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A method for the synthesis of spiro-1,3,4-thiadiazolines

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SUPPLEMENTARY INFORMATION

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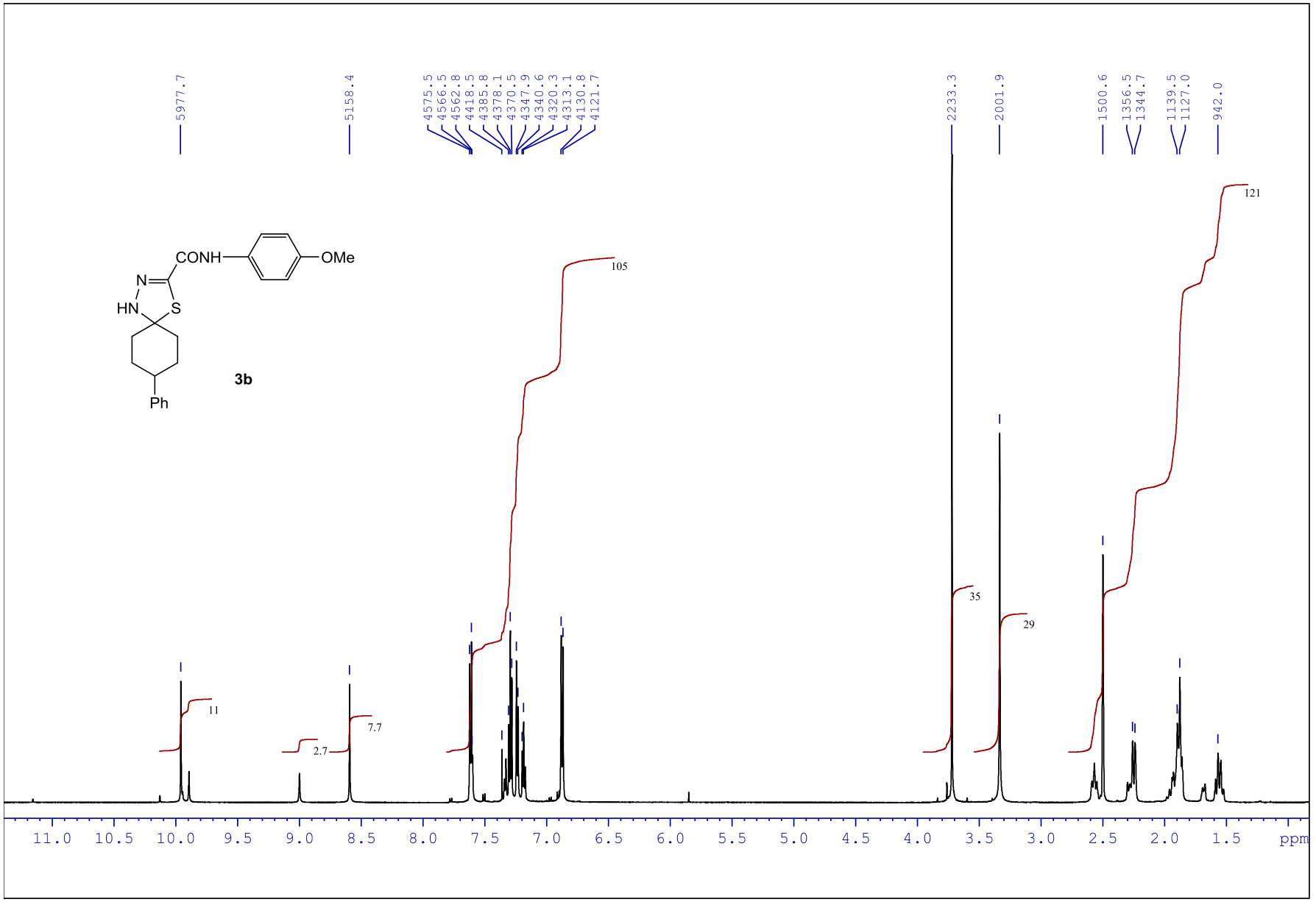
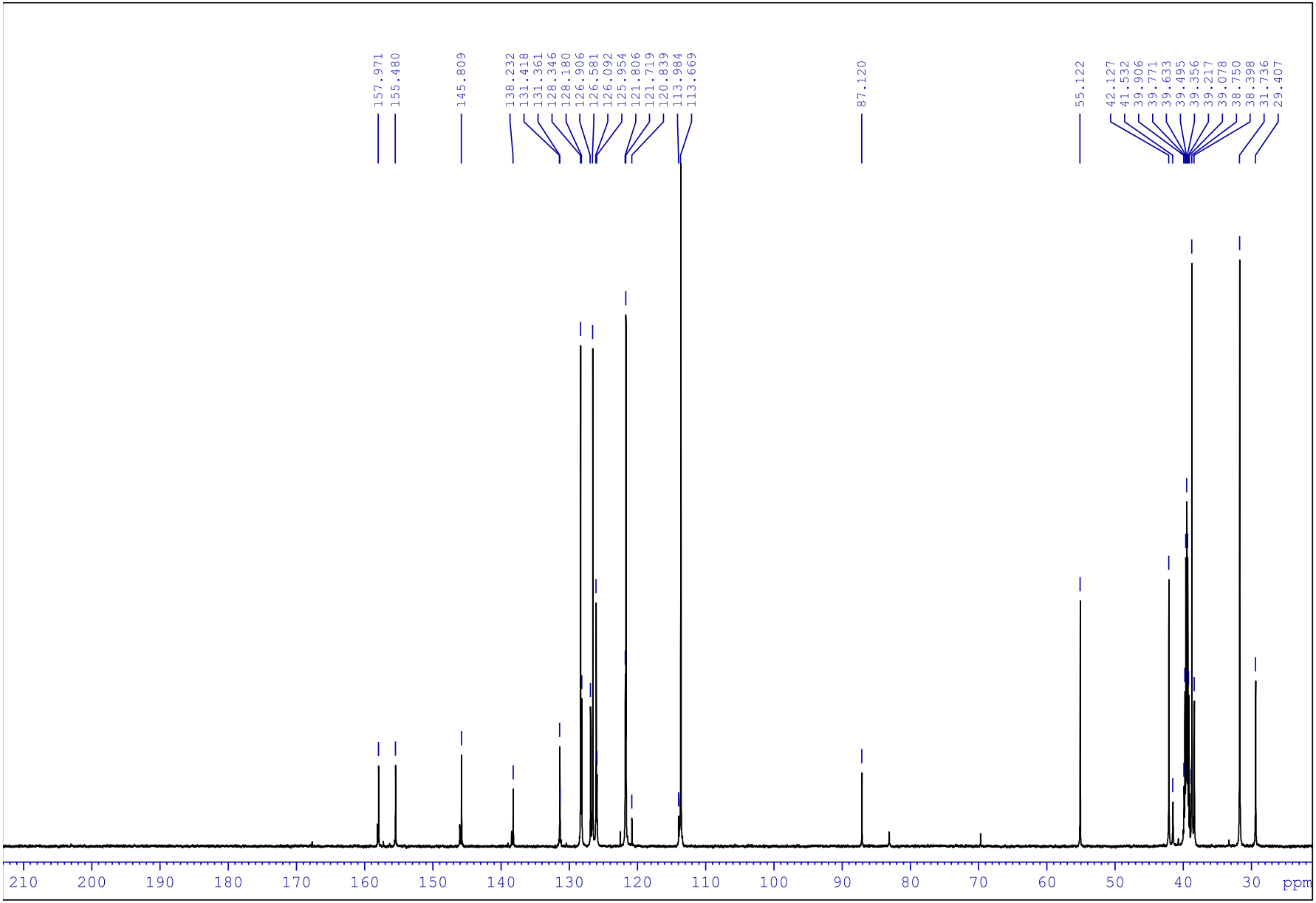
1. Experimental Section

^{1}H, ^{13}C, ^{19}F NMR, 1D NOESY NMR, 2D NMR HSQC, HMBC and ROESY experiments were recorded on Bruker AV-600 (600, 565 and 151 MHz, for ^{1}H, ^{19}F and ^{13}C respectively), Bruker AV-400 (400 and 100.6 MHz, respectively) and Bruker AM-300 (300, 282 and 75 MHz, for ^{1}H, ^{19}F and ^{13}C respectively). The chemical shifts (δ) were expressed in ppm and referenced to DMSO-d_6 (39.5 ppm) for ^{1}H and ^{13}C NMR, respectively. The coupling constants (*J*) are in Hertz. The assignment of the signals in the NMR spectra was based on the 2D NMR data. IR spectra were recorded on a Bruker Alpha spectrometer as KBr pellets, significant band (ν) reported in cm^{-1}. High-resolution mass spectra were obtained on a Bruker MicroTOF mass spectrometer by electrospray ionization (ESI) using Q-TOF detection. The melting points were determined on a Kofler hot stage apparatus and are uncorrected. TLC was performed using Silicagel 60 F254 plates. The chromatograms were visualized with an UV lamp (254 and 365 nm) and [$Ce(SO_4)_2/H_2SO_4$] developing solution. Column chromatography was carried out on silica gel 60 (0.063–0.200 mm, Merck). Commercial reagents were used without further purification.

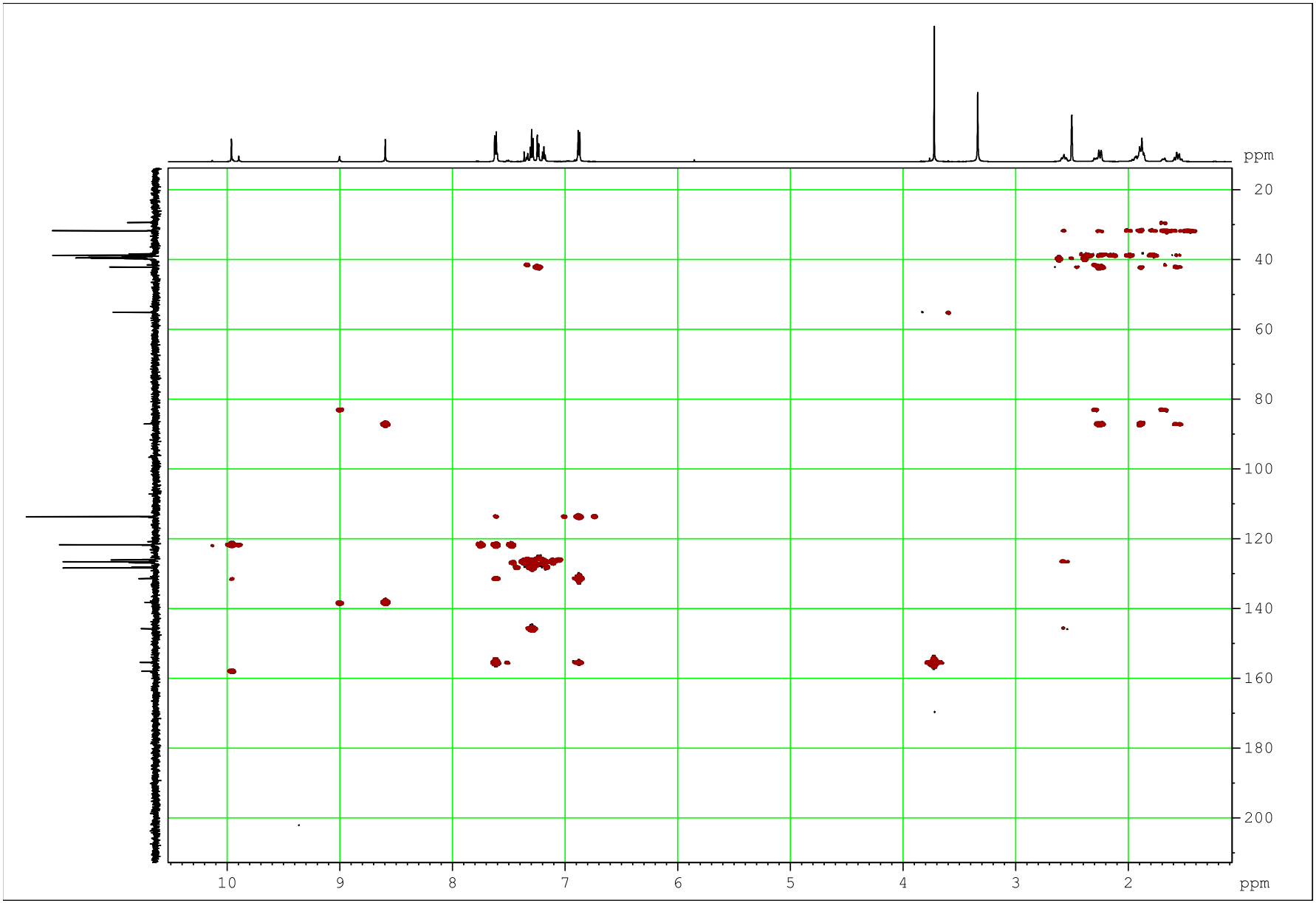
2. NMR spectra (Bruker AV-600)



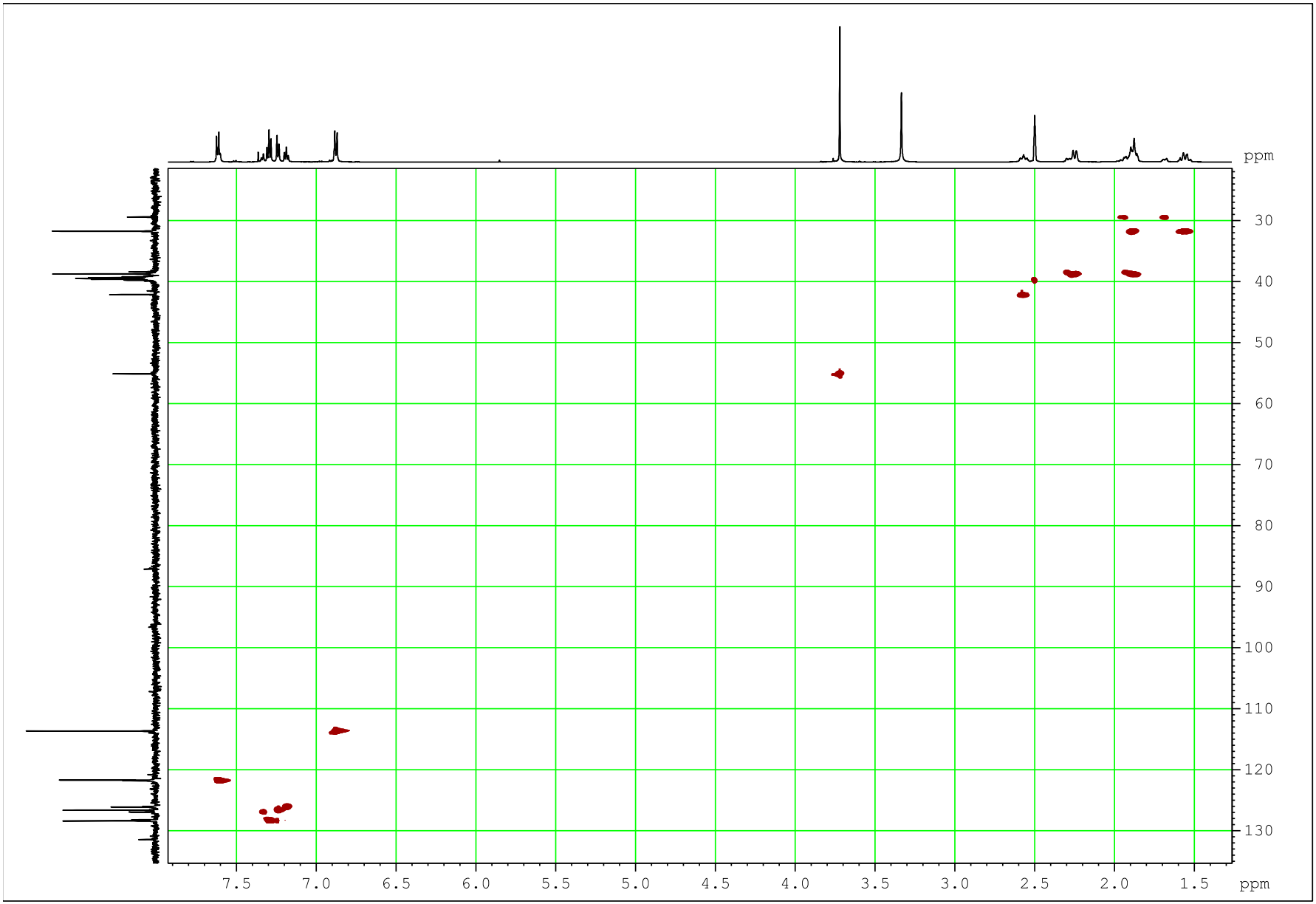
^{1}H NMR spectrum of **3b** (DMSO-d_6).



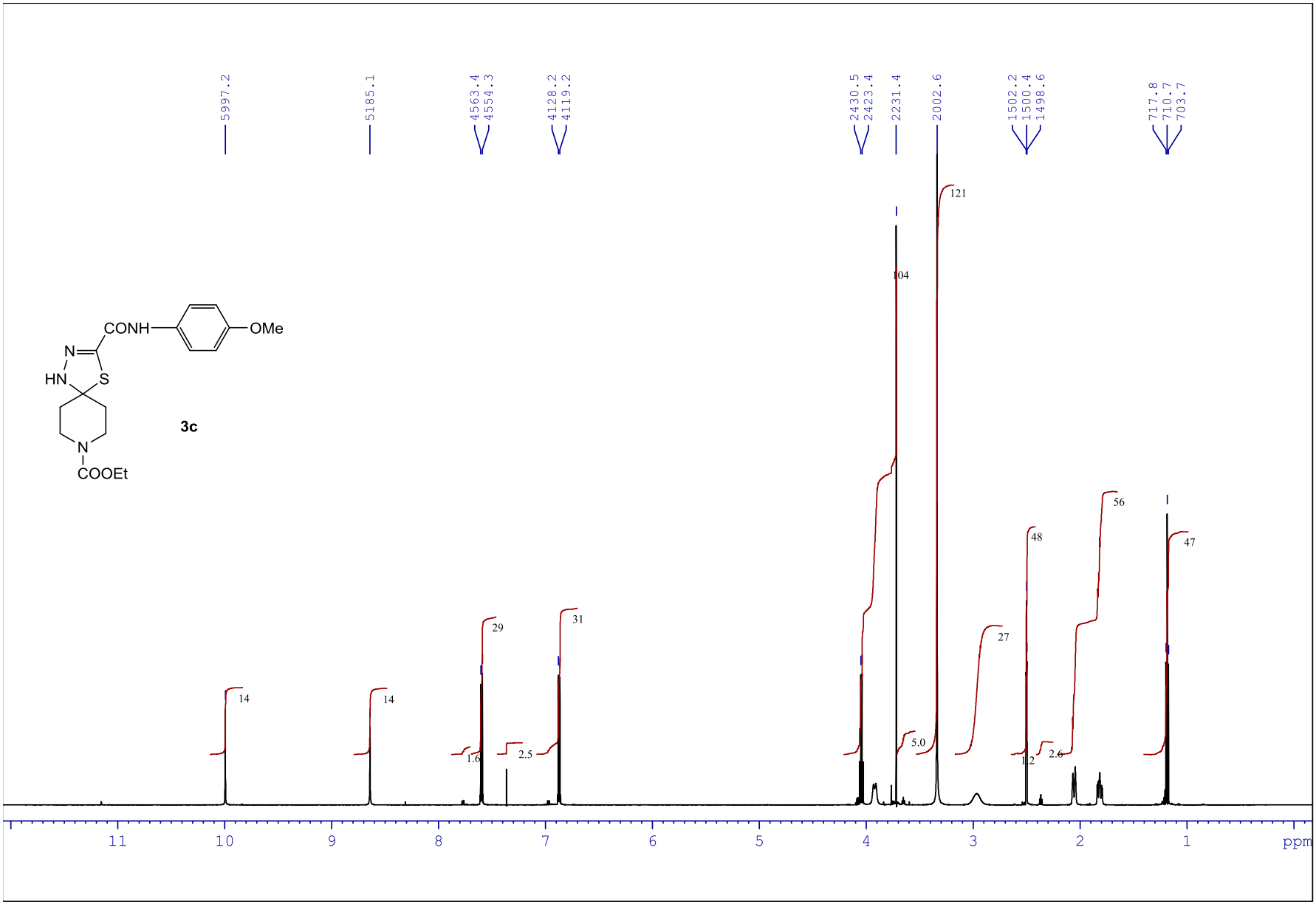
^{13}C NMR spectrum of **3b** (DMSO-d_6).



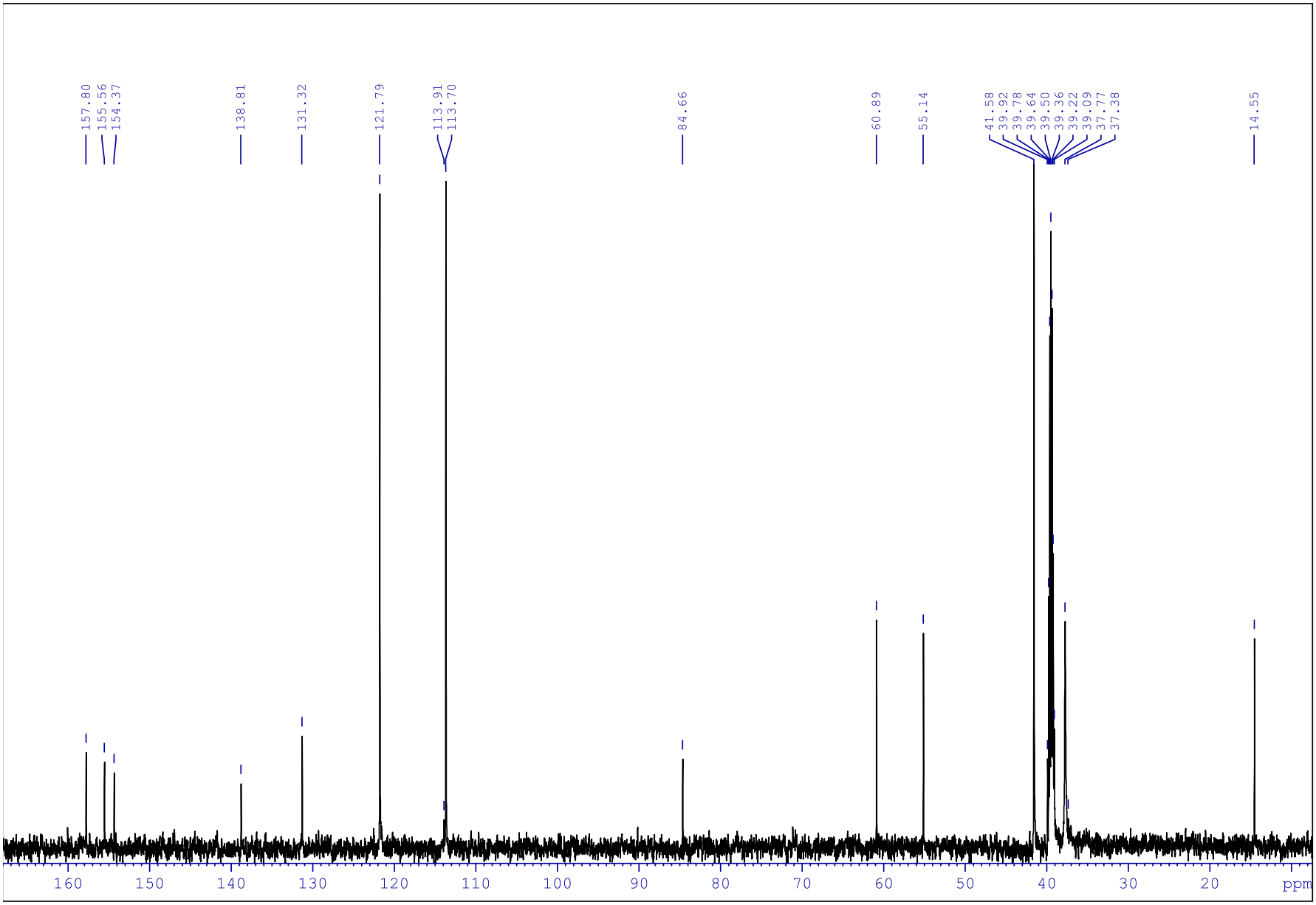
2D ^{1}H-^{13}C HMBC NMR spectrum of **3b** (DMSO-d_6).



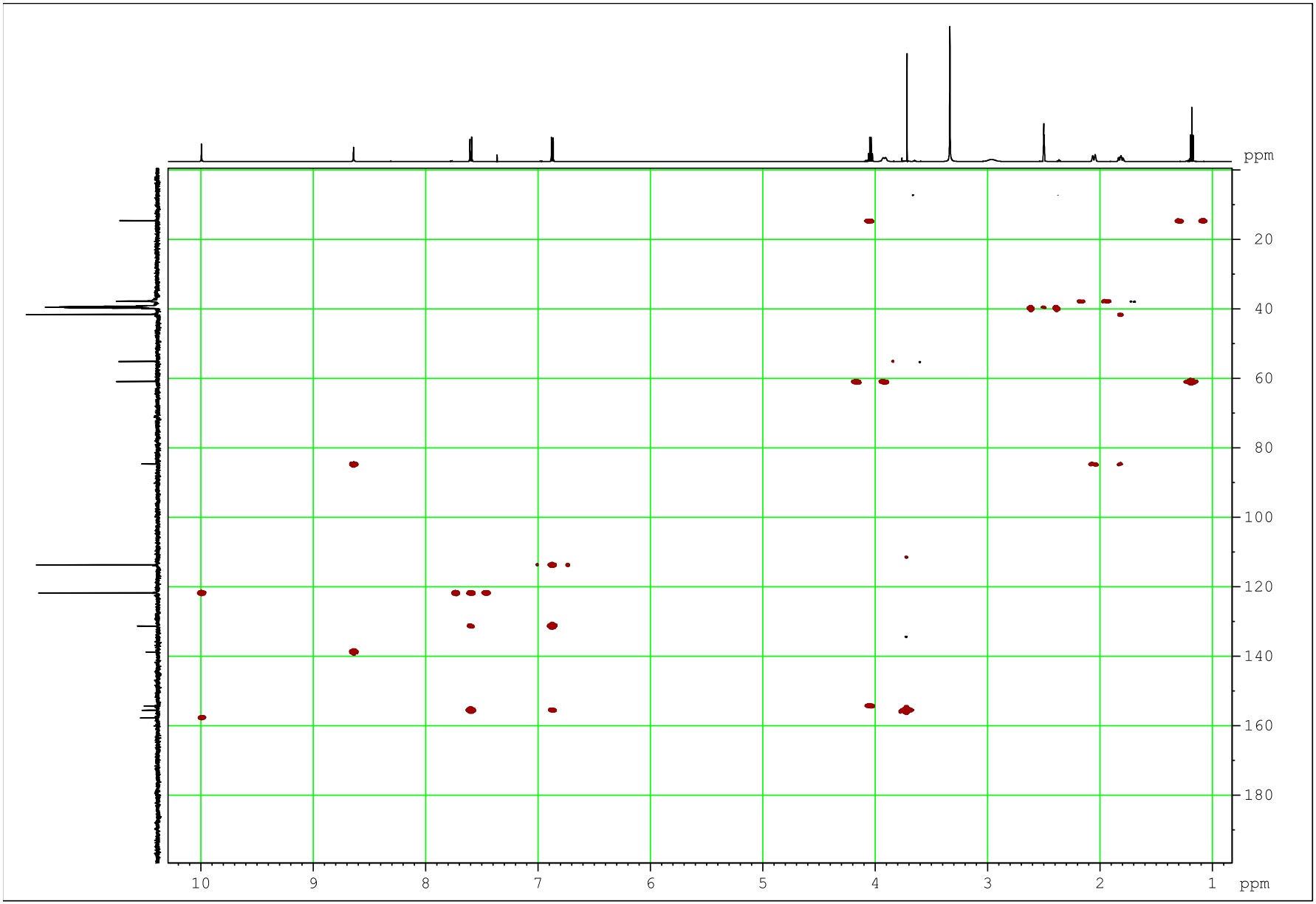
2D ^{1}H-^{13}C HSQC NMR spectrum of **3b** (DMSO-d_6).



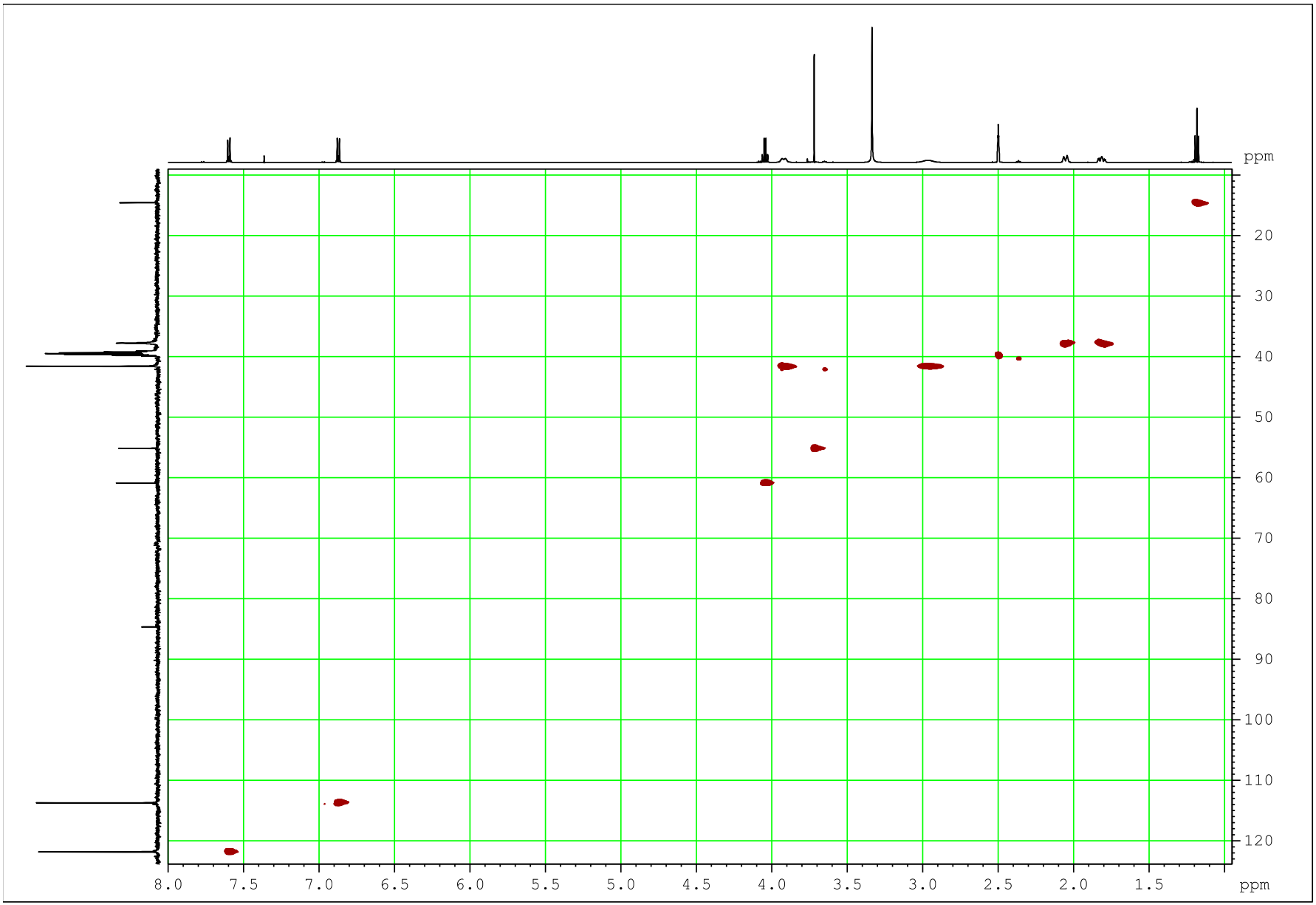
^{1}H NMR spectrum of **3c** (DMSO-d_6).



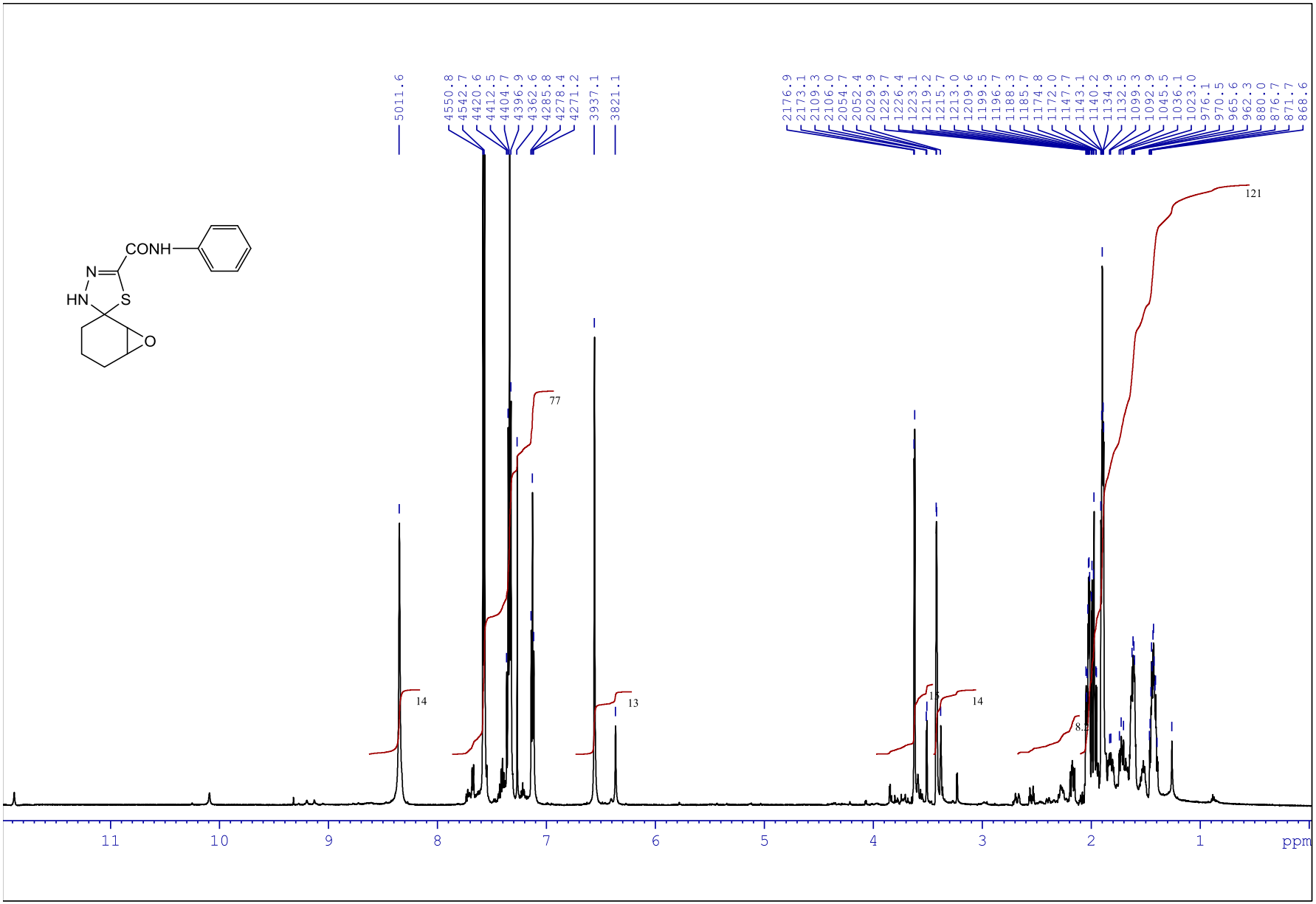
^{13}C NMR spectrum of **3c** (DMSO-d_6).



