

One-Pot Synthesis of Thioesters with Sodium Thiosulfate as Sulfur Surrogate under Transition Metal-Free Conditions

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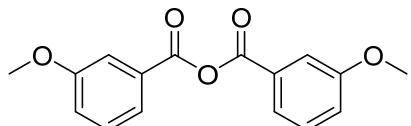
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General procedure for synthesis of anhydrides¹ 2-10:

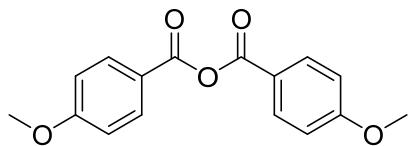
A solution of triethylamine (3.42 equiv.) in THF (0.30 M) was added dropwise to a THF solution (0.34 M) containing organic acid (2.00 equiv.) and methanesulfonyl chloride (1.10 equiv.) at 0 °C. The resulting mixture was stirred for 1 h and concentrated under vacuum. The mixture was extracted with NaHCO_{3(aq)} and ethyl acetate for three times, and the combined organic phase was washed with brine, dried over MgSO₄, filtered and concentrated to obtain the pure anhydride.

3-methoxybenzoic anhydride (2)²



Following general procedure, using 3-methoxybenzoic acid (500.0 mg, 3.288 mmol), methanesulfonyl chloride (207.2 mg, 1.809 mmol), triethylamine (569.0 mg, 5.623 mmol) to afford **2** (461.5 mg, 98% yield) as a colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 7.74 (d, *J* = 7.9 Hz, 2H), δ 7.65 (t, *J* = 2.4 Hz, 2H), δ 7.43 (t, *J* = 8.0 Hz, 2H), δ 7.21 (dd, *J* = 8.2, 2.6 Hz, 2H), δ 3.88 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 162.2, 159.8, 130.0, 129.8, 122.8, 121.0, 114.9, 55.5.

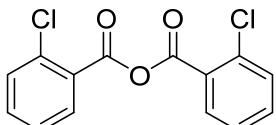
4-methoxybenzoic anhydride (3)³



Following general procedure, using 4-methoxybenzoic acid (265.5 mg, 1.746 mmol), methanesulfonyl chloride (110.0 mg, 0.960 mmol), triethylamine (302.1 mg, 2.985 mmol) to afford **3** (227.2 mg, 91% yield) as a white solid; ¹H NMR (400 MHz, CDCl₃): δ 8.10 (d, *J* = 9.0 Hz, 4H), δ 6.98 (d, *J* = 9.0 Hz, 4H), δ 3.90 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 162.2, 159.8, 130.0, 129.8, 122.8, 121.0, 114.9, 55.5.

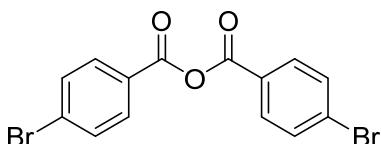
NMR (100 MHz, CDCl₃): δ 164.5, 162.2, 132.7, 121.1, 114.1, 55.5.

2-chlorobenzoic anhydride (4)²



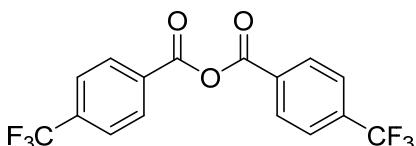
Following general procedure, using 2-chlorobenzoic acid (500.0 mg, 3.193 mmol), methanesulfonyl chloride (201.2 mg, 1.756 mmol), triethylamine (552.6 mg, 5.461 mmol) to afford **4** (399.6 mg, 85% yield) as a white solid; ¹H NMR (400 MHz, CDCl₃): δ 8.03 (dt, *J* = 7.8, 1.0 Hz, 2H), δ 7.54-7.53 (m, 4H), δ 7.43-7.37 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 160.4, 135.1, 134.2, 132.6, 131.6, 127.9, 126.9.

4-bromobenzoic anhydride (5)⁴



Following general procedure, using 4-bromobenzoic acid (400.0 mg, 2.001 mmol), methanesulfonyl chloride (126.1 mg, 1.101 mmol), triethylamine (346.2 mg, 3.421 mmol) to afford **5** (160.9 mg, 42% yield) as a white solid; ¹H NMR (400 MHz, CDCl₃): δ 8.00 (d, *J* = 8.8 Hz, 4H), δ 7.68 (d, *J* = 8.8 Hz, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 161.4, 132.4, 131.9, 130.2, 127.5.

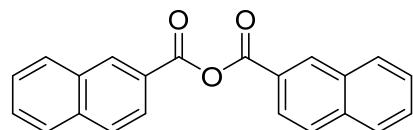
4-(trifluoromethyl)benzoic anhydride (6)⁵



Following general procedure, using 4-(trifluoromethyl)benzoic acid (400.0 mg, 2.104

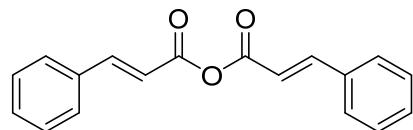
mmol), methanesulfonyl chloride (132.6 mg, 1.158 mmol), triethylamine (364.1 mg, 3.598 mmol) to afford **6** (349.6 mg, 92% yield) as a white solid; ¹H NMR (400 MHz, CDCl₃): δ 8.28 (d, *J* = 8.1 Hz, 4H), δ 7.82 (d, *J* = 8.2 Hz, 4H); ¹³C NMR (100 MHz, CDCl₃): δ 160.7, 136.0 (*J* = 33.0 Hz), 131.6, 130.9, 126.0 (*J* = 4.0 Hz), 123.3 (*J* = 271.0 Hz).

2-naphthoic anhydride (7)⁶



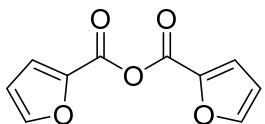
Following general procedure, using 2-naphthoic acid (500.0 mg, 2.904 mmol), methanesulfonyl chloride (183.0 mg, 1.598 mmol), triethylamine (502.5 mg, 4.966 mmol) to afford **7** (471.5 mg, quant. yield) as a brown solid; ¹H NMR (400 MHz, CDCl₃): δ 8.77 (s, 2H), δ 8.18 (dd, *J* = 8.6, 1.8 Hz, 2H), δ 8.01 (d, *J* = 8.1 Hz, 2H), δ 7.97 (d, *J* = 8.6 Hz, 2H), δ 7.93 (d, *J* = 8.1 Hz, 2H), δ 7.68-7.54 (m, 2H), δ 7.61-7.57 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 162.7, 136.2, 132.8, 132.4, 129.6, 129.2, 128.8, 127.9, 127.1, 126.0, 125.3.

cinnamic anhydride (8)²



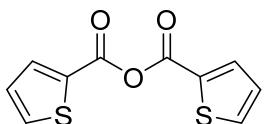
Following general procedure, using cinnamic acid (400.0 mg, 2.700 mmol), methanesulfonyl chloride (170.1 mg, 1.485 mmol), triethylamine (468.5 mg, 4.630 mmol) to afford **8** (375.1 mg, quant. yield) as a colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 7.86 (d, *J* = 16.0 Hz, 2H), δ 7.60-7.58 (m, 4H), δ 7.46-7.41 (m, 6H), δ 6.54 (d, *J* = 15.9 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 162.4, 148.6, 133.7, 131.2, 129.0, 128.5, 116.7.

furan-2-carboxylic anhydride (**9**)⁷



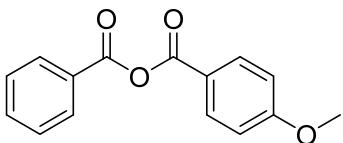
Following general procedure, using furan-2-carboxylic acid (400.0 mg, 3.569 mmol), methanesulfonyl chloride (224.8 mg, 1.962 mmol), triethylamine (617.5 mg, 6.102 mmol) to afford **9** (332.0 mg, 90% yield) as a white solid; ¹H NMR (400 MHz, CDCl₃): δ 7.71 (dd, *J* = 1.7, 0.8 Hz, 2H), δ 7.42 (dd, *J* = 3.6, 0.8 Hz, 2H), δ 6.62 (dd, *J* = 3.6, 1.7 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 152.7, 148.5, 142.7, 121.7, 112.6.

thiophene-2-carboxylic anhydride (**10**)⁸



Following general procedure, using thiophene-2-carboxylic acid (500.0 mg, 3.906 mmol), methanesulfonyl chloride (246.1 mg, 2.148 mmol), triethylamine (676.0 mg, 6.681 mmol) to afford **10** (459.9 mg, 99% yield) as a yellow oil; ¹H NMR (400 MHz, CDCl₃): δ 7.99 (dd, *J* = 3.8, 1.2 Hz, 2H), δ 7.74 (dd, *J* = 4.9, 1.1 Hz, 2H), δ 7.20 (dd, *J* = 4.9, 3.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 156.6, 136.0, 135.3, 131.9, 128.4.

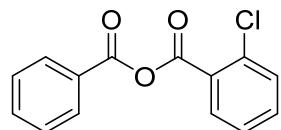
benzoic 4-methoxybenzoic anhydride (**12**)⁹



A solution of 4-methoxybenzoic acid (200.0 mg, 1.314 mmol, 1.00 equiv.) and triethylamine (454.9, 4.496 mmol, 3.42 equiv.) in THF (0.34 M) was added dropwise of benzoyl chloride (277.2 mg, 1.972 mmol, 1.20 equiv.) in THF (0.30 M) at 0 °C. The mixture was stirred for 1 hour and concentrated under vacuum. An EtOAc was

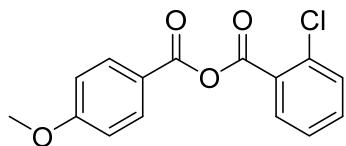
then added, and the organic layer was extracted by $\text{NaHCO}_3\text{(aq.)}$ for three times. The combined organic layer was washed with brine, dried over MgSO_4 , filtered and concentrated. The crude products were purified by flash column chromatography (hexane/EtOAc, 8:1) to afford **12** (335.1 mg, quant.) as a colorless oil; ^1H NMR (400 MHz, CDCl_3): δ 8.18-8.15 (m, 2H), δ 8.11 (d, $J = 9.0$ Hz, 2H), δ 7.67 (tt, $J = 7.5, 1.3$ Hz, 1H), δ 7.55-7.50 (m, 2H), δ 6.99 (d, $J = 9.0$ Hz, 2H), δ 3.90 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 164.6, 162.5, 161.9, 134.3, 132.8, 130.4, 128.9, 128.7, 120.8, 114.1, 55.5.

benzoic 2-chlorobenzoic anhydride (13)¹⁰



A solution of 2-chlorobenzoic acid (200.0 mg, 1.277 mmol, 1.00 equiv.) and triethylamine (442.1 mg, 4.369 mmol, 3.42 equiv.) in THF (0.34 M) was added dropwise of benzoyl chloride (215.5 mg, 1.533 mmol, 1.20 equiv.) in THF (0.30 M) at 0 °C. The mixture was stirred for 1 hour and concentrated under vacuum. An EtOAc was then added, and the organic layer was extracted by $\text{NaHCO}_3\text{(aq.)}$ for three times. The combined organic layer was washed with brine, dried over MgSO_4 , filtered and concentrated. The crude products were purified by flash column chromatography (hexane/EtOAc, 8:1) to afford **13** (301.4 mg, 91% yield) as a colorless oil; ^1H NMR (400 MHz, CDCl_3): δ 8.17-8.14 (m, 2H), δ 8.04-8.01 (m, 1H), δ 7.70-7.66 (m, 1H), δ 7.55-7.50 (m, 4H), δ 7.44-7.37 (m, 1H).

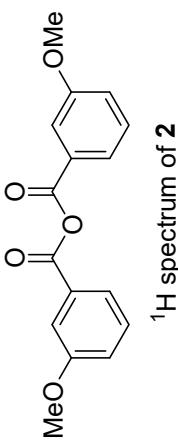
2-chlorobenzoic 4-methoxybenzoic anhydride (14)



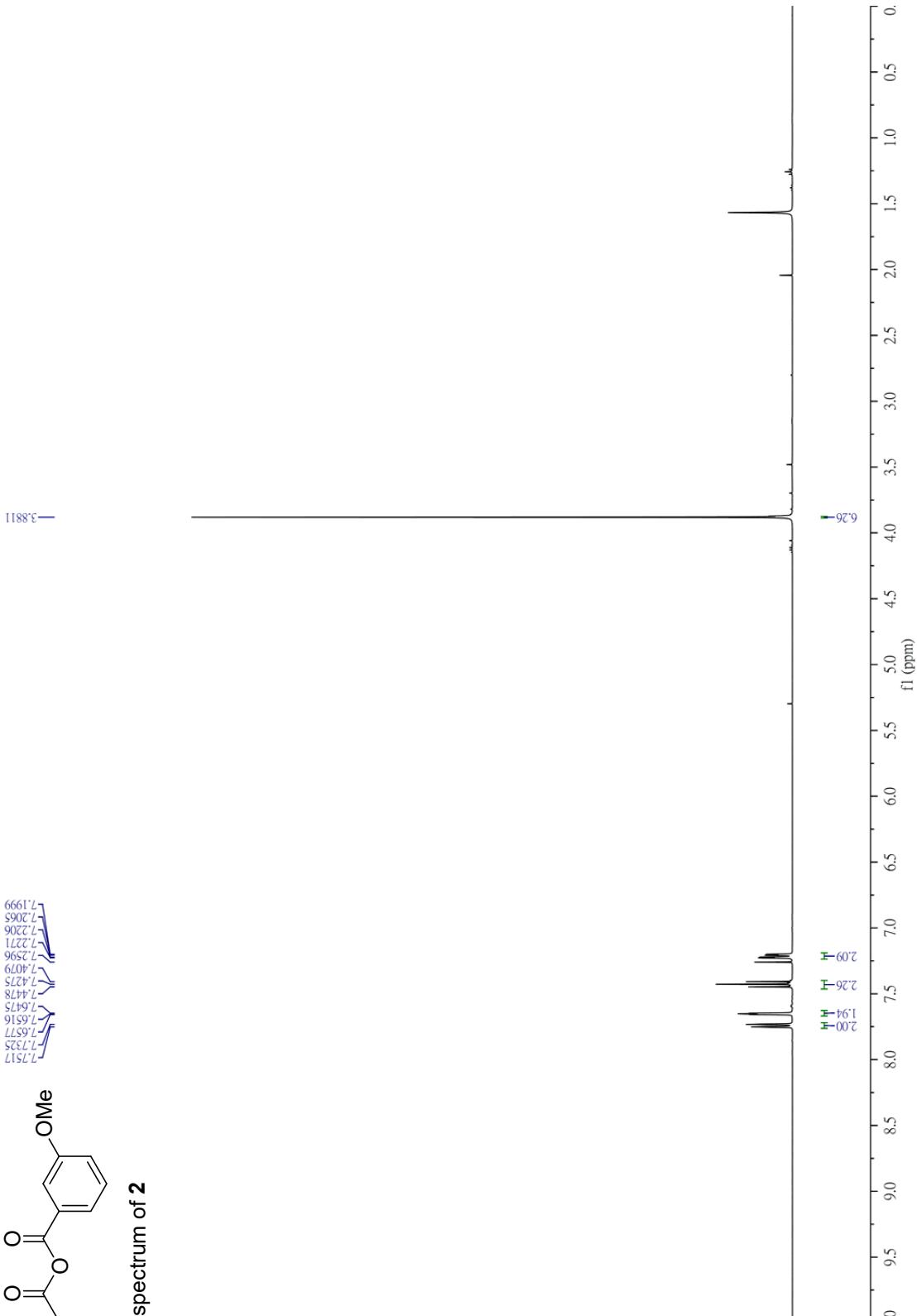
4-Methoxybenzoic acid (500.0 mg, 3.286 mmol, 1.00 equiv.) was dissolved in dichloromethane (0.2 M), then sulfurous chloride (469.2 mg, 3.944 mmol, 1.20 equiv.) and DMF (12.0 mg, 0.164 mmol, 0.05 equiv.) were added to the solution in order. The mixture was then stirred at room temperature and monitored by TLC. After the reaction was completed, the solvent was removed under reduced pressure to give acid chloride. The crude product was then added to the mixture of 2-chlorobenzoic acid (514.5 mg, 3.286 mmol, 1.00 equiv.) and triethylamine (1137.3 mg, 11.239 mmol, 3.42 equiv.) in THF (0.30 M) at 0 °C. The mixture was stirred for 1 hour and concentrated under vacuum. An EtOAc was then added, and the organic layer was extracted by NaHCO_{3(aq)} for three times. The combined organic layer was washed with brine, dried over MgSO₄, filtered and concentrated. The crude products were purified by flash column chromatography (hexane/EtOAc, 8:1) to afford **14** (755.2 mg, 79% yield) as a colorless oil; ¹H NMR (400 MHz, CDCl₃): δ 8.10 (d, *J* = 8.8 Hz, 2H), 8.02-8.00 (m, 1H), 7.54-7.52 (m, 2H), 7.43-7.37 (m, 1H), 6.98 (d, *J* = 8.9 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 164.7, 161.6, 161.2, 134.6, 133.9, 133.0, 132.4, 131.5, 128.6, 126.9, 120.5, 114.1, 55.6; IR (KBr): ν = 3077, 3009, 1758, 1723, 1603, 1510, 1213, 1019, 989, 752 cm⁻¹; HRMS (EI) m/z: [M]⁺ calcd. for C₁₅H₁₁Cl₁O₄: 290.0346, found: 290.0340

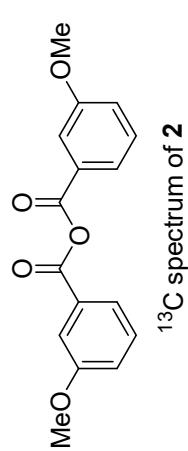
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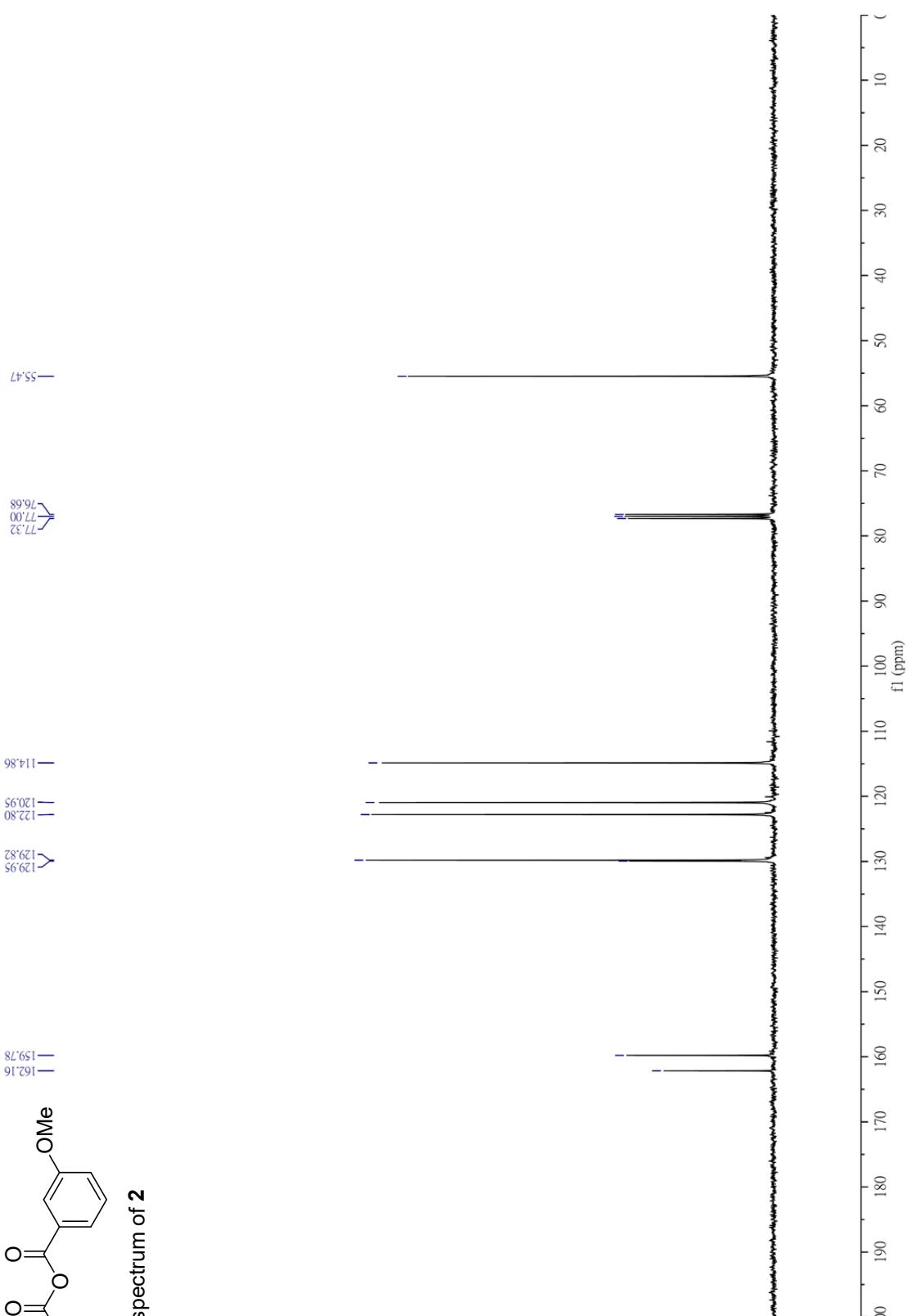


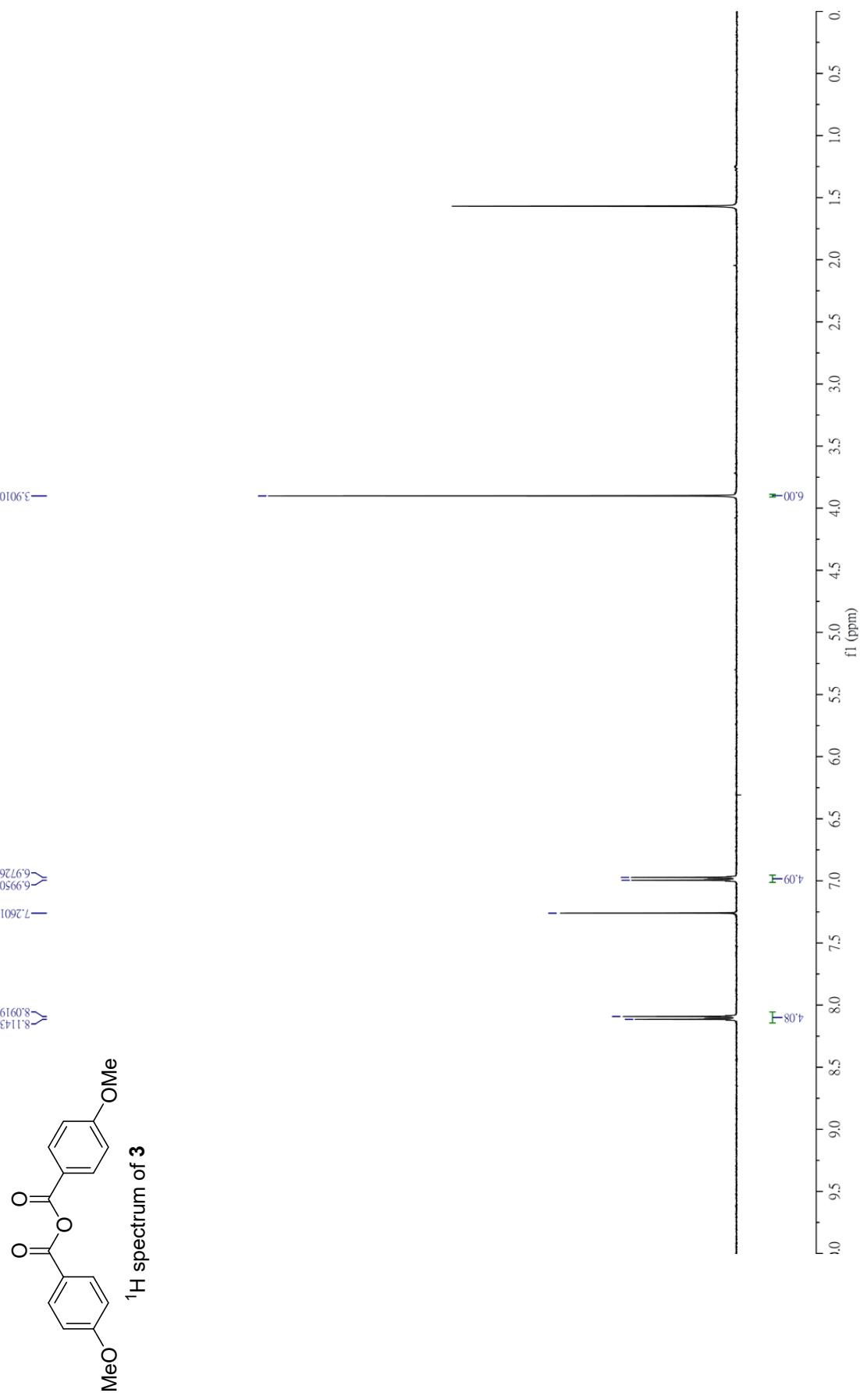
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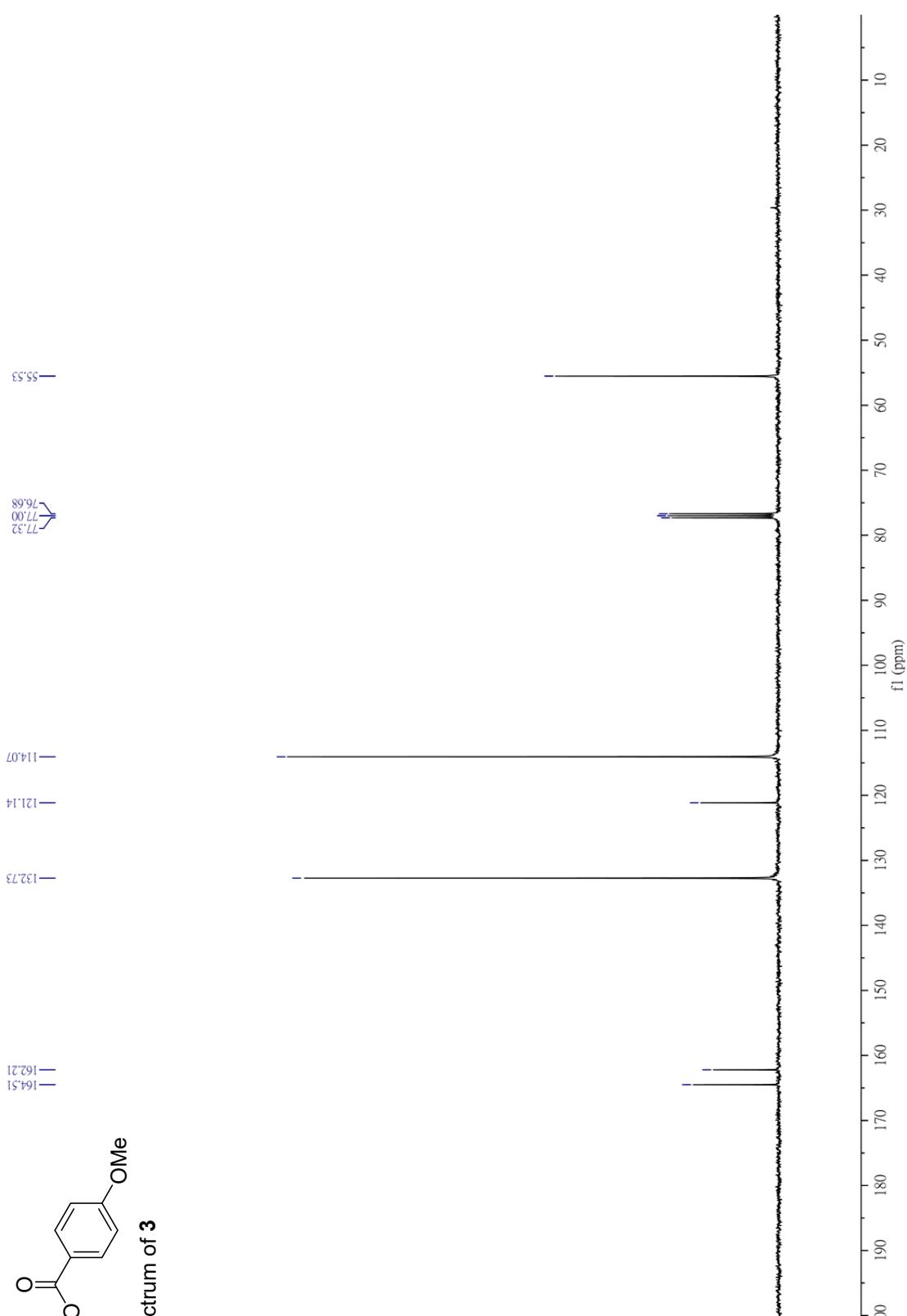
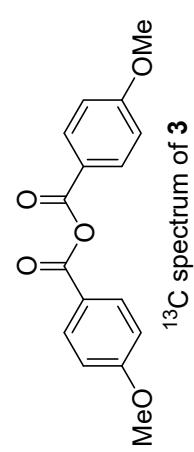


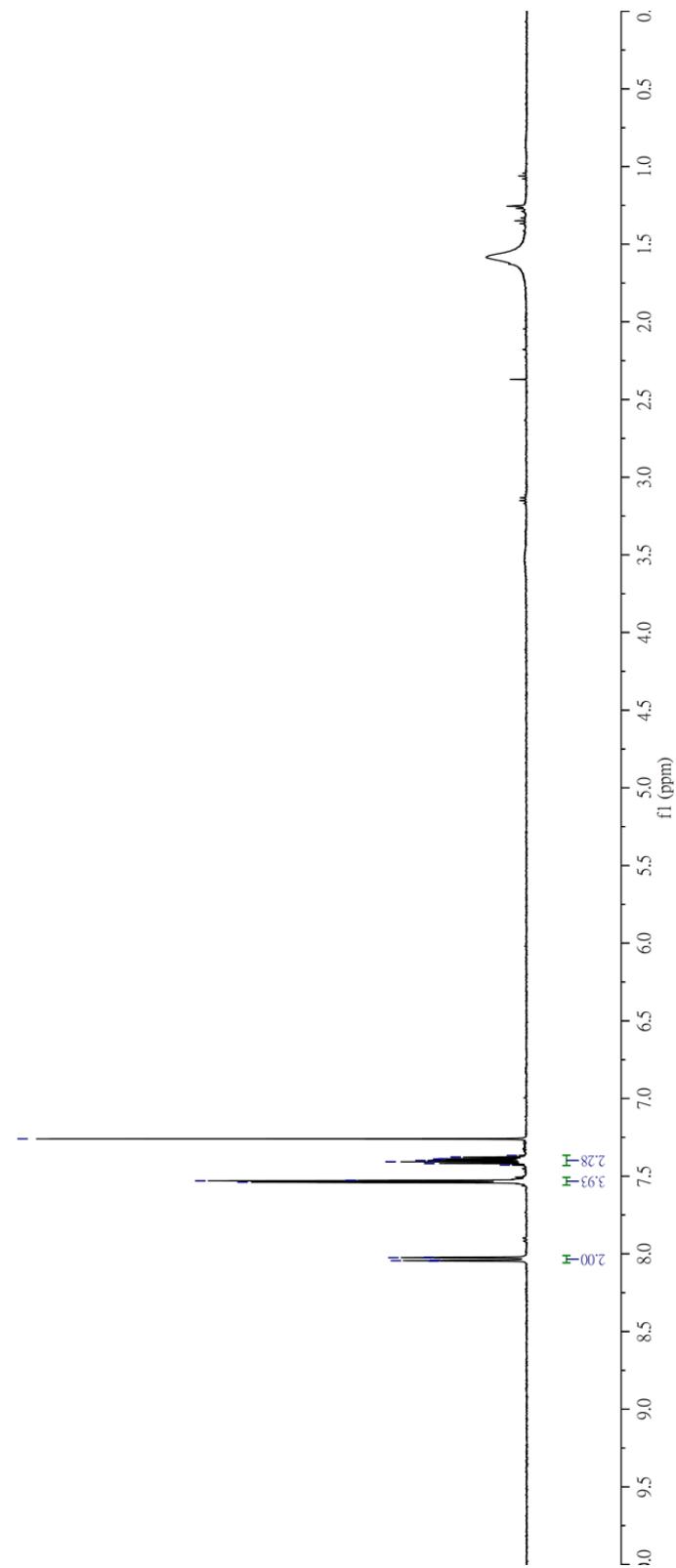
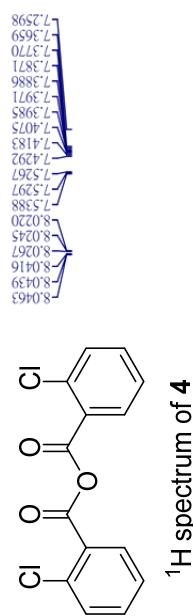


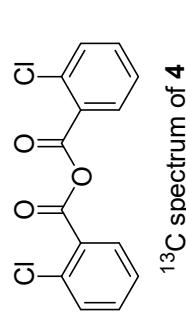
^{13}C spectrum of **2**



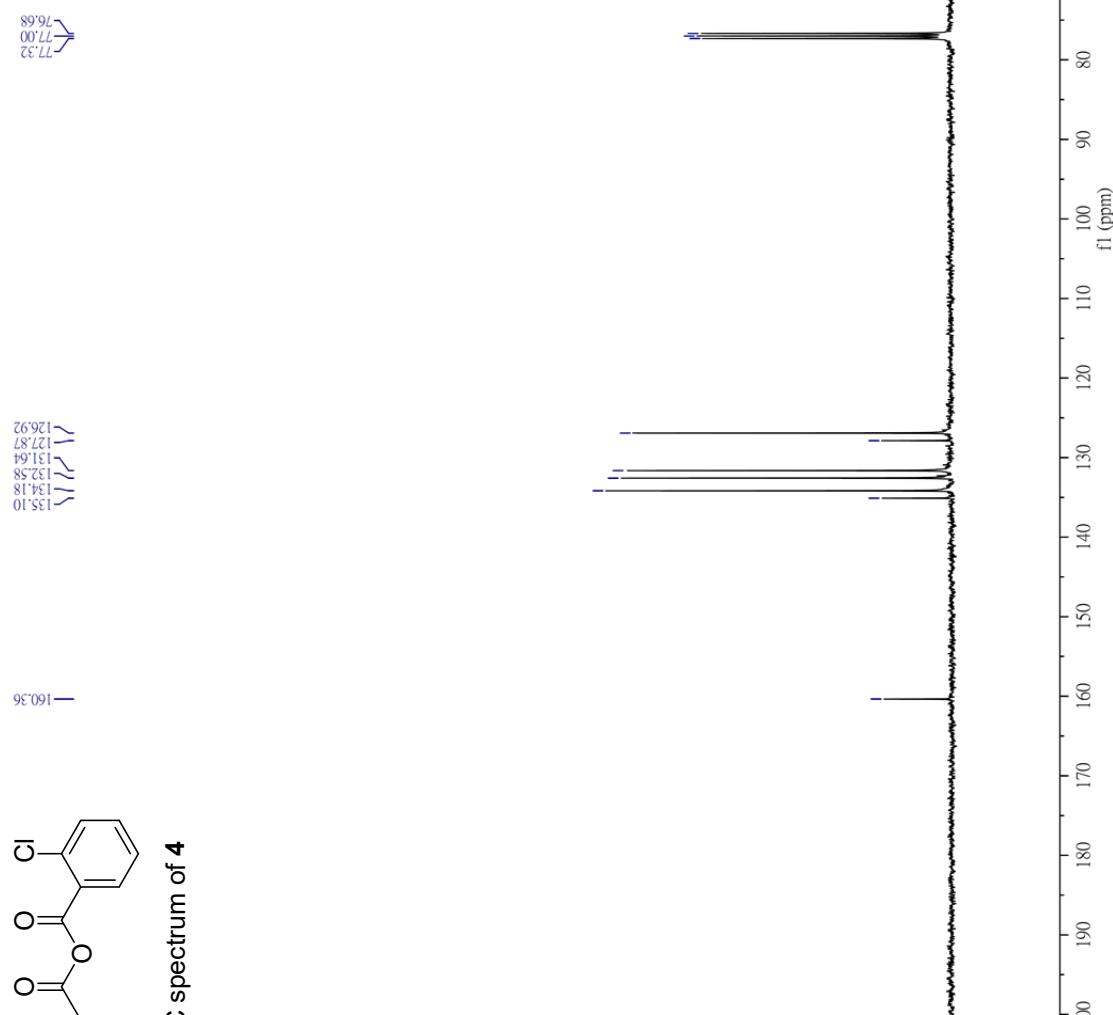


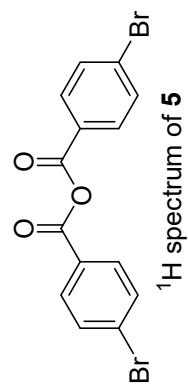




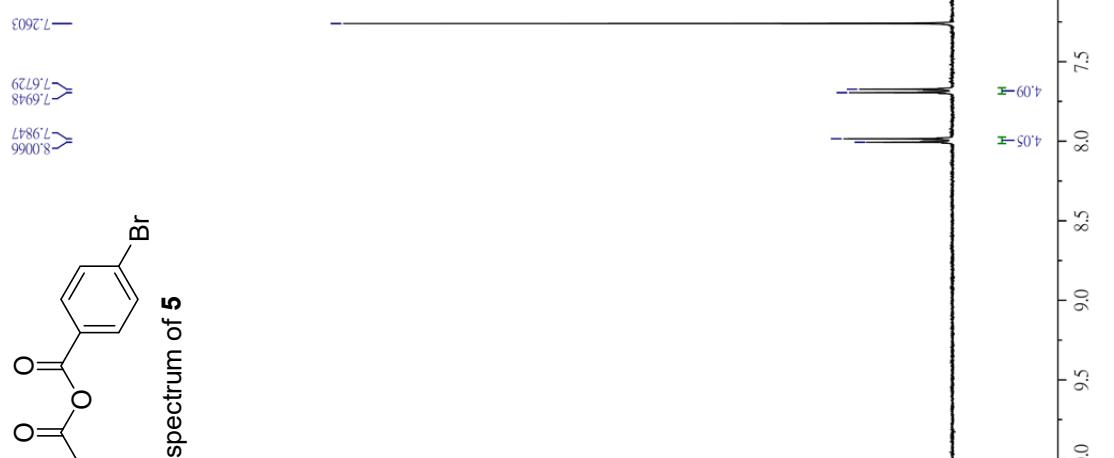


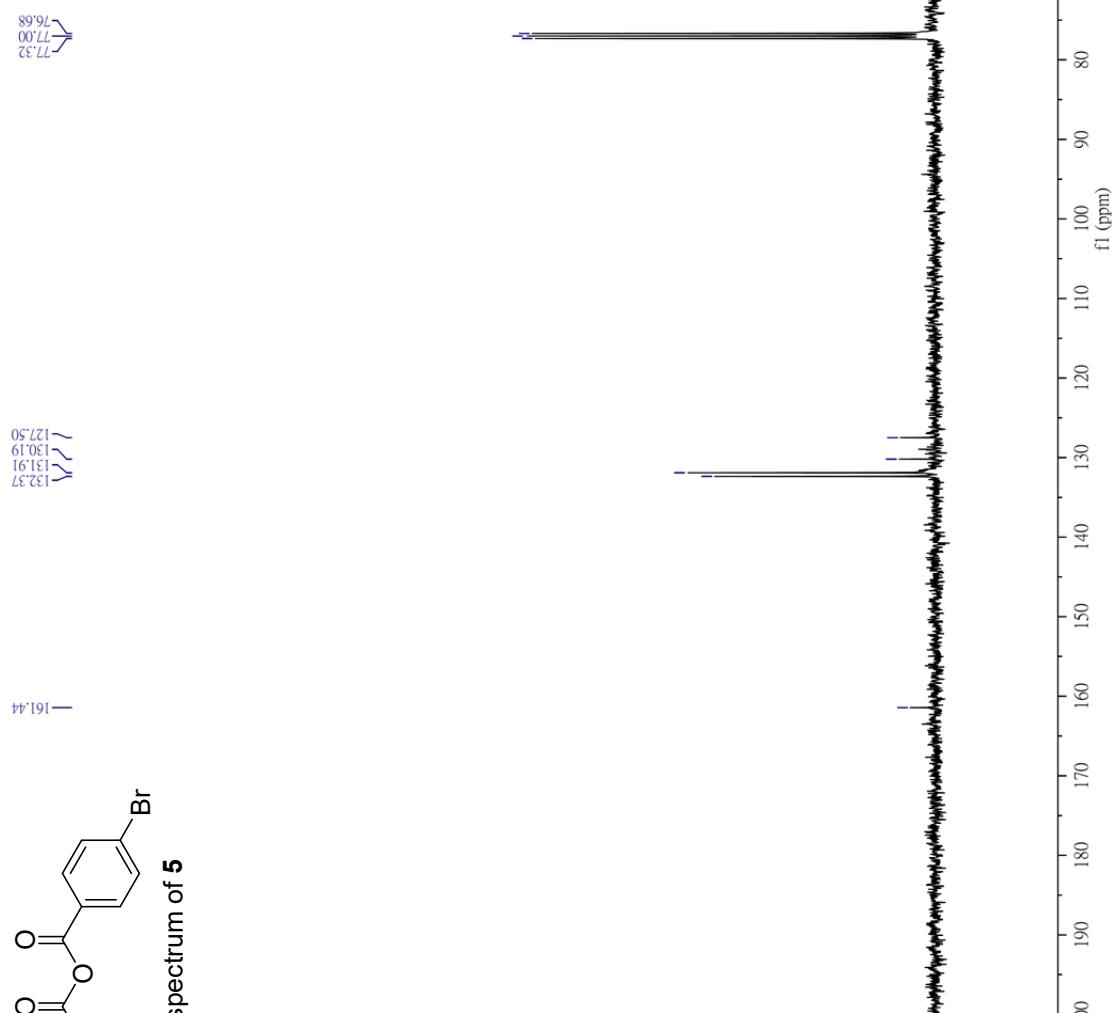
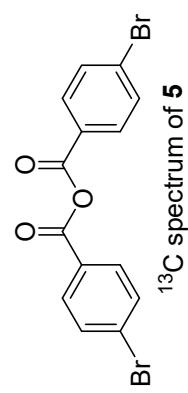
^{13}C spectrum of **4**

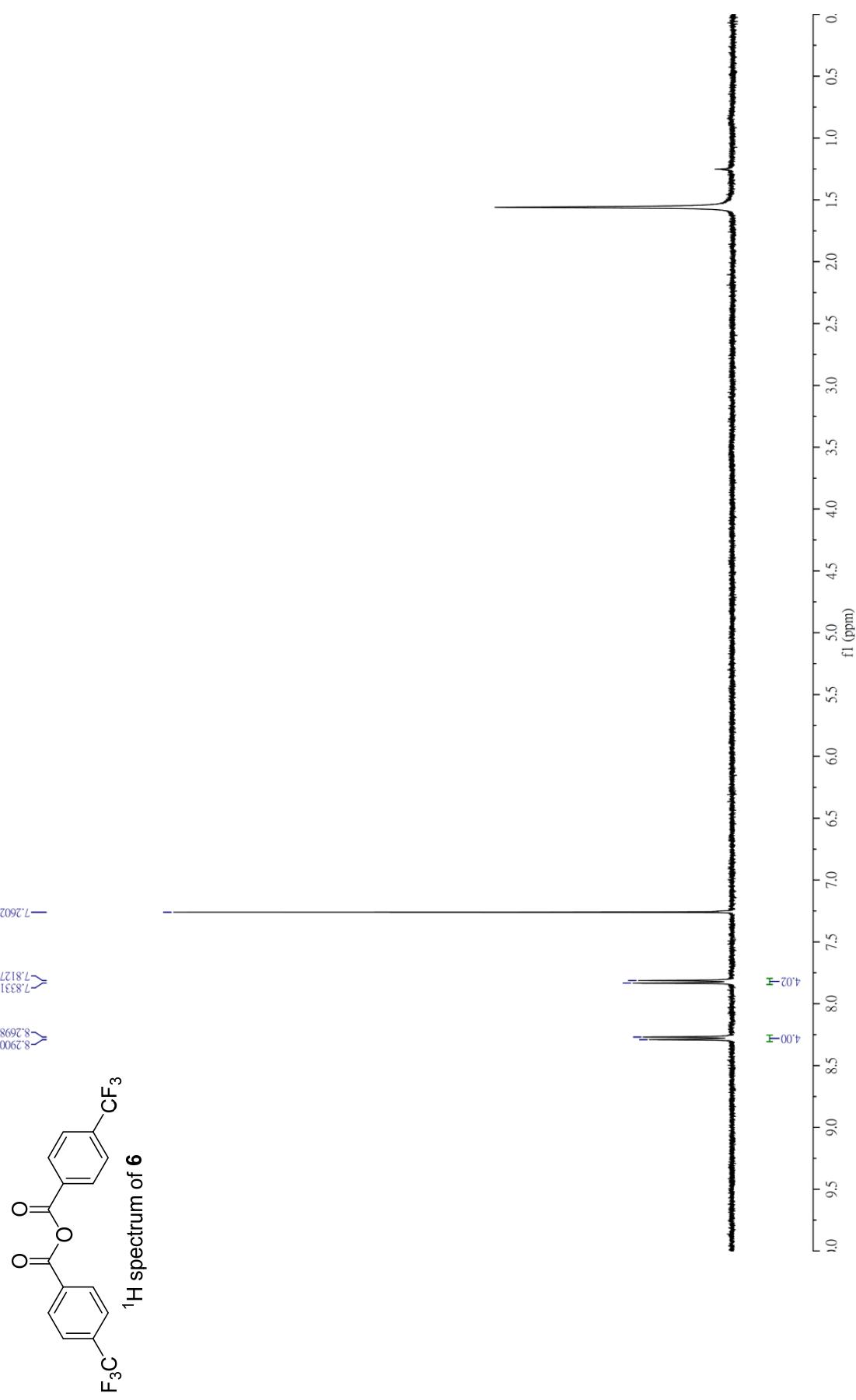


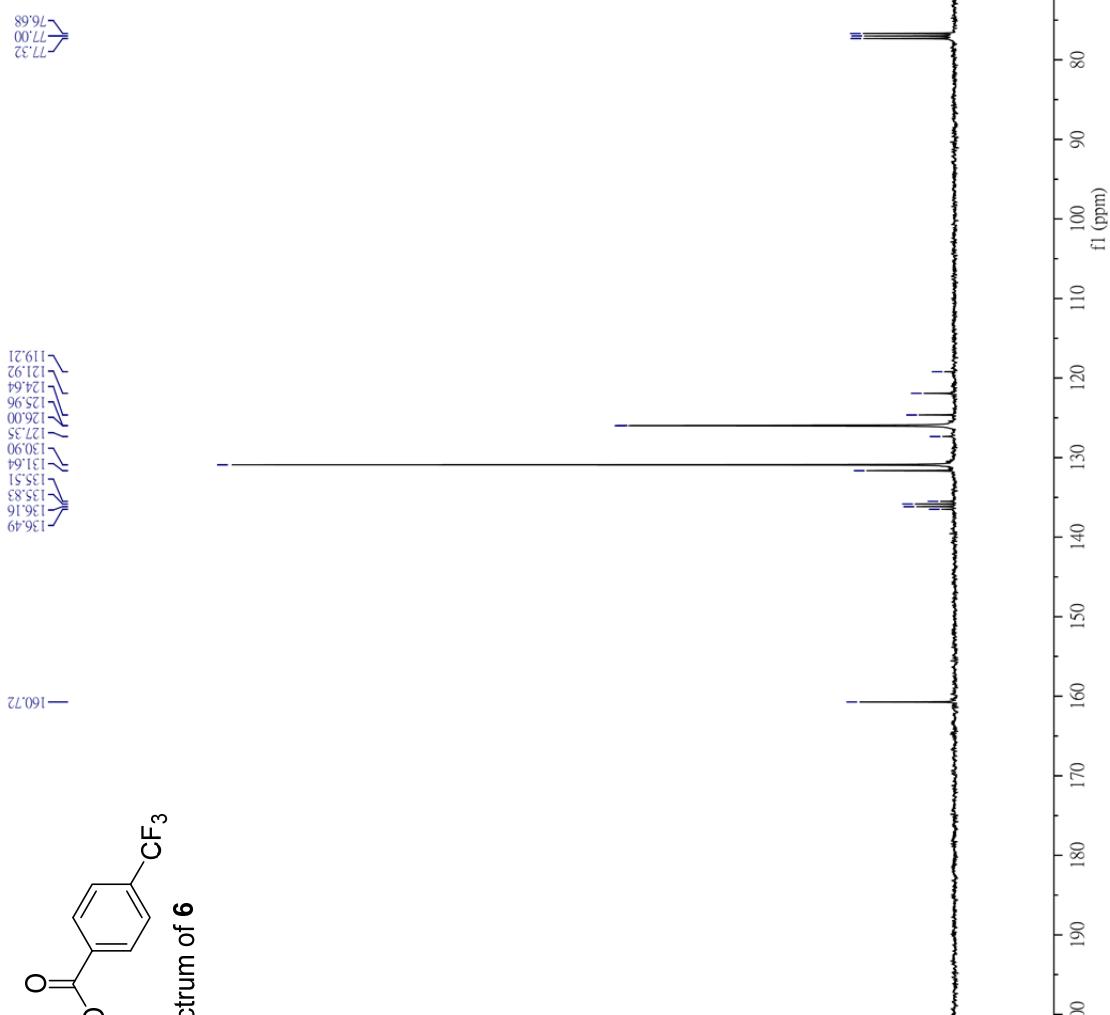
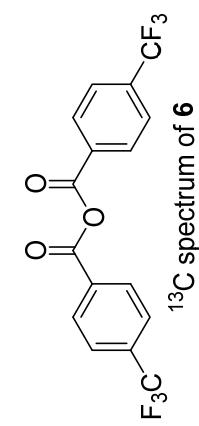


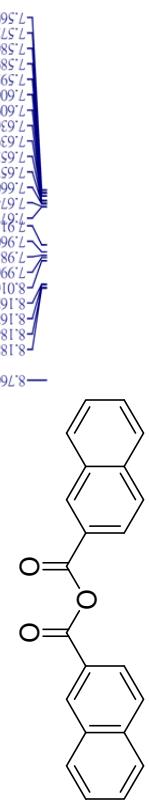
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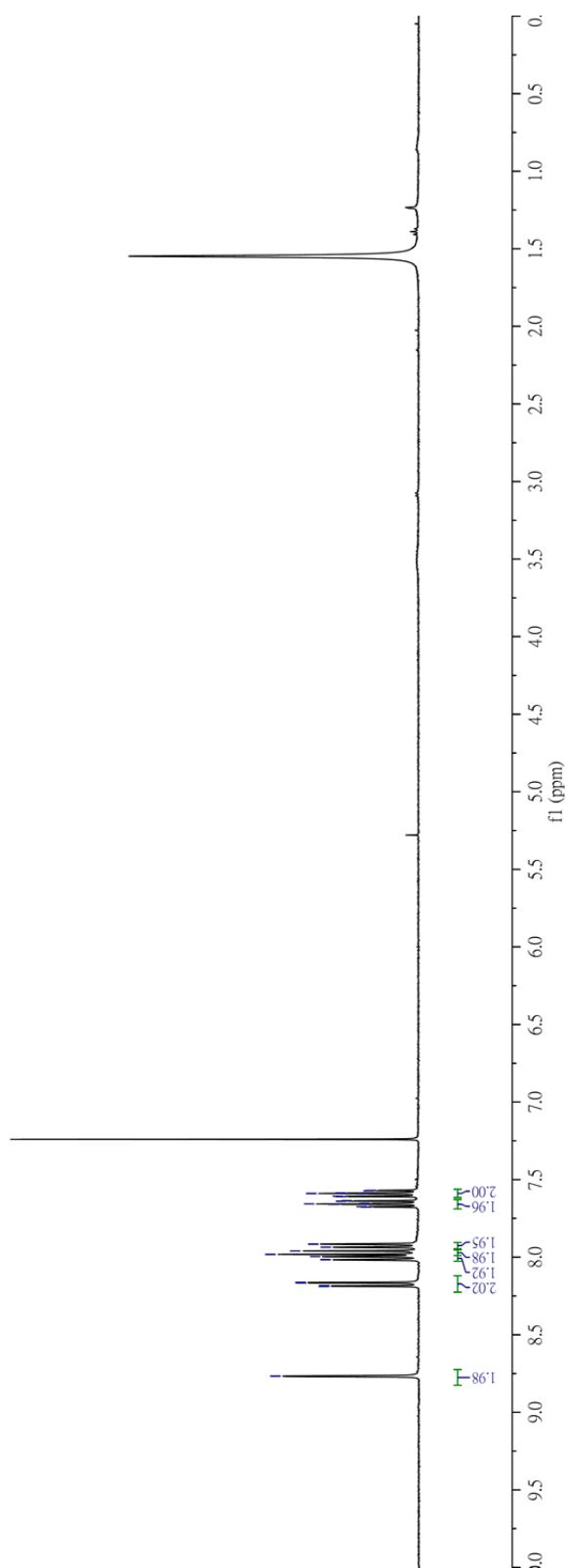


