

# **A transition-metal-free azide-alkyne cycloaddition/oxetane ring opening cascade reaction for the construction of hydroxymethyl decorated triazole-fused piperazin-2-ones and [1,4]diazepin-4-one**

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## **Supporting Information**

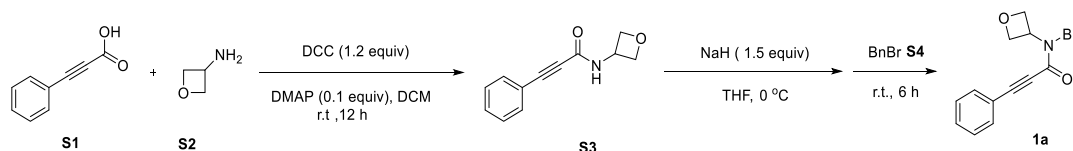
### **Table of Contents**

<b>I. General Remarks.....</b>	<b>S2</b>
<b>II. Synthesis of Substrates.....</b>	<b>S2</b>
<b>III. Procedure for Tandem Reactions.....</b>	<b>S11</b>
<b>IV. Synthetic Transformations.....</b>	<b>S22</b>
<b>V. X-Ray Crystallographic Data of 2a.....</b>	<b>S23</b>
<b>VI. NMR Spectra .....</b>	<b>S25</b>

## I. General Remarks

$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker AV-400 or 500 MHz spectrometer. Chemical shifts ( $\delta$ ) are given in relative to tetramethylsilane ( $\delta$  0.00 ppm) in  $\text{CDCl}_3$ . Coupling constants,  $J$ , were reported in hertz unit (Hz). High resolution mass spectra (HRMS) were obtained on a Q-STAR Elite ESI-LC-MS/MS Spectrometer. Chemical names were generated using Cambridge Soft. ChemDraw Ultra 16.0. Commercially obtained reagents were used without further purification.

## II. Synthesis of Substrates

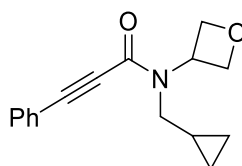


A solution of **S1** (1.46 g, 10.0 mmol, 1.0 equiv.), DCC (2.5 g, 12.0 mmol, 1.2 equiv.), DMAP (0.122 g, 0.1 equiv.) in  $\text{CH}_2\text{Cl}_2$  (20 mL) was stirred at  $0^\circ\text{C}$ . Then **S2** (0.73 g, 10.0 mmol, 1.0 equiv.) was added dropwise to the solution. The reaction mixture was stirred at room temperature until full consumption of the starting material as monitored by thin layer chromatography. After completion, the reaction mixture was diluted with  $\text{CH}_2\text{Cl}_2$  and washed 3 times with 0.5 M aq. HCl, dried over  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. The obtained **S3** was used directly in the next step without further purification.

NaH (420 mg, 60% in mineral oil, 10.5 mmol, 1.5 equiv) was added to a solution of **S3** (1.4 g, 7.0 mmol, 1.0 equiv.) in THF (20.0 mL) at  $0^\circ\text{C}$  in portions. The above solution was stirred for 20 mins at  $0^\circ\text{C}$  then BnBr **S4** (1.43 g, 8.4 mmol, 1.2 equiv.) was added dropwise into the flask. The reaction mixture was allowed to stirred at room temperature for another 6 h. After completion, the reaction was quenched with water and extract with ethyl acetate three times. The organic phase was dried over  $\text{Na}_2\text{SO}_4$ , and concentrated under reduced pressure. The crude residue was purified by a silica gel column chromatography to give the corresponding desired **1a** as white solid. (1.8 g, 84% yield)  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.62-7.47 (m, 1H), 7.46-7.38 (m, 4H), 7.36-7.32 (m, 2H), 7.32-7.26 (m, 3H), 5.67&5.22 (2m, 1H), 5.08&5.00 (2s, 2H), 4.83& 4.75 (2q,  $J = 4.0$  Hz, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.4, 137.1, 136.7, 132.5, 130.5, 130.3, 129.1, 128.9, 128.7, 128.5, 128.0, 127.5, 126.7, 126.5, 120.0, 90.6, 81.6, 75.4, 52.8, 50.3, 49.9, 45.5. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{18}\text{NO}_2^+(\text{M}+\text{H})^+$  292.1332, found 292.1324.

The propiolamides **1b**~**1u** were prepared according to similar procedure of **1a**.

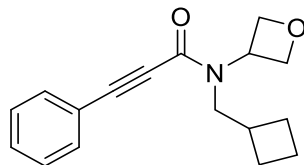
*N*-(cyclopropylmethyl)-*N*-(oxetan-3-yl)-3-phenylpropiolamide (**1b**)



The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.1 g, 63 %, yellow oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.55-7.50 (m, 2H), 7.43-7.33 (m, 3H), 5.57&5.12 (m, 1H), 4.93-4.77 (m, 4H), 3.63&3.54 (2d,  $J = 6.8$  Hz, 2H), 1.09-0.97 (m, 1H), 0.62-

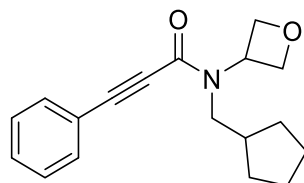
0.53 (m, 2H), 0.37-0.32 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  154.8, 154.3, 132.4, 132.3, 130.3, 130.2, 128.6, 120.2, 120.1, 90.9, 89.9, 81.8, 81.5, 76.2, 75.4, 52.3, 51.2, 50.1, 46.5, 11.3, 10.7, 4.4, 4.1. HRMS (ESI) calcd for  $\text{C}_{16}\text{H}_{18}\text{NO}_2^+(\text{M}+\text{H})^+$  256.1332, found 256.1325.

*N*-(cyclobutylmethyl)-*N*-(oxetan-3-yl)-3-phenylpropiolamide (**1c**)



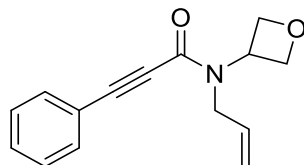
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.0 g, 56%, yellow oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.57-7.54 (m, 2H),  $\delta$  7.47-7.36 (m, 3H), 5.47&4.96 (m, 1H), 4.91&4.73 (m, 4H), 3.78&3.67 (2d,  $J=7.2$  Hz, 2H), 2.63&2.46 (m, 1H), 2.13-2.02 (m, 2H), 1.96-1.74 (m, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  154.9, 154.4, 132.4, 132.4, 130.3, 130.2, 128.6, 120.3, 120.2, 90.9, 90.1, 81.5, 81.9, 76.2, 75.4, 52.3, 51.9, 50.3, 47.6, 35.7, 35.2, 26.9, 26.2, 18.3, 18.2. HRMS (ESI) calcd for  $\text{C}_{17}\text{H}_{20}\text{NO}_2^+(\text{M}+\text{H})^+$  270.1489, found 270.1482.

*N*-(cyclopentylmethyl)-*N*-(oxetan-3-yl)-3-phenylpropiolamide (**1d**)



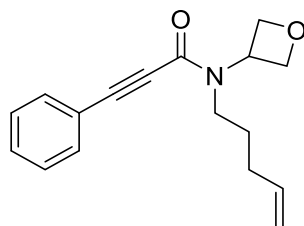
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.1 g, 60%, yellow oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.54-7.49 (m, 2H), 7.43-7.32 (m, 3H), 5.42& 4.90 (m, 1H), 4.88-4.75 (m, 4H), 3.64&3.56 (2d,  $J=7.6$  Hz, 2H), 2.16&1.97 (m, 1H), 1.76-1.68 (m, 2H), 1.66-1.60 (m, 2H), 1.58-1.51 (m, 2H), 1.30-1.20 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  154.8, 154.4, 132.3, 132.3, 130.3, 130.2, 128.6, 120.3, 120.2, 90.8, 90.0, 81.9, 81.7, 76.1, 75.2, 52.2, 51.6, 50.5, 47.1, 39.9, 39.6, 30.5, 30.1, 24.8, 24.8. HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{22}\text{NO}_2^+(\text{M}+\text{H})^+$  284.1645, found 284.1637.

*N*-allyl-*N*-(oxetan-3-yl)-3-phenylpropiolamide (**1e**)



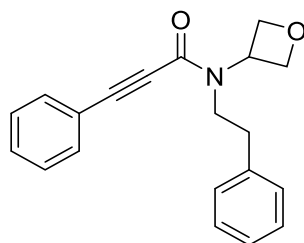
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.4 g, 85%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.59-7.53 (m, 2H), 7.49-7.36 (m, 3H), 6.01-5.90 (m, 1H), 5.69&5.36 (m, 1H), 5.31-5.18 (m, 2H), 4.94-4.76 (m, 4H), 4.47&4.37 (2dt,  $J=5.2, 1.6$  Hz, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.1, 153.9, 133.8, 133.2, 132.5, 132.4, 132.3, 130.4, 130.3, 129.9, 128.7, 128.6, 128.5, 120.6, 120.2, 120.0, 117.5, 116.6, 91.2, 90.1, 81.6, 81.1, 76.0, 75.5, 52.8, 49.5, 48.5, 44.4, 38.4, 34.1. HRMS (ESI) calcd for  $\text{C}_{15}\text{H}_{16}\text{NO}_2^+(\text{M}+\text{H})^+$  242.1176, found 242.1168.

*N*-(oxetan-3-yl)-*N*-(pent-4-en-1-yl)-3-phenylpropiolamide (**1f**)



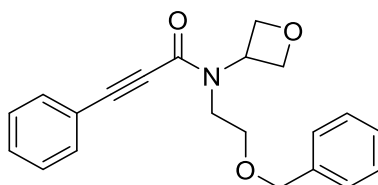
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.3 g, 72 %, colorless oil, <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, two rotamers) δ 7.57-7.53 (m, 2H), 7.47-7.36 (m, 3H), 5.86-5.76 (m, 1H), 5.62&5.17 (m, 1H), 5.11&5.07 (2q, *J* = 1.6 Hz, 1H), 5.04&5.02 (m, 1H), 4.94-4.74 (m, 4H), 3.76&3.65 (m, 2H), 2.18-2.13 (m, 2H), 1.80-1.72 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, two rotamers) δ 154.8, 154.0, 137.3, 136.9, 132.4, 132.4, 130.3, 128.6, 120.3, 120.1, 116.0, 115.5, 90.8, 89.9, 81.7, 81.3, 76.1, 75.5, 52.6, 49.7, 46.1, 42.2, 31.2, 30.9, 29.4, 27.9. HRMS (ESI) calcd for C<sub>17</sub>H<sub>20</sub>NO<sub>2</sub><sup>+</sup>(M+H)<sup>+</sup> 270.1489, found 270.1479.

*N*-(oxetan-3-yl)-*N*-phenethyl-3-phenylpropiolamide (**1g**)



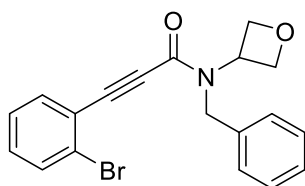
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.4 g, 66 %, white solid, <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, two rotamers) δ 7.60-7.55 (m, 2H), 7.50-7.39 (m, 3H), 7.37-7.21 (m, 5H), 5.54&5.15 (m, 1H), 4.80&4.64 (m, 4H), 4.00&2.88 (2t, *J* = 7.6 Hz, 2H), 3.02-2.98(m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, two rotamers) δ 154.9, 138.7, 137.7, 132.5, 132.5, 130.4, 130.4, 128.9, 128.9, 128.8, 128.8, 128.7, 127.0, 126.8, 120.2, 120.1, 90.9, 90.0, 81.7, 81.3, 76.1, 75.5, 52.8, 50.0, 48.2, 44.7, 37.1, 34.6, 29.7. HRMS (ESI) calcd for C<sub>20</sub>H<sub>20</sub>NO<sub>2</sub><sup>+</sup>(M+H)<sup>+</sup> 306.1489, found 306.1479.

*N*-(2-(benzyloxy)ethyl)-*N*-(oxetan-3-yl)-3-phenylpropiolamide (**1h**)



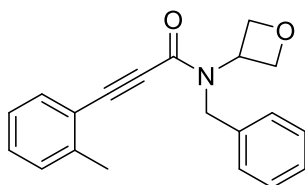
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 0.98 g, 42 %, yellow solid, <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, two rotamers) δ 7.59-7.51 (m, 2H), 7.48-7.42 (m, 2H), 7.38-7.30 (m, 6H), 5.58&5.15 (m, 1H), 4.94&4.87 (2t, *J* = 8.0 Hz, 2H), 4.79&4.53 (2d, *J* = 7.6Hz, 4H), 3.97&3.89 (2t, *J* = 5.6 Hz, 2H), 3.74&3.70 (2t, *J* = 5.2Hz, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, two rotamers) δ 154.9, 154.3, 137.9, 137.6, 132.5, 130.4, 130.3, 128.6, 128.6, 128.5, 128.5, 120.2, 120.1, 90.9, 90.2, 81.7, 81.4, 76.4, 75.6, 73.5, 73.4, 71.5, 69.3, 67.8, 61.9, 53.0, 50.7, 46.4, 42.9. HRMS (ESI) calcd for C<sub>21</sub>H<sub>22</sub>NO<sub>3</sub><sup>+</sup>(M+H)<sup>+</sup> 336.1594, found 336.1585.

*N*-benzyl-3-(2-bromophenyl)-*N*-(oxetan-3-yl)propiolamide (**1i**)



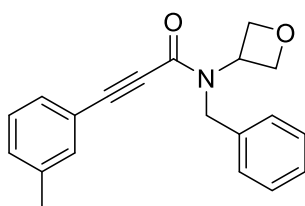
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 2.2 g, 88 %, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.68-7.55 (m, 2H), 7.40-7.26 (m, 7H), 5.99&5.18 (m, 1H), 5.17&5.05 (2s, 2H), 4.89-4.70 (m, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  154.9, 137.3, 136.6, 134.9, 134.9, 132.8, 132.6, 131.7, 131.5, 129.0, 128.9, 127.9, 127.5, 127.3, 126.7, 126.2, 122.6, 88.2, 85.3, 75.8, 75.4, 53.0, 50.4, 49.9, 45.2. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{18}\text{BrNO}_2^+(\text{M}+\text{H})^+$  370.0437, found 370.0426.

*N*-benzyl-*N*-(oxetan-3-yl)-3-(*o*-tolyl)propiolamide (**1j**)



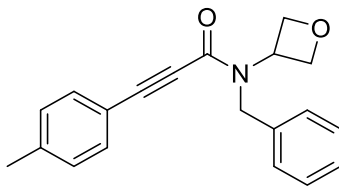
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.9 g, 92 %, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.56-7.33 (m, 3H), 7.32-7.23 (m, 4H), 7.21-7.11 (m, 2H), 5.74&5.23(m, 1H), 5.09&5.00 (2s, 2H), 4.80&4.73 (2d,  $J = 7.2$  Hz, 4H), 2.52&2.27 (2s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.6, 154.8, 141.6, 137.3, 136.7, 133.1, 133.0, 130.5, 130.3, 129.9, 129.7, 129.1, 128.9, 127.9, 127.5, 126.7, 126.4, 126.0, 125.8, 119.9, 89.6, 85.3, 75.8, 75.4, 52.9, 50.2, 49.8, 45.4, 20.8, 20.5. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{20}\text{NO}_2^+(\text{M}+\text{H})^+$  306.1489, found 306.1479.

*N*-benzyl-*N*-(oxetan-3-yl)-3-(*m*-tolyl)propiolamide (**1k**)



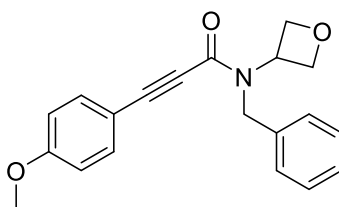
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.9 g, 91 %, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.42-7.38 (m, 2H), 7.36-7.33 (m, 1H), 7.33-7.25 (m, 4H), 7.23-7.21 (m, 2H), 5.66&5.20 (m, 1H), 5.08&4.99 (2s, 2H), 4.84&4.71 (m, 4H), 2.39&2.32 (2s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.4, 154.7, 138.5, 138.4, 137.2, 136.7, 133.0, 132.9, 131.5, 131.3, 129.6, 129.1, 128.8, 128.6, 128.4, 127.9, 127.5, 126.7, 126.6, 119.8, 92.1, 90.9, 81.3, 80.86, 75.8, 75.4, 52.7, 50.3, 49.8, 45.5, 21.1. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{20}\text{NO}_2^+(\text{M}+\text{H})^+$  306.1489, found 306.1479.

*N*-benzyl-*N*-(oxetan-3-yl)-3-(*p*-tolyl)propiolamide (**1l**)



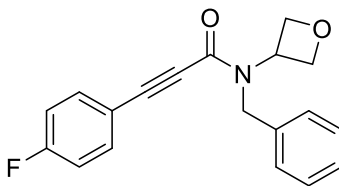
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.8 g, 87 %, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.49-7.36 (m, 2H), 7.33-7.24 (m, 5H), 7.21&7.12 (2d,  $J$  = 8.0 Hz, 2H), 5.64&5.20 (m, 1H), 5.05&4.97(2s, 2H), 4.81&4.72 (2d,  $J$  = 7.2 Hz, 4H), 2.40&2.35 (2s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.5, 140.9, 136.8, 132.5, 129.5, 129.3, 129.1, 128.9, 127.9, 127.5, 126.7, 126.6, 116.9, 75.9, 75.4, 52.7, 50.3, 49.8, 45.5, 21.6. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{20}\text{NO}_2^+(\text{M}+\text{H})^+$  306.1489, found 306.1479.

*N*-benzyl-3-(4-methoxyphenyl)-*N*-(oxetan-3-yl)propiolamide (**1m**)



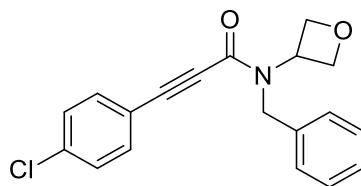
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 2.1g, 95 %, white solid ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.56-7.33 (m, 4H), 7.33-7.24 (m, 3H), 6.94-6.79 (m, 2H), 5.64&5.20 (m, 1H), 5.06&4.97 (2s, 2H), 4.82-4.69 (m, 4H), 3.84&3.80 (2s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  161.2, 154.9, 155.7, 137.3, 136.9, 134.4, 129.1, 128.8, 127.9, 127.4, 126.7, 126.6, 114.4, 114.2, 111.8, 92.4, 91.2, 81.1, 80.7, 75.9, 75.4, 55.4, 55.4, 52.7, 50.2, 49.8, 45.4. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{20}\text{NO}_3^+(\text{M}+\text{H})^+$  322.1438, found 322.1428.

*N*-benzyl-3-(4-fluorophenyl)-*N*-(oxetan-3-yl)propiolamide (**1n**)



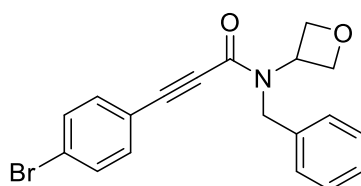
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.7 g, 82 %, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.62-7.19 (m, 7H), 7.11-6.90 (m, 2H), 5.60&5.16 (m, 1H), 5.02&4.94 (2s, 2H), 4.79-4.67 (m, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  164.9, 163.7&163.6 (2d,  $J$  = 252.0 Hz), 162.3, 155.1, 154.4, 137.2, 136.8, 134.8&134.7(2d,  $J$  = 8.0 Hz ), 129.0, 128.8, 127.9, 127.4, 126.7, 126.5, 116.2&116.0 (2d,  $J$  = 22.0 Hz ), 115.9, 90.5, 89.4, 81.6&81.1 (2d,  $J$  = 1.0 Hz), 75.7, 75.2, 52.7, 50.2, 49.9, 45.5. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{17}\text{FNO}_2^+(\text{M}+\text{H})^+$  310.1238, found 310.1230.

*N*-benzyl-3-(4-chlorophenyl)-*N*-(oxetan-3-yl)propiolamide (**1o**)



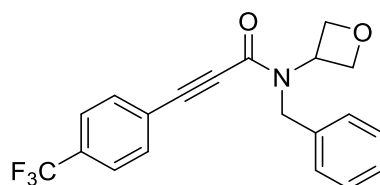
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 2.2g, 87 %, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.55-7.37 (m, 3H), 7.36-7.25 (m, 6H), 5.63&5.21 (m, 1H), 5.06&4.99 (2s, 2H), 4.85&4.71 (m 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.1, 154.3, 137.0, 136.9, 136.7, 136.7, 133.7, 129.2, 129.1, 129.0, 128.9, 128.0, 127.6, 126.7, 126.5, 118.5, 90.5, 89.3, 82.4, 82.0, 75.8, 75.3, 52.8, 50.3, 49.9, 45.6. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{17}\text{ClNO}_2^+(\text{M}+\text{H})^+$  326.0942, found 326.0934.

*N*-benzyl-3-(4-bromophenyl)-*N*-(oxetan-3-yl)propiolamide (**1p**)



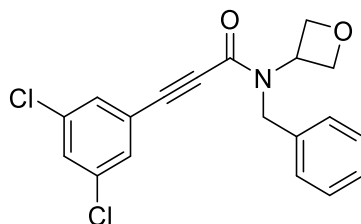
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 2.2g, 86 %, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.58-7.38 (m, 4H), 7.36-7.26 (m, 5H), 5.63&5.22 (m, 1H), 5.06&4.98 (2d,  $J = 7.2$  Hz, 2H), 4.83-4.72 (m, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.1, 154.3, 137.0, 136.6, 133.8, 132.1, 131.9, 129.1, 128.9, 128.0, 127.6, 126.8, 126.5, 125.2, 125.1, 118.9, 90.6, 89.4, 82.6, 82.1, 75.8, 75.3, 52.8, 50.3, 49.9, 45.6. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{17}\text{BrNO}_2^+(\text{M}+\text{H})^+$  370.0437, found 370.0430.

*N*-benzyl-*N*-(oxetan-3-yl)-3-(4-(trifluoromethyl)phenyl)propiolamide (**1q**)



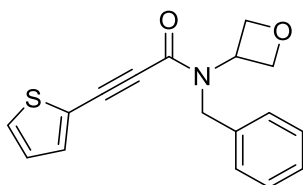
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 2.2g, 90 %, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.73-7.68 (m, 1H), 7.62&7.51 (m, 3H), 7.45-7.31 (m, 3H), 7.31-7.24 (m, 2H), 5.64&5.24 (m, 1H), 5.07-5.01 (2s, 2H), 4.86-4.74 (m, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  154.79, 154.04, 136.93, 136.52, 131.9 (q,  $J = 33.0$  Hz), 128.06, 127.62, 126.75, 126.42, 125.7&125.5 (2q,  $J = 3.0$  Hz), 124.89, 123.82, 122.18, 89.72, 88.50, 83.30, 82.80, 75.27, 52.83, 50.26, 49.94, 45.63. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{17}\text{F}_3\text{NO}_2^+(\text{M}+\text{H})^+$  360.1206, found 360.1197.

*N*-benzyl-3-(3,5-dichlorophenyl)-*N*-(oxetan-3-yl)propiolamide (**1r**)



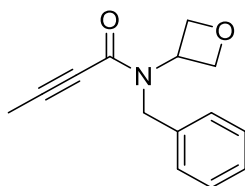
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 2.2 g, 89%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.46 (s, 1H), 7.43-7.39 (m, 2H), 7.38-7.27 (m, 3H), 7.26-7.25 (m, 2H), 5.60&5.22 (m, 1H), 5.04&4.99 (2s, 2H), 4.82&4.74 (2d,  $J = 7.2$  Hz, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  154.5, 153.7, 137.0, 136.5, 135.4, 135.2, 130.7, 130.6, 130.4, 129.2, 128.9, 128.1, 127.6, 126.7, 126.4, 122.8, 88.2, 87.0, 83.3, 82.8, 75.6, 75.2, 52.8, 50.2, 50.0, 45.6. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{16}\text{Cl}_2\text{NO}_2^+(\text{M}+\text{H})^+$  360.0553, found 360.0544.

*N*-benzyl-*N*-(oxetan-3-yl)-3-(thiophen-2-yl)propionamide (**1s**)



The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.5 g, 76 %, yellow solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.49-7.37 (m, 3H), 7.36-7.30 (m, 2H), 7.29-7.25 (m, 2H), 7.11-7.01 (m, 1H), 5.59&5.21 (m, 1H), 5.04&4.99 (2s, 2H), 4.77-4.71 (m, 4H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.2, 137.1, 136.7, 135.7, 135.6, 130.7, 130.6, 129.1, 128.9, 128.0, 127.6, 127.5, 127.5, 126.8, 126.6, 119.7, 85.8, 75.8, 75.3, 52.6, 50.2, 49.9, 45.5. HRMS (ESI) calcd for  $\text{C}_{17}\text{H}_{16}\text{NO}_2\text{S}^+(\text{M}+\text{H})^+$  298.0896, found 298.0887.

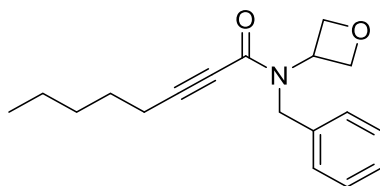
*N*-benzyl-*N*-(oxetan-3-yl)but-2-ynamide (**1t**)



The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.3 g, 83 %, colorless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.41-7.30 (m, 2H), 7.36-7.23 (m, 1H), 7.22-7.17 (m, 2H), 5.60&5.08 (m, 1H), 4.96&4.92 (2s, 2H), 4.75-4.62 (m, 4H), 2.05&1.95 (2s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.4, 137.3, 136.8, 129.0, 128.8, 127.9, 127.4, 126.6, 126.5, 89.6, 75.8, 75.3, 73.4, 52.7, 50.3, 49.7, 45.1, 4.1. HRMS (ESI) calcd for  $\text{C}_{14}\text{H}_{16}\text{NO}_2^+(\text{M}+\text{H})^+$ , 230.1176, found 230.1170.

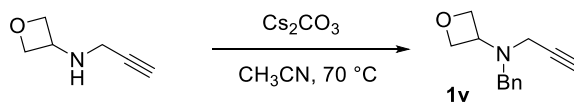
*N*-benzyl-*N*-(oxetan-3-yl)oct-2-ynamide (**1u**)





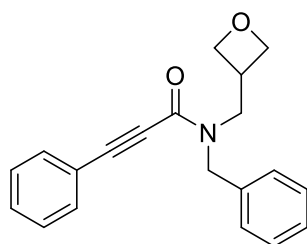
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.5 g, 79%, colorless oil;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.40-7.25 (m, 3H), 7.23-7.20 (m, 2H), 5.60&5.14 (m, 1H), 4.98&4.93 (2s, 2H), 4.76&4.65 (m, 4H), 2.40&2.29 (2t,  $J = 7.2$  Hz, 2H), 1.67&1.44 (m, 2H), 1.44-1.34 (m, 1H), 1.30-1.21 (m, 3H), 0.93&0.83 (2t,  $J = 8.0$  Hz, 3H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.5, 137.4, 136.9, 129.0, 128.8, 127.8, 127.4, 126.7, 126.4, 95.0, 95.2, 93.8, 75.8, 75.4, 52.7, 50.2, 49.7, 45.2, 31.1, 30.9, 27.4, 27.3, 22.1, 22.0, 19.0, 18.8, 13.9, 13.8. HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{24}\text{NO}_2^+(\text{M}+\text{H})^+$  286.1802, found 286.1793.

### Synthesis of substrate **1v**



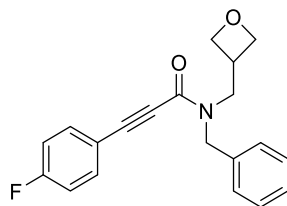
$\text{Cs}_2\text{CO}_3$  (780 mg, 2.4 mmol, 1.2 equiv) was added to a solution of *N*-(prop-2-yn-1-yl)oxetan-3-amine (222 mg, 2.0 mmol, 1.0 equiv.) in  $\text{CH}_3\text{CN}$  (20.0 mL). Then *BnBr* **S4** (424 mg, 2.4 mmol, 1.2 equiv.) was added dropwise into the flask. The reaction mixture was allowed to stirred at 70 °C for another 3 h. After completion, the reaction was quenched with water and extract with ethyl acetate three times. The organic phase was dried over  $\text{Na}_2\text{SO}_4$ , and concentrated under reduced pressure. The crude residue was purified by a silica gel column chromatography (ethyl acetate/petroleum ether = 1:5) to give the corresponding desired **1v** as yellow oil (381 mg, 95% yield).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40 – 7.30 (m, 5H), 4.71 – 4.64 (m, 4H), 4.09 (m,  $J = 6.7$  Hz, 1H), 3.59 (s, 2H), 3.23 (d,  $J = 2.4$  Hz, 2H), 2.25 (t,  $J = 2.4$  Hz, 1H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  129.2, 128.4, 127.5, 127.0, 76.1, 73.5, 56.2, 53.6, 38.6. HRMS (ESI) calcd for  $\text{C}_{13}\text{H}_{16}\text{NO}^+(\text{M}+\text{H})^+$  202.1226, found 202.1219.

### *N*-benzyl-*N*-(oxetan-3-ylmethyl)-3-phenylpropiolamide(**3a**)



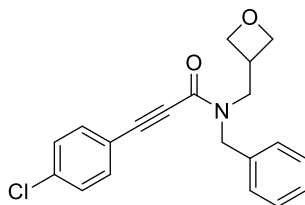
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.9g, 93%, white solid;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.62-7.48 (m, 2H), 7.47-7.37 (m, 3H), 7.37-7.23 (m, 5H), 4.87&4.66 (2s, 2H), 4.70&4.64 (2t, 2H), 4.46&4.38 (2t,  $J = 6.4$  Hz, 2H), 4.00&3.71 (2d,  $J = 7.2$  Hz, 2H), 3.35-3.21 (m, 1H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.3, 155.1, 136.4, 136.3, 132.5, 132.5, 130.4, 130.3, 129.0, 128.8, 128.7, 128.6, 128.2, 127.8, 127.3, 120.2, 91.5, 90.9, 81.5, 75.6, 74.9, 53.8, 51.4, 48.0, 47.7, 34.4, 34.1. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{20}\text{NO}_2^+(\text{M}+\text{H})^+$  306.1489, found 306.1481.

### *N*-benzyl-3-(4-fluorophenyl)-*N*-(oxetan-3-ylmethyl)propiolamide (**3b**)



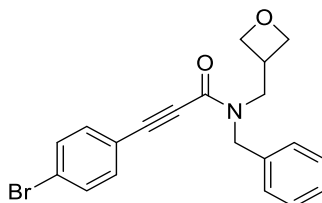
The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 2.2g, 97%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.62-7.43 (m, 2H), 7.43-7.32 (m, 3H), 7.31-7.22 (m, 2H), 7.21-7.02 (m, 2H), 4.85&4.65 (2s, 2H), 4.70&4.65 (2t,  $J = 6.4$  Hz, 2H), 4.45&4.37 (2t,  $J = 6.4$  Hz, 2H), 4.00&3.72 (2d,  $J = 7.2$  Hz, 2H), 3.32-3.23 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  163.7&163.6 (2d,  $J = 251.0$  Hz), 155.2, 155.0, 136.3, 136.2, 134.7&134.6 (2d,  $J = 9.0$  Hz), 129.1, 128.8, 128.2, 127.8, 127.3, 116.3, 116.2, 116.1, 115.9, 90.5, 89.8, 75.6, 74.8, 53.8, 51.3, 48.0, 47.8, 34.3, 34.0. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{19}\text{FNO}_2^+(\text{M}+\text{H})^+$  324.1394, found 324.1385.

*N*-benzyl-3-(4-chlorophenyl)-*N*-(oxetan-3-ylmethyl)propiolamide (**3c**)



The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 2.2g, 93%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.56-7.41 (m, 2H), 7.41-7.33 (m, 4H), 7.33-7.22 (m, 3H), 4.85&4.66 (2s, 2H), 4.70&4.64 (2t,  $J = 6.8$  Hz, 2H), 4.44&4.37 (2t,  $J = 6.4$  Hz, 2H), 3.99&3.72 (2d,  $J = 7.2$  Hz, 2H), 3.32-3.22 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.1, 154.8, 136.6, 136.3, 136.1, 133.7, 133.7, 129.1, 129.1, 129.0, 128.9, 128.2, 127.8, 127.8, 127.3, 118.7, 90.3, 89.6, 82.3, 75.4, 74.8, 53.8, 51.3, 47.8, 34.3, 34.0. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{19}\text{ClNO}_2^+(\text{M}+\text{H})^+$  340.1099, found 340.1090.

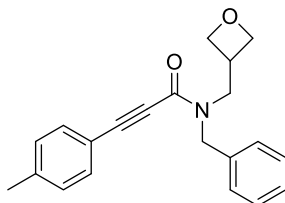
*N*-benzyl-3-(4-bromophenyl)-*N*-(oxetan-3-ylmethyl)propiolamide (**3d**)



The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 2.3g, 91%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.56-7.45 (m, 3H), 7.43-7.32 (m, 4H), 7.31-7.23 (m, 2H), 4.85&4.65 (2s, 2H), 4.70&4.64 (2q,  $J = 6.4$  Hz, 2H), 4.44&4.37 (2t,  $J = 6.0$  Hz, 2H), 3.99 & 3.72 (2d,  $J = 7.2$  Hz, 2H), 3.30-3.28 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  155.0, 154.8, 136.1, 133.8, 133.8, 132.1, 131.9, 129.1, 128.9, 128.2, 127.9, 127.8, 127.3, 124.9, 119.1, 90.4, 89.6, 82.4, 75.6, 74.8, 53.8, 51.3, 48.0, 47.8, 34.3, 34.0. HRMS (ESI) calcd

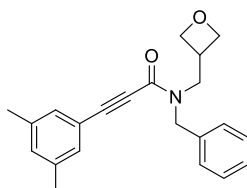
for  $C_{20}H_{19}BrNO_2^+(M+H)^+$  384.0594, found 384.0581.

*N*-benzyl-*N*-(oxetan-3-ylmethyl)-3-(*p*-tolyl)propiolamide (**3e**)



The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.9g, 88%, colorless oil;  $^1H$  NMR (400 MHz,  $CDCl_3$ , two rotamers)  $\delta$  7.53-7.39 (m, 2H), 7.39-7.29 (m, 4H), 7.29-7.23 (m, 1H), 7.22-7.15 (m, 2H), 4.87&4.66 (2s, 2H), 4.70&4.64 (2q,  $J = 6.0$  Hz, 2H), 4.47&4.38 (2t,  $J = 6.0$  Hz, 2H), 4.00&3.72 (2d,  $J = 7.6$  Hz, 2H), 3.35-3.24 (m, 1H), 2.41&2.38 (2s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ , two rotamers)  $\delta$  155.5, 155.2, 141.0, 140.8, 136.5, 136.4, 132.5, 132.4, 129.5, 129.3, 129.0, 128.8, 128.1, 127.8, 127.8, 127.4, 117.1, 92.0, 91.3, 81.1, 75.6, 74.9, 53.8, 51.3, 48.0, 47.7, 34.4, 34.1, 21.7, 21.7. HRMS (ESI) calcd for  $C_{21}H_{22}NO_2^+(M+H)^+$  320.1645, found 320.1636.

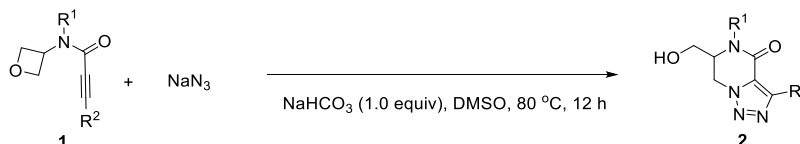
*N*-benzyl-3-(3,5-dimethylphenyl)-*N*-(oxetan-3-ylmethyl)propiolamide (**3f**)



The product was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:5). 1.9g, 83%, colorless oil;  $^1H$  NMR (400 MHz,  $CDCl_3$ , two rotamers)  $\delta$  7.43-7.35 (m, 2H), 7.35-7.31 (m, 2H), 7.30-7.20 (m, 2H), 7.13-7.03 (m, 2H), 4.87&4.66 (2s, 2H), 4.69 &4.64 (2q,  $J = 6.4$  Hz, 1H), 4.47&4.38 (2t,  $J = 6.0$  Hz, 2H), 3.99 &3.71 (2d,  $J = 7.2$  Hz, 2H), 3.33-3.26 (m, 2H), 2.33&2.29 (2s, 6H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ , two rotamers)  $\delta$  155.4, 155.2, 138.3, 138.2, 136.5, 136.4, 132.3, 132.2, 130.1, 129.0, 128.8, 128.1, 127.8, 127.4, 119.8, 92.1, 91.4, 81.0, 75.6, 75.0, 53.8, 51.3, 48.0, 47.7, 34.4, 34.1, 21.1, 21.0. HRMS (ESI) calcd for  $C_{22}H_{24}NO_2^+(M+H)^+$  334.1802, found 334.1792.

### III. Procedure for the tandem azide-alkyne cycloaddition/oxetane ring opening cascade reaction

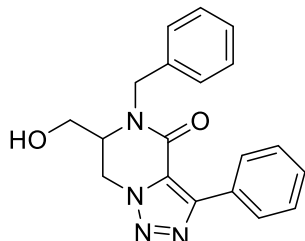
#### General procedure for the Synthesis of [1,2,3]triazolo[1,5-a]pyrazin-4(5H)-ones.



A mixture of **1** (0.2 mmol, 1.0 equiv),  $NaN_3$  (0.2 mmol, 12.6 mg, 1.0 equiv),  $NaHCO_3$  (0.2 mmol, 16.8 mg, 1.0 equiv) in DMSO (2 mL) was stirred at 80 °C for 12 hours. After the reaction was completed (monitored by TLC),  $H_2O$  (15.0 mL) and ethyl acetate (50.0 mL) were added. The organic phase was separated, and the aqueous phase was extracted with ethyl acetate (10.0 mL  $\times$  3). The combined organic

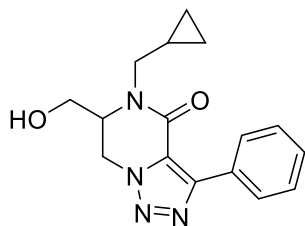
phase was washed with H<sub>2</sub>O (10.0 mL × 5) and brine, dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (dichloromethane/methanol = 100/1) to afford the desired products **2**.

5-benzyl-6-(hydroxymethyl)-3-phenyl-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2a**)



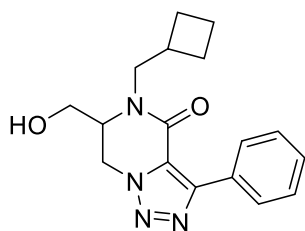
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 62.4 mg, 93%, white solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.28-8.14 (m, 2H), 7.44 (m, 3H), 7.39-7.29 (m, 5H), 5.43 (d, *J* = 14.8 Hz, 1H), 4.90 (d, *J* = 13.6 Hz, 1H), 4.65 (s, 1H), 4.23 (dd, *J* = 13.6, 4.8 Hz, 1H), 4.14 (d, *J* = 14.8 Hz, 1H), 3.84-3.80 (m, 1H), 3.68 (dd, *J* = 11.6, 4.4 Hz, 1H), 3.57 (t, *J* = 9.2 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 156.3, 148.4, 136.5, 129.5, 129.1, 128.9, 128.8, 128.5, 128.3, 128.3, 123.9, 59.1, 56.0, 48.6, 45.7. HRMS (ESI) calcd for C<sub>19</sub>H<sub>19</sub>N<sub>4</sub>O<sub>2</sub><sup>+</sup>(M+H)<sup>+</sup> 335.1503, found 335.1493

5-(cyclopropylmethyl)-6-(hydroxymethyl)-3-phenyl-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2b**)



The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 49.3 mg, 83%, white solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.23-8.11 (m, 2H), 7.51-7.35 (m, 3H), 5.03 (d, *J* = 13.6 Hz, 1H), 4.45 (dd, *J* = 13.6, 4.8 Hz, 1H), 4.04-3.99 (m, 1H), 3.86-3.77 (m, 2H), 3.56 (t, *J* = 10.4 Hz, 1H), 3.37 (s, 1H), 3.14-3.11 (dd, *J* = 14.4, 6.8 Hz, 1H), 1.12-1.06 (m, 1H), 0.64-0.54 (m, 2H), 0.39-0.30 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 156.1, 148.1, 129.5, 128.9, 128.7, 128.5, 124.1, 59.2, 56.9, 50.1, 45.6, 10.1, 4.2, 3.6. HRMS (ESI) calcd for C<sub>16</sub>H<sub>19</sub>N<sub>4</sub>O<sub>2</sub><sup>+</sup>(M+H)<sup>+</sup> 299.1503, found 299.1493.

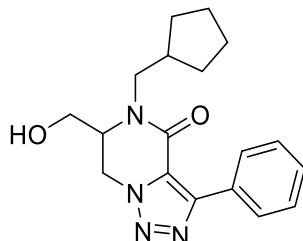
5-(cyclobutylmethyl)-6-(hydroxymethyl)-3-phenyl-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2c**)



The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 52.1 mg, 84%, white solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.17 (d, *J* = 12.0 Hz, 2H), 7.48-7.39 (m, 3H), 5.19 (s, 1H), 4.98 (d, *J* = 13.6 Hz, 1H), 4.36 (d, *J* = 13.6 Hz, 1H), 4.18-4.13 (m, 1H), 3.84-3.79 (m, 1H),

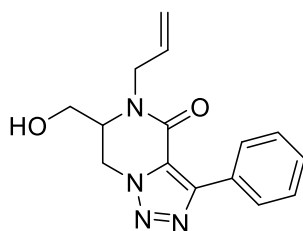
3.69 (d,  $J = 12.0$  Hz, 1H), 3.51 (t,  $J = 11.6$  Hz, 1H), 3.11-3.05 (m, 1H), 2.72-2.64(m, 2H), 1.96-1.87 (m, 3H), 1.83-1.75 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.2, 148.1, 129.4, 128.7, 128.4, 124.1, 59.0, 57.3, 50.8, 45.4, 34.3, 26.3, 26.1, 18.4. HRMS (ESI) calcd for  $\text{C}_{17}\text{H}_{21}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  313.1659, found 313.1649.

5-(cyclopentylmethyl)-6-(hydroxymethyl)-3-phenyl-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2d**)



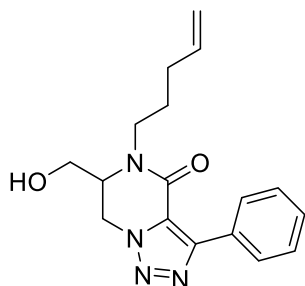
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 55.1 mg, 84%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.27-8.16 (m, 2H), 7.50-7.42 (m, 3H), 5.05 (d,  $J = 13.6$  Hz, 1H), 4.46-4.44(dd,  $J = 13.6, 8.8$ Hz, 1H), 4.22-4.19 (dd,  $J = 13.6, 8.0$ Hz, 1H), 3.95-3.90(m, 1H), 3.77 (dd,  $J = 11.6, 4.8$ Hz, 1H), 3.58 (m, 1H), 2.93-2.90 (dd,  $J = 13.6, 7.6$ Hz, 1H), 2.36-2.28 (m, 1H), 1.83-1.74 (m, 2H), 1.73-1.68(m, 2H), 1.65-1.56 (m, 2H), 1.32-1.27 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 148.2, 129.4, 129.0, 128.7, 128.4, 124.1, 59.1, 57.2, 50.4, 45.4, 39.0, 30.6, 30.2, 25.1, 24.8. HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{23}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  327.1816, found 327.1807.

5-allyl-6-(hydroxymethyl)-3-phenyl-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2e**)



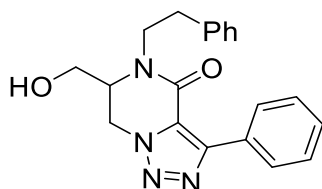
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 46.7 mg, 82%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.27-8.19 (m, 2H), 7.54-7.39 (m, 3H), 5.93-5.83 (m, 1H), 5.34 (d,  $J = 11.6$  Hz, 1H), 5.31 (d,  $J = 4.4$  Hz, 1H), 5.05 (d,  $J = 13.6$  Hz, 1H), 4.74 (dd,  $J = 15.2, 4.8$  Hz, 1H), 4.44 (dd,  $J = 13.6, 4.8$  Hz, 1H), 4.36 (t,  $J = 5.6$  Hz, 1H), 3.94-3.89 (m, 1H), 3.80-3.72 (m, 2H), 3.63-3.60 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  155.9, 148.4, 132.3, 129.5, 128.9, 128.7, 128.5, 123.9, 119.1, 59.3, 56.2, 48.1, 45.6. HRMS (ESI) calcd for  $\text{C}_{15}\text{H}_{17}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  285.1346, found 285.1338.

6-(hydroxymethyl)-5-(pent-4-en-1-yl)-3-phenyl-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2f**)



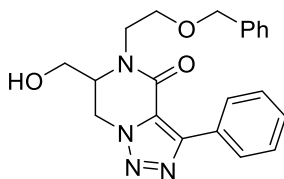
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 59.4 mg, 95%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.22-8.14 (m, 2H), 7.51-7.39 (m, 3H), 5.87-5.77 (m, 1H), 5.10-4.99 (m, 3H), 4.43-4.39 (dd,  $J = 13.6, 4.8$  Hz, 1H), 4.10-4.07 (m, 1H), 3.87-3.83 (m, 1H), 3.75-3.71 (dd,  $J = 11.6, 4.4$  Hz, 1H), 3.57 (t,  $J = 10.0$  Hz, 1H), 3.10-3.03 (m, 1H), 2.17-2.11 (m, 2H), 1.82-1.74 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.0, 148.1, 137.2, 129.5, 128.9, 128.7, 128.5, 124.1, 115.7, 59.2, 57.4, 46.0, 45.5, 31.0, 27.5. HRMS (ESI) calcd for  $\text{C}_{17}\text{H}_{21}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  313.1659 found 313.1649.

6-(hydroxymethyl)-5-phenethyl-3-phenyl-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2g**)



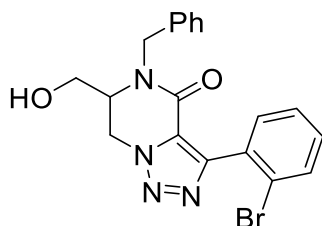
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 64.1 mg, 93%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.15 (d,  $J = 7.6$  Hz, 2H), 7.52-7.36 (m, 3H), 7.35-7.27 (m, 2H), 7.29-7.22 (m, 1H), 7.21 (d,  $J = 7.6$  Hz, 2H), 4.70 (d,  $J = 16.4$  Hz, 1H), 4.45-4.39 (m, 1H), 3.92-3.89 (dt,  $J = 4.0$  Hz, 1H), 3.62-3.59 (d,  $J = 13.6, 4.0$  Hz, 1H), 3.48-3.42 (m, 1H), 3.37-3.34 (m, 1H), 3.21-3.13 (m, 1H), 3.05-2.93 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.0, 148.1, 138.3, 129.5, 129.0, 128.9, 128.7, 128.5, 127.0, 124.0, 59.2, 58.5, 49.0, 45.1, 34.3. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{21}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  349.1659, found 349.1647.

5-(2-(benzyloxy)ethyl)-6-(hydroxymethyl)-3-phenyl-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2h**)



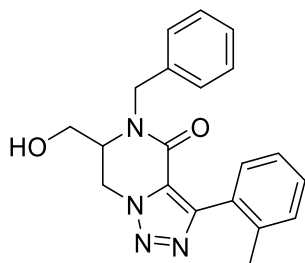
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 71.6 mg, 96%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.21-8.18 (m, 2H), 7.49-7.39 (m, 3H), 7.37-7.28 (m, 5H), 4.89 (dd,  $J = 13.6, 1.6$  Hz, 1H), 4.66 (t,  $J = 6.0$  Hz, 1H), 4.52 (s, 2H), 4.36 (dd,  $J = 13.6, 4.8$  Hz, 1H), 4.21 (dt,  $J = 14.4, 4.0$  Hz, 1H), 4.10-4.04 (m, 1H), 3.76-3.73 (m, 2H), 3.72-3.69 (m, 1H), 3.56-3.50 (m, 1H), 3.42-3.36 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.4, 148.1, 137.6, 129.4, 129.1, 128.7, 128.6, 128.4, 128.0, 127.8, 124.0, 73.5, 68.7, 59.7, 58.7, 46.7, 45.6. HRMS (ESI) calcd for  $\text{C}_{21}\text{H}_{23}\text{N}_4\text{O}_3^+(\text{M}+\text{H})^+$  379.1765, found 379.1755.

5-benzyl-3-(2-bromophenyl)-6-(hydroxymethyl)-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2i**)



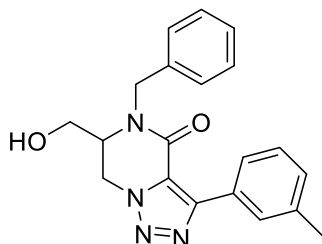
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 75.2 mg, 91%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 (d,  $J = 7.6$  Hz, 1H), 7.52 (d,  $J = 7.6$  Hz, 1H), 7.41 (t,  $J = 7.6$  Hz, 1H), 7.31 (s, 6H), 5.30 (d,  $J = 14.4$  Hz, 1H), 4.92 (d,  $J = 13.6$  Hz, 1H), 4.25 (d,  $J = 13.6$  Hz, 1H), 4.12 (d,  $J = 14.4$  Hz, 1H), 3.79 (s, 1H), 3.63 (d,  $J = 7.2$  Hz, 2H), 3.28 (s, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  155.7, 147.0, 136.4, 133.0, 131.9, 130.9, 130.4, 129.1, 128.3, 128.3, 127.4, 125.9, 123.8, 58.9, 56.3, 48.3, 45.5. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{18}\text{BrN}_4\text{O}_2^+(\text{M}+\text{H})^+$  413.0608, found 413.0595.

5-benzyl-6-(hydroxymethyl)-3-(o-tolyl)-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2j**)



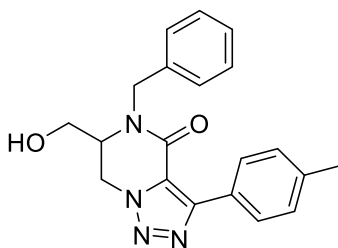
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 65.1 mg, 94%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 (d,  $J = 8.0$  Hz, 1H), 7.32 (d,  $J = 9.6$  Hz, 4H), 7.27 (d,  $J = 8.0$  Hz, 4H), 5.32 (d,  $J = 14.8$  Hz, 1H), 4.76 (d,  $J = 13.2$  Hz, 1H), 4.20 (d,  $J = 13.2$  Hz, 1H), 4.05 (d,  $J = 14.8$  Hz, 1H), 3.73 (s, 1H), 3.64-3.54 (m, 2H), 3.22 (s, 1H), 2.32 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.0, 148.0, 137.4, 136.4, 130.7, 130.5, 129.5, 129.0, 128.4, 128.3, 128.2, 125.6, 125.2, 59.1, 56.0, 48.2, 45.6, 20.1. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{21}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  349.1659, found 349.1650.

5-benzyl-6-(hydroxymethyl)-3-(m-tolyl)-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2k**)



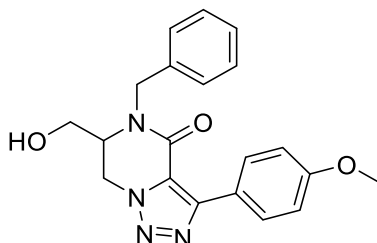
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 63.2mg, 92%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.97 (d,  $J = 8.8$  Hz, 2H), 7.36-7.29 (m, 6H), 7.22 (d,  $J = 6.8$  Hz, 1H), 5.44 (d,  $J = 16.0$  Hz, 1H), 4.88 (d,  $J = 14.8$  Hz, 1H), 4.22 (d,  $J = 13.2$  Hz, 1H), 4.11 (d,  $J = 14.8$  Hz, 1H), 3.79 (s, 1H), 3.67 (d,  $J = 11.2$  Hz, 1H), 3.55 (t,  $J = 10.8$  Hz, 1H), 3.47 (s, 1H), 2.41 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 148.5, 138.1, 136.5, 130.3, 129.3, 129.1, 129.1, 128.8, 128.4, 128.2, 126.0, 123.8, 59.1, 56.0, 48.5, 45.8, 21.6. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{21}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  349.1659, found 349.1650.

5-benzyl-6-(hydroxymethyl)-3-(p-tolyl)-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2l**)



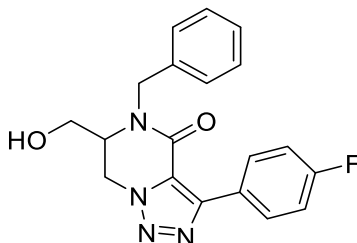
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 57.2 mg, 79%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.09 (d,  $J = 7.6$  Hz, 2H), 7.34 (t,  $J = 7.6$  Hz, 5H), 7.27 (d,  $J = 7.2$  Hz, 2H), 5.44 (d,  $J = 14.8$  Hz, 1H), 4.90 (d,  $J = 14.0$  Hz, 1H), 4.69 (s, 1H), 4.22 (dd,  $J = 13.6, 4.8$  Hz, 1H), 4.14 (d,  $J = 14.8$  Hz, 1H), 3.84-3.19 (m, 1H), 3.69 (dd,  $J = 11.2, 4.4$  Hz, 1H), 3.58 (t,  $J = 10.4$  Hz, 1H), 2.39 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 148.5, 139.6, 136.5, 129.2, 129.1, 128.6, 128.3, 126.0, 123.6, 59.0, 56.0, 48.6, 45.7, 21.4. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{21}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  349.1659, found 349.1650.

5-benzyl-6-(hydroxymethyl)-3-(4-methoxyphenyl)-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2m**)



The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 59.3 mg, 82%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.19 (d,  $J = 8.0$  Hz, 2H), 7.38-7.31 (m, 5H), 6.98 (d,  $J = 8.0$  Hz, 2H), 5.44 (d,  $J = 14.8$  Hz, 1H), 4.91 (d,  $J = 13.6$  Hz, 1H), 4.63 (s, 1H), 4.23 (dd,  $J = 13.6, 4.8$  Hz, 1H), 4.15 (d,  $J = 14.8$  Hz, 1H), 3.85 (s, 3H), 3.83-3.80 (m, 1H), 3.69 (dd,  $J = 11.6, 4.4$  Hz, 1H), 3.57 (t,  $J = 10.4$  Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  160.6, 156.4, 148.3, 136.5, 130.2, 129.1, 128.2, 128.2, 123.2, 121.4, 113.9, 59.0, 56.0, 55.4, 48.6, 45.6. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{21}\text{N}_4\text{O}_3^+(\text{M}+\text{H})^+$  365.1608, found 365.1598.

5-benzyl-3-(4-fluorophenyl)-6-(hydroxymethyl)-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2n**)

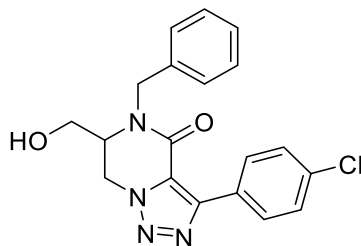


The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 68.6 mg, 98%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.25 (t,  $J = 5.2$  Hz, 2H), 7.38-7.31 (m, 5H), 7.14 (t,  $J = 8.4$  Hz, 2H), 5.44 (d,  $J = 14.8$  Hz, 1H), 4.93 (d,  $J = 13.6$  Hz, 1H), 4.27 (dd,  $J = 13.2, 4.0$  Hz, 1H), 4.17 (d,  $J = 14.8$  Hz, 1H), 3.87-3.82 (m, 1H), 3.70 (dd,  $J = 11.6, 4.8$  Hz, 1H), 3.56 (t,  $J = 10.4$  Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  163.5 (d,  $J = 124.0$  Hz), 156.31, 147.59, 136.35, 130.8 (d,  $J = 9.0$  Hz), 129.14, 128.34, 128.23, 125.1 (d,  $J = 3.0$  Hz), 123.67, 115.5 (d,  $J = 21.0$  Hz), 59.24, 55.89, 48.65,



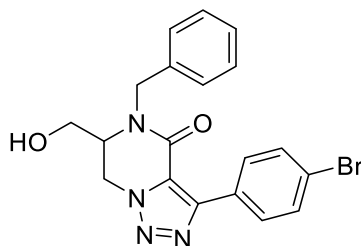
45.76. HRMS (ESI) calcd for  $C_{19}H_{18}FN_4O_2^+(M+H)^+$  353.1408, found 353.1404.

5-benzyl-3-(4-chlorophenyl)-6-(hydroxymethyl)-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one  
(**2o**)



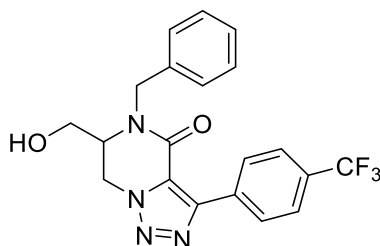
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 70.1 mg, 95%, white solid;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.18 (d,  $J$  = 10.4 Hz, 2H), 7.43 (d,  $J$  = 9.2 Hz, 2H), 7.37-7.32 (m, 5H), 5.42 (dd,  $J$  = 14.8, 3.6 Hz, 1H), 4.91 (dd,  $J$  = 13.6, 3.2 Hz, 1H), 4.72 (q,  $J$  = 5.6 Hz, 1H), 4.26 (dt,  $J$  = 12.0, 4.0 Hz, 1H), 4.17 (dd,  $J$  = 14.8, 4.0 Hz, 1H), 3.86-3.81 (m, 1H), 3.70-3.66 (m, 1H), 3.57-3.50 (m, 1H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  156.2, 147.3, 136.3, 135.6, 130.0, 129.1, 128.7, 128.3, 128.2, 127.4, 124.0, 59.2, 56.0, 48.7, 45.8. HRMS (ESI) calcd for  $C_{19}H_{18}ClN_4O_2^+(M+H)^+$  369.1113, found 369.1104.

5-benzyl-3-(4-bromophenyl)-6-(hydroxymethyl)-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one  
(**2p**)



The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 78.6 mg, 95%, white solid;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.14 (d,  $J$  = 8.0 Hz, 2H), 7.59 (d,  $J$  = 8.0 Hz, 2H), 7.40-7.33 (m, 5H), 5.44 (d,  $J$  = 14.8 Hz, 1H), 4.93 (d,  $J$  = 13.6 Hz, 1H), 4.38 (s, 1H), 4.28 (dd,  $J$  = 14.0, 4.4 Hz, 1H), 4.18 (d,  $J$  = 14.8 Hz, 1H), 3.88-3.83 (m, 1H), 3.70 (d,  $J$  = 10.8 Hz, 1H), 3.54 (t,  $J$  = 10.4 Hz, 1H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  156.2, 147.4, 136.3, 131.7, 130.3, 129.1, 128.3, 128.2, 127.9, 124.0, 123.9, 59.2, 55.9, 48.7, 45.8. HRMS (ESI) calcd for  $C_{19}H_{18}BrN_4O_2^+(M+H)^+$  413.0608, found 413.0595.

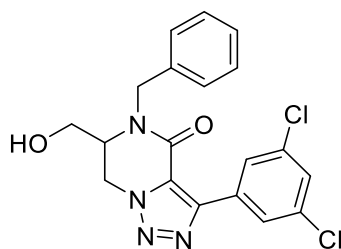
5-benzyl-6-(hydroxymethyl)-3-(4-(trifluoromethyl)phenyl)-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2q**)



The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 79.2 mg, 98%, white solid;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  8.44 (d,  $J$  = 8.0 Hz, 2H), 7.74 (d,  $J$  = 8.0 Hz,

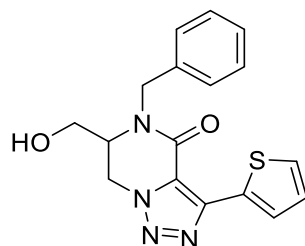
2H), 7.43-7.31 (m, 5H), 5.47 (d,  $J = 14.8$  Hz, 1H), 5.00 (d,  $J = 13.6$  Hz, 1H), 4.36 (dd,  $J = 13.6, 4.4$  Hz, 1H), 4.23 (d,  $J = 16.0$  Hz, 1H), 3.93-3.88 (m, 1H), 3.74 (dd,  $J = 11.2, 4.4$  Hz, 1H), 3.57 (t,  $J = 10.0$  Hz, 1H), 1.97 (s, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.1, 147.1, 136.2, 132.5, 131.1 (q,  $J = 32.0$  Hz), 129.2, 129.0, 128.4, 128.3, 125.4 (q,  $J = 4.0$  Hz), 124.56, 122.68, 59.54, 55.78, 48.74, 45.91. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{18}\text{F}_3\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  403.1376, found 403.1363.

5-benzyl-3-(3,5-dichlorophenyl)-6-(hydroxymethyl)-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2r**)



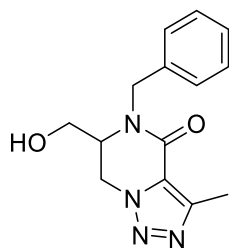
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 76.4 mg, 95%, white solid;  $^1\text{H}$  NMR (400 MHz, DMSO)  $\delta$  8.42 (d,  $J = 2.0$  Hz, 2H), 7.66 (t,  $J = 2.0$  Hz, 1H), 7.45-7.34 (m, 4H), 7.33-7.28 (m, 1H), 5.25 (d,  $J = 15.2$  Hz, 1H), 5.19 (t,  $J = 5.2$  Hz, 1H), 4.93 (d,  $J = 14.0$  Hz, 1H), 4.70 (dd,  $J = 13.6, 5.2$  Hz, 1H), 4.42 (d,  $J = 15.2$  Hz, 1H), 3.93 (q,  $J = 4.8$  Hz, 1H), 3.6-3.50 (m, 1H), 3.44-3.39 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz, DMSO)  $\delta$  156.56, 144.0, 137.6, 134.6, 133.6, 129.1, 128.6, 128.1, 127.9, 126.9, 125.7, 60.2, 56.6, 48.6, 46.5. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{17}\text{Cl}_2\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  403.0723, found 403.0713.

5-benzyl-6-(hydroxymethyl)-3-(thiophen-2-yl)-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2s**)



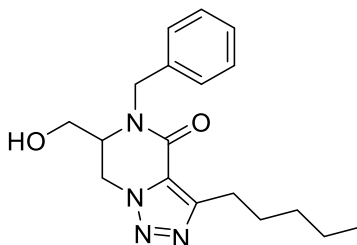
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 57.2 mg, 85%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.30 (t,  $J = 3.6$  Hz, 1H), 7.40 (t,  $J = 3.6$  Hz, 1H), 7.36-7.32 (m, 5H), 7.12 (q,  $J = 4.0$  Hz, 1H), 5.44 (dd,  $J = 15.2, 2.8$  Hz, 1H), 4.94 (d,  $J = 13.2$  Hz, 1H), 4.24 (dd,  $J = 14.0, 4.0$  Hz, 1H), 4.18 (d,  $J = 14.4$  Hz, 1H), 3.87-3.82 (m, 1H), 3.71 (dd,  $J = 11.6, 3.6$  Hz, 1H), 3.57 (t,  $J = 10.4$  Hz, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.1, 143.6, 136.4, 130.8, 129.7, 129.1, 128.3, 128.3, 128.0, 127.7, 122.4, 59.0, 56.0, 48.5, 45.7. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{18}\text{BrNO}_2^+(\text{M}+\text{H})^+$  341.1067, found 341.1059.

5-benzyl-6-(hydroxymethyl)-3-methyl-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2t**)



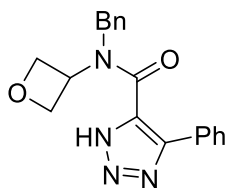
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 40.2 mg, 72%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40-7.32 (m, 5H), 5.43 (d,  $J$  = 14.8 Hz, 1H), 4.89 (d,  $J$  = 13.6 Hz, 1H), 4.21 (dt,  $J$  = 13.6, 4.0 Hz, 2H), 4.14 (d,  $J$  = 14.4 Hz), 3.86-3.80 (m, 1H), 3.72-3.67 (m, 1H), 3.54 (t,  $J$  = 10.4 Hz, 1H), 2.59 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.8, 145.9, 136.5, 129.1, 128.2, 128.2, 124.5, 58.8, 56.3, 48.0, 45.2, 11.0. HRMS (ESI) calcd for  $\text{C}_{14}\text{H}_{17}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  273.1346, found 274.1336.

5-benzyl-6-(hydroxymethyl)-3-pentyl-6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one (**2u**)



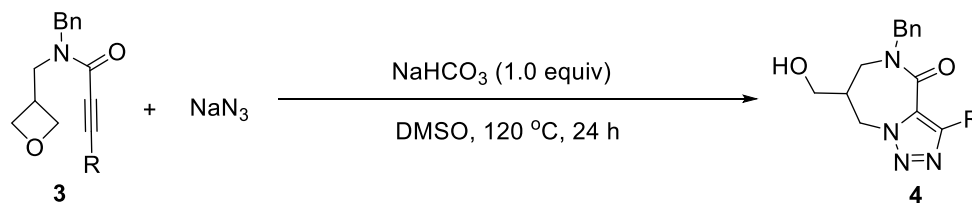
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 51.3 mg, 78%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41-7.34 (m, 5H), 5.43 (d,  $J$  = 14.8 Hz, 1H), 4.89 (d,  $J$  = 13.6 Hz, 1H), 4.21 (d,  $J$  = 11.2 Hz, 1H), 4.16 (d,  $J$  = 15.6 Hz, 1H), 3.84-3.80 (m, 1H), 3.70 (dd,  $J$  = 11.6, 4.4 Hz, 1H), 3.54 (t,  $J$  = 10.4 Hz, 1H), 3.00 (t,  $J$  = 8.0 Hz, 2H), 1.77 (q,  $J$  = 8.4 Hz, 2H), 1.39-1.35 (m, 4H), 0.91 (t,  $J$  = 6.4 Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  156.6, 150.4, 136.5, 129.1, 128.3, 128.2, 124.2, 58.6, 56.3, 48.0, 45.1, 31.4, 28.6, 25.2, 22.4, 14.0. HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{25}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  329.1972, found 329.1964.

N-benzyl-N-(oxetan-3-yl)-4-phenyl-1H-1,2,3-triazole-5-carboxamide (**2a'**)



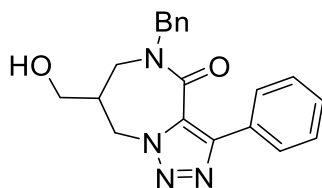
The product was purified by silica gel column chromatography (dichloromethane/methanol = 200/1). 18.1 mg, 27%, colorless oil,  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  7.80-7.77 (m, 1H), 7.53-7.42 (m, 3H), 7.40-7.35 (m, 4H), 7.33-7.28 (m, 2H), 4.75 (d,  $J$  = 15.2 Hz, 1H), 4.54 (dd,  $J$  = 14.4, 4.0 Hz, 1H), 4.46-4.37 (m, 2H), 4.30 (d,  $J$  = 15.2 Hz, 1H), 4.28-4.20 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ , two rotamers)  $\delta$  158.1, 148.3, 135.6, 129.9, 129.2, 129.0, 128.6, 128.2, 125.8, 120.4, 65.2, 54.5, 50.7, 47.4. HRMS (ESI) calcd for  $\text{C}_{19}\text{H}_{19}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  335.1503, found 335.1501.

