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Straightforward chemoselective 4-nitration of 5-aminoisoxazoles

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1. General

NMR spectra were recorded on spectrometer Agilent 400-MR (400.0 MHz for ^{1}H; 100.6 MHz for ^{13}C, 162.0 MHz for ^{31}P) at room temperature; the chemical shifts δ were measured in ppm with respect to the solvent (^{1}H: $CDCl_3$, δ = 7.26 ppm, CD_3OD, δ = 3.31 ppm, ^{13}C: $CDCl_3$, δ = 77.16 ppm, CD_3OD, δ = 49.0 ppm), and H_3PO_4 as external standard for ^{31}P. Chemical shifts (δ) are given in ppm; *J* values are given in Hz. When necessary, assignments of signals in NMR spectra were made using 2D techniques. Accurate mass measurements (HRMS) were performed on a Bruker micrOTOF II instrument using electrospray ionization (ESI). The measurements were done in a positive ion mode (interface capillary voltage 4500 V) or in a negative ion mode (3200 V). Melting points (mp) are uncorrected. Analytical thin layer chromatography was carried out with Silufol silica gel plates (supported on aluminum); the detection was done by UV lamp (254 and 365 nm) and chemical staining (5% aqueous solution of $KMnO_4$). Column chromatography was performed on silica gel (230–400 mesh, Merck). (1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl acrylate[S1] and 5-aminoizoxazoles **1a-f**[S2] were synthesized by described methods.

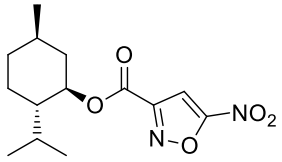
All other starting materials were commercially available.

All reagents except commercial products of satisfactory quality were purified by literature procedures prior to use.

1.1. Synthesis of (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 5-aminoisoxazole-3-carboxylate (1g)

Step 1. *(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl 5-nitroisoxazole-3-carboxylate.* Triethylamine (0.56 mL, 0.40 g, 4 mmol) was added dropwise to a solution of tetranitromethane (0.6 mL, 0.98 g, 5 mmol) in 1,4-dioxane (4 mL) at 0 °C (ice bath). The reaction mixture was stirred for 5 min, and (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl acrylate (0.42 g, 2 mmol) in 1,4-dioxane (0.5 mL) was added dropwise. The cooling was removed, and the mixture was stirred at 70 °C for 2 h. The solvent was removed under reduced pressure, and the product was isolated by column chromatography.

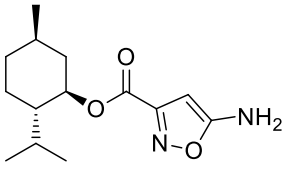
Colourless solid, 0.40 g (67%), mp. = 101–102 °C, R_f 0.20 (petroleum ether:CH_2Cl_2 = 2:1).



^{1}H-NMR ($CDCl_3$) δ: 0.77 (d, ^3J = 7.0 Hz, 3H, CH_3), 0.84–0.89 (m, 1H, CH_2), 0.90 (d, ^3J = 7.0 Hz, 3H, CH_3), 0.93 (d, ^3J = 6.6 Hz, 3H, CH_3), 1.03–1.14 (m, 1H, CH_2), 1.13-1.22 (m, 1H, CH_2), 1.49–1.62 (m, 2H, 2CH), 1.68–1.78 (m, 2H, 2CH_2), 1.83–1.92 (m, 1H, CH), 2.06– 2.14 (m, 1H, CH_2), 5.00 (td, ^3J = 4.4 Hz, ^3J = 11.0 Hz, 1H, CHO), 7.38 (s, 1H, CH). ^{13}C-NMR ($CDCl_3$) δ: 16.4 (CH_3), 20.7 (CH_3), 22.0 (CH_3), 23.5 (CH_2), 26.5 (CH), 31.6 (CH), 34.1 (CH_2), 40.6 (CH_2), 46.9 (CH), 78.1 (CH), 102.5 (CH), 157.4 (C=O), 158.6 (C), 165.6 (CNO_2). HRMS-ESI (M+K^+): Found: 335.1005. Calculated for $C_{14}H_{20}KN_2O_5^+$: 335.1004.

Step 2. *Compound **1g***. Sodium dithionite (588 mg, 2.7 mmol) was added to a solution of (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 5-nitroisoxazole-3-carboxylate (266 mg, 0.9 mmol) in mixture MeOH-H_2O (6 mL). The mixture was stirred at 90 °C for 1 h. The solvent was removed under reduced pressure, and the product was extracted with EtOAc (4×10 mL). The combined extracts were dried over $MgSO_4$, the solvent was removed under reduced pressure, and the product was isolated by column chromatography.

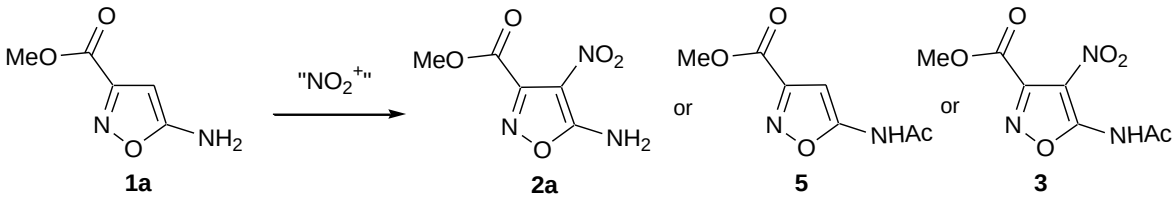
Colourless solid, 96 mg (40%), mp. = 110–111 °C, R_f 0.29 (petroleum ether:EtOAc = 3:1).



^{1}H-NMR ($CDCl_3$) δ: 0.77 (d, ^3J = 7.0 Hz, 3H, CH_3), 0.84–0.90 (m, 1H, CH_2), 0.89 (d, ^3J = 7.0 Hz, 3H, CH_3), 0.91 (d, ^3J = 6.6 Hz, 3H, CH_3), 1.03–1.19 (m, 2H, 2CH_2), 1.46–1.60 (m, 2H, 2CH), 1.65–1.75 (m, 2H, 2CH_2), 1.87–1.99 (m, 1H, CH), 2.04–2.13 (m, 1H, CH_2), 4.71 (br. s, 2H, NH_2), 4.93 (td, ^3J = 4.4 Гц, ^3J = 11.0 Гц, 1H, CHO), 5.52 (s, 1H, CH). ^{13}C-NMR ($CDCl_3$) δ: 16.4 (CH_3), 20.8 (CH_3), 22.1 (CH_3), 23.5 (CH_2), 26.4 (CH), 31.6 (CH), 34.2 (CH_2), 40.7 (CH_2), 46.9 (CH), 76.2 (CH), 80.8 (CH), 157.9 (C=O), 160.2 (C), 169.7 (CNH_2). HRMS-ESI (M+Na^+): Found: 289.1531. Calculated for $C_{14}H_{22}N_2O_3Na^+$: 289.1523.

1.2. Optimization of the Reaction Conditions

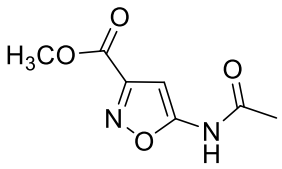
Table S1. Optimization of the conditions for the niration of 5-aminoisoxazole **1a**[a]



Entry	Nitrating reagent (NO_2^+ source)	Ratio, eq. **1a** : (NO_2^+)	Solvent	t, h	Product and yield, %[c]
1	HNO_3	1 : 1	Ac_2O	24	-[d]
2		1 : 1	CH_2Cl_2	12	-[d]
3	$Ce(NO_3)_3$	1 : 1	Ac_2O	12	**5**, 10 **3**, 26
4		1 : 2		12	**5**, 8 **3**, 34
5	$(NH_4)_2Ce(NO_3)_6$	1 : 1	Ac_2O	14	**3**, 40
6		1 : 1[b]	MeCN	14	0[e]
7	NO_2BF_4	1 : 1	MeCN	24	**2a**, 20
8	Me_4NNO_3	1 : 2	CH_2Cl_2	12	-[d]
9		1 : 1		12	-[d]
10		1 : 1		0.5	0[e]
11	NH_4NO_3	**1 : 1**	**$(CF_3CO)_2O$**	**12**	**2a**, 70
12		1 : 1[b]	MeCN	12	**2a**, 5[e]
13		1 : 1	$(CH_3CO)_2O$	12	**5**, 5[e]
14	Me_4NNO_3	**1 : 1**	**$(CF_3CO)_2O$**	**12**	**2a**, 72
15		1 : 1[b]	$CHCl_3$	12	-[d]
16		1 : 1[b]	MeCN	12	-[d]

[a]Reaction conditions: **1a** (0.25 mmol), nitration reagent NO_2^+, solvent (2 mL); [b] entry 6: 2 eq. Ac_2O was added; entry 12: 20 eq. $(CF_3CO)_2O$ was added; entries 14,15: 2 eq. $(CF_3CO)_2O$ was added; [c] yield after column chromatography; [d] no identified products; [e] no reaction or incomplete reaction.

1.3. Synthesis of methyl 5-(acetylamino)isoxazole-3-carboxylate (5) (counter synthesis).



Cerium (III) chloride (86 mg, 0.35 mmol) was added to a solution of 5-aminoisoxazole **1a** (50 mg, 0.35 mmol) and Ac_2O (0.07 ml, 76 mg, 0.74 mmol) in MeCN (2 mL). The mixture was stirred for 24 h and then was poured into water and neutralized with $NaHCO_3$ (aq.) to reach pH of 7–8. The product was extracted with CH_2Cl_2 (4×10 mL). The combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and the product was isolated by column chromatography. Light yellow solid, 57 mg, 91% yield, mp. = 151-154ºC, R_f 0.16 (petroleum ether:EtOAc = 6:1). ^{1}H-NMR ($CDCl_3$) δ: 2.24 (s, 3H, CH_3), 3.93 (s, 3H, OCH_3), 6.72 (s, 1H, CH), 9.73 (br.s, 1H, NH). ^{13}C-NMR ($CDCl_3$) δ: 23.4 (CH_3), 52.9 (CH_3O), 89.3 (CH), 157.0 (C), 160.2 (C=O), 162.3 (C-NH), 166.8 (C=O). HRMS-ESI ($M+K^+$): Found: 223.0117. Calculated for $C_7H_8KN_2O_4^+$: 223.0116.

1.4. Synthesis of methyl 5-acetamido-4-nitroisoxazole-3-carboxylate (3). Cerium (IV) ammonium nitrate (35 mg, 0.063 mmol) was added to a solution of 5-aminoisoxazole **1a** (35 mg, 0.25 mmol) in Ac_2O (2 mL). The mixture was stirred for 24 h and then poured into water and neutralized with $NaHCO_3$ (aq.) to pH 7–8. The product was extracted with CH_2Cl_2 (4×10 mL). The combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and the product was isolated by column chromatography. Colorless solid, yield 23 mg (40%), mp. = 154-156ºC, R_f 0.18 (petroleum ether:ЭА = 4:1). ^{1}H-NMR ($CDCl_3$) δ: 2.45 (s, 3H, CH_3), 4.03 (s, 3H, CH_3), 9.65 (br.s, 1H, NH). ^{13}C-NMR ($CDCl_3$) δ: 24.7 (CH_3), 54.2 (OCH_3), 112.8 (CNO_2), 150.4 (C), 157.6 (C=O), 160.4 (C), 165.9 (C=O). HRMS-ESI ($M+Na^+$): Found: 252.0223. Calculated for $C_7H_7N_3O_6Na^+$: 252.0227.

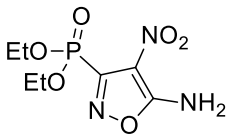
1.5. General procedure for the synthesis of 5-amino-4-nitroisoxazoles 2a-g. Ammonium nitrate (20 mg, 0.25 mmol) was added to a solution of 5-aminoisoxazole **1a-g** (0.25 mmol) in $(CF_3CO)_2O$ (2 mL). The mixture was stirred for 12 h and then poured into ice water and neutralized with $NaHCO_3$ (aq.) to pH of 7–8. The product was extracted with CH_2Cl_2 (4×10 mL). The combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and the product was isolated by column chromatography.

1-(5-Amino-4-nitroisoxazol-3-yl)ethanone **2b.** Yellow solid, yield 33 mg (78%), mp. = 137 °C, R_f 0.24 (CH_2Cl_2:CH_3OH = 30:1). ^{1}H-NMR ($CDCl_3$) δ: 2.62 (s, 3H, CH_3), 7.01 (br.s, 2H, NH_2). ^{13}C-NMR ($CDCl_3$) δ: 30.3 (CH_3), 109.4 (CNO_2), 156.4 (C), 166.0 (C), 190.1 (C=O). HRMS-ESI ($M+Na^+$): Found: 194.0175. Calculated for $C_5H_5N_3O_4Na^+$: 194.0172.

1-(5-Amino-4-nitroisoxazol-3-yl)propan-1-one **2c.** Yellow solid, yield 16 mg (35%), mp. = 132 °C, R_f 0.29 (petroleum ether:EtOAc= 2:1). ^{1}H-NMR ($CDCl_3$) δ: 1.23 (t, ^3J = 7.2 Hz, 3H, CH_3), 2.94 (q, ^3J = 7.2 Hz, 2H, CH_2), 6.76 (br.s, 2H, NH_2). ^{13}C-NMR ($CDCl_3$) δ: 7.0 (CH_3), 36.8 (CH_2), 109.6 (CNO_2), 156.5 (C), 165.6 (C), 193.2 (C=O). HRMS-ESI ($M+H^+$): Found: 186.0512. Calculated for $C_6H_8N_3O_4^+$: 186.0509.

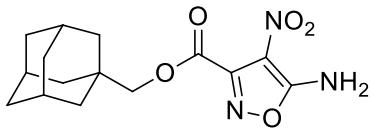
(5-Amino-4-nitroisoxazol-3-yl)(phenyl)methanone **2d.** Colorless solid, yield 37 mg (64%), mp. = 136 °C, R_f = 0.17 (petroleum ether:EtOAc = 2:1). ^{1}H-NMR ($CDCl_3$-CD_3OD) δ: 7.35-7.45 (m, 2H, 2CH), 7.50-7.60 (m, H, CH), 7.79-7.90 (m, 2H, 2CH). The signal of NH_2-group is aligned with the signals of solvent. ^{13}C-NMR ($CDCl_3$-CD_3OD) δ: 110.0 (CNO_2), 128.9 (2CH), 129.8 (2CH), 134.8 (C), 135.1 (CH), 155.8 (C), 165.9 (C), 184.5 (C=O). HRMS-ESI ($M+H^+$): Found: 234.0508. Calculated for $C_{10}H_8N_3O_4^+$: 234.0509. HRMS-ESI ($M+H^+$): Found: 234.0508. Calculated for $C_{10}H_8N_3O_4^+$: 234.0509.

Diethyl (5-amino-4-nitroisoxazol-3-yl)phosphonate **2e.** Light yellow solid, yield 53 mg (80%), mp. = 98 °C, R_f 0.18 (CH_2Cl_2:MeOH = 40:1).



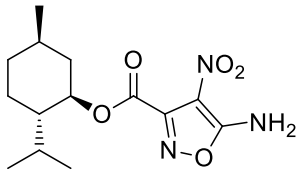
^{1}H-NMR ($CDCl_3$) δ: 1.40 (dt, $^3J_{HH}$ = 7.1 Hz, $^4J_{PH}$ = 0.6 Hz, 6H, $2CH_3$), 4.37 (m, 4H, $2CH_2$), 7.49 (br.s, 2H, NH_2). ^{13}C-NMR ($CDCl_3$) δ: 16.2 (J_{CP} = 6.8 Hz, $2CH_3$), 65.2 (J_{CP} = 6.5 Hz, $2CH_2$), 112.0 (J_{CP} = 16.0 Hz, CH), 150.8 (J_{CP} = 215.0 Hz, C), 166.5 (J_{CP} = 7.6 Hz, C). ^{31}P-NMR ($CDCl_3$) δ: -0.04. HRMS-ESI ($M+Na^+$): Found: 288.0353. Calculated for $C_7H_{12}N_3O_6PNa^+$: 288.0356.

Adamantan-1-ylmethyl 5-amino-4-nitroisoxazole-3-carboxylate **2f.** Colourless solid, yield 44 mg (55%), mp. = 177 °C, R_f 0.36 (petroleum ether:EtOAc = 4:1).