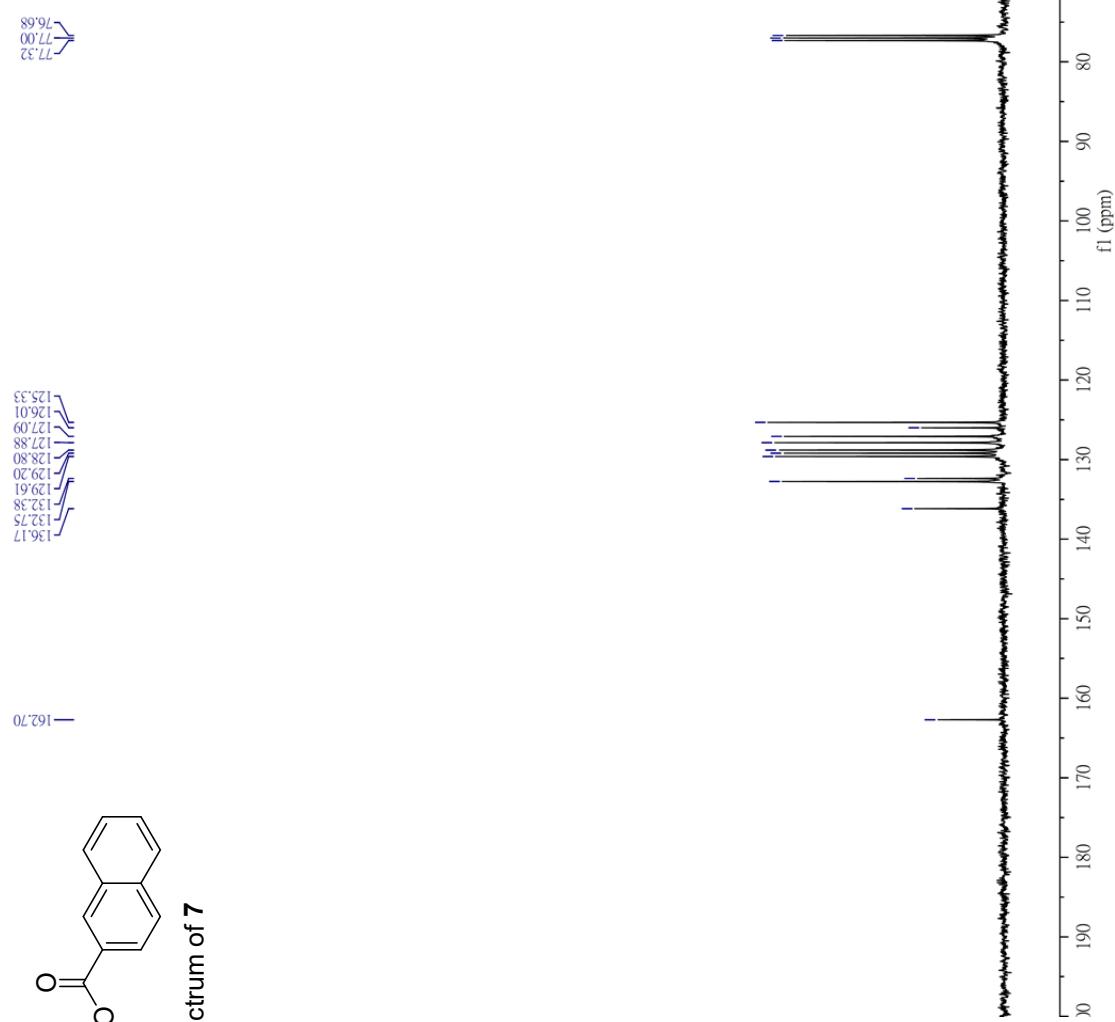
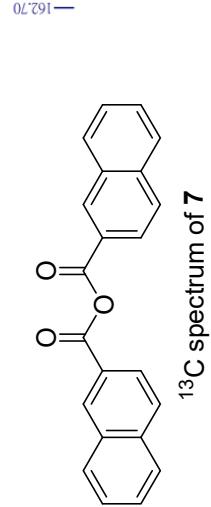


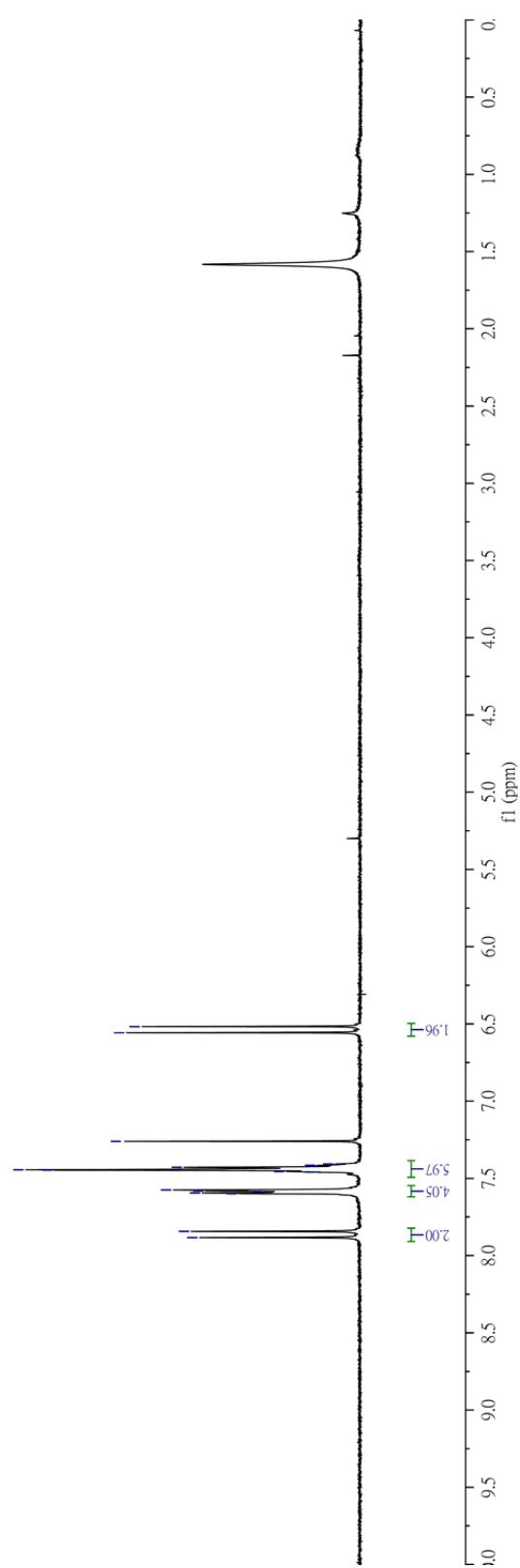
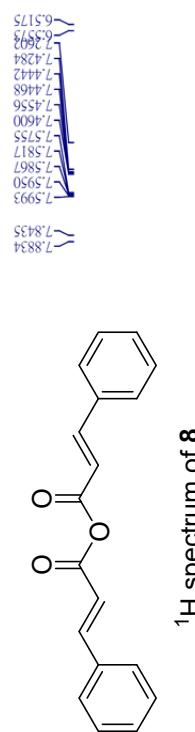


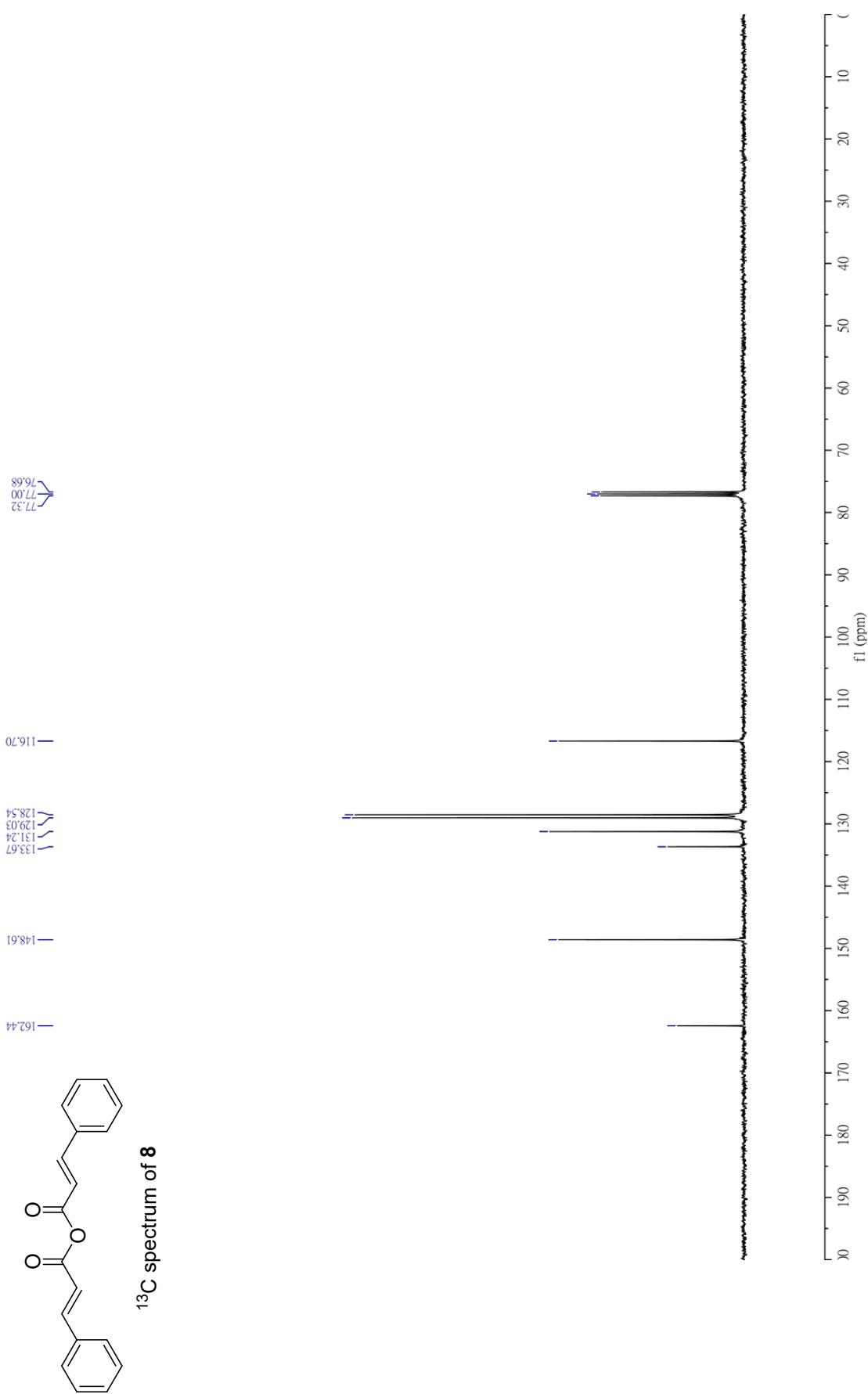


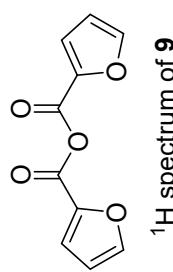
^1H spectrum of 7



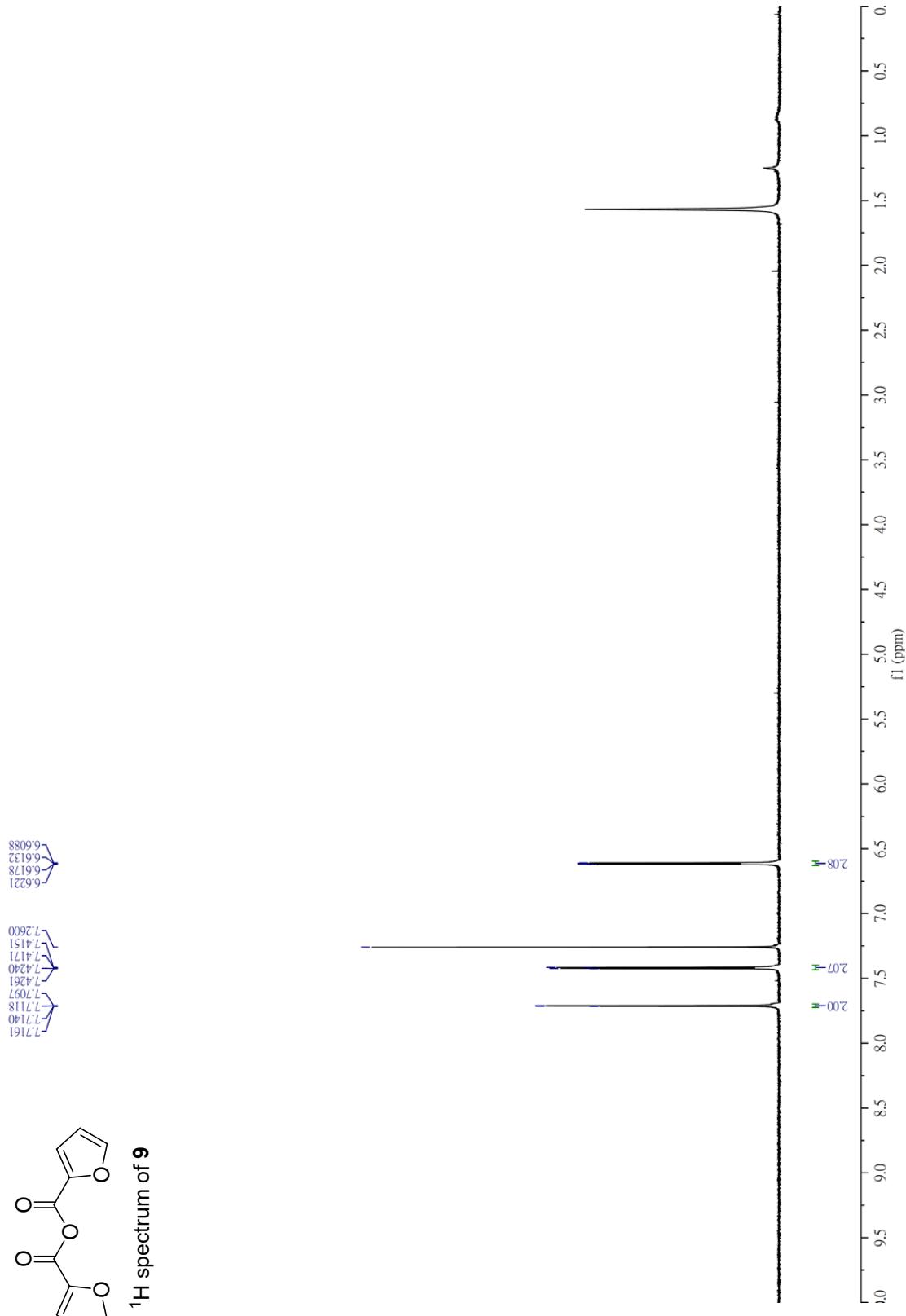


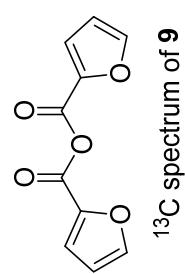




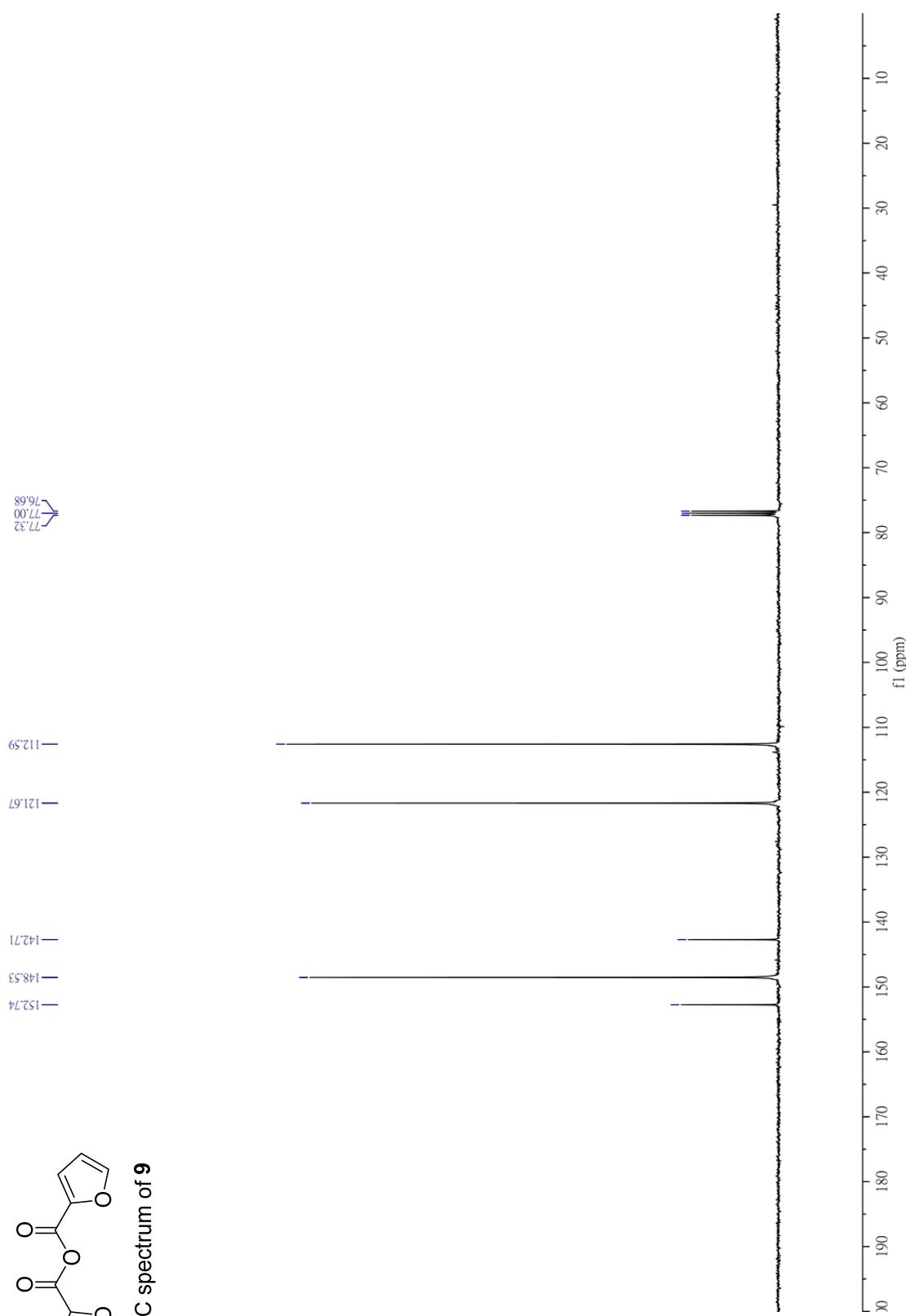


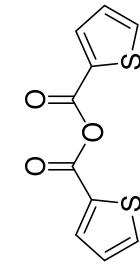
1H spectrum of 9



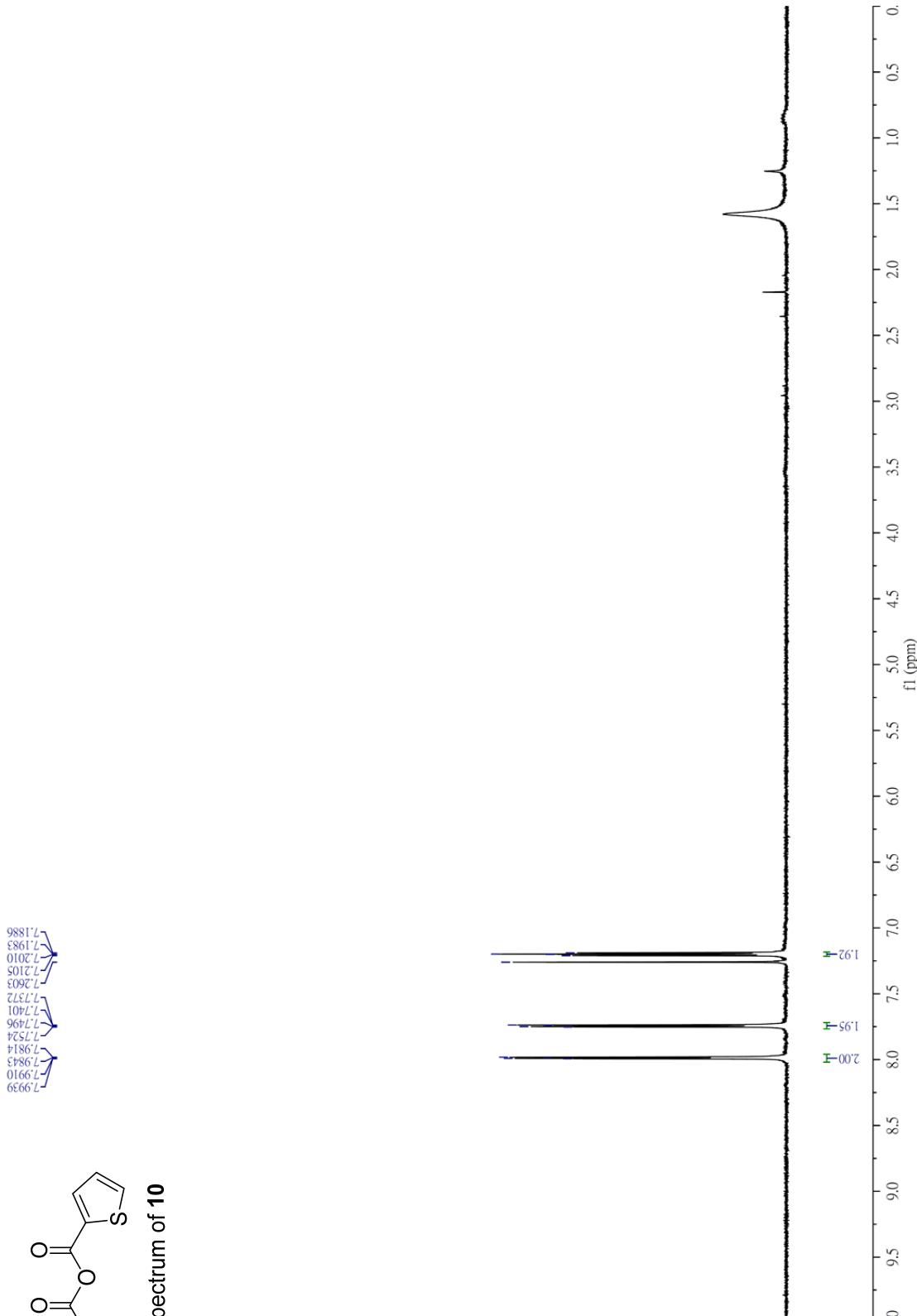


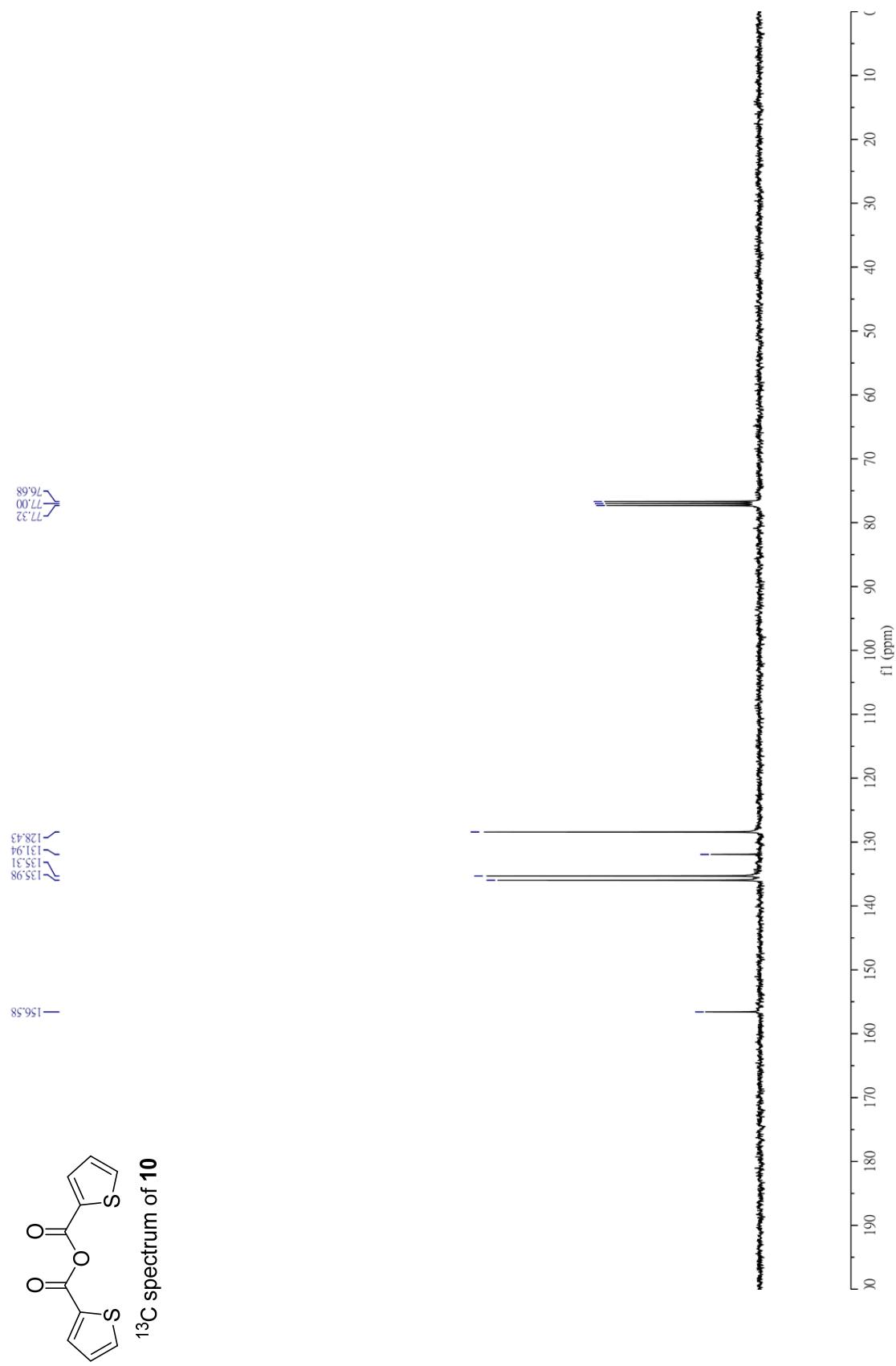
¹³C spectrum of **9**

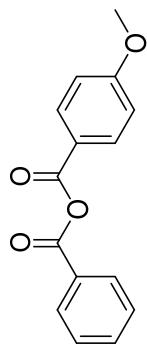




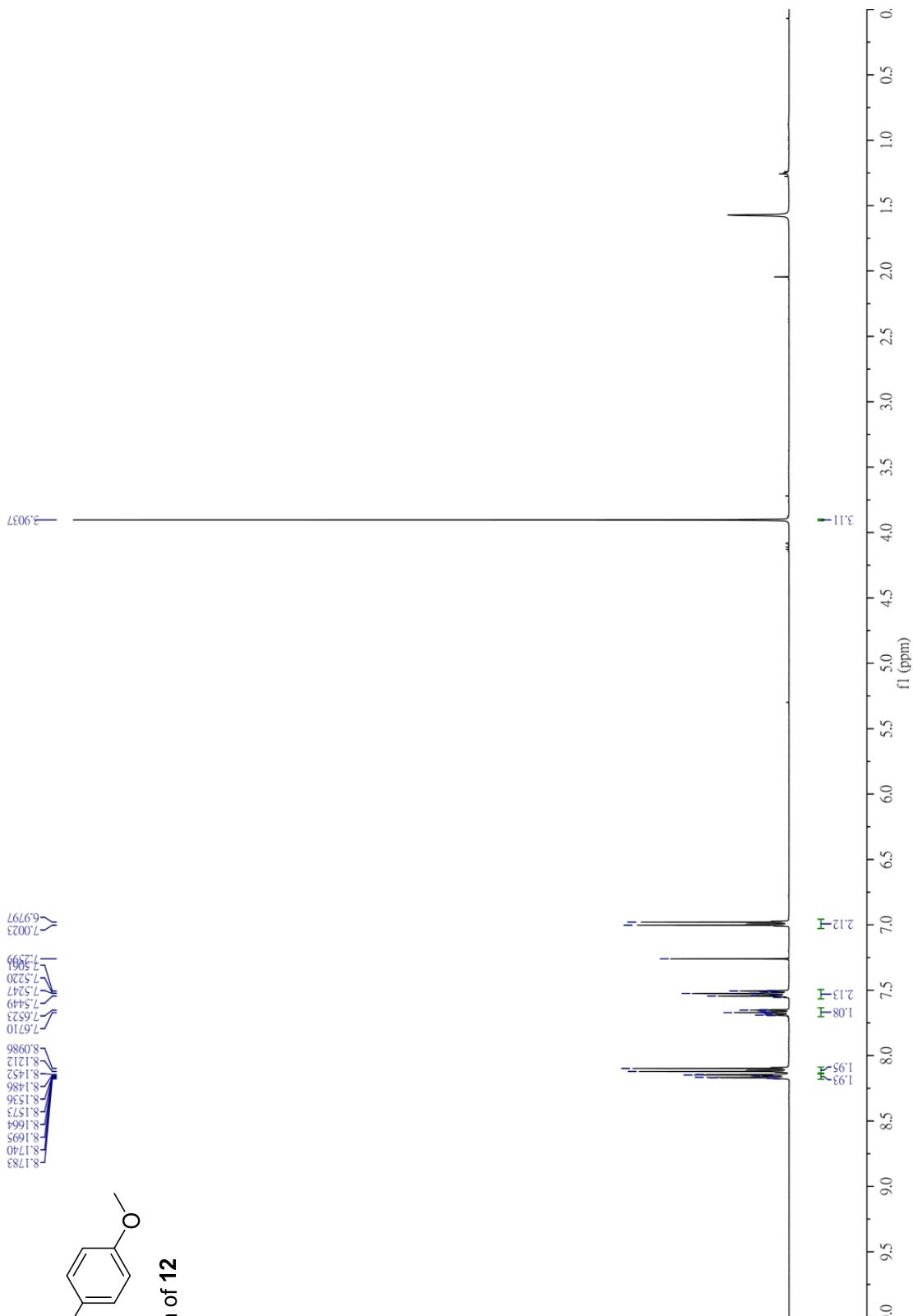
1H spectrum of 10

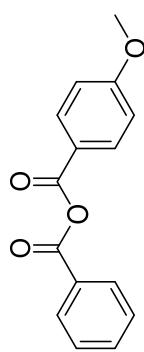
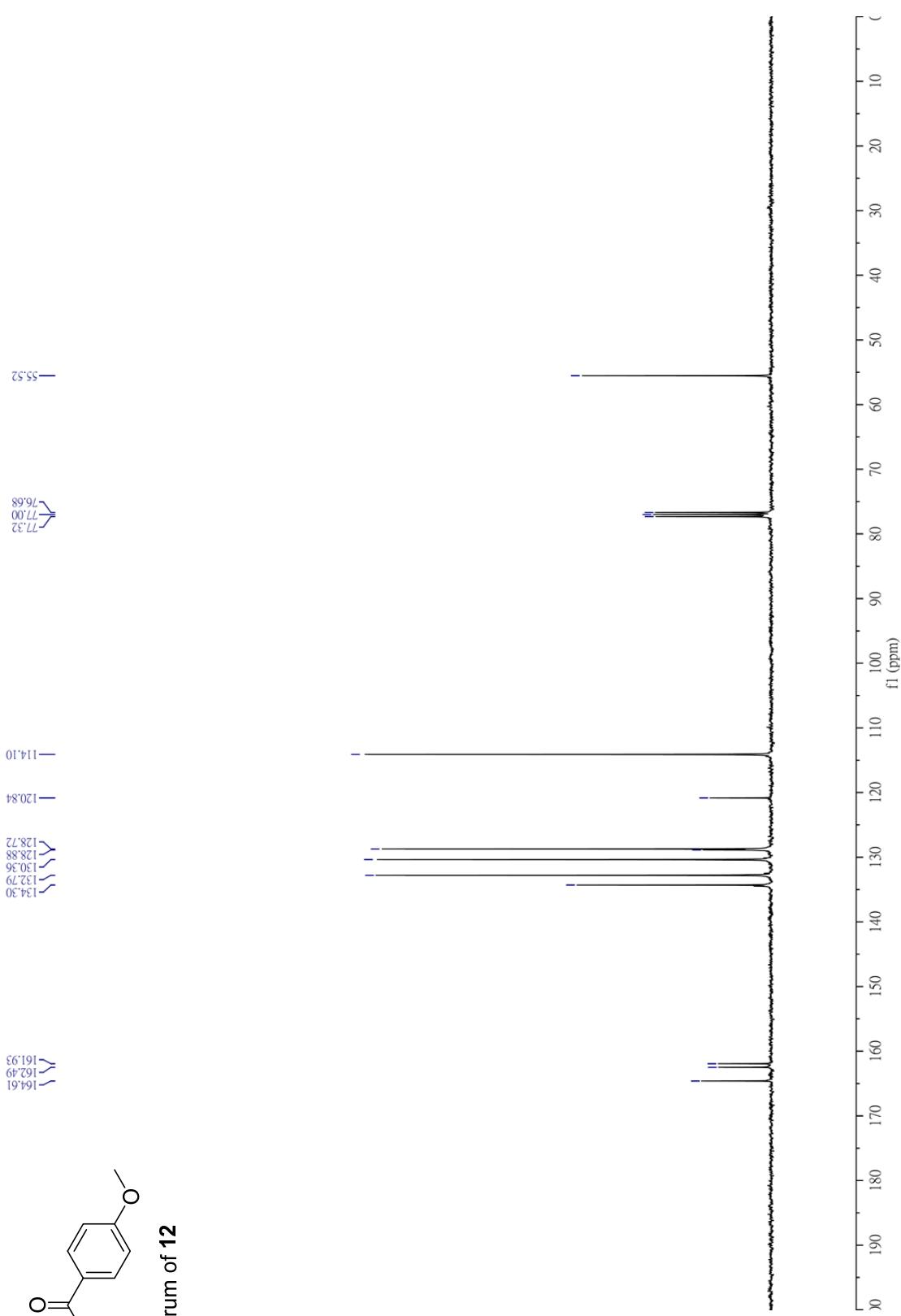




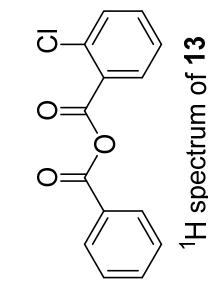


^1H spectrum of 12

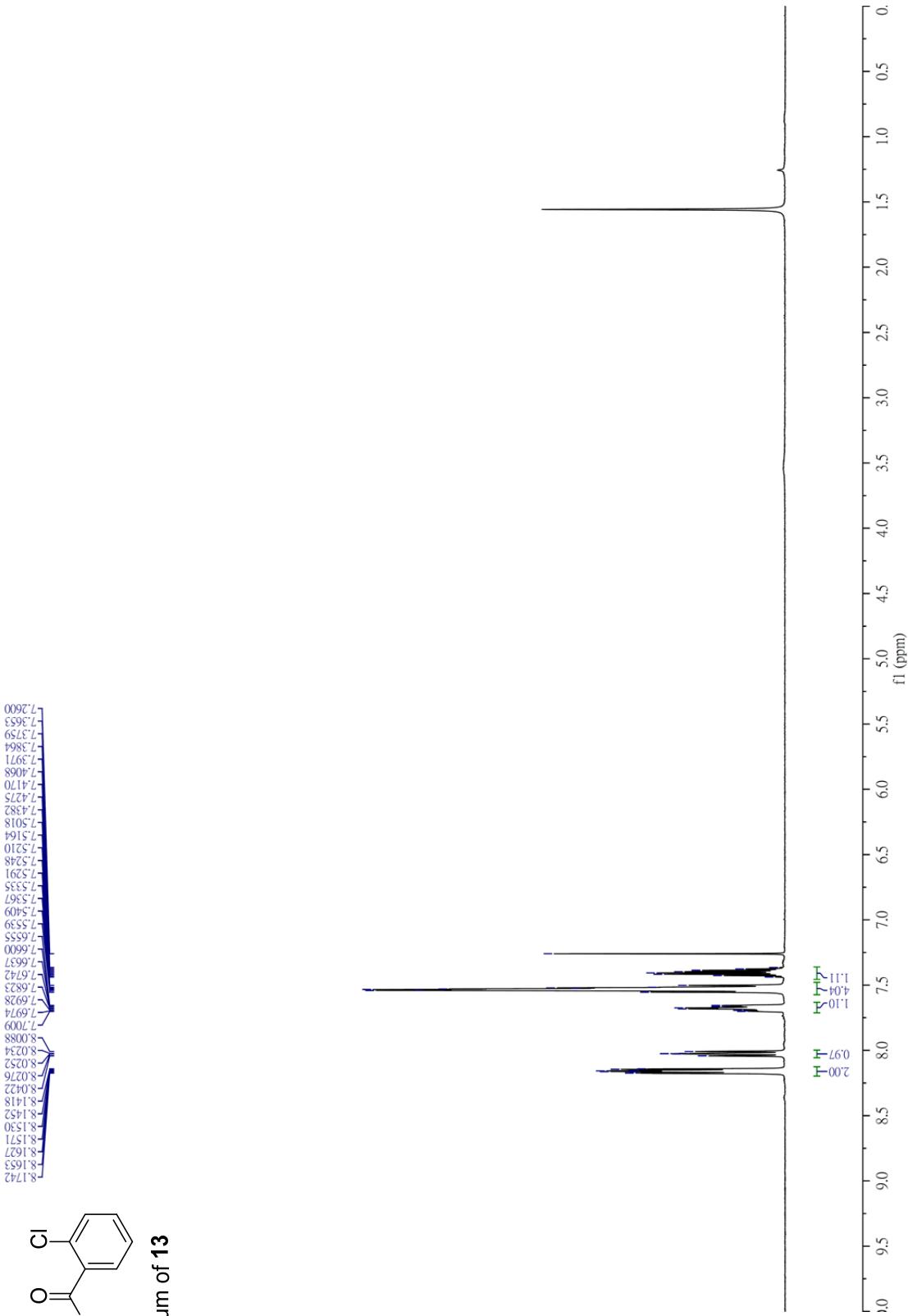


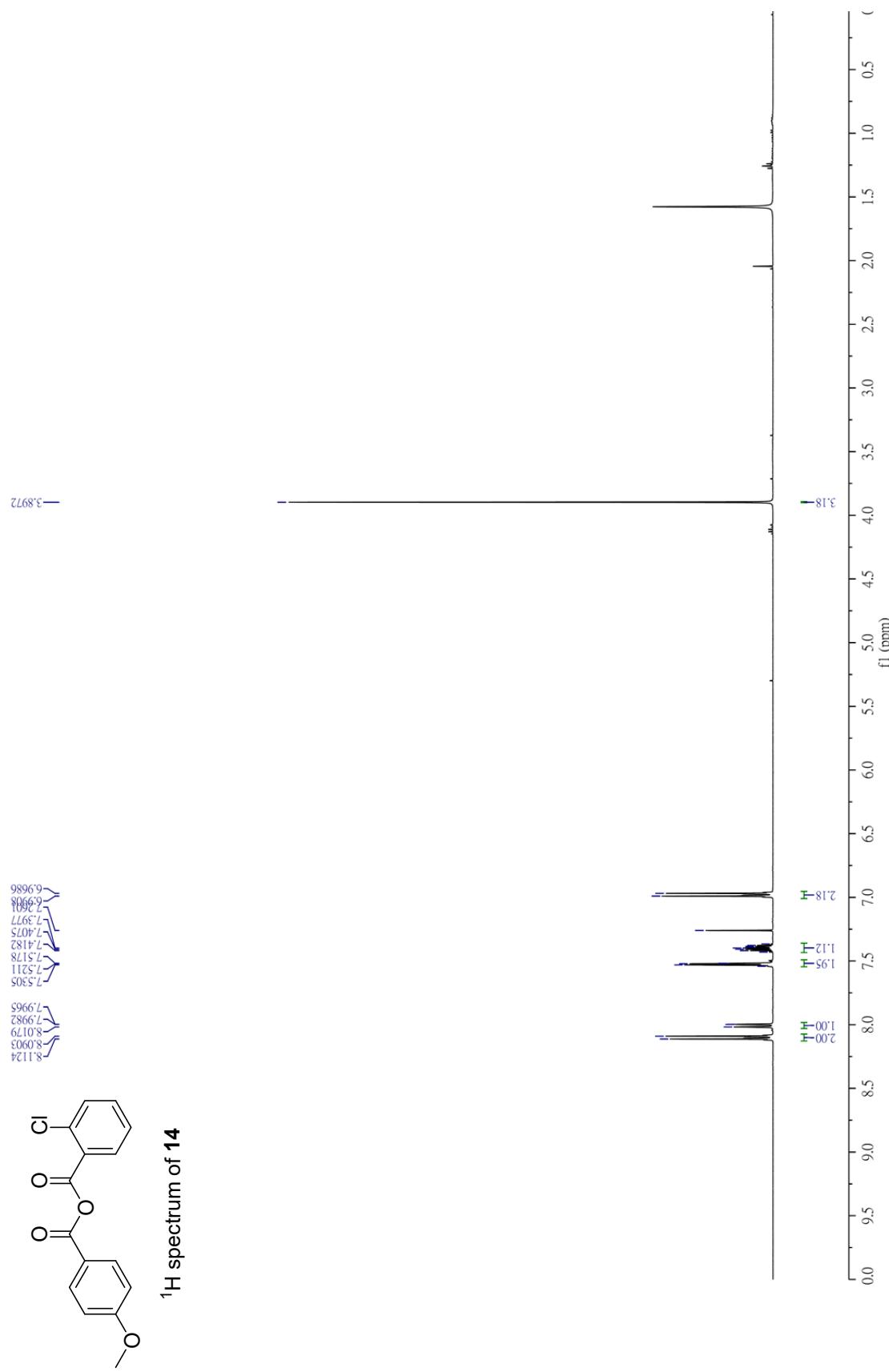


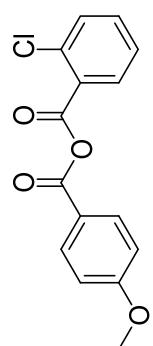
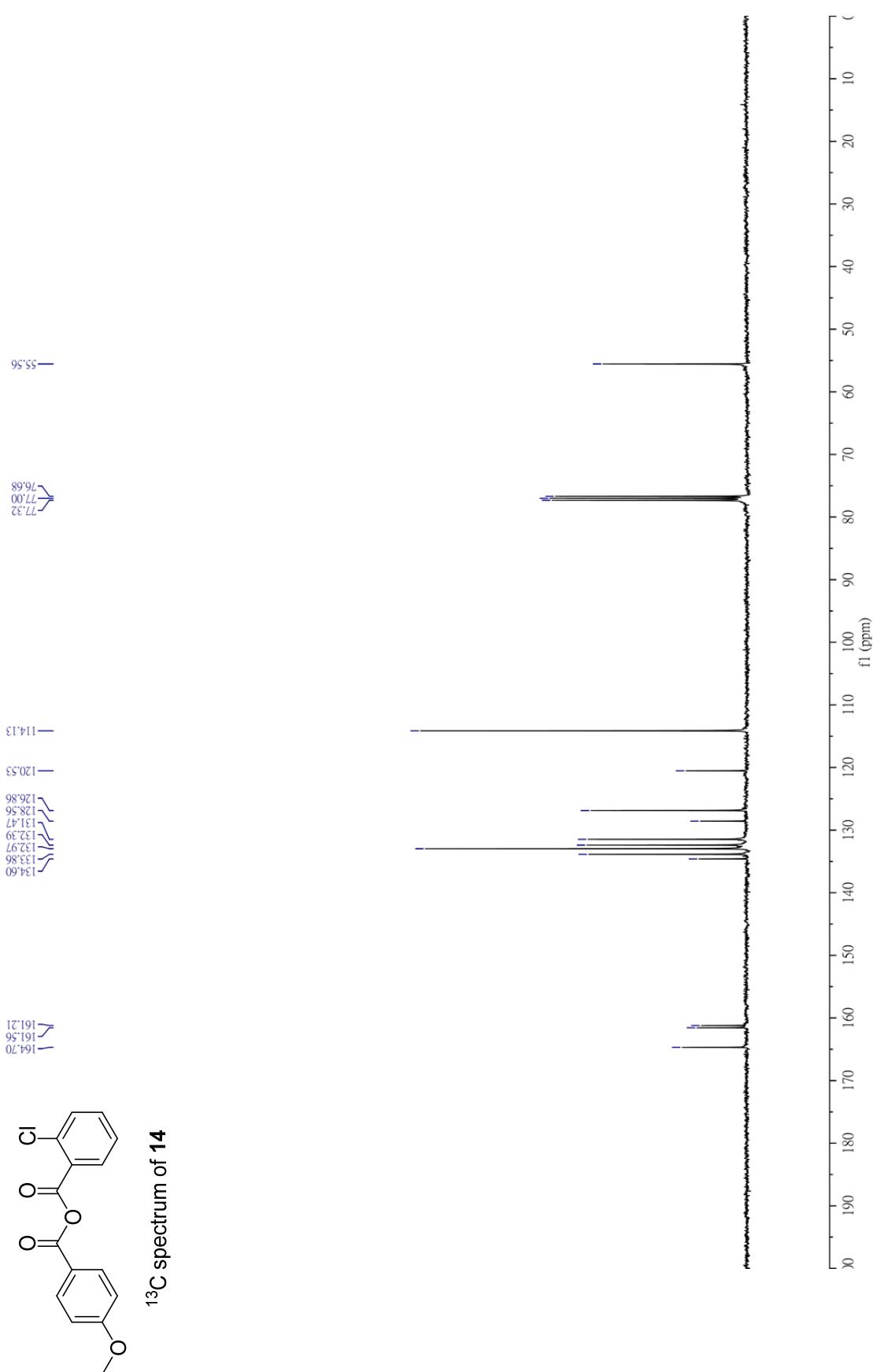
13C spectrum of **12**



