Supplementary information for

Highly Stereoselective Synthesis of Allylic β-lactams via Enzymatic Intramolecular C(sp^3)–H Amidation

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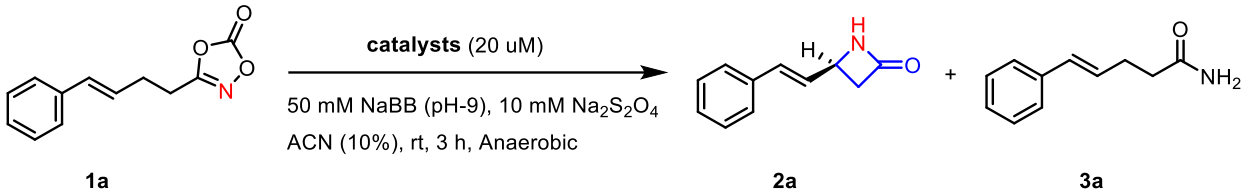
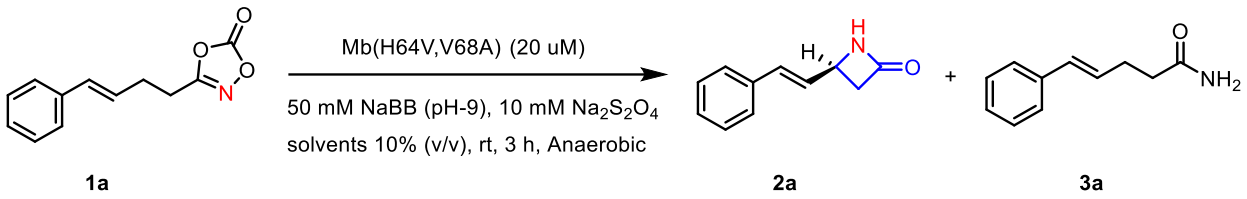
Supplementary Tables

Table S1. Activity and selectivity of wild-type sperm whale myoglobin (Mb) engineered Mb variants, other hemoprotein, and other porphyrin-based catalysts in the intramolecular allylic C-H amidation with dioxazolone **1a**. All reactions were performed at 400μL scale using 20 μM catalyst, 10 mM **1a**, 10 mM sodium dithionite, 3 hours, room temperature (RT), and under anaerobic conditions.



#	Catalyst	Yield of 2a (%)	Yield of 3a (%)	ee of 2a (%)
1	Cytochrome $P450_{BM3}$	0	N/A	N/A
2	CYP119 (*Sulfolobus acidocaldarius*)	0	N/A	N/A
3	Cytochrome *c* (Equine Heart)	0	N/A	N/A
4	Ht-Cc552 (*H. Thermophilus*)	0	N/A	N/A
5	Ht-Cc552 variant (G50T,M59G,P60E,Q62R)	0	N/A	N/A
6	Protoglobin (Pgb from *Aeropyrum Pernix*)	0	N/A	N/A
7	Dehaloperoxidase (*Amphitrite Ornate*)	0	N/A	N/A
8	Horseradish peroxidase	0	N/A	N/A
9	Catalase (bovine liver)	0	N/A	N/A

Table S2. Screening of dioxazolone (**1a**) with different solvents.



#	Solvents	2a	3a
1	ACN	57	43
2	MeOH	10	90
3	EtOH	8	92
4	THF	5	95
5	DMF	13	87
6	Ethyl acetate	28	72

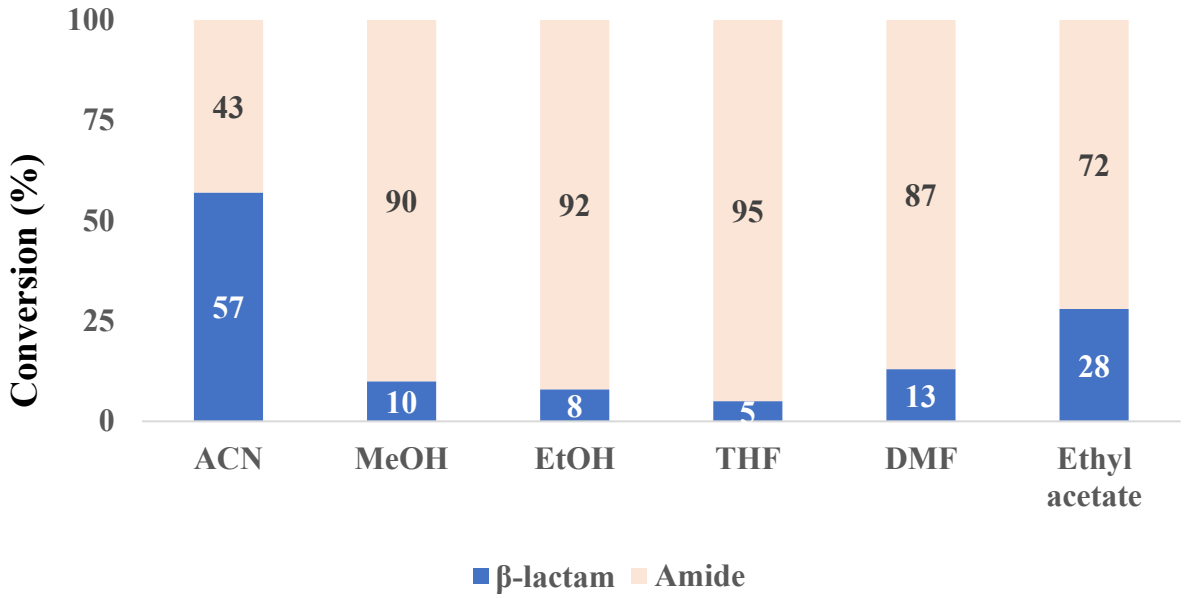
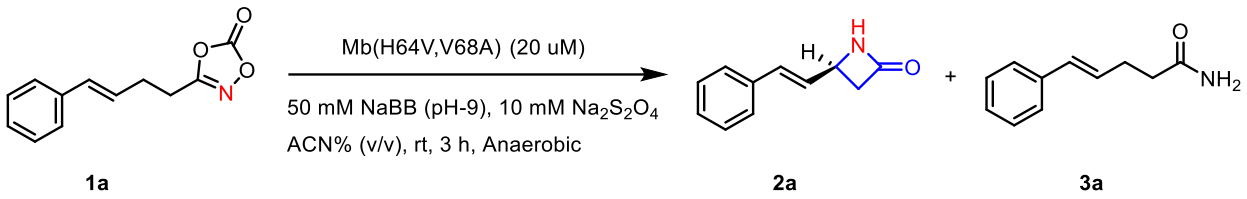


Table S3. Screening of dioxazolone (**1a**) with different ACN concentrations.



#	ACN concentrations (%)	2a	3a
1	5	49	51
2	10	57	43
3	15	36	64
4	20	22	78
5	25	11	89
6	30	9	91

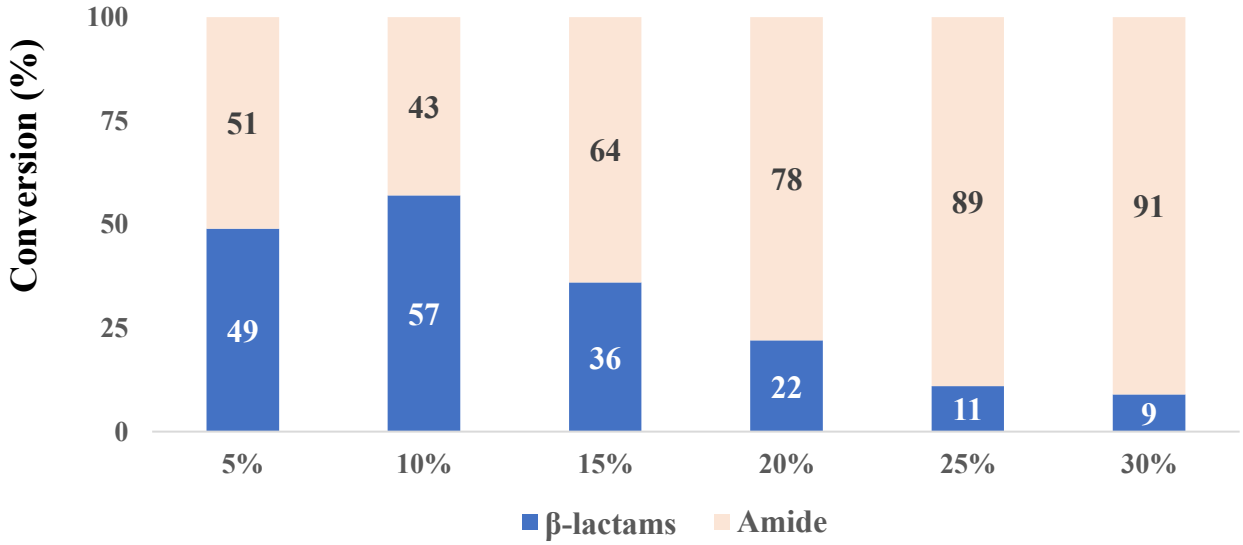
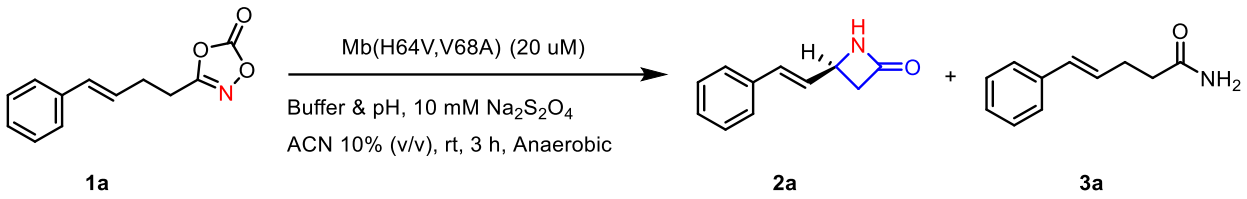


Table S4. Screening of dioxazolone (**1a**) with different buffers and pH.



#	Buffer (pH)	2a	3a
1	NaBB (pH 9)	57	43
2	NaBB (pH 9.5)	55	45
3	NaBB (pH 10)	54	46
4	Kpi (pH 6)	26	74
5	Kpi (pH 7)	41	59
6	Kpi (pH 8)	47	53

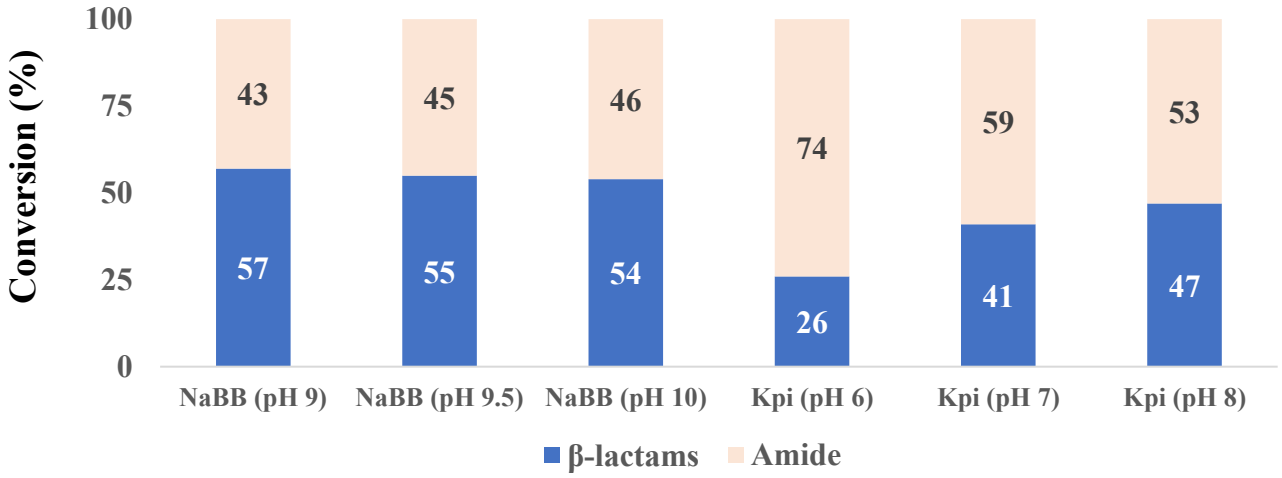
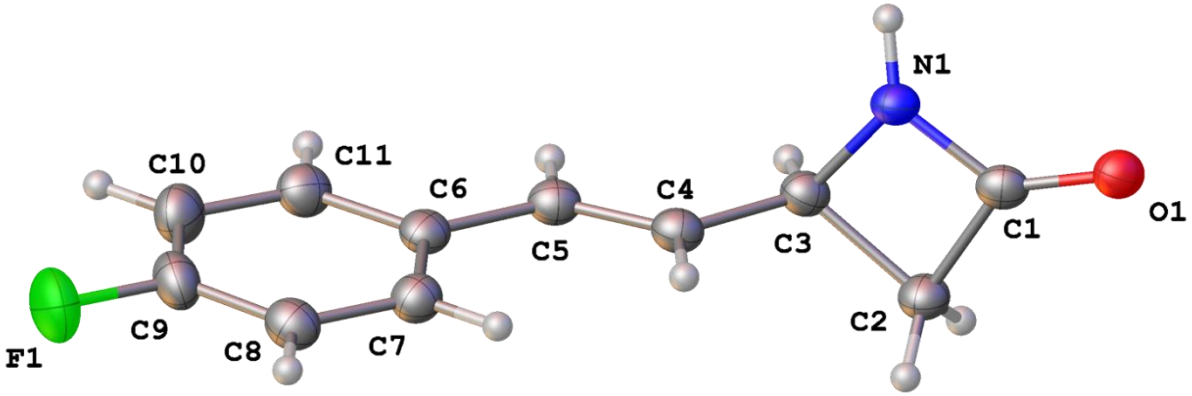


Table S5. Crystal data and structure refinement for compound **2b**. Cambridge Crystallographic Data Centre (CCDC) Entry 2495142.

Identification code	fassr02	
Empirical formula	C11 H10 F N O	
Formula weight	191.20	
Temperature	100.00(10) K	
Wavelength	1.54184 Å	
Crystal system	orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.18760(5) Å	α = 90°
	b = 7.88139(5) Å	β = 90°
	c = 33.6858(2) Å	γ = 90°
Volume	1908.24(2) Å^3	
Z	8	
Density (calculated)	1.331 Mg/m^3	
Absorption coefficient	0.826 mm^{-1}	
F(000)	800	
Crystal color, morphology	colourless, needle	
Crystal size	0.247 x 0.227 x 0.084 mm^3	
Theta range for data collection	5.252 to 80.393°	
Index ranges	$-8 \le h \le 9$, $-10 \le k \le 10$, $-42 \le l \le 42$	
Reflections collected	32458	
Independent reflections	4116 [R(int) = 0.0382]	
Observed reflections	4012	
Completeness to theta = 67.684°	100.0%	
Absorption correction	Multi-scan	
Max. and min. transmission	1.00000 and 0.76894	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4116 / 0 / 261	
Goodness-of-fit on F^2	1.057	
Final R indices [I>2sigma(I)]	$R1$ = 0.0290, $wR2$ = 0.0719	
R indices (all data)	$R1$ = 0.0299, $wR2$ = 0.0727	
Absolute structure parameter	-0.03(4)	
Largest diff. peak and hole	0.133 and -0.188 e.Å^{-3}	

Supplementary Figures

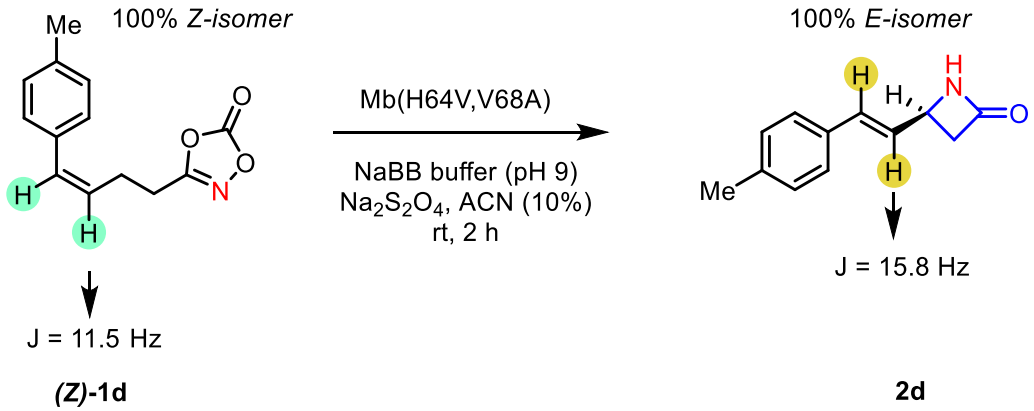
Figure S1. ORTEP of (*S,E*)-4-(4-fluorostyryl)azetidin-2-one (**2b**) with ellipsoids drawn at the 50% probability level. Hydrogen atoms were located in the difference Fourier map and refined freely. They are represented here as spheres of arbitrary radius for clarity.



Mechanistic Experiments

I. Rearrangement Experiment

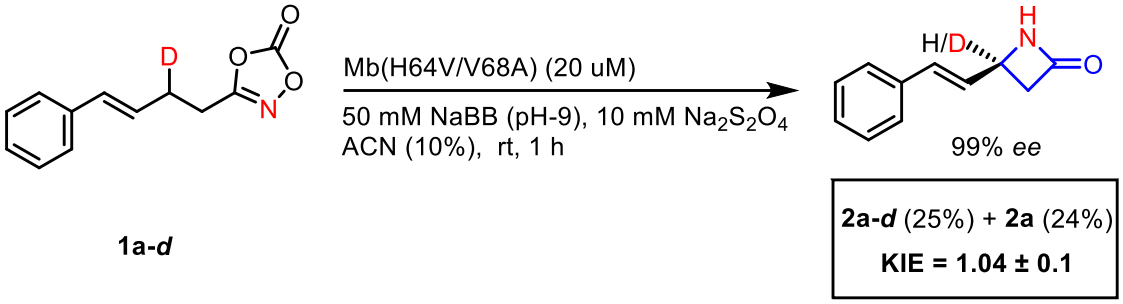
The intramolecular C-H amidation reaction of substrate ***(Z)*-1d** catalyzed by Mb(H64V,V68A) was tested in order to determine the presence of a radical intermediate in the reaction. Upon purification, the resulting *β*-lactam motif was analyzed via ^{1}HNMR spectroscopy which revealed a complete *Z*→*E* isomerization of the double bond as determined by the *J* values of the two vinyl H atoms. The reaction was conducted following **General Procedure B** obtaining 2.0 mg of **2d** as white solid in 12%. R_f = 0.5 (5% 2-propanaol in DCM).



(*E*)-4-(4-methylstyryl)azetidin-2-one (2d)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 – 7.10 (m, 7H), 6.60 (d, *J* = 15.8 Hz, 1H), 6.23 – 6.14 (m, 2H), 4.29 (s, 1H), 3.38 – 3.23 (m, 2H), 2.34 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 167.6, 138.1, 133.0, 132.2, 129.4, 126.4, 125.6, 49.6, 45.4, 21.2.

II. Intramolecular kinetic isotope study using 1a-*d*



1a-*d*

Intramolecular kinetic isotope study was conducted following **General Procedure B** for enzymatic reactions using **1a-*d***. The product (**2a**-*d* and **2a** mixture) was isolated using preparative thin layer chromatography and **2a-d/2a** ratio was determined by ^{1}H NMR spectroscopy.

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. The recombination variants were prepared by combining the desired mutations using a similar cloning procedure and mutagenizing primers reported previously.

Protein Expression and Purification. Engineered Mb variants were expressed in *E. coli* BL21(DE3) cells as described previously.1 Briefly, cells were grown in terrific broth (TB) medium (ampicillin, 100 mg L^{-1}) at 37 °C (150 rpm) until OD600 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)) $\varepsilon_{410} = 157\ mM^{-1}\ cm^{-1}$.

Analytical Reactions. Analytical reactions were carried out at a 400 μL scale using 20 μM purified 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).

Product Analysis. All products excepts **2k** and **2m** were analyzed by adding 20 μL of internal standard (50 mM benzodioxole in EtOH) to the reaction mixture, followed by extraction with 400 μL of CH_2Cl_2 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). Stereoselectivity determination was performed via chiral GC-FID. Product **2k** and **2m** were analyzed by Supercritical Fluid Chromatography-Mass Spectrometry (SFC-MS), using a Shimadzu Analytical SFC-MS instrument equipped with a column oven (40 °C). All samples were eluted using a constant gradient system with the indicated modifier in liquid CO_2 at an elution rate of 2 mL/min and detected by PDA mode. Calibration curves for quantification of the different 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. For each experiment, negative control samples containing no protein were included.

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.

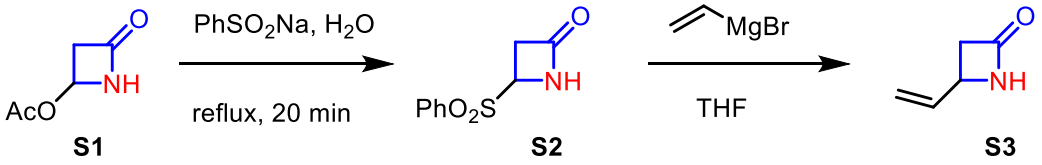
SFC-MS Separation Method 1: Detector wavelength- 254 nm, Chiral IG Column, 20% ^{i}PrOH in liquid CO_2 over 10 min with flow rate of 2 mL/min.

SFC-MS Separation Method 2: Detector wavelength- 254 nm, Chiral IG Column, 15% ^{i}PrOH in liquid CO_2 over 10 min with flow rate of 2 mL/min.

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.

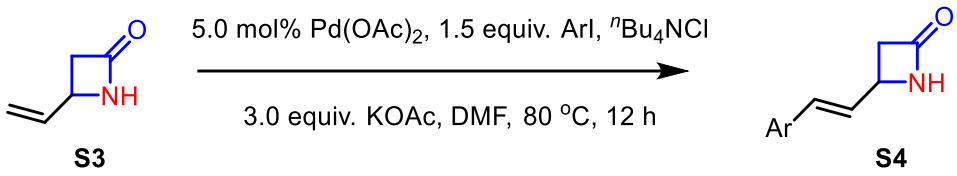
Preparation of racemic allylic β-lactam:



The following procedure was carried out according to Cho et al. (*Science*, 2019, 364: 575-578), without further optimization. Acetoxyazetidinone (2.7 g, 21 mmol) was dissolved in water (11 mL) and treated with sodium phenyl sulfinate (3.5 g, 21.3 mmol). The mixture was refluxed for 20 min, and the yellow reaction mixture was then cooled to room temperature. The reaction was then extracted with dichloromethane (5×15 mL), the combined extracts were dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure to give the pure sulfone product as a white powder (3.6 g, 82%). The sulfone was used in the next reaction without any further purification.

A -78°C solution of sulfone (3.6 g, 17.2 mmol) in anhydrous THF (62 mL) was treated with vinylmagnesium bromide (1.0 M in THF, 42.6 mL, 42.6 mmol), and the reaction was vigorously stirred at -78°C for 30 min. The mixture was then consequently allowed to warm to 0°C and stirred for 50 min. The reaction was then warmed to room temperature and stirred for 2 h. The reaction was quenched with saturated aq ammonium chloride (20 mL) and stirred for a further 15 min. The crude mixture was then extracted with dichloromethane (3×50 mL). The combined organic extracts were collected and dried over anhydrous sodium sulfate and the solvents evaporated under vacuum to give the crude product as an orange/brown oil. The crude product was purified by flash chromatography (silica gel, 50% ethyl acetate in Hexane) to give the pure vinylazetidinone as a colorless and slightly viscous oil. The spectroscopic data are in accordance with those reported.

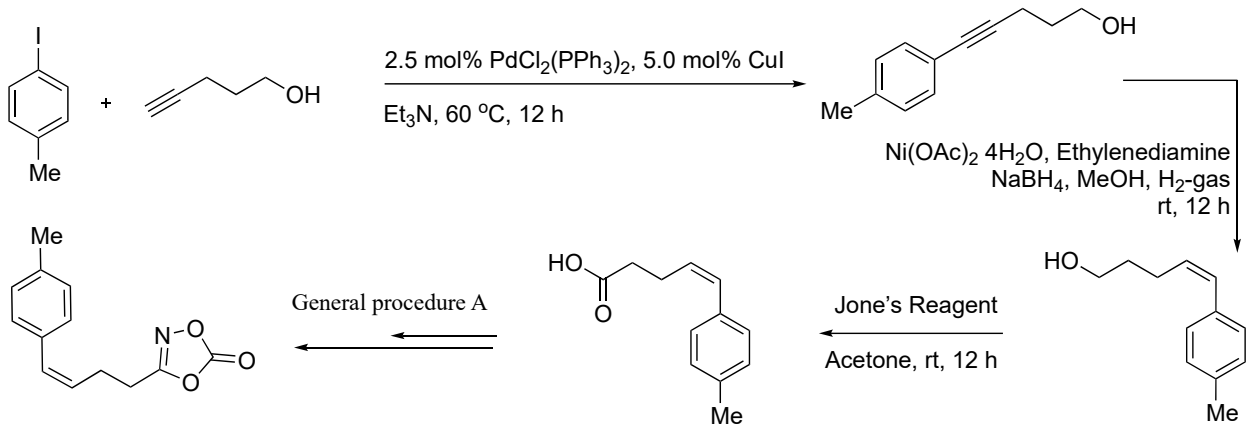
The following procedure was carried out according to Satake et al. (*Synlett*, 1994, 10, 839-841), without further optimization. The average yield of the product ranged from 10% to 34%.



S3 **S4**

Add substituted beta-lactam (1.0 mmol) in DMF (1 mL) to a mixture of $Pd(OAc)_2$ (0.05 mmol), tetrabutylammonium chloride (1.2 mmol), KOAc (3 mmol) and iodobenzene (1.5 mmol) in DMF (4 mL) under argon. Then the reaction mixture was stirred at 80 °C for over night. After completion, add water (5 mL) to the resulting mixture. Extract the organic layer with ethylacetate (20 mL x 3). Then the combined organic layer was wash with brine, dried the extracts over $MgSO_4$ and concentrate the extracts in vacuo. The crude product was purified by column chromatography.

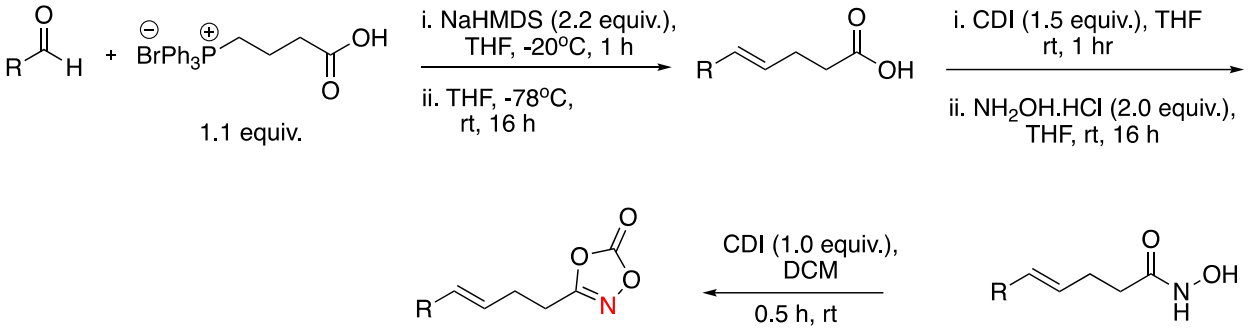
Preparation of (Z)-3-(4-(p-tolyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (Z)-1d:



Following the methods reported in Roy et al. (*Nat. Catal.* **2024**, *7*, 65-76), (Z)-3-(4-(p-tolyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one ***(Z)*-1d** was obtained in as colorless liquid in 34% yield over 4 steps. R_f = 0.5 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 – 7.08 (m, 4H), 6.54 (d, J = 11.5 Hz, 1H), 5.55 (dt, J = 11.5, 6.5 Hz, 1H), 2.72 (q, J = 4.9 Hz, 4H), 2.35 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.0, 154.0, 137.1, 133.6, 132.00, 129.1, 128.5, 126.8, 25.1, 23.5, 21.2.

Preparation of *trans*-dioxazolones from aldehyde (General procedure A):



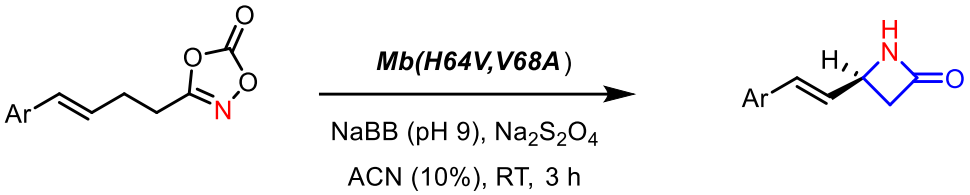
Witting reagent (1.1 equiv.) was added to dry THF. NaHMDS (2.2 equiv.) was added when the mixture was cooled down to -20°C and stirred for 1 h. Aldehyde (1.0 equiv. in 5ml dry THF) was added at -78°C and the mixture stirred at rt for 16 h. The mixture was quenched with water and ether and the aqueous layer was extracted. NaOH was added to the ether layer and aqueous layer extracted again which was then acidified with HCl solution. The organic layers were then extracted with EtOAc (3x20mL) and dried over Na_2SO_4. The extract was filtered and concentrated under reduced pressure to afford desired crude carboxylic acid which was used for the next step without further purification.

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 trans-dioxazolones.

Procedure for myoglobin-catalyzed enantioselective allylic C-H amination reactions (General procedure B)



Analytical scale reactions were carried out at a 400 µL scale: 24-well plates or crimp vials containing a concentrated amount of Mb (H64V, V68A) were introduced to an anaerobic chamber. Then, a corresponding amount of degassed 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 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 MeCN). 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 analyzed by adding 20 µL of internal standard (50 mM benzodioxole in EtOH) to the reaction mixture, followed by extraction with 400 µL of CH_2Cl_2 and analysis by GC-FID or SFC-MS.

Preparative-scale reaction (2.0 mmol scale). NaBB buffer (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) in NaBB (50 mM, pH 9.0) was added dropwise and the

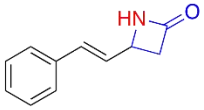
headspace of the flask was evacuated with Ar for 10 mins. The enzyme was reduced by the addition of a buffered solution of $Na_2S_2O_4$ (10 mM final conc.) in NaBB (50 mM, pH 9.0) via syringe. A solution of desired dioxazolone (10 mM final conc.) in acetonitrile (5% vol/vol final conc.) was then added via syringe. The resulting mixture was left stirring for 3 hours under Ar. The crude product was extracted with DCM (3 x 20 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 1:1 Hexane:Ethyl Acetate solution as eluent to afford the desired lactam products.

Determination of enantiomeric excess

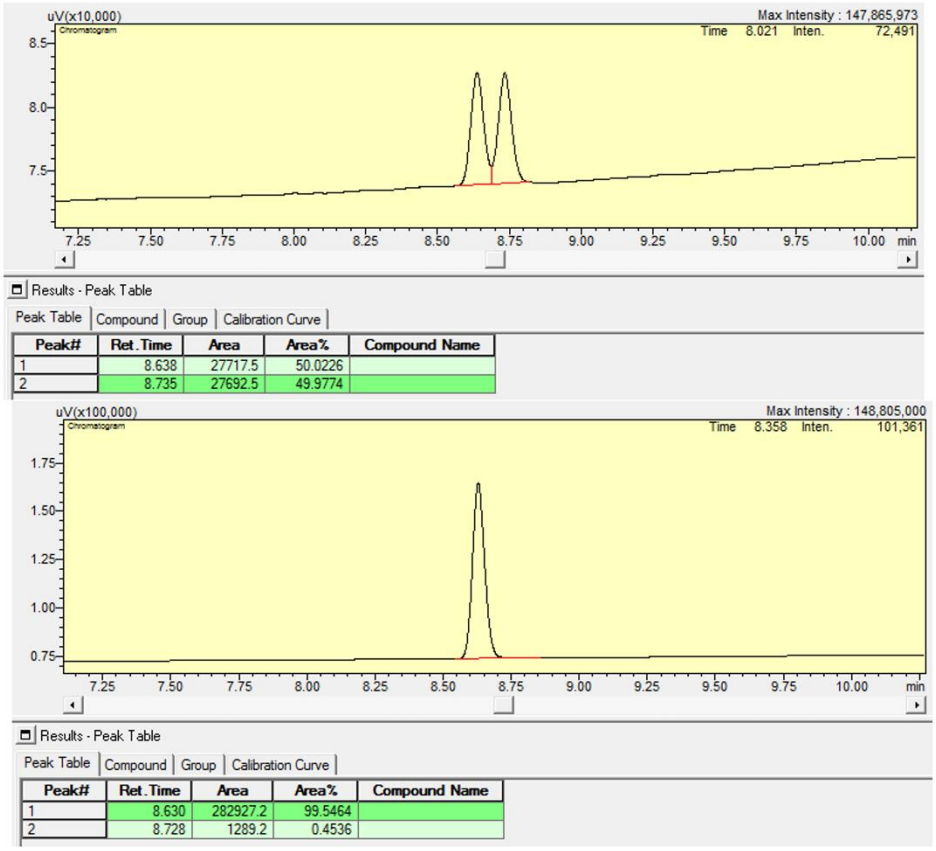
Chiral GC-FID and SFC-MS chromatograms for determination of enantiomeric excess in the C-H amidation of dioxazolonne substrates catalyzed by Mb(H64V,V68A). Reference racemic samples were prepared using Pd-catalyzed Heck reaction as described in the experimental procedures. GC and SFC-MS method used for separation is described for each substrate, see Product Analysis section for details.

a) **(*E*)-4-styrylazetidin-2-one (2a)** GC analysis for diastereomeric and enantiomeric determination of compound **2a** using **GC Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

Racemic →

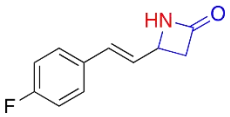


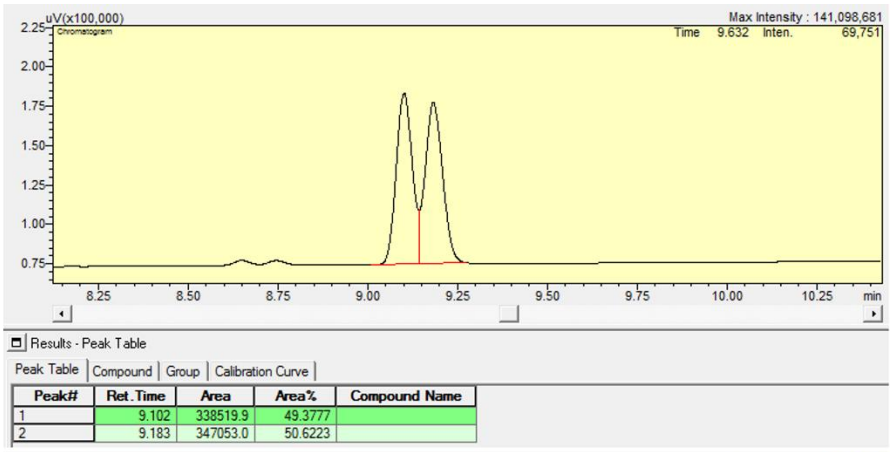
Mb(H64V,V68A) →



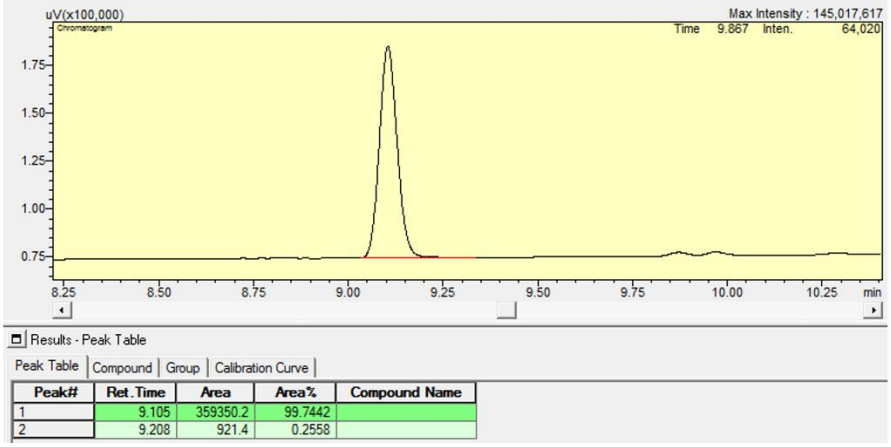
b) **(*E*)-4-(4-fluorostyryl)azetidin-2-one (2b)** GC analysis for diastereomeric and enantiomeric determination of compound **2b** using **GC Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

Racemic →



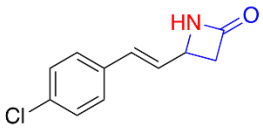


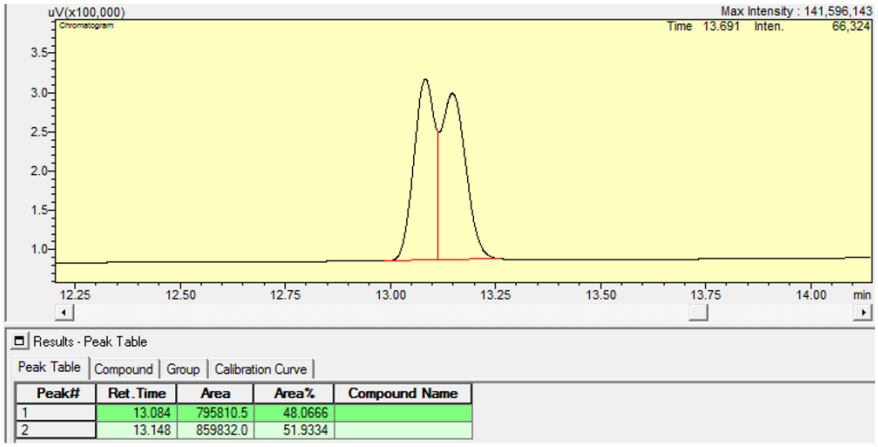
Mb(H64V,V68A) →



c) **(*E*)-4-(4-chlorostyryl)azetidin-2-one (2c)** GC analysis for diastereomeric and enantiomeric determination of compound **2c** using **GC Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

Racemic →



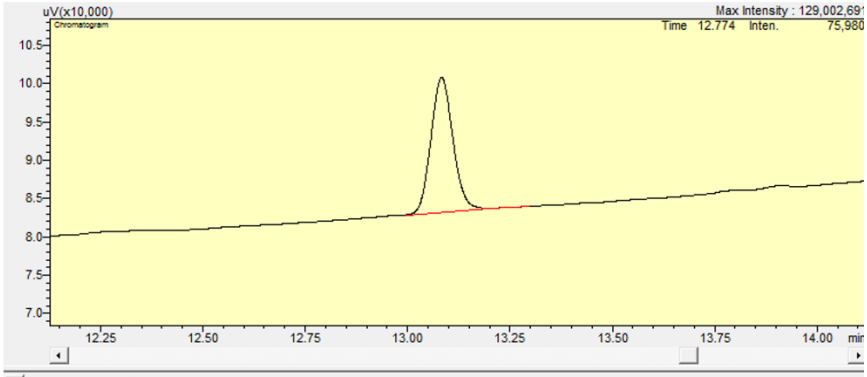


Results - Peak Table

Peak Table | Compound | Group | Calibration Curve

Peak#	Ret.Time	Area	Area%	Compound Name
1	13.084	795810.5	48.0666	
2	13.148	859832.0	51.9334	

