

Nickel-Catalyzed Denitrogenative Cross-Coupling Reaction of 1,2,3-Benzotriazin-4(3H)-ones with Organoboronic Acids: An Easy Access to *Ortho*-Arylated and Alkenylated Benzamides

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Supporting Information

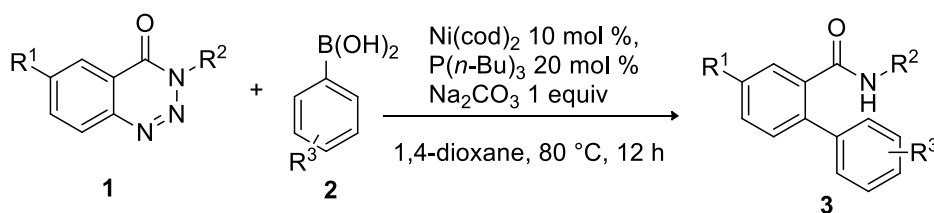
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Experimental Section:

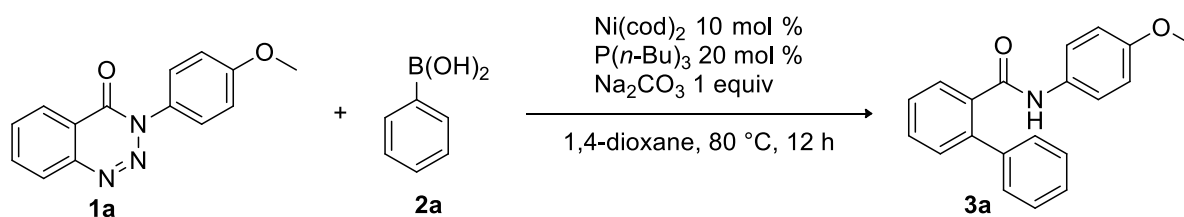
All experiments were carried out in oven-dried glassware, in an atmosphere of nitrogen, unless specified otherwise, by standard Schenk techniques. All the solvents used for extraction, filtration and flash chromatography were used without further purification. All reagents were purchased from Sigma-Aldrich, Alfa Aesar or Avra and were used without further purification. Flash column chromatography was performed on 100-200 mesh silica gel. ^1H -, and ^{13}C NMR spectroscopy was performed on Bruker BBFO (500 MHz) spectrometer. Chemical shifts were determined relative to the residual solvent peaks (CHCl_3 , $\delta = 7.26$ ppm for ^1H NMR, $\delta = 77.0$ ppm for ^{13}C NMR). The mass spectra (ESI-MS) were recorded on an Agilent 6200 Series TOF LC/MS spectrometer. $\text{Ni}(\text{cod})_2$ were purchased from Sigma Aldrich and used. The starting materials, benzotriazin-4(3H)-ones **1a-f**¹, **1j**¹, **1g-h**^{2,3}, **1i**⁴ were prepared according to literature procedure. Organo boronic acids **2** are purchased from spectrochem, sigma aldrich and Alfa Aesar, and used. Tri *n*-Butyl phosphine was purchased from Alfa Aesar and used.

General preparation of *ortho*-arylated benzamides (**3**)



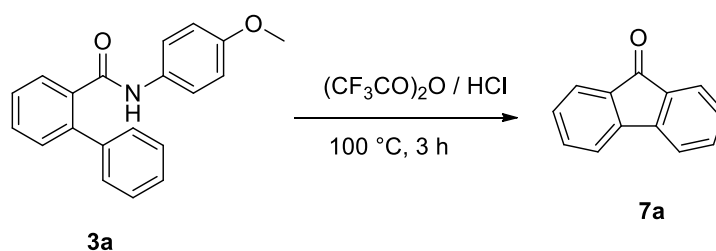
A sealed tube containing 1,2,3-benzotriazin-4(3H)-ones **1** (0.40 mmol), $\text{Ni}(\text{cod})_2$ (0.040 mmol), $\text{P}(\text{n-Bu})_3$ (0.080 mmol), Na_2CO_3 (0.40 mmol) and organo boronic acid **2** (0.60 mmol) was evacuated and purged with nitrogen gas three times. To this mixture, dry 1,4-dioxane (2 mL) was added via syringe under nitrogen atmosphere at room temperature and stirred for 2 min. The seal tube was then placed in a preheated oil bath at 80°C for 12 h. After completion of reaction the mixture was cooled and diluted with Ethyl acetate (10 mL). The mixture was filtered through a Celite and silica gel pad and was washed with Ethyl acetate (3×10 mL). The filtrate was concentrated and the residue was purified by silica gel column chromatography using suitable eluent to afford the desired pure product **3**.

Procedure for the preparation of *ortho*-arylated benzamides **3a** (1.00 mmol scale)



A sealed tube containing 1,2,3-benzotriazin-4(3*H*)-ones **1a** (253 mg, 1.0 mmol), Ni(cod)_2 (27.6 mg, 0.1 mmol), $\text{P}(n\text{-Bu})_3$ (40 mg, 0.2 mmol), Na_2CO_3 (106 mg, 1 mmol) and organo boronic acid **2a** (183 mg, 1.5 mmol) was evacuated and purged with nitrogen gas three times. To this mixture, dry 1,4-dioxane (3 mL) was added via syringe under nitrogen atmosphere at room temperature and stirred for 2 min. The seal tube was then placed in a preheated oil bath at 80 °C for 12 h. After completion of reaction, the mixture was cooled and diluted with Ethyl acetate (10 mL). The mixture was filtered through a Celite and silica gel pad and was washed with Ethyl acetate (3×10 mL). The filtrate was concentrated and the residue was purified by silica gel column chromatography using hexane/ethyl acetate (85/15) as eluent to afford the desired pure product **3a** (267 mg, 88 % yield).

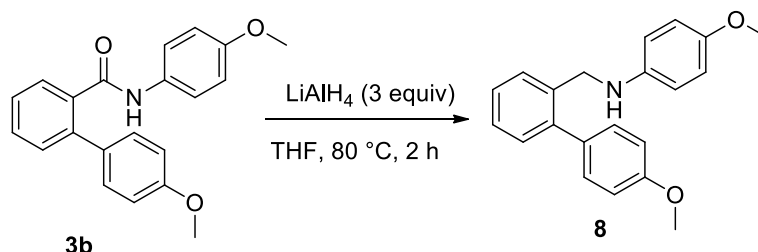
General procedure for the preparation of fluorenones (**7**)



Fluorenones (**7**) has been prepared according to the literature procedure⁴. *Ortho*-arylated benzamides **3a** (121 mg, 0.40 mmol scale reaction) and $(\text{CF}_3\text{CO})_2\text{O}$ (3 mL) were taken in a sealed pressure tube. The reaction mixture was allowed to stir at 100 °C for 2 h. Then, the reaction mixture was refluxed in the presence of conc. HCl (1.5 mL) at 100 °C for additional 1 h. After completion of the reaction, the reaction mixture was allowed to cool to room temperature and was extracted with ethyl acetate, washed with water and brine, and dried with anhydrous Na_2SO_4 . The filtrate was concentrated and the residue was purified through a silica gel column chromatography using hexanes and ethyl acetate as eluent to give pure **7a** (64 mg,

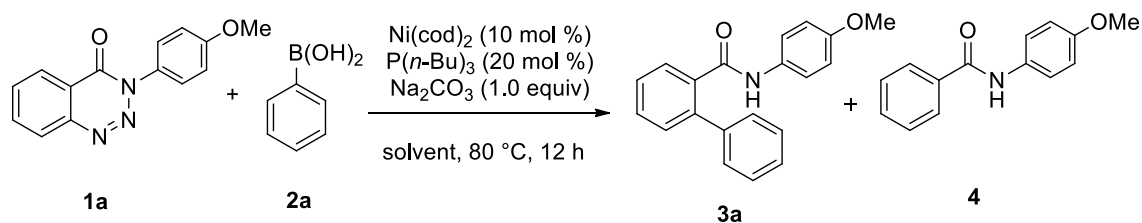
90 % yield). **7b-c** were prepared by following the same procedure mentioned above with **3c** and **3b** as starting material accordingly.

Procedure for the preparation of 4-Methoxy-N-((4'-methoxy-[1,1'-biphenyl]-2-yl)methyl)aniline (8**)**



4-Methoxy-N-((4'-methoxy-[1,1'-biphenyl]-2-yl)methyl)aniline **8** was prepared according to the literature procedure⁶. In a sealed pressure tube LiAlH₄ (39 mg, 1.2 mmol) was suspended in dry THF (3mL). To this **3b** (133 mg, 0.4 mmol) in THF solution was added drop wisely for 15 minutes at room temperature under nitrogen atmosphere. Then, the reaction mixture was stirred at 80 °C for 3 h and it was cooled to 0-5 °C and quenched with 15% NaOH solution (10 mL) and filtered through celite bed. The celite bed washed with ethylacetate (5mL) 3 times. The filtrate was extracted with ethyl acetate (10 mL) 2 times. The ethyl acetate layers were combined and dried with anhydrous sodium sulphate and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography with hexane and ethyl acetate as eluent to afford pure product **8** (108 mg, 85 % yield)

Table-1: Effect of Solvents^a



Entry	Solvent	Yield (%) ^b	
		3a	4a
1	1,4-Dioxane	95 (92) ^c	5
2	THF	91	7
3	Toluene	47	35
4	ACN	54	8
5	DCE	43	7

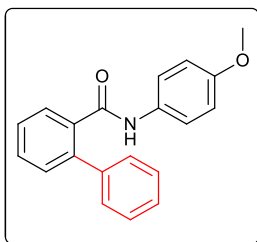
^aAll the reactions were carried out using **1a** (0.40 mmol), **2a** (0.60 mmol), Ni(cod)₂ (0.04 mmol), P(*n*-Bu)₃ (0.08 mmol), sodium carbonate (0.40 mmol) and solvent 1.5 mL (dry) at 80 °C and 12 h under N₂. ^bGC yields. ^cIsolated yield.

References

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5. Ravi Kiran, C; Jeganmohan, M.; *Org. Lett.* **2012**, *14*, 5246–5249.
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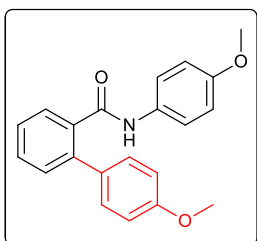
Spectral data of ^1H , ^{13}C NMR

N-(4-Methoxyphenyl)-[1,1'-biphenyl]-2-carboxamide (3a)



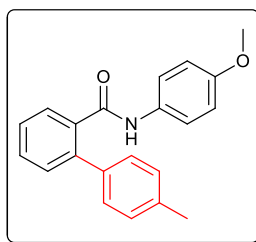
White fine solid (111 mg, 92% yield); mp: 152-153 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.87 (d, J = 7.6 Hz, 1H), 7.53 (td, J = 7.5, 1.1 Hz, 1H), 7.51 – 7.36 (m, 7H), 7.04 – 6.95 (m, 2H), 6.77 (dd, J = 9.9, 6.3 Hz, 3H), 3.75 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.0, 156.4, 140.0, 139.4, 135.3, 130.5, 130.2, 129.5, 128.9, 128.8, 128.0, 127.8, 121.8, 113.9, 55.4; HRMS calculated for $\text{C}_{20}\text{H}_{18}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 304.1332, found 304.1330; Purification: Flash chromatography; Eluent: hexane/EtOAc = 85/15.

4'-Methoxy-*N*-(4-methoxyphenyl)-[1,1'-biphenyl]-2-carboxamide (3b)



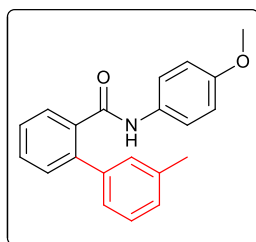
White fine solid (126 mg, 95% yield); mp: 133-134 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.80 (d, J = 7.5 Hz, 1H), 7.49 (t, J = 7.3 Hz, 1H), 7.40 (dd, J = 15.1, 7.9 Hz, 4H), 7.07 (d, J = 8.8 Hz, 2H), 6.95 (d, J = 8.5 Hz, 3H), 6.77 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.3, 159.4, 156.4, 139.0, 135.2, 132.1, 130.6, 130.4, 130.2, 129.9, 129.3, 127.3, 121.8, 114.2, 113.9, 55.3, 55.3; HRMS calculated for $\text{C}_{21}\text{H}_{20}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 334.1438, found 334.1441; Purification: Flash chromatography; Eluent: hexane/EtOAc = 8/2.

***N*-(4-Methoxyphenyl)-4'-methyl-[1,1'-biphenyl]-2-carboxamide (3c)**



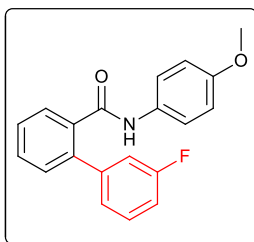
White fine solid (113 mg, 89% yield); mp:147-148 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.81 – 7.74 (m, 1H), 7.44 (ddd, J = 7.5, 4.5, 1.4 Hz, 1H), 7.37 (ddd, J = 7.5, 4.4, 1.3 Hz, 1H), 7.35 – 7.31 (m, 1H), 7.29 (d, J = 8.0 Hz, 2H), 7.18 (dd, J = 8.1, 5.5 Hz, 2H), 7.00 – 6.92 (m, 2H), 6.77 (s, 1H), 6.73 – 6.66 (m, 2H), 3.68 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.1, 156.4, 139.4, 137.8, 137.0, 135.2, 130.7, 130.5, 130.2, 129.5, 129.4, 128.7, 127.6, 121.7, 113.9, 55.4, 21.1; HRMS calculated for $\text{C}_{21}\text{H}_{20}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 318.1489, found 318.1482; Purification: Flash chromatography; Eluent: hexane/EtOAc = 8/2.

***N*-(4-Methoxyphenyl)-3'-methyl-[1,1'-biphenyl]-2-carboxamide (3d)**



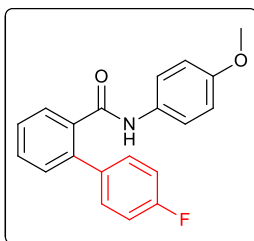
White solid (107 mg, 85% yield); mp:118-119 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.83 (dd, J = 7.7, 1.2 Hz, 1H), 7.50 (td, J = 7.5, 1.3 Hz, 1H), 7.43 (td, J = 7.5, 1.2 Hz, 1H), 7.39 (dd, J = 7.5, 1.0 Hz, 1H), 7.31 (t, J = 7.5 Hz, 1H), 7.28 – 7.22 (m, 2H), 7.20 (d, J = 7.5 Hz, 1H), 7.03 – 6.96 (m, 2H), 6.92 (s, 1H), 6.77 – 6.72 (m, 2H), 3.73 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.1, 156.4, 139.9, 139.5, 138.5, 135.1, 130.5, 130.4, 130.1, 129.4, 129.4, 128.7, 128.6, 127.6, 125.8, 121.8, 113.8, 55.3, 21.3; HRMS calculated for $\text{C}_{21}\text{H}_{20}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 318.1489, found 318.1488; Purification: Flash chromatography; Eluent: hexane/EtOAc = 8/2.

3'-Fluoro-*N*-(4-methoxyphenyl)-[1,1'-biphenyl]-2-carboxamide (3e)



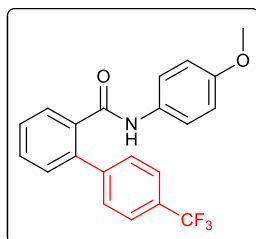
White solid (91 mg, 71% yield); mp: 162-163 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.81 (d, J = 7.6 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.41 (d, J = 7.4 Hz, 1H), 7.40 – 7.34 (m, 1H), 7.25 (d, J = 6.3 Hz, 1H), 7.21 (d, J = 9.5 Hz, 1H), 7.08 (dd, J = 12.2, 5.7 Hz, 3H), 6.84 (s, 1H), 6.79 (d, J = 8.9 Hz, 2H), 3.76 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.03, 162.84 (d, $J_{\text{C-F}}$ = 247.5 Hz), 156.66, 142.16 (d, $J_{\text{C-F}}$ = 7.7 Hz), 138.18, 135.66, 130.60, 130.41 (d, $J_{\text{C-F}}$ = 2.6 Hz), 130.36, 130.14, 129.19, 128.28, 124.62 (d, J = 2.8 Hz), 121.93, 115.68 (d, J = 21.9 Hz), 114.87 (d, $J_{\text{C-F}}$ = 20.9 Hz), 114.07, 55.43; HRMS calculated for $\text{C}_{20}\text{H}_{17}\text{NO}_2\text{F}$ $[\text{M}+\text{H}]^+$: 322.1238, found 322.1239; Purification: Flash chromatography; Eluent: toluene/diethyl ether = 85/15.

4'-Fluoro-*N*-(4-methoxyphenyl)-[1,1'-biphenyl]-2-carboxamide (3f)



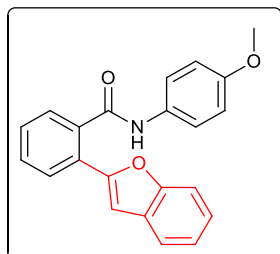
White fine solid (102 mg, 80% yield); mp: 167-168 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.79 (d, J = 7.6 Hz, 1H), 7.52 (td, J = 7.5, 1.4 Hz, 1H), 7.49 – 7.42 (m, 3H), 7.39 (dd, J = 7.6, 1.0 Hz, 1H), 7.15 – 7.06 (m, 4H), 6.88 (s, 1H), 6.83 – 6.75 (m, 2H), 3.76 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.1, 162.5 (d, $J_{\text{C-F}}$ = 247.9 Hz), 156.6, 138.3, 135.9, 135.6, 130.5 (d, $J_{\text{C-F}}$ = 10.0 Hz), 130.3 (d, $J_{\text{C-F}}$ = 15.8 Hz), 129.1, 127.9, 121.7, 115.9, 115.7, 114.0, 55.4; HRMS calculated for $\text{C}_{20}\text{H}_{17}\text{NO}_2\text{F}$ $[\text{M}+\text{H}]^+$: 322.1238, found 322.1236. Purification: Flash chromatography; Eluent: hexane/EtOAc = 75/25.

***N*-(4-Methoxyphenyl)-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxamide (3g)**



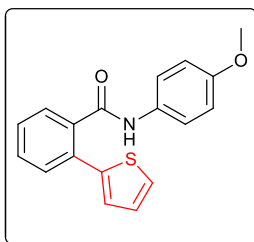
White solid (108 mg, 73% yield); mp:185-186 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.77 (d, J = 7.6 Hz, 1H), 7.67 (d, J = 8.2 Hz, 2H), 7.59 (d, J = 8.5 Hz, 2H), 7.55 (dd, J = 7.5, 1.4 Hz, 1H), 7.49 (dd, J = 10.8, 4.2 Hz, 1H), 7.43 (dd, J = 7.6, 1.1 Hz, 1H), 7.10 – 7.04 (m, 2H), 6.92 (s, 1H), 6.82 – 6.75 (m, 2H), 3.76 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 166.9, 156.7, 143.6, 138.1, 135.9, 130.6, 130.3, 130.2, 129.9 (d, $J_{\text{C-F}}$ = 32.8 Hz), 129.0, 128.9, 128.4, 125.6 (d, $J_{\text{C-F}}$ = 3.7 Hz), 124.0 (d, $J_{\text{C-F}}$ = 272.2 Hz), 121.8, 114.0, 55.4; HRMS calculated for $\text{C}_{21}\text{H}_{17}\text{NO}_2\text{F}_3$ $[\text{M}+\text{H}]^+$: 372.1206, found 372.1204. Purification: Flash chromatography; Eluent: hexane/EtOAc = 8/2.

2-(Benzofuran-2-yl)-*N*-(4-methoxyphenyl)benzamide (3h)



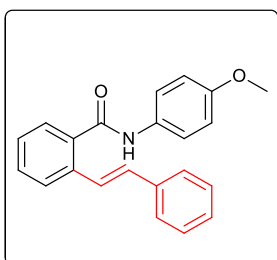
Light brown solid (86 mg, 63% yield); mp: 173-174 °C; ^1H NMR (500 MHz, DMSO) δ 10.37 (d, J = 6.4 Hz, 1H), 7.97 (d, J = 7.8 Hz, 1H), 7.69 – 7.52 (m, 6H), 7.49 (d, J = 8.2 Hz, 1H), 7.36 – 7.28 (m, 1H), 7.24 (dd, J = 10.9, 4.0 Hz, 1H), 7.17 (d, J = 3.1 Hz, 1H), 7.00 – 6.88 (m, 2H), 3.75 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 167.7, 156.0, 154.6, 154.1, 136.6, 132.7, 130.0, 129.2, 129.0, 128.4, 127.8, 127.3, 125.2, 123.6, 121.8, 121.8, 114.3, 111.4, 104.7, 55.6; HRMS calculated for $\text{C}_{22}\text{H}_{18}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 344.1281, found 344.1278. Purification: Flash chromatography; Eluent: hexane/EtOAc = 7/3.

***N*-(4-Methoxyphenyl)-2-(thiophen-2-yl)benzamide (3i)**



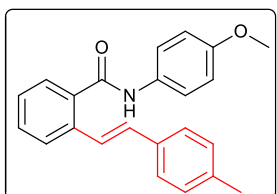
White fine solid (111 mg, 90% yield); mp: 124-125 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.79 – 7.73 (m, 1H), 7.55 – 7.42 (m, 3H), 7.38 (dd, J = 5.1, 1.1 Hz, 1H), 7.25 – 7.17 (m, 3H), 7.13 (s, 1H), 7.11 – 7.05 (m, 1H), 6.86 – 6.77 (m, 2H), 3.77 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.0, 156.5, 140.9, 135.9, 131.7, 130.7, 130.6, 130.2, 129.0, 128.2, 127.9, 127.1, 126.7, 121.9, 114.0, 55.4; HRMS calculated for $\text{C}_{18}\text{H}_{16}\text{NO}_2\text{S}$ $[\text{M}+\text{H}]^+$: 310.0896, found 310.0886. Purification: Flash chromatography; Eluent: hexane/EtOAc = 85/15.

***(E)*-N-(4-Methoxyphenyl)-2-styrylbenzamide (3j)**



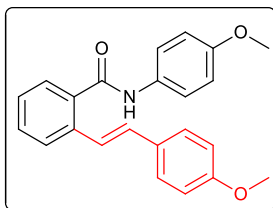
Light yellow solid (110 mg, 84% yield); mp: 182-183 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.73 (d, J = 7.9 Hz, 1H), 7.61 (d, J = 7.6 Hz, 1H), 7.57 – 7.44 (m, 7H), 7.34 (dd, J = 14.0, 7.1 Hz, 3H), 7.30 – 7.23 (m, 1H), 7.10 (d, J = 16.2 Hz, 1H), 6.89 (d, J = 8.9 Hz, 2H), 3.81 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.3, 156.6, 136.8, 135.7, 135.5, 131.9, 130.9, 130.5, 128.7, 128.0, 127.8, 127.6, 126.8, 126.4, 125.6, 121.7, 114.2, 55.4; HRMS calculated for $\text{C}_{22}\text{H}_{20}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 330.1489, found 330.1482. Purification: Flash chromatography; Eluent: hexane/EtOAc = 85/15.

***(E)*-N-(4-Methoxyphenyl)-2-(4-methylstyryl)benzamide (3k)**



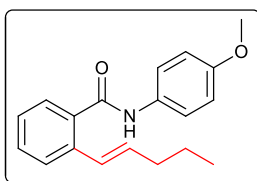
Light yellow solid (116 mg, 85% yield); mp:189-190 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.64 (d, J = 7.8 Hz, 1H), 7.54 (d, J = 6.9 Hz, 1H), 7.41 (dt, J = 15.8, 7.6 Hz, 5H), 7.32 (d, J = 8.0 Hz, 2H), 7.26 (t, J = 7.4 Hz, 1H), 7.07 (d, J = 7.9 Hz, 2H), 7.00 (d, J = 16.3 Hz, 1H), 6.82 (d, J = 8.9 Hz, 2H), 3.74 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.3, 156.6, 138.1, 135.8, 135.3, 134.0, 131.9, 130.9, 130.5, 129.4, 127.8, 127.4, 126.7, 126.4, 124.5, 121.7, 114.2, 55.4, 21.2; HRMS calculated for $\text{C}_{23}\text{H}_{22}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 344.164 found 344.1645; Purification: Flash chromatography; Eluent: toluene/diethyl ether = 85/15.

(*E*)-*N*-(4-Methoxyphenyl)-2-(4-methoxystyryl)benzamide (3l)



Light yellow solid (125 mg, 87% yield); mp: 192-193 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.69 (d, J = 7.9 Hz, 1H), 7.60 (dd, J = 7.6, 0.8 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.47 – 7.35 (m, 5H), 7.31 (t, J = 8.0 Hz, 1H), 7.08 – 7.00 (m, 1H), 6.88 (dd, J = 11.7, 8.8 Hz, 4H), 3.81 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.3, 159.6, 156.6, 135.9, 135.2, 131.4, 130.9, 130.5, 129.6, 128.0, 127.8, 127.2, 126.2, 123.4, 121.7, 114.2, 114.1, 55.5, 55.3; HRMS calculated for $\text{C}_{23}\text{H}_{22}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 360.1594, found 360.1596; Purification: Flash chromatography; Eluent: toluene/diethyl ether = 8/2.

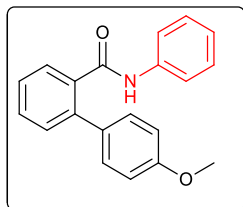
(*E*)-*N*-(4-Methoxyphenyl)-2-(pent-1-en-1-yl)benzamide (3m)



Light brown solid (97 mg, 82% yield); mp: 100-101 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.61 – 7.47 (m, 5H), 7.39 (t, J = 7.6 Hz, 1H), 7.27 (dt, J = 7.4, 3.4 Hz, 1H), 7.03 – 6.85 (m, 2H), 6.75 (d, J = 15.7 Hz, 1H), 6.30 – 6.16 (m, 1H), 3.81 (s, 3H), 2.20 (q, J = 7.2 Hz, 2H), 1.48 (dd, J = 14.7, 7.4 Hz, 2H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.3, 156.4, 136.0, 134.7, 134.7, 131.0, 130.3, 127.7, 127.2, 126.9, 126.6, 121.5, 114.1, 55.4, 35.2, 22.4, 13.7;

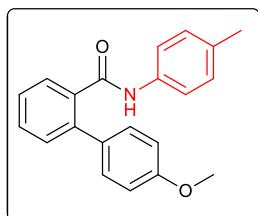
HRMS calculated for $C_{19}H_{22}NO_2$ $[M+H]^+$: 296.1645, found 296.164; Purification: Flash chromatography; Eluent: hexane/EtOAc = 75/25.