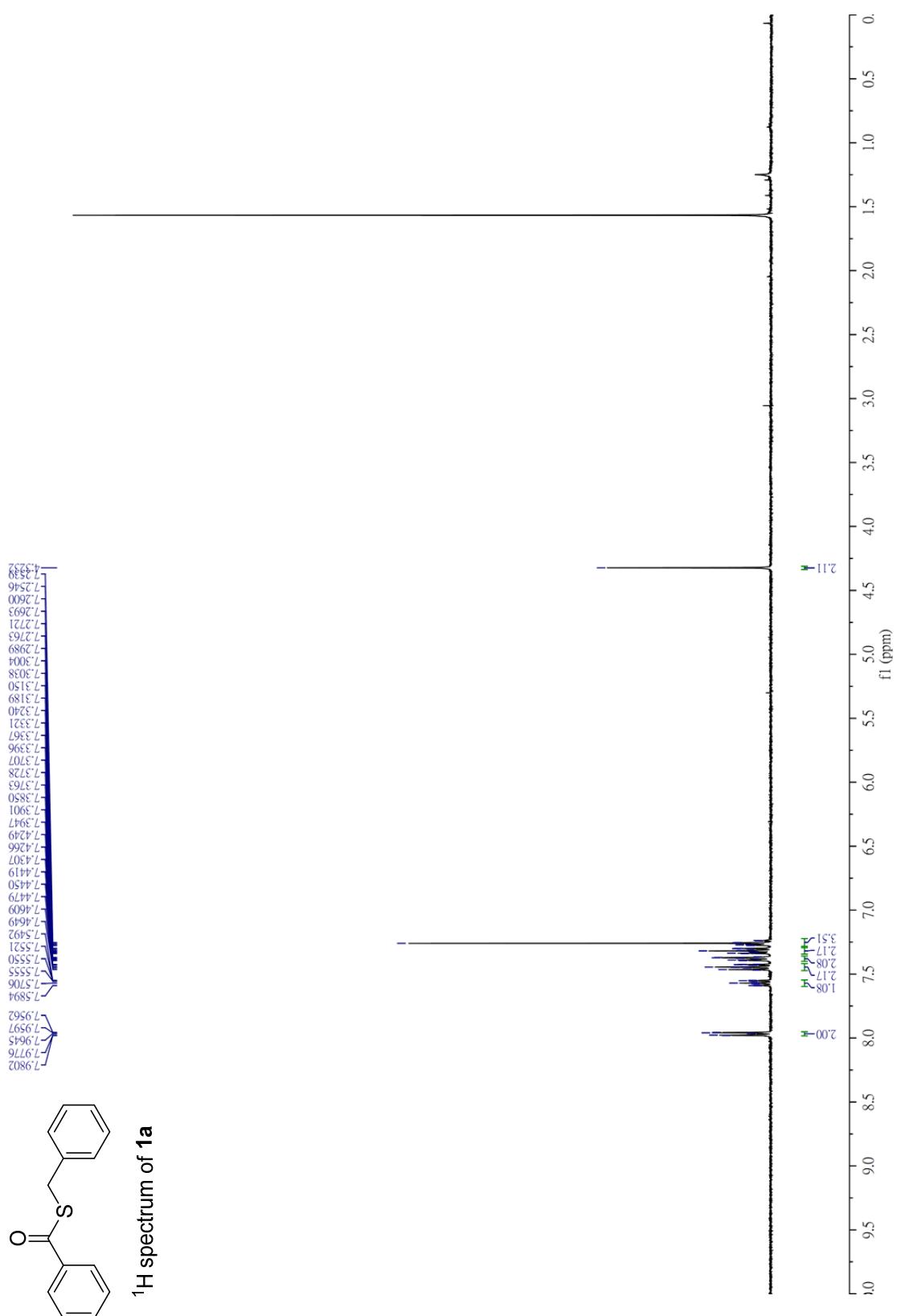
¹H spectrum of 13



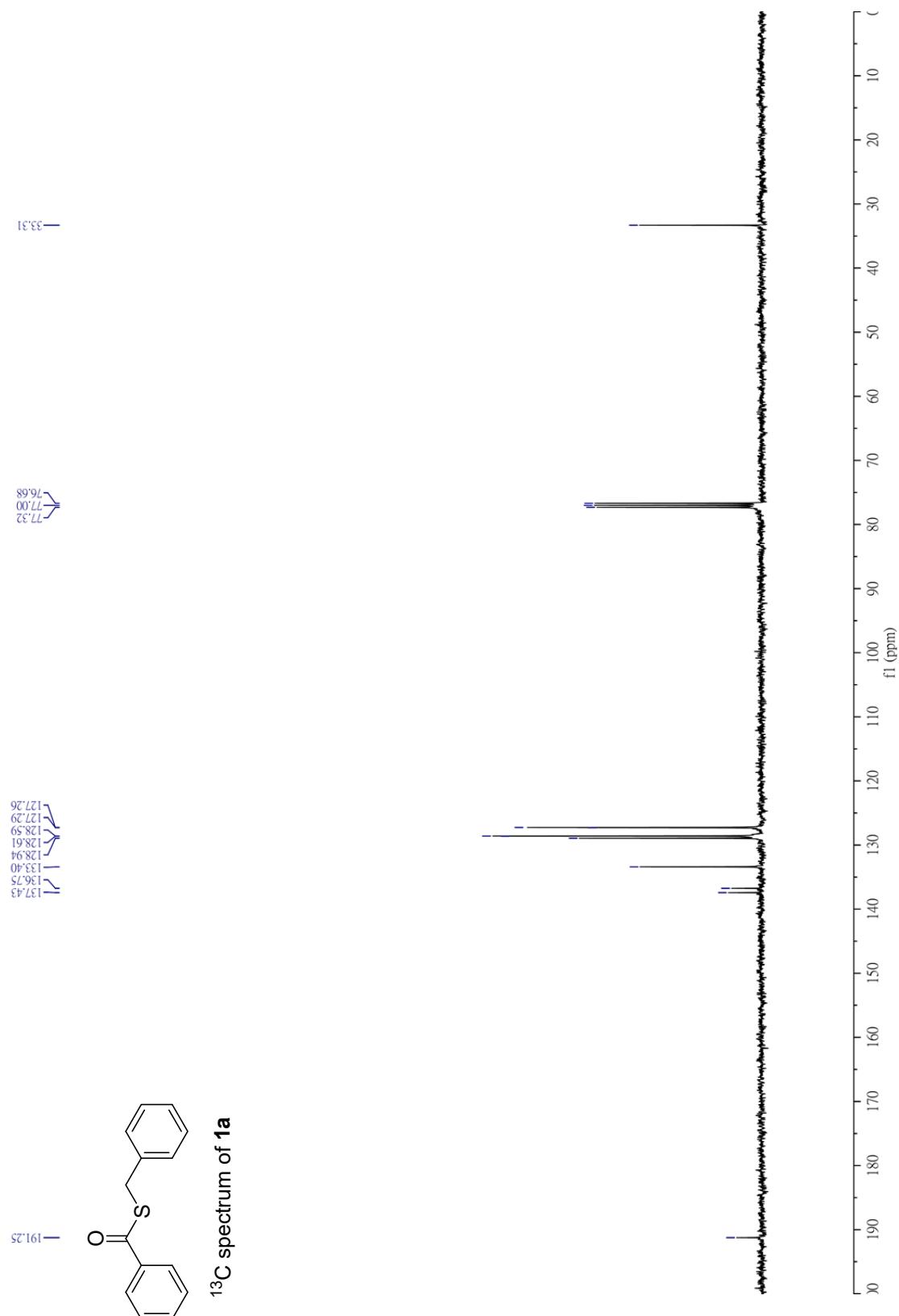




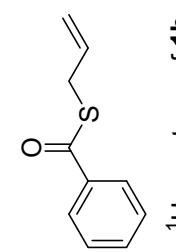
^{13}C spectrum of 14



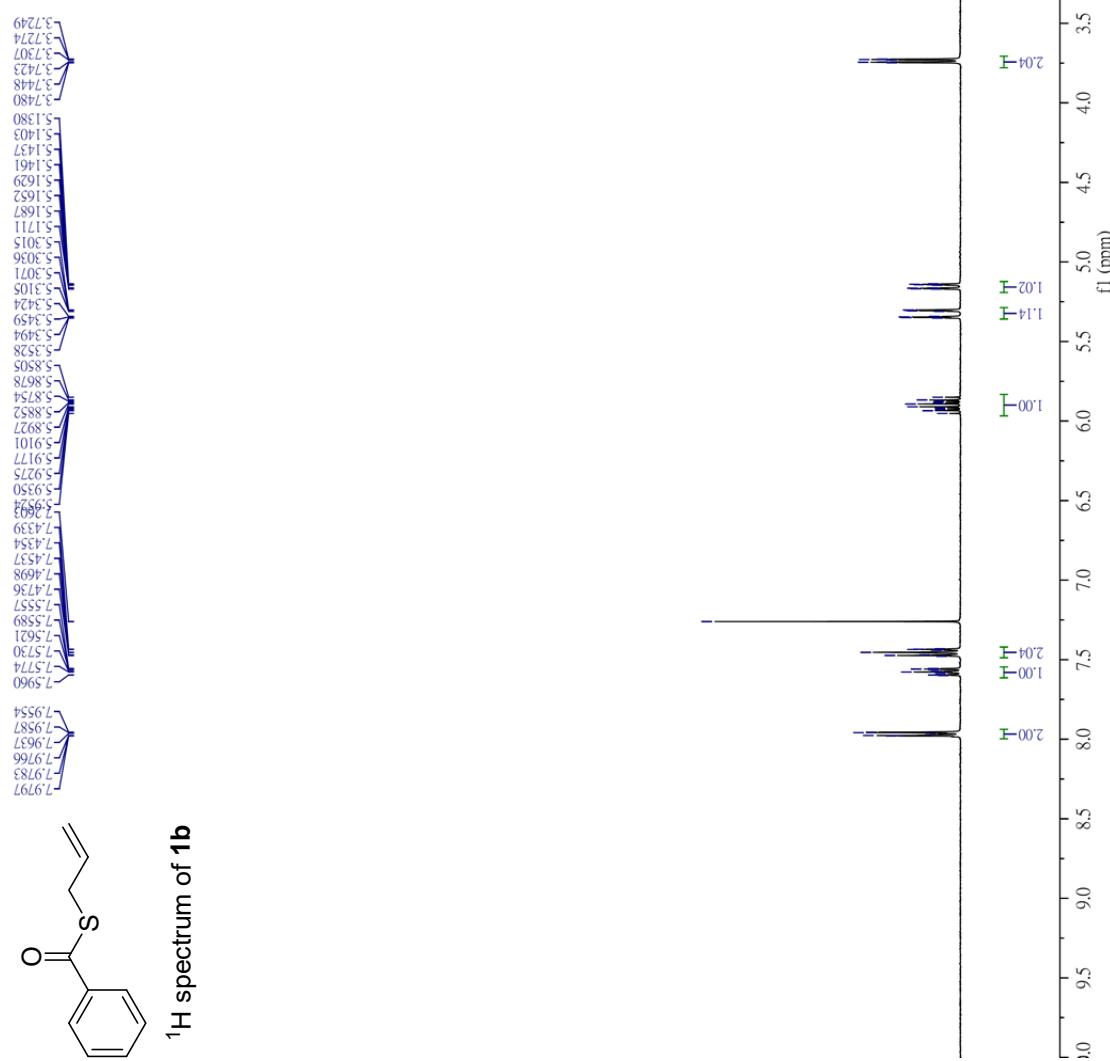
¹H spectrum of **1a**

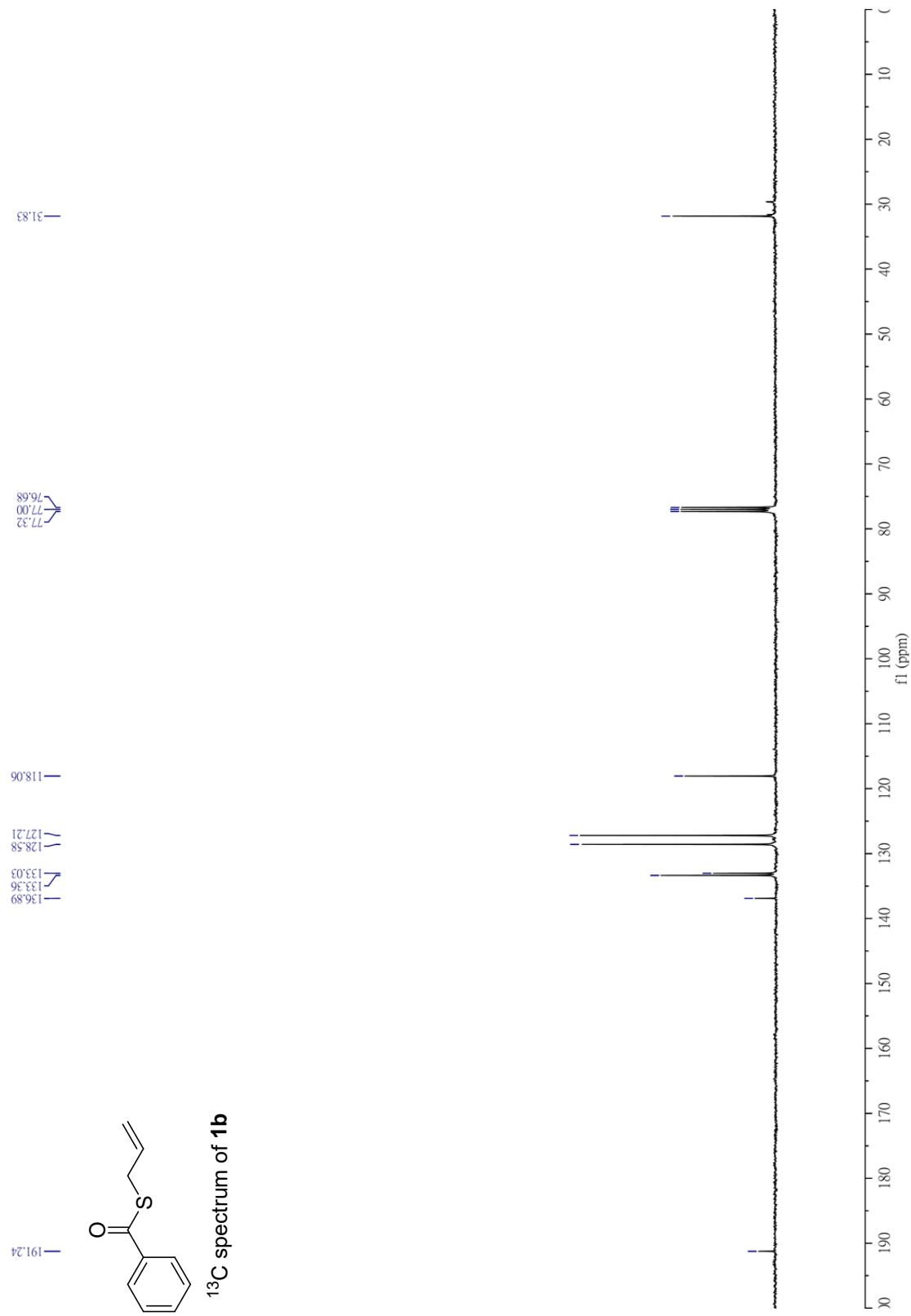
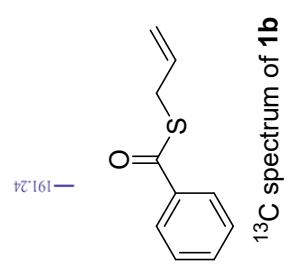


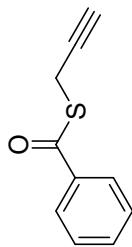
^{13}C spectrum of **1a**



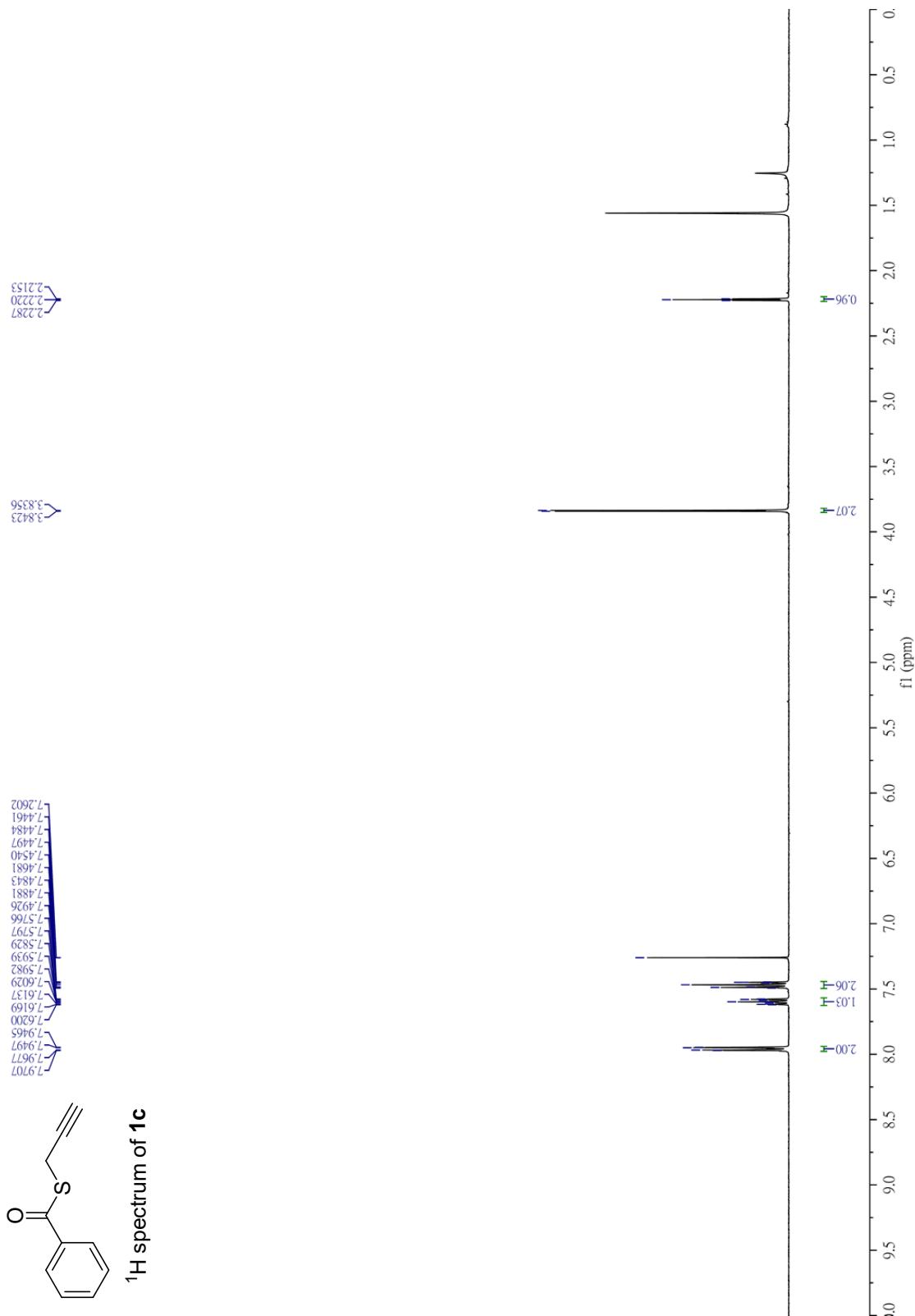
¹H spectrum of **1b**

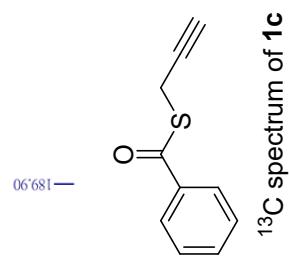




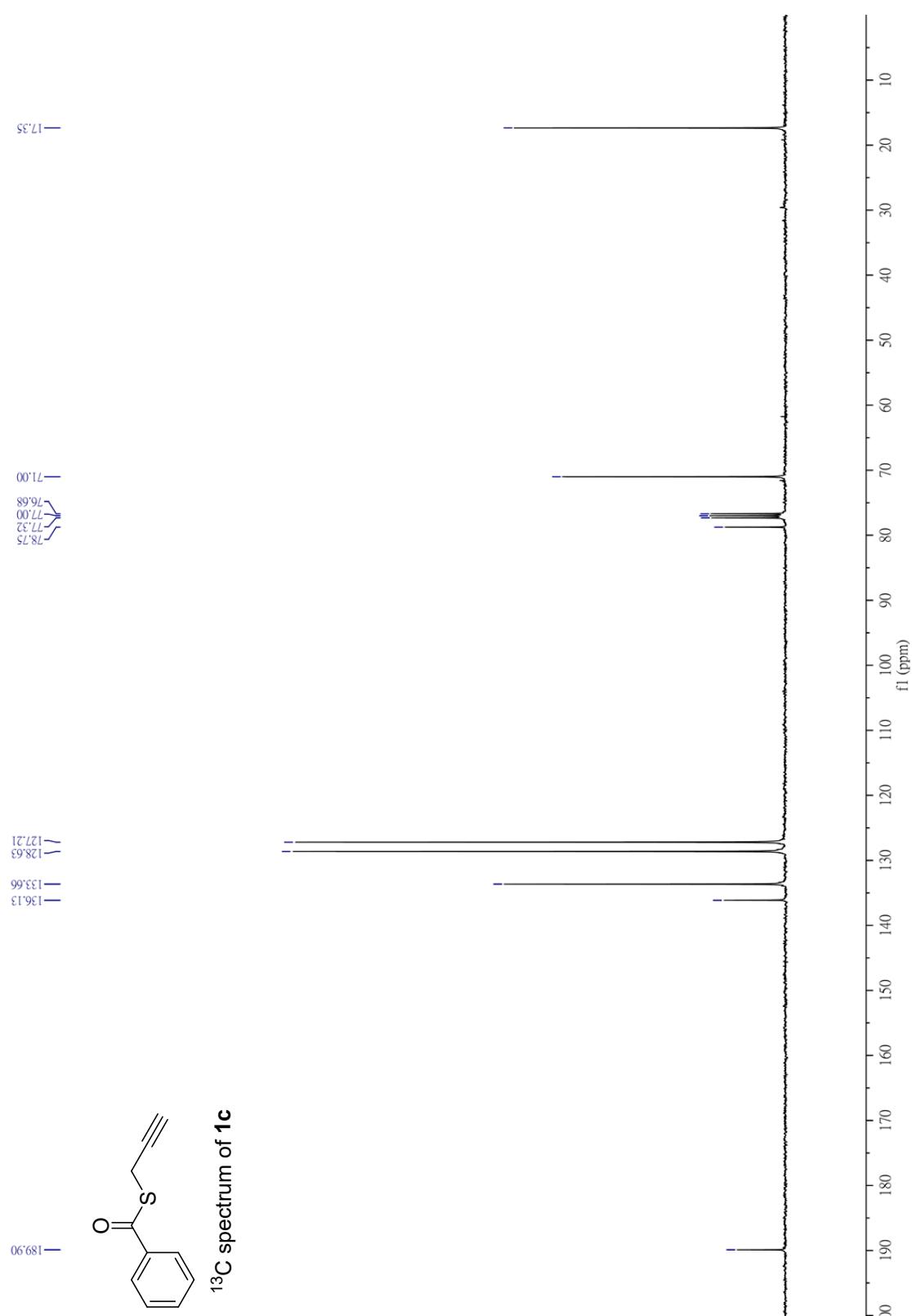


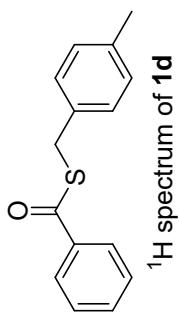
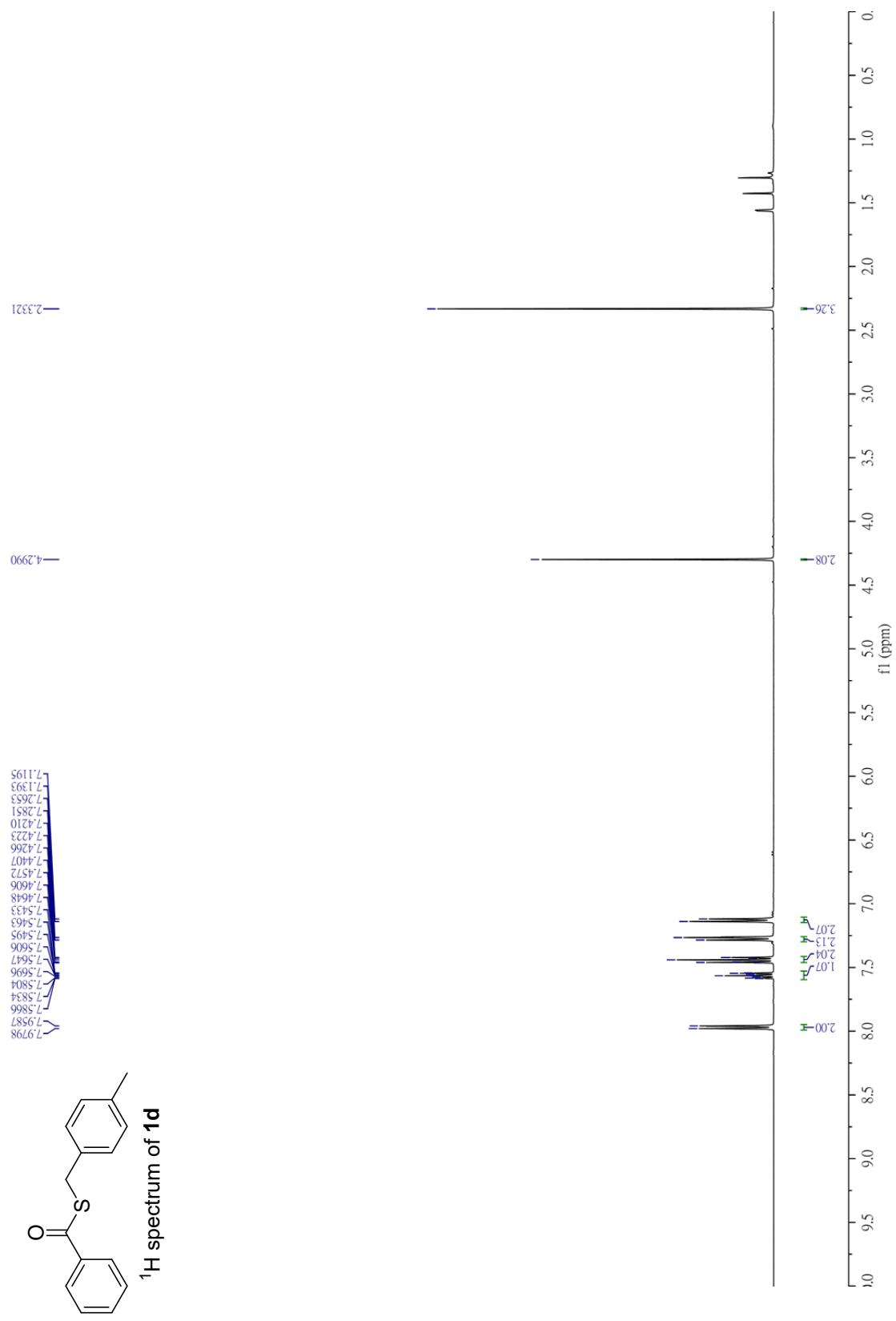
¹H spectrum of 1c



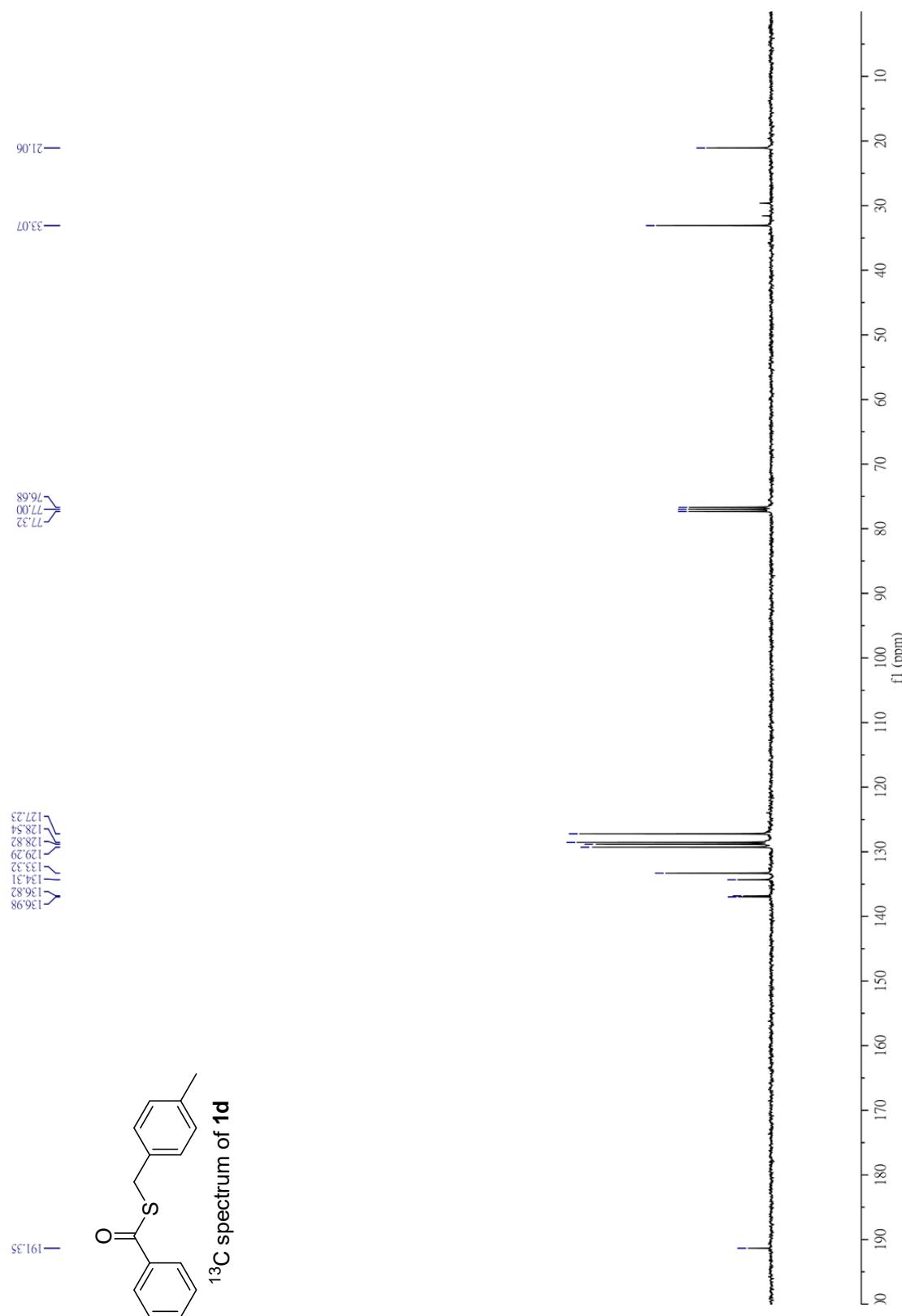


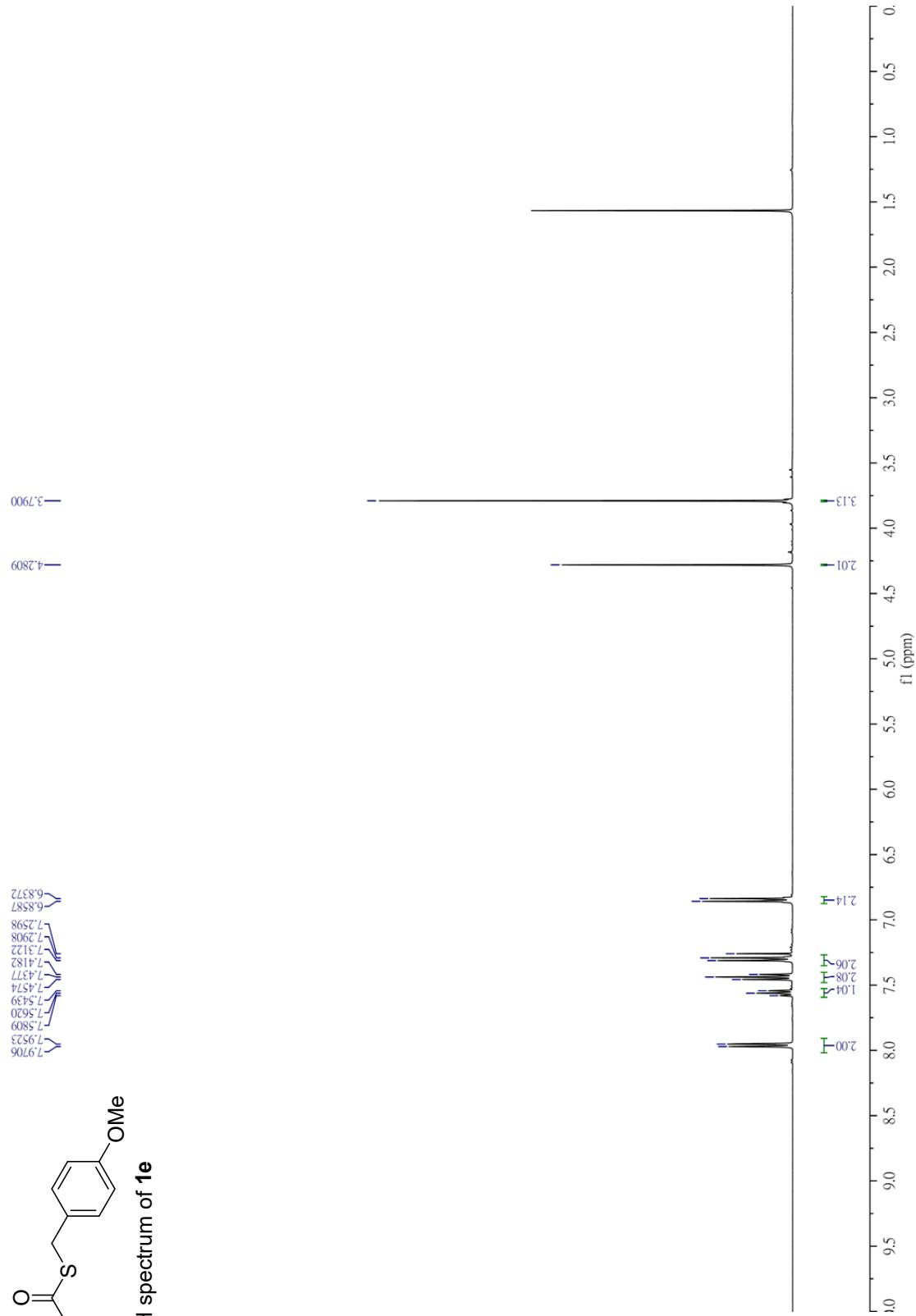
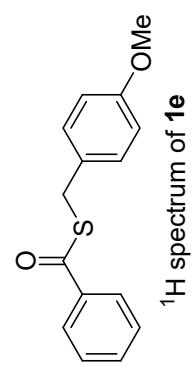
^{13}C spectrum of **1c**

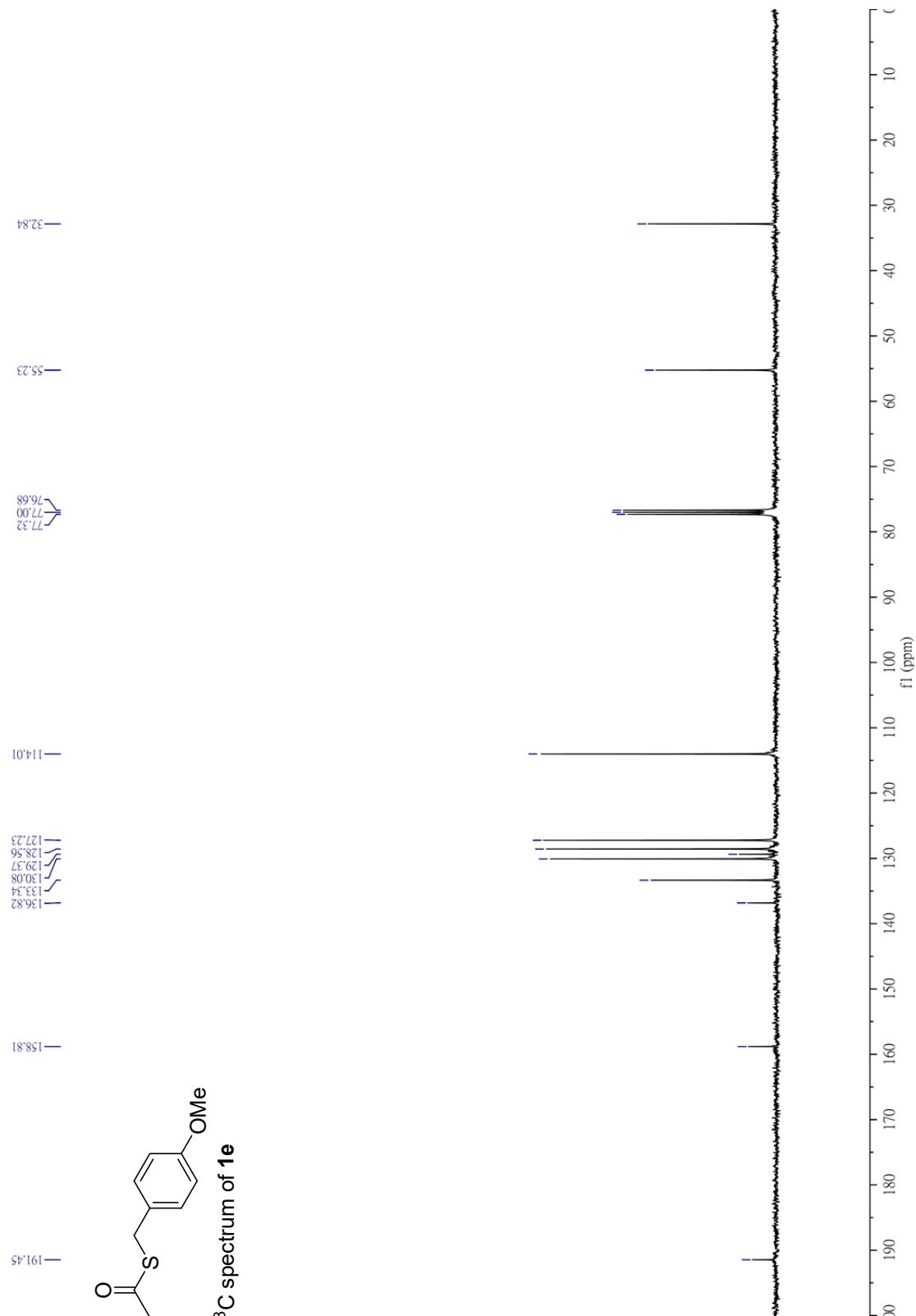
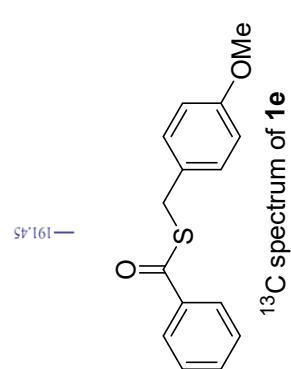


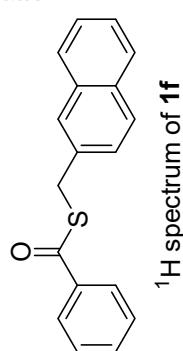


¹H spectrum of 1d

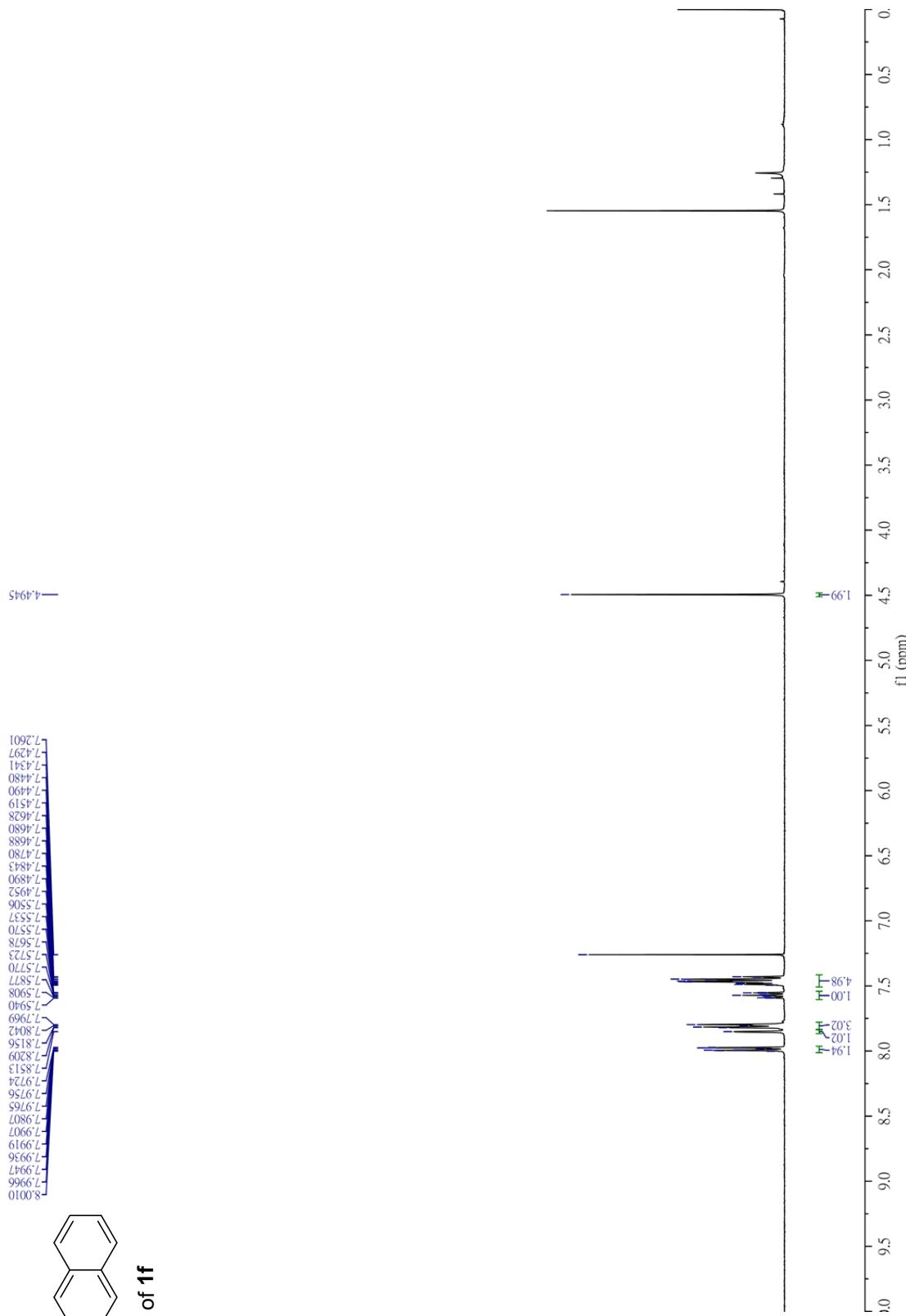


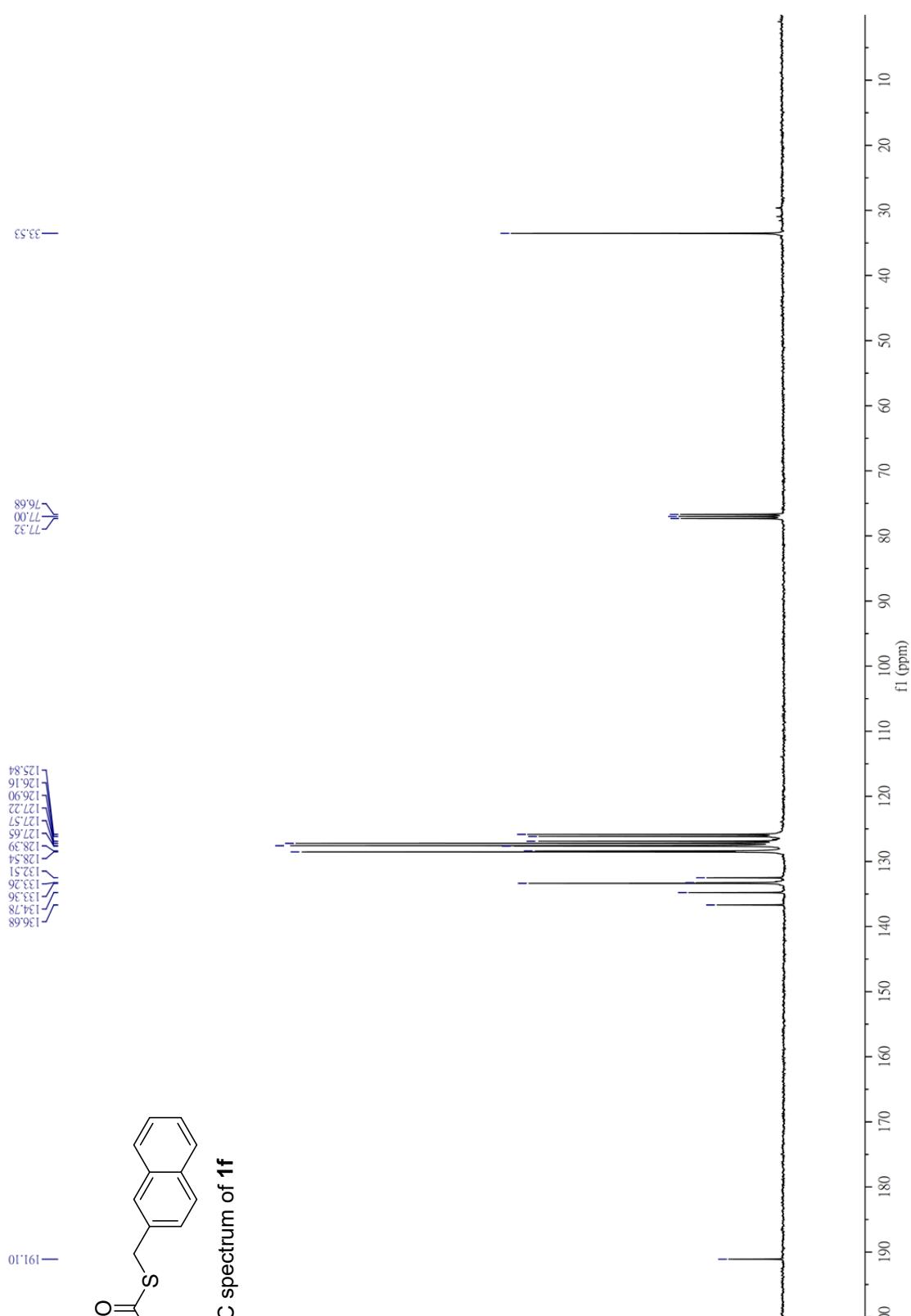
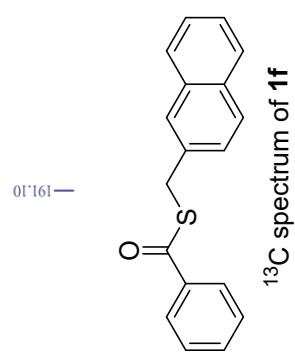


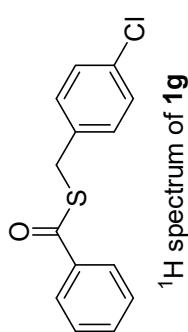




^1H spectrum of 1f

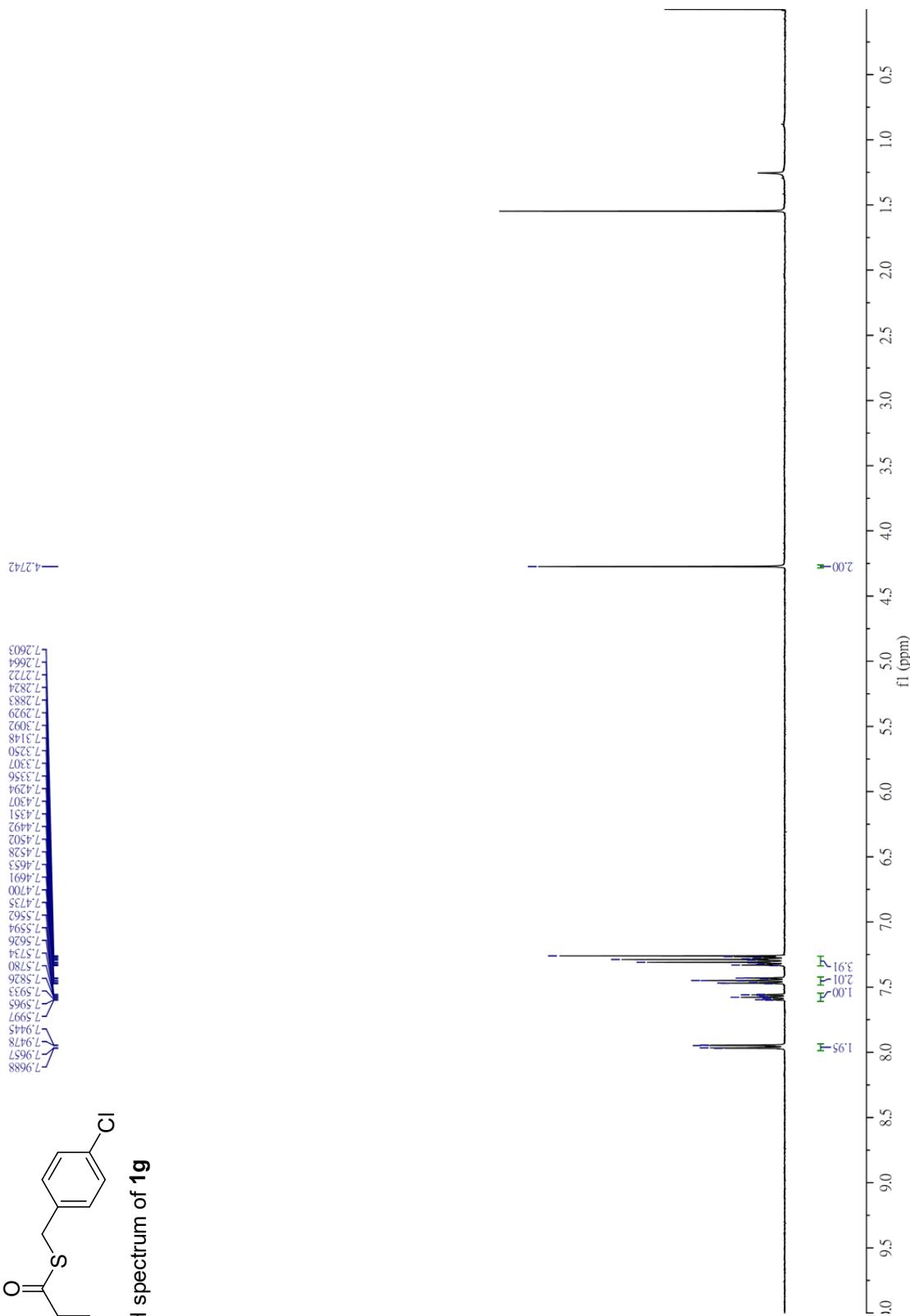


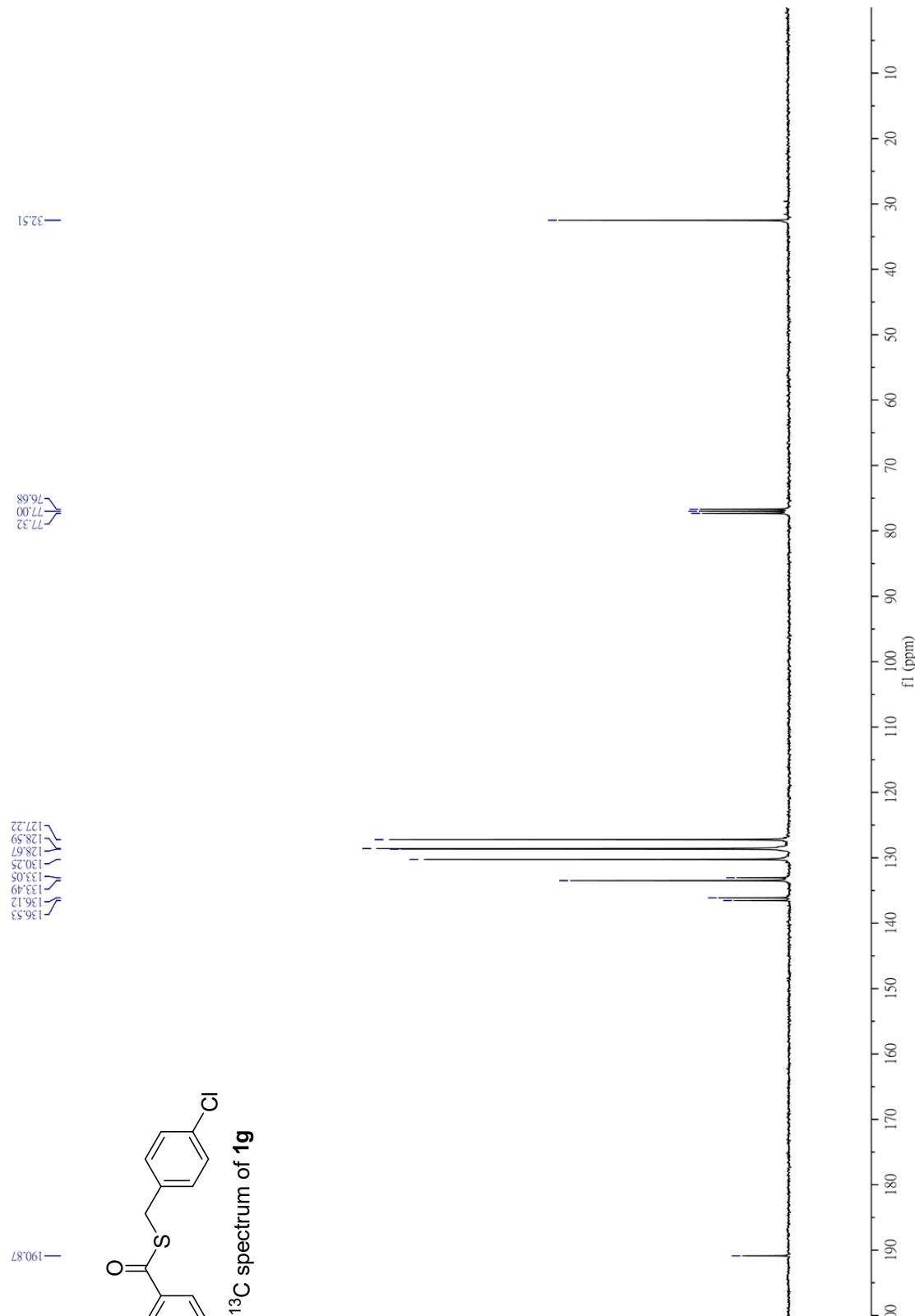
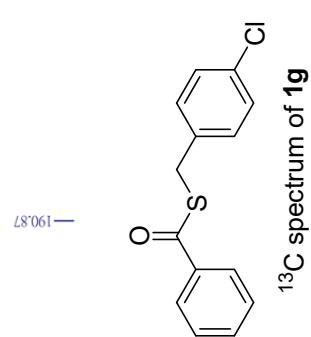


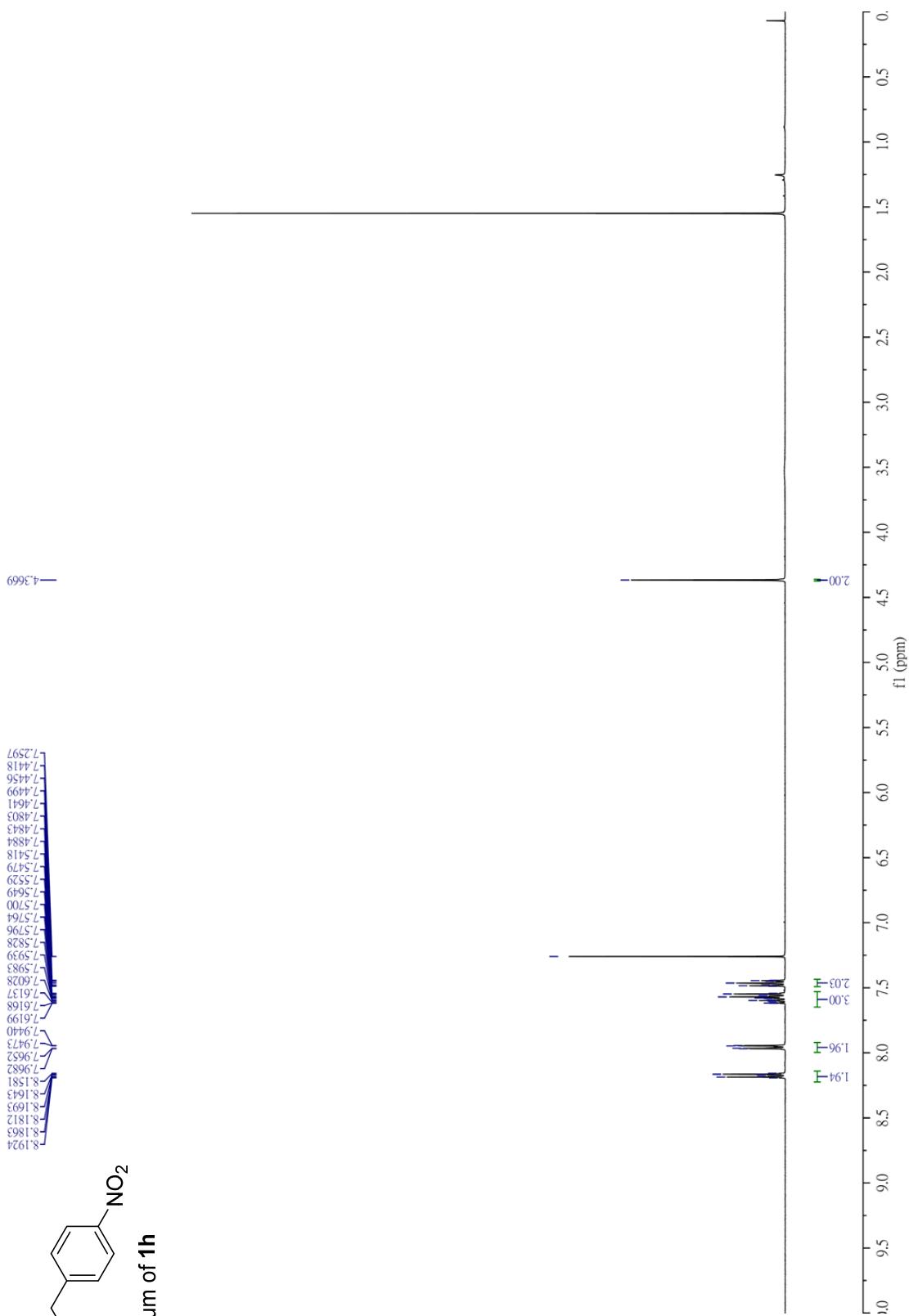
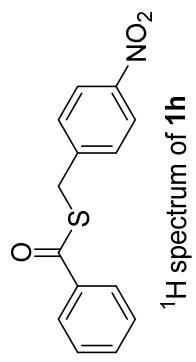


