

## Synthesis and antimutagenic activity of novel 5-aminoisoxazoles bearing alkoxyaryl moieties

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### 1. Chemistry

NMR spectra were recorded on Agilent 400-MR spectrometer (400.0 MHz for  $^1\text{H}$ ; 100.6 MHz for  $^{13}\text{C}$ ) at room temperature; chemical shifts were measured with reference to the solvent ( $\text{CDCl}_3$ ,  $\delta_{\text{H}} = 7.24$  ppm,  $\delta_{\text{C}} = 77.0$  ppm). Chemical shifts ( $\delta$ ) are given in ppm;  $J$  values are given in Hz. When necessary, assignments of signals in NMR spectra were made using 2D techniques. Accurate mass measurements (HRMS) were measured on JEOL GCMate II mass spectrometer (70 eV). Analytical thin layer chromatography was carried out with Silufol silica gel plates; the detection was done by UV lamp (254 and 365 nm). Column chromatography was performed on silica gel (230–400 mesh, Merck). X-ray data were collected on STADI VARI Pilatus-100 K diffractometer [1]. For structure solving and refinement the software package SHELX-97 and SHELXL-2014 [2] were used. The drawings were created with the PLATON program [3].

Starting benzylic alcohols were synthesized as described [4, 5]. All other starting materials were commercially available. All solvents were purified by standard procedures prior to use.

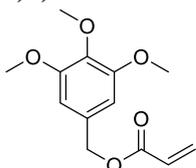
#### 1.1. General procedure for the preparation of compounds **2a-f**, **4a**, **4b**

**GPI.** To a solution of starting alcohol (2.5 mmol) in dichloromethane (2 mL) was added  $\text{Et}_3\text{N}$  (0.35 mL, 250 mg, 2.5 mmol) under argon. The mixture was cooled to 0...–5 °C and acryloyl chloride (0.2 mL, 226 mg, 2.5 mmol) in dichloromethane (2 mL) was added dropwise. The

resulting mixture was stirred at this temperature for 1 h and then at room temperature for 24 h. The mixture was poured into water (10 mL) and extracted with dichloromethane (4×10 mL). The combined organic layer was washed with brine (3×10 mL) and was dried over anhydrous MgSO<sub>4</sub>. The solvent was evaporated *in vacuo*; the residue was purified by preparative column chromatography on silica gel.

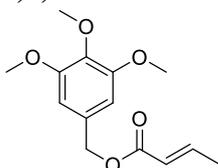
**GP2.** To a solution of starting alcohol (2.5 mmol) in dichloromethane (5 mL) was added pyridine (0.20 mL, 200 mg, 2.5 mmol) under argon. The mixture was cooled to −5...−10 °C and then crotonoyl chloride (0.2 mL, 226 mg, 2.5 mmol) in dichloromethane (2 mL) was added dropwise. The work-up of resulting mixture was carrying out as described above (GP1).

### 3,4,5-Trimethoxybenzyl acrylate (2a)



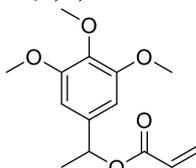
Obtained by **GP1** as colorless oil (0.44 g, 70 %); R<sub>f</sub> 0.22 (petroleum ether:EtOAc 10:1). δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>): 3.81 (s, 3H, OCH<sub>3</sub>), 3.83 (s, 6H, 2OCH<sub>3</sub>), 5.09 (s, 2H, CH<sub>2</sub>), 5.83 (dd, <sup>2</sup>J = 1.5 Hz, <sup>3</sup>J = 10.4 Hz, 1H, =CH<sub>2</sub>), 6.14 (dd, <sup>3</sup>J = 10.4 Hz, <sup>3</sup>J = 17.4 Hz, 1H, =CHCO), 6.42 (dd, <sup>2</sup>J = 1.5 Hz, <sup>3</sup>J = 17.4 Hz, 1H, =CH<sub>2</sub>), 6.57 (s, 2H, 2CH(Ar)); δ<sub>C</sub> (101 MHz, CDCl<sub>3</sub>): 56.1 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>), 66.6 (CH<sub>2</sub>), 105.5 (2CH(Ar)), 128.3 (=CH), 131.2 (C(Ar)), 131.4 (=CH<sub>2</sub>), 138.0(C(Ar)), 153.3 (2C(Ar)), 166.0 (C=O). HRMS (ESI, m/z): calcd for C<sub>13</sub>H<sub>16</sub>O<sub>5</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 275.0890; found 275.0898.

### 3,4,5-Trimethoxybenzyl (2E)-but-2-enoate (2b)



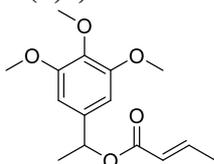
Obtained by **GP2** as colorless oil (0.35 g, 59 %); R<sub>f</sub> 0.22 (petroleum ether:EtOAc 10:1); δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>): 1.81 (dd, <sup>3</sup>J = 6.9 Hz, <sup>4</sup>J = 1.7 Hz, 3H, CH<sub>3</sub>), 3.76 (s, 3H, OCH<sub>3</sub>), 3.78 (s, 6H, 2OCH<sub>3</sub>), 5.01 (s, 2H, CH<sub>2</sub>), 5.82 (dq, <sup>3</sup>J = 15.6, <sup>4</sup>J = 1.7 Hz, 1H, =CH), 6.53 (s, 2H, 2CH(Ar)), 6.95 (dq, <sup>3</sup>J = 6.9 Hz, <sup>3</sup>J = 15.6 Hz, 1H, =CH). δ<sub>C</sub> (101 MHz, CDCl<sub>3</sub>): 17.9 (CH<sub>3</sub>), 56.0 (2OCH<sub>3</sub>), 60.7 (OCH<sub>3</sub>), 66.1 (CH<sub>2</sub>O), 105.4 (2CH(Ar)), 122.4 (=CH(CO)), 131.7 (C(Ar)), 137.9 (C(Ar)), 145.1 (=CH(CH<sub>3</sub>)), 153.2 (2C(Ar)), 166.1 (C=O). HRMS (ESI, m/z): calcd for C<sub>14</sub>H<sub>18</sub>O<sub>5</sub>K<sup>+</sup> [M+K]<sup>+</sup> 305.0786; found 304.0778.

### 1-(3,4,5-Trimethoxyphenyl)ethyl acrylate (2c)



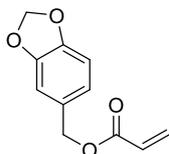
Obtained by **GP1** as colorless oil (0.43 g, 64 %); R<sub>f</sub> 0.24 (petroleum ether:EtOAc 10:1); δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>): 1.58 (d, <sup>3</sup>J = 6.6 Hz, 3H, CH<sub>3</sub>), 3.85 (s, 3H, OCH<sub>3</sub>), 3.88 (s, 6H, 2OCH<sub>3</sub>), 5.85 (dd, <sup>2</sup>J = 1.5 Hz, <sup>3</sup>J = 10.4 Hz, 1H, =CH<sub>2</sub>), 5.91 (q, <sup>3</sup>J = 6.6 Hz, 1H, CH), 6.17 (dd, <sup>3</sup>J = 10.4 Hz, <sup>3</sup>J = 17.4 Hz, 1H, =CHCO), 6.44 (dd, <sup>2</sup>J = 1.5 Hz, <sup>3</sup>J = 17.4 Hz, 1H, =CH<sub>2</sub>), 6.61 (s, 2H, 2CH(Ar)). δ<sub>C</sub> (101 MHz, CDCl<sub>3</sub>): 22.2 (CH<sub>3</sub>), 56.1 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>), 72.6 (OCH), 103.2 (2CH(Ar)), 128.7 (=CH), 130.9 (=CH<sub>2</sub>), 137.2 (C(Ar)), 137.6 (C(Ar)), 153.2 (2C(Ar)), 165.4 (C=O). HRMS (ESI, m/z): calcd for C<sub>14</sub>H<sub>18</sub>O<sub>5</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 289.1046; found 289.1046.

### 1-(3,4,5-Trimethoxyphenyl)ethyl (2E)-but-2-enoate (2d)



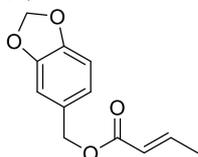
Obtained by **GP2** as colorless oil (0.24 g, 34 %); *R<sub>f</sub>* 0.54 (petroleum ether:EtOAc 10:1);  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 1.55 (d,  $^3J = 6.6$  Hz, 3H, CH<sub>3</sub>), 1.89 (dd,  $^3J = 6.9$  Hz,  $^4J = 1.7$  Hz, 3H, CH<sub>3</sub>), 3.83 (s, 3H, OCH<sub>3</sub>), 3.87 (s, 6H, 2OCH<sub>3</sub>), 5.87 (q,  $^3J = 6.6$  Hz, 1H, -CH), 5.89 (dq,  $^3J = 15.6$ ,  $^4J = 1.7$  Hz, 1H, =CH), 6.59 (s, 2H, 2CH(Ar)), 7.01 (dq,  $^3J = 6.9$  Hz,  $^3J = 15.5$  Hz, 1H, =CH(CH<sub>3</sub>)).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 18.0 (CH<sub>3</sub>), 22.2 (CH<sub>3</sub>), 56.1 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>), 72.1 (CHO), 103.1 (2CH(Ar)), 122.8 (=CH), 137.47 (C(Ar)), 137.50 (C(Ar)), 145.0 (=CH), 153.2 (2C(Ar)), 165.7 (C=O). HRMS (ESI, *m/z*): calcd for C<sub>15</sub>H<sub>24</sub>O<sub>5</sub>N<sup>+</sup> [M+NH<sub>4</sub>]<sup>+</sup> 298.1649; found 298.1647.

### (1,3-Benzodioxol-5-yl)methyl acrylate (2e)



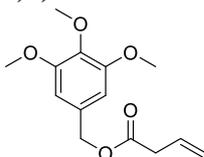
Obtained by **GPI** as colorless oil (0.34 g, 66 %); *R<sub>f</sub>* 0.68 (petroleum ether:EtOAc 10:1);  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 5.07 (s, 2H, OCH<sub>2</sub>), 5.82 (dd,  $^2J = 1.5$  Hz,  $^3J = 10.5$  Hz, 1H, =CH<sub>2</sub>), 5.94 (s, 2H, OCH<sub>2</sub>O), 6.12 (dd,  $^3J = 10.5$  Hz,  $^3J = 17.5$  Hz, 1H, =CHCO), 6.41 (dd,  $^2J = 1.5$  Hz,  $^3J = 17.5$  Hz, 1H, =CH<sub>2</sub>), 6.75-6.79 (m, 1H, CH(Ar)), 6.82-6.87 (m, 2H, 2CH(Ar)).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 66.3 (OCH<sub>2</sub>), 101.1 (OCH<sub>2</sub>O), 108.2 (CH(Ar)), 109.0 (CH(Ar)), 122.3 (CH(Ar)), 128.3 (CH=), 129.6 (C(Ar)), 131.0 (CH<sub>2</sub>=), 147.6(C(Ar)), 147.8 (C(Ar)), 166.0 (C=O). HRMS (ESI, *m/z*): calcd for C<sub>11</sub>H<sub>10</sub>O<sub>4</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 229.0471; found 229.0478.

### (1,3-Benzodioxol-5-yl)methyl (2E)-but-2-enoate (2f)



Obtained by **GP2** as colorless oil (0.21 g, 39 %); *R<sub>f</sub>* 0.70 (petroleum ether:EtOAc 10:1);  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 1.81 (d,  $^3J = 6.9$  Hz, 3H, CH<sub>3</sub>), 5.01 (s, 2H, OCH<sub>2</sub>), 5.82 (d,  $^3J = 15.5$  Hz, 1H, CH=), 5.88 (s, 2H, OCH<sub>2</sub>O), 6.69-6.75 (m, 1H, CH(Ar)), 6.76-6.84 (m, 2H, 2CH(Ar)), 6.95 (dq,  $^3J = 15.5$ ,  $^3J = 6.9$  Hz, 1H, CH=).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 17.9 (CH<sub>3</sub>), 65.8 (OCH<sub>2</sub>), 101.1 (OCH<sub>2</sub>O), 108.1 (CH(Ar)), 108.9 (CH(Ar)), 122.1 (CH(Ar)), 122.5 (CH=), 129.9 (C(Ar)), 145.0 (CH=), 147.5 (C(Ar)), 147.7 (C(Ar)), 166.2 (C=O). HRMS (ESI, *m/z*): calcd for C<sub>12</sub>H<sub>12</sub>O<sub>4</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 243.0628; found 243.0637.

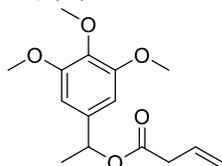
### 3,4,5-Trimethoxybenzyl but-3-enoate (4a)



Obtained by **GPI** from crotonoyl chloride (0.2 mL, 226 mg, 2.5 mmol) as colorless oil (0.54 g, 85 %); *R<sub>f</sub>* 0.40 (petroleum ether:EtOAc 10:1);  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 3.14-3.19 (m, 2H, CH<sub>2</sub>), 3.85 (s, 3H, OCH<sub>3</sub>), 3.88 (s, 6H, 2OCH<sub>3</sub>), 5.07 (s, 2H, CH<sub>2</sub>), 5.16-5.20 (m, 1H, =CH<sub>2</sub>), 5.20-5.23 (m, 1H, =CH<sub>2</sub>), 5.90-6.02 (m, 1H, =CH), 6.59 (s, 2H, 2CH(Ar)).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 38.9 (CH<sub>2</sub>), 55.9 (2OCH<sub>3</sub>), 60.5 (OCH<sub>3</sub>), 66.4 (CH<sub>2</sub>O), 105.2 (2CH(Ar)), 118.5 (CH<sub>2</sub>=), 129.9 (CH=),

131.2 (C(Ar)), 137.7 (C(Ar)), 153.1 (2C(Ar)), 171.0 (C=O). HRMS (ESI, m/z): calcd for C<sub>14</sub>H<sub>18</sub>O<sub>5</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 289.1046; found 289.1044.

### 1-(3,4,5-trimethoxyphenyl)ethyl but-3-enoate (4b)

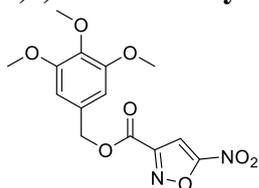


Obtained by **GPI** from crotonoyl chloride (0.2 mL, 226 mg, 2.5 mmol) as yellow oil (0.39 g, 52 %); R<sub>f</sub> 0.40 (petroleum ether:EtOAc 10:1);  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 1.54 (d, <sup>3</sup>J = 6.6 Hz, 3H, CH<sub>3</sub>), 3.11-3.15 (m, 2H, CH<sub>2</sub>), 3.84 (s, 3H, OCH<sub>3</sub>), 3.87 (s, 6H, 2OCH<sub>3</sub>), 5.14-5.17 (m, 1H, =CH<sub>2</sub>), 5.18-5.22 (m, 1H, =CH<sub>2</sub>), 5.84 (q, <sup>3</sup>J = 6.6 Hz, 1H, -CH), 5.87-6.01 (m, 1H, =CH), 6.57 (s, 2H, 2CH(Ar)).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 22.3 (CH<sub>3</sub>), 39.4 (CH<sub>2</sub>), 56.1 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>), 72.7 (CHO), 103.1 (2CH(Ar)), 118.6 (=CH<sub>2</sub>), 130.2 (=CH), 137.3 (C(Ar)), 137.5 (C(Ar)), 153.3 (2C(Ar)), 170.7 (C=O). HRMS (ESI, m/z): calcd for C<sub>15</sub>H<sub>20</sub>O<sub>5</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 303.1203; found 303.1193.

### 1.2. General procedure for the preparation of compounds 3a-f, 5

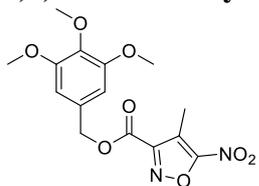
To the solution of C(NO<sub>2</sub>)<sub>4</sub> (0.45 mL, 0.74 g, 3.75 mmol) in 1,4-dioxane (4 mL) was added Et<sub>3</sub>N (0.41 mL, 300 mg, 2.96 mmol) in 1,4-dioxane (1 mL) in atmosphere of Ar for 30 min at -10...-5 °C. The resulting mixture was stirred at this temperature for 10 min and then the alkene **2** (1.48 mmol) in 1,4-dioxane (1 mL) was added dropwise. The reaction mixture was stirred at 80°C for 2 h and then the solvent was evaporated *in vacuo*; the residue was purified by preparative column chromatography on silica gel.

### 3,4,5-Trimethoxybenzyl 5-nitroisoxazole-3-carboxylate (3a)



Obtained as yellow solid (190 mg, 38 %); m.p. 122-123 °C; R<sub>f</sub> 0.30 (petroleum ether:EtOAc 3:1);  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 3.81 (s, 3H, OCH<sub>3</sub>), 3.84 (s, 6H, 2OCH<sub>3</sub>), 5.34 (s, 2H, CH<sub>2</sub>), 6.65 (s, 2H, 2CH(Ar)), 7.37 (s, 1H, CH).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 56.2 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>), 69.0 (CH<sub>2</sub>), 102.3 (CH), 106.3 (2CH(Ar)), 129.4 (C(Ar)), 138.7 (C(Ar)), 153.4 (2C(Ar)), 157.5 (C=O), 158.1 (C), 165.6 (CNO<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>8</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 361.0642; found 361.0630. Anal. Calcd for C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>8</sub>: C, 49.71; H, 4.17; N, 8.28%. Found: C, 49.75; H, 4.14; N, 8.38.

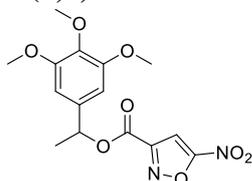
### 3,4,5-Trimethoxybenzyl 4-methyl-5-nitroisoxazole-3-carboxylate (3b)



Obtained as yellowish solid (170 mg, 33 %); m.p. 135-137 °C; R<sub>f</sub> 0.45 (petroleum ether:EtOAc 3:1);  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 2.57 (s, 3H, CH<sub>3</sub>), 3.81 (s, 3H, OCH<sub>3</sub>), 3.84 (s, 6H, 2OCH<sub>3</sub>), 5.34 (s, 2H, CH<sub>2</sub>), 6.65 (s, 2H, 2CH(Ar)).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 8.6 (CH<sub>3</sub>), 56.1 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>),

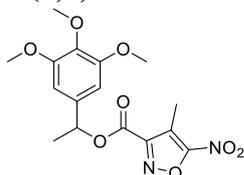
68.6 (CH<sub>2</sub>), 106.0 (2CH(Ar)), 115.7 (C), 129.6 (C(Ar)), 138.5 (C(Ar)), 153.4 (2C(Ar)), 157.0 (C), 158.4 (C=O), 162.1 (CNO<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>15</sub>H<sub>16</sub>N<sub>2</sub>O<sub>8</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 375.0799; found 375.0793. Anal. Calcd for C<sub>15</sub>H<sub>16</sub>N<sub>2</sub>O<sub>8</sub>: C, 51.14; H, 4.58; N, 7.95%. Found: C, 51.04; H, 4.59; N, 7.97.

### 1-(3,4,5-Trimethoxyphenyl)ethyl 5-nitroisoxazole-3-carboxylate (3c)



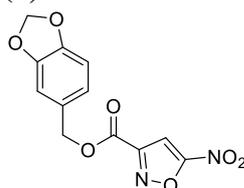
Obtained as brownish oil (150 mg, 29 %); R<sub>f</sub> 0.51 (petroleum ether:EtOAc 3:1); δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>): 1.75 (d, <sup>3</sup>J = 6.6 Hz, 3H, CH<sub>3</sub>), 3.86 (s, 3H, OCH<sub>3</sub>), 3.91 (s, 6H, 2OCH<sub>3</sub>), 6.14 (q, <sup>3</sup>J = 6.6 Hz, 1H, CH), 6.69 (s, 2H, 2CH(Ar)), 7.41 (s, 1H, CH). δ<sub>C</sub> (101 MHz, CDCl<sub>3</sub>): 21.9 (CH<sub>3</sub>), 56.2 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>), 76.1 (CH), 102.4 (CH), 103.5 (2CH(Ar)), 135.3 (C(Ar)), 138.2 (C(Ar)), 153.4 (2C(Ar)), 157.0 (C=O), 158.3 (C), 165.6 (CNO<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>15</sub>H<sub>16</sub>N<sub>2</sub>O<sub>8</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 375.0799; found 375.0793.

### 1-(3,4,5-Trimethoxyphenyl)ethyl 4-methyl-5-nitroisoxazole-3-carboxylate (3d)



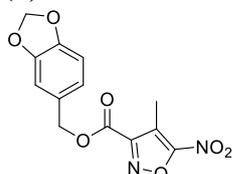
Obtained as yellowish solid (200 mg, 37 %); m.p. 87-90 °C; R<sub>f</sub> 0.33 (petroleum ether:EtOAc 5:1); δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>): 1.70 (d, <sup>3</sup>J = 6.5 Hz, 3H, CH<sub>3</sub>), 2.57 (s, 3H, CH<sub>3</sub>), 3.81 (s, 3H, OCH<sub>3</sub>), 3.85 (s, 6H, 2OCH<sub>3</sub>), 6.08 (q, <sup>3</sup>J = 6.5 Hz, 1H, CH), 6.64 (s, 2H, 2CH(Ar)). δ<sub>C</sub> (101 MHz, CDCl<sub>3</sub>): 8.6 (CH<sub>3</sub>), 22.1 (CH<sub>3</sub>), 56.2 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>), 75.6 (CH), 103.4 (2CH(Ar)), 115.6 (C), 135.6 (C(Ar)), 138.1 (C(Ar)), 153.4 (2C(Ar)), 157.2 (C), 157.9 (C=O), 162.1 (CNO<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>16</sub>H<sub>18</sub>N<sub>2</sub>O<sub>8</sub>K<sup>+</sup> [M+K]<sup>+</sup> 405.0695; found 405.0692.

### (1,3-Benzodioxol-5-yl)methyl 5-nitroisoxazole-3-carboxylate (3e)



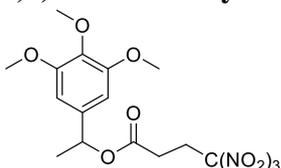
Obtained as yellowish solid (250 mg, 58 %); m.p. 83-84 °C; R<sub>f</sub> 0.53 (petroleum ether:EtOAc 5:1). δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>): 5.32 (s, 2H, OCH<sub>2</sub>), 5.96 (s, 2H, OCH<sub>2</sub>O), 6.77-6.81 (m, 1H, CH(Ar)), 6.90-6.93 (m, 2H, 2CH(Ar)), 7.36 (s, 1H, CH). δ<sub>C</sub> (101 MHz, CDCl<sub>3</sub>): 68.8 (CH<sub>2</sub>), 101.4 (OCH<sub>2</sub>O), 102.3 (CH), 108.4 (CH(Ar)), 109.5 (CH(Ar)), 123.2 (CH(Ar)), 127.6 (C(Ar)), 148.0 (C(Ar)), 148.3 (C(Ar)), 157.5 (C=O), 158.1 (C), 165.6 (CNO<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>12</sub>H<sub>8</sub>N<sub>2</sub>O<sub>7</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 315.0224; found 315.0221. Anal. Calcd for C<sub>12</sub>H<sub>8</sub>N<sub>2</sub>O<sub>7</sub>: C, 49.33; H, 2.76; N, 9.59%. Found: C, 49.34; H, 2.71; N, 9.47.

### (1,3-Benzodioxol-5-yl)methyl 4-methyl-5-nitroisoxazole-3-carboxylate (3f)



Obtained as yellowish solid (260 mg, 57 %); m.p. 71-73 °C; R<sub>f</sub> 0.64 (petroleum ether:EtOAc 5:1).  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 2.55 (s, 3H, CH<sub>3</sub>), 5.30 (s, 2H, OCH<sub>2</sub>), 5.93 (s, 2H, OCH<sub>2</sub>O), 6.74-6.78 (m, 1H, CH(Ar)), 6.88-6.92 (m, 2H, 2CH(Ar)).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 8.6 (CH<sub>3</sub>), 68.4 (CH<sub>2</sub>), 101.3 (OCH<sub>2</sub>O), 108.3 (CH(Ar)), 109.4 (CH(Ar)), 115.6 (C), 123.1 (CH(Ar)), 127.8 (C(Ar)), 147.9 (C(Ar)), 148.2 (C(Ar)), 157.1 (C), 158.4 (C=O), 162.0 (CNO<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>13</sub>H<sub>10</sub>N<sub>2</sub>O<sub>7</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 329.0380; found 329.0376.

### 3,4,5-Trimethoxybenzyl 4,4,4-trinitrobutanoate (5)

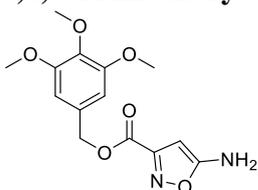


Obtained as yellowish oil (123 mg, 20 %); R<sub>f</sub> 0.48 (petroleum ether:EtOAc 3:1);  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 1.57 (d, <sup>3</sup>J = 6.6 Hz, 3H, CH<sub>3</sub>), 2.71-2.87 (m, 2H, CH<sub>2</sub>), 3.32-3.48 (m, 2H, CH<sub>2</sub>), 3.88 (s, 3H, OCH<sub>3</sub>), 3.89 (s, 6H, 2OCH<sub>3</sub>), 5.86 (q, <sup>3</sup>J = 6.6 Hz, 1H, CH), 6.57 (s, 2H, 2CH(Ar)).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 21.9 (CH<sub>3</sub>), 28.7 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 56.1 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>), 74.4 (OCH), 103.4 (2CH(Ar)), 128.8 (C(NO<sub>2</sub>)<sub>3</sub>), 136.1 (C(Ar)), 138.0 (C(Ar)), 153.4 (2C(Ar)), 168.6 (C=O). HRMS (ESI, m/z): calcd for C<sub>15</sub>H<sub>19</sub>N<sub>3</sub>O<sub>11</sub>K<sup>+</sup> [M+K]<sup>+</sup> 456.0651; found 456.0639.

### 1.3. General procedure for the preparation of compounds 1a-f

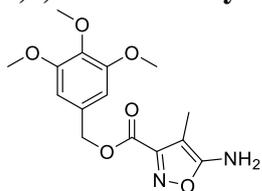
To a stirred solution of 5-nitroisoxazole **4** (0.15 mmol) in a mixture (1:1) THF-H<sub>2</sub>O (2 mL) Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> (75 mg, 0.45 mmol) was added in one portion at room temperature. The resulting mixture was stirred for 1 h at 90°C. Then the mixture was cooled to room temperature, the water (5 mL) was added and extracted with EtOAc (3×10 mL). The combined organic layer was dried over anhydrous MgSO<sub>4</sub>. The solvent was evaporated in vacuo; the residue was purified by preparative column chromatography on silica gel (petroleum ether-ethyl acetate 1:1).

### 3,4,5-Trimethoxybenzyl 5-aminoisoxazole-3-carboxylate (1a)



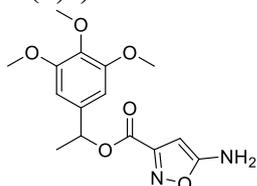
Obtained as colorless solid (31 mg, 67 %); m.p. 144-145 °C; R<sub>f</sub> 0.4 (petroleum ether:EtOAc 1:1).  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>-CD<sub>3</sub>OD): 3.20 (br s 2H, NH<sub>2</sub>), 3.74 (s, 3H, OCH<sub>3</sub>), 3.77 (s, 6H, 2OCH<sub>3</sub>), 5.19 (s, 2H, CH<sub>2</sub>), 5.39 (s, 1H, CH), 6.58 (s, 2H, 2CH(Ar)).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>-CD<sub>3</sub>OD): 56.0 (2OCH<sub>3</sub>), 60.7 (OCH<sub>3</sub>), 67.5 (CH<sub>2</sub>), 79.6 (CH), 105.8 (2CH(Ar)), 130.6 (C(Ar)), 137.9 (C(Ar)), 153.1 (2C(Ar)), 156.9 (C), 160.4 (C=O), 170.8 (CNH<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>14</sub>H<sub>16</sub>N<sub>2</sub>O<sub>6</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 331.0901; found 331.0901. Anal. Calcd for C<sub>14</sub>H<sub>16</sub>N<sub>2</sub>O<sub>6</sub>: C, 54.54; H, 5.23; N, 9.09%. Found: C, 54.62; H, 5.27; N, 8.70.

### 3,4,5-Trimethoxybenzyl 5-amino-4-methylisoxazole-3-carboxylate (1b)



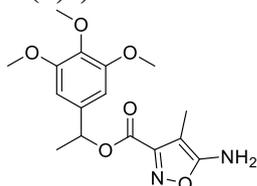
Obtained as colorless solid (24 mg, 50 %); m.p. 102-103 °C; *R<sub>f</sub>* 0.47 (petroleum ether:EtOAc 1:1).  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 1.96 (s, 3H, CH<sub>3</sub>), 3.80 (s, 3H, OCH<sub>3</sub>), 3.83 (s, 6H, 2OCH<sub>3</sub>), 4.48 (br s 2H, NH<sub>2</sub>), 5.26 (s, 2H, CH<sub>2</sub>), 6.64 (s, 2H, 2CH(Ar)).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 6.5 (CH<sub>3</sub>), 56.1 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>), 67.3 (CH<sub>2</sub>), 89.9 (C), 105.8 (2CH(Ar)), 130.7 (C(Ar)), 138.0 (C(Ar)), 153.3 (2C(Ar)), 155.1 (C), 160.9 (C=O), 167.1 (CNH<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>15</sub>H<sub>18</sub>N<sub>2</sub>O<sub>6</sub>K<sup>+</sup> [M+K]<sup>+</sup> 361.0796; found 361.0793. Anal. Calcd for C<sub>15</sub>H<sub>18</sub>N<sub>2</sub>O<sub>6</sub>: C, 55.90; H, 5.63; N, 8.69%. Found: C, 56.10; H, 5.64; N, 8.70.

### 1-(3,4,5-Trimethoxyphenyl)ethyl 5-aminoisoxazole-3-carboxylate (1c)



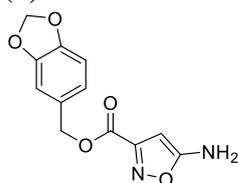
Obtained as colorless solid (14 mg, 30 %); m.p. 112-113 °C; *R<sub>f</sub>* 0.47 (petroleum ether:EtOAc 1:1).  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 1.65 (d, <sup>3</sup>*J* = 6.6 Hz, 3H, CH<sub>3</sub>), 3.81 (s, 3H, OCH<sub>3</sub>), 3.85 (s, 6H, 2OCH<sub>3</sub>), 4.61 (br s, 2H, NH<sub>2</sub>), 5.51 (s, 1H, CH), 6.02 (q, <sup>3</sup>*J* = 6.6 Hz, 1H, CH), 6.64 (s, 2H, 2CH(Ar)).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 22.1 (CH<sub>3</sub>), 56.1 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>), 74.2 (CH<sub>2</sub>), 80.7 (C), 103.3 (2CH(Ar)), 136.5 (C(Ar)), 137.7 (C(Ar)), 153.3 (2C(Ar)), 157.5 (C), 159.7 (C=O), 169.5 (CNH<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>15</sub>H<sub>18</sub>N<sub>2</sub>O<sub>6</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 345.1057; found 345.1057.

### 1-(3,4,5-Trimethoxyphenyl)ethyl 5-amino-4-methylisoxazole-3-carboxylate (1d)



Obtained as colorless solid (25 mg, 50 %); m.p. 139-140 °C; *R<sub>f</sub>* 0.51 (petroleum ether:EtOAc 1:1).  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>): 1.64 (d, <sup>3</sup>*J* = 6.7 Hz, 3H, CH<sub>3</sub>), 1.97 (s, 3H, CH<sub>3</sub>), 3.80 (s, 3H, OCH<sub>3</sub>), 3.84 (s, 6H, 2OCH<sub>3</sub>), 4.38 (br s, 2H, NH<sub>2</sub>), 6.02 (q, <sup>3</sup>*J* = 6.7 Hz, 1H, CH), 6.64 (s, 2H, 2CH(Ar)).  $\delta_{\text{C}}$  (101 MHz, CDCl<sub>3</sub>): 6.5 (CH<sub>3</sub>), 22.3 (CH<sub>3</sub>), 56.1 (2OCH<sub>3</sub>), 60.8 (OCH<sub>3</sub>), 73.9 (CH), 90.0 (C), 103.2 (2CH(Ar)), 136.7 (C(Ar)), 137.6 (C(Ar)), 153.3 (2C(Ar)), 155.4 (C), 160.4 (C=O), 166.9 (CNH<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>16</sub>H<sub>20</sub>N<sub>2</sub>O<sub>6</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 359.1214; found 359.1210.

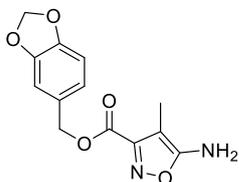
### (1,3-Benzodioxol-5-yl)methyl 5-aminoisoxazole-3-carboxylate (1e)



Obtained as colorless solid (25 mg, 65 %); m.p. 151-152°C; *R<sub>f</sub>* 0.75 (petroleum ether:EtOAc 1:1).  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>-CD<sub>3</sub>OD): 2.95 (br s, 2H, NH<sub>2</sub>), 5.17 (s, 2H, OCH<sub>2</sub>), 5.38 (s, 1H, CH), 5.88 (s, 2H, OCH<sub>2</sub>O), 6.69-6.73 (m, 1H, CH(Ar)), 6.80-6.86 (m, 2H, 2CH(Ar)).  $\delta_{\text{C}}$  (101 MHz,

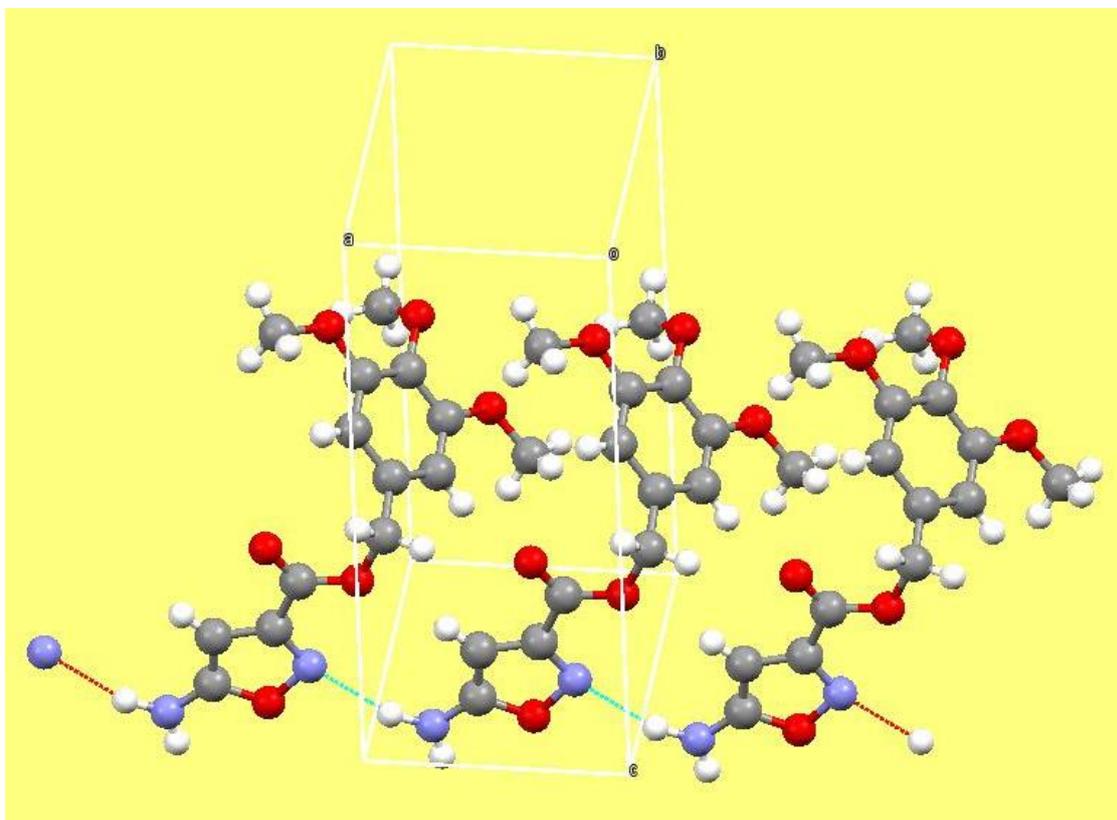
CDCl<sub>3</sub>-CD<sub>3</sub>OD): 67.3 (CH<sub>2</sub>), 79.7 (CH), 101.1 (OCH<sub>2</sub>O), 108.2 (CH(Ar)), 109.2 (CH(Ar)), 122.7 (CH(Ar)), 128.6 (C(Ar)), 147.7 (C(Ar)), 147.8 (C(Ar)), 157.0 (C), 160.4 (C=O), 170.7 (CNH<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>12</sub>H<sub>10</sub>N<sub>2</sub>O<sub>5</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 285.0482; found 285.0486.