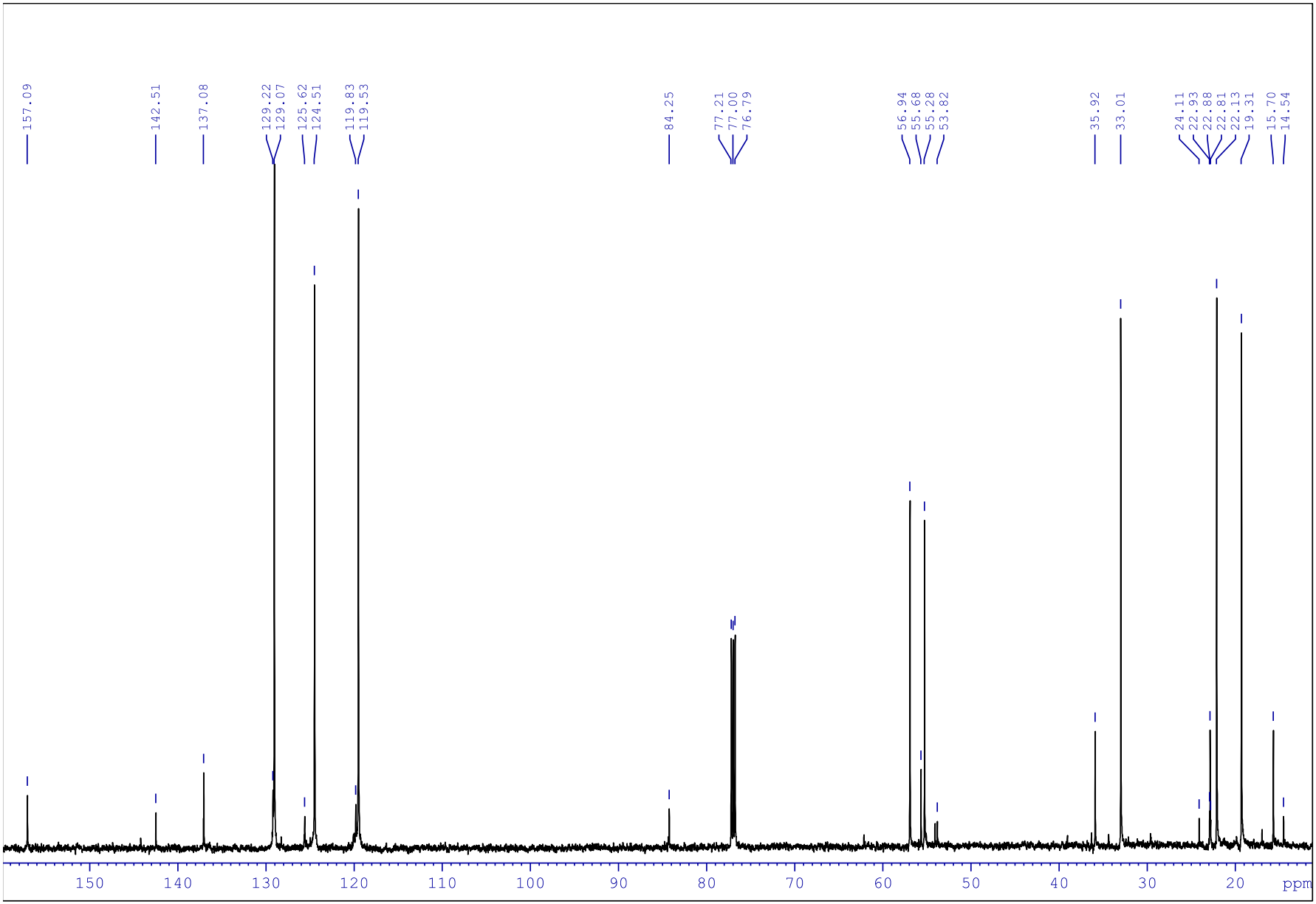
2D ^{1}H-^{13}C HMBC NMR spectrum of **3c** (DMSO-d_6).



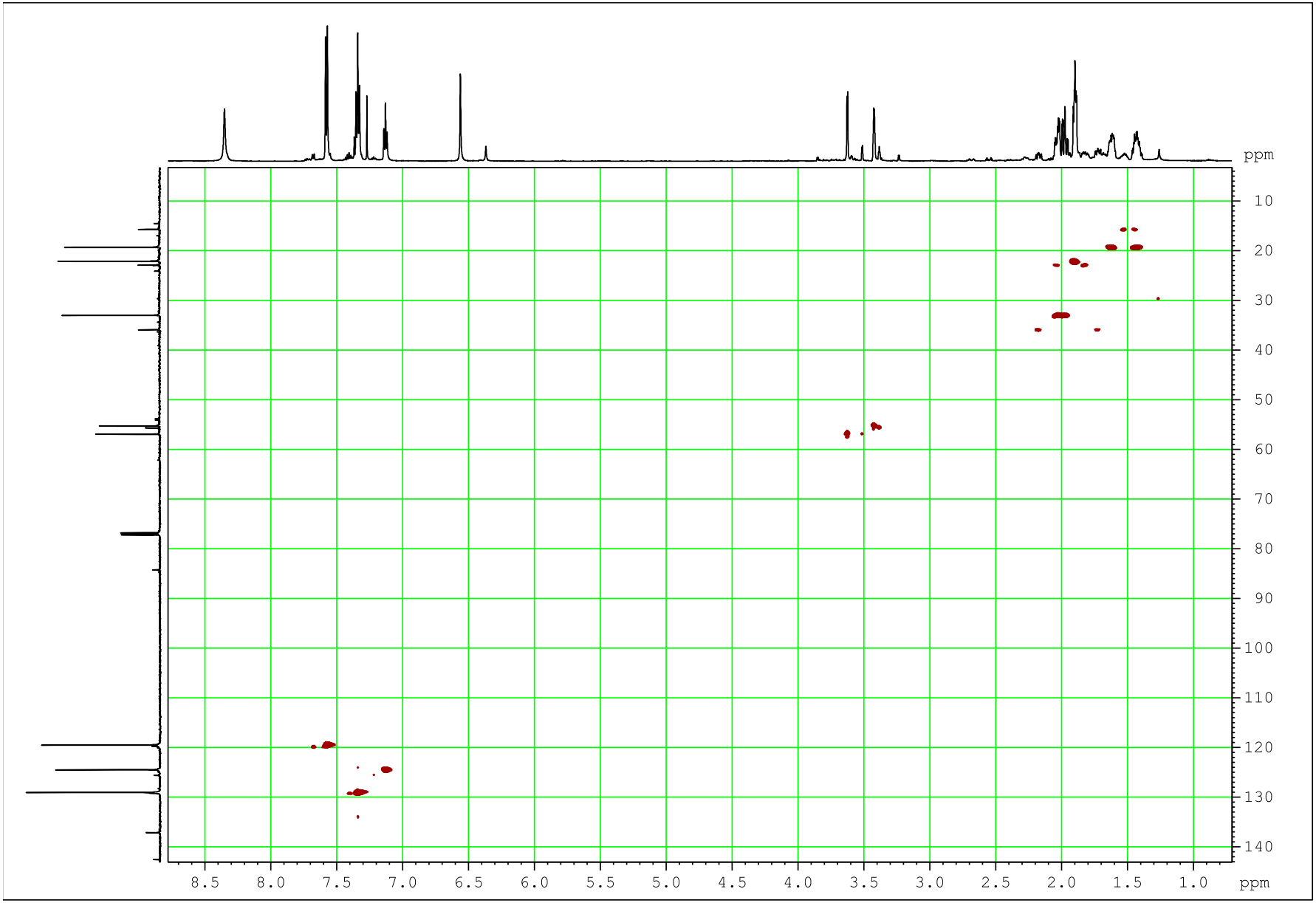
2D ^{1}H-^{13}C HSQC NMR spectrum of **3c** (DMSO-d_6).



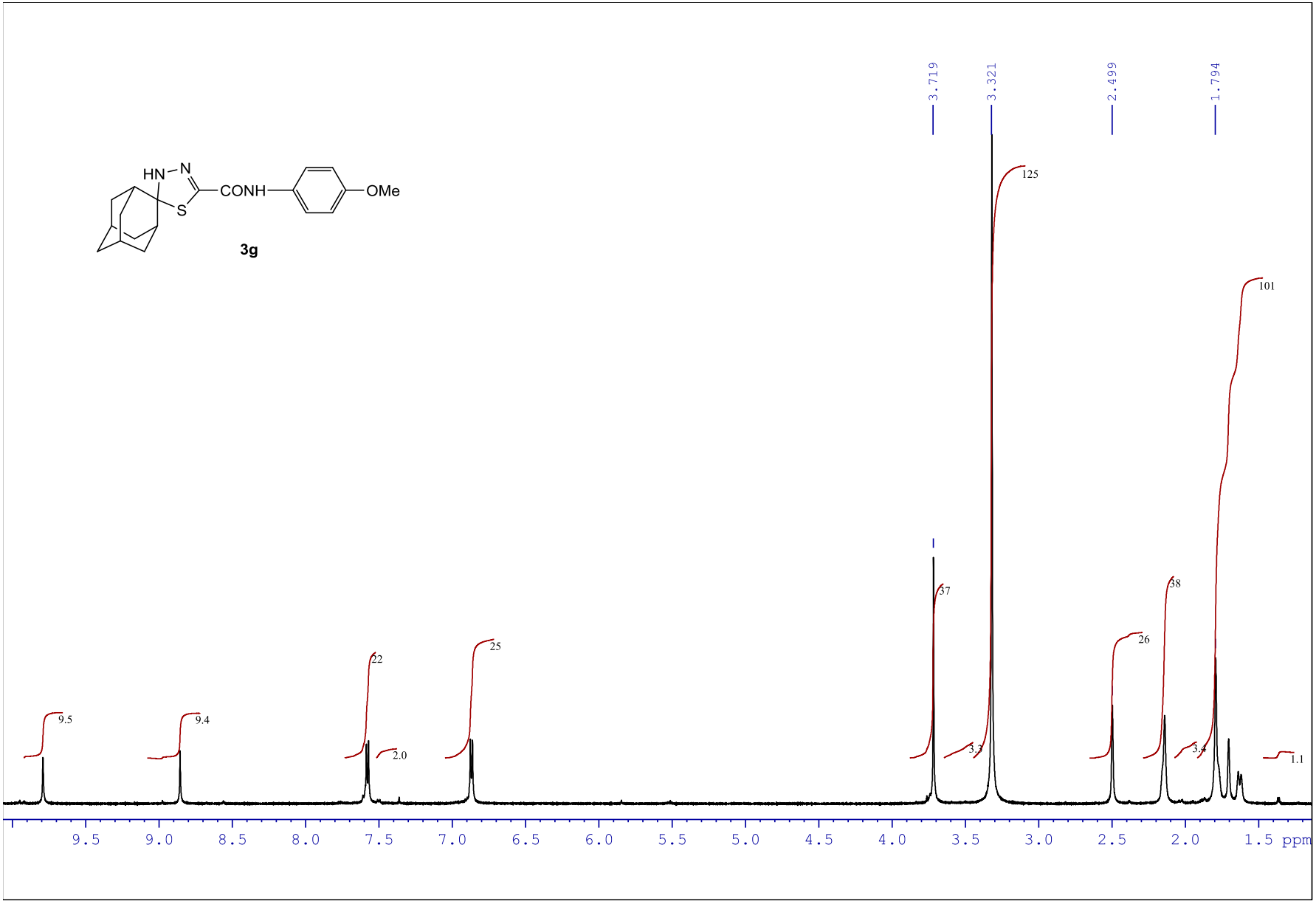
^{1}H NMR spectrum of **3f** ($CDCl_3$).



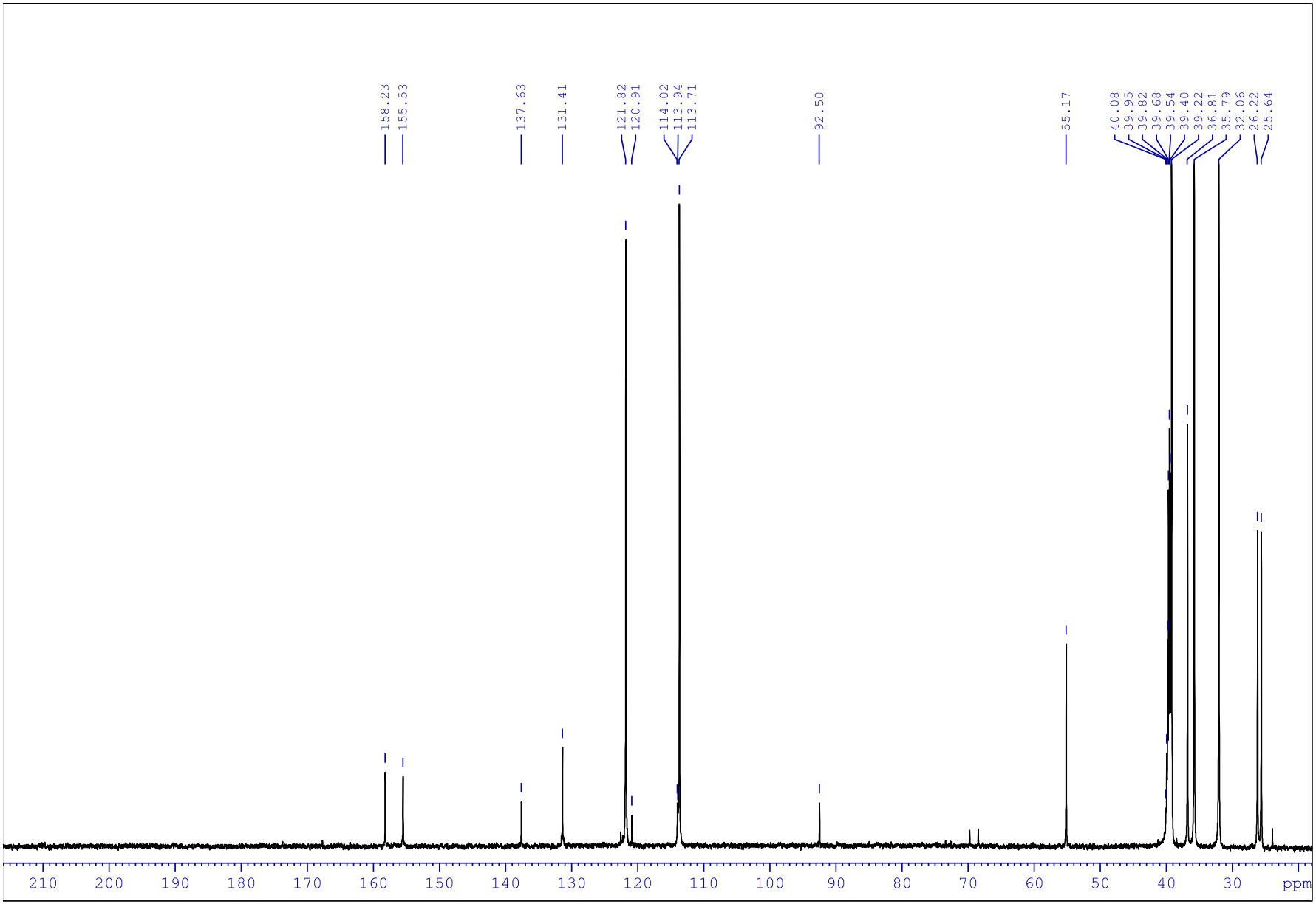
^{13}C NMR spectrum of **3f** ($CDCl_3$).



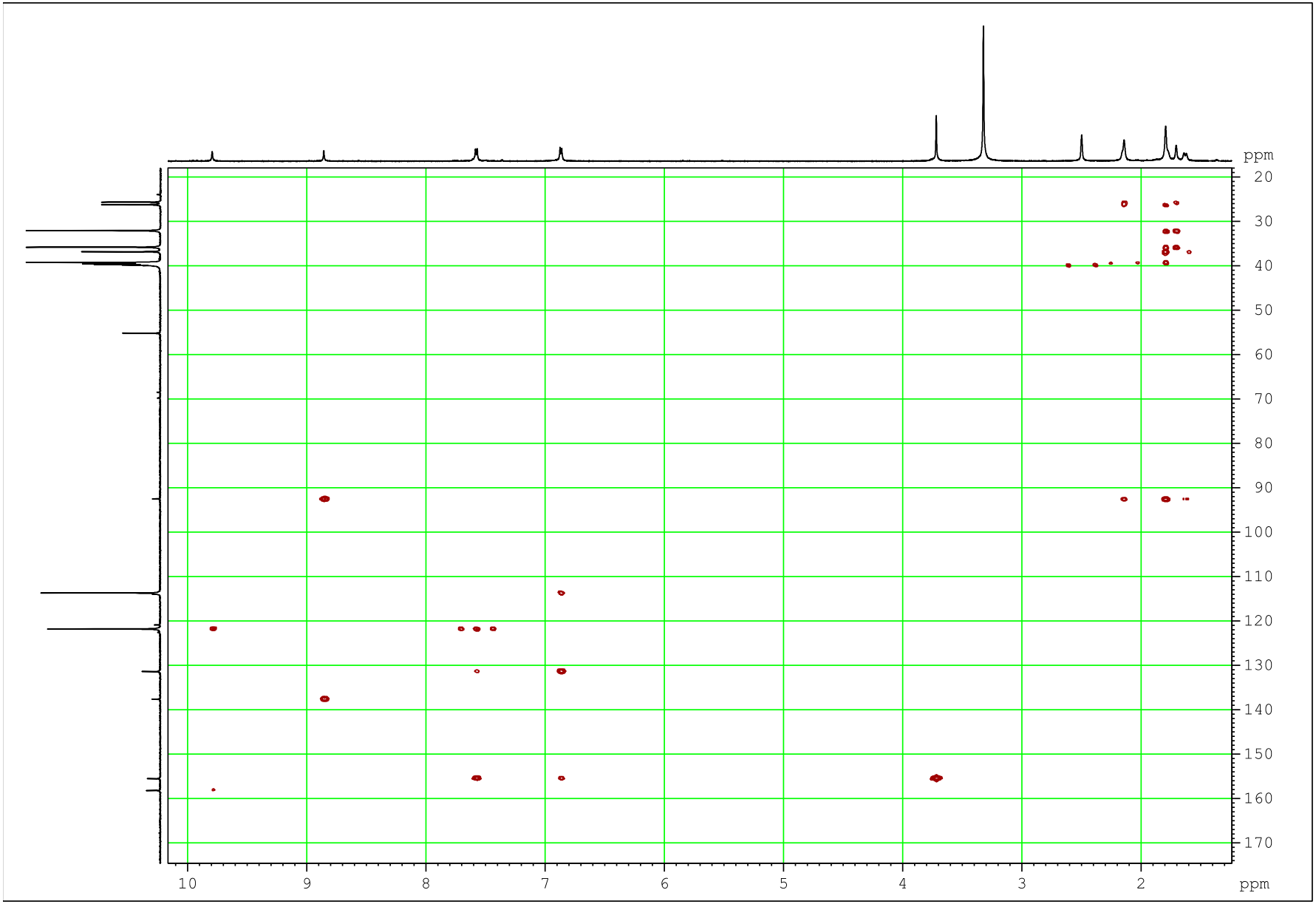
2D ^{1}H-^{13}C HSQC NMR spectrum of **3f** ($CDCl_3$).



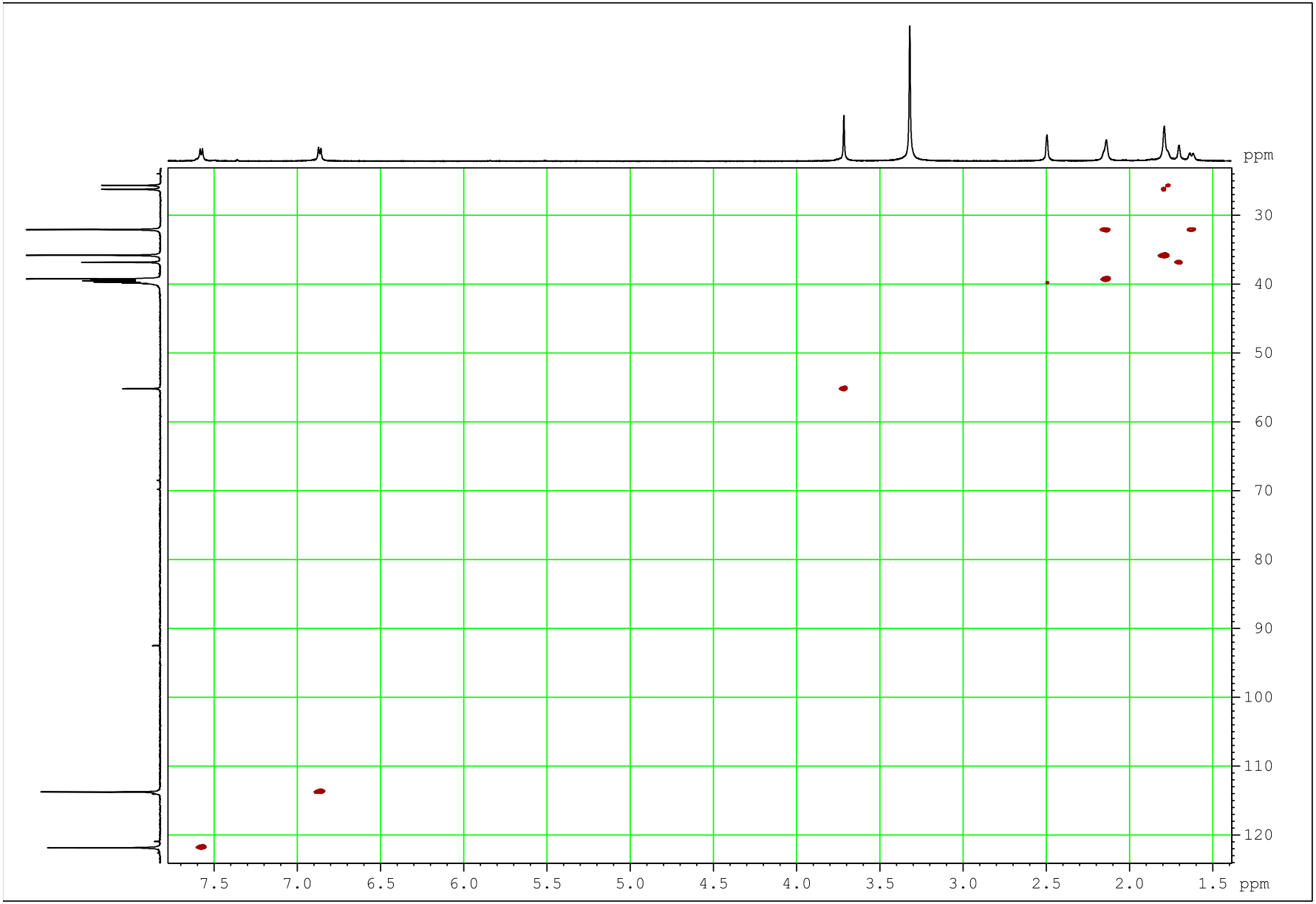
^{1}H NMR spectrum of **3g** (DMSO-d_6).



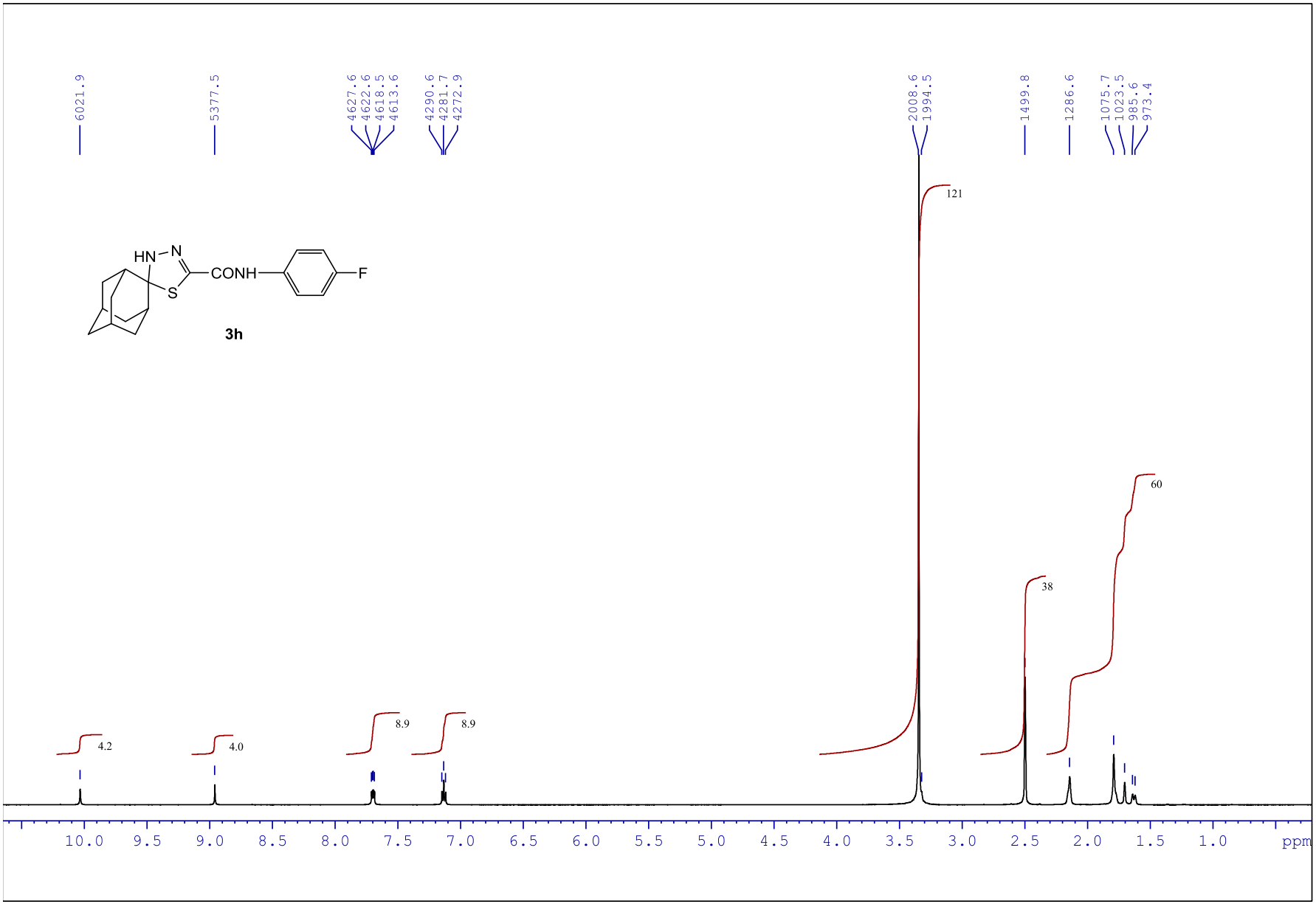
^{13}C NMR spectrum of **3g** (DMSO-d_6).



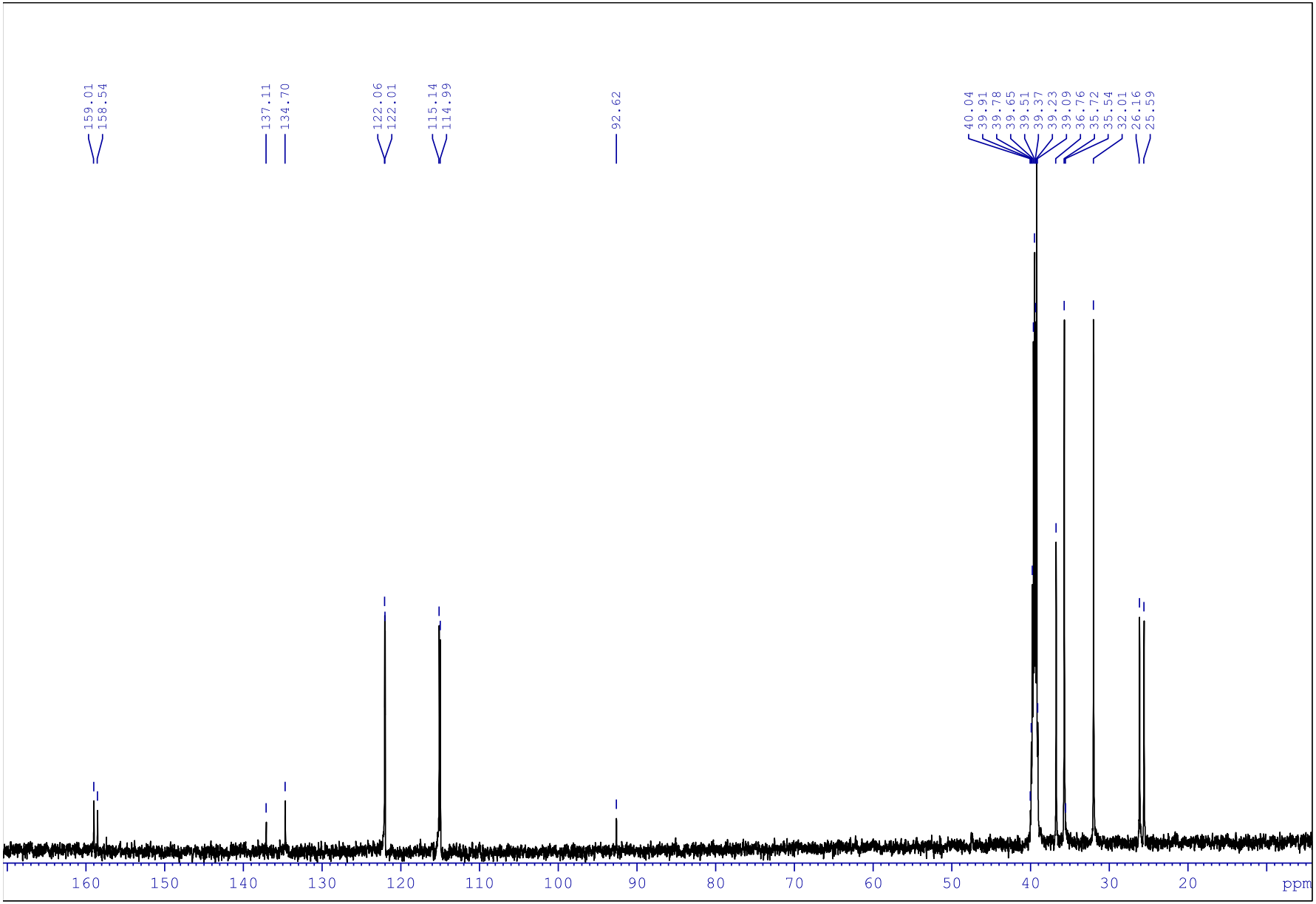
2D ^{1}H-^{13}C HMBC NMR spectrum of **3g** (DMSO-d_6).



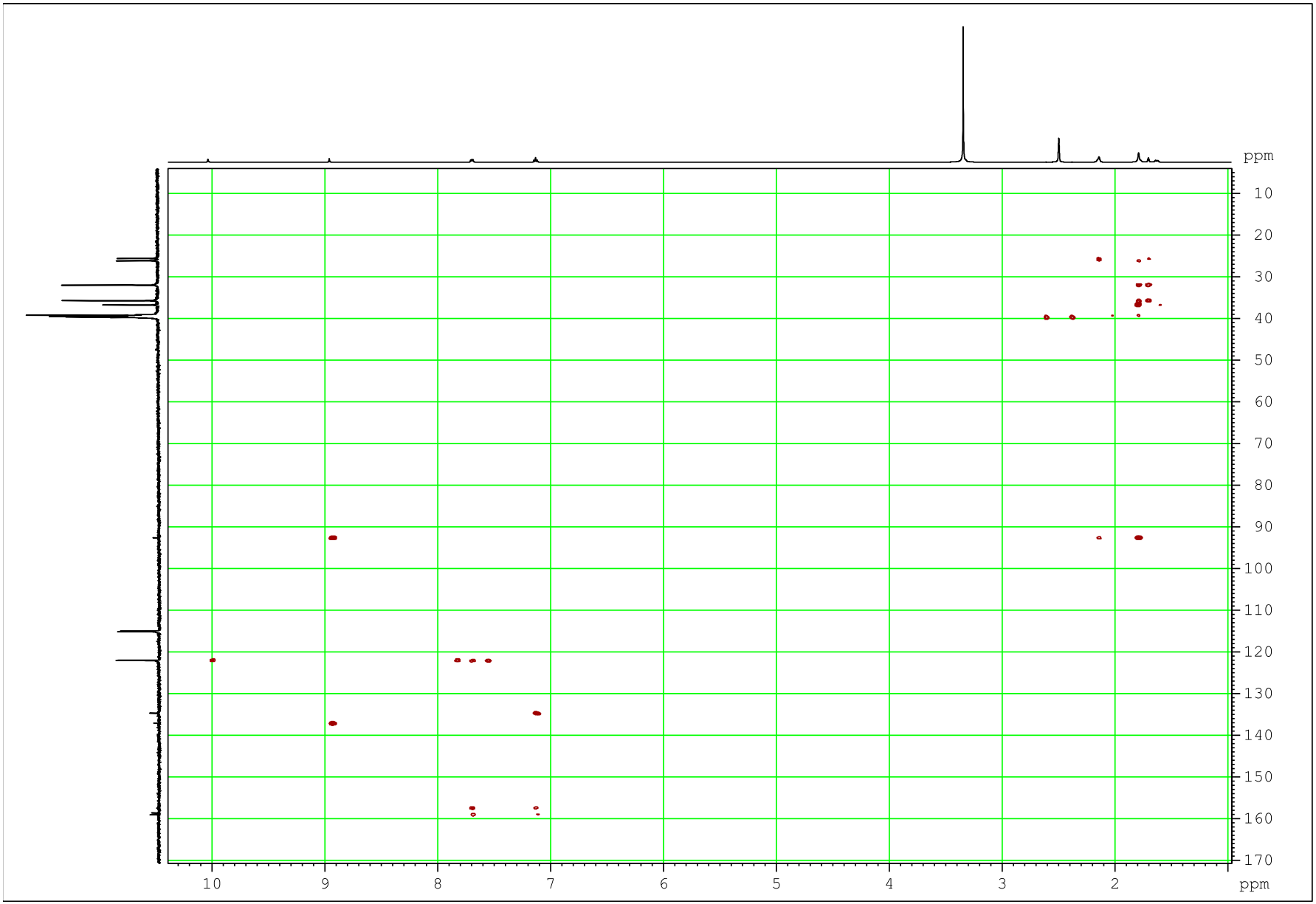
2D ^{1}H-^{13}C HSQC NMR spectrum of **3g** (DMSO-d_6).