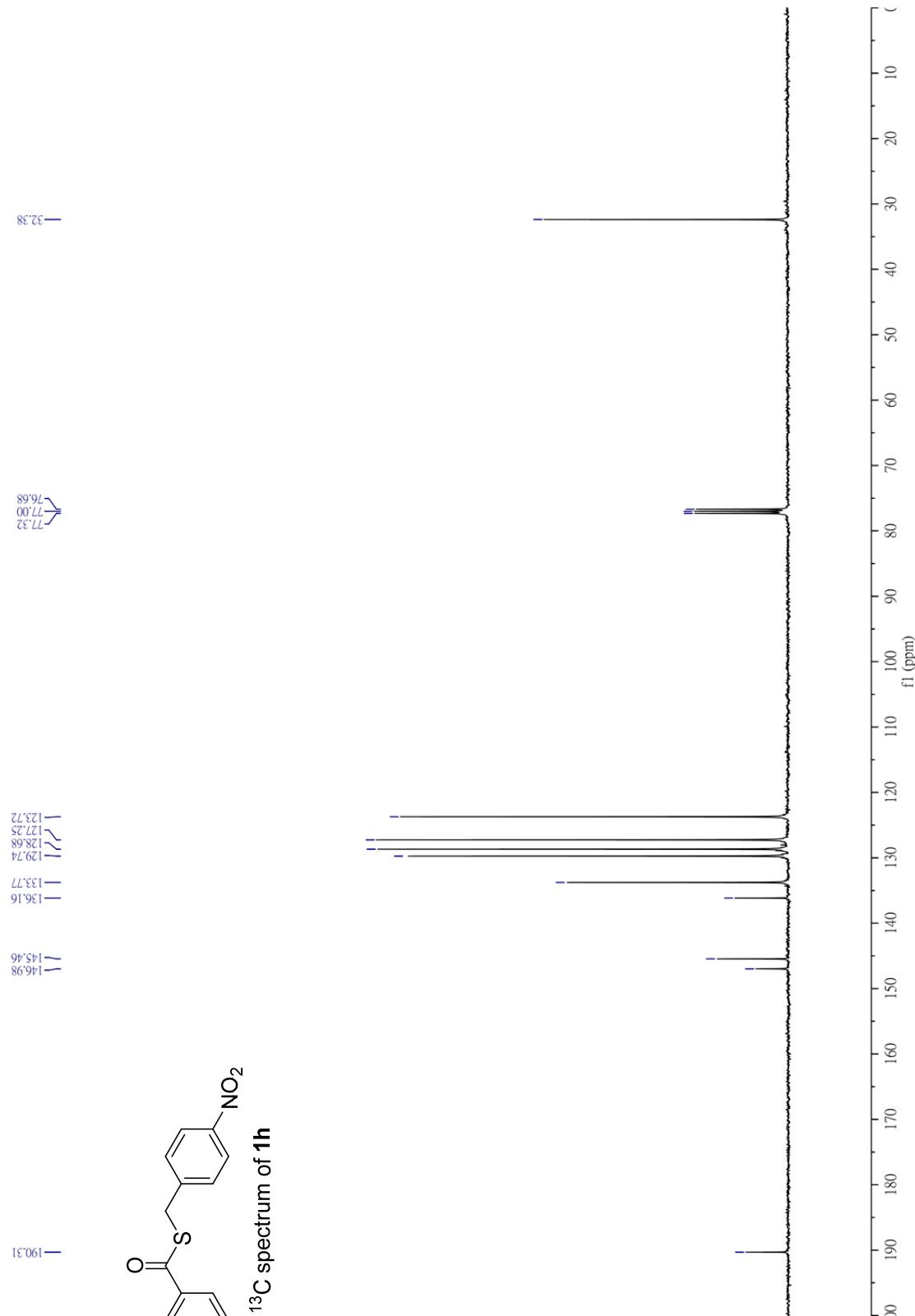
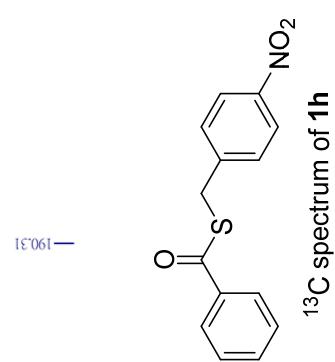
7.9688
7.9657
7.9478
7.9445
7.9397
7.9365
7.9333
7.9268
7.9178
7.9045
7.8997
7.8965
7.8933
7.8865
7.8780
7.8734
7.8626
7.8594
7.8562
7.8532
7.8475
7.8431
7.8386
7.8356
7.8326
7.8291
7.8244
7.8222
7.8164
7.8063

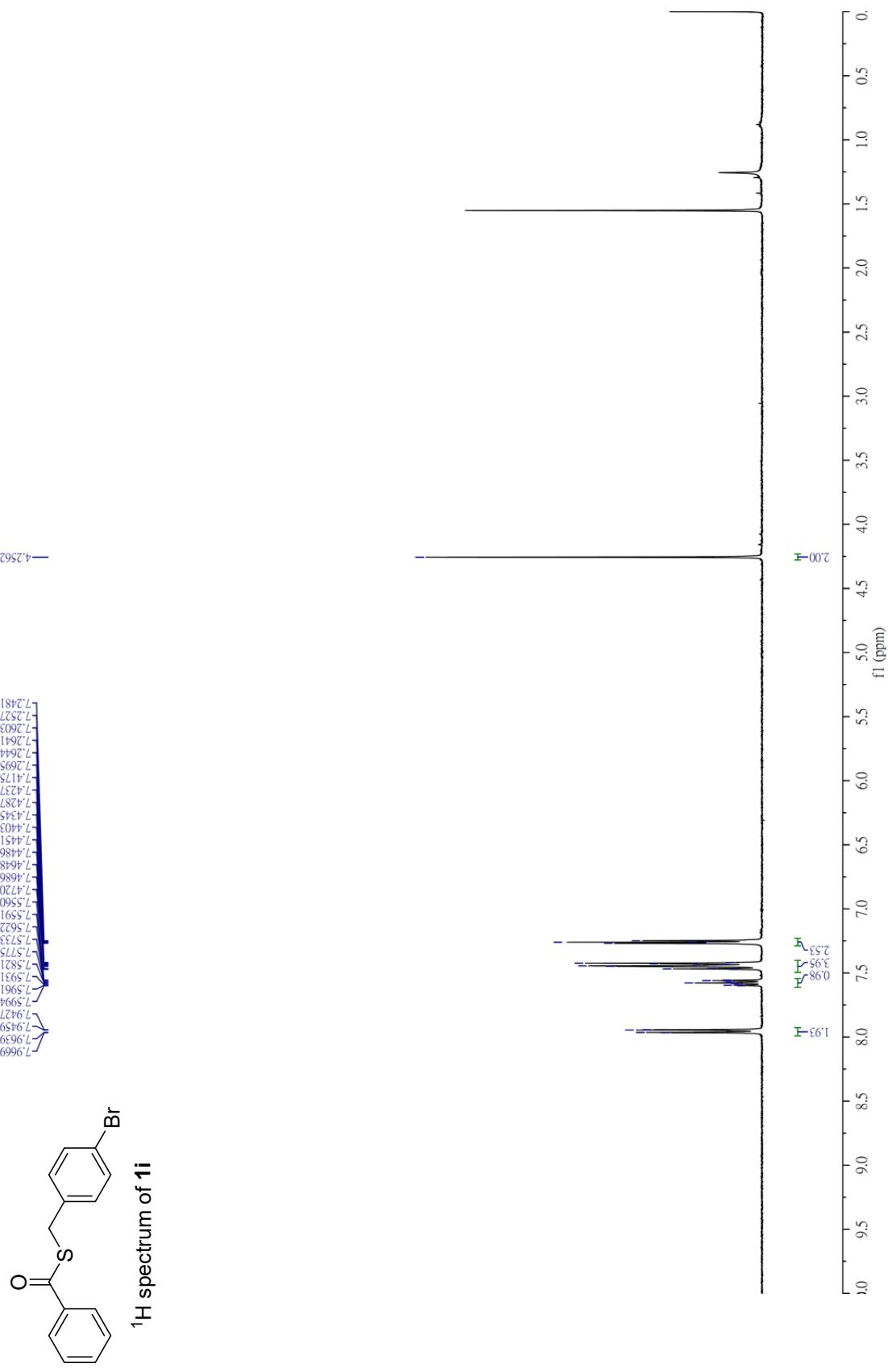
—4.2742

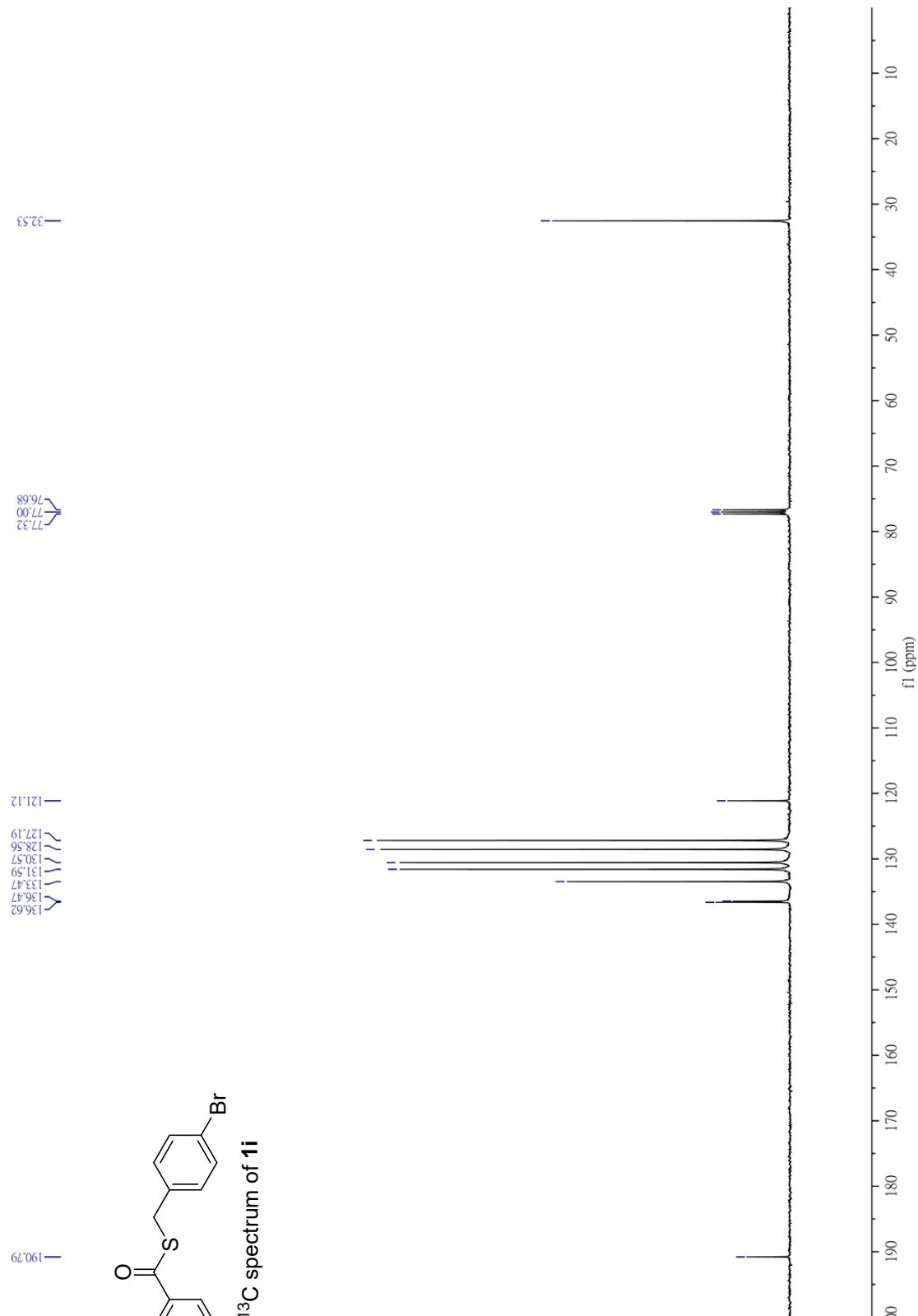
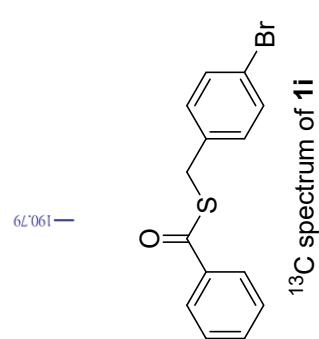


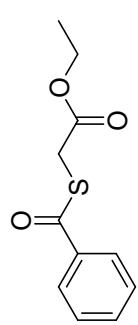




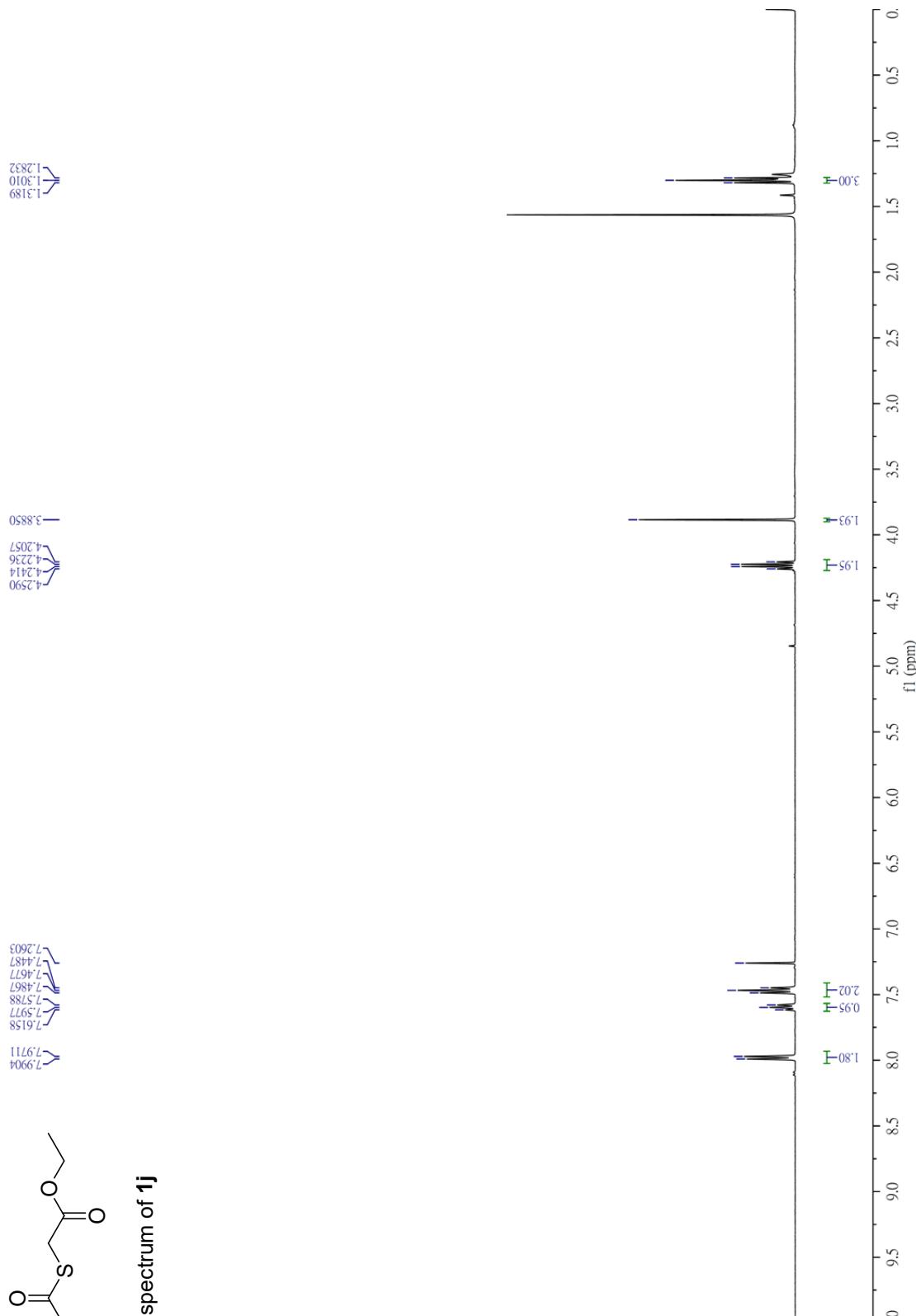


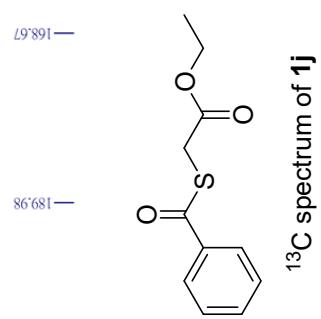






^1H spectrum of 1j



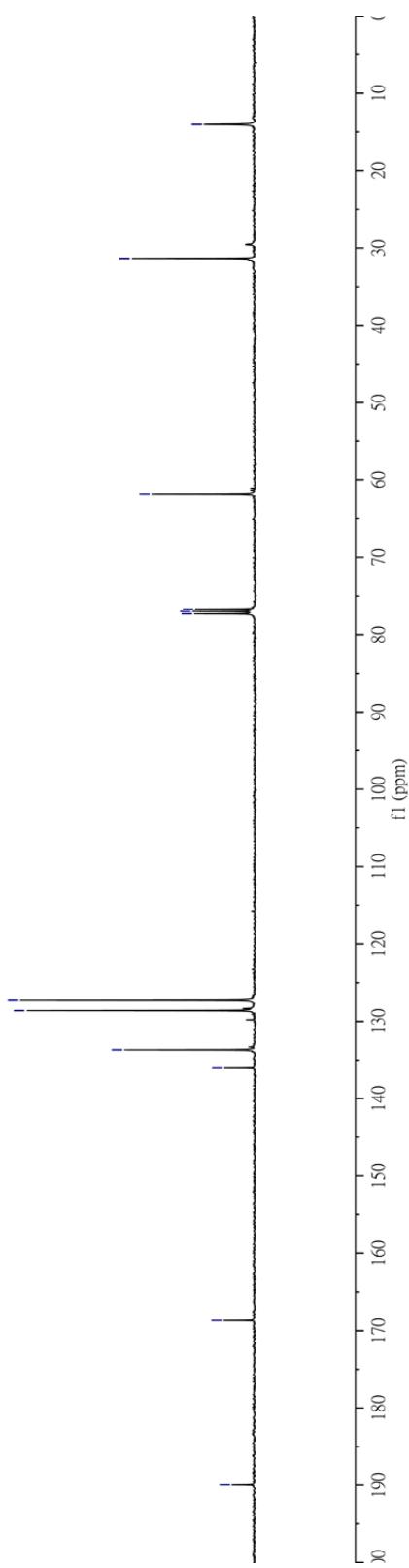


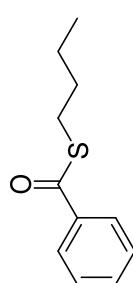
^{13}C spectrum of **1j**

168.67
189.98

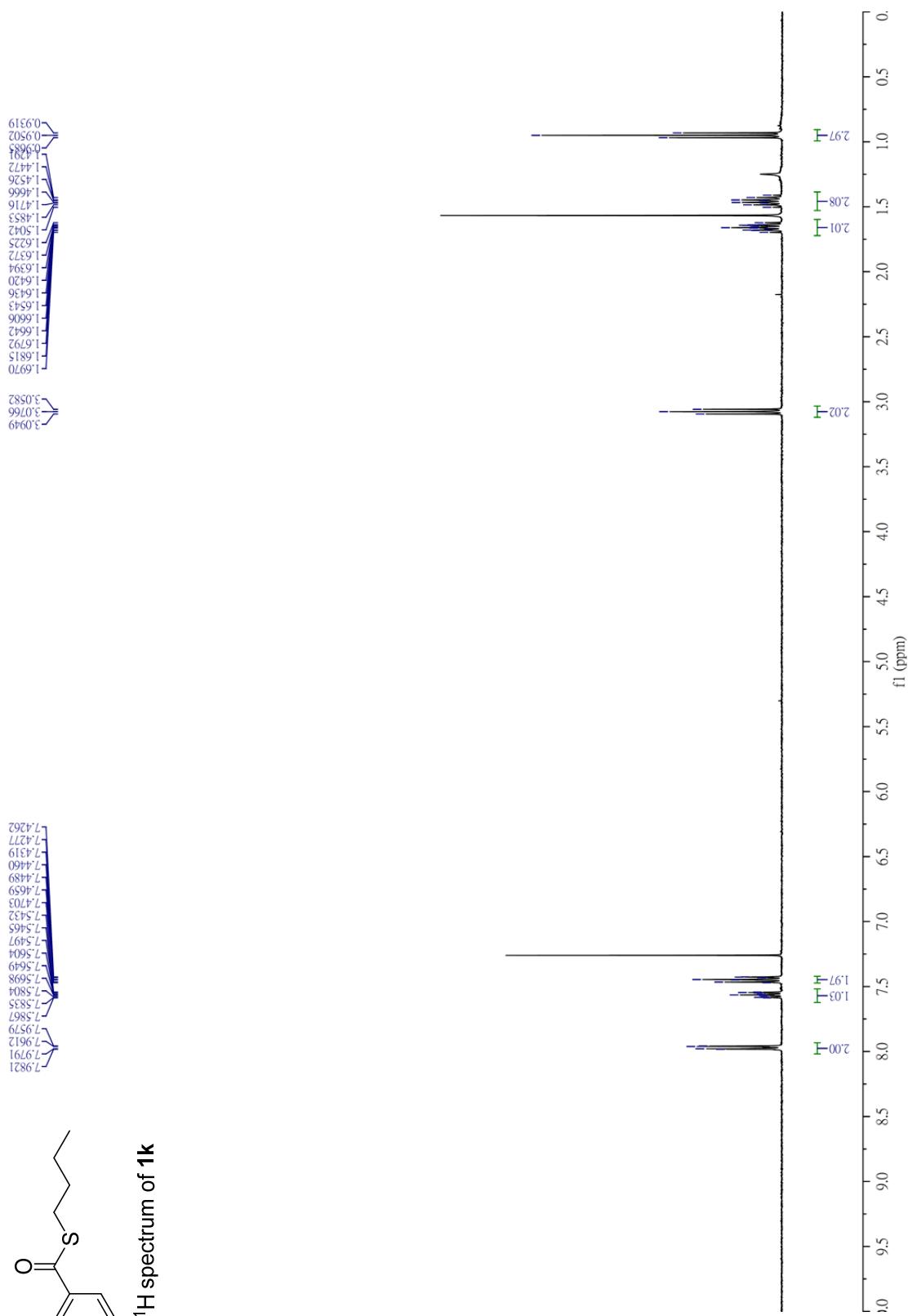
127.30
128.61
133.69
136.06
77.32
77.00
76.68

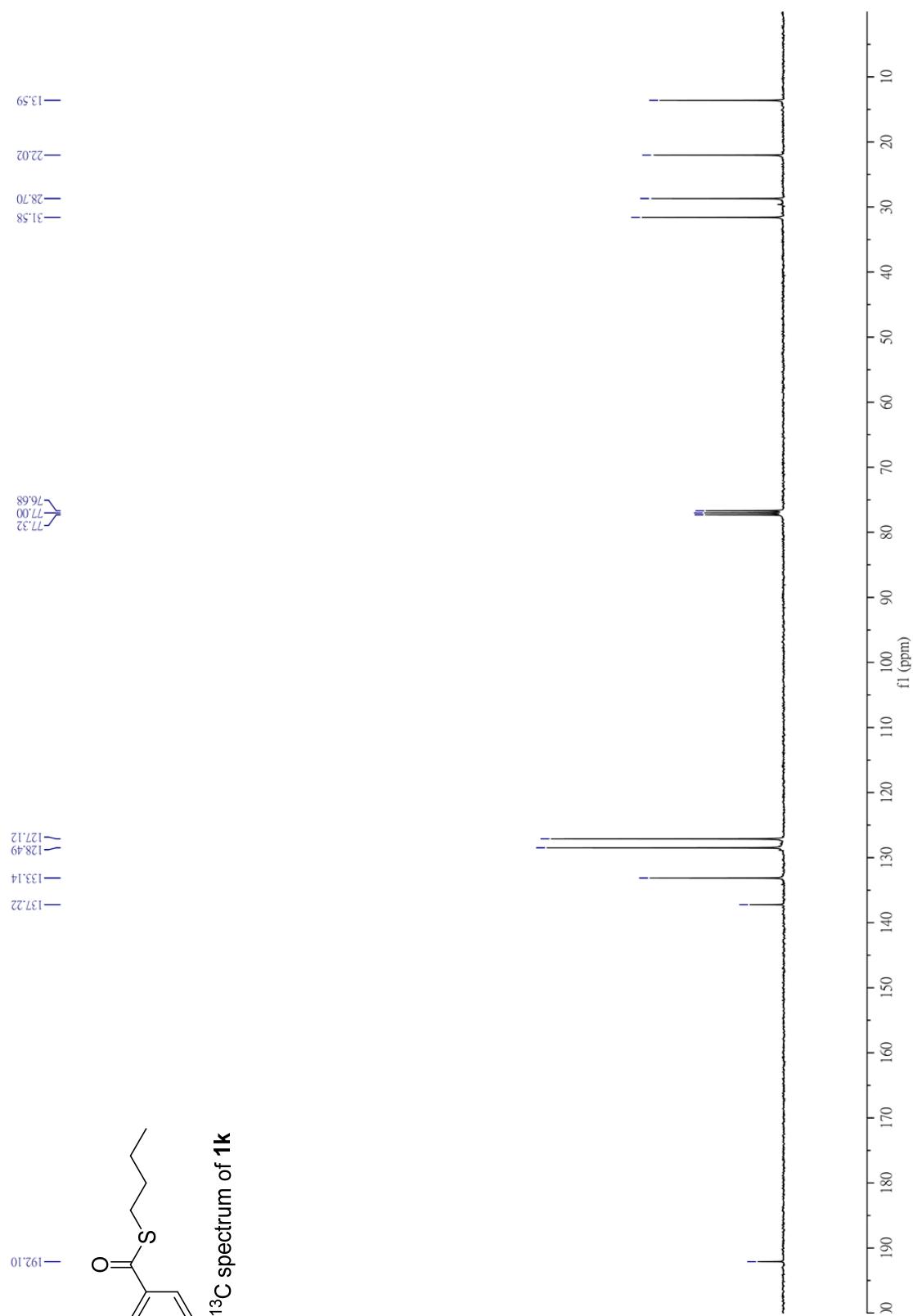
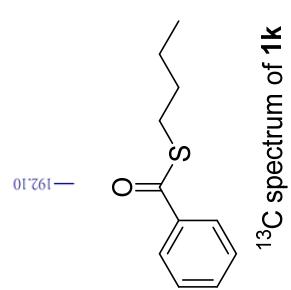
141.04
131.34
61.80

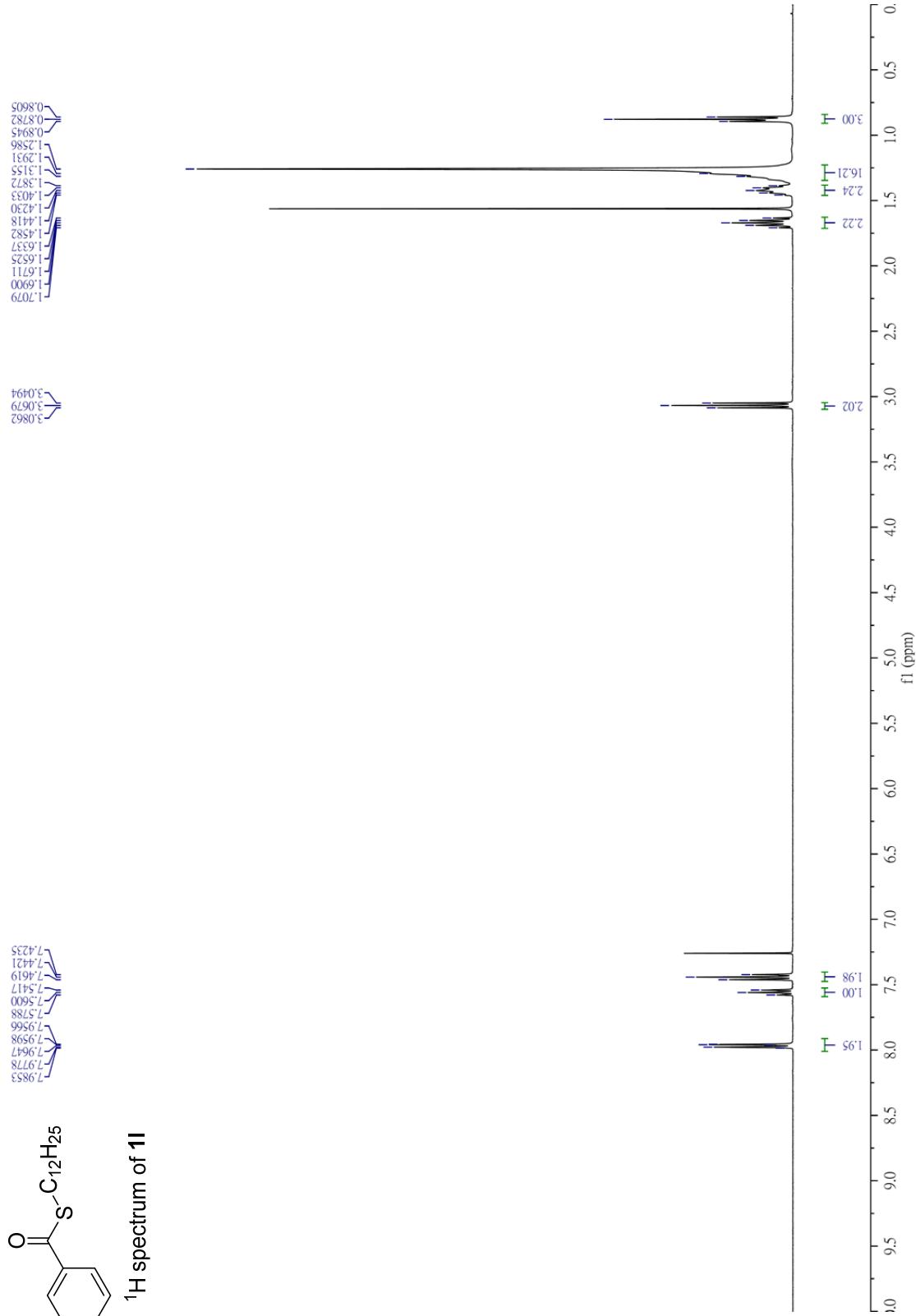
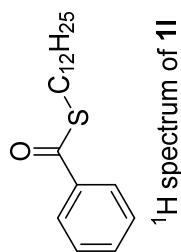


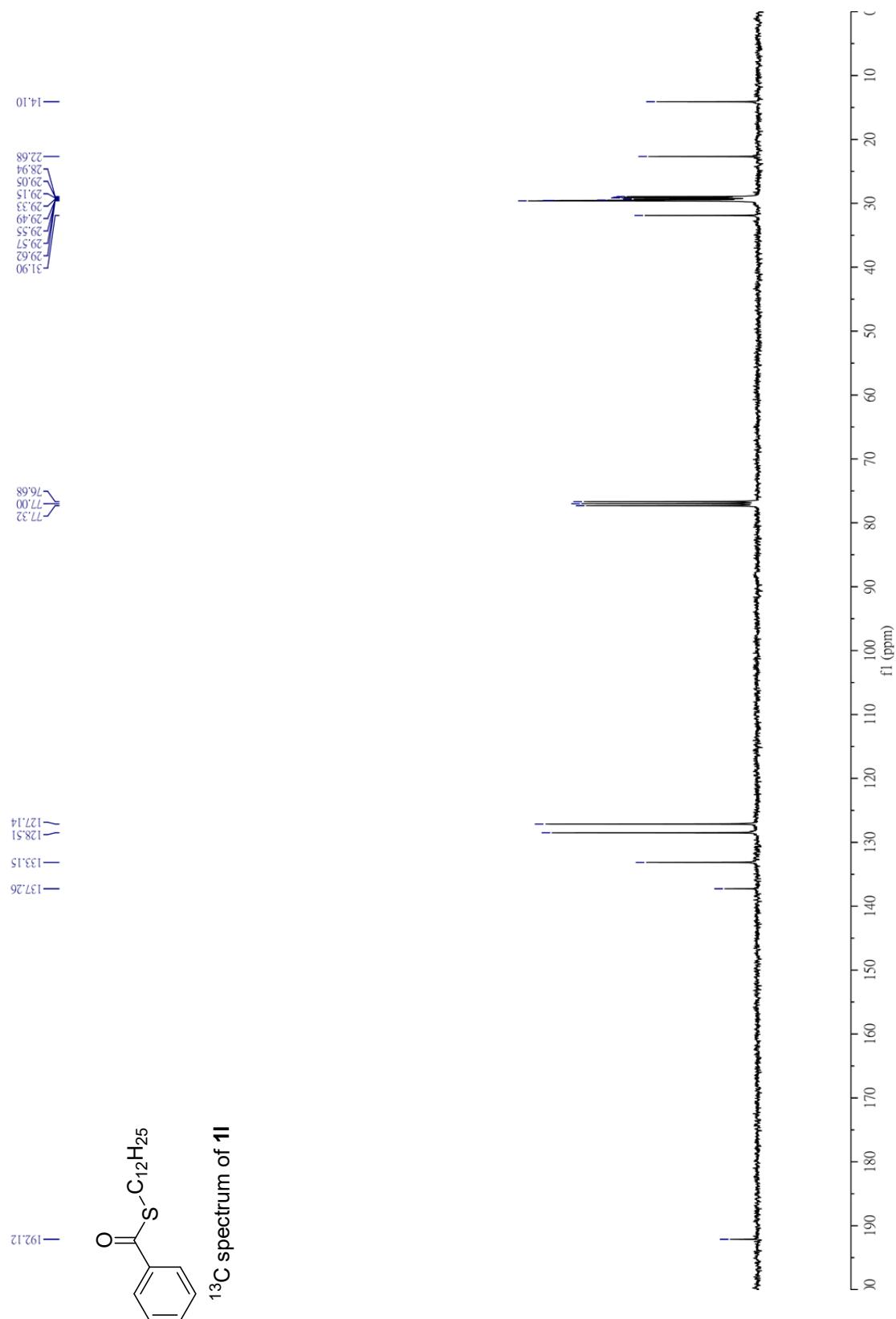


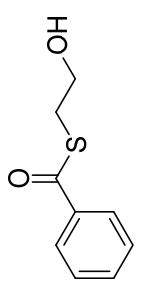
¹H spectrum of 1k



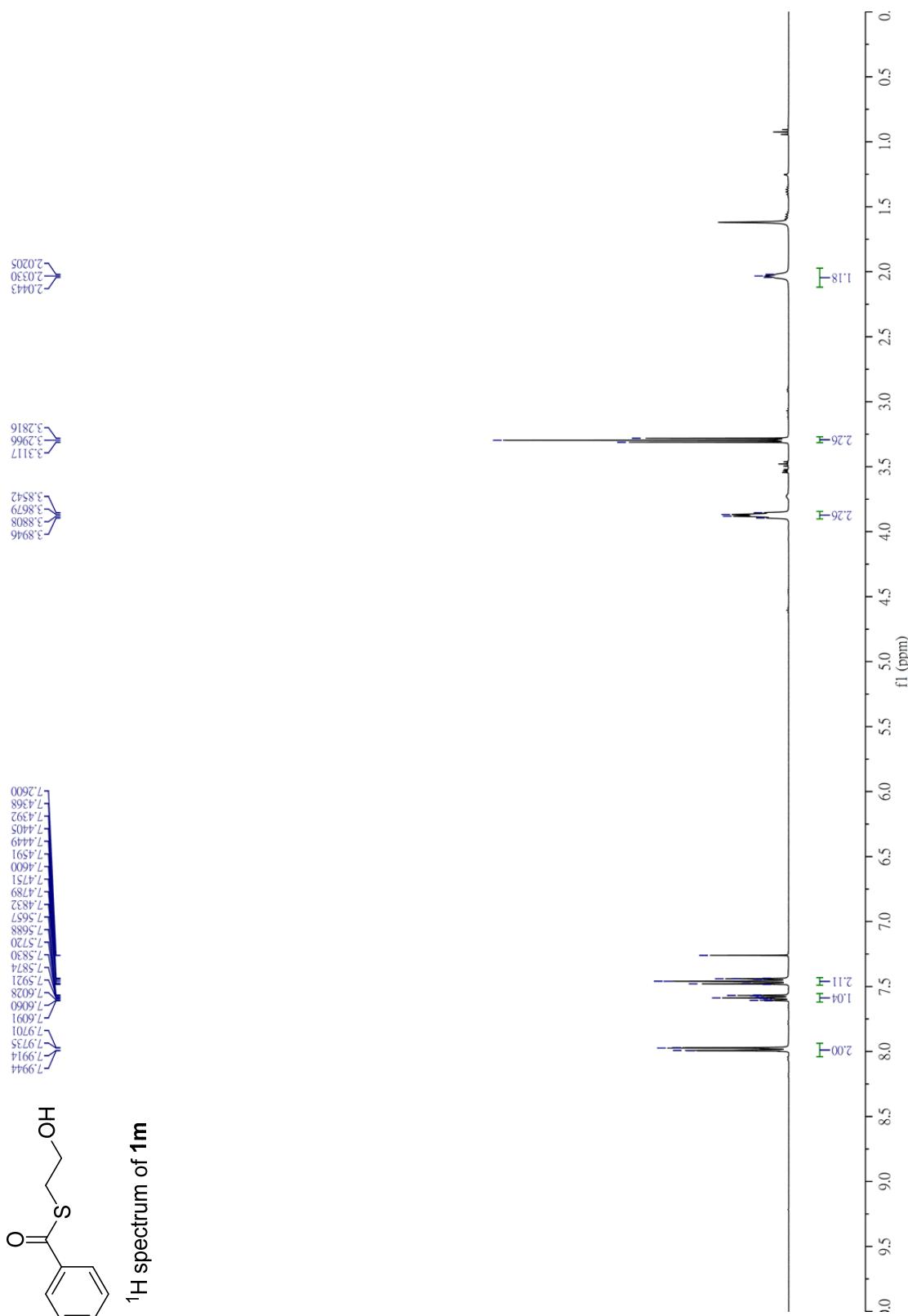


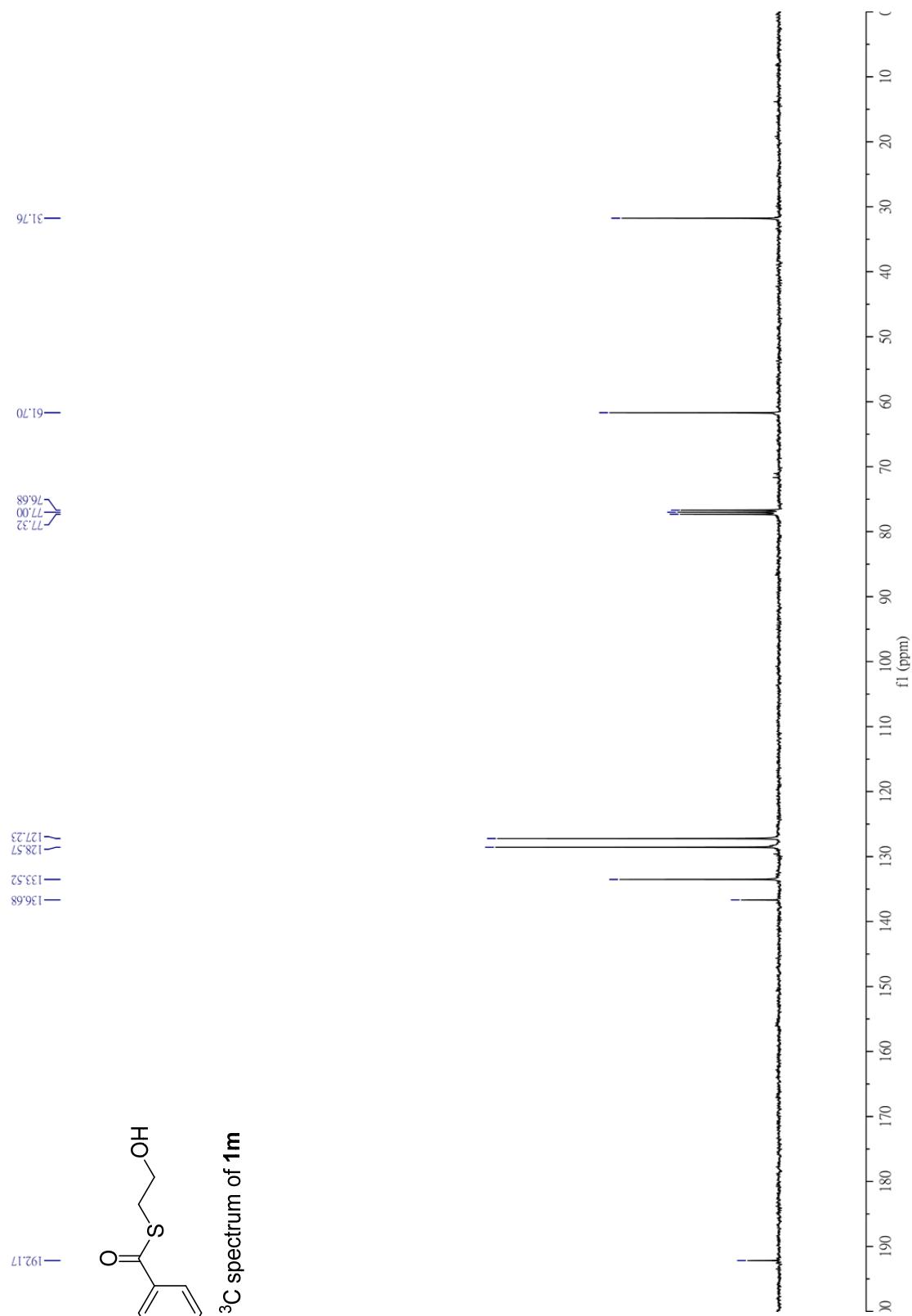
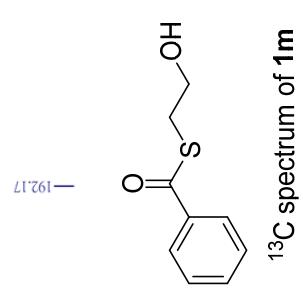


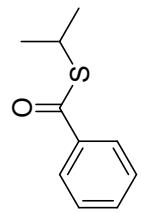




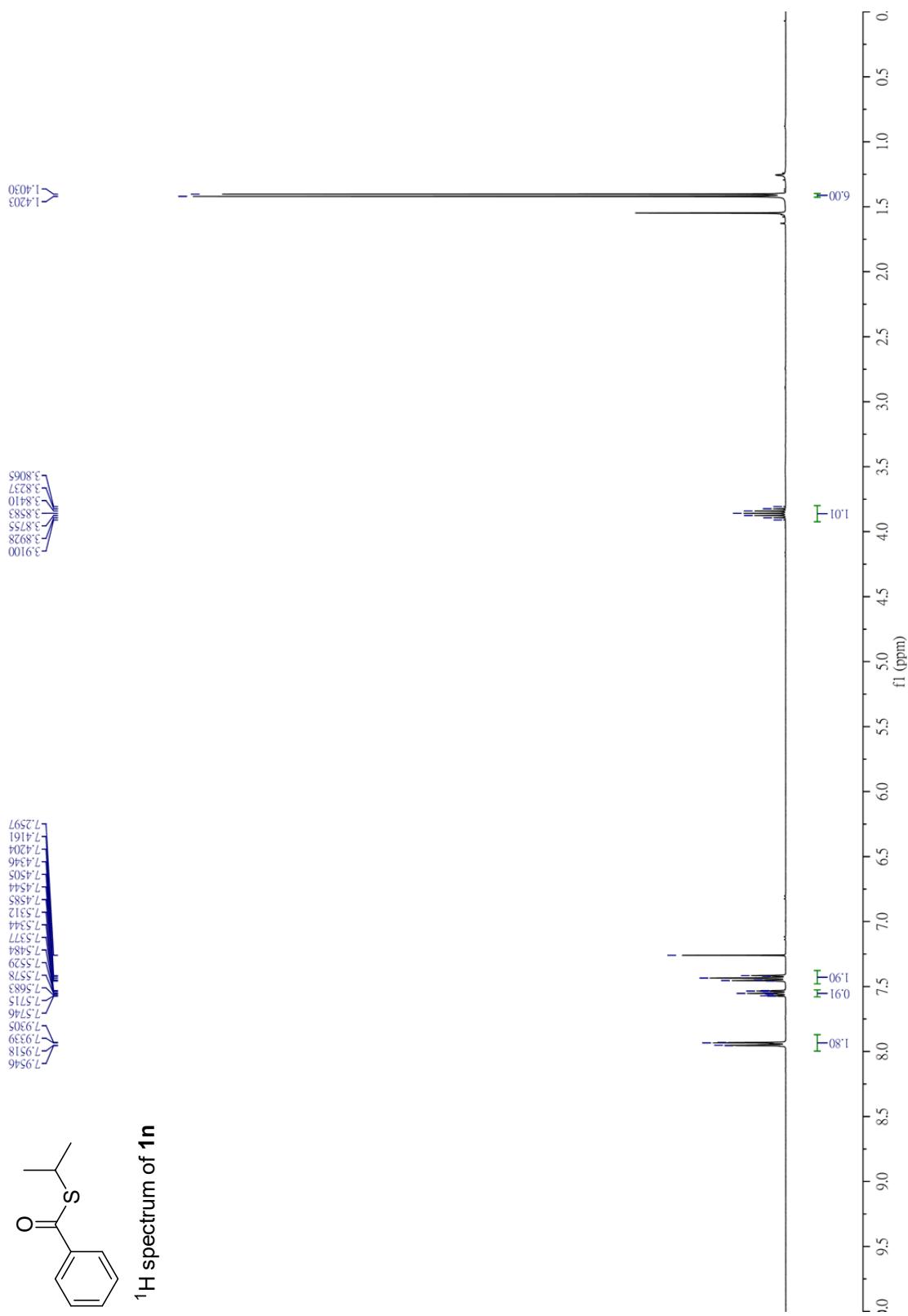
¹H spectrum of 1m

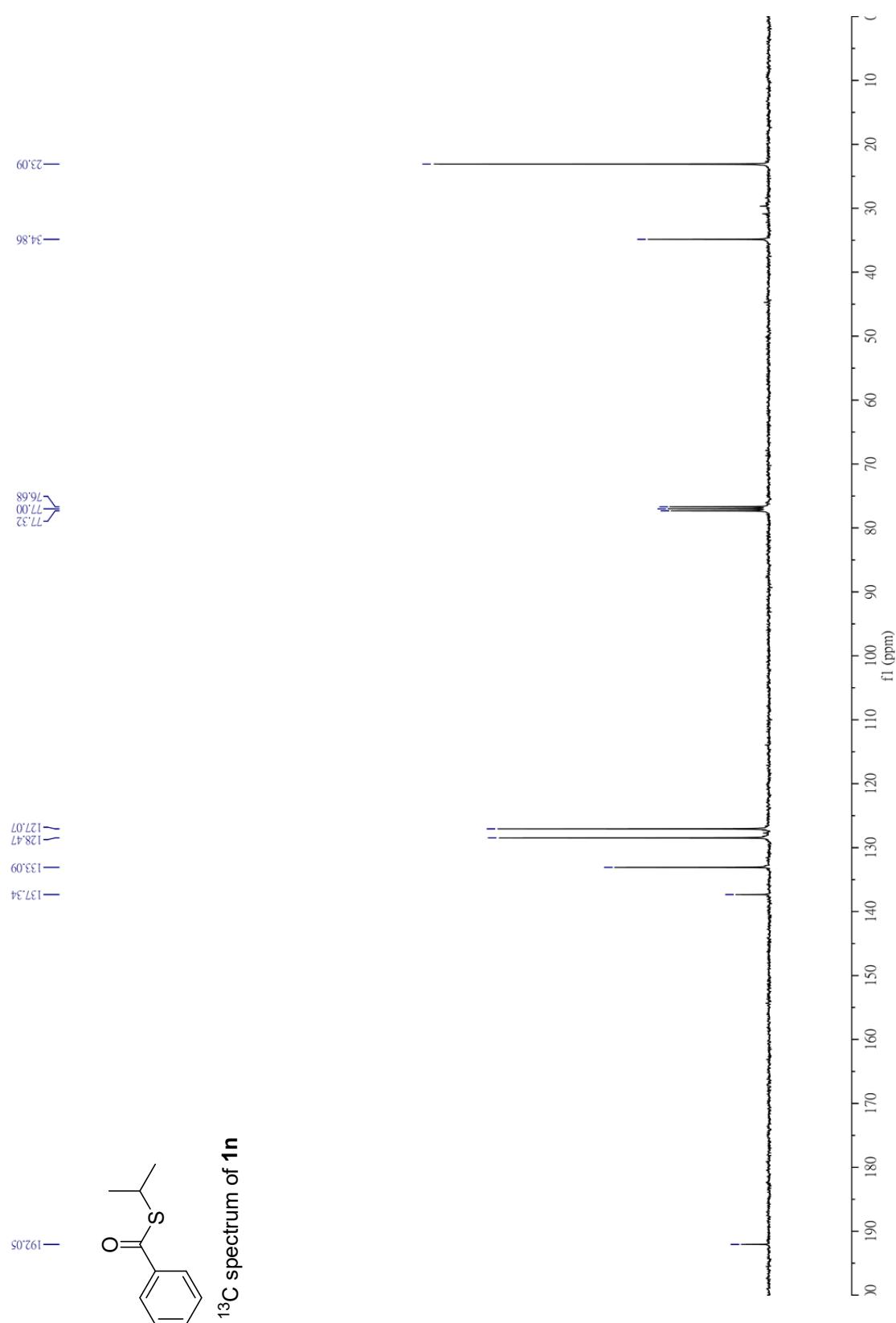


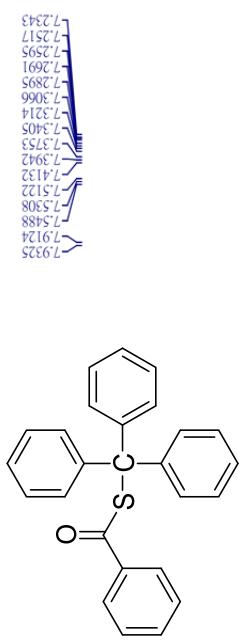




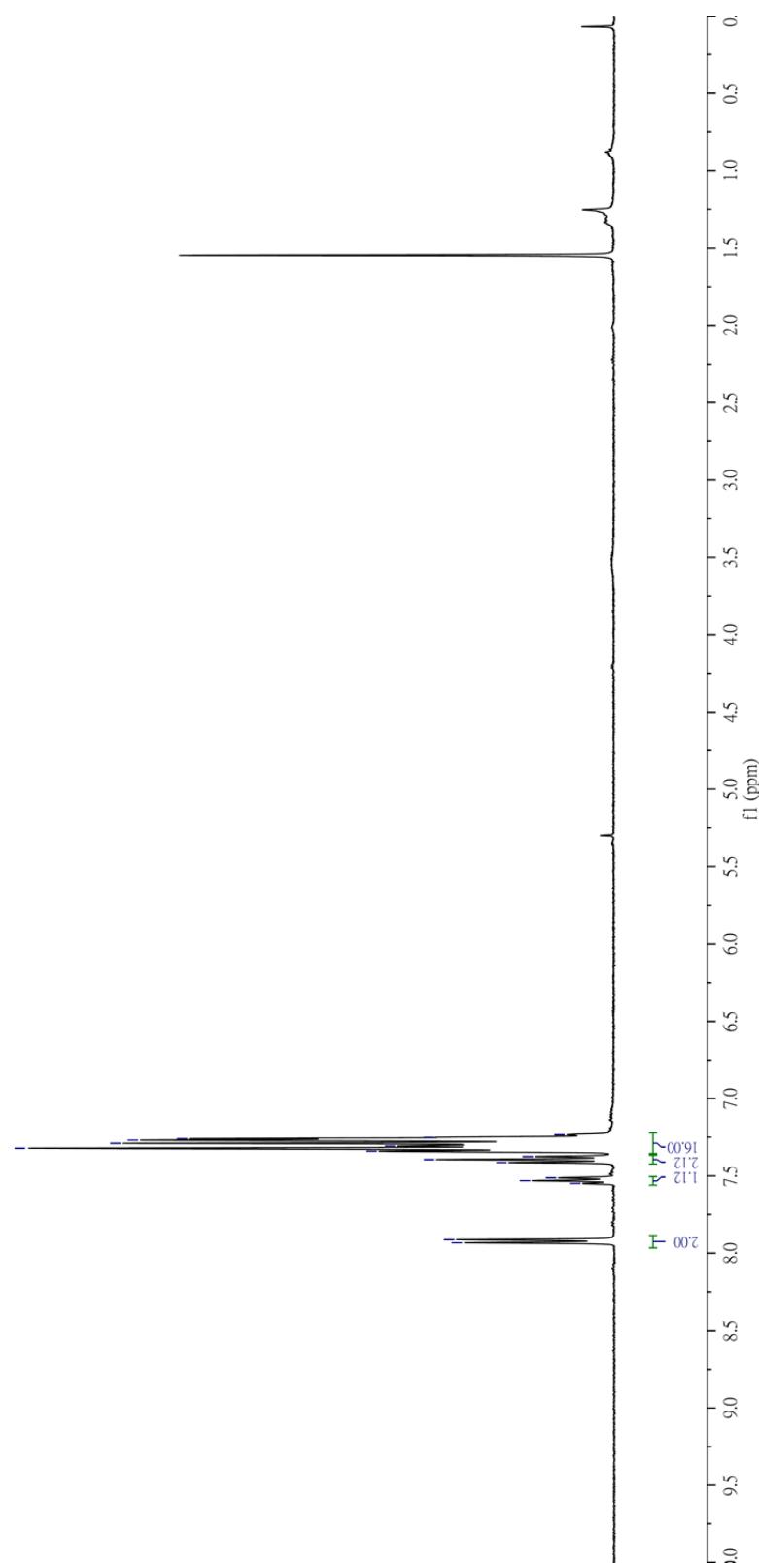
^1H spectrum of 1n

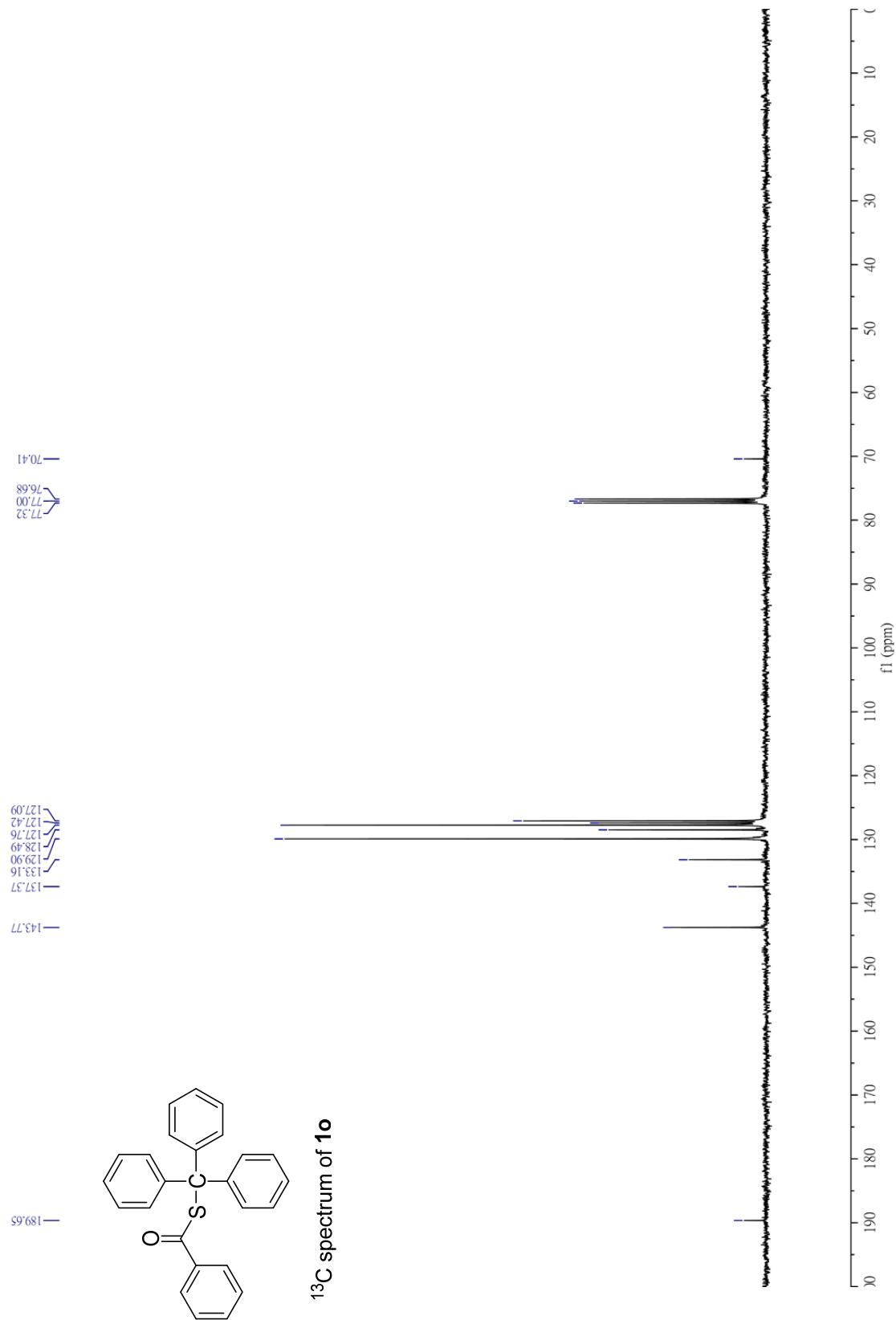


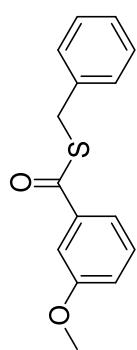
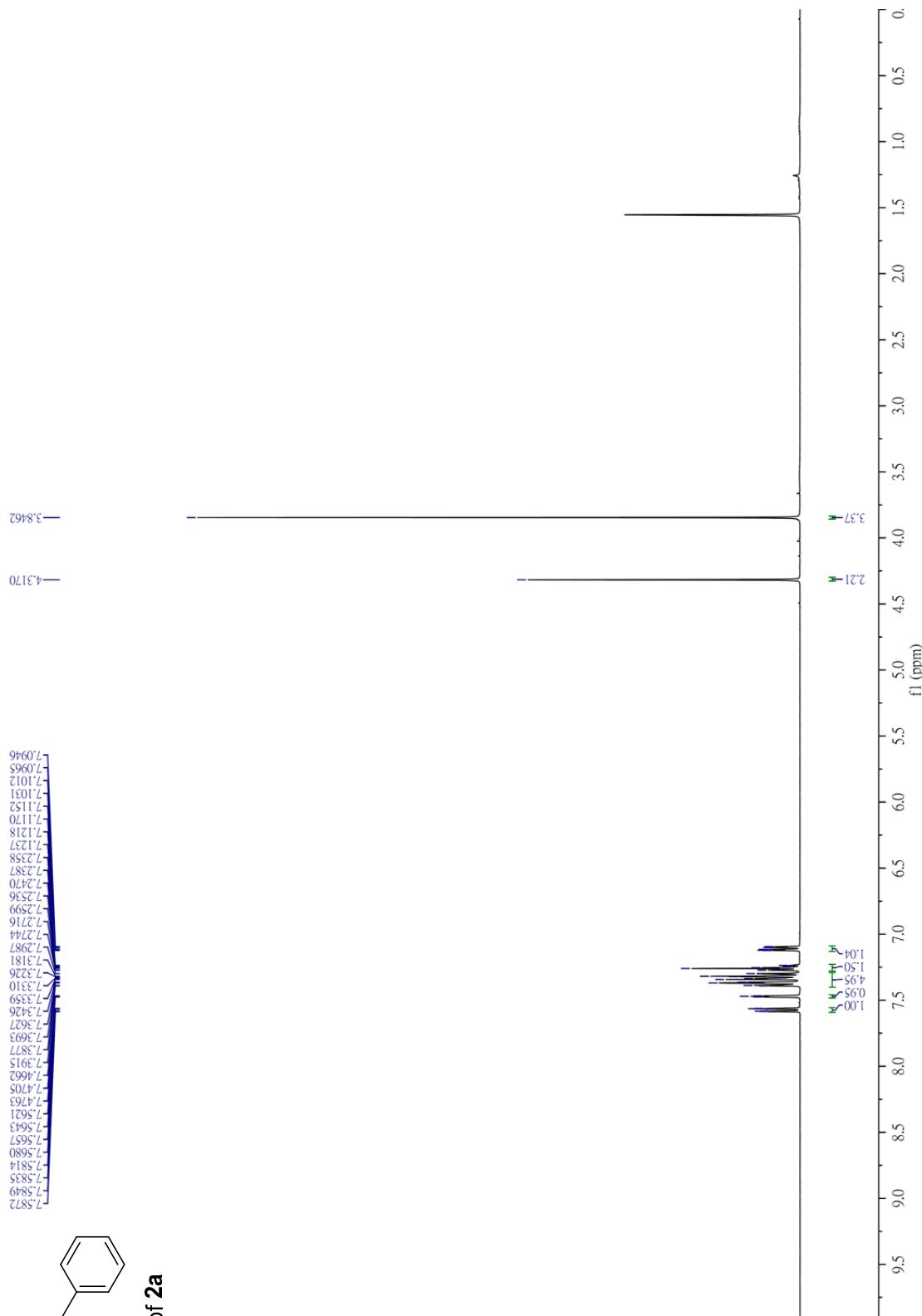


