Stereoselective Construction of β-, γ-, and δ-Lactam Rings via Enzymatic C–H Amidation

Satyajit Roy[a,‡], David A. Vargas[a,b,‡], Pengchen Ma[c,d,‡], Arkajyoti Sengupta[c], Ledong Zhu[e], K. N. Houk[c,*] and Rudi Fasan[a,*]

[a] *Department of Chemistry, University of Rochester, 120 Trustee Road, Rochester, New York, 14627, United States*

[b] *Current affiliation: Process Research and Development, Merck & Co., Inc., Rahway, NJ, 07065, USA.*

[c] *Department of Chemistry and Biochemistry, University of California, Los Angeles, California, 90095, United States*

[d] *School of Chemistry, Xi'an Key Laboratory of Sustainable Energy Materials Chemistry, MOE Key Laboratory for Nonequilibrium Synthesis and Modulation of Condensed Matter, Xi'an Jiaotong University, Xi'an, China*

[e] *Environment Research Institute, Shandong University, Qingdao 266237, PR China*

[‡] These authors contributed equally to this work.

Corresponding authors: rfasan@ur.rochester.edu, houk@chem.ucla.edu.

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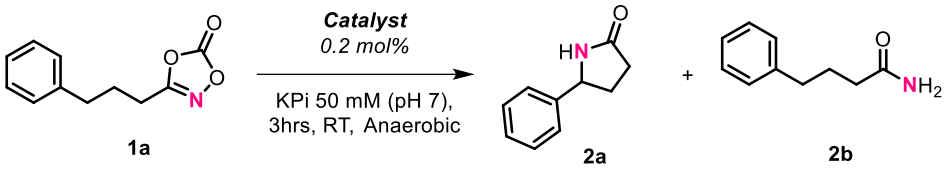
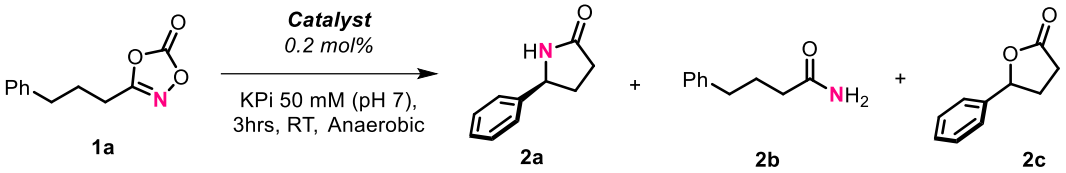
Table S1. Enzyme screening. Screening of various heme-dependent enzymes, proteins, and chemocatalysts for activity toward the intramolecular C-H amidation with dioxazolone **1a**. Reactions were performed at 400 µL scale using 20 µM catalyst, 10 mM 3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (**1a**), 10 mM sodium dithionite in phosphate buffer (50 mM, pH 7), 3 hours, room temperature (RT), under anaerobic conditions. Product yield was determined by GC analysis using calibration curve with racemic (±)-**2a**. N/A = not determinable due to low activity. Reported values are mean values from n ≥ 2 experiments (SE).



Entry	Catalyst	% Yield (GC) 2a	2a : 2b	*ee* (2a)
1	Cytochrome $P450_{BM3}$	0	0:100	N/A
2	CYP119 (*Sulfolobus acidocaldarius*)	0	0:100	N/A
3	Cytochrome *c* (Equine Heart)	0	0:100	N/A
4	Ht-Cc552 (*H. Thermophilus*)	0	0:100	N/A
5	Ht-Cc552 variant (G50T,M59G,P60E,Q62R)	0	0:100	N/A
6	Protoglobin (Pgb from *Aeropyrum Pernix*)	0	0:100	N/A
7	Dehaloperoxidase (*Amphitrite Ornate*)	0	0:100	N/A
8	Horseradish peroxidase	0	0:100	N/A
9	Catalase (bovine liver)	0	0:100	N/A
10	Mb (sperm whale)	0	0:100	N/A
11	Mb(H64V)	2	3:97	96%
12	Fe(TPP)(Cl)[a]	3	33:67	0
13	Co(TPP)[a]	0	N/A	N/A
14	Hemin[b]	3	25:75	0

[a] Reaction was carried out in dichloromethane (DCM). [b] Reaction was carried out in dimethylformamide (DMF). N/A = not determinable due to low activity.

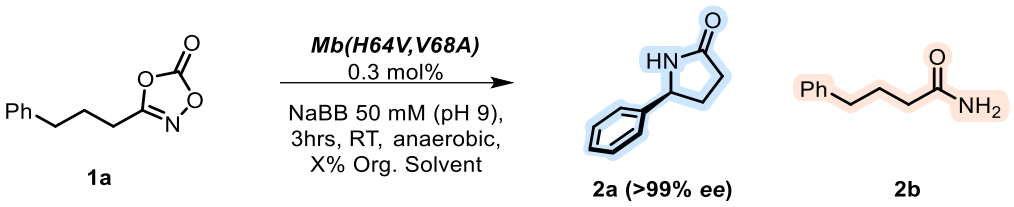
Table S2. **Screening of Mb variants.** Activity and selectivity of representative engineered Mb variants in the intramolecular C-H amidation with dioxazolone **1a**. Reactions were performed at 400 µL scale using 20 µM catalyst, 10 mM 3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (**1a**), 10 mM sodium dithionite in phosphate buffer (50 mM, pH 7), 3 hours, room temperature (RT), under anaerobic conditions. Product yield and enantioselectivity was determined by chiral GC analysis using calibration curve with racemic (±)-**2a**. N/A = not determinable due to low activity. Reported values are mean values from n ≥ 2 experiments (SE).

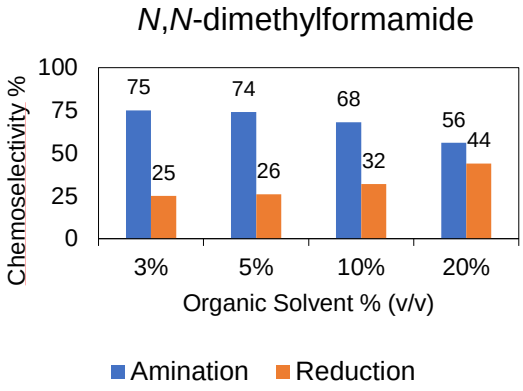


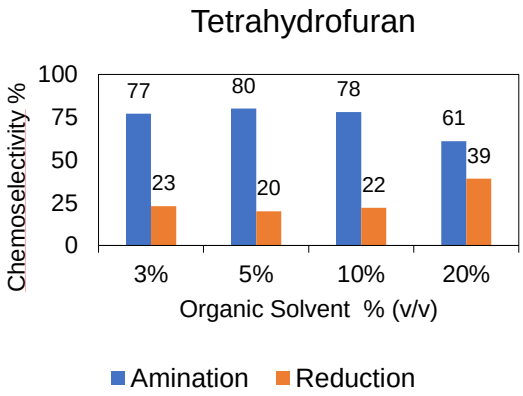
Entry	Catalyst	% Yield (GC) 2a	2a : 2b : 2c	*ee* (2a)
1	Mb (sperm whale)	0	0:100:0	N/A
2	Mb(H64V)	2	2:96:2	96%
3	Mb(H64V,V68G)	5	5:90:5	80%
4	Mb(H64A,V68A)	5	5:90:5	0
5	Mb(H64G,V68A)	10	10:75:15	74%
6	Mb(H64G,V68G)	10	10:80:10	11%
7	Mb(H64V,V68A) (= **Mb***)	50	50:40:10	99%
8	Mb(L29S,H64V)	1	1:99:0	-3%
9	Mb(F43I,H64V)	4	5:92:3	-3%
10	Mb(F43S,H64V)	4	5:92:3	67%
11	Mb(H64V,I107Y)	9	10:70:20	8%
12	Mb(H64W,V68A)	28	30:60:10	76%
13	Mb(F43V,H64W)	3	3:94:3	0
14	Mb(L29A,H64V)	1	1:97:2	-1%
15	Mb(L29T,H64V)	5	5:85:10	9%
16	Mb(L29A,H64V,V68G)	1	1:97:2	4%

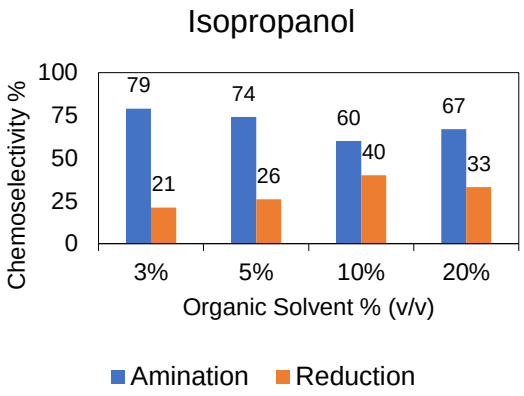
17	Mb(L29S,H64V,V68G)	1	1:97:2	3%
18	Mb(L29T,H64V,V68L)	15	15:80:5	-65%
19	Mb(L29T,H64V,V68F)	1	1:95:4	15%
20	Mb(H64A,V68G,I107A)	5	5:92:3	-1%
21	Mb(H64V,V68G,I107V)	5	5:92:3	8%
22	Mb(H64L,V68G,I107V)	5	5:90:5	6%
23	Mb(R45S,H64G,V68A)	10	10:80:10	48%
24	Mb(L29T,H64A,V68F,I107L)	3	3:94:3	-6%

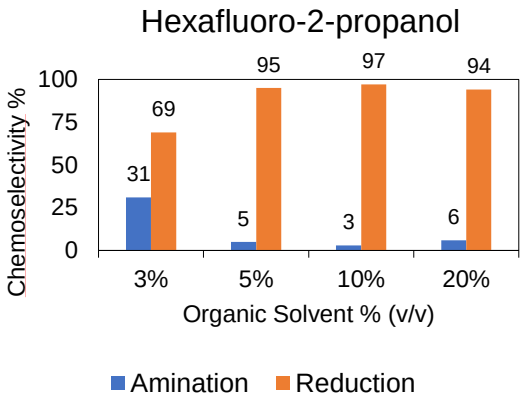
Figure S1. Organic co-solvent screen. Reactions were performed at 400 µL scale using 20 µM Mb*, 10 mM 3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (**1a**), 10 mM sodium dithionite in sodium borate buffer (50 mM, pH 9) containing the indicated amount of organic co-solvent, 3 hours, room temperature (RT), under anaerobic conditions.

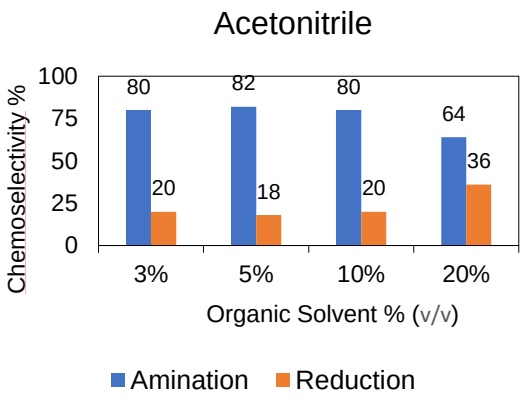







Isopropanol
Chemoselectivity %
100
75
50
25
0
79
21
74
26
60
40
67
33
3%
5%
10%
20%
Organic Solvent % (v/v)
Amination
Reduction


Hexafluoro-2-propanol
Chemoselectivity %
100
75
50
25
0
31
69
5
95
3
97
6
94
3%
5%
10%
20%
Organic Solvent % (v/v)
Amination
Reduction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75
50
25
0
80
20
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18
80
20
64
36
3%
5%
10%
20%
Organic Solvent % (v/v)
Amination
Reduction

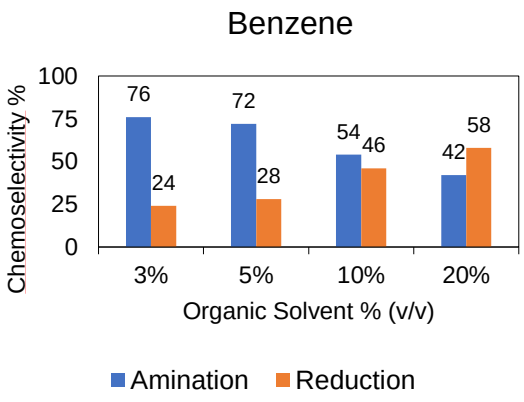
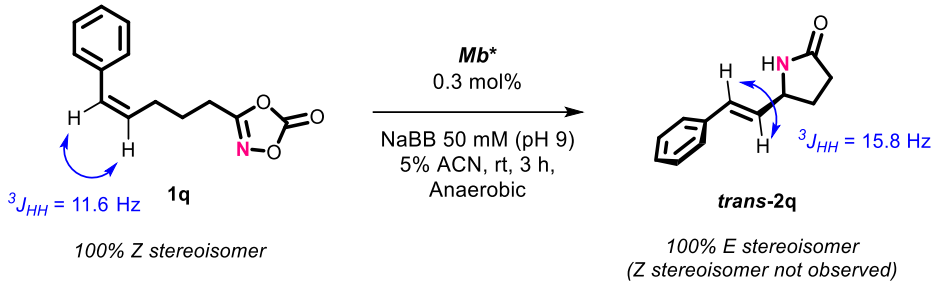

Benzene
Chemoselectivity %
100
75
50
25
0
76
24
72
28
54
46
42
58
3%
5%
10%
20%
Organic Solvent % (v/v)
Amination
Reduction

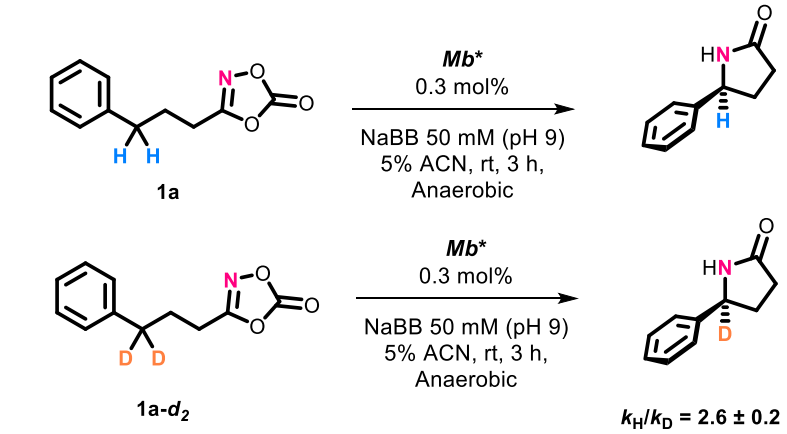
Figure S2. Rearrangement experiment. The Mb(H64V,V68A)-catalyzed intramolecular C-H amidation of substrate **1q** was carried out at a semipreparative scale (7 mg) using the **General Procedure D**. After purification, the resulting γ-lactam product was analyzed via ^{1}H-NMR spectroscopy which revealed a complete *Z*→*E* isomerization of the double bond by the *J* values of the vinylic H.



(*S*,*E*)-5-styrylpyrrolidin-2-one (2q) (7 mg, 12% yield; R_f = 0.5 (5% 2-propanol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.24 (m, 5H), 6.55 (d, *J* = 15.8 Hz, 1H), 6.13 (dd, *J* = 15.8 Hz, *J* = 7.4 Hz, 1H), 5.90 (s, 1H), 4.34 (q, *J* = 6.8 Hz, 1H), 2.40 (td, *J* = 12.4 Hz, *J* = 8.2 Hz, 3H), 1.94 (ddt, *J* = 10.2 Hz, *J* = 7.6 Hz, *J* = 4.1 Hz, 1H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 178.0, 136.0, 131.2, 129.8, 128.7, 128.0, 126.5, 56.4, 29.9, 28.5.

Figure S3. Intermolecular kinetic isotope effect experiments. Mb(H64V,V68A) catalyzed reactions were conducted in parallel using **1a** or **1a-*d*$_2$** as the substrate, under standard reaction conditions. Product formation over time was measured by GC and the KIE was calculated by comparing the slopes of the two plots, which yielded a KIE (k_H/k_D) of 2.6 ± 0.2 from independent experiments (n = 2). A representative plot is shown, and further experimental details can be found under the **Experimental Procedures** section.



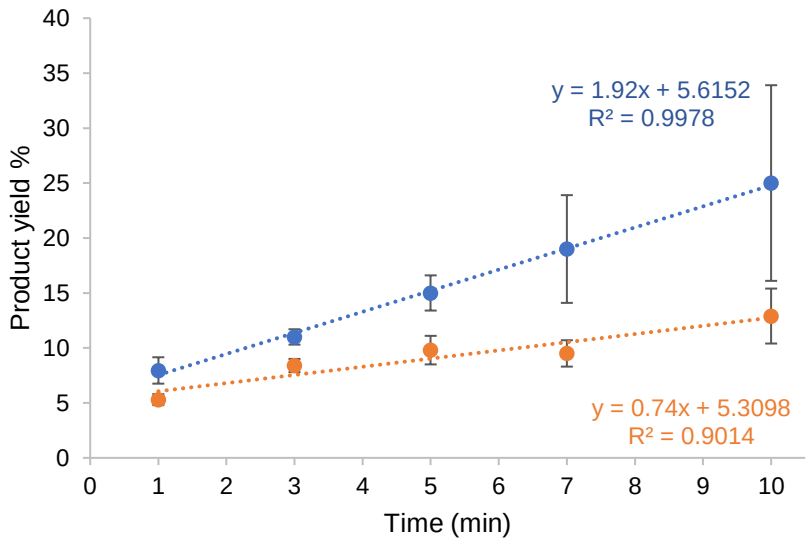
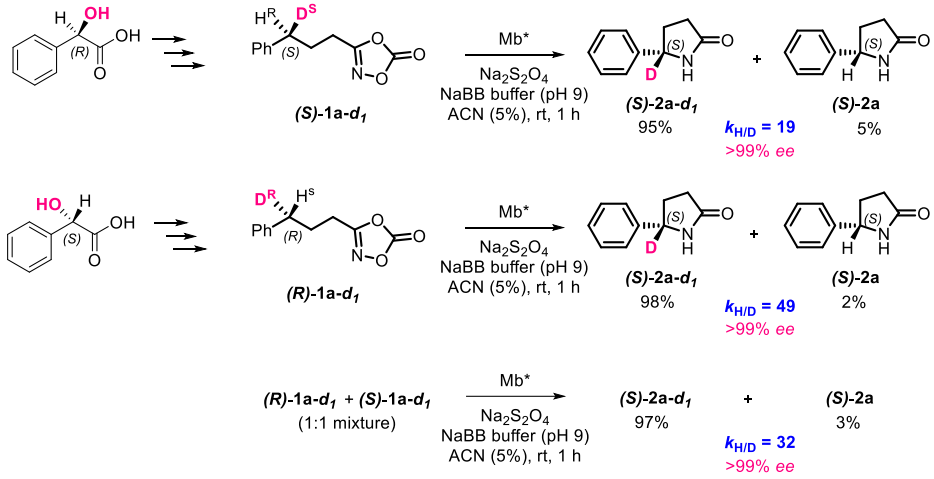


Figure S4. Intramolecular H/D competition experiments. Parallel reactions were carried out on a preparative scale (~30 mg product) using Mb(H64V,V68A) (= Mb*) as the catalyst, and either ***(S)*-1a-*d*$_1$**, or ***(R)*-1a-*d*$_1$**, or an equimolar mixture of ***(S)*-1a-*d*$_1$** and ***(R)*-1a-*d*$_1$** as the substrate, following the **General Procedure D** over 1 hour. After isolation of the γ-lactam product, the relative amount of **(*S*)-2a** vs. **(*S*)-2a-d$_1$** was determined via ^{1}H-NMR spectroscopy. The K_{HDE} ratio, which accounts for both the intrinsic KIE (k_H/k_D) and $k_{(proS)}/k_{(proR)}$, was determined to be 19, 49 and 32, respectively. The synthesis of ***(S)*-1a-*d*$_1$** and ***(R)*-1a-*d*$_1$** from enantiopure mandelic acid precursors is described in **Scheme S4**.



***(S)*-1a-*d*$_1$.** **^{1}H NMR (500 MHz, CDCl3):** δ 7.55 – 7.13 (m, 5H), 6.46 (s, 1H), 4.75 (t, *J* = 8.5 Hz, 0.05H), 2.55 (t, *J* = 11.2 Hz, 1H), 2.51 – 2.31 (m, 2H), 1.95 (t, *J* = 8.5 Hz, 1H).

***(R)*-1a-*d*$_1$**. **^{1}H NMR (500 MHz, CDCl3):** δ 7.55 – 7.13 (m, 5H), 6.46 (s, 1H), 4.75 (t, *J* = 8.5 Hz, 0.02H), 2.55 (t, *J* = 11.2 Hz, 1H), 2.51 – 2.31 (m, 2H), 1.95 (t, *J* = 8.5 Hz, 1H).

***Racemic* 1a-*d*$_1$**. **^{1}H NMR (500 MHz, CDCl3):** δ 7.55 – 7.13 (m, 5H), 6.46 (s, 1H), 4.75 (t, *J* = 8.5 Hz, 0.03H), 2.55 (t, *J* = 11.2 Hz, 1H), 2.51 – 2.31 (m, 2H), 1.95 (t, *J* = 8.5 Hz, 1H).

Figure S5. Gibbs free energy diagram for the Mb-catalyzed formation of γ-lactam **2a** from 3-phenylpropyl-dioxazolone **1a** for all possible spin states.

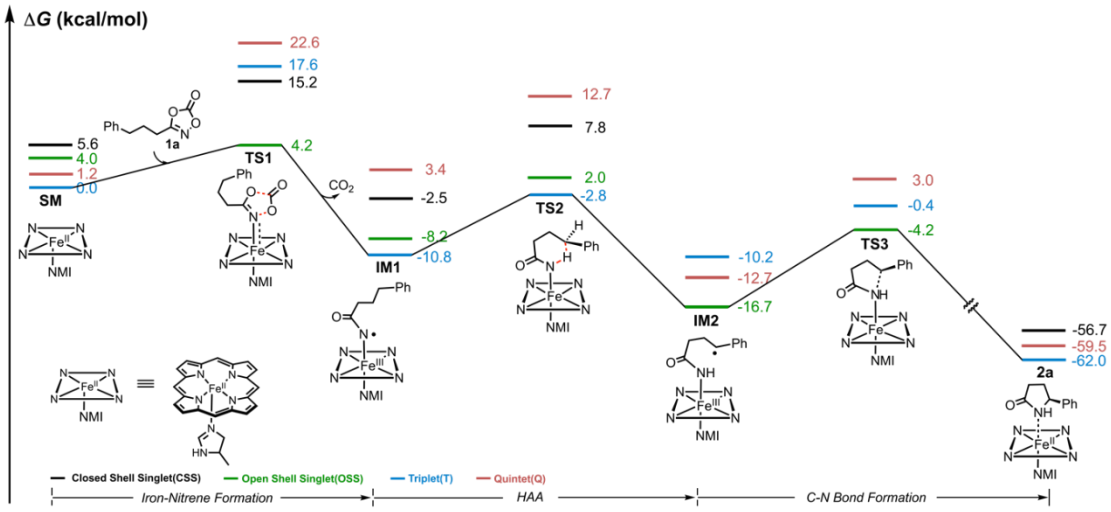


Figure S6. Analysis of enantioselectivity via MD simulations. Three independent MD simulations (1000 ns) were carried out using **1a**-derived nitrene intermediate **IM1** docked into the active site of Mb*. The figure reports representative snapshots of the complex (*left*) and the corresponding plot of the nitrene N···H^1 and nitrene N···H^2 distances (*right*) over the entire 1000 ns MD simulation.

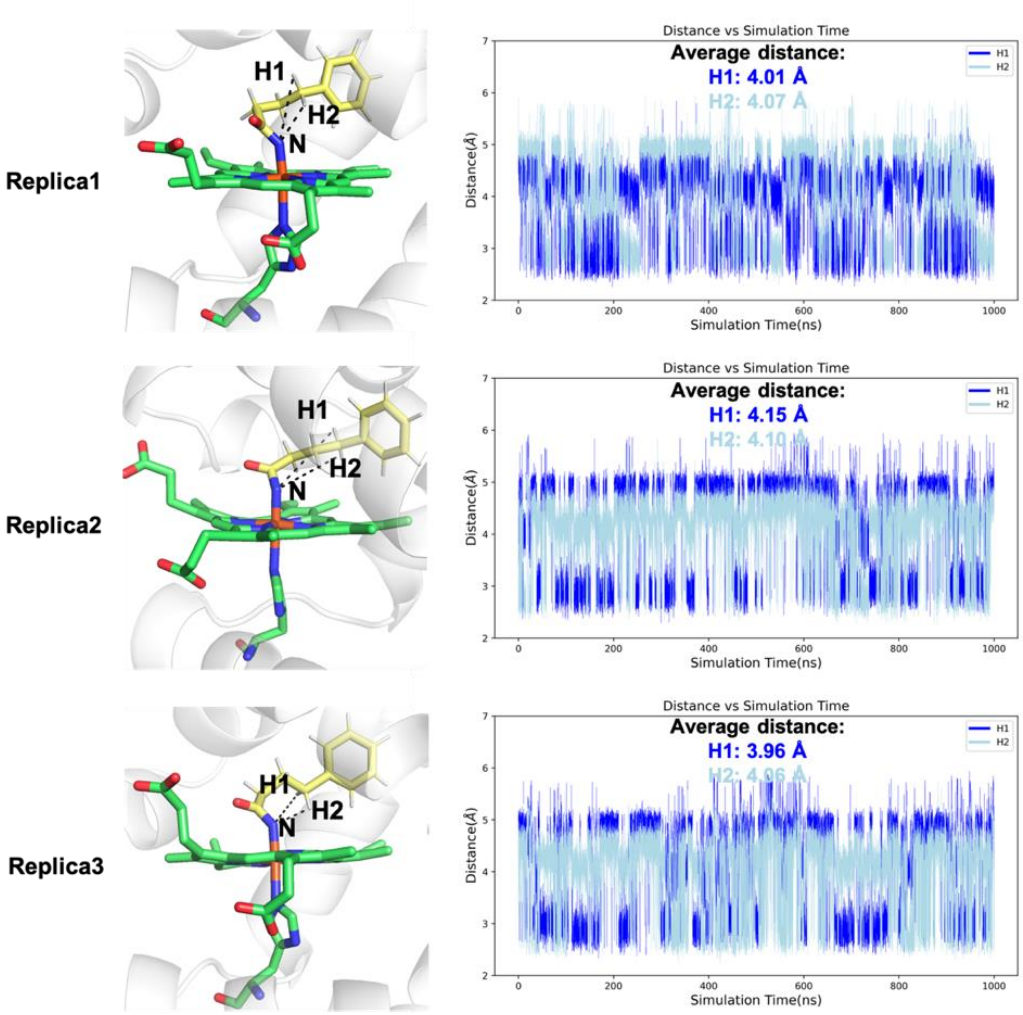


Figure S7. Mb*-bound carbon radical intermediate (IM2) in the pro-(*S*) and pro-(*R*) conformations. Docked complexes of the C-centered radical intermediate **IM2** derived from substrate **1a** in the active site of Mb* in both a conformation that could lead to the *S* lactam product (**IM2$_{pro(S)}$**; *left*) and a conformation that could lead to the *R* lactam product (**IM2$_{pro(R)}$**; *right*).

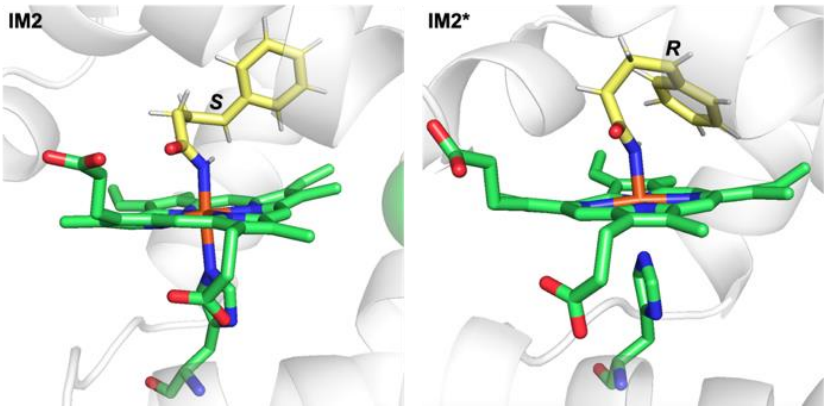


Figure S8. DFT analysis of pro-(*S*) vs. pro-(*R*) radical rebound step in C–H amidation of dioxazolone 1. Calculated models of the two **TS3** transition states for the radical rebound step in C–H amidation of substrate **1a** (see **Figure 5**) leading to the formation of *S*-configured product (*left*) and *R*-configured product (*right*). Active site residues involved in the interaction with the substrate phenyl group (yellow) are highlighted. The calculated energy for $TS3_{(pro\text{-}S)}$ is 3.1 kcal/mol lower than that of $TS3_{(pro\text{-}R)}$, explaining the enzyme's enantiopreference toward formation of *S*-configured product **2b** (over **ent-2b**).

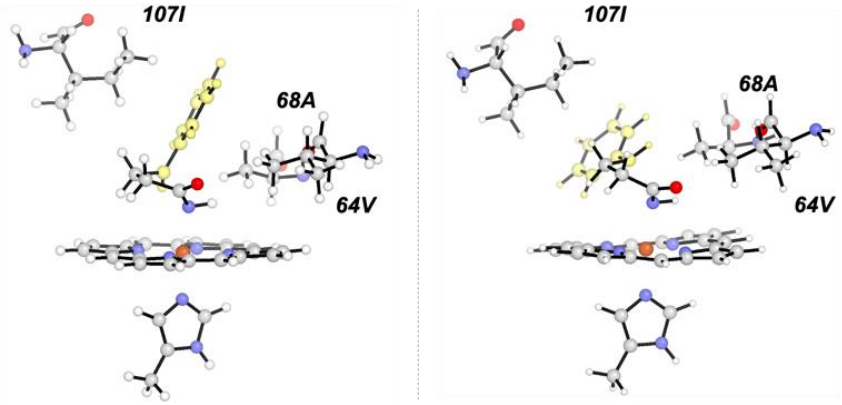


Figure S9. Analysis of regioselectivity toward γ- vs. δ-C-H amidation via MD simulations. Three independent MD simulations (1000 ns) were carried out using **5a**-derived nitrene intermediate **IM1** docked into the active site of Mb*. The figure reports representative snapshots of the complex (*left*) and the corresponding plot (*middle*) and Boltzmann distribution (*right*) of the nitrene N···γ-H and nitrene N···δ-H distances over the entire 1000 ns MD simulation.

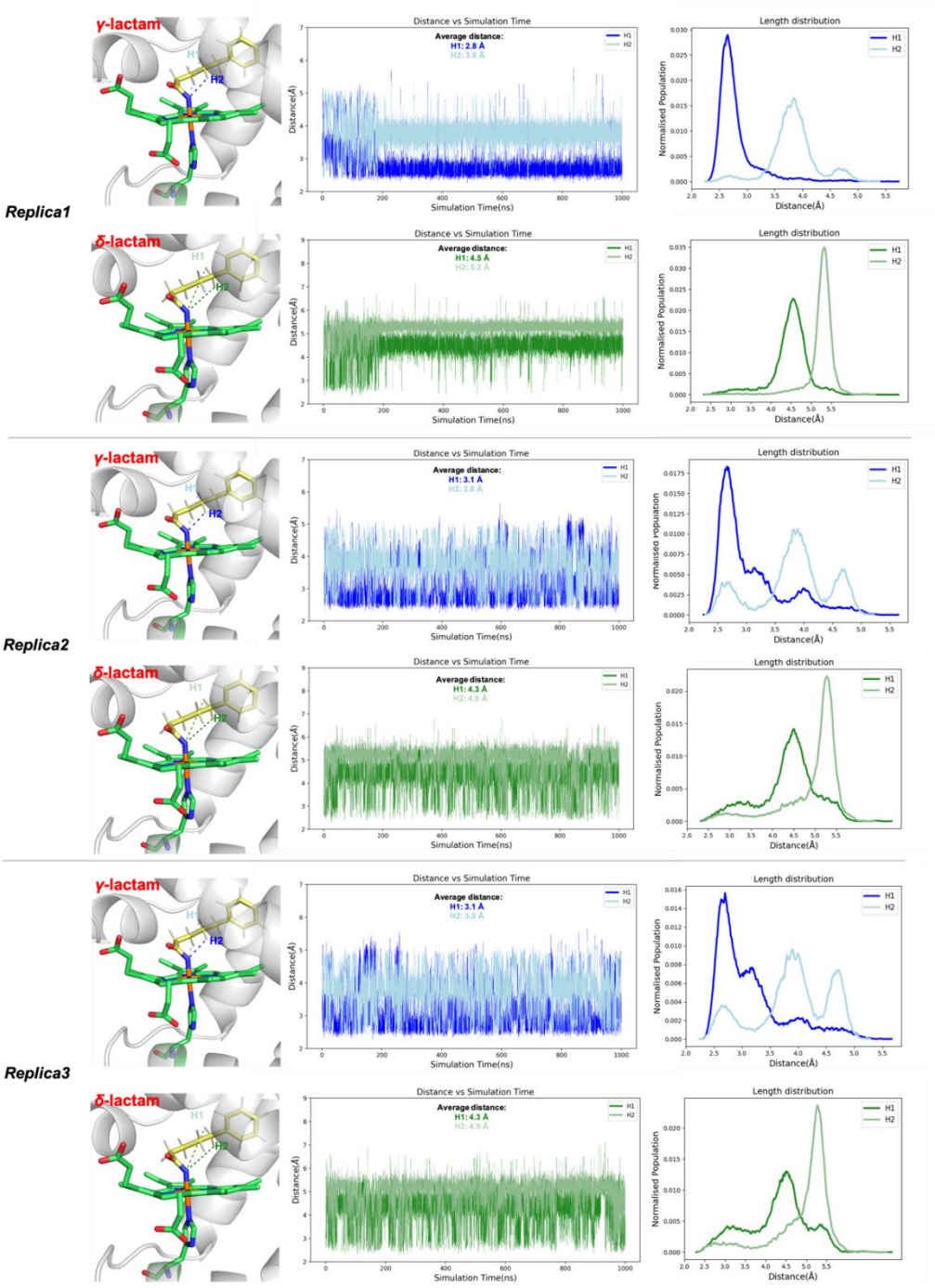


Figure S10. ORTEP of (*S*)-5-phenylpyrrolidin-2-one (**2a**) with ellipsoids drawn at the 50% probability level. Hydrogen atoms were located in the difference Fourier map and refined freely. They are represented here as spheres of arbitrary radius for clarity.

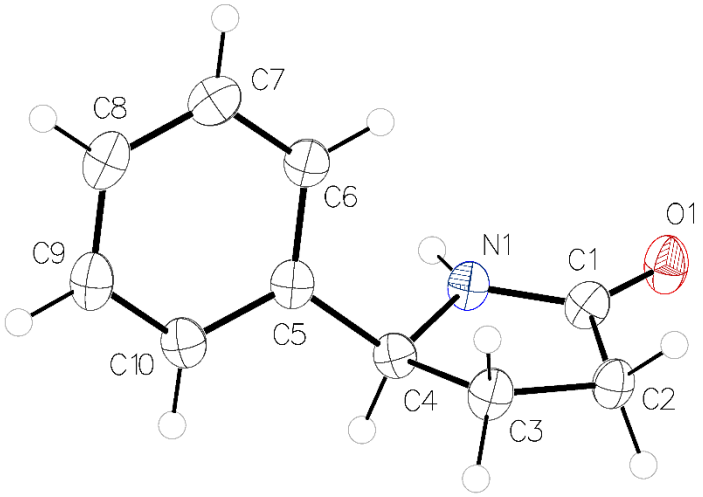


Figure S11. ORTEP of (*S*)-5-(thiophen-2-yl)pyrrolidin-2-one (**2m**) with ellipsoids drawn at the 50% probability level. Hydrogen atoms were located in the difference Fourier map and refined freely. They are represented here as spheres of arbitrary radius for clarity.

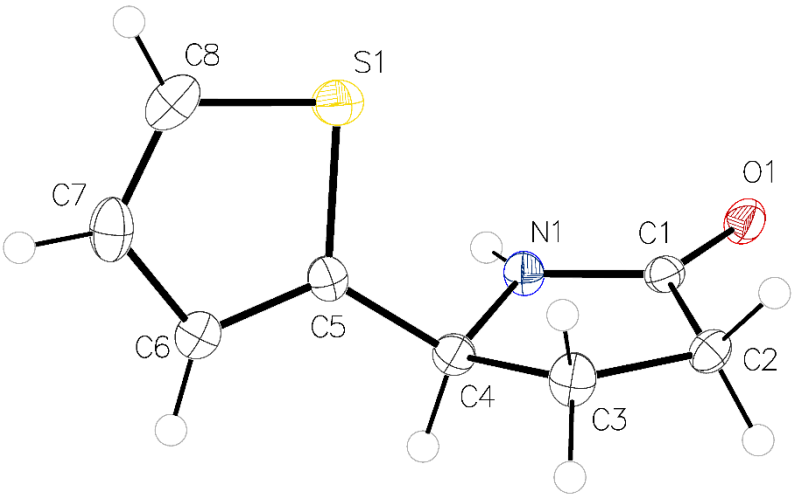


Figure S12. ORTEP of (*S*)-4-(thiophen-2-yl)azetidin-2-one (**4j**) with ellipsoids drawn at the 50% probability level. Hydrogen atoms were located in the difference Fourier map and refined freely. They are represented here as spheres of arbitrary radius for clarity.

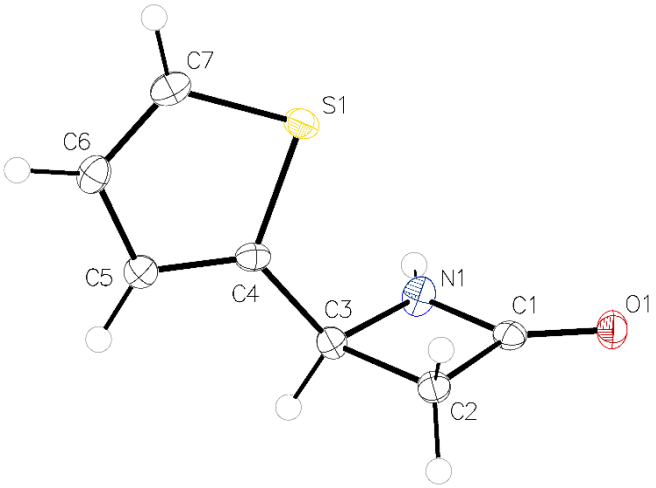
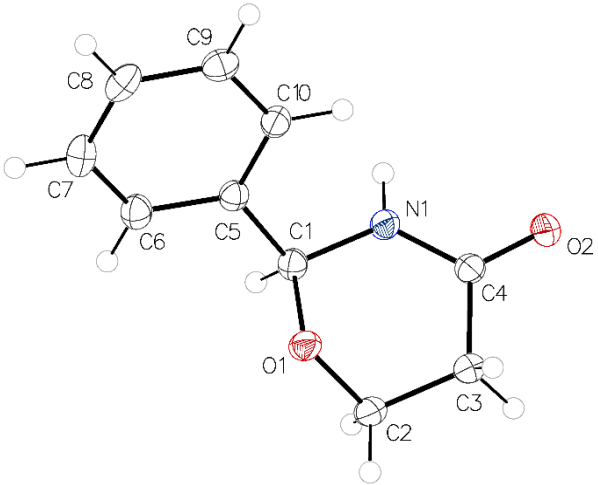
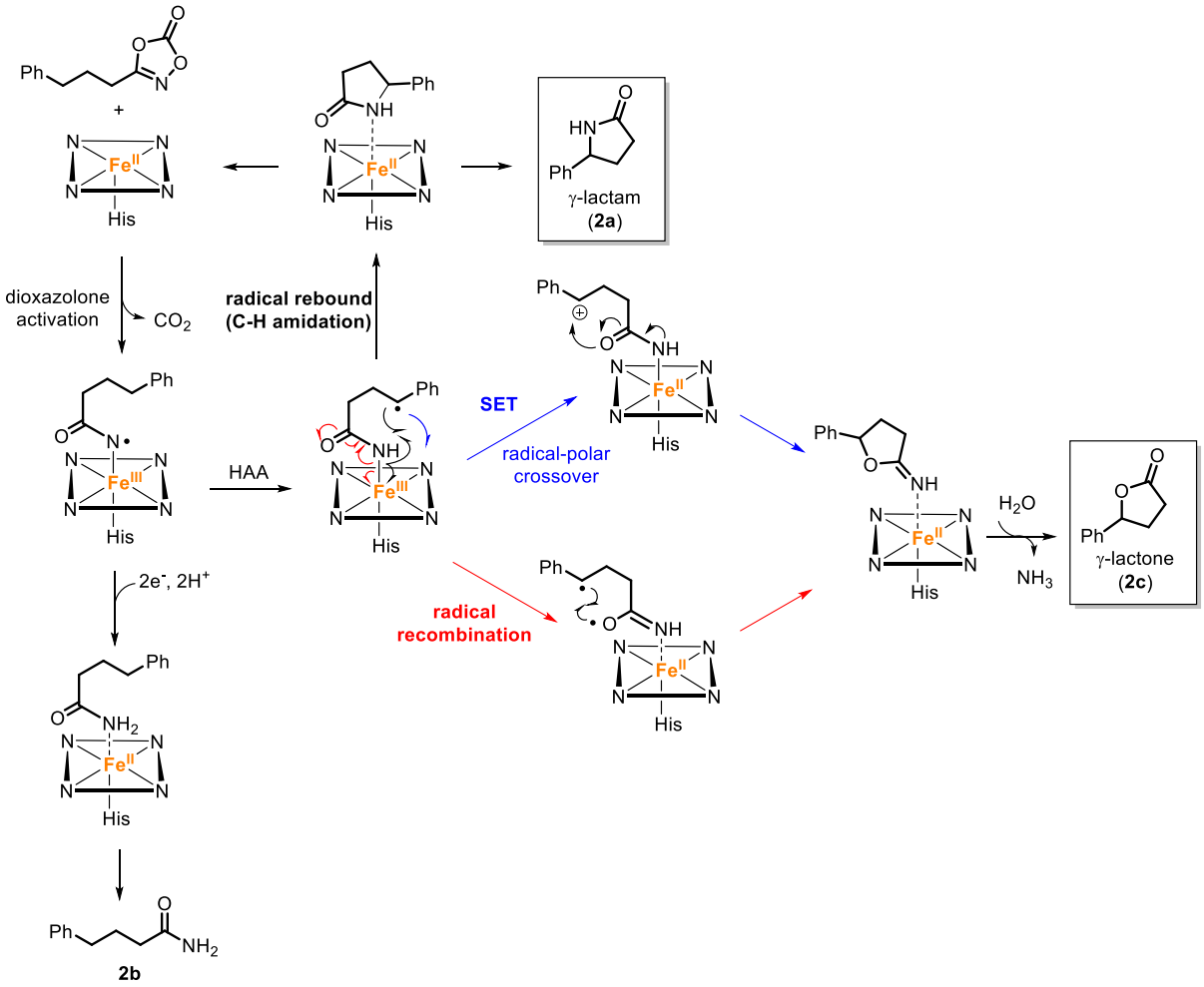


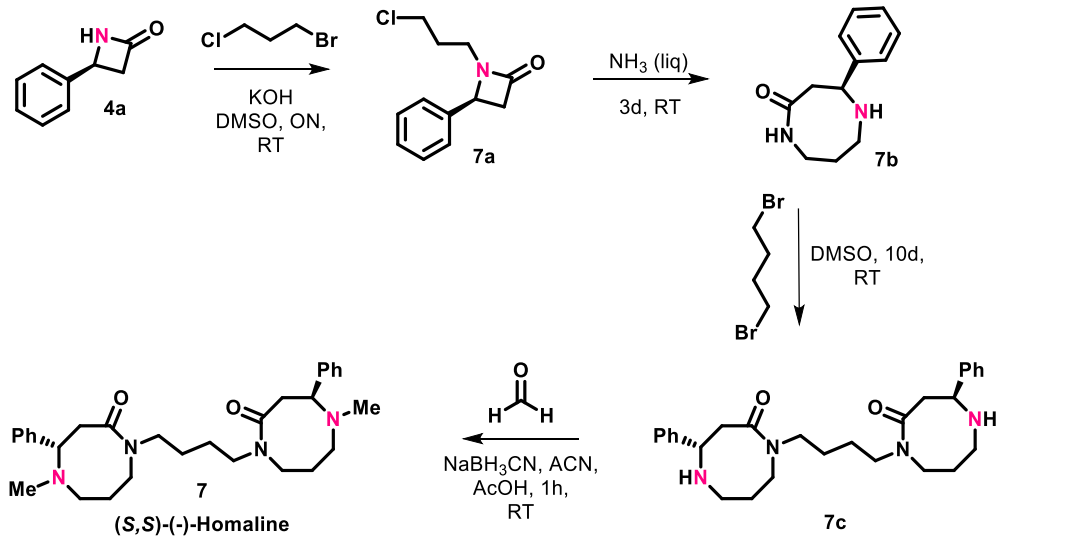
Figure S13. ORTEP of (*S*)-2-phenyl-1,3-oxazinan-4-one (**6c**) with ellipsoids drawn at the 50% probability level. Hydrogen atoms were located in the difference Fourier map and refined freely. They are represented here as spheres of arbitrary radius for clarity.

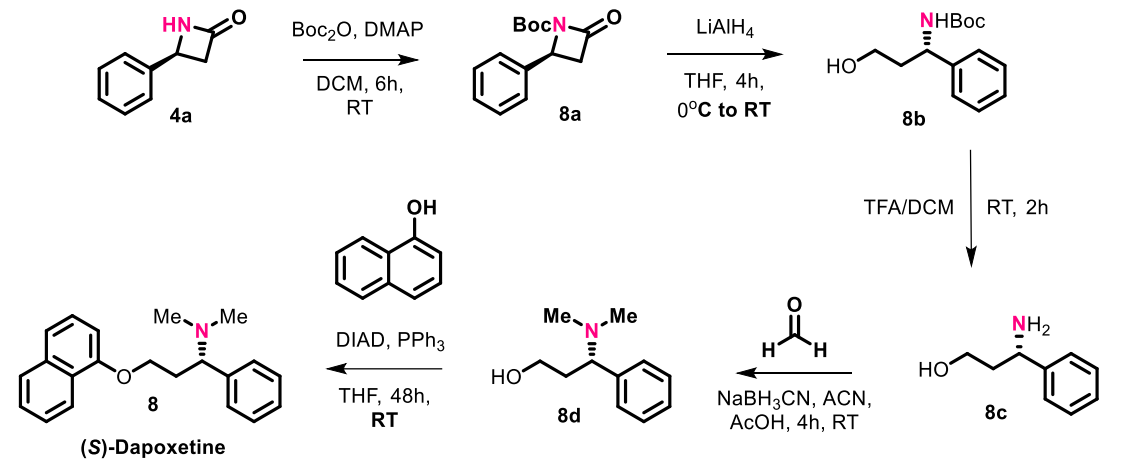


Scheme S1. Plausible mechanism for γ-lactone formation. Formation of the γ-lactone product (**2c**) from dioxazolone **1a** (**Figure 2**) may occur through two alternative, and not mutually exclusive pathways, namely through a radical-polar crossover mechanism proceeding via a carbocation intermediate (blue arrows) and/or via a diradical intermediate (red arrows). Both pathways produce the observed γ-lactone product.



Scheme S2. Syntheses of (*S*,*S*)-(-)-Homaline and (*S*)-Dapoxetine from enzymatically produced 4a. Starting from enantiopure β-lactam **4a** prepared enzymatically, the natural product alkaloid (*S*,*S*)-(-)-Homaline **7** and drug molecule (*S*)-Dapoxetine **8** were prepared according to reported procedures[1,2,3] as described in the following scheme.





Experimental Procedures

General Information. All the chemicals and reagents were purchased from commercial suppliers (Sigma-Aldrich, Alfa Aesar, ACS Scientific, Acros) and used without any further purification. All dry reactions were carried out under argon in flame-dried glassware with magnetic stirring using standard gas-tight syringes, cannula and septa. ^{1}H and ^{13}C NMR spectra were measured on Bruker DPX-500 (operating at 500 MHz for ^{1}H and 125 MHz for ^{13}C) or Bruker DPX-400 (operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C), ^{19}F was measured on Bruker DPX-400 (operating at 375 MHz). Tetramethylsilane (TMS) served as the internal standard (0 ppm) for $^{1}HNMR$, $CDCl_3$ was used as the internal standard (77.0 ppm) for $^{13}CNMR$, and trifluorotoluene served as the internal standard (-63 ppm) for ^{19}F NMR. Silica gel chromatography purifications were carried out using AMD Silica Gel 60 230-400 mesh. Thin Layer Chromatography (TLC) was carried out using Merck Millipore TLC silica gel 60 F254 glass plates.

Molecular Cloning. pET22b(+) (Novagen) was used as the recipient plasmid vector for expression of all of the myoglobin variants. In this construct, the Mb gene is C-terminally fused to a polyhistidine tag and it is under the control of an IPTG-inducible T7 promoter. The cloning of the single-site Mb variants tested in this study was described previously[42]. The recombination variants were prepared by combining the desired mutations using a similar cloning procedure and mutagenizing primers reported previously[43].

Protein Expression and Purification. Engineered Mb variants were expressed in *E. coli* C41(DE3) or BL21(DE3) cells as described previously[43]. Briefly, cells were grown in terrific broth (TB) medium (ampicillin, 100 mg L^{-1}) at 37 °C (150 rpm) until OD_{600} reached 0.9-1.2. Cells were then induced with 0.25 mM β-d-1-thiogalactopyranoside (IPTG) and 0.3 mM δ-aminolevulinic acid (ALA). After induction, cultures were shaken at 180 rpm and 27 °C and harvested after 18-20 h by centrifugation at 4000 rpm at 4°C. After cell lysis by sonication, the proteins were purified by Ni-affinity chromatography. The lysate was transfer to a Ni-NTA column equilibrated with Ni-NTA Lysis Buffer. The resin was washed with 50 mL of Ni-NTA Lysis Buffer and then 50 mL of Ni-NTA Wash Buffer (50 mM KPi, 250 mM, NaCl, 20 mM imidazole, pH 8.0). Proteins were eluted with Ni-NTA Elution Buffer (50 mM KPi, 250 mM, NaCl, 250 mM histidine, pH 7.0). After elution, the proteins were buffer exchanged against 50 mM KPi buffer (pH 7.0 or 8.0) using 10 KDa Centricon filters. Myoglobin concentration was determined using an extinction coefficient (Fe(III)) ε_{410} = 157 mM^{-1} cm^{-1}.

Purified Protein Reactions.

Analytical reactions were carried out at a 400 μL scale using 20 μM myoglobin, 10 mM dioxazolone compound, and 10 mM sodium dithionite under anaerobic conditions unless otherwise noted. In a typical procedure, 24-well plates or crimp vials containing a concentrated amount of Mb were introduced to an anaerobic chamber. Then, a corresponding amount of degassed potassium phosphate buffer (KPi, 50 mM, pH 7.0) or sodium borate buffer (NaBB 50 mM, pH 9) was added to each well/vial followed by

the addition of 40 μL of sodium dithionite solution (100 mM stock solution) in KPi or NaBB, producing a 20 μM myoglobin solution. The reactions were initiated by addition of 10 μL of the dioxazolone compound (400 mM stock solution in organic solvent). The plates were covered with aluminum foil (vials were capped) and left shaking at 120 rpm (or under magnetic agitation for vials) for 3-16 hours at room temperature. The reactions were then analyzed outside of the chamber following the **Product Analysis** protocol shown below.

Reactions with hemin or Fe(TPP)(Cl) were carried out using an identical procedure with the exception that the purified Mb was replaced by hemin (20 μM in DMF) or Fe(TPP)(Cl) (20 μM in DCM).

For each experiment, negative control samples containing no protein were included.

Intermolecular Kinetic Isotope Effect Experiments. These reactions were carried out using 20 μM myoglobin (50 mM NaBB, pH 9.0), 7.5 mM **1a** or **1a-d**$_2$ (5% ACN v/v), 10 mM sodium dithionite (50 mM NaBB, pH 9.0) and a certain volume of sodium borate buffer (NaBB, 50 mM, pH 9.0) to get to a final volume of 400 μL. Under anaerobic conditions, the reactions were set up in the following order: NaBB buffer, Mb, reductant, and finally the addition of the dioxazolone substrate initiated the reactions. Then, the reaction mixtures were left under magnetic agitation for the indicated time under argon. At the indicated time, the reactions were quenched by exposure to air and immediate transfer to an Eppendorf tube containing CH_2Cl_2 (400 μL) and internal standard (20 μL, 2.5 mM final concentration). The tube was

immediately vortexed for 30 seconds, centrifuged at 13,000 × g for 5 min, and the CH_2Cl_2 layer was extracted for GC analysis as described in the **Product Analysis** section. All measurements were performed in triplicates.

Product Analysis. After completion, the reactions were analyzed by adding 20 μL of internal standard (50 mM benzodioxole in EtOH) to the reaction mixture along with with 400 μL of CH_2Cl_2. After mixing the aqueous and organic layers, the organic phase was extracted and analyzed by GC-FID using a Shimadzu GC-2010 gas chromatograph equipped with an FID detector, and a chiral Cyclosil-B column (30 m x 0.25 mm x 0.25 μm film). **Separation and quantification method:** 1 μL injection, injector temperature: 250 °C, detector temperature: 300 °C. Gradient: column temperature set at 180 °C for 3 min, then to 185 °C for 1.0 °C/min then 190 for 2.0 °C/min then to 245 °C at 80 °C/min with a 0 min hold. Total run time: 16.19 min. Stereoselectivity determination was performed via chiral GC-FID of HPLC as described below. Calibration curves for quantification of the different cyclopropanation products were constructed with authentic standards prepared using purified protein biotransformations with Mb(H64V,V68A) or FePc as described in **Synthetic Procedures**. All measurements were performed at least in duplicate.

Determination of diastereomeric and enantiomeric excess

Chiral GC-FID and HPLC chromatograms for determination of diastereomeric and enantiomeric excess in the amidation reactions of dioxazolone substrates catalyzed by Mb(H64V,V68A). Reference racemic samples were prepared described in the

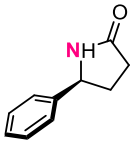
experimental procedures. GC method used for separation is described for each substrate, see **Product Analysis** section for details.

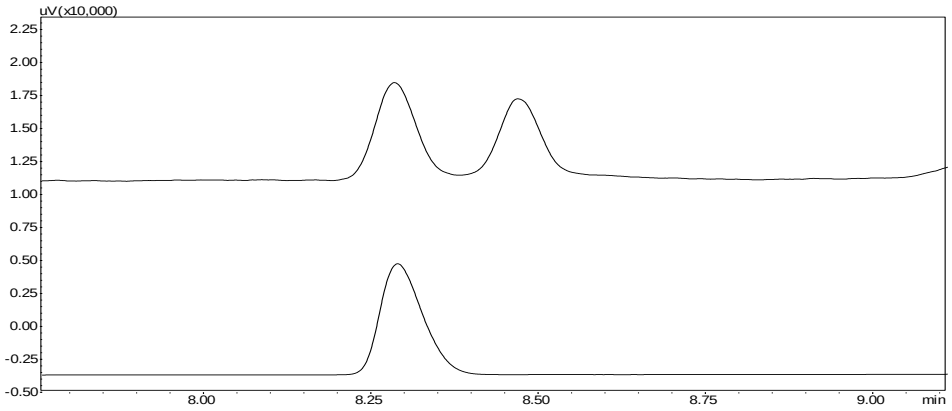
GC Separation Method 1: 1 μL injection, injector temperature: 250 °C, detector temperature: 300 °C. Gradient: column temperature set at 180 °C for 3 min, then to 185 °C for 1.0 °C/min then 190 for 2.0 °C/min then to 245 °C at 80 °C/min with a 0 min hold. Total run time: 16.19 min.

GC Separation Method 2: 1 μL injection, injector temperature: 240 °C, detector temperature: 300 °C. Gradient: column temperature set at 80 °C for 2 min, then to 120 °C for 1.5 °C/min for 1 min hold then to 150 °C for 1.2 °C/min for 1 min hold then to 180 °C for 1.1 °C/min for 5 min hold then to 245 °C at 35 °C/min with a 3 min hold. Total run time: 92.80 min.

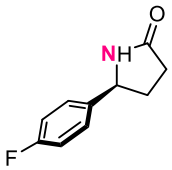
GC Separation Method 3: 1 μL injection, injector temperature: 240 °C, detector temperature: 300 °C. Gradient: column temperature set at 120 °C for 2 min, then to 120 °C for 1.0 °C/min for 1 min hold then to 150 °C for 1.0 °C/min for 1 min hold then to 180 °C for 1.0 °C/min for 5 min hold then to 245 °C at 35 °C/min with a 3 min hold. Total run time: 73.86 min.

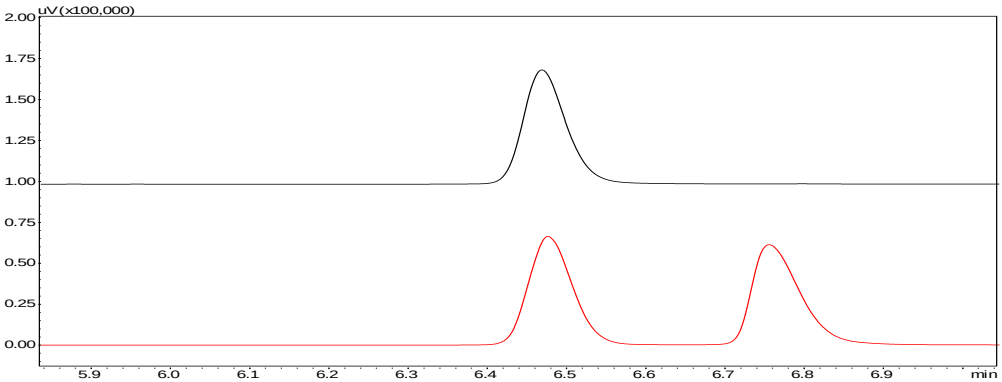
❖ **5-phenylpyrrolidin-2-one (2a)** GC analysis for enantiomeric determination of compound **2a** using **GC Separation Method 1**. Enzymatically generated (top) and racemic (bottom) products are shown below.



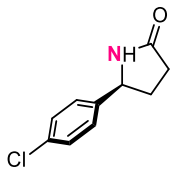


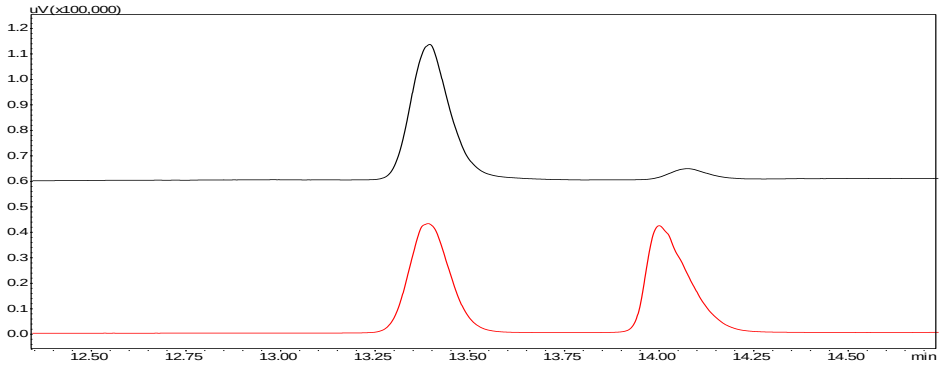
❖ **5-(4-fluorophenyl)pyrrolidin-2-one (2d)** GC analysis for enantiomeric determination of compound **2d** using **GC Separation Method 1**. Enzymatically generated (top) and racemic (bottom) products are shown below.



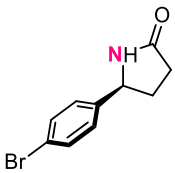


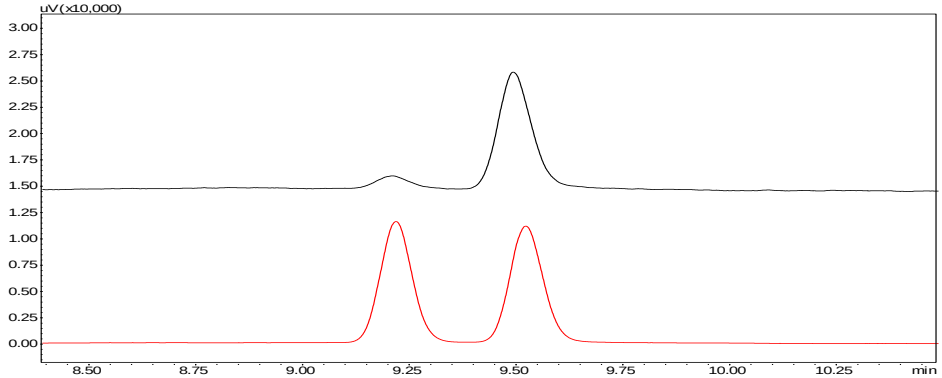
❖ **5-(4-chlorophenyl)pyrrolidin-2-one (2e)** GC analysis for enantiomeric determination of compound **2e** using **GC Separation Method 1**. Enzymatically generated (top) and racemic (bottom) products are shown below.



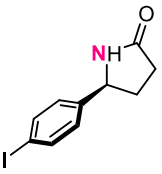


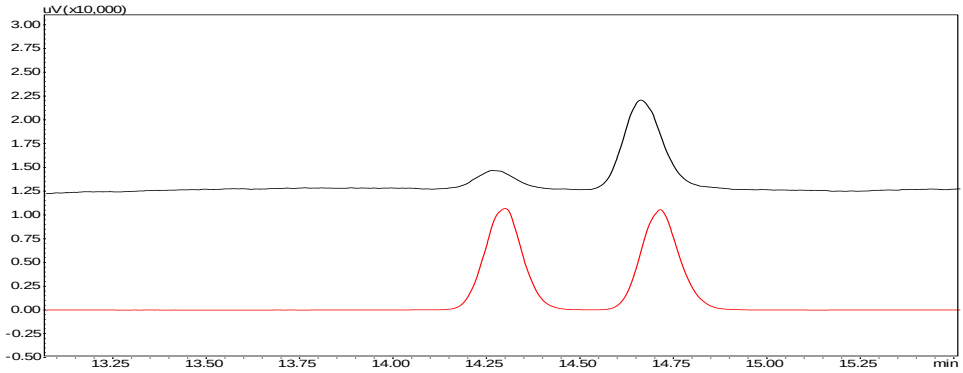
❖ **5-(4-bromophenyl)pyrrolidin-2-one (2f)** GC analysis for enantiomeric determination of compound **2f** using **GC Separation Method 1**. Enzymatically generated (top) and racemic (bottom) products are shown below.



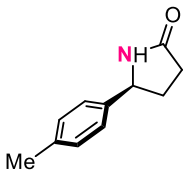


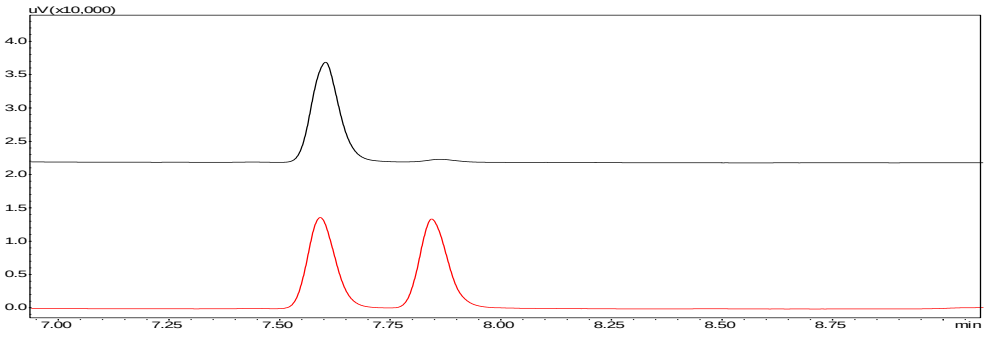
❖ **5-(4-iodophenyl)pyrrolidin-2-one (2g)** GC analysis for enantiomeric determination of compound **2g** using **GC Separation Method 1.** Enzymatically generated (top) and racemic (bottom) products are shown below.



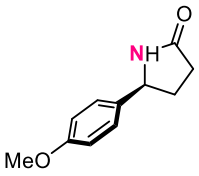


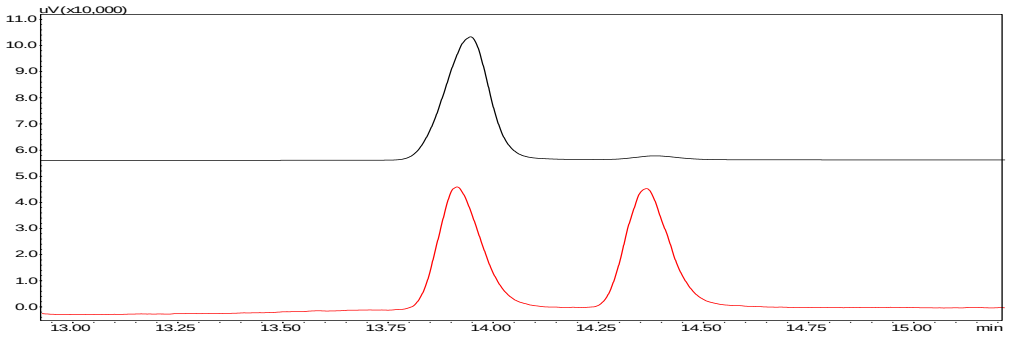
❖ **5-(p-tolyl)pyrrolidin-2-one (2h)** GC analysis for enantiomeric determination of compound **2h** using **GC Separation Method 1.** Enzymatically generated (top) and racemic (bottom) products are shown below.



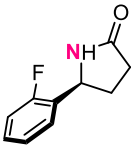


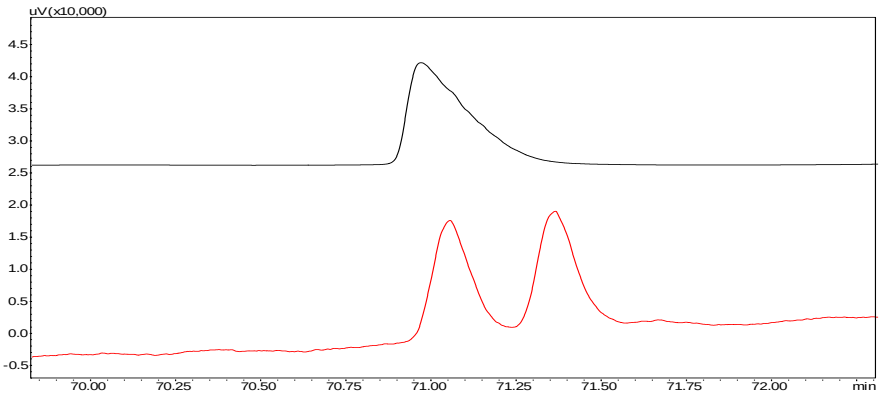
❖ **5-(4-methoxyphenyl)pyrrolidin-2-one (2i)** GC analysis for enantiomeric determination of compound **2i** using **GC Separation Method 1.** Enzymatically generated (top) and racemic (bottom) products are shown below.



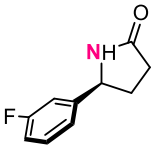


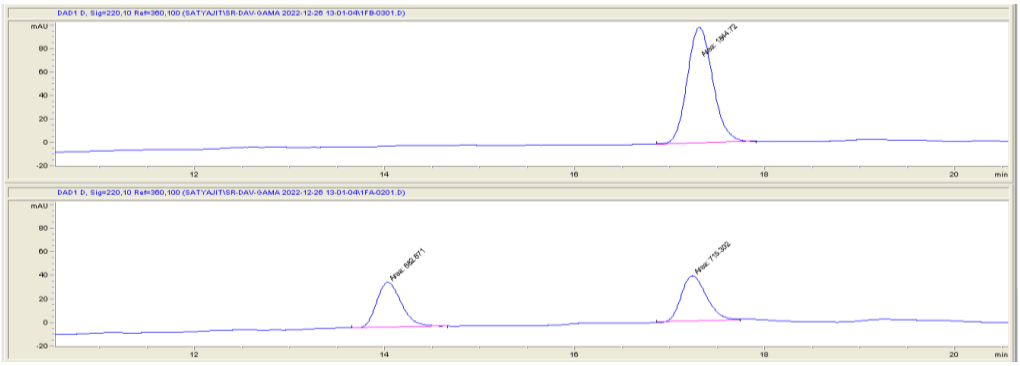
❖ **5-(2-fluorophenyl)pyrrolidin-2-one (2j)** GC analysis for enantiomeric determination of compound **2j** using **GC Separation Method 2.** Enzymatically generated (top) and racemic (bottom) products are shown below.



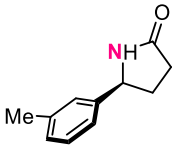


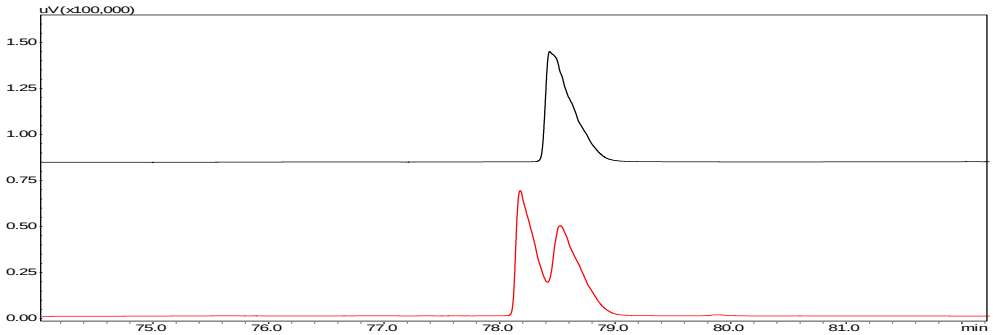
❖ **5-(3-fluorophenyl)pyrrolidin-2-one (2k)** HPLC analysis for enantiomeric determination of compound **2k** using HPLC HPLC Conditions: Detector wavelength- 254 nm, Chiral IA Column, 15% iPrOH/hexanes, 1.0 mL/min: tR (major) = 17.3 min. tR (minor) = NA, %ee = >99%. Enzymatically generated (top) and racemic (bottom) products are shown below.



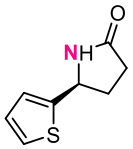


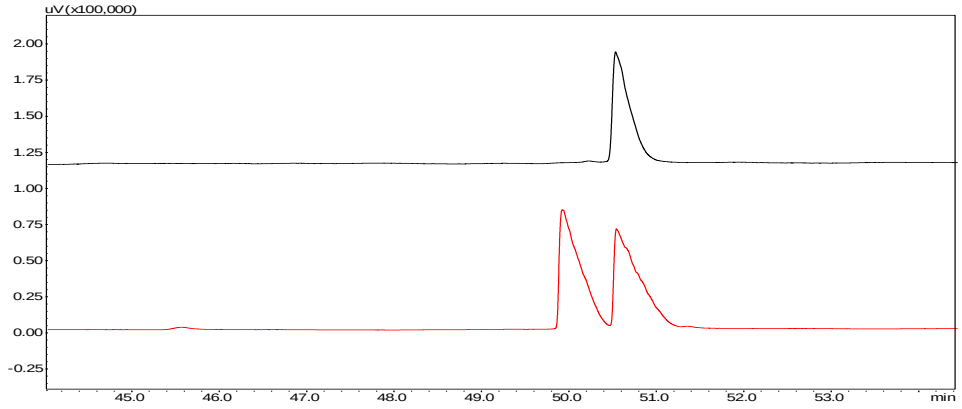
❖ **5-(m-tolyl)pyrrolidin-2-one (2l)** GC analysis for enantiomeric determination of compound **2l** using **GC Separation Method 2.** Enzymatically generated (top) and racemic (bottom) products are shown below.



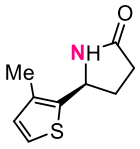


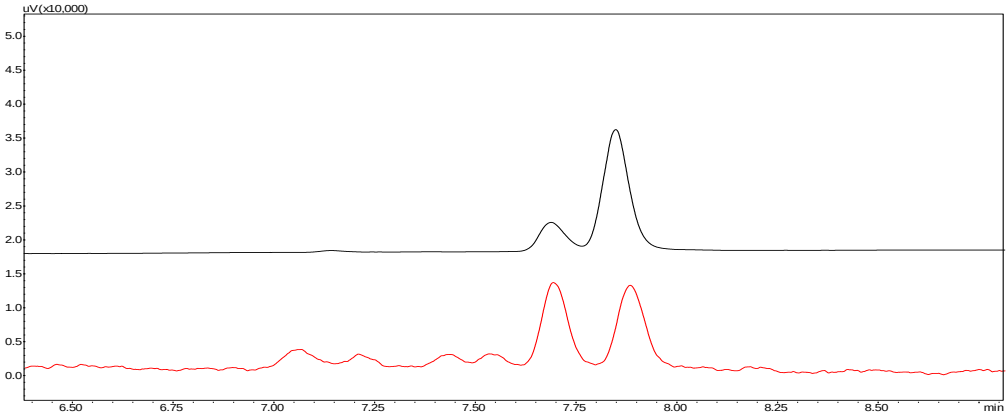
❖ **5-(thiophen-2-yl)pyrrolidin-2-one (2m)** GC analysis for enantiomeric determination of compound **2m** using **GC Separation Method 3.** Enzymatically generated (top) and racemic (bottom) products are shown below.



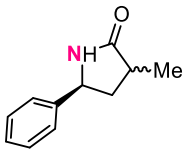


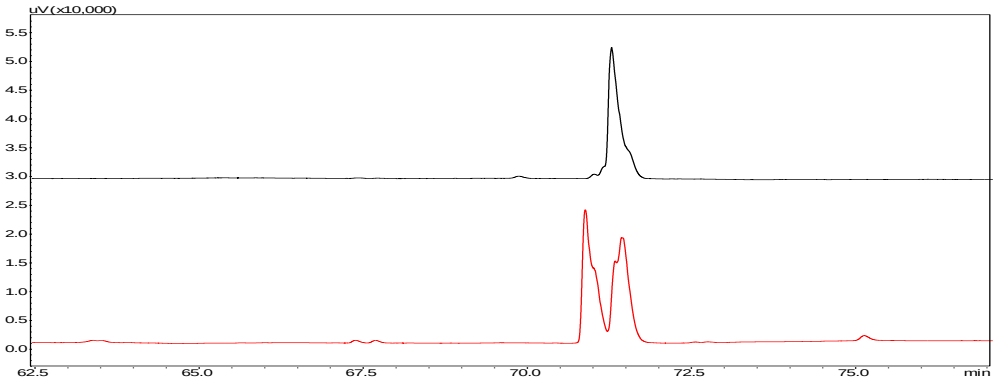
❖ **5-(3-methylthiophen-2-yl)pyrrolidin-2-one (2n)** GC analysis for enantiomeric determination of compound **2n** using **GC Separation Method 1.** Enzymatically generated (top) and racemic (bottom) products are shown below.



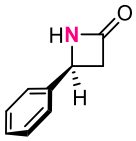


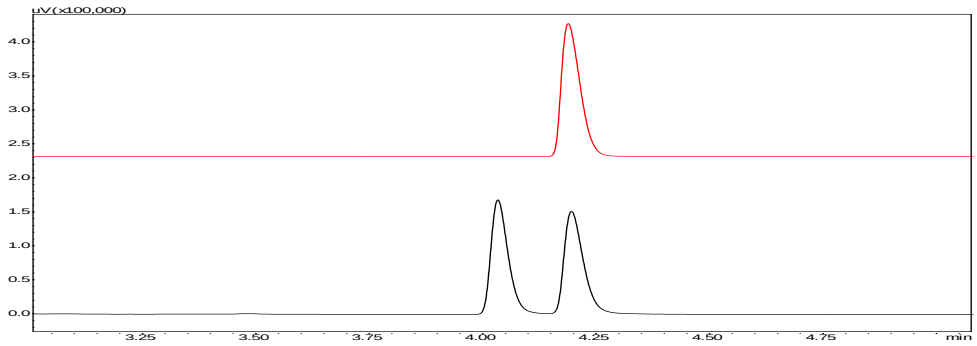
❖ **3-methyl-5-phenylpyrrolidin-2-one (2p)** GC analysis for enantiomeric determination of compound **2p** using **GC Separation Method 3.** Enzymatically generated (top) and racemic (bottom) products are shown below.



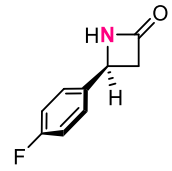


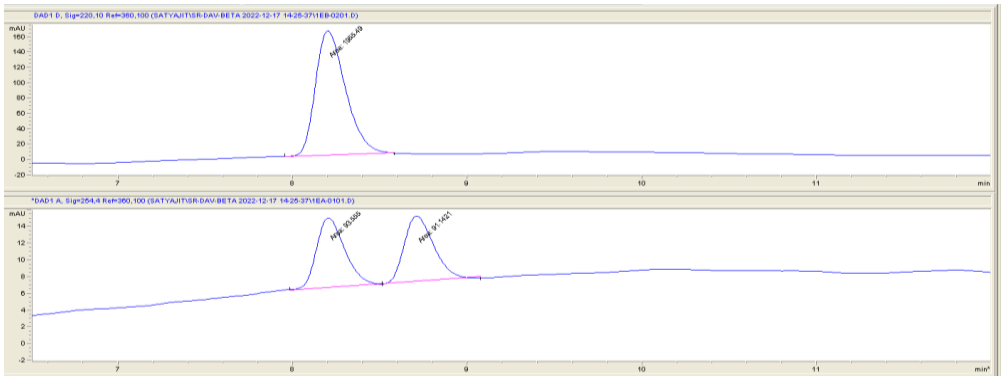
❖ **4-phenylazetidin-2-one (4a)** GC analysis for enantiomeric determination of compound **4a** using **GC Separation Method 1.** Enzymatically generated (top) and racemic (bottom) products are shown below.



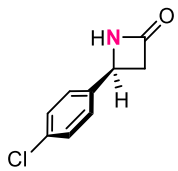


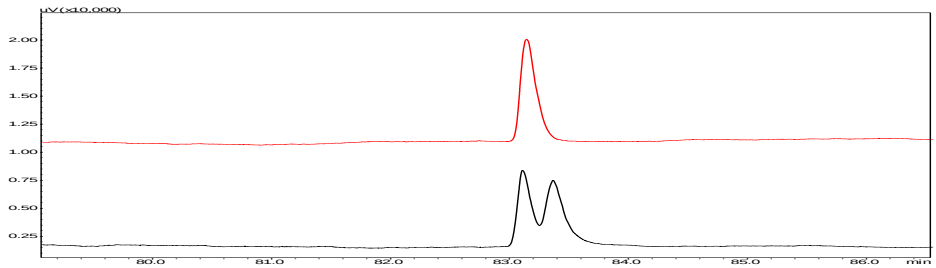
❖ **4-(4-fluorophenyl)azetidin-2-one (4b)** HPLC analysis for enantiomeric determination of compound **4b** using HPLC Conditions: Detector wavelength-254 nm, Chiral IA Column, 15% iPrOH/hexanes, 1.0 mL/min:tR (major) = 8.2 min. tR (minor) = NA, %ee = >99%. Enzymatically generated (top) and racemic (bottom) products are shown below.



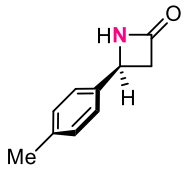


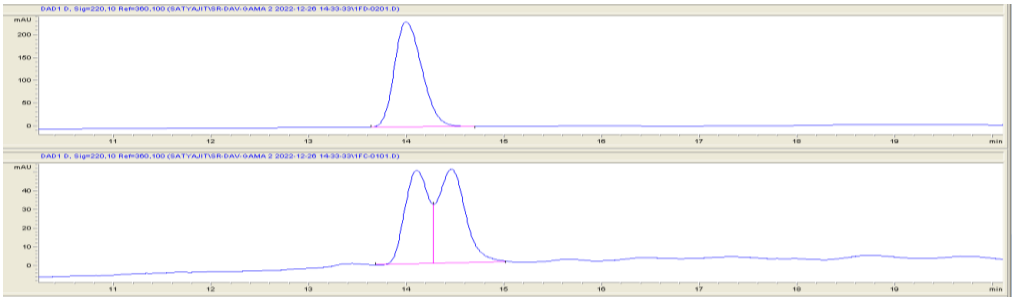
❖ **4-(4-chlorophenyl)azetidin-2-one (4c)** GC analysis for enantiomeric determination of compound **4c** using **GC Separation Method 2.** Enzymatically generated (top) and racemic (bottom) products are shown below.



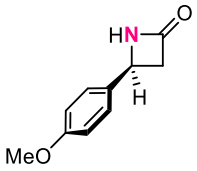


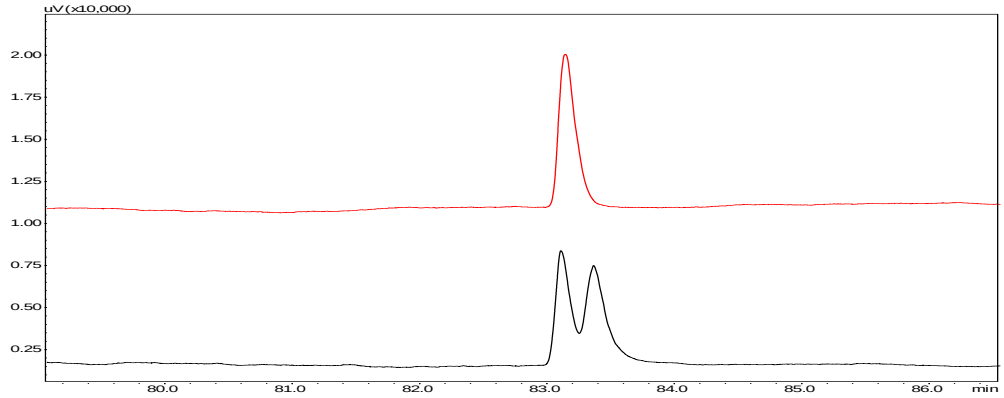
❖ **4-(p-tolyl)azetidin-2-one (4d)** HPLC analysis for enantiomeric determination of compound **4d** using HPLC Conditions: Detector wavelength- 254 nm, Chiral IA Column, 15% iPrOH/hexanes, 0.7 mL/min:tR (major) = 14.0 min. tR (minor) = NA, %ee = >99%. Enzymatically generated (top) and racemic (bottom) products are shown below.



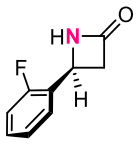


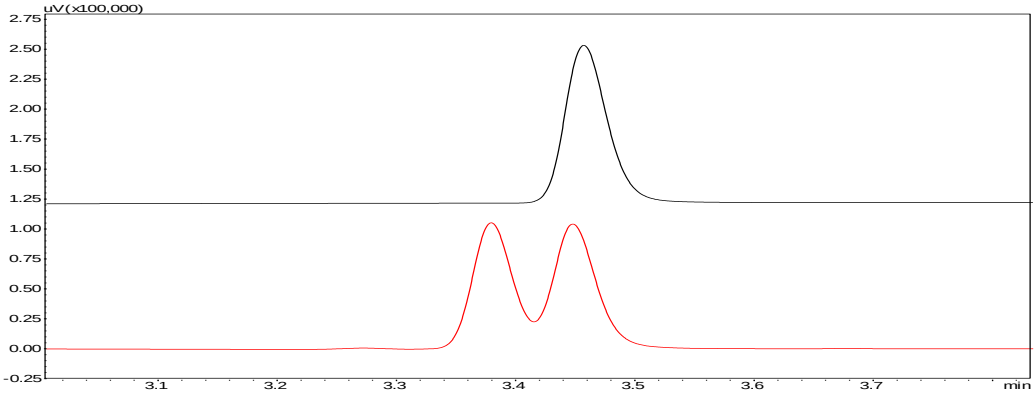
❖ **4-(4-methoxyphenyl)azetidin-2-one (4e)** GC analysis for enantiomeric determination of compound **4e** using **GC Separation Method 2.** Enzymatically generated (top) and racemic (bottom) products are shown below.



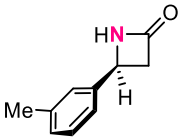


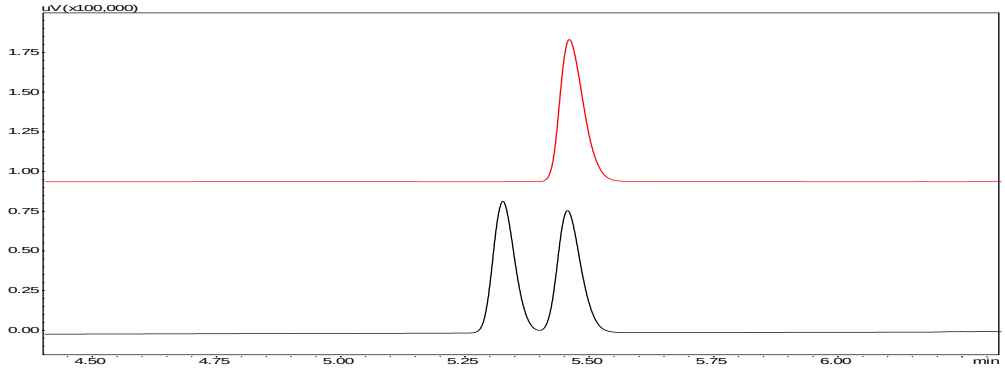
❖ **4-(2-fluorophenyl)azetidin-2-one (4f)** GC analysis for enantiomeric determination of compound **4f** using **GC Separation Method 1.** Enzymatically generated (top) and racemic (bottom) products are shown below.



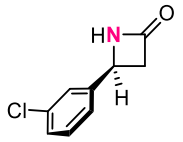


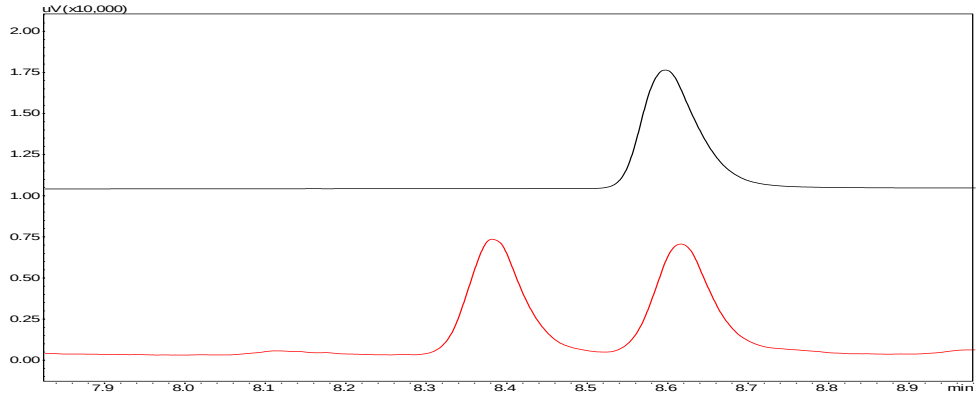
❖ **4-(m-tolyl)azetidin-2-one (4g)** GC analysis for enantiomeric determination of compound **4g** using **GC Separation Method 1.** Enzymatically generated (top) and racemic (bottom) products are shown below.



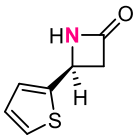


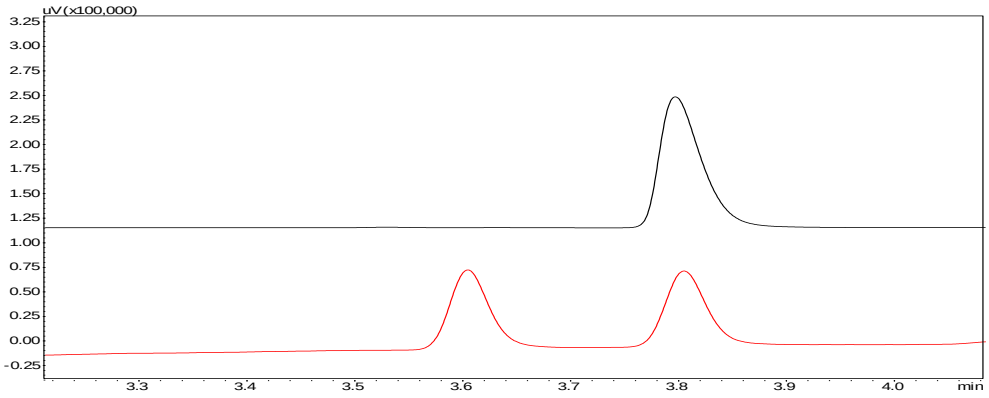
❖ **4-(3-chlorophenyl)azetidin-2-one (4h)** GC analysis for enantiomeric determination of compound **4h** using **GC Separation Method 1.** Enzymatically generated (top) and racemic (bottom) products are shown below.





❖ **4-(thiophen-2-yl)azetidin-2-one (4j)** GC analysis for enantiomeric determination of compound **4j** using **GC Separation Method 1.** Enzymatically generated (top) and racemic (bottom) products are shown below.



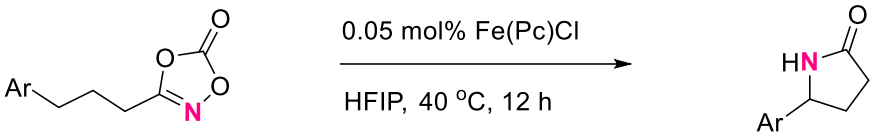


Synthetic Procedures

Safety Note: The C-H amidation reactions described in this work produce stoichiometric amounts of CO_2 gas. Therefore, caution is advised when performing the reactions at larger scales and it is recommended to follow safety protocols for reactions run under high pression.

Preparation of racemic compounds

Procedure I:

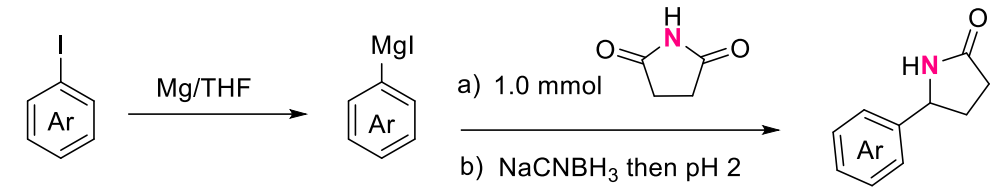


0.1 mmol

2a, 2d, 2e, 2f, 2g, 2h, 2n, 2p

The racemic compounds **2a, 2d, 2e, 2f, 2g, 2h, 2n, 2p** were made using the following procedure reported by Chang and co-workers[4] . A solution of PcFe(III)Cl in HFIP (1.0 mL) was added to dioxazolones (0.1 mmol) placed in a 4 mL vial. The reaction mixture was stirred at 40 °C for 12 h. The solvent was evaporated under vacuum and 1.0 mL of DCM was added. From this crude mixture, a 20 uL aliquot of the reaction mixture was taken and analyzed by chiral GC.

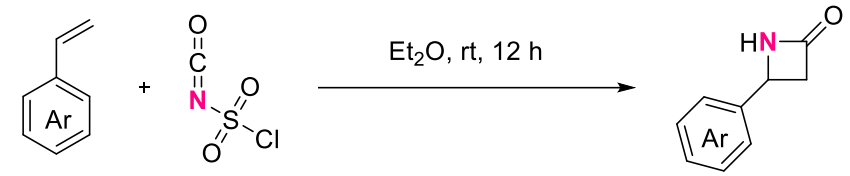
Procedure II:



3.0 mmol **2i, 2j, 2k, 2l, 2m**

The racemic compounds **2i, 2j, 2k, 2l** and **2m** were synthesized using the following procedure. To a solution of aryl iodide (3.0 mmol) in anhydrous THF (10 mL) was added magnesium (3.0 mmol, 1.0 equiv.) at room temperature. Upon complete consumption of magnesium, a cold solution of succinimide (1.0 mmol) in THF (10 mL) was added and stirred at room temperature for 12 hours. Subsequently, solid $NaCNBH_3$ (1.2 mmol) was added. The reaction was acidified to pH 2-4 with 6 M HCl, stirred for 30 minutes and neutralized with 3M NaOH. The organic layer was separated, and the aqueous layers extracted with DCM (3 x 10 mL). The combined organic extracts were washed with brine, dried over magnesium sulfate, filtered and reduced to dryness. The crude product was analyzed by either chiral GC or HPLC.

Procedure III:

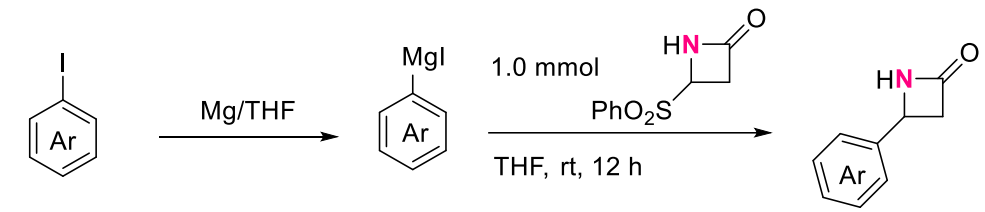


1.0 mmol 1.0 equiv. **4a, 4b, 4c, 4d, 4f**

The racemic compounds **4a, 4b, 4c, 4d** and **4f** were synthesized using the reported procedure[5] . Add the N-chlorosulfonyl isocyanate (1.0 mmol) dropwise over 10 minutes to a solution of styrene (1.0 mmol) in anhydrous diethyl ether (2 ml) at room temperature under an inert atmosphere. The mixture was stirred at room temperature

for 12 hours. After completion, the solvent was removed under reduced pressure. The crude residue was dissolved in diethyl ether (10 ml), poured dropwise over 10 minutes to a vigorously stirred solution of sodium carbonate (5.0 mmol, 5 equiv.) and sodium sulfite (5.0 mmol, 5 equiv.) in water (10 ml) containing ice (10 g). The solution was the stirred for 1 hour and later filtered. The organic layers were separated, and the aqueous layer was extracted with diethyl ether (3x10 ml). The combined organic extracts were dried over anhydrous Na_2SO_4 and filtered. The solvent was removed under reduced pressure to obtain **4a, 4b, 4c, 4d** and **4f** which was analyzed by chiral GC and HPLC.

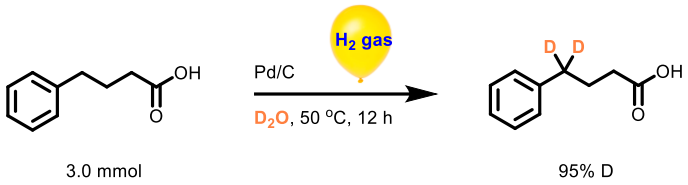
Procedure IV:



3.0 mmol **4e, 4g, 4h, 4j**

The racemic compounds **4e, 4g, 4h** and **4j** were synthesized using the following procedure. To a solution of aryl iodide (3.0 mmol) in anhydrous THF (10 mL) was added magnesium (3.0 mmol, 1.0 equiv.) at room temperature. Upon complete consumption of magnesium, a cold solution of 4-(phenylsulfonyl)azetidin-2-one (1.0 mmol) in THF (10 mL) was added and stirred at room temperature for 12 hours. The crude product analyzed by either chiral GC or HPLC.

Preparation of 4-phenylbutanoic-4,4-d2 acid

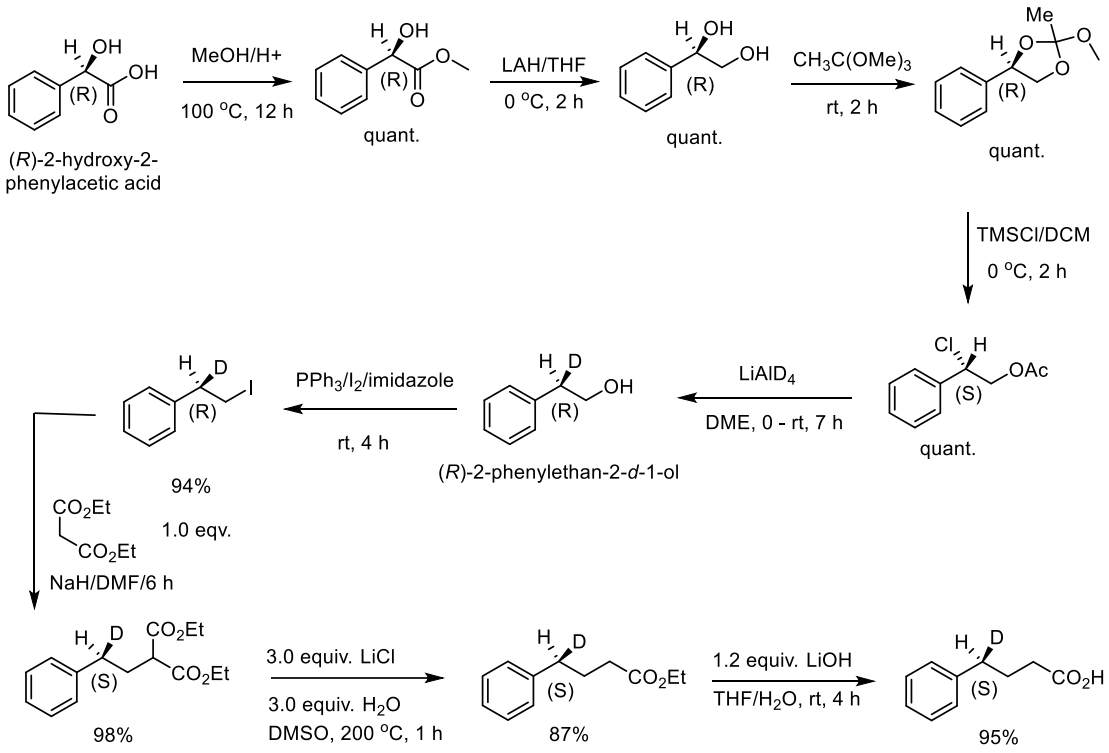


3.0 mmol 95% D

The synthesis of 4-phenylbutanoic-4,4-d2 acid was performed following a reported procedure.[4] A suspension of the carboxylic acid (1.00 mmol) and 10% Pd/C (10 wt% of the substrate) in D_2O (0.5mL) was stirred at room temperature or 50°C in a sealed test tube filled with hydrogen gas. After the appropriate time, the mixture was diluted with diethyl ether (10mL), and then filtered using celite to remove the Pd catalyst. The filtrate was partitioned between diethyl ether and aqueous layers. The aqueous layers were extracted with diethyl ether (2x15mL). The combined organic layers were washed with brine (3x30mL) and dried over $MgSO_4$. After filtration, the crude was concentrated *in vacuo* and purified using silica gel chromatography (20-30% ethyl acetate in hexane as eluent) to afford 4-phenylbutanoic-4,4-d2 acid in 91% yield. Spectroscopic data obtained was in accordance with the reported data[6].

^{1}H NMR (400 MHz, $CDCl_3$): δ 11.31 (s, 1H), 7.29 (td, *J* = 6.9, 1.5 Hz, 1H), 7.23 – 7.11 (m, 2H), 2.38 (t, *J* = 7.4 Hz, 1H), 1.96 (t, *J* = 7.4 Hz, 1H).

Preparation of (S)-4-phenylbutanoic-4-d acid



(*R*)-Methyl Mandelate. (*R*)-Methyl Mandelate was prepared according to a known procedure[7]. (*R*)-Mandelic acid (2.28 g, 15 mmol), 2,2-dimethoxypropane (1.85 mL, 15 mmol), were refluxed in concentrated H_2SO_4 (150 µL) and MeOH (15 mL) for 4–5 h. The mixture was concentrated and the residual oil was dissolved in Et_2O (20 mL) and washed with a 5% aqueous solution $NaHCO_3$. The organic phase was washed with brine, dried with MgSO4 and concentrated to afford the ester compound which was used for the next step without any further purification. The spectral data were in accordance with the reported literature[8].

(*R*)-Phenylethylene Glycol. To a cooled (0 °C) mixture of $LiAlH_4$ (0.57 g, 15 mmol) in dry DME (30 mL), under N_2 atmosphere, was added dropwise a solution of (*R*)-Methyl Mandelate (2.24 g, 13.5 mmol) in dry DME (30 mL). After 2-3 h of stirring at

room temperature, the reaction mixture was quenched at 0°C by addition of 1 mL of H_2O, 1 mL of 15% NaOH solution, and 2.5 mL of H_2O and then filtered. The organic layer was washed with a 5% solution of $NaHCO_3$, dried over $MgSO_4$, and concentrated. The residue was used without any further purification for the next step. The spectral data were in accordance with the reported literature[8].

(2*SR*,4*R*)-2-Methoxy-2-methyl-4-phenyl-1,3-dioxolane. A mixture of (*R*)-Phenylethylene Glycol (1.61 g, 11.5 mmol), trimethyl orthoacetate (3.9 mL, 31.1 mmol) and concentrated H_2SO_4 (23 µL) was stirred at room temperature for 1 h. The red oil was distilled (bp 86–88 ^oC) to give a 3/2 mixture of diastereomers **5** which was used without any further purification. The spectral data were in accordance with the reported literature[8].

(*S*)-2-Chloro-2-phenylethyl Acetate. (*S*)-2-Chloro-2-phenylethylacetate was prepared according to a reported procedure. To a solution of (2*SR*,4*R*)-2-Methoxy-2-methyl-4-phenyl-1,3-dioxolane (1.96 g, 10 mmol) and dry CH_2Cl_2 (10 mL) at 0^oC was added chlorotrimethylsilane (3.8 mL, 30 mmol). After 2 h at 0^oC the mixture was concentrated under reduced pressure and the residual oil was distilled (bp 72–74 ^oC) to give (*S*)-2-Chloro-2-phenylethyl Acetate which was used without any further purification. The spectral data were in accordance with the reported literature[8].

(*R*)-2-Phenylethanol-2-d1. To a cooled (0 °C) mixture of LiAlD4 (0.42 g, 10 mmol) in dry DME (20 mL), under N_2 atmosphere, was added dropwise a solution of compound (*S*)-2-Chloro-2-phenylethylacetate (1.59 g, 8 mmol) in dry DME (10 mL).

After 7 h of stirring at room temperature, the reaction mixture was quenched at 0°C by addition of 1 mL of H_2O, 1 mL of 15% NaOH solution, and 2.5 mL of H_2O and then filtered. The organic layer was washed with a 5% aqueous solution of $NaHCO_3$, dried over $MgSO_4$, and concentrated. The crude product was chromatographed on silica gel (hexanes:EtOAc = 4:1 v/v) to give (1.1 g) (*R*)-2-Phenylethanol-2-d1. Overall yield was 62% (over 5 steps) and the spectral data were in accordance with the reported literature[8].