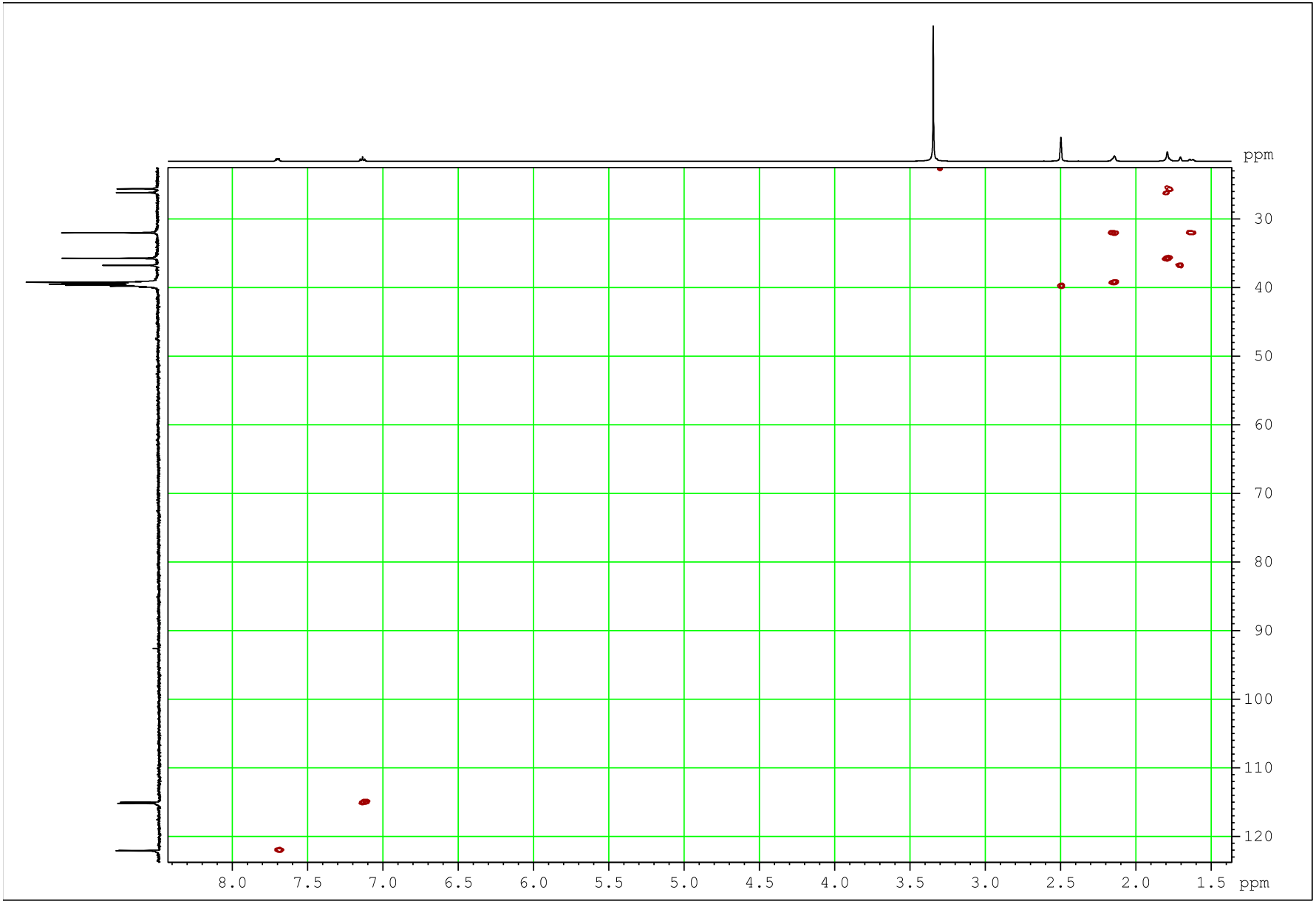
^{1}H NMR spectrum of **3h** (DMSO-d_6).



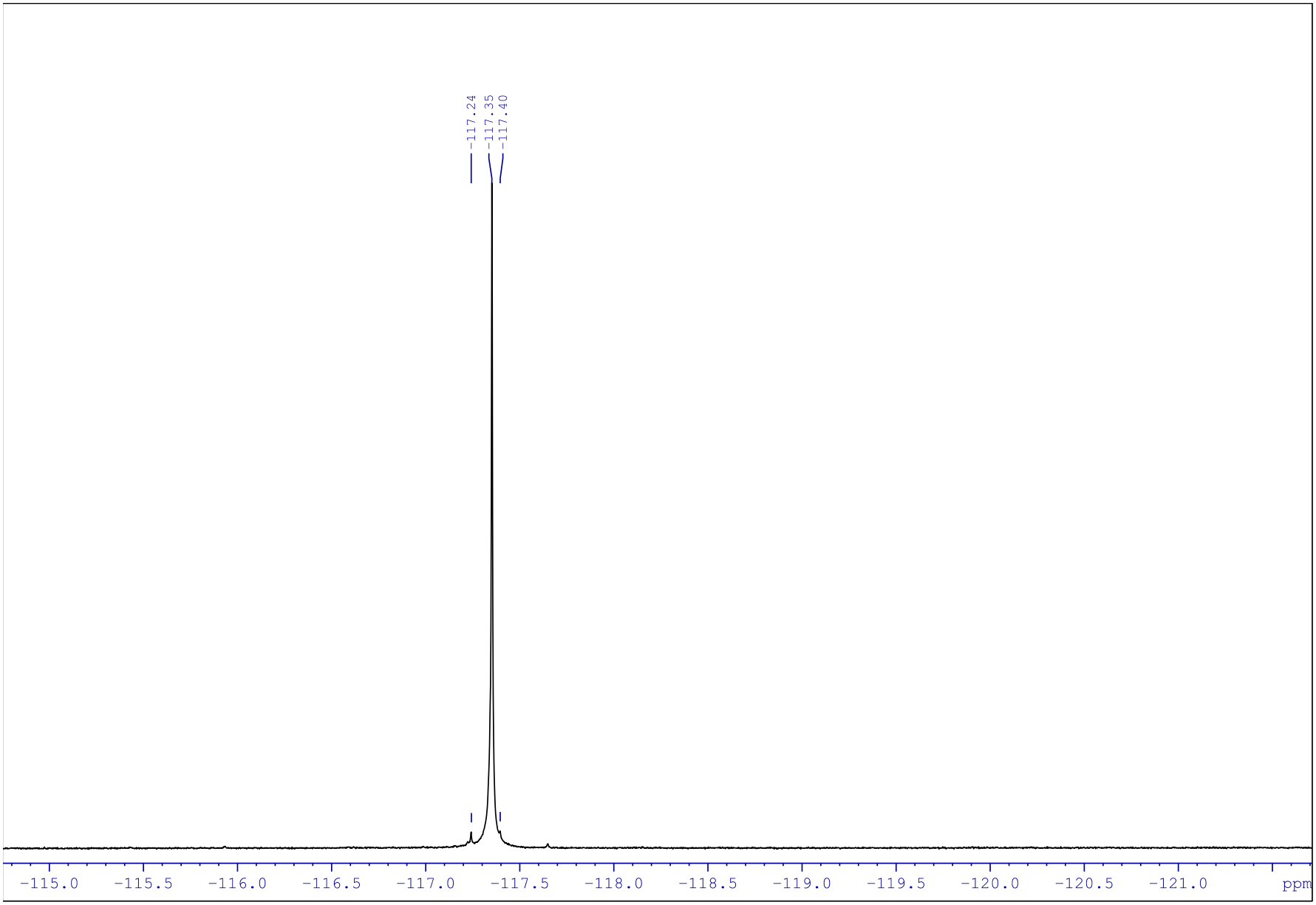
^{13}C NMR spectrum of **3h** (DMSO-d_6).



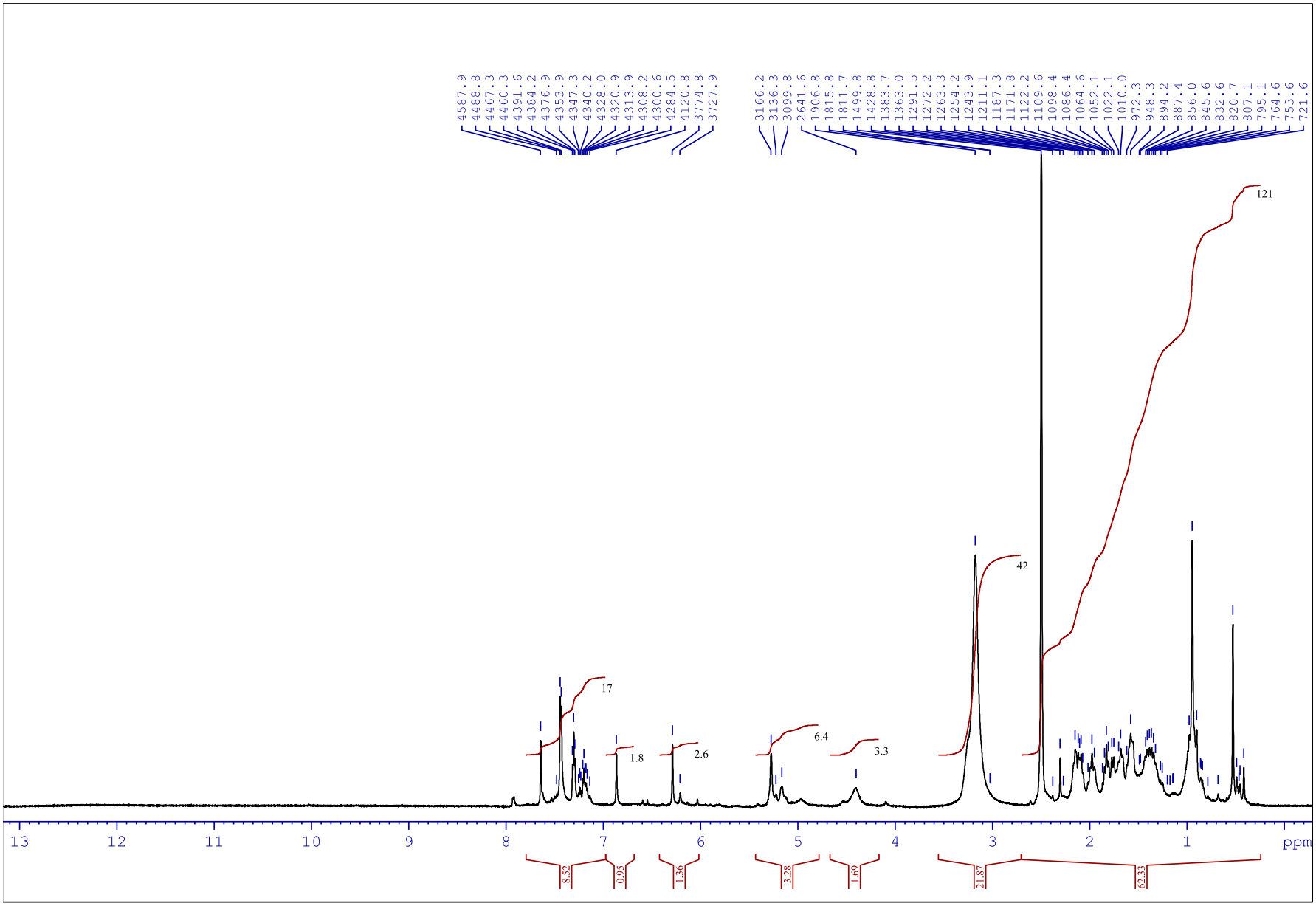
2D ^{1}H-^{13}C HMBC NMR spectrum of **3h** (DMSO-d_6).



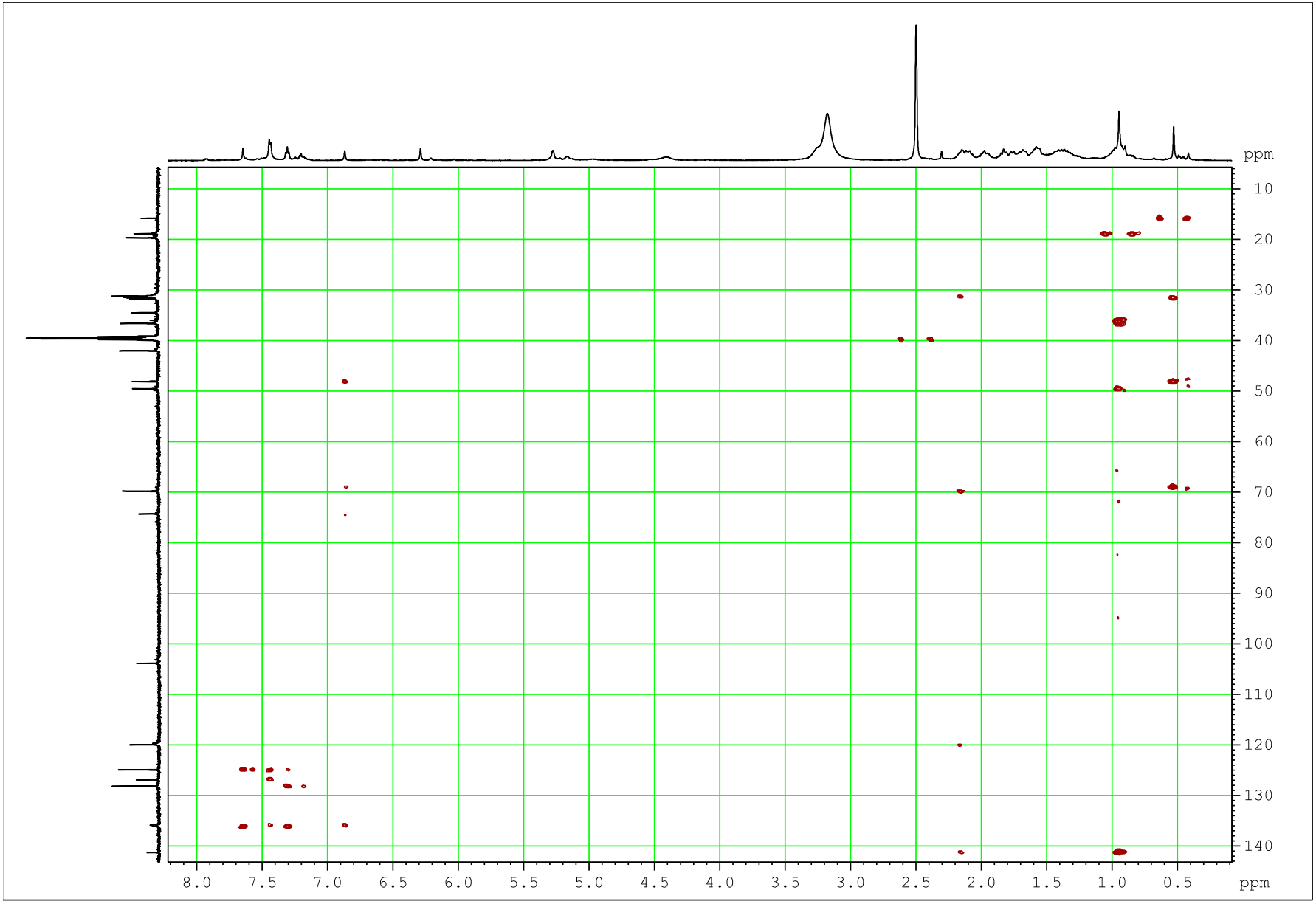
2D ^{1}H-^{13}C HSQC NMR spectrum of **3h** (DMSO-d_6).



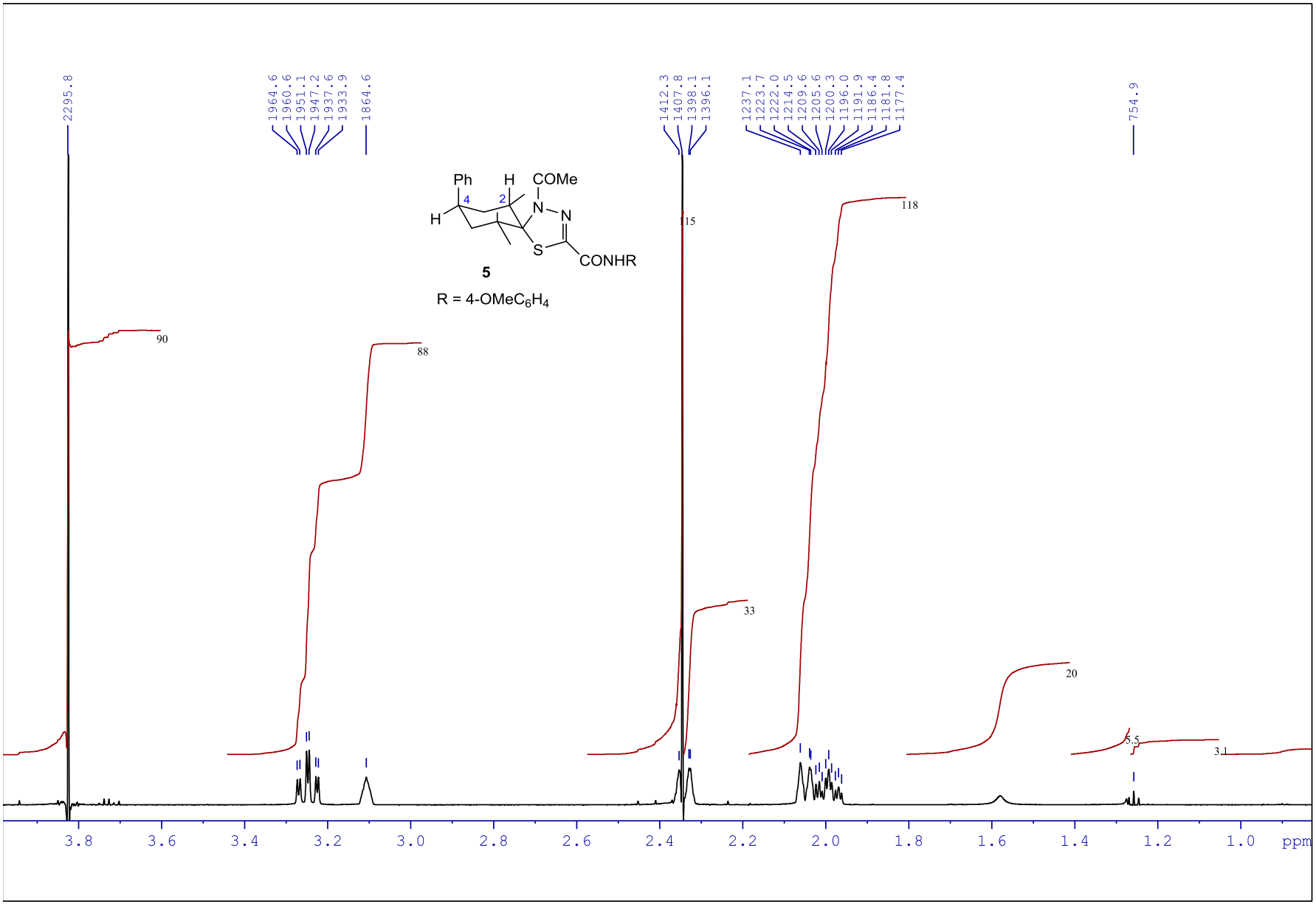
^{19}F NMR spectrum of **3h** (DMSO-d_6).



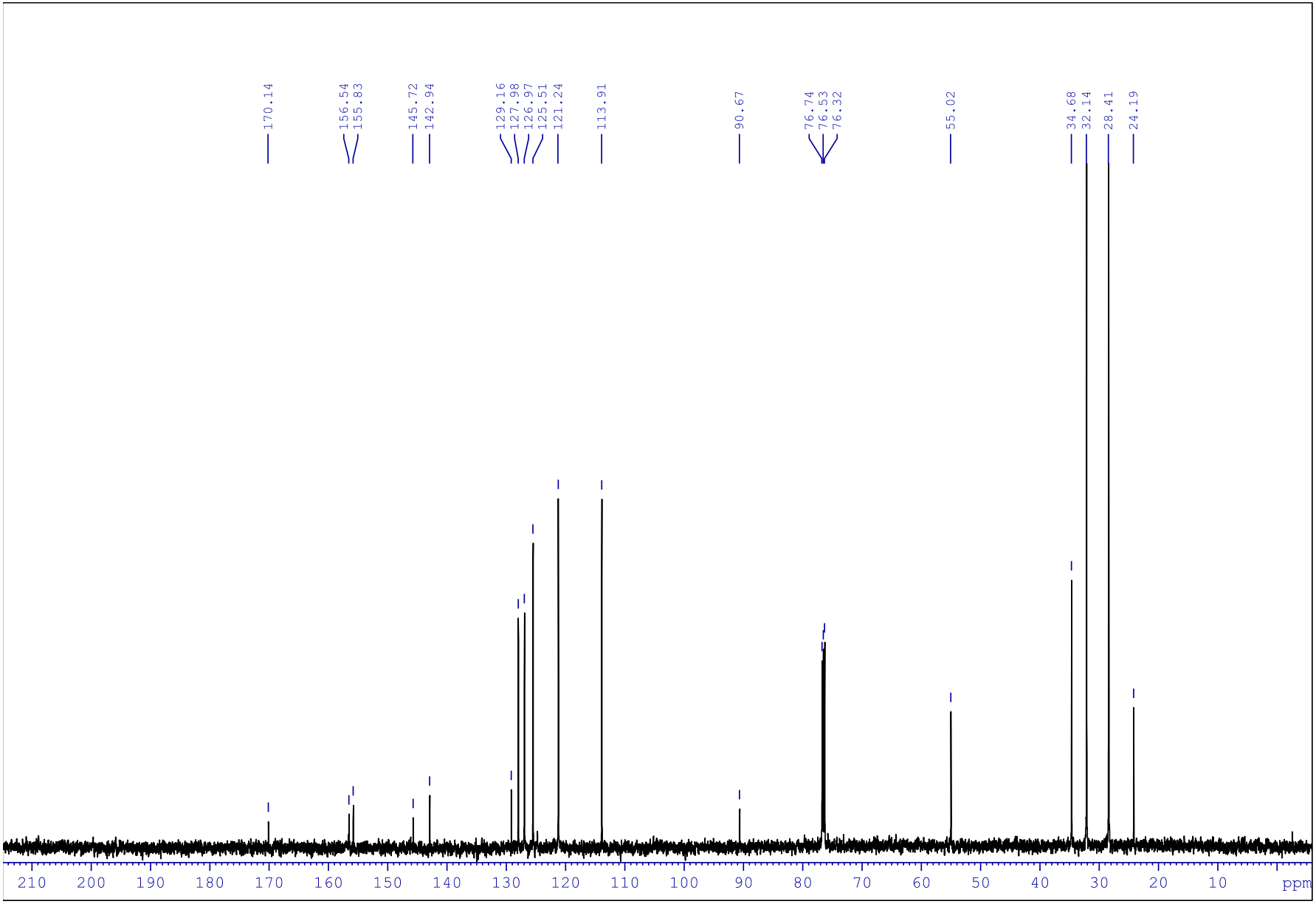
^{1}H NMR spectrum of **3i** (DMSO-d_6).



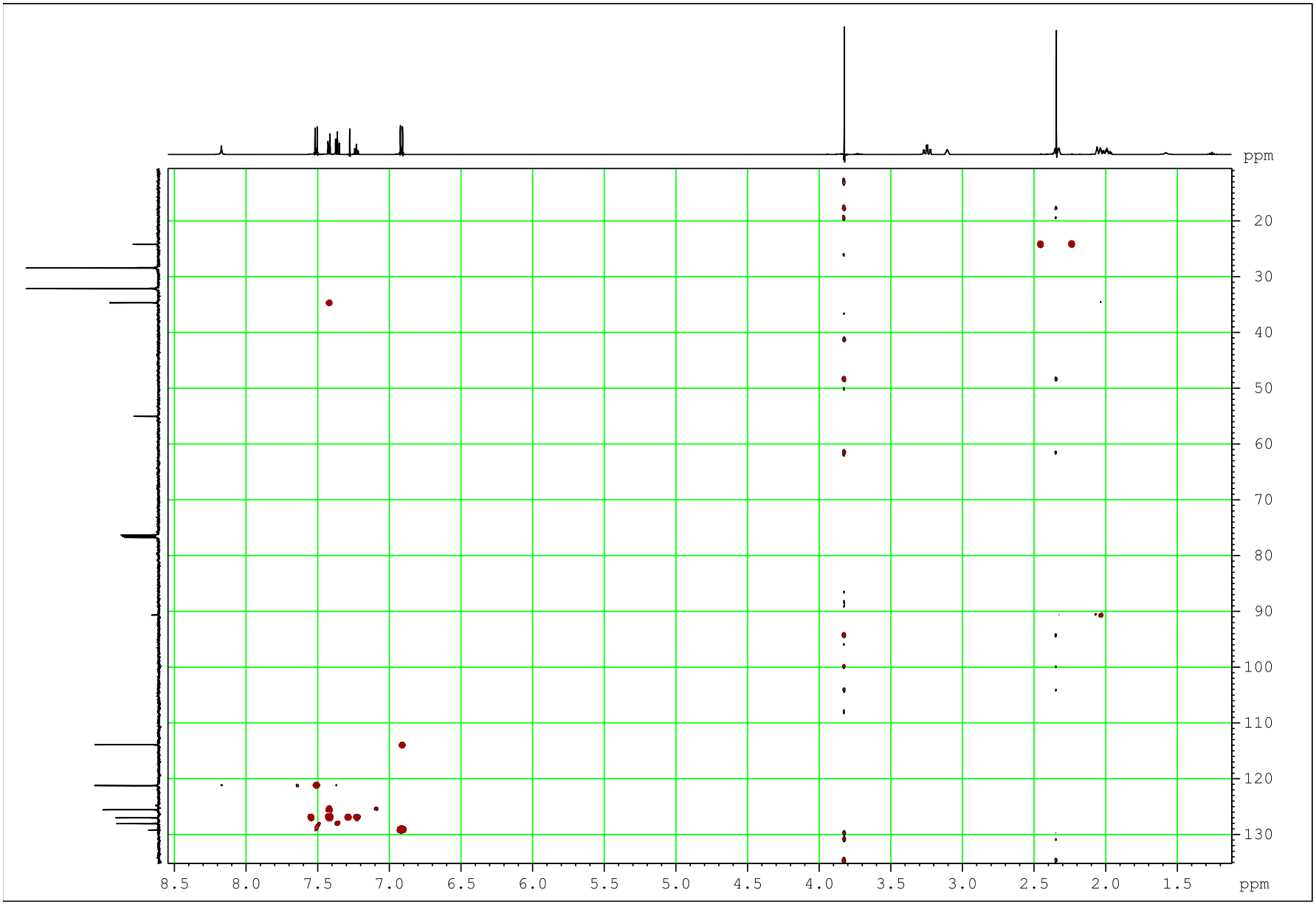
2D ^{1}H-^{13}C HMBC NMR spectrum of **3i** (DMSO-d_6).



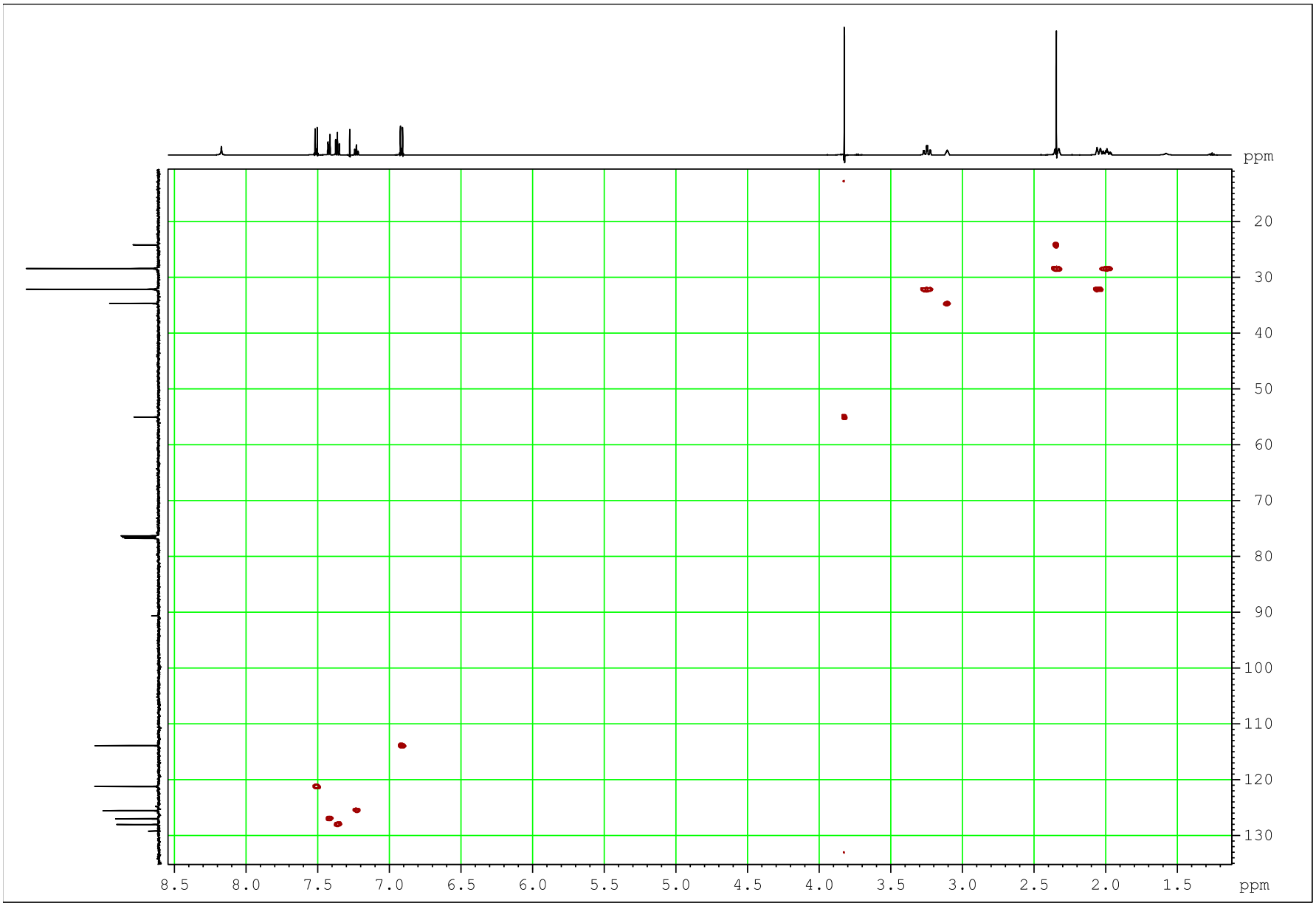
^{1}H NMR spectrum of **5** ($CDCl_3$).