Mb(H64V,V68A) →



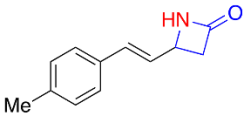
Results - Peak Table

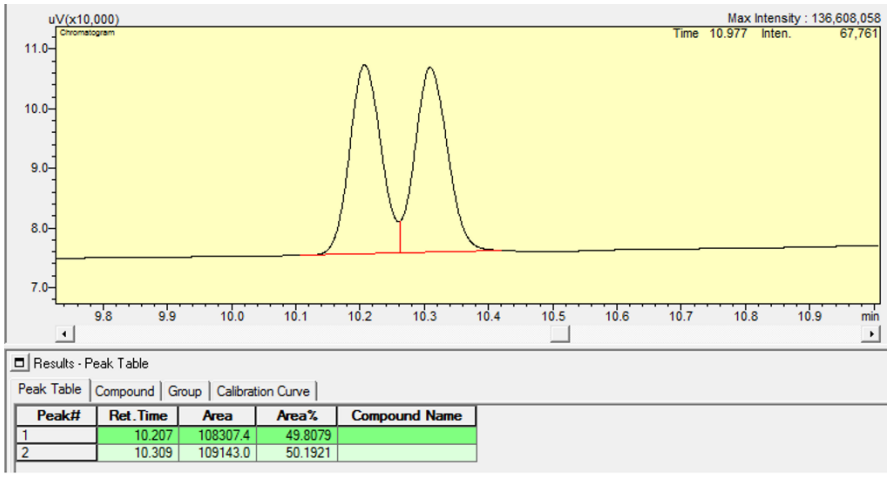
Peak Table | Compound | Group | Calibration Curve

Peak#	Ret.Time	Area	Area%	Compound Name
1	13.083	66169.2	99.6833	
2	13.296	210.3	0.3167	

d) **(*E*)-4-(4-methylstyryl)azetidin-2-one (2d)** GC analysis for diastereomeric and enantiomeric determination of compound **2d** using **GC Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

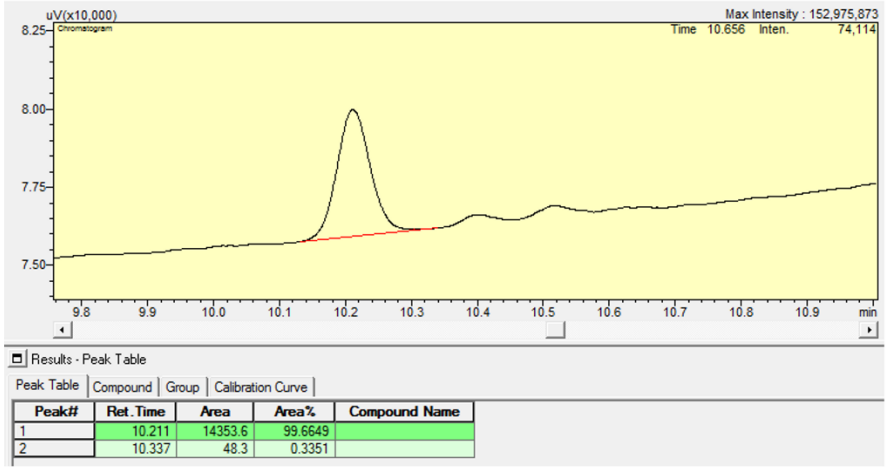
Racemic →





Peak#	Ret.Time	Area	Area%	Compound Name
1	10.207	108307.4	49.8079	
2	10.309	109143.0	50.1921	

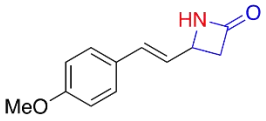
Mb(H64V,V68A) →



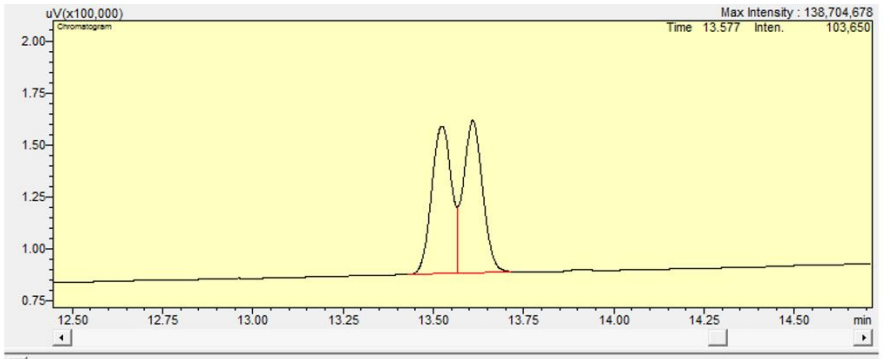
Peak#	Ret.Time	Area	Area%	Compound Name
1	10.211	14353.6	99.6649	
2	10.337	48.3	0.3351	

e) **(*E*)-4-(4-methoxystyryl)azetidin-2-one (2e)** GC analysis for diastereomeric and enantiomeric determination of compound **2e** using **GC Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

Racemic →



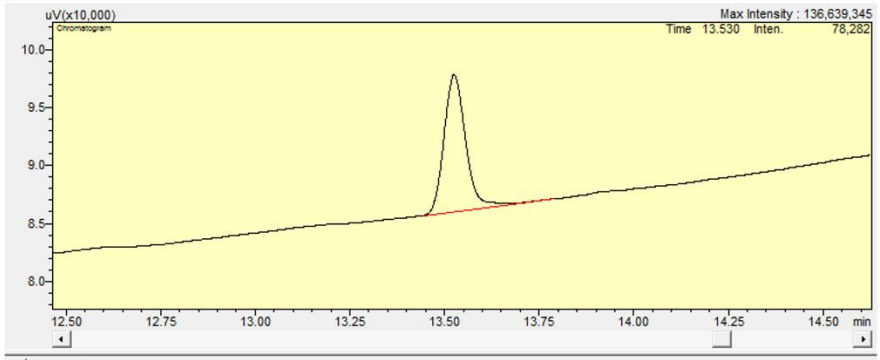
Mb(H64V,V68A) →



Results - Peak Table

Peak Table | Compound | Group | Calibration Curve

Peak#	Ret.Time	Area	Area%	Compound Name
1	13.524	271991.0	49.9578	
2	13.609	272450.4	50.0422	



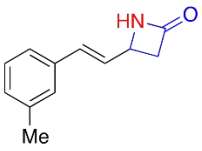
Results - Peak Table

Peak Table | Compound | Group | Calibration Curve

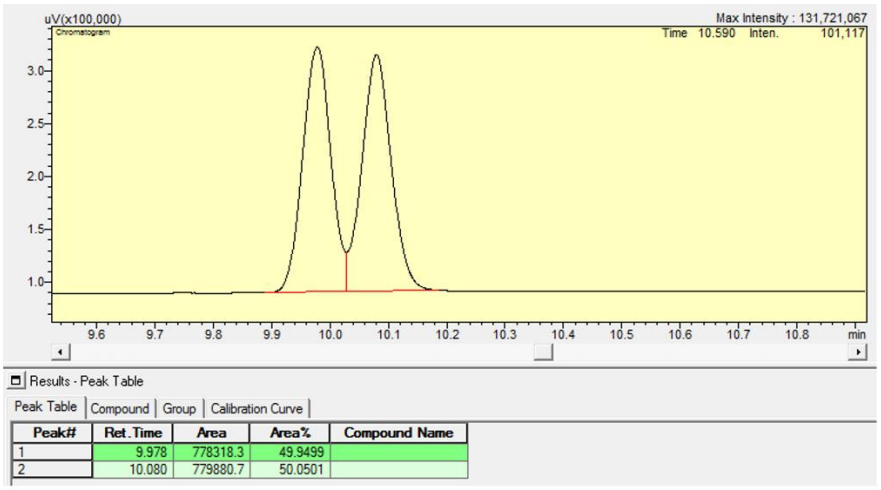
Peak#	Ret.Time	Area	Area%	Compound Name
1	13.525	46947.2	99.4011	
2	13.786	282.9	0.5989	

f) **(*E*)-4-(3-methylstyryl)azetidin-2-one (2f)** GC analysis for diastereomeric and enantiomeric determination of compound **2f** using **GC Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

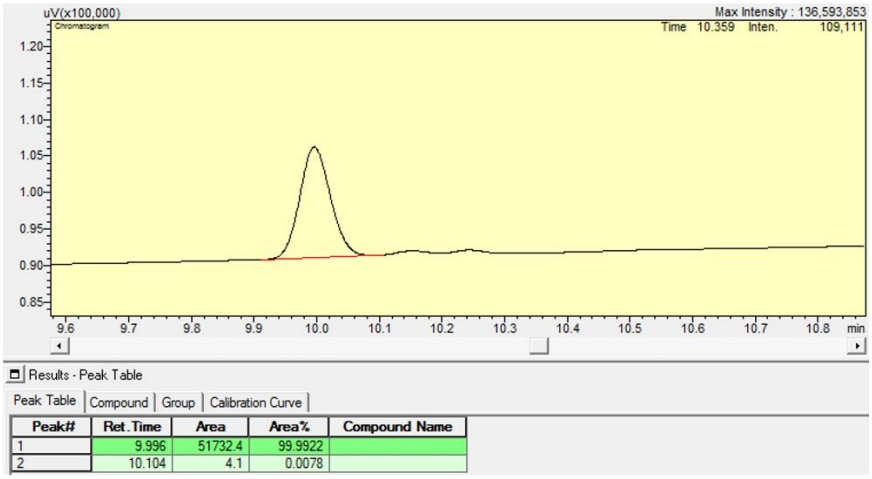
Racemic →



Mb(H64V,V68A) →



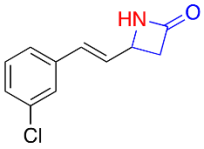
Peak#	Ret.Time	Area	Area%	Compound Name
1	9.978	778318.3	49.9499	
2	10.080	779880.7	50.0501	

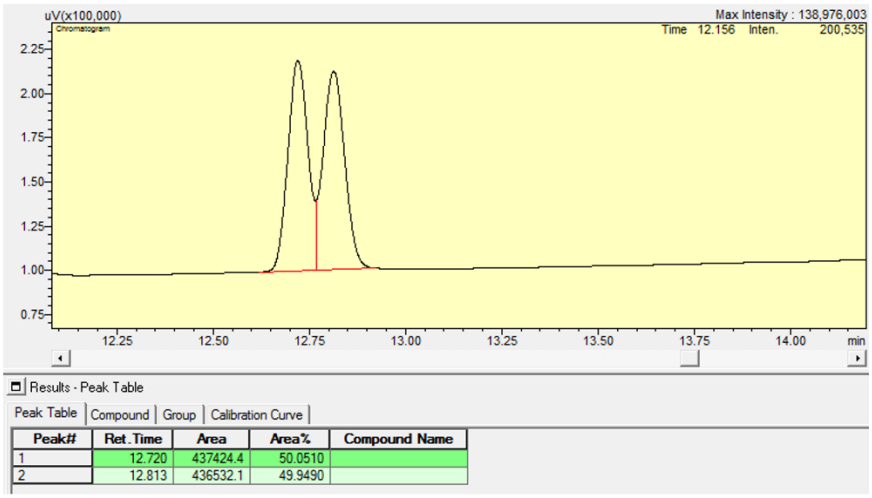


Peak#	Ret.Time	Area	Area%	Compound Name
1	9.996	51732.4	99.9922	
2	10.104	4.1	0.0078	

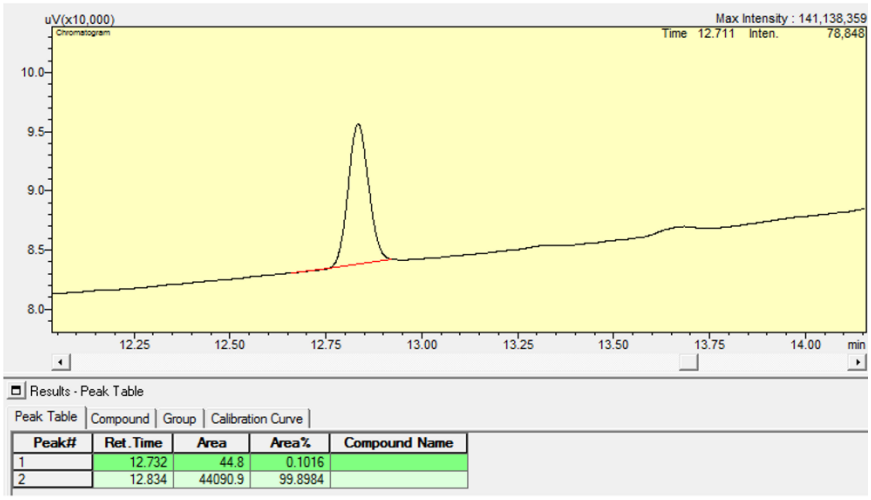
g) **(*E*)-4-(3-chlorostyryl)azetidin-2-one (2g)** GC analysis for diastereomeric and enantiomeric determination of compound **2g** using **GC Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

Racemic →



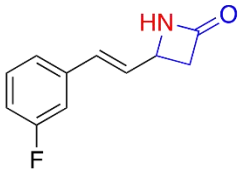


Mb(H64V,V68A) →

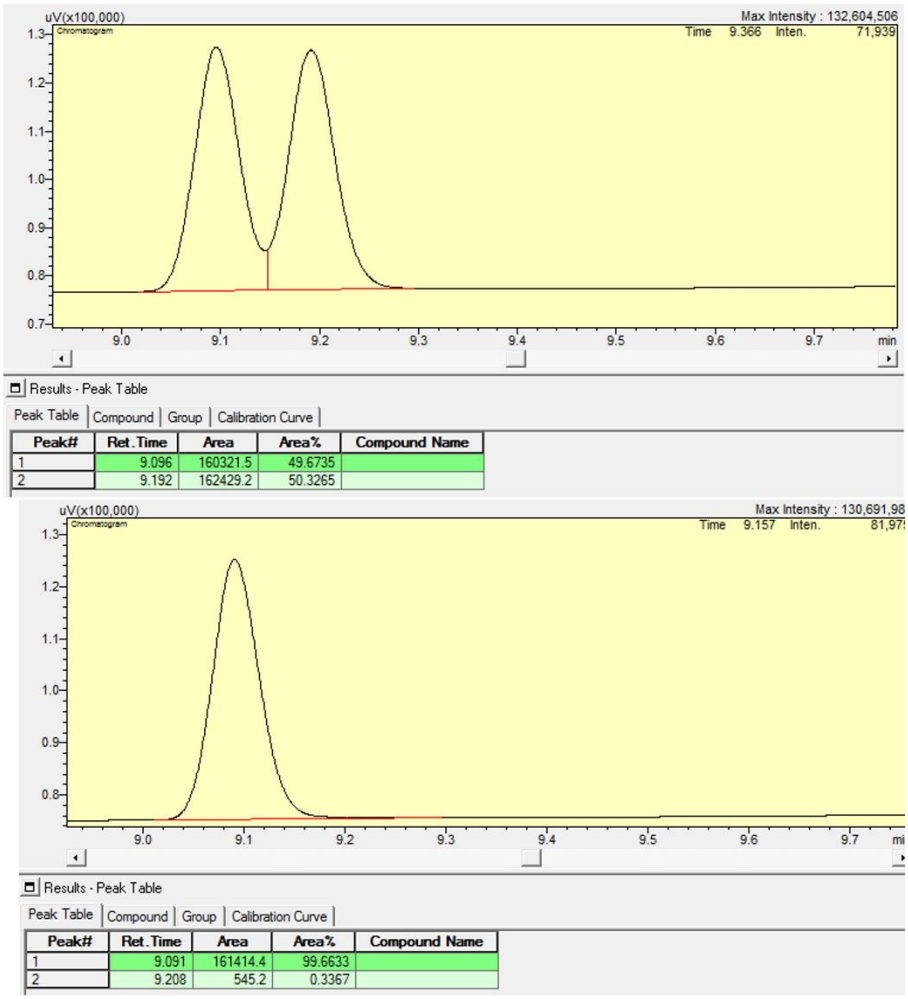


h) **(*E*)-4-(3-fluorostyryl)azetidin-2-one (2h)** GC analysis for diastereomeric and enantiomeric determination of compound **2h** using **GC Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

Racemic →

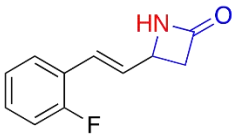


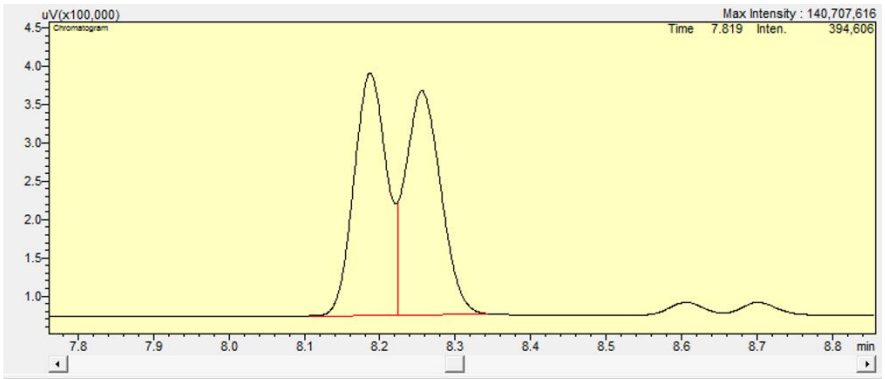
Mb(H64V,V68A) →



i) **(*E*)-4-(2-fluorostyryl)azetidin-2-one (2i)** GC analysis for diastereomeric and enantiomeric determination of compound **2i** using **GC Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

Racemic →



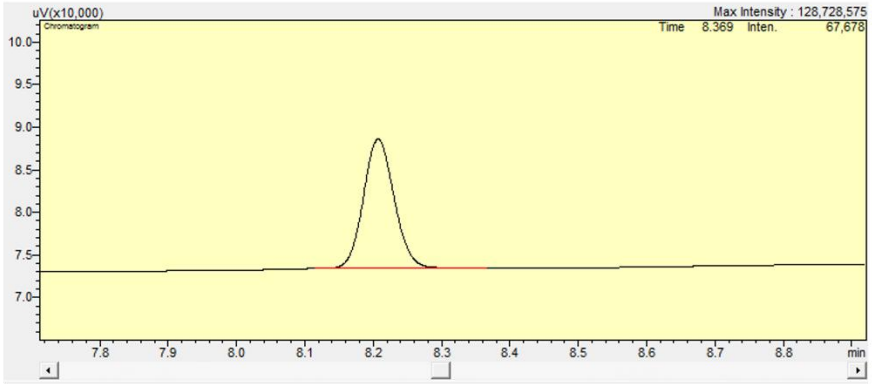


Results - Peak Table

Peak Table | Compound | Group | Calibration Curve

Peak#	Ret.Time	Area	Area%	Compound Name
1	8.187	955188.6	50.1410	
2	8.256	949815.4	49.8590	

Mb(H64V,V68A) →



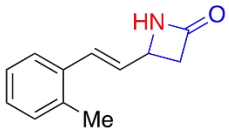
Results - Peak Table

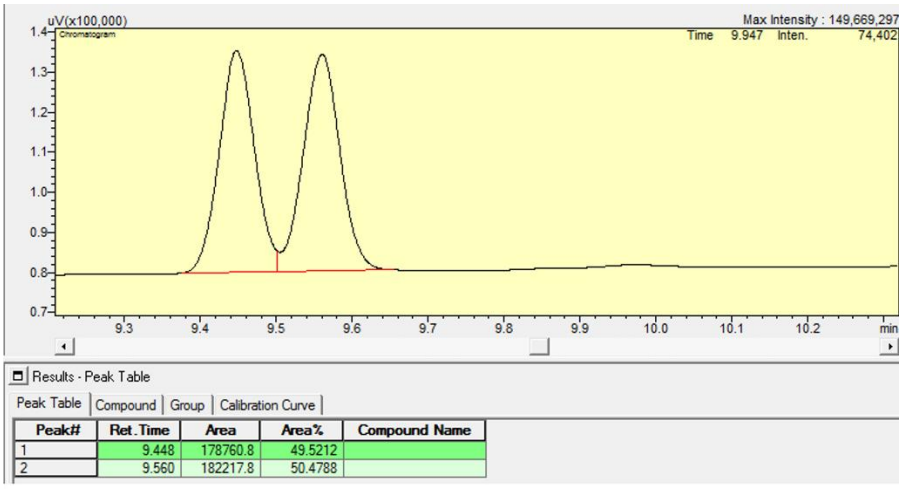
Peak Table | Compound | Group | Calibration Curve

Peak#	Ret.Time	Area	Area%	Compound Name
1	8.207	47363.8	99.8803	
2	8.313	56.8	0.1197	

j) **(*E*)-4-(2-methylstyryl)azetidin-2-one (2j)** GC analysis for diastereomeric and enantiomeric determination of compound **2j** using **GC Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

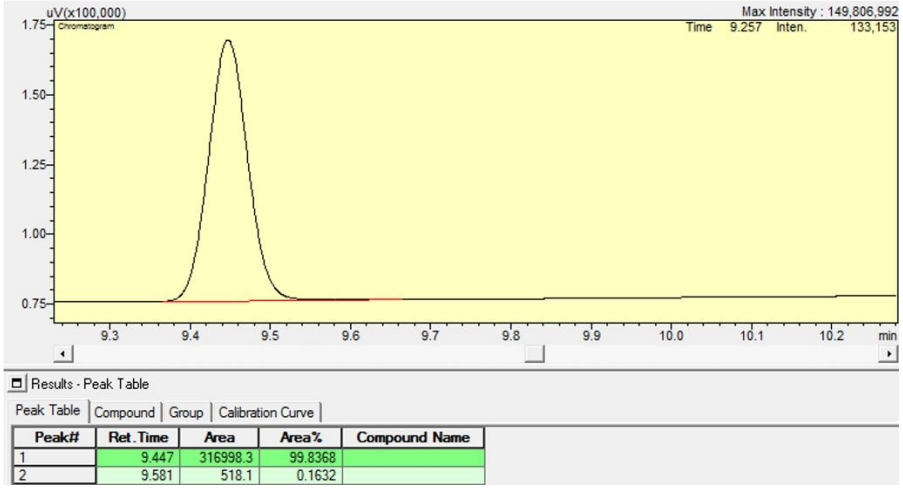
Racemic →





Peak#	Ret. Time	Area	Area%	Compound Name
1	9.448	178760.8	49.5212	
2	9.560	182217.8	50.4788	

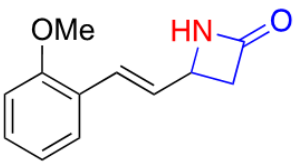
Mb(H64V,V68A) →



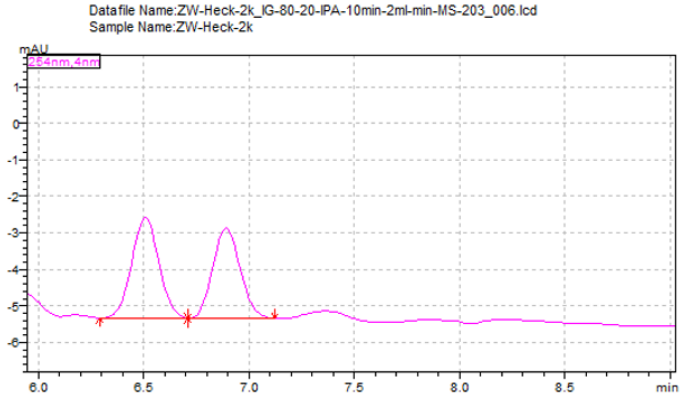
Peak#	Ret. Time	Area	Area%	Compound Name
1	9.447	316998.3	99.8368	
2	9.581	518.1	0.1632	

k) **(E)-4-(2-methoxystyryl)azetidin-2-one (2k):** SFC-MS analysis for diastereomeric and enantiomeric determination of compound **2k** using **SFC-MS Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

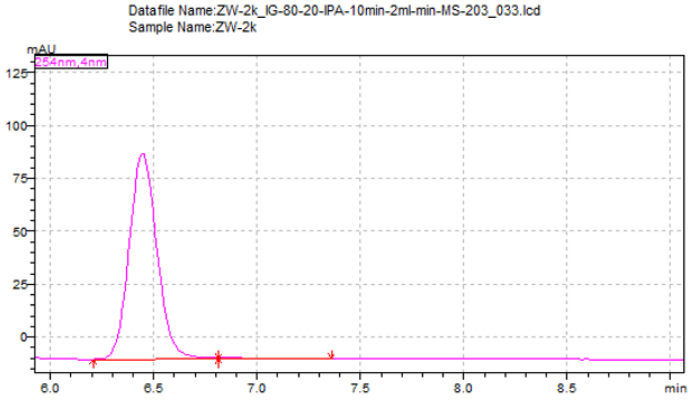
Racemic →



Mb(H64V, V68A) →



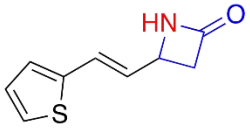
Peak#	Ret. Time	Area	Height	ID#	Name	Area%
1	6.507	24649	2771			52.490
2	6.891	22310	2465			47.510
Total		46959	5237			100.000

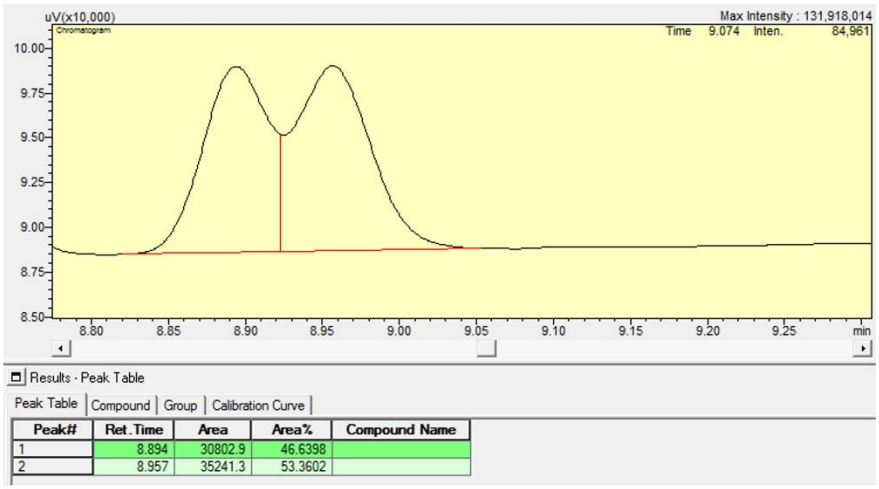


Peak#	Ret. Time	Area	Height	ID#	Name	Area%
1	6.447	901115	97164			99.184
2	6.821	7411	671			0.816
Total		908526	97835			100.000

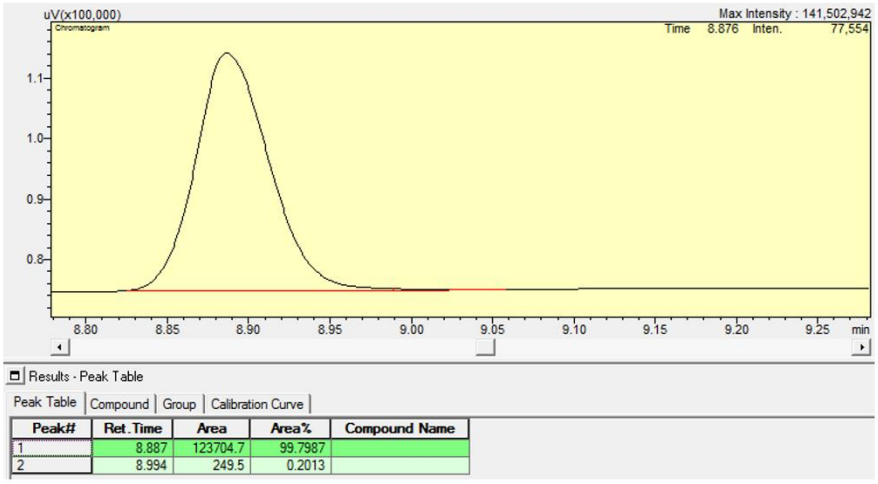
l) **(S,E)-4-(2-(thiophen-2-yl)vinyl)azetidin-2-one (2l)** GC analysis for diastereomeric and enantiomeric determination of compound **2l** using **GC Separation Method 1**. Racemic (top) and enzymatically (bottom) generated products are shown below

Racemic →



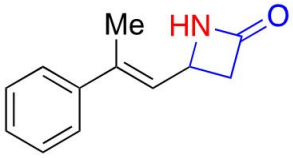


Mb(H64V,V68A) →

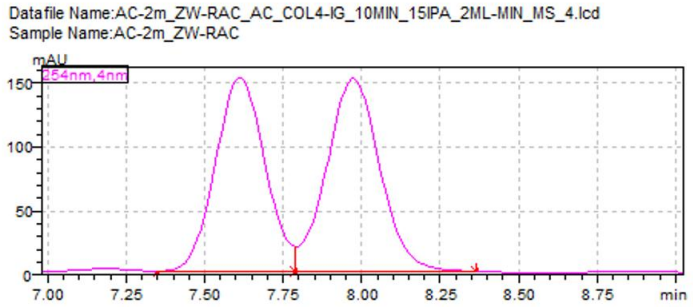


m) **((E)-4-(2-phenylprop-1-en-1-yl)azetidin-2-one (2m):** SFC-MS analysis for diastereomeric and enantiomeric determination of compound **2m** using **SFC Separation Method 2**. Racemic (top) and enzymatically (bottom) generated products are shown below

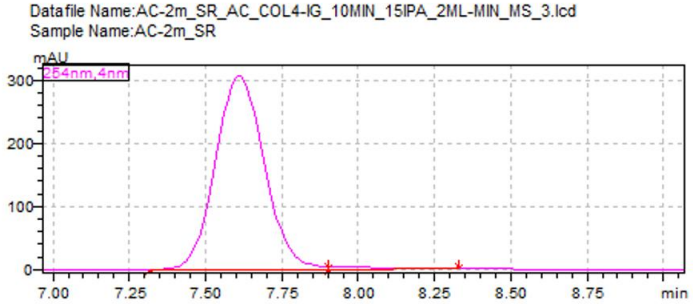
Racemic →



Mb(H64V, V68A) →



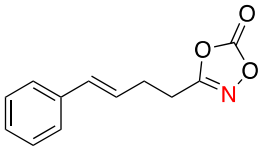
Peak#	Ret. Time	Area	Height	I	N	Area%
1	7.613	1663680	151079			48.399
2	7.973	1773781	150412			51.601



Peak#	Ret. Time	Area	Height	I	N	Area%
1	7.610	3423898	307651			98.857
2	7.920	39603	3913			1.143

Compound Characterization Data

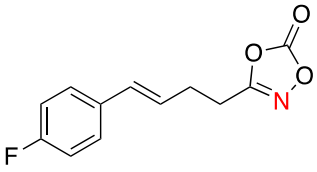
Compound 1a:



1a was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 927 mg of the desired product as mixture of the *E* and *Z* isomers in a d.r. ratio of 8.5:1 in a form of colorless liquid in 61% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.20 (m, 6H), 6.49 (d, *J* = 15.8 Hz, 1H), 6.15 (dt, *J* = 15.8, 6.9 Hz, 1H), 2.80 (t, *J* = 7.4 Hz, 2H), 2.63 (qd, *J* = 7.2, 1.4 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 165.9, 154.0, 136.5, 132.8, 128.6, 128.5, 128.4, 127.7, 126.2, 125.5, 27.7, 24.9.

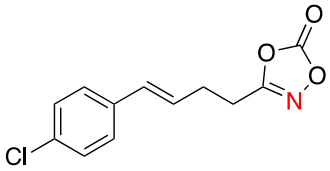
Compound 1b:



1b was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 372 mg of the desired product as mixture of the *E* and *Z* isomers in a d.r. ratio of 5.0:1 in a form of colorless liquid in 79% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.27 (m, 2H), 7.03 – 6.97 (m, 2H), 6.47 (d, *J* = 15.8 Hz, 1H), 6.07 (dt, *J* = 15.7, 6.9 Hz, 1H), 2.82 (t, *J* = 7.3 Hz, 2H), 2.65 – 2.62 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 131.7, 127.8, 127.7, 125.3, 115.6, 115.4, 27.7, 24.9.

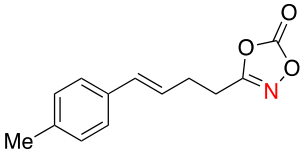
Compound 1c:



1c was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 888 mg of the desired product as colorless liquid in 63% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (s, 4H), 6.45 (dt, *J* = 15.9, 1.5 Hz, 1H), 6.14 (dt, *J* = 15.7, 6.9 Hz, 1H), 2.81 (t, *J* = 7.3 Hz, 2H), 2.69 – 2.58 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.8, 154.0, 135.0, 133.3, 131.7, 128.8, 127.4, 126.2, 27.7, 24.8.

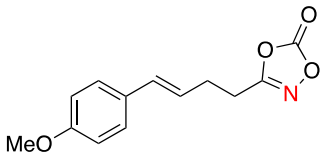
Compound 1d::



1d was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 650 mg of the desired product as mixture of the *E* and *Z* isomers in a d.r. ratio of 15.0:1 as colorless liquid in 76% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 – 7.03 (m, 1H), 2.77 (t, *J* = 7.4 Hz, 1H), 2.32 (s, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.0, 154.0, 137.5, 133.7, 132.6, 129.3, 129.1, 128.4, 126.0, 124.5, 27.7, 25.0, 24.9, 23.4, 21.1.

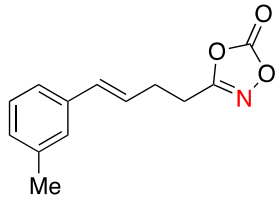
Compound 1e:



1e was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 979 mg of the desired product as colorless liquid in 60% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.25 (m, 1H), 6.97 – 6.74 (m, 1H), 3.81 (s, 2H), 2.80 (t, *J* = 7.5 Hz, 1H), 2.68 – 2.56 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.0, 159.3, 132.3, 129.4, 127.4, 123.3, 114.1, 55.3, 27.8, 25.1.

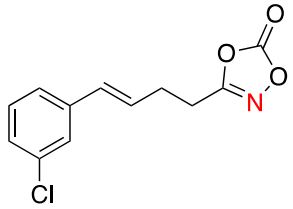
Compound 1f:



(*E*)-3-(4-(*m*-tolyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (**1g**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 856 mg of the desired product as a mixture of the *E* and *Z* isomers in a d.r. ratio of 10.1:1 in a form of 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 6.38 – 6.19 (m, 3H), 6.17 – 6.05 (m, 1H), 5.64 – 5.46 (m, 1H), 5.22 (dt, J = 15.8, 6.9 Hz, 1H), 1.82 (td, J = 7.4, 0.9 Hz, 2H), 1.71 – 1.62 (m, 2H), 1.47 – 1.40 (m, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.9, 153.9, 137.9, 136.4, 132.5, 128.3, 128.2, 126.7, 125.4, 123.2, 27.4, 24.5, 21.1.

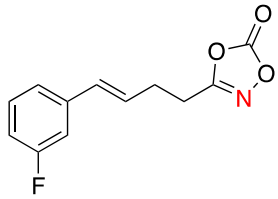
Compound 1g:



1g was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 876 mg of the desired product as a mixture of the *E* and *Z* isomers in a d.r. ratio of 5.1:1 in a form of colorless liquid in 58% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (t, J = 1.8 Hz, 1H), 7.15 – 7.08 (m, 3H), 6.38 – 6.28 (m, 1H), 6.07 (dt, J = 15.8, 6.8 Hz, 1H), 2.70 (t, J = 7.3 Hz, 2H), 2.56 – 2.49 (m, 2H).. **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.8, 165.8, 153.9, 138.4, 138.2, 134.4, 131.4, 130.6, 129.8, 129.6, 128.8, 128.5, 127.5, 127.2, 127.2, 126.6, 126.0, 124.4, 27.5, 24.8, 24.6, 23.3.

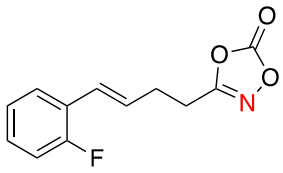
Compound 1h:



1h was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 514 mg of the desired product as a mixture of the *E* and *Z* isomers in a d.r. ratio of 8.1:1 in a form of colorless liquid in 56% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (td, J = 7.9, 5.8 Hz, 1H), 7.10 (dd, J = 7.8, 1.5 Hz, 1H), 7.04 (dd, J = 10.1, 2.4 Hz, 1H), 6.93 (td, J = 8.4, 2.5 Hz, 1H), 6.47 (d, J = 15.8 Hz, 1H), 6.17 (dt, J = 15.6, 6.9 Hz, 1H), 2.82 (t, J = 7.3 Hz, 2H), 2.64 (q, J = 7.2 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.8, 164.3, 161.8, 154.0, 138.9, 138.8, 131.8, 131.7, 130.1, 130.0, 127.0, 122.1, 122.1, 114.6, 114.4, 112.7, 112.5, 27.6, 24.7.

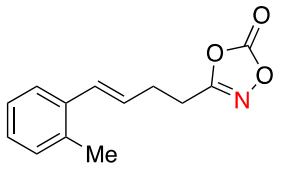
Compound 1i:



1i was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 386 mg of the desired product as mixture of the *E* and *Z* isomers in a d.r. ratio of 2.0:1 in a form of colorless liquid in 82% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 – 6.95 (m, 4H), 6.73 – 6.49 (m, 1H), 6.25 (dt, *J* = 15.9, 6.9 Hz, 1H), 2.91 – 2.70 (m, 2H), 2.67 (dd, *J* = 15.7, 8.5 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.9, 161.2, 160.9, 158.8, 158.5, 154.0, 130.2, 130.2, 129.9, 129.2, 129.1, 128.9, 128.9, 128.4, 128.3, 127.3, 127.3, 125.3, 125.2, 124.9, 124.3, 124.2, 124.1, 124.1, 124.0, 123.9, 123.8, 115.8, 115.7, 115.6, 115.5, 28.0, 24.7, 24.6, 23.8.

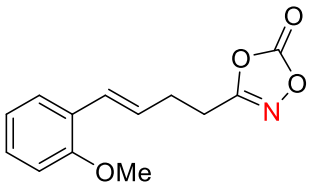
Compound 1j:



1j was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 733 mg of the desired product as mixture of the *E* and *Z* isomers in a d.r. ratio of 10.2:1 in a form of colorless liquid in 52% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (td, *J* = 5.4, 2.5 Hz, 1H), 7.18 – 7.13 (m, 3H), 6.71 (d, *J* = 16.6 Hz, 1H), 6.02 (dd, *J* = 15.8, 6.8 Hz, 1H), 2.82 (td, *J* = 7.3, 2.3 Hz, 2H), 2.69 – 2.65 (m, 2H), 2.32 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 166.0, 135.8, 135.2, 131.0, 130.3, 127.6, 126.9, 126.1, 125.6, 28.0, 25.0, 23.3, 19.7.