(*R*)-(2-iodoethyl-1-d)benzene.Triphenylphosphine (512 mg, 2.0 mmol) and Iodine (533 mg, 2.1 mmol) were dissolved in 6 mL CH_2Cl_2, then the reaction mixture was stirred under argon at room temperature for 30 min. Subsequently, imidazole (153 mg, 2.2 mmol) was added to the reaction mixture, stirred for additional 15 min. Then (*R*)-2-Phenylethanol-2-d1 (186 mg, 1.5 mmol) was added to the reaction mixture. After completion of the reaction, excess iodine was quenched by adding $Na_2S_2O_3$ (10% aq.). The mixture was extracted with CH_2Cl_2 and the combined organic layers were washed with brine. The combined organic extracts were dried with Na_2SO_4 and concentrated to give the residue, which was purified by column chromatography to give (R)-(2-iodoethyl-1-d)benzene (329 mg) in 94% yield. The spectral data were in accordance with the reported literature[9].

Diethyl (S)-2-(2-phenylethyl-2-d)malonate: To an ice cooled solution of sodium hydride (48.0 mg, 2.0 equiv) in dry DMF, dimethyl malonate (160 mg, 1.0 equiv) was added dropwise with continuous stirring. The reaction mixture was slightly warmed to 40 ^oC. After stirring for 1 h was added (R)-(2-iodoethyl-1-d)benzene (233 mg, 1.0 mmol) at 0 ^oC. The reaction mixture was stirred at 70 ^oC for 4 h. After completion of

the reaction as indicated by TLC, the reaction mixture was quenched with saturated solution of NH_4Cl. The reaction mixture was diluted with 5 mL water and extracted with ether (2 x 20 mL). The organic layer was washed with brine (2 x 80 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting crude product was purified by silica gel column chromatography using ethyl acetate/n-hexane gradients to afford 260 mg (98%) of pure product. The spectral data were in accordance with the reported literature[9].

Ethyl (*S*)-4-phenylbutanoate-4-d. Diethyl alkyl malonate (1.5 mmol), lithium chloride (166 mg, 1.5 mmol) and deionized H_2O (3.0 mL) were added to a 25 mL round bottom flask equiped with condenser. The reaction mixture was heated to 200°C for 2 h. The reaction contents were poured into saturated $NaHCO_3$ (10 mL). The contents were extracted with EtOAc (2 x 15 mL), washed sequentially with $NaHCO_3$ (15 mL) and brine (15 mL). The combined organic phases were dried over Na_2SO_4. After filtration the combined organic phases were concentrated *in vacuo* and the crude was used without any further purification for the next step.

(*S*)-4-phenylbutanoic-4-d acid. A 50 mL round bottom flask was charged with Ethyl (*R*)-4-phenylbutanoate-4-d (193 mg, 1.0 mmol) and LiOH (46 mg, 2.0 equivalent). Then, 1:1 THF and H_2O was added via syringe (10 mL). The reaction mixture was then stirred at room tempetature for 12 h. After completion (checked by TLC), reaction was diluted with 20 mL of Et_2O. separate the organic layer and washed the aquous layer with 20 mL of Et_2O two times. The combine organic layer was dried over Na_2SO_4 and concentrated the organic layer under vacuuo. The resulting crude product was purified

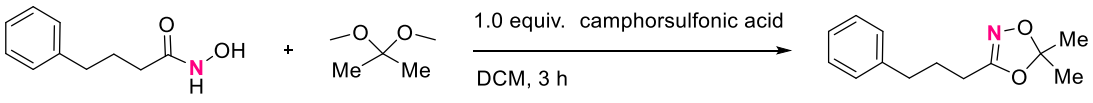
by silica gel column chromatography using ethyl acetate/n-hexane gradients to afford 157 mg (yield, 95%) of pure product.

Preparation of (R)-4-phenylbutanoic-4-d acid

(*R*)-4-phenylbutanoic-4-d acid was prepared identically as (*S*)-4-phenylbutanoic-4-d acid, using (*S*)-Mandelic acid as the starting material instead.

Scheme 5. Preparation of other nitrene precursors

Preparation of 5,5-dimethyl-3-(3-phenylpropyl)-1,4,2-dioxazole (1aa):

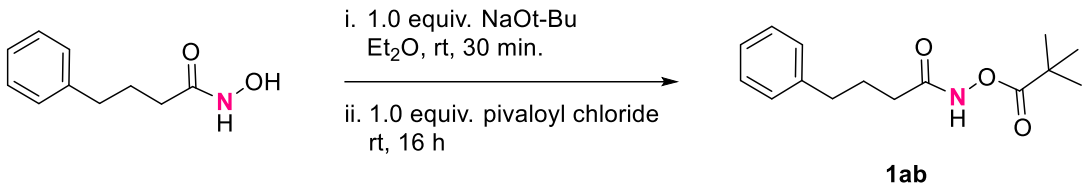


1aa

Compound 5,5-dimethyl-3-(3-phenylpropyl)-1,4,2-dioxazole (**1aa**) was synthesized following the reported procedure[10]. To a stirred solution of N-hydroxy-4-phenylbutanamide (1.8 g, 10 mmol) and 2,2-dimethylpropane (3.1 g, 30 mmol) in 150 mL of CH_2Cl_2 was added camphorsulfonic acid (2.3 g, 10 mmol). Reaction mixture was stirred at room temperature for 3 h and quenched with a saturated sodium bicarbonate (20 mL). The aqueous layer was extracted with diethyl ether (100 mL x 3) and dried over Na_2SO_4 and purified by silica gel column chromatography (eluent: n-hexane/EtOAc, 10:1) to obtain the desired products (**1aa**, 1.8 g, 84%) as white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.22 (m, 2H), 7.18 (ddd, J = 8.5 Hz, J = 7.0 Hz, J = 1.8 Hz, 3H), 2.67 (t, J = 7.7 Hz, 2H), 2.30 (t, J = 7.5 Hz, 2H), 1.96-1.89 (m, 2H), 1.55 (s, 6H).

Preparation of 4-phenyl-N-(pivaloyloxy)butanamide (1ab):

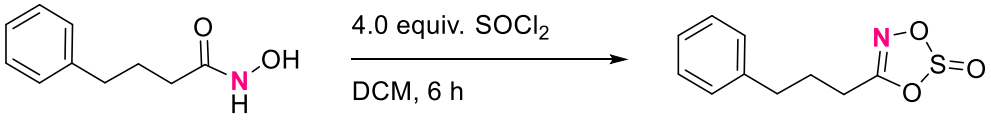


1ab

Compound 4-phenyl-N-(pivaloyloxy)butanamide (**1ab**) was synthesized following the reported procedure[11]. A solution of N-hydroxy-4-phenylbutanamide (3.0 mmol) and sodium tert-butoxide (1.0 equiv) in diethyl ether (20 ml) was stirred for 30 min at room temperature. Benzoyl chloride, pivaloyl chloride or 2,3,4,5,6-pentafluorobenzoyl chloride (1.0 equiv.) was added to the solution via dropwise addition. The reaction mixture was stirred for 16 h, diluted by EtOAc, and washed by $NaHCO_3$ solution and water. The organic phase was dried over $MgSO_4$ and purified by silica gel column chromatography (eluent: n-hexane/EtOAc, 10:1) to obtain the desired products (**1ab**) as white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.79 (s, 1H), 7.26 (dd, J = 8.7 Hz, J = 6.8 Hz, 2H), 7.21 – 7.11 (m, 3H), 2.66 (t, J = 7.5 Hz, 2H), 2.21 (t, J = 7.4 Hz, 2H), 2.02 – 1.92 (m, 2H), 1.28 (s, 9H).

Preparation of 5-(3-phenylpropyl)-1,3,2,4-dioxathiazole 2-oxide (1ac):



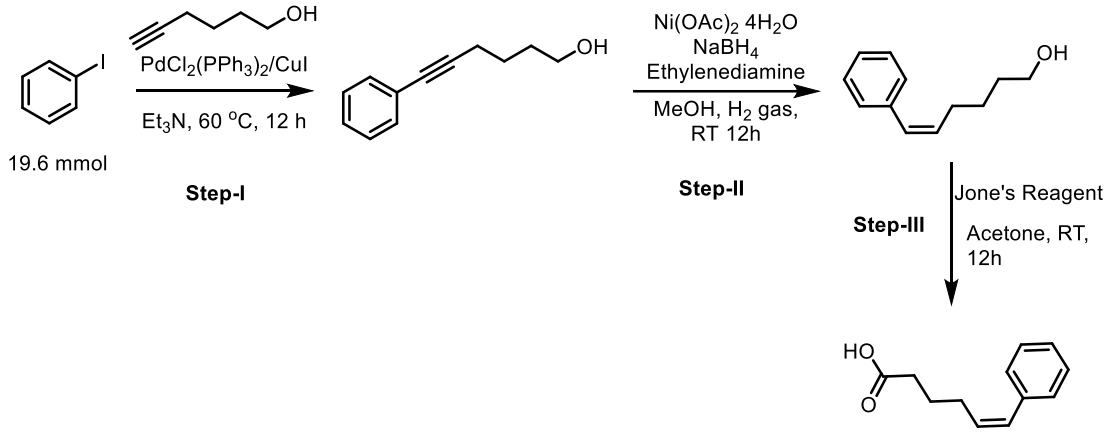
1ac

Compound 5-(3-phenylpropyl)-1,3,2,4-dioxathiazole 2-oxide (**1ac**) was synthesized following the reported procedure[10]. To a solution of thionyl chloride (40 mmol, 40 mL of 1 M solution in CH_2Cl_2) was added N-hydroxy-4-phenylbutanamide (1.8 g, 10

mmol). The mixture was stirred for 6 h at room temperature. Excessive thionyl chloride and solvent were removed under reduced pressure to give 5- phenyl-1,3,2,4-dioxathiazole 2-oxide (**1ac**,1.5 g, 66%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.14 (m, 6H), 2.77 – 2.61 (m, 4H), 2.08 (p, J = 7.4 Hz, 2H).

Preparation of (Z)-6-phenylhex-5-enoic acid:



Step-I:

To a solution of hex-5-yn-1-ol (1 g, 10.2 mmol) and Iodobenzene (11.2 mmol) in THF (5 mL) and Et_3N (30 mL) was added successively CuI (39 mg, 0.204 mmol) and $Pd(PPh_3)_4$ (121 mg, 0.102 mmol). After being stirred overnight at room temperature, the reaction mixture was filtrated with celite and solvents were evaporated under reduced pressure. The residue was purified by column chromatography on silica gel with Pentane/Et_2O as eluent to afford coupling products[12].

Step-II:

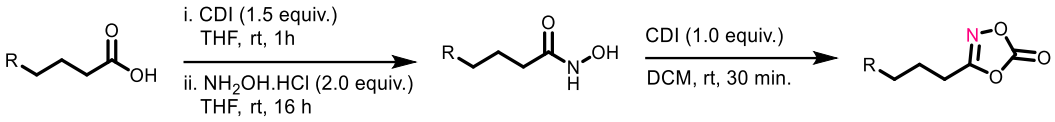
To a solution of $Ni(OAc)_2$ (416 mg, 1.67 mmol) in EtOH (20 mL) under H_2 atmosphere (1 bar) was added a solution of $NaBH_4$ (63 mg, 1.67 mmol) in EtOH (5 mL) at room temperature. After being stirred for 1 h, a solution of alkyne (8.35 mmol) and ethylenediamine (350 mg, 5.84 mmol) in EtOH (5 mL) was added and the reaction was stirred overnight. Solvent was evaporated and the residue was purified by filtration on silica gel with Et_2O as eluent to afford olefinic products which were used in the next step without further purification[12].

Step-III:

Following a literature procedure[13], to a solution of (Z)-6-phenylhex-5-en-1-ol (870.0 mg, 4.94 mmol, 1 equiv.) in acetone (75 mL) at 0 ºC was added Jones reagent (4.0 mL, 2 equiv.) dropwise. The reaction mixture was stirred at 0 ºC for 3 hours. After completion, the reaction was quenched by addition of ^{i}PrOH (20 mL). The precipitate was filtered off and the filtrate was concentrated by evaporation under reduced pressure. To the residue was added water (25 mL), and the mixture was extracted with CH_2Cl_2 for five times. The combined organic layer was dried over anhydrous sodium sulfate. After filtration, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (silica gel, eluent: EtOAc/nhexane = 1/5 with 0.1% TFA) to afford (Z)-6-phenylhex-5-enoic acid as an orange oil (658.0 mg, 70% yield).

Preparation of dioxazolones from carboxylic acids

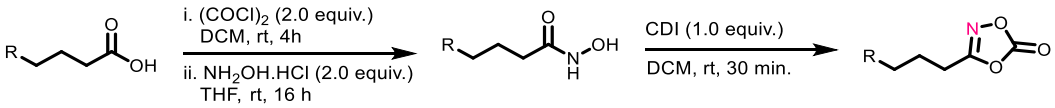
General procedure A



1,1'-Carbonyldiimidazole (CDI, 1.5 equiv.) was added to a solution of carboxylic acid (1.0 equiv.) in dry THF (2 mL/mmol). The reaction mixture was stirred at rt for 1 h and hydroxylamine hydrochloride (2.0 equiv.) was added. The resulting mixture was stirred for 16 h. The mixture was diluted with 5% aqueous $KHSO_4$ and extracted with EtOAc (3x20 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The extract was filtered and concentrated under reduced pressure to afford desired crude hydroxamic acid which was used for the next step without further purification.

To a solution of hydroxamic acid in dry CH_2Cl_2 (10 mL/mmol) was added 1,1'-carbonyldiimidazole (1.0 equiv.) at room temperature. After stirring for 30 min, the reaction mixture was quenched with aqueous 1 M HCl, extracted with CH_2Cl_2 (3x20 mL) and dried over Na_2SO_4. After filtration, the solvent was concentrated *in vacuo* and the crude mixture was purified using silica gel chromatography (0-10% EtOAc/hexanes gradient) to afford desired 1,4,2-dioxazol-5-ones.

General procedure B:



To a mixture of carboxylic acid (1.0 equiv.) in anhydrous DCM (0.2 M), DMF (2 drops), and oxalyl chloride ($(COCl_2)_2$, 2.0 equiv.) were added dropwise at 0°C. After

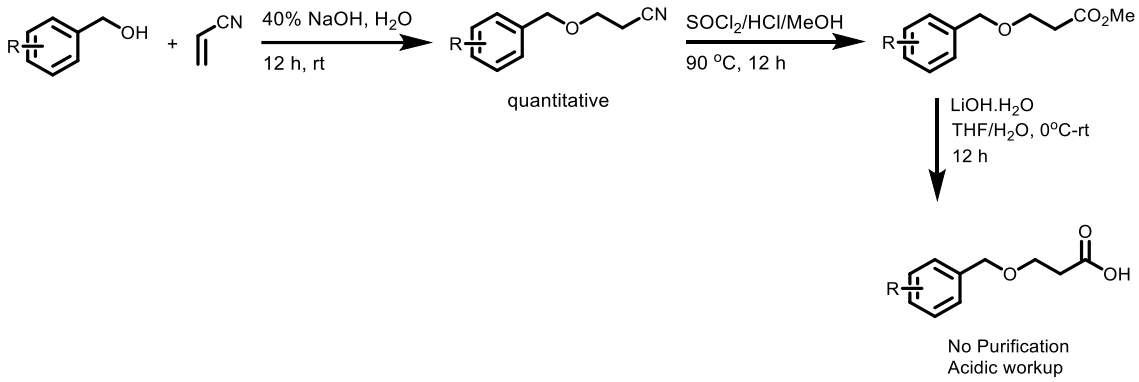
the addition was completed, the mixture was stirred for 4-5 h. After that, the solution was concentrated under reduced pressure to remove DCM and excess $(COCl_2)_2$. The residue was dried under high vacuum for 1 h, the crude product was used for next step without further purification.

To a stirred solution of hydroxylamine hydrochloride (2.0 equiv.) and K_2CO_3 (2.0 equiv.) in EtOAc/H_2O (1:1, 0.5 M, v/v) was added an EtOAc solution of the acid chloride (1.2 eq) dropwise at 0 °C. The reaction mixture was stirred for 30 min. Afterward, the reaction mixture was warmed to room temperature under vigorously magnetically stirring overnight. The mixture was extracted with EtOAc (3x20mL) and the combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to afford the crude hydroxamic acid which was used for the next step without further purification.

To a solution of hydroxamic acid in dry CH_2Cl_2 (10 mL/mmol) was added 1,1'-carbonyldiimidazole (1.0 equiv.) at room temperature. After stirring for 30 min, the reaction mixture was quenched with aqueous 1 M HCl, extracted with CH_2Cl_2 (3x20mL) and dried over Na_2SO_4. The solvent was concentrated in vacuo. The crude mixture was purified using silica gel chromatography (0-10% EtOAc/hexanes gradient) to afford desired 1,4,2-dioxazol-5-ones.

General Procedure C

Preparation of 3-(benzyloxy)propyl propanoic acid derivatives



Step I:

The synthesis of 3-(benzyloxy)propyl dioxazolones was performed following reported procedures[14]. Acrylonitrile was added to a mixture of alcohol and aqueous NaOH (40%) while maintaining the temperature below 30°C. The reaction mixture was stirred for 6 h at room temperature, neutralized with aqueous HCL (1N), and diluted with $CHCl_3$. The organic layer was washed with 5% aqueous NaOH followed by brine, evaporated *in vacuo*, and dried thoroughly to afford the desired ether compound.

Step II:

To a mixture of methanol (40 mL) and hydrochloric acid (12N, 3.2 mL), thionyl chloride (3.8 mL, 52.3 mmol) was added dropwise for 10 min at 0ºC. To the mixture, 3-benzyloxypropionitrile (17.0 g, 105 mmol) was added at rt dropwise for 20 min, then the solution was heated to reflux after which it was left stiring for 11 h. After being cooled to rt, the mixture was filtered and washed with MeOH. To the filtrate, sodium carbonate (3 g) was added, filtered, and concentrated under reduced pressure. The

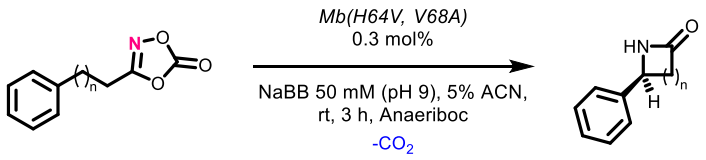
resulting residue was dissolved in toluene (20 mL), filtered, and concentrated under reduced pressure to obtain crude methyl 3-benzyloxypropionate which was used for the next step without further purification.

Step II:

The methylester crude was dissolved in THF (30 mL), and to this solution, a solution of LiOH-H_2O (5.0 g, 12 mmol) in H_2O (20 mL) was added and stirred for 12 h at room temperature. An additional quantity of 1N aqueous NaOH (3m1, 3mmole) was then added and stirring was continued for 1.5 h at room temperature. The resulting solution was diluted with 5% aqueous NaCl (80ml) and the mixture was extracted with ether (3x80ml). The aqueous solution was then acidified with 3N aqueous HCl to pH2 and the liberated acid was isolated by ether extraction (3x80ml). The acid was dried over Na_2SO_4, filtrated, and evaporated to afford the 6-benzyloxypropionic acid.

Procedure for myoglobin-catalyzed enantioselective amidation reactions

General procedure D

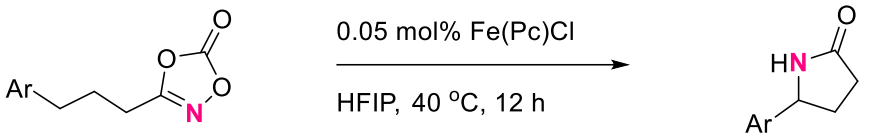


In a typical procedure, NaBB (50 mM, pH 9.0) was placed in a round-bottom flask equipped with a stir bar and degassed over Ar for 10 mins. Then, a buffered solution containing Mb(H64V, V68A) (0.3 mol%) in NaBB (50 mM, pH 9.0) was added dropwise and the headspace of the flask was evacuated with Ar for 10 mins. The enzyme was reduced by the addition of a buffered solution of $Na_2S_2O_4$ (10 mM final conc.) in NaBB (50 mM, pH 9.0) via syringe. A solution of desired dioxazolone (7.5 mM final conc.) in acetonitrile (5% vol/vol final conc.) was then added via syringe. The

resulting mixture was left stirring overnight under Ar. The crude product was extracted with DCM (3x20 mL) and dried over Na_2SO_4. After filtration, the crude was concentrated *in vacuo* and purified by silica gel column chromatography using a step gradient of 100% DCM to a final ratio of 20:1 DCM:^{i}PrOH solution as eluent to afford the desired lactam products.

Procedure for Fe(Pc)-catalyzed amidation reactions

General procedure E



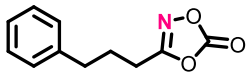
0.1 mmol

2e, 2f & 2g

Compounds **2e, 2f** and **2g** were synthesized following known methods[15]. Briefly, a solution of PcFe(III)Cl (0.05 mol%) in HFIP (1.0 mL) was added to dioxazolones (0.1 mmol) placed in a 4 mL vial. The reaction mixture was stirred at 40 °C for 12 h. The solvent was evaporated under vacuum and the residue was purified by silica gel column chromatography using a step gradient of 100% DCM to a final ratio of 20:1 DCM:^{i}PrOH solution as eluent to afford the desired lactam products.

Compound Characterization

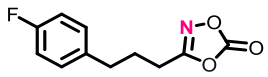
3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (1a):



3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (**1**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 443 mg of the desired product as colorless liquid in 72% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.07 (m, 5H), 2.73 (t, *J* = 7.4 Hz, 2H), 2.60 (t, *J* = 7.5 Hz, 2H), 2.05 (p, *J* = 7.5 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.4, 154.0, 139.8, 128.6, 128.4, 126.5, 34.5, 25.8, 23.9.

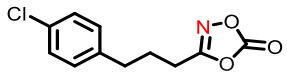
3-(3-(4-fluorophenyl)propyl)-1,4,2-dioxazol-5-one (1d):



3-(3-(4-methoxyphenyl)propyl)-1,4,2-dioxazol-5-one (**1d)** was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 535 mg of the desired product as colorless liquid in 80% yield over 3 steps. R_f = 0.45 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 3.79 (s, 3H), 2.68 (t, *J* = 7.3 Hz, 2H), 2.59 (t, *J* = 7.5 Hz, 2H), 2.12 – 1.97 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 166.5, 158.2, 154.1, 131.7, 129.3, 114.0, 55.2, 33.6, 26.0, 23.9.

3-(3-(4-chlorophenyl)propyl)-1,4,2-dioxazol-5-one (1e):

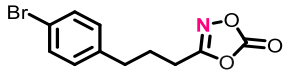


3-(3-(4-chlorophenyl)propyl)-1,4,2-dioxazol-5-one (**1e**) was prepared according to the general procedure **A** and purified by silica gel column

chromatography to afford 481 mg of the desired product as colorless liquid in 67% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 2.71 (t, *J* = 7.4 Hz, 2H), 2.62 (t, *J* = 7.4 Hz, 2H), 2.04 (p, *J* = 7.5 Hz, 2H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.2, 154.0, 138.2, 132.3, 129.7, 128.8, 33.8, 25.7, 23.9.

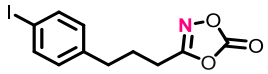
3-(3-(4-bromophenyl)propyl)-1,4,2-dioxazol-5-one (1f):



3-(3-(4-bromophenyl)propyl)-1,4,2-dioxazol-5-one (**1f**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 528 mg of the desired product as colorless liquid in 62% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.4 Hz, 2H), 2.70 (t, *J* = 7.5 Hz, 2H), 2.62 (t, *J* = 7.5 Hz, 2H), 2.04 (p, *J* = 7.5 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.2, 154.0, 138.7, 131.7, 130.1, 120.3, 33.9, 25.7, 23.9.

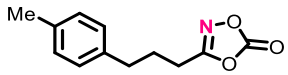
3-(3-(4-iodophenyl)propyl)-1,4,2-dioxazol-5-one (1g):



3-(3-(4-iodophenyl)propyl)-1,4,2-dioxazol-5-one (**1g**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 705 mg of the desired product as colorless liquid in 71% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.3 Hz, 2H), 6.94 (d, *J* = 8.3 Hz, 2H), 2.68 (t, *J* = 7.5 Hz, 2H), 2.61 (t, *J* = 7.4 Hz, 2H), 2.06 – 2.00 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.2, 154.0, 139.4, 137.7, 130.5, 34.0, 25.6, 23.9.

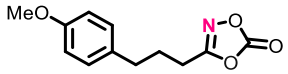
3-(3-(p-tolyl)propyl)-1,4,2-dioxazol-5-one (1h):



3-(3-(p-tolyl)propyl)-1,4,2-dioxazol-5-one (**1h**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 427 mg of the desired product as colorless liquid in 65% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (d, *J* = 7.7 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 2H), 2.70 (t, *J* = 7.3 Hz, 2H), 2.60 (t, *J* = 7.5 Hz, 2H), 2.33 (s, 3H), 2.04 (p, *J* = 7.5 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.5, 154.1, 136.6, 136.1, 129.3, 128.3, 34.1, 25.9, 24.0, 21.0.

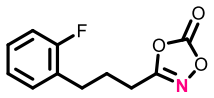
3-(3-(4-methoxyphenyl)propyl)-1,4,2-dioxazol-5-one (1i):



3-(3-(4-methoxyphenyl)propyl)-1,4,2-dioxazol-5-one (**1i**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 564 mg of the desired product as colorless liquid in 80% yield over 3 steps. R_f = 0.45 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 3.79 (s, 3H), 2.68 (t, *J* = 7.3 Hz, 2H), 2.59 (t, *J* = 7.5 Hz, 2H), 2.12 – 1.97 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 166.5, 158.2, 154.1, 131.7, 129.3, 114.0, 55.2, 33.6, 26.0, 23.9.

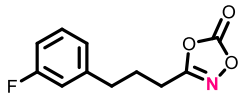
3-(3-(2-fluorophenyl)propyl)-1,4,2-dioxazol-5-one (1j):



3-(3-(2-fluorophenyl)propyl)-1,4,2-dioxazol-5-one (**1j**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 462 mg of the desired product as colorless liquid in 69% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23-7.16 (m, 2H), 7.12 – 6.98 (m, 2H), 2.78 (t, *J* = 7.4 Hz, 2H), 2.64 (t, *J* = 7.5 Hz, 2H), 2.06 (p, *J* = 7.4 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.3, 162.3, 159.8, 154.0, 130.7, 130.6, 128.4, 128.3, 126.8, 126.6, 124.2, 124.2, 115.5, 115.3, 27.9, 27.9, 24.6, 24.0.

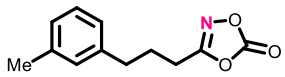
3-(3-(3-fluorophenyl)propyl)-1,4,2-dioxazol-5-one (1k):



3-(3-(3-fluorophenyl)propyl)-1,4,2-dioxazol-5-one (**1k**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 422 mg of the desired product as colorless liquid in 63% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (td, *J* = 7.9 Hz, J = 6.0 Hz, 1H), 7.00 – 6.85 (m, 3H), 2.74 (t, *J* = 7.5 Hz, 2H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.06 (p, *J* = 7.5 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.2, 164.2, 161.7, 154.0, 142.4, 142.3, 130.2, 130.1, 124.1, 124.1, 115.4, 115.1, 113.5, 113.3, 34.2, 25.6, 23.9.

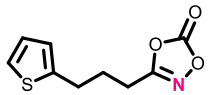
3-(3-(m-tolyl)propyl)-1,4,2-dioxazol-5-one (1l):



3-(3-(m-tolyl)propyl)-1,4,2-dioxazol-5-one (**1l**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 447 mg of the desired product as colorless liquid in 68% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (t, *J* = 7.5 Hz, 1H), 7.08 – 6.94 (m, 3H), 2.69 (t, *J* = 7.3 Hz, 2H), 2.61 (t, *J* = 7.5 Hz, 2H), 2.33 (s, 3H), 2.04 (p, *J* = 7.5 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.5, 154.1, 139.7, 138.2, 129.2, 128.5, 127.2, 125.4, 34.4, 25.8, 24.0, 21.3.

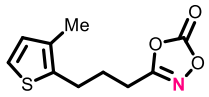
3-(3-(thiophen-2-yl)propyl)-1,4,2-dioxazol-5-one (1m):



3-(3-(thiophen-2-yl)propyl)-1,4,2-dioxazol-5-one (**1m**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 545 mg of the desired product as colorless liquid in 86% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.16 (dd, *J* = 5.1 Hz, *J* = 1.2 Hz, 1H), 6.94 (dd, *J* = 5.2 Hz, *J* = 3.4 Hz, 1H), 6.85 – 6.78 (m, 1H), 2.97 (t, *J* = 7.2 Hz, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 2.10 (p, *J* = 7.3 Hz, 2H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 166.2, 154.0, 142.2, 127.0, 125.2, 123.9, 28.6, 26.2, 23.8.

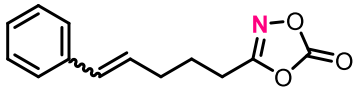
3-(3-(3-methylthiophen-2-yl)propyl)-1,4,2-dioxazol-5-one (1n):



3-(3-(3-methylthiophen-2-yl)propyl)-1,4,2-dioxazol-5-one (**1n**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 520 mg of the desired product as colorless liquid in 77% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06 (d, *J* = 5.1 Hz, 1H), 6.80 (d, *J* = 5.1 Hz, 1H), 2.87 (t, *J* = 7.2 Hz, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 2.16 (s, 3H) 2.06 (p, *J* = 7.4 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.2, 154.0, 135.3, 133.7, 130.2, 121.8, 26.5, 25.9, 23.9, 13.6.

3-(5-phenylpent-4-en-1-yl)-1,4,2-dioxazol-5-one (1o):



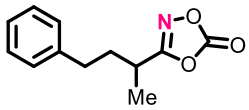
E:Z = 7:3

3-(5-phenylpent-4-en-1-yl)-1,4,2-dioxazol-5-one (**1o**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 734 mg of the desired product as colorless liquid in 53% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): 7.43 – 7.14 (m, 8H), 6.54 (d, J = 11.6 Hz, 0.42H), 6.44 (dt, J = 15.9 Hz, J = 1.5 Hz, 1H), 6.14 (dt, J = 15.8 Hz, J = 7.0 Hz, 1H), 5.60 (dt, J = 11.6 Hz, J = 7.3 Hz, 0.44H), 2.73 – 2.55 (m, 3H), 2.52 – 2.27 (m, 3H), 1.97 – 1.82 (m, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.5, 137.0, 132.0, 131.0, 129.9, 128.6, 128.6, 128.7, 127.7, 127.4, 126.9, 126.0, 31.8, 27.2, 24.5, 24.2, 24.0.

NMR showed 7:3 mixture of E/Z isomer. THe mixture as a substrate for the biocatalytic reaction.

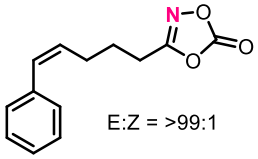
3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (1p):



3-(4-phenylbutan-2-yl)-1,4,2-dioxazol-5-one (**1p**) was prepared according to the general procedure **B** and purified by silica gel column chromatography to afford 375 mg of the desired product as colorless liquid in 57% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.13 (m, 5H), 2.83 (h, *J* = 7.1 Hz, 1H), 2.69 (td, *J* = 7.6 Hz, *J* =1.7 Hz, 2H), 2.17 – 2.00 (m, 1H), 1.98 – 1.80 (m, 1H), 1.34 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 169.3, 154.1, 140.0, 128.6, 128.3, 126.4, 34.0, 32.7, 30.5, 16.2.

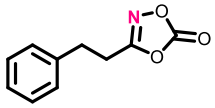
(Z)-3-(5-phenylpent-4-en-1-yl)-1,4,2-dioxazol-5-one (1q):



3-(5-phenylpent-4-en-1-yl)-1,4,2-dioxazol-5-one (**1q**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 734 mg of the desired product as colorless liquid in 53% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.30 (m, 2H), 7.27 – 7.20 (m, 3H), 6.54 (d, J = 11.6 Hz, 1H), 5.60 (dt, J = 11.6 Hz, J = 7.3 Hz, 1H), 2.61 (t, J = 7.5 Hz, 2H), 2.45 (qd, J = 7.4 Hz, J = 1.8 Hz, 2H), 1.86 (q, J = 7.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.3, 154.0, 137.0, 131.0, 129.8, 128.6, 128.4, 128.3, 126.9, 27.3, 24.5, 24.2.

3-phenylethyl-1,4,2-dioxazol-5-one (3):

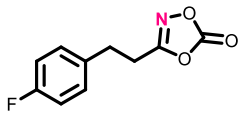


3-phenethyl-1,4,2-dioxazol-5-one (**3a**) was prepared according to the general procedure **A** and purified by silica gel column

chromatography to afford 482 mg of the desired product as colorless liquid in 84% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (dd, *J* = 8.1, 6.6 Hz, 2H), 7.30 – 7.23 (m, 1H), 7.20 (d, *J* = 7.1 Hz, 2H), 3.03 (t, *J* = 7.3 Hz, 2H), 2.94 (t, *J* = 7.1 Hz, 2H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 165.8, 154.0, 138.0, 128.9, 128.2, 127.1, 30.4, 26.6.

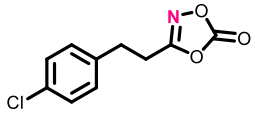
3-(4-fluorophenethyl)-1,4,2-dioxazol-5-one (3b):



3-(4-fluorophenethyl)-1,4,2-dioxazol-5-one (**3b**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 527 mg of the desired product as colorless liquid in 84% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (dd, *J* = 8.5 Hz, *J* = 5.3 Hz, 2H), 7.02 (t, *J* = 8.7 Hz, 2H), 3.05 – 2.98 (m, 2H), 2.92 (ddd, *J* = 8.6 Hz, *J* = 7.3 Hz, *J* = 1.8 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.6, 163.1, 160.6, 153.9, 133.7, 133.6, 129.8, 129.7, 115.9, 115.7, 29.6, 26.7.

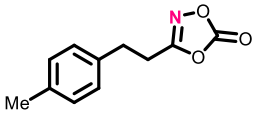
3-(4-chlorophenethyl)-1,4,2-dioxazol-5-one (3c):



3-(4-chlorophenethyl)-1,4,2-dioxazol-5-one (**3c**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 406 mg of the desired product as colorless liquid in 60% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 3.05 – 2.97 (m, 2H), 2.92 (ddd, *J* = 8.6 Hz, *J* = 7.0 Hz, *J* = 1.6 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.5, 153.9, 136.4, 133.0, 129.5, 129.0, 29.7, 26.5.

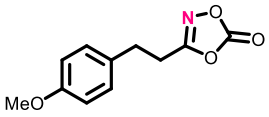
3-(4-methylphenethyl)-1,4,2-dioxazol-5-one (3d):



3-(4-methylphenethyl)-1,4,2-dioxazol-5-one (**3d)** was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 474 mg of the desired product as colorless liquid in 77% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (d, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 3.04 – 2.96 (m, 2H), 2.91 (ddd, *J* = 8.8Hz, *J* = 6.8 Hz, *J* = 1.8 Hz, 2H), 2.33 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.9, 154.0, 136.8, 134.9, 129.5, 128.0, 30.0, 26.7, 21.0.

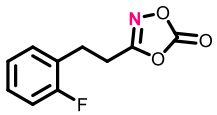
3-(4-methoxyphenethyl)-1,4,2-dioxazol-5-one (3e):



3-(4-methoxyphenethyl)-1,4,2-dioxazol-5-one (**3e**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 398 mg of the desired product as colorless liquid in 60% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 3.01 – 2.94 (m, 2H), 2.90 (ddd, *J* = 8.8 Hz, *J* = 6.7 Hz, *J* = 1.8 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$): δ** 165.9, 158.6, 154.0, 129.9, 129.2, 114.2, 55.2, 29.6, 26.9.

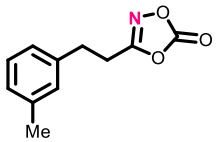
3-(2-fluorophenethyl)-1,4,2-dioxazol-5-one (3f):



3-(2-fluorophenethyl)-1,4,2-dioxazol-5-one (**3f**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 470 mg of the desired product as colorless liquid in 75% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.23 (m, 1H), 7.20 (td, *J* = 7.6 Hz, *J* = 1.8 Hz, 1H), 7.14 – 6.97 (m, 2H), 3.07 (t, *J* = 7.5 Hz, 2H), 2.95 (t, *J* = 7.2 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.7, 162.3, 159.8, 154.0, 130.5, 130.5, 129.2, 129.1, 125.0, 124.8, 124.5, 124.5, 115.7, 115.5, 25.3, 24.6, 24.5.

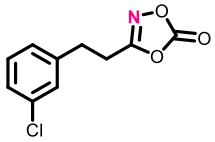
3-(3-methylphenethyl)-1,4,2-dioxazol-5-one (3g):



3-(3-methylphenethyl)-1,4,2-dioxazol-5-one (**3g**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 523 mg of the desired product as colorless liquid in 85% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.03 – 6.93 (m, 2H), 3.02 – 2.95 (m, 2H), 2.96 – 2.89 (m, 2H), 2.34 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.9, 154.0, 138.6, 137.9, 128.9, 128.8, 127.8, 125.1, 30.3, 26.6, 21.3.

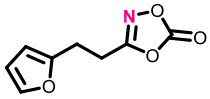
3-(3-chlorophenethyl)-1,4,2-dioxazol-5-one (3h):



3-(3-chlorophenethyl)-1,4,2-dioxazol-5-one (**3h**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 420 mg of the desired product as colorless liquid in 62% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.16 (m, 3H), 7.09 (dt, *J* = 6.7 Hz, *J* = 2.0 Hz, 1H), 3.08 – 2.98 (m, 2H), 2.94 (ddd, *J* = 8.9 Hz, *J* = 6.8 Hz, *J* = 1.8 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.5, 153.8, 139.9, 134.6, 130.2, 128.3, 127.4, 126.4, 29.9, 26.3.

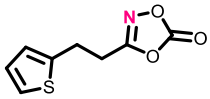
3-(2-(furan-2-yl)ethyl)-1,4,2-dioxazol-5-one (3i):



3-(2-(furan-2-yl)ethyl)-1,4,2-dioxazol-5-one (**3i**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 429 mg of the desired product as colorless liquid in 79% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 1.9 Hz, 1H), 6.30 (dd, *J* = 3.2 Hz, *J* = 1.9 Hz, 1H), 6.11 (d, J = 3.2 Hz, 1H), 3.08 (t, J = 6.9 Hz, 2H), 2.98 (td, J = 7.1 Hz, J = 1.5 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.6, 153.9, 151.3, 142.0, 110.4, 106.6, 23.8, 23.1.

3-(2-(thiophen-2-yl)ethyl)-1,4,2-dioxazol-5-one (3j):

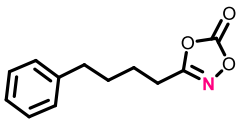


3-(2-(thiophen-2-yl)ethyl)-1,4,2-dioxazol-5-one (**3j**) was prepared according to the general procedure **A** and purified by silica gel

column chromatography to afford 331 mg of the desired product as colorless liquid in 56% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (dd, *J* = 5.2 Hz, *J* = 1.2 Hz, 1H), 6.96 -6.86 (m, 2H), 3.48 – 3.21 (m, 2H), 3.21 – 2.92 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.3, 153.9, 140.0, 127.1, 125.6, 124.5, 27.1, 24.7.

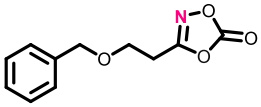
3-(4-phenylbutyl)-1,4,2-dioxazol-5-one (5a):



3-(4-phenylbutyl)-1,4,2-dioxazol-5-one (a**5**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 60 mg of the desired product as colorless liquid in 16% yield over 2 steps. R_f = 0.5 (15% ethyl acetate in hexane). R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (dd, *J* = 8.1, 6.9 Hz, 2H), 7.23 – 7.11 (m, 3H), 2.64 (ddq, *J* = 17.3, 7.5, 3.4 Hz, 2H), 1.81 – 1.68 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 167.24, 154.89, 141.93, 129.24, 129.09, 126.87, 35.90, 31.09, 25.40, 24.75.

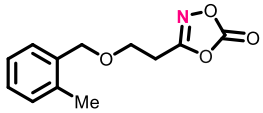
3-(2-(benzyloxy)ethyl)-1,4,2-dioxazol-5-one (5c):



3-(2-(benzyloxy)ethyl)-1,4,2-dioxazol-5-one (**5c**) was prepared according to general procedures **A** and **C** and purified by silica gel column chromatography to afford 597 mg of the desired product as colorless liquid in 90% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane). R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 – 7.14 (m, 5H), 4.54 (s, 2H), 3.76 (t, *J* = 6.1 Hz, 2H), 2.90 (t, *J* = 6.1 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 164.8, 154.0, 137.1, 128.5, 128.0, 127.7, 73.2, 63.7, 26.0.

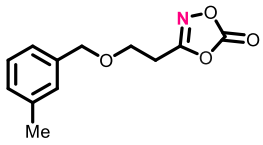
3-(2-((2-methylbenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (5d):



3-(2-((2-methylbenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (**5d**) was prepared according to the general procedures **A** and **C** and purified by silica gel column chromatography to afford 338 mg of the desired product as colorless liquid in 48% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 – 7.12 (m, 4H), 4.54 (s, 2H), 3.78 (t, *J* = 6.1 Hz, 2H), 2.89 (t, *J* = 6.1 Hz, 2H), 2.31 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 164.8, 154.0, 136.8, 134.9, 130.4, 128.7, 128.2, 125.8, 71.7, 63.8, 26.0, 18.6.

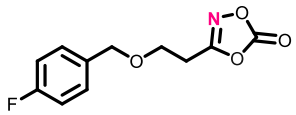
3-(2-((3-methylbenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (5e):



3-(2-((3-methylbenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (**5e**) was prepared according to the general procedure **A** and **C** and purified by silica gel column chromatography to afford 494 mg of the desired product as colorless liquid in 70% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 – 7.06 (m, 4H), 4.50 (s, 2H), 3.76 (t, *J* = 6.1 Hz, 2H), 2.89 (t, *J* = 6.1 Hz, 2H), 2.35 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 164.8, 154.0, 138.2, 137.0, 128.7, 128.5, 128.4, 124.8, 73.2, 63.7, 26.0, 21.3.

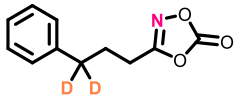
3-(2-((4-fluorobenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (5f):



3-(2-((4-fluorobenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (**5f**) was prepared according to the general procedures **A** and **C** and purified by silica gel column chromatography to afford 523 mg of the desired product as colorless liquid in 73% yield over 3 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (dd, *J* = 8.5, 5.6 Hz, 2H), 7.04 (t, *J* = 8.7 Hz, 2H), 4.51 (s, 2H), 3.77 (t, *J* = 6.1 Hz, 2H), 2.91 (t, *J* = 6.1 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 164.7, 163.7, 161.2, 153.9, 132.9, 132.9, 129.5, 129.4, 115.5, 115.3, 72.5, 63.7, 26.0.

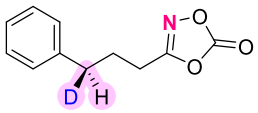
3-(3-phenylpropyl-3,3-d_2)-1,4,2-dioxazol-5-one (1a-1d_2):



3-(3-phenylpropyl-3,3-d2)-1,4,2-dioxazol-5-one (**1a-d_2**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 528 mg of the desired product as colorless liquid in 85% yield over 2 steps. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 – 6.90 (m, 5H), 2.72 – 2.70 (m, 0.15 H), 2.67 – 2.50 (m, 2H), 2.05 (t, *J* = 7.4 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.4, 154.0, 139.8, 128.6, 128.4, 126.5, 34.5, 25.8, 23.9.

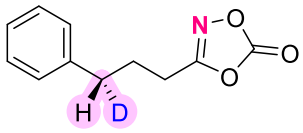
(*R*)-3-(3-phenylpropyl-3-d)-1,4,2-dioxazol-5-one [(*R*)-1a-d$_1$]:



(*R*)-3-(3-phenylpropyl-3-d)-1,4,2-dioxazol-5-one **[(R)-1a-d$_1$]** was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 160 mg of the desired product as colorless liquid in 78% yield. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.28 – 7.08 (m, 6H), 2.65 (tt, J = 5.7 Hz, J = 2.4 Hz, 1H), 2.54 (t, J = 7.5 Hz, 2H), 1.99 (q, J = 7.4 Hz, 2H). **^{13}C NMR (101 MHz, CDCl$_3$):** δ 166.4, 154.1, 139.7, 128.7, 128.4, 126.5, 34.2 (t, J = 20.2 Hz), 25.8, 24.0.

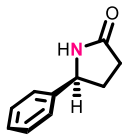
(*S*)-3-(3-phenylpropyl-3-d)-1,4,2-dioxazol-5-one [(*S*)-1a-d$_1$]:



(*R*)-3-(3-phenylpropyl-3-d)-1,4,2-dioxazol-5-one **[(S)-1a-d$_1$]** was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 150 mg of the desired product as colorless liquid in 73% yield. R_f = 0.5 (15% ethyl acetate in hexane).

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.28 – 7.08 (m, 6H), 2.65 (tt, J = 5.7 Hz, J = 2.4 Hz, 1H), 2.54 (t, J = 7.5 Hz, 2H), 1.99 (q, J = 7.4 Hz, 2H). **^{13}C NMR (101 MHz, CDCl$_3$):** δ 166.4, 154.1, 139.7, 128.7, 128.4, 126.5, 34.2 (t, J = 20.2 Hz), 25.8, 24.0.

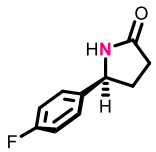
(*S*)-5-phenylpyrrolidin-2-one (2a):



(S)-5-phenylpyrrolidin-2-one (**2a**) was prepared according to the general procedure **D** to afford 21 mg of the desired amide product as white solid in 45% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (t, *J* = 7.4 Hz, 2H), 7.29 – 7.23 (m, 2H), 7.21 (s, 1H), 5.77 (s, 1H), 4.71 (t, *J* = 7.1 Hz, 1H), 2.54 (dtd, *J* = 12.7, 8.3, 4.7 Hz, 1H), 2.49 – 2.32 (m, 2H), 1.94 (ddt, *J* = 15.4, 12.7, 7.9 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 178.93, 143.18, 129.69, 128.74, 126.38, 58.75, 32.19, 30.92. **HRMS (ESI)** m/z calcd for $C_{10}H_{12}NO$ $[M+H]^+$ 162.0919, found 162.0910.

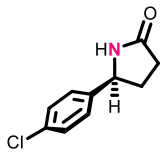
(*S*)-5-(4-fluorophenyl)pyrrolidin-2-one (2d):



(S)-5-(4-fluorophenyl)pyrrolidin-2-one (**2d**) was prepared according to the general procedure **D** to afford 14mg of the desired amide product as white solid in 44% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (dd, *J* = 8.7, 5.0 Hz, 2H), 7.06 (t, *J* = 8.4 Hz, 2H), 6.46 (s, 1H), 4.75 (t, *J* = 7.1 Hz, 1H), 2.67 – 2.52 (m, 1H), 2.52 – 2.36 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 179.1, 163.1 (d, *J* = 246.1 Hz), 138.9, 128.0 (d, *J* = 8.1 Hz), 116.4 (d, *J* = 21.6 Hz), 58.2, 32.2, 30.9. **^{19}F {^{1}H}NMR (376 MHz, $CDCl_3$):** δ -114.58. **HRMS (ESI)** m/z calcd. for $C_{10}H_{11}FNO$ $[M+H]^+$ 180.0824, found 180.0815.

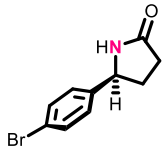
(*S*)-5-(4-chlorophenyl)pyrrolidin-2-one (2e):



(*S*)-5-(4-chlorophenyl)pyrrolidin-2-one (**2e**) was prepared according to the general procedure **E** to afford 21 mg of the desired amide product as white solid in 46% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.88 (s, 1H), 4.74 (t, *J* = 7.1 Hz, 1H), 2.63 – 2.51 (m, 1H), 2.41 – 2.31 (m, 2H), 1.98 – 1.85 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 178.78, 141.08, 133.62, 129.08, 127.03, 57.56, 31.29, 30.30**. HRMS (ESI)** m/z calcd for $C_{10}H_{11}ClNO$ $[M+H]^+$ 196.0529, found 196.0522.

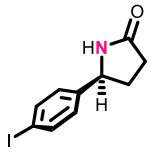
(*S*)-5-(4-bromophenyl)pyrrolidin-2-one (2f):



(*S*)-5-(4-bromophenyl)pyrrolidin-2-one (**2f**) was prepared according to the general procedure **E** to afford 16 g of the desired amide product as white solid in 37% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 – 7.46 (m, 2H), 7.25 – 7.14 (m, 2H), 6.83 (s, 1H), 4.72 (t, *J* = 7.1 Hz, 1H), 2.57 (dddd, *J* = 12.6, 9.2, 7.6, 5.1 Hz, 1H), 2.51 – 2.27 (m, 2H), 1.98 – 1.85 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 178.77, 141.61, 132.03, 127.38, 121.69, 57.61, 31.25, 30.27. **HRMS (ESI)** m/z calcd for $C_{10}H_{11}BrNO$ $[M+H]^+$ 240.0024, found 240.0015.

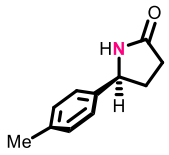
(*S*)-5-(4-iodophenyl)pyrrolidin-2-one (2g):



(*S*)-5-(4-iodophenyl)pyrrolidin-2-one (**2g**) was prepared according to the general procedure **E** to afford 15 mg of the desired amide product as white solid in 34% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 – 7.61 (m, 2H), 7.06 (s, 1H), 7.04 – 6.97 (m, 2H), 4.66 (t, *J* = 7.1 Hz, 1H), 2.52 (dddd, *J* = 12.6, 9.2, 7.7, 5.1 Hz, 1H), 2.46 – 2.26 (m, 2H), 1.93 – 1.79 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 178.91, 142.35, 137.96, 127.62, 93.18, 57.71, 31.18, 30.31. **HRMS (ESI)** m/z calcd for $C_{10}H_{11}INO$ $[M+H]^+$ 287.9885, found 287.9871.

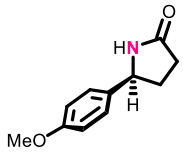
(*S*)-5-(p-tolyl)pyrrolidin-2-one (2h):



(*S*)-5-(p-tolyl)pyrrolidin-2-one (**2h**) was prepared according to the general procedure **D** to afford 5.2 mg of the desired amide product as white solid in 16% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 – 7.12 (m, 4H), 5.95 (s, 1H), 4.71 (q, *J* = 8.4 Hz, 1H), 2.54 (dddd, *J* = 16.9, 13.7, 8.8, 4.7 Hz, 1H), 2.50 – 2.39 (m, 2H), 2.38 (s, 1H), 1.96 (dtd, *J* = 12.6, 8.5, 6.8 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 179.0, 140.2, 138.5, 130.3, 126.4, 58.6, 32.3, 31.0, 21.8. **HRMS (ESI)** m/z calcd for $C_{10}H_{14}NO$ $[M+H]^+$ 176.1075, found 176.1067.

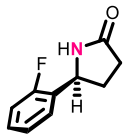
(*S*)-5-(4-methoxyphenyl)pyrrolidin-2-one (2i):



(*S*)-5-(4-methoxyphenyl)pyrrolidin-2-one (**2i**) was prepared according to the general procedure **D** to afford 10 mg of the desired amide product as white solid in 25% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (d, *J* = 8.2 Hz, 2H), 6.90 (d, *J* = 8.2 Hz, 2H), 4.71 (t, *J* = 7.1 Hz, 1H), 3.81 (s, 2H), 2.54 (ddd, *J* = 20.0, 10.3, 5.7 Hz, 1H), 2.49 – 2.35 (m, 2H), 2.01 – 1.90 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 179.02, 160.08, 135.15, 127.65, 115.00, 58.38, 56.08, 32.32, 31.15. **HRMS (ESI)** m/z calcd for $C_{11}H_{14}NO_2$ $[M+H]^+$ 192.1024, found 192.1015.

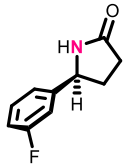
(*S*)-5-(2-fluorophenyl)pyrrolidin-2-one (2j):



(*S*)-5-(2-fluorophenyl)pyrrolidin-2-one (**2j**) was prepared according to the general procedure **D** to afford 21 mg of the desired amide product as white solid in 44% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (td, *J* = 7.6, 1.8 Hz, 1H), 7.28 (tdd, *J* = 7.5, 5.2, 1.8 Hz, 1H), 7.16 (td, *J* = 7.5, 1.2 Hz, 1H), 7.06 (ddd, *J* = 10.6, 8.2, 1.2 Hz, 1H), 6.86 (s, 1H), 5.07 (dd, *J* = 8.0, 5.8 Hz, 1H), 2.64 (dddd, *J* = 13.4, 9.6, 7.9, 5.9 Hz, 1H), 2.51 – 2.35 (m, 2H), 2.04 – 1.95 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 179.64, 160.82 (d, *J* = 246.6 Hz), 130.31 (d, *J* = 13.0 Hz), 129.99 (d, *J* = 8.1 Hz), 127.01 (d, *J* = 4.0 Hz), 125.26 (d, *J* = 3.6 Hz), 116.38 (d, *J* = 21.2 Hz), 52.60 (d, *J* = 4.1 Hz), 30.64, 30.19. **^{19}F {^{1}H}NMR (376 MHz, $CDCl_3$):** δ -119.6. **HRMS (ESI)** m/z calcd for $C_{10}H_{11}FNO$ $[M+H]^+$ 180.0824, found 180.0815.

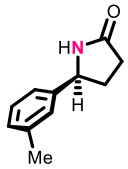
(*S*)-5-(3-fluorophenyl)pyrrolidin-2-one (2k):



(*S*)-5-(3-fluorophenyl)pyrrolidin-2-one (**2k**) was prepared according to the general procedure **D** to afford the desired amide product as white solid in 68% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (td, J = 7.8, 5.8 Hz, 1H), 7.08 (d, J = 7.7 Hz, 1H), 7.05 – 6.94 (m, 2H), 6.45 (s, 1H), 4.76 (t, J = 7.1 Hz, 1H), 2.66 – 2.54 (m, 1H), 2.52 – 2.37 (m, 2H), 2.03 – 1.89 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 178.5, 164.1, 162.6, 145.2, 145.2, 130.6, 130.5, 121.2, 121.1, 114.9, 114.7, 112.7, 112.5, 57.6, 31.2, 30.1. **HRMS (ESI)** m/z calcd for $C_{10}H_{11}FNO$ $[M+H]^+$ 180.0824, found 180.0815.

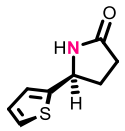
(*S*)-5-(m-tolyl)pyrrolidin-2-one (2l):



(*S*)-5-(m-tolyl)pyrrolidin-2-one (**2l**) was prepared according to the general procedure **D** to afford 22 mg of the desired amide product as white solid in 55% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.20 (m, 1H), 7.13 – 7.04 (m, 3H), 6.45 (s, 1H), 4.71 (t, *J* = 7.1 Hz, 1H), 2.55 (dddd, *J* = 12.4, 9.6, 7.6, 4.9 Hz, 1H), 2.49 – 2.38 (m, 2H), 2.35 (s, 3H), 2.02 – 1.89 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 179.33, 143.27, 139.38, 129.53, 129.36, 127.04, 123.45, 58.80, 32.08, 31.06, 22.17. **HRMS (ESI)** m/z calcd for $C_{10}H_{14}NO$ $[M+H]^+$ 176.1075, found 176.1066.

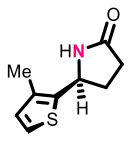
(*S*)-5-(thiophen-2-yl)pyrrolidin-2-one (2m):



(*S*)-5-(thiophen-2-yl)pyrrolidin-2-one (**2m**) was prepared according to the general procedure **D** to afford 12 mg of the desired amide product as white solid in 52% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (s, 1H), 6.98 (d, *J* = 8.1 Hz, 2H), 5.74 (s, 1H), 5.03 (t, *J* = 6.9 Hz, 1H), 2.67 – 2.58 (m, 1H), 2.58 – 2.49 (m, 1H), 2.42 (dt, *J* = 17.1, 8.4 Hz, 1H), 2.20 – 2.09 (m, 1H). **HRMS (ESI)** m/z calcd for $C_8H_{10}NOS$ $[M+H]^+$ 168.0483, found 168.0475.

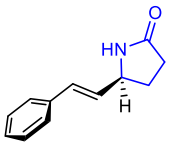
(*S*)-5-(3-methylthiophen-2-yl)pyrrolidin-2-one (2n):



(*S*)-5-(3-methylthiophen-2-yl)pyrrolidin-2-one (**2n**) was prepared according to the general procedure **D** to afford 15 mg of the desired amide product as white solid in 35% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, CDCl3): δ 7.12 (d, J = 5.0 Hz, 1H), 6.79 (t, J = 5.2 Hz, 1H), 5.83 (s, 1H), 5.04 (t, J = 7.1 Hz, 1H), 2.61 – 2.48 (m, 2H), 2.46 – 2.36 (m, 1H), 2.20 (s, 3H), 2.08 (ddd, J = 15.3 Hz, J = 13.3 Hz, J = 7.9 Hz, 1H).**^{13}C NMR (126 MHz, $CDCl_3$):** δ 178.2, 143.3, 140.2, 131.3, 123.8, 52.8, 31.7, 30.9, 14.4. **HRMS (ESI)** m/z calcd for $C_8H_{12}NOS$ $[M+H]^+$ 182.0639, found 182.0631.

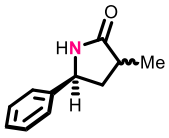
(S,E)-5-styrylpyrrolidin-2-one (2o):



(*S*,*E*)-5-styrylpyrrolidin-2-one (**2o**) was prepared according to the general procedure **D** to afford 15 mg of the desired amide product as white solid in 35% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, CDCl3): δ 7.39 – 7.24 (m, 5H), 6.55 (d, J = 15.8 Hz, 1H), 6.13 (dd, J = 15.8 Hz, J = 7.4 Hz, 1H), 5.90 (s, 1H), 4.34 (q, J = 6.8 Hz, 1H), 2.40 (td, J = 12.4 Hz, J = 8.2 Hz, 3H), 1.94 (ddt, J = 10.2 Hz, J = 7.6 Hz, J = 4.1 Hz, 1H).**^{13}C NMR (126 MHz, $CDCl_3$):** δ 178.0, 136.0, 131.2, 129.8, 128.7, 128.0, 126.5, 56.4, 29.9, 28.5. **HRMS (ESI)** m/z calcd for $C_{12}H_{14}NO$ $[M+H]^+$ 188.1075, found 188.1067.

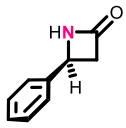
3-methyl-5-phenylpyrrolidin-2-one (2p):



3-methyl-5-phenylpyrrolidin-2-one (**2p**) was prepared according to the general procedure **D** to afford 14mg of a 4:1 diastereomeric mixture of the desired amide products as white solid in 17% yield. R_f = 0.5 (5% 2-propanaol in DCM).

Major Diastereomer. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.41 – 7.33 (m, 1H), 7.34 – 7.25 (m, 2H), 5.92 (s, 0H), 4.64 (dd, *J* = 9.2, 6.5 Hz, 0H), 2.72 (ddd, *J* = 12.6, 8.4, 6.5 Hz, 0H), 2.59 (dtt, *J* = 14.0, 10.8, 7.0 Hz, 1H), 1.61 (ddd, *J* = 12.6, 10.8, 9.2 Hz, 0H), 1.25 (d, *J* = 7.1 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 181.02, 142.87, 129.65, 126.58, 126.21, 57.11, 41.78, 37.87, 16.49. **HRMS (ESI)** m/z calcd for $C_{10}H_{14}NO$ $[M+H]^+$ 176.1075, found 176.1067.

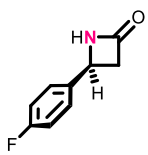
(*S*)-4-phenylazetidin-2-one (4a):



(*S*)-4-phenylazetidin-2-one (**4a**) was prepared according to the general procedure **D** to afford 510 mg of the desired amide product as white solid in 45% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 – 7.36 (m, 4H), 7.33 (ddt, *J* = 5.6, 3.7, 2.2 Hz, 1H), 6.18 (s, 1H), 4.73 (dt, *J* = 4.6, 2.2 Hz, 1H), 3.45 (ddt, *J* = 15.0, 4.5, 2.2 Hz, 1H), 2.89 (dd, *J* = 14.8, 2.6 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 168.59, 140.92, 129.61, 129.00, 126.38, 51.11, 48.81. **HRMS (ESI)** m/z calcd for $C_9H_{10}NO$ $[M+H]^+$ 148.0762, found 148.0755.

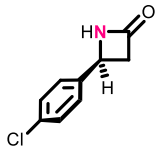
(*S*)-4-(4-fluorophenyl)azetidin-2-one (4c):



(*S*)-4-(4-fluorophenyl)azetidin-2-one (**4c**) was prepared according to the general procedure **D** to afford 13 mg of the desired amide product as white solid in 34% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 – 7.31 (m, 2H), 7.07 (t, *J* = 8.6 Hz, 2H), 6.42 (s, 1H), 4.72 (dd, *J* = 5.4, 2.5 Hz, 1H), 3.44 (ddd, *J* = 14.9, 5.3, 2.6 Hz, 1H), 2.84 (dd, *J* = 14.9, 2.5 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 168.7, 163.3 (d, *J* = 246.9 Hz), 136.7, 128.1 (d, *J* = 8.1 Hz), 116.5 (d, *J* = 21.7 Hz), 50.5, 48.9. **^{19}F {^{1}H}NMR (376 MHz, $CDCl_3$):** δ -113.96. **HRMS (ESI)** m/z calcd for C_9H_9FNO $[M+H]^+$ 166.0668, found 166.0660.

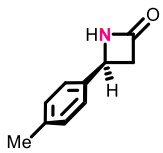
(*S*)-4-(4-chlorophenyl)azetidin-2-one (4d):



(*S*)-4-(4-chlorophenyl)azetidin-2-one (**4d**) was prepared according to the general procedure **D** to afford 3 mg of the desired amide product as white solid in 8% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H), 6.10 (s, 1H), 4.71 (dd, *J* = 5.4, 2.5 Hz, 1H), 3.46 (ddd, *J* = 15.0, 5.4, 2.6 Hz, 1H), 2.85 (dd, *J* = 15.0, 2.6 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 168.23, 143.02, 139.43, 129.81, 127.77, 50.54, 48.98. **HRMS (ESI)** m/z calcd for C_9H_9ClNO $[M+H]^+$ 182.0372, found 182.0365.

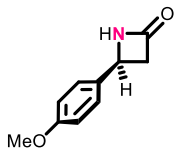
(*S*)-4-(p-tolyl)azetidin-2-one (4e):



(*S*)-4-(p-tolyl)azetidin-2-one (**4e**) was prepared according to the general procedure **D** to afford 8 mg of the desired amide product as white solid in 21% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 – 7.25 (m, 2H), 7.19 (d, *J* = 7.8 Hz, 2H), 6.13 (s, 1H), 4.69 (dd, *J* = 5.4, 2.5 Hz, 1H), 3.43 (ddd, *J* = 14.9, 5.3, 2.4 Hz, 1H), 2.86 (dd, *J* = 14.9, 2.5 Hz, 1H), 2.36 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 168.8, 138.9, 137.9, 130.3, 126.3, 50.9, 48.8, 30.4, 21.9. **HRMS (ESI)** m/z calcd for $C_{10}H_{12}NO$ $[M+H]^+$ 162.0919, found 162.0911.

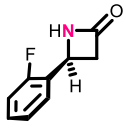
(*S*)-4-(4-methoxyphenyl)azetidin-2-one (4f):



(*S*)-4-(4-methoxyphenyl)azetidin-2-one (**4f**) was prepared according to the general procedure **D** to afford 4 mg of the desired amide product as white solid in 12% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.10 (s, 1H), 4.68 (dd, *J* = 5.4, 2.5 Hz, 1H), 3.82 (s, 3H), 3.42 (ddd, *J* = 15.0, 5.3, 2.5 Hz, 1H), 2.86 (dd, *J* = 14.9, 2.5 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 168.8, 160.4, 132.8, 127.7, 114.9, 56.1, 50.7, 48.8. **HRMS (ESI)** m/z calcd for $C_{10}H_{12}NO_2$ $[M+H]^+$ 178.0868, found 178.0861.

(*S*)-4-(2-fluorophenyl)azetidin-2-one (4g):

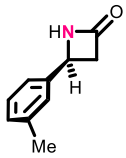


(*S*)-4-(2-fluorophenyl)azetidin-2-one (**4g**) was prepared according to the general procedure **D** to afford 22 mg of the desired amide product as white solid in 56% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (t, *J* = 7.6 Hz, 1H), 7.30 (p, *J* = 7.0 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.06 (t, *J* = 9.3 Hz, 1H), 6.52 (s, 1H), 4.99 (dd, *J* = 5.6, 2.6 Hz, 1H),

3.49 (ddd, *J* = 14.9, 5.5, 2.6 Hz, 1H), 2.94 (dd, *J* = 15.0, 2.6 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 168.68, 161.17 (d, *J* = 246.8 Hz), 130.38 (d, *J* = 8.1 Hz), 127.99 (d, *J* = 13.2 Hz), 127.37 (d, *J* = 3.9 Hz), 125.21 (d, *J* = 3.6 Hz), 116.28 (d, *J* = 20.9 Hz), 47.39, 45.46 (d, *J* = 4.7 Hz). **^{19}F {^{1}H}NMR (376 MHz, $CDCl_3$):** δ -119.32. **HRMS (ESI)** m/z calcd for C_9H_9FNO $[M+H]^+$ 166.0668, found 166.0660.

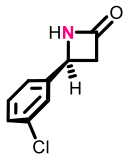
(*S*)-4-(m-tolyl)azetidin-2-one (4h):



(*S*)-4-(m-tolyl)azetidin-2-one (**4h**) was prepared according to the general procedure **D** to afford 17 mg of the desired amide product as white solid in 40% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 – 7.23 (m, 1H), 7.20 – 7.09 (m, 3H), 6.38 – 6.34 (m, 1H), 4.68 (dd, *J* = 5.3, 2.5 Hz, 1H), 3.42 (ddd, *J* = 14.9, 5.3, 2.4 Hz, 1H), 2.86 (ddd, *J* = 14.8, 2.5, 1.0 Hz, 1H), 2.36 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 168.9, 140.9, 139.4, 129.7, 129.5, 127.0, 123.5, 51.1, 48.7, 22.1. **HRMS (ESI)** m/z calcd for $C_{10}H_{12}NO$ $[M+H]^+$ 162.0919, found 162.0916.

(*S*)-4-(3-chlorophenyl)azetidin-2-one (4i):

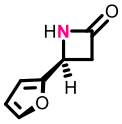


(S)-4-(3-chlorophenyl)azetidin-2-one (**4i**) was prepared according to the general procedure **D** to afford 26 mg of the desired amide product as white solid in 65% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.21 (m, 4H), 6.63 (s, 1H), 4.70 (dt, *J* = 4.8, 2.2 Hz, 1H), 3.45 (ddt, *J* = 14.9, 5.2, 2.6 Hz, 1H), 2.84 (ddd, *J* = 14.9, 9.0, 2.5 Hz, 1H). **^{13}C**

NMR (101 MHz, $CDCl_3$): δ 167.92, 142.39, 134.84, 130.21, 128.38, 125.89, 123.81, 49.87, 48.06. **HRMS (ESI)** m/z calcd for C_9H_9ClNO $[M+H]^+$ 182.0372, found 182.0366.

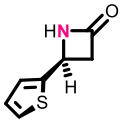
(*S*)-4-(furan-2-yl)azetidin-2-one (4j):



(*S*)-4-(furan-2-yl)azetidin-2-one (**4j**) was prepared according to the general procedure **D** to afford 7 mg of the desired amide product as white solid in 51% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.38 (m, 1H), 6.39 – 6.29 (m, 2H), 6.21 (s, 1H), 4.71 (dd, *J* = 5.3, 2.6 Hz, 1H), 3.36 (ddd, *J* = 14.8, 5.3, 2.0 Hz, 1H), 3.17 (ddd, *J* = 14.8, 2.6, 1.4 Hz, 1H).**^{13}C NMR (101 MHz, $CDCl_3$):** δ 167.60, 152.41, 142.83, 110.52, 107.67, 44.89, 43.83. **HRMS (ESI)** m/z calcd for $C_7H_8NO_2$ $[M+H]^+$ 138.0555, found 138.0549.

(*S*)-4-(thiophen-2-yl)azetidin-2-one (4k):

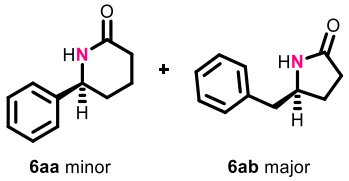


(*S*)-4-(thiophen-2-yl)azetidin-2-one (**4k**) was prepared according to the general procedure **D** to afford 28mg of the desired amide product as white solid in 71% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 – 7.24 (m, 1H), 7.05 (d, *J* = 3.5 Hz, 1H), 6.98 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.63 (s, 1H), 4.97 (dd, *J* = 5.2, 2.5 Hz, 1H), 3.46 (ddd, *J* = 14.9, 5.2, 2.4 Hz, 1H), 3.01 (dd, *J* = 14.9, 2.5 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ

168.5, 145.2, 127.8, 125.9, 125.6, 78.1, 77.82, 77.6, 49.4, 47.2. **HRMS (ESI)** m/z calcd for C_7H_8NOS $[M+H]^+$ 154.0326, found 154.0320.

(*S*)-6-phenylpiperidin-2-one (6aa) & (S)-5-benzylpyrrolidin-2-one (6ab):

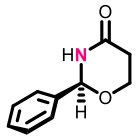


6aa minor **6ab** major

(S)-6-phenylpiperidin-2-one (**6aa**) & (S)-5-benzylpyrrolidin-2-one (**6ab**) was prepared according to the general procedure **D** to afford 4.0 mg (mixture of **6aa** and **6ab**) of the desired amide product as yellow liquid in 12% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.12 (m, 8H), 5.69 (s, 0.06 H), 5.69 (s, 1H), 5.57 (m, 0.14 H), 3.90 (q, J = 6.9 Hz, 1H), 2.86 (dd, J = 13.4, 5.4 Hz, 1H), 2.71 (dd, J = 13.4 Hz, J = 8.4 Hz, 1H), 2.49 – 2.44 (m, 0.39 H), 2.39 – 2.19 (m, 3.76H), 2.13 – 2.10 (m, 0.19 H), 1.89 -1.83 (m, 1H). **HRMS (ESI)** m/z calcd for $C_{11}H_{14}NO$ $[M+H]^+$ 176.1075, found 176.1069.

(*S*)-2-phenyl-1,3-oxazinan-4-one (6c):

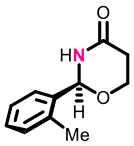


(*S*)-2-phenyl-1,3-oxazinan-4-one (**6c**) was prepared according to the general procedure **D** to afford 34 mg of the desired amide product as white solid in 78% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 – 7.29 (m, 5H), 6.94 (s, 1H), 5.73 (s, 1H), 4.22 (ddd, *J* = 11.7, 7.1, 2.3 Hz, 1H), 3.95 (td, *J* = 11.3, 4.4 Hz, 1H), 2.69 (ddd, *J* = 17., 10.9, 7.2 Hz, 1H), 2.43 (ddd, *J* = 17.5, 4.4, 2.2 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ

169.0, 137.8, 129.8, 128.8, 126.7, 85.6, 63.7, 31.6. **HRMS (ESI)** m/z calcd for $C_{10}H_{12}NO_2$ $[M+H]^+$ 178.0868, found 178.0860.

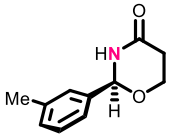
(*S*)-2-(o-tolyl)-1,3-oxazinan-4-one (6d):



(*S*)-2-(o-tolyl)-1,3-oxazinan-4-one (**6d**) was prepared according to the general procedure **D** to afford 8.6 mg of the desired amide product as white solid in 45% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.34 – 7.16 (m, 3H), 6.22 (s, 1H), 5.95 (s, 1H), 4.26 (ddd, *J* = 11.6, 7.1, 2.3 Hz, 1H), 3.99 (td, *J* = 11.3, 4.5, 1H), 2.75 (ddd, *J* = 17.9, 10.9, 7.2 Hz, 1H), 2.49 (ddd, *J* = 17.5, 4.6, 2.3 Hz, 1H), 2.43 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 169.0, 136.1, 135.3, 131.1, 129.6, 126.7, 126.4, 83.5, 63.9, 31.7, 18.7**. HRMS (ESI)** m/z calcd for $C_{11}H_{14}NO_2$ $[M+H]^+$ 192.1024, found 192.1016.

(*S*)-2-(m-tolyl)-1,3-oxazinan-4-one (6e):

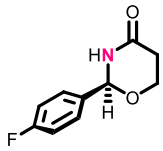


(*S*)-2-(m-tolyl)-1,3-oxazinan-4-one (**6e**) was prepared according to the general procedure **D** to afford 17 mg of the desired amide product as white solid in 90% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.16 (m, 4H), 6.26 (s, 1H), 5.70 (s, 1H), 4.26 (ddd, *J* = 11.7, 7.2, 2.0 Hz, 1H), 3.98 (td, *J* = 11.4, 4.4 Hz, 1H), 2.76 (ddd, *J* = 18.0, 11.1, 7.2 Hz, 1H), 2.52 – 2.43 (m, 1H), 2.38 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ

168.7, 138.8, 137.7, 130.7, 128.8, 127.3, 123.8, 85.9, 64.0, 31.7, 21.3. **HRMS (ESI)** m/z calcd for $C_{11}H_{14}NO_2$ $[M+H]^+$ 192.1024, found 192.1016.

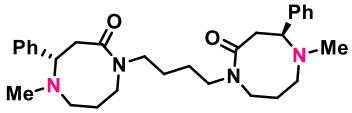
(*S*)-2-(4-fluorophenyl)-1,3-oxazinan-4-one (6f):



(*S*)-2-(4-fluorophenyl)-1,3-oxazinan-4-one (**8e**) was prepared according to the general procedure **D** to afford 18 mg of the desired amide product as white solid in 93% yield. R_f = 0.5 (5% 2-propanaol in DCM).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.11 (t, *J* = 8.6 Hz, 2H), 6.84 (s, 1H), 5.73 (s, 1H), 4.24 (ddd, *J* = 11.7, 7.2Hz, 2.1 Hz, 1H), 3.97 (td, *J* = 11.4, 4.4 Hz, 1H), 2.72 (ddd, *J* = 18.0, 11.1, 7.2 Hz, 1H), 2.45 (ddd, *J* = 17.5, 4.3, 2.1 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 169.0, 133.8, 128.7, 128.7, 116.0, 115.7, 85.0, 63.8, 31.6. **^{19}F {^{1}H}NMR (376 MHz, $CDCl_3$):** δ -111.3. **HRMS (ESI)** m/z calcd for $C_{10}H_{11}FNO_2$ $[M+H]^+$ 196.0774, found 196.0767.

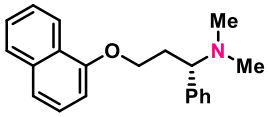
(*S*,*S*)-(-)-Homaline (7):



(*S*,*S*)-(-)-Homaline was prepared according to known methods[ref] to afford 25 mg of the desired alkaloid as a white solid in 16% overall yield over 4 steps. R_f = 0.8 (5% methanol in ether).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (tq, *J* = 15.4, 7.6 Hz, 10H), 3.99 (dd, *J* = 11.7, 3.4 Hz, 2H), 3.81 (d, *J* = 13.4 Hz, 4H), 3.32 (dt, *J* = 15.3, 3.7 Hz, 2H), 3.15 (t, *J* = 12.1 Hz, 2H), 3.09 – 2.90 (m, 4H), 2.51 (ddd, *J* = 14.9, 9.3, 4.4 Hz, 4H), 2.26 (s, 6H), 1.88 – 1.73 (m, 2H), 1.62 (q, *J* = 6.9 Hz, 7H).

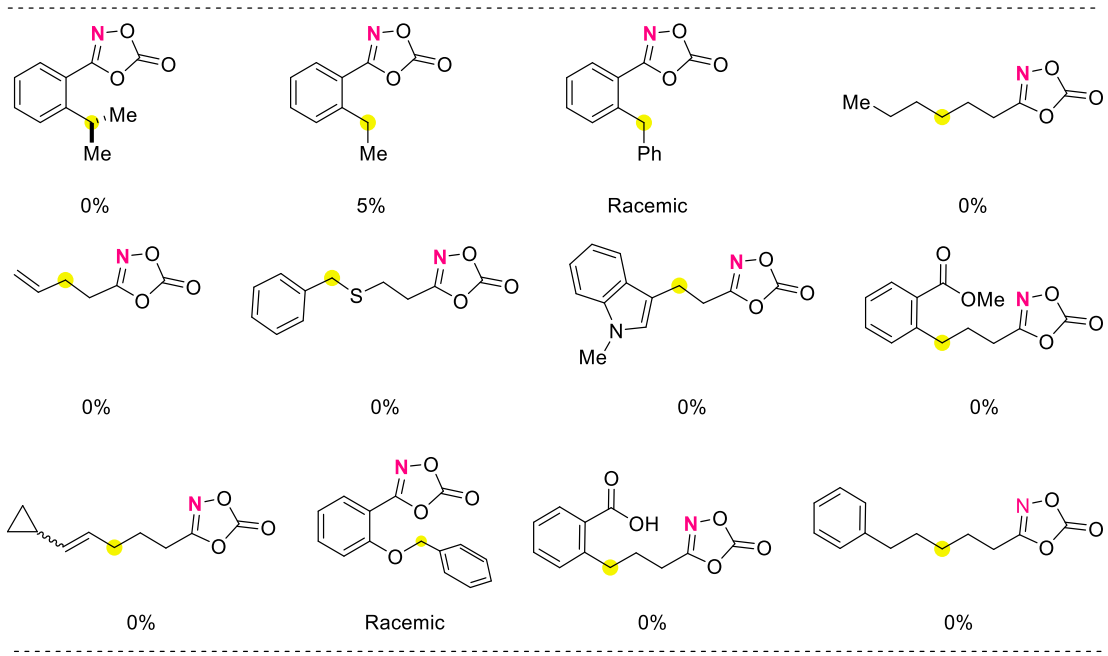
(*S*)-Dapoxetine (8):



(*S*)-Dapoxetine was prepared according to known methods[ref] to afford 70 mg of the desired drug as a white solid in 56% overall yield over 4 steps. R_f = 0.4 (50% EtOAc in DCM).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 – 8.21 (m, 1H), 7.77 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.48 – 7.46 (m, 2H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.33 – 7.26 (m, 6H), 6.64 (d, *J* = 7.5 Hz, 1H), 4.07 (ddd, *J* = 9.3, 6.7, 5.2 Hz, 1H), 3.90 (ddd, J = 9.2, 7.6, 6.2 Hz, 1H), 3.60 (dd, *J* = 9.3, 5.4 Hz, 1H), 2.68 – 2.58 (m, 1H), 2.32 – 2.26 (m, 1H), 2.25 (s, 6H). **^{13}C NMR (125 MHz, $CDCl_3$):** δ 154.5, 139.5, 134.3, 128.4, 128.1, 127.3, 127.2, 126.2, 125.7, 125.5, 124.9, 121.9, 119.9, 104.4, 67.5, 65.5, 42.7, 32.9.

Scheme S11. Unsuccessful Dioxazolones



Computational data

Quantum Mechanics (Density Functional Theory) calculations

Density Functional Theory (DFT) calculations were carried out using Gaussian09[17] software on the Cluster at XJTU. A truncated model containing the porphyrin pyrrole core, Fe center and a 4-Methylimidazole to mimic Fe-axial histidine. Geometry optimizations and frequency calculations were performed using dispersion corrected (U)B3LYP-D3(BJ)[18,19,20] functional with the SDD basis set for iron and 6-31G(d) on all other atoms. Transition states had one negative force constant corresponding to the desired transformation. All the optimized transition states were confirmed by the intrinsic reaction coordinate (IRC) calculations, which connect the corresponding reactants and intermediates (or intermediates and products). All stationary points were verified as minima or first-order saddle points by a vibrational frequency analysis. A quasi-harmonic corrections to entropy using Grimme's method[21] with a frequency cut-off value of 100 cm^{-1} was applied to the entropy calculations using the Goodvibes software[22]. Single-point energy calculations were carried out in water at Def2TZVP level, using SMD solvation model[23] continuum solvation model based on the gas-phase optimized geometries.

In the DFT calculations, the initial guess for the molecular orbital coefficients of open-shell singlet (OSS) structures was generated by using "stable = opt" calculation[24,25,26] from the close-shell singlet (CSS) optimized geometry, followed by a full optimization of the system starting from this guess. Wavefunction stability tests were carried out with "stable" to ensure the calculated wavefunctions in all open-shell calculations are stable. The stability test suggested that the closed-shell singlet (CSS) wavefunction is unstable in this iron porphyrin nitrene system. The closed-shell singlet structures lead to higher energies than corresponding open-shell singlet states. Optimized DFT structures are illustrated with CYLview[27].

Molecular Dynamics (MD) simulations

Molecular Dynamics simulations were prepared and equilibrated using the GPU code (pmemd)[28] (12) of the AMBER 16 package[29]. Parameters for the Iron porphyrin nitrene complexes were generated within the *antechamber* and MCPB.py[30] modules using the general AMBER force field (*gaff*)[31], with partial charges set to fit the electrostatic potential generated at the B3LYP/6-31G(d) level by the RESP model[32]. The partial charges were calculated according to the Merz–Singh–Kollman scheme[33,34] using the Gaussian 09 package.

Protonation states of protein residues were predicted using H++ server. Each protein was immersed in a pre-equilibrated truncated cuboid box with a 10 Å buffer of OPC[35] water molecules using the leap module, resulting in the addition of 7248 solvent molecules. The systems were neutralized by addition of explicit counter ions (Na^+ and Cl^-).

All subsequent calculations were done using the most current protein force field. The new *ff19SB* forcefield has shown to improve amino-acid dependent properties such as helical propensities and reproduces the differences in amino acid-specific Ramachandram Map using amino acid specific CMAPS. The *ff19SB* force field contains amino-acid specific backbone parameters. *ff19SB* pairs best with the more accurate OPC water model[36]. Water molecules were treated with the SHAKE algorithm such that the angle between the hydrogen atoms was kept fixed, long-range electrostatic effects were modelled using the particle-mesh-Ewald method[37]. An 8 Å cut-off was applied to Lennard–Jones and electrostatic interactions. Frist, a two-stage geometry optimization approach has been performed. The first stage minimizes the positions of solvent molecules and ions imposing positional restraints on the solute by a harmonic potential with a force constant of 500 $kcal \cdot mol^{-1} \cdot Å^{-2}$. The second stage minimizes all the atoms in the simulation cell except those involved in the harmonic distance restraint, with a force constant of 2 $kcal \cdot mol^{-1} \cdot Å^{-2}$. Second, the systems were gently heated using six 50 ps steps, incrementing the temperature by 50 K for each step (0–300 K) under

constant-volume and periodic-boundary conditions. Harmonic restraints of 30 kcal·mol^{-1} were applied to the to the protein backbone and ligands, and the Andersen equilibration scheme was used to control and equalize the temperature. The time step was kept at 1 fs during the heating stages, allowing potential inhomogeneities to self-adjust. Third, each system was then equilibrated for a total of 4 ns at constant pressure of 1 atm with a Berendson barostat with a 2 fs time step; harmonic restraints of 30 kcal·mol^{-1} were applied for the first 2 ns and harmonic restraints of 0.5 kcal·mol^{-1} were applied for the second 2 ns to the protein backbone and ligands. Finally, production trajectories were then run for an additional 1000 ns (1 μs) under the same simulation conditions. Trajectories were processed and analyzed using the *cpptraj*[38] module from AmberTools utilities. Snapshots for QM/MM calculations were obtained from a clusterization analysis of MD trajectories using *cpptraj*, where a representative snapshot from the most populated cluster was selected.

1a

N 0.894492 1.723095 1.157211

C 1.298837 1.142438 0.084366

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H 3.224697 0.996588 -0.753111

H 3.068395 0.399690 0.901774

C 2.442612 -1.016896 -0.642498

H 1.998839 -0.966001 -1.643108

H 3.457287 -1.412763 -0.766308

C 1.624417 -1.986837 0.234138

C 0.139834 -1.689645 0.240334

C -0.622173 -1.888373 -0.919295

C -1.969936 -1.537908 -0.958679

C -2.582217 -0.984248 0.168200

C -1.840052 -0.800183 1.334610

C -0.490266 -1.156591 1.369447

H 0.087123 -0.989461 2.274502

H -2.305045 -0.367128 2.215208

H -3.627337 -0.692452 0.133506

H -2.540971 -1.685741 -1.870607

H -0.149157 -2.307234 -1.804763

H 2.013768 -1.967156 1.259705

H 1.794382 -3.002607 -0.144900

O 0.437074 1.235920 -0.961386

C -0.667017 1.927098 -0.480526

O -1.649367 2.193312 -1.099681

O -0.386746 2.246669 0.810679

SM(Closed Shell Singlet)

C -0.124999 -3.416033 -0.664461

C -3.537530 0.000425 -0.357395

C -0.124139 3.416007 -0.664642

C 3.269840 -0.000453 -1.124228

N -1.544190 -1.417144 -0.555011

C -1.353126 -2.780282 -0.552079

C -2.618301 -3.467400 -0.423528

C -3.580492 -2.507098 -0.345322

C -2.902765 -1.232763 -0.424441

N -1.543834 1.417481 -0.555088

C -2.902455 1.233449 -0.424508

C -3.579861 2.507960 -0.345455

C -2.617428 3.468014 -0.423717

C -1.352425 2.780571 -0.552228

N 1.283536 1.416926 -0.870140

C 1.098138 2.779968 -0.825689

C 2.360479 3.467082 -0.982227

C 3.315151 2.506574 -1.120792

C	2.636373	1.232313	-1.046252
N	1.283179	-1.417318	-0.870066
C	2.636063	-1.233055	-1.046188
C	3.314520	-2.507491	-1.120659
C	2.359605	-3.467751	-0.982047
C	1.097438	-2.780310	-0.825542
Fe	-0.116030	-0.000012	-0.589619
H	-0.122972	-4.501946	-0.646051
H	4.347236	-0.000592	-1.261178
H	-0.121838	4.501920	-0.646290
H	-4.618418	0.000564	-0.250737
H	2.478051	-4.543908	-0.990760
H	4.380947	2.629603	-1.266535
H	-2.734726	4.544220	-0.406485
H	-4.652009	-2.630794	-0.250713
H	-2.735870	-4.543575	-0.406237
H	-4.651346	2.631930	-0.250851
H	4.380285	-2.630797	-1.266395
H	2.479197	4.543208	-0.990995
C	1.017504	0.000084	3.382673
C	1.282076	-0.000111	2.037378
N	-0.368062	0.000010	3.474014
C	-0.888088	0.000133	2.217054
N	0.093154	0.000013	1.332624
H	-1.940944	0.000223	1.983364
H	2.230707	-0.000221	1.524748
H	-0.903680	0.000007	4.329093
C	1.911754	0.000183	4.576103
H	1.758067	0.886787	5.204497
H	1.758038	-0.886312	5.204642
H	2.955577	0.000138	4.251793

TS1(Closed Shell Singlet)

C	-5.794499	0.181557	-2.500359
C	-4.701379	0.071825	-1.491973
C	-3.336890	0.132940	-1.603691
N	-2.760776	-0.028589	-0.358764
C	-3.743838	-0.186497	0.507956
N	-4.937210	-0.132357	-0.137048
H	-5.843515	-0.227161	0.297211
H	-3.624890	-0.338283	1.568846
Fe	-0.782972	-0.046137	0.097847
N	0.904873	0.005035	0.519076
C	1.852781	0.378325	1.310042
C	1.885497	1.885721	1.596363
H	1.492239	1.998988	2.613790
H	1.203639	2.405372	0.923664

C	3.298894	2.474181	1.498403	C	-1.263569	3.305741	0.579571
H	3.981060	1.869658	2.103824	C	-1.404799	2.479991	1.688358
H	3.263482	3.475590	1.947310	N	-1.242489	1.116907	1.694054
C	3.839539	2.599584	0.059964	C	-1.374475	0.713228	2.998137
C	4.091614	1.269314	-0.616400	C	-1.354303	-0.609081	3.428017
C	5.126546	0.434058	-0.175855	C	-1.258592	-1.713454	2.591818
C	5.312023	-0.828741	-0.732950	N	-1.116767	-1.666352	1.228385
C	4.465187	-1.274449	-1.750869	C	-1.104135	-2.965334	0.793778
C	3.442620	-0.445913	-2.209090	C	-0.887710	-3.380545	-0.512120
C	3.261538	0.818148	-1.646336	C	-0.562773	-2.551541	-1.576069
H	2.446152	1.447562	-1.988628	N	-0.483041	-1.185666	-1.527332
H	2.765992	-0.790810	-2.984204	C	-0.098050	-0.773996	-2.776207
H	4.594260	-2.267476	-2.171674	C	0.044846	0.546683	-3.179270
H	6.100526	-1.474289	-0.358123	C	-0.222878	1.653594	-2.382572
H	5.773007	0.764668	0.633578	C	-0.186112	3.025660	-2.835862
H	3.129485	3.186095	-0.537727	C	-0.595853	3.796521	-1.788868
H	4.772024	3.178400	0.099376	H	-0.703734	4.872808	-1.745956
O	2.771374	-0.336941	1.836787	H	0.105626	3.338432	-3.830265
C	2.749534	-1.991708	1.225054	H	0.355615	0.728649	-4.203241
O	3.662480	-2.580368	1.712600	C	0.078538	-1.919827	-3.643179
O	1.792084	-2.042638	0.472061	C	-0.220297	-3.021028	-2.901293
N	-0.625159	1.602993	-1.073741	H	-0.203315	-4.061241	-3.199758
C	-0.865248	2.898341	-0.688241	H	0.383786	-1.865728	-4.680400

H	-0.902826	-4.449092	-0.701725
C	-1.273102	-3.862993	1.915140
C	-1.352022	-3.088487	3.031583
H	-1.463974	-3.398516	4.062564
H	-1.296600	-4.942393	1.839810
H	-1.463510	-0.793292	4.492081
C	-1.618310	1.856974	3.846510
C	-1.654055	2.950396	3.031601
H	-1.815409	3.986286	3.301547
H	-1.755475	1.811057	4.919338
H	-1.413913	4.370057	0.732597
H	-2.730416	0.279281	-2.482788
H	-5.363286	0.339143	-3.492267
H	-6.405847	-0.728760	-2.543465
H	-6.464025	1.025216	-2.289878

IM1(Closed Shell Singlet)

C	1.194980	-2.239066	-3.079985
C	1.966132	-2.394305	-1.935903
N	1.906582	-1.609481	-0.811896
C	2.815034	-2.127775	0.072851
C	3.010839	-1.699579	1.376947
C	2.278957	-0.705275	2.009102
N	1.292963	0.047533	1.421571
C	0.835817	0.907547	2.390004
C	-0.119958	1.895819	2.195207
C	-0.737525	2.183139	0.985696
N	-0.547084	1.502465	-0.191967
C	-1.322317	2.131543	-1.133087
C	-1.499125	1.721068	-2.447003
C	-0.932925	0.587357	-3.014720
N	-0.050415	-0.249449	-2.387407
C	0.259853	-1.233224	-3.289262
C	-0.460202	-1.017806	-4.525777
C	-1.194001	0.117766	-4.358043
H	-1.858434	0.601959	-5.062342
H	-0.394179	-1.656194	-5.397572
Fe	0.578481	-0.145363	-0.460412
N	-0.624472	-1.262631	-0.006657
C	-0.631683	-2.072263	1.080632
O	-0.129771	-3.197911	1.084827
C	-3.659811	-2.532981	1.385788
H	-3.156011	-2.916342	0.491309
N	2.070566	1.173947	-1.114077
C	2.643367	1.167165	-2.301663
N	3.577180	2.153186	-2.370827
C	3.597004	2.828637	-1.157039

C	2.650119	2.197654	-0.391610
H	2.342980	2.406480	0.620713
C	4.503987	3.979843	-0.880695
H	4.338994	4.339906	0.138108
H	5.561614	3.699919	-0.967782
H	4.322719	4.819205	-1.564190
H	4.157221	2.358671	-3.170990
H	2.416075	0.481922	-3.102798
H	-2.166169	2.312005	-3.067188
C	-2.000921	3.260237	-0.537369
C	-1.650892	3.283081	0.777682
H	-1.971037	3.970015	1.550315
H	-2.674141	3.921193	-1.067996
H	-0.381316	2.514752	3.047701
C	1.540532	0.677249	3.629902
C	2.440255	-0.318797	3.391317
H	3.151912	-0.762916	4.075351
H	1.364034	1.221387	4.548945
H	3.760306	-2.219447	1.964991
C	3.504268	-3.247629	-0.526659
C	2.973220	-3.417849	-1.767639
H	3.218038	-4.165413	-2.511135
H	4.274028	-3.828247	-0.035093
H	1.353291	-2.950133	-3.884790
C	-1.460106	-1.530952	2.246969
H	-1.805030	-0.515090	2.033907
H	-0.782636	-1.481491	3.107954
C	-2.641653	-2.462537	2.542206
H	-2.251980	-3.467194	2.738757
H	-3.147959	-2.117675	3.452777
C	-4.304584	-1.199678	1.079632
C	-5.320314	-0.701169	1.906791
C	-5.902908	0.541756	1.660494
C	-5.479111	1.307735	0.572419
C	-4.470756	0.820756	-0.259326
C	-3.883687	-0.419879	-0.005888
H	-5.659671	-1.298544	2.750733
H	-6.691266	0.908938	2.312762
H	-5.933220	2.275155	0.374567
H	-4.129730	1.406776	-1.106017
H	-3.079673	-0.779431	-0.641266
H	-4.433748	-3.264745	1.650190

TS2(Closed Shell Singlet)

C	0.484638	-2.595563	-2.389595
C	1.515904	-2.663412	-1.457479
N	1.749623	-1.729599	-0.486458

C	2.865950	-2.142387	0.189760
C	3.410026	-1.512231	1.302237
C	2.871636	-0.413020	1.957866
N	1.758354	0.280968	1.573801
C	1.532605	1.214918	2.544788
C	0.510857	2.156378	2.525369
C	-0.405159	2.319217	1.493095
N	-0.487208	1.526184	0.375663
C	-1.442100	2.093242	-0.428667
C	-1.878135	1.574555	-1.639622
C	-1.455993	0.373547	-2.194570
N	-0.488054	-0.451688	-1.669568
C	-0.426404	-1.552178	-2.500921
C	-1.404834	-1.427334	-3.554484
C	-2.029775	-0.226461	-3.374089
H	-2.818573	0.217956	-3.967768
H	-1.567606	-2.160430	-4.334725
Fe	0.598409	-0.120623	-0.028729
N	-0.410310	-1.288573	1.005229
C	-0.583815	-1.729682	2.265775
O	0.303081	-1.680409	3.128370
C	-2.660843	-1.919290	0.225929
H	-1.377120	-1.534143	0.347067
N	1.883621	1.013240	-1.087933
C	2.429904	0.678188	-2.241355
N	3.235741	1.682205	-2.678100
C	3.201015	2.714032	-1.747354
C	2.351097	2.272350	-0.766824
H	2.045068	2.762014	0.143660
C	3.975192	3.978719	-1.905845
H	3.787180	4.632453	-1.050201
H	5.056386	3.795676	-1.953687
H	3.688180	4.526194	-2.812869
H	3.771470	1.675364	-3.533278
H	2.266565	-0.250839	-2.764095
H	-2.663303	2.113496	-2.159579
C	-1.981285	3.280316	0.198200
C	-1.350833	3.411246	1.398387
H	-1.486919	4.176016	2.152822
H	-2.757615	3.902005	-0.228767
H	0.455205	2.851750	3.357546
C	2.547067	1.122534	3.574442
C	3.386822	0.120286	3.202410
H	4.261488	-0.255047	3.718026
H	2.590618	1.749770	4.455707
H	4.298051	-1.960001	1.738375

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H 2.567281 -4.557083 -2.067039

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H 0.411797 -3.399465 -3.116278

C -1.940429 -2.373781 2.608430

H -2.549225 -1.625288 3.128045

H -1.736080 -3.166059 3.334034

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H -3.699631 -3.191711 1.617456

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C -5.335339 1.426139 0.142913

C -4.450836 1.280622 1.215108

C -3.559994 0.213781 1.253039

H -4.373504 -1.265644 -1.696246

H -5.975096 0.620653 -1.753835

H -6.027818 2.262863 0.116454

H -4.433272 2.018174 2.011150

H -2.831202 0.156345 2.051668

H -2.595452 -2.392362 -0.756018

IM2(Closed Shell Singlet)

C 0.329849 -2.303270 -2.395637

C 1.162337 -2.316205 -1.283789

N 1.213875 -1.327743 -0.324365

C 2.139032 -1.757394 0.603758

C 2.485504 -1.074092 1.761572

C 1.987468 0.162169 2.145896

N 1.092584 0.918459 1.425746

C 0.901628 2.066199 2.157577

C 0.071465 3.116874 1.792448

C -0.731789 3.144148 0.661363

N -0.807905 2.145763 -0.279640

C -1.736661 2.569319 -1.199013

C -2.147994 1.852196 -2.312486

C -1.691951 0.592015 -2.670787

N -0.735810 -0.128281 -1.994056

C -0.569775 -1.292576 -2.710582

C -1.457357 -1.313668 -3.852261

C -2.155427 -0.144532 -3.825797

H -2.914048 0.203829 -4.515345

H -1.525951 -2.125456 -4.565454

Fe 0.257242 0.447470 -0.339874

N -0.855650 -3.182881 1.160884

C	-1.198850	-4.012766	2.194408
O	-0.428436	-4.526954	2.989082
C	-1.974038	-2.563344	0.471718
H	0.085410	-2.821641	1.085089
N	1.683390	1.276537	-1.360919
C	2.261618	0.775675	-2.438040
N	3.217702	1.634335	-2.883412
C	3.248689	2.740301	-2.044536
C	2.283210	2.494989	-1.102638
H	1.976046	3.098565	-0.263887
C	4.184831	3.884517	-2.240420
H	4.021777	4.629668	-1.457528
H	5.234839	3.569650	-2.187295
H	4.032098	4.378994	-3.208245
H	3.806201	1.487792	-3.689834
H	2.019331	-0.169101	-2.897704
H	-2.902104	2.307728	-2.947625
C	-2.259303	3.866877	-0.828398
C	-1.633710	4.224929	0.326092
H	-1.763611	5.124637	0.914308
H	-3.009848	4.411666	-1.387108
H	0.022995	3.971357	2.461037
C	1.686033	2.027788	3.372940
C	2.356848	0.843657	3.367814
H	3.039325	0.450077	4.110244
H	1.702796	2.810174	4.121189
H	3.199401	-1.552448	2.425027
C	2.670652	-3.046791	0.223660
C	2.067909	-3.390644	-0.949066
H	2.196383	-4.293382	-1.532415
H	3.393560	-3.609017	0.800281
H	0.370085	-3.162063	-3.059112
C	-2.725855	-4.143692	2.160017
H	-3.131610	-3.541898	2.982528
H	-3.029976	-5.179883	2.324931
C	-3.115497	-3.574318	0.789517
H	-3.105696	-4.369234	0.035910
H	-4.096660	-3.094808	0.771547
C	-2.304884	-1.159362	0.958809
C	-3.262416	-0.408916	0.260966
C	-3.677473	0.831107	0.735540
C	-3.132854	1.348248	1.913967
C	-2.161593	0.623599	2.599306
C	-1.746296	-0.622880	2.123020
H	-3.675702	-0.802302	-0.664640
H	-4.410570	1.405926	0.177655

H -3.444240 2.323967 2.273978

H -1.706959 1.030027 3.497366

H -0.987563 -1.181037 2.660851

H -1.780645 -2.526462 -0.603828 ss

SM(Open Shell Singlet)

C 0.140078 3.414905 -0.672291

C 3.549659 -0.000048 -0.289305

C 0.139996 -3.414927 -0.672202

C -3.249693 0.000022 -1.195028

N 1.561706 1.419211 -0.526096

C 1.367425 2.780687 -0.531785

C 2.629493 3.468684 -0.378373

C 3.591183 2.509151 -0.278345

C 2.916402 1.234022 -0.369183

N 1.561674 -1.419266 -0.526063

C 2.916373 -1.234105 -0.369154

C 3.591124 -2.509247 -0.278284

C 2.629410 -3.468760 -0.378287

C 1.367360 -2.780736 -0.531716

N -1.269874 -1.419063 -0.901538

C -1.081183 -2.780360 -0.856275

C -2.339771 -3.468361 -1.038223

C -3.293459 -2.508692 -1.193660

C -2.617936 -1.233651 -1.104568

N -1.269841 1.419069 -0.901581

C -2.617907 1.233684 -1.104604

C -3.293400 2.508738 -1.193731

C -2.339688 3.468389 -1.038319

C -1.081117 2.780363 -0.856352

Fe 0.128080 -0.000010 -0.587318

H 0.137955 4.500878 -0.657311

H -4.324099 0.000032 -1.353520

H 0.137846 -4.500899 -0.657194

H 4.628231 -0.000059 -0.161608

H -2.457835 4.544585 -1.050166

H -4.356070 -2.633654 -1.359425

H 2.746522 -4.545001 -0.359835

H 4.660262 2.634725 -0.161530

H 2.746631 4.544923 -0.359951

H 4.660200 -2.634845 -0.161465

H -4.356007 2.633721 -1.359500

H -2.457943 -4.544555 -1.050043

C -1.098587 0.000078 3.455167

C -1.336568 0.000023 2.104443

N 0.286245 0.000042 3.570899

C 0.825112 0.000044 2.321766

N	-0.137608	0.000022	1.420239
H	1.882664	0.000043	2.106701
H	-2.276194	0.000008	1.573982
H	0.805994	0.000045	4.436102
C	-2.012592	0.000130	4.633691
H	-1.869724	-0.886330	5.264908
H	-1.869705	0.886628	5.264851
H	-3.050896	0.000130	4.291985

TS1(Open Shell Singlet)