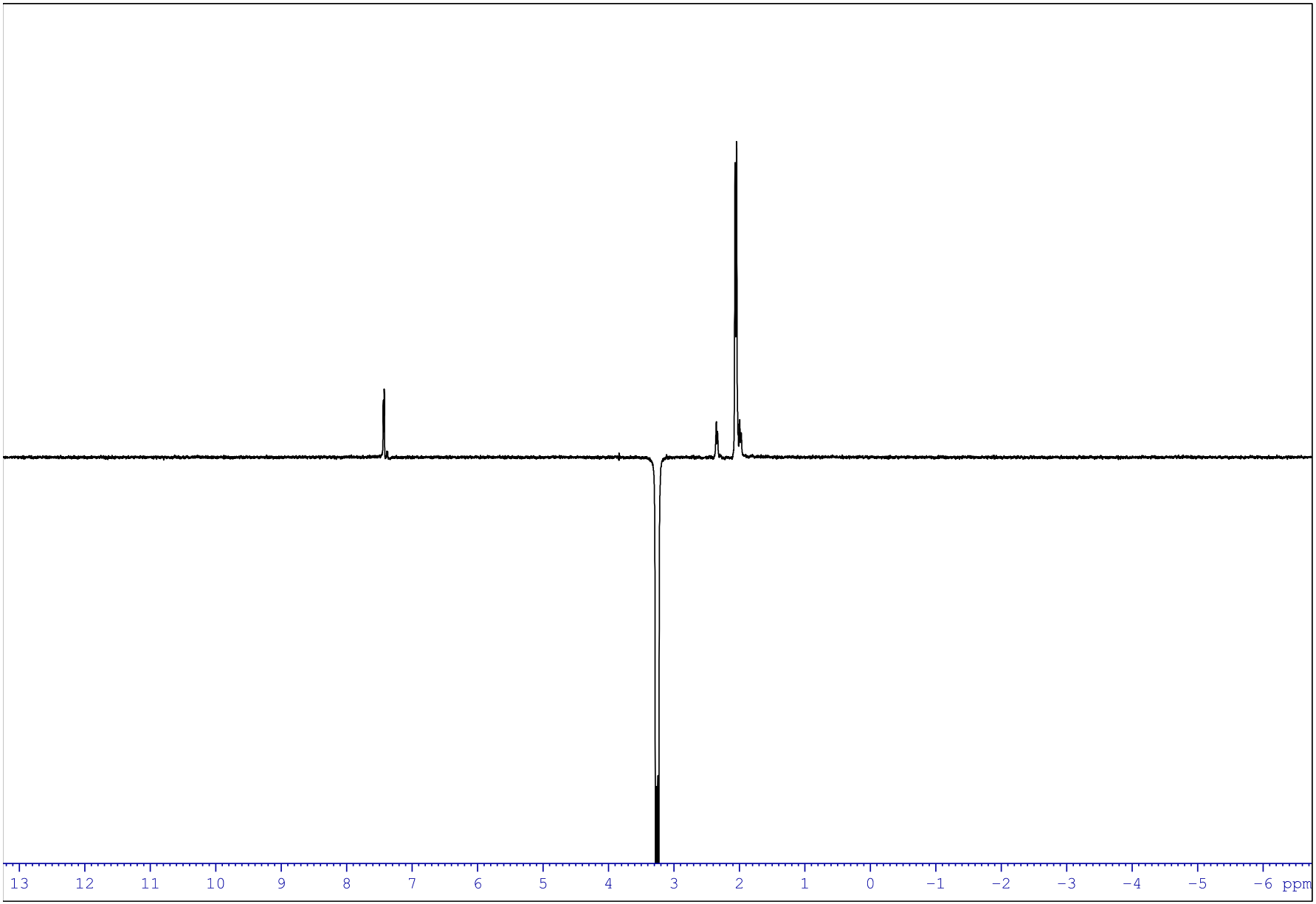
^{13}C NMR spectrum of **5** ($CDCl_3$).



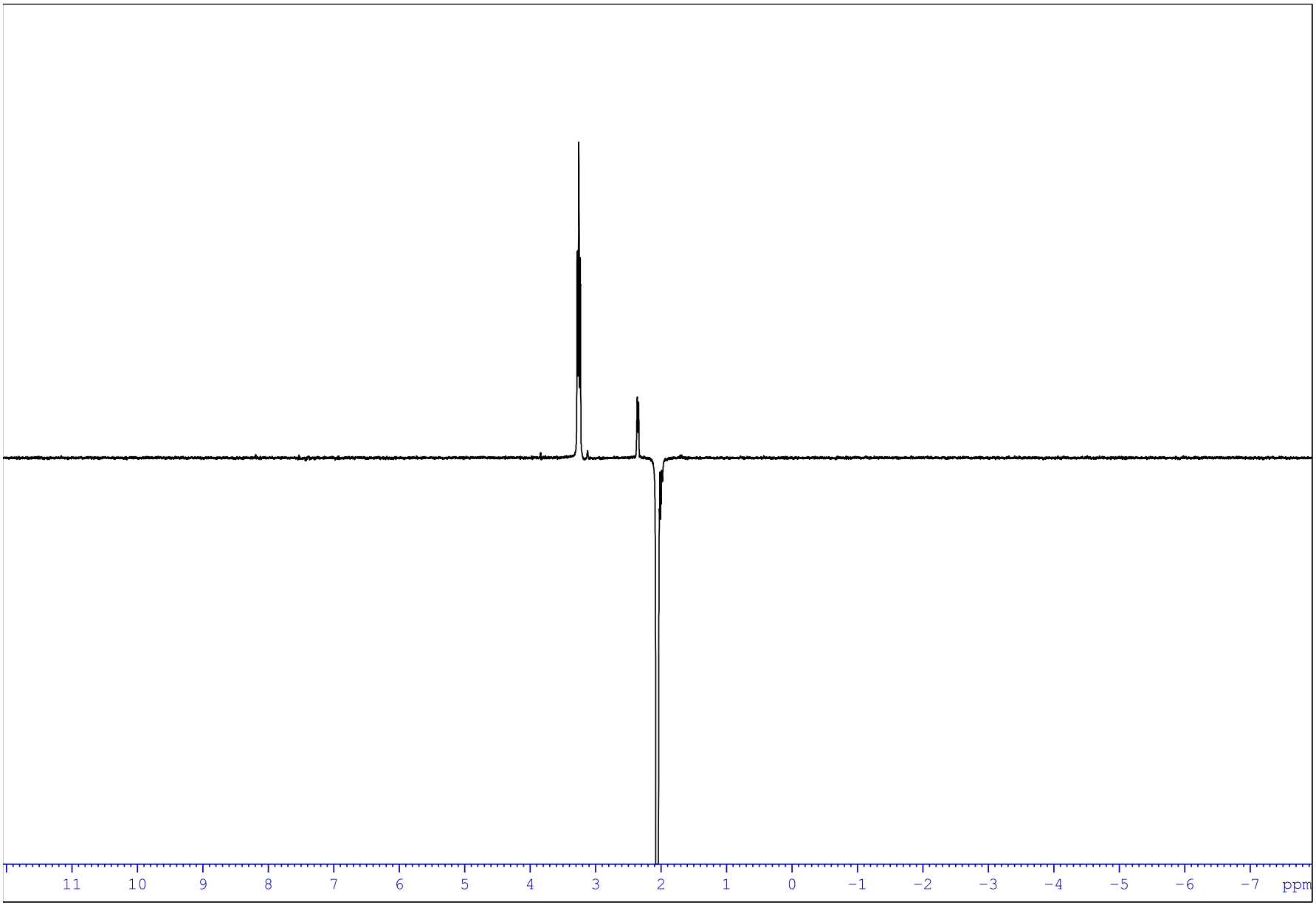
2D ^{1}H-^{13}C HMBC NMR spectrum of **5** ($CDCl_3$).



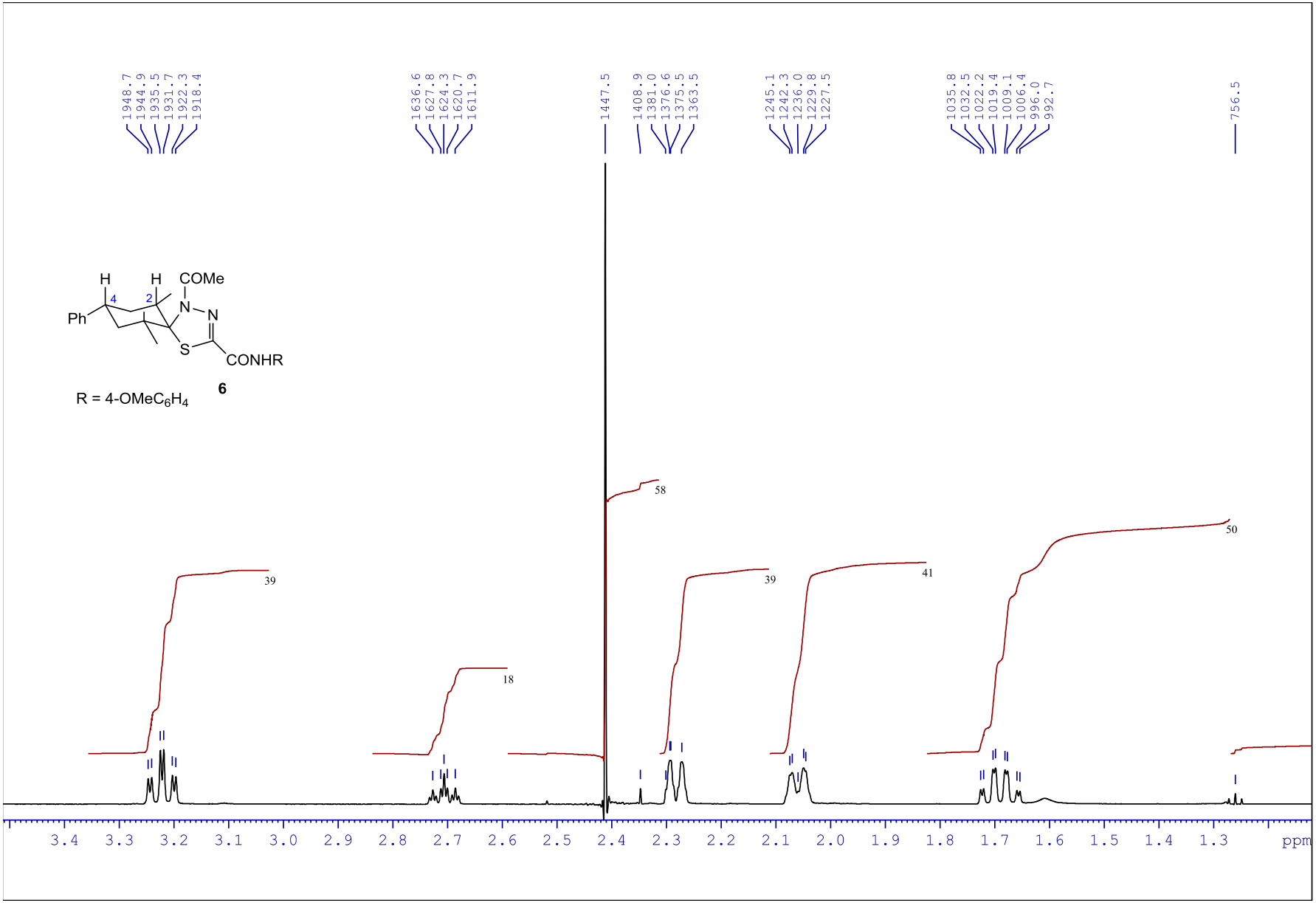
2D ^{1}H-^{13}C HSQC NMR spectrum of **5** ($CDCl_3$).



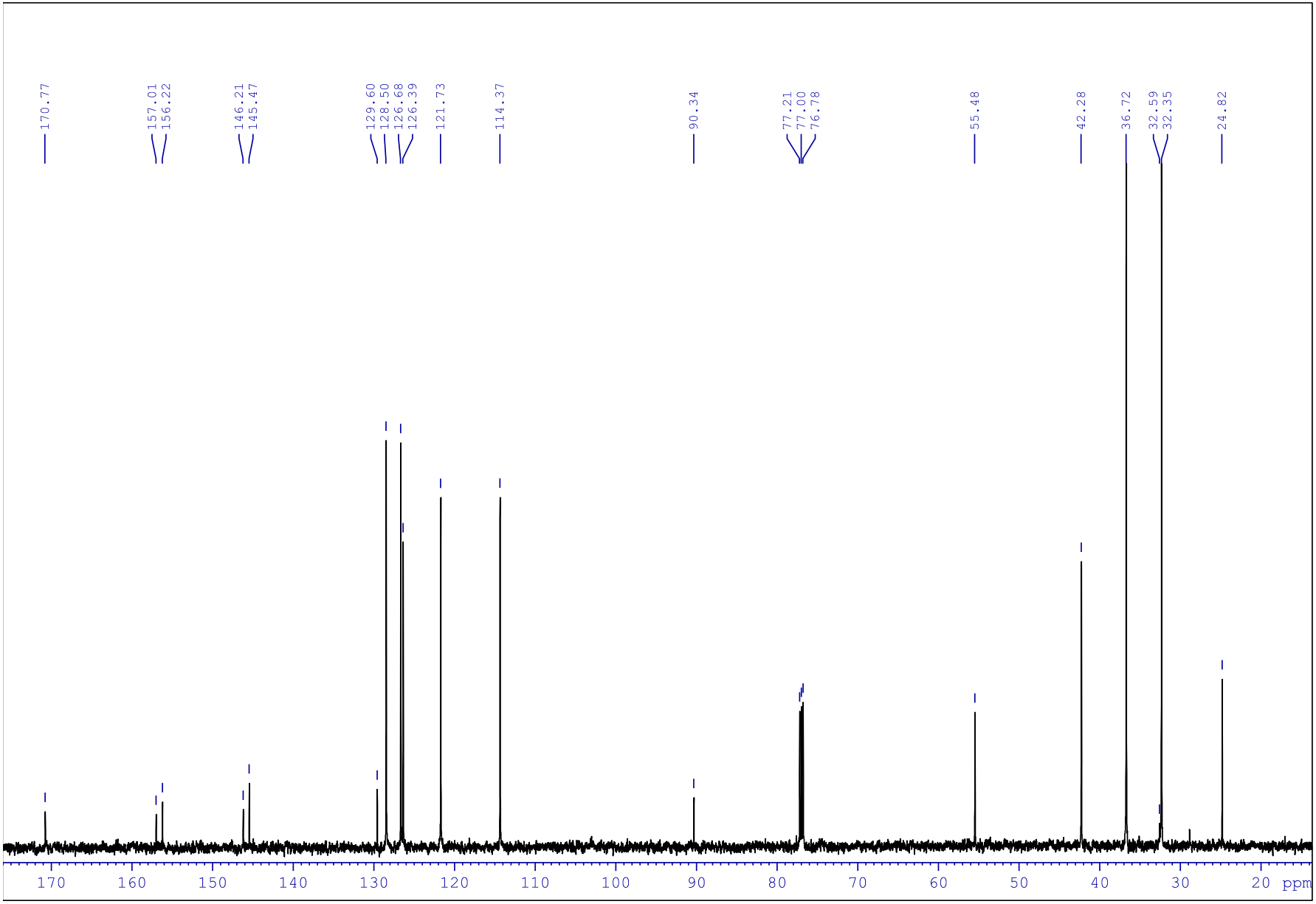
1D ^{1}H NOESY (3.25 ppm) NMR spectrum of **5** ($CDCl_3$).



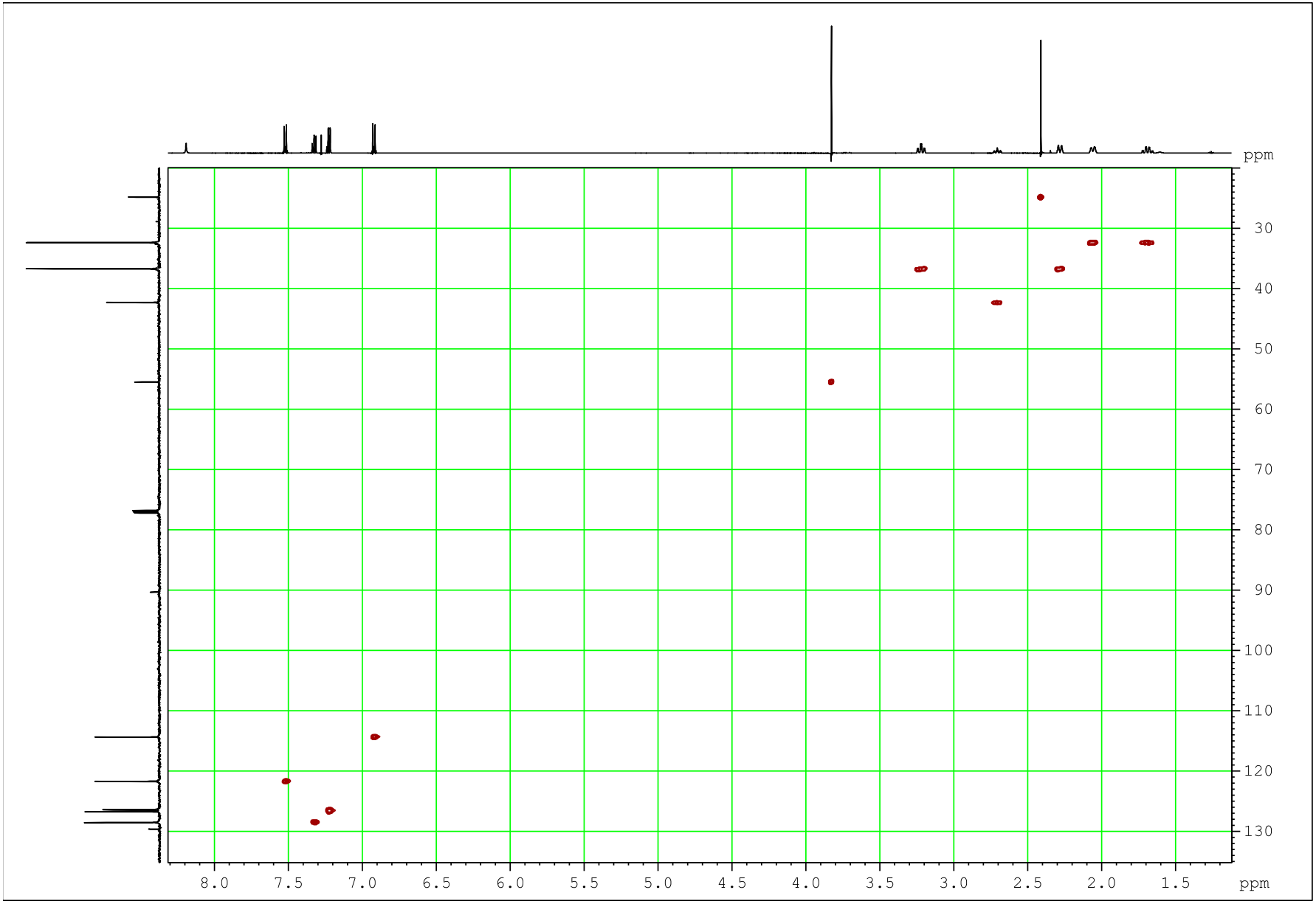
1D ^{1}H NOESY (2.04 ppm) NMR spectrum of **5** ($CDCl_3$).



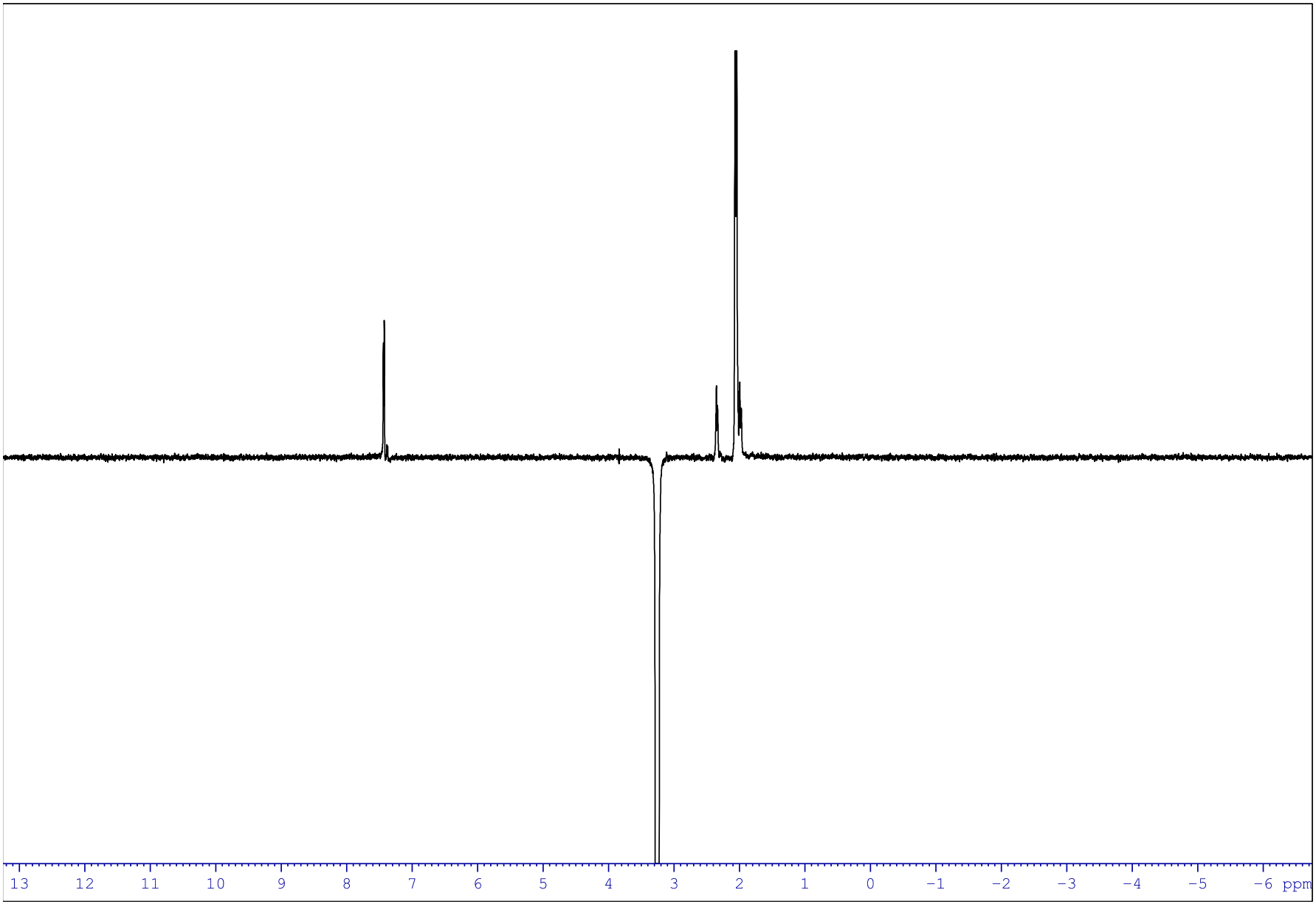
^{1}H NMR spectrum of **6** ($CDCl_3$).



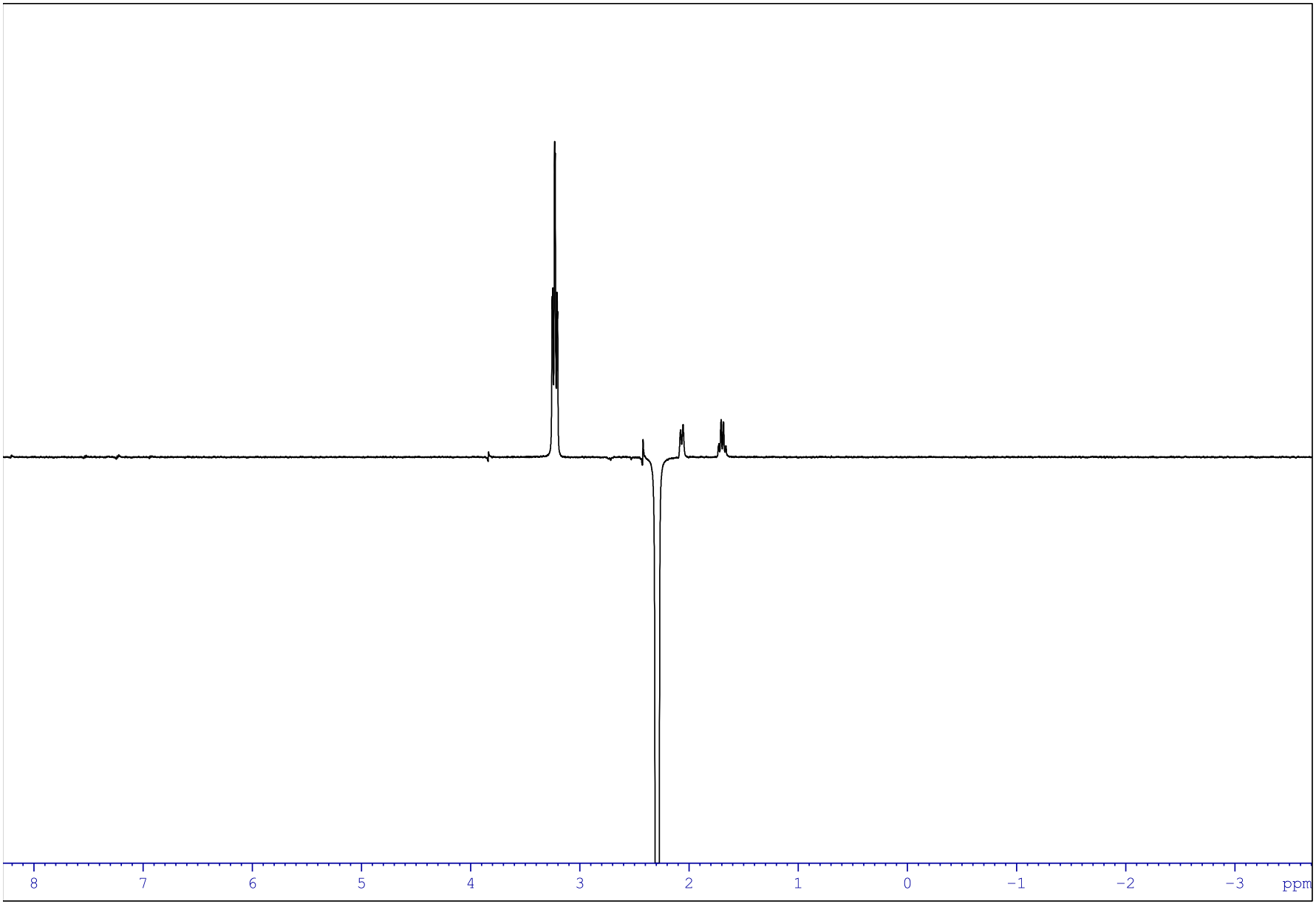
^{13}C NMR spectrum of **6** ($CDCl_3$).



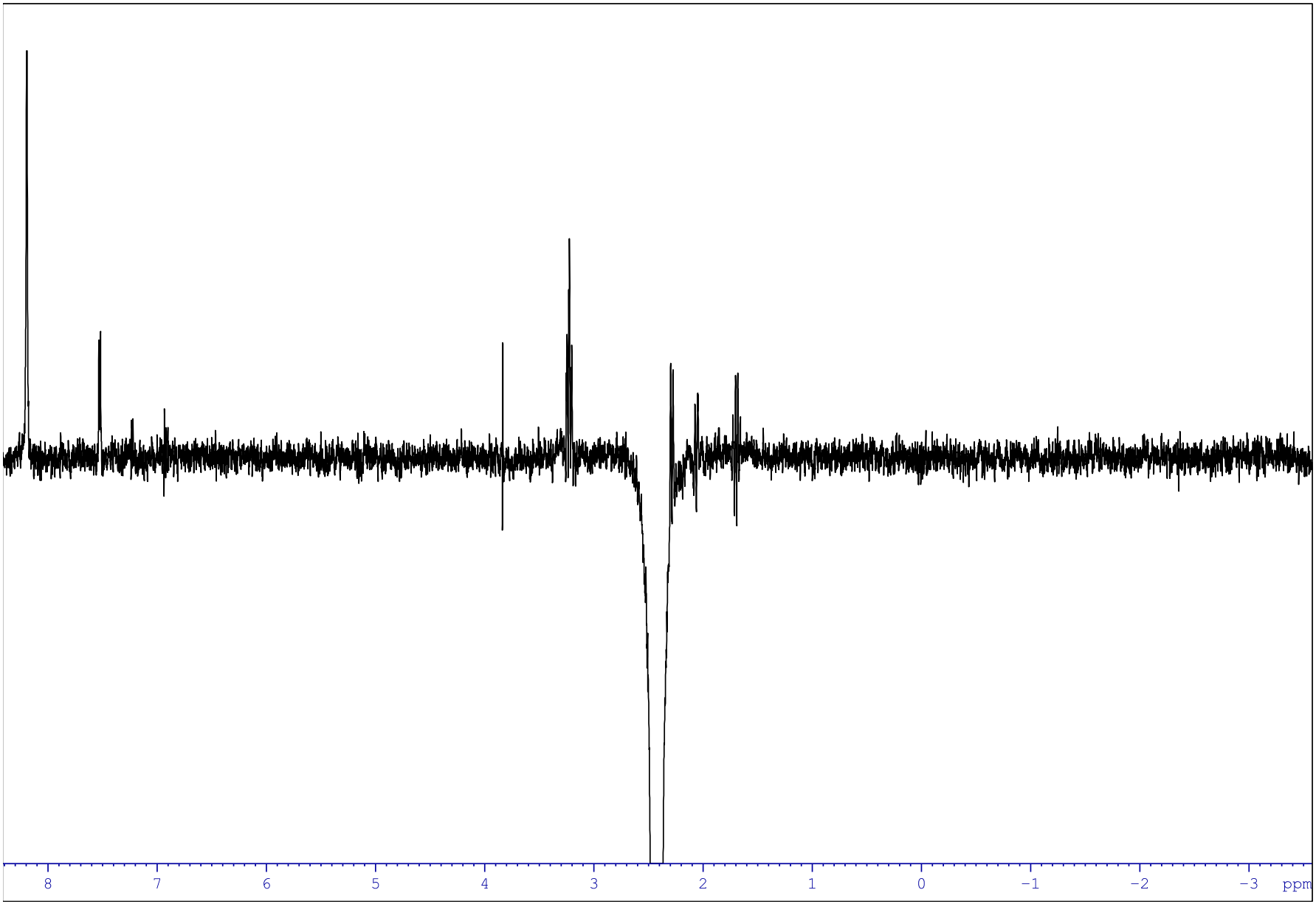
2D ^{1}H-^{13}C HSQC NMR spectrum of **6** ($CDCl_3$).



1D ^{1}H NOESY (3.25 ppm) NMR spectrum of **6** ($CDCl_3$).

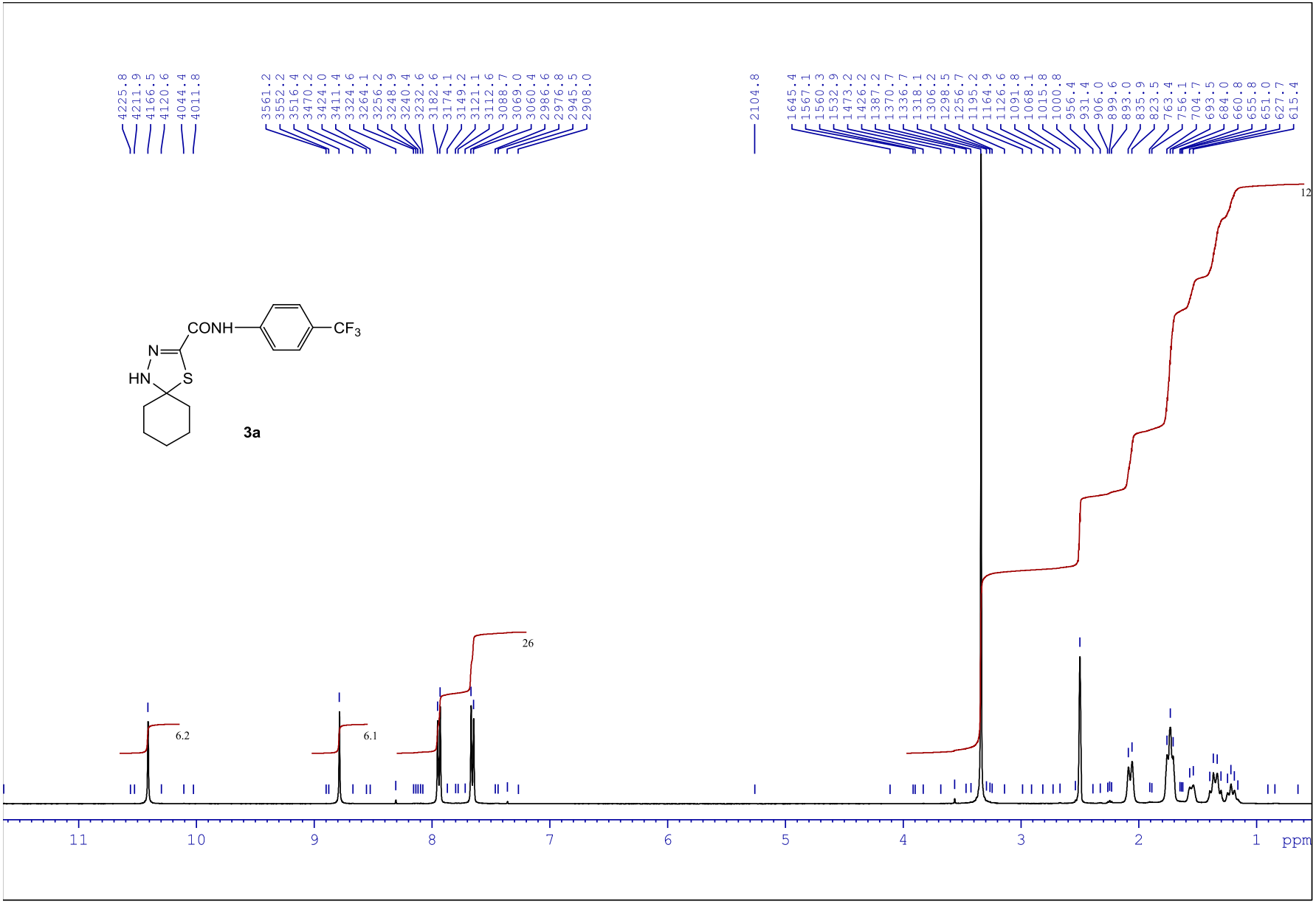


1D ^{1}H NOESY (2.28 ppm) NMR spectrum of **6** ($CDCl_3$).