### (1,3-Benzodioxol-5-yl)methyl 5-amino-4-methylisoxazole-3-carboxylate (**1f**)



Obtained as colorless solid (24 mg, 58 %); m.p. 173-174 °C; R<sub>f</sub> 0.78 (petroleum ether:EtOAc 1:1). δ<sub>H</sub> (400 MHz, CD<sub>3</sub>OD): 1.92 (s, 3H, CH<sub>3</sub>), 5.22 (s, 2H, OCH<sub>2</sub>), 5.93 (s, 2H, OCH<sub>2</sub>O), 6.76-6.81 (m, 1H, CH(Ar)), 6.90-6.94 (m, 2H, 2CH(Ar)). δ<sub>C</sub> (101 MHz, CD<sub>3</sub>OD): 4.9 (CH<sub>3</sub>), 66.6 (CH<sub>2</sub>), 87.2 (C), 101.1 (OCH<sub>2</sub>O), 107.7 (CH(Ar)), 108.8 (CH(Ar)), 122.3 (CH(Ar)), 129.2 (C(Ar)), 147.85 (C(Ar)), 147.88 (C(Ar)), 154.6 (C), 160.8 (C=O), 169.6 (CNH<sub>2</sub>). HRMS (ESI, m/z): calcd for C<sub>13</sub>H<sub>12</sub>N<sub>2</sub>O<sub>5</sub>Na<sup>+</sup> [M+Na]<sup>+</sup> 299.0638; found 299.0633.

## 2. The crystal packing of compound **1a**



**Figure S1** The crystal packing of **1a** showing a layer of molecules connected through intermolecular hydrogen bonds between amino group and sp<sup>2</sup>-nitrogen atom of isoxazole ring.

### 3. Biological evaluation

#### MTT Cytotoxicity Assay

A549 human lung epithelial carcinoma cells (CCL-185™) were seeded in 96-well plates at a density of 3000 cells per well. Stock solutions of test compounds were prepared in DMSO. Cells were treated for 24 h with selected compounds at 10–100  $\mu$ M (8 wells for each concentration). DMSO (0.5%) served as a negative control. MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide), Roth GmbH, Karlsruhe, Germany) was prepared at 5 mg/mL in phosphate buffered saline (PBS) and filtered through a 0.22  $\mu$ m filter. 20  $\mu$ L of sterile MTT solution (final concentration 0.5 mg/mL) was added to each well 2 h before the end of compound exposure. Then the supernatant was removed, and 100  $\mu$ L of DMSO containing 10% SDS and 0.6% acetic acid was added to each well. The resulting formazan crystals were solubilized by thorough mixing on a plate shaker. Optical density was measured at 590 nm with 690 nm reference filter using a EL808 Ultra Microplate Reader (BioTek Instruments, Winooski, USA). Experiments for all compounds were repeated at least 3 times and EC<sub>50</sub> values were determined by sigmoidal curve fitting using Excel-based software.

#### Proliferation assay

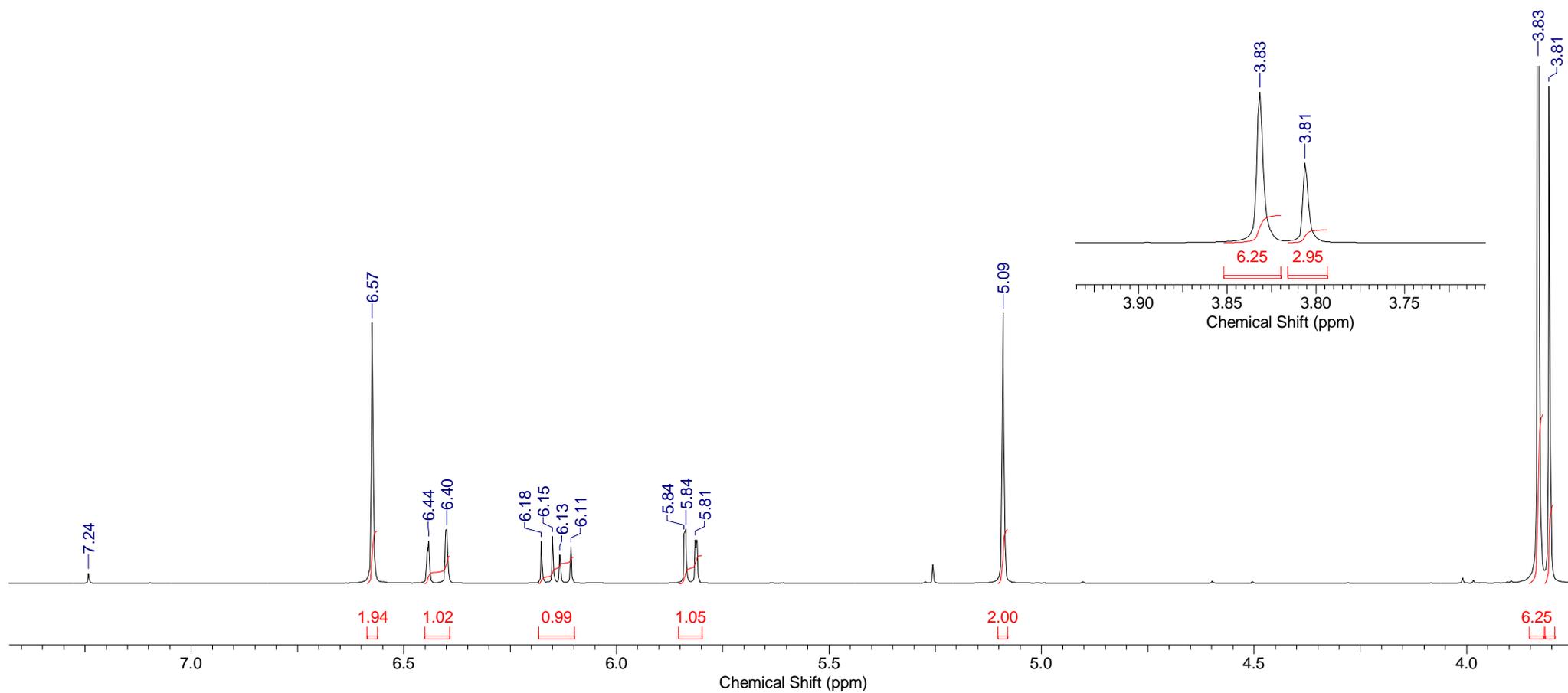
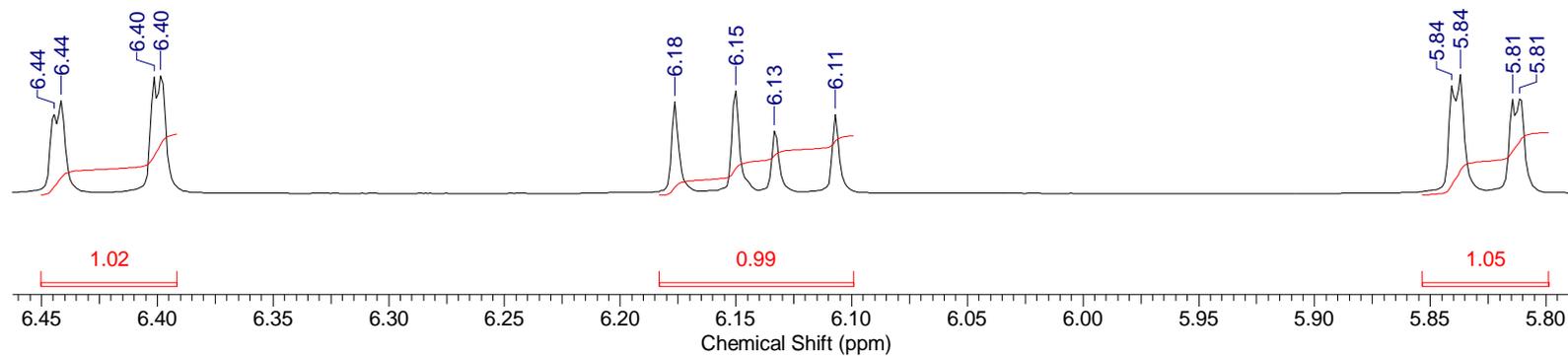
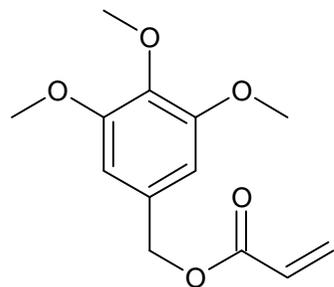
A 549 cells were incubated with 100  $\mu$ M of each tested compound for 24, 48 and 72 h. 1% DMSO was used as a control. After culturing the cells were re-suspended in PBS and counted directly by phase-contrast microscopy using hemocytometer. The percentage of cell growth inhibition was calculated for the cell cultivated during 48 h (the difference between cell number in control after 48 h and 0 h was taken as 100%).

#### 4. References

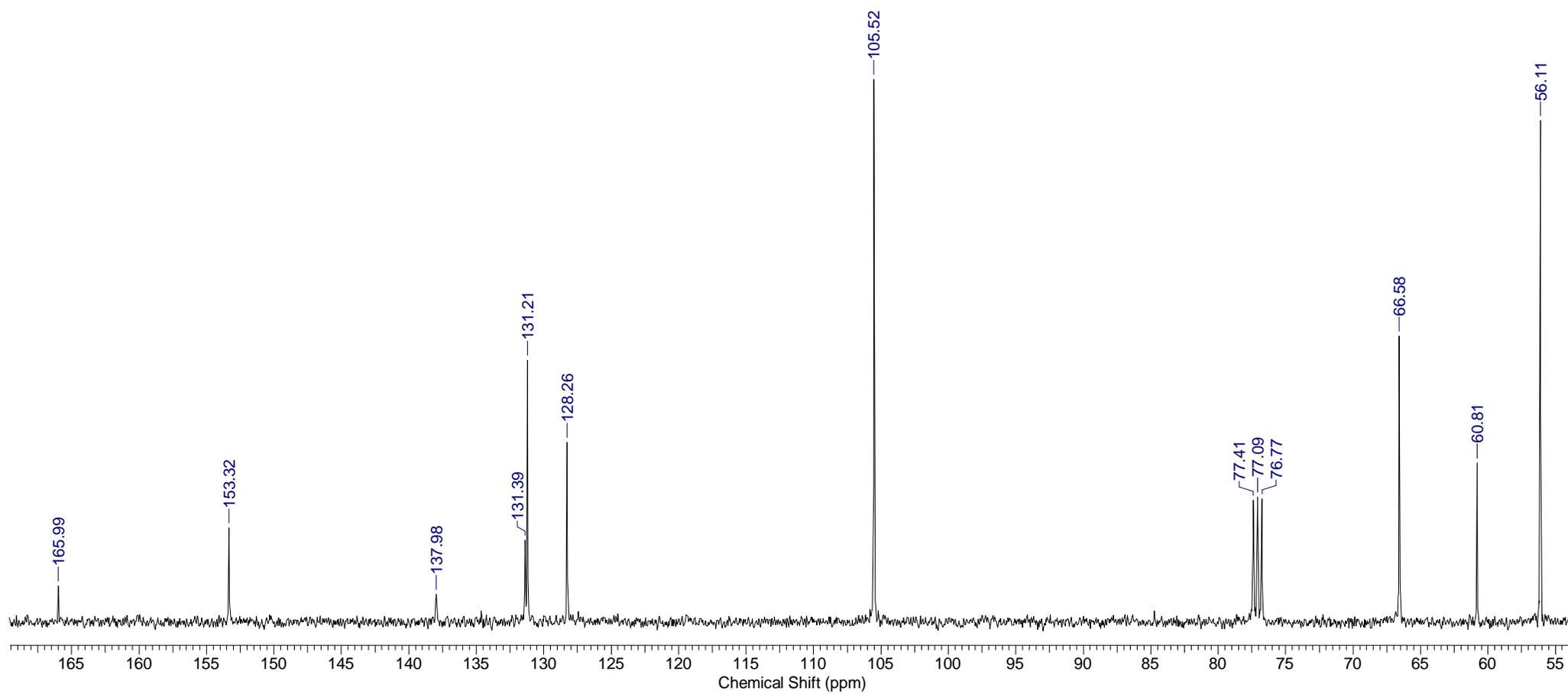
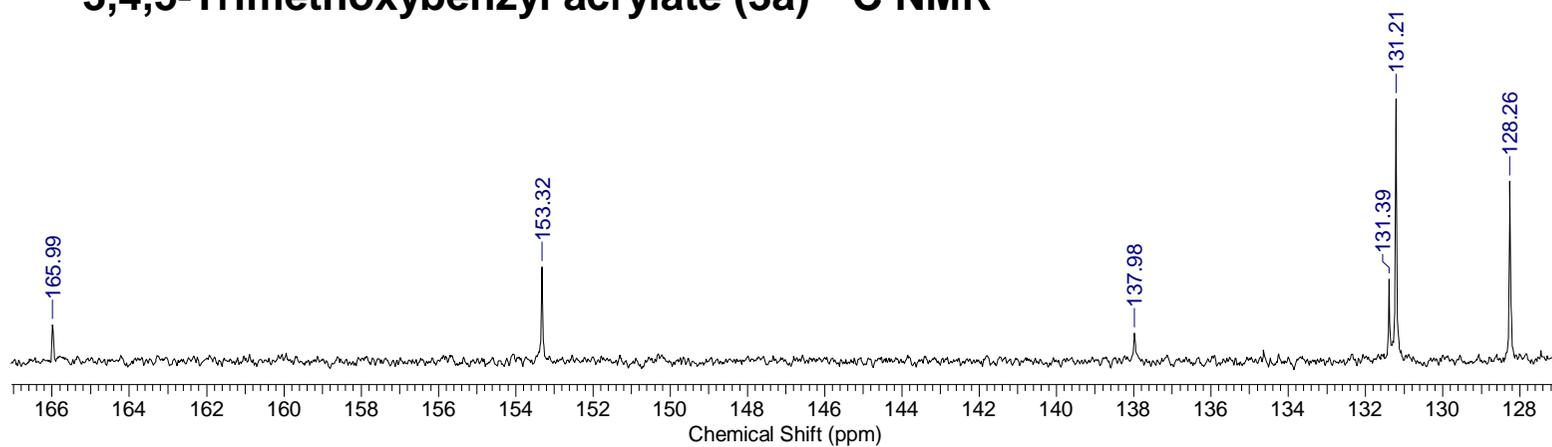
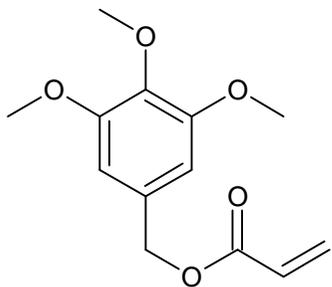
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2. G. M. Sheldrick, *Acta Crystallogr.*, 2015, **C71**, 3.
3. A. L. Spek, *Acta Crystallogr.*, 2009, **D65**, 148.
4. R. P. Tanpure, A. R. Harkrider, T. E. Strecker, E. Hamel, M. L. Trawick and K. G. Pinney, *Bioorg. Med. Chem.*, 2009, **17**, 6993.
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## 5. NMR-Spectra

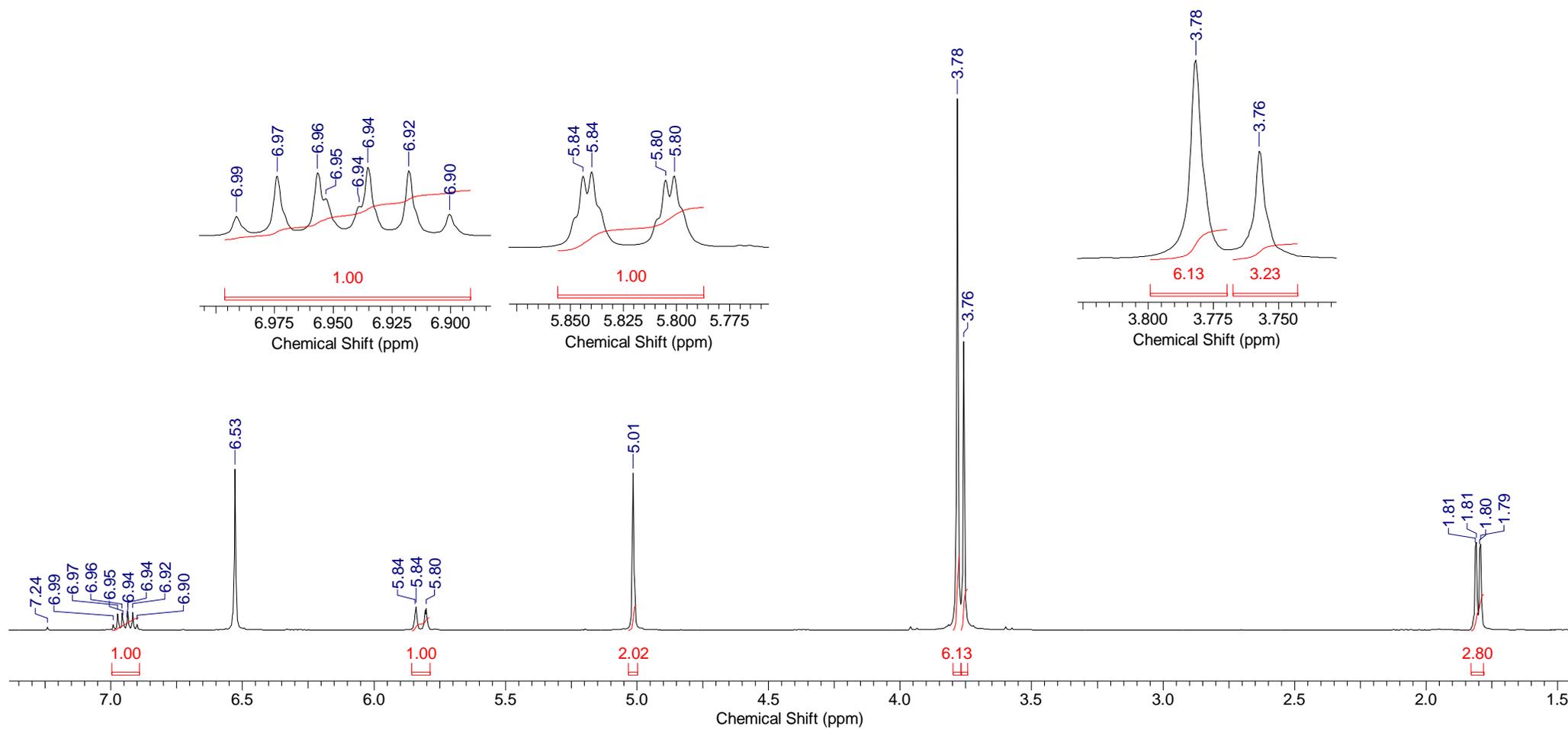
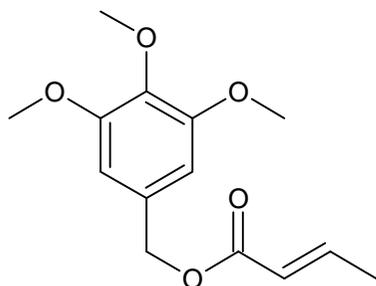
### 3,4,5-Trimethoxybenzyl acrylate (3a) $^1\text{H}$ NMR



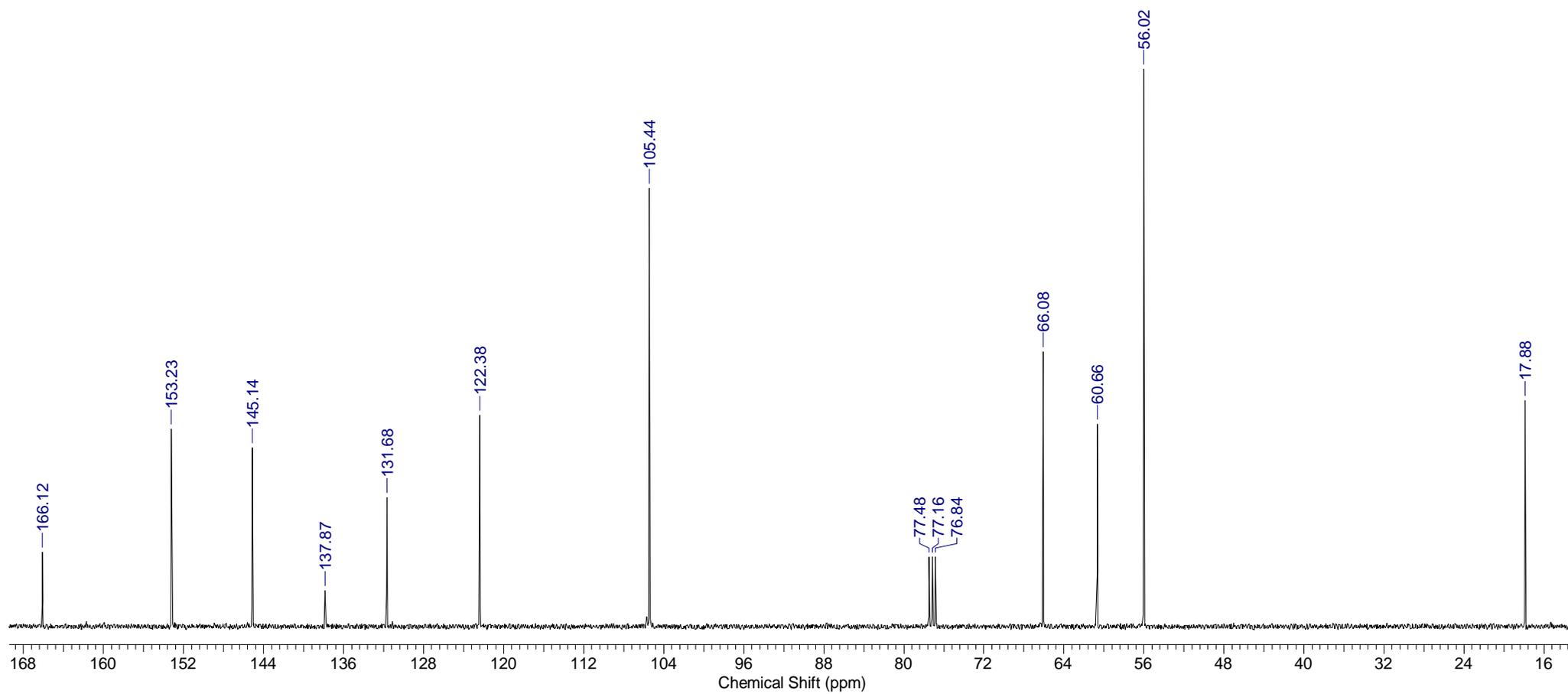
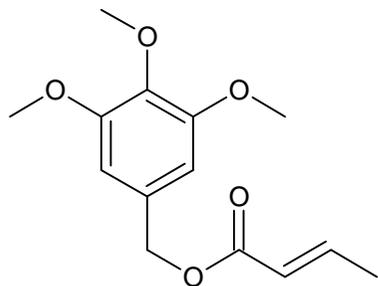
### 3,4,5-Trimethoxybenzyl acrylate (3a) $^{13}\text{C}$ NMR



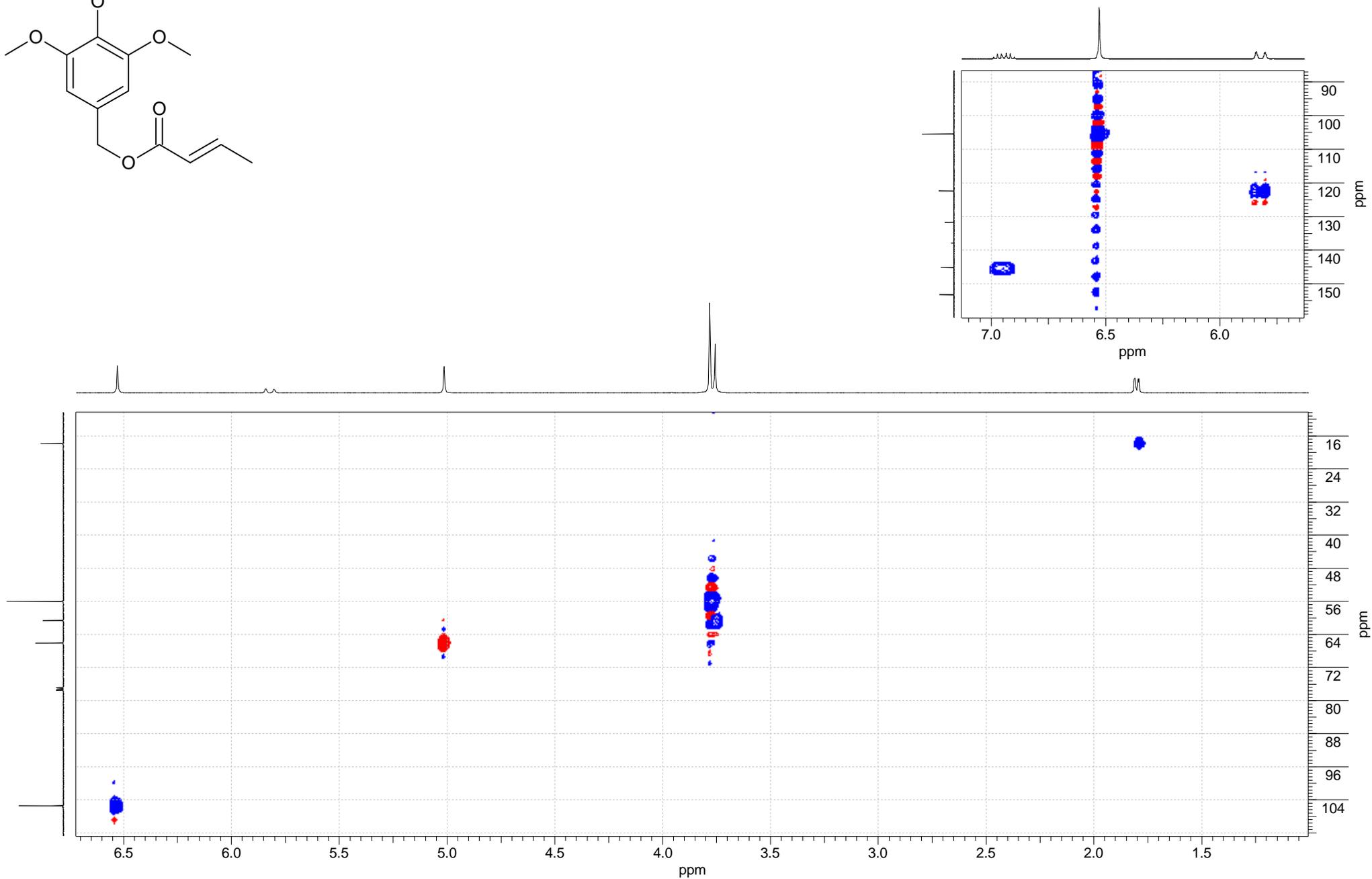
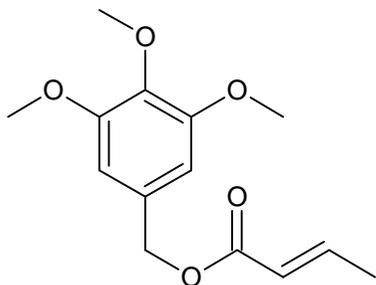
# 3,4,5-Trimethoxybenzyl (2E)-but-2-enoate (3b) <sup>1</sup>H NMR



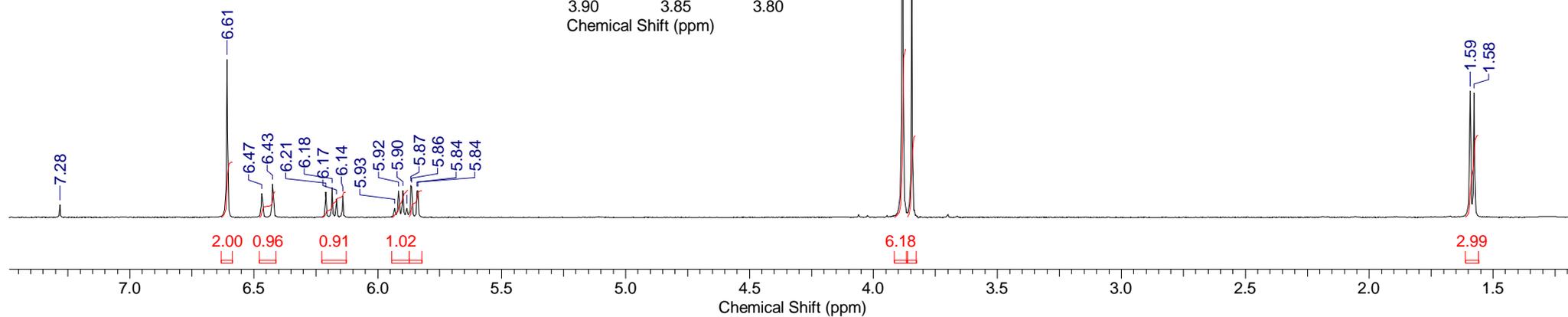
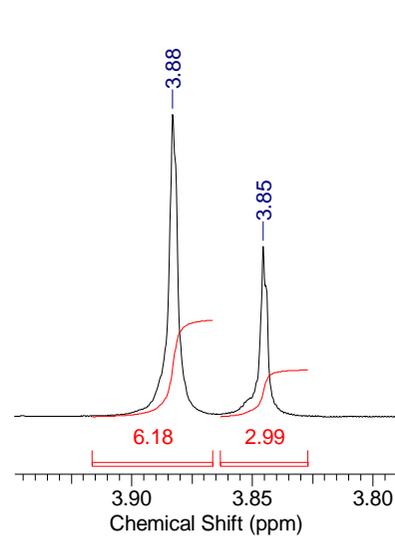
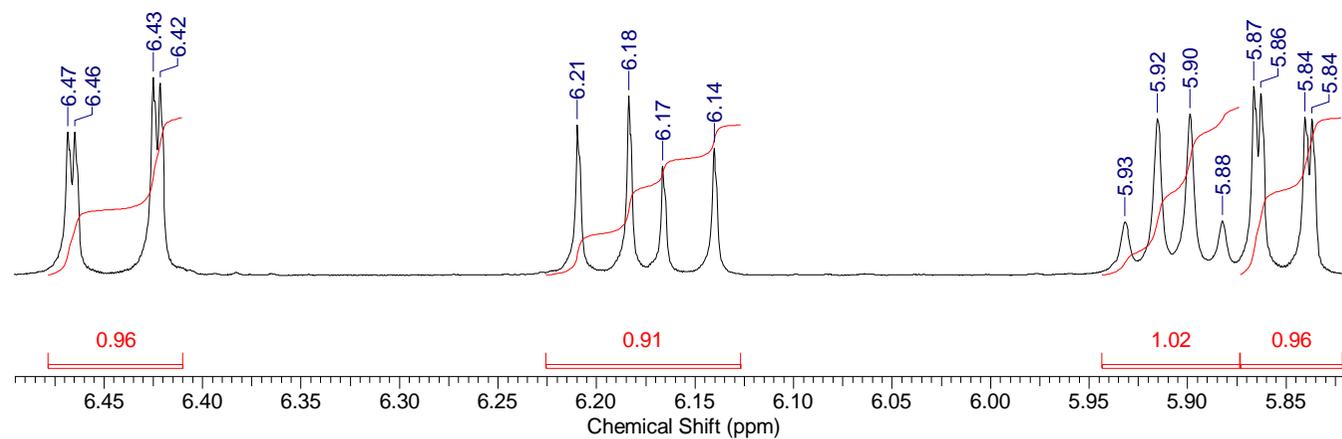
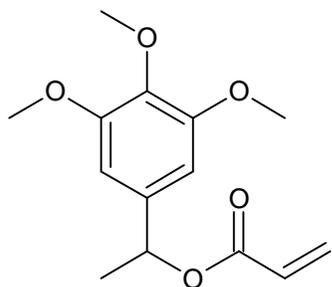
# 3,4,5-Trimethoxybenzyl (2E)-but-2-enoate (3b) <sup>13</sup>C NMR



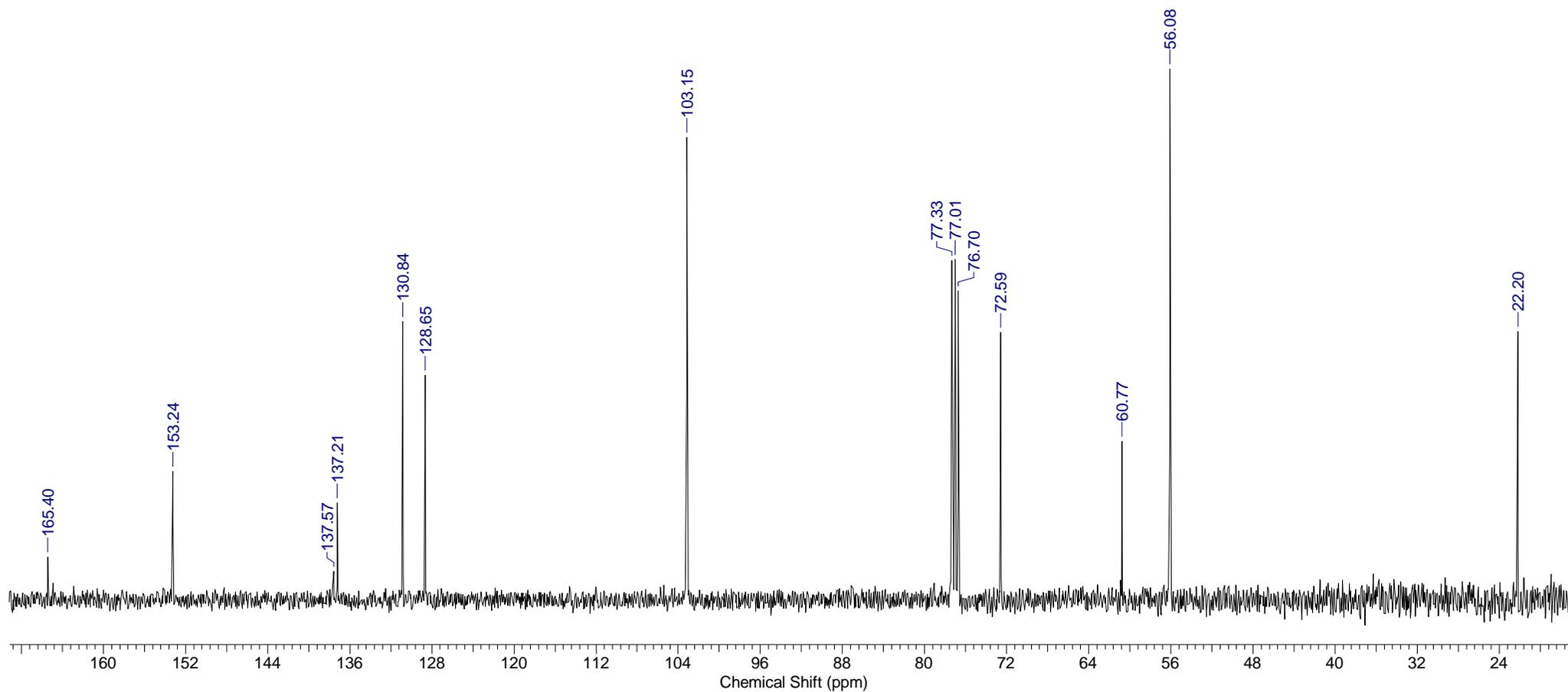
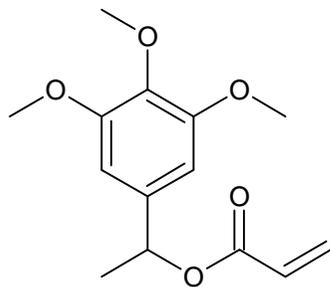
# 3,4,5-Trimethoxybenzyl (2E)-but-2-enoate (3b) gHSQC