^{1}H-NMR ($CDCl_3$-CD_3OD) δ: 1.53–1.56 (m, 6H, $3CH_2$(Ad)), 1.56–1.64 (m, 3H, $3CH_2$(Ad)), 1.64–1.71 (m, 3H, $3CH_2$(Ad)), 1.92–1.96 (m, 3H, 3CH(Ad)), 3.97 (s, 2H, CH_2O). The signal of NH_2-group is aligned with the signals of solvent. ^{13}C-NMR ($CDCl_3$-CD_3OD) δ: 28.0 (3CH(Ad)), 33.4 (C(Ad)), 36.8 ($3CH_2$(Ad)), 39.0 ($3CH_2$(Ad)), 76.8 (CH_2O), 109.2 (CNO_2), 151.6 (C), 158.7 (C), 166.1 (CNH_2). HRMS-ESI ($M+Na^+$): Found: 344.1218. Calculated for $C_{15}H_{19}N_3O_5Na^+$: 344.1217.

(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl 5-amino-4-nitroisoxazole-3-carboxylate **2g.** Colourless solid, yield 51 mg (66%), mp. = 112 °C, R_f 0.22 (petroleum ether:EtOAc = 4:1).

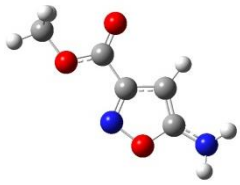


^{1}H-NMR ($CDCl_3$-CD_3OD) δ: 0.78 (d, ^3J = 6.9 Hz, 3H, CH_3), 0.83–0.89 (m, 1H, CH_2), 0.86 (d, ^3J = 7.0 Hz, 3H, CH_3), 0.90 (d, ^3J = 6.6 Hz, 3H, CH_3), 1.01–1.17 (m, 2H, $2CH_2$), 1.41–1.56 (m, 2H, 2CH), 1.64–1.72 (m, 2H, $2CH_2$), 1.90–1.98 (m, 1H, CH), 2.15–2.21 (m, 1H, CH_2), 4.99 (td, ^3J = 4.4 Hz, ^3J = 11.0 Hz, 1H, CHO). The signal of NH_2-group is aligned with the signals of solvent. ^{13}C-NMR ($CDCl_3$-CD_3OD) δ: 16.1 (CH_3), 20.7 (CH_3), 22.0 (CH_3), 23.3 (CH_2), 26.0 (CH), 31.6 (CH), 34.1 (CH_2), 40.3 (CH_2), 46.9 (CH), 78.5 (CH), 109.2 (CNO_2), 151.8 (C=O), 158.2 (C), 166.0 (CNH_2). HRMS-ESI ($M+K^+$): Found: 350.1106. Calculated for $C_{14}H_{21}N_3O_5K^+$: 350.1113.

2. DFT Calculations

Density functional theory (DFT) calculations were performed using Gaussian 09 package.[3] B3LYP functional and 6-31+G(d,p) basis set were used in all calculations. After the optimization calculations, we performed the frequency calculations to confirm the optimized structure (Table S3 and S4). No imaginary frequencies were found. The obtained energy values were corrected with the zero-point vibrational energy correction provided by frequency calculations. Kohn-Sham orbitals of **2a** and **4** were generated from these optimized structure using Gaussian 09 and GaussView 5.0.8 (isovalue: 0.05).

Table S2. Cartesian coordinate of optimized structure of **1a**.

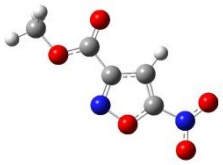


Number of imaginary frequency: 0

Sum of electronic and zero-point Energies= -529.162258 (Hartree)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	2.243213	0.129610	-0.008320
2	6	0	1.138163	0.939236	-0.008829
3	6	0	0.066099	0.009708	-0.001497
4	8	0	1.867569	-1.166813	0.001942
5	1	0	1.074489	2.014378	-0.019644
6	7	0	0.460586	-1.248525	0.005118
7	6	0	-1.373440	0.388536	0.001917
8	8	0	-1.745317	1.544724	0.007194
9	8	0	-2.191509	-0.675149	-0.001555
10	6	0	-3.595414	-0.365582	0.000902
11	1	0	-3.862161	0.215171	-0.885449
12	1	0	-4.104858	-1.328391	-0.002753
13	1	0	-3.860838	0.207758	0.892490
14	7	0	3.592616	0.362720	-0.071349
15	1	0	3.892115	1.264648	0.269039
16	1	0	4.171168	-0.404068	0.244246

Table S3. Cartesian coordinate of optimized structure of **4**.



Number of imaginary frequency: 0

Sum of electronic and zero-point Energies= -678.294545 (Hartree)

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	1.550522	-0.049569	0.000023
2	6	0	0.512619	0.824689	0.000106
3	6	0	-0.609585	-0.048336	-0.000177
4	8	0	1.129151	-1.324808	-0.000226
5	1	0	0.528374	1.901500	0.000245
6	7	0	-0.254737	-1.321744	-0.000105
7	6	0	-2.034112	0.397376	-0.000299
8	8	0	-2.335081	1.572029	0.000071
9	8	0	-2.890382	-0.627377	-0.000127
10	7	0	2.978292	0.182475	0.000104
11	8	0	3.712052	-0.798365	0.000014
12	8	0	3.320335	1.363924	0.000295
13	6	0	-4.286317	-0.264687	0.000157
14	1	0	-4.526101	0.321083	-0.889853
15	1	0	-4.828696	-1.208546	0.000088
16	1	0	-4.525817	0.320775	0.890448

3. Biological activity

Two Gram-positive *Bacillus subtilis* ATCC 6633 and *Staphylococcus aureus* ATCC 43300 and one Gram-negative *Escherichia coli* ATCC 25922 strains were used for antibacterial assays. Antifungal properties of tested compounds were evaluated on *Aspergillus niger* INA 00760 and *Candida albicans* ATCC 2091. For antibacterial assay, bacterial suspension in saline solution (3 mL) with 0.5 McFarland turbidity was added to sterile melted Mueller-Hinton agar (100 mL), inoculated medium was poured in Petri dishes and solidified. For fungi and yeasts Sabouraud

medium with 0.2% of glucose was prepared and inoculated with cell suspension, yielding 10^6 CFU in 100 mL of the resulting medium.

The antimicrobial testing of obtained compounds was carried out *in vitro* using the disk diffusion assay. Paper disks (6 mm in diameter), bearing 100 μg of analytes, were placed of the plates, then the plates were incubated at 37 °C for 24 hours. Culture growth inhibition zones were measured after 24 hours. As a positive control, standard antibiotic discs of 30 μg vancomycin (for *B. subtilis* and MRSA), 10 μg of gentamicin (for *E. coli*) and 40 μg of fluconazole (for *A. niger* and *C. albicans*) were used.

Table S4. Evaluation of antibacterial activities of **2d, 2g** and **3**.

Compound	Inhibition zones (mm)		
	B. subtilis ATCC 6633	*MRSA* ATCC 43300	*E. coli* ATCC 25922
3	20	18*	10
2d	7	9*	0
2g	10	11	0

*Diffuse inhibition zones.

4. References

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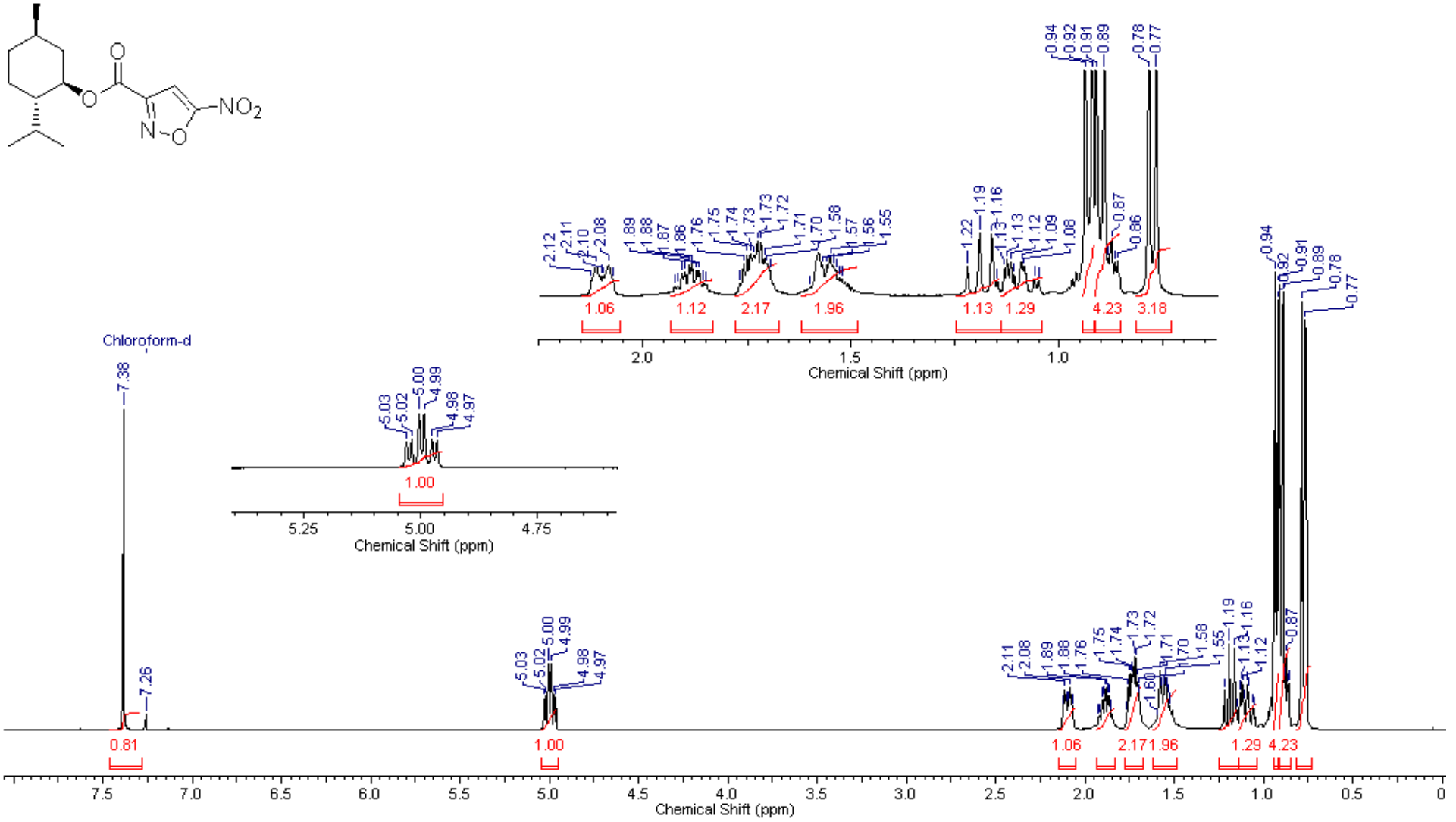
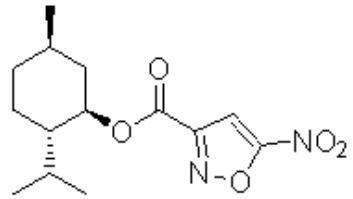
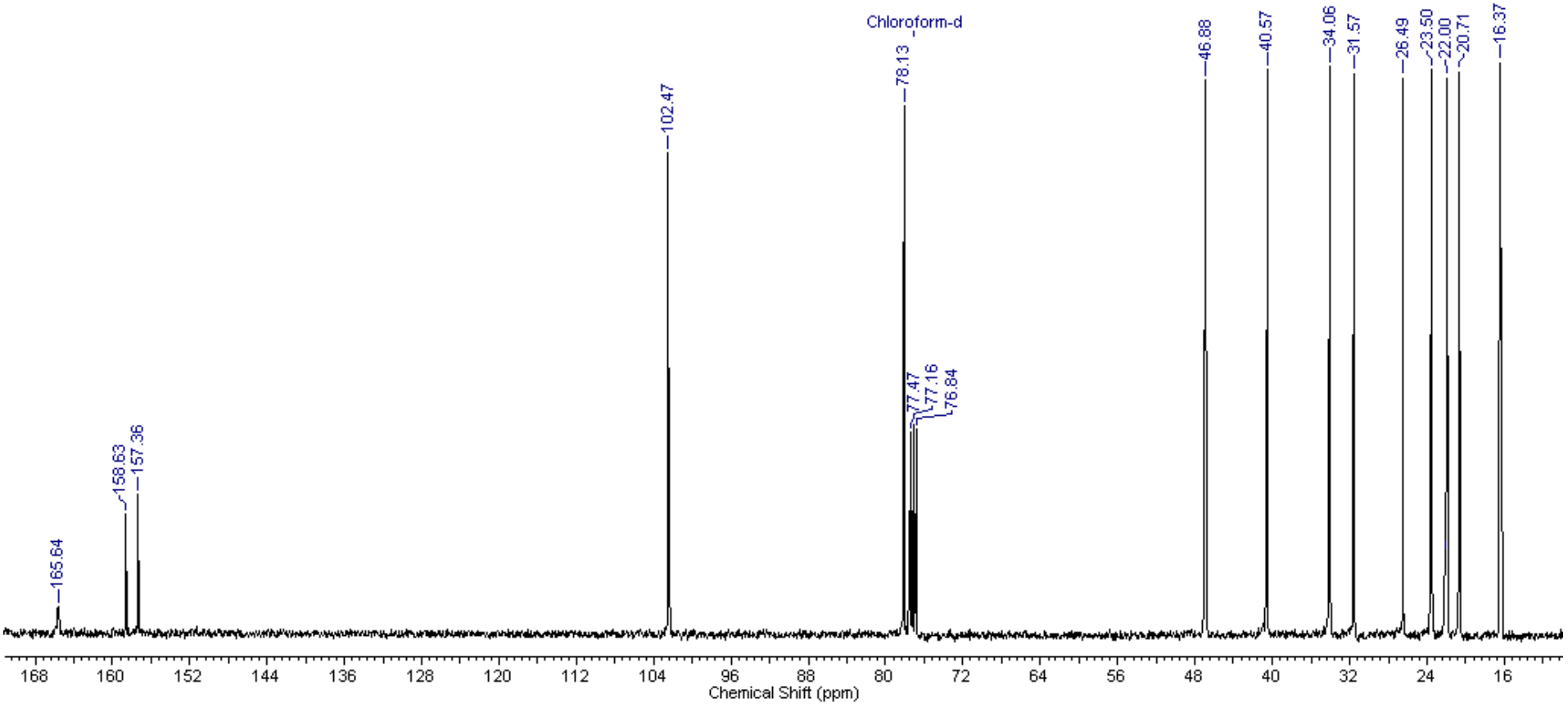
5. NMR Spectra

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 5-nitroisoxazole-3-carboxylate (^{1}H NMR)

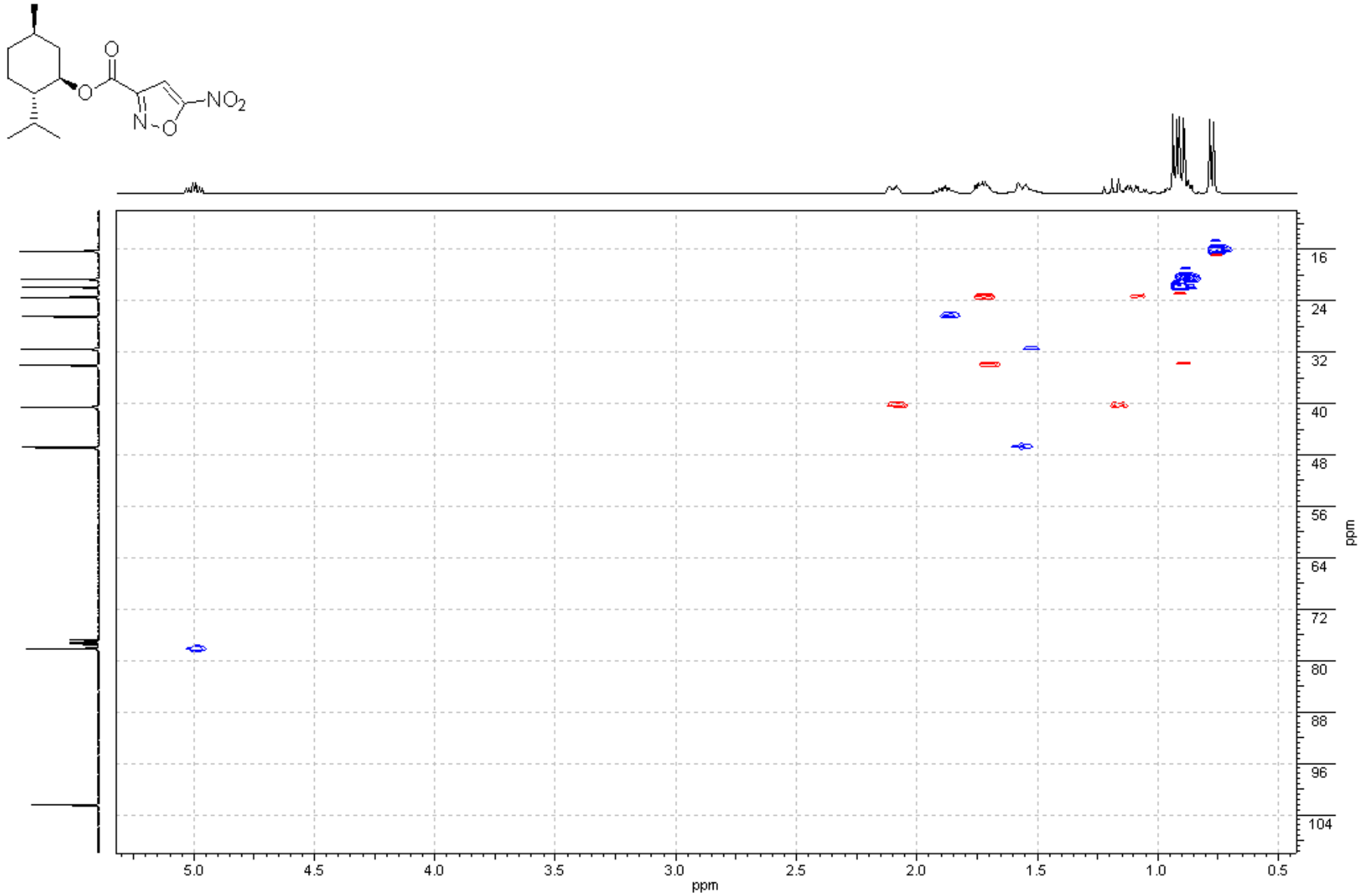


(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 5-nitroisoxazole-3-carboxylate (^{13}C NMR)