C	5.694959	2.667037	0.234672
C	4.631508	1.637785	0.052281
C	3.271103	1.683546	0.206653
N	2.731427	0.446471	-0.088110
C	3.731400	-0.350992	-0.417895
N	4.900205	0.332358	-0.346031
H	5.813909	-0.047571	-0.546352
H	3.639046	-1.387596	-0.700063
Fe	0.792270	-0.095201	-0.019646
N	-0.960803	-0.600425	0.001375
C	-1.889050	-1.343663	-0.475918
C	-2.137128	-1.324225	-1.982969
H	-1.688292	-2.246975	-2.370833
H	-1.593647	-0.488793	-2.427088
C	-3.627141	-1.269646	-2.350404
H	-4.172101	-1.975115	-1.716806
H	-3.736933	-1.620261	-3.384525
C	-4.247235	0.136521	-2.252559
C	-4.127133	0.796079	-0.894191
C	-4.615979	0.170409	0.261122
C	-4.458189	0.759325	1.513912
C	-3.843159	2.007676	1.629031
C	-3.382174	2.654006	0.483526
C	-3.509286	2.044230	-0.765129
H	-3.109918	2.538146	-1.647644
H	-2.905714	3.626399	0.559312
H	-3.715296	2.465401	2.606048
H	-4.796416	0.227376	2.397603
H	-5.078637	-0.808792	0.194267
H	-3.773152	0.784244	-3.001572
H	-5.306266	0.060531	-2.536970
O	-2.686929	-2.109971	0.205815
C	-2.583180	-1.949064	1.822810
O	-3.524950	-2.491215	2.341614
O	-1.574534	-1.304792	2.106645
N	0.344733	1.642489	-0.951114
C	0.328477	1.853525	-2.307249

C	0.643948	0.912906	-3.278672
C	0.961811	-0.417875	-3.041200
N	1.057281	-1.011117	-1.805455
C	1.280508	-2.347786	-2.032532
C	1.467289	-3.306518	-1.044739
C	1.501548	-3.040758	0.316551
N	1.333354	-1.803708	0.888045
C	1.482339	-1.979243	2.239293
C	1.324572	-0.999539	3.206696
C	0.901585	0.298904	2.969441
N	0.649976	0.849454	1.741149
C	0.206181	2.126520	1.973340
C	-0.118731	3.053456	0.996066
C	-0.043372	2.821918	-0.370165
C	-0.320533	3.807579	-1.387516
C	-0.084898	3.208947	-2.589499
H	-0.181352	3.628386	-3.582747
H	-0.649456	4.819789	-1.190351
H	-0.444926	4.035146	1.323043
C	0.179199	2.391373	3.393370
C	0.620210	1.261448	4.010368
H	0.730991	1.068895	5.069493
H	-0.140127	3.324909	3.838287
H	1.471775	-1.293435	4.240690
C	1.778276	-3.363559	2.528140
C	1.776902	-4.024593	1.337971
H	1.942398	-5.077358	1.148985
H	1.936241	-3.762451	3.521643
H	1.621848	-4.332793	-1.361852
C	1.334556	-2.604417	-3.450843
C	1.149545	-1.405775	-4.075759
H	1.121089	-1.196999	-5.137538
H	1.497996	-3.578221	-3.894346
H	0.589819	1.232261	-4.314742
H	2.644146	2.506913	0.508065
H	5.241726	3.610064	0.550476
H	6.422079	2.372845	1.001938
H	6.245875	2.856213	-0.695221

IM1(Open Shell Singlet)

C	1.256828	-2.228016	-3.128800
C	1.971168	-2.417581	-1.953302
N	1.889314	-1.635487	-0.828875
C	2.761830	-2.175186	0.081090
C	2.942519	-1.736875	1.383687
C	2.222840	-0.716418	1.986423
N	1.263526	0.050640	1.370833

C	0.786757	0.912617	2.328346	C	2.569852	2.290606	-0.443103
C	-0.176573	1.891127	2.122808	H	2.139836	2.580253	0.502464
C	-0.789196	2.167872	0.908085	C	4.416612	4.090564	-0.889771
N	-0.571664	1.493371	-0.268119	H	4.121583	4.538906	0.062418
C	-1.334440	2.122734	-1.220218	H	5.484281	3.844958	-0.825821
C	-1.460519	1.729724	-2.544928	H	4.294453	4.853220	-1.669375
C	-0.850983	0.617362	-3.108458	H	4.387880	2.249512	-3.035025
N	0.023403	-0.218062	-2.464374	H	2.705738	0.318316	-2.983541
C	0.355002	-1.198213	-3.363251	H	-2.118894	2.315438	-3.178905
C	-0.328162	-0.972666	-4.617702	C	-2.037832	3.238357	-0.631589
C	-1.070215	0.159031	-4.461897	C	-1.711692	3.257317	0.690392
H	-1.719513	0.644785	-5.178986	H	-2.054459	3.935733	1.460782
H	-0.239058	-1.606909	-5.490429	H	-2.707729	3.895846	-1.170644
Fe	0.608300	-0.122202	-0.529588	H	-0.455013	2.505049	2.973387
N	-0.717980	-1.286231	-0.084250	C	1.461108	0.679253	3.583689
C	-0.674794	-2.115105	0.990132	C	2.355603	-0.326932	3.369864
O	-0.180512	-3.245079	0.958850	H	3.042541	-0.780048	4.072888
C	-3.685890	-2.538668	1.456479	H	1.264090	1.224170	4.498040
H	-3.238383	-2.921552	0.532462	H	3.664586	-2.268749	1.994642
N	2.110482	1.181467	-1.124532	C	3.439393	-3.311579	-0.496039
C	2.818520	1.084511	-2.232787	C	2.943936	-3.466987	-1.754384
N	3.723797	2.096884	-2.290240	H	3.193850	-4.219916	-2.490734
C	3.581422	2.883602	-1.154141	H	4.177990	-3.912289	0.018546

H	1.428098	-2.935522	-3.933960
C	-1.423961	-1.594645	2.219491
H	-1.761443	-0.567494	2.054831
H	-0.703825	-1.584137	3.046405
C	-2.607172	-2.509362	2.558604
H	-2.227847	-3.525362	2.713623
H	-3.059608	-2.175800	3.501433
C	-4.312119	-1.186281	1.198814
C	-5.272532	-0.671595	2.080188
C	-5.834803	0.588333	1.875062
C	-5.446328	1.355433	0.774666
C	-4.493098	0.852137	-0.111020
C	-3.926261	-0.405263	0.101109
H	-5.584753	-1.269245	2.934384
H	-6.580422	0.967892	2.569276
H	-5.885097	2.335987	0.608967
H	-4.179207	1.439125	-0.967826
H	-3.160385	-0.776792	-0.572937
H	-4.463845	-3.254579	1.751436

TS2(Open Shell Singlet)

C	1.981766	-2.666057	-1.845742
C	2.557868	-2.404232	-0.609121
N	2.204883	-1.382604	0.235911
C	3.053830	-1.456912	1.309970
C	3.002587	-0.646009	2.433113
C	2.022063	0.301437	2.678846
N	1.017924	0.650479	1.812768
C	0.241640	1.570195	2.468843
C	-0.855920	2.232079	1.932617
C	-1.316796	2.093518	0.631094
N	-0.790405	1.247172	-0.312452
C	-1.517687	1.448760	-1.459266
C	-1.369617	0.737609	-2.640259
C	-0.504234	-0.333452	-2.820561
N	0.387388	-0.800676	-1.888081
C	0.981028	-1.908656	-2.440928
C	0.451015	-2.144840	-3.763534
C	-0.462927	-1.161473	-4.002947
H	-1.069245	-1.004338	-4.886000
H	0.752381	-2.958054	-4.411634
Fe	0.673133	-0.114122	-0.004115
N	-0.517101	-1.314494	0.647012
C	-0.606345	-2.181844	1.677780
O	0.276952	-2.353732	2.525737
C	-2.756639	-1.847531	-0.382392
H	-1.607493	-1.396323	-0.089590

N	2.029687	1.261601	-0.762470	C	3.985934	-2.544603	1.129307
C	3.020075	0.989908	-1.589021	C	3.670664	-3.141004	-0.054037
N	3.698199	2.130519	-1.884761	H	4.135611	-3.998660	-0.523353
C	3.104455	3.187250	-1.205368	H	4.758492	-2.815588	1.837263
C	2.066047	2.618466	-0.513495	H	2.365673	-3.513732	-2.404950
H	1.346568	3.082271	0.142576	C	-1.941367	-2.947348	1.787413
C	3.595160	4.592535	-1.297973	H	-2.561643	-2.409200	2.514850
H	2.969402	5.240459	-0.678802	H	-1.710654	-3.915522	2.242014
H	4.629295	4.690759	-0.943868	C	-2.694846	-3.127517	0.460231
H	3.555529	4.974611	-2.326046	H	-2.169126	-3.884845	-0.133596
H	4.499911	2.196226	-2.494515	H	-3.704603	-3.516551	0.650725
H	3.262472	0.012700	-1.976293	C	-3.743578	-0.788767	-0.061692
H	-2.027329	0.994938	-3.464479	C	-4.642886	-0.348746	-1.049020
C	-2.520124	2.465455	-1.237995	C	-5.594342	0.632401	-0.777315
C	-2.402697	2.857414	0.059859	C	-5.660318	1.211420	0.491054
H	-2.998362	3.579700	0.601987	C	-4.753844	0.809490	1.474217
H	-3.236236	2.794260	-1.979048	C	-3.804333	-0.172320	1.201492
H	-1.372849	2.940711	2.572216	H	-4.594782	-0.796454	-2.038625
C	0.773753	1.811308	3.791540	H	-6.285261	0.944398	-1.556402
C	1.885665	1.035184	3.915479	H	-6.400663	1.976856	0.707008
H	2.552014	0.939930	4.763022	H	-4.776870	1.272057	2.457499
H	0.341657	2.493034	4.512997	H	-3.075806	-0.433884	1.959715
H	3.736990	-0.821847	3.212491	H	-2.716475	-2.053551	-1.454714

IM2(Open Shell Singlet)

C 0.482319 0.286355 -3.157321

C -0.318735 1.311552 -2.675745

N -0.918557 1.353956 -1.439774

C -1.698281 2.483112 -1.424804

C -2.497203 2.908403 -0.375241

C -2.567719 2.296590 0.865636

N -1.896430 1.158405 1.228266

C -2.186174 0.937779 2.551228

C -1.706976 -0.116360 3.314952

C -0.890946 -1.137249 2.846294

N -0.411540 -1.257232 1.564648

C 0.281793 -2.442677 1.516939

C 0.909587 -2.973029 0.398725

C 0.980821 -2.359256 -0.844366

N 0.474449 -1.118147 -1.146863

C 0.805867 -0.868671 -2.456384

C 1.520672 -1.995081 -3.004604

C 1.623178 -2.922116 -2.005356

H 2.099976 -3.893511 -2.035433

H 1.893825 -2.054713 -4.019080

Fe -0.565435 0.127424 0.102435

N 1.044606 1.107211 0.784988

C 1.269122 2.439417 0.866246

O 0.425841 3.306761 0.603370

C 3.663670 1.604936 -0.734802

H 1.854335 0.541899 1.025398

N -2.493900 -1.151025 -0.640120

C -2.504103 -2.077066 -1.575871

N -3.756094 -2.601974 -1.712295

C -4.593869 -1.968281 -0.803706

C -3.781791 -1.072495 -0.152050

H -4.034852 -0.376219 0.633489

C -6.044374 -2.290545 -0.671973

H -6.489930 -1.663558 0.104929

H -6.594215 -2.105958 -1.603978

H -6.210218 -3.338236 -0.389361

H -4.028454 -3.326232 -2.360872

H -1.651507 -2.390357 -2.159621

H 1.394822 -3.937379 0.509090

C 0.248933 -3.081448 2.810230

C -0.471511 -2.269704 3.635295

H -0.715069 -2.414793 4.679894

H 0.721280 -4.028010 3.039619

H -2.014632 -0.161664 4.354722

C -3.088727 1.957481 3.032725

C	-3.332232	2.794198	1.984433
H	-3.951996	3.681152	1.959840
H	-3.471935	2.013035	4.043522
H	-3.069679	3.818469	-0.520041
C	-1.581323	3.177681	-2.683566
C	-0.718869	2.458952	-3.454852
H	-0.382948	2.663648	-4.463261
H	-2.094456	4.099526	-2.924558
H	0.846549	0.373506	-4.176018
C	2.693768	2.872988	1.238304
H	3.133449	2.183891	1.968754
H	2.641562	3.870050	1.685492
C	3.594476	2.922949	-0.028243
H	3.185182	3.681166	-0.704297
H	4.596132	3.263983	0.269790
C	4.351007	0.467408	-0.247635
C	4.181106	-0.790246	-0.893043
C	4.794629	-1.936120	-0.415048
C	5.616105	-1.881611	0.719932
C	5.811336	-0.653702	1.365999
C	5.195724	0.499392	0.899463
H	3.536895	-0.842121	-1.763762
H	4.630015	-2.882196	-0.924342
H	6.096689	-2.780541	1.095118
H	6.449652	-0.601550	2.244382
H	5.359461	1.440058	1.415270
H	3.019241	1.459969	-1.597649

TS3(Open Shell Singlet)

C	0.482319	0.286355	-3.157321
C	-0.318735	1.311552	-2.675745
N	-0.918557	1.353956	-1.439774
C	-1.698281	2.483112	-1.424804
C	-2.497203	2.908403	-0.375241
C	-2.567719	2.296590	0.865636
N	-1.896430	1.158405	1.228266
C	-2.186174	0.937779	2.551228
C	-1.706976	-0.116360	3.314952
C	-0.890946	-1.137249	2.846294
N	-0.411540	-1.257232	1.564648
C	0.281793	-2.442677	1.516939
C	0.909587	-2.973029	0.398725
C	0.980821	-2.359256	-0.844366
N	0.474449	-1.118147	-1.146863
C	0.805867	-0.868671	-2.456384
C	1.520672	-1.995081	-3.004604
C	1.623178	-2.922116	-2.005356

H	2.099976	-3.893511	-2.035433	H	-0.715069	-2.414793	4.679894
H	1.893825	-2.054713	-4.019080	H	0.721280	-4.028010	3.039619
Fe	-0.565435	0.127424	0.102435	H	-2.014632	-0.161664	4.354722
N	1.044606	1.107211	0.784988	C	-3.088727	1.957481	3.032725
C	1.269122	2.439417	0.866246	C	-3.332232	2.794198	1.984433
O	0.425841	3.306761	0.603370	H	-3.951996	3.681152	1.959840
C	3.663670	1.604936	-0.734802	H	-3.471935	2.013035	4.043522
H	1.854335	0.541899	1.025398	H	-3.069679	3.818469	-0.520041
N	-2.493900	-1.151025	-0.640120	C	-1.581323	3.177681	-2.683566
C	-2.504103	-2.077066	-1.575871	C	-0.718869	2.458952	-3.454852
N	-3.756094	-2.601974	-1.712295	H	-0.382948	2.663648	-4.463261
C	-4.593869	-1.968281	-0.803706	H	-2.094456	4.099526	-2.924558
C	-3.781791	-1.072495	-0.152050	H	0.846549	0.373506	-4.176018
H	-4.034852	-0.376219	0.633489	C	2.693768	2.872988	1.238304
C	-6.044374	-2.290545	-0.671973	H	3.133449	2.183891	1.968754
H	-6.489930	-1.663558	0.104929	H	2.641562	3.870050	1.685492
H	-6.594215	-2.105958	-1.603978	C	3.594476	2.922949	-0.028243
H	-6.210218	-3.338236	-0.389361	H	3.185182	3.681166	-0.704297
H	-4.028454	-3.326232	-2.360872	H	4.596132	3.263983	0.269790
H	-1.651507	-2.390357	-2.159621	C	4.351007	0.467408	-0.247635
H	1.394822	-3.937379	0.509090	C	4.181106	-0.790246	-0.893043
C	0.248933	-3.081448	2.810230	C	4.794629	-1.936120	-0.415048
C	-0.471511	-2.269704	3.635295	C	5.616105	-1.881611	0.719932

C	5.811336	-0.653702	1.365999
C	5.195724	0.499392	0.899463
H	3.536895	-0.842121	-1.763762
H	4.630015	-2.882196	-0.924342
H	6.096689	-2.780541	1.095118
H	6.449652	-0.601550	2.244382
H	5.359461	1.440058	1.415270
H	3.019241	1.459969	-1.597649

2a(Open Shell Singlet)

C	0.293488	-2.307989	-2.419514
C	1.134793	-2.331151	-1.313886
N	1.203958	-1.345891	-0.353300
C	2.134863	-1.782054	0.565260
C	2.484275	-1.111057	1.730417
C	1.980599	0.116745	2.138118
N	1.082390	0.882059	1.433427
C	0.885977	2.016608	2.183155
C	0.057862	3.073763	1.829745
C	-0.735021	3.122960	0.691554
N	-0.806022	2.141497	-0.266778
C	-1.724529	2.580652	-1.187971
C	-2.135314	1.877690	-2.311712
C	-1.693642	0.614133	-2.680203
N	-0.747293	-0.122865	-2.009644
C	-0.596979	-1.286467	-2.728817
C	-1.485688	-1.290715	-3.869417
C	-2.166799	-0.110917	-3.838279
H	-2.920271	0.250310	-4.526901
H	-1.566300	-2.097917	-4.586520
Fe	0.255689	0.437963	-0.349271
N	-0.834000	-3.138494	1.241849
C	-1.165442	-3.963677	2.282530
O	-0.390487	-4.443276	3.094403
C	-1.960514	-2.565381	0.526465
H	0.097388	-2.751688	1.169627
N	1.745241	1.307650	-1.397639
C	2.342411	0.800603	-2.459100
N	3.295894	1.661632	-2.906147
C	3.305101	2.779293	-2.080755
C	2.329156	2.534038	-1.148967
H	2.003929	3.144477	-0.321086
C	4.233077	3.929650	-2.280410
H	4.052859	4.683821	-1.509973
H	5.285341	3.625893	-2.209478
H	4.088516	4.409669	-3.256768
H	3.896602	1.511720	-3.703256

H	2.114870	-0.153206	-2.909248
H	-2.882642	2.346570	-2.945179
C	-2.243533	3.875773	-0.803024
C	-1.628513	4.213180	0.363594
H	-1.760775	5.104464	0.963928
H	-2.985968	4.433057	-1.360298
H	0.005707	3.917116	2.512012
C	1.669709	1.959868	3.397666
C	2.346982	0.778905	3.371101
H	3.031776	0.376569	4.106697
H	1.683860	2.728771	4.159772
H	3.201327	-1.596798	2.385016
C	2.658284	-3.071613	0.173713
C	2.039607	-3.410436	-0.992210
H	2.158564	-4.311812	-1.579687
H	3.385532	-3.638755	0.740041
H	0.321740	-3.165256	-3.085577
C	-2.687488	-4.140554	2.231203
H	-3.121332	-3.539417	3.039719
H	-2.962747	-5.182880	2.407779
C	-3.076636	-3.603321	0.847538
H	-3.035910	-4.409265	0.106762
H	-4.070458	-3.151692	0.810732
C	-2.336469	-1.162183	0.980727
C	-3.272870	-0.436491	0.231046
C	-3.719593	0.808028	0.664484
C	-3.227745	1.353621	1.852831
C	-2.278947	0.651291	2.591782
C	-1.833341	-0.599547	2.157750
H	-3.642944	-0.850922	-0.703660
H	-4.435237	1.363920	0.066221
H	-3.561875	2.333304	2.180290
H	-1.866140	1.079581	3.500000
H	-1.089583	-1.138284	2.735043
H	-1.752916	-2.542687	-0.547016

SM (Triplet)

C	0.146402	3.412686	-0.717008
C	3.560953	-0.000056	-0.337065
C	0.146311	-3.412713	-0.716929
C	-3.244165	0.000025	-1.264794
N	1.570675	1.417648	-0.570030
C	1.373457	2.778319	-0.573182
C	2.633954	3.466049	-0.415300
C	3.597779	2.507642	-0.317682
C	2.925845	1.232734	-0.413769
N	1.570638	-1.417711	-0.570007

C	2.925813	-1.232830	-0.413749
C	3.597712	-2.507753	-0.317626
C	2.633863	-3.466137	-0.415239
C	1.373384	-2.778376	-0.573127
N	-1.264576	-1.417517	-0.956840
C	-1.074127	-2.777974	-0.906482
C	-2.331367	-3.465698	-1.090858
C	-3.285636	-2.507212	-1.254540
C	-2.611938	-1.232397	-1.167648
N	-1.264537	1.417522	-0.956875
C	-2.611904	1.232433	-1.167683
C	-3.285567	2.507263	-1.254605
C	-2.331271	3.465728	-1.090963
C	-1.074051	2.777975	-0.906553
Fe	0.136945	-0.000013	-0.654411
H	0.143884	4.498473	-0.699627
H	-4.317493	0.000038	-1.429036
H	0.143764	-4.498500	-0.699521
H	4.639356	-0.000069	-0.209730
H	-2.449406	4.541977	-1.097036
H	-4.347600	-2.633441	-1.422664
H	2.749360	-4.542436	-0.390884
H	4.666222	2.634460	-0.197551
H	2.749479	4.542345	-0.390964
H	4.666150	-2.634597	-0.197485
H	-4.347528	2.633516	-1.422729
H	-2.449533	-4.541944	-1.096895
C	-1.119595	0.000079	3.608208
C	-1.359451	-0.000073	2.256531
N	0.265939	0.000050	3.718062
C	0.794279	0.000128	2.461828
N	-0.167528	-0.000001	1.563035
H	1.852559	0.000206	2.245332
H	-2.303854	-0.000167	1.732260
H	0.788773	0.000069	4.581766
C	-2.028124	0.000153	4.791299
H	-1.883040	-0.886057	5.422635
H	-1.883095	0.886473	5.422494
H	-3.068182	0.000094	4.454539

TS1(Triplet)

C	-6.243647	1.592021	1.724675
C	-5.079104	0.798266	1.235752
C	-3.776979	1.138294	0.960436
N	-3.074944	0.032590	0.527645
C	-3.922500	-0.974743	0.533858
N	-5.151937	-0.559990	0.955585

H	-5.973538	-1.139162	1.050130
H	-3.689421	-1.989744	0.248800
Fe	-0.752068	-0.151626	-0.084376
N	1.157534	-0.381276	-0.673540
C	2.074241	0.068846	-1.442471
C	2.015903	1.426460	-2.090797
H	1.800158	1.257356	-3.153834
H	1.168599	1.968117	-1.672347
C	3.307212	2.251128	-1.951762
H	4.147679	1.684735	-2.366554
H	3.184073	3.146616	-2.573705
C	3.636430	2.687669	-0.509176
C	4.047434	1.537134	0.384171
C	5.269600	0.882150	0.180802
C	5.606426	-0.246209	0.924679
C	4.725139	-0.735098	1.892546
C	3.515436	-0.080184	2.118120
C	3.186161	1.052452	1.371962
H	2.233131	1.542822	1.533859
H	2.813809	-0.459445	2.854661
H	4.975796	-1.630354	2.453903
H	6.545801	-0.757602	0.736487
H	5.949736	1.243460	-0.587437
H	2.764186	3.197945	-0.080373
H	4.445082	3.428854	-0.558094
O	3.147522	-0.666327	-1.731305
C	3.112679	-1.927224	-1.012102
O	4.045026	-2.678210	-1.142485
O	2.023628	-2.023126	-0.333852
N	-0.648611	1.815865	0.399820
C	-0.894380	2.890512	-0.425311
C	-1.287357	2.812378	-1.755552
C	-1.489336	1.634958	-2.464144
N	-1.341876	0.366810	-1.957235
C	-1.642087	-0.497910	-2.979402
C	-1.670220	-1.884189	-2.883244
C	-1.426591	-2.620059	-1.731492
N	-1.115150	-2.098424	-0.500298
C	-0.914522	-3.169566	0.335047
C	-0.529225	-3.091457	1.665027
C	-0.270676	-1.915591	2.355657
N	-0.363416	-0.648692	1.836172
C	-0.059369	0.213294	2.859236
C	-0.042792	1.598866	2.771700
C	-0.323254	2.337835	1.629211
C	-0.336546	3.779670	1.570816

C	-0.691887	4.122570	0.298418
H	-0.814759	5.112014	-0.123072
H	-0.107760	4.431388	2.404319
H	0.212227	2.151266	3.670558
C	0.242655	-0.532308	4.059719
C	0.114092	-1.852813	3.746221
H	0.260478	-2.714815	4.384072
H	0.516132	-0.087755	5.008088
H	-0.402532	-4.024898	2.203796
C	-1.141142	-4.403669	-0.380731
C	-1.456521	-4.063521	-1.661693
H	-1.678327	-4.715624	-2.496750
H	-1.047686	-5.391607	0.051139
H	-1.911247	-2.438962	-3.784675
C	-1.966372	0.246006	-4.173958
C	-1.876354	1.568519	-3.853350
H	-2.054859	2.428996	-4.485402
H	-2.235496	-0.199809	-5.123001
H	-1.441773	3.747135	-2.285353
H	-3.298050	2.102383	1.045842
H	-5.941448	2.631896	1.874997
H	-6.626517	1.215500	2.682066
H	-7.075613	1.587750	1.008557

IM1(Triplet)

C	1.266603	-2.494464	-1.763400
C	1.997427	-2.341572	-0.592943
N	1.908338	-1.278982	0.271283
C	2.841856	-1.495470	1.252176
C	3.042486	-0.695888	2.365922
C	2.257836	0.393668	2.710345
N	1.233821	0.906151	1.957668
C	0.682489	1.926901	2.690460
C	-0.347610	2.757238	2.270932
C	-0.945849	2.716412	1.017736
N	-0.645903	1.816581	0.026474
C	-1.408187	2.166030	-1.059653
C	-1.484880	1.458533	-2.251118
C	-0.851885	0.250267	-2.502753
N	0.020912	-0.386035	-1.654456
C	0.362184	-1.567249	-2.265016
C	-0.318558	-1.682878	-3.533846
C	-1.062293	-0.551010	-3.685664
H	-1.712780	-0.275974	-4.505823
H	-0.226852	-2.525491	-4.207194
Fe	0.569069	0.204751	0.205583
N	-0.612843	-0.772882	1.015953

C	-0.755952	-1.738394	1.948108
O	0.167660	-2.139572	2.668691
C	-2.634260	-2.652003	-0.491427
H	-1.702371	-2.138885	-0.739727
N	2.065618	1.364902	-0.702174
C	2.859171	0.969595	-1.677728
N	3.695603	1.981433	-2.030227
C	3.416938	3.084196	-1.231566
C	2.397010	2.672788	-0.412508
H	1.879744	3.218570	0.360692
C	4.149162	4.378294	-1.347308
H	3.754150	5.089264	-0.617079
H	5.222767	4.261746	-1.151819
H	4.036796	4.826163	-2.342915
H	4.400682	1.937500	-2.751317
H	2.852933	-0.008520	-2.132704
H	-2.155265	1.839062	-3.014816
C	-2.202661	3.331797	-0.749997
C	-1.927485	3.664293	0.543633
H	-2.334836	4.475862	1.132913
H	-2.889851	3.807384	-1.437880
H	-0.680719	3.527138	2.959770
C	1.385932	2.064976	3.945989
C	2.371181	1.125261	3.951061
H	3.103105	0.918279	4.720966
H	1.145623	2.795995	4.707295
H	3.818178	-0.994814	3.063359
C	3.559612	-2.720245	0.987309
C	3.026801	-3.252890	-0.146753
H	3.294044	-4.172178	-0.652015
H	4.349392	-3.115845	1.612651
H	1.444736	-3.389496	-2.351078
C	-2.163535	-2.328389	2.046287
H	-2.904260	-1.521390	2.065371
H	-2.206504	-2.858449	3.002915
C	-2.490600	-3.304120	0.900104
H	-1.704496	-4.068957	0.852056
H	-3.425846	-3.823567	1.147150
C	-3.789061	-1.681581	-0.587650
C	-5.057720	-2.113923	-0.995236
C	-6.133165	-1.227013	-1.061449
C	-5.955553	0.114886	-0.718148
C	-4.696710	0.558839	-0.309399
C	-3.625164	-0.332130	-0.244803
H	-5.200757	-3.157382	-1.268965
H	-7.108375	-1.582676	-1.384429

H	-6.791372	0.807715	-0.771547
H	-4.538621	1.600774	-0.044215
H	-2.648038	0.015428	0.071449
H	-2.768423	-3.450615	-1.231853

TS2(Triplet)

C	1.981766	-2.666057	-1.845742
C	2.557868	-2.404232	-0.609121
N	2.204883	-1.382604	0.235911
C	3.053830	-1.456912	1.309970
C	3.002587	-0.646009	2.433113
C	2.022063	0.301437	2.678846
N	1.017924	0.650479	1.812768
C	0.241640	1.570195	2.468843
C	-0.855920	2.232079	1.932617
C	-1.316796	2.093518	0.631094
N	-0.790405	1.247172	-0.312452
C	-1.517687	1.448760	-1.459266
C	-1.369617	0.737609	-2.640259
C	-0.504234	-0.333452	-2.820561
N	0.387388	-0.800676	-1.888081
C	0.981028	-1.908656	-2.440928
C	0.451015	-2.144840	-3.763534
C	-0.462927	-1.161473	-4.002947
H	-1.069245	-1.004338	-4.886000
H	0.752381	-2.958054	-4.411634
Fe	0.673133	-0.114122	-0.004115
N	-0.517101	-1.314494	0.647012
C	-0.606345	-2.181844	1.677780
O	0.276952	-2.353732	2.525737
C	-2.756639	-1.847531	-0.382392
H	-1.607493	-1.396323	-0.089590
N	2.029687	1.261601	-0.762470
C	3.020075	0.989908	-1.589021
N	3.698199	2.130519	-1.884761
C	3.104455	3.187250	-1.205368
C	2.066047	2.618466	-0.513495
H	1.346568	3.082271	0.142576
C	3.595160	4.592535	-1.297973
H	2.969402	5.240459	-0.678802
H	4.629295	4.690759	-0.943868
H	3.555529	4.974611	-2.326046
H	4.499911	2.196226	-2.494515
H	3.262472	0.012700	-1.976293
H	-2.027329	0.994938	-3.464479
C	-2.520124	2.465455	-1.237995
C	-2.402697	2.857414	0.059859

H	-2.998362	3.579700	0.601987
H	-3.236236	2.794260	-1.979048
H	-1.372849	2.940711	2.572216
C	0.773753	1.811308	3.791540
C	1.885665	1.035184	3.915479
H	2.552014	0.939930	4.763022
H	0.341657	2.493034	4.512997
H	3.736990	-0.821847	3.212491
C	3.985934	-2.544603	1.129307
C	3.670664	-3.141004	-0.054037
H	4.135611	-3.998660	-0.523353
H	4.758492	-2.815588	1.837263
H	2.365673	-3.513732	-2.404950
C	-1.941367	-2.947348	1.787413
H	-2.561643	-2.409200	2.514850
H	-1.710654	-3.915522	2.242014
C	-2.694846	-3.127517	0.460231
H	-2.169126	-3.884845	-0.133596
H	-3.704603	-3.516551	0.650725
C	-3.743578	-0.788767	-0.061692
C	-4.642886	-0.348746	-1.049020
C	-5.594342	0.632401	-0.777315
C	-5.660318	1.211420	0.491054
C	-4.753844	0.809490	1.474217
C	-3.804333	-0.172320	1.201492
H	-4.594782	-0.796454	-2.038625
H	-6.285261	0.944398	-1.556402
H	-6.400663	1.976856	0.707008
H	-4.776870	1.272057	2.457499
H	-3.075806	-0.433884	1.959715
H	-2.716475	-2.053551	-1.454714

IM2(Triplet)

C	1.026329	-2.370161	-1.909297
C	1.804158	-2.318891	-0.759584
N	1.817007	-1.289417	0.147071
C	2.806517	-1.580433	1.050136
C	3.125262	-0.820944	2.165030
C	2.398838	0.275758	2.602509
N	1.333013	0.833926	1.948018
C	0.854286	1.828171	2.760197
C	-0.193378	2.687433	2.455877
C	-0.877999	2.719980	1.246878
N	-0.656457	1.875379	0.187879
C	-1.467529	2.309480	-0.831482
C	-1.578762	1.708980	-2.077928
C	-0.963239	0.519115	-2.441996

N	-0.137472	-0.225539	-1.635759	H	2.979892	-0.056913	-1.942625
C	0.166507	-1.364634	-2.337967	H	-2.244447	2.170648	-2.800107
C	-0.479507	-1.335288	-3.630097	C	-2.220662	3.465299	-0.404836
C	-1.165707	-0.157728	-3.700659	C	-1.865830	3.711659	0.888195
H	-1.776400	0.219201	-4.511195	H	-2.221754	4.492834	1.547795
H	-0.402304	-2.116504	-4.375718	H	-2.933631	3.997219	-1.021682
Fe	0.552338	0.261795	0.201326	H	-0.464170	3.427553	3.202470
N	-0.788758	-0.708374	1.028970	C	1.647890	1.903305	3.967812
C	-0.749652	-1.602942	2.050168	C	2.616491	0.952828	3.860887
O	0.271851	-1.965348	2.637140	H	3.397092	0.701518	4.567246
C	-2.657693	-2.905413	0.042612	H	1.473431	2.602223	4.775887
H	-1.717016	-0.533002	0.657778	H	3.941637	-1.165512	2.791551
N	2.004810	1.402646	-0.729613	C	3.446712	-2.826860	0.698807
C	2.891730	0.961929	-1.600068	C	2.813723	-3.295214	-0.412201
N	3.684332	1.988164	-2.008525	H	3.004278	-4.206610	-0.964594
C	3.279746	3.146636	-1.357189	H	4.257564	-3.279527	1.254809
C	2.229989	2.754618	-0.566808	H	1.150668	-3.231245	-2.558739
H	1.624137	3.341265	0.105200	C	-2.103748	-2.216738	2.429769
C	3.936847	4.469220	-1.564891	H	-2.888204	-1.450998	2.427182
H	3.442748	5.224491	-0.948308	H	-2.009595	-2.615086	3.443792
H	4.997151	4.449926	-1.282390	C	-2.503744	-3.363810	1.459146
H	3.874637	4.799201	-2.609736	H	-1.733471	-4.140635	1.513818
H	4.441467	1.917186	-2.672264	H	-3.436950	-3.812658	1.828382

C	-3.715703	-2.089399	-0.425640
C	-3.665384	-1.557660	-1.745612
C	-4.652921	-0.710289	-2.219885
C	-5.742599	-0.364303	-1.408549
C	-5.825130	-0.887563	-0.111357
C	-4.837927	-1.731845	0.376822
H	-2.819249	-1.811354	-2.374633
H	-4.575131	-0.309281	-3.227300
H	-6.515955	0.301440	-1.780594
H	-6.669409	-0.628603	0.522443
H	-4.921421	-2.126228	1.384366
H	-1.834101	-3.088498	-0.642028

TS3(Triplet)

C	1.420507	-2.415050	-2.065897
C	2.165475	-2.316767	-0.896779
N	2.029646	-1.334738	0.052781
C	2.996554	-1.565813	0.994508
C	3.190301	-0.823125	2.152045
C	2.390856	0.227844	2.584817
N	1.316127	0.743654	1.908166
C	0.782046	1.726789	2.707731
C	-0.303791	2.530221	2.378353
C	-0.984109	2.503119	1.164554
N	-0.707080	1.645223	0.129028
C	-1.545560	1.991786	-0.901559
C	-1.597660	1.373575	-2.144682
C	-0.871210	0.252612	-2.534169
N	0.047545	-0.408159	-1.761478
C	0.451795	-1.505045	-2.480173
C	-0.234497	-1.539826	-3.751797
C	-1.043454	-0.439856	-3.791067
H	-1.710846	-0.124662	-4.583568
H	-0.097836	-2.302110	-4.508552
Fe	0.640671	0.113664	0.123072
N	-0.879239	-1.049085	0.988095
C	-0.685567	-1.743073	2.185963
O	0.384777	-2.183499	2.573190
C	-2.673375	-2.321701	0.458936
H	-1.607725	-0.345300	1.100677
N	2.177840	1.590005	-0.897158
C	2.706659	1.432198	-2.091031
N	3.560480	2.459439	-2.367719
C	3.571221	3.321662	-1.277904
C	2.701507	2.754286	-0.378874
H	2.416781	3.099399	0.604159
C	4.398983	4.561733	-1.230743

H	4.241455	5.071141	-0.276323
H	5.471632	4.345376	-1.318792
H	4.134309	5.265364	-2.030762
H	4.094035	2.575341	-3.216895
H	2.500194	0.612822	-2.763478
H	-2.313102	1.768688	-2.858517
C	-2.388218	3.094446	-0.497632
C	-2.047270	3.405704	0.785647
H	-2.460161	4.176479	1.424050
H	-3.144621	3.551493	-1.122548
H	-0.619839	3.265999	3.111699
C	1.547620	1.833932	3.929218
C	2.550094	0.913829	3.846964
H	3.325456	0.697976	4.571001
H	1.336314	2.530723	4.730409
H	4.003640	-1.125917	2.804296
C	3.774632	-2.728949	0.627326
C	3.251689	-3.202863	-0.537447
H	3.564118	-4.062390	-1.116862
H	4.599997	-3.125088	1.205104
H	1.643174	-3.244533	-2.730510
C	-2.003260	-2.104452	2.875466
H	-2.550033	-1.188520	3.133418
H	-1.806955	-2.664056	3.793452
C	-2.796260	-2.929720	1.837748
H	-2.382760	-3.943741	1.815669
H	-3.849345	-3.016343	2.132865
C	-3.611437	-1.367583	-0.063451
C	-3.665826	-1.127815	-1.456142
C	-4.549146	-0.198712	-1.989601
C	-5.393724	0.536965	-1.152535
C	-5.348824	0.322394	0.229852
C	-4.479349	-0.617374	0.768722
H	-2.994969	-1.678171	-2.108604
H	-4.572858	-0.038169	-3.064193
H	-6.078836	1.269188	-1.570015
H	-5.999202	0.891869	0.888233
H	-4.460171	-0.772567	1.843248
H	-2.097282	-2.871962	-0.276081

2a(Triplet)

C	0.573289	-1.838299	-2.917309
C	1.229436	-2.091122	-1.719908
N	1.178430	-1.295631	-0.601277
C	1.990450	-1.899314	0.330451
C	2.267348	-1.397521	1.595847
C	1.743016	-0.225636	2.123142

N	0.845663	0.600887	1.480157	C	3.878006	2.700202	-1.394626
C	0.561325	1.614231	2.371143	C	3.075007	1.957147	-0.565313
C	-0.366655	2.626393	2.161408	H	3.269045	1.612908	0.439732
C	-1.129374	2.796291	1.013172	C	5.243300	3.275701	-1.221506
N	-1.048875	2.021684	-0.119226	H	5.623544	3.024533	-0.227804
C	-1.943200	2.563887	-1.011897	H	5.953677	2.880538	-1.959178
C	-2.156486	2.110166	-2.306063	H	5.243822	4.369736	-1.310950
C	-1.530562	1.012955	-2.880200	H	3.428793	3.350403	-3.385543
N	-0.603650	0.211526	-2.255077	H	1.166219	2.163920	-3.139544
C	-0.282523	-0.772519	-3.158665	H	-2.883008	2.644915	-2.910432
C	-1.008570	-0.573551	-4.392531	C	-2.619067	3.695452	-0.420196
C	-1.783922	0.533880	-4.220277	C	-2.114475	3.838825	0.837174
H	-2.476411	0.988551	-4.917299	H	-2.372742	4.574736	1.587894
H	-0.934206	-1.215242	-5.261535	H	-3.375964	4.290340	-0.915321
Fe	0.165612	0.440349	-0.411628	H	-0.526556	3.328279	2.973714
N	-1.460386	-0.961254	2.934028	C	1.306478	1.425840	3.593969
C	-2.441988	-1.027143	3.885199	C	2.038064	0.286149	3.440321
O	-2.726255	-0.151840	4.687131	H	2.705476	-0.185958	4.149674
C	-1.437519	-2.066164	1.991749	H	1.246468	2.076260	4.456880
H	-0.983607	-0.089888	2.743606	H	2.945750	-1.967664	2.223112
N	1.882984	1.664019	-1.194839	C	2.545925	-3.120551	-0.205253
C	1.942739	2.212039	-2.390695	C	2.075031	-3.237713	-1.479083
N	3.134383	2.852002	-2.558321	H	2.274894	-4.019168	-2.201425

H	3.210432	-3.784630	0.332646
H	0.718356	-2.551457	-3.723379
C	-3.115264	-2.395350	3.723470
H	-4.090484	-2.233890	3.248030
H	-3.293445	-2.856790	4.697520
C	-2.157032	-3.176402	2.814003
H	-1.414664	-3.707827	3.419321
H	-2.653655	-3.900689	2.164454
C	-2.143482	-1.772798	0.676357
C	-1.939136	-2.634887	-0.408728
C	-2.624374	-2.445724	-1.605715
C	-3.520613	-1.382917	-1.738766
C	-3.715897	-0.509598	-0.670645
C	-3.030685	-0.702151	0.530537
H	-1.224915	-3.449511	-0.314940
H	-2.443944	-3.113589	-2.442801
H	-4.039333	-1.223071	-2.679062
H	-4.388365	0.336839	-0.772842
H	-3.176248	-0.009577	1.352863
H	-0.404509	-2.354696	1.776114

SM (Quintet)

C	1.024168	-0.000159	3.695449
C	1.304916	-0.000199	2.352646
N	-0.364258	-0.000272	3.764377
C	-0.859077	-0.000372	2.497684
N	0.130958	-0.000338	1.626380
H	-1.909264	-0.000457	2.247022
H	2.261894	-0.000123	1.852613
N	-0.138010	2.055987	-0.815336
N	1.941007	0.000735	-0.983606
N	-2.196587	-0.000587	-0.486607
C	-2.555269	2.425629	-0.505696
C	2.283349	2.426409	-1.089274
C	2.284944	-2.424711	-1.089605
C	-2.553665	-2.427075	-0.506091
C	-1.237903	2.866021	-0.687281
C	2.737974	1.106010	-1.121991
C	0.962204	-2.865535	-0.952505
C	-3.003787	-1.106398	-0.430887
C	-0.820535	4.248947	-0.761006
C	4.112489	0.683479	-1.329803
C	0.539698	-4.248560	-0.925275
C	-4.387573	-0.683719	-0.303722
C	0.536942	4.249099	-0.924686
C	4.112929	-0.680554	-1.329894
C	-0.817783	-4.249283	-0.761615

C	-4.388036	0.681022	-0.303612
C	0.960316	2.866342	-0.952104
C	2.738697	-1.104012	-1.122140
C	-1.236017	-2.866623	-0.687712
C	-3.004542	1.104656	-0.430697
N	-0.136636	-2.055893	-0.815648
Fe	-0.100315	0.000011	-0.525648
H	-3.314312	3.200044	-0.434703
H	3.037126	3.201129	-1.200643
H	3.039236	-3.198917	-1.201064
H	-3.312222	-3.201975	-0.435214
H	-0.912105	-0.000262	4.612556
H	-5.238569	-1.350800	-0.242863
H	-5.239486	1.347514	-0.242640
H	-1.484127	5.102401	-0.697991
H	1.196346	5.102671	-1.020923
H	4.953260	1.350930	-1.472545
H	4.954139	-1.347440	-1.472716
H	1.199636	-5.101706	-1.021606
H	-1.480841	-5.103160	-0.698723
C	1.897268	-0.000018	4.904716
H	1.732522	0.886433	5.530486
H	1.732705	-0.886449	5.530563
H	2.946695	0.000077	4.598913

TS1(Quintet)

C	5.947754	-1.673203	-1.643691
C	4.807791	-0.878506	-1.102473
C	3.468634	-1.149055	-0.991869
N	2.823776	-0.070951	-0.418042
C	3.739147	0.848852	-0.176659
N	4.956343	0.397995	-0.573645
H	5.823669	0.909517	-0.499204
H	3.555210	1.811901	0.271486
Fe	0.783927	0.134048	0.020545
N	-0.986500	0.465108	0.385875
C	-1.889763	0.259354	1.285075
C	-1.822552	-0.897579	2.264538
H	-1.415062	-0.481113	3.194690
H	-1.102346	-1.626421	1.898437
C	-3.176849	-1.568188	2.540897
H	-3.913423	-0.802115	2.801116
H	-3.052455	-2.212334	3.420809
C	-3.703047	-2.427603	1.372471
C	-4.006217	-1.621592	0.129034
C	-5.101118	-0.747965	0.099430
C	-5.315216	0.091817	-0.990258

C	-4.439664	0.060651	-2.078848
C	-3.361259	-0.821815	-2.072991
C	-3.150842	-1.658677	-0.975744
H	-2.291770	-2.322145	-0.963036
H	-2.667001	-0.842639	-2.906882
H	-4.591194	0.732742	-2.918510
H	-6.145599	0.790845	-0.978433
H	-5.767135	-0.695701	0.957347
H	-2.960431	-3.201748	1.138073
H	-4.607435	-2.948320	1.713977
O	-2.920398	1.041118	1.436264
C	-3.034143	2.234667	0.405312
O	-4.057584	2.848629	0.561262
O	-2.030976	2.266898	-0.327400
N	0.761343	-1.902764	0.271265
C	1.101353	-2.574303	1.422039
C	1.490209	-1.991364	2.631885
C	1.585987	-0.627864	2.922748
N	1.368680	0.378793	2.023007
C	1.505109	1.569724	2.679022
C	1.386432	2.829394	2.080622
C	1.144228	3.100517	0.731128
N	1.024361	2.162575	-0.258497
C	0.751353	2.818773	-1.427284
C	0.458362	2.224555	-2.656557
C	0.291233	0.864069	-2.929774
N	0.429173	-0.145388	-2.020919
C	0.139394	-1.321627	-2.647990
C	0.146314	-2.571718	-2.024783
C	0.443626	-2.837020	-0.683423
C	0.549182	-4.156907	-0.100347
C	0.960710	-3.995171	1.192389
H	1.154500	-4.761577	1.932013
H	0.346154	-5.081316	-0.625951
H	-0.093288	-3.430650	-2.644622
C	-0.176733	-1.054064	-4.038348
C	-0.085198	0.297947	-4.210973
H	-0.261912	0.868381	-5.113876
H	-0.445786	-1.804217	-4.771218
H	0.277989	2.905331	-3.483210
C	0.757117	4.247515	-1.179067
C	0.995029	4.421878	0.151005
H	1.047215	5.350130	0.705390
H	0.572129	5.004605	-1.929992
H	1.486566	3.689787	2.735808
C	1.822538	1.309256	4.068714

C	1.882148	-0.048467	4.217110
H	2.093140	-0.611795	5.117335
H	1.980734	2.069512	4.823185
H	1.703287	-2.677632	3.446361
H	2.925805	-2.032761	-1.285567
H	5.584266	-2.641234	-1.997794
H	6.433487	-1.169680	-2.489039
H	6.713710	-1.863038	-0.881221

IM1(Quintet)

C	6.087703	-1.661653	-0.153357
C	4.775797	-1.023612	-0.464238
C	3.579100	-0.995313	0.207389
N	2.653449	-0.259624	-0.503196
C	3.259816	0.161046	-1.593404
N	4.549609	-0.277550	-1.614831
H	5.225859	-0.092192	-2.341112
H	2.810466	0.765757	-2.366642
Fe	0.420446	0.149651	0.062690
N	-1.345948	0.625918	0.441701
C	-2.233143	1.580203	0.159727
C	-3.007548	2.093492	1.382550
H	-2.635728	3.111861	1.553362
H	-2.760402	1.501258	2.271633
C	-4.520786	2.122539	1.125086
H	-4.674727	2.435846	0.086686
H	-4.989428	2.883283	1.762024
C	-5.213119	0.770848	1.389895
C	-4.567535	-0.394689	0.673509
C	-4.590935	-0.477350	-0.724575
C	-3.955771	-1.525079	-1.386943
C	-3.293359	-2.514818	-0.658592
C	-3.252987	-2.440692	0.732543
C	-3.888332	-1.386615	1.389333
H	-3.848684	-1.325044	2.474486
H	-2.713655	-3.191737	1.302741
H	-2.799209	-3.330929	-1.174281
H	-3.967568	-1.564886	-2.472670
H	-5.087520	0.300477	-1.298224
H	-5.203584	0.573571	2.469555
H	-6.268665	0.855626	1.097649
O	-2.421256	2.051429	-0.972415
N	1.247692	0.632621	1.925211
C	1.623843	1.887585	2.319073
C	1.646126	3.022803	1.502287
C	1.284864	3.111363	0.155123
N	0.867795	2.069080	-0.628670

C	0.570019	2.565497	-1.867278
C	0.119873	1.805257	-2.950002
C	-0.111531	0.428974	-2.965568
N	0.061791	-0.415133	-1.900869
C	-0.193294	-1.690509	-2.327272
C	-0.122344	-2.840168	-1.538357
C	0.154310	-2.914078	-0.170978
N	0.448410	-1.850462	0.638022
C	0.642590	-2.328333	1.907391
C	1.033293	-1.559648	3.007901
C	1.326646	-0.191784	3.013378
C	1.784321	0.573385	4.154787
C	1.970915	1.856797	3.725124
H	2.308292	2.710236	4.299650
H	1.940268	0.173027	5.148641
H	1.147092	-2.085227	3.951599
C	0.443849	-3.762290	1.907165
C	0.151275	-4.124887	0.621938
H	-0.053004	-5.116717	0.238713
H	0.530803	-4.400932	2.777178
H	-0.340506	-3.780131	-2.037098
C	-0.553532	-1.654868	-3.729165
C	-0.510024	-0.347047	-4.120686
H	-0.720731	0.064436	-5.099597
H	-0.808946	-2.522223	-4.324723
H	-0.074096	2.341535	-3.873809
C	0.827579	3.990110	-1.880144
C	1.271056	4.327001	-0.633347
H	1.555788	5.305572	-0.267904
H	0.676850	4.639164	-2.733282
H	1.958924	3.948772	1.976489
H	3.319765	-1.451793	1.150500
H	6.020332	-2.191809	0.800339
H	6.383223	-2.390754	-0.918901
H	6.895263	-0.923170	-0.066955

TS2(Quintet)

C	0.973641	-2.515596	-2.339818
C	1.901085	-2.535508	-1.293777
N	1.968277	-1.612293	-0.290704
C	2.961371	-1.986326	0.567517
C	3.299429	-1.306938	1.742064
C	2.660854	-0.188533	2.281833
N	1.601390	0.477252	1.726796
C	1.266493	1.509983	2.557643
C	0.241864	2.437320	2.344166
C	-0.638367	2.498634	1.259041

N	-0.627006	1.643993	0.194290	H	5.887468	2.308599	-1.207958
C	-1.654230	1.993445	-0.636781	H	5.581996	2.514626	-2.937739
C	-1.996643	1.316781	-1.810151	H	5.250900	3.844018	-1.812030
C	-1.392950	0.163563	-2.325871	H	2.755768	3.268503	-3.253352
N	-0.306426	-0.478656	-1.790079	H	0.645156	2.060070	-2.453717
C	-0.046867	-1.582843	-2.560203	H	-2.860340	1.690915	-2.350699
C	-1.006692	-1.636296	-3.643771	C	-2.339443	3.147182	-0.086552
C	-1.835058	-0.558137	-3.500442	C	-1.712187	3.459418	1.085382
H	-2.674775	-0.273111	-4.121889	H	-1.954442	4.253514	1.780697
H	-1.035618	-2.402695	-4.408318	H	-3.202459	3.625213	-0.531367
Fe	0.615030	-0.057488	0.022502	H	0.111619	3.191561	3.115221
N	-0.559646	-1.139300	0.889125	C	2.163915	1.505253	3.697867
C	-0.553515	-1.954858	1.973252	C	3.024540	0.462161	3.524813
O	0.402625	-2.127139	2.730656	H	3.829515	0.144128	4.175030
C	-2.781037	-1.897342	-0.020967	H	2.126411	2.213196	4.516165
H	-1.640539	-1.374526	0.187658	H	4.119366	-1.719430	2.322575
N	1.962510	1.172723	-1.027480	C	3.583204	-3.197992	0.069371
C	1.635724	1.951880	-2.040768	C	2.925624	-3.540143	-1.077840
N	2.735966	2.610144	-2.488343	H	3.104446	-4.393936	-1.719448
C	3.827131	2.226071	-1.716560	H	4.401792	-3.719029	0.549640
C	3.317406	1.330468	-0.813030	H	1.038908	-3.329244	-3.057033
H	3.823094	0.788882	-0.029566	C	-1.905426	-2.644712	2.261488
C	5.204394	2.754470	-1.935526	H	-2.490962	-1.960567	2.888131

H	-1.681655	-3.521476	2.875427
C	-2.696383	-3.031075	1.004265
H	-2.190802	-3.877019	0.523621
H	-3.701429	-3.376063	1.283226
C	-3.763174	-0.799224	0.143216
C	-4.711357	-0.556898	-0.865619
C	-5.629988	0.485208	-0.756394
C	-5.611000	1.320054	0.362835
C	-4.659904	1.106159	1.363059
C	-3.745086	0.062215	1.254411
H	-4.718411	-1.196796	-1.744224
H	-6.358963	0.647699	-1.546188
H	-6.321322	2.137819	0.448487
H	-4.612707	1.771273	2.220371
H	-2.970006	-0.049234	2.003767
H	-2.743444	-2.259199	-1.050935

IM2(Quintet)

C	0.482319	0.286355	-3.157321
C	-0.318735	1.311552	-2.675745
N	-0.918557	1.353956	-1.439774
C	-1.698281	2.483112	-1.424804
C	-2.497203	2.908403	-0.375241
C	-2.567719	2.296590	0.865636
N	-1.896430	1.158405	1.228266
C	-2.186174	0.937779	2.551228
C	-1.706976	-0.116360	3.314952
C	-0.890946	-1.137249	2.846294
N	-0.411540	-1.257232	1.564648
C	0.281793	-2.442677	1.516939
C	0.909587	-2.973029	0.398725
C	0.980821	-2.359256	-0.844366
N	0.474449	-1.118147	-1.146863
C	0.805867	-0.868671	-2.456384
C	1.520672	-1.995081	-3.004604
C	1.623178	-2.922116	-2.005356
H	2.099976	-3.893511	-2.035433
H	1.893825	-2.054713	-4.019080
Fe	-0.565435	0.127424	0.102435
N	1.044606	1.107211	0.784988
C	1.269122	2.439417	0.866246
O	0.425841	3.306761	0.603370
C	3.663670	1.604936	-0.734802
H	1.854335	0.541899	1.025398
N	-2.493900	-1.151025	-0.640120
C	-2.504103	-2.077066	-1.575871
N	-3.756094	-2.601974	-1.712295

C	-4.593869	-1.968281	-0.803706
C	-3.781791	-1.072495	-0.152050
H	-4.034852	-0.376219	0.633489
C	-6.044374	-2.290545	-0.671973
H	-6.489930	-1.663558	0.104929
H	-6.594215	-2.105958	-1.603978
H	-6.210218	-3.338236	-0.389361
H	-4.028454	-3.326232	-2.360872
H	-1.651507	-2.390357	-2.159621
H	1.394822	-3.937379	0.509090
C	0.248933	-3.081448	2.810230
C	-0.471511	-2.269704	3.635295
H	-0.715069	-2.414793	4.679894
H	0.721280	-4.028010	3.039619
H	-2.014632	-0.161664	4.354722
C	-3.088727	1.957481	3.032725
C	-3.332232	2.794198	1.984433
H	-3.951996	3.681152	1.959840
H	-3.471935	2.013035	4.043522
H	-3.069679	3.818469	-0.520041
C	-1.581323	3.177681	-2.683566
C	-0.718869	2.458952	-3.454852
H	-0.382948	2.663648	-4.463261
H	-2.094456	4.099526	-2.924558
H	0.846549	0.373506	-4.176018
C	2.693768	2.872988	1.238304
H	3.133449	2.183891	1.968754
H	2.641562	3.870050	1.685492
C	3.594476	2.922949	-0.028243
H	3.185182	3.681166	-0.704297
H	4.596132	3.263983	0.269790
C	4.351007	0.467408	-0.247635
C	4.181106	-0.790246	-0.893043
C	4.794629	-1.936120	-0.415048
C	5.616105	-1.881611	0.719932
C	5.811336	-0.653702	1.365999
C	5.195724	0.499392	0.899463
H	3.536895	-0.842121	-1.763762
H	4.630015	-2.882196	-0.924342
H	6.096689	-2.780541	1.095118
H	6.449652	-0.601550	2.244382
H	5.359461	1.440058	1.415270
H	3.019241	1.459969	-1.597649

TS3(Quintet)

C	-0.373399	-0.750090	3.398205
C	-1.188468	-1.547966	2.619558

N	-1.436414	-1.379405	1.274764
C	-2.402398	-2.303819	0.930823
C	-2.908631	-2.517819	-0.332580
C	-2.426969	-1.909750	-1.493896
N	-1.468641	-0.925607	-1.533160
C	-1.203717	-0.685427	-2.865923
C	-0.317279	0.277411	-3.350986
C	0.367457	1.185332	-2.564165
N	0.327850	1.239046	-1.185573
C	1.037875	2.361311	-0.814567
C	1.243230	2.793590	0.480784
C	0.880882	2.085472	1.628608
N	0.261630	0.848341	1.632914
C	0.242889	0.424499	2.945649
C	0.862184	1.404384	3.779260
C	1.236290	2.451241	2.960478
H	1.740787	3.369077	3.234859
H	0.977902	1.317849	4.852059
Fe	-0.512256	-0.118125	0.039880
N	1.176463	-1.416535	-0.362034
C	1.084267	-2.794433	-0.588463
O	0.063660	-3.456152	-0.478903
C	2.917602	-1.495630	0.825933
H	1.759149	-0.970294	-1.068449
N	-2.345146	1.341014	0.239275
C	-2.599878	2.117287	1.272063
N	-3.737350	2.834448	1.051121
C	-4.234085	2.491605	-0.200492
C	-3.347576	1.560333	-0.681950
H	-3.359627	1.030674	-1.622711
C	-5.476862	3.085546	-0.772885
H	-5.663132	2.661223	-1.763007
H	-6.357175	2.877628	-0.150961
H	-5.398730	4.174521	-0.886872
H	-4.148983	3.501753	1.687162
H	-1.999886	2.187652	2.166876
H	1.788747	3.721143	0.619360
C	1.555462	3.017212	-1.991087
C	1.158765	2.282454	-3.068001
H	1.357959	2.463391	-4.116603
H	2.156571	3.917171	-1.974904
H	-0.205459	0.357270	-4.427468
C	-2.026184	-1.530044	-3.680672
C	-2.799493	-2.277110	-2.826349
H	-3.539575	-3.027261	-3.073694
H	-2.016128	-1.541634	-4.762998

H	-3.666285	-3.285707	-0.448344
C	-2.771778	-3.070395	2.096706
C	-2.005717	-2.626047	3.130104
H	-1.996797	-2.966148	4.157860
H	-3.511272	-3.860968	2.098377
H	-0.289416	-0.987038	4.453664
C	2.465360	-3.424520	-0.732040
H	2.964315	-3.046634	-1.633038
H	2.391362	-4.512060	-0.803010
C	3.216142	-2.957024	0.538902
H	2.871846	-3.563077	1.383708
H	4.296384	-3.115997	0.442002
C	3.763718	-0.444984	0.317532
C	3.773282	0.819865	0.946922
C	4.536552	1.865986	0.445639
C	5.307939	1.690825	-0.708244
C	5.317057	0.443752	-1.344463
C	4.564592	-0.610141	-0.842158
H	3.177527	0.962313	1.841090
H	4.526844	2.825729	0.955151
H	5.897521	2.511962	-1.105433
H	5.918790	0.295531	-2.237327
H	4.591687	-1.570743	-1.347008
H	2.401048	-1.273417	1.753388

2a(Quintet)

C	-1.530430	2.537471	1.172459
C	-0.955258	1.667548	2.105121
N	-0.104144	0.627555	1.813194
C	0.276417	0.057594	3.005771
C	1.159254	-1.022343	3.143851
C	1.790006	-1.733987	2.122752
N	1.676452	-1.449342	0.788292
C	2.319072	-2.445537	0.103962
C	2.329035	-2.579399	-1.284352
C	1.678916	-1.765728	-2.222251
N	0.928249	-0.654321	-1.931432
C	0.494197	-0.123696	-3.122334
C	-0.290814	1.027773	-3.261306
C	-0.814121	1.823188	-2.238215
N	-0.616762	1.601618	-0.900203
C	-1.381226	2.508784	-0.215064
C	-2.051285	3.382564	-1.160386
C	-1.701108	2.960237	-2.410399
H	-2.028709	3.355055	-3.364236
H	-2.726669	4.184875	-0.891696
Fe	0.715568	0.208399	-0.054421

N	-1.542192	-2.039775	0.604080
C	-1.108791	-3.318478	0.358460
O	-0.378854	-3.982194	1.075278
C	-2.275326	-1.435363	-0.502520
H	-1.075314	-1.468359	1.298814
H	-1.583721	-0.910183	-1.174498
N	2.398013	1.546596	-0.031079
C	2.386667	2.796331	-0.454041
N	3.615005	3.354189	-0.287395
C	4.459410	2.403762	0.275272
C	3.675791	1.287844	0.424103
H	3.931292	0.318069	0.824263
C	5.889942	2.677346	0.596658
H	6.346009	1.782846	1.028610
H	5.998714	3.491561	1.324420
H	6.467182	2.947591	-0.296734
H	3.871852	4.299897	-0.530894
H	1.530183	3.304530	-0.871037
H	-0.544648	1.315736	-4.277920
C	0.974858	-0.944520	-4.210277
C	1.704355	-1.959797	-3.654548
H	2.216701	-2.767396	-4.162318
H	0.775356	-0.764620	-5.259352
H	2.876140	-3.428237	-1.684869
C	2.925278	-3.368200	1.049499
C	2.599632	-2.928475	2.295385
H	2.838492	-3.383362	3.248155
H	3.485028	-4.254392	0.779056
H	1.337017	-1.368825	4.157886
C	-0.383686	0.744824	4.091265
C	-1.143664	1.737408	3.535022
H	-1.776859	2.454690	4.041963
H	-0.276129	0.495781	5.139506
H	-2.192580	3.299542	1.572689
C	-1.707786	-3.731140	-0.989728
H	-0.907566	-3.648382	-1.737280
H	-2.046600	-4.769540	-0.969829
C	-2.810009	-2.692513	-1.233890
H	-3.746177	-3.008373	-0.760519
H	-3.009505	-2.488860	-2.289126
C	-3.336965	-0.455996	-0.064080
C	-3.831294	-0.434254	1.243326
C	-4.804808	0.493677	1.615700
C	-5.302267	1.403817	0.682075
C	-4.817217	1.381595	-0.627282
C	-3.838487	0.460628	-0.993791

H	-3.439983	-1.138293	1.970558
H	-5.171084	0.506859	2.638838
H	-6.057945	2.128532	0.973233
H	-5.184631	2.095564	-1.359110
H	-3.431843	0.473444	-2.001332

CRYSTAL STRUCTURE REPORT

A crystal (0.513 x 0.069 x 0.050 mm^3) was placed onto a thin glass optical fiber or a nylon loop and mounted on a Rigaku XtaLAB Synergy-S Dualflex diffractometer equipped with a HyPix-6000HE HPC area detector for data collection at 99.97(16) K. A preliminary set of cell constants and an orientation matrix were calculated from a small sampling of reflections.[39] A short pre-experiment was run, from which an optimal data collection strategy was determined. The full data collection was carried out using a PhotonJet (Cu) X-ray source with frame times of 0.42 and 1.68 seconds and a detector distance of 34.0 mm. Series of frames were collected in 0.50º steps in *w* at different 2*q*, *k*, and *f* settings. After the intensity data were corrected for absorption, the final cell constants were calculated from the xyz centroids of 10147 strong reflections from the actual data collection after integration.[40] See Table 1 for additional crystal and refinement information.

Structure solution and refinement

The structure was solved using SHELXT[40] and refined using SHELXL.[41] The space group $P2_1$ was determined based on systematic absences and intensity statistics. Most or all non-hydrogen atoms were assigned from the solution. Full-matrix least squares / difference Fourier cycles were performed which located any remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. The N-H and O-H hydrogen atoms were found from the difference Fourier map and refined freely. All other hydrogen atoms were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters. The final full matrix least squares refinement converged to $R1 = 0.0418$ (F^2, $I > 2s(I)$) and $wR2 = 0.1225$ (F^2, all data).

Structure description

The structure is the one suggested. The asymmetric unit contains one lactam molecule and one hydrate molecule in general positions. Hydrogen bonding links molecules along [010] (see figure and Table 7).

Structure manipulation and figure generation were performed using Olex2.[4] Unless noted otherwise all structural diagrams containing anisotropic displacement ellipsoids are drawn at the 50 % probability level.

Data collection, structure solution, and structure refinement were conducted at the X-ray

Crystallographic Facility, B04 Hutchison Hall, Department of Chemistry, University of Rochester. The instrument was purchased with funding from NSF MRI program grant CHE-1725028. All publications arising from this report MUST either 1) include William W. Brennessel as a coauthor or 2) acknowledge William W. Brennessel and the X-ray Crystallographic Facility of the Department of Chemistry at the University of Rochester.

Some equations of interest:

$$R_{int} = S\,|F_o^2 - \langle F_o^2 \rangle| \,/\, S|F_o^2|$$

$$R1 = S||F_o| - |F_c|| \,/\, S|F_o|$$

$$wR2 = [S[w(F_o^2 - F_c^2)^2] \,/\, S\,[w(F_o^2)^2]]^{1/2}$$

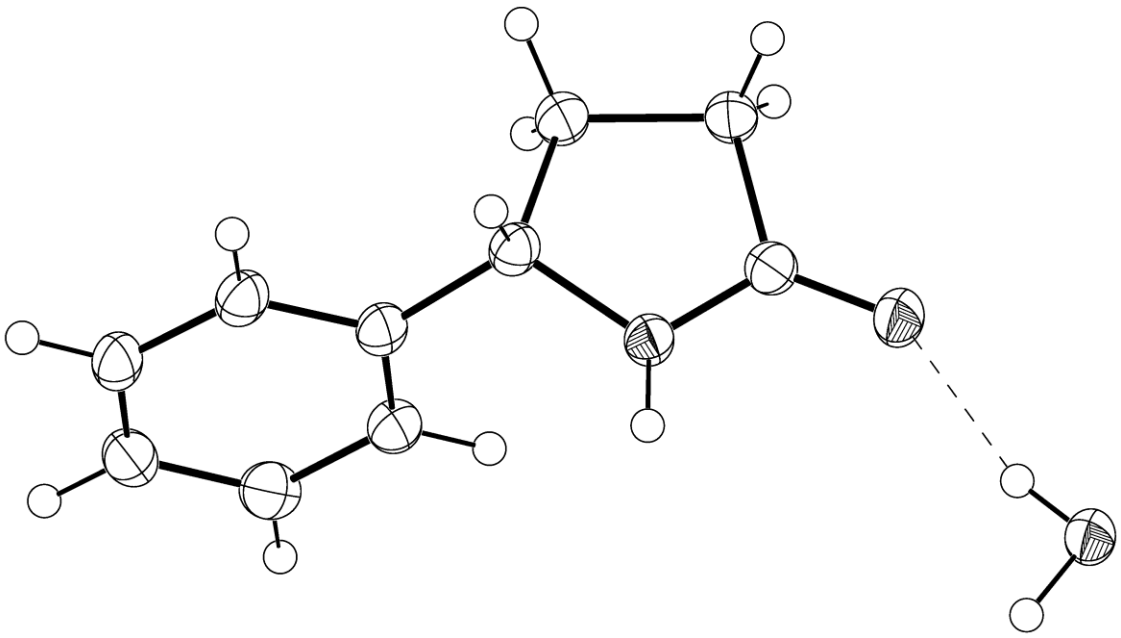
where $w = 1 / [s^2 (F_o^2) + (aP)^2 + bP]$ and

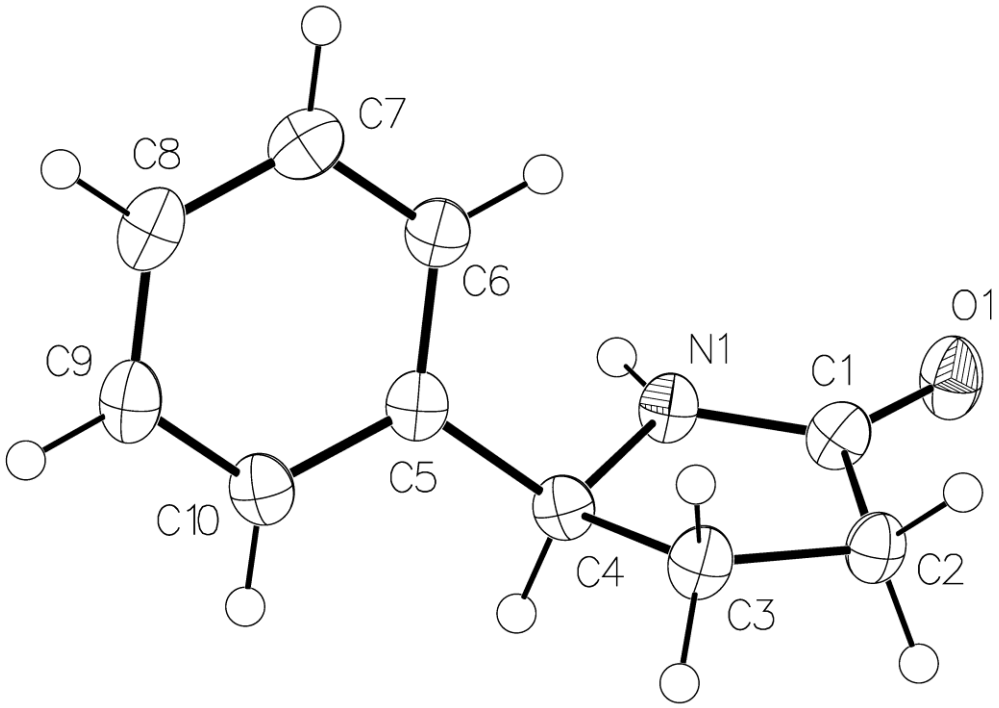
$$P = 1/3 \max (0, F_o^2) + 2/3\, F_c^2$$

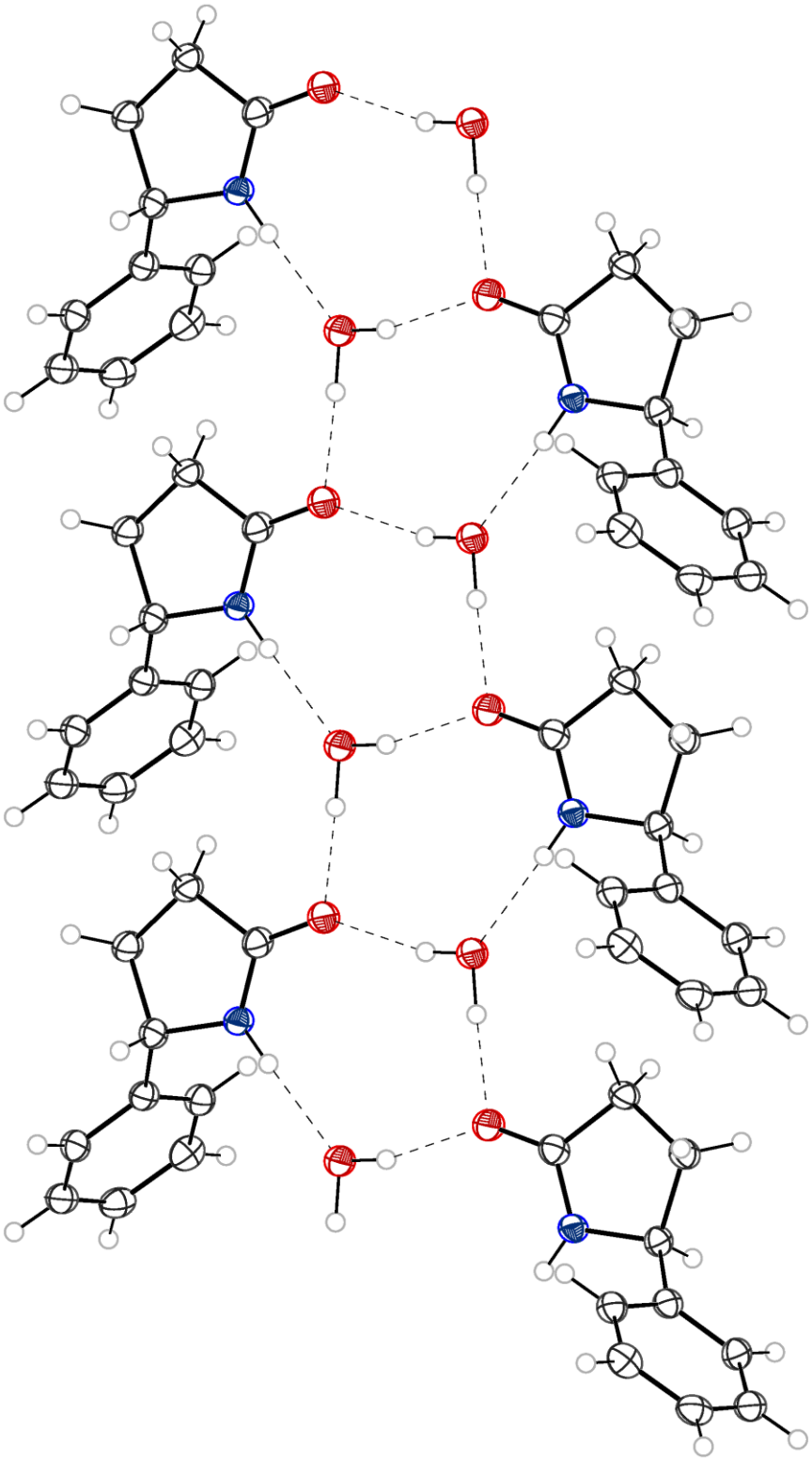
$$GOF = S = [S[w(F_o^2 - F_c^2)^2] / (m-n)]^{1/2}$$

where m = number of reflections and n = number of parameters

Structure of 2a




C7
C8
C6
O1
N1
C9
C1
C5
C10
C4
C2
C3



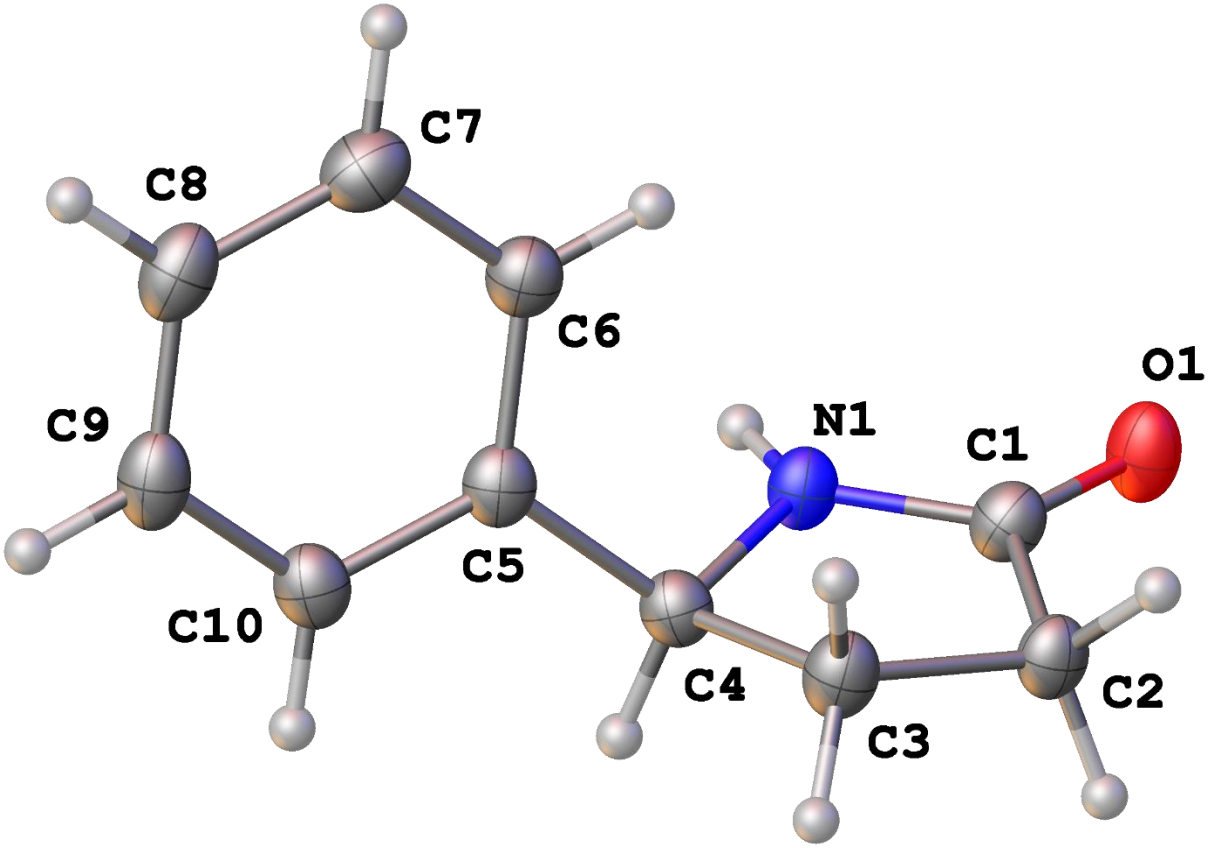
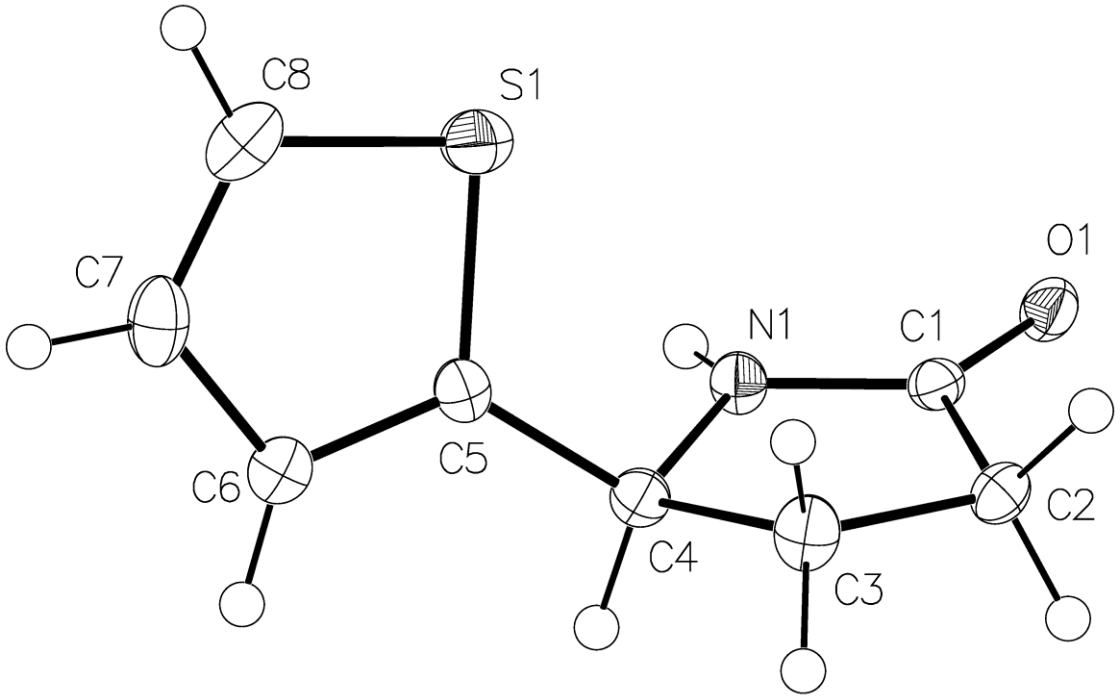
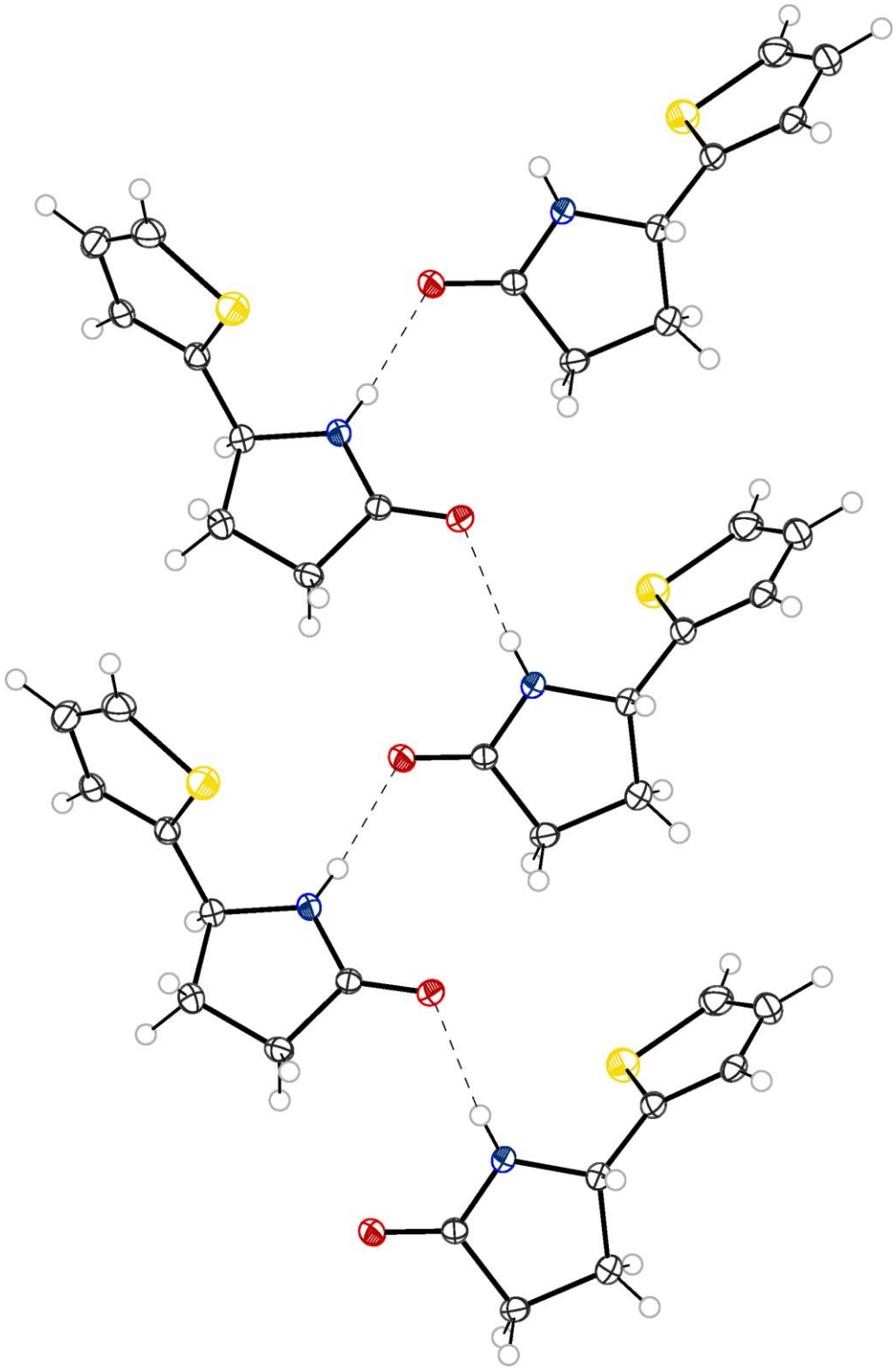

C7
C8
C6
O1
C9
N1
C1
C5
C10
C4
C2
C3

Table S3. Crystal data and structure refinement for (*S*)-5-phenylpyrrolidin-2-one (**1b**). Cambridge Crystallographic Data Centre (CCDC) entry: 1893087.

Identification code	fasdv12	
Empirical formula	C10 H13 N O2	
Formula weight	179.21	
Temperature	99.97(16) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 5.70230(10) Å	α = 90°
	b = 6.7587(2) Å	β = 98.893(2)°
	c = 12.4558(3) Å	γ = 90°
Volume	474.28(2) $Å^3$	
Z	2	
Density (calculated)	1.255 Mg/m^3	
Absorption coefficient	0.712 mm^{-1}	
F(000)	192	
Crystal color, morphology	colourless, needle	
Crystal size	0.513 x 0.069 x 0.050 mm^3	
Theta range for data collection	3.592 to 80.439°	
Index ranges	$-7 \le h \le 7$, $-8 \le k \le 7$, $-15 \le l \le 15$	
Reflections collected	14442	
Independent reflections	1996 [R(int) = 0.0921]	
Observed reflections	1922	
Completeness to theta = 74.504°	99.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	1.00000 and 0.78400	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1996 / 1 / 130	
Goodness-of-fit on F^2	1.159	
Final R indices [I>2sigma(I)]	$R1$ = 0.0418, $wR2$ = 0.1189	
R indices (all data)	$R1$ = 0.0433, $wR2$ = 0.1225	
Absolute structure parameter	0.1(2)	
Largest diff. peak and hole	0.192 and -0.192 $e.Å^{-3}$	

Structure of 2m





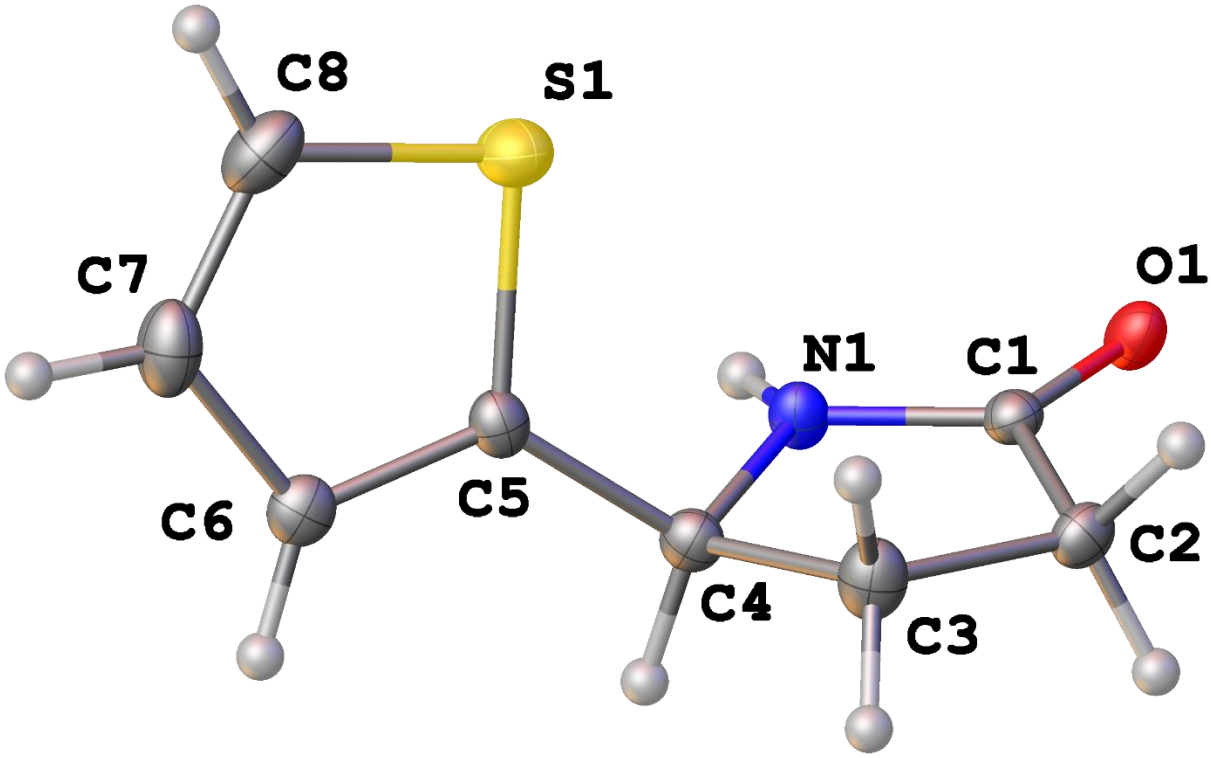
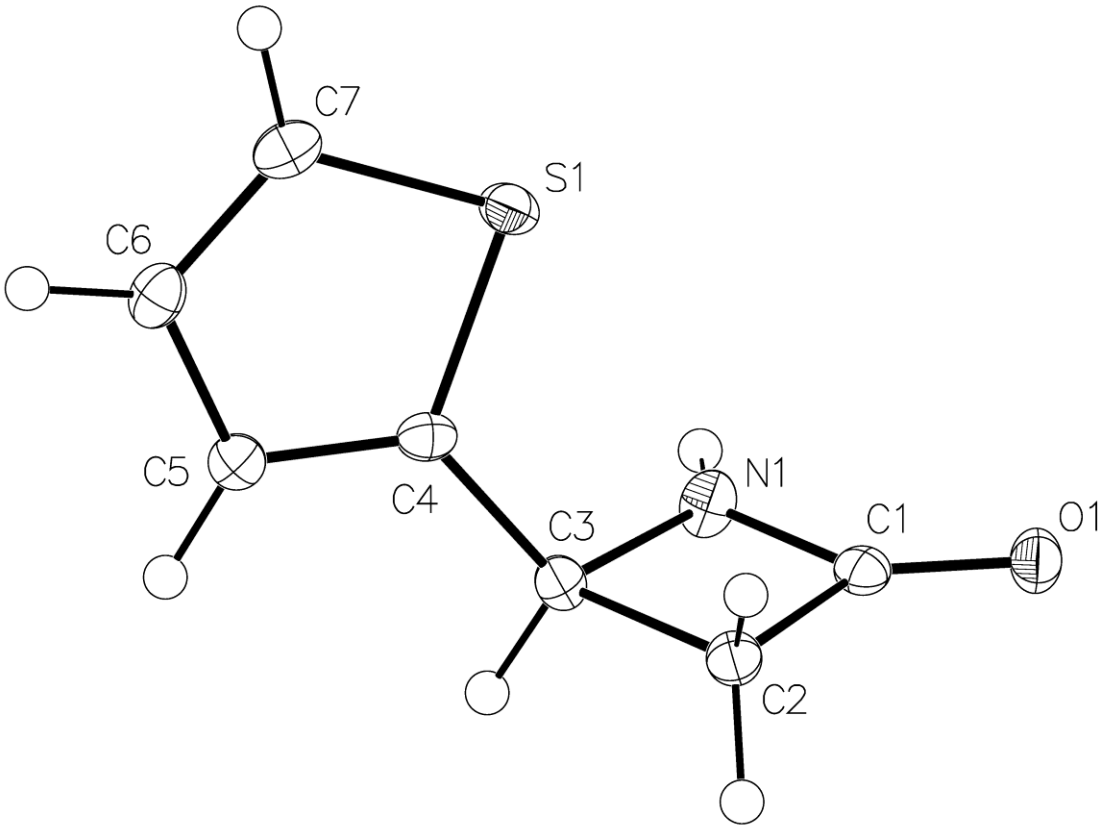
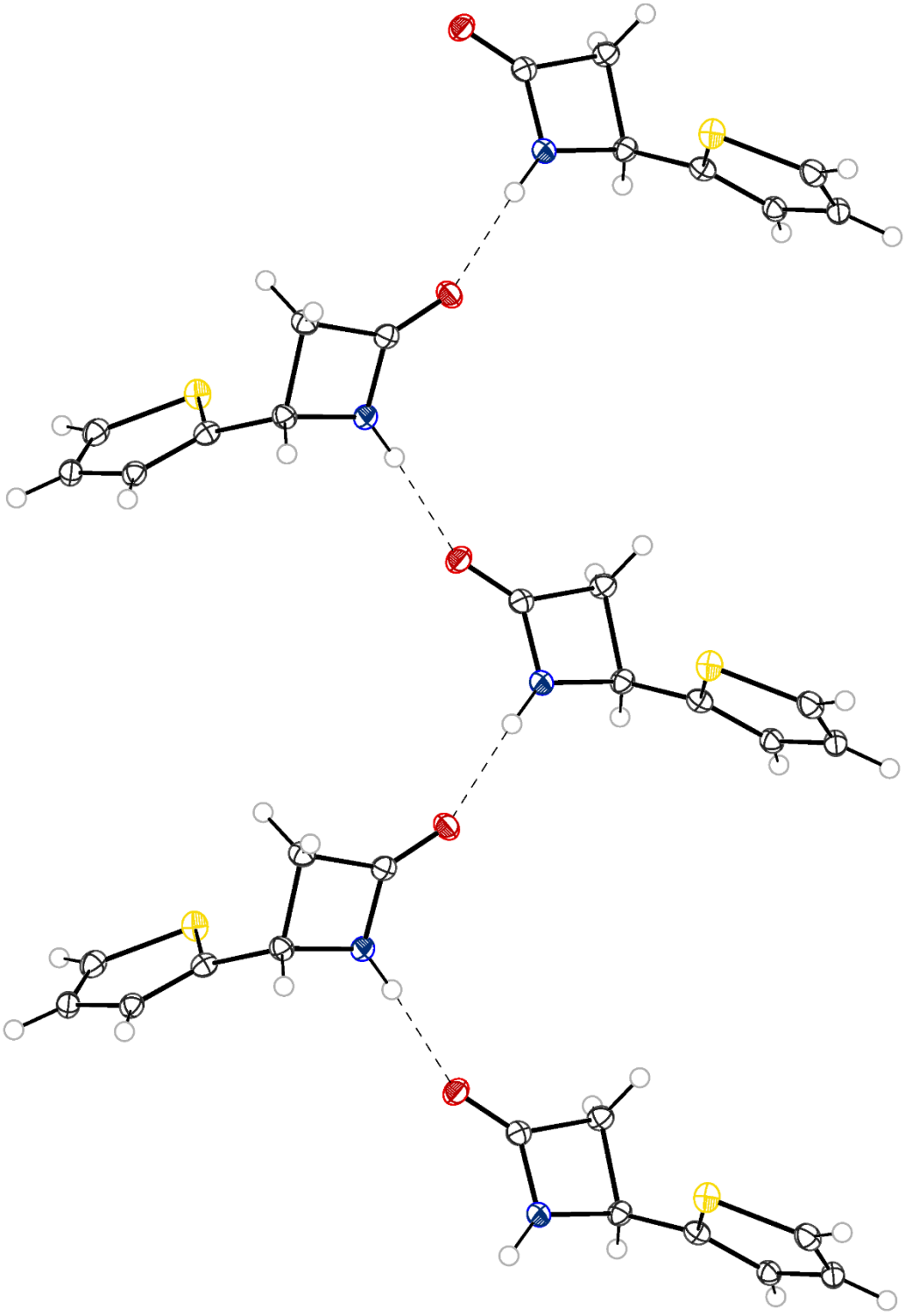

C8
S1
C7
O1
N1
C1
C6
C5
C2
C4
C3

Table S4. Crystal data and structure refinement for (*S*)-5-(thiophen-2-yl)pyrrolidin-2-one (**1m**). Cambridge Crystallographic Data Centre (CCDC) entry: 1893087.

Identification code	fasdv14	
Empirical formula	C8 H9 N O S	
Formula weight	167.22	
Temperature	100.00(10) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 6.28600(10) Å	α = 90°
	b = 7.14490(10) Å	β = 106.6810(10)°
	c = 9.17890(10) Å	γ = 90°
Volume	394.902(10) Å^3	
Z	2	
Density (calculated)	1.406 Mg/m^3	
Absorption coefficient	3.126 mm^{-1}	
F(000)	176	
Crystal color, morphology	colourless, block	
Crystal size	0.268 x 0.176 x 0.112 mm^3	
Theta range for data collection	5.030 to 80.397°	
Index ranges	$-6 \le h \le 7$, $-9 \le k \le 9$, $-11 \le l \le 11$	
Reflections collected	13408	
Independent reflections	1686 [R(int) = 0.0656]	
Observed reflections	1675	
Completeness to theta = 74.504°	100.0%	
Absorption correction	Multi-scan	
Max. and min. transmission	1.00000 and 0.26185	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1686 / 1 / 104	
Goodness-of-fit on F^2	1.079	
Final R indices [I>2sigma(I)]	R1 = 0.0338, wR2 = 0.0869	
R indices (all data)	R1 = 0.0341, wR2 = 0.0872	
Absolute structure parameter	0.009(12)	
Largest diff. peak and hole	0.245 and -0.358 e.Å^{-3}	

Structure of 4j





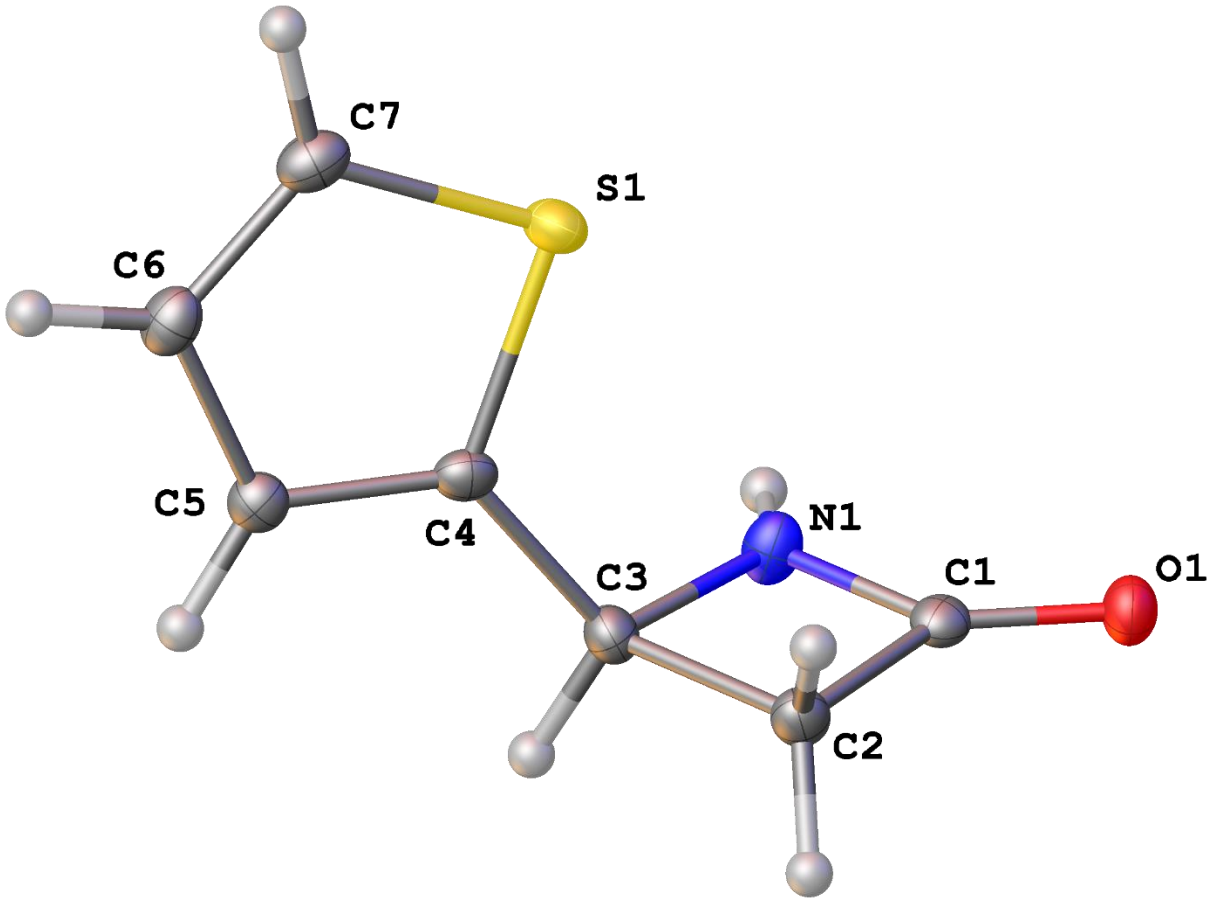
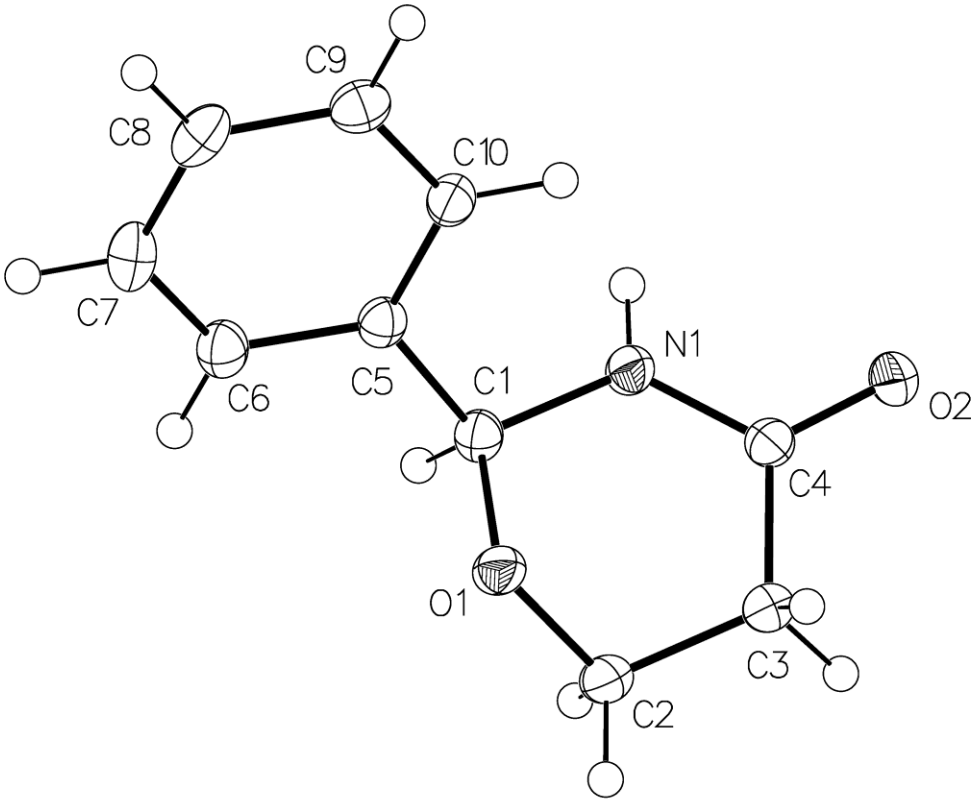
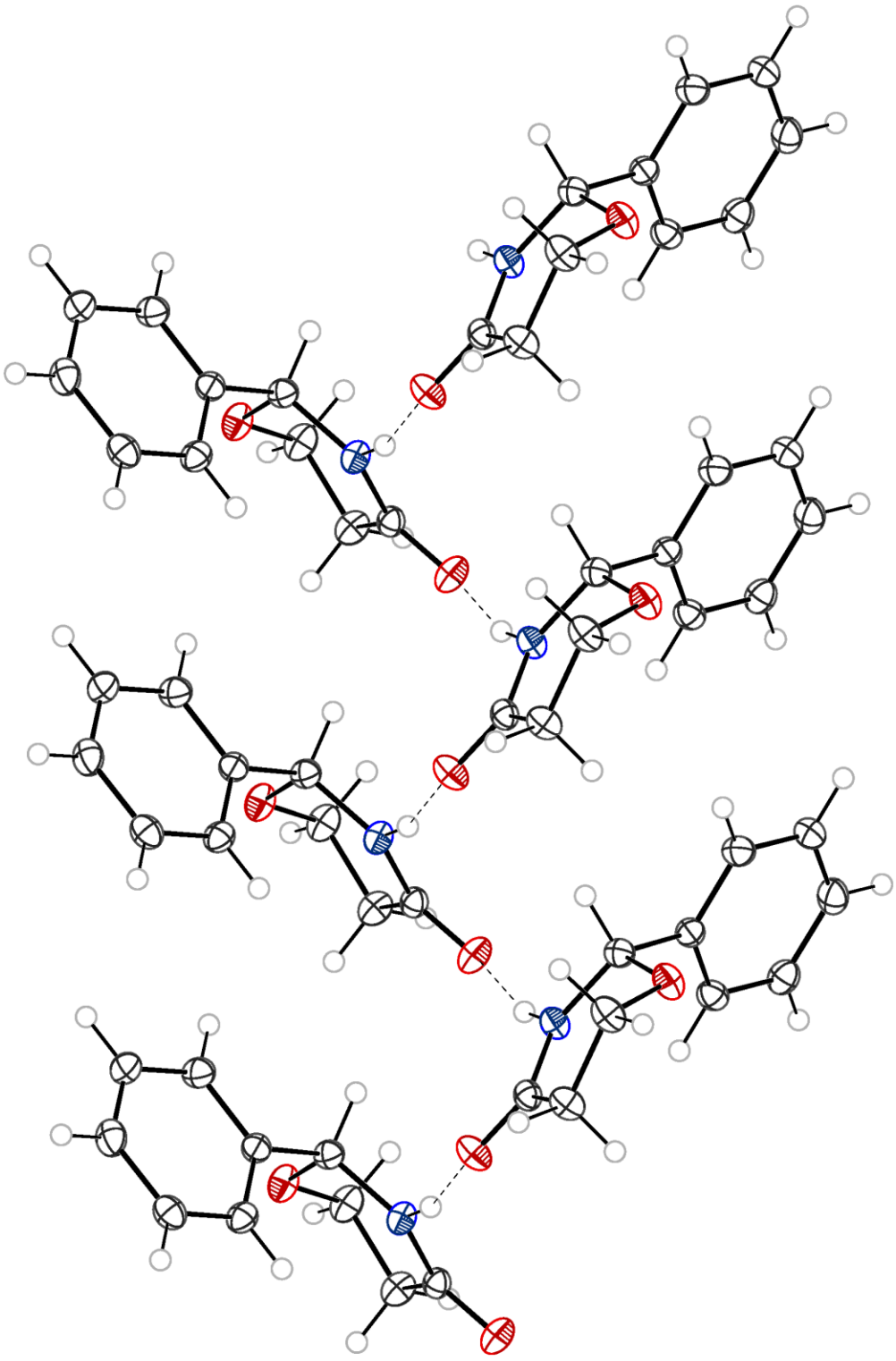

C7
S1
C6
C5
C4
C3
N1
C1
O1
C2

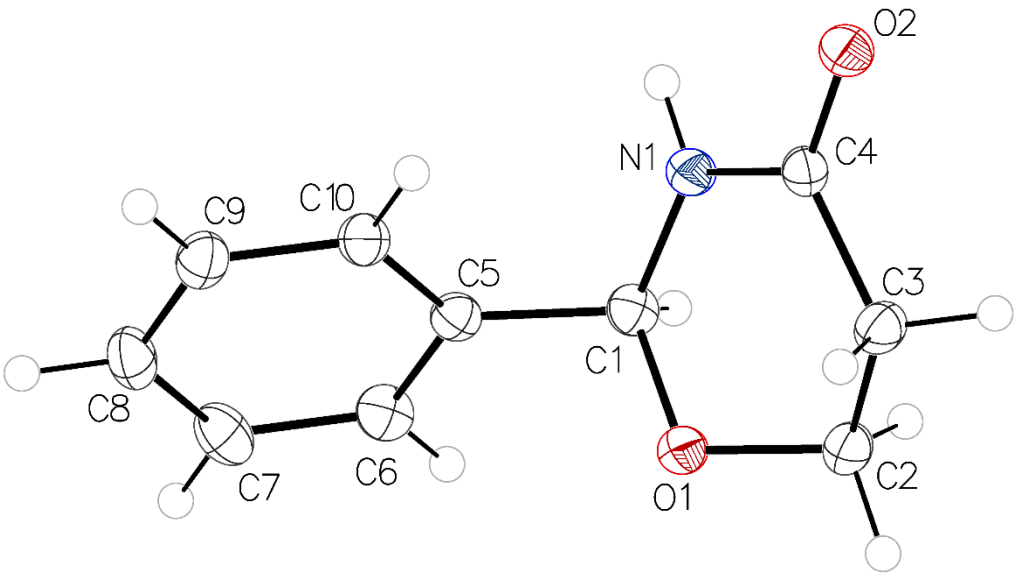
Table S5. Crystal data and structure refinement for (*S*)-4-(thiophen-2-yl)azetidin-2-one (**4k**). Cambridge Crystallographic Data Centre (CCDC) entry: 1893087.