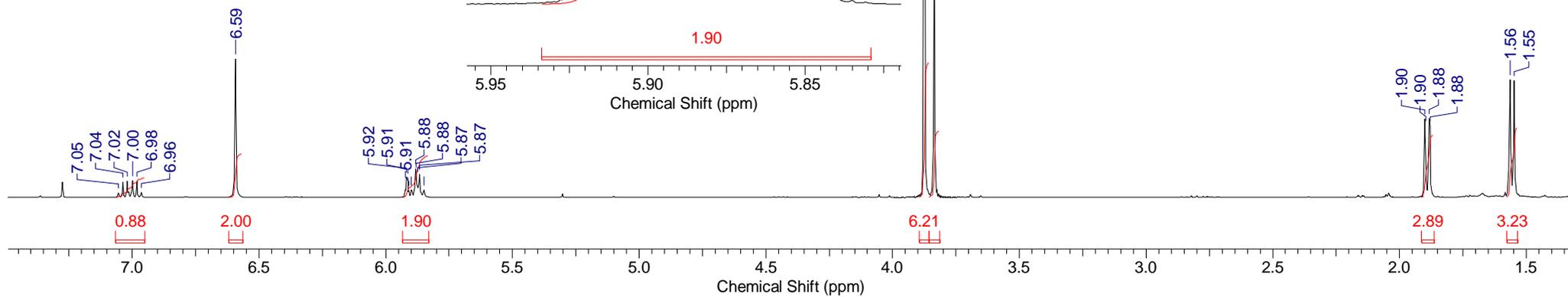
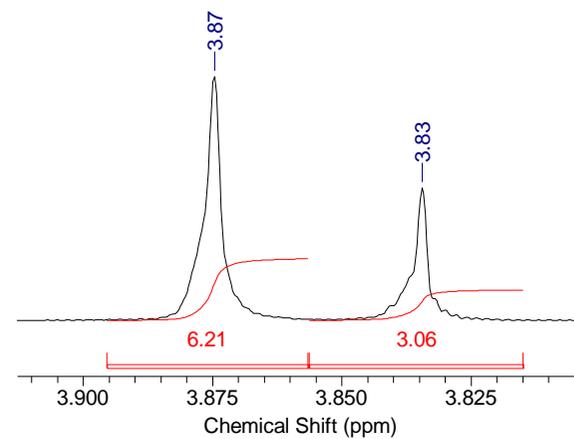
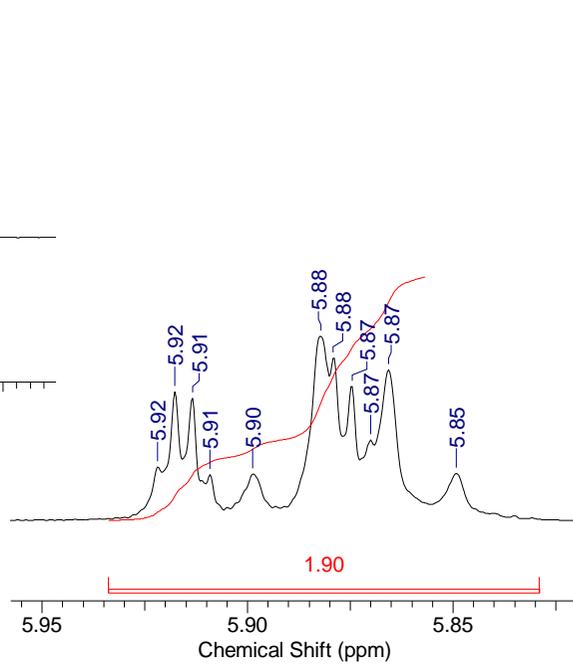
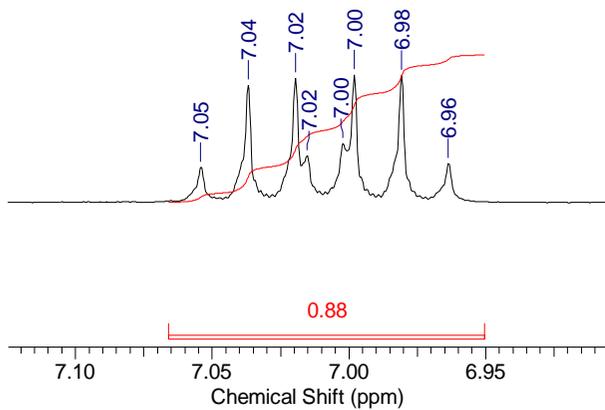
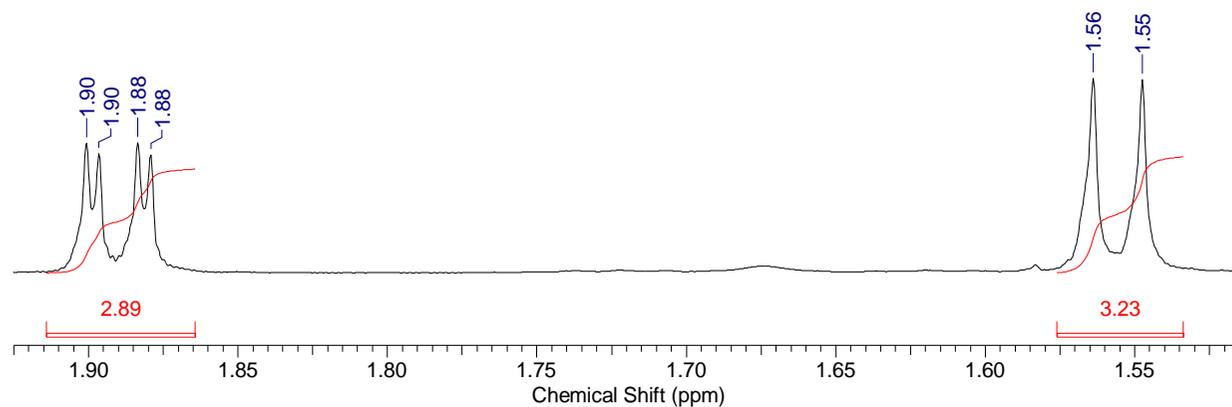
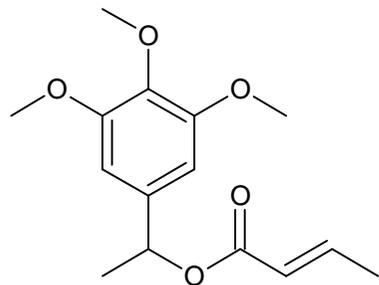
# 1-(3,4,5-Trimethoxyphenyl)ethyl acrylate (3c) <sup>1</sup>H NMR



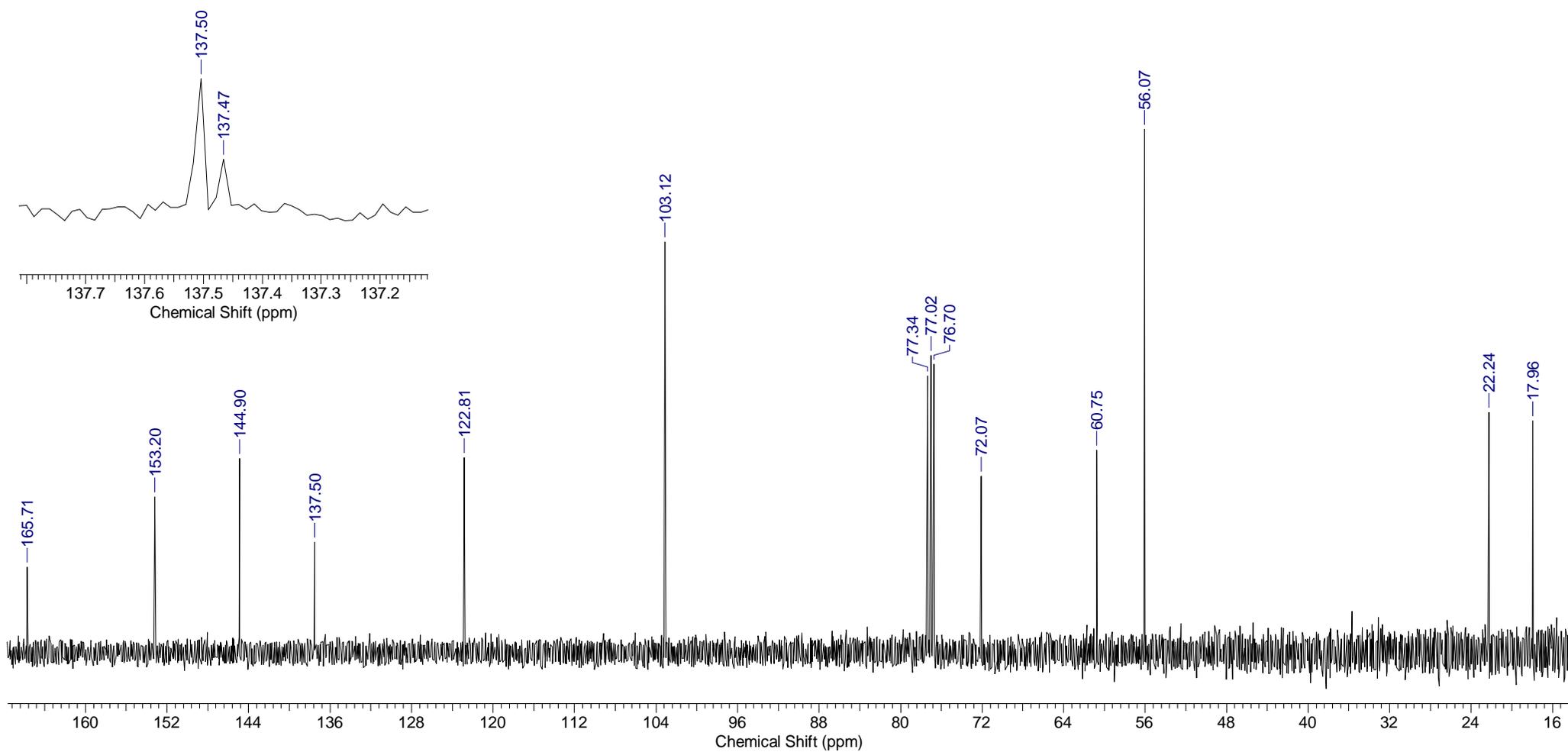
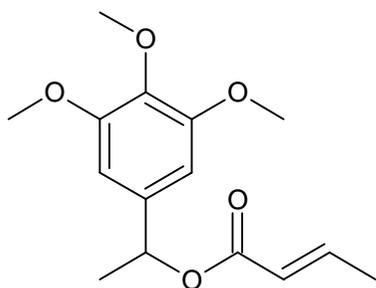
# 1-(3,4,5-Trimethoxyphenyl)ethyl acrylate (3c) <sup>13</sup>C NMR



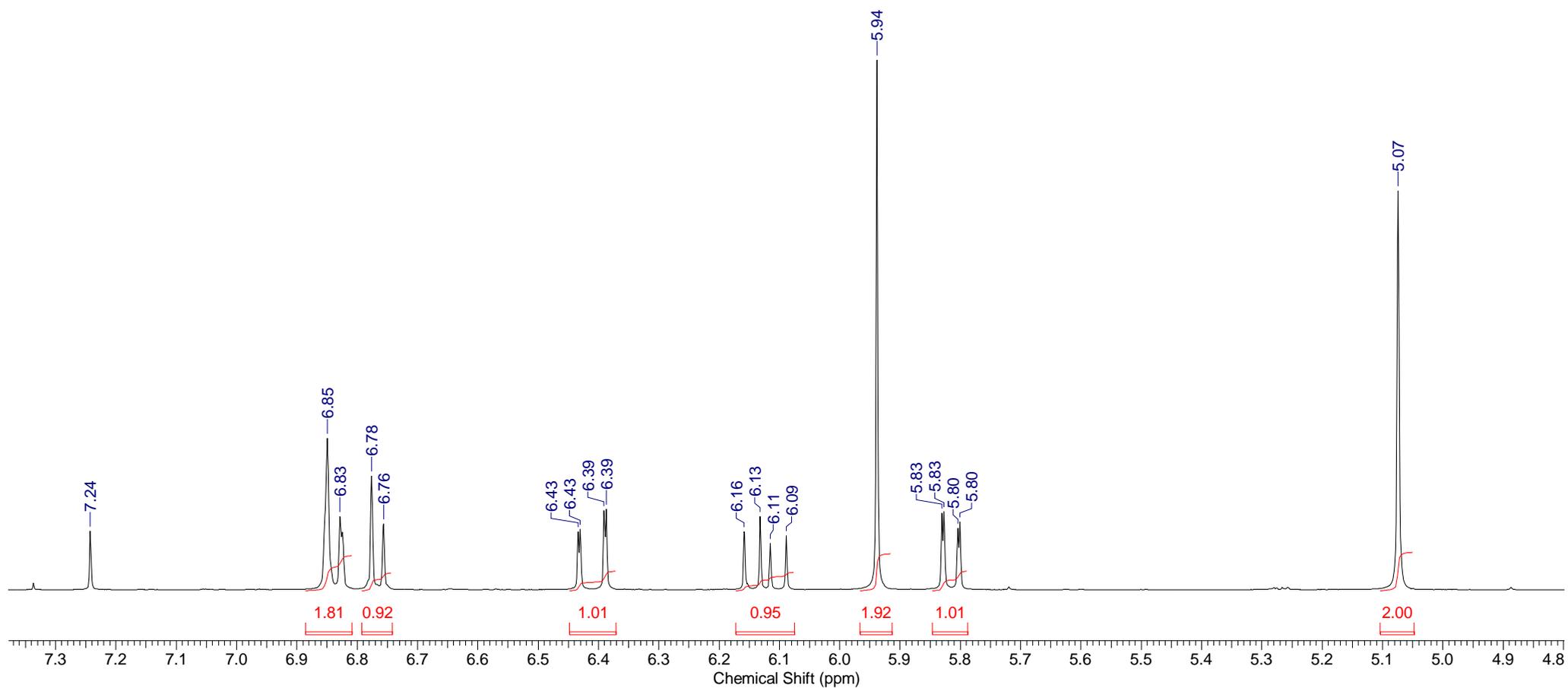
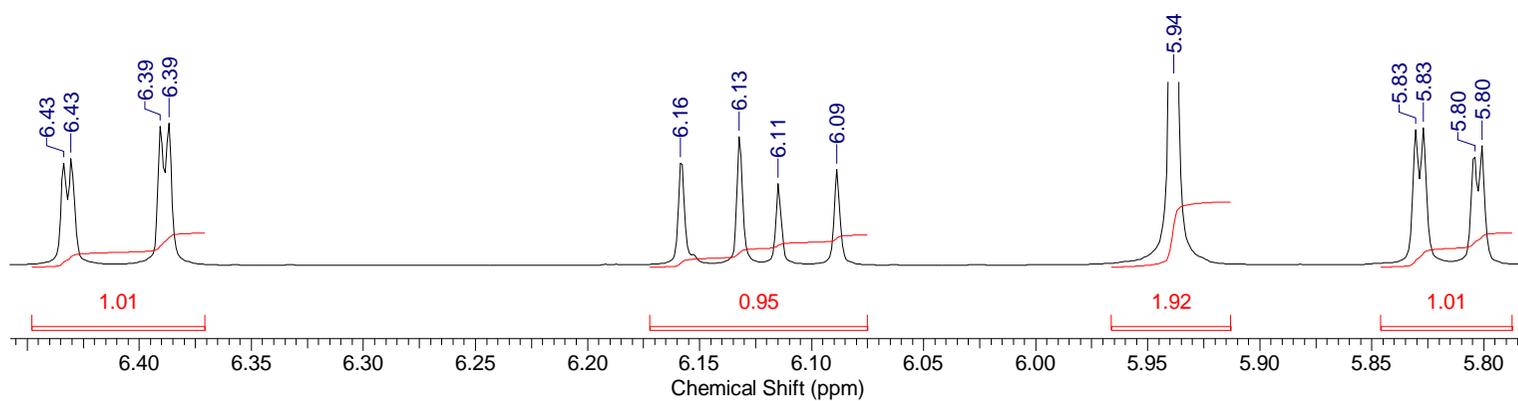
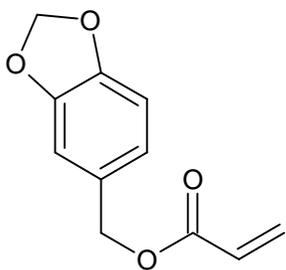
# 1-(3,4,5-trimethoxyphenyl)ethyl (2E)-but-2-enoate (3d) <sup>1</sup>H NMR



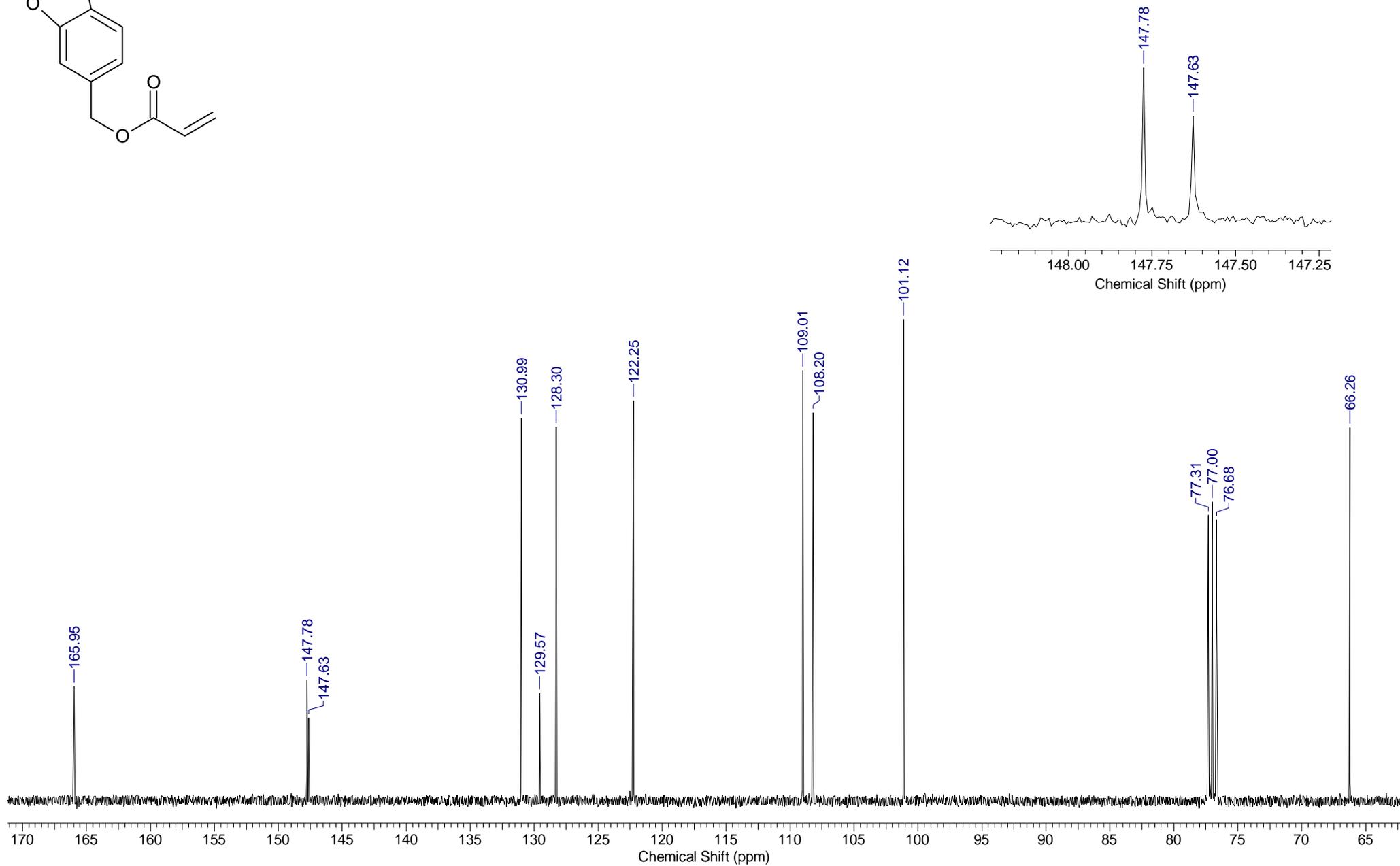
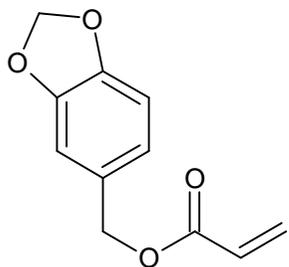
# 1-(3,4,5-trimethoxyphenyl)ethyl (2E)-but-2-enoate (3d) <sup>13</sup>C NMR



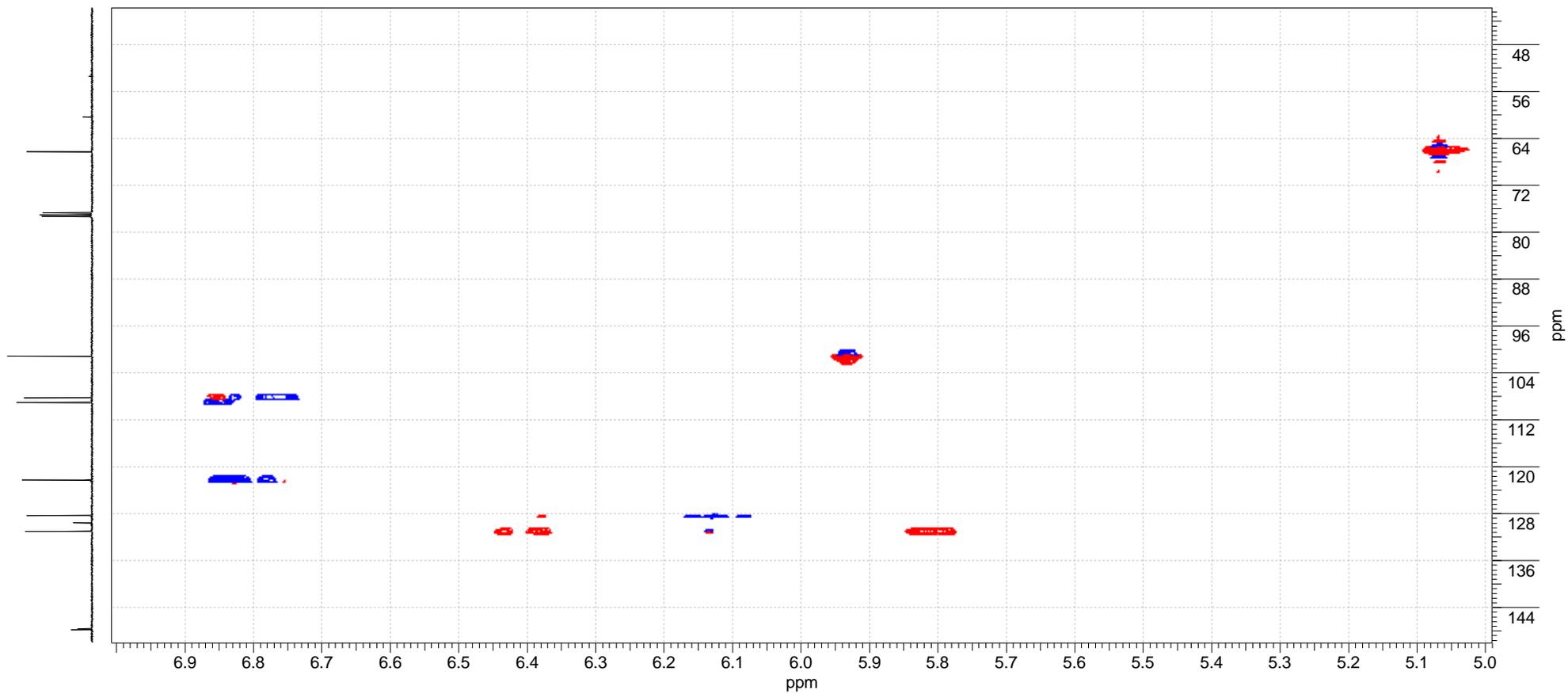
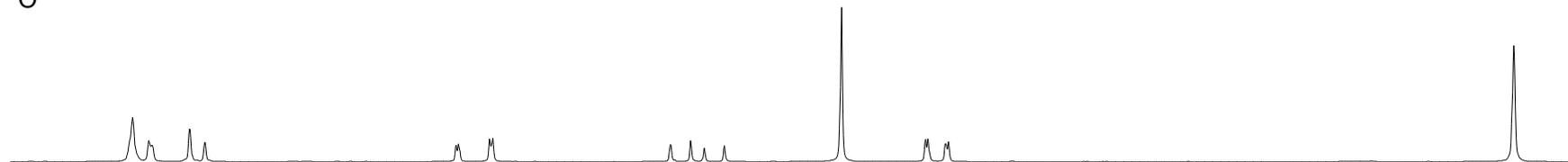
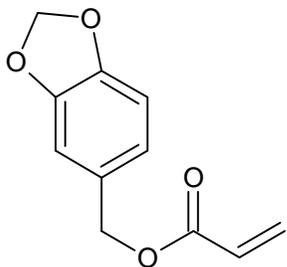
# 1,3-benzodioxol-5-ylmethyl acrylate (3e) <sup>1</sup>H NMR



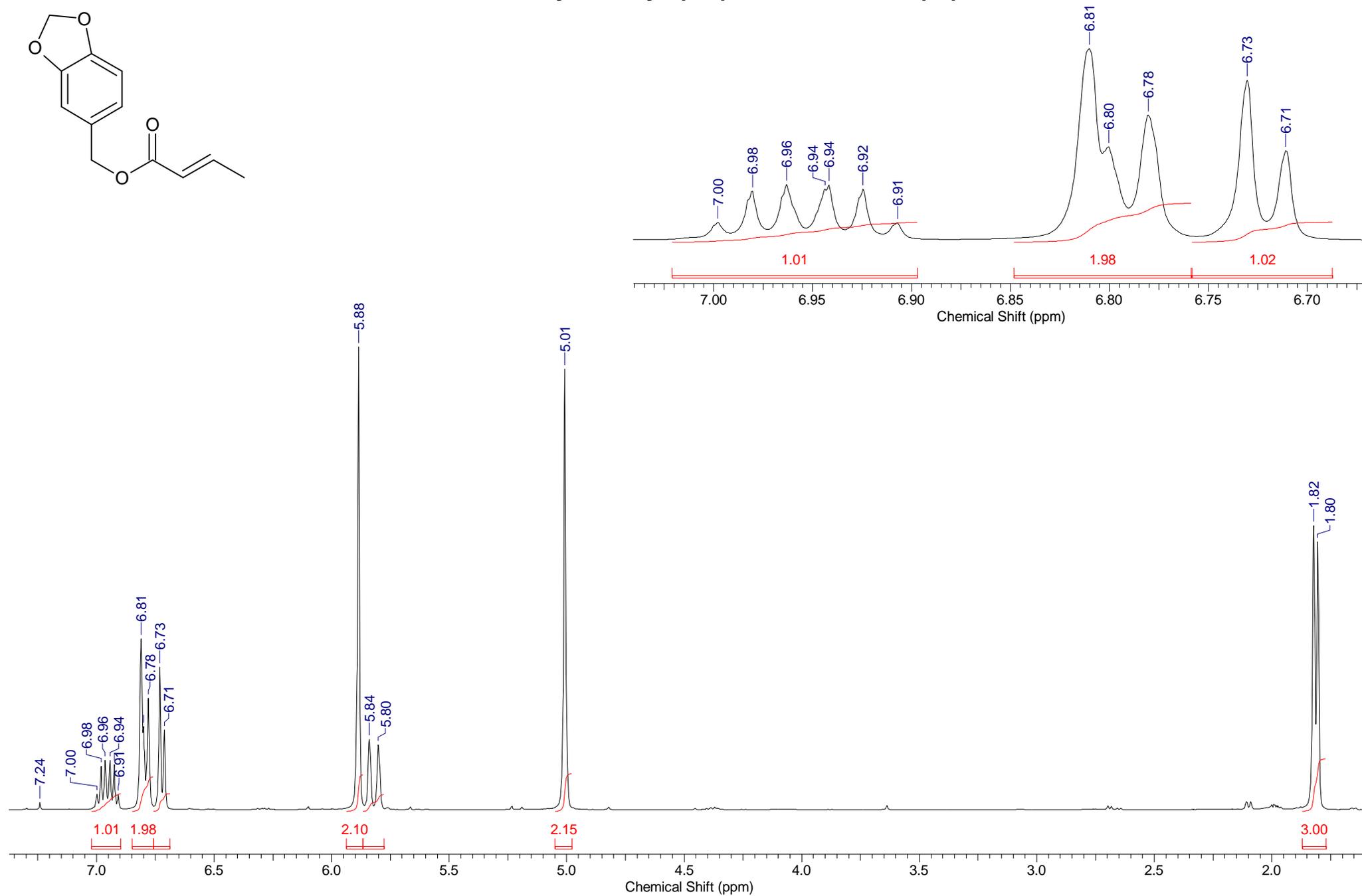
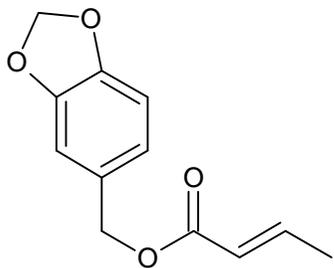
# 1,3-benzodioxol-5-ylmethyl acrylate (3e) <sup>13</sup>C NMR



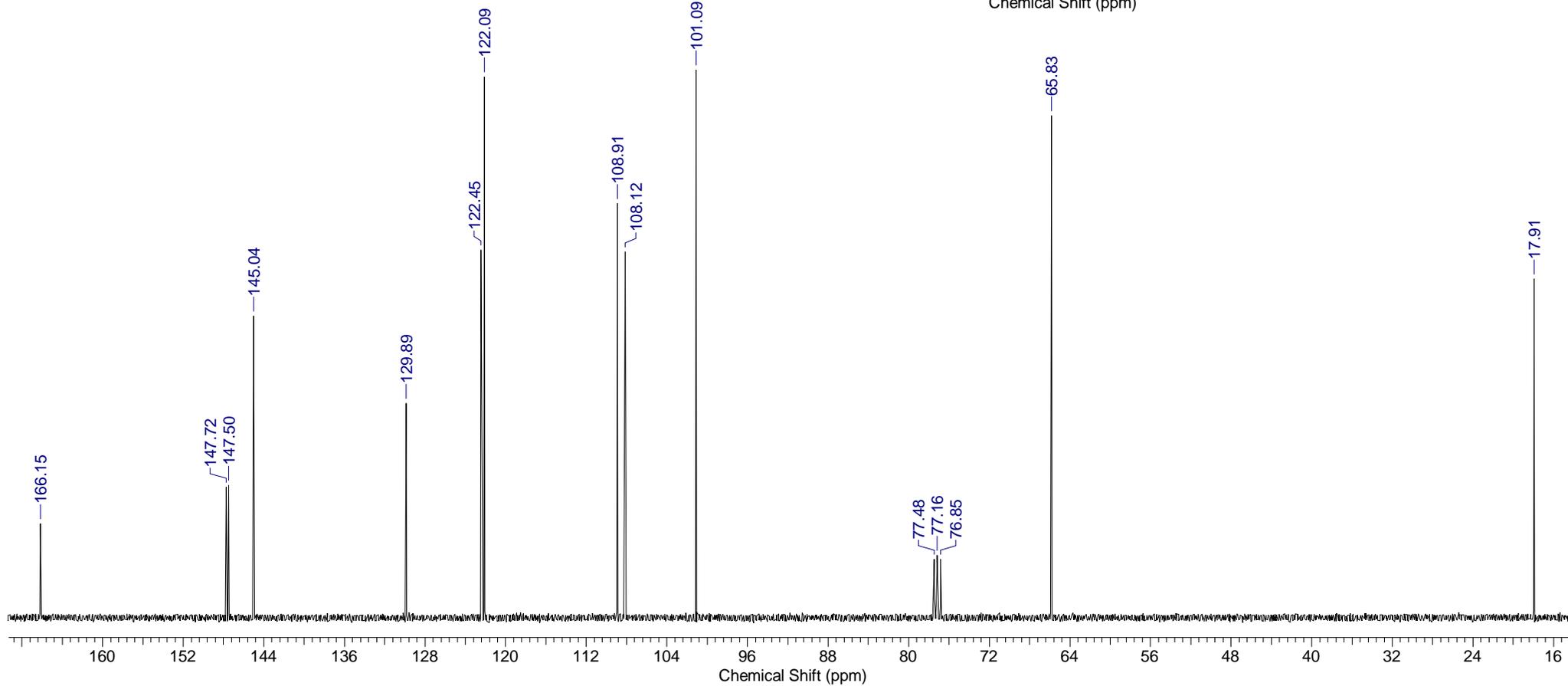
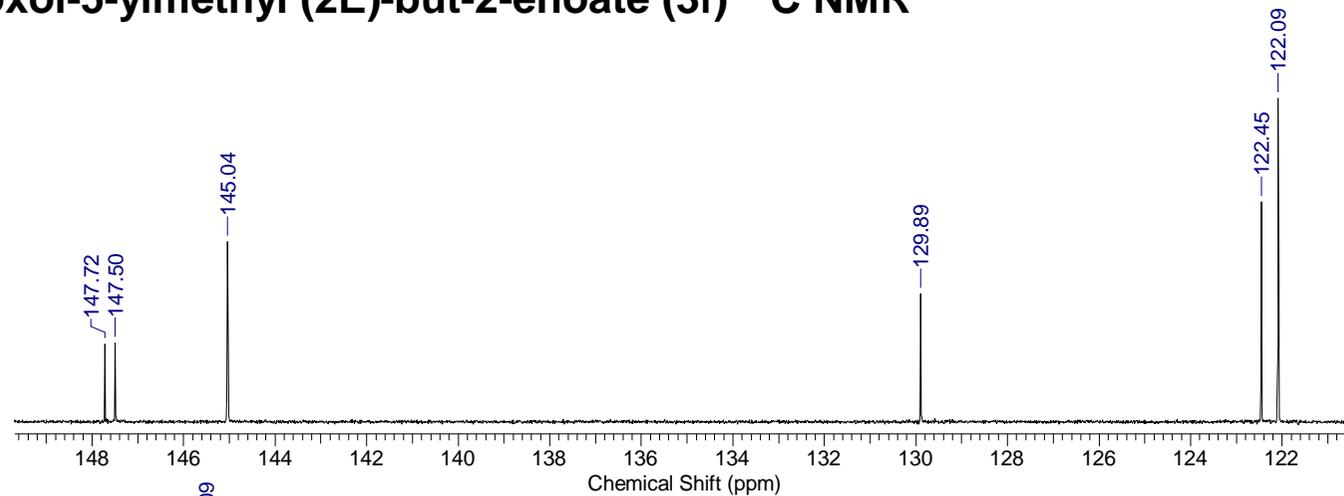
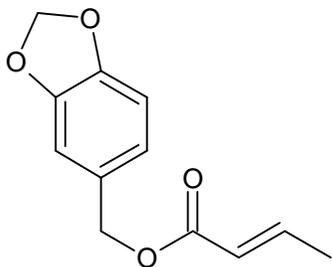
# 1,3-benzodioxol-5-ylmethyl acrylate (3e) gHSQC



