

HClO₄ catalysed aldol-type reaction of fluorinated silyl enol ethers with acetals or ketals toward fluoroalkyl ethers

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General information: Reactions were monitored by thin layer chromatography using UV light to visualize the course of reaction. Purification of reaction products was carried out by flash chromatography on silica gel. Chemical yields refer to pure isolated substances. The infrared (IR) spectra were obtained using a Bruker tensor 27 infrared spectrometer. ^1H , ^{13}C , ^{19}F NMR spectra were obtained using a Bruker DPX-600, 500, 400 or 300 MHz spectrometer. Chemical shifts are reported in ppm from CDCl_3 with the solvent resonance as the internal standard. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad.

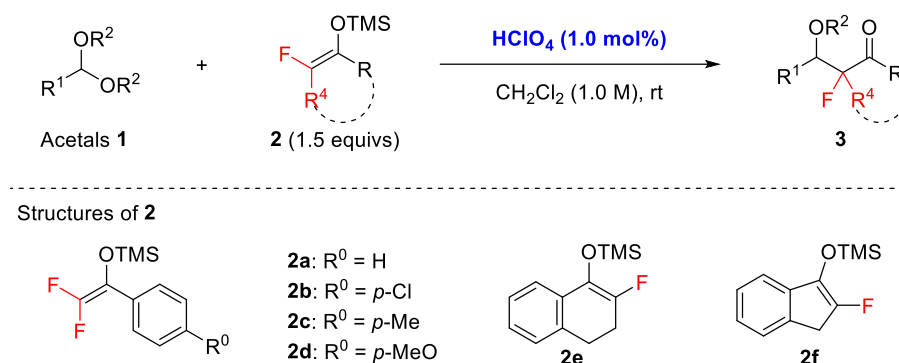
Anhydrous CH_2Cl_2 and CH_3CN were prepared by first distillation over P_2O_5 and then from CaH_2 . Anhydrous THF and toluene were prepared by distillation over sodium-benzophenone ketyl prior to use. Anhydrous EtOAc was prepared by first distillation over activated CaSO_4 and then stored in 5Å molecular sieves. Absolute MeOH was treated by stirring commercial anhydrous methanol over magnesium chips, then distilled and stored under N_2 atmosphere. HClO_4 (70% wt., aq.) is purchased from Sinopharm Chemical Reagent Co., Ltd and used as received. The substrates acetal **1** or ketals **4**,¹ were prepared following literature reports. The fluorinated silyl enol ethers **2** were prepared according to the literature reports.²

¹ a) M. Blümel, S. Nagasawa, K. Blackford, S. R. Hare, D. J. Tantillo, R. Sarpong, *J. Am. Chem. Soc.*, 2018, **140**, 9291; b) K. Wu, A. G. Doyle, *Nature Chem.*, 2017, **9**, 779.

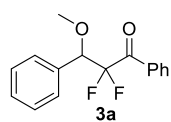
² a) H. Amii, T. Kobayashi, Y. Hatamoto and K. Uneyama, *Chem. Commun.*, **1999**, 1323; b) G. K. S. Prakash, J. Hu and G. A. Olah, *J. Fluorine Chem.*, 2001, **112**, 355; c) É. Bélanger, K. Cantin, O. Messe, M. Tremblay and J.-F. Paquin, *J. Am. Chem. Soc.*, 2007, **129**, 1034.

Part I. General procedure for the catalytic aldol-type reactions.

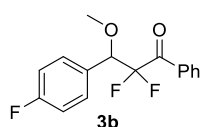
1) Procedure for the catalytic aldol-type reactions with acetals **1**



General procedure: To a stirred mixture of acetals **1** (1.0 mmol, 1.0 equiv) and fluorinated silyl enol ethers **2** (1.5 mmol, 1.5 equivs) in anhydrous CH₂Cl₂ (1.0 mL) in 5 mL vial was added HClO₄ (1.4 mg, 1.0 mol%, 70% wt., aq.) at room temperature under air conditions. The resulting mixture was then stirred at room temperature. After full conversion of acetals **1** by TLC analysis, the reaction was directly purified by flash column chromatography on silica gel to afford the desired fluoroalkyl ethers **3** using the petroleum ether (PE)/Et₂O as eluents.



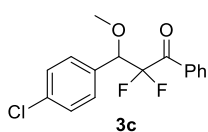
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3a**³ in 98% yield as colorless oil; ¹H NMR (300 MHz, CDCl₃): δ 8.06 (d, *J* = 7.8 Hz, 2H), 7.65-7.59 (m, 1H), 7.51-7.41 (m, 7H), 4.88 (dd, *J* = 19.1, 5.7 Hz, 1H), 3.30 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 191.09 (dd, *J* = 31.8, 25.6 Hz), 133.88, 133.47 (d, *J* = 2.6 Hz), 132.80, 130.02 (dd, *J* = 4.9, 2.0 Hz), 129.18, 128.77, 128.43, 128.35, 116.13 (dd, *J* = 265.7, 252.7 Hz), 82.15 (dd, *J* = 30.1, 22.1 Hz), 57.78; ¹⁹F NMR (376 MHz, CDCl₃): δ -103.55 (d, *J* = 274.0 Hz, 1F), -117.73 (d, *J* = 273.5 Hz, 1F); IR (ATR): 2939, 1699, 1598, 1448, 1276, 1217, 1001, 979, 903, 669.



Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3b** in 91% yield as colorless oil; ¹H NMR (300 MHz, CDCl₃): δ 8.05 (d, *J* = 8.0 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.51-7.44 (m, 4H), 7.18-7.07 (m, 2H), 4.86 (dd, *J* = 18.9, 5.6 Hz, 1H), 3.28 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 190.92 (dd, *J* = 31.8, 25.7 Hz), 163.36 (d, *J* = 247.8 Hz), 134.01, 133.40 (d, *J* = 2.8 Hz), 130.55 (d, *J* = 8.4 Hz), 130.04 (dd, *J* = 5.0, 2.0 Hz), 128.64 (d, *J* = 3.4 Hz), 128.50, 115.98 (dd, *J* = 266.0, 252.5 Hz), 115.45 (d, *J* = 21.6 Hz), 81.50 (dd, *J* = 30.3, 22.1 Hz), 57.81; ¹⁹F NMR (376 MHz, CDCl₃): δ -103.82 (d, *J* = 275.3 Hz, 1F), -112.52 (s, 1F), -118.08 (d, *J* = 275.5 Hz, 1F); IR

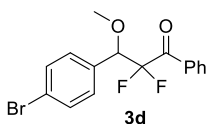
³ Y. Kodama, H. Yamane, M. Okumura, M. Shiro and T. Taguchi, *Tetrahedron*, 1995, **51**(45), 12217.

(ATR): 3030, 1693, 1597, 1448, 1290, 1219, 1101, 1074, 979, 852, 657, 586; HRMS (ESI): Exact mass calcd for C₁₆H₁₃F₃NaO₂ [M+Na]⁺: 317.0760, Found: 317.0758.



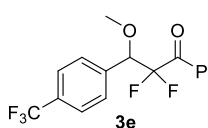
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3c** in 98% yield as colorless oil; ¹H NMR (600 MHz, CDCl₃): δ 8.05 (d, *J* = 7.9 Hz, 2H), 7.63 (t, *J* = 6.5 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 2H), 7.43-7.39 (m, 4H), 4.85 (d, *J* = 18.8 Hz, 1H), 3.29

(s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 190.78 (dd, *J* = 31.8, 25.7 Hz), 135.25, 134.07, 133.33 (d, *J* = 2.9 Hz), 131.46, 130.13, 130.05 (dd, *J* = 5.0, 1.9 Hz), 128.69, 128.53, 115.90 (dd, *J* = 266.3, 252.9 Hz), 81.50 (dd, *J* = 30.2, 22.1 Hz), 57.92; ¹⁹F NMR (376 MHz, CDCl₃): δ -103.66 (d, *J* = 276.3 Hz, 1F), -118.03 (d, *J* = 276.6 Hz, 1F); IR (ATR): 3032, 1751, 1697, 1579, 1490, 1219, 1001, 858, 740; HRMS (ESI): Exact mass calcd for C₁₆H₁₃ClF₂NaO₂ [M+Na]⁺: 333.0464, Found: 333.0457.



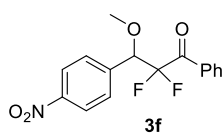
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3d** in 70% yield as colorless oil; ¹H NMR (300 MHz, CDCl₃): δ 8.05 (d, *J* = 7.8 Hz, 2H), 7.65-7.55 (m, 3H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 4.84 (dd, *J* = 18.9, 5.4 Hz, 1H), 3.29 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 190.76 (dd, *J* = 31.8, 25.6 Hz), 134.08, 133.31 (d, *J* = 3.0 Hz), 131.98, 131.64, 130.43, 130.05 (dd, *J* = 4.9, 2.0 Hz), 128.53, 123.49, 115.83 (dd, *J* = 266.3, 252.9 Hz), 81.55 (dd, *J* = 30.3, 22.1 Hz), 57.95; ¹⁹F NMR (282 MHz, CDCl₃): δ -103.62 (dd, *J* = 276.4, 5.4 Hz, 1F), -118.03 (dd, *J* = 276.6, 17.4 Hz, 1F); IR (ATR): 2935, 1751, 1597, 1579, 1487, 1404, 1280, 1188,

1001, 896, 796; HRMS (ESI): Exact mass calcd for C₁₆H₁₃BrF₂NaO₂ [M+Na]⁺: 376.9959, Found: 376.9950.

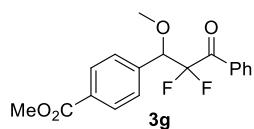


Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3e** in 93% yield as colorless oil; ¹H NMR (300 MHz, CDCl₃): δ 8.06 (d, *J* = 8.0 Hz, 2H), 7.71-7.61 (m, 5H), 7.52-7.47 (m, 2H), 4.95 (dd, *J* = 19.0, 5.2 Hz, 1H), 3.32 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 190.52 (dd, *J* = 31.7, 25.6 Hz), 137.12, 134.15, 133.23 (d, *J* = 3.1 Hz), 131.39 (q, *J* = 32.5 Hz), 130.05 (dd, *J* = 4.9, 1.9 Hz), 129.16, 128.56, 125.34 (q, *J* = 3.8 Hz), 124.00 (q, *J* = 273.2 Hz), 115.84 (dd, *J* = 266.7, 253.2 Hz), 81.54 (dd, *J* = 30.2, 22.1 Hz), 58.14; ¹⁹F NMR (282 MHz, CDCl₃): δ -62.73 (s, CF₃), -103.28 (dd, *J* = 278.5, 5.0 Hz, 1F), -117.91 (dd, *J* = 278.2, 15.6 Hz, 1F); IR (ATR): 3032,

3001, 1751, 1653, 1598, 1579, 1450, 1323, 1278, 1001, 980, 879, 790; HRMS (ESI): Exact mass calcd for C₁₇H₁₃F₅NaO₂ [M+Na]⁺: 367.0728, Found: 367.0716.

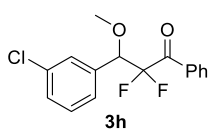


Column chromatography (PE/Et₂O = 20:1, v/v) afforded product **3f** in 72% yield as white solid, Mp: 84-86°C; ¹H NMR (300 MHz, CDCl₃): δ 8.31-8.28 (m, 2H), 8.06 (d, *J* = 7.9 Hz, 2H), 7.70-7.62 (m, 3H), 7.53-7.48 (m, 2H), 5.01 (dd, *J* = 18.7, 5.1 Hz, 1H), 3.34 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 190.12 (dd, *J* = 31.7, 25.6 Hz), 148.61, 140.41, 134.31, 133.03 (d, *J* = 2.9 Hz), 130.05 (dd, *J* = 5.0, 1.9 Hz), 129.68, 128.63, 123.51, 115.67 (dd, *J* = 267.4, 254.1 Hz), 81.23 (dd, *J* = 30.0, 22.2 Hz), 58.43; ¹⁹F NMR (282 MHz, CDCl₃): δ -102.91 (dd, *J* = 280.4, 3.4 Hz, 1F), -117.60 (dd, *J* = 280.4, 12.8 Hz, 1F); IR (ATR): 3030, 1708, 1598, 1448, 1213, 1168, 1112, 977, 1059, 979, 833, 775; HRMS (ESI): Exact mass calcd for C₁₆H₁₃F₂NNaO₄ [M+Na]⁺: 344.0705, Found: 344.0701.



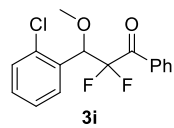
Column chromatography (PE/Et₂O = 30:1, v/v) afforded product **3g** in 95% yield as white solid, Mp: 74 –76°C; ¹H NMR (300 MHz, CDCl₃): δ 8.11-8.04 (m, 4H), 7.65-7.46 (m, 5H), 4.94 (dd, *J* = 19.0, 5.3 Hz, 1H), 3.94 (s, 3H), 3.31 (s, 3H); ¹³C

NMR (101 MHz, CDCl₃): δ 190.63 (dd, *J* = 31.7, 25.5 Hz), 166.70, 138.02, 134.09, 133.28 (d, *J* = 2.9 Hz), 131.01, 130.05 (dd, *J* = 5.0, 1.9 Hz), 129.59, 128.79, 128.53, 115.91 (dd, *J* = 266.7, 253.3 Hz), 81.74 (dd, *J* = 30.1, 22.2 Hz), 58.10, 52.20; ¹⁹F NMR (282 MHz, CDCl₃): δ -103.45 (dd, *J* = 277.0, 5.0 Hz, 1F), -117.72 (dd, *J* = 277.0, 15.9 Hz, 1F); IR (ATR): 3003, 1701, 1598, 1448, 1215, 1134, 1018, 854, 752; HRMS (ESI): Exact mass calcd for C₁₈H₁₆F₂NaO₄ [M+Na]⁺: 357.0909, Found: 357.0905.



Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3h** in 93% yield as colorless oil; ¹H NMR (600 MHz, CDCl₃): δ 8.06 (d, *J* = 7.7 Hz, 2H), 7.64-7.62 (m, 1H), 7.51-7.48 (m, 3H), 7.39-7.36 (m, 3H), 4.85 (d, *J* = 19.2 Hz, 1H), 3.30 (s, 3H); ¹³C

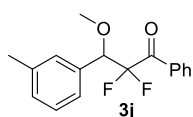
NMR (101 MHz, CDCl₃): δ 190.70 (dd, *J* = 31.9, 25.4 Hz), 135.09, 134.52, 134.08, 133.32 (d, *J* = 3.0 Hz), 130.06 (dd, *J* = 5.0, 1.9 Hz), 129.65, 129.41, 128.79, 128.53, 127.03, 115.85 (dd, *J* = 266.7, 253.1 Hz), 81.51 (dd, *J* = 30.3, 22.0 Hz), 58.07; ¹⁹F NMR (376 MHz, CDCl₃): δ -103.36 (d, *J* = 276.9 Hz, 1F), -118.07 (d, *J* = 277.1 Hz, 1F); IR (ATR): 3030, 1751, 1598, 1475, 1431, 1190, 999, 896, 719; HRMS (ESI): Exact mass calcd for C₁₆H₁₃ClF₂NaO₂ [M+Na]⁺: 333.0464, Found: 333.0461.



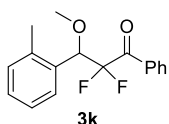
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3i** in 89% yield as colorless oil; ¹H NMR (600 MHz, CDCl₃): δ 8.11 (d, *J* = 7.9 Hz, 2H), 7.68-7.63 (m, 2H), 7.52-7.50 (m, 2H), 7.45-7.44 (m, 1H), 7.39-7.34 (m, 2H), 5.55 (dd, *J* = 20.3, 3.3 Hz, 1H),

3.25 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 189.77 (dd, *J* = 31.1, 25.9 Hz), 135.32, 134.10, 133.10 (t,

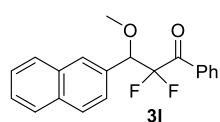
$J = 1.8$ Hz), 131.02, 130.33, 130.16 (d, $J = 2.3$ Hz), 130.03 (dd, $J = 4.3, 2.3$ Hz), 129.60, 128.60, 127.02, 116.17 (dd, $J = 266.1, 253.7$ Hz), 77.74 (dd, $J = 30.8, 21.3$ Hz), 57.86; ^{19}F NMR (376 MHz, CDCl_3): δ -103.63 (d, $J = 278.8$ Hz, 1F), -118.46 (d, $J = 278.7$ Hz, 1F); IR (ATR): 3030, 2856, 1598, 1473, 1284, 1188, 981, 700; HRMS (ESI): Exact mass calcd for $\text{C}_{16}\text{H}_{13}\text{ClF}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 333.0464, Found: 333.0460.



Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3j** in 96% yield as colorless oil; ^1H NMR (300 MHz, CDCl_3): δ 8.06 (d, $J = 7.8$ Hz, 2H), 7.65-7.59 (m, 1H), 7.51-7.46 (m, 2H), 7.34-7.27 (m, 3H), 7.23-7.21 (m, 1H), 4.84 (dd, $J = 19.2, 5.6$ Hz, 1H), 3.29 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 191.20 (dd, $J = 31.8, 25.6$ Hz), 138.08, 133.90, 133.57 (d, $J = 2.8$ Hz), 132.73, 130.07 (dd, $J = 4.9, 2.1$ Hz), 130.02, 129.42, 128.46, 128.27, 125.94, 116.21 (dd, $J = 265.7, 252.5$ Hz), 82.25 (dd, $J = 30.2, 22.1$ Hz), 57.81, 21.43; ^{19}F NMR (282 MHz, CDCl_3): δ -103.81 (dd, $J = 273.2, 6.2$ Hz, 1F), -117.87 (dd, $J = 273.3, 17.7$ Hz, 1F); IR (ATR): 3032, 1751, 1608, 1579, 1489, 1284, 1188, 1001, 746, 669; HRMS (ESI): Exact mass calcd for $\text{C}_{17}\text{H}_{16}\text{F}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 313.1011, Found: 313.1004.

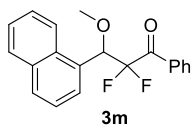


Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3k** in 83% yield as colorless oil; ^1H NMR (300 MHz, CDCl_3): δ 8.08 (d, $J = 7.7$ Hz, 2H), 7.65-7.57 (m, 2H), 7.49 (t, $J = 7.8$ Hz, 2H), 7.33-7.28 (m, 2H), 7.25-7.22 (m, 1H), 5.23 (dd, $J = 20.3, 3.7$ Hz, 1H), 3.24 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 191.25 (dd, $J = 32.3, 25.4$ Hz), 138.01, 133.89, 133.55 (d, $J = 2.9$ Hz), 131.12, 130.55, 130.05 (dd, $J = 5.0, 1.8$ Hz), 128.86, 128.54 (d, $J = 1.8$ Hz), 128.46, 126.05, 116.80 (dd, $J = 266.7, 251.4$ Hz), 78.11 (dd, $J = 31.2, 21.9$ Hz), 57.51, 19.52 (d, $J = 3.2$ Hz); ^{19}F NMR (282 MHz, CDCl_3): δ -103.41 (dd, $J = 275.2, 3.4$ Hz, 1F), -118.08 (dd, $J = 275.6, 11.6$ Hz, 1F); IR (ATR): 3030, 2856, 1751, 1598, 1579, 1490, 1448, 1286, 1209, 977, 717; HRMS (ESI): Exact mass calcd for $\text{C}_{17}\text{H}_{16}\text{F}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 313.1011, Found: 313.1009.



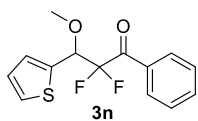
Column chromatography (PE/Et₂O = 20:1, v/v) afforded product **3l** in 94% yield as white solid, Mp: 103-104°C. ^1H NMR (300 MHz, CDCl_3): δ 8.09 (d, $J = 7.9$ Hz, 2H), 7.95 (s, 1H), 7.93-7.86 (m, 3H), 7.65-7.60 (m, 2H), 7.56-7.47 (m, 4H), 5.05 (dd, $J = 19.2, 5.6$ Hz, 1H), 3.34 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 191.12 (dd, $J = 31.8, 25.6$ Hz), 133.96, 133.82, 133.52 (d, $J = 2.8$ Hz), 133.01, 130.39, 130.09 (dd, $J = 5.0, 2.0$ Hz), 128.83, 128.50, 128.21, 128.18, 127.77, 126.61, 126.34, 125.74, 116.30 (dd, $J = 266.0, 252.5$ Hz), 82.37 (dd, $J = 30.4,$

22.1 Hz), 57.91; ^{19}F NMR (282 MHz, CDCl_3): δ -103.46 (dd, J = 274.7, 2.8 Hz, 1F), -117.60 (dd, J = 274.8, 10.6 Hz, 1F); IR (ATR): 3062, 2921, 1739, 1598, 1448, 1080, 896, 754; HRMS (ESI): Exact mass calcd for $\text{C}_{20}\text{H}_{16}\text{F}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 349.1011, Found: 349.1001.



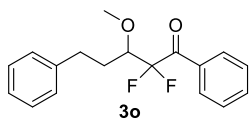
Column chromatography (PE/Et₂O = 20:1, v/v) afforded product **3m** in 94% yield as white solid, Mp: 86-87°C; ^1H NMR (300 MHz, CDCl_3): δ 8.23 (d, J = 8.3 Hz, 1H), 8.10 (d, J = 8.0 Hz, 2H), 7.92 (d, J = 8.1 Hz, 2H), 7.80 (d, J = 7.2 Hz, 1H), 7.66-7.47

(m, 6H), 5.77 (dd, J = 20.1, 3.7 Hz, 1H), 3.31 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 191.39 (dd, J = 32.4, 25.4 Hz), 133.98, 133.85, 133.62 (d, J = 3.0 Hz), 132.68, 130.12 (dd, J = 5.3, 1.7 Hz), 129.83, 128.87, 128.70, 128.53, 127.31, 126.54, 125.75, 125.24, 123.61, 116.80 (dd, J = 267.3, 252.6 Hz), 78.71 (dd, J = 30.3, 23.2 Hz), 57.88; ^{19}F NMR (282 MHz, CDCl_3): δ -102.05 (dd, J = 275.3, 3.2 Hz, 1F), -117.77 (dd, J = 277.4, 16.5 Hz, 1F). IR (ATR): 3001, 1752, 1685, 1597, 1448, 1280, 1149, 1070, 948, 790; HRMS (ESI): Exact mass calcd for $\text{C}_{20}\text{H}_{16}\text{F}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 349.1011, Found: 349.1006.



Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3n** in 82% yield as colorless oil; ^1H NMR (300 MHz, CDCl_3): δ 8.06 (d, J = 8.1 Hz, 2H), 7.65-7.60 (m, 1H), 7.52-7.47 (m, 2H), 7.43 (dd, J = 5.0, 1.2 Hz, 1H), 7.21 (d, J = 3.4 Hz, 1H), 7.07

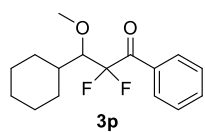
(dd, J = 5.1, 3.5 Hz, 1H), 5.17 (dd, J = 18.4, 5.6 Hz, 1H), 3.35 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 190.70 (dd, J = 31.7, 25.8 Hz), 135.35, 134.10 (d, J = 2.1 Hz), 133.28 (d, J = 2.9 Hz), 130.06 (dd, J = 4.9, 2.0 Hz), 129.02 (d, J = 2.9 Hz), 128.55, 127.52 (d, J = 2.0 Hz), 126.79 (d, J = 1.9 Hz), 115.56 (dd, J = 266.6, 253.4 Hz), 78.43 (ddd, J = 30.7, 22.2, 2.2 Hz), 57.89; ^{19}F NMR (282 MHz, CDCl_3): δ -103.92 (d, J = 274.8 Hz, 1F), -117.58 (d, J = 273.1 Hz, 1F); IR (ATR): 3030, 2856, 1699, 1599, 1579, 1448, 1307, 1280, 1199, 974, 846, 754; HRMS (ESI): Exact mass calcd for $\text{C}_{14}\text{H}_{12}\text{F}_2\text{NaO}_2\text{S}$ $[\text{M}+\text{Na}]^+$: 305.0418, Found: 305.0424.



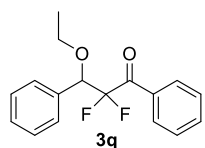
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3o** in 82% yield as colorless oil; ^1H NMR (300 MHz, CDCl_3): δ 8.08 (d, J = 7.5 Hz, 2H), 7.66-7.61 (m, 1H), 7.50 (t, J = 7.7 Hz, 2H), 7.34-7.20 (m, 5H), 3.91-3.79 (m, 1H), 3.45 (s,

3H), 2.98-2.89 (m, 1H), 2.81-2.71 (m, 1H), 2.09-2.00 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3): δ 190.89 (dd, J = 30.3, 27.7 Hz), 141.12 (d, J = 2.5 Hz), 134.17 (d, J = 2.0 Hz), 133.28, 130.07 (d, J = 3.6 Hz), 128.62 (d, J = 2.4 Hz), 128.57 (d, J = 2.6 Hz), 128.47 (d, J = 2.7 Hz), 126.18 (d, J = 2.6 Hz), 118.05 (t, J = 262.0 Hz), 80.14 (ddd, J = 25.9, 23.0, 2.5 Hz), 60.38, 31.48, 30.27; ^{19}F NMR (282 MHz, CDCl_3): δ -105.50 (dd, J = 276.6, 8.7 Hz), -108.53 (dd, J = 276.4, 8.7 Hz); IR (ATR): 3001, 2837, 1751, 1653, 1587,

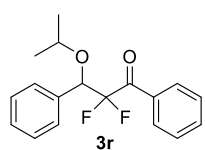
1498, 1282, 1016, 781; HRMS (ESI): Exact mass calcd for C₁₈H₁₈F₂NaO₂ [M+Na]⁺: 327.1167, Found: 327.1158.



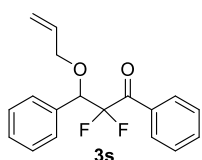
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3p** in 76% yield as colorless oil; ¹H NMR (300 MHz, CDCl₃): δ 8.06 (d, *J* = 7.9 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 3.65-3.54 (m, 1H), 3.37 (s, 3H), 1.96-1.59 (m, 6H), 1.30-1.14 (m, 5H); ¹³C NMR (101 MHz, CDCl₃): δ 191.62 (dd, *J* = 31.4, 26.9 Hz), 133.87, 133.49 (d, *J* = 2.3 Hz), 130.03 (dd, *J* = 4.4, 2.5 Hz), 128.48, 118.70 (dd, *J* = 263.5, 258.0 Hz), 84.65 (dd, *J* = 26.1, 22.1 Hz), 61.31, 38.61 (d, *J* = 1.8 Hz), 30.18 (t, *J* = 1.8 Hz), 27.88 (d, *J* = 1.5 Hz), 26.29, 26.24, 26.07; ¹⁹F NMR (282 MHz, CDCl₃): δ -102.75 (d, *J* = 273.7 Hz, 1F), -113.05 (d, *J* = 276.4 Hz, 1F); IR (ATR): 3064, 1751, 1598, 1579, 1448, 1278, 1182, 1041, 952, 846, 786; HRMS (ESI): Exact mass calcd for C₁₆H₂₀F₂NaO₂ [M+Na]⁺: 305.1324, Found: 305.1321.



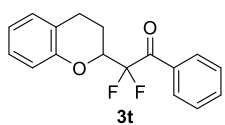
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3q** in 84% yield as colorless oil; ¹H NMR (300 MHz, CDCl₃): δ 8.07 (d, *J* = 7.7 Hz, 2H), 7.65-7.59 (m, 1H), 7.51-7.46 (m, 4H), 7.44-7.40 (m, 3H), 4.96 (dd, *J* = 19.5, 5.6 Hz, 1H), 3.58-3.48 (m, 1H), 3.43-3.33 (m, 1H), 1.08 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 191.58 (dd, *J* = 31.9, 25.3 Hz), 133.83, 133.76 (d, *J* = 2.7 Hz), 133.60, 130.09 (dd, *J* = 4.9, 1.9 Hz), 129.10, 128.71, 128.40, 128.33, 116.31 (dd, *J* = 265.6, 252.4 Hz), 80.47 (dd, *J* = 30.3, 22.2 Hz), 65.82, 14.89; ¹⁹F NMR (282 MHz, CDCl₃): δ -103.75 (dd, *J* = 269.9, 5.4 Hz, 1F), -118.12 (dd, *J* = 270.5, 15.7 Hz, 1F); IR (ATR): 3035, 1751, 1597, 1539, 1448, 1325, 823; HRMS (ESI): Exact mass calcd for C₁₇H₁₆F₂NaO₂ [M+Na]⁺: 313.1011, Found: 313.1006



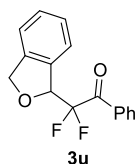
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3r** in 96% yield as colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 8.10 (d, *J* = 8.4 Hz, 2H), 7.64-7.59 (m, 1H), 7.55-7.44 (m, 4H), 7.43-7.40 (m, 3H), 5.05 (dd, *J* = 19.8, 5.4 Hz, 1H), 3.63-3.57 (m, 1H), 1.04 (d, *J* = 6.2 Hz, 3H), 0.98 (d, *J* = 6.0 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃): δ 191.96 (dd, *J* = 32.0, 24.9 Hz), 134.29, 133.83 (d, *J* = 2.6 Hz), 133.71, 130.09 (dd, *J* = 4.9, 1.5 Hz), 128.92, 128.69, 128.28, 128.17, 116.41 (dd, *J* = 265.8, 252.3 Hz), 78.21 (dd, *J* = 30.5, 22.2 Hz), 71.42, 22.95, 20.65; ¹⁹F NMR (376 MHz, CDCl₃) δ -103.29 (d, *J* = 266.4 Hz, 1F), -118.24 (d, *J* = 266.4 Hz, 1F); IR (ATR): 1712, 1699, 1598, 1579, 1496, 1448, 1379, 1307, 1215, 1028, 1001, 837, 710; HRMS (ESI): Exact mass calcd for C₁₈H₁₈F₂NaO₂ [M+Na]⁺: 327.1167, Found: 327.1170.



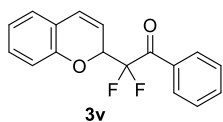
Run on a 0.5 mmol scale in this case, and column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3s** in 93% yield as colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 8.09 (d, *J* = 8.2 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.53-7.47 (m, 4H), 7.45-7.42 (m, 3H), 5.76-5.67 (m, 1H), 5.15-5.03 (m, 3H), 4.06 (dd, *J* = 12.6, 5.0 Hz, 1H), 3.84 (dd, *J* = 12.7, 6.2 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃): δ 191.15 (dd, *J* = 31.6, 25.4 Hz), 133.84, 133.49 (d, *J* = 2.5 Hz), 133.21, 132.97, 130.00 (dd, *J* = 4.8, 1.8 Hz), 129.13, 128.77, 128.36, 128.31, 117.89, 116.23 (dd, *J* = 265.5, 252.4 Hz), 79.43 (dd, *J* = 30.5, 22.3 Hz), 70.46; ¹⁹F NMR (376 MHz, CDCl₃): δ -103.60 (d, *J* = 271.5 Hz, 1F), -117.39 (d, *J* = 271.5 Hz, 1F); IR (ATR): 3064, 1697, 1598, 1579, 1494, 1448, 1425, 1361, 1286, 1159, 1001, 842, 788, 761; HRMS (ESI): Exact mass calcd for C₁₈H₁₆F₂NaO₂ [M+Na]⁺: 325.1011, Found: 325.1015



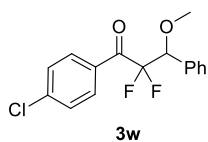
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3t** in 78% yield as colorless oil; ¹H NMR (300 MHz, CDCl₃) δ 8.08 (d, *J* = 7.8 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.52-7.43 (m, 3H), 7.33-7.27 (m, 2H), 7.22-7.17 (m, 1H), 5.50 (dd, *J* = 20.2, 5.2 Hz, 1H), 4.17-4.10 (m, 1H), 3.76-3.68 (m, 1H), 3.00-2.90 (m, 1H), 2.76-2.68 (m, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 190.46 (dd, *J* = 29.7, 25.7 Hz), 135.60, 133.92, 133.55, 129.97 (dd, *J* = 4.2, 2.7 Hz), 128.87, 128.82 (d, *J* = 1.9 Hz), 128.56, 128.00, 126.78 (d, *J* = 5.6 Hz), 126.43, 117.43 (dd, *J* = 265.4, 255.3 Hz), 75.25 (dd, *J* = 28.0, 24.9 Hz), 63.29, 28.79; ¹⁹F NMR (282 MHz, CDCl₃): δ -101.14 (dd, *J* = 264.4, 6.1 Hz, 1F), -115.18 (dd, *J* = 264.7, 17.9 Hz, 1F); IR (ATR): 3032, 1579, 1494, 1448, 1278, 1001, 979, 812, 680; HRMS (ESI): Exact mass calcd for C₁₇H₁₄F₂NaO₂ [M+Na]⁺: 311.0854, Found: 311.0851



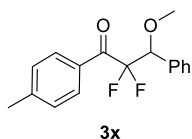
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3u** in 83% yield as colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 8.10 (d, *J* = 7.3 Hz, 2H), 7.66-7.60 (m, 1H), 7.51-7.46 (m, 3H), 7.41-7.32 (m, 2H), 7.28-7.25 (m, 1H), 5.87 (dd, *J* = 16.5, 6.2 Hz, 1H), 5.22-5.12 (m, 2H); ¹³C NMR (101 MHz, CDCl₃): δ 189.75 (dd, *J* = 30.5, 27.5 Hz), 140.33, 134.28, 133.72 (t, *J* = 2.0 Hz), 132.88 (t, *J* = 2.2 Hz), 130.15 (t, *J* = 3.4 Hz), 129.04, 128.61, 127.70, 123.48 (d, *J* = 2.4 Hz), 120.99, 116.69 (dd, *J* = 262.2, 257.1 Hz), 82.75 (dd, *J* = 29.6, 26.2 Hz), 74.52; ¹⁹F NMR (282 MHz, CDCl₃): δ -107.19 (d, *J* = 283.5 Hz, 1F), -115.04 (d, *J* = 283.7 Hz, 1F); IR (ATR): 3005, 1751, 1598, 1448, 1381, 1219, 1174, 977, 903, 846, 775; HRMS (ESI): Exact mass calcd for C₁₆H₁₂F₂NaO₂ [M+Na]⁺: 297.0698, Found: 297.0690.



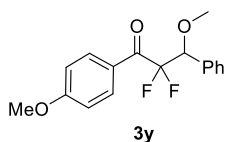
Run on a 0.5 mmol scale in this case, and column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3v** in 93% yield as colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 7.98 (d, *J* = 8.1 Hz, 2H), 7.66-7.55 (m, 1H), 7.43 (t, *J* = 7.9 Hz, 2H), 7.28-7.21 (m, 2H), 7.08-7.04 (m, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 6.75 (d, *J* = 6.1 Hz, 1H), 5.04 (t, *J* = 5.5 Hz, 1H), 4.46-4.38 (m, 1H); ¹³C NMR (126 MHz, CDCl₃): δ 189.94 (t, *J* = 30.6 Hz), 152.48, 144.36, 134.17, 132.74 (t, *J* = 2.4 Hz), 130.56 (d, *J* = 2.2 Hz), 130.04 (t, *J* = 3.5 Hz), 129.03, 128.51, 123.53, 117.55 (dd, *J* = 260.2, 259.1 Hz), 116.73, 115.23 (t, *J* = 2.7 Hz), 96.66 (dd, *J* = 5.9, 3.5 Hz), 38.99 (t, *J* = 23.8 Hz); ¹⁹F NMR (376 MHz, CDCl₃): δ -101.29 (d, *J* = 277.6 Hz, 1F), -106.64 (d, *J* = 277.9 Hz, 1F); IR (ATR): 1701, 1597, 1581, 1487, 1458, 1307, 1271, 1178, 1153, 1001, 817, 665; HRMS (ESI): Exact mass calcd for C₁₇H₁₂F₂NaO₂ [M+Na]⁺: 309.0698, Found: 309.0692.



Run on a 0.5 mmol scale in this case, and column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3w** in 82% yield as colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 8.00 (dd, *J* = 8.7, 1.5 Hz, 2H), 7.49-7.41 (m, 7H), 4.84 (dd, *J* = 18.9, 5.7 Hz, 1H), 3.30 (s, 3H); ¹³C NMR (126 MHz, CDCl₃): δ 190.17 (dd, *J* = 32.1, 25.8 Hz), 140.61, 132.55, 131.76 (d, *J* = 3.2 Hz), 131.52 (d, *J* = 2.0 Hz), 129.28, 128.82, 128.71, 128.40, 116.10 (dd, *J* = 265.2, 252.6 Hz), 82.13 (dd, *J* = 30.2, 22.3 Hz), 57.78; ¹⁹F NMR (376 MHz, CDCl₃): δ -103.91 (d, *J* = 273.3 Hz, 1F), -117.54 (d, *J* = 273.3 Hz, 1F); IR (ATR): 2831, 1699, 1587, 1558, 1489, 1456, 1361, 1309, 1274, 1029, 956, 659; HRMS (ESI): Exact mass calcd for C₁₆H₁₃ClF₂NaO₂ [M+Na]⁺: 333.0464, Found: 333.0472.

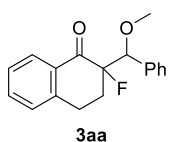


Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3x** in 74% yield as colorless oil; ¹H NMR (300 MHz, CDCl₃): δ 7.96 (d, *J* = 7.9 Hz, 2H), 7.50-7.45 (m, 2H), 7.43-7.40 (m, 3H), 7.29 (s, 2H), 4.86 (dd, *J* = 18.9, 5.8 Hz, 1H), 3.29 (s, 3H), 2.43 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 190.47 (dd, *J* = 31.2, 25.7 Hz), 145.07, 132.97, 130.91 (d, *J* = 2.8 Hz), 130.25 (dd, *J* = 5.0, 2.1 Hz), 129.21, 129.16, 128.81, 128.36, 116.24 (dd, *J* = 265.7, 252.7 Hz), 82.21 (dd, *J* = 30.1, 22.2 Hz), 57.83, 21.78; ¹⁹F NMR (282 MHz, CDCl₃): δ -104.03 (dd, *J* = 274.0, 5.1 Hz, 1F), -117.58 (dd, *J* = 273.9, 16.8 Hz, 1F); IR (ATR): 3035, 1751, 1699, 1606, 1494, 1276, 1219, 1188, 1066, 979, 806, 781; HRMS (ESI): Exact mass calcd for C₁₇H₁₆F₂NaO₂ [M+Na]⁺: 313.1011, Found: 313.1007.



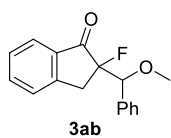
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3y** in 68% yield as colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 8.07 (dd, *J* = 8.8, 1.4 Hz, 2H), 7.49-7.47 (m, 2H), 7.43-7.40 (m, 3H), 6.96-6.93 (m, 2H), 4.86 (dd, *J* = 18.8, 5.8 Hz, 1H), 3.89

(s, 3H), 3.30 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 189.01 (dd, *J* = 30.8, 25.8 Hz), 164.24, 133.08, 132.71 (dd, *J* = 5.4, 2.3 Hz), 129.09, 128.79, 128.31, 126.30 (d, *J* = 2.8 Hz), 116.42 (dd, *J* = 265.5, 252.9 Hz), 113.77, 82.21 (dd, *J* = 29.9, 22.2 Hz), 57.82, 55.49; ¹⁹F NMR (376 MHz, CDCl₃): δ -103.96 (d, *J* = 273.6 Hz, 1F), -116.88 (d, *J* = 273.6 Hz, 1F); IR (ATR): 2831, 1712, 1685, 1573, 1494, 1442, 1361, 1290, 1219, 1066, 952, 765, 669; HRMS (ESI): Exact mass calcd for C₁₇H₁₆F₂NaO₃ [M+Na]⁺: 329.0960, Found: 329.0964.



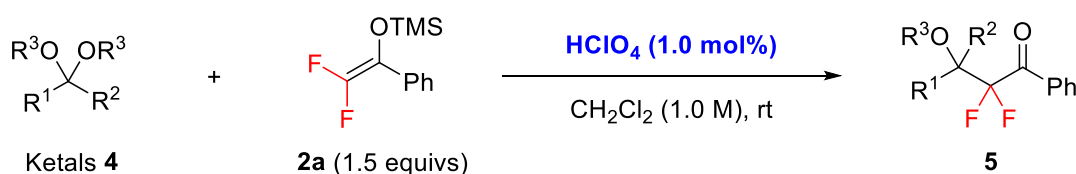
Run on a 0.5 mmol scale in this case, and column chromatography (PE/Et₂O = 50:1, v/v)

afforded product **3aa** in 83% yield as colorless oil; ¹H, ¹⁹F NMR analysis of crude mixture revealed that the dr value was 1.1:1. ¹H NMR for the major diastereomer (300 MHz, CDCl₃): δ 8.04 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.53-7.44 (m, 3H), 7.38-7.31 (m, 4H), 7.23 (d, *J* = 7.7 Hz, 1H), 4.75 (d, *J* = 19.1 Hz, 1H), 3.19 (s, 3H), 3.09 (dd, *J* = 7.7, 5.4 Hz, 2H), 2.48-2.34 (m, 1H), 2.14-2.00 (m, 1H); ¹³C NMR for the major diastereomer (101 MHz, CDCl₃): δ 192.54 (d, *J* = 18.0 Hz), 142.21, 135.11 (d, *J* = 2.9 Hz), 133.91, 131.68 (d, *J* = 1.0 Hz), 128.85 (d, *J* = 1.7 Hz), 128.63 (d, *J* = 2.3 Hz), 128.32, 128.27 (d, *J* = 1.5 Hz), 127.10, 96.14 (d, *J* = 191.5 Hz), 82.82 (d, *J* = 20.2 Hz), 57.64, 29.44 (d, *J* = 21.8 Hz), 25.72 (d, *J* = 9.3 Hz); ¹⁹F NMR for the major diastereomer (282 MHz, CDCl₃): δ -169.33 (s, 1F); IR (ATR): 2937, 1708, 1685, 1602, 1490, 1438, 1309, 1300, 1222, 1091, 983, 916, 769; HRMS (ESI): Exact mass calcd for C₁₈H₁₇FNaO₂ [M+Na]⁺: 307.1105, Found: 307.1107. ¹H NMR for the minor diastereomer (400 MHz, CDCl₃): δ 8.10 (d, *J* = 7.8 Hz, 1H), 7.53-7.50 (m, 1H), 7.41-7.34 (m, 6H), 7.25 (d, *J* = 6.4 Hz, 1H), 4.98 (d, *J* = 10.5 Hz, 1H), 3.26 (s, 3H), 3.04-2.99 (m, 2H), 2.47-2.33 (m, 1H), 2.10-2.00 (m, 1H); ¹³C NMR for the minor diastereomer (101 MHz, CDCl₃): δ 192.67 (d, *J* = 17.3 Hz), 143.97, 135.79, 133.95, 131.89, 128.58, 128.24, 128.17, 128.05, 128.03, 126.92, 93.21 (d, *J* = 181.5 Hz), 82.60 (d, *J* = 28.6 Hz), 57.92, 28.00 (d, *J* = 21.8 Hz), 24.68 (d, *J* = 7.0 Hz); ¹⁹F NMR for the minor diastereomer (376 MHz, CDCl₃): δ -161.59 (s, 1F); IR (ATR): 3032, 1693, 1600, 1494, 1454, 1307, 1282, 1219, 1190, 941, 877, 740; HRMS (ESI): Exact mass calcd for C₁₈H₁₇FNaO₂ [M+Na]⁺: 307.1105, Found: 307.1122.

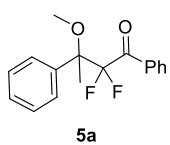


Run on a 0.5 mmol scale in this case, and column chromatography (PE/Et₂O = 50:1, v/v) afforded product **3ab** in 96% yield as colorless oil; ¹H, ¹⁹F NMR analysis of crude mixture revealed that the dr value was 1.1:1. ¹H NMR for the major diastereomer (400 MHz, CDCl₃): δ 7.85 (d, *J* = 7.7 Hz, 1H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.50-7.48 (m, 2H), 7.45-7.38 (m, 5H), 4.89 (d, *J* = 6.7 Hz, 1H), 3.63 (t, *J* = 17.9 Hz, 1H), 3.24 (s, 3H), 2.80 (dd, *J* = 25.9, 18.0 Hz, 1H); ¹³C NMR for the major diastereomer (126 MHz, CDCl₃): δ 200.47 (d, *J* = 16.9 Hz), 151.80 (d, *J* = 2.2 Hz), 136.10, 135.95, 134.59, 128.32, 128.20, 127.76, 127.46 (d, *J* = 1.9 Hz), 126.47, 124.65, 95.46 (d, *J* = 186.0 Hz), 81.24 (d, *J* = 30.1 Hz), 57.45, 33.77 (d, *J* = 23.7 Hz); ¹⁹F NMR for the major diastereomer (376 MHz, CDCl₃): δ -156.88 (s, 1F); IR (ATR): 1724, 1606, 1587, 1465, 1454, 1307, 1288, 1207, 1161, 1101, 975, 902, 835, 636; HRMS (ESI): Exact mass calcd for C₁₇H₁₅FNaO₂ [M+Na]⁺: 293.0948, Found: 293.0955. ¹H NMR for the minor diastereomer (400 MHz, CDCl₃): δ 7.54 (d, *J* = 7.9 Hz, 1H), 7.46 (td, *J* = 7.5, 1.3 Hz, 1H), 7.28-7.25 (m, 3H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.17-7.08 (m, 3H), 4.81 (d, *J* = 12.9 Hz, 1H), 3.78 (dd, *J* = 18.0, 10.5 Hz, 1H), 3.42 (s, 3H), 3.29-3.18 (m, 1H); ¹³C NMR for the minor diastereomer (126 MHz, CDCl₃): δ 199.93 (d, *J* = 17.6 Hz), 151.05 (d, *J* = 4.6 Hz), 135.93, 134.58 (d, *J* = 1.3 Hz), 134.33 (d, *J* = 8.1 Hz), 128.41, 128.21, 127.81, 127.71, 126.07 (d, *J* = 1.8 Hz), 124.50, 99.55 (d, *J* = 194.6 Hz), 83.99 (d, *J* = 24.2 Hz), 57.95, 34.05 (d, *J* = 24.4 Hz); ¹⁹F NMR for the minor diastereomer (376 MHz, CDCl₃): δ -158.32 (s, 1F); IR (ATR): 1722, 1608, 1454, 1203, 1134, 1105, 1074, 1047, 912, 767, 702; HRMS (ESI): Exact mass calcd for C₁₇H₁₅FNaO₂ [M+Na]⁺: 293.0948, Found: 293.0948.

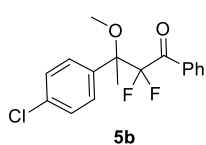
2) Procedure for the catalytic aldol-type reaction with ketals **4**



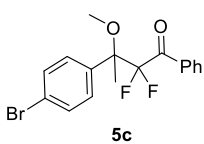
General procedure: To a stirred mixture of ketals **4** (1.0 mmol, 1.0 equiv) and difluoroenoxy silanes **2a** (1.5 mmol, 1.5 equivs) in anhydrous CH₂Cl₂ (1.0 mL) in 5 mL vial was added HClO₄ (1.4 mg, 1.0 mol%, 70% wt., aq.) at room temperature under air conditions. The resulting mixture was then stirred at room temperature. After full conversion of ketals **4** by TLC analysis, the reaction was directly purified by flash column chromatography on silica gel to afford the desired products **5** using the mixture solvent of PE and Et₂O as eluents.



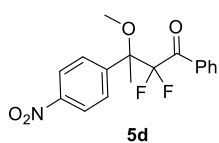
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **5a** in 94% yield as white solid, Mp: 63-65°C; ¹H NMR (300 MHz, CDCl₃): δ 8.04 (d, *J* = 7.9 Hz, 2H), 7.59-7.53 (m, 1H), 7.48-7.35 (m, 7H), 3.19 (s, 3H), 1.85 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 191.34 (dd, *J* = 30.4, 26.9 Hz), 136.69, 134.57 (d, *J* = 2.1 Hz), 133.47, 130.78 (dd, *J* = 4.4, 2.8 Hz), 128.48, 128.28, 128.10, 128.05, 117.71 (dd, *J* = 262.0, 259.8 Hz), 81.48 (dd, *J* = 26.9, 24.3 Hz), 50.43, 17.58 (t, *J* = 3.4 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -107.84 (d, *J* = 252.8 Hz, 1F), -109.43 (d, *J* = 253.0 Hz, 1F); IR (ATR): 3007, 1739, 1687, 1595, 1446, 1379, 1278, 1217, 1143, 1047, 972, 883, 781, 696; HRMS (ESI): Exact mass calcd for C₁₇H₁₆F₂NaO₂ [M+Na]⁺: 313.1011, Found: 313.1007.



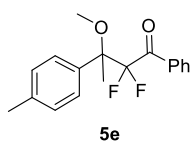
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **5b** in 88% yield as white solid, Mp: 90-92°C; ¹H NMR (300 MHz, CDCl₃): δ 8.05 (d, *J* = 7.6 Hz, 2H), 7.61-7.55 (m, 1H), 7.46-7.34 (m, 6H), 3.17 (s, 3H), 1.82 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 191.06 (dd, *J* = 30.1, 26.9 Hz), 135.34, 134.65, 134.42 (d, *J* = 2.0 Hz), 133.61, 130.75 (dd, *J* = 4.4, 2.9 Hz), 129.68, 128.31, 128.11, 117.42 (dd, *J* = 262.0, 260.4 Hz), 81.18 (dd, *J* = 27.1, 24.4 Hz), 50.46, 17.56; ¹⁹F NMR (282 MHz, CDCl₃): δ -107.86 (d, *J* = 254.0 Hz, 1F), -109.42 (d, *J* = 254.0 Hz, 1F); IR (ATR): 3005, 2970, 1751, 1693, 1597, 1504, 1487, 1446, 1367, 1276, 1217, 1103, 1070, 970, 846, 748, 700; HRMS (ESI): Exact mass calcd for C₁₇H₁₅ClF₂NaO₂ [M+Na]⁺: 347.0621, Found: 347.0617.



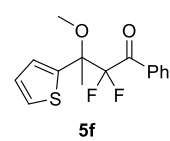
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **5c** in 80% yield as white solid, Mp: 96-98°C; ¹H NMR (300 MHz, CDCl₃): δ 8.05 (d, *J* = 7.8 Hz, 2H), 7.61-7.58 (m, 1H), 7.57-7.49 (m, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 3.17 (s, 3H), 1.82 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 191.03 (dd, *J* = 30.2, 27.0 Hz), 135.89, 134.41 (d, *J* = 2.0 Hz), 133.61, 131.28, 130.75 (dd, *J* = 4.3, 2.9 Hz), 130.00, 128.11, 122.94, 117.35 (dd, *J* = 262.0, 260.4 Hz), 81.24 (dd, *J* = 27.0, 24.4 Hz), 50.48, 17.51 (t, *J* = 3.6 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -107.87 (d, *J* = 254.0 Hz, 1F), -109.42 (d, *J* = 254.2 Hz, 1F); IR (ATR): 3014, 1693, 1633, 1558, 1446, 1278, 1037, 902, 680, 744, 669; HRMS (ESI): Exact mass calcd for C₁₇H₁₅BrF₂NaO₂ [M+Na]⁺: 391.0116, Found: 391.0108.



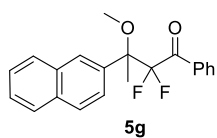
Column chromatography (PE/Et₂O = 20:1, v/v) afforded product **5d** in 77% yield as white solid, Mp: 80-82°C; ¹H NMR (300 MHz, CDCl₃) δ 8.26-8.23 (m, 2H), 8.07 (d, *J* = 7.7 Hz, 2H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 3.22 (s, 3H), 1.89 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 190.58 (dd, *J* = 28.9, 27.8 Hz), 147.99, 144.37, 134.19, 133.87, 130.72 (t, *J* = 3.6 Hz), 129.25 (d, *J* = 1.5 Hz), 128.24, 123.16, 117.11 (t, *J* = 262.3 Hz), 81.39 (dd, *J* = 26.7, 25.0 Hz), 50.84, 17.62 (t, *J* = 3.4 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -107.78 (d, *J* = 255.8 Hz, 1F), -108.88 (d, *J* = 255.5 Hz, 1F); IR (ATR): 3361, 1691, 1516, 1350, 1280, 1151, 1074, 941, 746, 696; HRMS (ESI): Exact mass calcd for C₁₇H₁₅F₂NNaO₄ [M+Na]⁺: 358.0861, Found: 358.0860.



Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **5e** in 74% yield as white solid, Mp: 65-67°C; ¹H NMR (300 MHz, CDCl₃) δ 8.05 (d, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 3.17 (s, 3H), 2.37 (s, 3H), 1.83 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 191.45 (dd, *J* = 30.4, 27.0 Hz), 138.29, 134.59 (d, *J* = 1.9 Hz), 133.59, 133.40, 130.81 (dd, *J* = 4.3, 2.8 Hz), 128.83, 128.19, 128.00, 117.73 (dd, *J* = 261.5, 259.9 Hz), 81.38 (dd, *J* = 26.7, 24.4 Hz), 50.30, 21.09, 17.55 (t, *J* = 3.4 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -107.91 (d, *J* = 252.4 Hz, 1F), -109.46 (d, *J* = 252.3 Hz, 1F); IR (ATR): 2970, 1689, 1597, 1579, 1274, 1141, 1105, 1074, 977, 839, 756, 705; HRMS (ESI): Exact mass calcd for C₁₈H₁₈F₂NaO₂ [M+Na]⁺: 327.1167, Found: 327.1165.

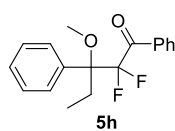


Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **5f** in 81% yield as white solid, Mp: 44-46 °C; ¹H NMR (300 MHz, CDCl₃): δ 8.05 (d, *J* = 7.8 Hz, 2H), 7.60-7.54 (m, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.38-7.36 (m, 1H), 7.10 (d, *J* = 3.6 Hz, 1H), 7.03 (dd, *J* = 5.0, 3.6 Hz, 1H), 3.25 (s, 3H), 1.87 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 191.04 (dd, *J* = 30.9, 26.4 Hz), 140.92, 134.42, 133.61, 133.59, 130.71 (dd, *J* = 4.8, 2.6 Hz), 128.12, 127.97, 126.85, 117.11 (t, *J* = 261.9 Hz), 80.48 (dd, *J* = 27.9, 24.1 Hz), 50.86, 18.44 (t, *J* = 3.3 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -107.29 (d, *J* = 252.6 Hz, 1F), -109.21 (d, *J* = 252.7 Hz, 1F); IR (ATR): 3105, 1695, 1595, 1448, 1381, 1274, 1190, 1045, 937, 800, 754; HRMS (ESI): Exact mass calcd for C₁₅H₁₄F₂NaO₂S [M+Na]⁺: 319.0575, Found: 319.0589.



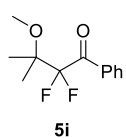
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **5g** in 98% yield as white solid, Mp: 125-127°C; ¹H NMR (300 MHz, CDCl₃): δ 8.08 (d, *J* = 7.9 Hz, 2H), 7.92 (s, 1H), 7.87-7.85 (m, 3H), 7.63-7.58 (m, 1H), 7.55-7.48 (m, 3H), 7.44-7.39 (m,

2H), 3.23 (s, 3H), 1.96 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 191.38 (dd, *J* = 30.7, 26.7 Hz), 134.59 (d, *J* = 2.1 Hz), 134.33, 133.49, 133.18, 132.96, 130.80 (dd, *J* = 4.6, 2.6 Hz), 128.44, 128.14, 128.05, 127.62, 127.51, 126.57, 126.16, 125.67, 117.83 (dd, *J* = 261.7, 261.6 Hz), 81.65 (dd, *J* = 27.1, 24.1 Hz), 50.58, 17.84 (t, *J* = 3.4 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -107.31 (d, *J* = 253.6 Hz, 1F), -109.27 (d, *J* = 253.8 Hz, 1F); IR (ATR): 3037, 2960, 1739, 1695, 1558, 1436, 1228, 1035, 813, 756; HRMS (ESI): Exact mass calcd for C₂₁H₁₈F₂NaO₂ [M+Na]⁺: 363.1167, Found: 363.1161.



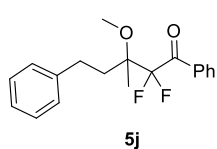
Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **5h** in 90% yield as colorless oil; ¹H NMR (300 MHz, CDCl₃): δ 7.63 (d, *J* = 7.5 Hz, 2H), 7.47-7.37 (m, 3H), 7.28-7.21 (m, 5H), 3.44 (s, 3H), 2.66-2.54 (m, 1H), 2.32-2.20 (m, 1H), 0.90 (t, *J* = 7.4

Hz, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 190.55 (t, *J* = 27.8 Hz), 136.86 (d, *J* = 3.6 Hz), 134.46, 133.14, 130.04 (t, *J* = 3.7 Hz), 128.11, 128.08, 127.96, 127.88, 119.18 (dd, *J* = 267.2, 264.7 Hz), 82.92 (t, *J* = 23.3 Hz), 51.66 (d, *J* = 2.6 Hz), 21.78 (t, *J* = 2.1 Hz), 7.50 (d, *J* = 2.2 Hz); ¹⁹F NMR (282 MHz, CDCl₃): δ -103.50 (d, *J* = 254.6 Hz, 1F), -107.16 (d, *J* = 254.7 Hz, 1F); IR (ATR): 3030, 1751, 1579, 1496, 1219, 1045, 789; HRMS (ESI): Exact mass calcd for C₁₈H₁₈F₂NaO₂ [M+Na]⁺: 327.1167, Found: 327.1166.



Column chromatography (PE/Et₂O = 70:1, v/v) afforded product **5i** in 68% yield as colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 8.08 (d, *J* = 7.5 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 3.22 (s, 3H), 1.40 (t, *J* = 1.6 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃): δ 192.06

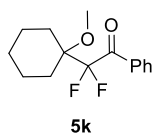
(t, *J* = 28.8 Hz), 134.66, 133.46, 130.63 (t, *J* = 3.7 Hz), 128.09, 118.82 (t, *J* = 260.2 Hz), 77.83 (t, *J* = 25.4 Hz), 49.80, 18.83 (t, *J* = 3.3 Hz); ¹⁹F NMR (376 MHz, CDCl₃): δ -110.81 (s, 2F); IR (ATR): 2991, 1751, 1653, 1598, 1579, 1448, 1369, 1280, 1174, 977, 806, 738; HRMS (ESI): Exact mass calcd for C₁₂H₁₄F₂NaO₂ [M+Na]⁺: 251.0854, Found: 251.0856.



Column chromatography (PE/Et₂O = 50:1, v/v) afforded product **5j** in 93% yield as colorless oil; ¹H NMR (300 MHz, CDCl₃): δ 8.09 (d, *J* = 7.9 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.32-7.17 (m, 5H), 3.29 (s, 3H), 2.82-2.66 (m, 2H),

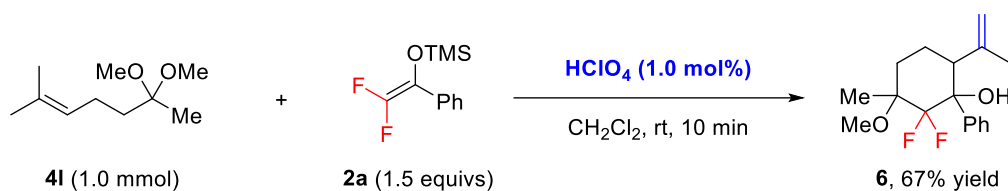
2.12-1.97 (m, 2H), 1.47 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 191.73 (dd, *J* = 29.9, 27.8 Hz), 142.06, 134.65, 133.63, 130.51 (t, *J* = 3.8 Hz), 128.51, 128.36, 128.28, 126.00, 119.67 (dd, *J* = 263.2, 262.0 Hz),

79.22 (t, $J = 24.0$ Hz), 51.07, 35.87, 29.79, 16.75 (t, $J = 3.5$ Hz); ^{19}F NMR (282 MHz, CDCl_3): δ -106.66 (d, $J = 260.3$ Hz, 1F), -109.54 (d, $J = 260.2$ Hz, 1F); IR (ATR): 3028, 1751, 1695, 1598, 1496, 1219, 1080, 977, 850, 746; HRMS (ESI): Exact mass calcd for $\text{C}_{19}\text{H}_{20}\text{F}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 341.1324, Found: 341.1322.



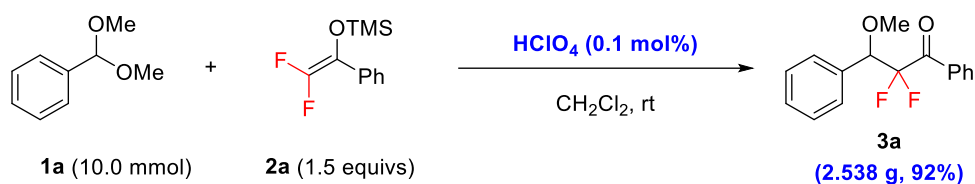
Column chromatography (PE/Et₂O = 30:1, v/v) afforded **5k** in 85% yield as colorless oil; ^1H NMR (300 MHz, CDCl_3): δ 8.06-8.02 (m, 2H), 7.61-7.56 (m, 1H), 7.49-7.43 (m, 2H), 3.32 (s, 3H), 1.96-1.92 (m, 2H), 1.68-1.38 (m, 7H), 1.25-1.16 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3): δ 191.24 (t, $J = 28.0$ Hz), 135.08 (d, $J = 1.8$ Hz), 133.54, 129.87 (t, $J = 4.2$ Hz), 128.43, 120.33 (t, $J = 264.3$ Hz), 77.79 (t, $J = 22.3$ Hz), 51.63 (t, $J = 2.0$ Hz), 27.88, 27.86, 27.83, 25.02, 21.00; ^{19}F NMR (282 MHz, CDCl_3): δ -108.25 (s, 2F); IR (ATR): 3030, 1751, 1579, 1448, 1219, 1014, 977, 830, 767; HRMS (ESI): Exact mass calcd for $\text{C}_{15}\text{H}_{18}\text{F}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 291.1167, Found: 291.1173.

3) Procedure for the cascade aldol/carbonyl-ene reaction



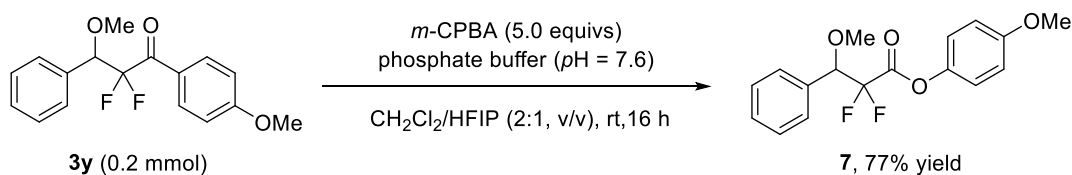
To a stirred mixture of ketal **4l** (172.3 mg, 1.0 mmol, 1.0 equiv) and difluoroenoxy silane **2a** (342.5 mg, 1.5 mmol, 1.5 equivs) in anhydrous CH_2Cl_2 (1.0 mL) in 5.0 mL vial was added HClO_4 (1.4 mg, 1 mol%, 70% wt., aq.) at room temperature. The resulting mixture was then stirred at room temperature. After full consumption of **4l** (ca. 10 min), the reaction mixture was concentrated under vacuum, and ^1H NMR analysis of the residue with 600 MHz spectrometer revealed that the dr value was 10:1. The residue was then purified by flash column chromatography on silica gel using PE/Et₂O (50:1, v/v) as eluents to afford the polysubstituted hexanol **6** in 67% yield as colorless oil (198.3 mg). The structure of **6** was confirmed by 2D NMR analysis. ^1H NMR (400 MHz, CDCl_3): δ 7.65 (dd, $J = 6.9, 1.8$ Hz, 2H), 7.36-7.28 (m, 3H), 5.37 (s, 1H), 4.78 (s, 1H), 4.65 (s, 1H), 3.42 (s, 3H), 3.01-2.96 (m, 1H), 2.15-2.05 (m, 2H), 1.79-1.70 (m, 1H), 1.60 (s, 4H), 1.35 (d, $J = 1.9$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 144.77 (d, $J = 1.8$ Hz), 138.32, 128.02 (d, $J = 3.0$ Hz), 127.29, 127.15, 117.73 (dd, $J = 268.7, 251.6$ Hz), 114.66, 79.72 (dd, $J = 29.9, 21.8$ Hz), 78.93 (dd, $J = 23.9, 21.2$ Hz), 50.11, 50.09 (d, $J = 3.9$ Hz), 31.89 (d, $J = 4.8$ Hz), 22.53, 22.50, 16.37 (t, $J = 2.9$ Hz); ^{19}F NMR (376 MHz, CDCl_3): δ -110.40 (d, $J = 260.5$ Hz, 1F), -128.48 (d, $J = 260.5$ Hz, 1F); IR (ATR): 3415, 3037, 2987, 2976, 1714, 1639, 1496, 1436, 1315, 1197, 1056, 964, 933, 840, 651; HRMS (ESI): Exact mass calcd for $\text{C}_{17}\text{H}_{22}\text{F}_2\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 319.1480, Found: 319.1486.

Part II. Gram-scale synthesis



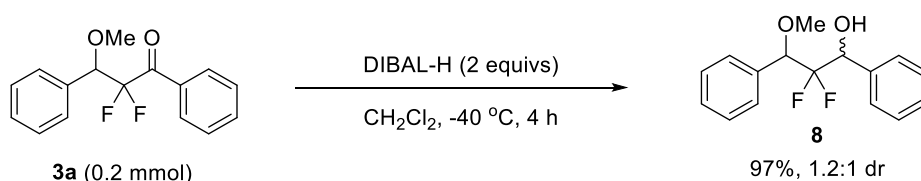
General procedure: To a stirred mixture of acetal **1a** (10.0 mmol, 1.0 equiv) and difluoroenoxy silanes **2a** (15 mmol, 1.5 equivs) in anhydrous CH_2Cl_2 (10.0 mL, 1.0 M) in 25 mL flame-dried Schleck tube was added HClO_4 (1.4 mg, 0.1 mol%, 70% wt., aq.) at room temperature. The resulting mixture was then stirred at room temperature. After 30 minutes, the reaction was concentration under vacuum and purified by flash column chromatography on silica gel using the PE/ Et_2O (50:1, v/v) as eluents to afford 2.538 g of products **3a** in 92% yield.