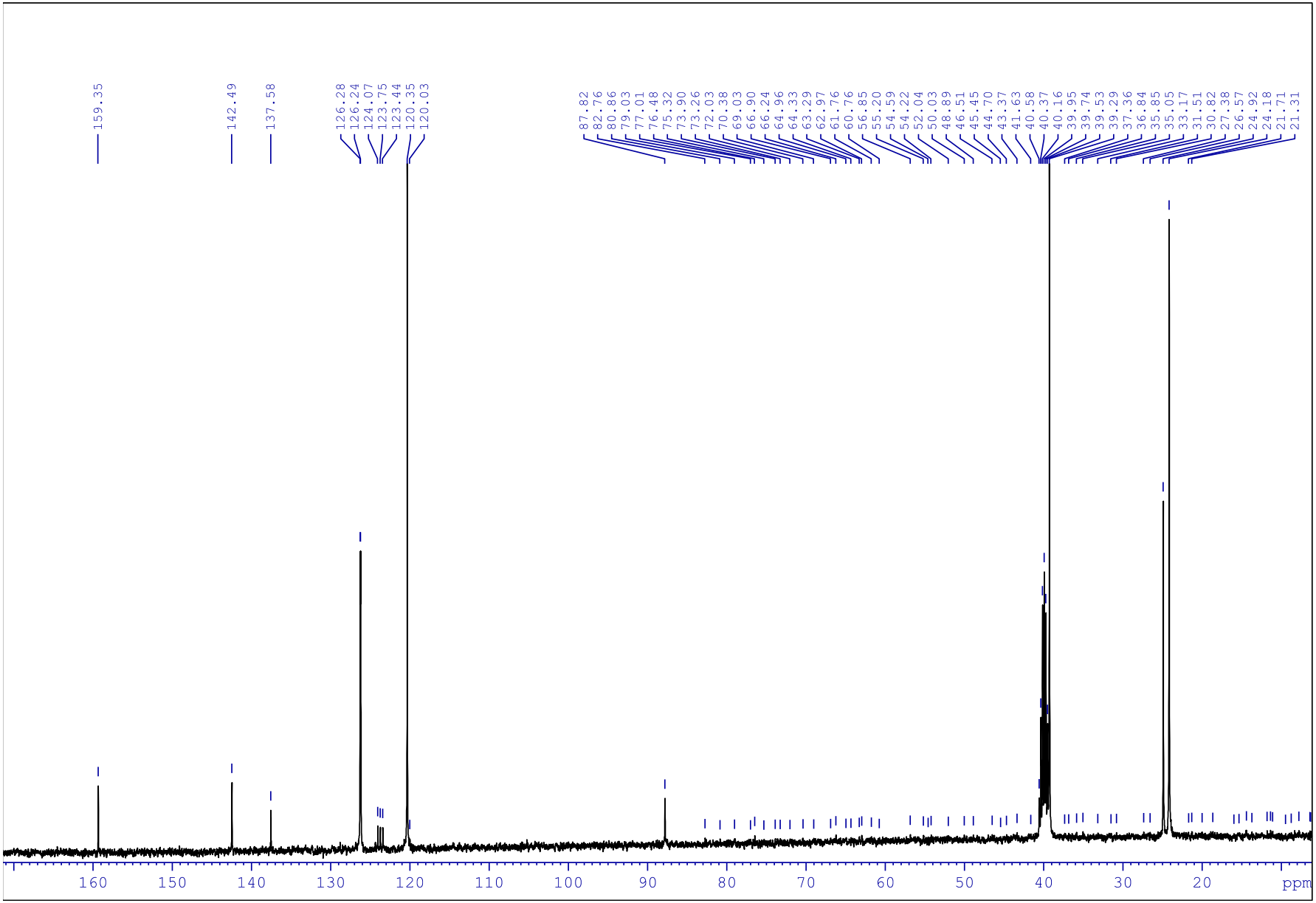


1D ^{1}H NOESY (2.41 ppm) NMR spectrum of **6** ($CDCl_3$).

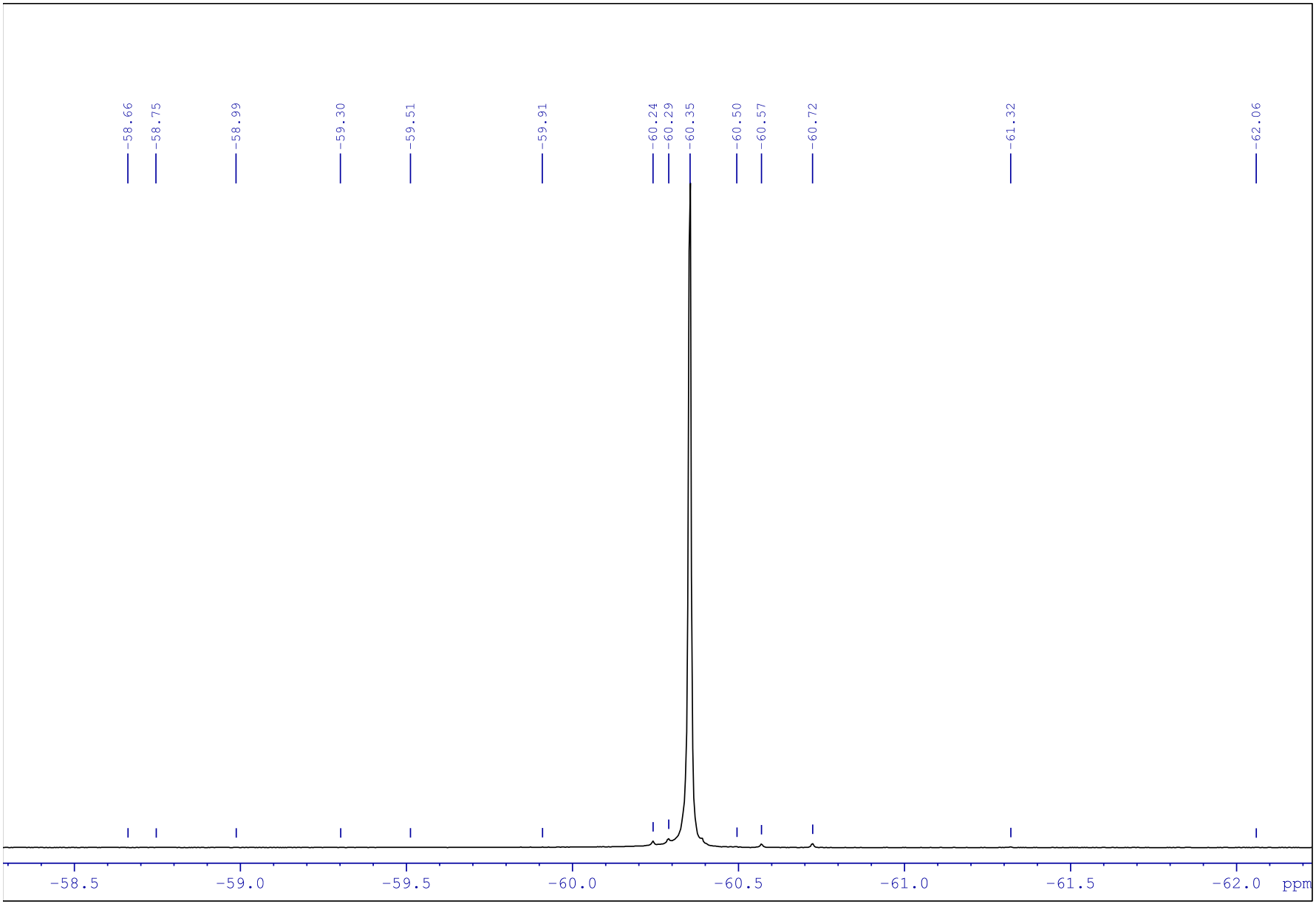
2. NMR spectra (Bruker AV-400)



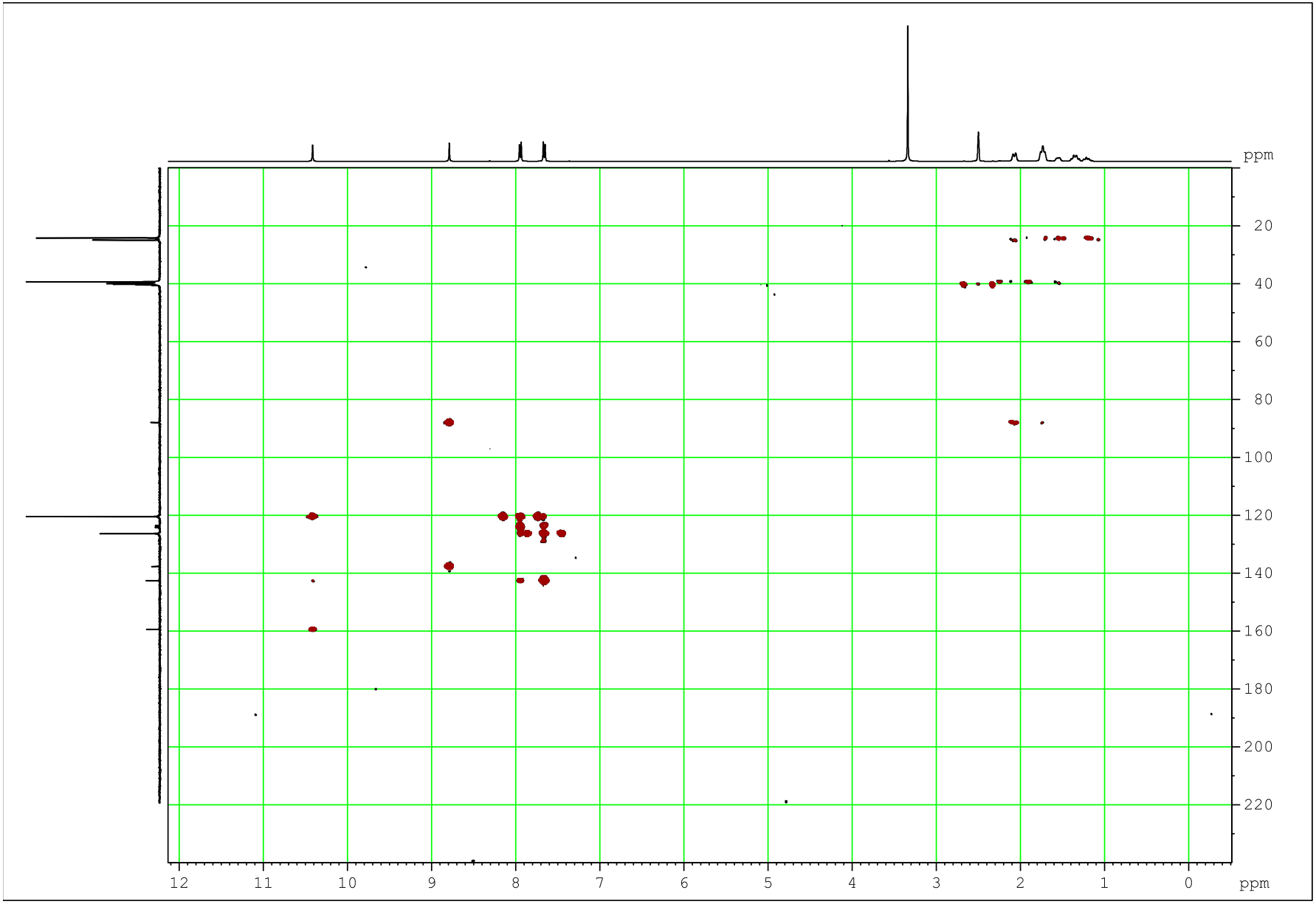
^{1}H NMR spectrum of **3a** (DMSO-d_6).



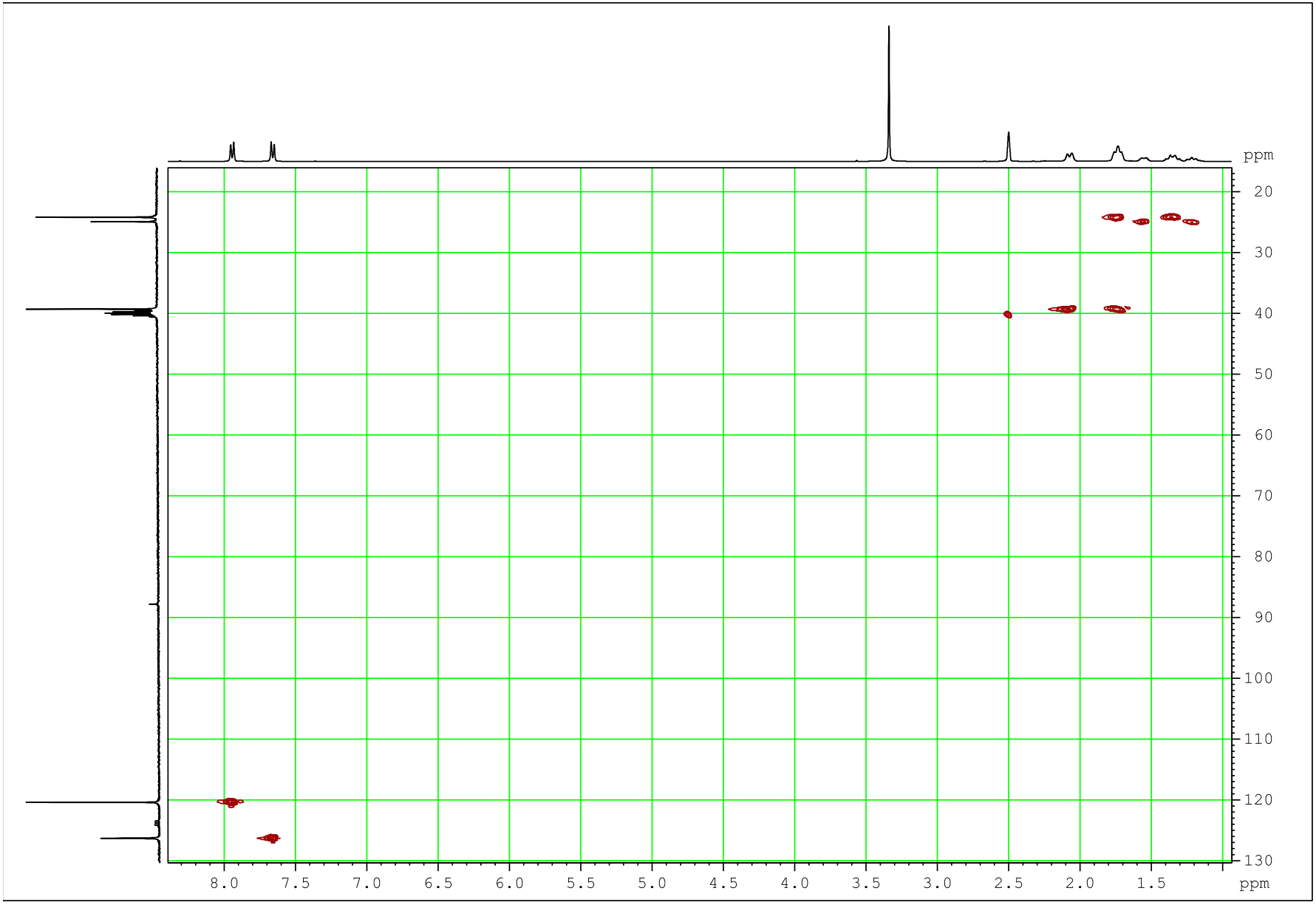
^{13}C NMR spectrum of **3a** (DMSO-d_6).



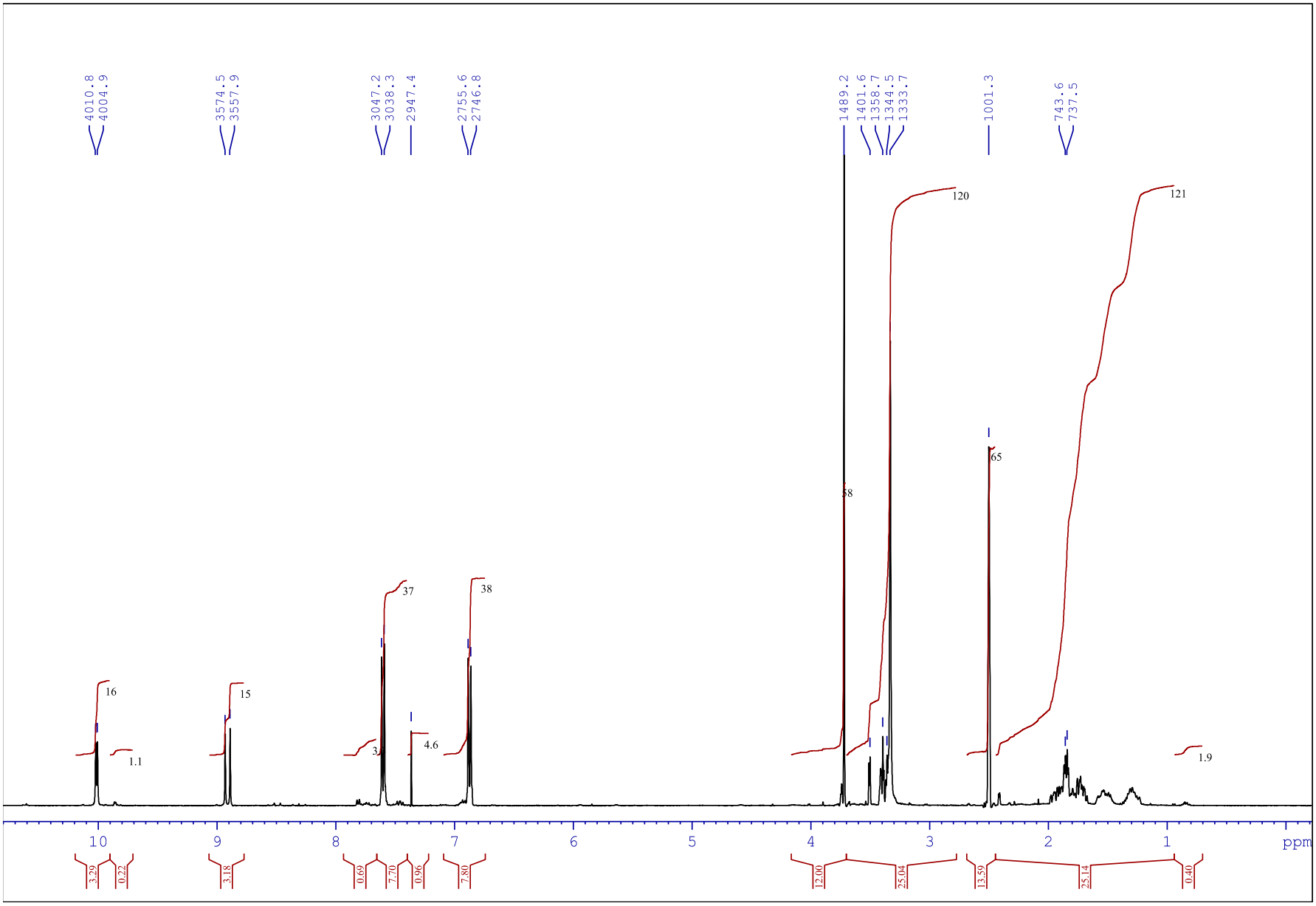
^{19}F NMR spectrum of **3a** (DMSO-d_6).



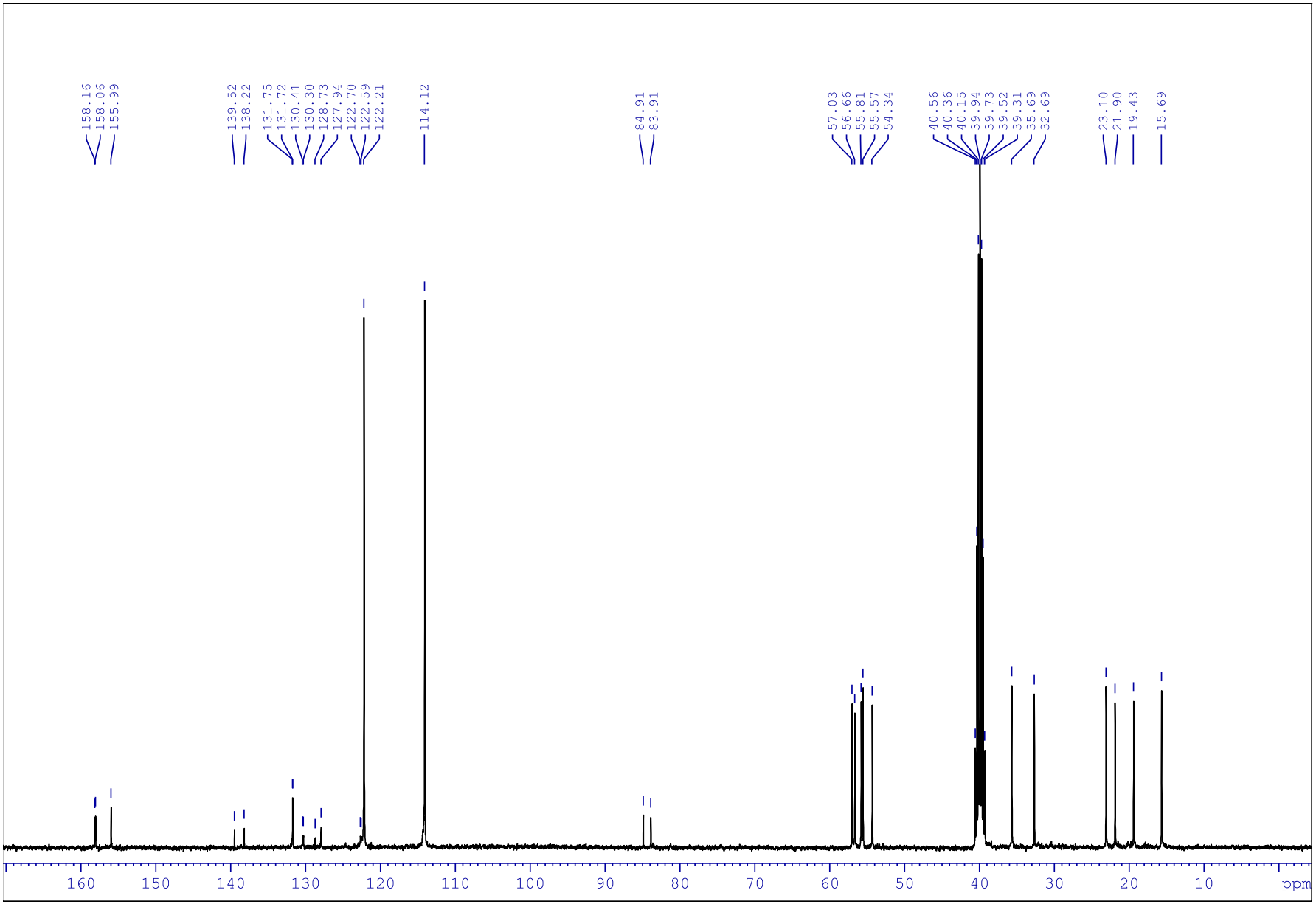
2D ^{1}H-^{13}C HMBC NMR spectrum of **3a** (DMSO-d_6).



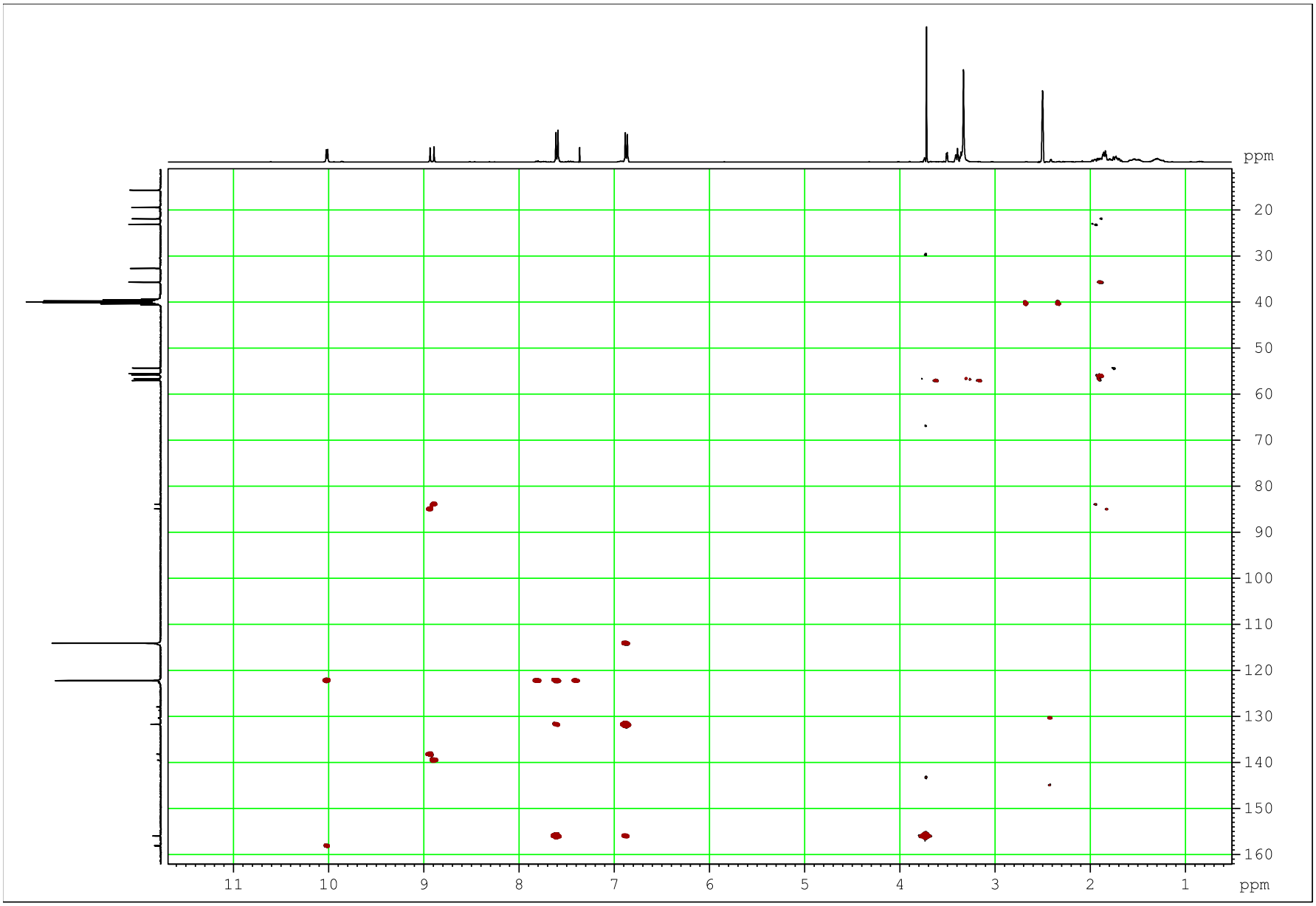
2D ^{1}H-^{13}C HSQC NMR spectrum of **3a** (DMSO-d_6).



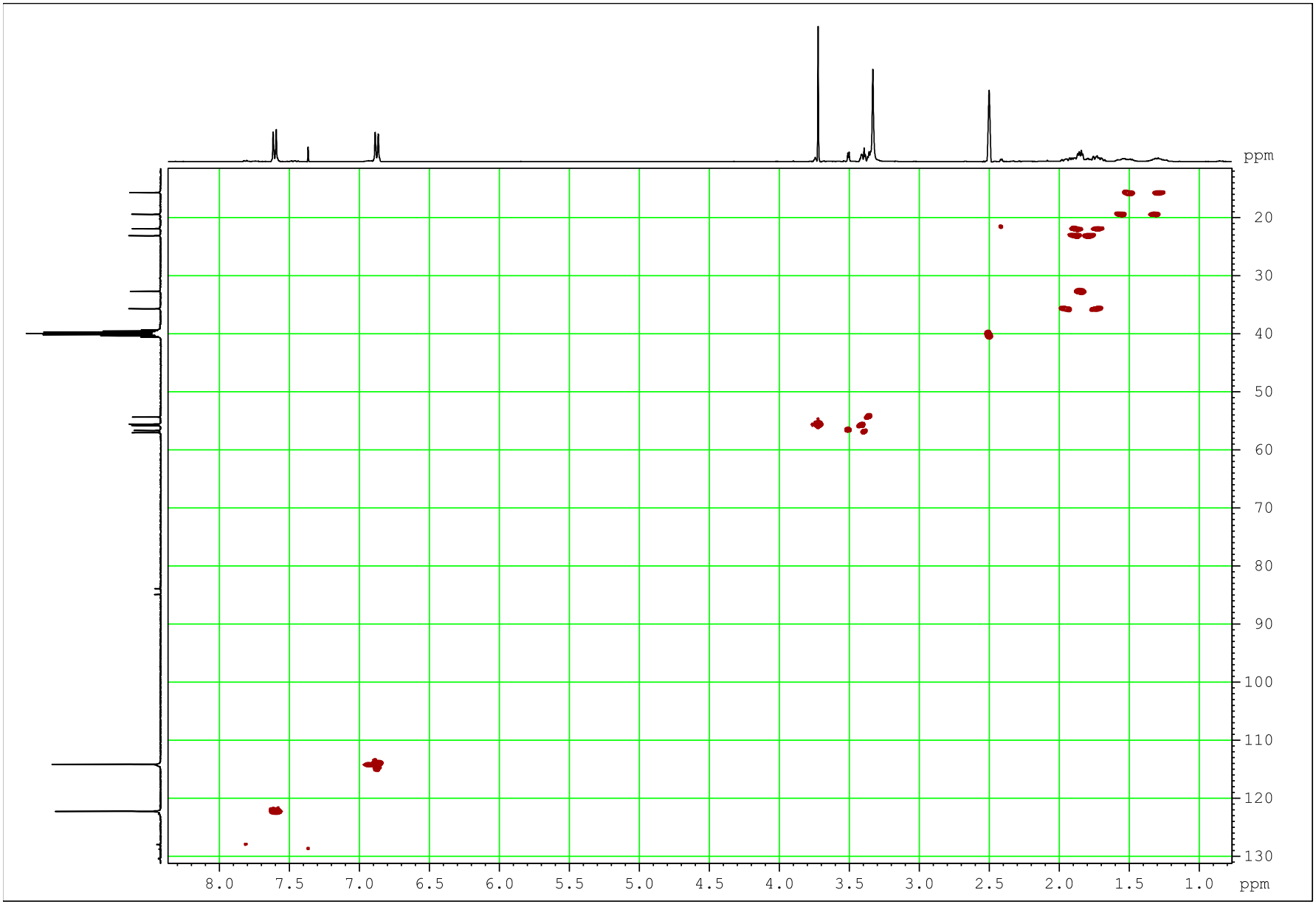
^{1}H NMR spectrum of **3e** (DMSO-d_6).



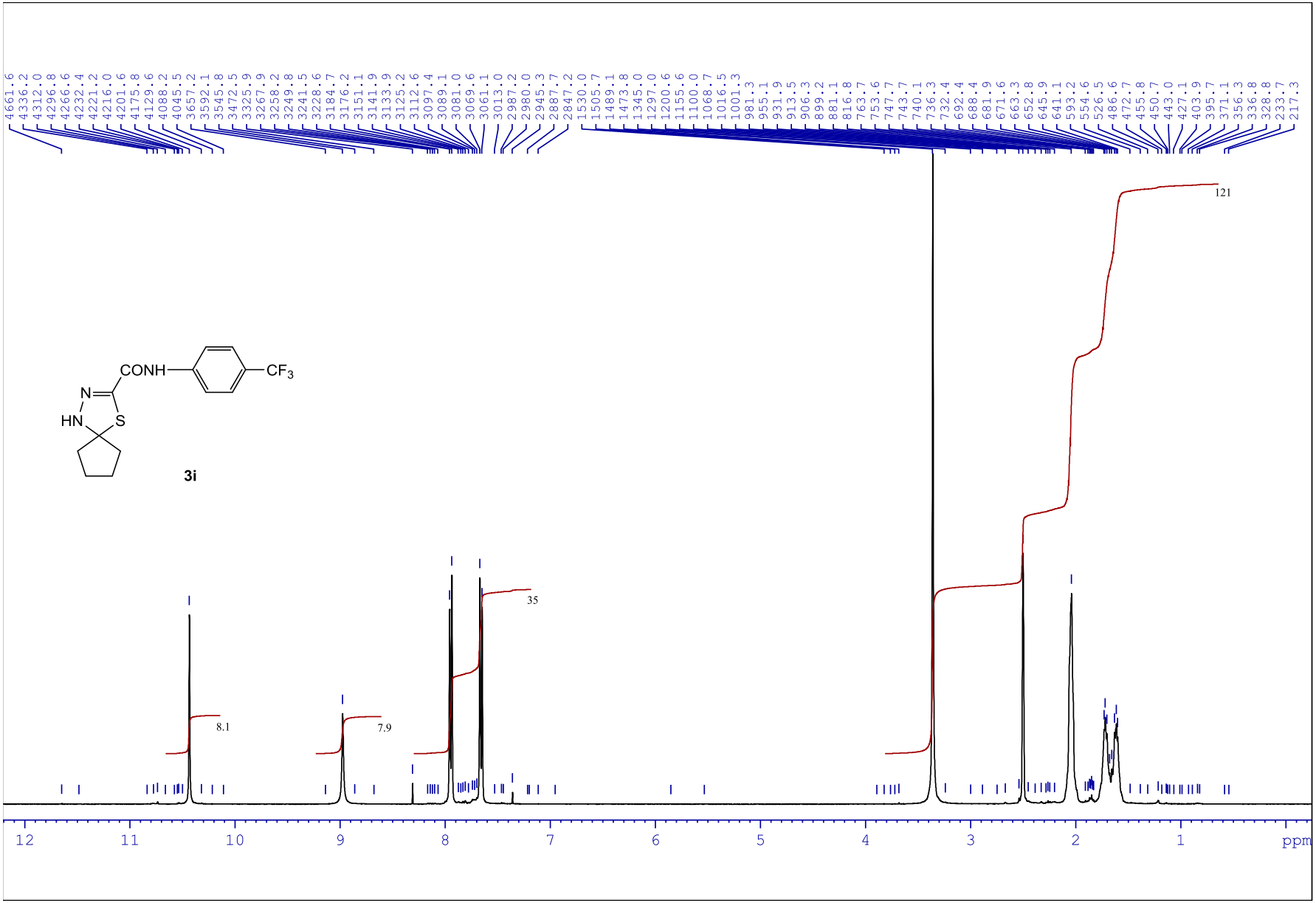
^{13}C NMR spectrum of **3e** (DMSO-d_6).