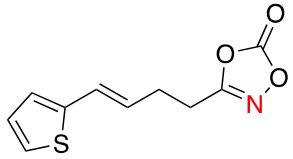
Compound 1k:



1k was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 445 mg of the desired product as a mixture of the *E* and *Z* isomers in a d.r. ratio of 4.3:1 in a form of colorless liquid in 36% yield over 3 steps. R_f = 0.2 (10% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.6 Hz, 1H), 7.24 – 7.19 (m, 1H), 6.91 (q, *J* = 7.1 Hz, 1H), 6.86 (d, *J* = 8.2 Hz, 1H), 6.79 (s, 1H), 6.15 (dt, *J* = 16.2, 6.9 Hz, 1H), 3.84 (s, 3H), 2.81 (t, *J* = 7.4 Hz, 2H), 2.64 (q, *J* = 7.1 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 166.06, 156.48, 154.11, 128.72, 127.75, 126.70, 126.16, 125.64, 120.63, 110.77, 55.38, 28.18, 24.99.

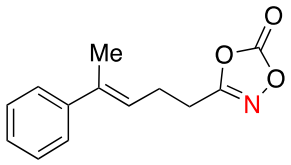
Compound 1l:



1n was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 738 mg of the desired product as colorless liquid in 59% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 – 7.12 (m, 1H), 6.98 – 6.91 (m, 2H), 6.66 – 6.59 (m, 1H), 5.99 (dt, *J* = 15.5, 7.0 Hz, 1H), 2.84 – 2.77 (m, 2H), 2.64 – 2.58 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.99, 154.16, 141.63, 127.52, 126.17, 125.78, 125.30, 124.41, 27.70, 24.98.

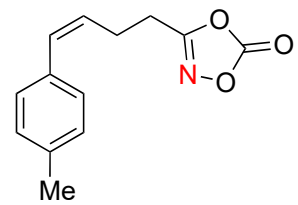
Compound 1m:



1m was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 738 mg of the desired product as colorless liquid in 55% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.18 (m, 5H), 5.68 (tq, *J* = 7.2, 1.4 Hz, 1H), 2.74 (td, *J* = 7.3, 1.0 Hz, 2H), 2.65 – 2.55 (m, 2H), 2.05 (q, *J* = 1.0 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.1, 154.0, 142.9, 138.2, 128.2, 127.1, 125.7, 123.2, 24.8, 23.7, 15.9.

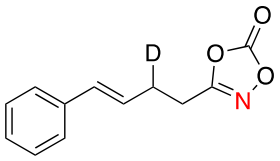
Compound (*Z*)-1d:



(*Z*)-1d was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 762 mg of the desired product as colorless liquid in 66% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 – 7.08 (m, 4H), 6.54 (d, J = 11.5 Hz, 1H), 5.55 (dt, J = 11.5, 6.5 Hz, 1H), 2.72 (q, J = 4.9 Hz, 4H), 2.35 (s, 3H).**^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.0, 154.0, 137.1, 133.6, 132.00, 129.1, 128.5, 126.8, 25.1, 23.5, 21.2.

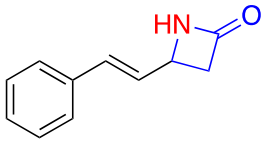
(*E*)-3-(4-phenylbut-3-en-1-yl-2-*d*)-1,4,2-dioxazol-5-one (1a-*D*$_1$):



(*E*)-3-(4-phenylbut-3-en-1-yl-2-*d*)-1,4,2-dioxazol-5-one (**1a-*D*$_1$**) was prepared according to the general procedure **A** and purified by silica gel column chromatography to afford 355 mg of the desired product as colorless liquid in 65% yield over 3 steps. R_f = 0.4 (10% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.23 (m, 5H), 6.54 – 6.44 (m, 1H), 6.15 (dd, *J* = 15.8, 6.8 Hz, 1H), 2.79 (d, *J* = 7.3 Hz, 2H), 2.65 – 2.57 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 165.9, 154.0, 136.5, 132.8, 128.6, 127.7, 126.2, 125.5, 27.6, 27.4, 27.2, 24.8.

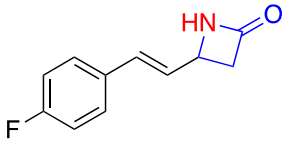
(*E*)-4-styrylazetidin-2-one (2a):



(*E*)-4-styrylazetidin-2-one (**2a**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 57% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.30 (m, 5H), 6.64 (d, *J* = 15.8 Hz, 1H), 6.24 (ddd, *J* = 15.8, 7.8, 2.0 Hz, 1H), 6.13 (s, 1H), 4.31 – 4.16 (m, 1H), 3.36 – 3.25 (m, 1H), 2.82 (d, *J* = 14.9 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 167.3, 135.9, 132.4, 128.7, 128.6, 128.2, 126.5, 125.9, 49.4, 45.6.

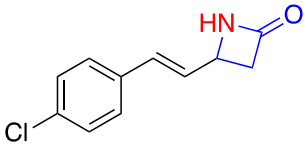
(*E*)-4-(4-fluorostyryl)azetidin-2-one (2b):



(*E*)-4-(4-fluorostyryl)azetidin-2-one (**2b**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 32% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 – 6.99 (m, 5H), 6.60 (d, *J* = 15.7 Hz, 1H), 6.16 (dd, *J* = 15.8, 7.6 Hz, 2H), 4.31 (dddd, *J* = 7.7, 5.2, 2.5, 0.9 Hz, 1H), 3.30 (ddd, *J* = 14.9, 5.3, 2.2 Hz, 1H), 2.82 (ddd, *J* = 14.9, 2.5, 1.3 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 163.6, 161.6, 132.0, 131.2, 128.4, 128.1, 128.0, 115.7, 115.6, 49.3, 45.6.

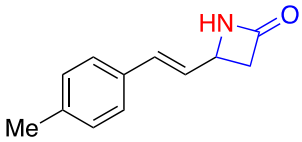
(*E*)-4-(4-chlorostyryl)azetidin-2-one (2c):



(*E*)-4-(4-chlorostyryl)azetidin-2-one (**2c**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 64% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (s, 4H), 6.51 (dd, *J* = 15.8, 1.0 Hz, 1H), 6.20 – 6.08 (m, 2H), 4.27 – 4.19 (m, 1H), 3.23 (ddd, *J* = 14.9, 5.2, 2.2 Hz, 1H), 2.74 (ddd, *J* = 14.9, 2.6, 1.3 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 167.4, 134.4, 133.8, 131.1, 129.3, 128.9, 49.2, 45.5.

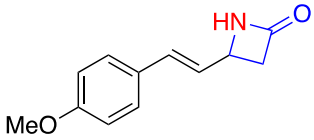
(*E*)-4-(4-methylstyryl)azetidin-2-one (2d):



(*E*)-4-(4-methylstyryl)azetidin-2-one (**2d**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 43% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 – 7.10 (m, 7H), 6.60 (d, *J* = 15.8 Hz, 1H), 6.23 – 6.14 (m, 2H), 4.29 (s, 1H), 3.38 – 3.23 (m, 2H), 2.34 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 167.6, 138.1, 133.0, 132.2, 129.4, 126.4, 125.6, 49.6, 45.4, 21.2.

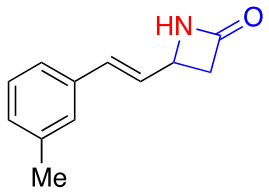
(*E*)-4-(4-methoxystyryl)azetidin-2-one (2e):



(*E*)-4-(4-methoxystyryl)azetidin-2-one (**2e**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 74% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 – 7.29 (m, 2H), 6.89 – 6.84 (m, 2H), 6.57 (d, *J* = 15.7 Hz, 1H), 6.09 (dd, *J* = 15.7, 7.8 Hz, 1H), 6.00 (s, 1H), 4.29 (d, *J* = 0.9 Hz, 1H), 3.82 (s, 3H), 3.27 (dd, *J* = 5.2, 2.1 Hz, 1H), 2.81 (ddd, *J* = 14.9, 2.5, 1.4 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 167.5, 159.7, 131.9, 128.6, 127.7, 126.3, 114.1, 55.3, 49.5, 45.6.

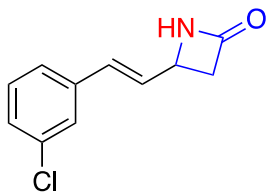
(*E*)-4-(3-methylstyryl)azetidin-2-one (2f):



(*E*)-4-(3-methylstyryl)azetidin-2-one (**2f**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 24% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 – 7.10 (m, 4H), 6.60 (d, *J* = 15.8 Hz, 1H), 6.23 (dd, *J* = 15.8, 7.7 Hz, 1H), 6.11 (s, 1H), 4.30 (dddd, *J* = 6.2, 5.2, 2.5, 1.3 Hz, 1H), 3.30 (ddd, *J* = 14.9, 5.2, 2.1 Hz, 1H), 2.82 (ddd, *J* = 14.9, 2.6, 1.4 Hz, 1H), 2.35 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 167.5, 138.3, 135.8, 132.5, 129.0, 128.6, 128.4, 127.2, 123.7, 49.4, 45.5, 21.3.

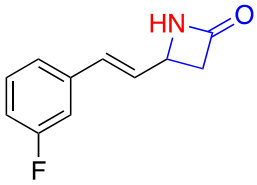
(*E*)-4-(3-chlorostyryl)azetidin-2-one (2g):



(*E*)-4-(3-chlorostyryl)azetidin-2-one (**2g**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 14% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.17 (m, 5H), 6.58 (d, *J* = 15.8 Hz, 1H), 6.27 (ddd, *J* = 15.8, 7.5, 0.9 Hz, 1H), 4.32 (dddd, *J* = 6.6, 5.3, 2.6, 1.3 Hz, 1H), 3.38 – 3.21 (m, 1H), 2.83 (ddt, *J* = 14.9, 2.4, 1.1 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 167.3, 137.7, 134.7, 131.0, 130.2, 130.0, 128.1, 126.4, 124.7, 49.1, 45.6.

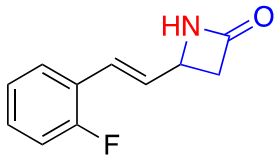
(*E*)-4-(3-fluorostyryl)azetidin-2-one (2h):



(*E*)-4-(3-fluorostyryl)azetidin-2-one (**2h**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 53% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (td, *J* = 8.0, 5.9 Hz, 1H), 7.14 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.08 (dt, *J* = 10.0, 2.1 Hz, 1H), 6.97 (tdd, *J* = 8.5, 2.6, 0.9 Hz, 1H), 6.61 (d, *J* = 15.8 Hz, 1H), 6.26 (dd, *J* = 15.8, 7.5 Hz, 1H), 6.21 (s, 1H), 4.32 (dddd, *J* = 7.6, 5.2, 2.5, 1.0 Hz, 1H), 3.31 (ddd, *J* = 14.9, 5.2, 2.2 Hz, 1H), 2.83 (ddd, *J* = 14.9, 2.6, 1.3 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 169.5, 164.1, 162.1, 144.2, 138.2, 131.2, 130.2, 130.1, 122.4, 115.1, 114.9, 113.1, 112.9, 49.1, 45.6.

(*E*)-4-(2-fluorostyryl)azetidin-2-one (2i):

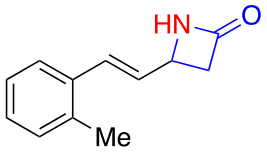


(*E*)-4-(2-fluorostyryl)azetidin-2-one (**2i**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 41% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 – 6.95 (m, 4H), 6.79 (d, *J* = 16.0 Hz, 1H), 6.39 – 6.30 (m, 1H), 6.15 (s, 1H), 4.38 – 4.30 (m, 1H), 3.32 (ddd, *J* = 14.9, 5.3, 2.1 Hz, 1H), 2.91 – 2.79 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.4, 161.5, 159.1, 131.3, 129.5, 129.4, 128.7, 127.6, 124.9, 124.2, 116.0, 115.7, 49.6, 45.5.

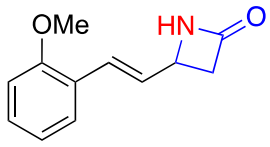
(*E*)-4-(2-methylstyryl)azetidin-2-one (2j):



(*E*)-4-(2-methylstyryl)azetidin-2-one (**2j**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 87% analytical yield. According to the typical 2.0 mmol scale procedure, **2j** was obtained with 72% isolated yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.78 – 5.46 (m, 5H), 5.18 (d, *J* = 15.6 Hz, 1H), 4.53 – 4.38 (m, 2H), 1.71 – 1.58 (m, 1H), 1.18 – 1.10 (m, 1H), 0.68 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 167.5, 135.5, 134.9, 130.4, 130.2, 129.9, 128.0, 126.2, 125.7, 49.6, 45.6, 19.7.

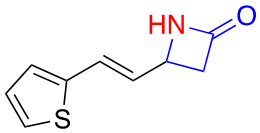
(E)-4-(2-methoxystyryl)azetidin-2-one (2k):



(E)-4-(2-methoxystyryl)azetidin-2-one (**2k**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 39% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (s, 1H), 6.97 – 6.86 (m, 4H), 6.26 (dd, J = 15.9, 7.8 Hz, 1H), 6.03 (s, 1H), 4.37 – 4.28 (m, 1H), 3.86 (s, 3H), 3.34 – 3.23 (m, 1H), 2.86 – 2.79 (m, 1H). **^{13}C NMR (151 MHz, $CDCl_3$):** δ 167.63, 156.95, 129.43, 129.40, 127.63, 127.28, 120.89, 111.04, 55.58, 50.06, 45.74.

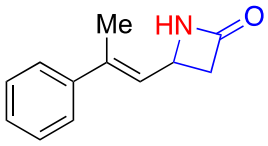
(E)-4-(2-(thiophen-2-yl)vinyl)azetidin-2-one (2l):



(E)-4-(2-(thiophen-2-yl)vinyl)azetidin-2-one (**2l**) was prepared according to the general procedure **B** to afford the desired *β*-lactam product as white solid in 11% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (s, 1H), 7.20 (d, J = 4.4 Hz, 1H), 6.98 (m, 2H), 6.77 (d, J = 15.6 Hz, 1H), 6.08 (dd, J = 15.6, 7.7 Hz, 1H), 5.90 (s, 1H), 3.29 (dd, J = 15.0, 4.5 Hz, 1H), 2.83 (d, J = 14.4 Hz, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 167.26, 140.81, 127.98, 127.53, 126.50, 125.56, 125.06, 49.20, 45.66.

((E)-4-(2-phenylprop-1-en-1-yl)azetidin-2-one (2m):



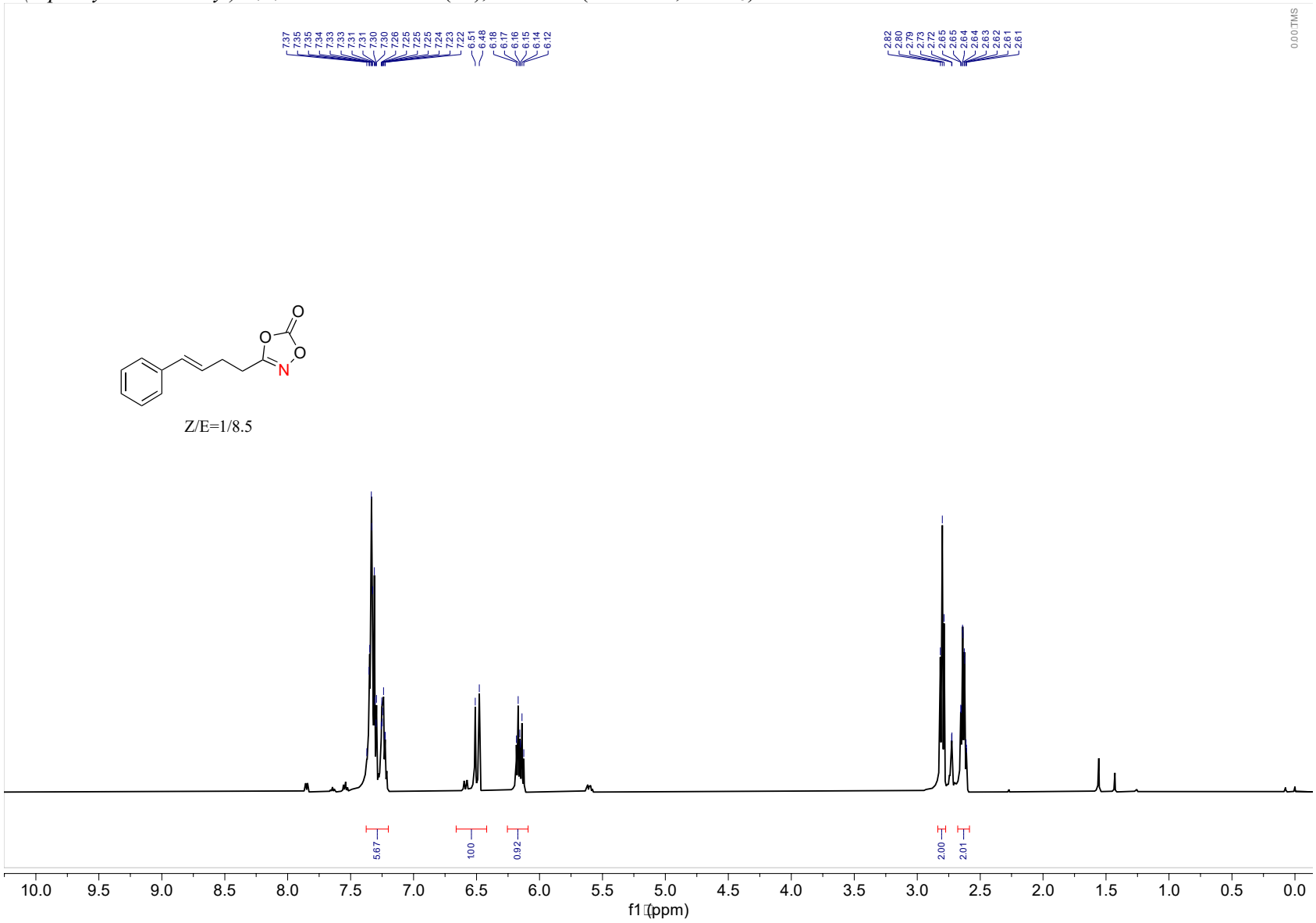
(E)-4-(2-phenylprop-1-en-1-yl)azetidin-2-one (**2m**) was prepared according to the general procedure **B** to afford the desired amide product as white solid in 24% analytical yield. R_f = 0.2 (50% ethyl acetate in hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.29 (m, 5H), 5.90 (s, 1H), 5.84 (d, J = 8.9 Hz, 1H), 4.59 (d, J = 6.2 Hz, 1H), 3.34 (dd, J = 14.9, 5.1 Hz, 1H), 2.81 (d, J = 15.5 Hz, 1H), 2.12 (d, J = 1.6 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 167.88, 142.38, 139.33, 128.57, 127.83, 127.30, 125.86, 45.84, 45.60, 16.43.

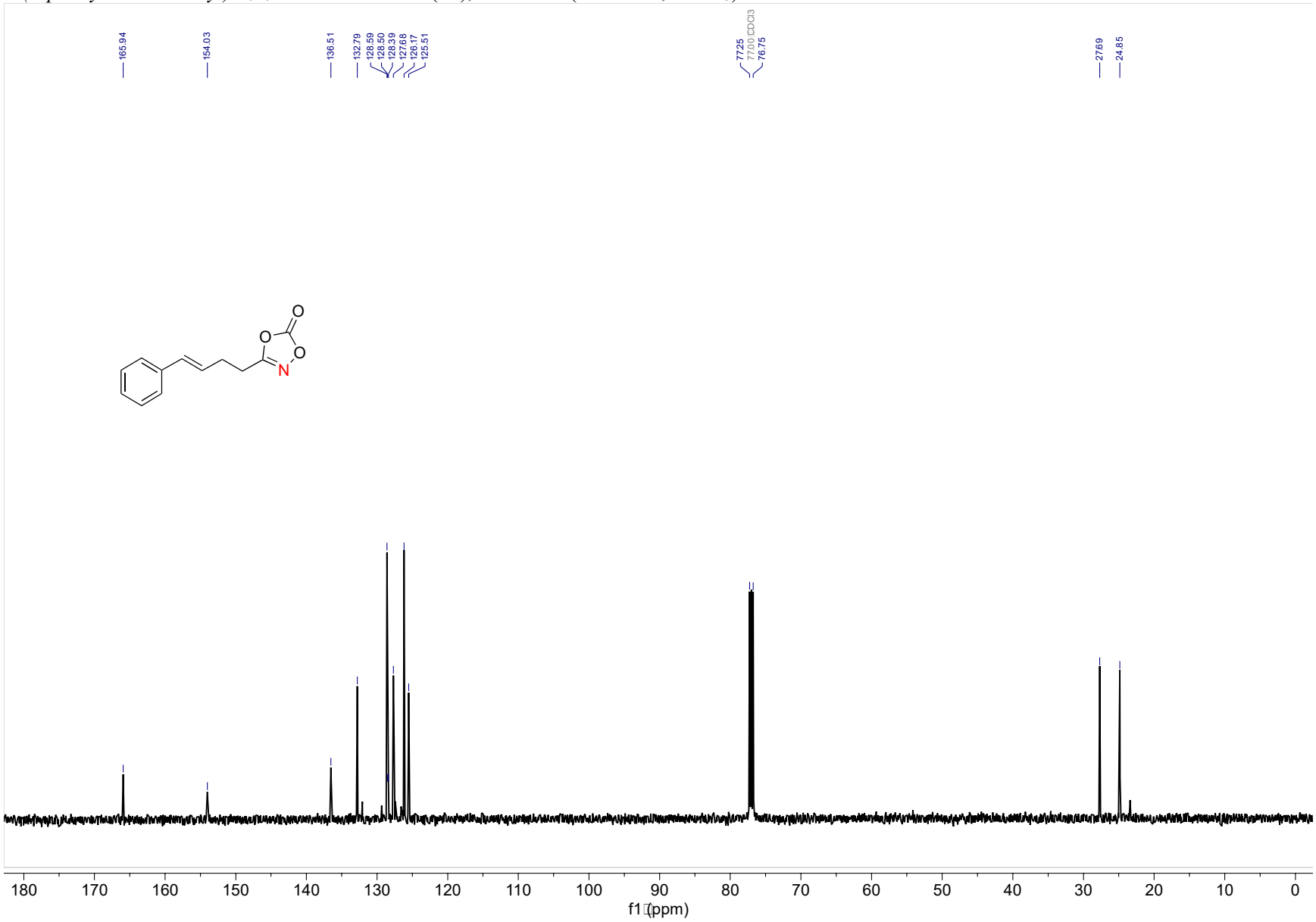
.

NMR Spectra

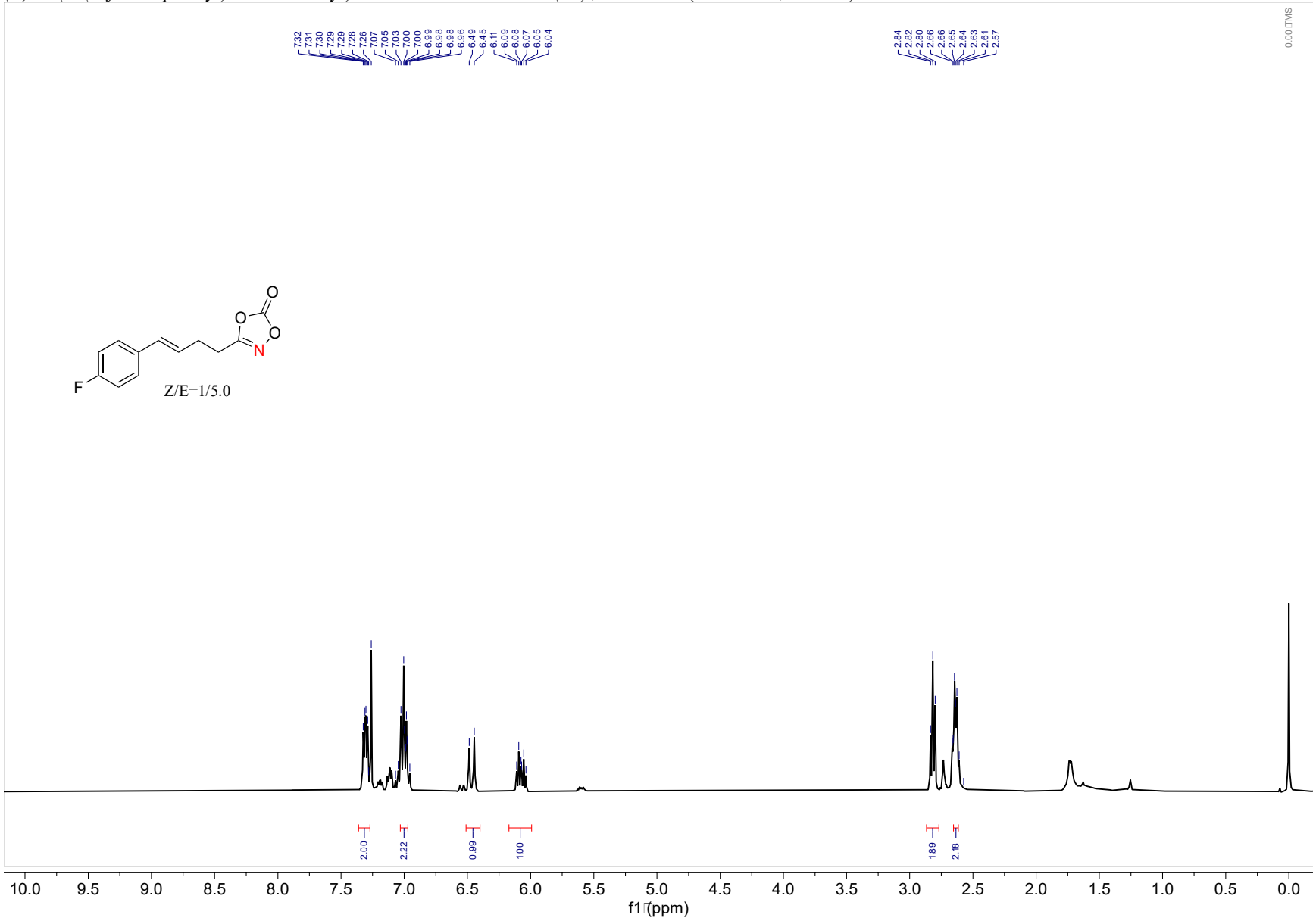
3-(4-phenylbut-3-en-1-yl)-1,4,2-dioxazol-5-one (**1a**), ^{1}H NMR (500 MHz, $CDCl_3$):



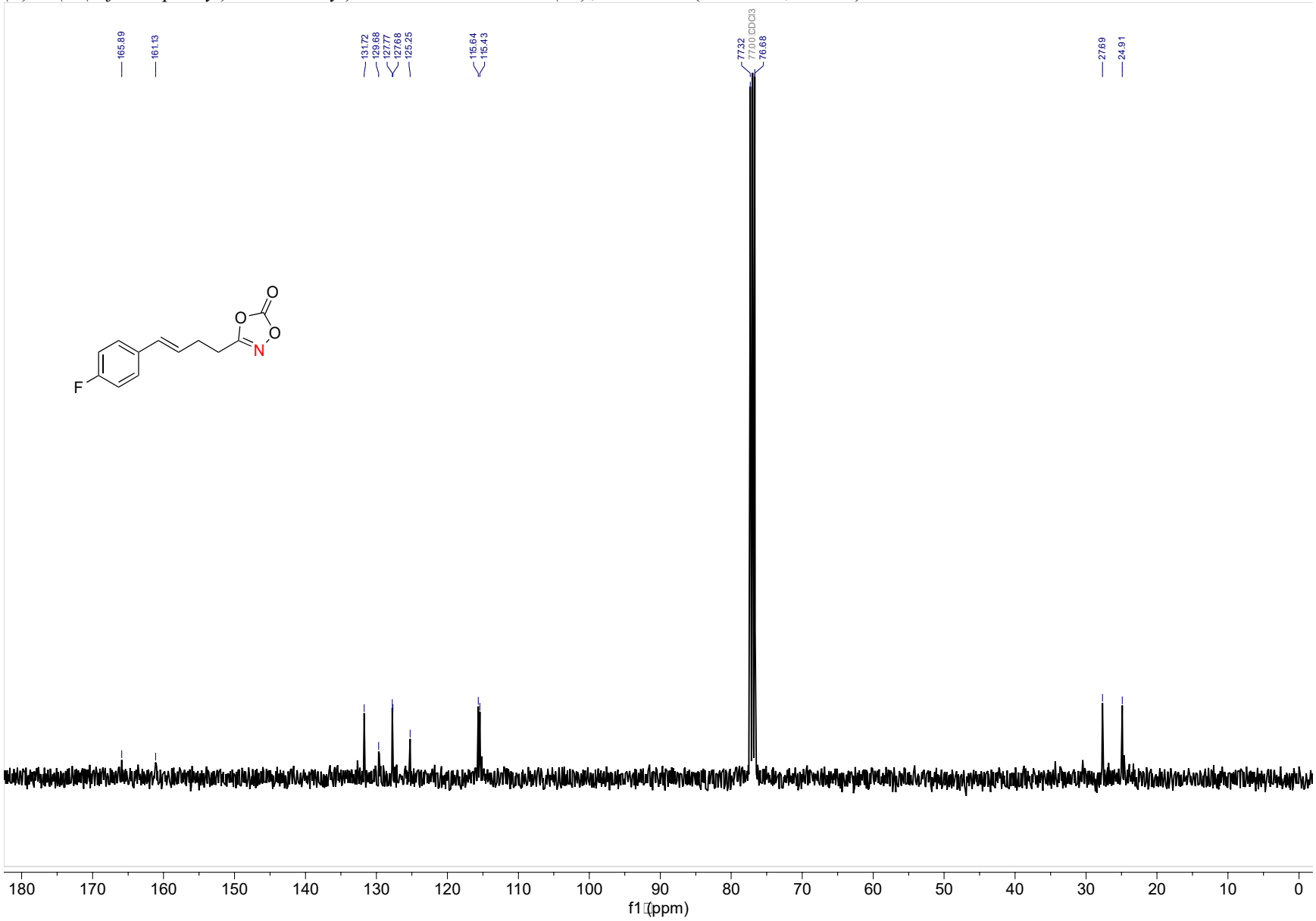
3-(4-phenylbut-3-en-1-yl)-1,4,2-dioxazol-5-one (**1a**), ^{13}C NMR (126 MHz, $CDCl_3$):



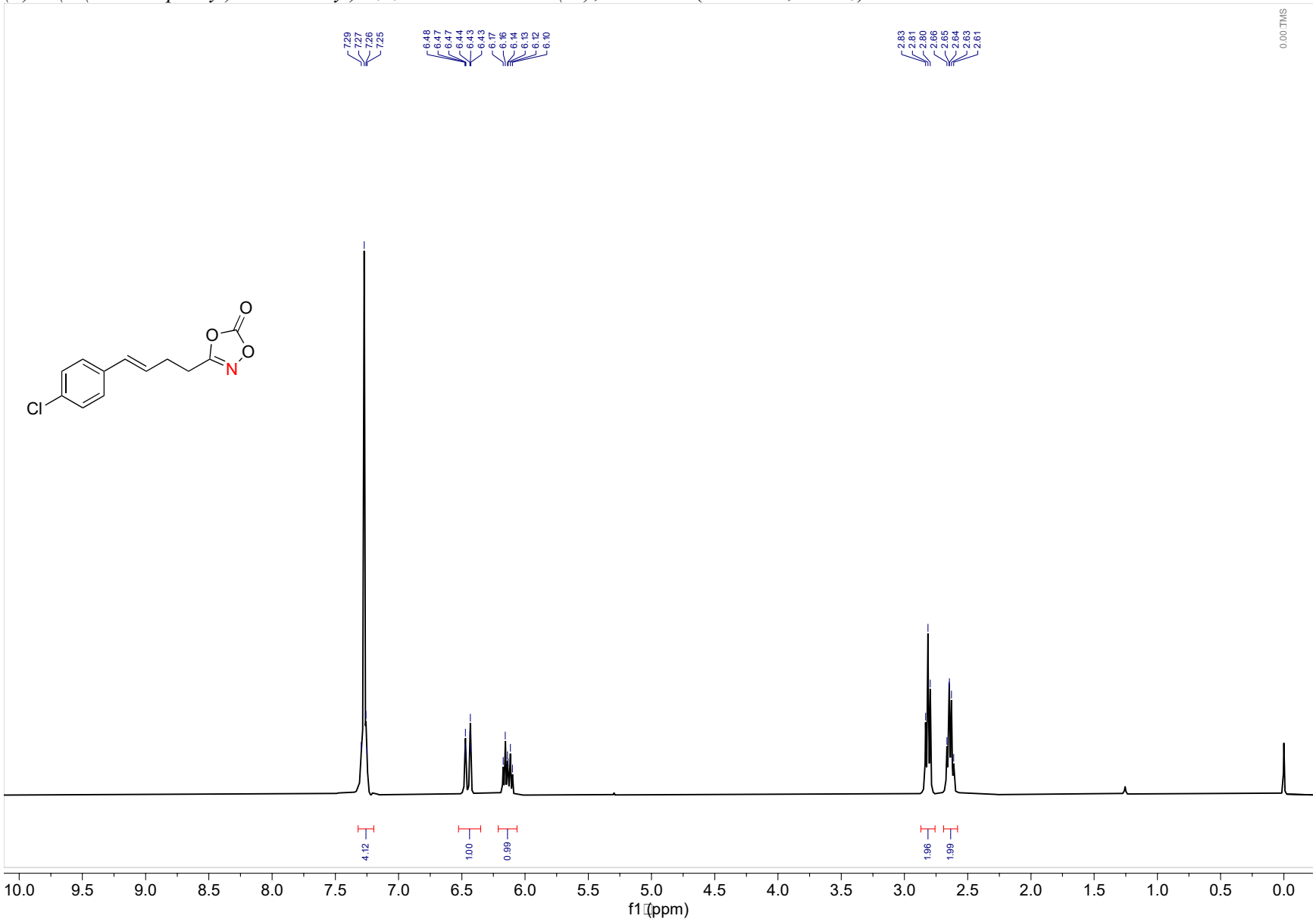
(E)-3-(4-(4-fluorophenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1b), ^{1}H NMR (400 MHz, $CDCl_3$):



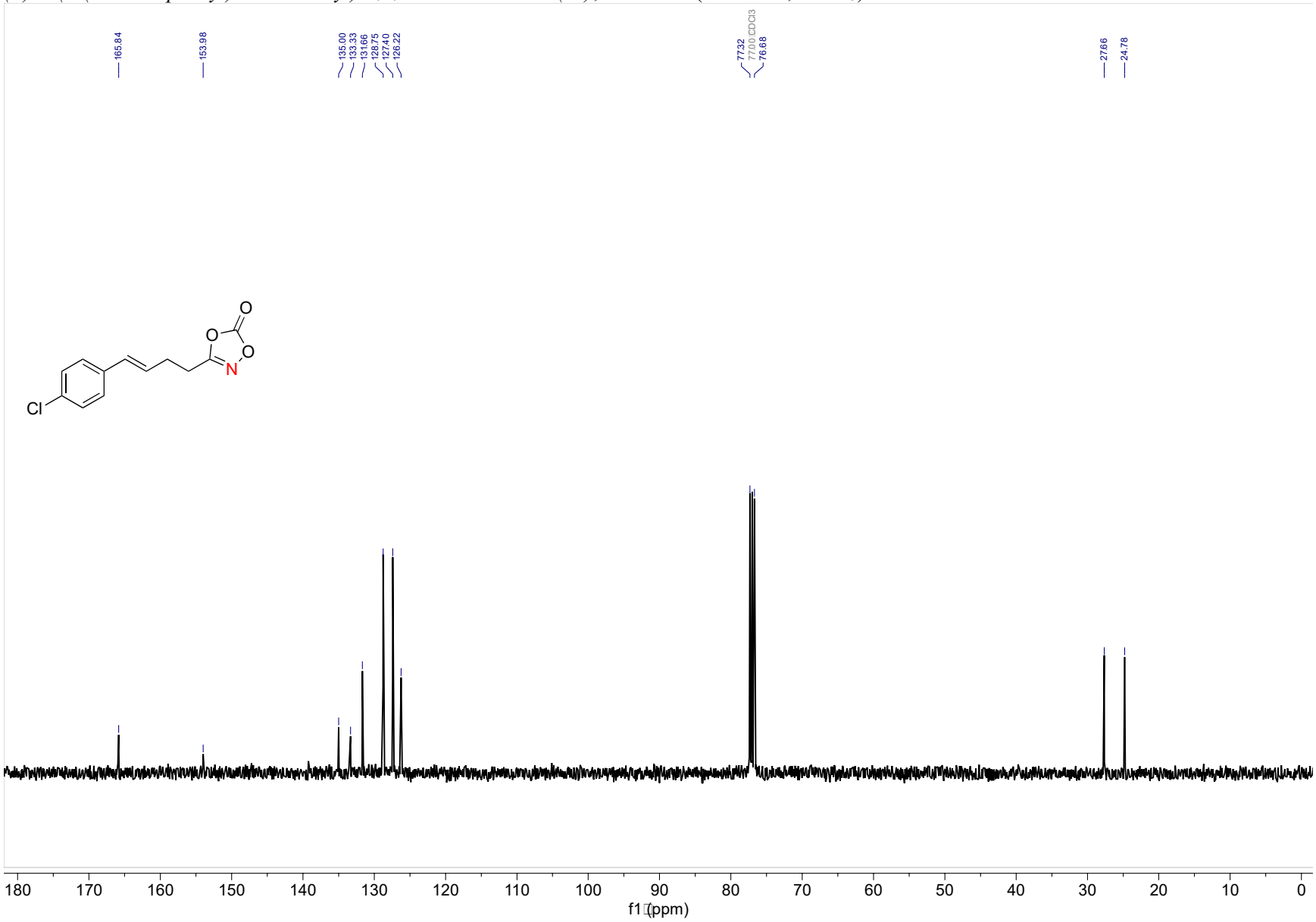
(E)-3-(4-(4-fluorophenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1b), ^{13}C NMR (100 MHz, $CDCl_3$):