Part III. Product transformation

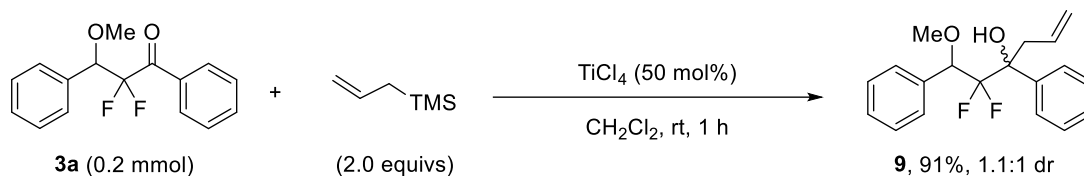


To a solution of compound **3y** (55.0 mg, 0.2 mmol, 1.0 equiv) in the mixed solvent of CH_2Cl_2 (2.0 mL) and HFIP (1.0 mL) was subsequently added *m*-chloroperoxybenzoic acid (*m*-CPBA, 202.0 mg, 1.0 mmol, 85% wt, 5.0 equivs) and phosphate buffer (0.2 mL, pH = 7.6).⁴ The resulting mixture was stirred at room temperature until full consumption of **3y** (about 16 h), then sat. aq. NaHCO_3 solution was added to quench the reaction. After extracting with CH_2Cl_2 (6 mL \times 3), the combined organic layer was washed with brine, then dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude residue was purified by column chromatography (PE/ EtOAc = 10/1, v/v) to give the ester **7** in 77% yield as colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 7.51-7.43 (m, 5H), 7.08-7.02 (m, 2H), 6.95-6.91 (m, 2H), 4.86 (dd, J = 17.4, 7.0 Hz, 1H), 3.82 (s, 3H), 3.42 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 162.46 (dd, J = 34.0, 31.0 Hz), 157.90, 143.37, 132.02 (d, J = 1.5 Hz), 129.52, 128.75, 128.53, 121.76, 114.67, 113.52 (dd, J = 262.3, 251.3 Hz), 82.48 (dd, J = 29.3, 22.6 Hz), 58.01, 55.62; ^{19}F NMR (282 MHz, CDCl_3): δ -111.17 (dd, J = 262.0, 6.8 Hz, 1F), -121.48 (dd, J = 261.6, 16.1 Hz, 1F); IR (ATR): 1793, 1714, 1506, 1363, 1290, 1186, 1091, 1064, 920, 715; HRMS (ESI): Exact mass calcd for $\text{C}_{17}\text{H}_{16}\text{F}_2\text{NaO}_4$ [$\text{M}+\text{Na}$] $^+$: 345.0909, Found: 345.0910.

⁴ S. Kobayashi, H. Tanaka, H. Amii and K. Uneyama, *Tetrahedron*, 2003, **59**, 1547.

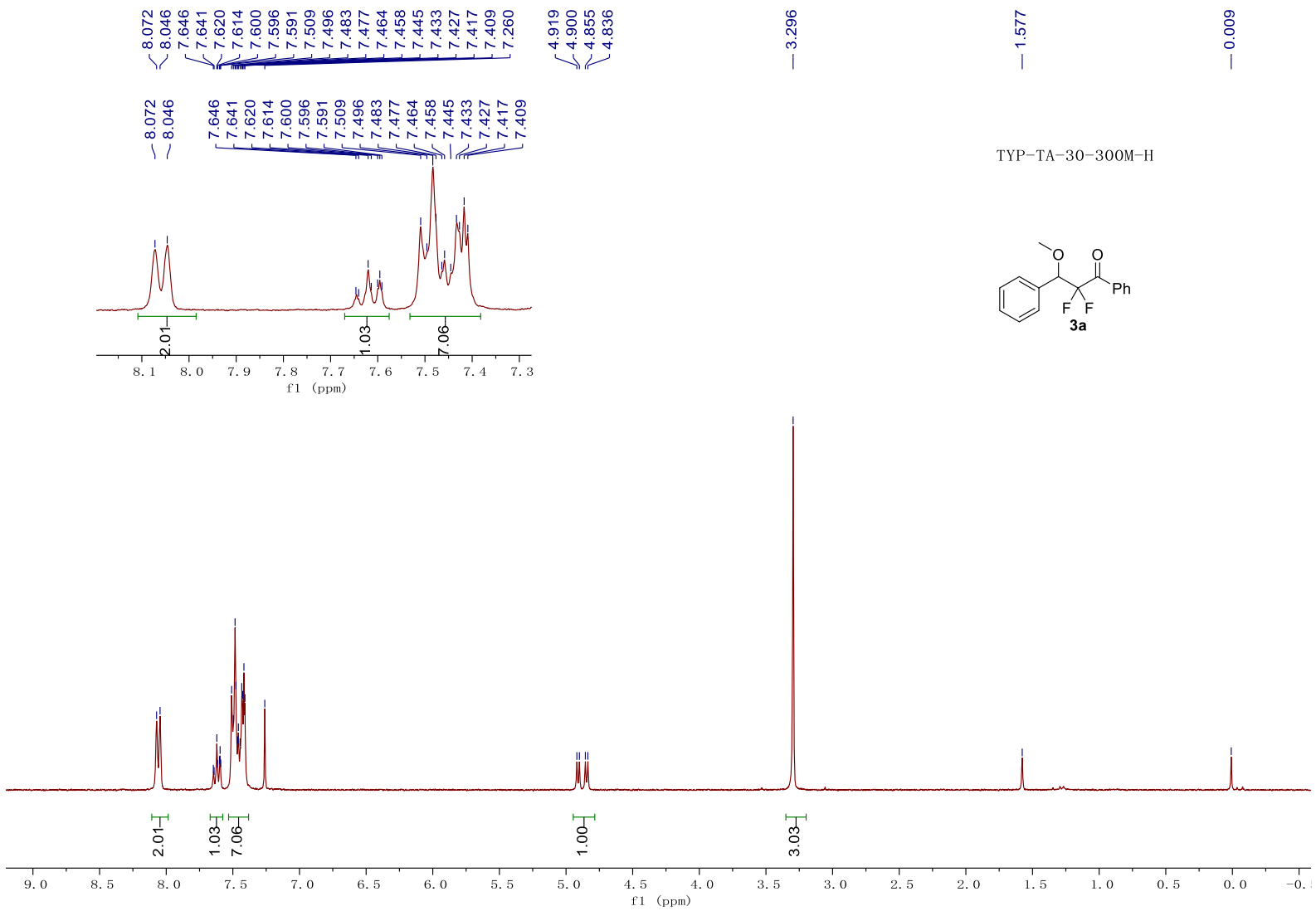


To a stirred solution of **3a** (55.0 mg, 0.2 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (2.0 mL) at $-40\text{ }^\circ\text{C}$ was added DIBAL-H (0.4 mL, 1.0 M in hexane, 0.4 mmol, 2.0 equivs). The resulting mixture was stirred at $-40\text{ }^\circ\text{C}$ until full consumption of **3a** by TLC analysis (about 4 h), and then quenched by saturated NaCl (aq.). The mixture was extracted with EtOAc (6 mL \times 3), then the combined organic layer was washed with brine, and dried over Na_2SO_4 , filtered, and concentrated under vacuo. ^1H , ^{19}F NMR analysis of crude mixture revealed that the dr value was 1.2:1. The crude residue was then purified by column chromatography (PE/toluene = 1/2, v/v) to give the corresponding product **8** in total 97% yield as colorless oil. *Notably, two diastereomers of 8 could be easily isolated by column chromatography.* **^1H NMR for the major diastereomer** (400 MHz, CDCl_3): δ 7.52-7.49 (m, 2H), 7.43-7.38 (m, 8H), 5.13 (t, $J = 12.7$ Hz, 1H), 4.20 (dd, $J = 18.4, 6.2$ Hz, 1H), 3.23 (s, 3H), 2.91 (s, 1H); **^{13}C NMR the major diastereomer** (101 MHz, CDCl_3): δ 136.46 (d, $J = 4.5$ Hz), 133.35 (d, $J = 1.7$ Hz), 128.95, 128.85, 128.81, 128.39, 128.26, 128.06, 119.54 (dd, $J = 256.9, 247.3$ Hz), 82.58 (dd, $J = 31.4, 23.1$ Hz), 74.23 (t, $J = 24.6$ Hz), 57.09; **^{19}F NMR the major diastereomer** (376 MHz, CDCl_3): δ -119.91 (d, $J = 256.0$ Hz, 1F), -124.60 (d, $J = 256.1$ Hz, 1F). IR (ATR): 3439, 1714, 1492, 1456, 1361, 1217, 1197, 1130, 1101, 1076, 1045, 980, 750, 642; HRMS (ESI): Exact mass calcd for $\text{C}_{16}\text{H}_{16}\text{F}_2\text{NaO}_2$ [$\text{M}+\text{Na}$] $^+$: 301.1011, Found: 301.1010. **^1H NMR for the minor diastereomer** (400 MHz, CDCl_3): δ 7.46 (d, $J = 6.5$ Hz, 2H), 7.41-7.34 (m, 8H), 5.11 (t, $J = 8.4$ Hz, 1H), 4.58 (dd, $J = 14.6, 8.4$ Hz, 1H), 3.45 (s, 1H), 3.37 (s, 3H); **^{13}C NMR for the minor diastereomer** (126 MHz, CDCl_3): δ 136.74, 133.27, 128.97, 128.68, 128.57, 128.31, 128.24, 127.68, 118.71 (dd, $J = 252.0, 252.6$ Hz), 82.39 (dd, $J = 31.3, 26.5$ Hz), 73.45 (dd, $J = 29.7, 26.5$ Hz), 57.65; **^{19}F NMR for the minor diastereomer** (376 MHz, CDCl_3): δ -117.29 (d, $J = 266.2$ Hz, 1F), -118.08 (d, $J = 266.2$ Hz, 1F); IR (ATR): 3460, 1714, 1456, 1361, 1219, 1157, 1103, 1076, 981, 977, 700; HRMS (ESI): Exact mass calcd for $\text{C}_{16}\text{H}_{16}\text{F}_2\text{NaO}_2$ [$\text{M}+\text{Na}$] $^+$: 301.1011, Found: 301.1013.

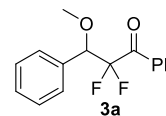


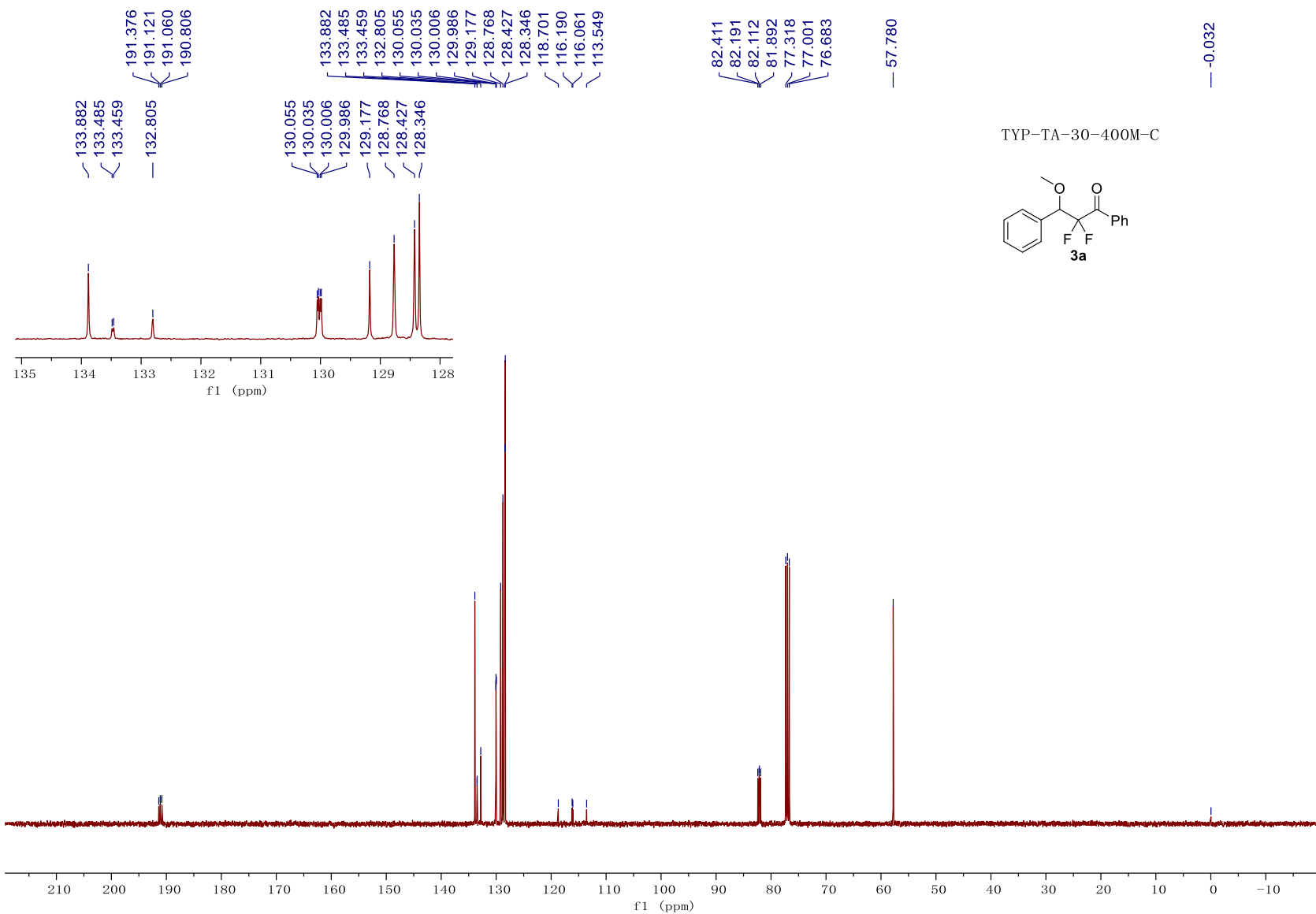
To a solution of compound **3a** (55.0 mg, 0.2 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (2.0 mL) was subsequently added allyltrimethylsilane (45.6 mg, 0.4 mmol, 2.0 equivs) and TiCl_4 (19.0 mg, 0.1 mmol, 50 mol%). The resulting mixture was stirred at room temperature until full consumption of **3a** (about 1 h), then saturated aq. NaHCO_3 solution was added to quench the reaction. After extracting with CH_2Cl_2 (6 mL \times 3), the combined organic layer was washed with brine, then dried over Na_2SO_4 , and concentrated under reduced pressure. ^1H , ^{19}F NMR analysis of crude mixture revealed that the dr value was 1.1:1. The combined crude residue was then purified by column chromatography (PE/EtOAc = 20/1, v/v) to afford product **9** in total 91% yield as colorless oil. *Notably, two diastereomers of 9 could be easily isolated by column chromatography.* **^1H NMR for the major diastereomer** (400 MHz, CDCl_3): δ 7.63 (d, $J = 7.7$ Hz, 2H), 7.46 (t, $J = 7.6$ Hz, 2H), 7.39-7.34 (m, 4H), 7.29-7.27 (m, 2H), 5.63-5.56 (m, 1H), 5.05-5.01 (m, 1H), 4.76 (s, 1H), 3.95 (dd, $J = 22.2, 2.6$ Hz, 1H), 3.01 (s, 3H), 2.98-2.92 (m, 1H), 2.85-2.80 (m, 1H); **^{13}C NMR for the major diastereomer** (101 MHz, CDCl_3): δ 141.03 (d, $J = 4.4$ Hz), 132.61, 132.37, 129.03, 128.82, 128.37, 128.16, 127.78, 126.14 (d, $J = 3.3$ Hz), 118.69 (dd, $J = 265.9, 249.5$ Hz), 118.27, 83.58 (dd, $J = 35.8, 23.8$ Hz), 79.40 (t, $J = 24.2$ Hz), 56.92, 39.72 (dd, $J = 4.4, 1.5$ Hz); **^{19}F NMR for the major diastereomer** (376 MHz, CDCl_3): δ -110.65 (d, $J = 266.3$ Hz, 1F), -126.53 (d, $J = 266.4$ Hz, 1F). IR (ATR): 3460, 3030, 1714, 1495, 1450, 1417, 1398, 1219, 1157, 1097, 1029, 985, 756; HRMS (ESI): Exact mass calcd for $\text{C}_{19}\text{H}_{20}\text{F}_2\text{NaO}_2$ [$\text{M}+\text{Na}$] $^+$: 341.1324, Found: 341.1321; **^1H NMR for the minor diastereomer** (400 MHz, CDCl_3): δ 7.51 (d, $J = 7.6$ Hz, 2H), 7.31-7.18 (m, 8H), 5.58-5.47 (m, 1H), 5.06 (dd, $J = 27.2, 13.3$ Hz, 1H), 4.51 (dd, $J = 19.4, 4.9$ Hz, 1H), 3.40 (s, 1H), 3.06-3.00 (m, 1H), 3.00 (s, 3H), 2.77 (dd, $J = 14.3, 7.6$ Hz, 1H); **^{13}C NMR for the minor diastereomer** (101 MHz, CDCl_3): δ 138.98 (d, $J = 2.1$ Hz), 133.80, 132.26, 128.88, 128.79, 128.10, 127.73, 127.53, 127.03 (d, $J = 1.8$ Hz), 119.69, 119.30 (dd, $J = 263.2, 249.9$ Hz), 82.33 (dd, $J = 34.4, 22.7$ Hz), 77.81 (dd, $J = 24.7, 25.4$ Hz), 56.85, 41.06 (dd, $J = 3.7, 1.9$ Hz); **^{19}F NMR for the minor diastereomer** (376 MHz, CDCl_3) δ -109.46 (d, $J = 264.8$ Hz, 1F), -122.04 (d, $J = 264.9$ Hz, 1F); IR (ATR): 3460, 3442, 3030, 1737, 1714, 1494, 1450, 1361, 1219, 1130, 1066, 920, 717; HRMS (ESI): Exact mass calcd for $\text{C}_{19}\text{H}_{20}\text{F}_2\text{NaO}_2$ [$\text{M}+\text{Na}$] $^+$: 341.1324, Found: 341.1322.

Part IV. ^1H , ^{13}C , ^{19}F NMR spectra



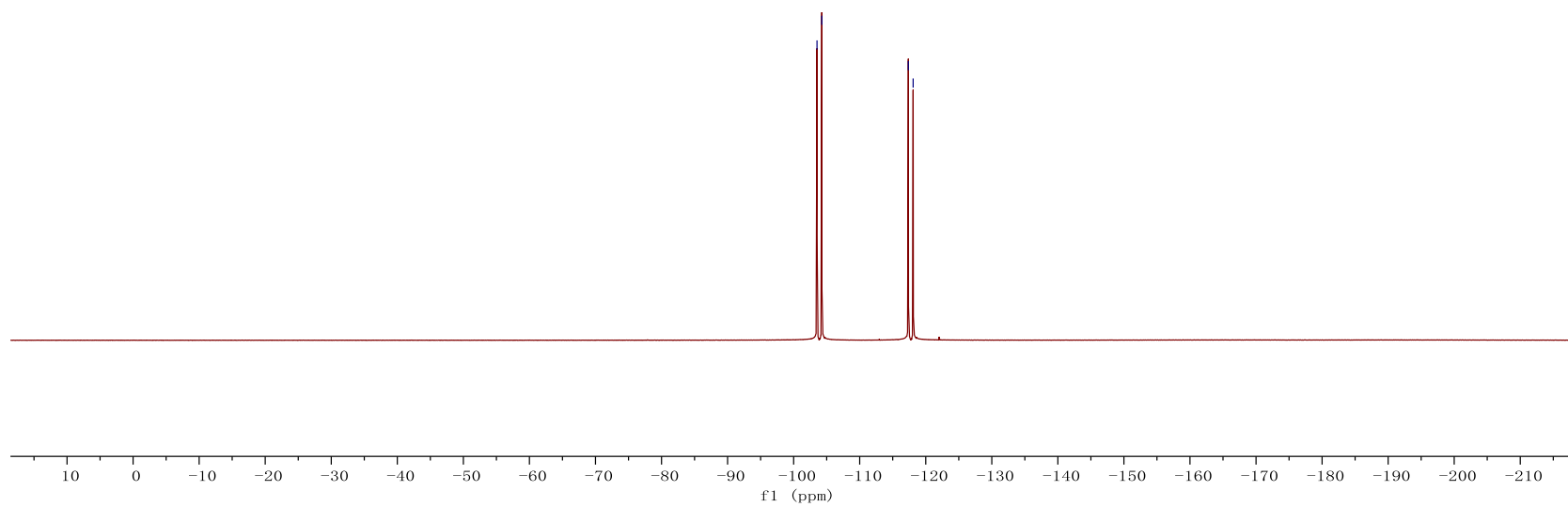
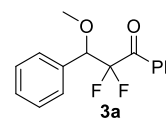
TYP-TA-30-300M-H

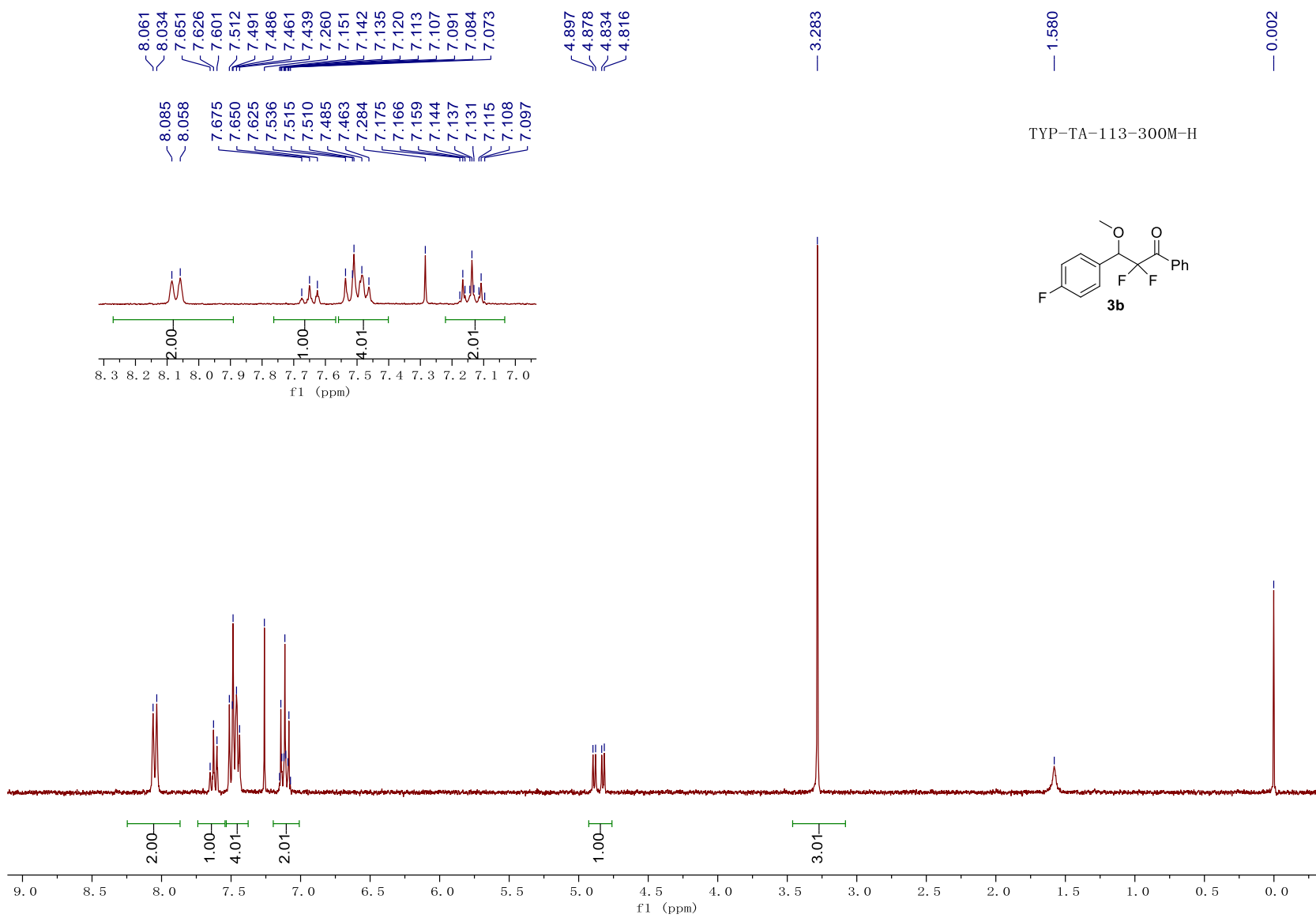


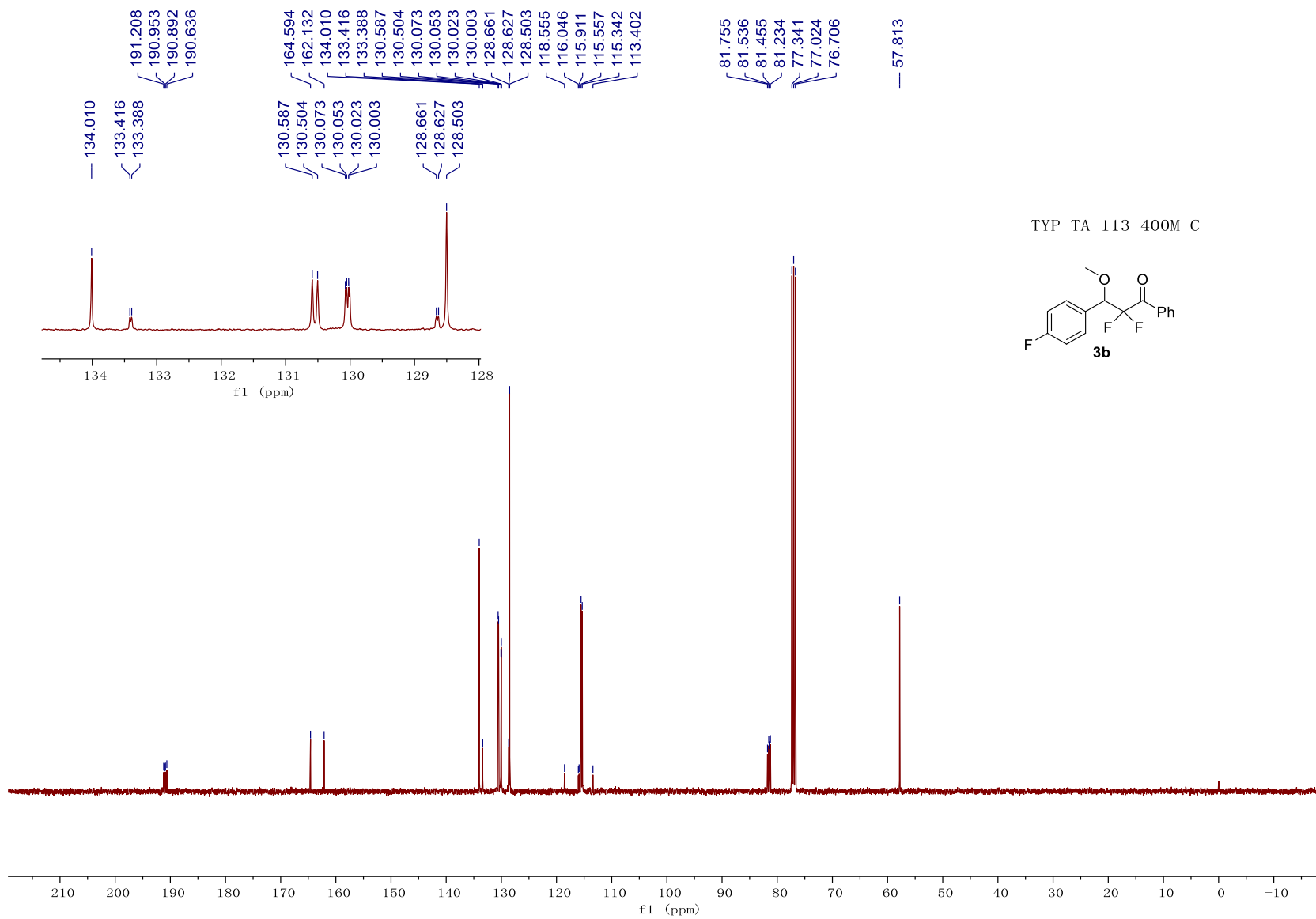


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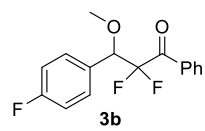
-103.537
-104.265
-117.366
-118.092



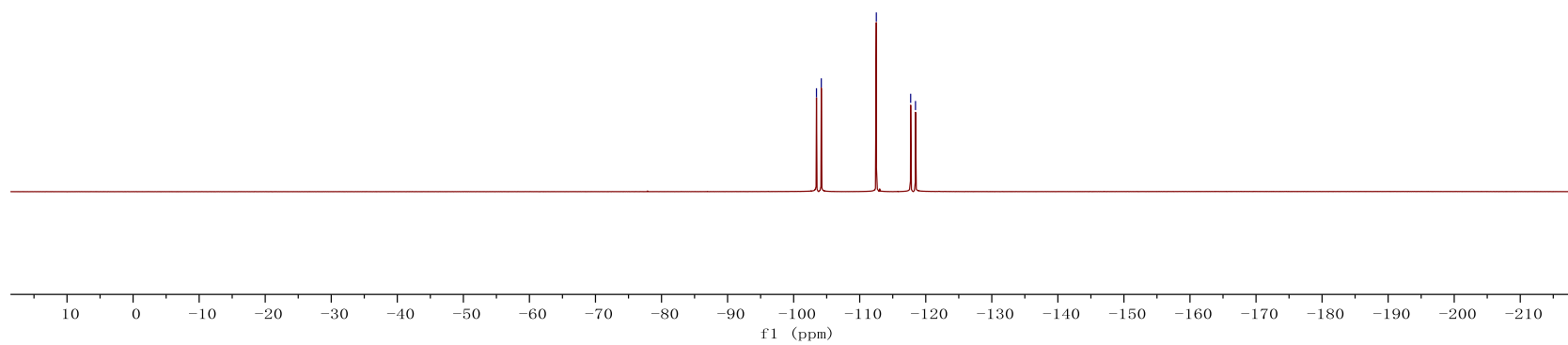


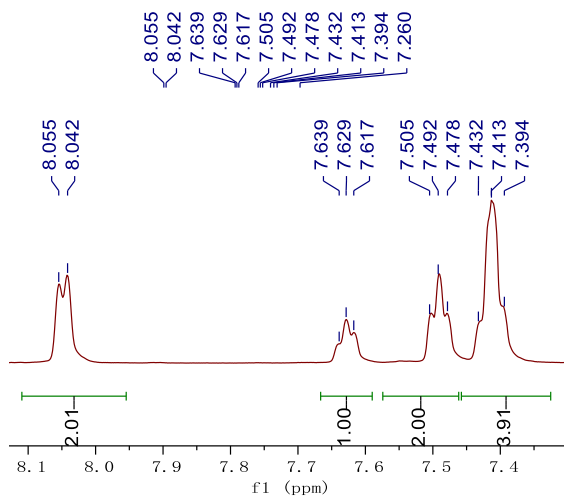


TYP-TA-113-400M-F

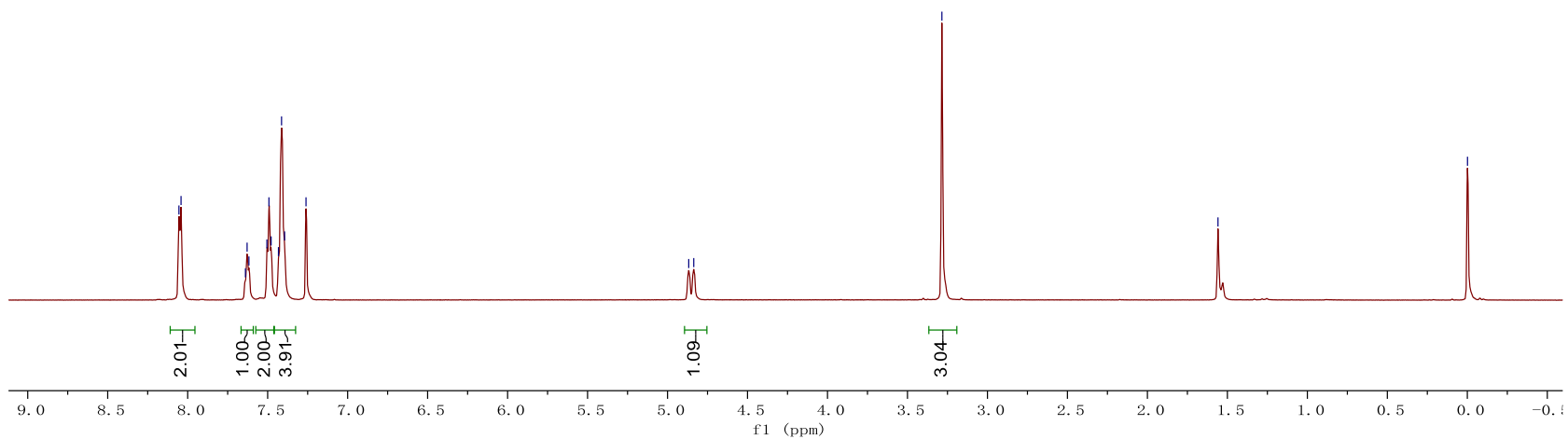
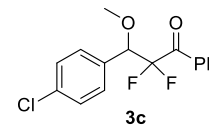


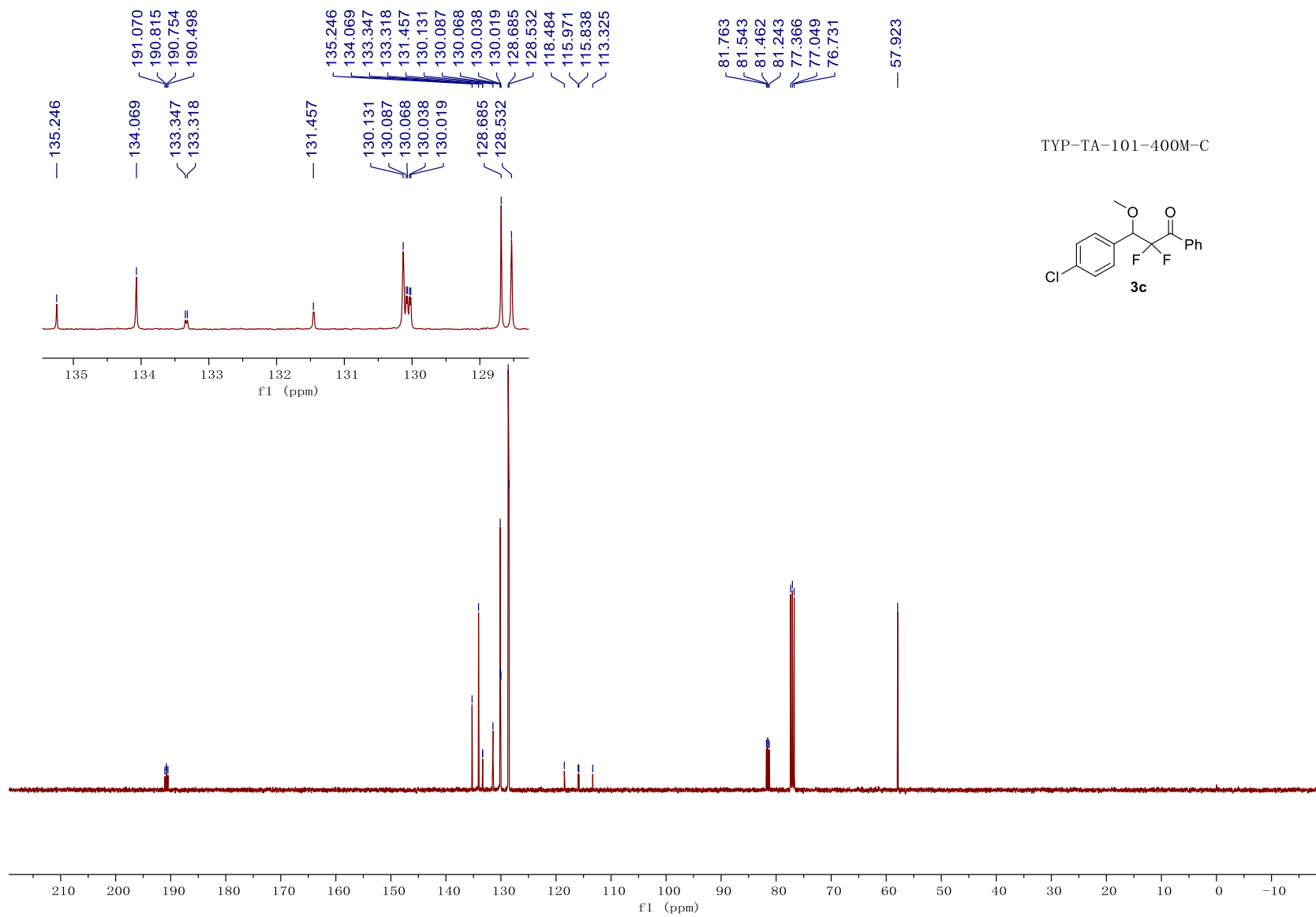
-103.457
-104.189
-112.515
-117.715
-118.447



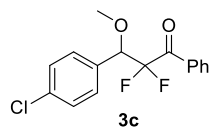


TYP-TA-101-600M-H



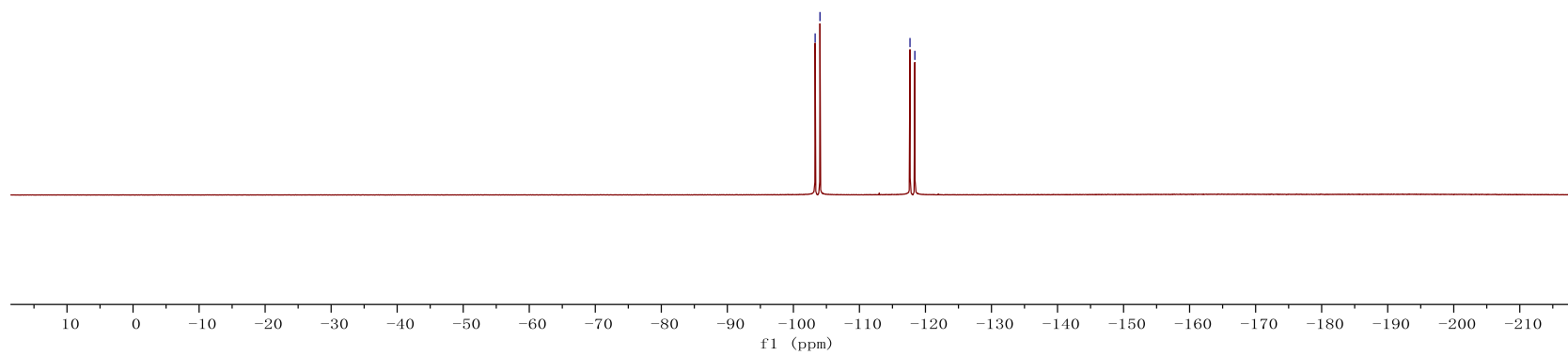


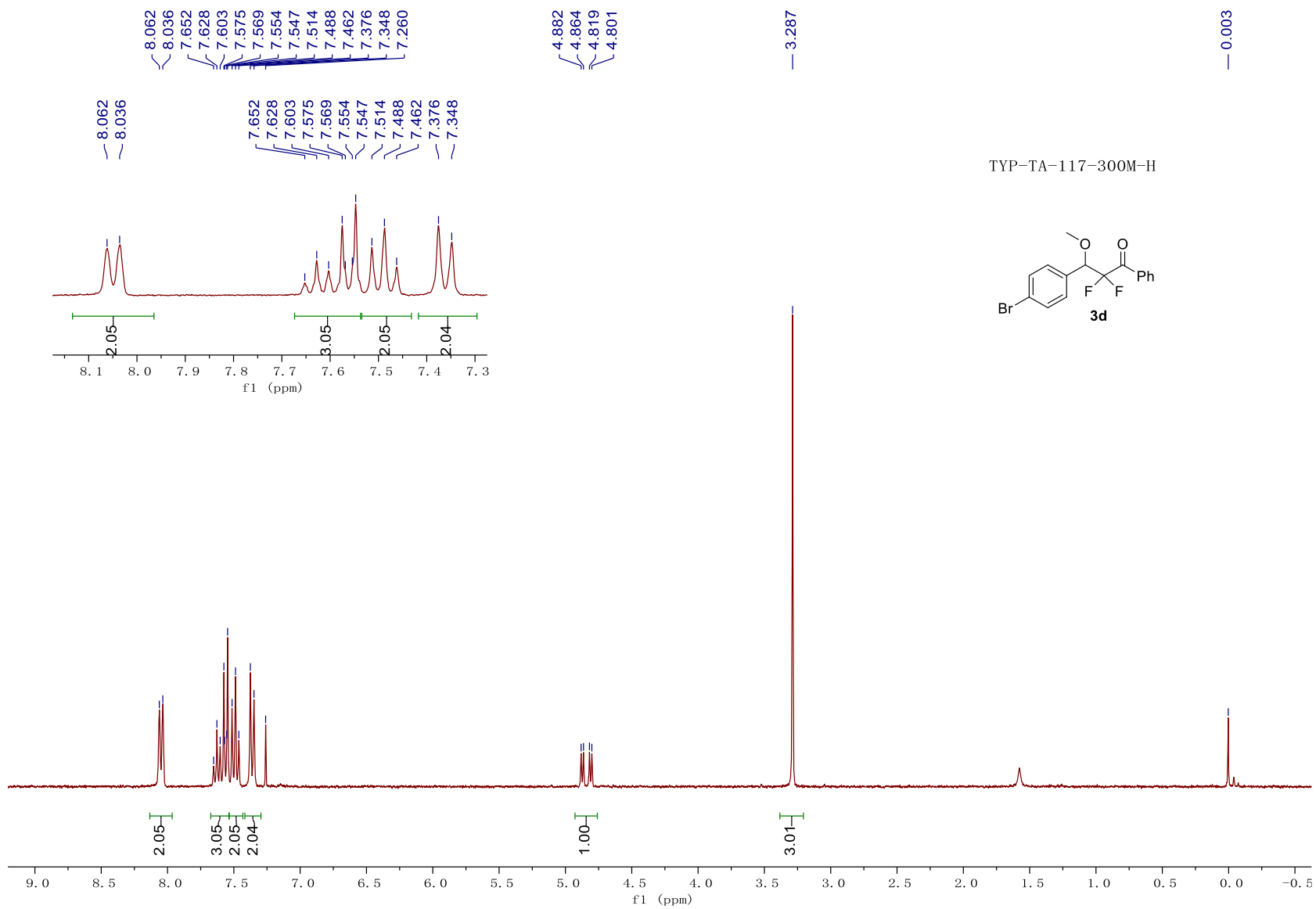
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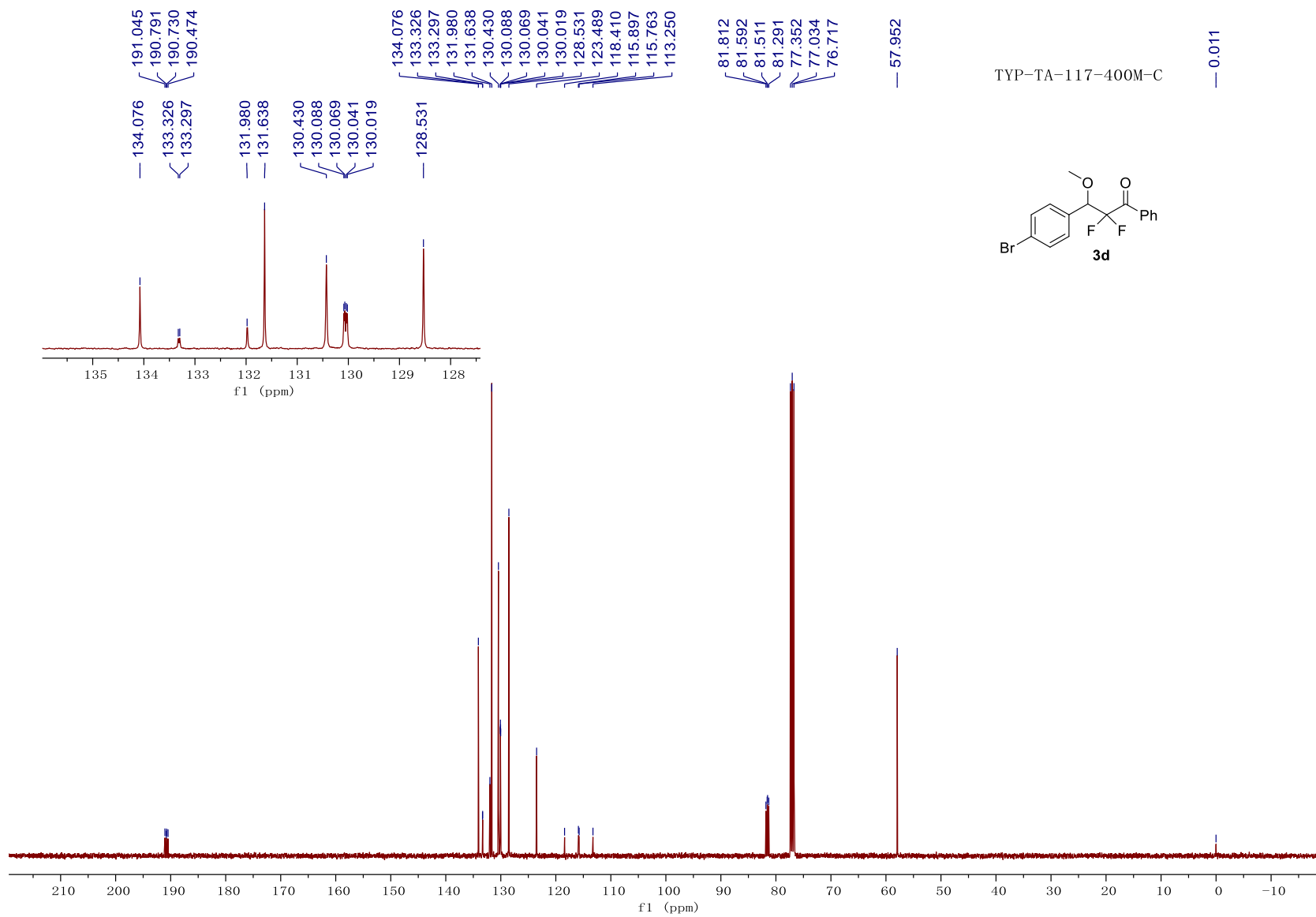


-103.291
-104.025

-117.660
-118.394

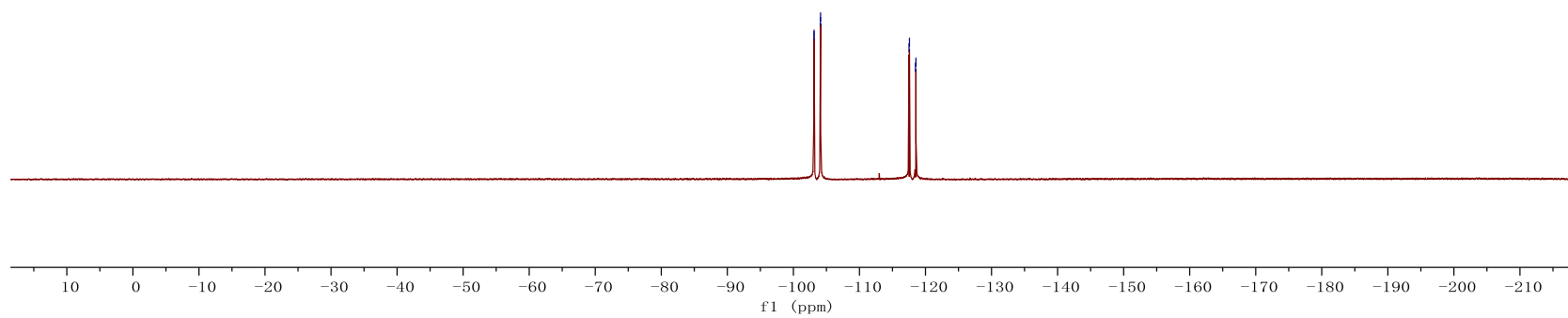
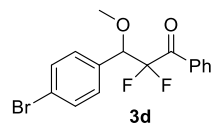


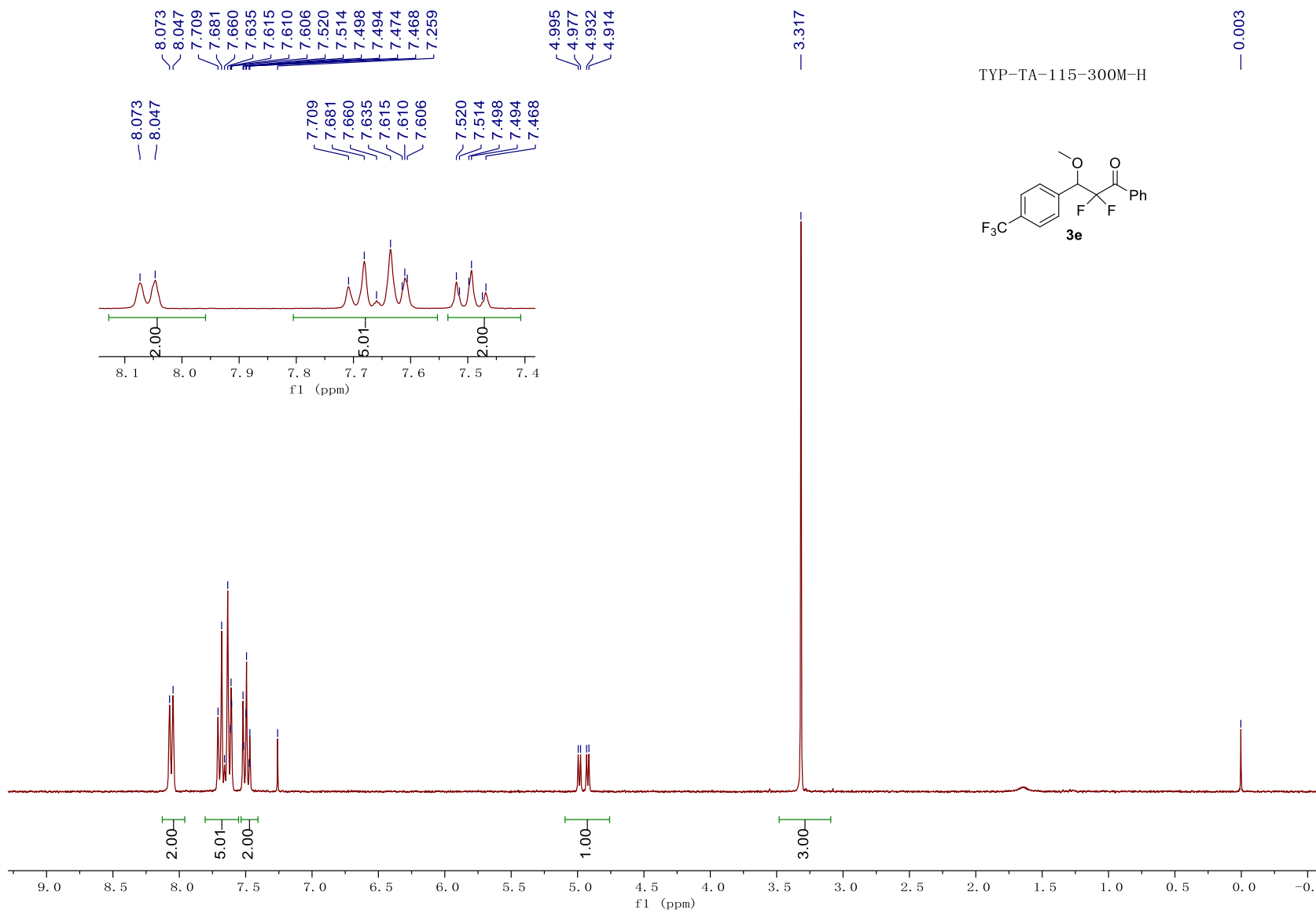


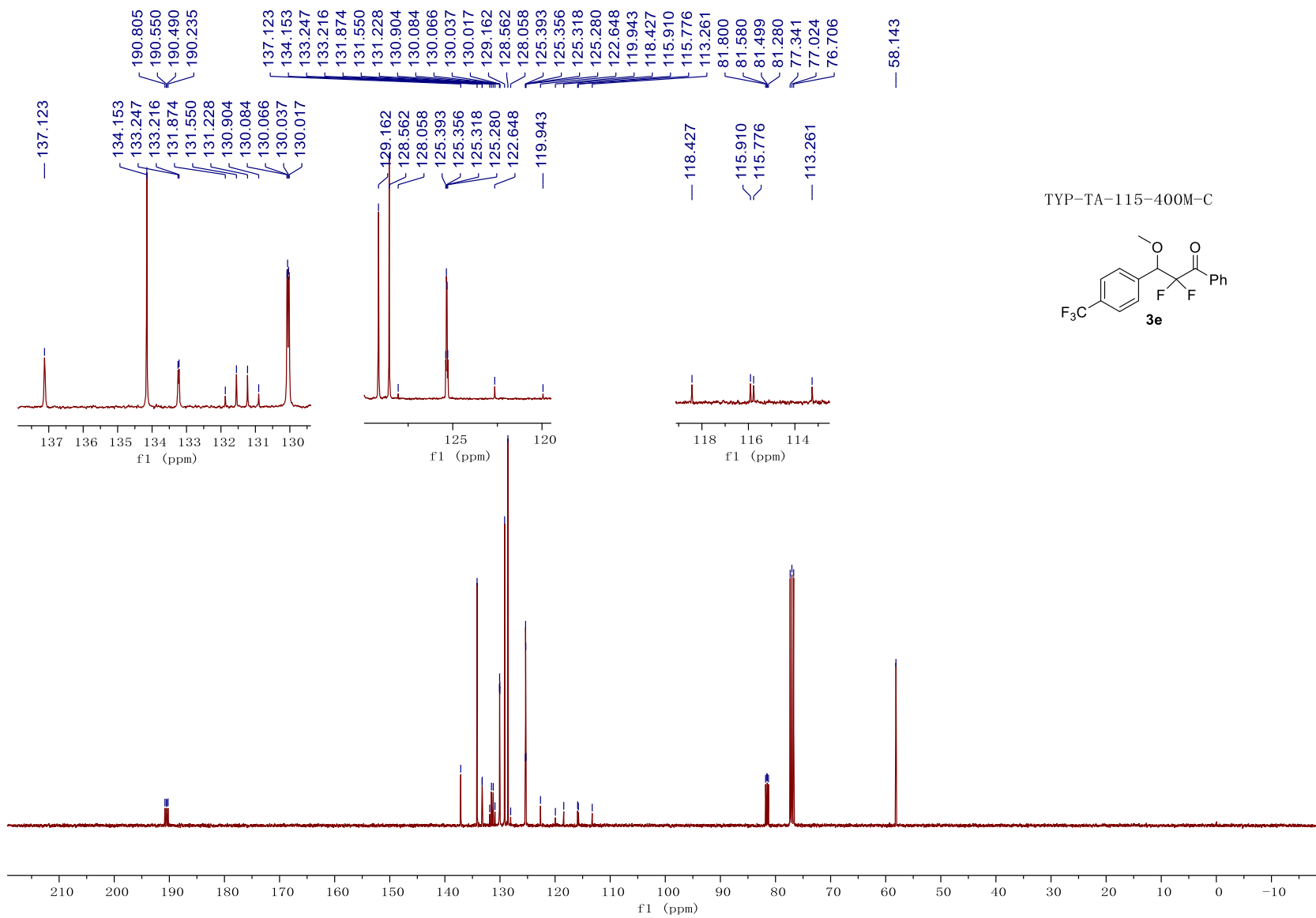


TYP-TA-117-300M-F

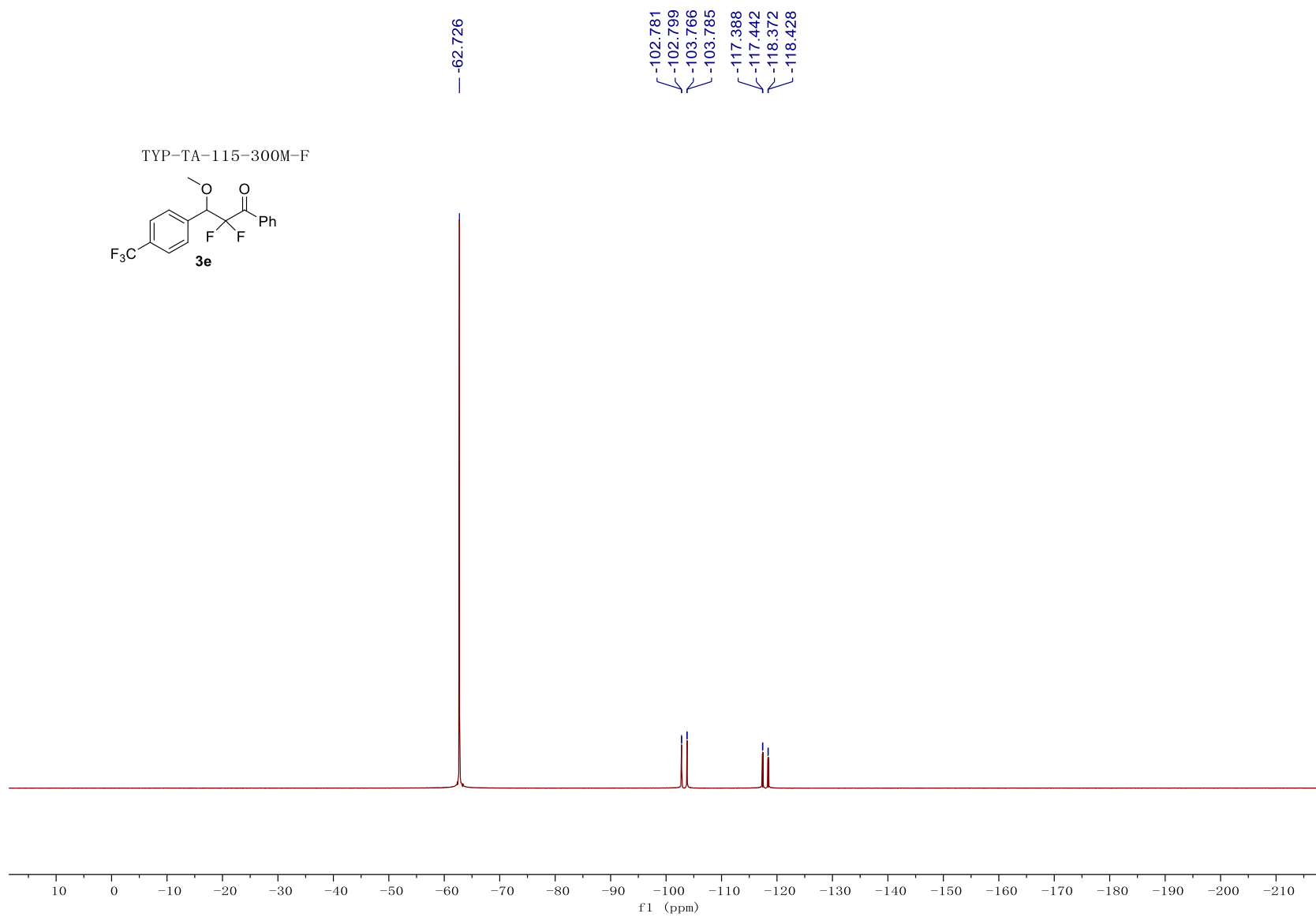
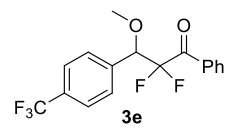
-103.116
-103.136
-104.095
-104.114
-117.509
-117.570
-118.488
-118.550

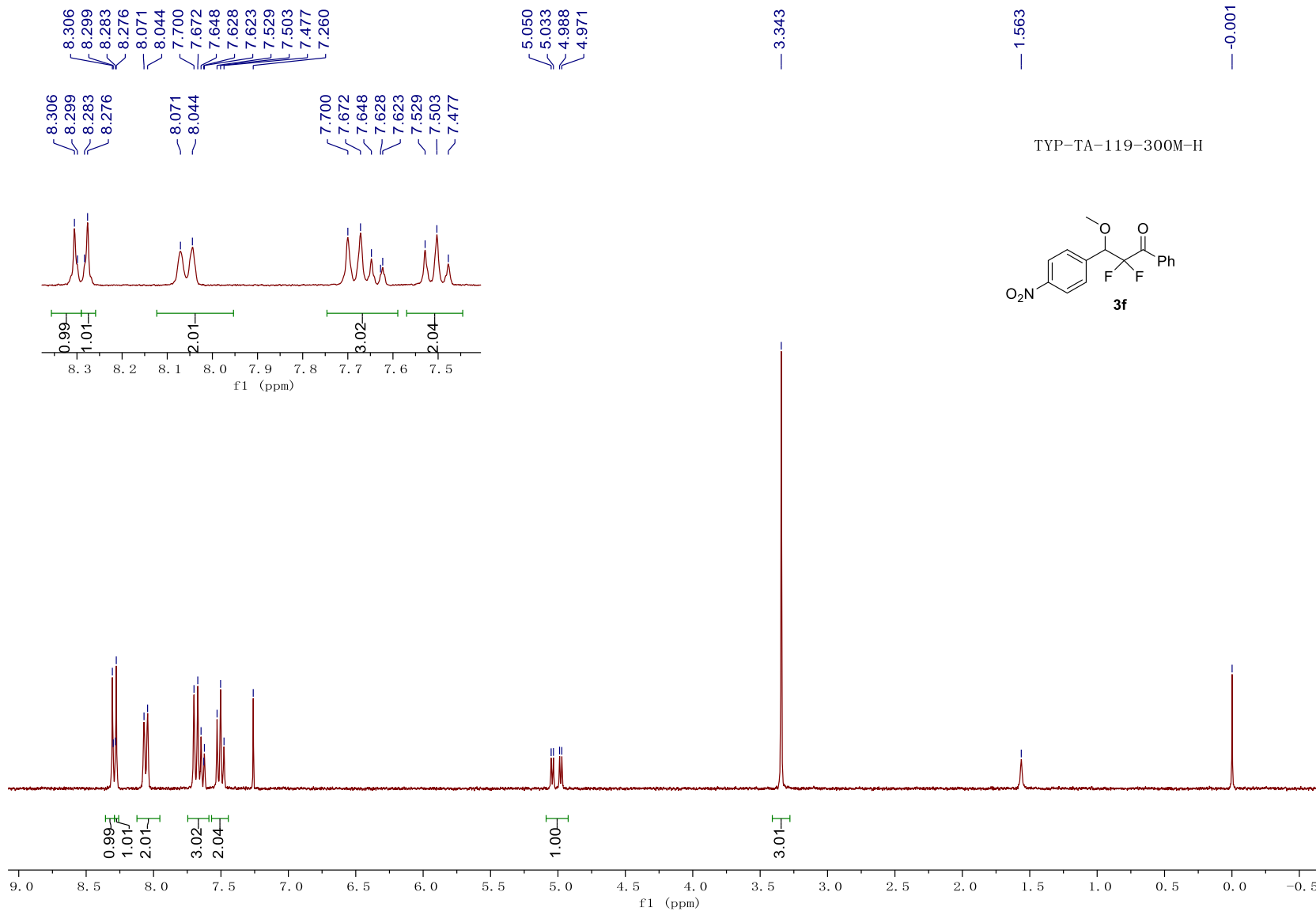


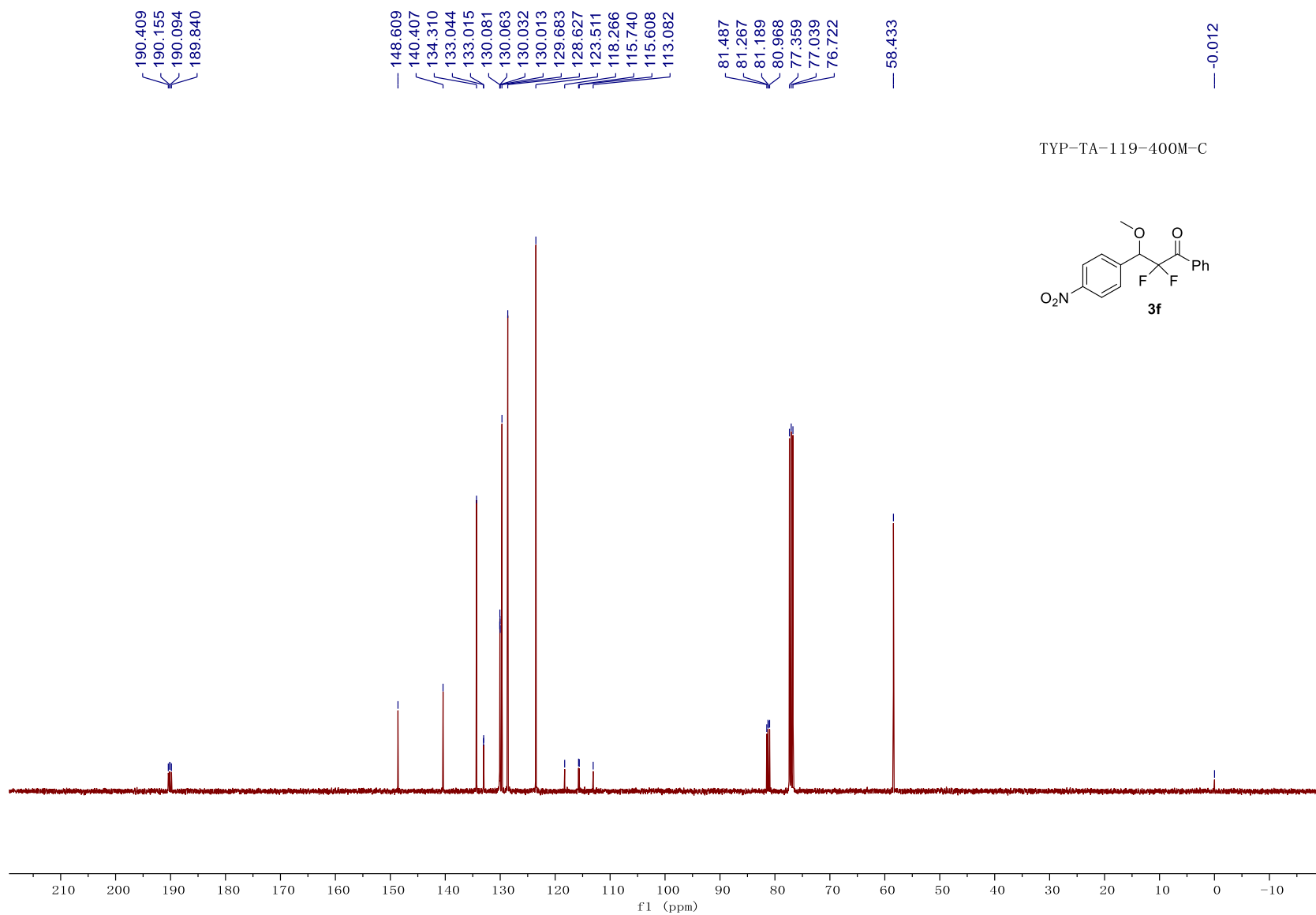




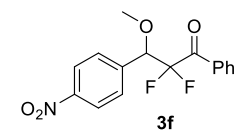
TYP-TA-115-300M-F



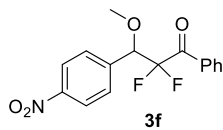




TYP-TA-119-400M-C

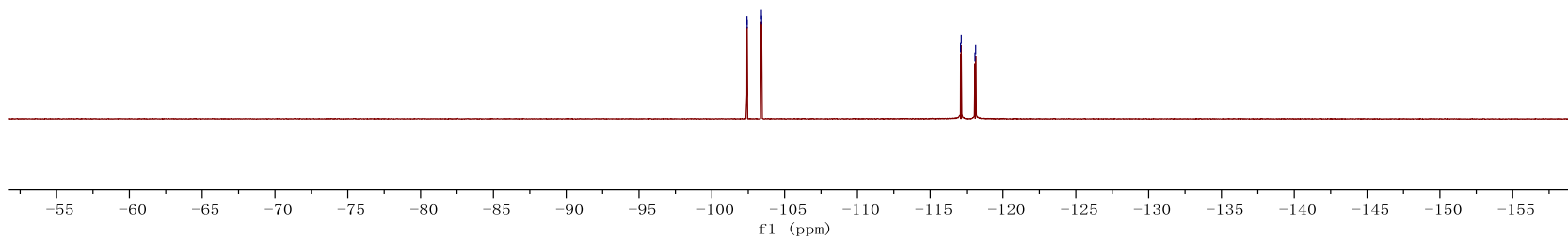


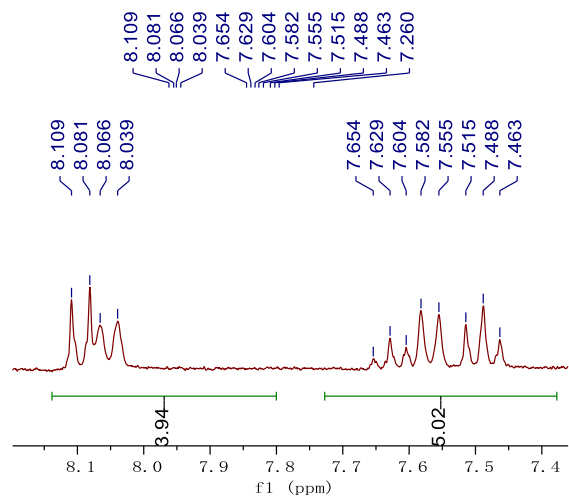
TYP-TA-119-300M-F



-102.413
-102.424
-103.404
-103.418

-117.086
-117.130
-118.078
-118.125





4.979
4.961
4.915
4.898

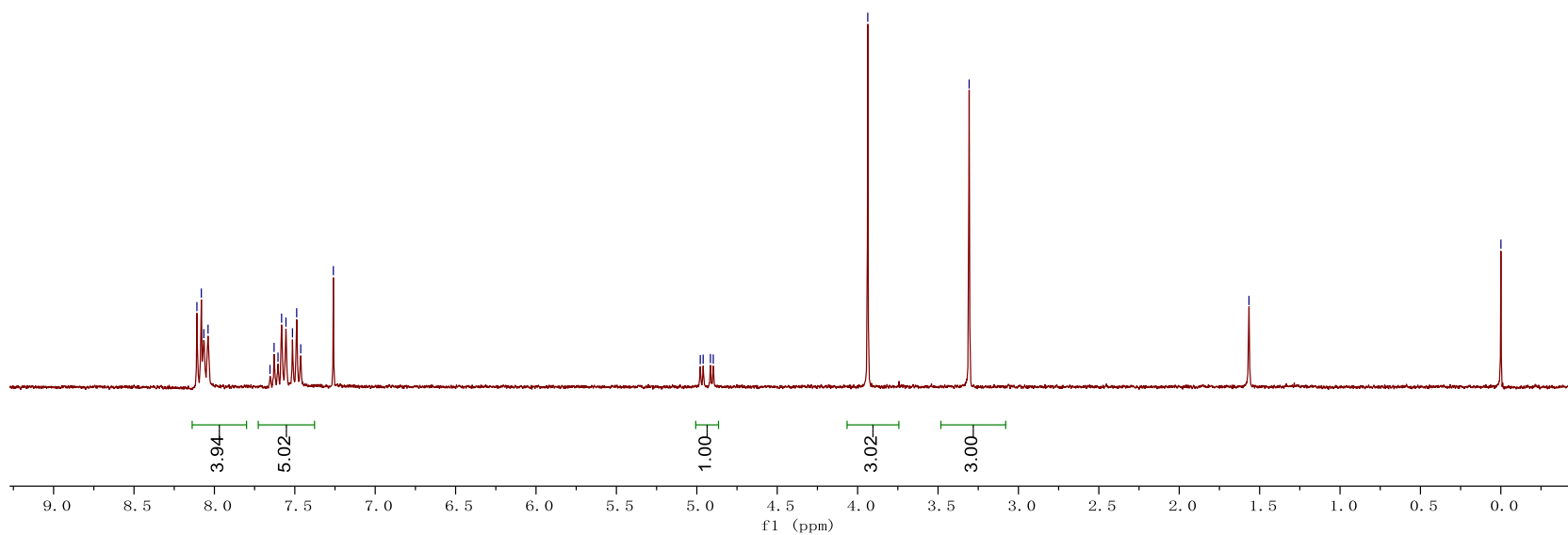
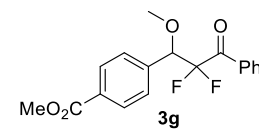
— 3.937