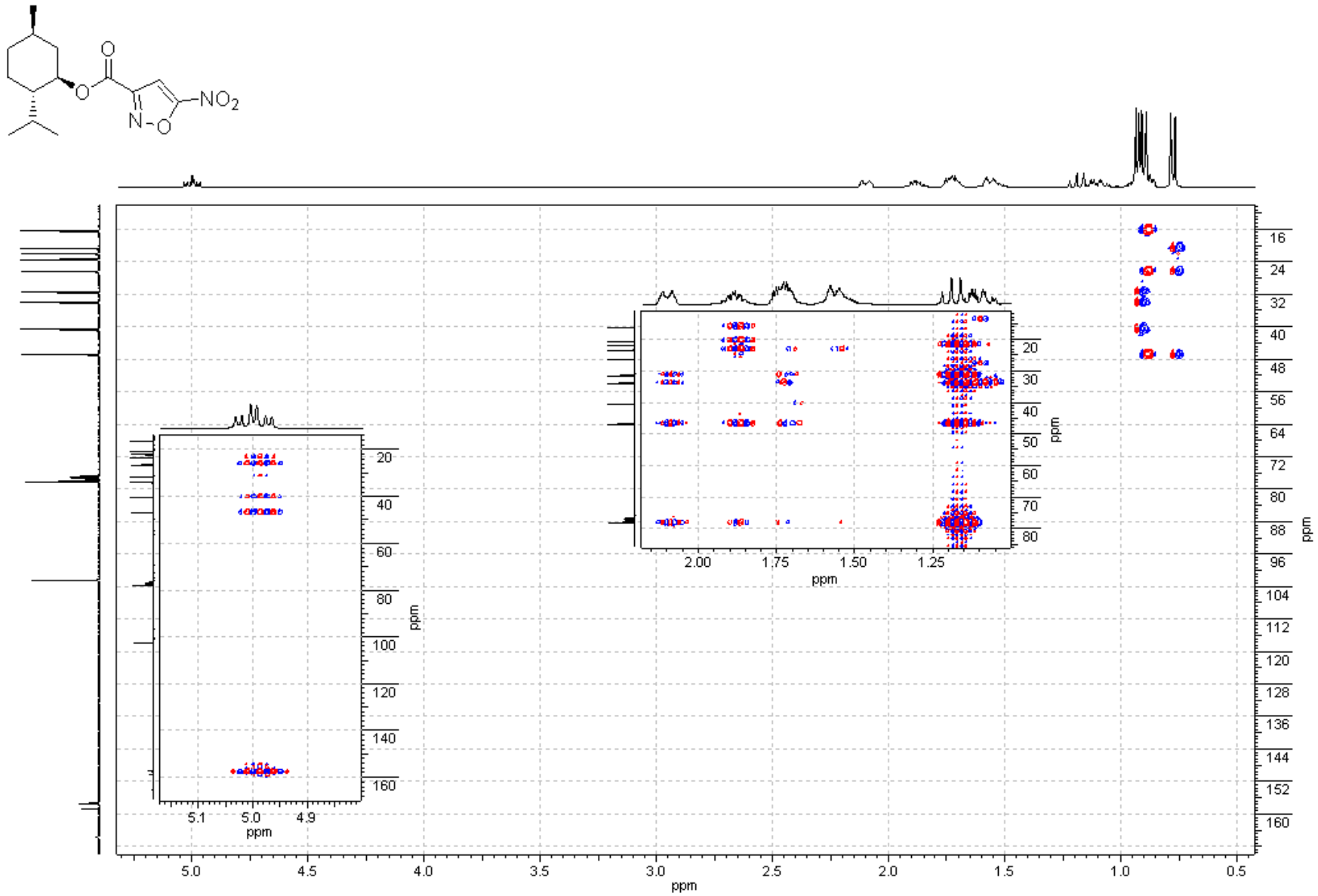




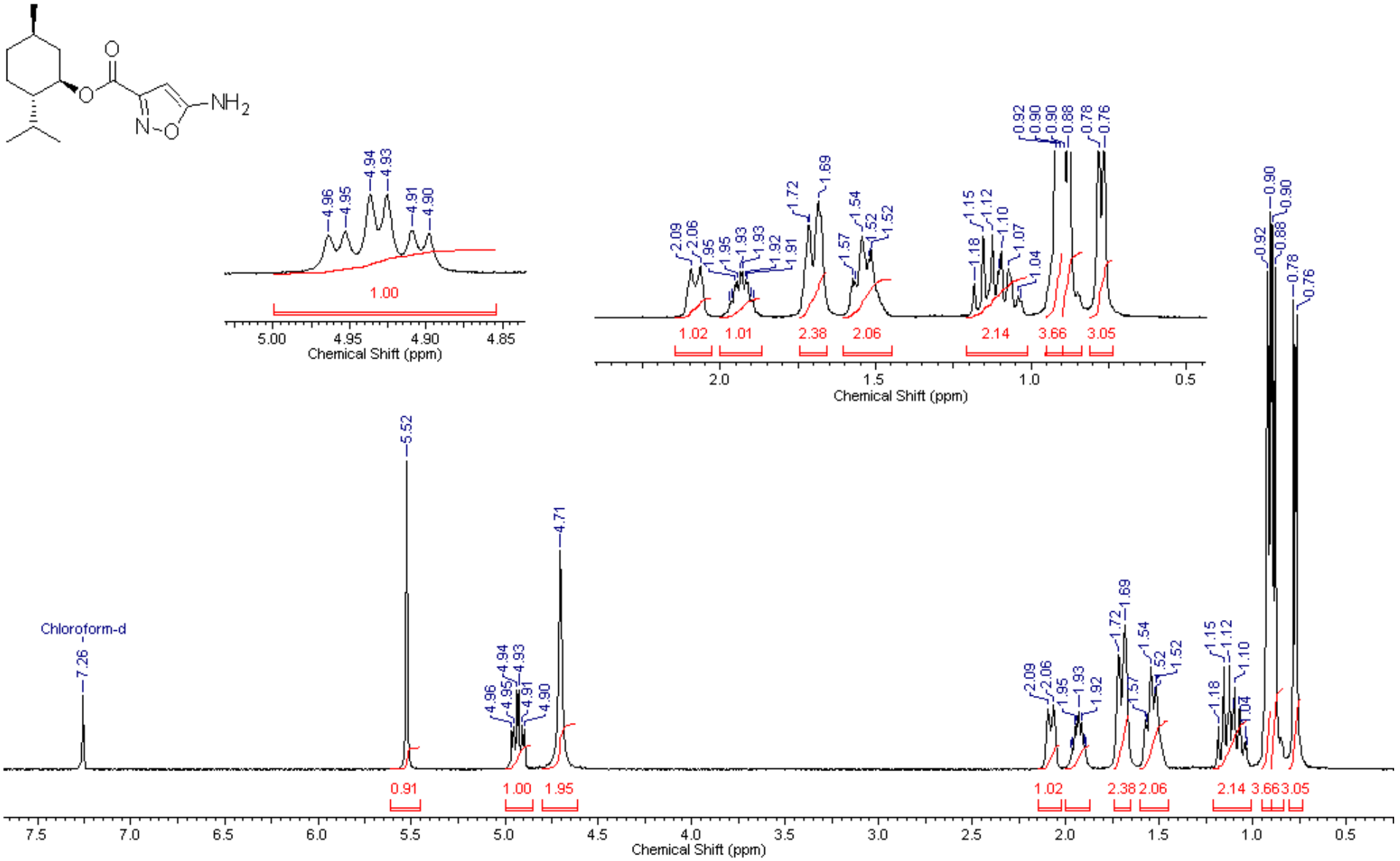
(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 5-nitroisoxazole-3-carboxylate (HSQC)



(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 5-nitroisoxazole-3-carboxylate (HMBC)



(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 5-aminoisoxazole-3-carboxylate (1g) (^{1}H NMR)



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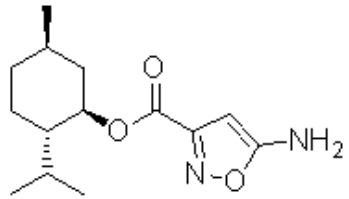
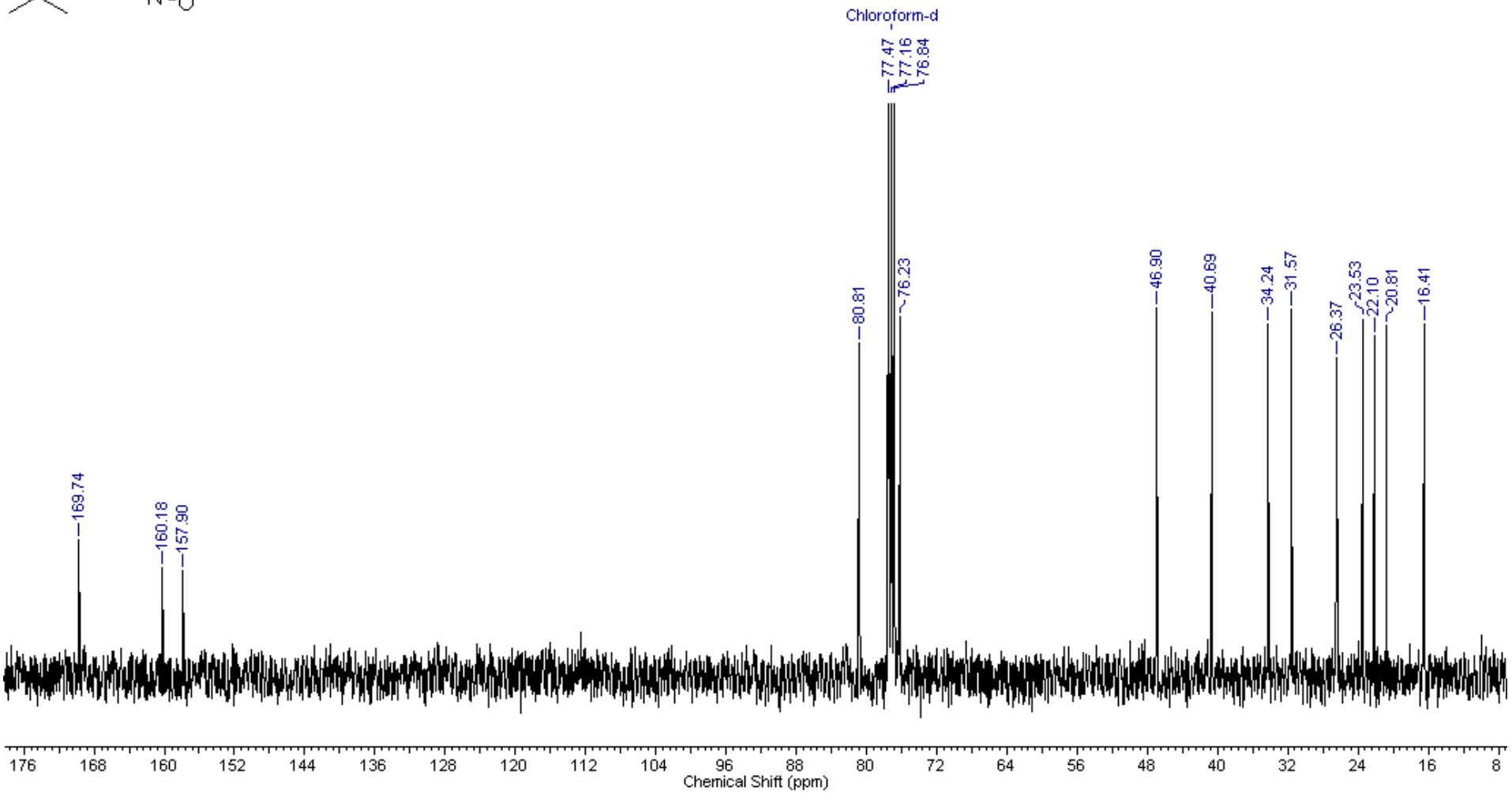
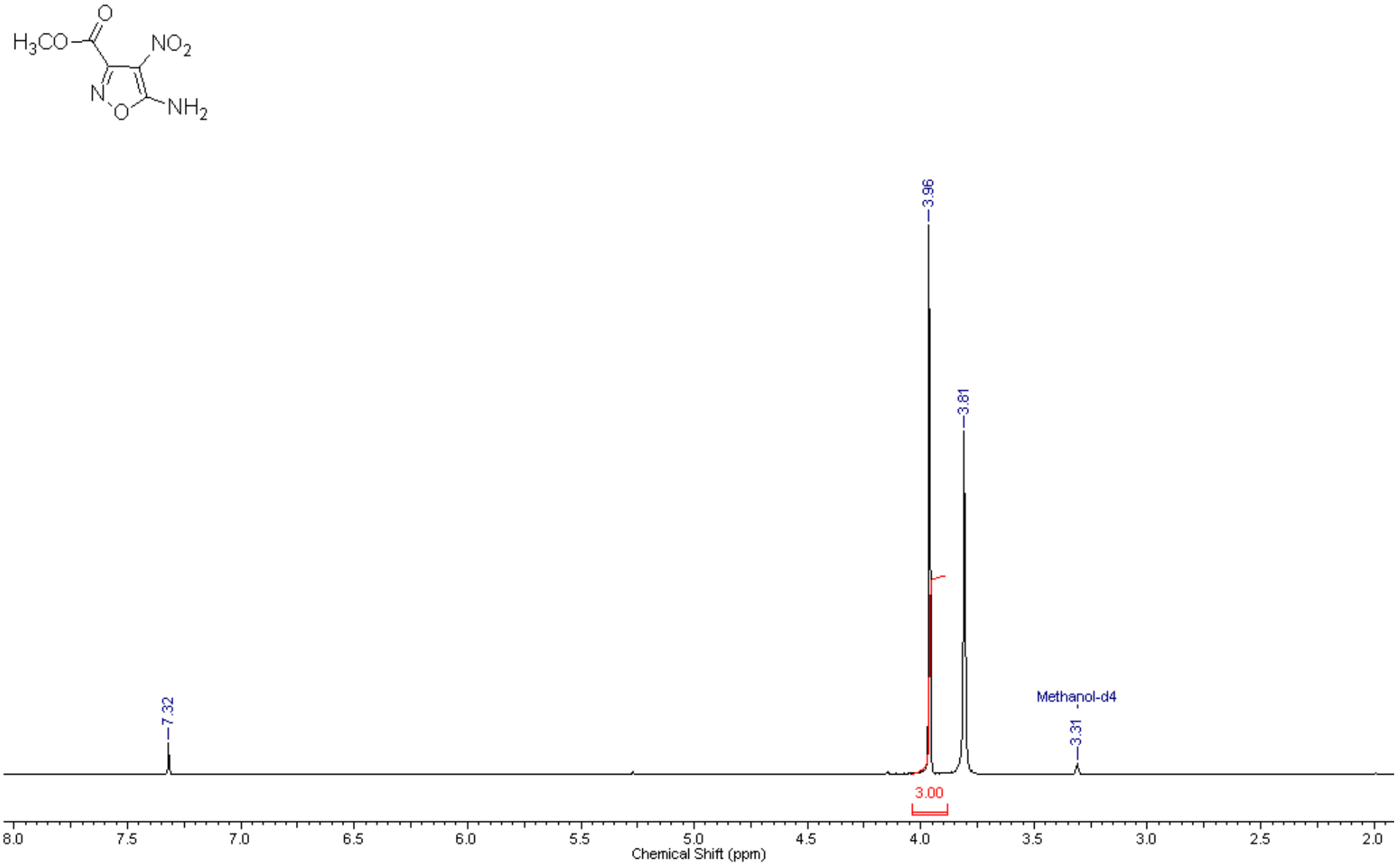
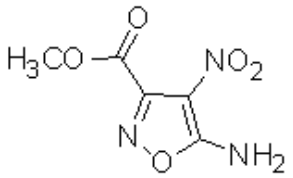