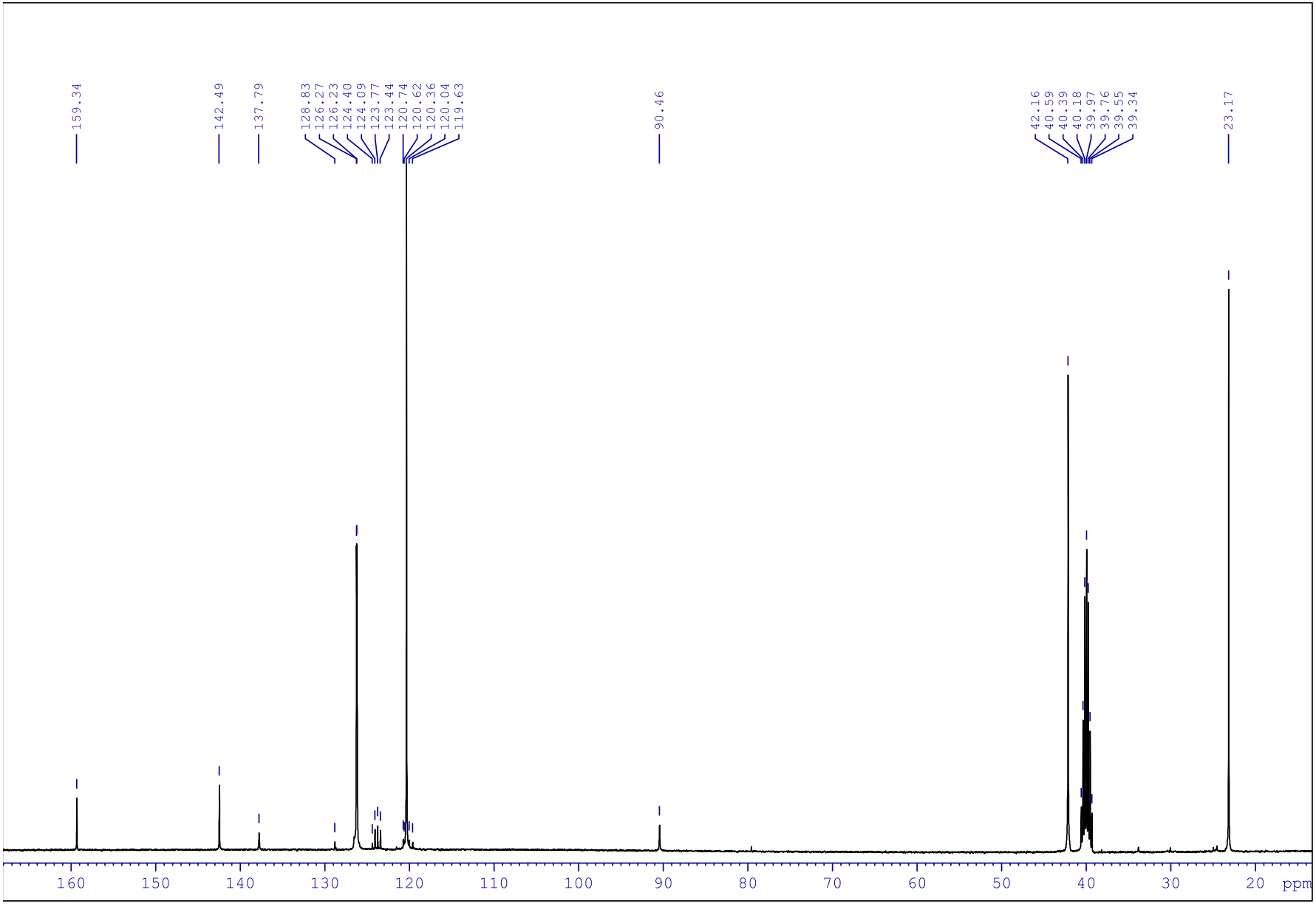
2D ^{1}H-^{13}C HMBC NMR spectrum of **3e** (DMSO-d_6).



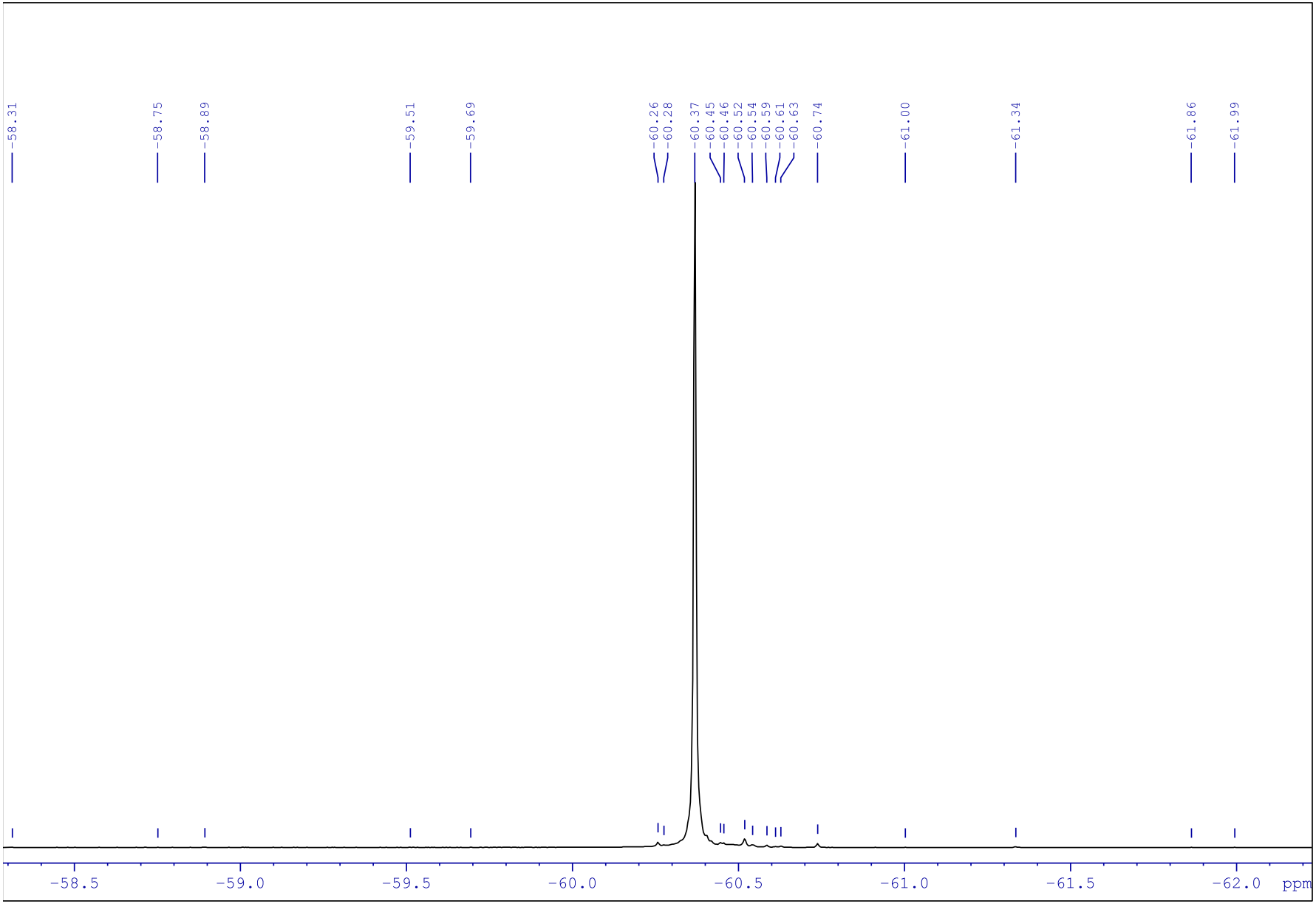
2D ^{1}H-^{13}C HSQC NMR spectrum of **3e** (DMSO-d_6).



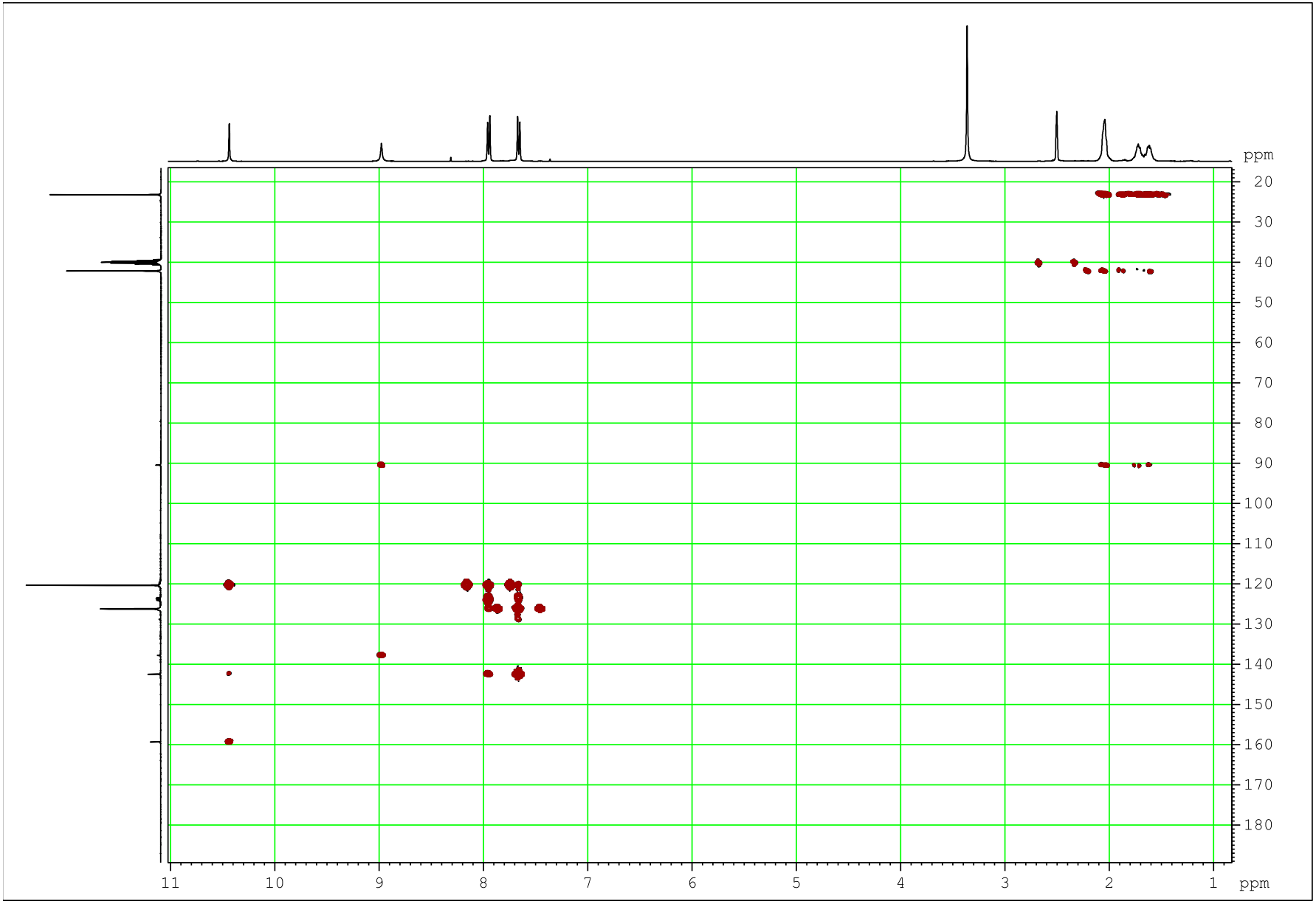
^{1}H NMR spectrum of **3i** (DMSO-d_6).



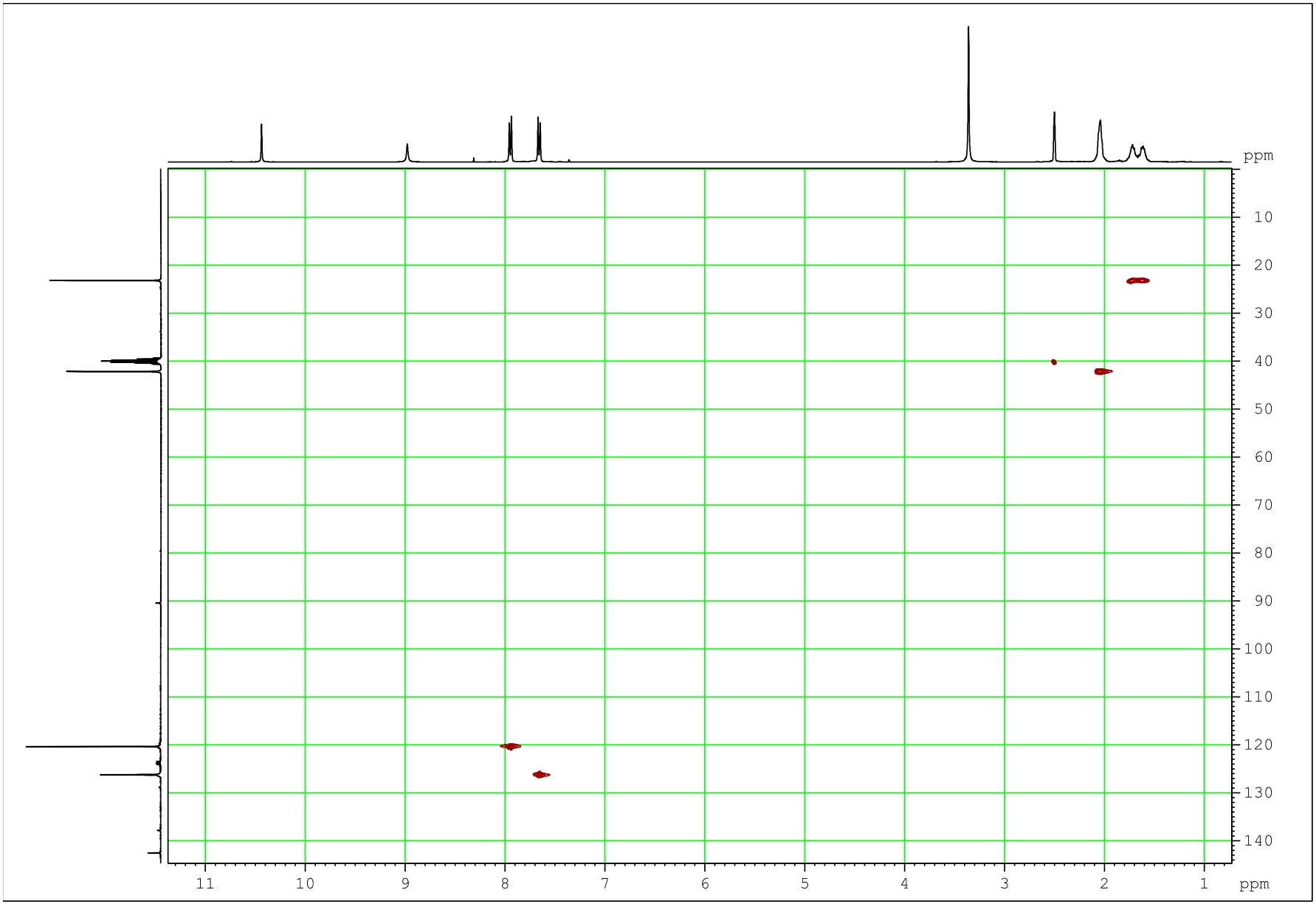
^{13}C NMR spectrum of **3i** (DMSO-d_6).



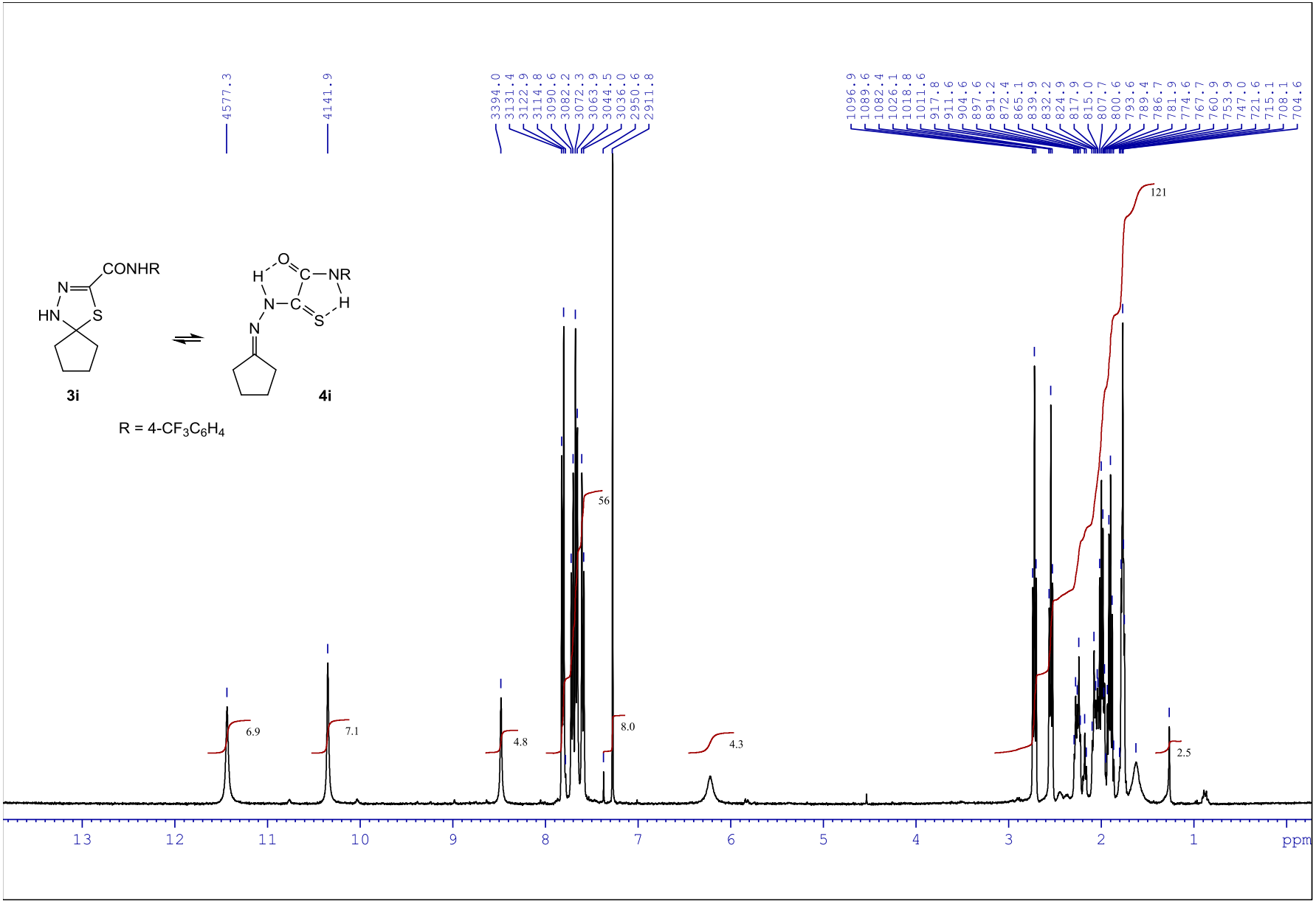
^{19}F NMR spectrum of **3i** (DMSO-d_6).



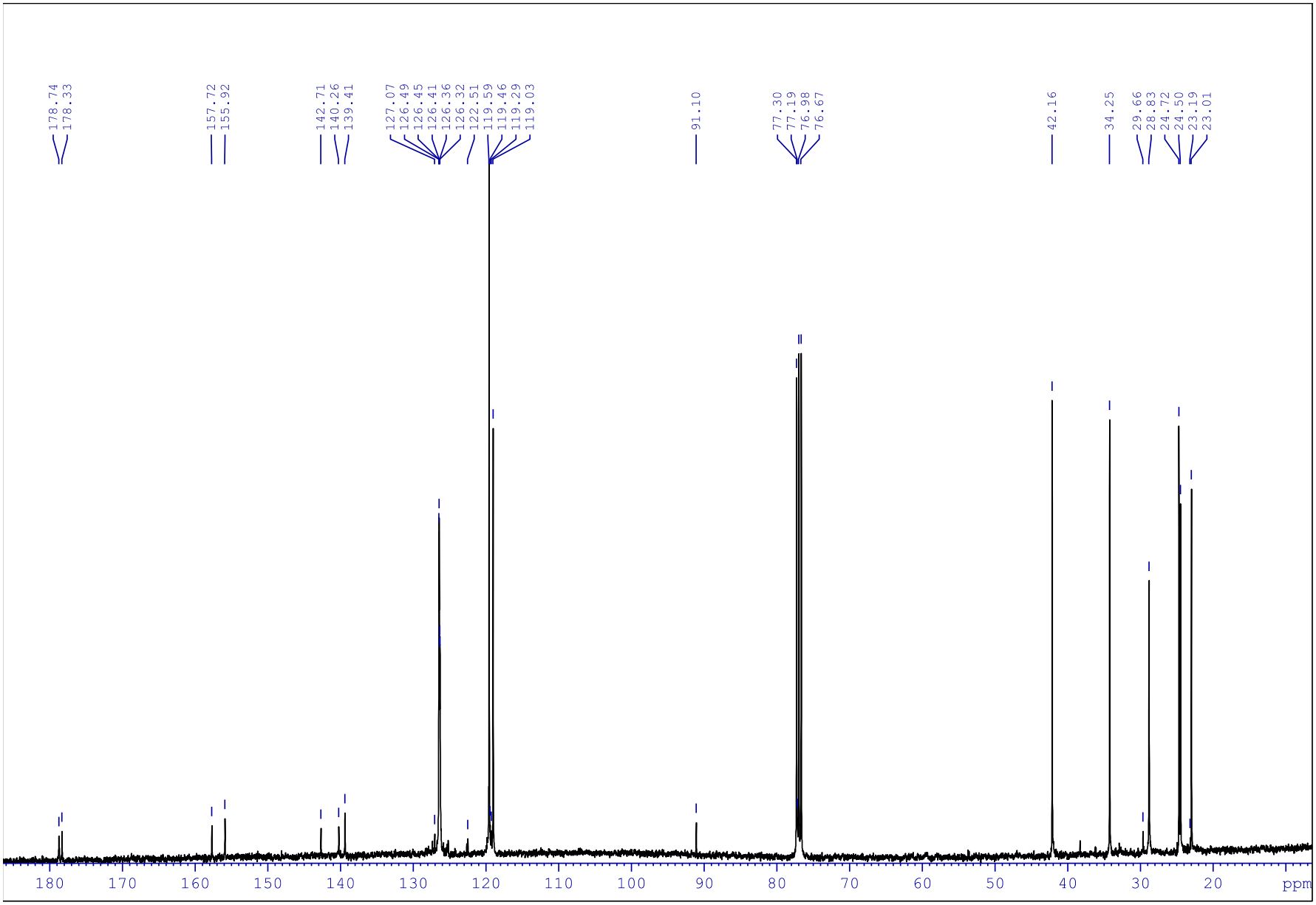
2D ^{1}H-^{13}C HMBC NMR spectrum of **3i** (DMSO-d_6).



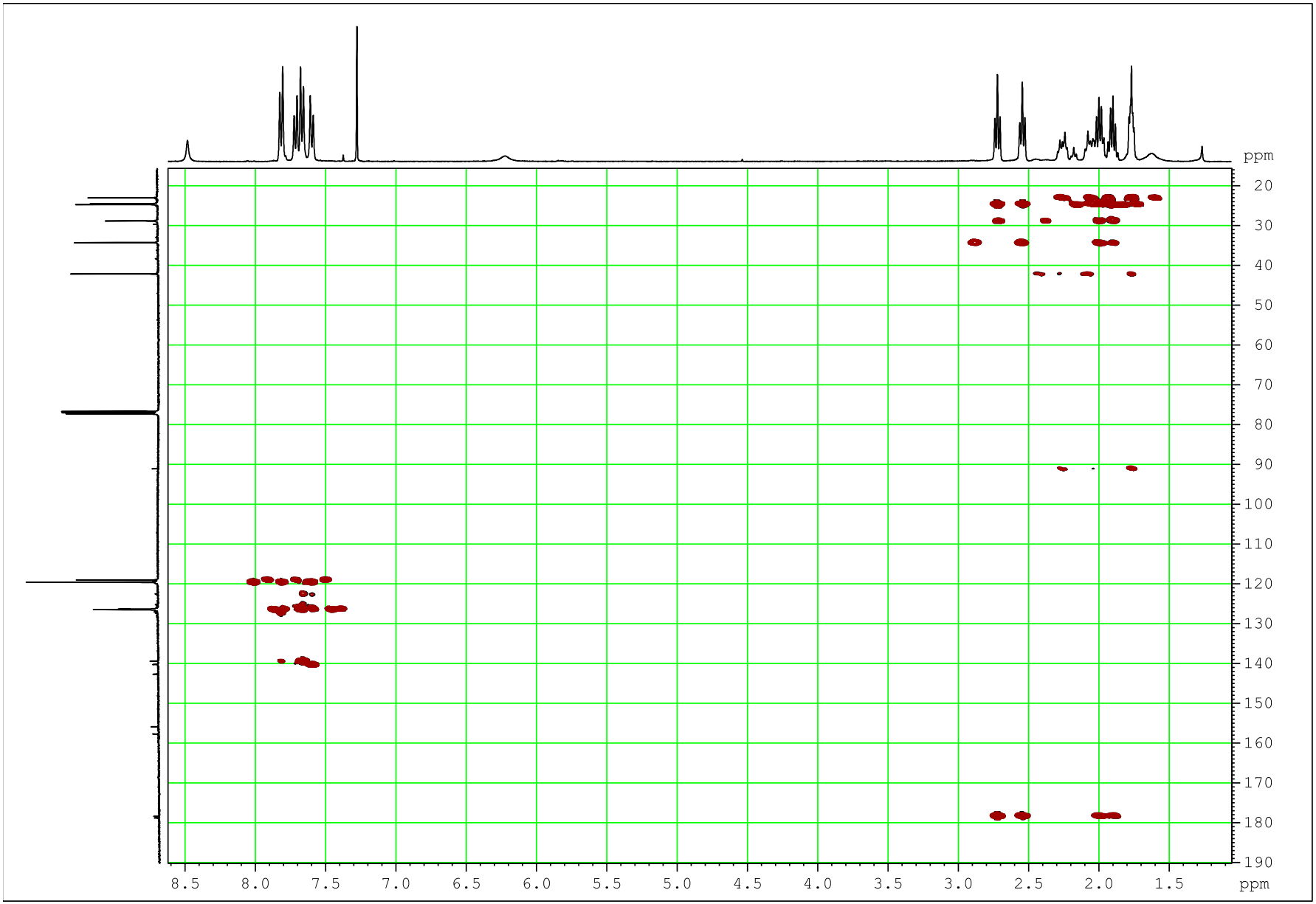
2D ^{1}H-^{13}C HSQC NMR spectrum of **3i** (DMSO-d_6).



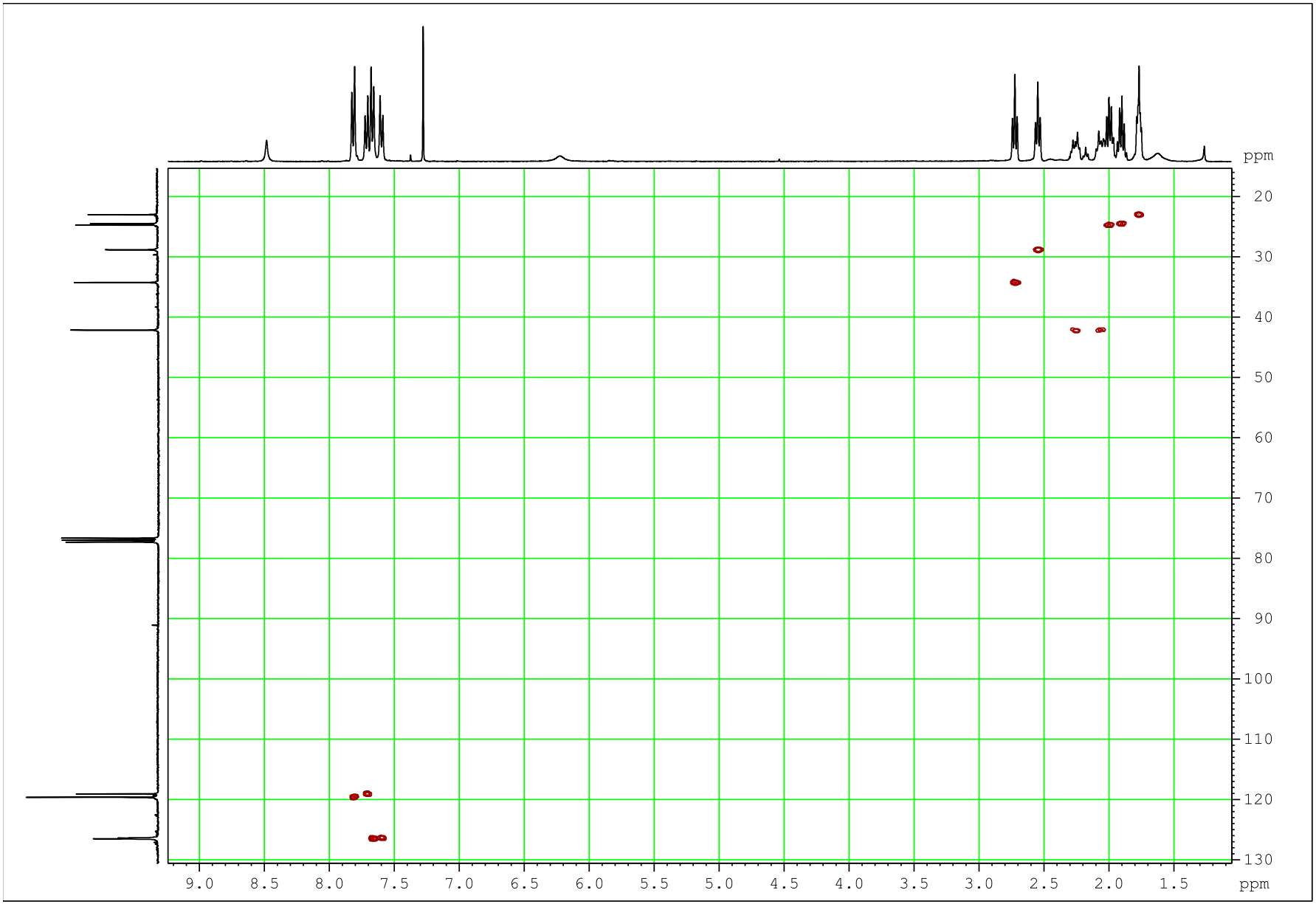
^{1}H NMR spectrum of **3i/4i** ($CDCl_3$).



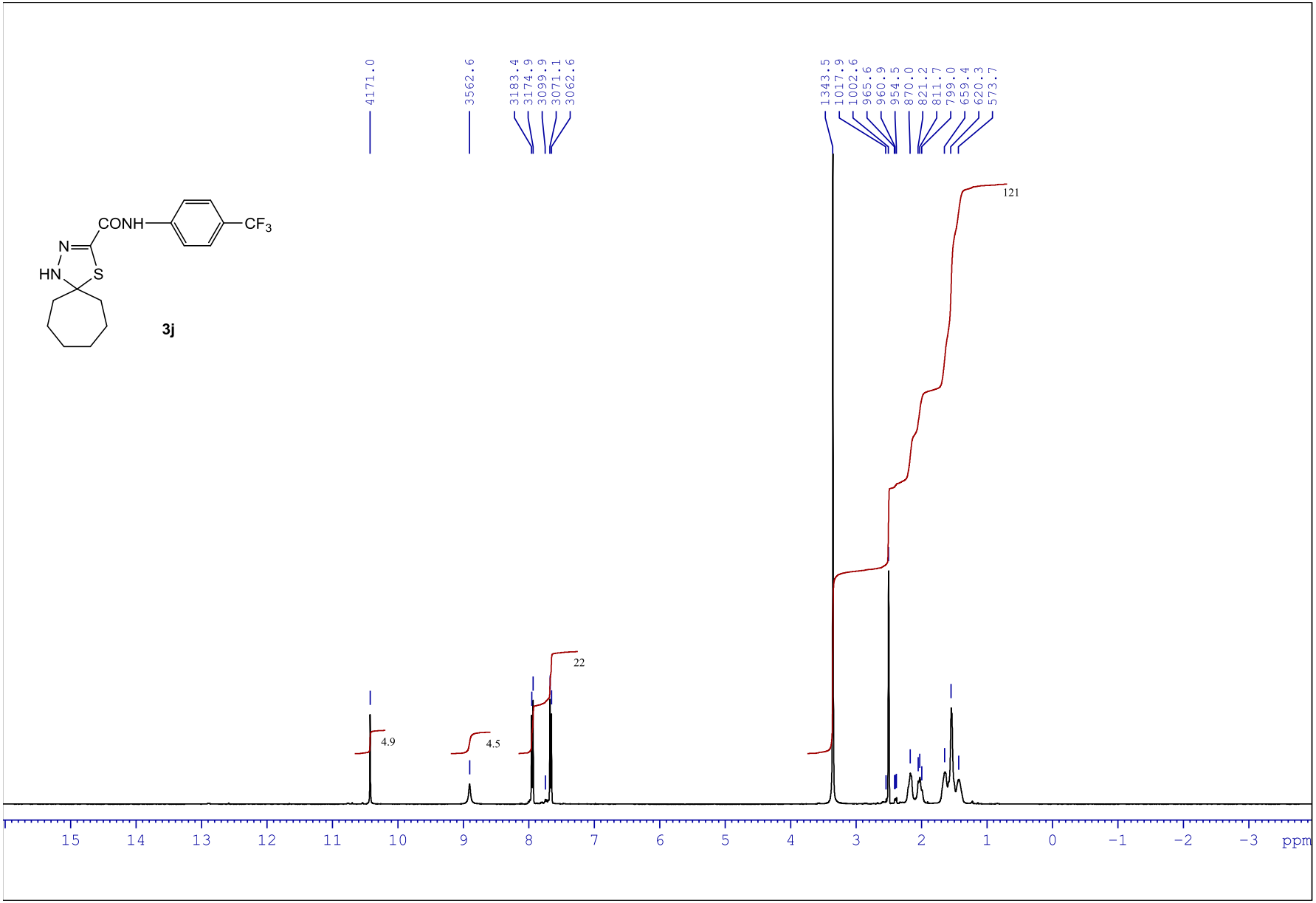
^{13}C NMR spectrum of **3i/4i** ($CDCl_3$).