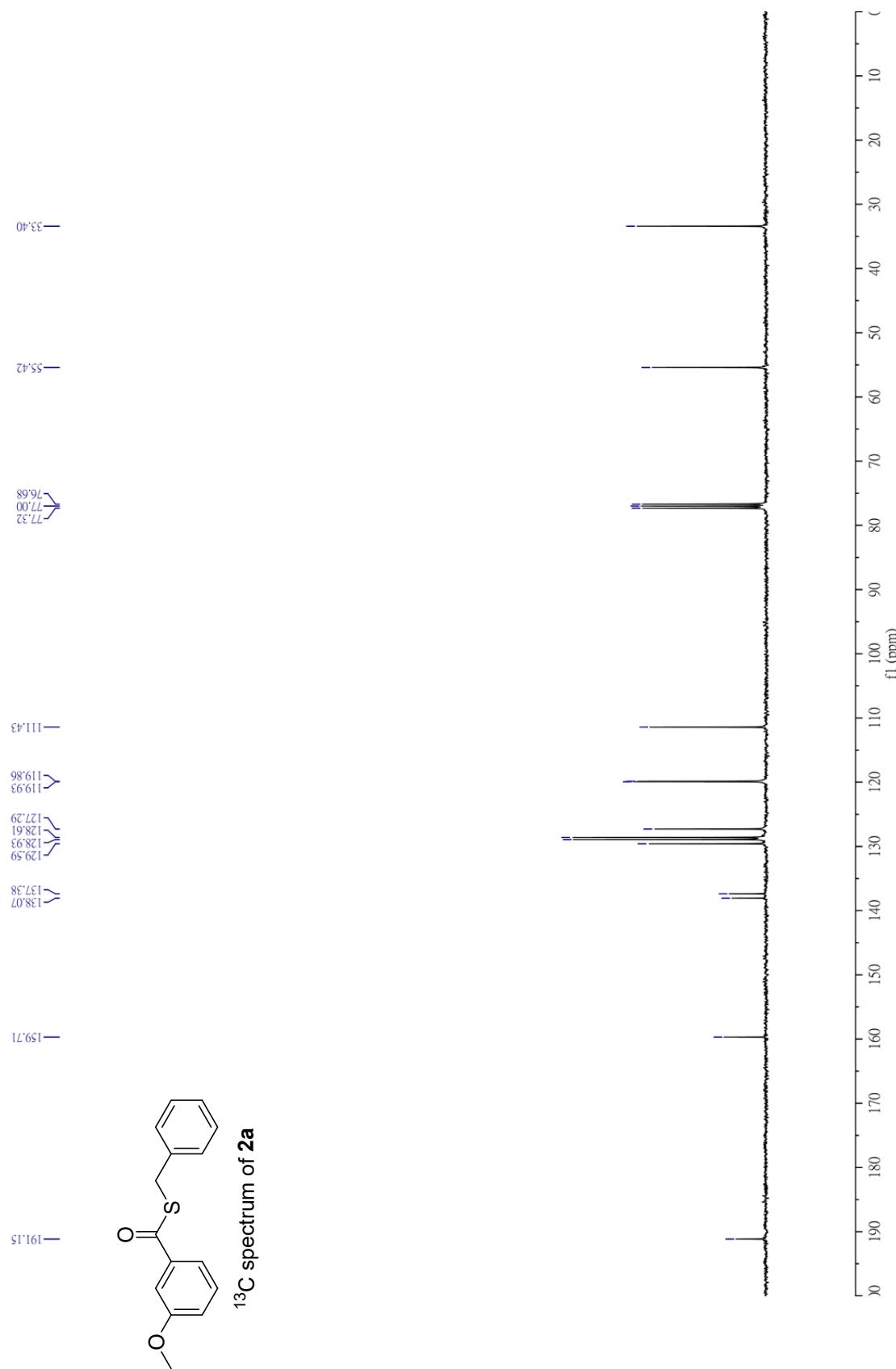


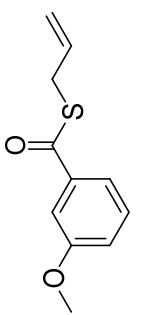
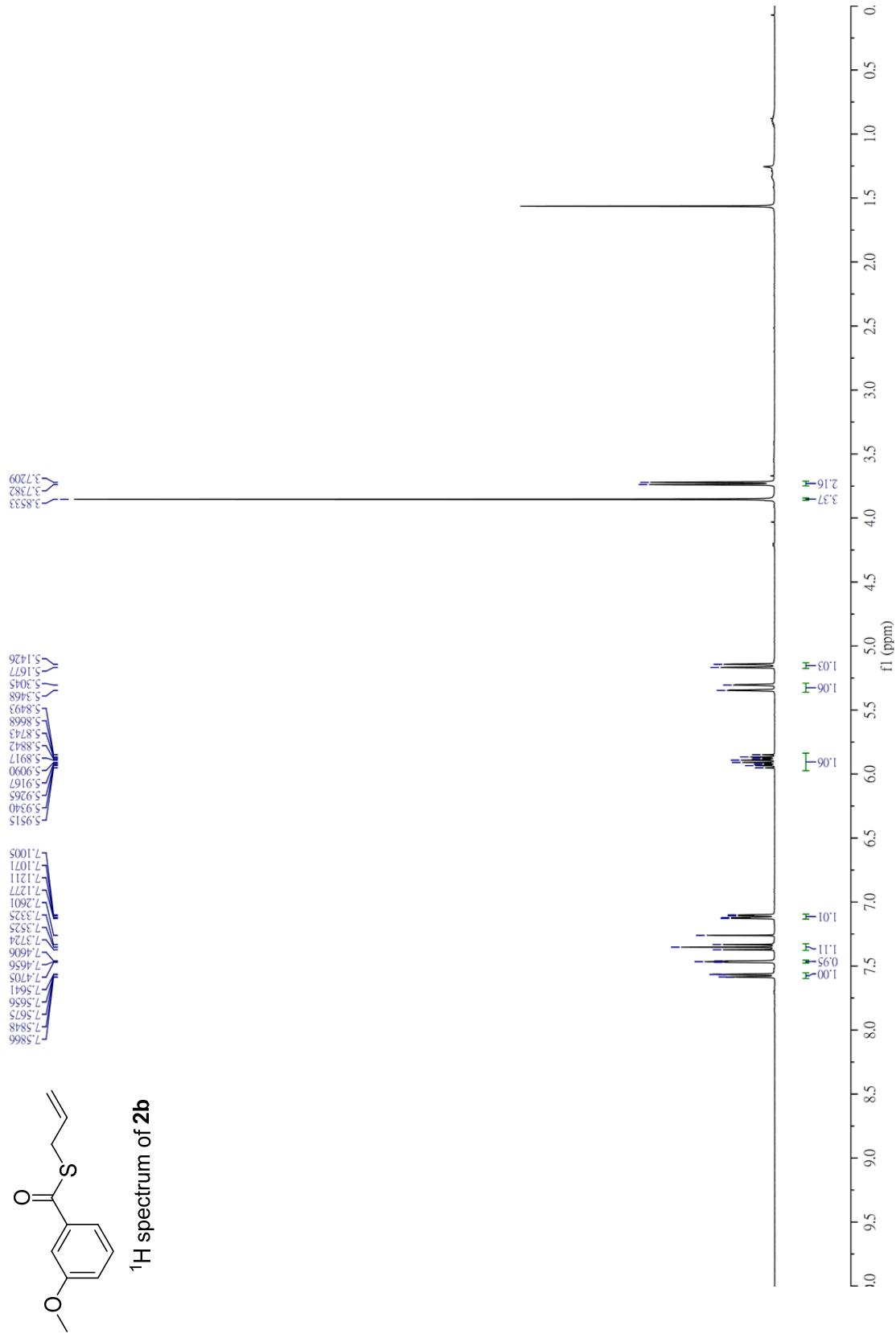
¹H spectrum of 1o



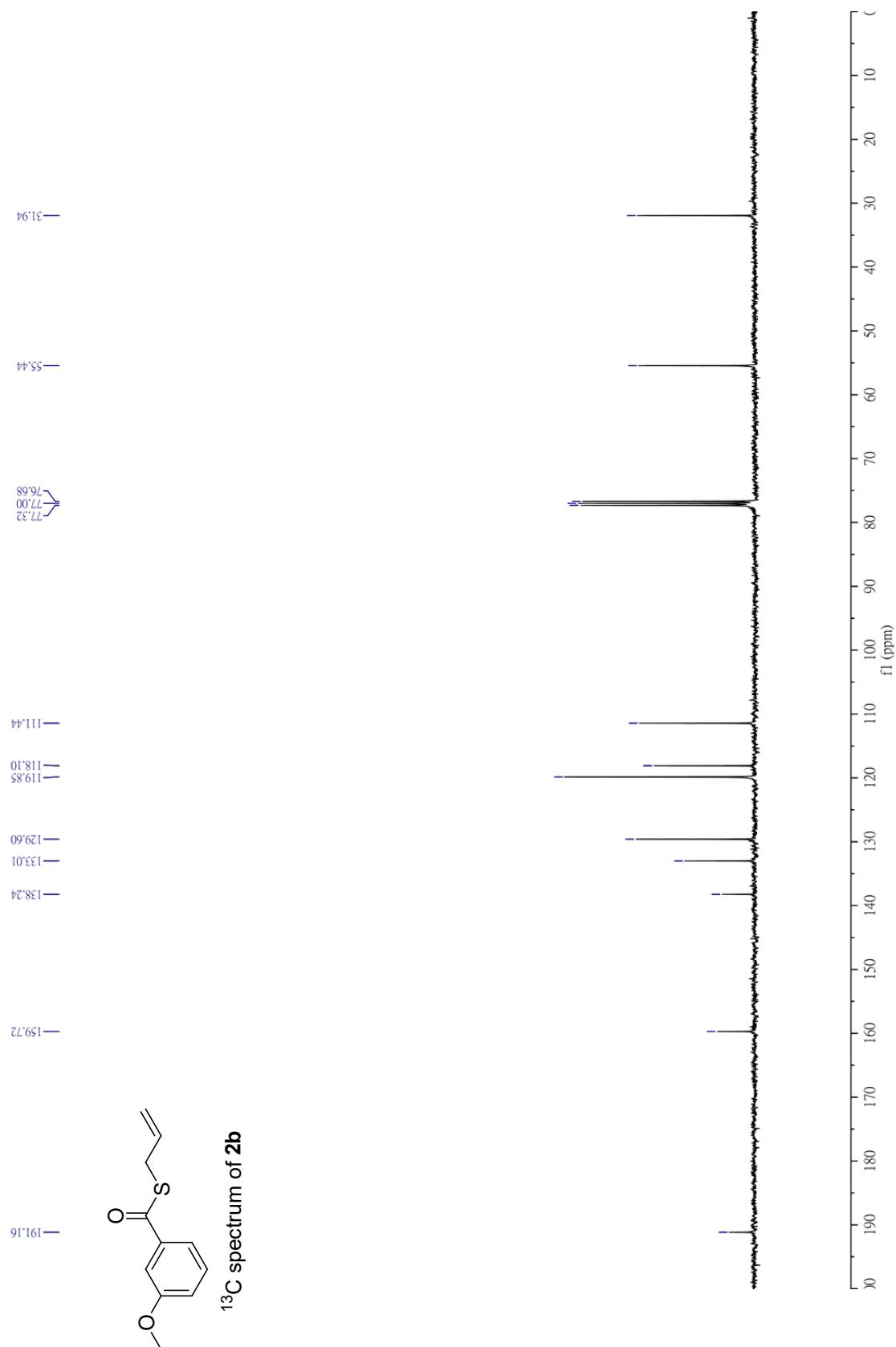


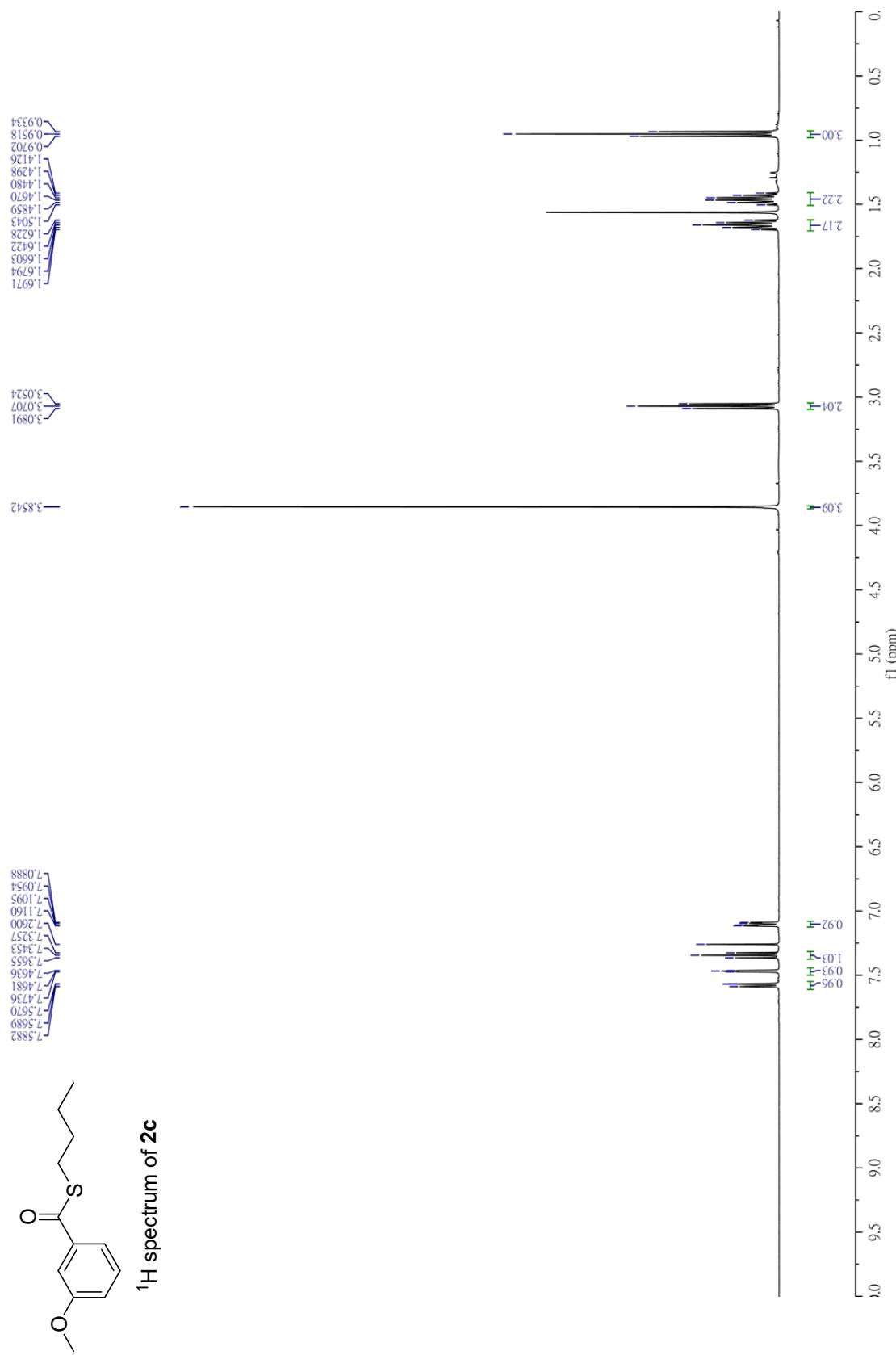


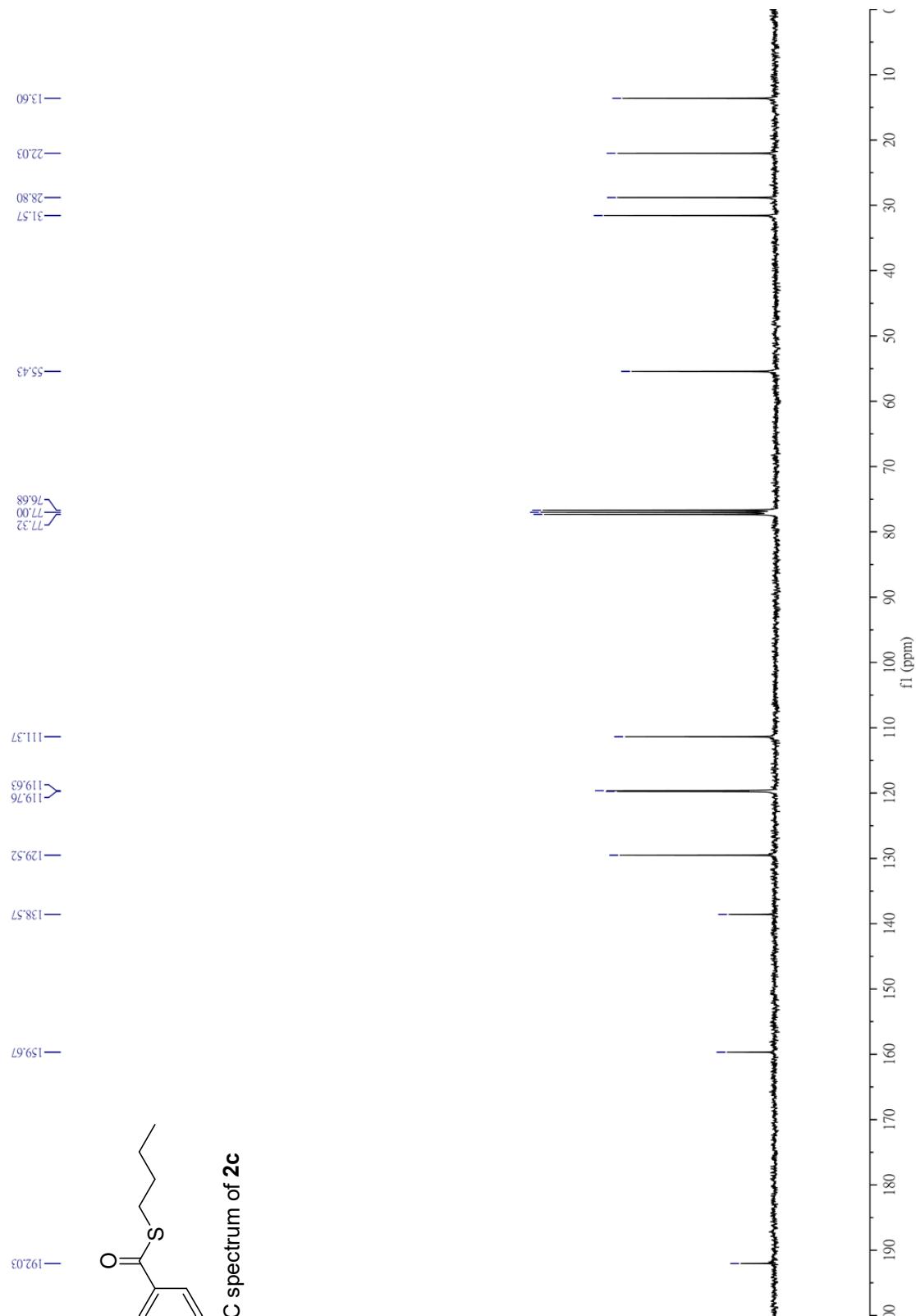
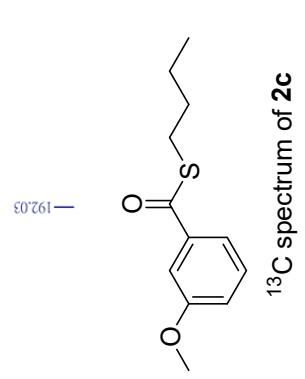


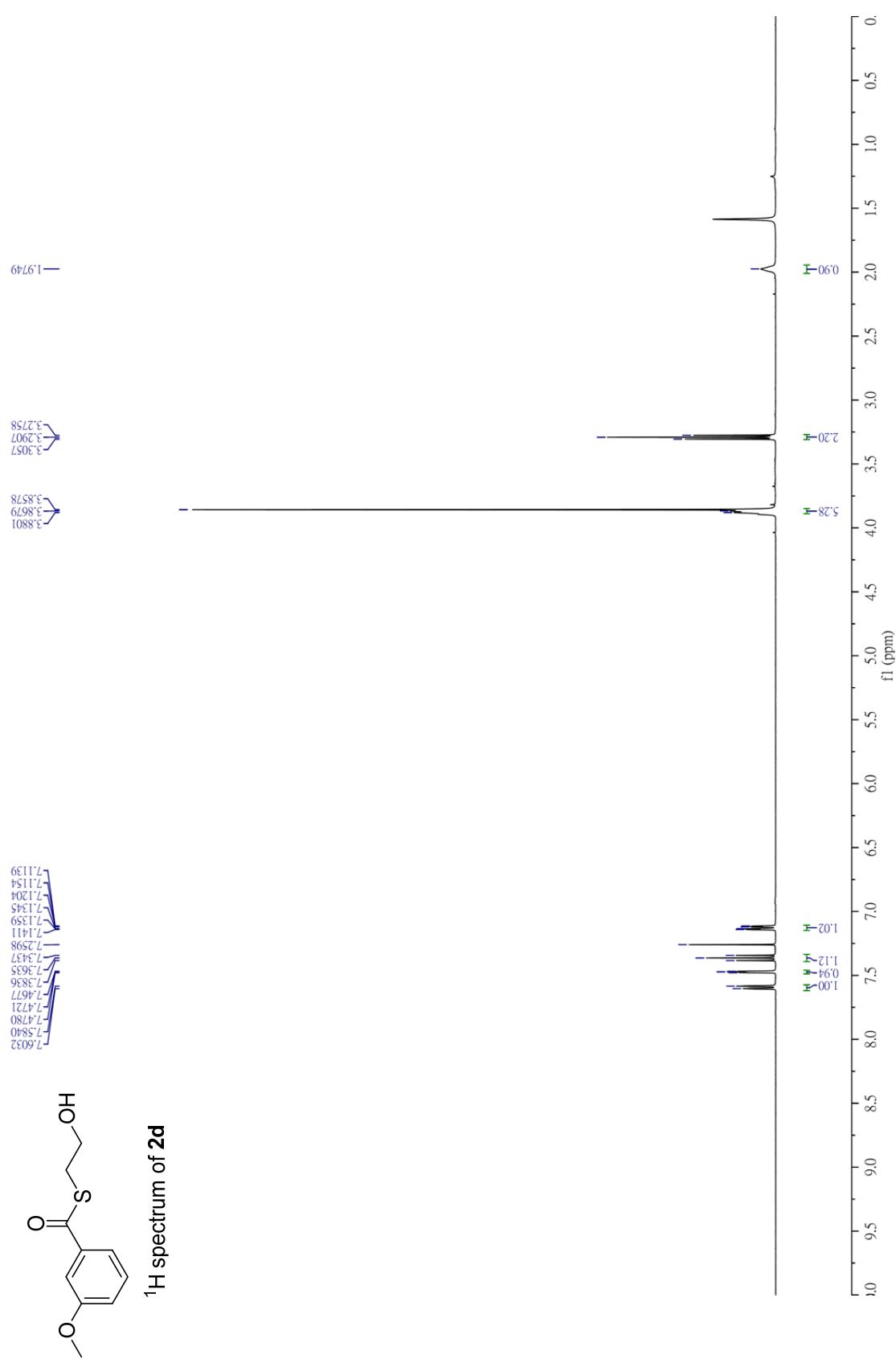


^1H spectrum of 2b

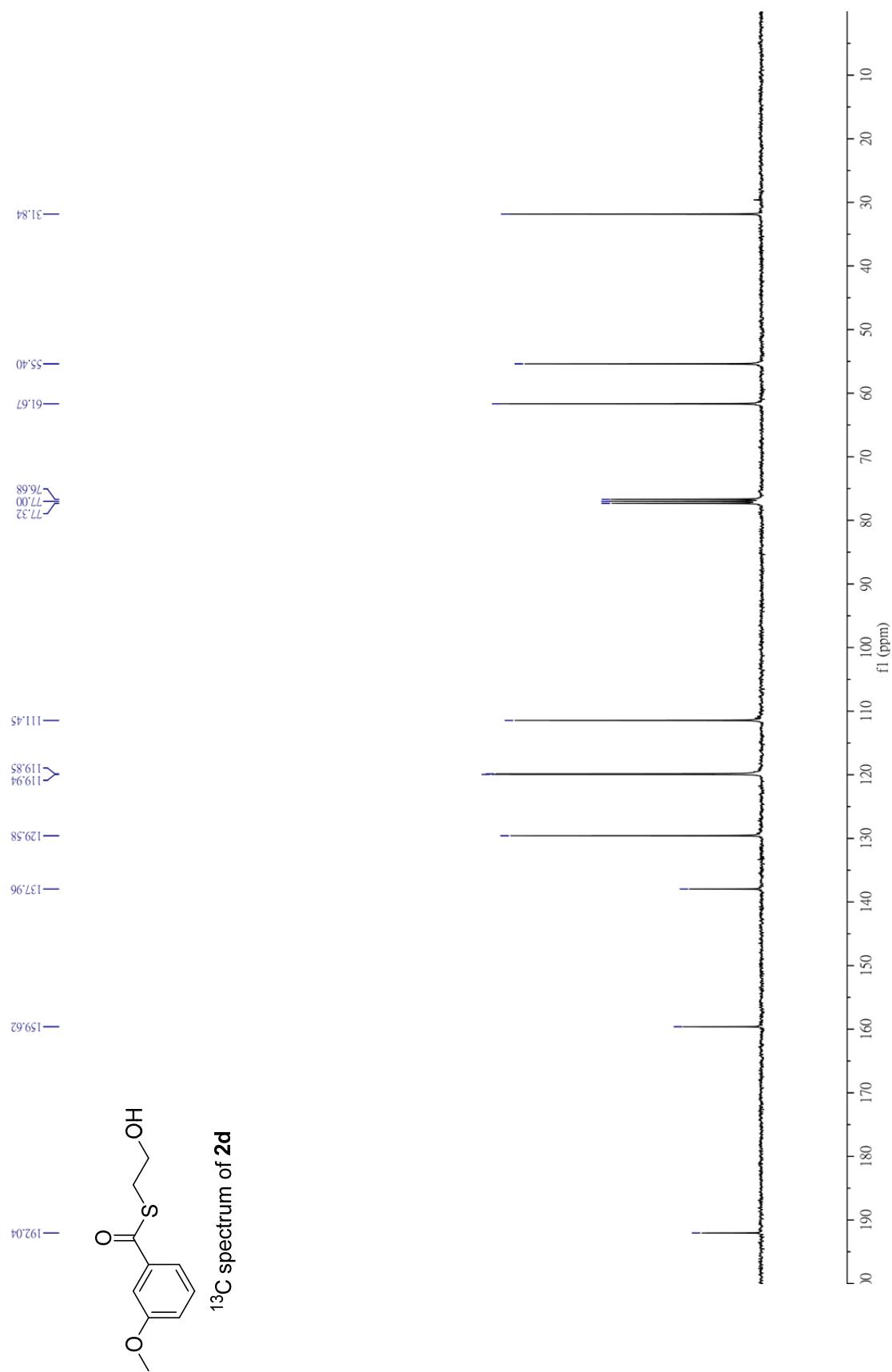


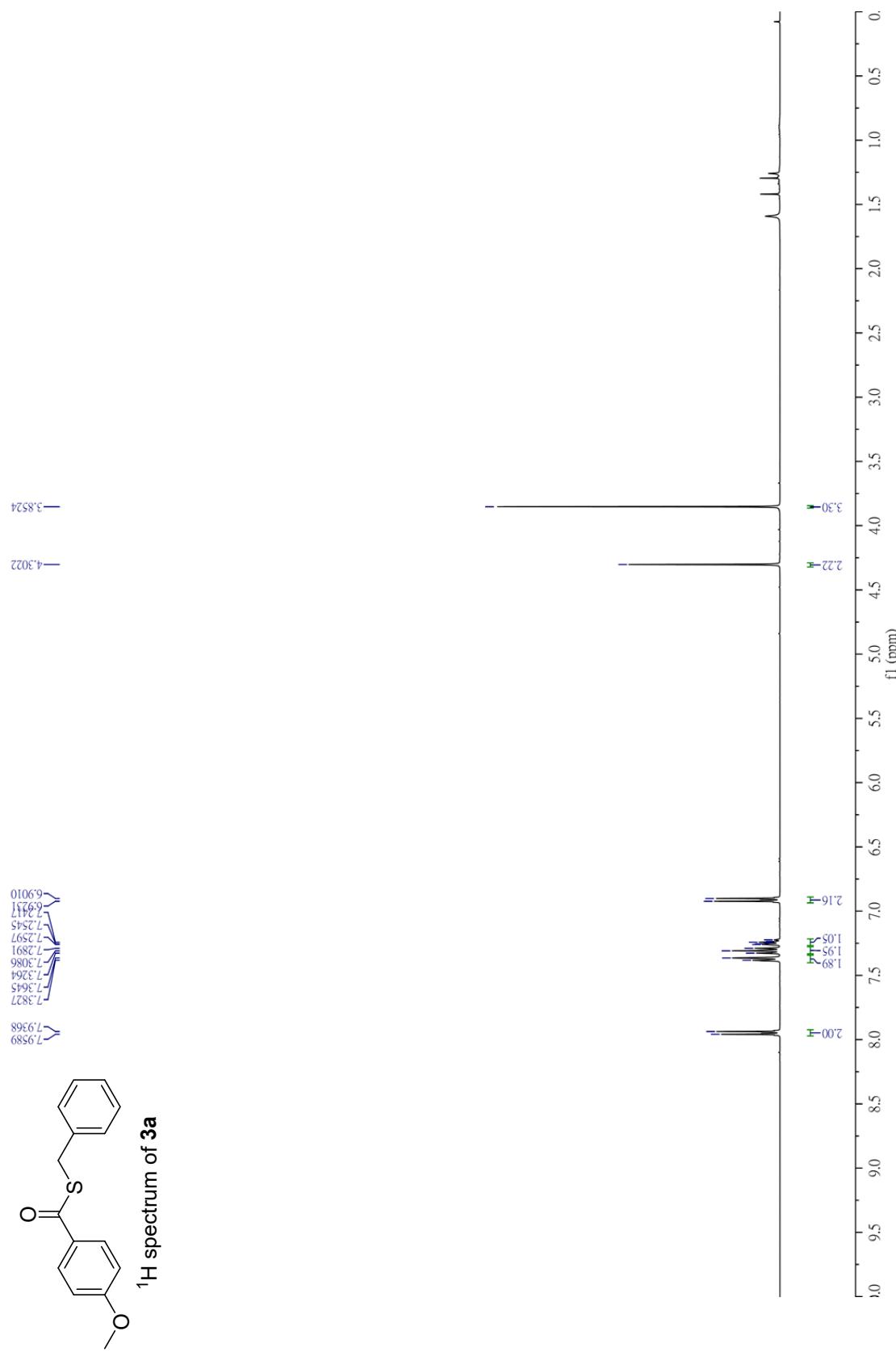


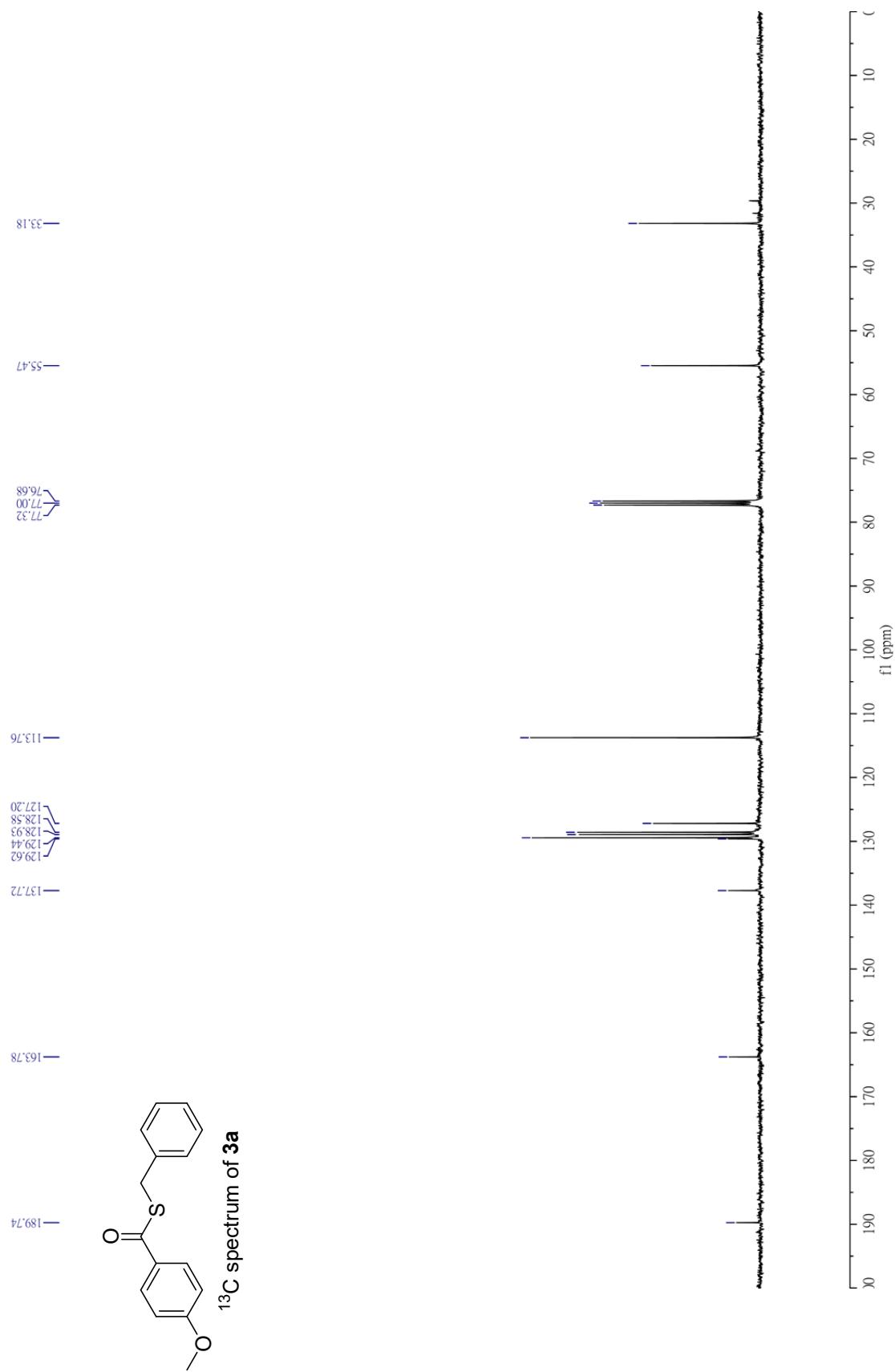


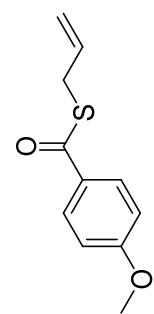


¹H spectrum of **2d**

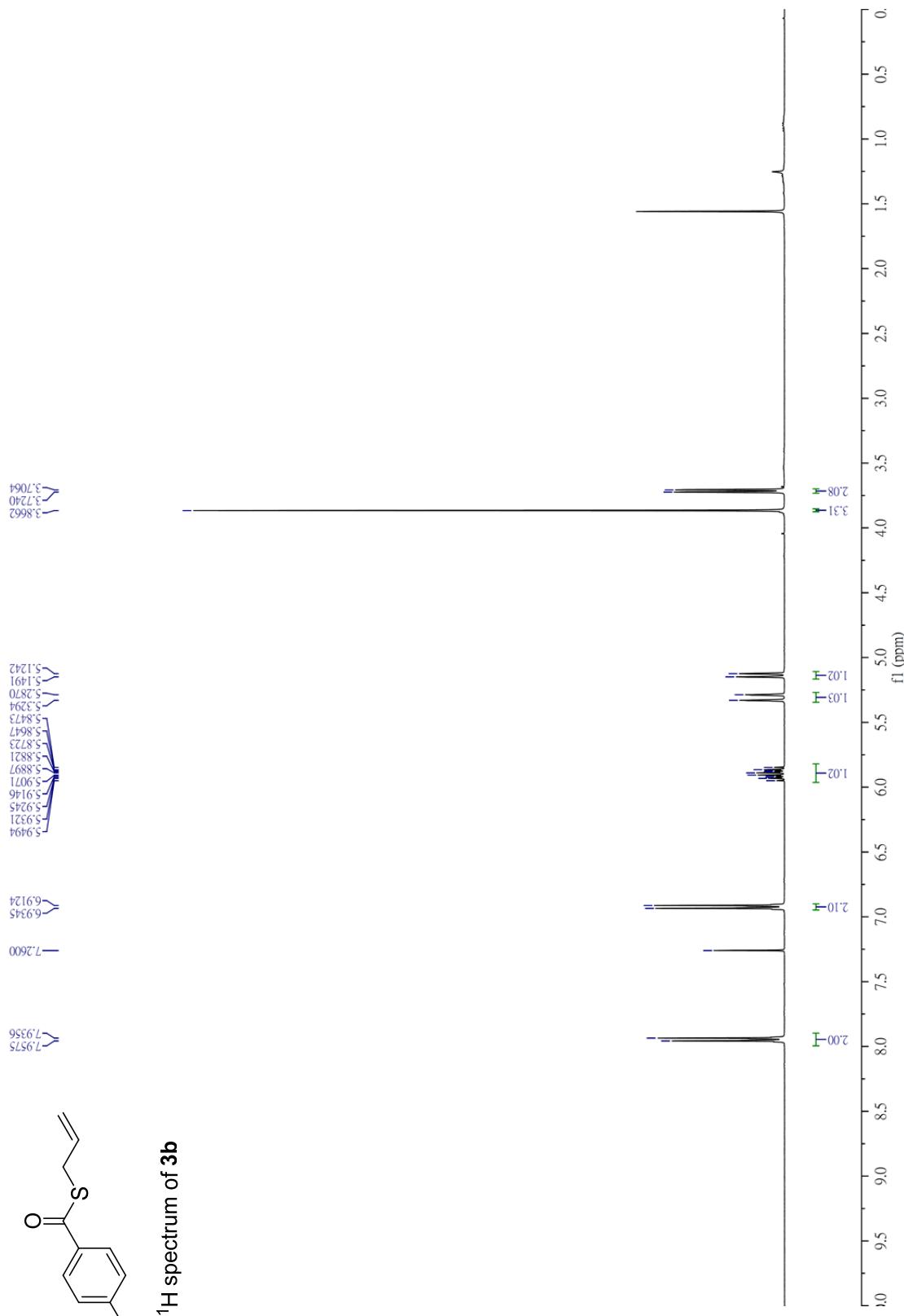


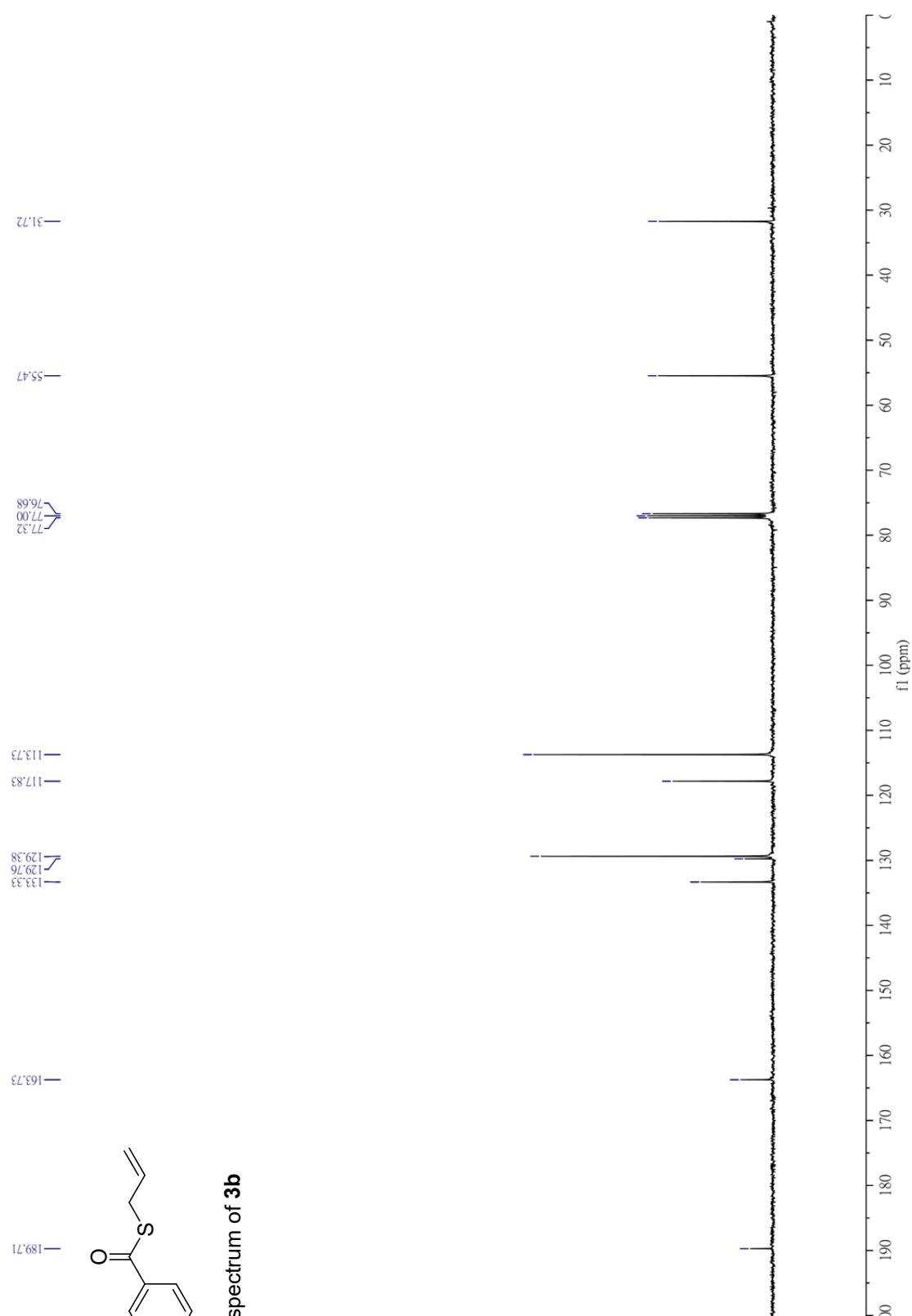
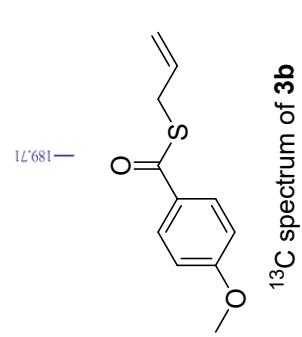


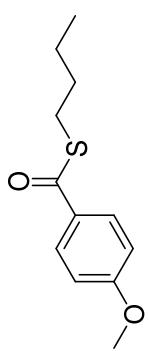
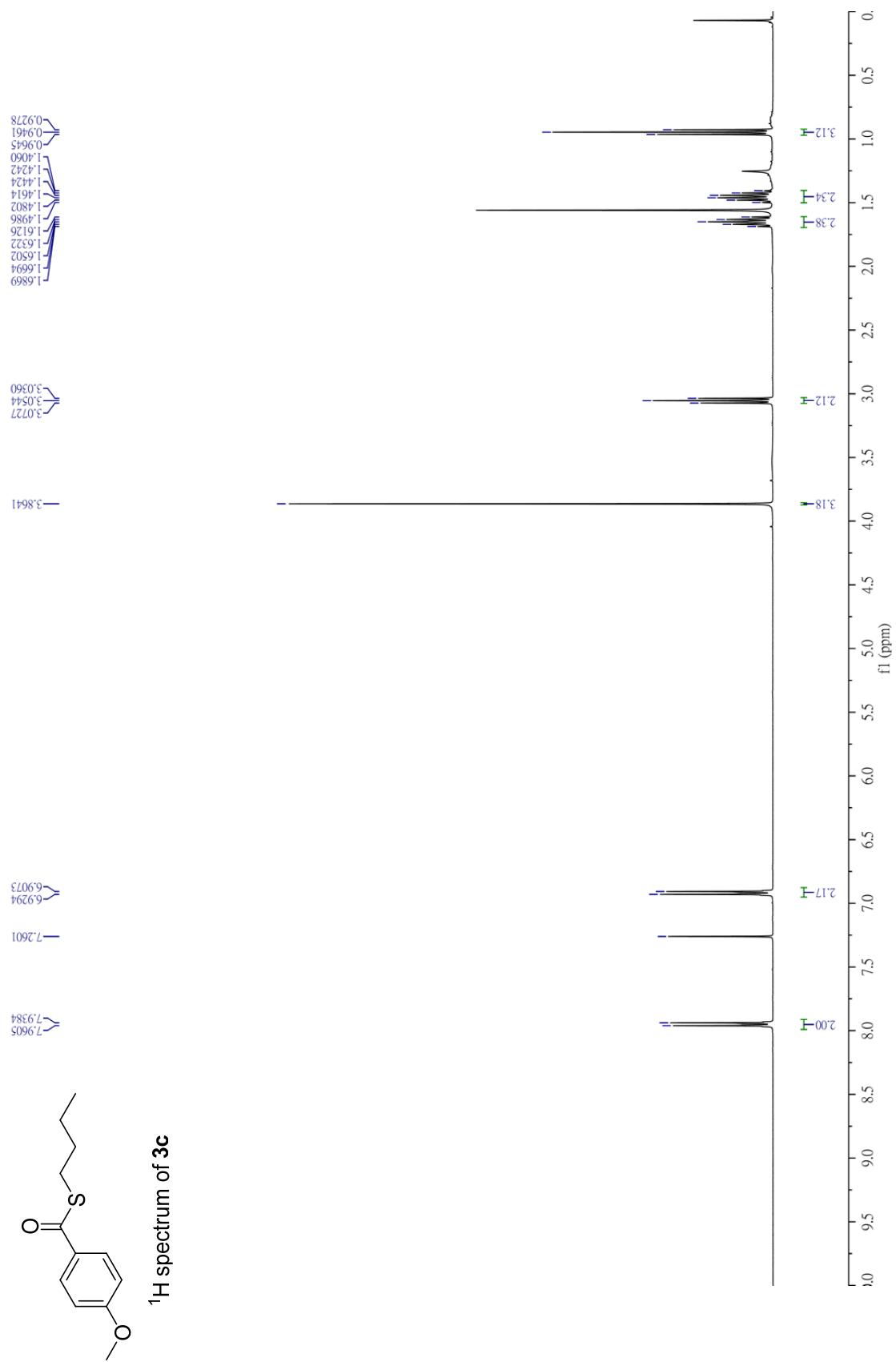