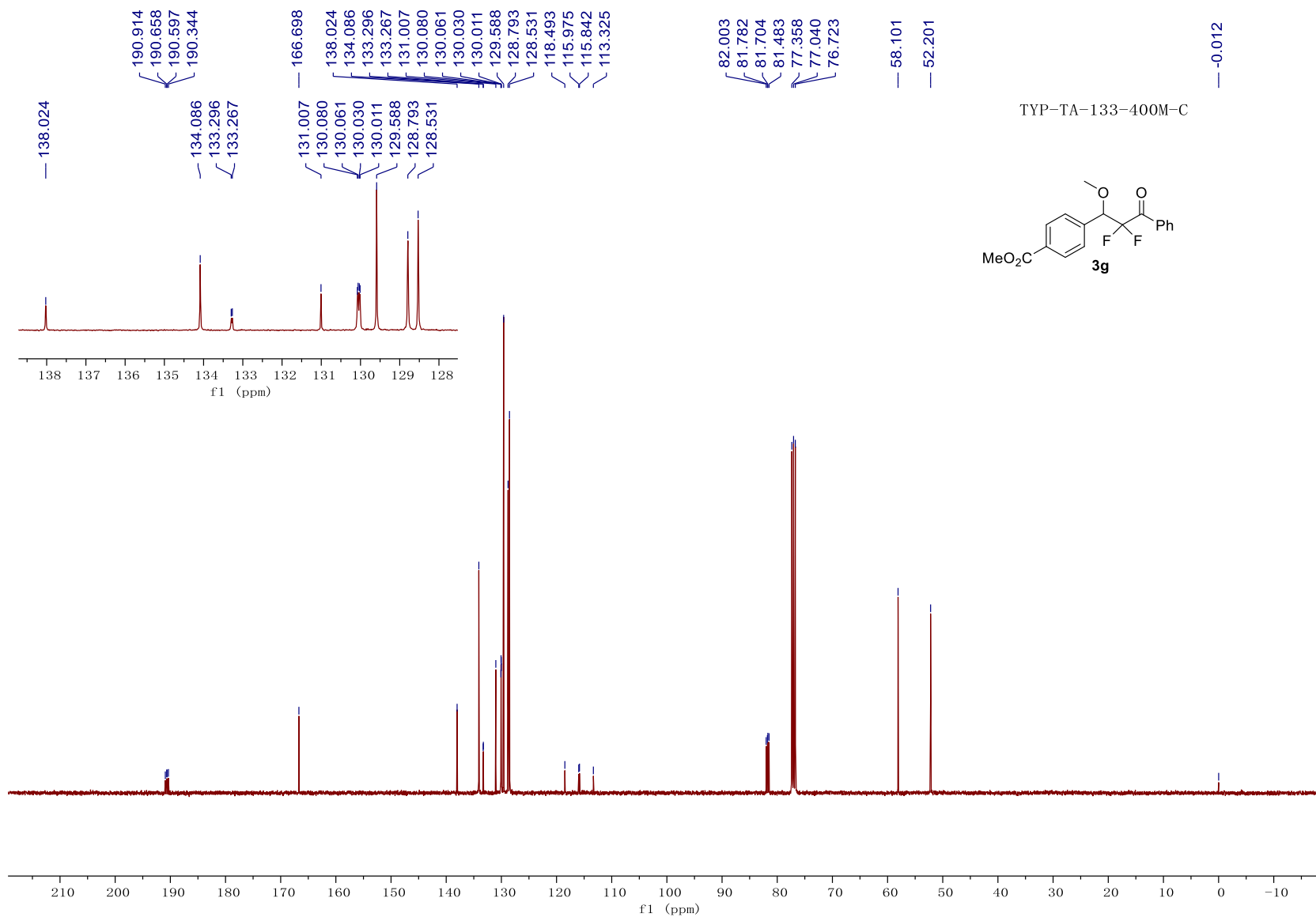
— 3.307

— 1.566

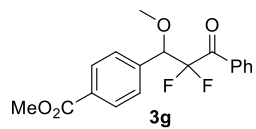
— -0.001

TYP-TA-133-300M-H

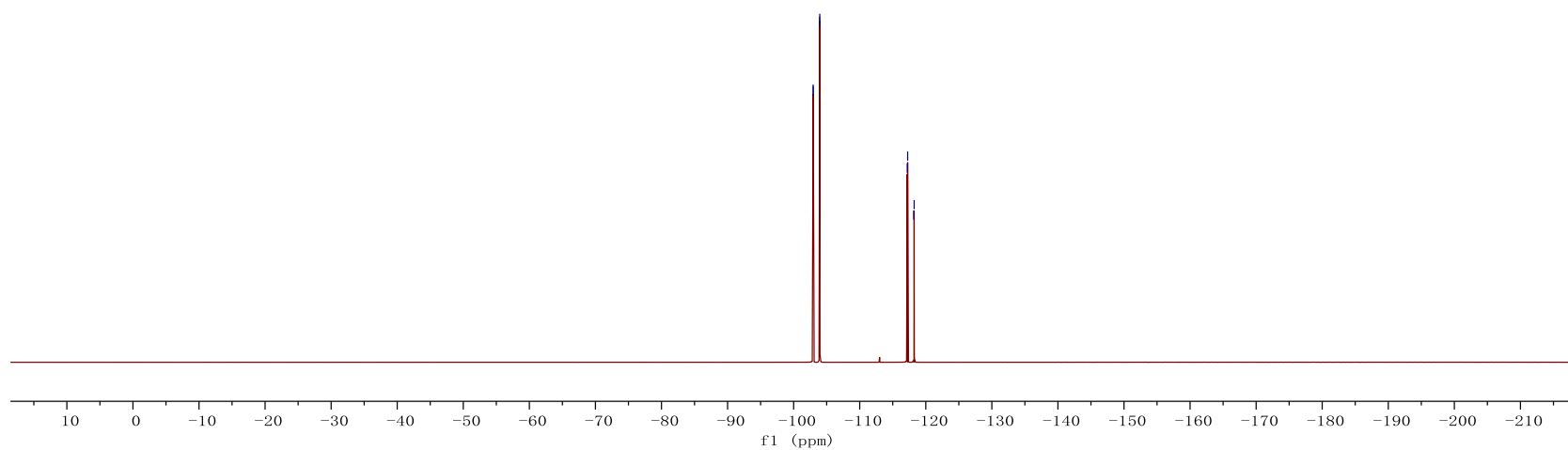


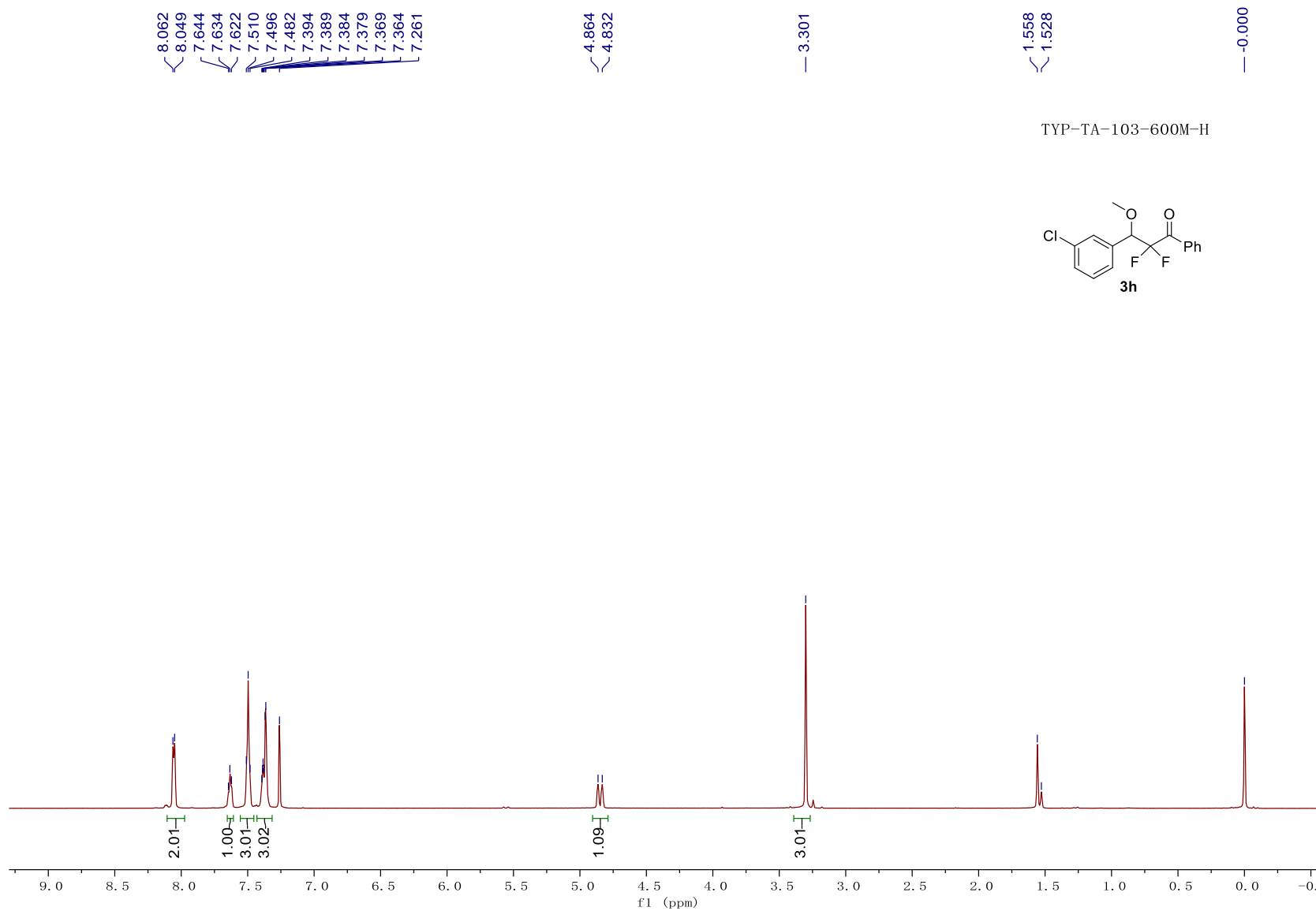


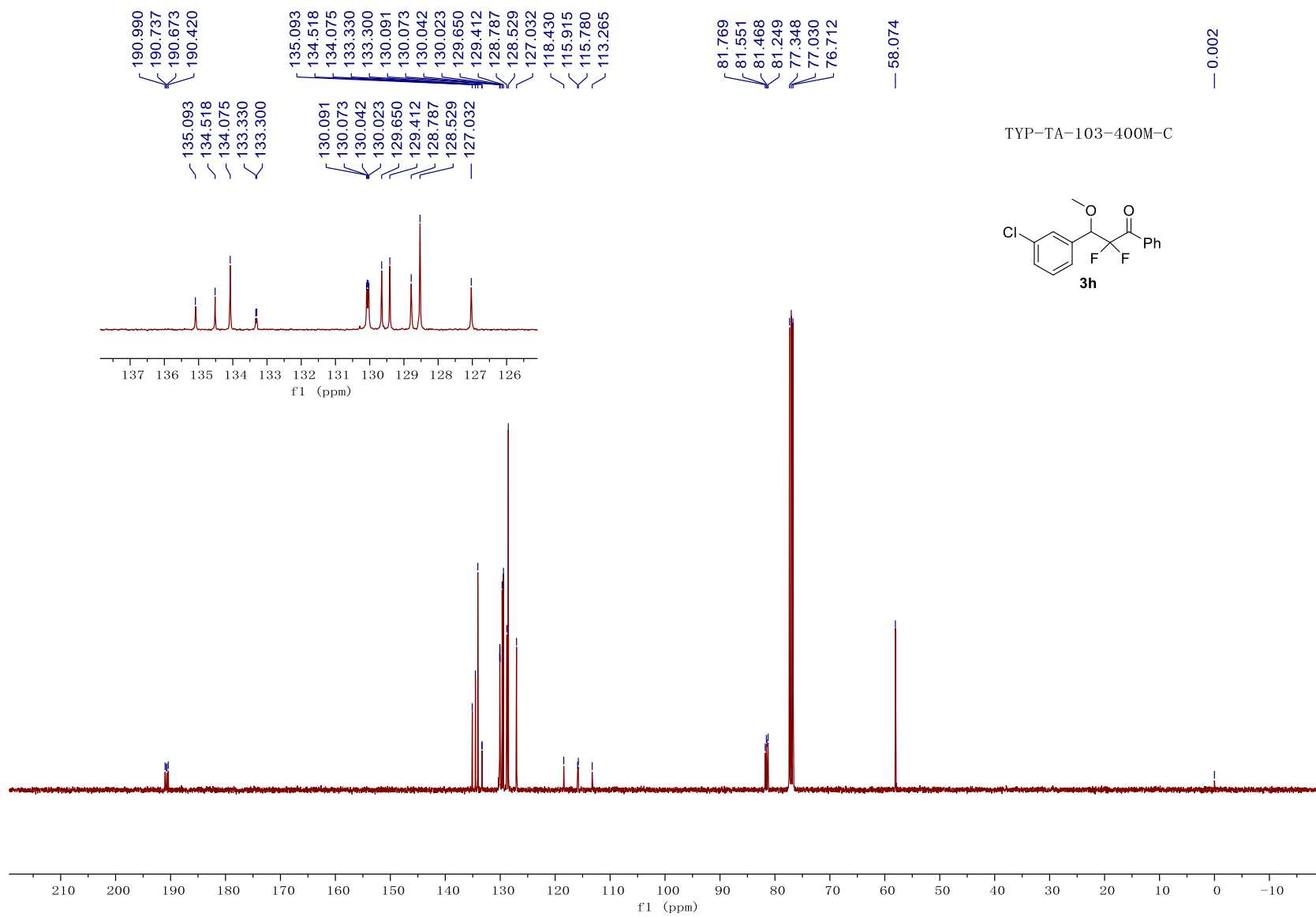
TYP-TA-133-300M-F



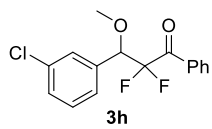
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-103.932
-103.951
-117.200
-117.255
-118.180
-118.237



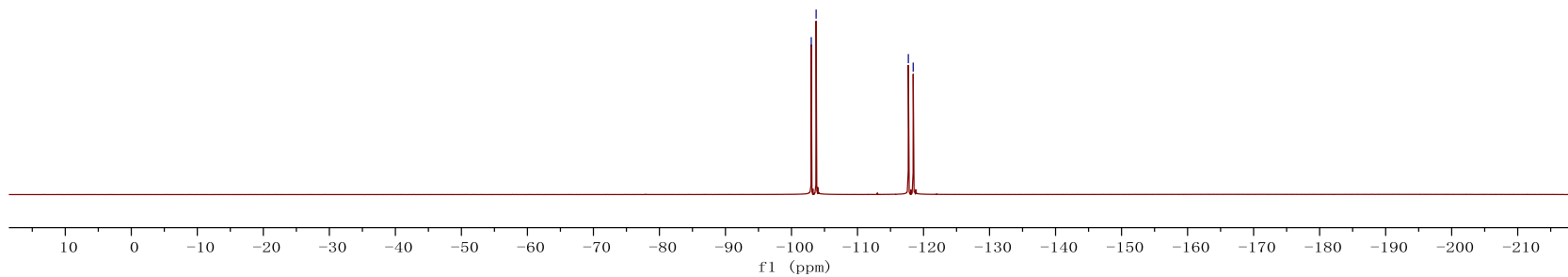


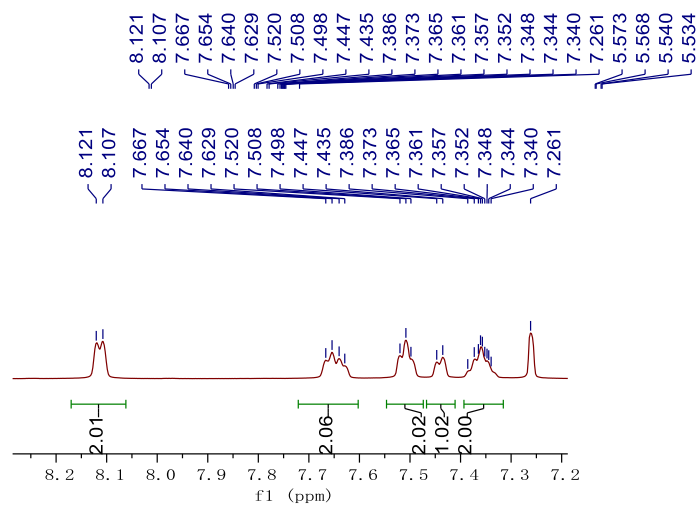


TYP-TA-103-400M-F



-102.997
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-117.702
-118.438



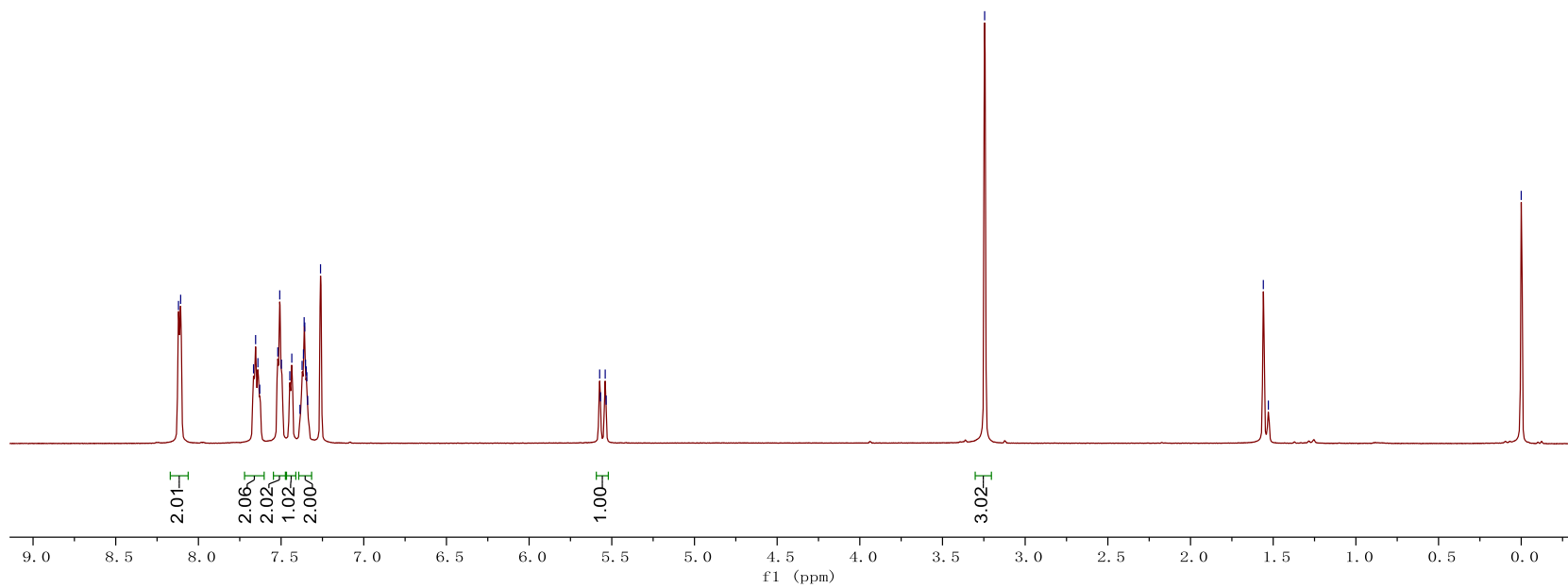
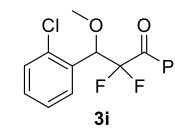


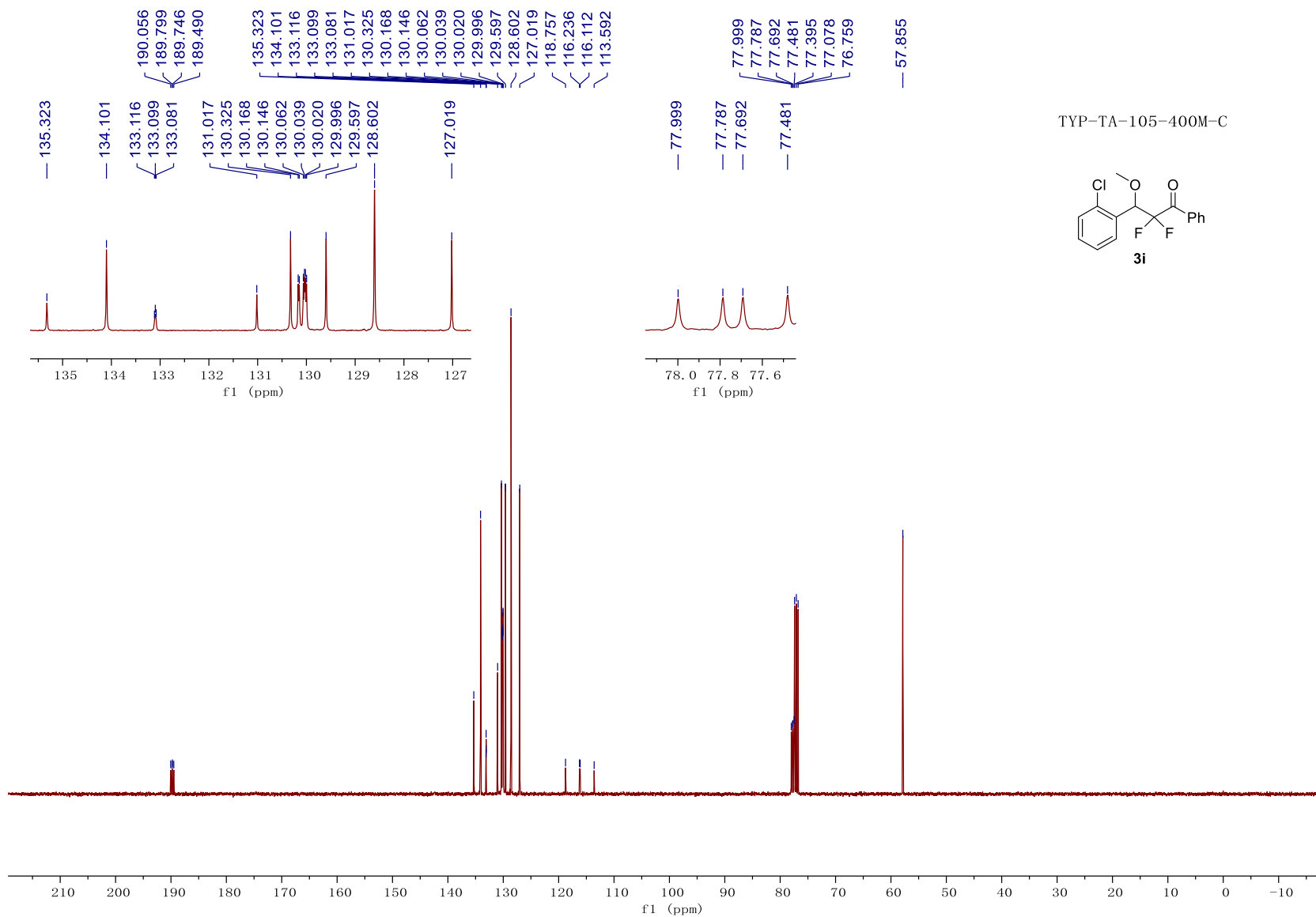
— 3.245

— 1.560
— 1.529

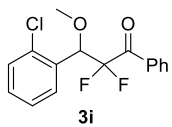
— 0.000

TYP-TA-105-600M-H



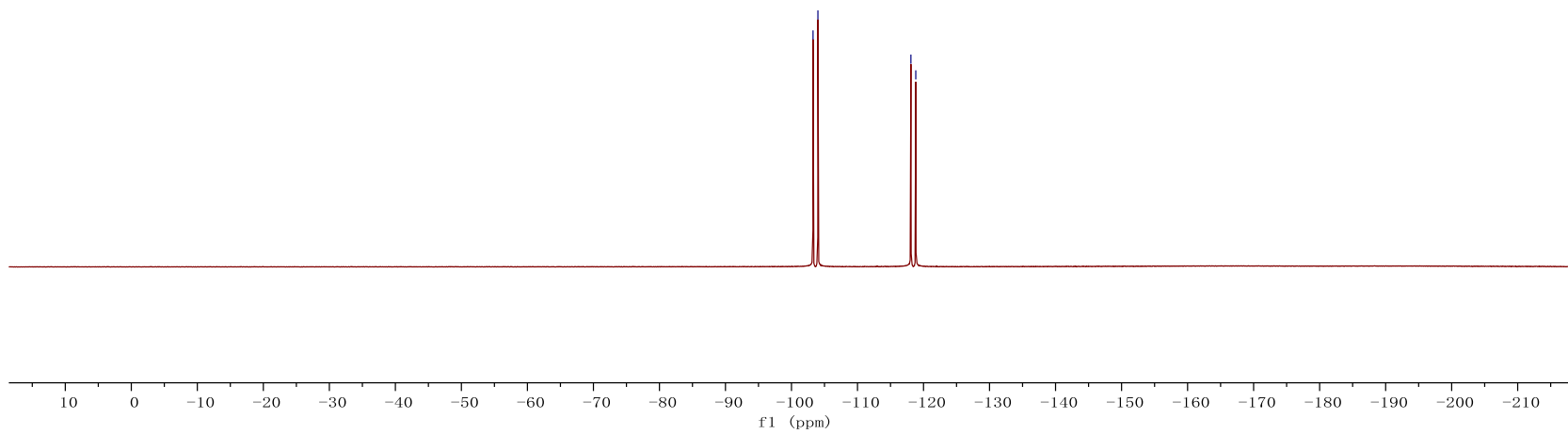


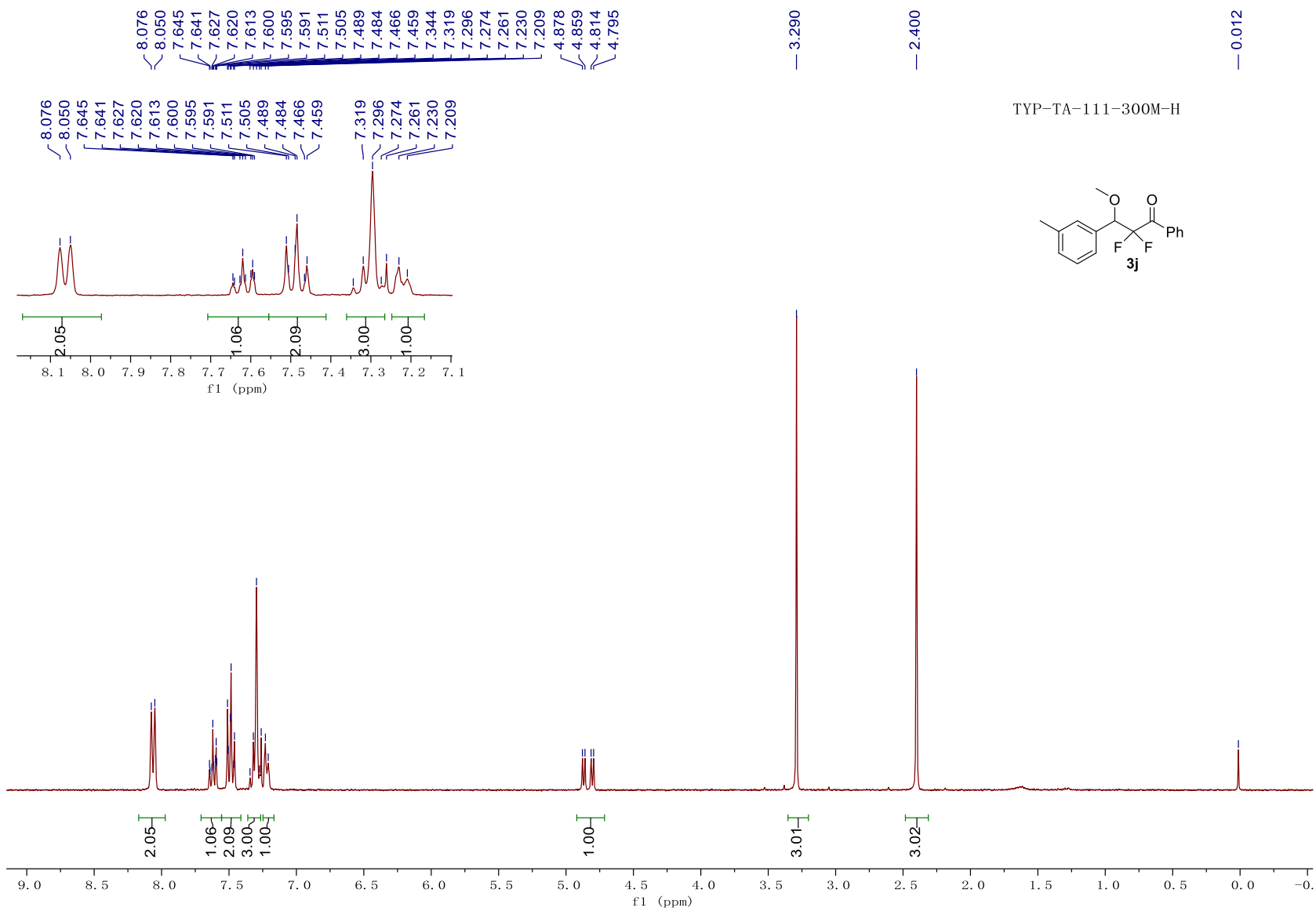
TYP-TA-105-400M-F

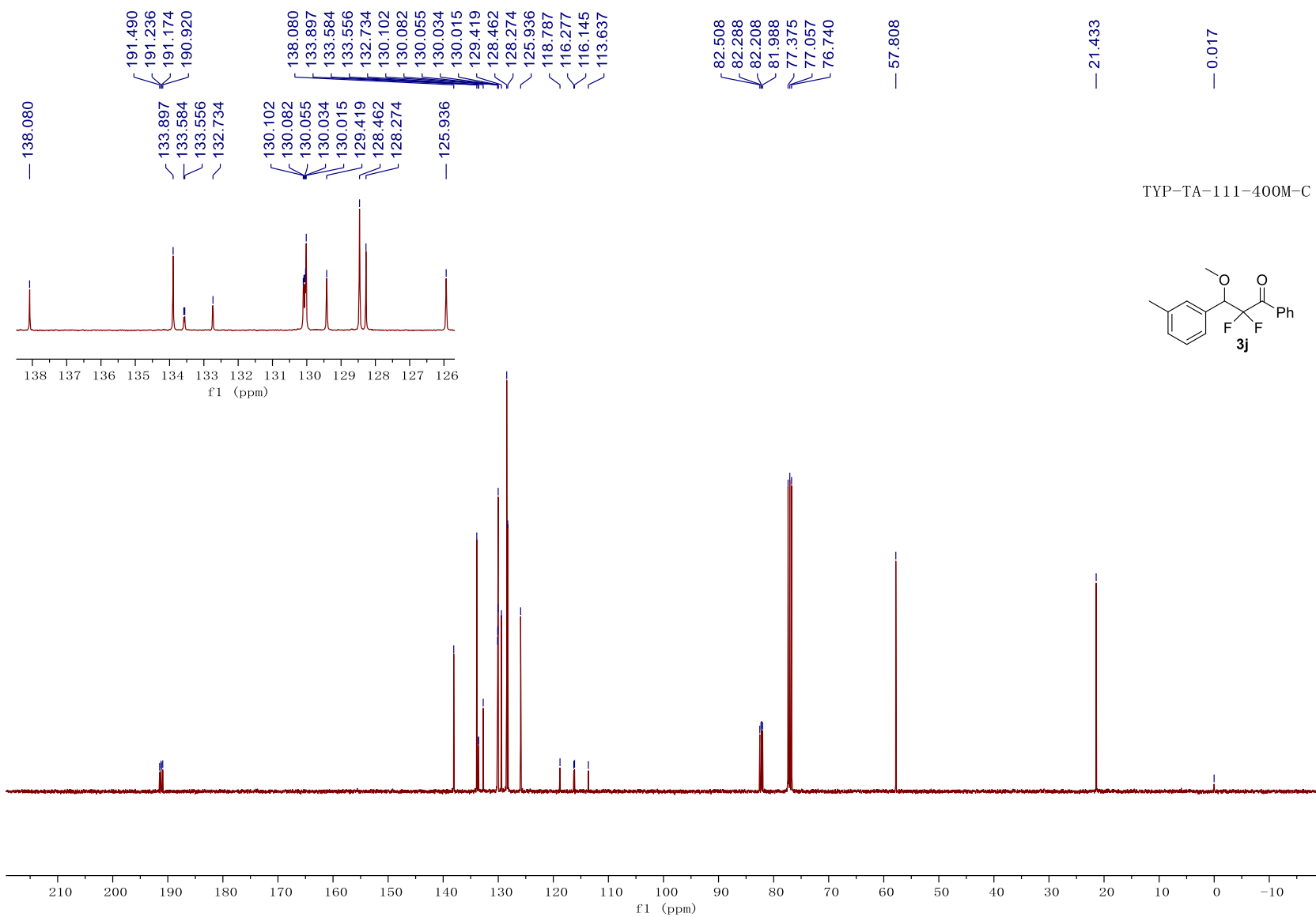


-103.264
-104.004

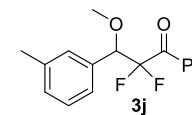
-118.088
-118.829



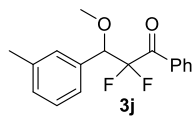




TYP-TA-111-400M-C

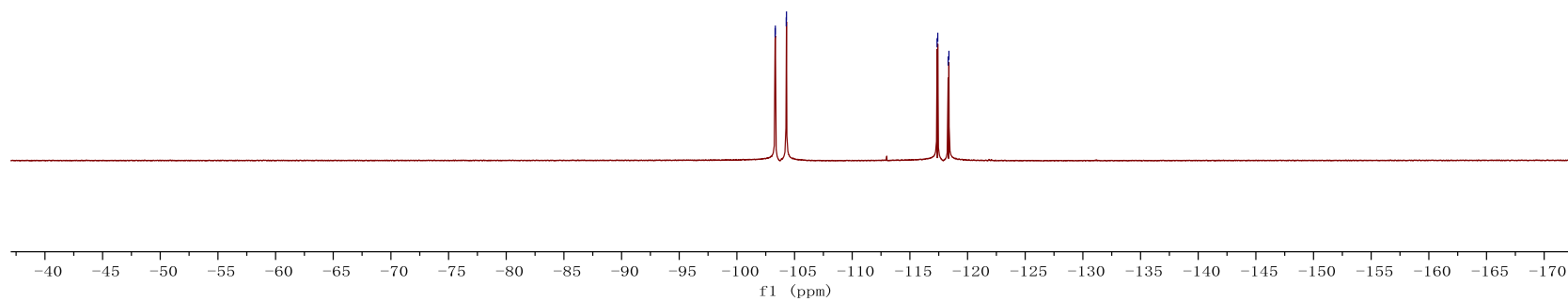


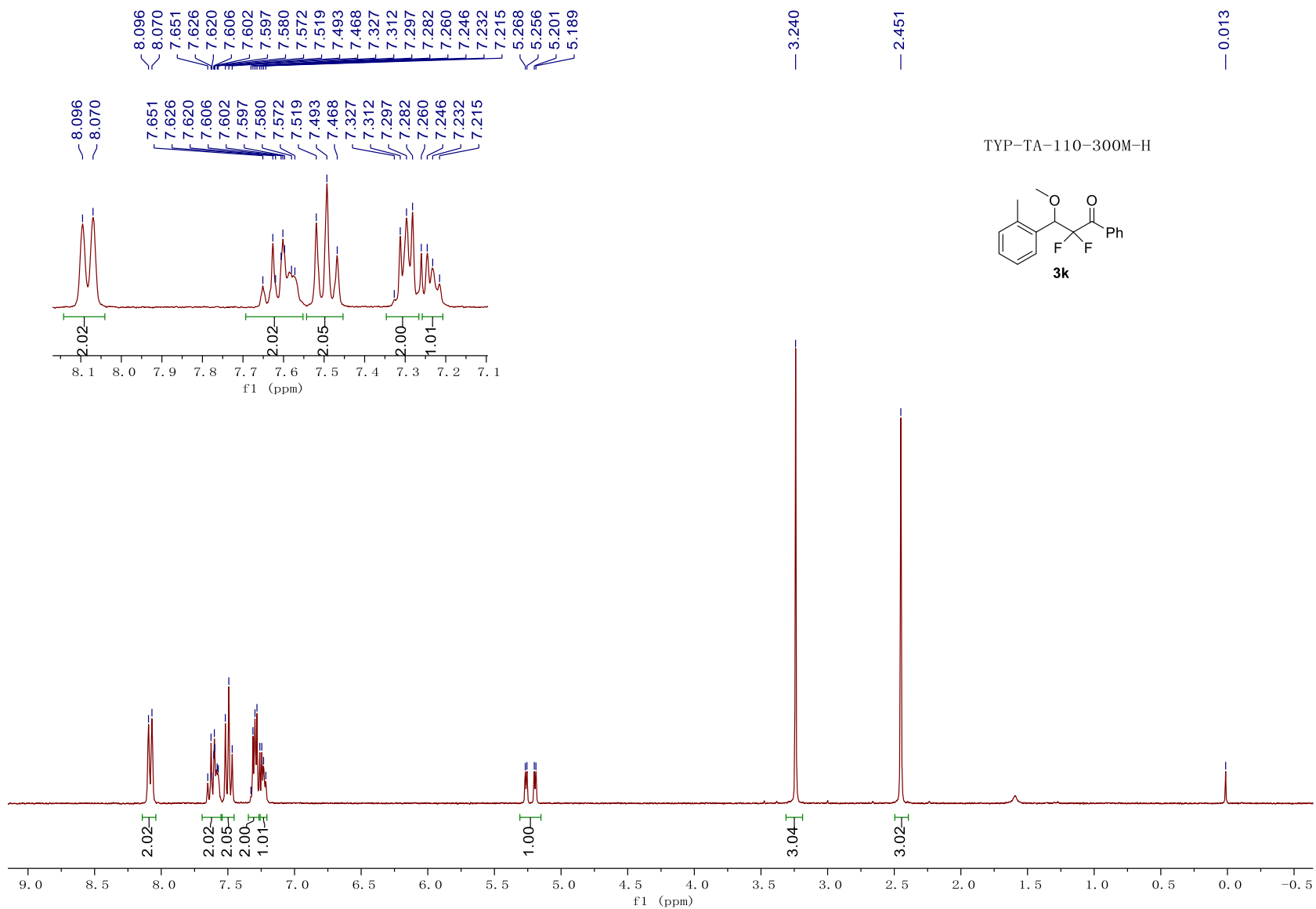
TYP-TA-111-300M-F

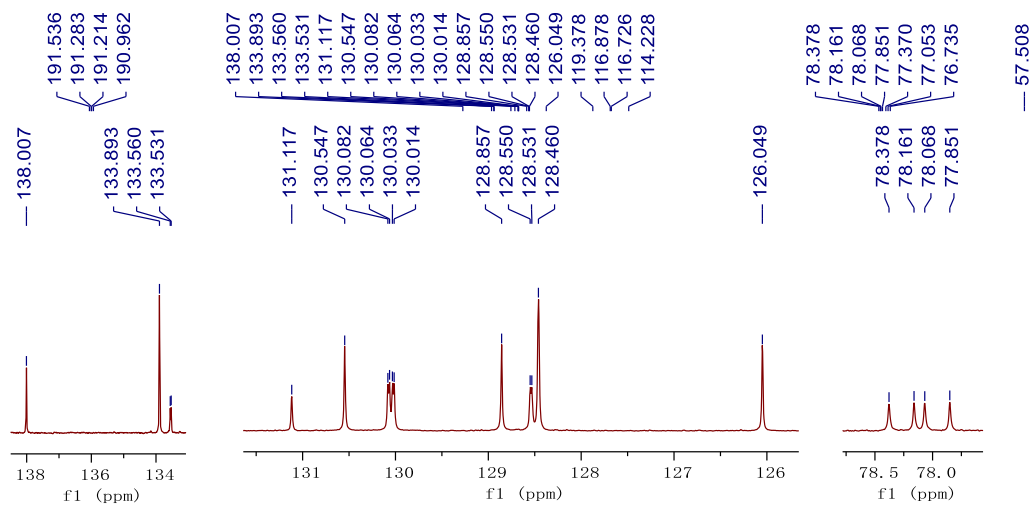


-103.313
-103.334
-104.280
-104.302

-117.355
-117.417
-118.322
-118.385

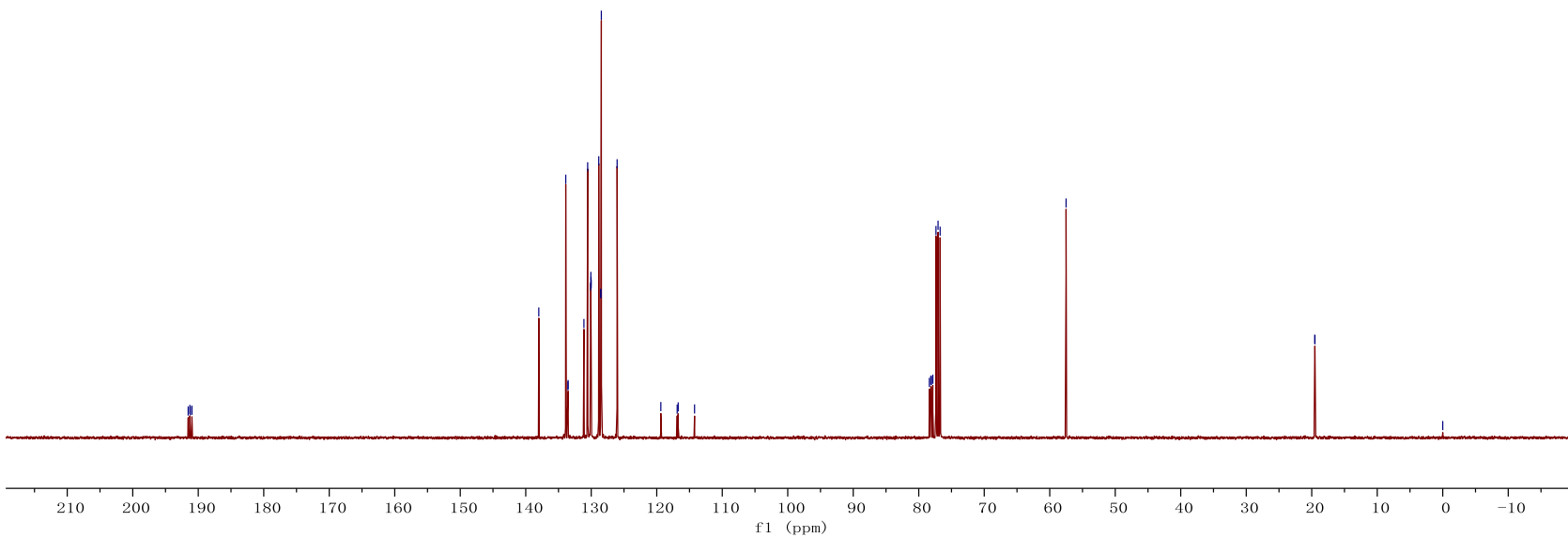
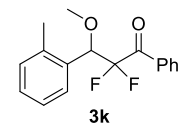




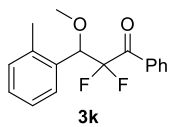


19.538
19.506
-0.001

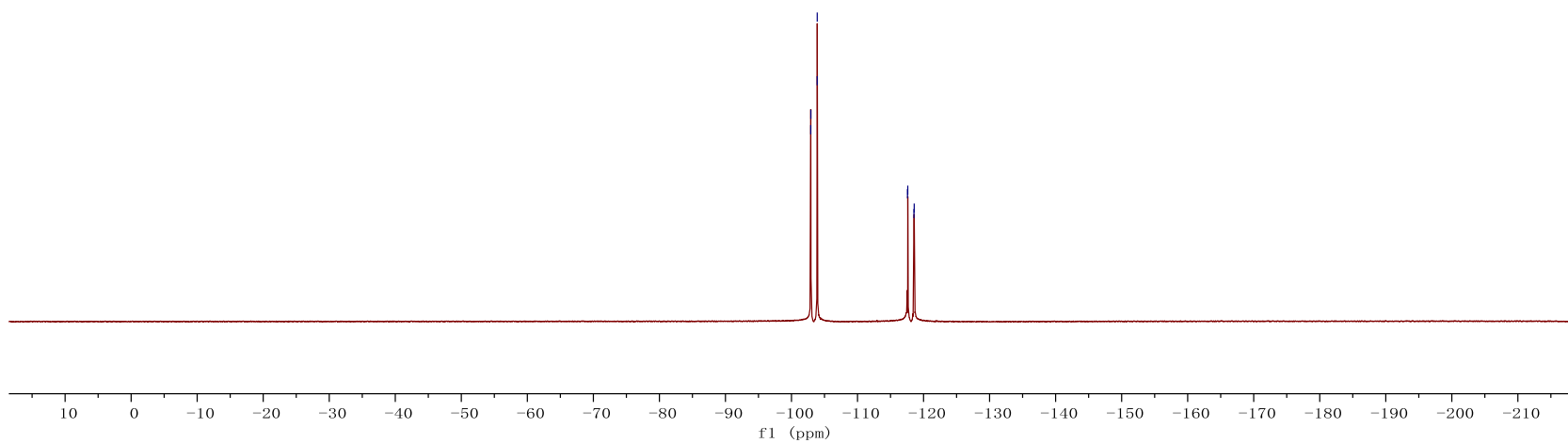
TYP-TA-110-400M-C



TYP-TA-110-300M-F

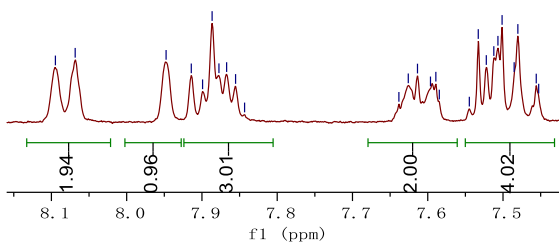


-102.918
-102.930
-103.894
-103.901
-117.569
-117.611
-118.546
-118.586



8.107
8.080
7.960
7.926
7.911
7.898
7.889
7.879
7.867
7.855
7.650
7.638
7.626
7.608
7.601
7.597
7.557
7.534
7.545
7.524
7.519
7.513
7.497
7.492
7.468
7.465
7.260
5.093
5.074
5.010

8.095
8.068
7.948
7.914
7.899
7.886
7.877
7.867
7.855
7.638
7.626
7.614
7.596
7.589
7.585
7.533
7.522
7.512
7.507
7.501
7.485
7.480
7.456
7.453

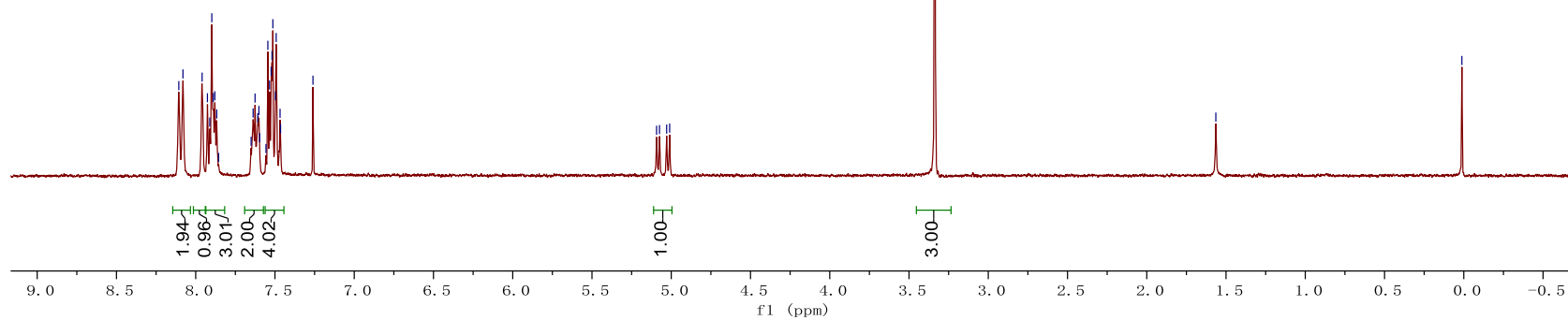
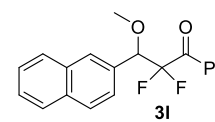


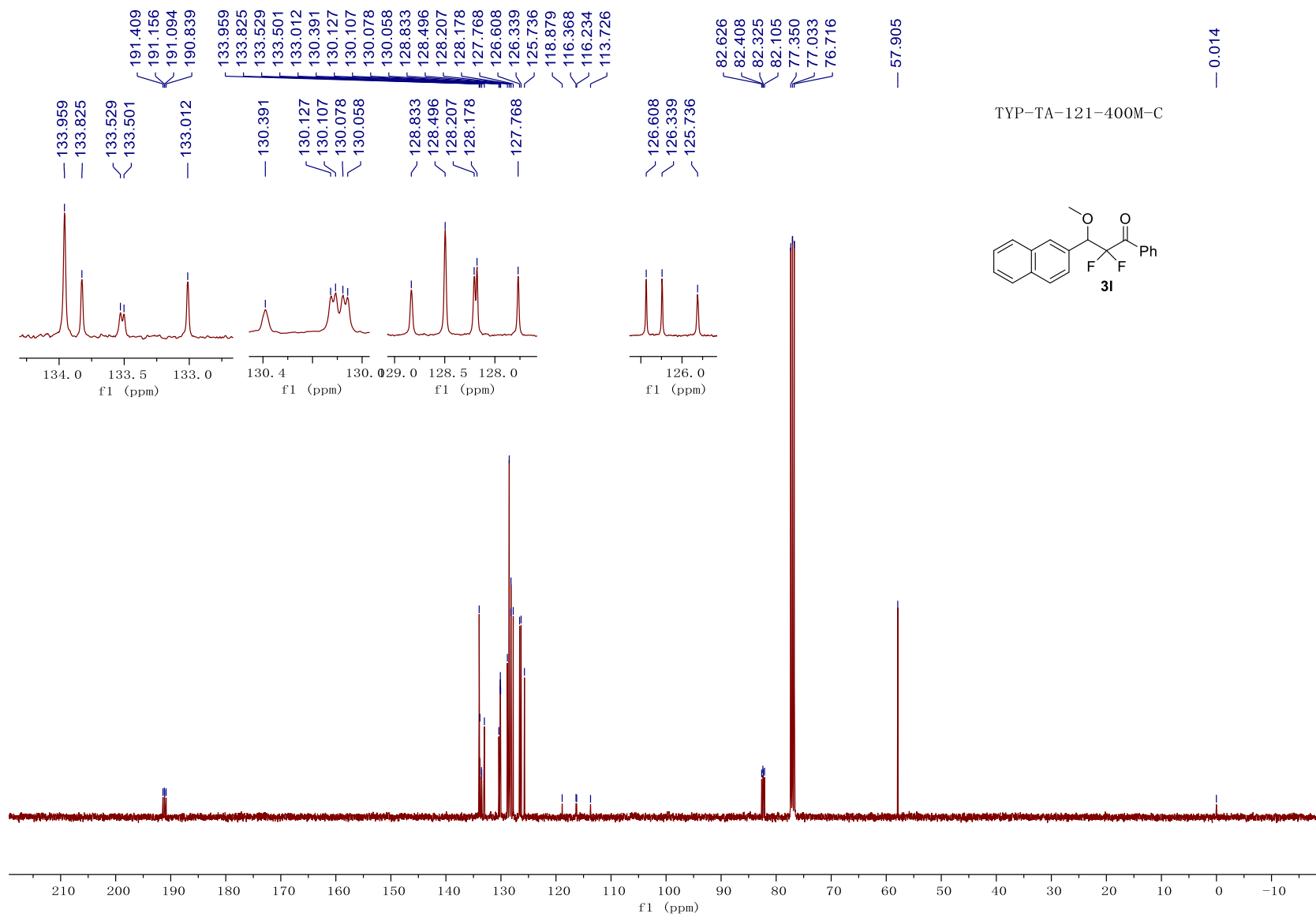
3.337

1.564

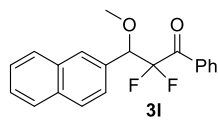
0.012

TYP-TA-121-300M-H

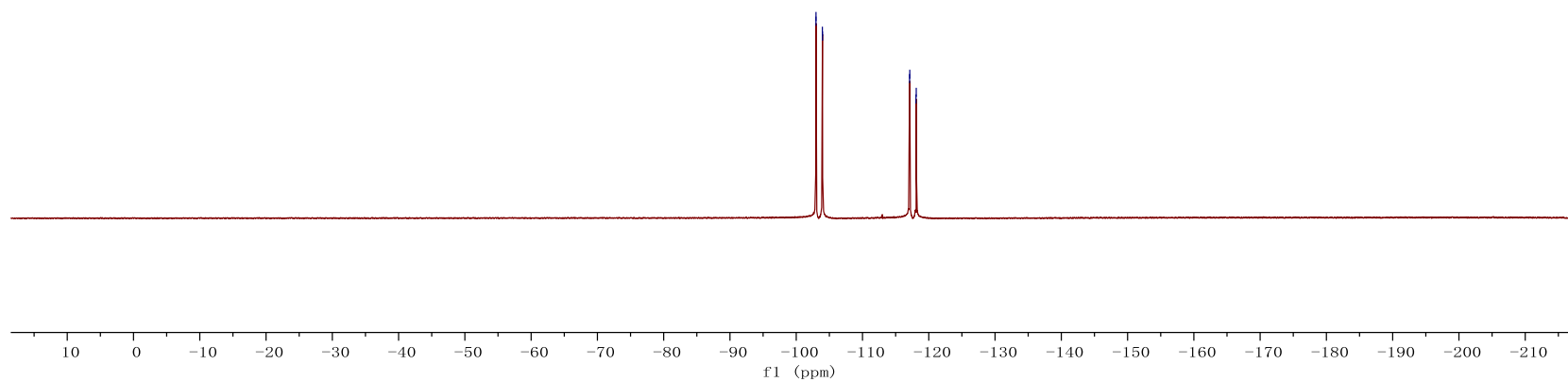


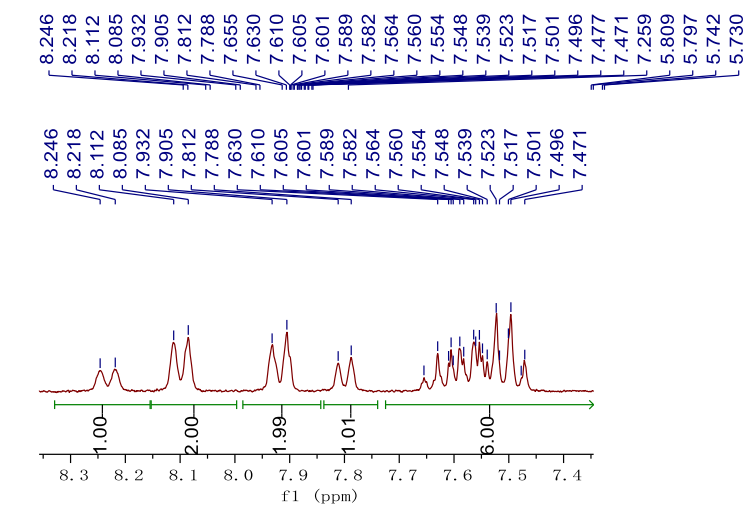


TYP-TA-121-300M-F



-102.975
-102.982
-103.945
-103.957
-117.098
-117.133
-118.069
-118.109



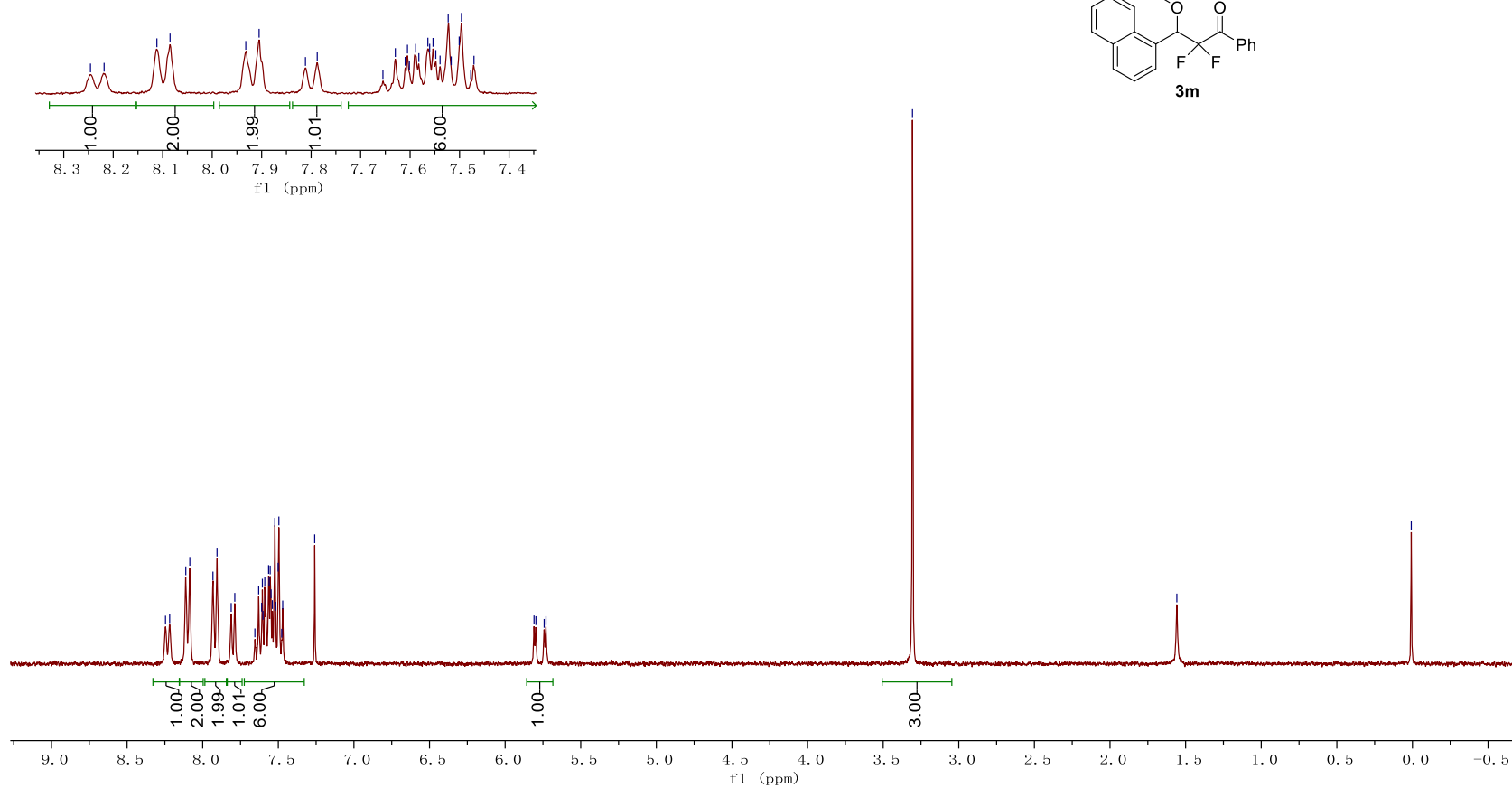
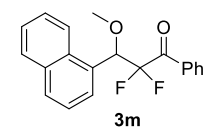