## General procedure for the synthesis of 6,7-dihydro-[1,2,3]triazolo[1,5-a]pyrazin-4(5H)-one



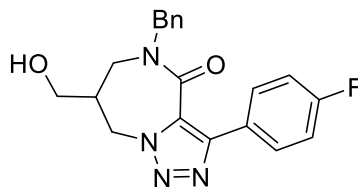
A mixture of **3** (0.2 mmol, 1.0 equiv),  $\text{NaN}_3$  (0.2 mmol, 12.6 mg, 1.0 equiv),  $\text{NaHCO}_3$  (0.2 mmol, 16.8 mg, 1.0 equiv) in DMSO (2 mL) was stirred at  $120\text{ }^\circ\text{C}$  for 12 hours. After the reaction was completed (monitored by TLC),  $\text{H}_2\text{O}$  (15.0 mL) and ethyl acetate (50.0 mL) were added. The organic phase was separated, and the aqueous phase was extracted with ethyl acetate (10.0 mL  $\times$  3). The combined organic phase was washed with brine (10.0 mL  $\times$  5) and further dried over  $\text{Na}_2\text{SO}_4$ . The solvent was removed under reduced pressure and the residue was purified by flash chromatography (dichloromethane/methanol = 100/1) to afford the desired products **4**.

### 5-benzyl-7-(hydroxymethyl)-3-phenyl-5,6,7,8-tetrahydro-4H-[1,2,3]triazolo[1,5-a][1,4]diazepin-4-one (**4a**)



The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 55.3 mg, 80%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.15 (d,  $J = 9.6$  Hz, 2H), 7.49-7.42 (m, 2H), 7.39-7.38 (m, 6H), 5.14 (d,  $J = 14.4$  Hz, 1H), 4.66 (d,  $J = 14.4$  Hz, 1H), 4.54 (d,  $J = 14.8$  Hz, 1H), 4.44-4.38 (m, 1H), 3.50-3.43 (m, 2H), 3.40-3.34 (m, 1H), 3.14-3.07 (m, 1H), 2.37-2.34 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  161.2, 148.0, 136.7, 129.6, 129.1, 129.0, 128.6, 128.4, 128.3, 127.9, 127.8, 61.7, 51.0, 48.2, 47.1, 42.0. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{21}\text{N}_4\text{O}_2^+(\text{M}+\text{H})^+$  349.1659, found 349.1651.

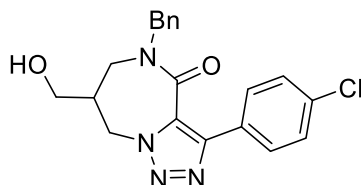
### 5-benzyl-3-(4-fluorophenyl)-7-(hydroxymethyl)-5,6,7,8-tetrahydro-4H-[1,2,3]triazolo[1,5-a][1,4]diazepin-4-one (**4b**)



The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 65.2 mg, 90%, white solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 (d,  $J = 8.0$  Hz, 2H), 7.59 (d,  $J = 8.0$  Hz, 2H), 7.41-7.35 (m, 5H), 5.13 (d,  $J = 14.0$  Hz, 1H), 4.65 (dd,  $J = 14.4, 3.6$  Hz, 1H), 4.55 (d,  $J = 14.4$  Hz, 1H), 4.43 (dd,  $J = 14.4, 6.8$  Hz, 1H), 3.53-3.43 (m, 2H), 3.38 (dd,  $J = 15.2, 6.0$  Hz, 1H), 3.13 (dd,  $J = 15.6, 9.2$  Hz, 1H), 2.40-2.35 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  163.2 (d,  $J = 247.0$  Hz), 161.16, 147.11, 136.61, 129.8 (d,  $J = 8.0$  Hz), 129.13, 128.40, 128.35, 127.73, 125.8 (d,  $J = 3.0$  Hz), 115.63 (d,  $J = 21.0$  Hz), 61.60, 51.04, 48.33, 47.18, 41.95. HRMS (ESI) calcd for  $\text{C}_{20}\text{H}_{20}\text{FN}_4\text{O}_2^+(\text{M}+\text{H})^+$  367.1565,

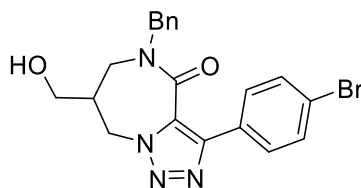
found 367.1556.

5-benzyl-3-(4-chlorophenyl)-7-(hydroxymethyl)-5,6,7,8-tetrahydro-4H-[1,2,3]triazolo[1,5-a][1,4]diazepin-4-one (**4c**)



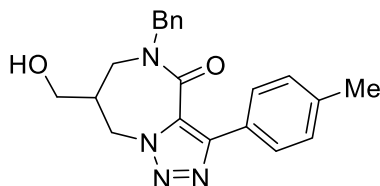
The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 66.2 mg, 87%, white solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.11 (d, *J* = 8.0 Hz, 2H), 7.44-7.38 (m, 7H), 5.13 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.54 (d, *J* = 16.0 Hz, 1H), 4.41 (dd, *J* = 16.0, 8.0 Hz, 1H), 3.46 (s, 2H), 3.38 (dd, *J* = 16.0, 4.0 Hz, 1H), 3.11 (t, *J* = 12.0 Hz, 1H), 2.71 (s, 1H), 2.37 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 161.1, 146.9, 136.6, 135.0, 129.1, 128.9, 128.4, 128.4, 128.1, 128.0, 61.6, 51.1, 48.3, 47.2, 41.9. HRMS (ESI) calcd for C<sub>20</sub>H<sub>20</sub>ClN<sub>4</sub>O<sub>2</sub><sup>+</sup>(M+H)<sup>+</sup> 383.1268, found 383.1259.

5-benzyl-3-(4-bromophenyl)-7-(hydroxymethyl)-5,6,7,8-tetrahydro-4H-[1,2,3]triazolo[1,5-a][1,4]diazepin-4-one (**4d**)



The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 69.2 mg, 81%, white solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.07 (d, *J* = 8.8 Hz, 2H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.44-7.33 (m, 5H), 5.13 (d, *J* = 14.4 Hz, 1H), 4.65 (dd, *J* = 14.4, 3.6 Hz, 1H), 4.55 (d, *J* = 14.4 Hz, 1H), 4.43 (dd, *J* = 14.4, 6.8 Hz, 1H), 3.54-3.43 (m, 2H), 3.38 (dd, *J* = 14.4, 6.8 Hz, 1H), 3.13 (dd, *J* = 15.2, 9.2 Hz, 1H), 2.41-2.34 (m, 1H), 2.23-2.21 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 161.1, 147.0, 136.6, 131.8, 129.4, 129.2, 128.6, 128.4, 128.4, 128.0, 123.3, 61.8, 51.1, 48.3, 47.1, 41.9. HRMS (ESI) calcd for C<sub>20</sub>H<sub>20</sub>BrN<sub>4</sub>O<sub>2</sub><sup>+</sup>(M+H)<sup>+</sup> 437.0764, found 437.0755.

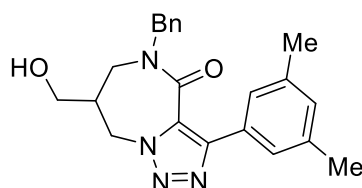
5-benzyl-7-(hydroxymethyl)-3-(p-tolyl)-5,6,7,8-tetrahydro-4H-[1,2,3]triazolo[1,5-a][1,4]diazepin-4-one (**4e**)



The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 52.3 mg, 72%, white solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.01 (d, *J* = 8.0 Hz, 2H), 7.38-7.34 (m, 5H), 7.27 (s 1H), 7.25 (s, 1H), 5.11 (d, *J* = 14.4 Hz, 1H), 4.61 (dd, *J* = 14.4, 3.6 Hz, 1H), 4.52 (d, *J* = 14.4 Hz, 1H), 4.39 (dd, *J* = 12.0, 4.0 Hz, 1H), 3.50-3.40 (m, 2H), 3.34 (dd, *J* = 13.6, 6.4 Hz, 1H), 3.09 (dd, *J* = 12.0, 8.0 Hz, 1H), 2.39 (s, 3H), 2.36-2.30 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 161.3, 139.0, 136.8, 129.3, 129.1, 128.4, 128.3, 127.7, 127.6, 126.8, 61.7, 51.0, 48.2, 47.1, 41.9, 21.4. HRMS (ESI) calcd for

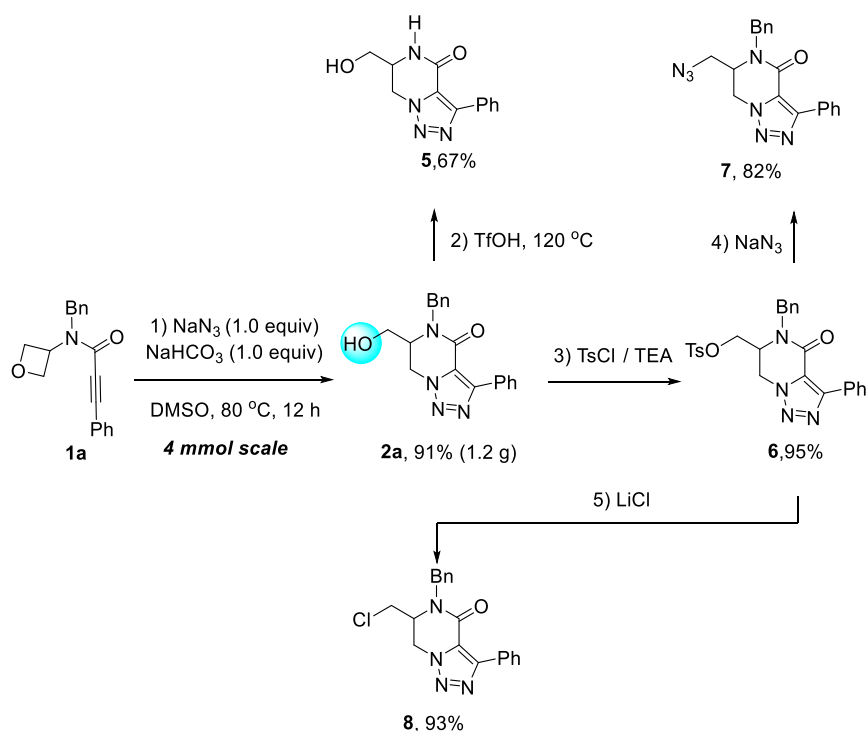
$C_{21}H_{23}N_4O_2^+(M+H)^+$  363.1816, found 363.1807.

5-benzyl-3-(3,5-dimethylphenyl)-7-(hydroxymethyl)-5,6,7,8-tetrahydro-4H-[1,2,3]triazolo[1,5-a][1,4]diazepin-4-one (**4f**)



The product was purified by silica gel column chromatography (dichloromethane/methanol = 100/1). 55.3 mg, 76%, colourless oil;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.71 (s, 2H), 7.43-7.32 (m, 5H), 7.05 (s, 1H), 5.11 (d,  $J$  = 15.6 Hz, 1H), 4.60 (dd,  $J$  = 14.4, 4.0 Hz, 1H), 4.55 (d,  $J$  = 14.4 Hz, 1H), 4.41 (dd,  $J$  = 16.0, 4.0 Hz, 1H), 3.50-3.43 (m, 2H), 3.35 (dd,  $J$  = 14.4, 6.8 Hz, 1H), 3.10 (dd,  $J$  = 15.6, 9.2 Hz, 1H), 2.89 (t,  $J$  = 4.4 Hz, 1H), 2.39 (s, 6H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  161.3, 148.2, 138.2, 136.8, 130.8, 129.3, 129.1, 128.4, 128.3, 127.8, 125.6, 61.6, 51.0, 48.2, 47.1, 42.0, 21.4. HRMS (ESI) calcd for  $C_{22}H_{25}N_4O_2^+(M+H)^+$  377.1972, found 377.1962.

#### IV. Synthetic Transformations



**Gram synthesis of 2a:** A mixture of **1a** (4 mmol, 1.16 g),  $NaN_3$  (4 mmol, 252 mg),  $NaHCO_3$  (4 mmol, 420 mg) in DMSO (10 mL) was stirred at 80 °C for 12 hours. After the reaction was completed (monitored by TLC),  $H_2O$  (15.0 mL) and ethyl acetate (50.0 mL) were added. The organic phase was separated, and the aqueous phase was extracted with ethyl acetate (10.0 mL  $\times$  3). The combined organic phase was washed with brine, dried over  $Na_2SO_4$ . The solvent was removed under reduced pressure and the residue was purified by flash chromatography (dichloromethane/methanol = 100/1) to afford the desired products **2a** in 91% yield. Notably, the

above resulting crude product was able to be recrystallized from petroleum ether and DCM to afford pure compound 4a as white solid (74% yield).

**Synthesis of 5:** A mixture of **2a** (0.2 mmol, 66.8 mg) in TfOH (2 mL) was stirred at 120 °C for 12 hours. After the reaction was completed, the mixture was concentrated in vacuum and then loaded on silica column (ethyl acetate/petroleum ether = 2:1) to afford the title compound **5** in 67% yield. White solid; <sup>1</sup>H NMR (400 MHz, DMSO) δ 8.56 (d, *J* = 3.6 Hz, 1H), 8.30-8.27 (m, 2H), 7.49-7.39 (m, 3H), 5.17 (t, *J* = 5.6 Hz, 1H), 4.76-4.64 (m, 2H), 3.82-3.86 (m, 1H), 3.58-3.52 (m, 1H), 3.41-3.37 (m, 1H). <sup>13</sup>C NMR (100 MHz, DMSO) δ 157.8, 146.8, 130.3, 129.3, 128.7, 128.7, 124.8, 61.6, 51.7, 46.7. HRMS (ESI) calcd for C<sub>12</sub>H<sub>13</sub>N<sub>4</sub>O<sub>2</sub>(M+H)<sup>+</sup> 245.1033, found 245.1030.

**Synthesis of 6:** A mixture of **2a** (1.5 mmol, 501.0 mg), TsCl (1.5 mmol, 285.0 mg), Et<sub>3</sub>N (2.25 mmol, 227.2 mg) in DCM (10 mL) was stirred at room temperature for 12 hours. After the reaction was completed, the mixture was concentrated in vacuum and then loaded on silica column (ethyl acetate/petroleum ether = 1:10) to afford the title compound **6** in 95% yield. White solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.27 (d, *J* = 7.2 Hz, 2H), 7.59 (d, *J* = 7.2 Hz, 2H), 7.45 (q, *J* = 8.0 Hz, 3H), 7.39-7.31 (m, 5H), 7.23 (d, *J* = 8.0 Hz, 2H), 5.32 (d, *J* = 14.8 Hz, 1H), 4.80 (d, *J* = 14.0 Hz, 1H), 4.35 (dt, *J* = 14.0, 4.0 Hz, 1H), 4.24 (d, *J* = 14.8 Hz, 1H), 4.11-4.06 (m, 1H), 4.00-3.95 (m, 1H), 3.78 (t, *J* = 8.8 Hz, 1H), 2.36 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 156.2, 148.7, 145.8, 136.1, 131.6, 130.2, 129.4, 129.3, 129.2, 128.8, 128.4, 128.4, 127.7, 123.3, 65.6, 53.3, 48.7, 46.0, 21.7. HRMS (ESI) calcd for C<sub>26</sub>H<sub>25</sub>N<sub>4</sub>O<sub>4</sub>S<sup>+</sup>(M+H)<sup>+</sup> 489.1591, found 489.1578.

**Synthesis of 7:** A mixture of **6** (0.3 mmol, 146 mg), NaN<sub>3</sub> (0.3 mmol, 18.9 mg) in DMSO (2 mL) was stirred at 80 °C for 24 hours. After the reaction was complete (monitored by TLC), H<sub>2</sub>O (15.0 mL) and ethyl acetate (50.0 mL) were added. The organic phase was separated, and the aqueous phase was extracted with ethyl acetate (10.0 mL × 3). The combined organic phase was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (ethyl acetate/petroleum ether = 1/5) to afford the desired products **7**. White solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.35 (d, *J* = 7.2 Hz, 2H), 7.52-7.41 (m, 3H), 7.40-7.34 (m, 5H), 5.40 (d, *J* = 14.8 Hz, 1H), 4.85 (d, *J* = 14.0 Hz, 1H), 4.37 (dd, *J* = 14.0, 4.8 Hz, 1H), 4.30 (d, *J* = 15.2 Hz, 1H), 3.86-3.81 (m, 1H), 3.43 (dd, *J* = 12.4, 5.2 Hz, 1H), 3.27 (dd, *J* = 12.8, 8.8 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 156.2, 149.0, 136.2, 129.5, 129.3, 129.2, 128.9, 128.5, 128.4, 128.3, 123.4, 53.8, 50.2, 48.7, 46.6. HRMS (ESI) calcd for C<sub>19</sub>H<sub>18</sub>N<sub>7</sub>O<sup>+</sup>(M+H)<sup>+</sup> 360.1567, found 360.1558.

**Synthesis of 8:** A mixture of **6** (0.3 mmol, 146 mg), LiCl (0.3 mmol, 15.2 mg) in DMF (2 mL) was stirred at room temperature for 12 hours. After the reaction was complete (monitored by TLC), H<sub>2</sub>O (15.0 mL) and ethyl acetate (50.0 mL) were added. The organic phase was separated, and the aqueous phase was extracted with ethyl acetate (10.0 mL × 3). The combined organic phase was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (ethyl acetate/petroleum ether = 1/5) to afford the desired products **8**. White solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.35 (d, *J* = 8.0 Hz, 2H), 7.51-7.44 (m, 3H), 7.40-7.35 (m, 5H), 5.39 (d, *J* = 14.8 Hz, 1H), 5.11 (d, *J* = 14.0 Hz, 1H), 4.41-4.36 (m, 1H), 4.29 (d, *J* = 14.8 Hz, 1H), 3.97 (q, *J* = 5.2 Hz, 1H), 3.50 (d, *J* = 10.4 Hz, 1H), 3.28 (t, *J* = 11.6 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 156.0, 149.0, 136.1, 129.5, 129.3, 129.2, 128.9, 128.5, 128.4, 128.3, 123.3, 56.1, 48.6, 46.1, 40.6. HRMS (ESI) calcd

for  $C_{19}H_{18}ClN_4O^+(M+H)^+$  353.1164, found 353.1155.

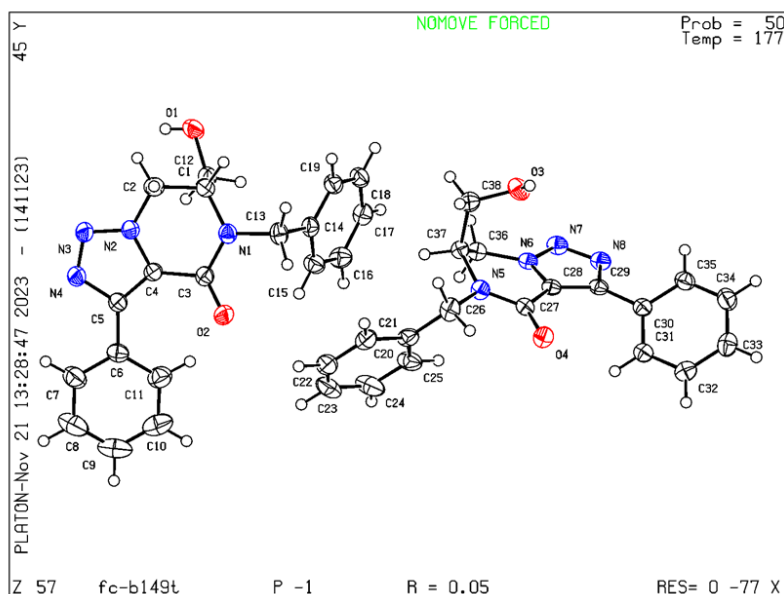
## V. X-Ray Crystallographic Data 2a

### X-Ray Crystallographic Data of 2a

Compounds **2a** were collected at 100 K on a Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu  $K\alpha$  radiation. The data were collected and processed using CrysAlisPro22.

Compound **2a** was completely dissolved in ethyl acetate (0.3 mL). Hexanes (1.0 mL) was added slowly to the solution at room temperature. The solvent diffused slowly, and the single crystal was obtained after two days. The structure in Figure S1 showed the absolute configuration of **2a**. The CCDC number is 2386562. These details can be obtained free of charge via [www.ccdc.com.ac.uk/data\\_request/cif](http://www.ccdc.com.ac.uk/data_request/cif) from the Cambridge Crystallographic Data Centre.

Figure S1. Thermal Ellipsoid Plot for 2a (50% probability level)



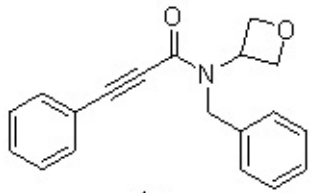
### Crystal Data for 2a

Table 1 Crystal data and structure refinement for FC-B149T.

Identification code	FC-B149T
Empirical formula	$C_{19}H_{18}N_4O_2$
Formula weight	334.37
Temperature/K	177(12)
Crystal system	triclinic
Space group	P-1
$a/\text{\AA}$	8.9365(3)



b/Å	9.5864(4)
c/Å	21.4457(8)
$\alpha$ /°	82.342(3)
$\beta$ /°	85.179(3)
$\gamma$ /°	65.019(4)
Volume/Å <sup>3</sup>	1649.71(12)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.346
$\mu/\text{mm}^{-1}$	0.732
F(000)	704.0
Crystal size/mm <sup>3</sup>	0.15 × 0.13 × 0.12
Radiation	Cu K $\alpha$ ( $\lambda$ = 1.54184)
2 $\theta$ range for data collection/°	4.16 to 148.054
Index ranges	-11 ≤ h ≤ 8, -11 ≤ k ≤ 10, -25 ≤ l ≤ 26
Reflections collected	11372
Independent reflections	6464 [R <sub>int</sub> = 0.0376, R <sub>sigma</sub> = 0.0464]
Data/restraints/parameters	6464/0/453
Goodness-of-fit on F <sup>2</sup>	1.026
Final R indexes [I ≥ 2 $\sigma$ (I)]	R <sub>1</sub> = 0.0507, wR <sub>2</sub> = 0.1362
Final R indexes [all data]	R <sub>1</sub> = 0.0565, wR <sub>2</sub> = 0.1454
Largest diff. peak/hole / e Å <sup>-3</sup>	0.30/-0.26

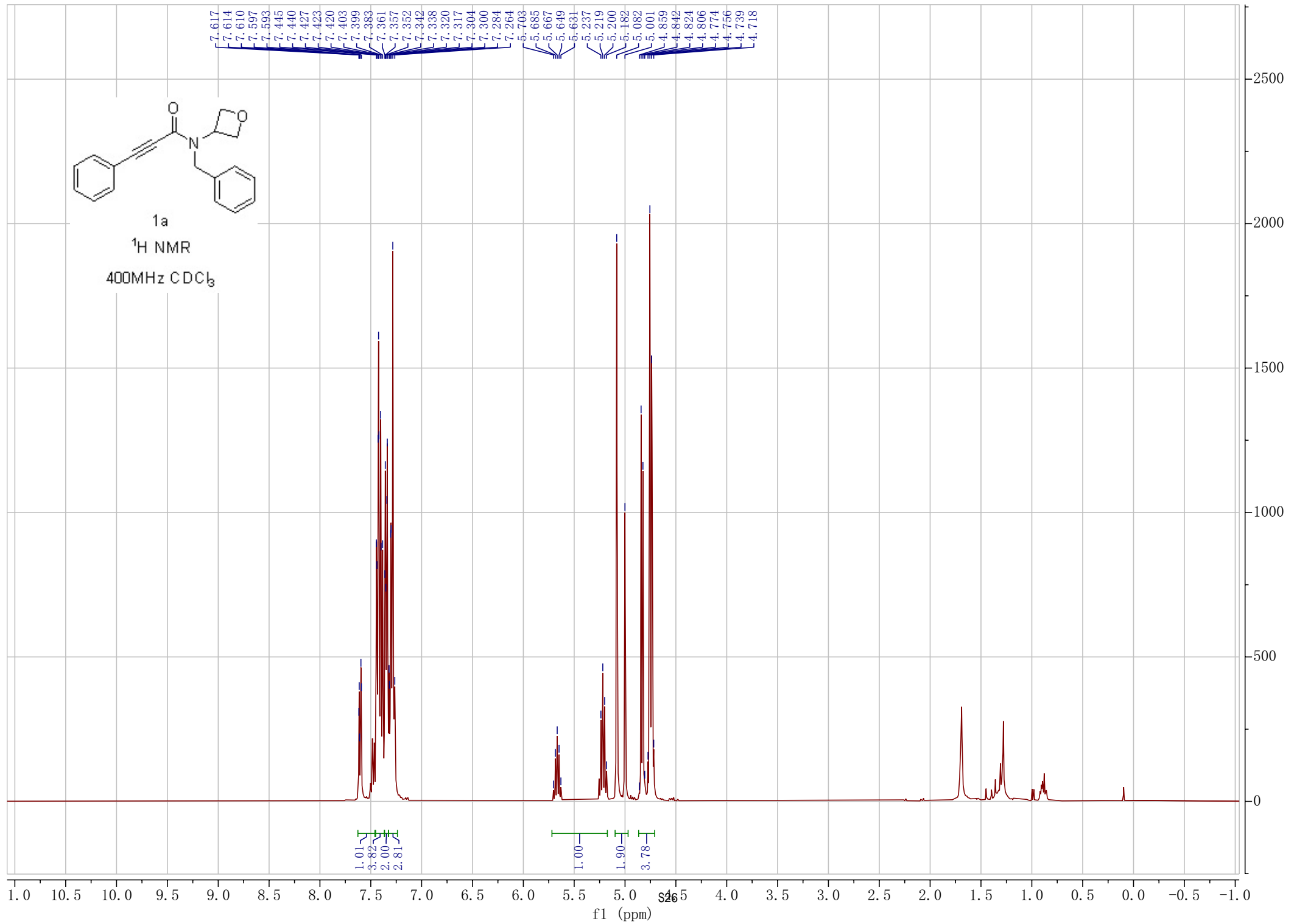


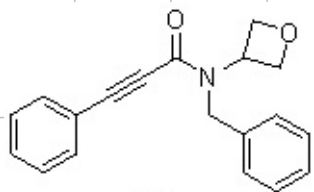
1a

<sup>1</sup>H NMR

400MHz CDCl<sub>3</sub>

7.617  
7.614  
7.610  
7.597  
7.593  
7.445  
7.440  
7.427  
7.423  
7.420  
7.403  
7.399  
7.383  
7.361  
7.357  
7.352  
7.342  
7.338  
7.320  
7.317  
7.304  
7.300  
7.284  
7.264  
5.708  
5.685  
5.667  
5.649  
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5.237  
5.219  
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4.718

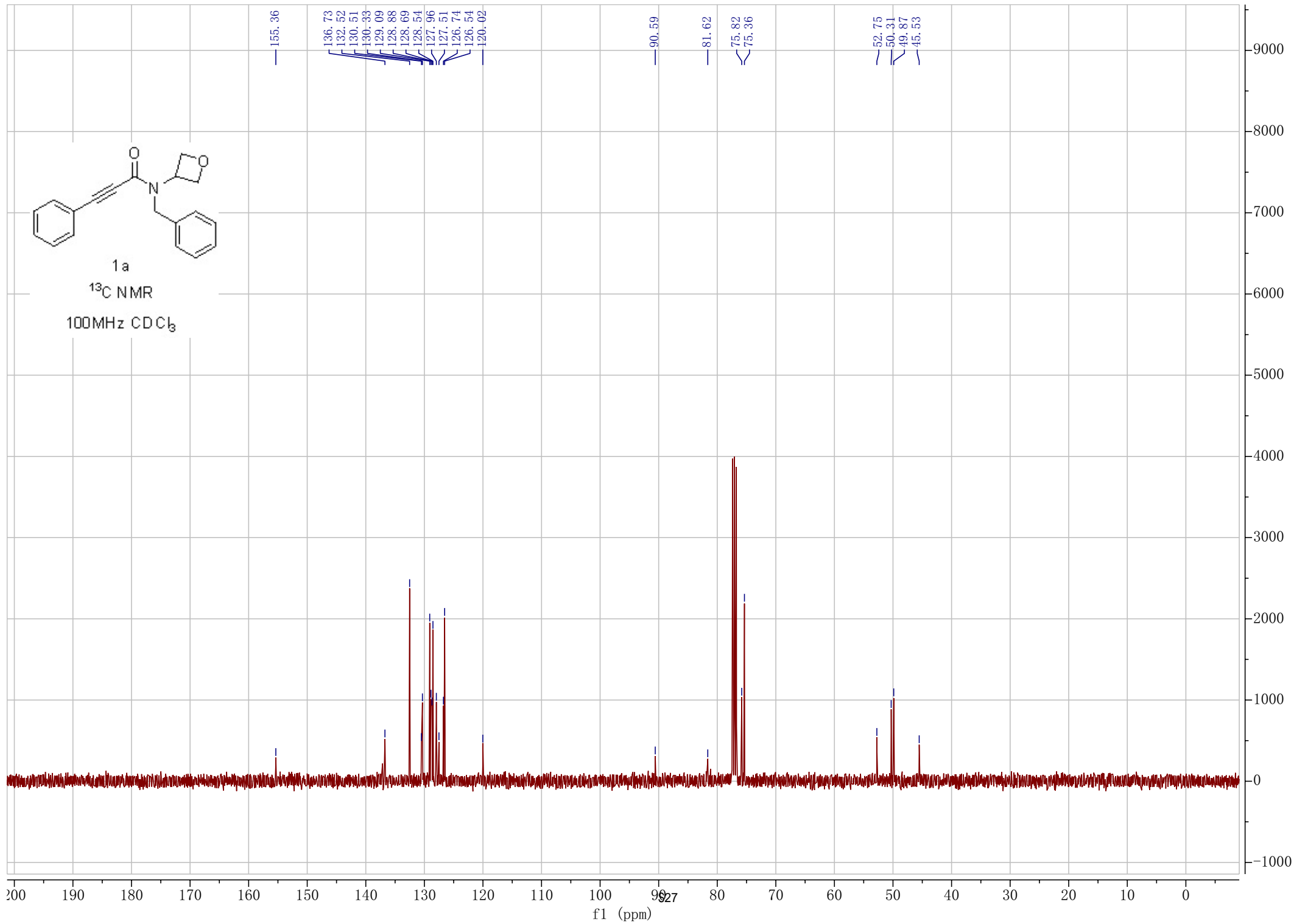


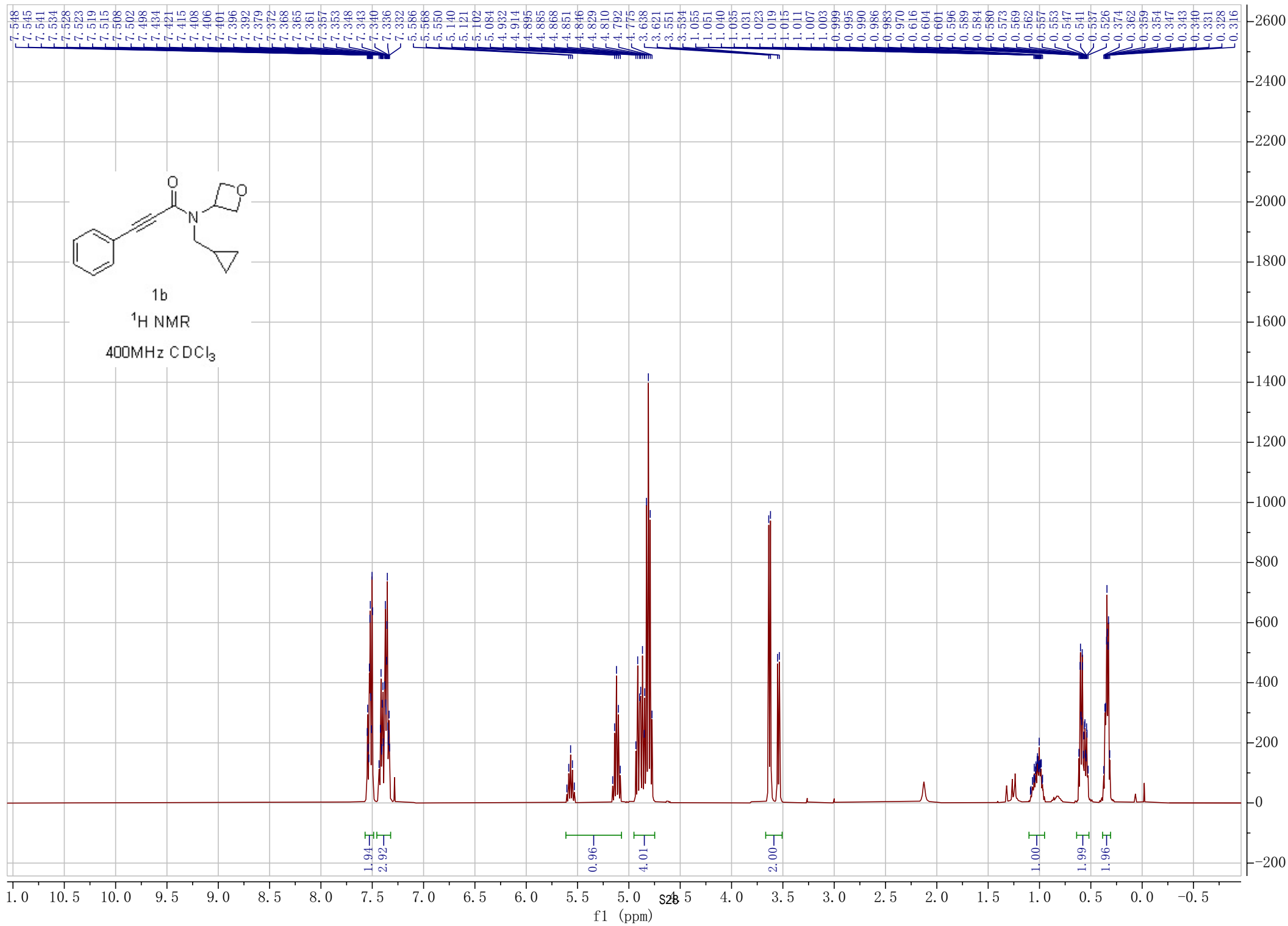


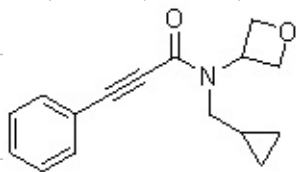
1a

$^{13}\text{C}$  NMR

100MHz  $\text{CDCl}_3$



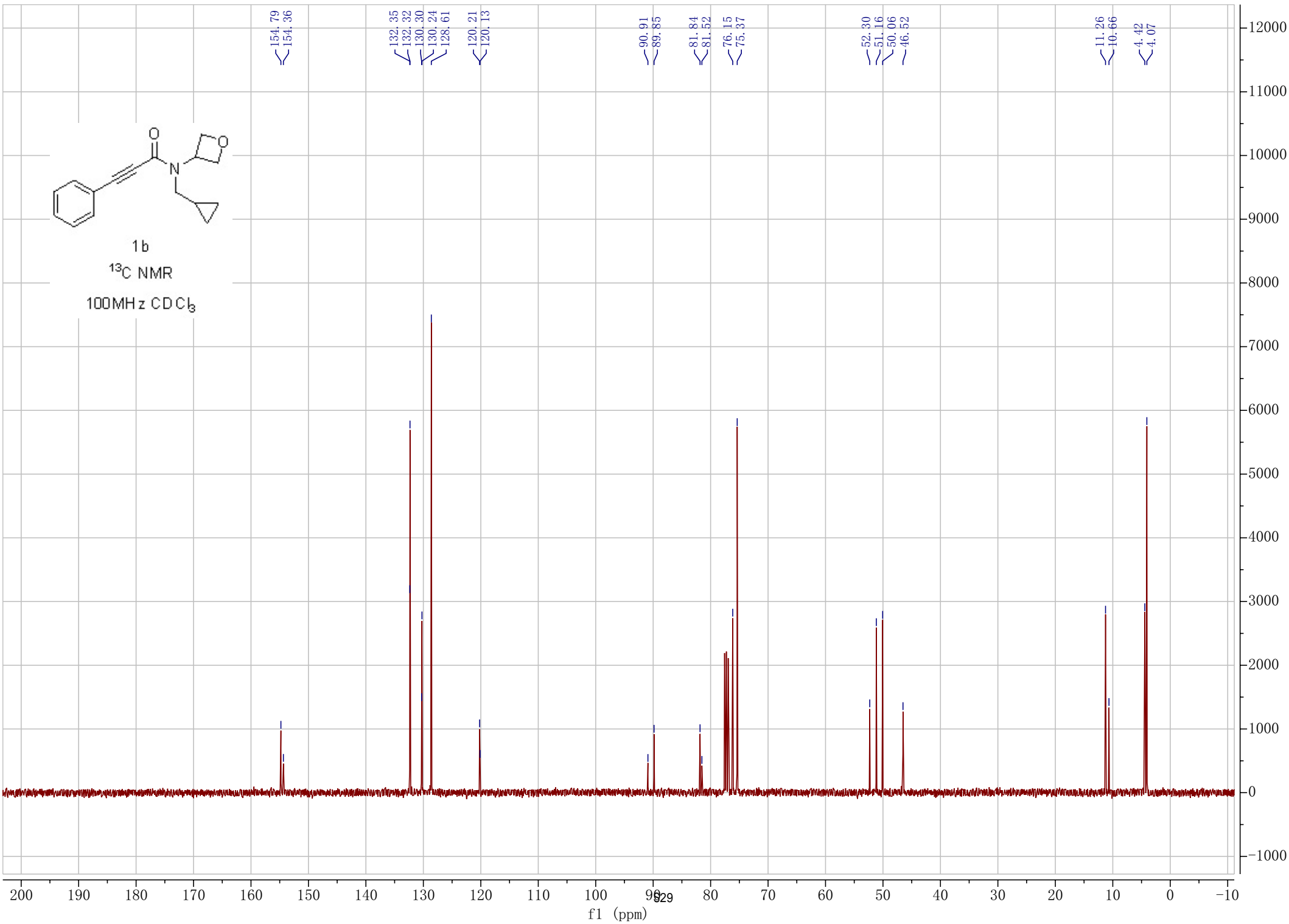


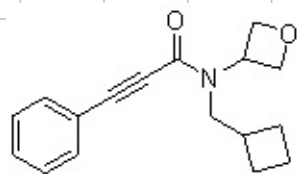


1b

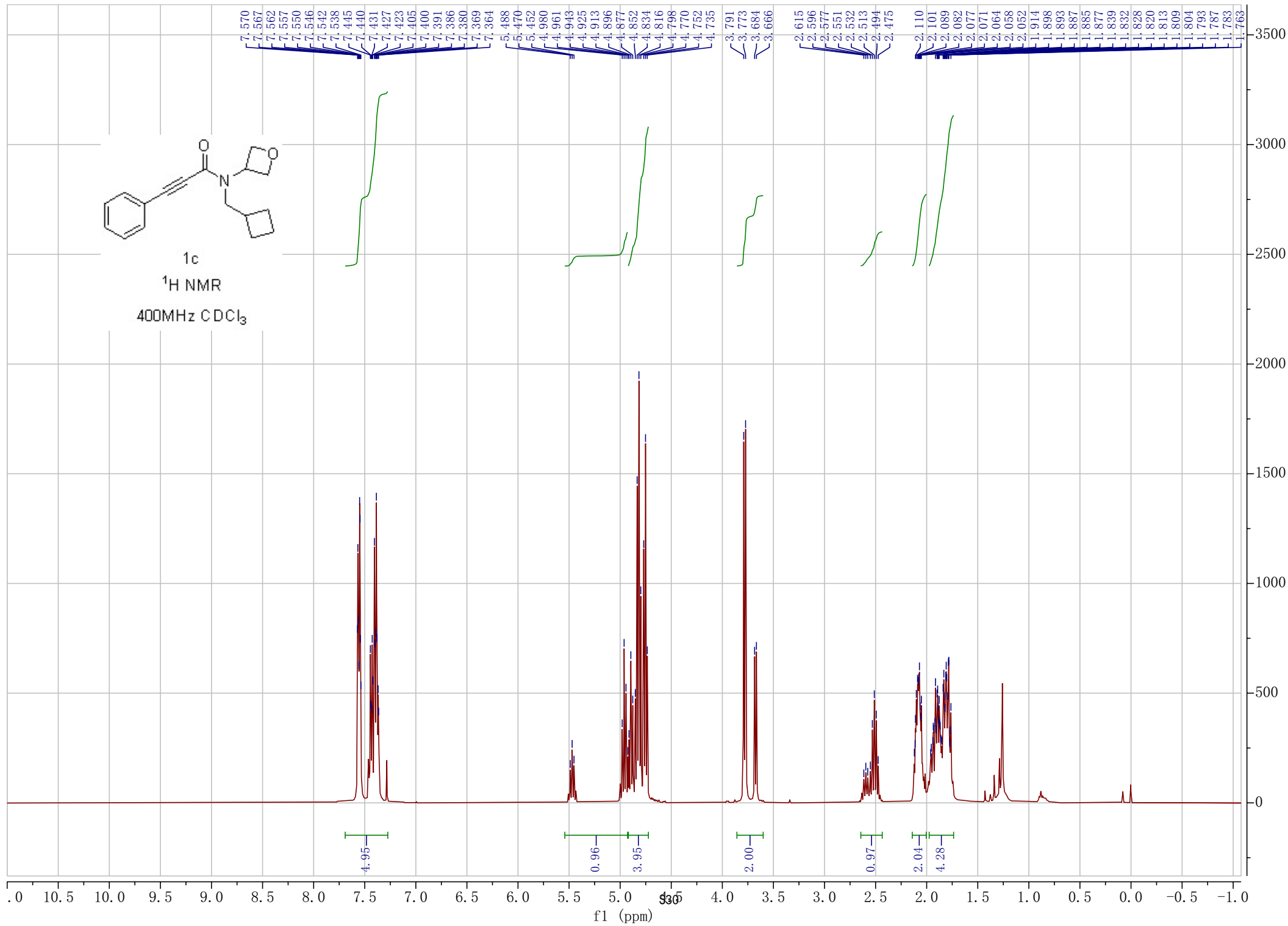
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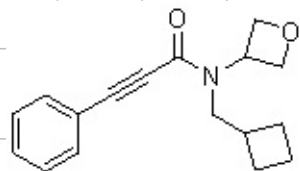
100MHz  $\text{CDCl}_3$