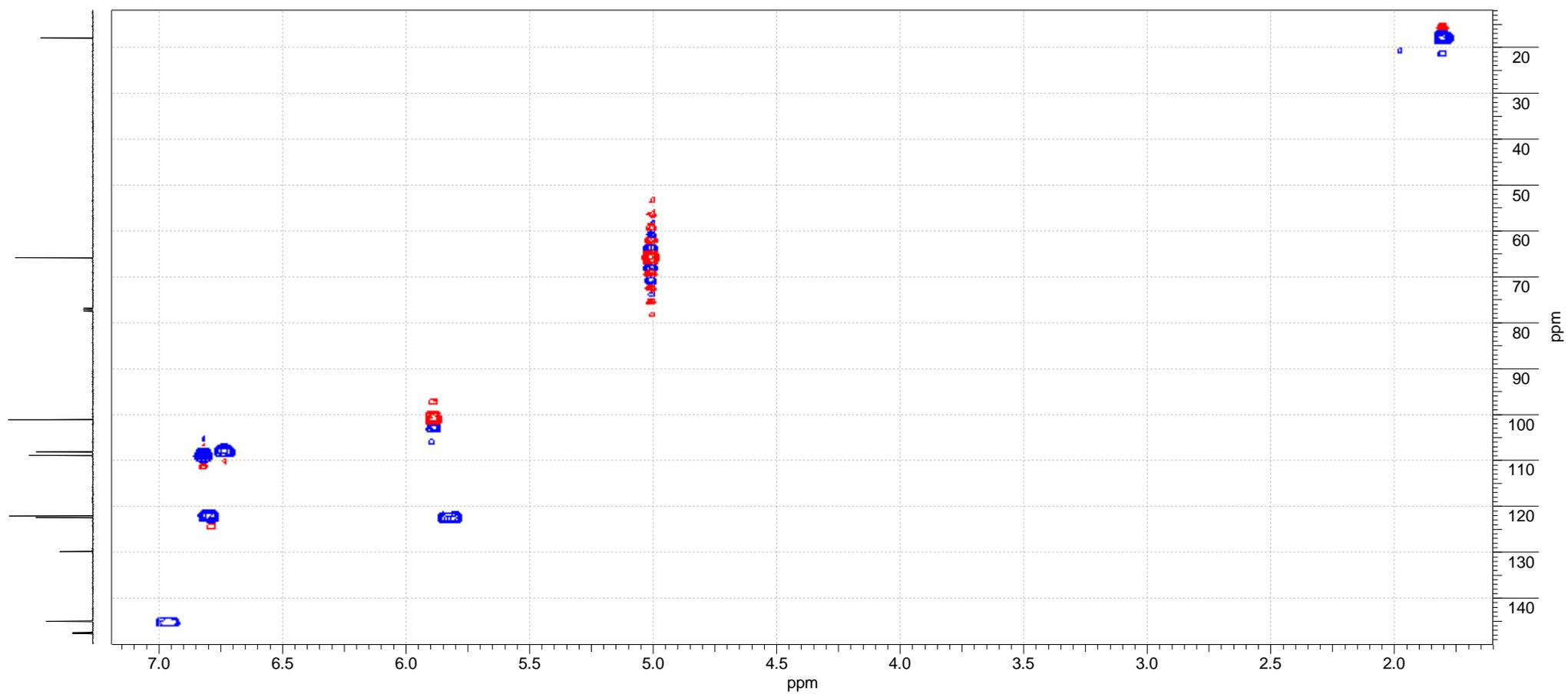
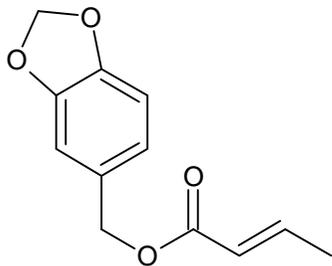
# 1,3-benzodioxol-5-ylmethyl (2E)-but-2-enoate (3f) <sup>1</sup>H NMR



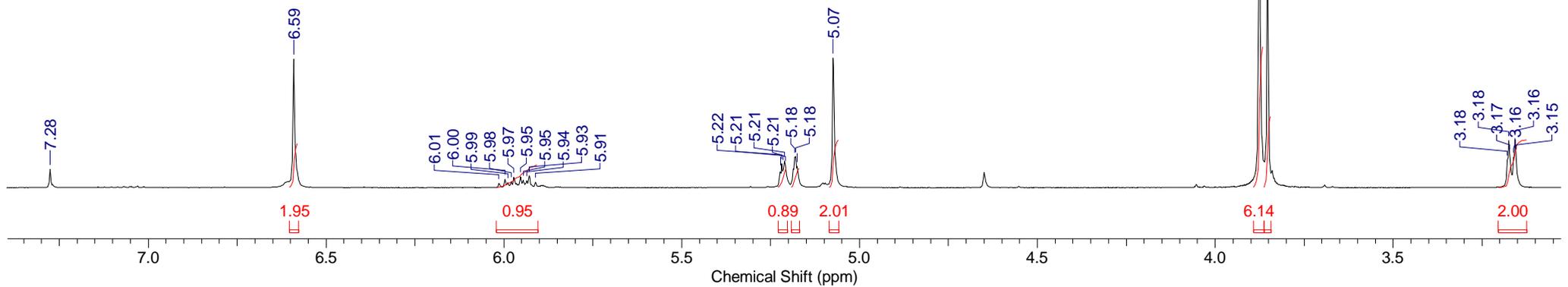
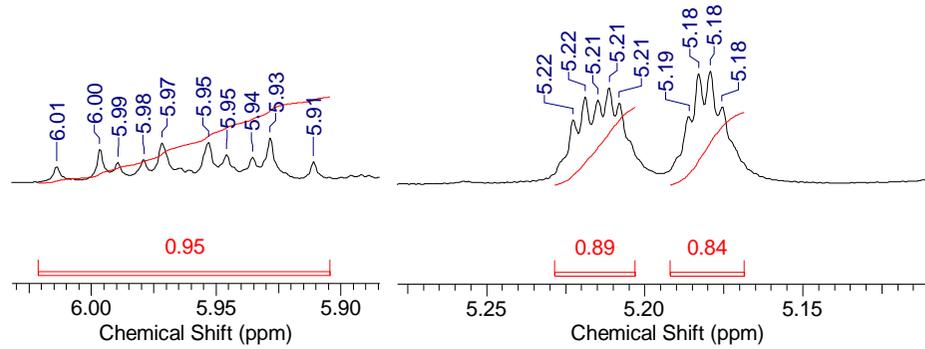
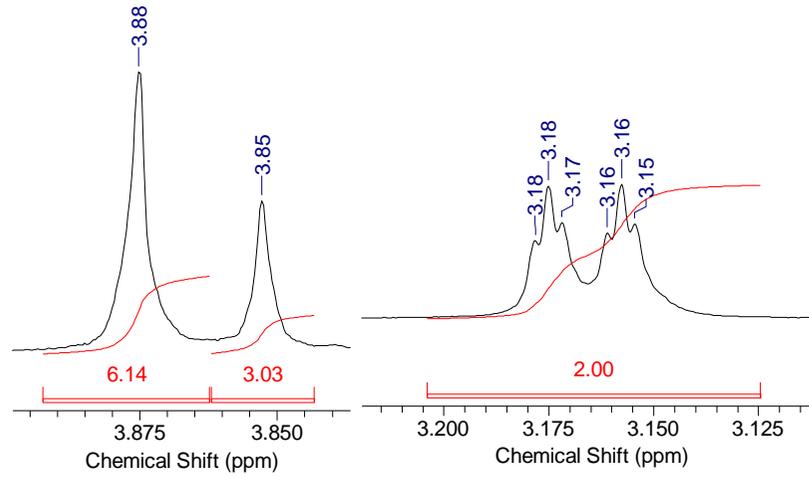
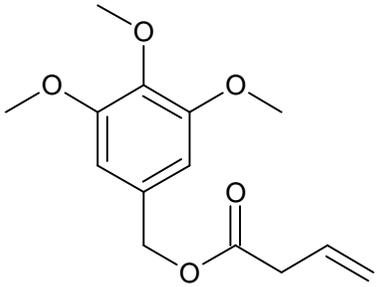
# 1,3-benzodioxol-5-ylmethyl (2E)-but-2-enoate (3f) <sup>13</sup>C NMR



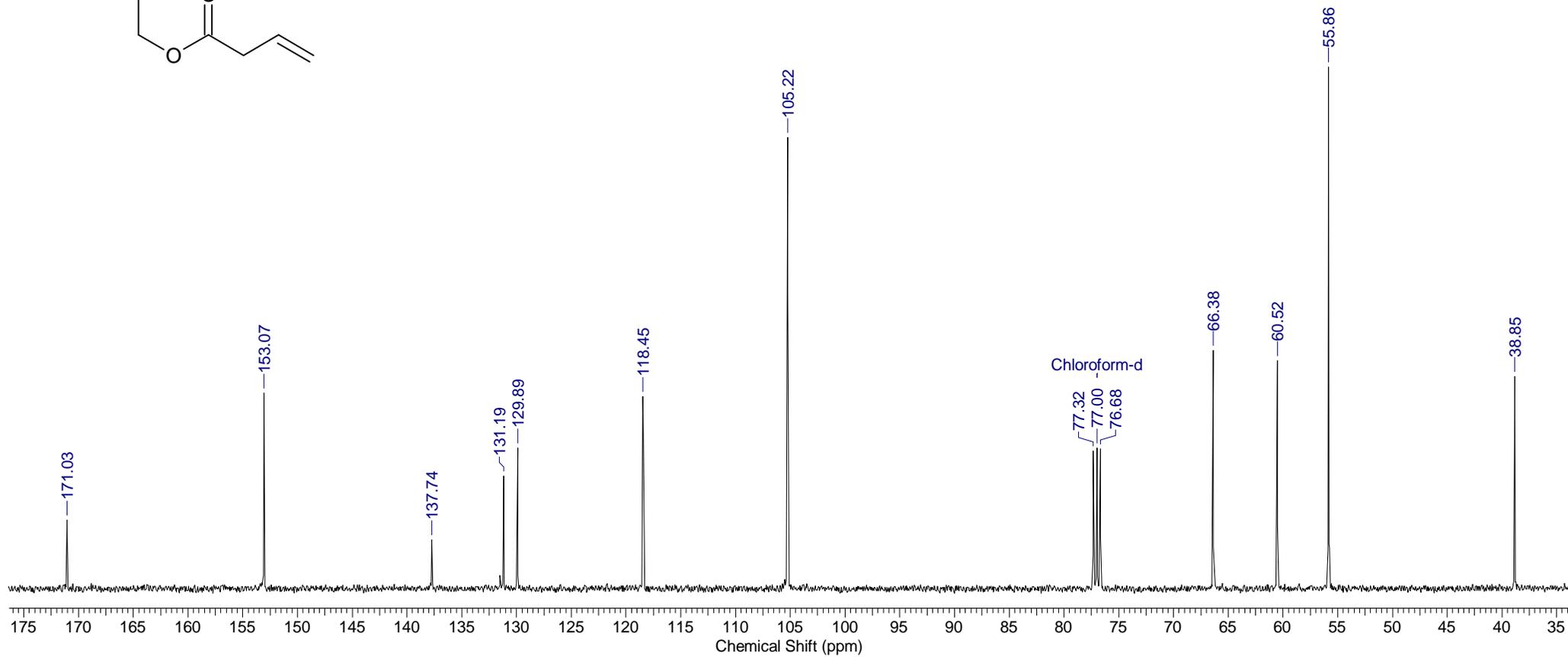
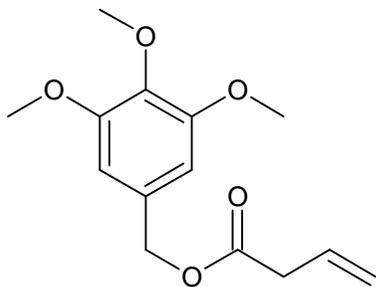
# 1,3-benzodioxol-5-ylmethyl (2E)-but-2-enoate (3f) gHSQC



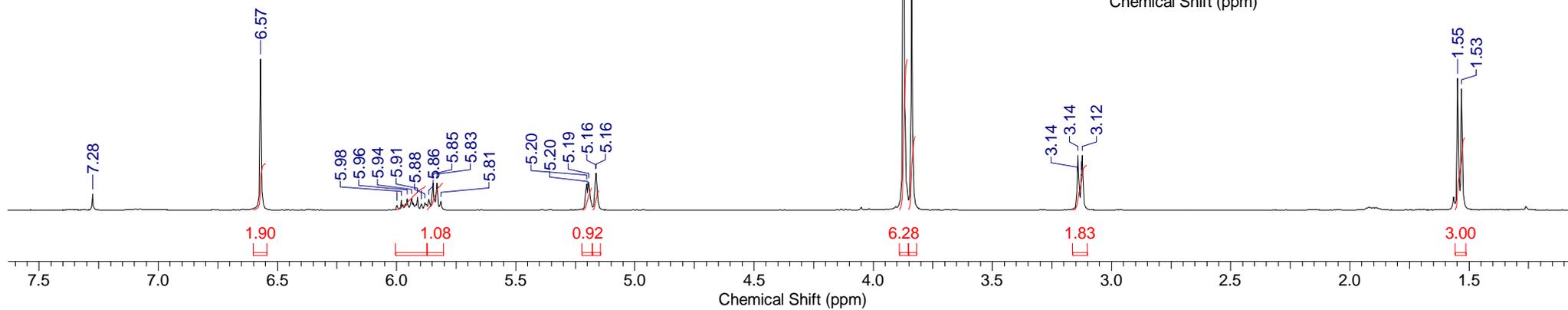
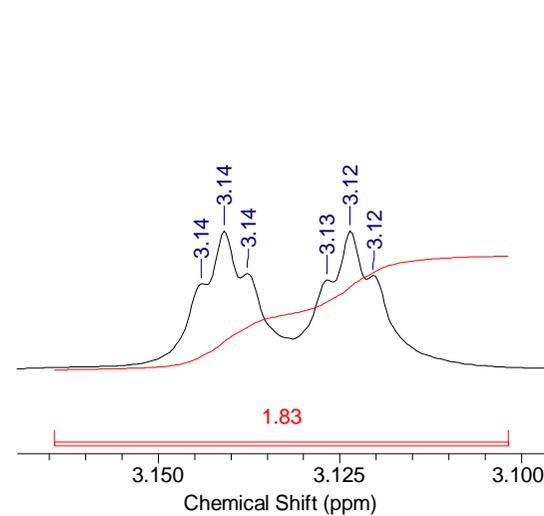
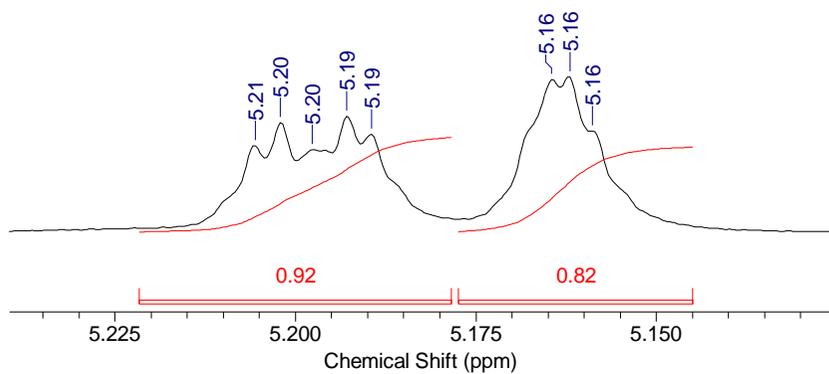
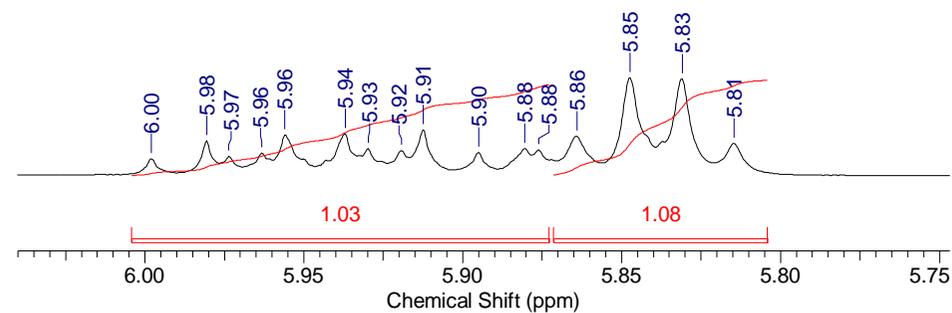
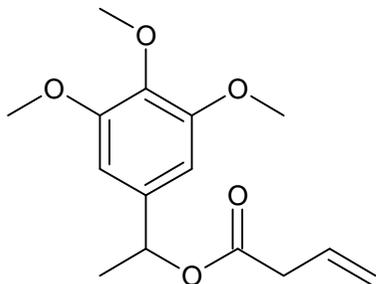
# 3,4,5-Trimethoxybenzyl but-3-enoate <sup>1</sup>H NMR



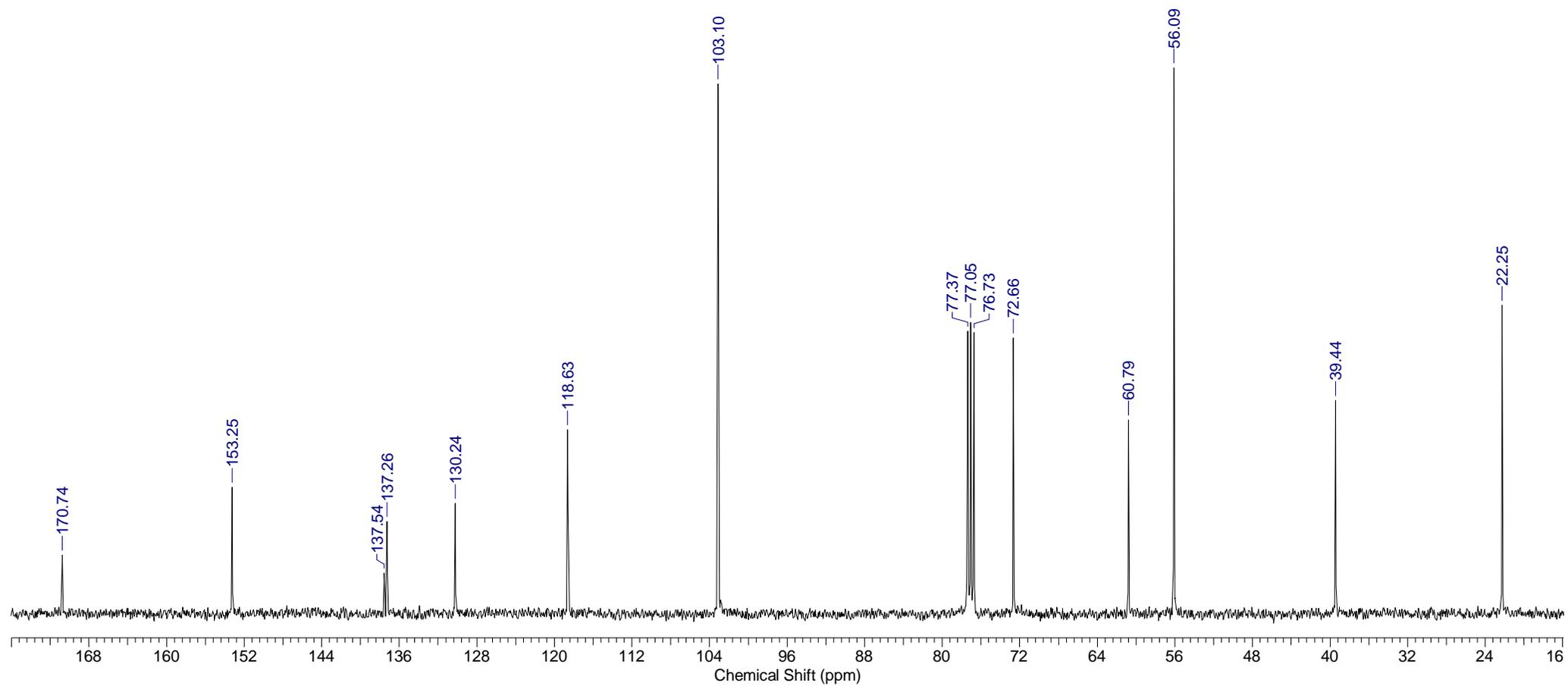
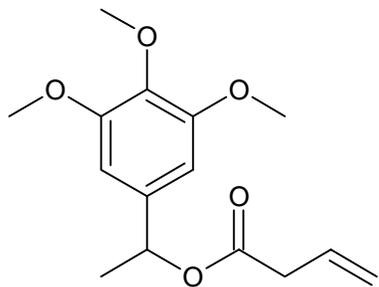
# 3,4,5-Trimethoxybenzyl but-3-enoate <sup>13</sup>C NMR



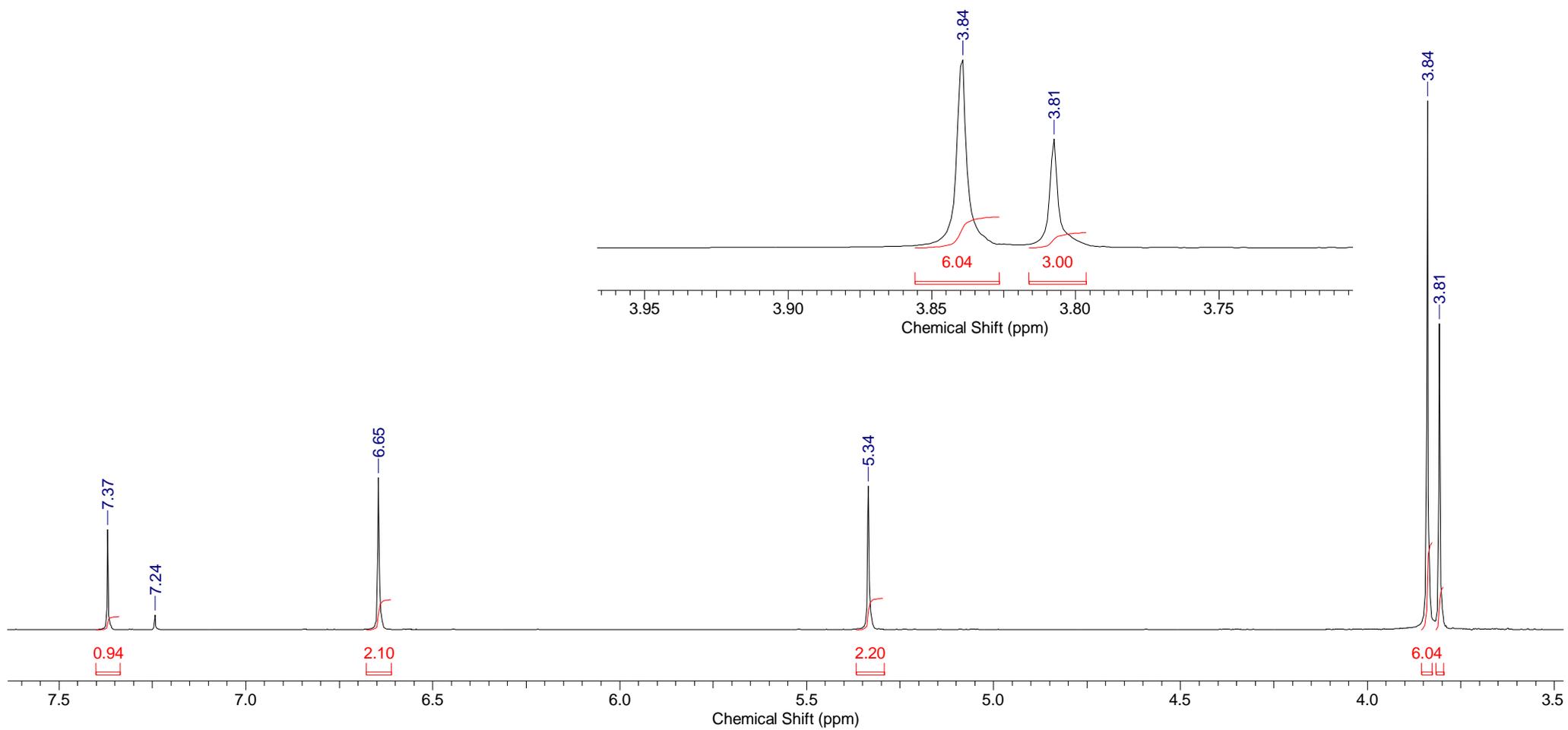
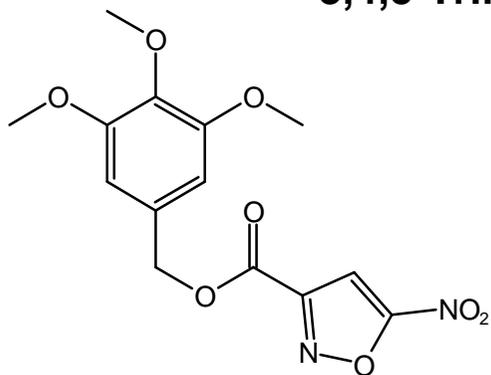
# 1-(3,4,5-Trimethoxyphenyl)ethyl but-3-enoate <sup>1</sup>H NMR



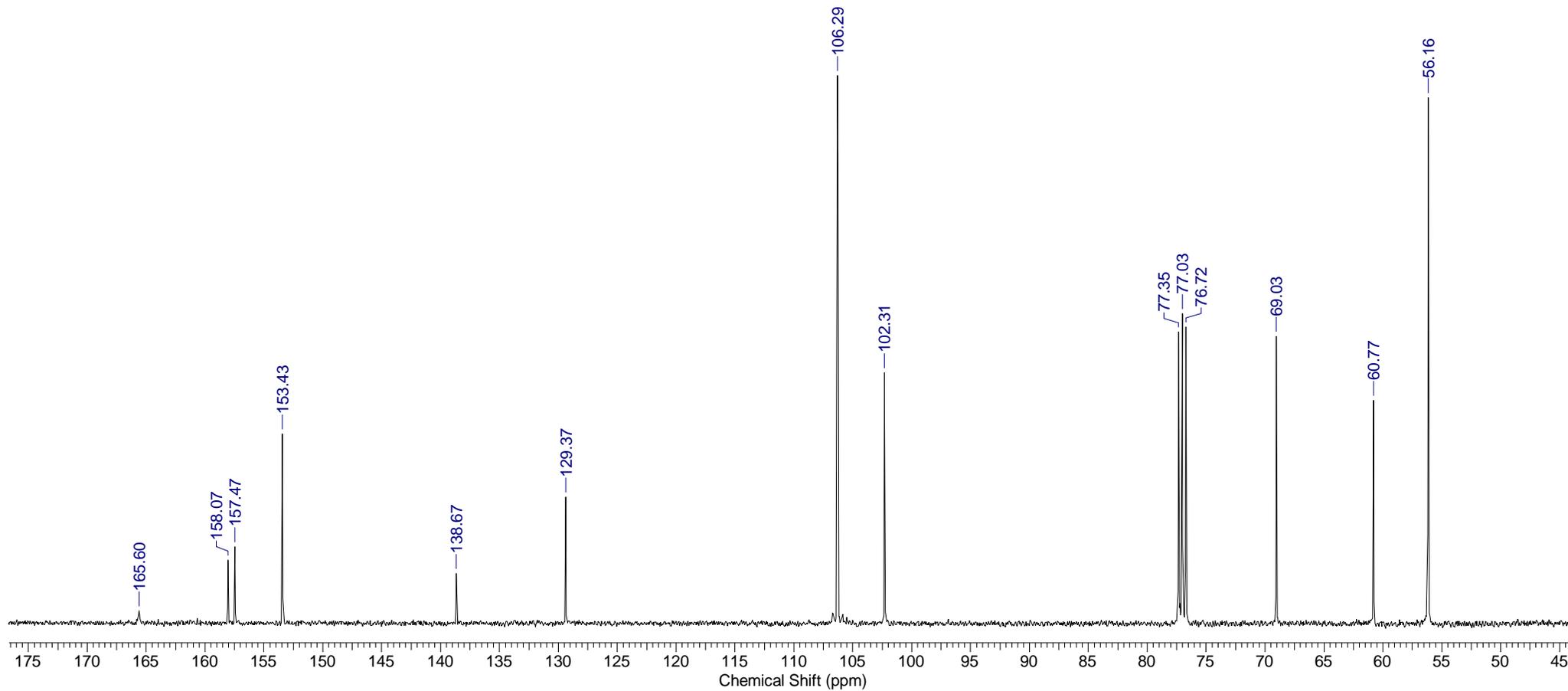
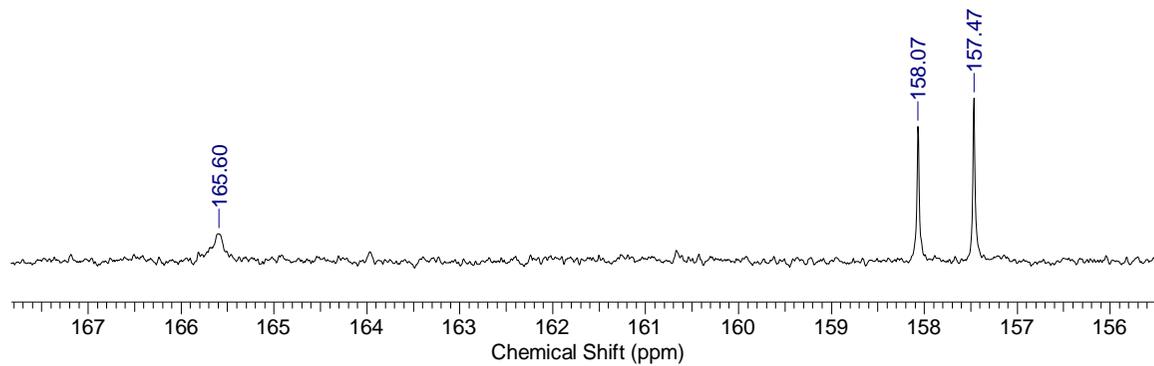
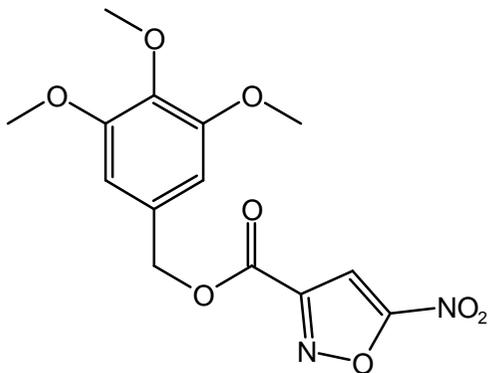
# 1-(3,4,5-Trimethoxyphenyl)ethyl but-3-enoate <sup>13</sup>C NMR



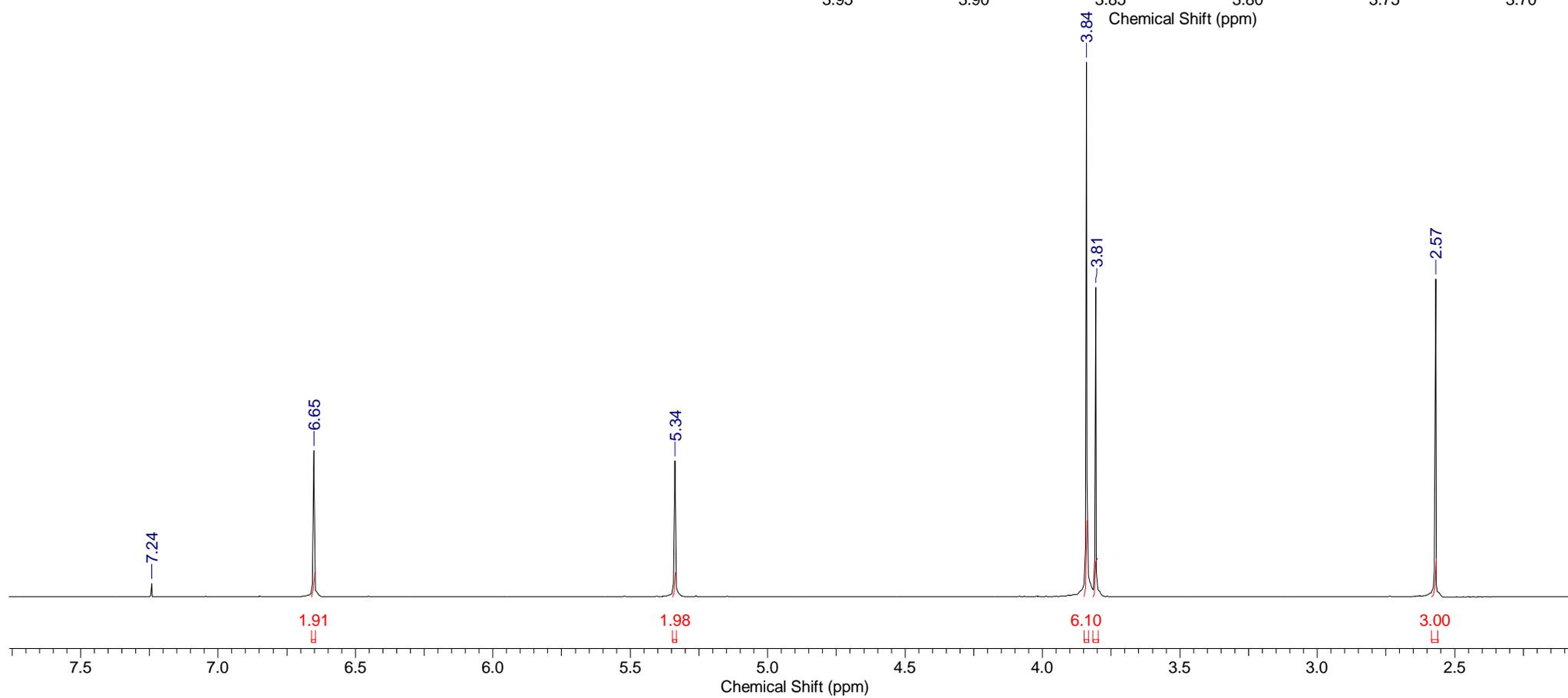
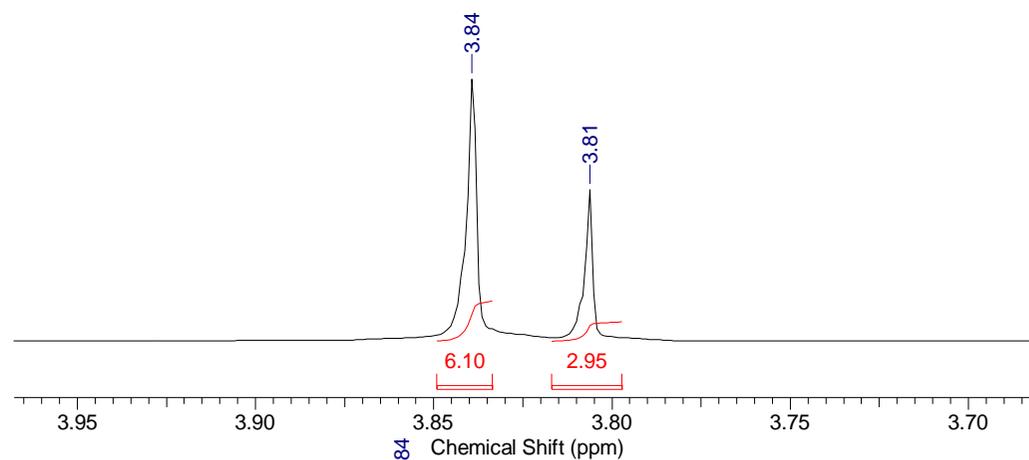
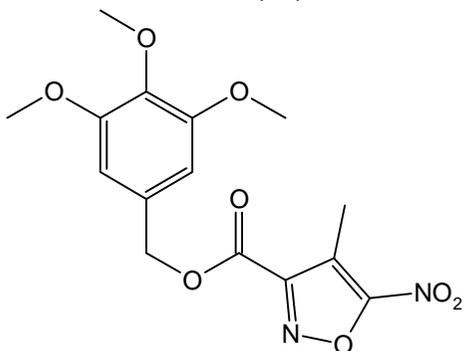
# 3,4,5-Trimethoxybenzyl 5-nitroisoxazole-3-carboxylate (4a) <sup>1</sup>H NMR