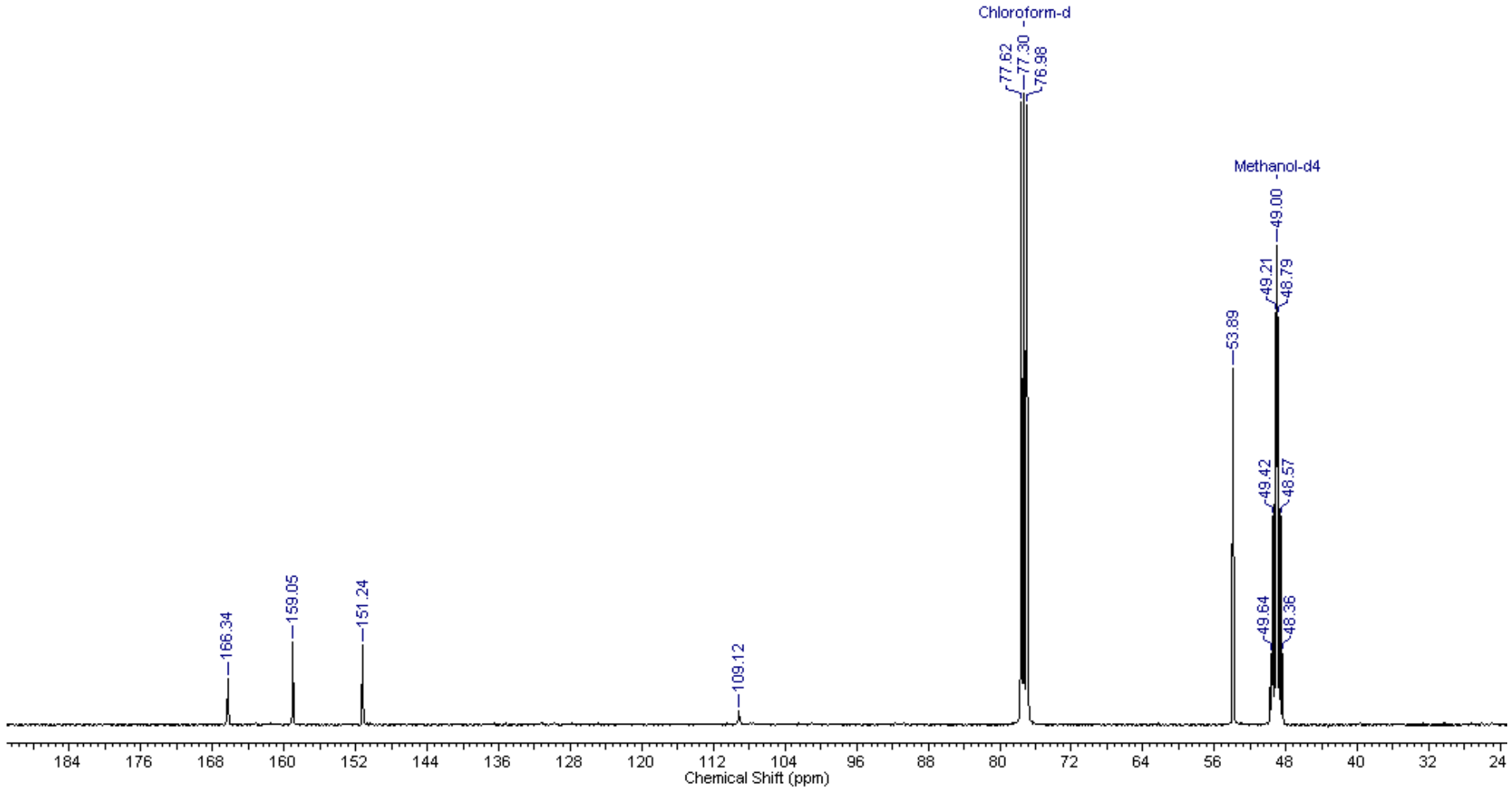


Methyl 5-amino-4-nitroisoxazole-3-carboxylate (2a) (^{1}H NMR)

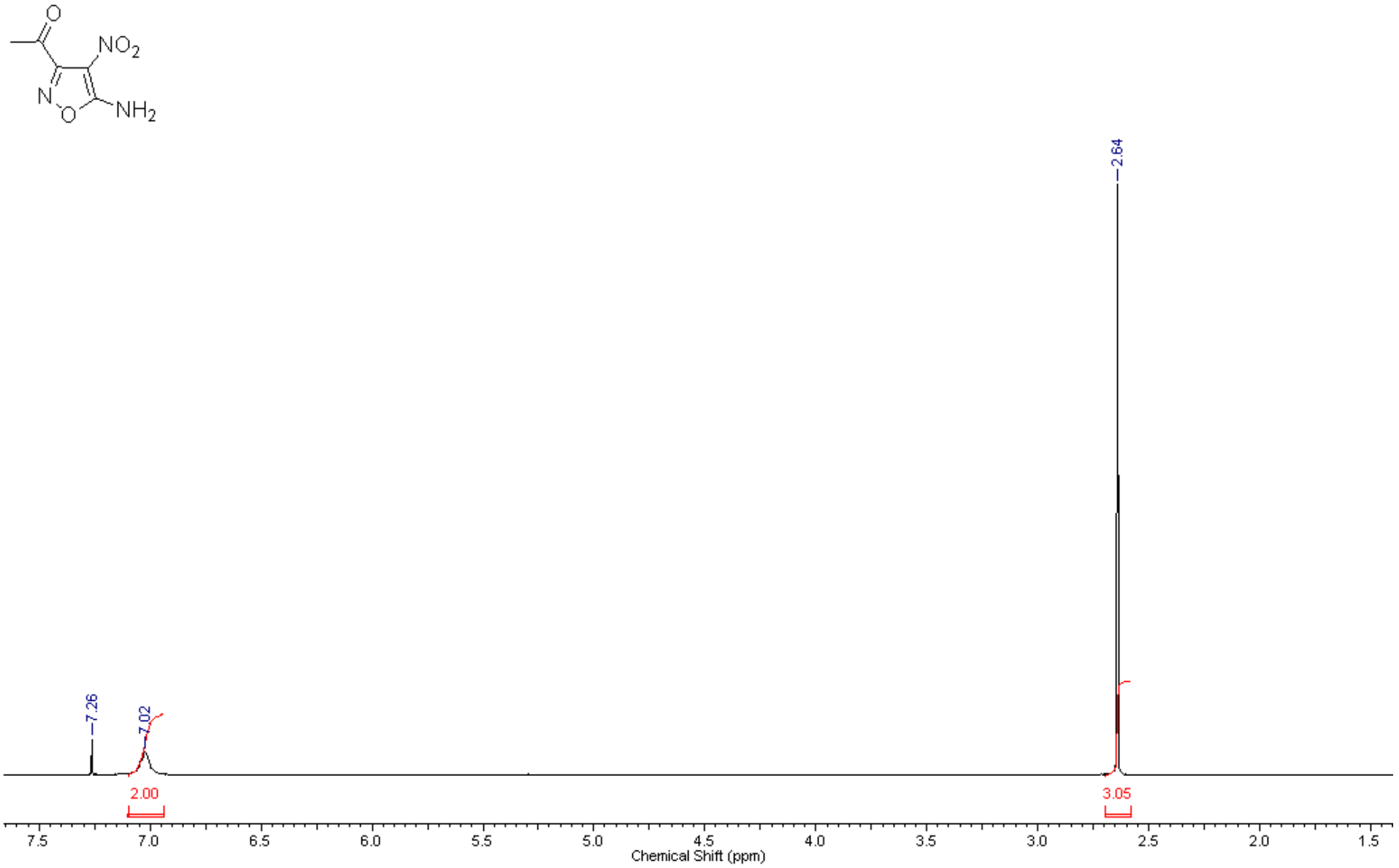


Methyl 5-amino-4-nitroisoxazole-3-carboxylate (2a) (^{13}C NMR)

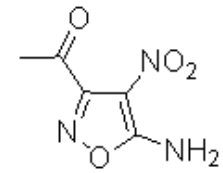


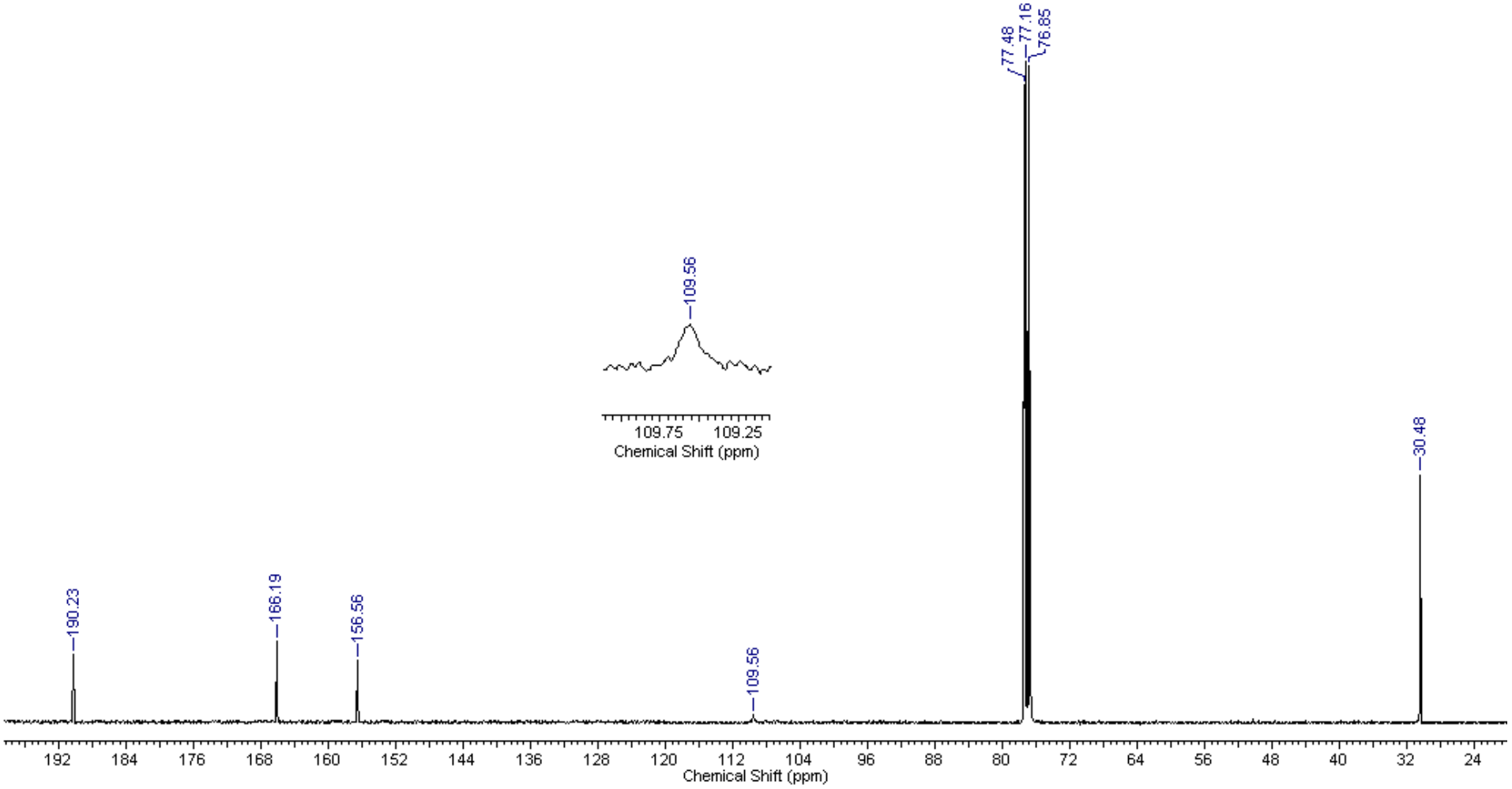


1-(5-Amino-4-nitroisoxazol-3-yl)ethanone (2b) (^{1}H NMR)

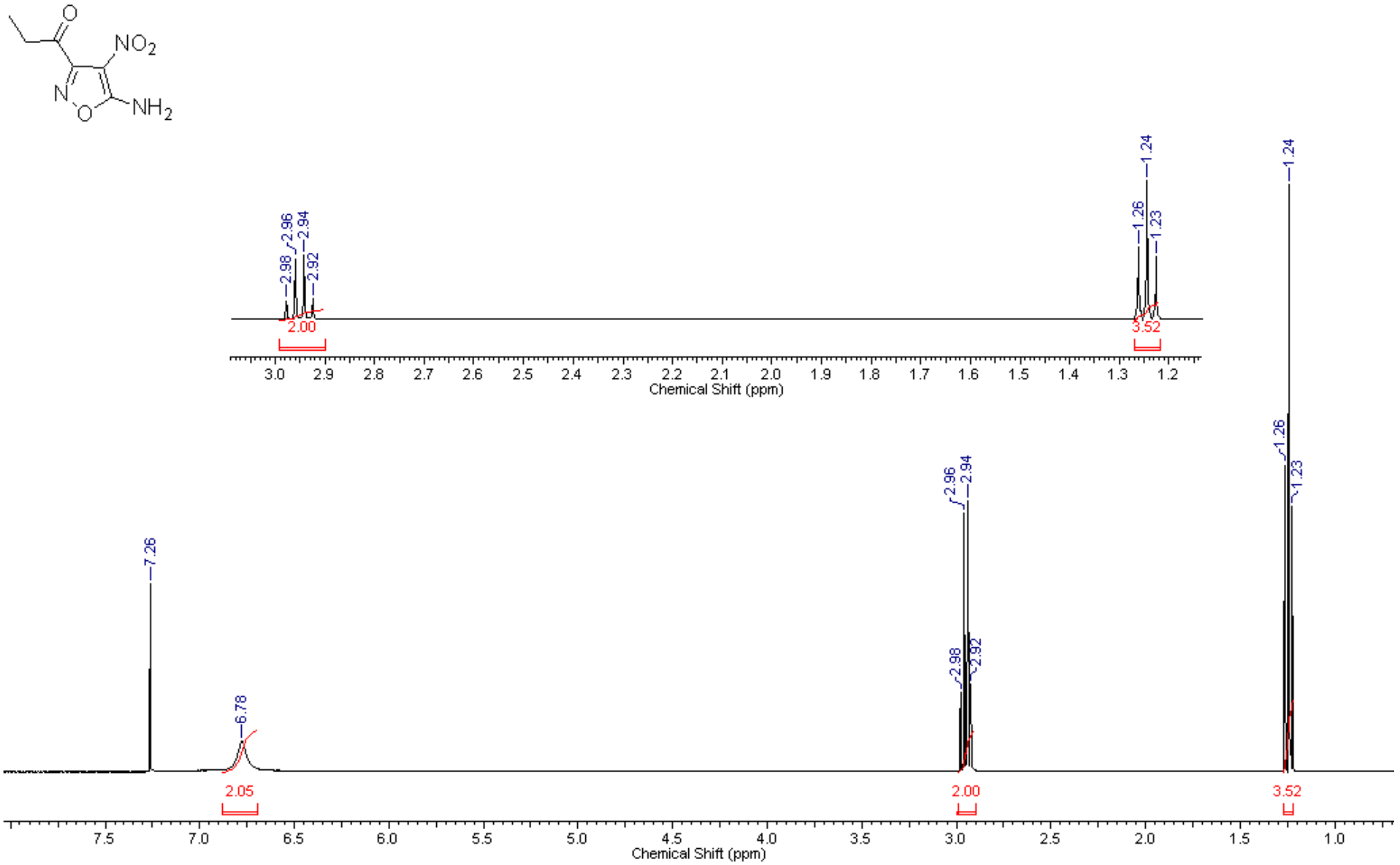


1-(5-Amino-4-nitroisoxazol-3-yl)ethanone (2b) (^{13}C NMR)