1c  
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>

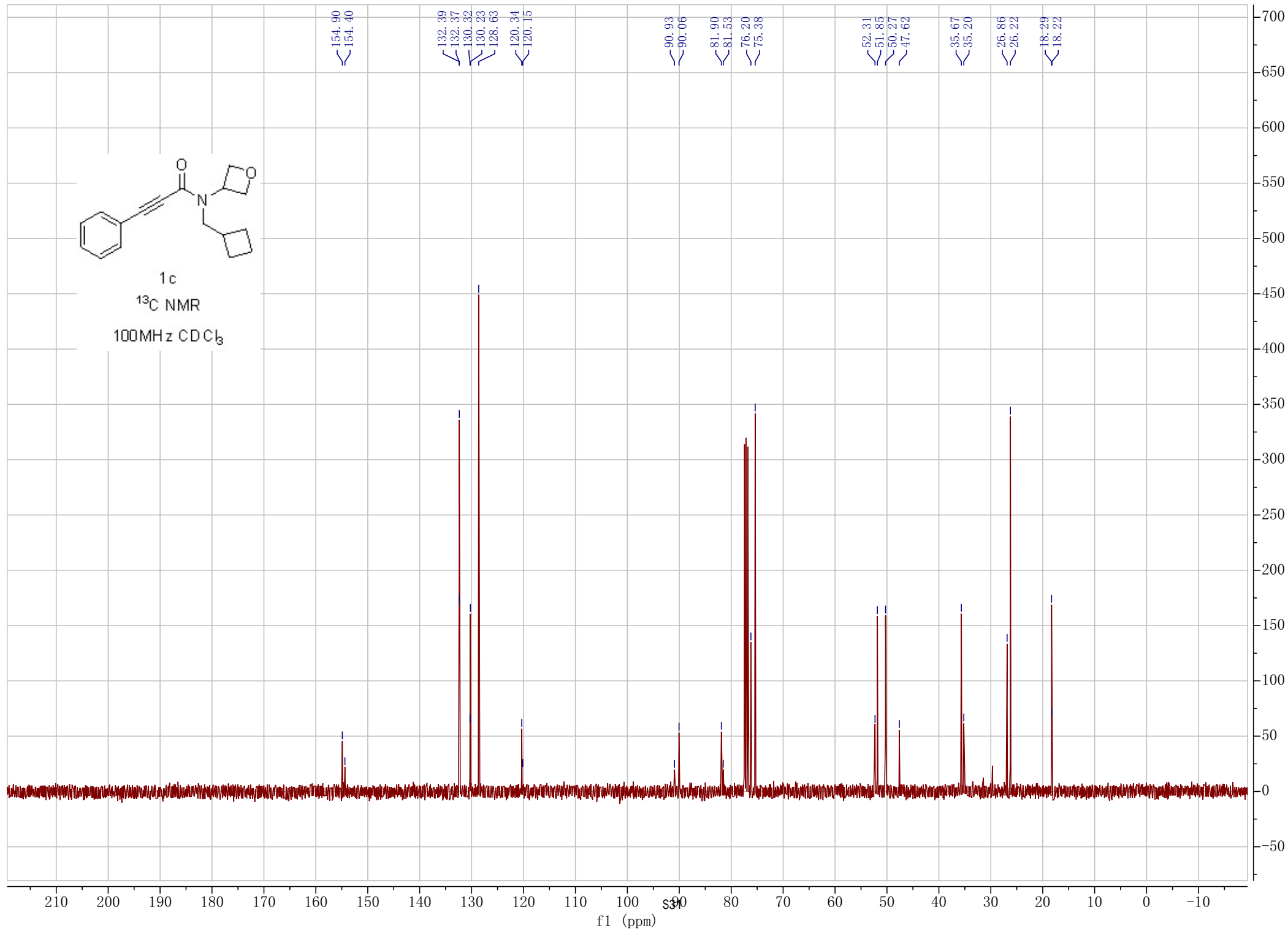


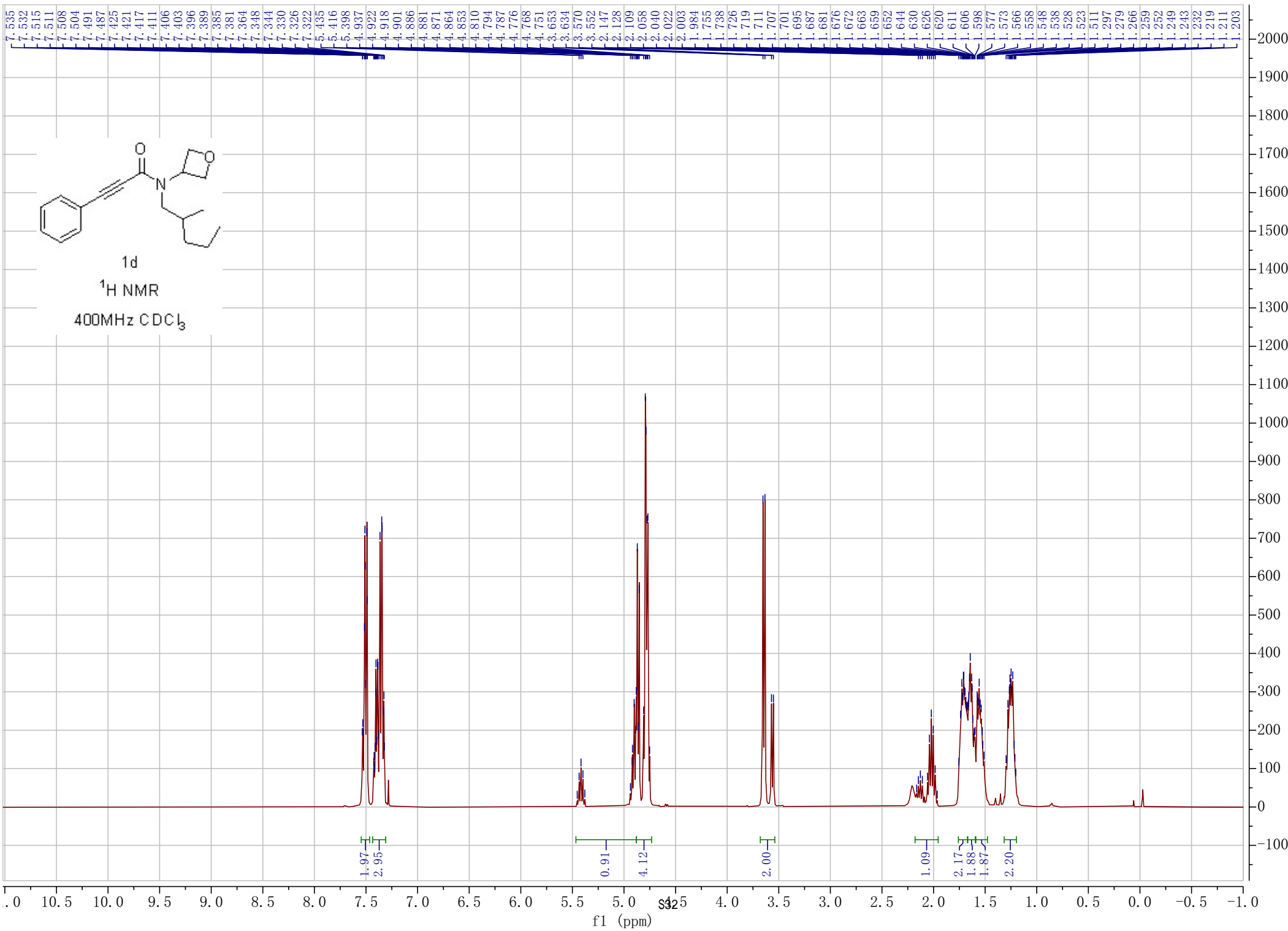


1c

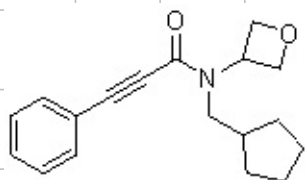
$^{13}\text{C}$  NMR

100MHz  $\text{CDCl}_3$





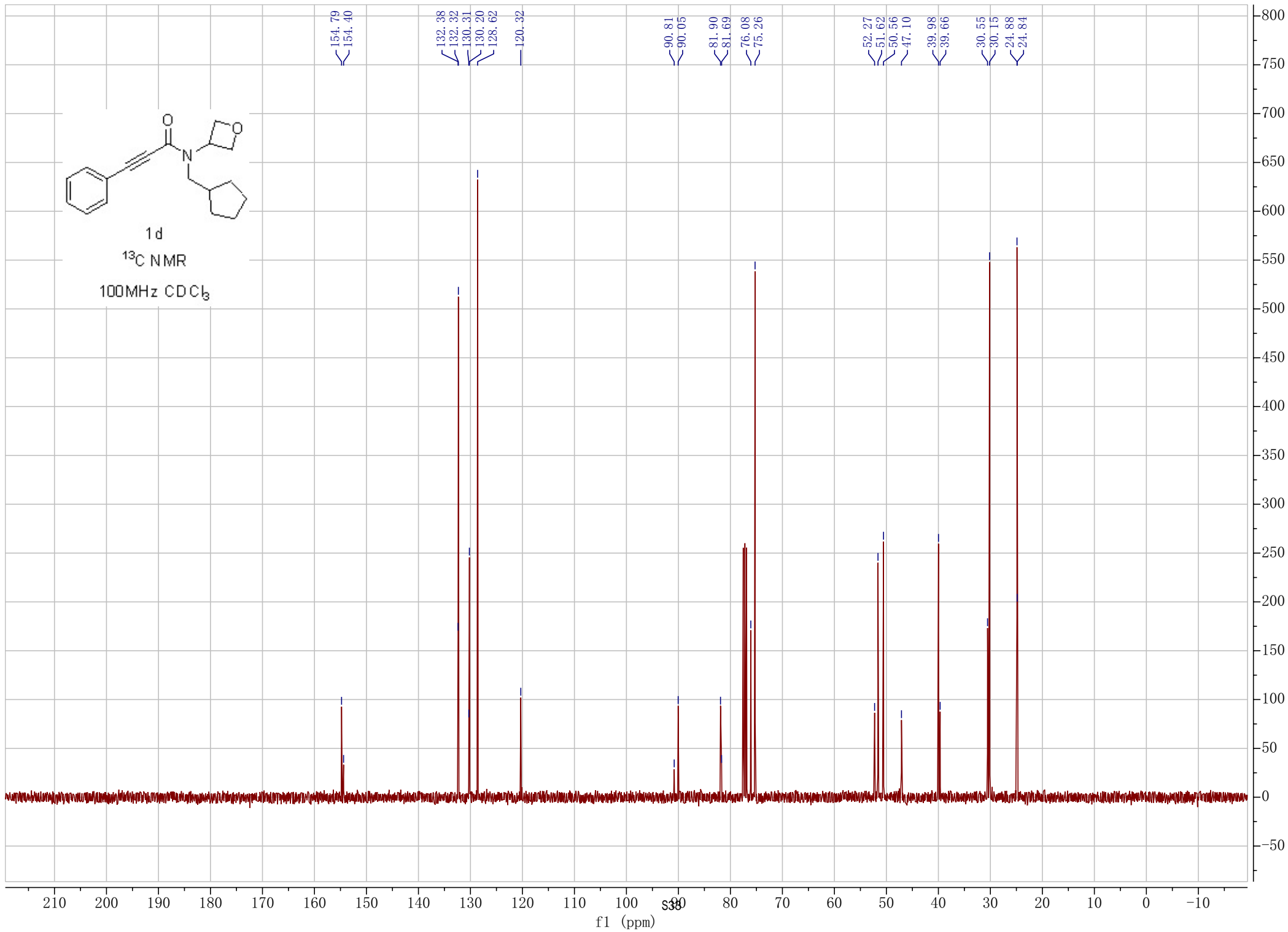




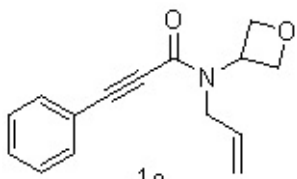
1d

$^{13}\text{C}$  NMR

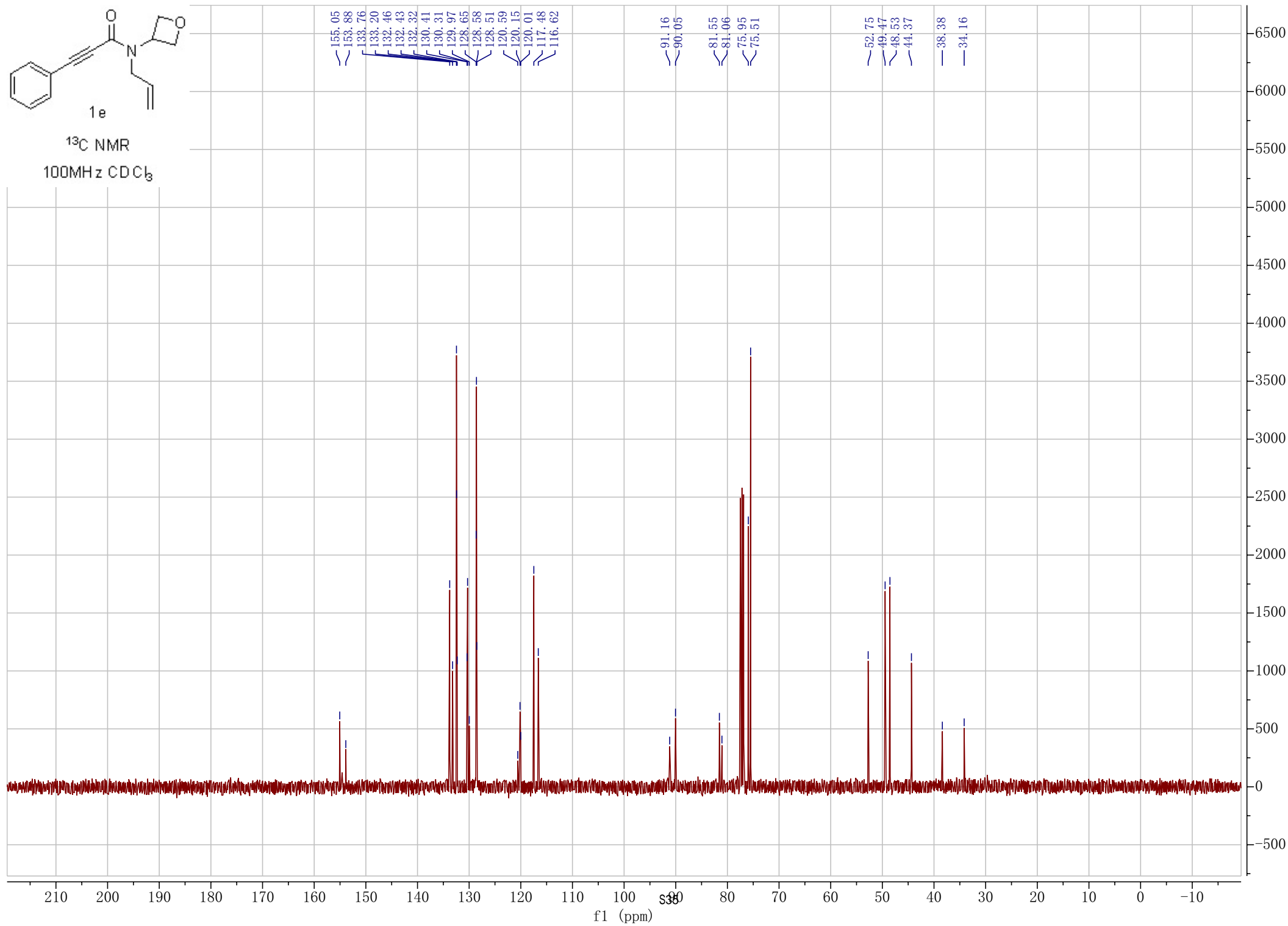
100MHz  $\text{CDCl}_3$

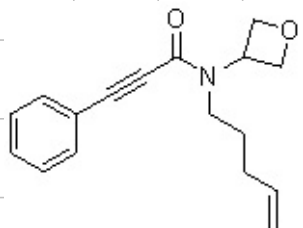






<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

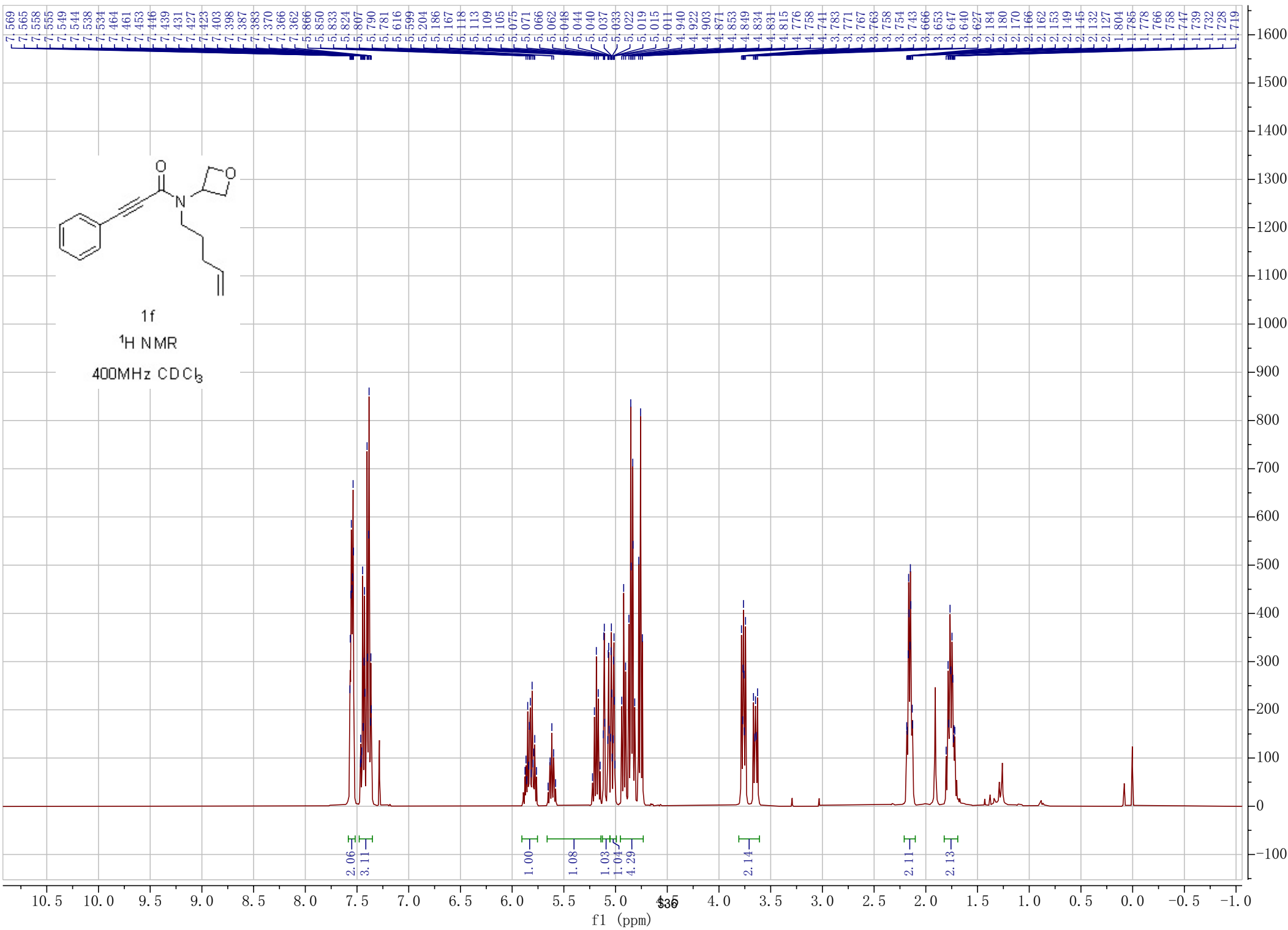


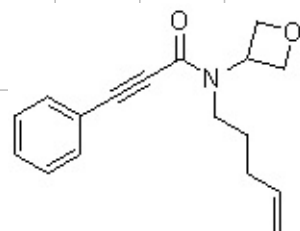


1f

<sup>1</sup>H NMR

400MHz CDCl<sub>3</sub>

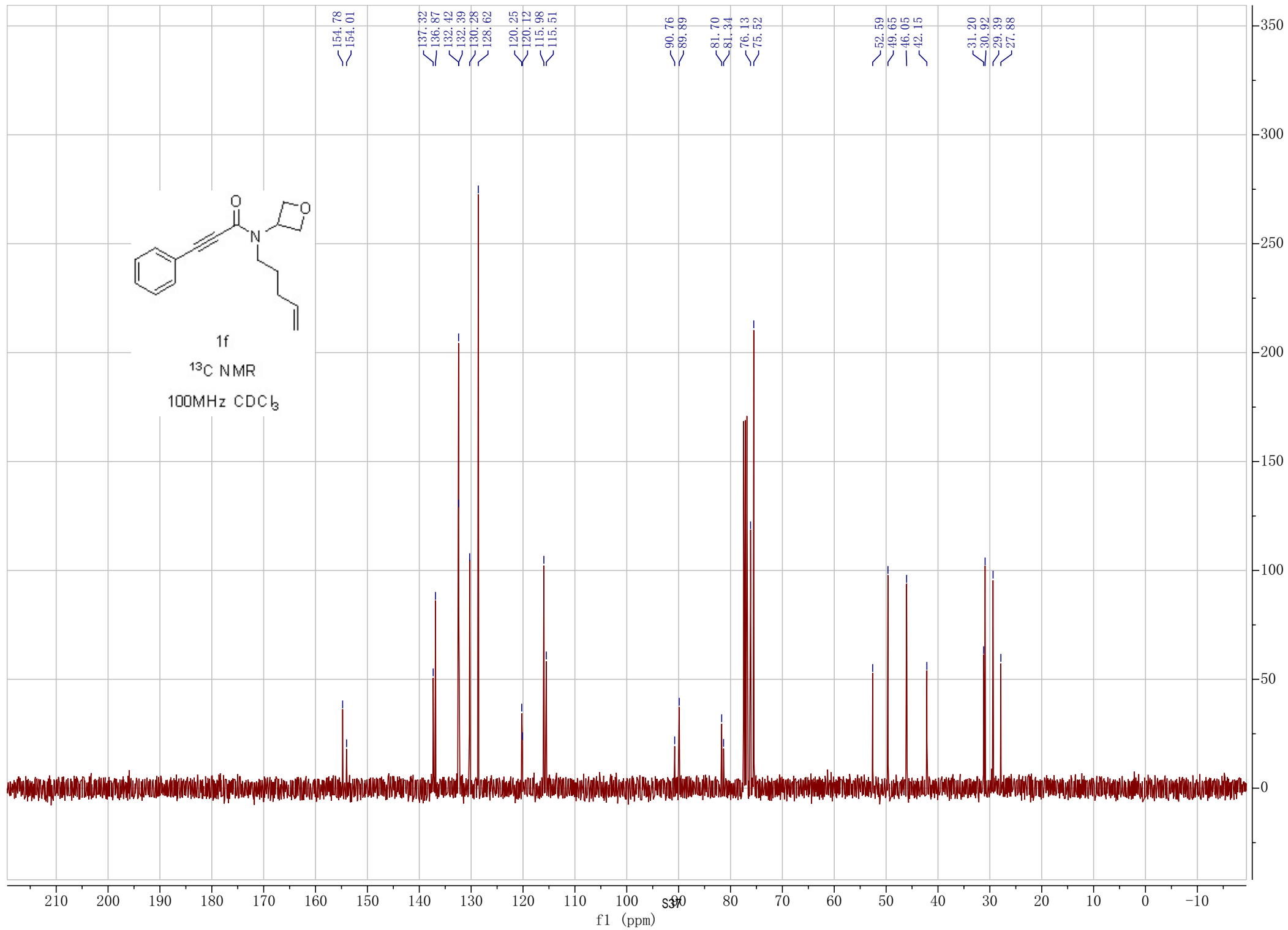


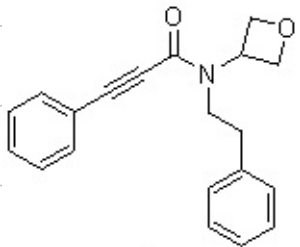


1f

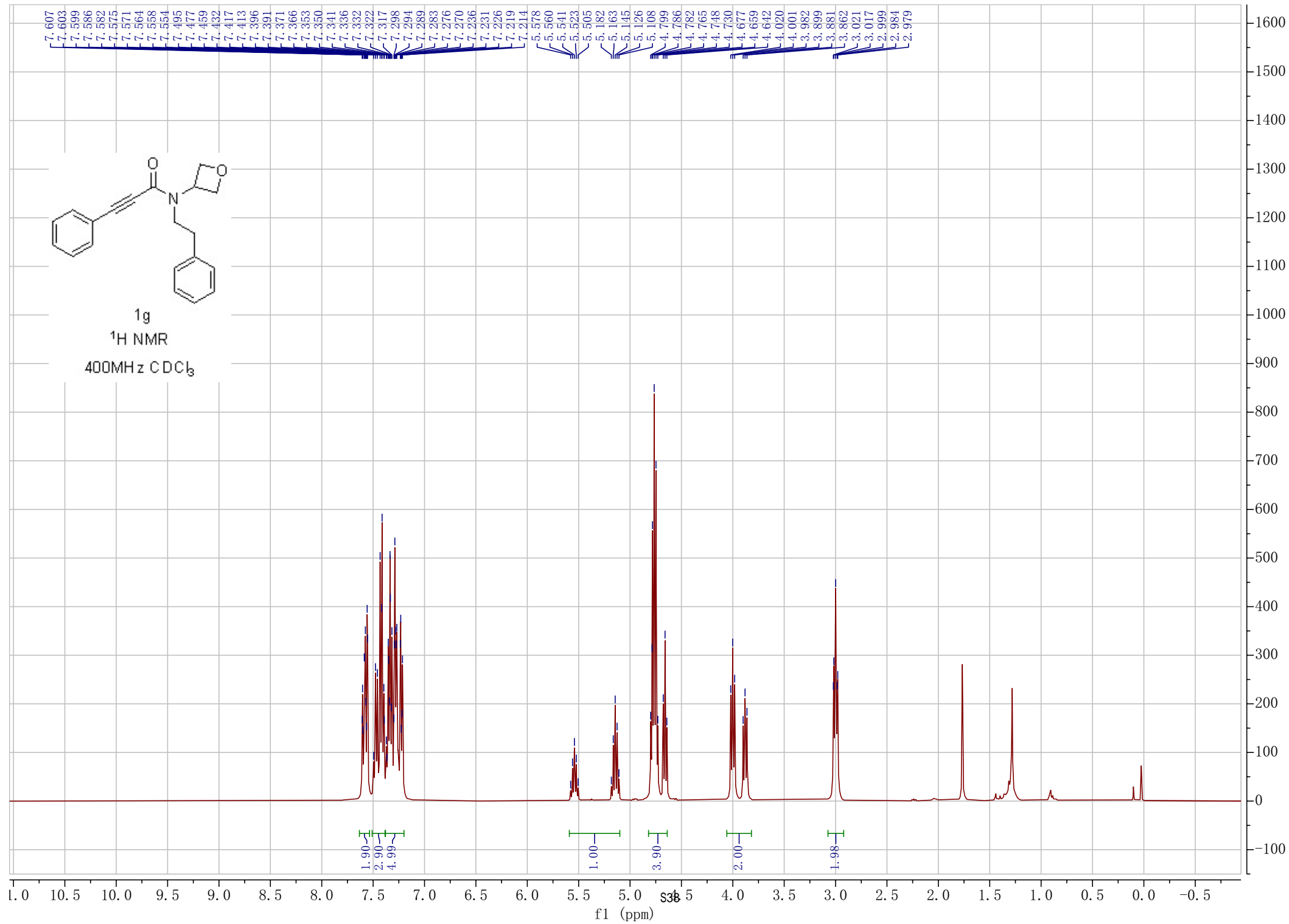
$^{13}\text{C}$  NMR

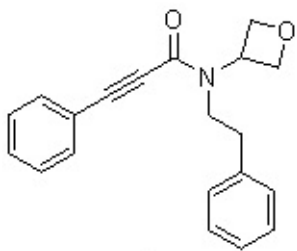
100MHz  $\text{CDCl}_3$





1g  
1H NMR  
400MHz CDCl<sub>3</sub>

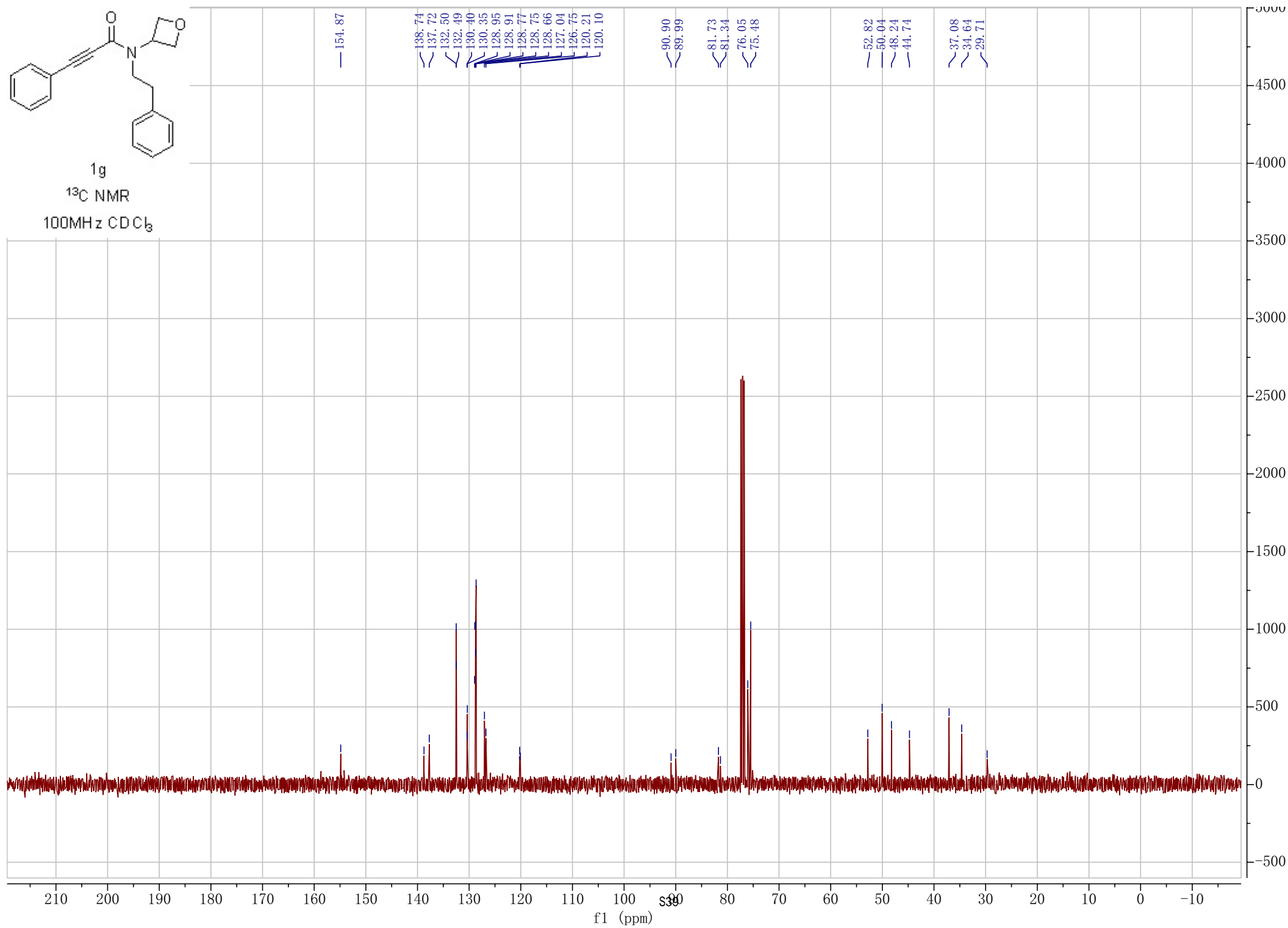


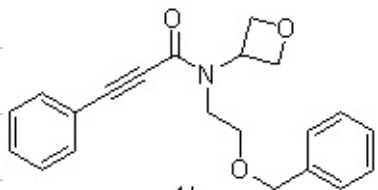


1g

$^{13}\text{C}$  NMR

100MHz  $\text{CDCl}_3$

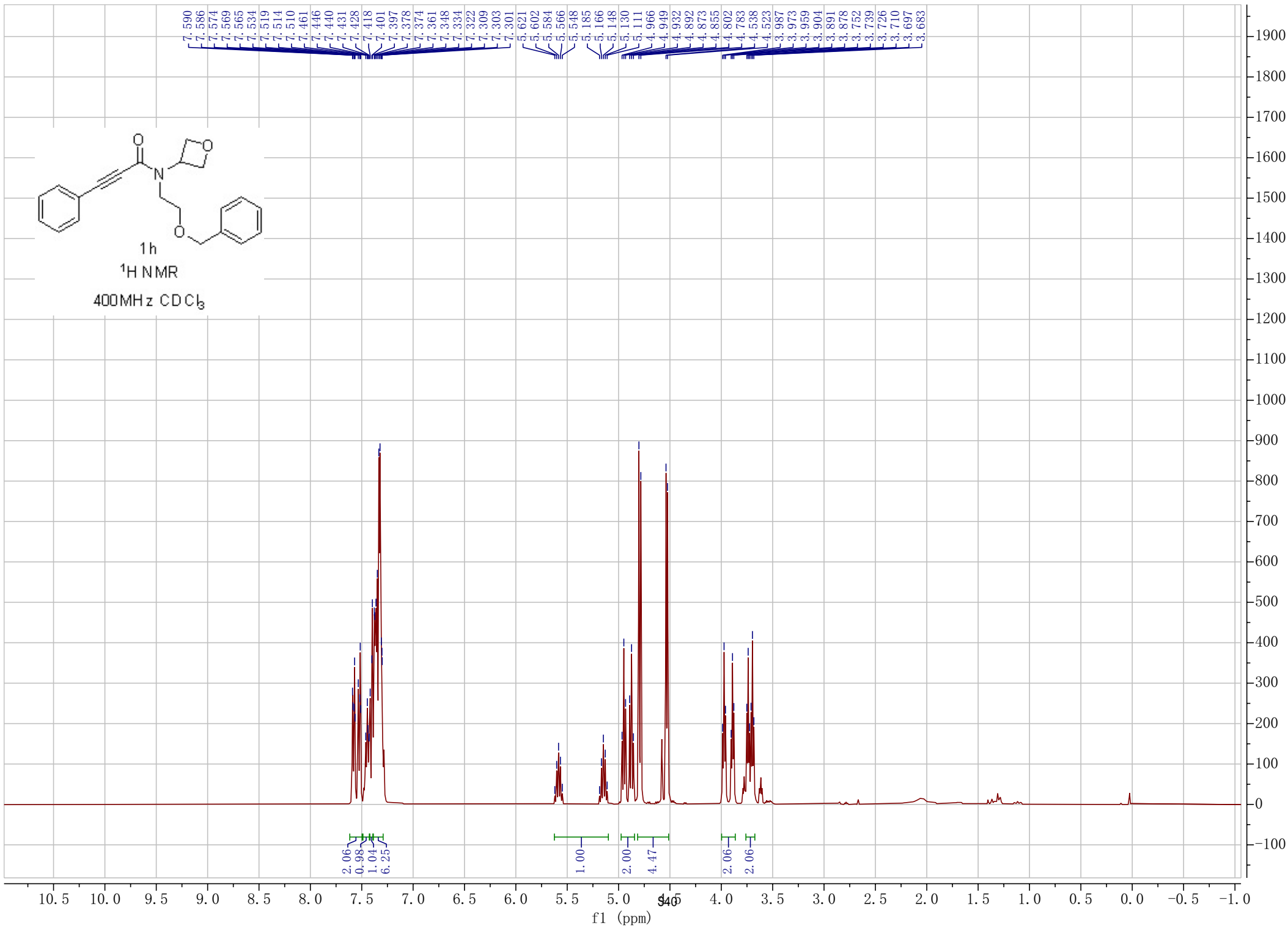




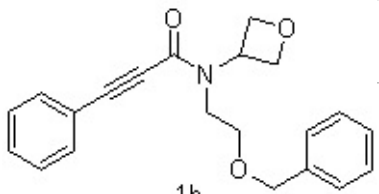
1h

$^1\text{H NMR}$

400MHz  $\text{CDCl}_3$



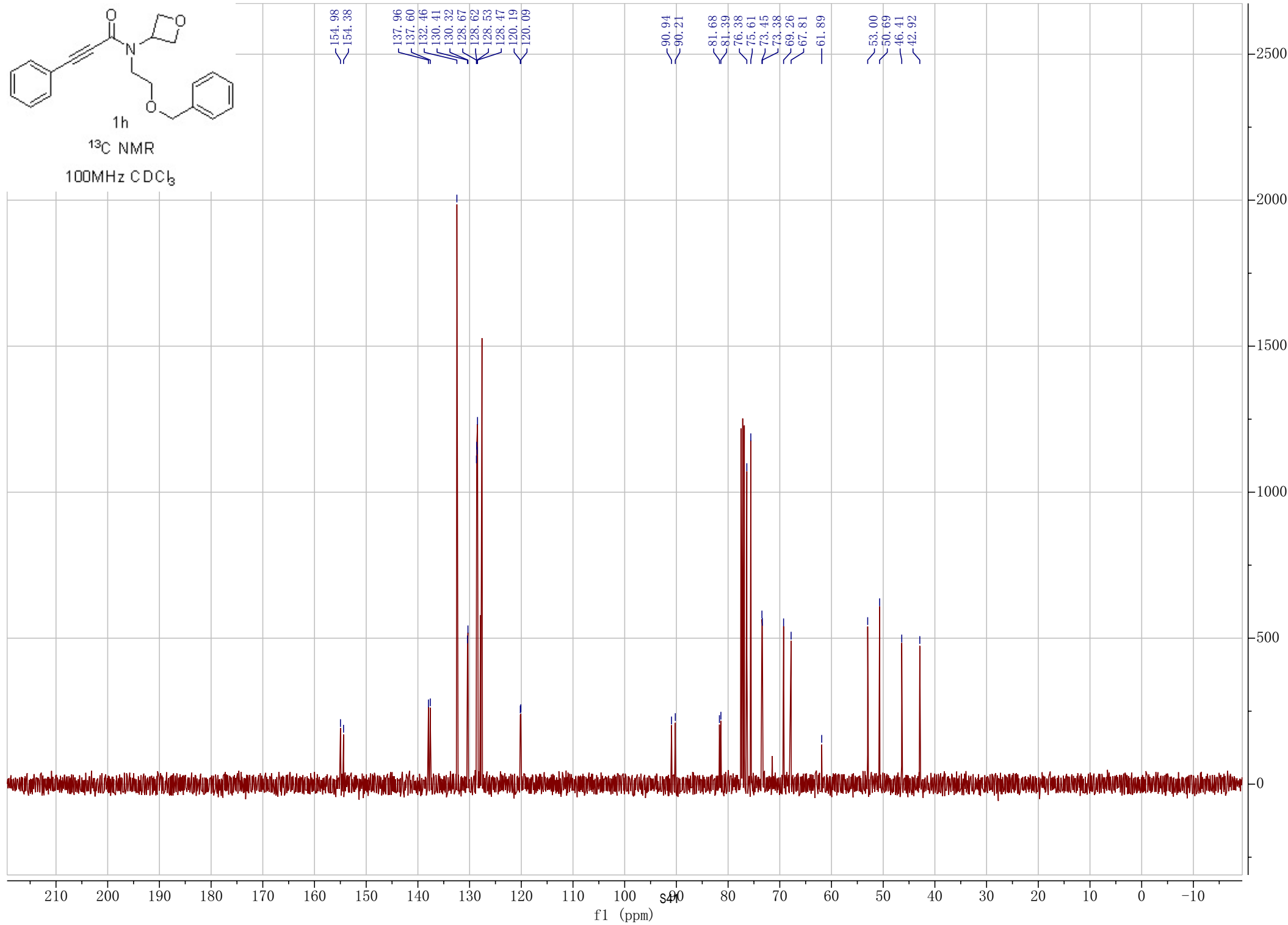


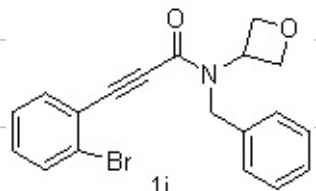


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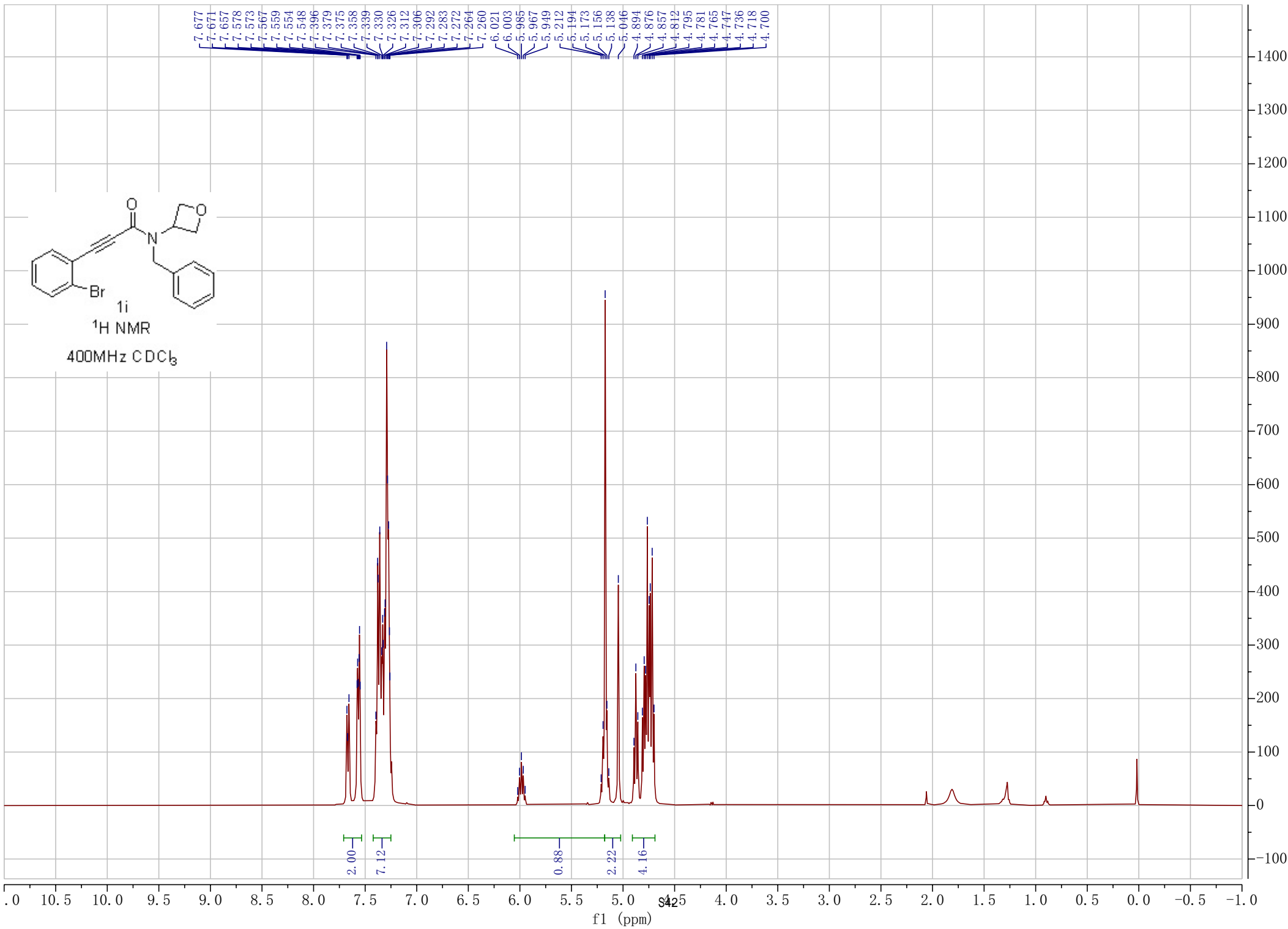
$^{13}\text{C}$  NMR

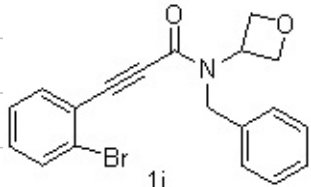
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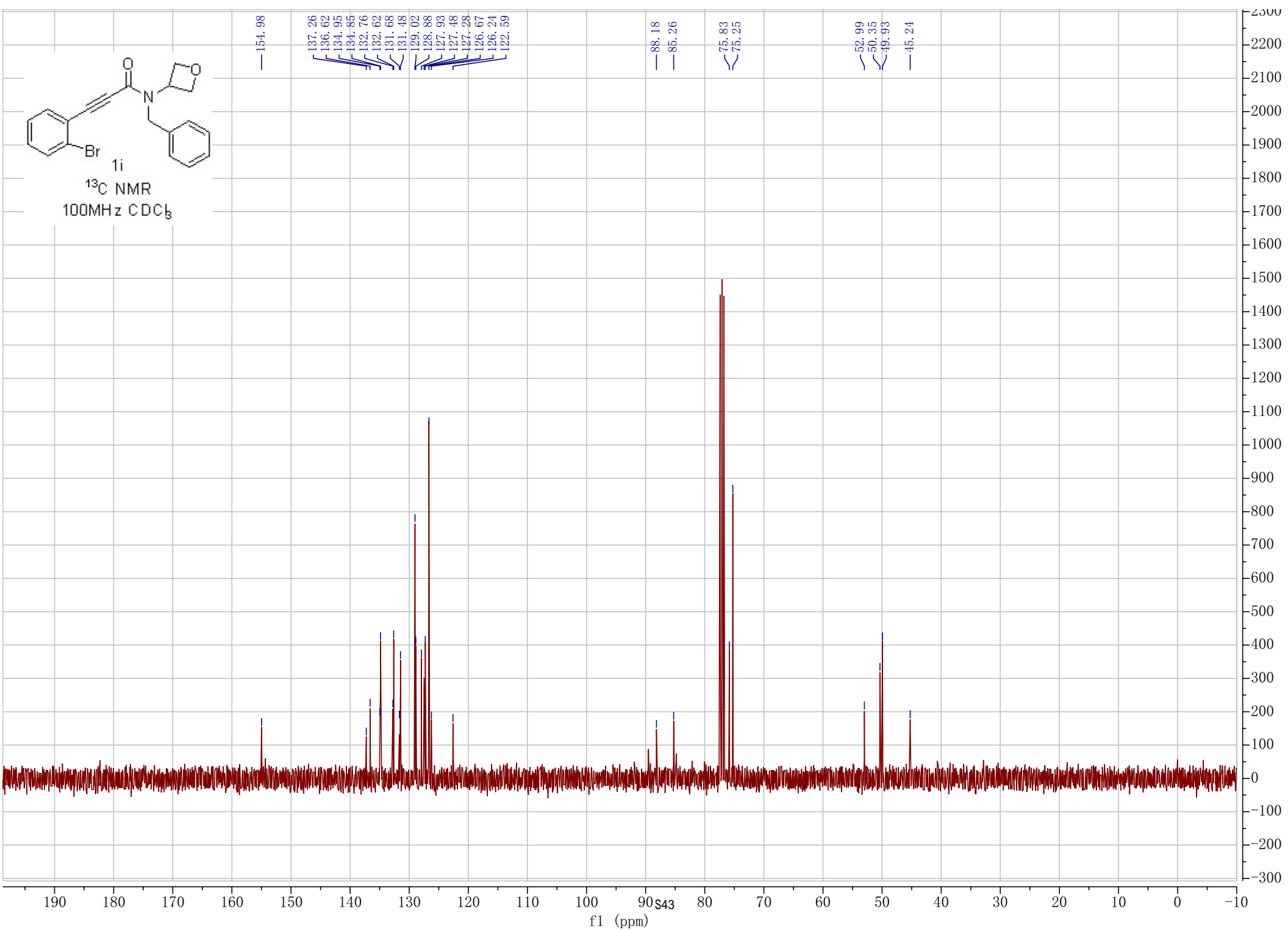
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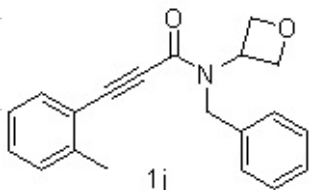




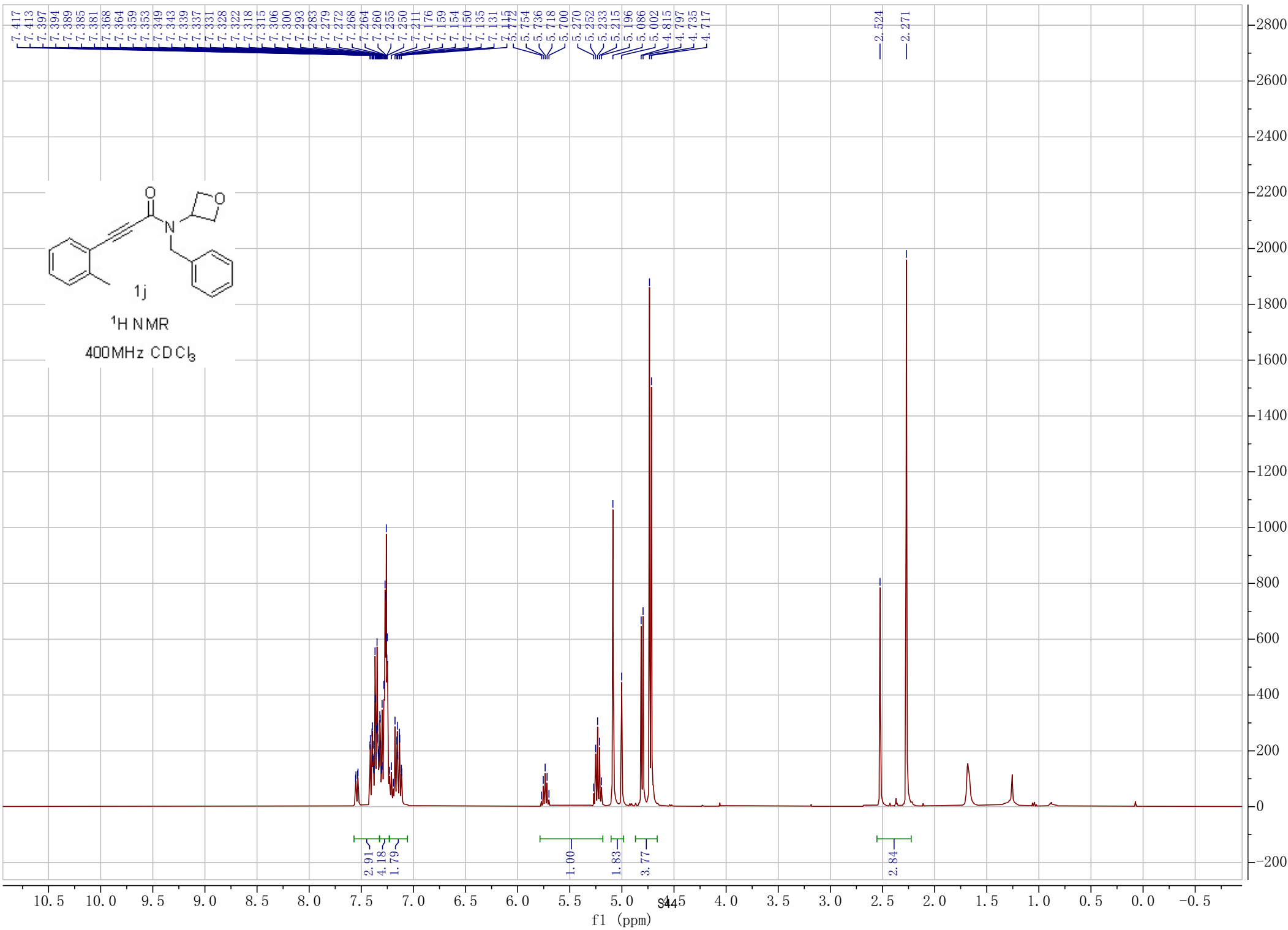
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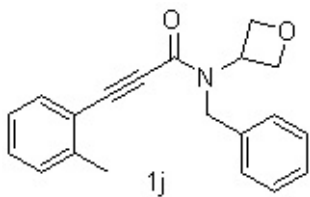
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45.24



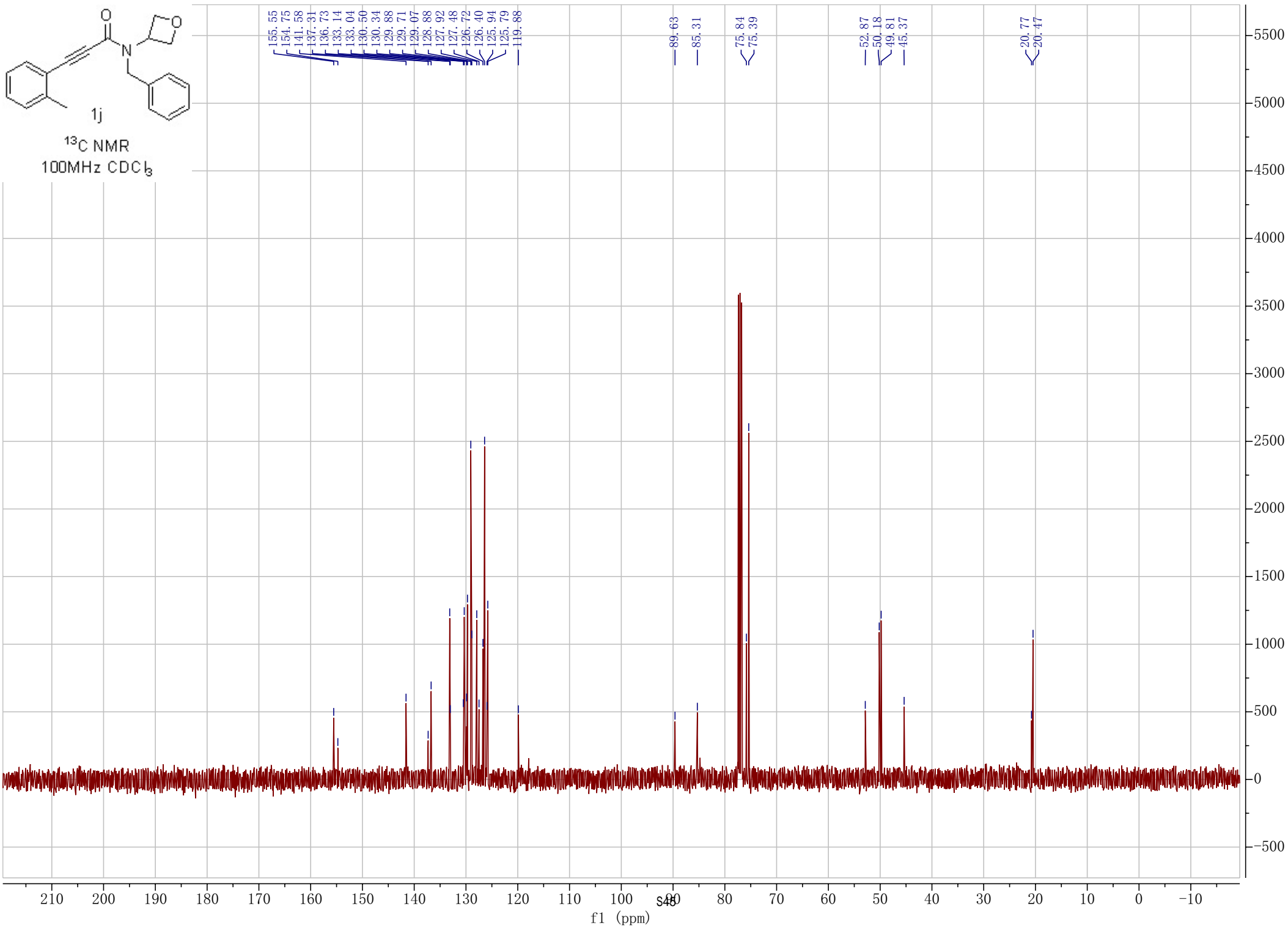


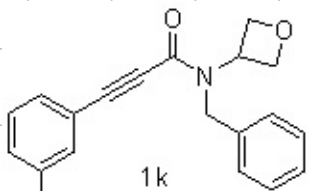
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400MHz CDCl<sub>3</sub>



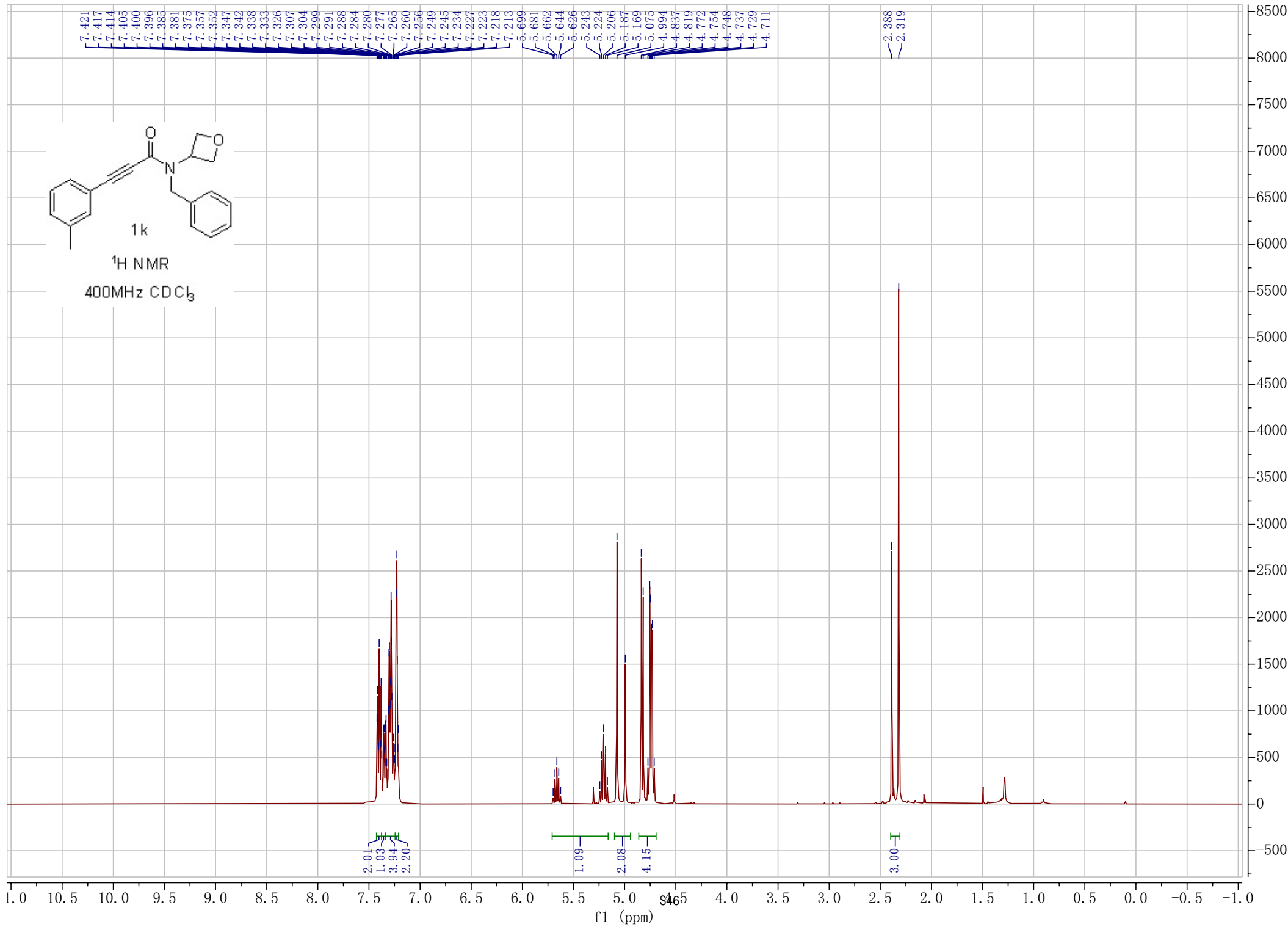


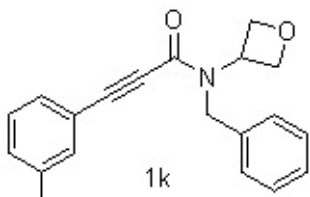
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100MHz CDCl<sub>3</sub>



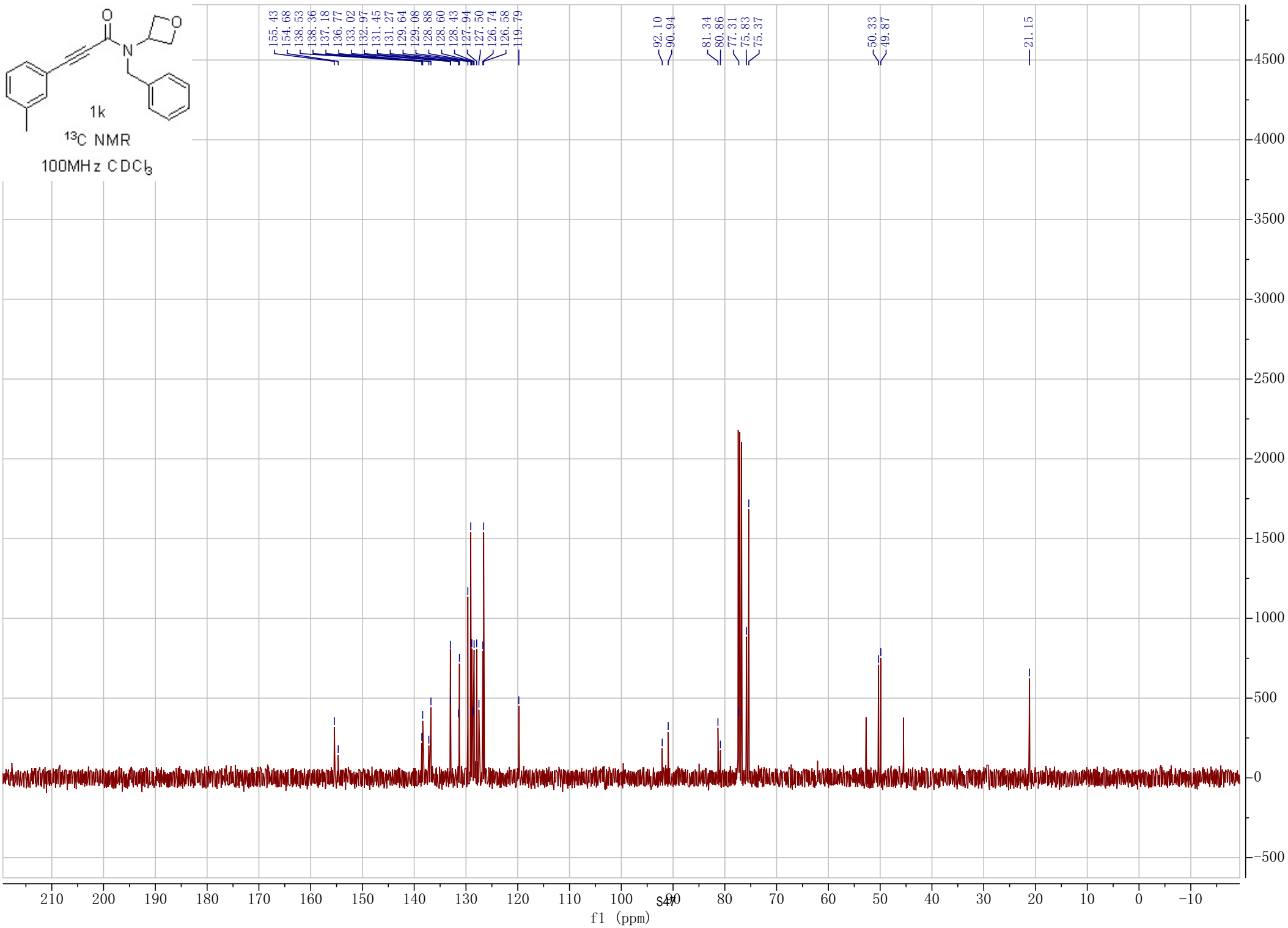


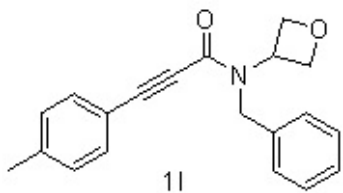
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>





<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

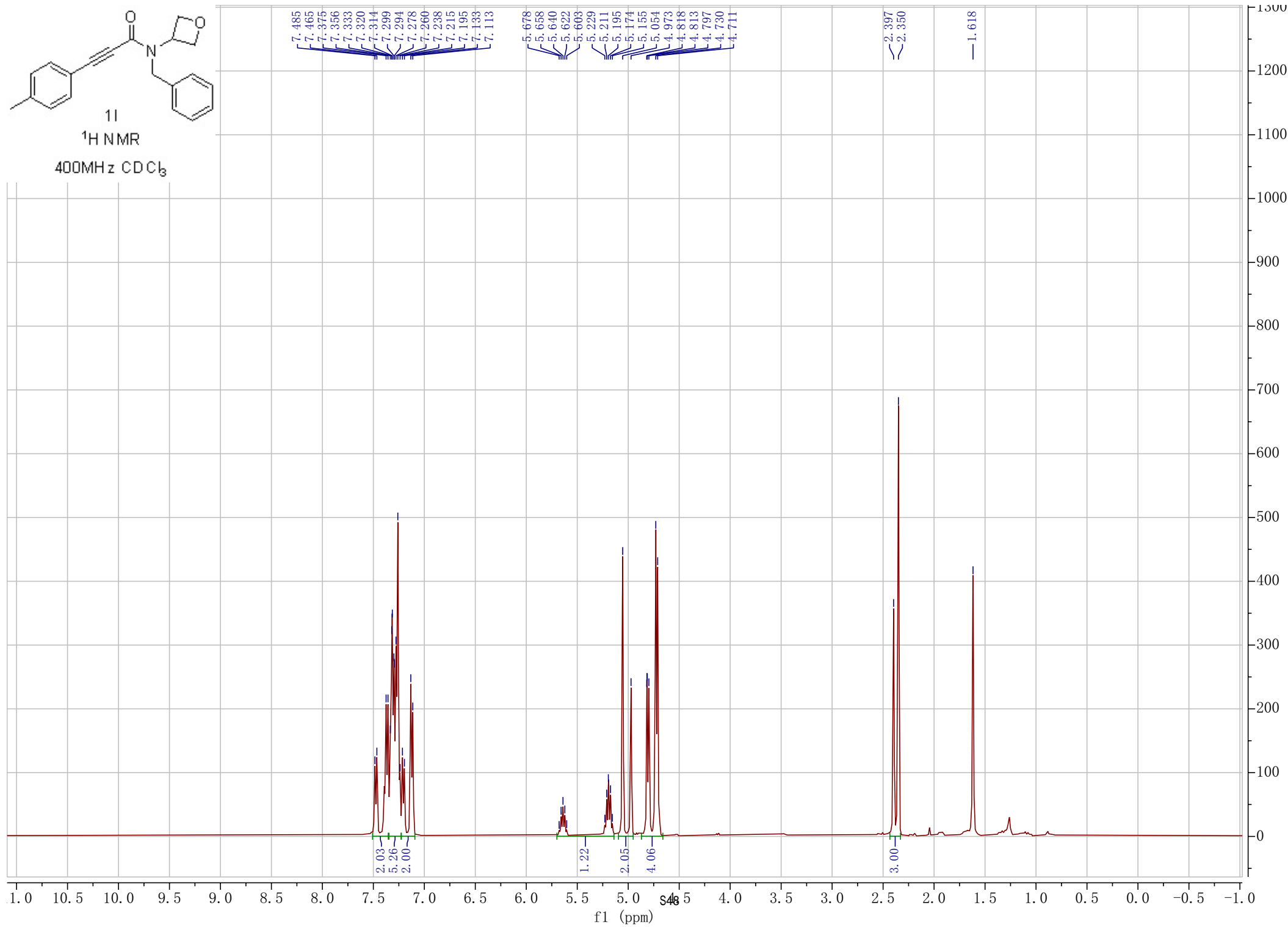




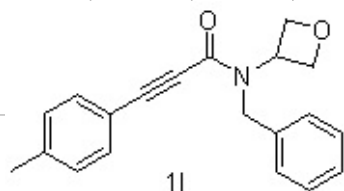
11

<sup>1</sup>H NMR

400MHz CDCl<sub>3</sub>

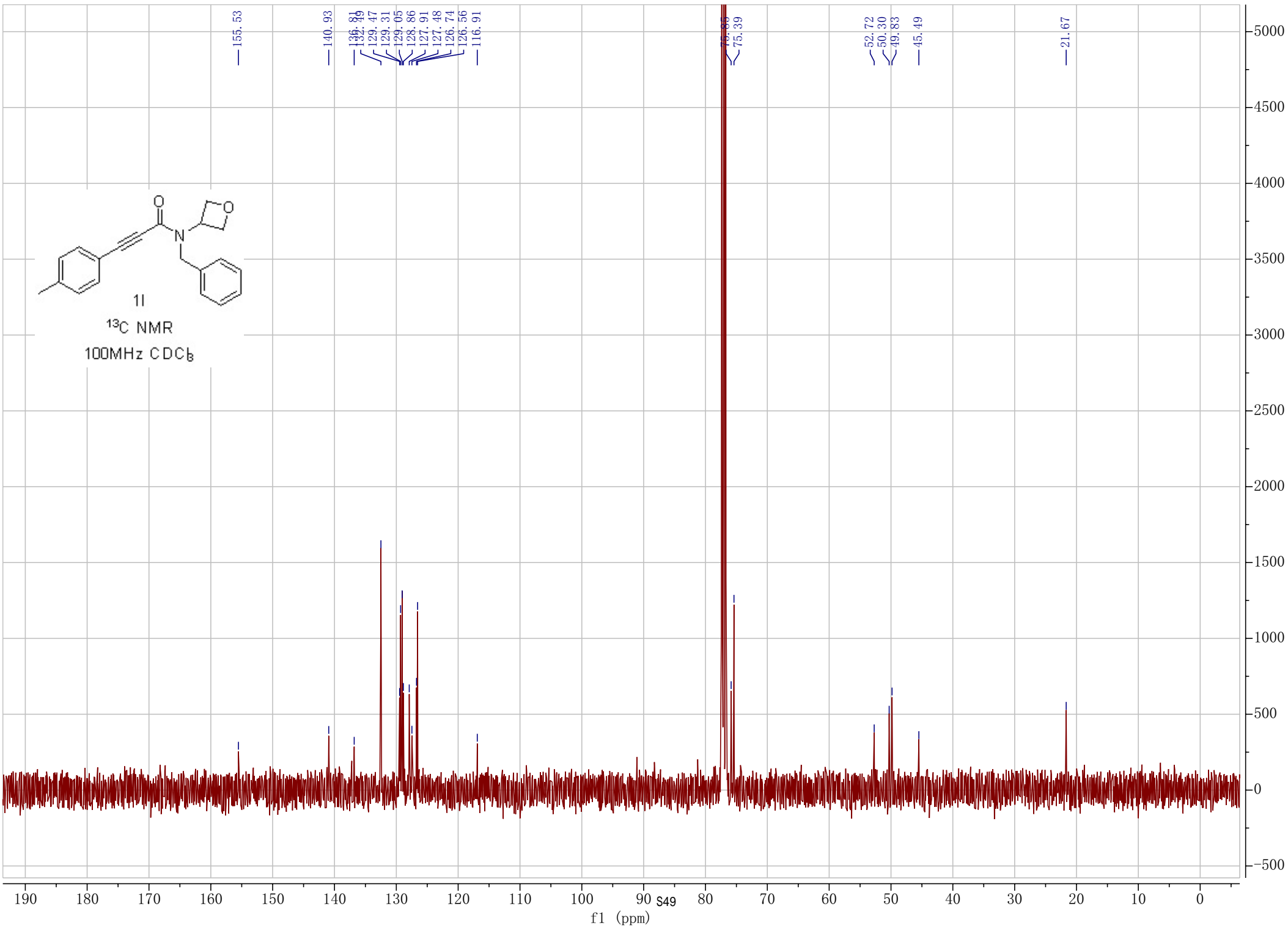


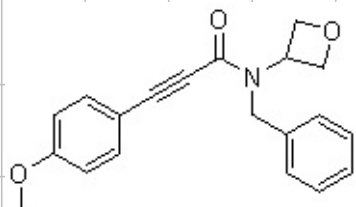




11

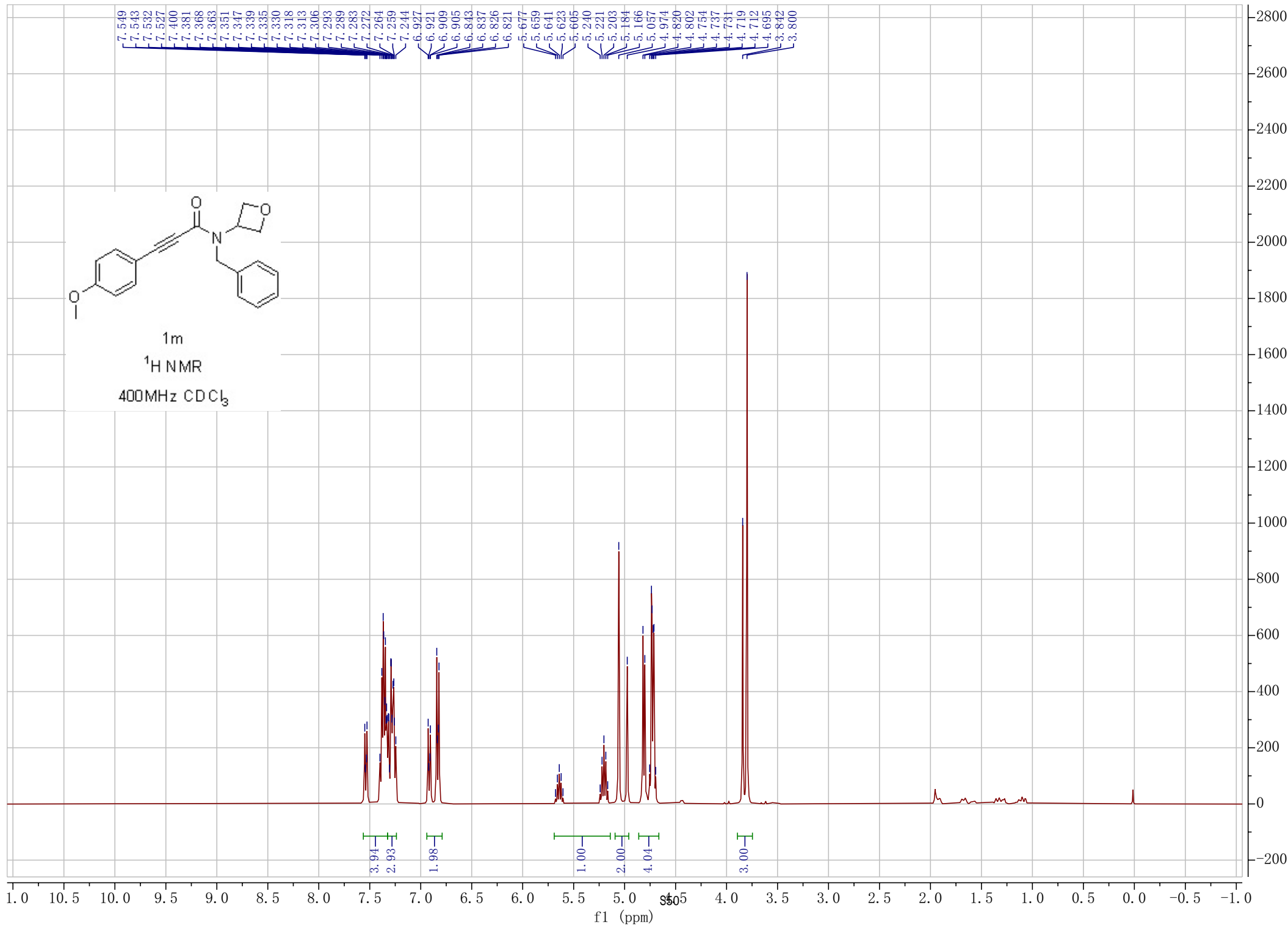
$^{13}\text{C}$  NMR  
100MHz  $\text{CDCl}_3$

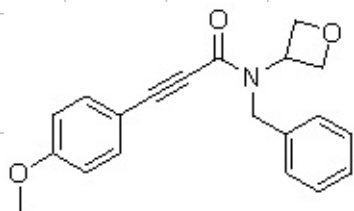




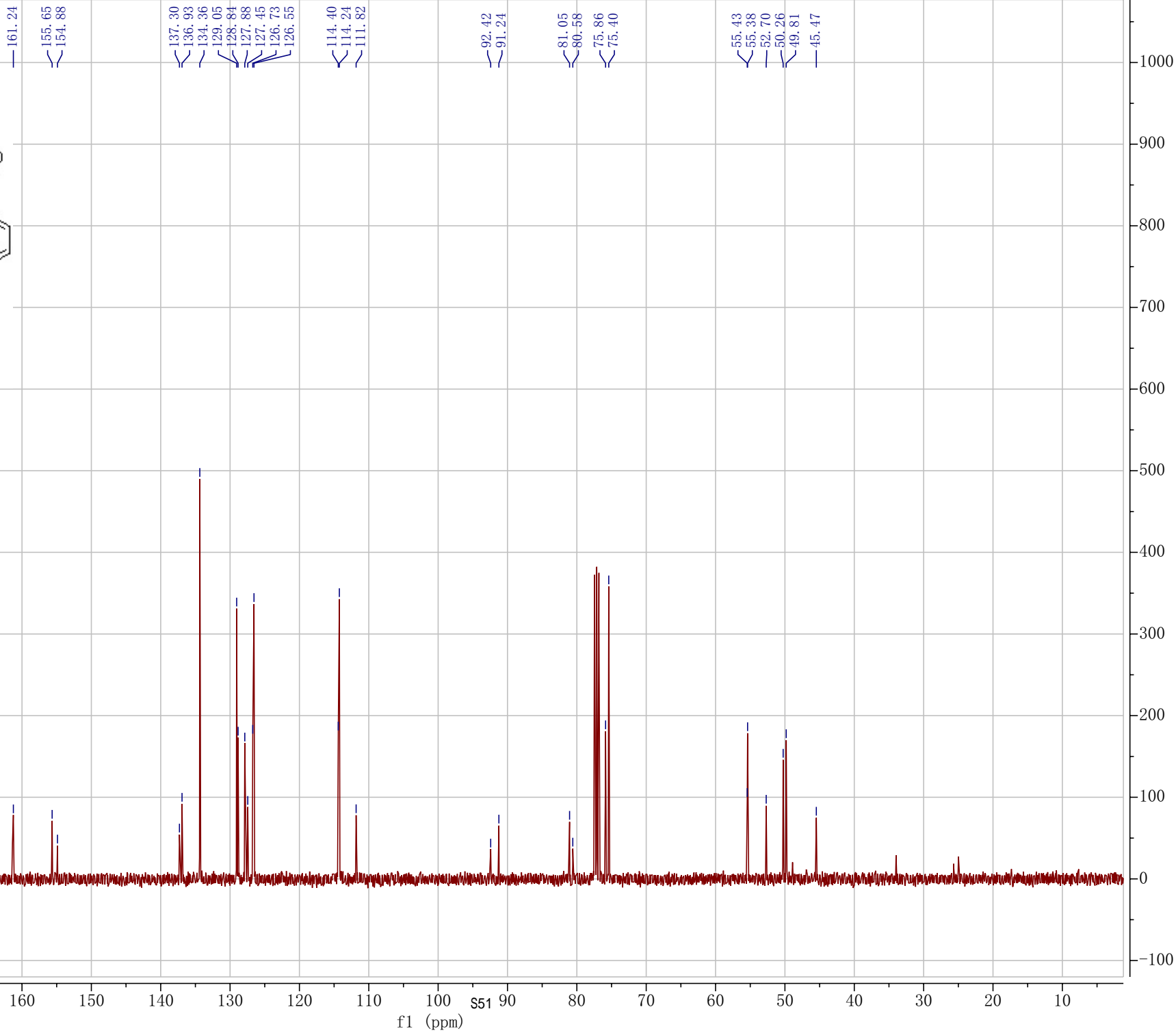
1m  
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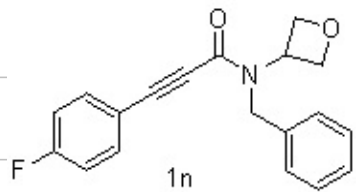
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7.339  
7.335  
7.330  
7.318  
7.313  
7.306  
7.293  
7.289  
7.283  
7.272  
7.264  
7.259  
7.244  
7.241  
6.921  
6.909  
6.905  
6.843  
6.837  
6.826  
6.821  
5.677  
5.659  
5.641  
5.623  
5.605  
5.240  
5.221  
5.203  
5.184  
5.166  
5.057  
4.974  
4.820  
4.802  
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4.731  
4.719  
4.712  
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3.842  
3.800



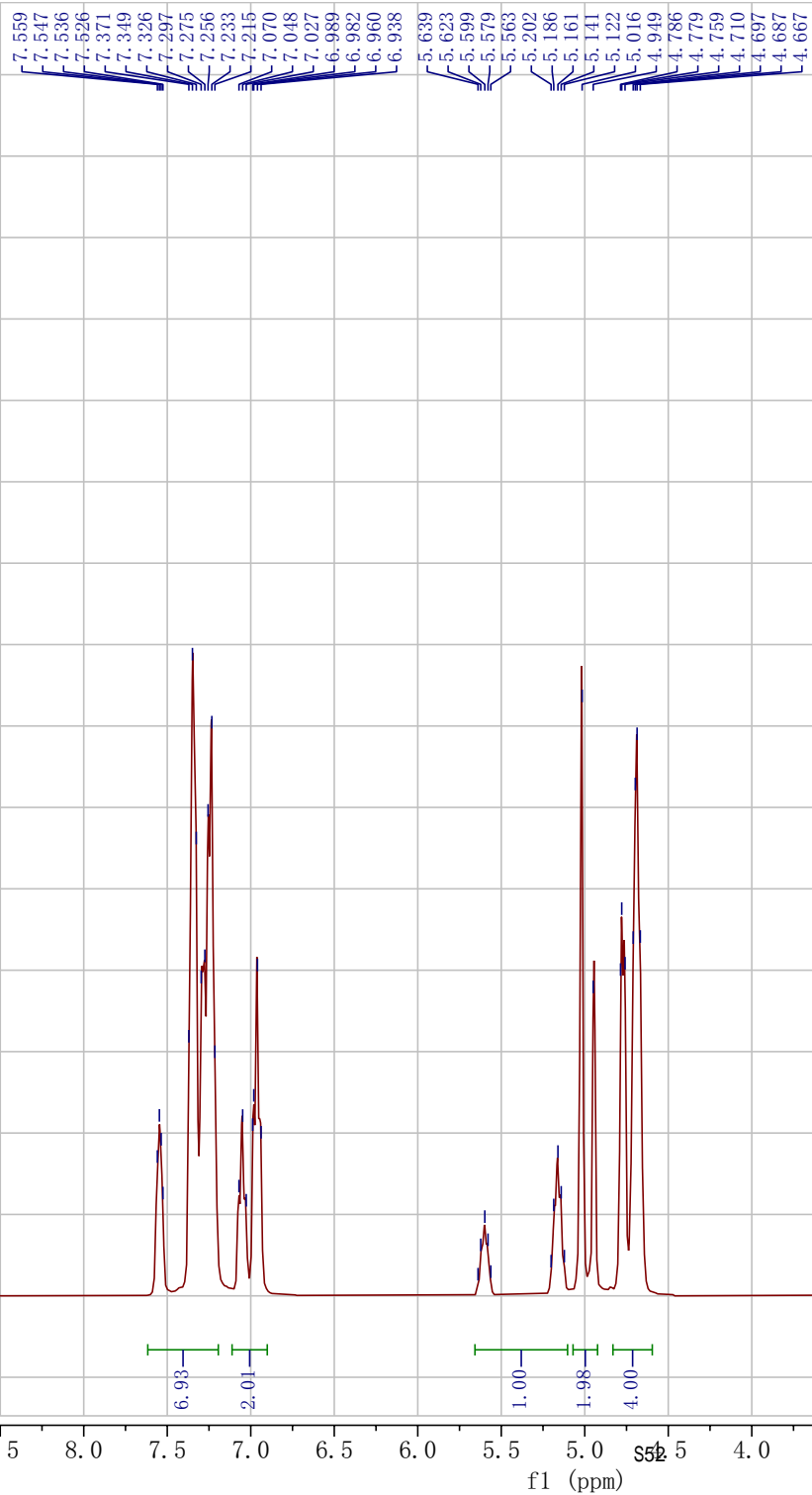


1m  
 $^{13}\text{C}$  NMR  
100MHz  $\text{CDCl}_3$



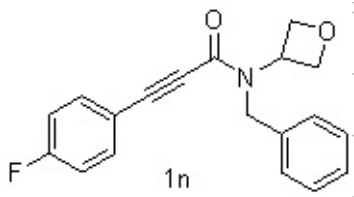


<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>

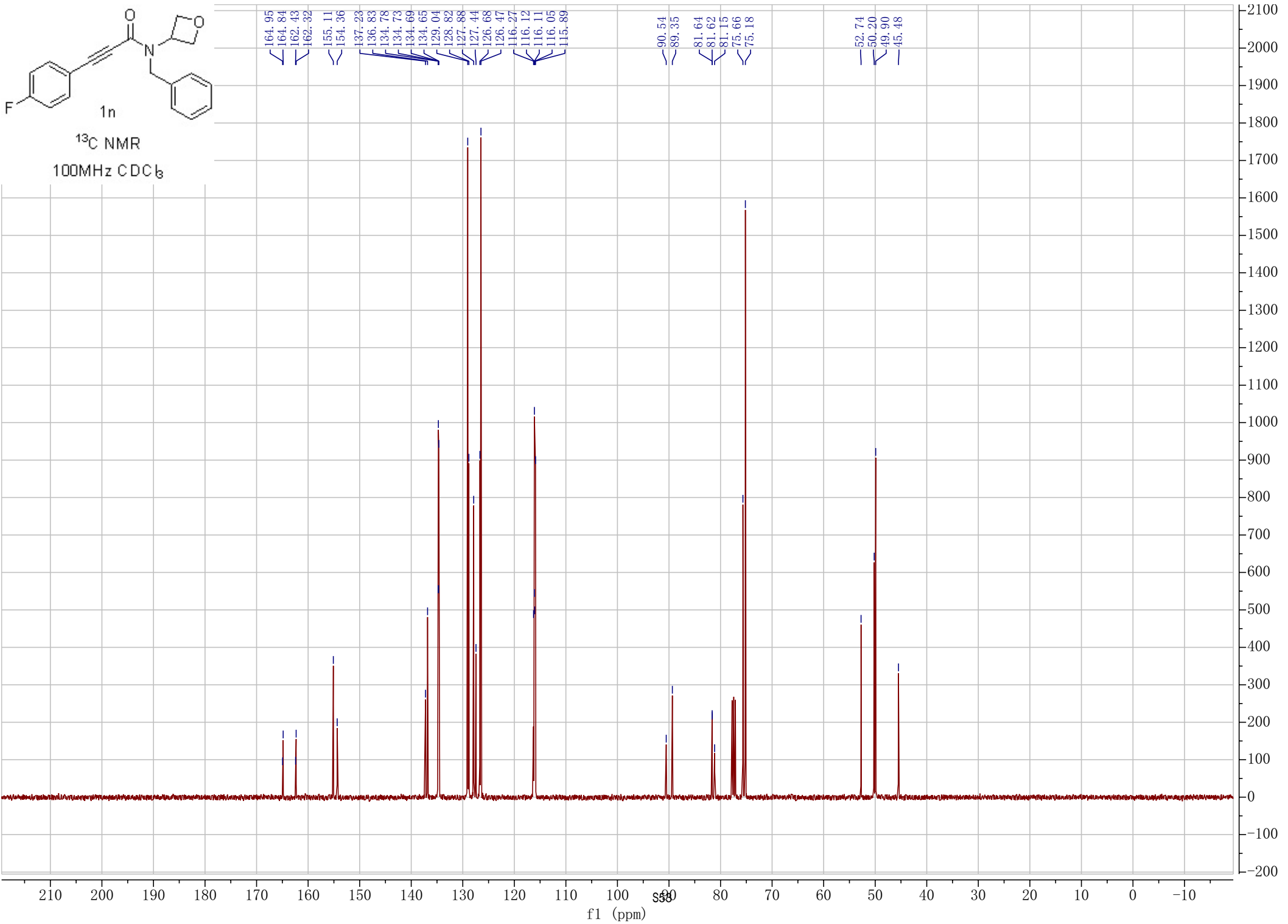


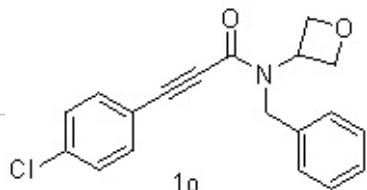
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f1 (ppm)

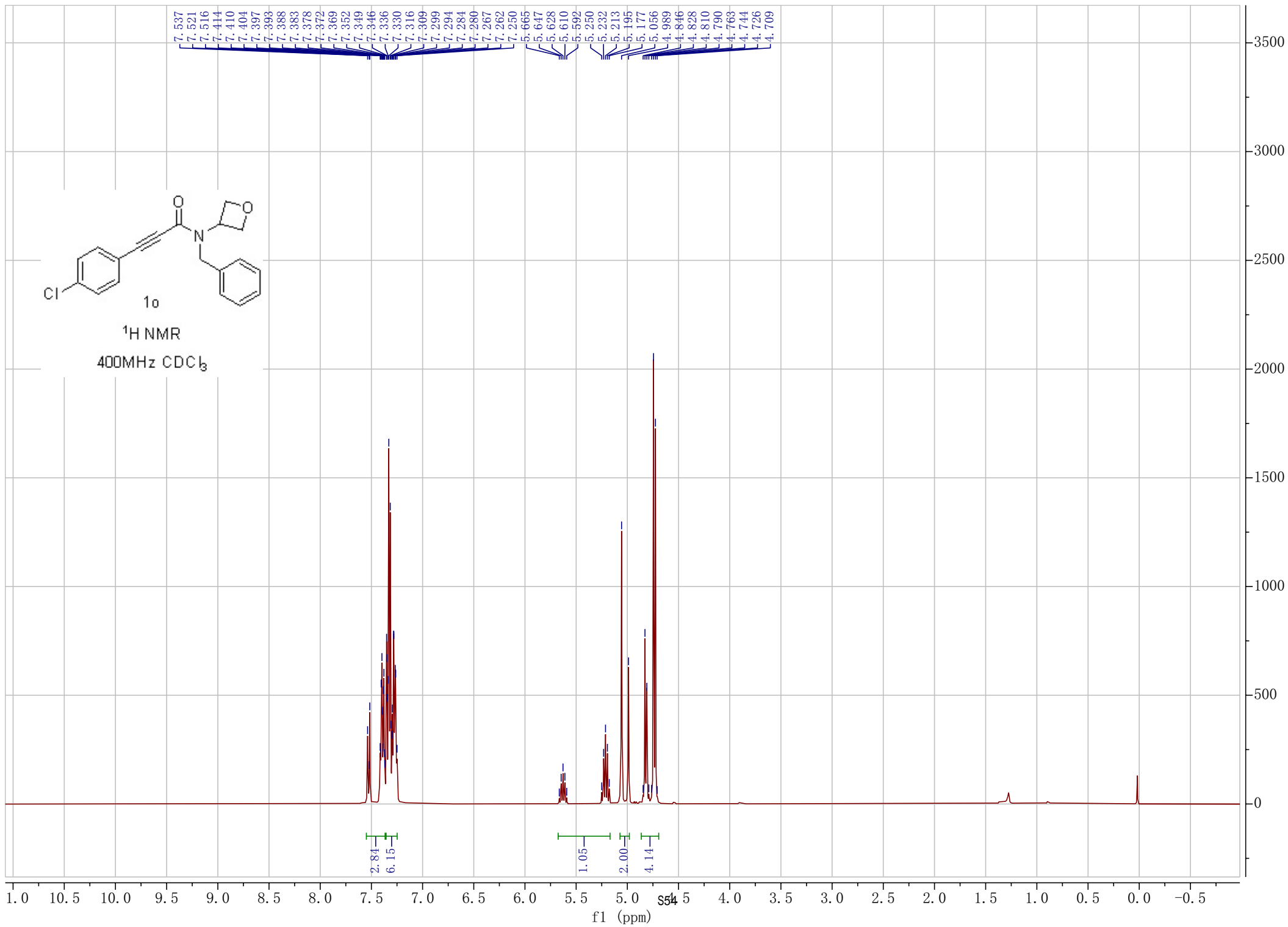


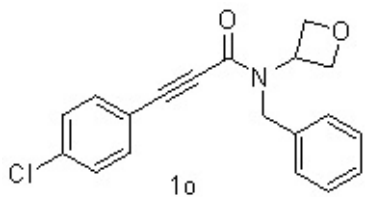
$^{13}\text{C}$  NMR  
100MHz  $\text{CDCl}_3$