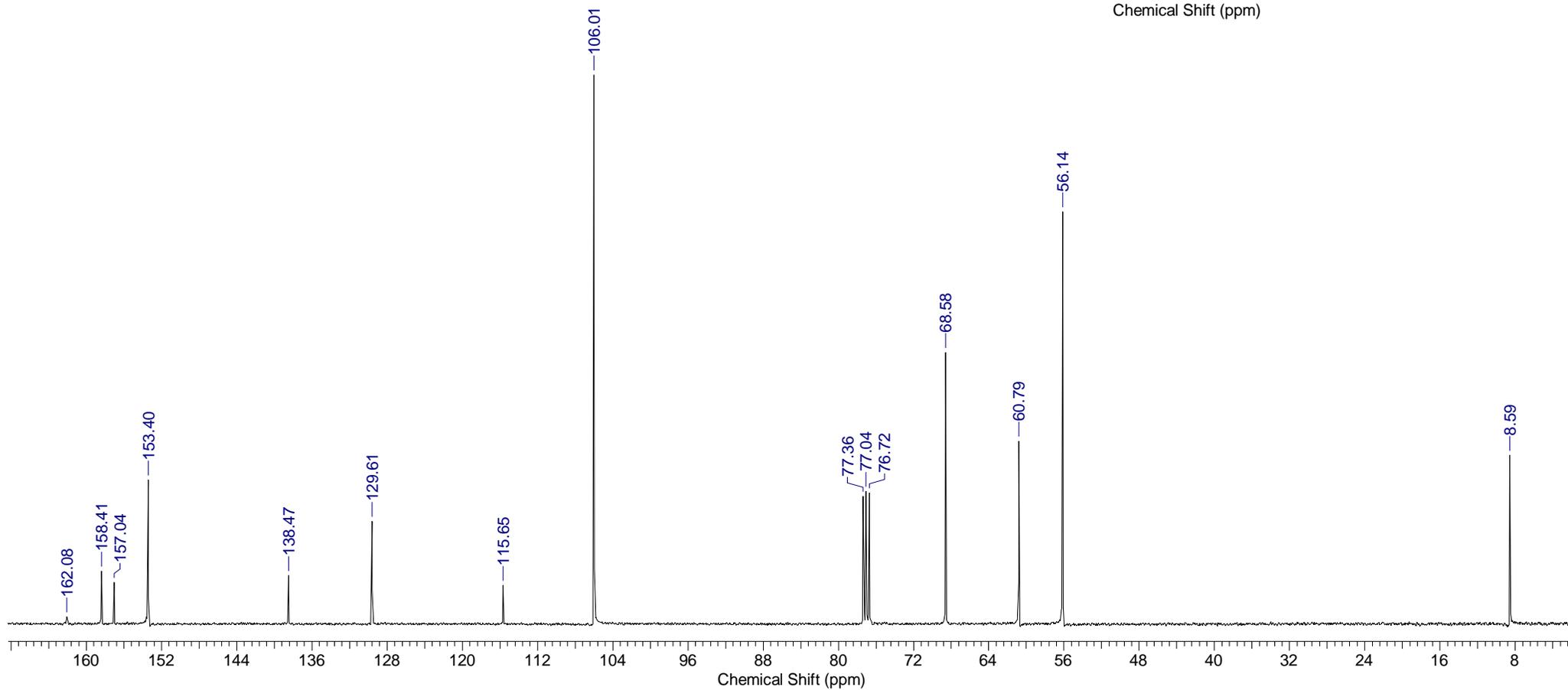
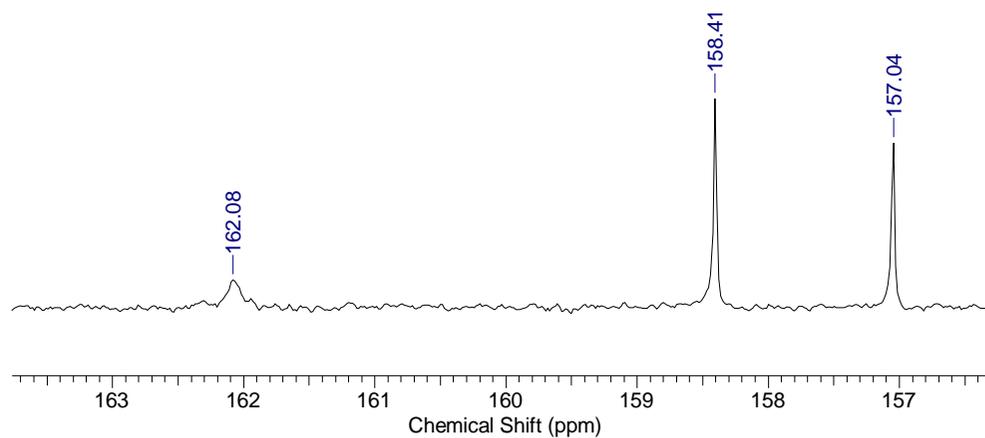
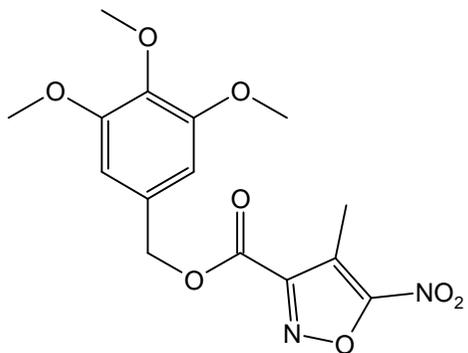
# 3,4,5-Trimethoxybenzyl 5-nitroisoxazole-3-carboxylate (4a) <sup>13</sup>C NMR



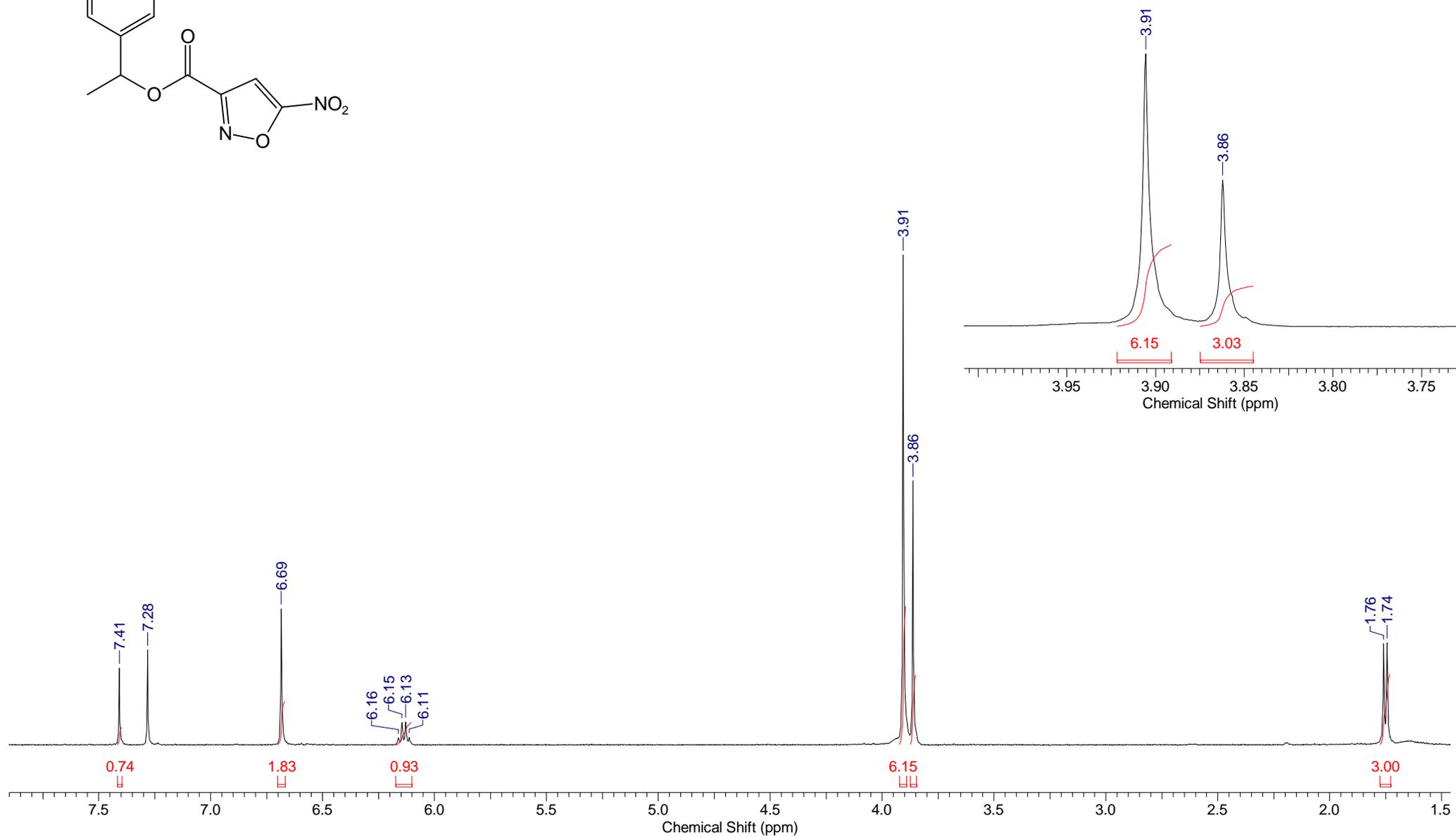
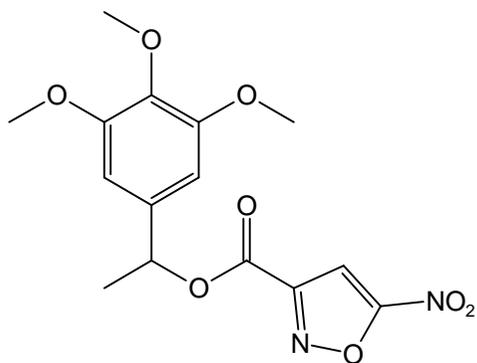
# 3,4,5-trimethoxybenzyl 4-methyl-5-nitroisoxazole-3-carboxylate (4b) <sup>1</sup>H NMR



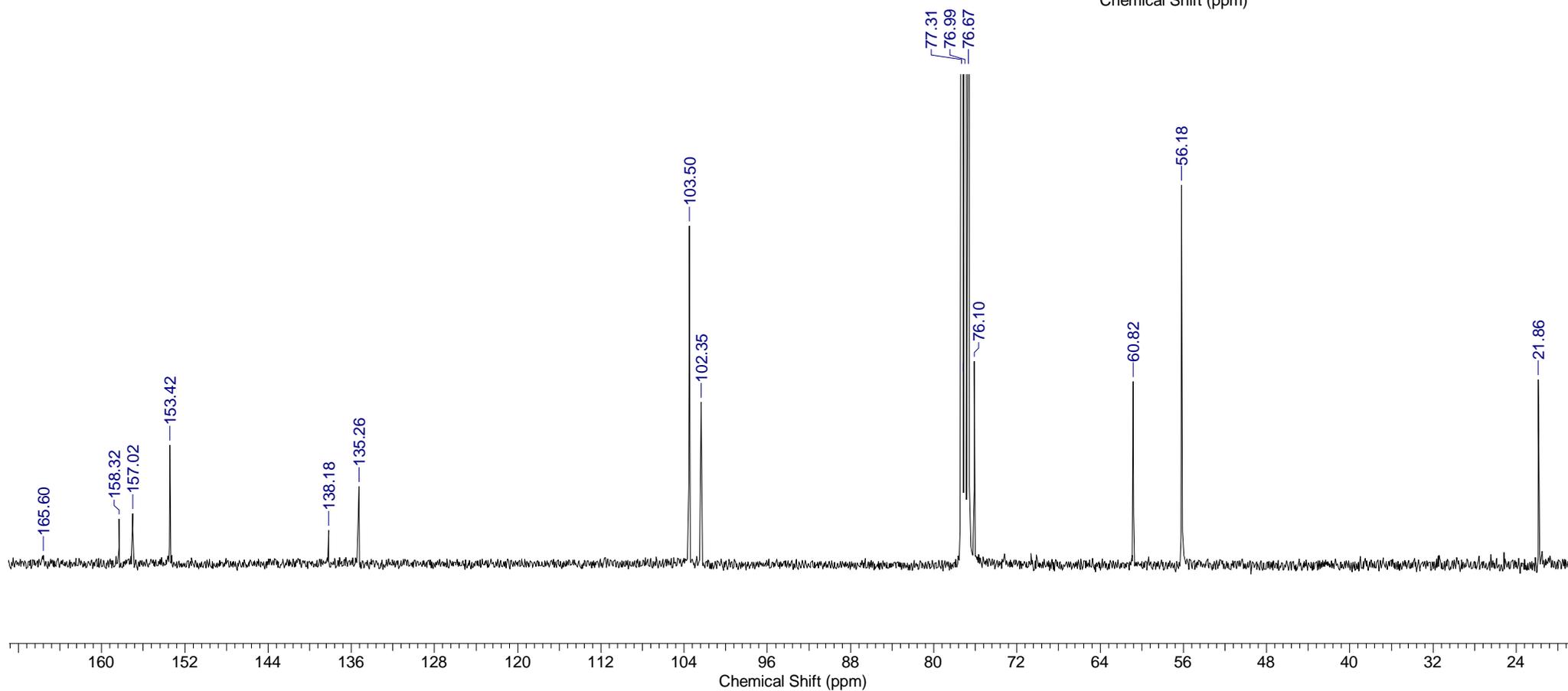
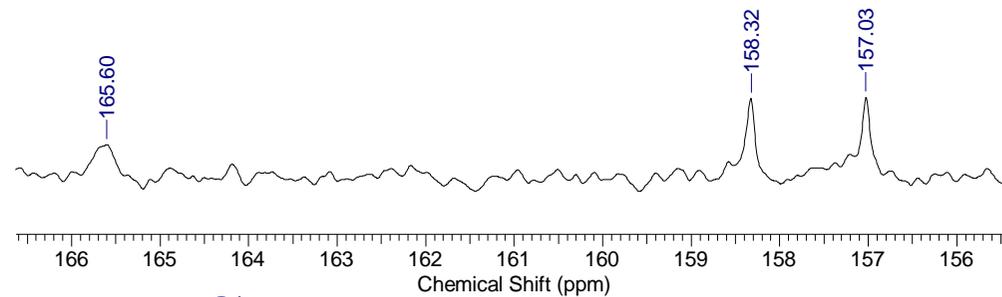
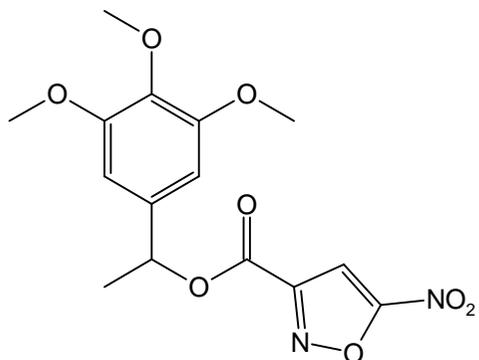
# 3,4,5-trimethoxybenzyl 4-methyl-5-nitroisoxazole-3-carboxylate (4b) <sup>13</sup>C NMR



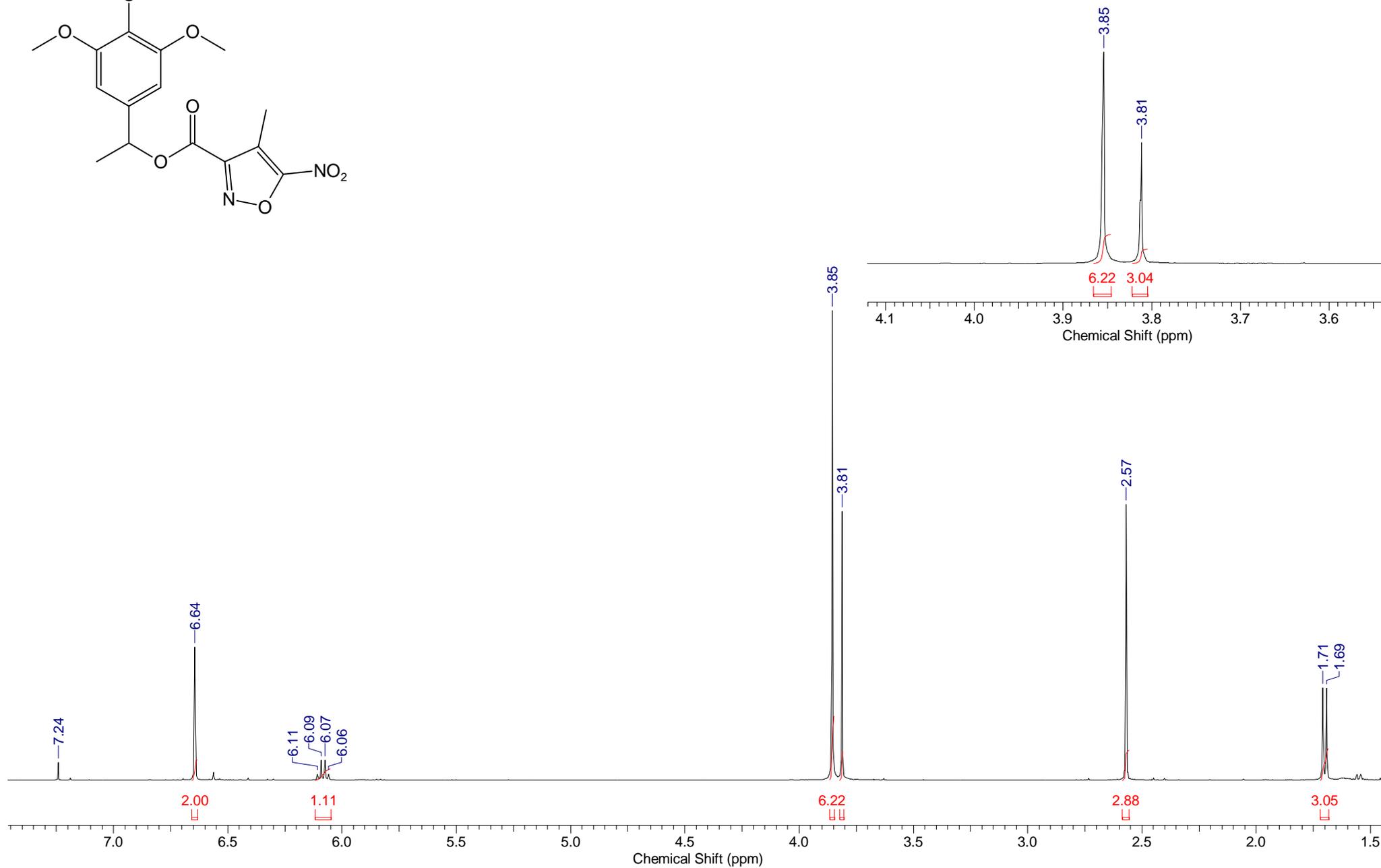
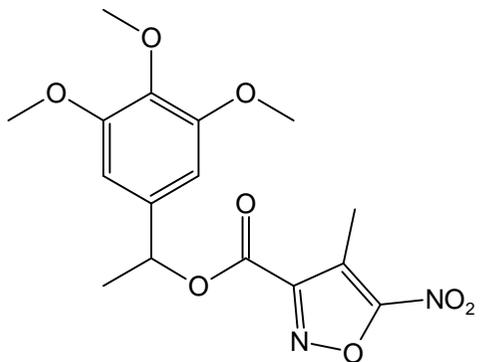
# 1-(3,4,5-Trimethoxyphenyl)ethyl 5-nitroisoxazole-3-carboxylate (4c) <sup>1</sup>H NMR



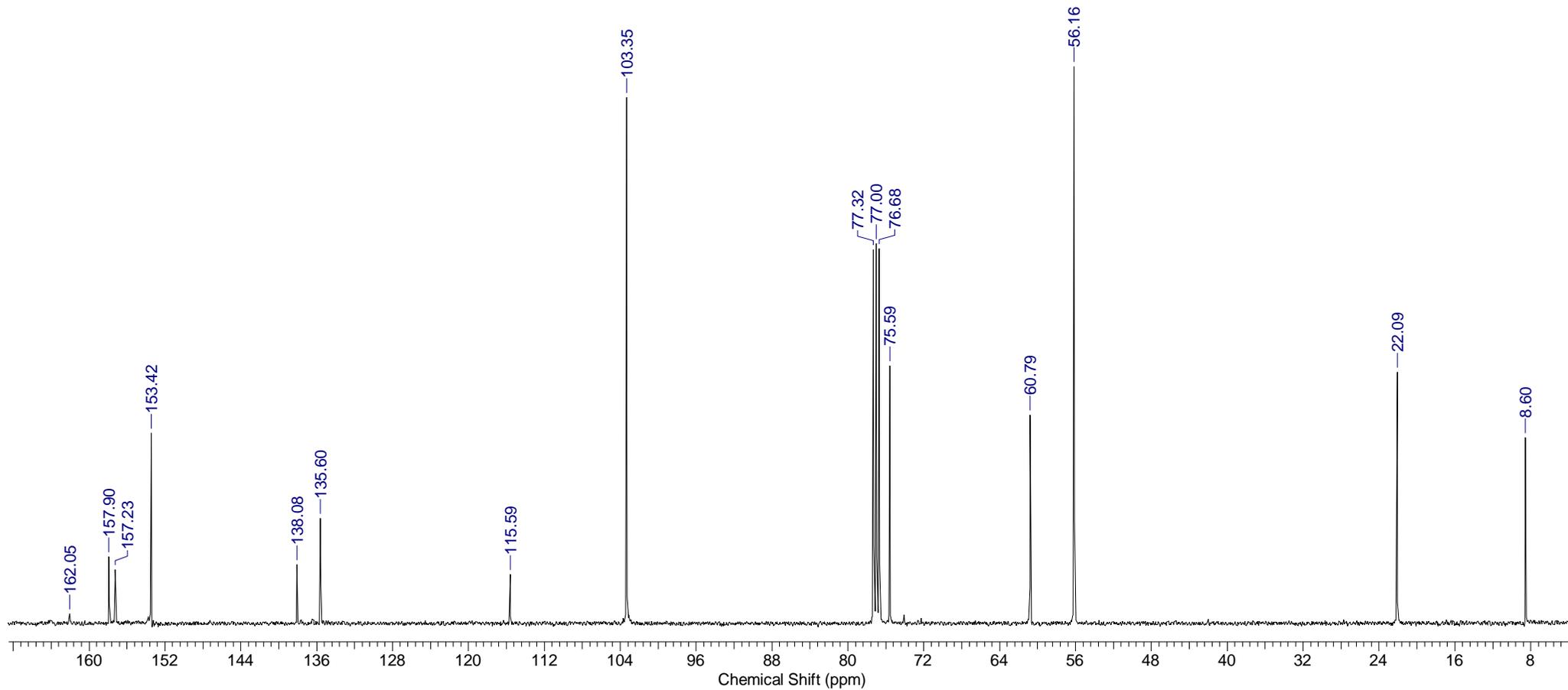
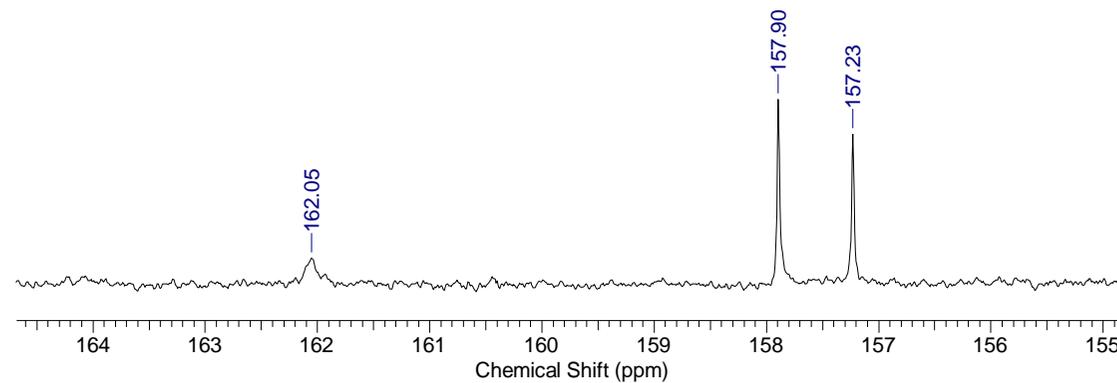
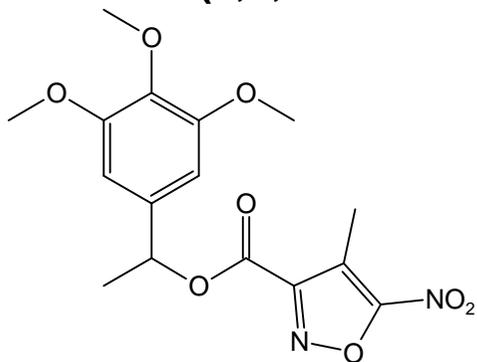
# 1-(3,4,5-Trimethoxyphenyl)ethyl 5-nitroisoxazole-3-carboxylate (4c) $^{13}\text{C}$ NMR



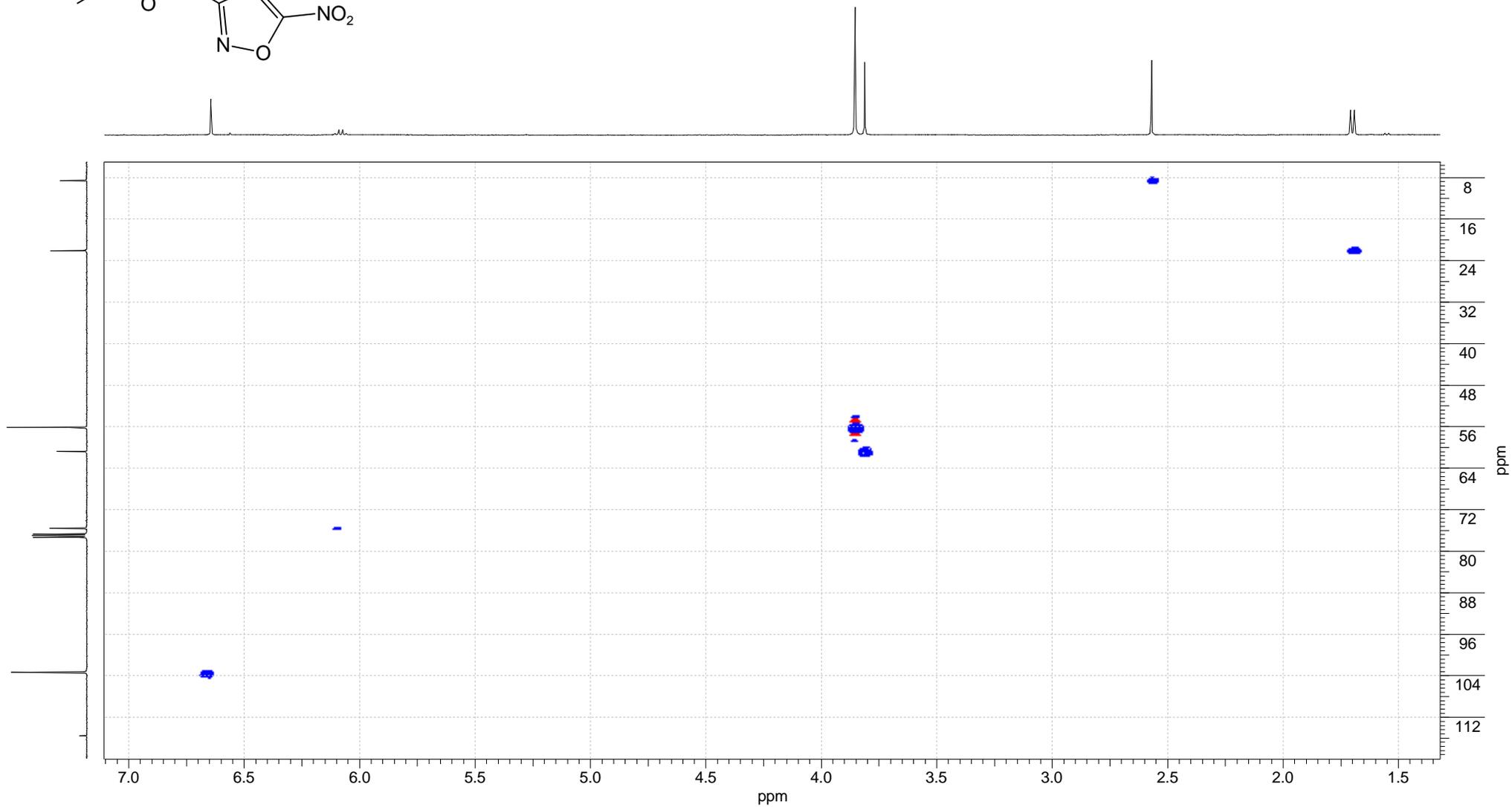
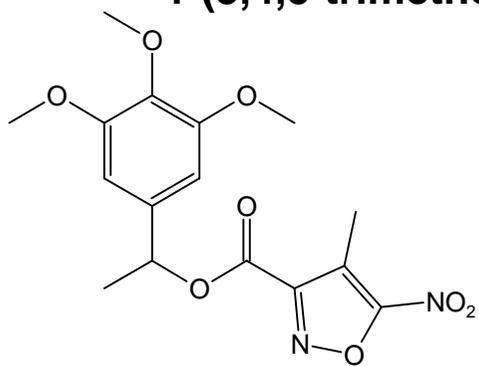
# 1-(3,4,5-trimethoxyphenyl)ethyl 4-methyl-5-nitroisoxazole-3-carboxylate (4d) <sup>1</sup>H NMR



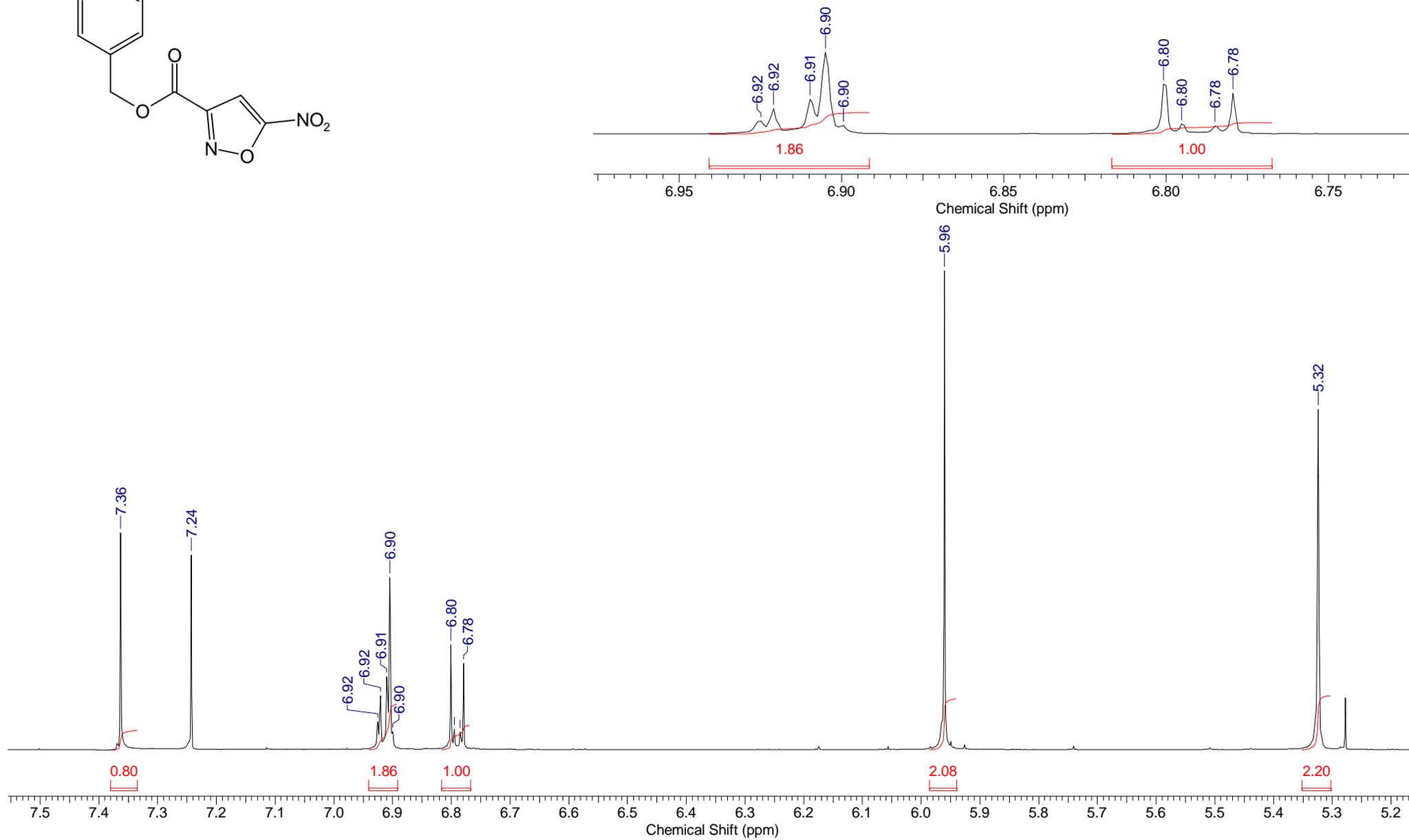
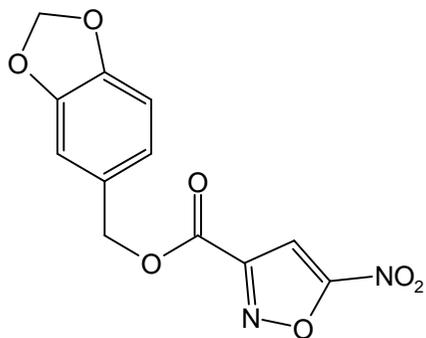
# 1-(3,4,5-trimethoxyphenyl)ethyl 4-methyl-5-nitroisoxazole-3-carboxylate (4d) <sup>13</sup>C NMR



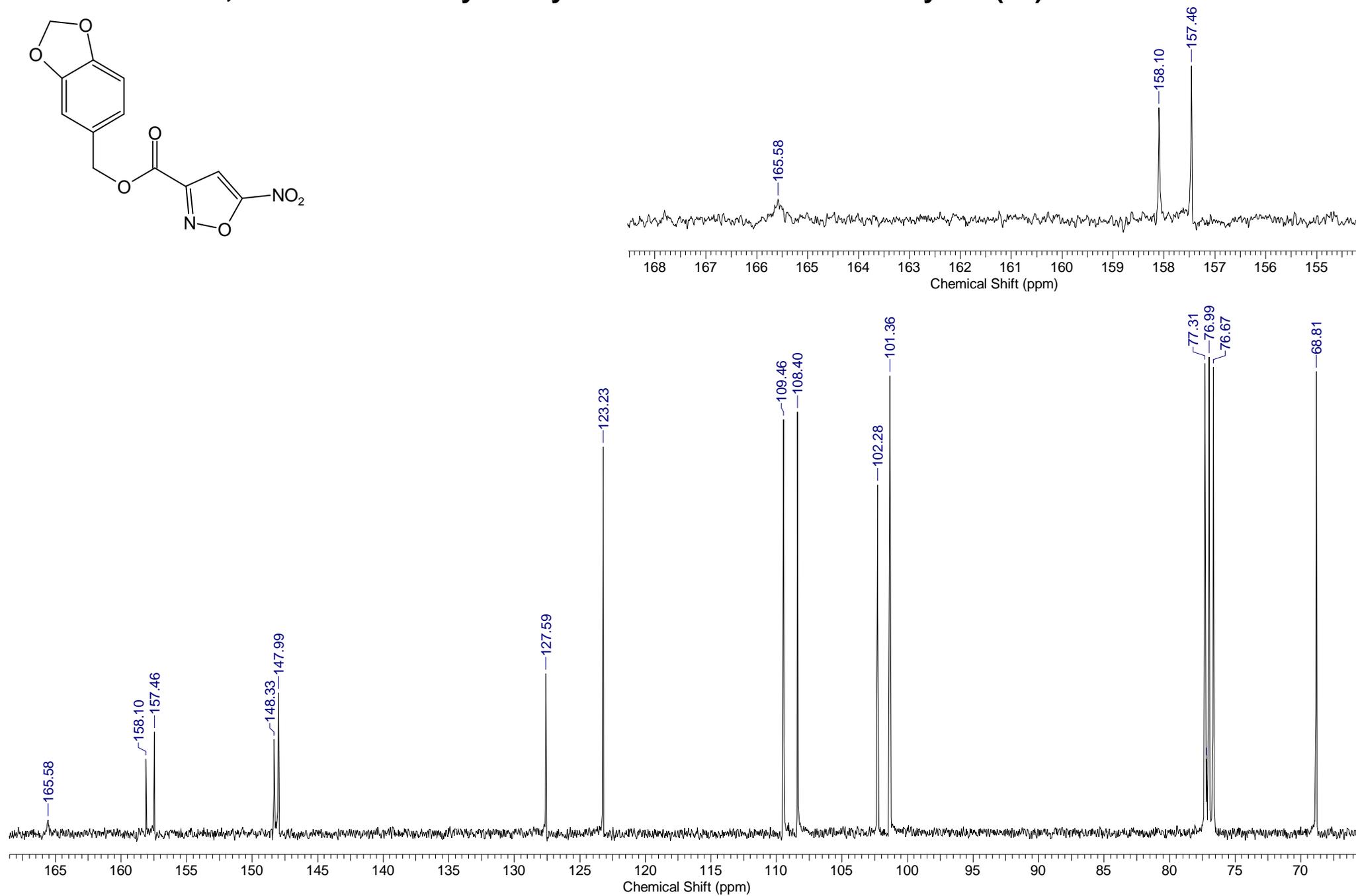
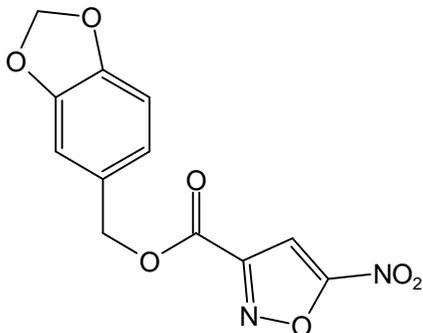
# 1-(3,4,5-trimethoxyphenyl)ethyl 4-methyl-5-nitroisoxazole-3-carboxylate (4d) gHSQC