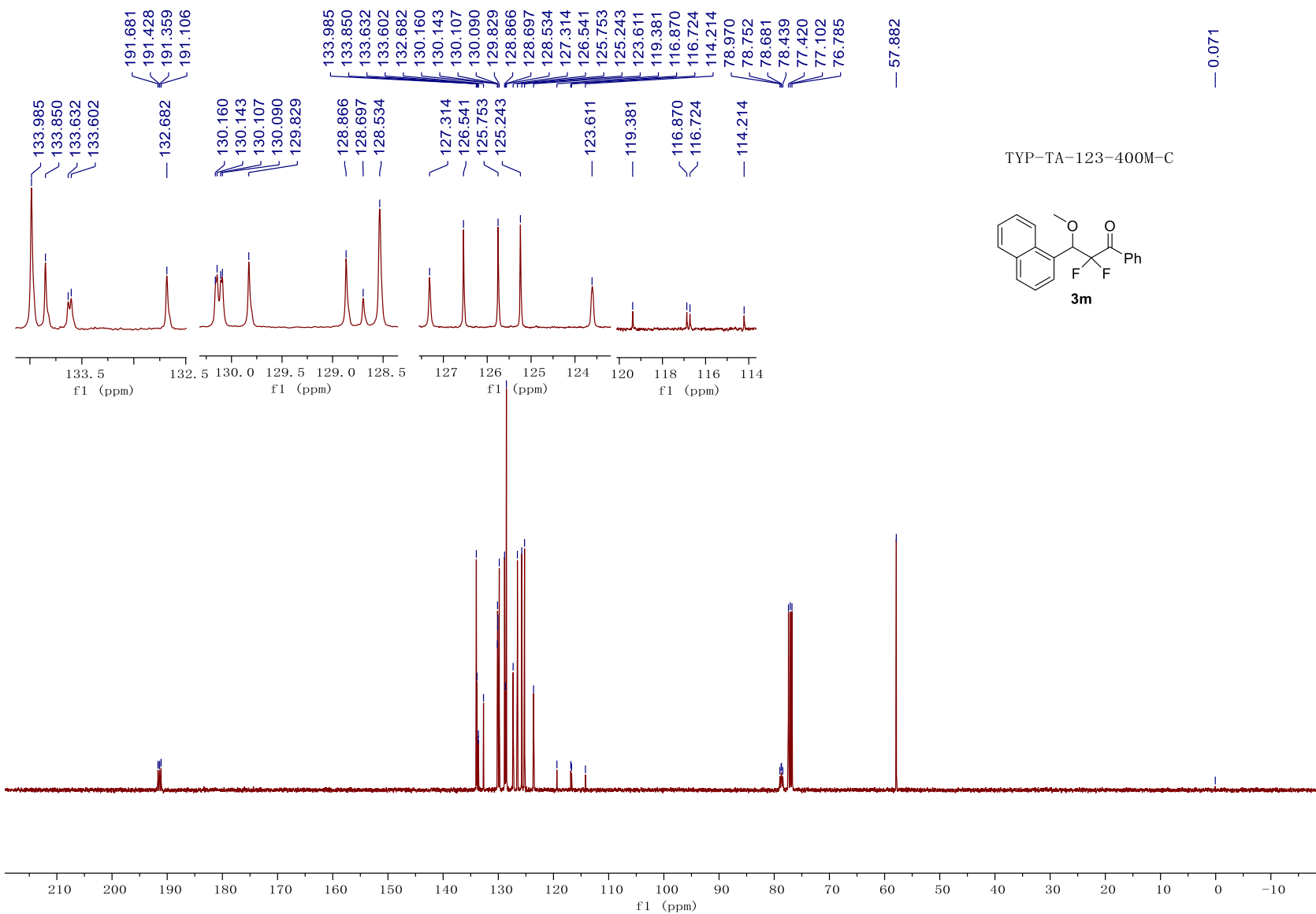
— 3.306

— 1.558

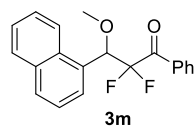
— 0.008

TYP-TA-123-300M-H

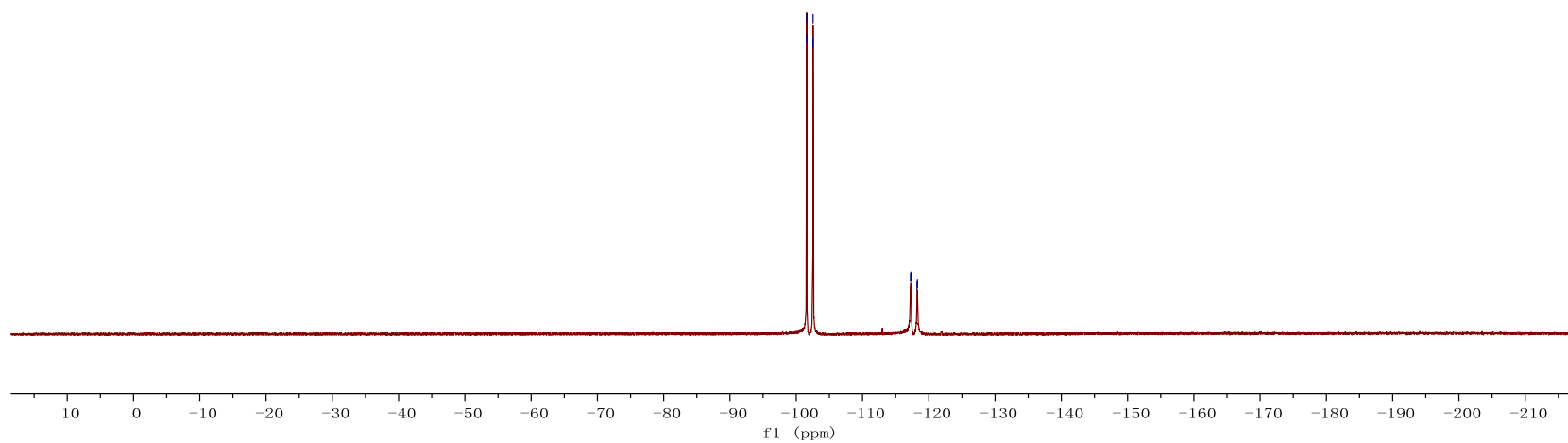




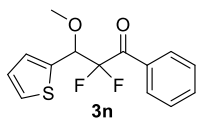
TYP-TA-123-300M-F



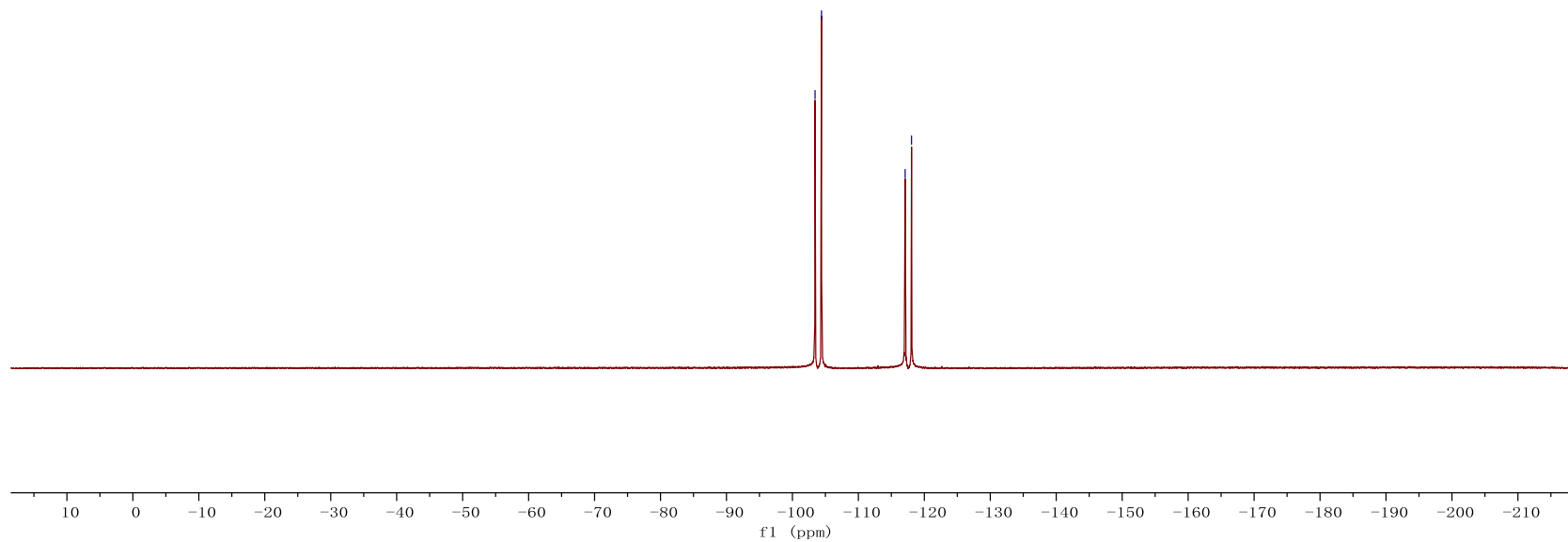
-101.557
-101.567
-102.530
-102.543
-117.244
-117.303
-118.227
-118.285

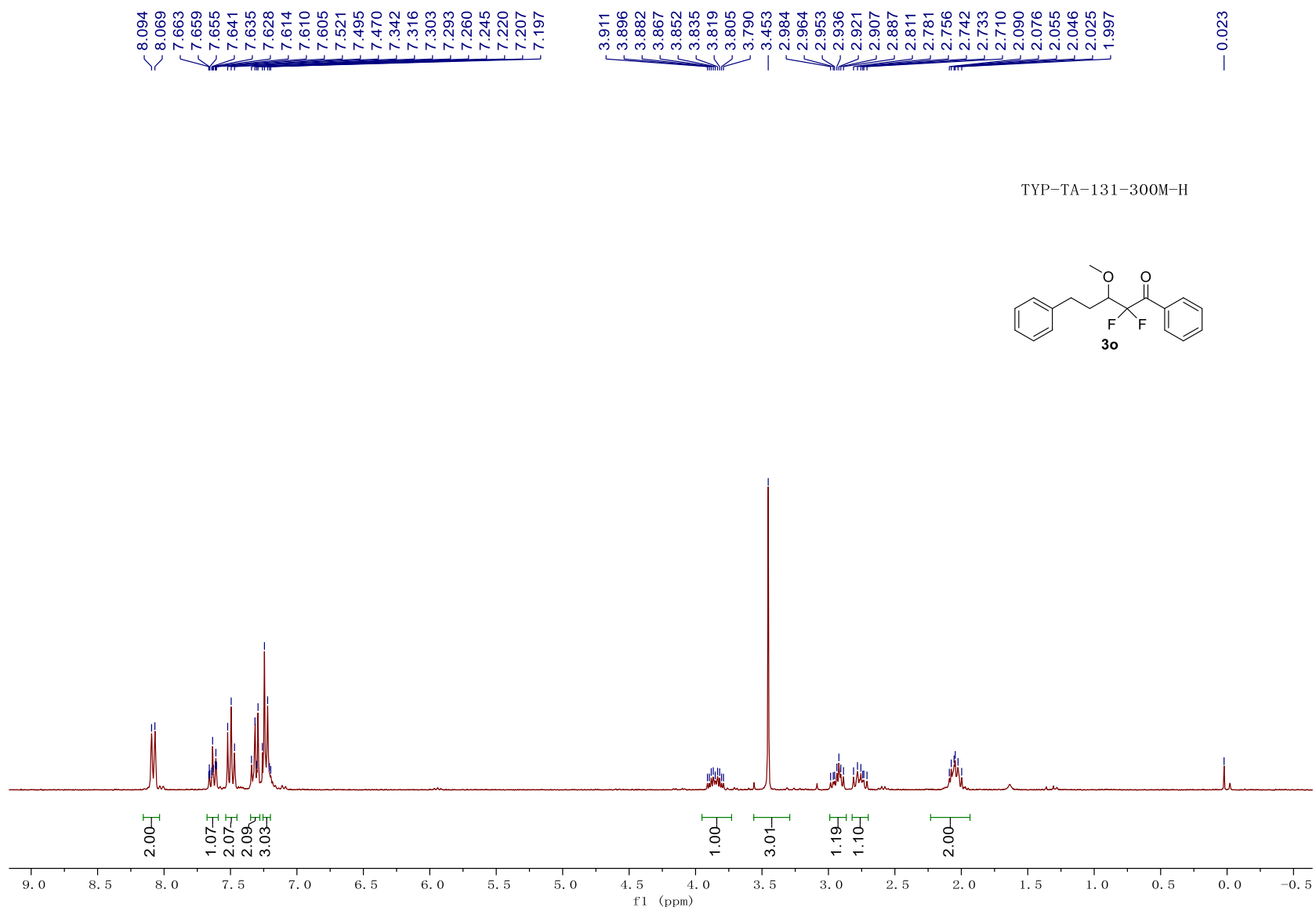


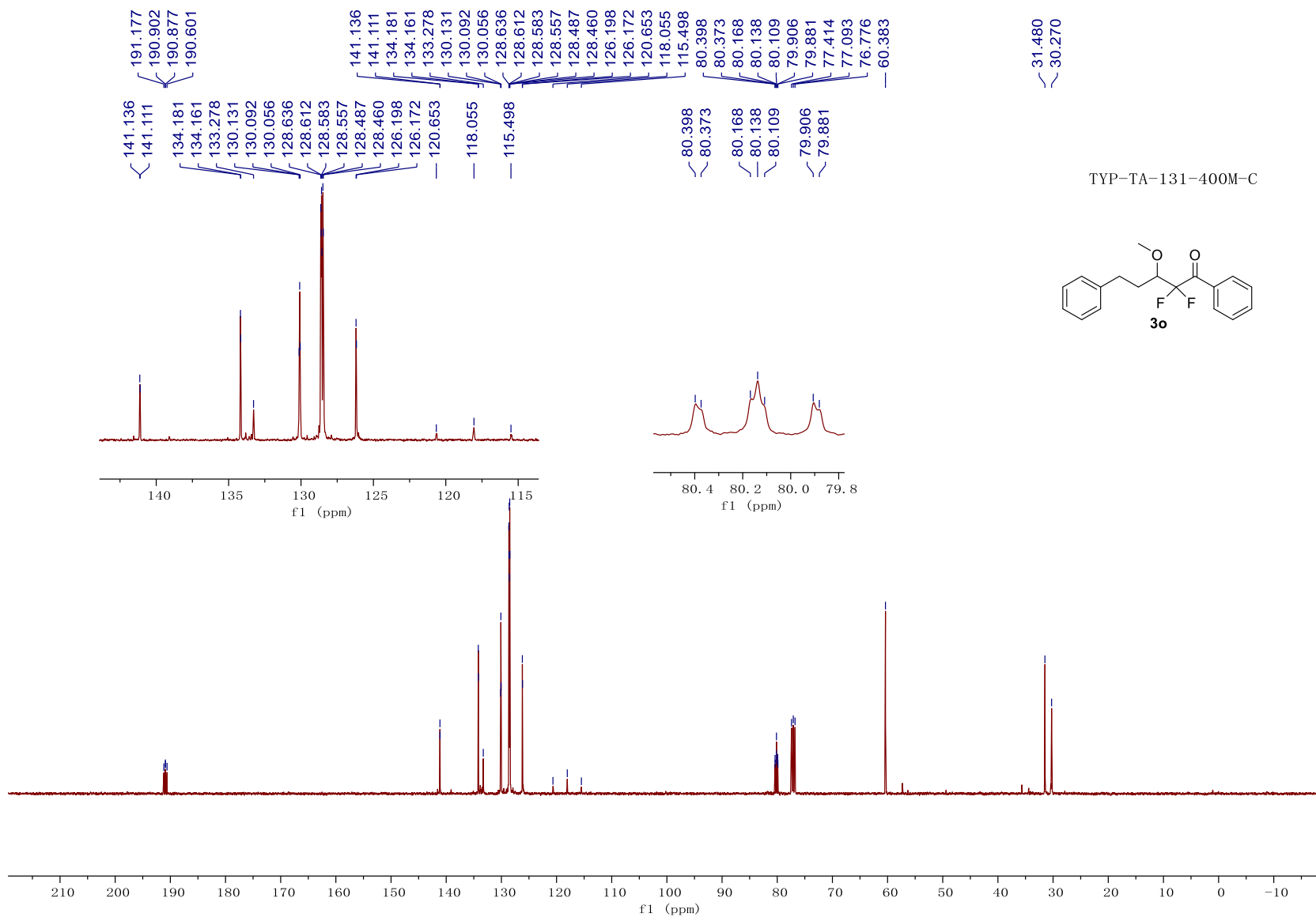
TYP-TB-78-300M-F



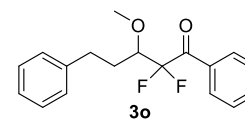
-103.434
-104.407
-117.094
-118.061



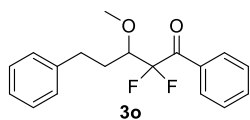




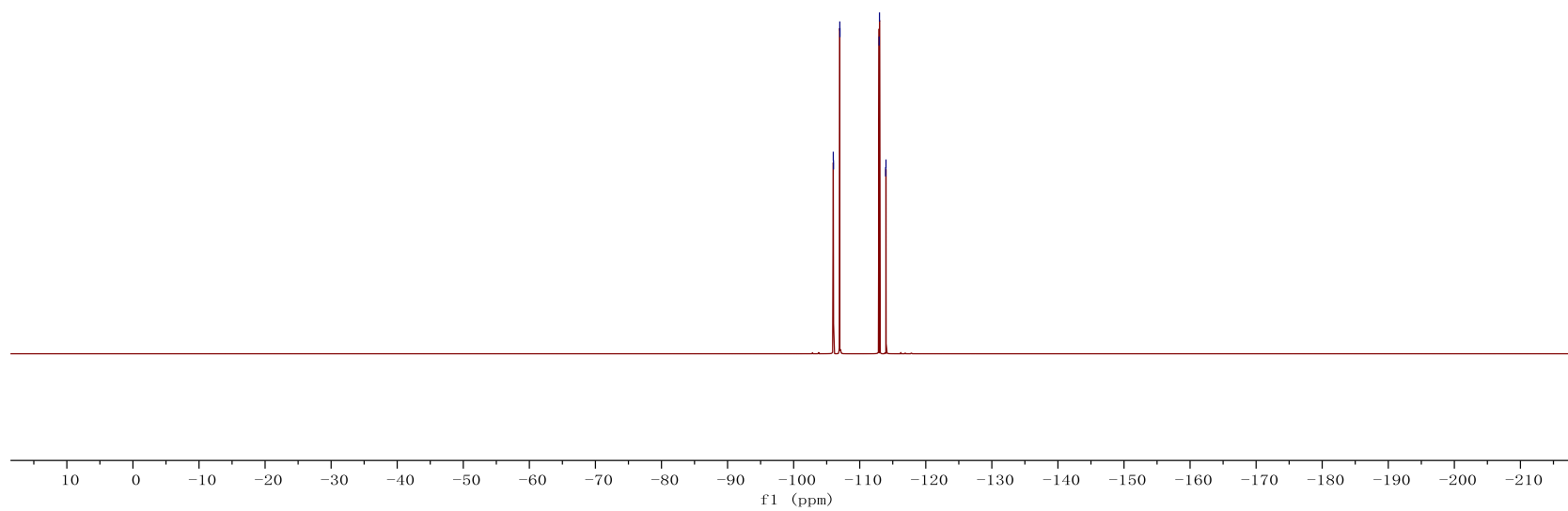
TYP-TA-131-400M-C



TYP-TA-131-300M-F



-106.003
-106.034
-106.984
-107.014
-112.946
-112.995
-113.926
-113.975



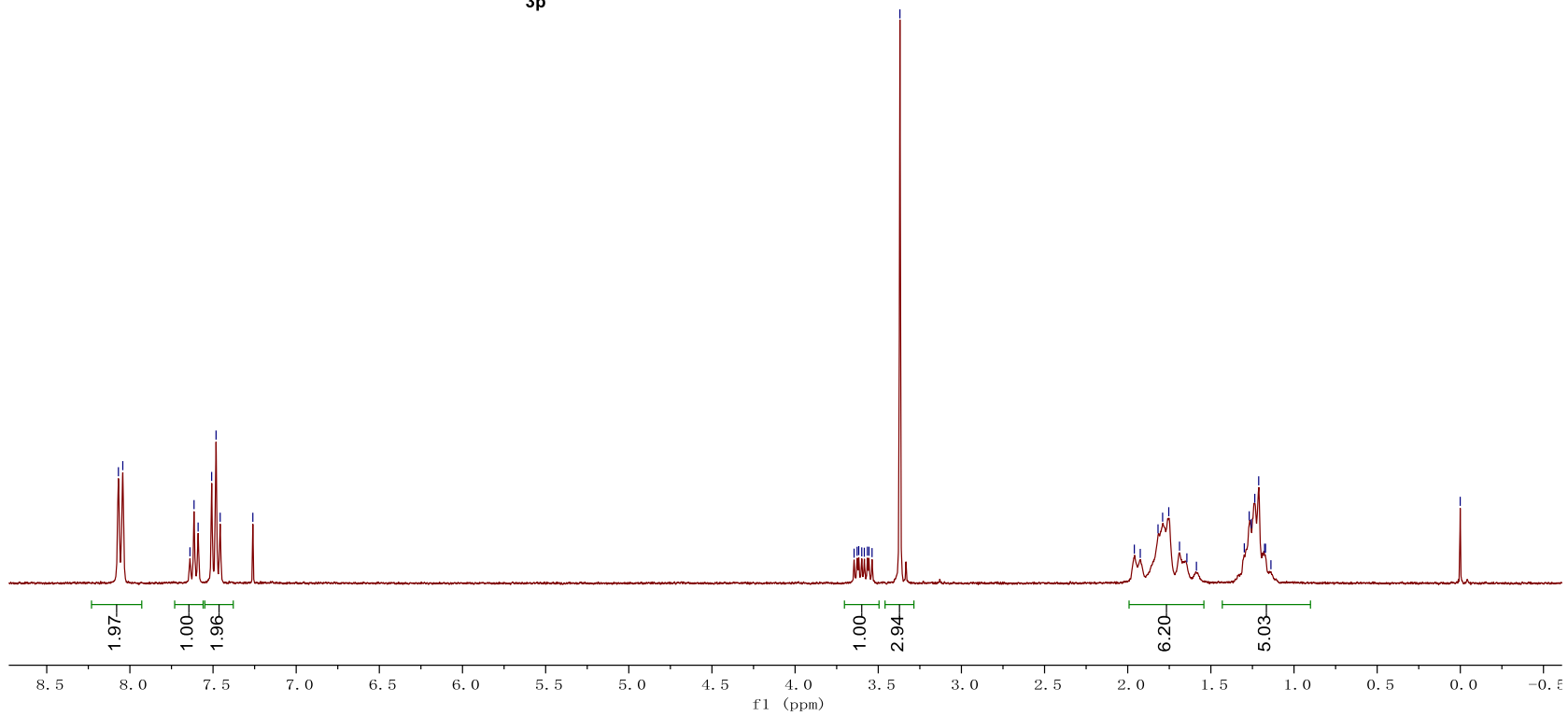
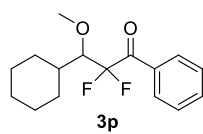
8.069
8.043
7.639
7.614
7.590
7.508
7.482
7.457
7.261

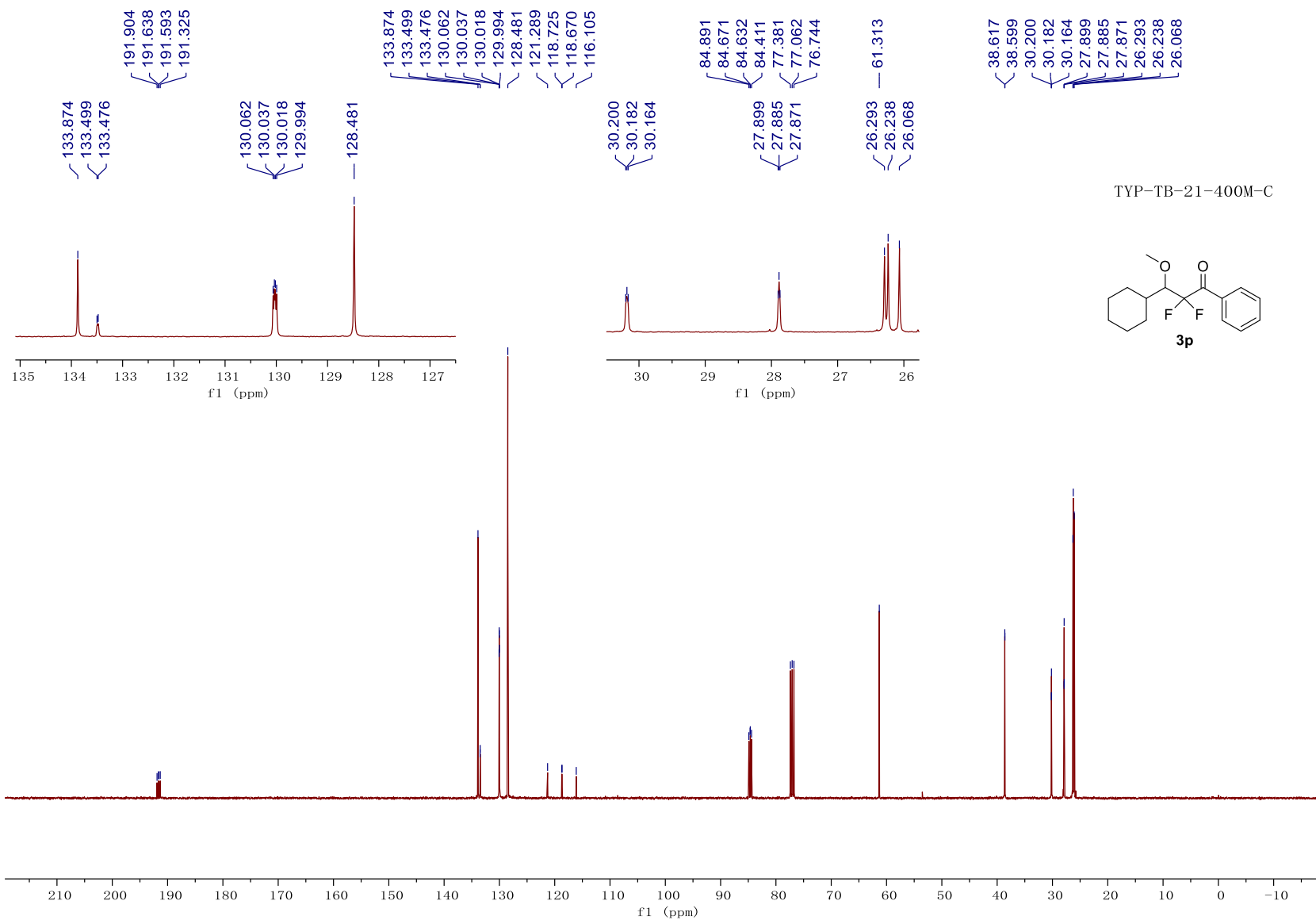
3.645
3.627
3.617
3.599
3.584
3.565
3.556
3.537
3.370

1.960
1.924
1.818
1.790
1.753
1.688
1.644
1.587
1.299
1.270
1.257
1.236
1.212
1.177
1.171
1.139

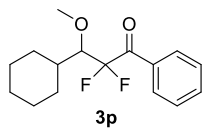
— 0.001

TYP-TB-21-300M-H

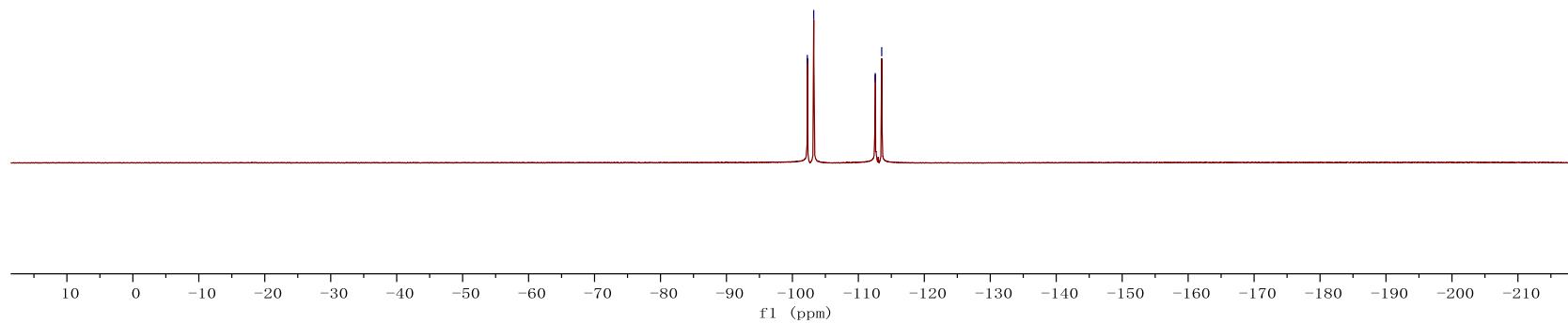


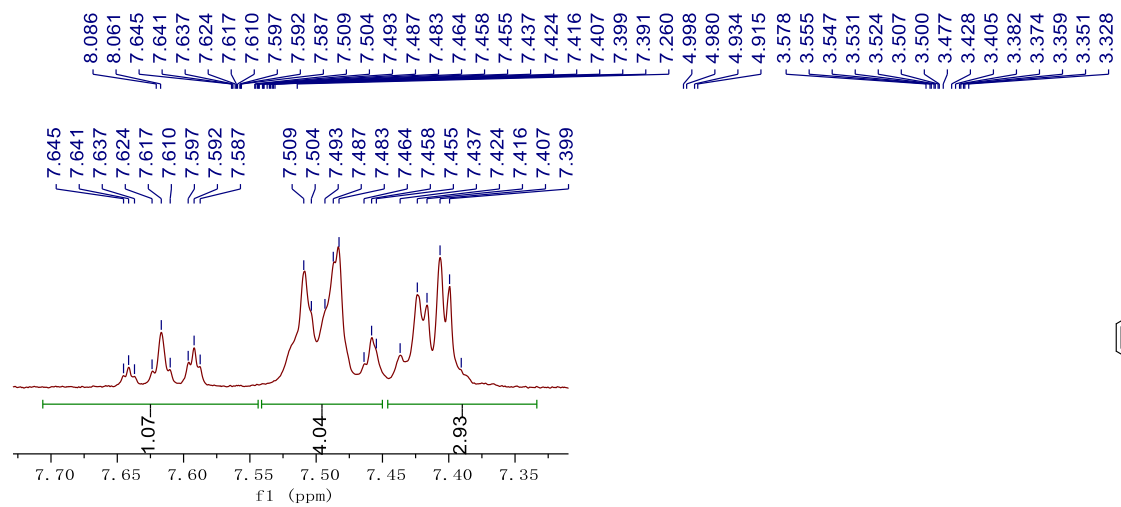


TYP-TB-21-300M-F

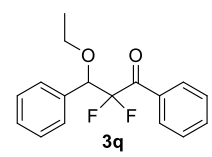


-102.263
-103.232
-112.557
-113.536



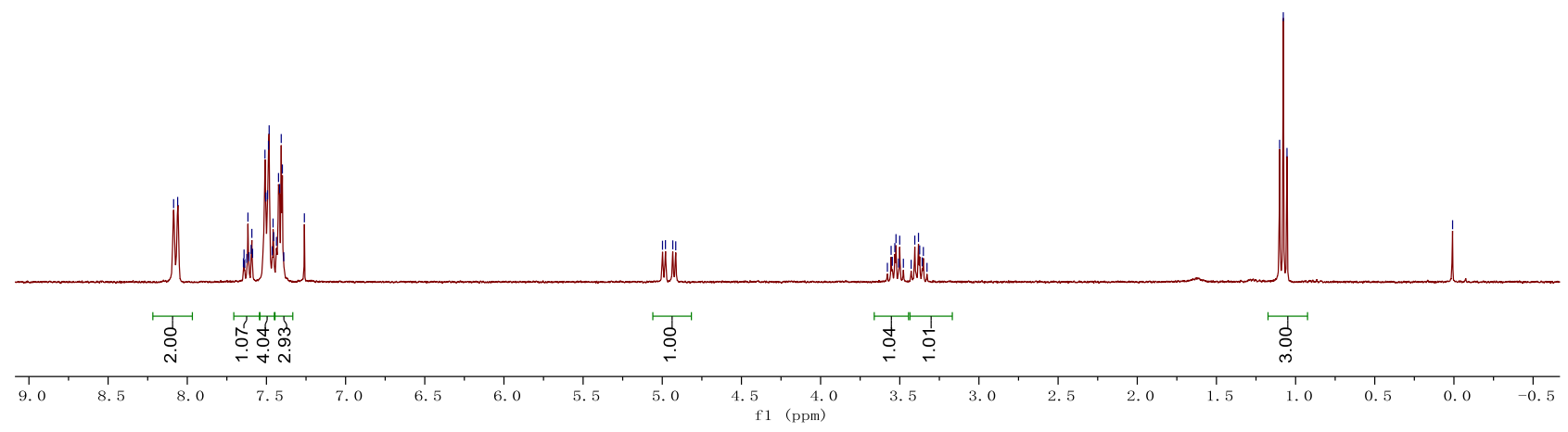


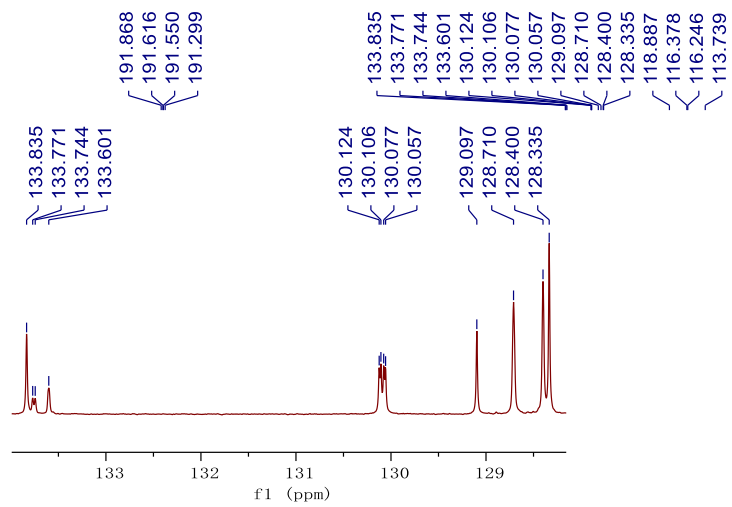
TYP-TA-146-300M-H



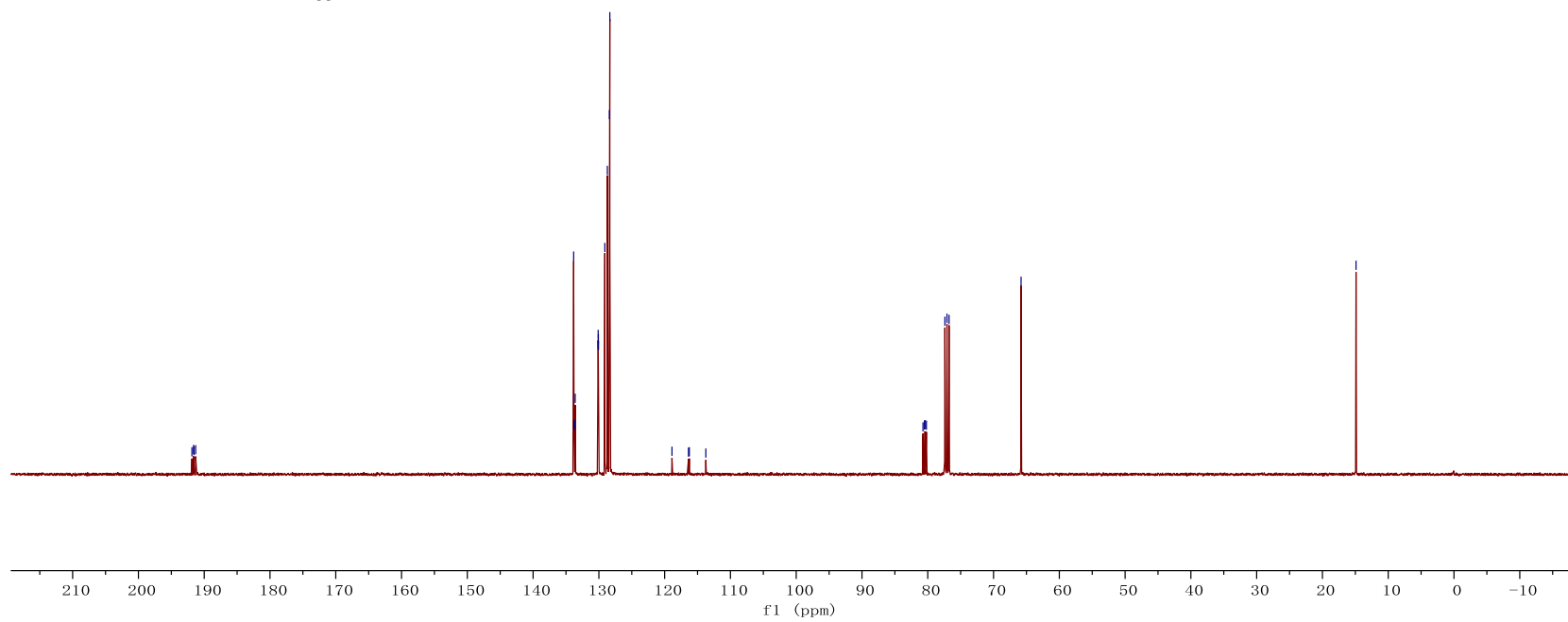
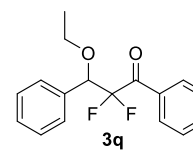
1.101
1.078
1.054

— 0.008

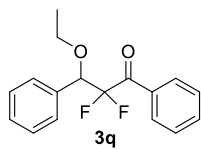




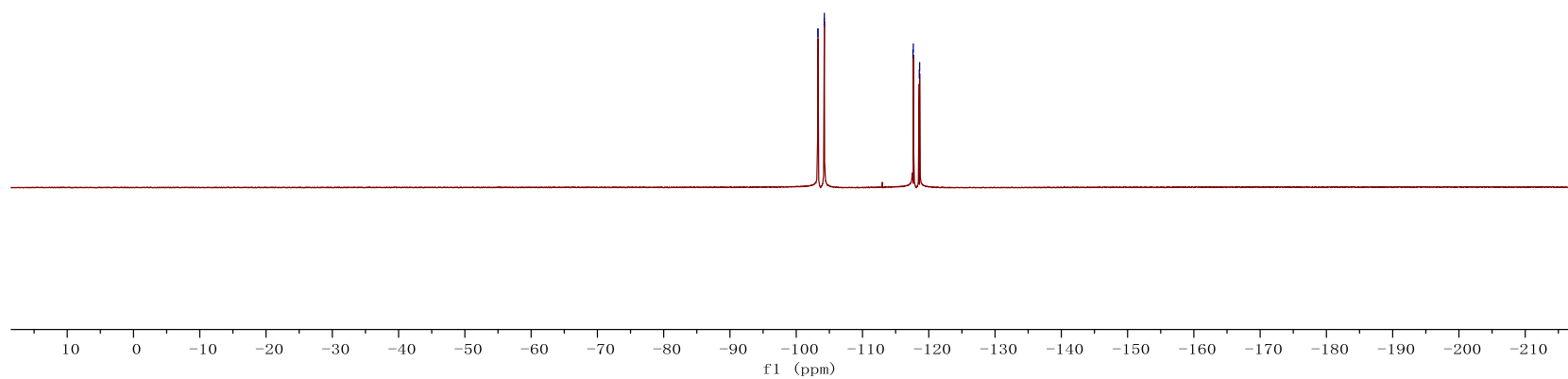
TYP-TB-146-400M-C

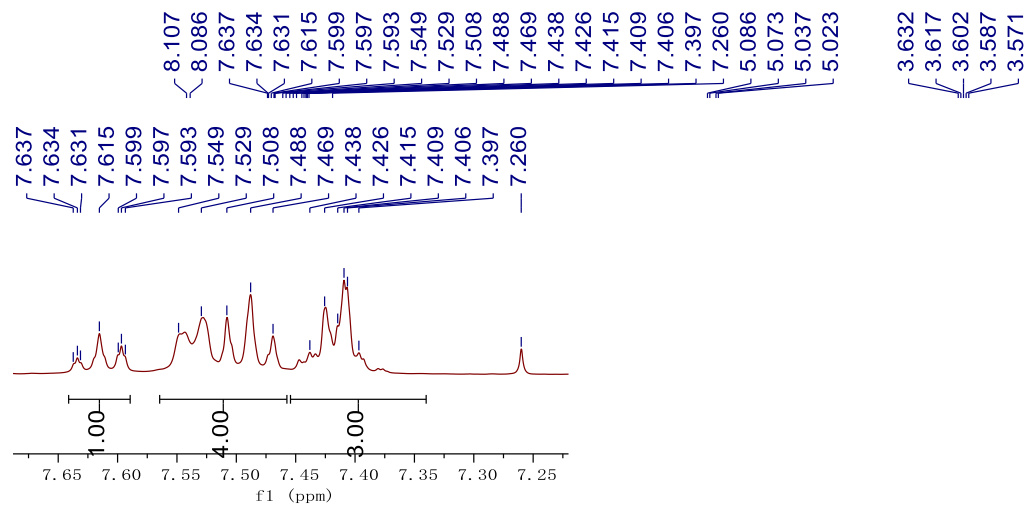


TYP-TA-146-300M-F

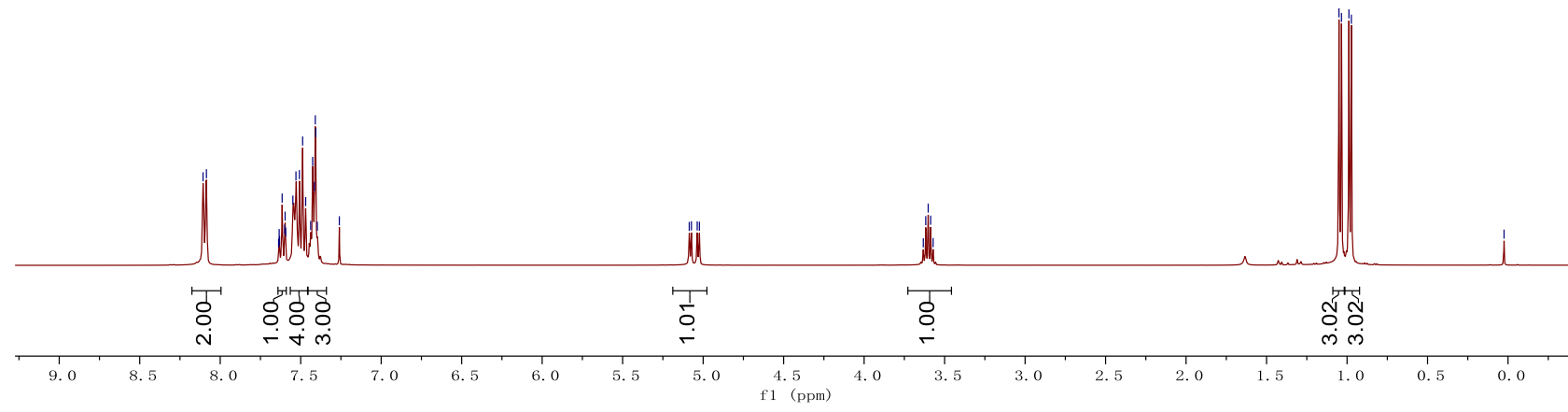
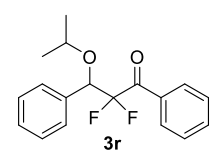


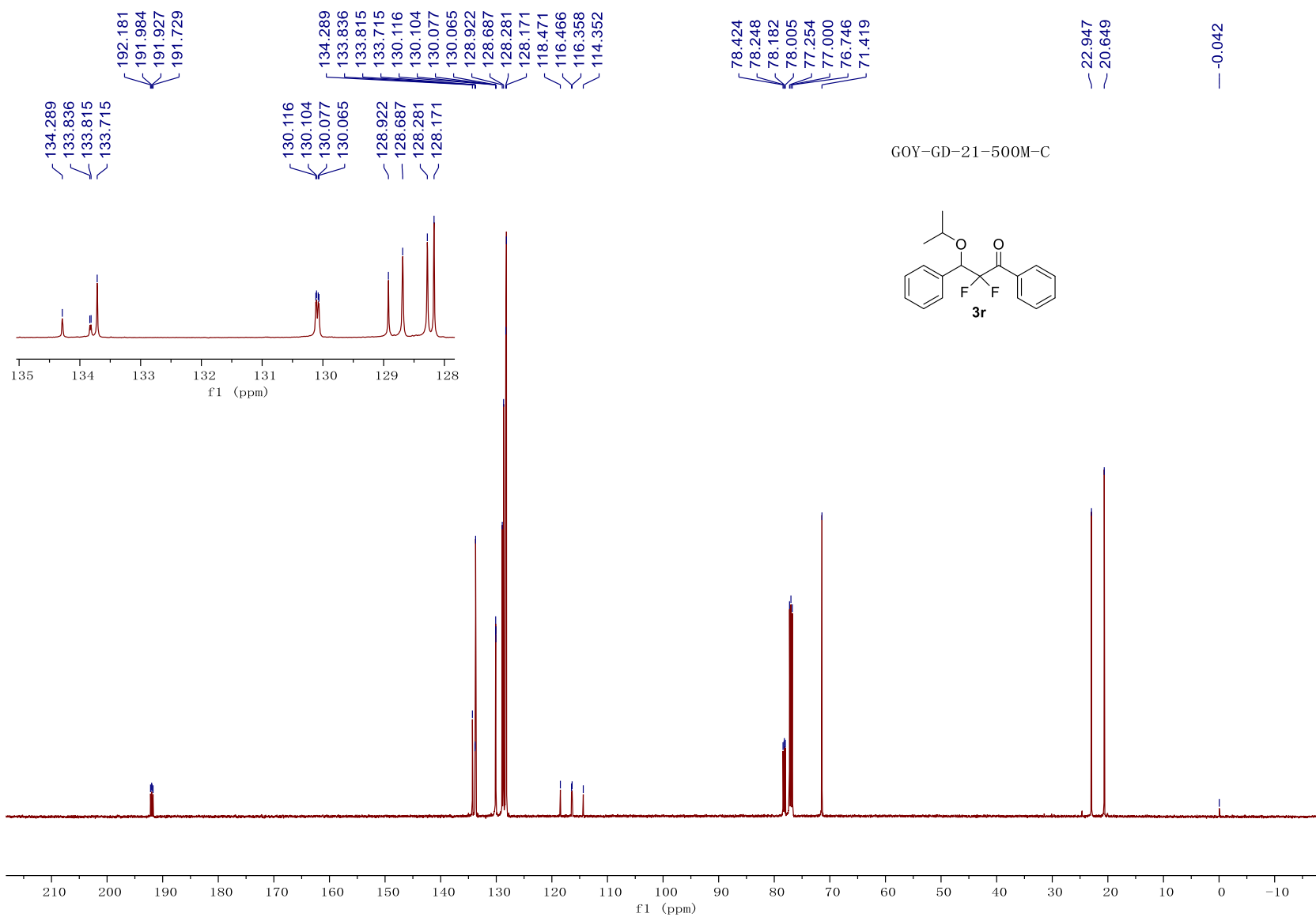
-103.266
-103.283
-104.220
-104.240
-117.611
-117.665
-118.568
-118.624



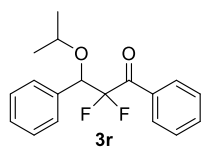


GOY-GD-21-400M-1H



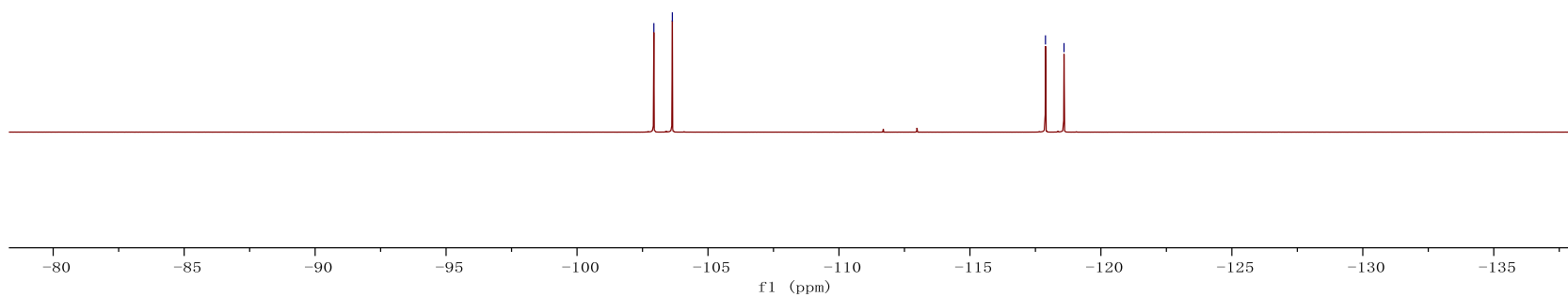


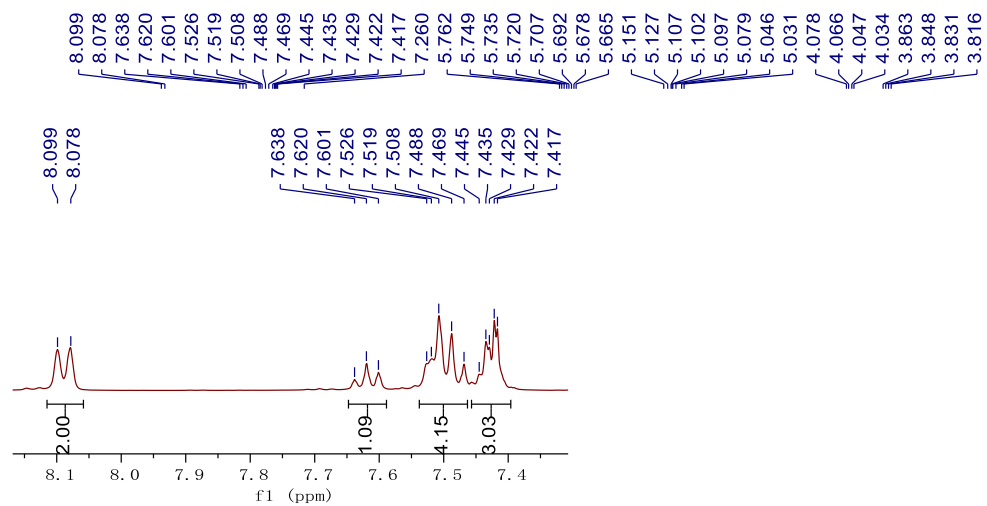
GOY-GD-21-400M-F



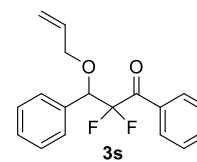
-102.933
-103.640

-117.885
-118.592

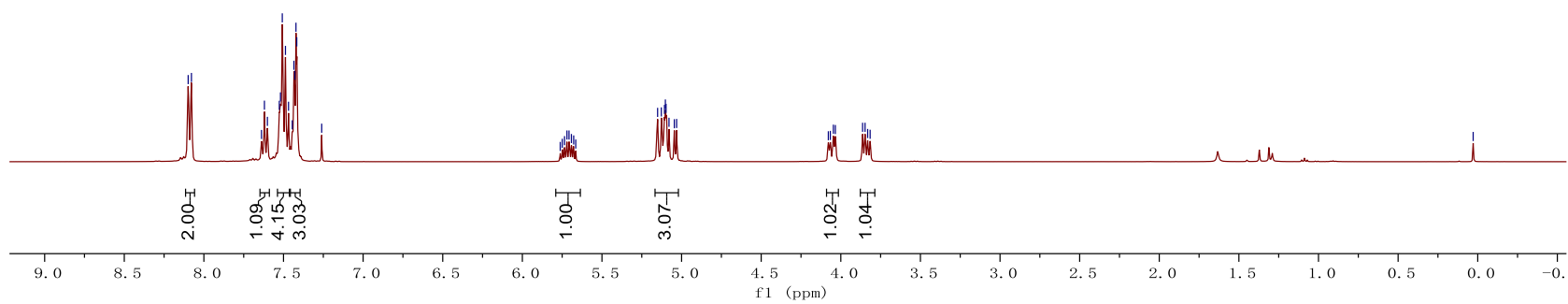


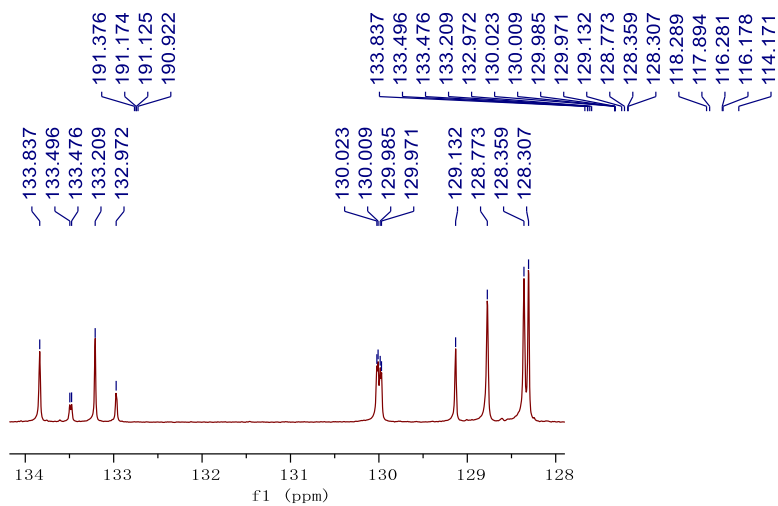


GOY-GA-34-400M-H

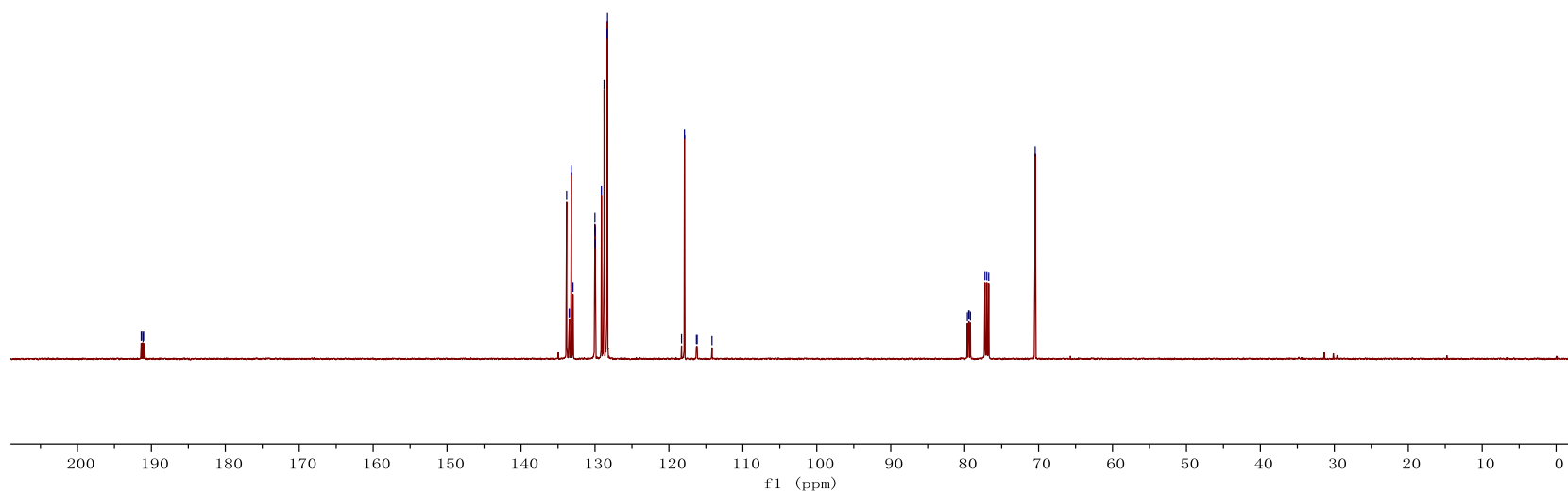
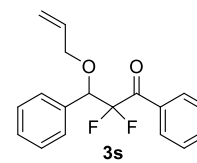


— 0.029

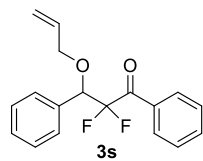




GOY-GD-34-500M-C

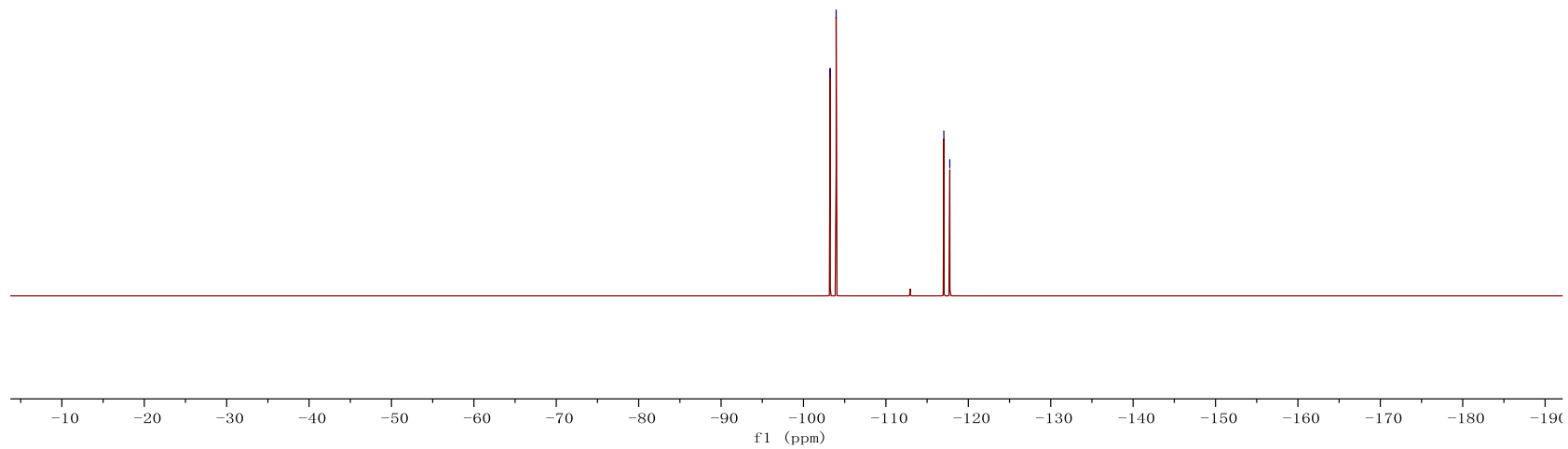


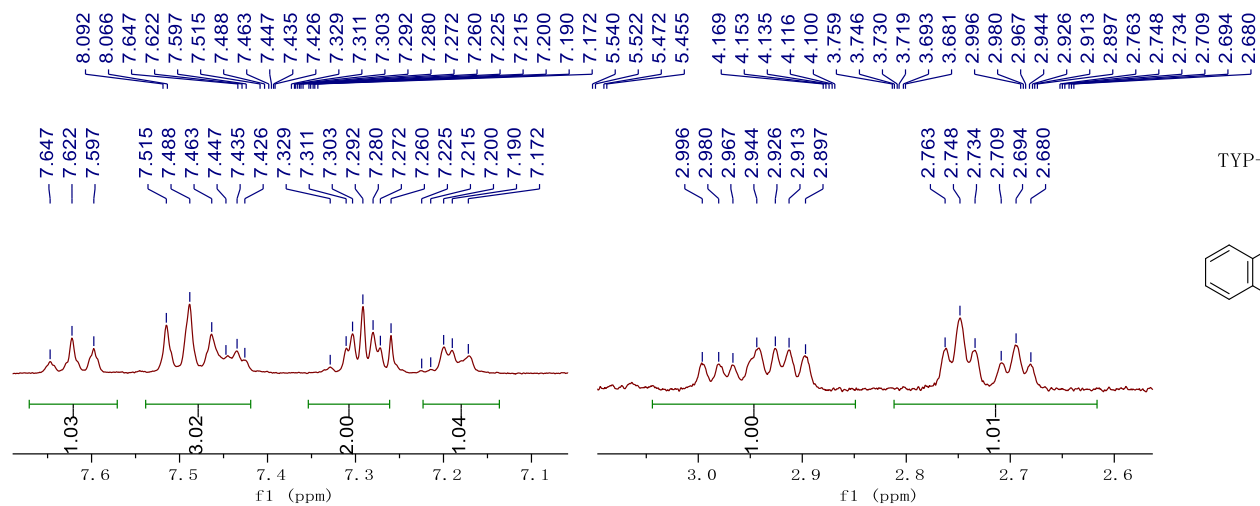
GOY-GA-34-400M-F



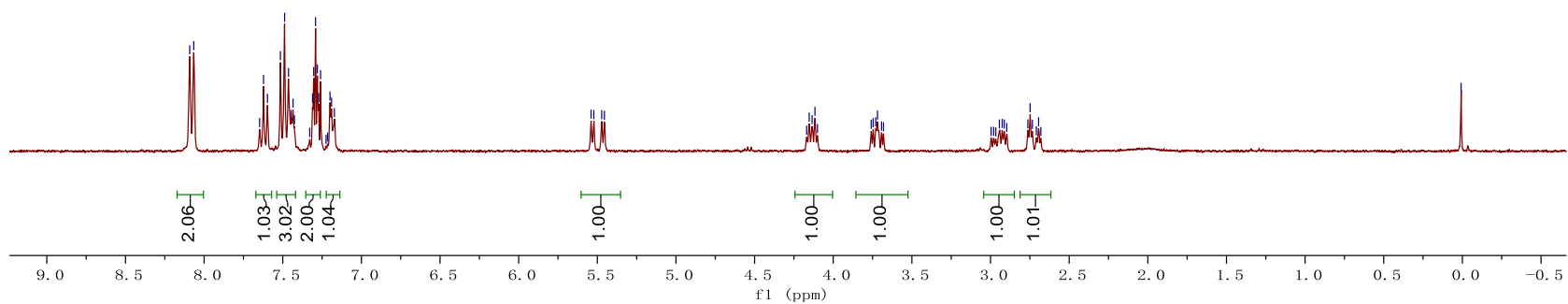
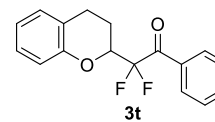
-103.241
-103.963

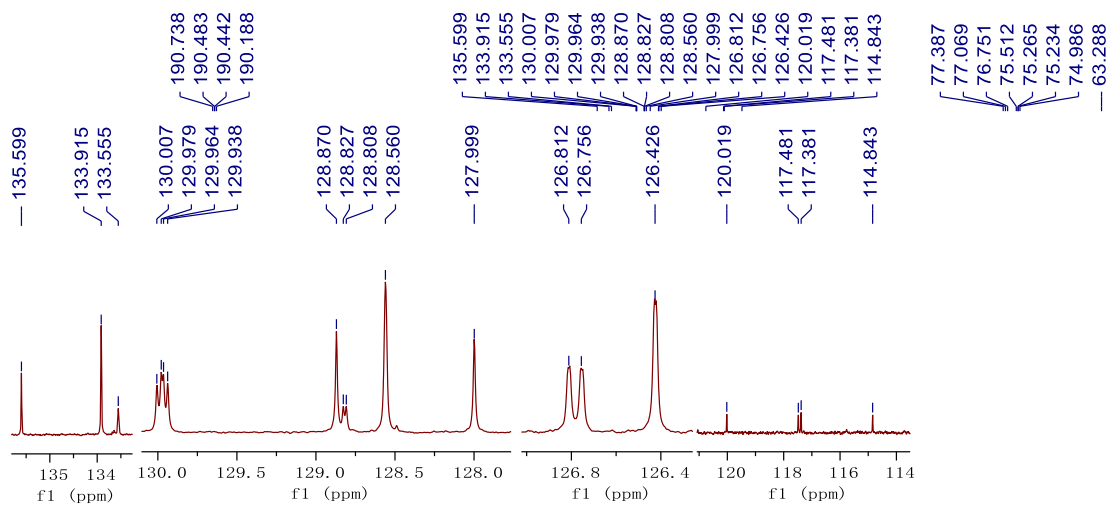
-117.032
-117.753



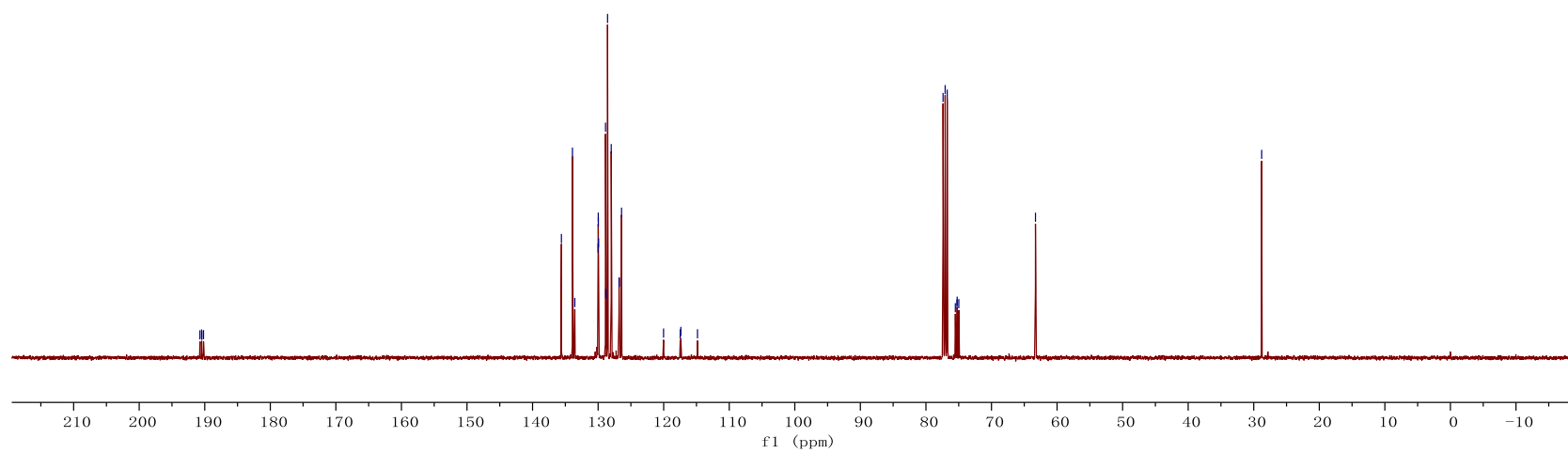
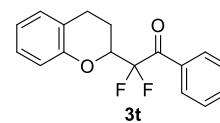


TYP-TA-125-300M-H

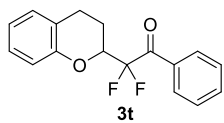




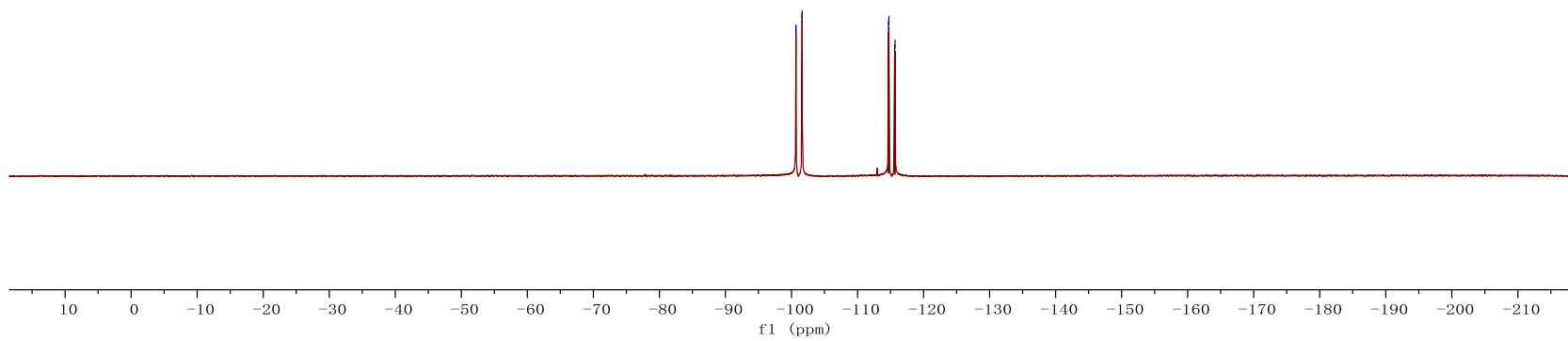
TYP-TA-125-400M-C

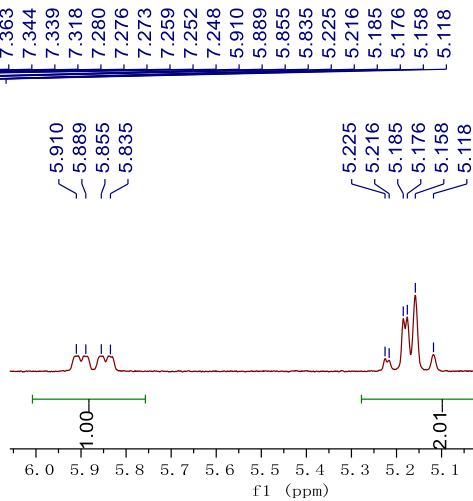
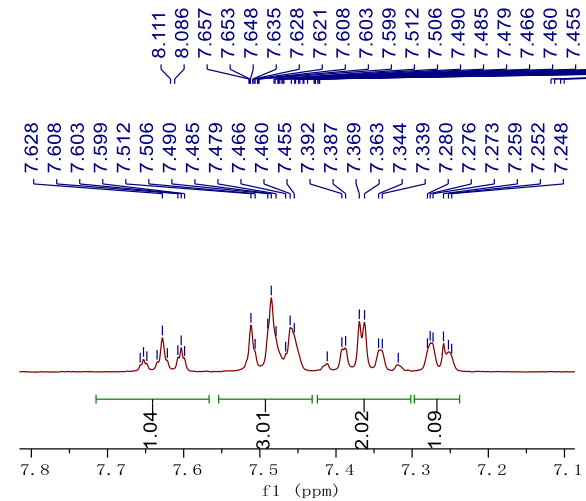