<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>





<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

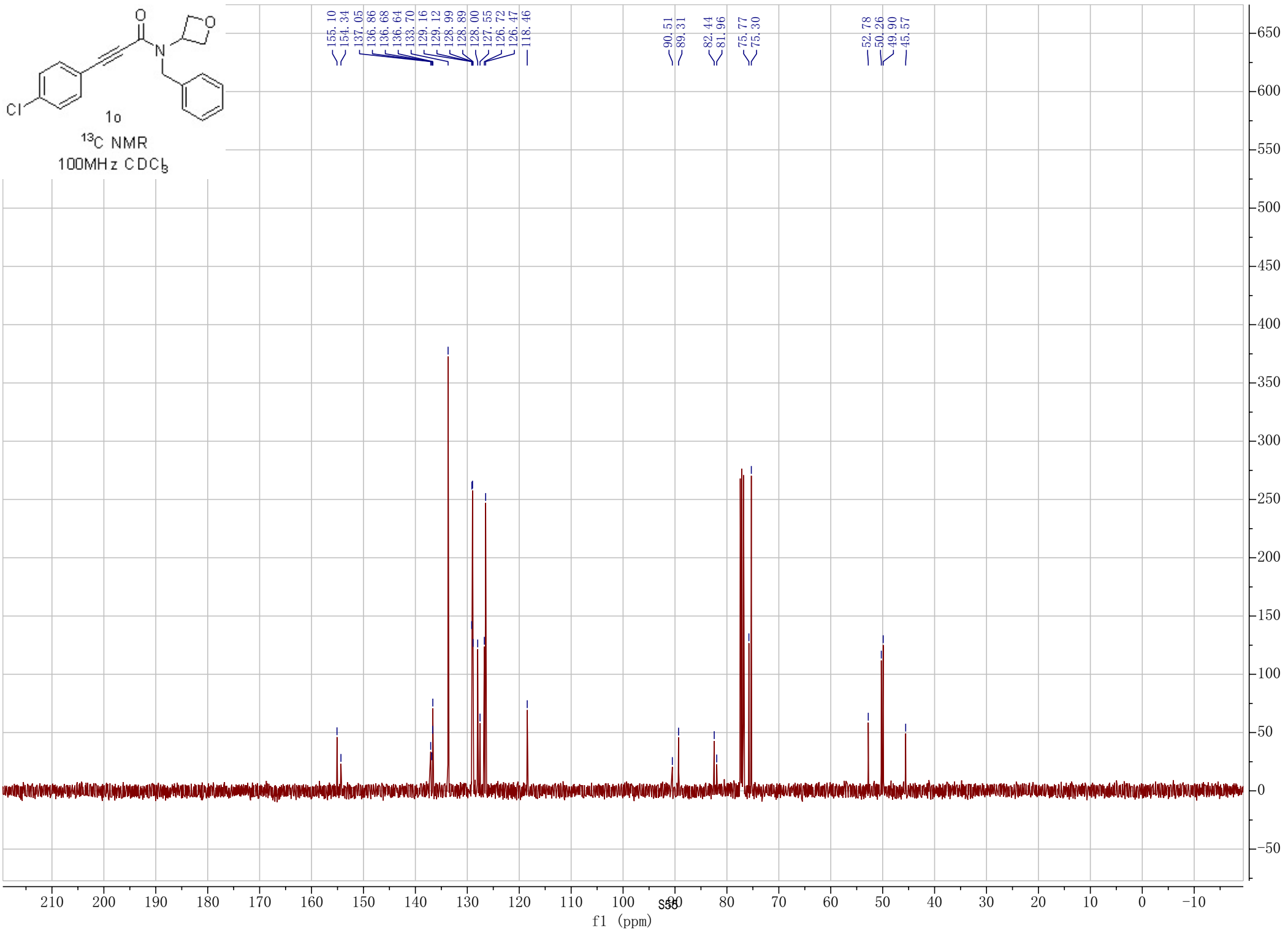
155.10  
154.34  
137.05  
136.86  
136.68  
136.64  
133.70  
129.16  
129.12  
128.99  
128.89  
128.00  
127.55  
126.72  
126.47  
118.46

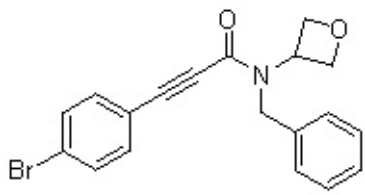
90.51  
89.31

82.44  
81.96

75.77  
75.30

52.78  
50.26  
49.90  
45.57

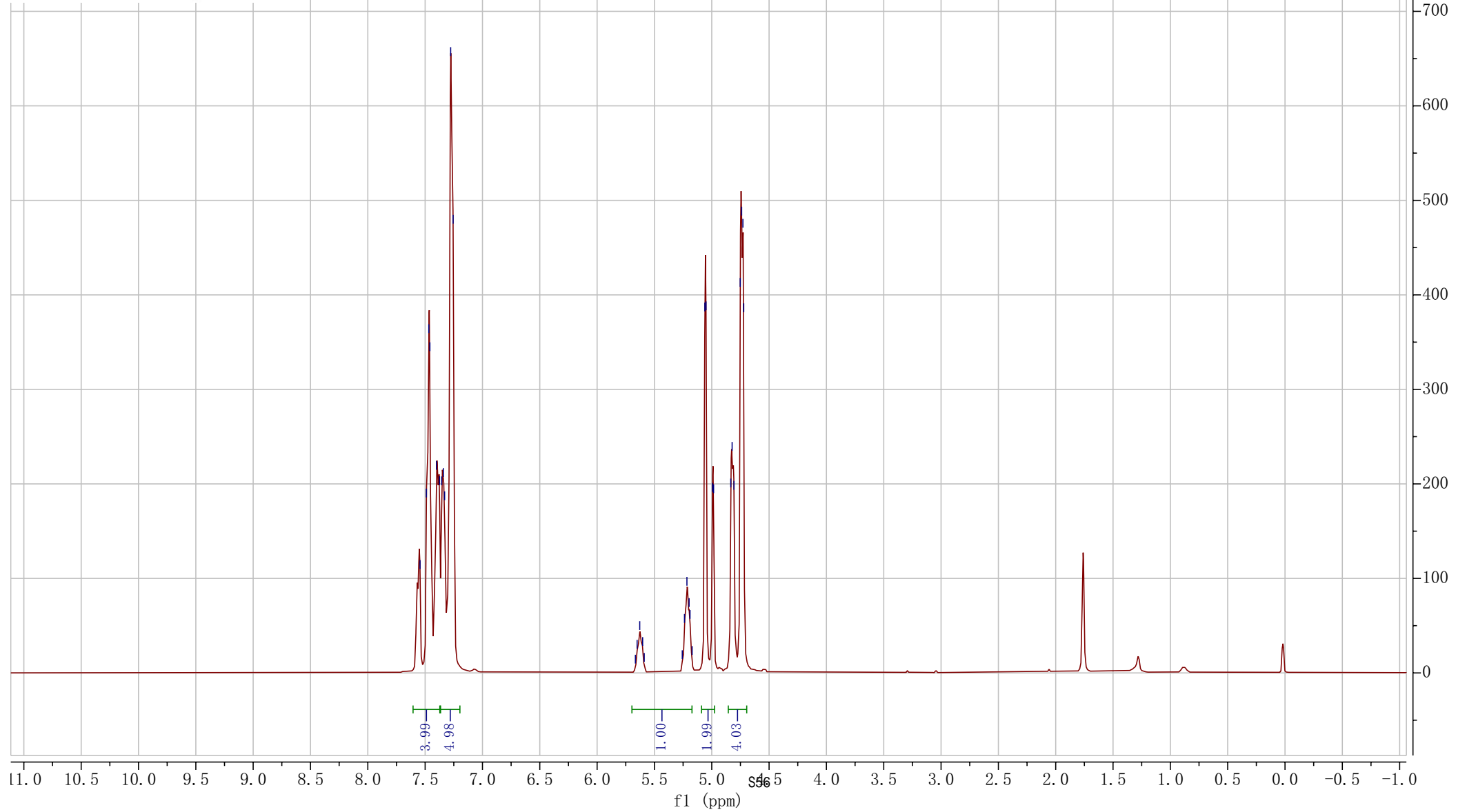




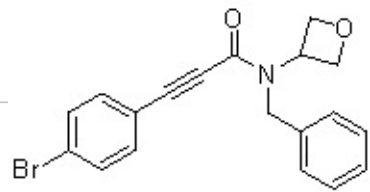
1p

<sup>1</sup>H NMR

400MHz CDCl<sub>3</sub>







1p

$^{13}\text{C}$  NMR

100MHz  $\text{CDCl}_3$

155.08  
154.33  
137.04  
136.63  
133.81  
132.09  
131.93  
129.12  
128.90  
128.00  
127.56  
126.74  
126.46  
125.23  
125.05  
118.93

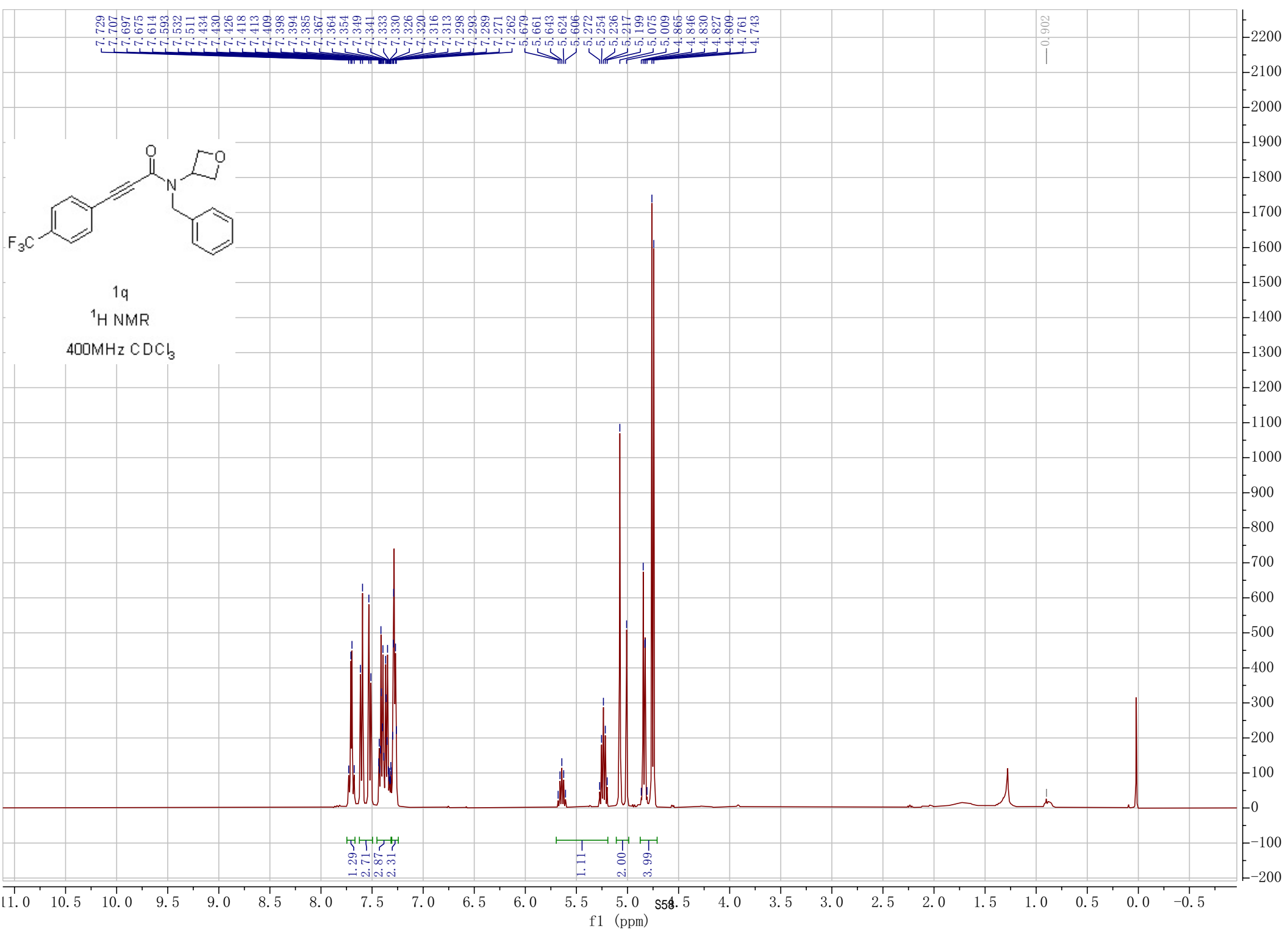
90.55  
89.35  
82.57  
82.08  
75.77  
75.30

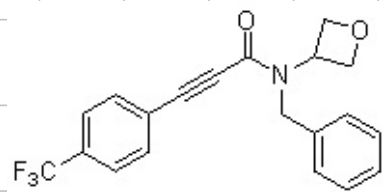
52.77  
50.25  
49.89  
45.57

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

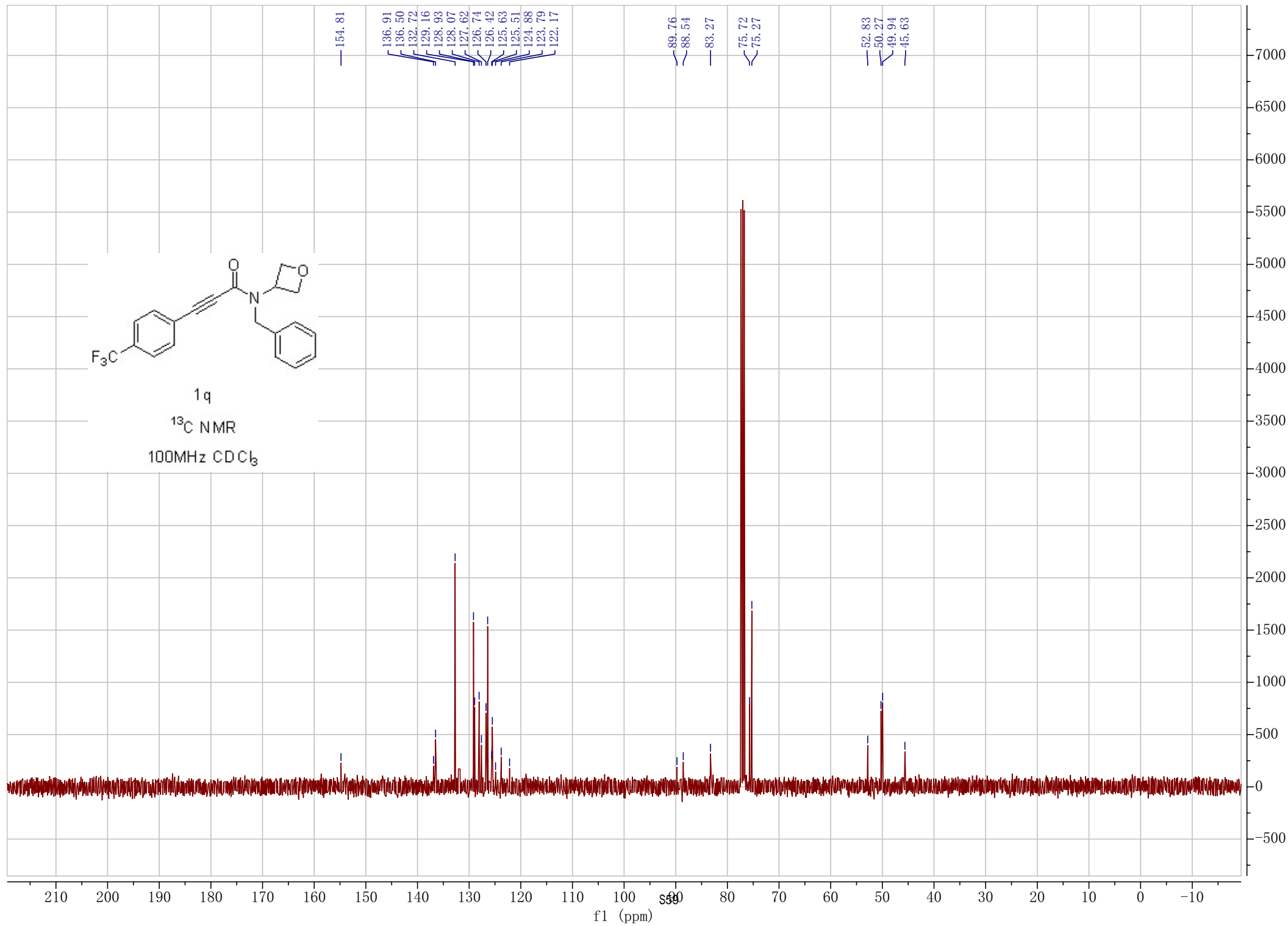
f1 (ppm)

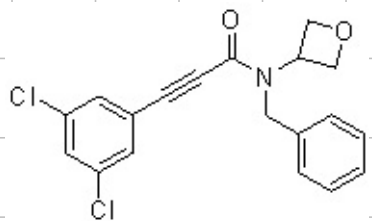
5000  
4500  
4000  
3500  
3000  
2500  
2000  
1500  
1000  
500  
0  
-500



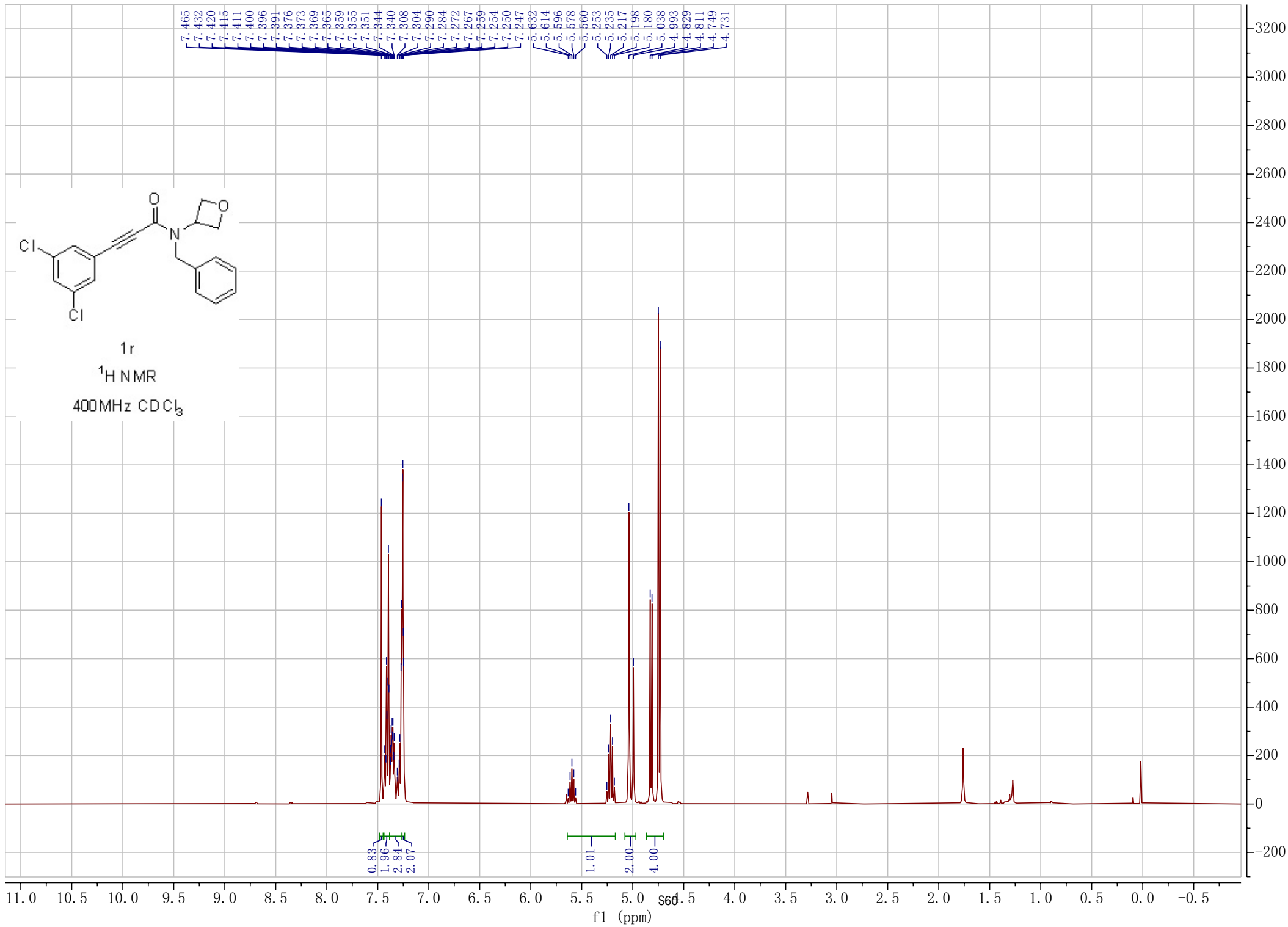


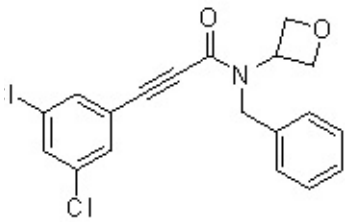
1q  
<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>





1r  
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>

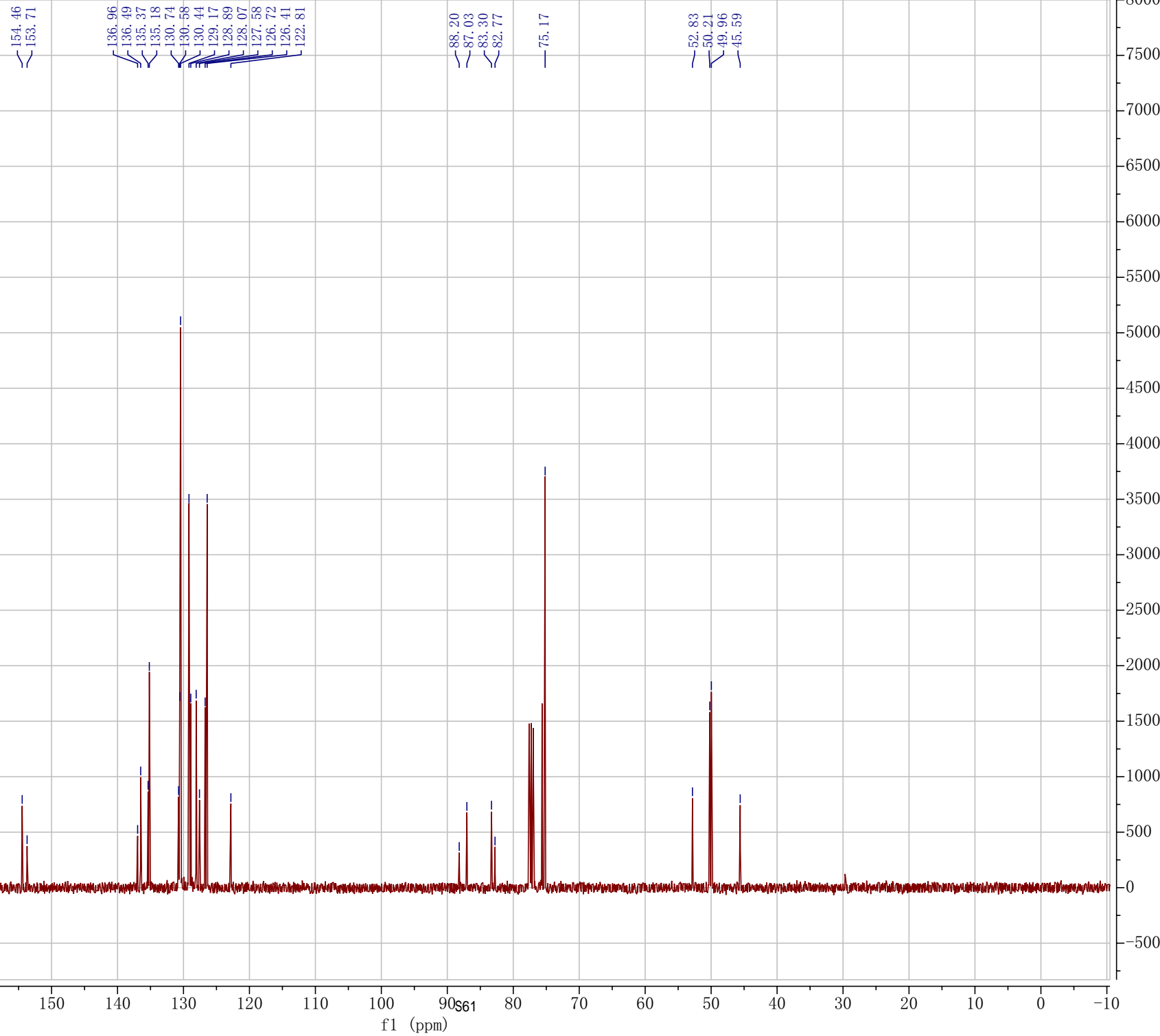


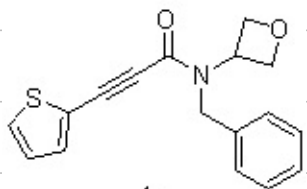


1r

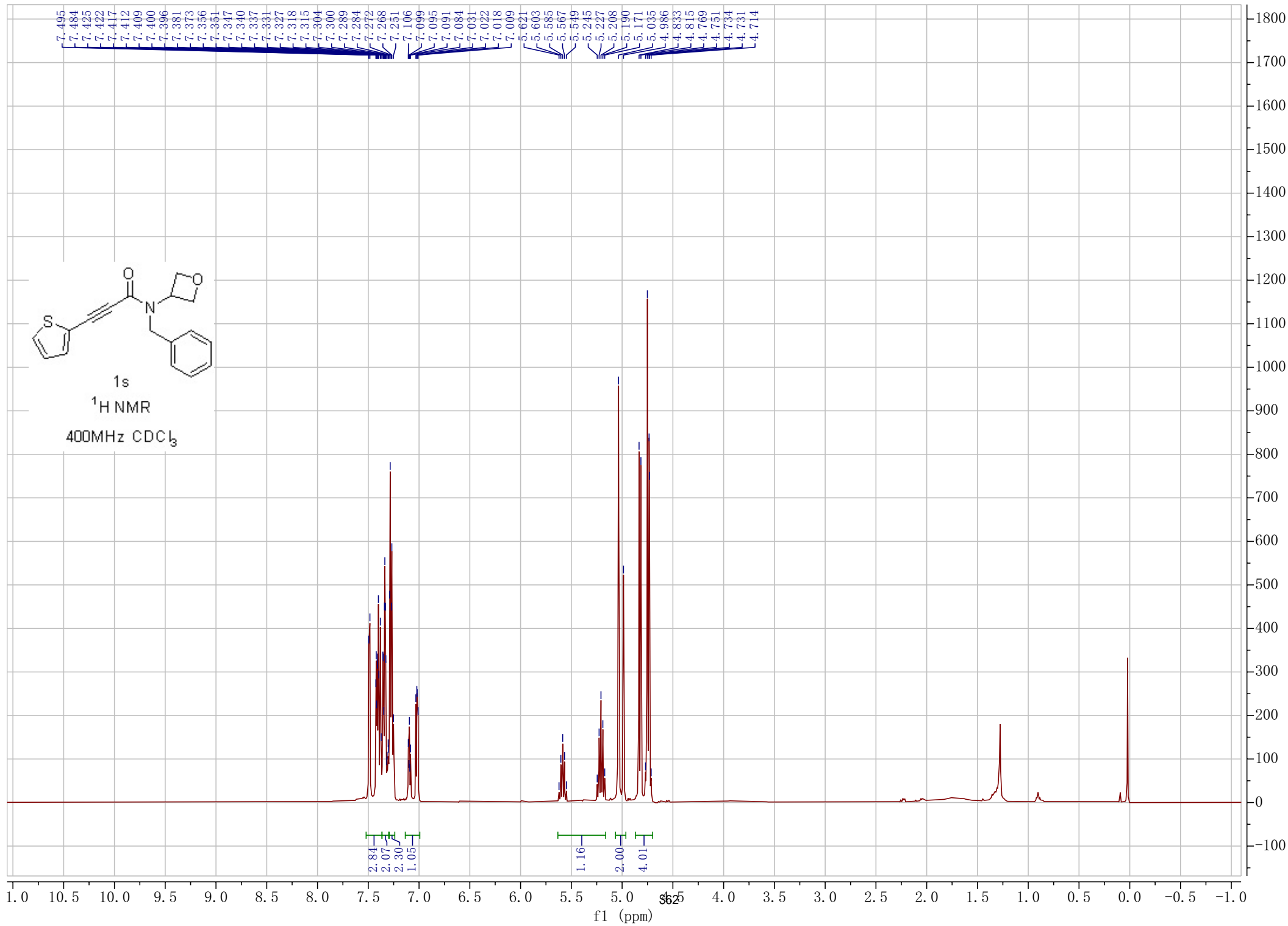
<sup>13</sup>C NMR

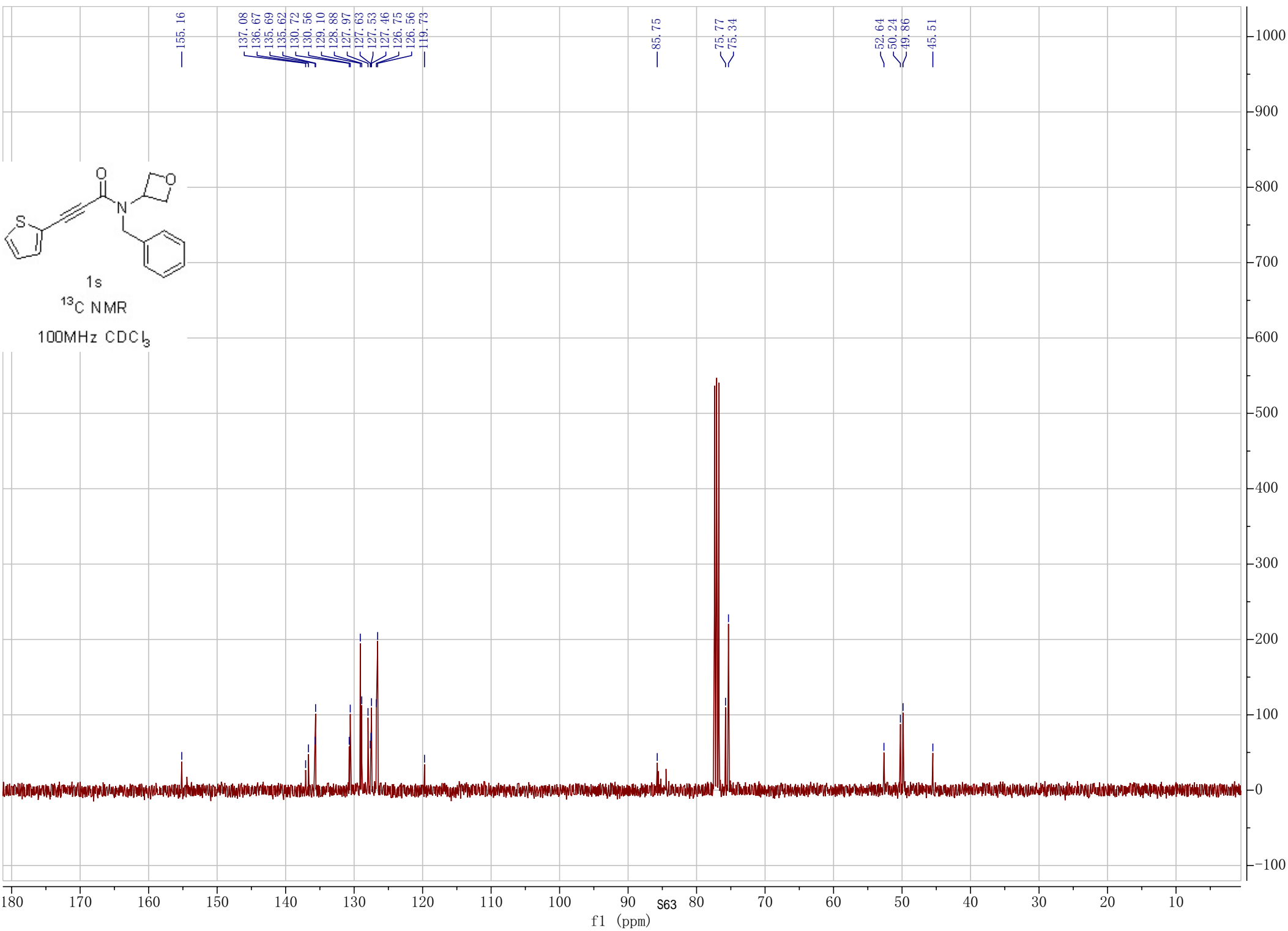
100MHz CDCl<sub>3</sub>

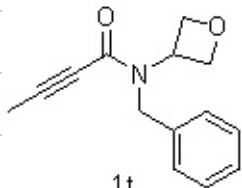




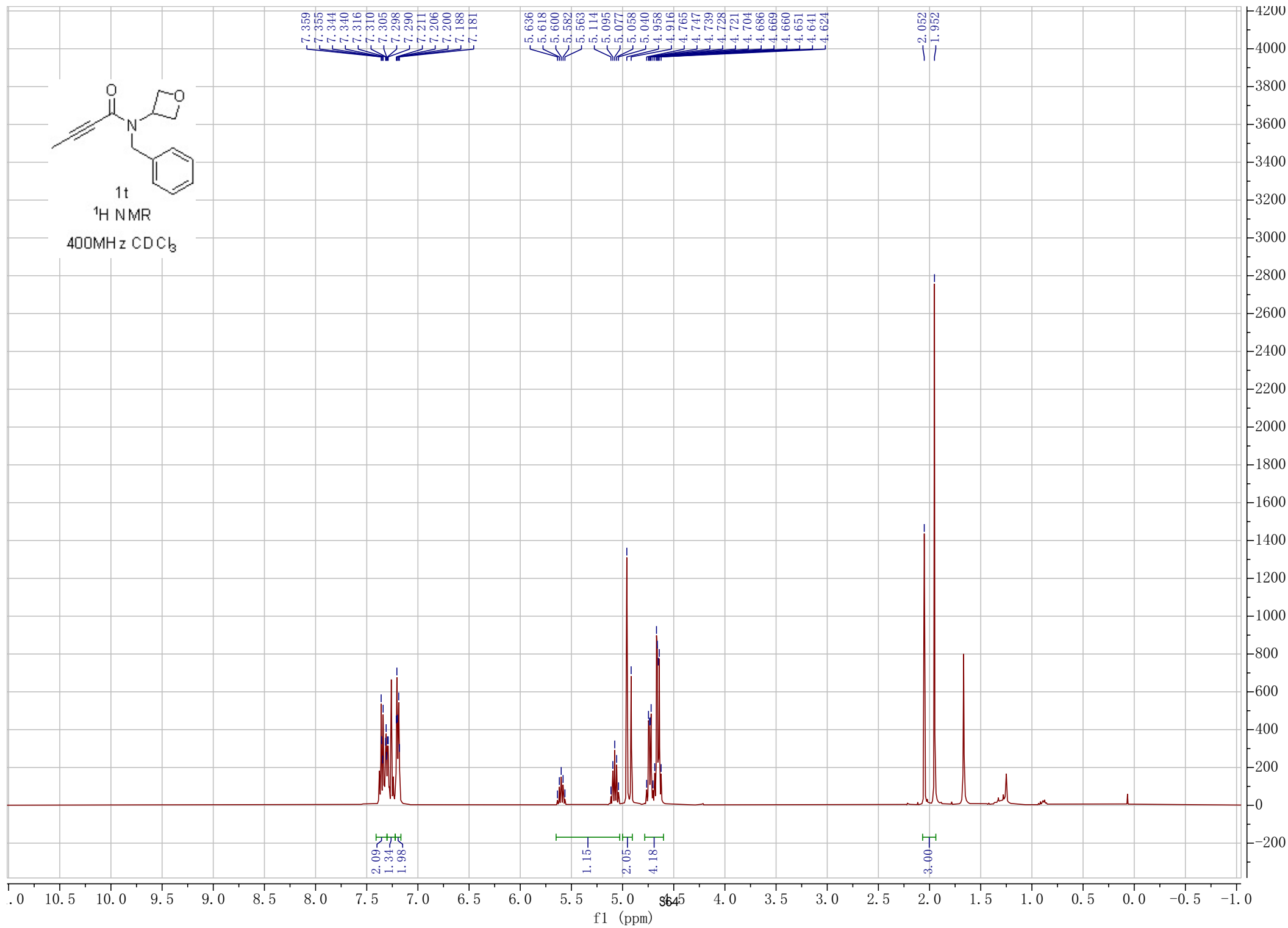
1s  
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>



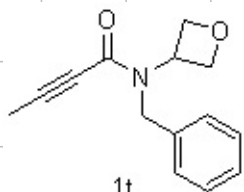




1t  
<sup>1</sup>H NMR  
400MHz z CDCl<sub>3</sub>

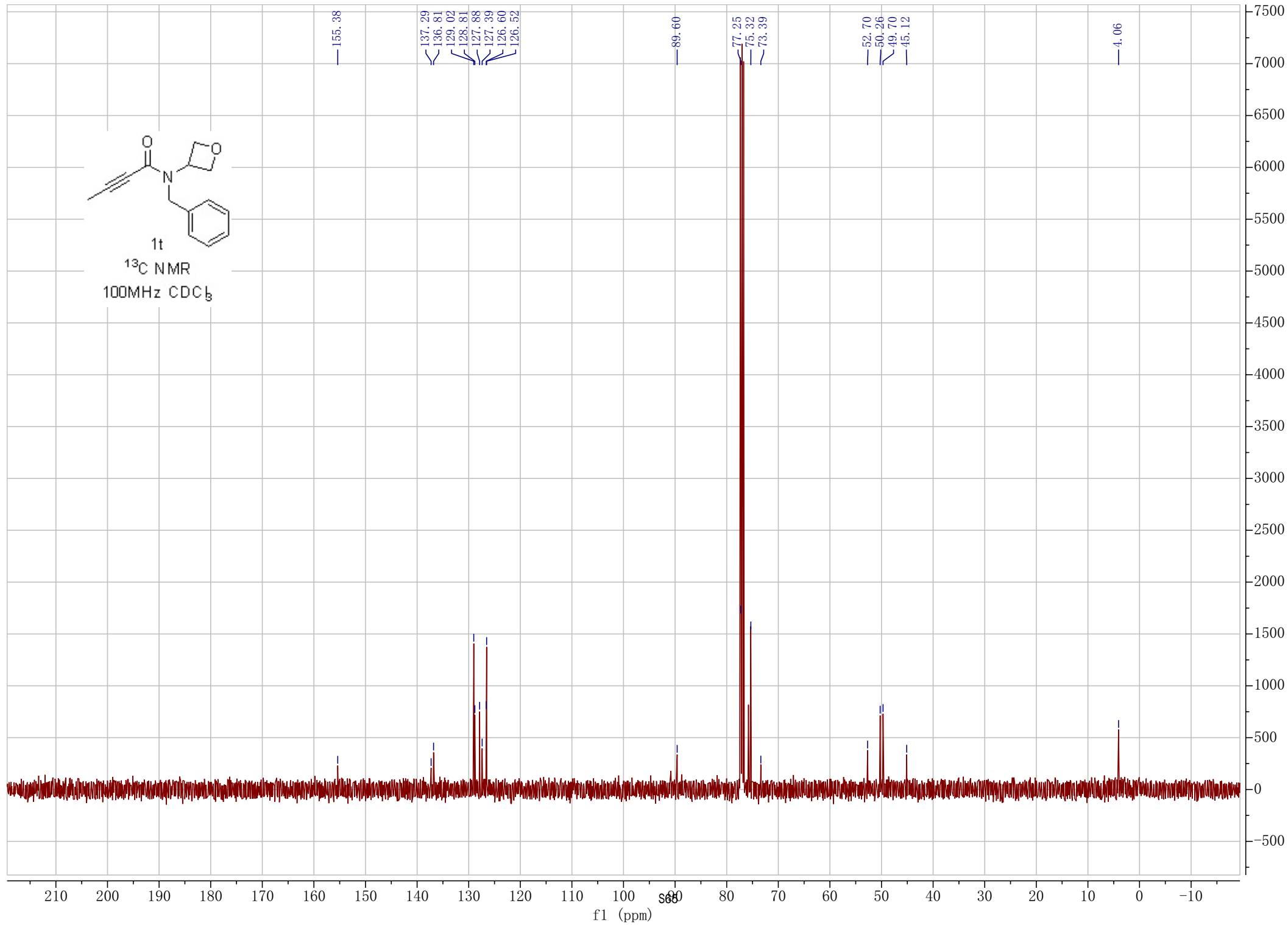


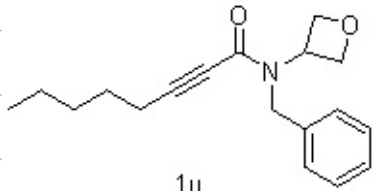




1t

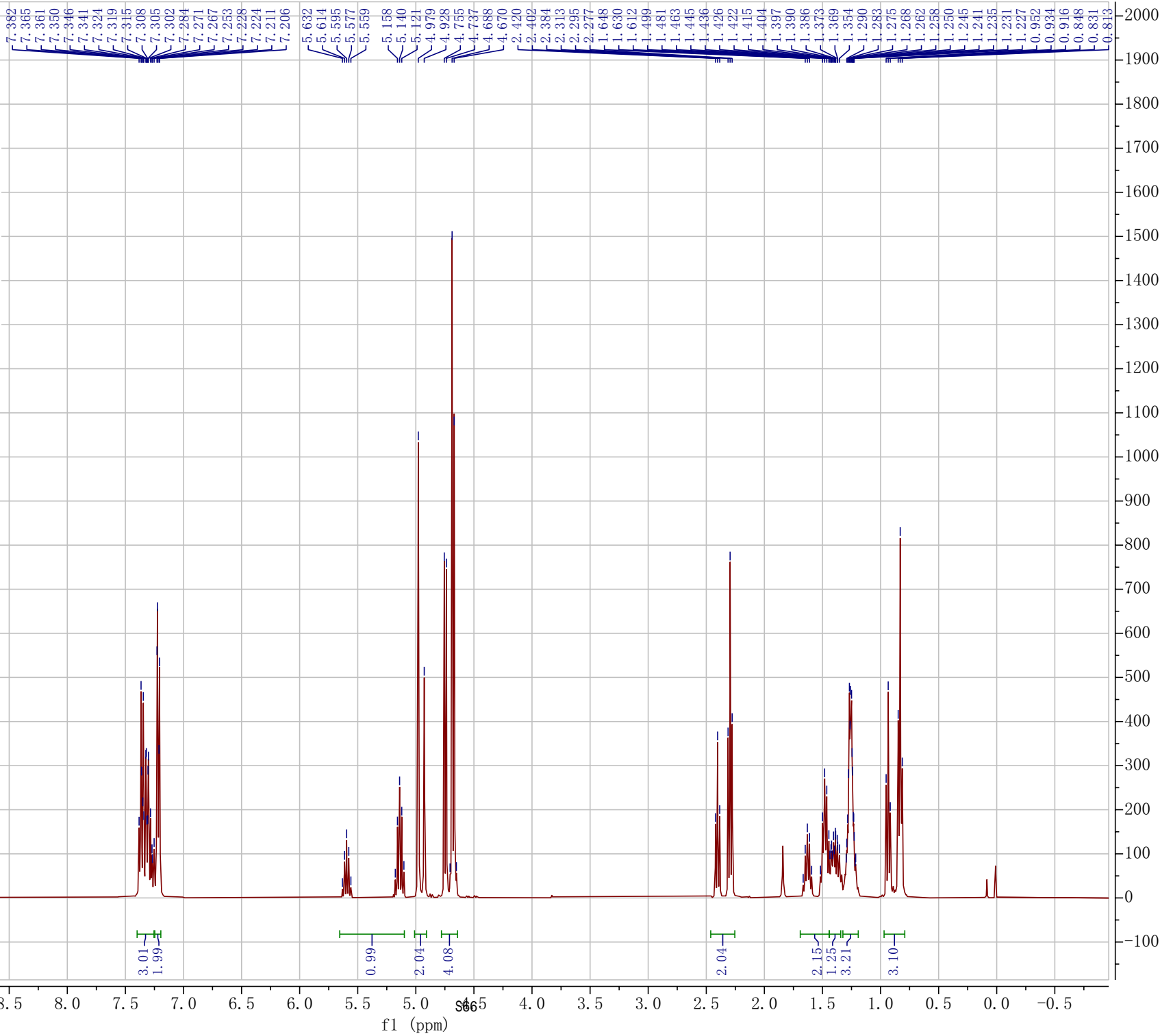
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100MHz CDCl<sub>3</sub>

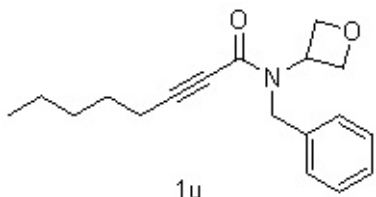




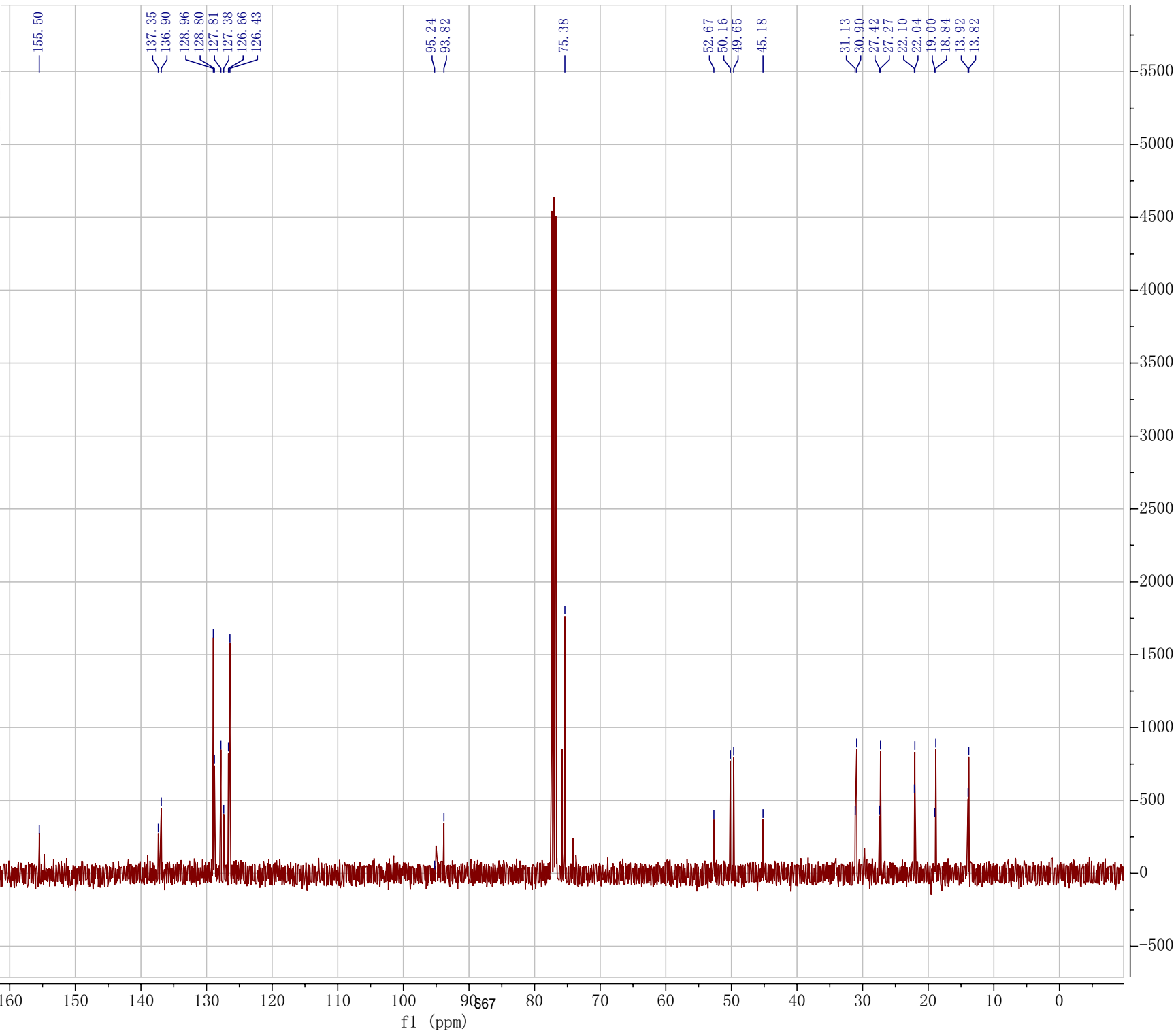
1u

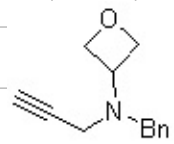
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>





1u  
<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

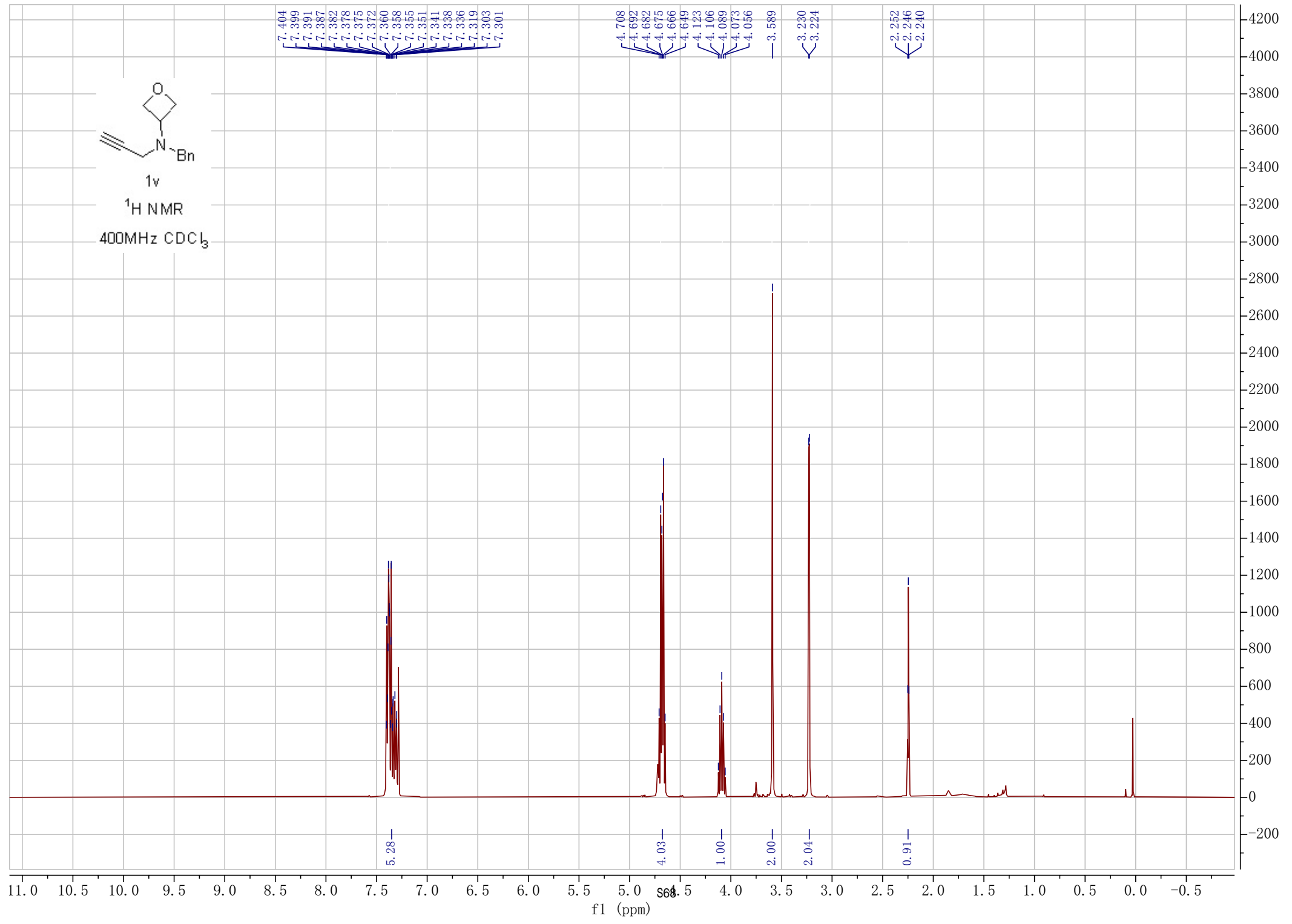


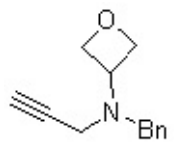


1v

<sup>1</sup>H NMR

400MHz CDCl<sub>3</sub>

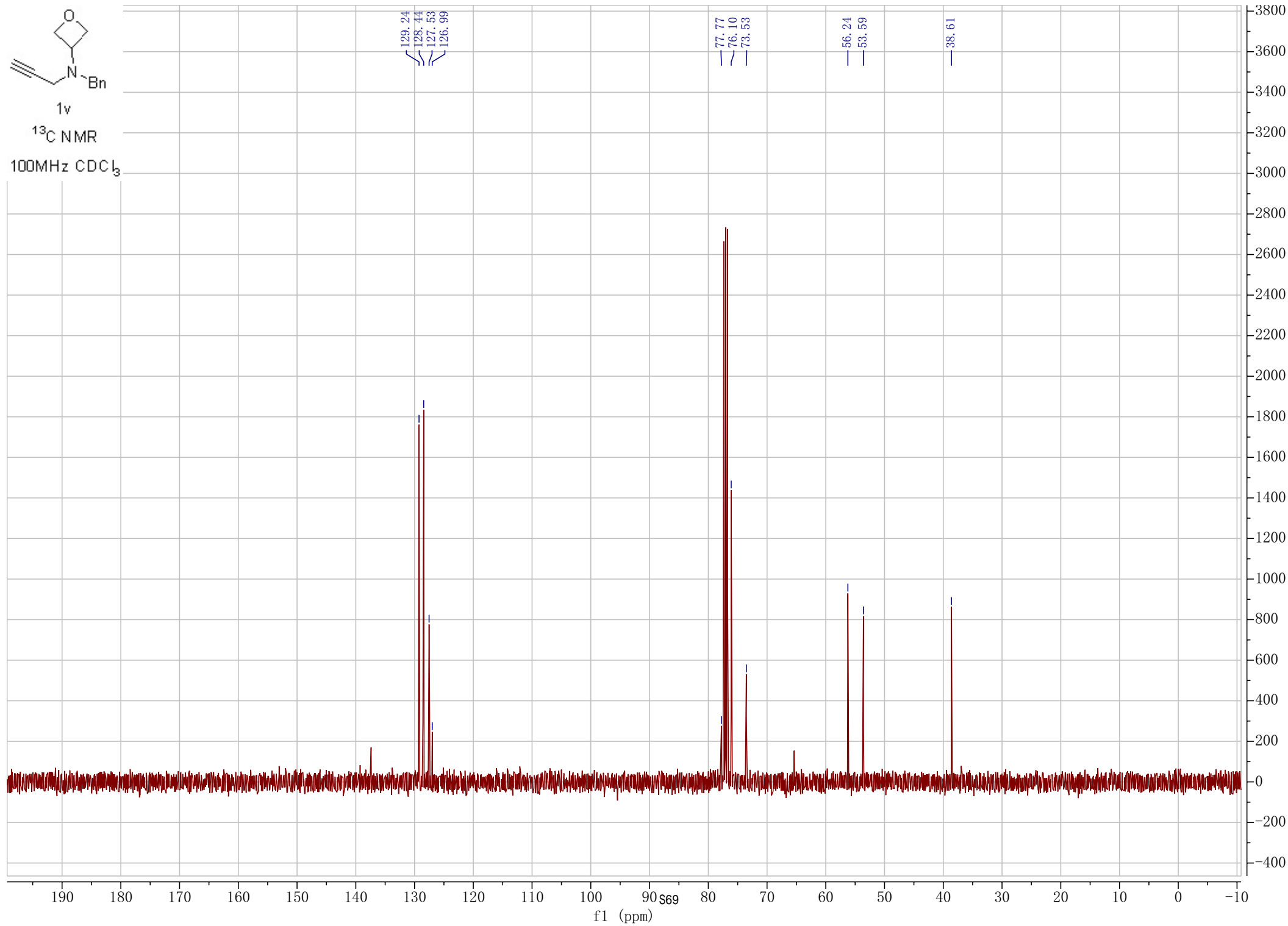


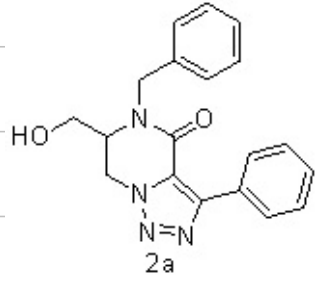


1v

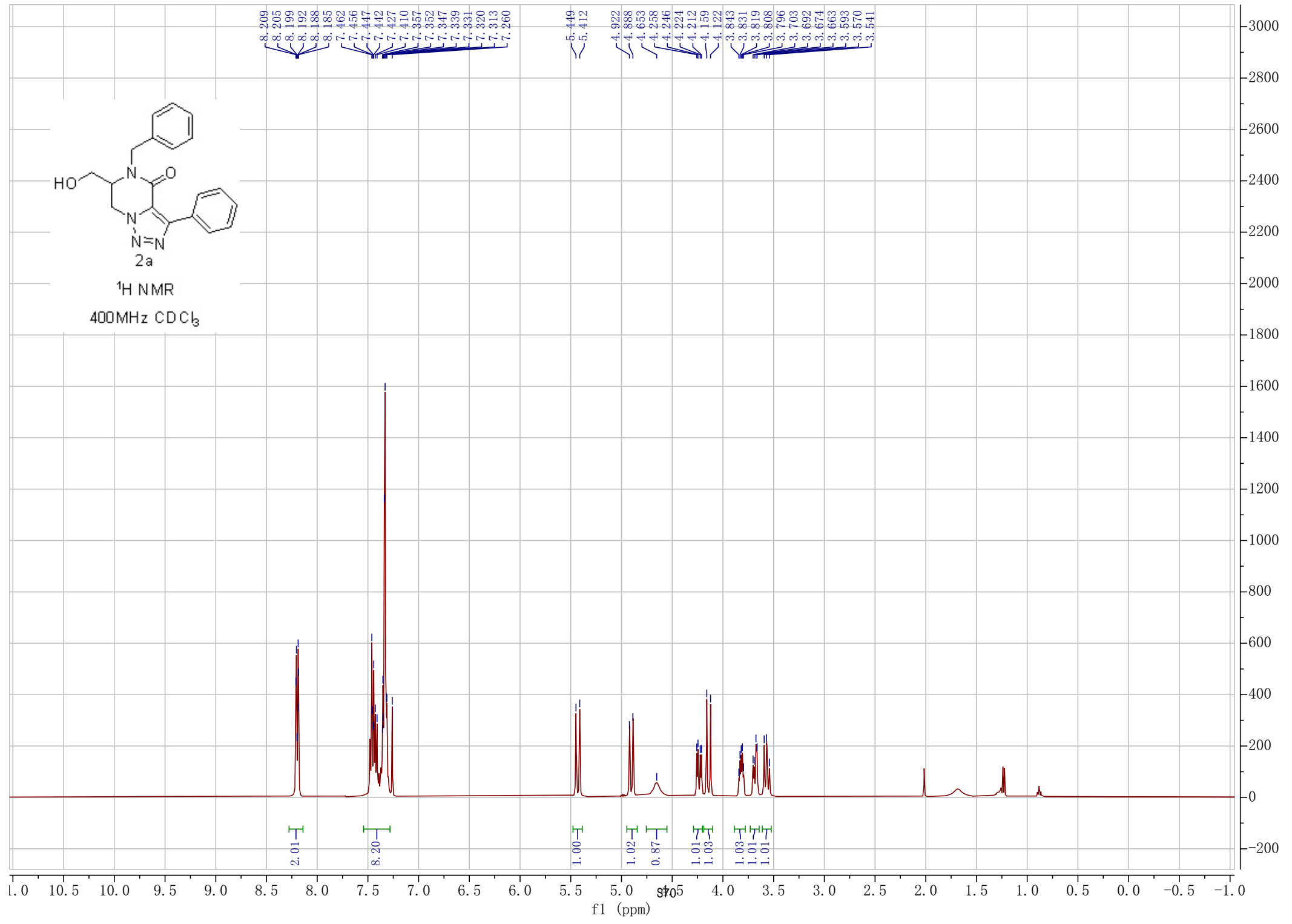
$^{13}\text{C}$  NMR

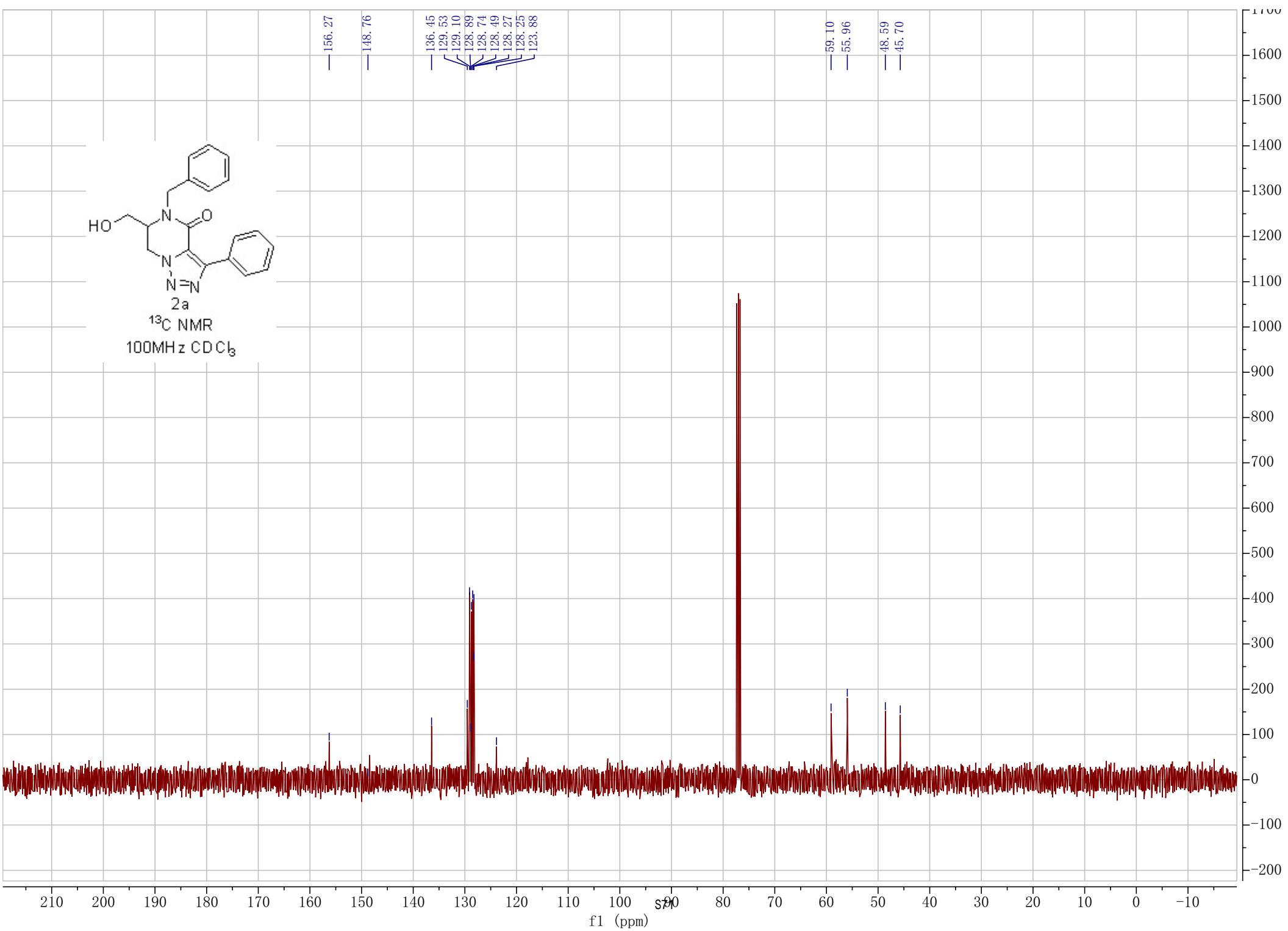
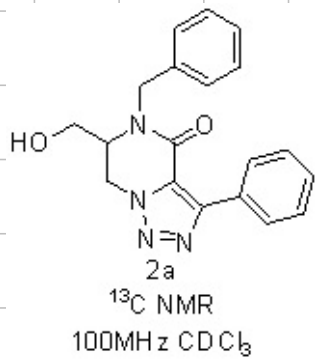
100MHz  $\text{CDCl}_3$