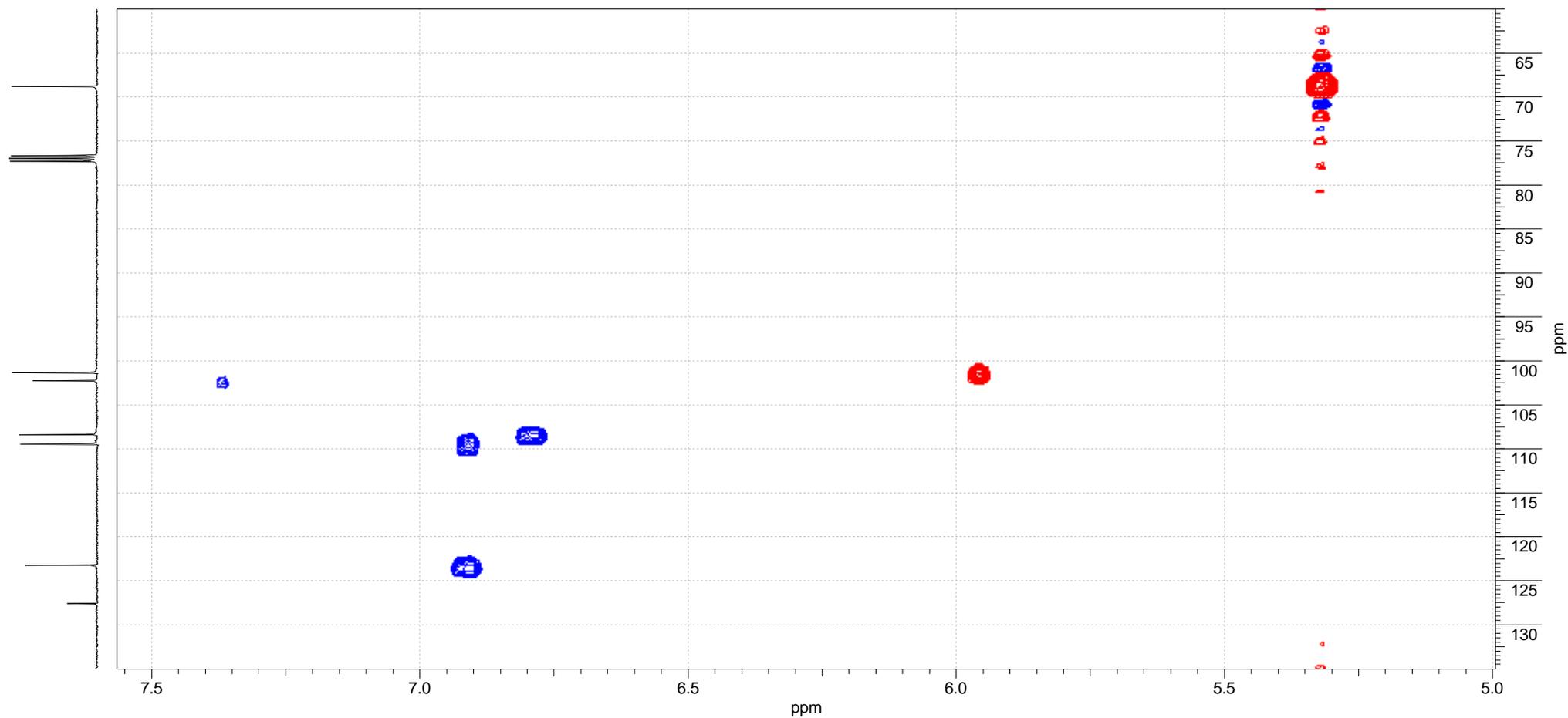
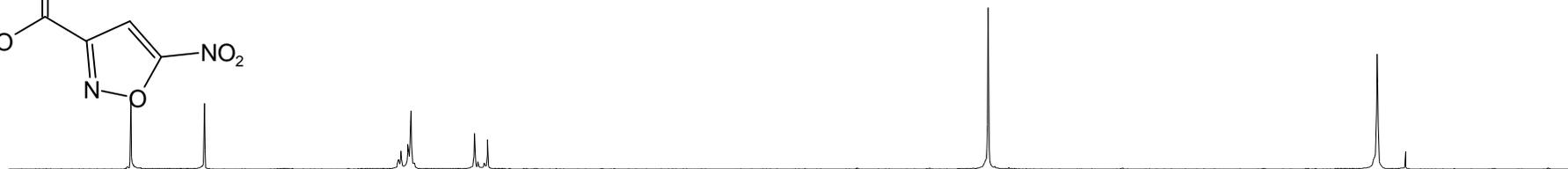
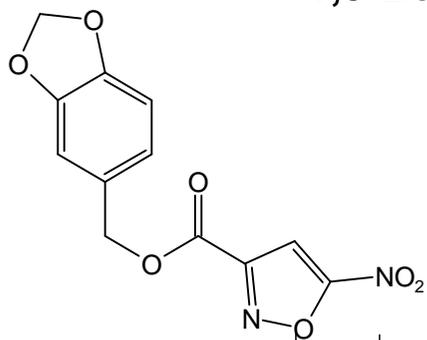
# 1,3-Benzodioxol-5-ylmethyl 5-nitroisoxazole-3-carboxylate (4e) <sup>1</sup>H NMR



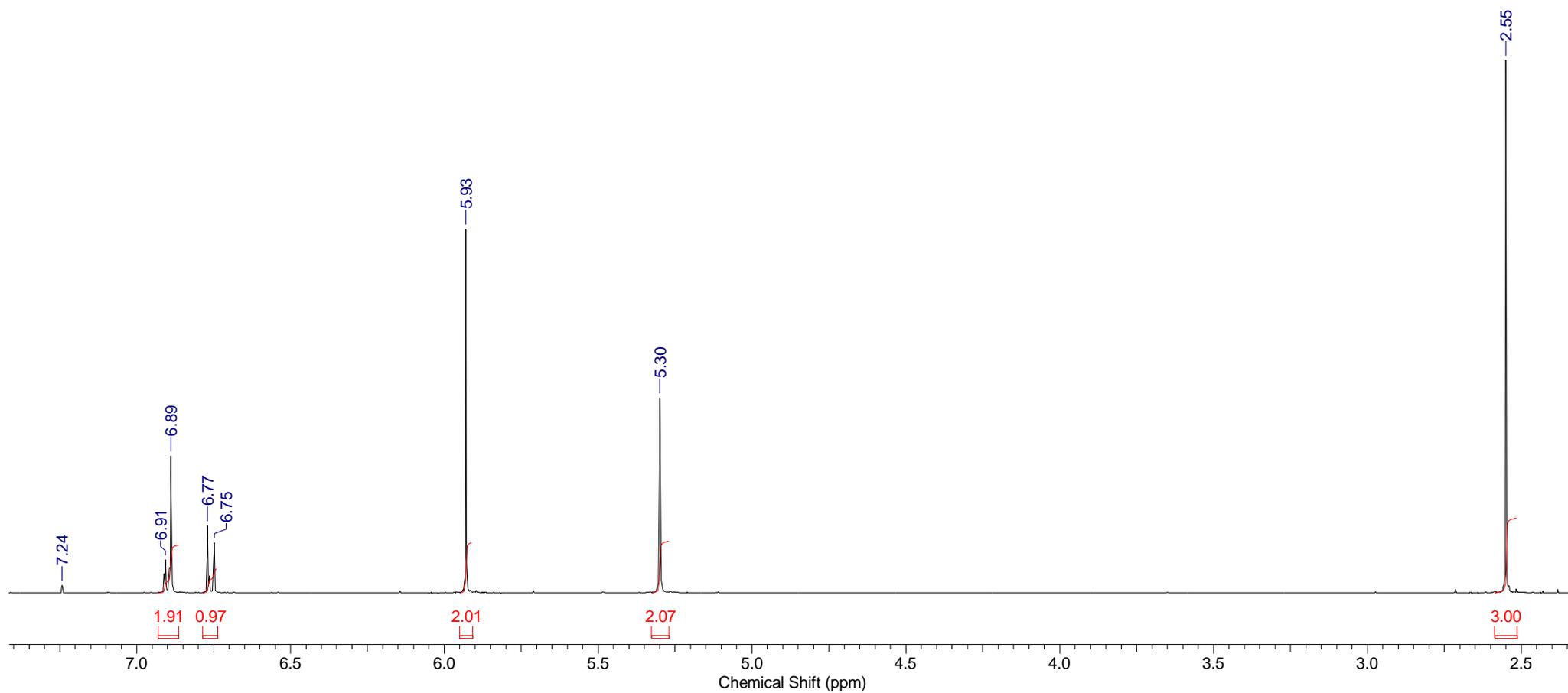
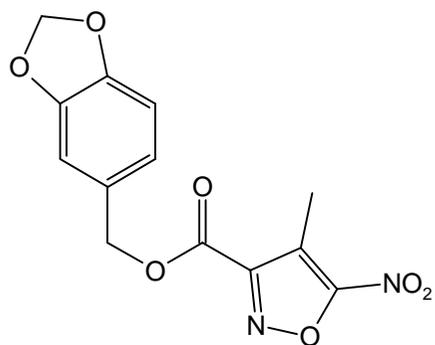
# 1,3-Benzodioxol-5-ylmethyl 5-nitroisoxazole-3-carboxylate (4e) $^{13}\text{C}$ NMR



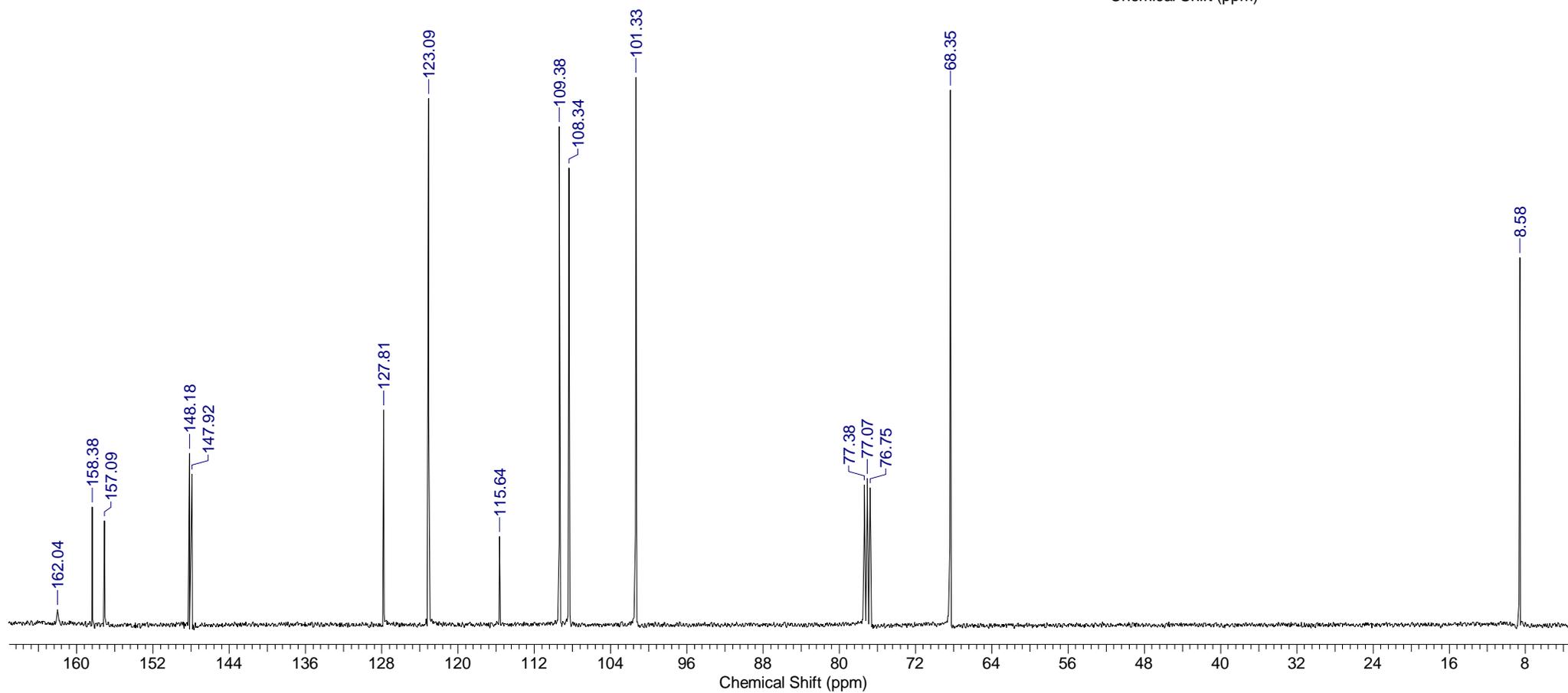
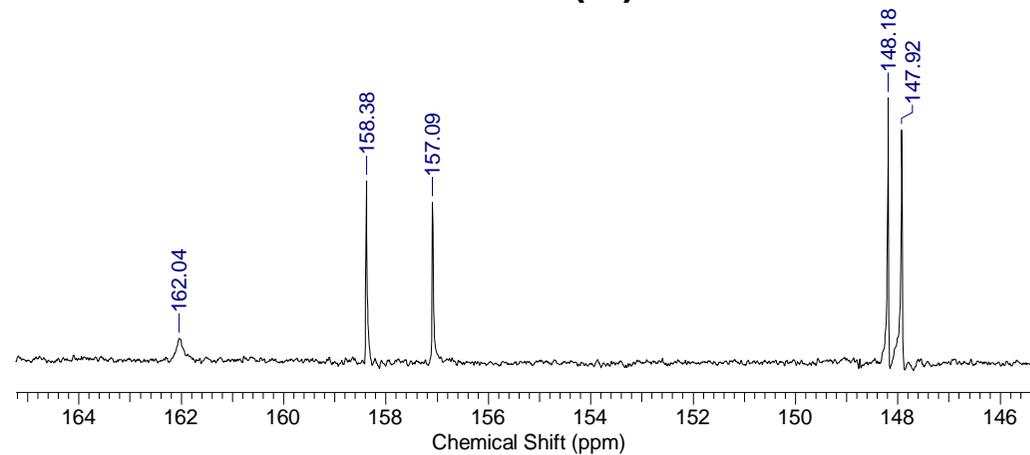
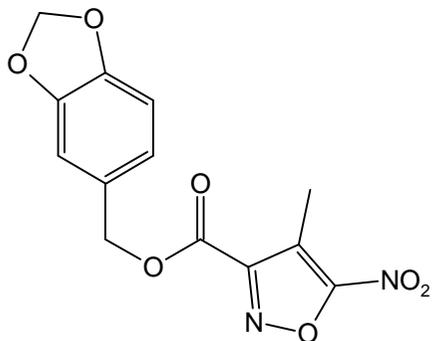
# 1,3-Benzodioxol-5-ylmethyl 5-nitroisoxazole-3-carboxylate (4e) gHSQC



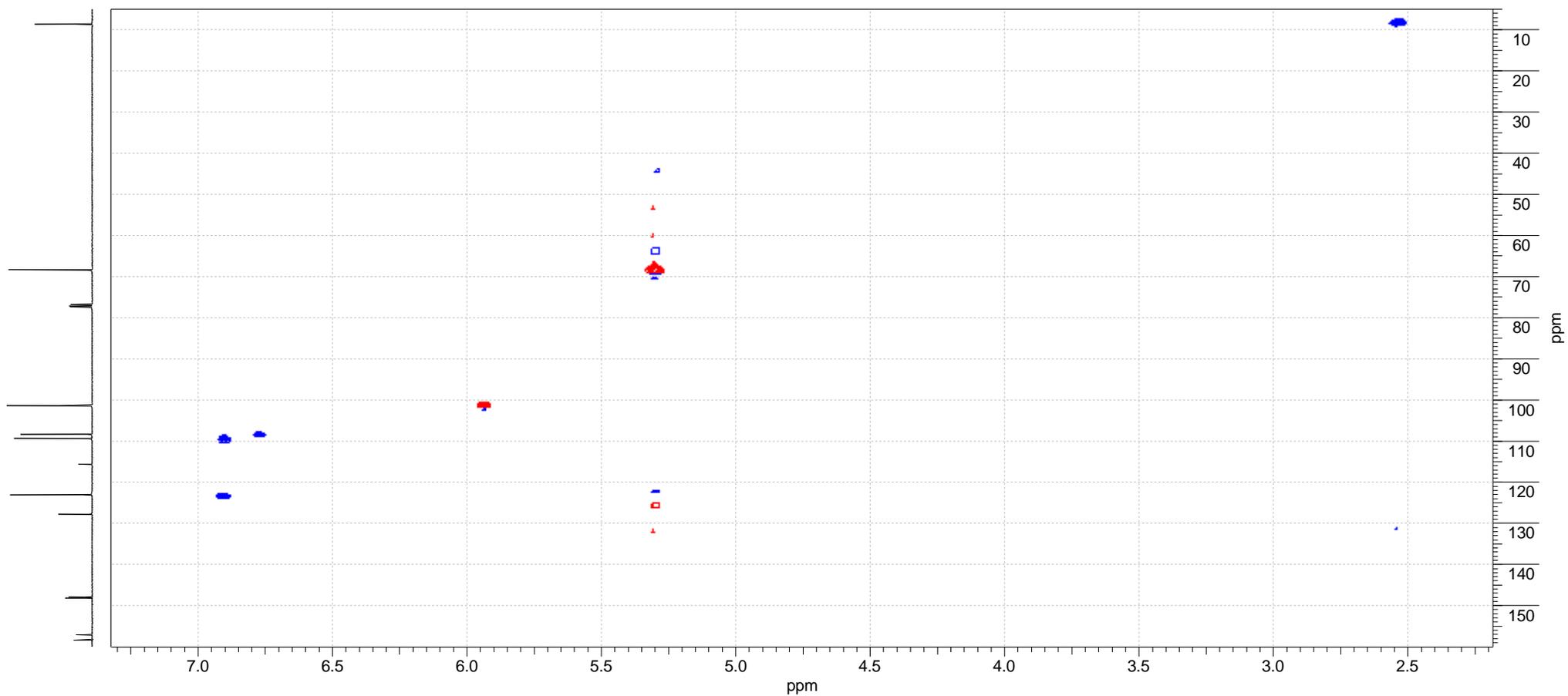
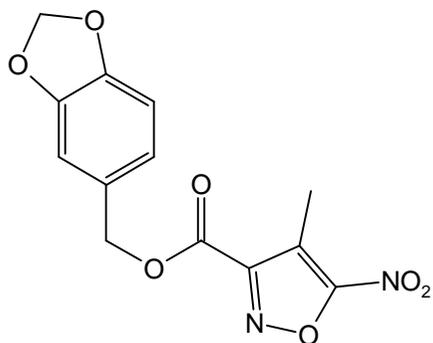
# 1,3-Benzodioxol-5-ylmethyl 4-methyl-5-nitroisoxazole-3-carboxylate (4f) <sup>1</sup>H NMR



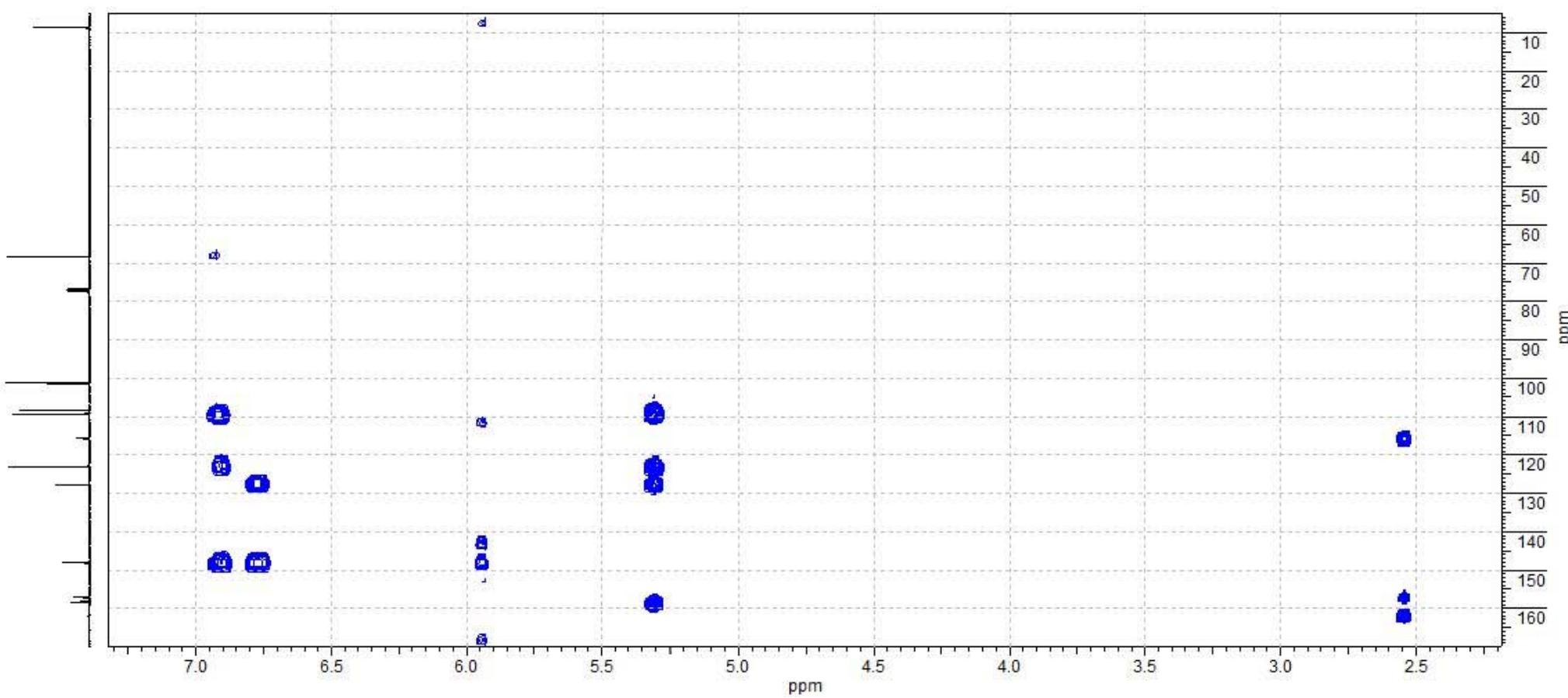
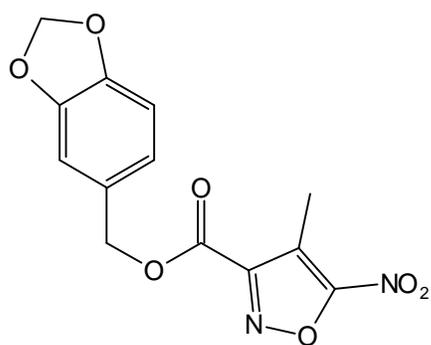
# 1,3-Benzodioxol-5-ylmethyl 4-methyl-5-nitroisoxazole-3-carboxylate (4f) <sup>13</sup>C NMR



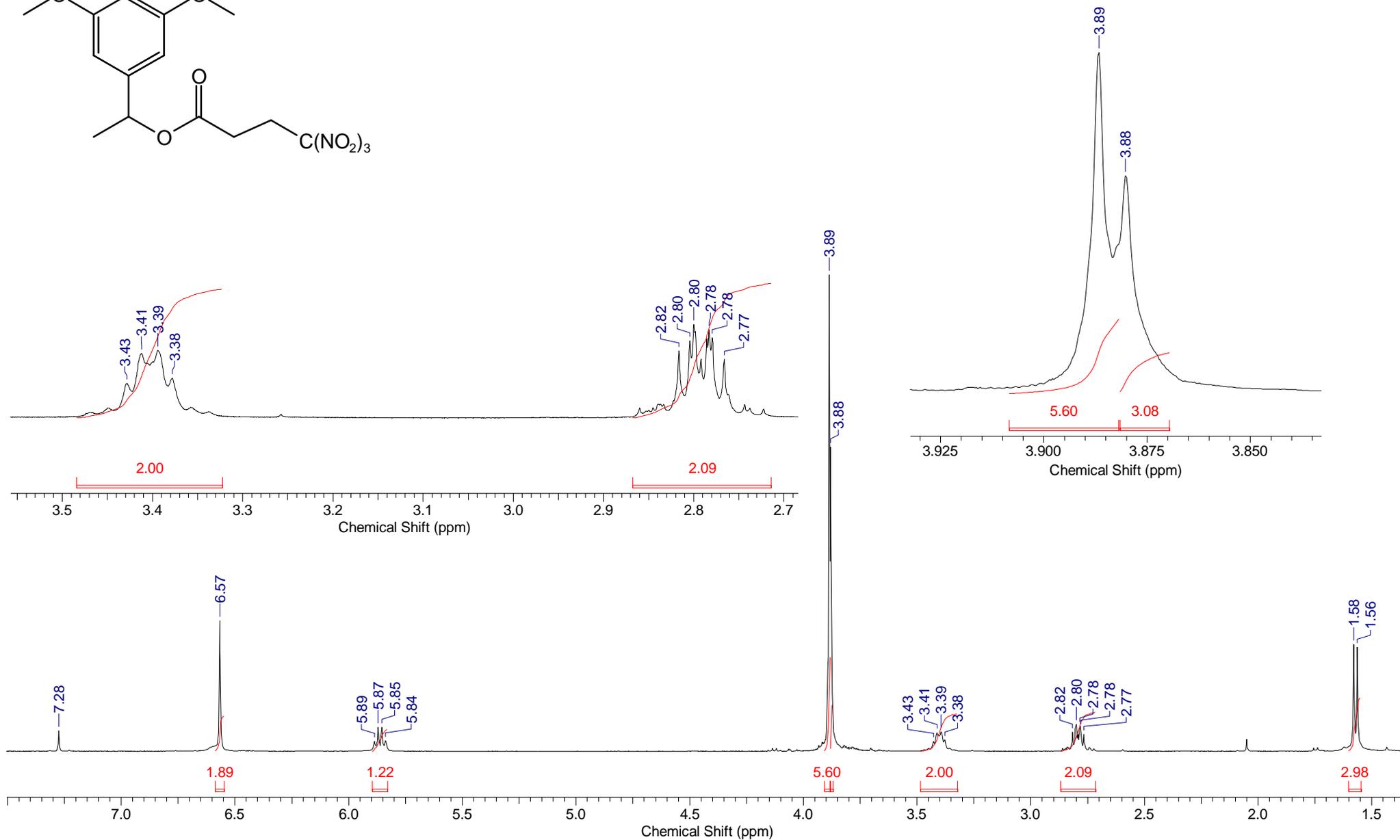
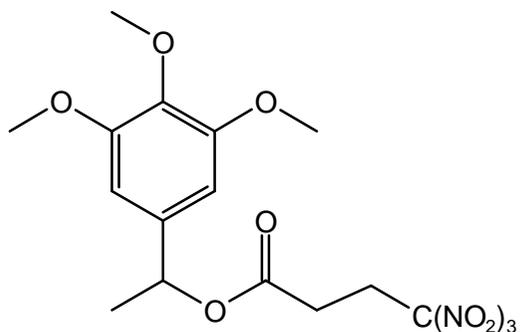
# 1,3-Benzodioxol-5-ylmethyl 4-methyl-5-nitroisoxazole-3-carboxylate (4f) gHSQC



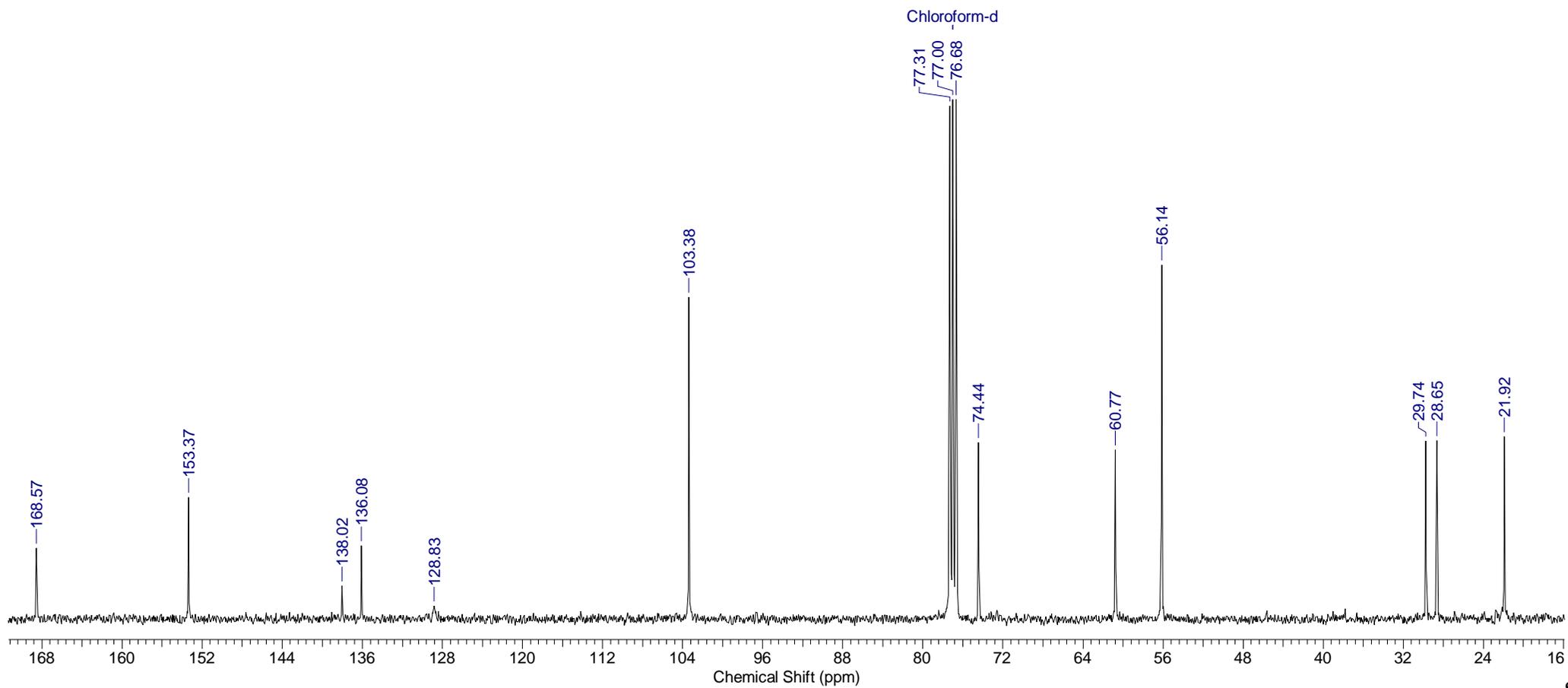
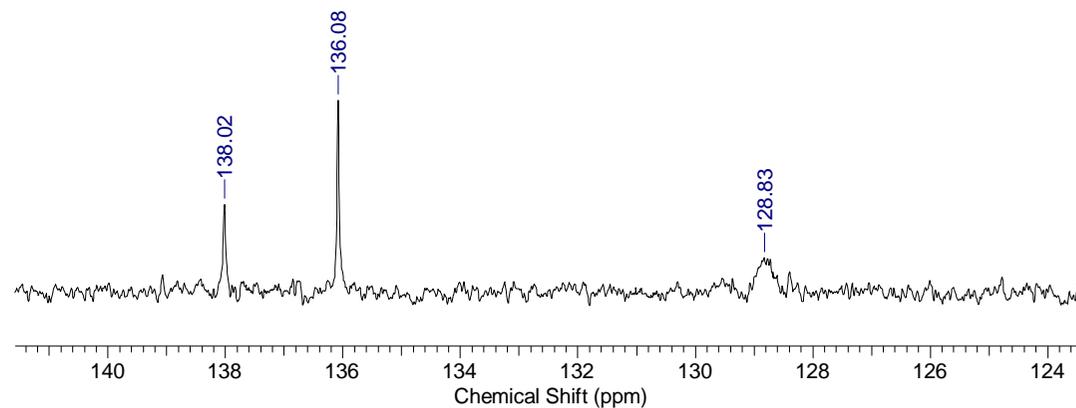
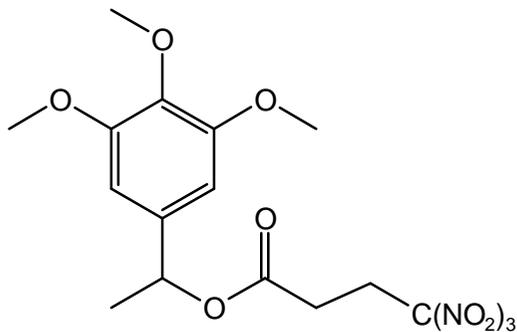
# 1,3-Benzodioxol-5-ylmethyl 4-methyl-5-nitroisoxazole-3-carboxylate (4f) gHMBC