TYP-TA-125-300M-F

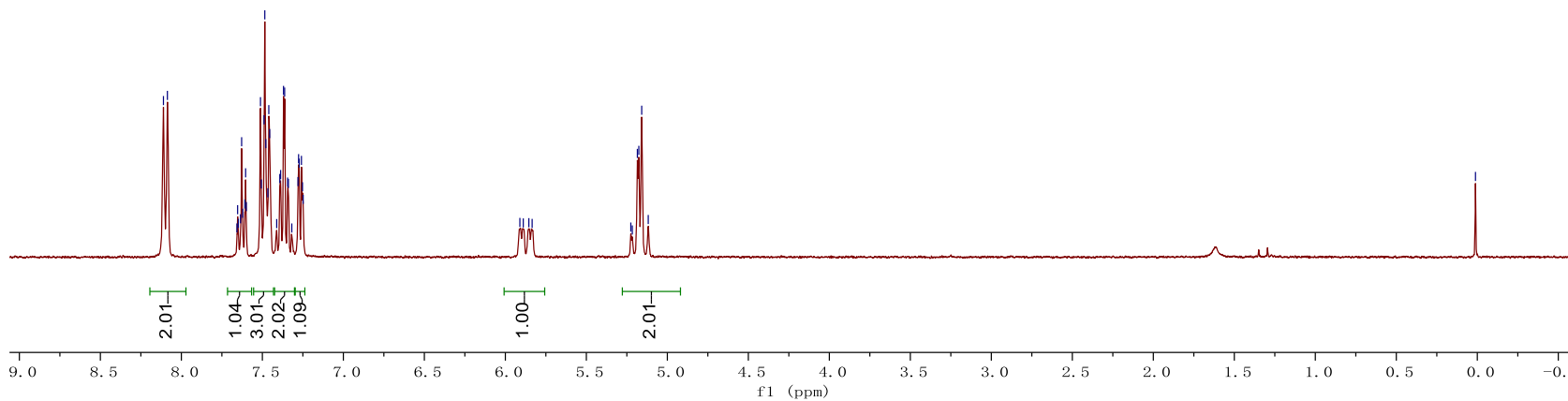
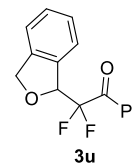


-100.657
-100.677
-101.592
-101.614
-114.683
-114.746
-115.621
-115.684

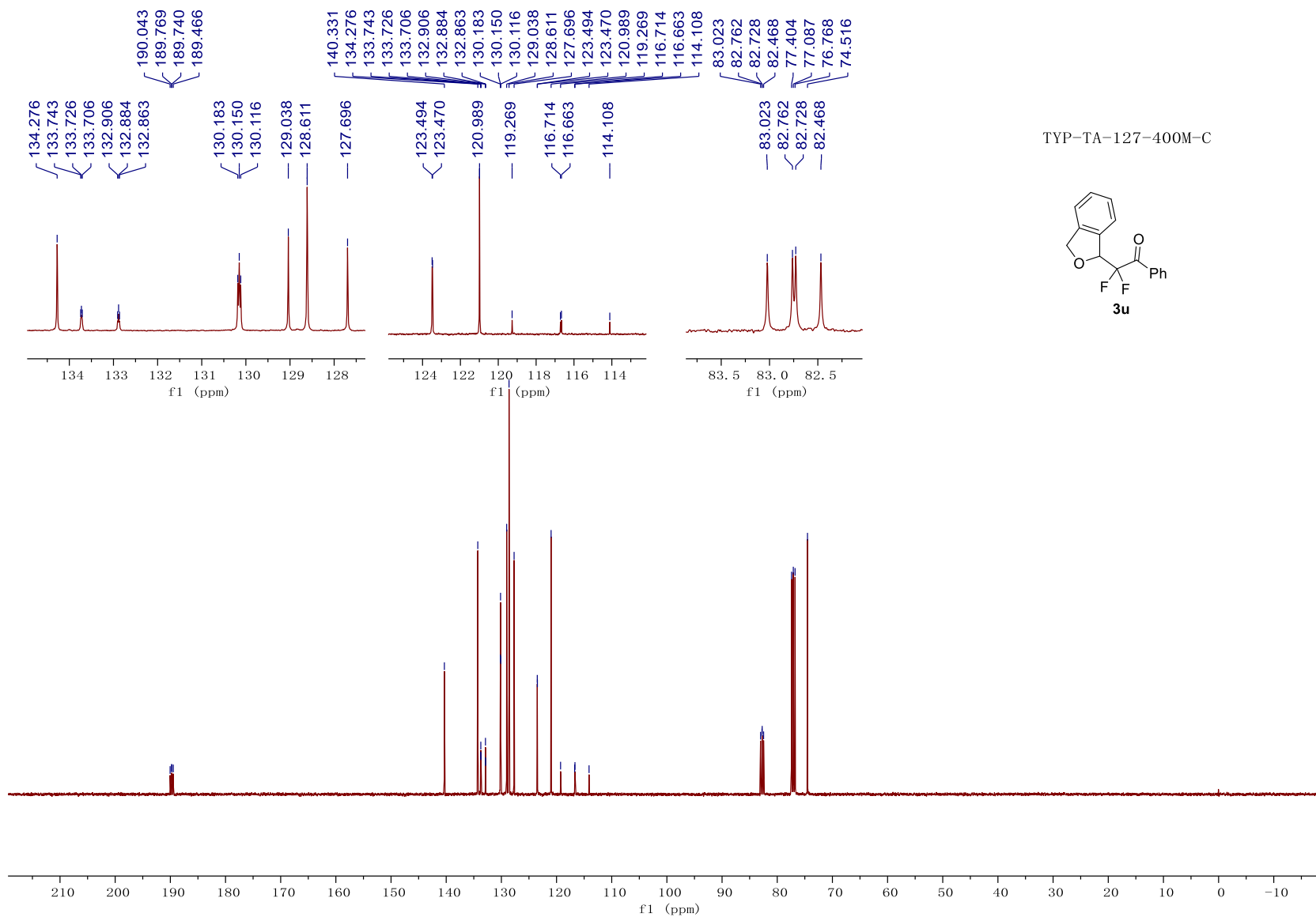




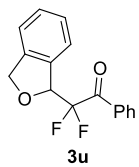
TYP-TA-127-300M-H



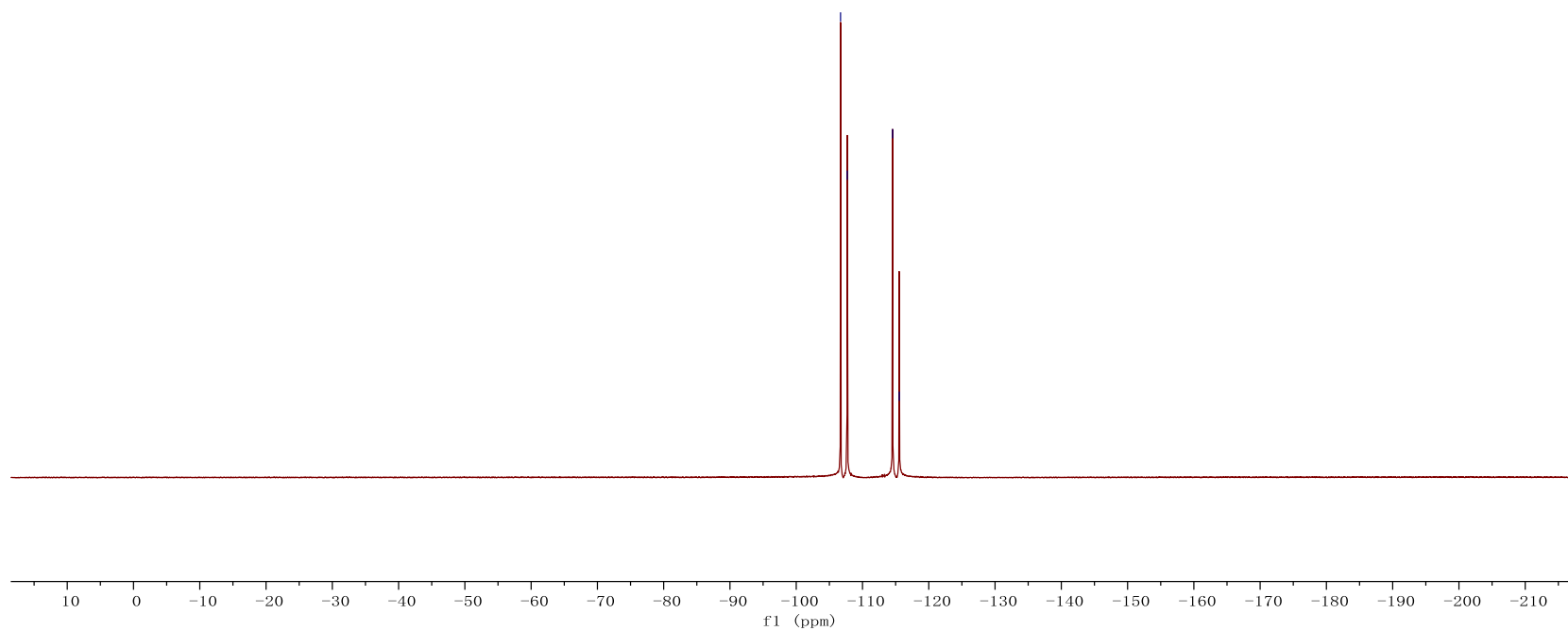
— 0.011

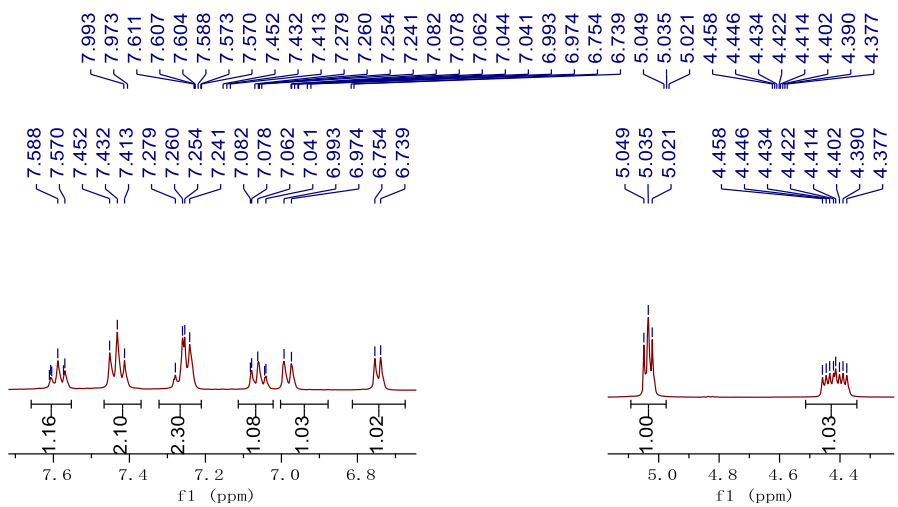


TYP-TA-127-300M-F

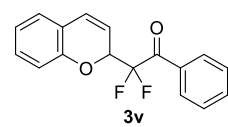


-106.689
-107.693
-114.537
-115.542

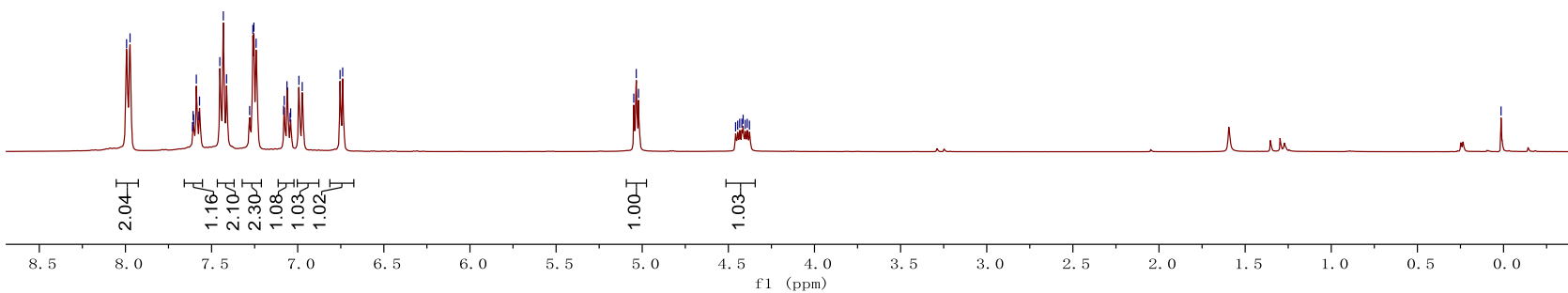


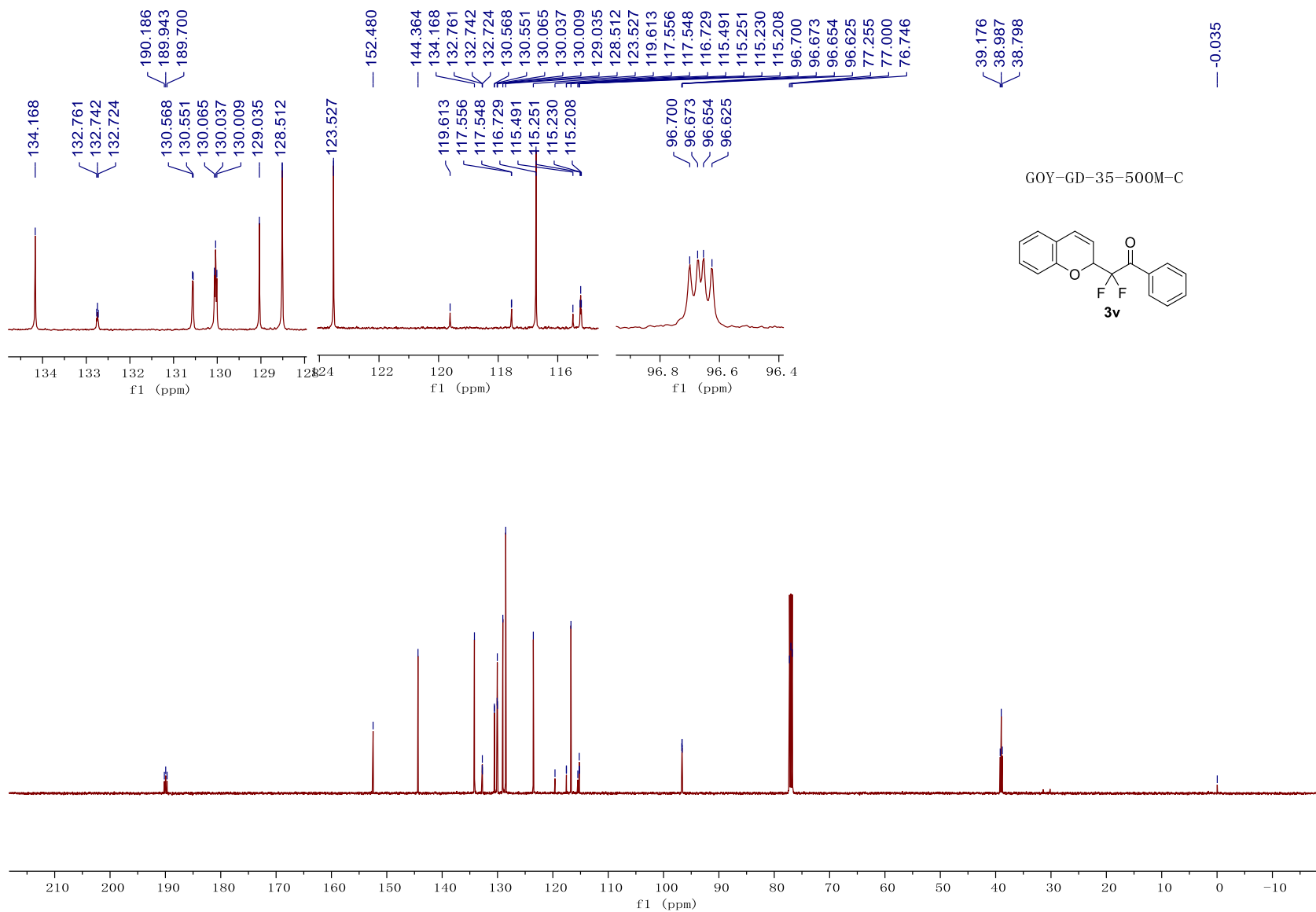


GOY-GA-35-400M-H

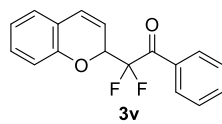


— 0.014



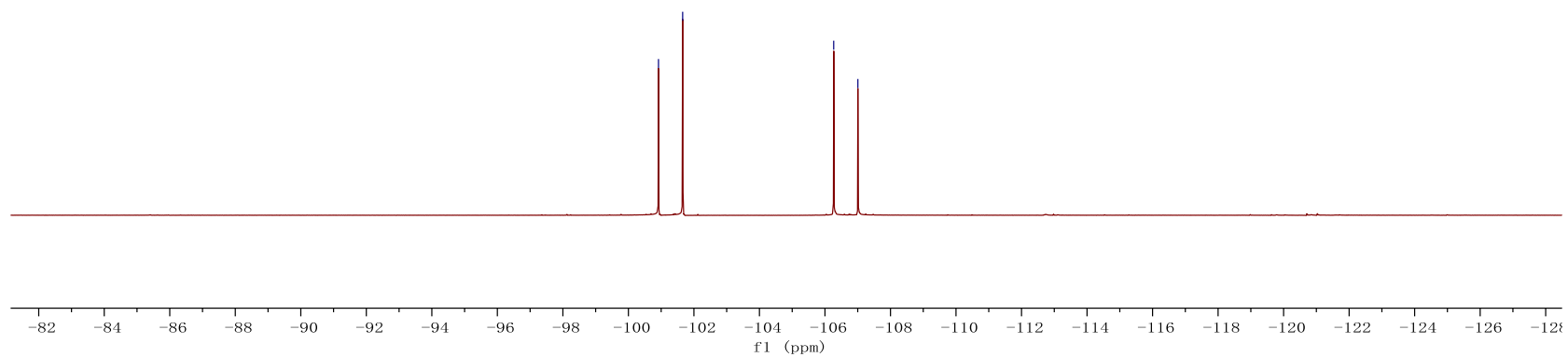


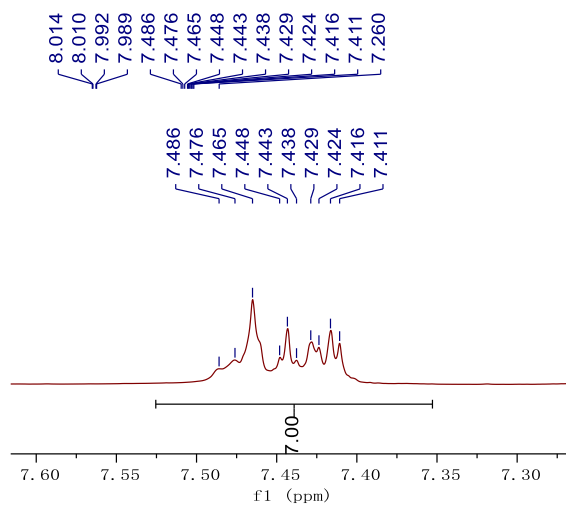
GOY-GA-35-400M-F



— -100.919
— -101.656

— -106.267
— -107.005





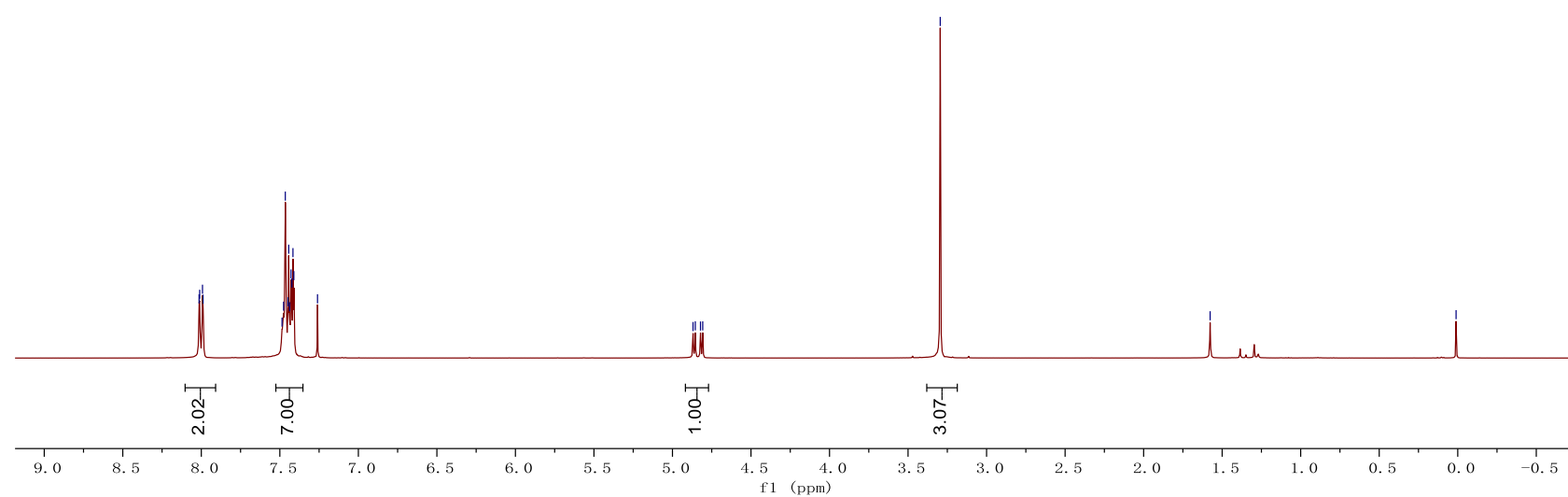
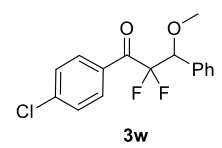
4.869
4.855
4.822
4.807

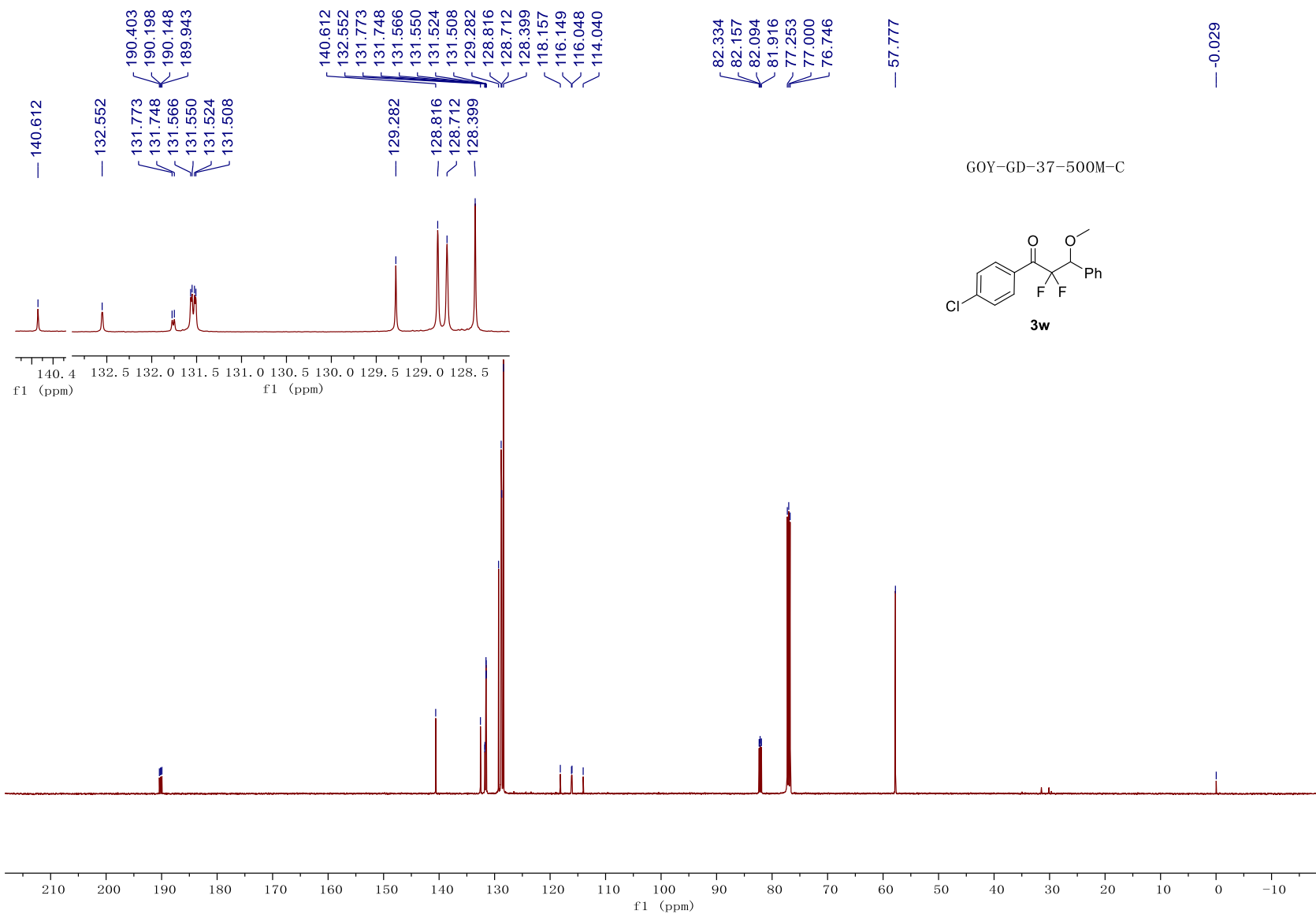
— 3.295

— 1.577

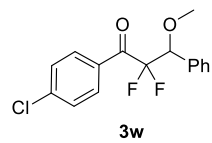
— 0.011

GOY-GA-37-400M-H



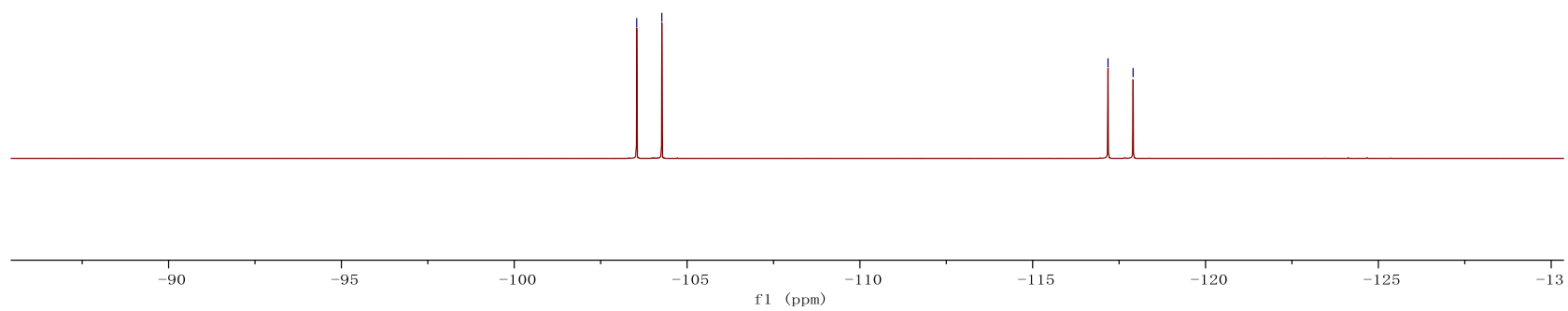


GOY-GA-37-400M-F



— -103.543
— -104.269

— -117.179
— -117.905



7.975
7.949
7.496
7.482
7.470
7.464
7.451
7.433
7.420
7.415
7.405
7.397
7.289
7.260

4.900
4.880
4.837
4.817

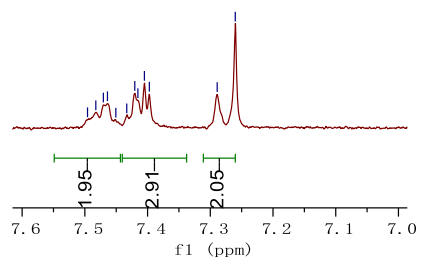
— 3.288

— 2.429

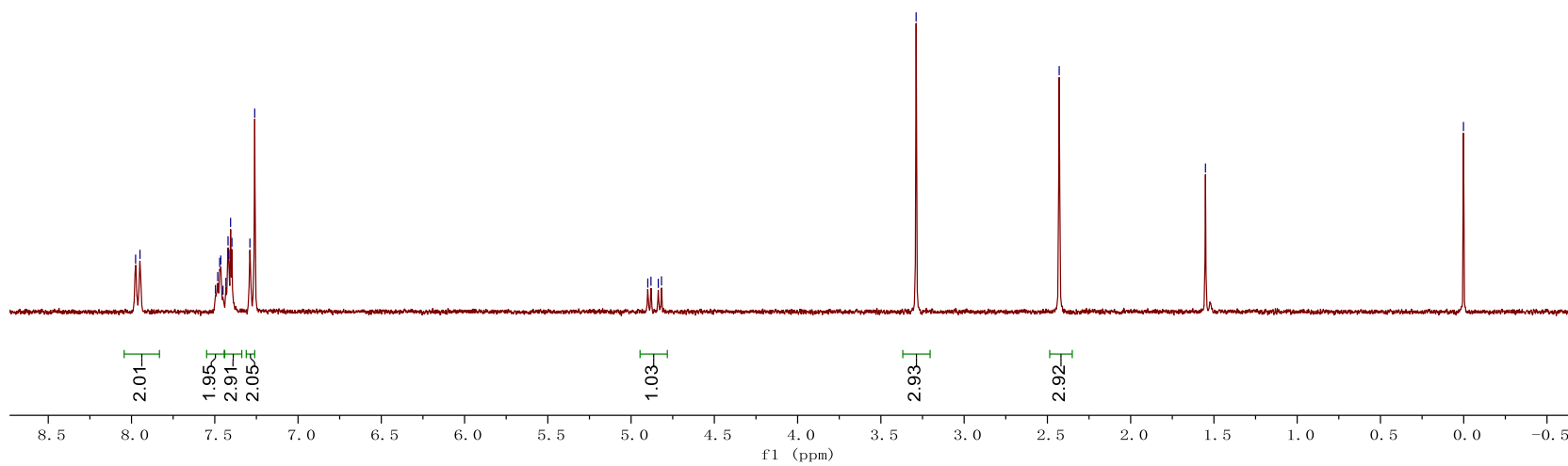
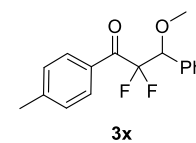
— 1.551

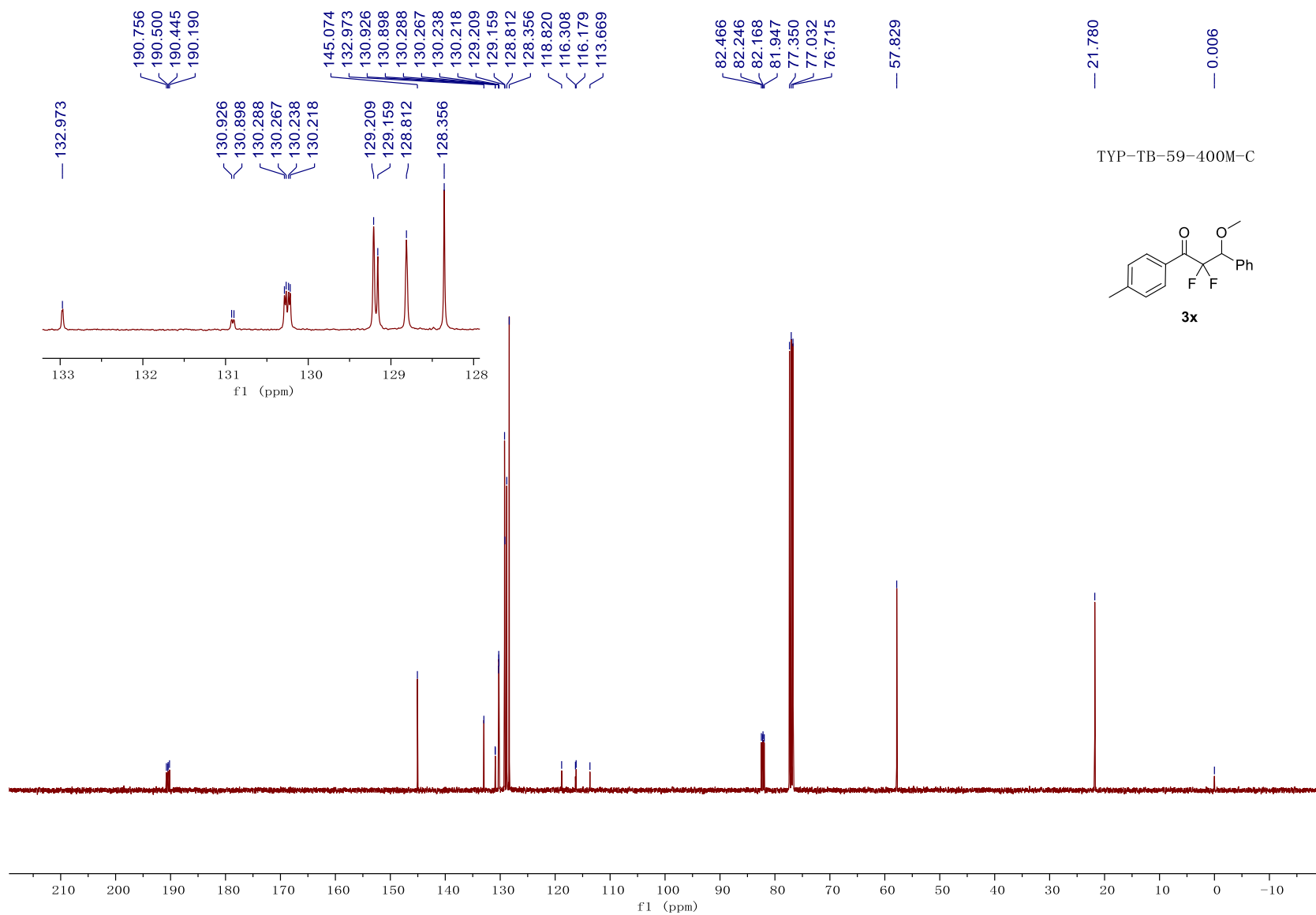
— 0.001

7.496
7.482
7.470
7.464
7.451
7.433
7.420
7.415
7.405
7.397
7.289
7.260

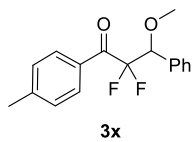


TYP-TB-59-300M-H

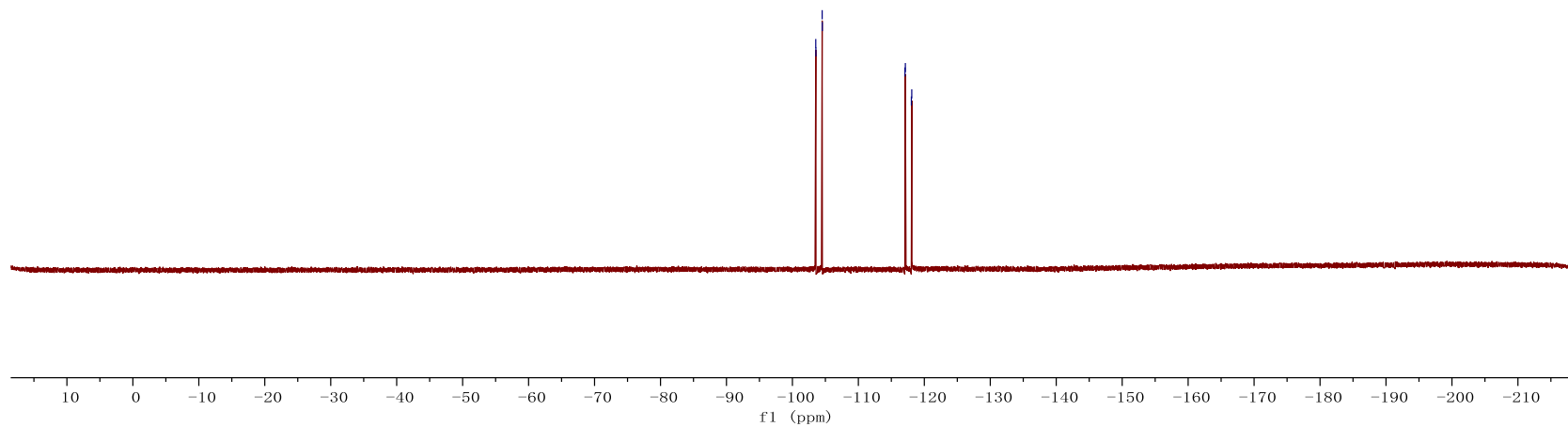


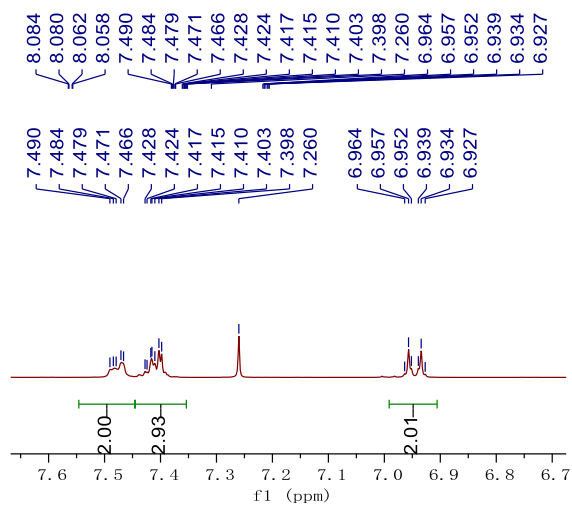


TYP-TB-59-300M-F



-103.540
-103.558
-104.510
-104.528
-117.066
-117.125
-118.035
-118.095





4.889
4.874
4.842
4.827

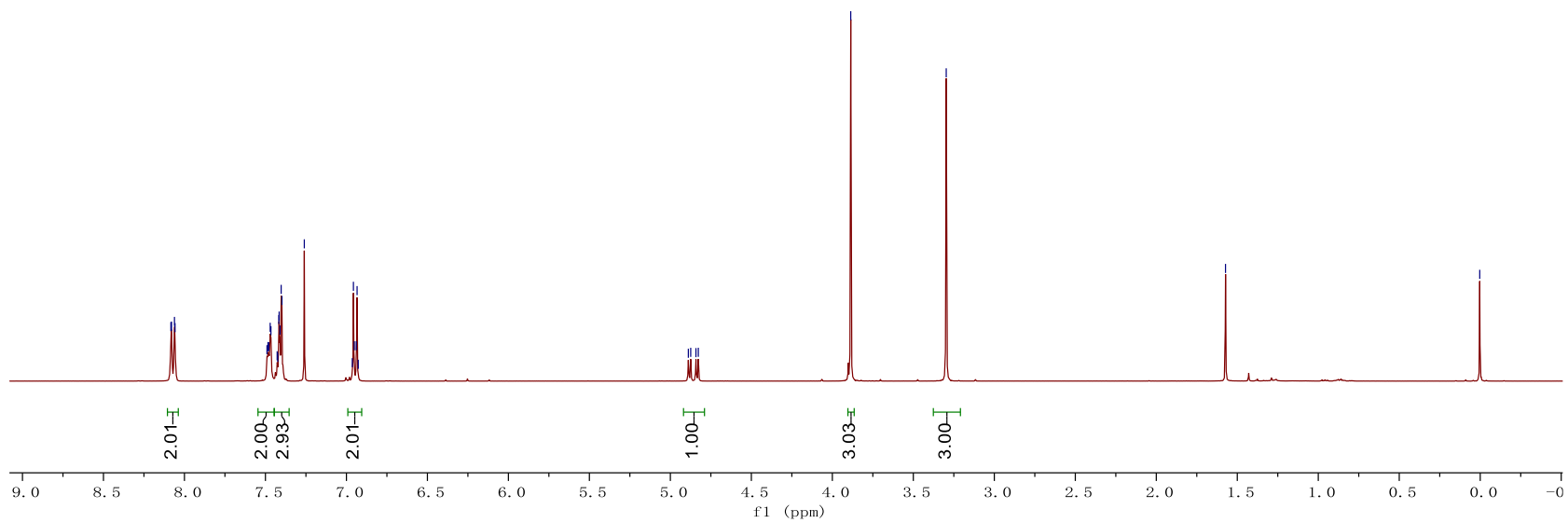
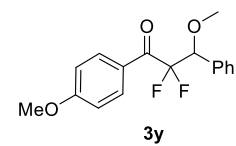
— 3.886

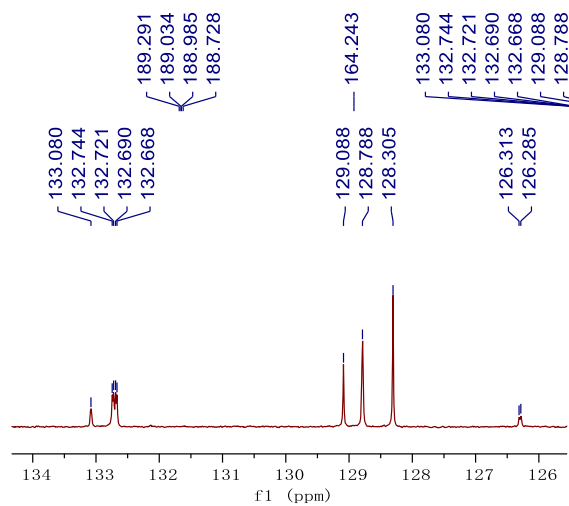
— 3.297

— 1.573

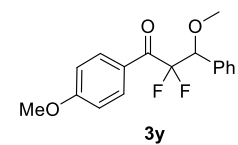
— 0.003

TYP-TB-91-400M-H

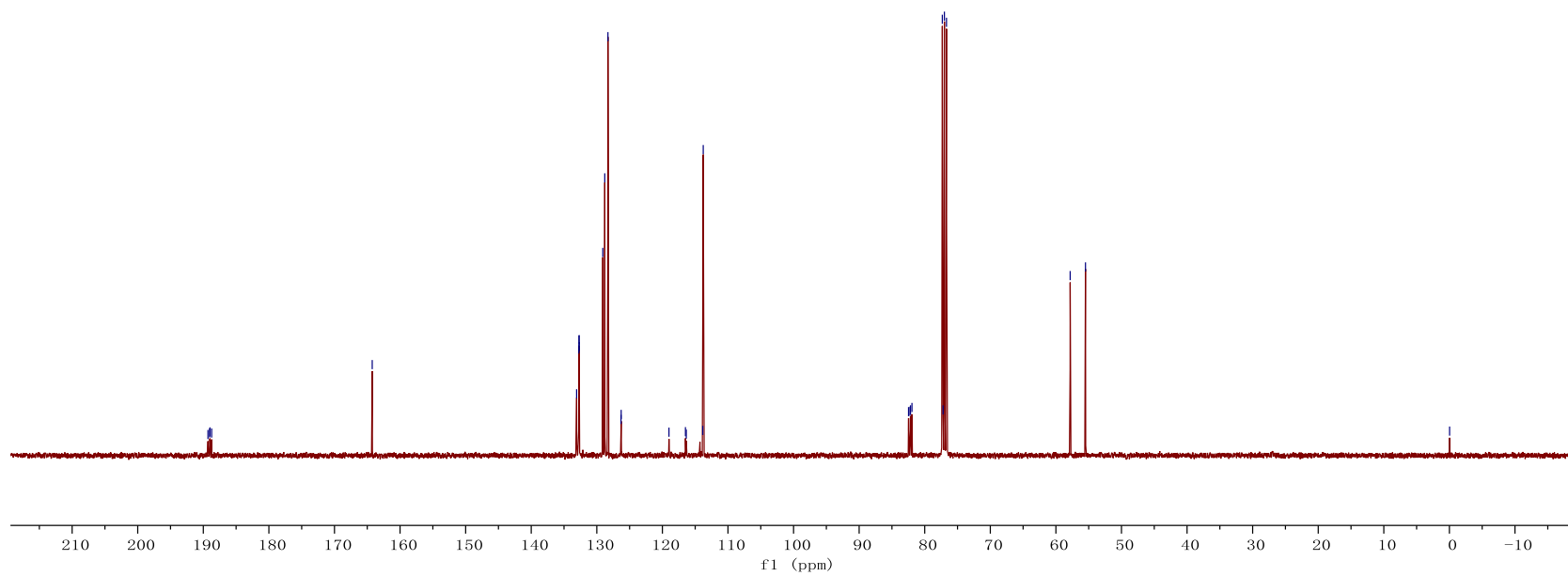




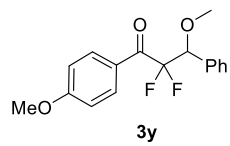
TYP-TB-91-400M-C



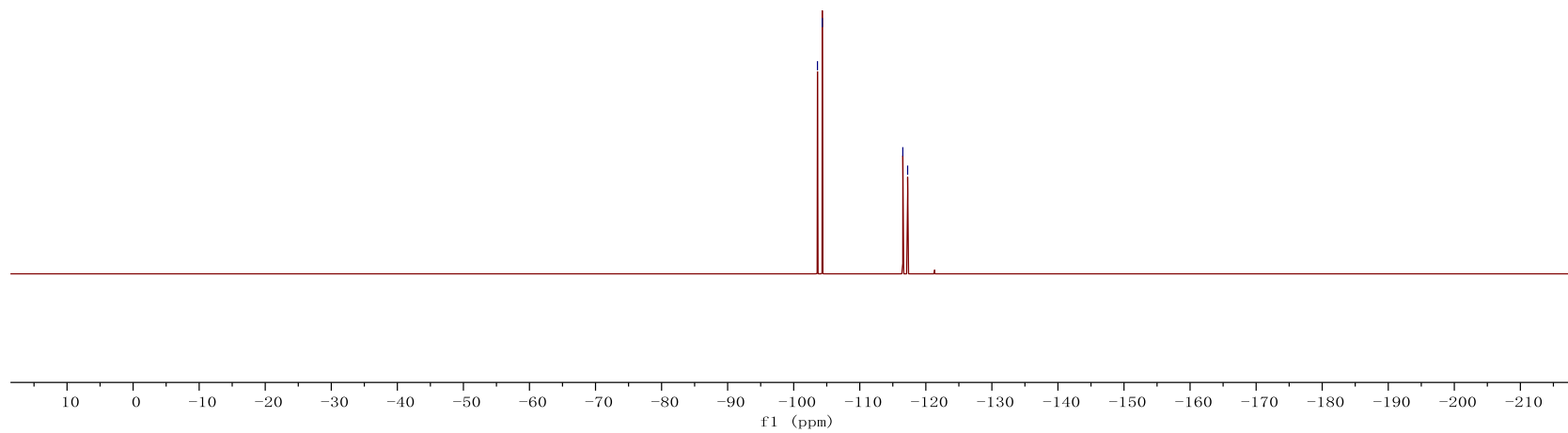
-0.031

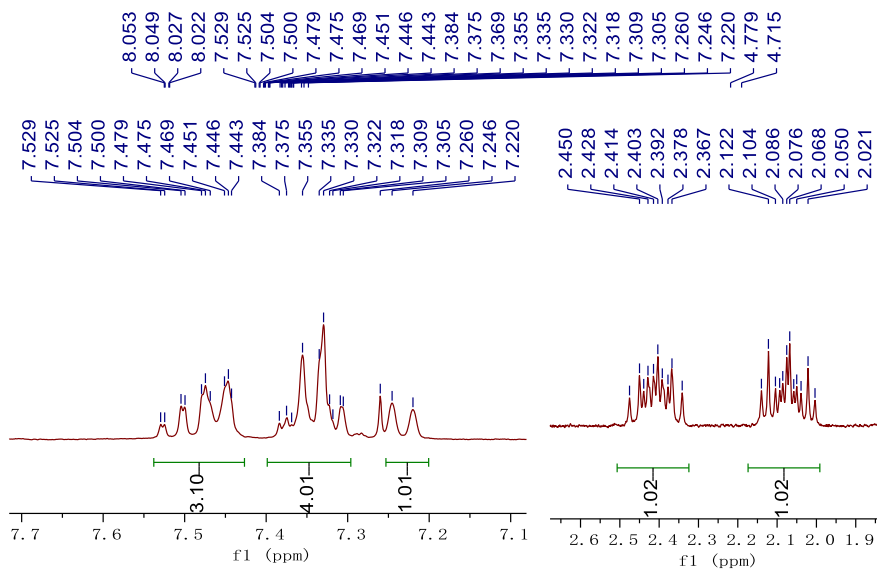


TYP-TB-91-400M-F

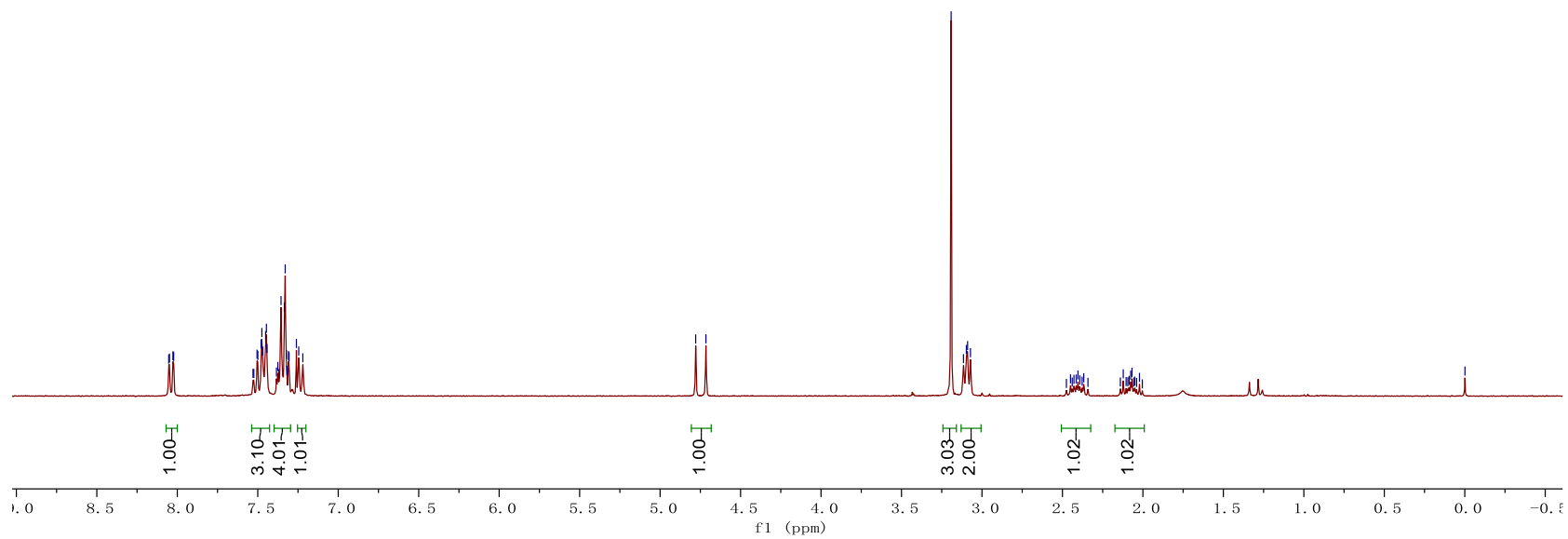
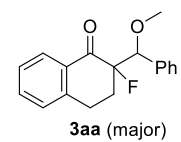


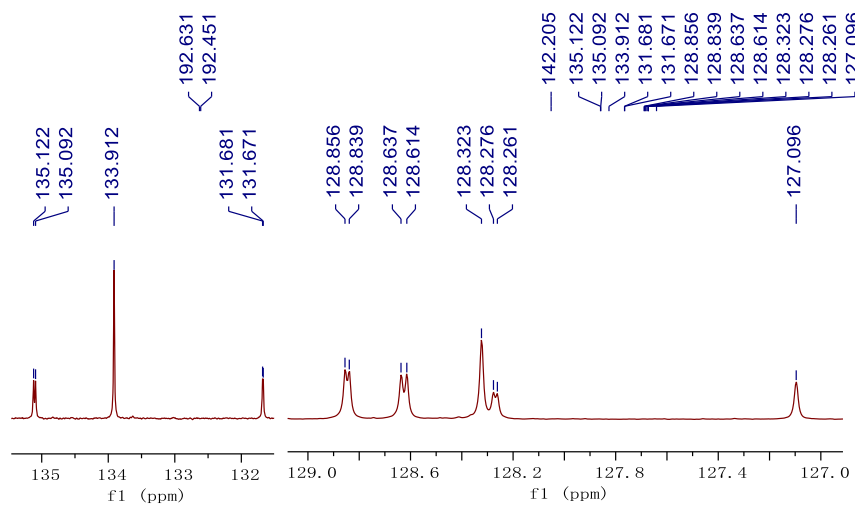
-103.596
-104.323
-116.519
-117.245



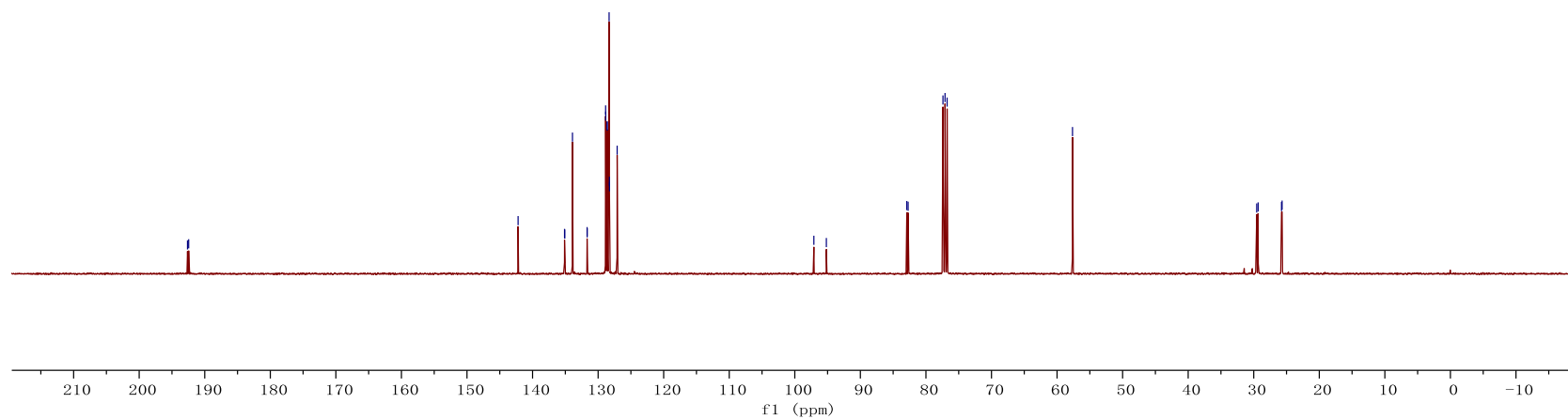
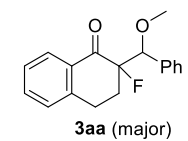


TYP-TB-81-300M-H

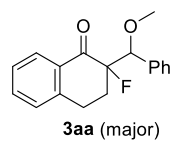




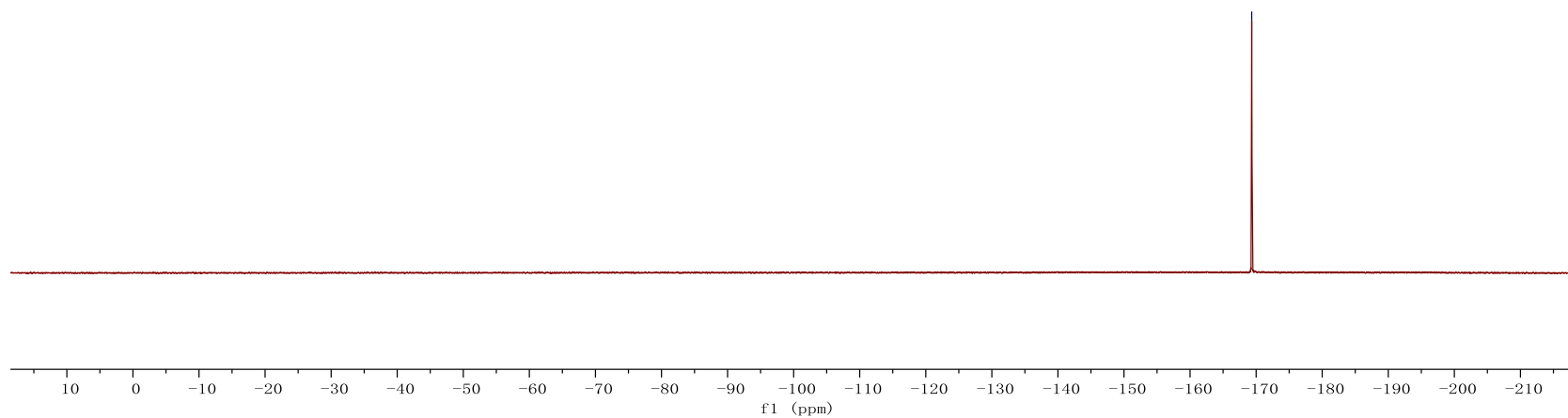
TYP-TB-81-400M-C



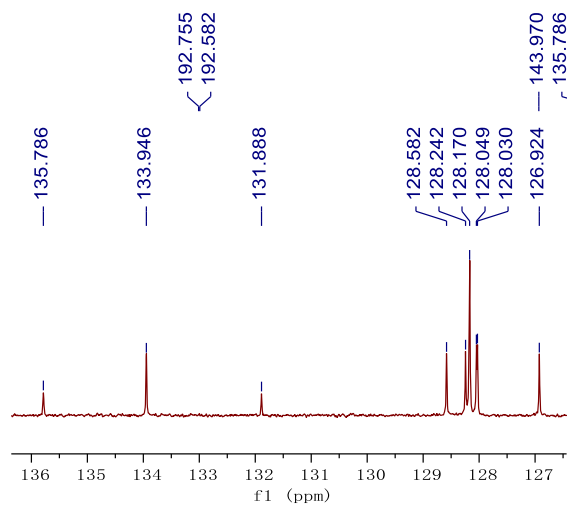
TYP-TB-81-300M-F



— -169.332







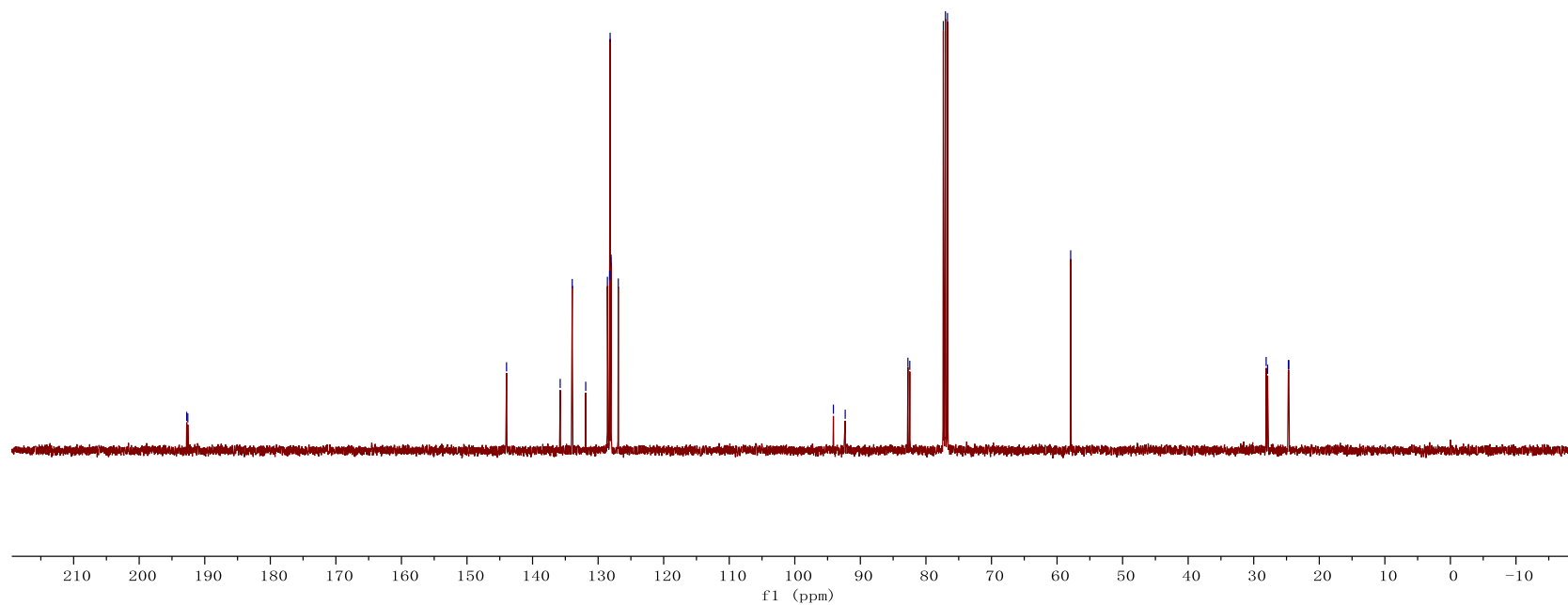
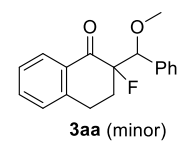
143.970
135.786
133.946
131.888
128.582
128.242
128.170
128.049
128.030
126.924

94.113
92.309
82.746
82.462
77.345
77.028
76.711

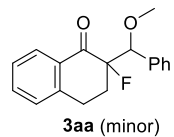
57.922

28.104
27.887
24.717
24.647

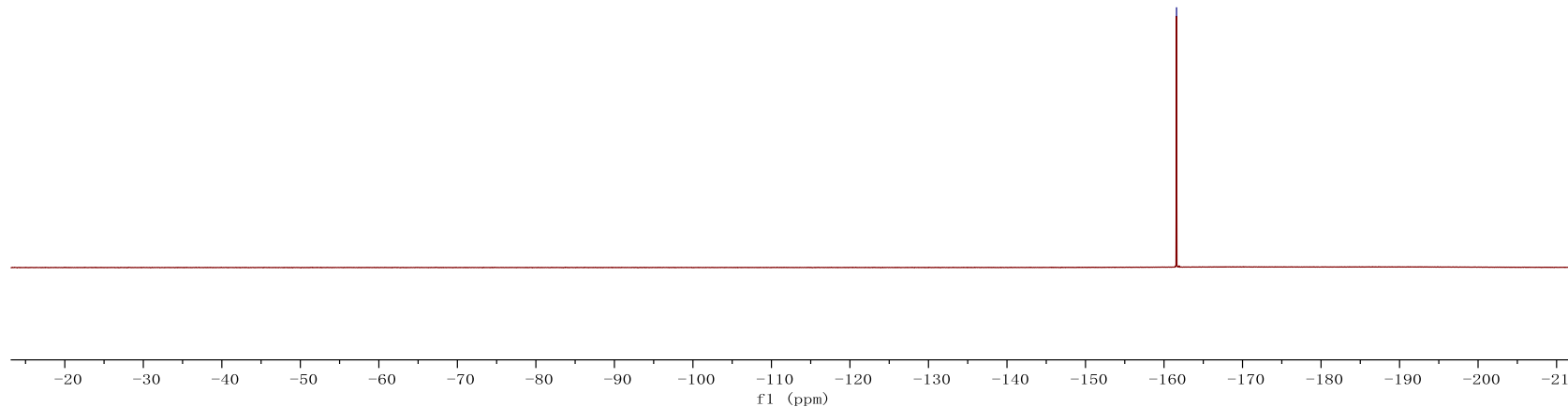
TYP-TB-81-400M-H



TYP-TB-81-400M-F



— -161.594



7.856
7.836
7.632
7.614
7.595
7.503
7.481
7.450
7.433
7.415
7.396
7.383
7.260

4.901
4.884

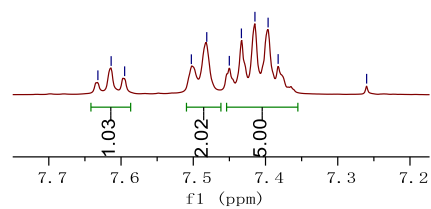
3.679
3.634
3.589

3.238

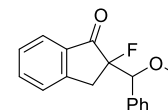
2.858
2.813
2.793
2.748

7.632
7.614
7.595
7.503
7.481
7.450
7.433
7.415
7.396
7.383

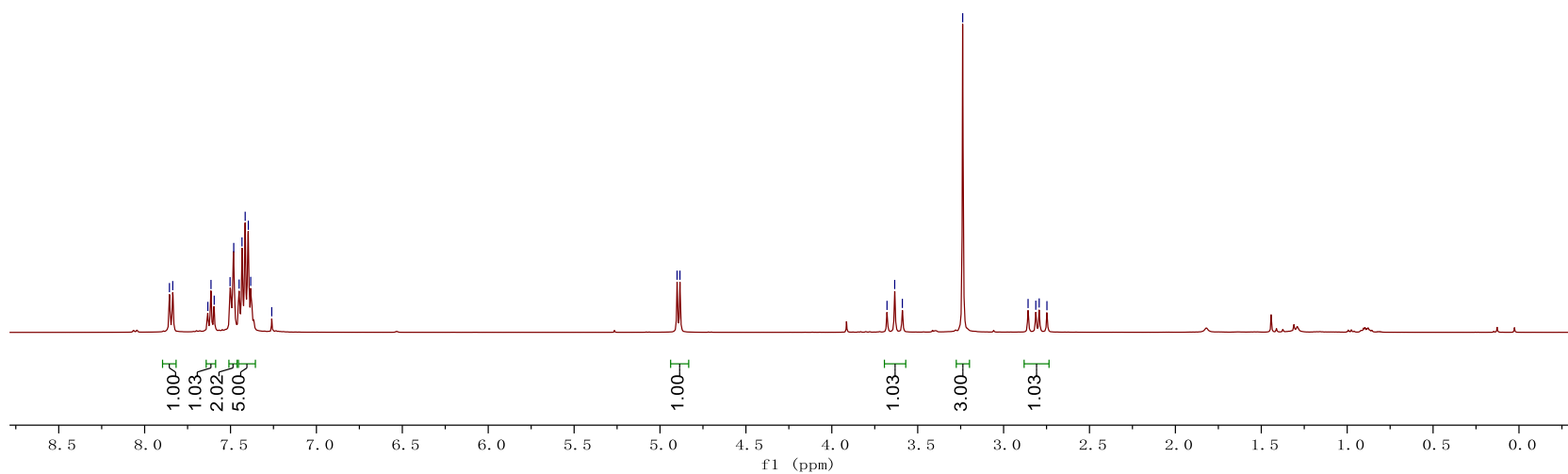
7.260

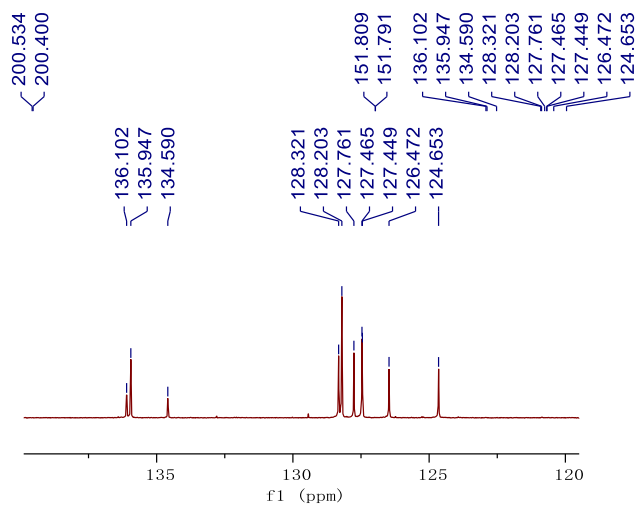


GOY-GA-38-400M-H



3ab (major)