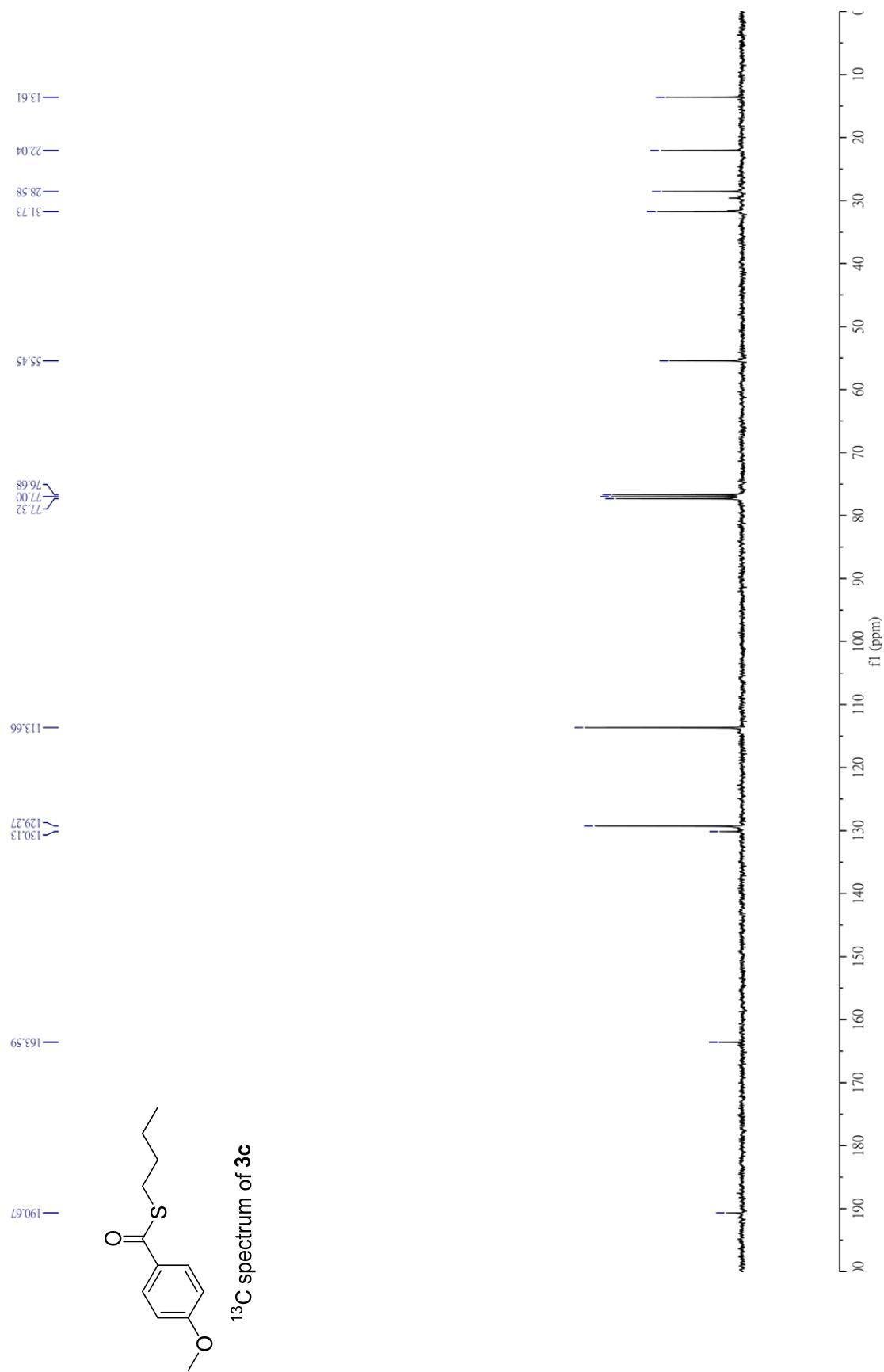
¹H spectrum of 3b

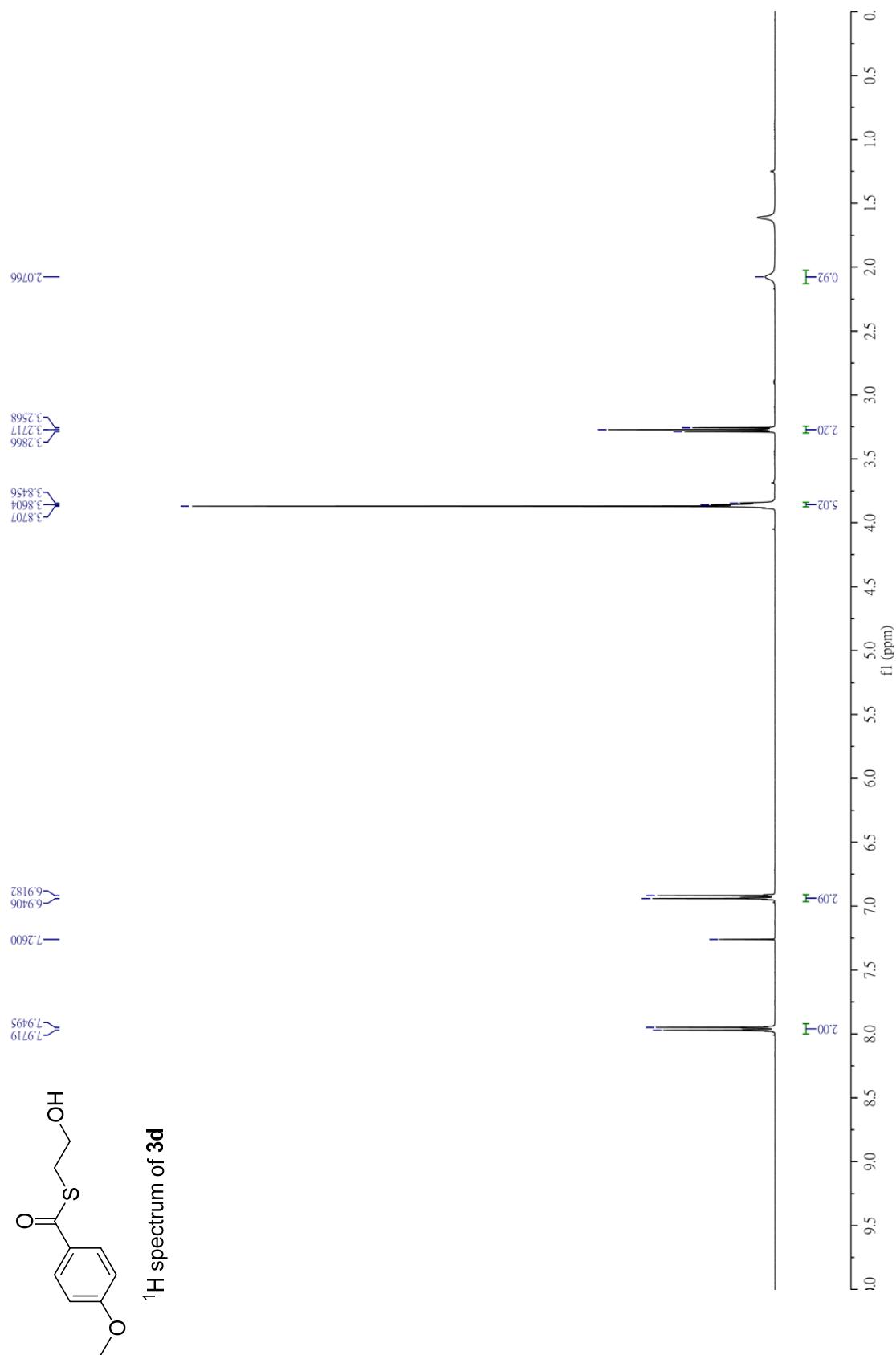


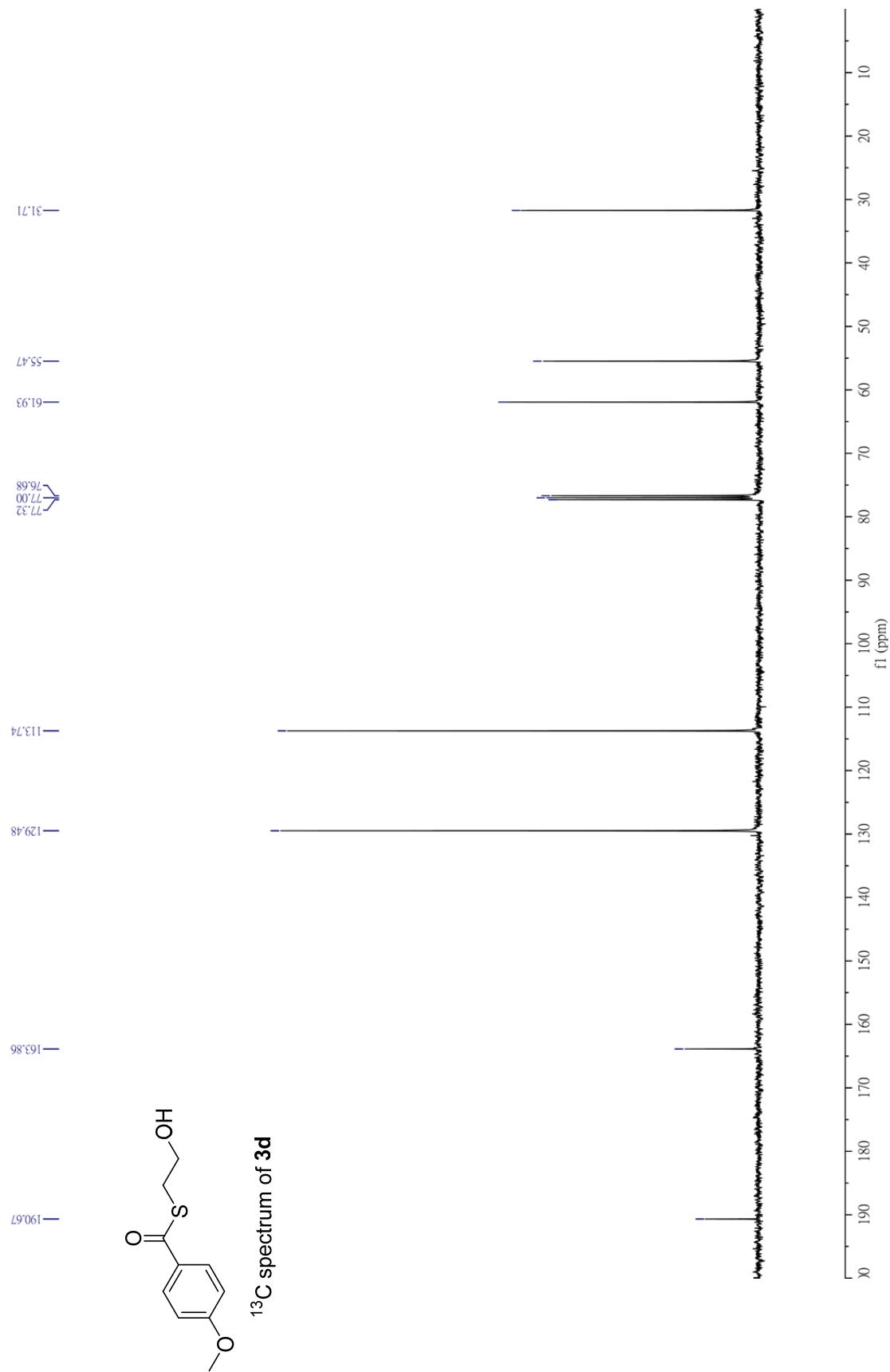


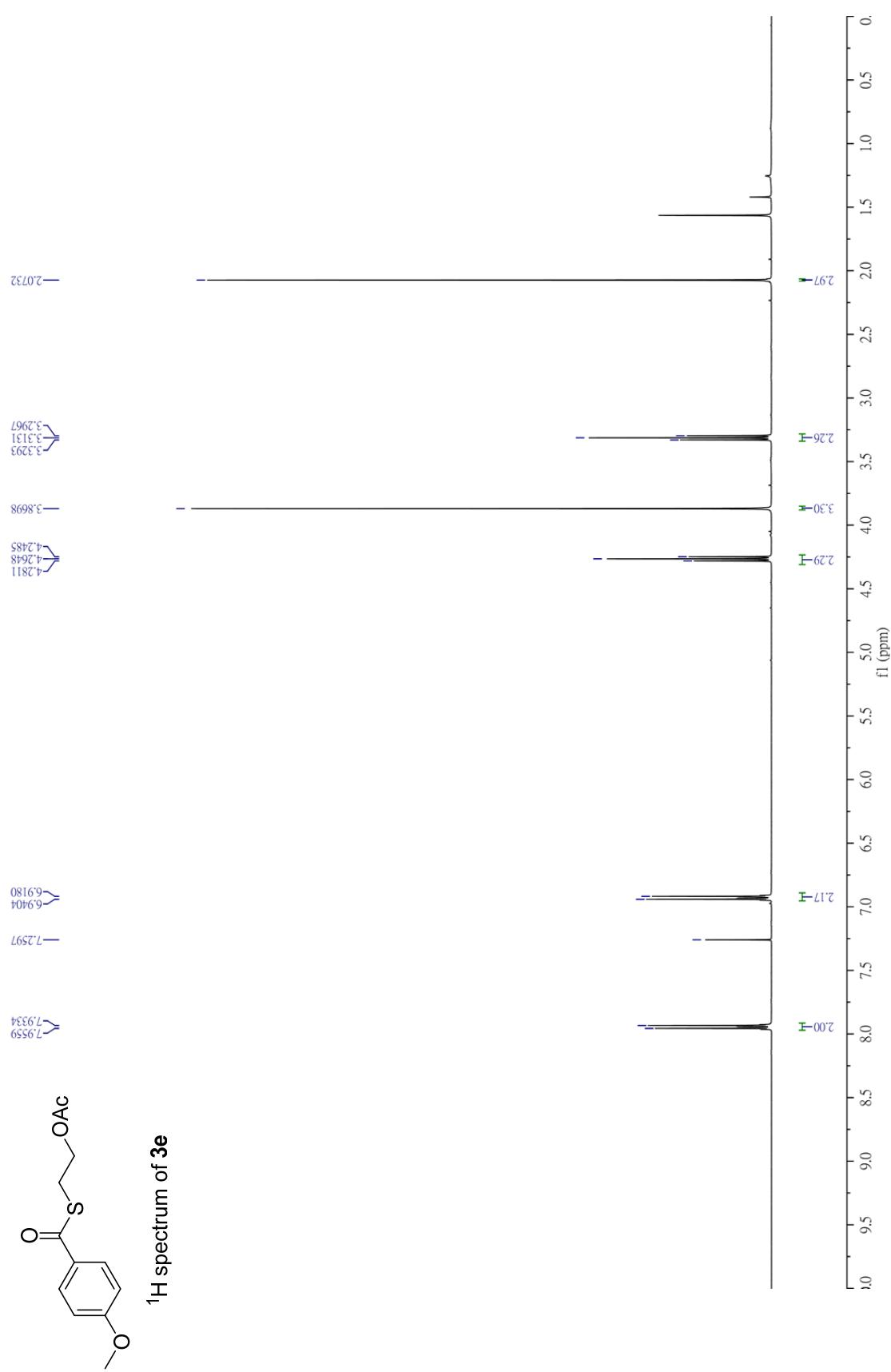


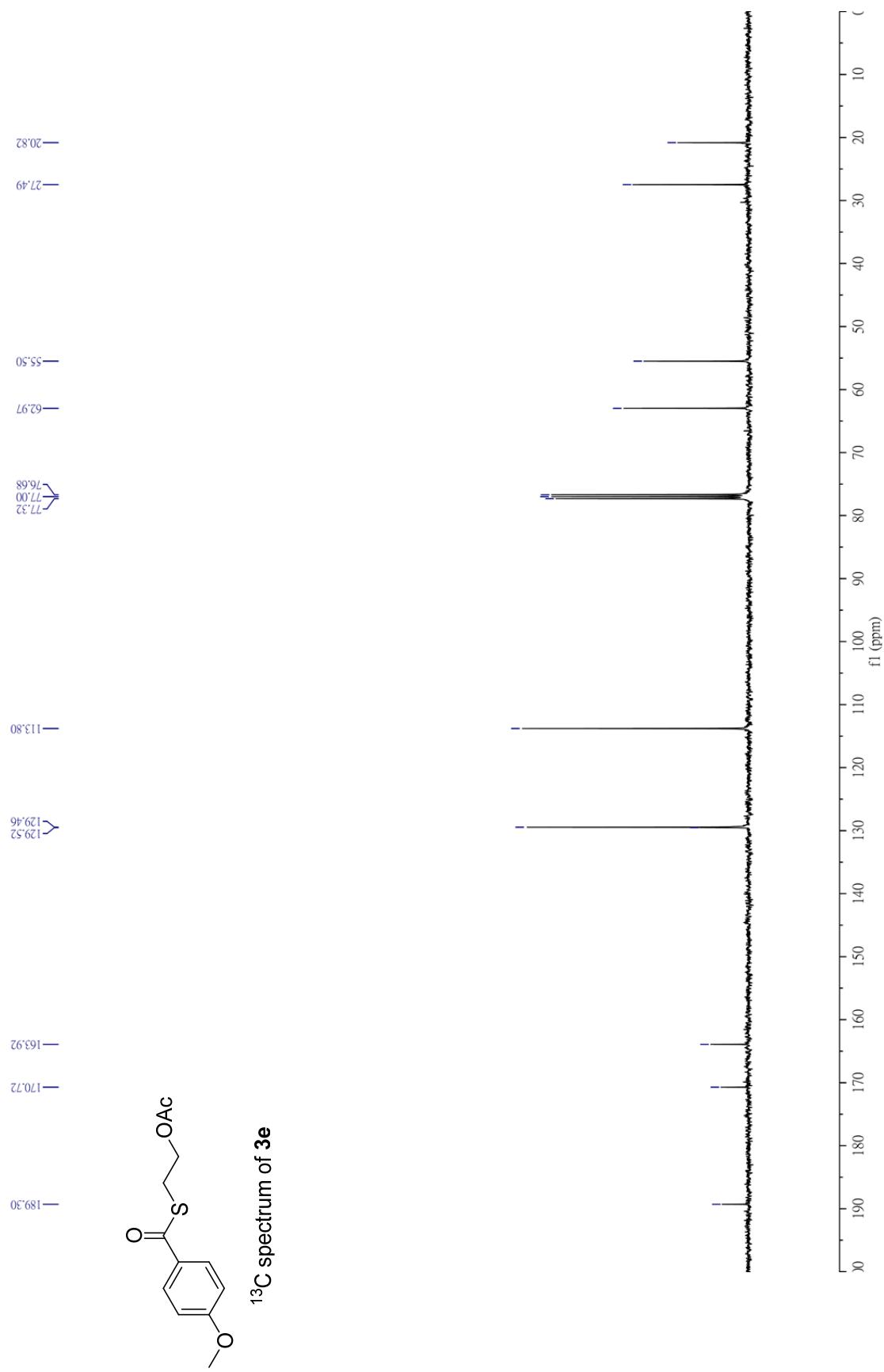
¹H spectrum of 3c

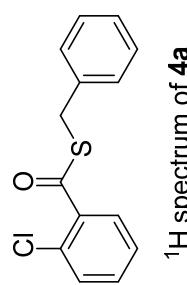
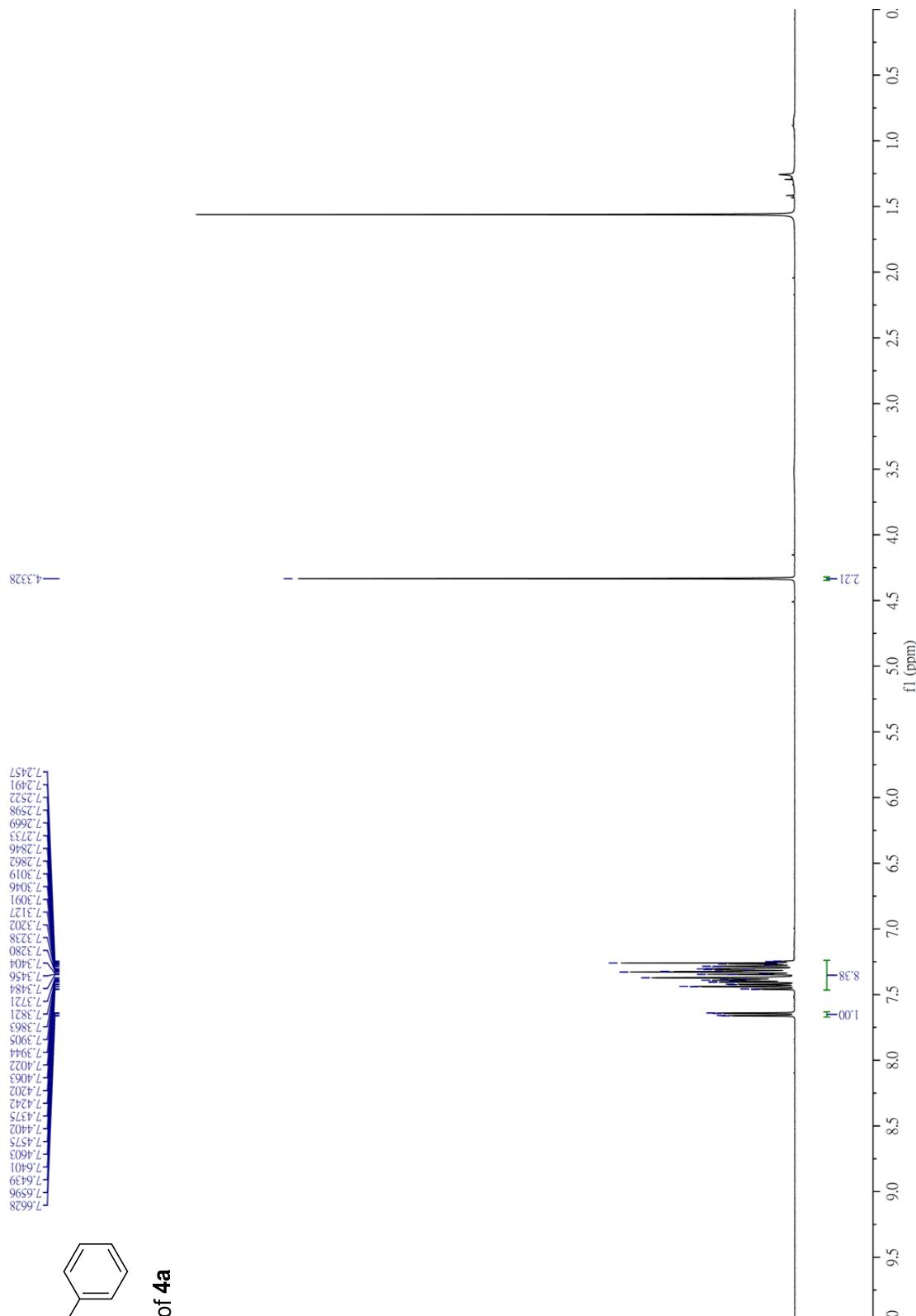




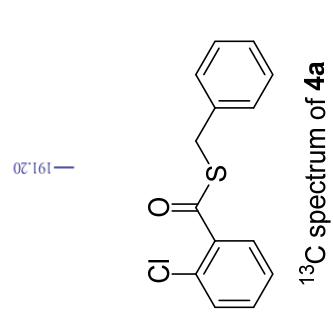








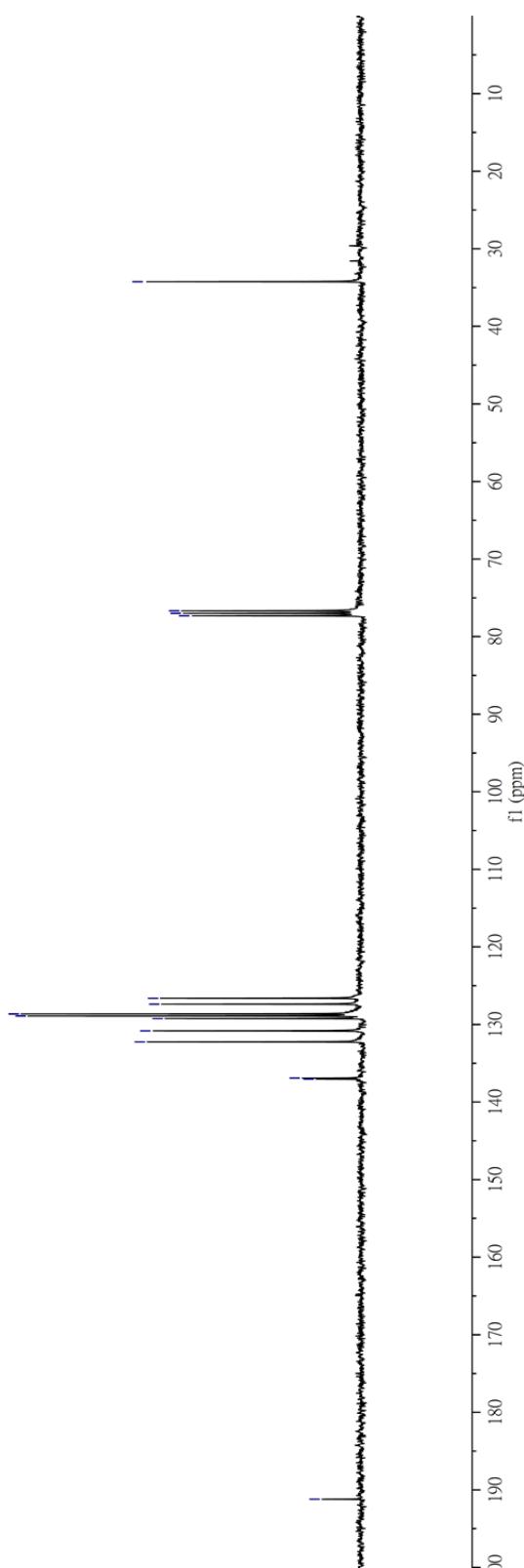
¹H spectrum of **4a**

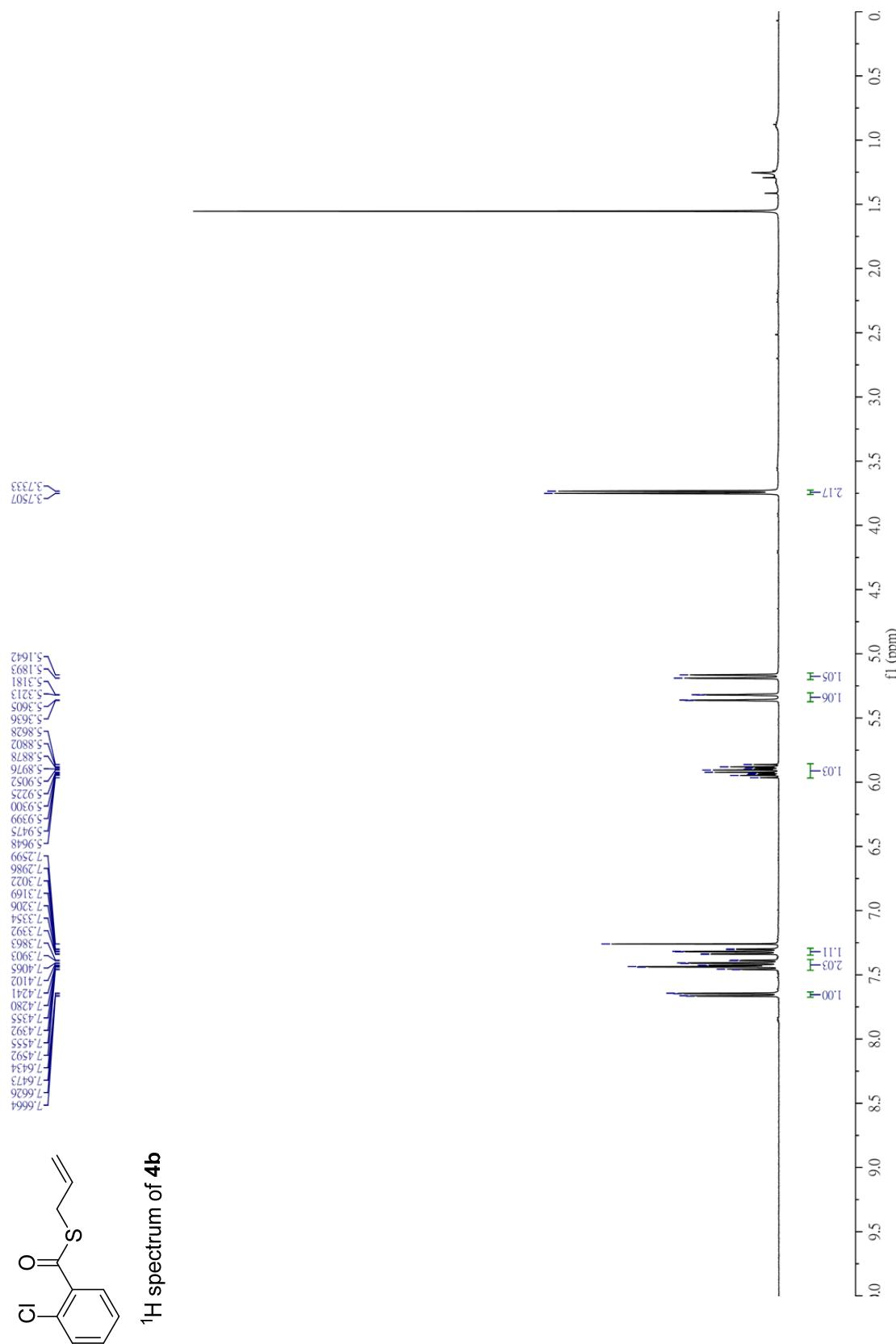


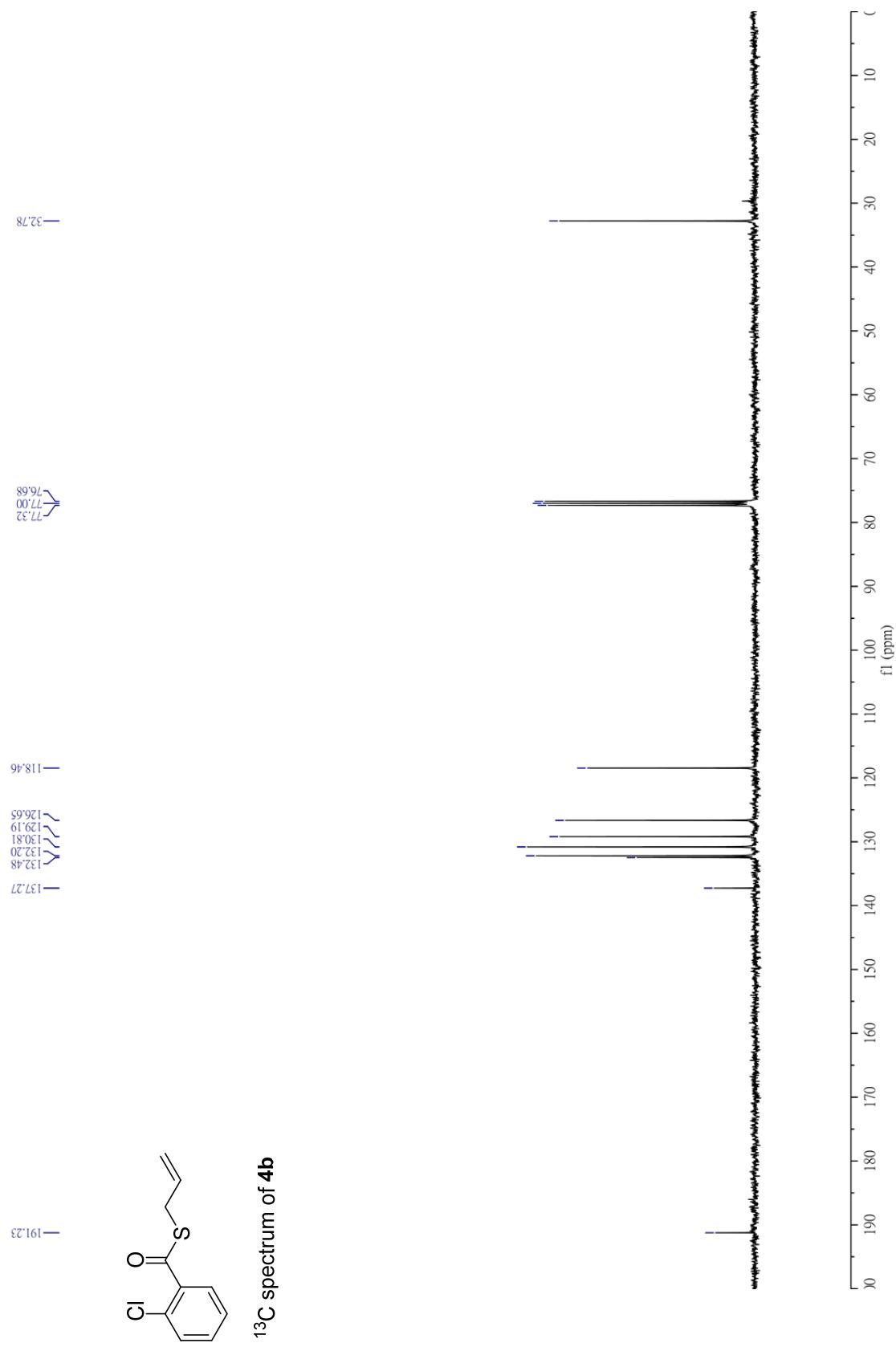
137.05
136.92
133.25
130.82
129.24
128.91
128.65
127.38
126.62

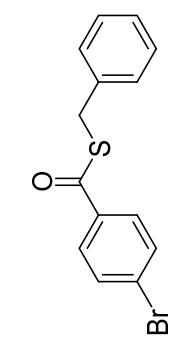
77.31
76.99
76.68

—34.24

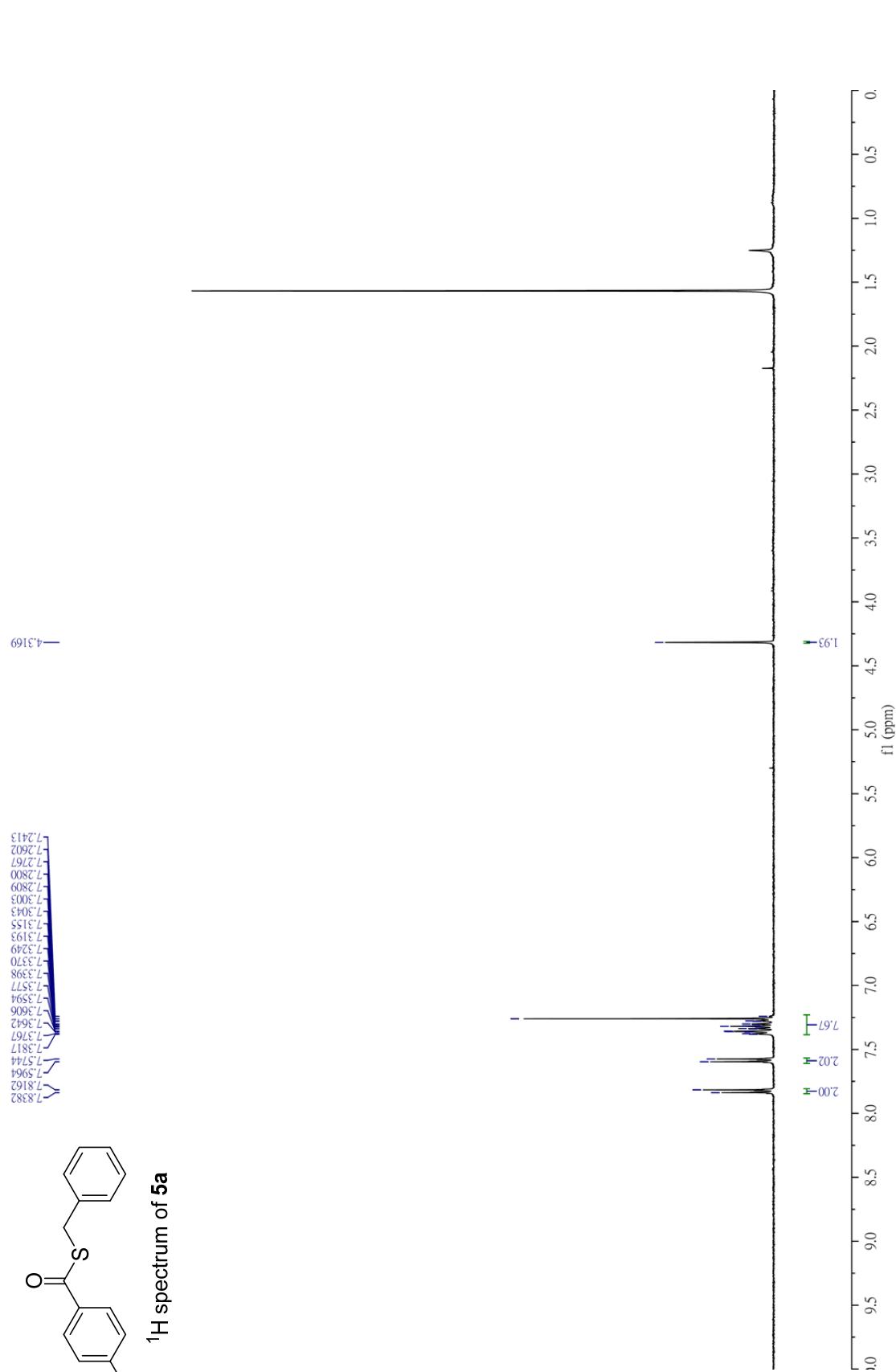


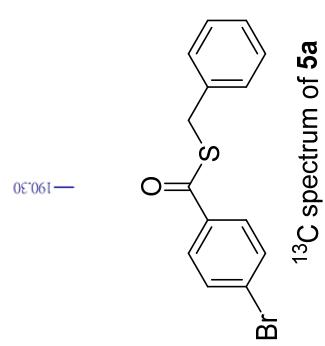




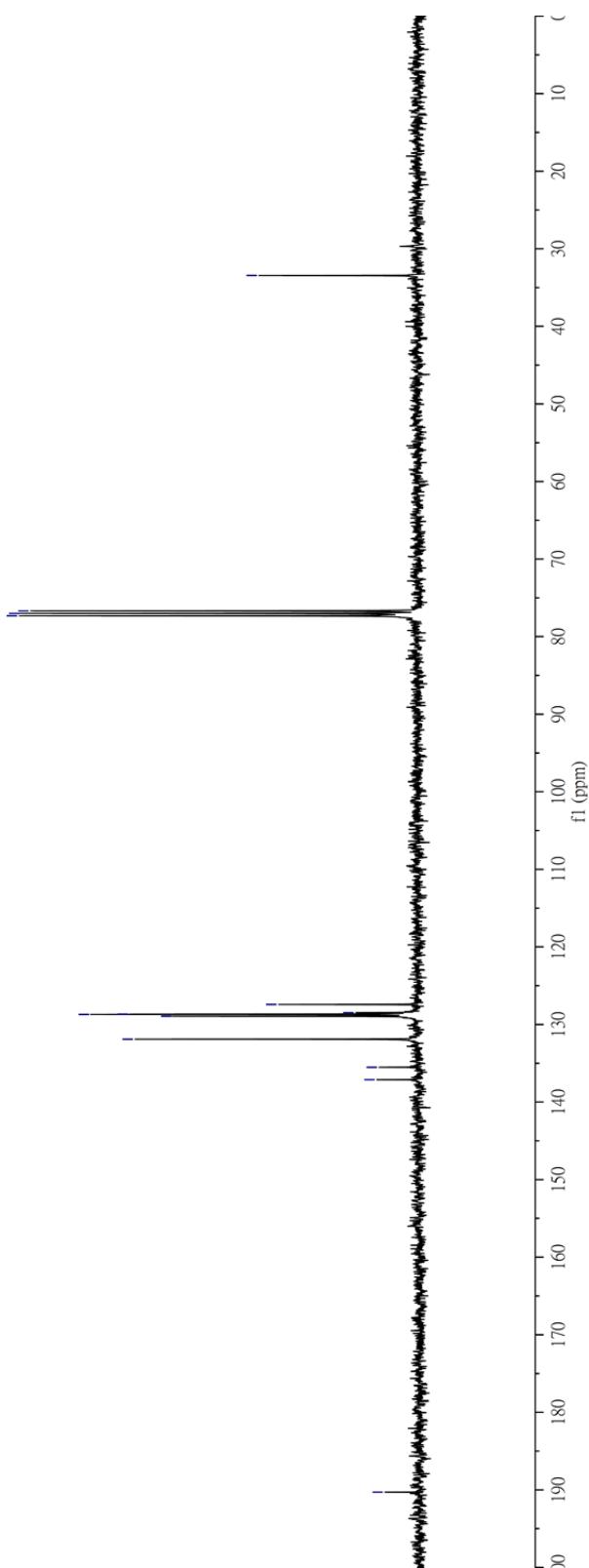


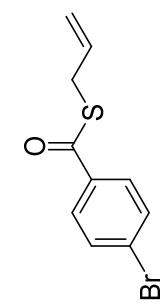
¹H spectrum of 5a



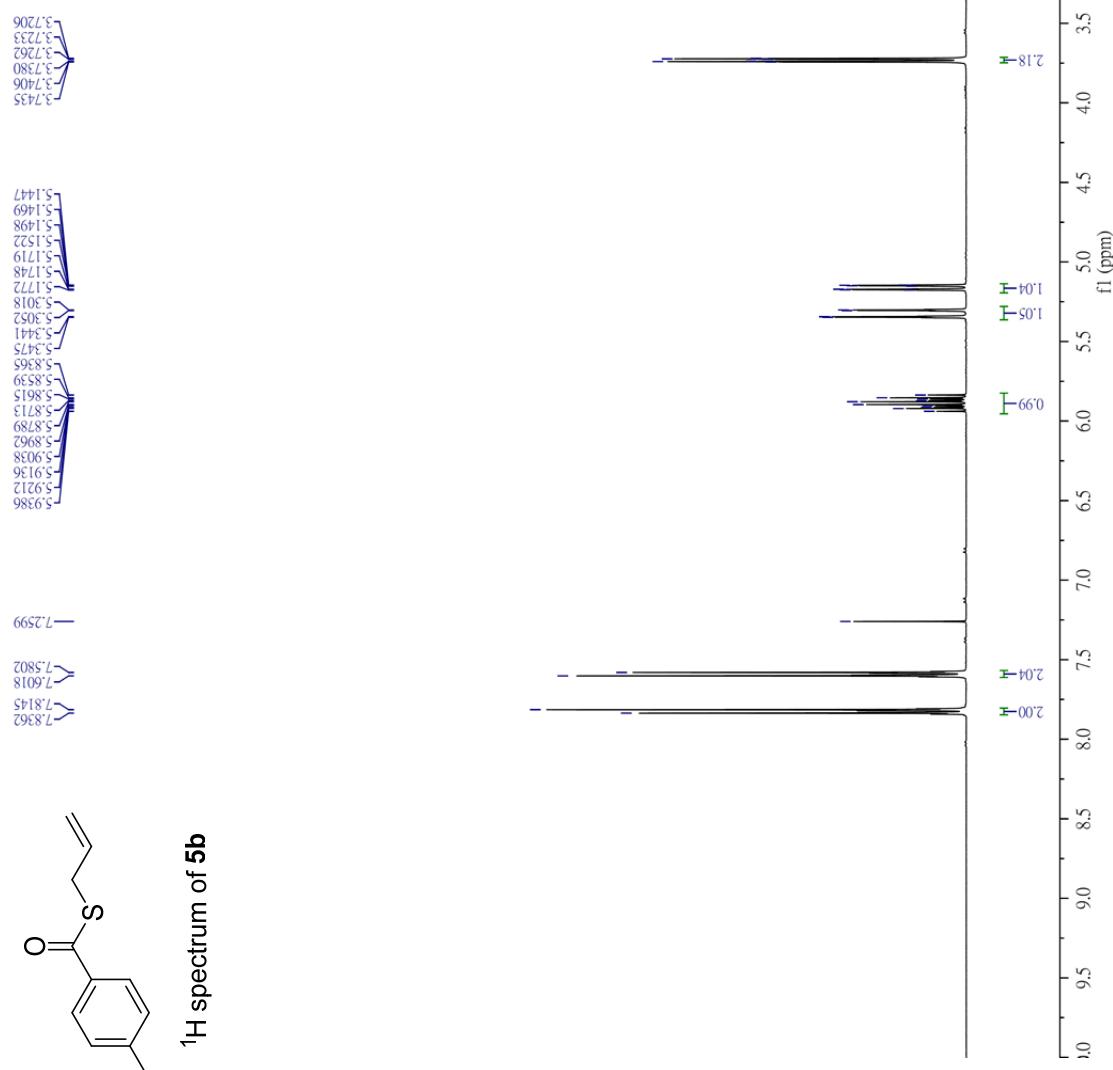


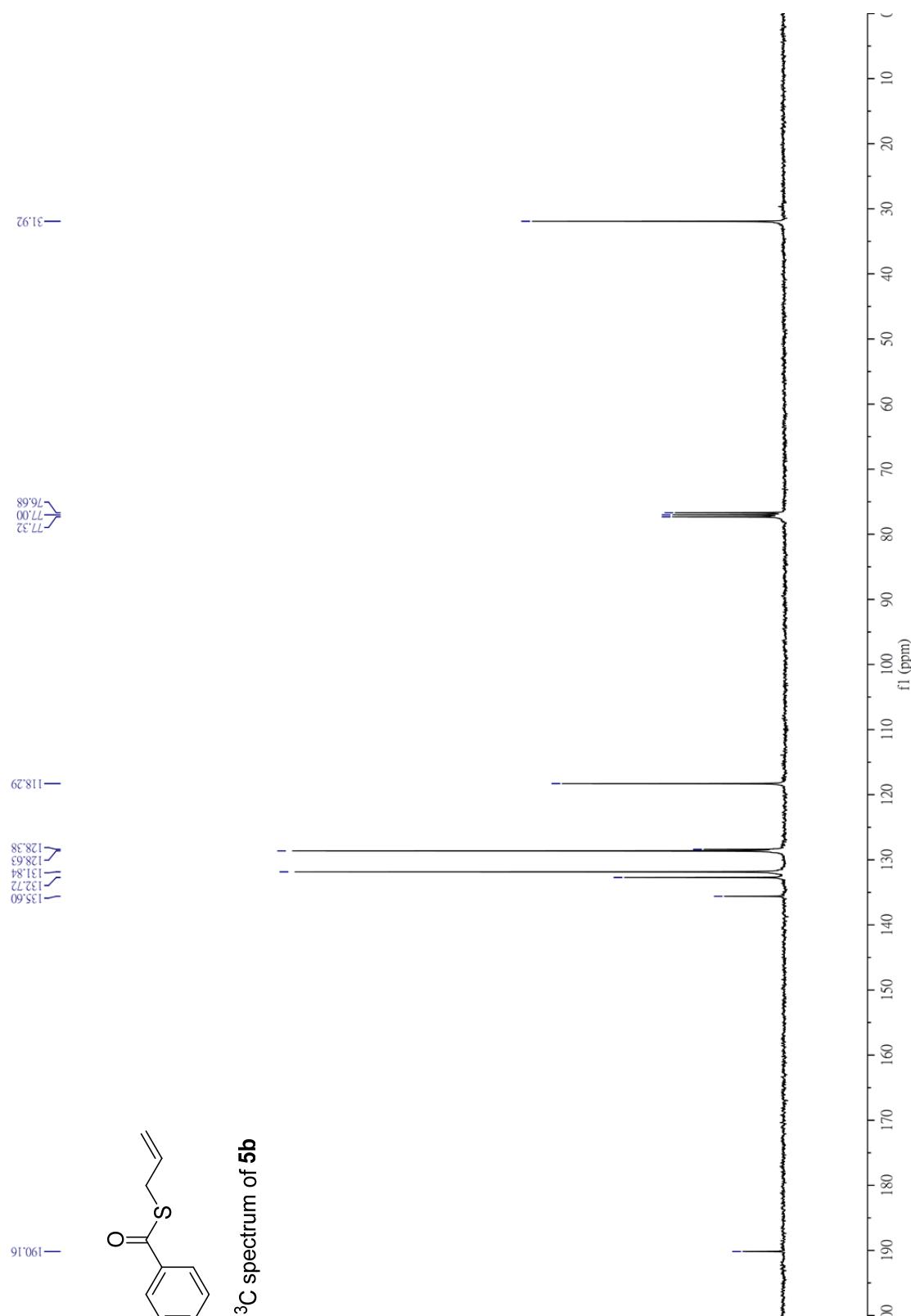
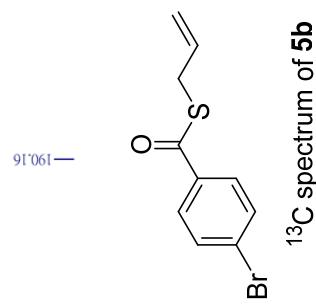
^{13}C spectrum of **5a**