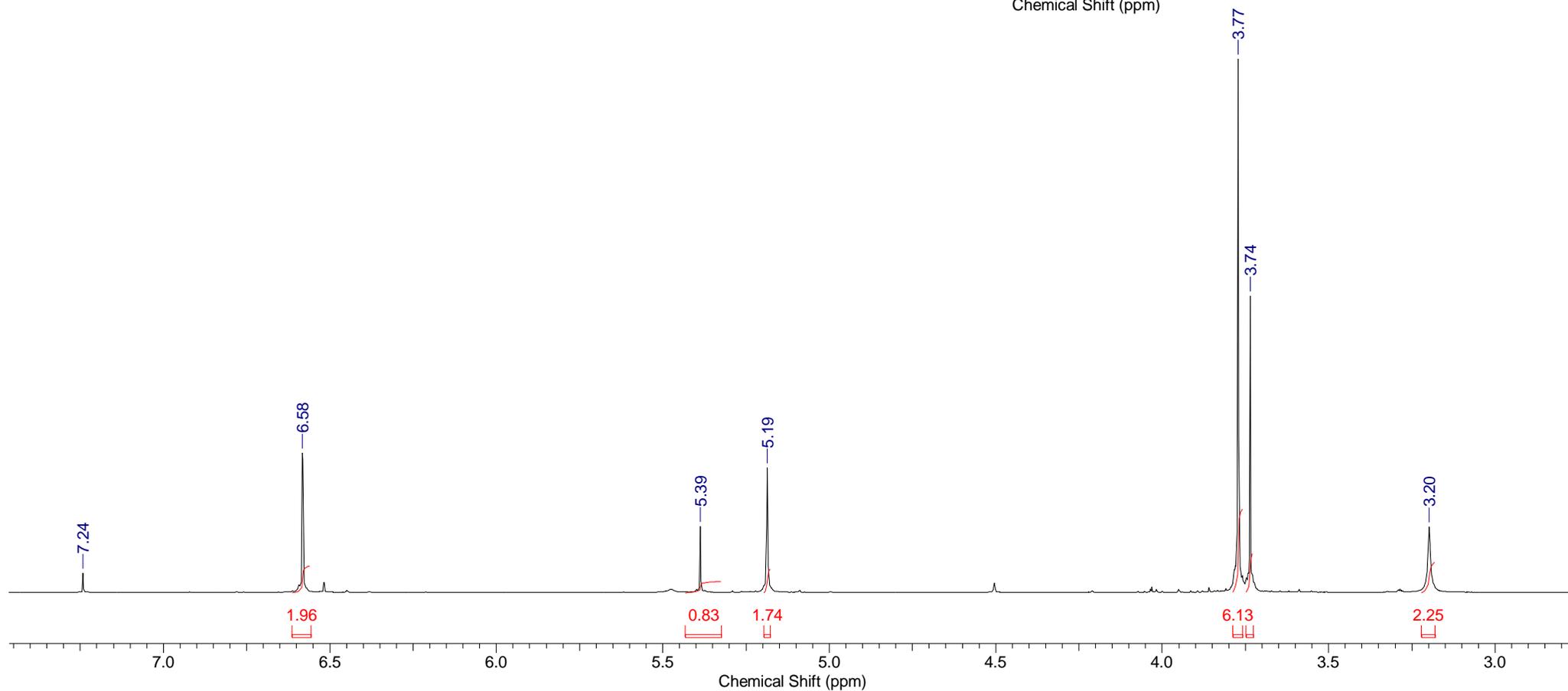
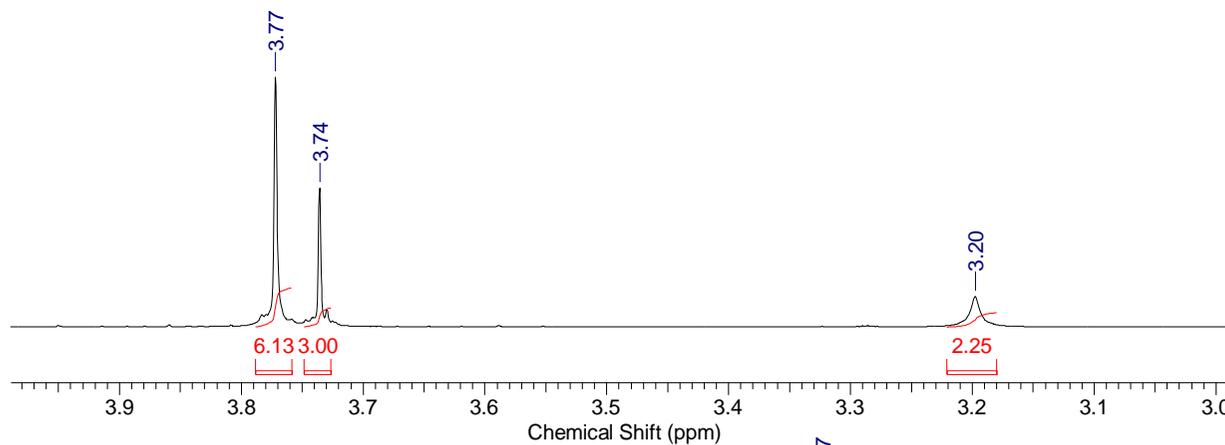
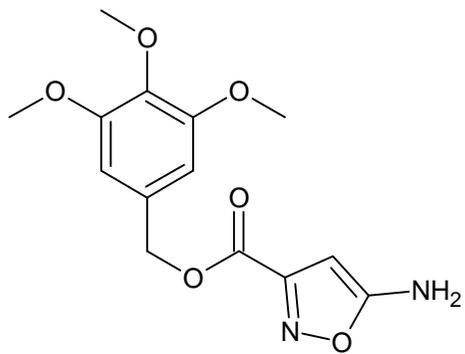
# 1-(3,4,5-Trimethoxyphenyl)ethyl 4,4,4-trinitrobutanoate <sup>1</sup>H NMR



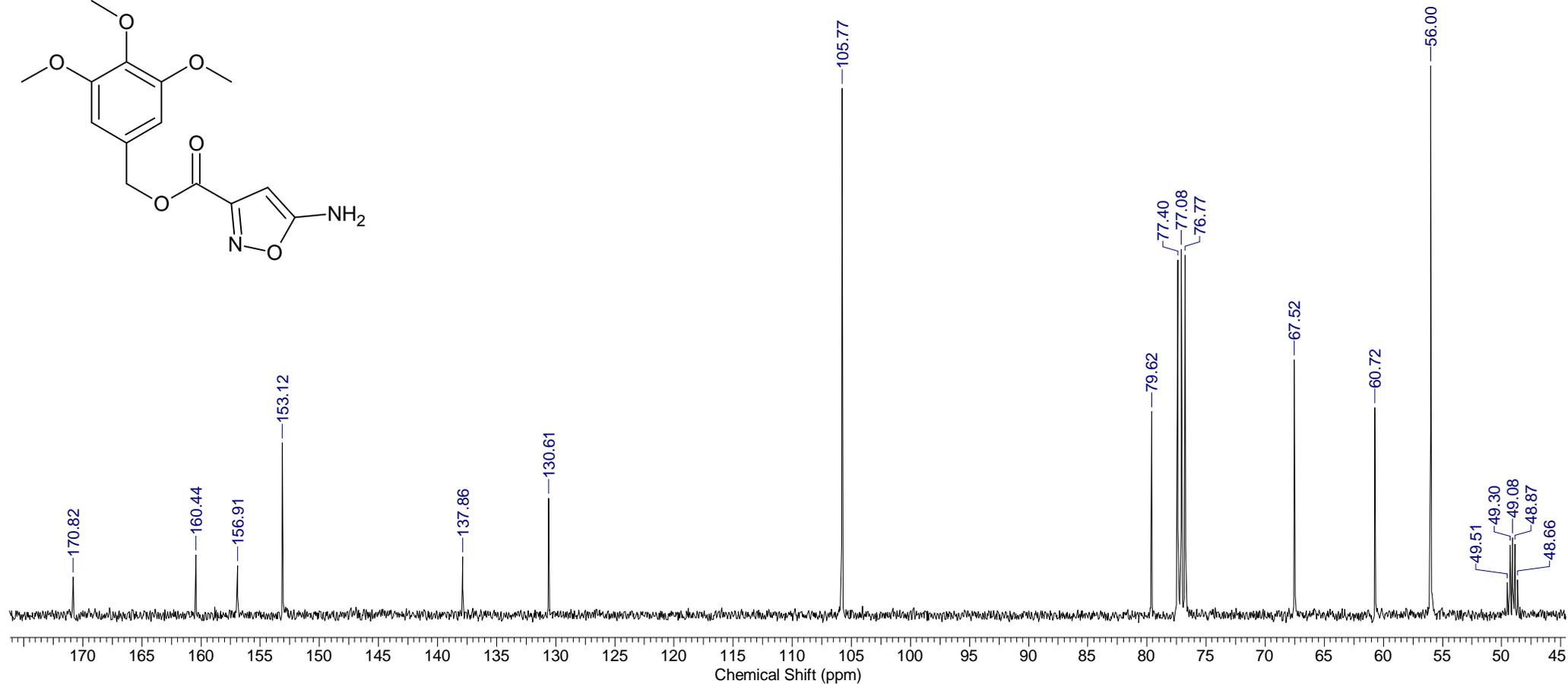
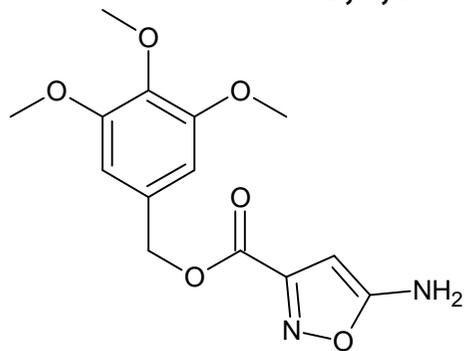
# 1-(3,4,5-Trimethoxyphenyl)ethyl 4,4,4-trinitrobutanoate <sup>13</sup>C NMR



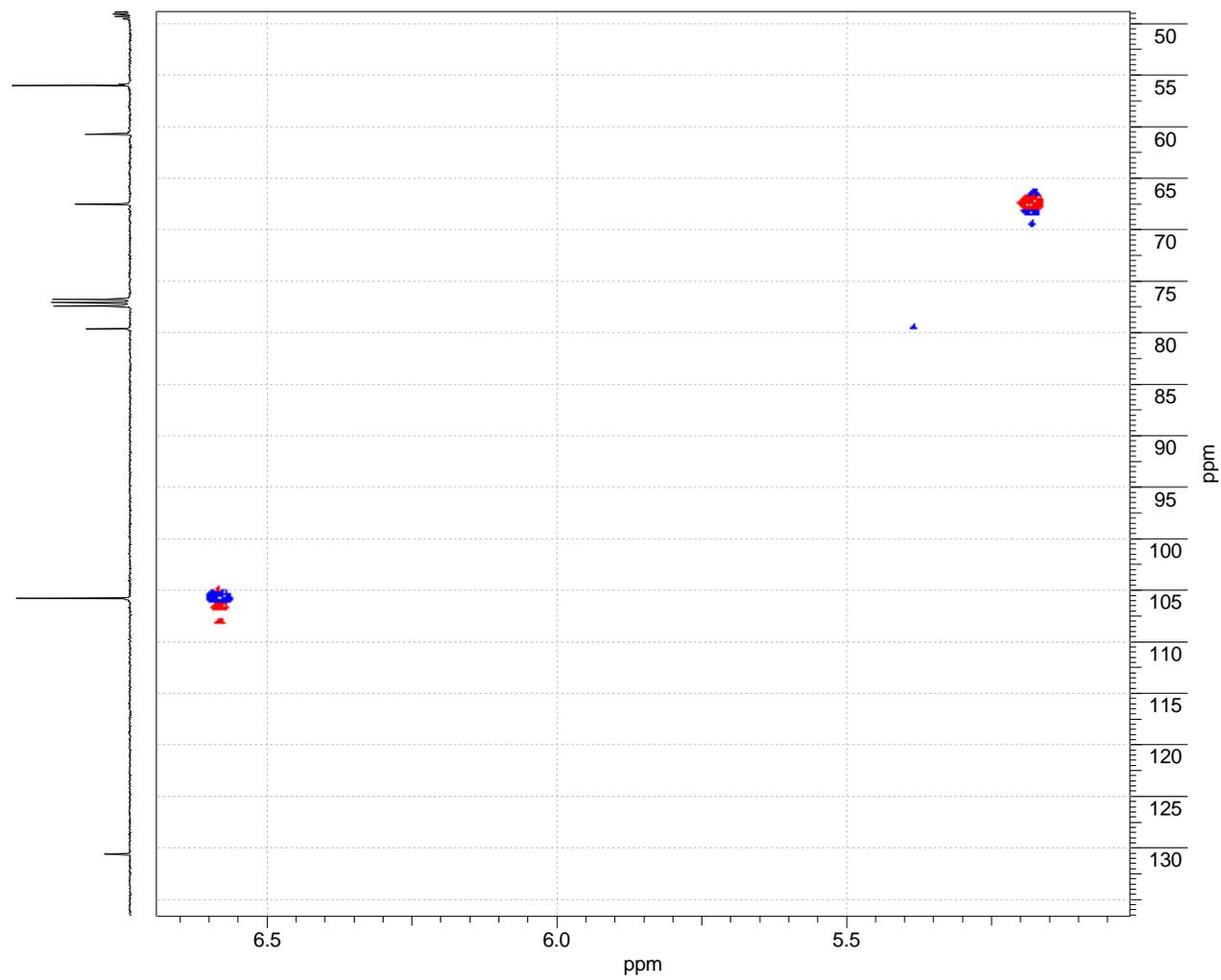
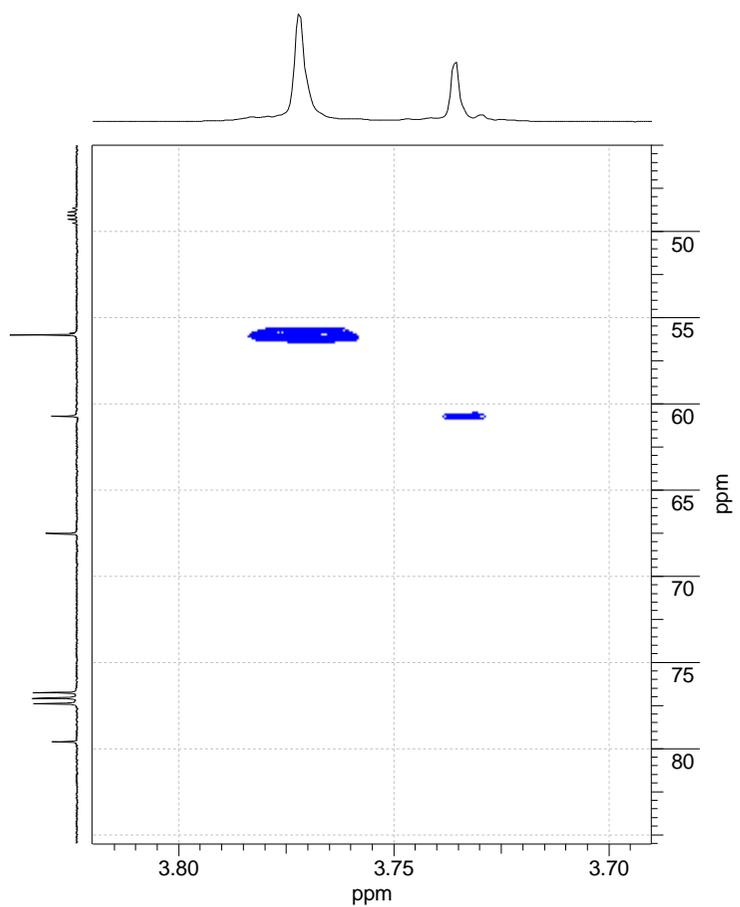
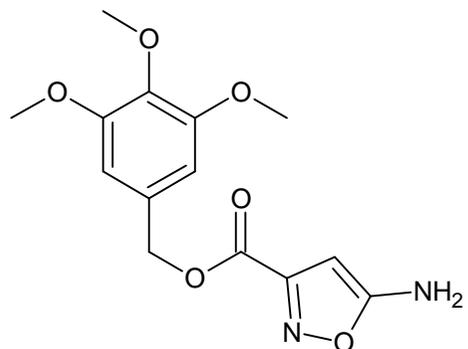
# 3,4,5-Trimethoxybenzyl 5-aminoisoxazole-3-carboxylate (1a) <sup>1</sup>H NMR



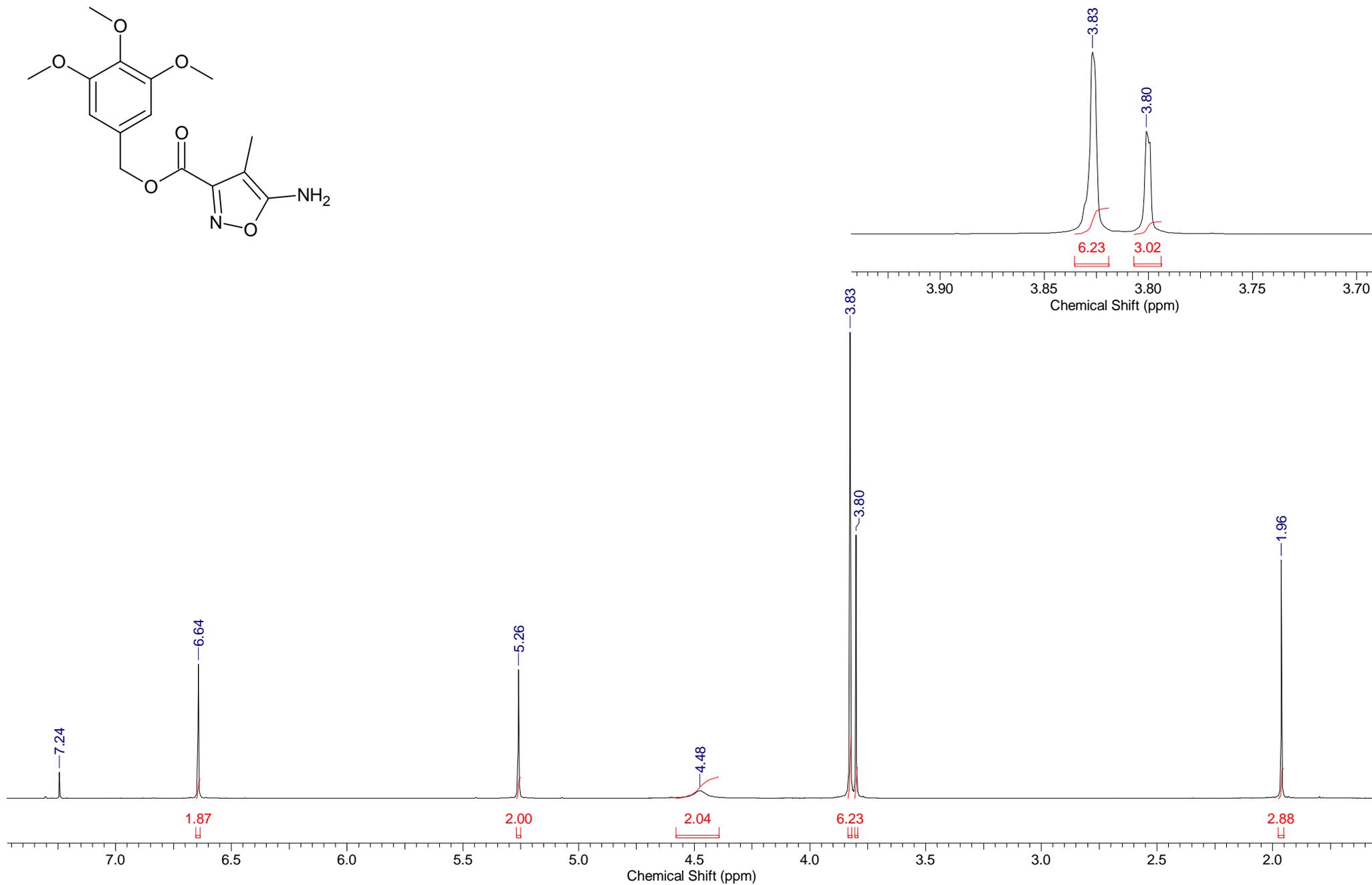
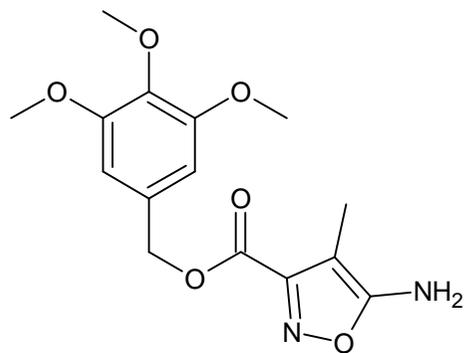
# 3,4,5-Trimethoxybenzyl 5-aminoisoxazole-3-carboxylate (1a) $^{13}\text{C}$ NMR



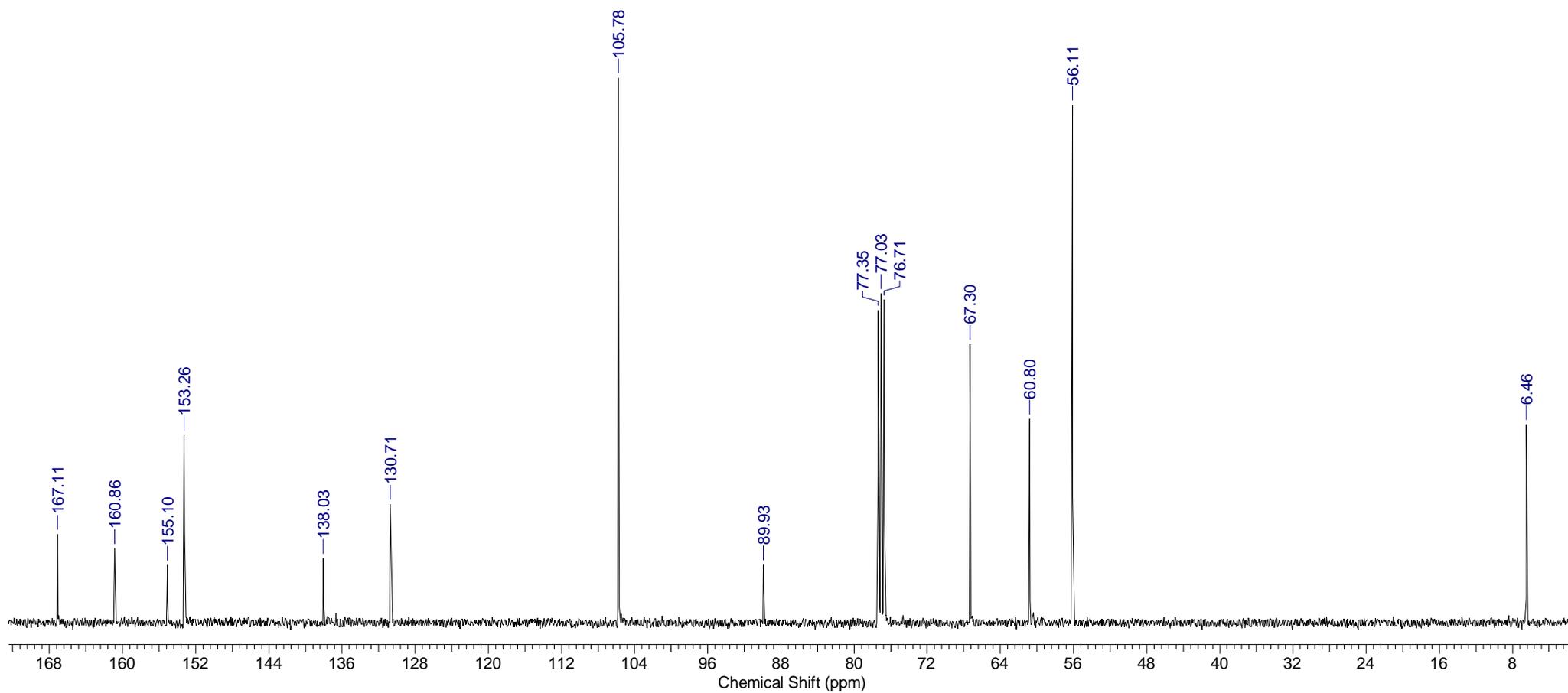
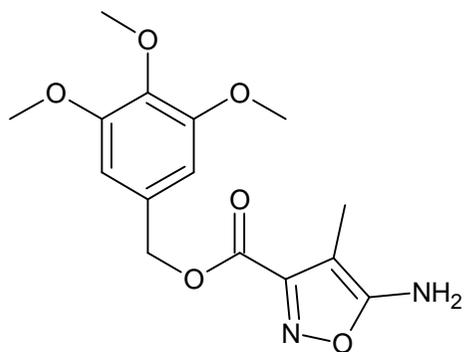
# 3,4,5-Trimethoxybenzyl 5-aminoisoxazole-3-carboxylate (1a) gHSQC



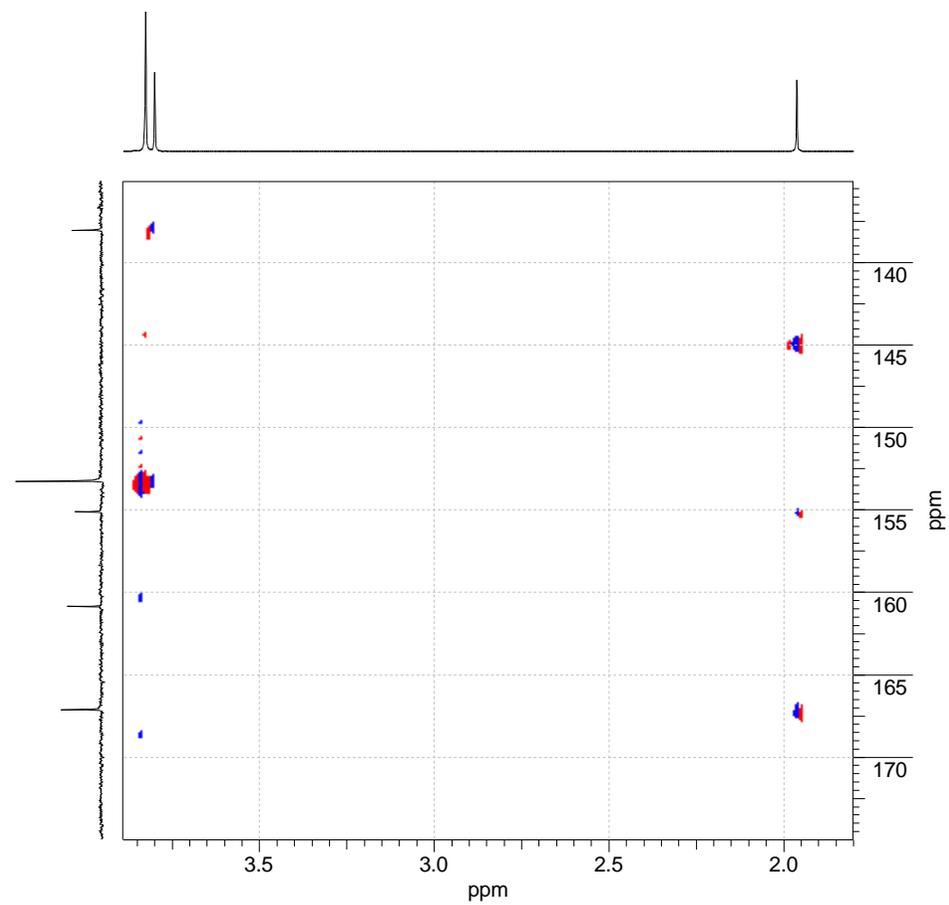
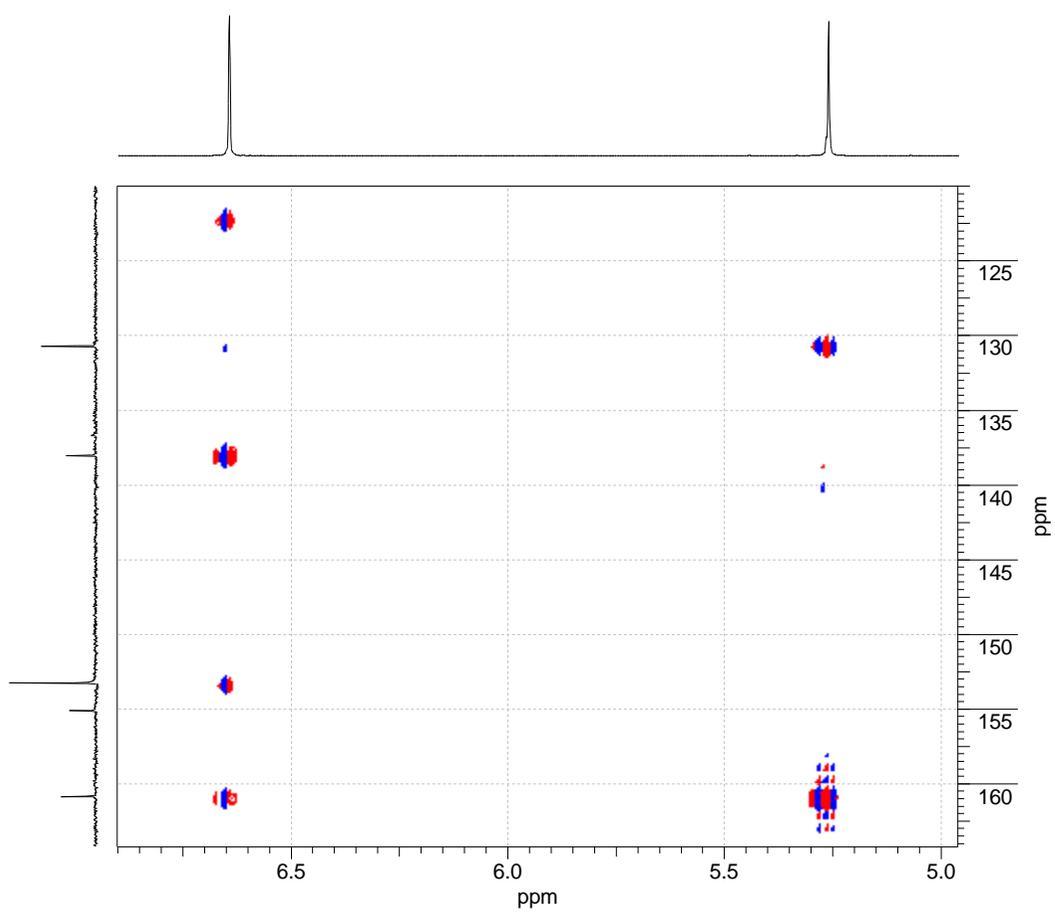
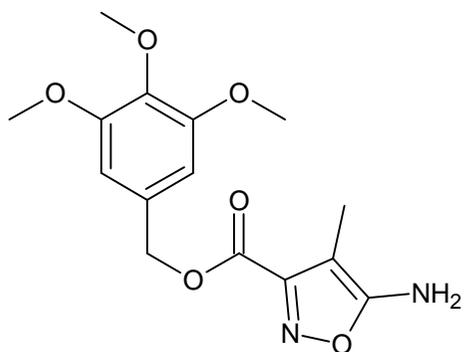
# 3,4,5-Trimethoxybenzyl 5-amino-4-methylisoxazole-3-carboxylate (1b) <sup>1</sup>H NMR



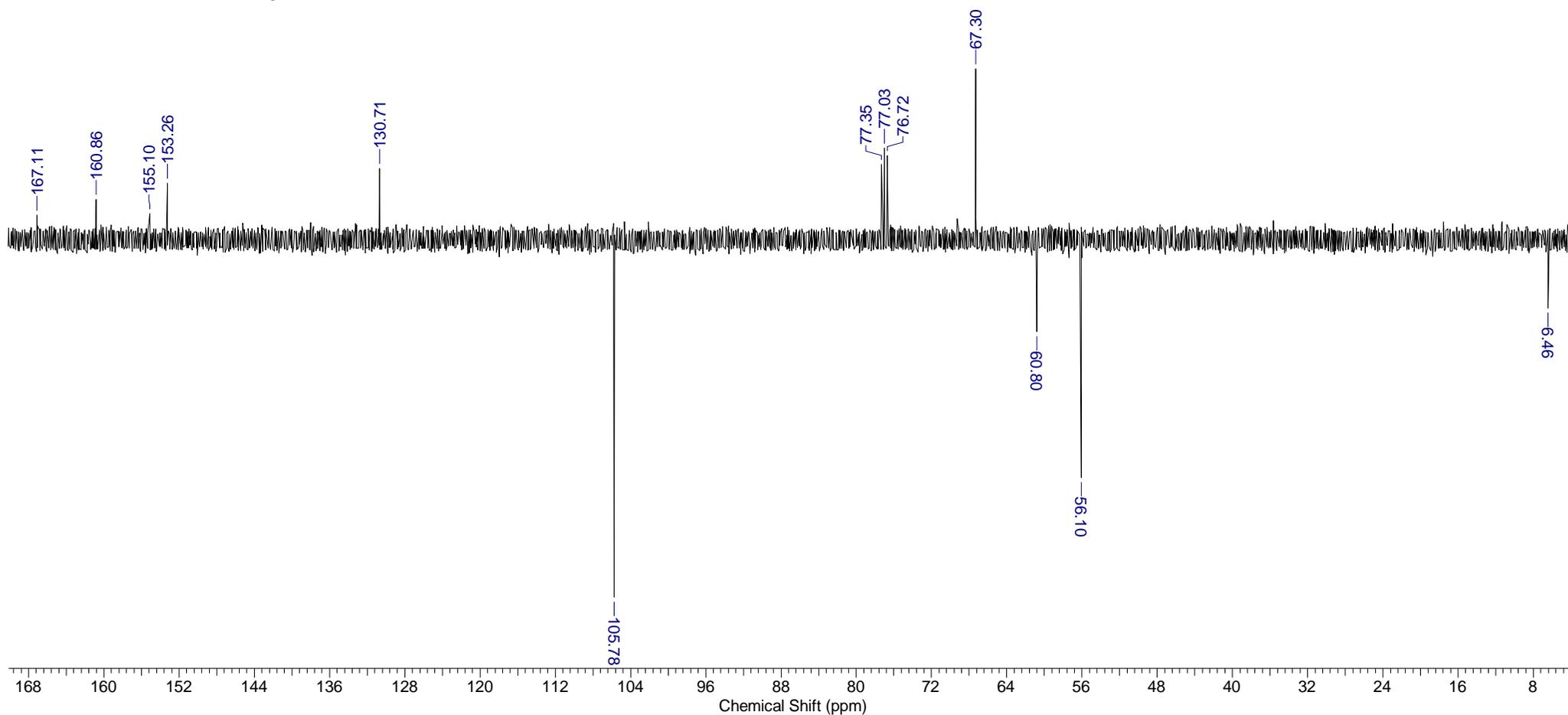
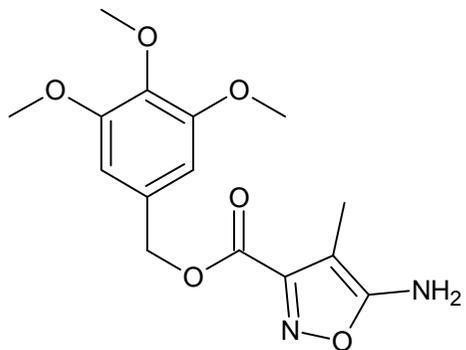
# 3,4,5-Trimethoxybenzyl 5-amino-4-methylisoxazole-3-carboxylate (1b) <sup>13</sup>C NMR