Identification code	fasdv15	
Empirical formula	C7 H7 N O S	
Formula weight	153.20	
Temperature	100.00(10) K	
Wavelength	1.54184 Å	
Crystal system	orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.3215(2) Å	α = 90°
	b = 8.4087(2) Å	β = 90°
	c = 9.8718(2) Å	γ = 90°
Volume	690.76(3) Å^3	
Z	4	
Density (calculated)	1.473 Mg/m^3	
Absorption coefficient	3.521 mm^{-1}	
F(000)	320	
Crystal color, morphology	colourless, block	
Crystal size	0.3 x 0.245 x 0.163 mm^3	
Theta range for data collection	6.917 to 80.738°	
Index ranges	$-10 \le h \le 10$, $-10 \le k \le 10$, $-11 \le l \le 12$	
Reflections collected	11717	
Independent reflections	1498 [R(int) = 0.0839]	
Observed reflections	1469	
Completeness to theta = 74.504°	99.9%	
Absorption correction	Multi-scan	
Max. and min. transmission	1.00000 and 0.81976	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1498 / 0 / 96	
Goodness-of-fit on F^2	1.176	
Final R indices [I>2sigma(I)]	R1 = 0.0377, wR2 = 0.1085	
R indices (all data)	R1 = 0.0395, wR2 = 0.1118	
Absolute structure parameter	-0.020(18)	
Extinction coefficient	0.028(4)	
Largest diff. peak and hole	0.509 and -0.417 e.Å^{-3}	

Structure of 6c






O2
N1
C4
C9
C10
C5
C3
C1
C8
C7
C6
O1
C2

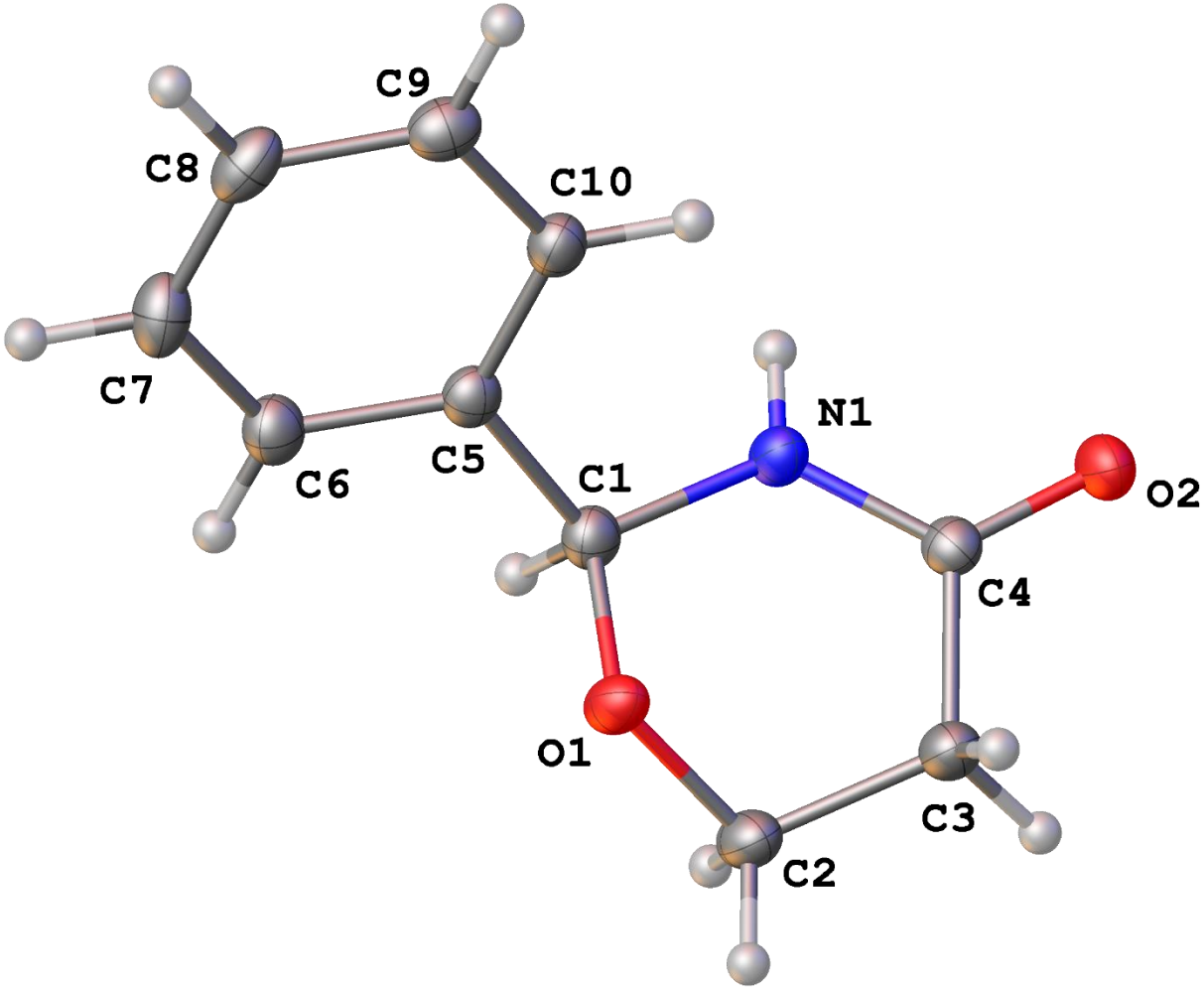

C9
C8
C10
C7
N1
C5
C6
C1
O2
C4
O1
C3
C2

Table S6. Crystal data and structure refinement for (*S*)-2-phenyl-1,3-oxazinan-4-one (**6c**). Cambridge Crystallographic Data Centre (CCDC) entry: 1893087.

Identification code	frosr02	
Empirical formula	C10 H11 N O2	
Formula weight	177.20	
Temperature	100.00(10) K	
Wavelength	1.54184 Å	
Crystal system	orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 5.58700(10) Å	α = 90°
	b = 8.52990(10) Å	β = 90°
	c = 18.4366(3) Å	γ = 90°
Volume	878.62(2) Å^3	
Z	4	
Density (calculated)	1.340 Mg/m^3	
Absorption coefficient	0.768 mm^{-1}	
F(000)	376	
Crystal color, morphology	colourless, block	
Crystal size	0.121 x 0.105 x 0.092 mm^3	
Theta range for data collection	4.797 to 80.960°	
Index ranges	$-7 \le h \le 7$, $-10 \le k \le 10$, $-21 \le l \le 23$	
Reflections collected	15564	
Independent reflections	1904 [R(int) = 0.0655]	
Observed reflections	1845	
Completeness to theta = 80.960°	99.4%	
Absorption correction	Multi-scan	
Max. and min. transmission	1.00000 and 0.53031	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1904 / 0 / 122	
Goodness-of-fit on F^2	1.131	
Final R indices [I>2sigma(I)]	R1 = 0.0344, wR2 = 0.0864	
R indices (all data)	R1 = 0.0357, wR2 = 0.0879	
Absolute structure parameter	-0.04(12)	
Largest diff. peak and hole	0.158 and -0.247 e.Å^{-3}	

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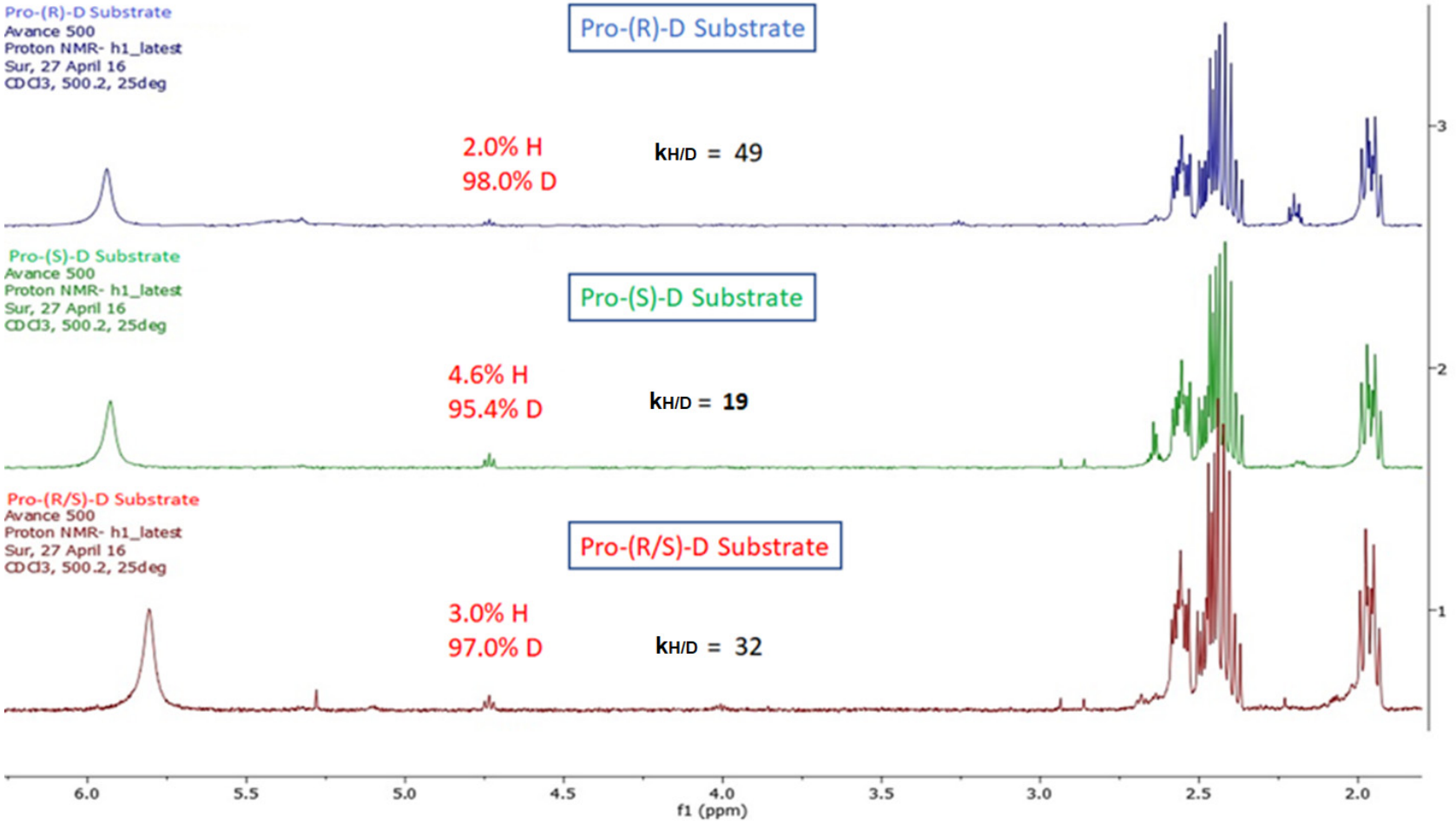
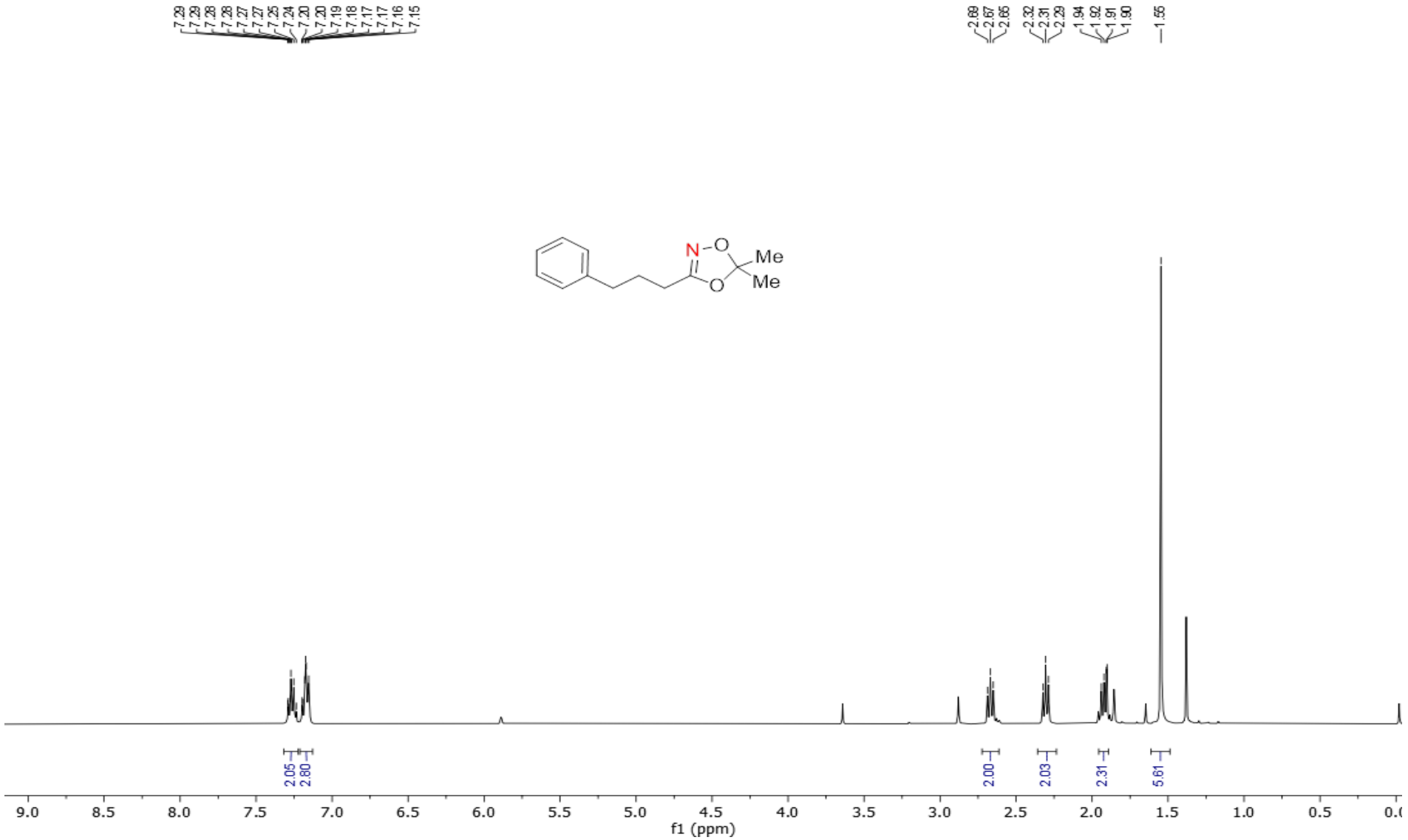
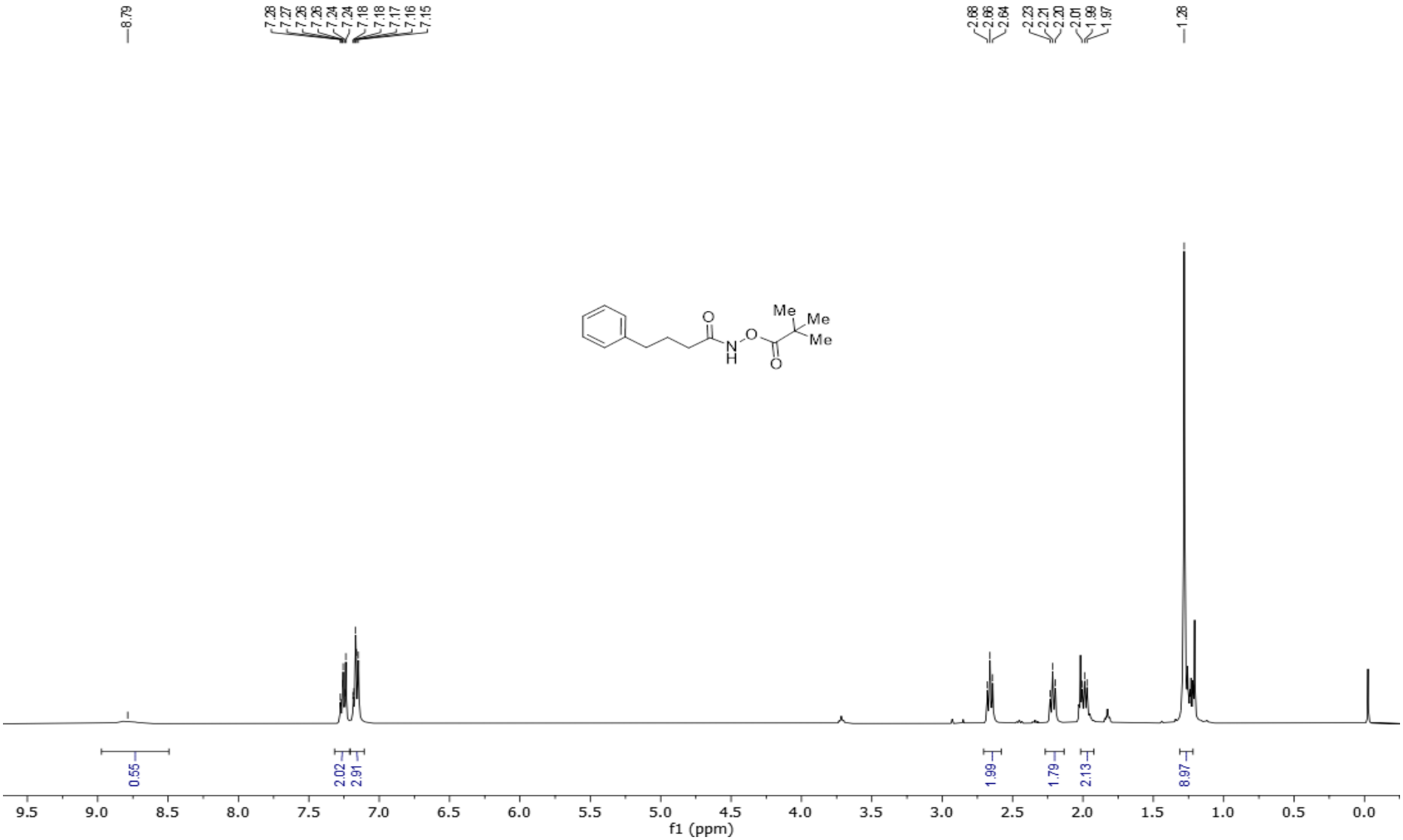


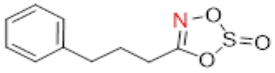
5,5-dimethyl-3-(3-phenylpropyl)-1,4,2-dioxazole (**1aa**), ^{1}H NMR (400 MHz, $CDCl_3$):

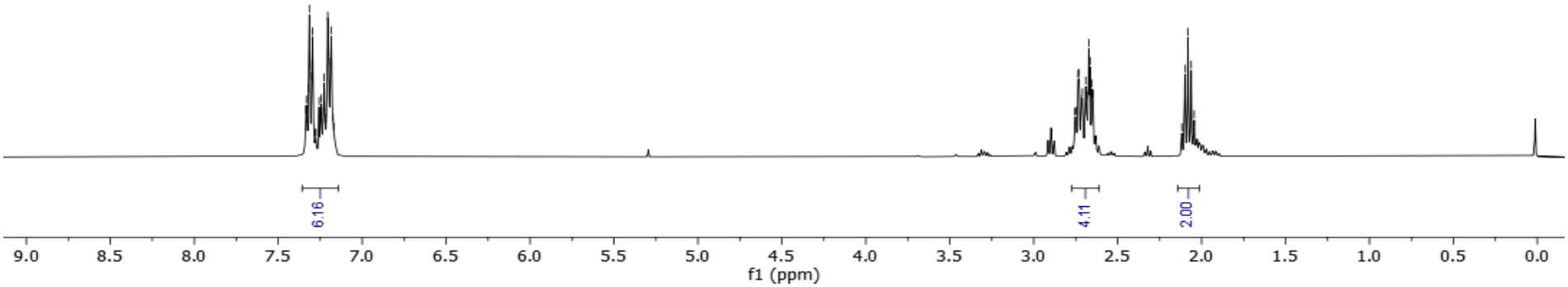


3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (**1ab**), ^{1}H NMR (400 MHz, $CDCl_3$):

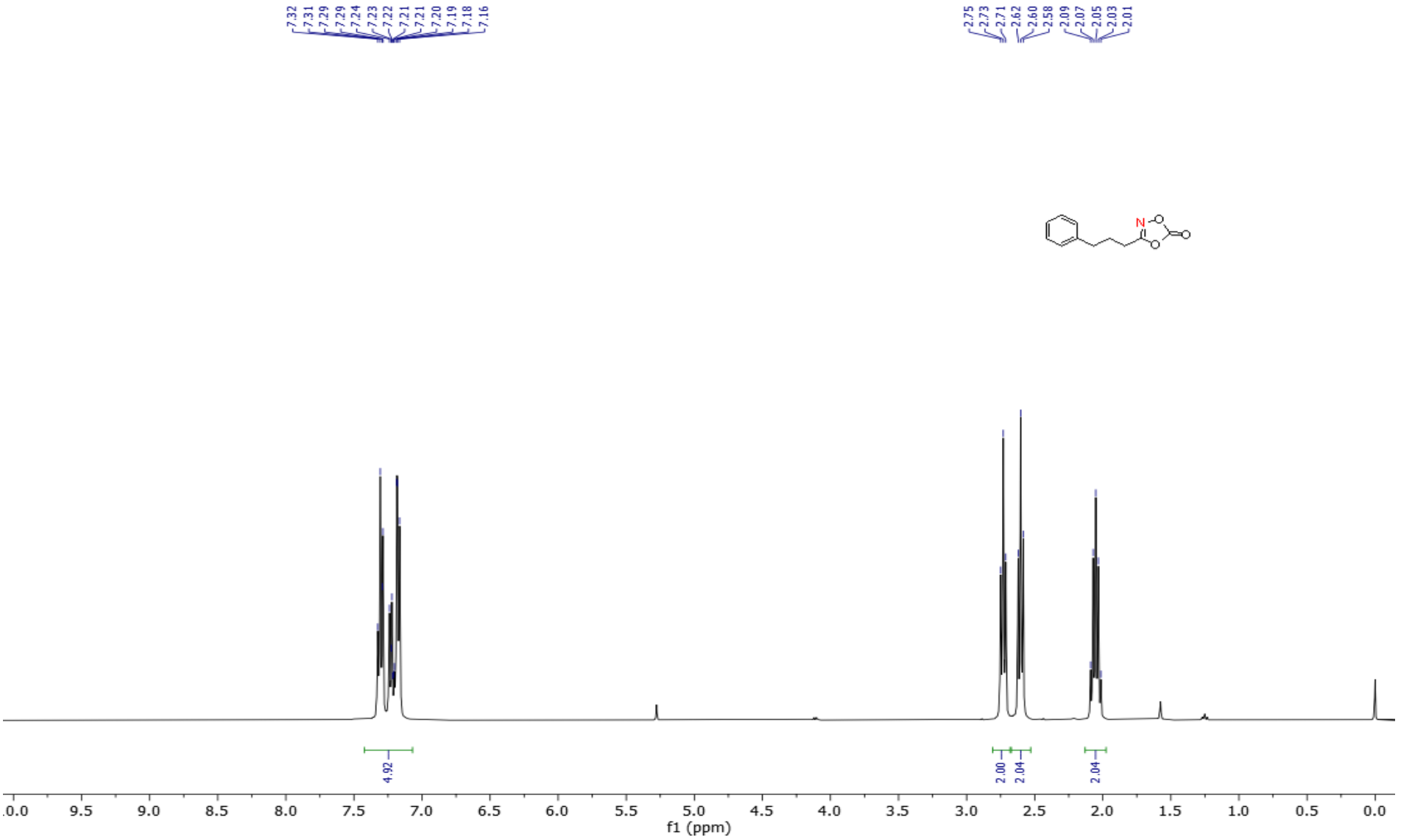


3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (**1ac**), ^{1}H NMR (400 MHz, $CDCl_3$):

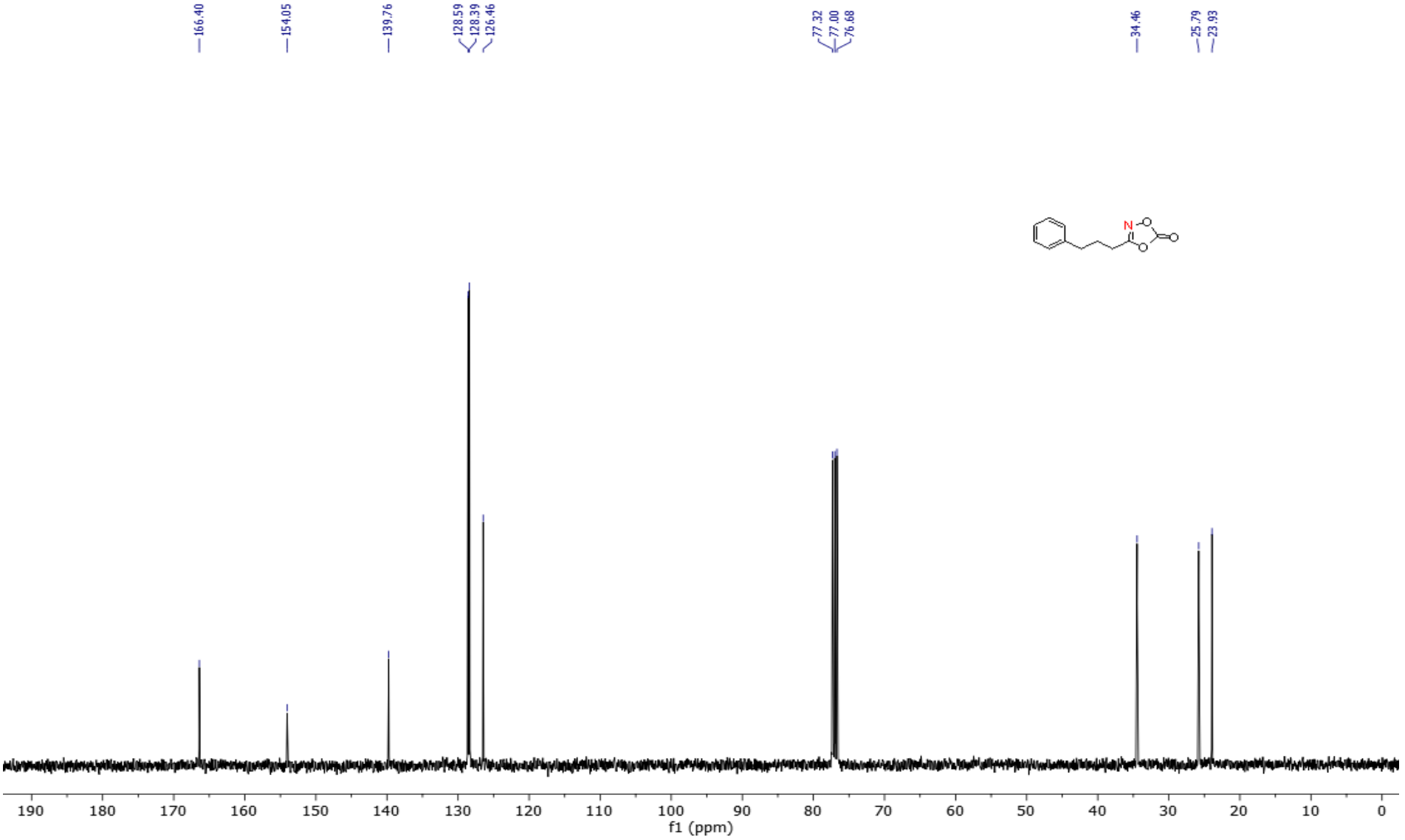




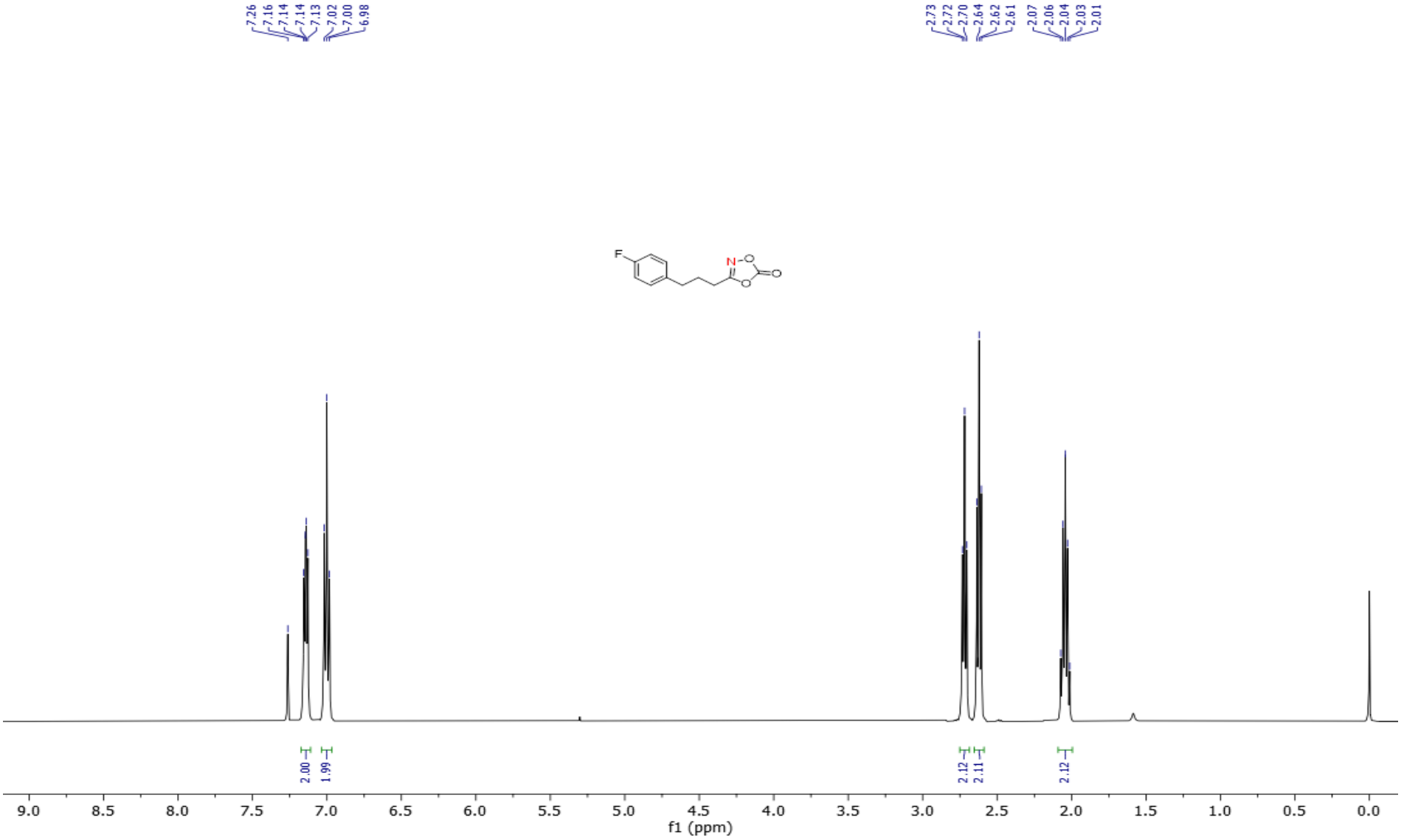
3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (**1a**), ^{1}H NMR (400 MHz, $CDCl_3$):



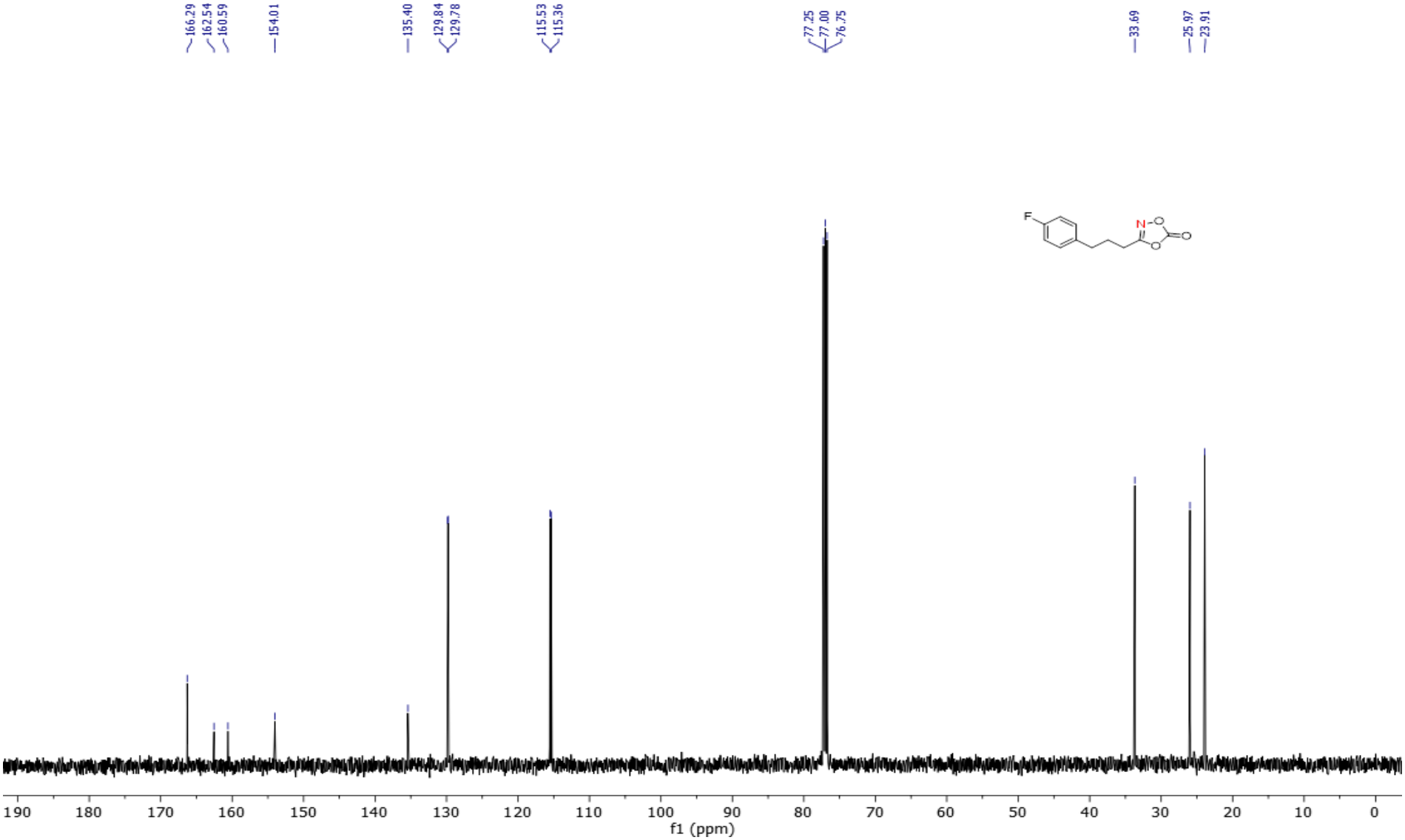
3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (**1a**), ^{13}C NMR (101 MHz, $CDCl_3$):



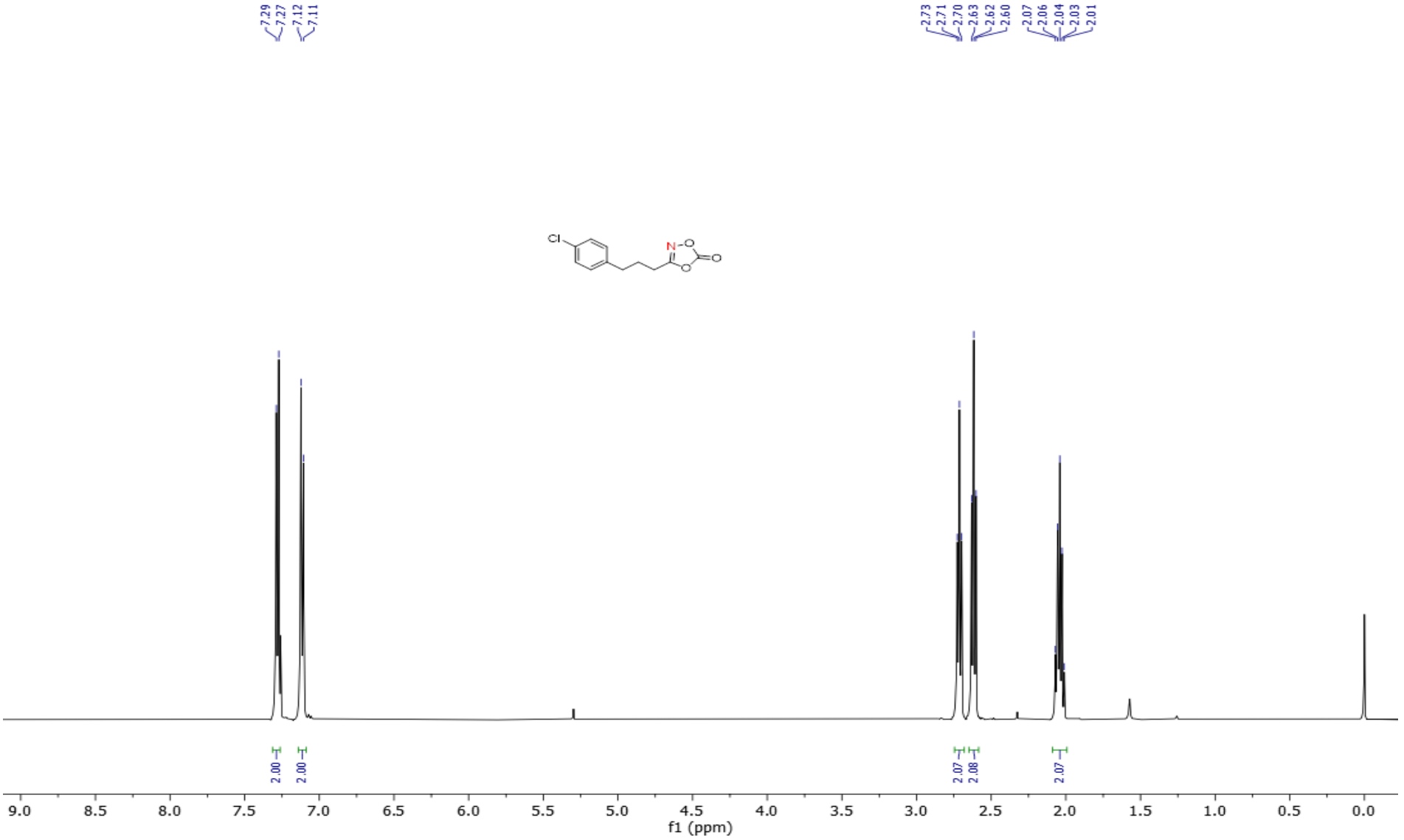
3-(3-(4-fluorophenyl)propyl)-1,4,2-dioxazol-5-one (**1d**), ^{1}H NMR (500 MHz, $CDCl_3$):



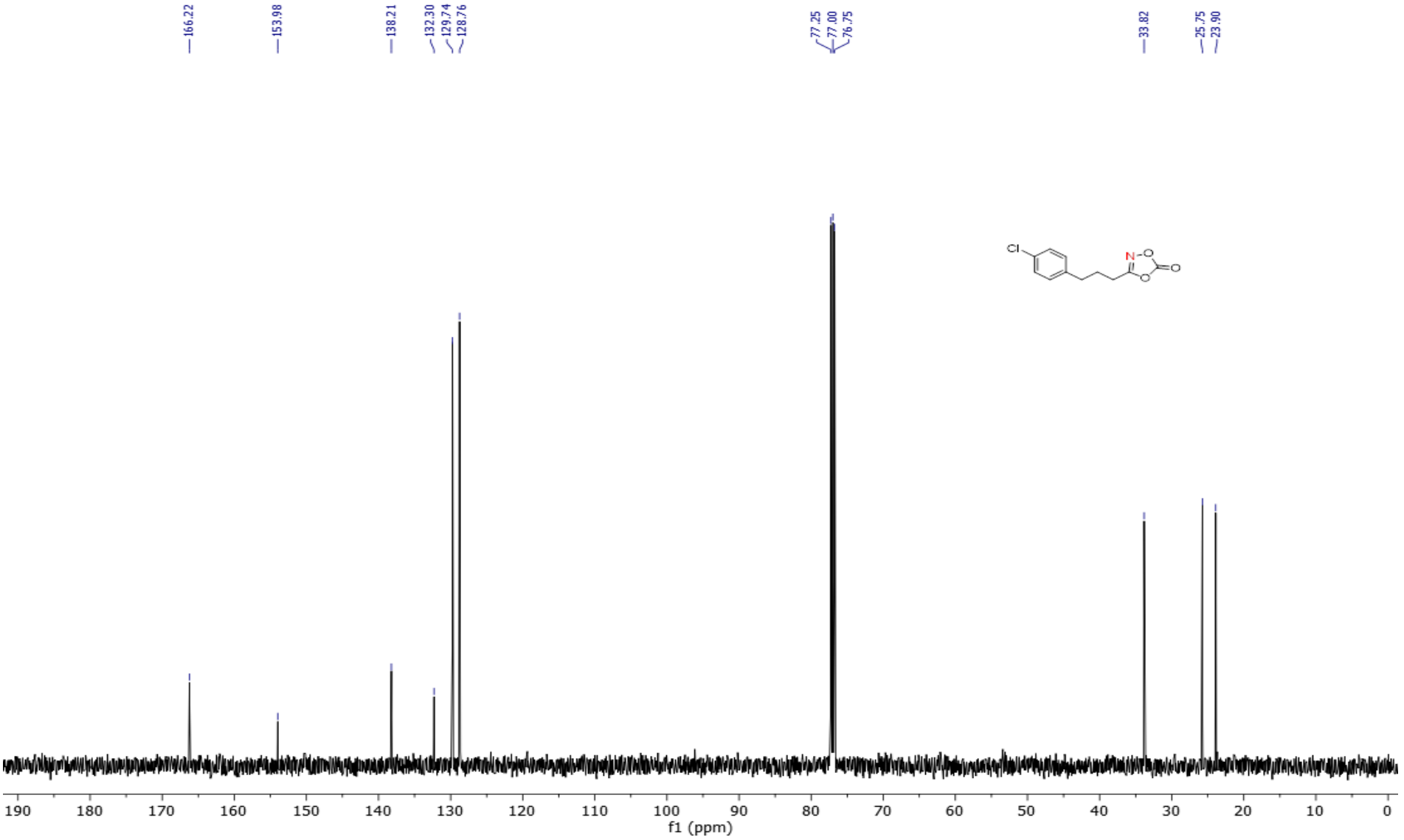
3-(3-(4-fluorophenyl)propyl)-1,4,2-dioxazol-5-one (**1d**), ^{13}C NMR (126 MHz, $CDCl_3$):



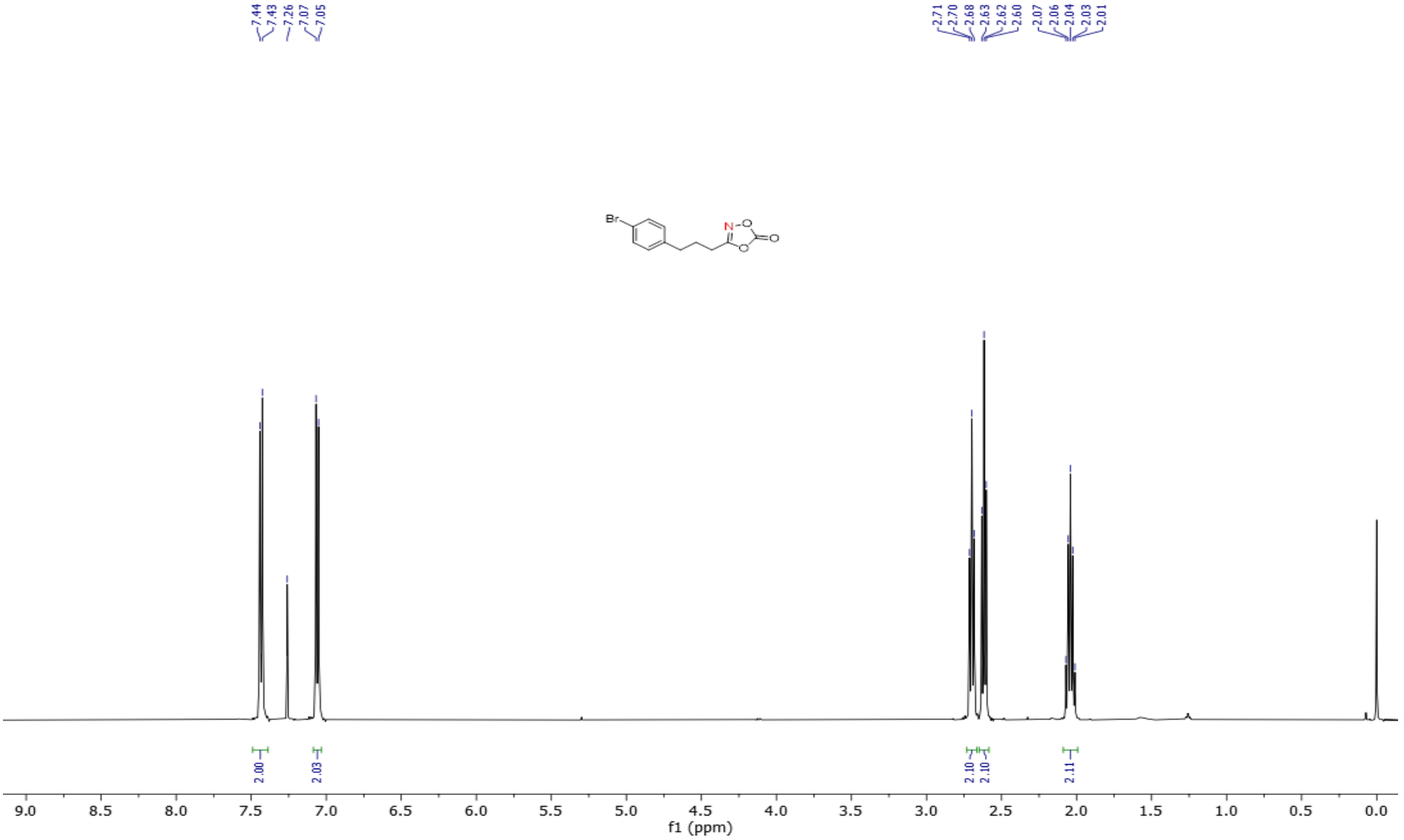
3-(3-(4-chlorophenyl)propyl)-1,4,2-dioxazol-5-one (**1e**), ^{1}H NMR (500 MHz, $CDCl_3$):



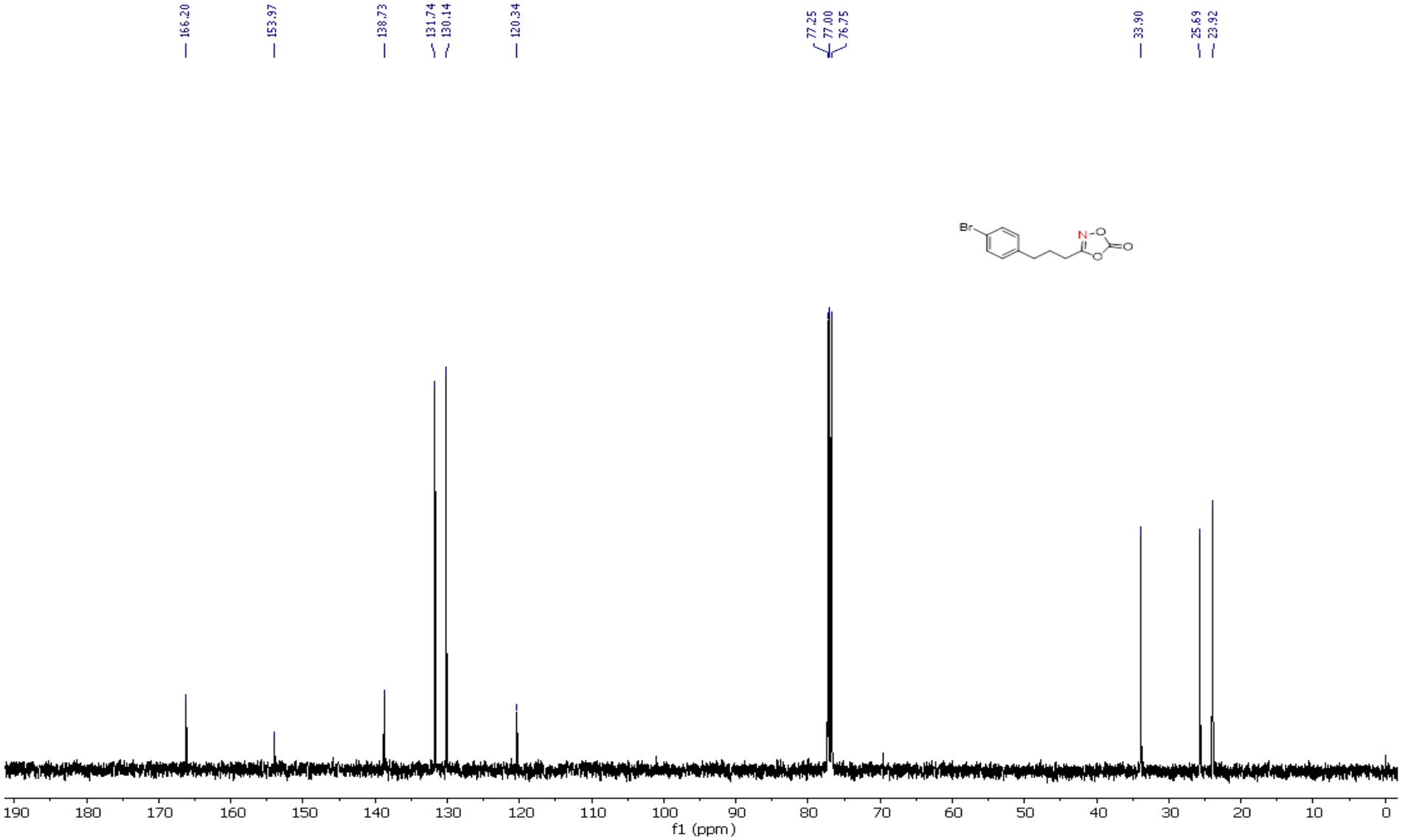
3-(3-(4-chlorophenyl)propyl)-1,4,2-dioxazol-5-one (**1e**), ^{13}C NMR (126 MHz, $CDCl_3$):



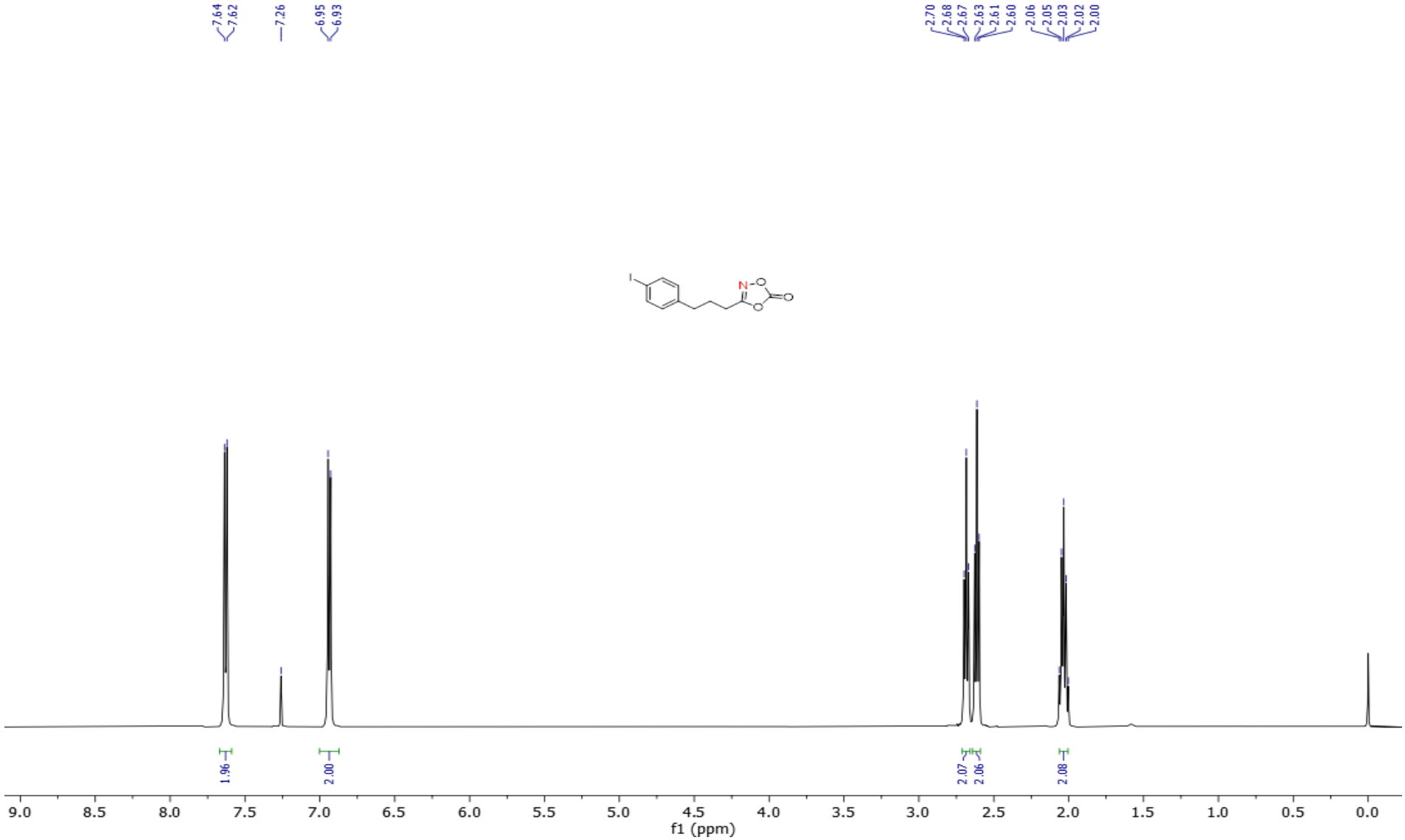
3-(3-(4-bromophenyl)propyl)-1,4,2-dioxazol-5-one (**1f**), ^{1}H NMR (400 MHz, $CDCl_3$):



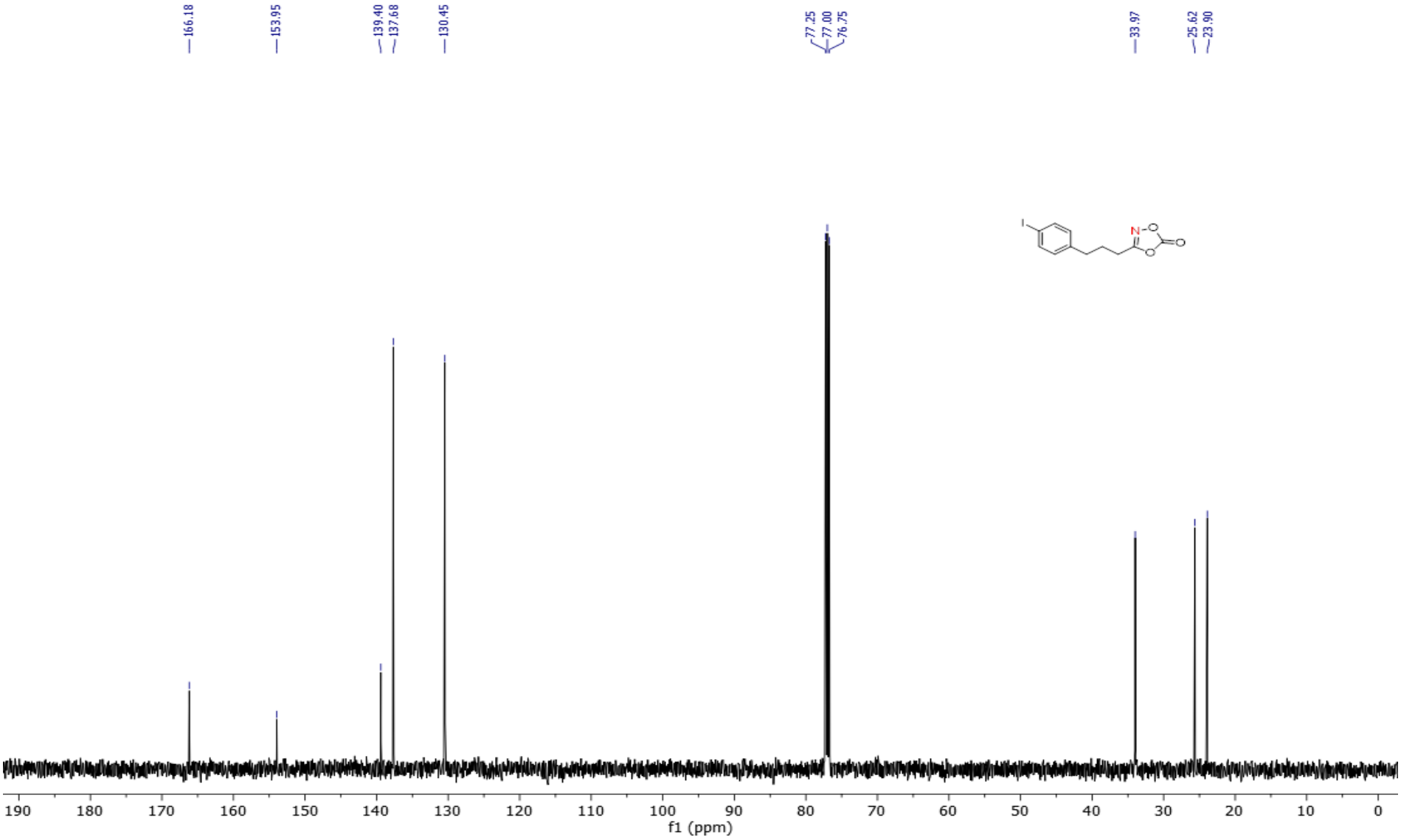
3-(3-(4-bromophenyl)propyl)-1,4,2-dioxazol-5-one (**1f**), ^{13}C NMR (101 MHz, $CDCl_3$):



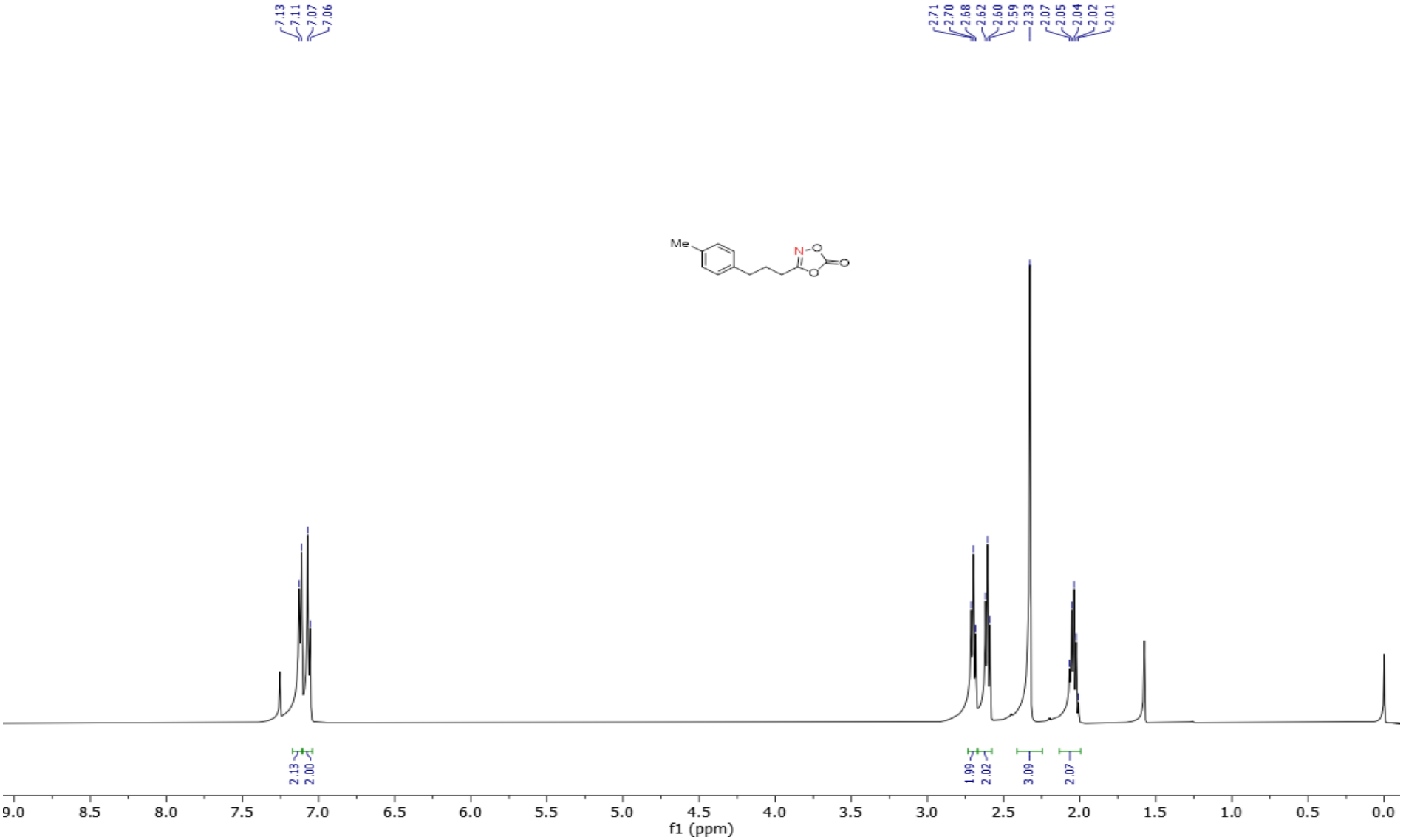
3-(3-(4-iodophenyl)propyl)-1,4,2-dioxazol-5-one (1g), ^{1}H NMR (400 MHz, $CDCl_3$):



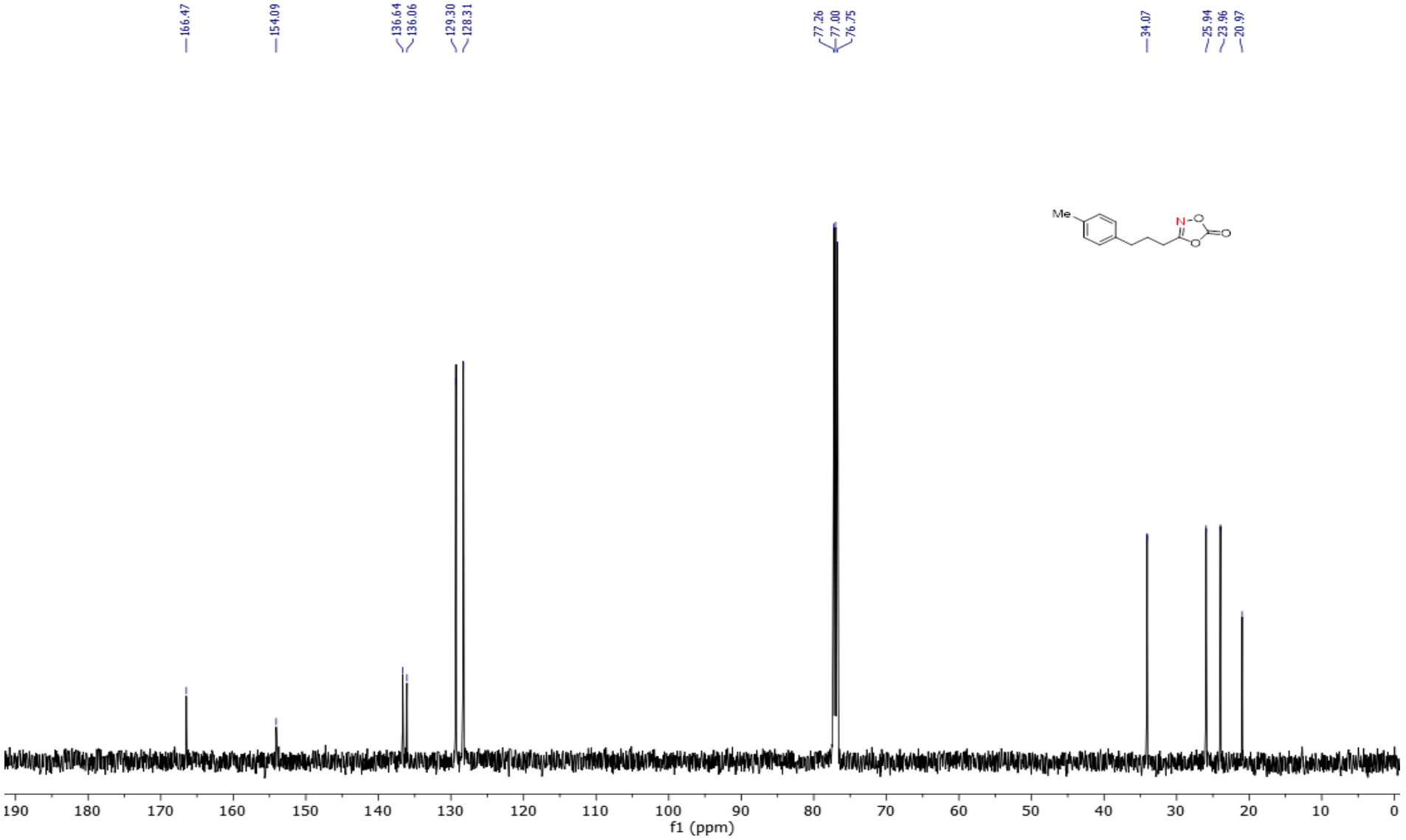
3-(3-(4-iodophenyl)propyl)-1,4,2-dioxazol-5-one (1g), ^{13}C NMR (101 MHz, $CDCl_3$):



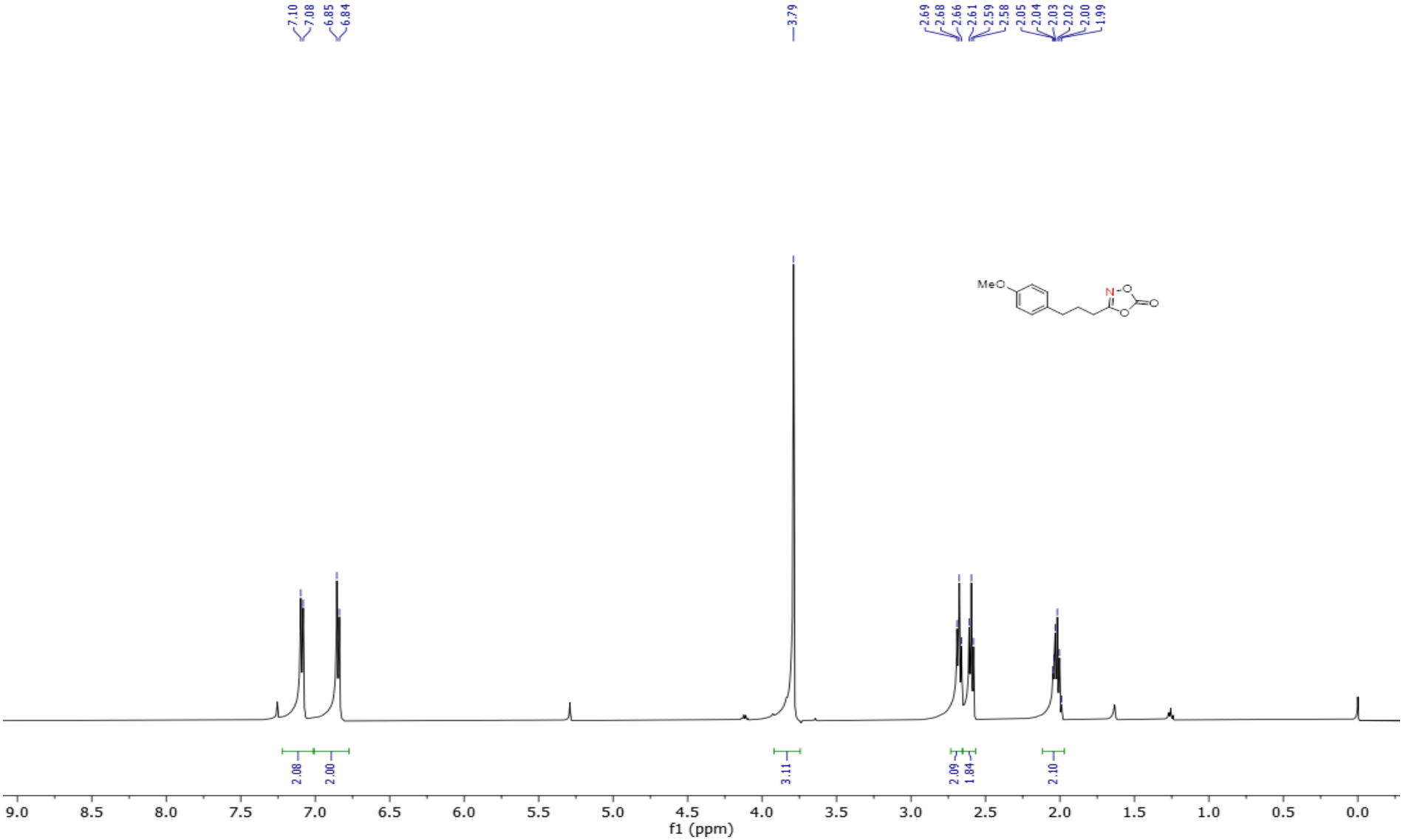
3-(3-(p-tolyl)propyl)-1,4,2-dioxazol-5-one (1h), ^{1}H NMR (400 MHz, $CDCl_3$):



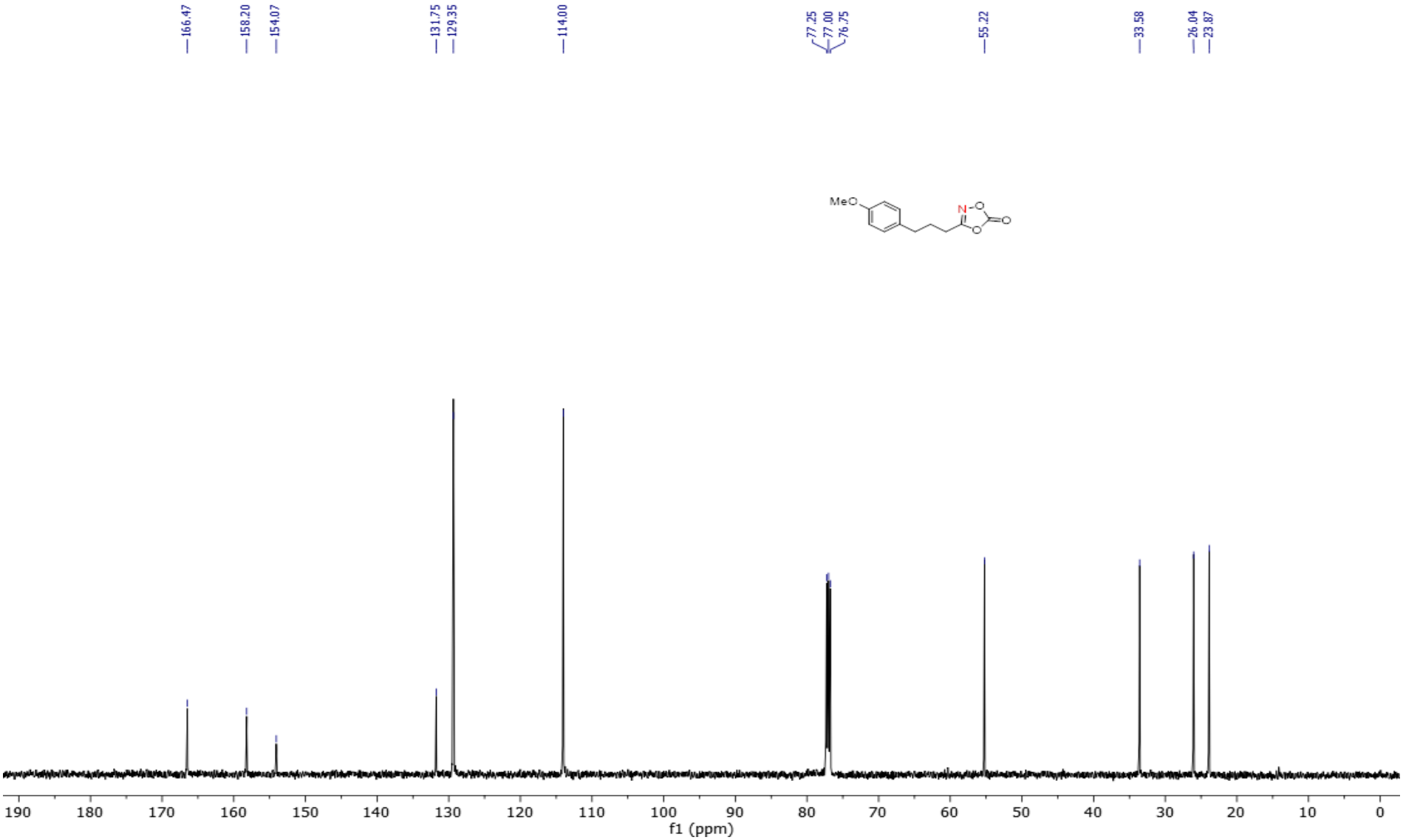
3-(3-(p-tolyl)propyl)-1,4,2-dioxazol-5-one (1h), ^{13}C NMR (101 MHz, $CDCl_3$):



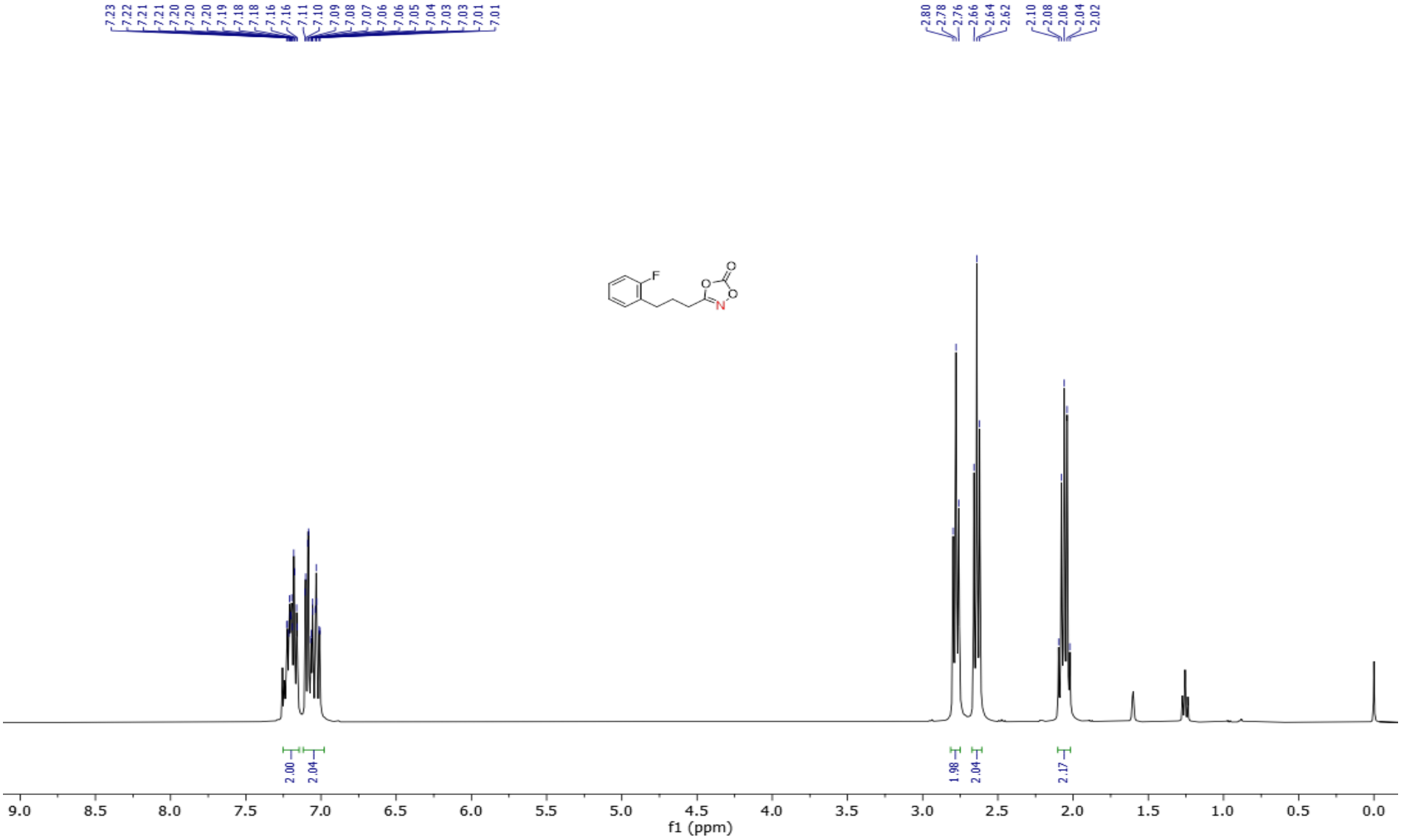
3-(3-(4-methoxyphenyl)propyl)-1,4,2-dioxazol-5-one (1i), ^{1}H NMR (400 MHz, $CDCl_3$):



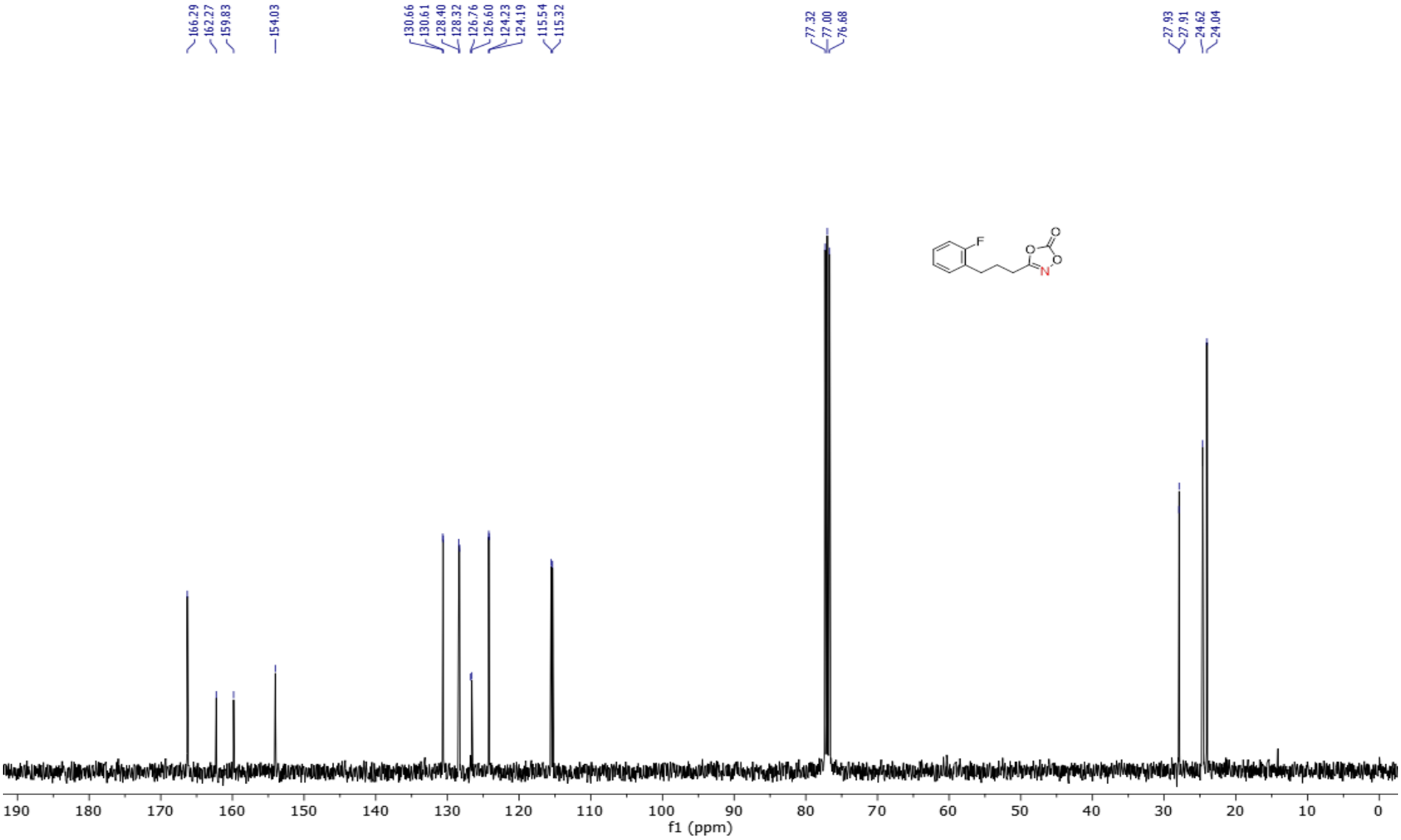
3-(3-(4-methoxyphenyl)propyl)-1,4,2-dioxazol-5-one (1i), ^{13}C NMR (101 MHz, $CDCl_3$):



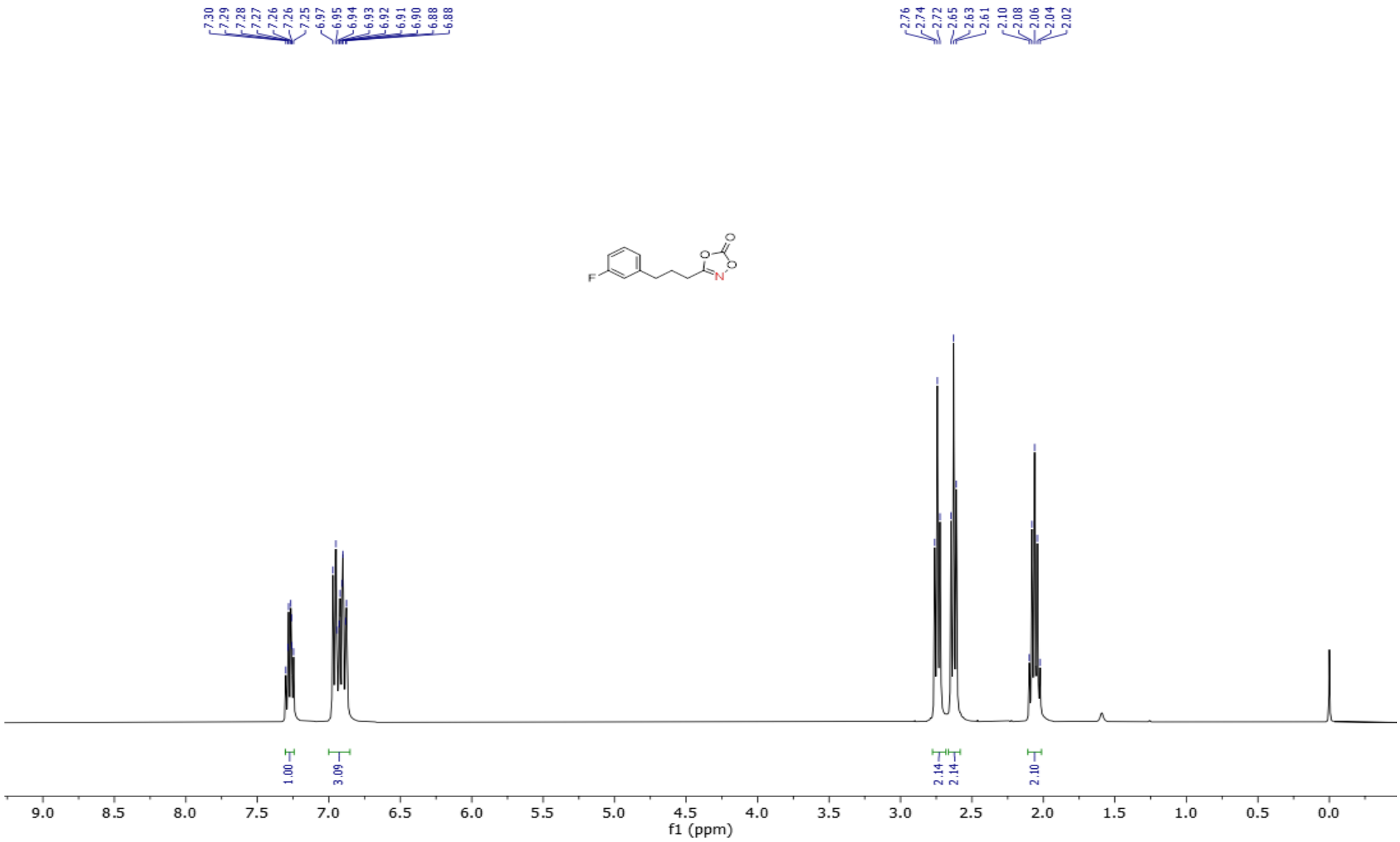
3-(3-(2-fluorophenyl)propyl)-1,4,2-dioxazol-5-one (1j), ^{1}H NMR (400 MHz, $CDCl_3$):



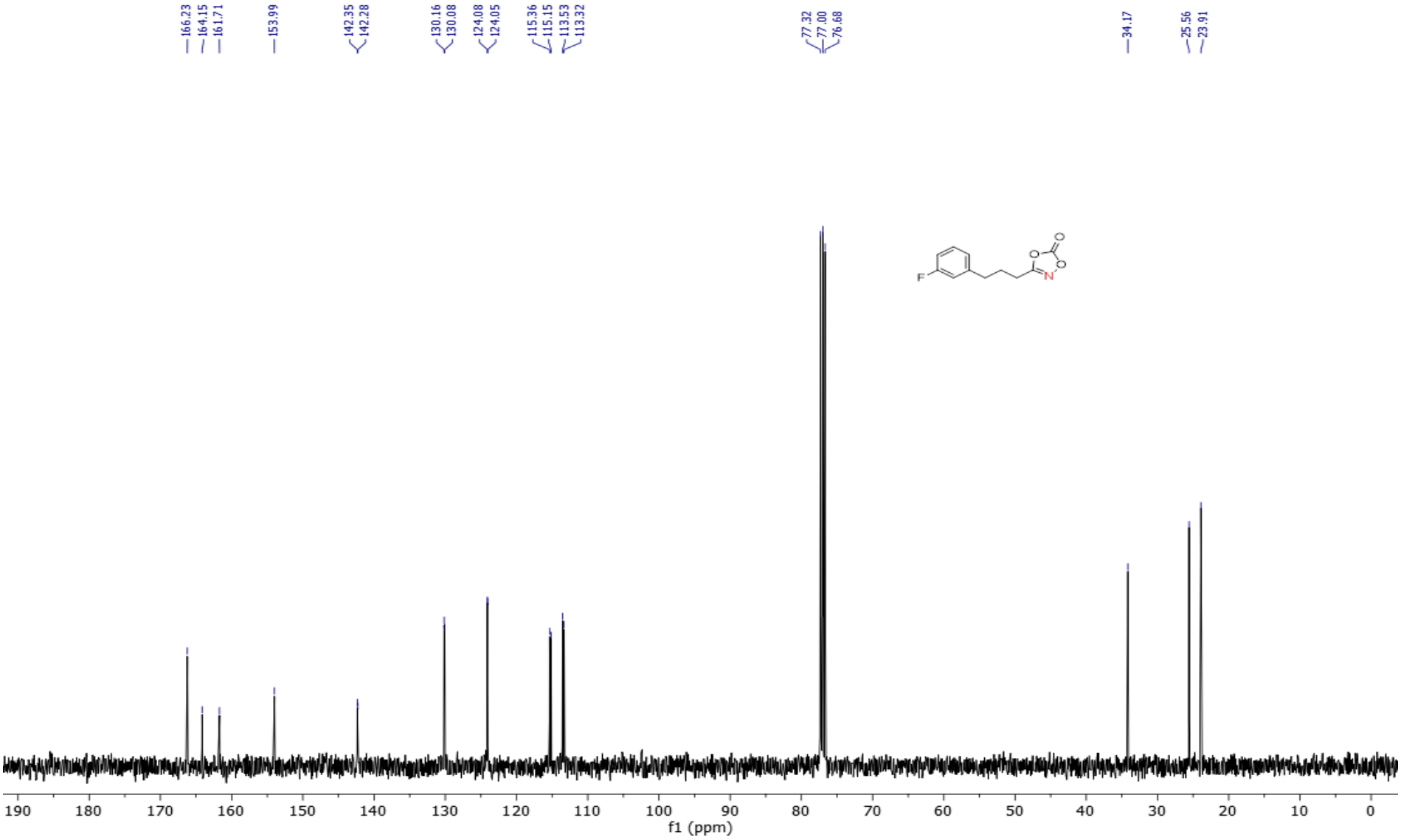
3-(3-(2-fluorophenyl)propyl)-1,4,2-dioxazol-5-one (1j), ^{13}C NMR (101 MHz, $CDCl_3$):



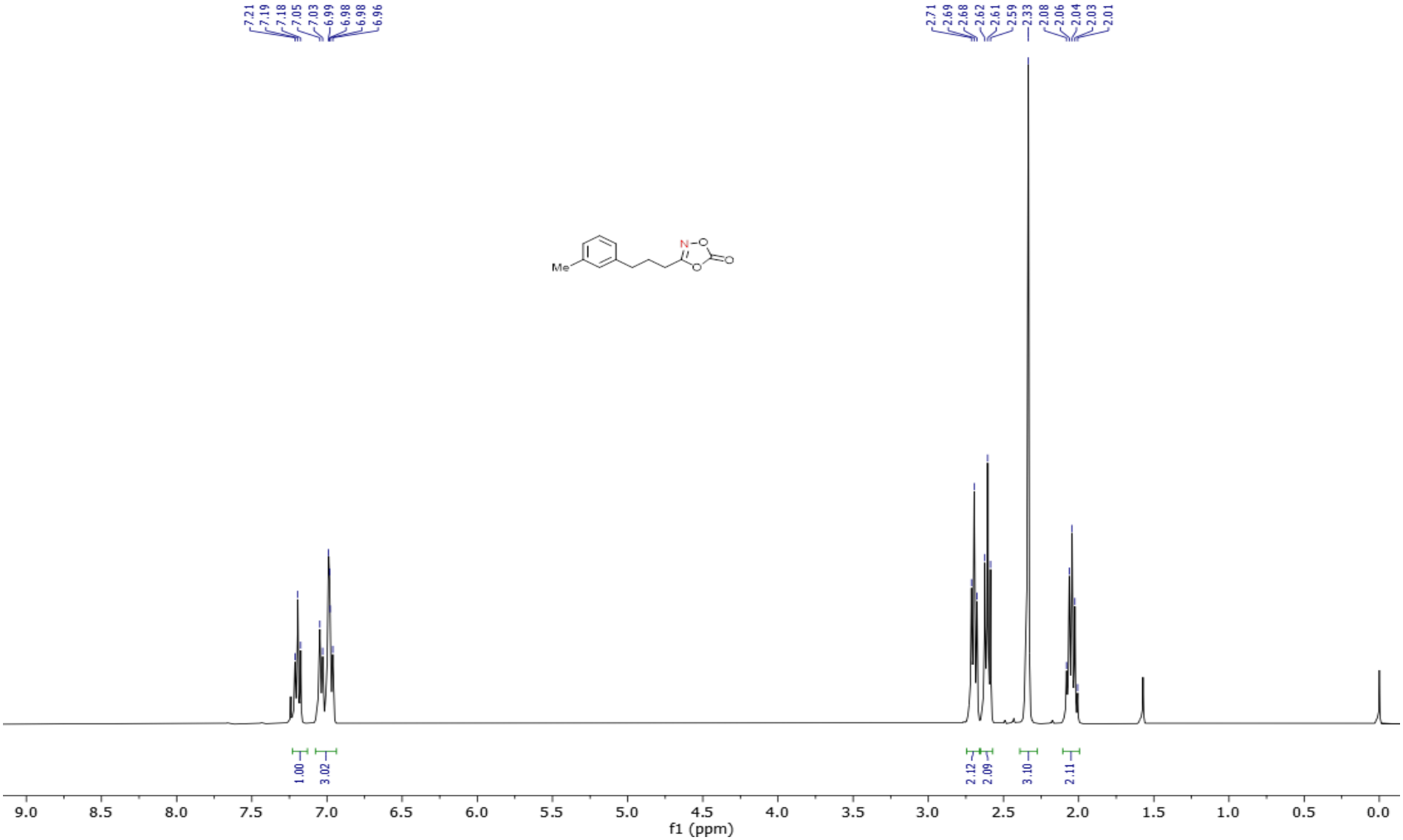
3-(3-(3-fluorophenyl)propyl)-1,4,2-dioxazol-5-one (1k), ^{1}H NMR (400 MHz, $CDCl_3$):



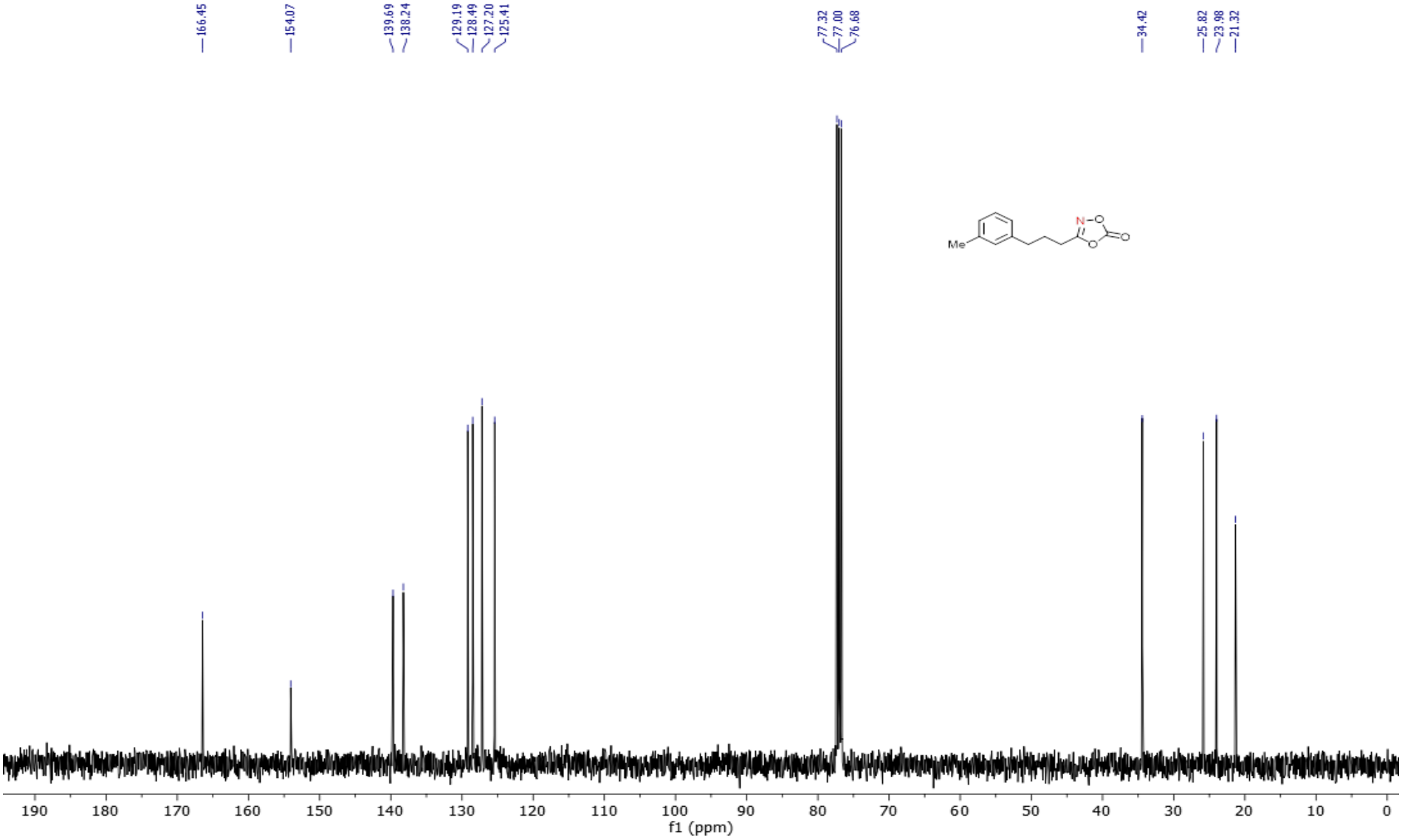
3-(3-(3-fluorophenyl)propyl)-1,4,2-dioxazol-5-one (1k), ^{13}C NMR (101 MHz, $CDCl_3$):