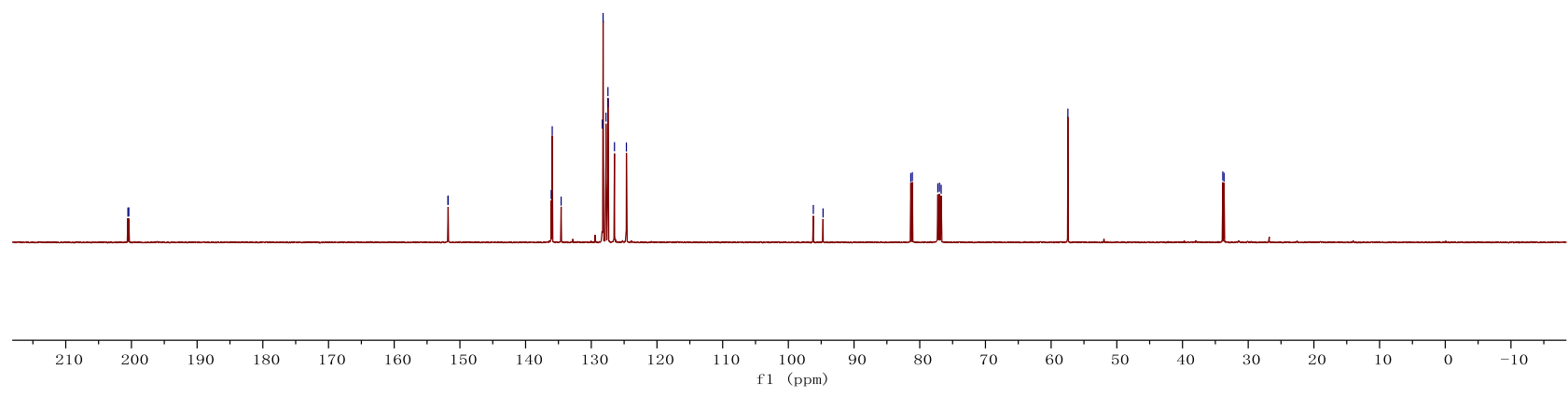
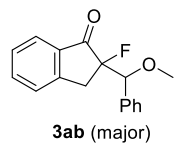
96.198
94.719

81.362
81.122
77.246
76.991
76.737

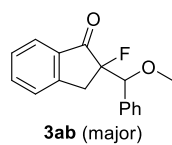
57.447

33.867
33.679

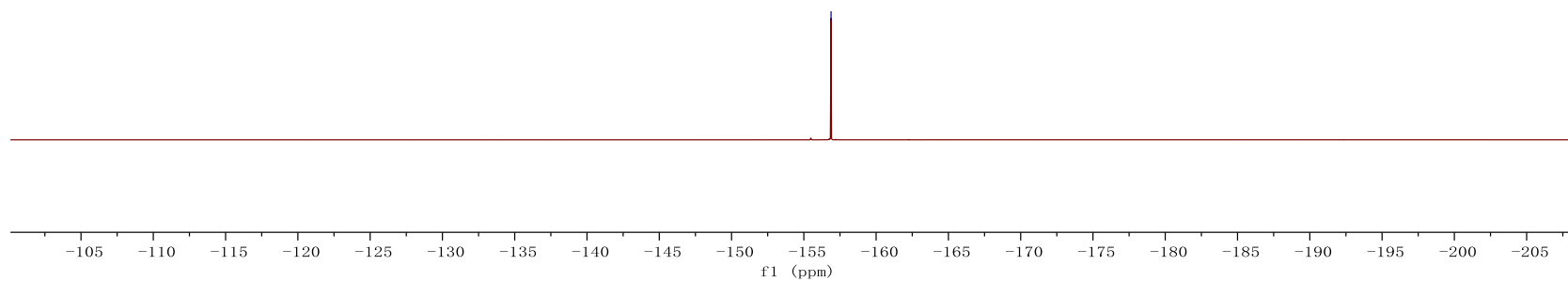
GOY-GD-38-500M-C

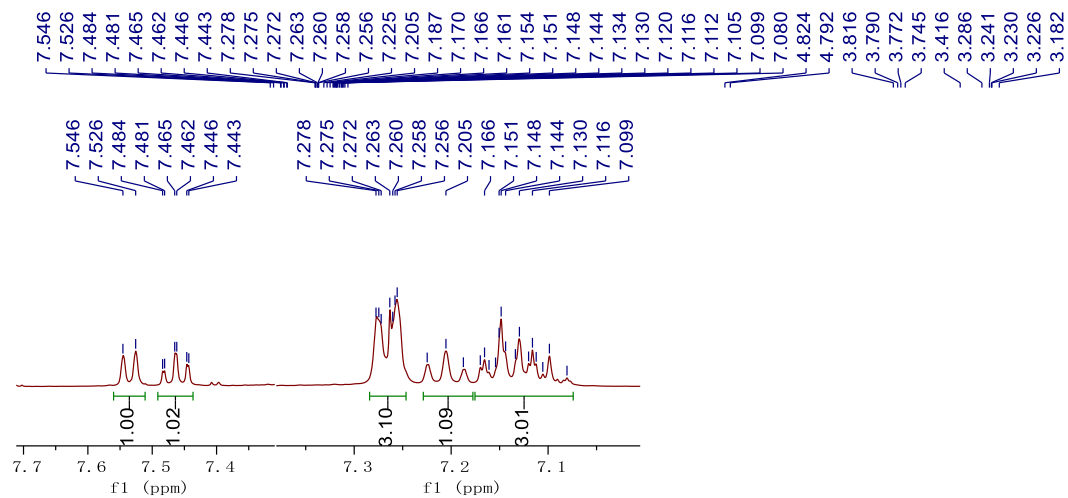


GOY-GA-38-400M-F



-156.882

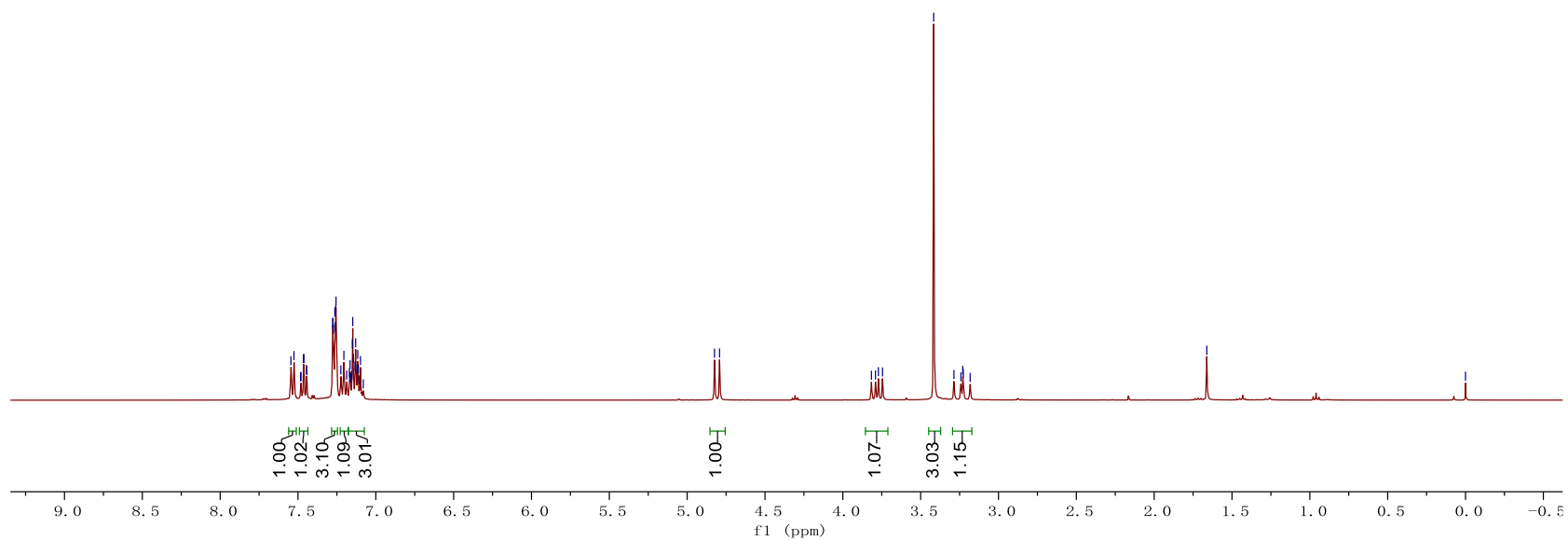
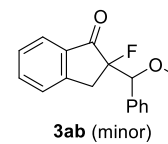




— 1.662

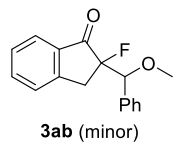
— -0.000

GOY-GD-38-400M-H

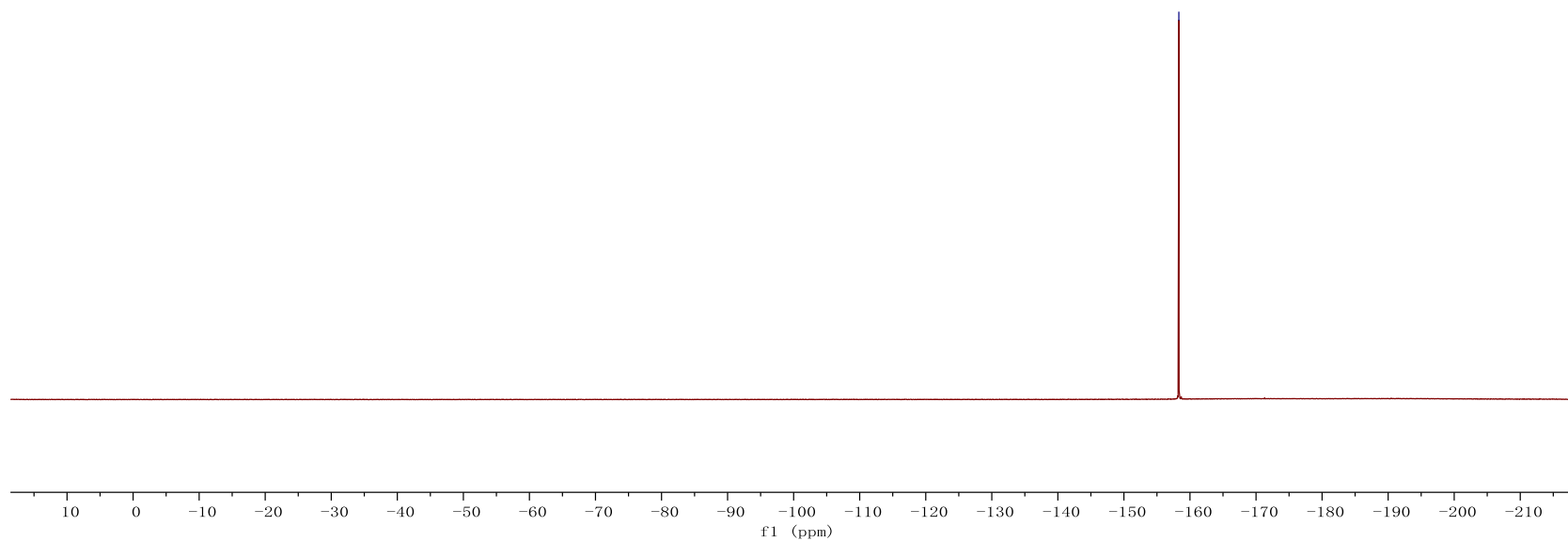


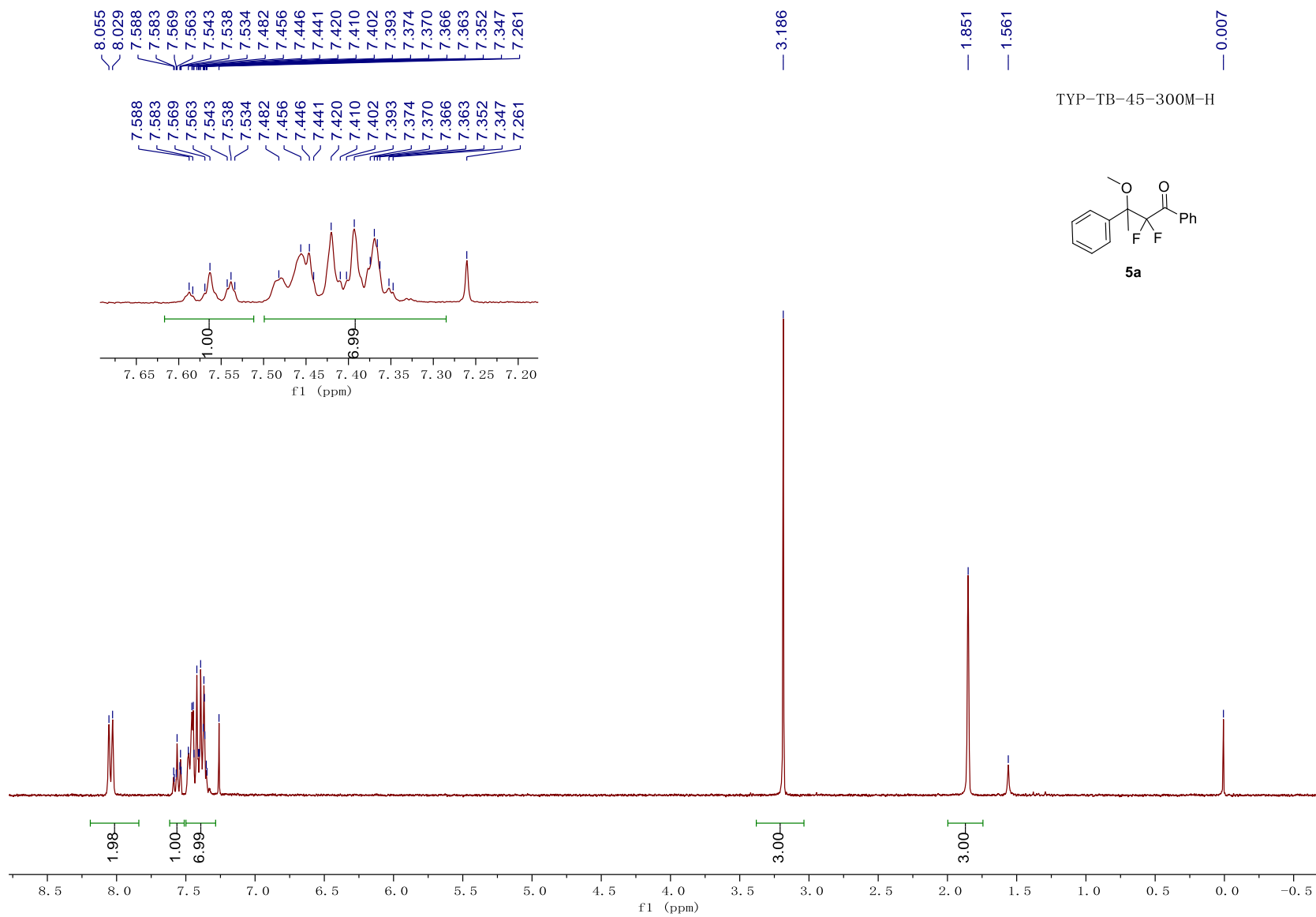


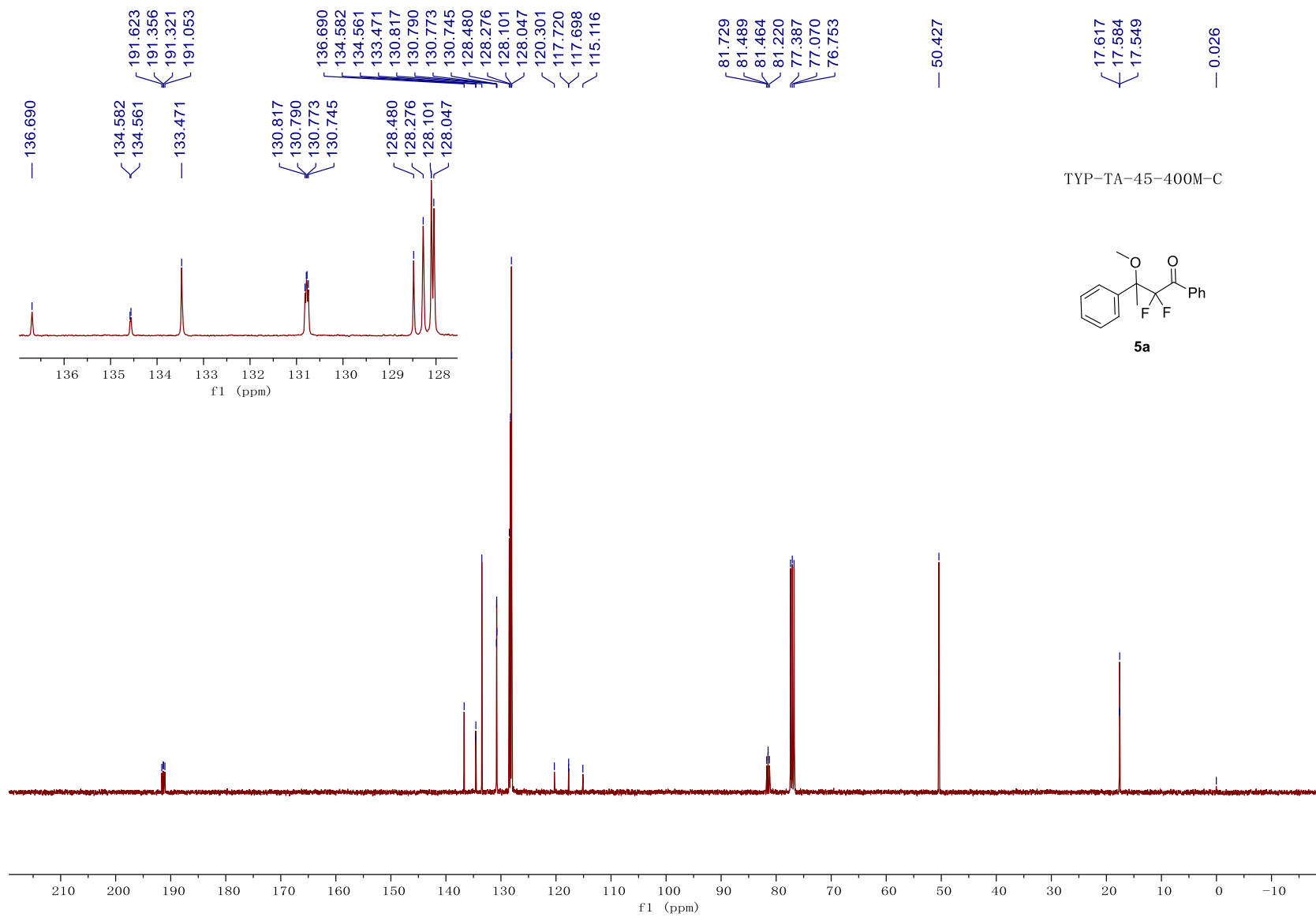
GOY-GD-38-400M-F



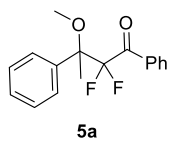
— -158.315



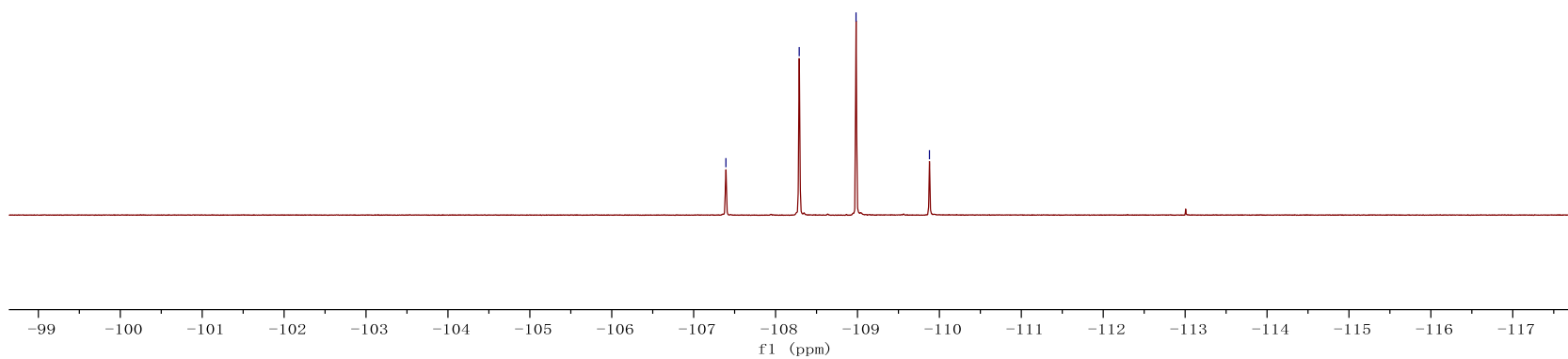


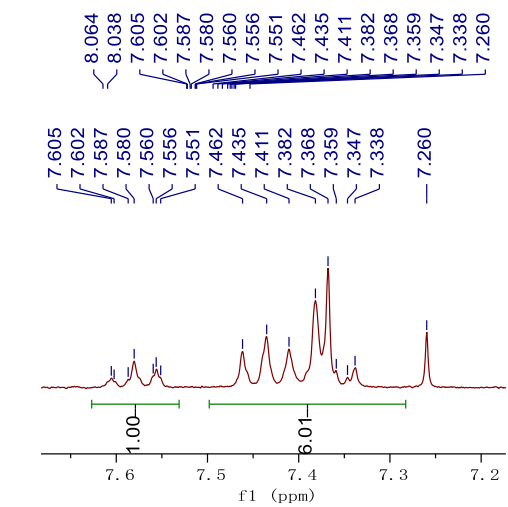


TYP-TB-45-300M-F

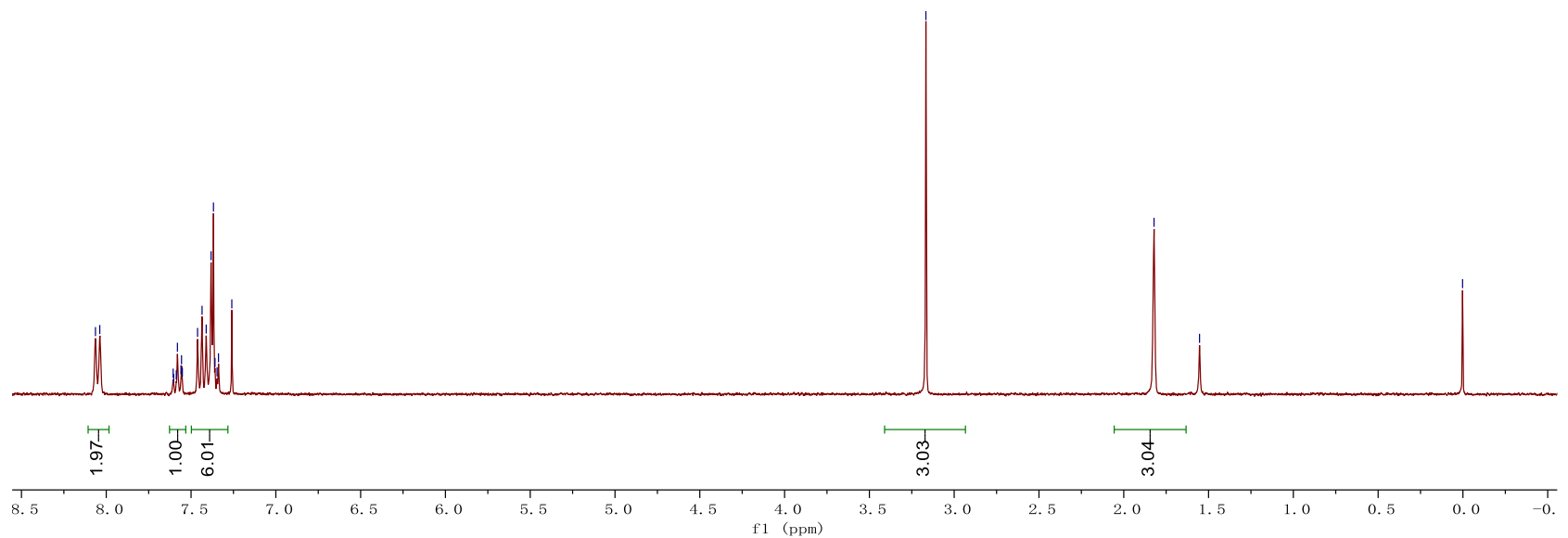
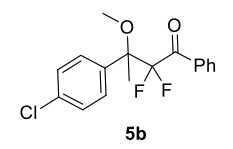


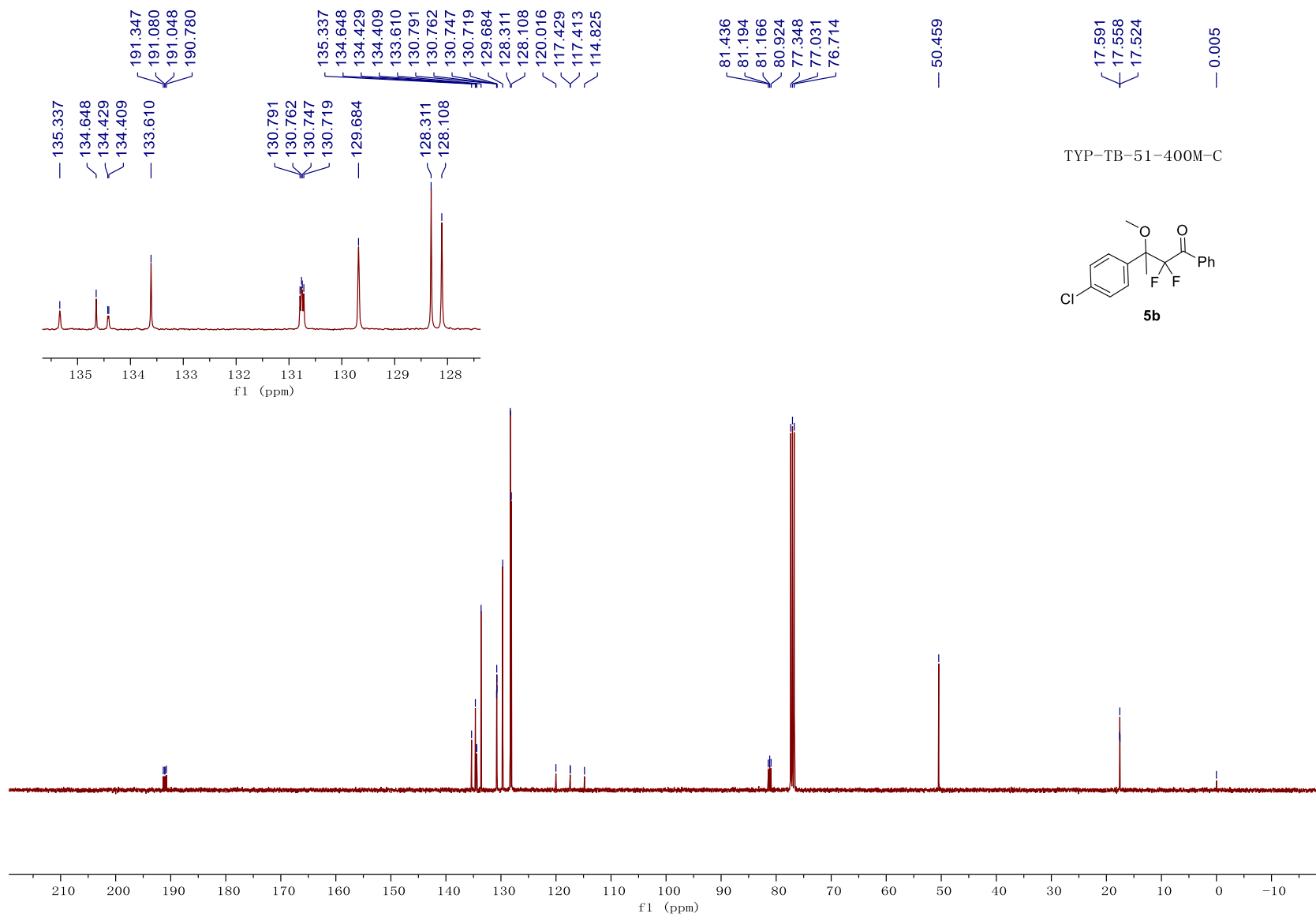
— -107.393
— -108.289
— -108.982
— -109.878



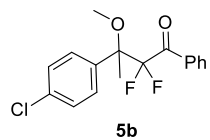


TYP-TB-51-300M-H

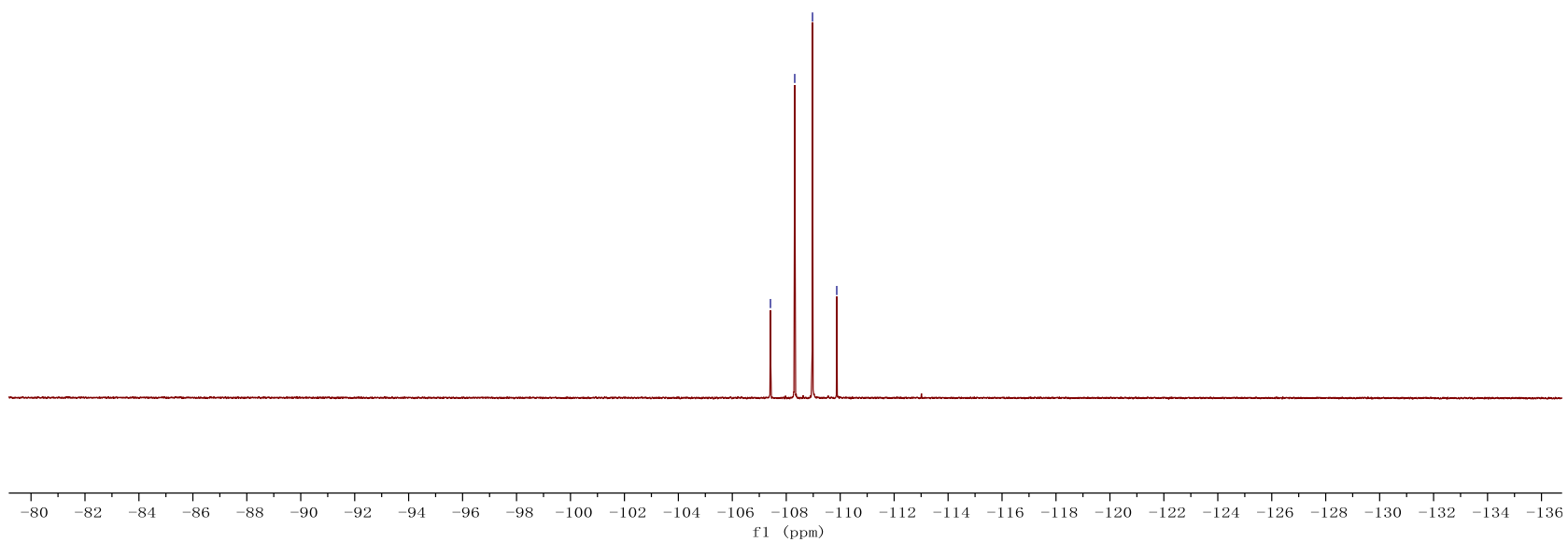


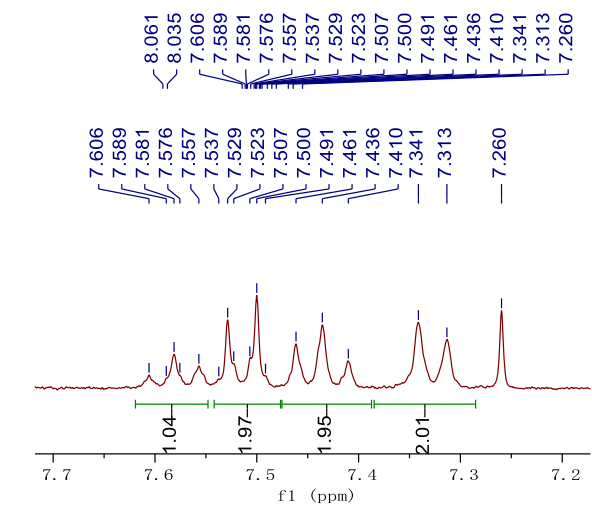


TYP-TB-51-300M-F



-107.414
-108.314
-108.973
-109.872





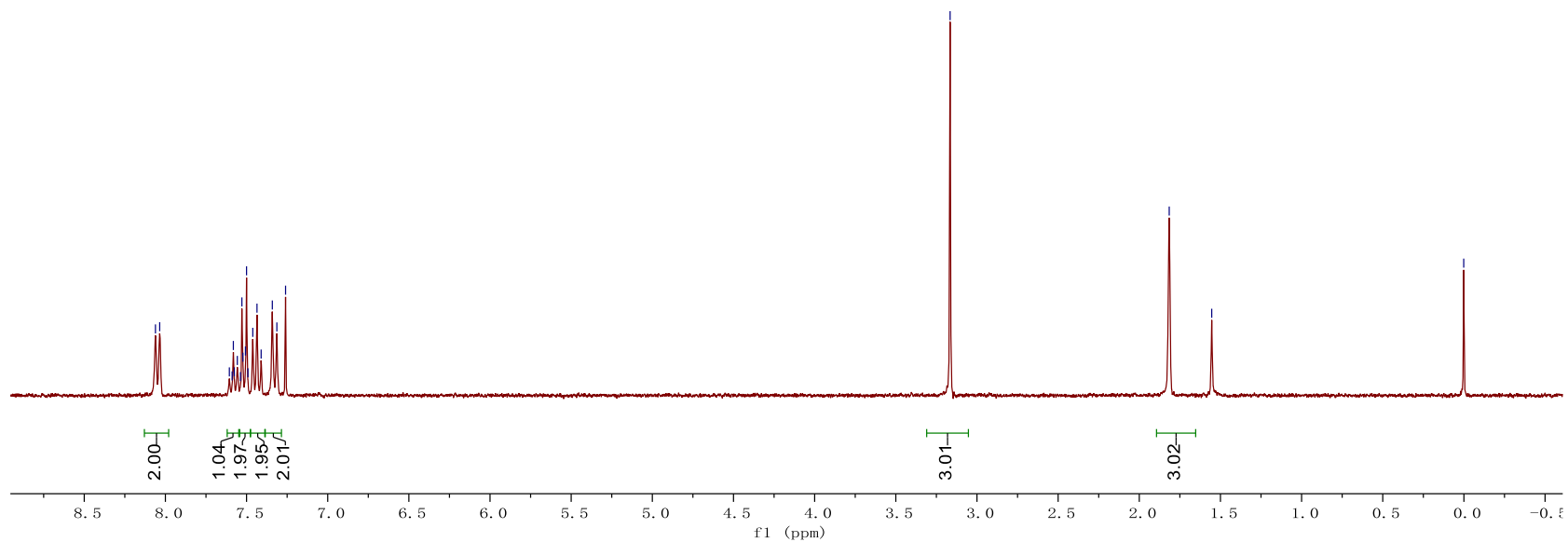
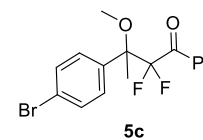
— 3.166