4'-Methoxy-N-phenyl-[1,1'-biphenyl]-2-carboxamide (3n)



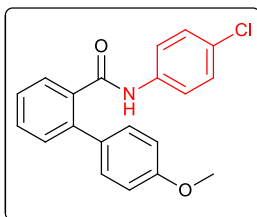
White solid (103 mg, 85% yield); mp: 143-144 °C; 1H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, J = 7.6 Hz, 1H), 7.55 – 7.49 (m, 1H), 7.45 (d, J = 7.5 Hz, 1H), 7.44 – 7.36 (m, 2H), 7.23 (d, J = 7.5 Hz, 2H), 7.17 (d, J = 7.7 Hz, 2H), 7.06 (t, J = 7.3 Hz, 1H), 6.97 (d, J = 8.6 Hz, 3H), 3.83 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 159.5, 139.1, 137.6, 135.1, 132.0, 130.6, 130.3, 130.0, 129.5, 128.8, 127.5, 124.3, 119.9, 114.4, 55.3; HRMS calculated for $C_{20}H_{18}NO_2$ $[M+H]^+$: 304.1332, found 304.1336; Purification: Flash chromatography; Eluent: hexane/EtOAc = 85/15.

4'-Methoxy-N-(p-tolyl)-[1,1'-biphenyl]-2-carboxamide (3o)



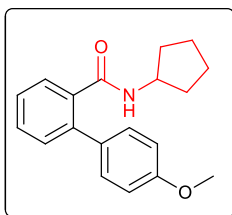
White solid (111 mg, 88% yield); mp: 129-130 °C; 1H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 7.7 Hz, 1H), 7.49 (td, J = 7.4, 1.0 Hz, 1H), 7.44 – 7.37 (m, 4H), 7.08 – 7.01 (m, 4H), 6.95 (t, J = 5.8 Hz, 3H), 3.81 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 159.4, 139.0, 135.2, 135.0, 133.9, 132.1, 130.4, 130.2, 129.9, 129.4, 129.2, 127.3, 120.0, 114.3, 55.3, 20.8; HRMS calculated for $C_{21}H_{20}NO_2$ $[M+H]^+$: 318.1489, found 318.1490; Purification: Flash chromatography; Eluent: hexane/EtOAc = 88/12.

***N*-(4-Chlorophenyl)-4'-methoxy-[1,1'-biphenyl]-2-carboxamide (3p)**



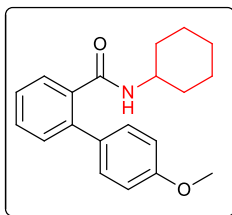
White solid (97 mg, 72% yield); mp: 146-147 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.80 (d, J = 7.4 Hz, 1H), 7.51 (t, J = 7.3 Hz, 1H), 7.47 – 7.33 (m, 4H), 7.18 (d, J = 8.6 Hz, 2H), 7.14 – 7.02 (m, 3H), 6.95 (d, J = 8.4 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.3, 159.5, 139.1, 136.1, 134.7, 131.9, 130.7, 130.3, 129.9, 129.5, 129.2, 128.8, 127.5, 121.0, 114.4, 55.3; HRMS calculated for $\text{C}_{20}\text{H}_{17}\text{NO}_2\text{Cl}$ $[\text{M}+\text{H}]^+$: 338.0942, found 338.0940; Purification: Flash chromatography; Eluent: hexane/EtOAc = 83/17.

***N*-Cyclopentyl-4'-methoxy-[1,1'-biphenyl]-2-carboxamide (3q)**



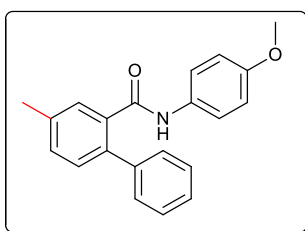
White solid (108 mg, 92% yield); mp: 123-124 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.70 (dd, J = 7.7, 1.2 Hz, 1H), 7.46 – 7.41 (m, 1H), 7.38 (dd, J = 7.6, 1.2 Hz, 1H), 7.35 – 7.30 (m, 3H), 6.97 – 6.93 (m, 2H), 5.19 (d, J = 7.4 Hz, 1H), 4.40 – 4.16 (m, 1H), 3.84 (s, 3H), 1.81 – 1.72 (m, 2H), 1.52 – 1.41 (m, 2H), 1.39 – 1.31 (m, 2H), 1.09 – 0.99 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ 168.7, 159.3, 138.9, 135.7, 132.5, 130.0, 129.8, 128.8, 127.1, 114.0, 55.3, 51.2, 32.4, 23.3; HRMS calculated for $\text{C}_{19}\text{H}_{22}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 296.1645 found 296.1644. Purification: Flash chromatography; Eluent: hexane/EtOAc = 7/3.

***N*-Cyclohexyl-4'-methoxy-[1,1'-biphenyl]-2-carboxamide (3r)**



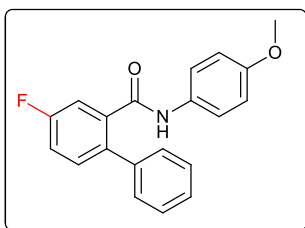
White solid (108 mg, 88% yield); mp: 143-144 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.68 (d, J = 7.5 Hz, 1H), 7.44 (td, J = 7.4, 0.8 Hz, 1H), 7.36 (dt, J = 15.4, 3.7 Hz, 4H), 6.95 (d, J = 8.6 Hz, 2H), 5.16 (d, J = 7.8 Hz, 1H), 3.84 (s, 3H), 3.81 – 3.72 (m, 1H), 1.71 – 1.61 (m, 2H), 1.51 (d, J = 10.6 Hz, 3H), 1.33 – 1.20 (m, 2H), 1.04 (tdd, J = 12.4, 9.5, 3.3 Hz, 1H), 0.79 (td, J = 12.9, 2.8 Hz, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ 168.4, 159.3, 138.9, 135.9, 132.5, 130.0, 129.8, 129.8, 128.7, 127.1, 114.0, 55.3, 48.1, 32.4, 25.3, 24.4; HRMS calculated for $\text{C}_{20}\text{H}_{24}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 310.1802 found 310.1795. Purification: Flash chromatography; Eluent: hexane/EtOAc = 7/3.

***N*-(4-Methoxyphenyl)-4-methyl-[1,1'-biphenyl]-2-carboxamide (3s)**



White solid (105 mg, 71% yield); mp: 147-148 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.70 – 7.69 (m, 1H), 7.47 – 7.37 (m, 6H), 7.33 (dt, J = 14.2, 4.5 Hz, 2H), 7.00 – 6.97 (m, 2H), 6.78 – 6.74 (m, 3H), 3.75 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.2, 156.4, 139.9, 137.8, 136.5, 135.0, 131.3, 130.5, 130.2, 130.0, 128.8, 128.8, 127.8, 121.8, 113.9, 55.4, 21.0; HRMS calculated for $\text{C}_{21}\text{H}_{20}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 318.1489 found 318.1491; Purification: Flash chromatography; Eluent: toluene/THF = 95/5.

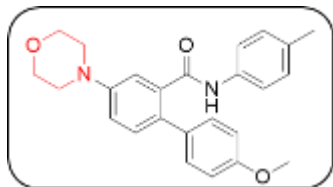
4-Fluoro-*N*-(4-methoxyphenyl)-[1,1'-biphenyl]-2-carboxamide (3t)



White solid (83 mg, 65% yield); mp: 162-163 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.62 (dd, J = 9.0, 2.7 Hz, 1H), 7.48 – 7.42 (m, 5H), 7.40 (dd, J = 8.5, 5.4 Hz, 1H), 7.25 – 7.20 (m, 1H), 7.00 – 6.95 (m, 2H), 6.79 – 6.74 (m, 3H), 3.76 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 165.54, 162.21 (d, $J_{\text{C-F}}$ = 248.7 Hz), 156.7, 139.1, 137.0, 135.5, 132.1 (d, J = 7.8 Hz), 130.2, 129.1, 128.9, 128.2, 121.2, 117.7 (d, $J_{\text{C-F}}$ = 21.3 Hz), 116.5 (d, J = 23.1 Hz), 114.0, 55.4; HRMS

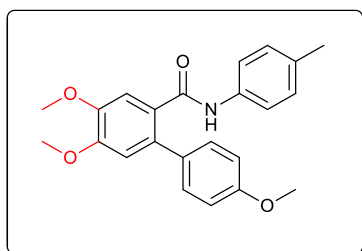
calculated for $C_{20}H_{17}NO_2F$ $[M+H]^+$: 322.1238 found 322.1239; Purification: Flash chromatography; Eluent: toluene/THF = 98/2.

4'-Methoxy-4-morpholino-*N*-(*p*-tolyl)-[1,1'-biphenyl]-2-carboxamide (3u)



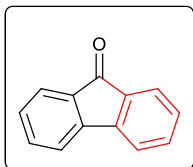
Light brown solid (116 mg, 72% yield); 1H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, J = 2.7 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.30 (d, J = 8.5 Hz, 1H), 7.06 – 7.01 (m, 5H), 6.96 – 6.91 (m, 3H), 3.82 (s, 3H), 3.89 – 3.87 (m, 4H), 3.27 – 3.23 (m, 4H), 2.28 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 159.1, 150.3, 135.7, 135.0, 134.0, 132.0, 131.2, 130.1, 130.0, 129.3, 119.9, 117.5, 115.9, 114.3, 66.7, 55.3, 48.8, 20.8; HRMS calculated for $C_{25}H_{27}N_2O_3$ 403.2016 found 403.2021; Purification: Flash chromatography; Eluent: $CHCl_3$ /diethyl ether = 95/5.

4,4',5-Trimethoxy-*N*-(*p*-tolyl)-[1,1'-biphenyl]-2-carboxamide (3v)



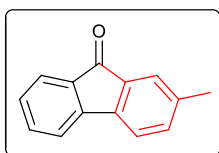
Light yellow solid (117 mg, 77% yield); 1H NMR (500 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.38 (d, J = 8.4 Hz, 2H), 7.05 – 6.96 (m, 6H), 6.92 (s, 1H), 6.81 (s, 1H), 3.97 (s, 3H), 3.94 (s, 3H), 3.84 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 159.5, 150.5, 148.3, 135.2, 133.8, 132.6, 132.2, 130.3, 129.3, 127.0, 119.8, 114.5, 112.9, 112.5, 56.1, 56.1, 55.4, 20.8; HRMS calculated for $C_{23}H_{24}NO_4$ $[M+H]^+$: 378.1700 found 378.1705; Purification: Flash chromatography; Eluent: DCM/THF = (98/2)

9H-Fluoren-9-one (7a)



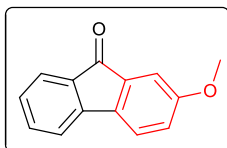
Light yellow solid (65 mg, 90% yield); m.p. 83-84 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.65 (d, J = 6.2 Hz, 2H), 7.50 (dd, J = 12.7, 7.3 Hz, 4H), 7.28 (t, J = 9.3 Hz, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ 193.9, 144.3, 134.6, 134.1, 129.0, 124.2, 120.2; HRMS calculated for $\text{C}_{13}\text{H}_9\text{O}$ $[\text{M}+\text{H}]^+$: 181.0648 found 181.0643; Purification: Flash chromatography; Eluent: Hexane/EtOAc = 95/5.

2-Methyl-9H-fluoren-9-one (7b)



Light yellow solid (68 mg, 88 % yield); m.p. 87-88 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.63 (d, J = 7.3 Hz, 1H), 7.48 – 7.45 (m, 3H), 7.40 – 7.38 (m, 1H), 7.29 – 7.26 (m, 1H), 7.26 – 7.23 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 194.2, 144.6, 141.8, 139.2, 135.1, 134.6, 134.3, 134.2, 128.5, 125.0, 124.2, 120.1, 119.9, 21.3; HRMS calculated for $\text{C}_{14}\text{H}_{11}\text{O}$ $[\text{M}+\text{H}]^+$: 195.0804, found 195.0798; Purification: Flash chromatography; Eluent: Hexane/EtOAc = 95/5.

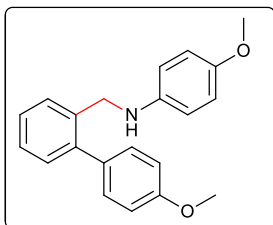
2-Methoxy-9H-fluoren-9-one (7c)



Bright yellow solid (75 mg, 90% yield); m.p. 78-79 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.58 (d, J = 7.3 Hz, 1H), 7.42 (t, J = 7.4 Hz, 1H), 7.37 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.1 Hz, 2H), 6.96 (dd, J = 8.1, 1.6 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 193.7, 160.7, 144.7, 136.8, 135.8, 134.7, 134.2, 127.7, 124.2, 121.2, 120.1, 119.5, 109.2, 55.6; HRMS

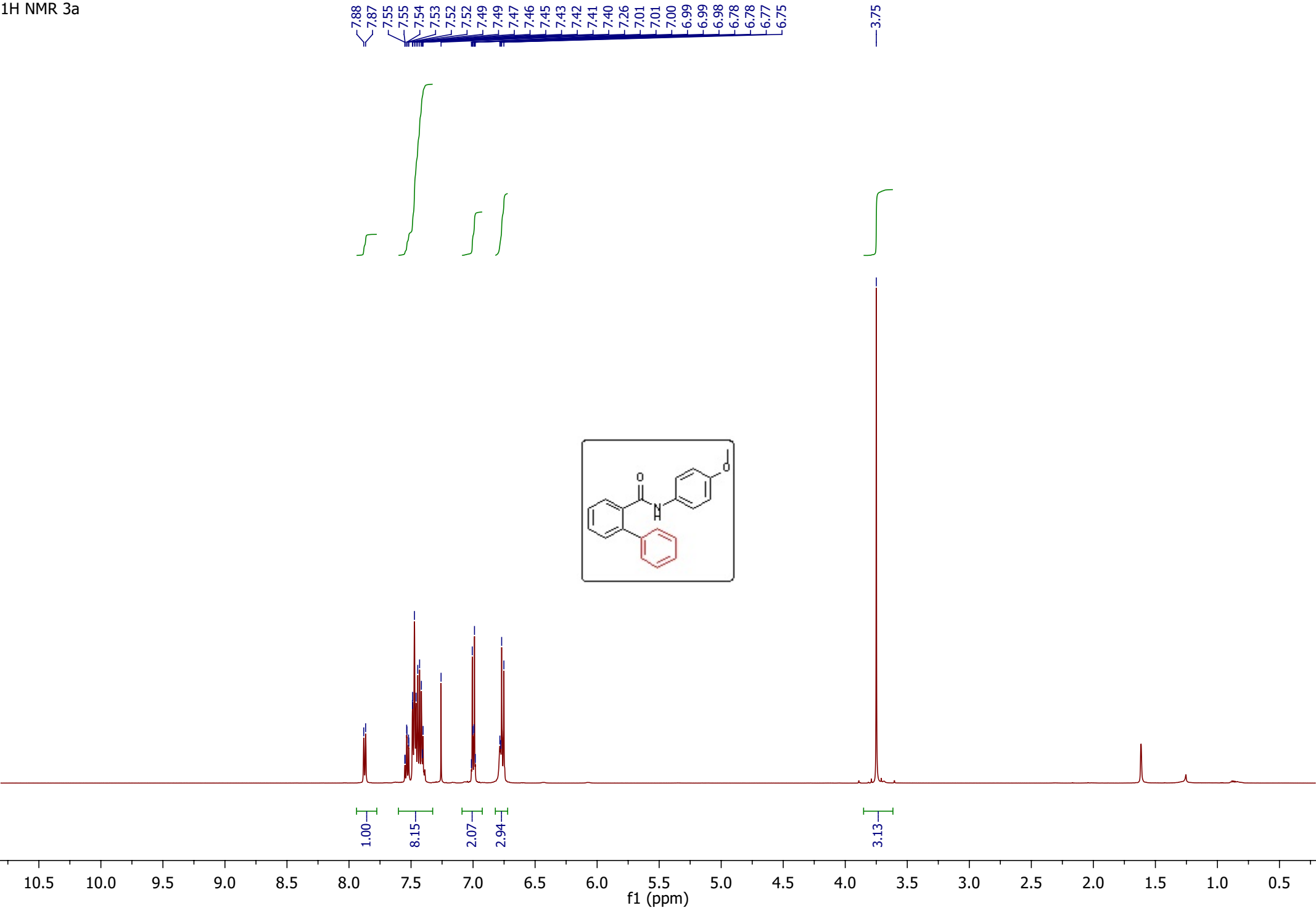
calculated for $C_{14}H_{11}O_2$ $[M+H]^+$: 211.0754 found 211.0745; Purification: Flash chromatography; Eluent: Hexane/EtOAc = 95/5.

4-Methoxy-N-((4'-methoxy-[1,1'-biphenyl]-2-yl)methyl)aniline (8)



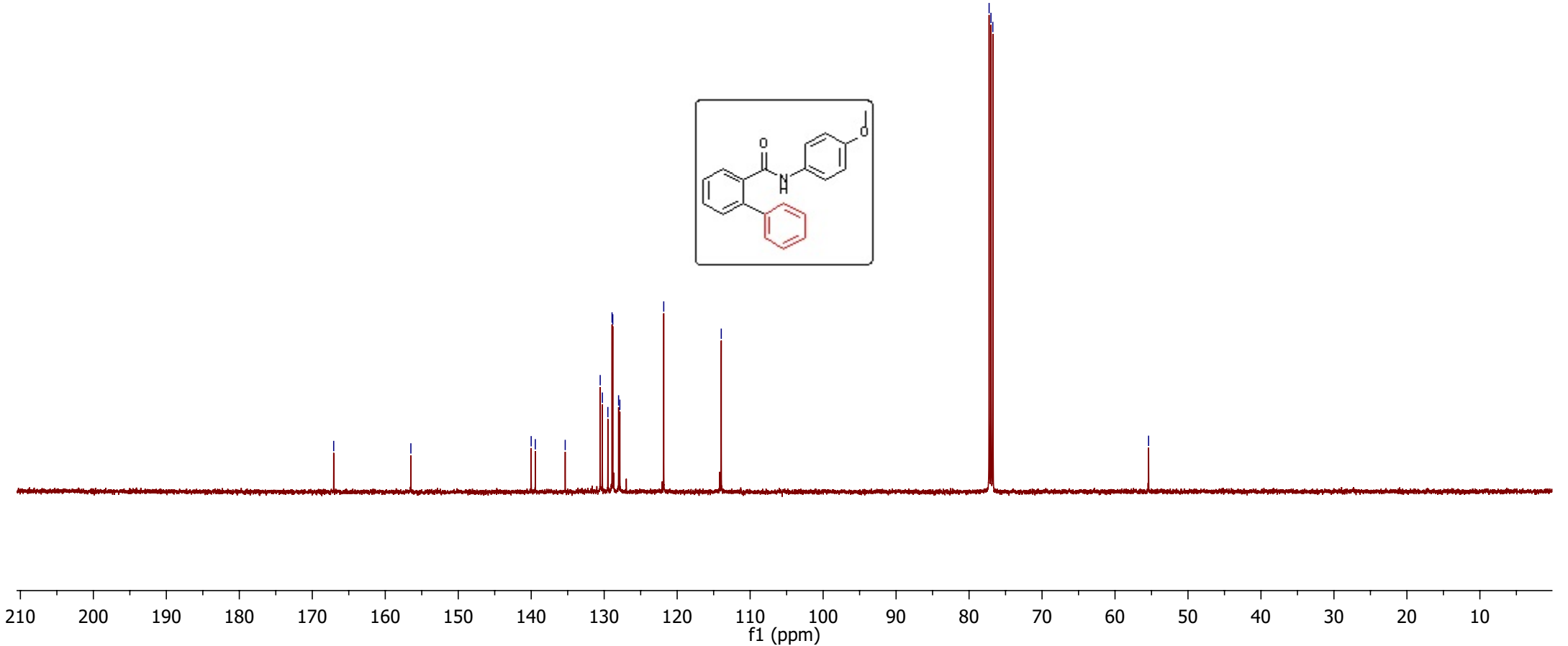
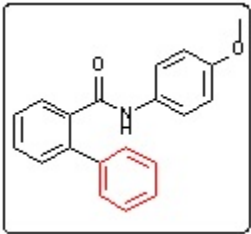
Brown oily liquid (108 mg, 85% yield); 1H NMR (500 MHz, $CDCl_3$) δ 7.50 (dq, J = 7.1, 3.6 Hz, 1H), 7.33 (dt, J = 6.9, 3.1 Hz, 4H), 7.28 (dd, J = 5.4, 3.7 Hz, 1H), 6.97 – 6.94 (m, 2H), 6.76 – 6.72 (m, 2H), 6.52 – 6.48 (m, 2H), 4.20 (s, 2H), 3.85 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 152.0, 142.2, 141.3, 136.6, 133.2, 130.3, 130.0, 128.7, 127.3, 127.2, 114.7, 114.1, 113.6, 55.7, 55.2, 47.2; HRMS calculated for $C_{21}H_{22}NO_2$ $[M+H]^+$: 322.1238 found 322.1239; Purification: Flash chromatography; Eluent: Hexane/EtOAc = 75/25.

1H NMR 3a

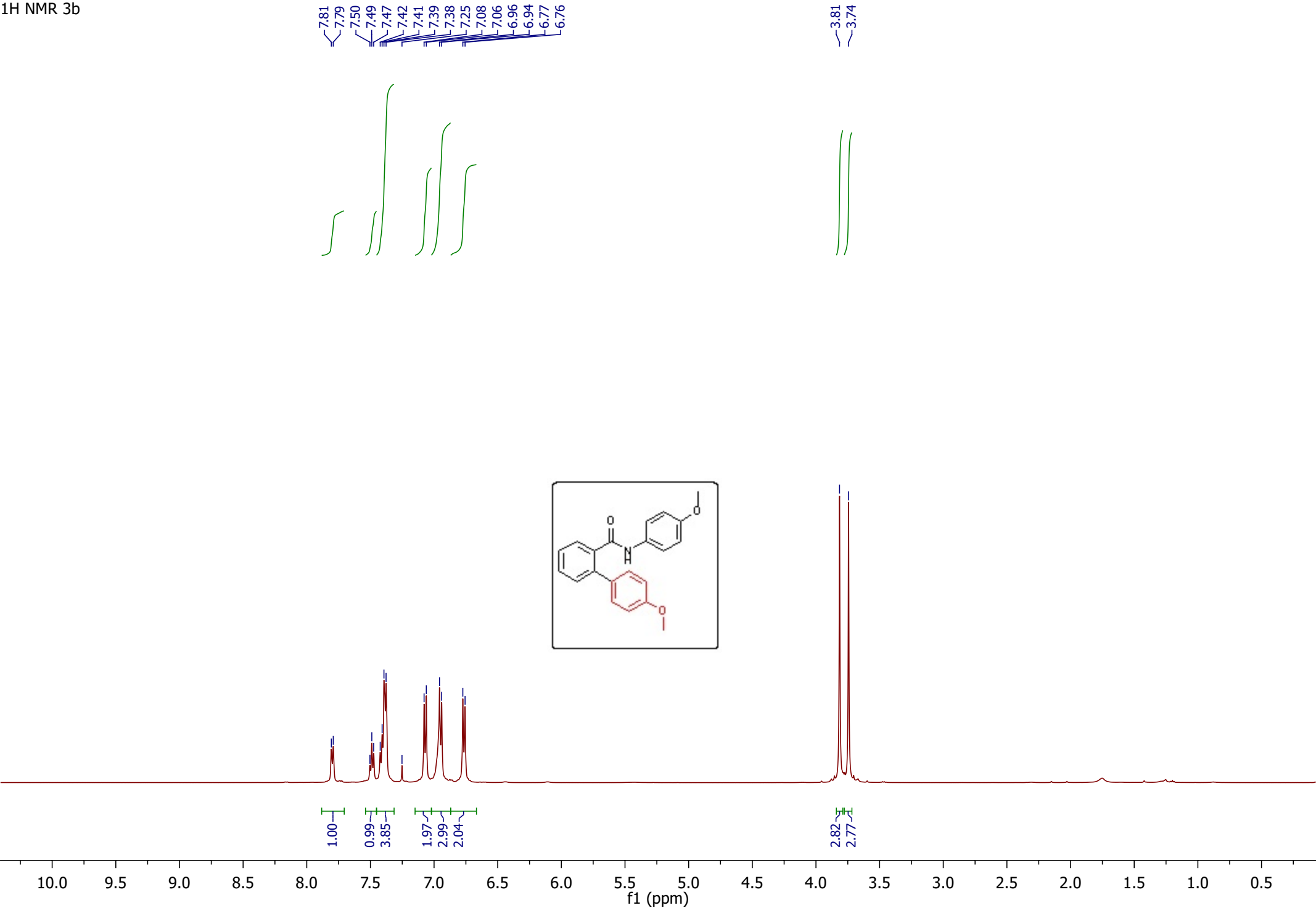


13C NMR 3a

167.07 156.49 140.00 139.44 135.34 130.55 130.25 129.50 128.92 128.82 128.03 127.86 121.84 113.96 77.25 77.00 76.75 55.40

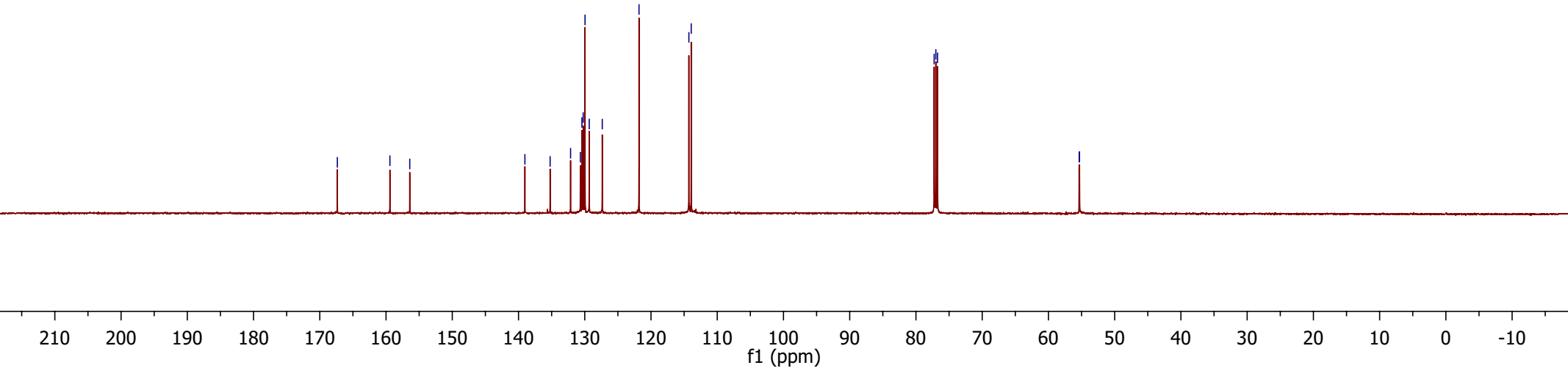
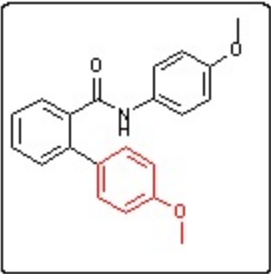