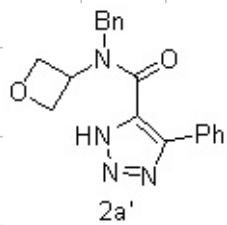




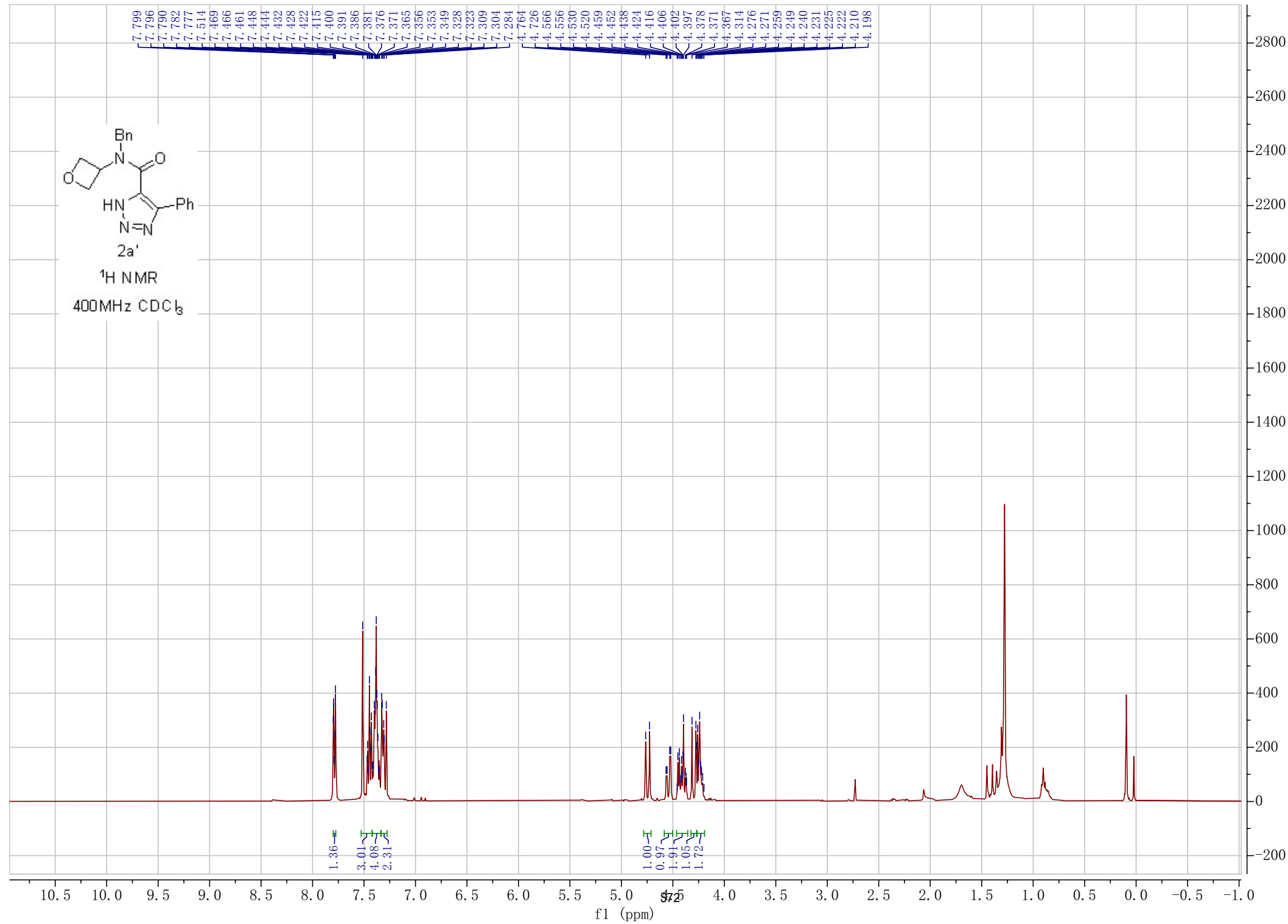
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>



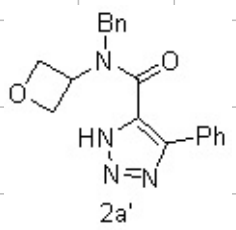




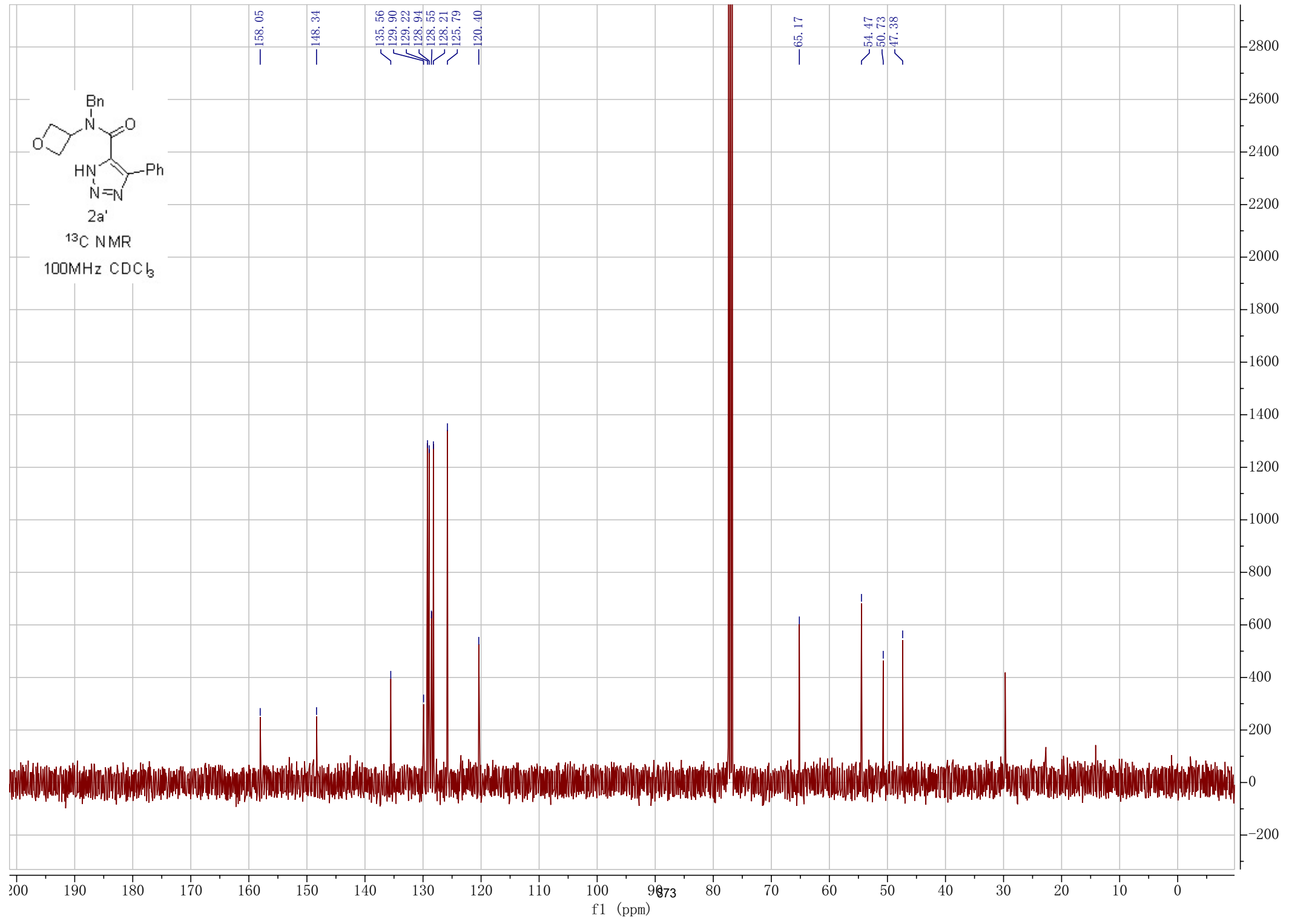
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400MHz CDCl<sub>3</sub>

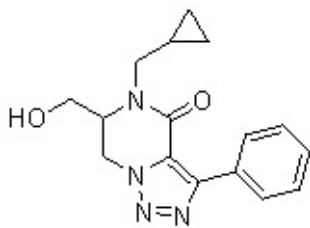






<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

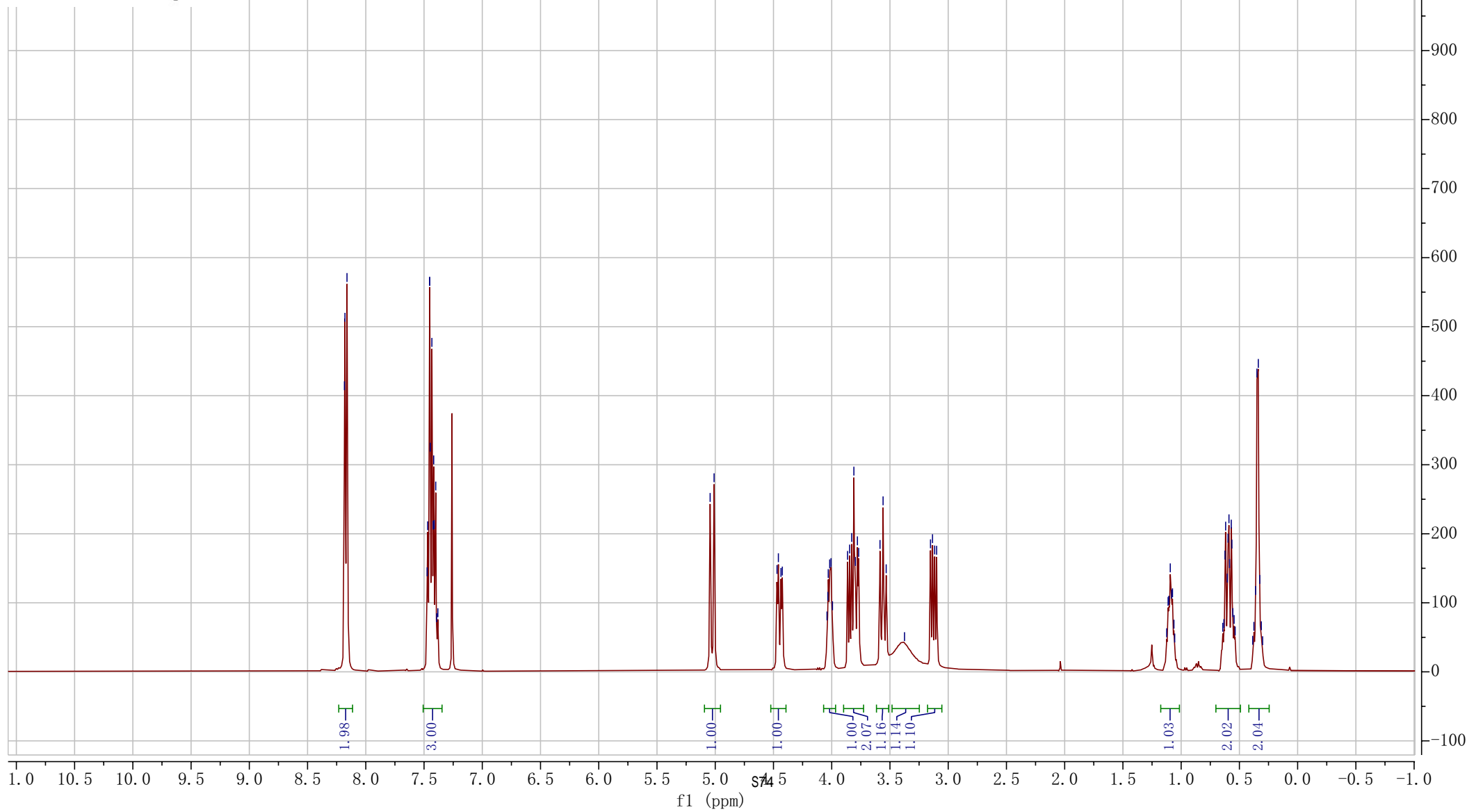


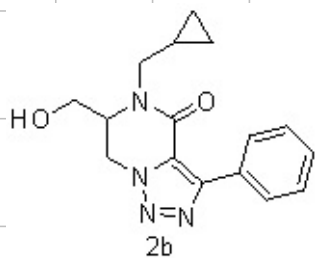


2b

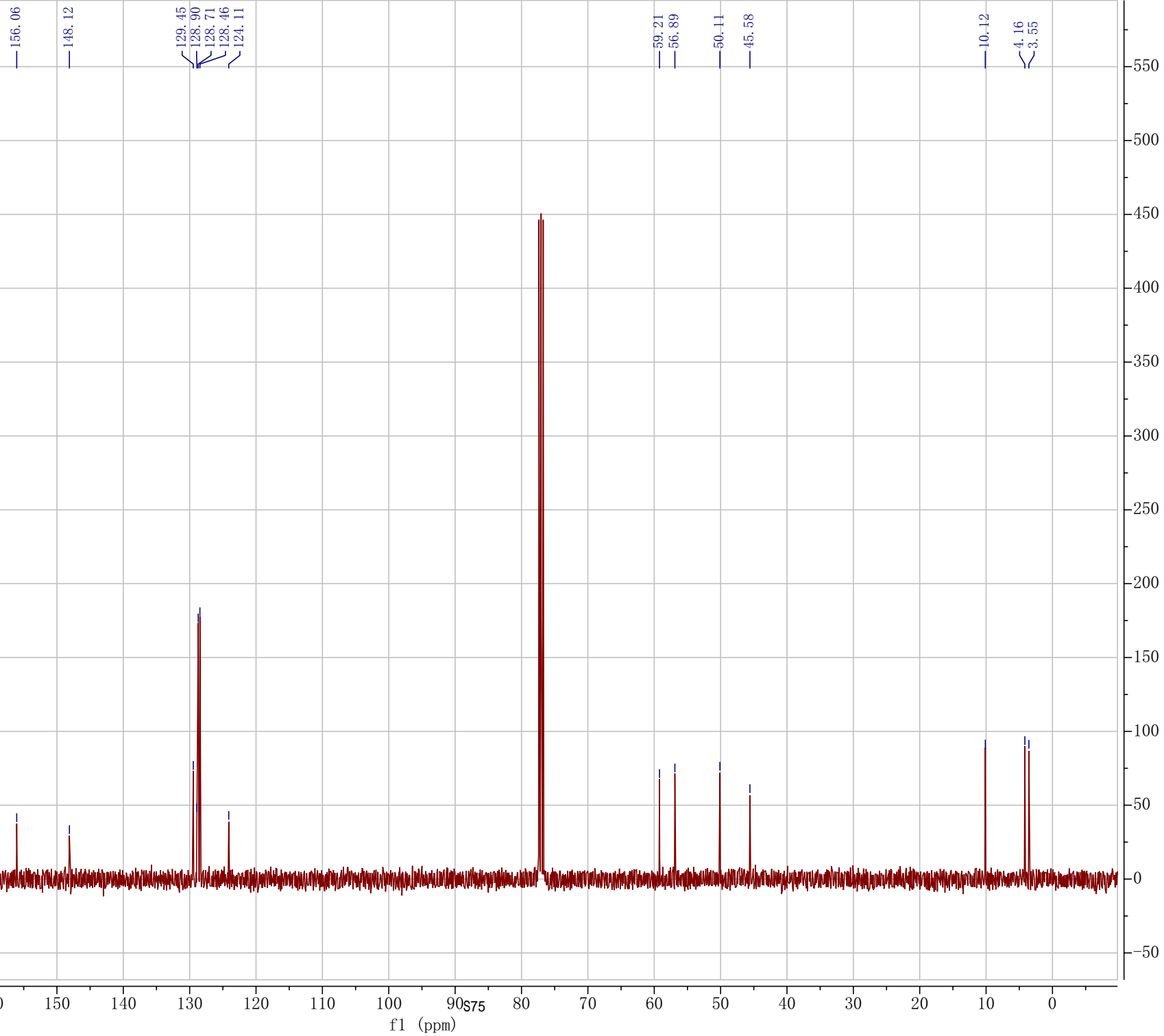
<sup>1</sup>H NMR

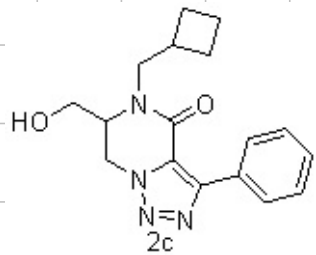
400MHz CDCl<sub>3</sub>



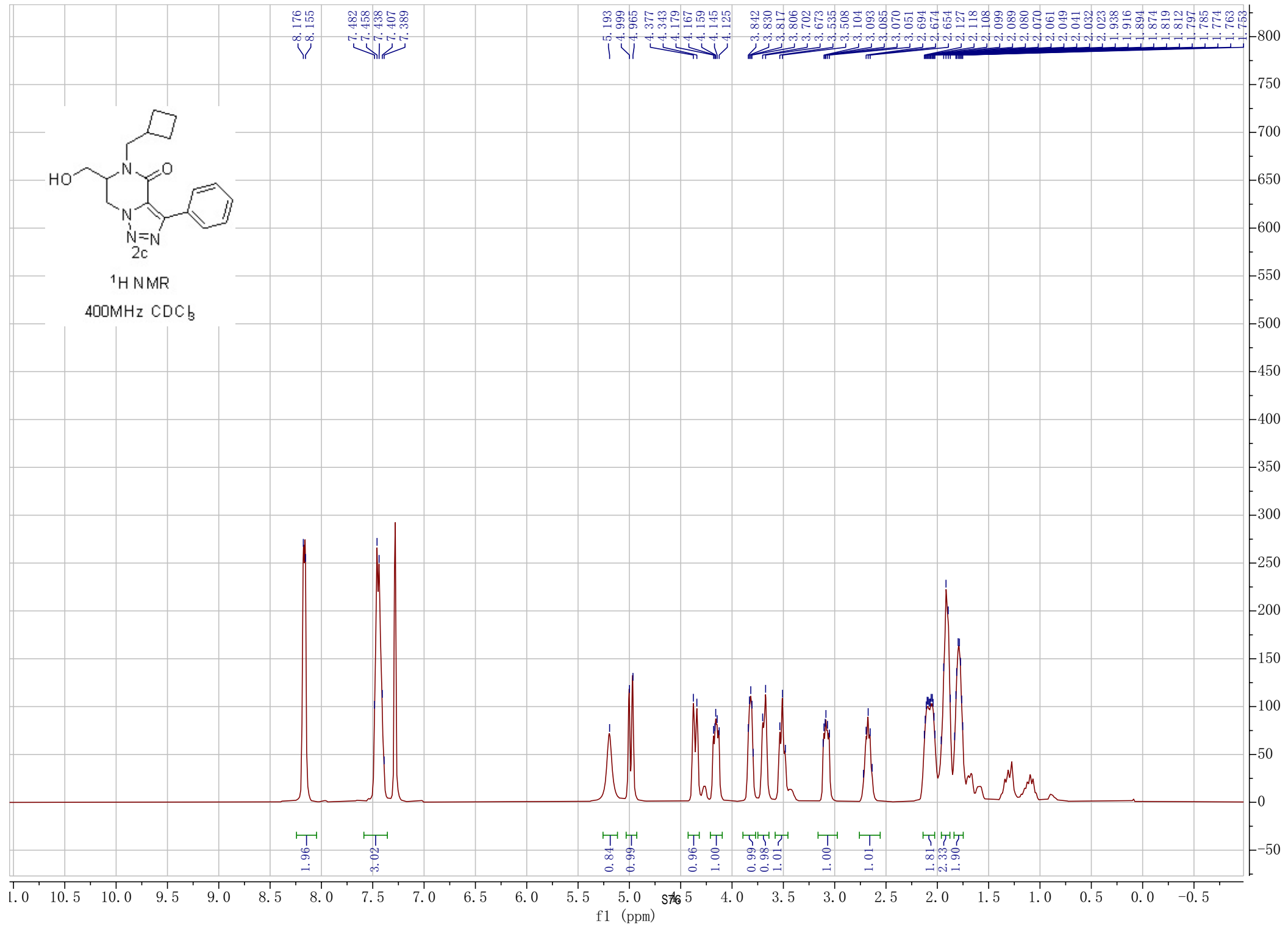


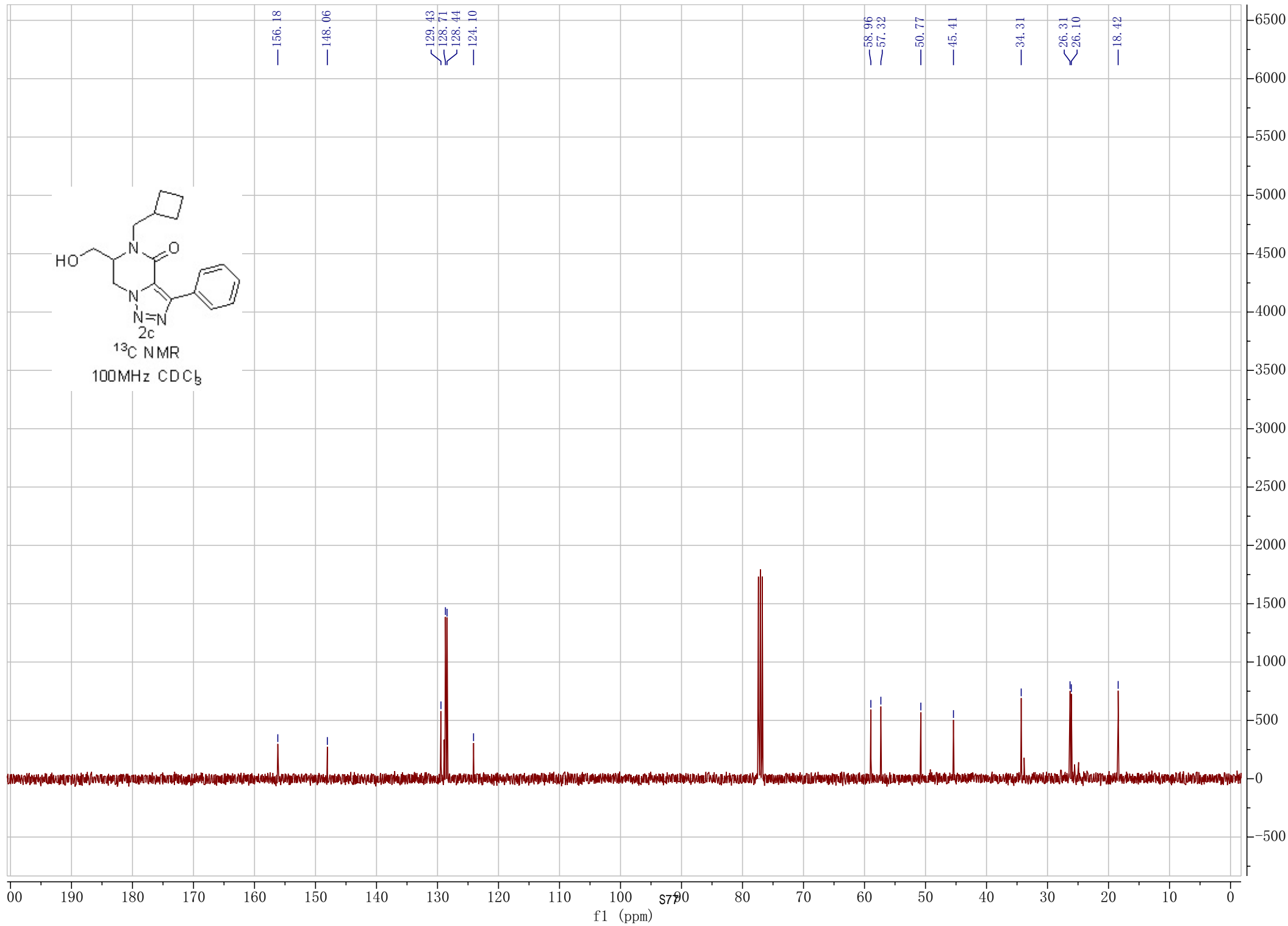
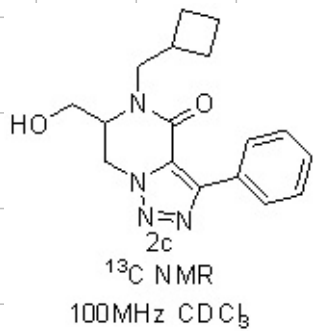
<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

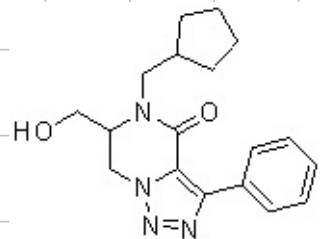




<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>

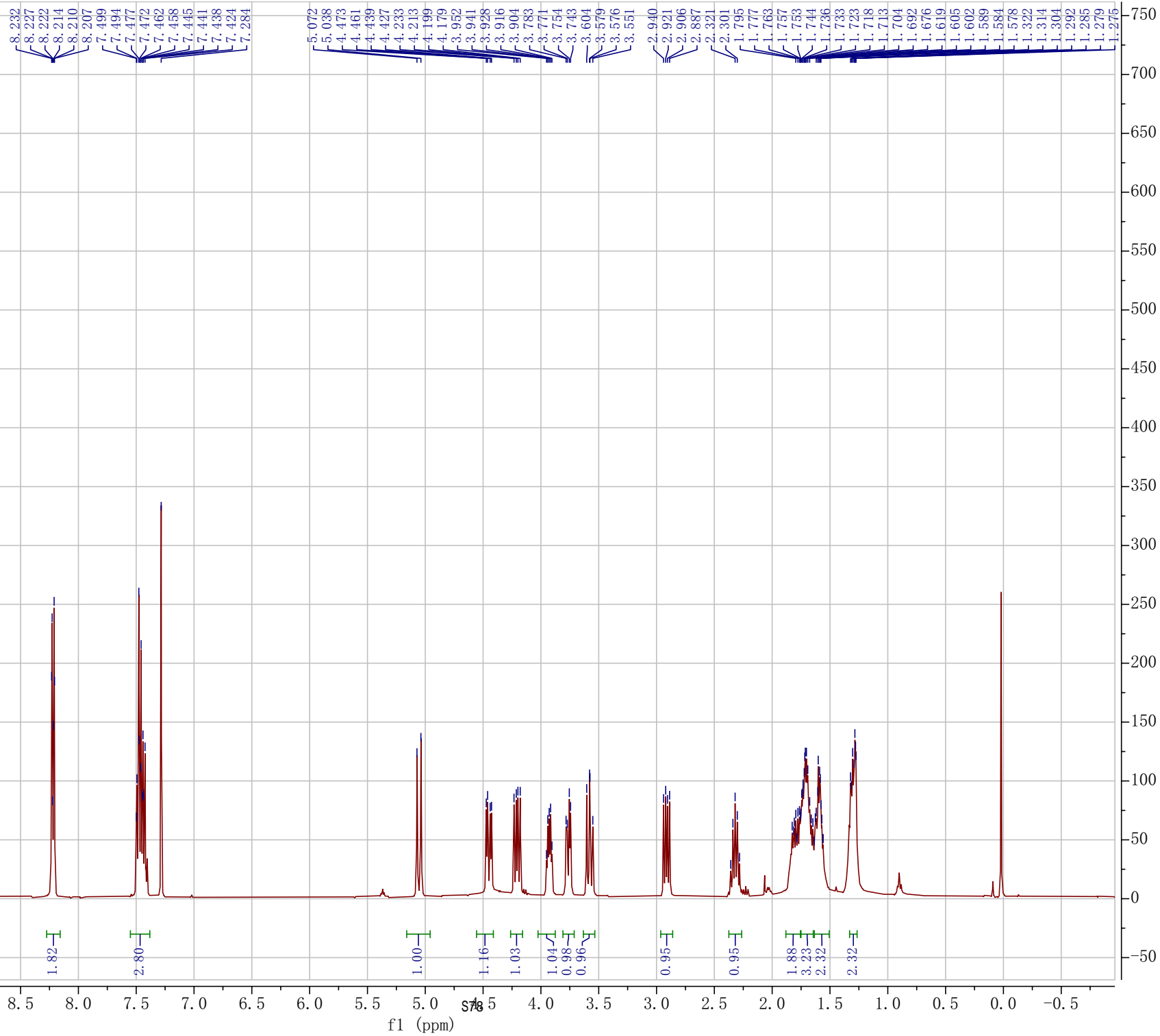


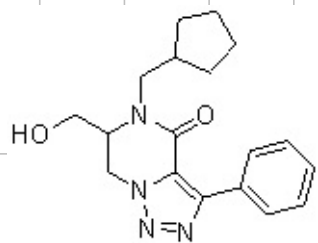




2d

<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>

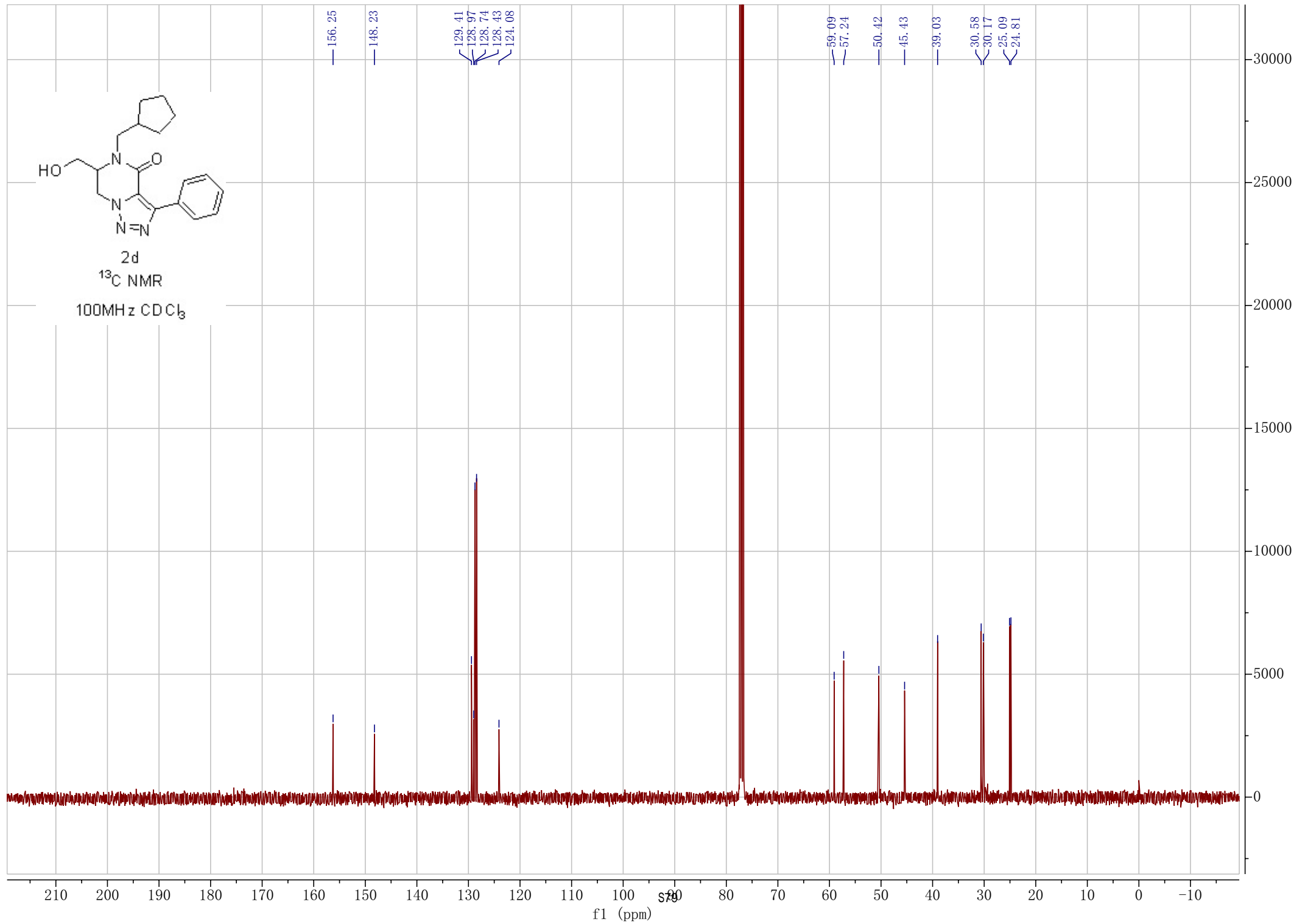


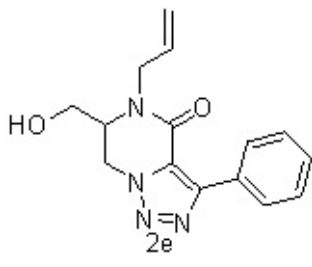


2d

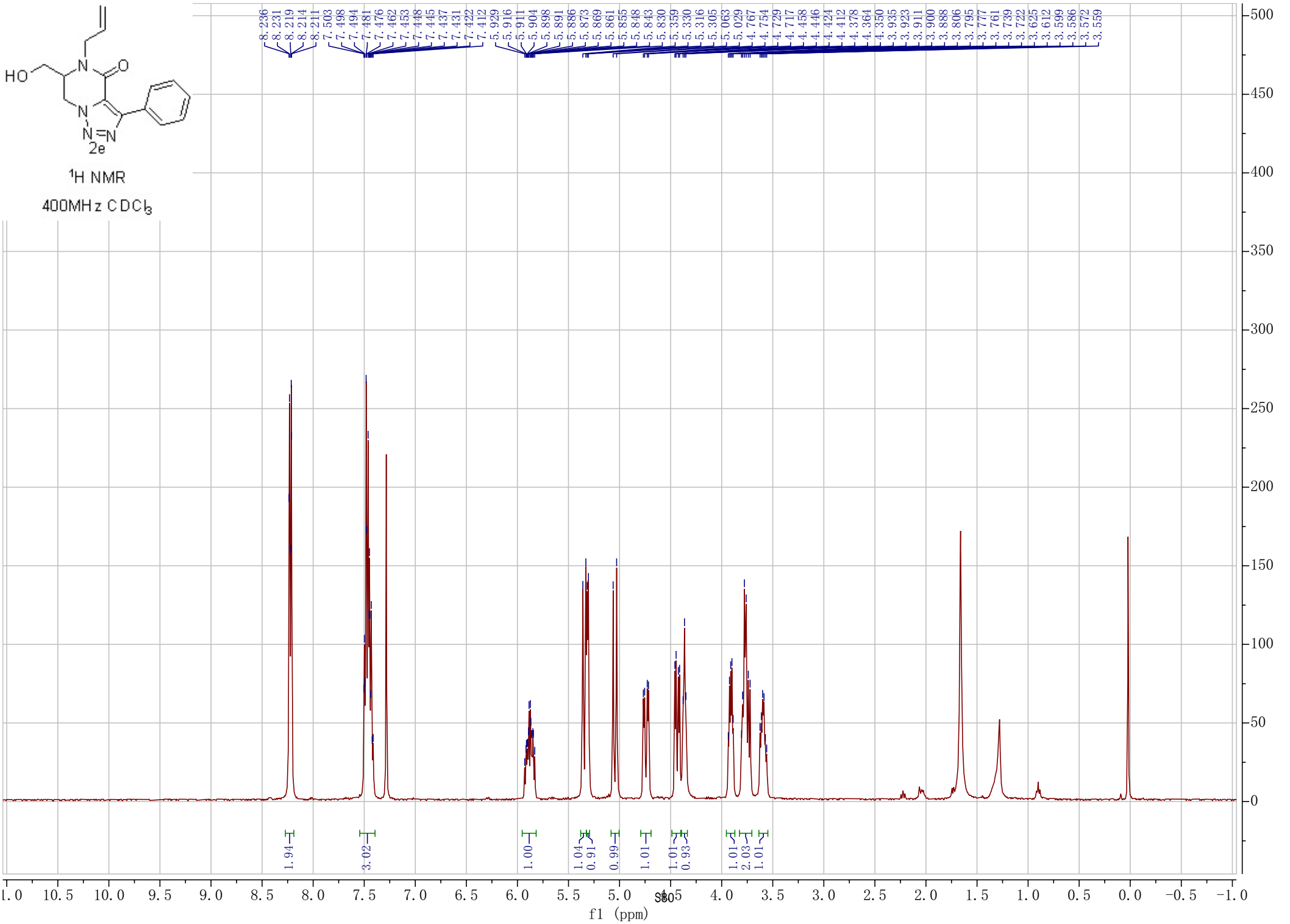
$^{13}\text{C}$  NMR

100MHz  $\text{CDCl}_3$

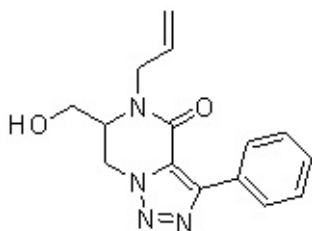




**1H NMR**  
400MHz  $CDCl_3$

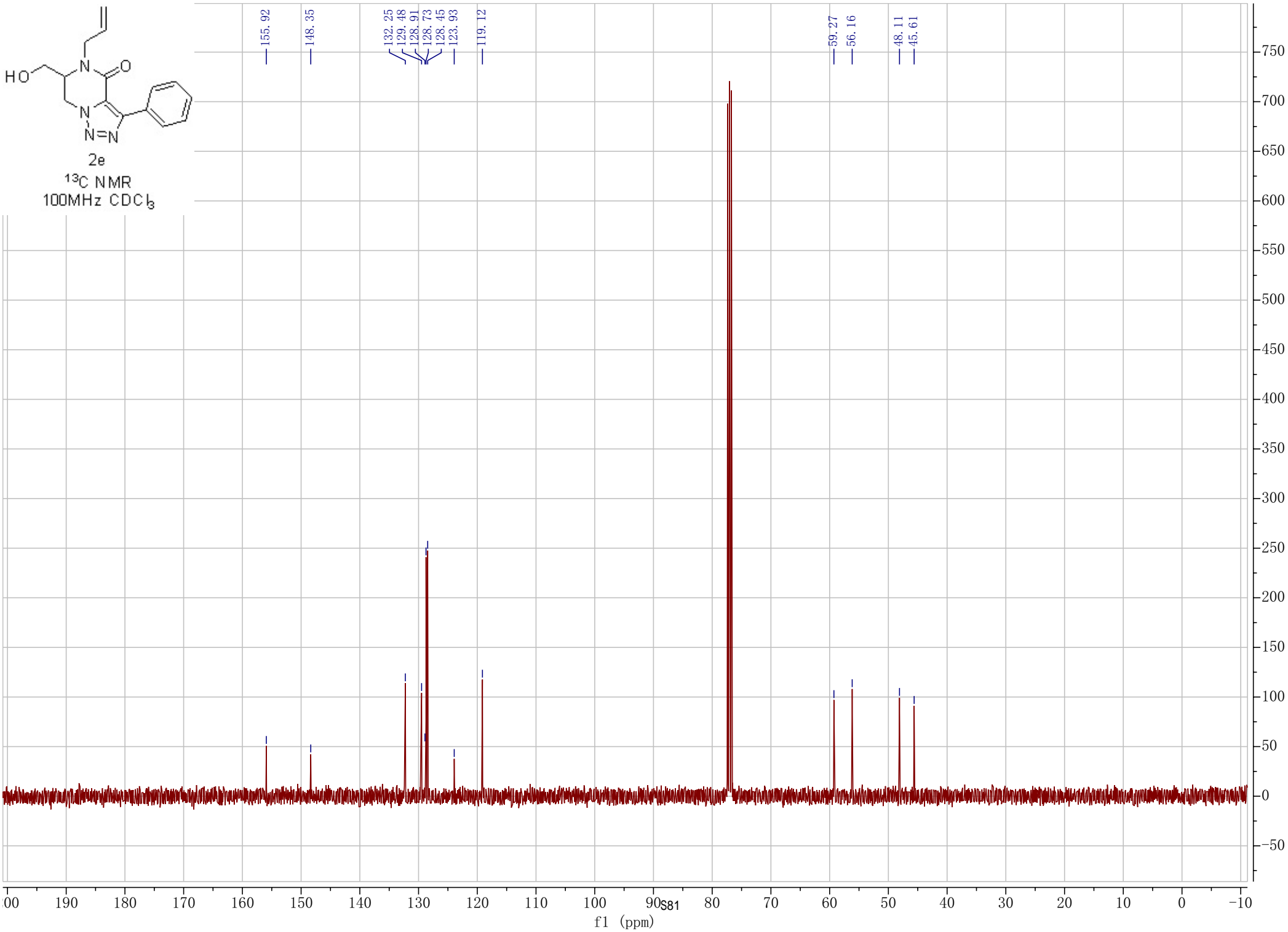


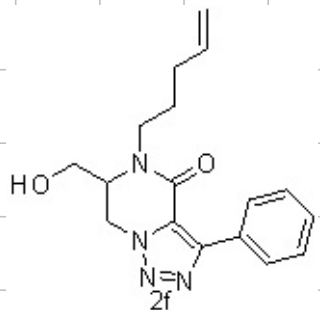




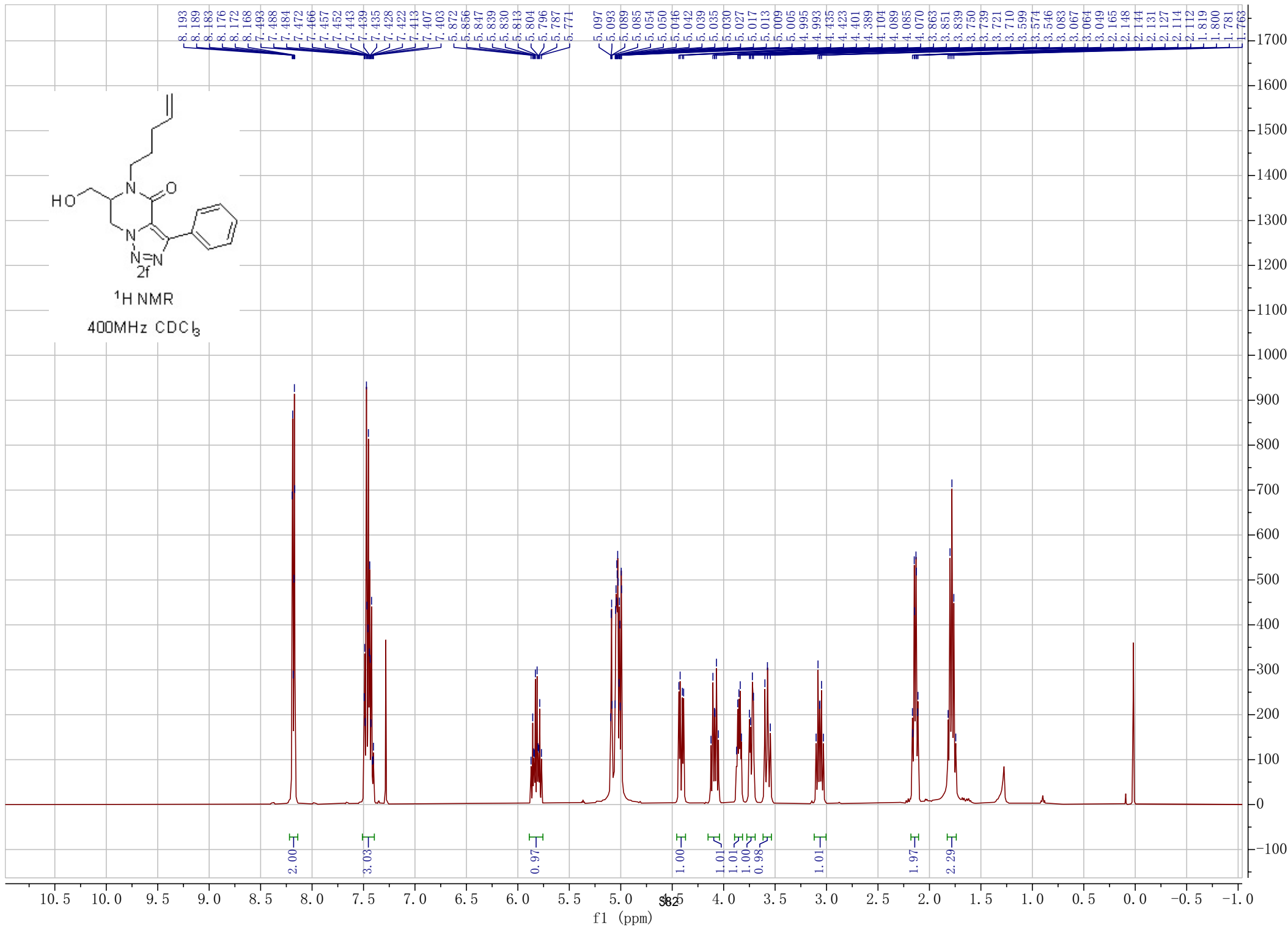
2e

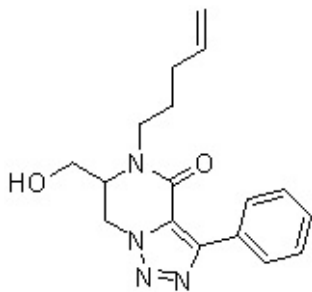
$^{13}\text{C}$  NMR  
100MHz  $\text{CDCl}_3$



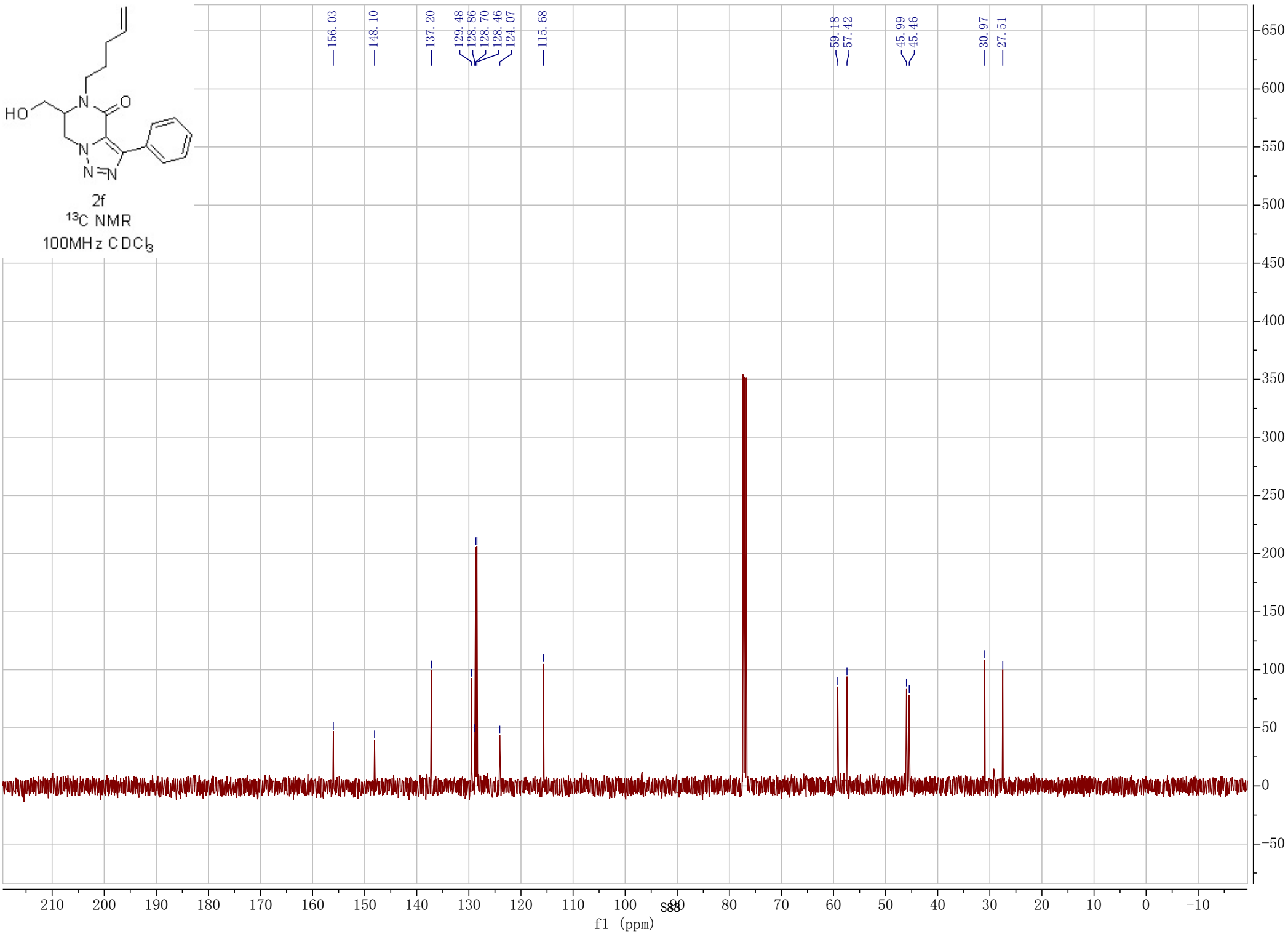


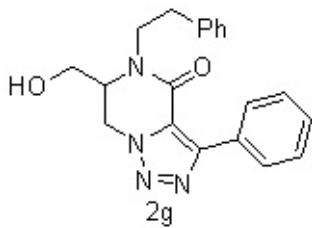
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>



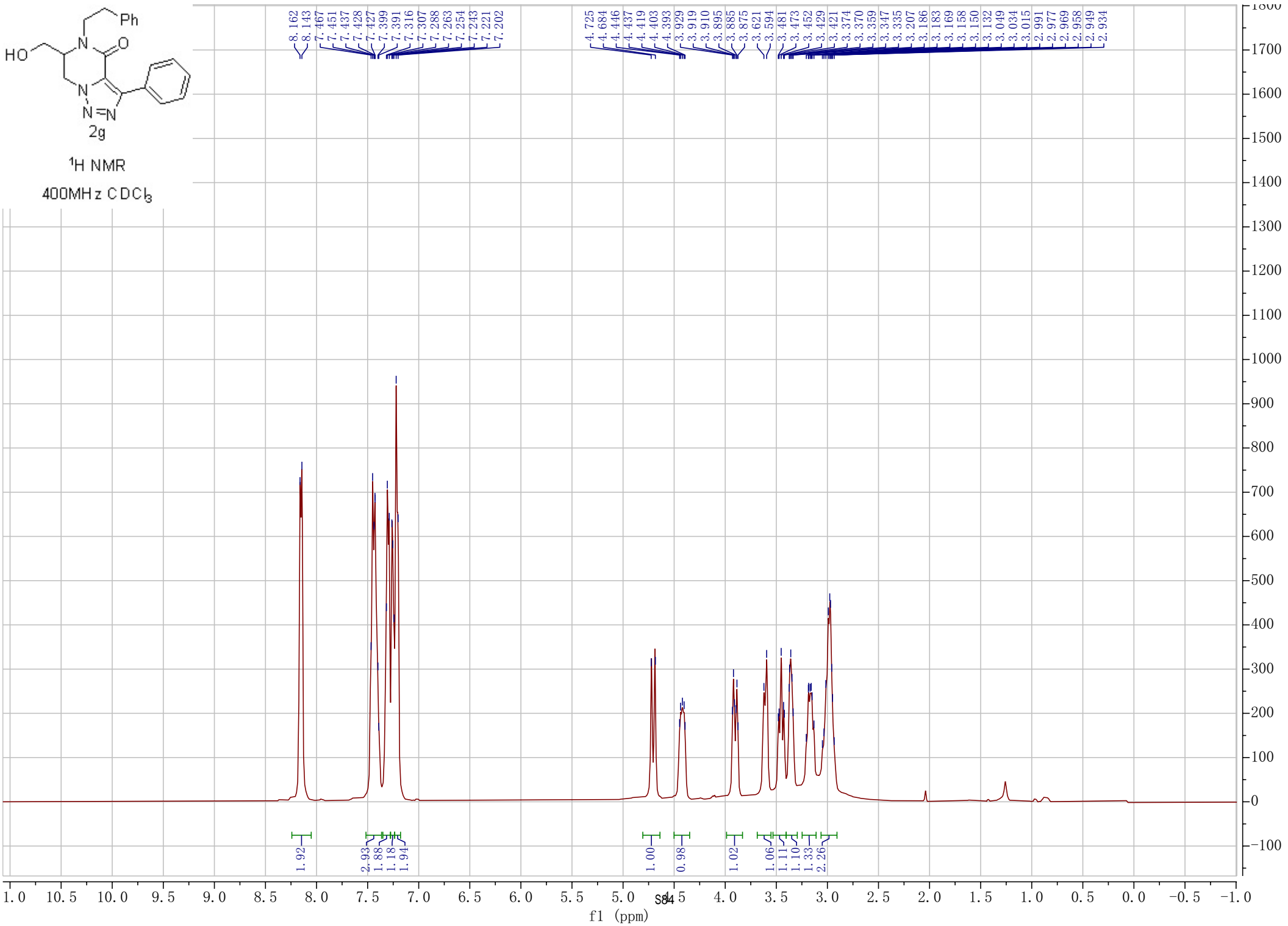


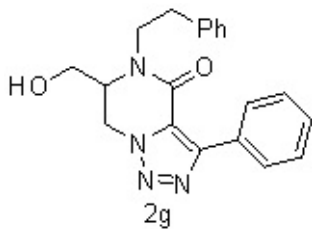
2f  
<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>



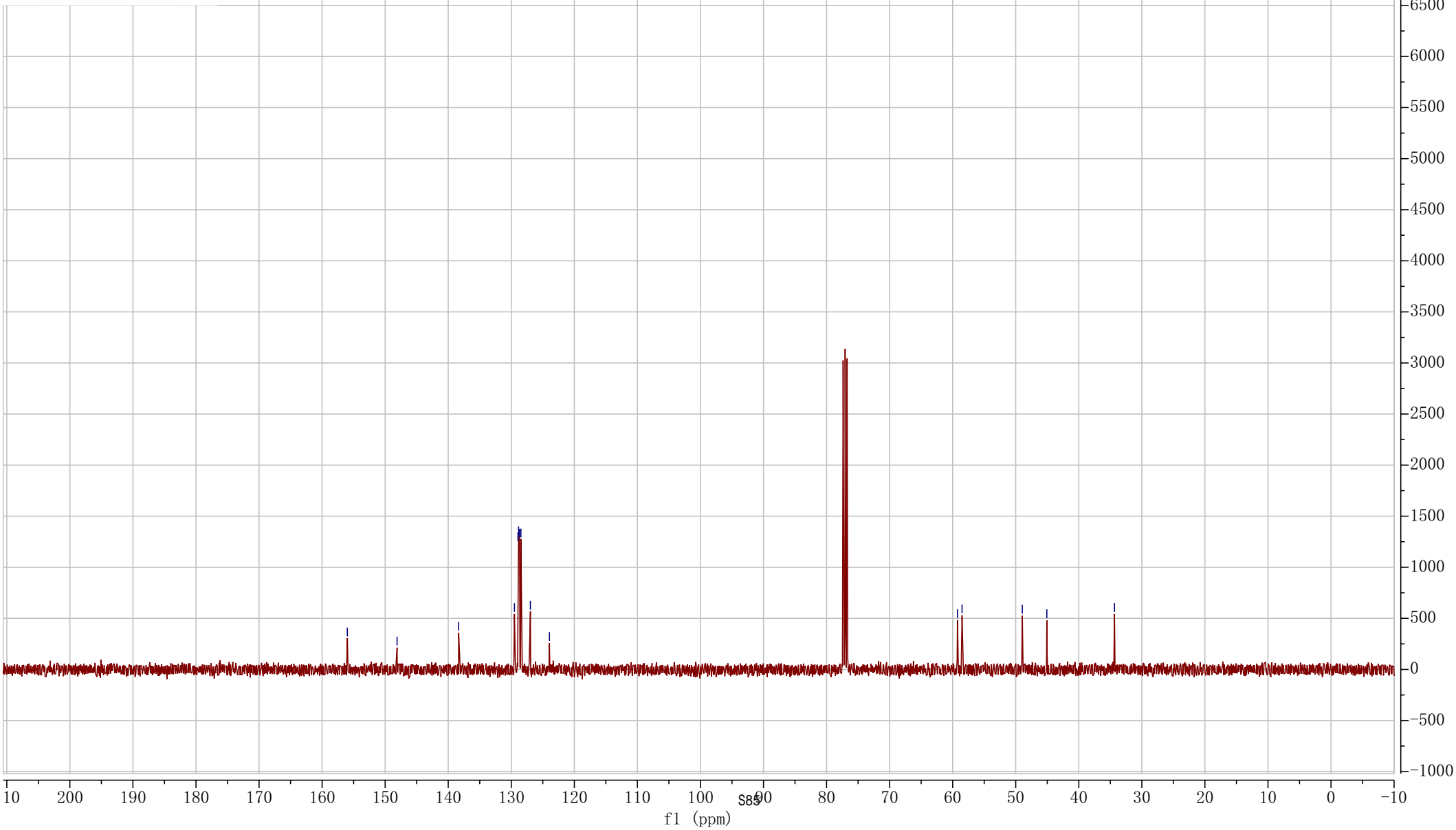


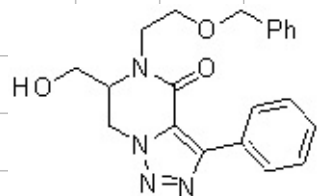
<sup>1</sup>H NMR  
400MHz  $\text{CDCl}_3$