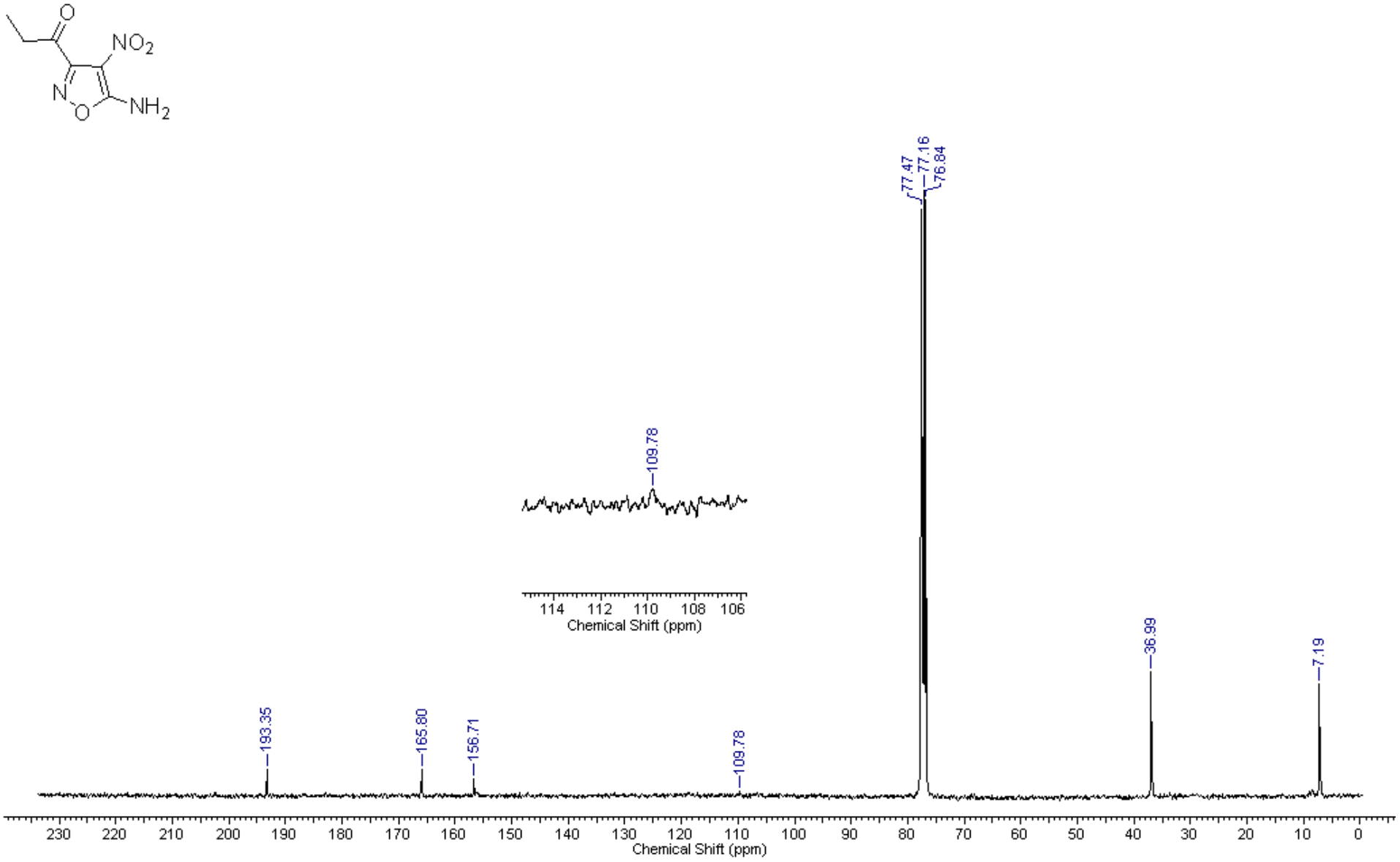




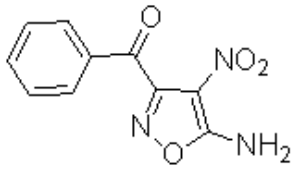
1-(5-Amino-4-nitroisoxazol-3-yl)propan-1-one (2c) (^{1}H NMR)

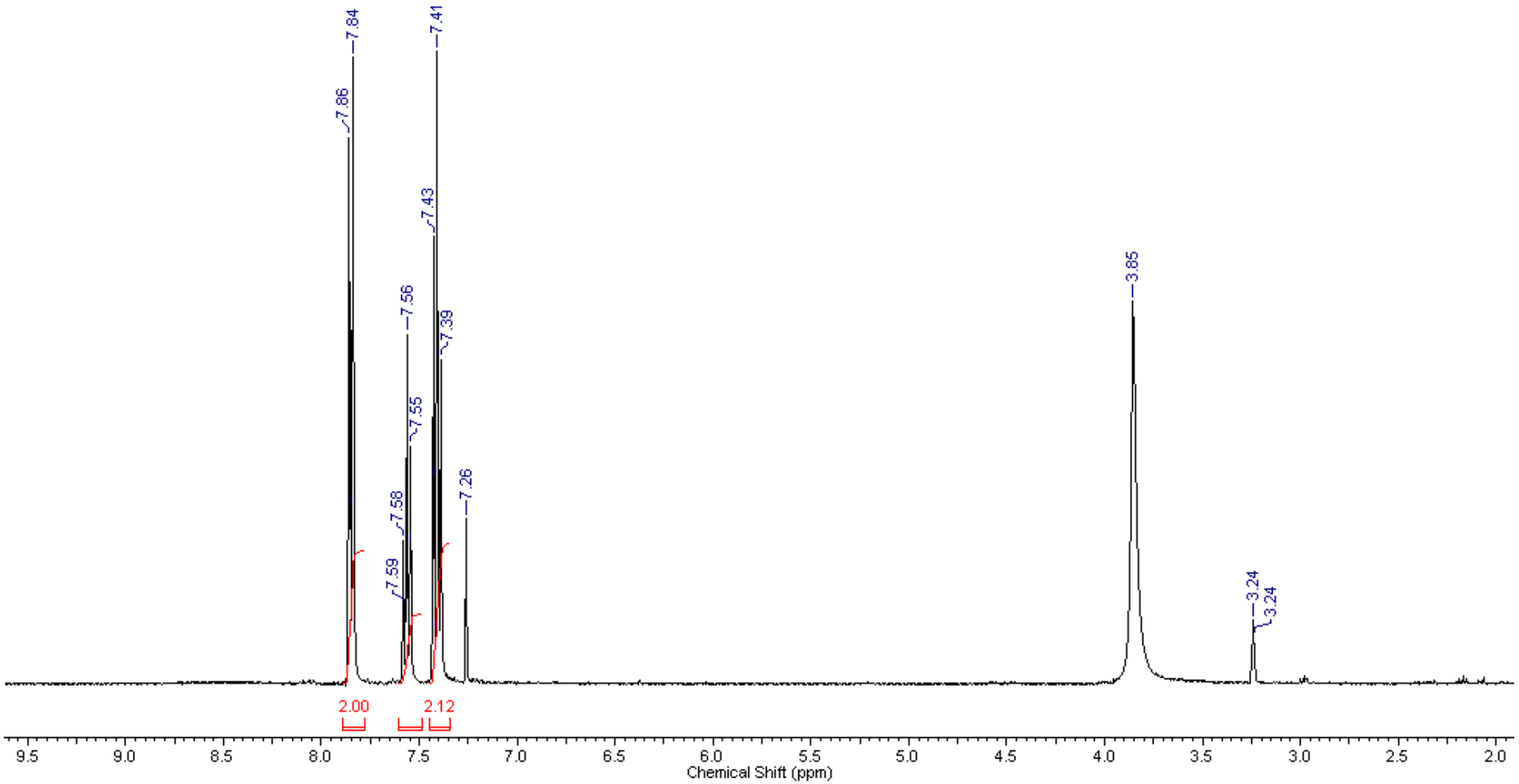


1-(5-Amino-4-nitroisoxazol-3-yl)propan-1-one (2c) (^{13}C NMR)

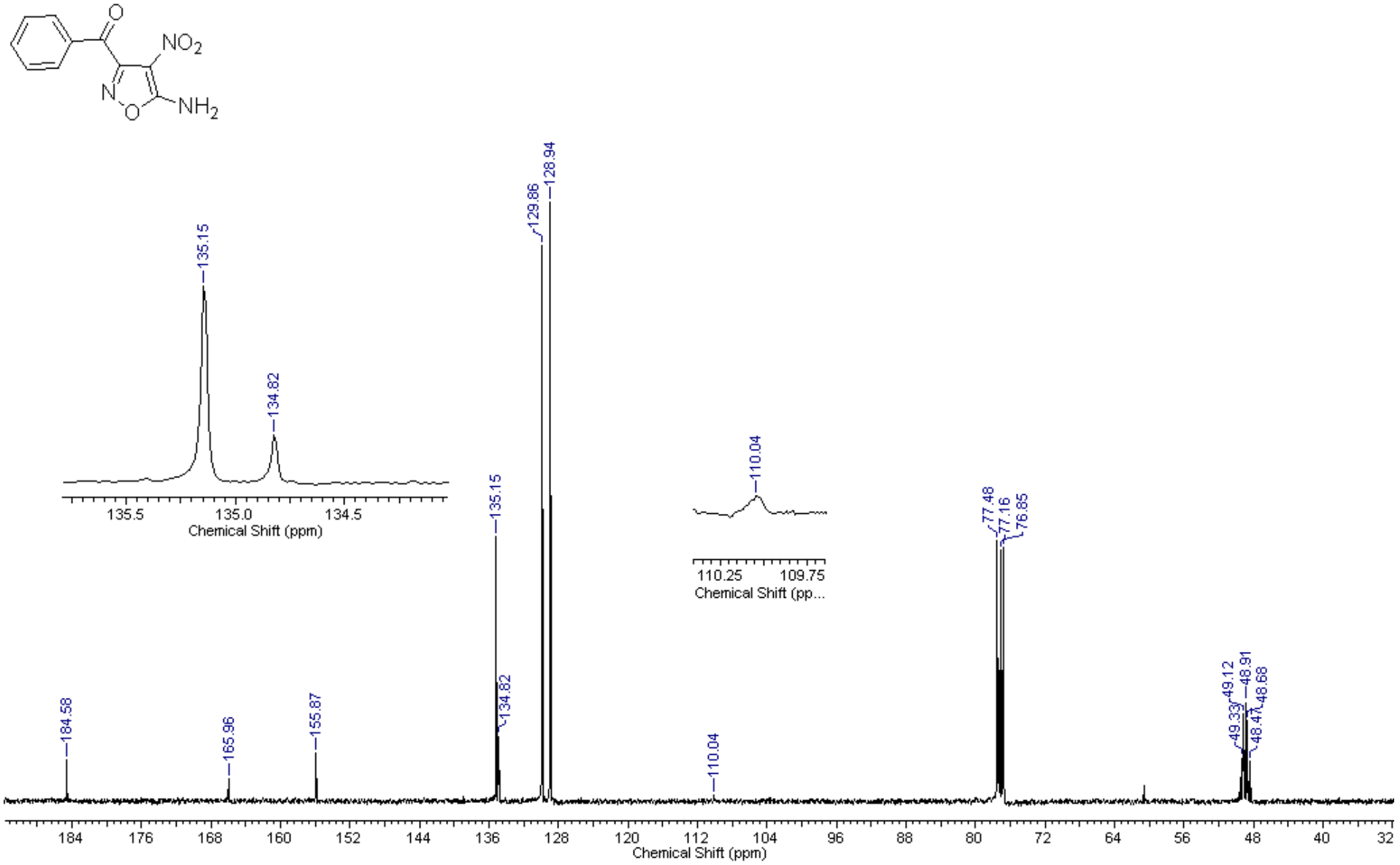


(5-Amino-4-nitroisoxazol-3-yl)(phenyl)methanone (2d) (^{1}H NMR)

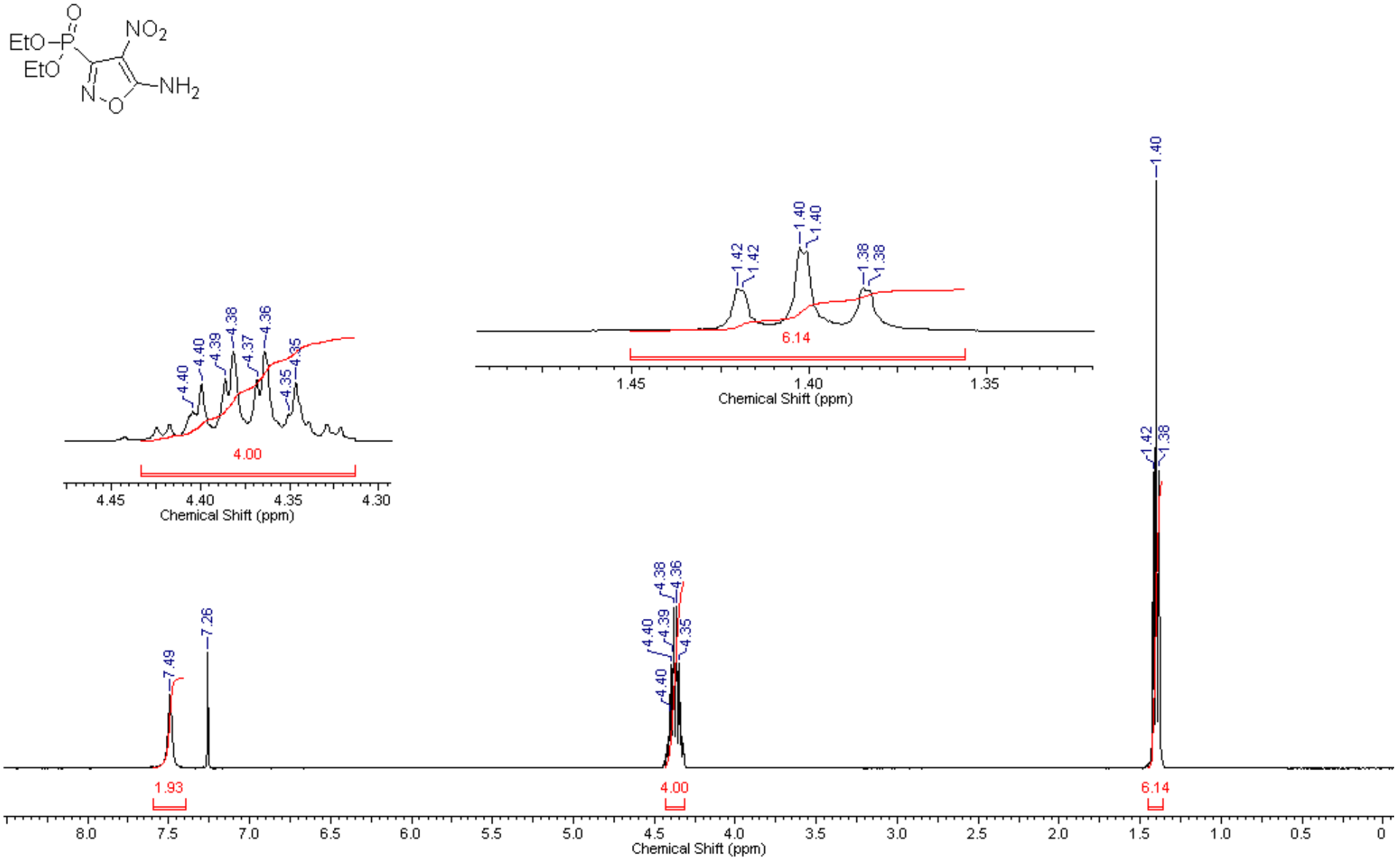




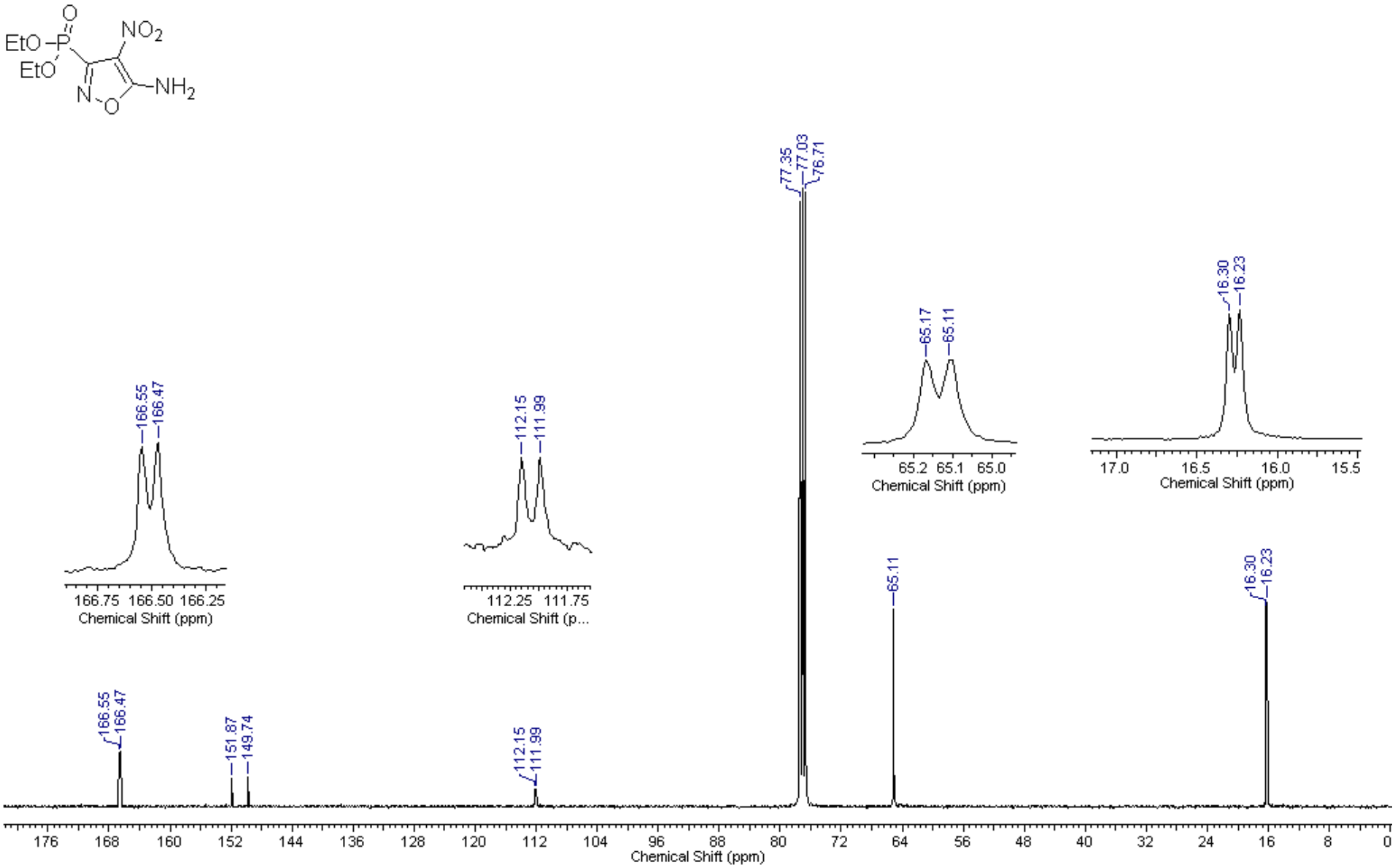
(5-Amino-4-nitroisoxazol-3-yl)(phenyl)methanone (2d) (^{13}C NMR)