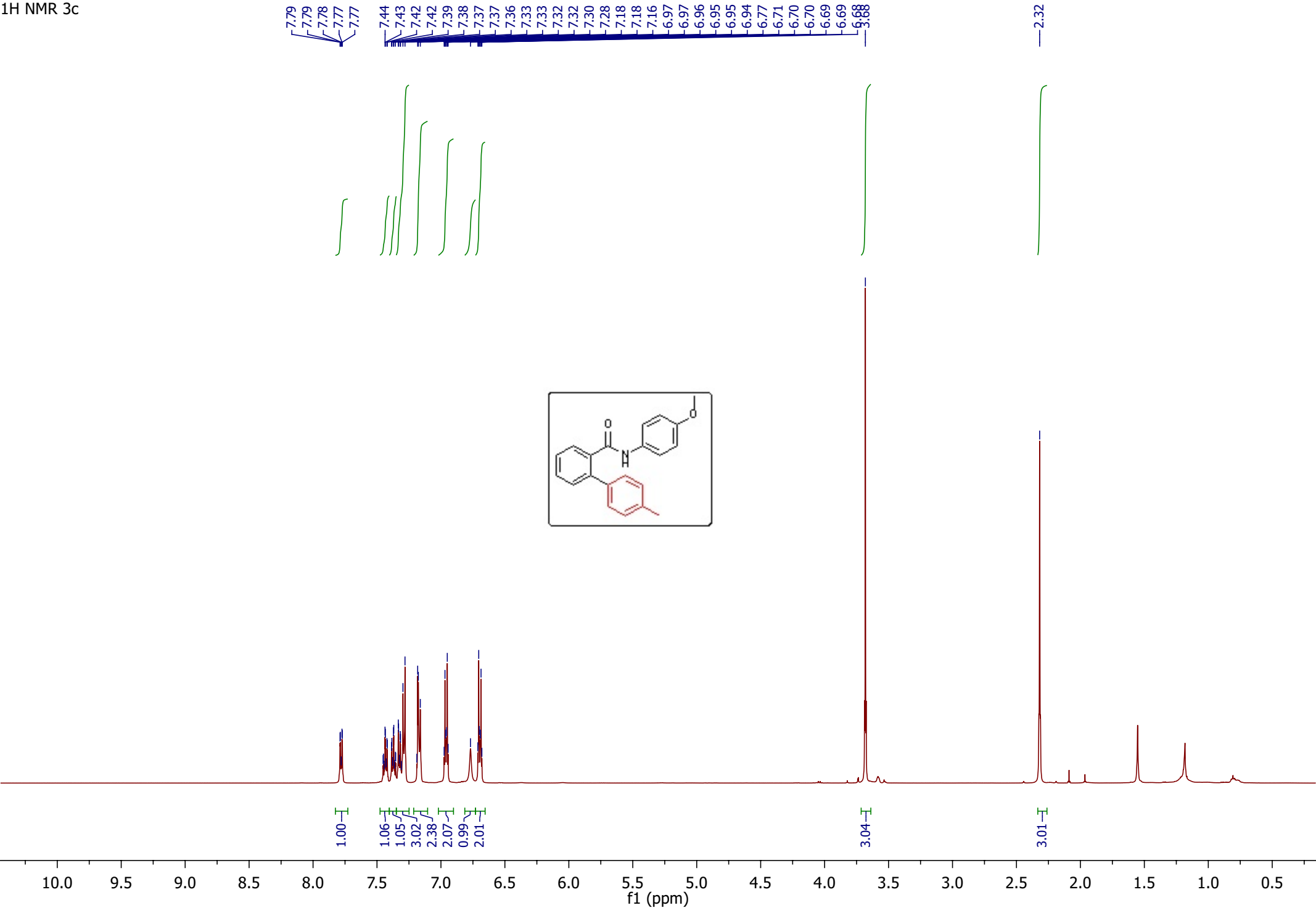
1H NMR 3b



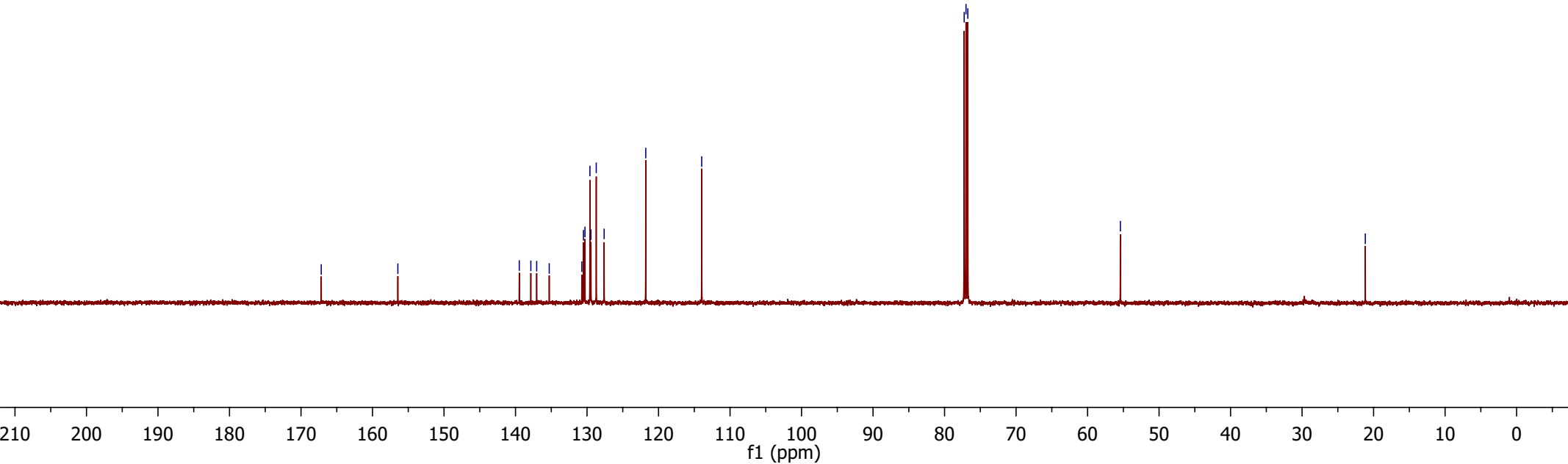
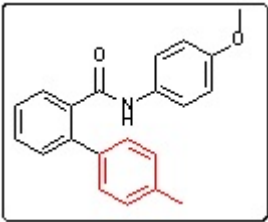
13C NMR3b

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139.04
135.23
132.14
130.66
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130.23
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127.36
121.81
114.28
113.93
77.25
77.00
76.75
55.36
55.31

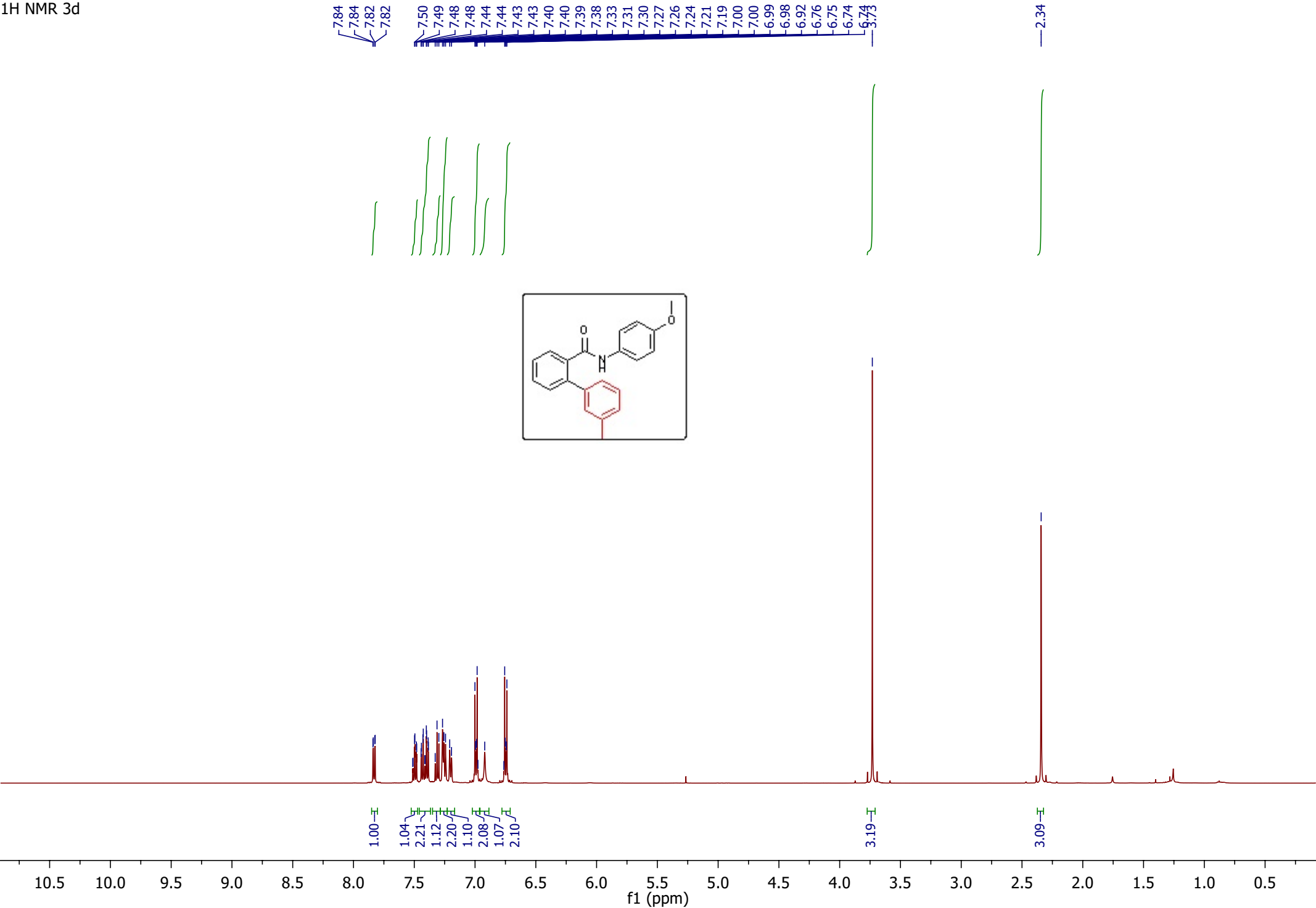




¹³C NMR 3c

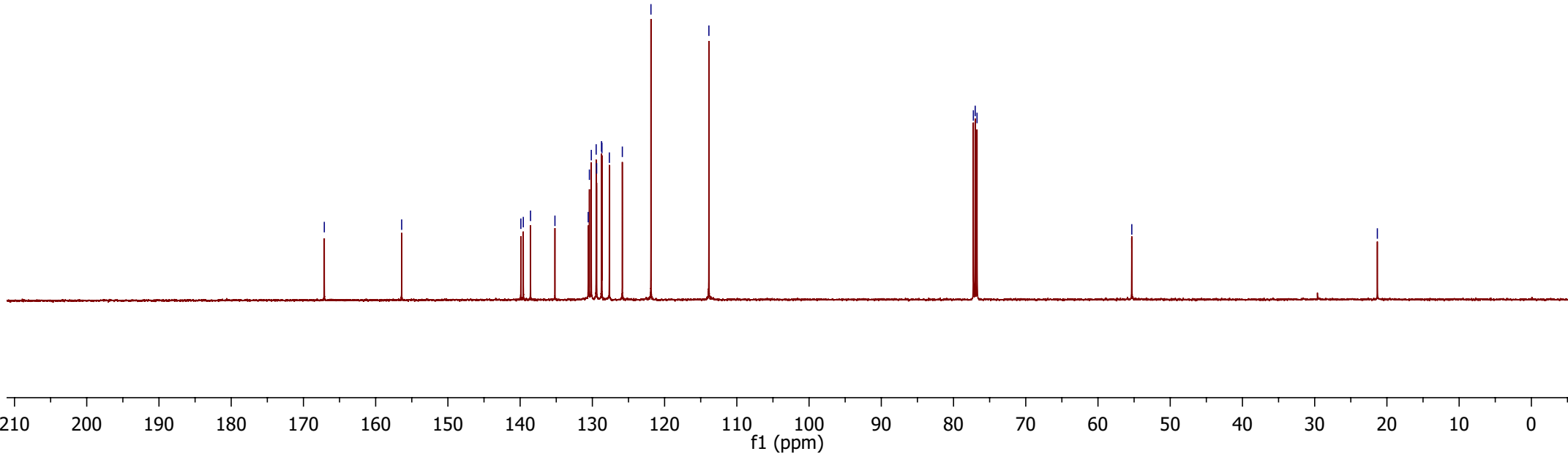
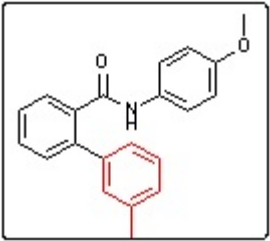


1H NMR 3d

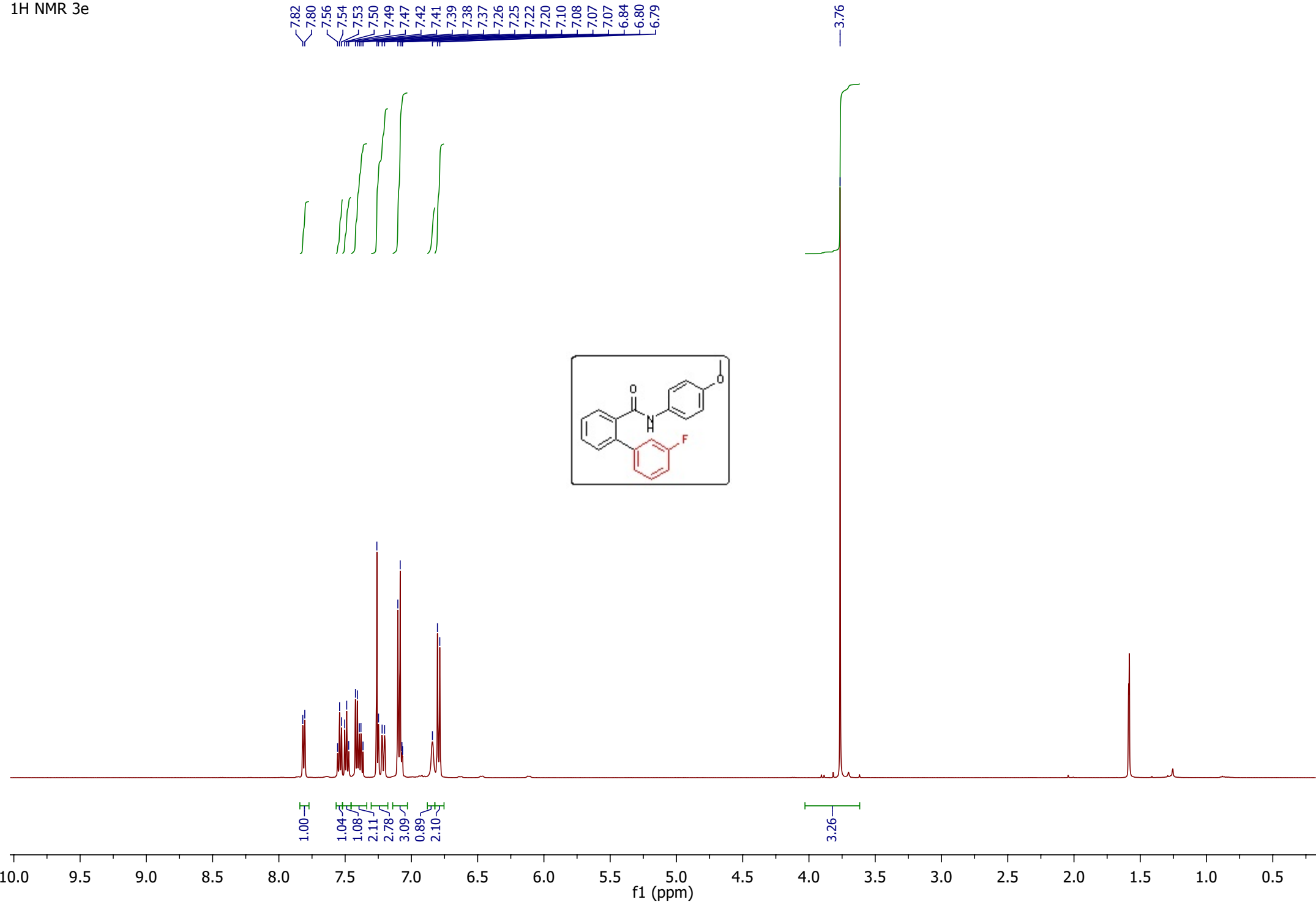


13C NMR 3d

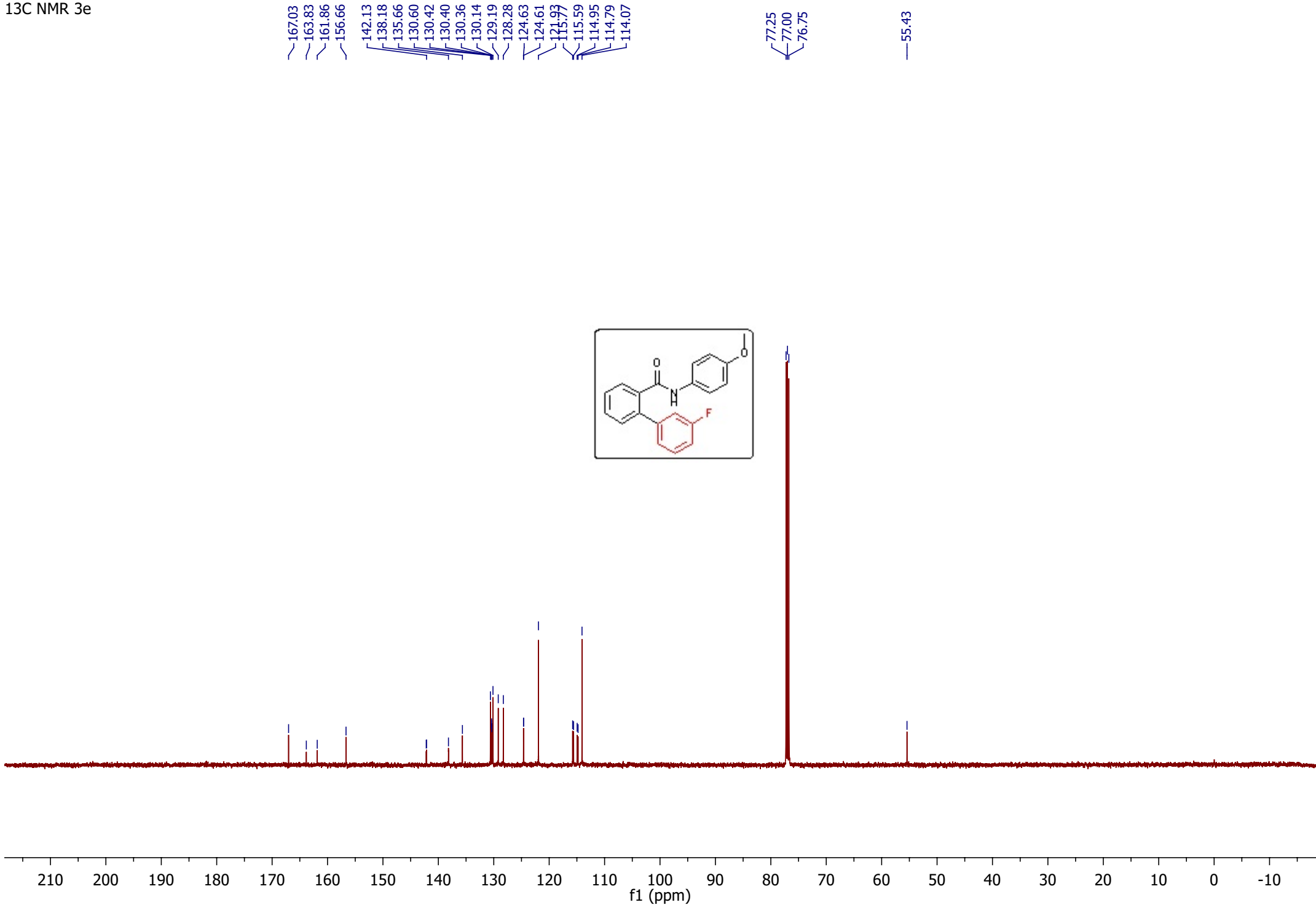
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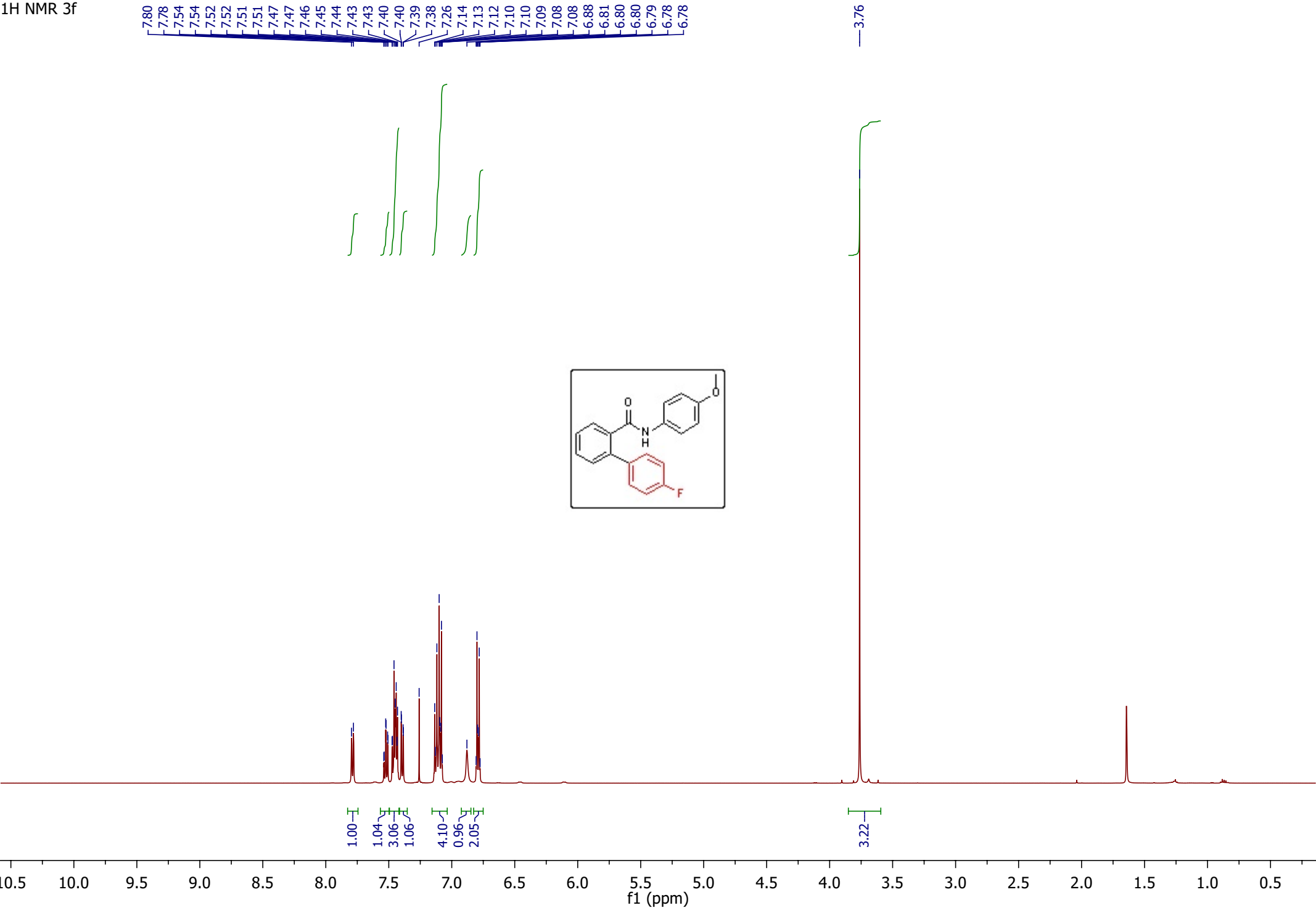
1H NMR 3e



13C NMR 3e

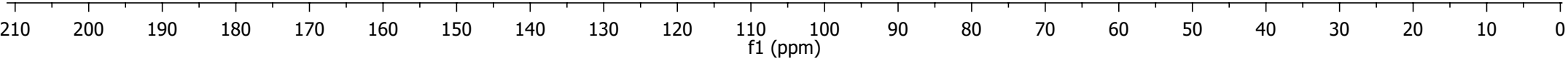
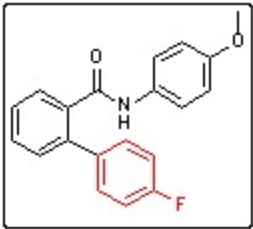