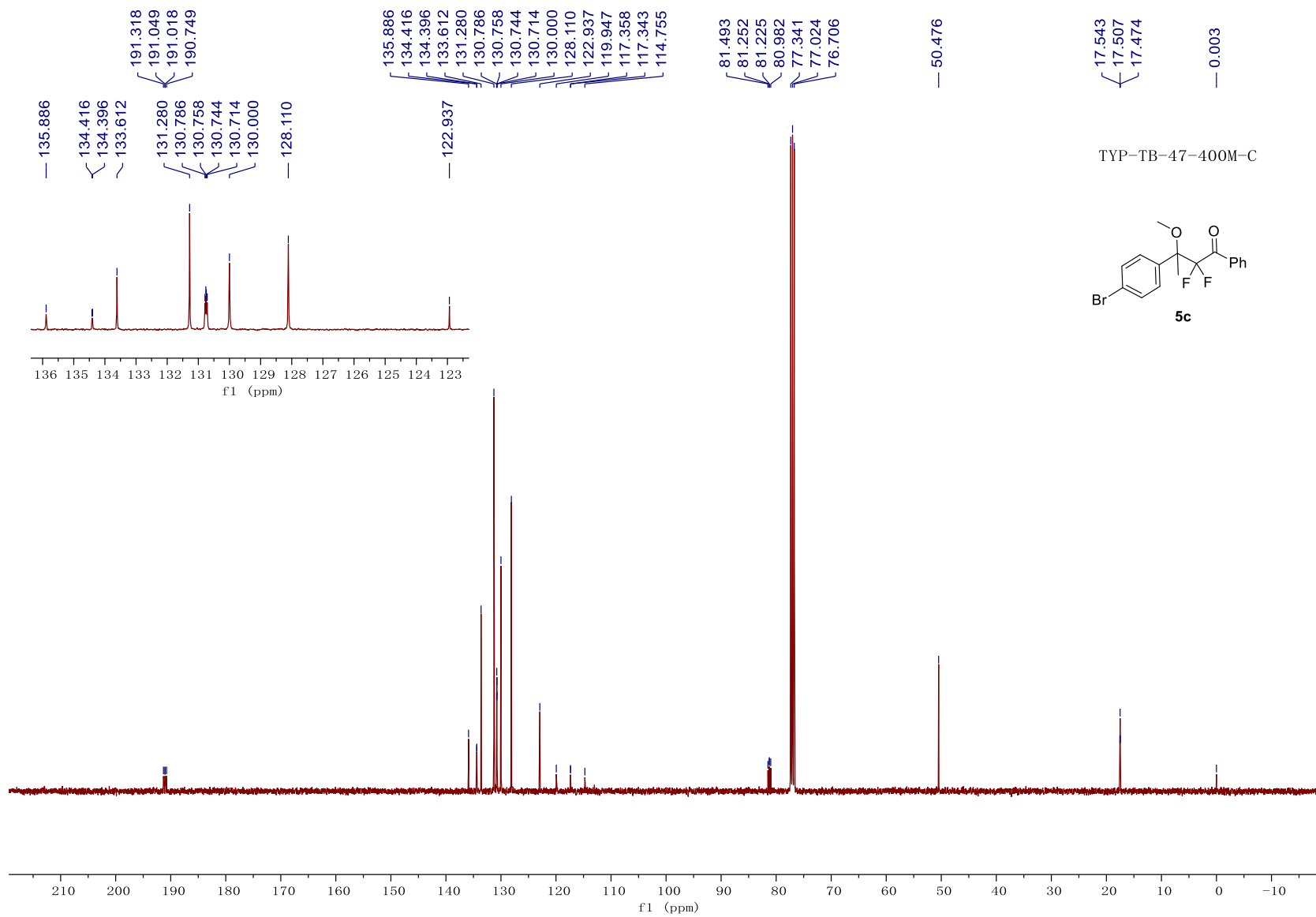
— 1.816

— 1.554

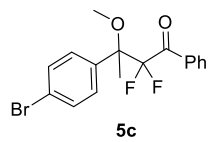
— 0.001

TYP-TB-47-300M-H

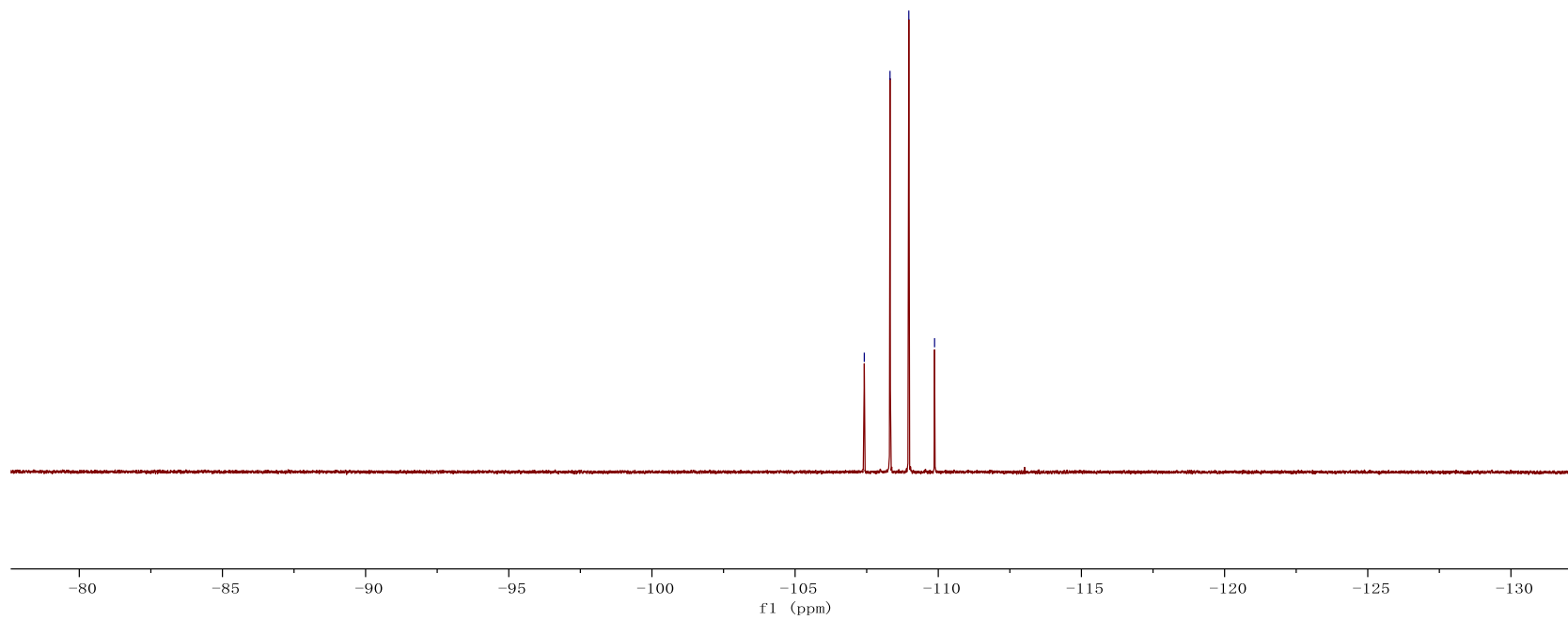


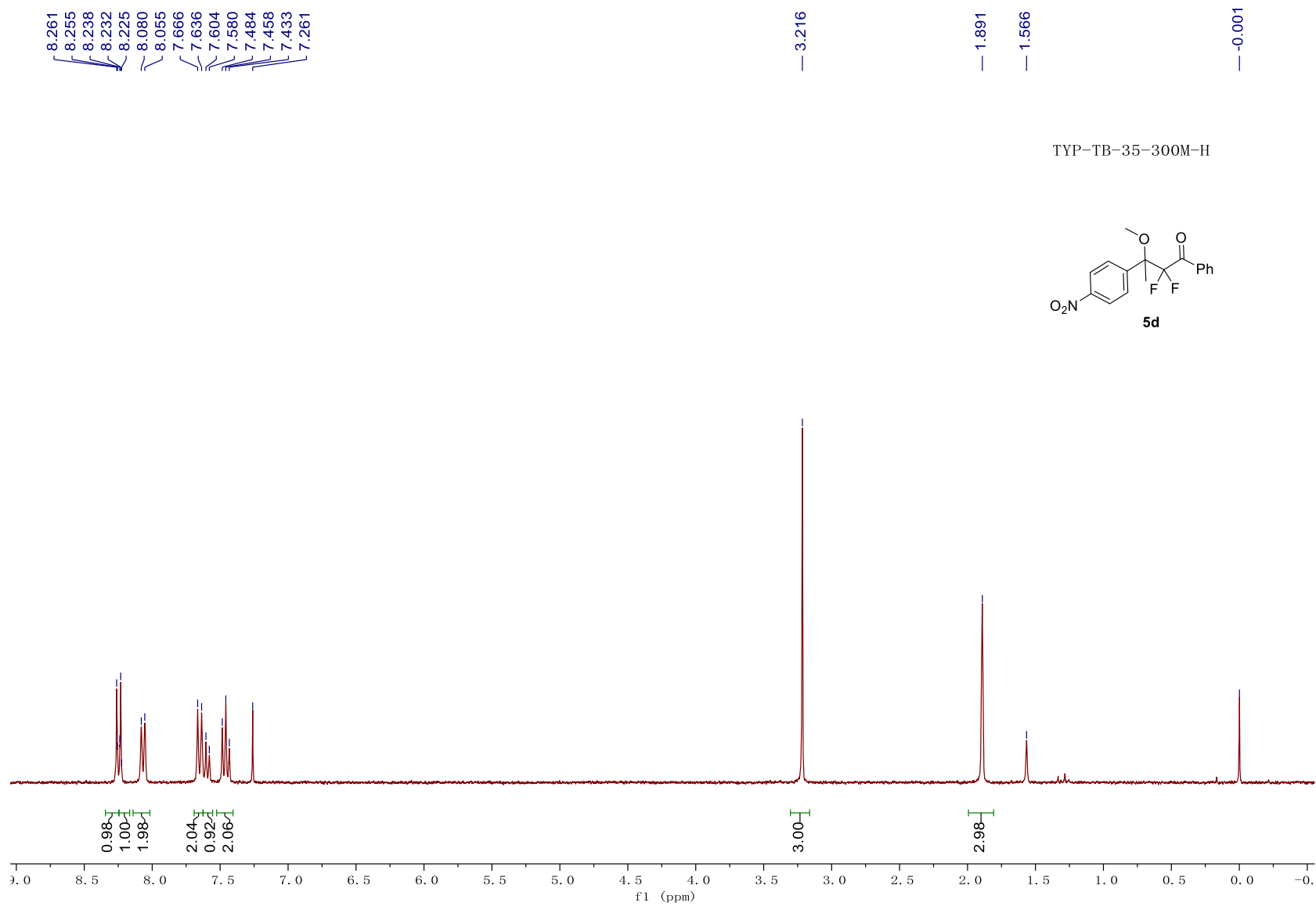


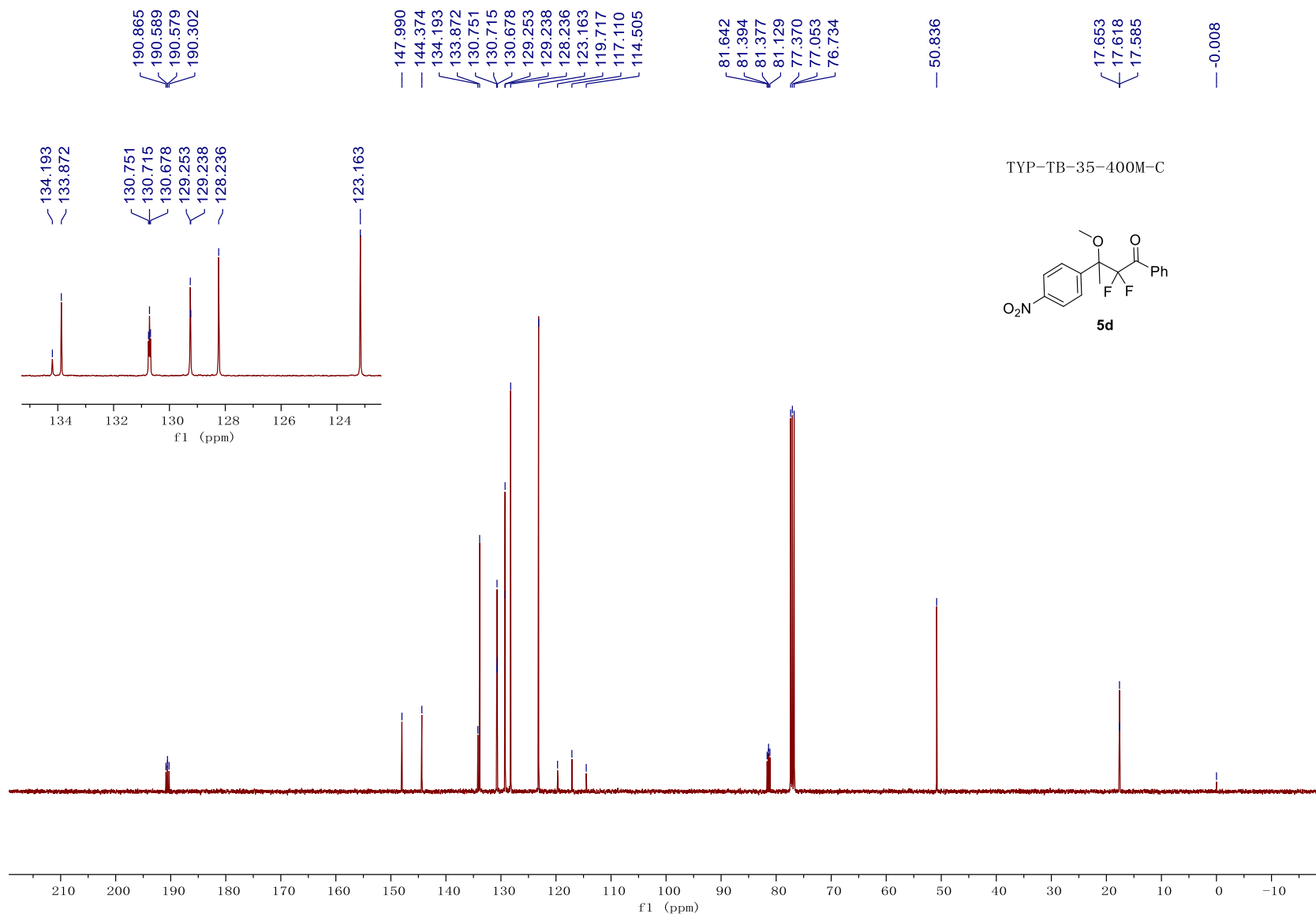
TYP-TB-47-300M-F



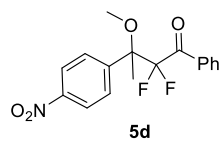
-107.416
-108.315
-108.971
-109.871







TYP-TB-35-300M-F

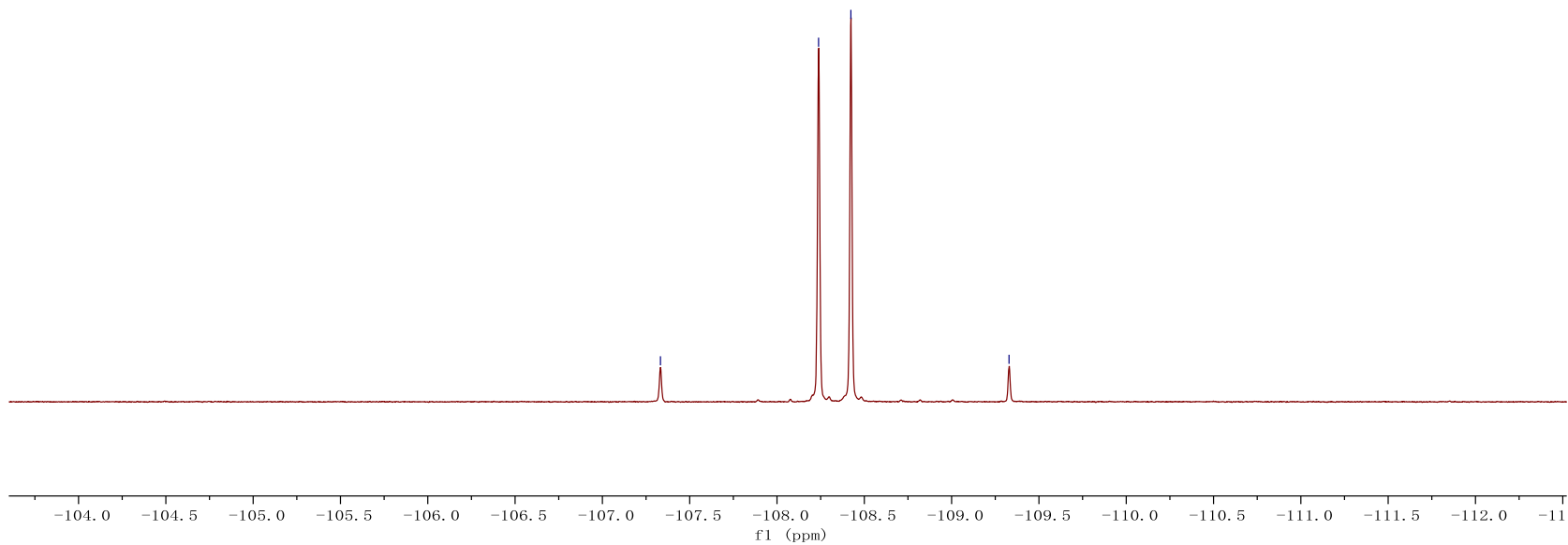


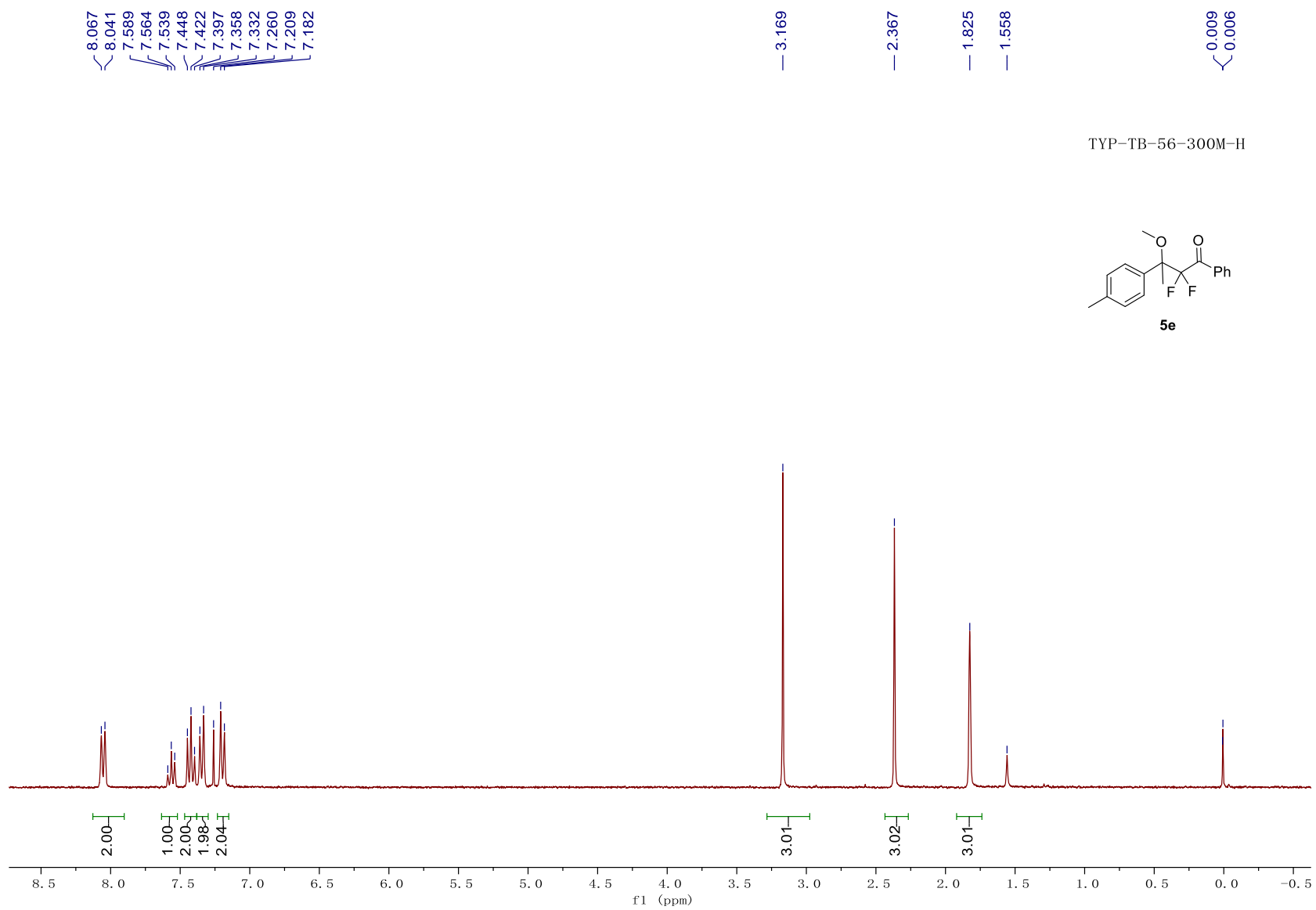
— -107.332

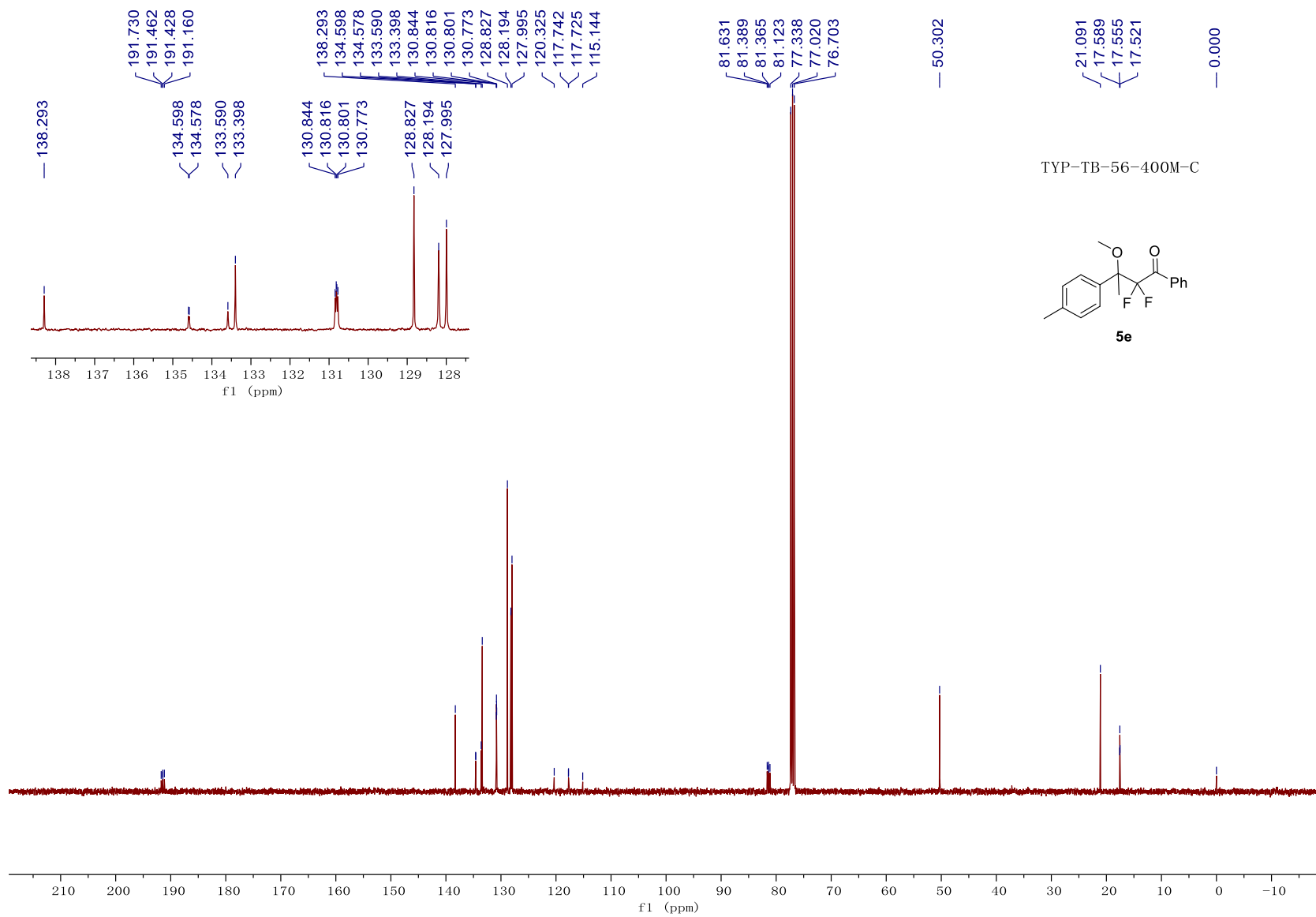
— -108.238

— -108.423

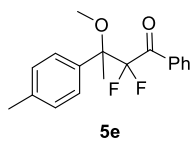
— -109.329



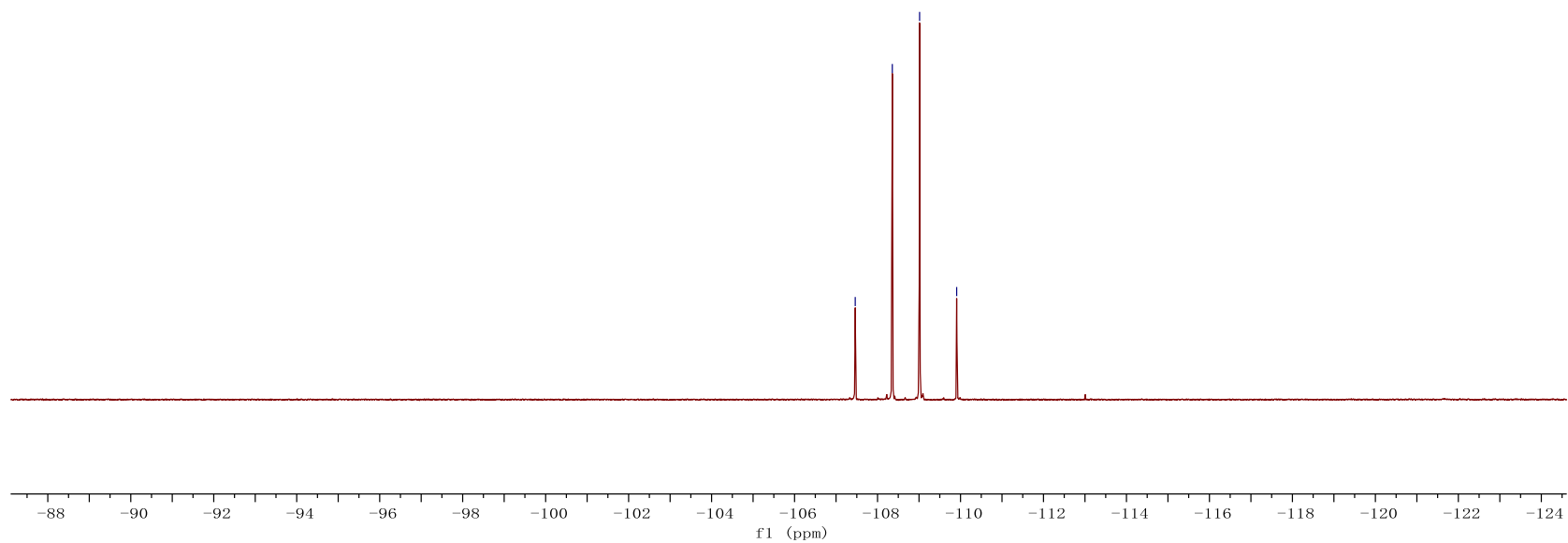


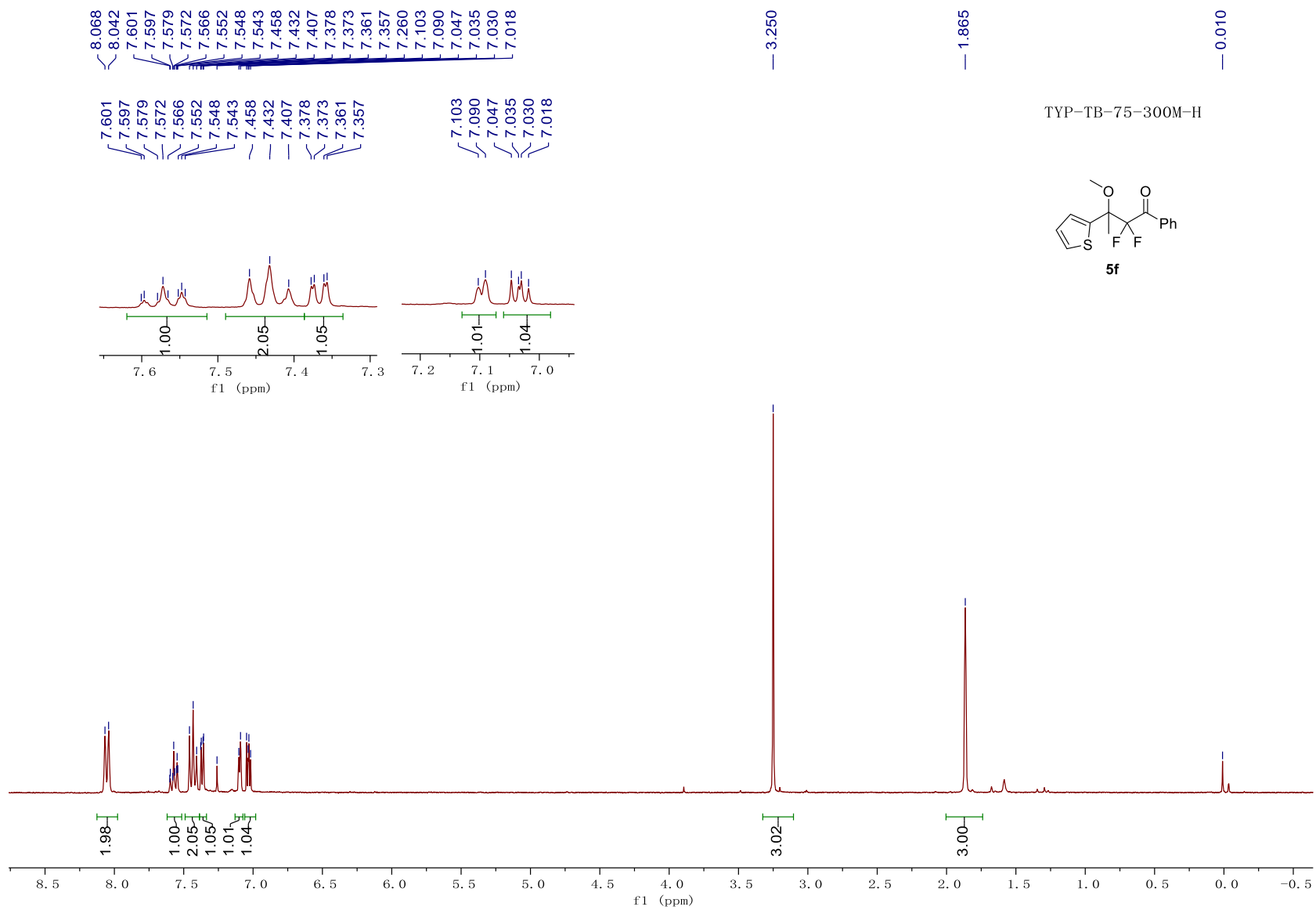


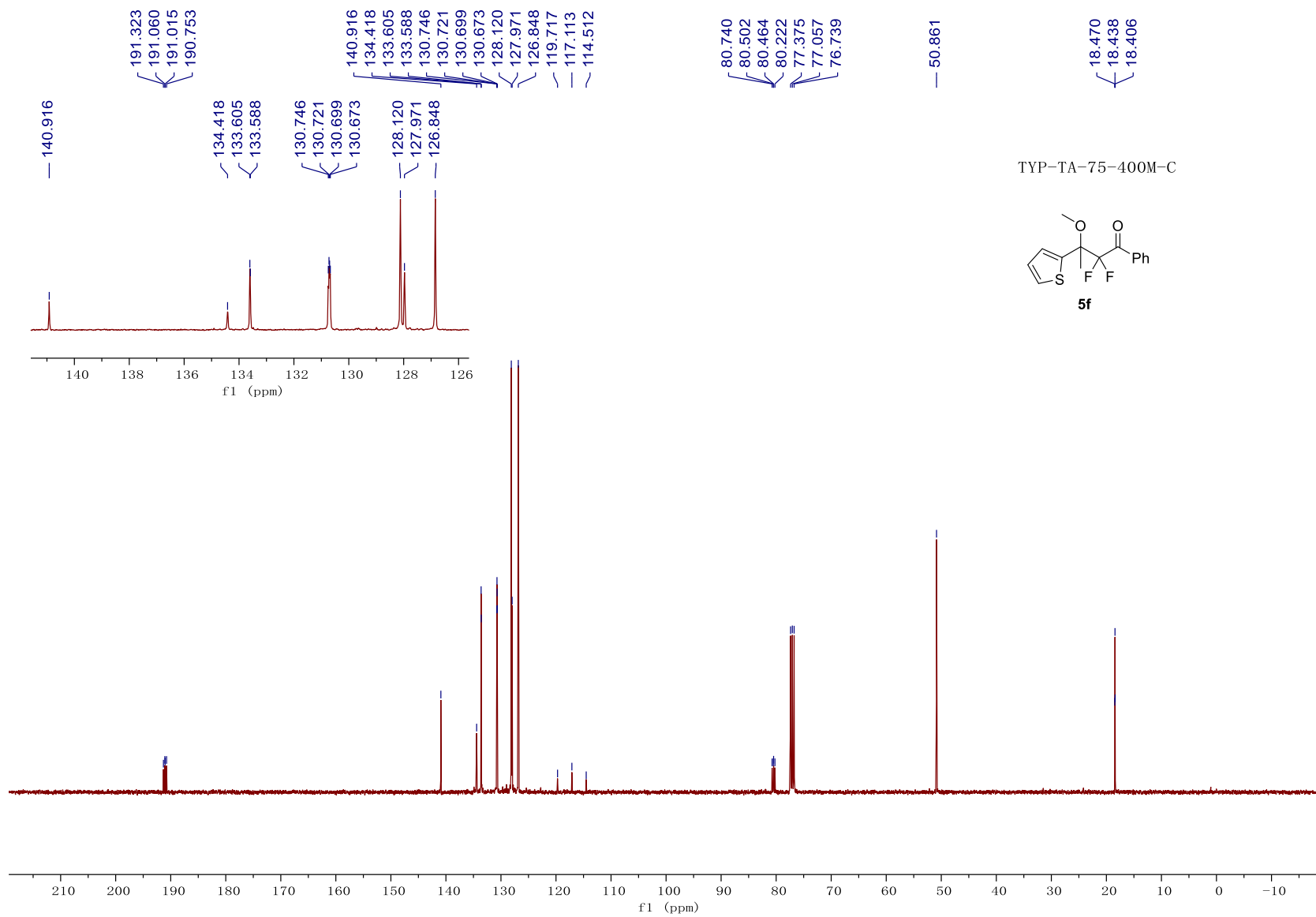
TYP-TB-56-300M-F



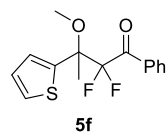
-107.462
-108.356
-109.014
-109.907



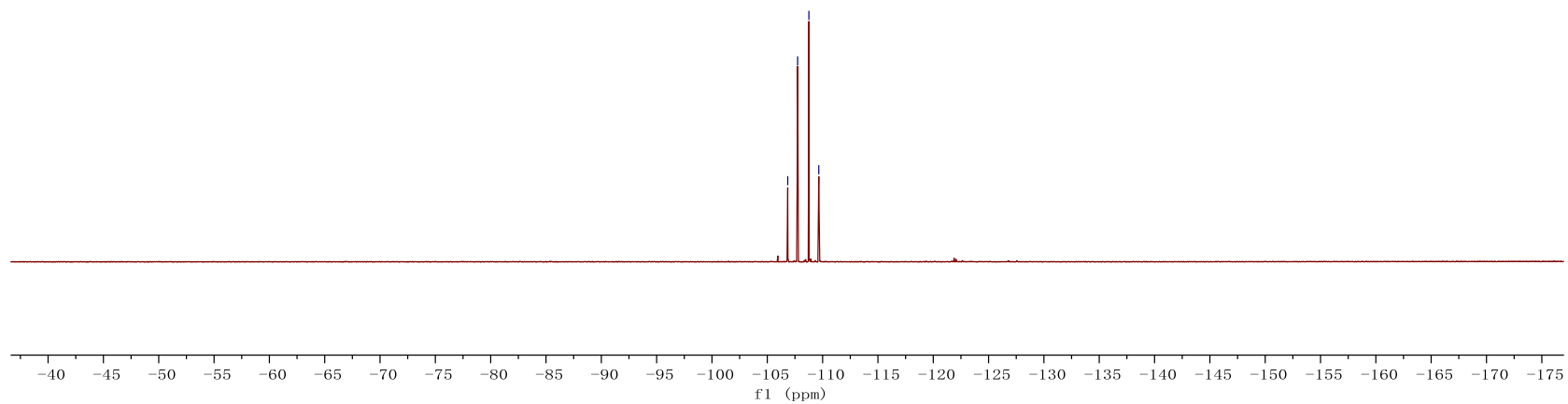


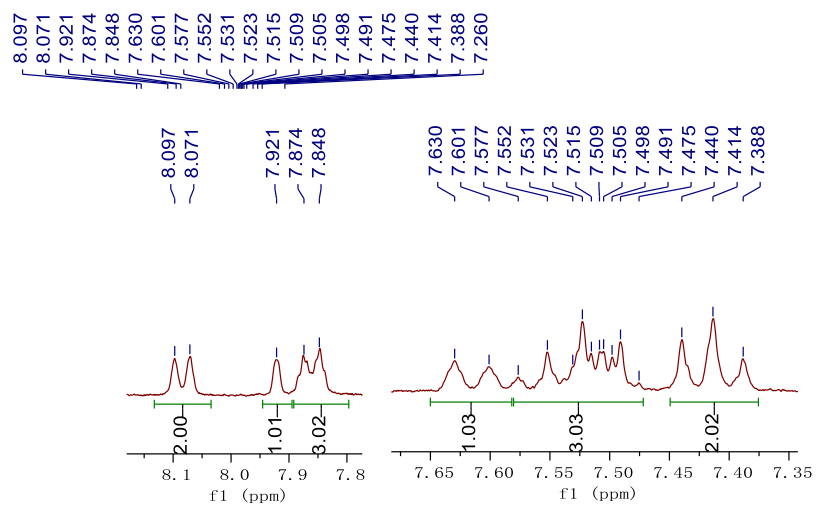


TYP-TB-75-300M-F



-106.847
-107.741
-108.759
-109.654





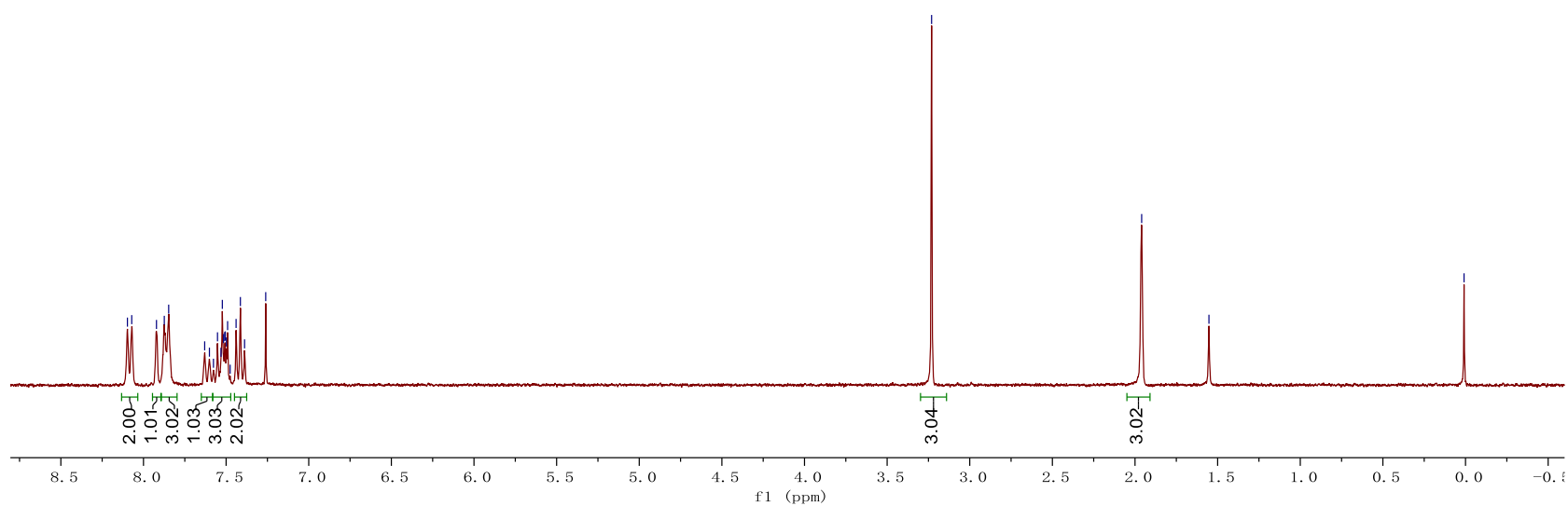
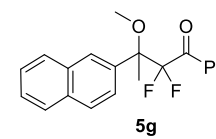
— 3.231

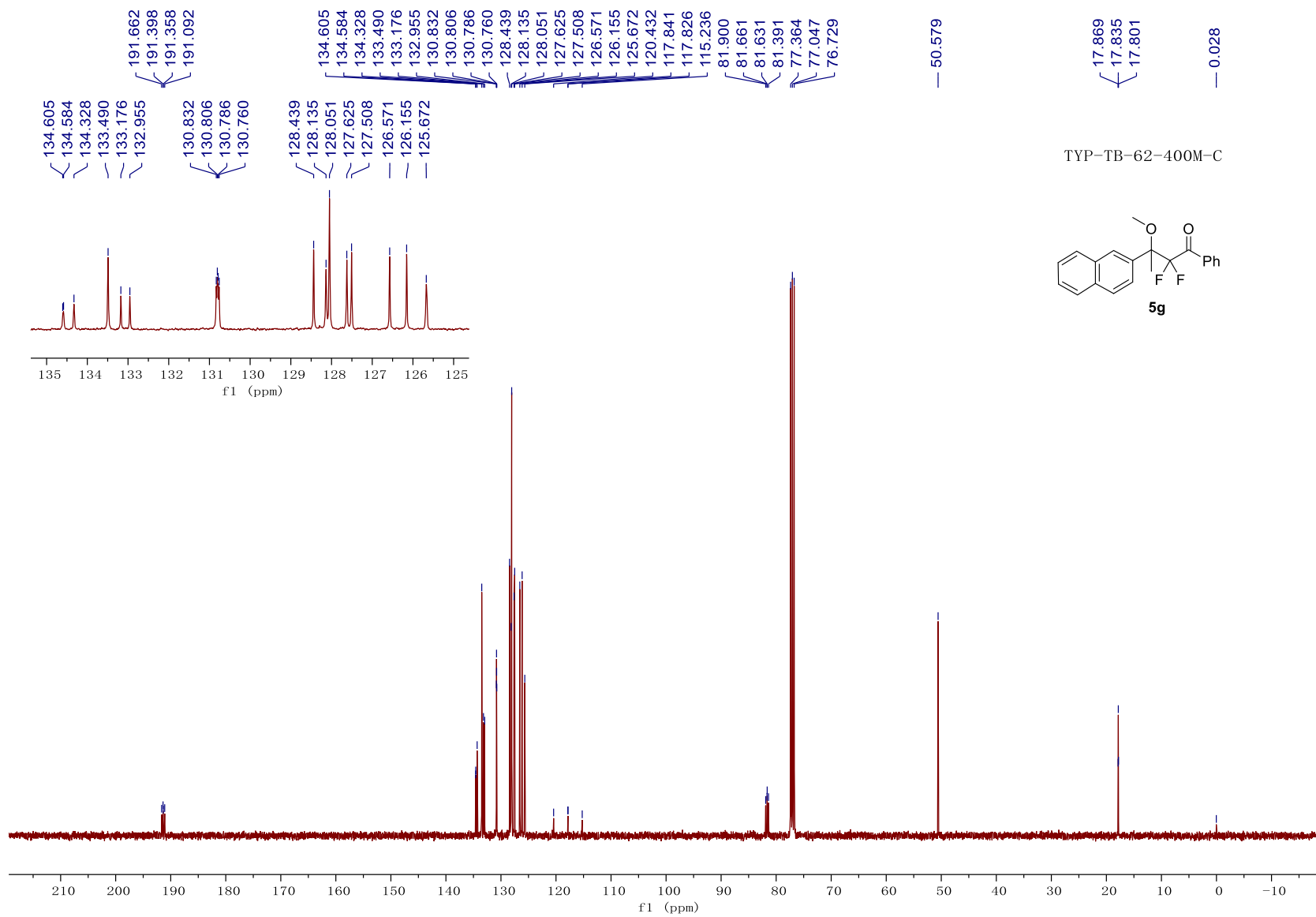
— 1.960

— 1.553

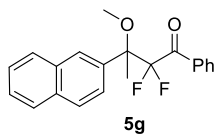
— 0.009

TYP-TB-62-300M-H

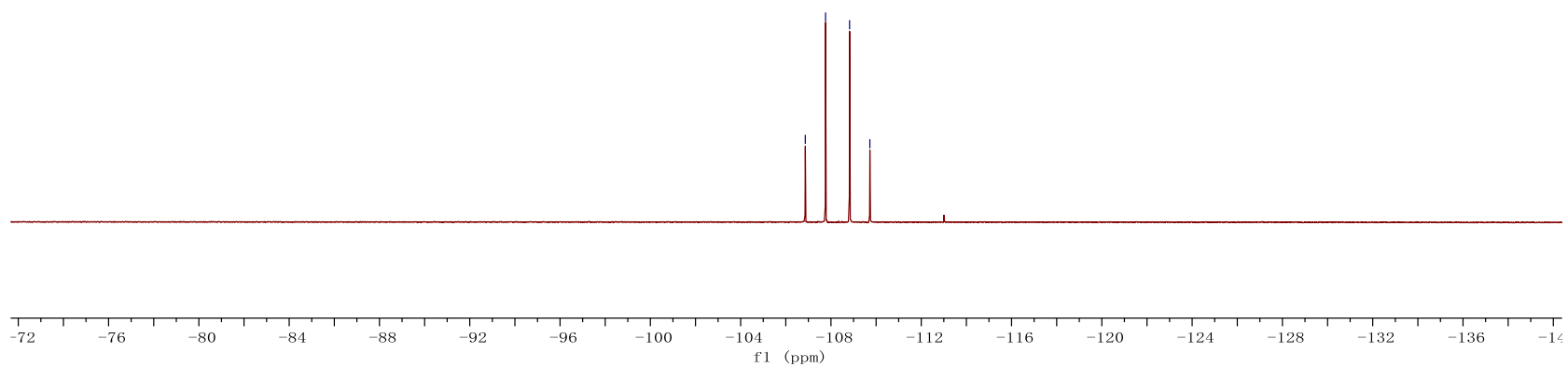


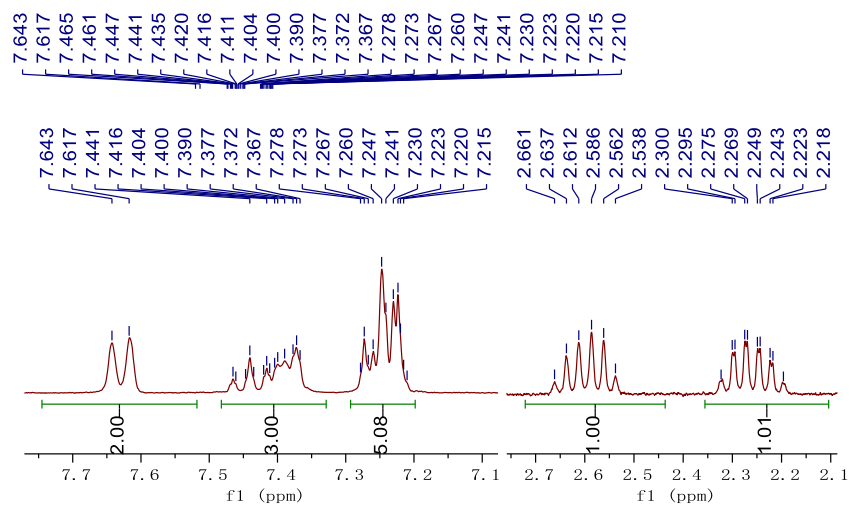


TYP-TB-62-300M-F

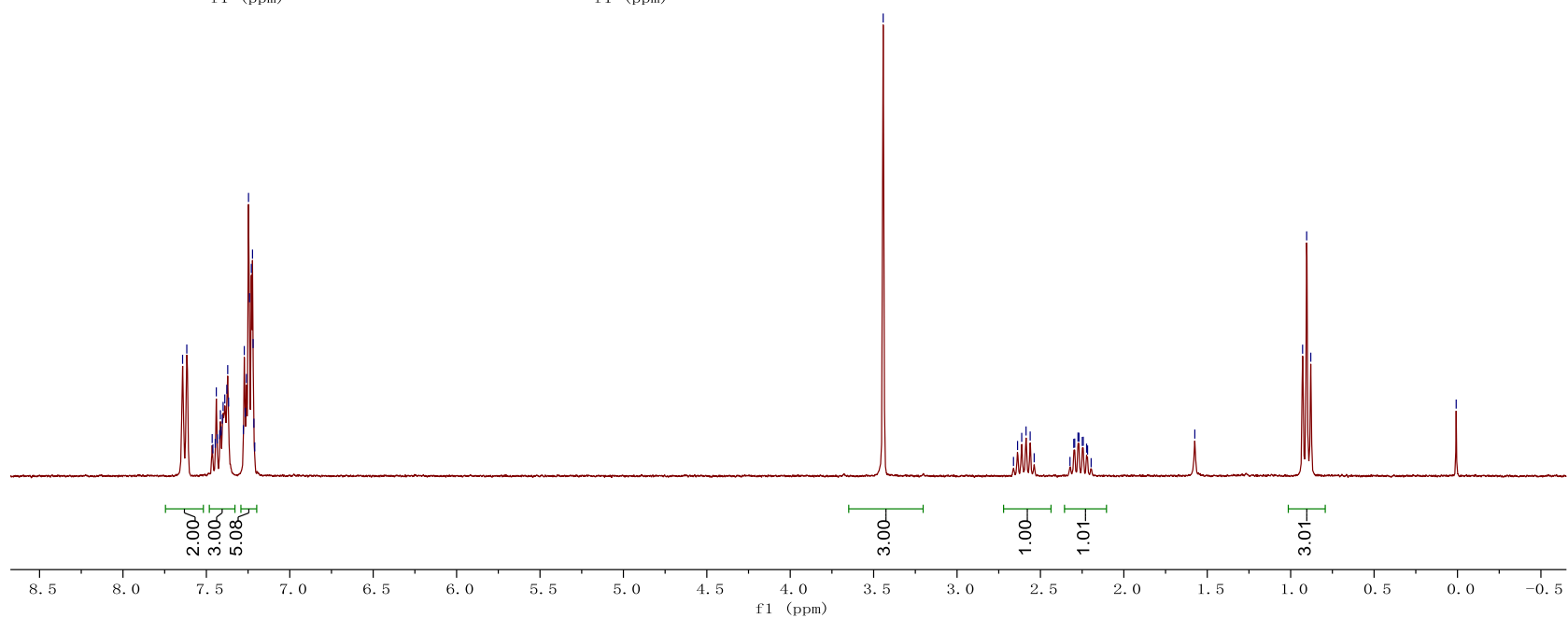
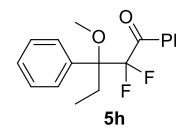


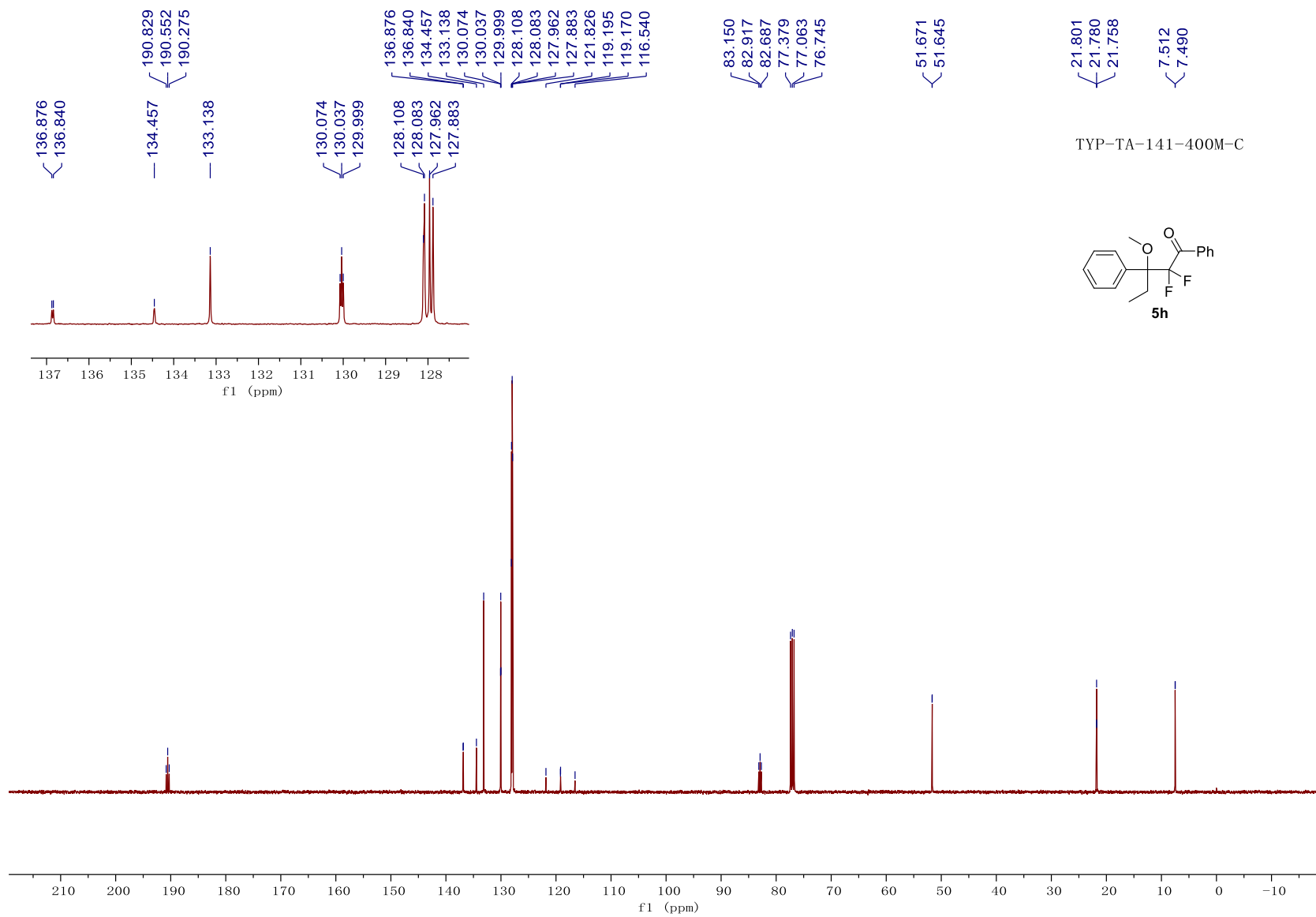
-106.863
-107.761
-108.825
-109.724



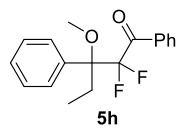


TYP-TA-141-300M-H

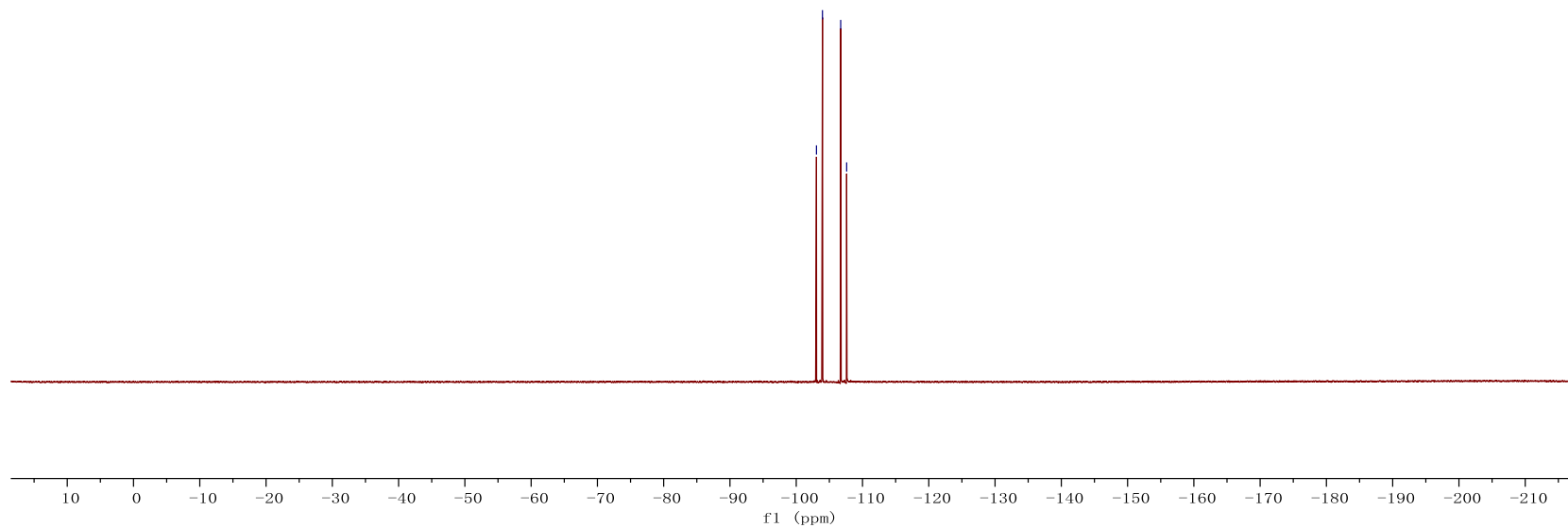


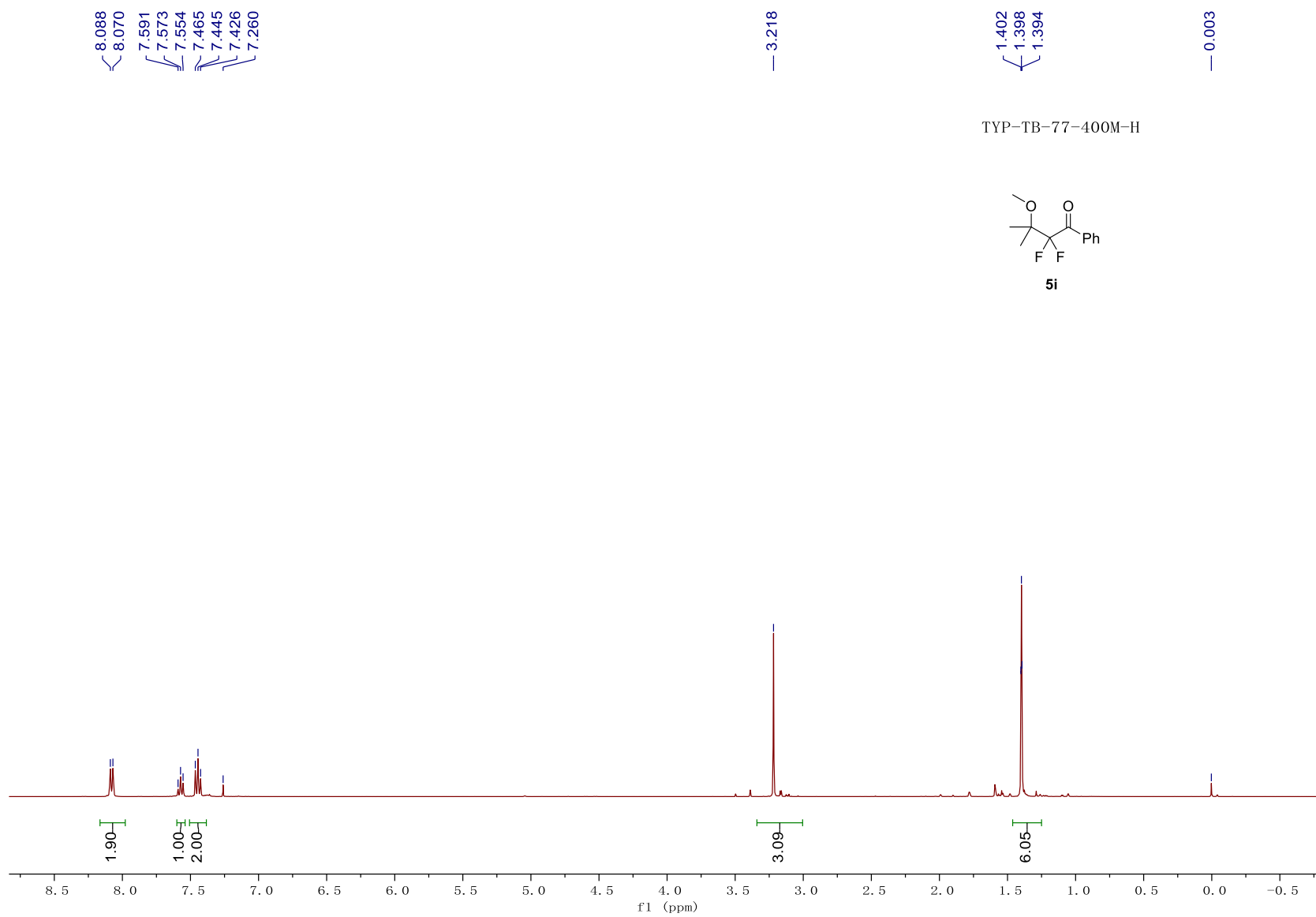


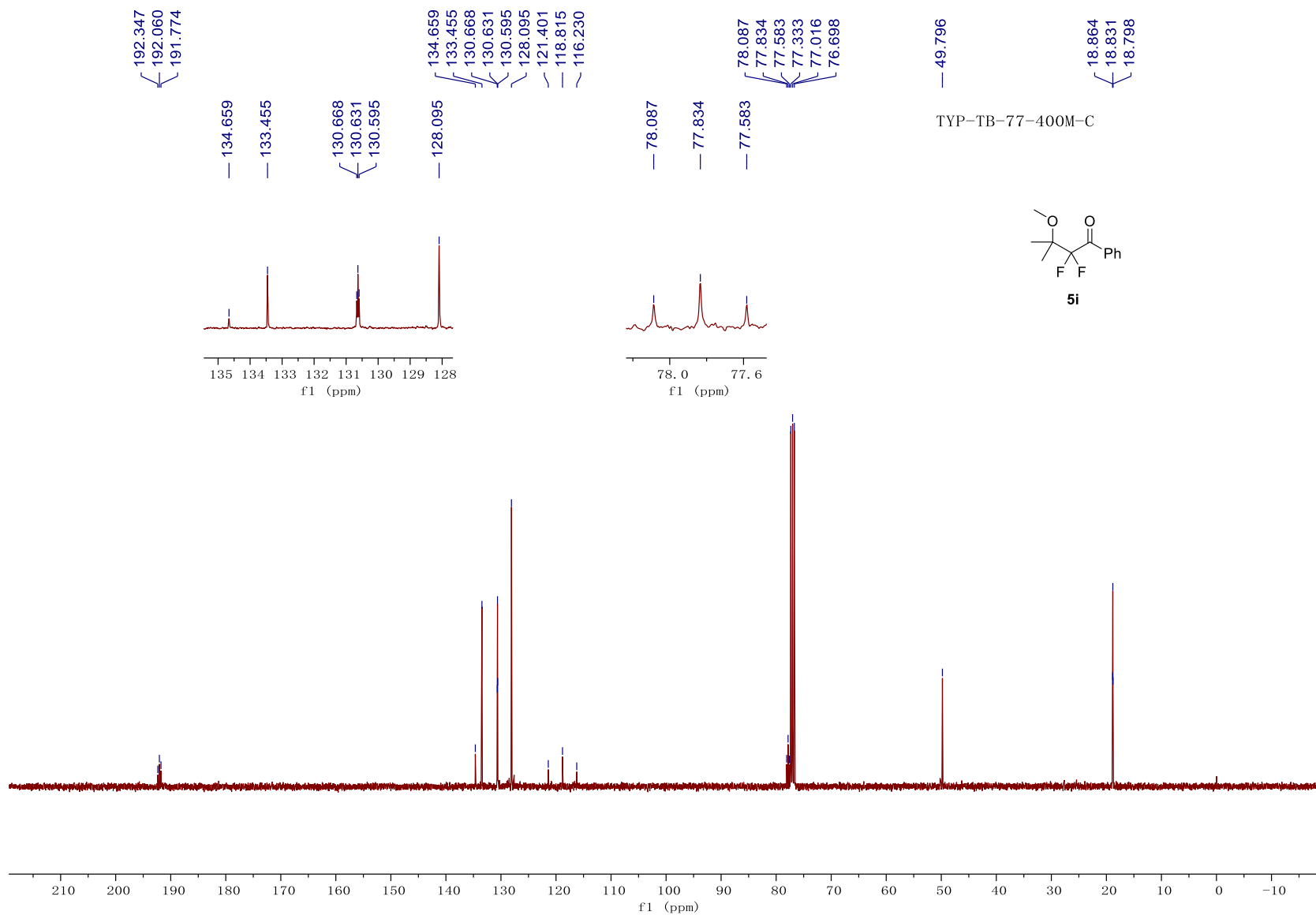
TYP-TA-141-300M-F



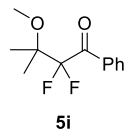
-103.053
-103.955
-106.706
-107.608



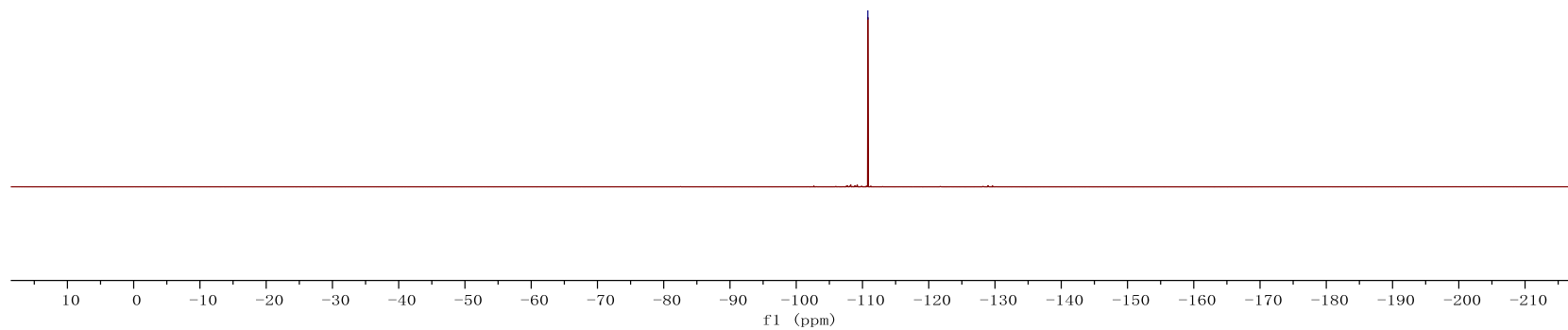




TYP-TB-77-400M-F



-110.807

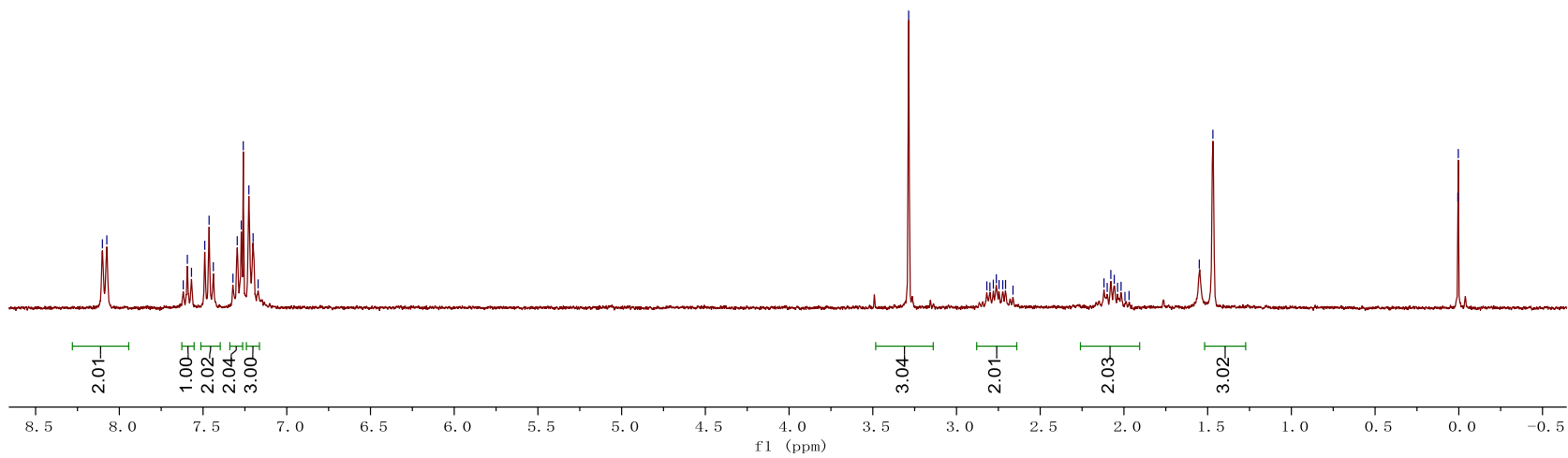
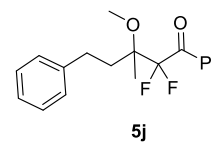


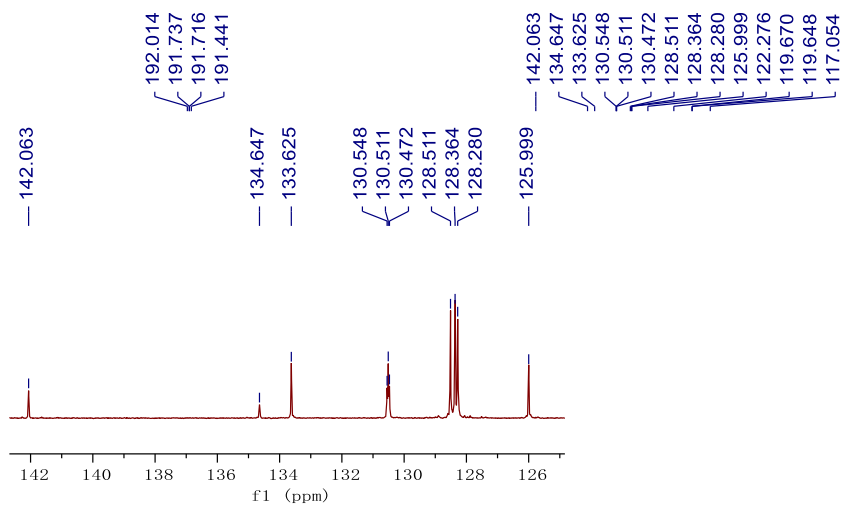
8.101
8.075
7.618
7.594
7.569
7.490
7.464
7.439
7.321
7.296
7.272
7.260
7.226
7.201
7.171

3.286
2.819
2.800
2.780
2.762
2.746
2.724
2.707
2.663
2.119
2.100
2.078
2.058
2.038
2.017
1.994
1.969
1.550
1.469

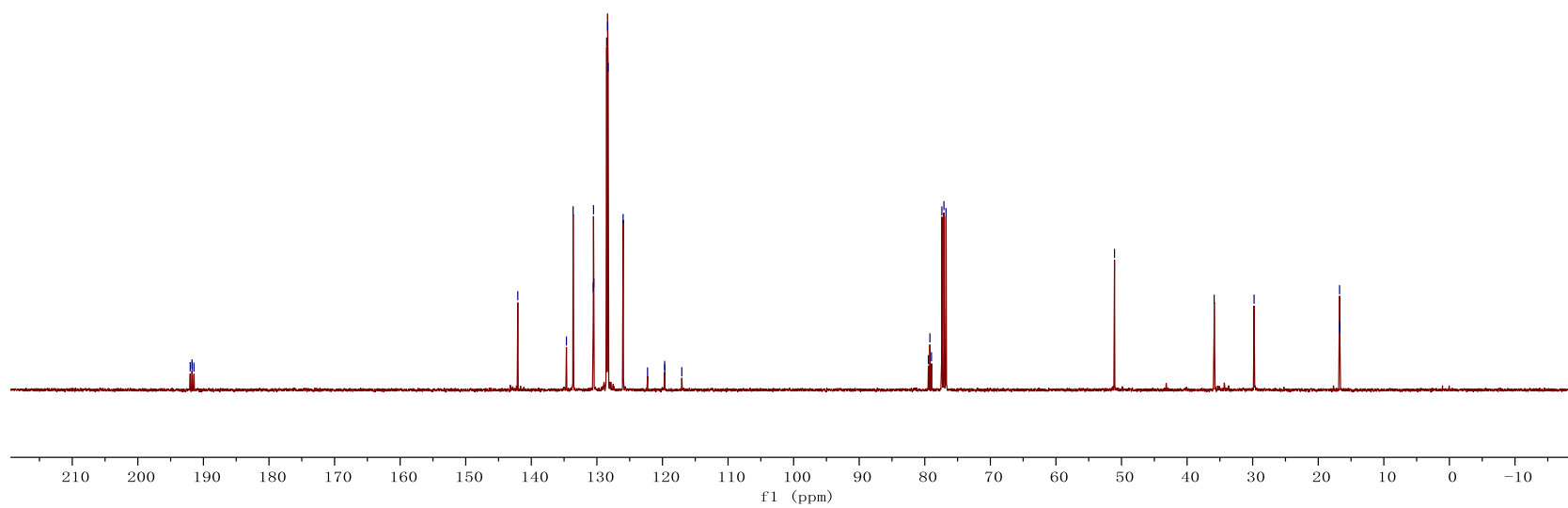
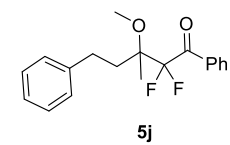
0.006
0.003

TYP-TB-53-300M-H

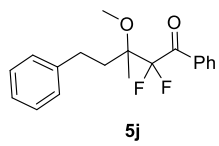




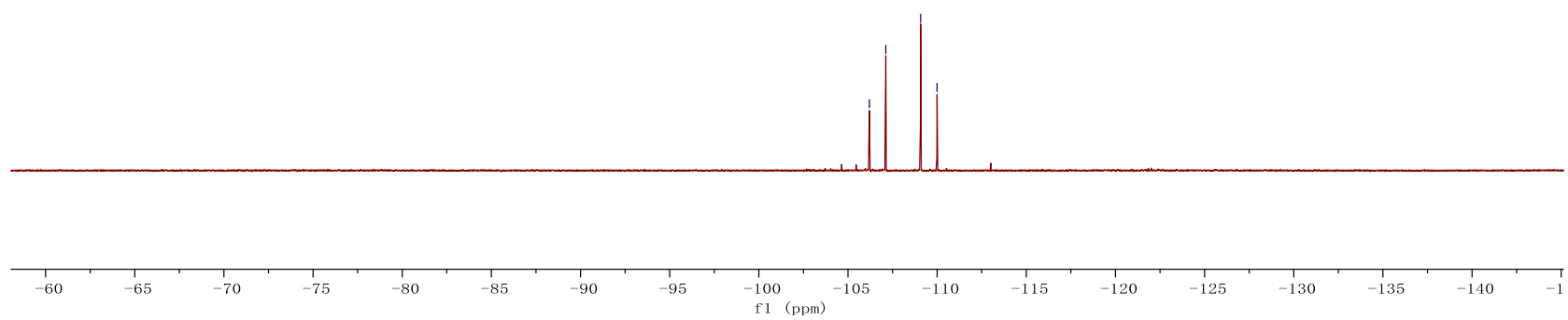
TYP-TB-53-400M-C

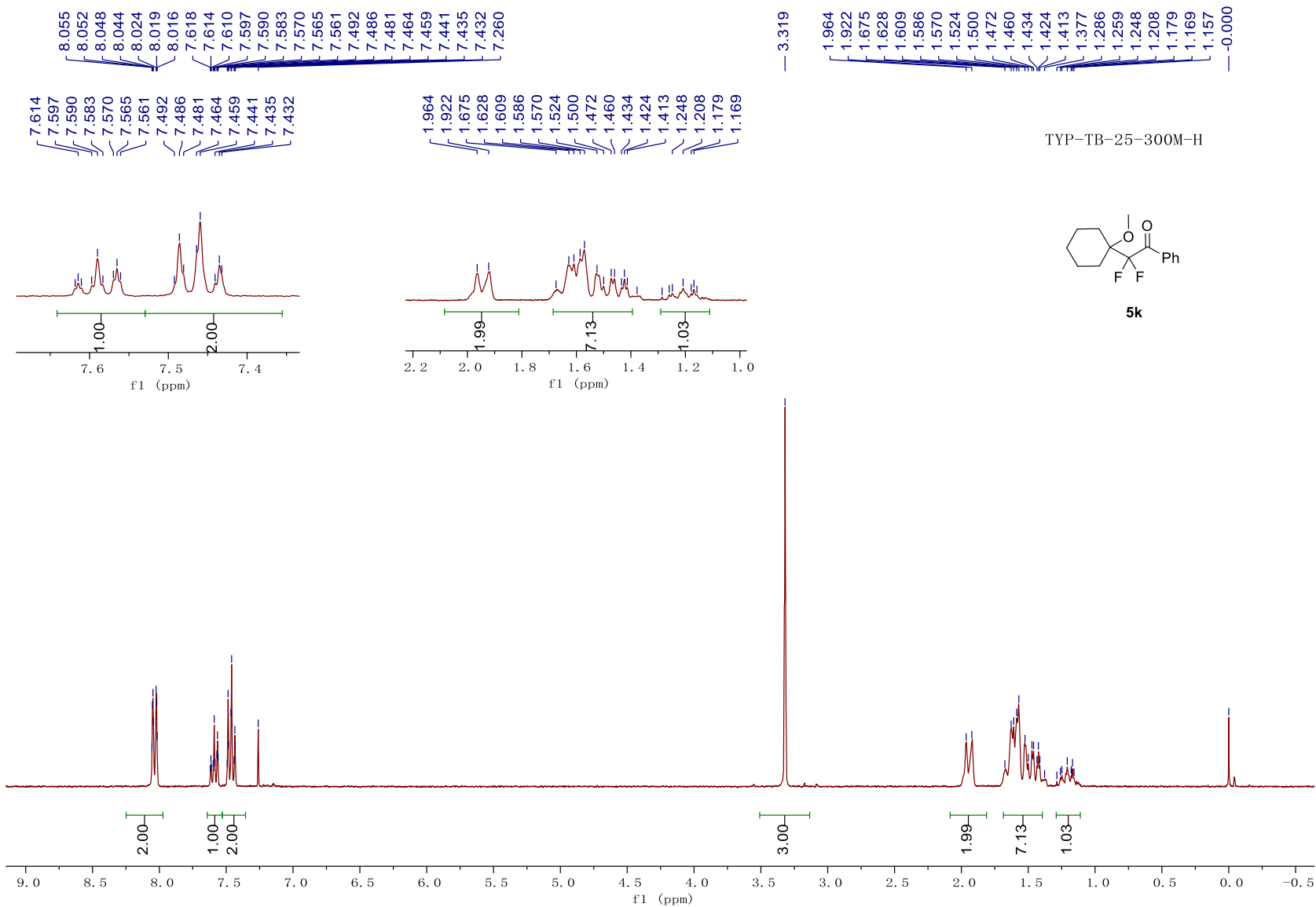


TYP-TB-53-300M-F



-106.199
-107.121
-109.075
-109.996





TYP-TB-25-300M-H

5k

191.521
191.243
190.964

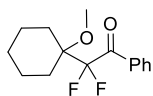
135.104
135.089
135.071
133.543
129.913
129.869
129.829
128.426
122.953
120.327
117.701

78.007
77.786
77.563
77.404
77.087
76.770

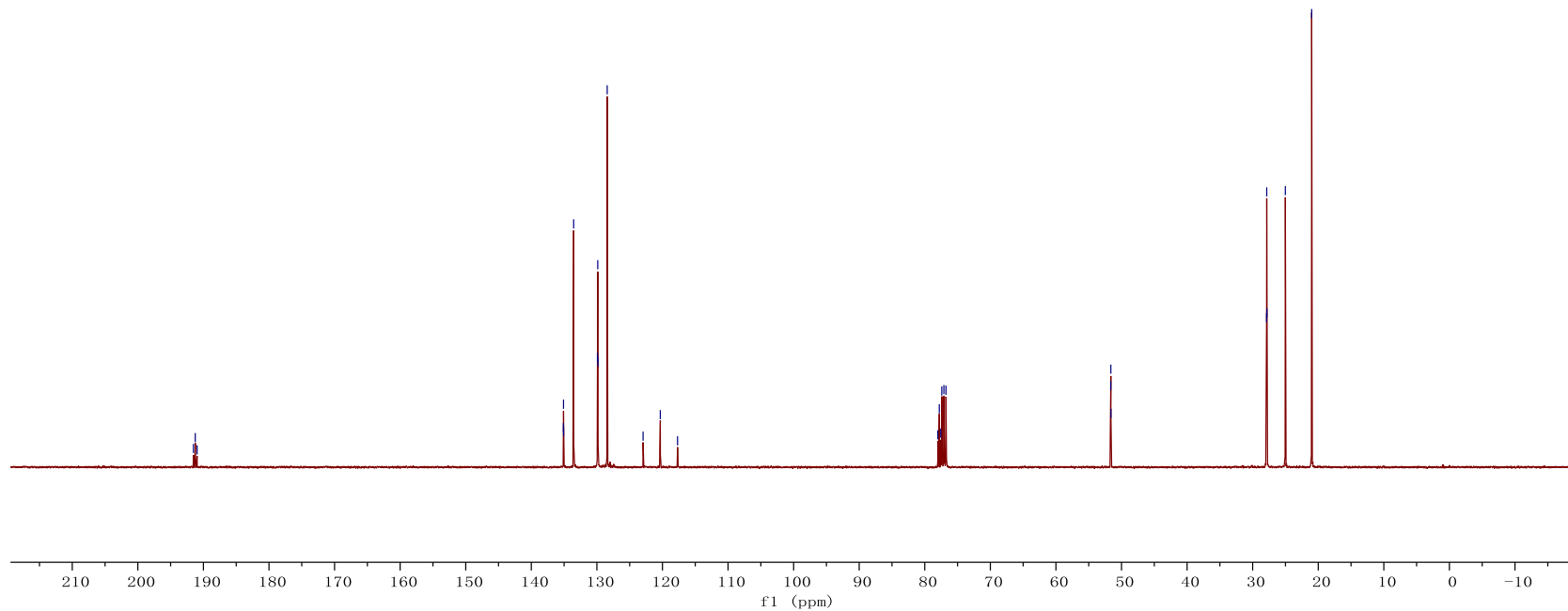
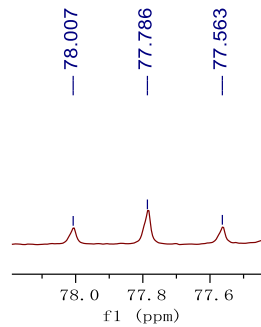
51.649
51.627
51.609

27.883
27.856
27.827
25.020
21.000

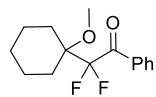
TYP-TB-25-400M-C



5k

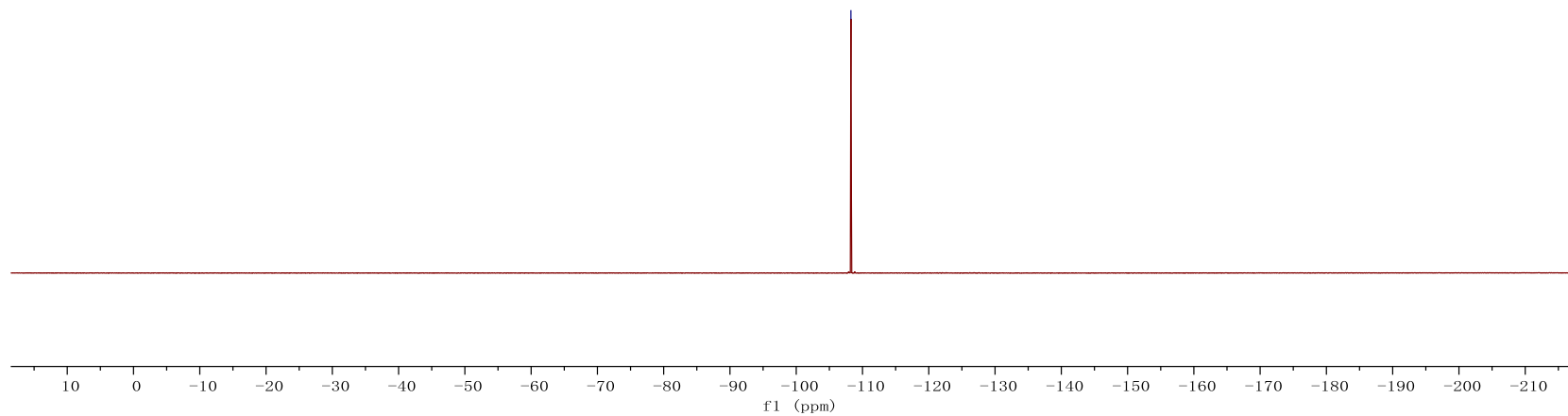


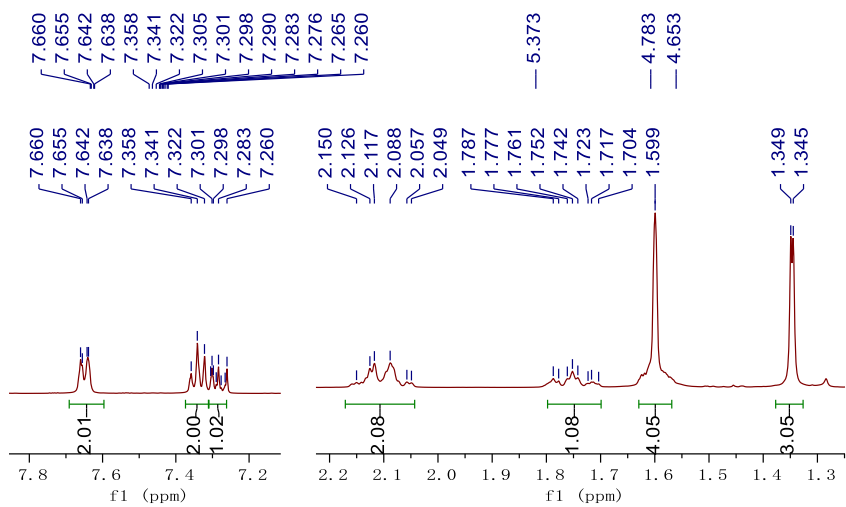
TYP-TB-25-300M-F



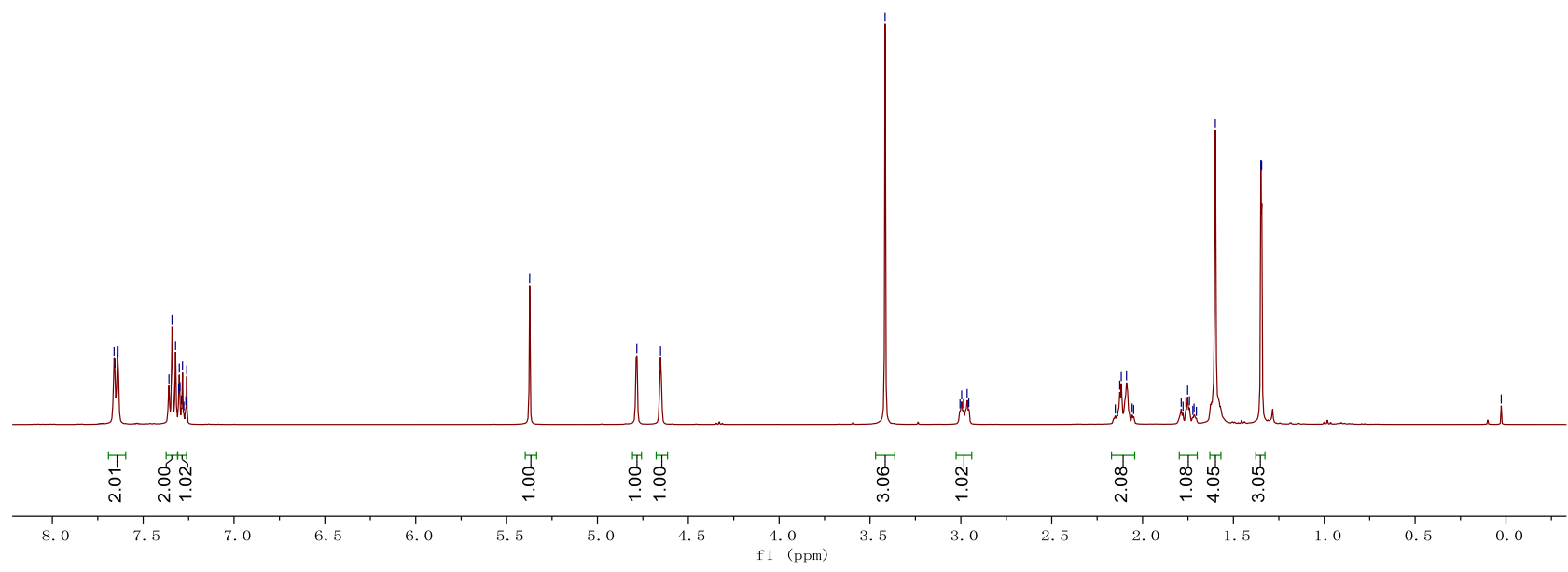
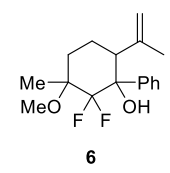
5k

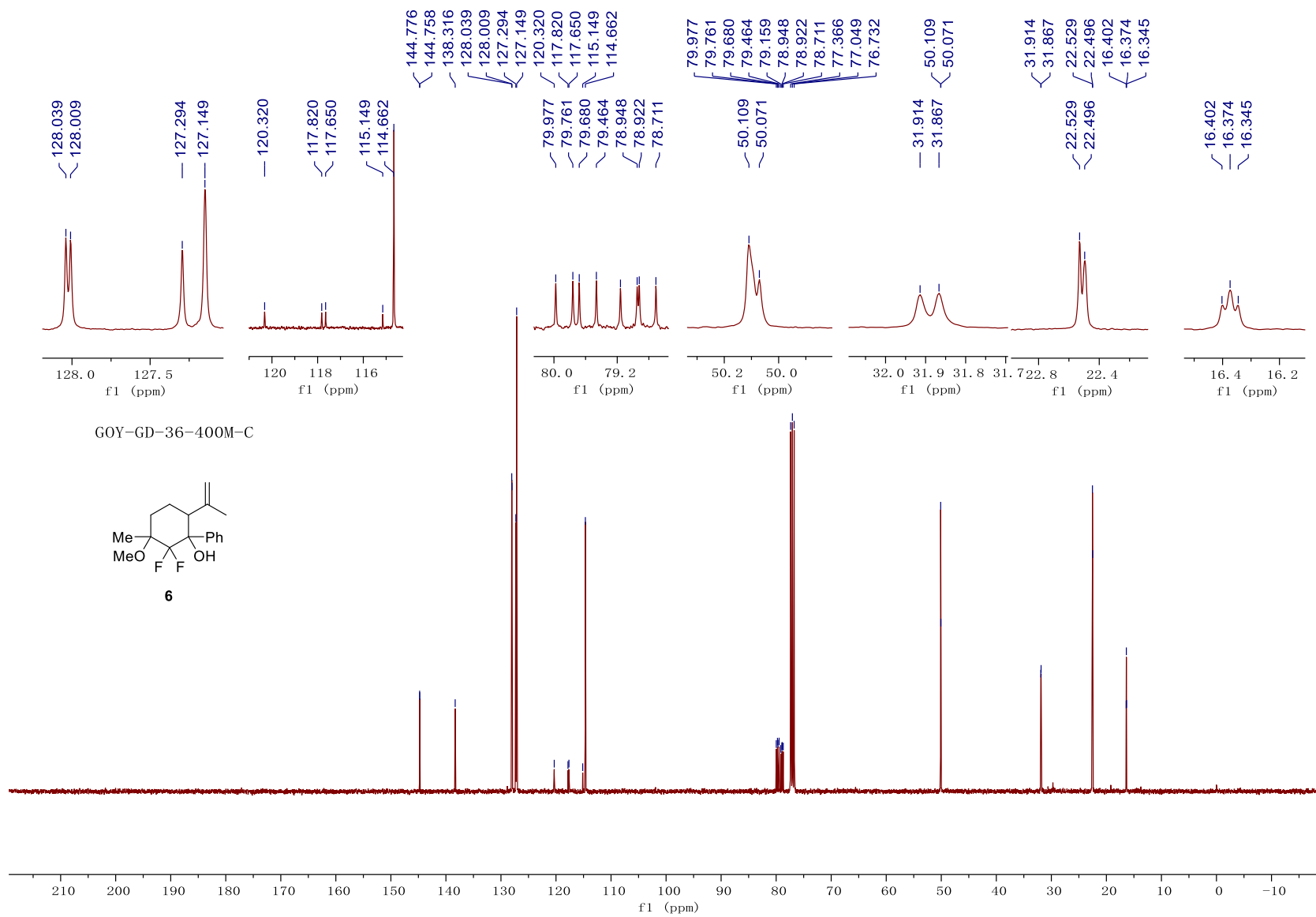
-108.252



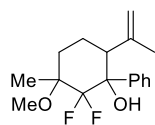


GOY-GD-36-400M-H





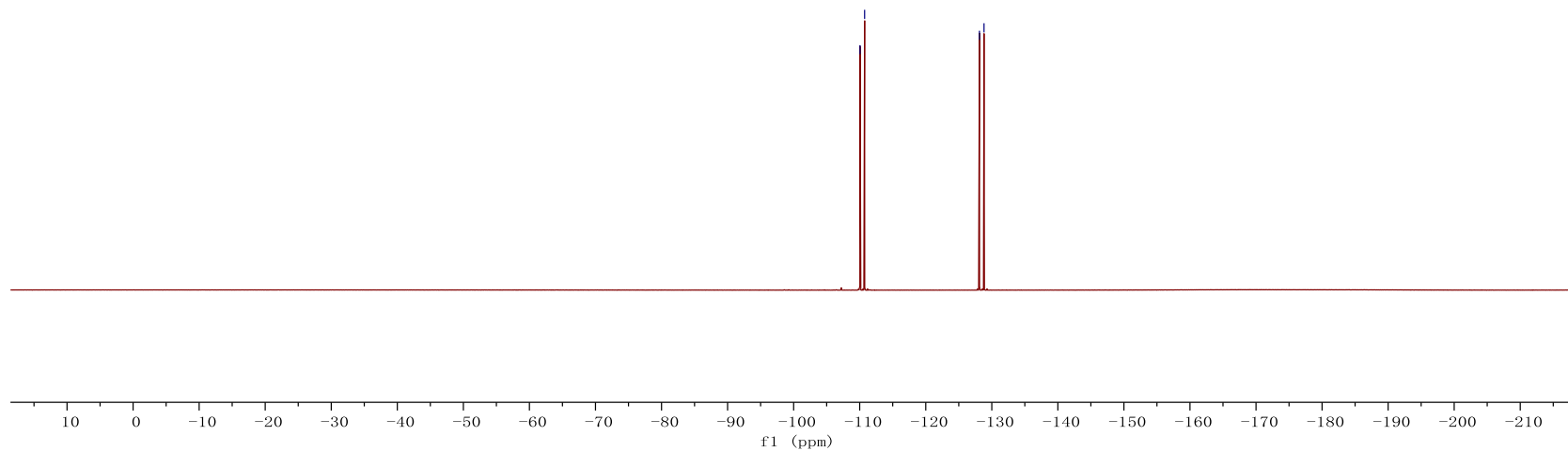
GOY-GD-36-400M-F



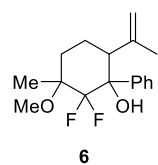
6

-110.051
-110.743

-128.130
-128.822



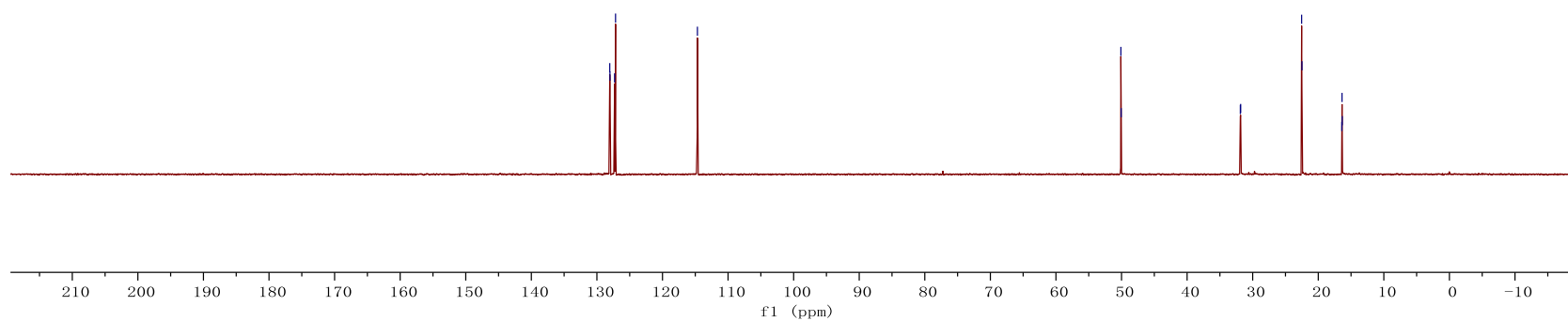
GOY-GD-36-400M-DEPT45



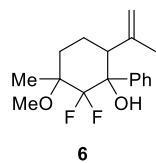
128.039
128.010
127.304
127.157
— 114.671