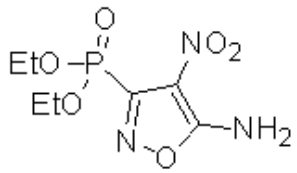
Diethyl (5-amino-4-nitroisoxazol-3-yl)phosphonate (2e) (^{1}H NMR)

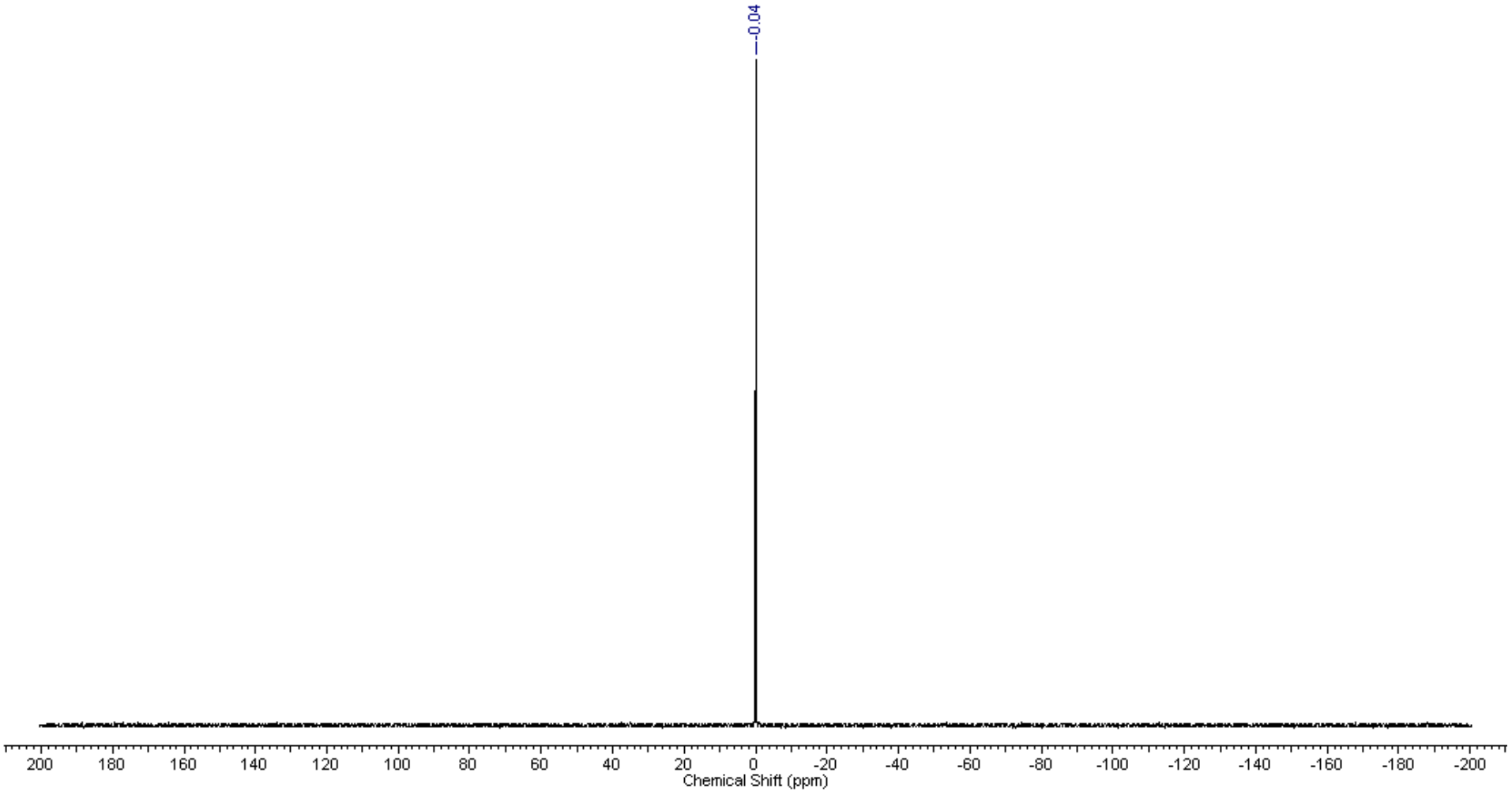


Diethyl (5-amino-4-nitroisoxazol-3-yl)phosphonate (2e) (^{13}C NMR)

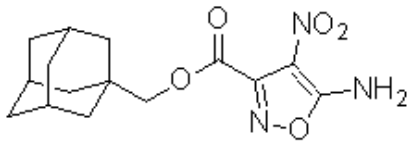


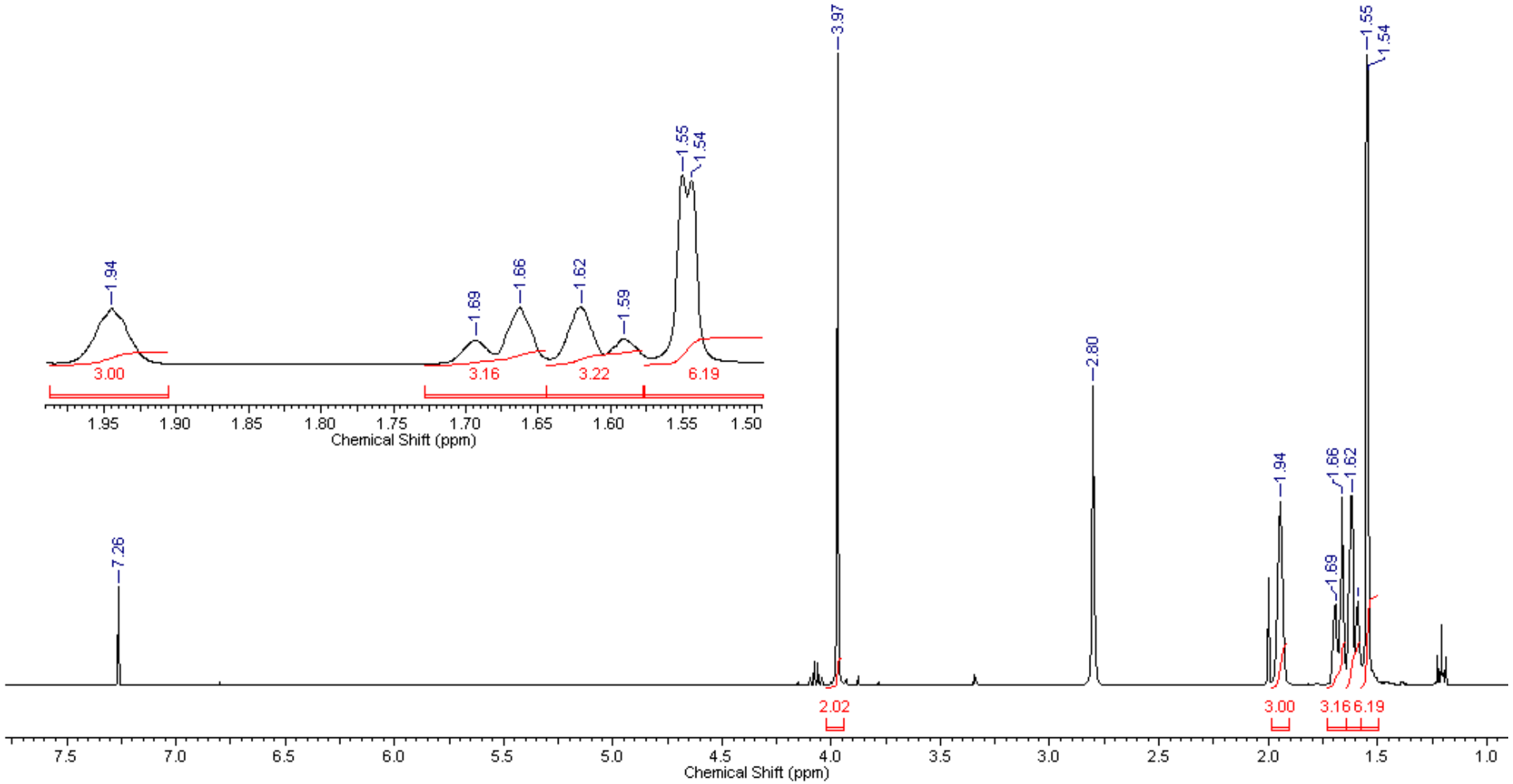
Diethyl (5-amino-4-nitroisoxazol-3-yl)phosphonate (2e) (^{31}P NMR)



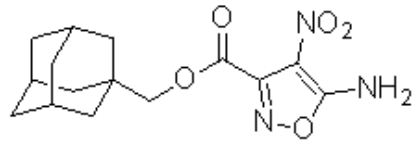


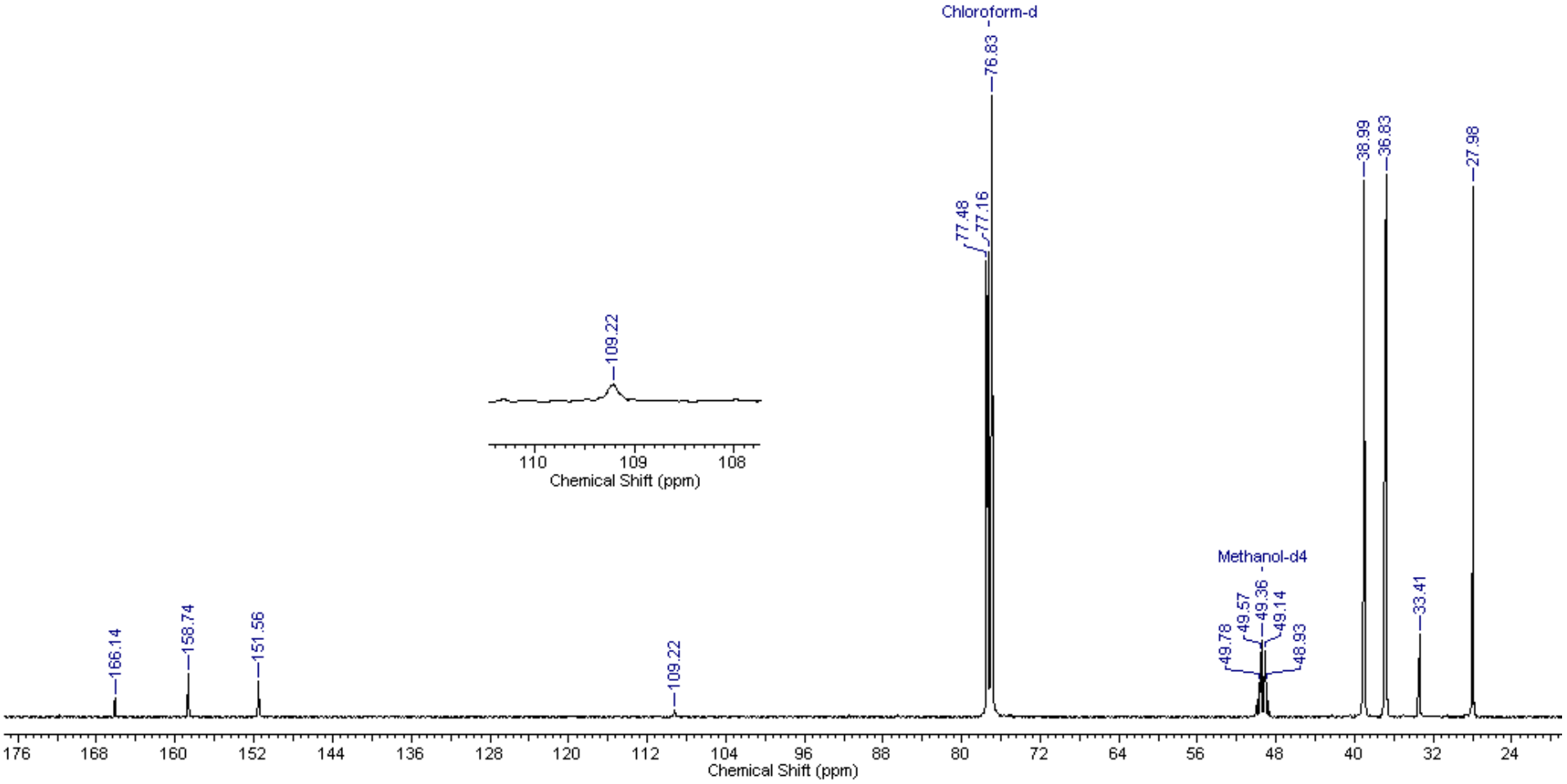
Adamantan-1-ylmethyl 5-amino-4-nitroisoxazole-3-carboxylate (2f) (^{1}H NMR)



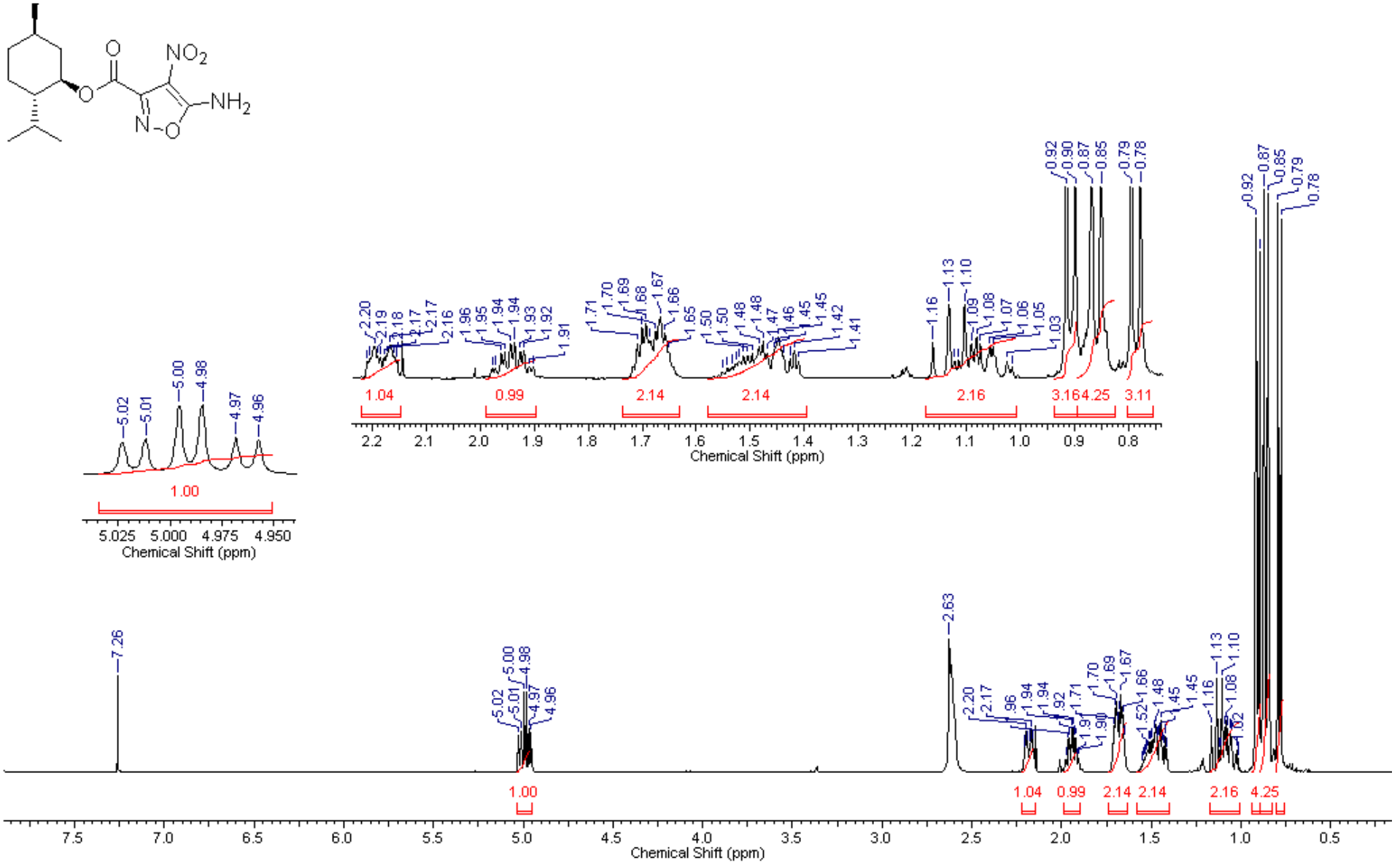


Adamantan-1-ylmethyl 5-amino-4-nitroisoxazole-3-carboxylate (2f) (^{13}C NMR)