1H NMR 3f

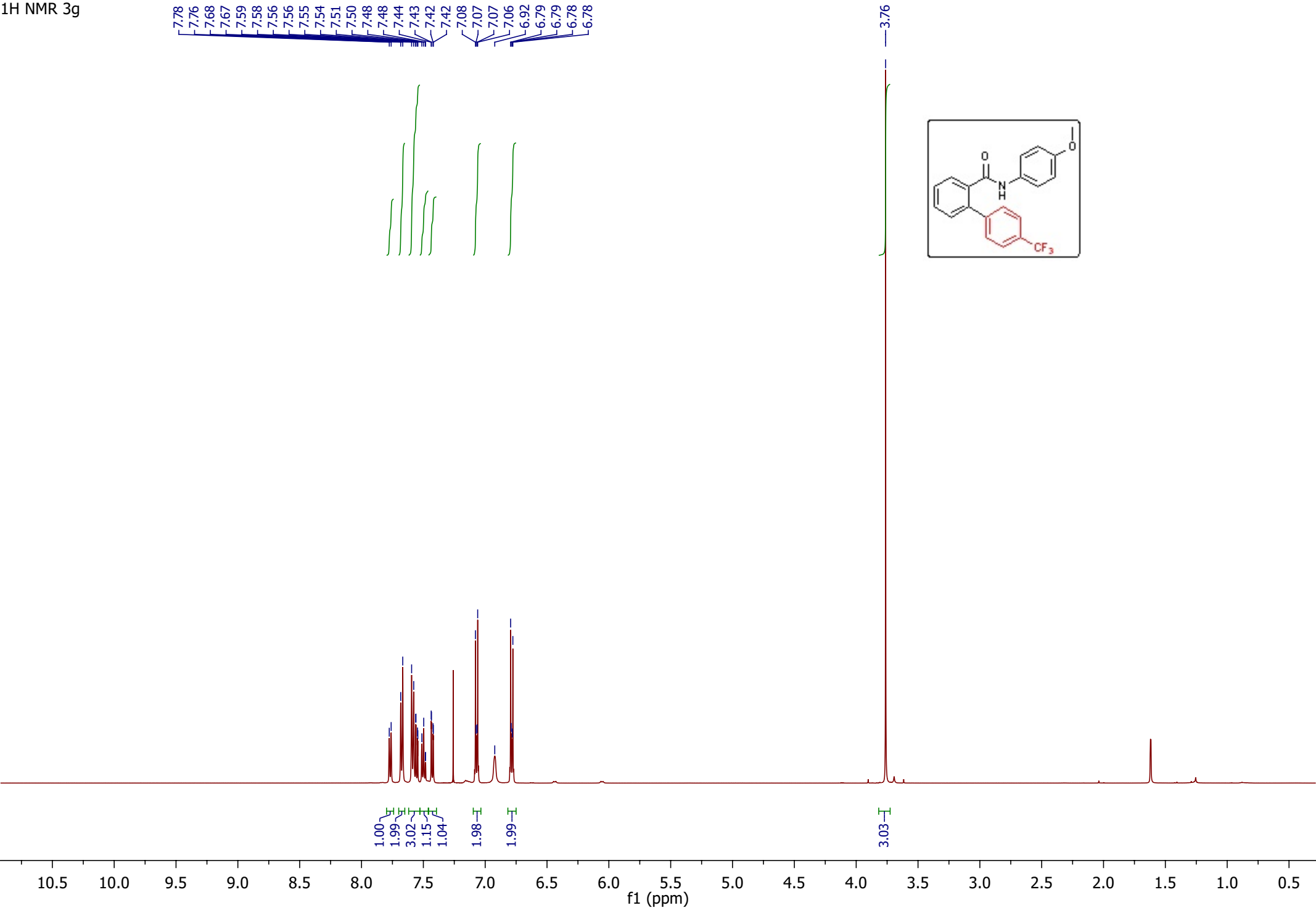


13C NMR 3f

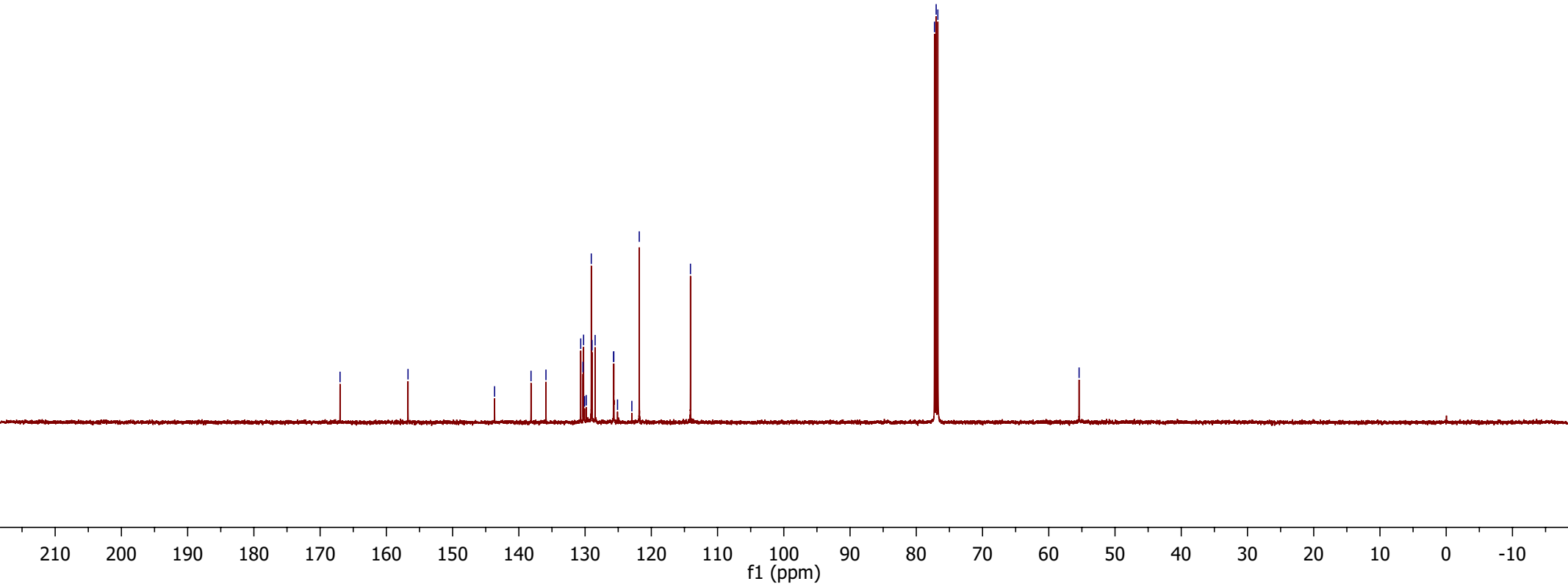
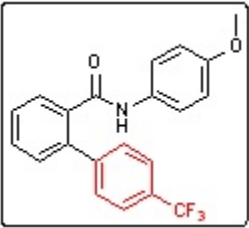
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76.75
55.42



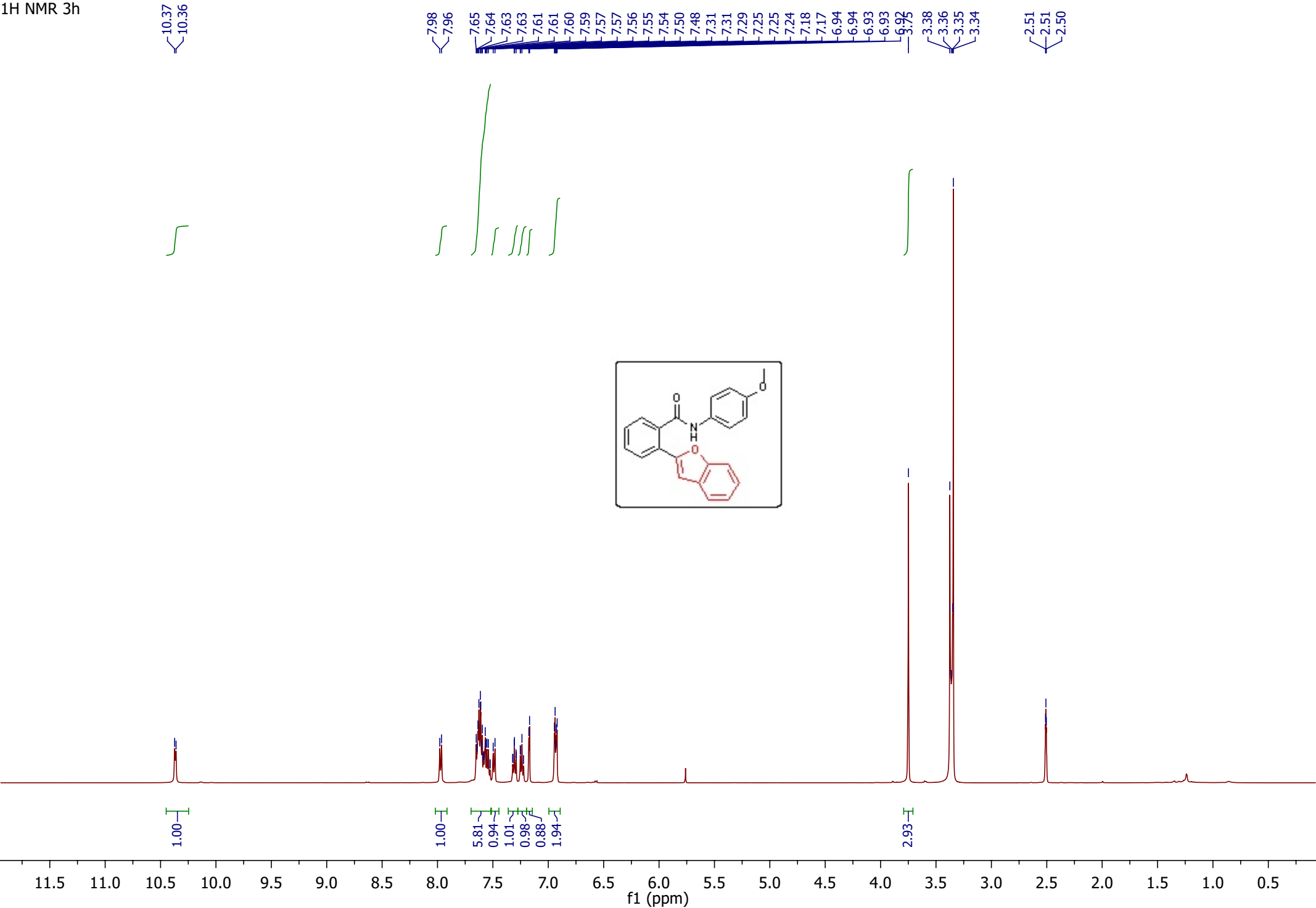
1H NMR 3g



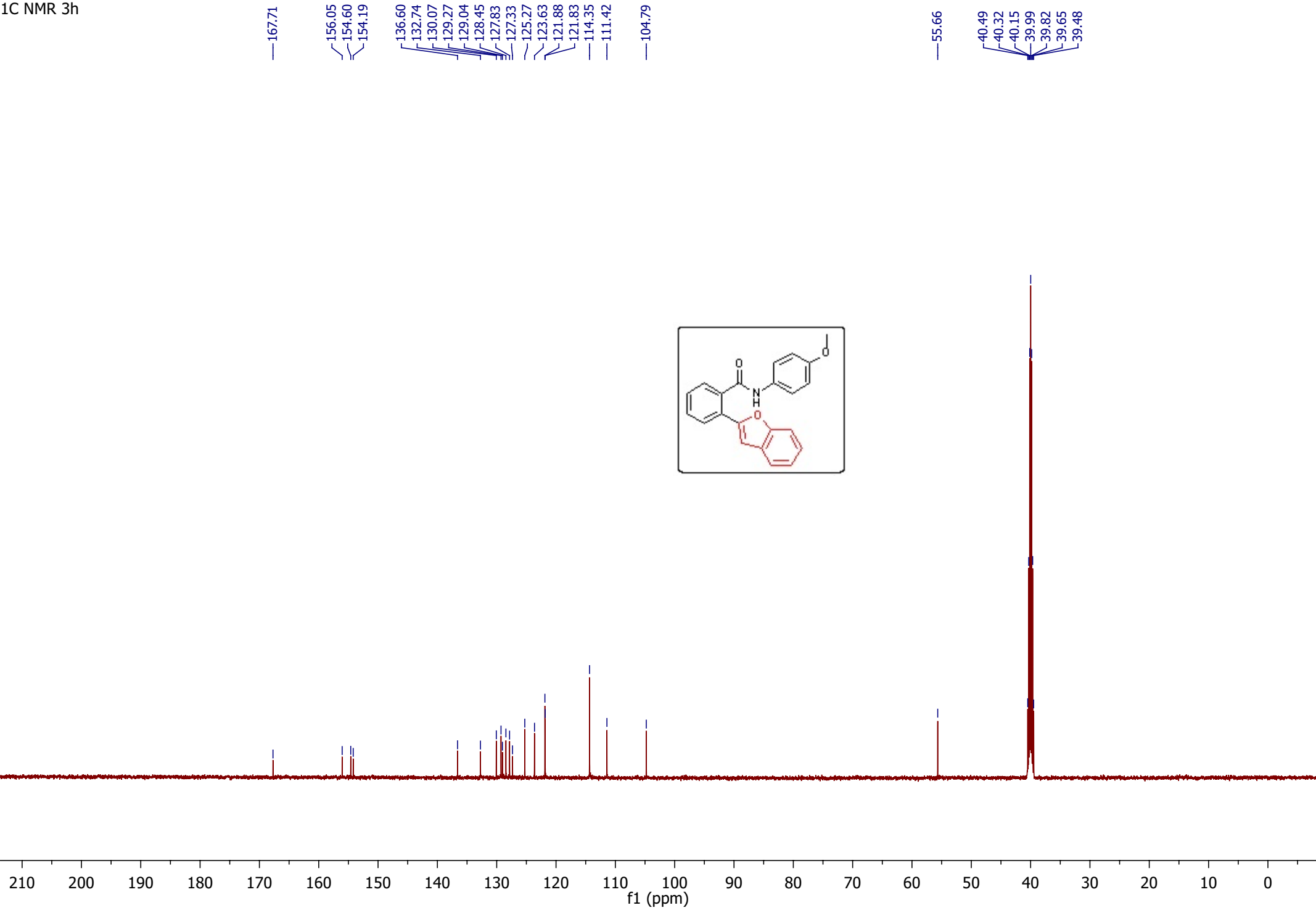
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76.75
55.42

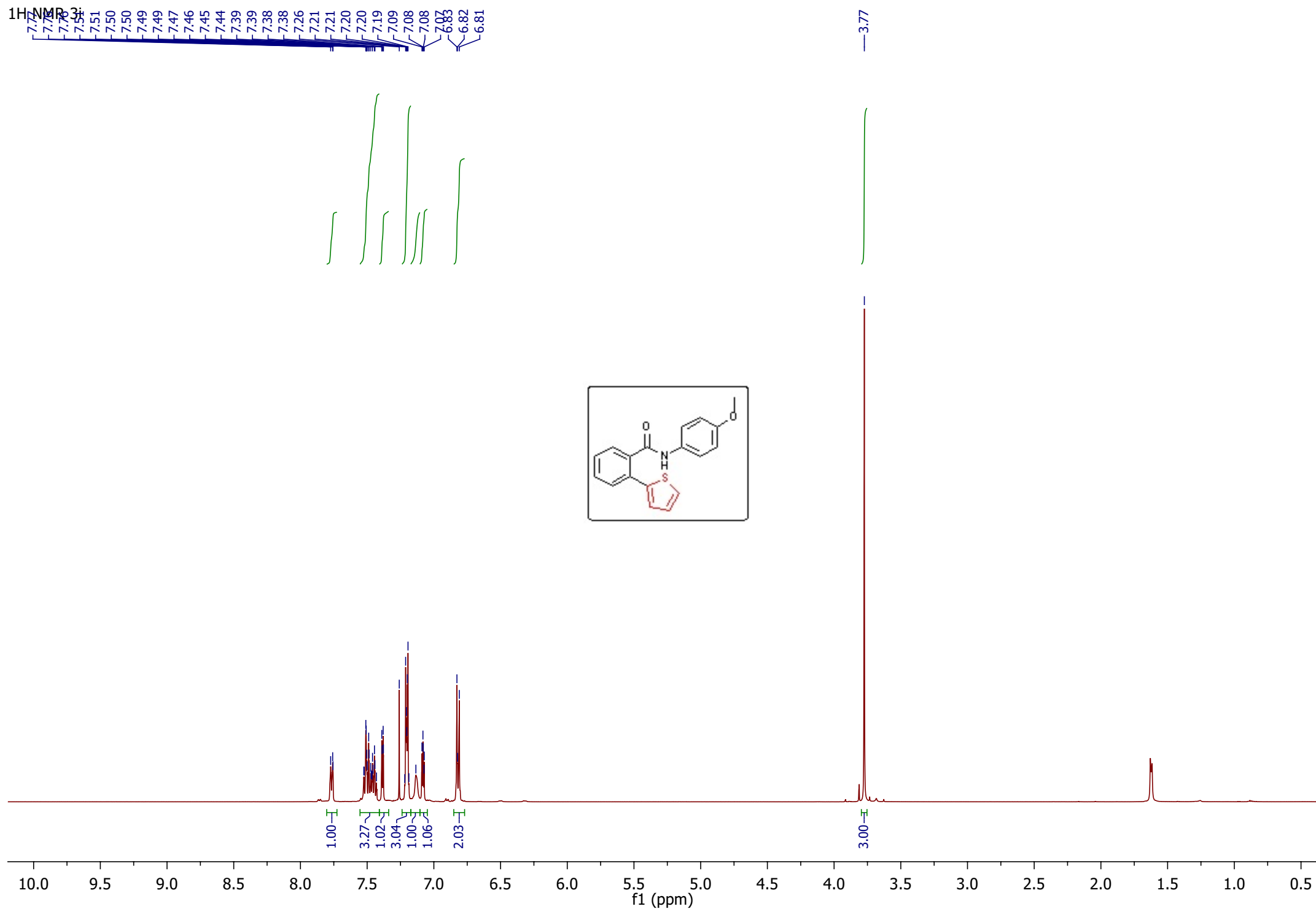


1H NMR 3h



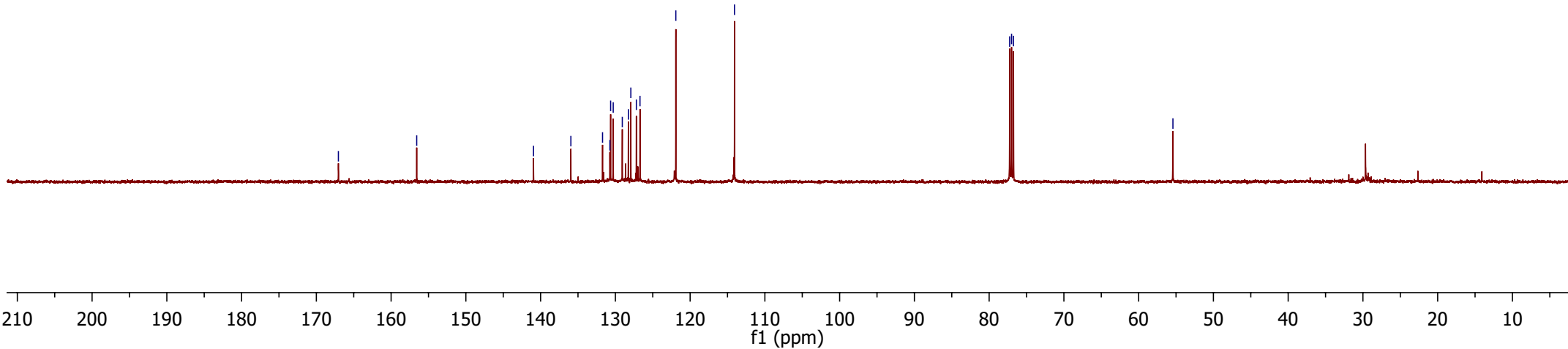
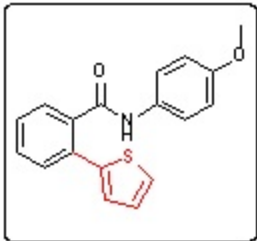
1C NMR 3h



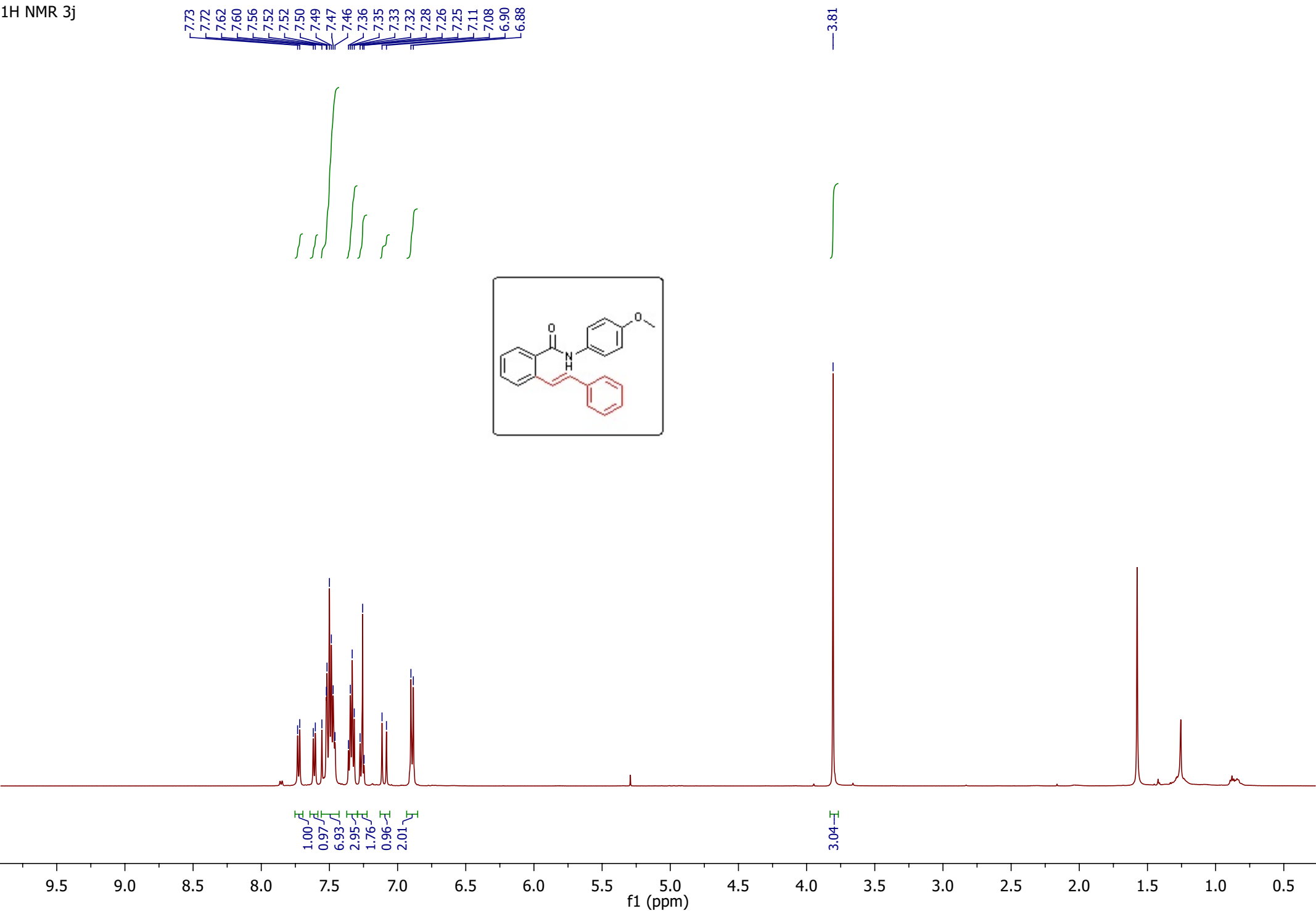


¹³C NMR 3i

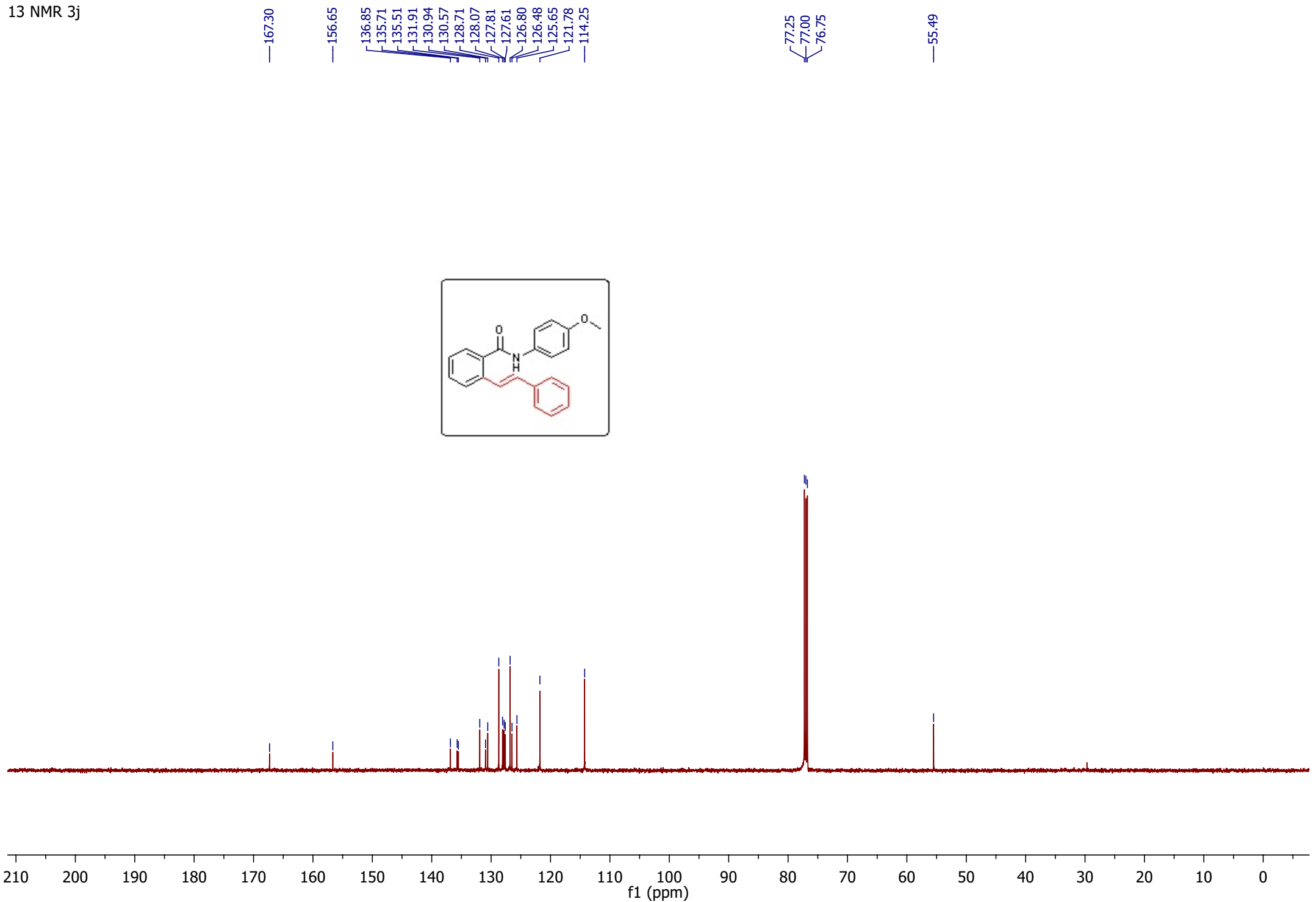
— 167.05 — 156.57 — 140.95 — 131.72 — 130.63 — 130.29 — 129.07 — 128.26 — 127.93 — 127.19 — 126.71 — 124.06 — 77.25 — 77.00 — 76.75 — 55.42