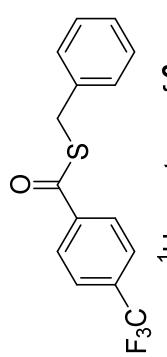




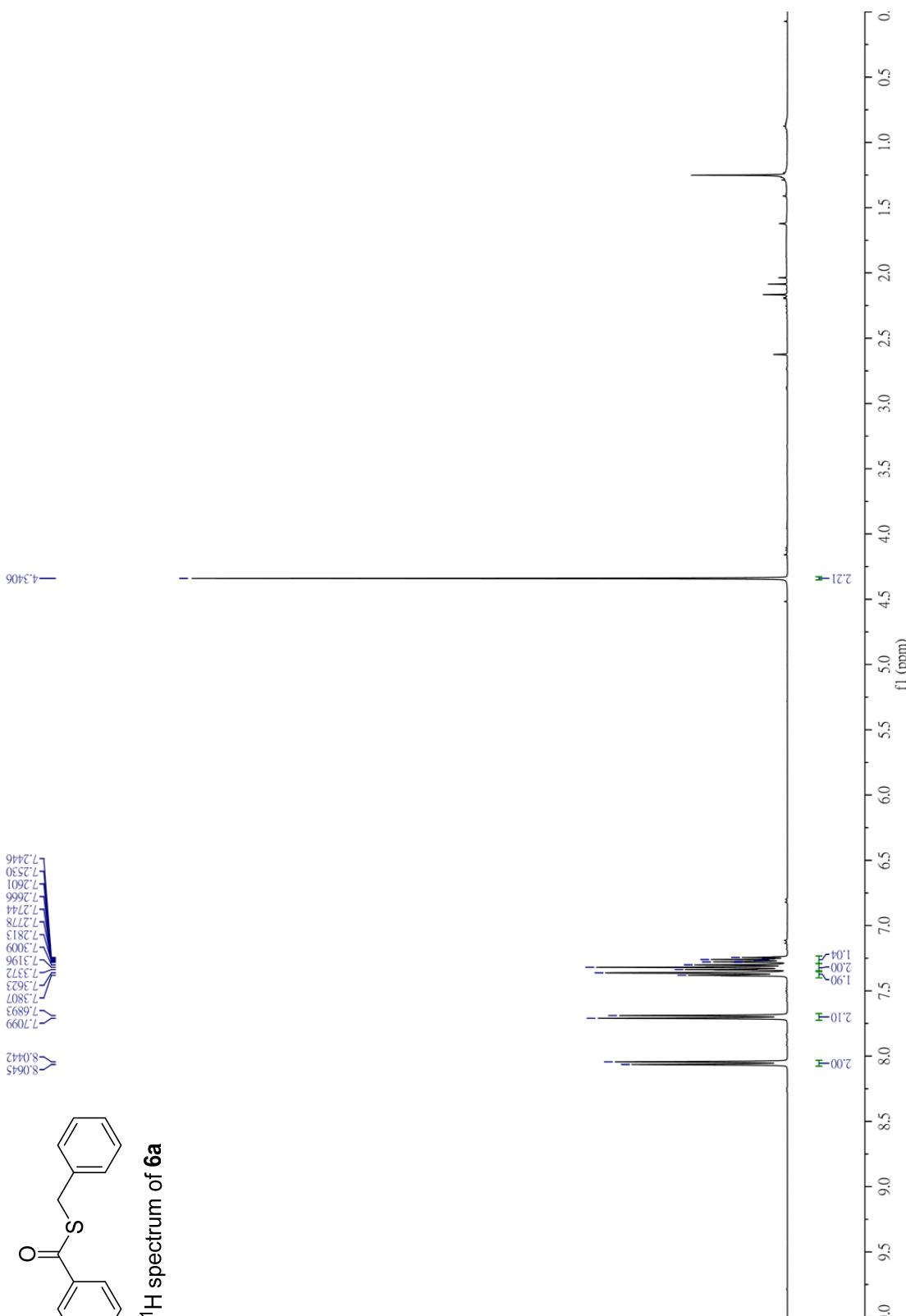
¹H spectrum of **5b**

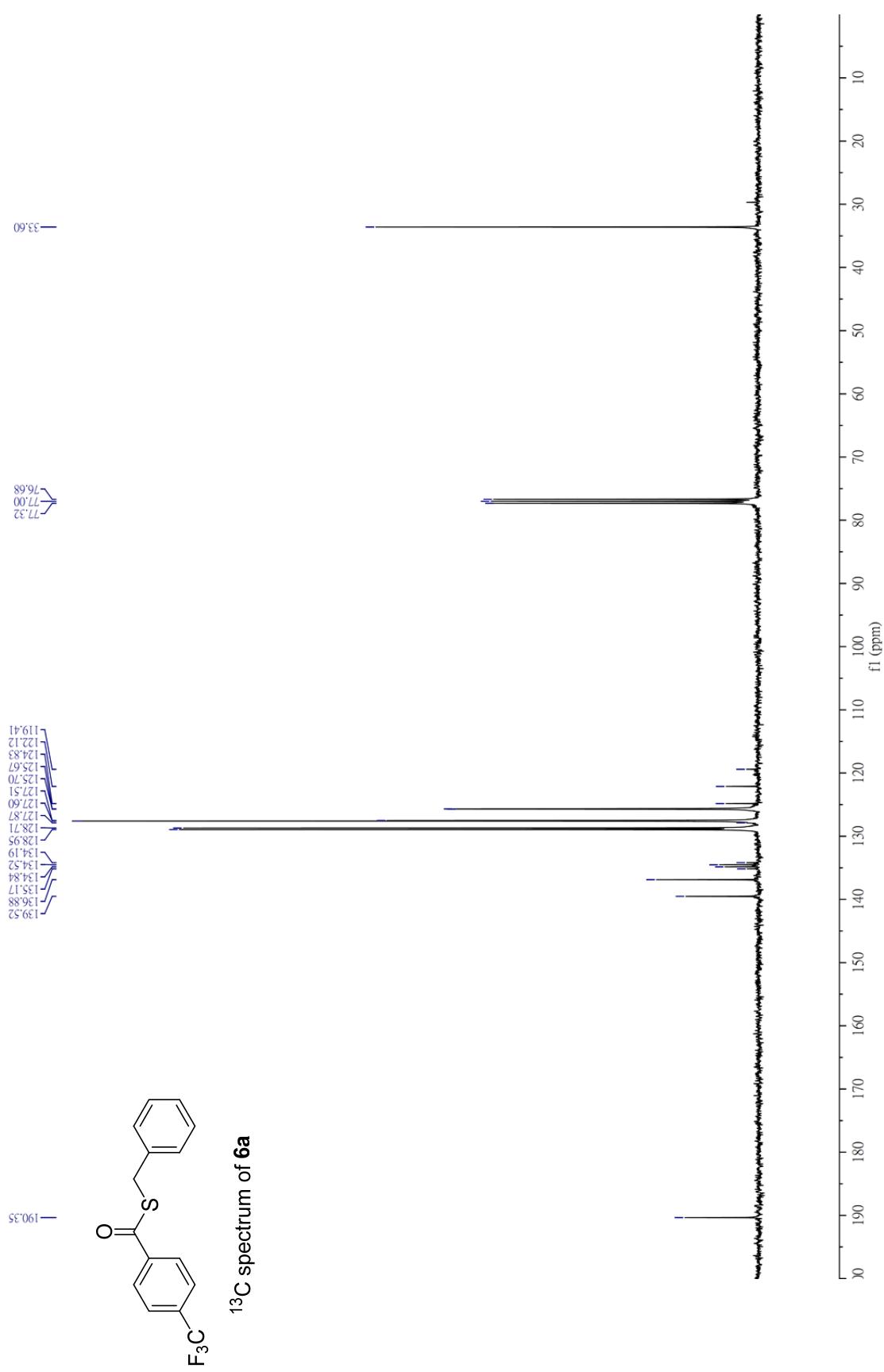




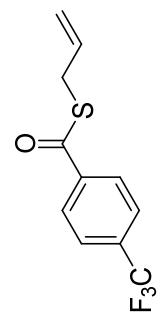


¹H spectrum of 6a

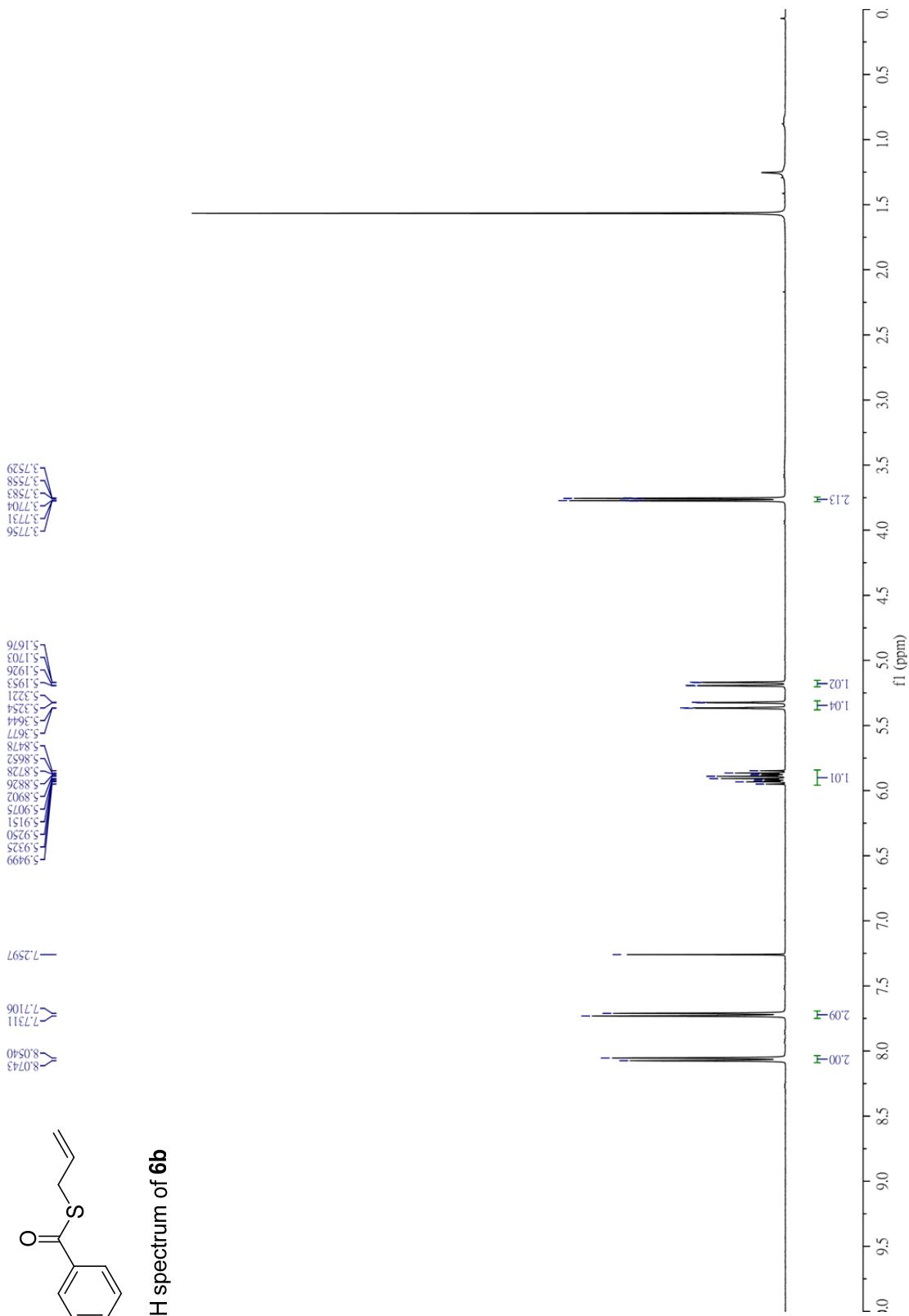


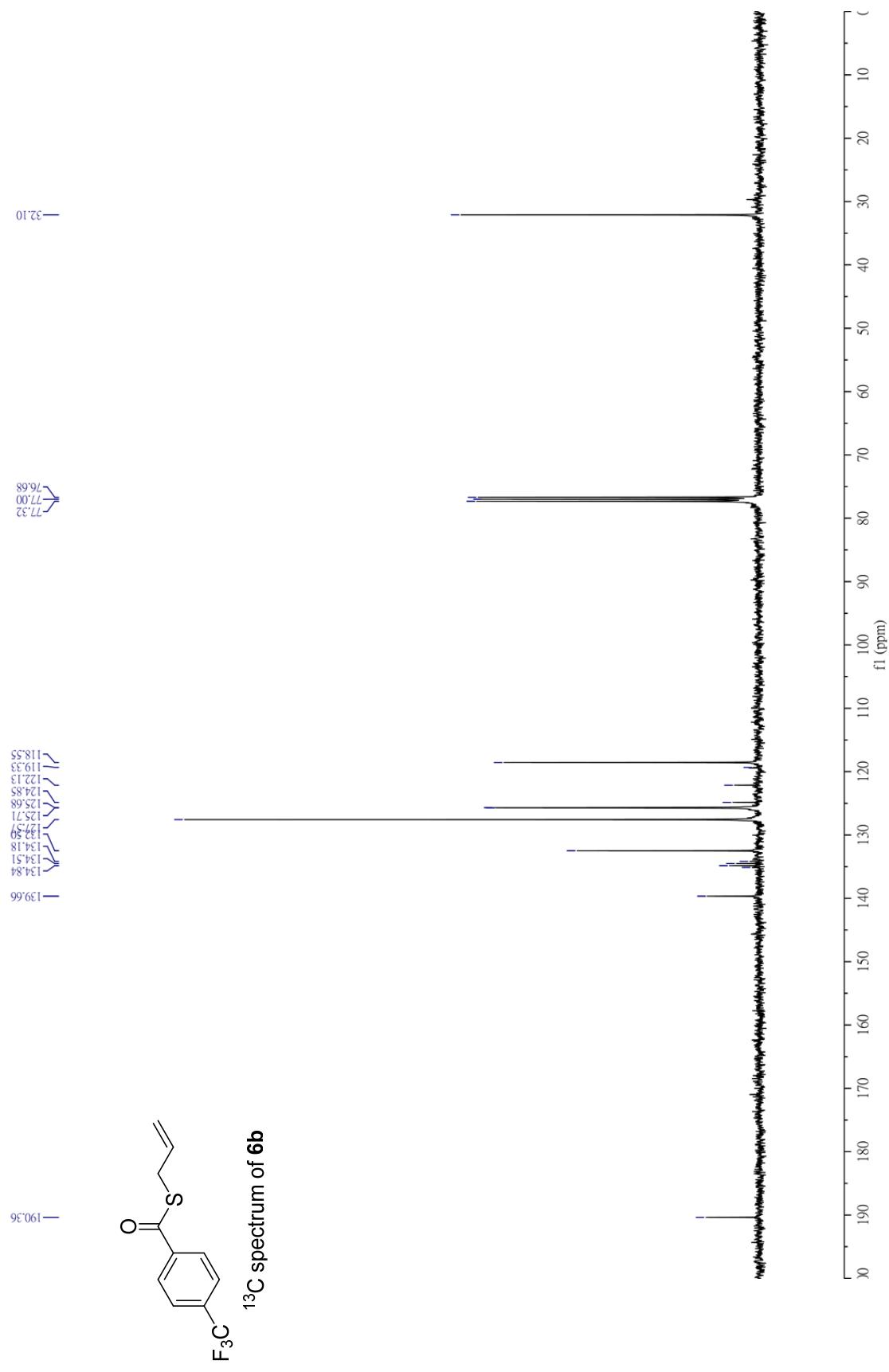


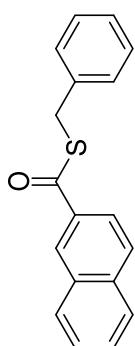
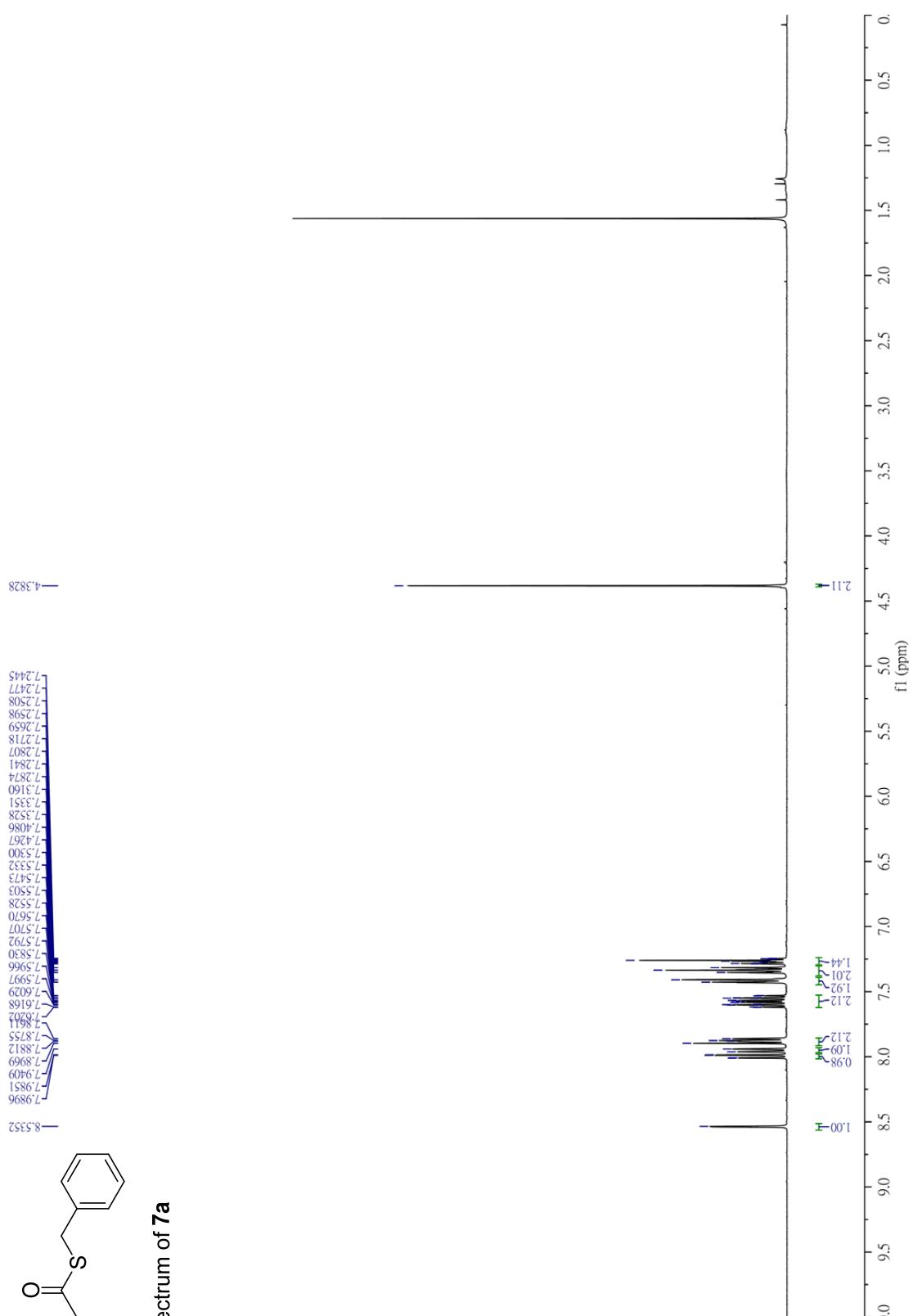
^{13}C spectrum of **6a**



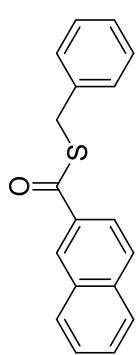
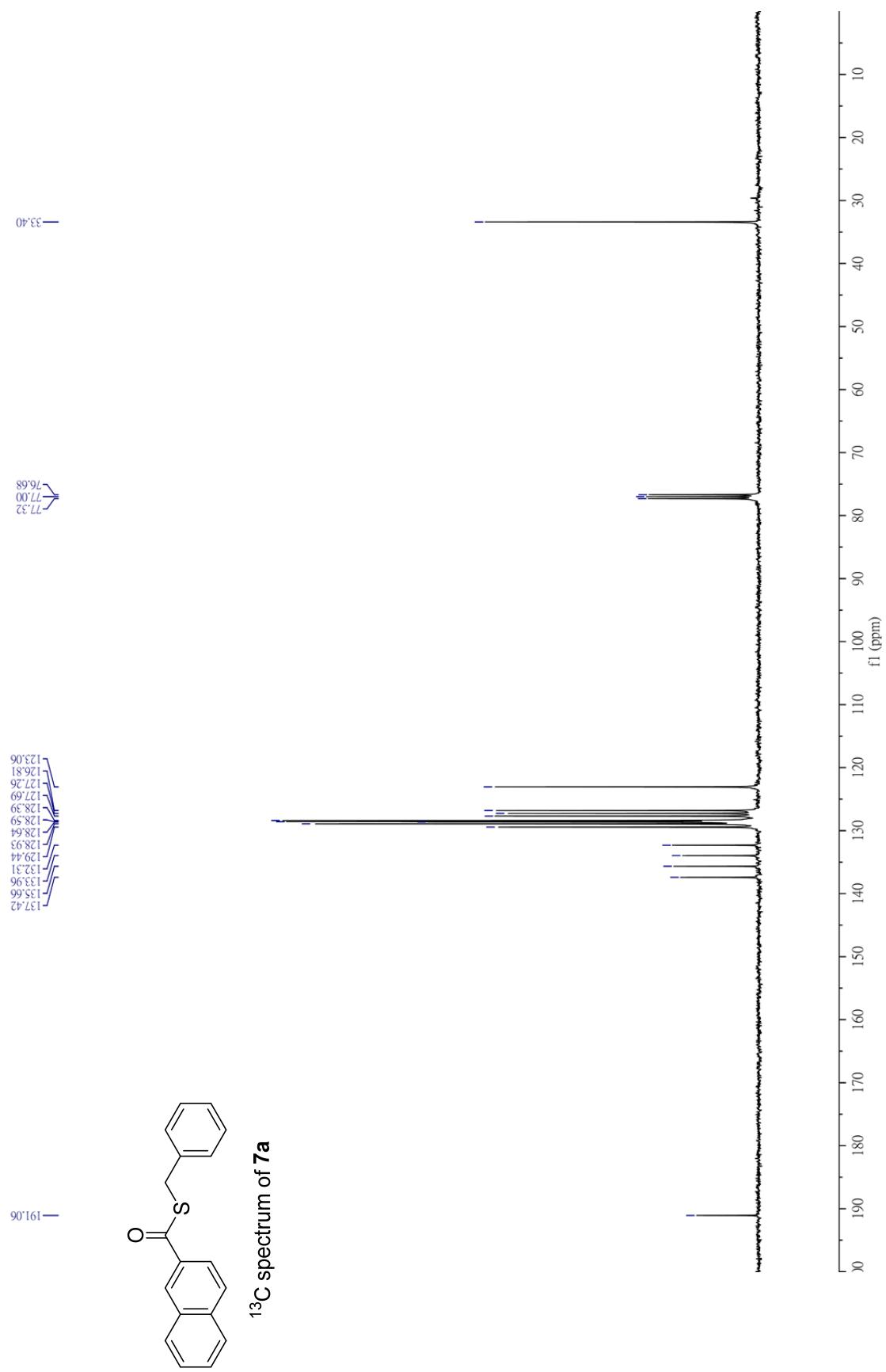
^1H spectrum of **6b**



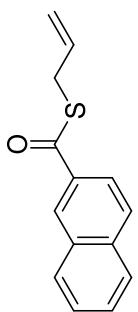
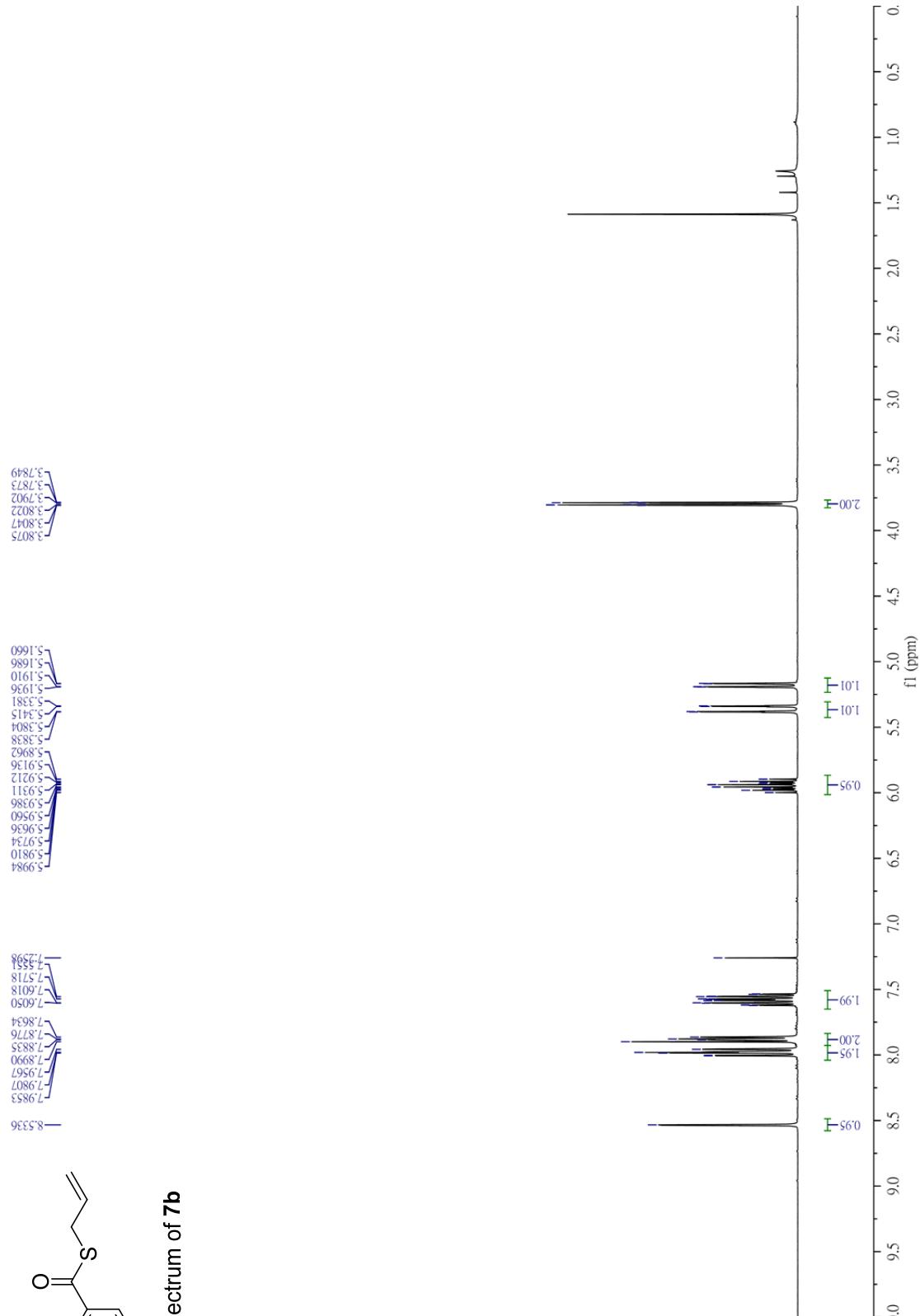




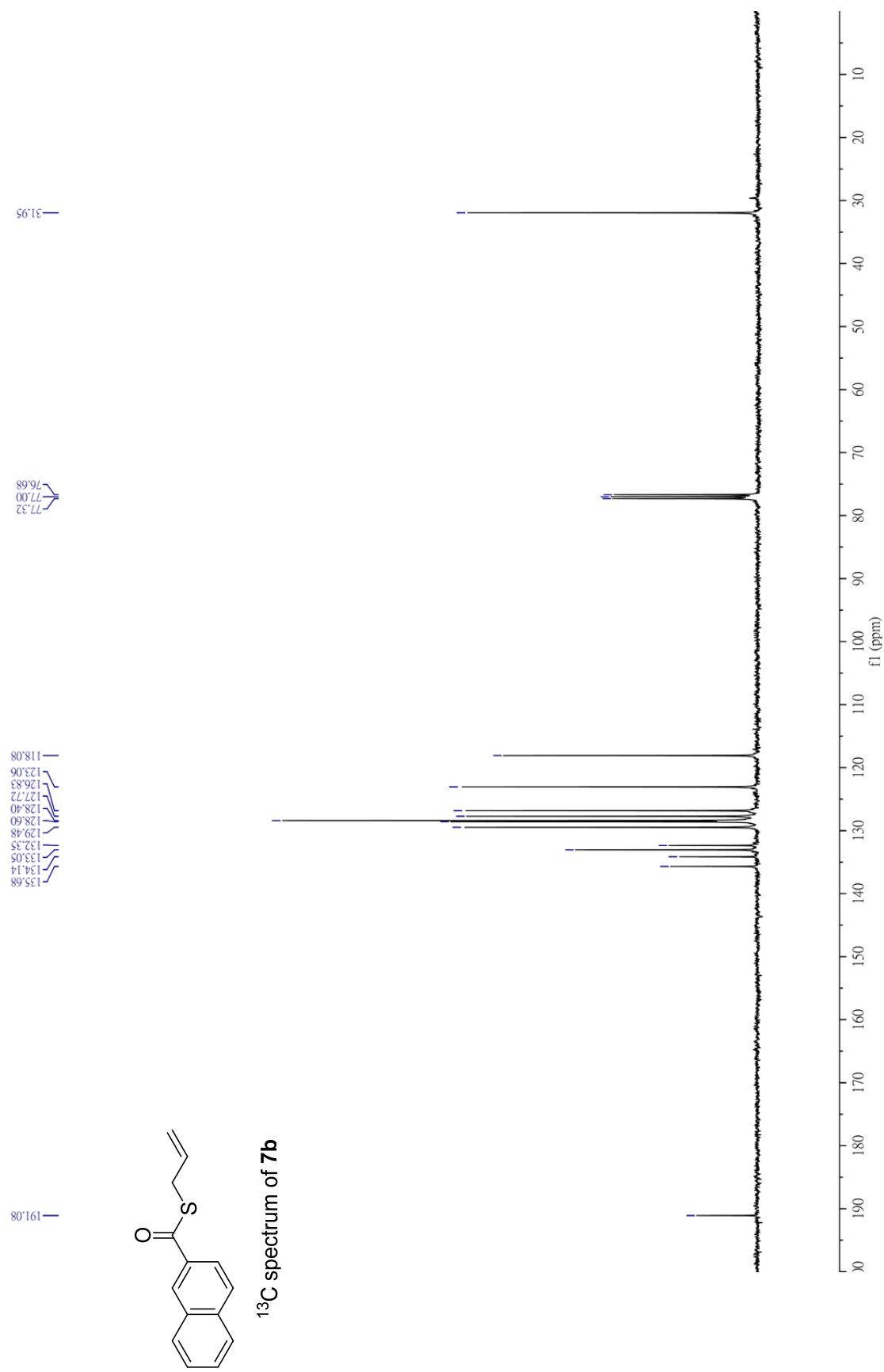
¹H spectrum of 7a



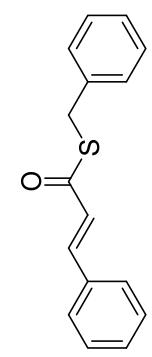
13C spectrum of 7a



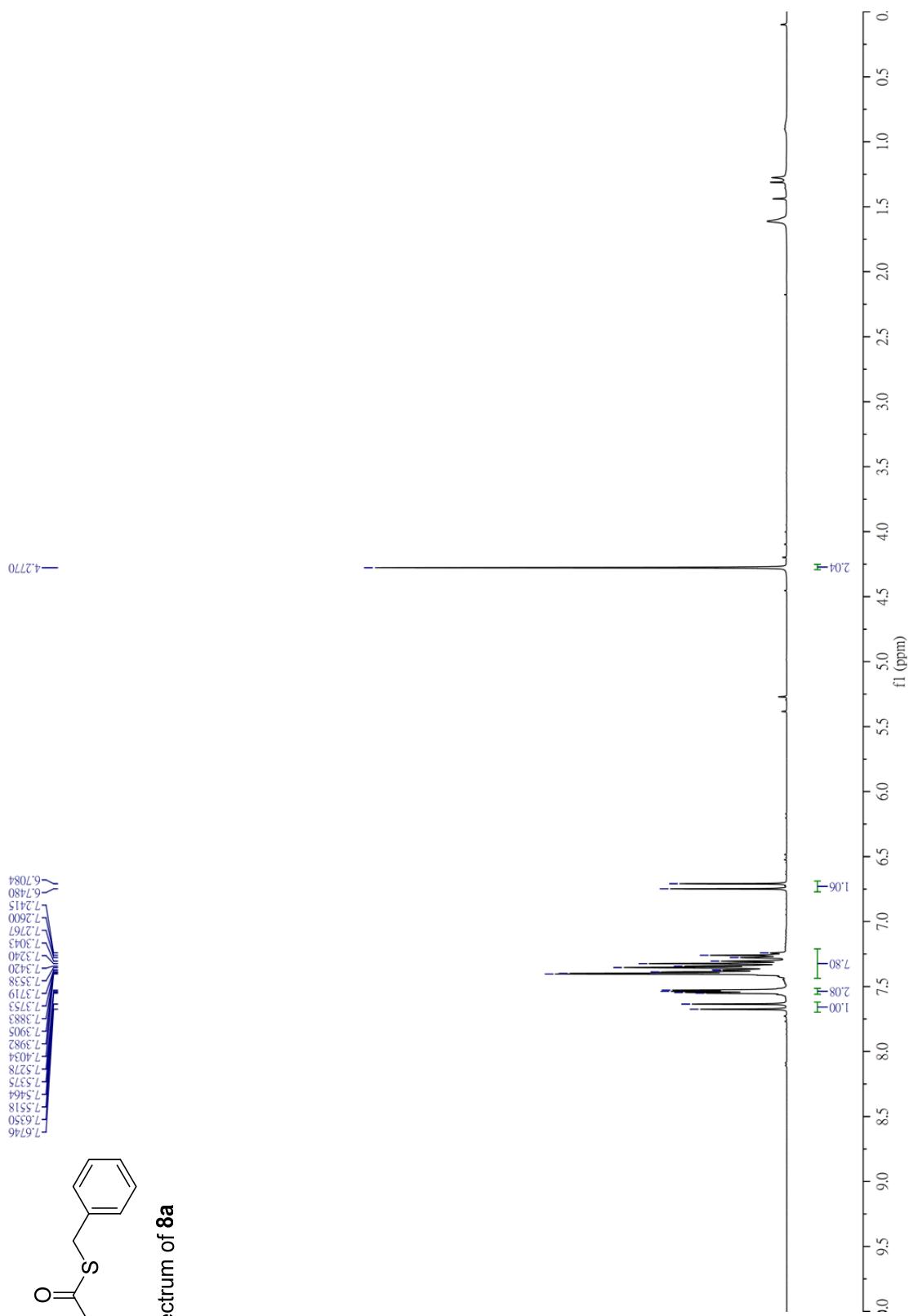
¹H spectrum of 7b

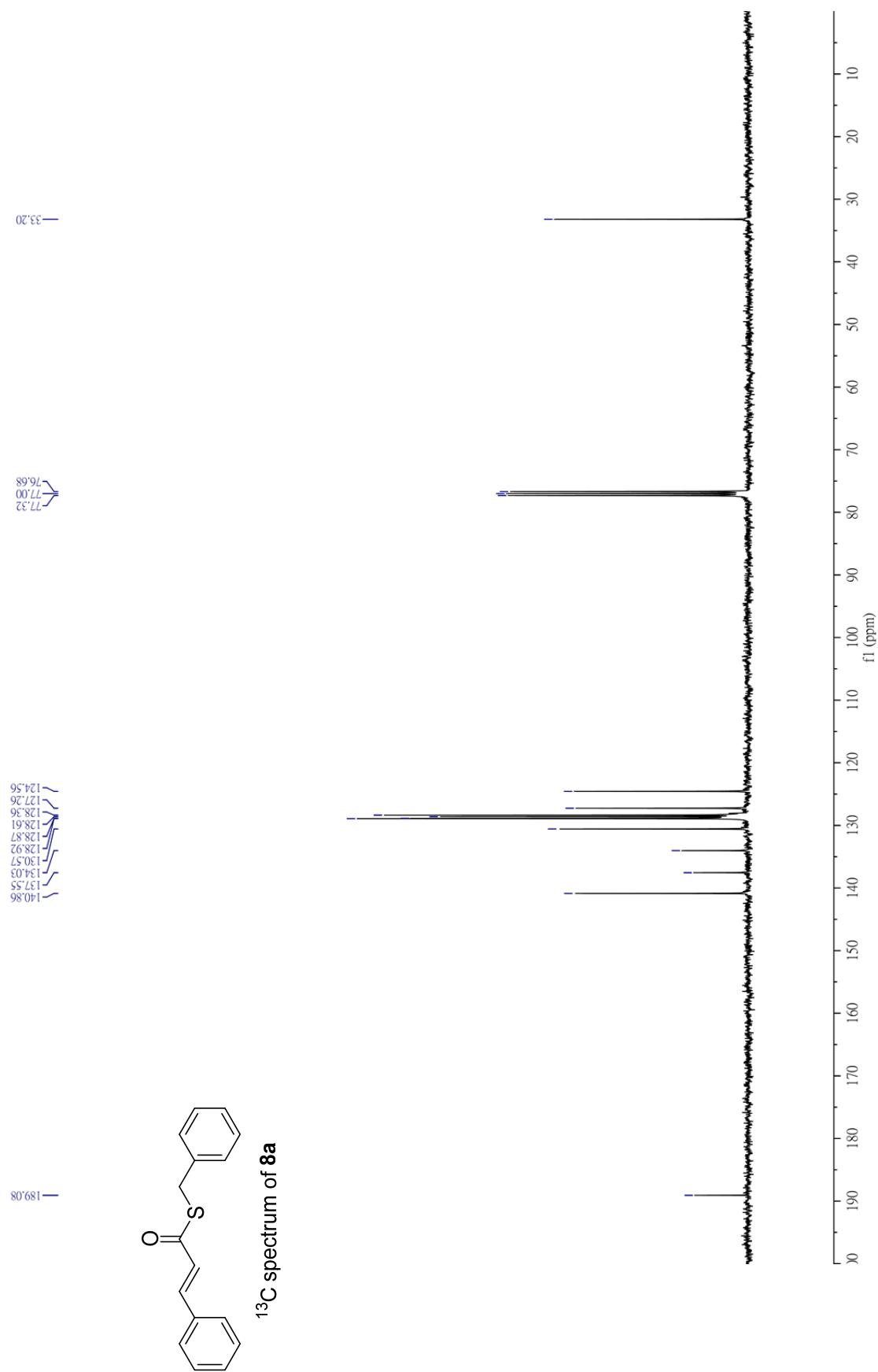


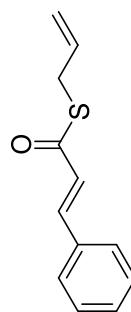
^{13}C spectrum of **7b**



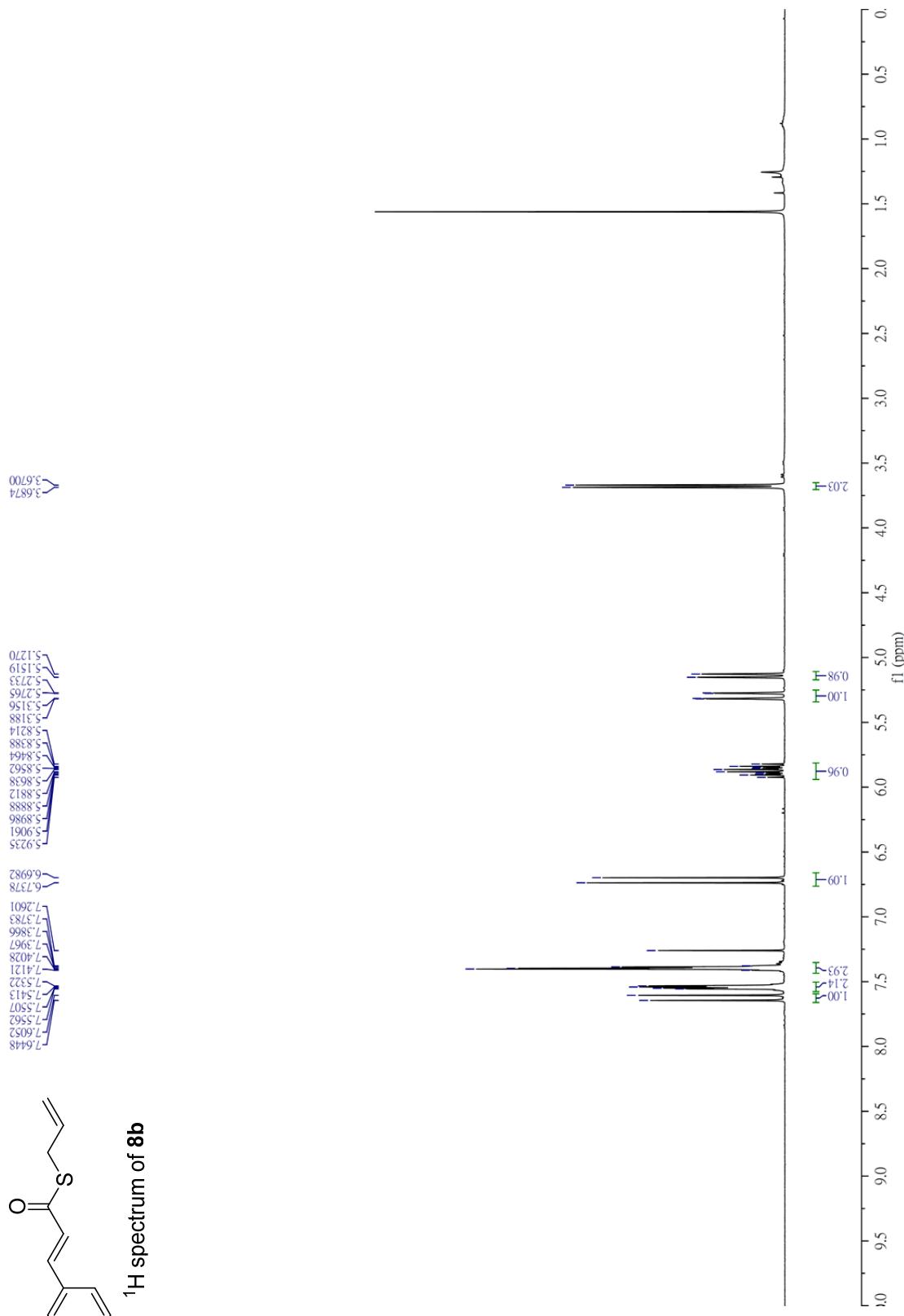
¹H spectrum of 8a

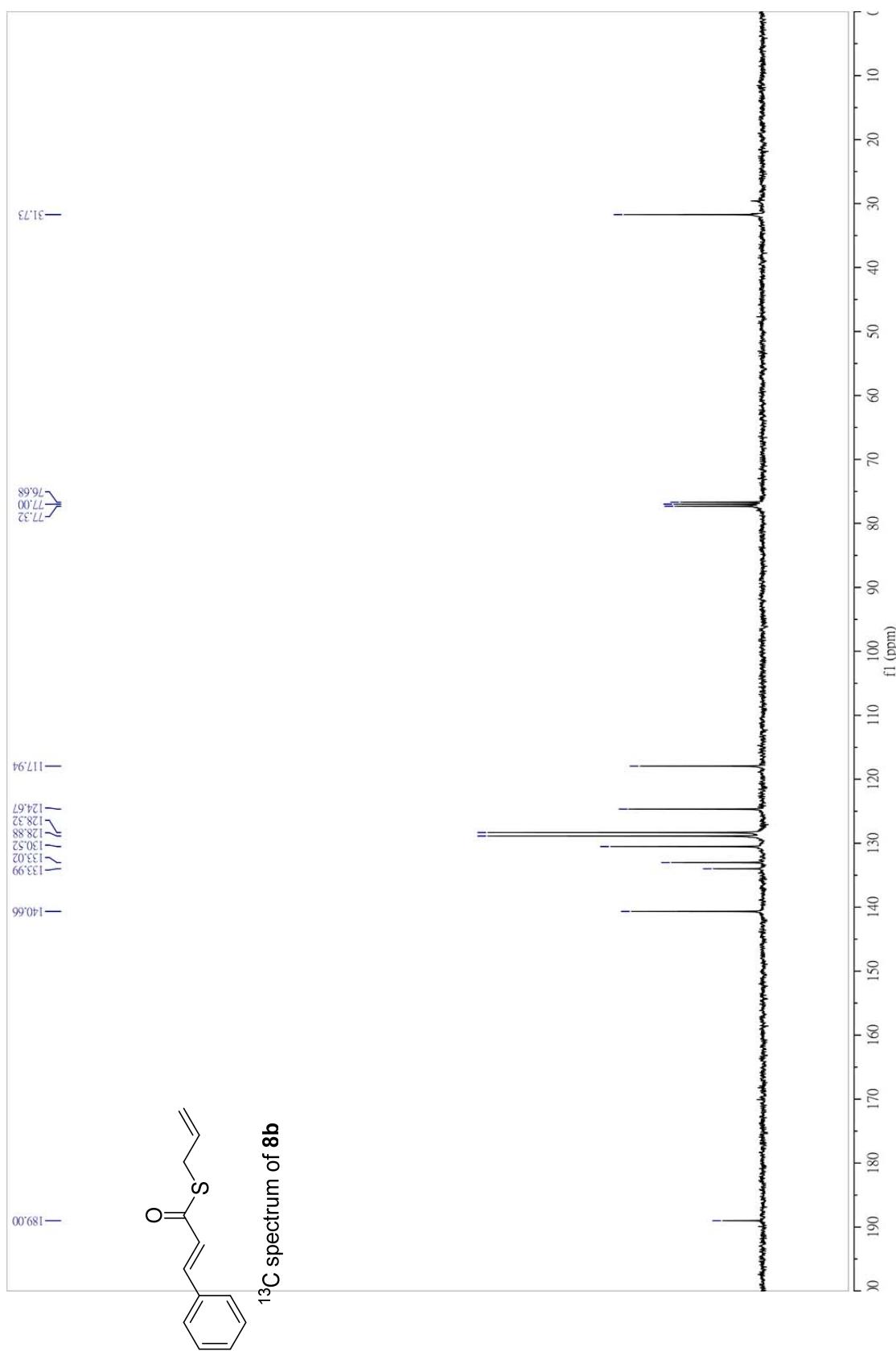


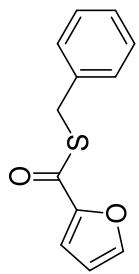




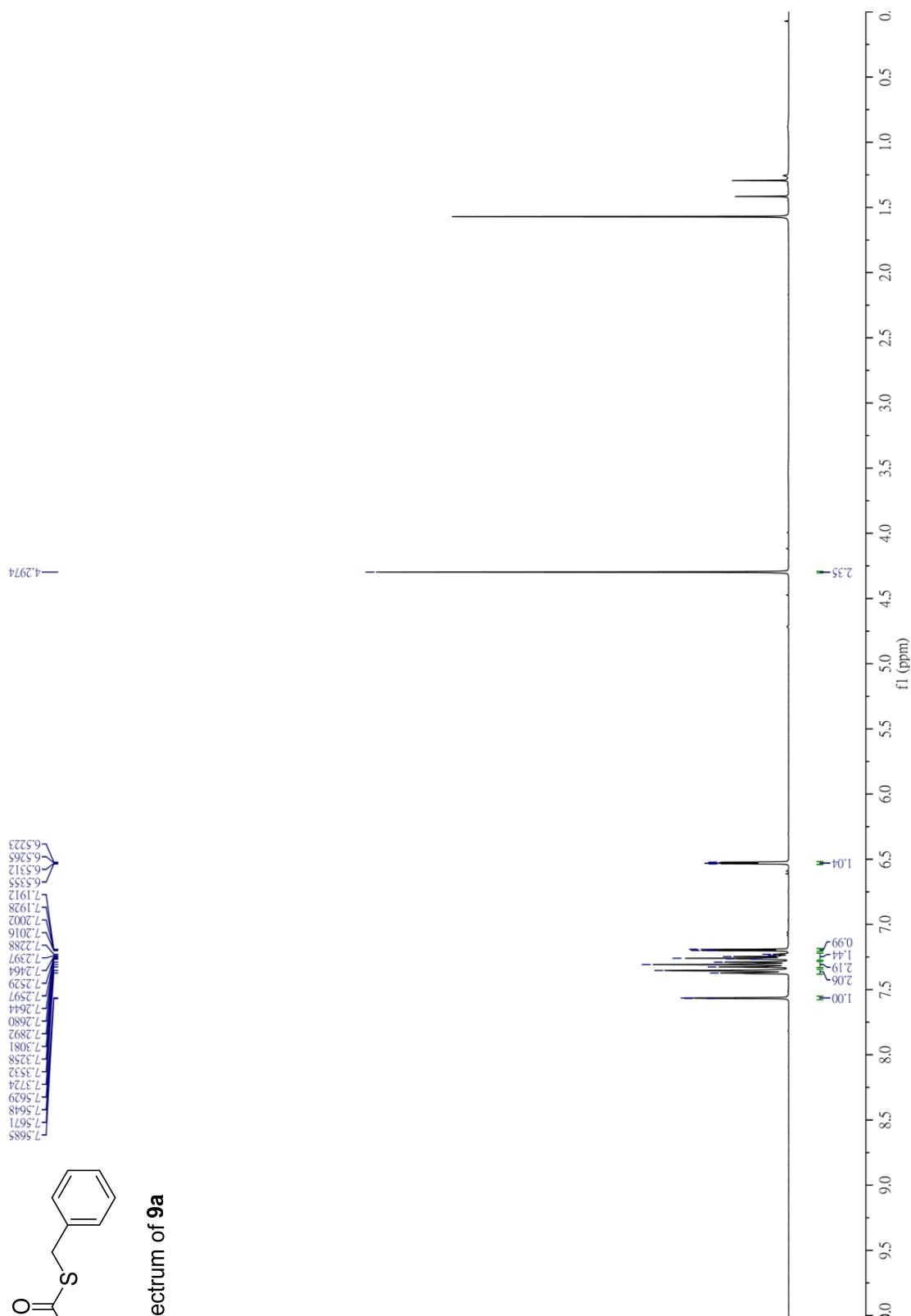
¹H spectrum of 8b

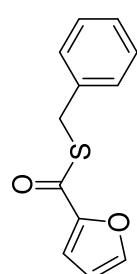
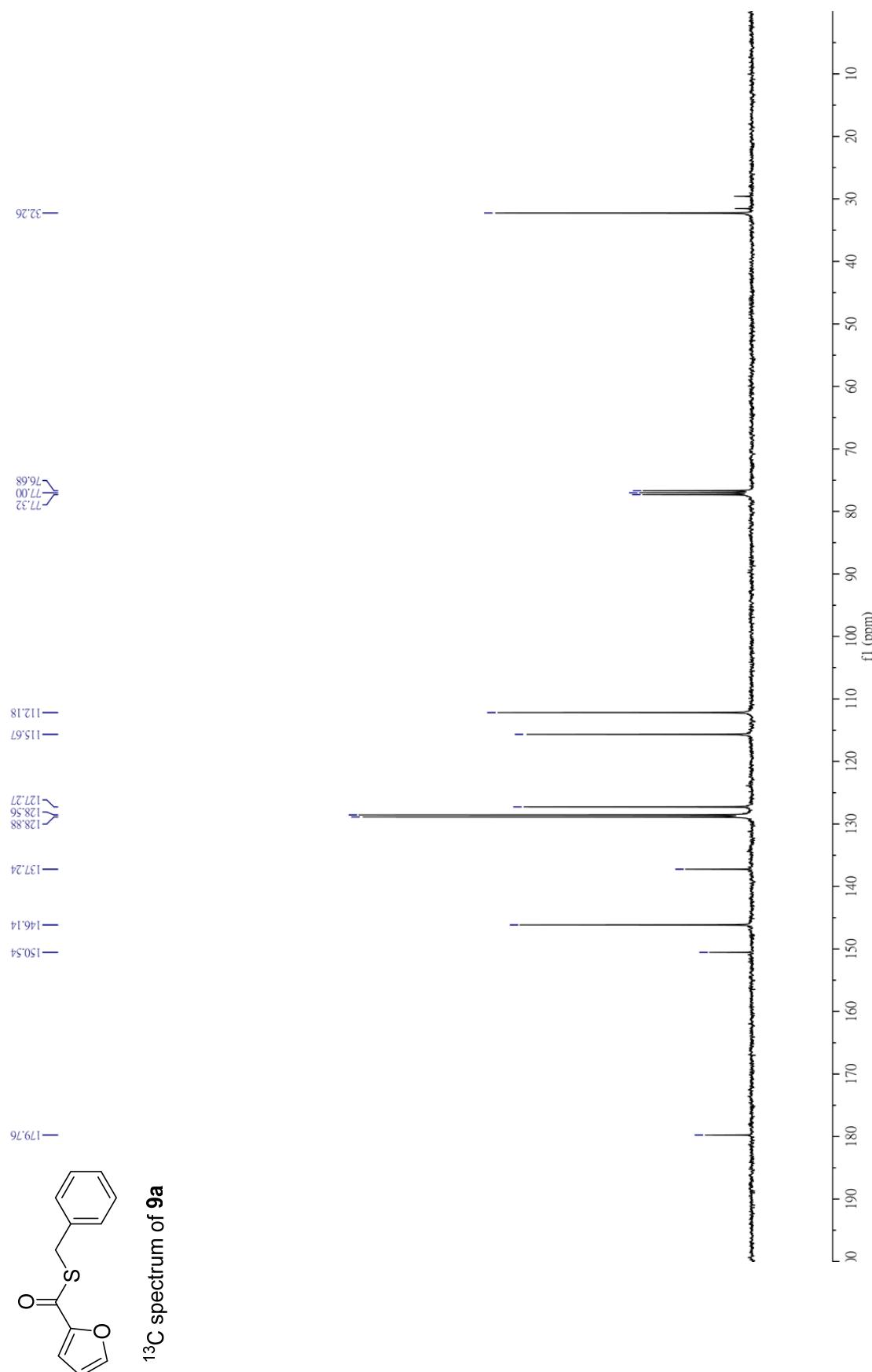