<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

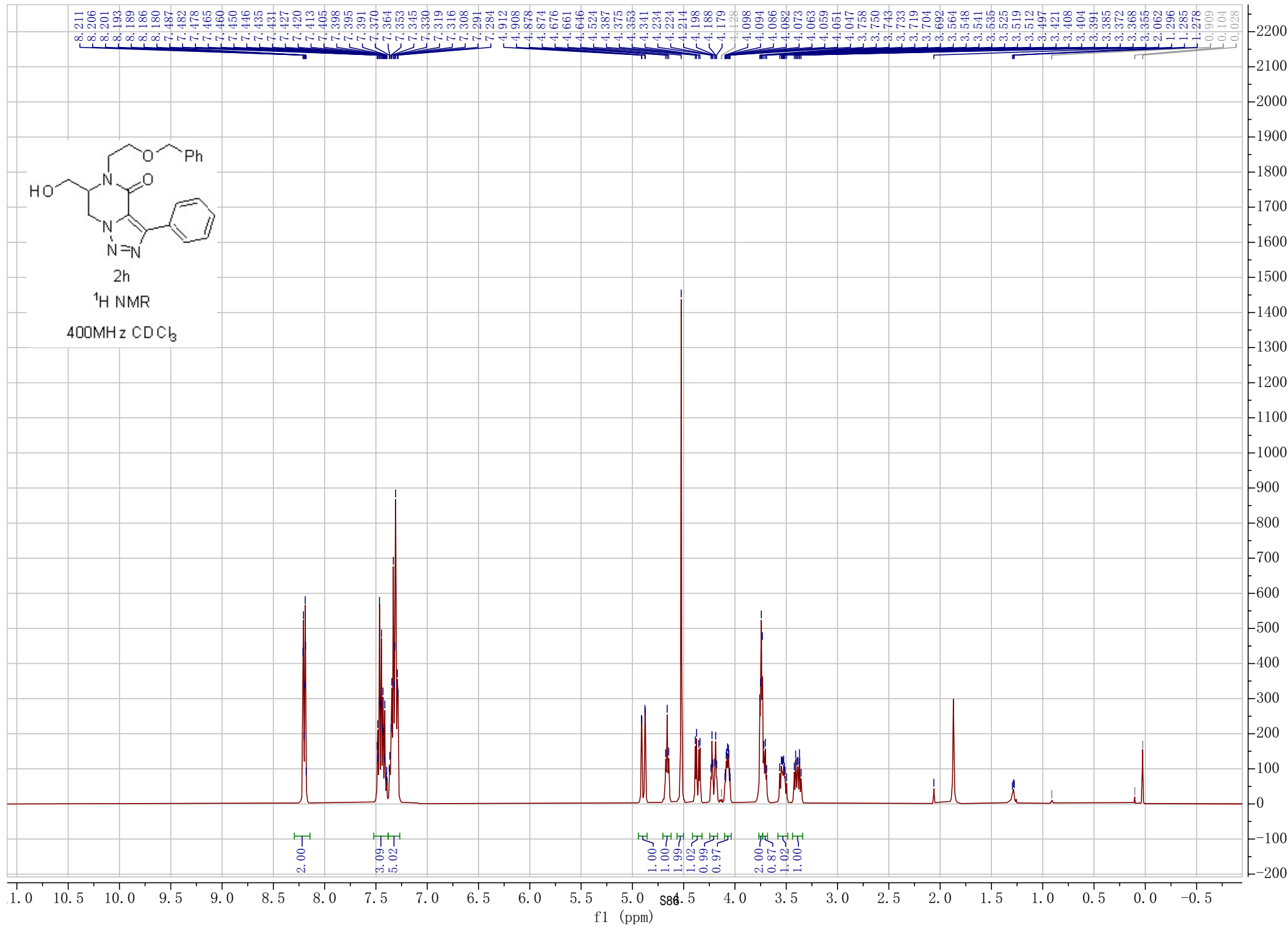


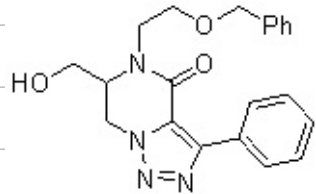


2h

<sup>1</sup>H NMR

400MHz z CDCl<sub>3</sub>

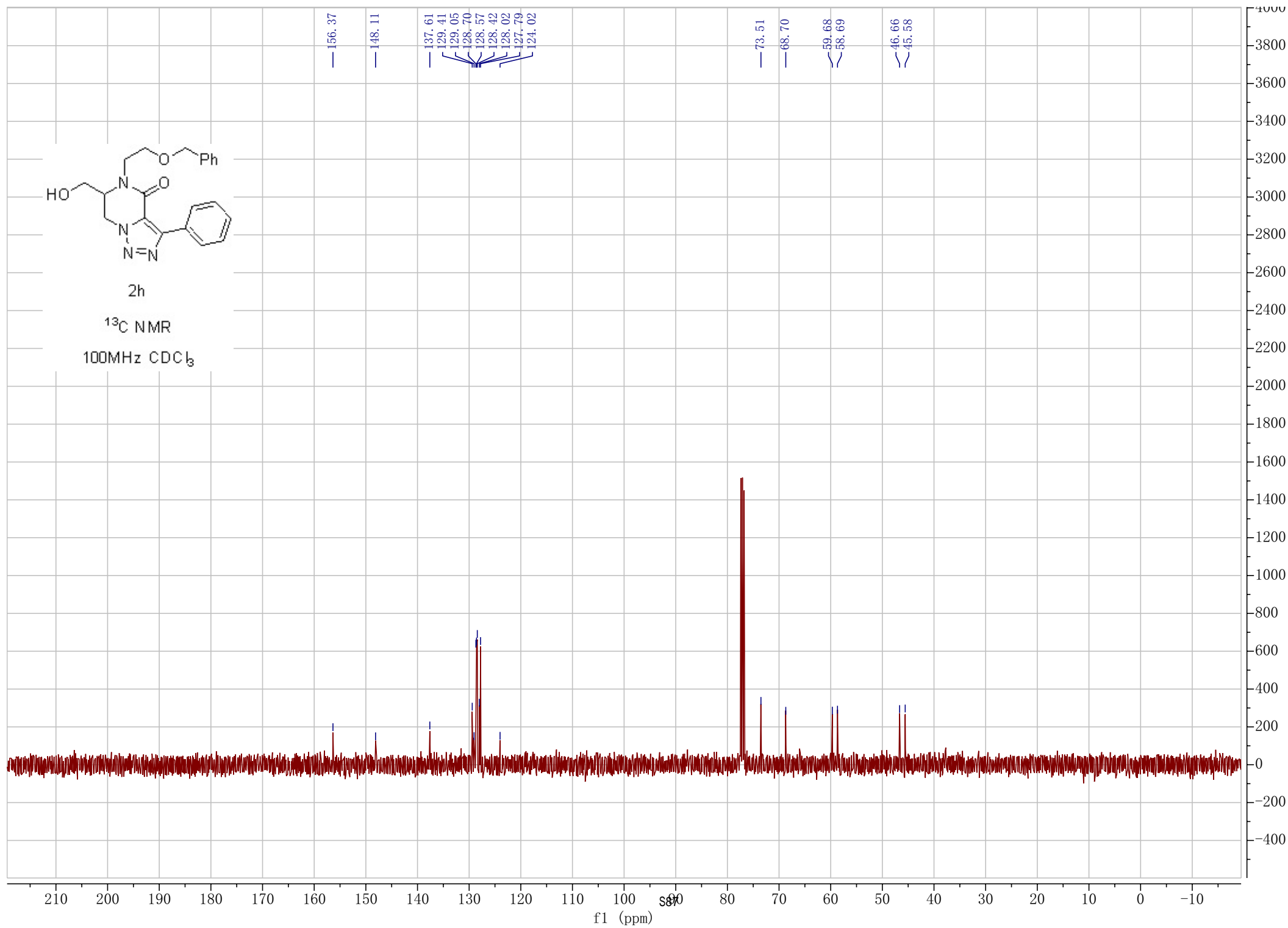


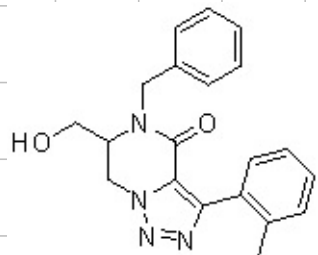


2h

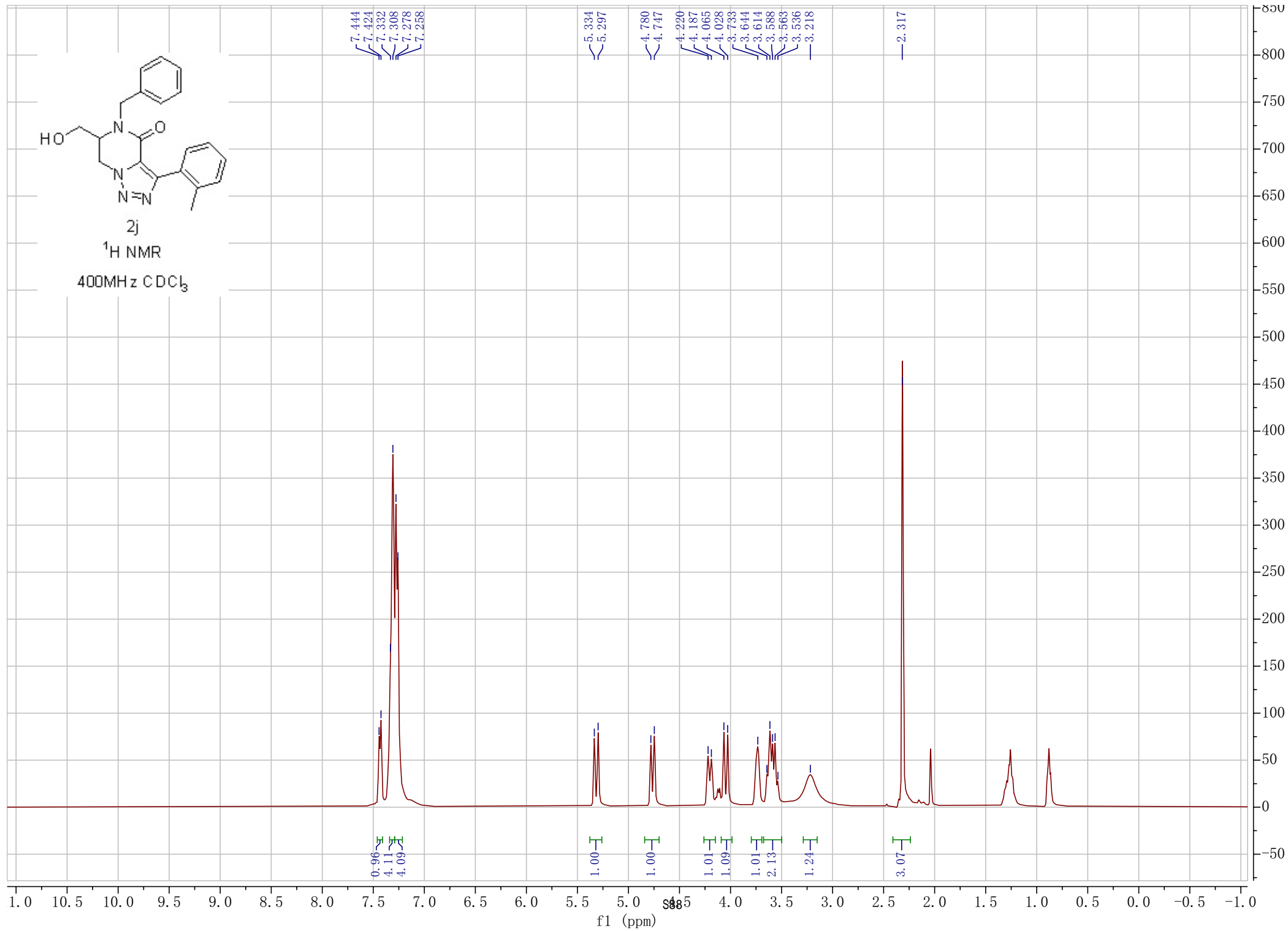
$^{13}\text{C}$  NMR

100MHz  $\text{CDCl}_3$

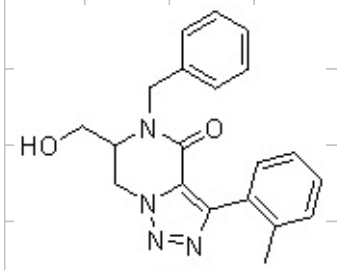




2j  
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>



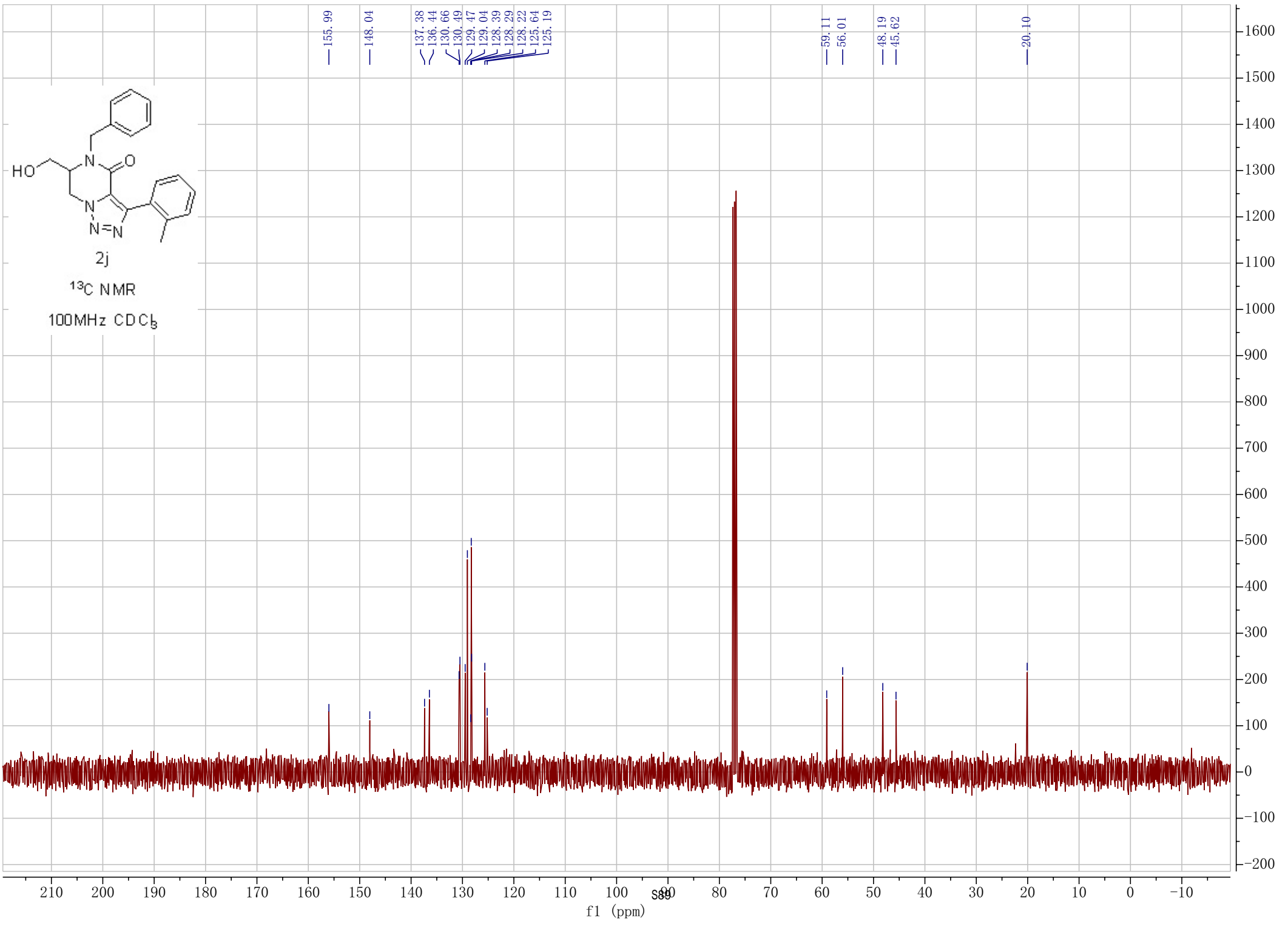


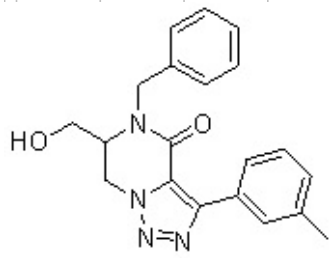


2j

<sup>13</sup>C NMR

100MHz CDCl<sub>3</sub>

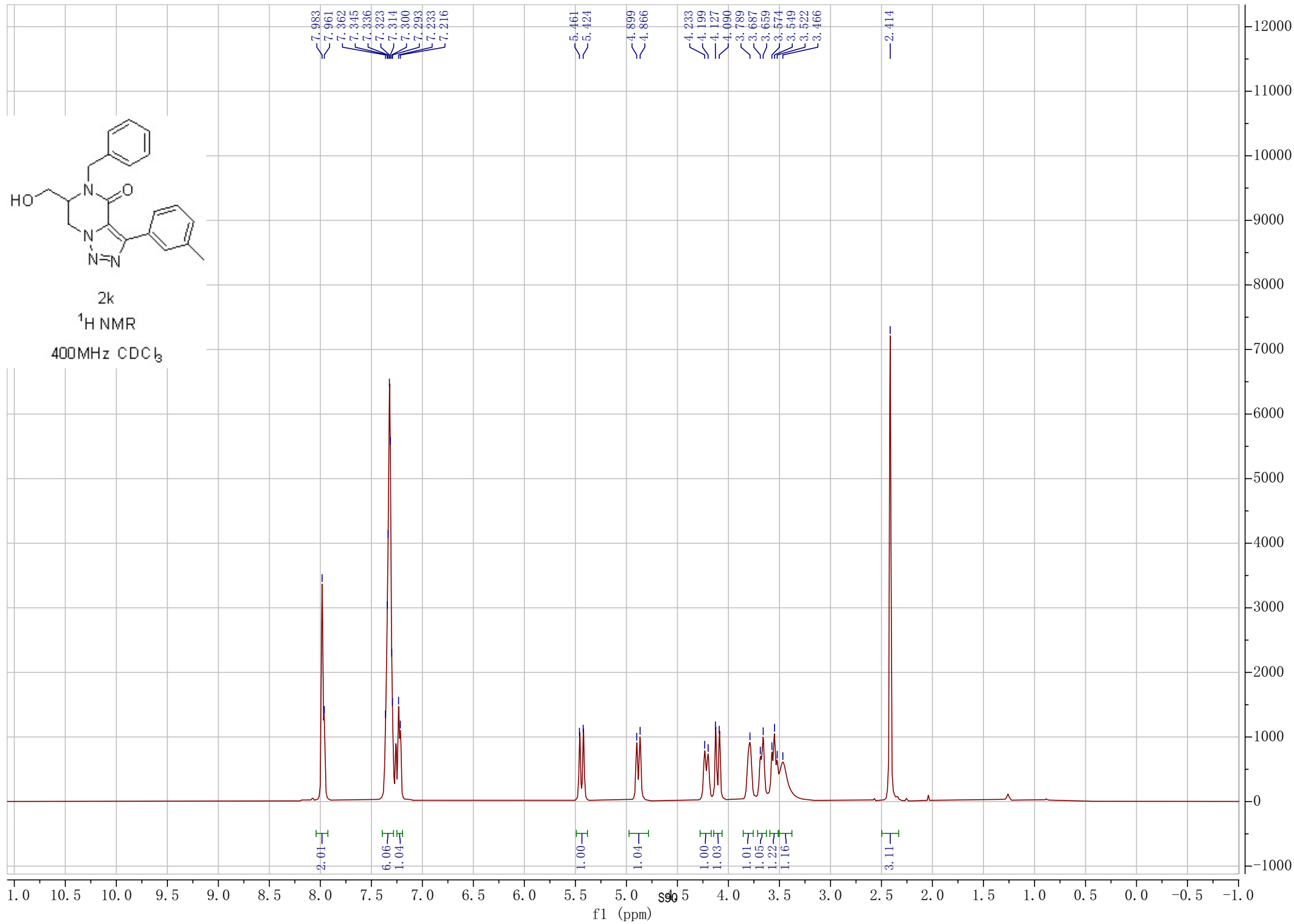


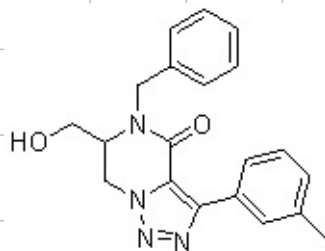


2k

<sup>1</sup>H NMR

400MHz CDCl<sub>3</sub>





2k

$^{13}\text{C}$  NMR

100MHz  $\text{CDCl}_3$

156.29  
148.54  
138.11  
136.47  
130.32  
129.31  
129.07  
129.07  
128.78  
128.38  
128.21  
125.95  
123.83

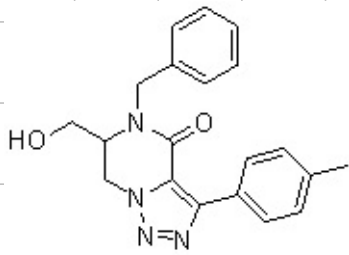
59.11  
55.95

48.53  
45.75

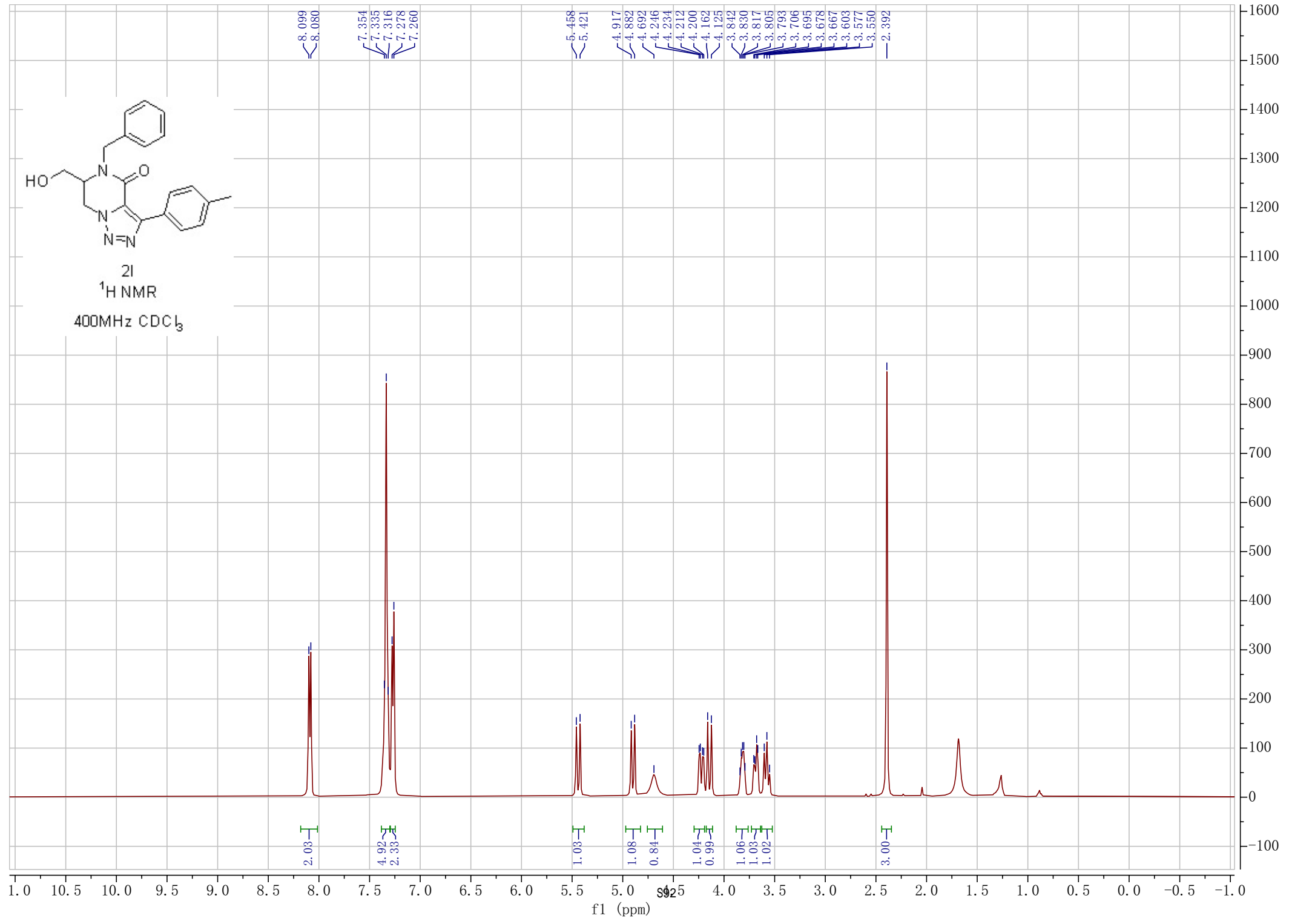
21.55

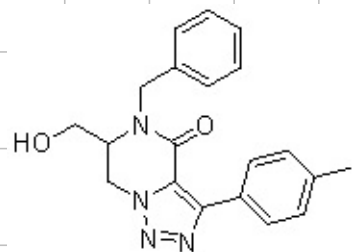
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10  
f1 (ppm)

7000  
6500  
6000  
5500  
5000  
4500  
4000  
3500  
3000  
2500  
2000  
1500  
1000  
500  
0  
-500



21  
<sup>1</sup>H NMR  
 400MHz CDCl<sub>3</sub>



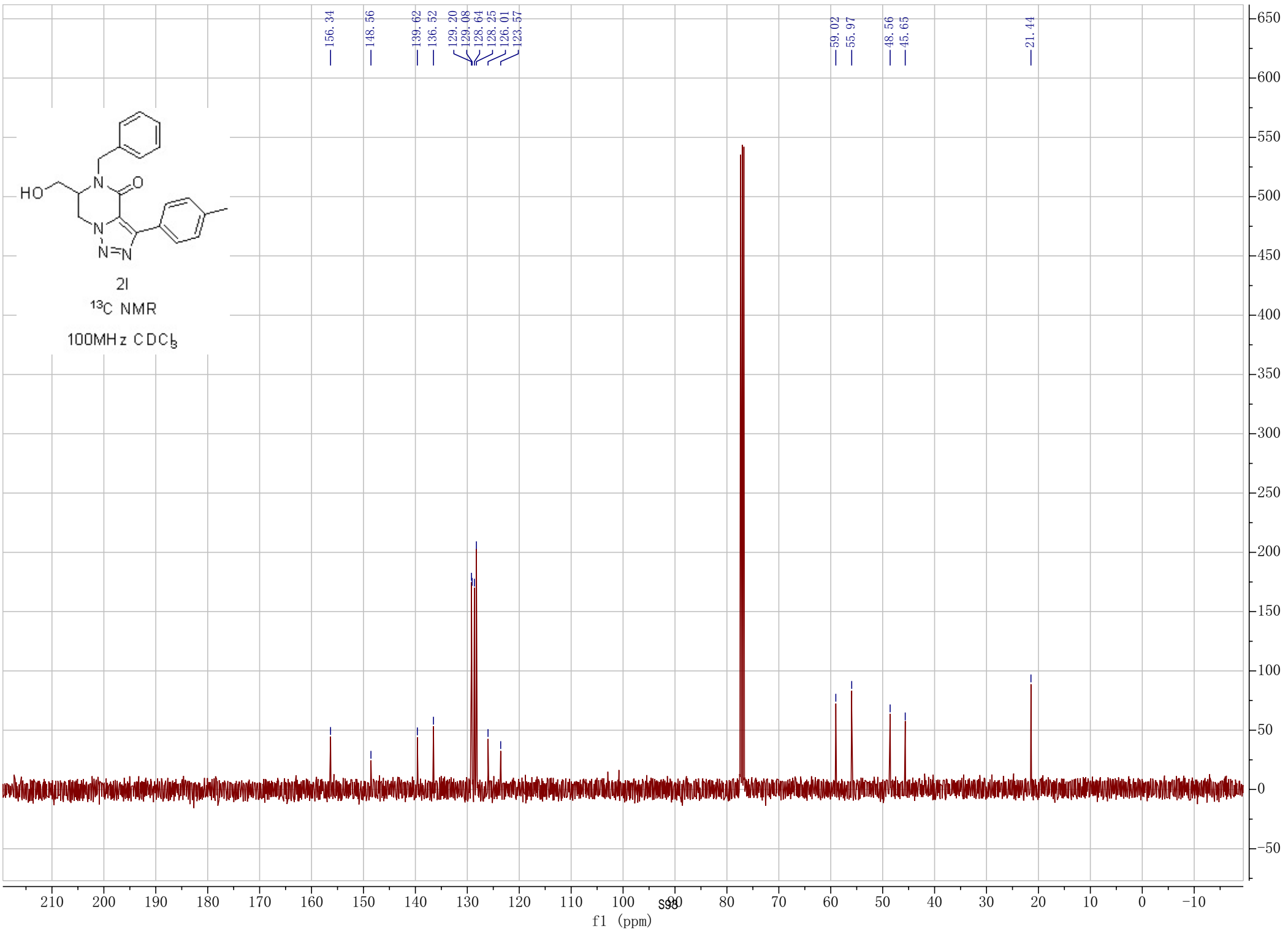


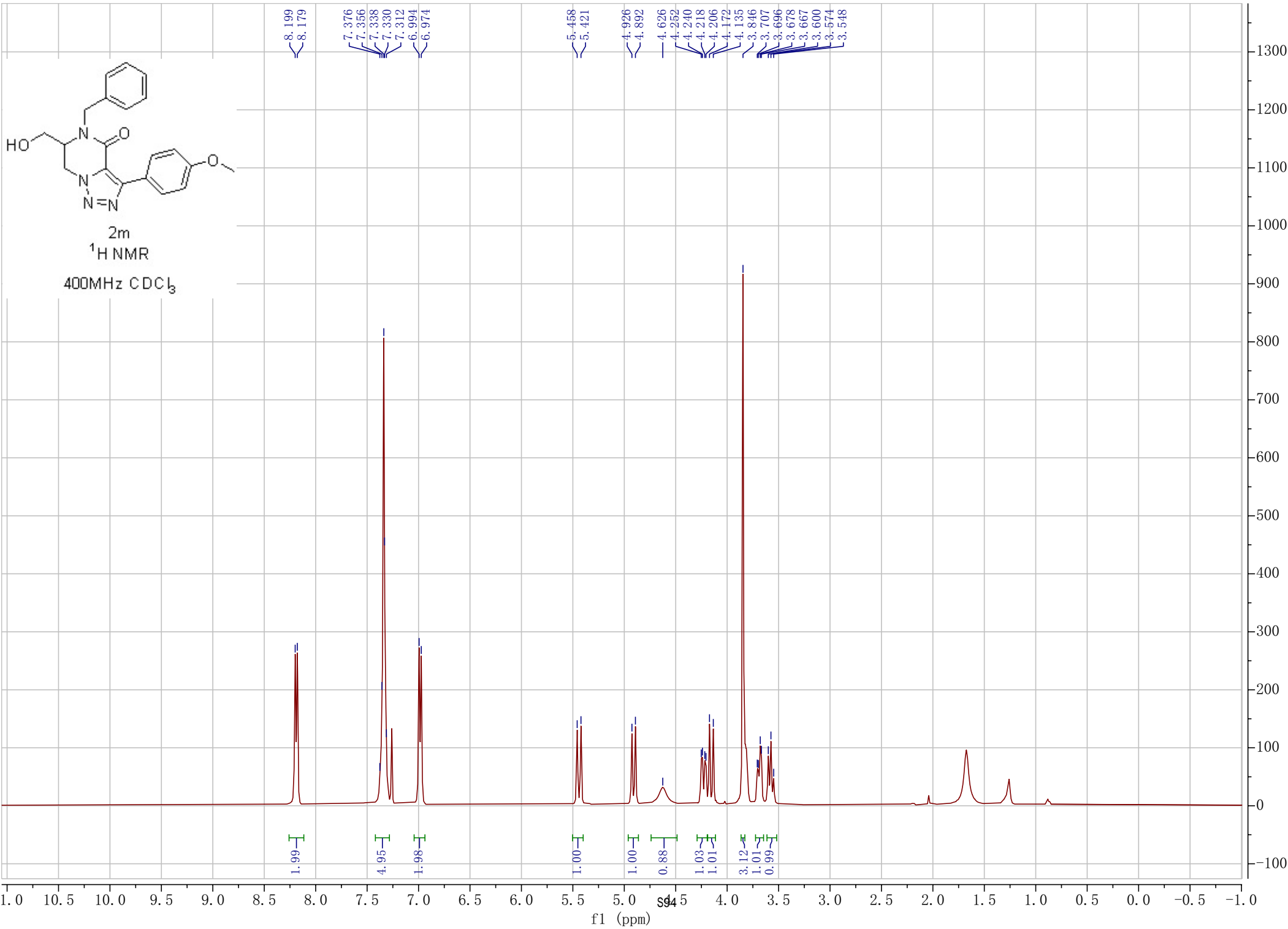
21

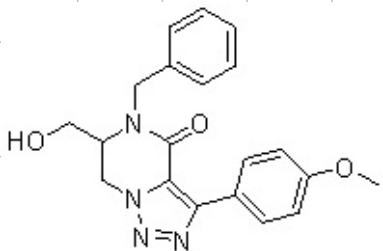
<sup>13</sup>C NMR

100MHz CDCl<sub>3</sub>

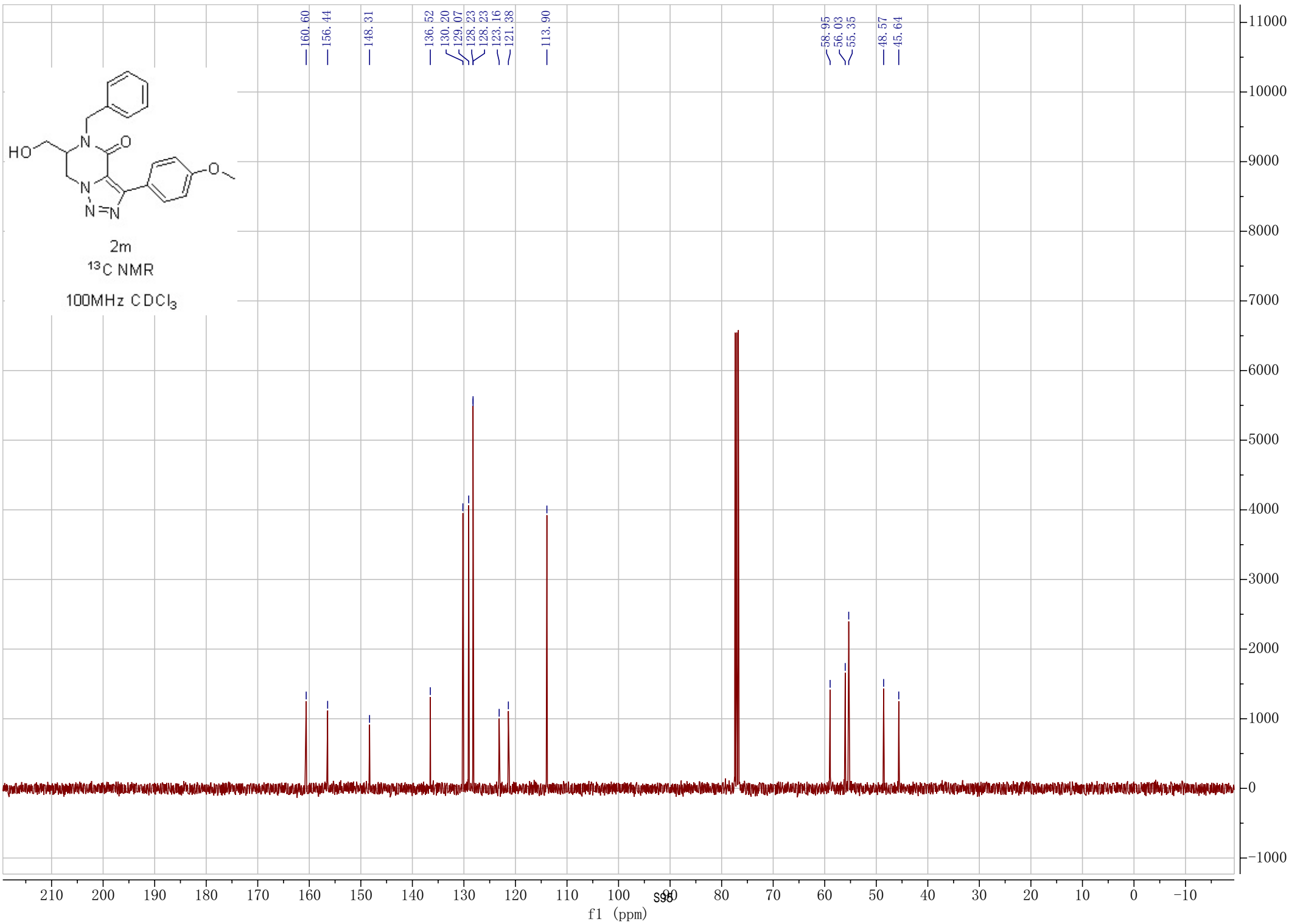
156.34  
148.56  
139.62  
136.52  
129.20  
129.08  
128.64  
128.25  
126.01  
123.57  
59.02  
55.97  
48.56  
45.65  
21.44

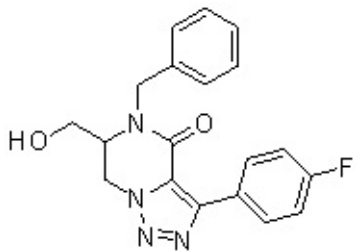






2m  
<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

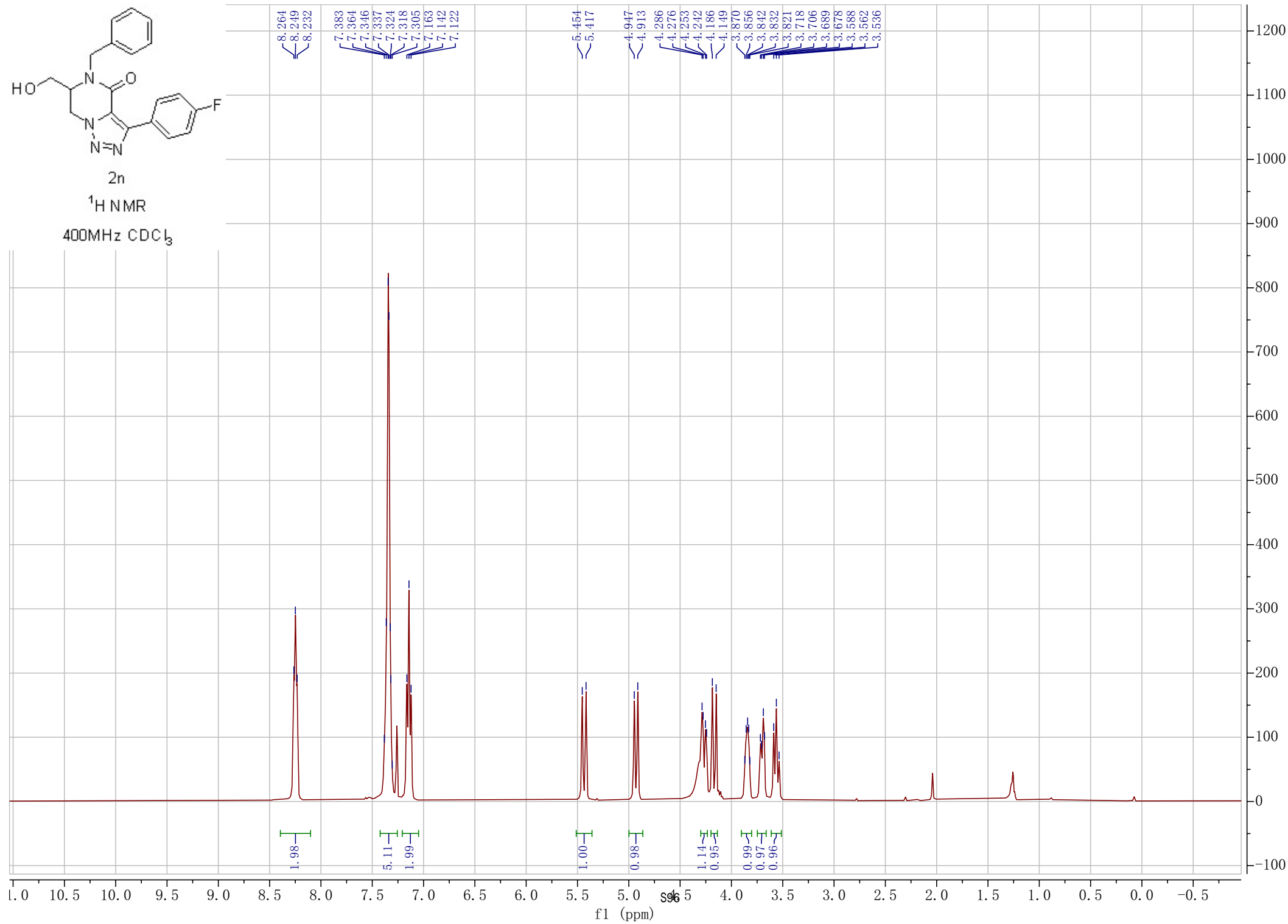




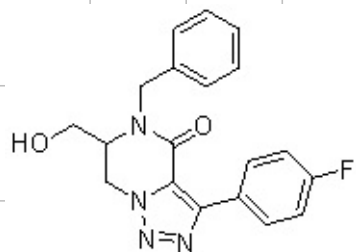
2n

<sup>1</sup>H NMR

400MHz CDCl<sub>3</sub>







2n

$^{13}\text{C}$  NMR

100MHz  $\text{CDCl}_3$

156.30

147.57

136.34

130.81

130.73

129.14

128.34

128.23

125.10

123.68

115.62

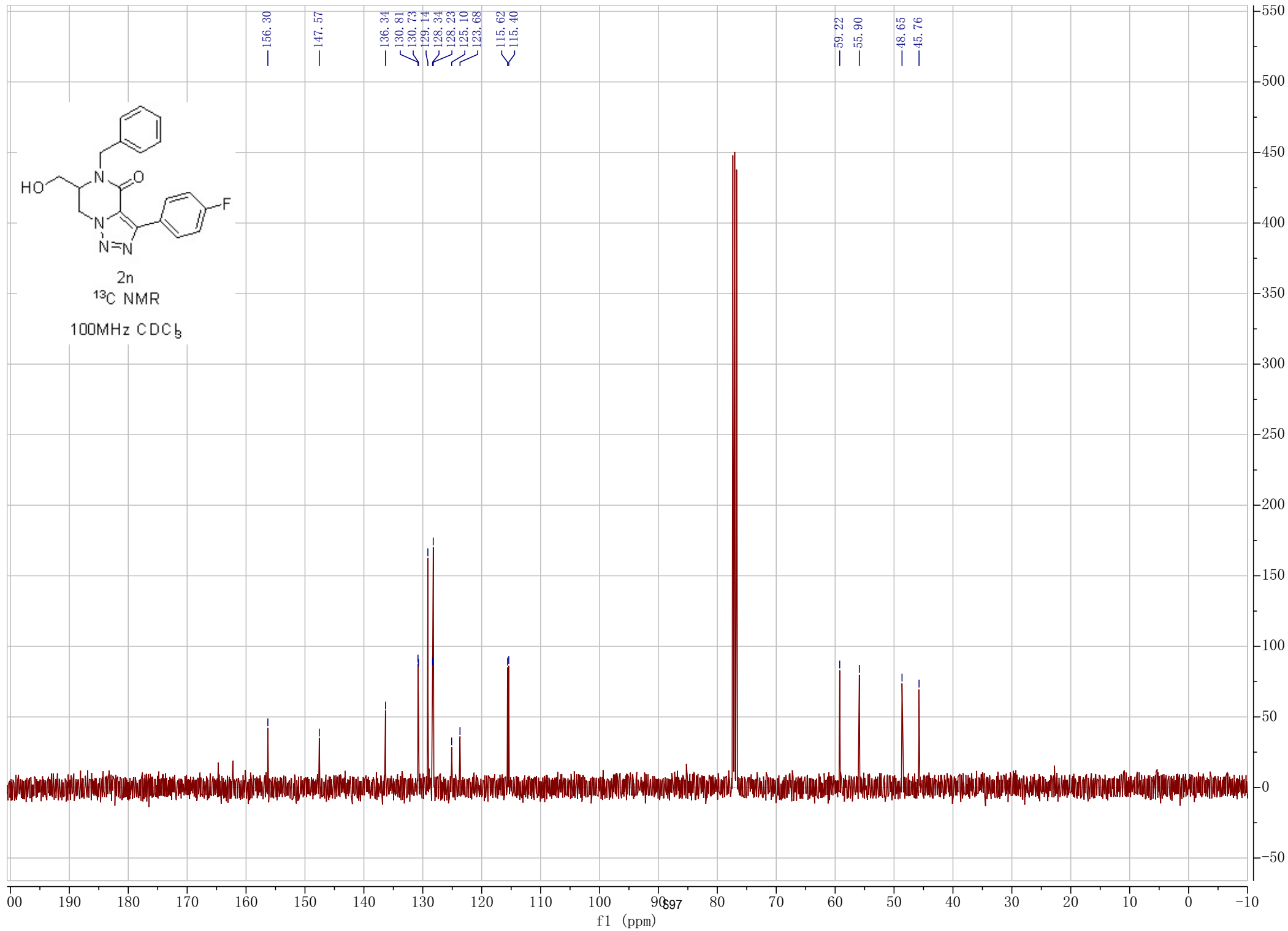
115.40

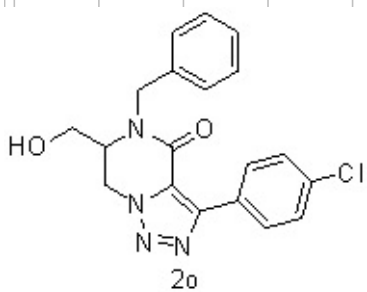
59.22

55.90

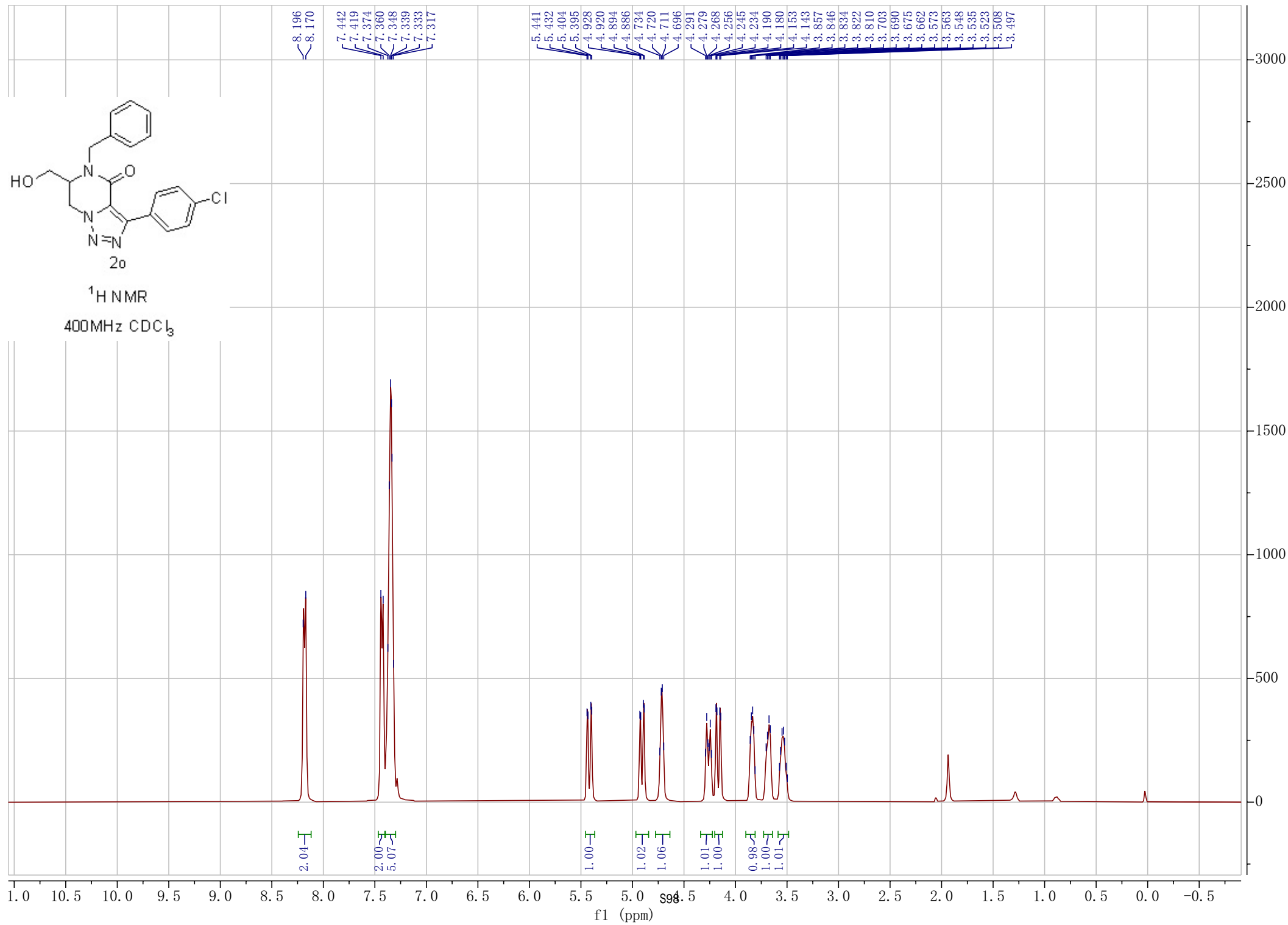
48.65

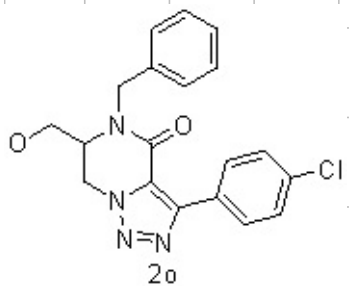
45.76



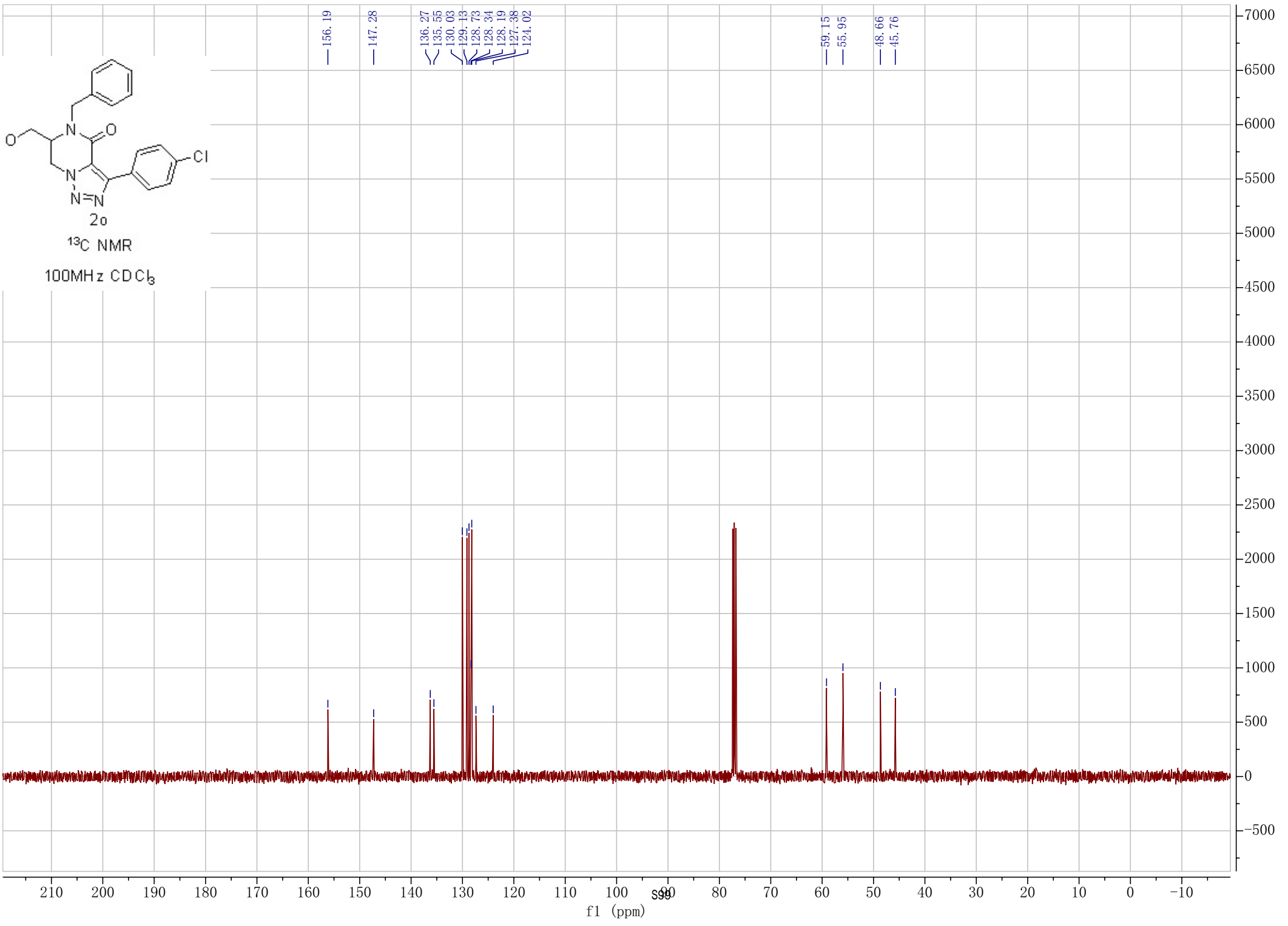


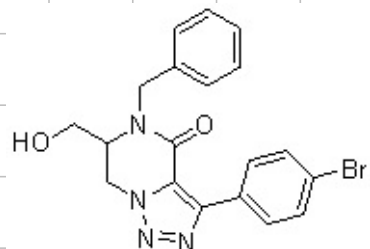
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>





<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

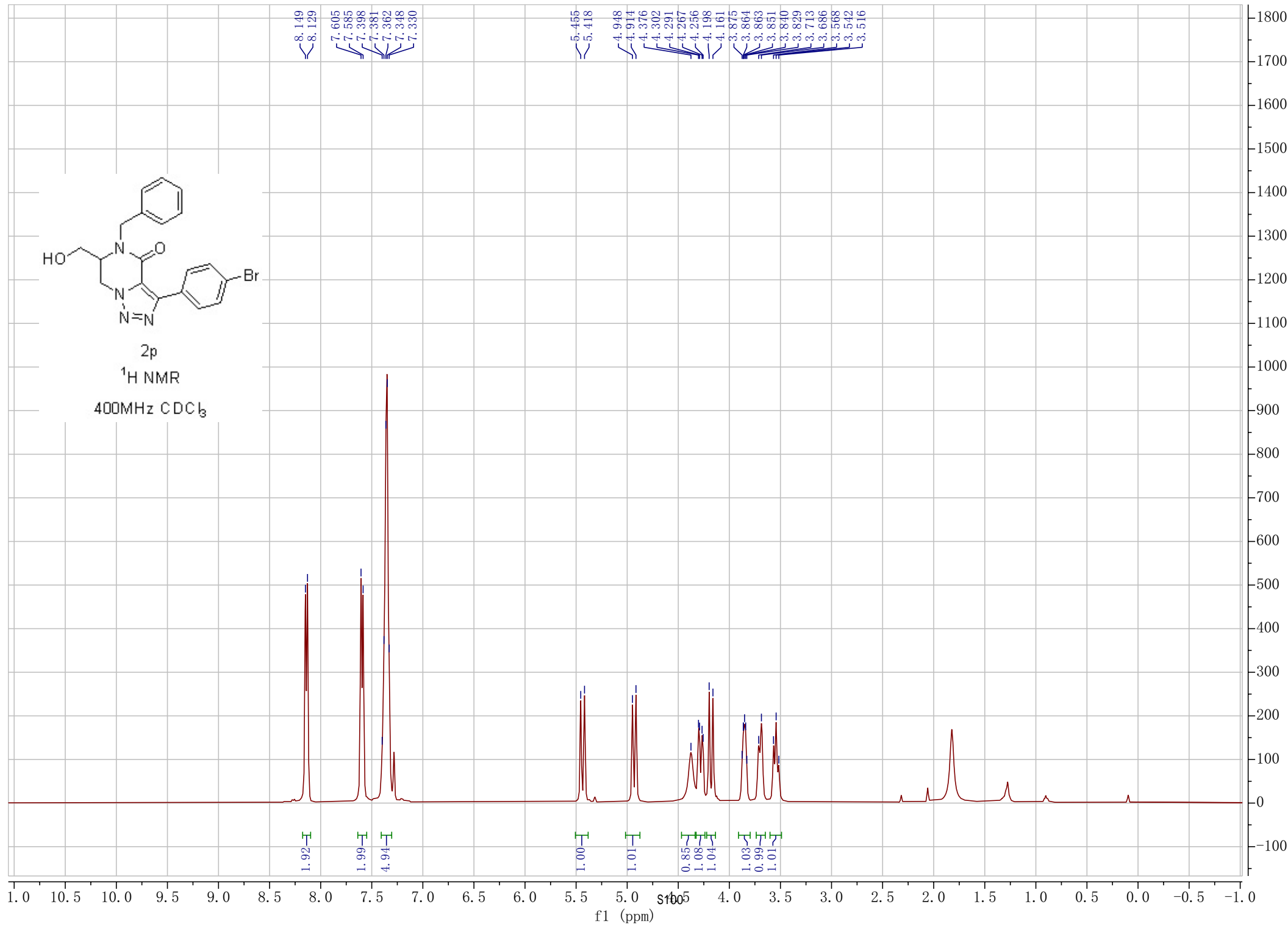


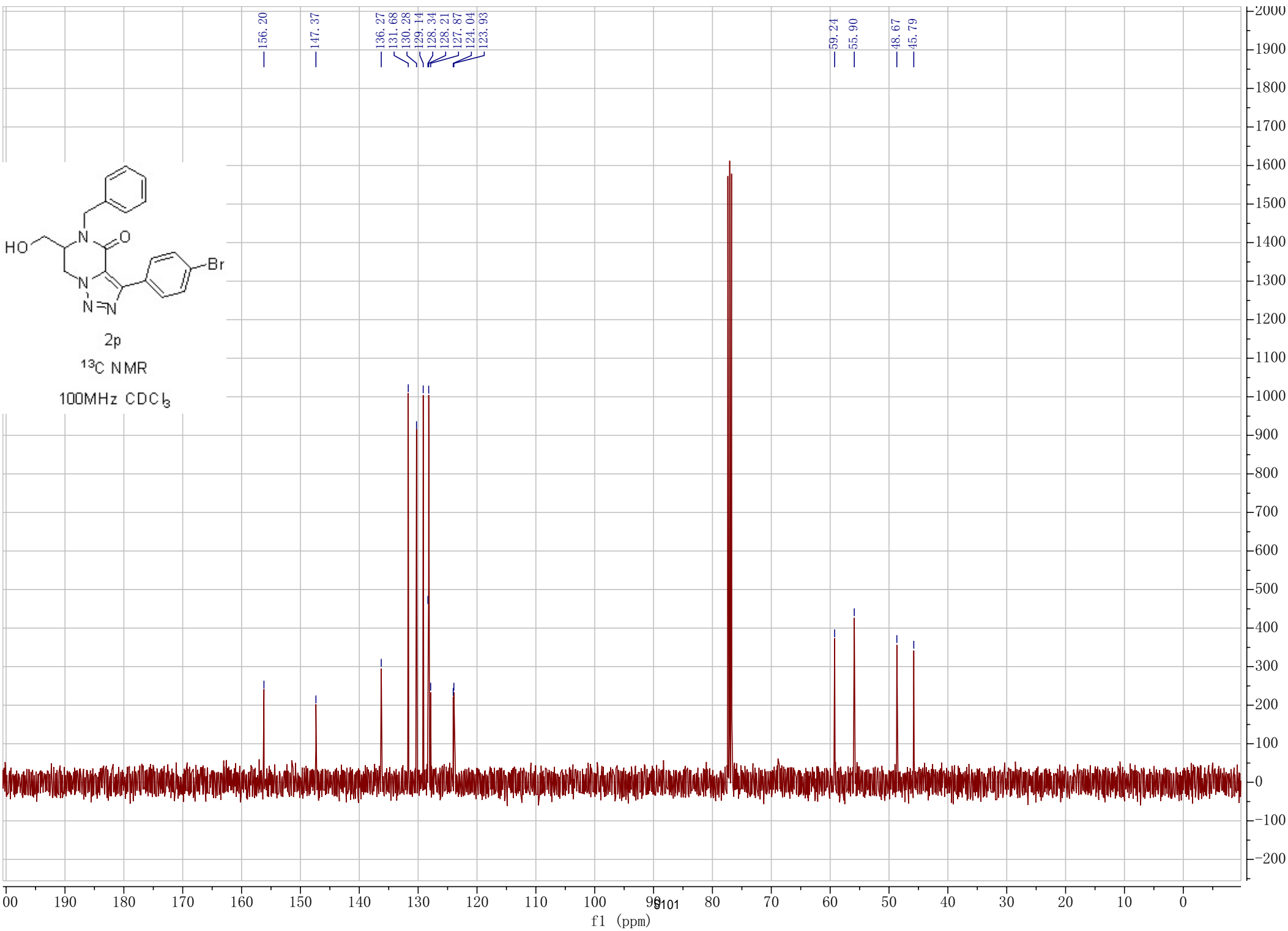


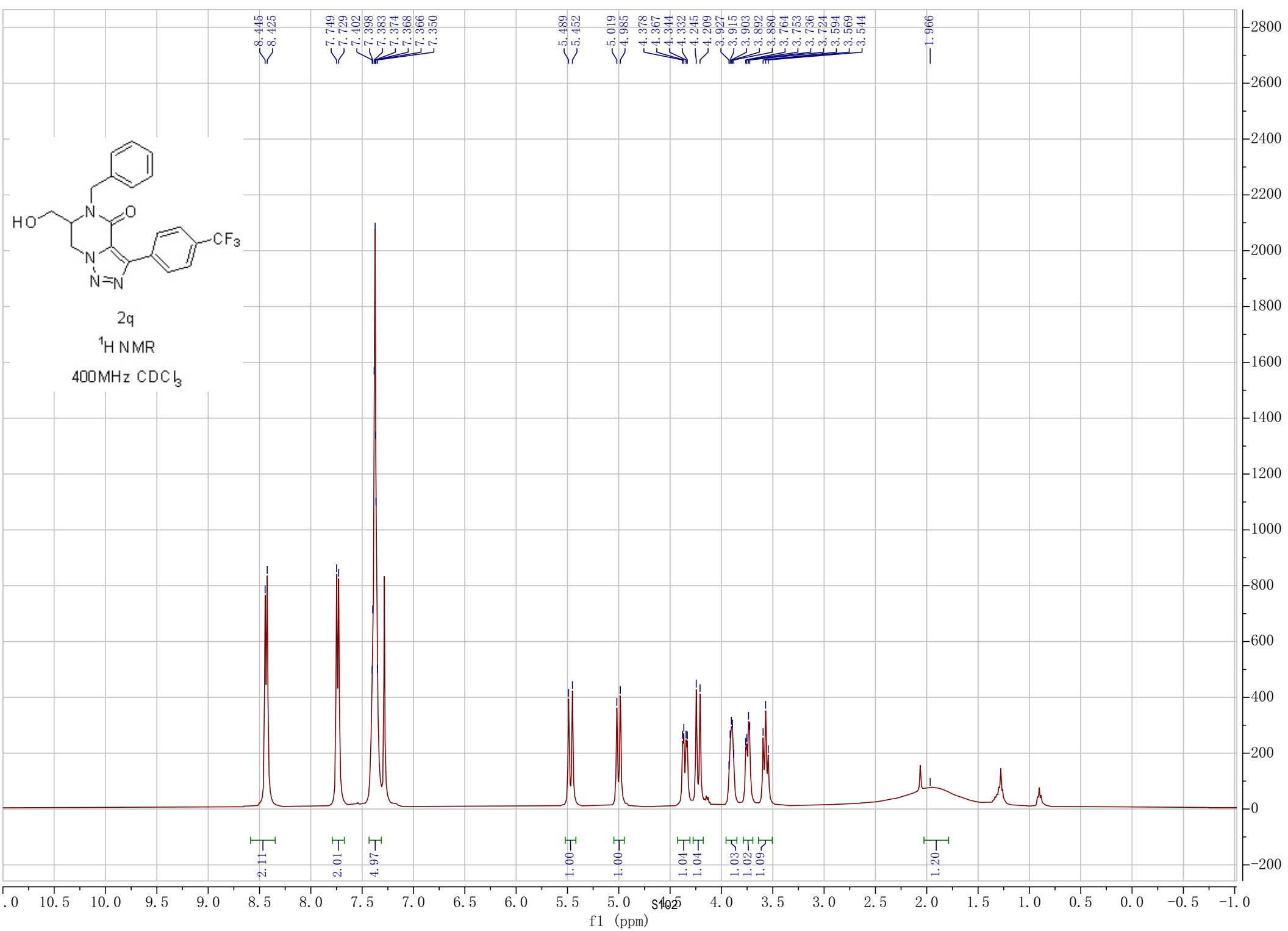
2p

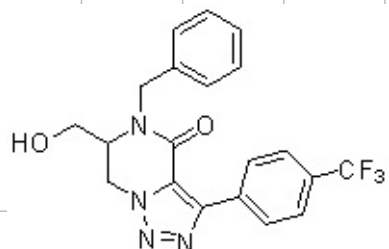
<sup>1</sup>H NMR

400MHz CDCl<sub>3</sub>







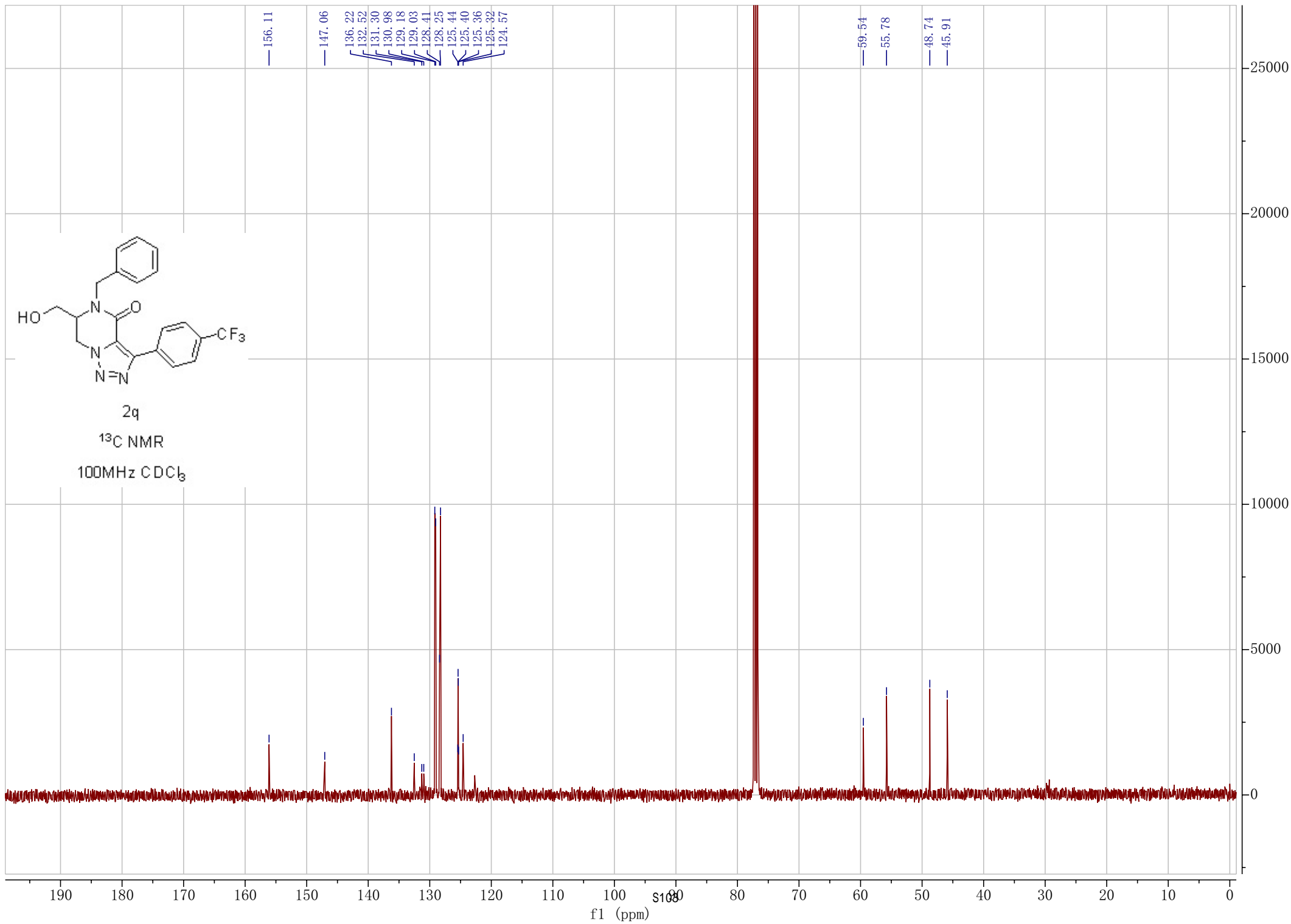


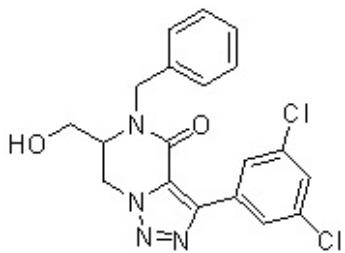
2q

<sup>13</sup>C NMR

100MHz CDCl<sub>3</sub>

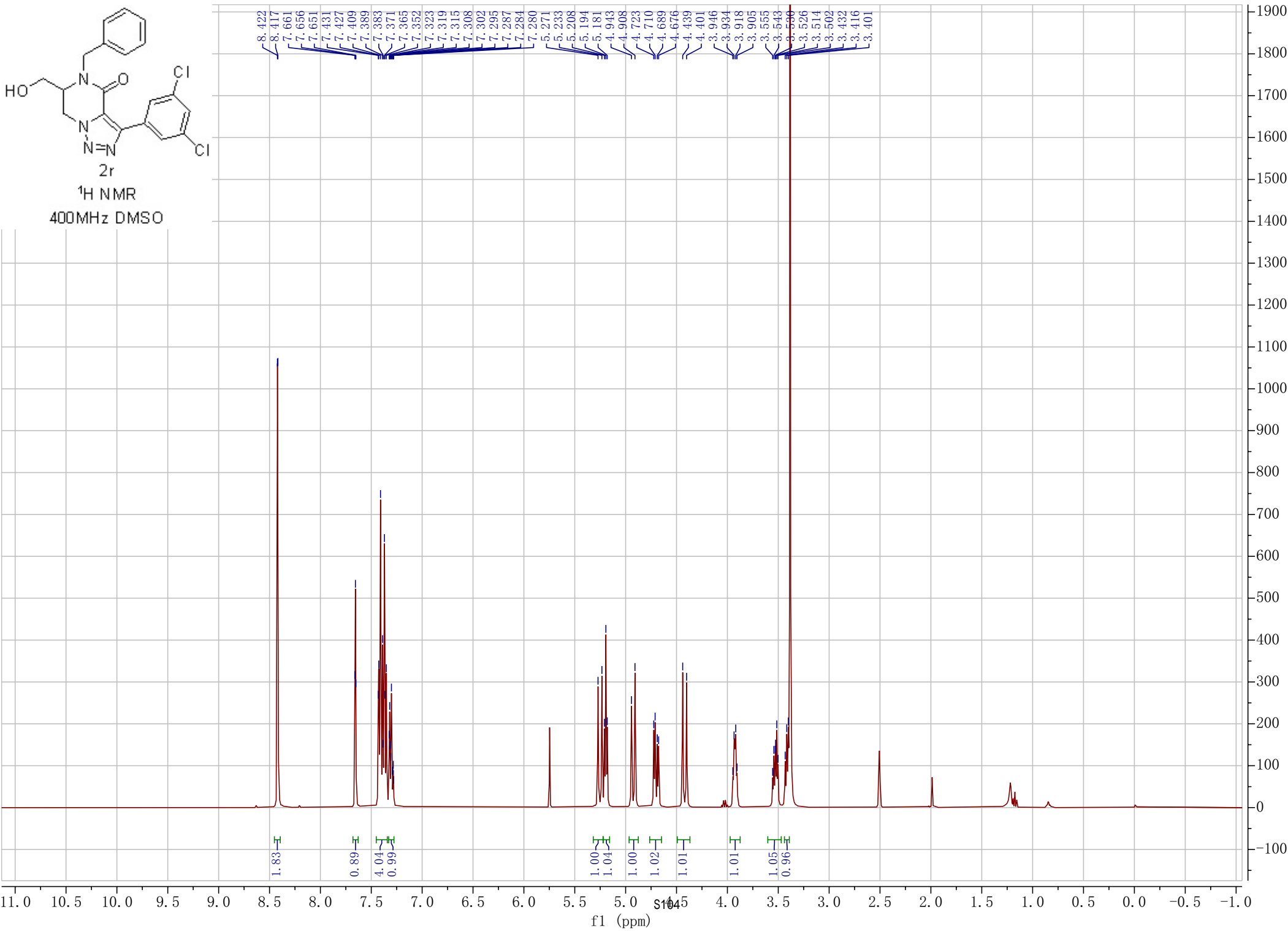
156.11  
147.06  
136.22  
132.52  
131.30  
130.98  
129.18  
129.03  
128.41  
128.25  
125.44  
125.40  
125.36  
125.32  
124.57  
59.54  
55.78  
48.74  
45.91