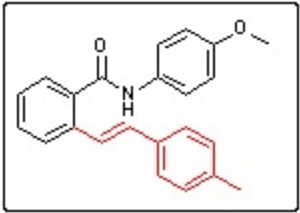
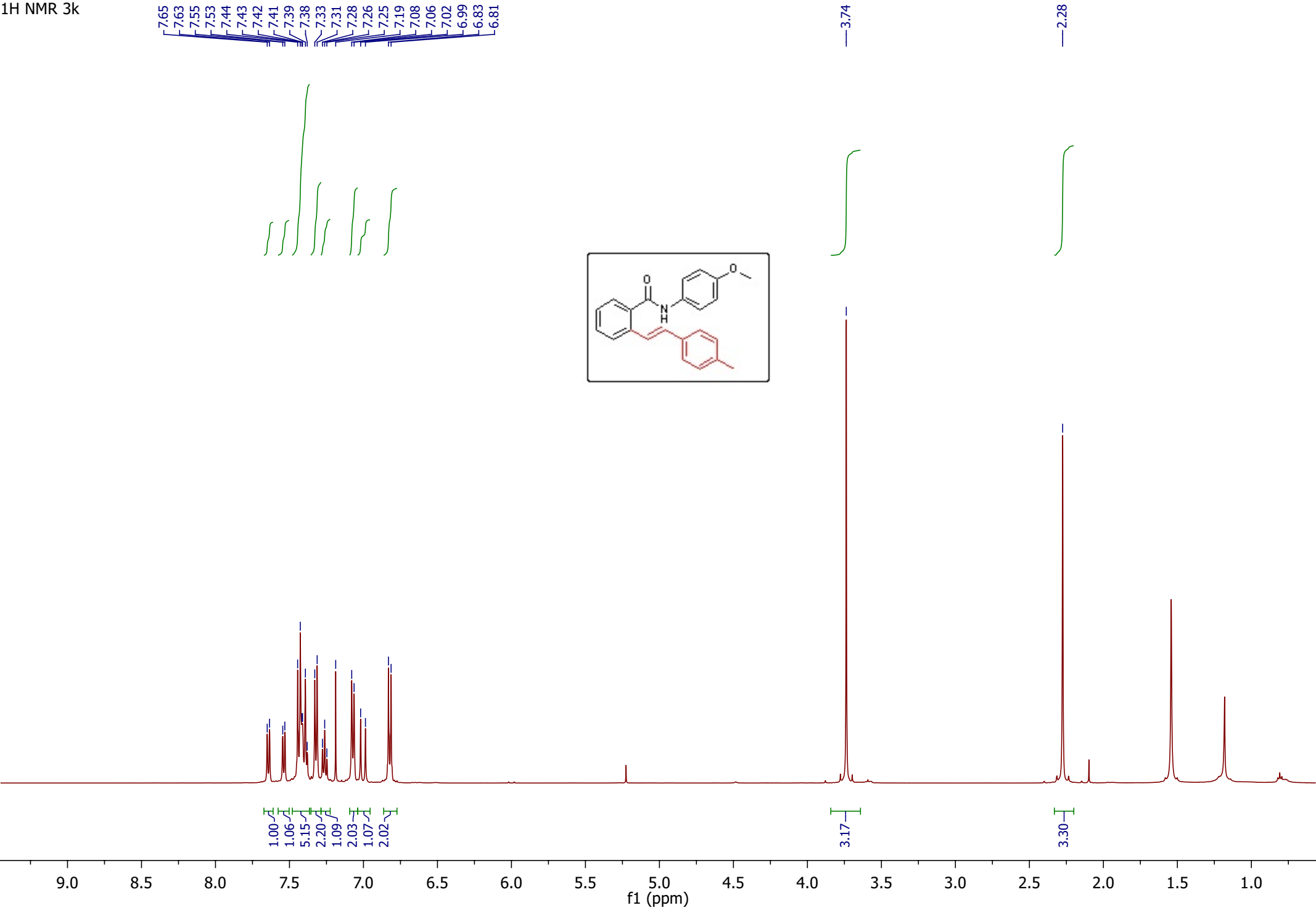


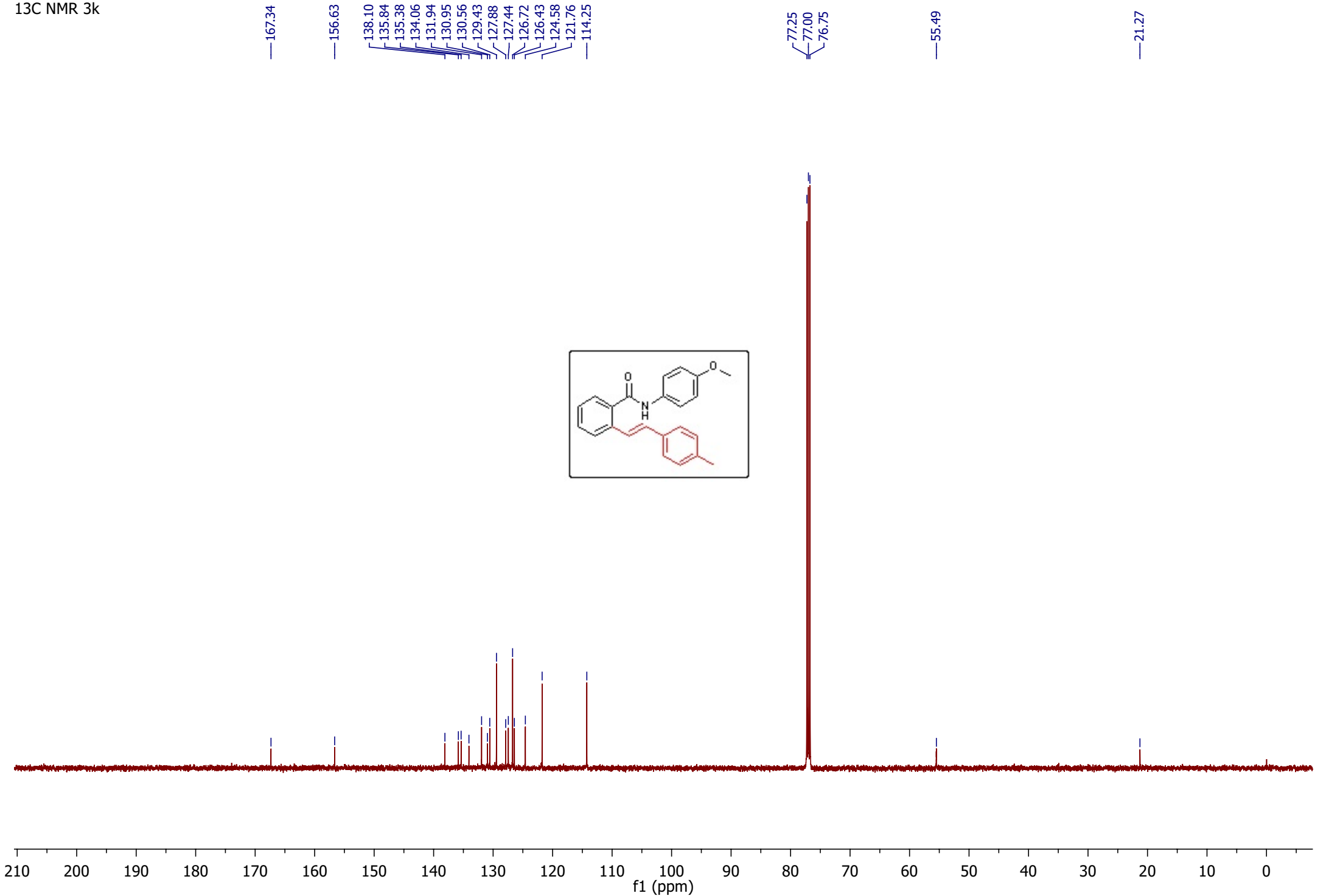
1H NMR 3j



13 NMR 3j



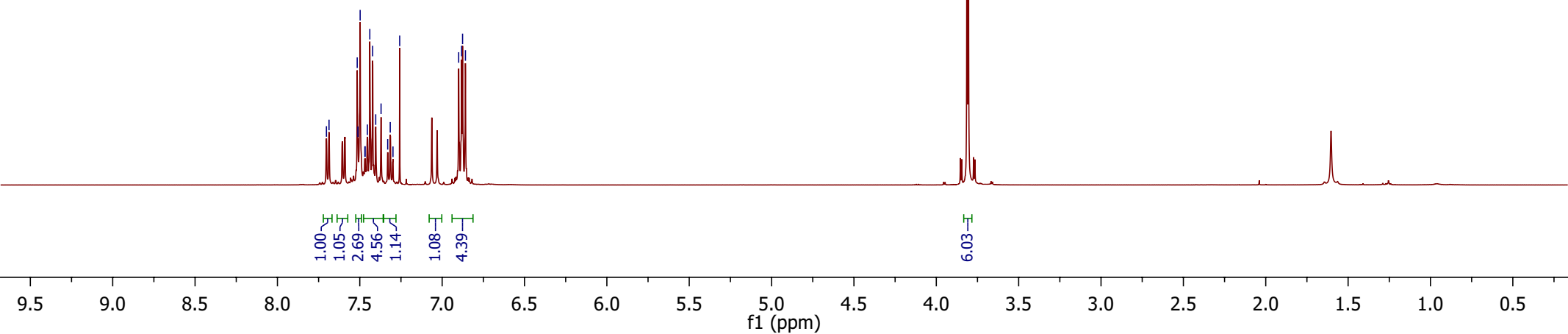
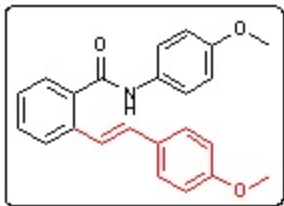


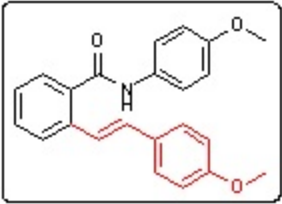
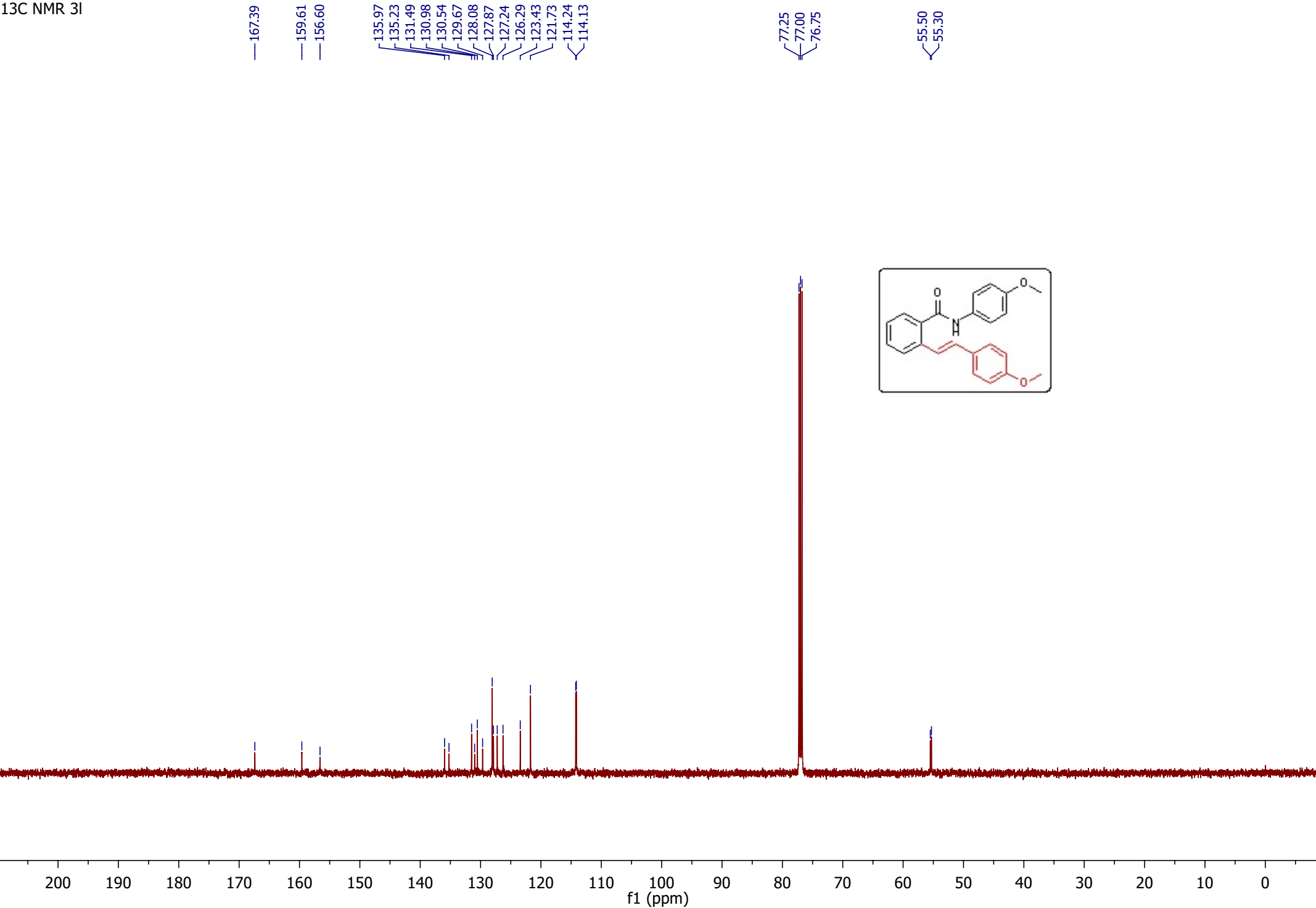


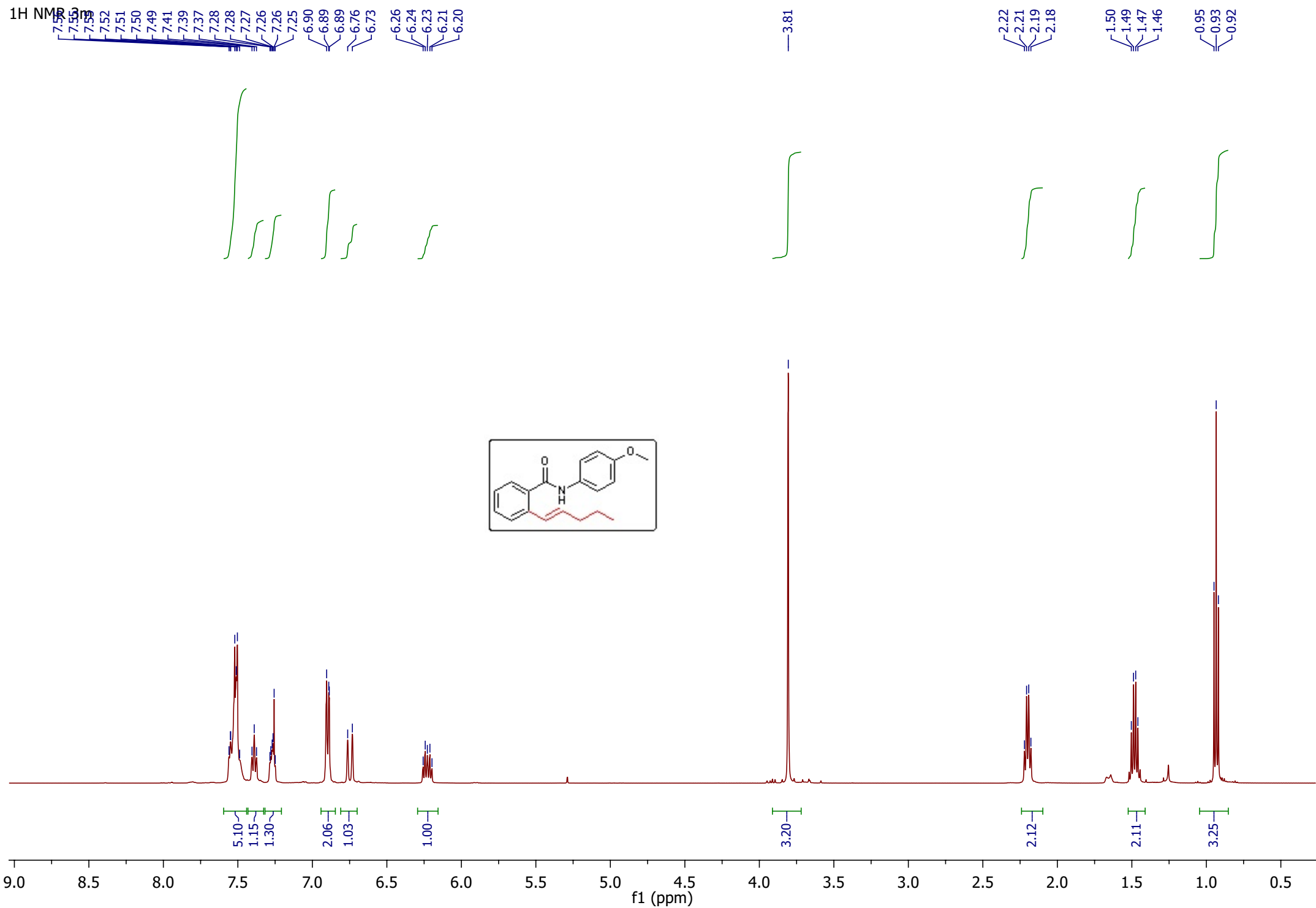
1H NMR 3I

7.70
7.69
7.52
7.51
7.50
7.47
7.47
7.45
7.44
7.42
7.40
7.37
7.33
7.32
7.30
7.26
6.90
6.88
6.86

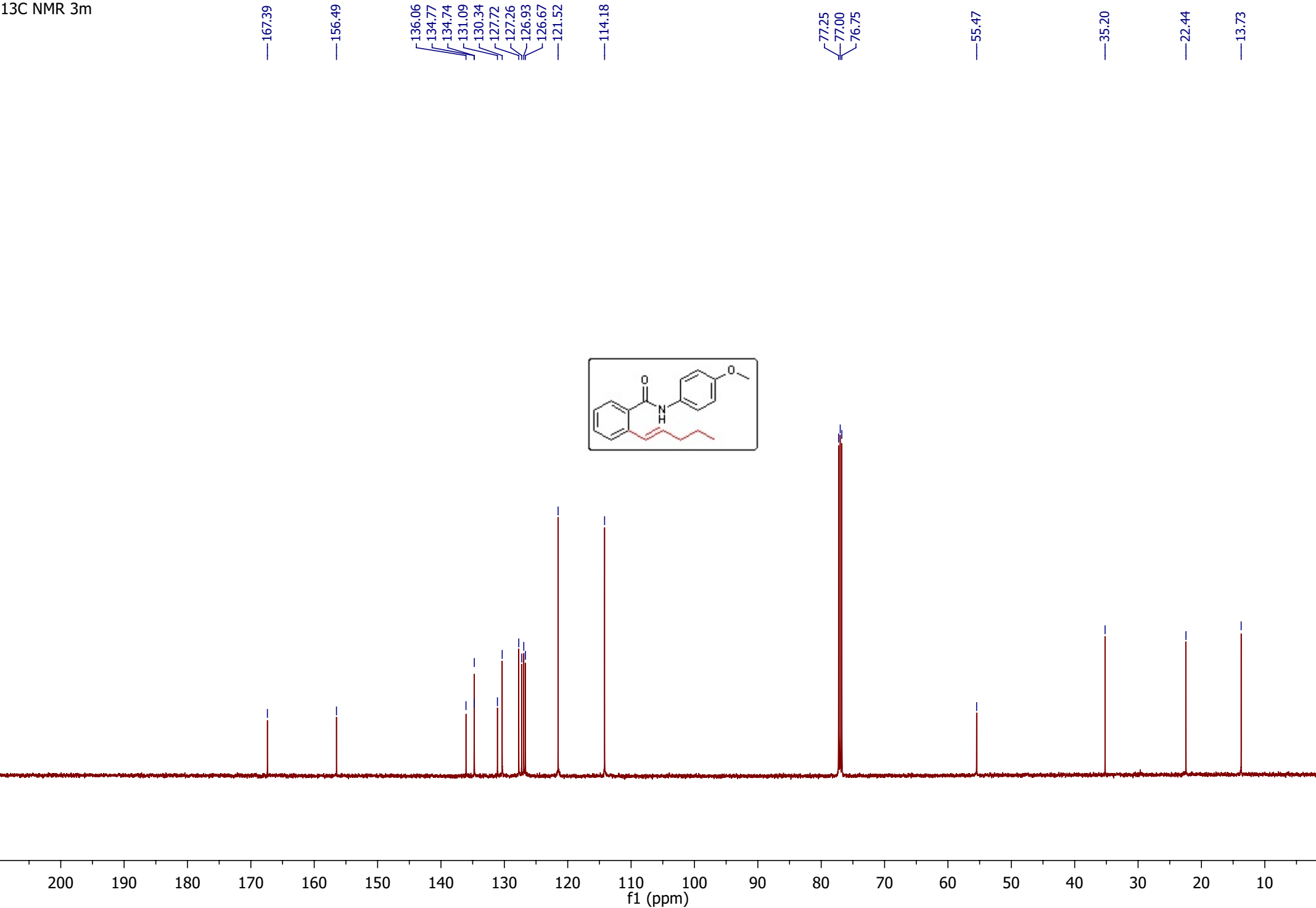
3.81
3.81



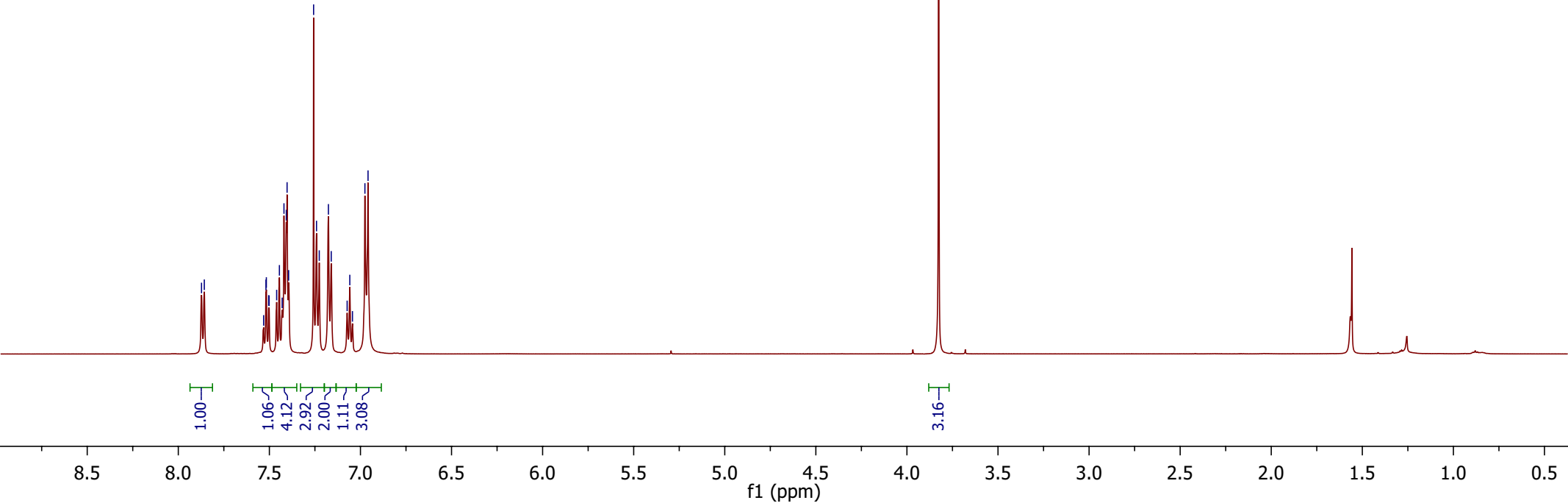
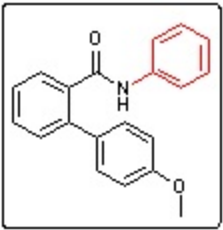
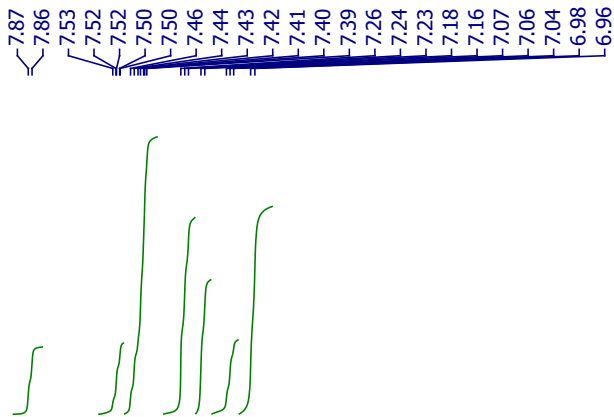