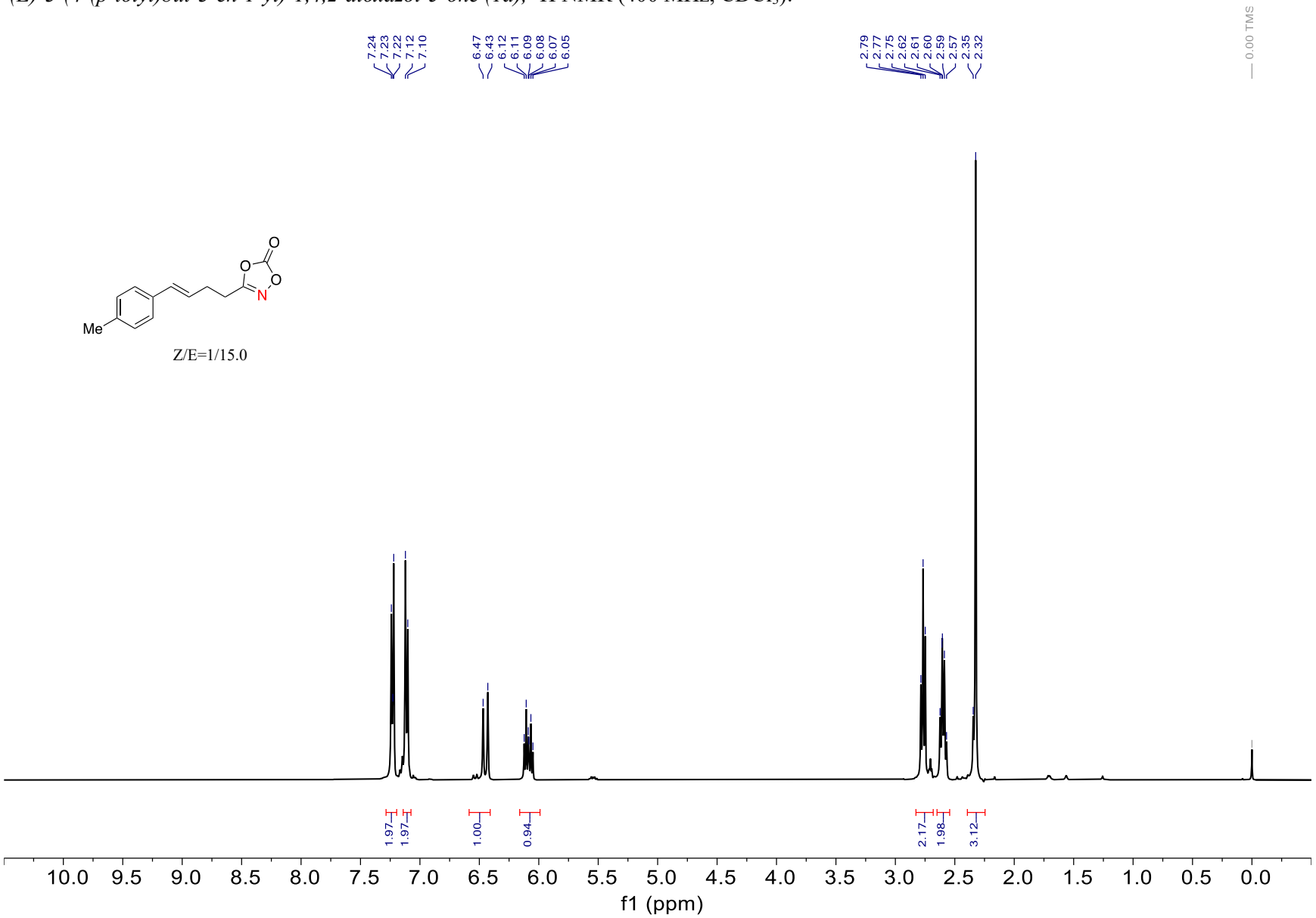
(E)-3-(4-(4-chlorophenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1c), ^{1}H NMR (400 MHz, $CDCl_3$):



(E)-3-(4-(4-chlorophenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1c), ^{13}C NMR (100 MHz, $CDCl_3$):

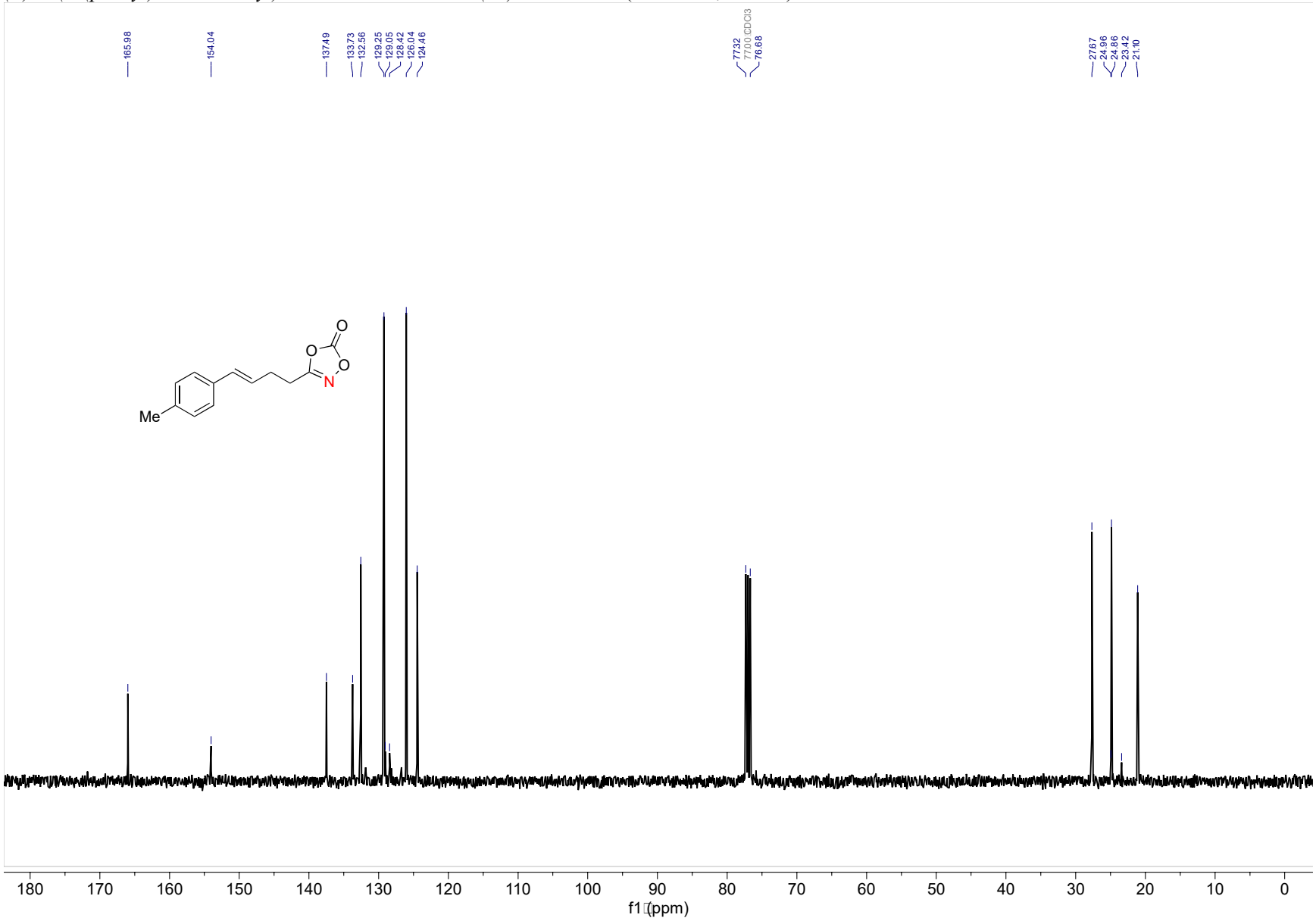


(E)-3-(4-(p-tolyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1d), ^{1}H NMR (400 MHz, $CDCl_3$):

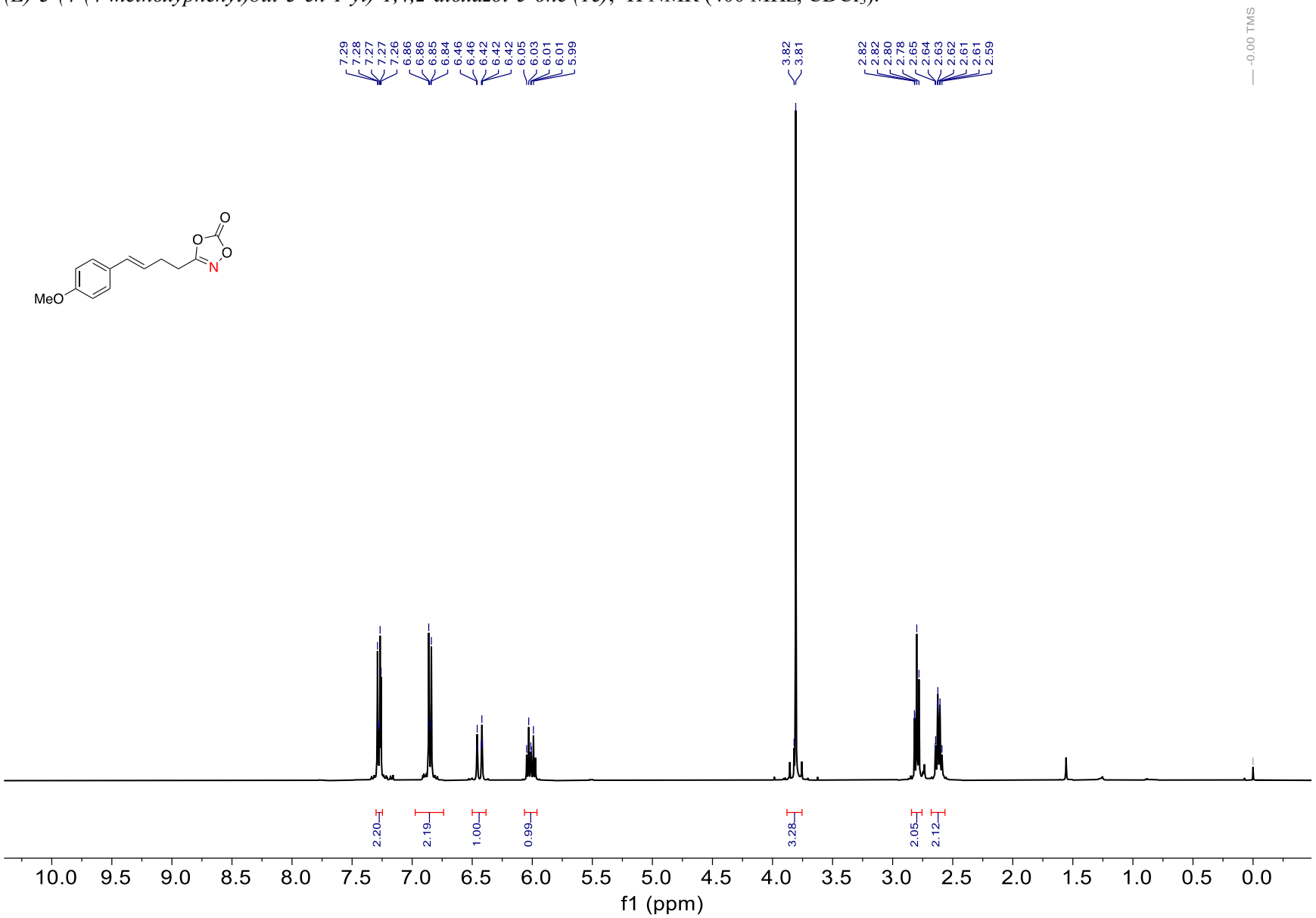


Z/E=1/15.0

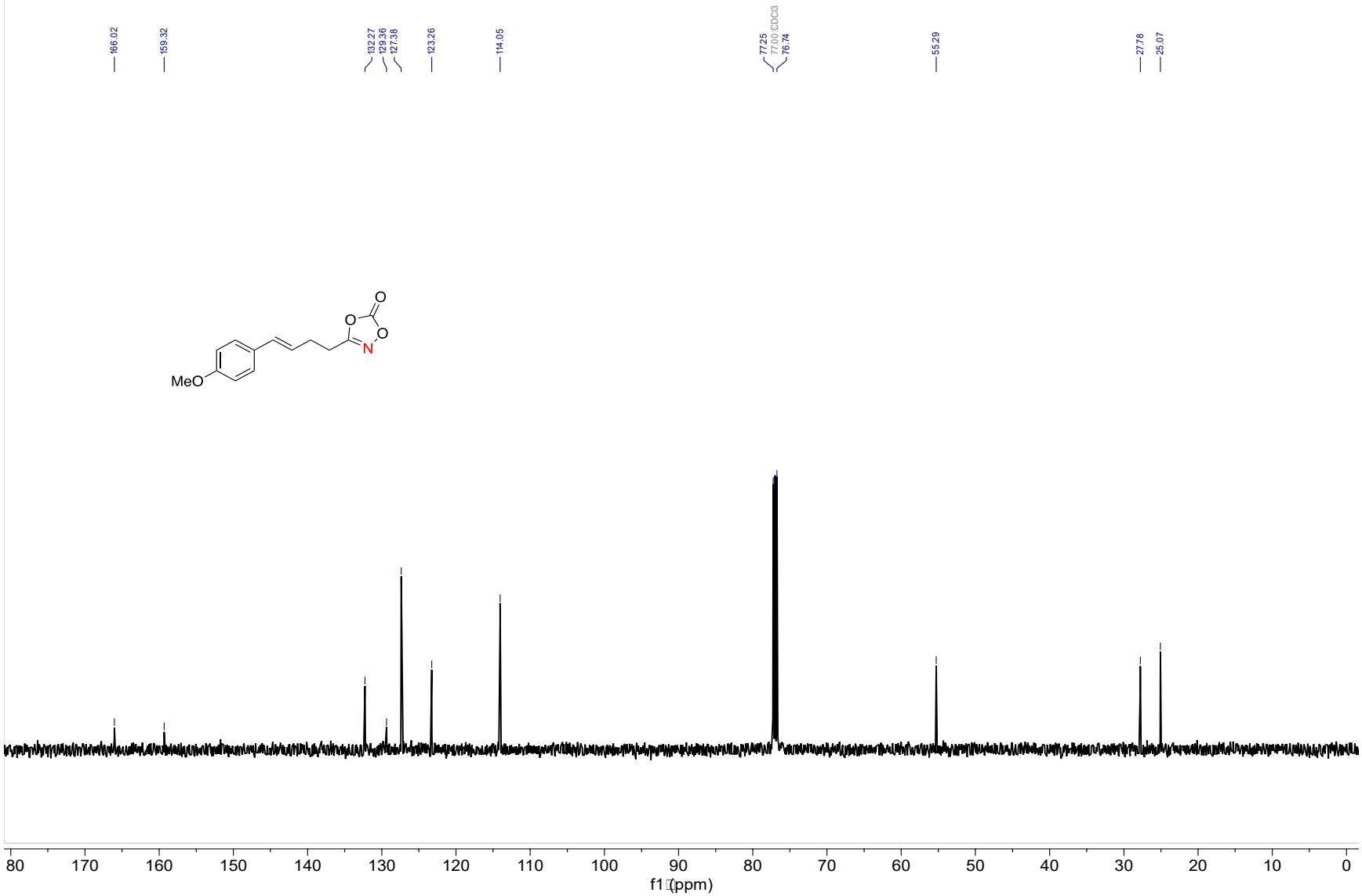
(E)-3-(4-(p-tolyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1d), ^{13}C NMR (100 MHz, $CDCl_3$):



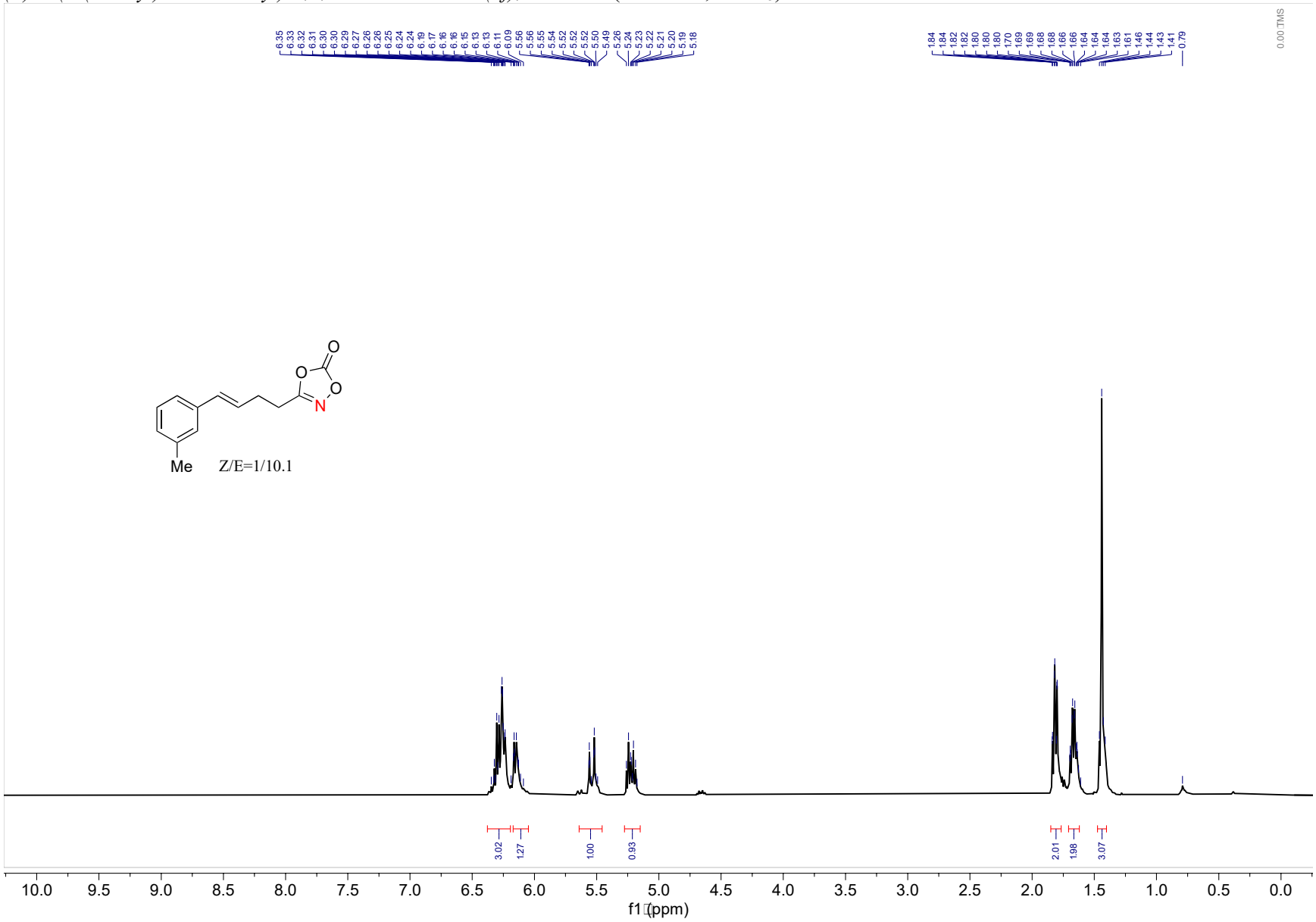
(E)-3-(4-(4-methoxyphenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1e), ^{1}H NMR (400 MHz, $CDCl_3$):



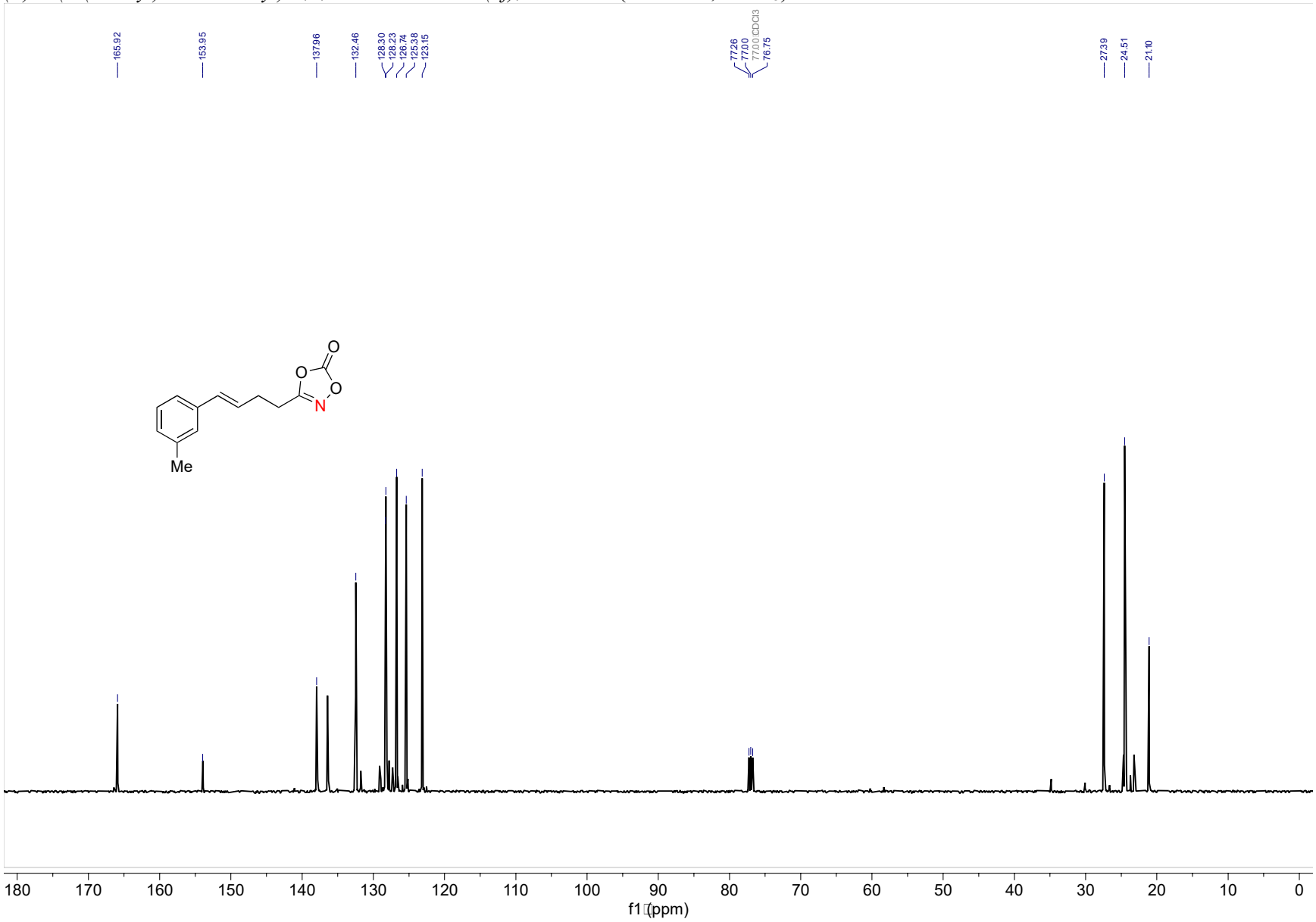
(E)-3-(4-(4-methoxyphenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1e), ^{13}C NMR (100 MHz, $CDCl_3$):



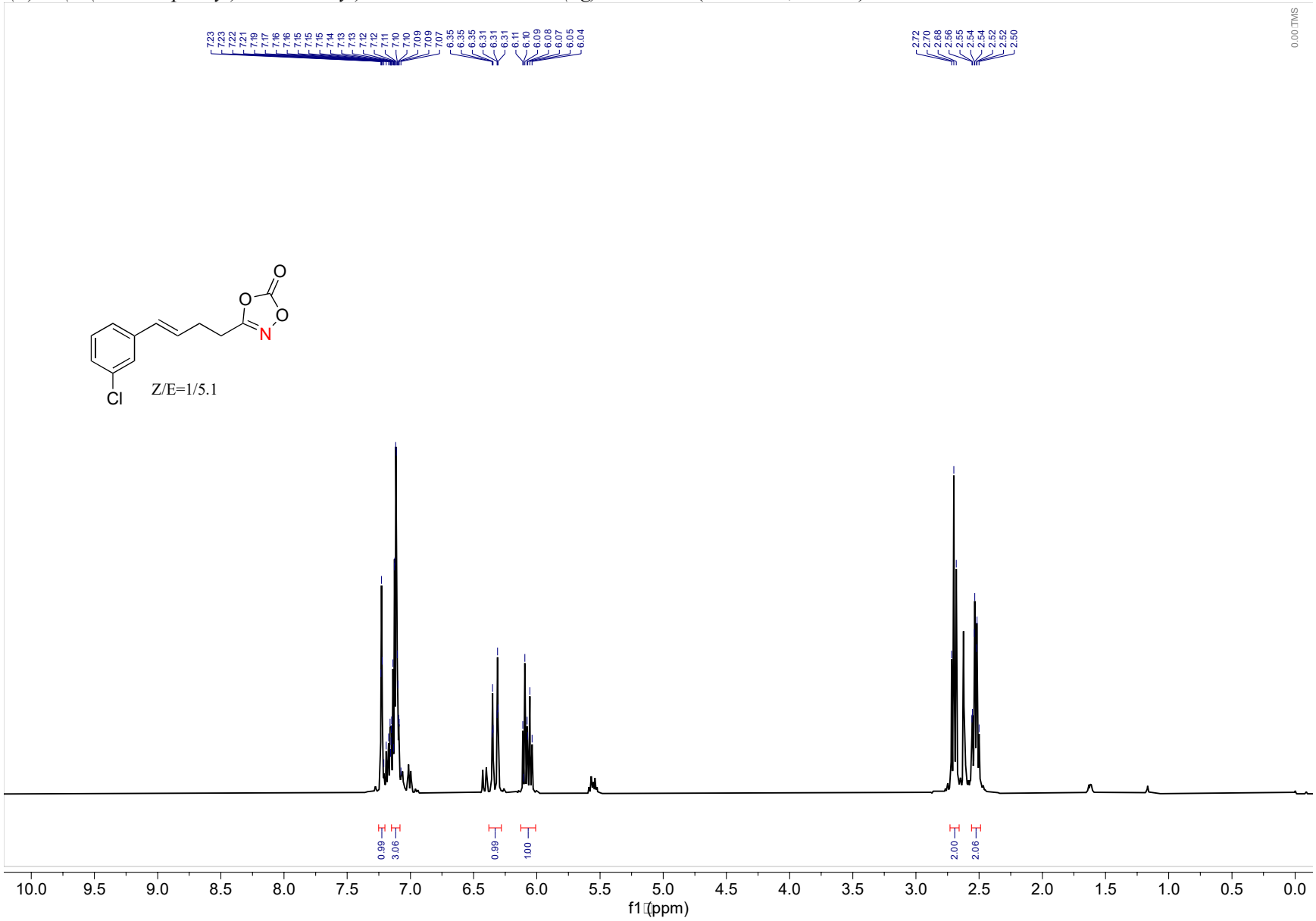
(E)-3-(4-(m-tolyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1f), ^{1}H NMR (400 MHz, $CDCl_3$):



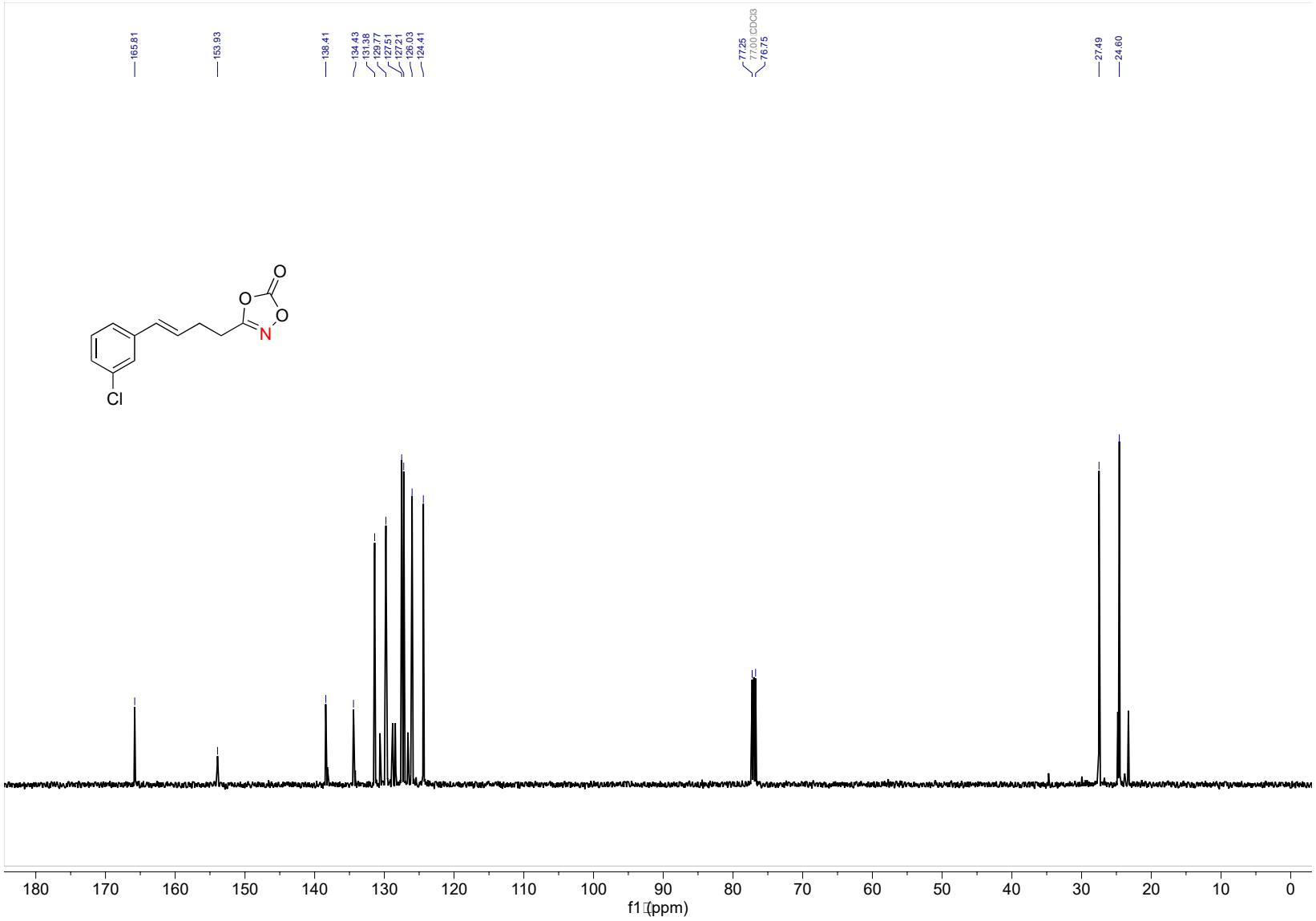
(E)-3-(4-(m-tolyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1f), ^{13}C NMR (100 MHz, $CDCl_3$):



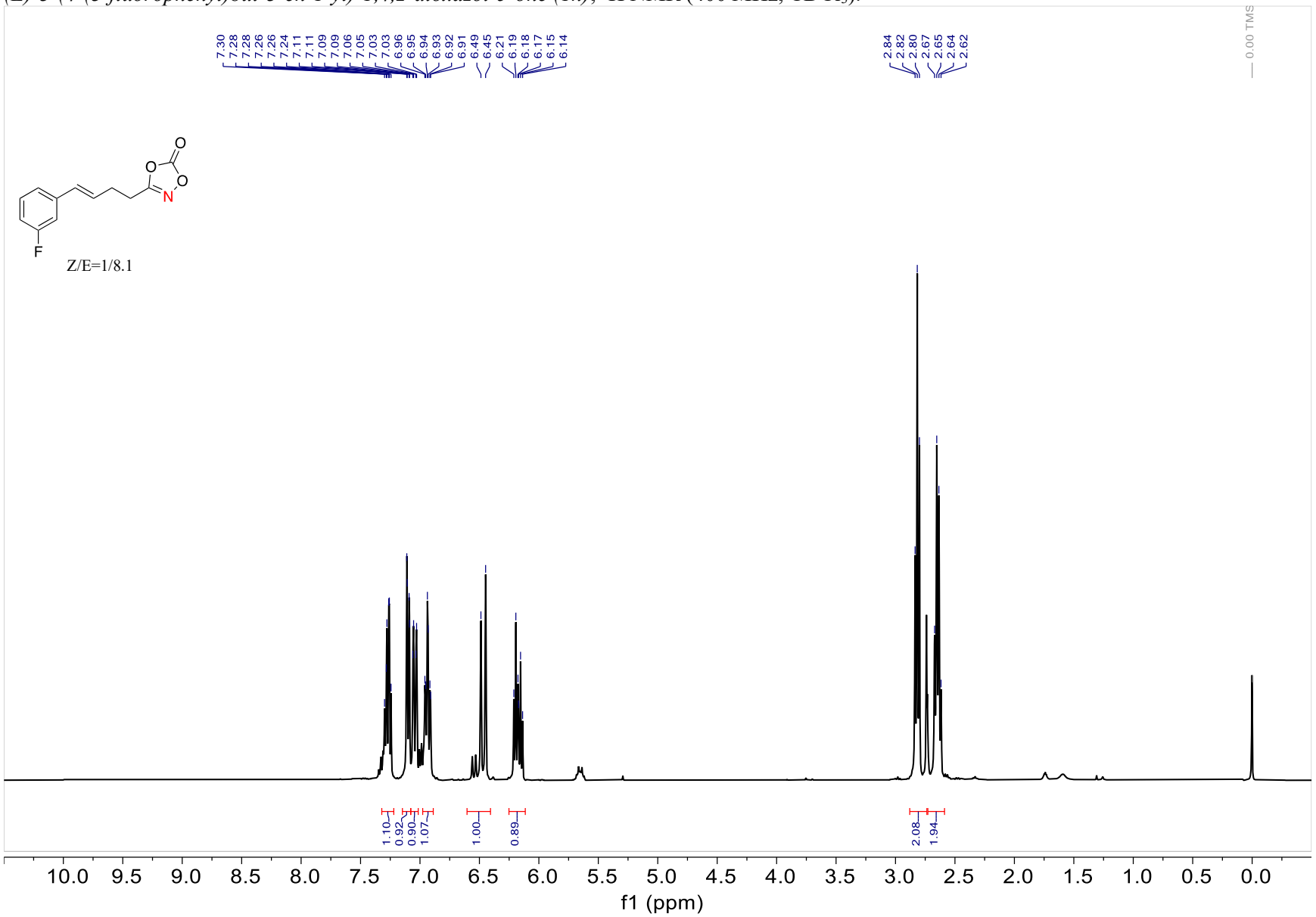
(E)-3-(4-(3-chlorophenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1g), ^{1}H NMR (400 MHz, $CDCl_3$):



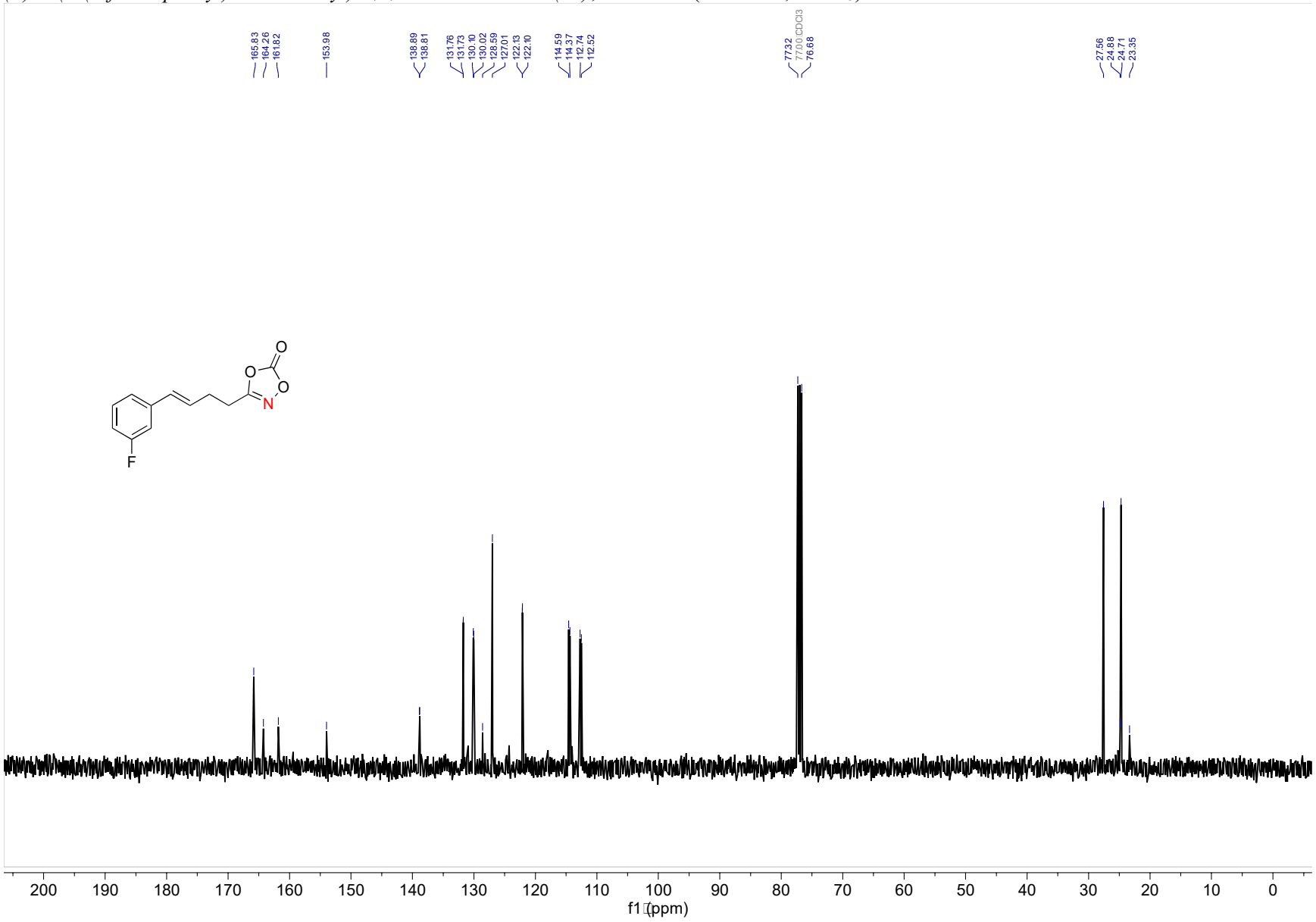
(E)-3-(4-(3-chlorophenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1g), ^{13}C NMR (100 MHz, $CDCl_3$):



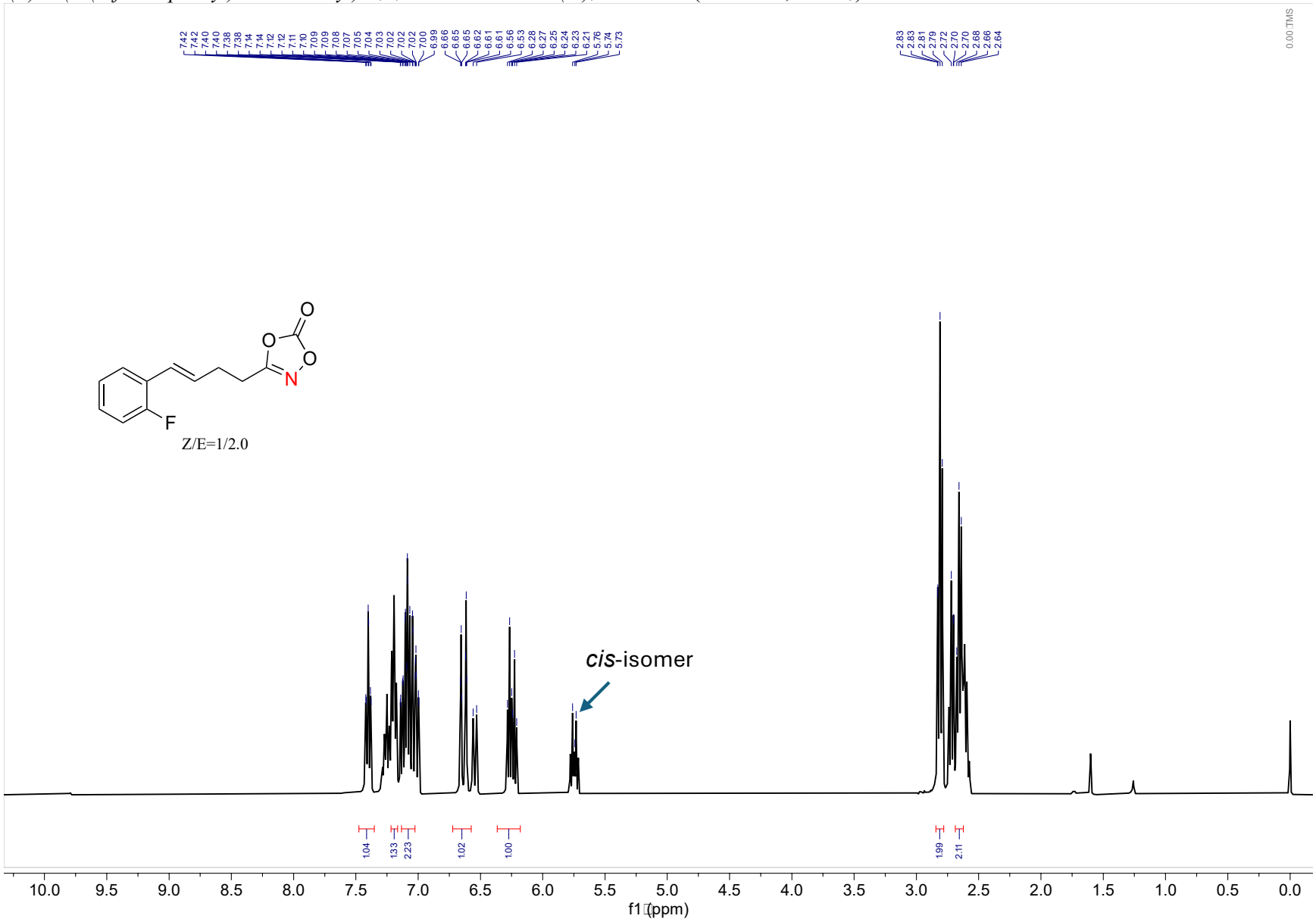
(E)-3-(4-(3-fluorophenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1h), ^{1}H NMR (400 MHz, $CDCl_3$):