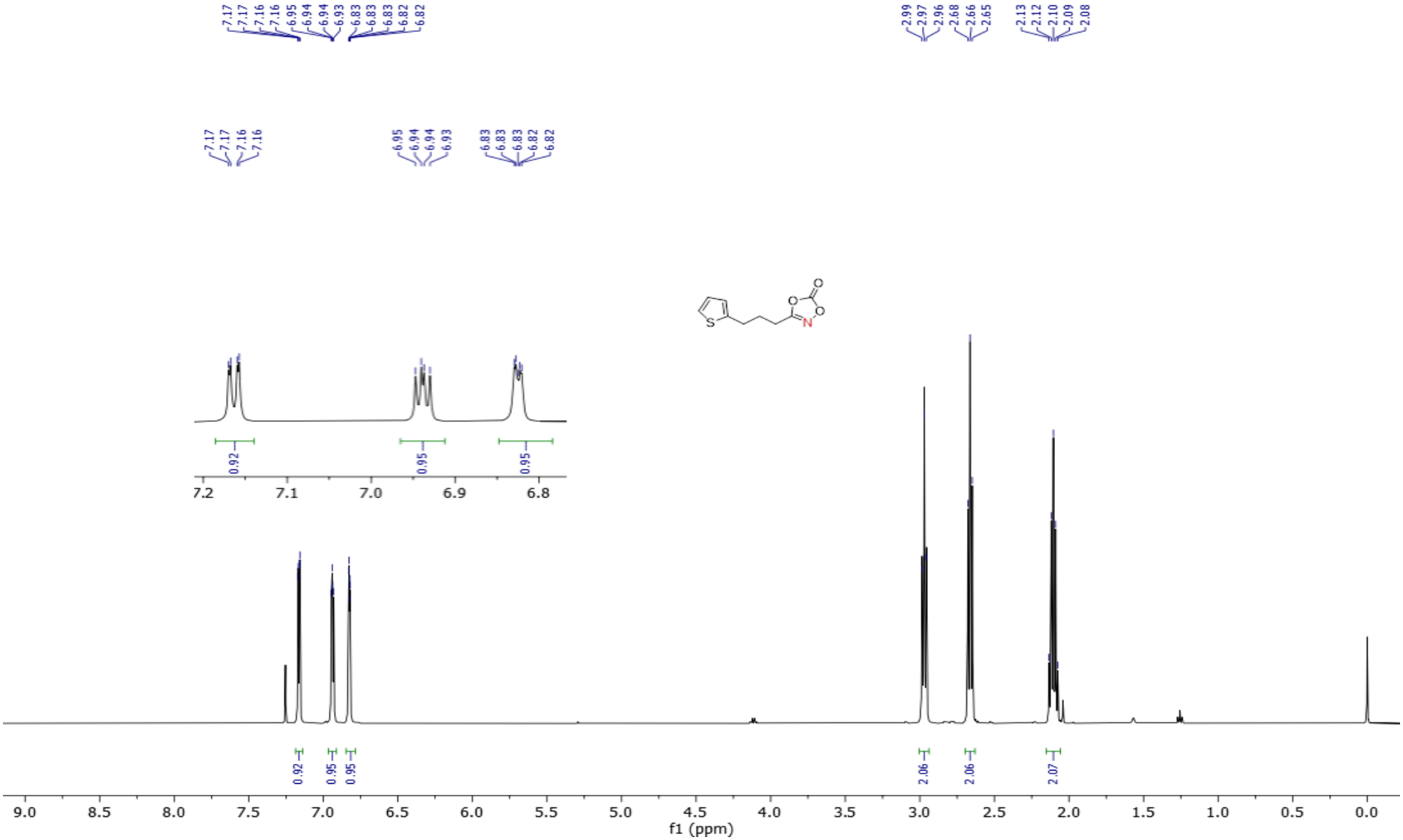
3-(3-(m-tolyl)propyl)-1,4,2-dioxazol-5-one (1l), ^{1}H NMR (400 MHz, $CDCl_3$):



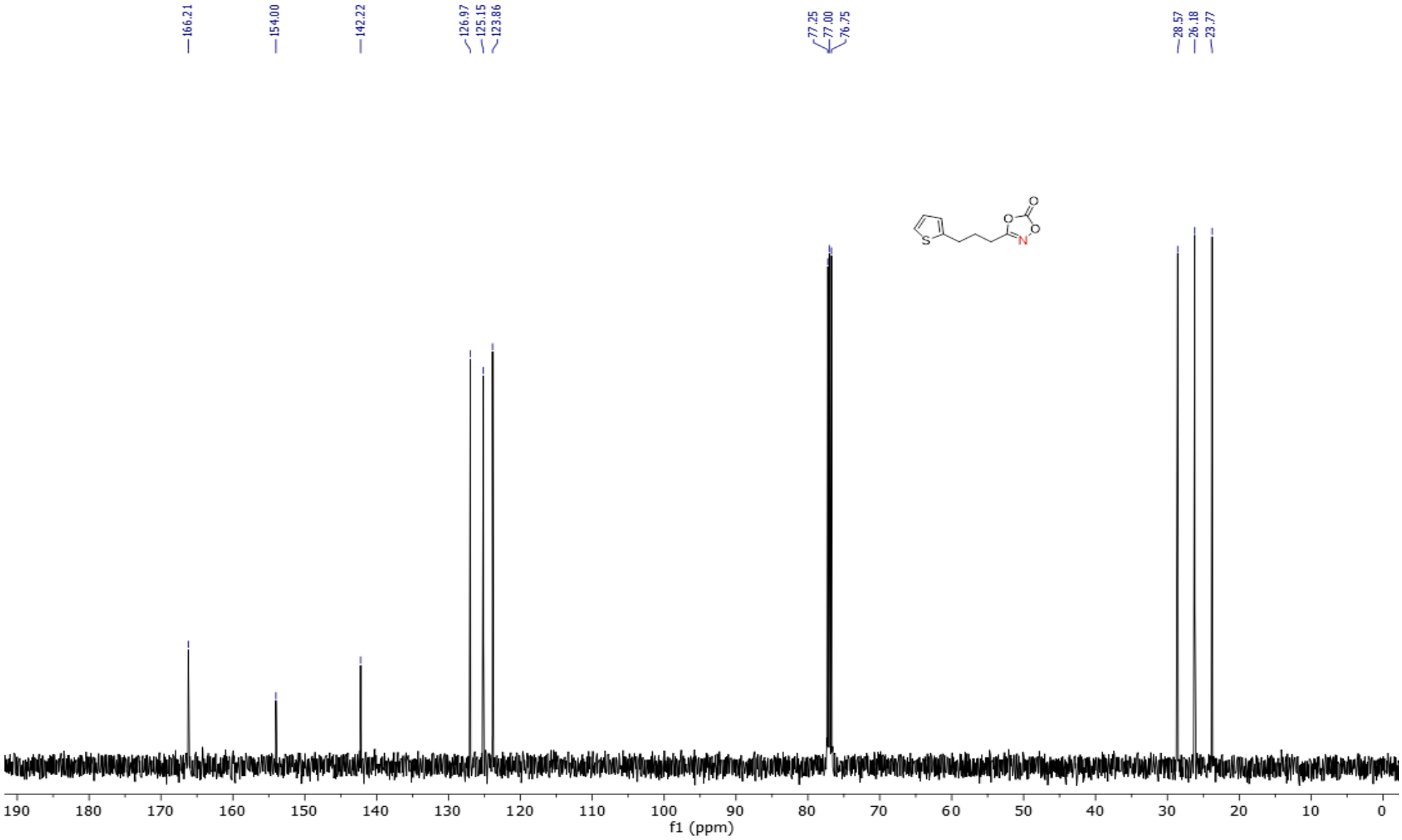
3-(3-(m-tolyl)propyl)-1,4,2-dioxazol-5-one (1l), ^{13}C NMR (101 MHz, $CDCl_3$):



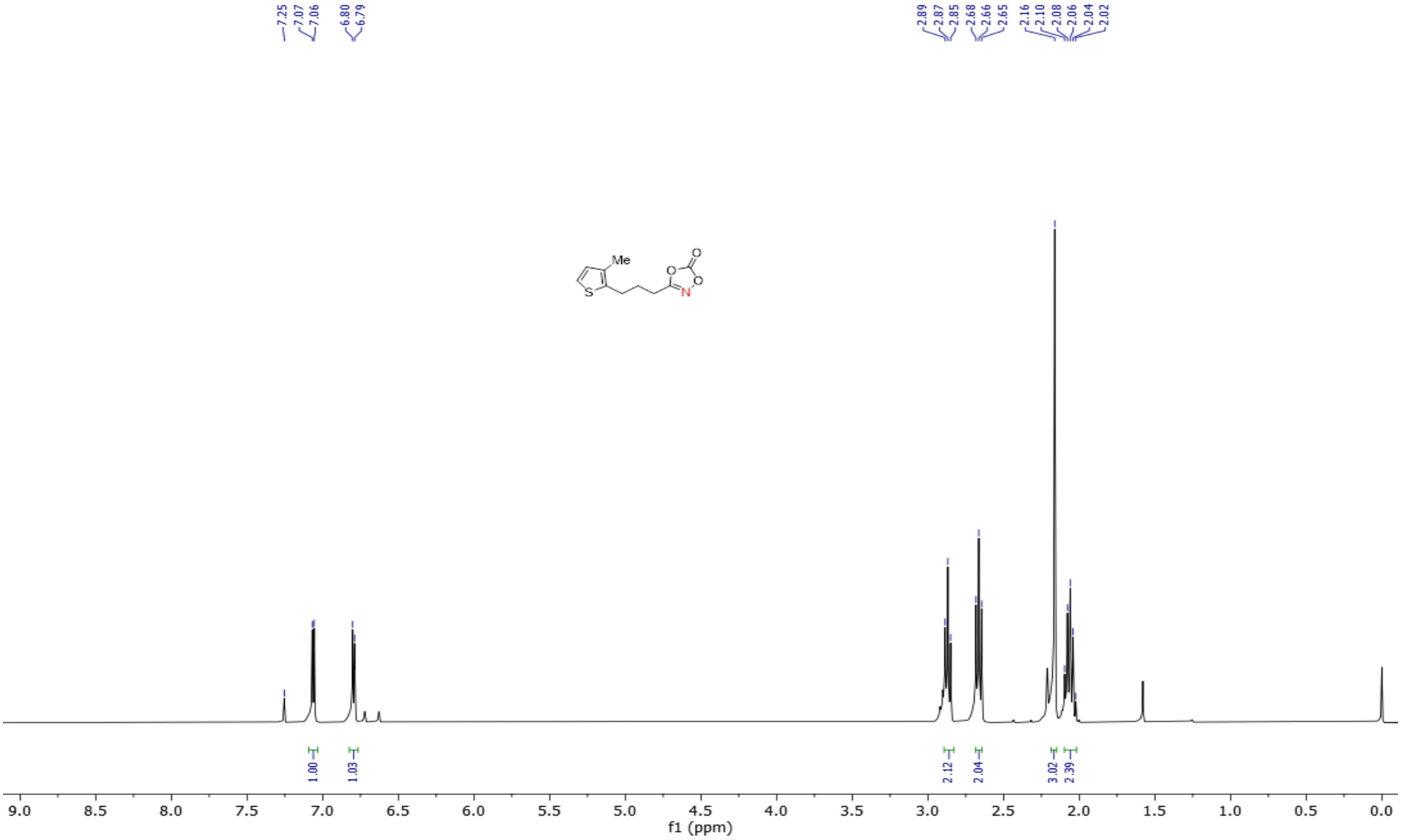
3-(3-(thiophen-2-yl)propyl)-1,4,2-dioxazol-5-one (1m), ^{1}H NMR (500 MHz, $CDCl_3$):



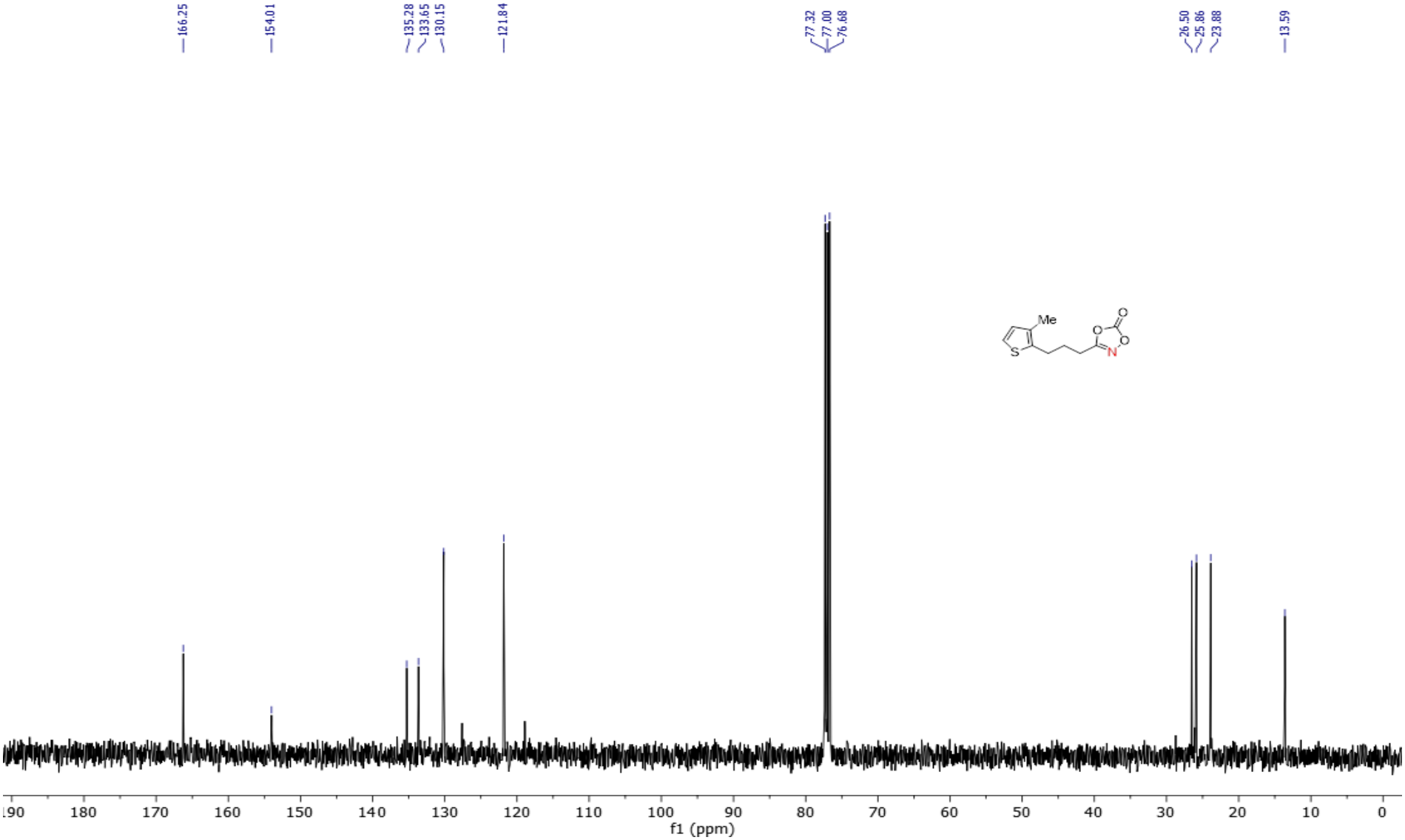
3-(3-(thiophen-2-yl)propyl)-1,4,2-dioxazol-5-one (1m), ^{13}C NMR (126 MHz, $CDCl_3$):



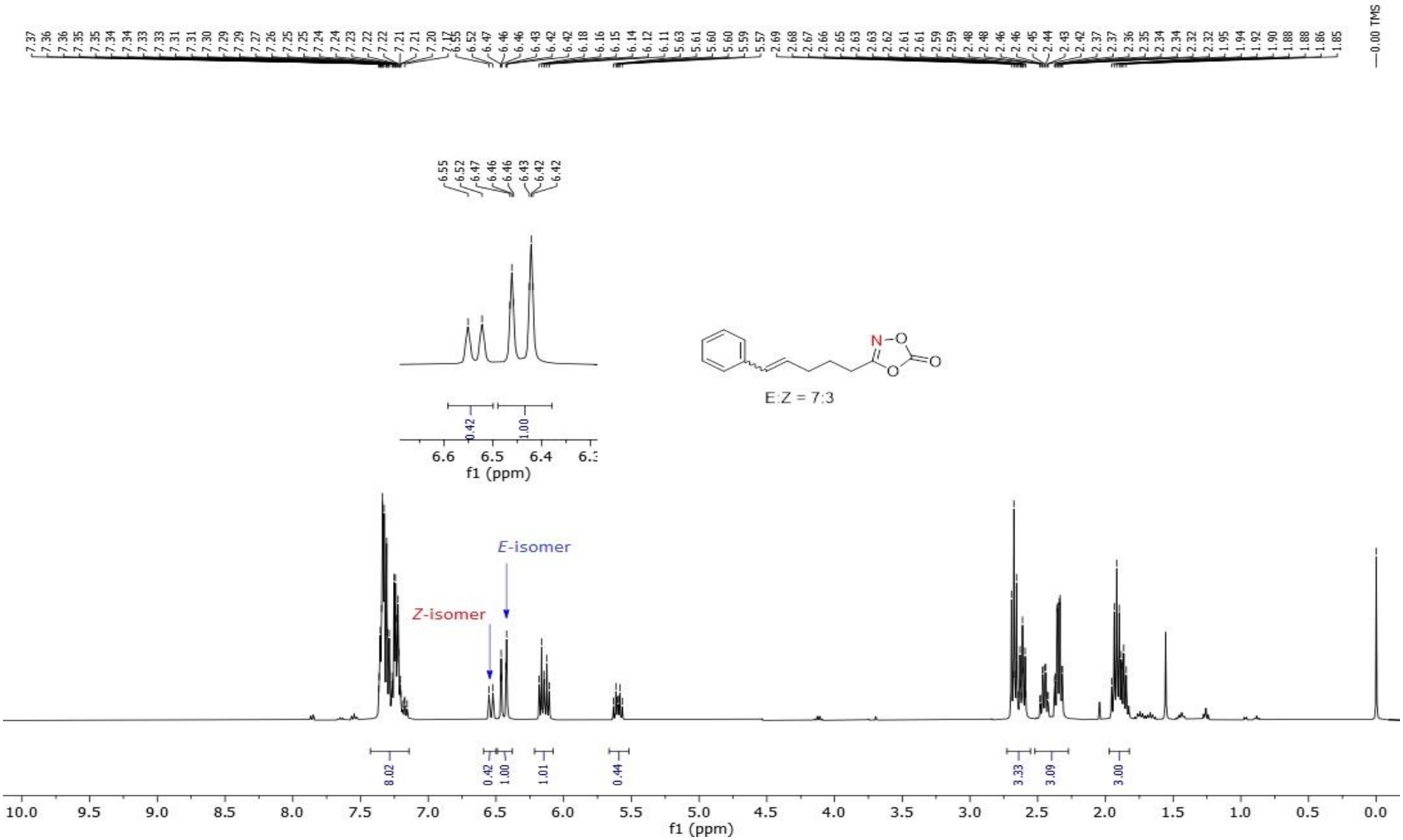
3-(3-(3-methylthiophen-2-yl)propyl)-1,4,2-dioxazol-5-one (1n), ^{1}H NMR (400 MHz, $CDCl_3$):



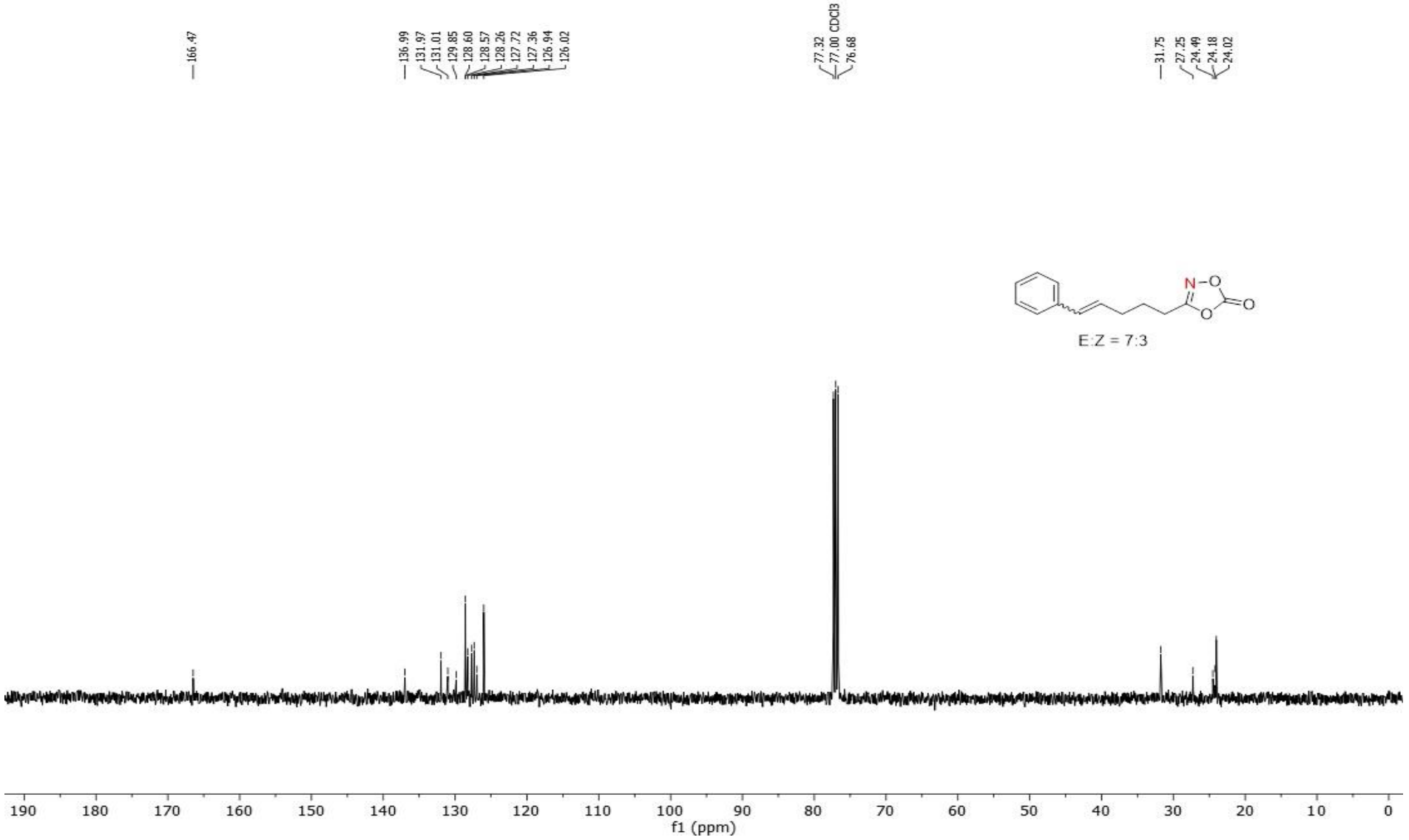
3-(3-(3-methylthiophen-2-yl)propyl)-1,4,2-dioxazol-5-one (1n), ^{13}C NMR (101 MHz, $CDCl_3$):



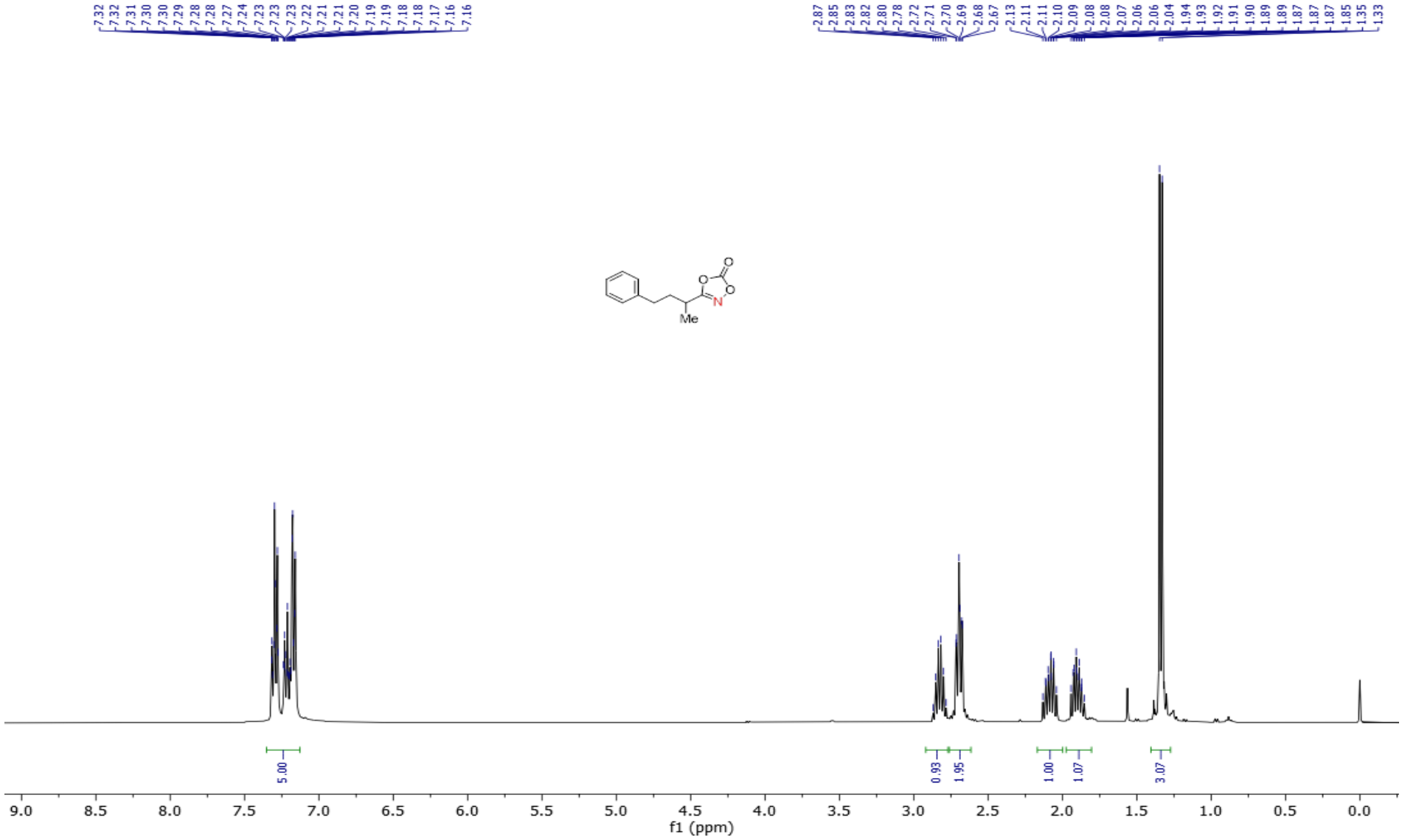
3-(5-phenylpent-4-en-1-yl)-1,4,2-dioxazol-5-one (1o), ^{1}H NMR (400 MHz, $CDCl_3$):



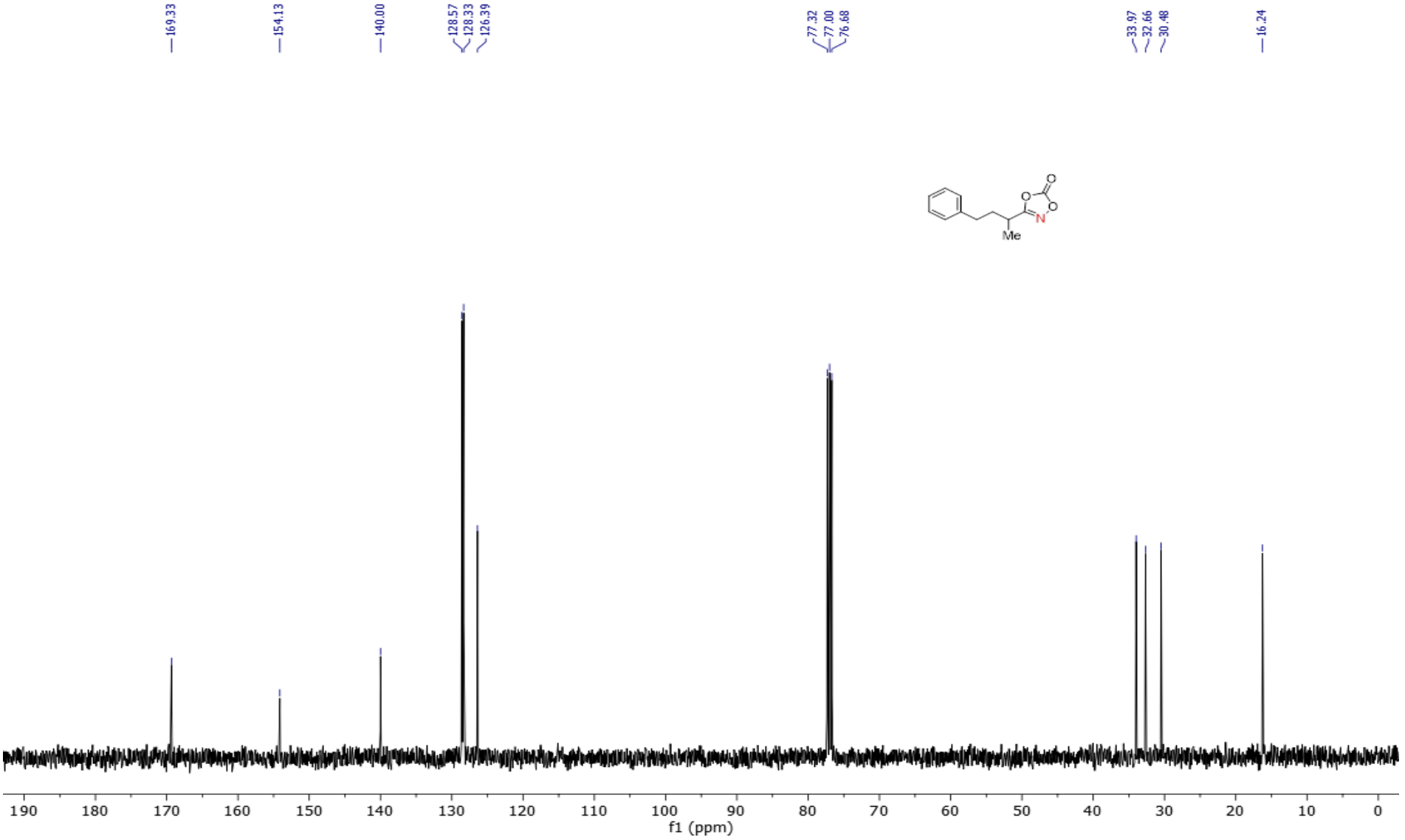
2,5-Dimethylbenzyl 3,3,3-trifluoro-2-(m-tolylamino)propanoate (5d), ^{13}C NMR (101 MHz, $CDCl_3$):



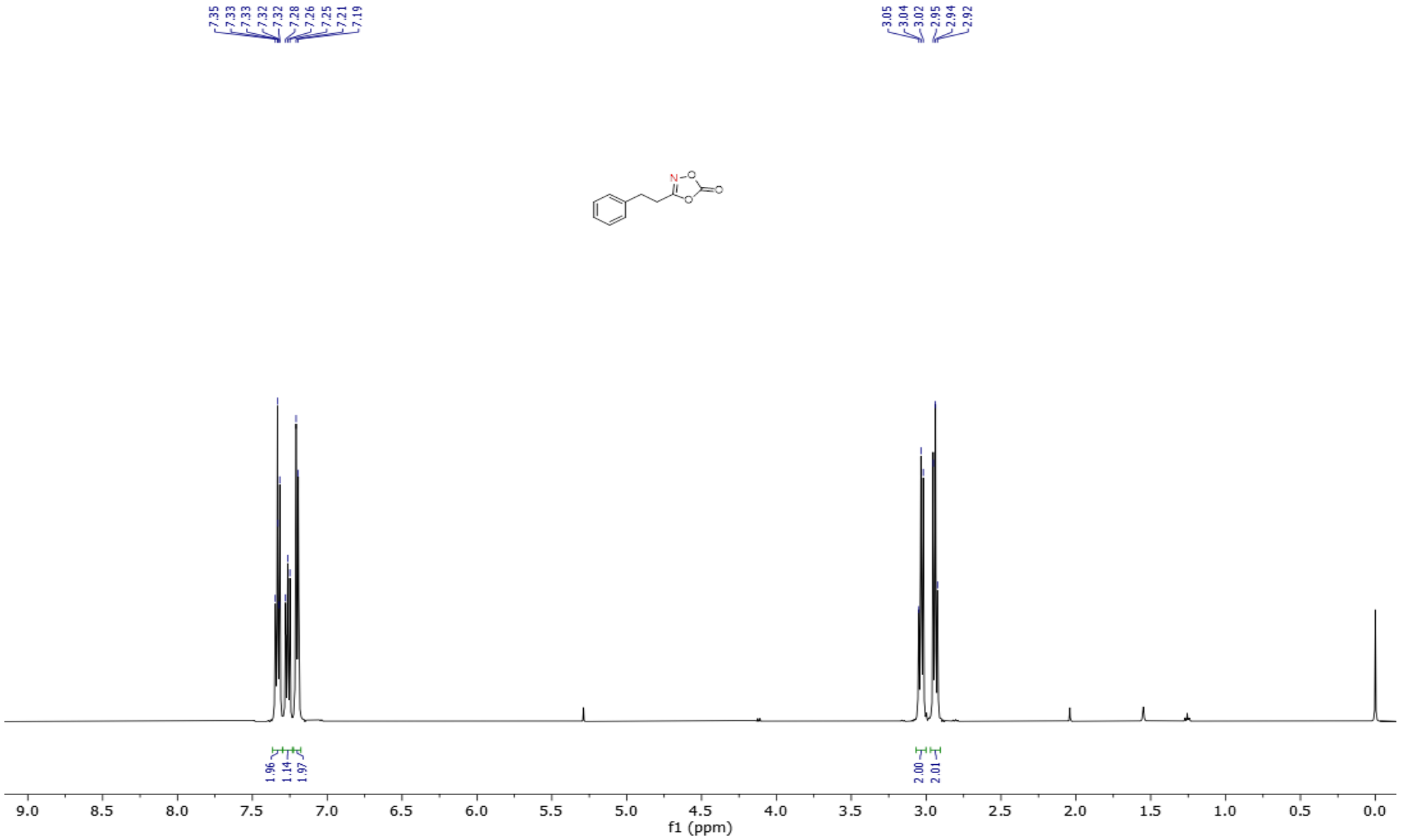
3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (1p), ^{1}H NMR (400 MHz, $CDCl_3$):



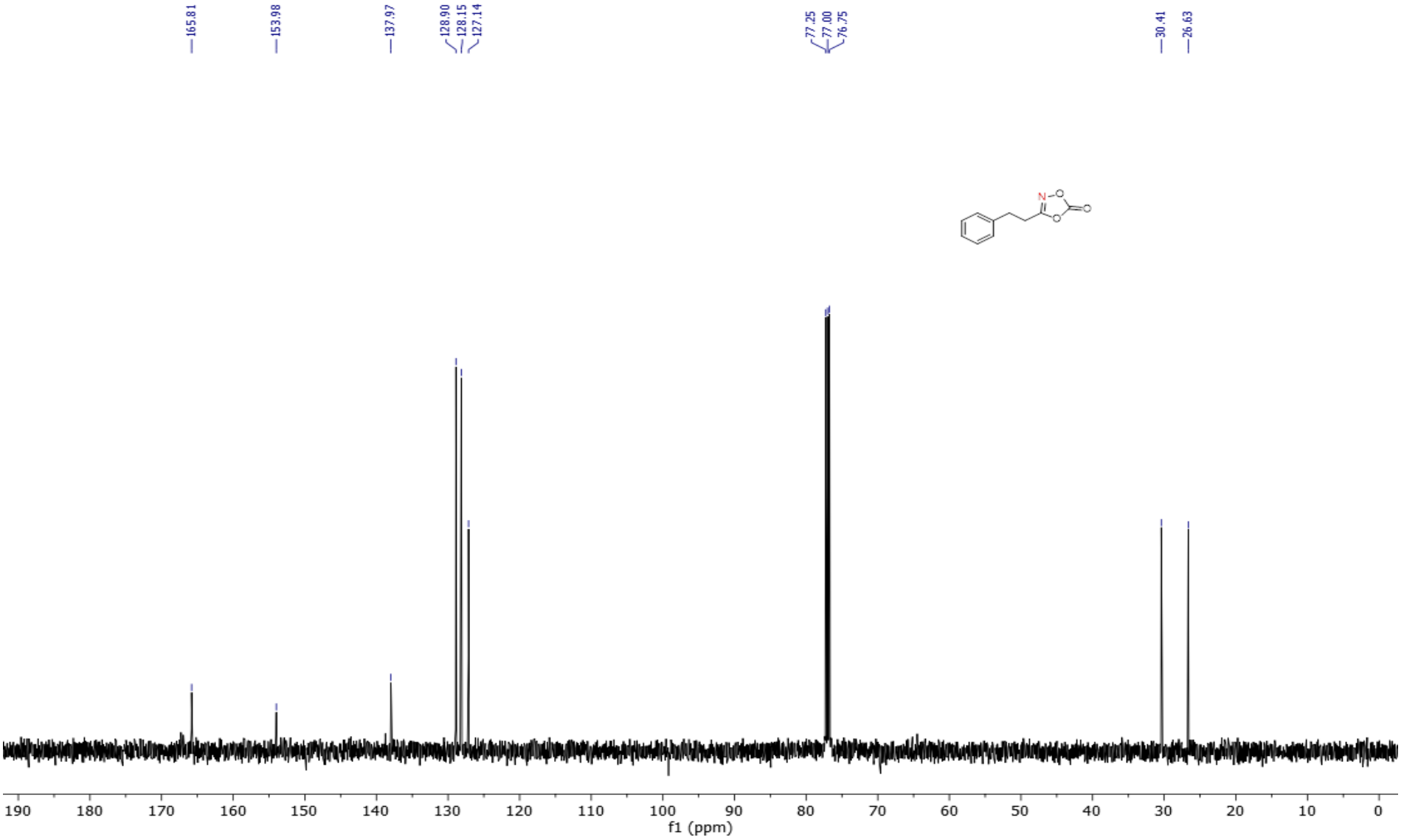
3-(3-phenylpropyl)-1,4,2-dioxazol-5-one (1p), ^{13}C NMR (101 MHz, $CDCl_3$):



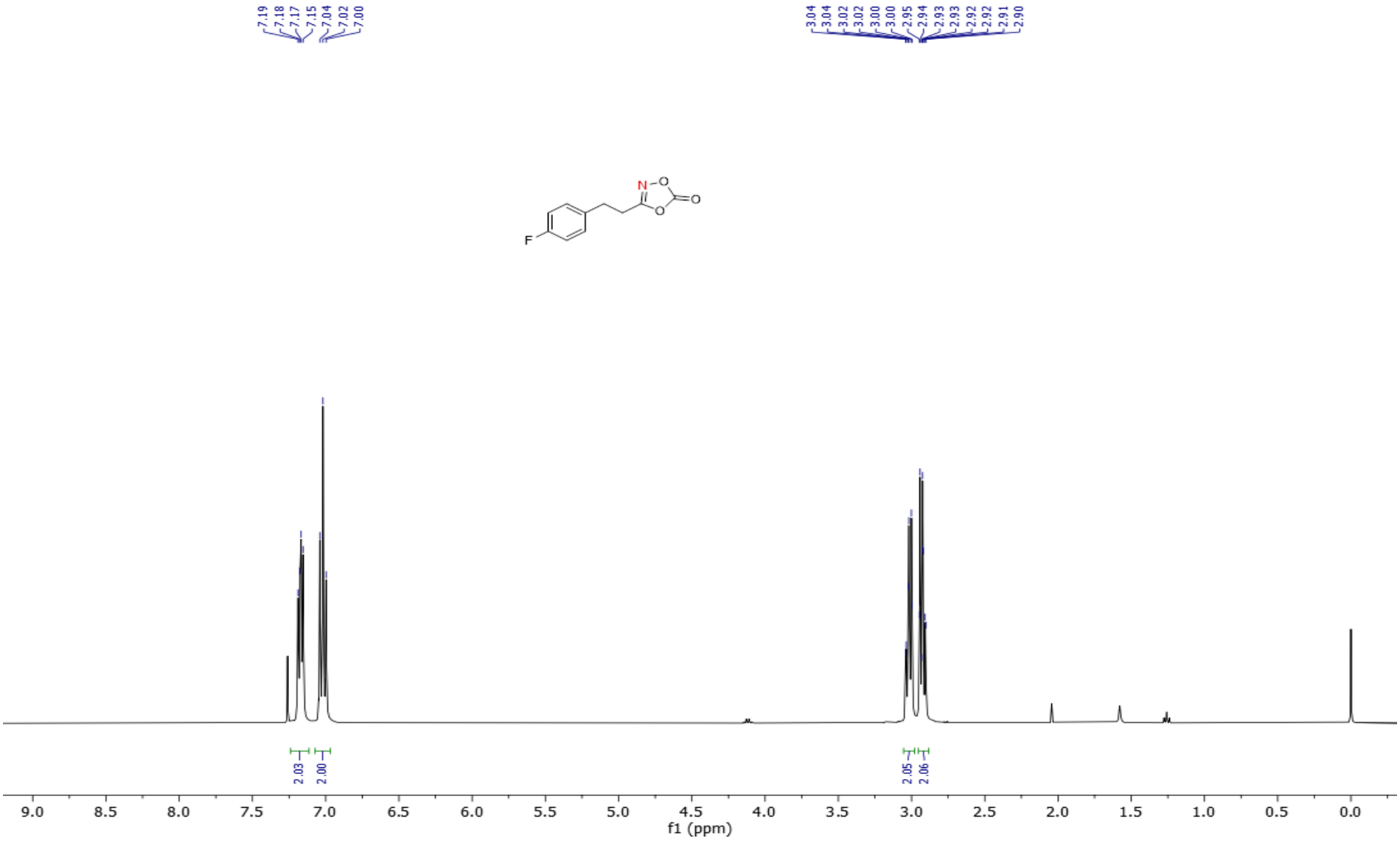
3-phenylethyl-1,4,2-dioxazol-5-one (3a), ^{1}H NMR (500 MHz, $CDCl_3$):



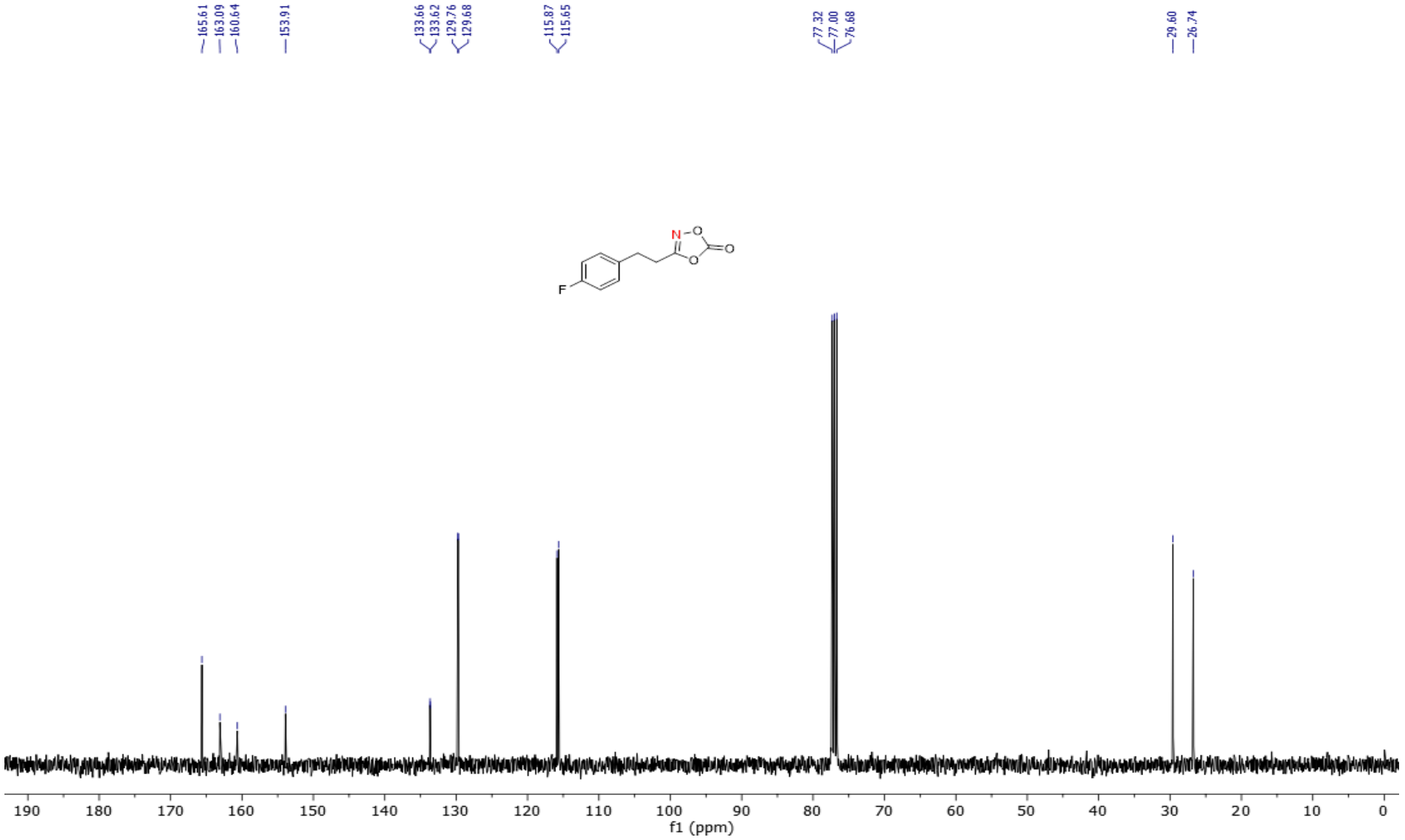
3-phenylethyl-1,4,2-dioxazol-5-one (3a), ^{13}C NMR (126 MHz, $CDCl_3$):



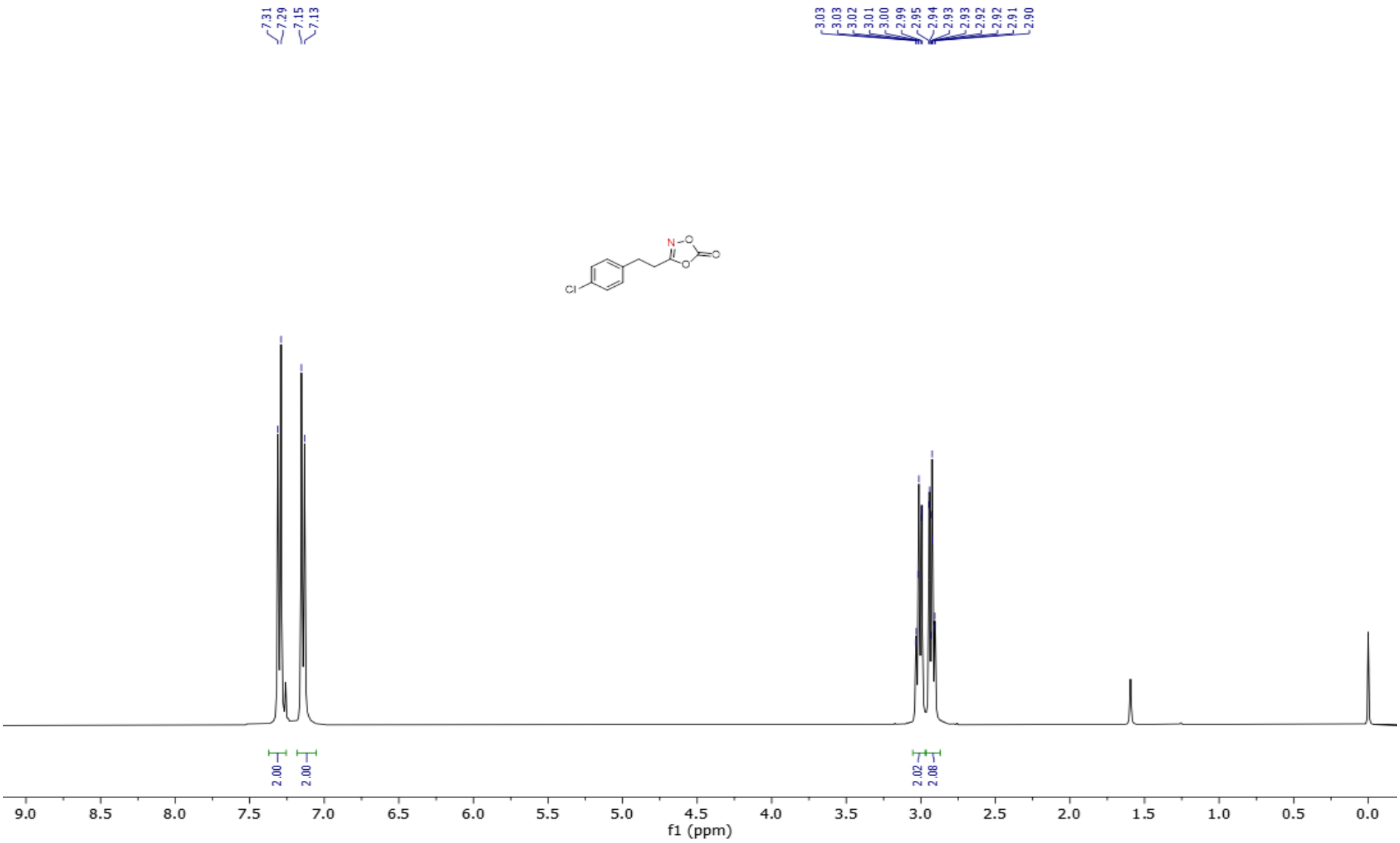
3-(4-fluorophenethyl)-1,4,2-dioxazol-5-one (**3b**), ^{1}H NMR (400 MHz, $CDCl_3$):



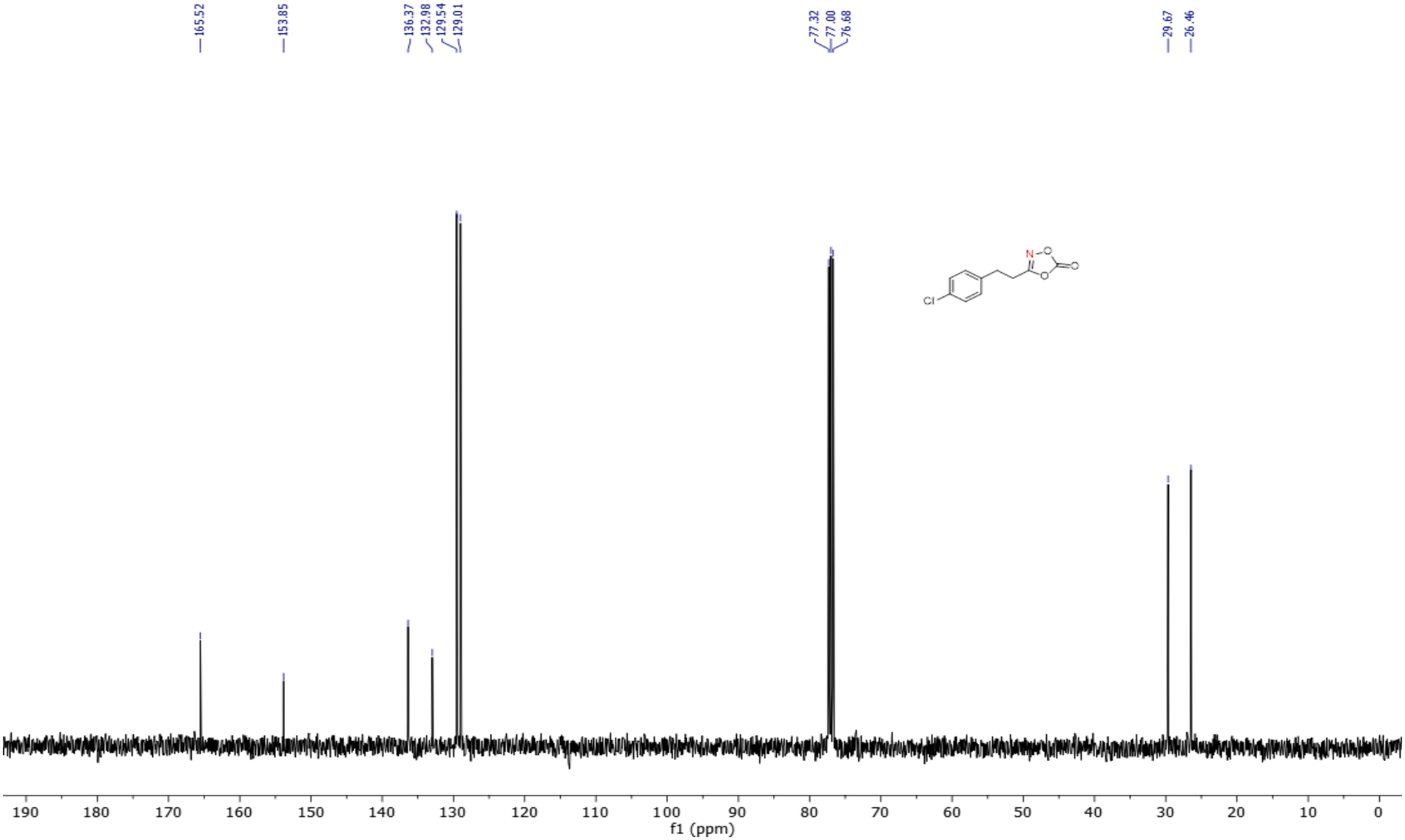
3-(4-fluorophenethyl)-1,4,2-dioxazol-5-one (**3b**), ^{13}C NMR (101 MHz, $CDCl_3$):



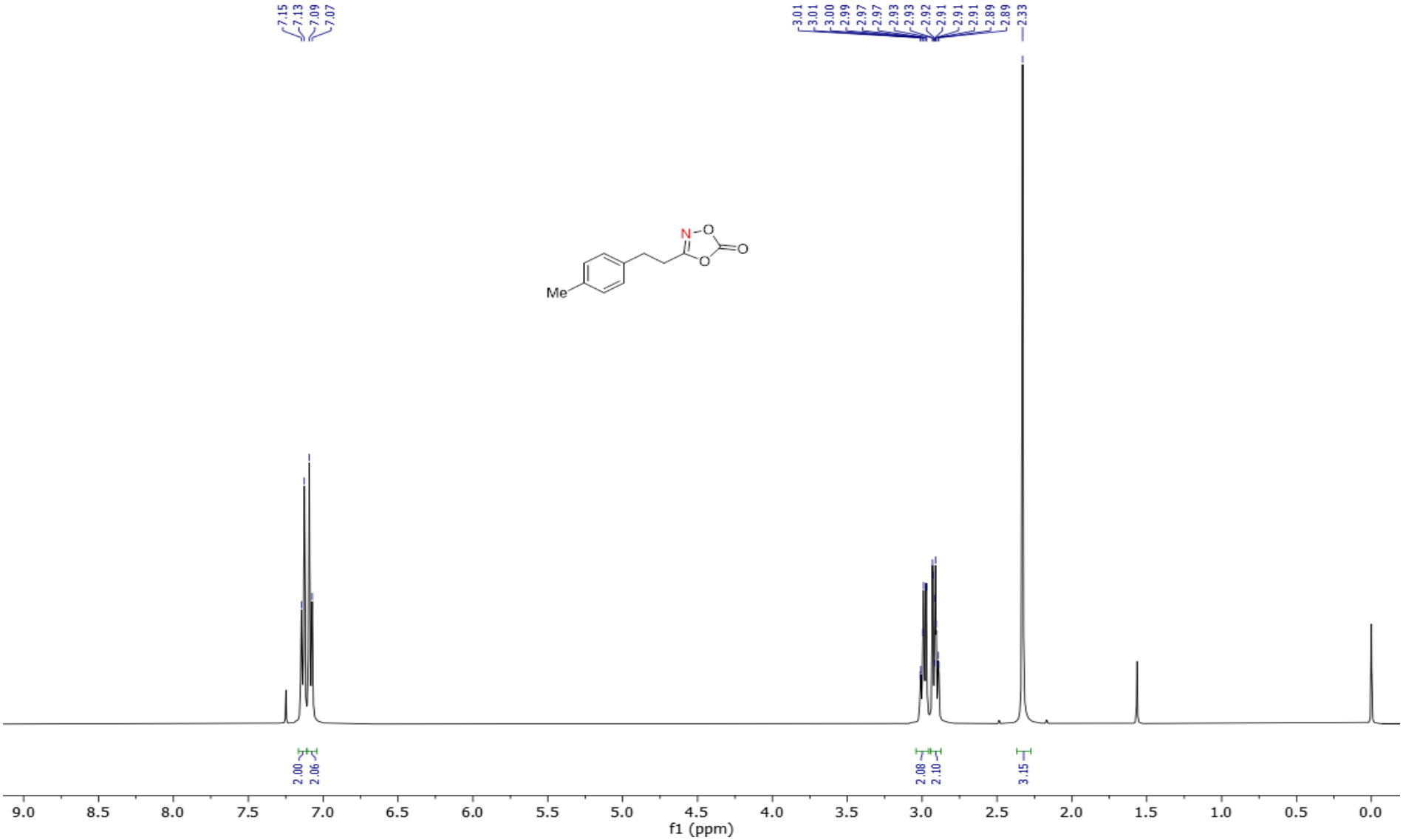
3-(4-chlorophenethyl)-1,4,2-dioxazol-5-one (**3c**), ^{1}H NMR (400 MHz, $CDCl_3$):



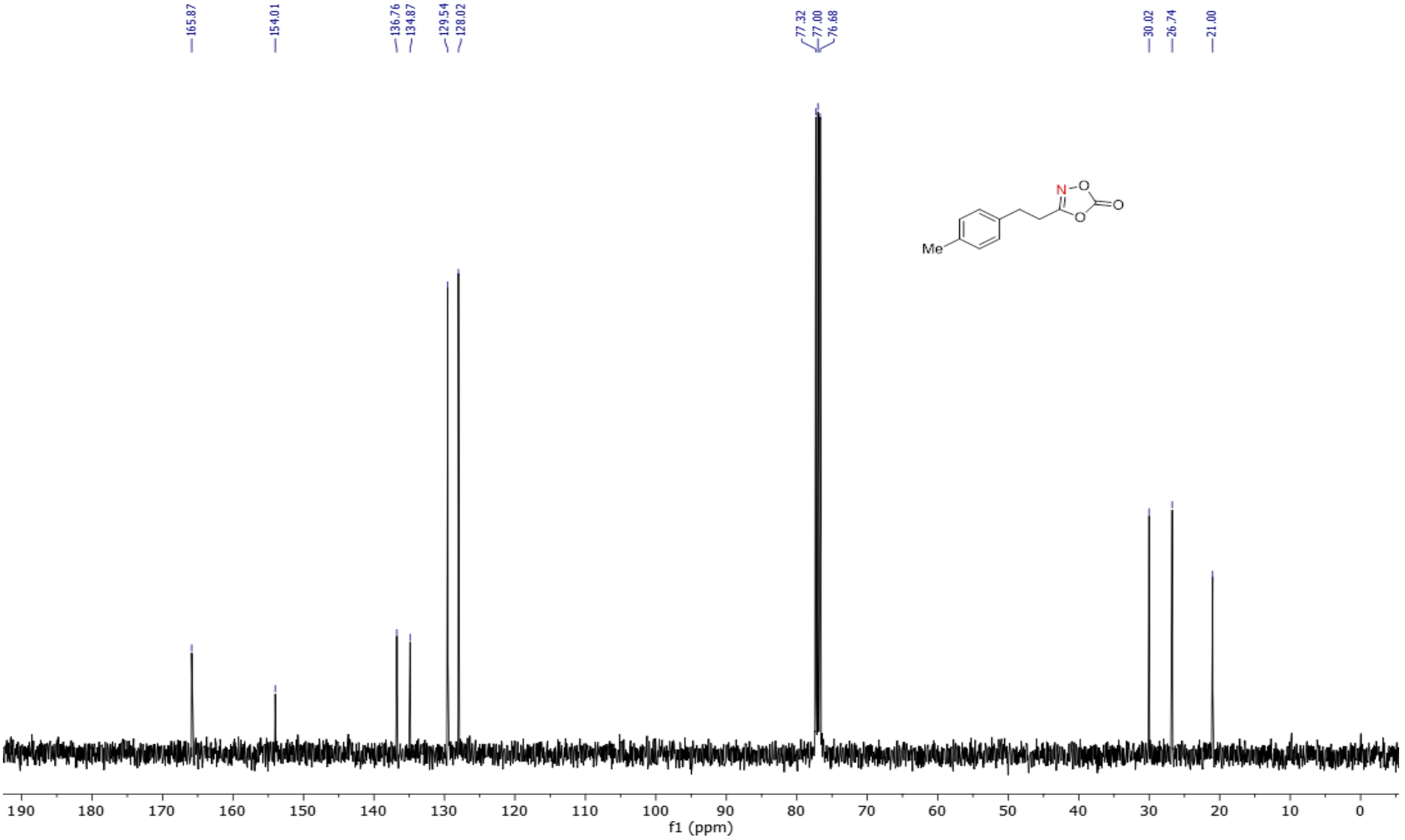
3-(4-chlorophenethyl)-1,4,2-dioxazol-5-one (**3c**), ^{13}C NMR (101 MHz, $CDCl_3$):



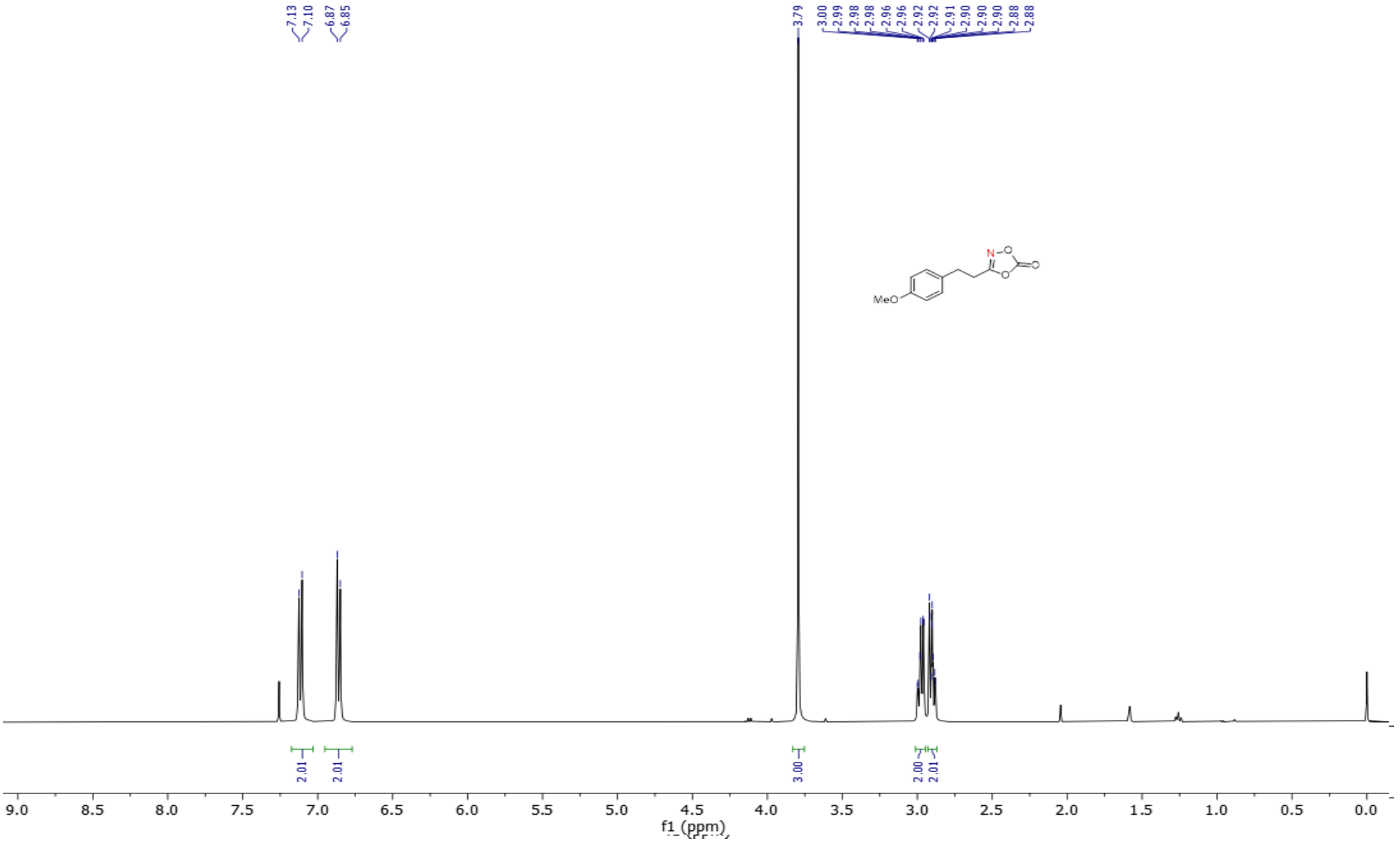
3-(4-methylphenethyl)-1,4,2-dioxazol-5-one (**3d**), ^{1}H NMR (400 MHz, $CDCl_3$):



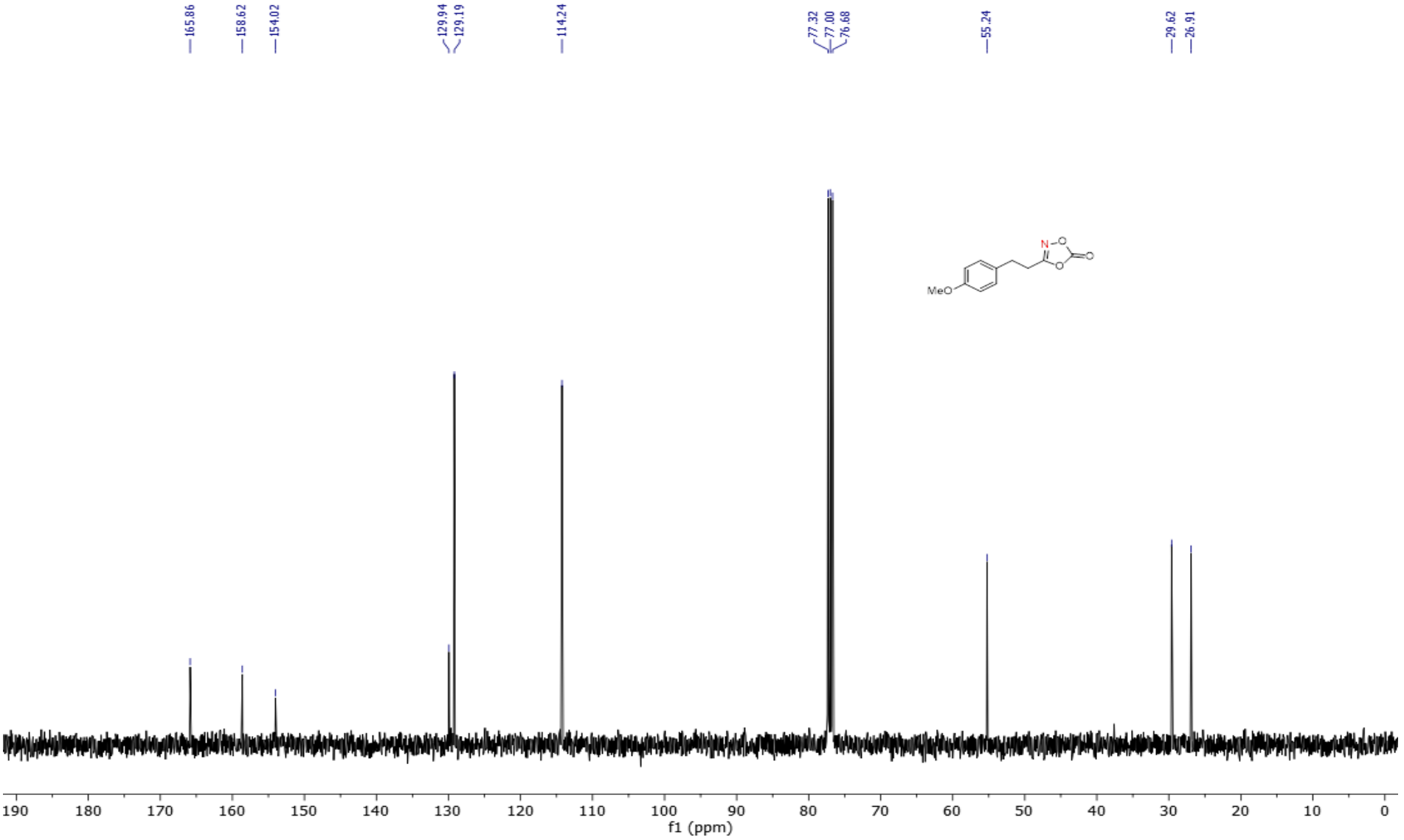
3-(4-methylphenethyl)-1,4,2-dioxazol-5-one (**3d**), ^{13}C NMR (101 MHz, $CDCl_3$):



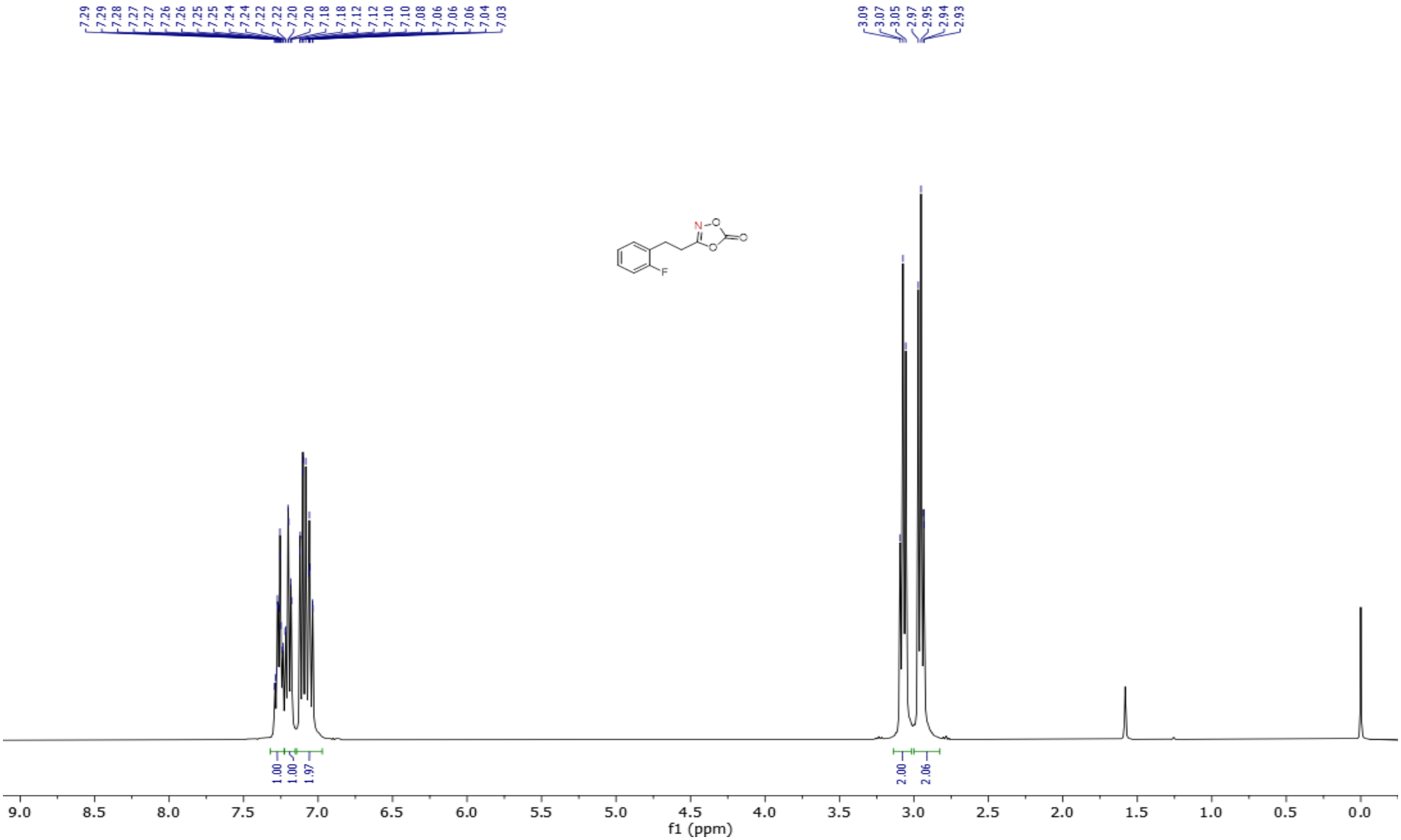
3-(4-methoxyphenethyl)-1,4,2-dioxazol-5-one (**3e**), ^{1}H NMR (400 MHz, $CDCl_3$):



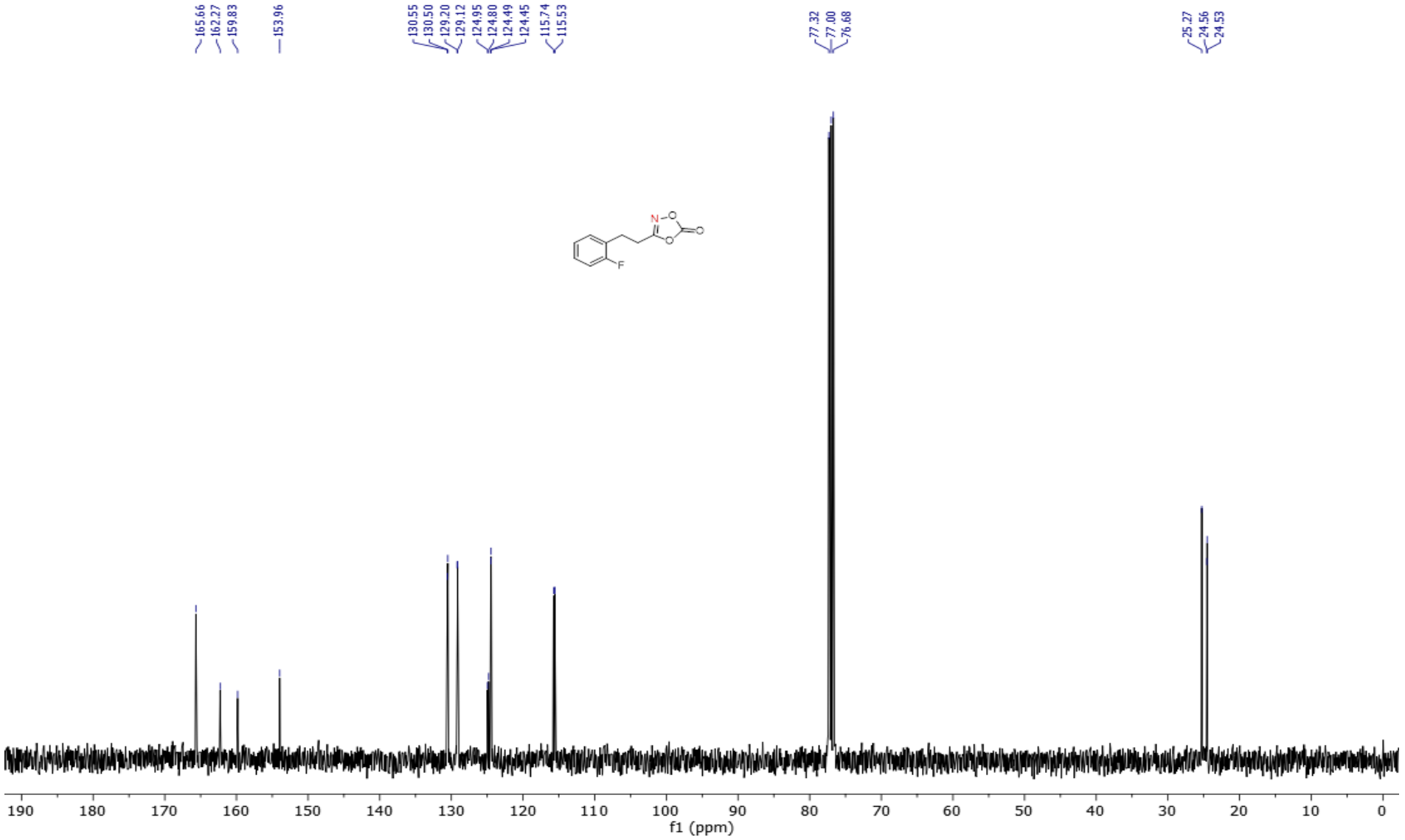
3-(4-methoxyphenethyl)-1,4,2-dioxazol-5-one (**3e**), ^{13}C NMR (101 MHz, $CDCl_3$):



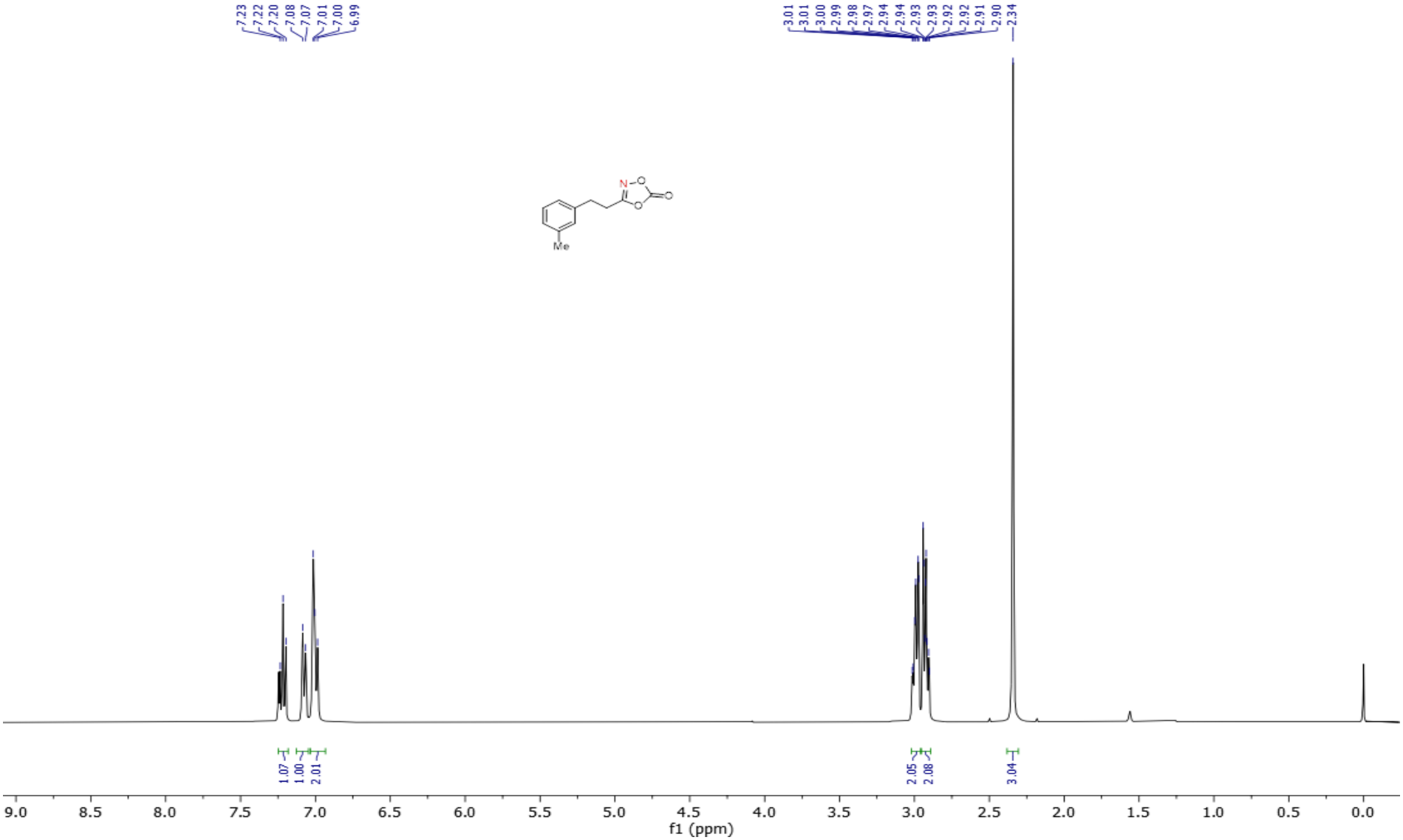
3-(2-fluorophenethyl)-1,4,2-dioxazol-5-one (**3f**), ^{1}H NMR (400 MHz, $CDCl_3$):



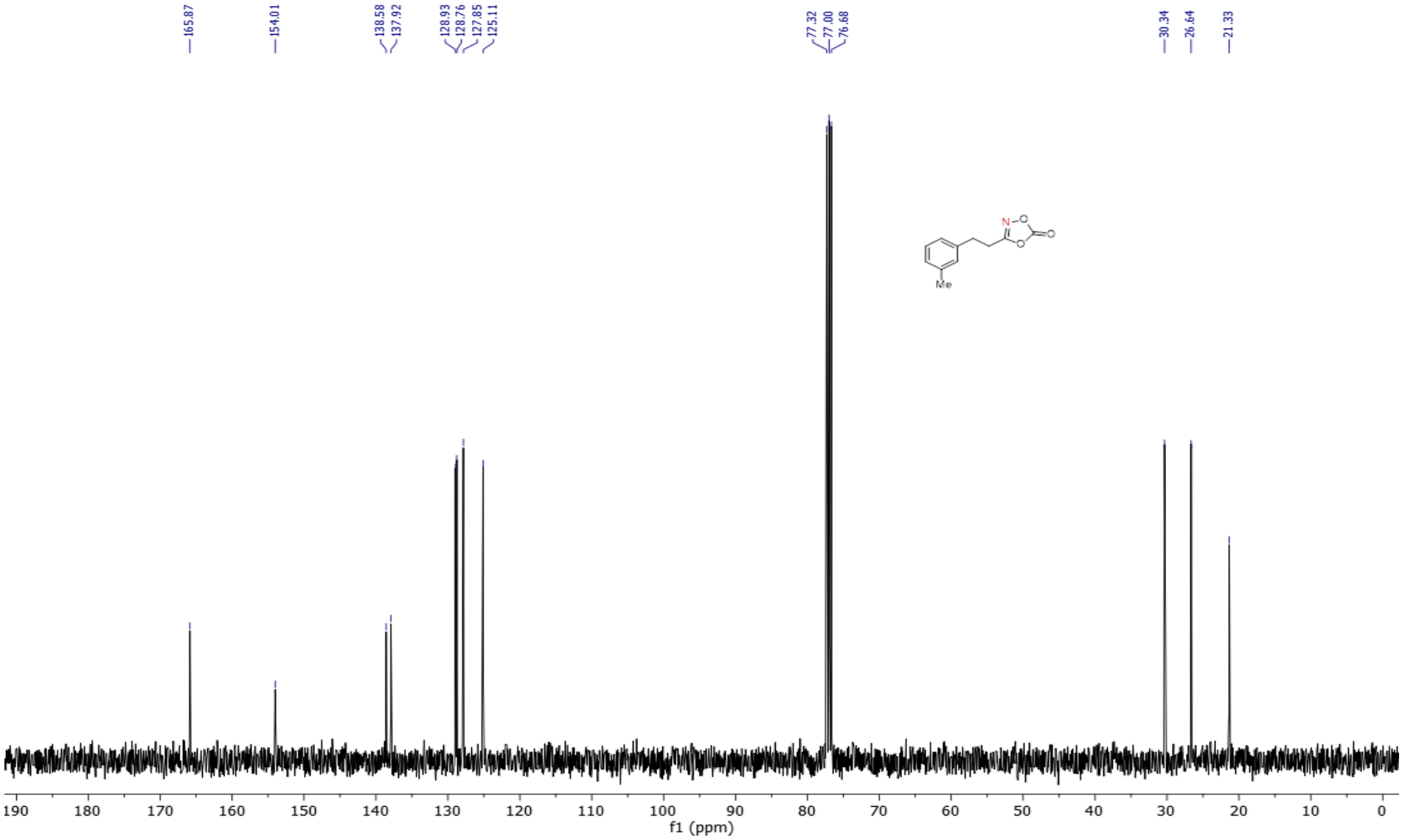
3-(2-fluorophenethyl)-1,4,2-dioxazol-5-one (**3f**), ^{13}C NMR (101 MHz, $CDCl_3$):



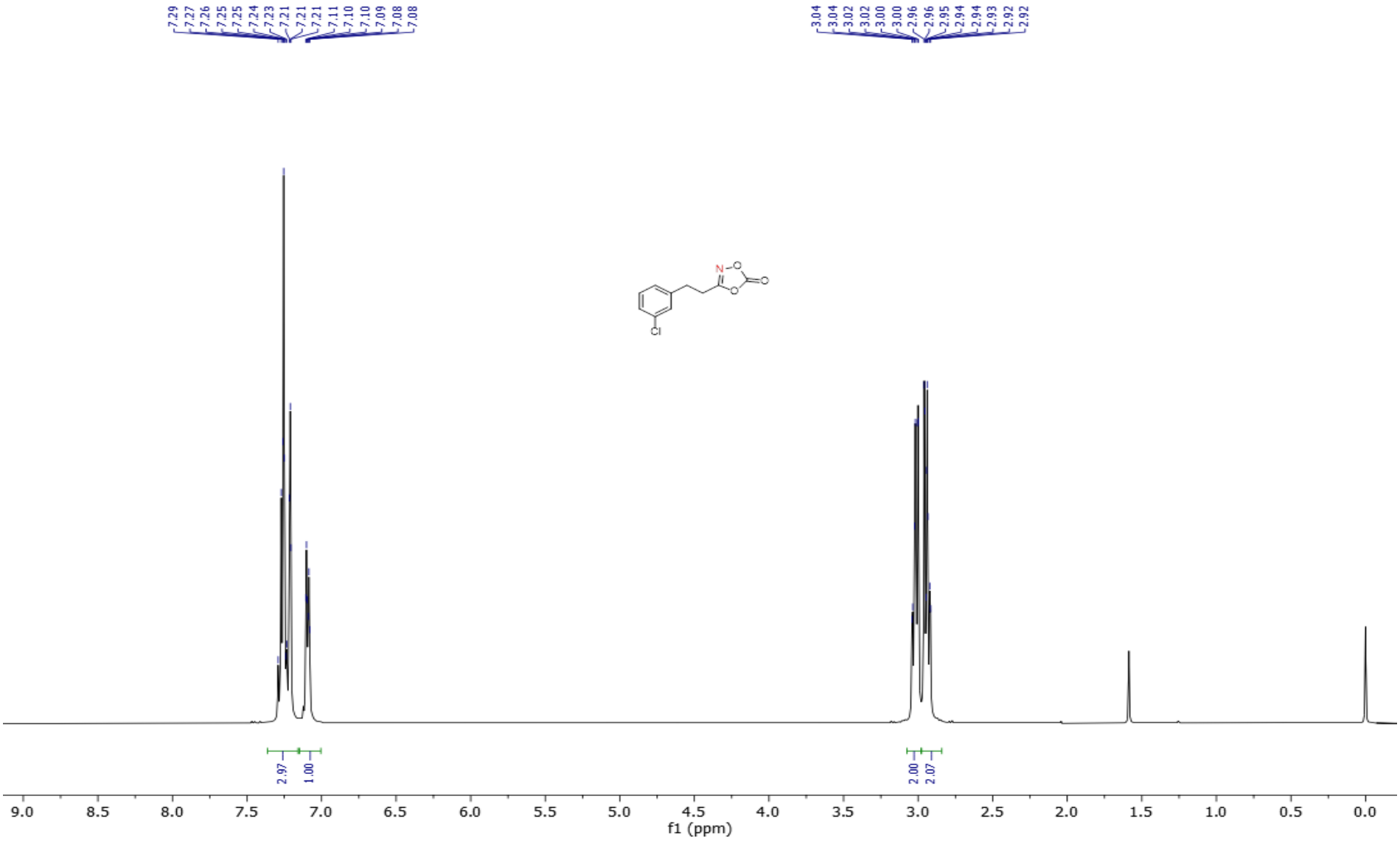
3-(3-methylphenethyl)-1,4,2-dioxazol-5-one (**3g**), ^{1}H NMR (400 MHz, $CDCl_3$):



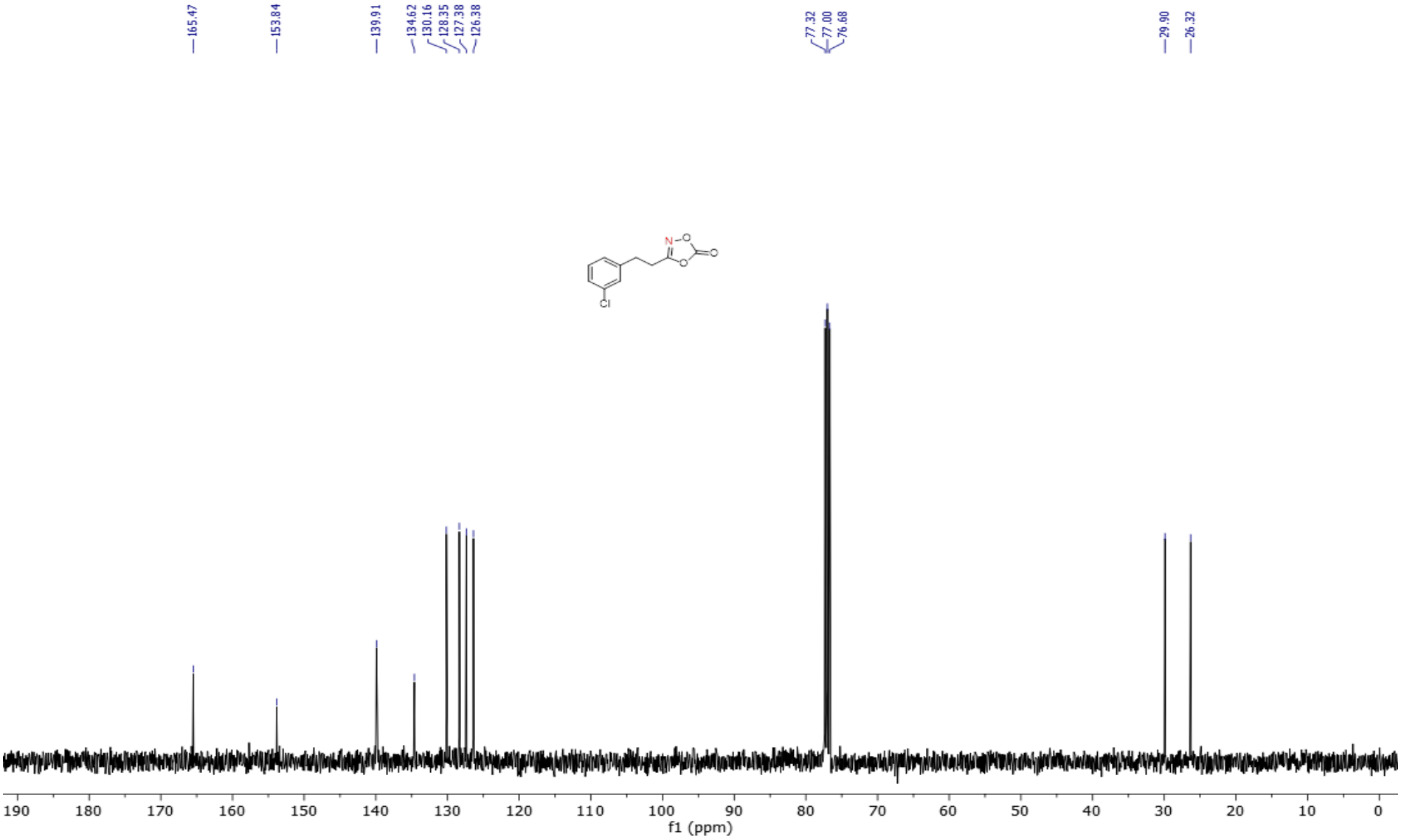
3-(3-methylphenethyl)-1,4,2-dioxazol-5-one (**3g**), ^{13}C NMR (101 MHz, $CDCl_3$):



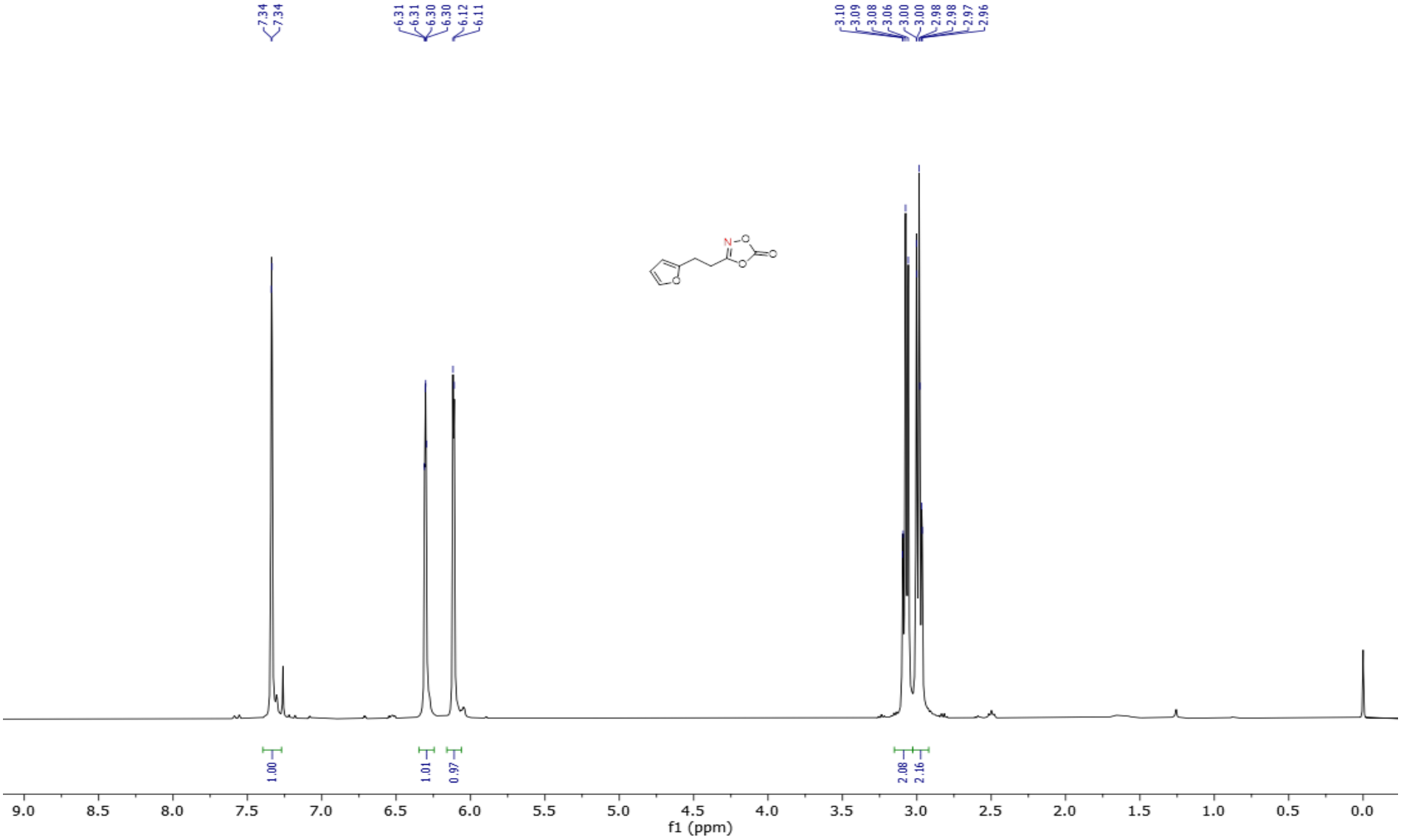
3-(3-chlorophenethyl)-1,4,2-dioxazol-5-one (**3h**), ^{1}H NMR (400 MHz, $CDCl_3$):



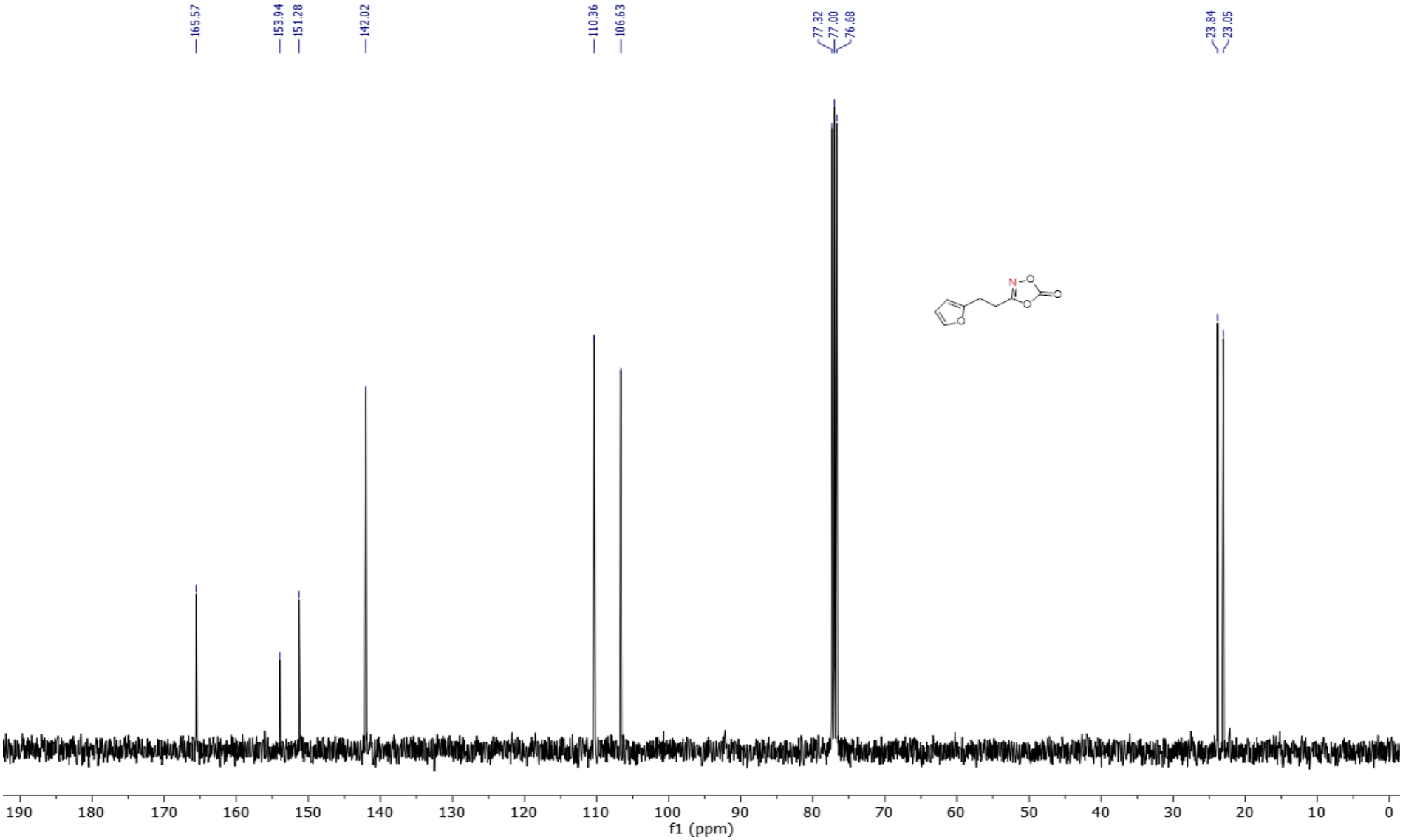
3-(3-chlorophenethyl)-1,4,2-dioxazol-5-one (**3h**), ^{13}C NMR (101 MHz, $CDCl_3$):



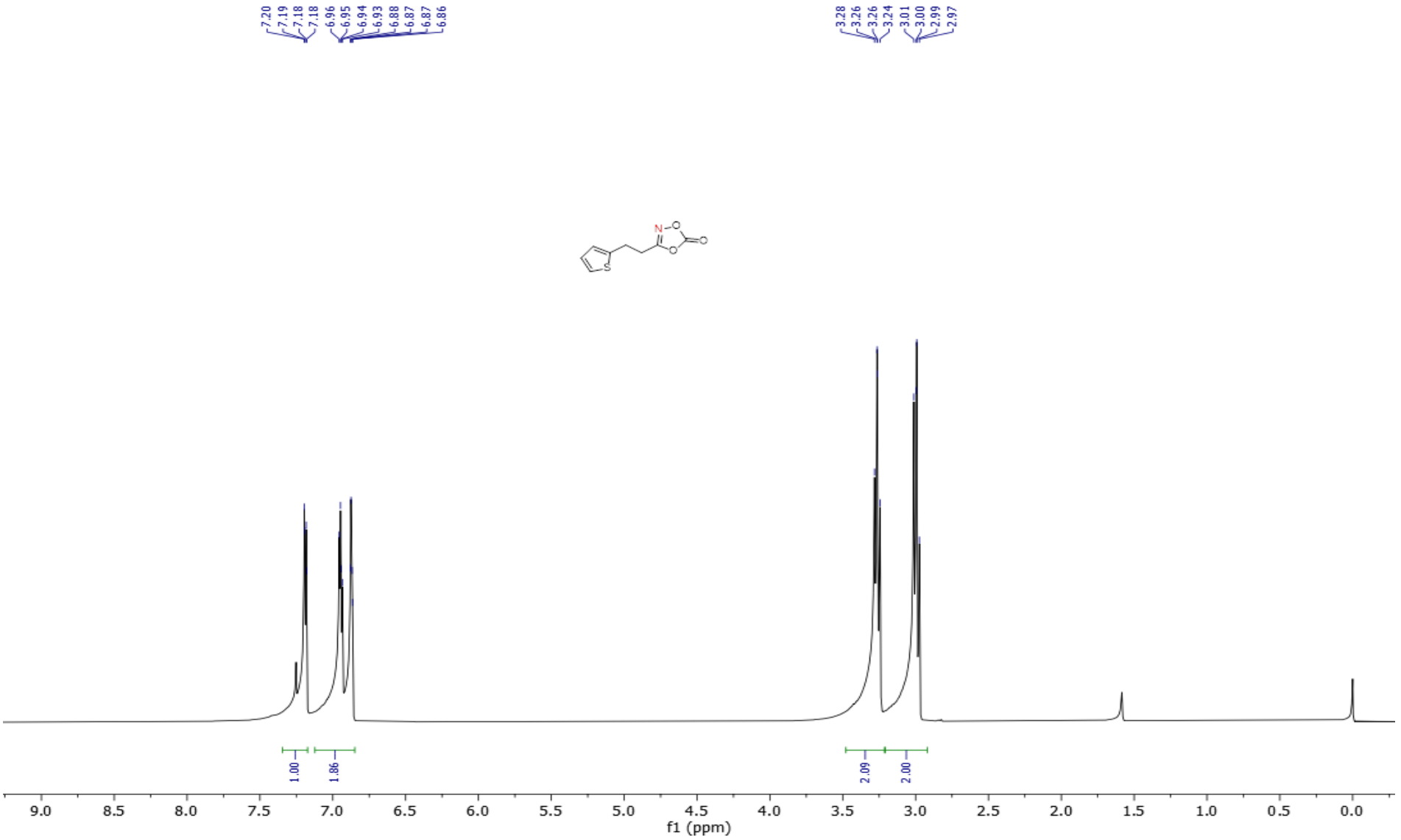
3-(2-(furan-2-yl)ethyl)-1,4,2-dioxazol-5-one (**3i**), ^{1}H NMR (400 MHz, $CDCl_3$):