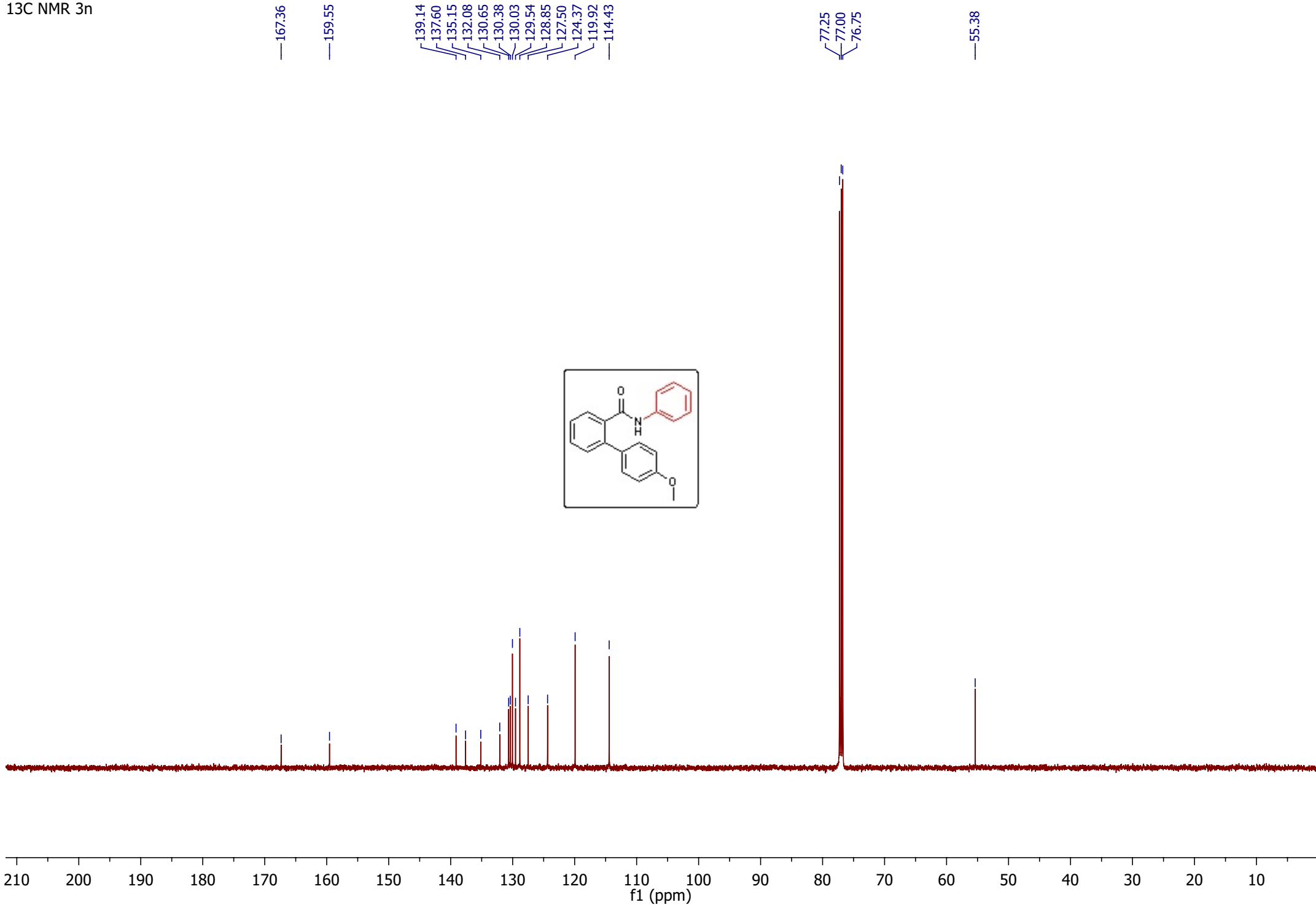
¹³C NMR 3m

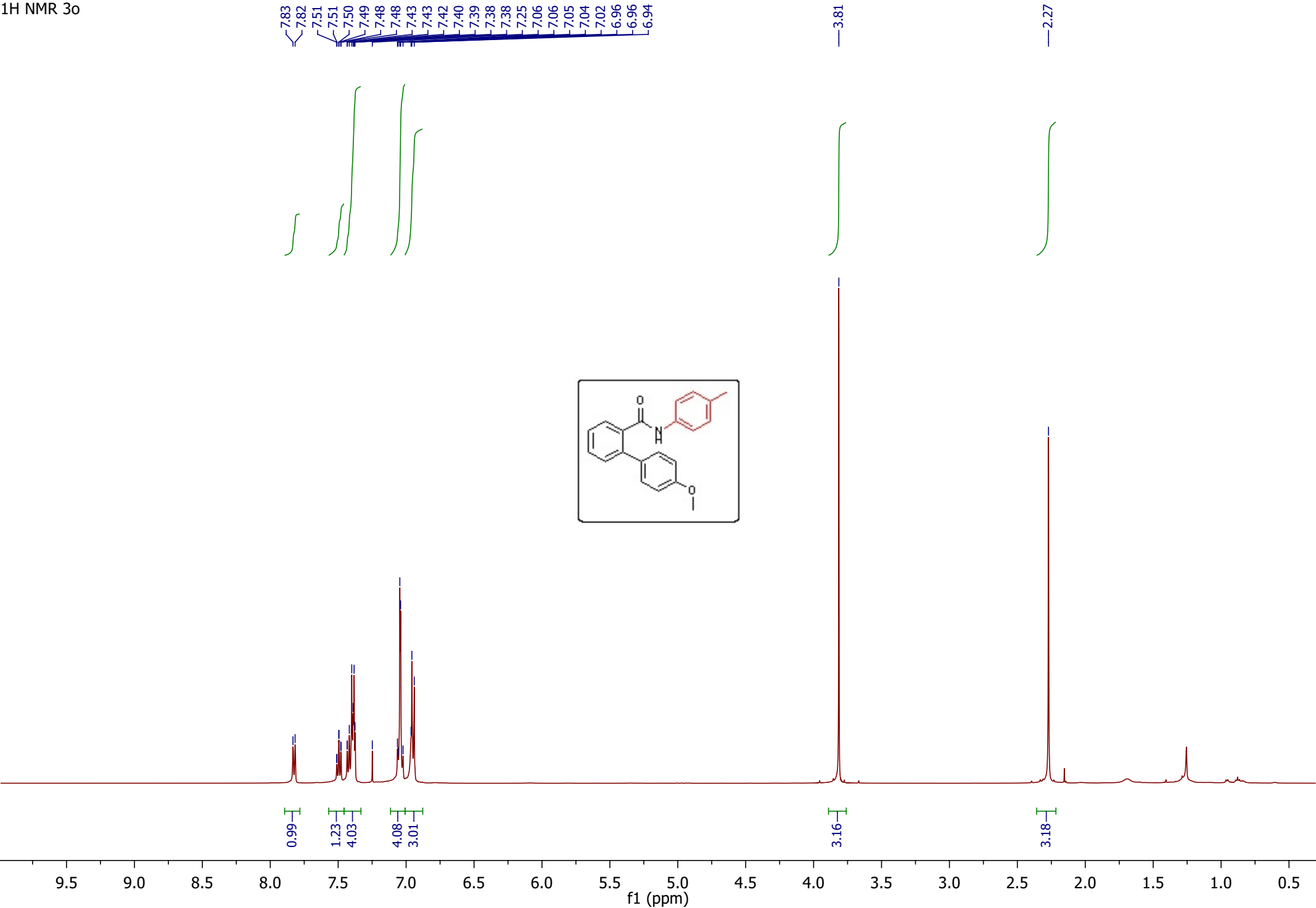


1H NMR 3n

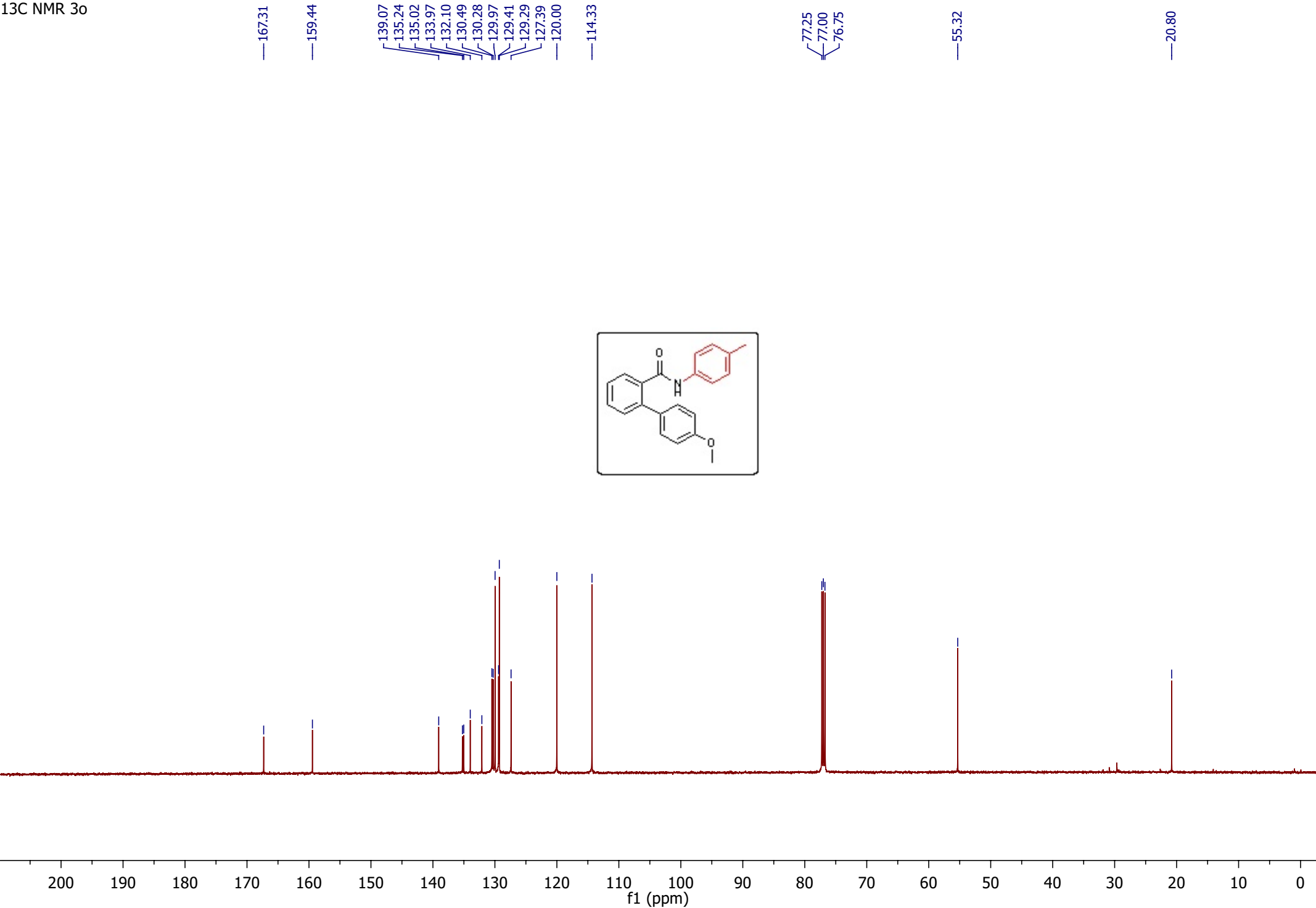


¹³C NMR 3n

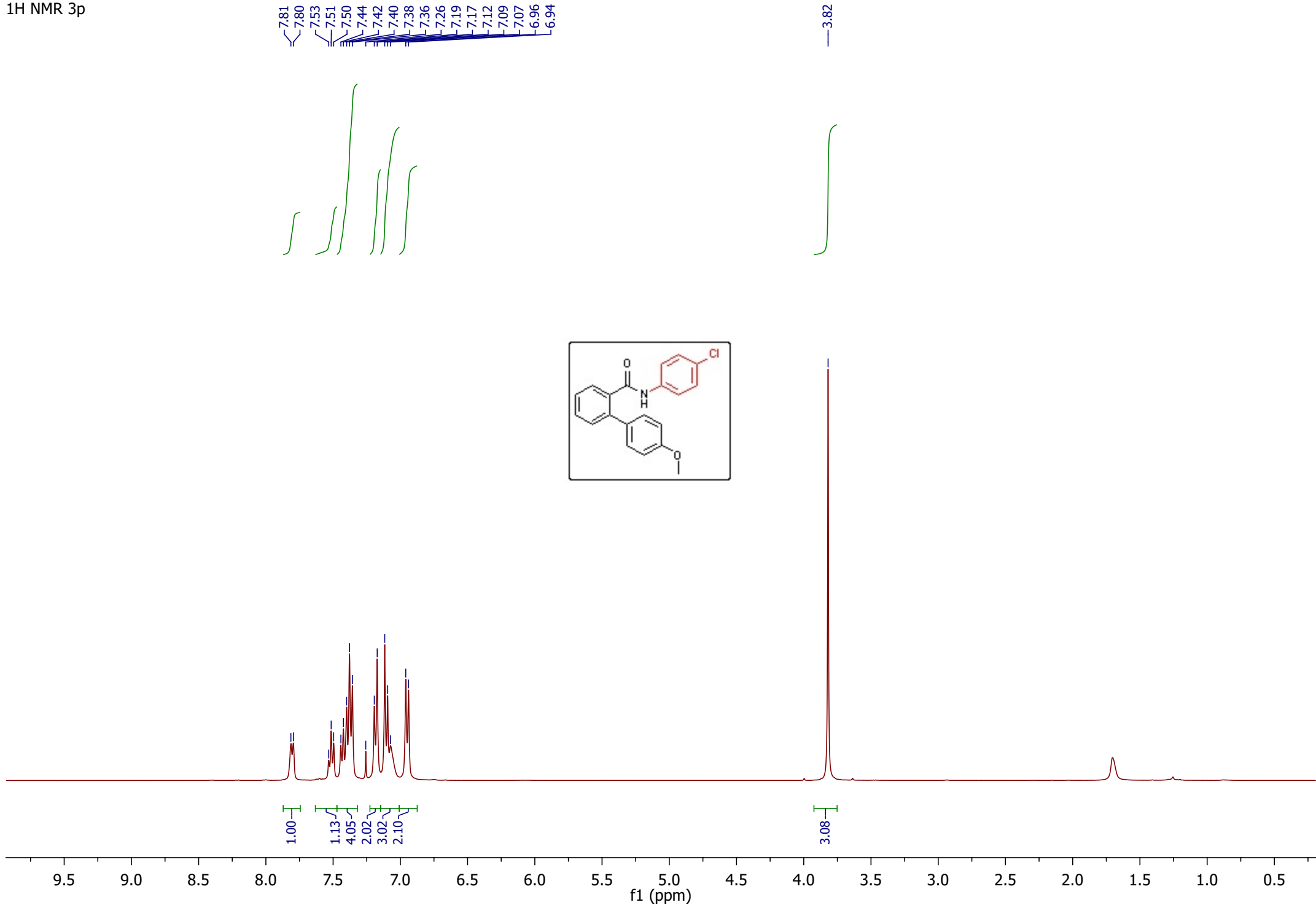


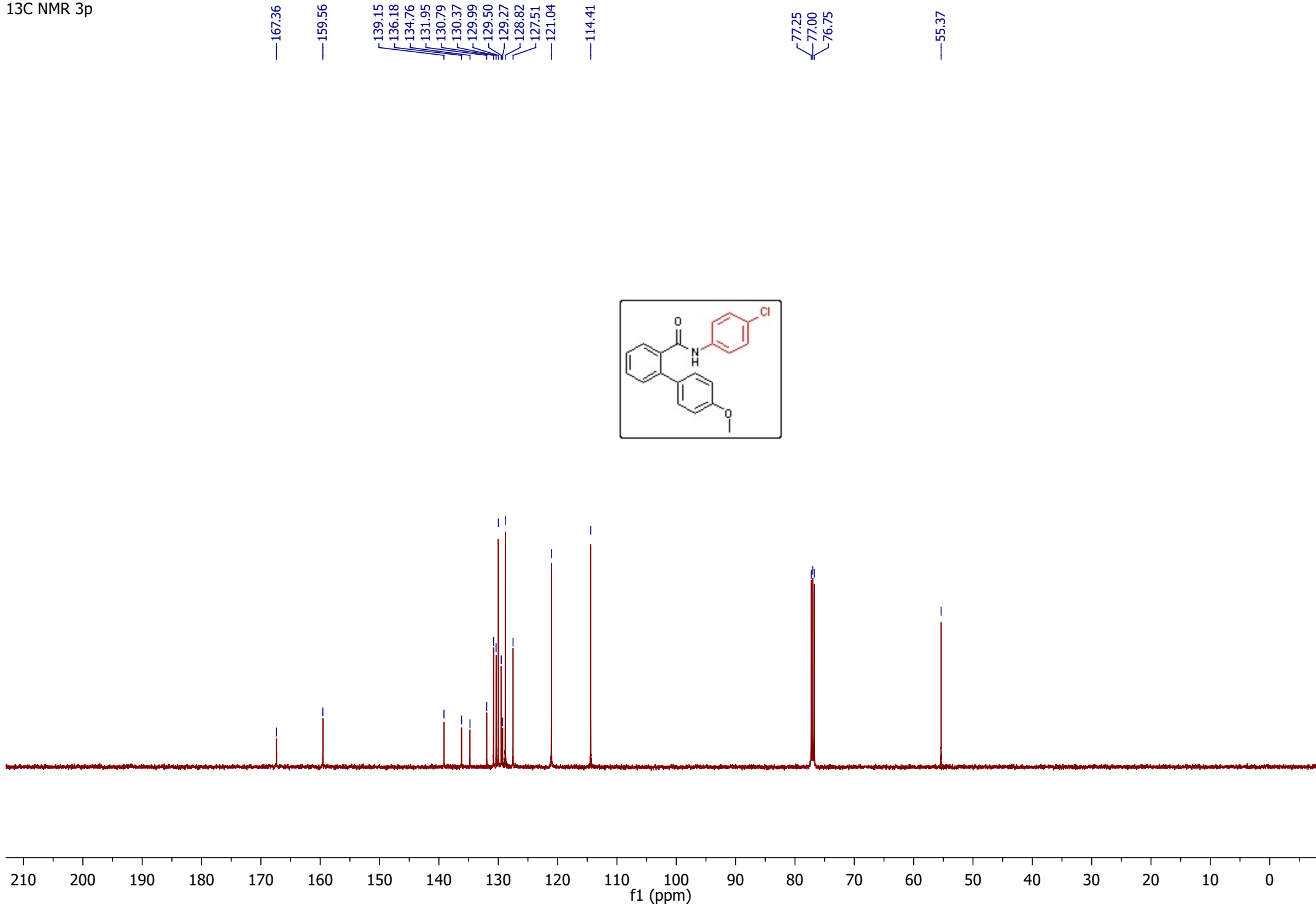


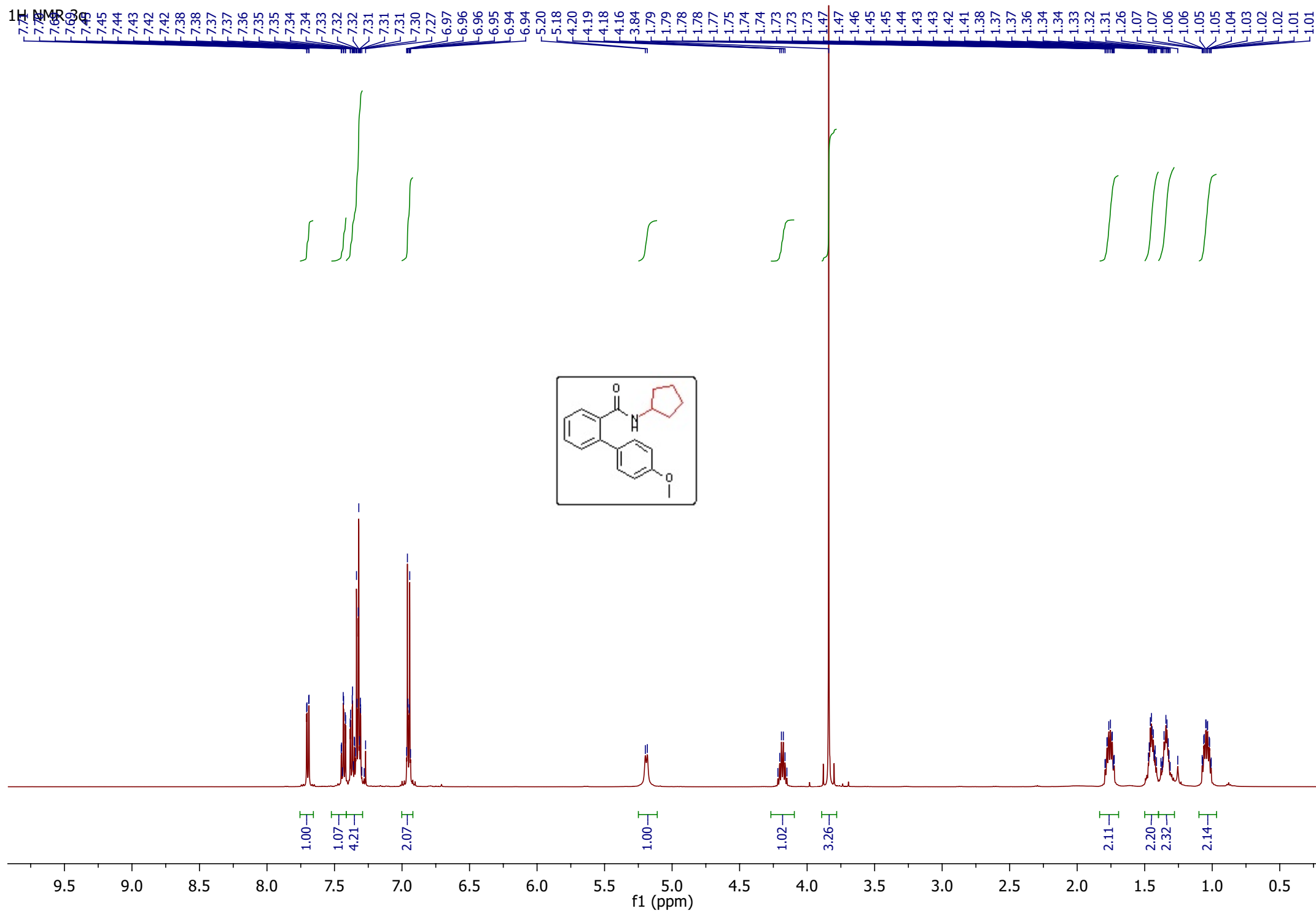
13C NMR 3o



1H NMR 3p

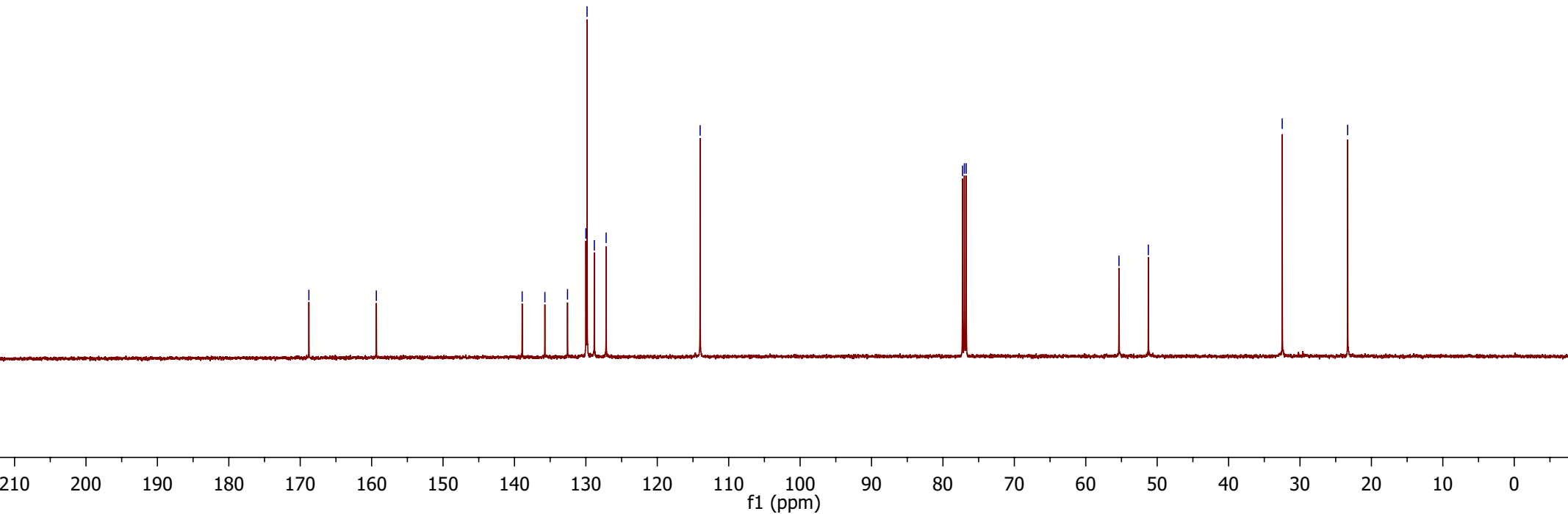
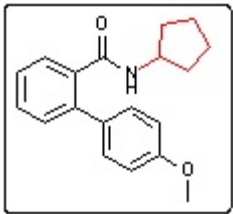




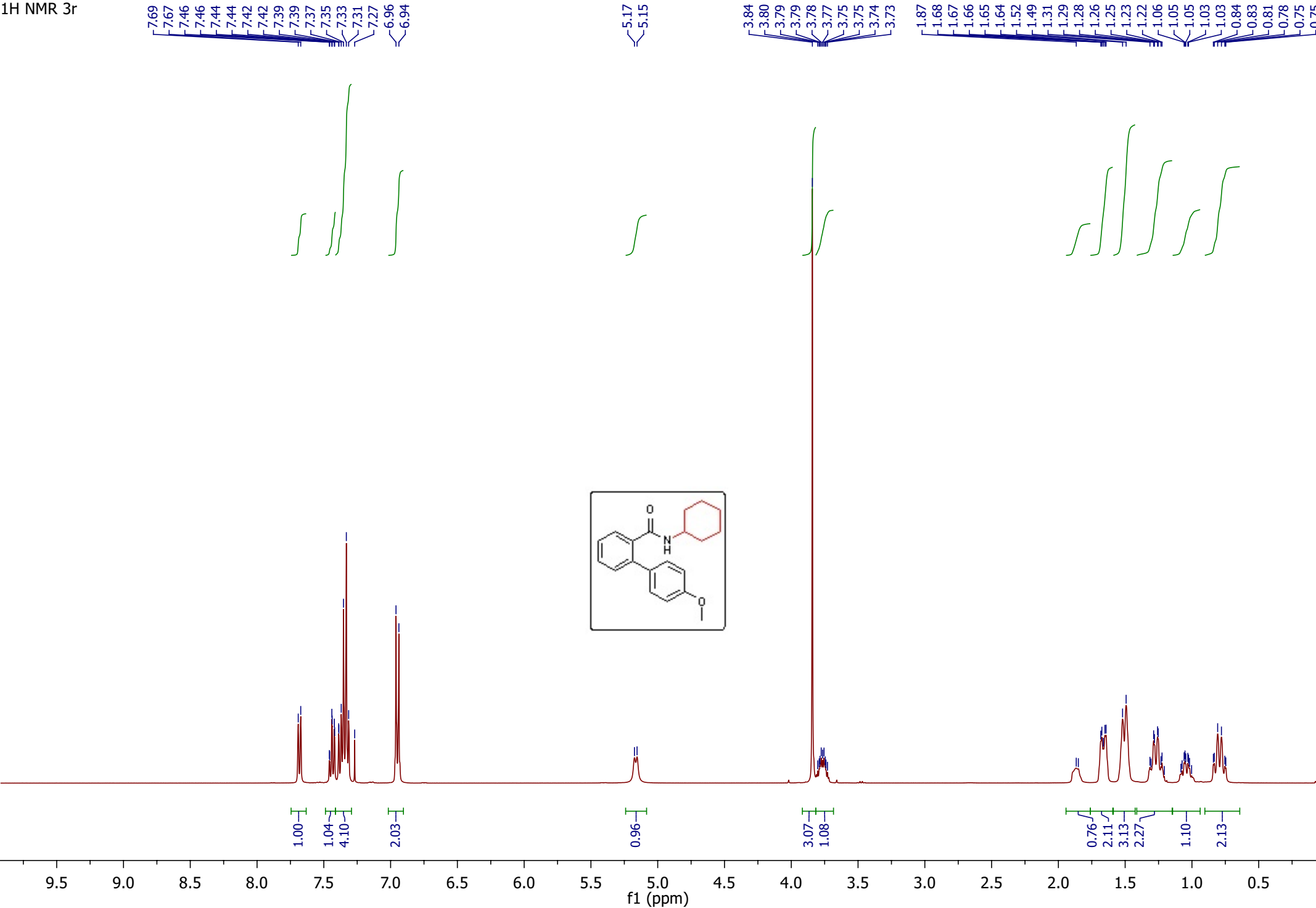


13C NMR 3q

168.79 159.34 138.92 135.74 132.57 130.00 129.84 128.82 127.16 114.00 77.25 77.00 76.75 55.35 51.24 32.49 23.33