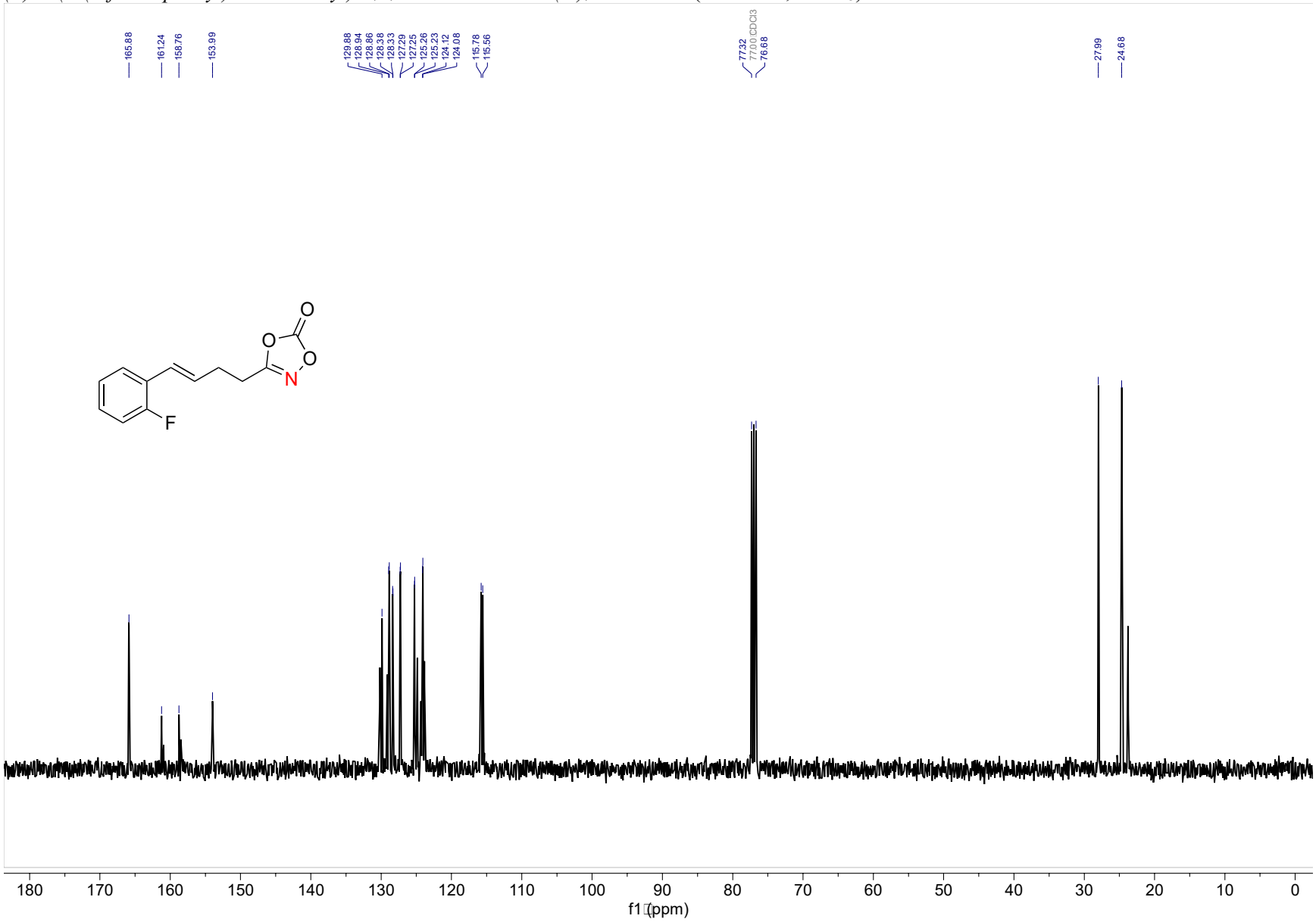
(E)-3-(4-(3-fluorophenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1h), ^{13}C NMR (400 MHz, $CDCl_3$):



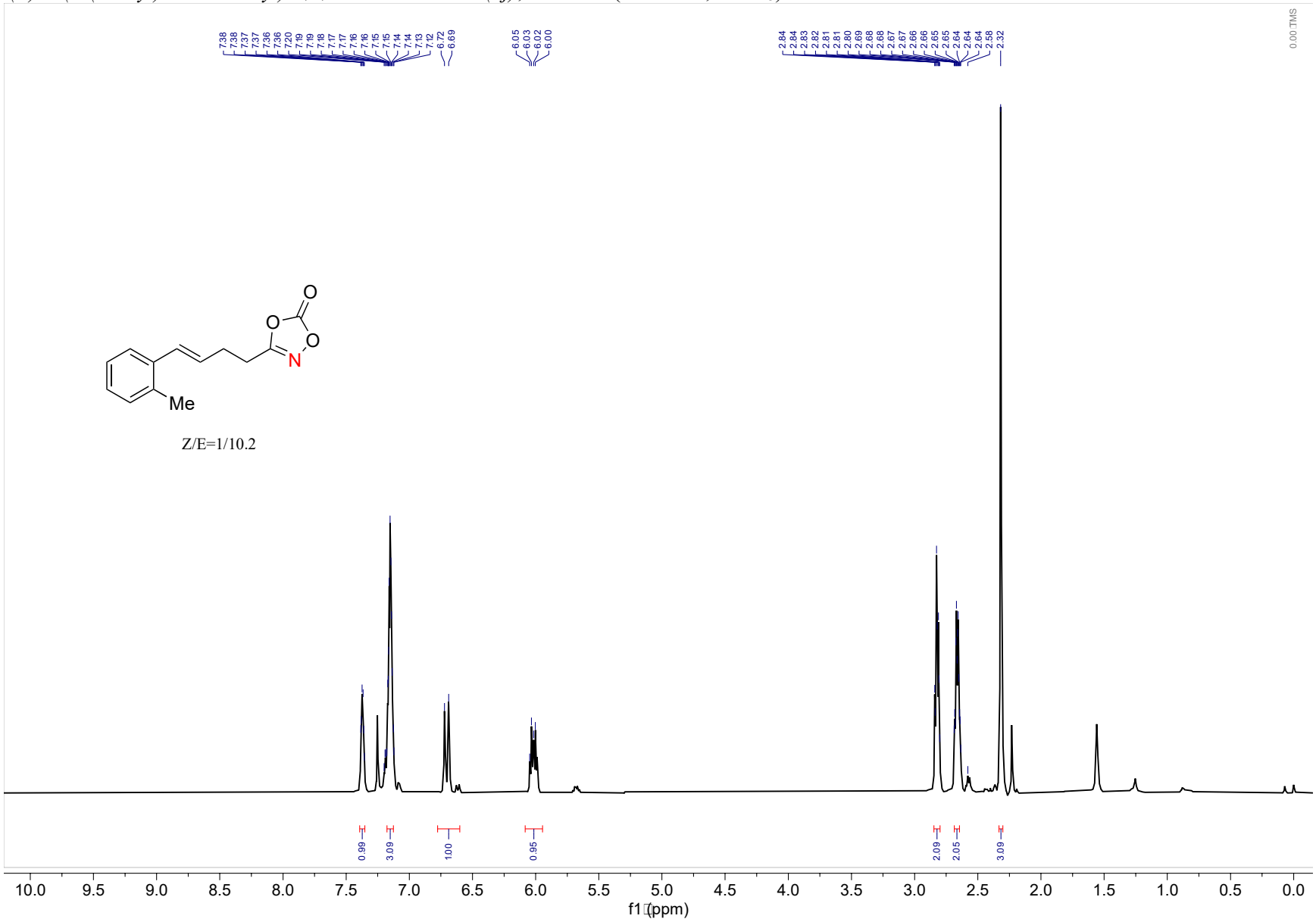
(E)-3-(4-(2-fluorophenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1i), ^{1}H NMR (400 MHz, $CDCl_3$):



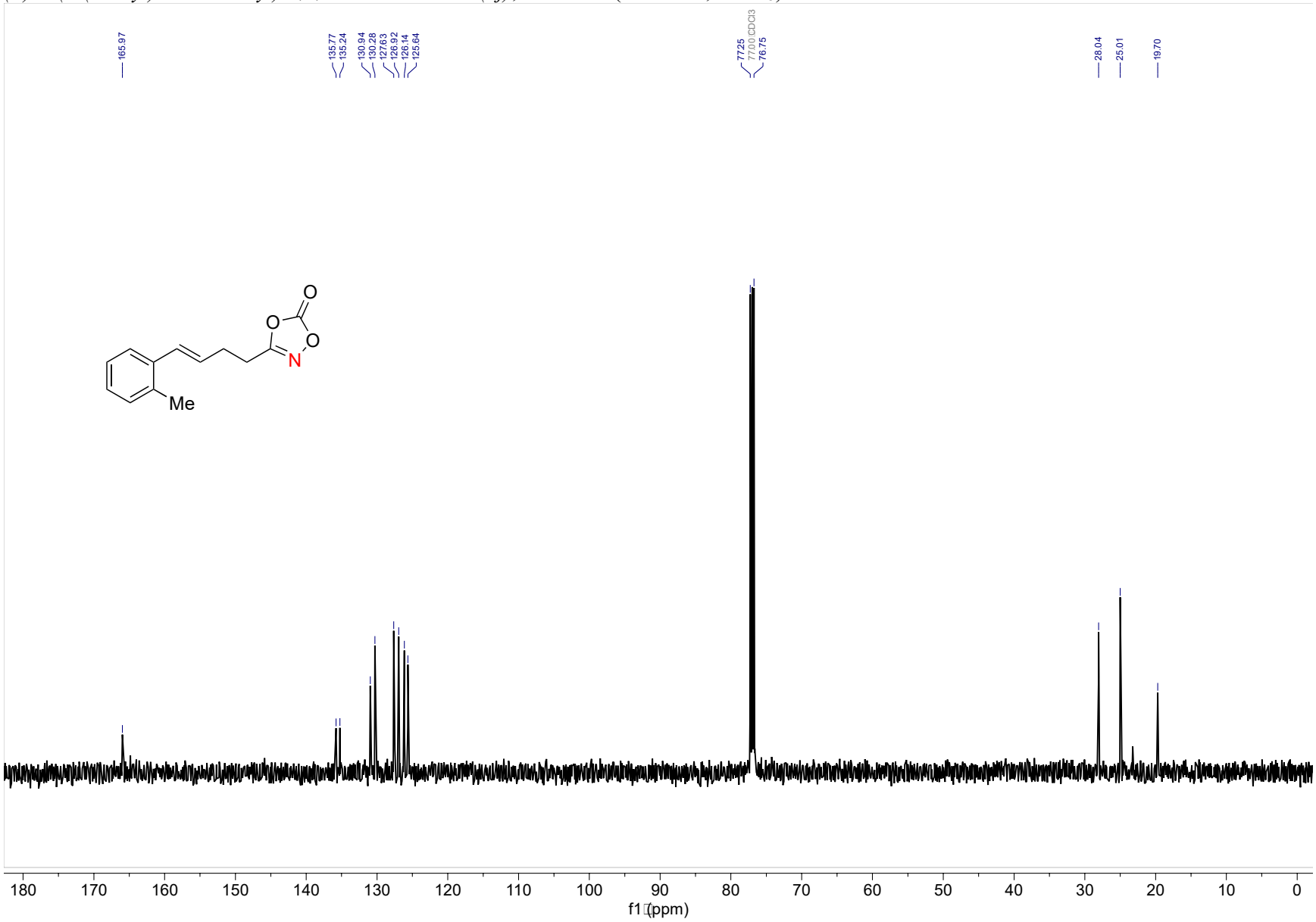
(E)-3-(4-(2-fluorophenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1i), ^{13}C NMR (100 MHz, $CDCl_3$):



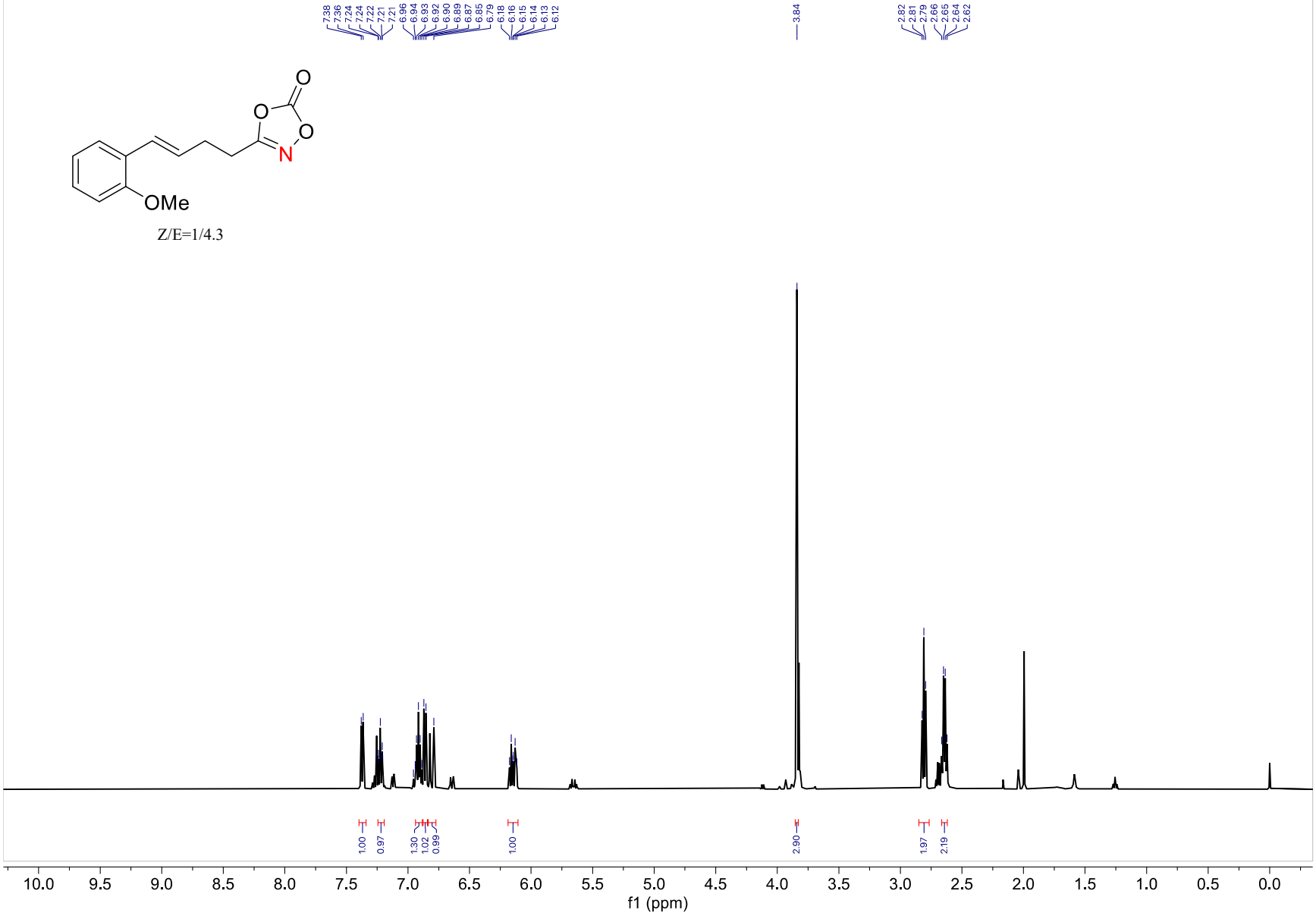
(E)-3-(4-(o-tolyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1j), ^{1}H NMR (500 MHz, $CDCl_3$):



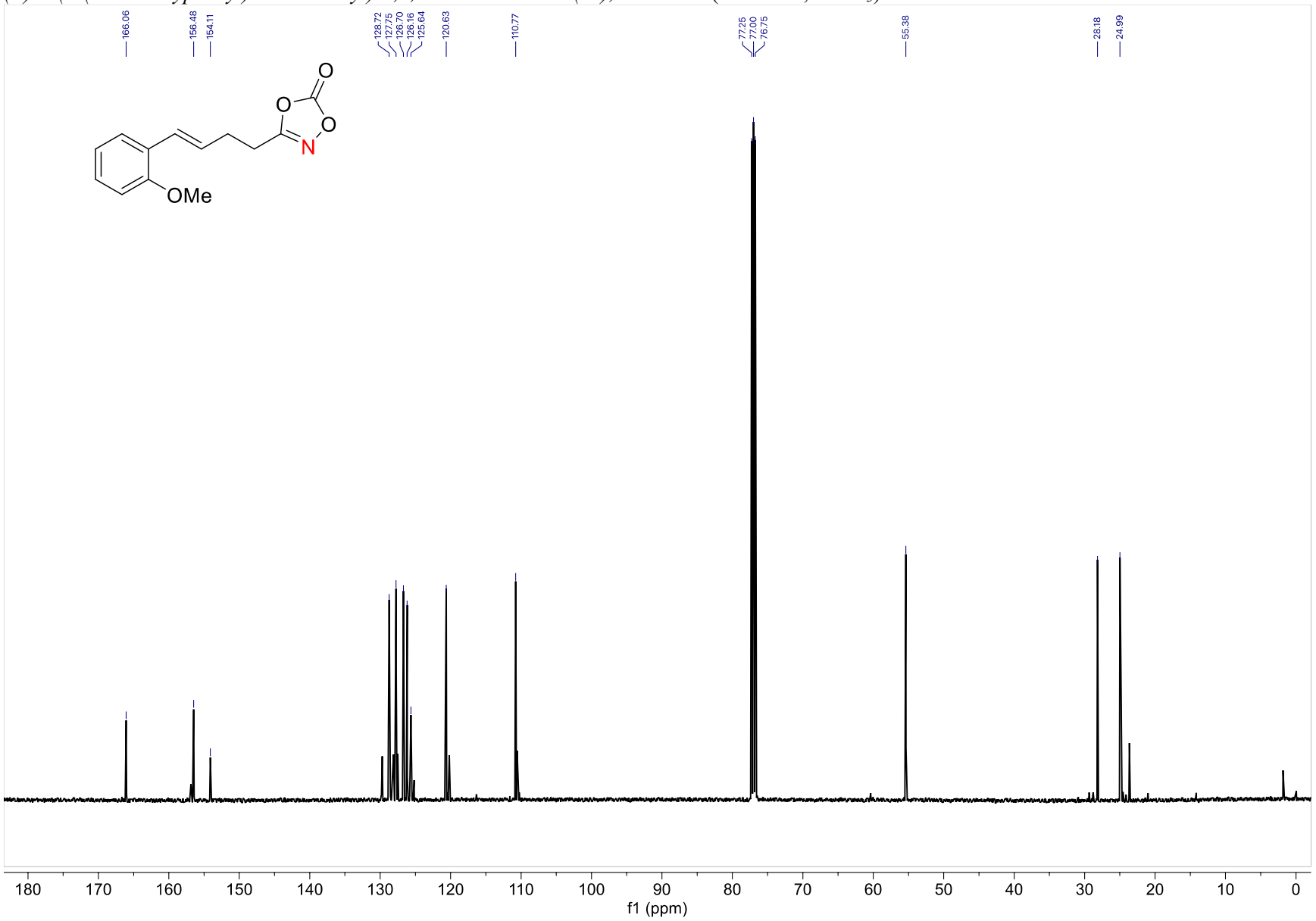
(E)-3-(4-(o-tolyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1j), ^{13}C NMR (126 MHz, $CDCl_3$):



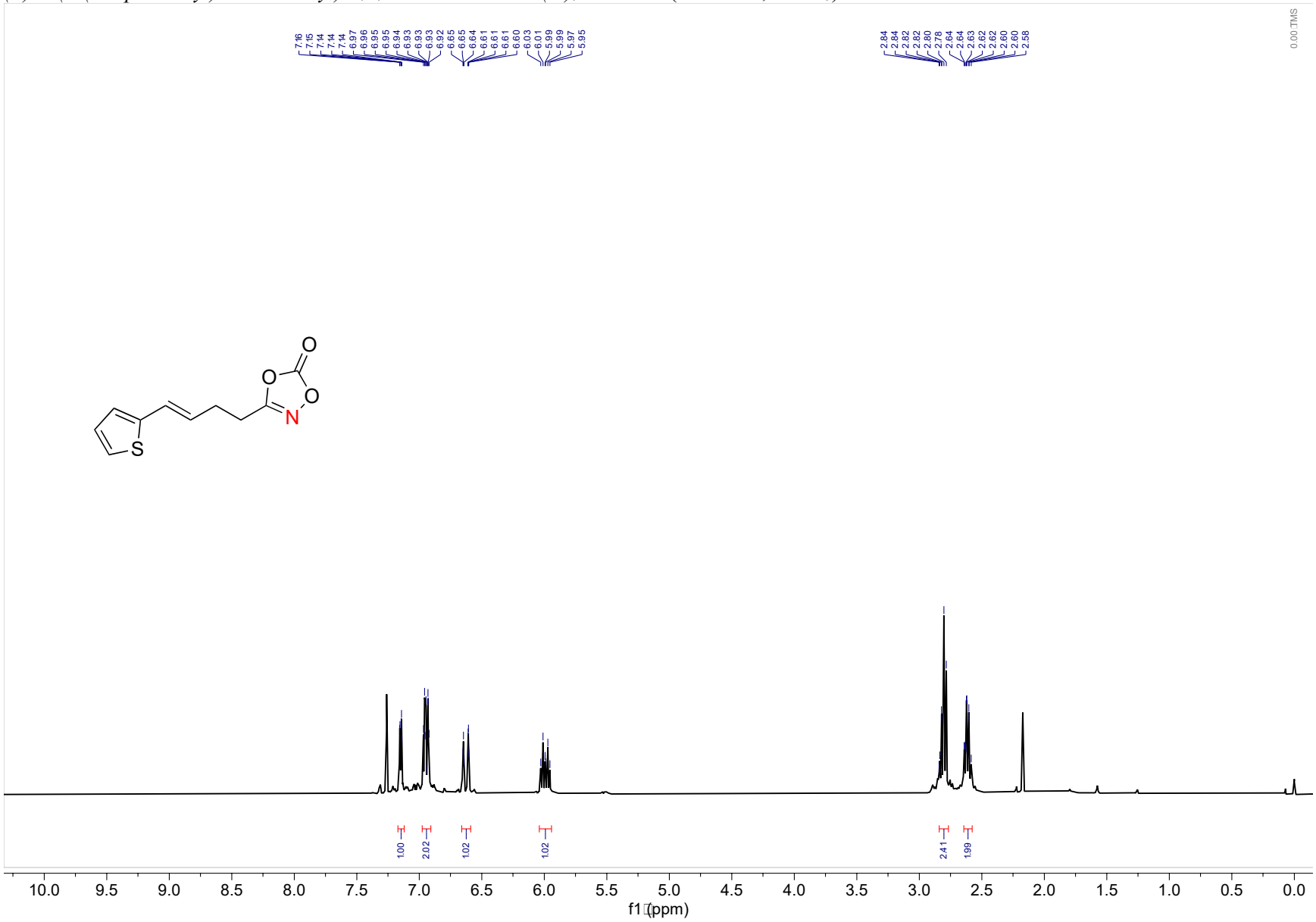
(E)-3-(4-(2-methoxyphenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1k), ^{1}H NMR (500 MHz, $CDCl_3$):



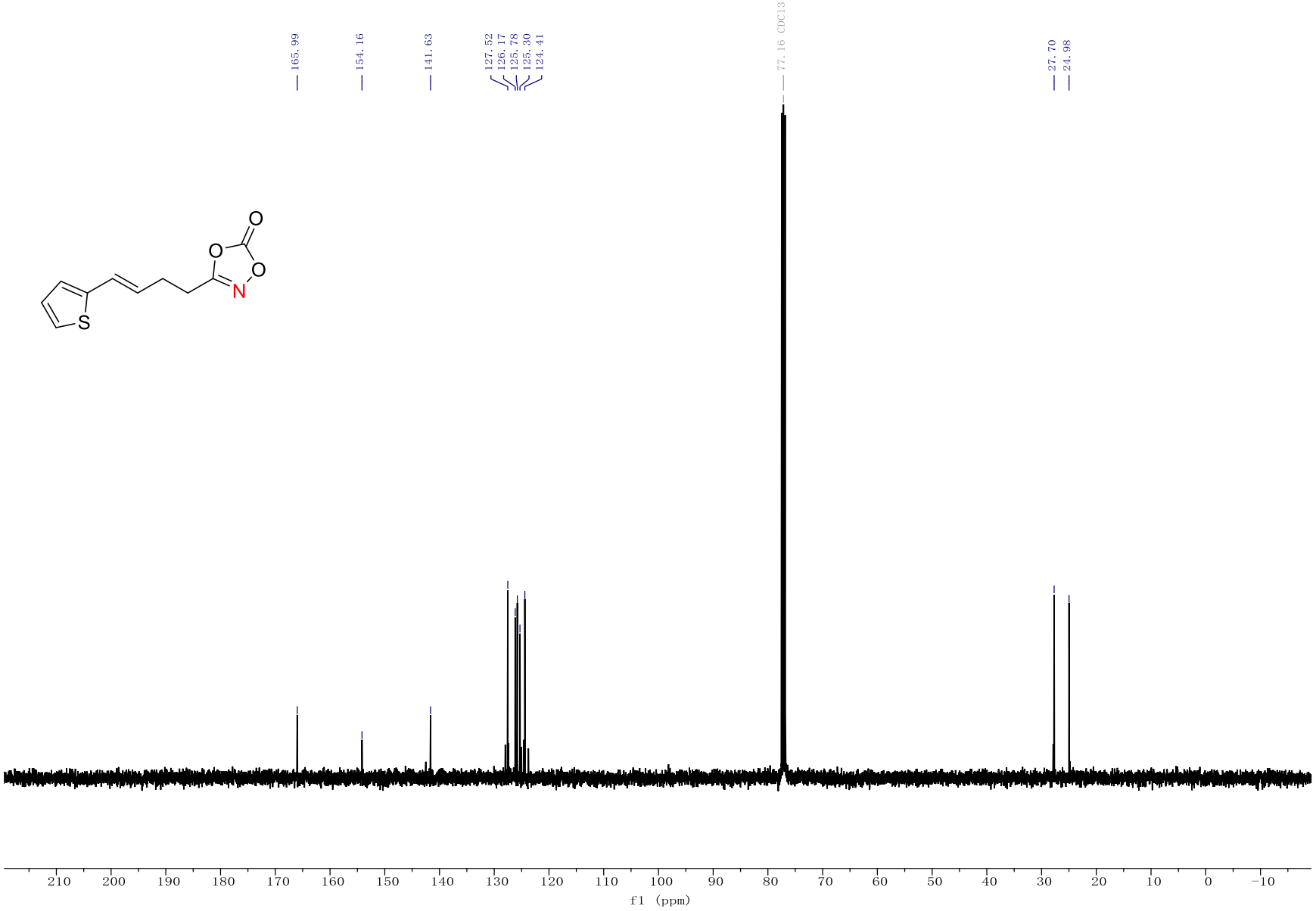
(E)-3-(4-(2-methoxyphenyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1k), ^{13}C NMR (126 MHz, $CDCl_3$):



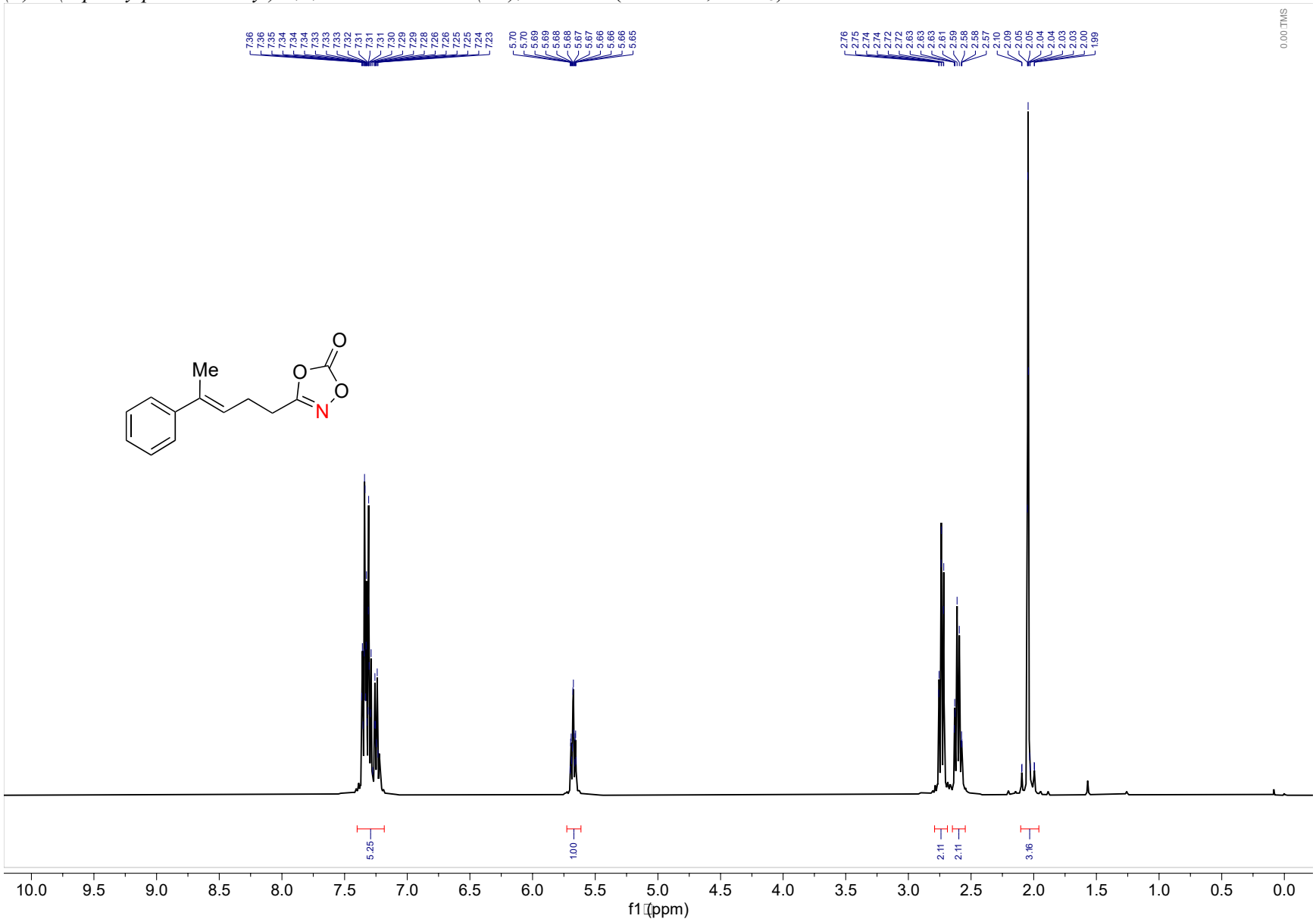
(E)-3-(4-(thiophen-2-yl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1l), ^{1}H NMR (400 MHz, $CDCl_3$):



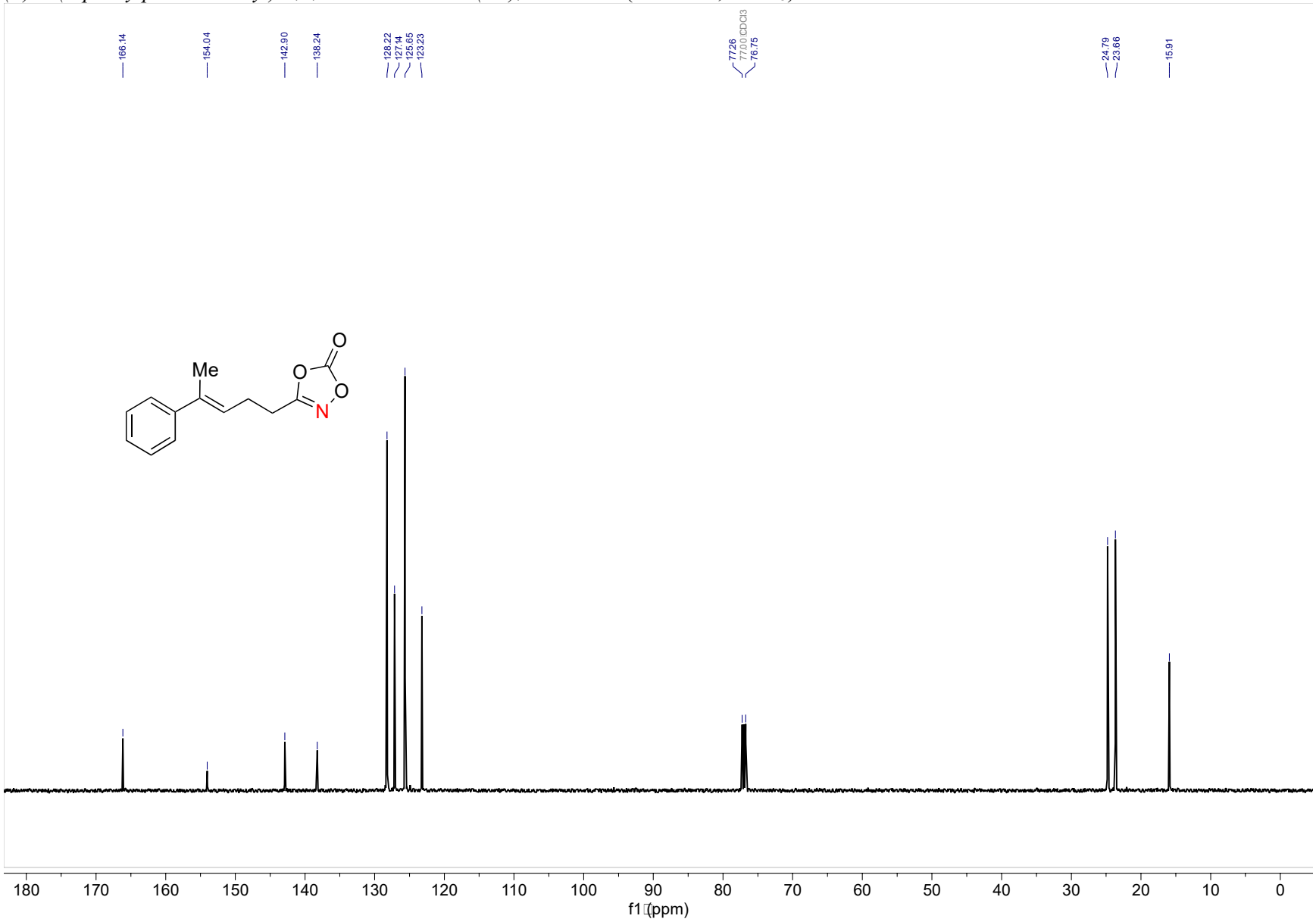
(E)-3-(4-(thiophen-2-yl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (1l), ^{13}C NMR (100 MHz, $CDCl_3$):



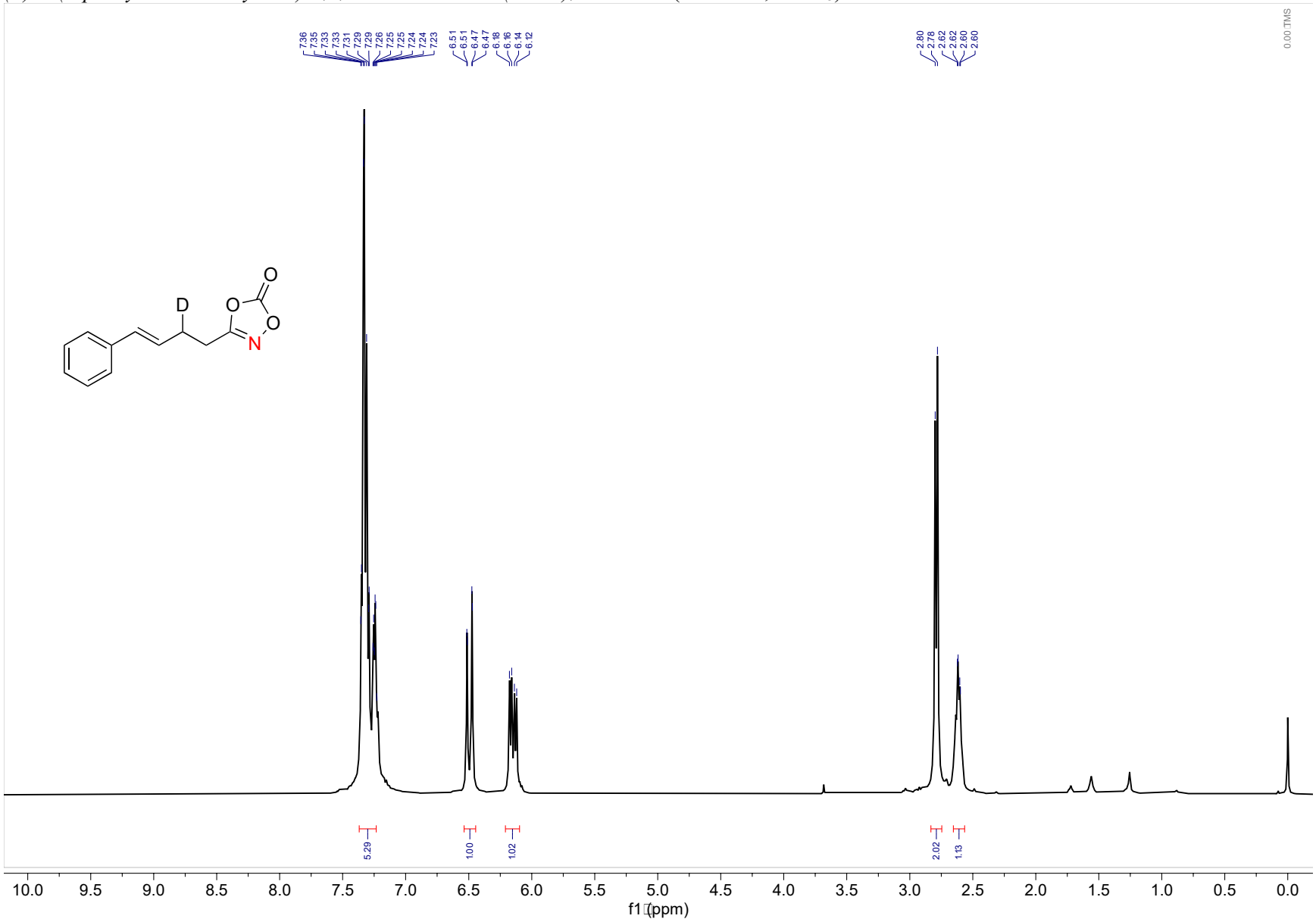
(E)-3-(4-phenylpent-3-en-1-yl)-1,4,2-dioxazol-5-one (1m), ^{1}H NMR (400 MHz, $CDCl_3$):