50.097
50.057

31.881
31.834
22.536
22.485
16.403
16.375
16.347

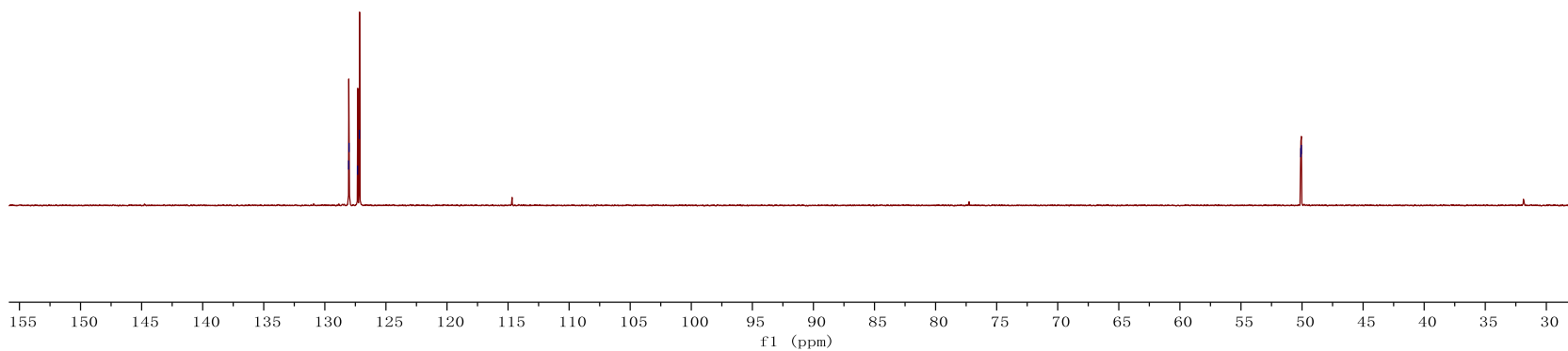


GOY-GD-36-400M-DEPT90

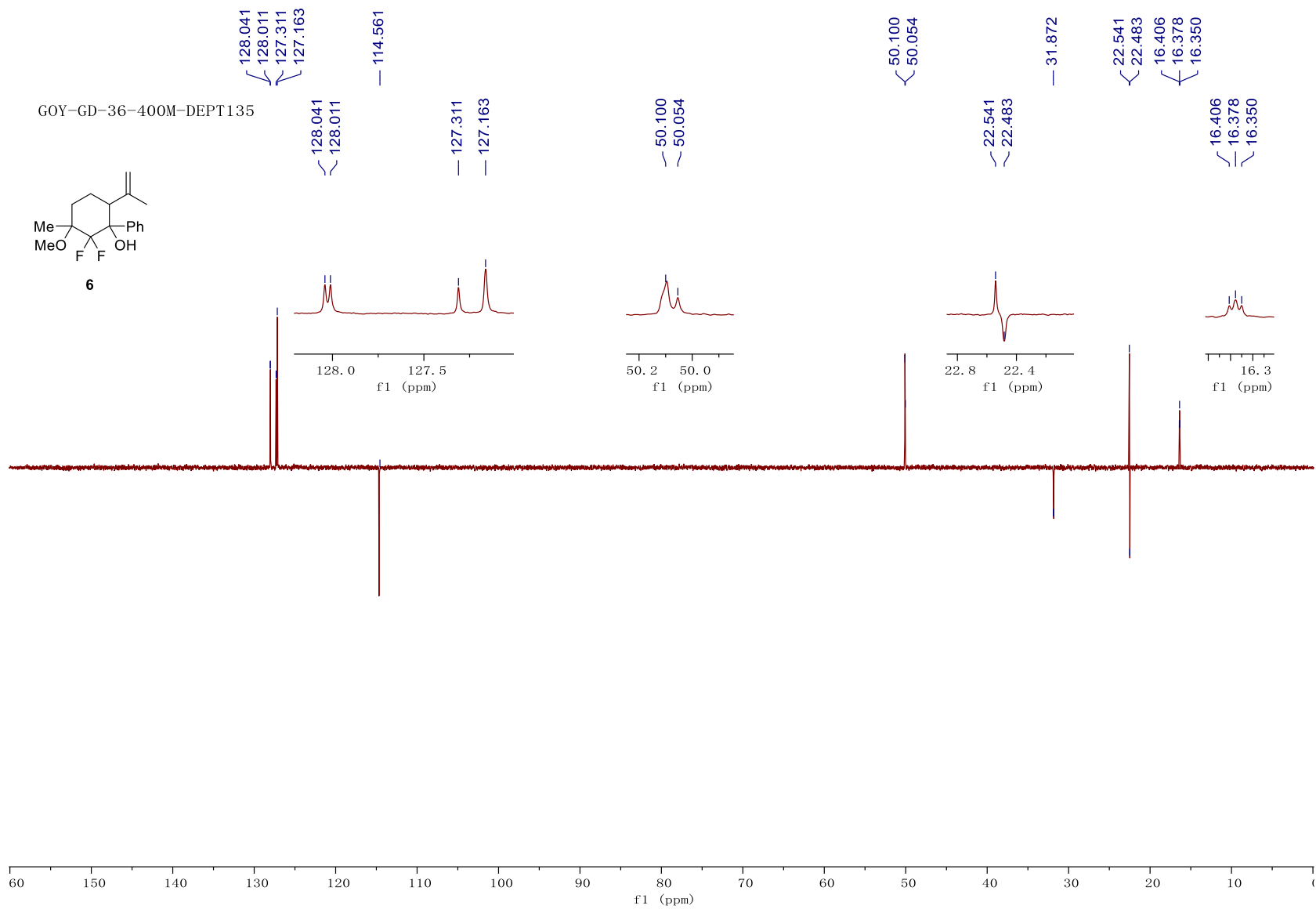
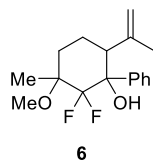


128.051
128.020
127.318
127.170

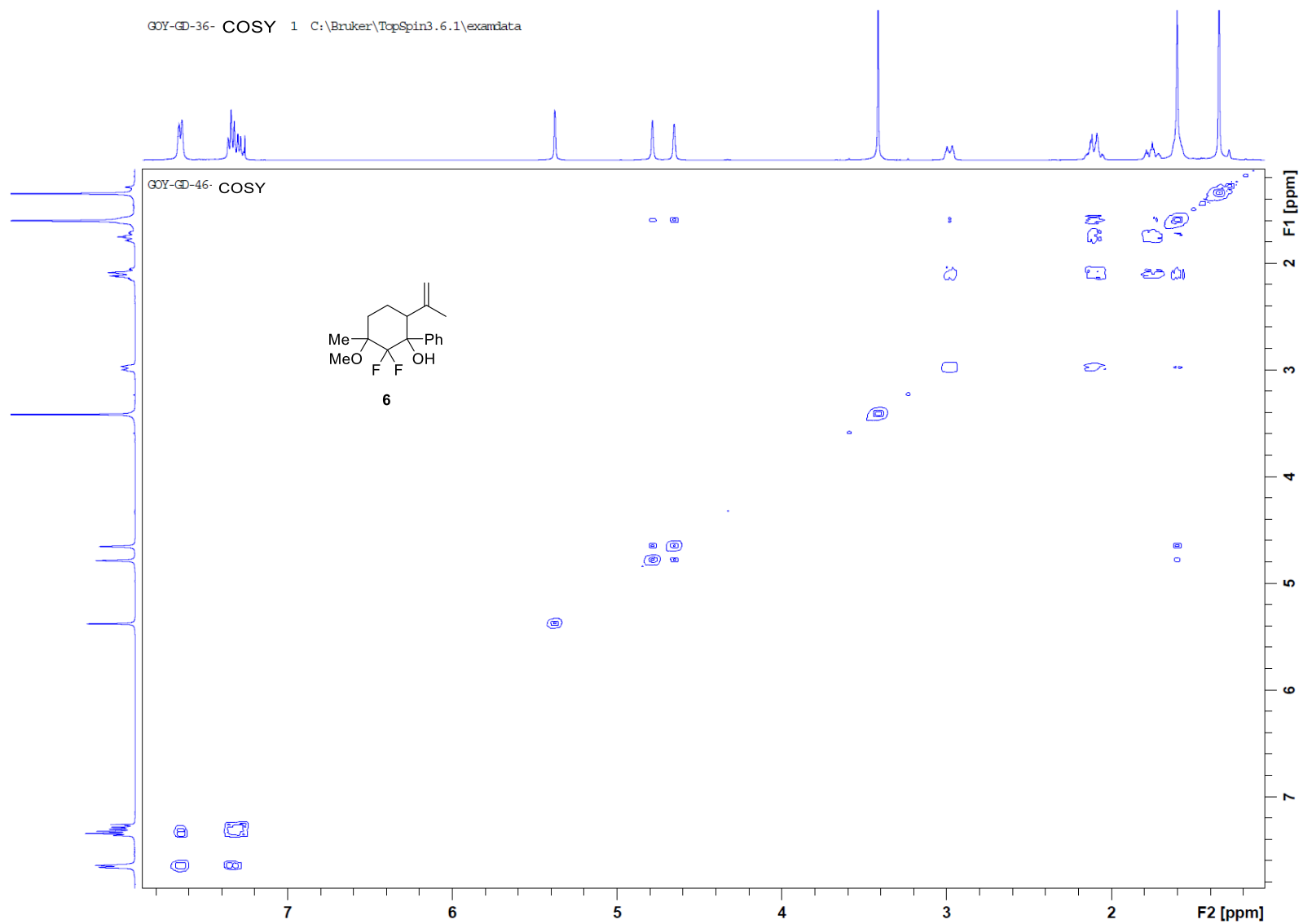
50.099
50.060



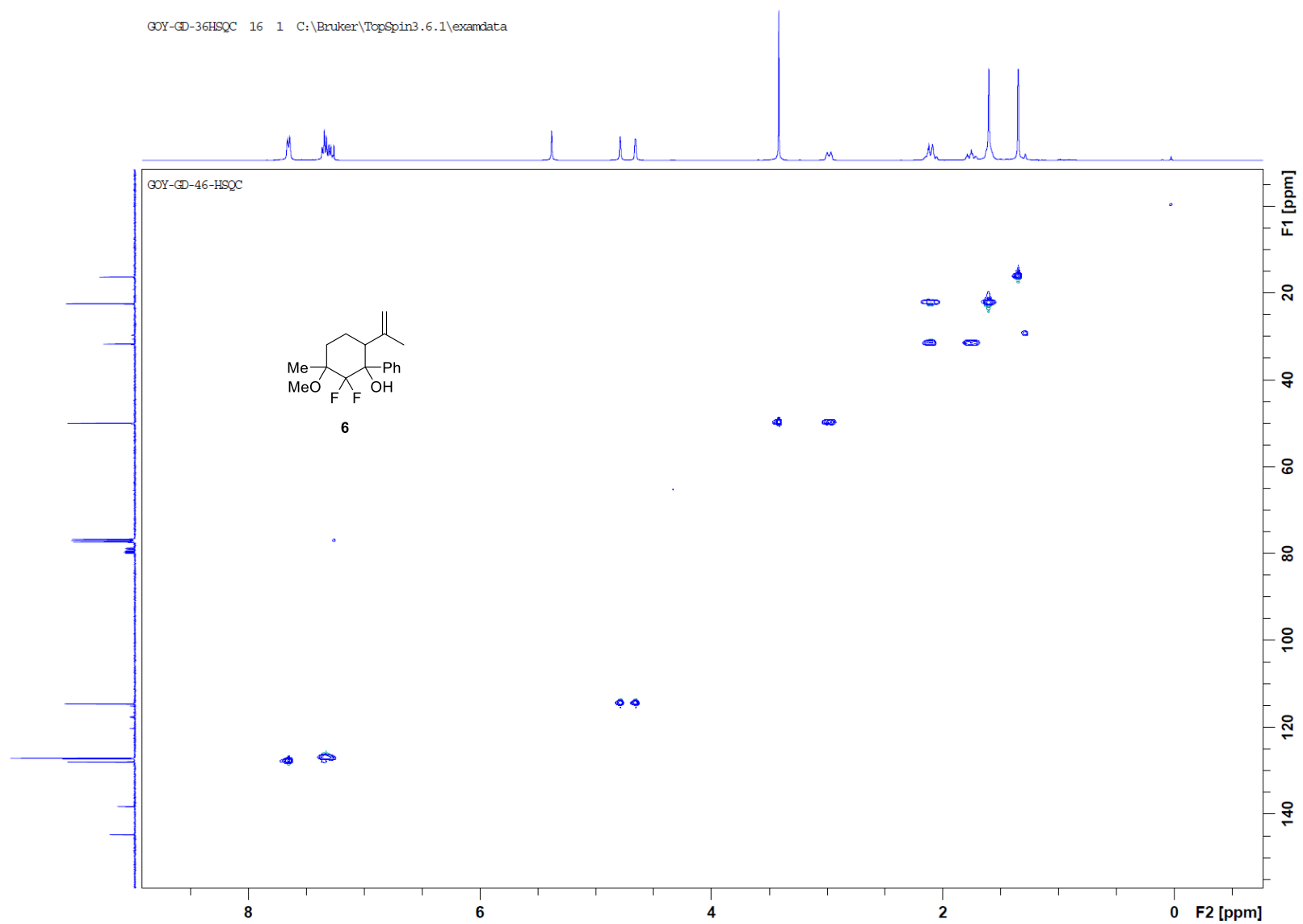
GOY-GD-36-400M-DEPT135



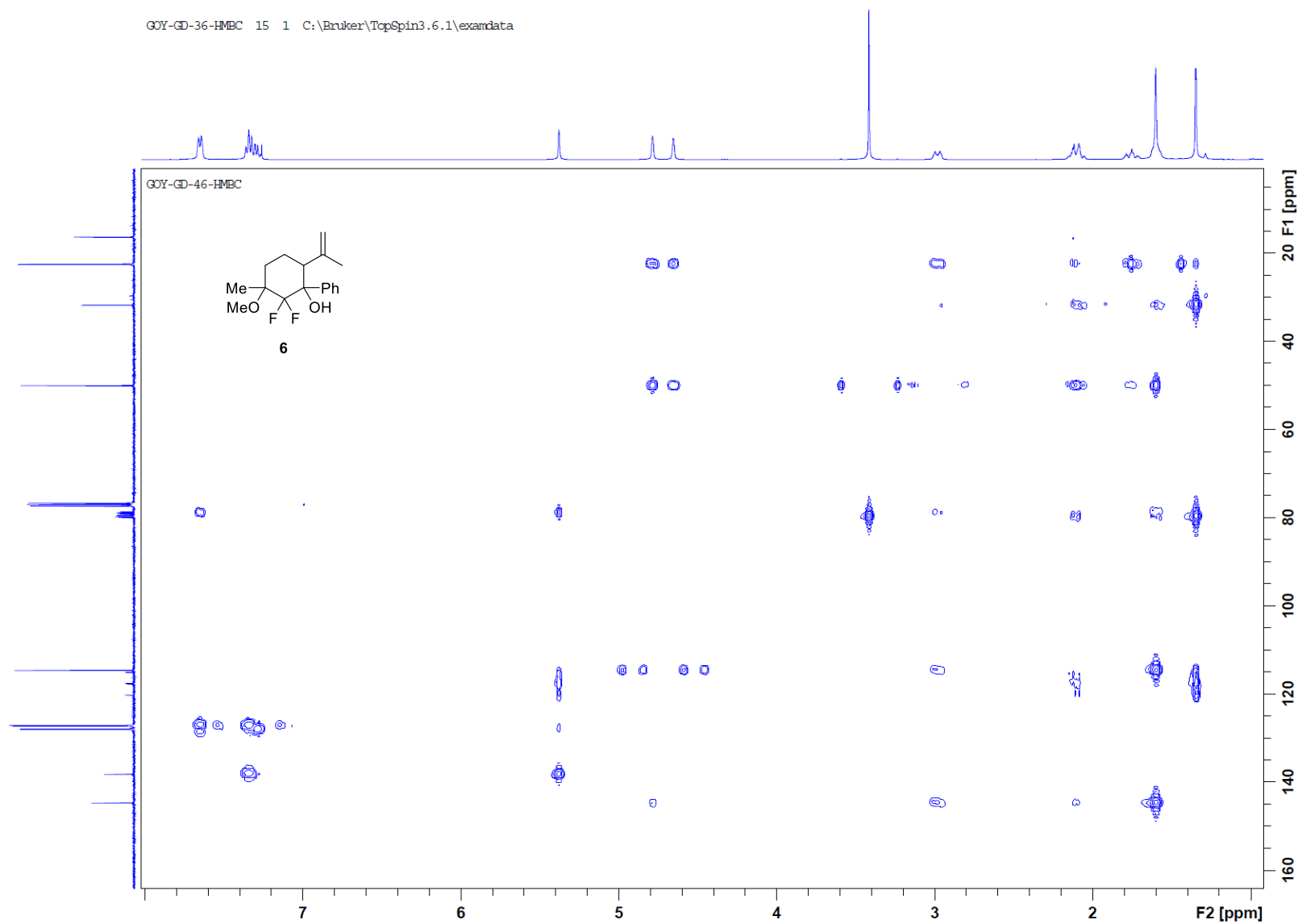
GOY-00-36- COSY 1 C:\Bruker\TopSpin3.6.1\exdata

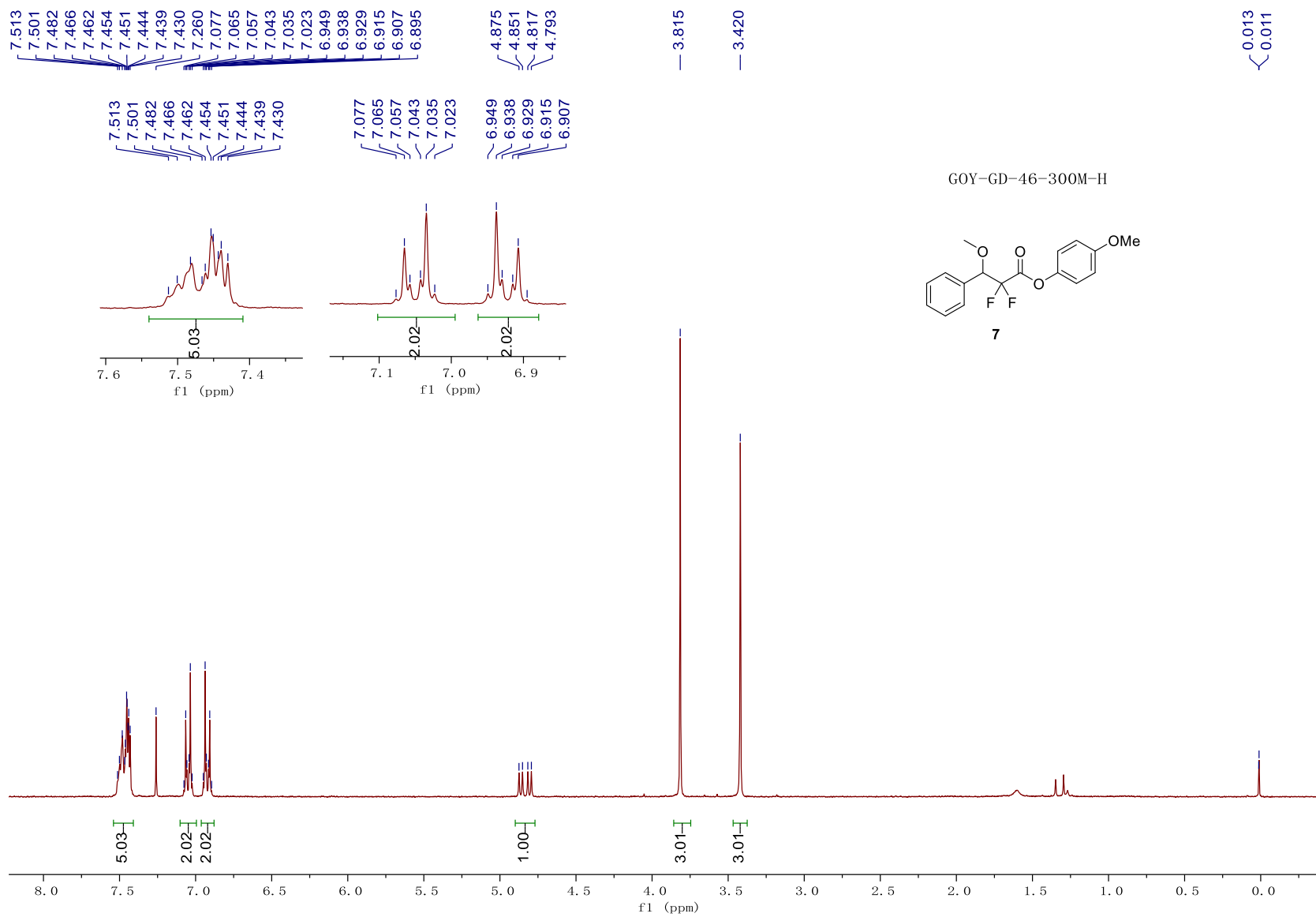


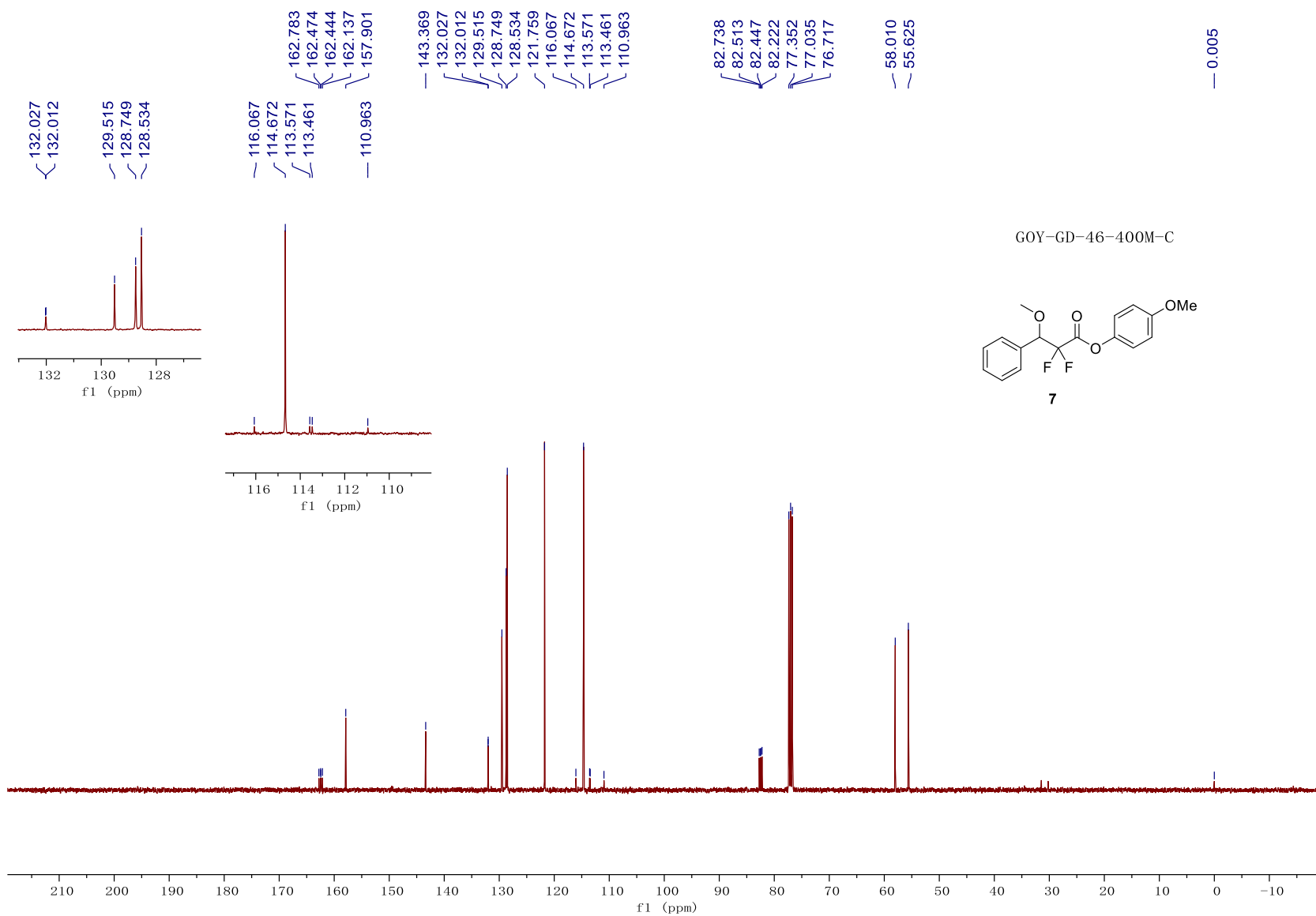
GOY-GD-36HSQC 16 1 C:\Bruker\TopSpin3.6.1\examdata



GOY-GD-36-HMBC 15 1 C:\Bruker\TopSpin3.6.1\examdata

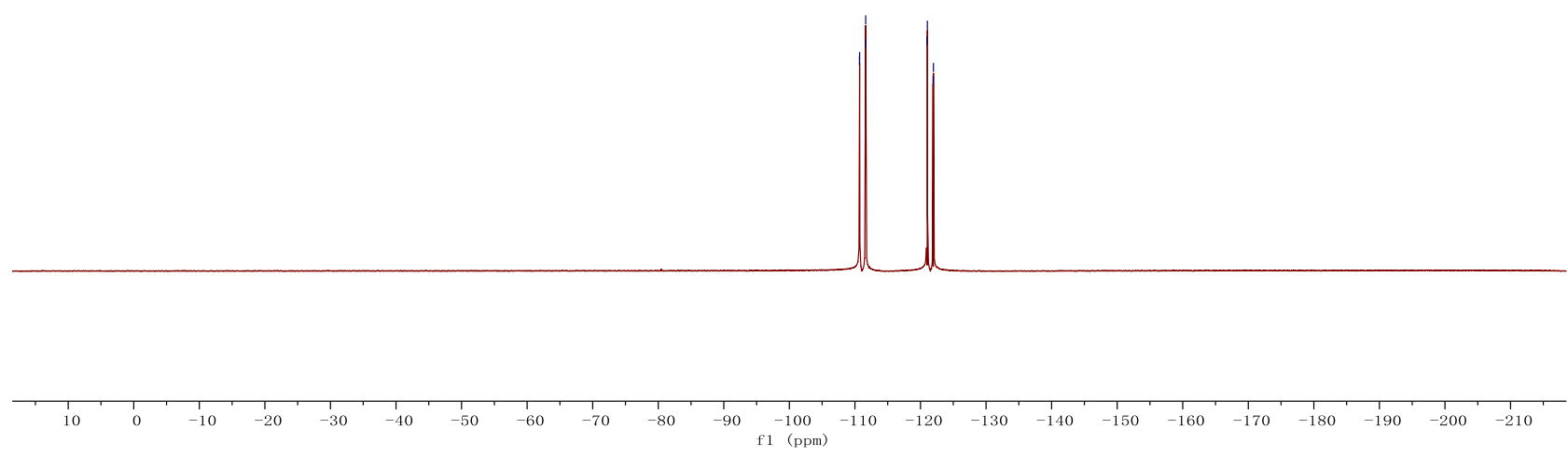
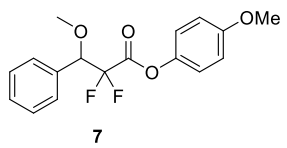


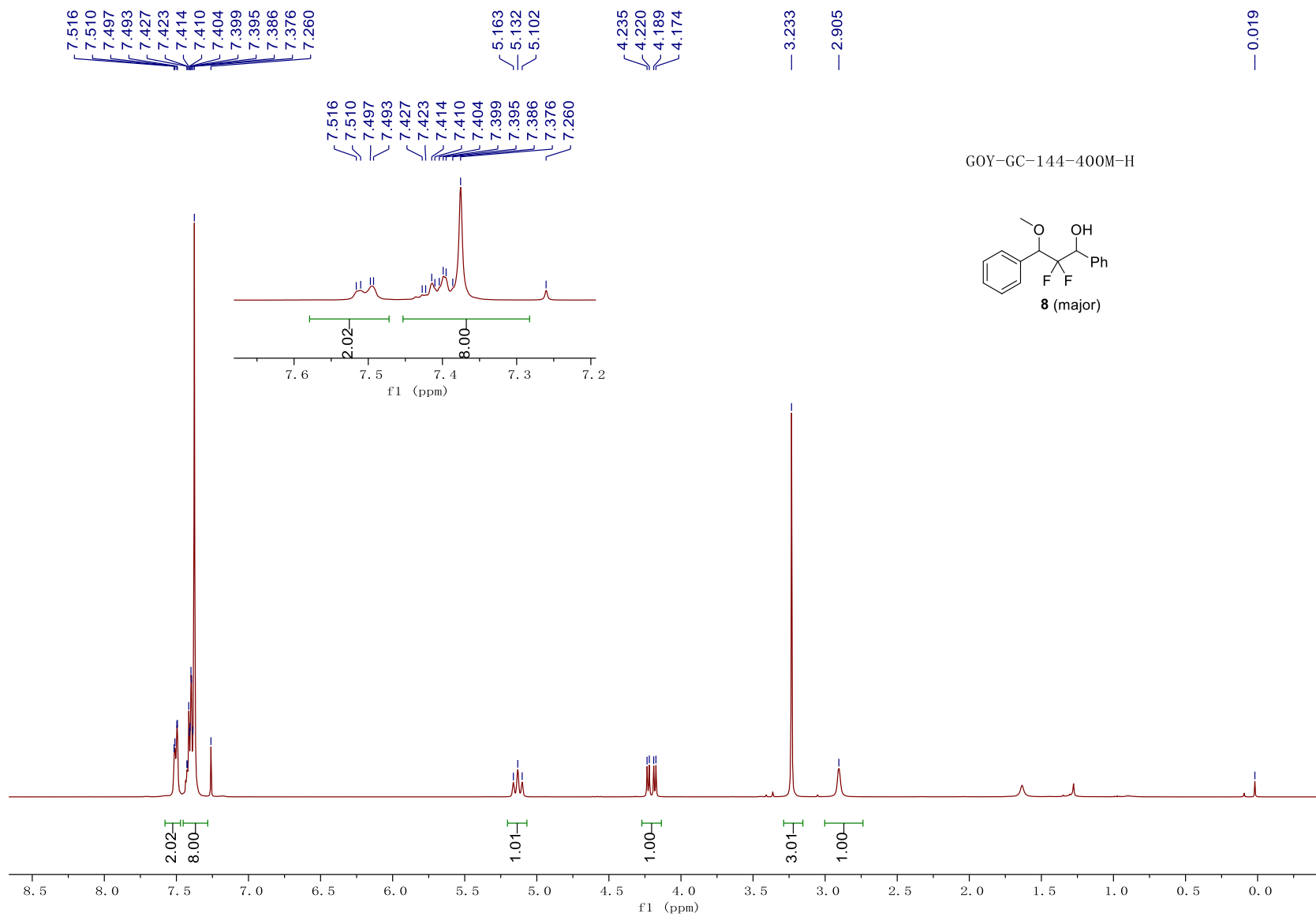


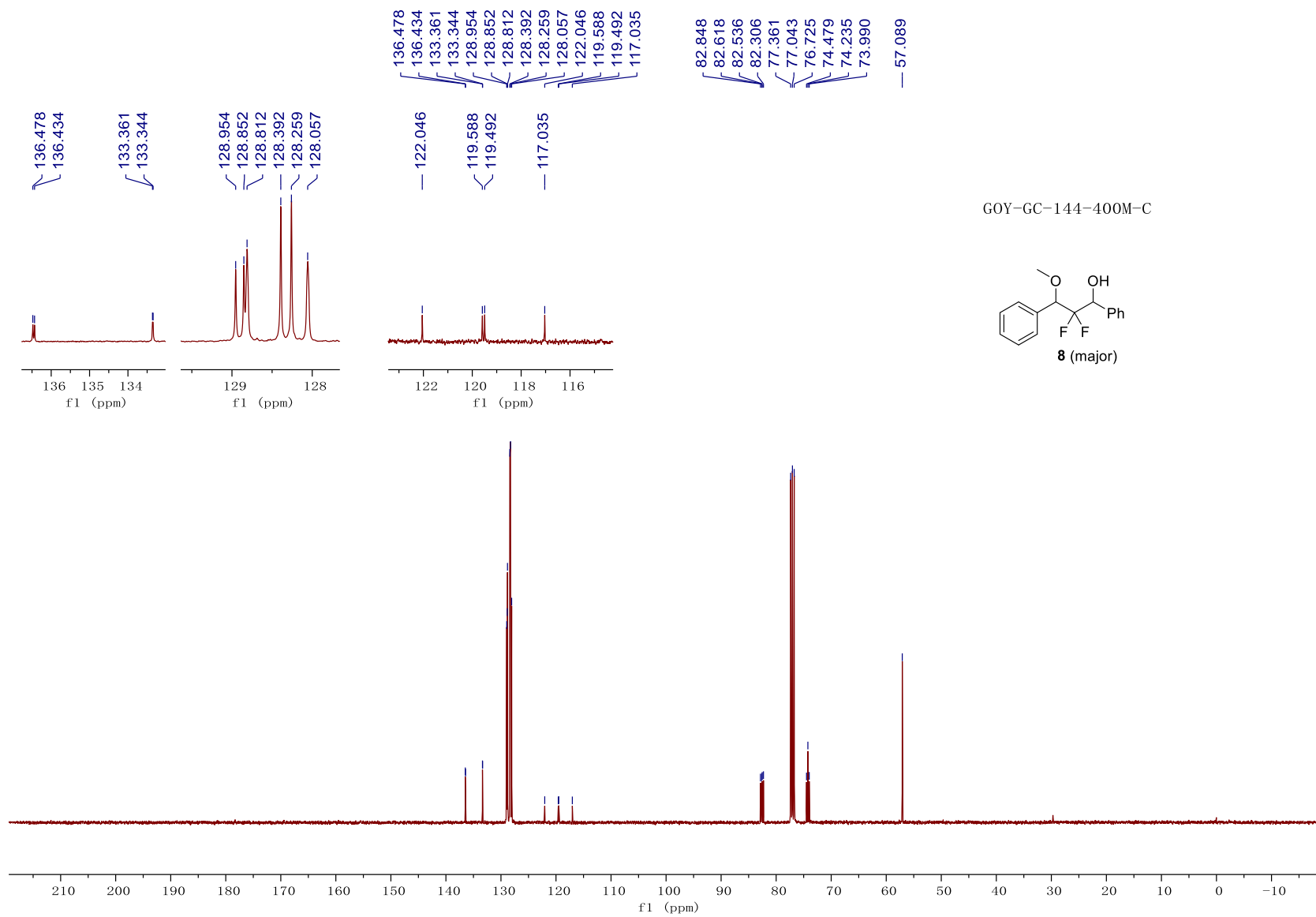


-110.691
-110.716
-111.620
-111.643
-120.991
-121.048
-121.917
-121.974

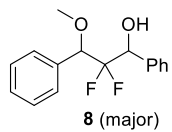
GOY-GD-46-300M-F



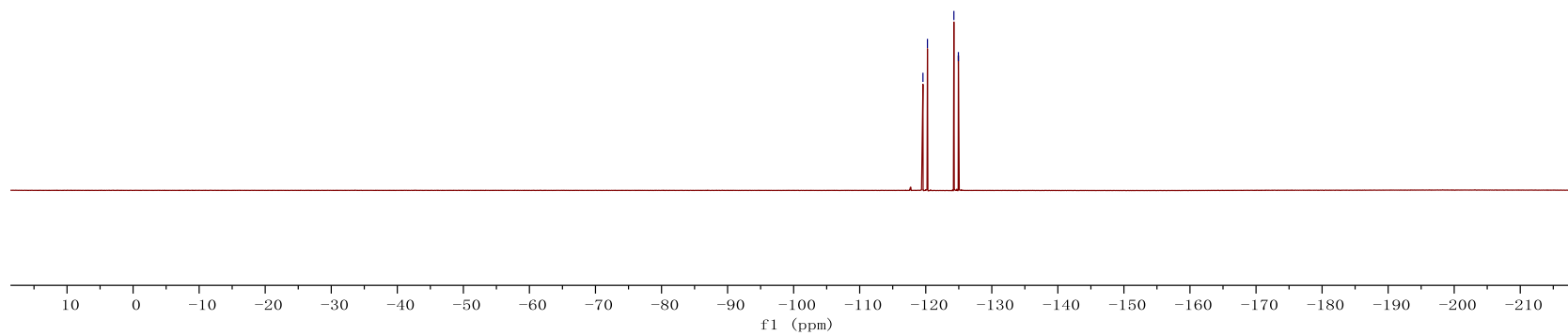


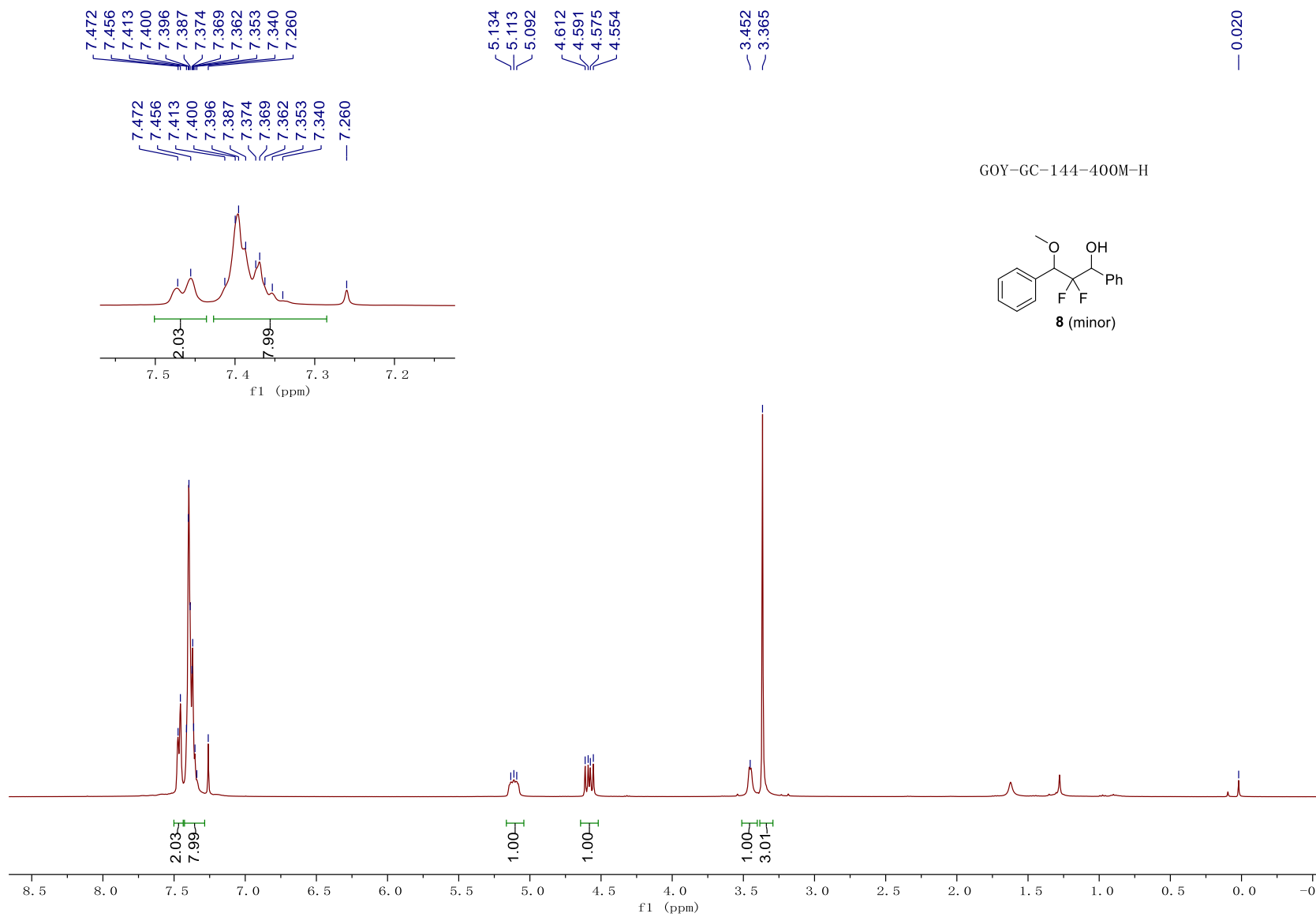


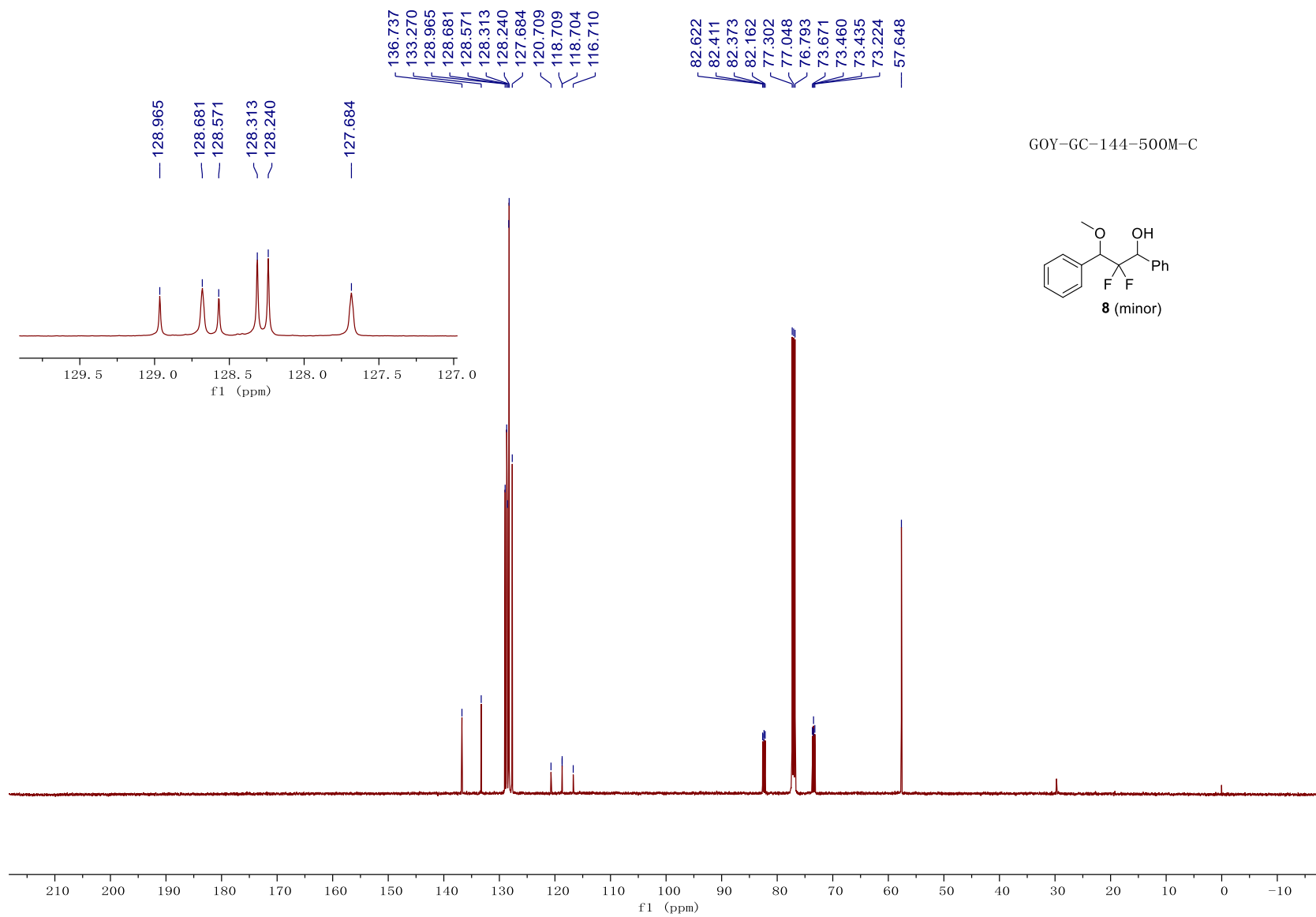
GOY-GC-144-400M-F



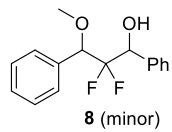
-119.574
-120.254
-124.260
-124.940



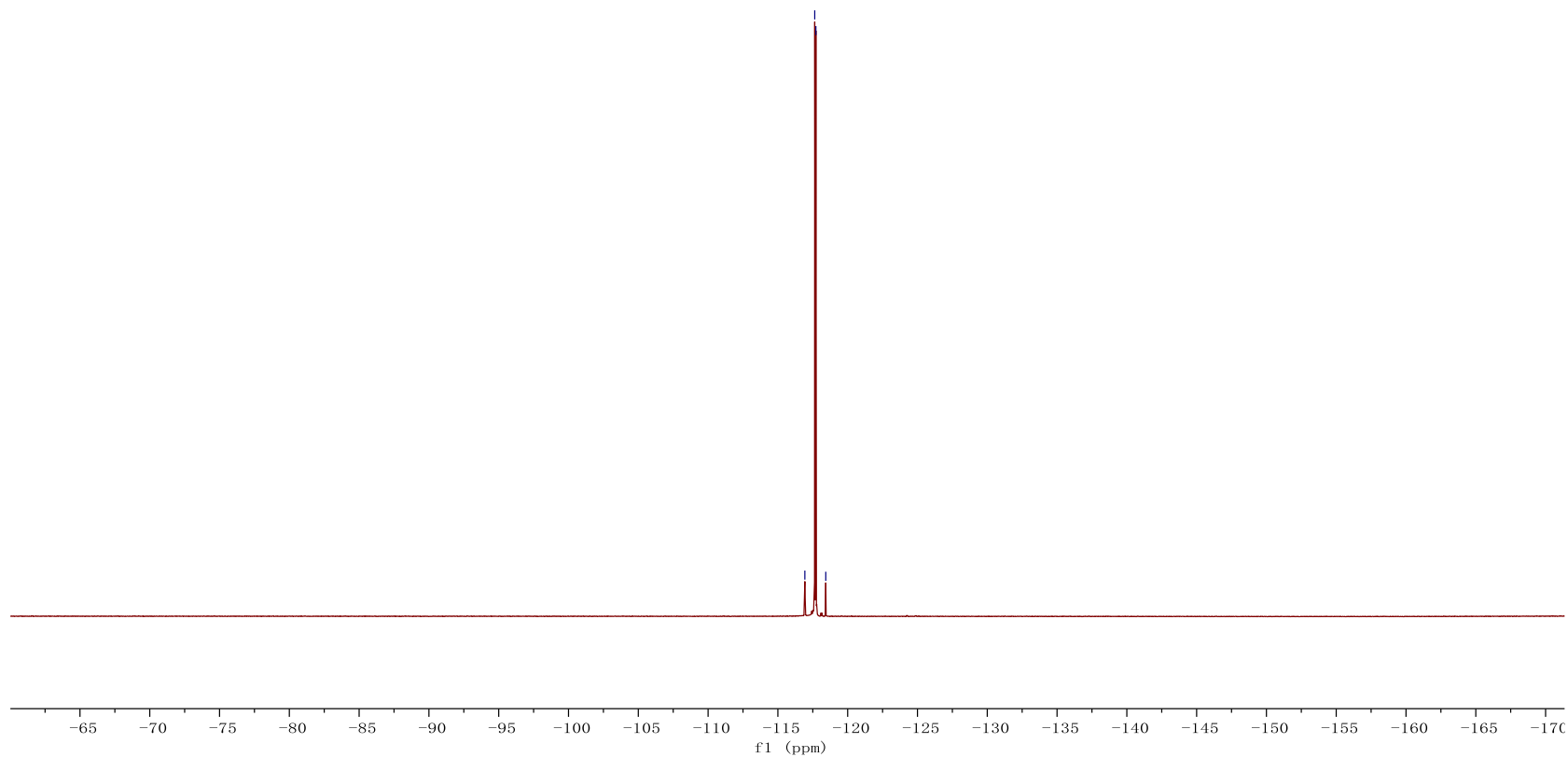


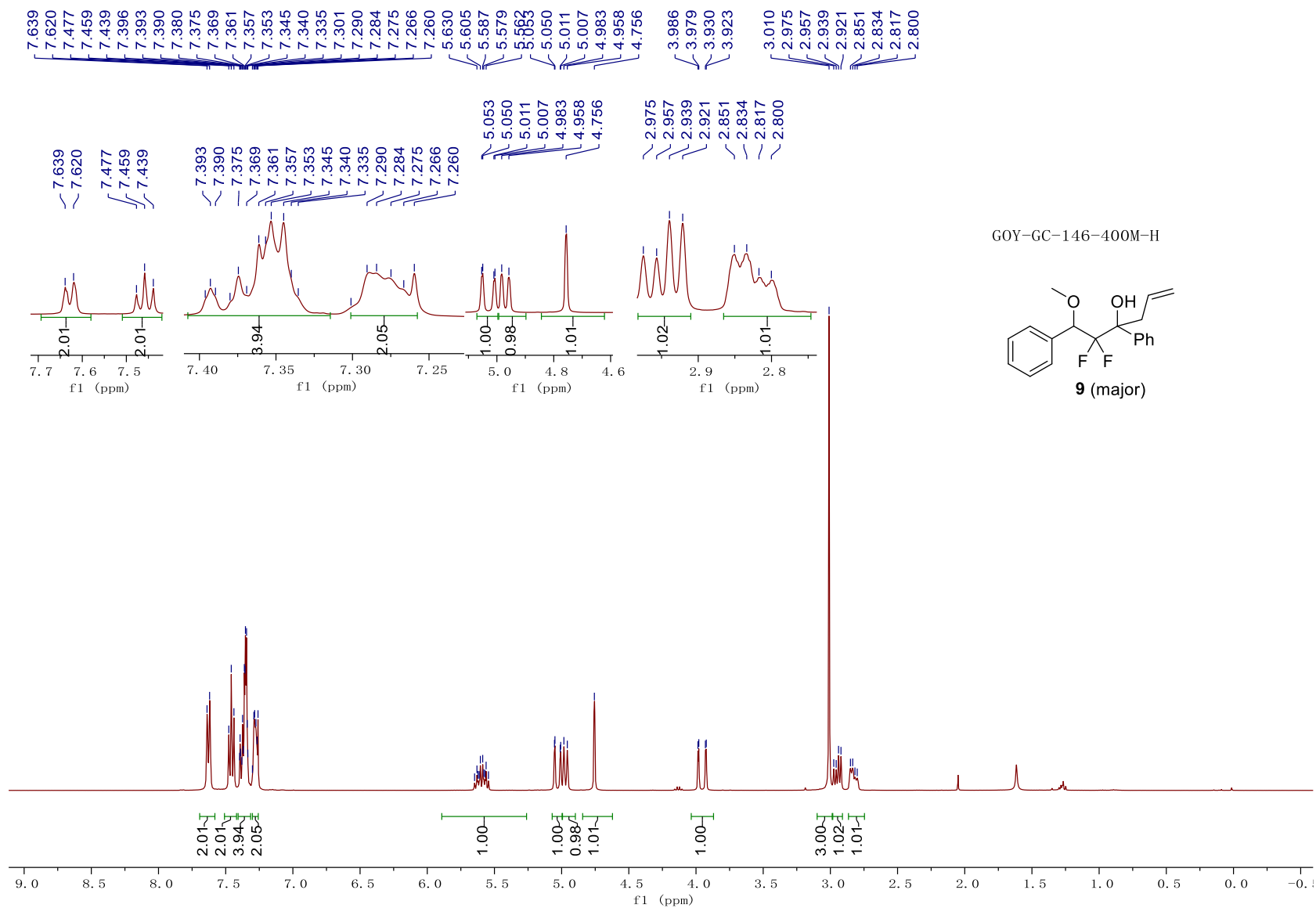


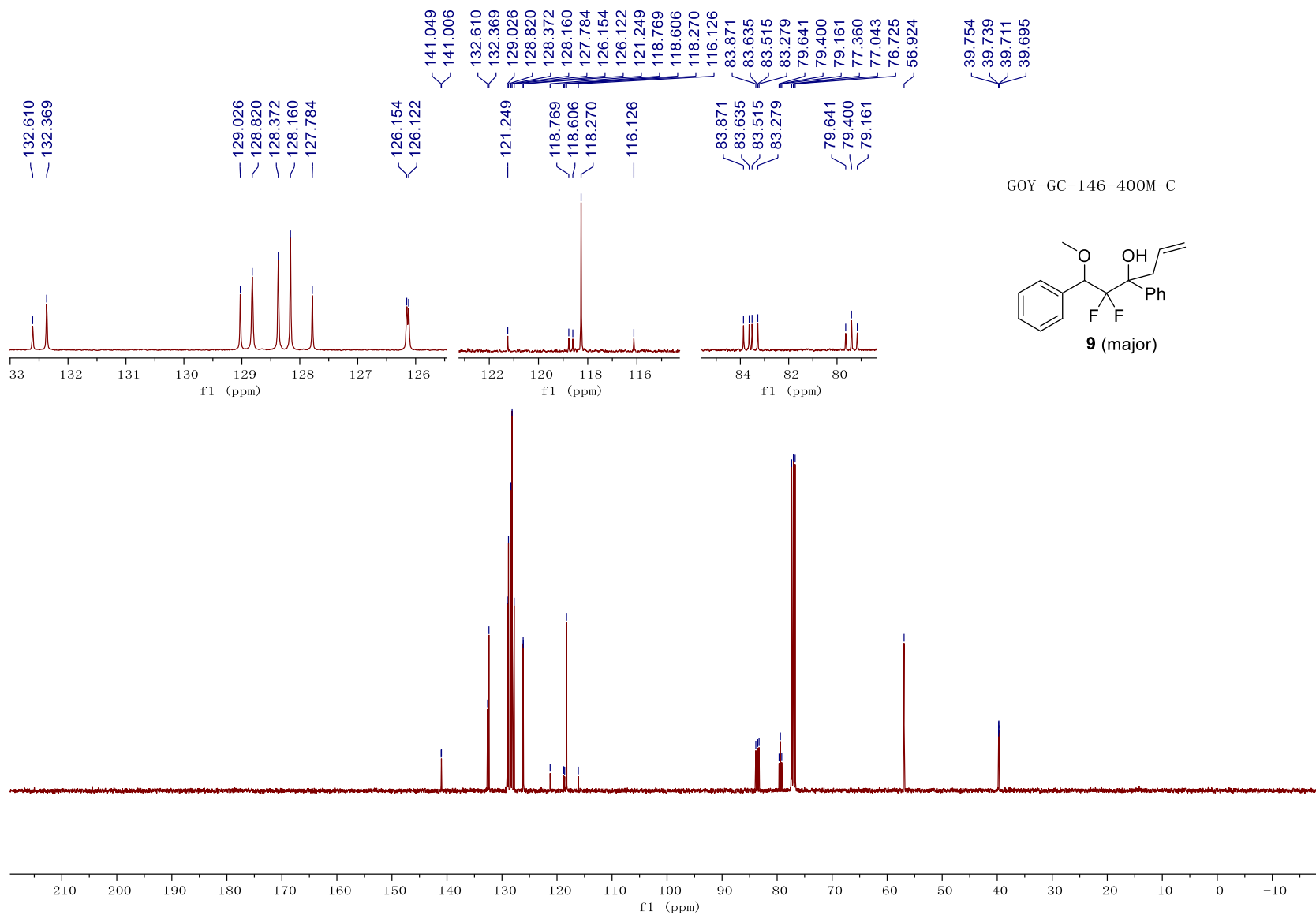
GOY-GC-144-400M-F



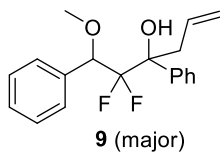
-116.932
-117.640
-117.723
-118.431





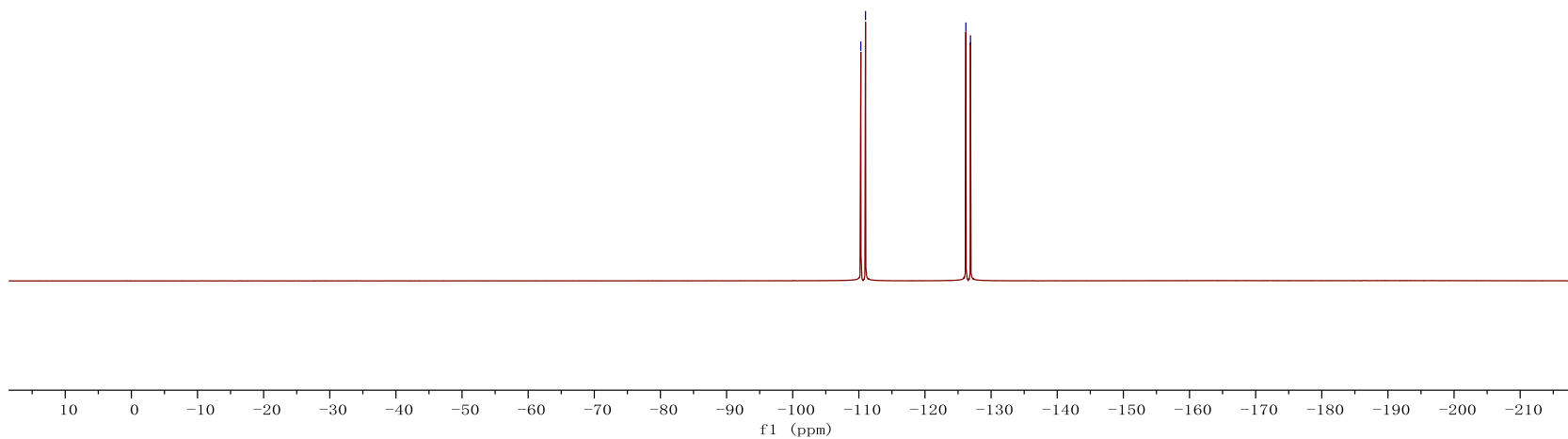


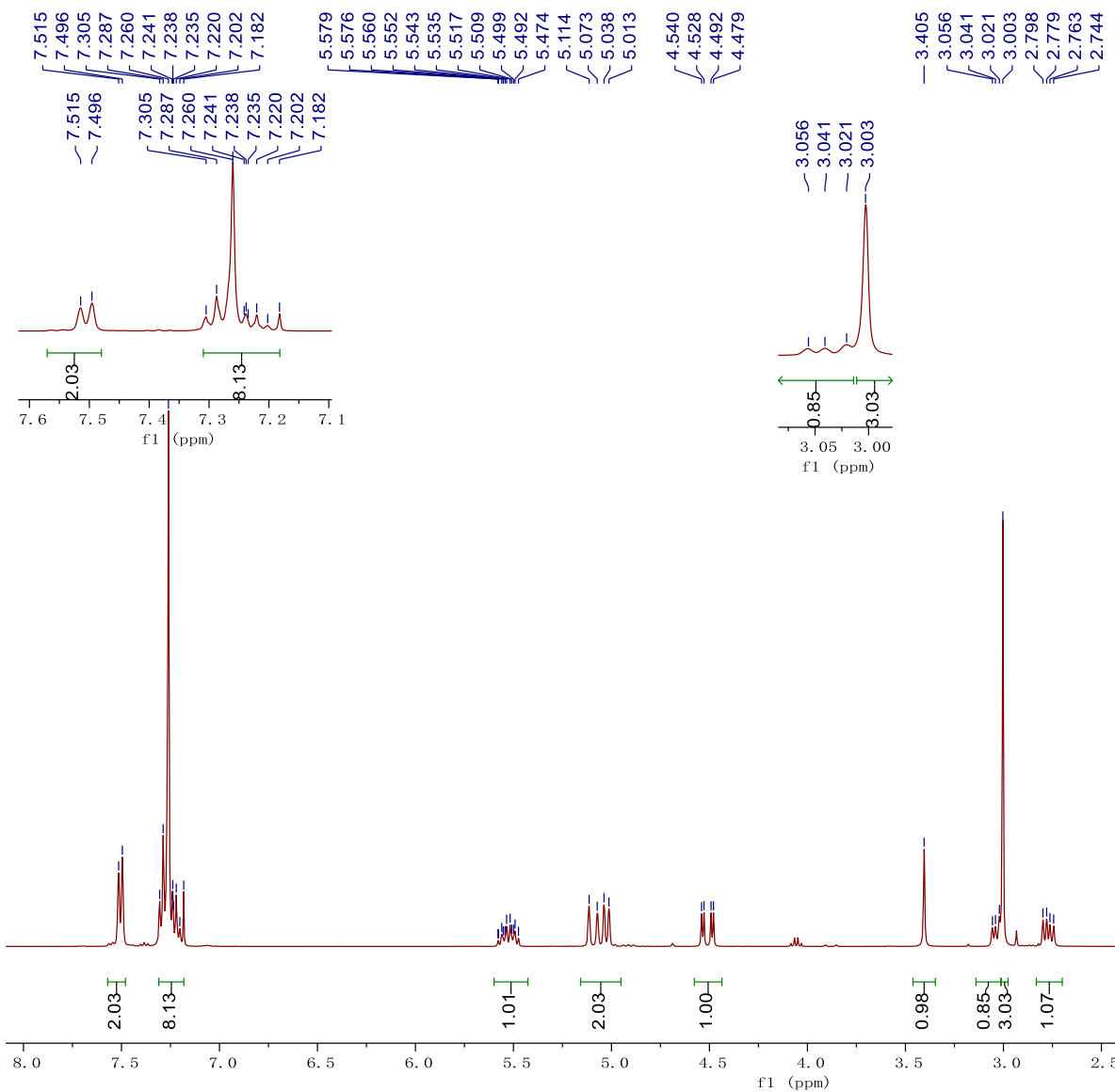
GOY-GC-146-400M-F



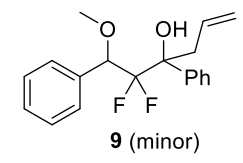
-110.301
-111.008

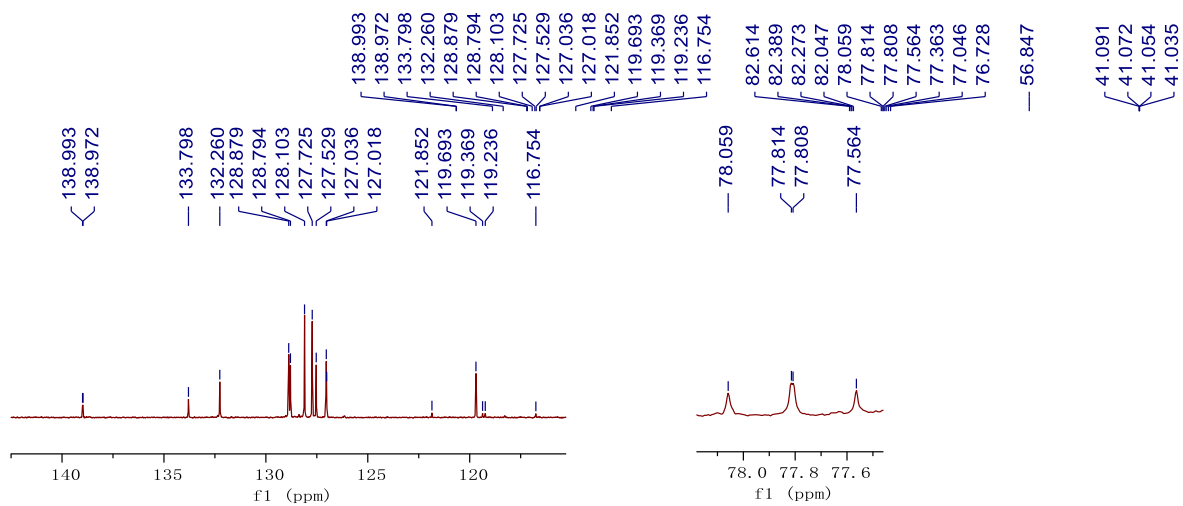
-126.179
-126.886



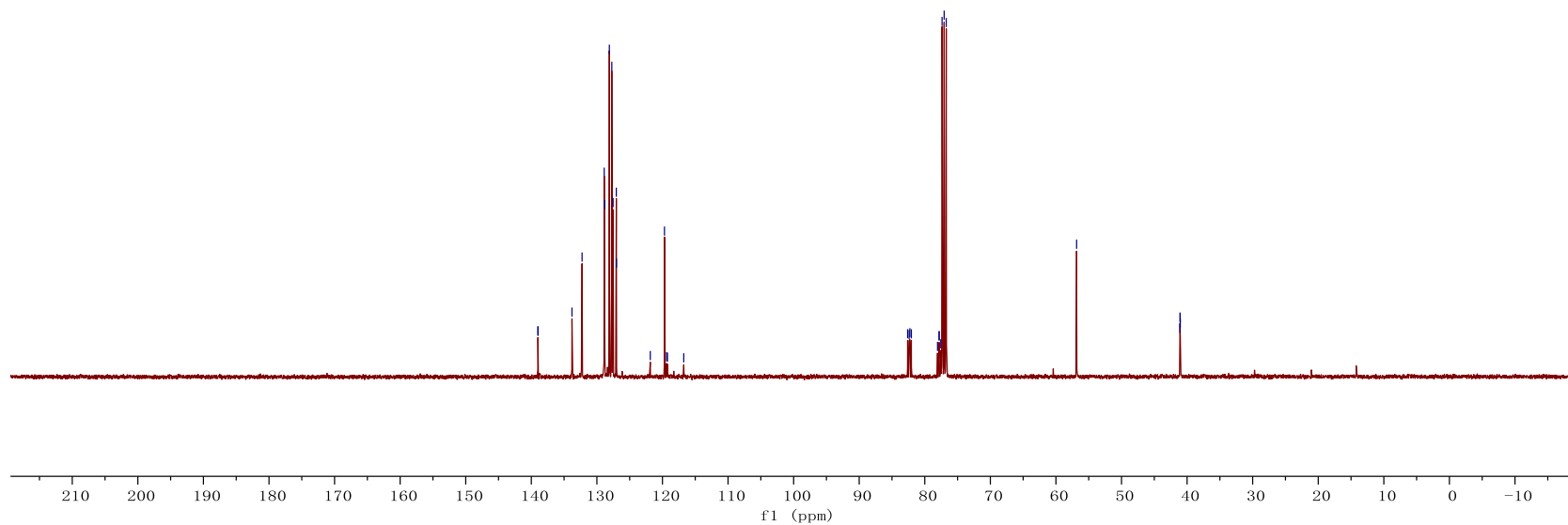
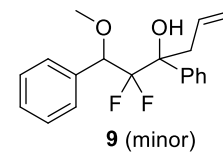


GOY-GC-146-400M-H

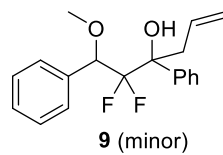




GOY-GC-146-400M-C



GOY-GC-146-400M-F



-109.109
-109.812

-121.689
-122.393