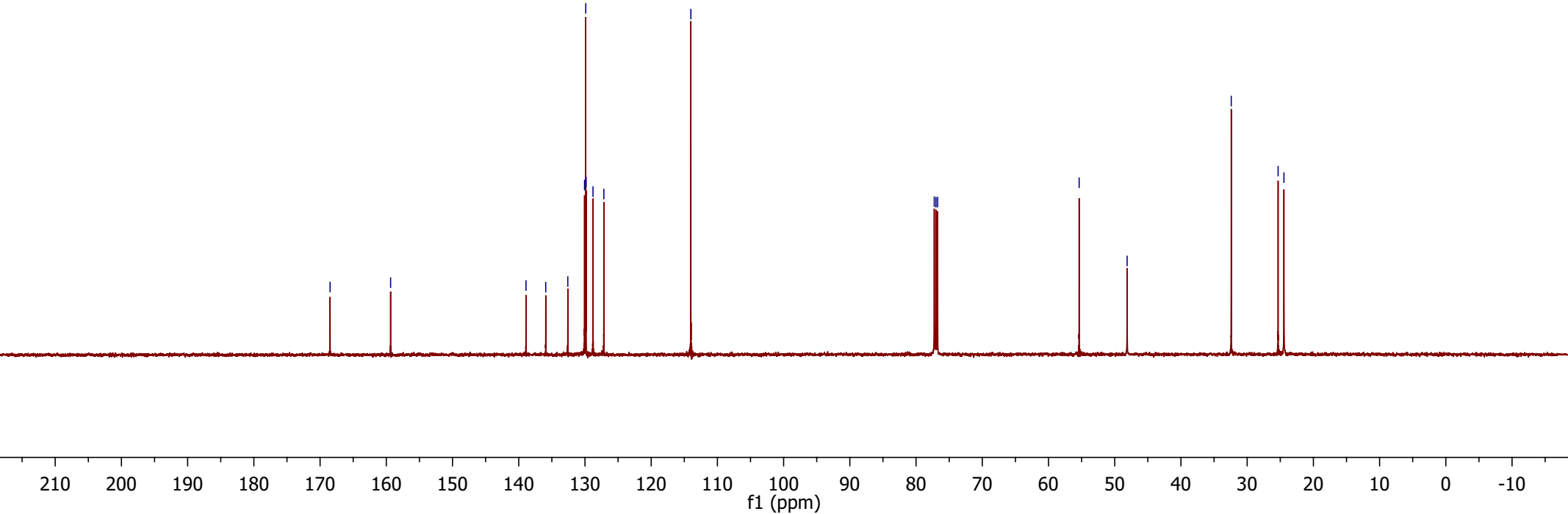
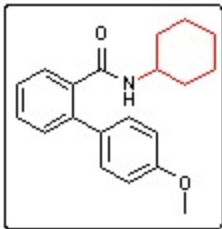


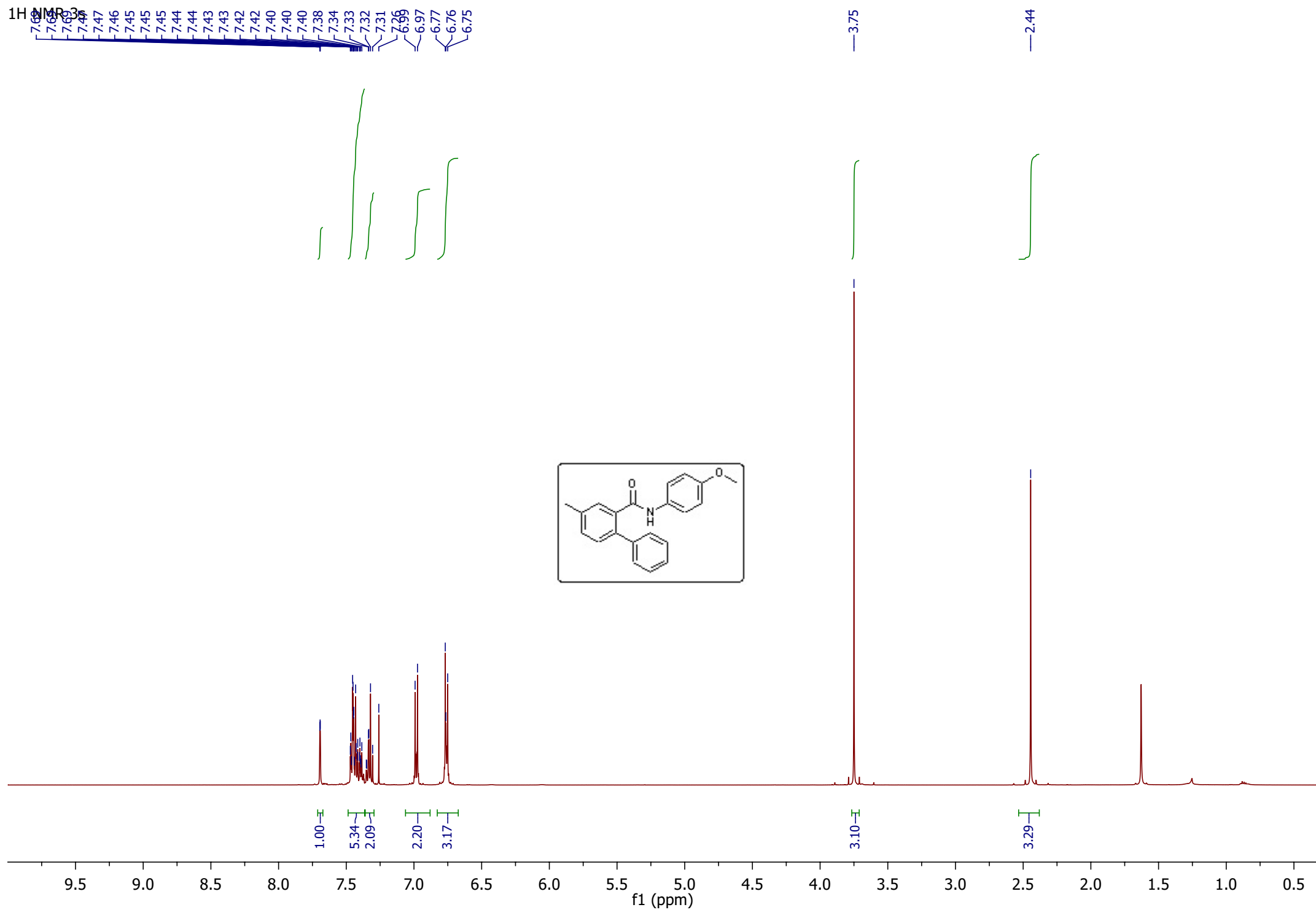
1H NMR 3r



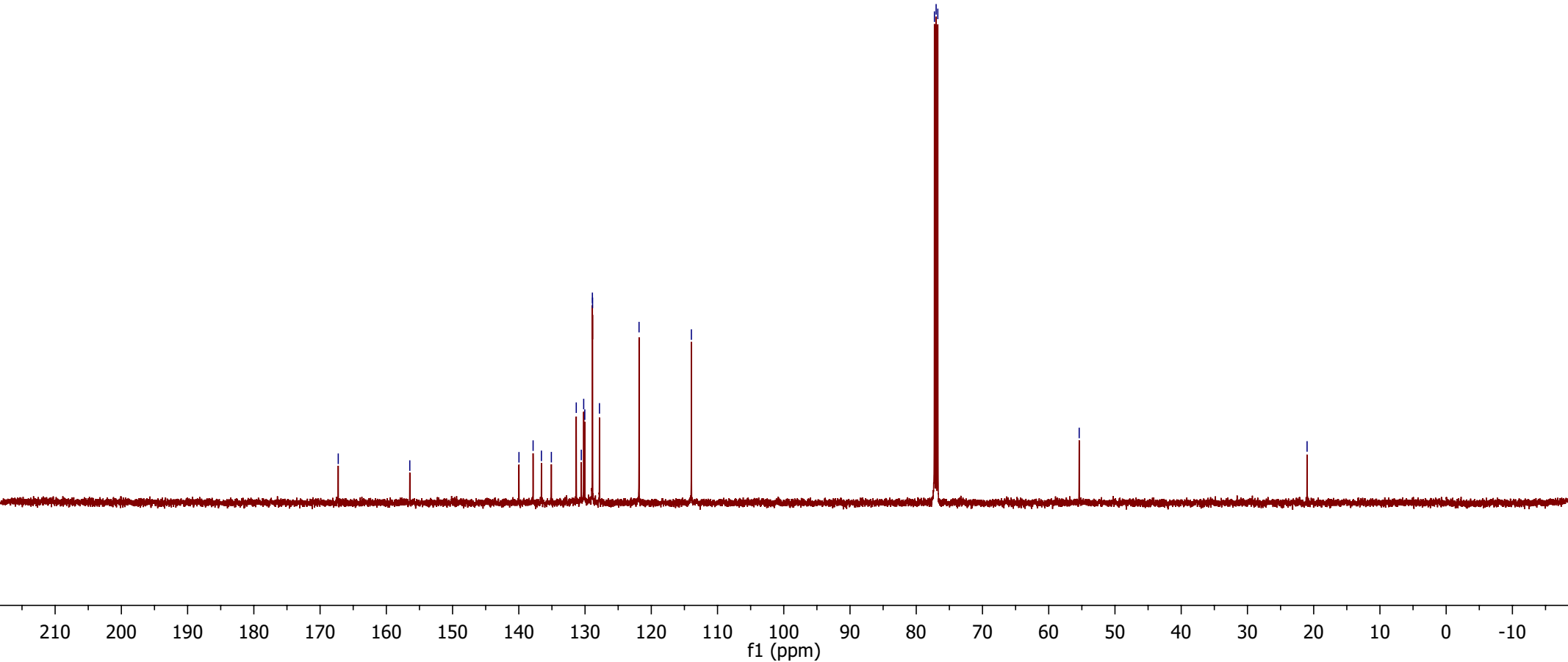
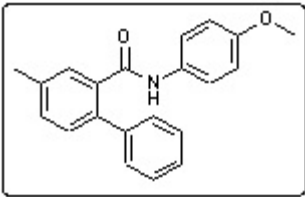
13C NMR 3r

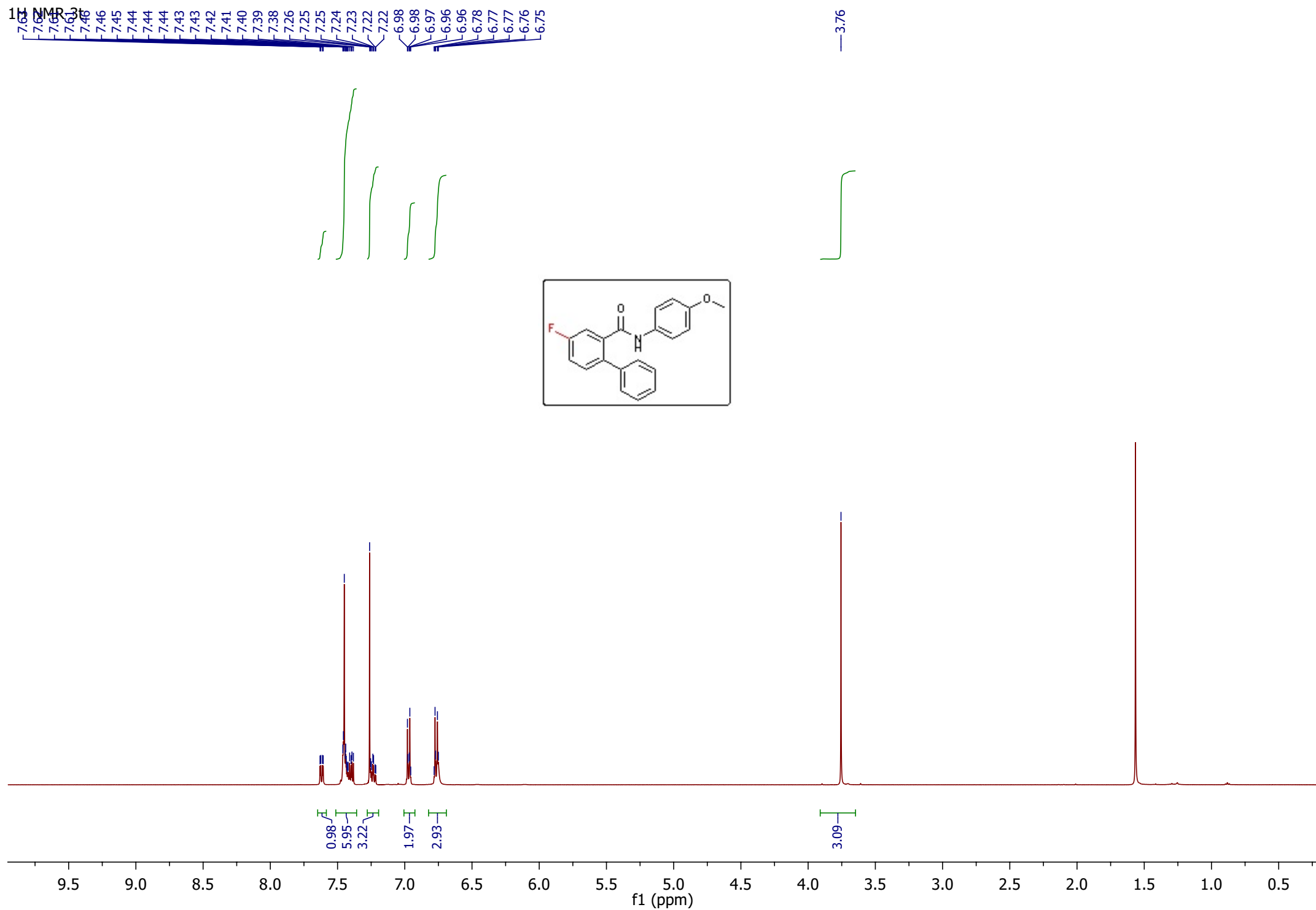
168.49 159.35 138.91 135.92 132.59 130.06 129.88 129.83 128.78 127.15 114.01 77.25 77.00 76.75 55.37 48.13 32.40 25.33 24.45





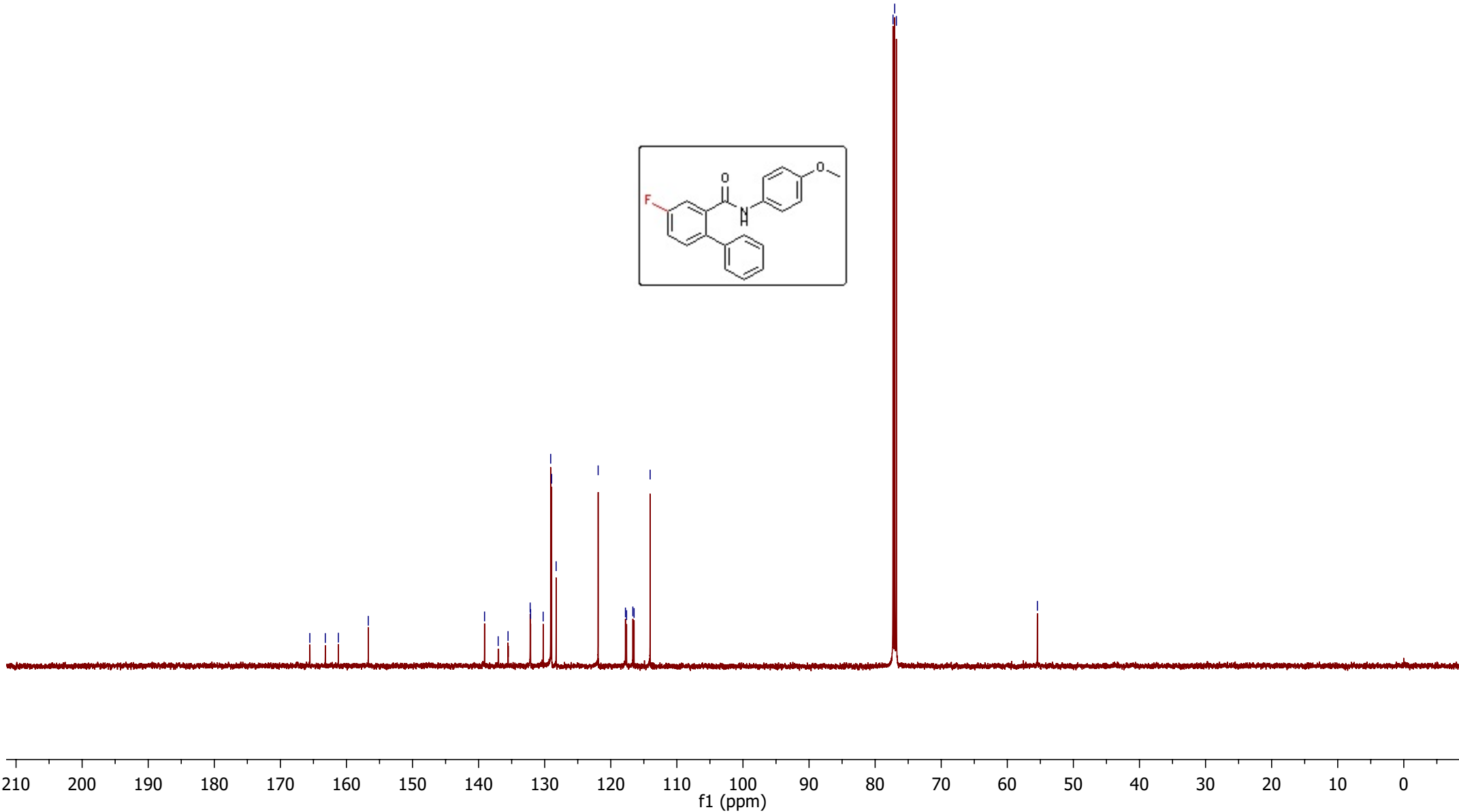
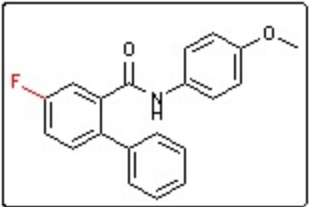
¹³C NMR 3s





¹³C NMR 3t

165.54
163.20
161.22
156.70
139.10
137.04
135.55
132.20
132.14
130.23
129.10
128.95
128.27
121.92
117.78
117.61
116.66
116.48
114.05
77.29
77.04
76.78
55.45



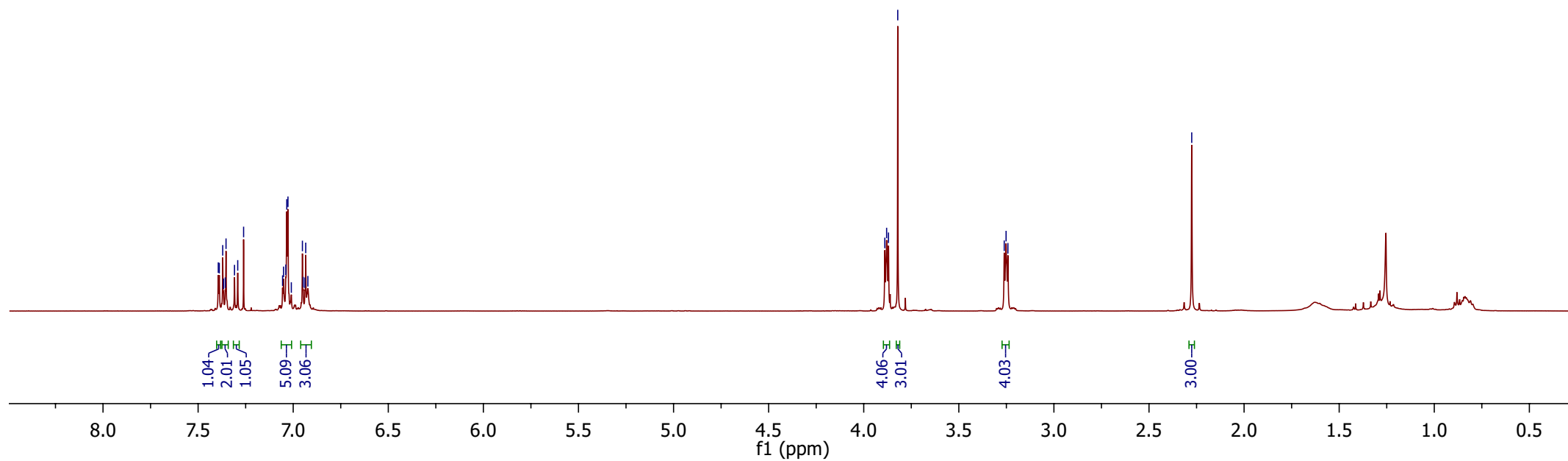
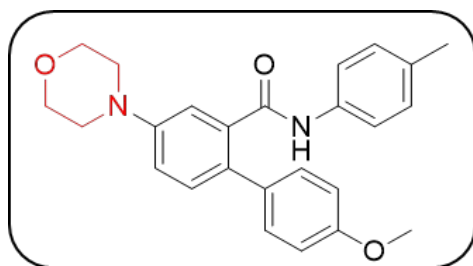
¹H NMR 3

7.39
7.39
7.37
7.37
7.36
7.35
7.31
7.29
7.26
7.06
7.05
7.04
7.03
7.01
6.95
6.95
6.94
6.93
6.92

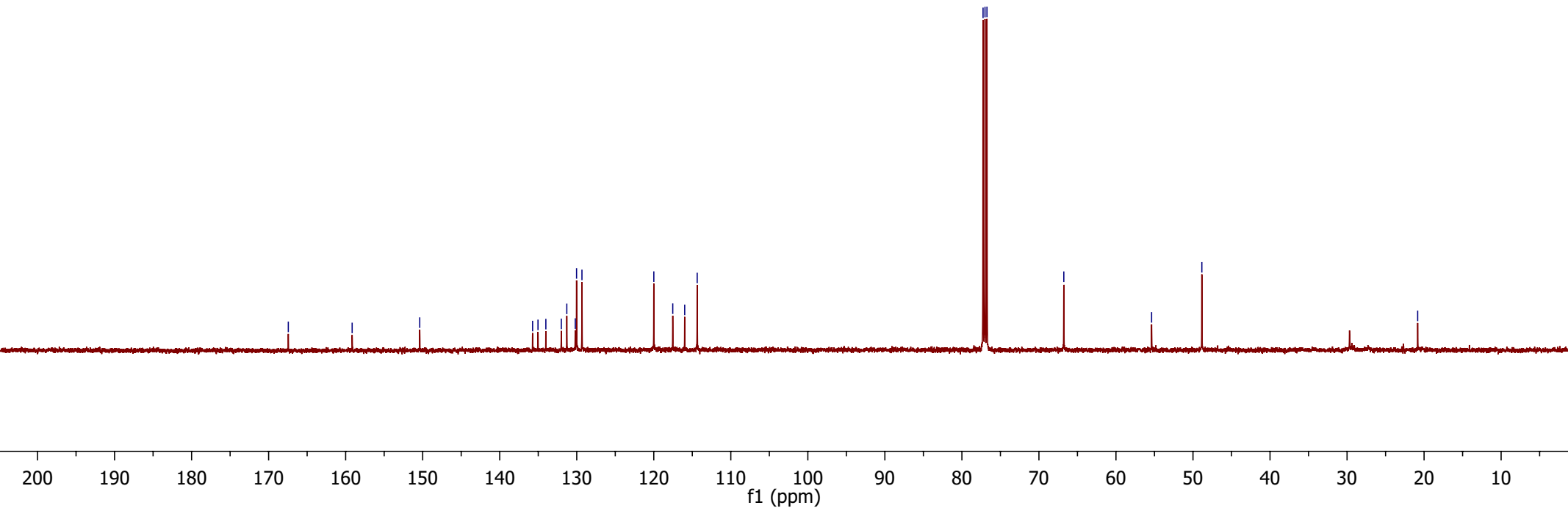
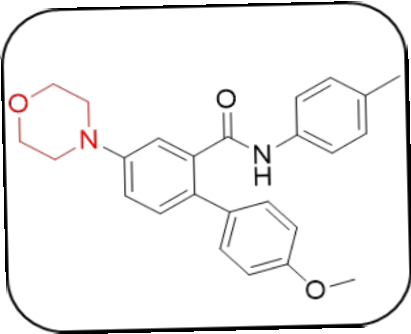
3.89
3.88
3.87
3.82