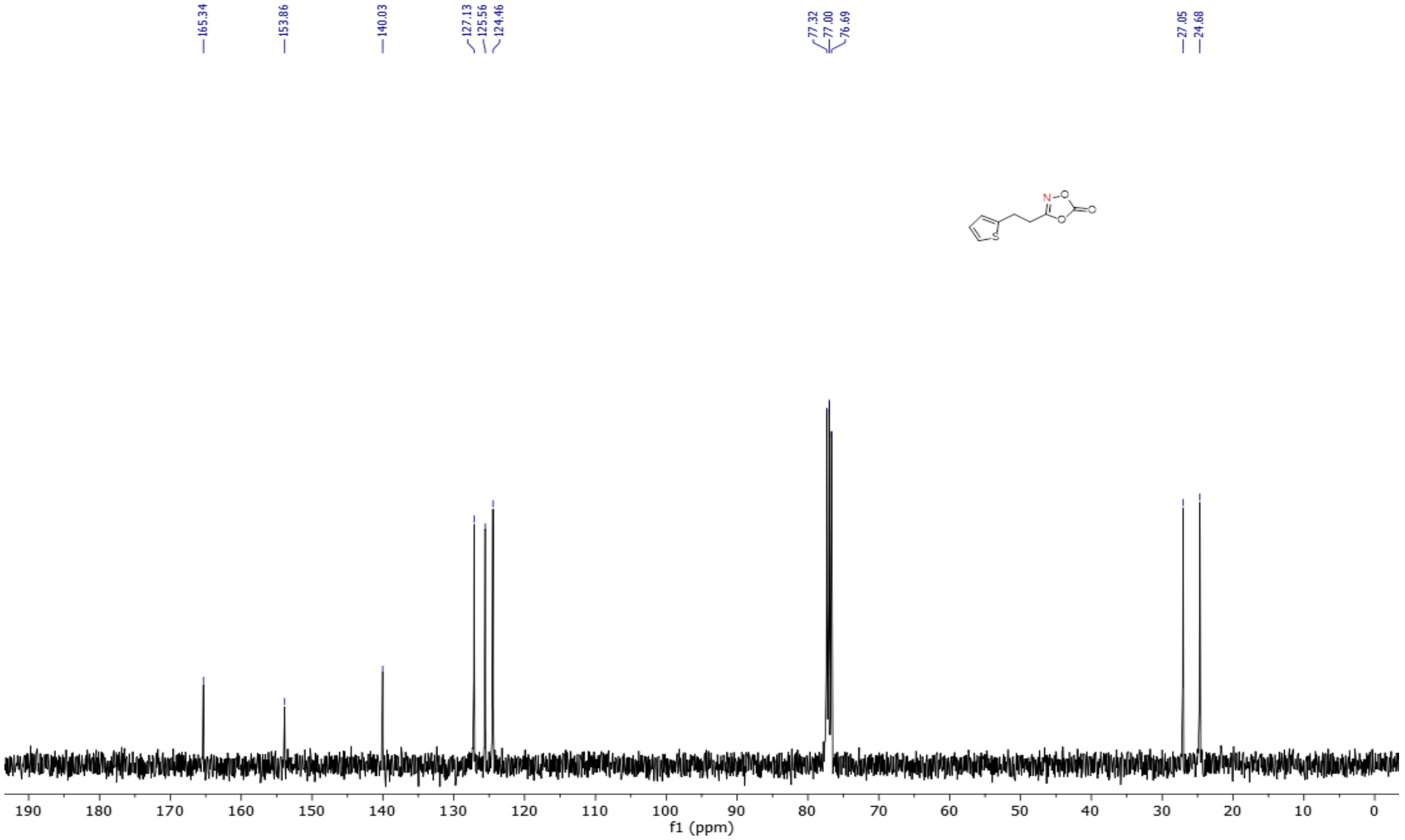
3-(2-(furan-2-yl)ethyl)-1,4,2-dioxazol-5-one (**3i**), ^{13}C NMR (101 MHz, $CDCl_3$):



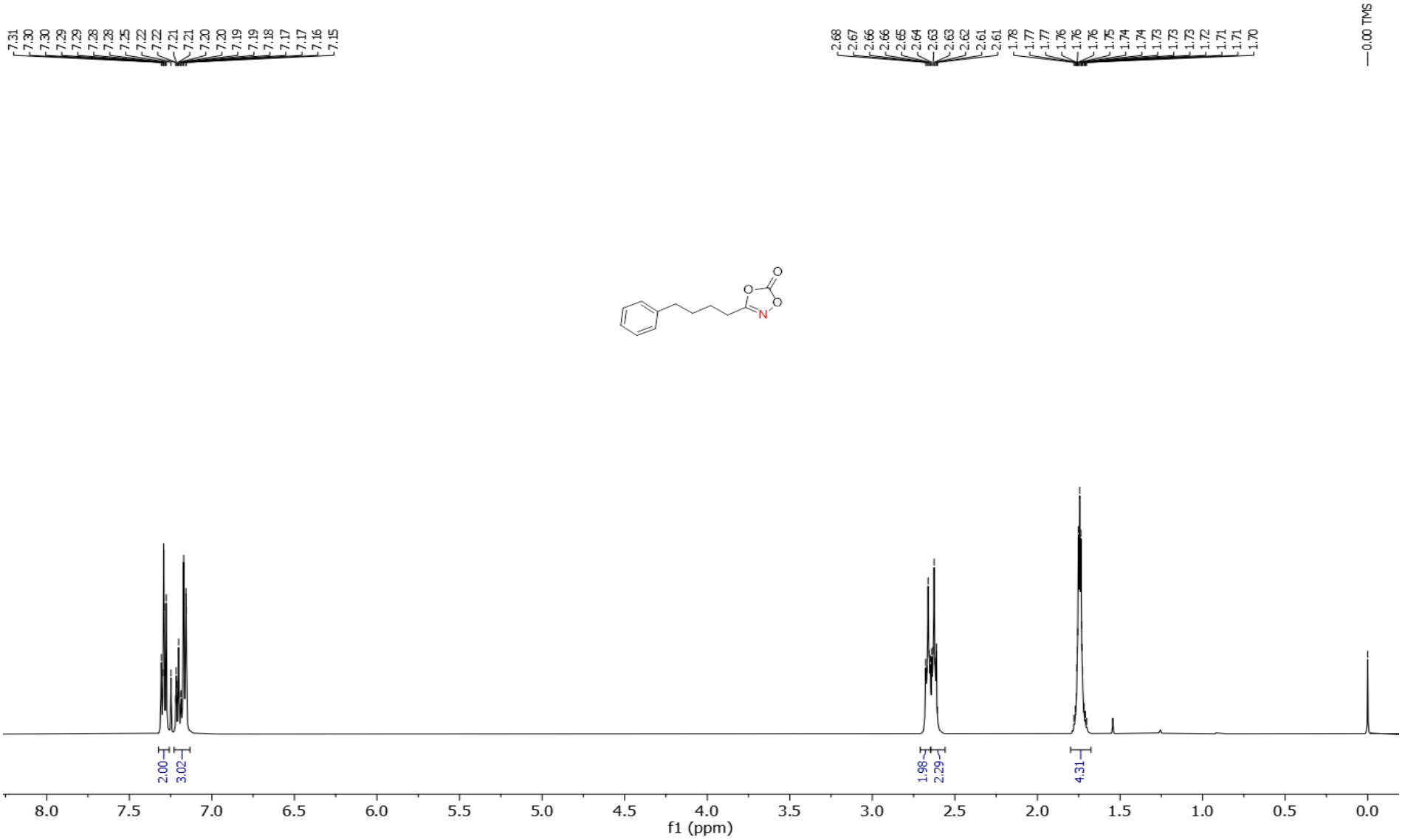
3-(2-(thiophen-2-yl)ethyl)-1,4,2-dioxazol-5-one (**3j**), ^{1}H NMR (400 MHz, $CDCl_3$):



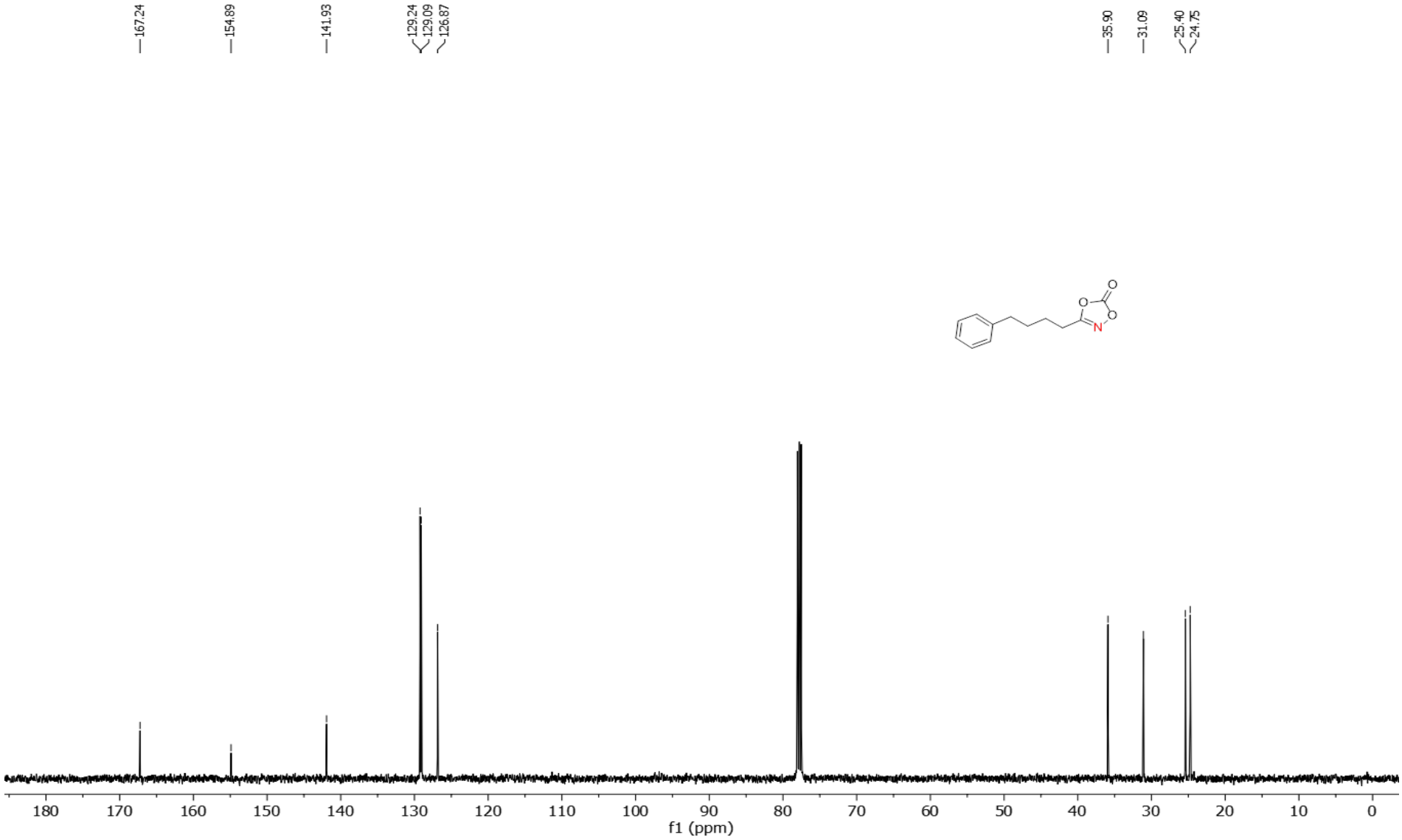
3-(2-(thiophen-2-yl)ethyl)-1,4,2-dioxazol-5-one (**3j**), ^{13}C NMR (101 MHz, $CDCl_3$):



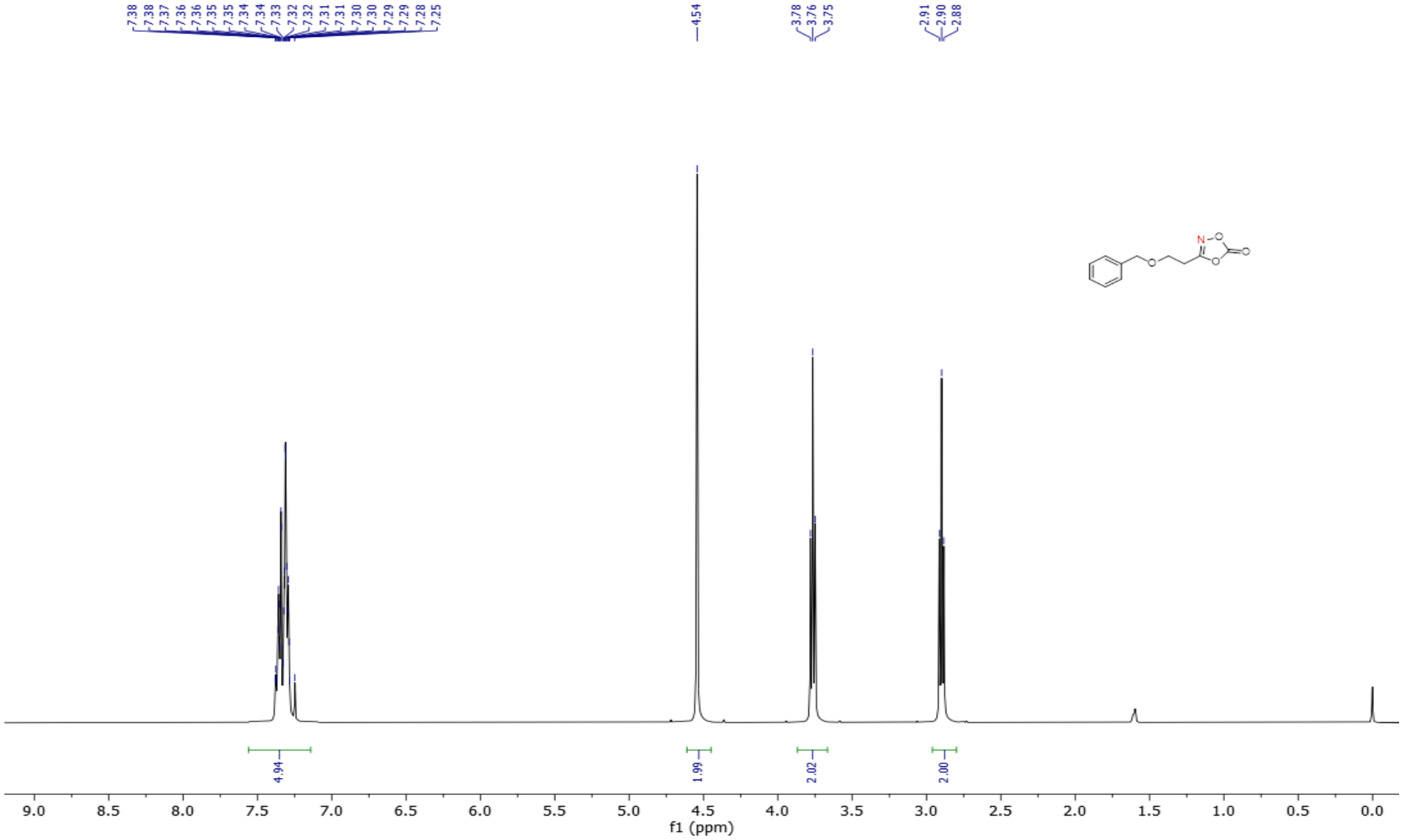
2,5-Dimethylbenzyl 3,3,3-trifluoro-2-(m-tolylamino)propanoate (**5a**), ^{1}H NMR (500 MHz, $CDCl_3$):



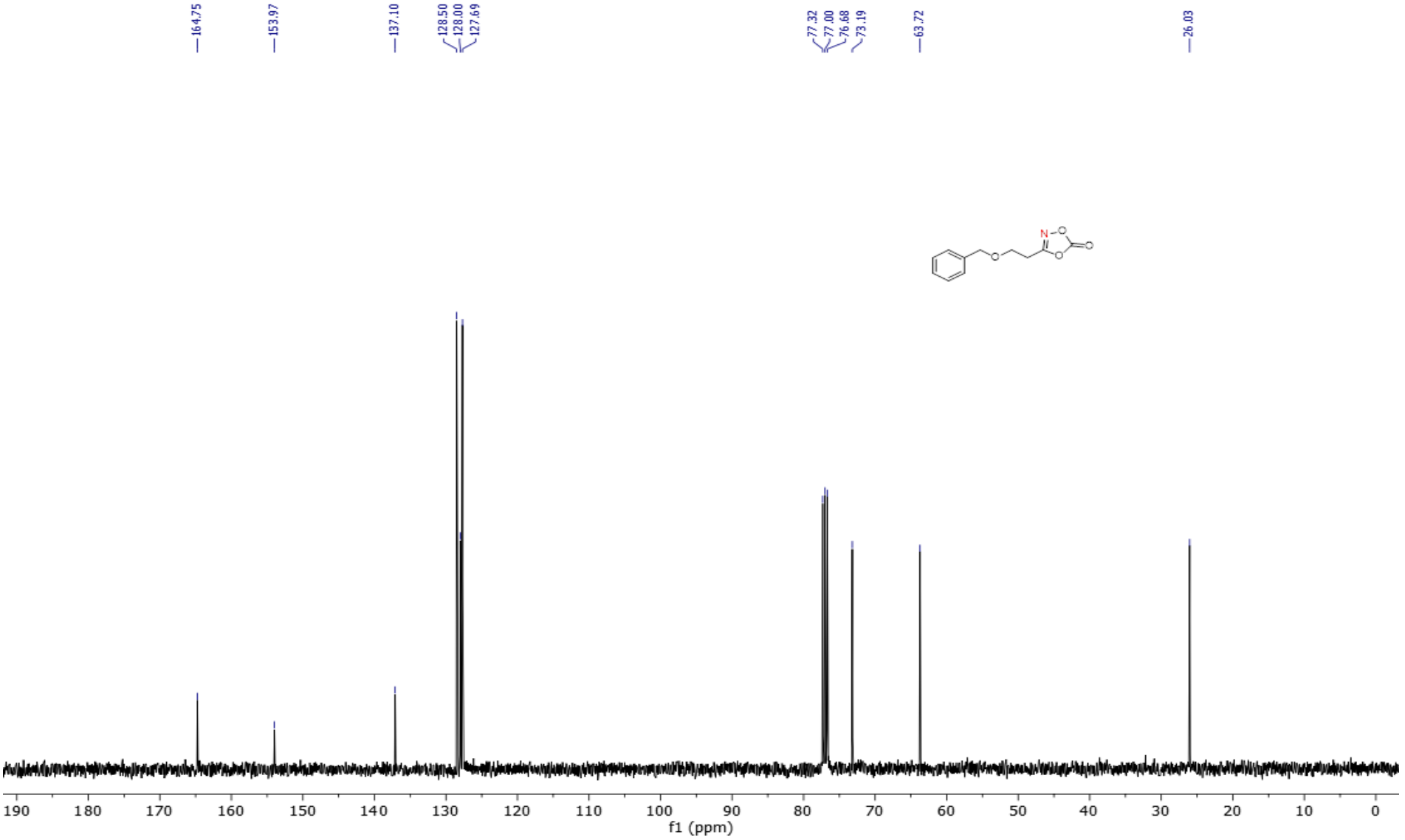
3-(4-phenylbutyl)-1,4,2-dioxazol-5-one (**5a**), ^{13}C NMR (126 MHz, $CDCl_3$):



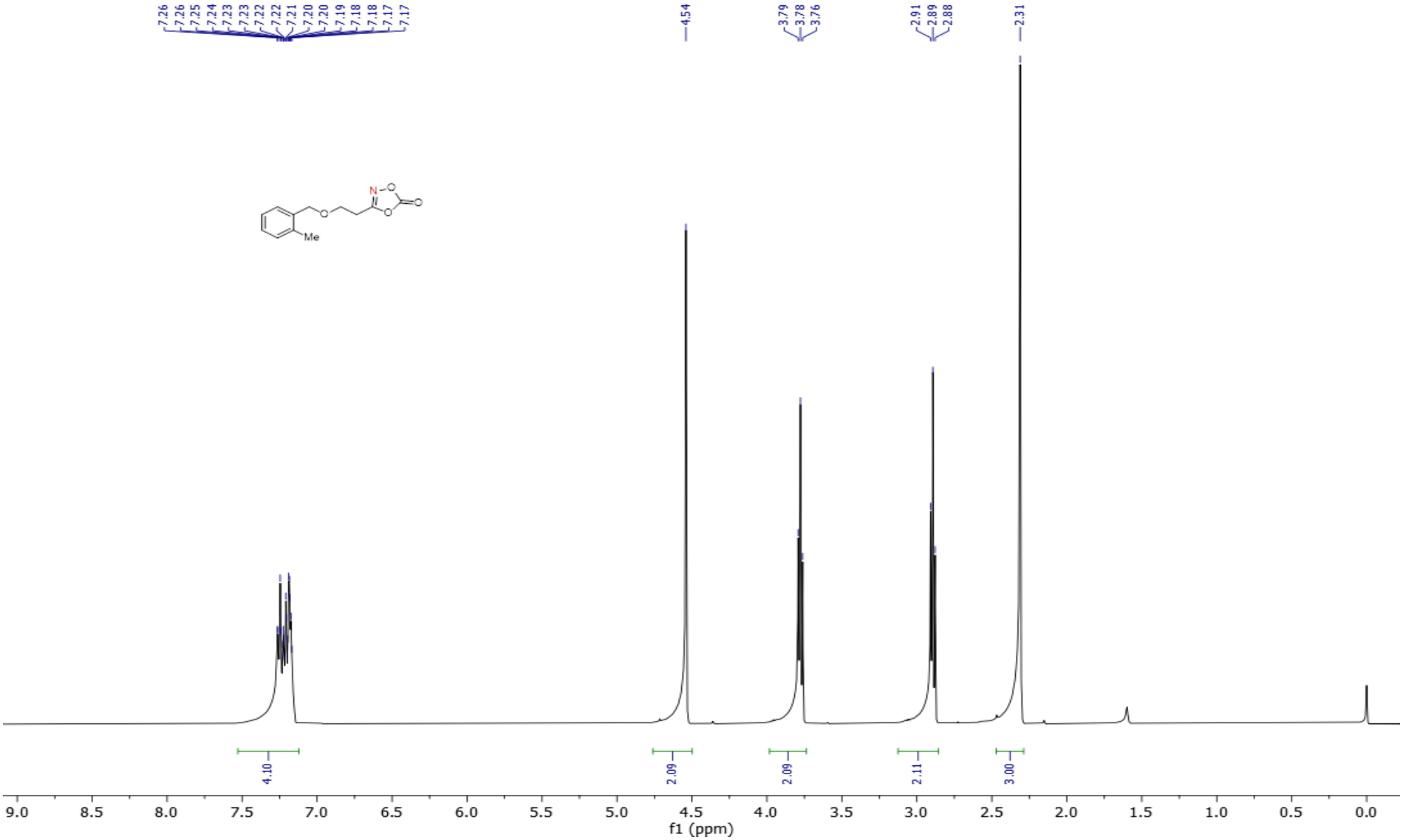
3-(2-(benzyloxy)ethyl)-1,4,2-dioxazol-5-one (**5c**), ^{1}H NMR (400 MHz, $CDCl_3$):



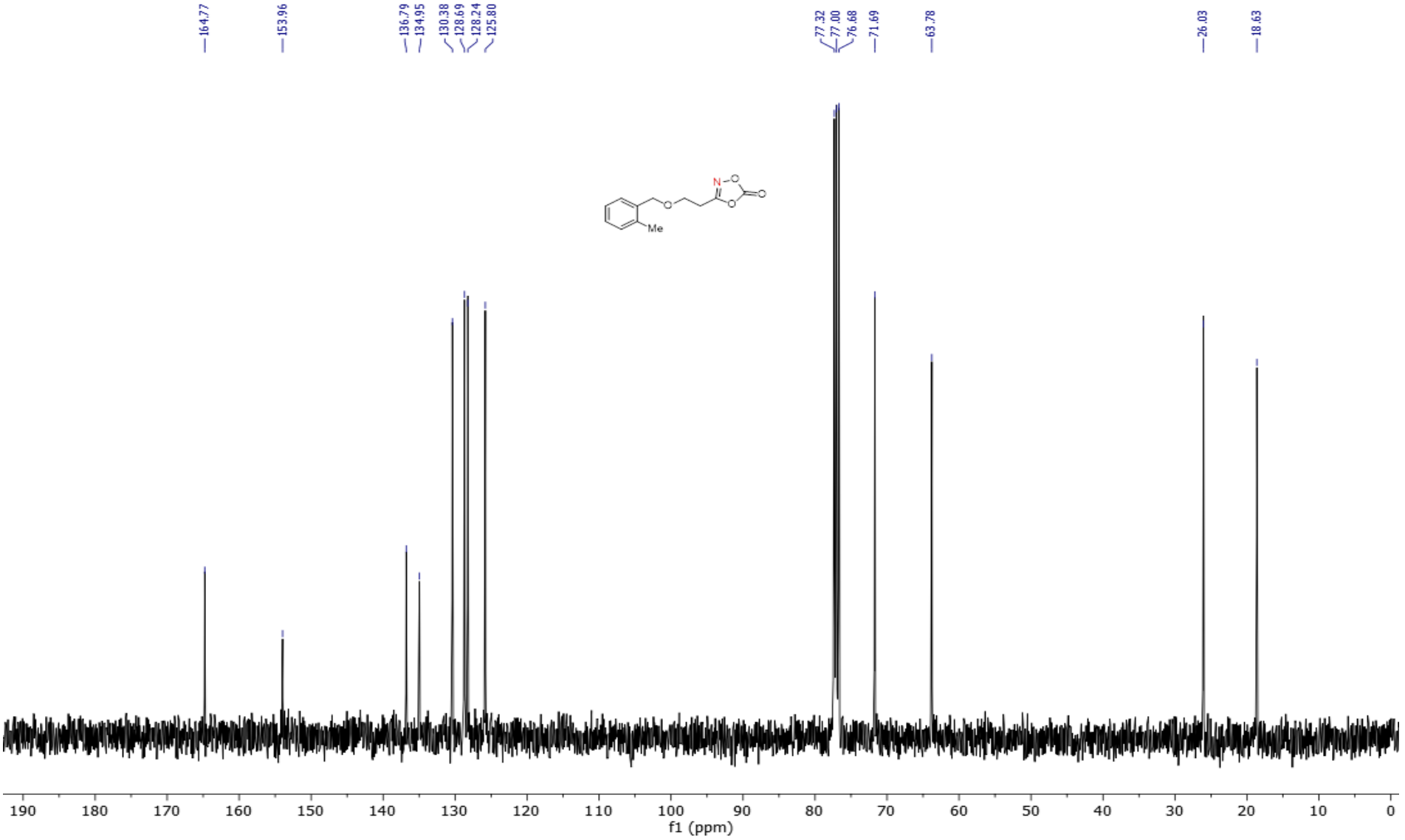
3-(2-(benzyloxy)ethyl)-1,4,2-dioxazol-5-one (**5c**), ^{13}C NMR (101 MHz, $CDCl_3$):



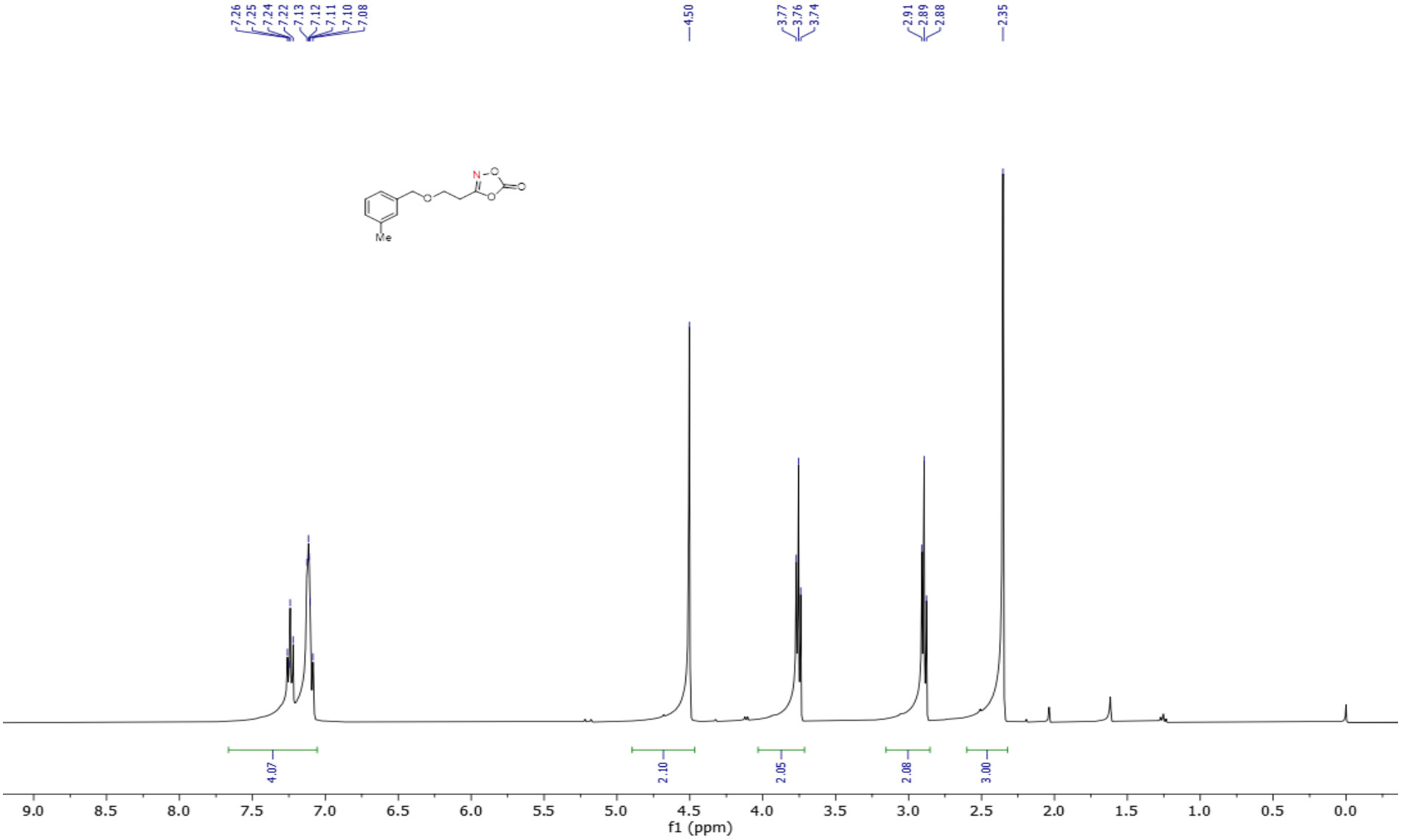
3-(2-((2-methylbenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (**5d**), ^{1}H NMR (400 MHz, $CDCl_3$):



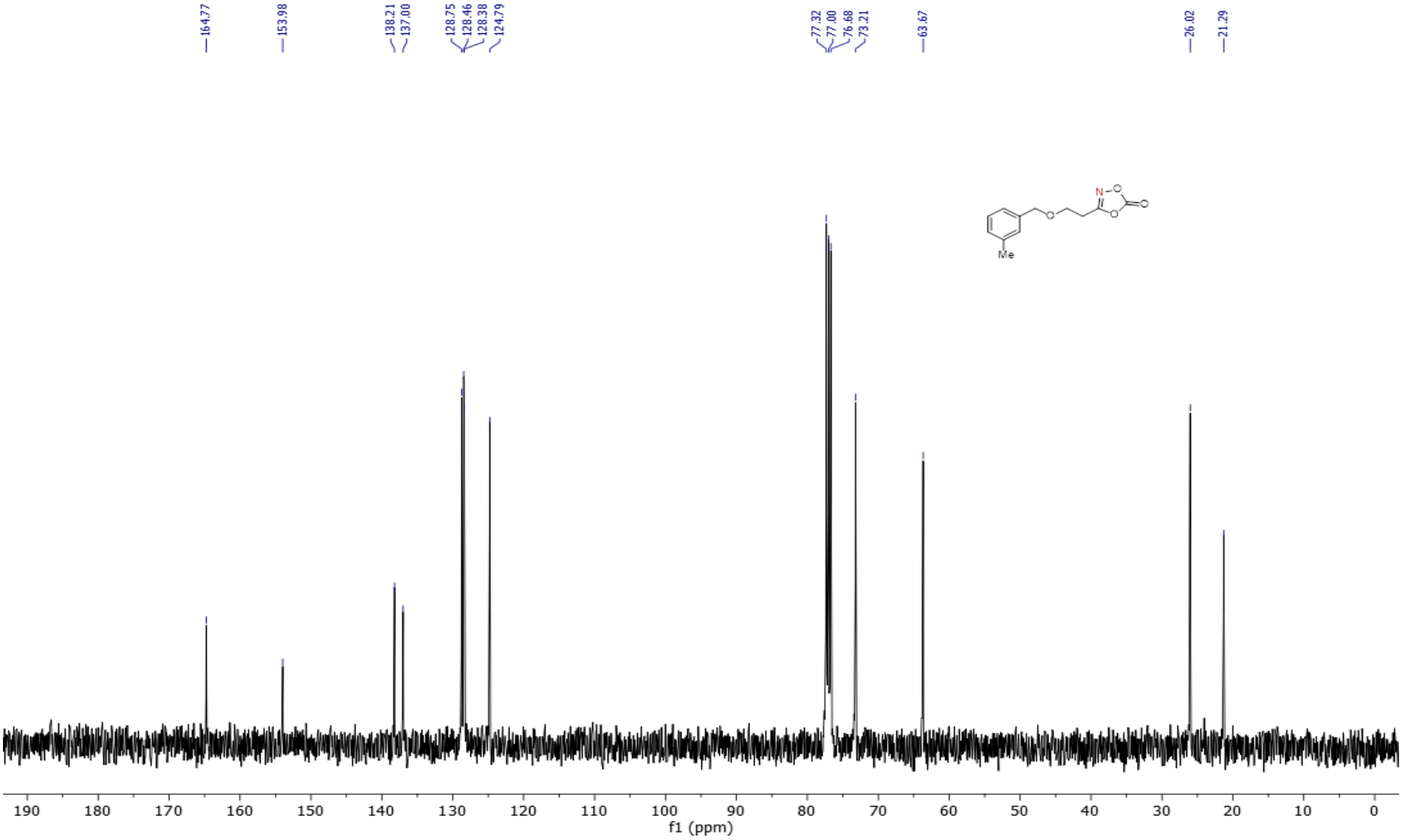
3-(2-((2-methylbenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (**5d**), ^{13}C NMR (101 MHz, $CDCl_3$):



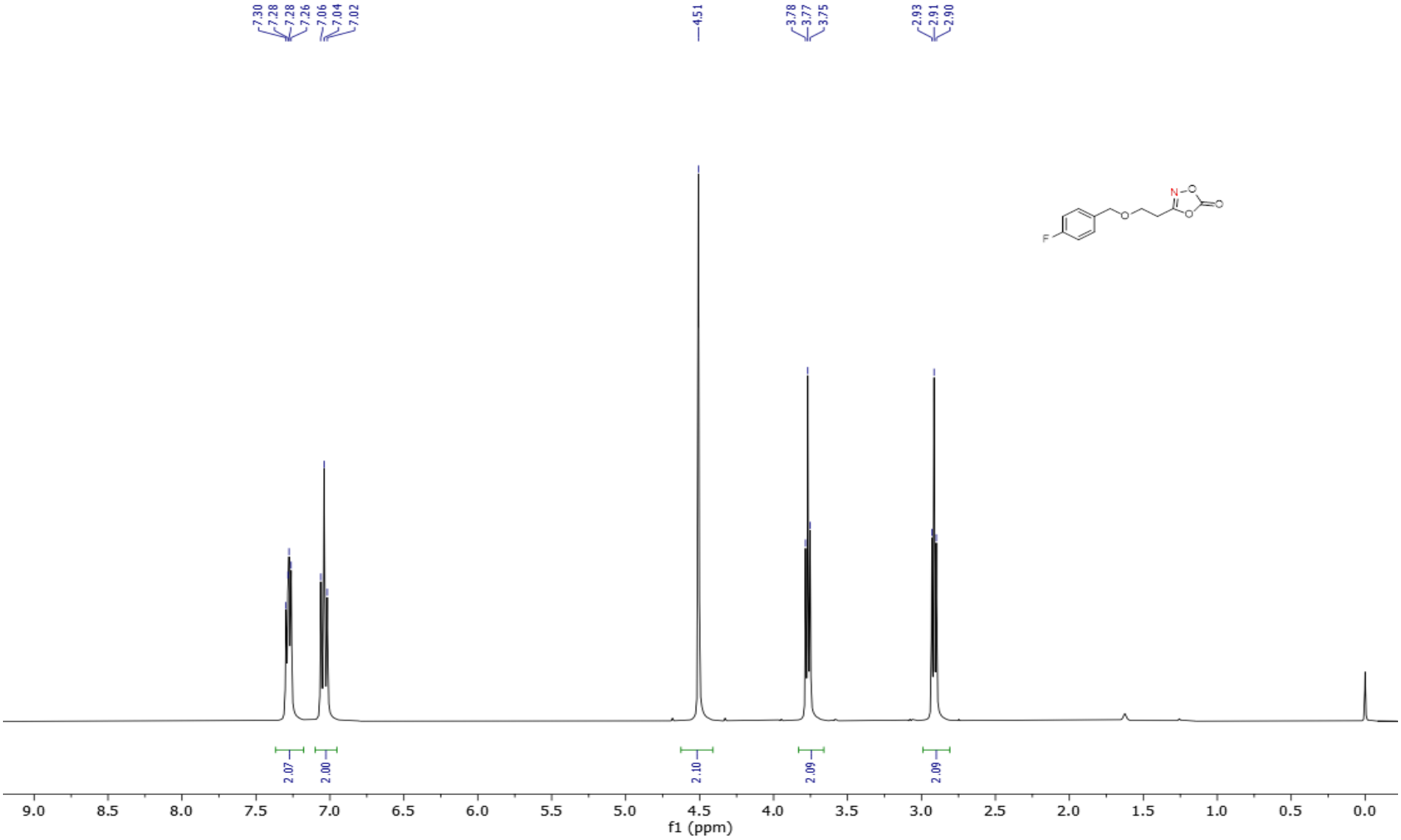
3-(2-((3-methylbenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (**5e**), ^{1}H NMR (400 MHz, $CDCl_3$):



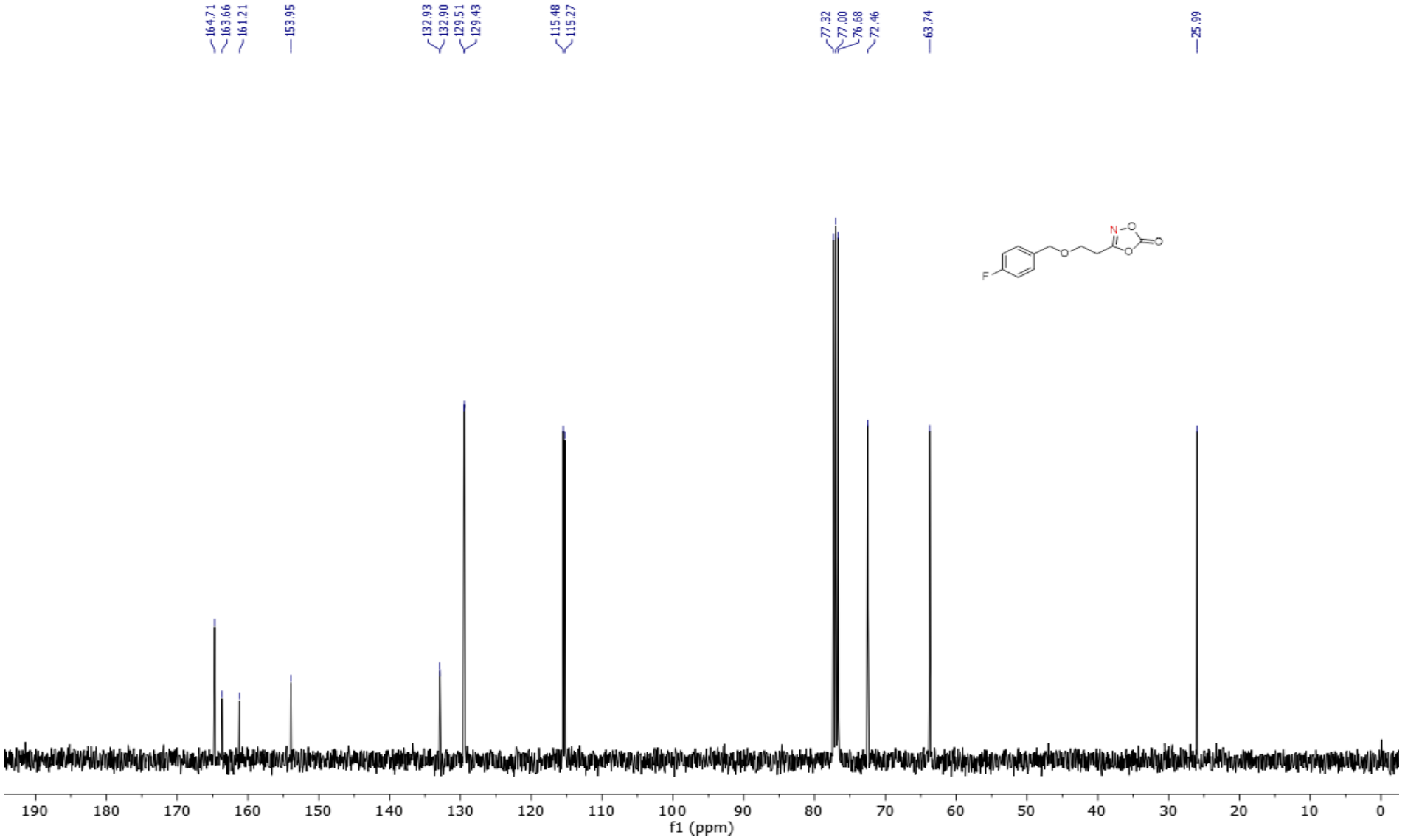
3-(2-((3-methylbenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (**5e**), ^{13}C NMR (101 MHz, $CDCl_3$):



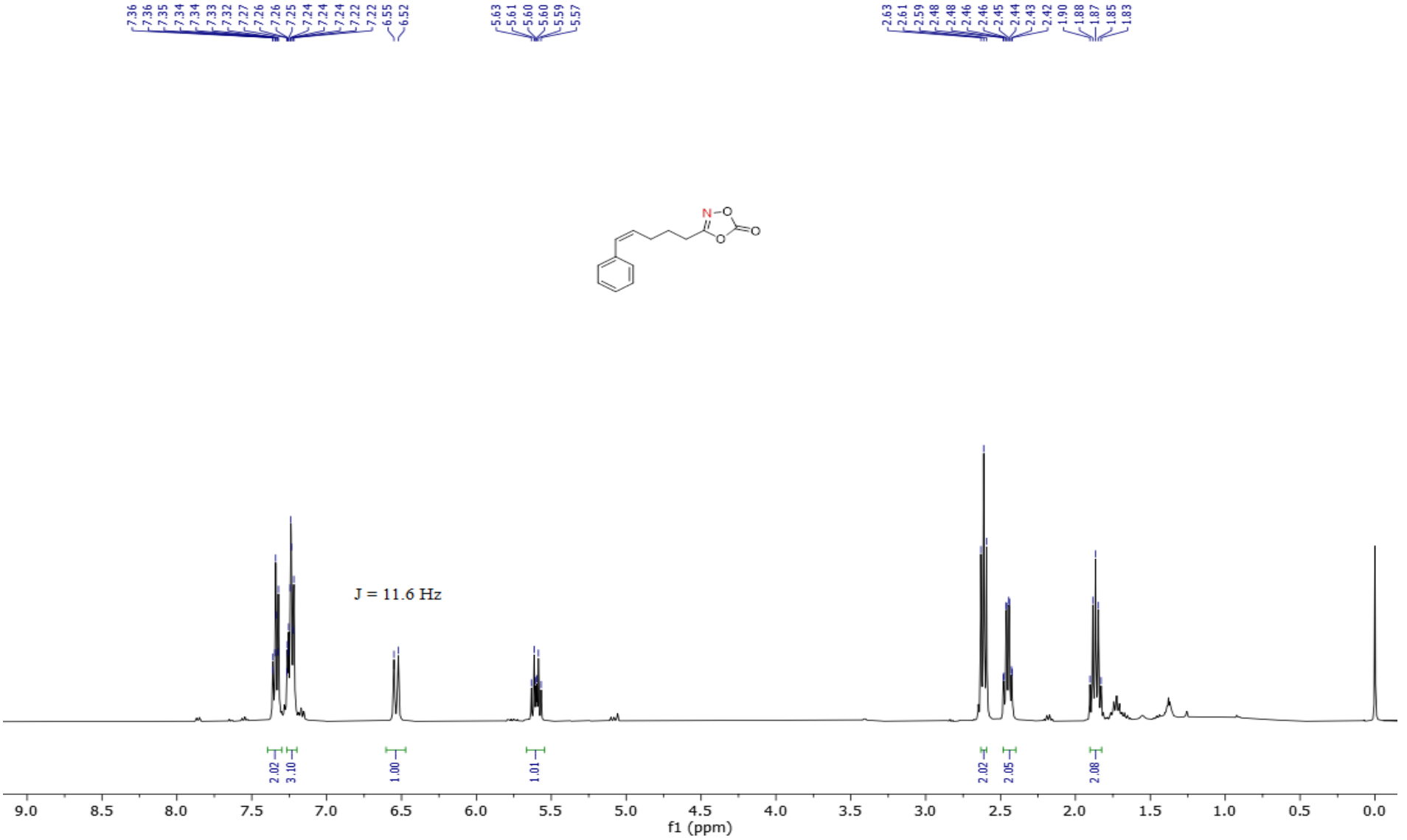
3-(2-((4-fluorobenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (**5f**), ^{1}H NMR (400 MHz, $CDCl_3$):



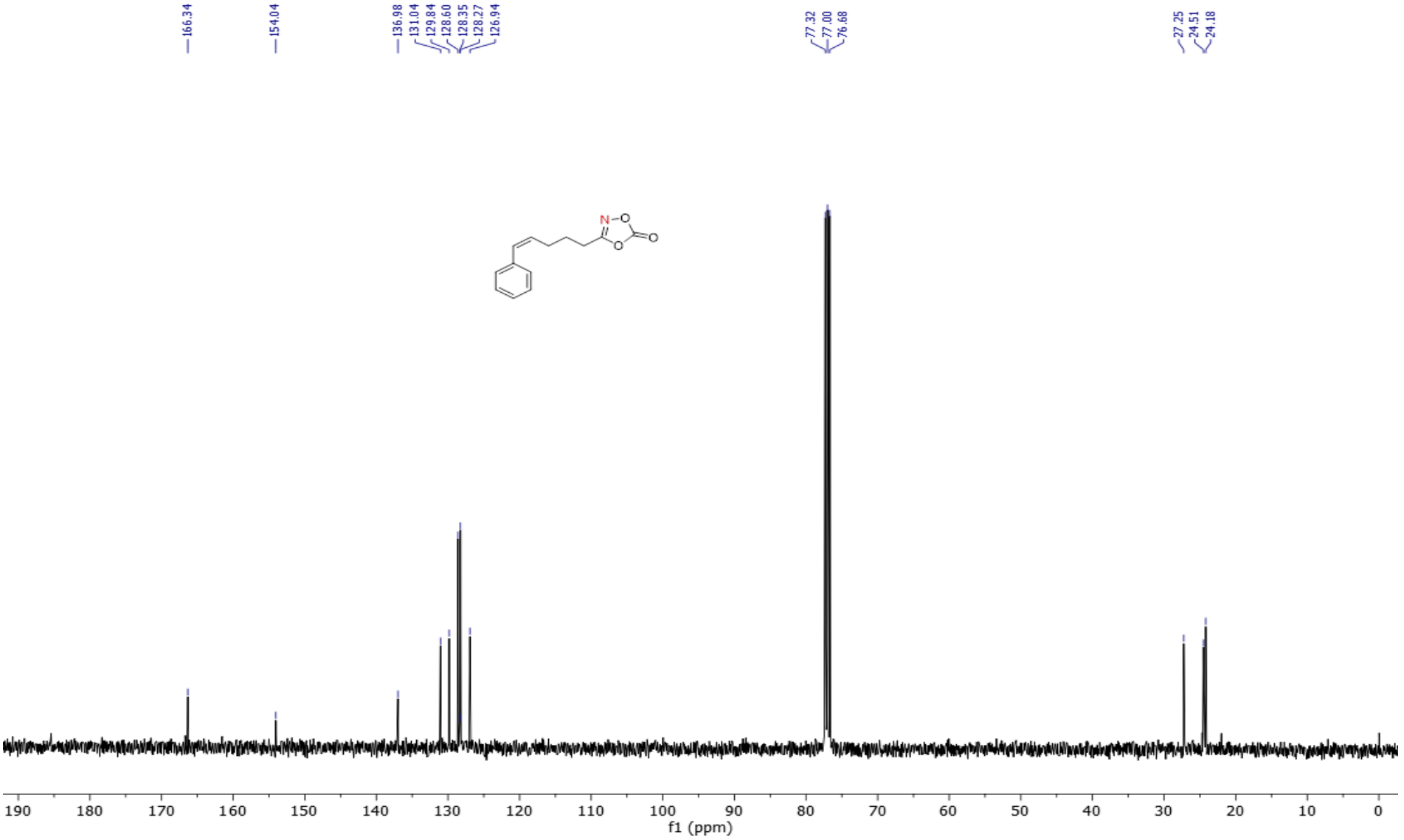
3-(2-((4-fluorobenzyl)oxy)ethyl)-1,4,2-dioxazol-5-one (**5f**), ^{13}C NMR (101 MHz, $CDCl_3$):



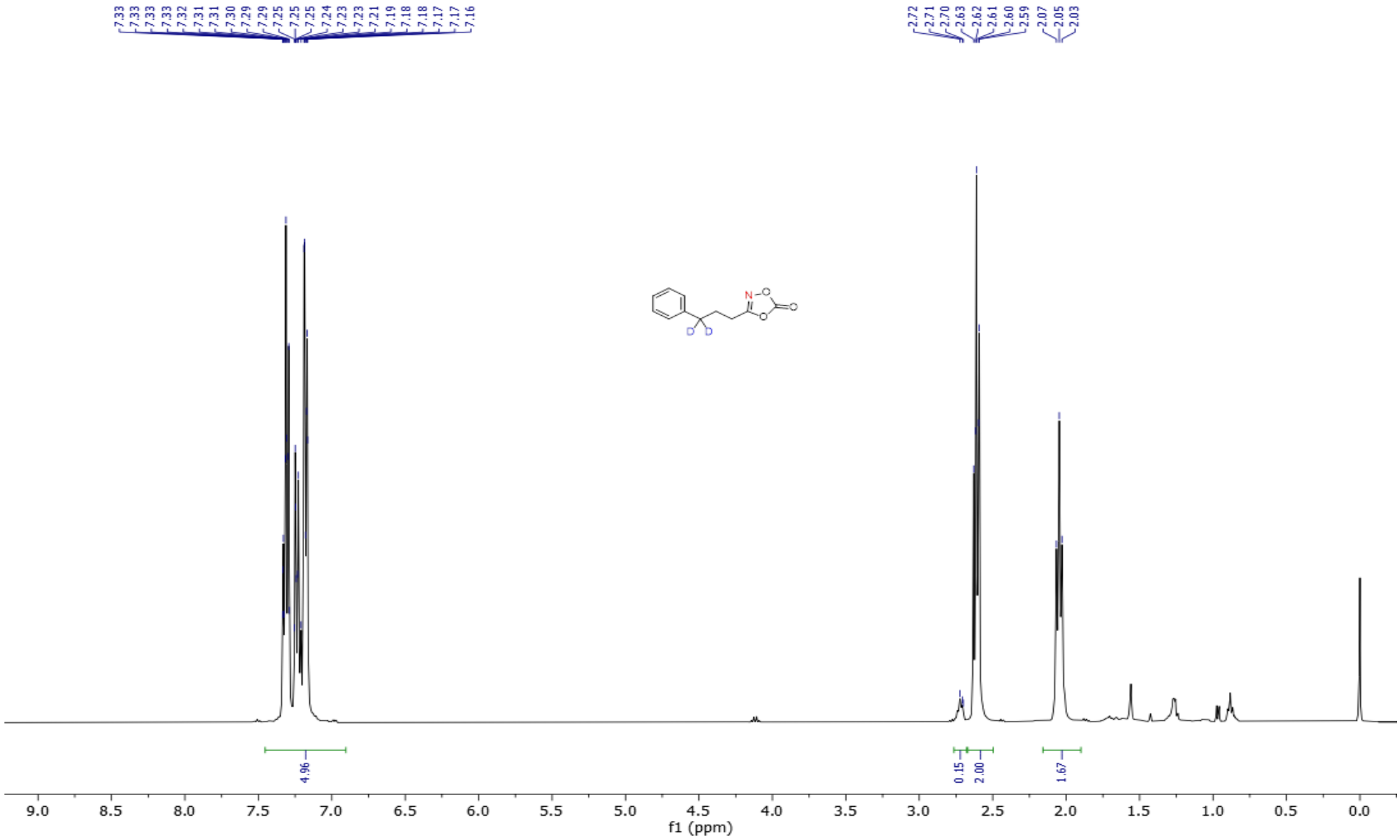
(Z)-3-(5-phenylpent-4-en-1-yl)-1,4,2-dioxazol-5-one (**1q**), ^{1}H NMR (400 MHz, $CDCl_3$):



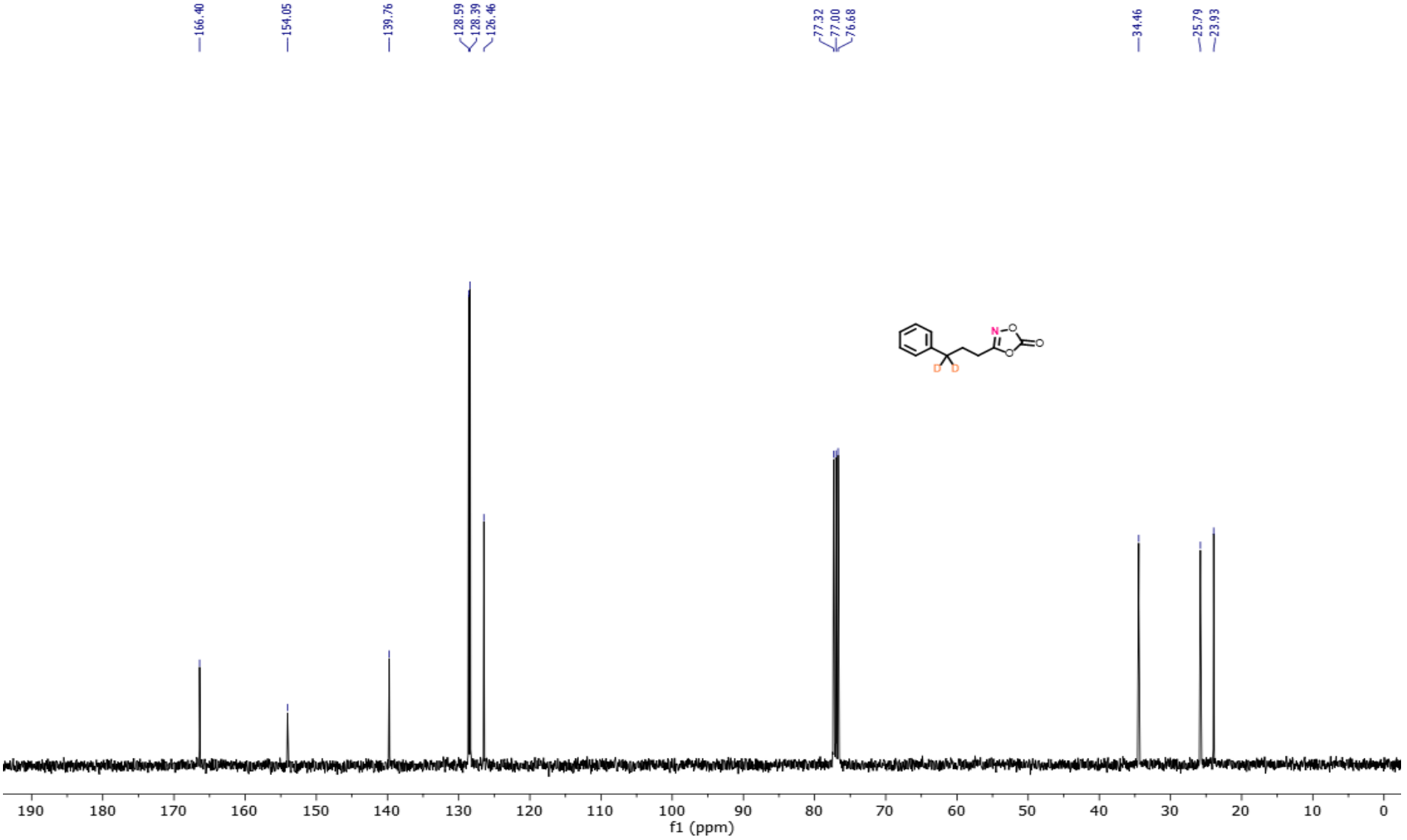
(Z)-3-(5-phenylpent-4-en-1-yl)-1,4,2-dioxazol-5-one (**1q**), ^{13}C NMR (101 MHz, $CDCl_3$):



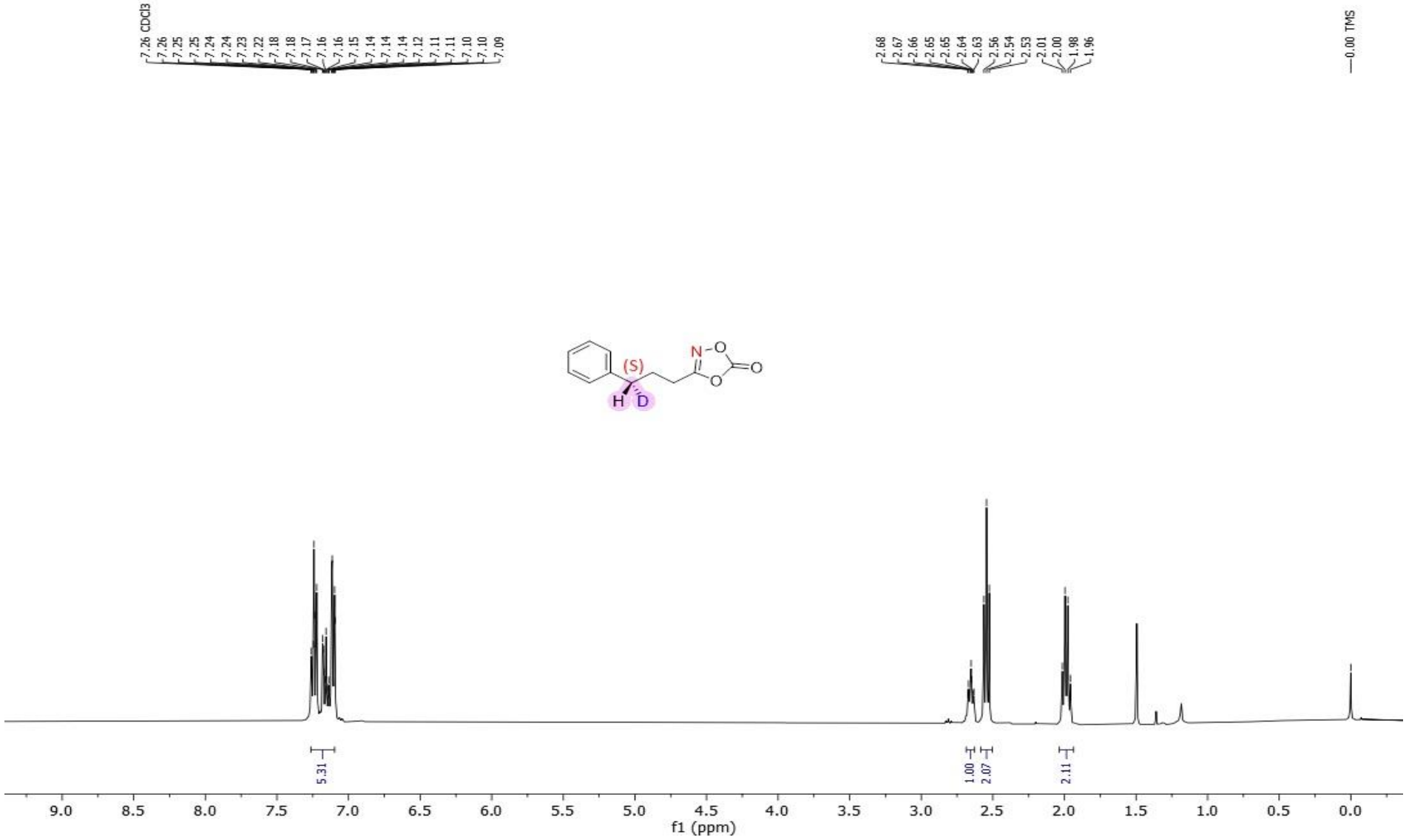
3-(3-phenylpropyl-3,3-d_2)-1,4,2-dioxazol-5-one (**1a-d_2**), ^{1}H NMR (400 MHz, $CDCl_3$):



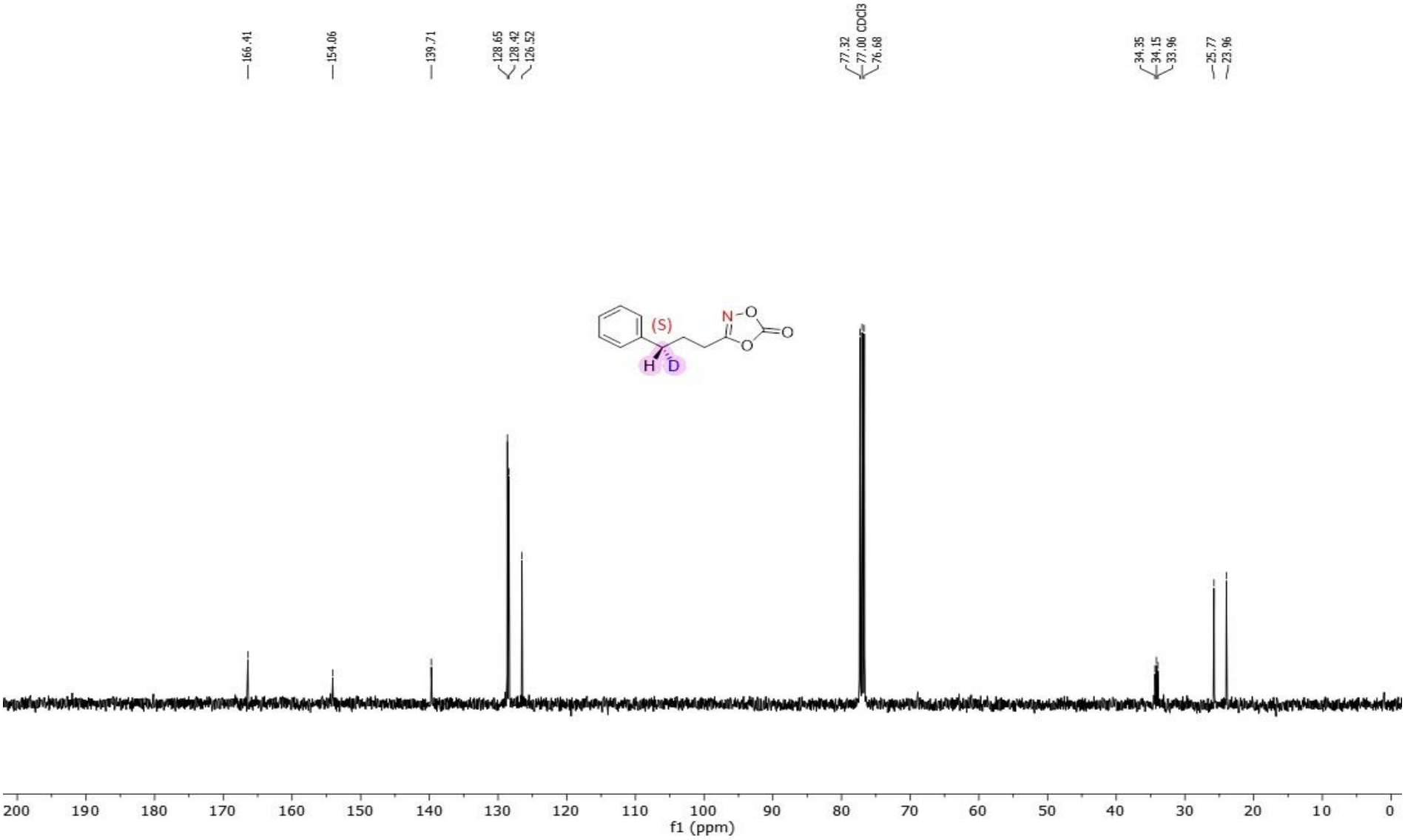
3-(3-phenylpropyl-3,3-d_2)-1,4,2-dioxazol-5-one (**1a-d_2**), ^{13}C NMR (101 MHz, $CDCl_3$):



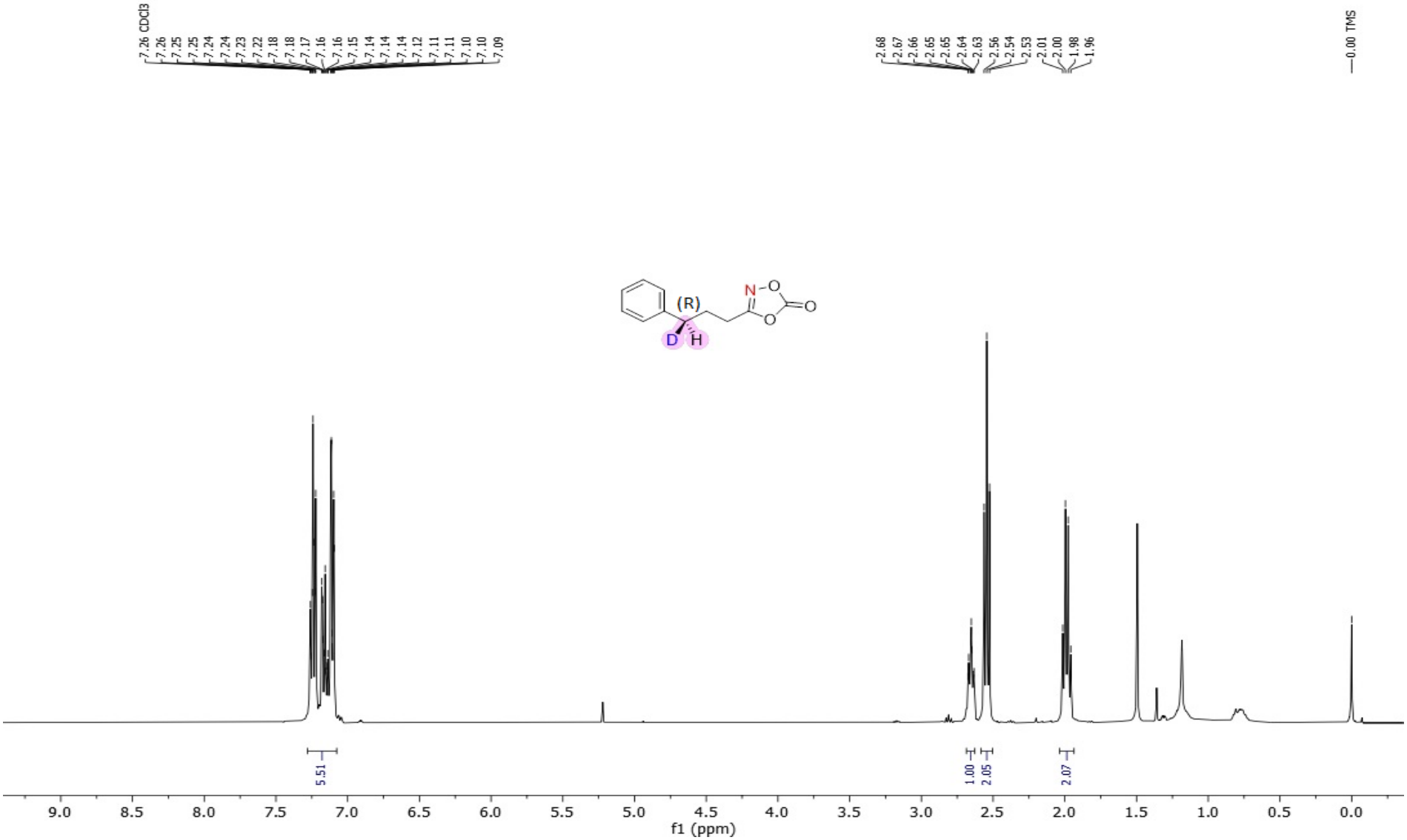
(S)-3-(3-phenylpropyl-3-d)-1,4,2-dioxazol-5-one [*(S)-1a-d*$_1$], ^{1}H NMR (400 MHz, $CDCl_3$):



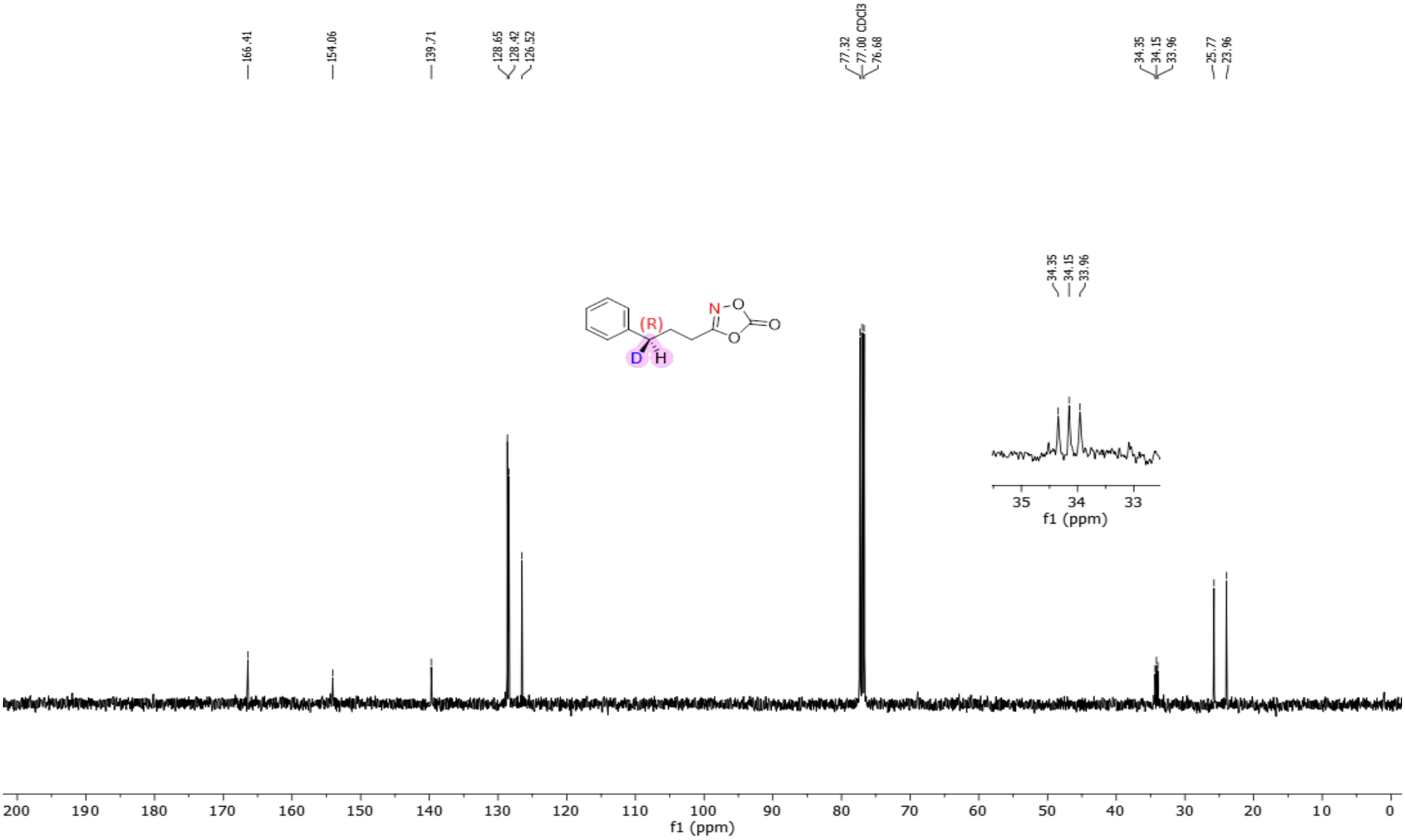
(S)-3-(3-phenylpropyl-3-d)-1,4,2-dioxazol-5-one [*(S)-1a-d*$_1$], ^{13}C NMR (101 MHz, $CDCl_3$):



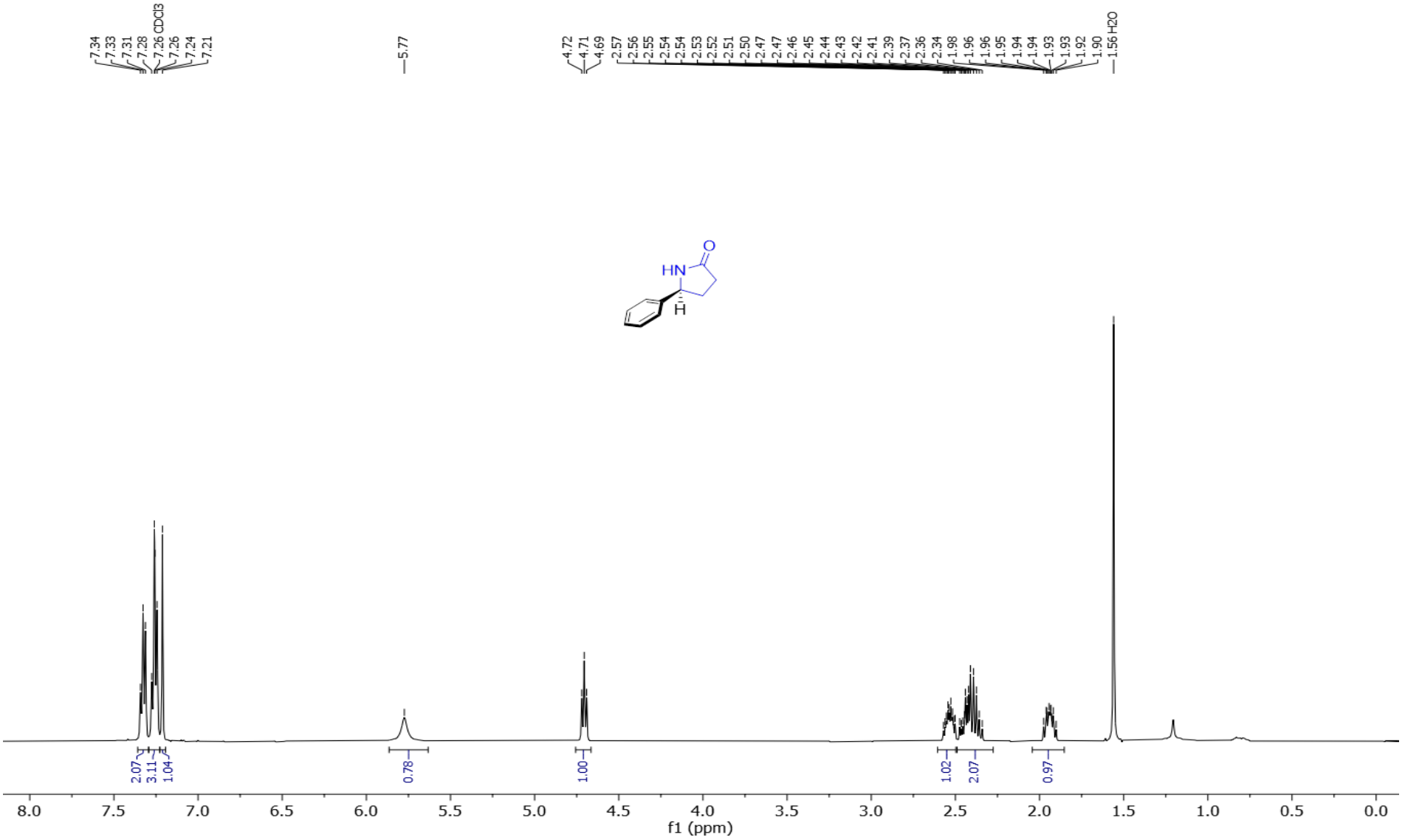
(R)-3-(3-phenylpropyl-3-d)-1,4,2-dioxazol-5-one [*(R)-1a-d*$_1$], ^{1}H NMR (400 MHz, $CDCl_3$):



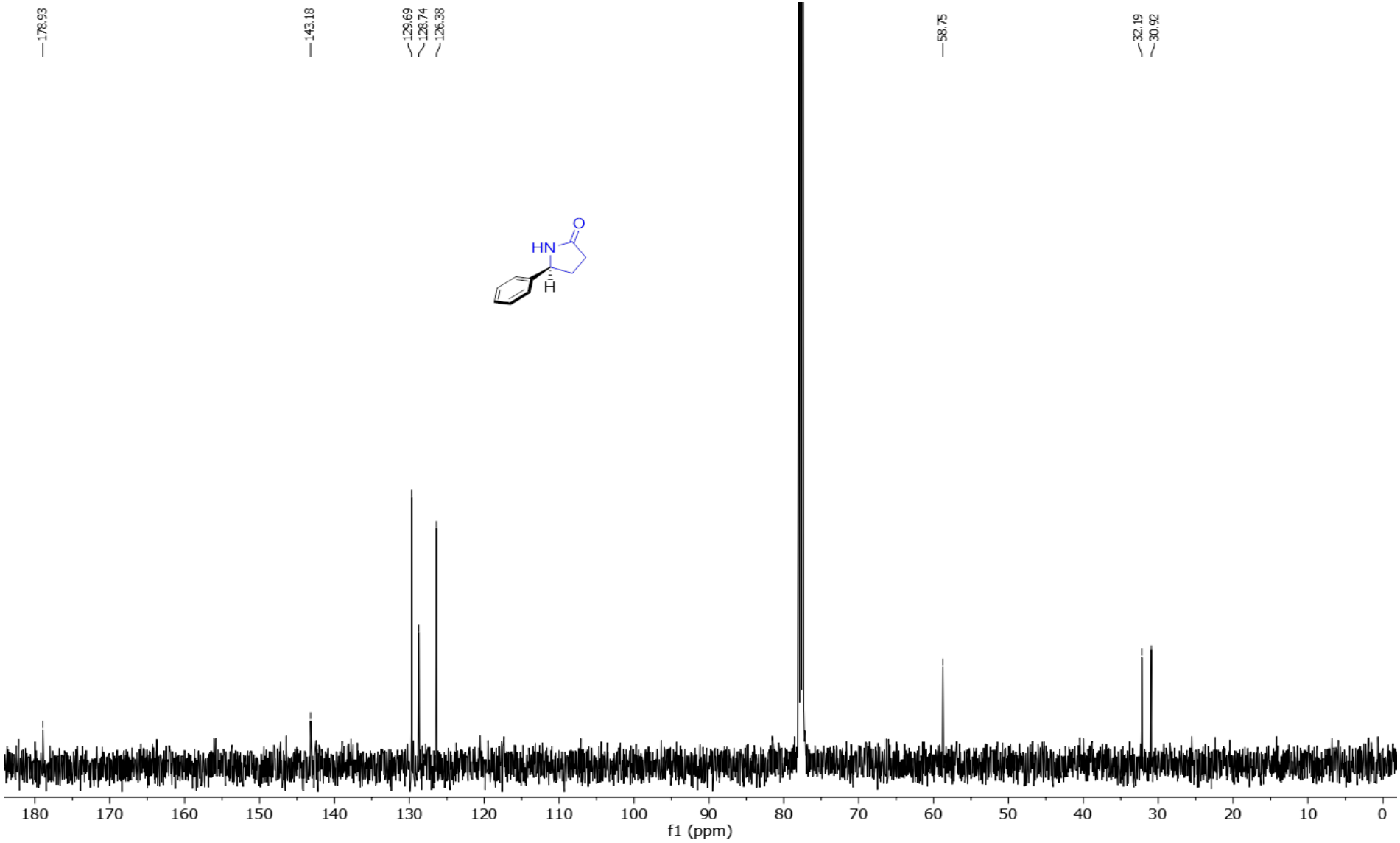
(R)-3-(3-phenylpropyl-3-d)-1,4,2-dioxazol-5-one [*(R)-1a-d*$_1$], ^{13}C NMR (101 MHz, $CDCl_3$):



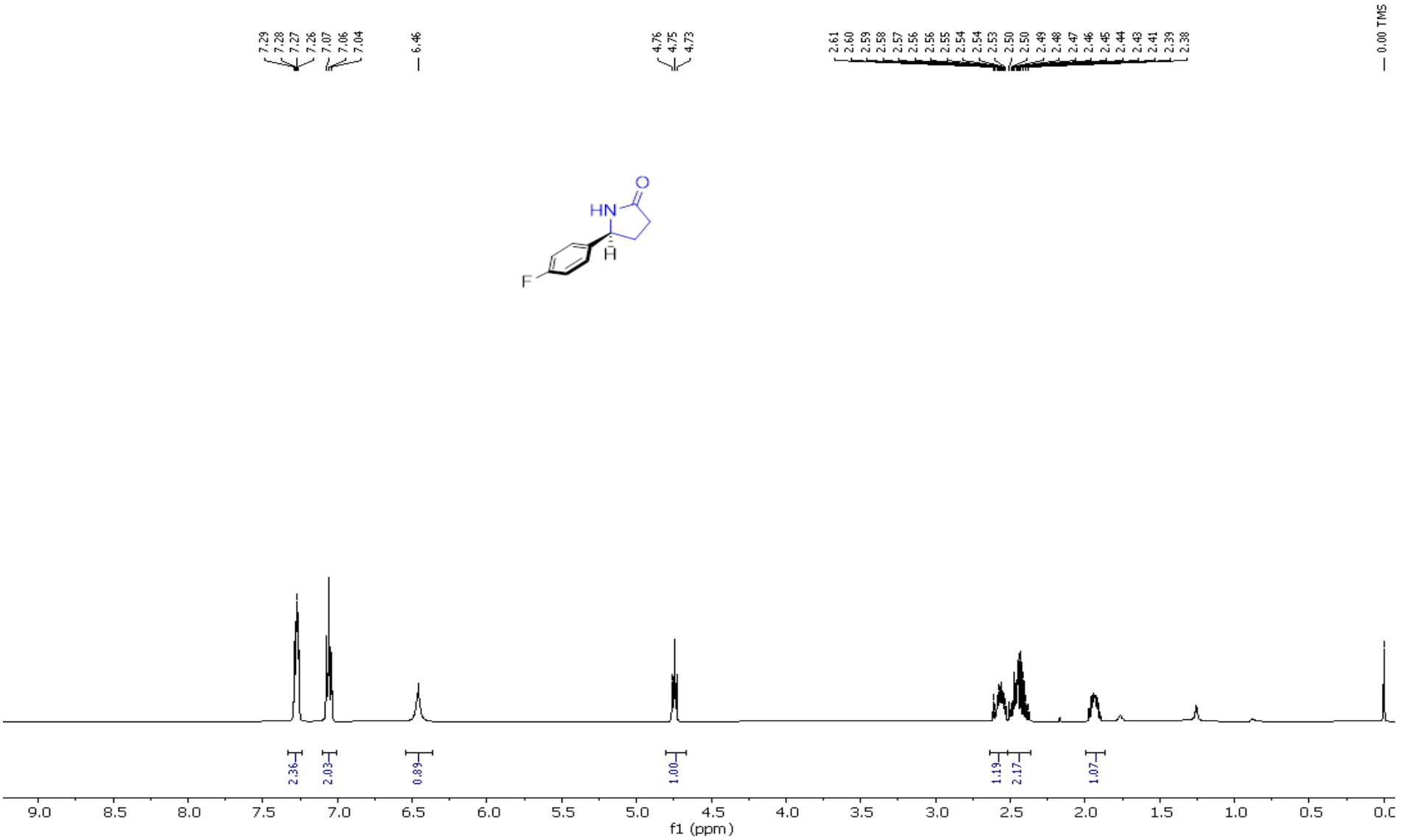
(S)-5-phenylpyrrolidin-2-one (**2a**), ^{1}H NMR (400 MHz, $CDCl_3$):



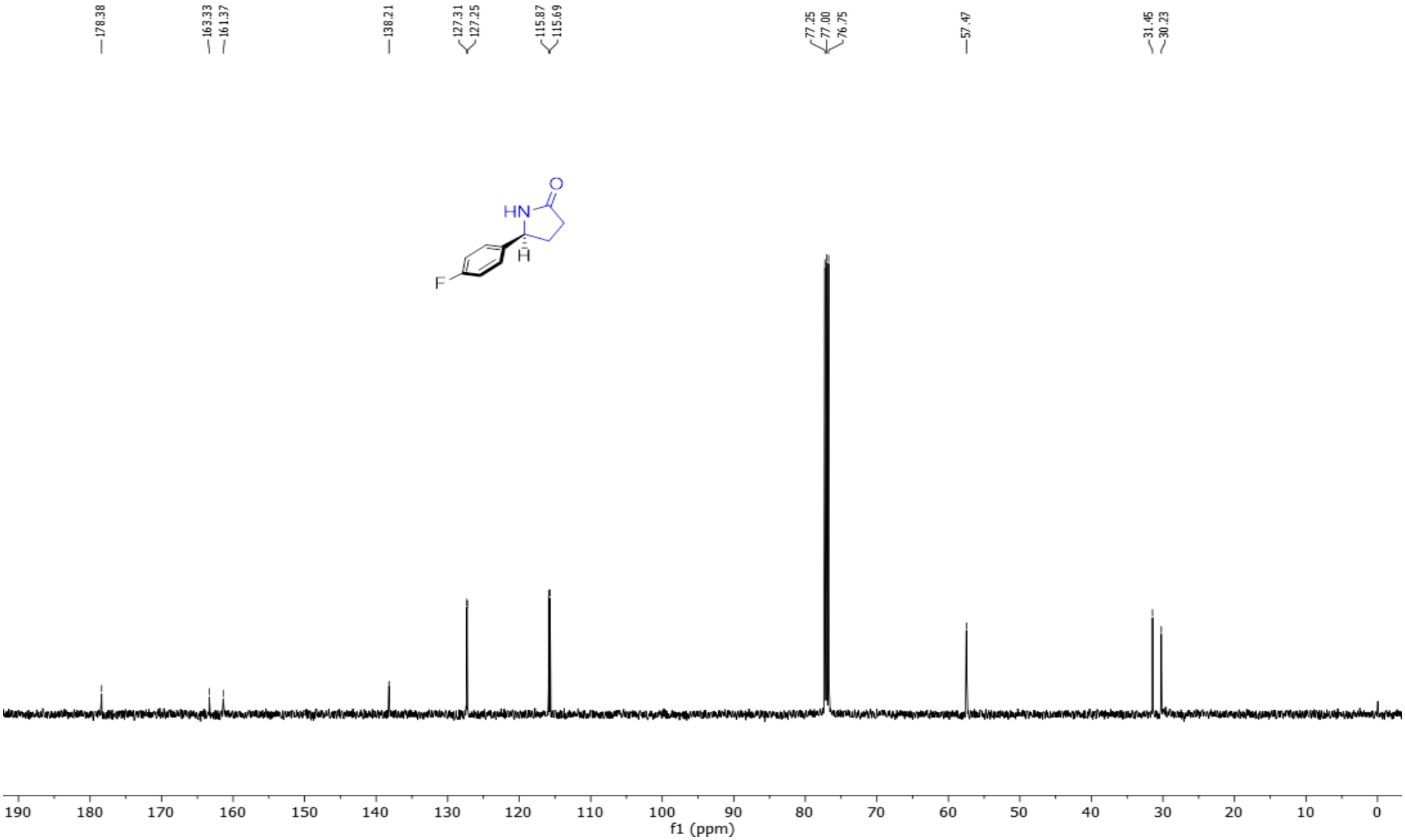
(S)-5-phenylpyrrolidin-2-one (**2a**), ^{13}C NMR (101 MHz, $CDCl_3$):



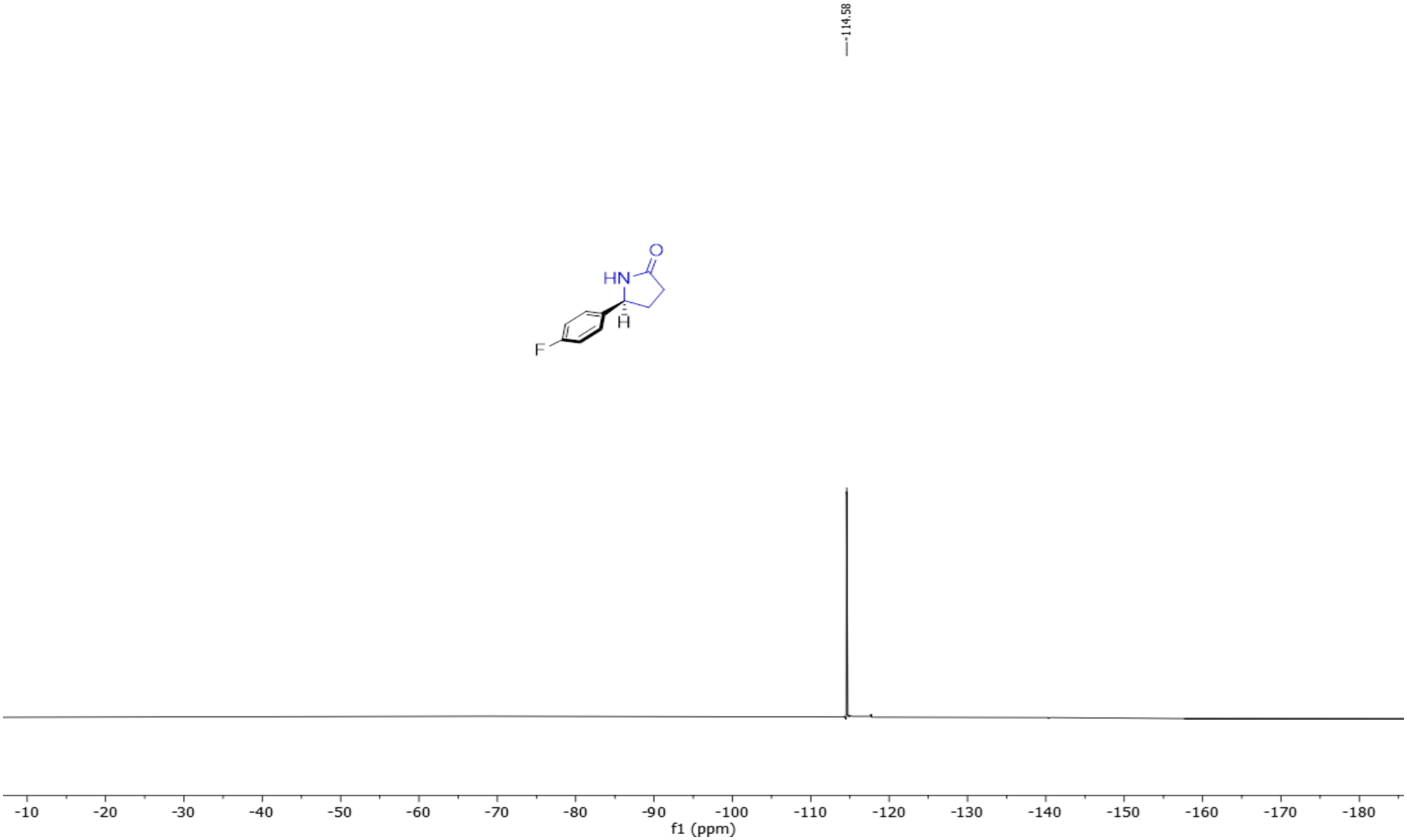
(S)-5-(4-fluorophenyl)pyrrolidin-2-one (**2b**), ^{1}H NMR (400 MHz, $CDCl_3$):



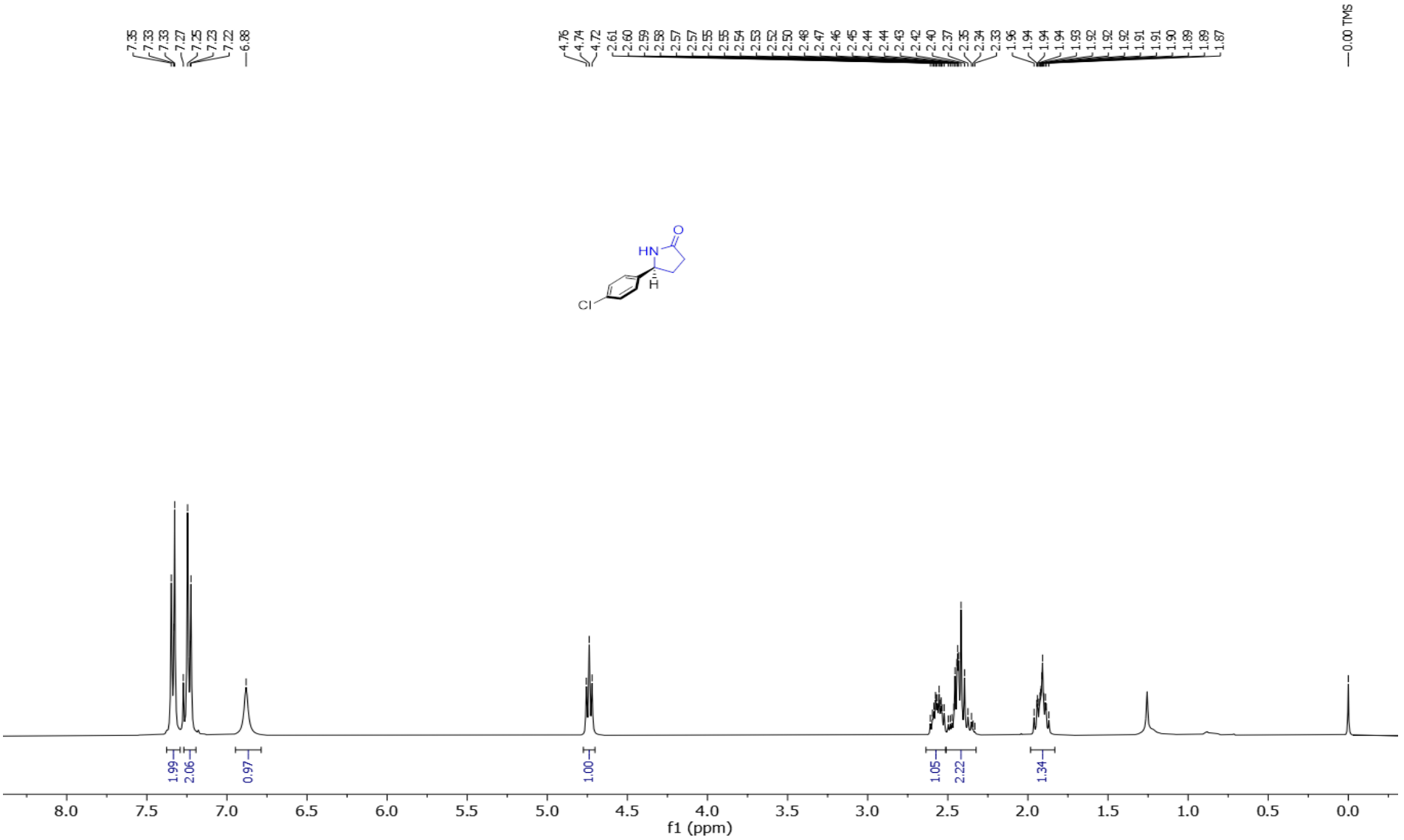
(S)-5-(4-fluorophenyl)pyrrolidin-2-one (**2d**), ^{13}C NMR (101 MHz, $CDCl_3$):



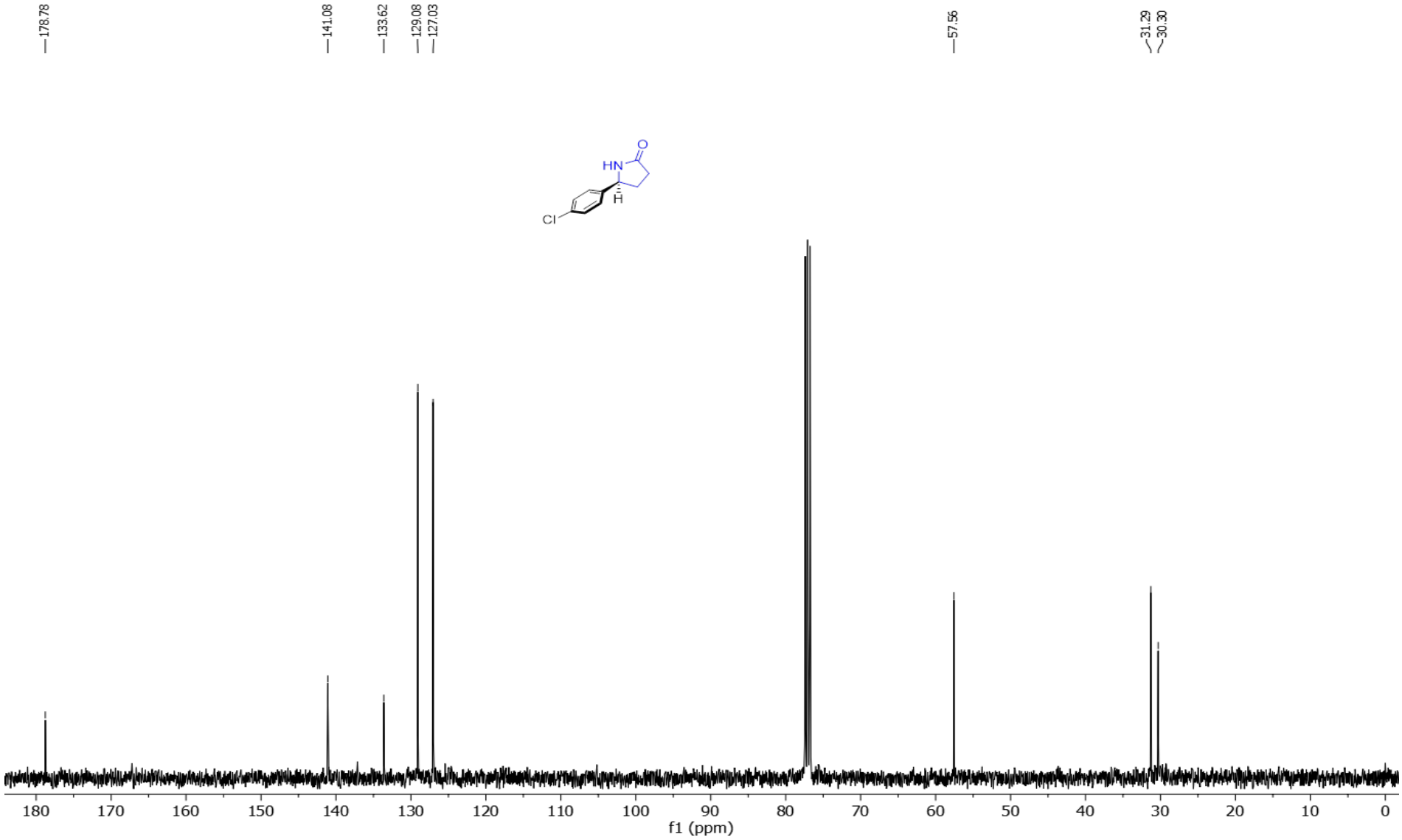
(S)-5-(4-fluorophenyl)pyrrolidin-2-one (**2d**), ^{19}FNMR (376 MHz, $CDCl_3$):



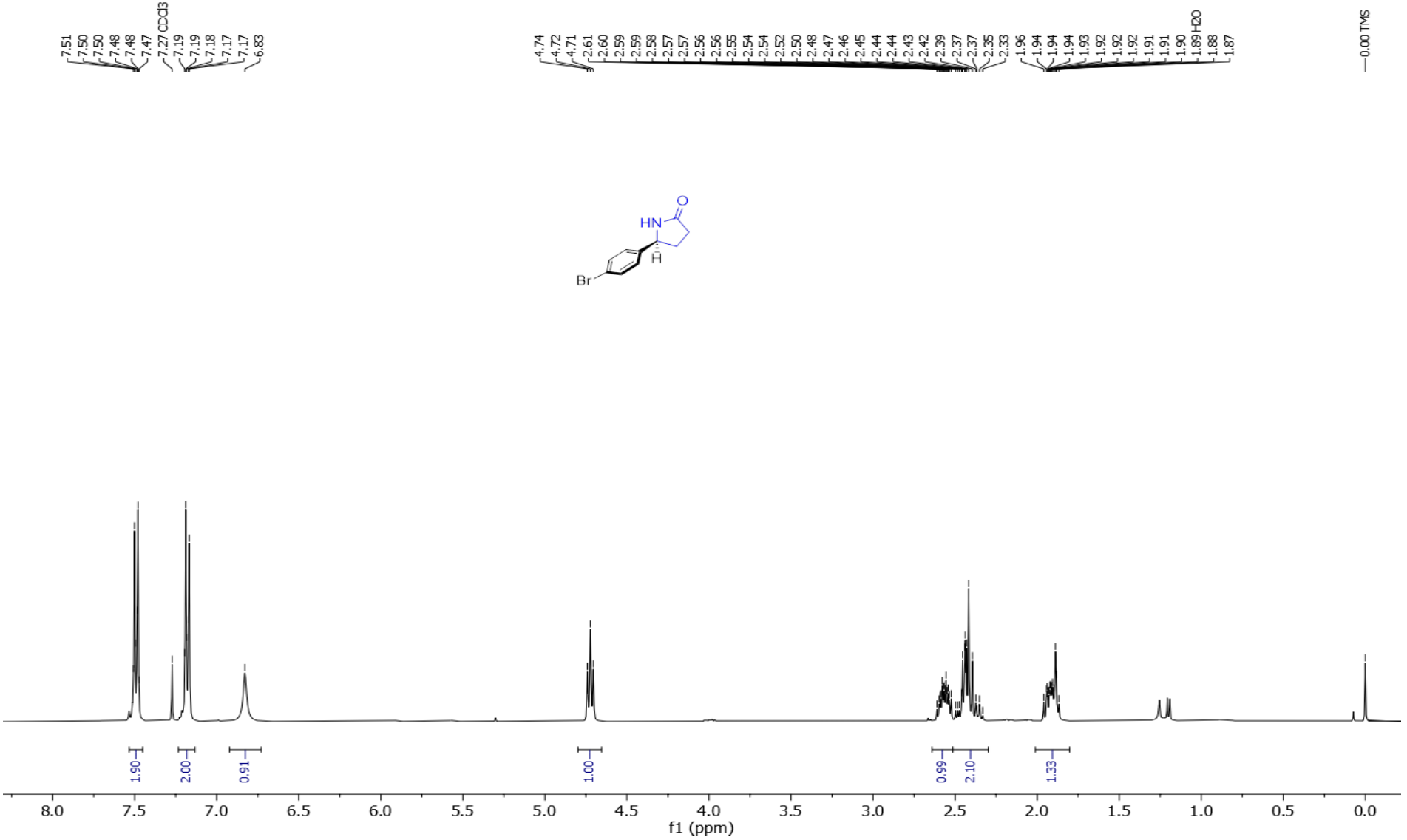
(S)-5-(4-chlorophenyl)pyrrolidin-2-one (**2e**), ^{1}H NMR (400 MHz, $CDCl_3$):