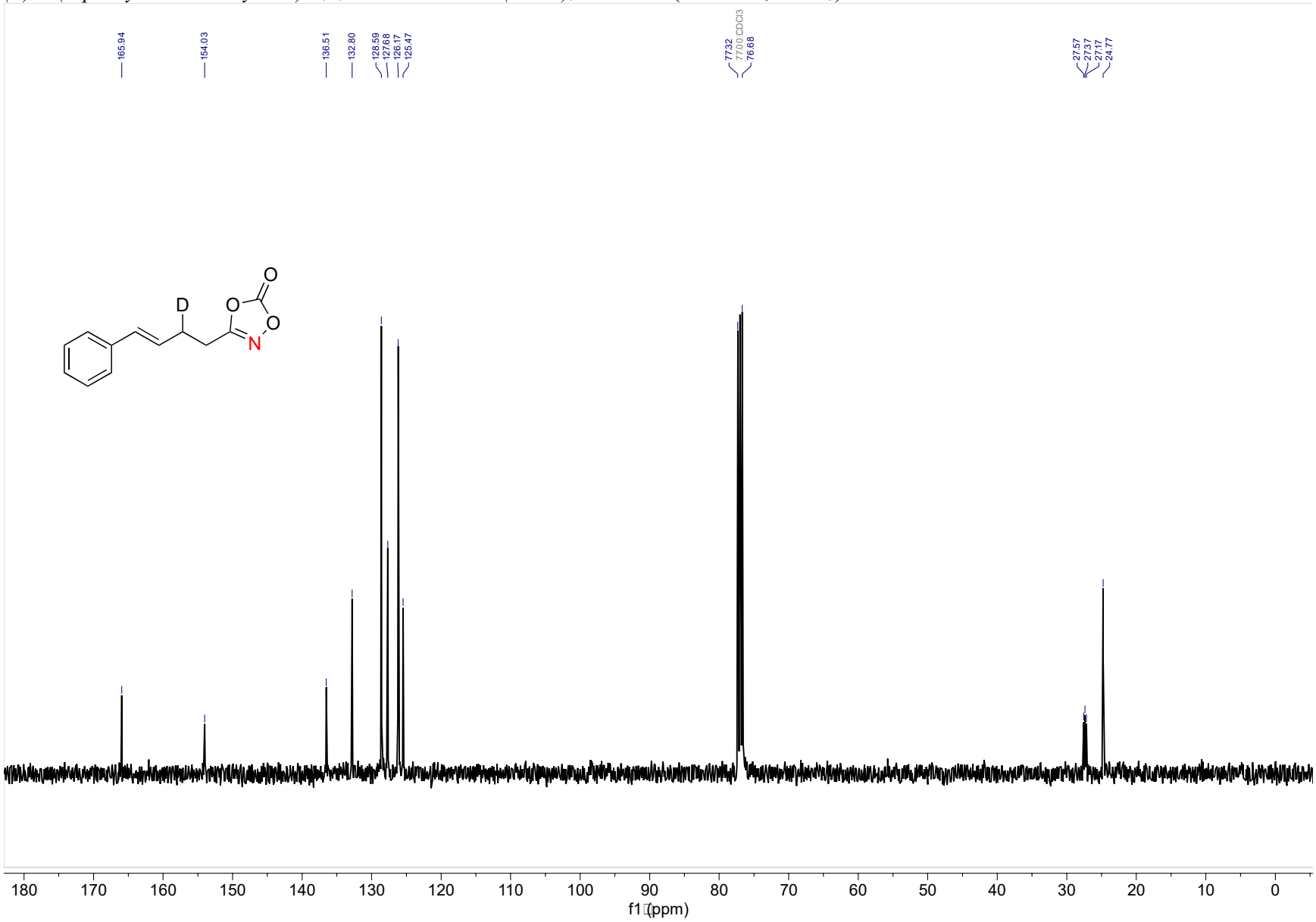
(E)-3-(4-phenylpent-3-en-1-yl)-1,4,2-dioxazol-5-one (1m), ^{13}C NMR (100 MHz, $CDCl_3$):



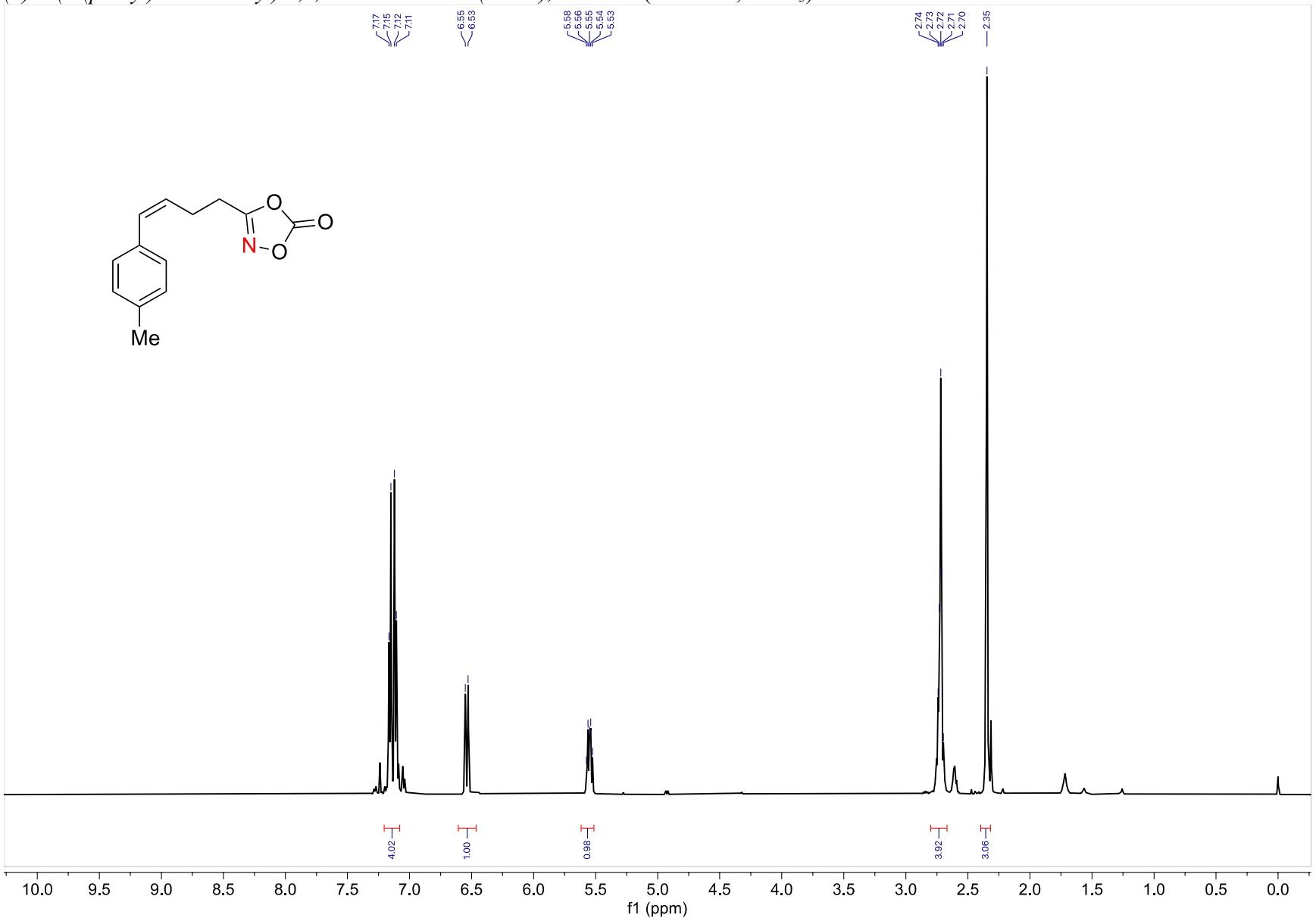
(E)-3-(4-phenylbut-3-en-1-yl-2-d)-1,4,2-dioxazol-5-one (1a-D$_1$), ^{1}H NMR (400 MHz, $CDCl_3$):



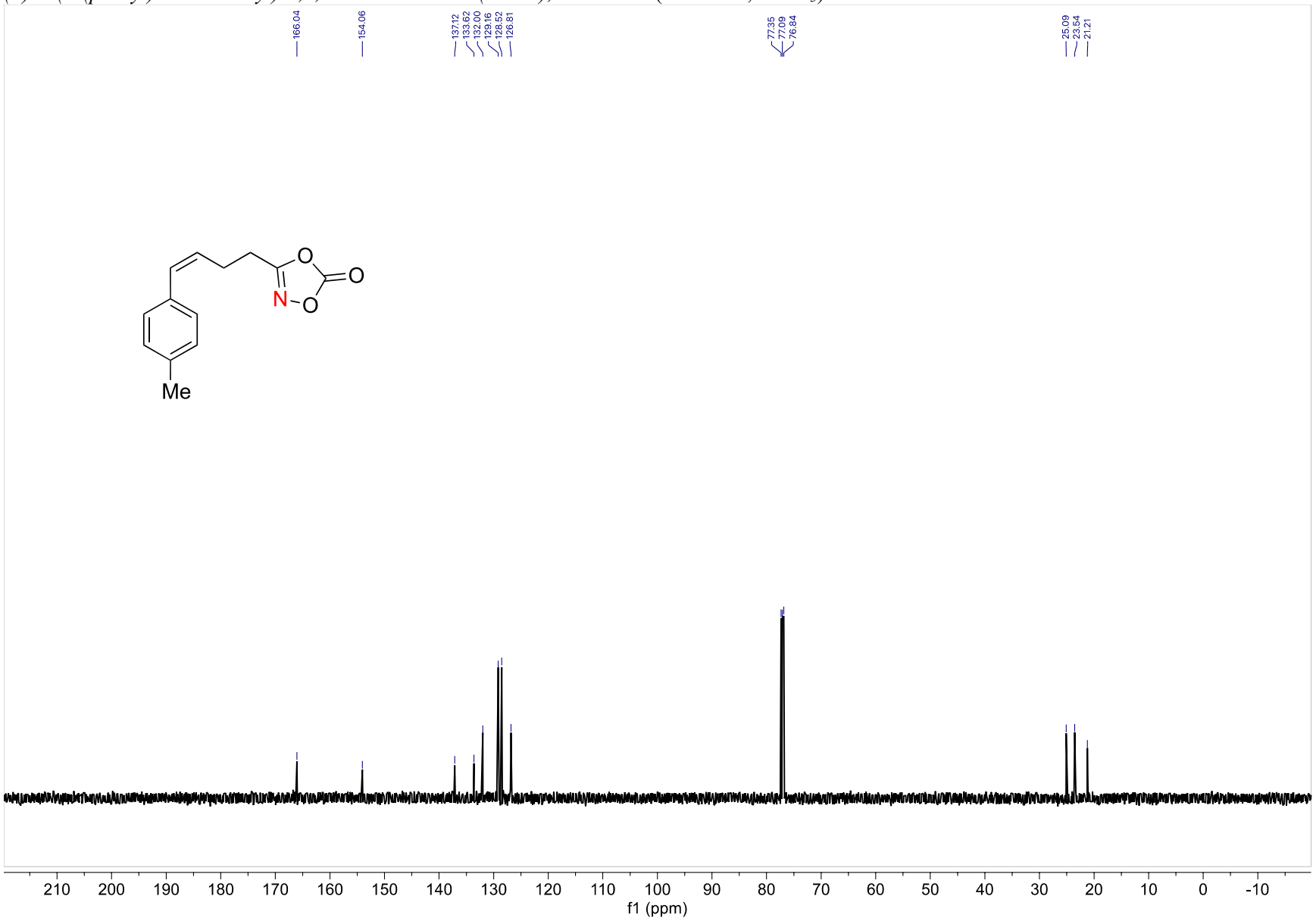
(E)-3-(4-phenylbut-3-en-1-yl-2-d)-1,4,2-dioxazol-5-one (1a-D_1), ^{13}C NMR (100 MHz, $CDCl_3$):



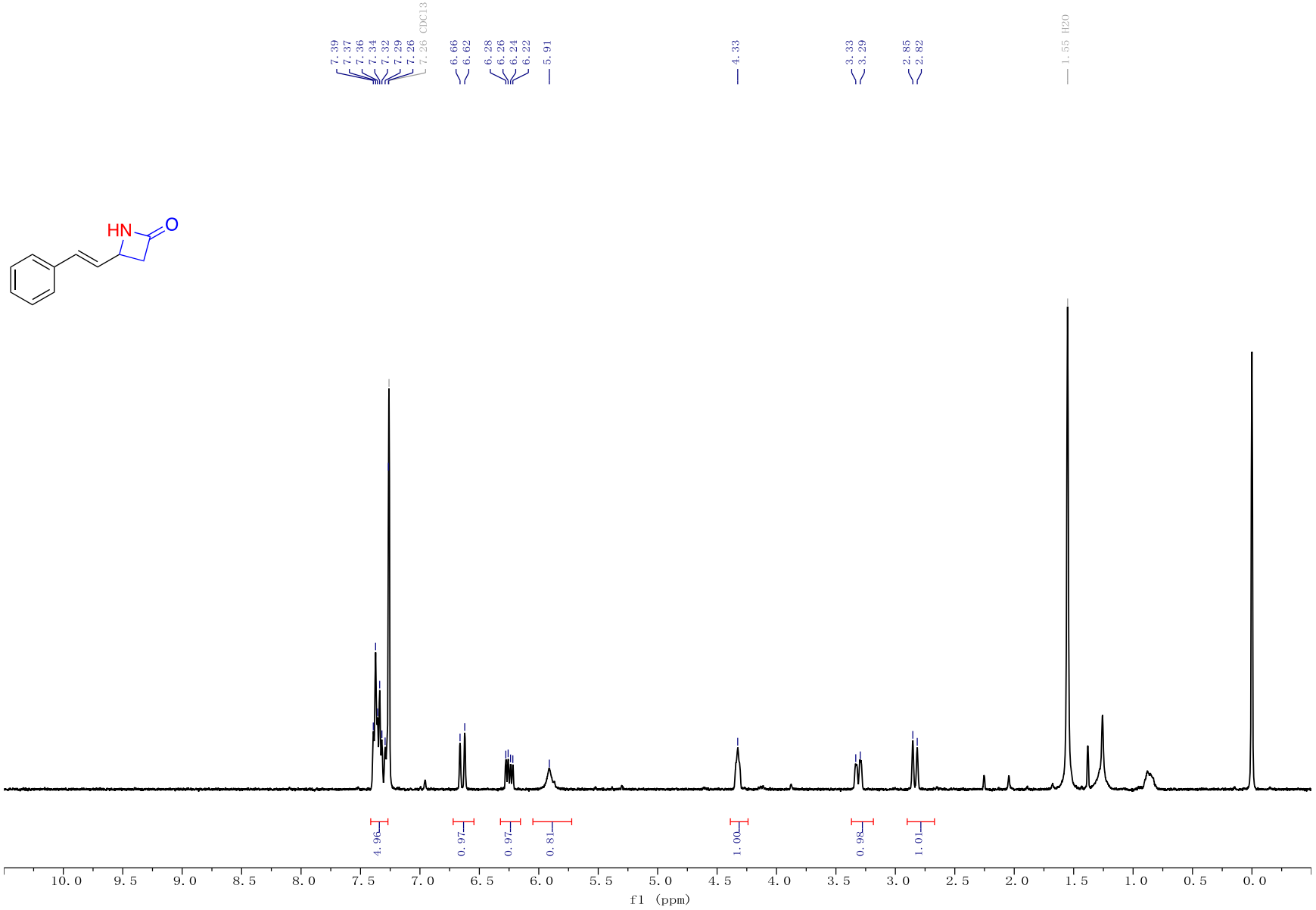
(Z)-3-(4-(p-tolyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (cis-1d), ^{1}H NMR (400 MHz, $CDCl_3$):



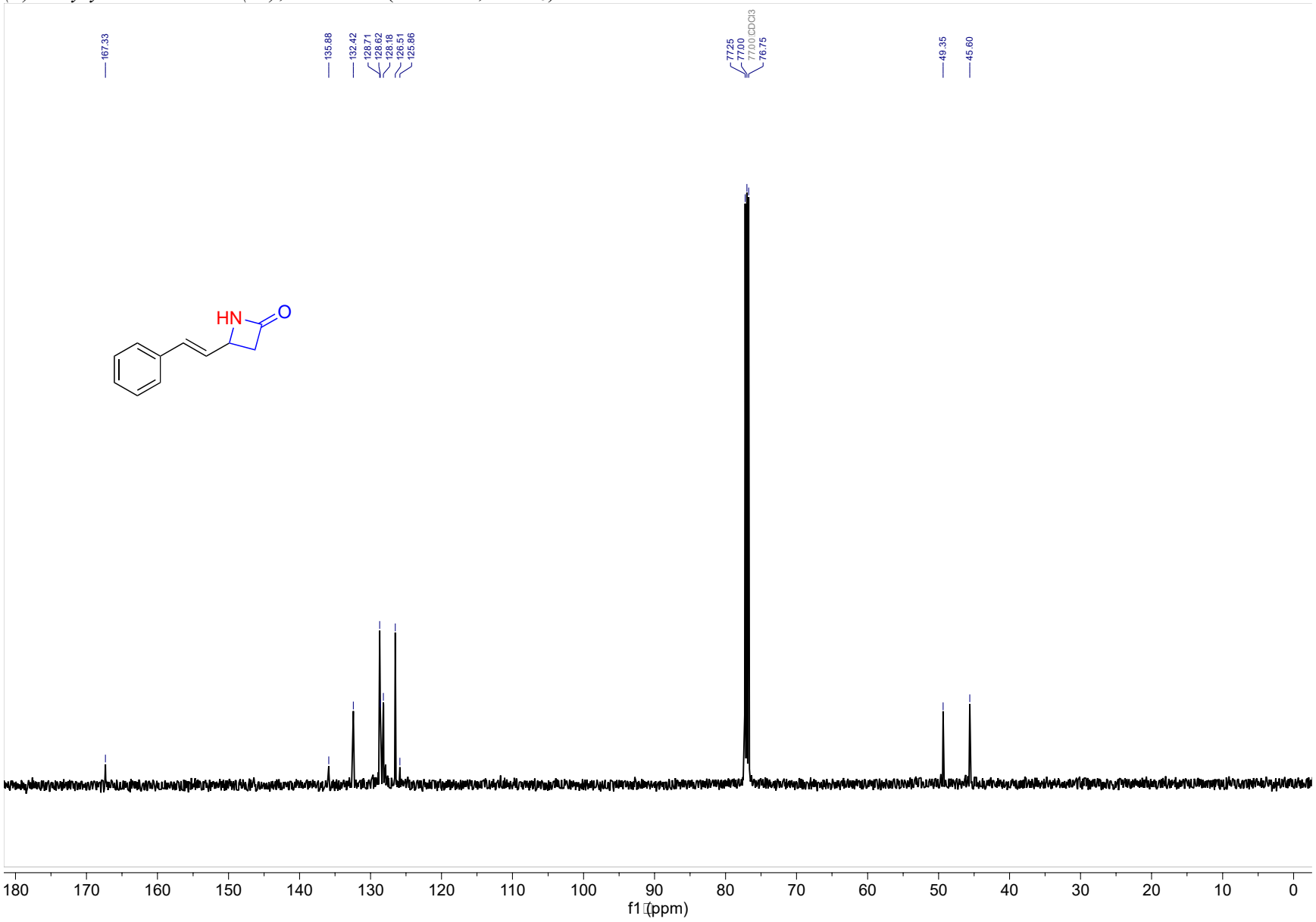
(Z)-3-(4-(p-tolyl)but-3-en-1-yl)-1,4,2-dioxazol-5-one (cis-1d), ^{13}C NMR (400 MHz, $CDCl_3$):



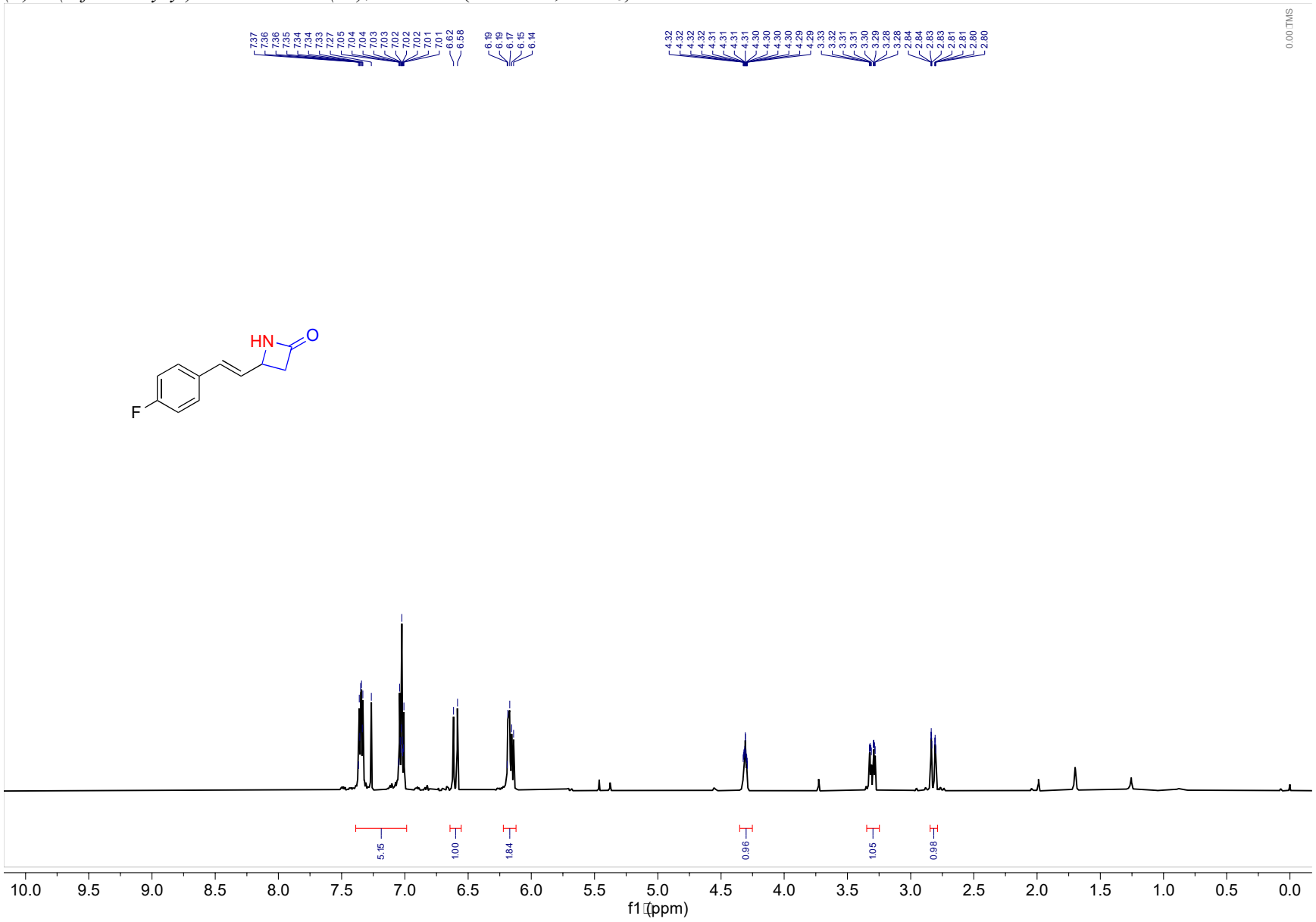
(E)-4-styrylazetidin-2-one (2a), ^{1}H NMR (400 MHz, $CDCl_3$):



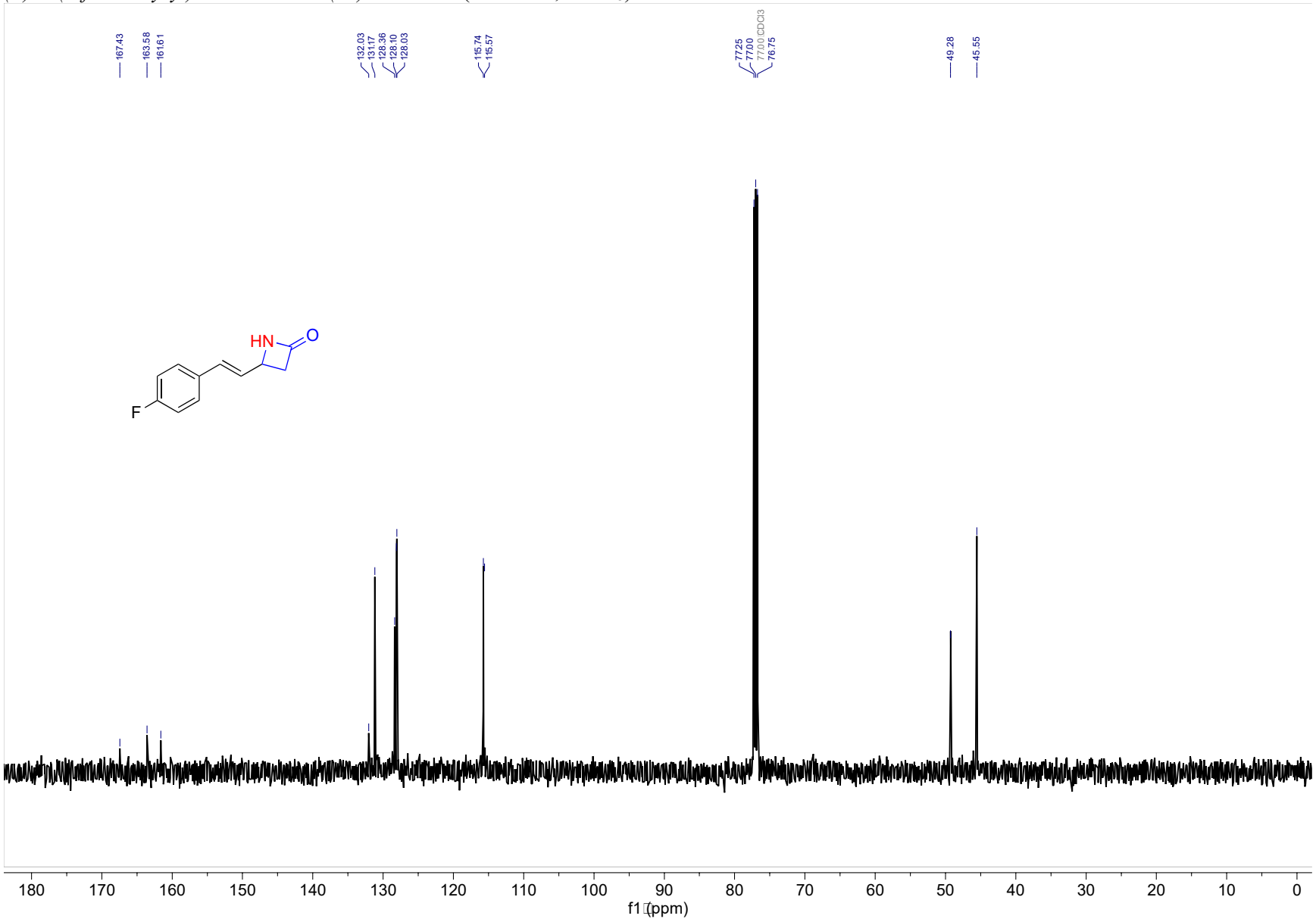
(E)-4-styrylazetidin-2-one (2a), ^{13}C NMR (126 MHz, $CDCl_3$):



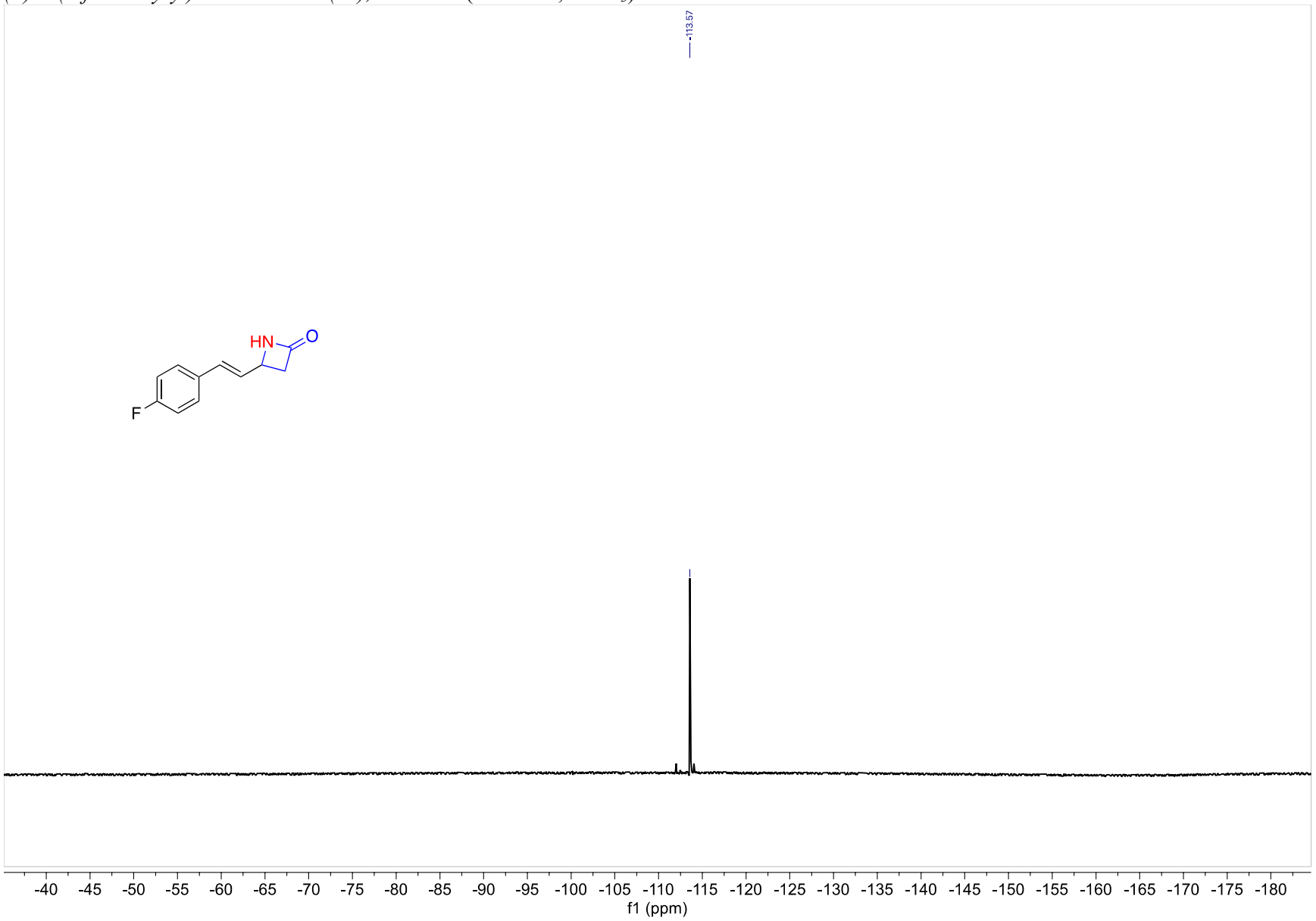
(E)-4-(4-fluorostyryl)azetidin-2-one (2b), ^{1}H NMR (500 MHz, $CDCl_3$):



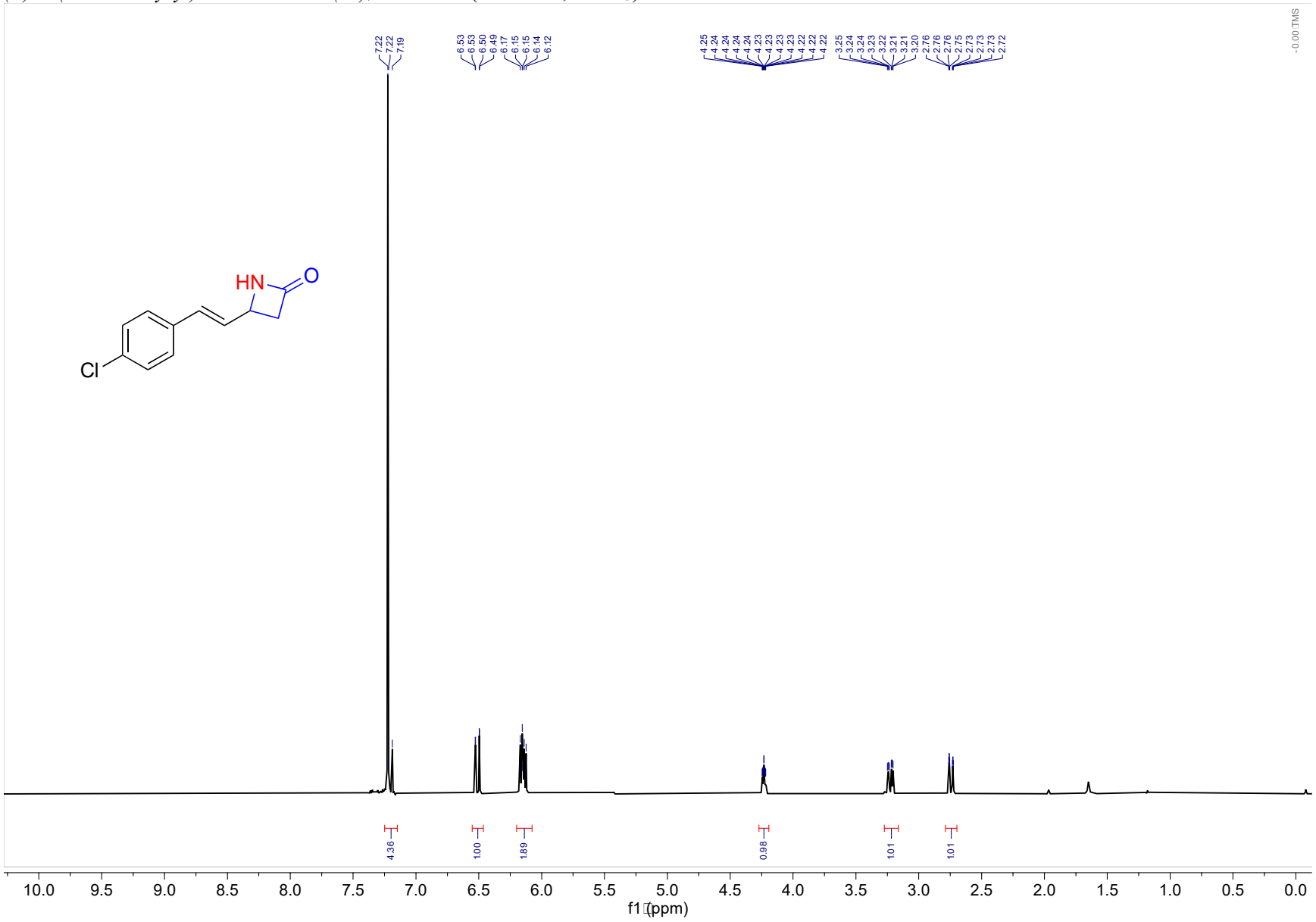
(E)-4-(4-fluorostyryl)azetidin-2-one (2b) ^{13}C NMR (126 MHz, $CDCl_3$):



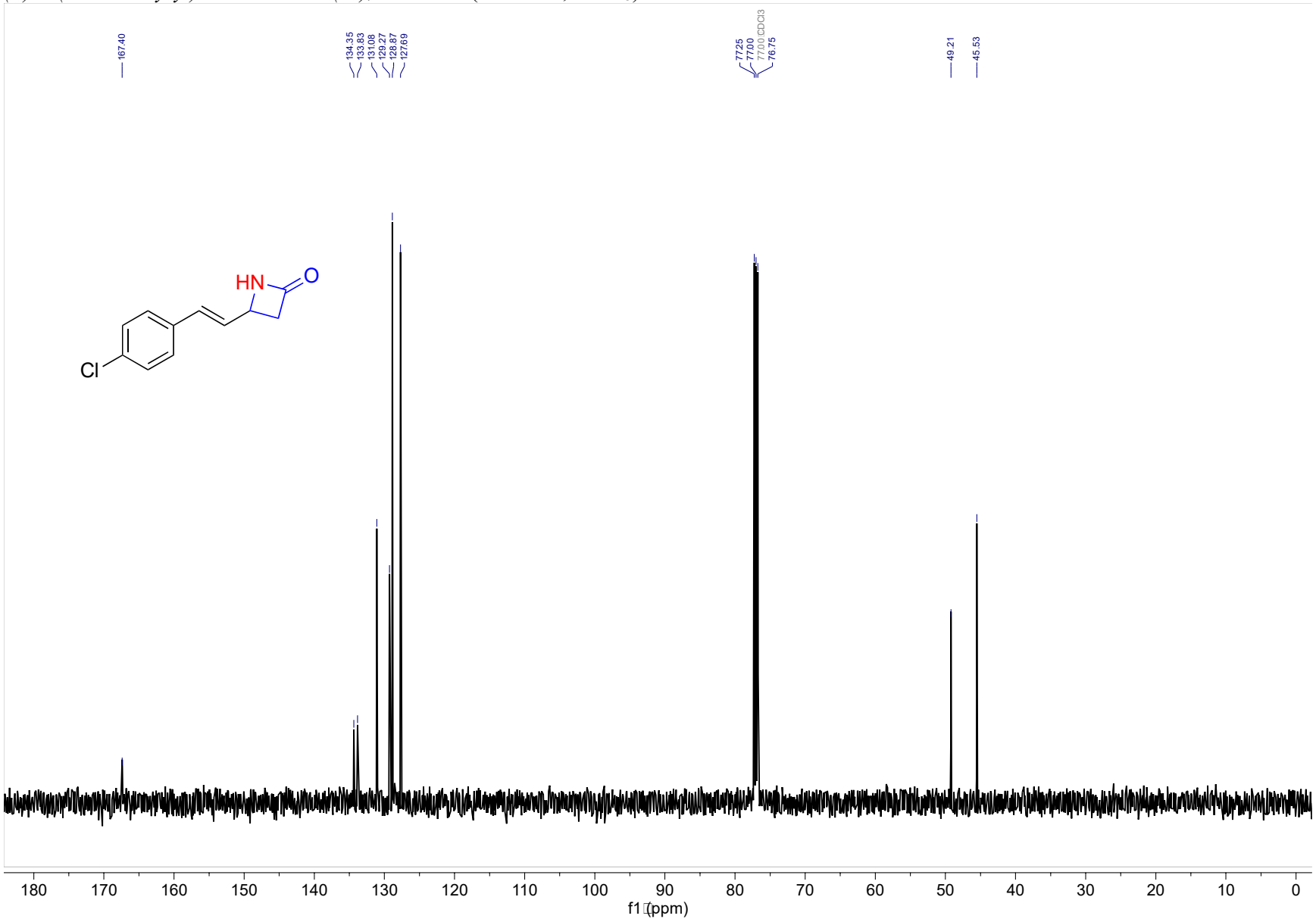
(E)-4-(4-fluorostyryl)azetidin-2-one (2b), ^{19}F NMR (376 MHz, $CDCl_3$):