3.26
3.25
3.24

2.28



¹³C NMR 3u

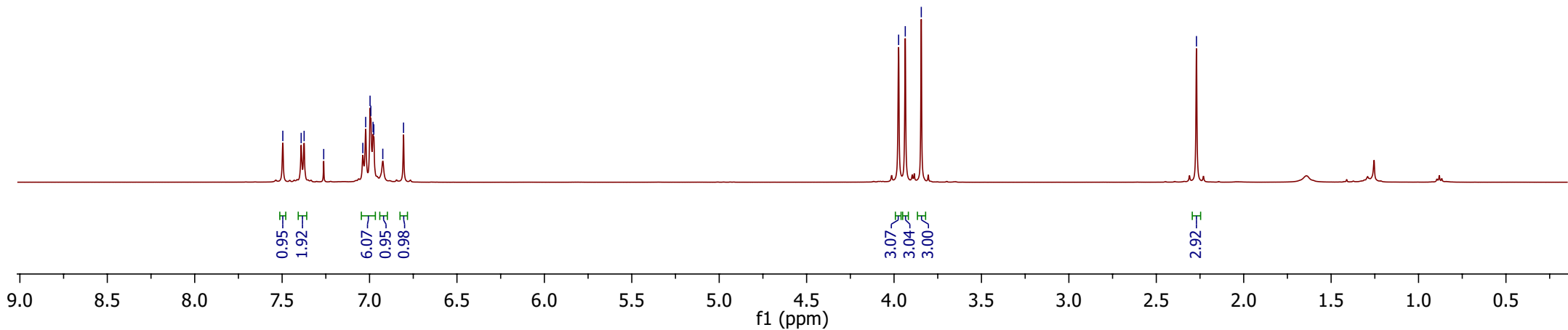
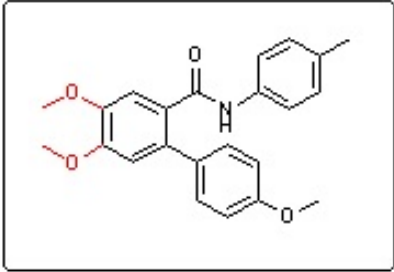


1H NMR 3v

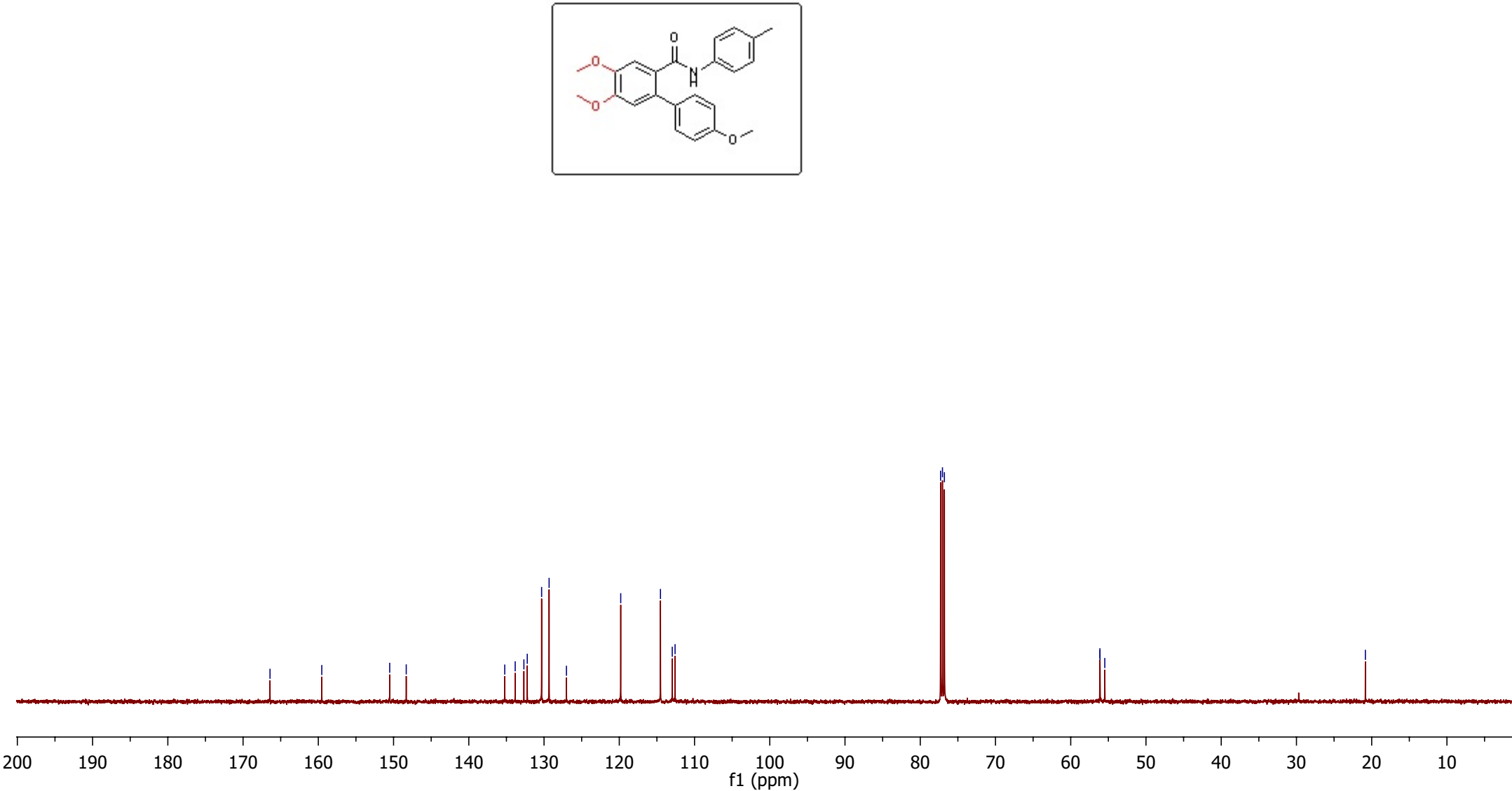
7.50
7.39
7.37
7.26
7.04
7.02
7.00
6.99
6.98
6.98
6.92
6.81

3.97
3.94
3.84

2.27

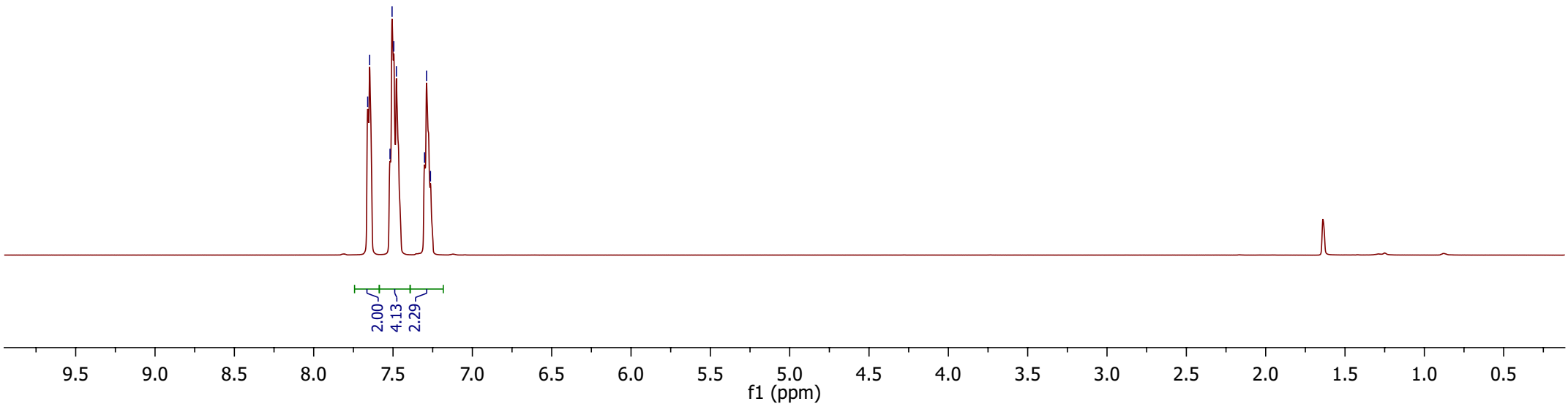
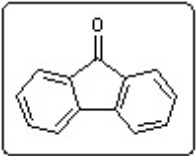
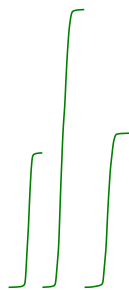


13 C NMR 3v



1H NMR 7a

7.66
7.65
7.52
7.51
7.50
7.48
7.30
7.29
7.26



13C NMR 7a

193.93

144.39

134.66

134.10

129.04

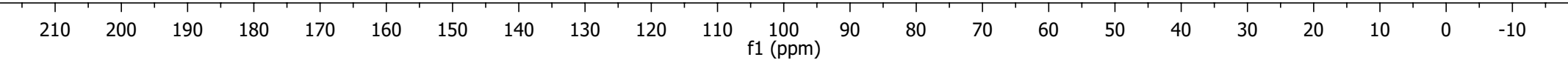
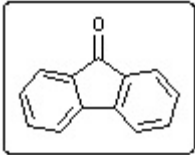
124.28

120.28

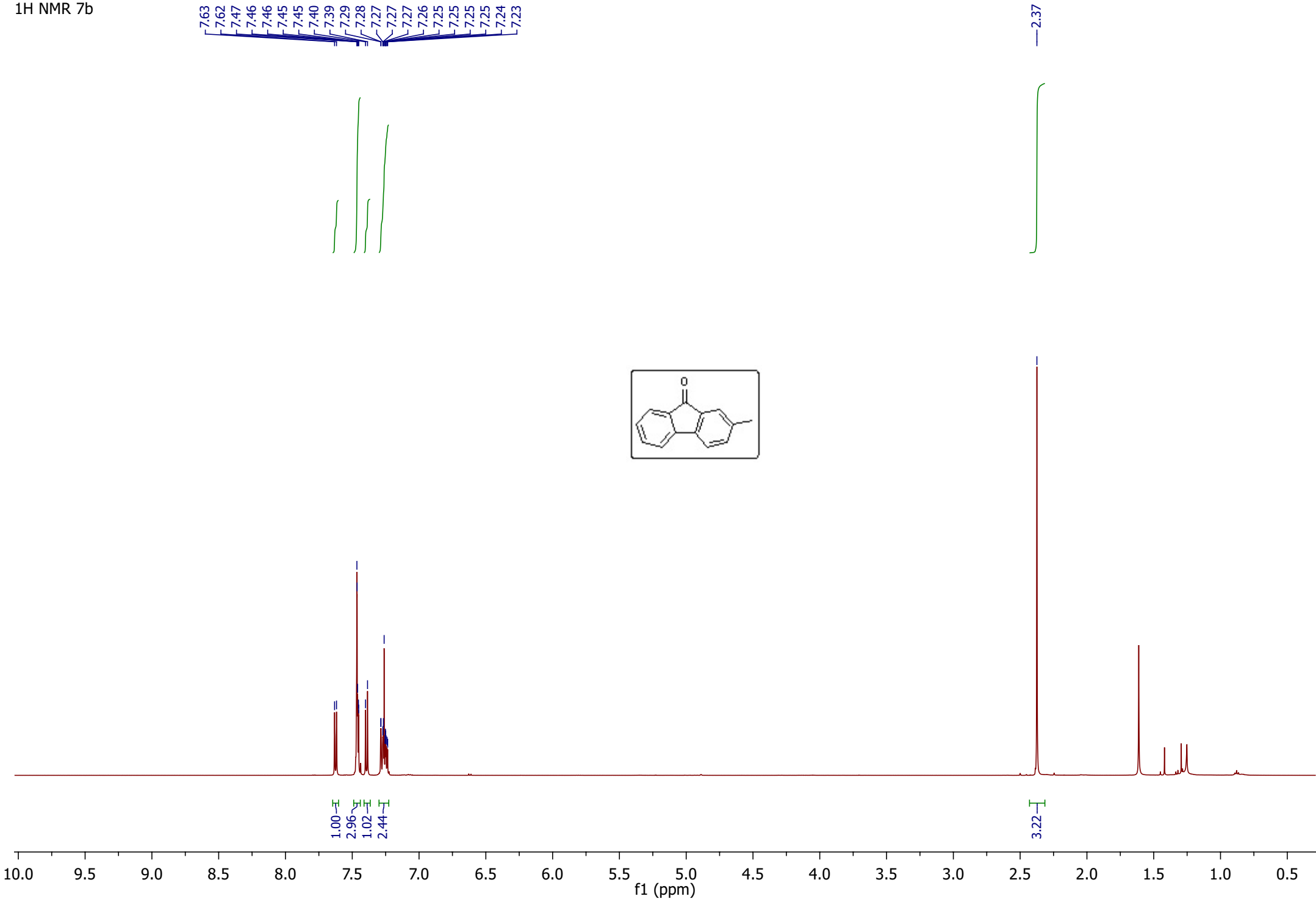
77.25

77.00

76.75



1H NMR 7b

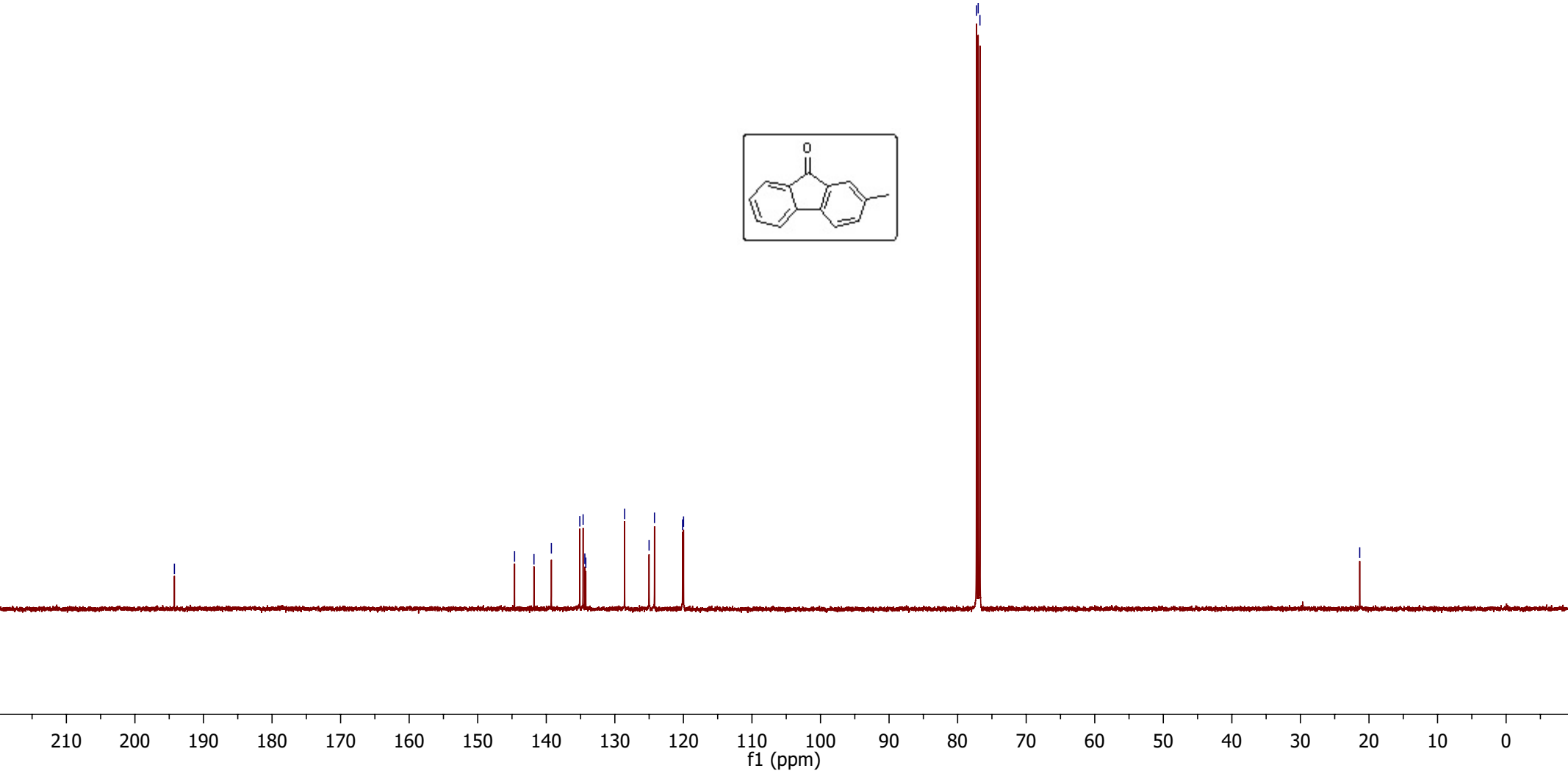
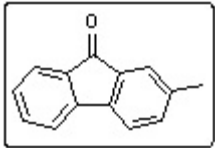


194.24

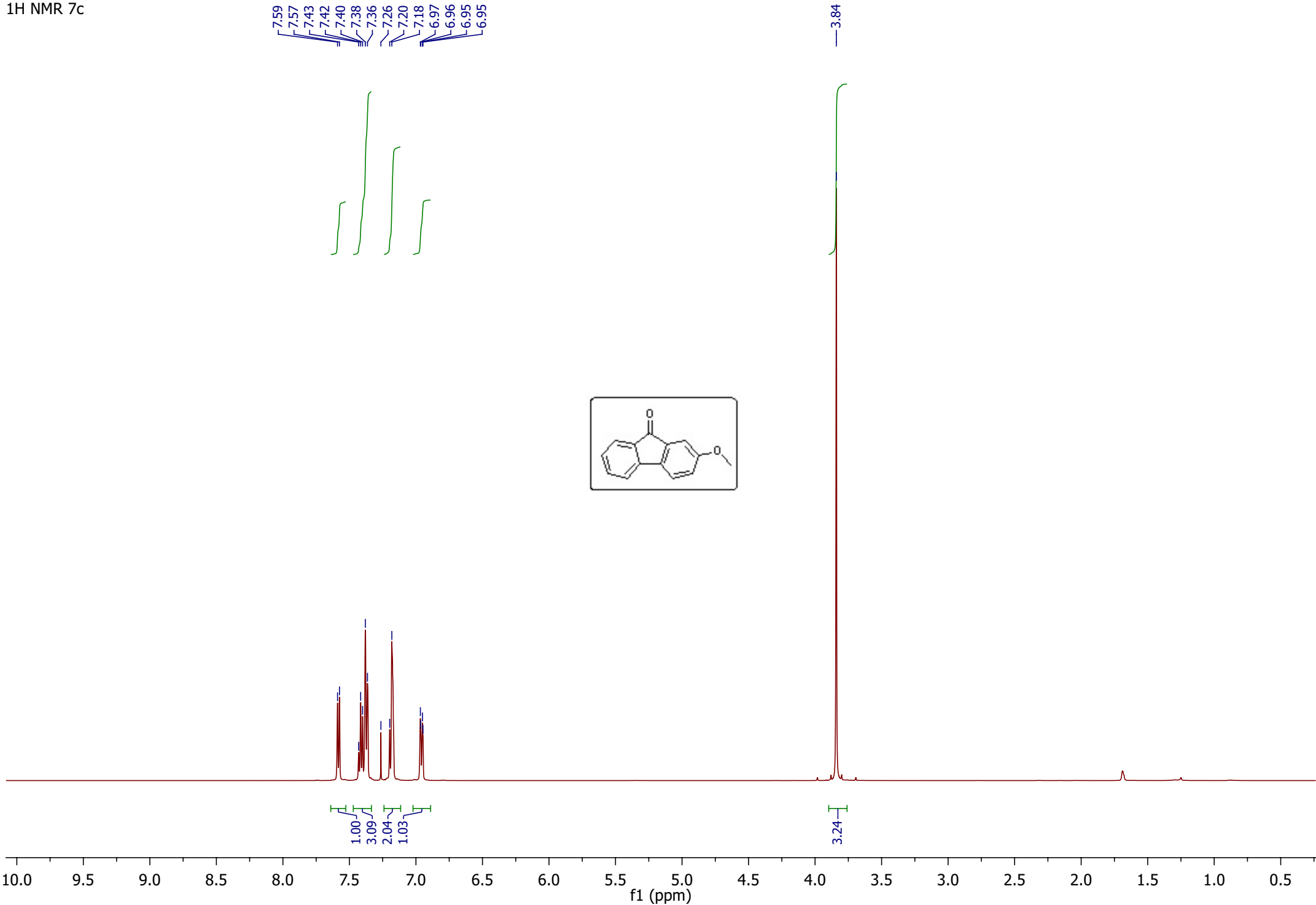
144.63
141.80
139.26
135.11
134.63
134.37
134.23
128.57
125.01
124.22
120.12
119.98

77.25
77.00
76.75

21.35



1H NMR 7c



¹³C NMR 7c

—193.78

—160.74

—144.79

136.89

135.80

134.77

134.21

127.78

124.22

121.26

120.14

119.50

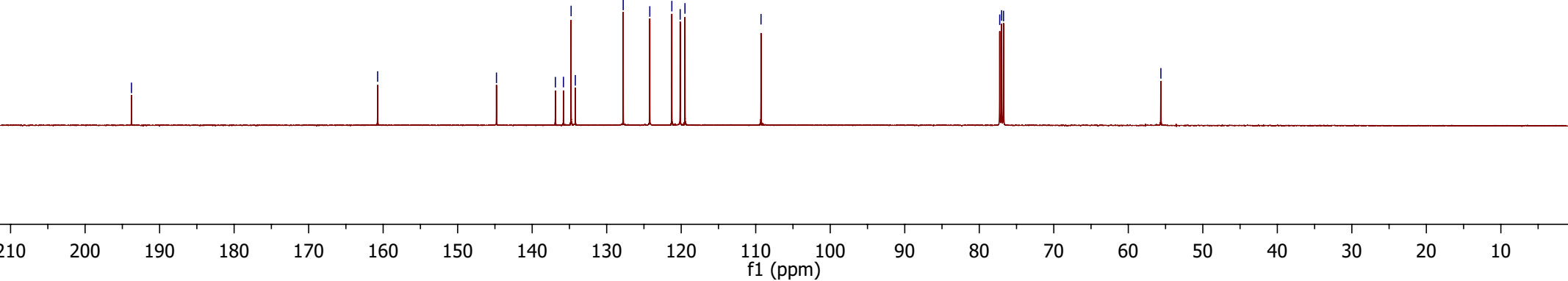
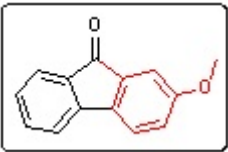
—109.29

77.25

77.00

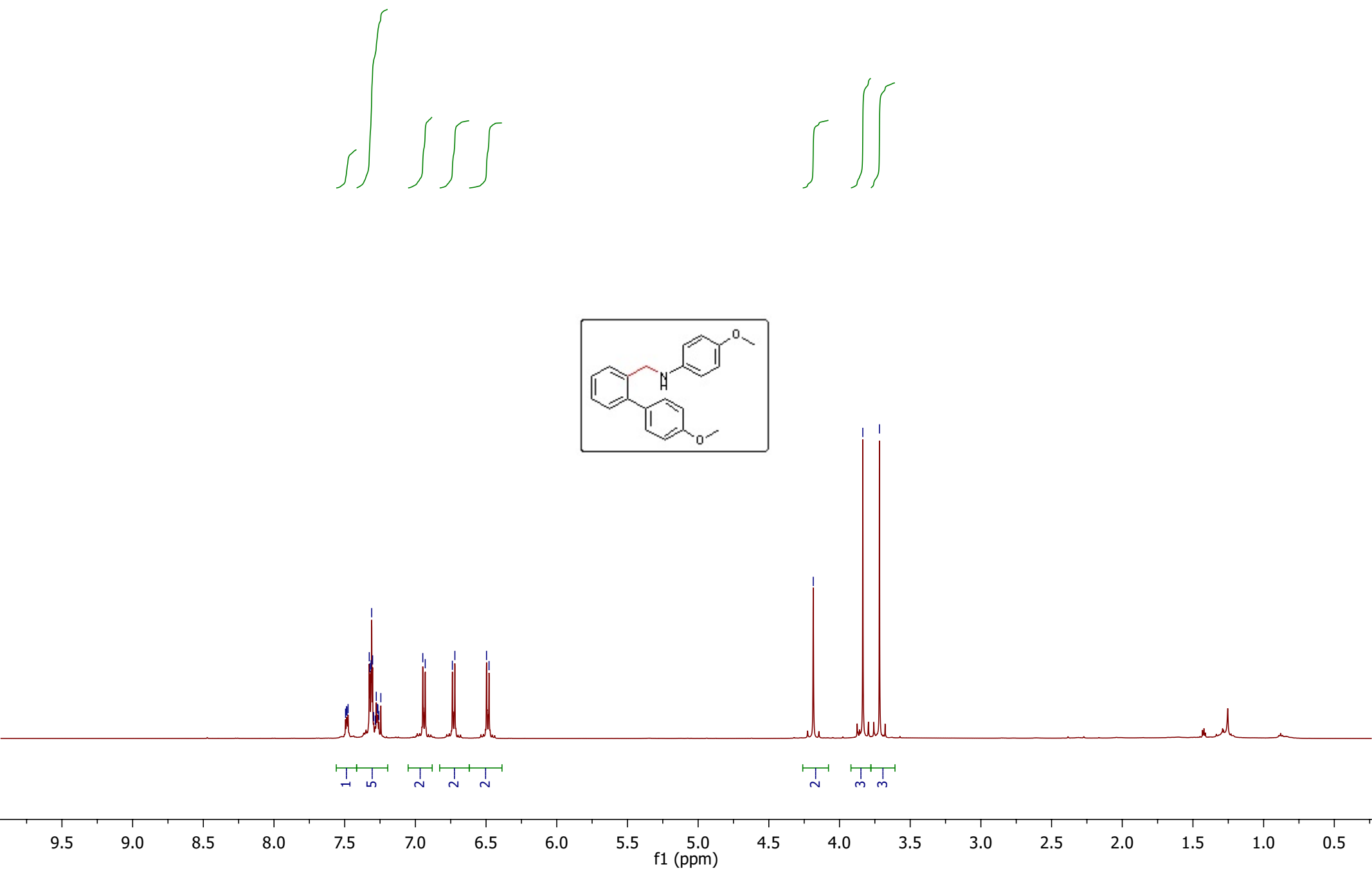
76.75

—55.63



1H NMR 8

7.49 7.49 7.48 7.48 7.33 7.32 7.31 7.31 7.30 7.30 7.28 7.28 7.27 7.27 7.26 7.24 6.95 6.93 6.74 6.72 6.50 6.48 4.19 3.84 3.72



13C NMR 8

158.79 152.07 142.20 141.35 136.66 133.22 130.31 130.08 128.78 127.35 127.21 114.75 114.15 113.69 77.25 77.00 76.75 55.76 55.26 47.20