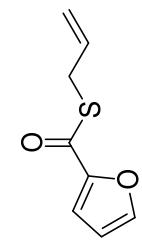


¹H spectrum of 9a

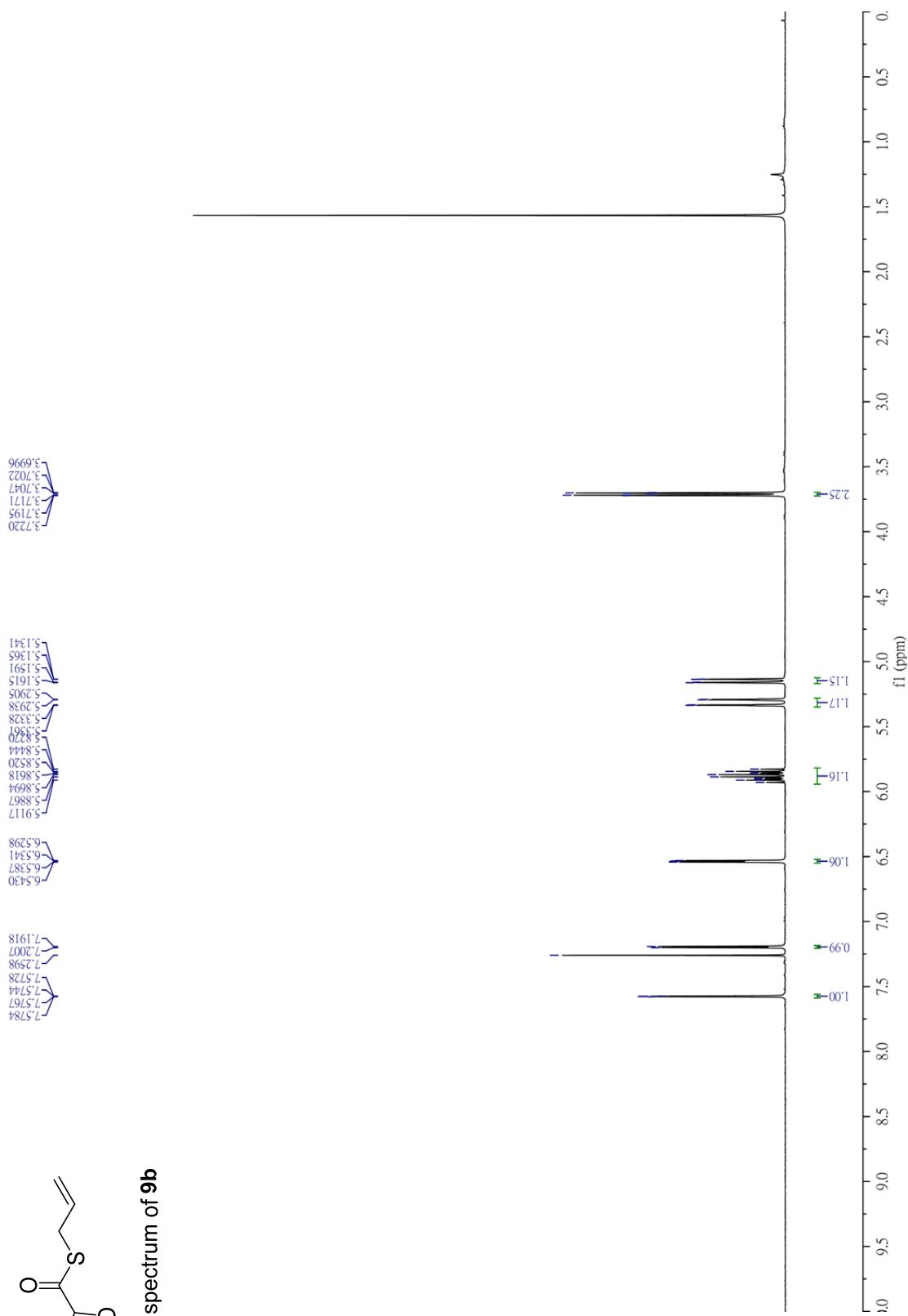


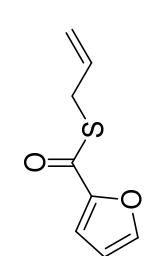


¹³C spectrum of 9a

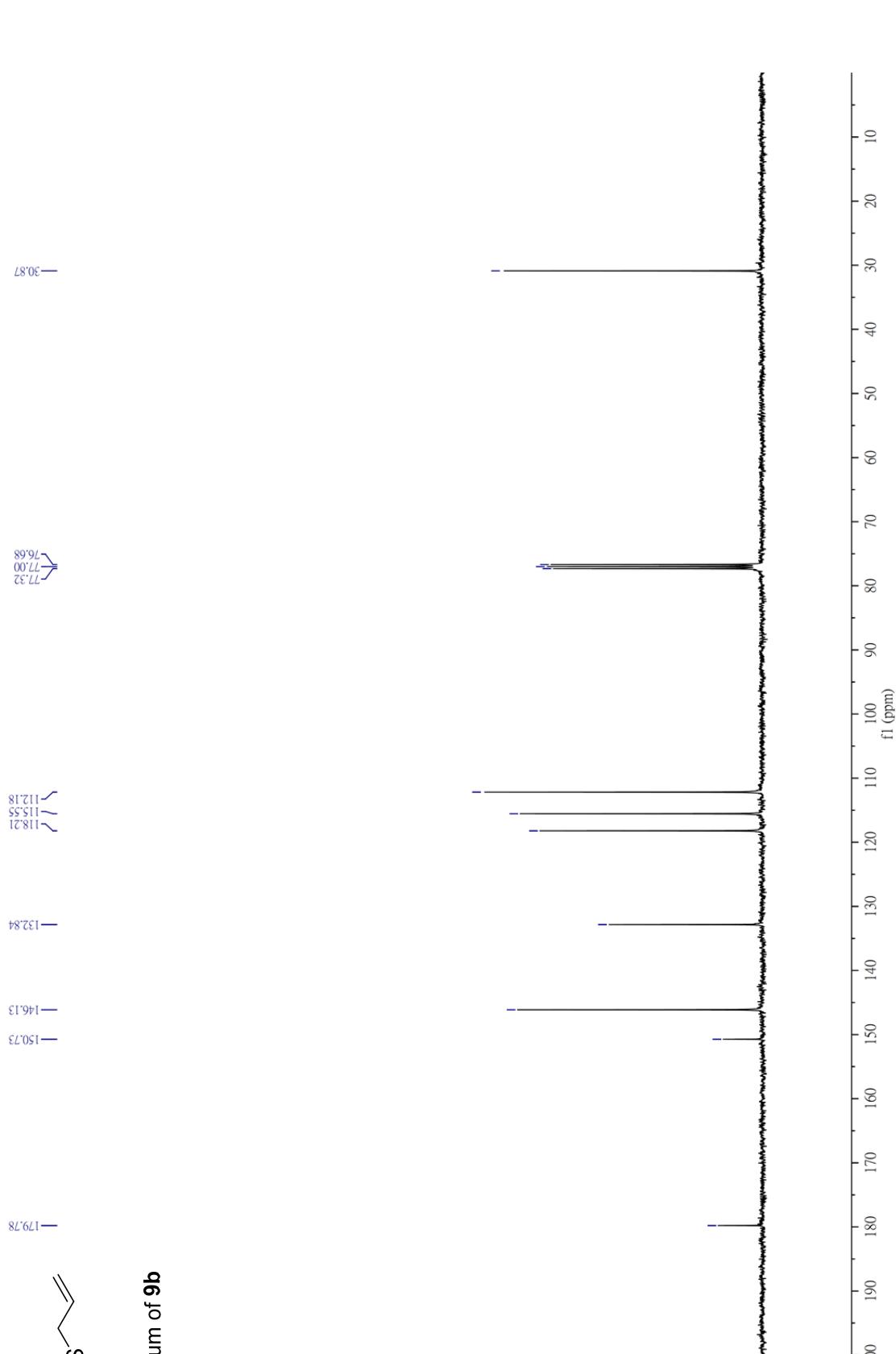


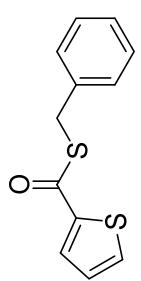
^1H spectrum of **9b**



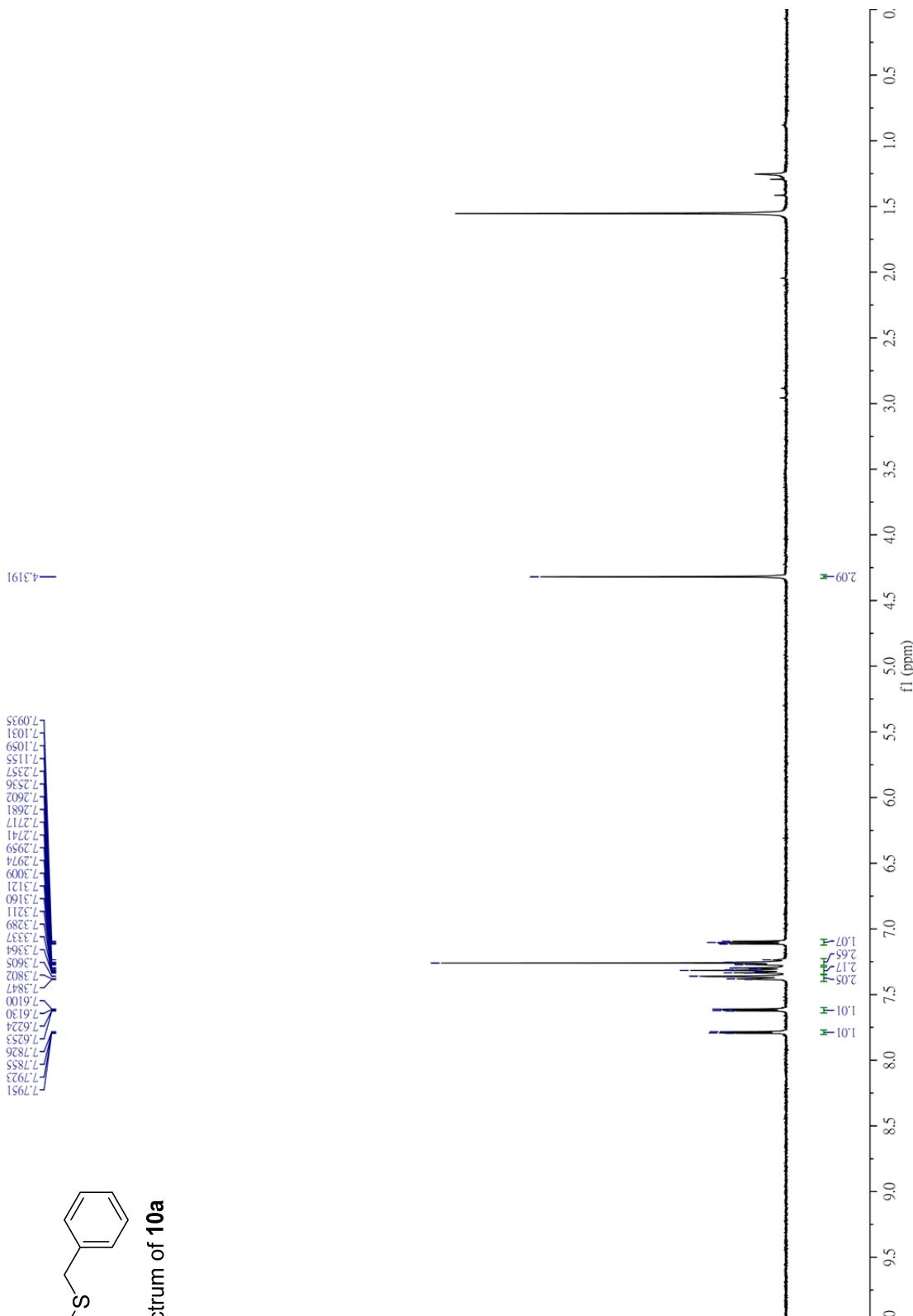


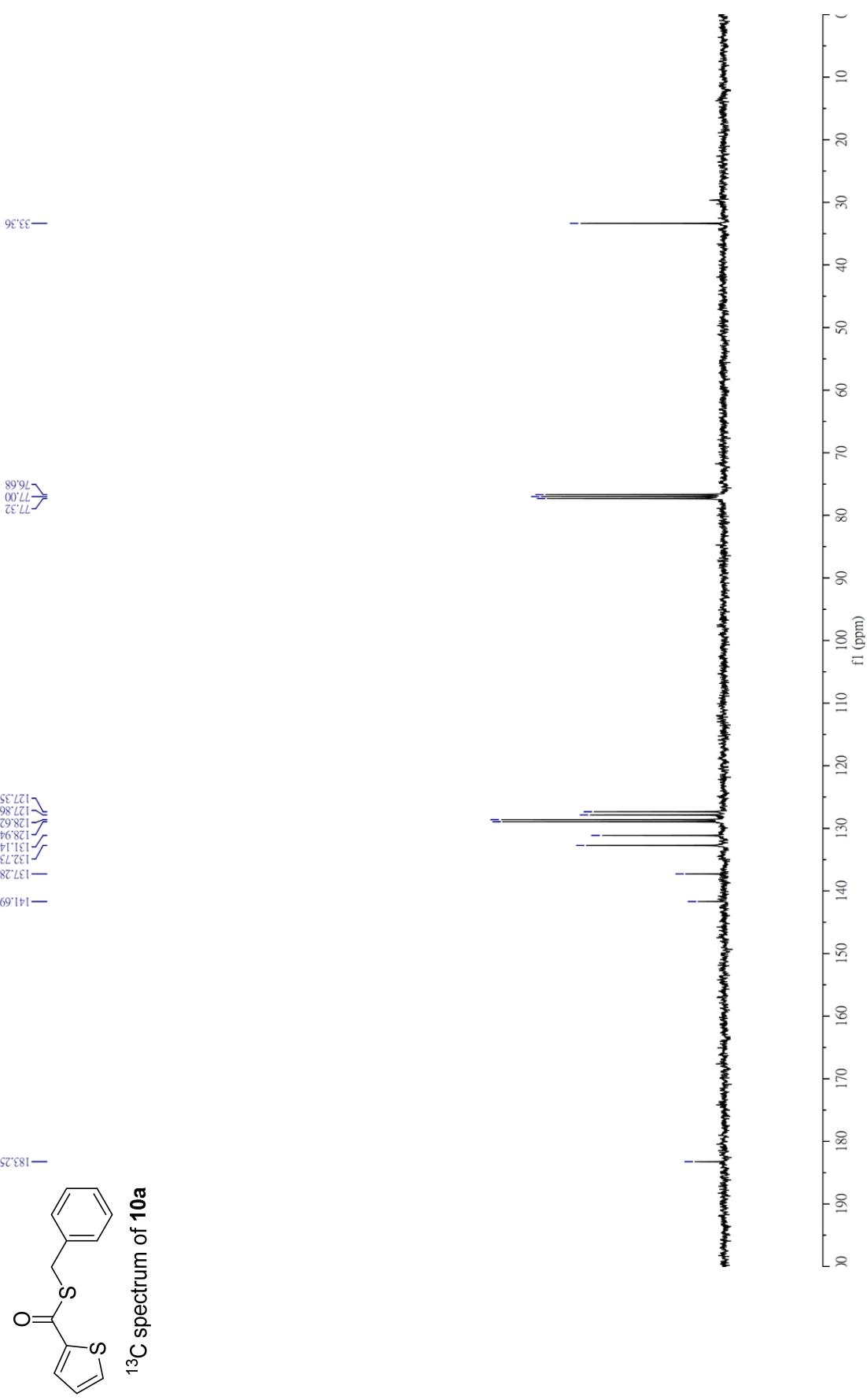
¹³C spectrum of **9b**

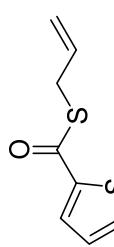




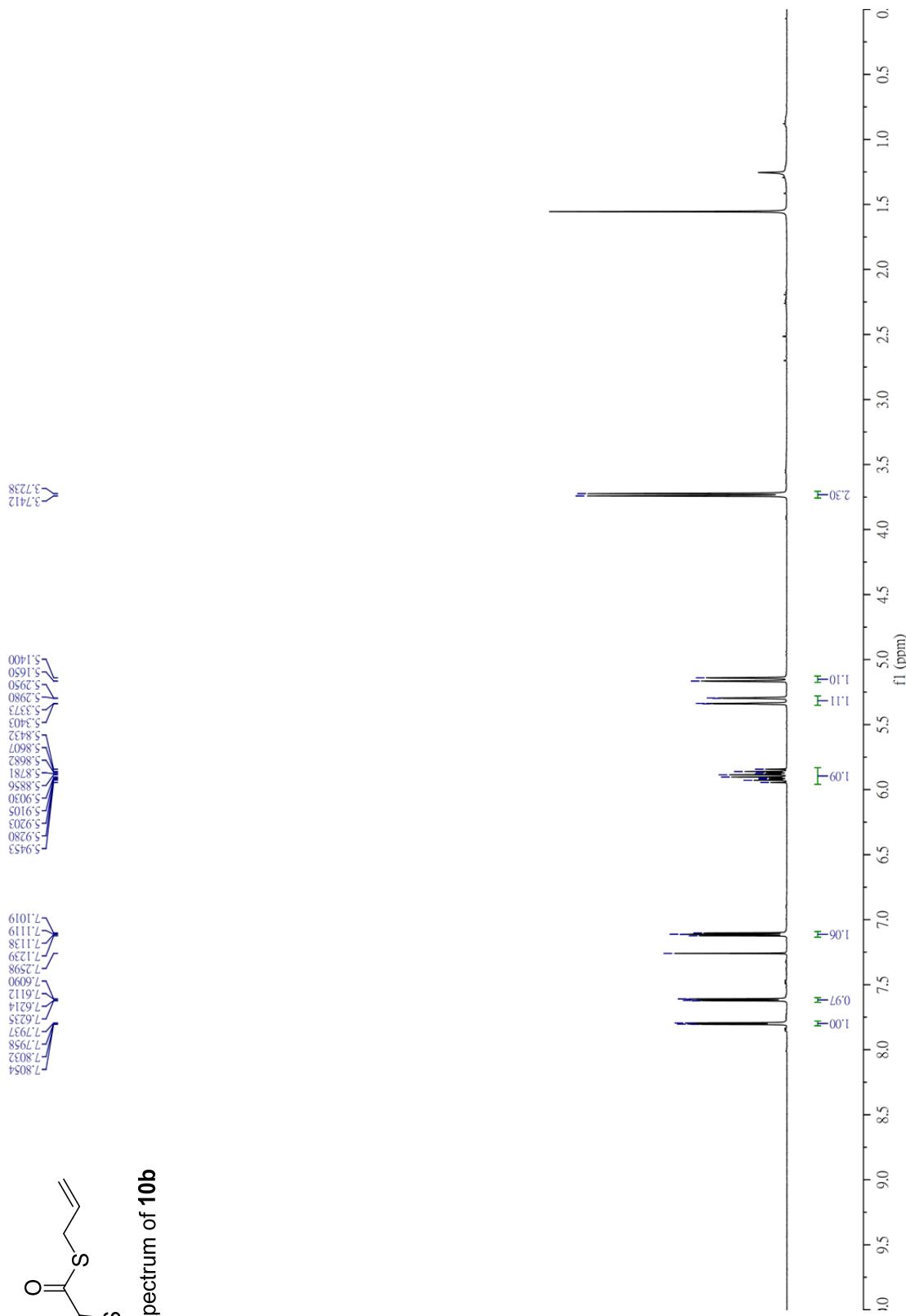
¹H spectrum of 10a

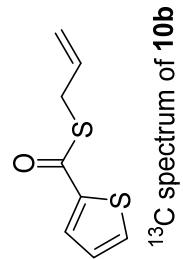






¹H spectrum of 10b





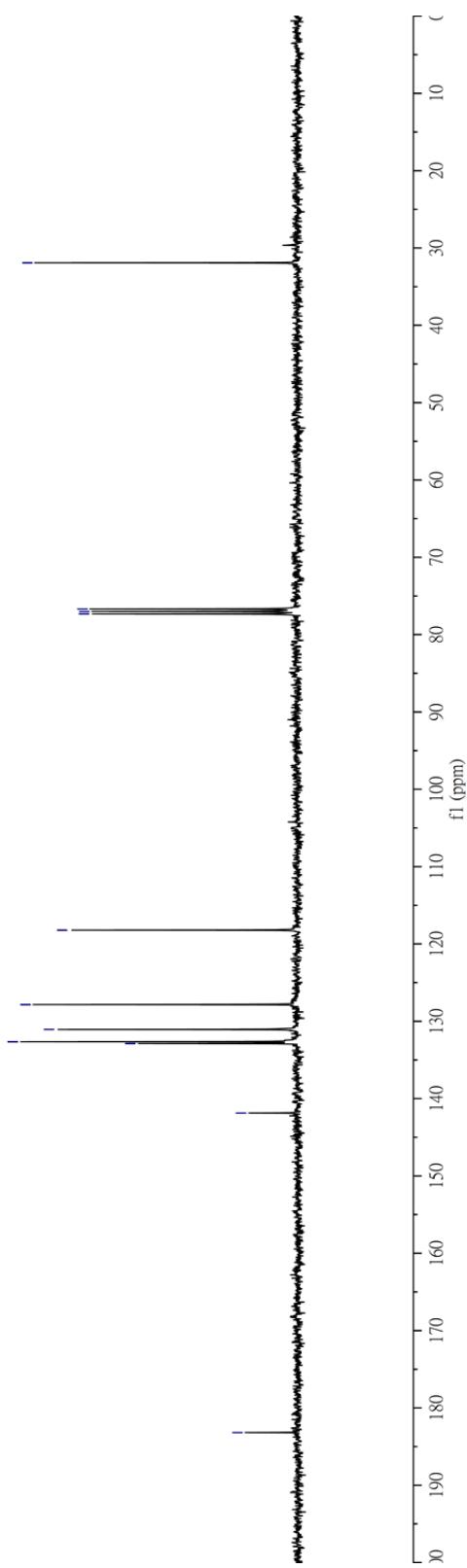
—183.19

—141.86

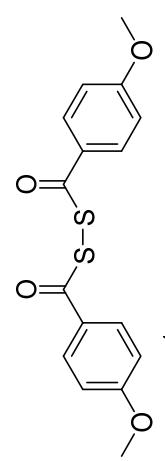
132.88
132.64
131.06
127.83

77.32
77.00
76.68

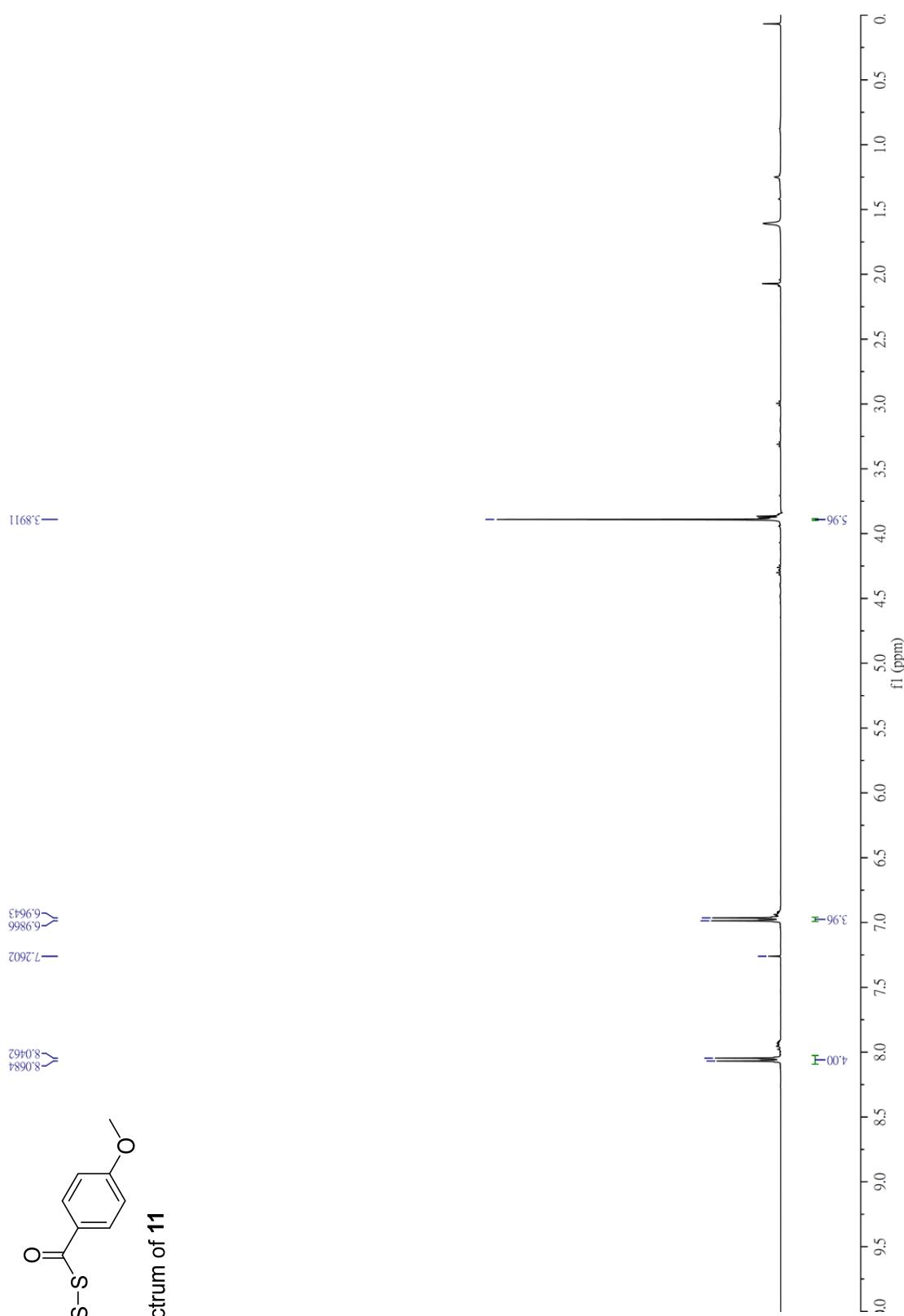
—31.91

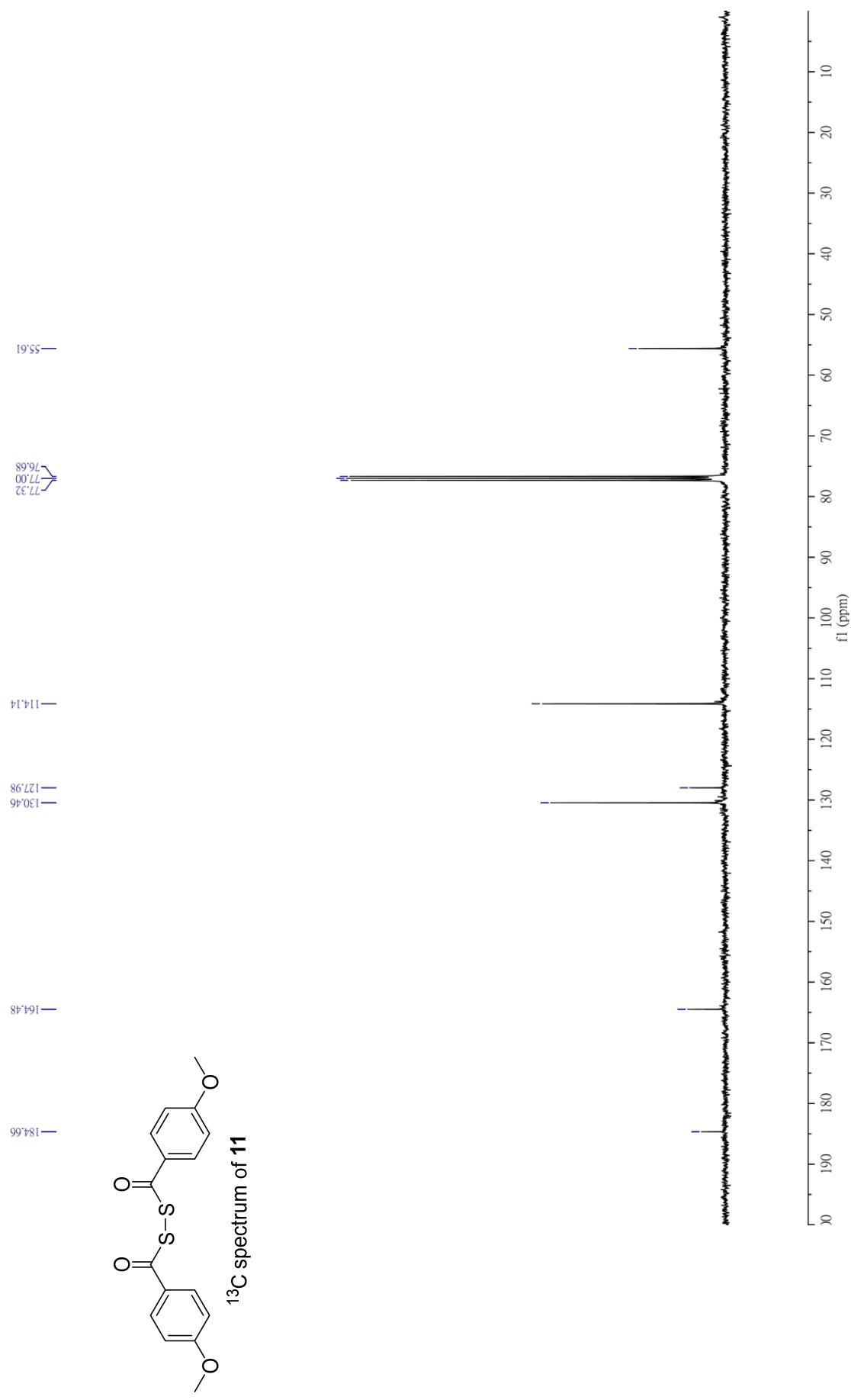


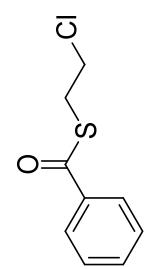
^{13}C spectrum of **10b**



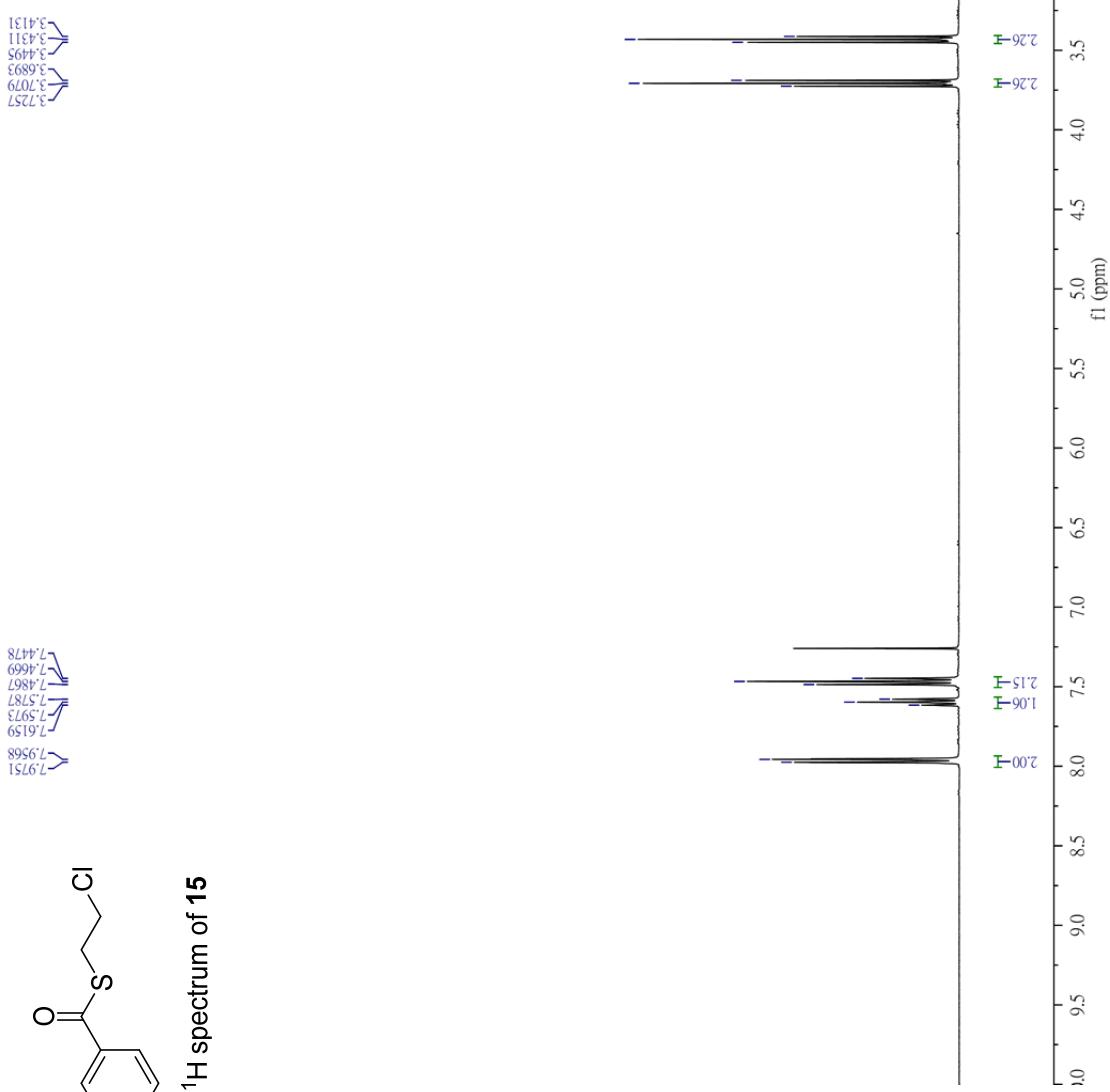
^1H spectrum of 11

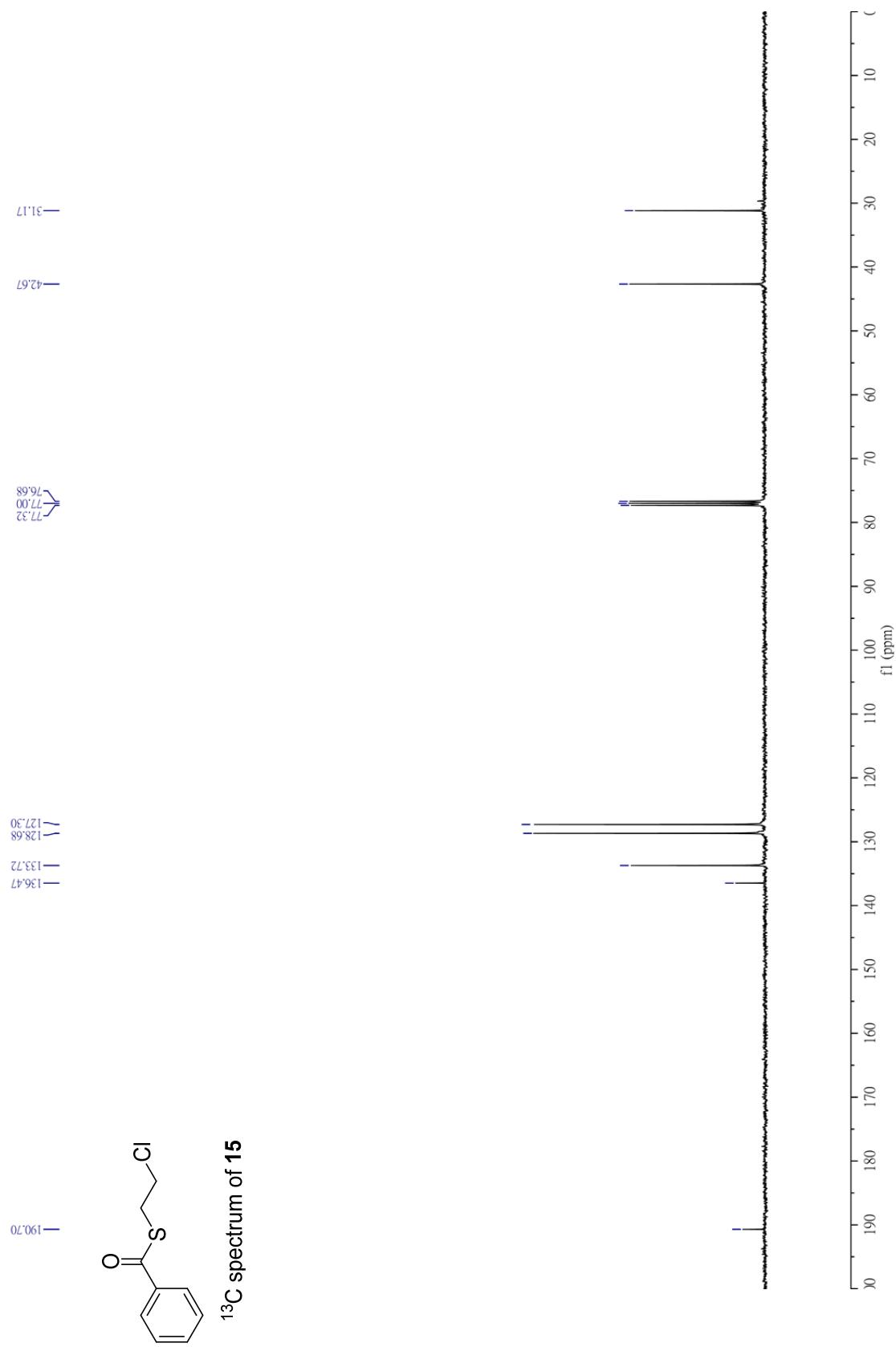


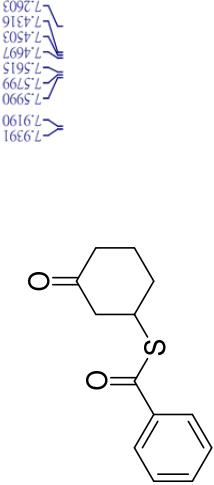




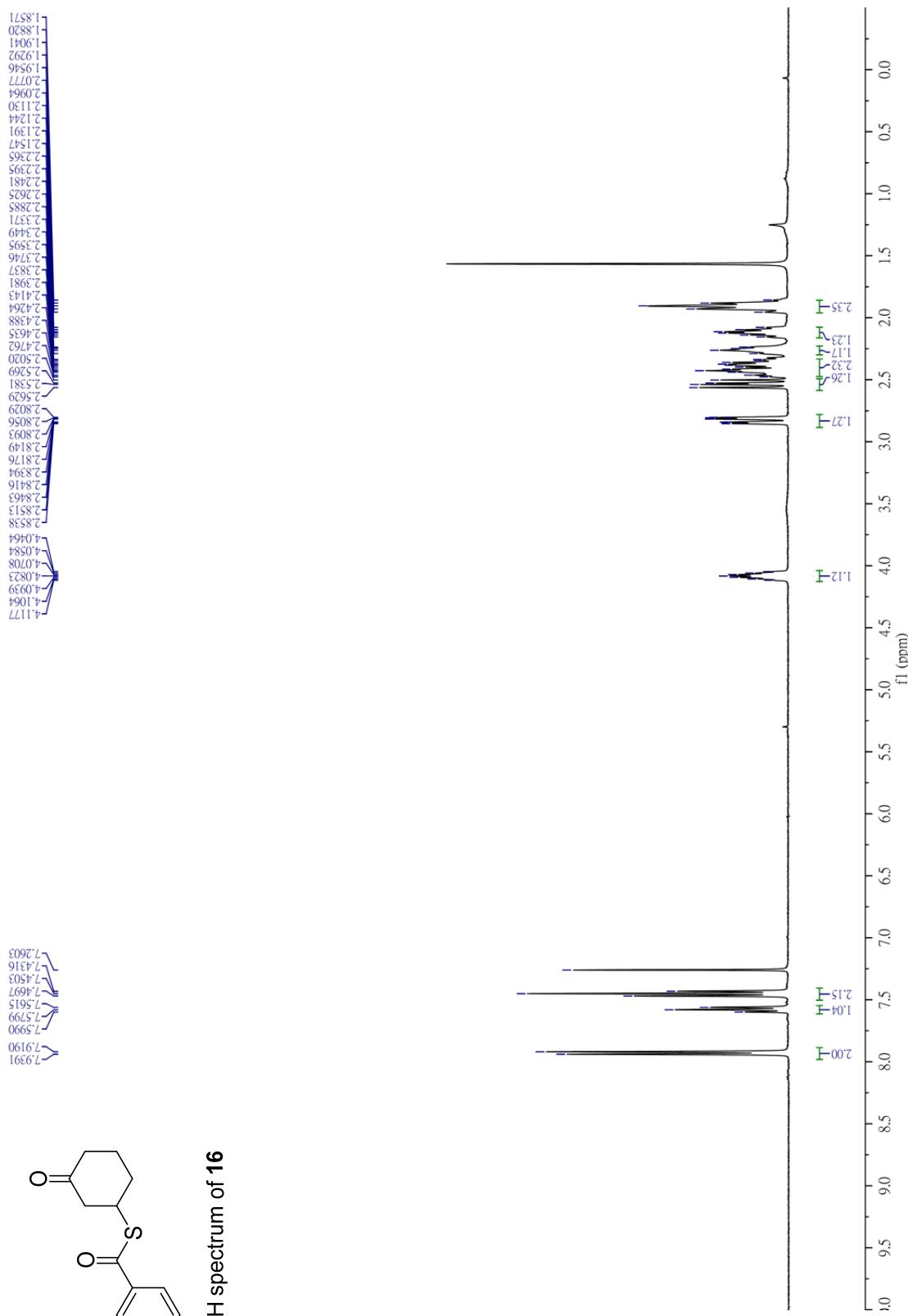
¹H spectrum of **15**

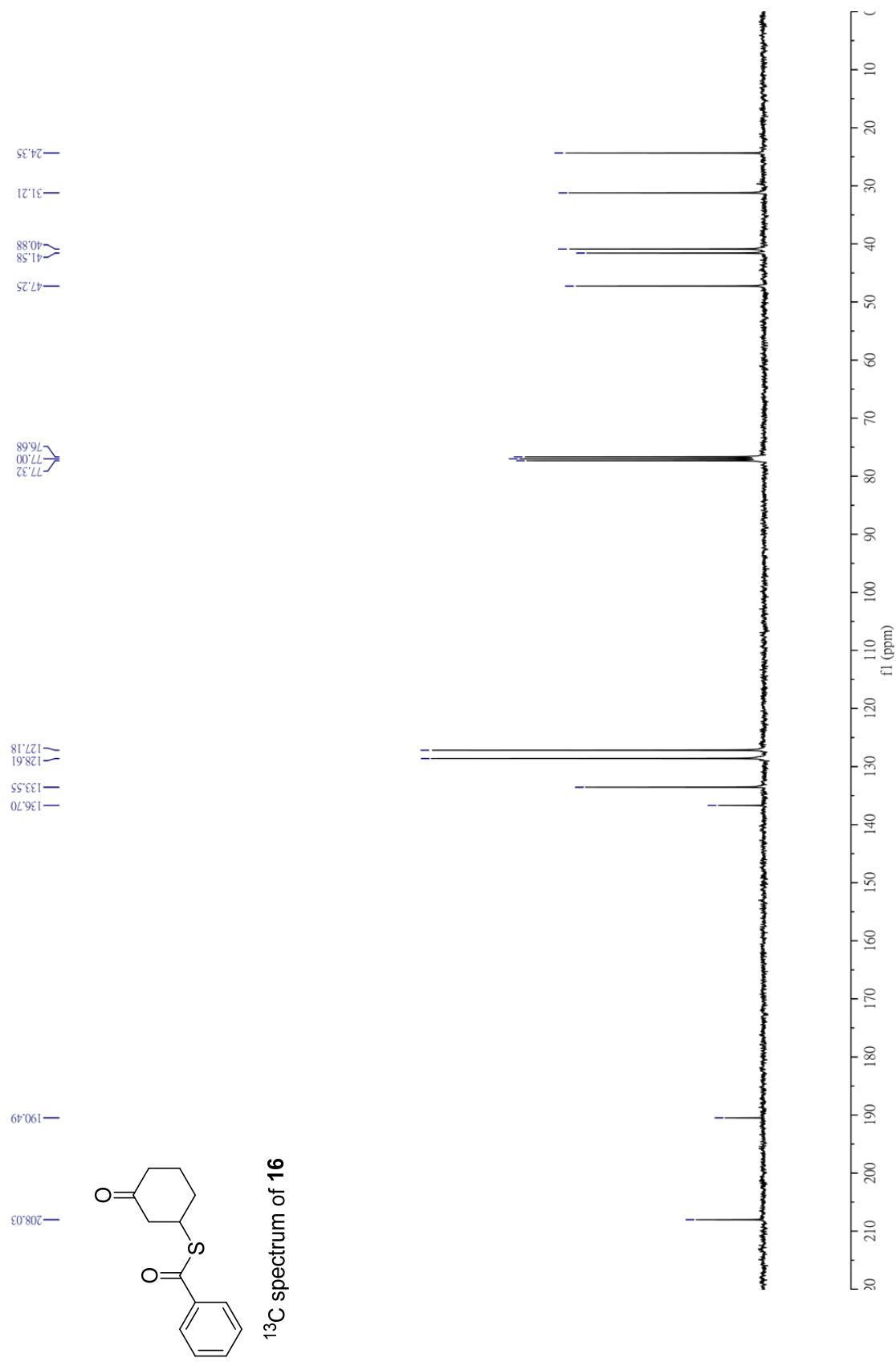


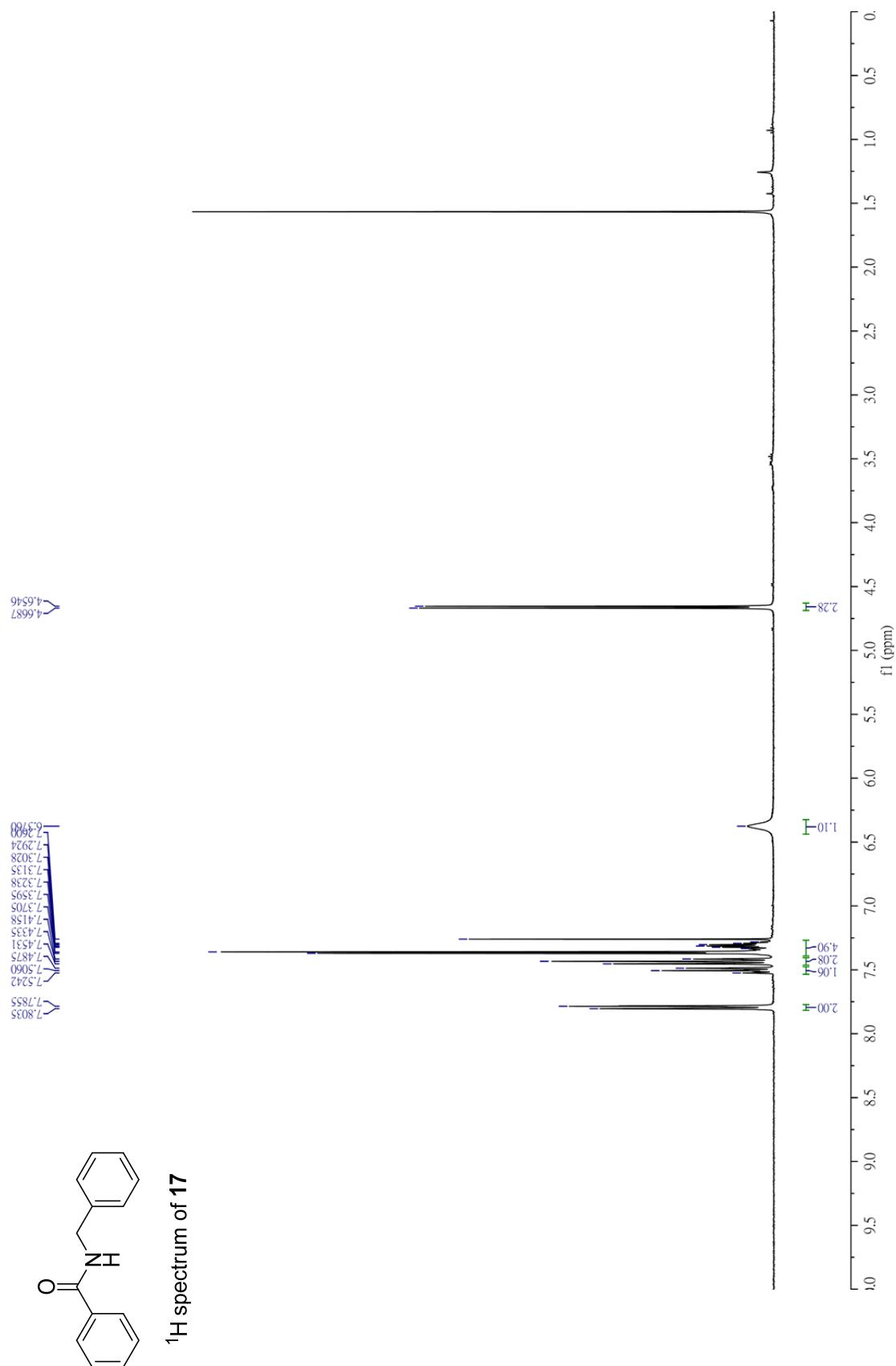




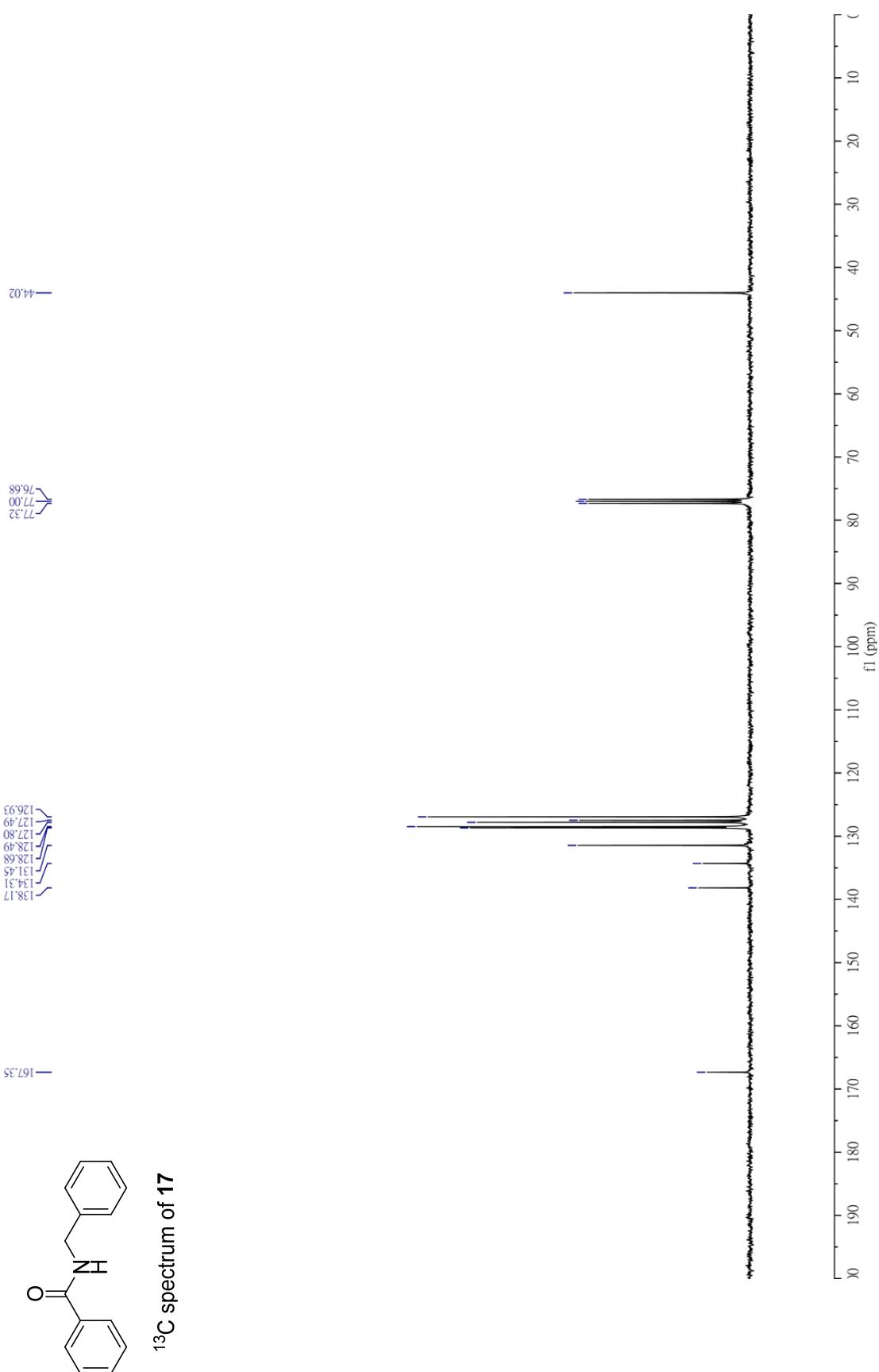
1H spectrum of 16

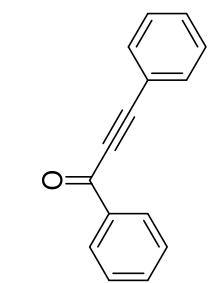




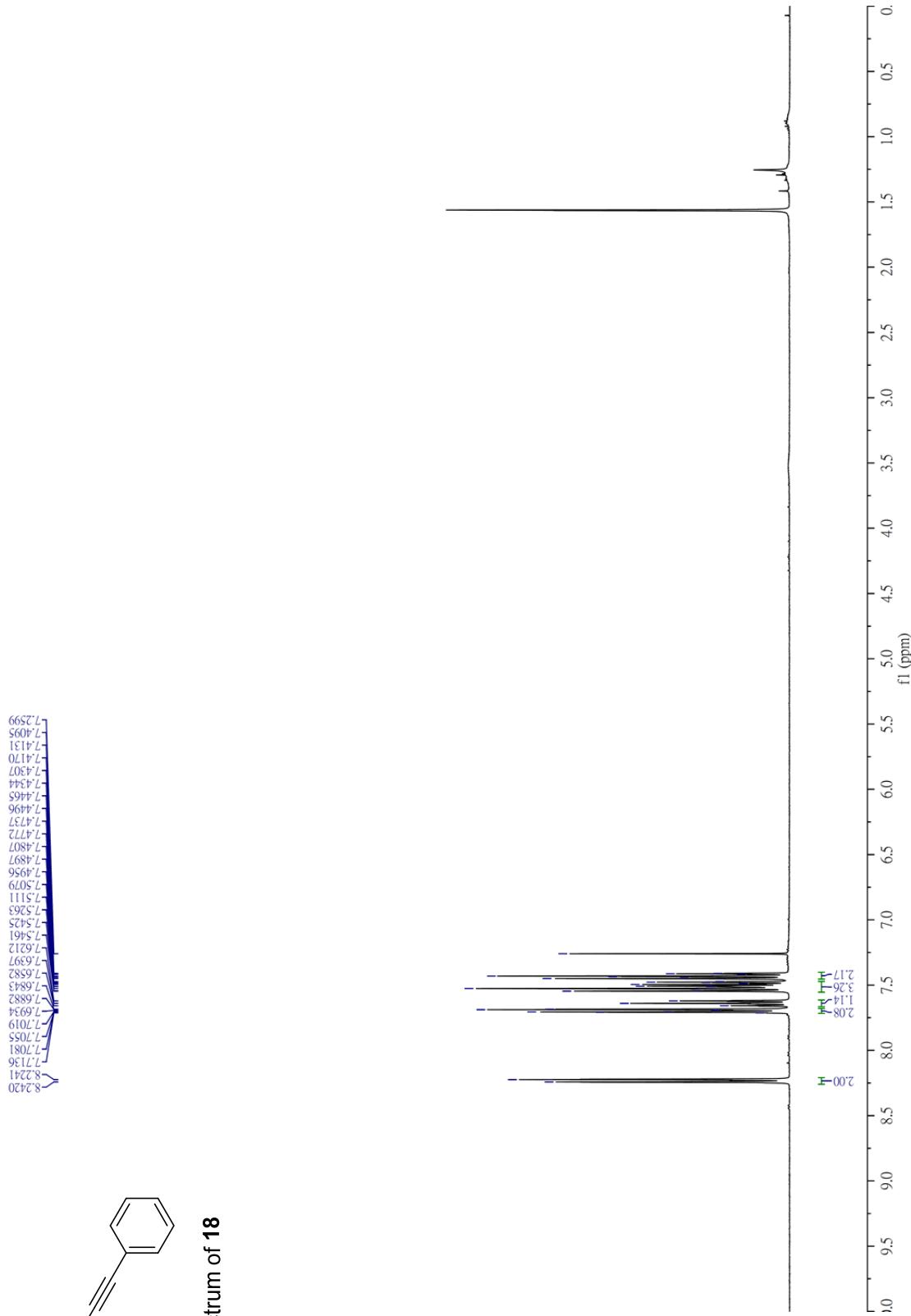


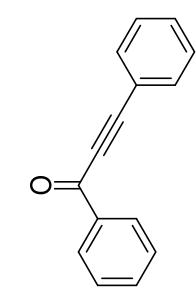
¹H spectrum of 17





^1H spectrum of 18





^{13}C spectrum of **18**