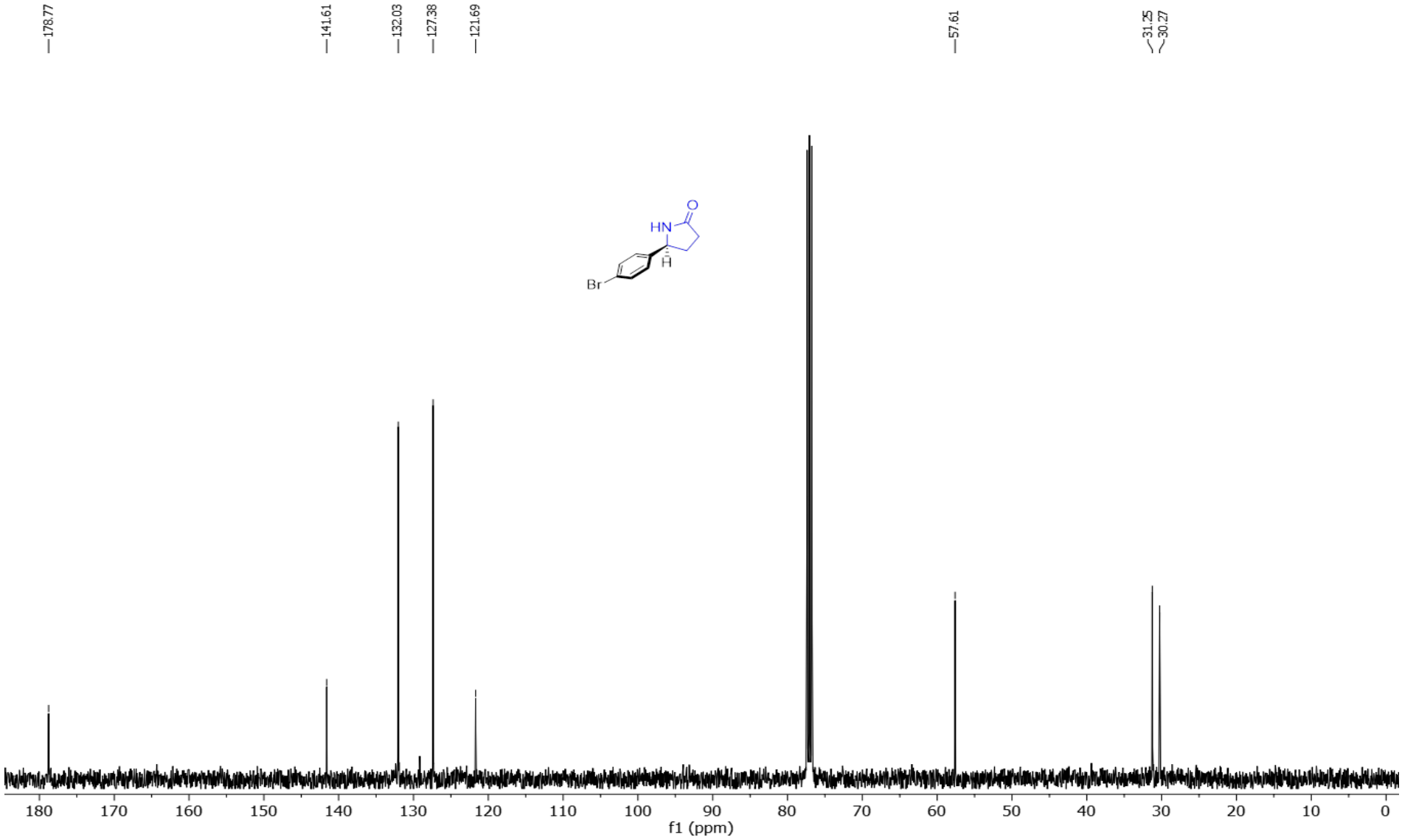
(S)-5-(4-chlorophenyl)pyrrolidin-2-one (**2e**), ^{13}C NMR (101 MHz, $CDCl_3$):



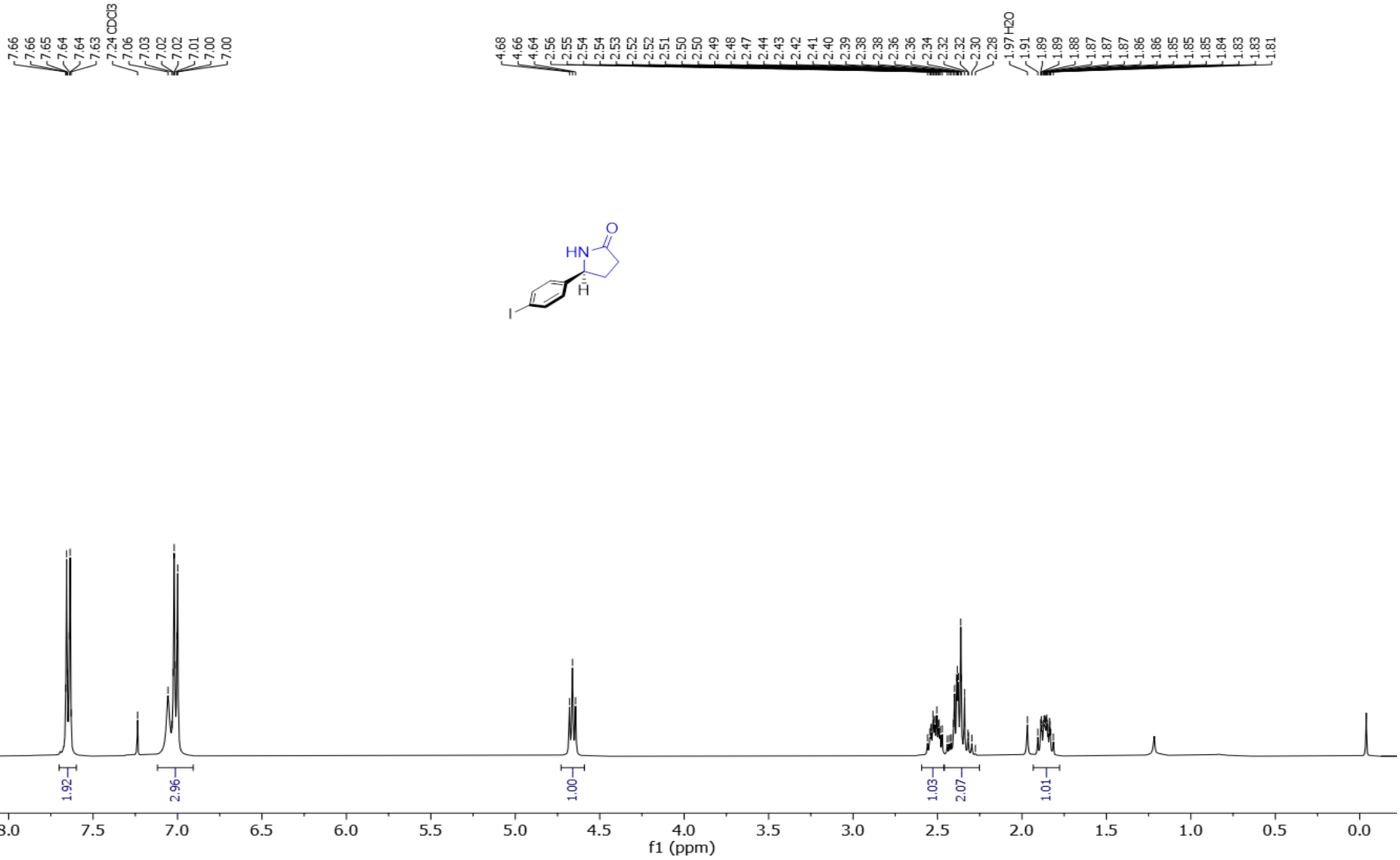
(S)-5-(4-bromophenyl)pyrrolidin-2-one (**2f**), ^{1}H NMR (400 MHz, $CDCl_3$):



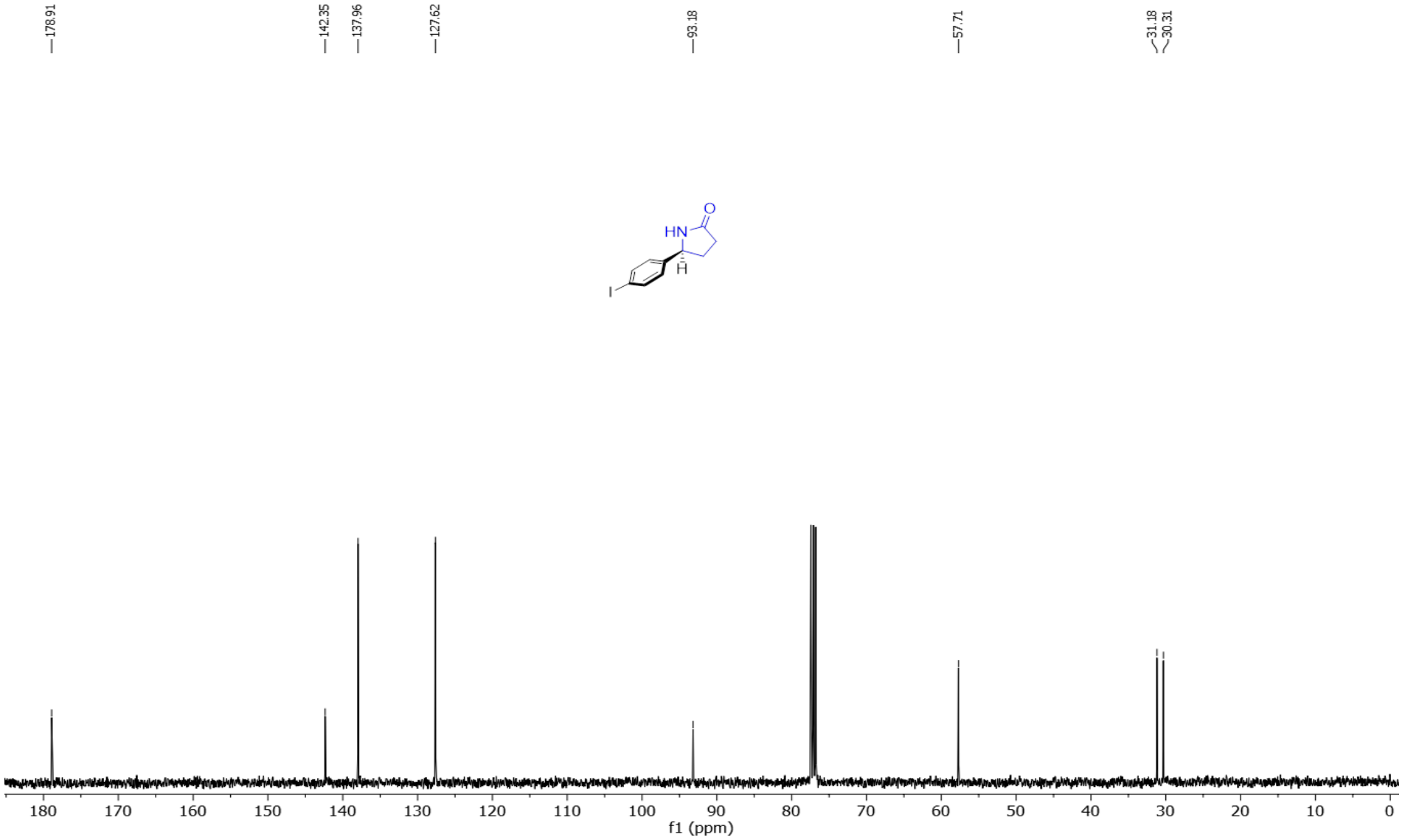
(S)-5-(4-bromophenyl)pyrrolidin-2-one (**2f**), ^{13}C NMR (101 MHz, $CDCl_3$):



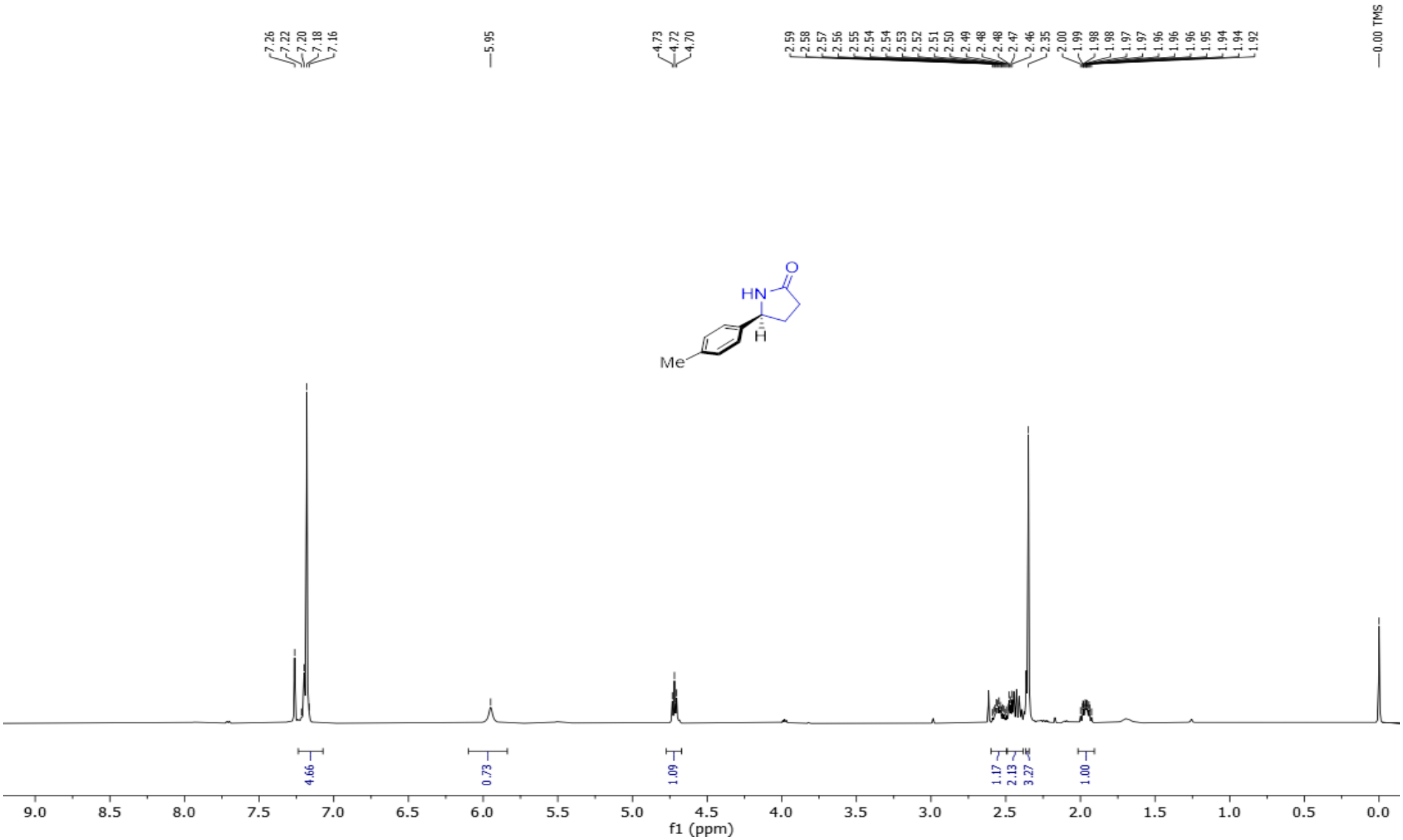
(S)-5-(4-iodophenyl)pyrrolidin-2-one (**2g**), ^{1}H NMR (400 MHz, $CDCl_3$):



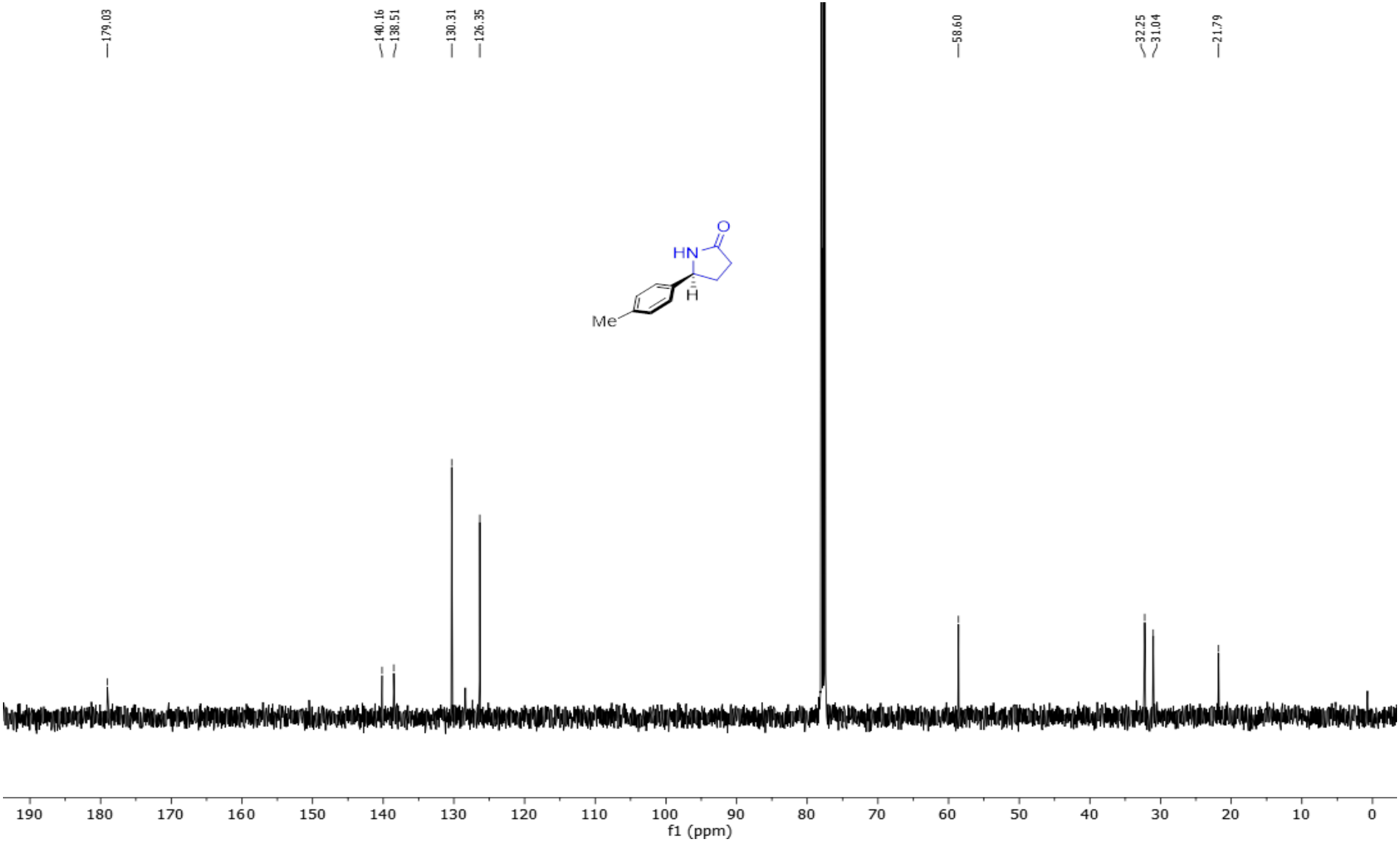
(S)-5-(4-iodophenyl)pyrrolidin-2-one (**2g**), ^{13}C NMR (101 MHz, $CDCl_3$):



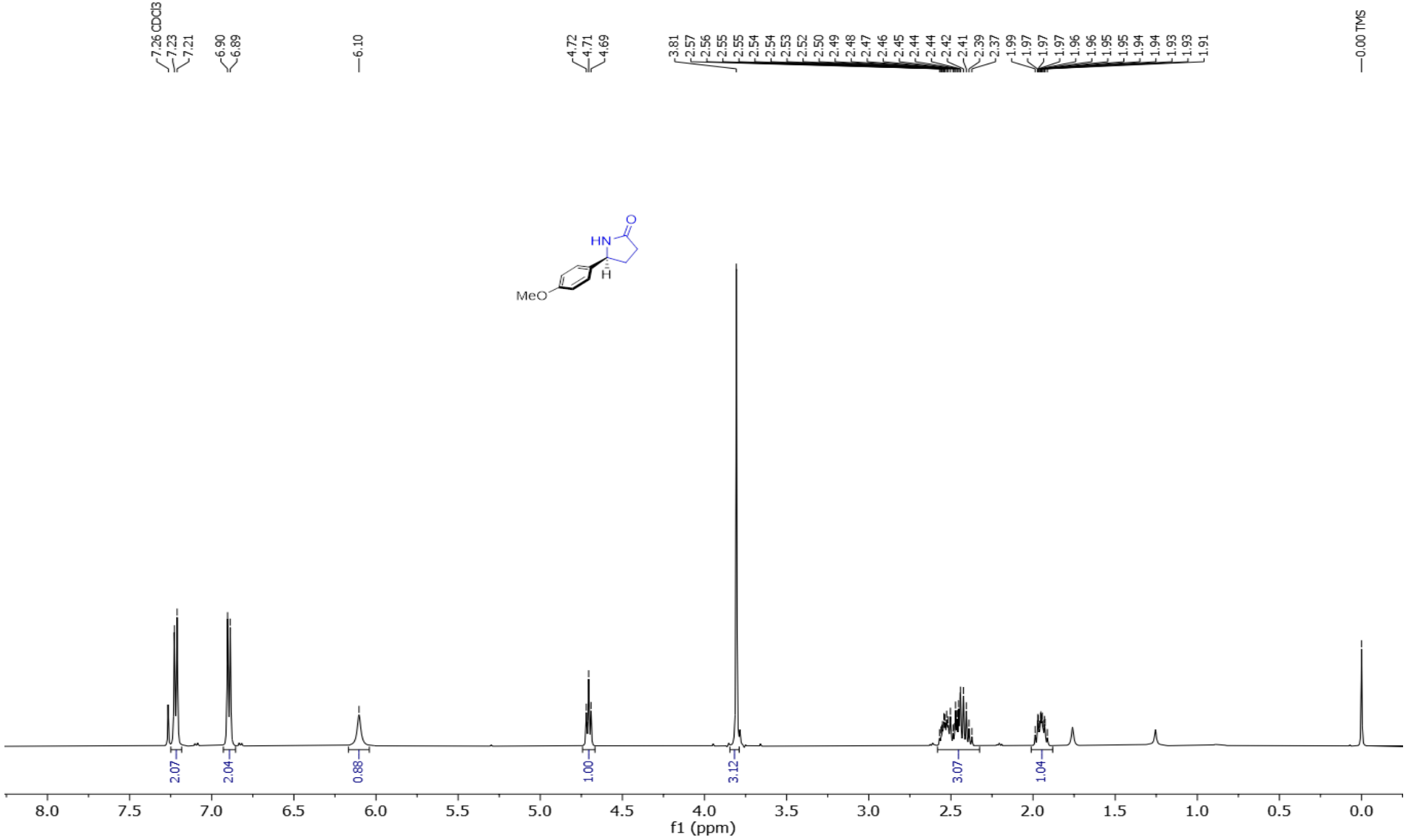
(S)-5-(p-tolyl)pyrrolidin-2-one (**2h**), ^{1}H NMR (400 MHz, $CDCl_3$):



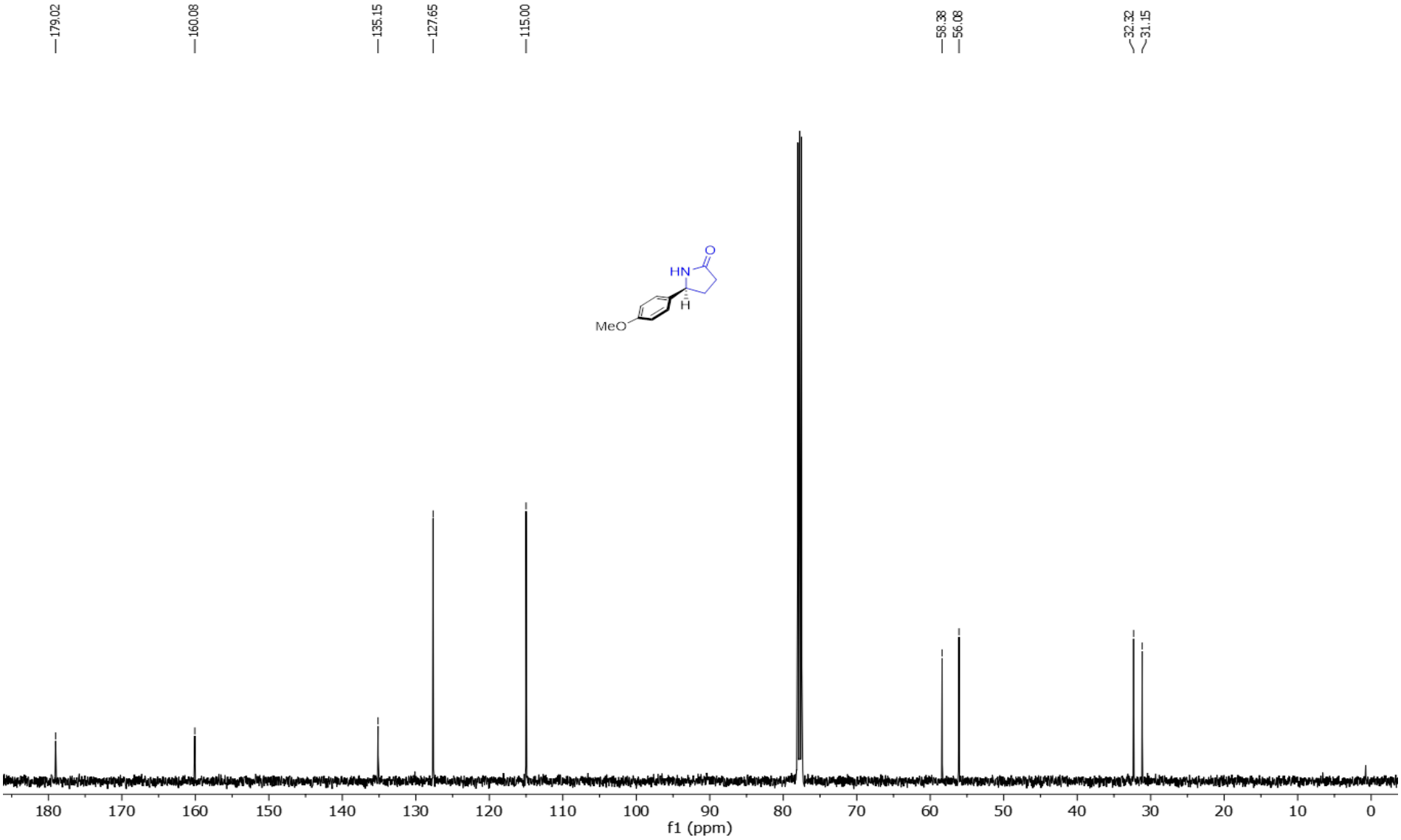
(S)-5-(p-tolyl)pyrrolidin-2-one (**2h**), ^{13}C NMR (101 MHz, $CDCl_3$):



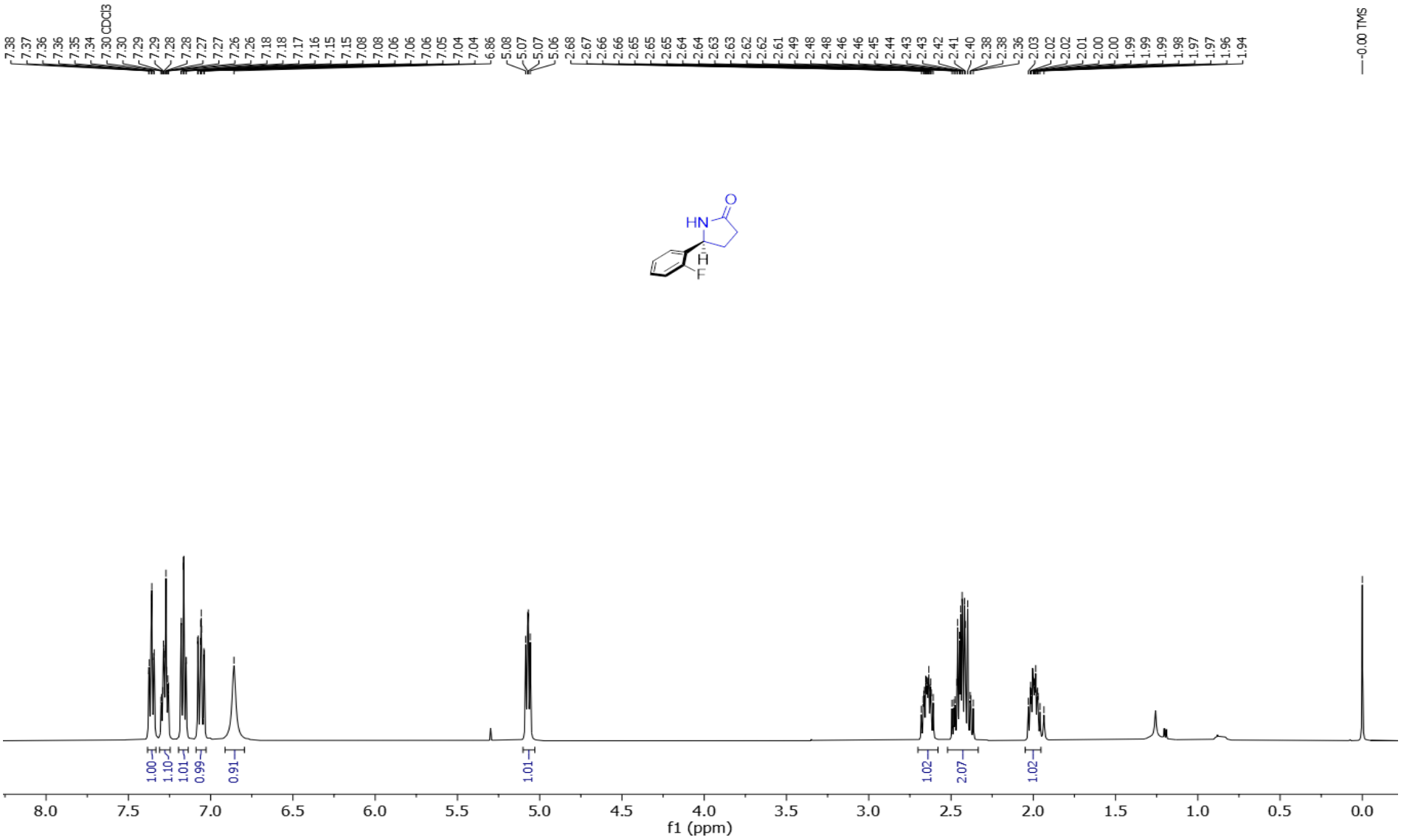
(S)-5-(4-methoxyphenyl)pyrrolidin-2-one (**2i**), ^{1}H NMR (400 MHz, $CDCl_3$):



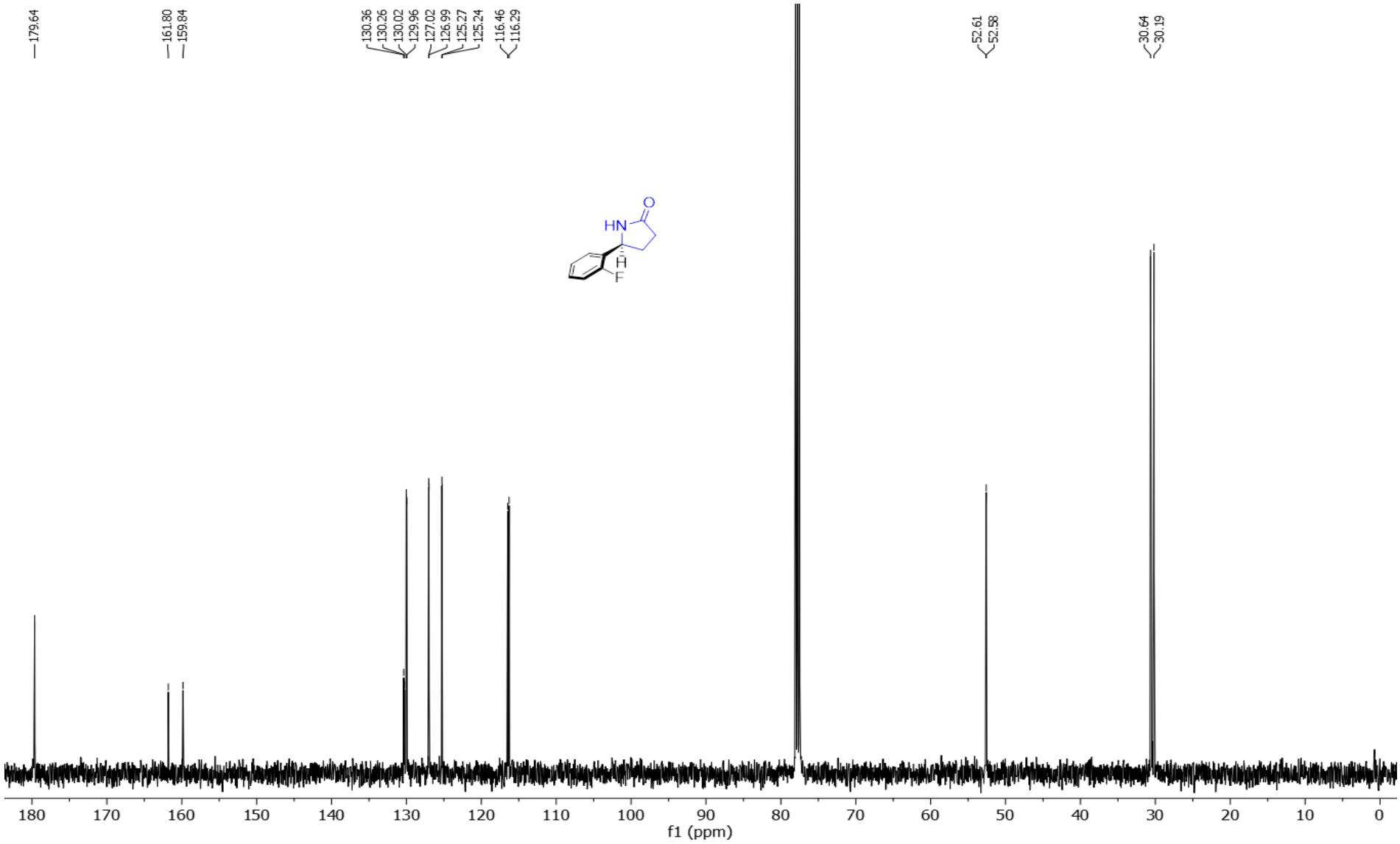
(S)-5-(4-methoxyphenyl)pyrrolidin-2-one (**2i**), ^{13}C NMR (101 MHz, $CDCl_3$):



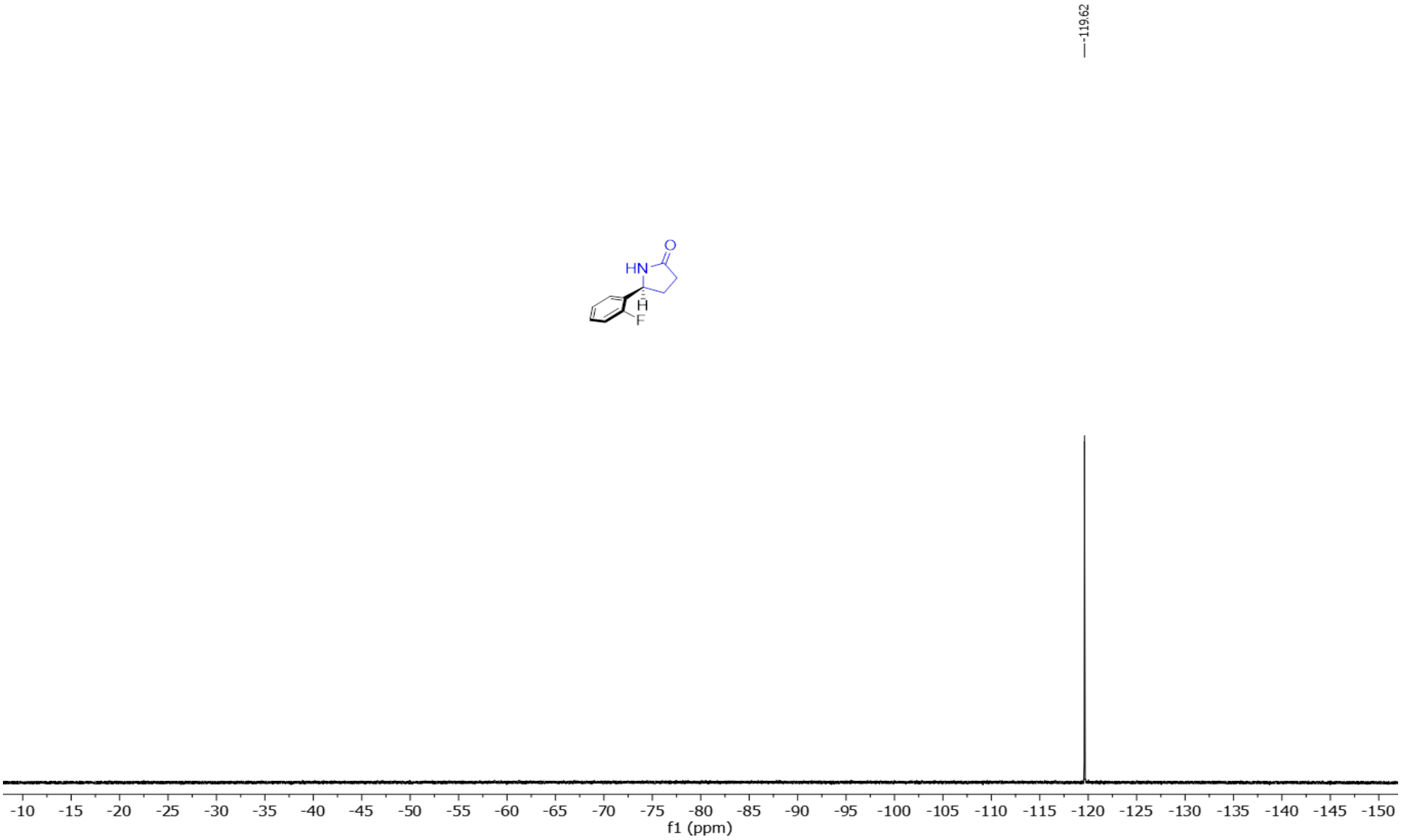
(S)-5-(2-fluorophenyl)pyrrolidin-2-one (**2j**), ^{1}H NMR (400 MHz, $CDCl_3$):



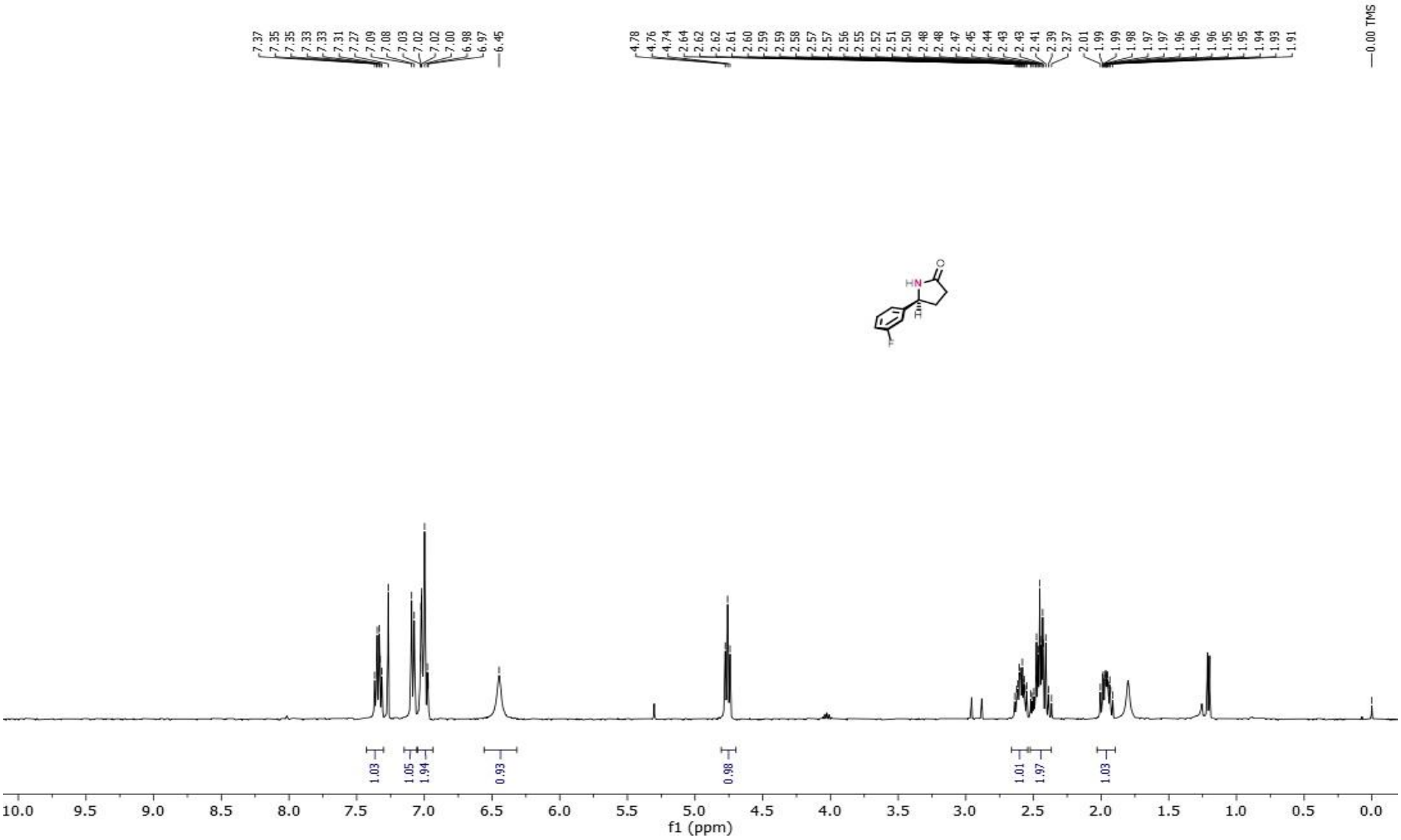
(S)-5-(2-fluorophenyl)pyrrolidin-2-one (**2j**), ^{13}C NMR (101 MHz, $CDCl_3$):



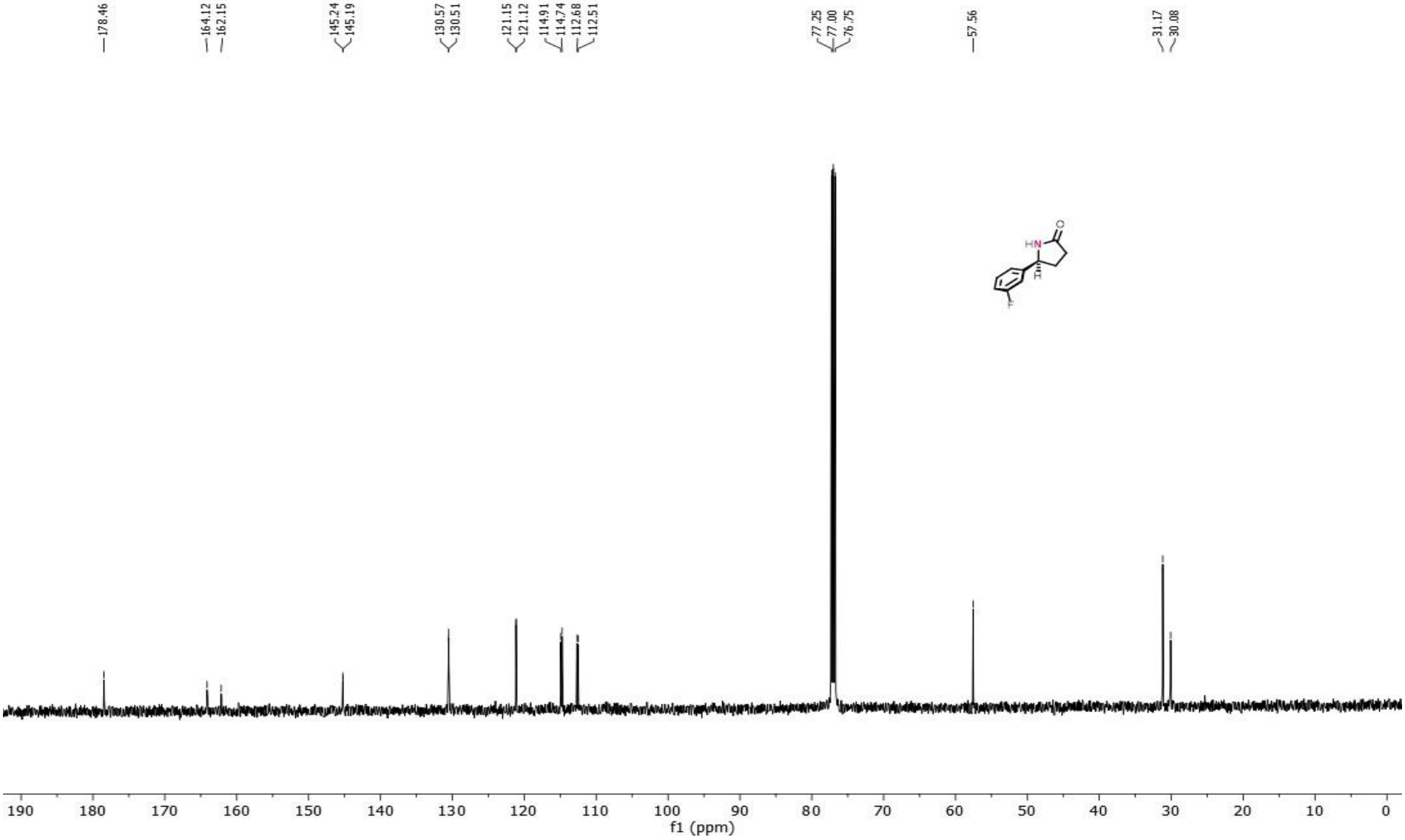
(S)-5-(2-fluorophenyl)pyrrolidin-2-one (**2j**), ^{19}F NMR (376 MHz, $CDCl_3$):



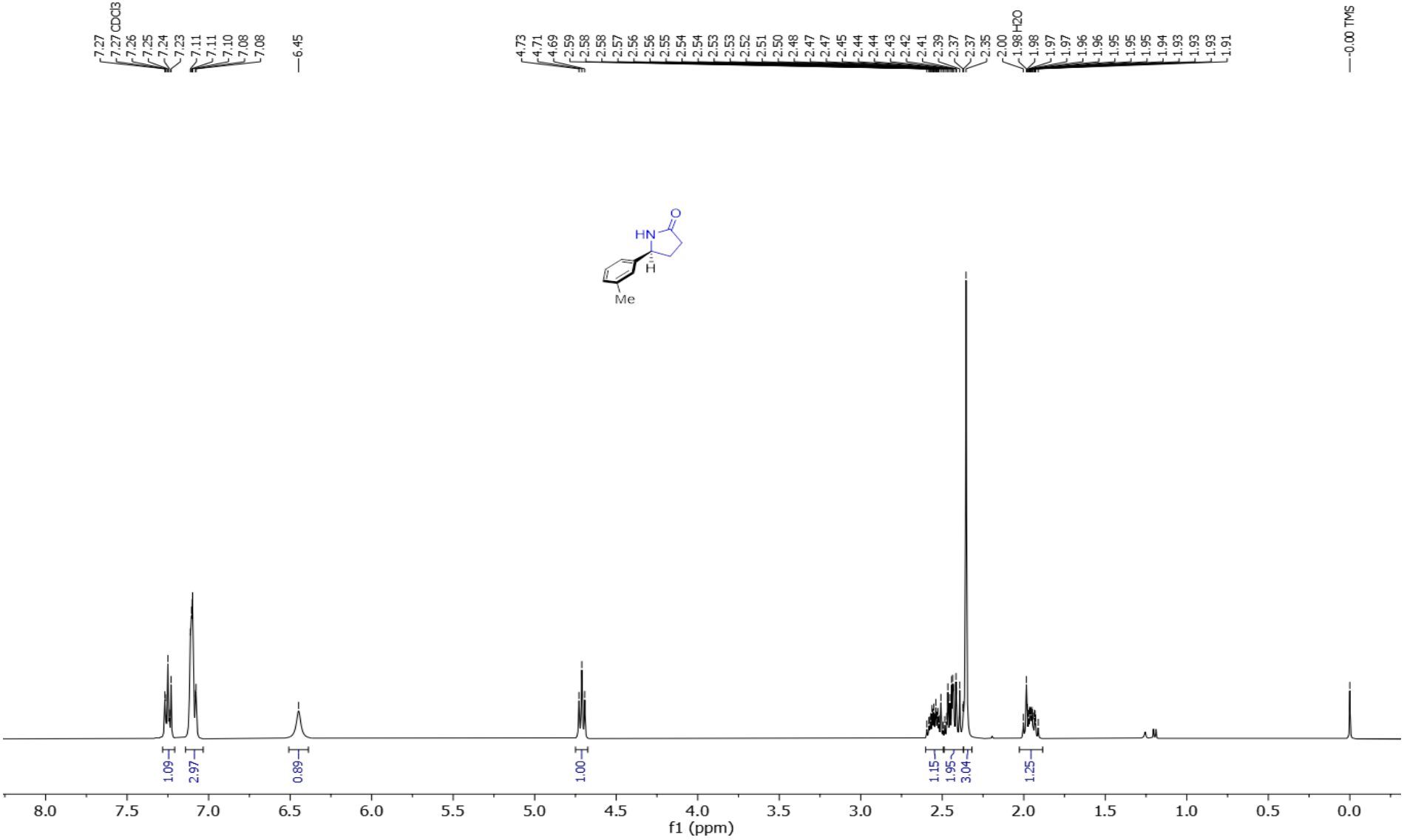
(S)-5-(3-fluorophenyl)pyrrolidin-2-one (**2k**), ^{1}H NMR (400 MHz, $CDCl_3$):



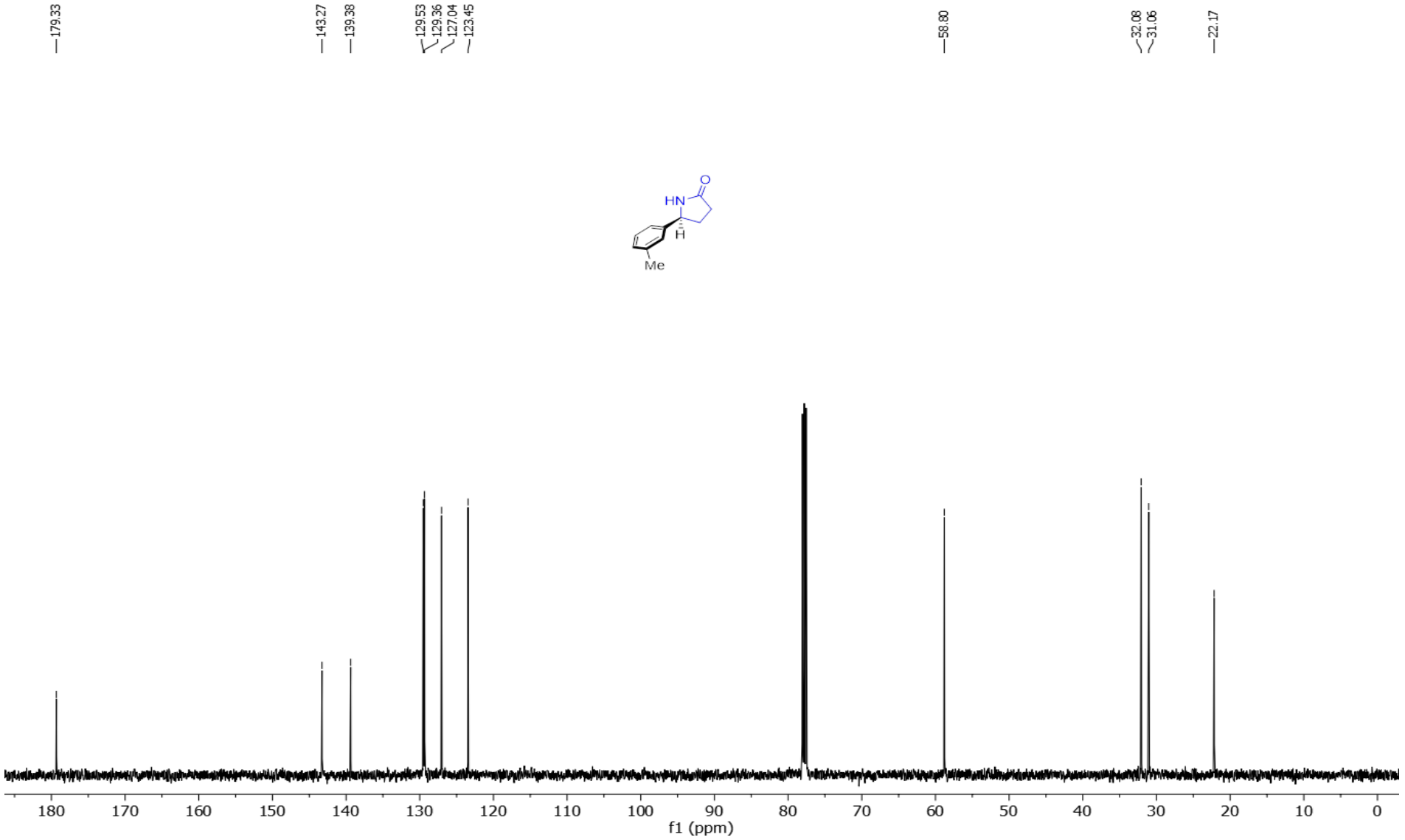
(S)-5-(3-fluorophenyl)pyrrolidin-2-one (**2k**), ^{13}C NMR (101 MHz, $CDCl_3$):



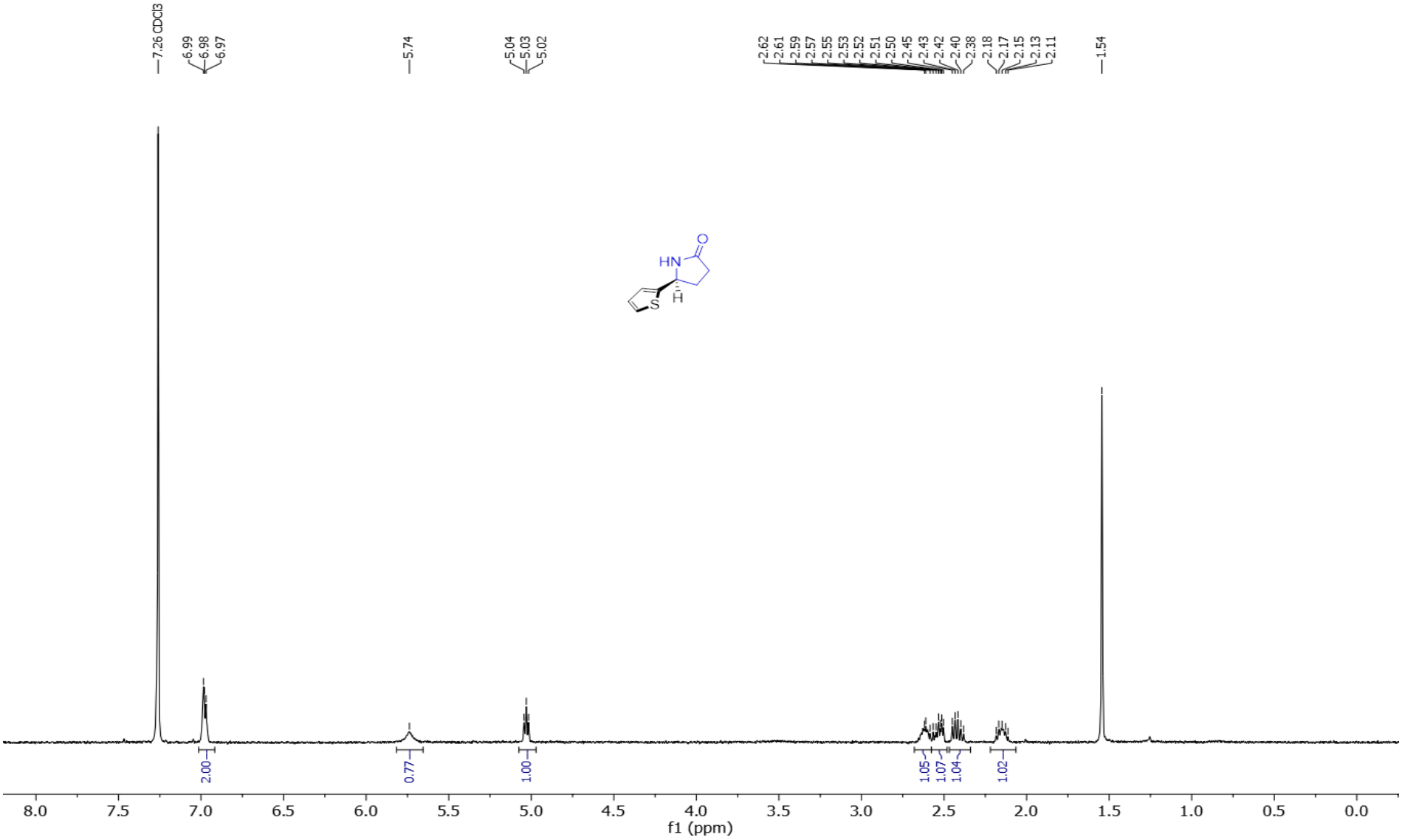
(S)-5-(m-tolyl)pyrrolidin-2-one (**2l**), ^{1}H NMR (400 MHz, $CDCl_3$):



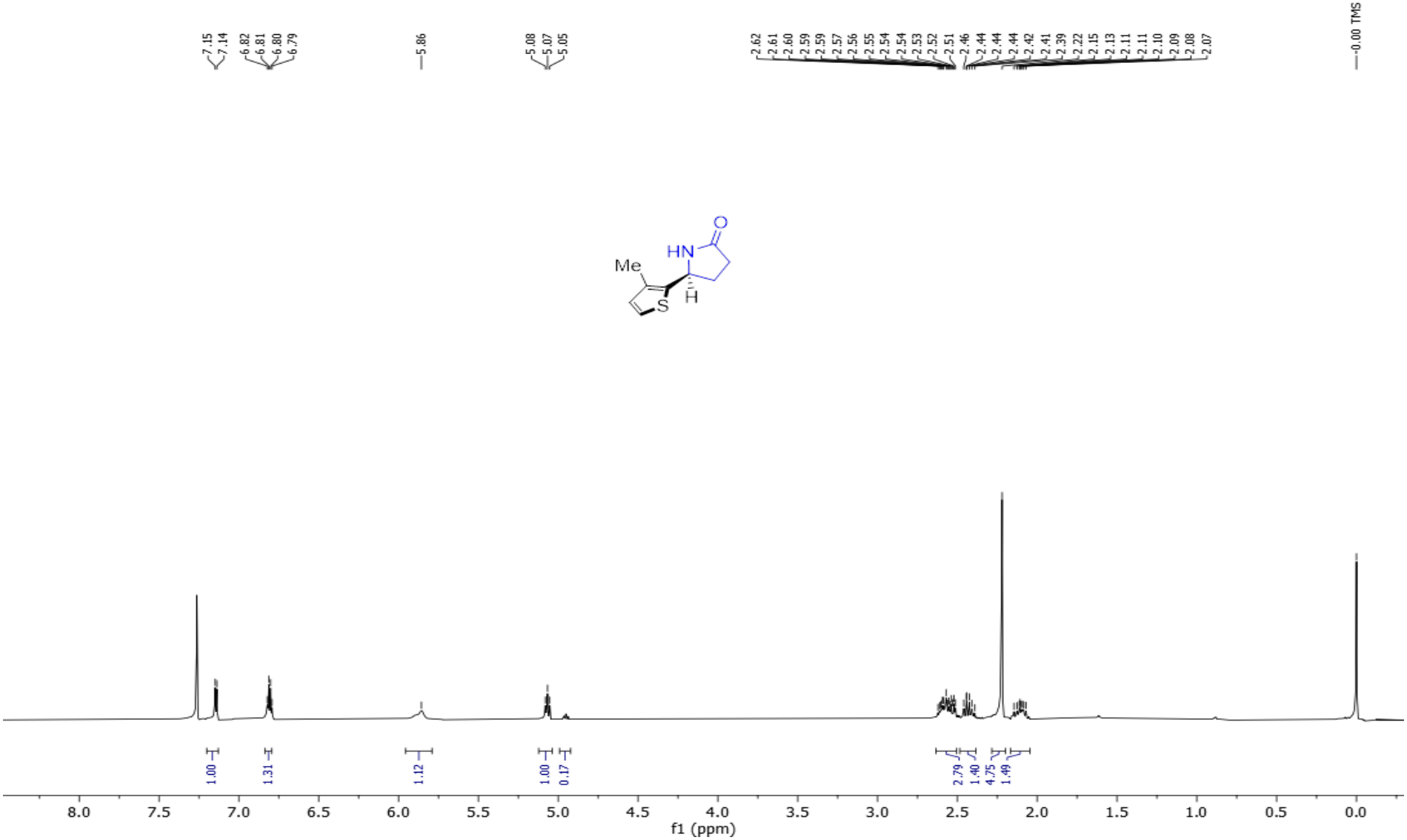
(S)-5-(m-tolyl)pyrrolidin-2-one (**2l**), ^{13}C NMR (101 MHz, $CDCl_3$):



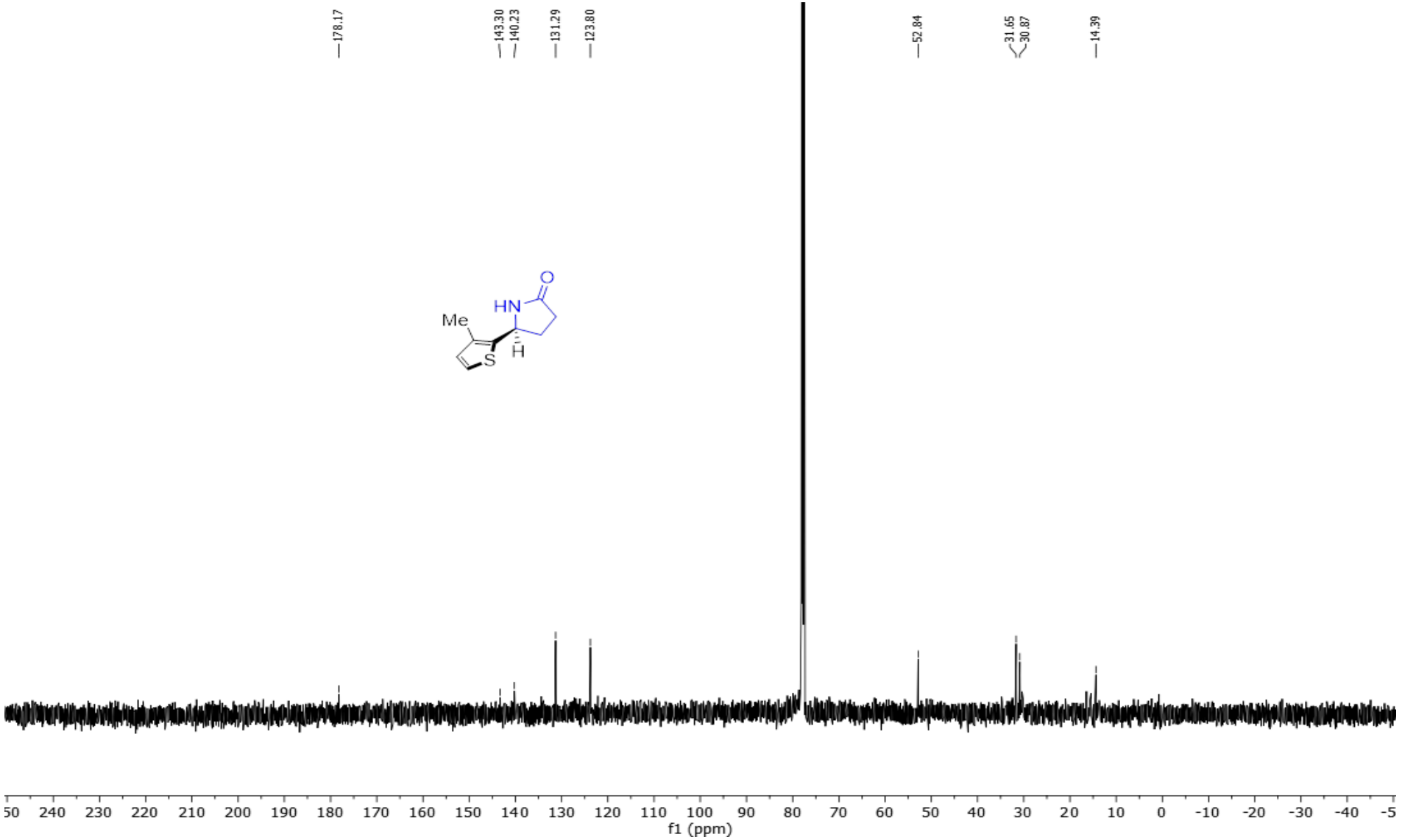
(S)-5-(thiophen-2-yl)pyrrolidin-2-one (**2m**), ^{1}H NMR (400 MHz, $CDCl_3$):



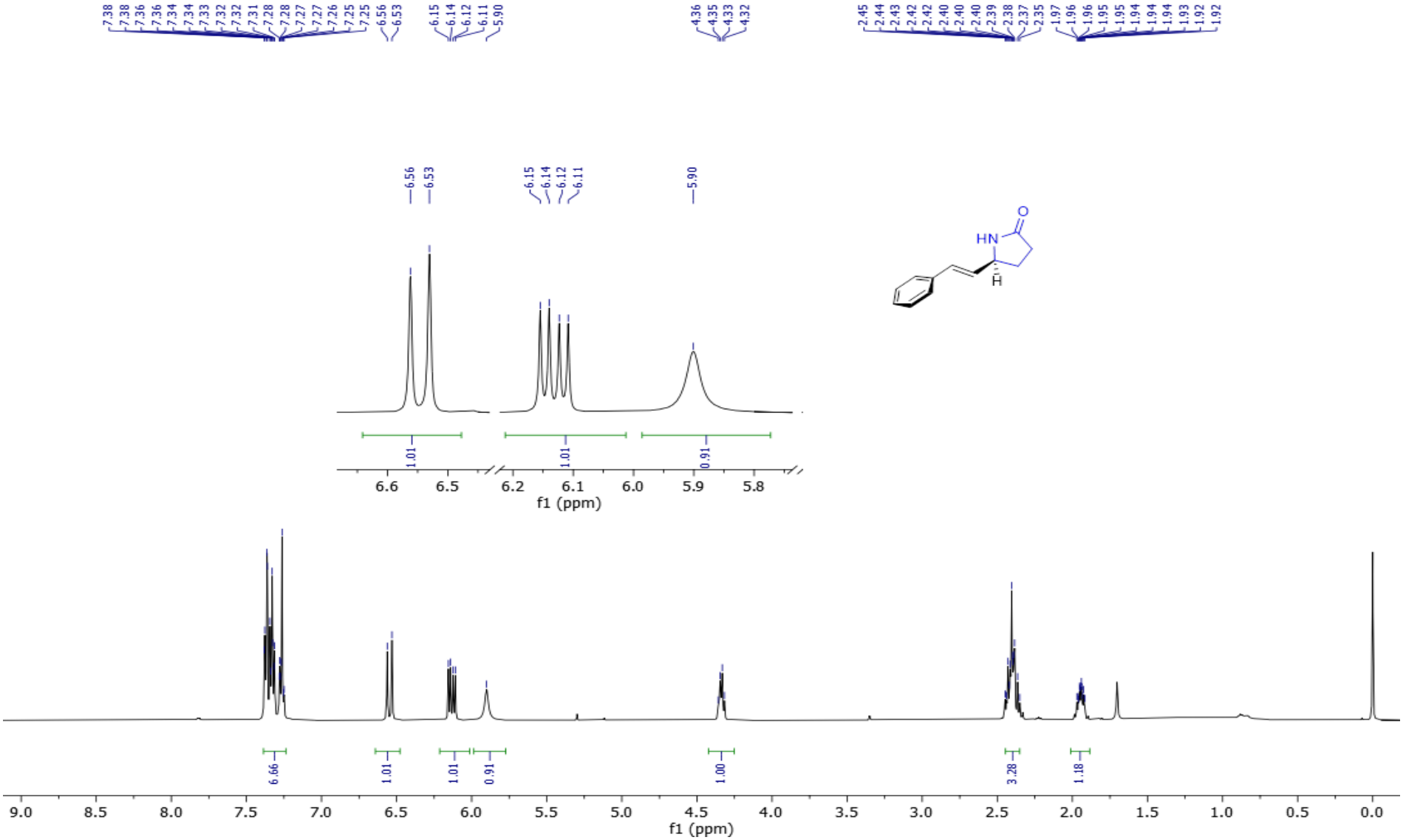
(S)-5-(3-methylthiophen-2-yl)pyrrolidin-2-one (**2n**), ^{1}H NMR (400 MHz, $CDCl_3$):



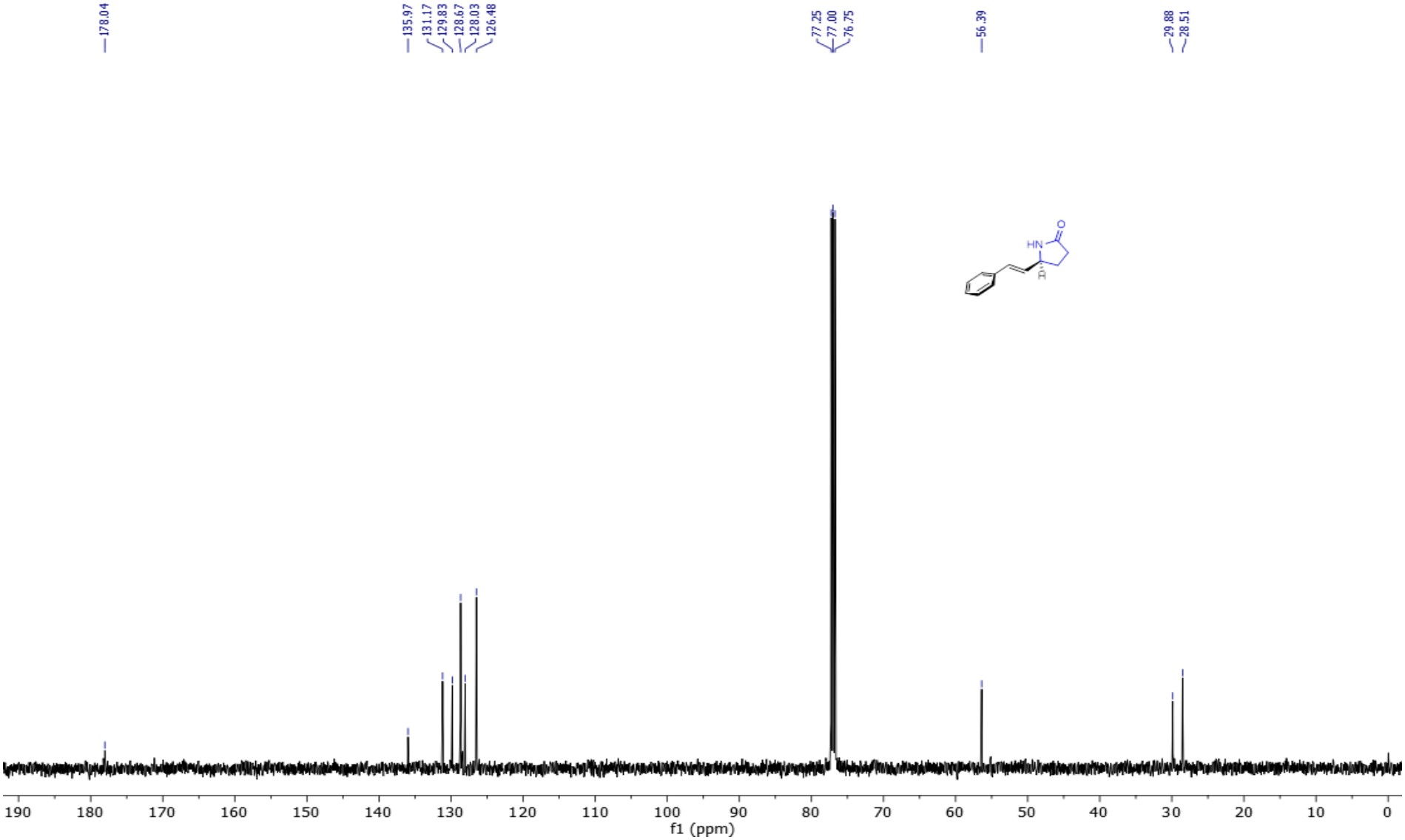
(S)-5-(3-methylthiophen-2-yl)pyrrolidin-2-one (**2n**), ^{13}C NMR (101 MHz, $CDCl_3$):



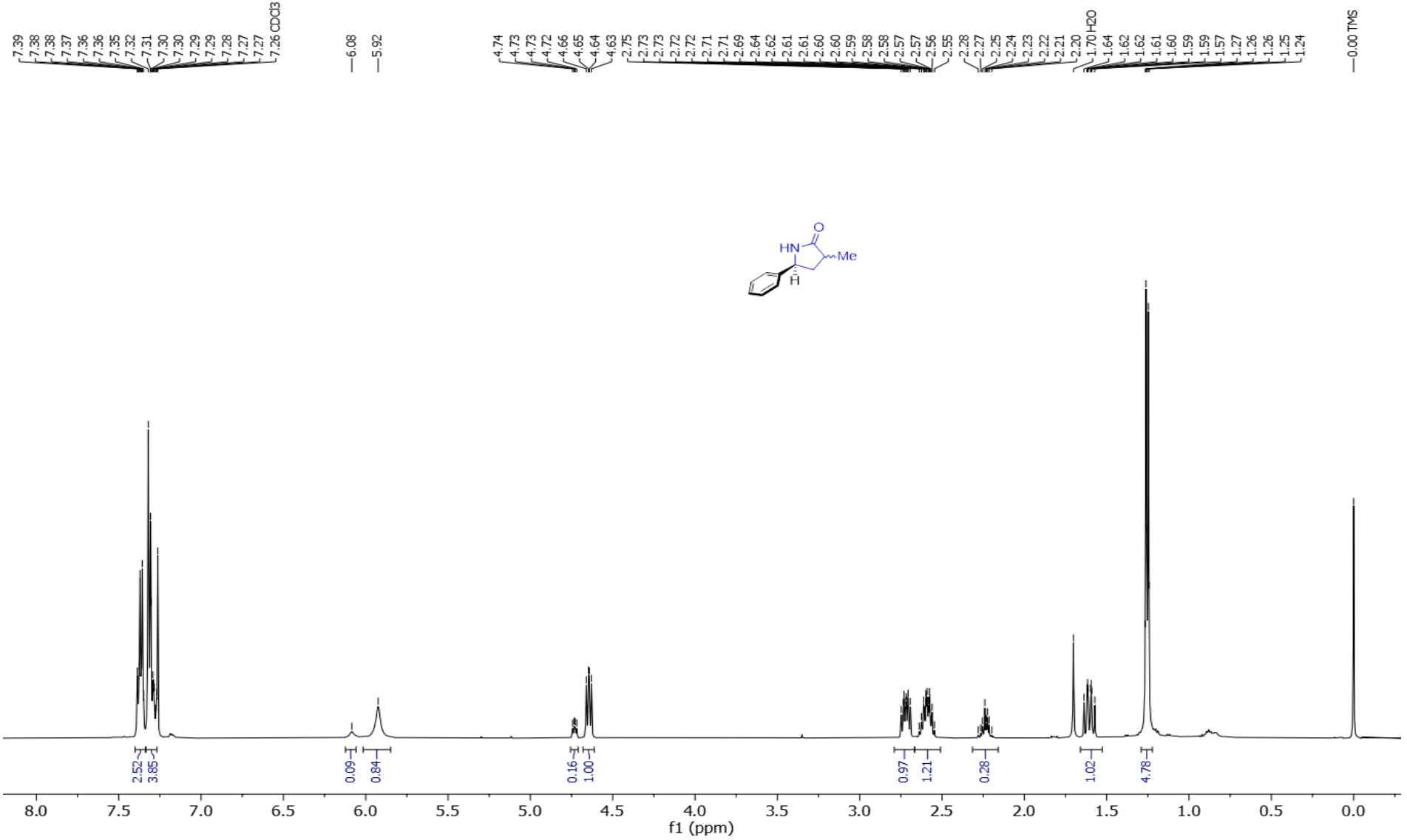
(S,E)-5-styrylpyrrolidin-2-one (**2o**), ^{1}H NMR (400 MHz, $CDCl_3$):



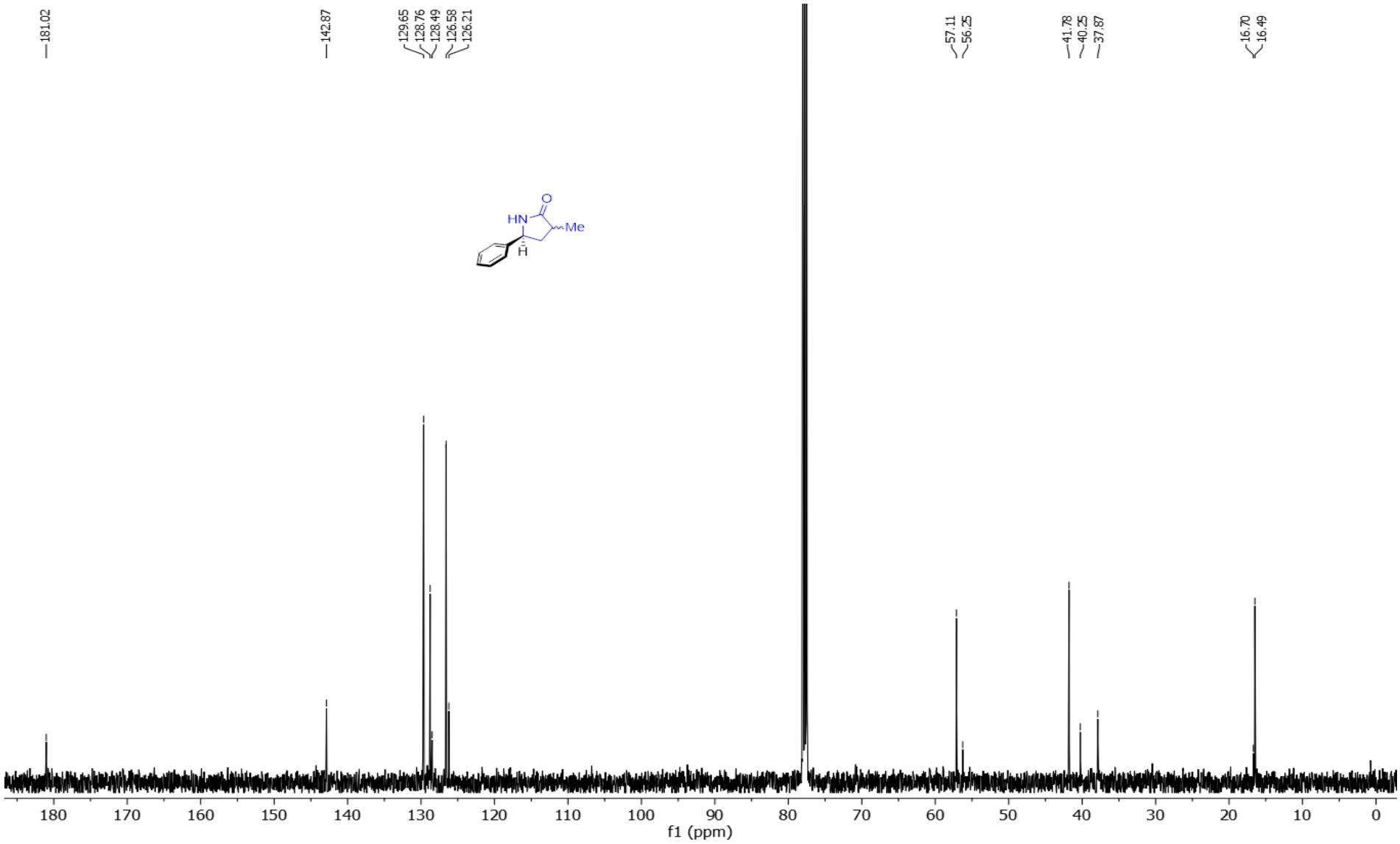
(S,E)-5-styrylpyrrolidin-2-one (**2o**), ^{13}C NMR (101 MHz, $CDCl_3$):



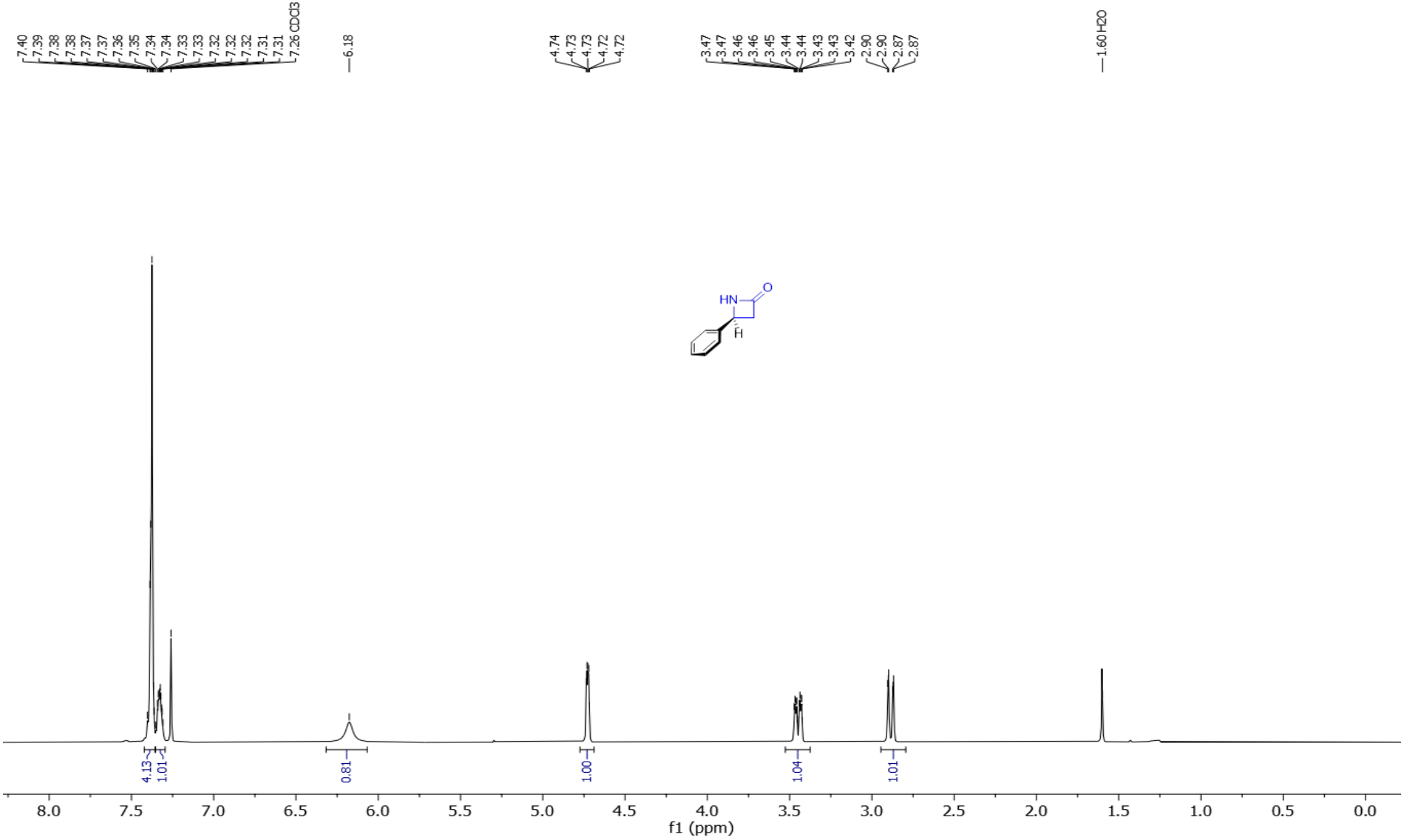
(5S)-3-methyl-5-phenylpyrrolidin-2-one (**2p**), ^{1}H NMR (400 MHz, $CDCl_3$):



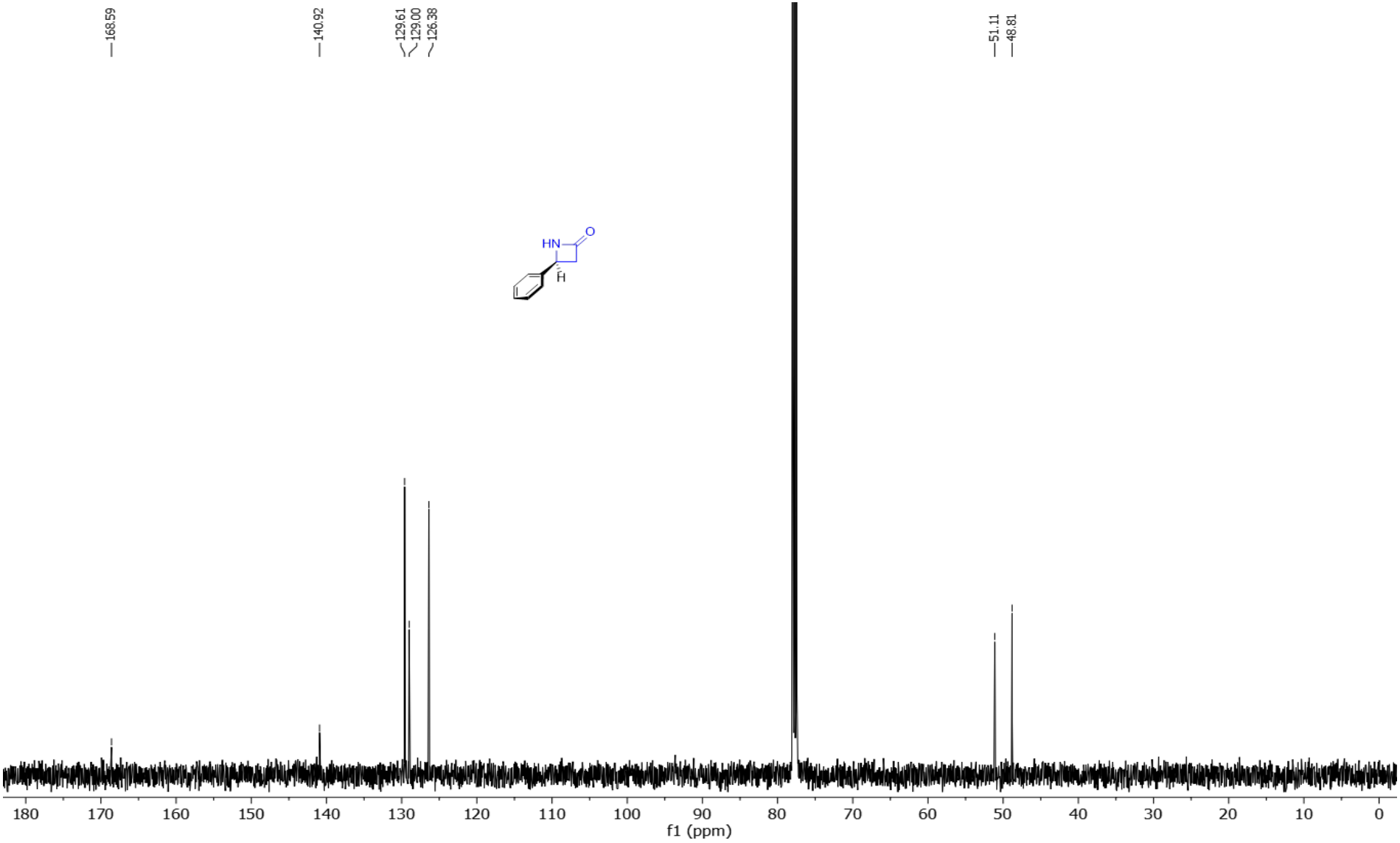
(5S)-3-methyl-5-phenylpyrrolidin-2-one (**2p**), ^{13}C NMR (101 MHz, $CDCl_3$):



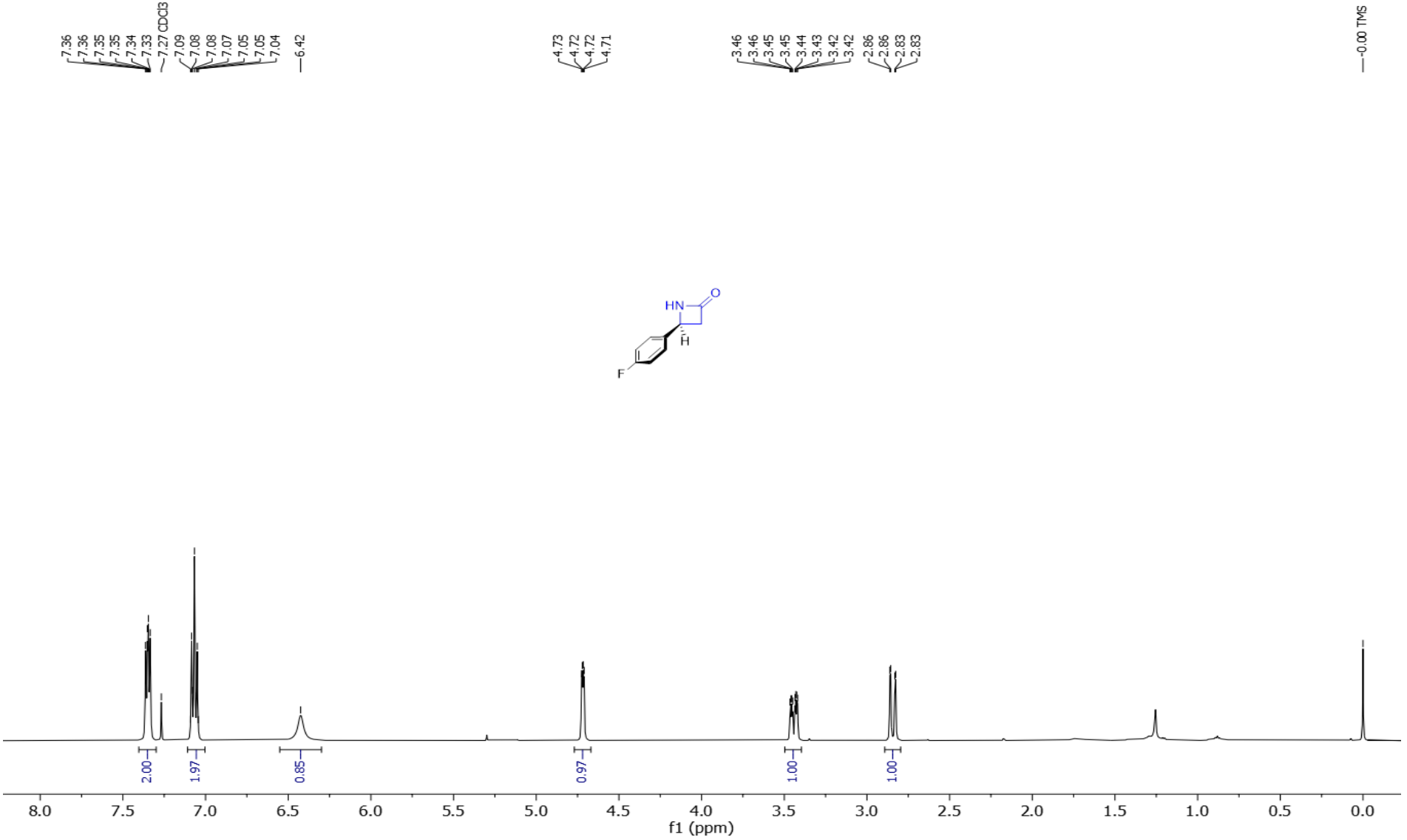
(S)-4-phenylazetidin-2-one (**4a**), ^{1}H NMR (500 MHz, $CDCl_3$):



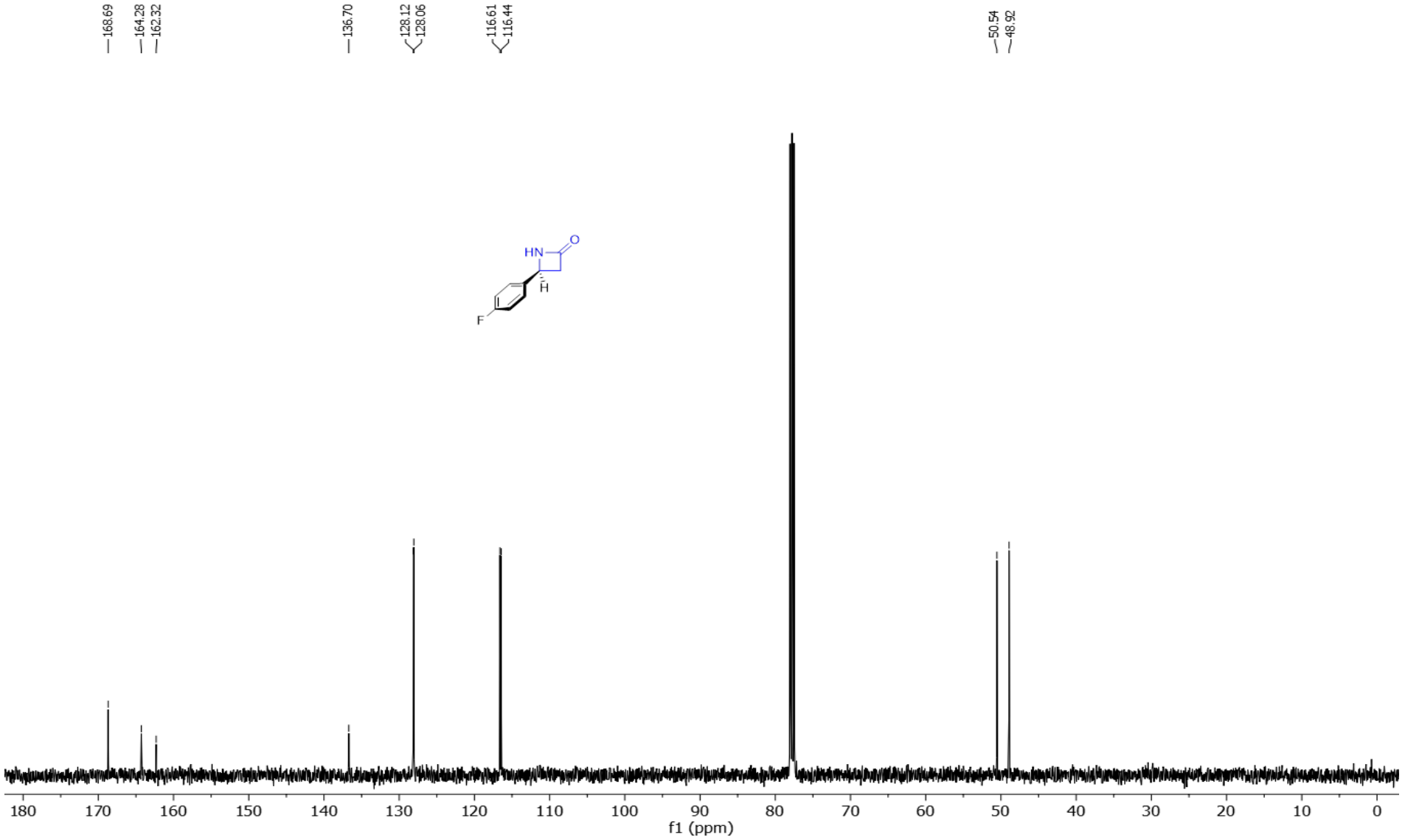
(S)-4-phenylazetidin-2-one (**4a**), ^{13}C NMR (126 MHz, $CDCl_3$):



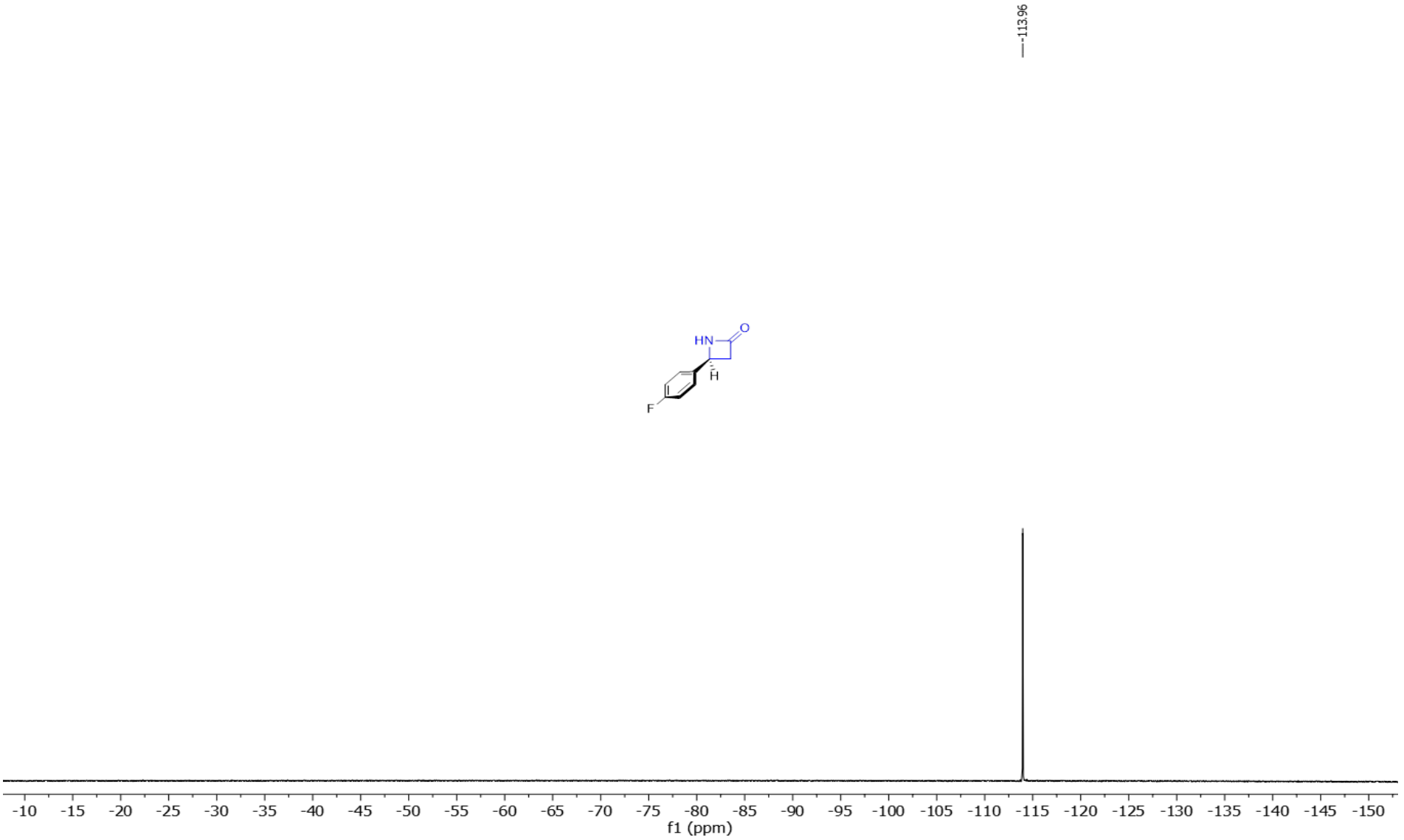
(S)-4-(4-fluorophenyl)azetidin-2-one (**4b**), ^{1}H NMR (400 MHz, $CDCl_3$):



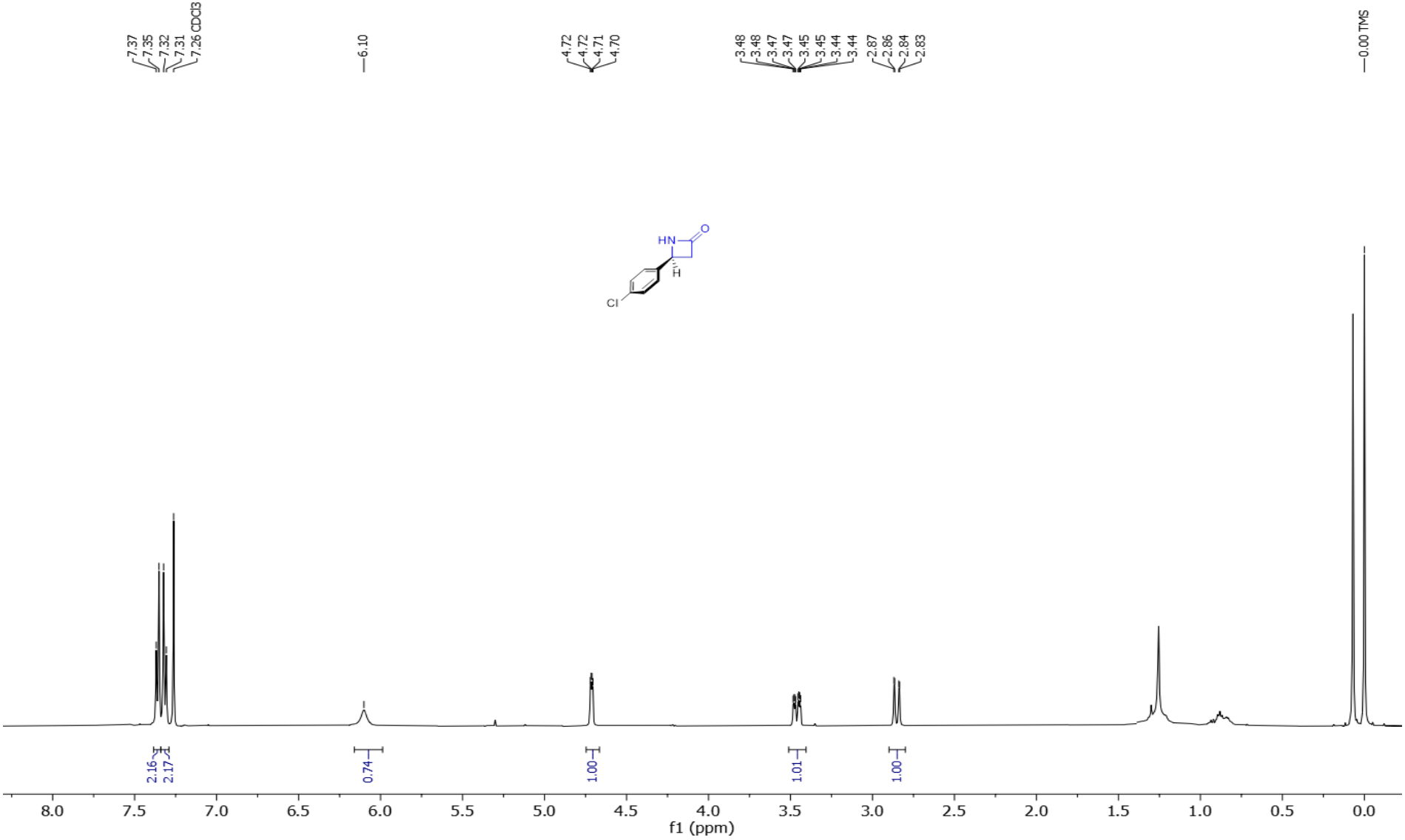
(S)-4-(4-fluorophenyl)azetidin-2-one (**4b**), ^{13}C NMR (101 MHz, $CDCl_3$):