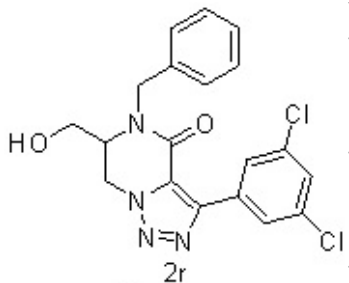


2r

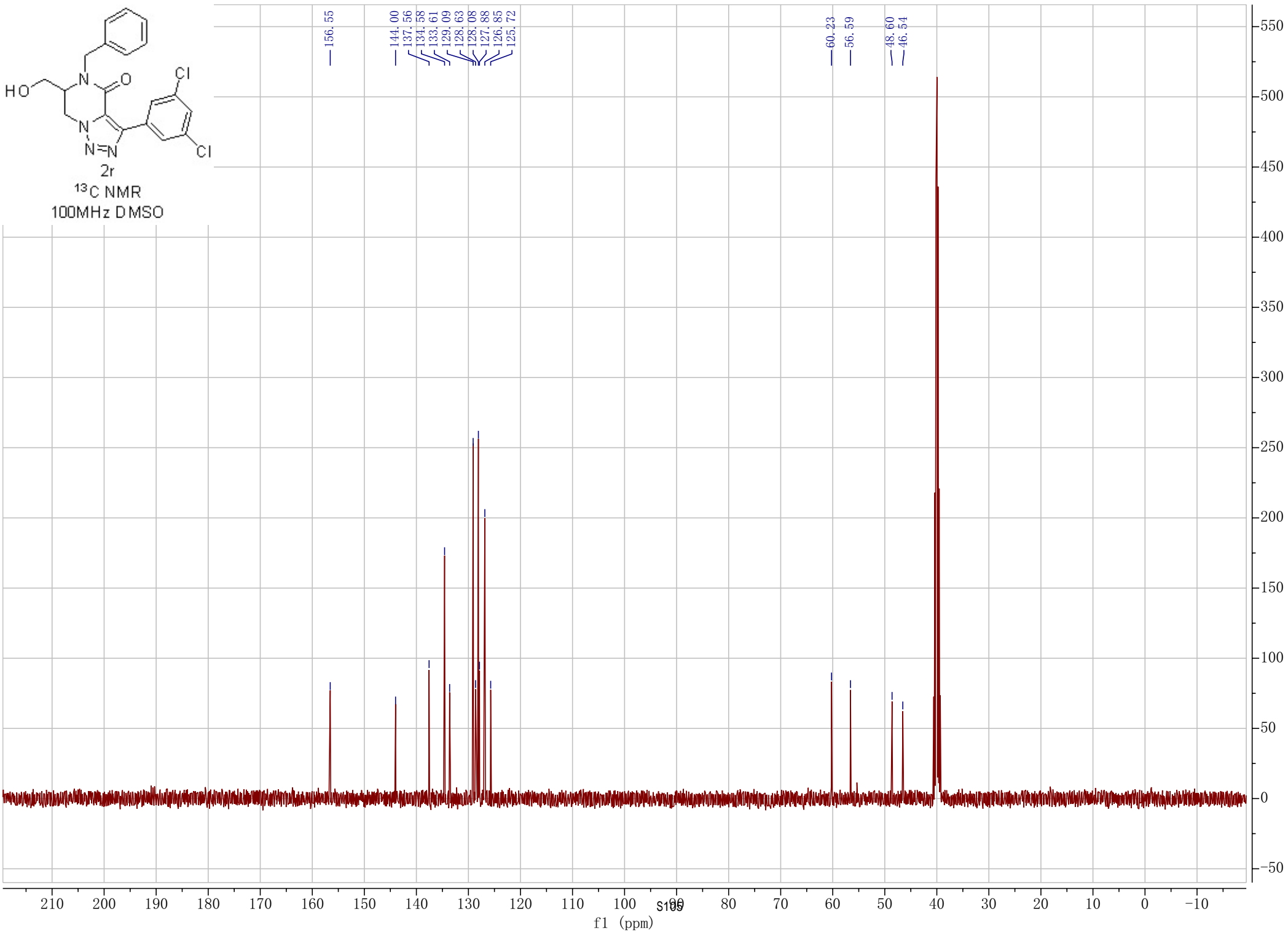
<sup>1</sup>H NMR  
400MHz DMSO

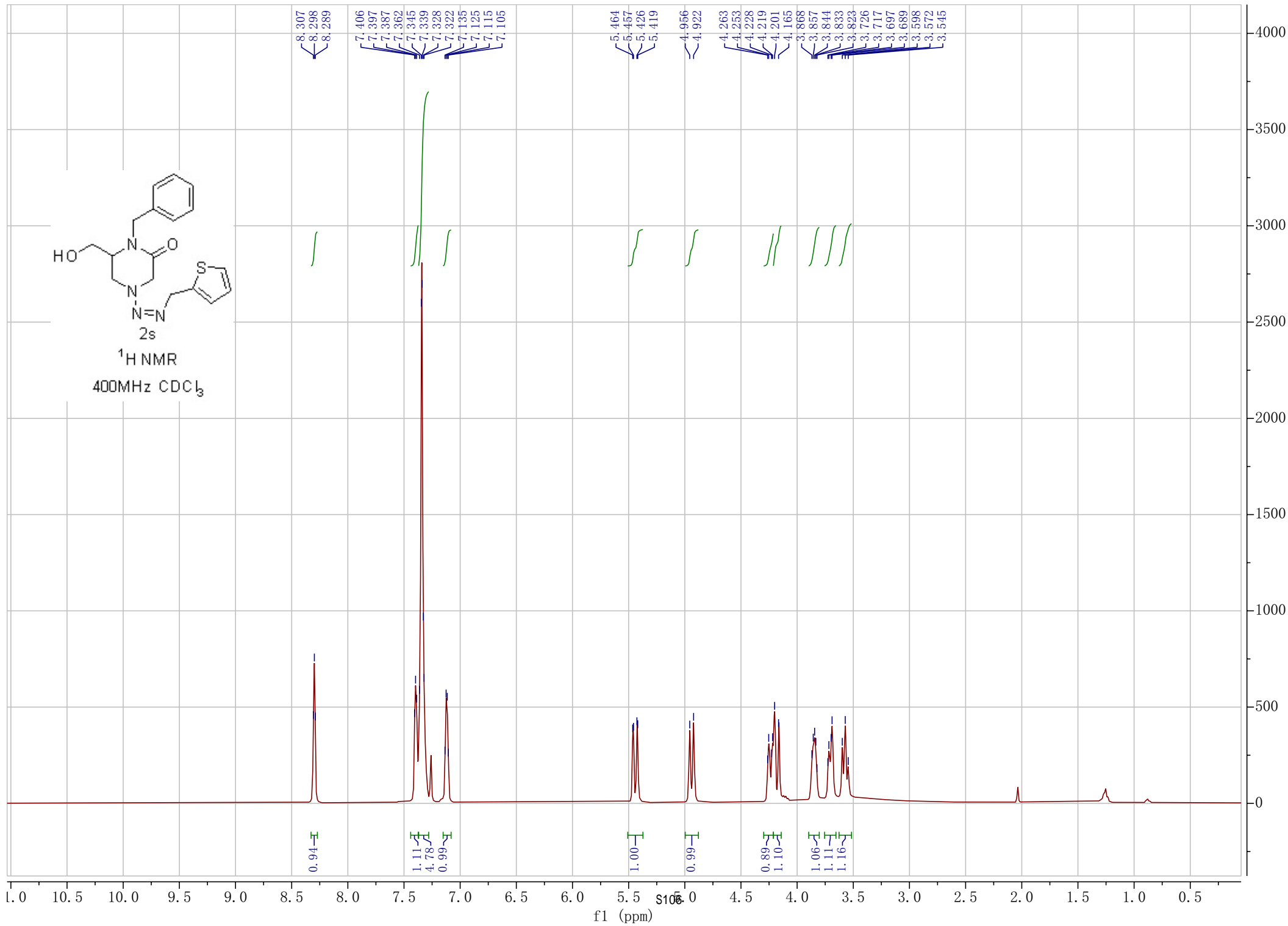
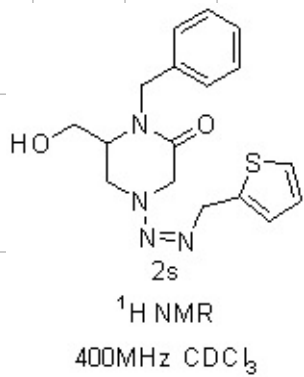


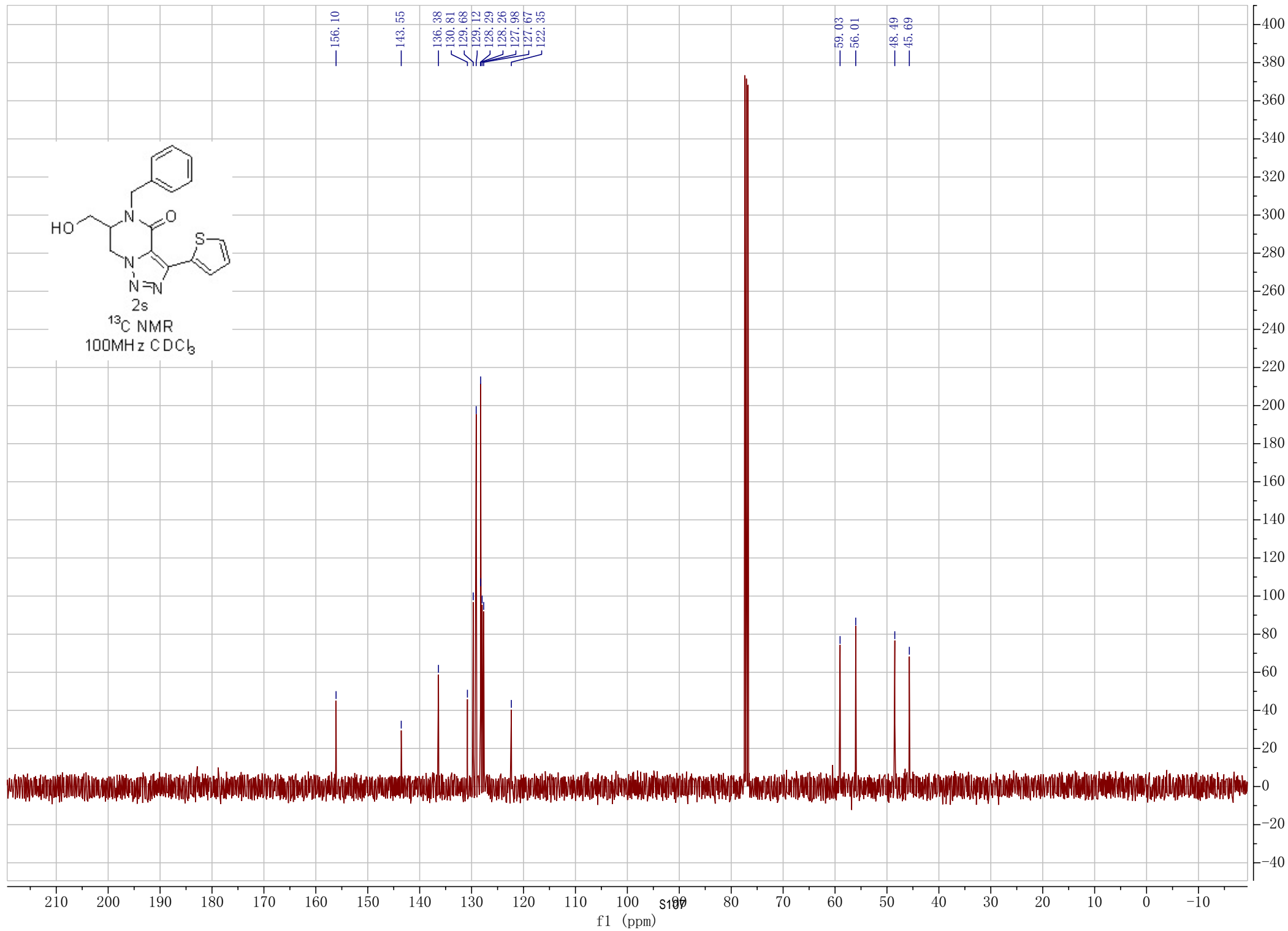
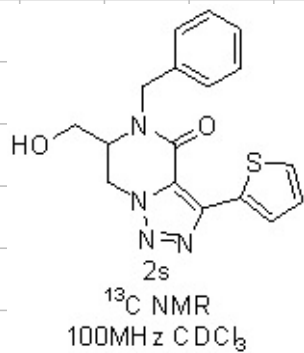


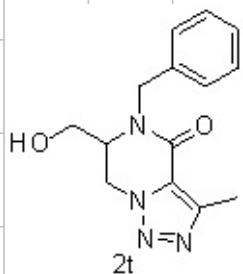


<sup>13</sup>C NMR  
100MHz DMSO

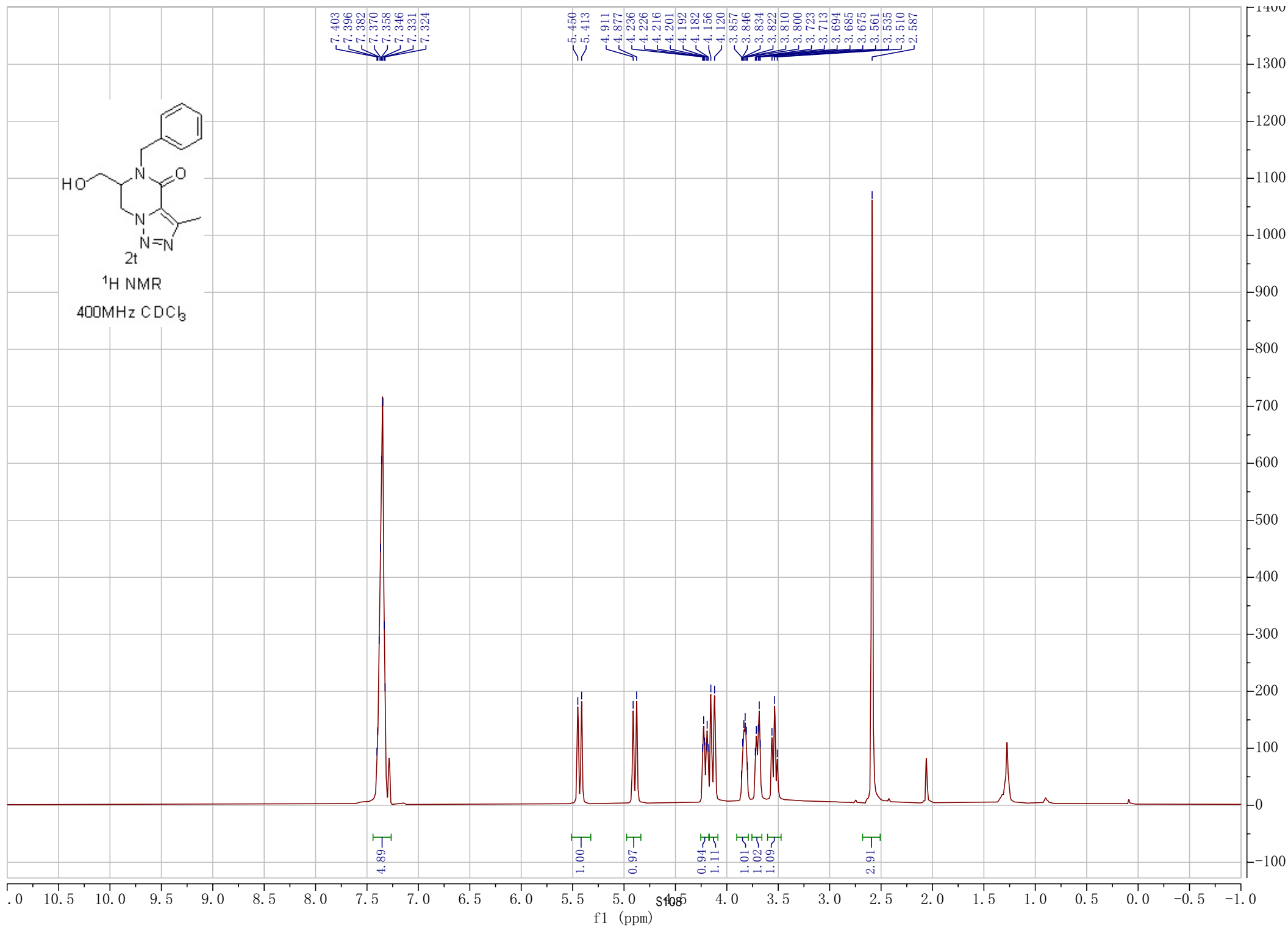


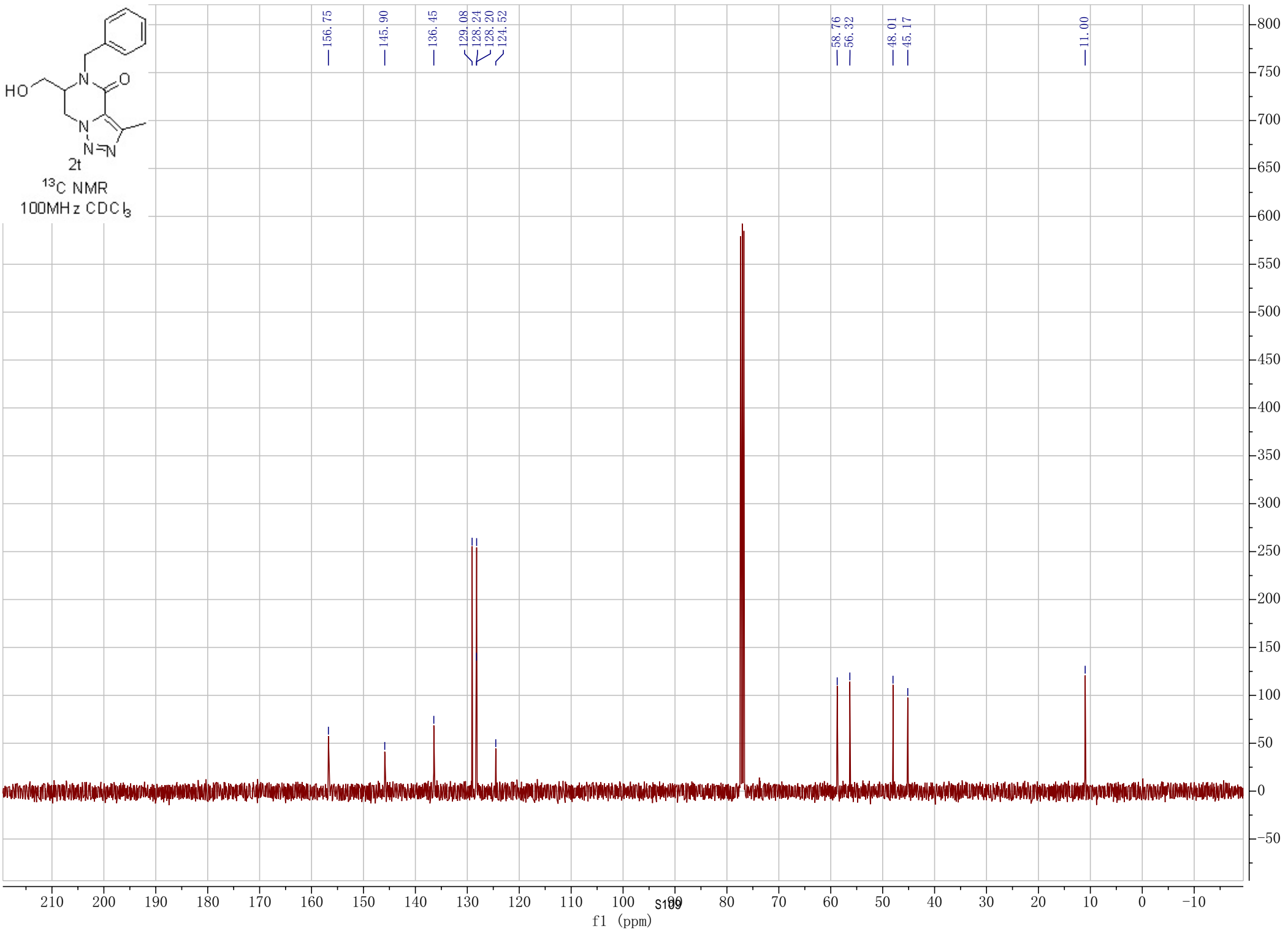
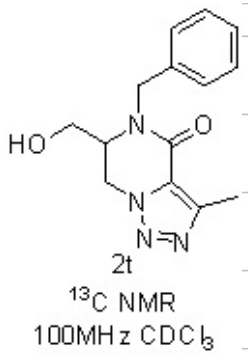


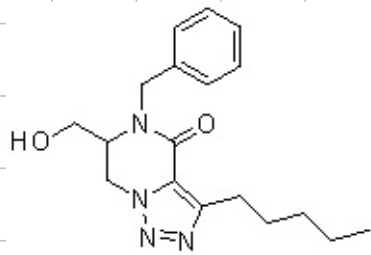




<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>

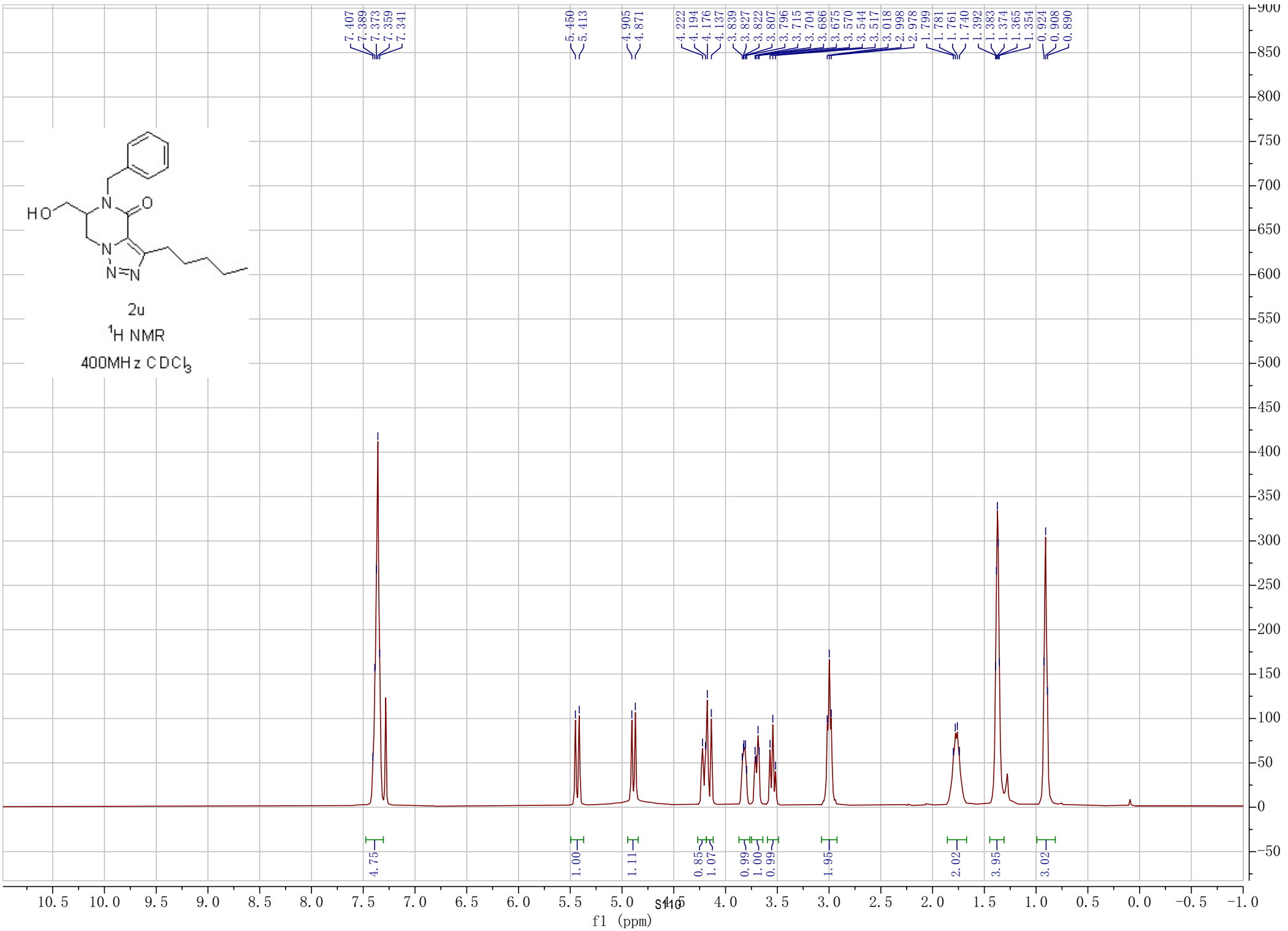


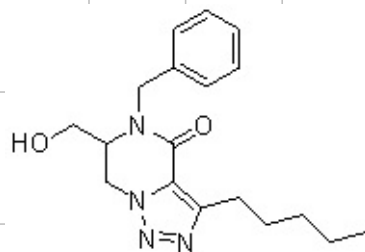




2u

<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>





2u

<sup>13</sup>C NMR

100MHz CDCl<sub>3</sub>

156.62

150.39

136.50

129.08

128.25

124.17

58.61

56.28

48.01

45.14

31.40

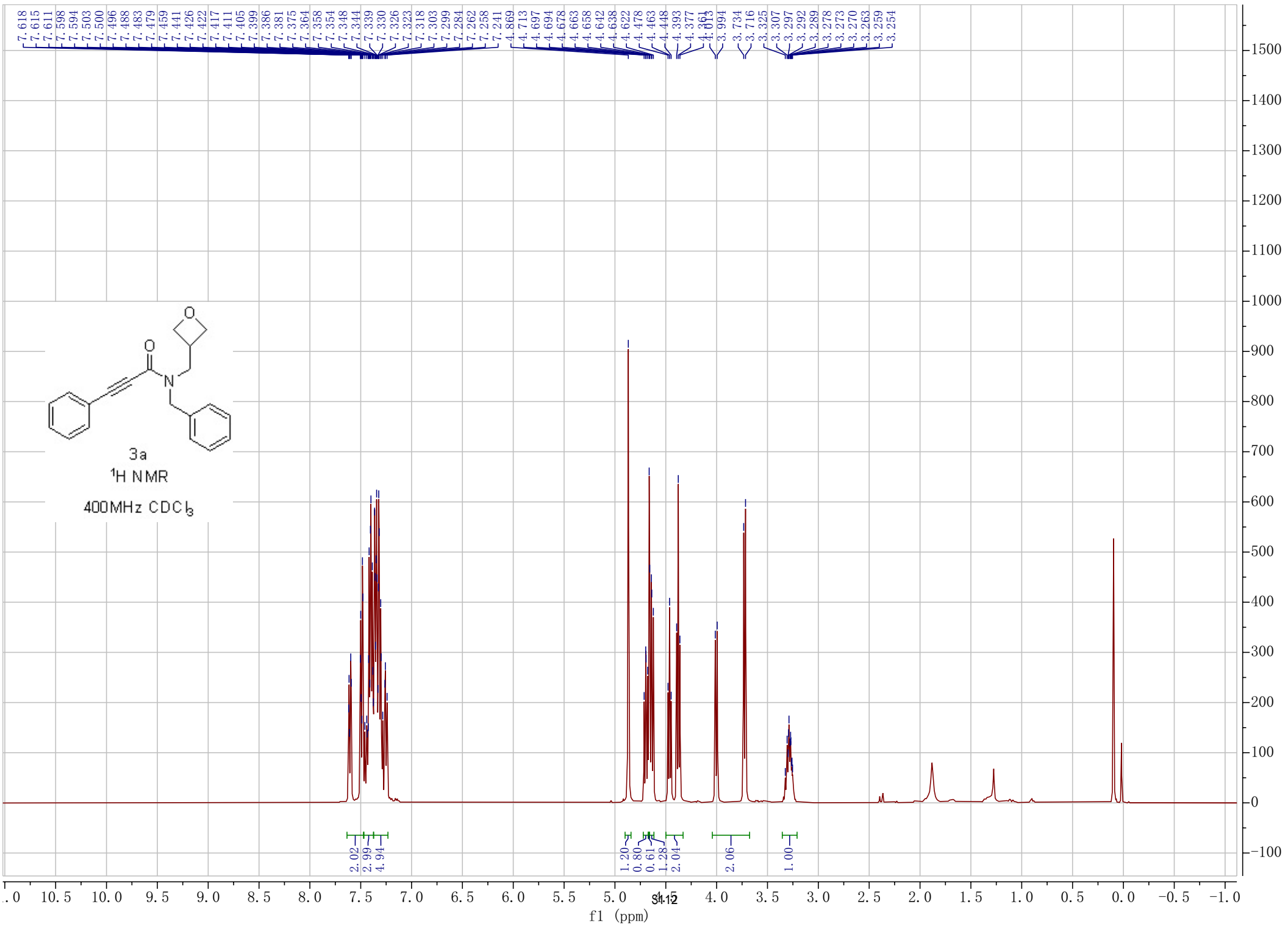
28.62

25.22

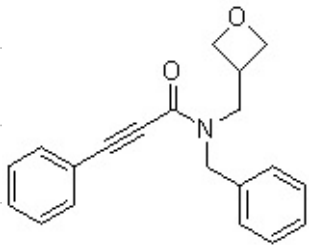
22.36

14.02

f1 (ppm)





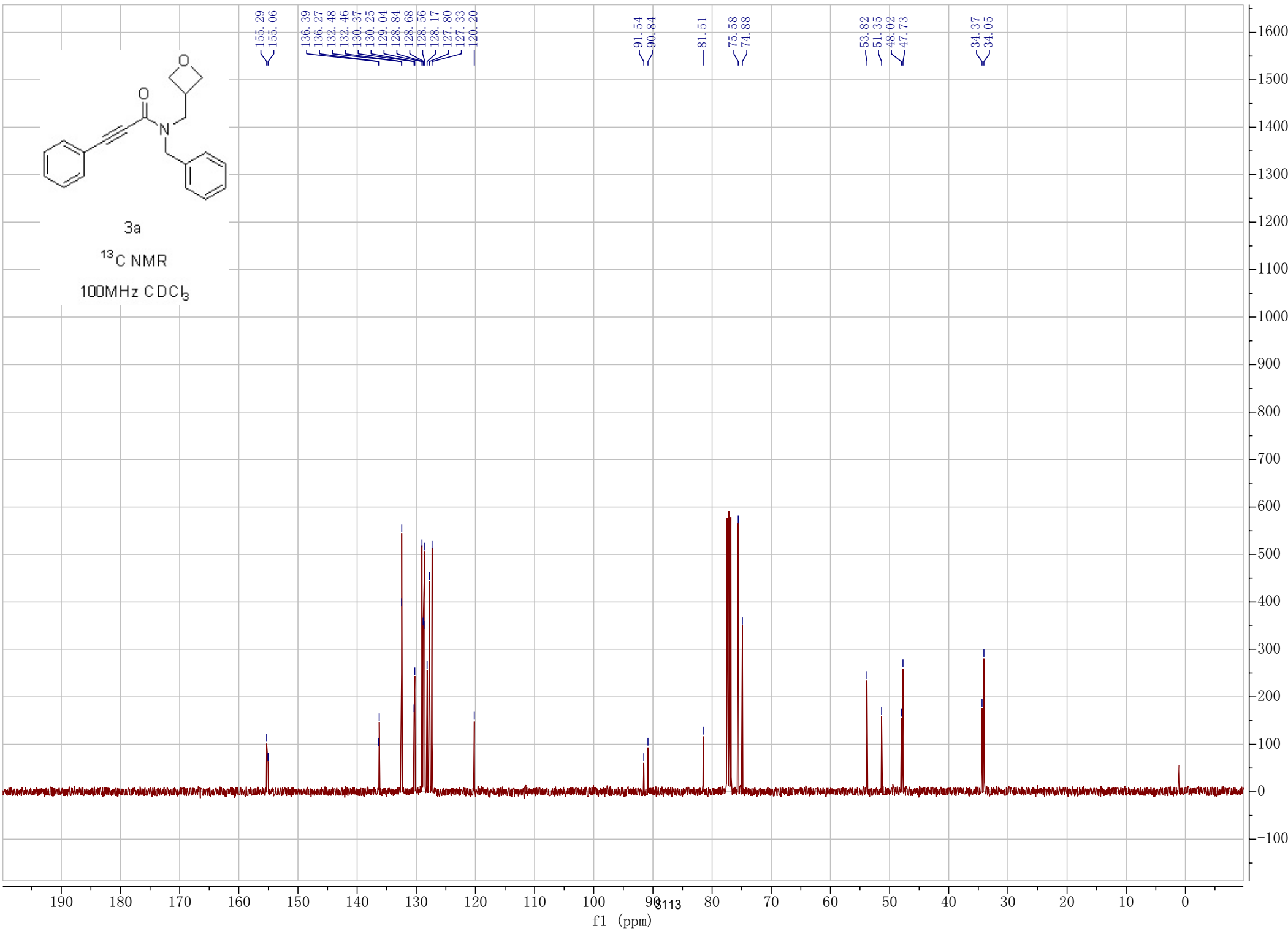


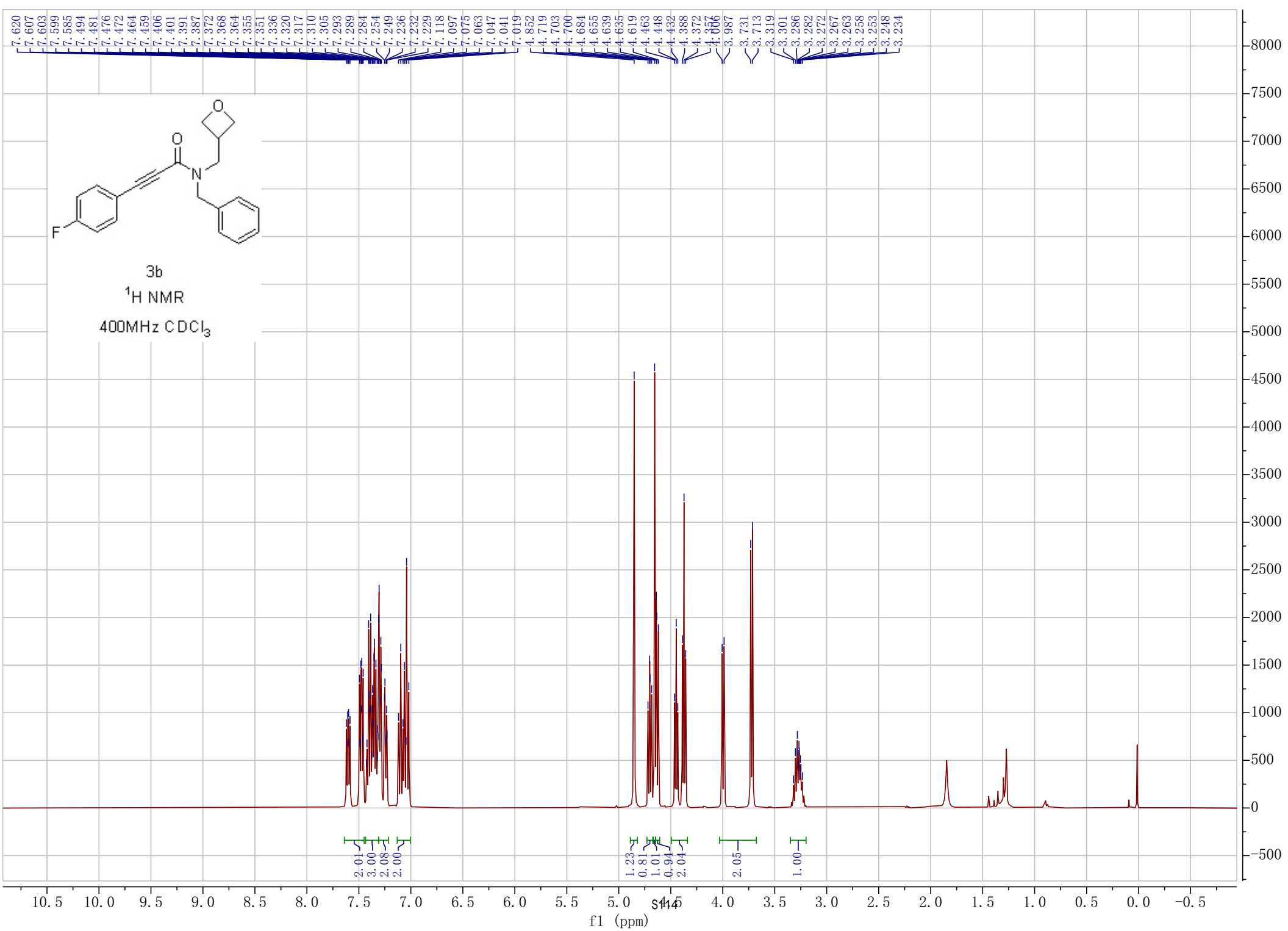
3a

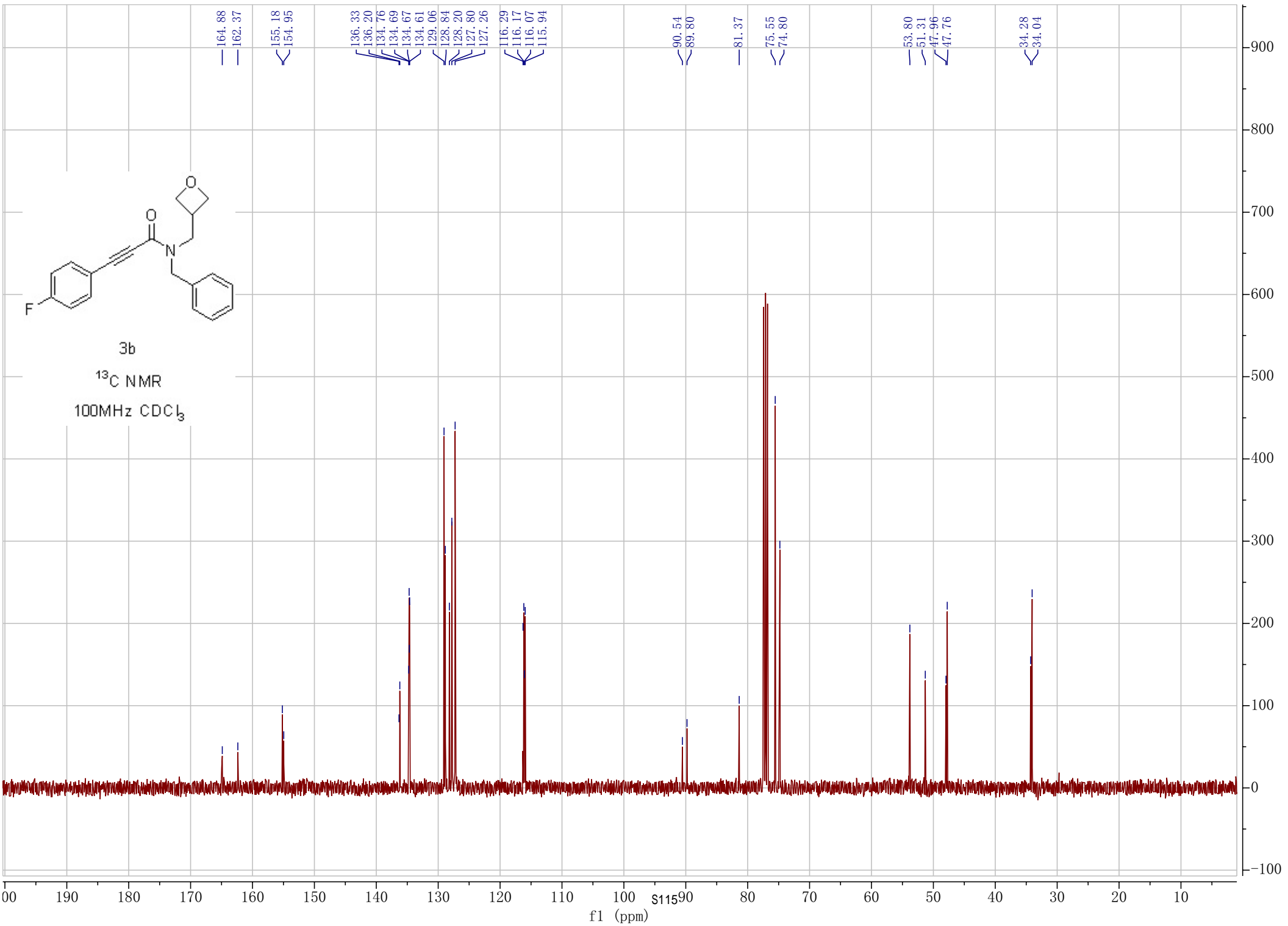
<sup>13</sup>C NMR

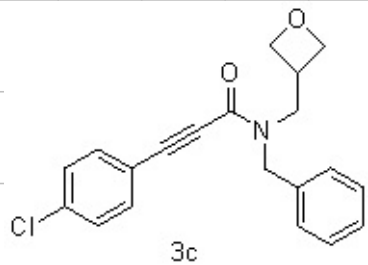
100MHz CDCl<sub>3</sub>

- 155.29
- 155.06
- 136.39
- 136.27
- 132.48
- 132.46
- 130.37
- 130.25
- 129.04
- 128.84
- 128.68
- 128.56
- 128.17
- 127.80
- 127.33
- 120.20
- 91.54
- 90.84
- 81.51
- 75.58
- 74.88
- 53.82
- 51.35
- 48.02
- 47.73
- 34.37
- 34.05

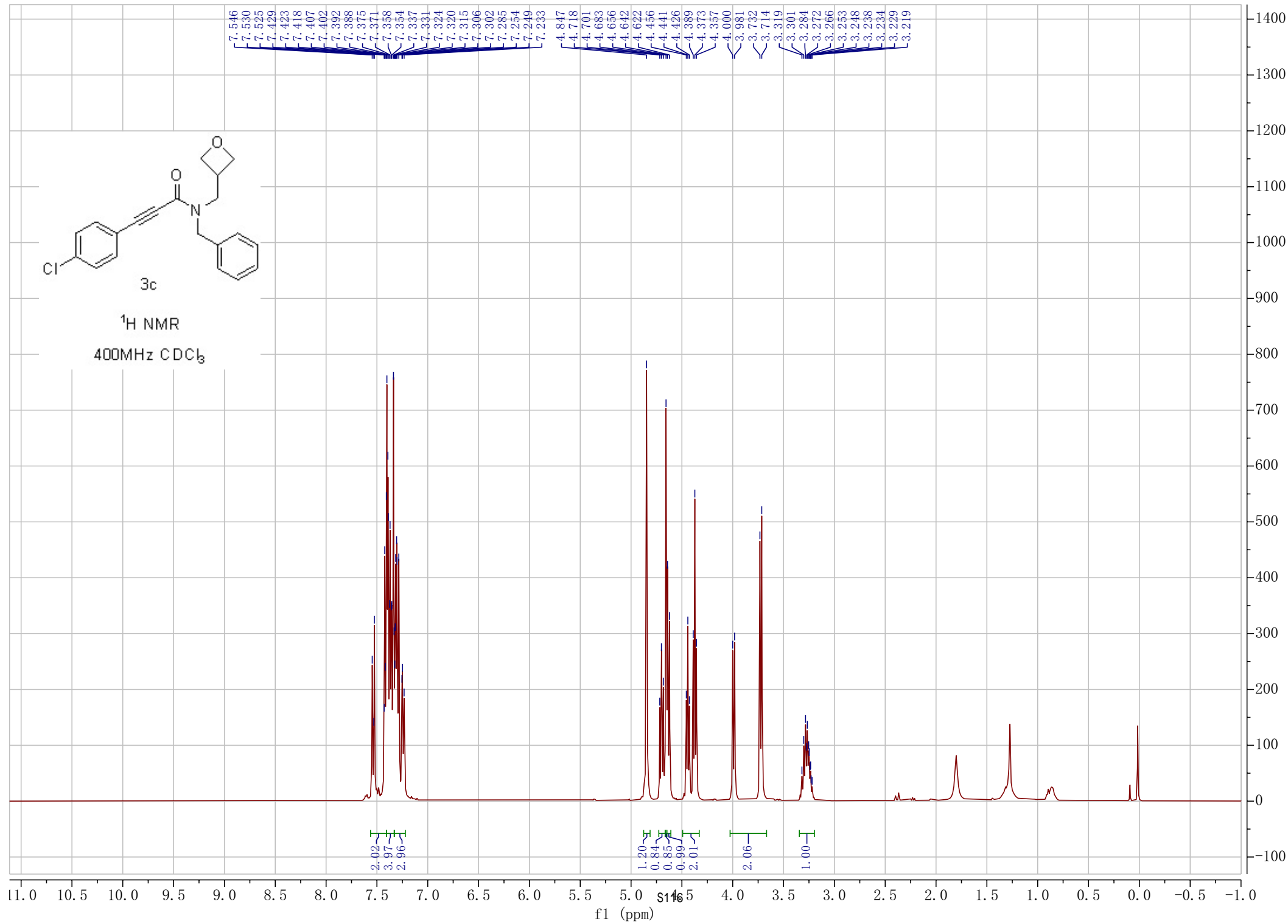


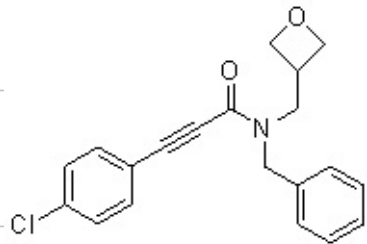




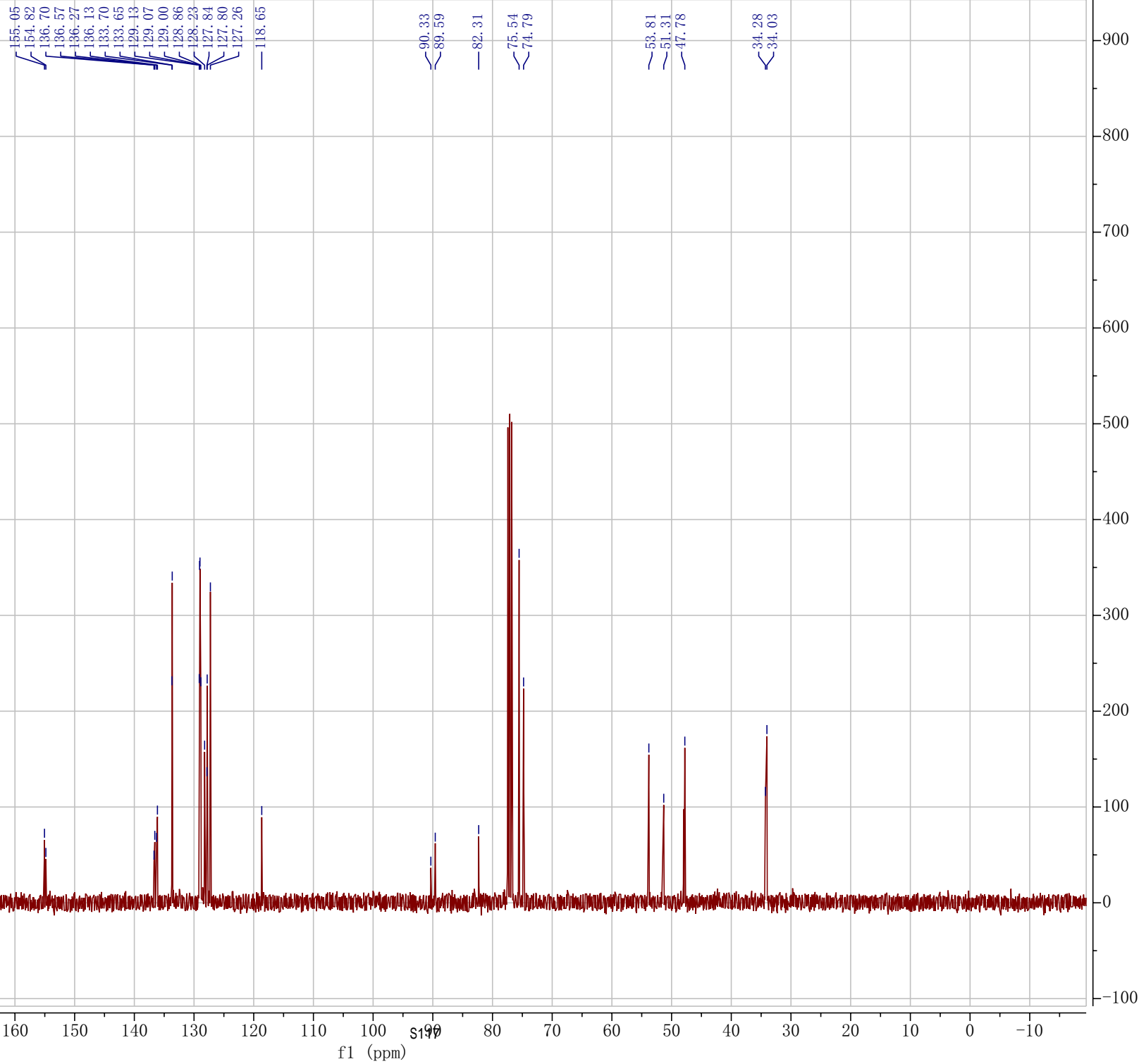


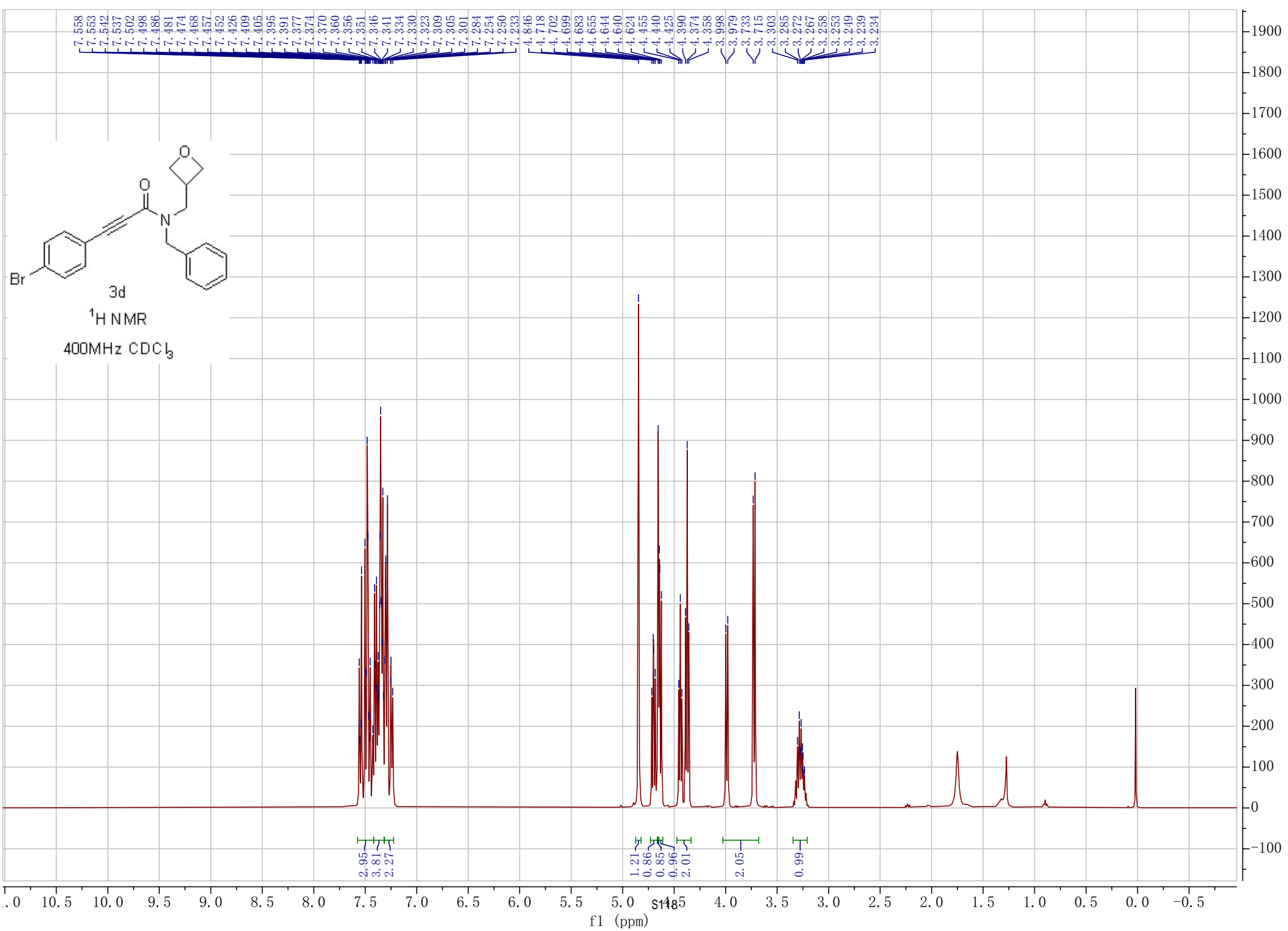
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>

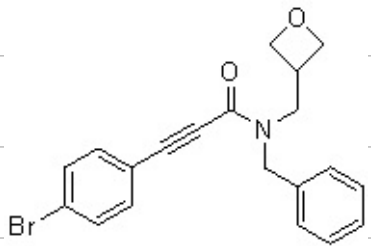




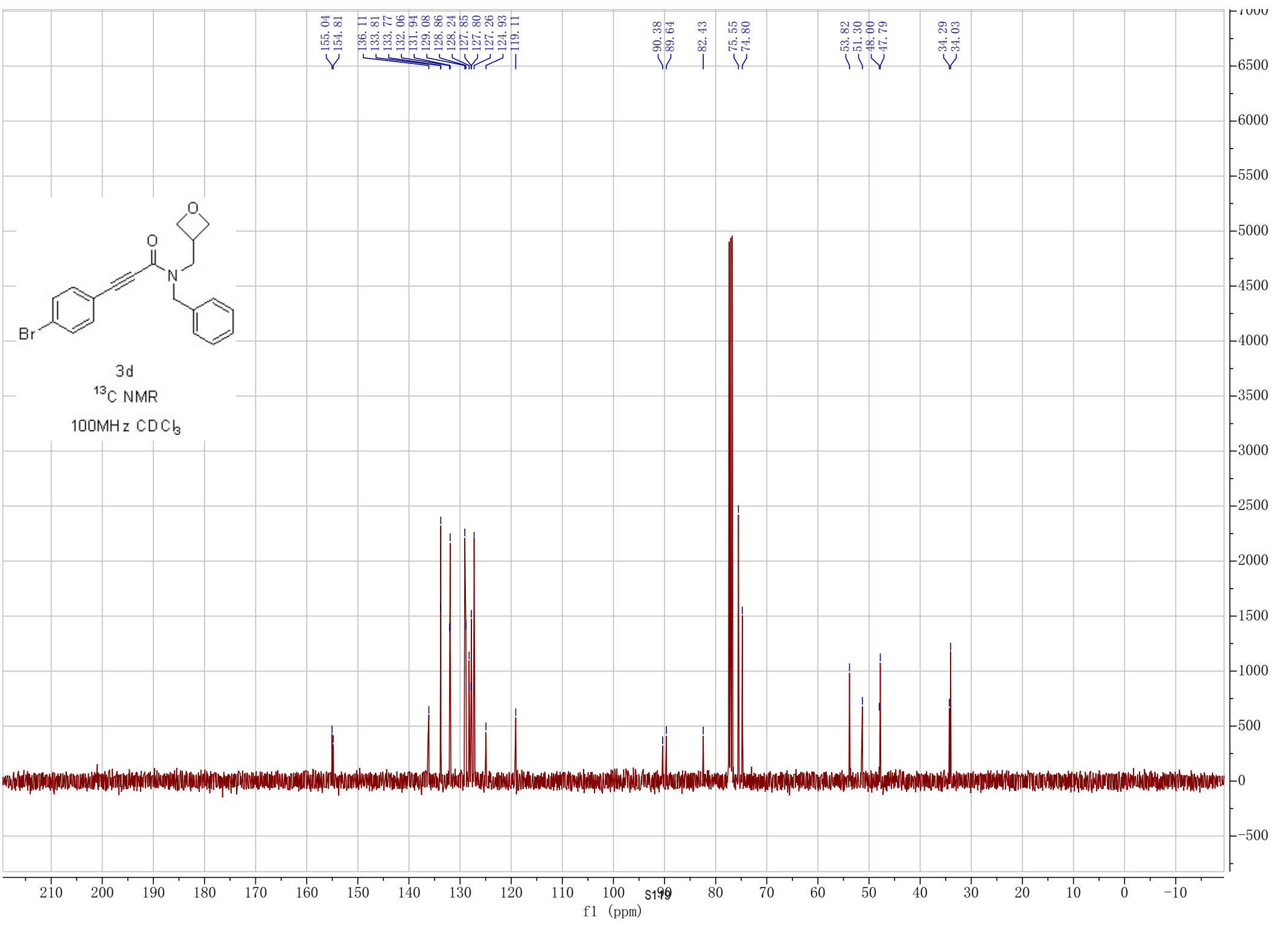
3c  
<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