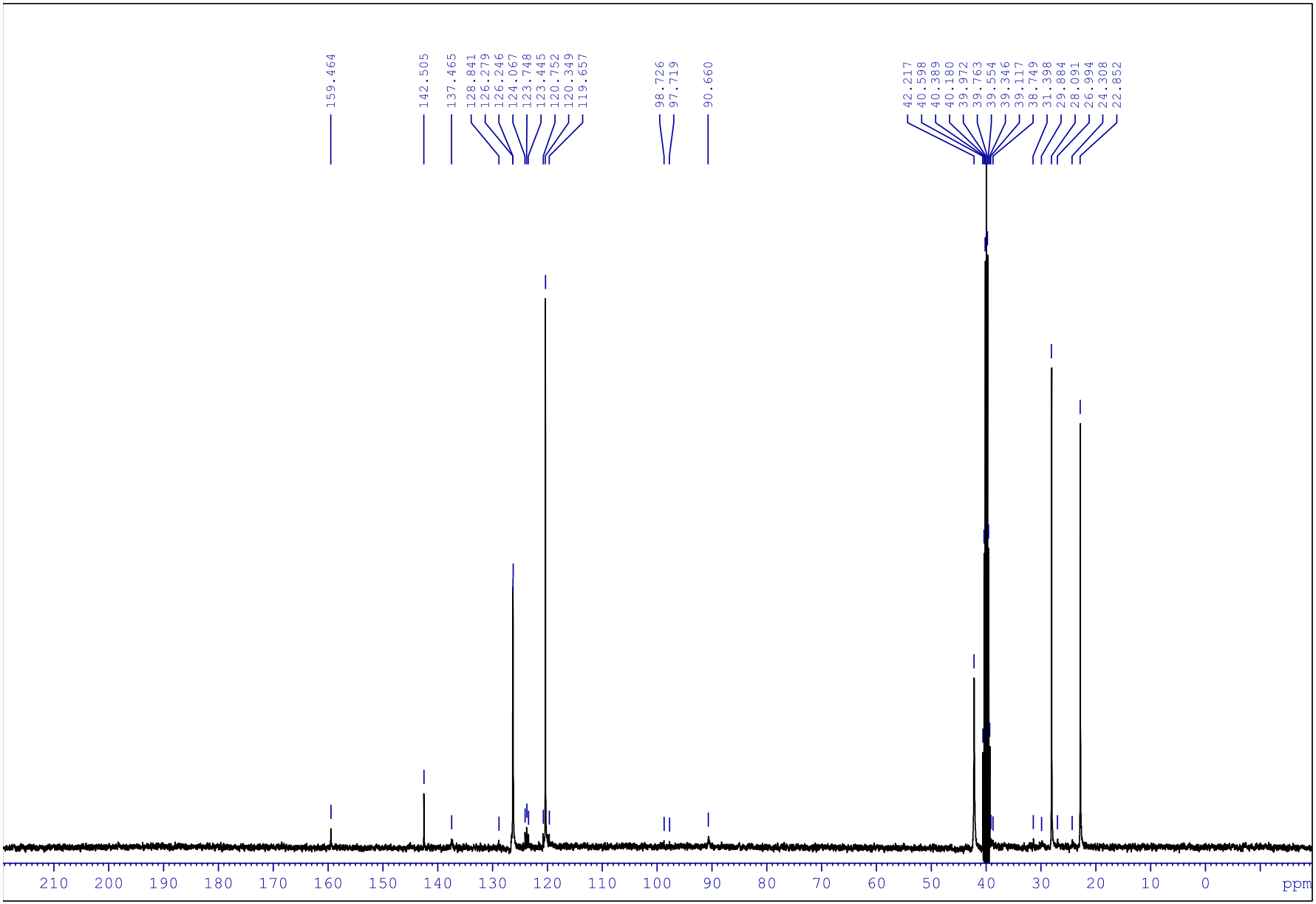
2D ^{1}H-^{13}C HMBC NMR spectrum of **3i/4i** ($CDCl_3$).



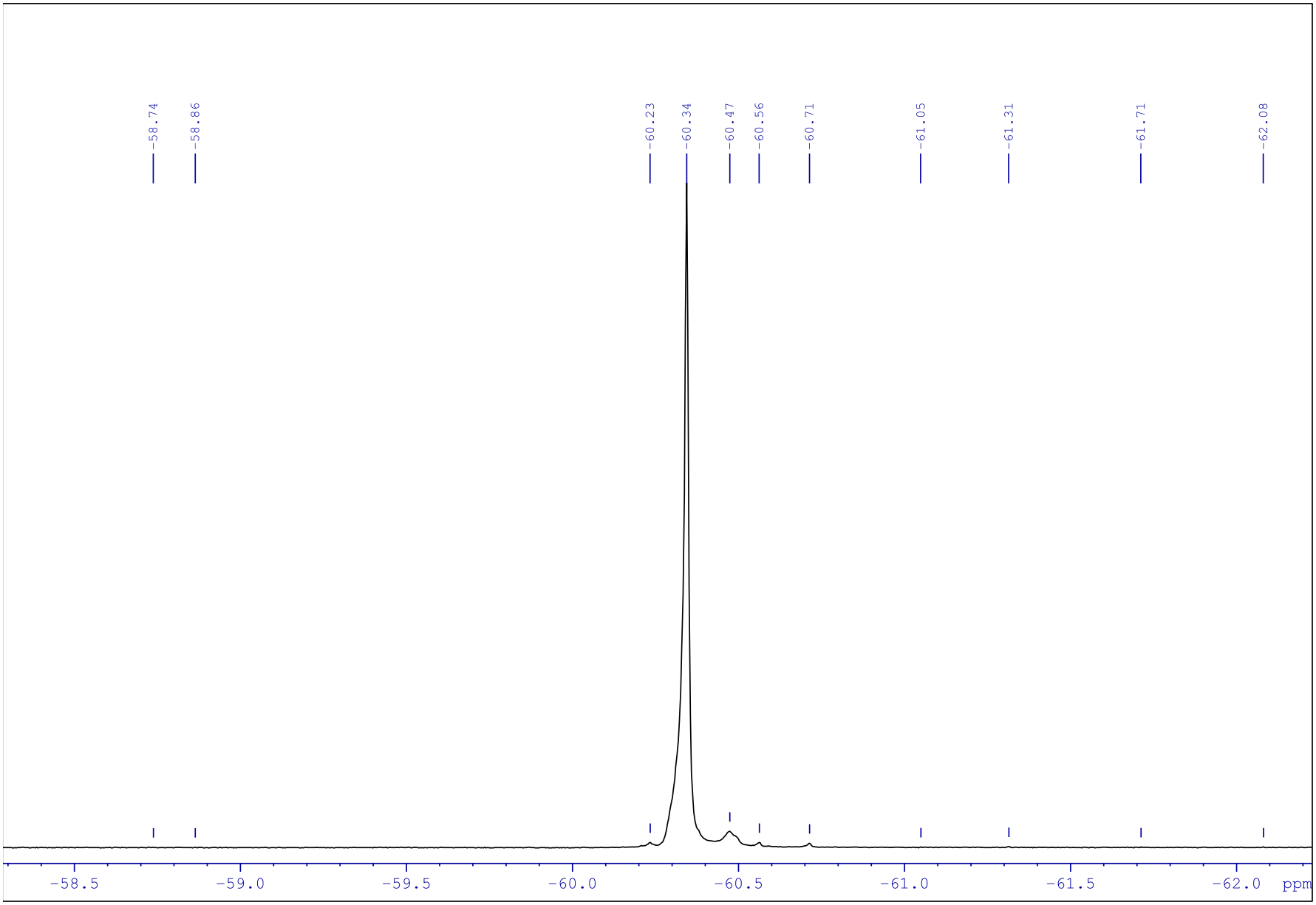
2D ^{1}H-^{13}C HSQC NMR spectrum of **3i/4i** ($CDCl_3$).



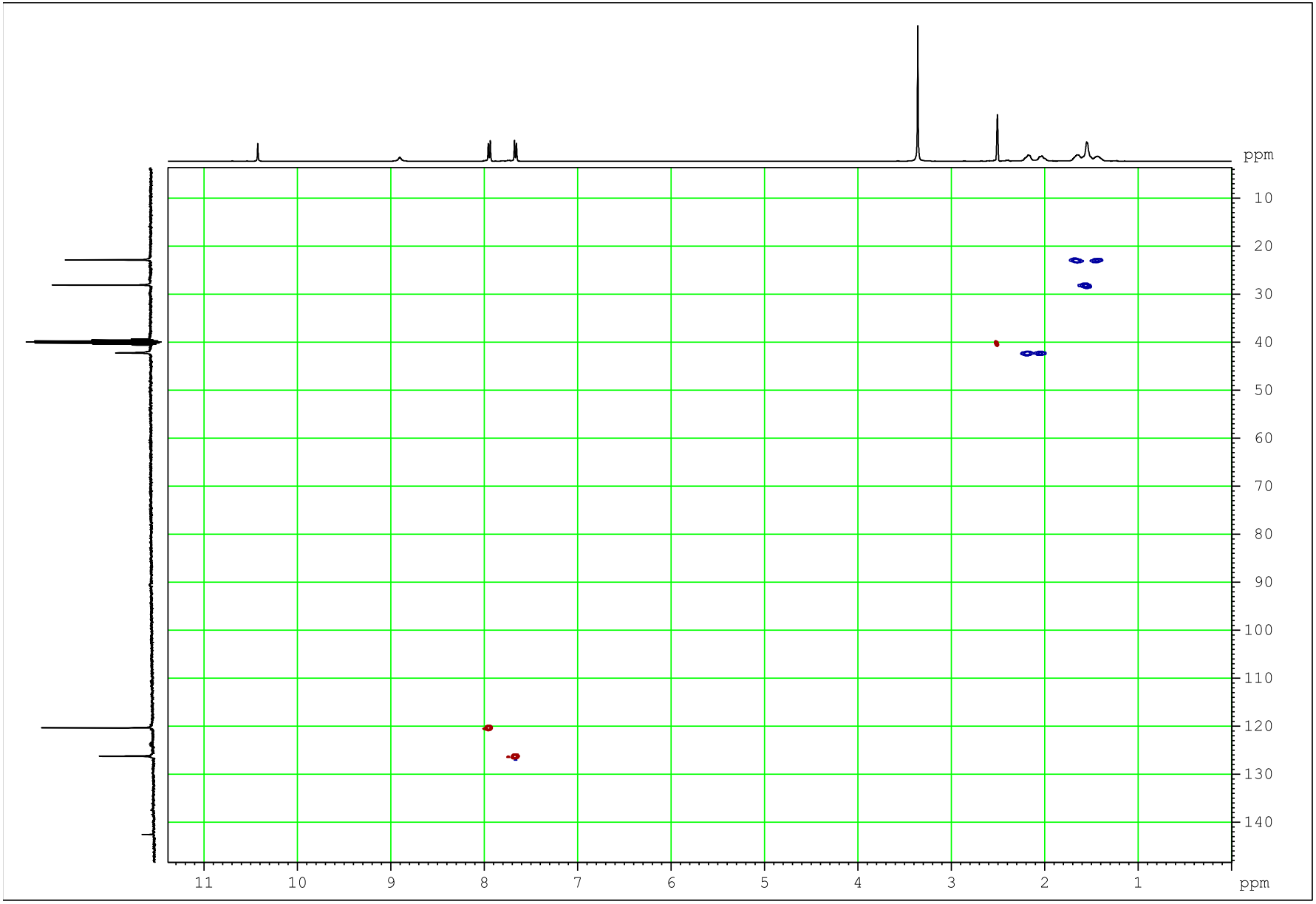
^{1}H NMR spectrum of **3j** (DMSO-d_6).



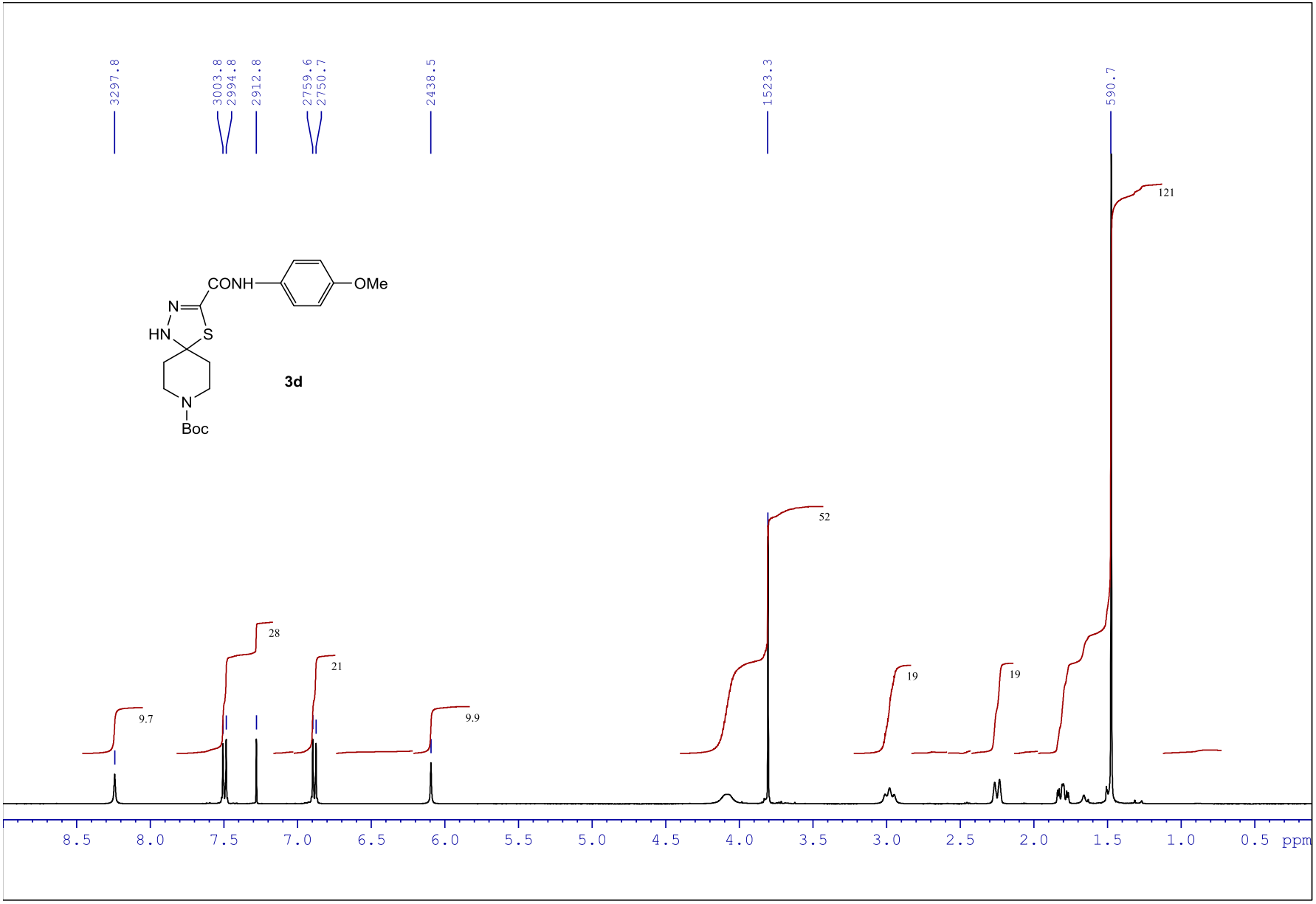
^{13}C NMR spectrum of **3j** (DMSO-d_6).



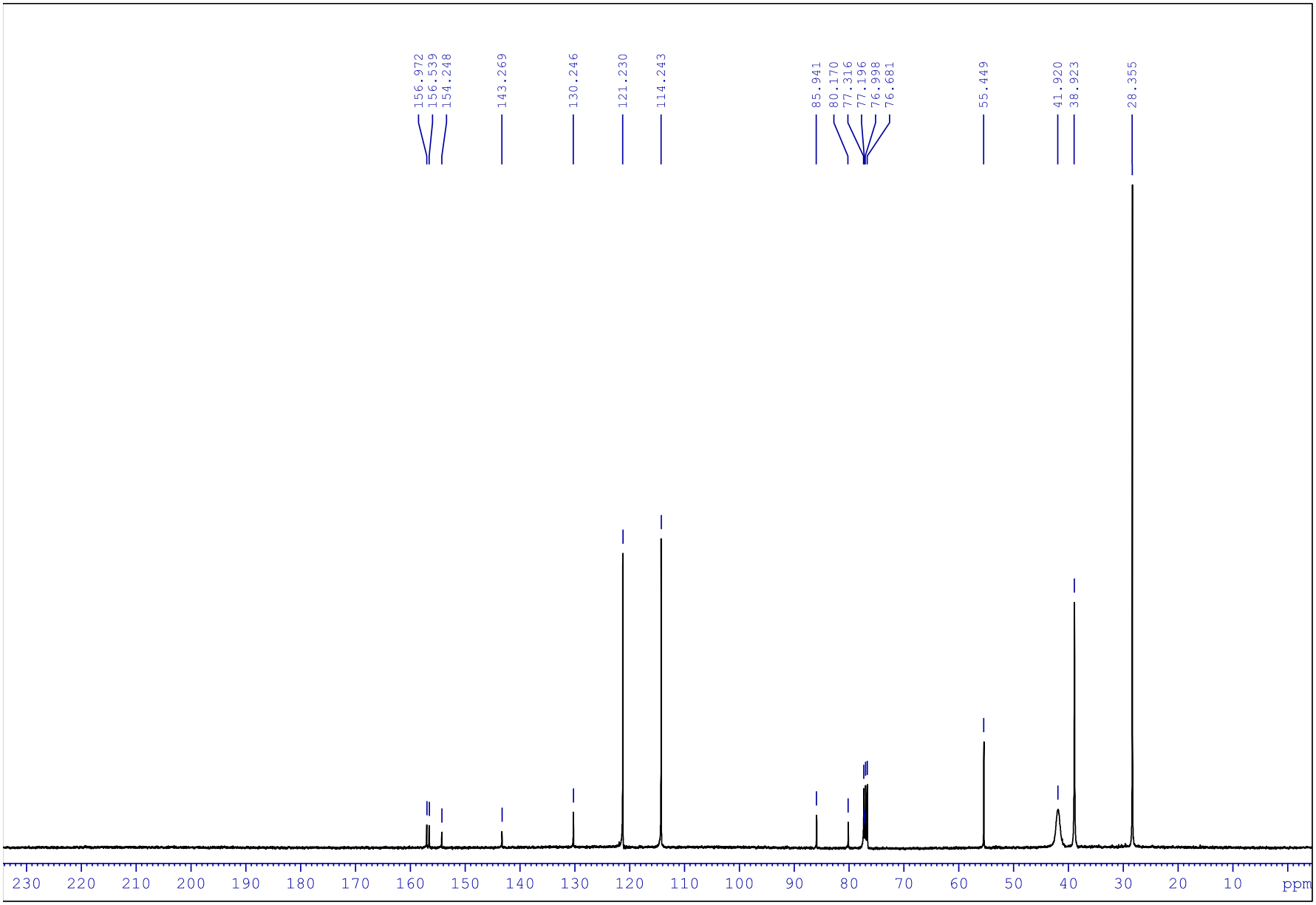
^{19}F NMR spectrum of **3j** (DMSO-d_6).



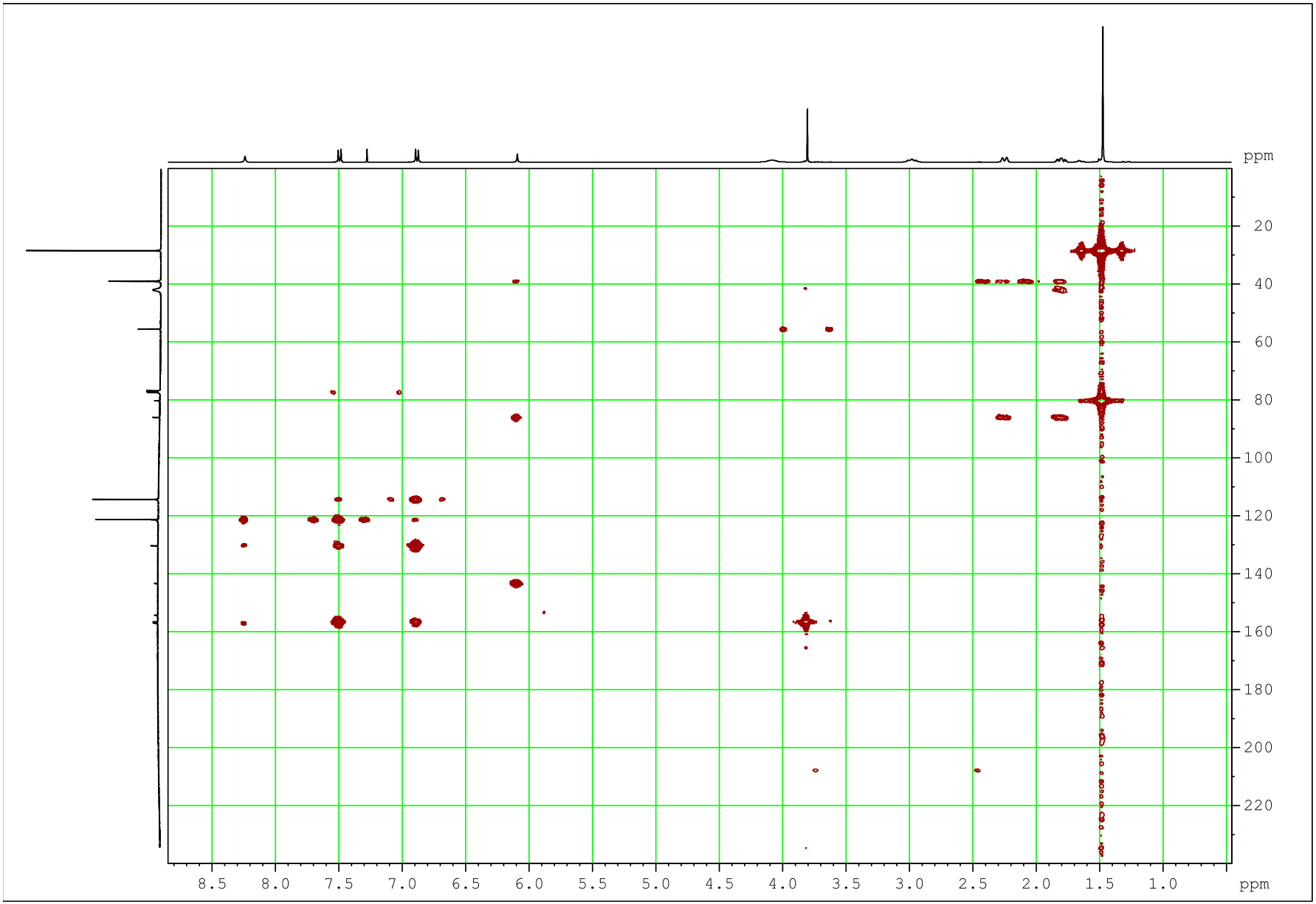
2D ^{1}H-^{13}C HSQC NMR spectrum of **3j** (DMSO-d_6).



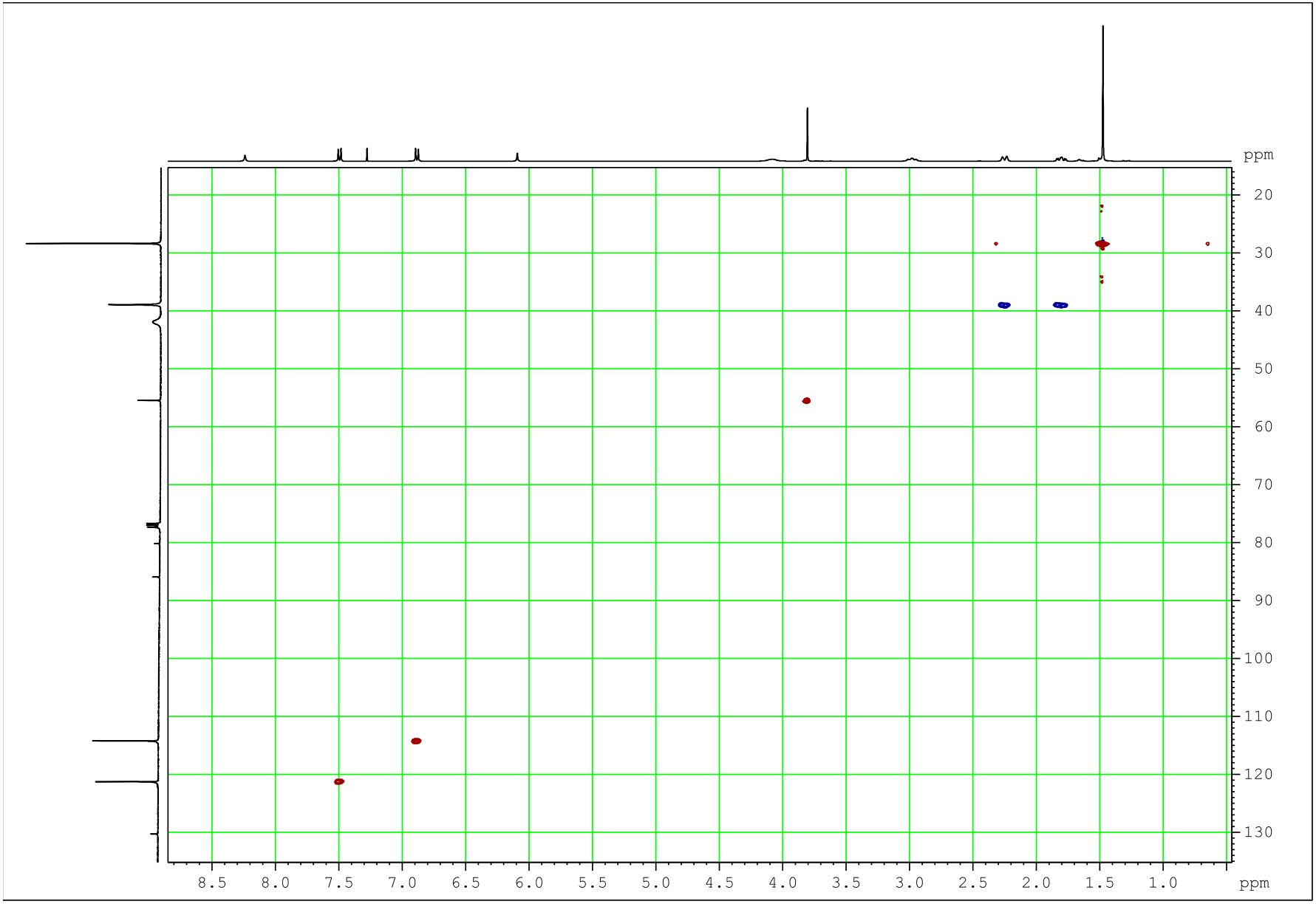
^{1}H NMR spectrum of **3d** (DMSO-d_6).



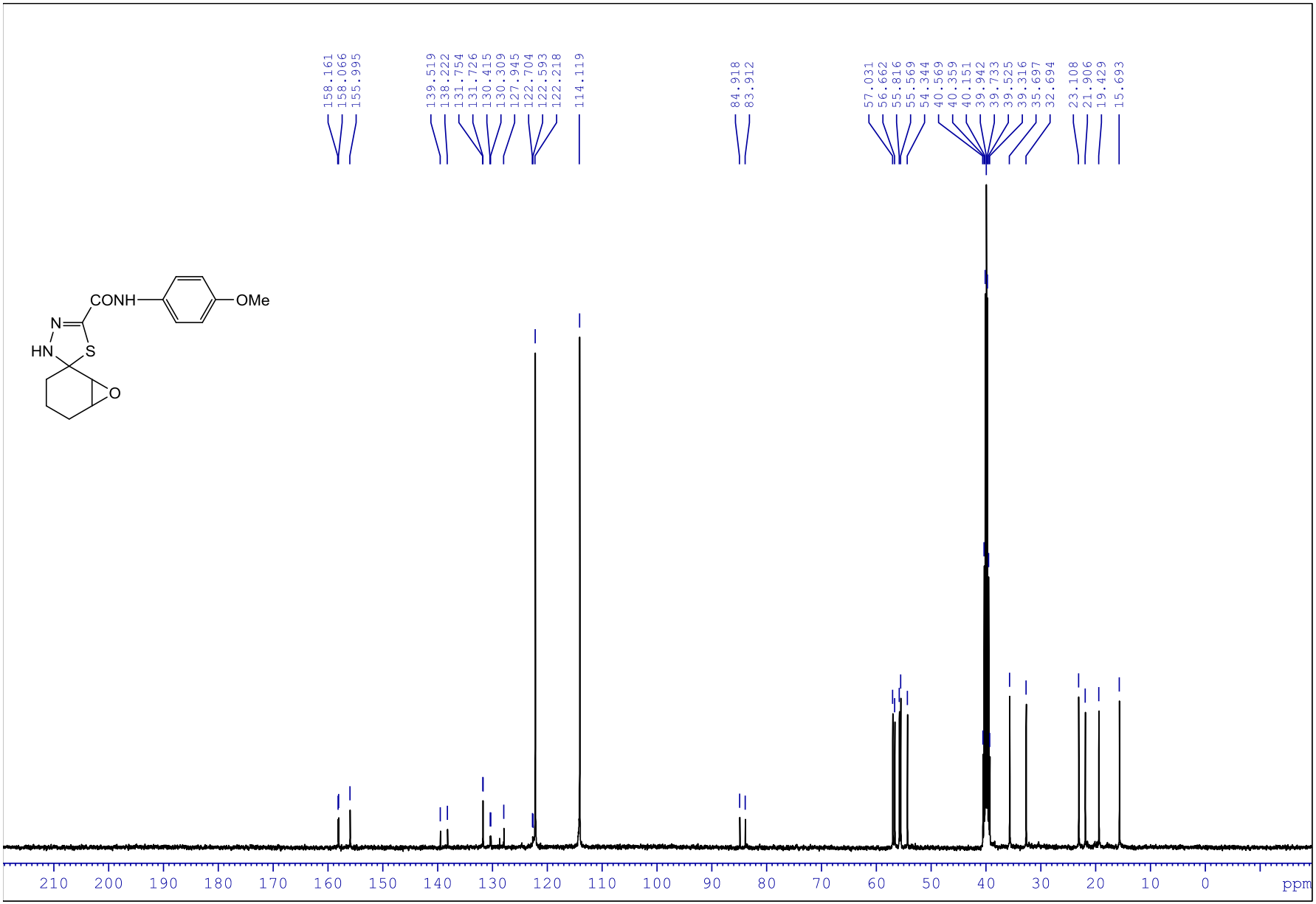
^{13}C NMR spectrum of **3d** (DMSO-d_6).



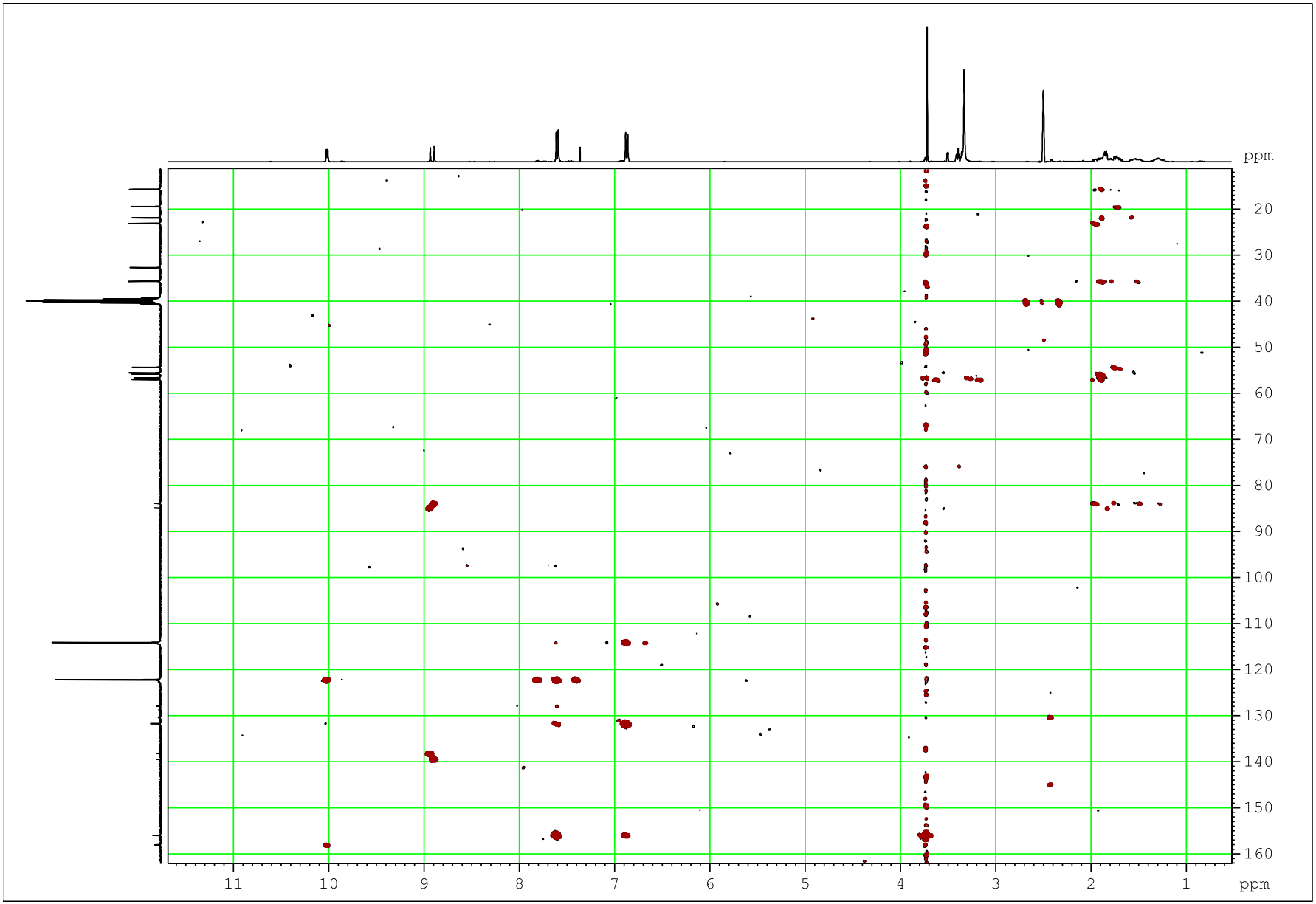
2D ^{1}H-^{13}C HMBC NMR spectrum of **3d** (DMSO-d_6).