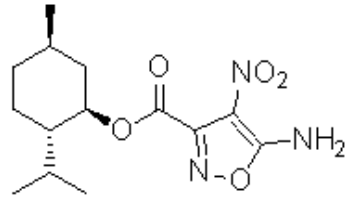


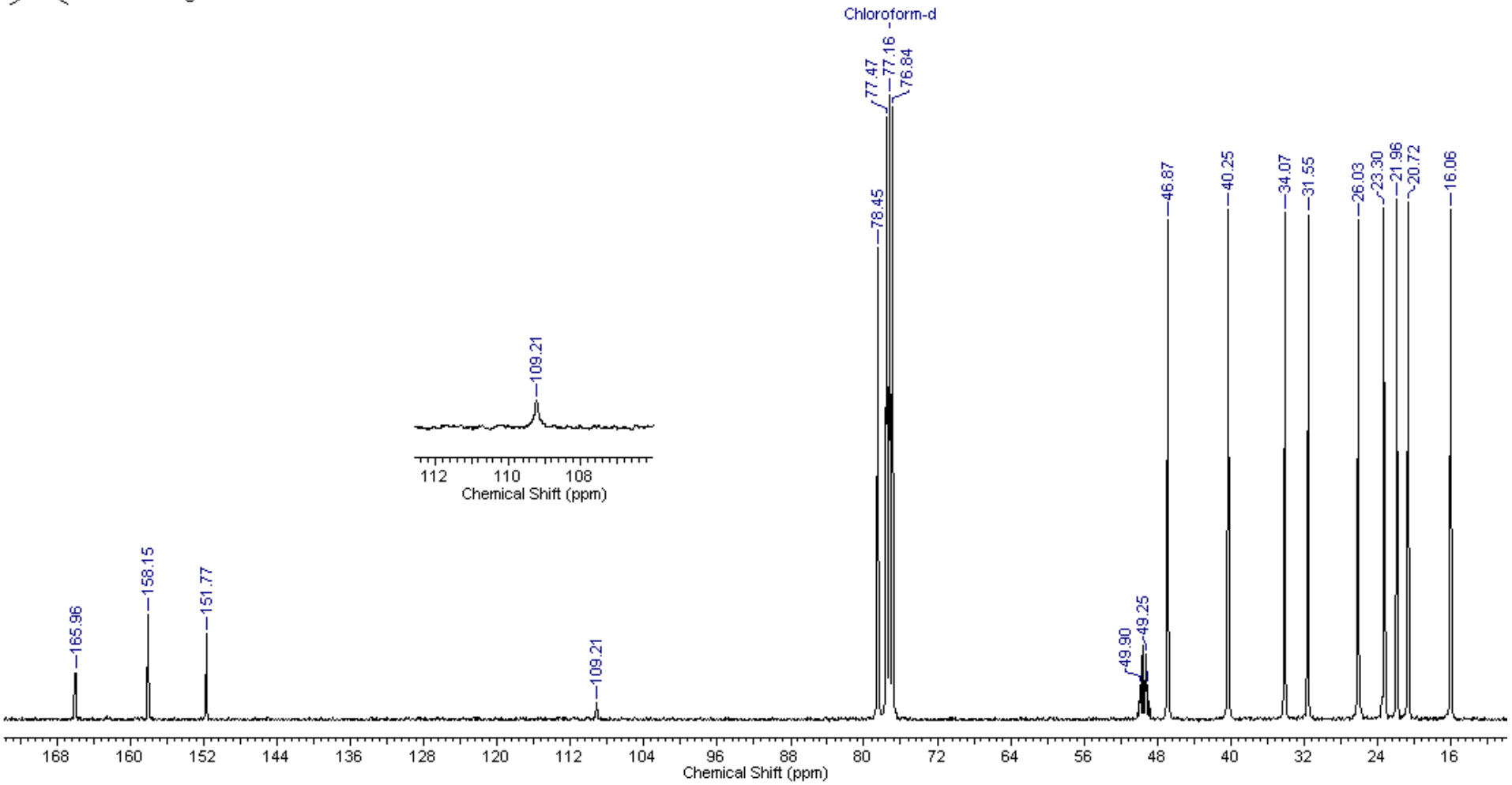


(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 5-amino-4-nitroisoxazole-3-carboxylate (2g) (^{1}H NMR)

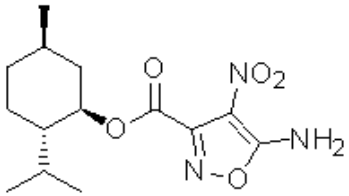


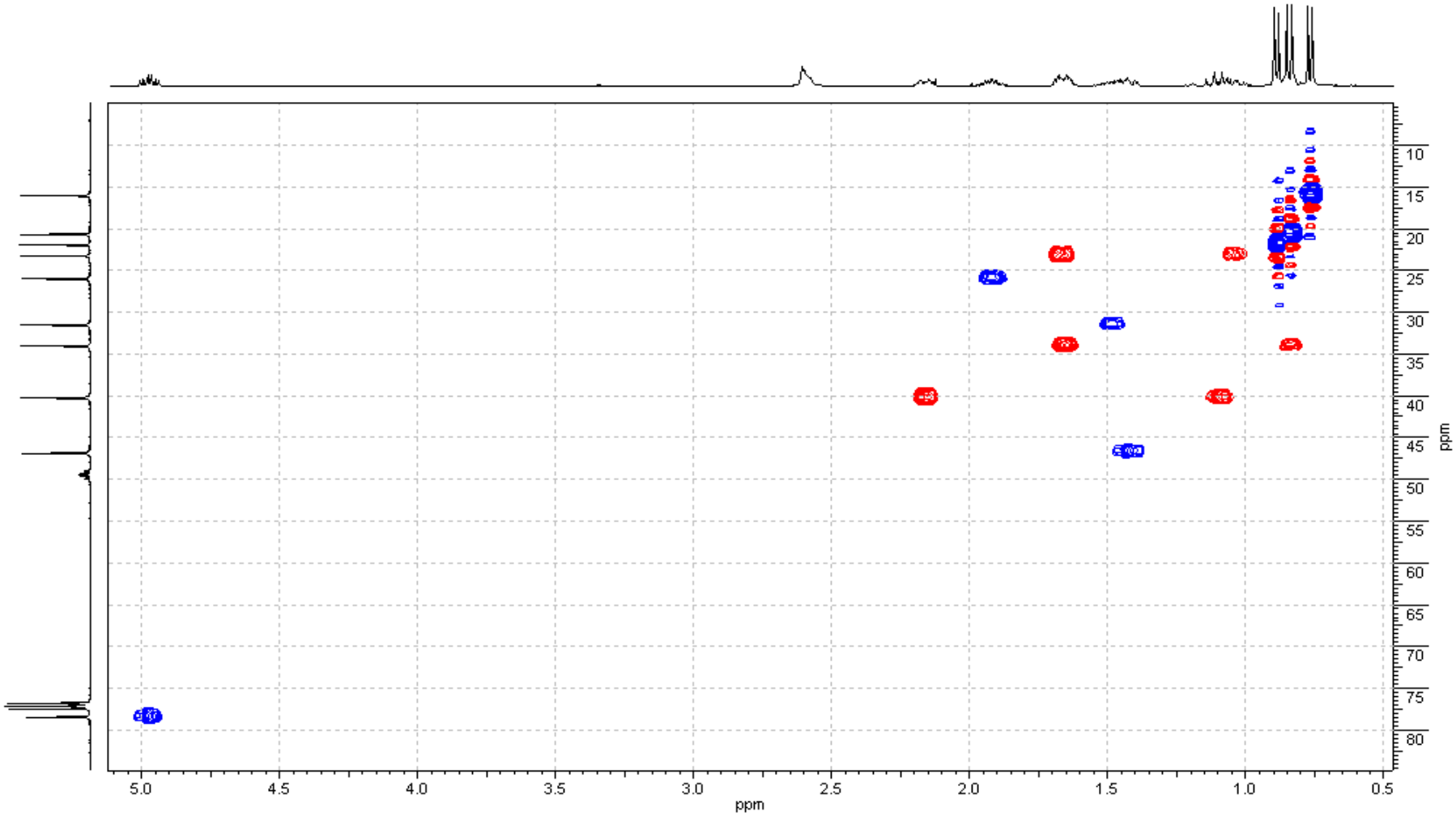
(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 5-amino-4-nitroisoxazole-3-carboxylate (2g) (^{13}C NMR)





(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 5-amino-4-nitroisoxazole-3-carboxylate (2g) (HSQC)





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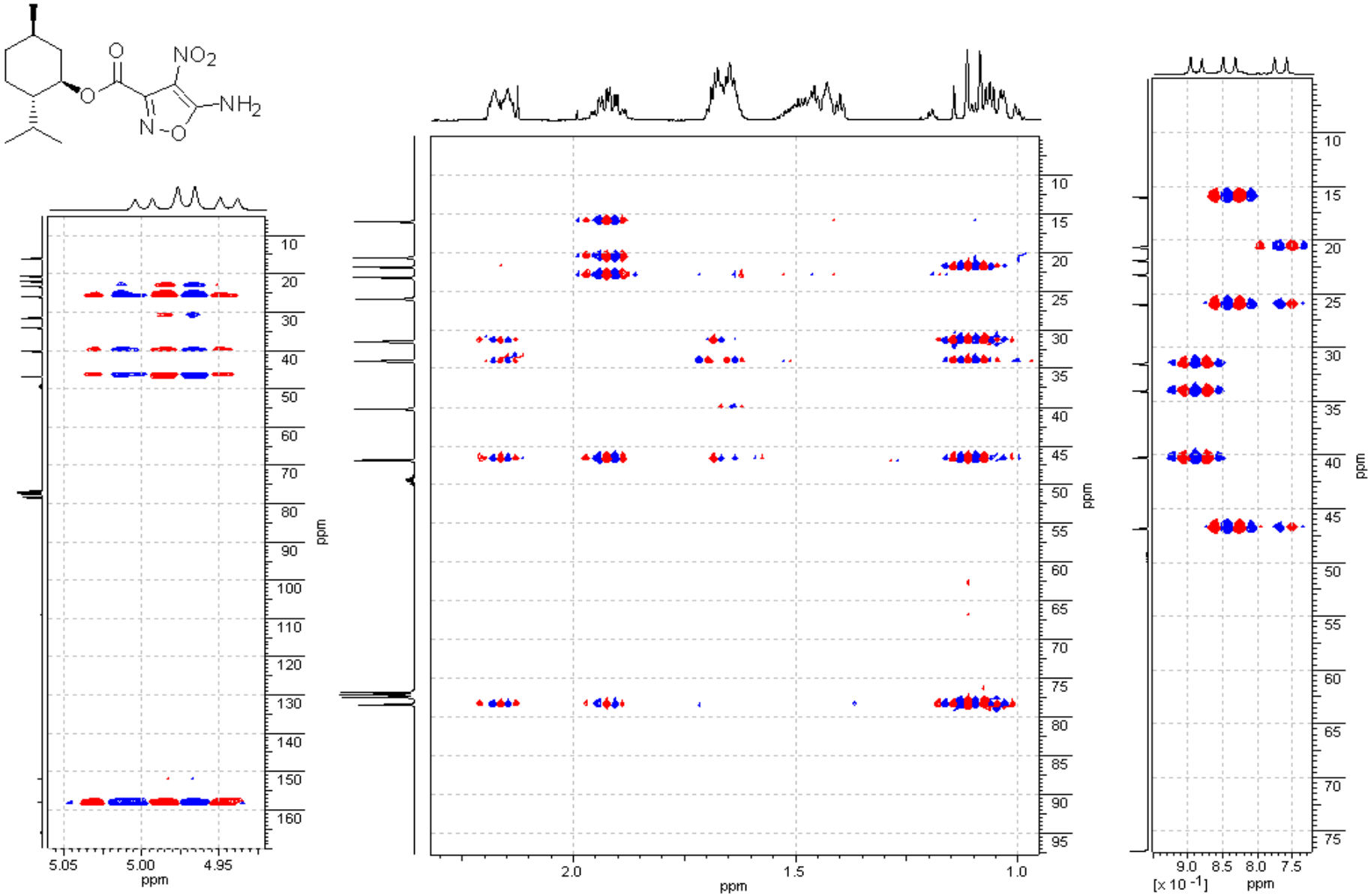
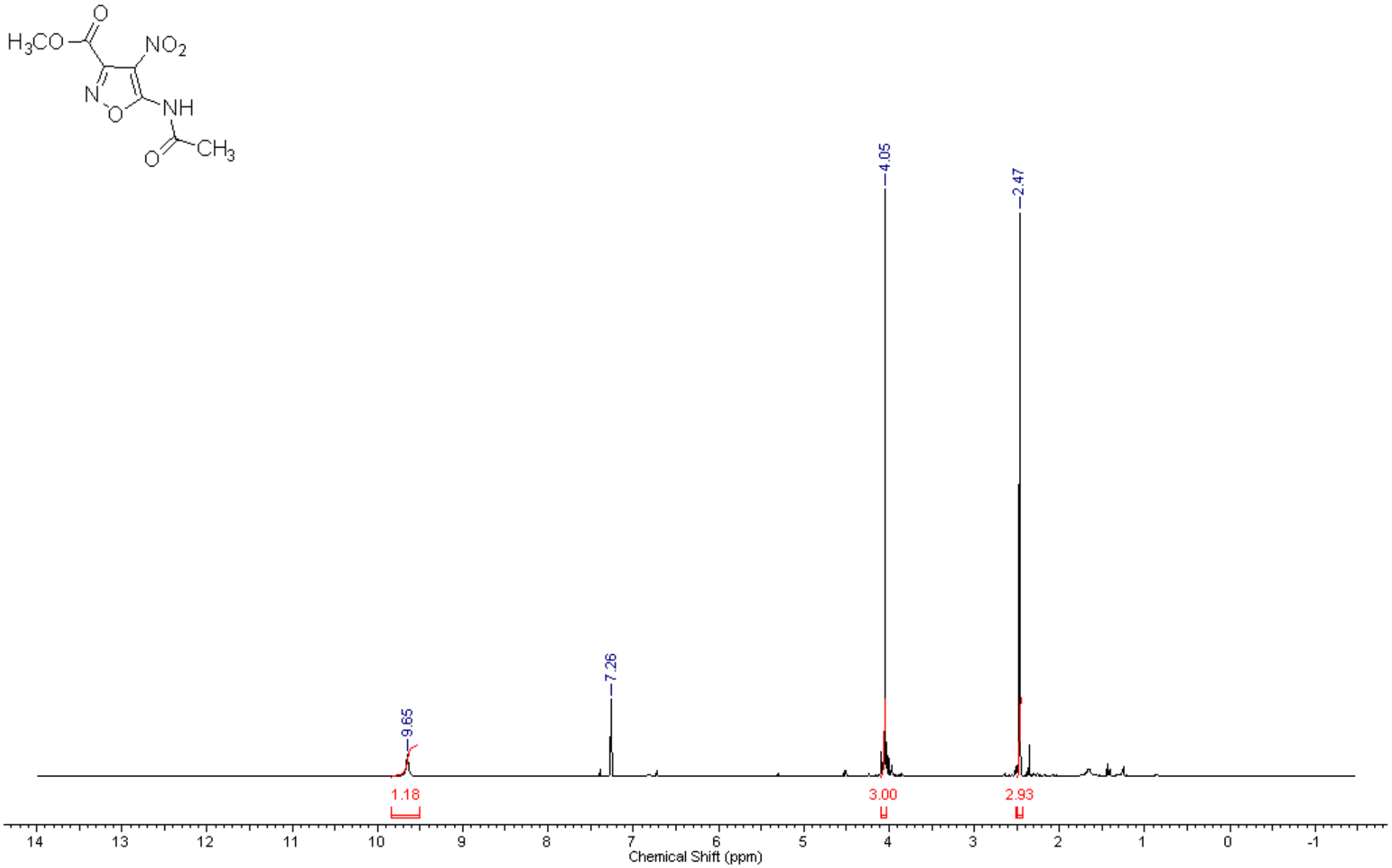
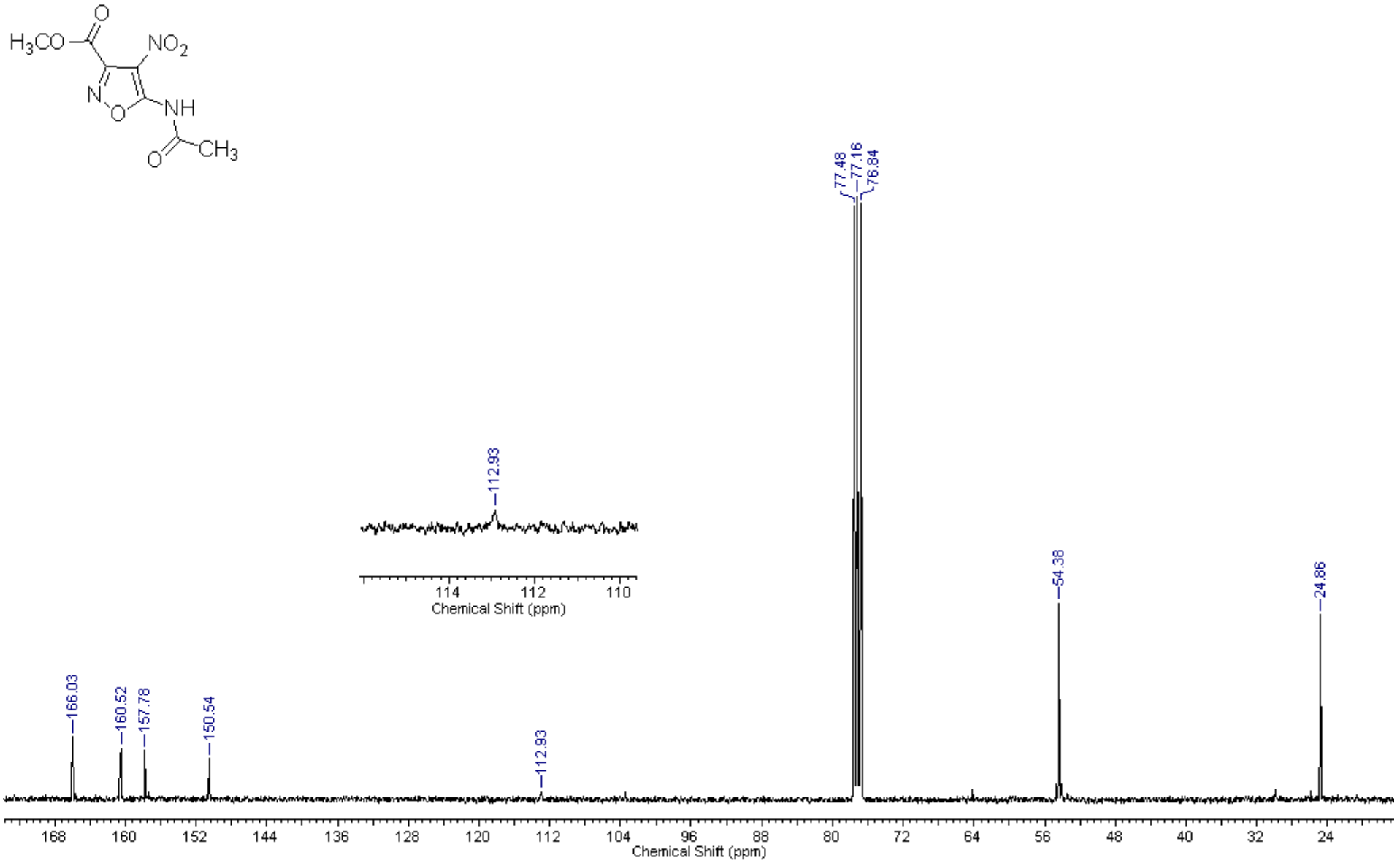