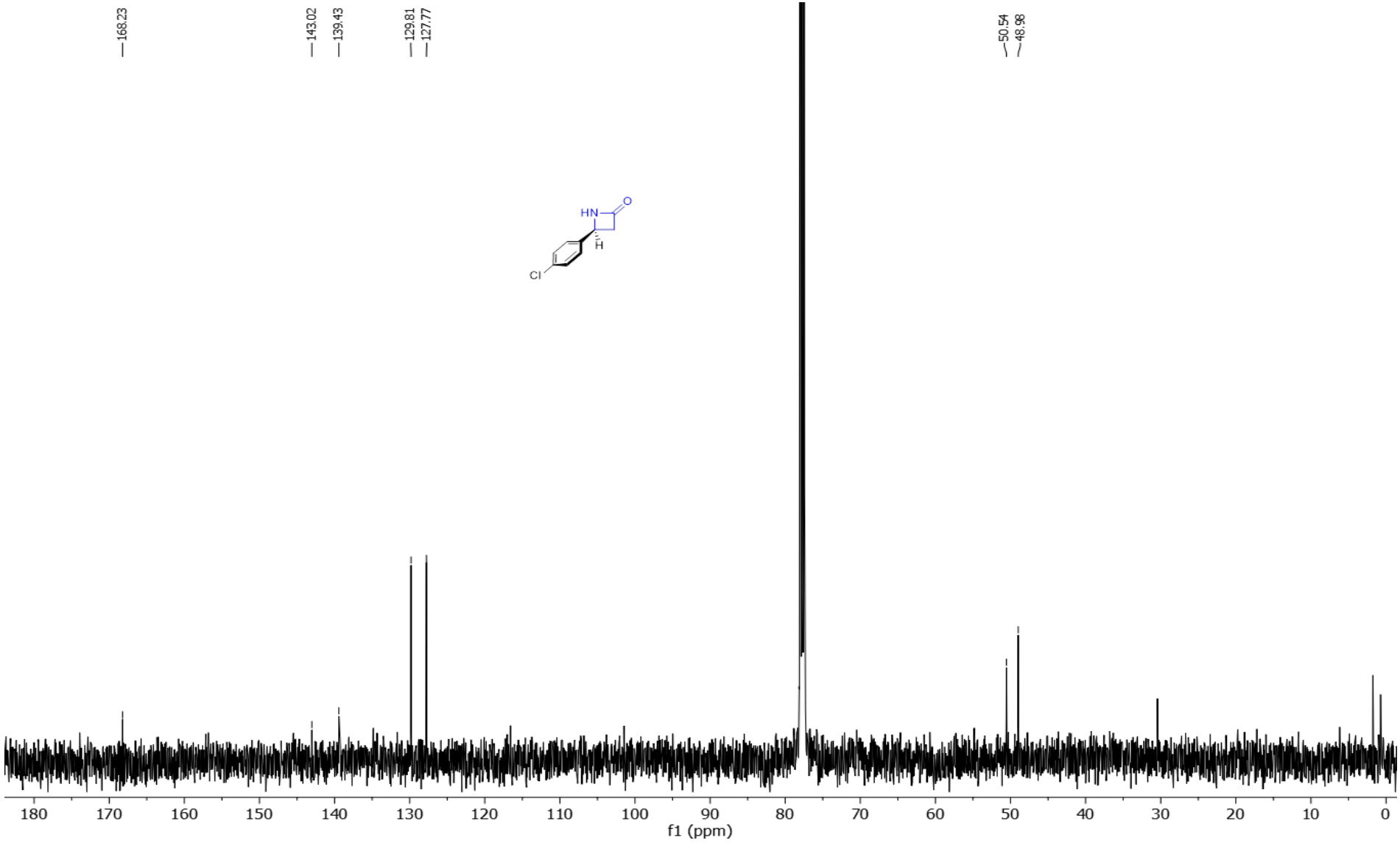
(S)-4-(4-fluorophenyl)azetidin-2-one (**4b**), ^{19}F NMR (376 MHz, $CDCl_3$):



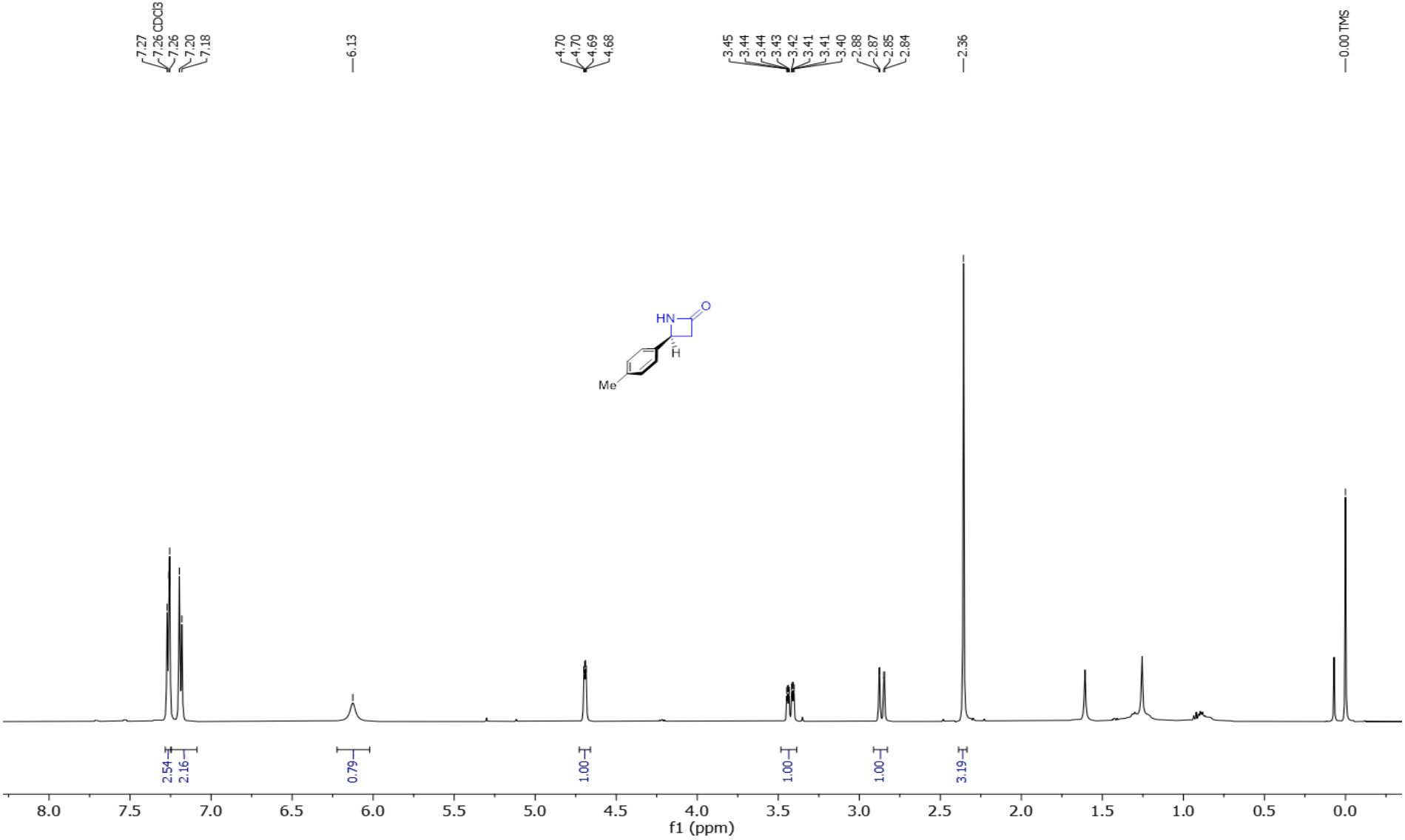
(S)-4-(4-chlorophenyl)azetidin-2-one (**4c**), ^{1}H NMR (400 MHz, $CDCl_3$):



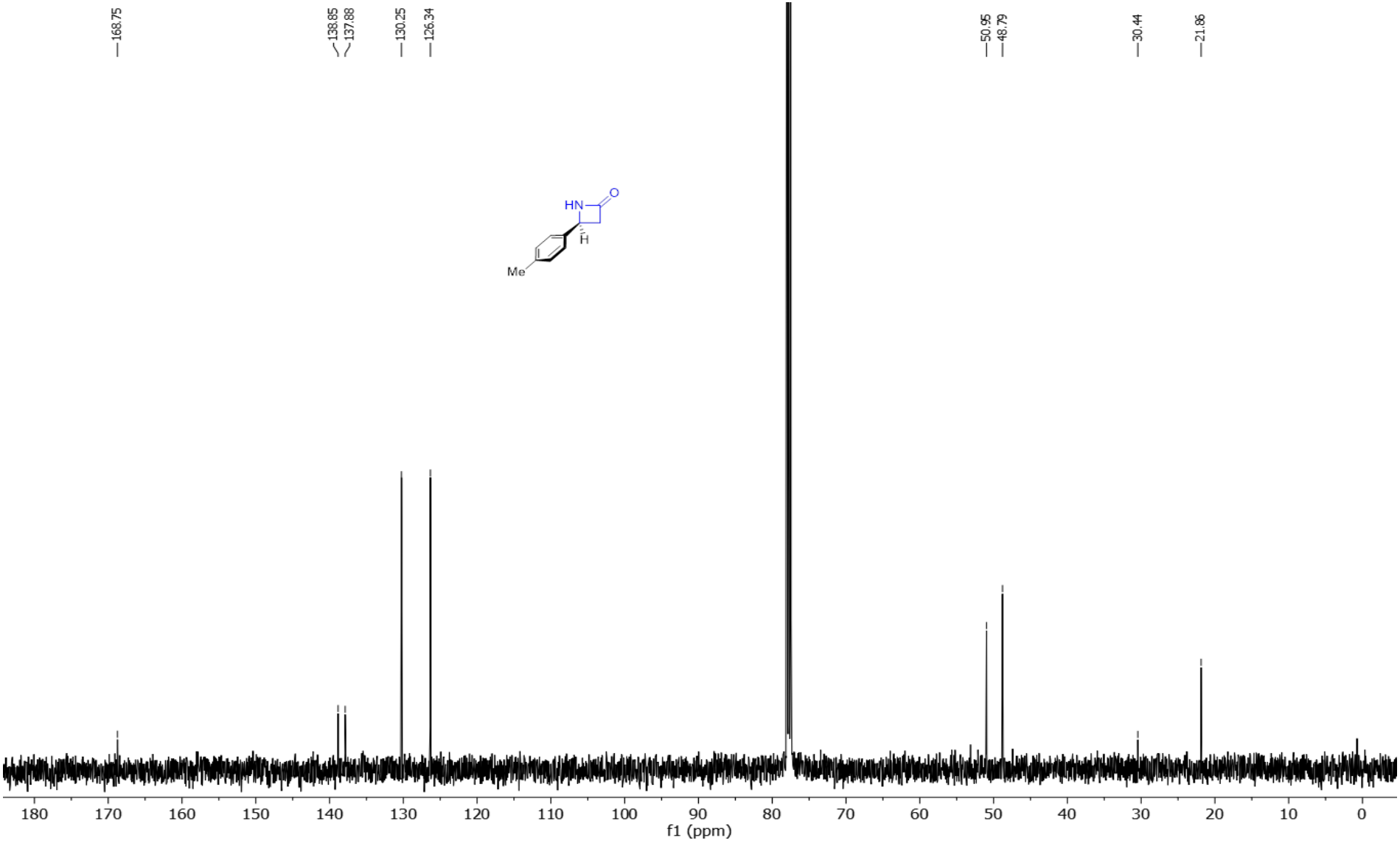
(S)-4-(4-chlorophenyl)azetidin-2-one (**4c**), ^{13}C NMR (101 MHz, $CDCl_3$):



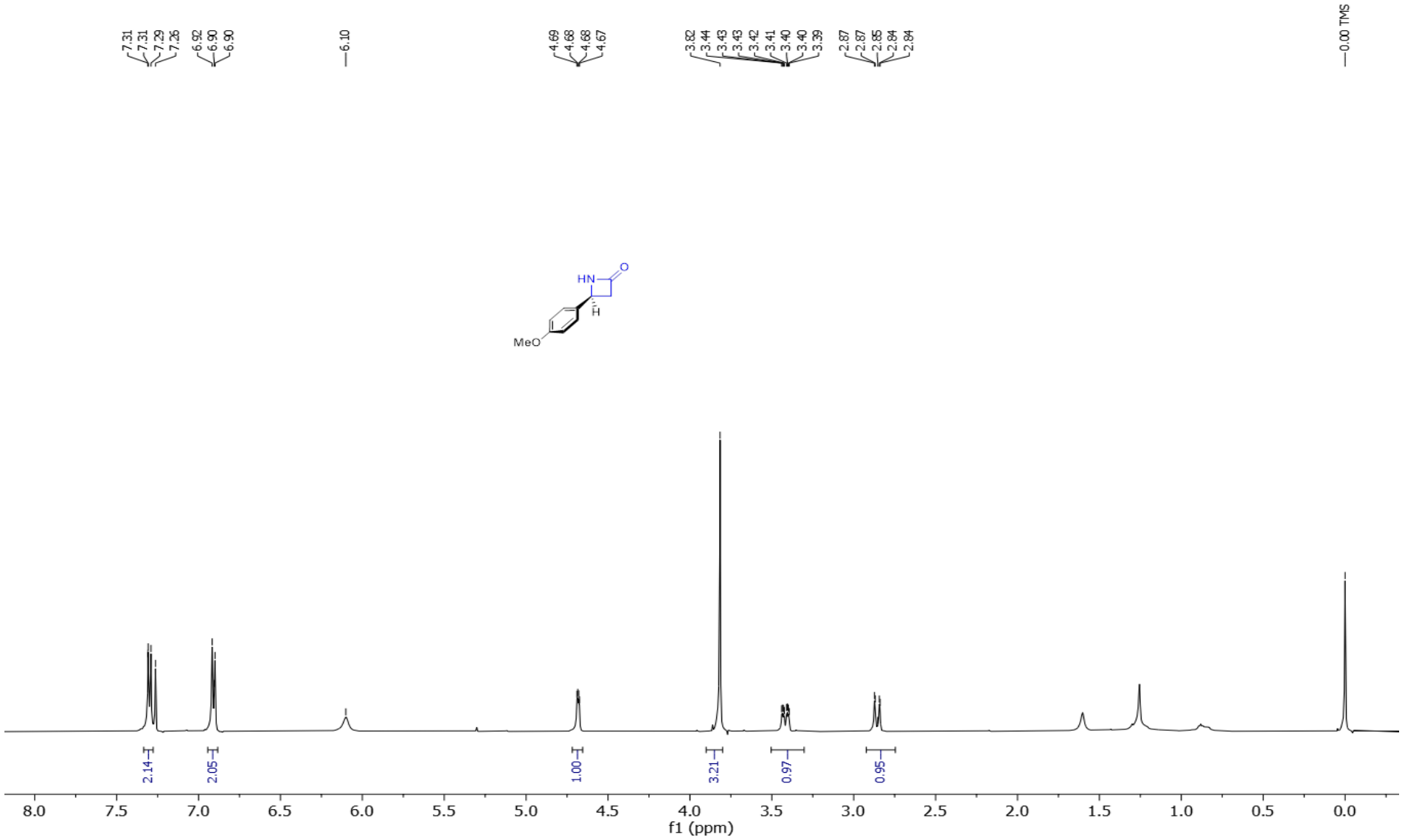
(S)-4-(p-tolyl)azetidin-2-one (**4d**), ^{1}H NMR (400 MHz, $CDCl_3$):



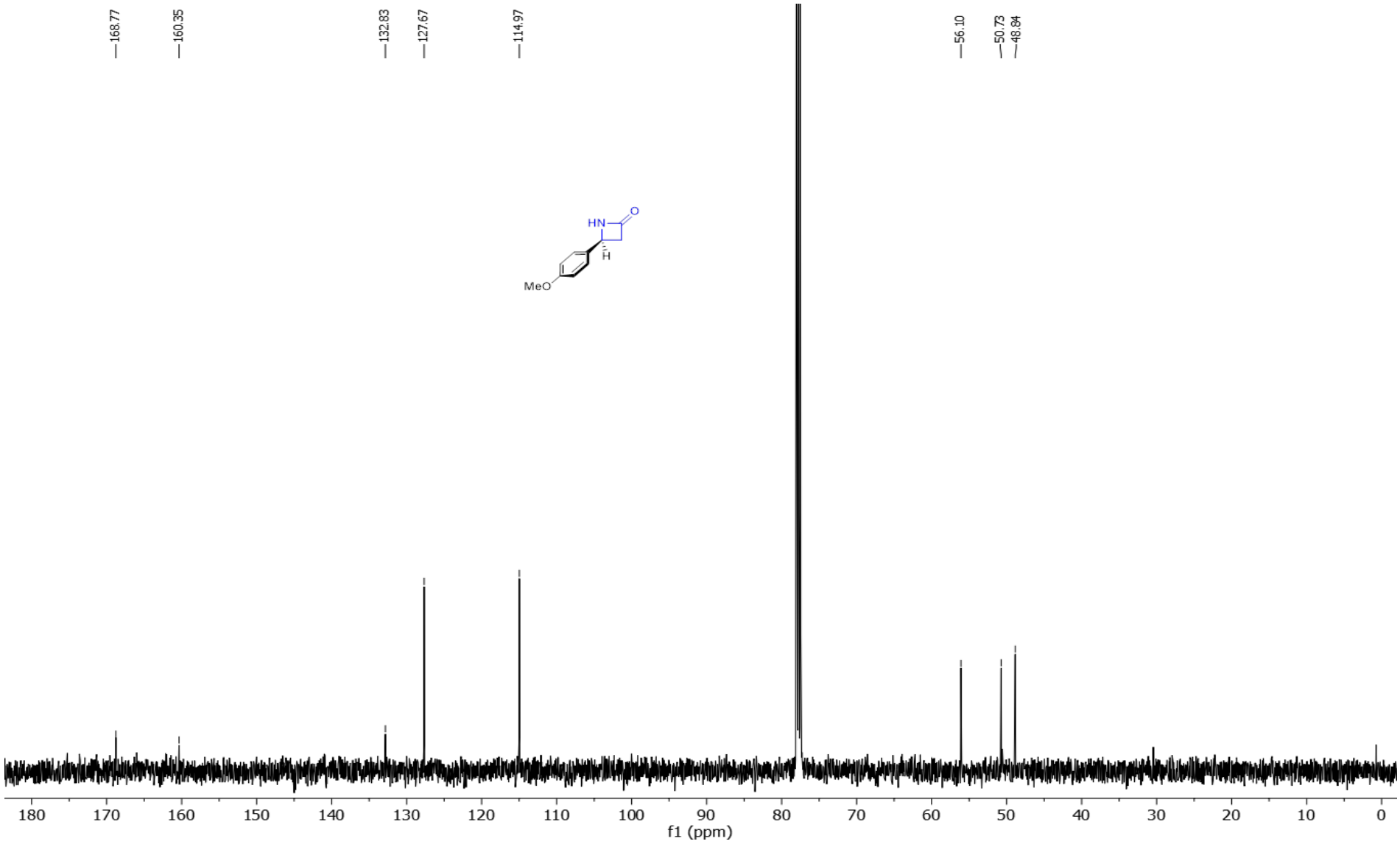
(S)-4-(p-tolyl)azetidin-2-one (**4d**), ^{13}C NMR (101 MHz, $CDCl_3$):



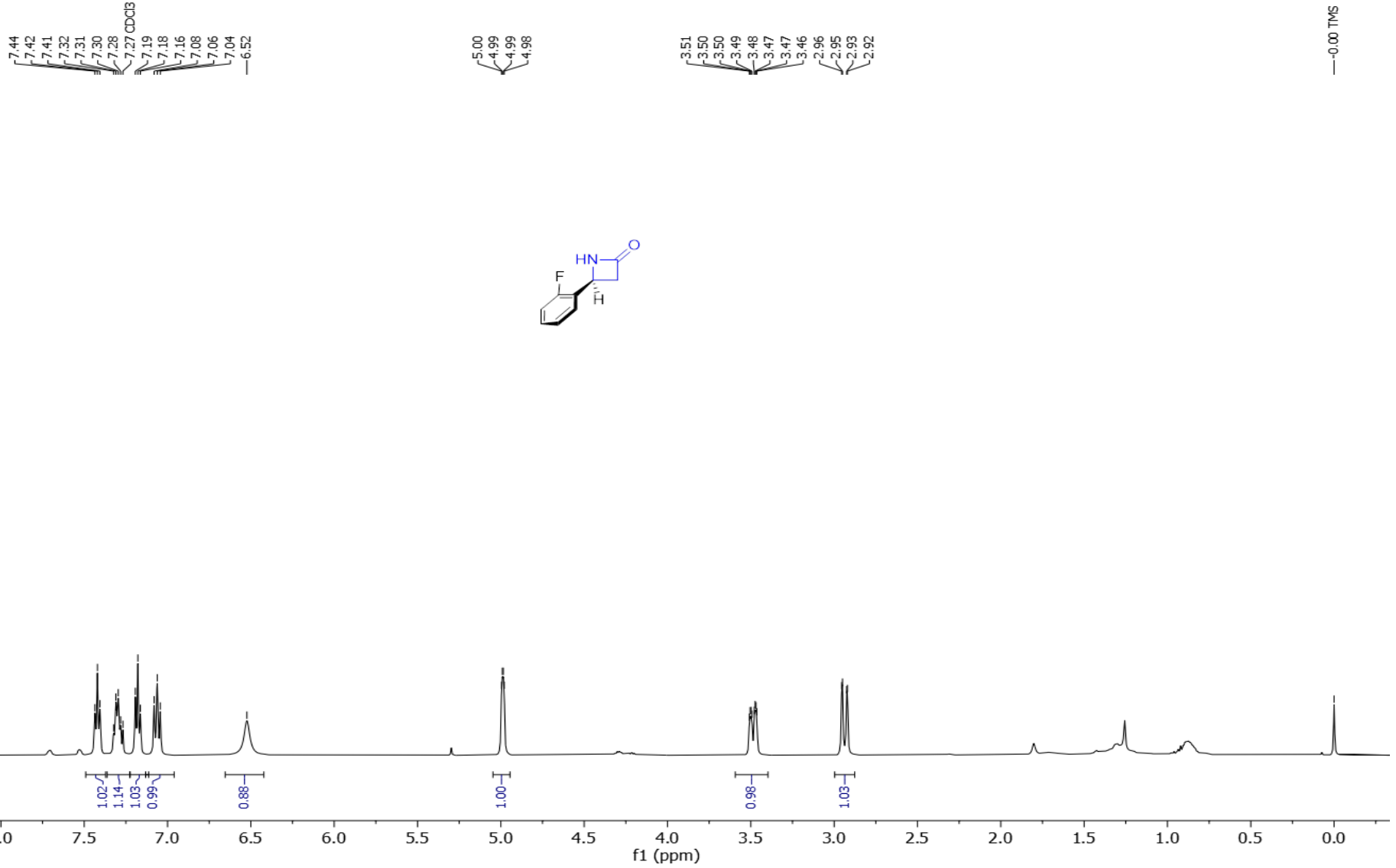
(S)-4-(4-methoxyphenyl)azetidin-2-one (**4e**), ^{1}H NMR (400 MHz, $CDCl_3$):



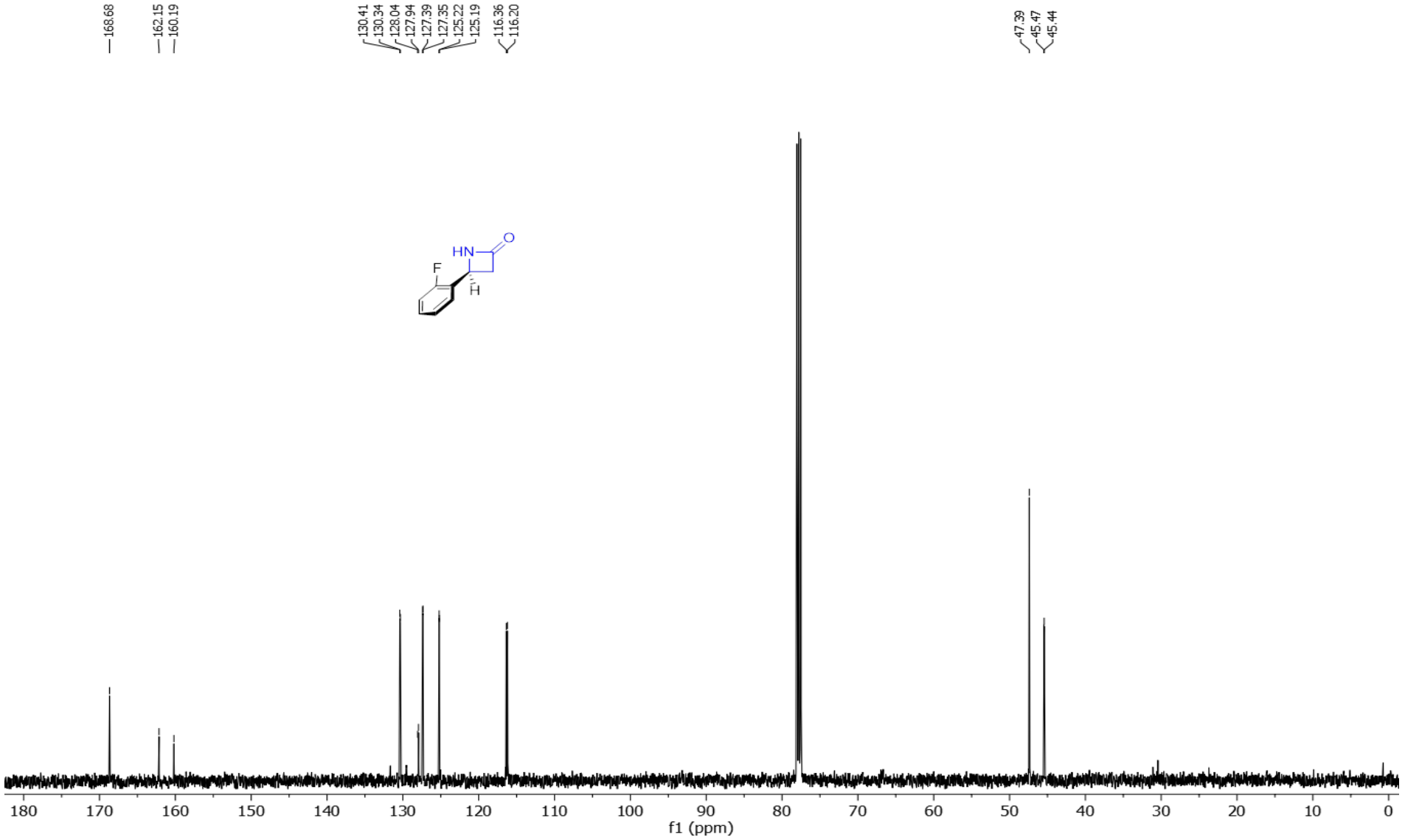
(S)-4-(4-methoxyphenyl)azetidin-2-one (**4e**), ^{13}C NMR (101 MHz, $CDCl_3$):



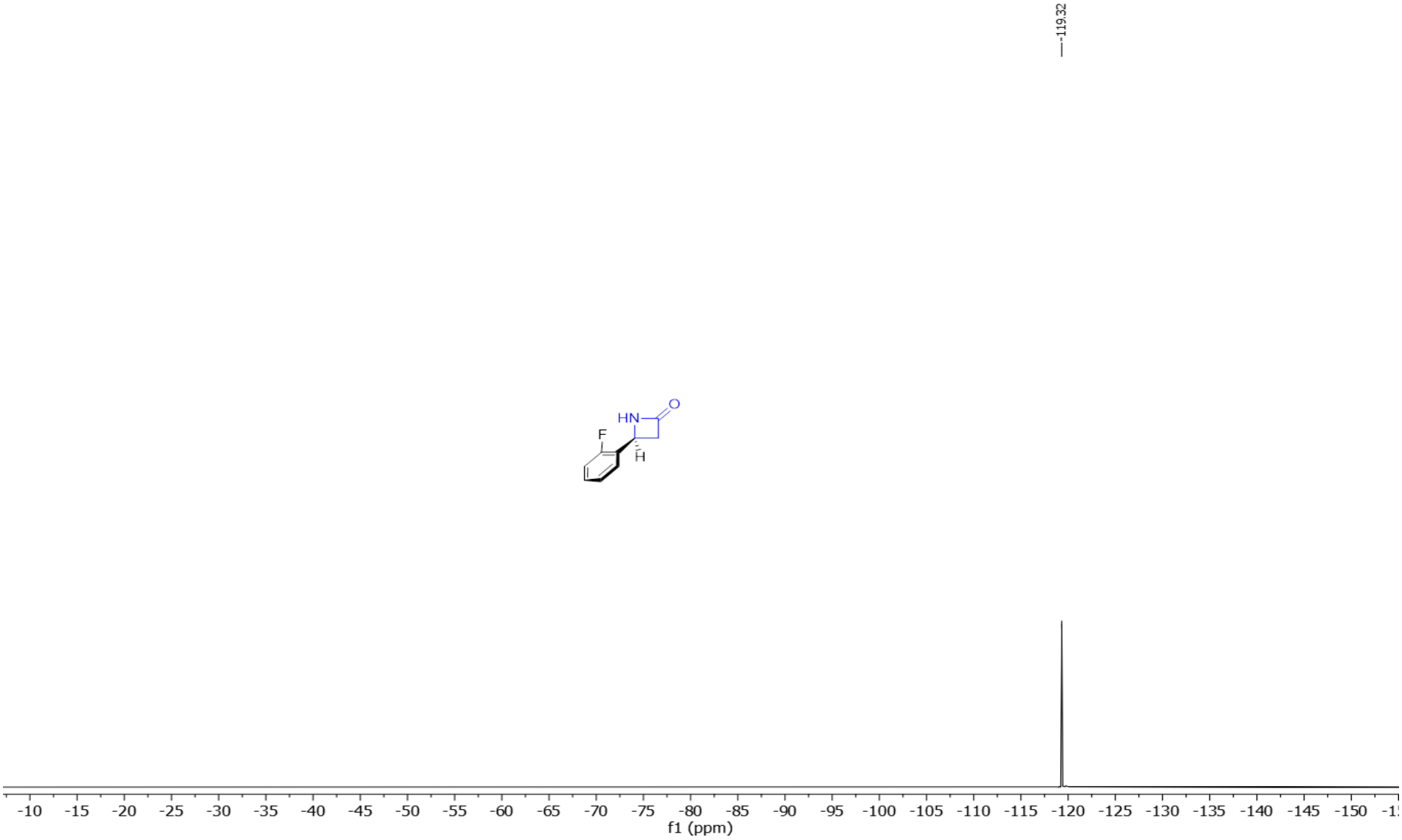
(S)-4-(2-fluorophenyl)azetidin-2-one (**4f**), ^{1}H NMR (400 MHz, $CDCl_3$):



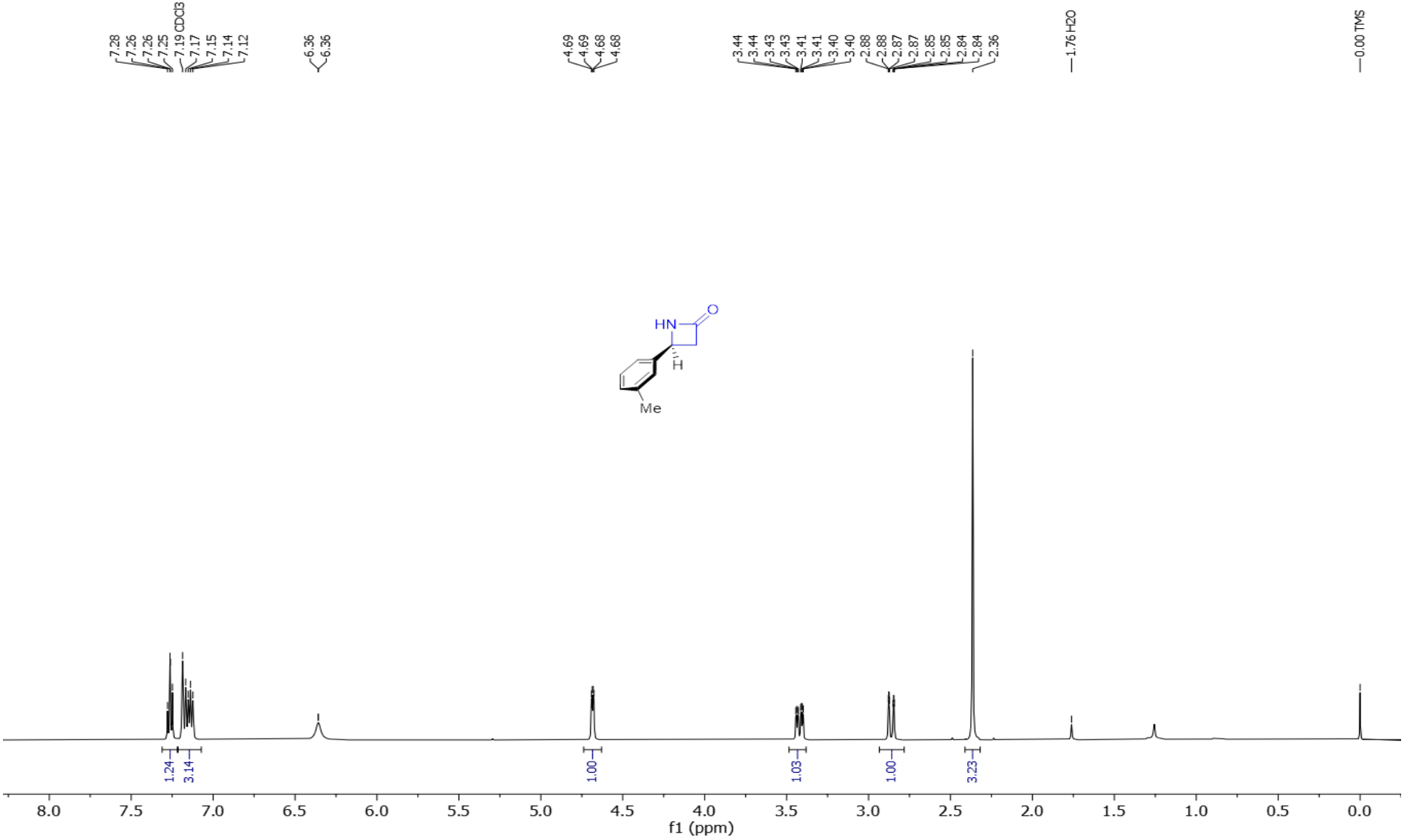
(S)-4-(2-fluorophenyl)azetidin-2-one (**4f**), ^{13}C NMR (101 MHz, $CDCl_3$):



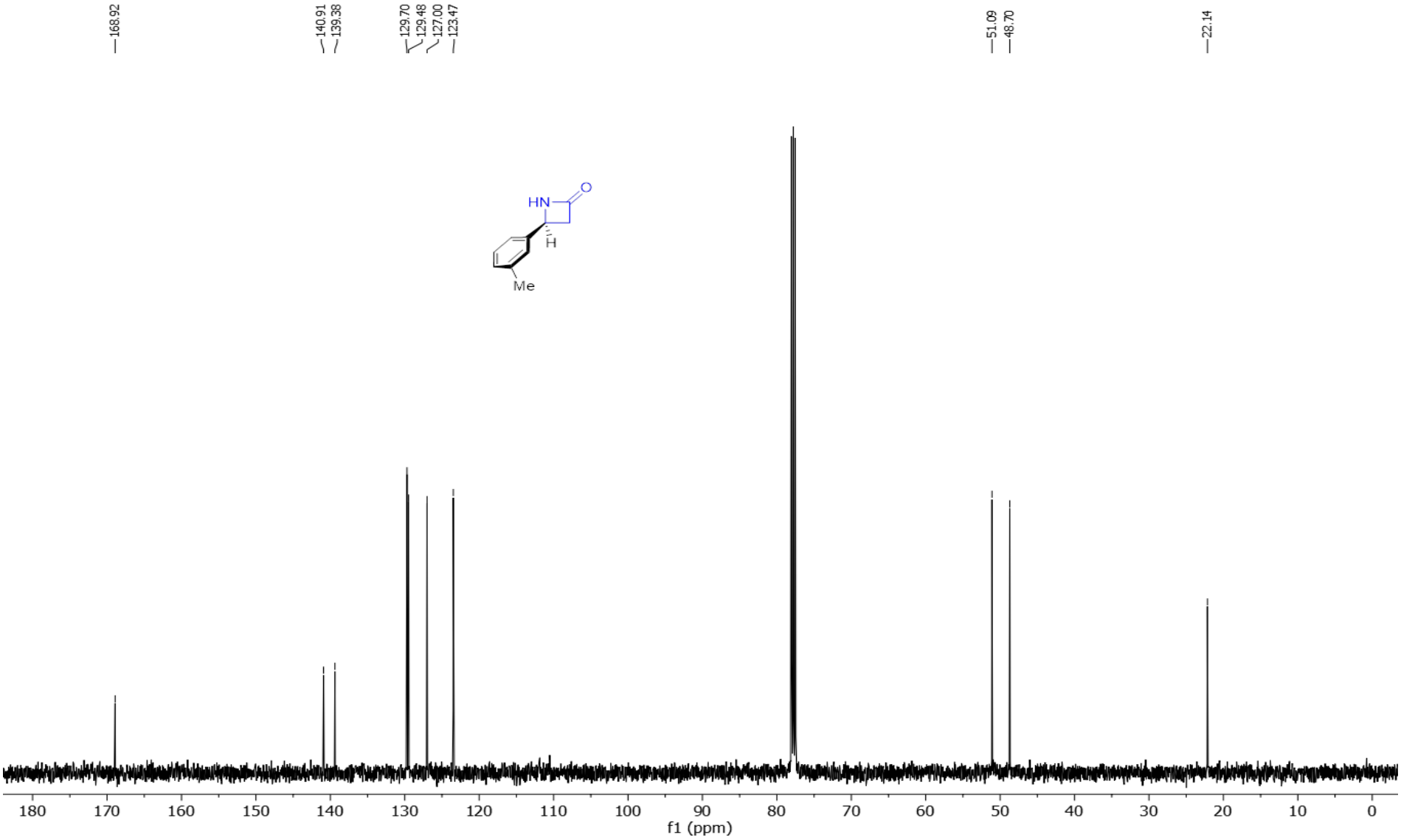
(S)-4-(2-fluorophenyl)azetidin-2-one (**4f**), ^{19}F NMR (376 MHz, $CDCl_3$):



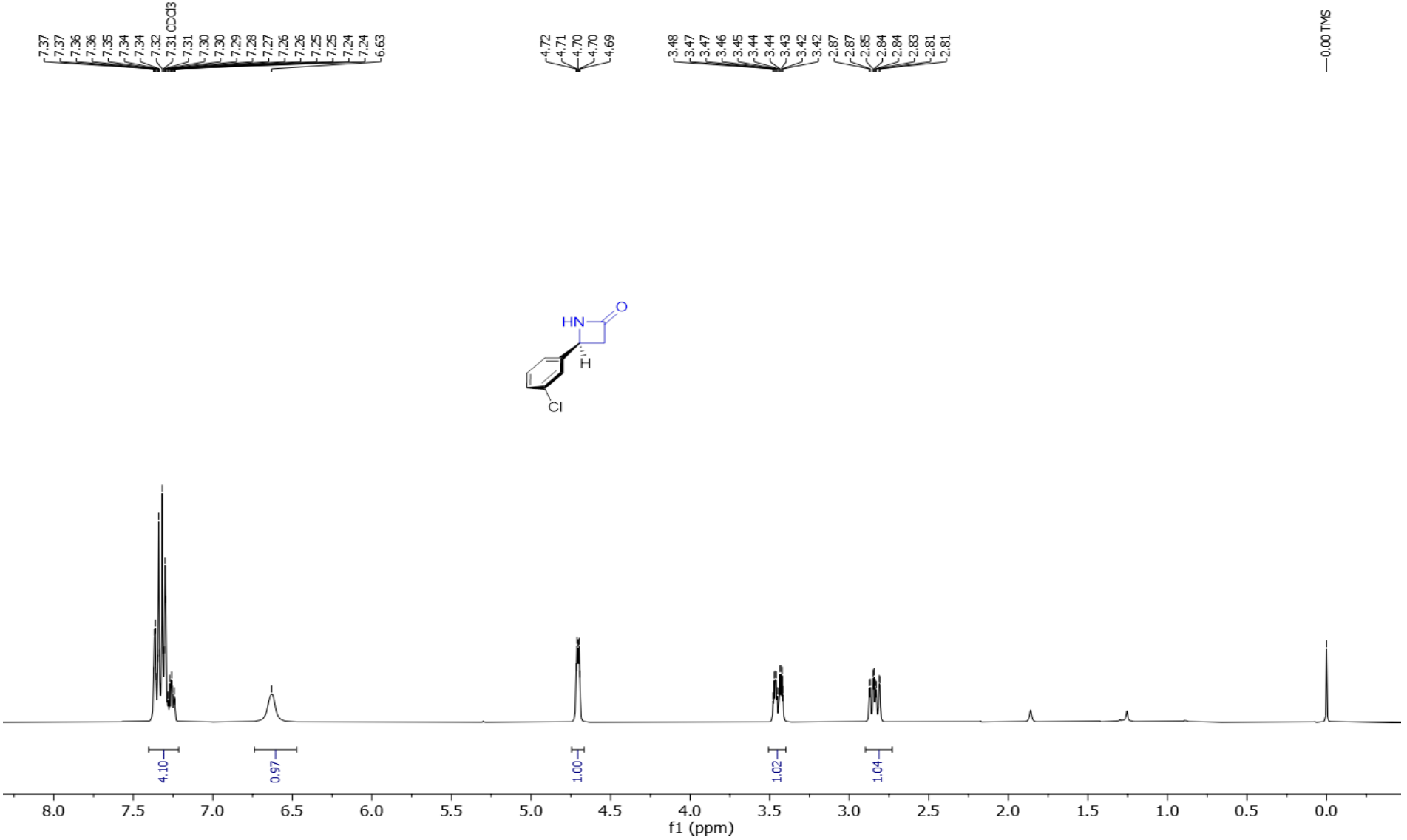
(S)-4-(m-tolyl)azetidin-2-one (**4g**), ^{1}H NMR (400 MHz, $CDCl_3$):



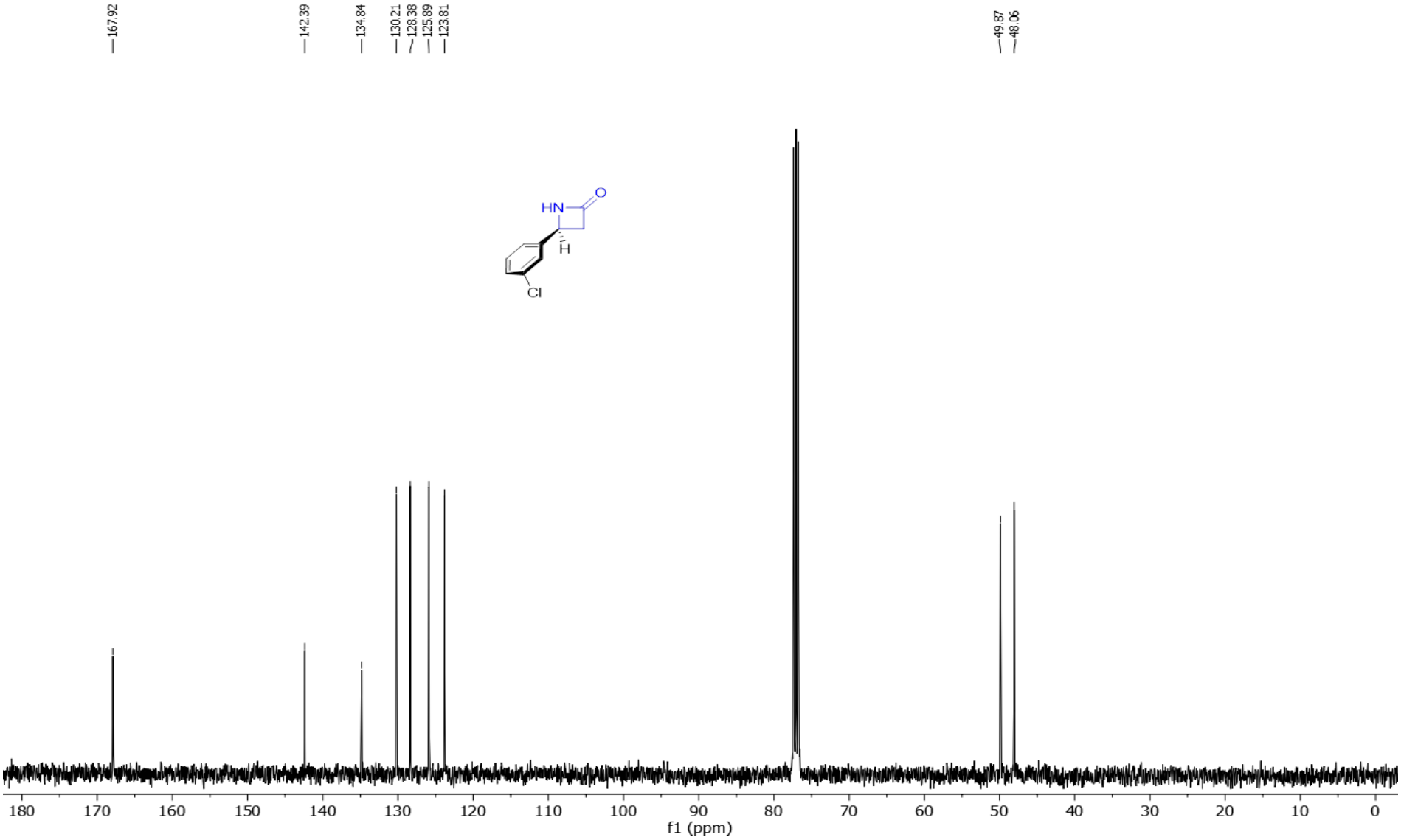
(S)-4-(m-tolyl)azetidin-2-one (**4g**), ^{13}C NMR (101 MHz, $CDCl_3$):



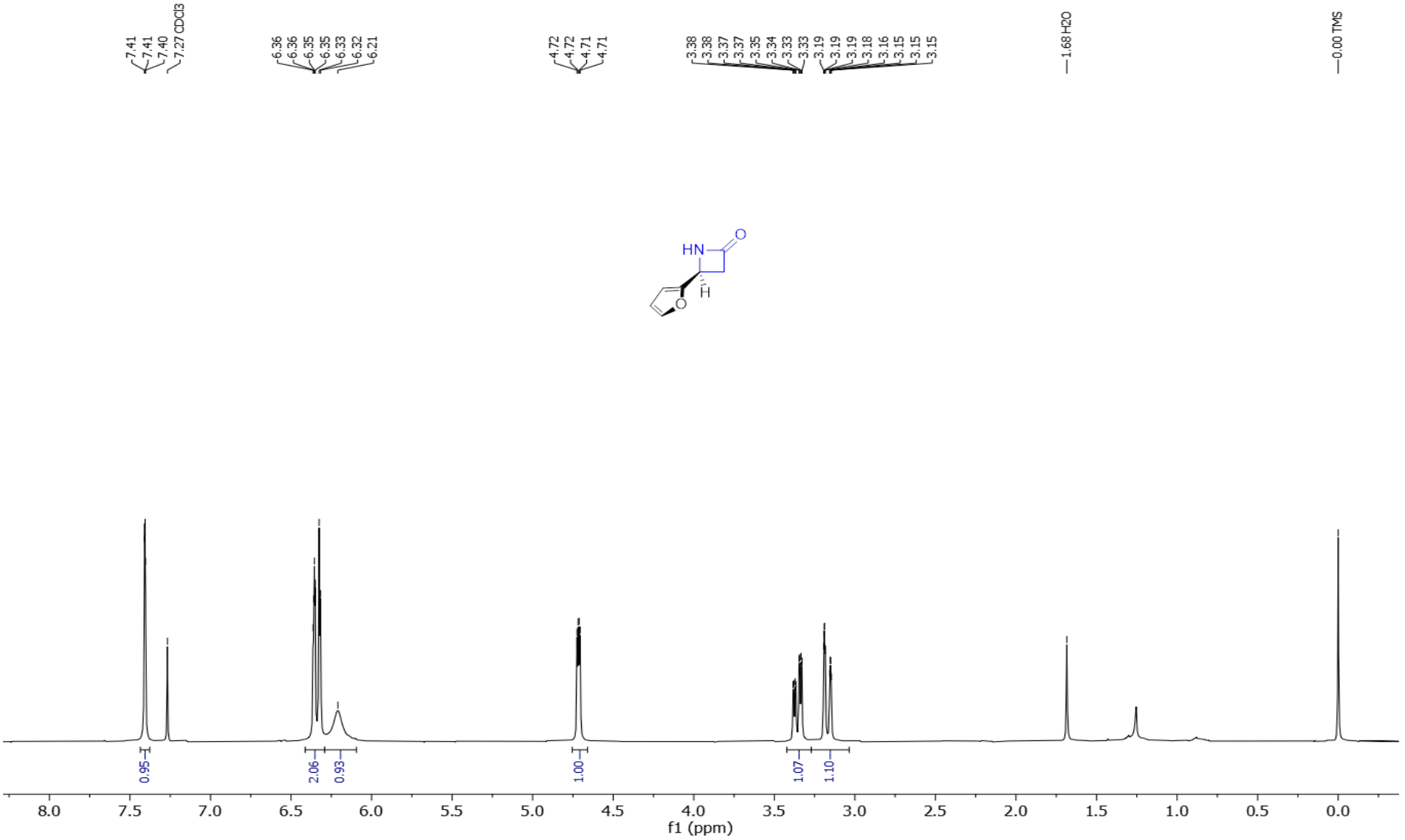
(S)-4-(3-chlorophenyl)azetidin-2-one (**4h**), ^{1}H NMR (400 MHz, $CDCl_3$):



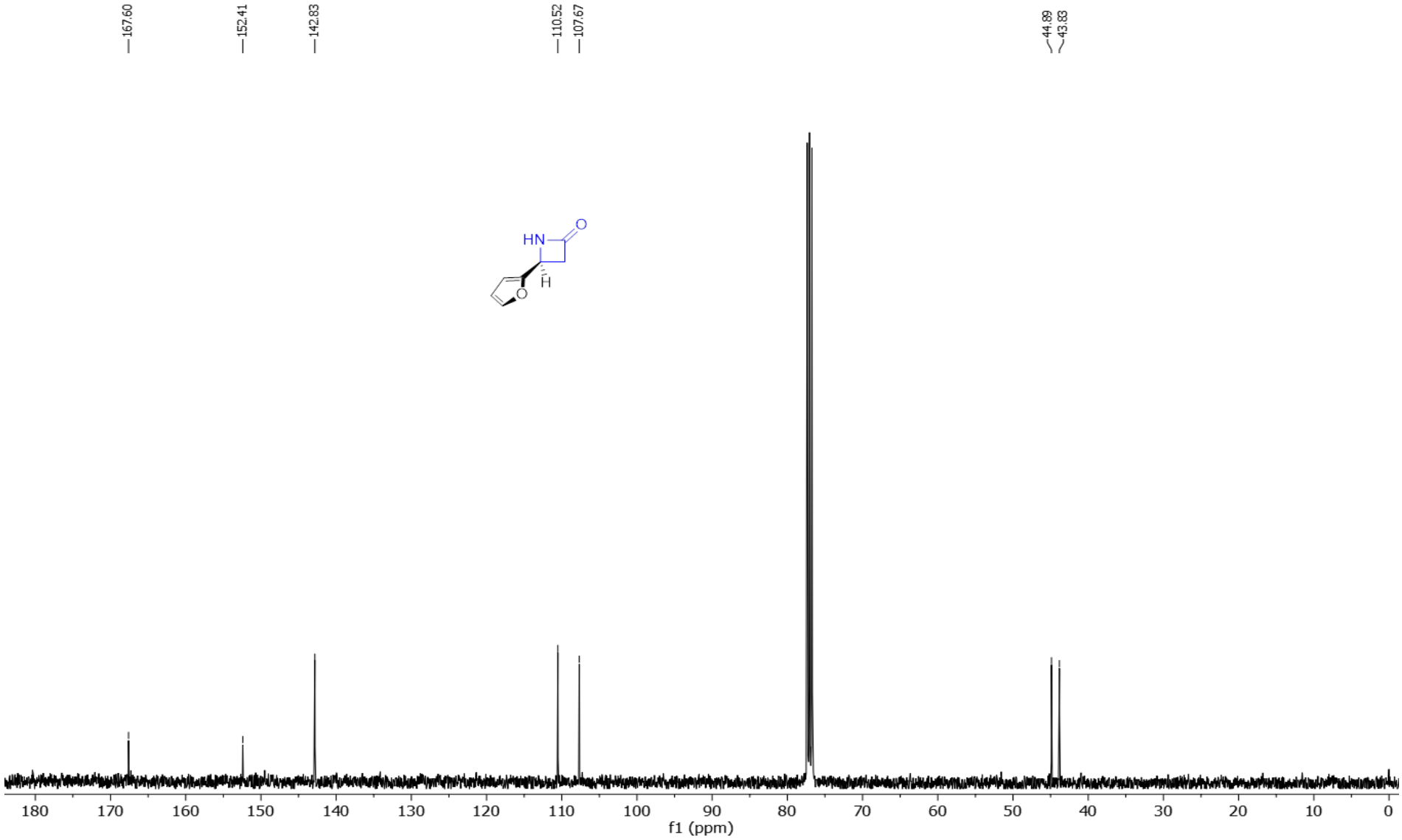
(S)-4-(3-chlorophenyl)azetidin-2-one (**4h**), ^{13}C NMR (101 MHz, $CDCl_3$):



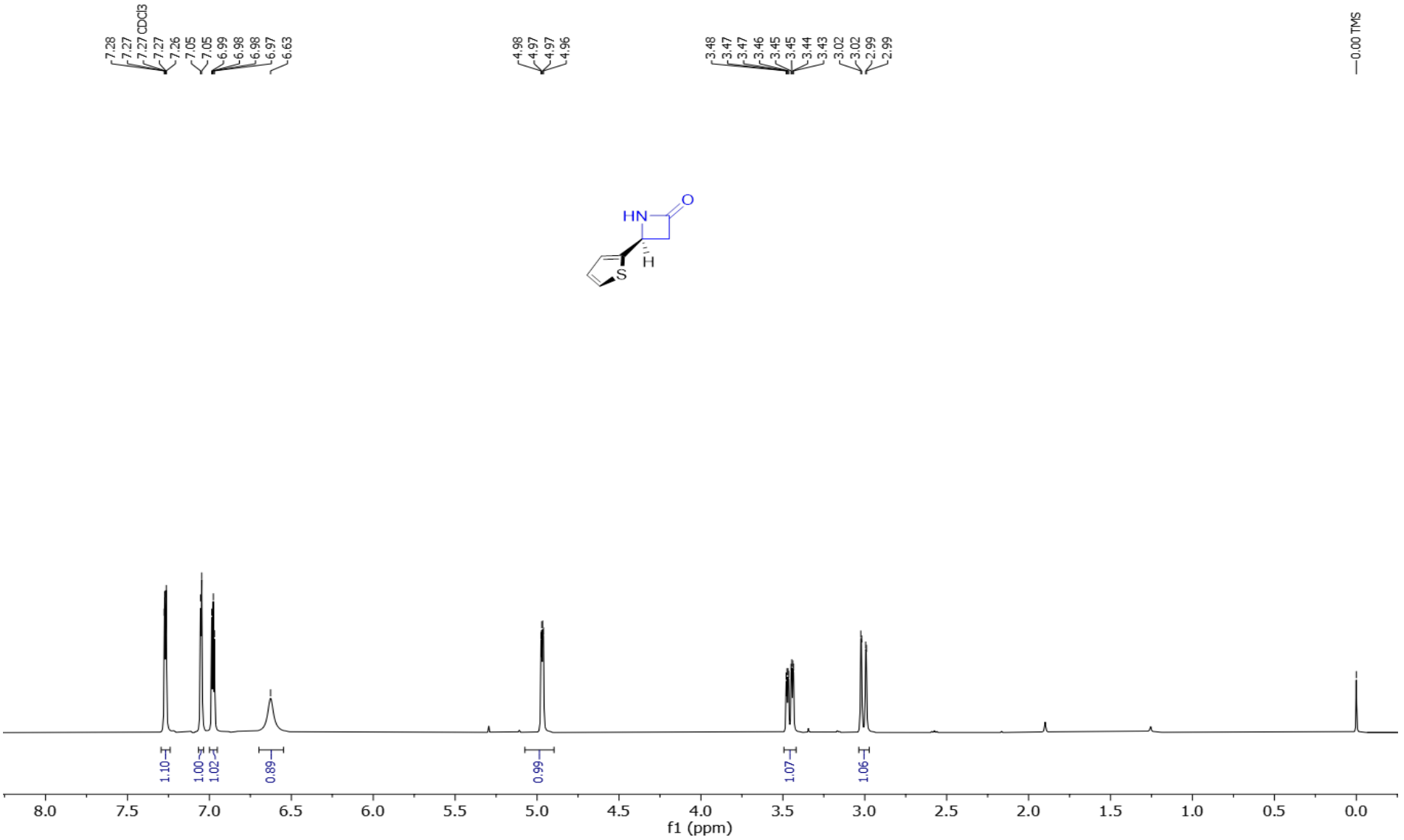
(S)-4-(furan-2-yl)azetidin-2-one (**4i**), ^{1}H NMR (400 MHz, $CDCl_3$):



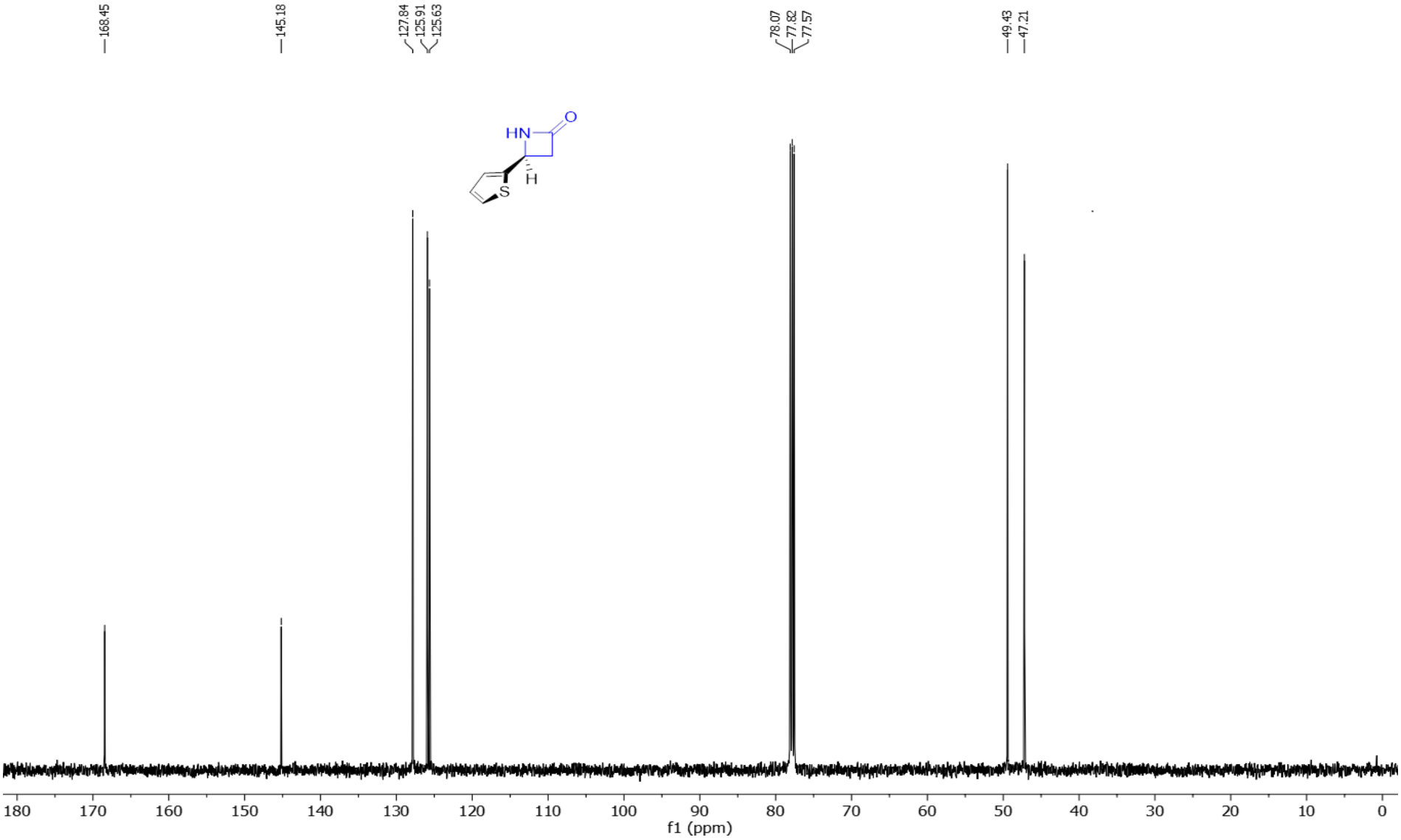
(S)-4-(furan-2-yl)azetidin-2-one (**4i**), ^{13}C NMR (101 MHz, $CDCl_3$):



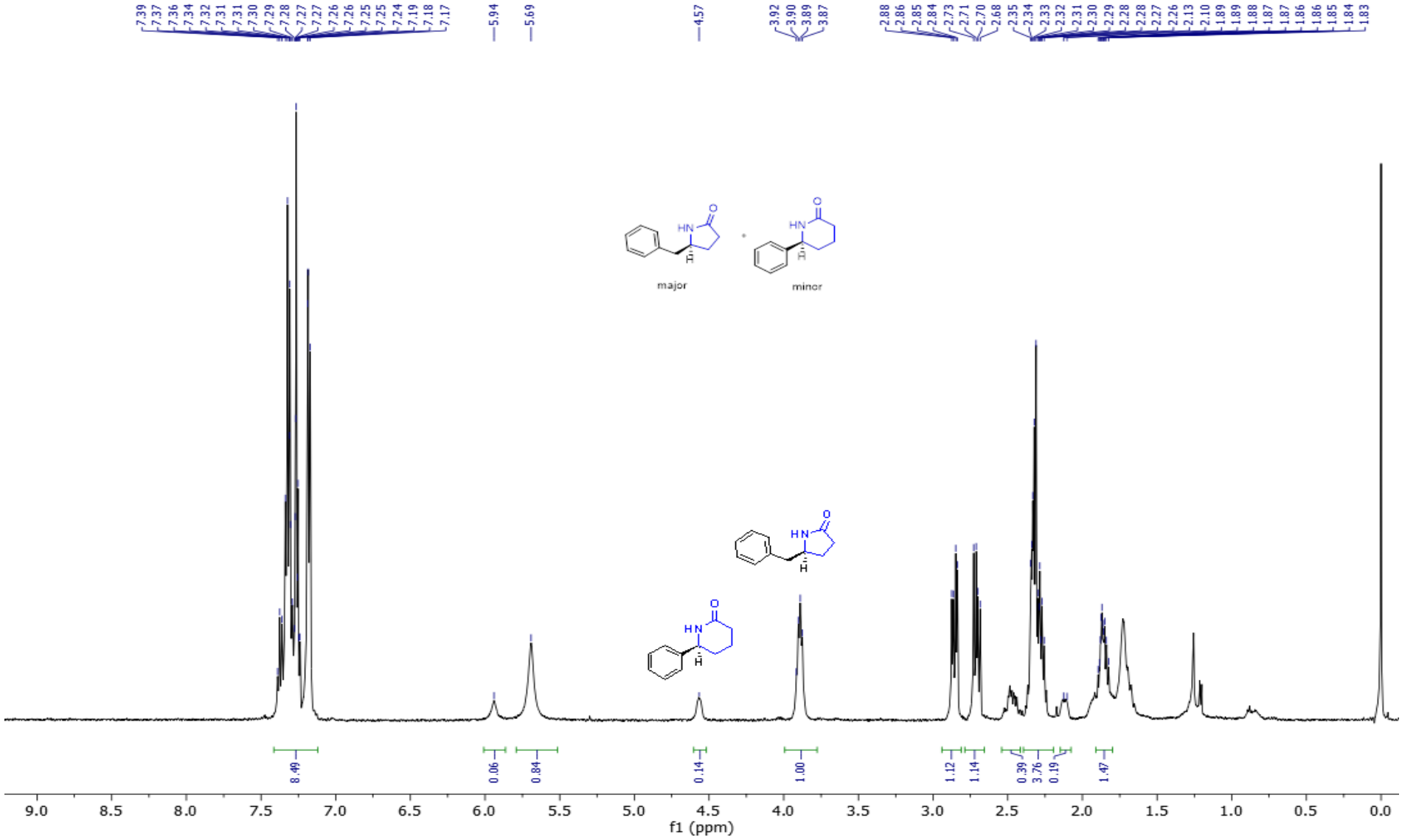
(S)-4-(thiophen-2-yl)azetidin-2-one (**4j**), ^{1}H NMR (400 MHz, $CDCl_3$):



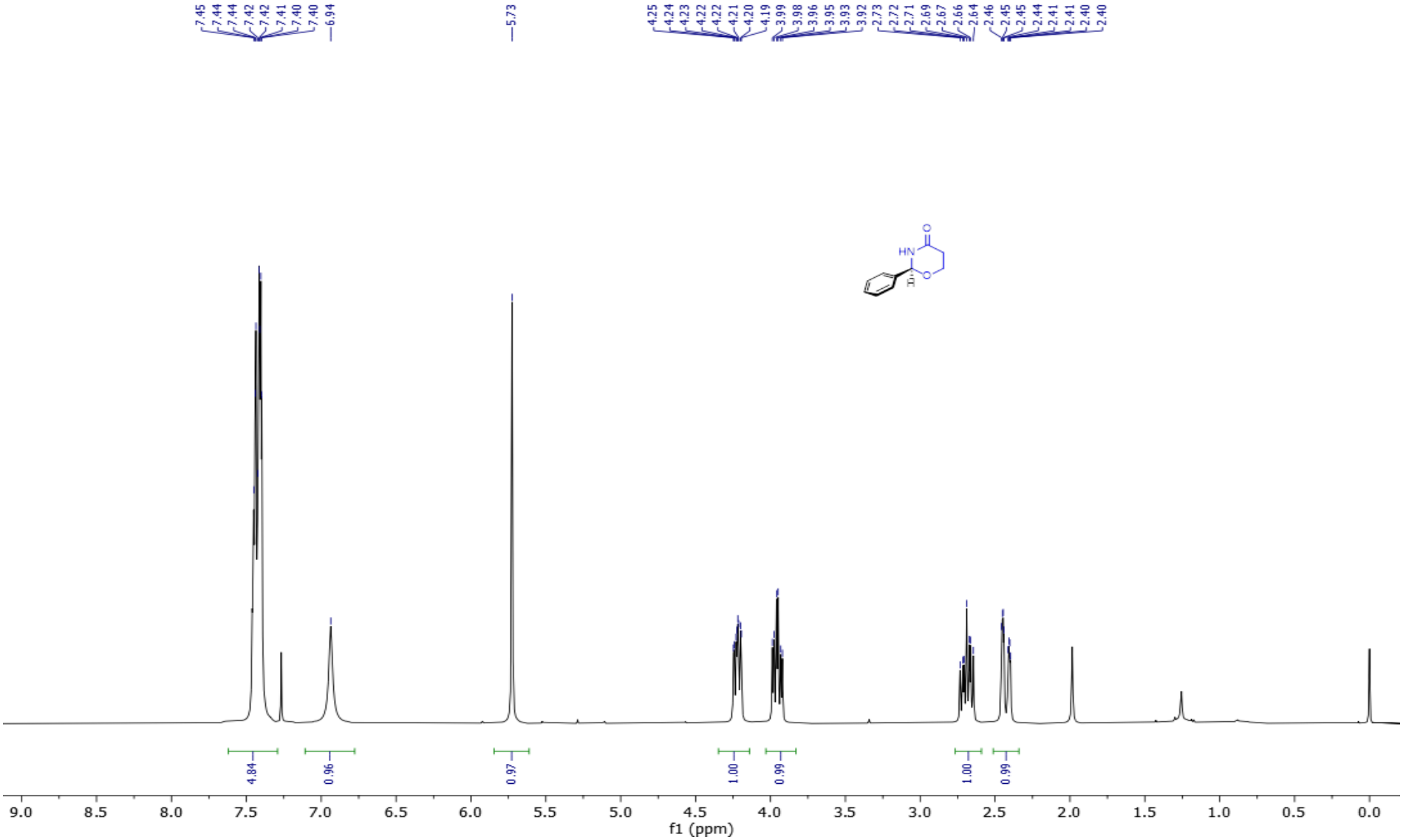
(S)-4-(thiophen-2-yl)azetidin-2-one (**4j**), ^{13}C NMR (101 MHz, $CDCl_3$):



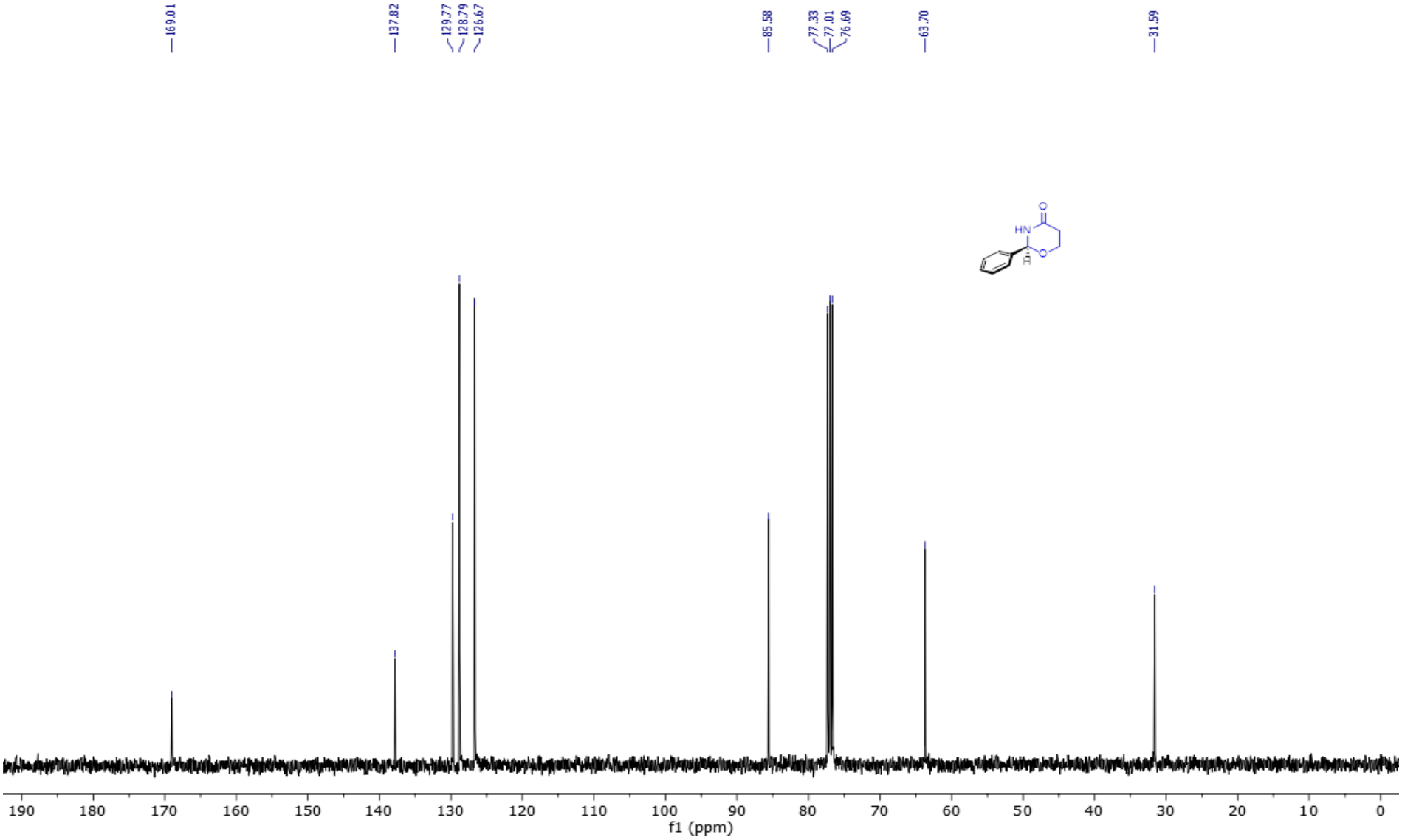
Mixture of Compound (**6aa**) and Compound (**6ab**), ^{1}H NMR (400 MHz, $CDCl_3$):



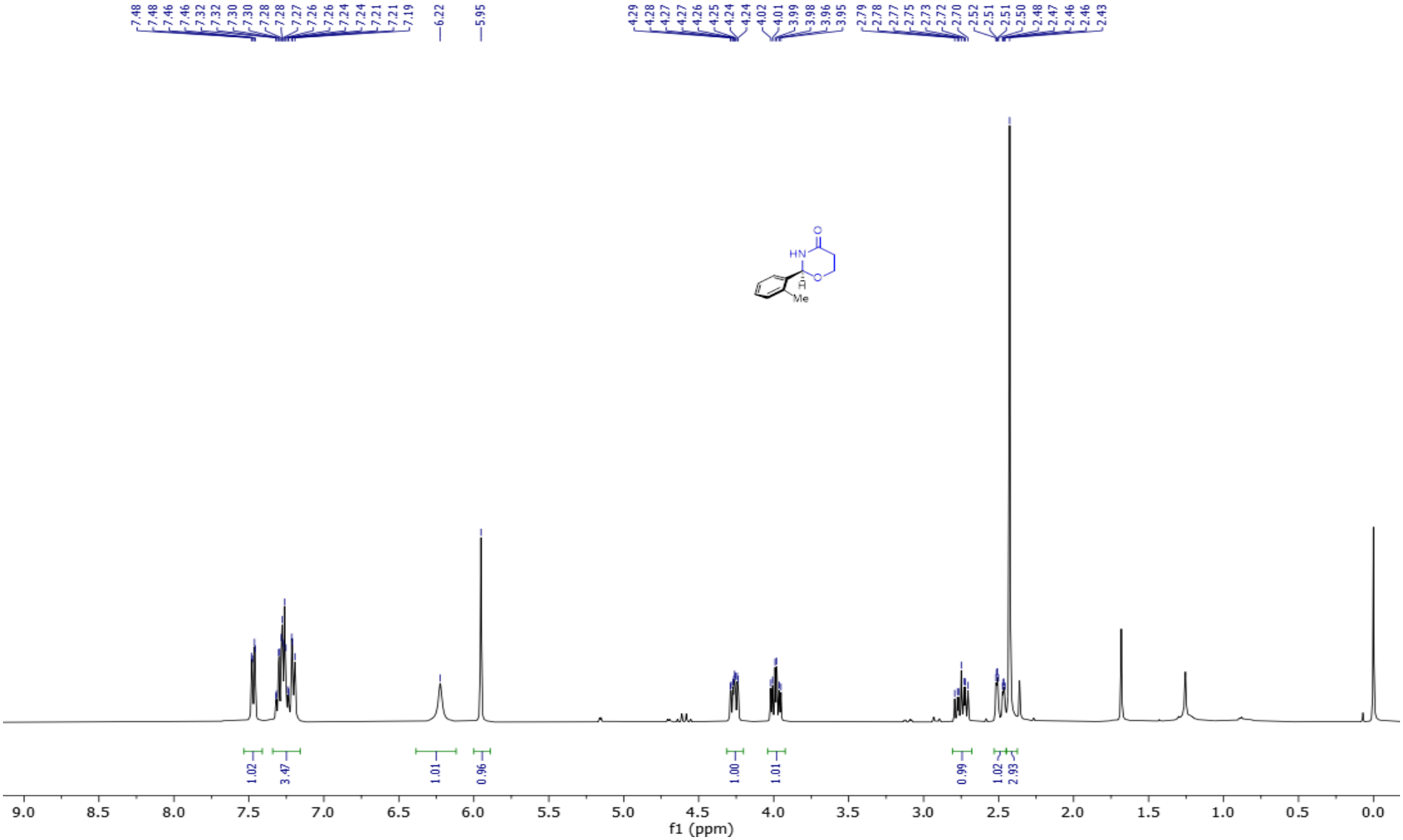
(S)-2-phenyl-1,3-oxazinan-4-one (**6c**), ^{1}H NMR (400 MHz, $CDCl_3$):



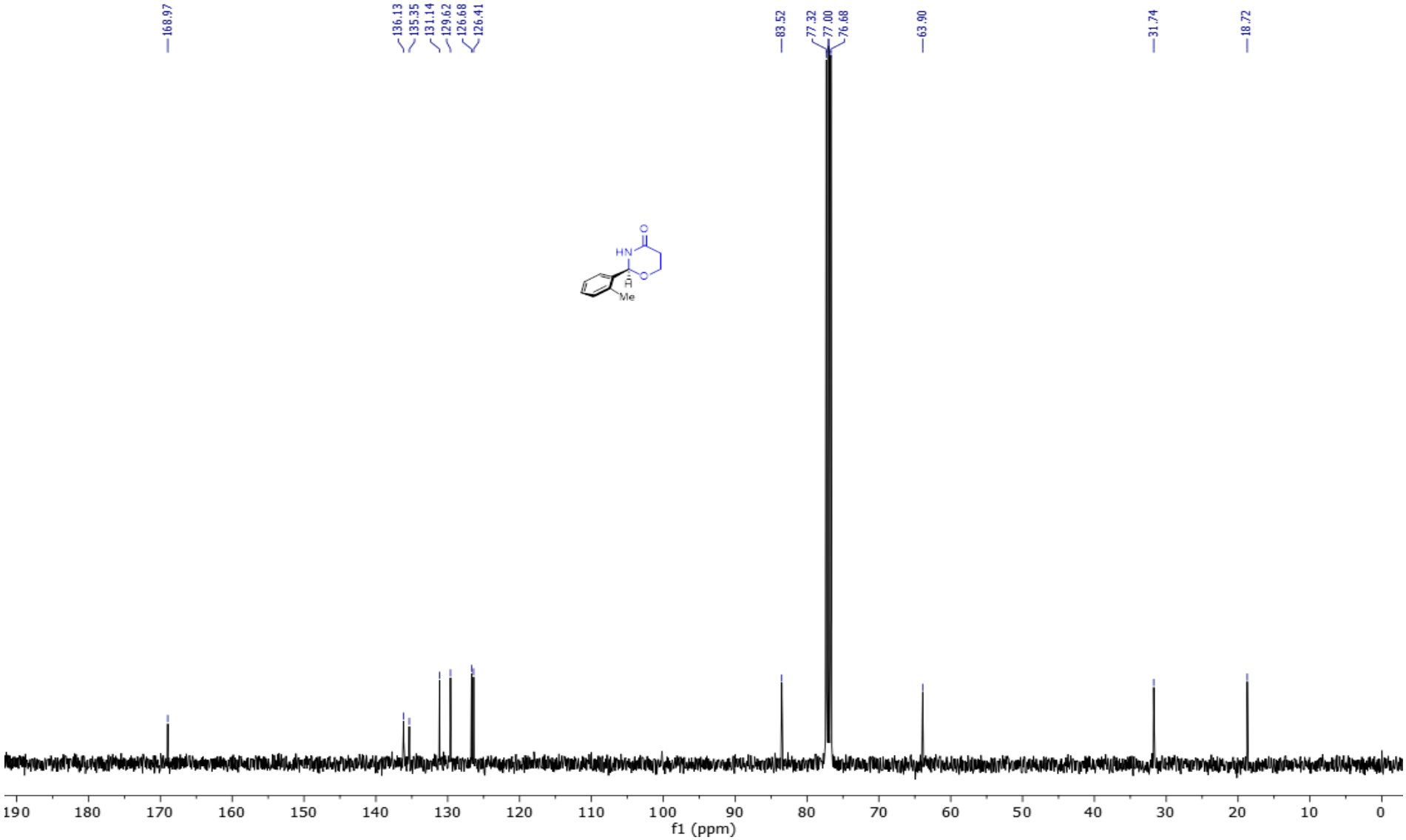
(S)-2-phenyl-1,3-oxazinan-4-one (**6c**), ^{13}C NMR (101 MHz, $CDCl_3$):



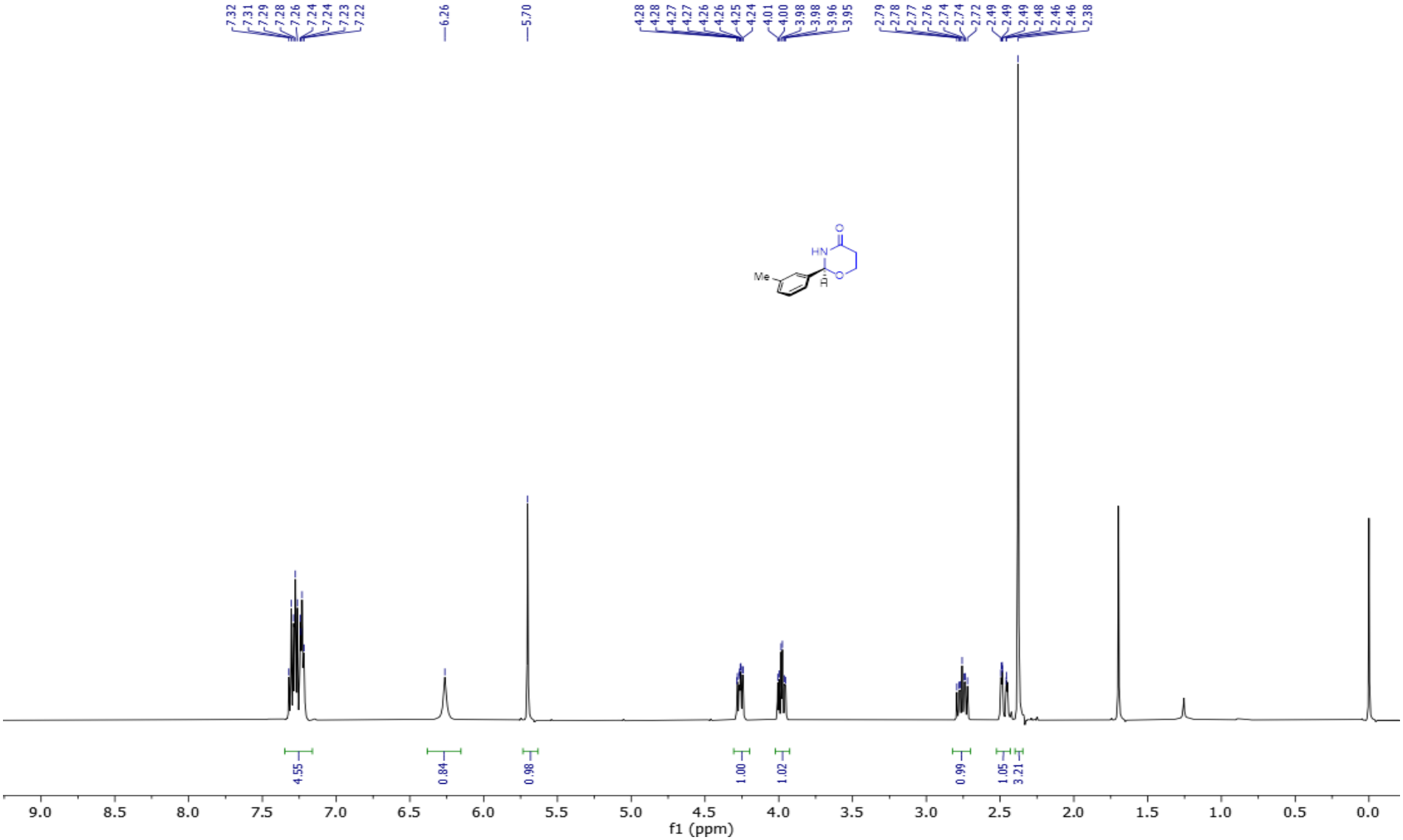
(S)-2-(o-tolyl)-1,3-oxazinan-4-one (**6d**), ^{1}H NMR (400 MHz, $CDCl_3$):



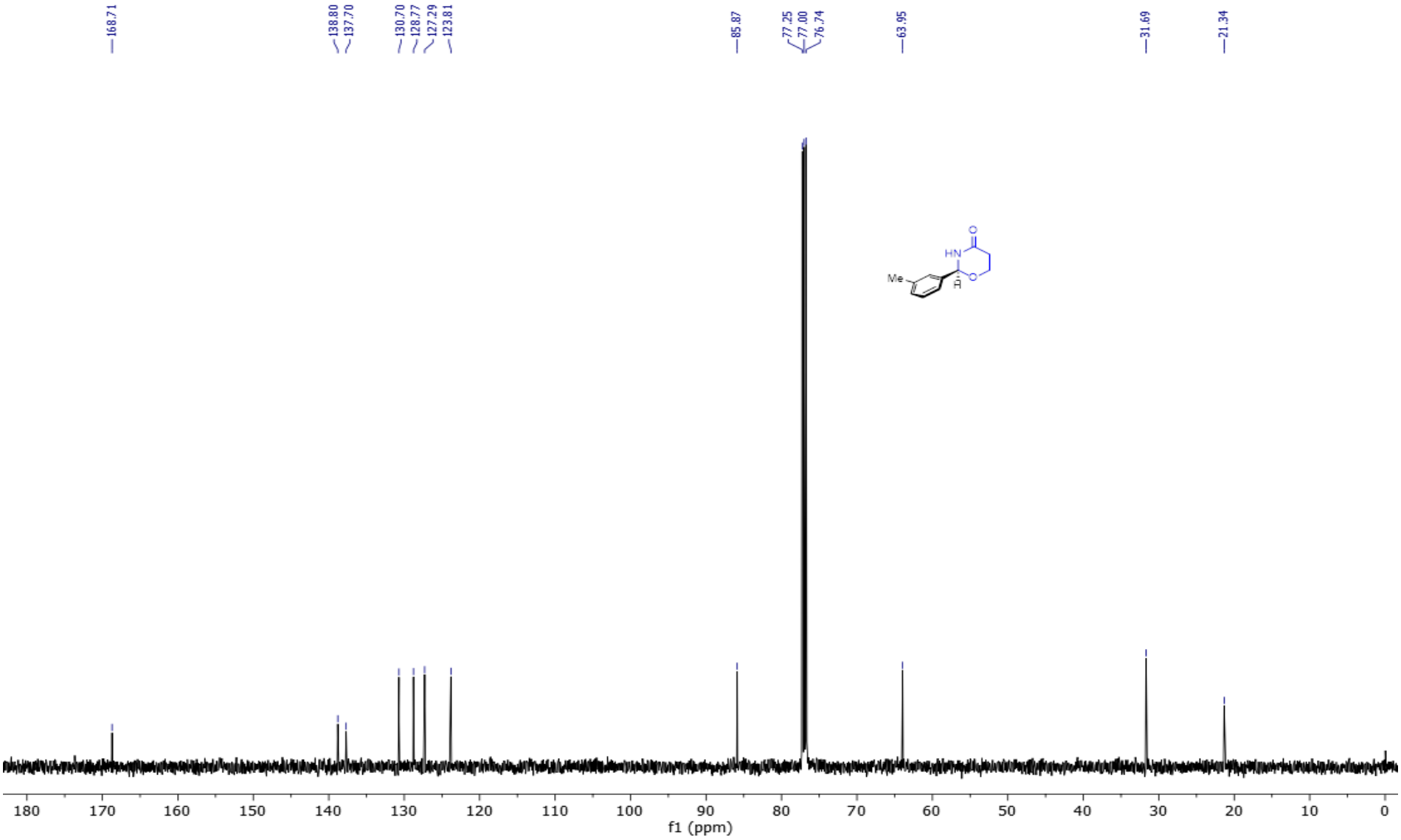
(S)-2-(o-tolyl)-1,3-oxazinan-4-one (**6d**), ^{13}C NMR (101 MHz, $CDCl_3$):



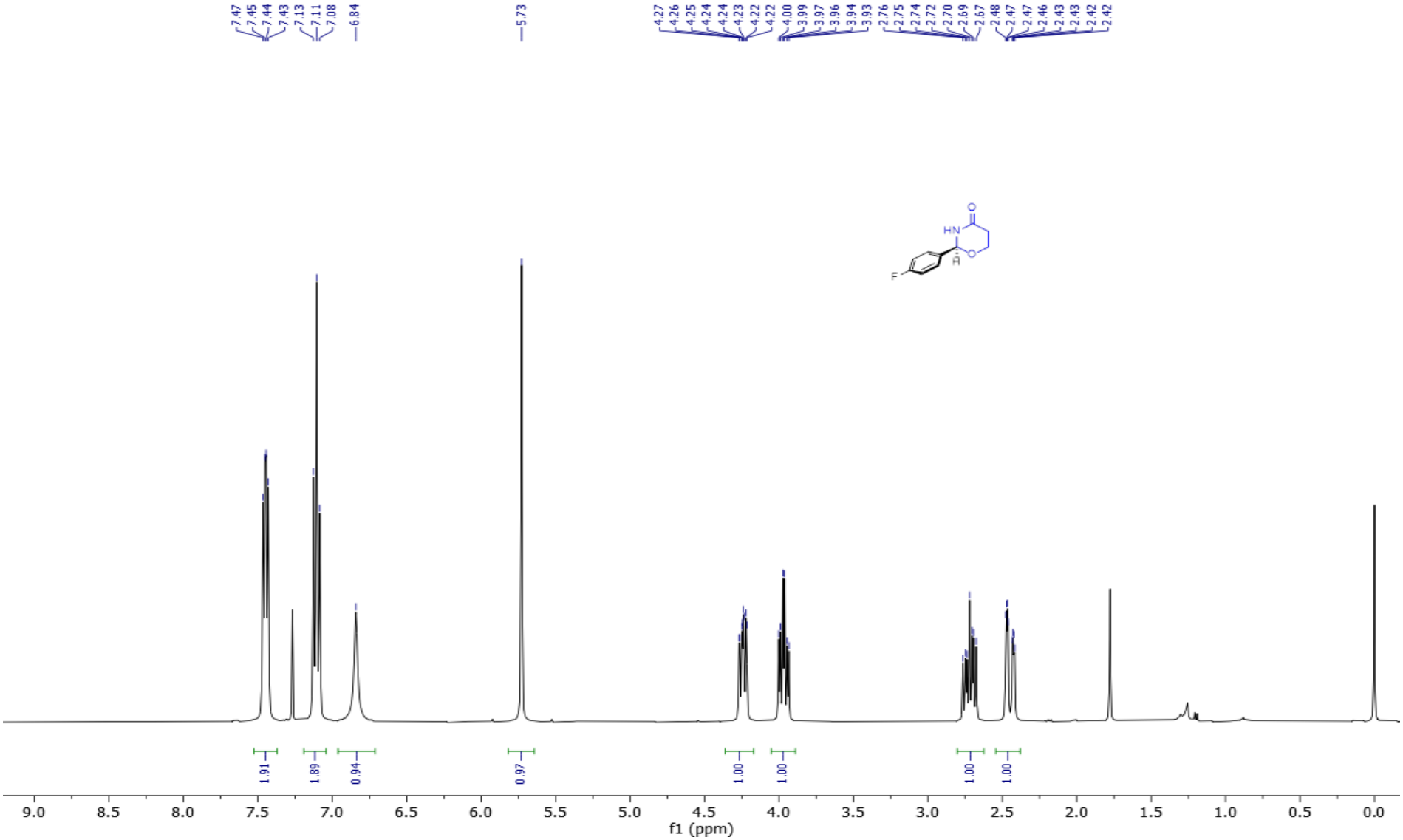
(S)-2-(m-tolyl)-1,3-oxazinan-4-one (**6e**), ^{1}H NMR (400 MHz, $CDCl_3$):



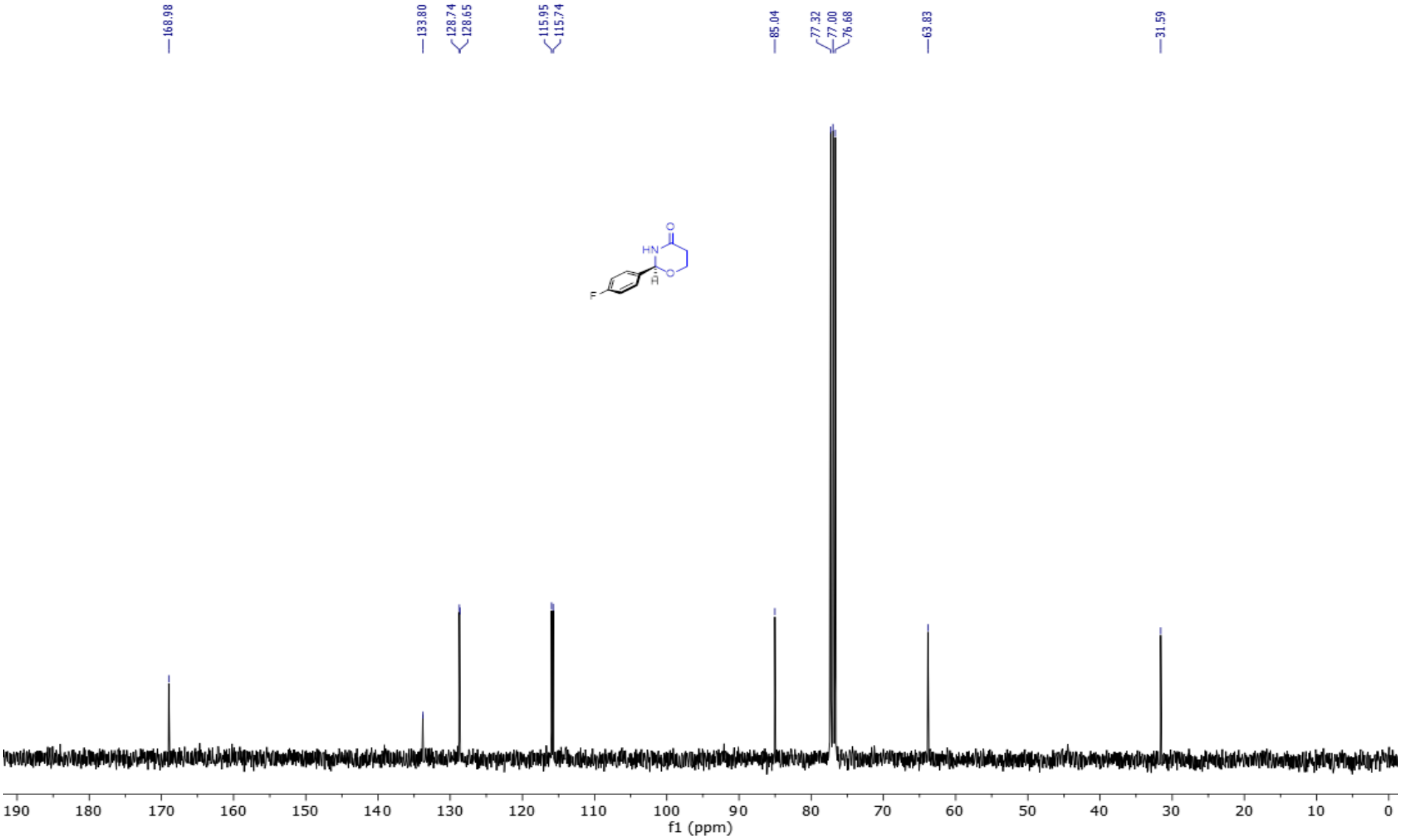
(S)-2-(m-tolyl)-1,3-oxazinan-4-one (**6e**), ^{13}C NMR (101 MHz, $CDCl_3$):



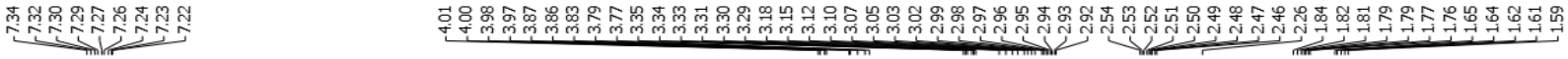
(S)-2-(4-fluorophenyl)-1,3-oxazinan-4-one (**6f**), ^{1}H NMR (400 MHz, $CDCl_3$):

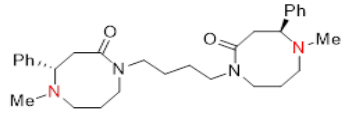


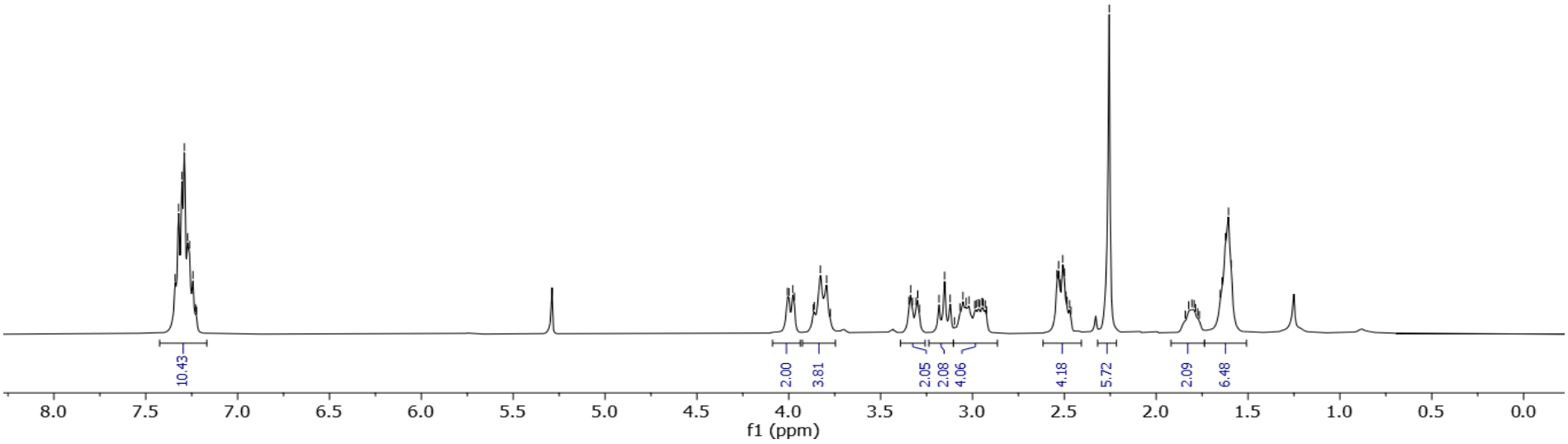
(S)-2-(4-fluorophenyl)-1,3-oxazinan-4-one (**6f**), ^{13}C NMR (101 MHz, $CDCl_3$):



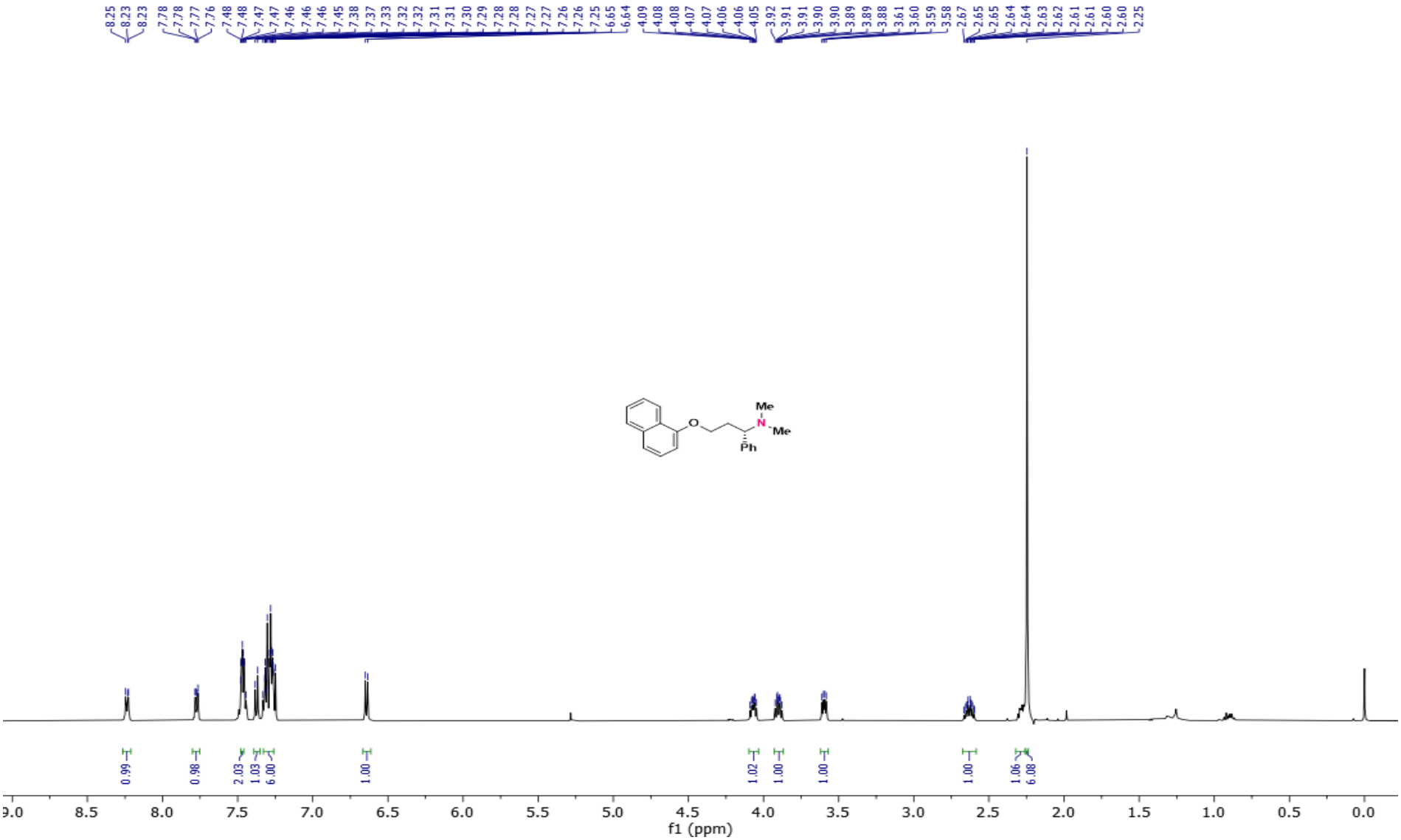
(S,S)-(-)-Homaline (**7**), ^{1}H NMR (400 MHz, $CDCl_3$):







(S)-Dafoxetine (**8**), ^{1}H NMR (400 MHz, $CDCl_3$):



(S)-Dafoxetine (**8**), ^{13}C NMR (101 MHz, $CDCl_3$):