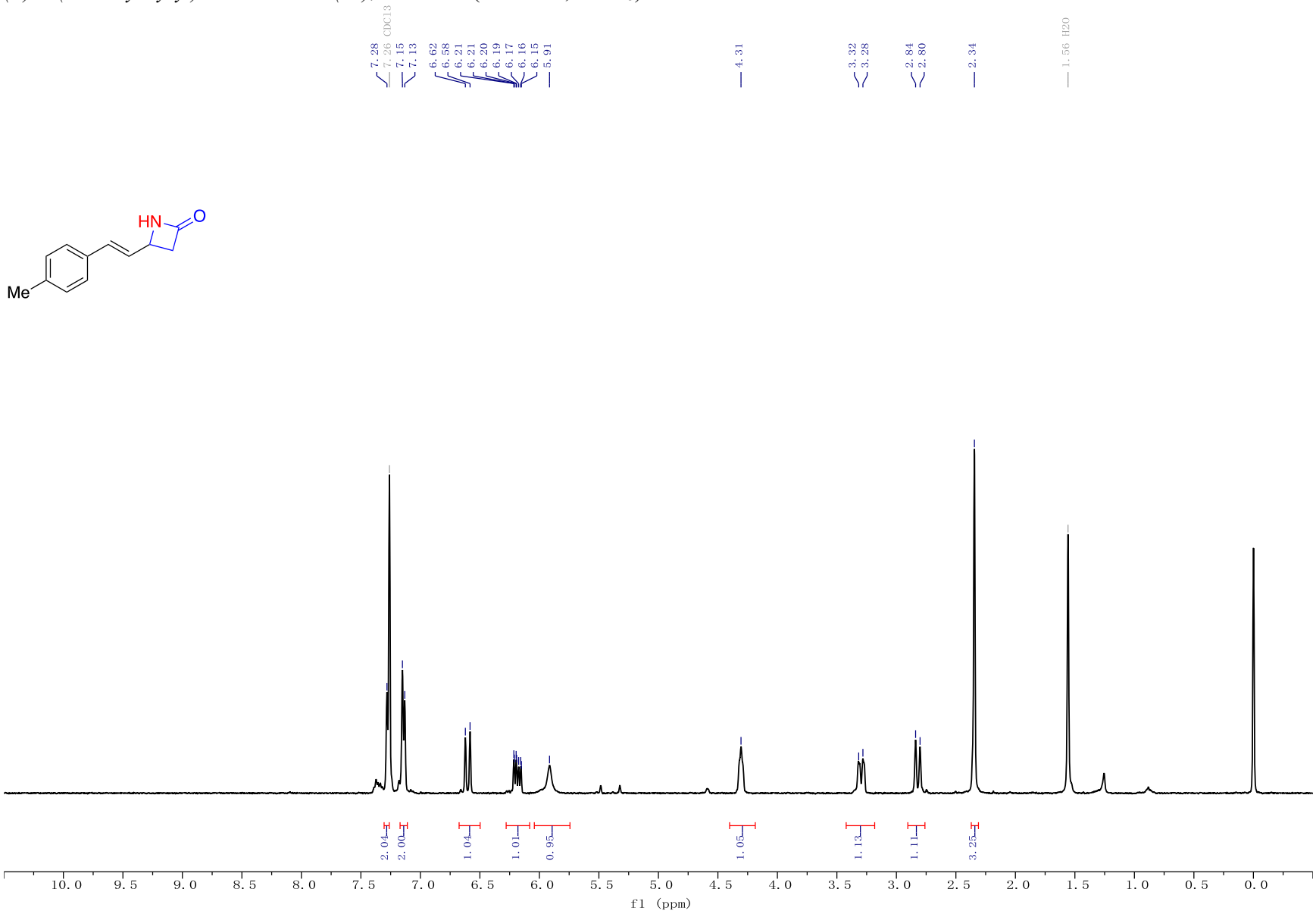
(E)-4-(4-chlorostyryl)azetidin-2-one (2c), ^{1}H NMR (500 MHz, $CDCl_3$):



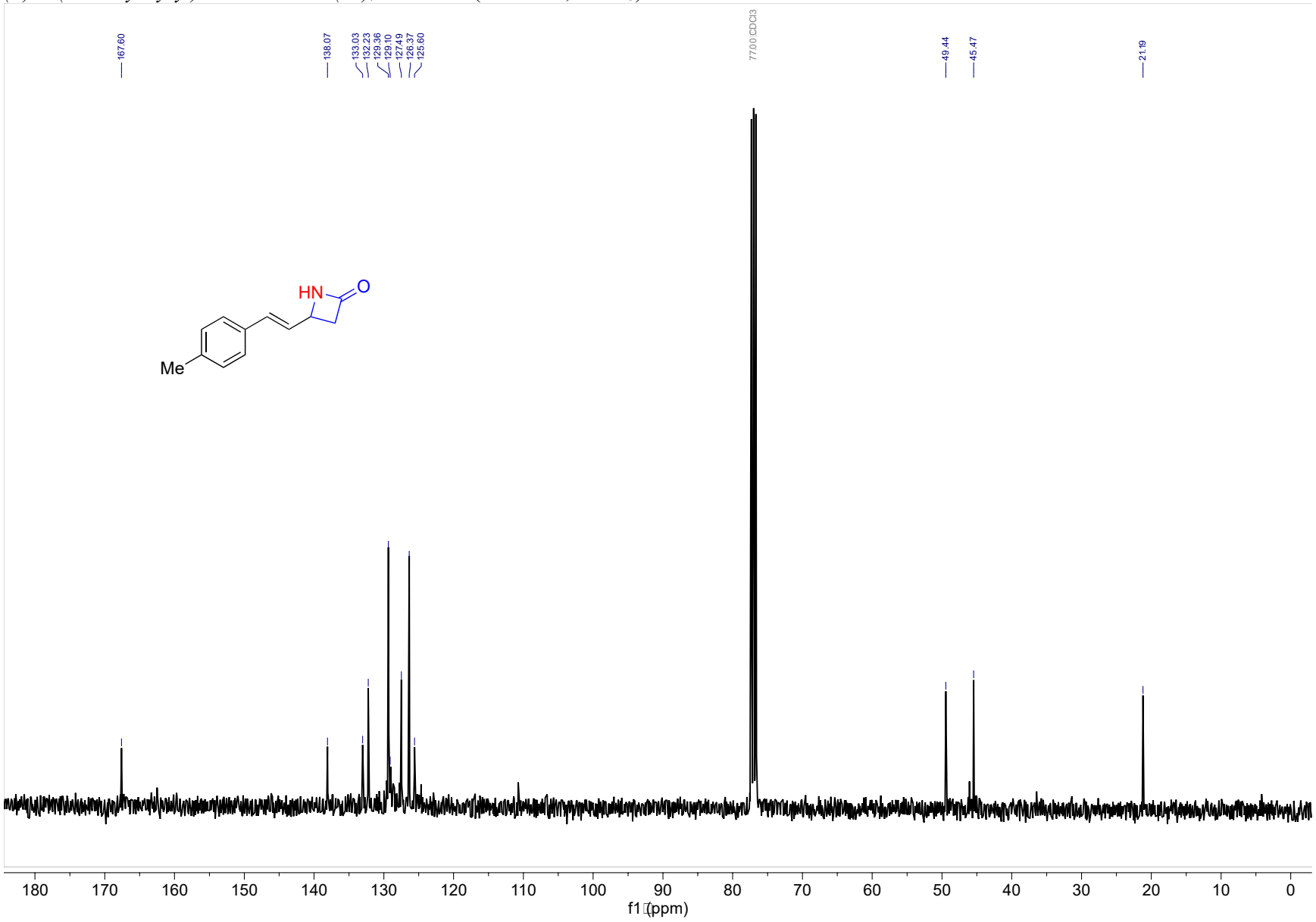
(E)-4-(4-chlorostyryl)azetidin-2-one (2c), ^{13}C NMR (126 MHz, $CDCl_3$):



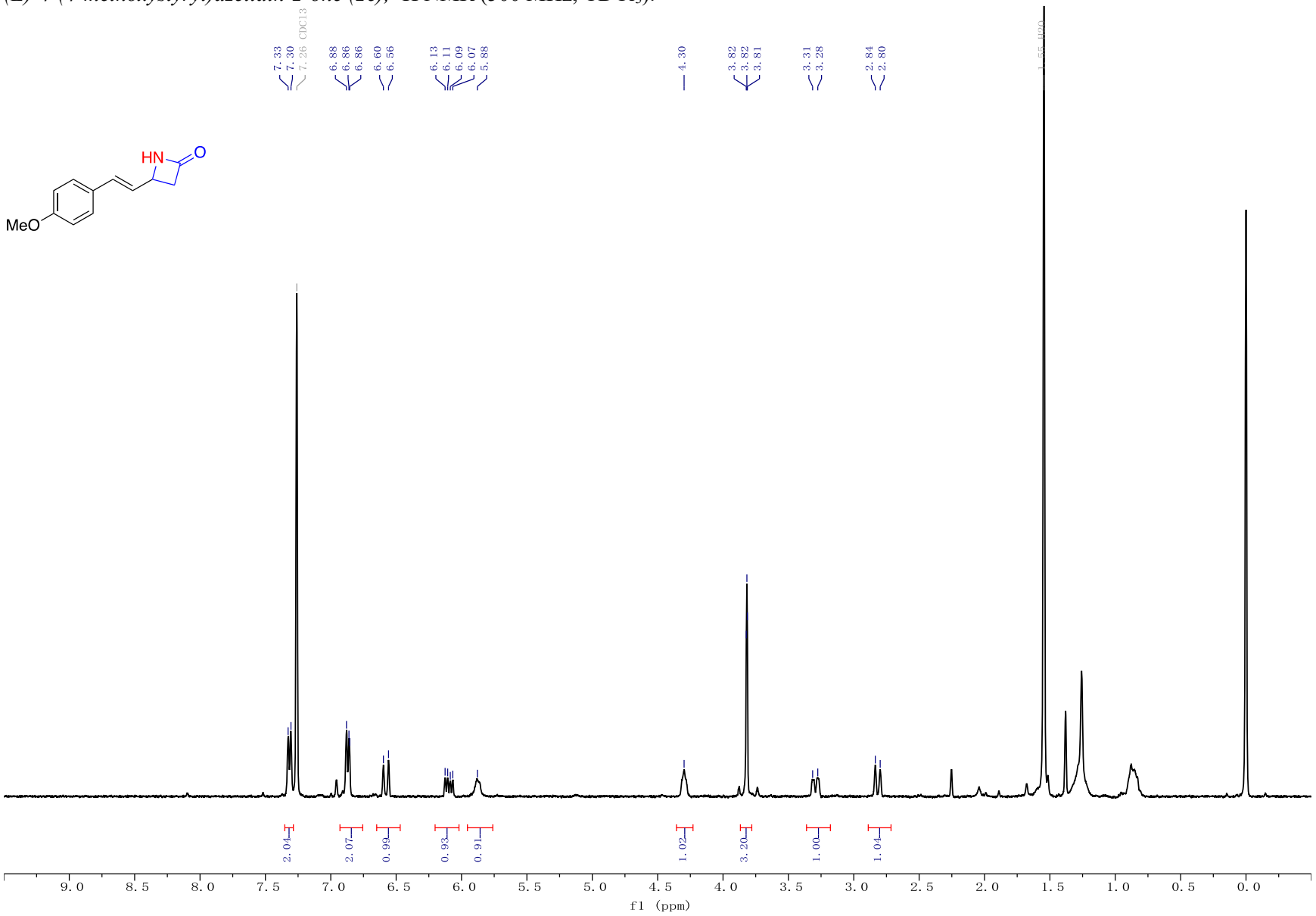
(E)-4-(4-methylstyryl)azetidin-2-one (2d), ^{1}H NMR (400 MHz, $CDCl_3$):



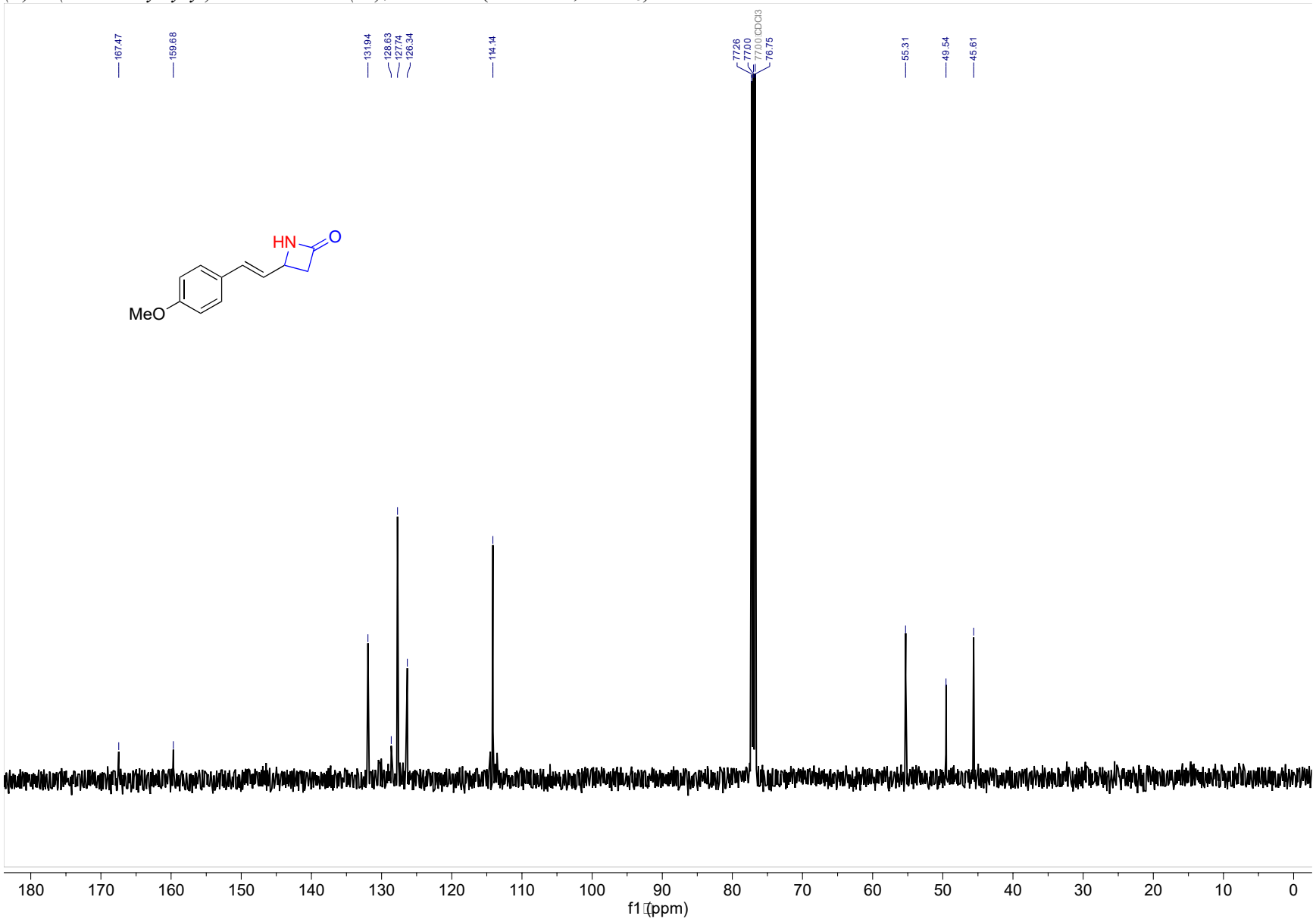
(E)-4-(4-methylstyryl)azetidin-2-one (2d), ^{13}C NMR (100 MHz, $CDCl_3$):



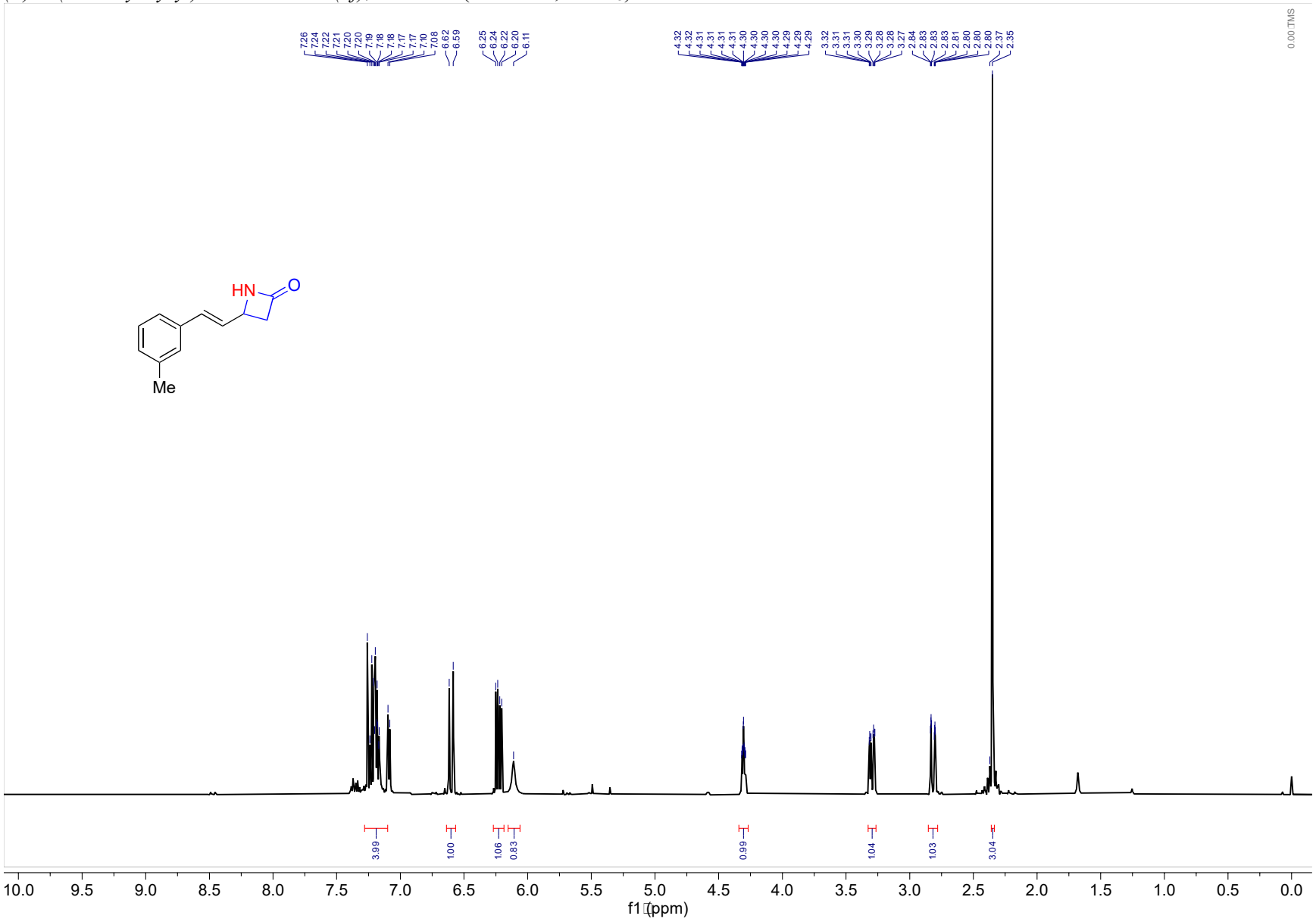
(E)-4-(4-methoxystyryl)azetidin-2-one (2e), ^{1}H NMR (500 MHz, $CDCl_3$):



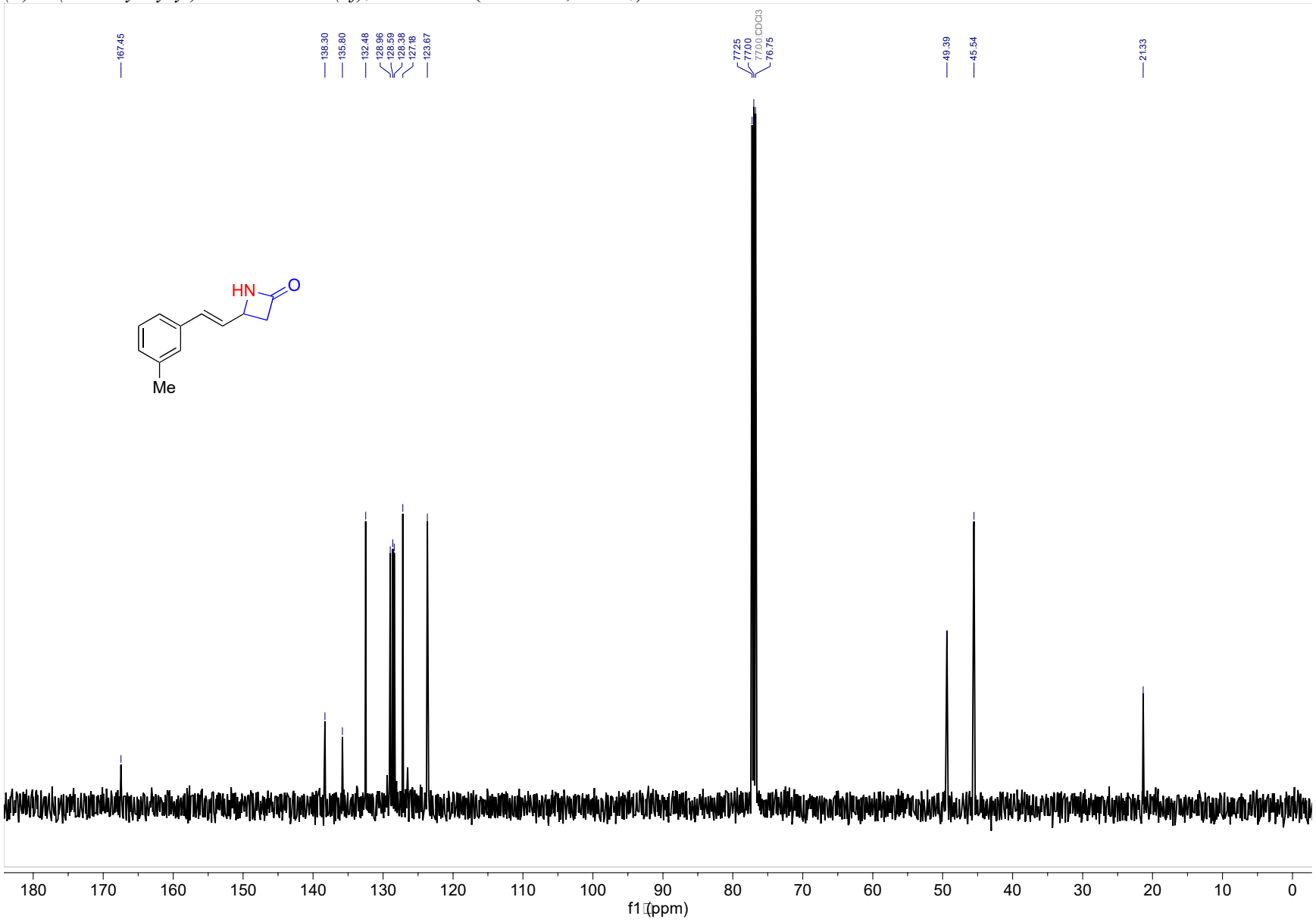
(E)-4-(4-methoxystyryl)azetidin-2-one (2e), ^{13}C NMR (126 MHz, $CDCl_3$):



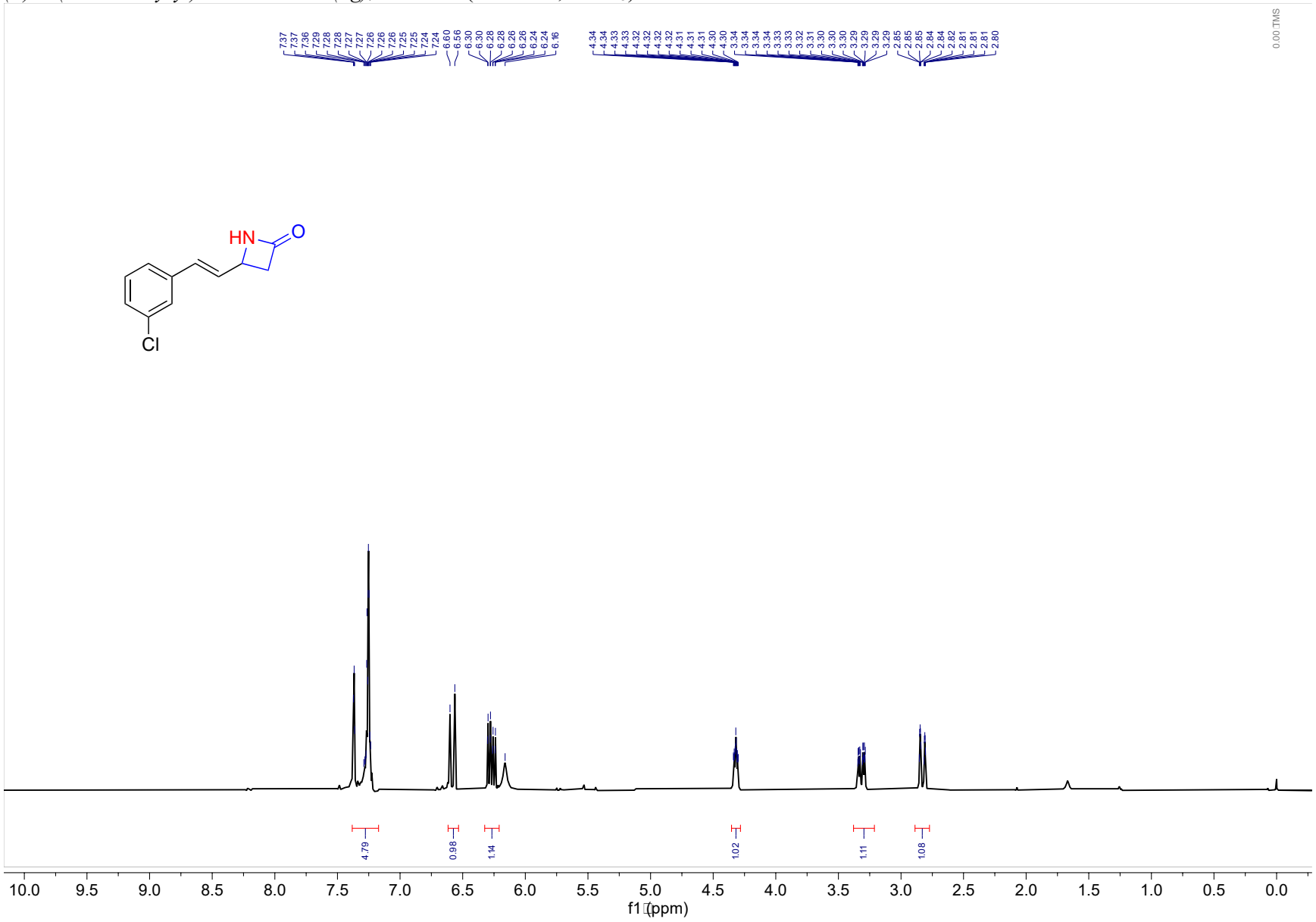
(E)-4-(3-methylstyryl)azetidin-2-one (2f), ^{1}H NMR (500 MHz, $CDCl_3$):



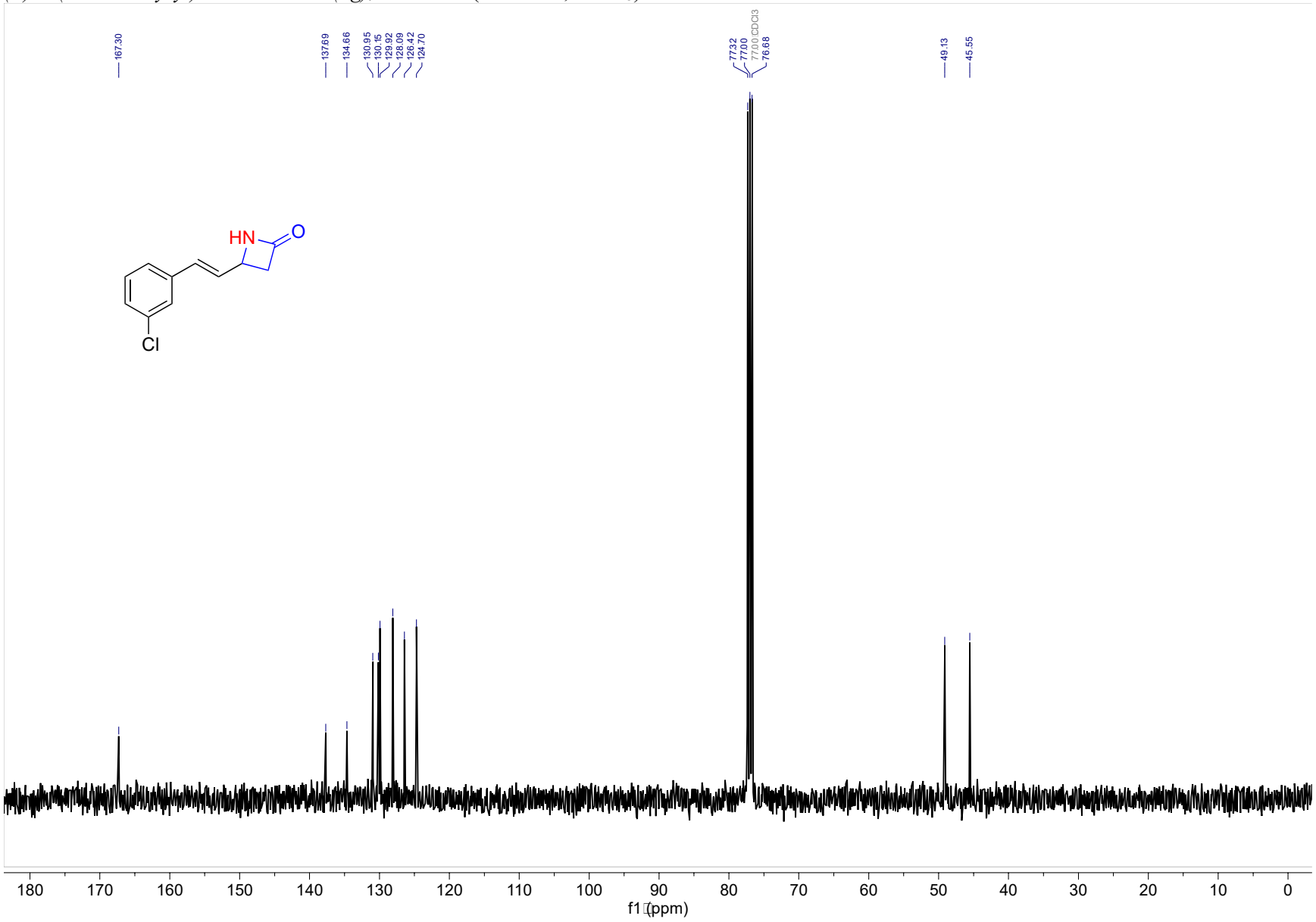
(E)-4-(3-methylstyryl)azetidin-2-one (2f), ^{13}C NMR (126 MHz, $CDCl_3$):



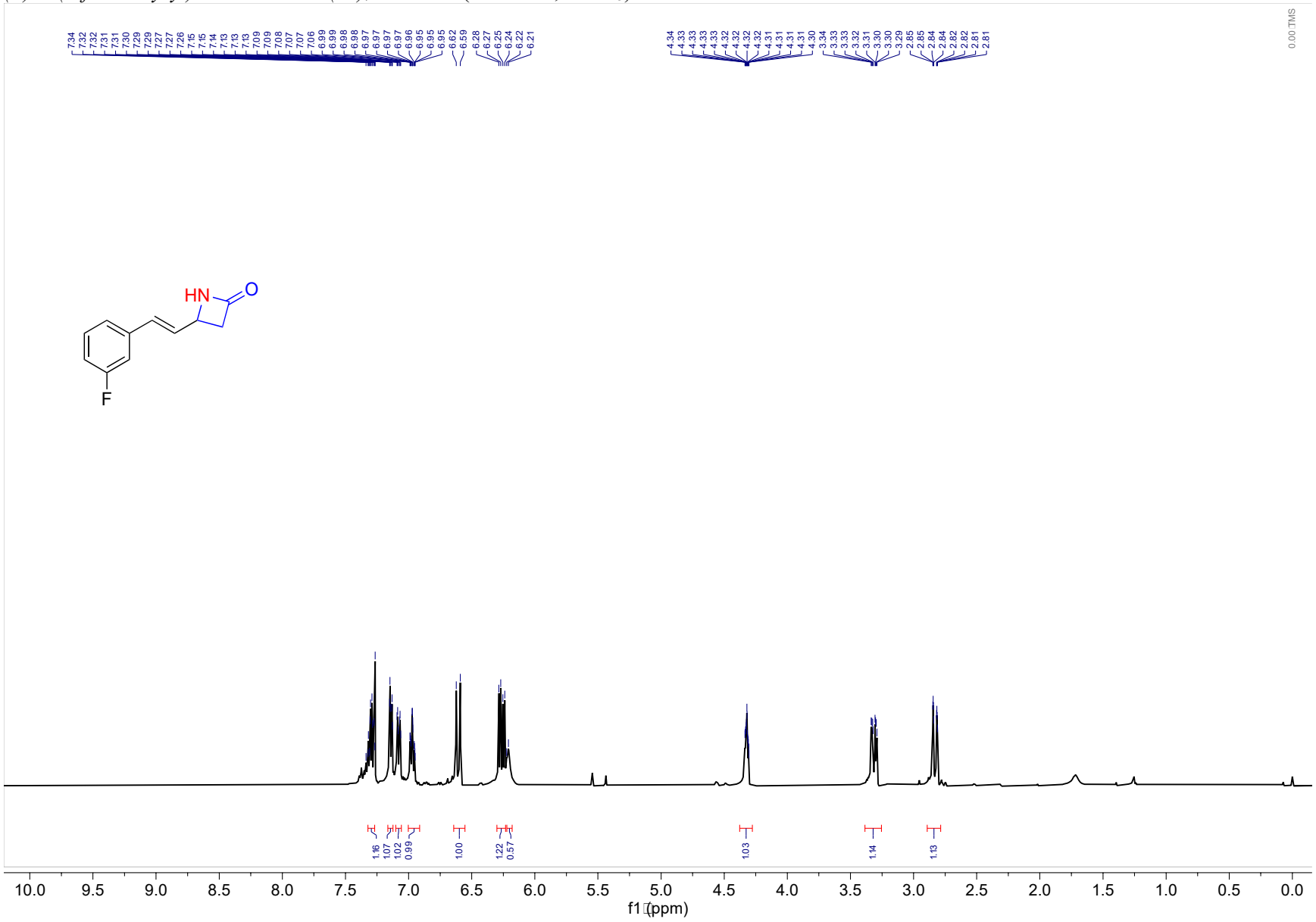
(E)-4-(3-chlorostyryl)azetidin-2-one (2g), ^{1}H NMR (400 MHz, $CDCl_3$):



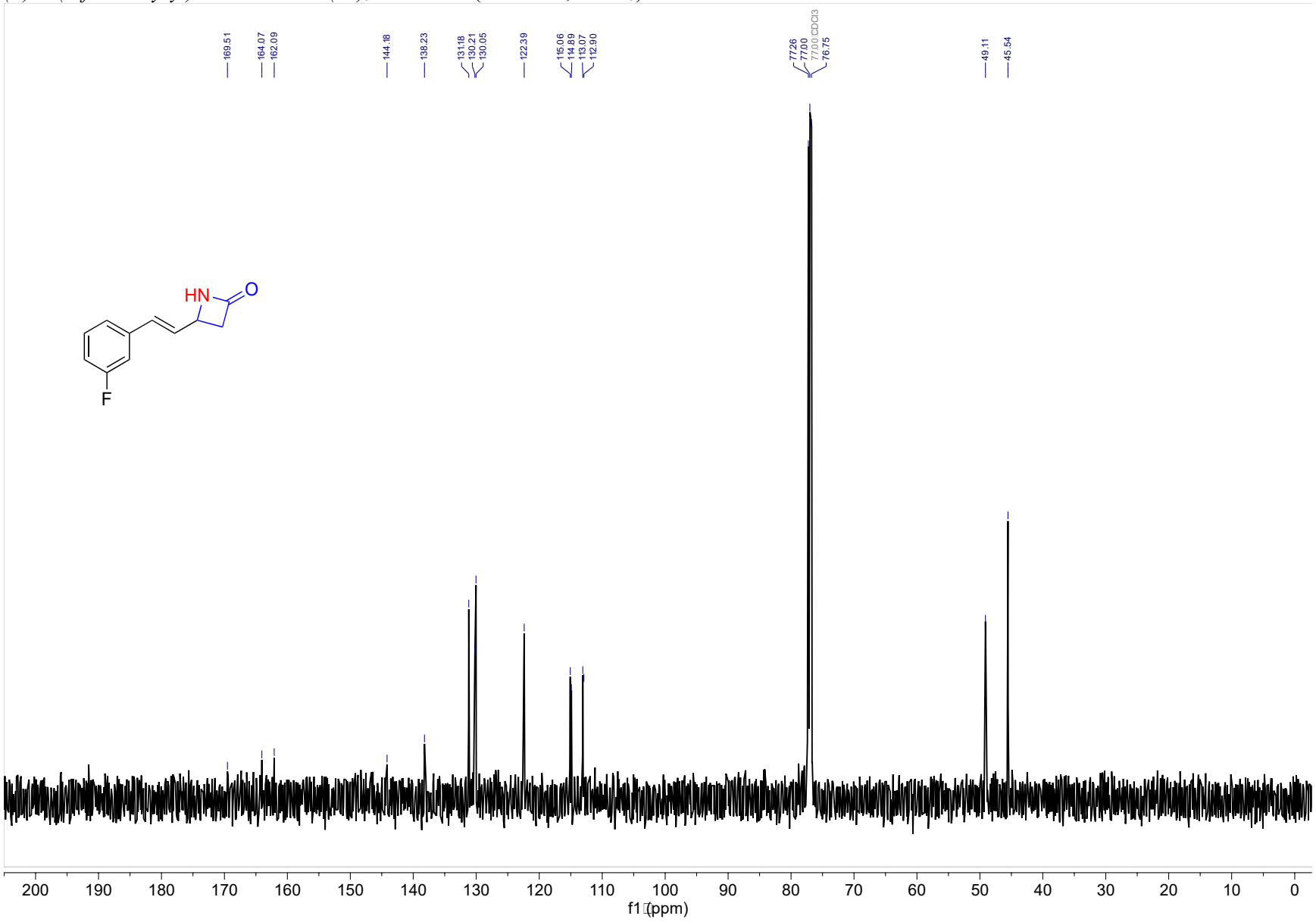
(E)-4-(3-chlorostyryl)azetidin-2-one (2g), ^{13}C NMR (100 MHz, $CDCl_3$):