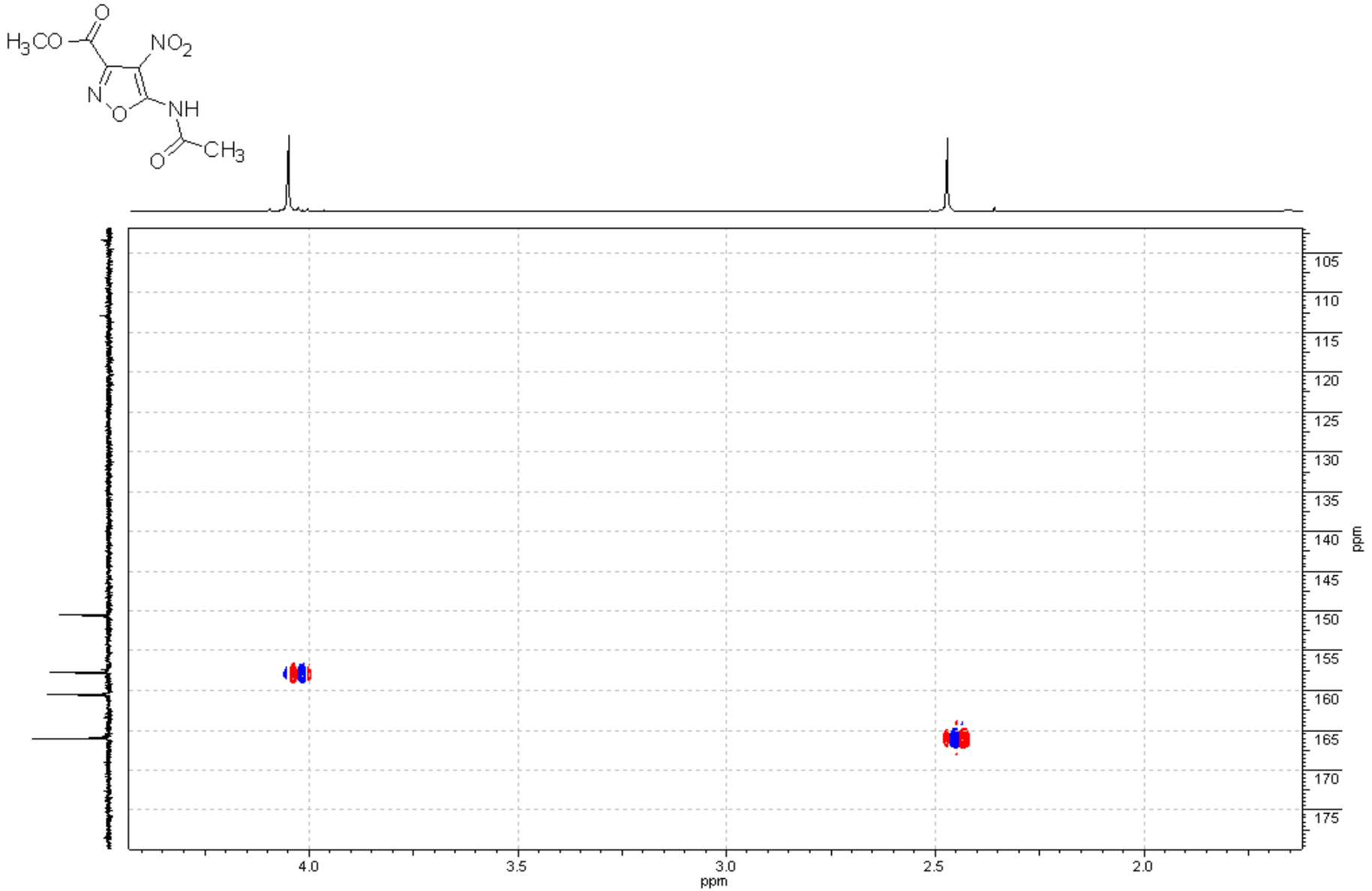
Methyl 5-acetylamino-4-nitroisoxazole-3-carboxylate (3) (^{1}H NMR)



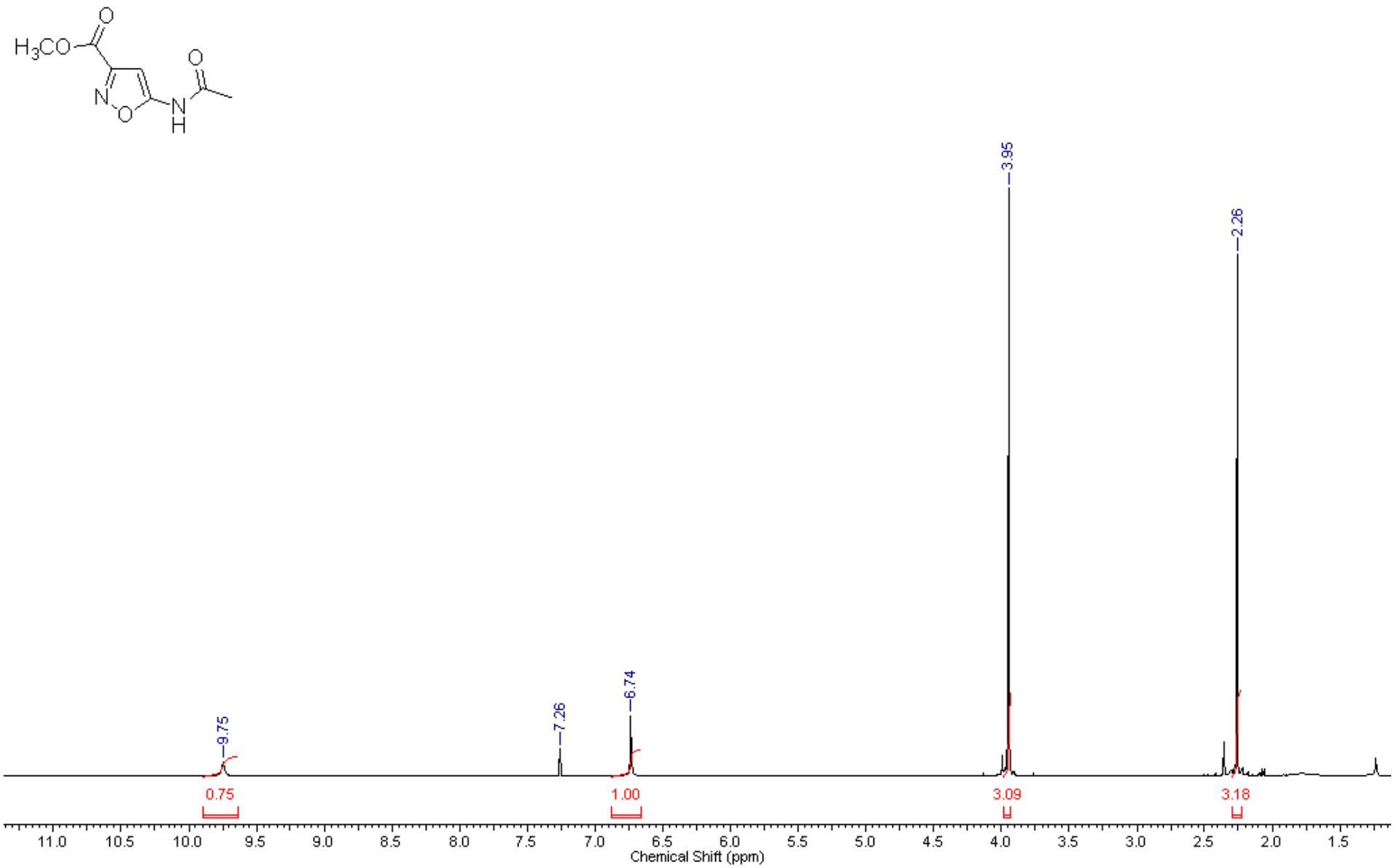
Methyl 5-acetylamino-4-nitroisoxazole-3-carboxylate (3) (^{13}C NMR)



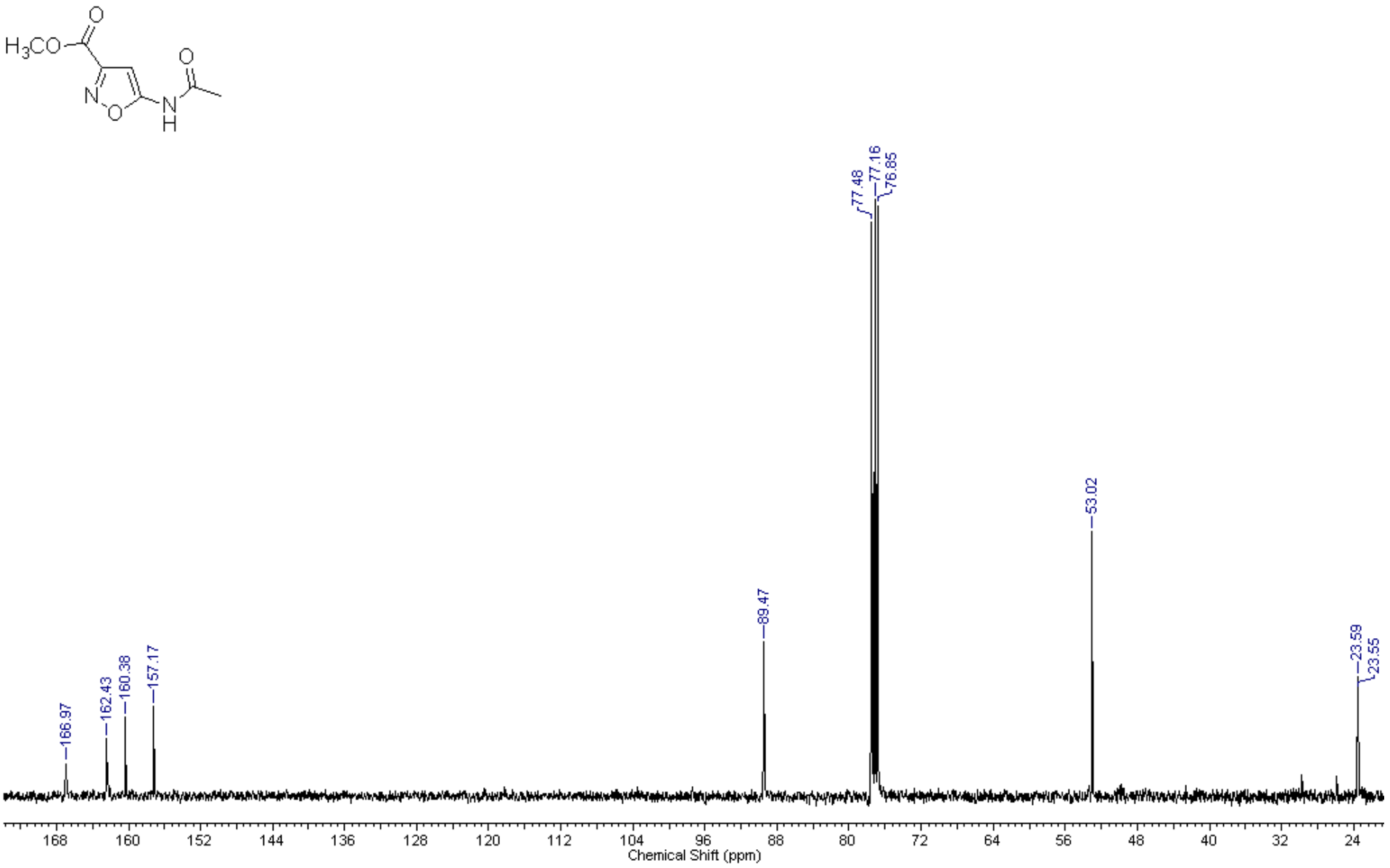
Methyl 5-acetylamino-4-nitroisoxazole-3-carboxylate (3) (HMBC)



Methyl 5-(acetylamino)isoxazole-3-carboxylate (5) (^{1}H NMR)



Methyl 5-(acetylamino)isoxazole-3-carboxylate (5) (^{13}C NMR)



Methyl 5-(acetylamino)isoxazole-3-carboxylate (5) (HMBC)