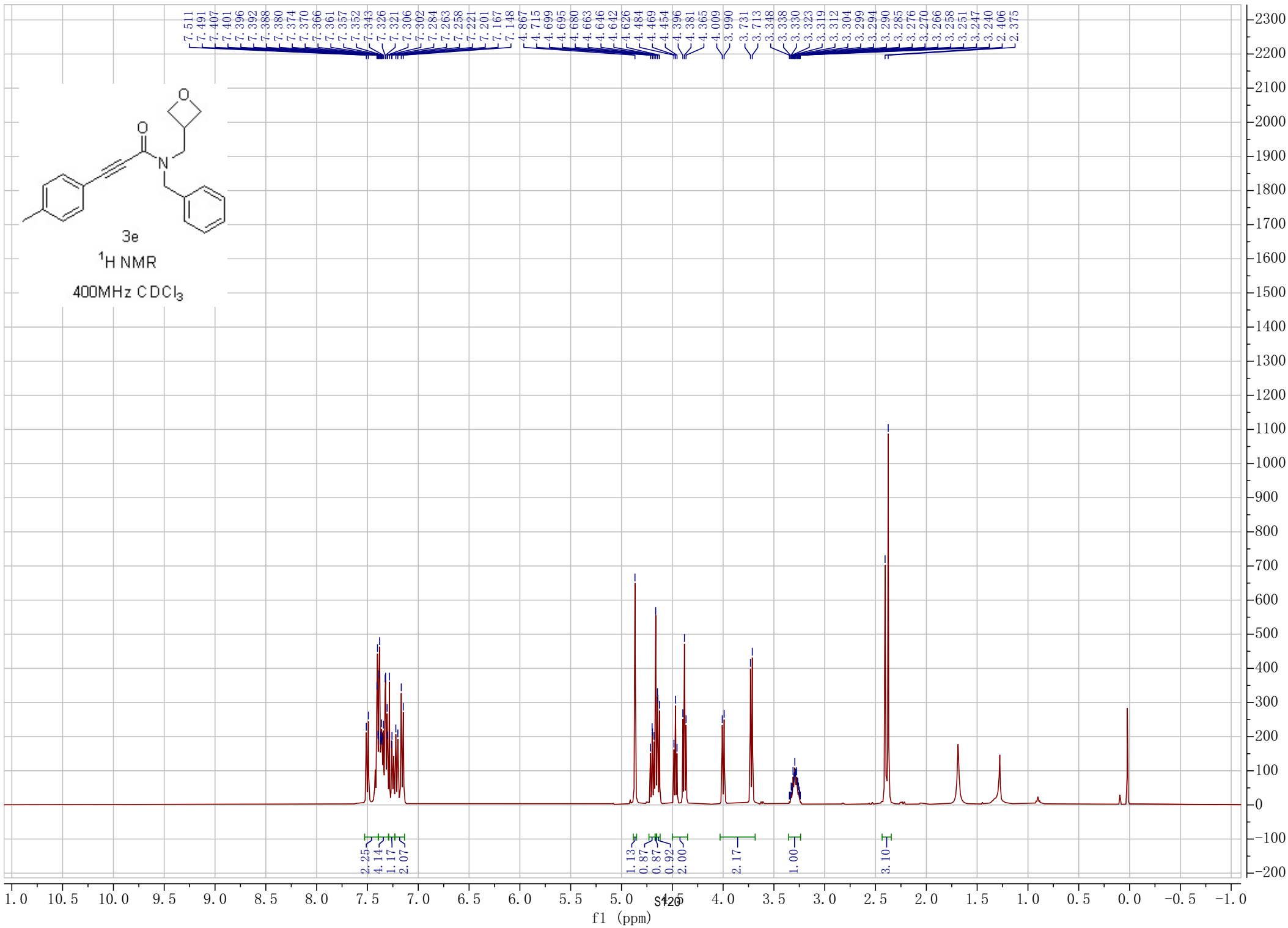




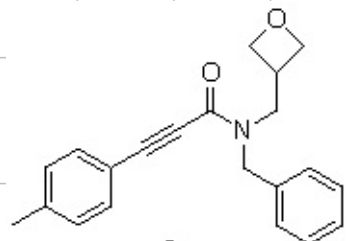


3d  
<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>





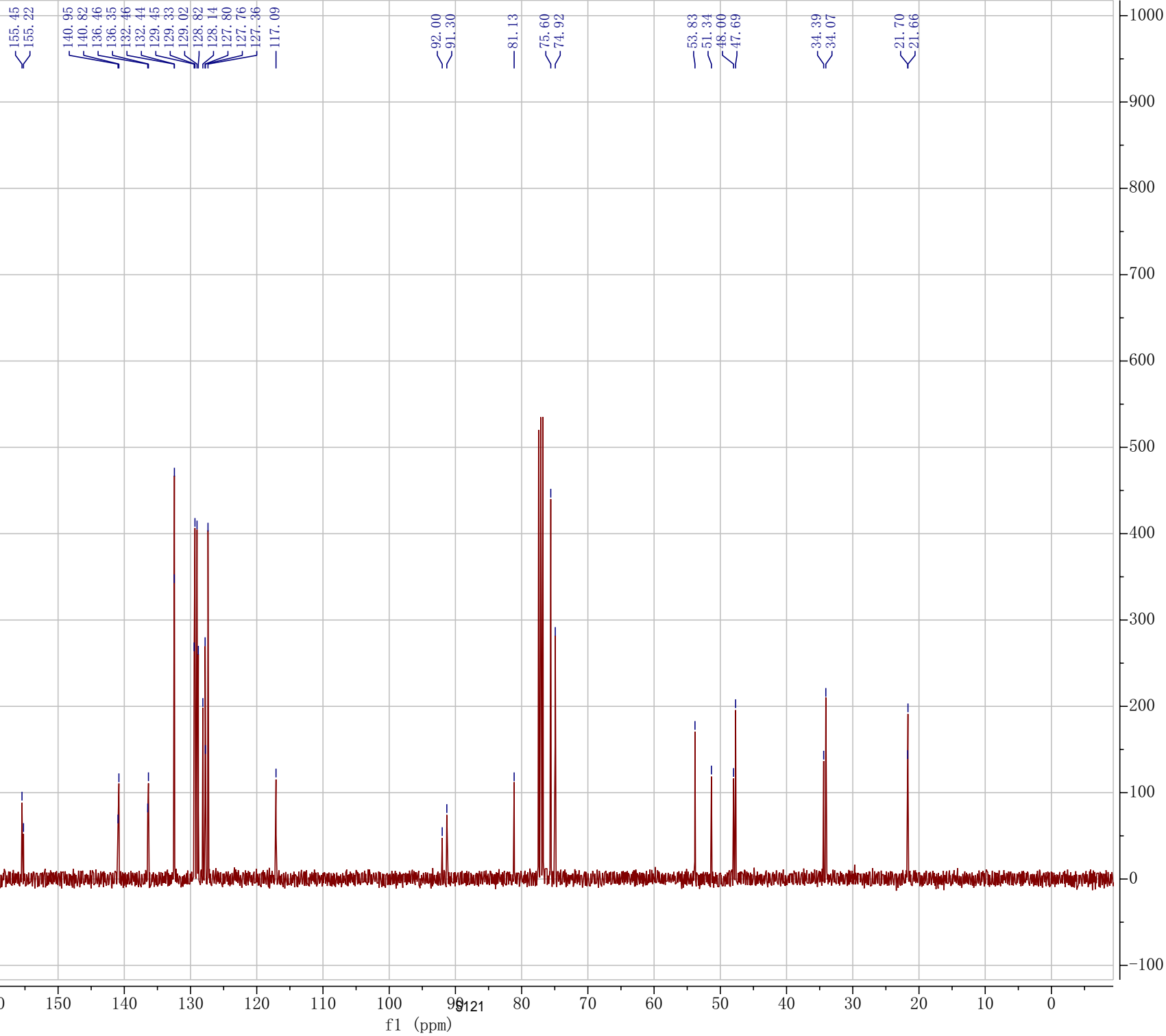


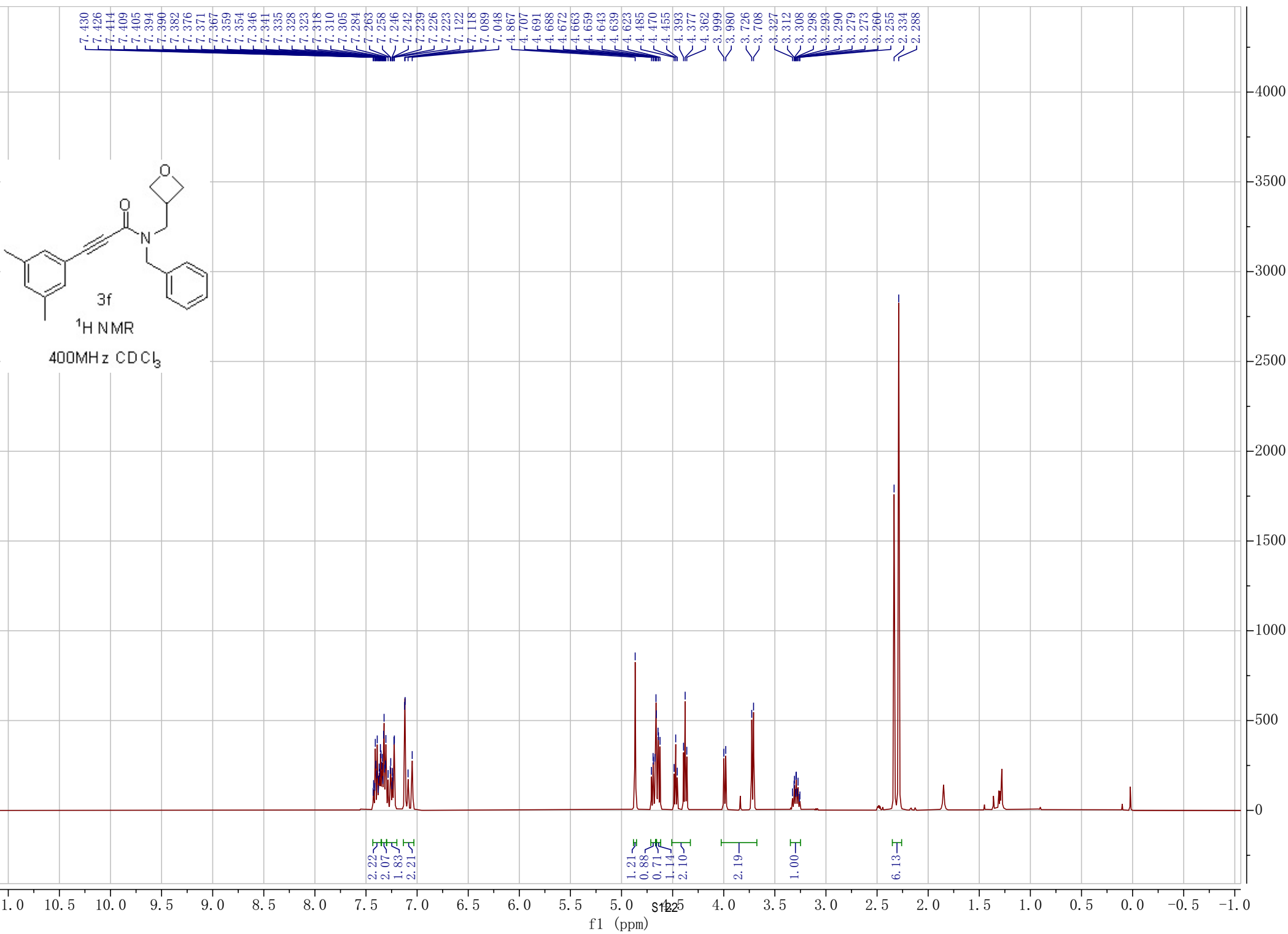


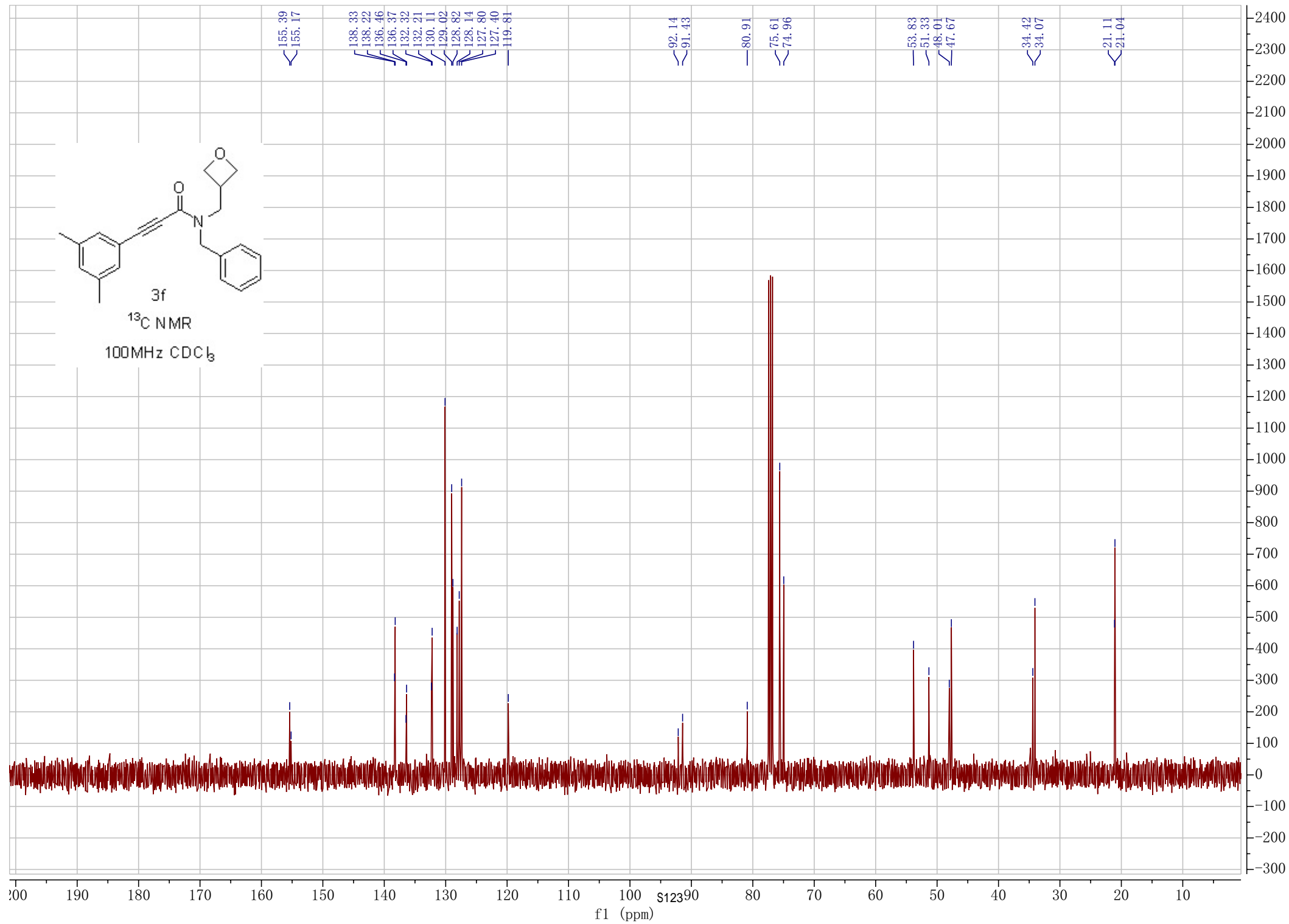
3e

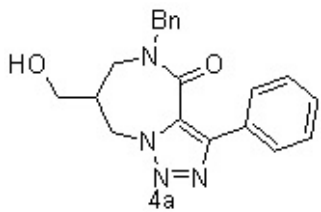
$^{13}\text{C}$  NMR

100MHz  $\text{CDCl}_3$

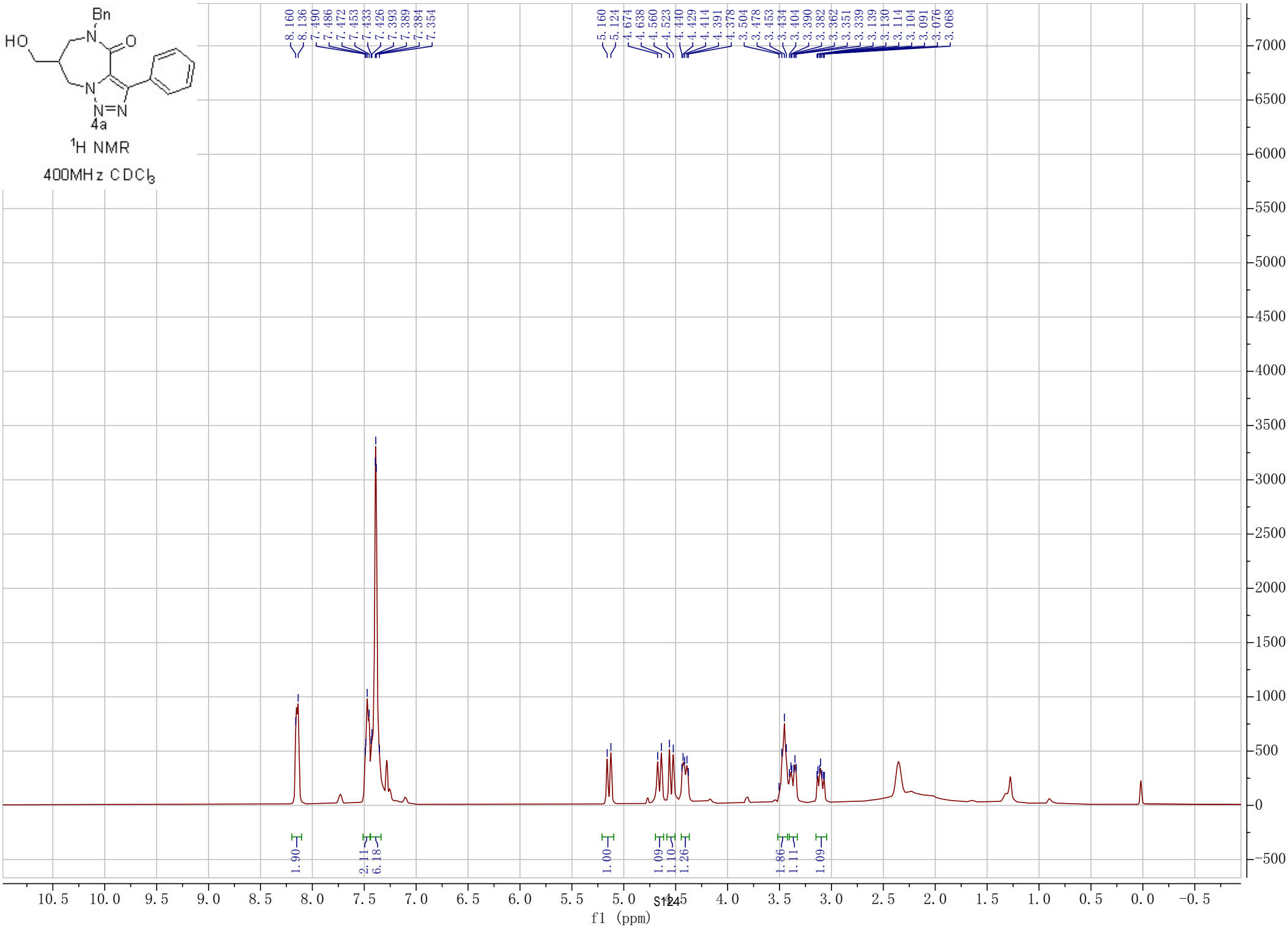


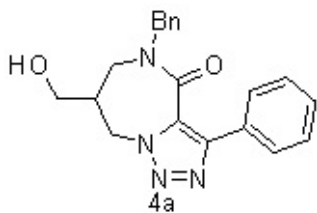




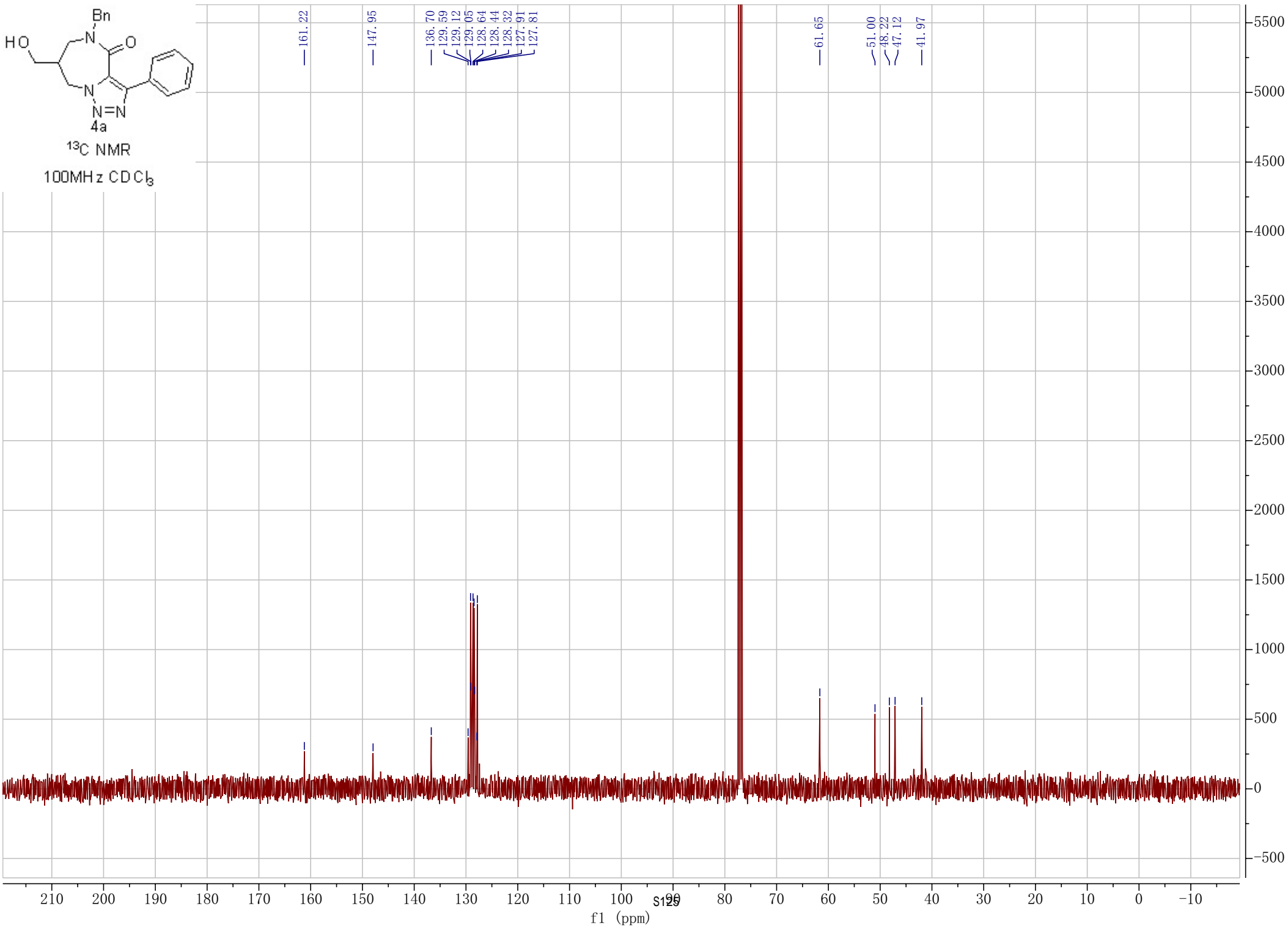


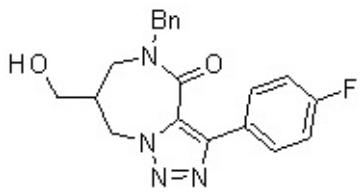
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>





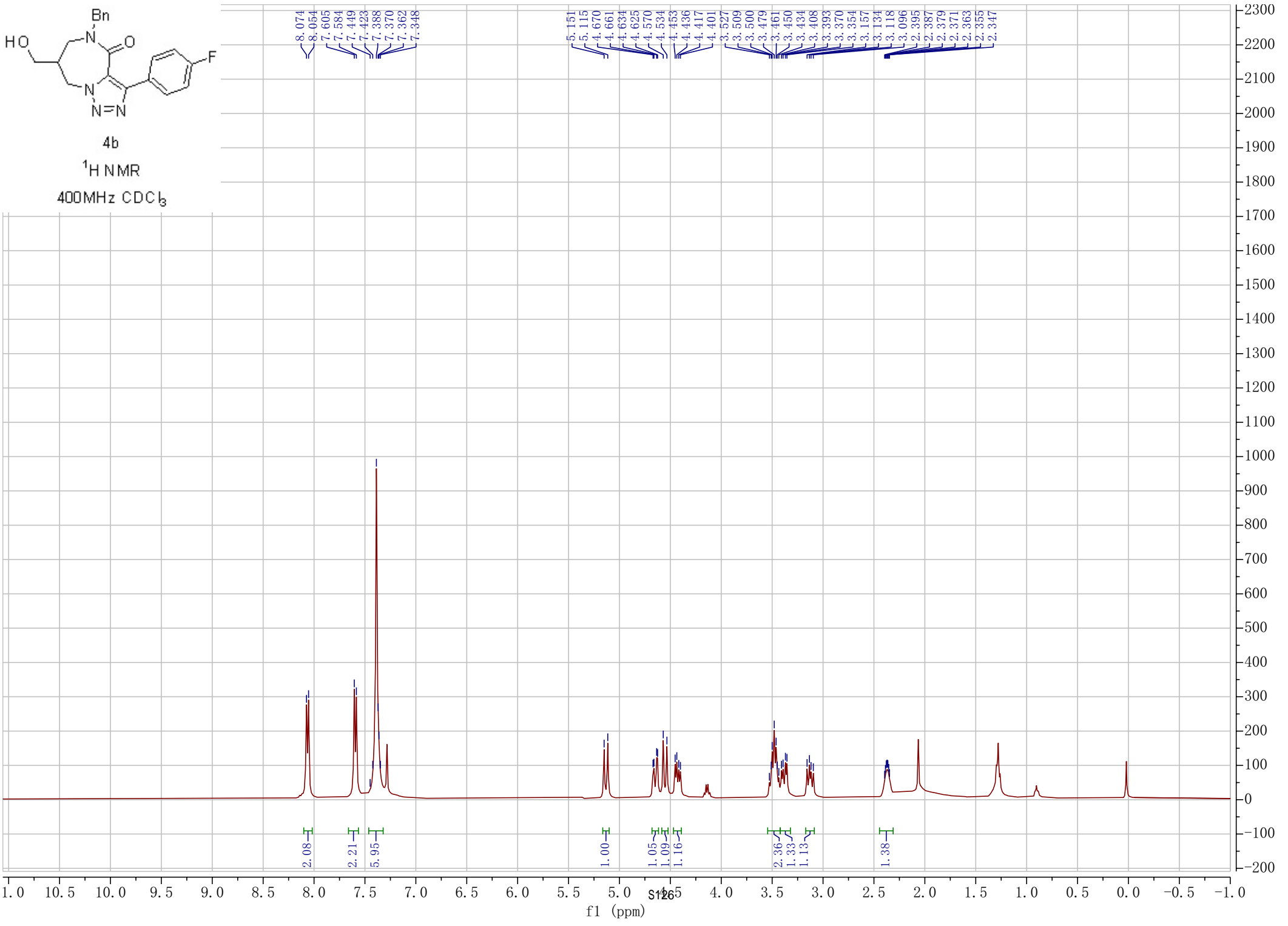
<sup>13</sup>C NMR  
100MHz z CDCl<sub>3</sub>

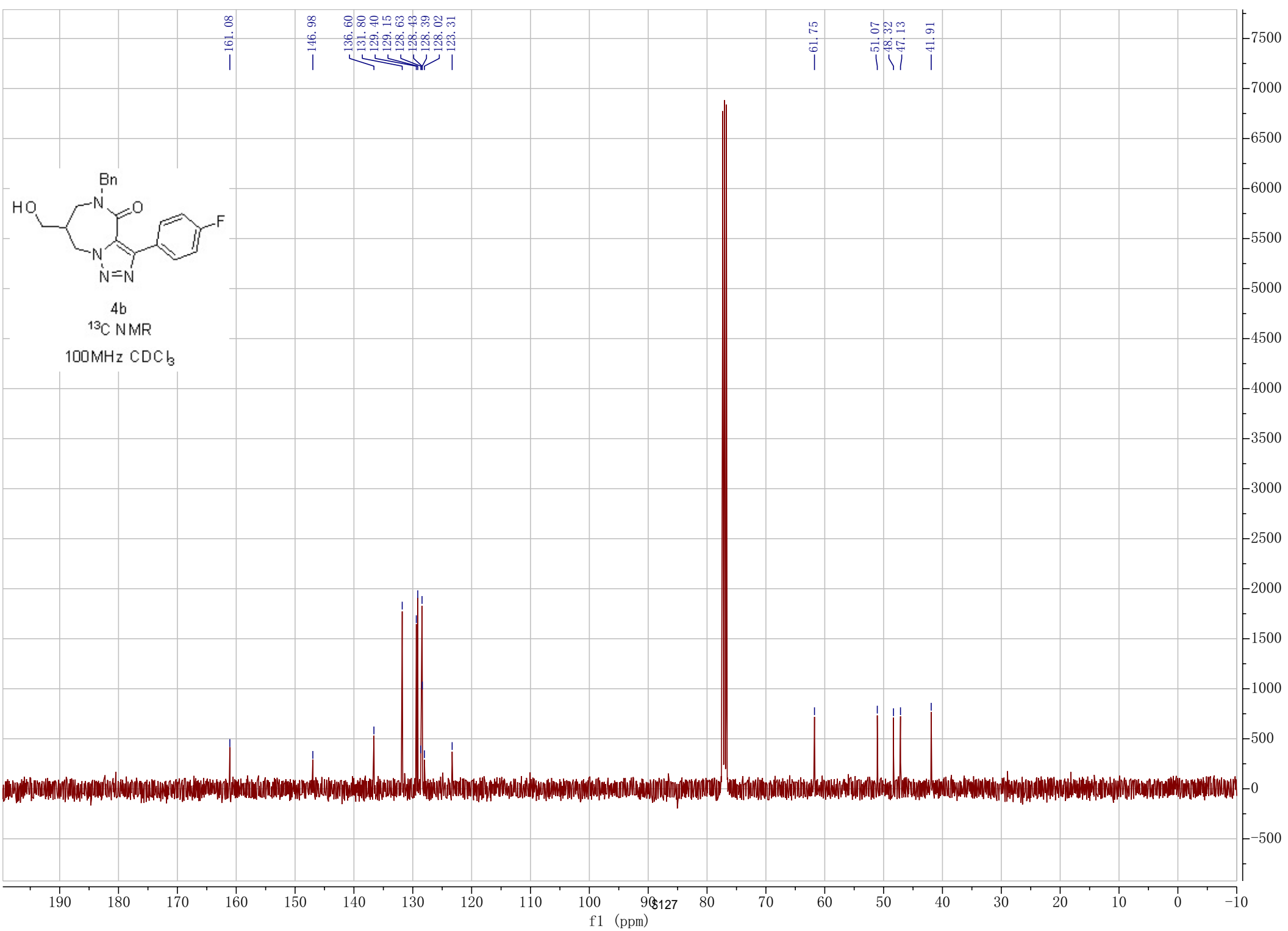


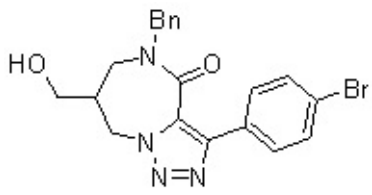


4b

<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>







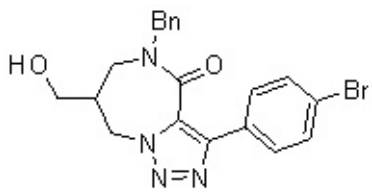
4d

<sup>1</sup>H NMR

400MHz CDCl<sub>3</sub>



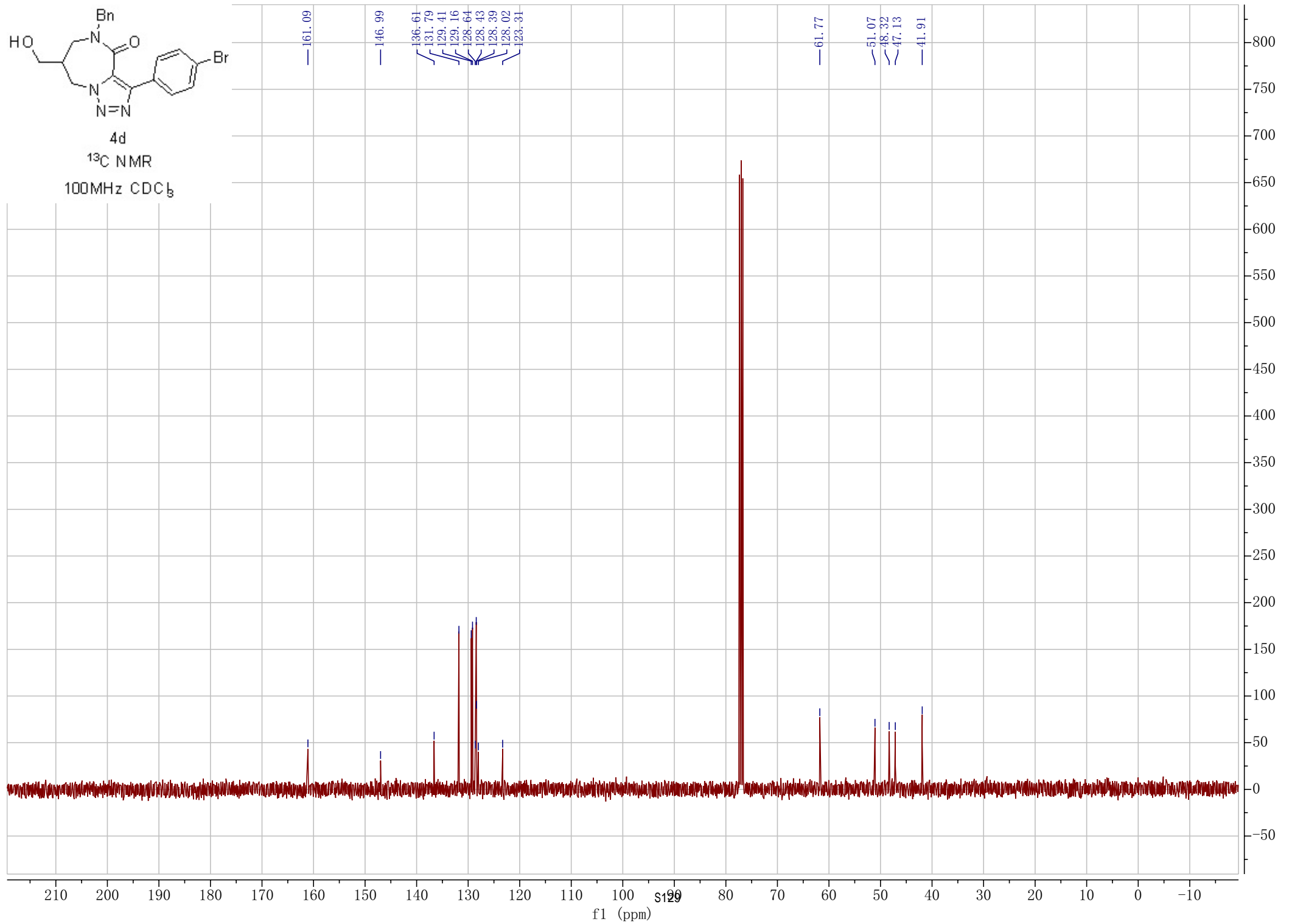


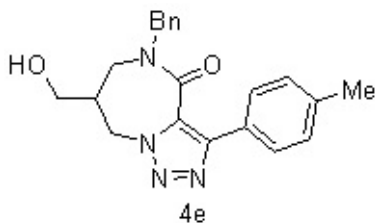


4d

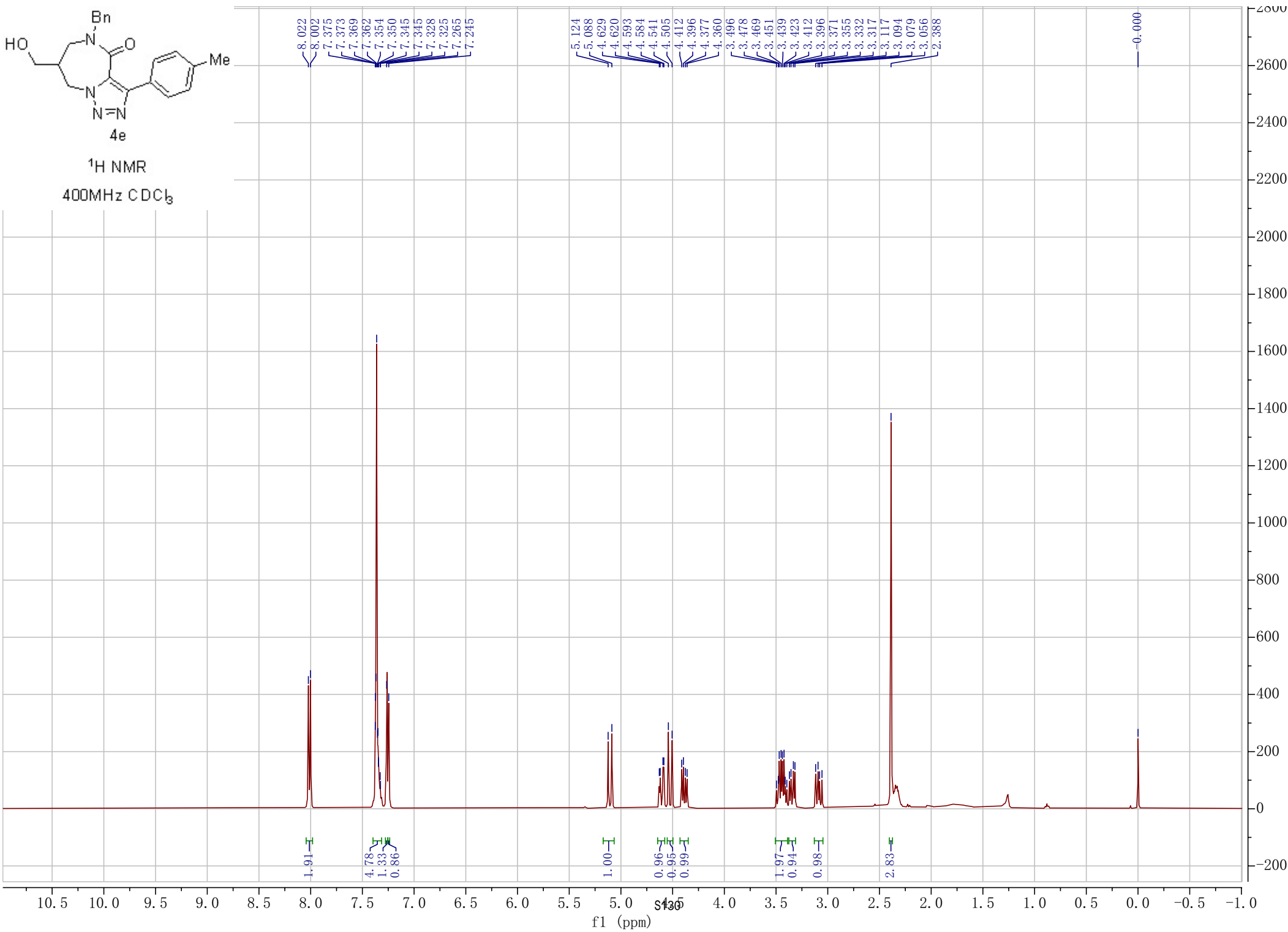
$^{13}\text{C}$  NMR

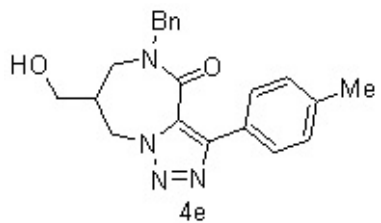
100MHz  $\text{CDCl}_3$



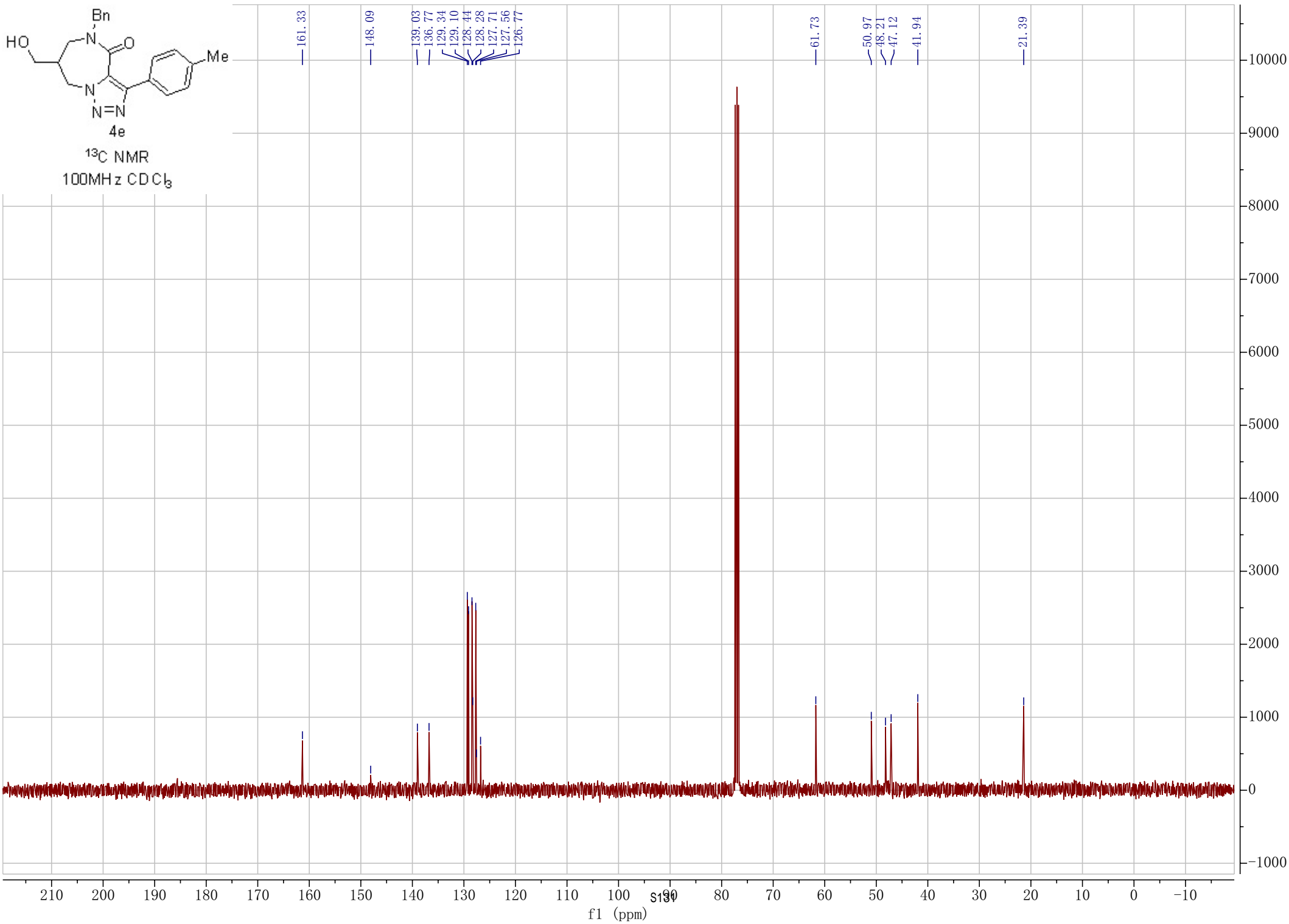


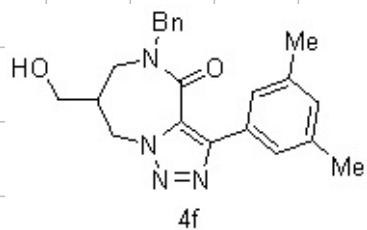
4e  
<sup>1</sup>H NMR  
 400MHz CDCl<sub>3</sub>



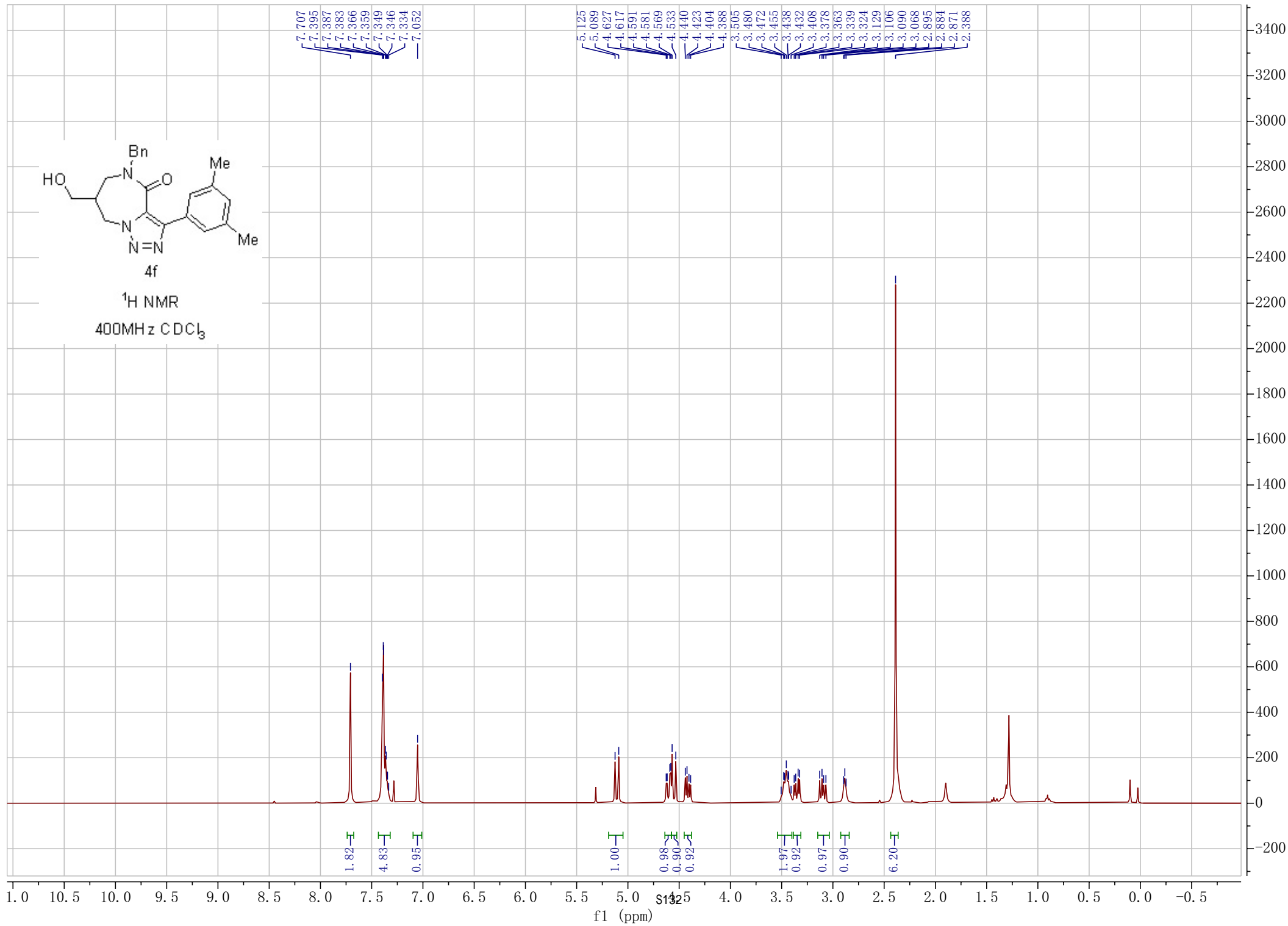


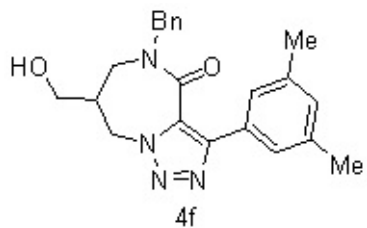
<sup>13</sup>C NMR  
100MHz z CDCl<sub>3</sub>



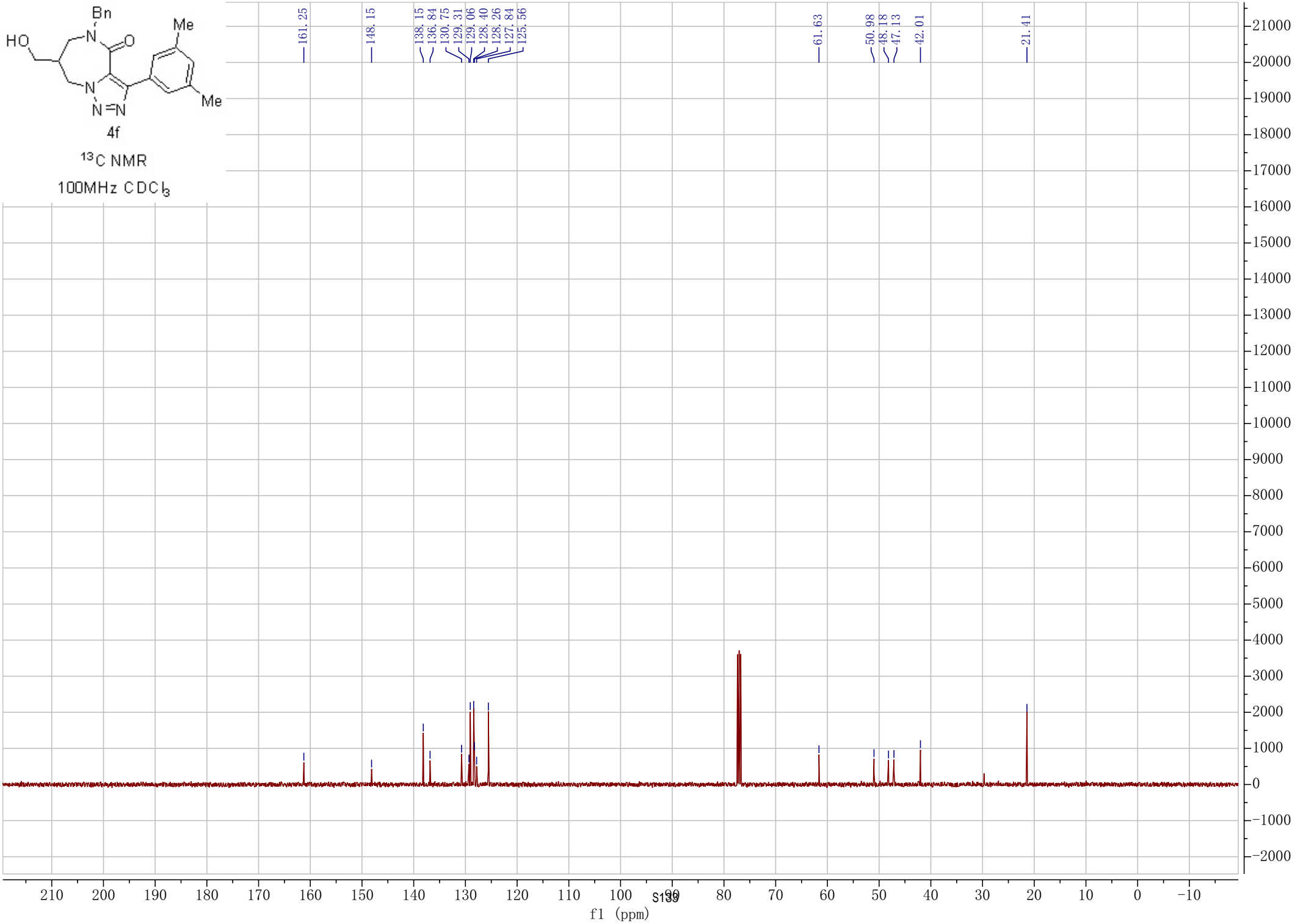


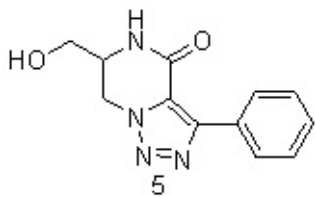
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>



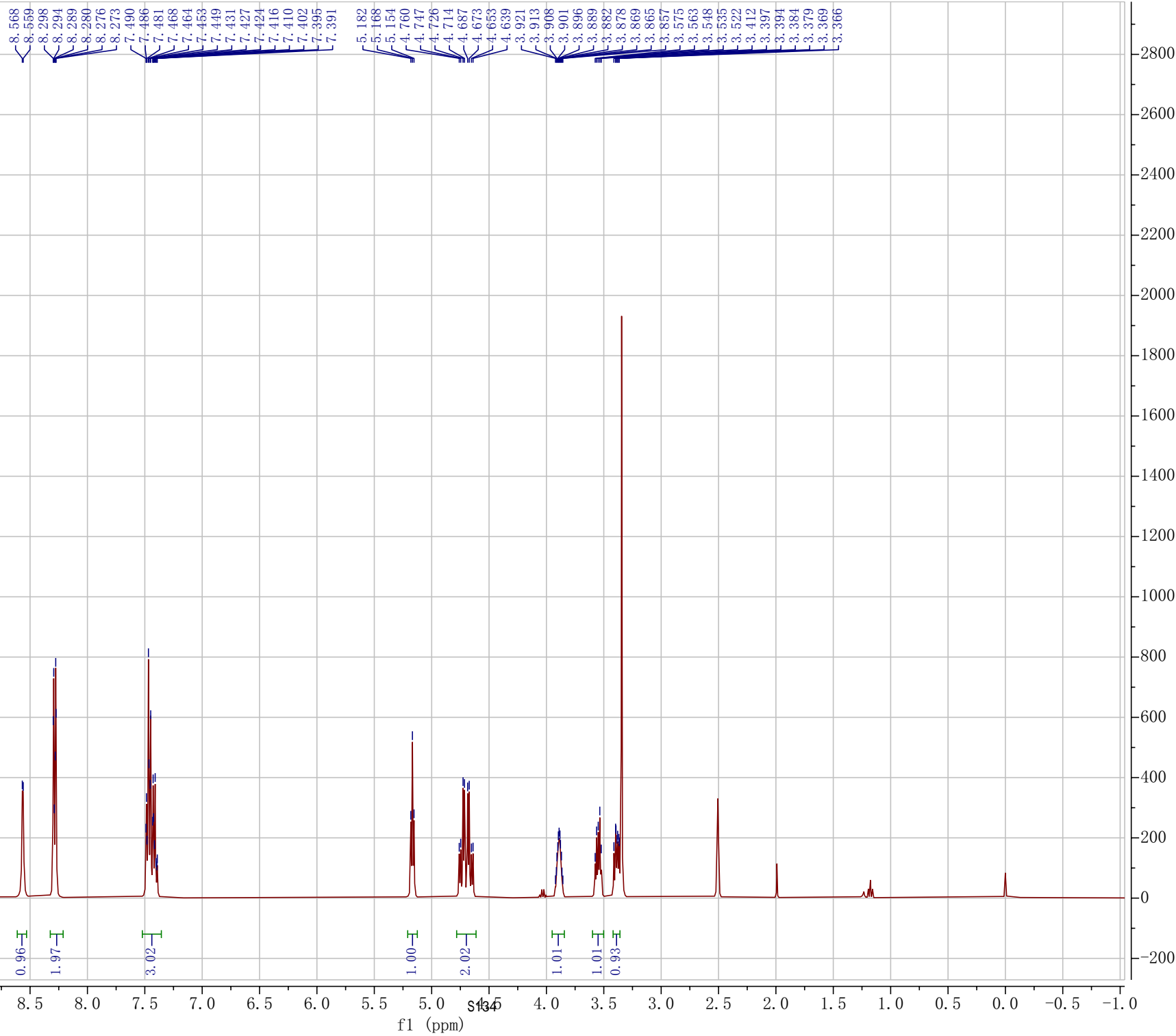


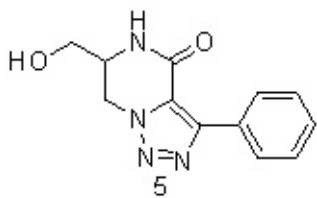
<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>



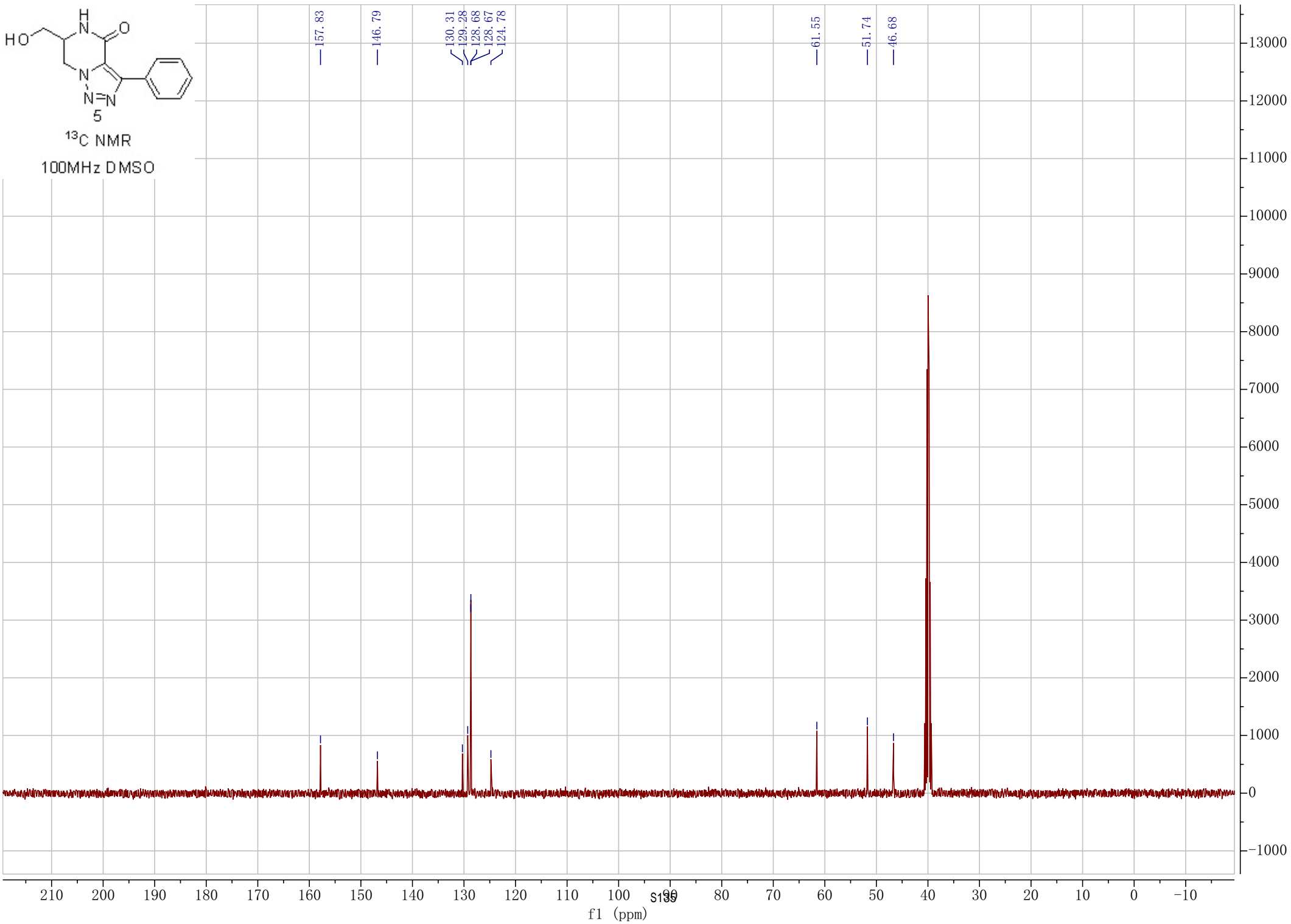


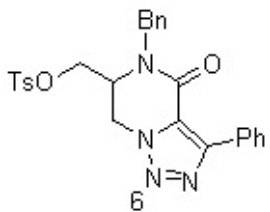
<sup>1</sup>H NMR  
400MHz DMSO



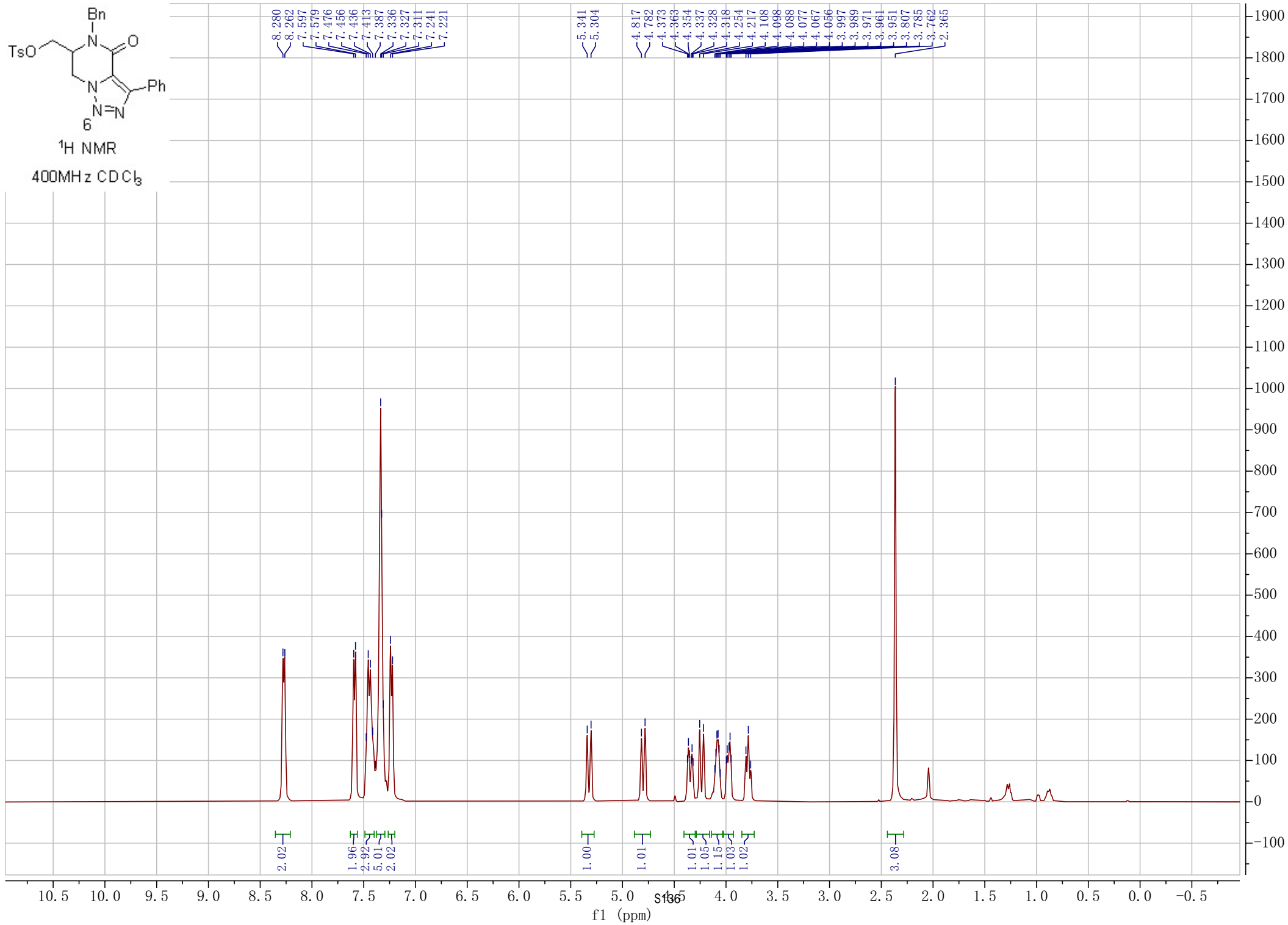


<sup>13</sup>C NMR  
100MHz DMSO

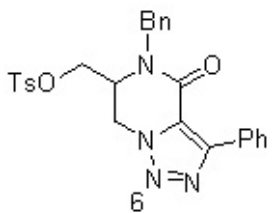




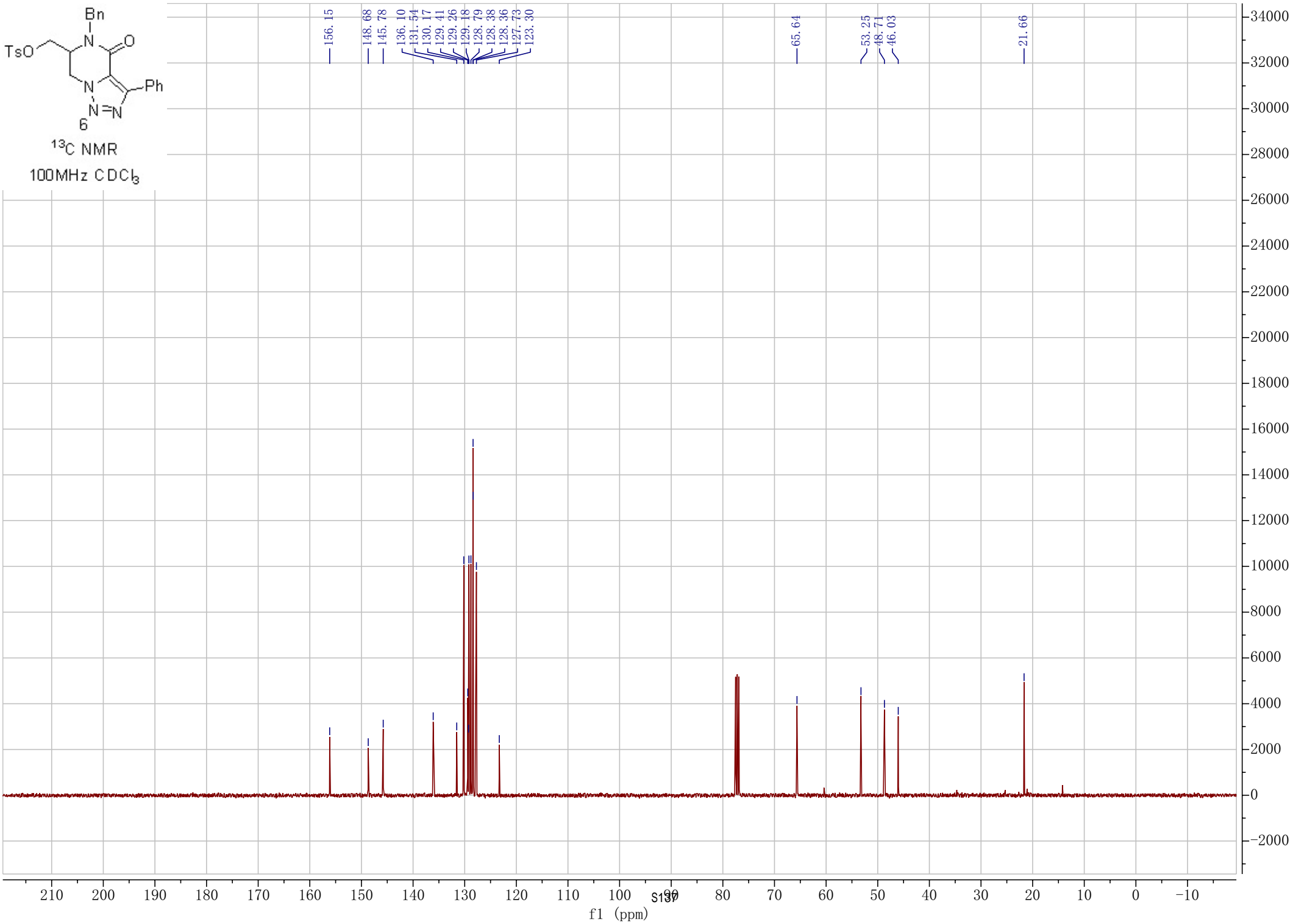
<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>

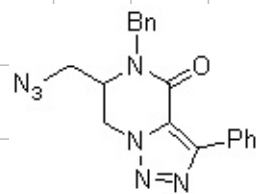






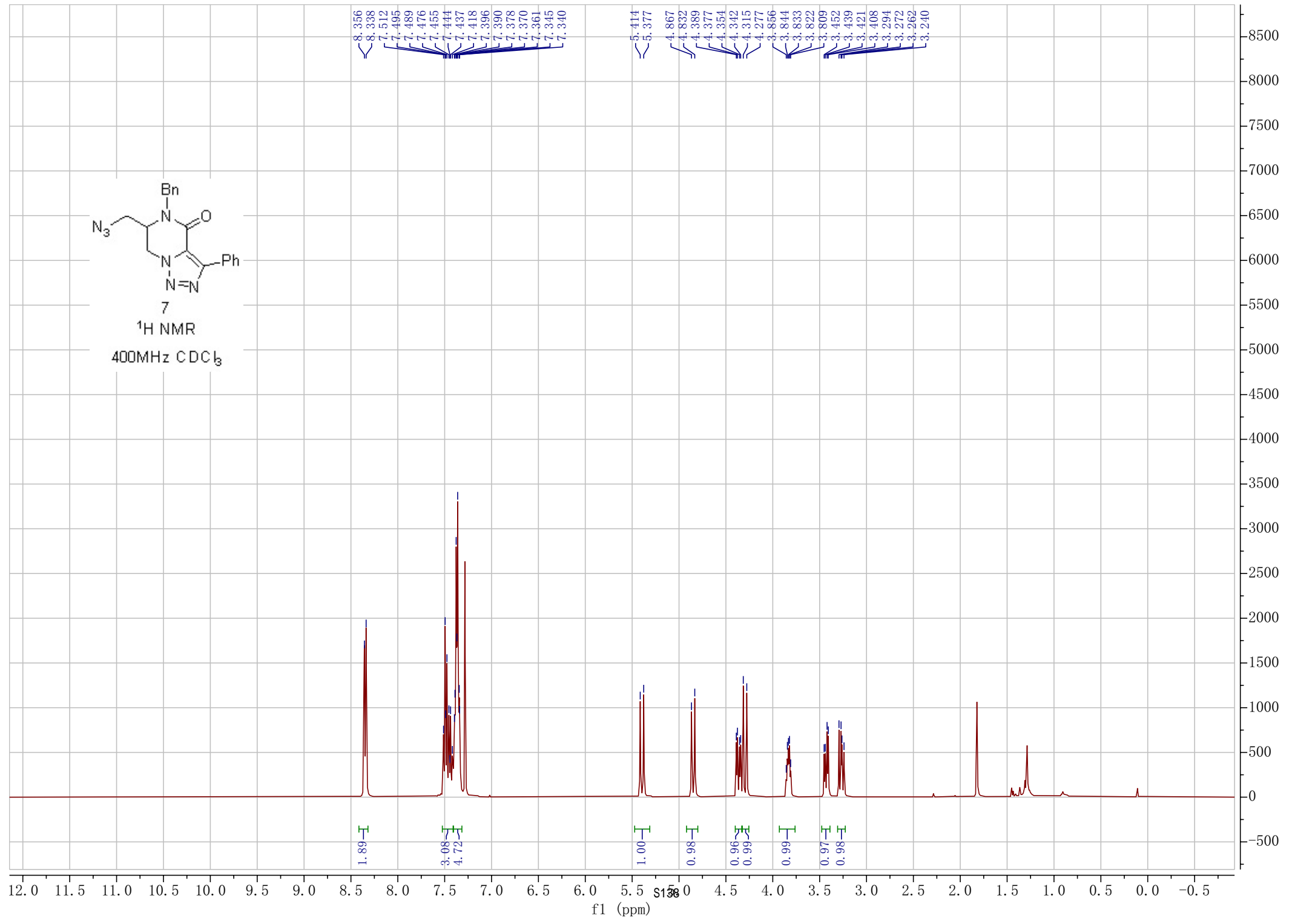
<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

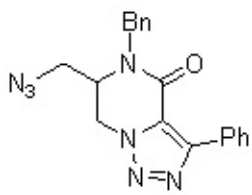




7

<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>

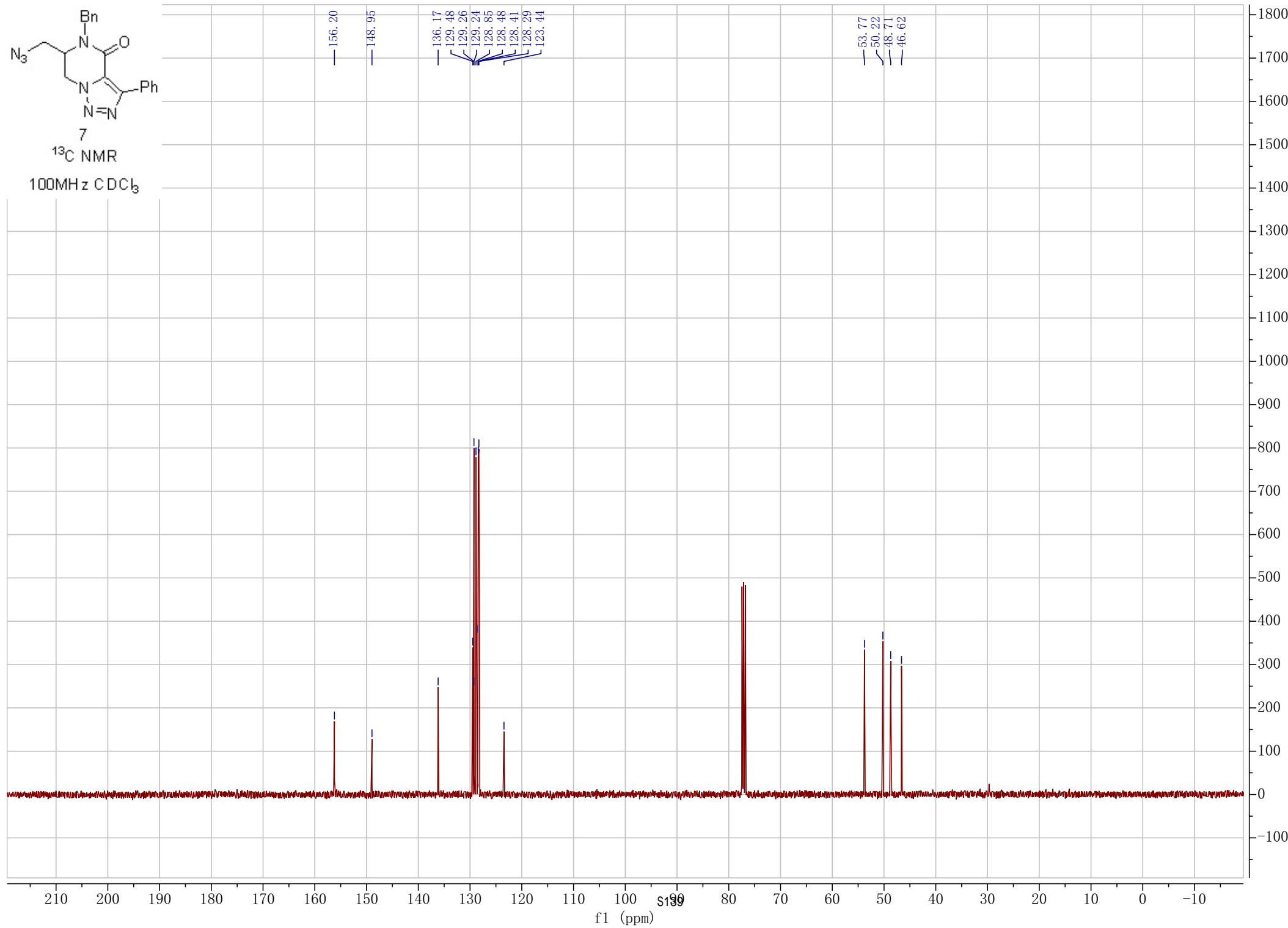


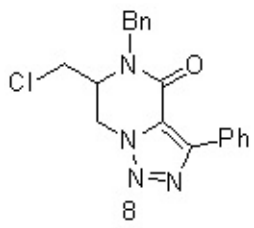


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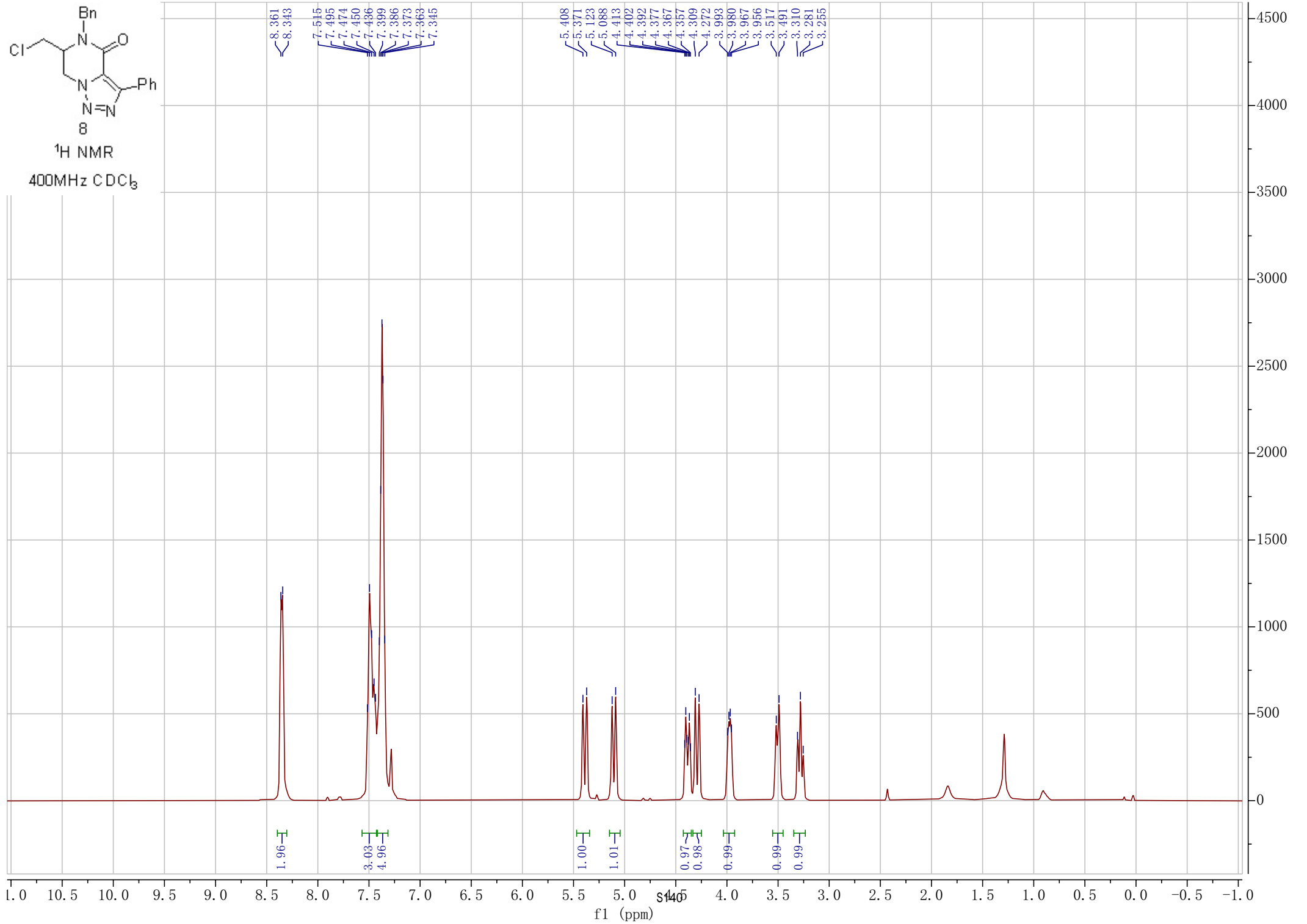
<sup>13</sup>C NMR

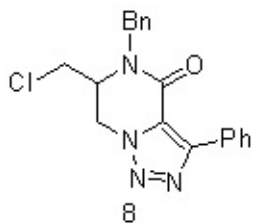
100MHz CDCl<sub>3</sub>





<sup>1</sup>H NMR  
400MHz CDCl<sub>3</sub>





<sup>13</sup>C NMR  
100MHz CDCl<sub>3</sub>