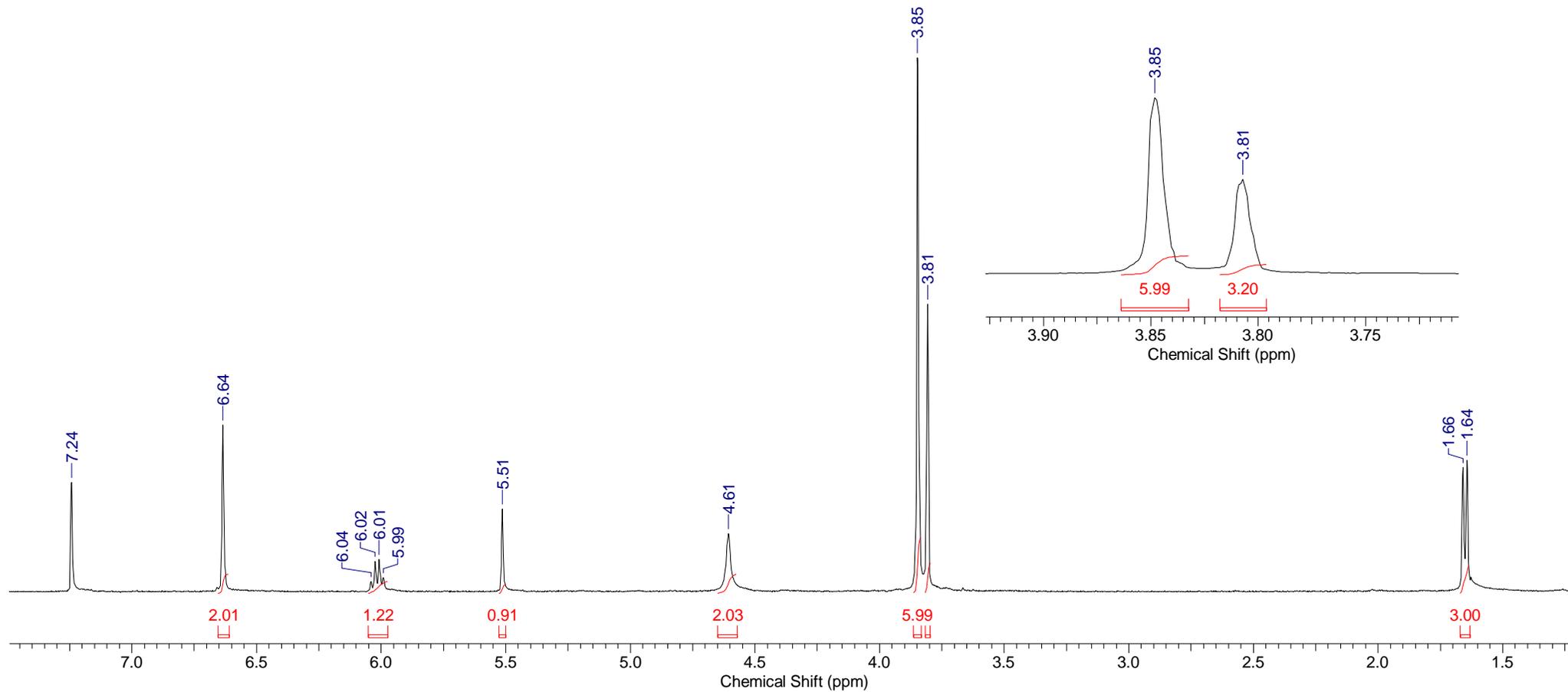
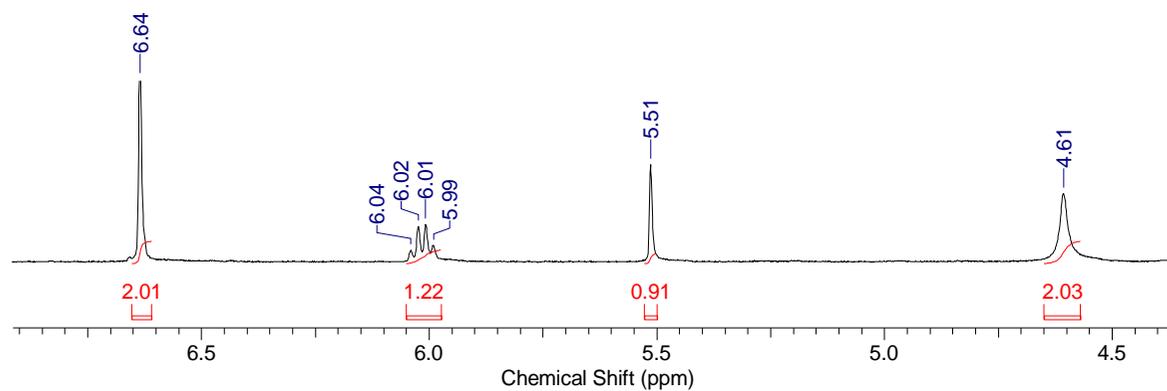
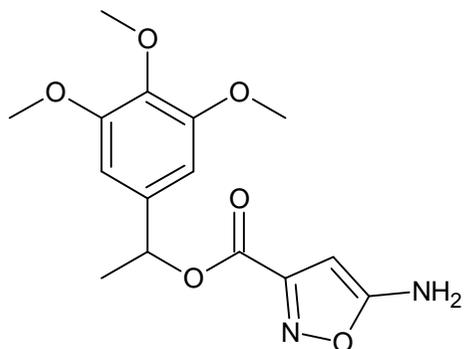
# 3,4,5-Trimethoxybenzyl 5-amino-4-methylisoxazole-3-carboxylate (1b) gHMBC



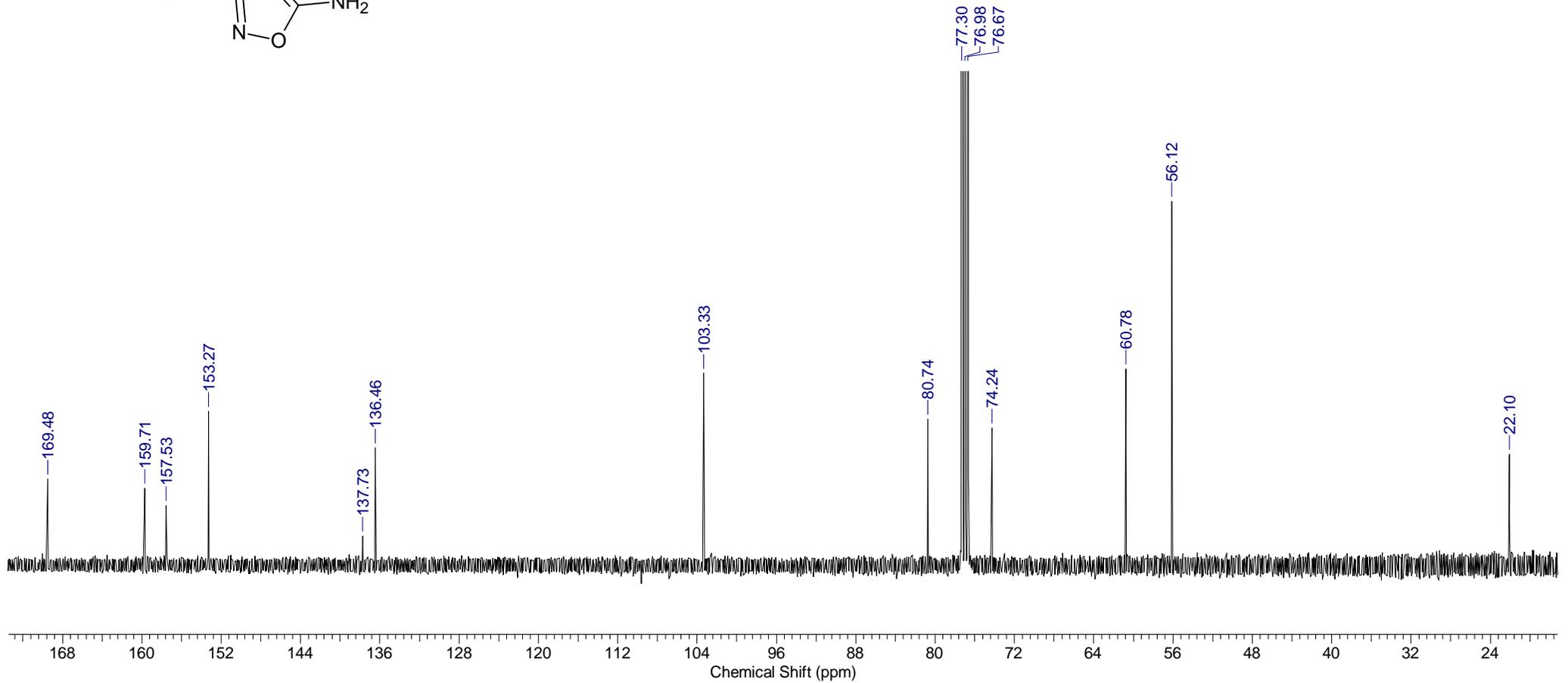
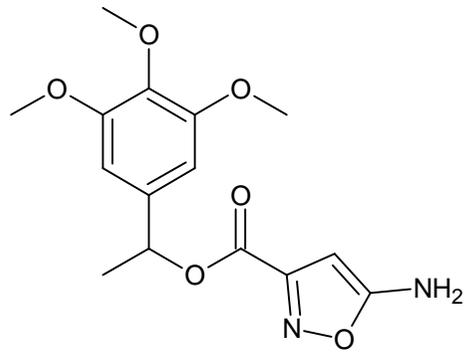
# 3,4,5-Trimethoxybenzyl 5-amino-4-methylisoxazole-3-carboxylate (1b) APT



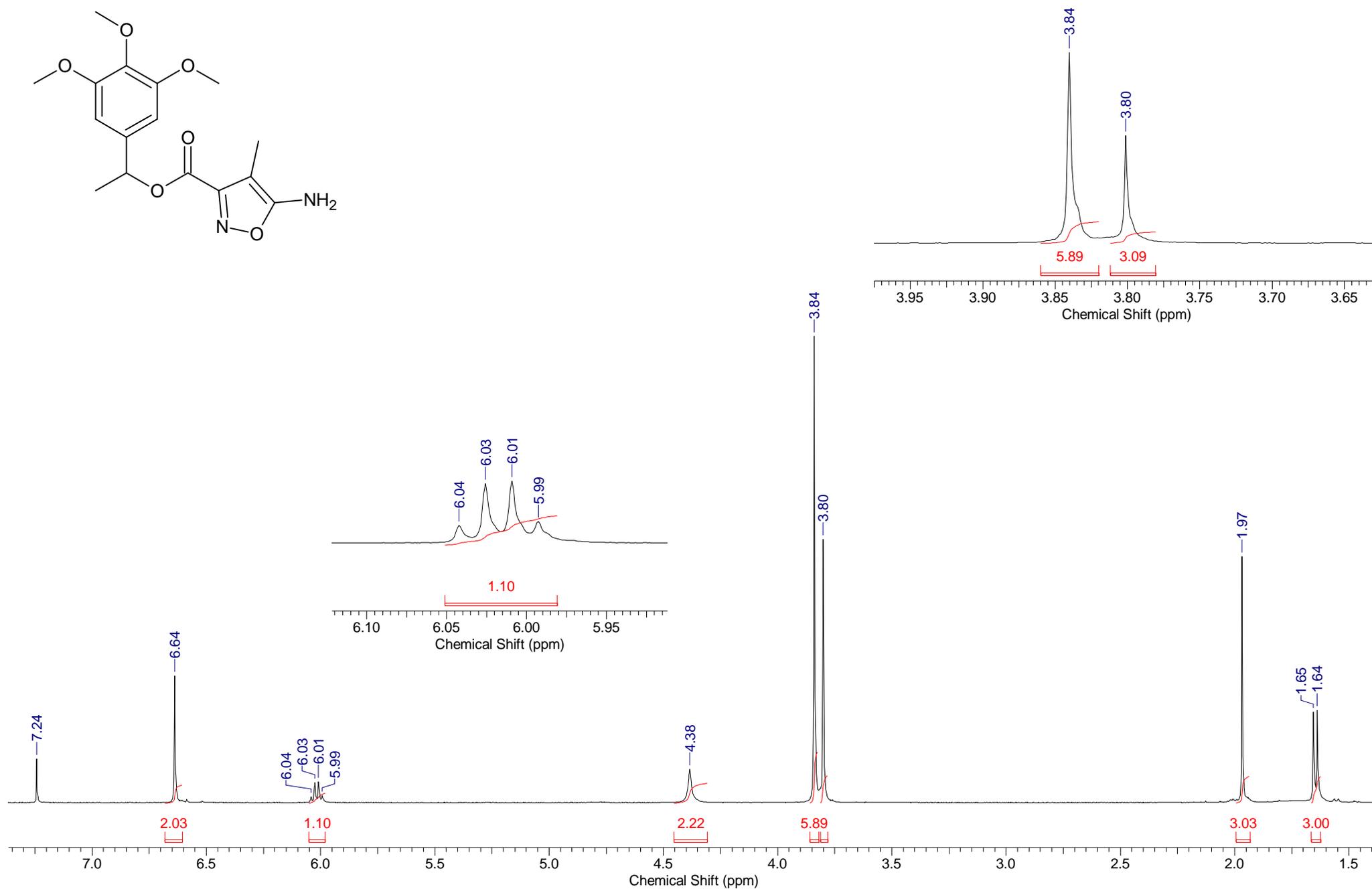
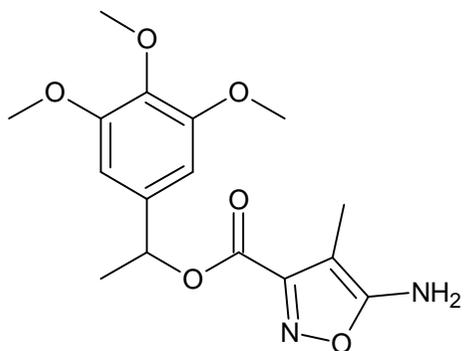
# 1-(3,4,5-trimethoxyphenyl)ethyl 5-aminoisoxazole-3-carboxylate (1c) <sup>1</sup>H NMR



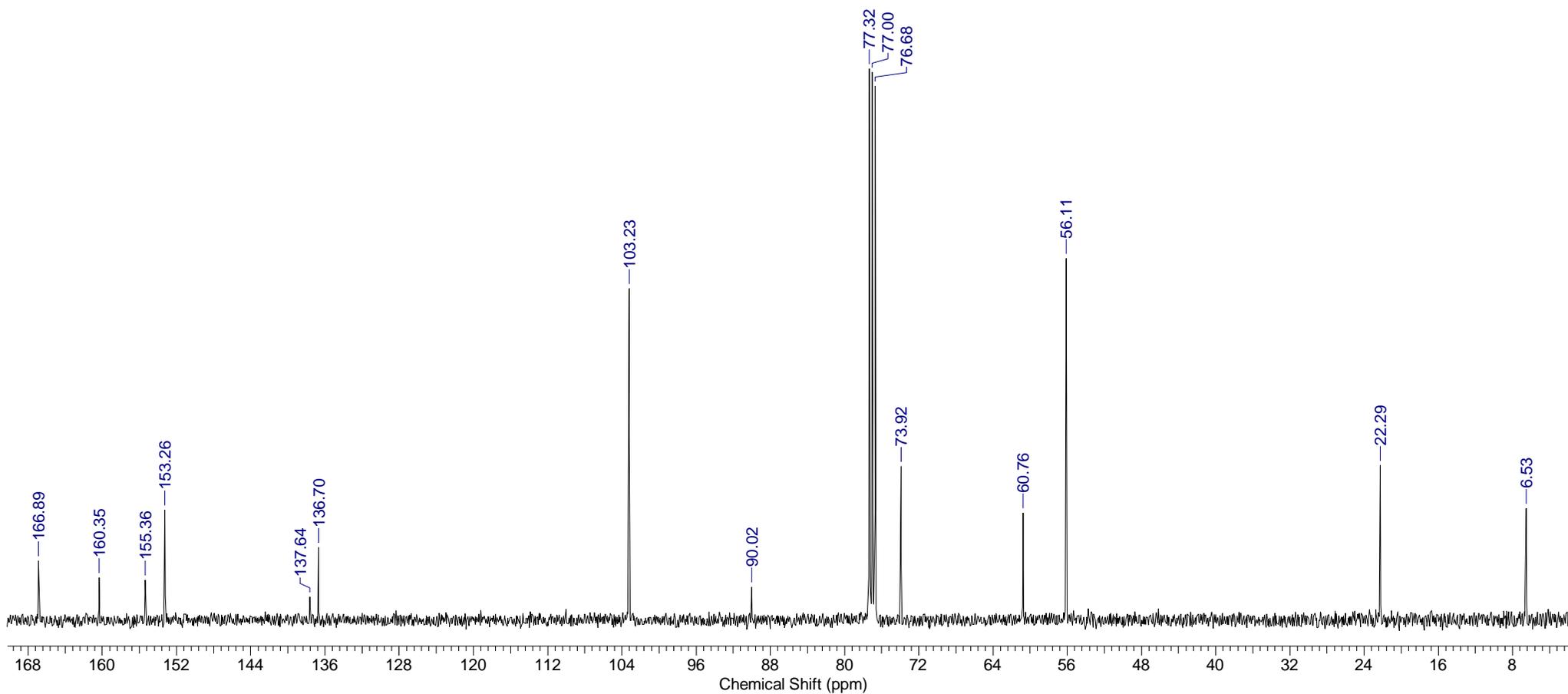
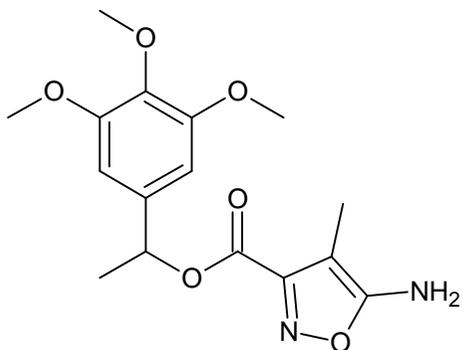
# 1-(3,4,5-trimethoxyphenyl)ethyl 5-aminoisoxazole-3-carboxylate (1c) $^{13}\text{C}$ NMR



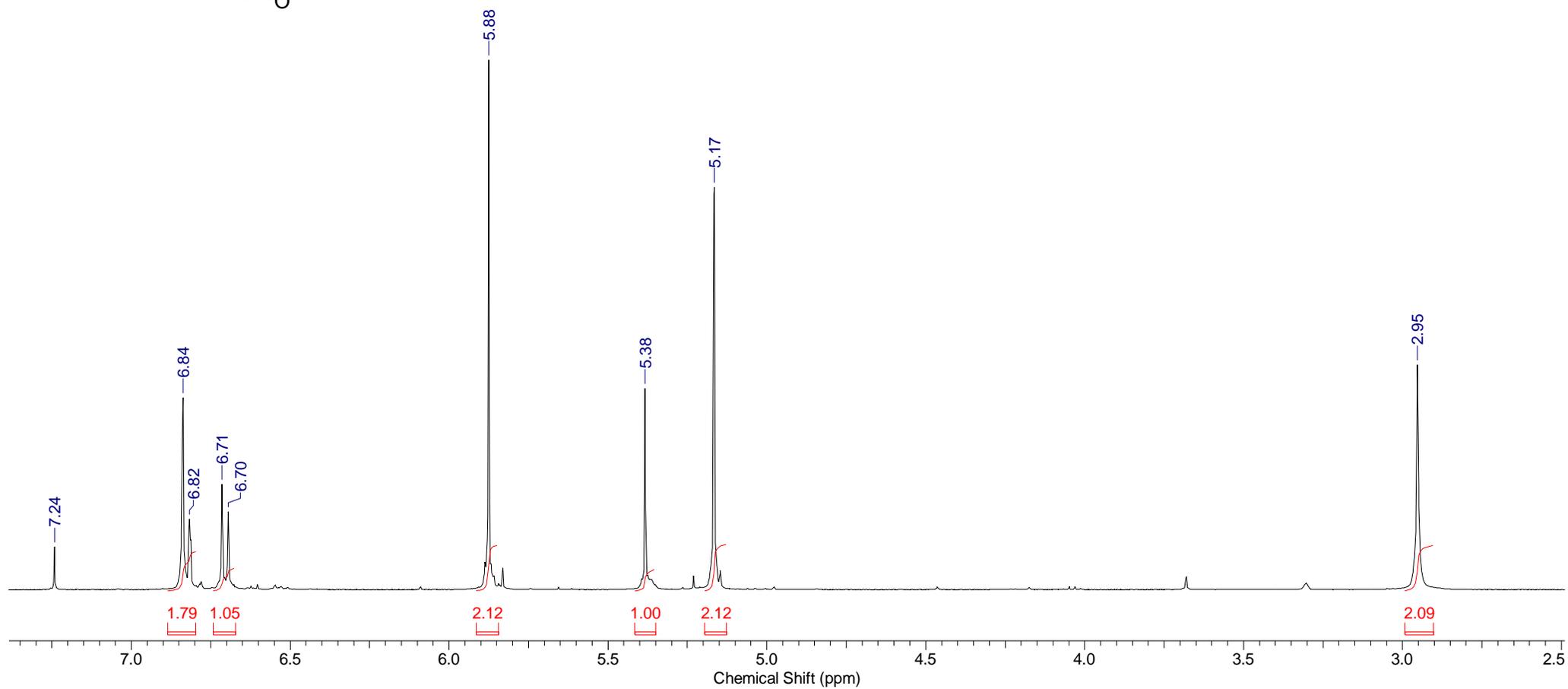
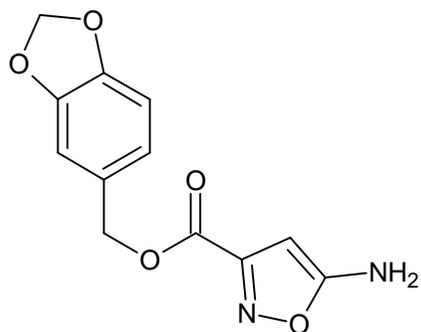
# 1-(3,4,5-trimethoxyphenyl)ethyl 5-amino-4-methylisoxazole-3-carboxylate (1d) <sup>1</sup>H NMR



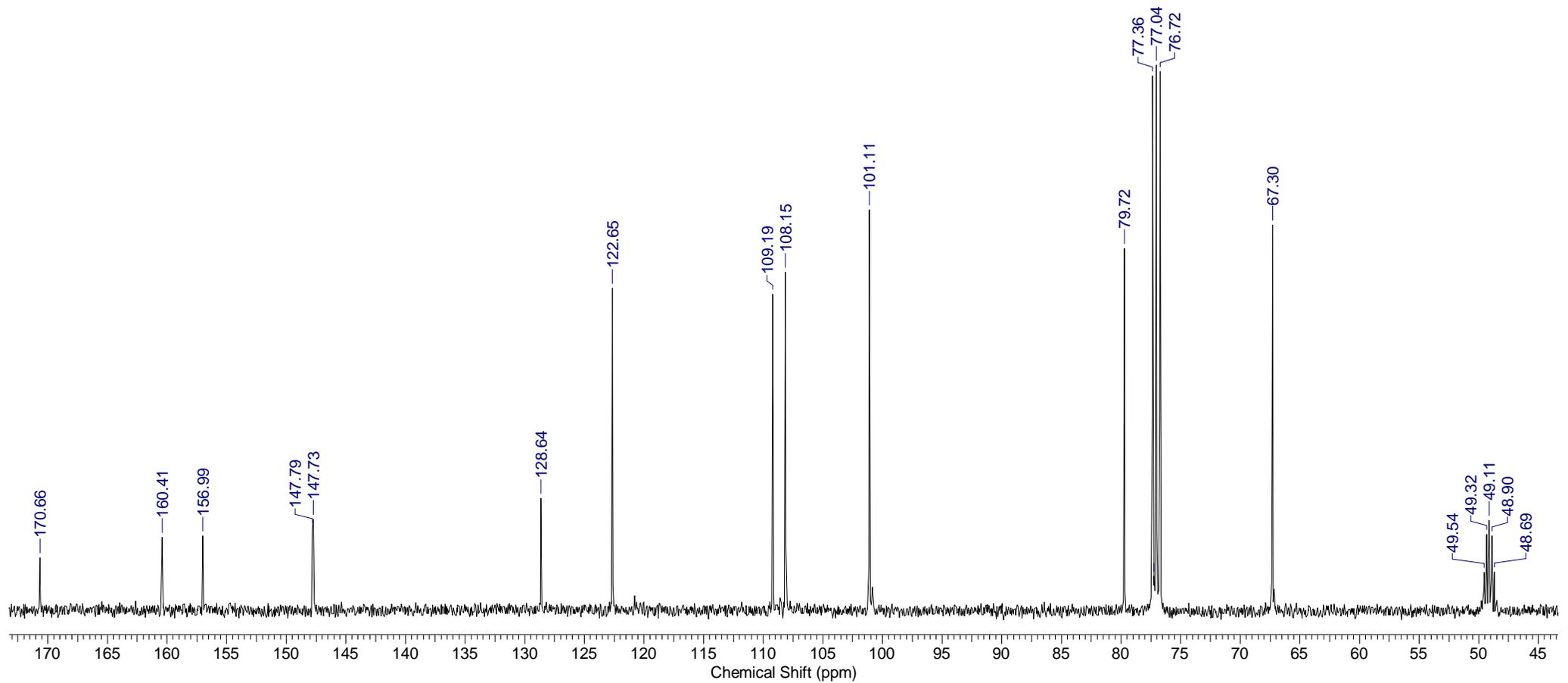
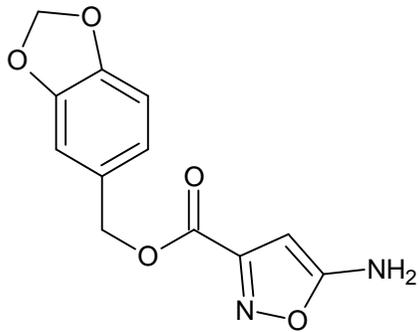
# 1-(3,4,5-trimethoxyphenyl)ethyl 5-amino-4-methylisoxazole-3-carboxylate (1d) $^{13}\text{C}$ NMR



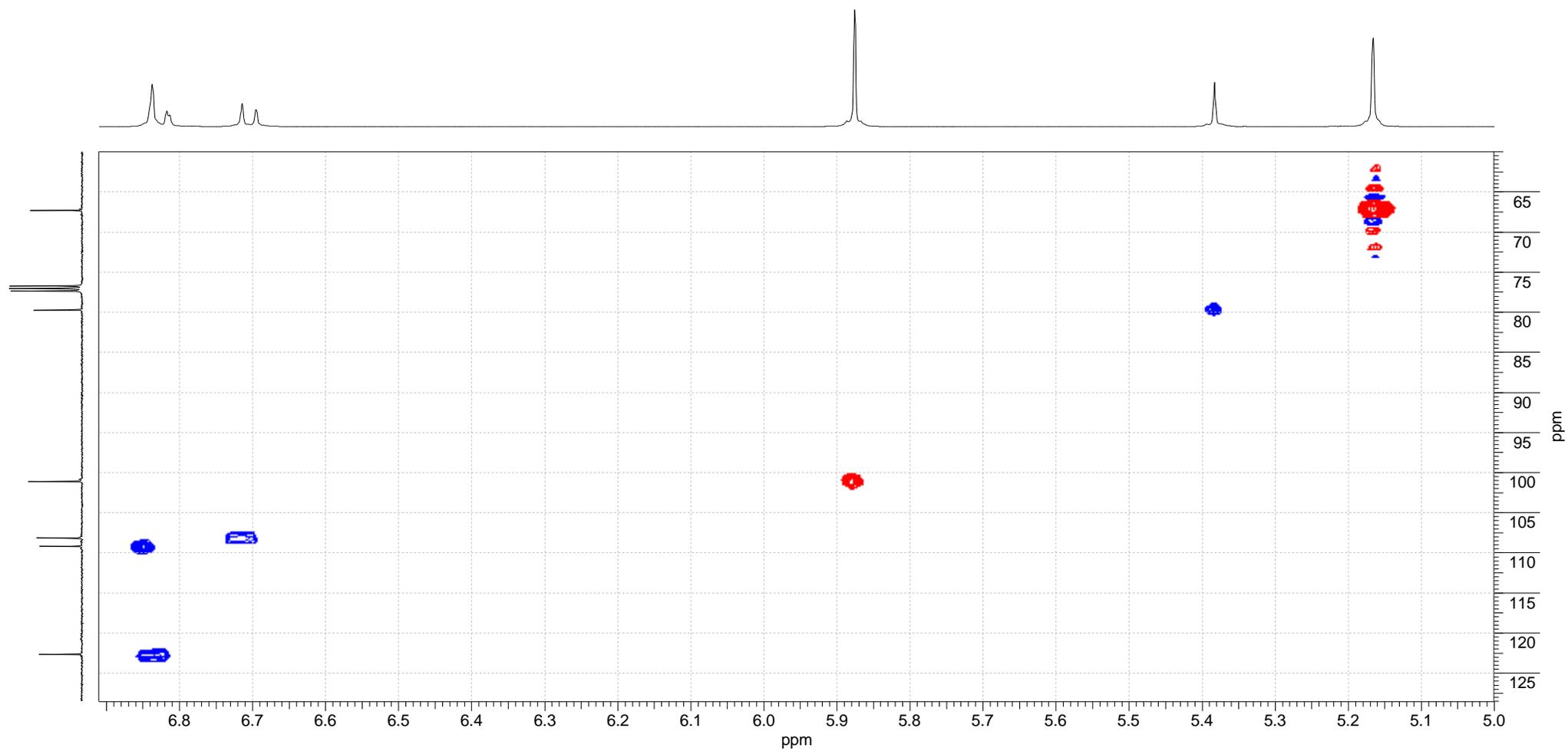
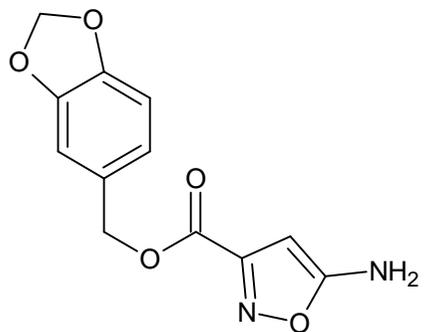
# 1,3-Benzodioxol-5-ylmethyl 5-aminoisoxazole-3-carboxylate (1e) <sup>1</sup>H NMR



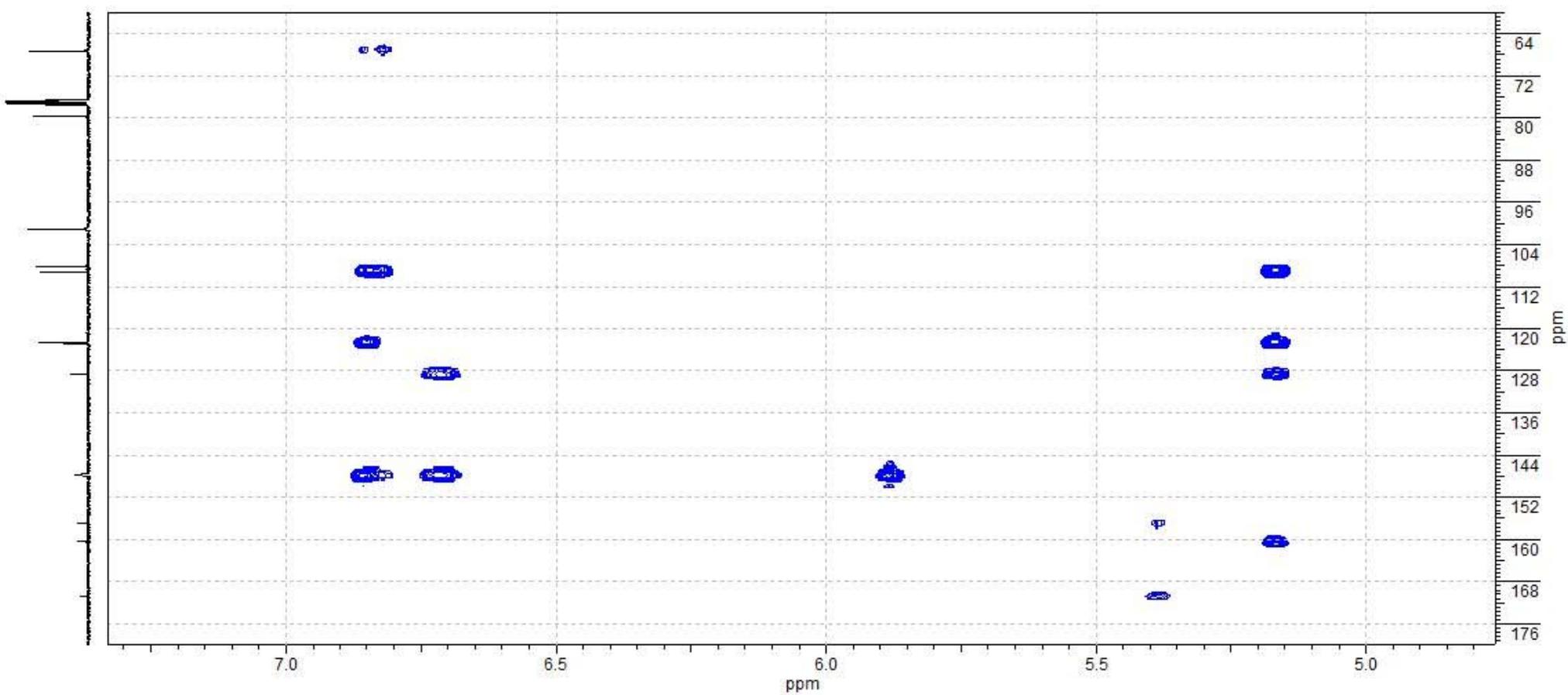
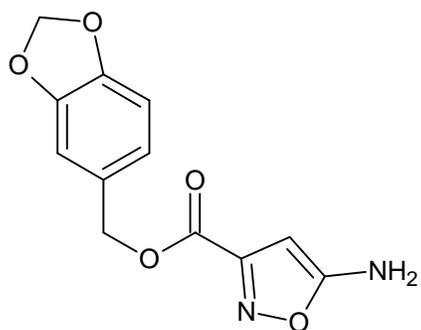
# 1,3-Benzodioxol-5-ylmethyl 5-aminoisoxazole-3-carboxylate (1e) $^{13}\text{C}$ NMR



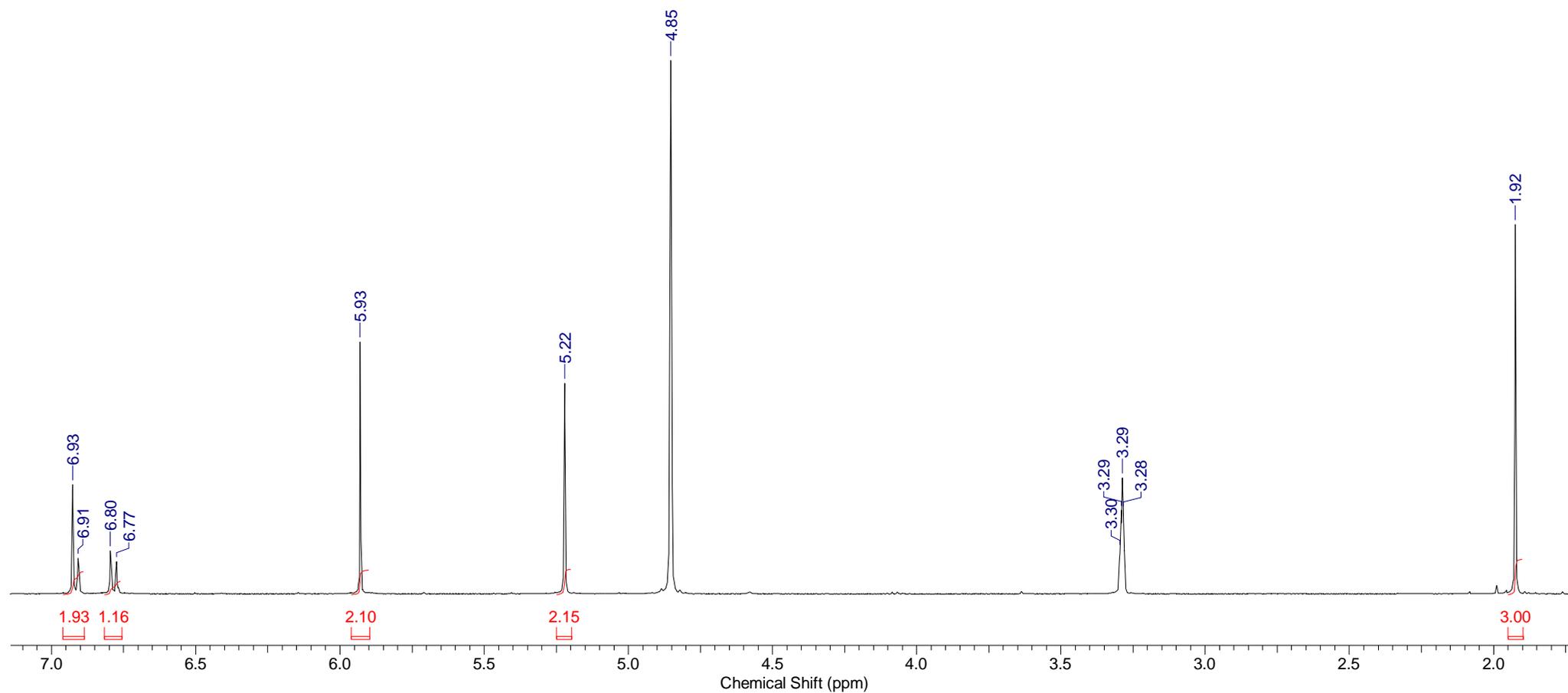
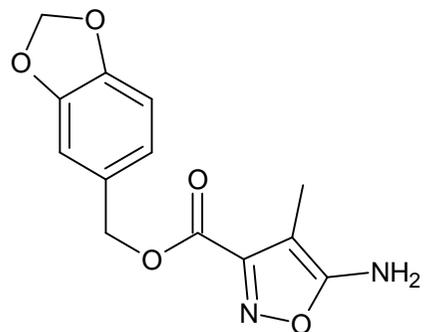
# 1,3-Benzodioxol-5-ylmethyl 5-aminoisoxazole-3-carboxylate (1e) gHSQC



# 1,3-Benzodioxol-5-ylmethyl 5-aminoisoxazole-3-carboxylate (1e) gHMBC



# 1,3-Benzodioxol-5-ylmethyl 5-amino-4-methylisoxazole-3-carboxylate (1f) $^1\text{H}$ NMR



# 1,3-Benzodioxol-5-ylmethyl 5-amino-4-methylisoxazole-3-carboxylate (1f) <sup>13</sup>C NMR