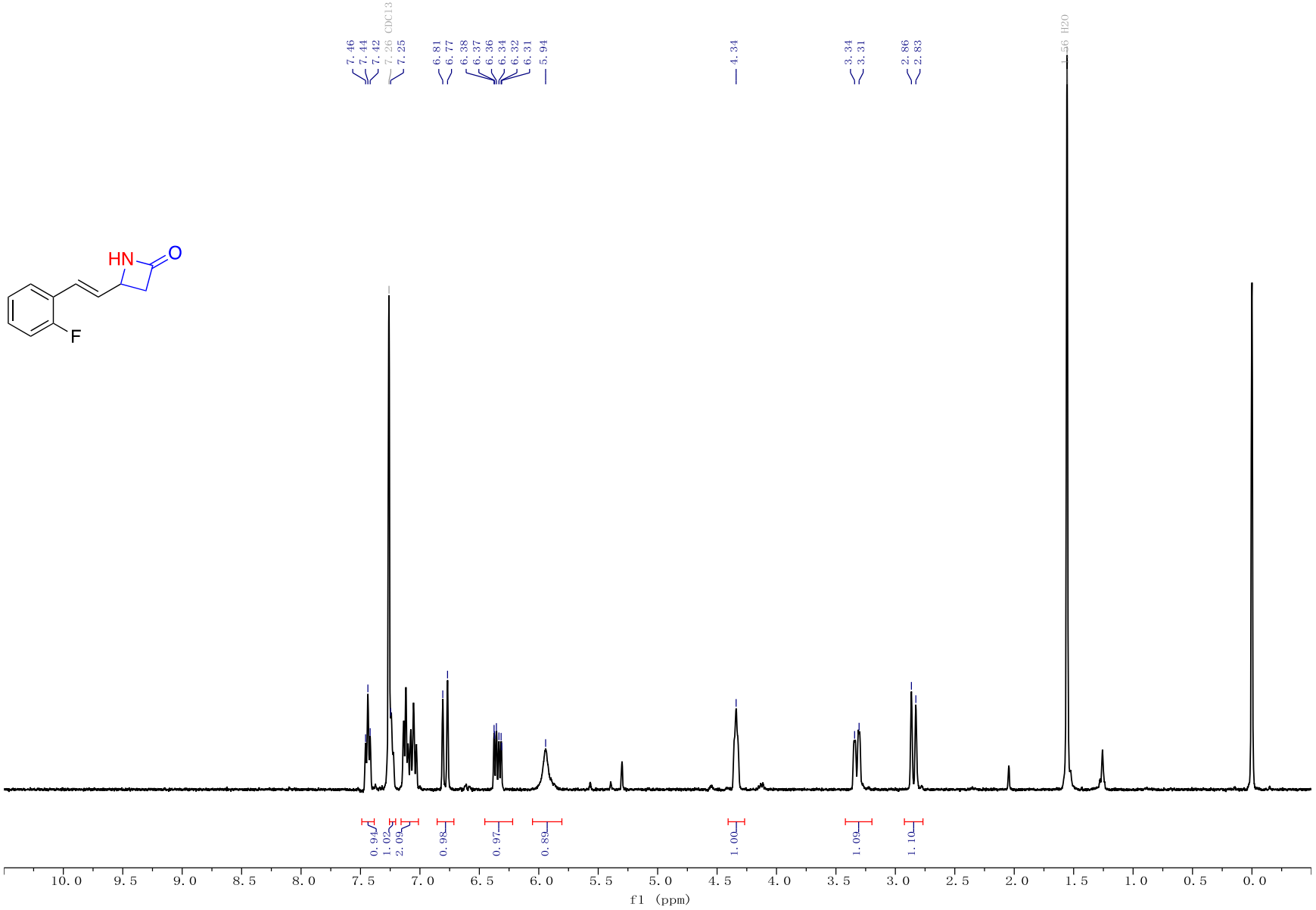
(E)-4-(3-fluorostyryl)azetidin-2-one (2h), ^{1}H NMR (500 MHz, $CDCl_3$):



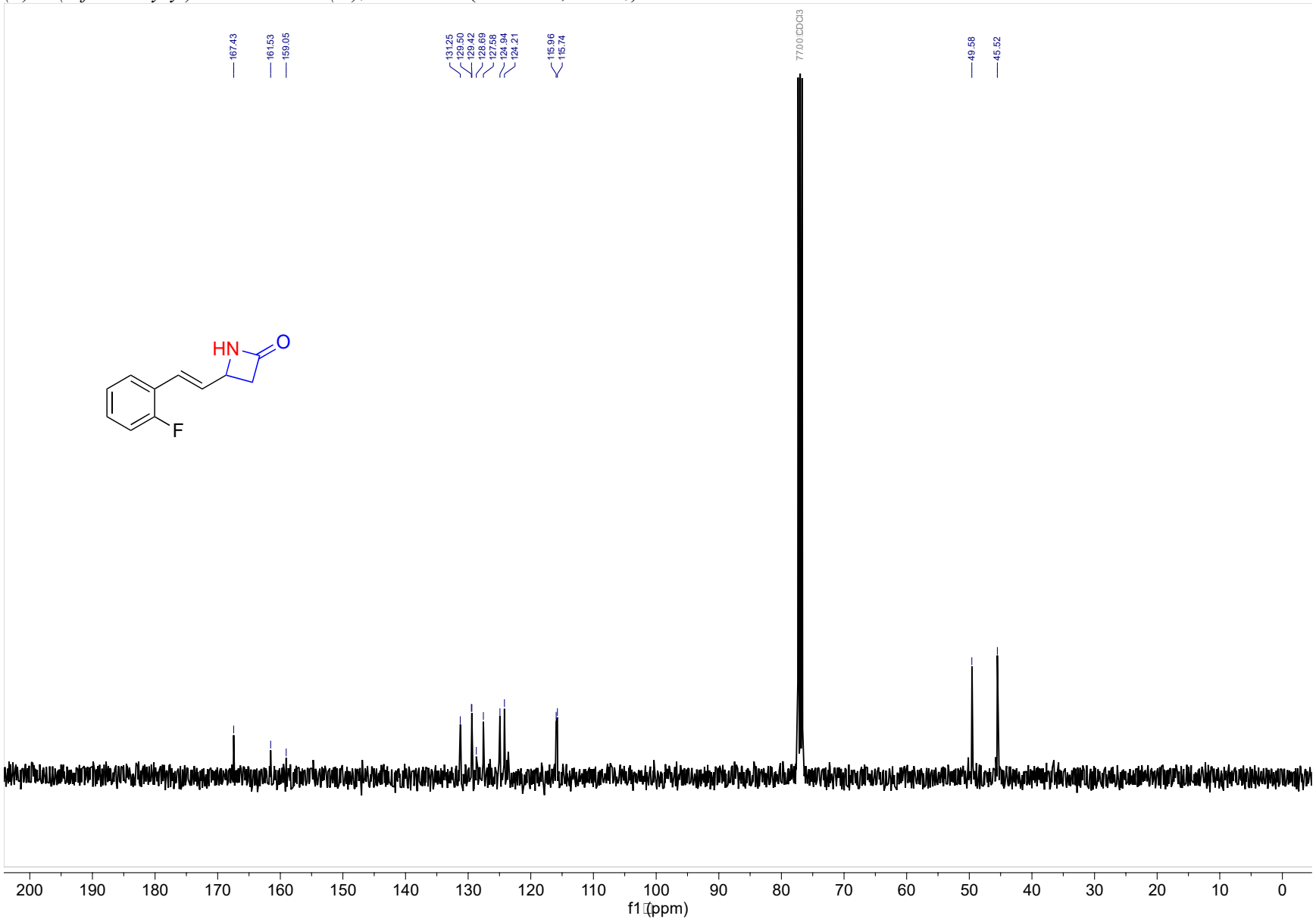
(E)-4-(3-fluorostyryl)azetidin-2-one (2h), ^{13}C NMR (126 MHz, $CDCl_3$):



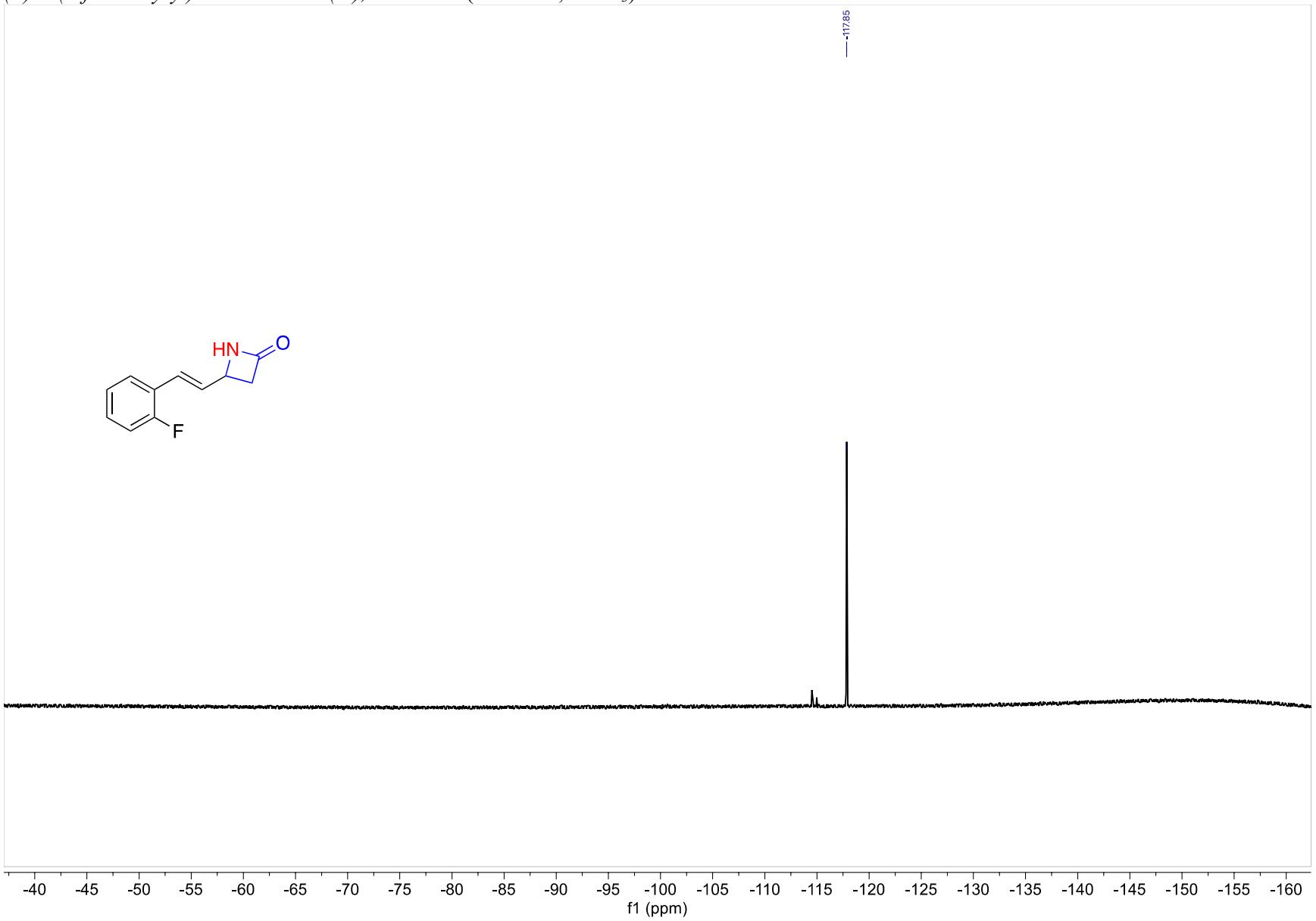
(E)-4-(2-fluorostyryl)azetidin-2-one (2i), ^{1}H NMR (400 MHz, $CDCl_3$):



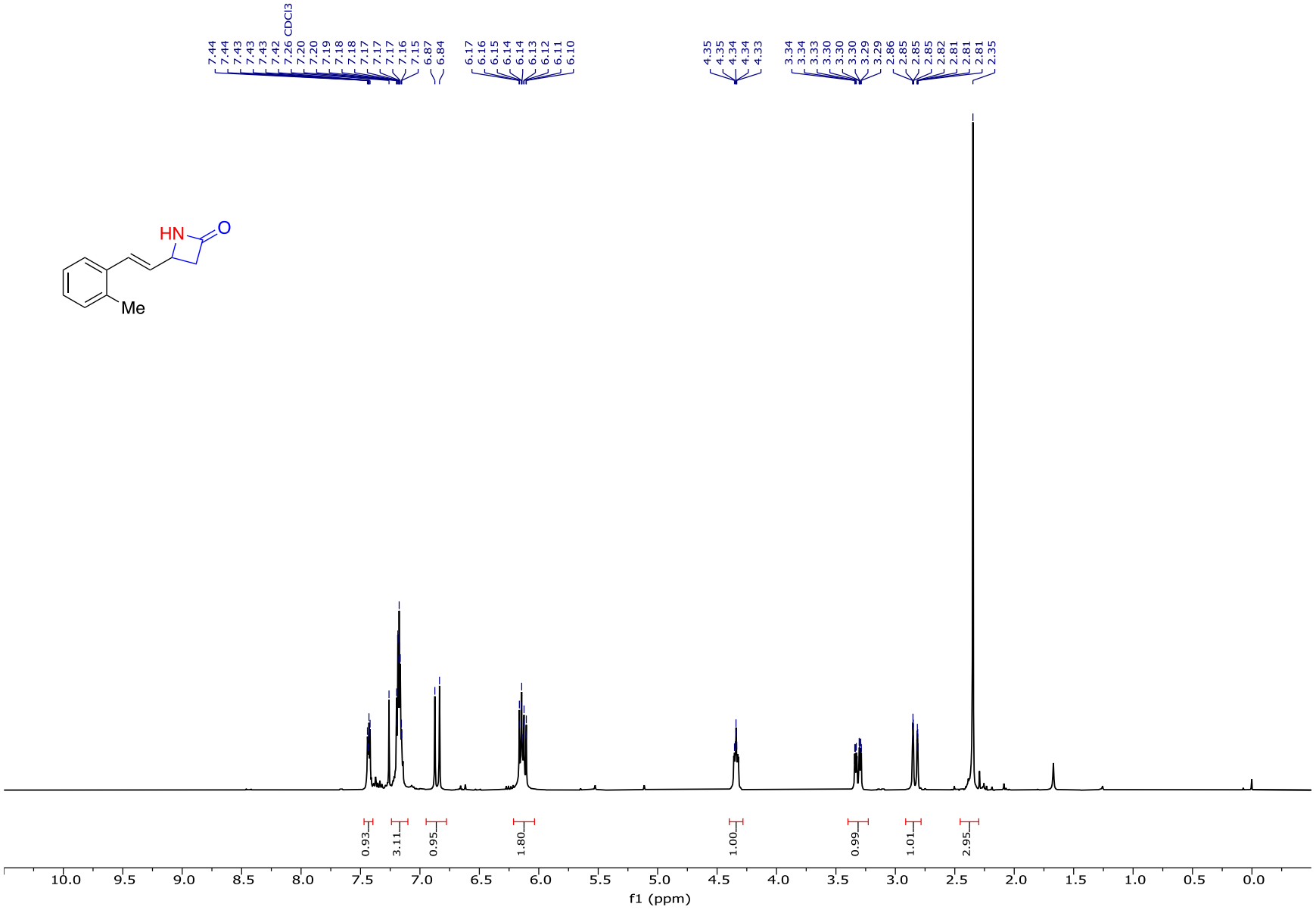
(E)-4-(2-fluorostyryl)azetidin-2-one (2i), ^{13}C NMR (400 MHz, $CDCl_3$):



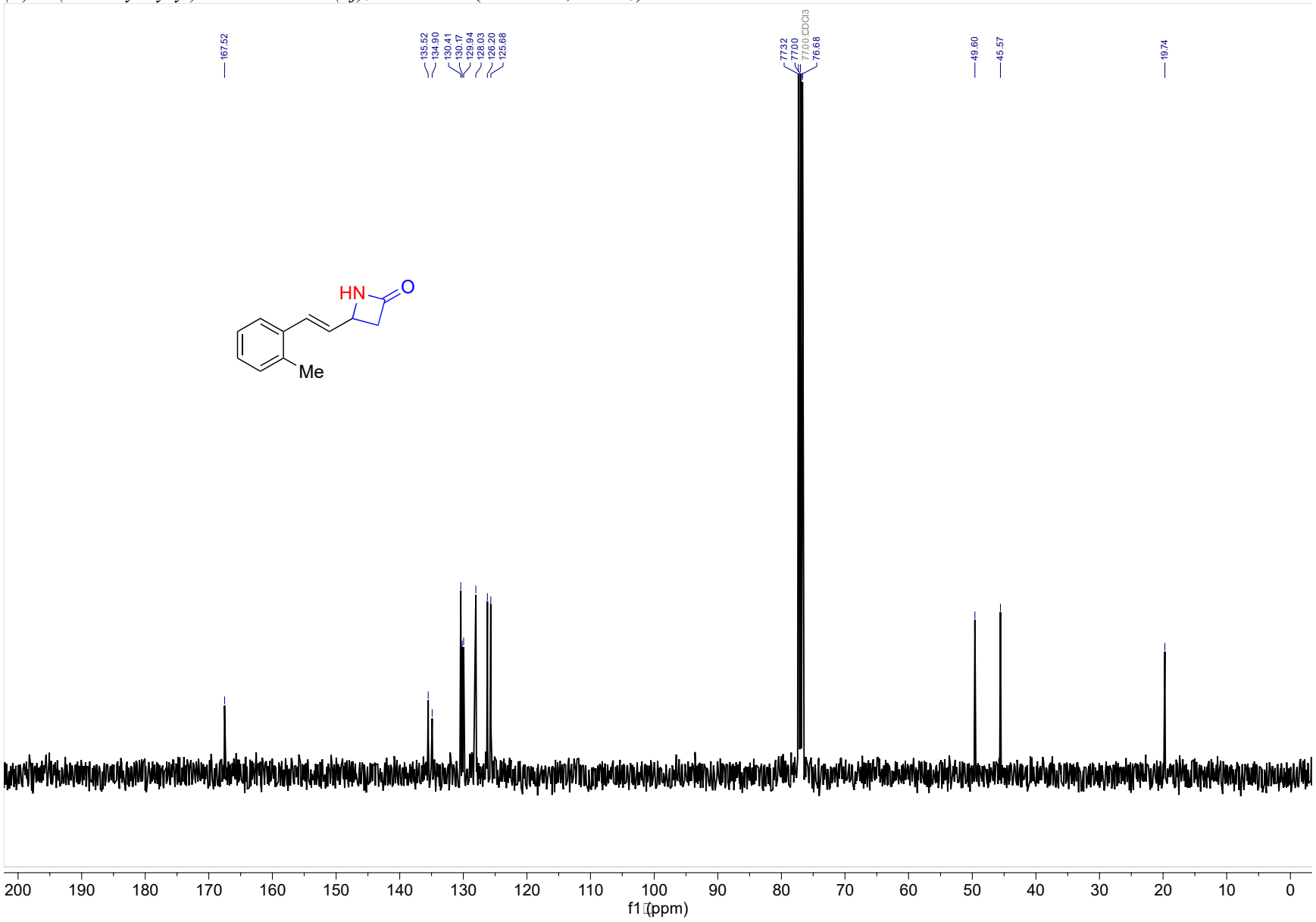
(E)-4-(2-fluorostyryl)azetidin-2-one (2i), ^{19}F NMR (376 MHz, $CDCl_3$):



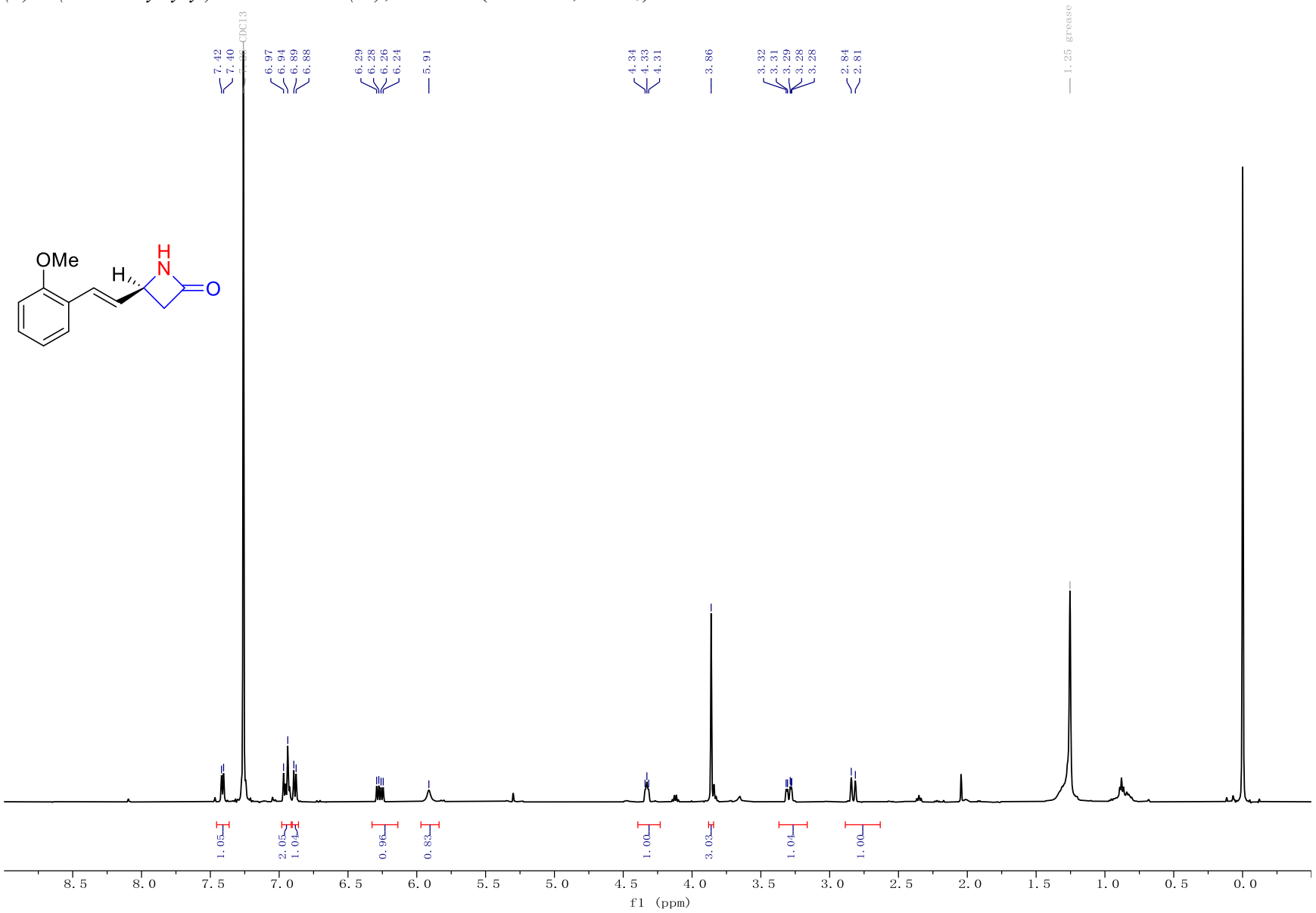
(E)-4-(2-methylstyryl)azetidin-2-one (2j), ^{1}H NMR (400 MHz, $CDCl_3$):



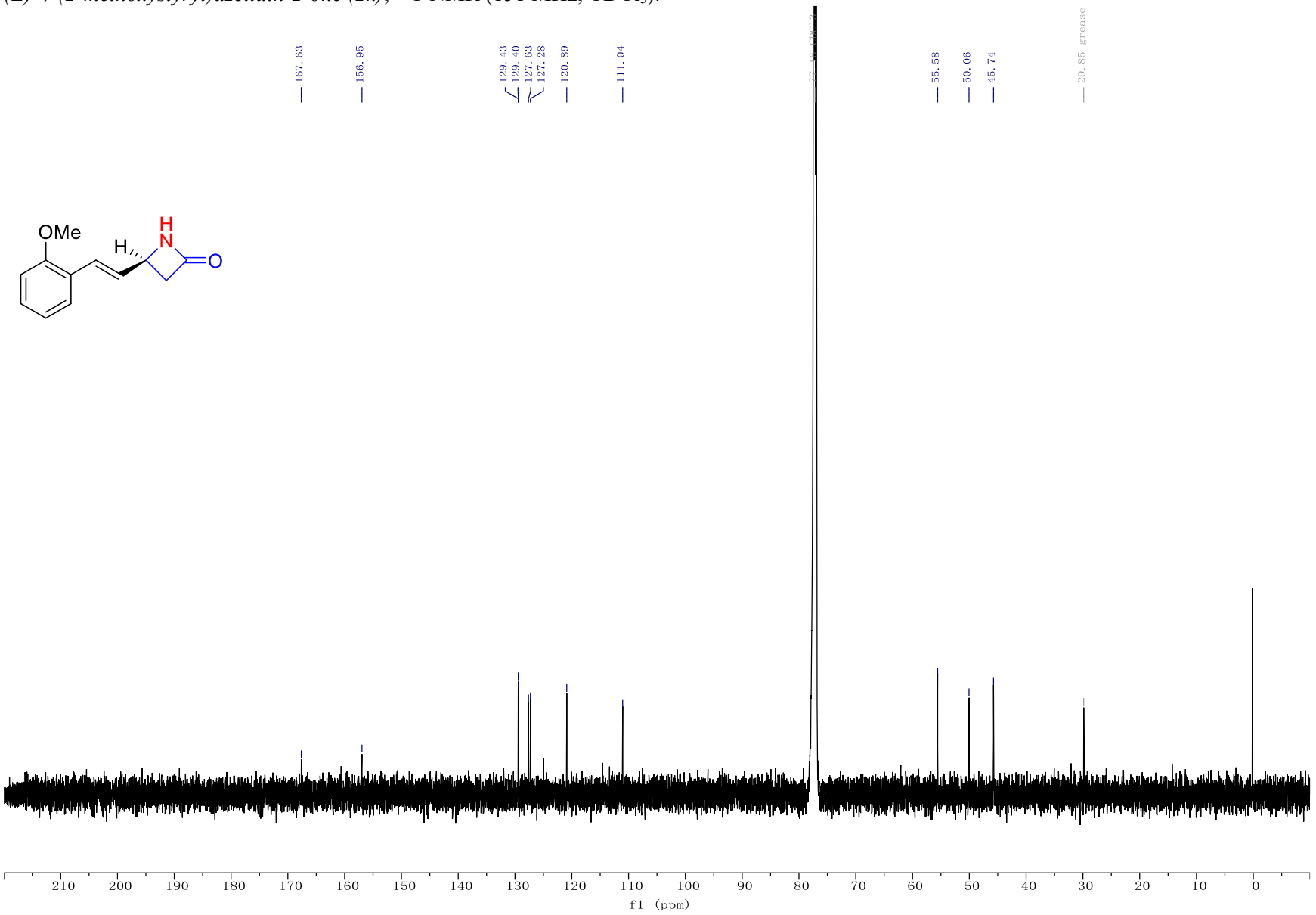
(E)-4-(2-methylstyryl)azetidin-2-one (2j), ^{13}C NMR (101 MHz, $CDCl_3$):



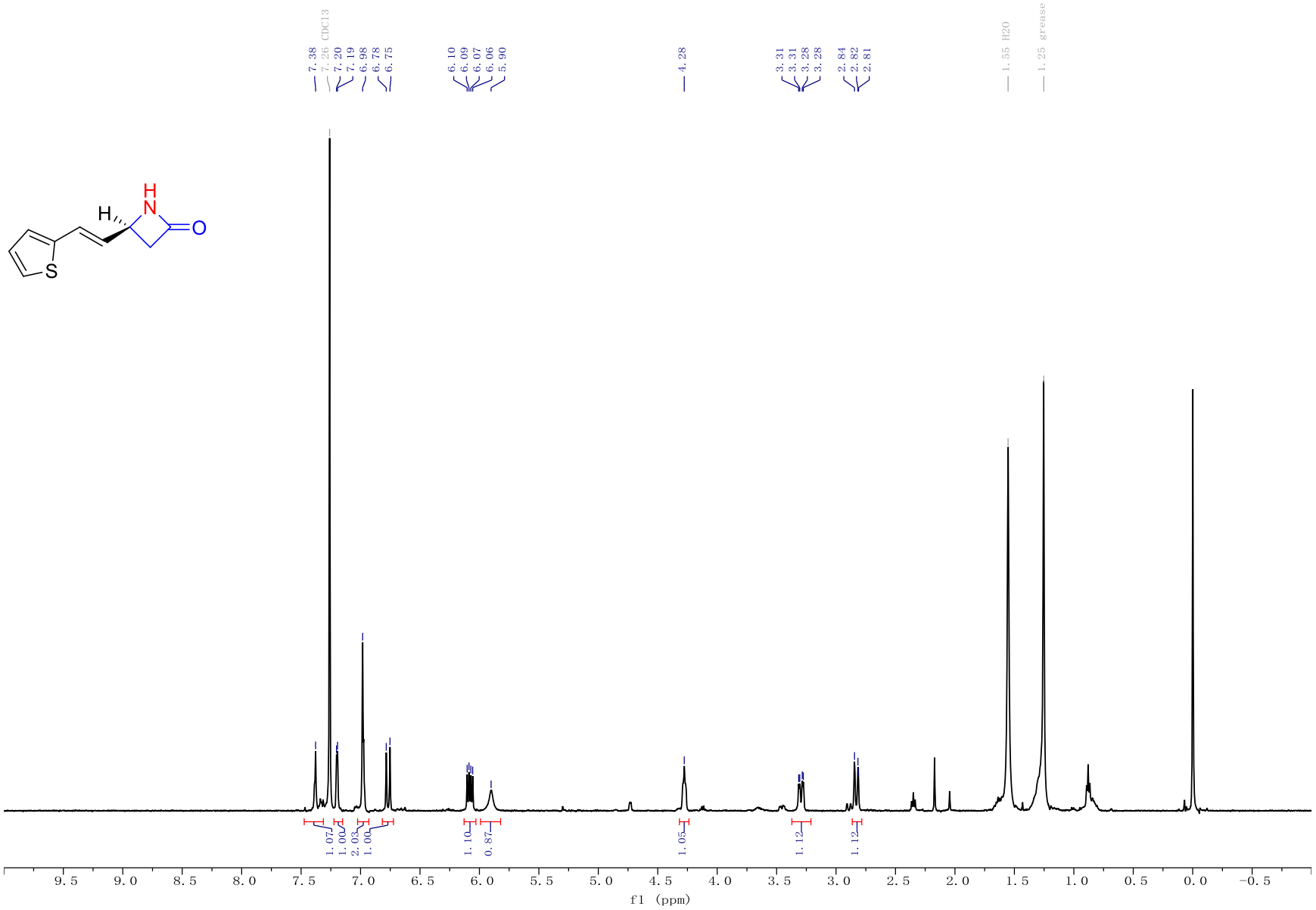
(E)-4-(2-methoxystyryl)azetidin-2-one (2k), ^{1}H NMR (500 MHz, $CDCl_3$):



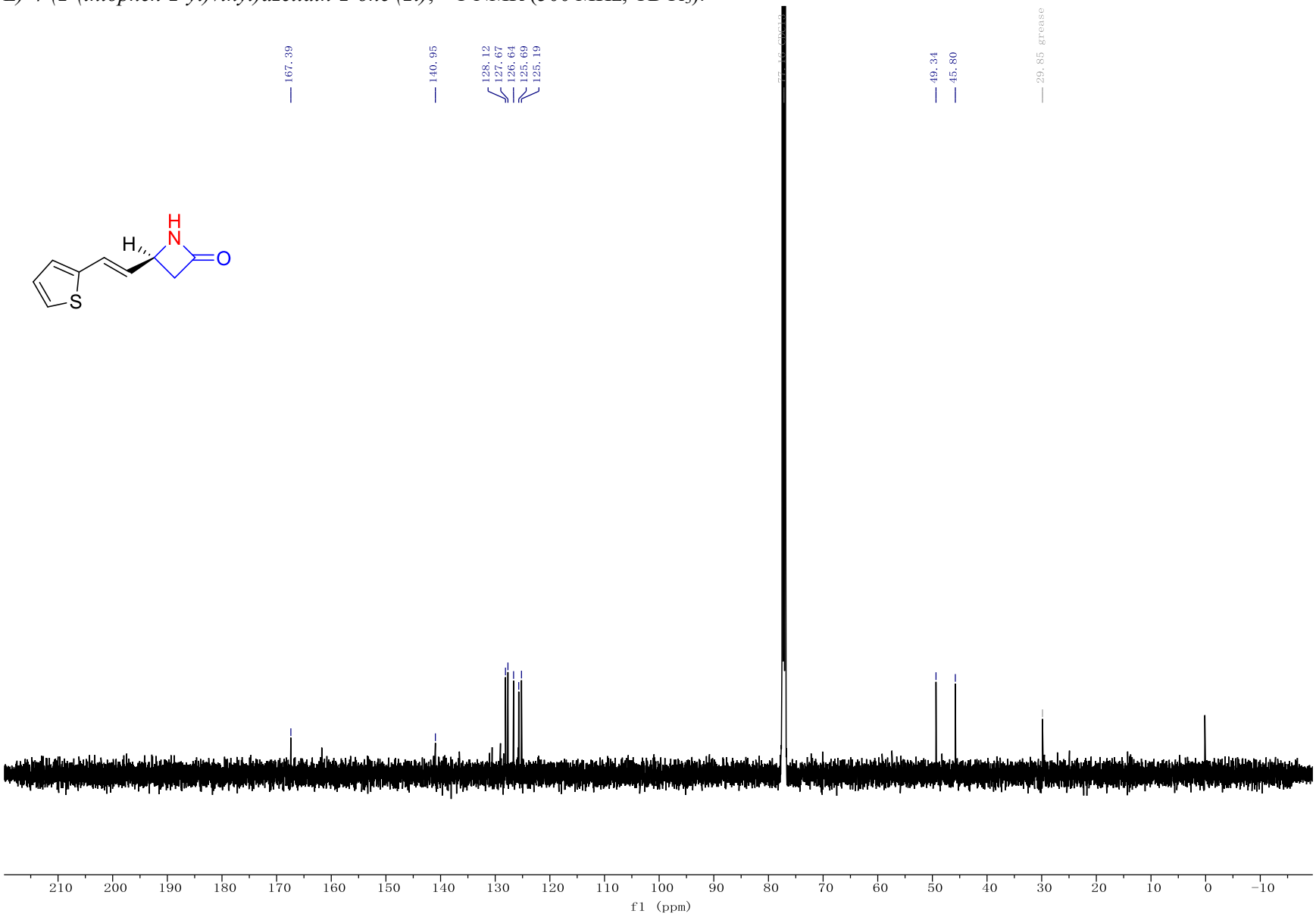
(E)-4-(2-methoxystyryl)azetidin-2-one (2k), ^{13}C NMR (151 MHz, $CDCl_3$):



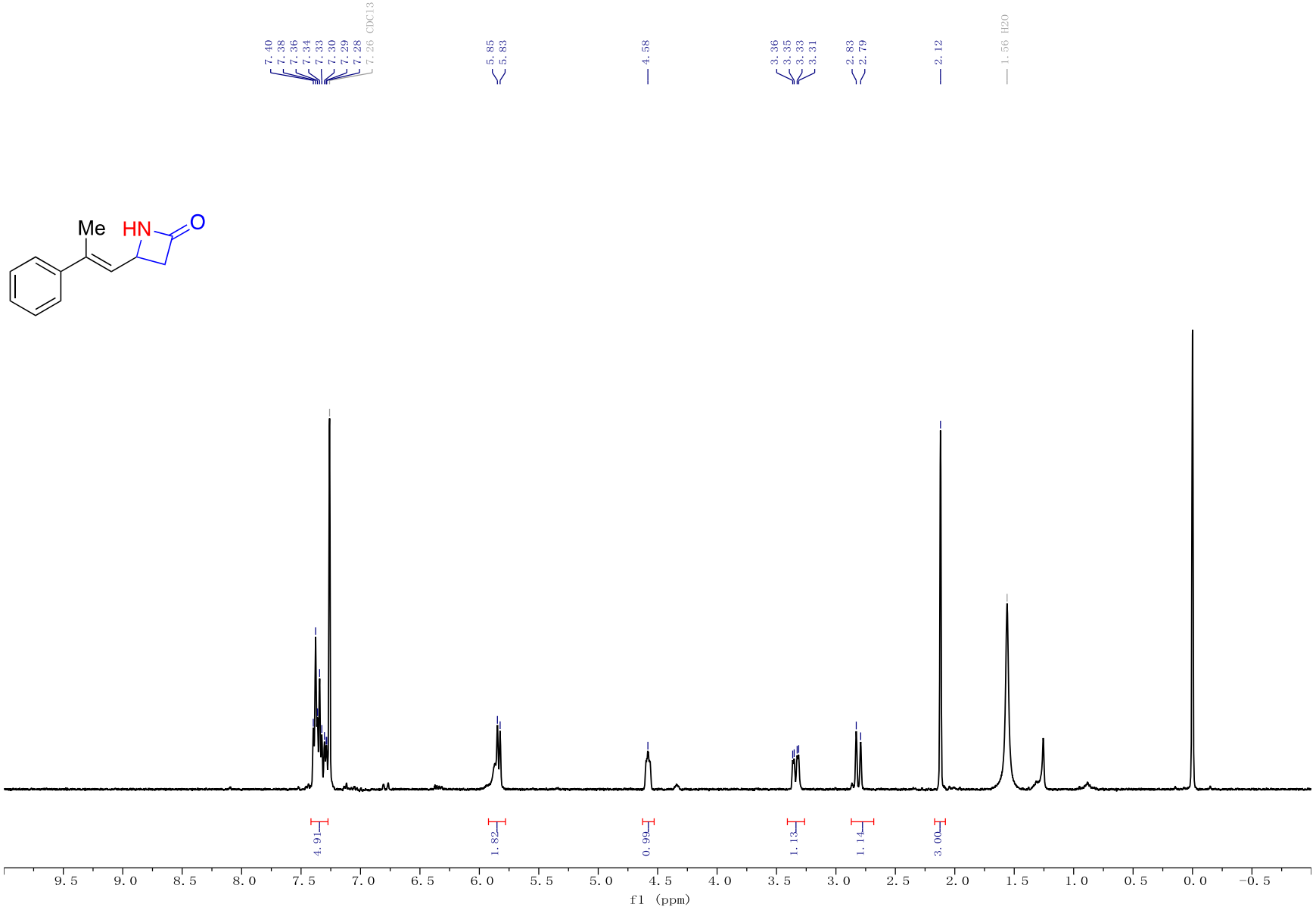
(E)-4-(2-(thiophen-2-yl)vinyl)azetidin-2-one (2l), ^{1}H NMR (500 MHz, $CDCl_3$):



E)-4-(2-(thiophen-2-yl)vinyl)azetidin-2-one (2l), ^{13}C NMR (500 MHz, $CDCl_3$):



((E)-4-(2-phenylprop-1-en-1-yl)azetidin-2-one (2m), ^{1}H NMR (400 MHz, $CDCl_3$):



((E)-4-(2-phenylprop-1-en-1-yl)azetidin-2-one (2m), ^{13}C NMR (500 MHz, $CDCl_3$):