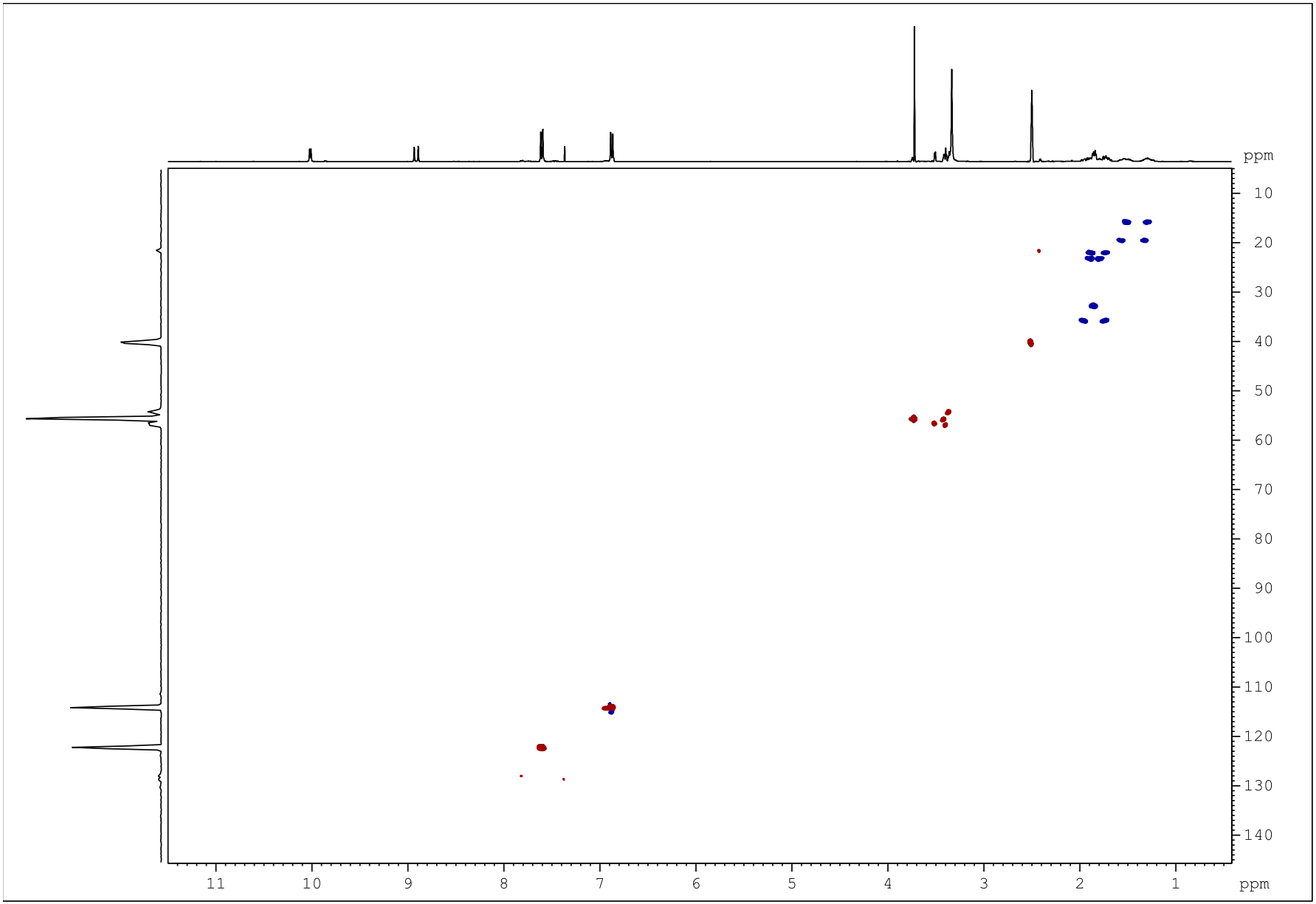
2D ^{1}H-^{13}C HSQC NMR spectrum of **3d** (DMSO-d_6).



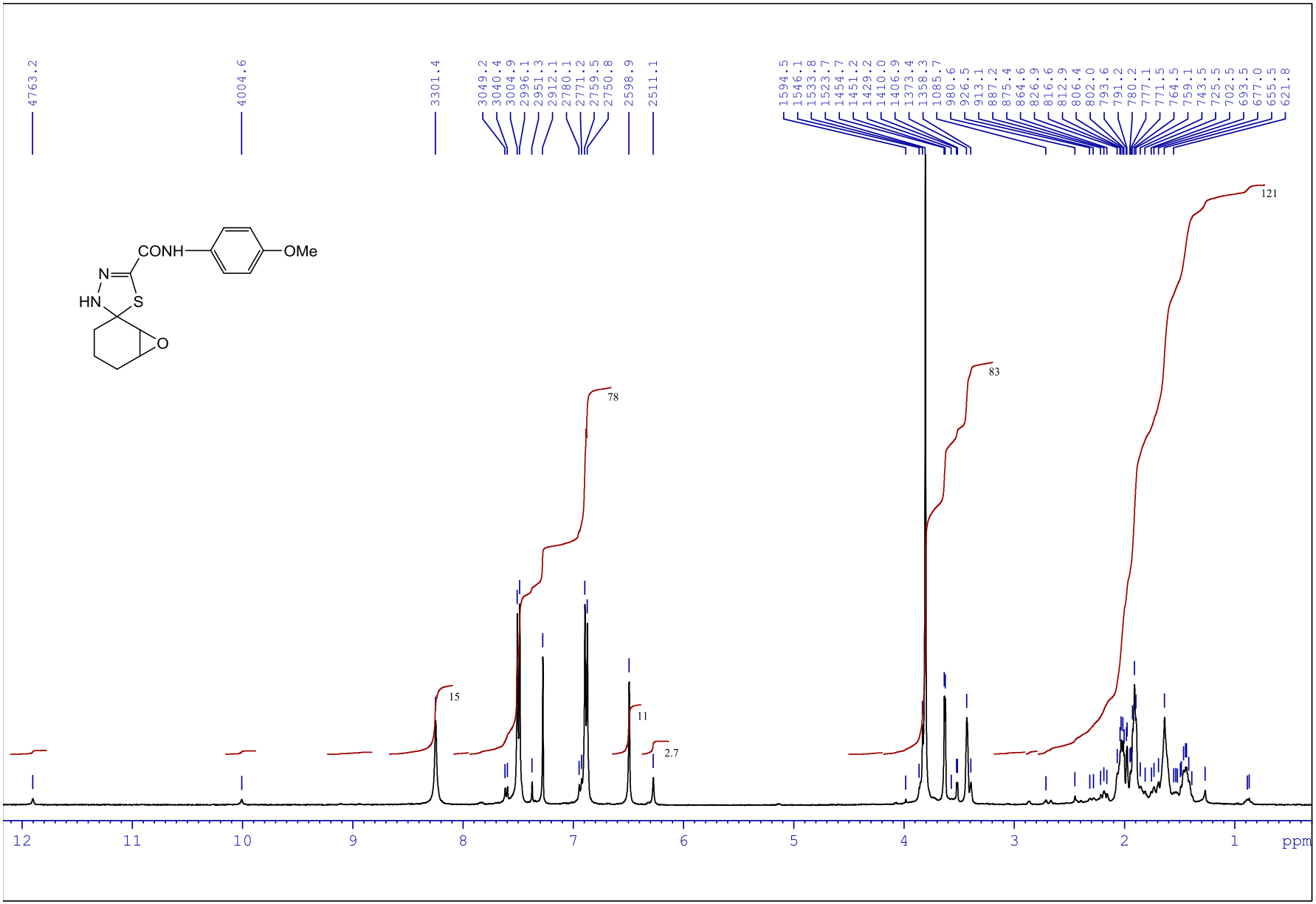
^{13}C NMR spectrum of **3e** (DMSO-d_6).



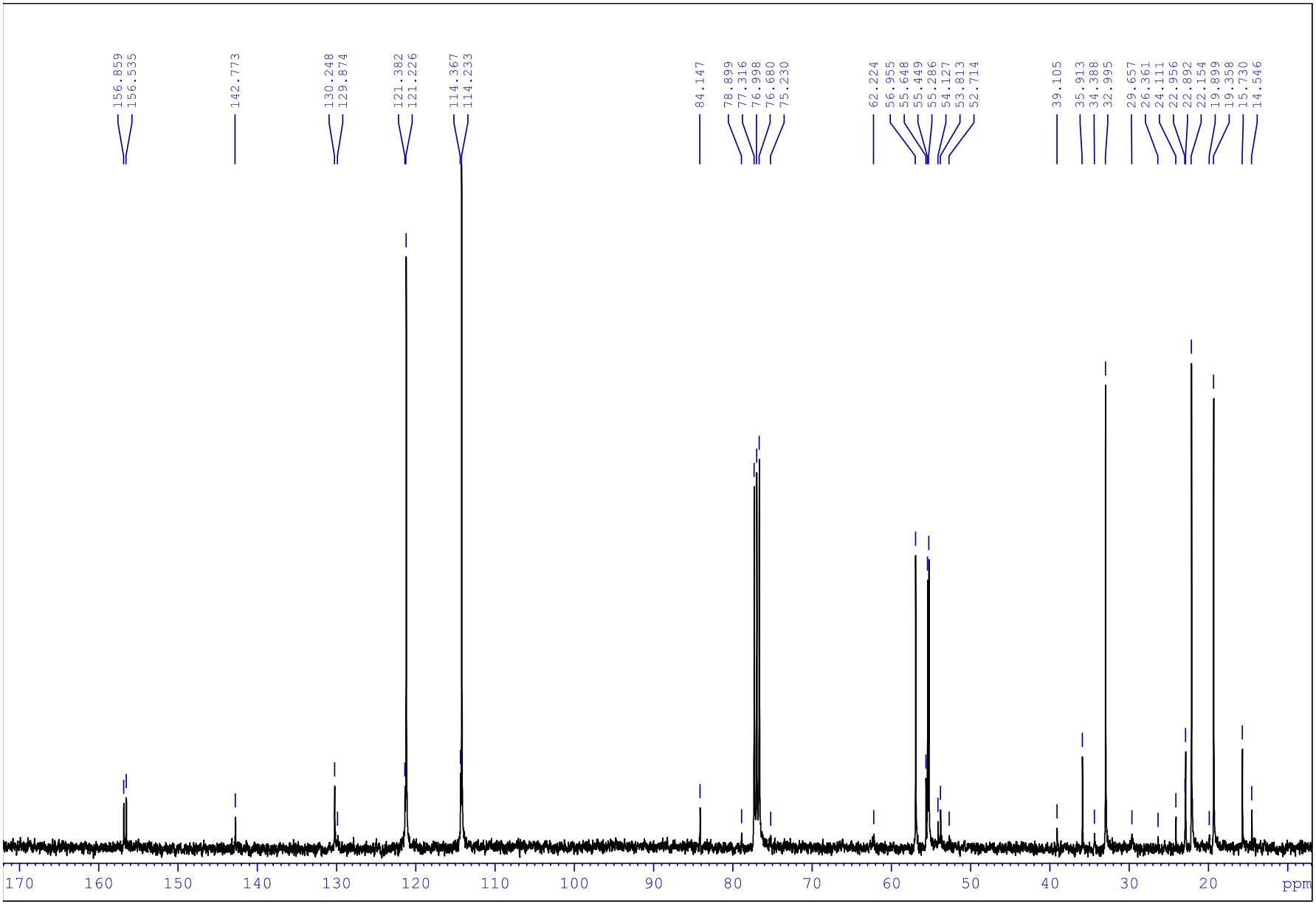
2D ^{1}H-^{13}C HMBC NMR spectrum of **3e** (DMSO-d_6).



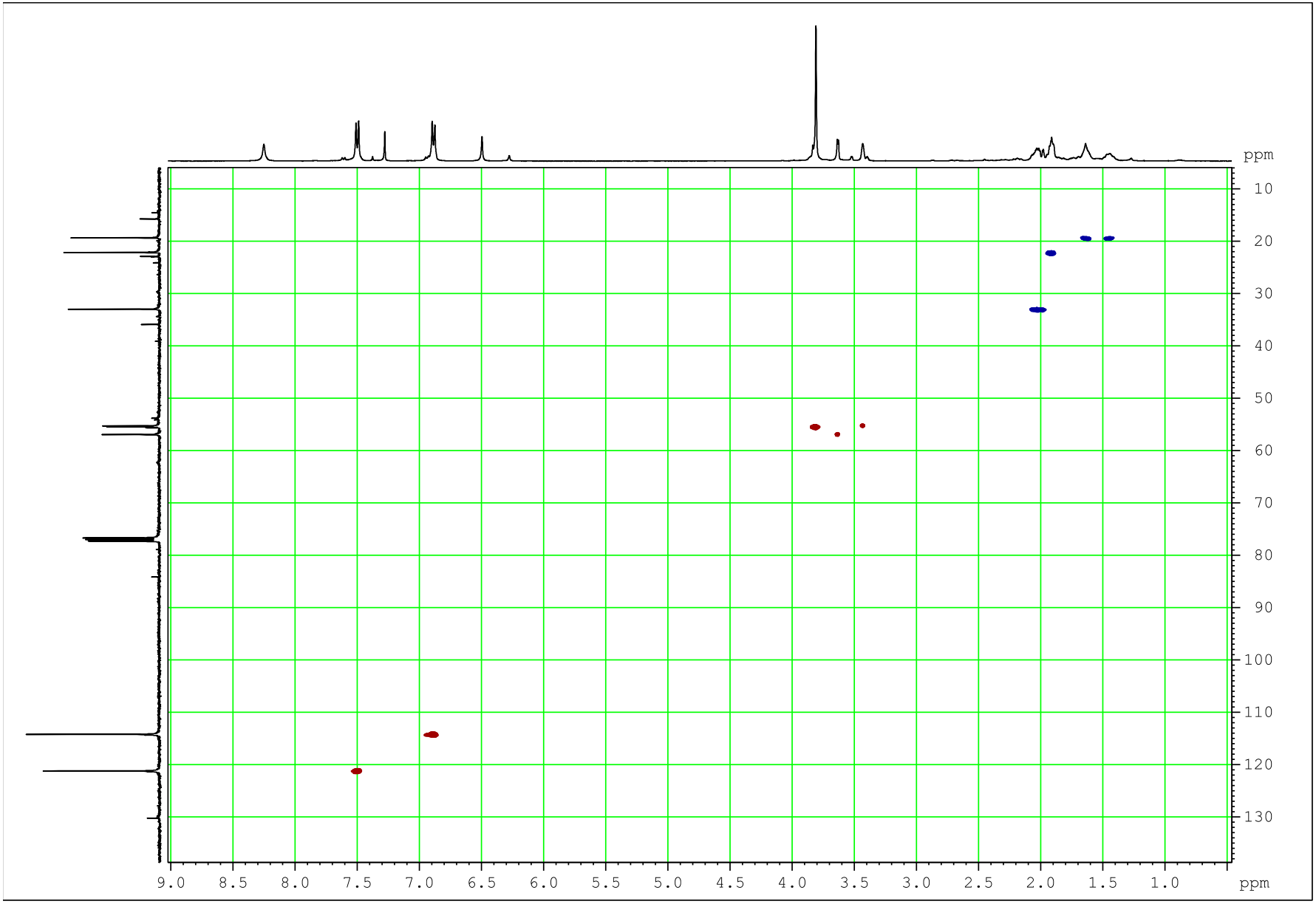
2D ^{1}H-^{13}C HSQC NMR spectrum of **3e** (DMSO-d_6).



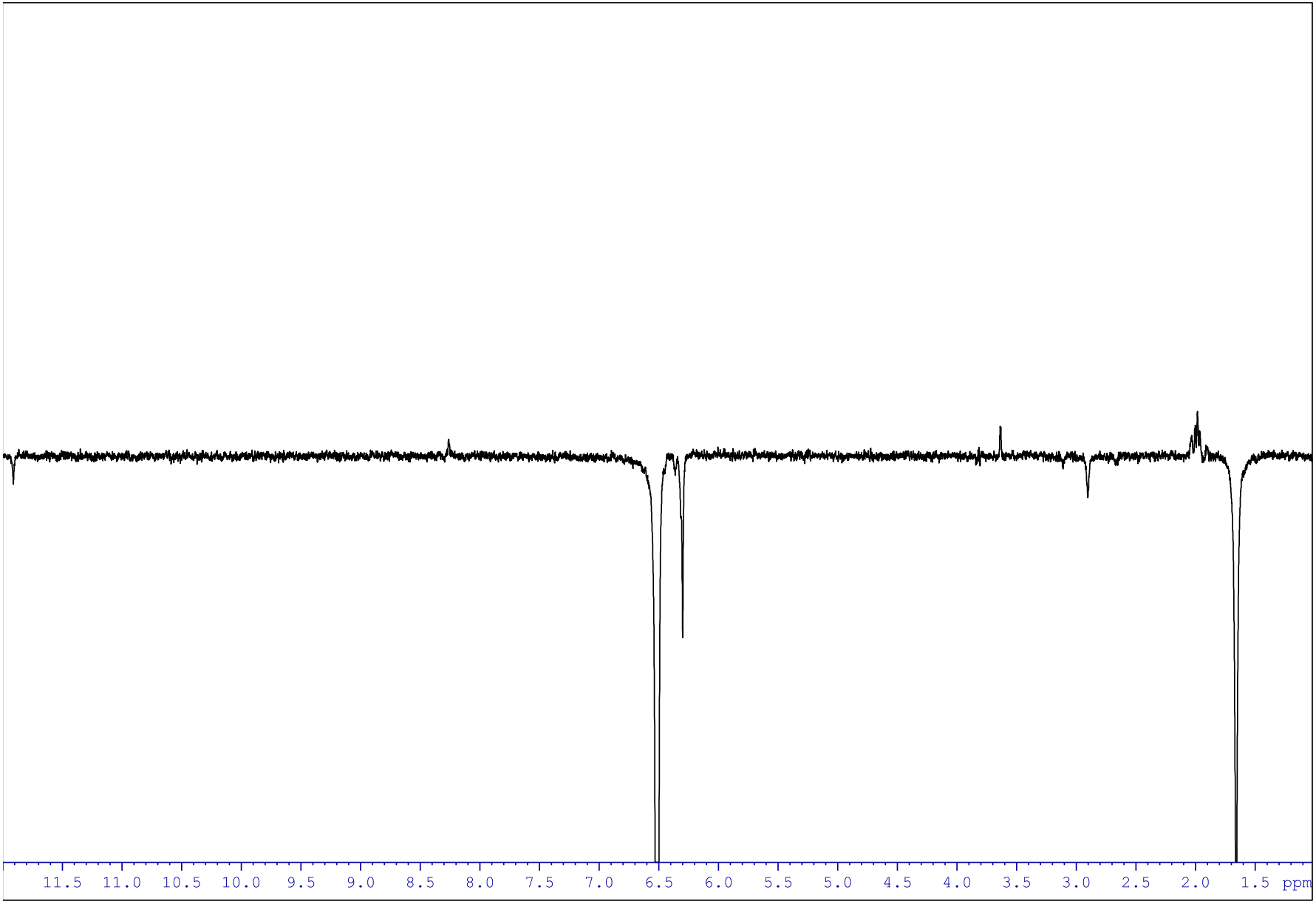
^{1}H NMR spectrum of **3e** ($CDCl_3$).



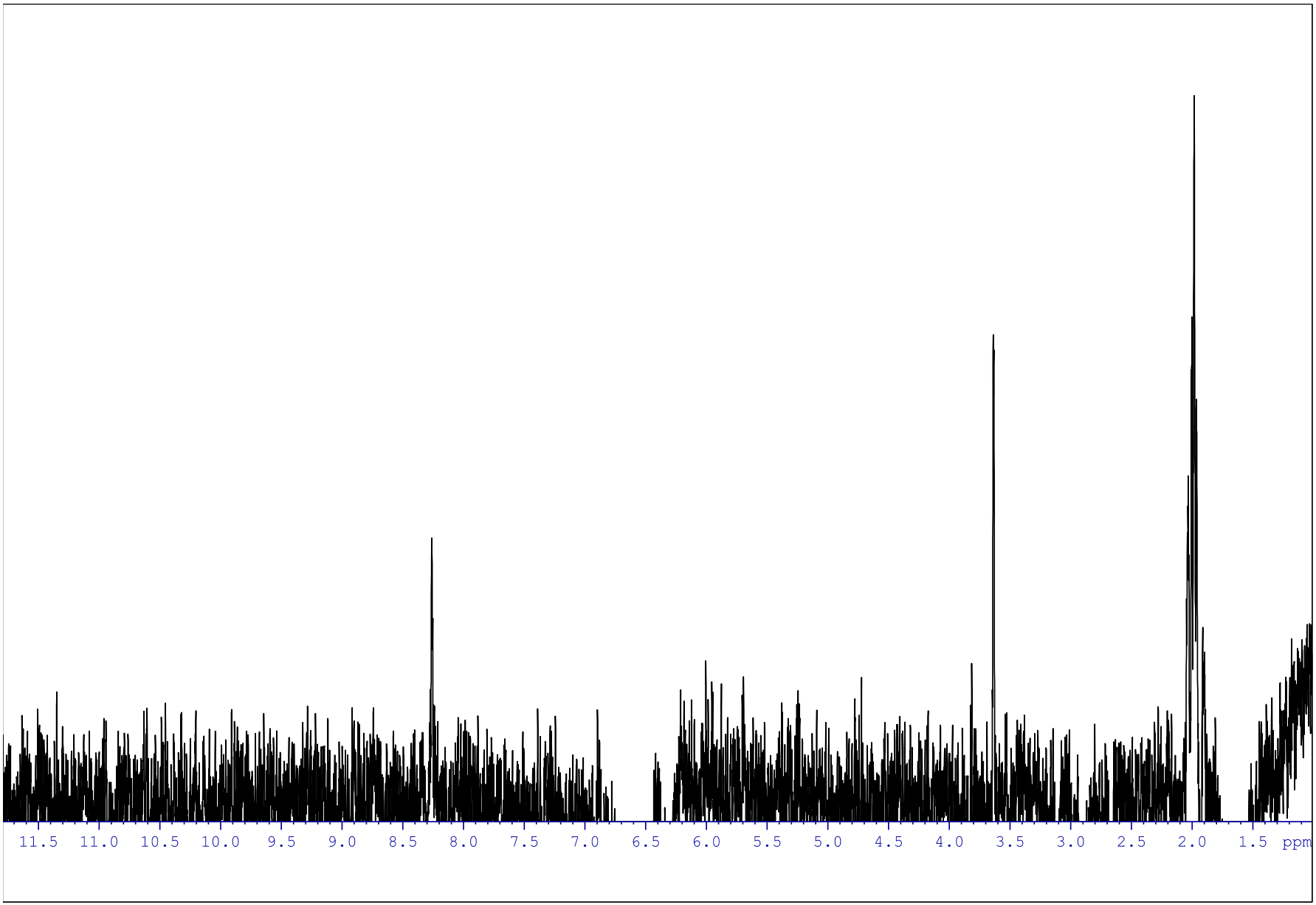
^{13}C NMR spectrum of **3e** ($CDCl_3$).



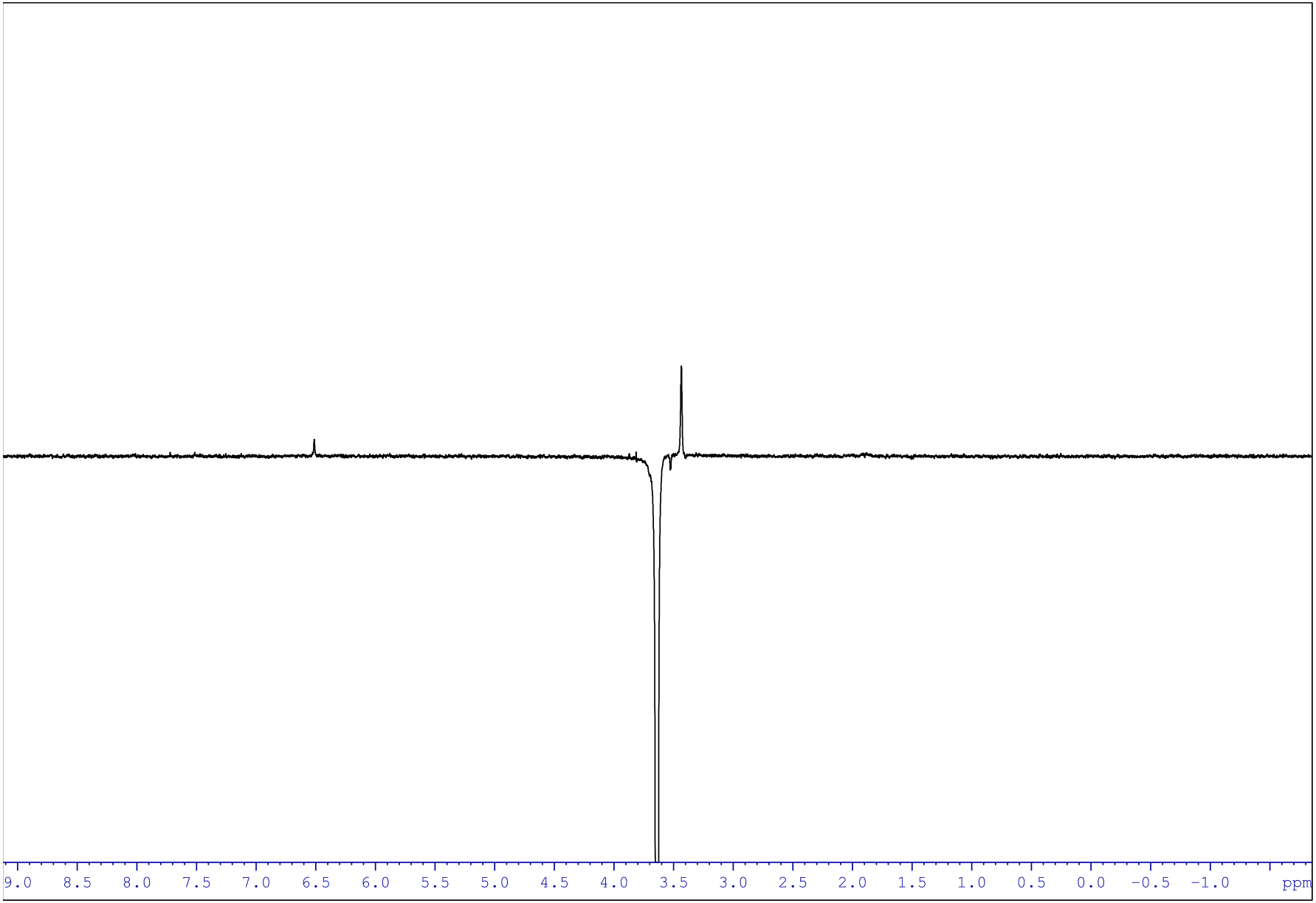
2D ^{1}H-^{13}C HSQC NMR spectrum of **3e** ($CDCl_3$).



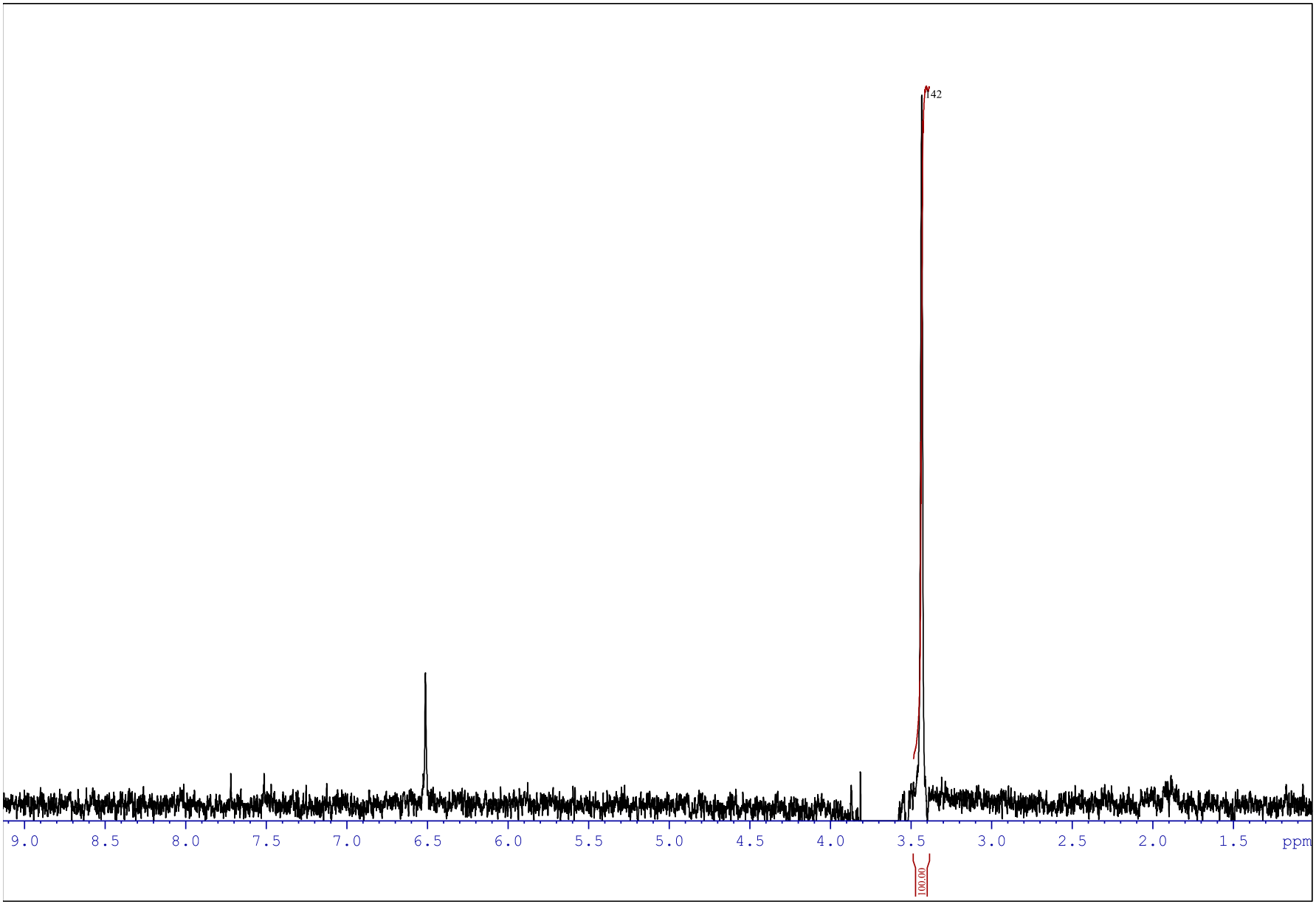
1D ^{1}H NOESY (6.51 ppm) NMR spectrum of **3e** ($CDCl_3$).



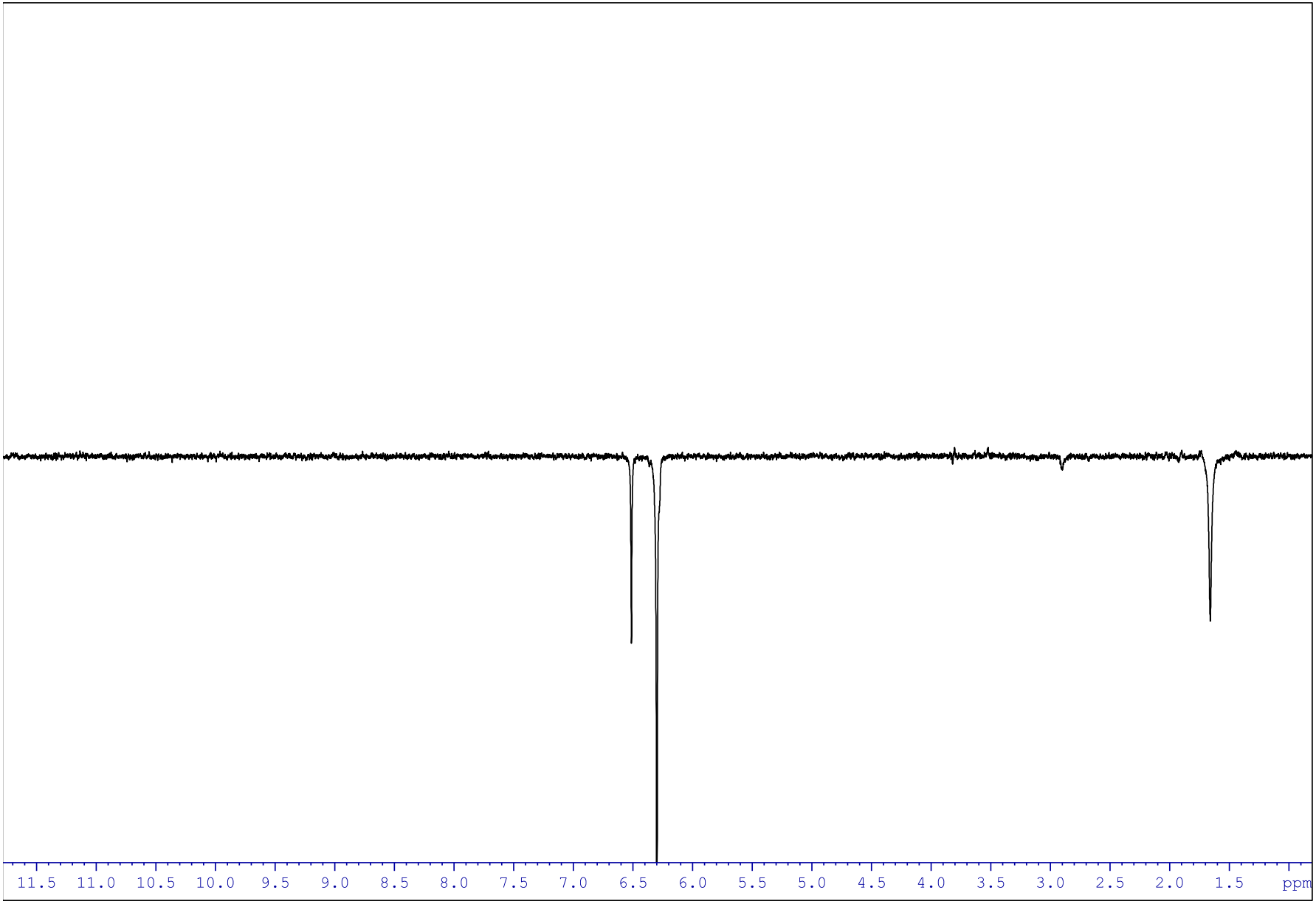
1D ^{1}H NOESY (6.51 ppm) NMR spectrum of **3e** ($CDCl_3$).



1D ^{1}H NOESY (3.63 ppm) NMR spectrum of **3e** ($CDCl_3$).

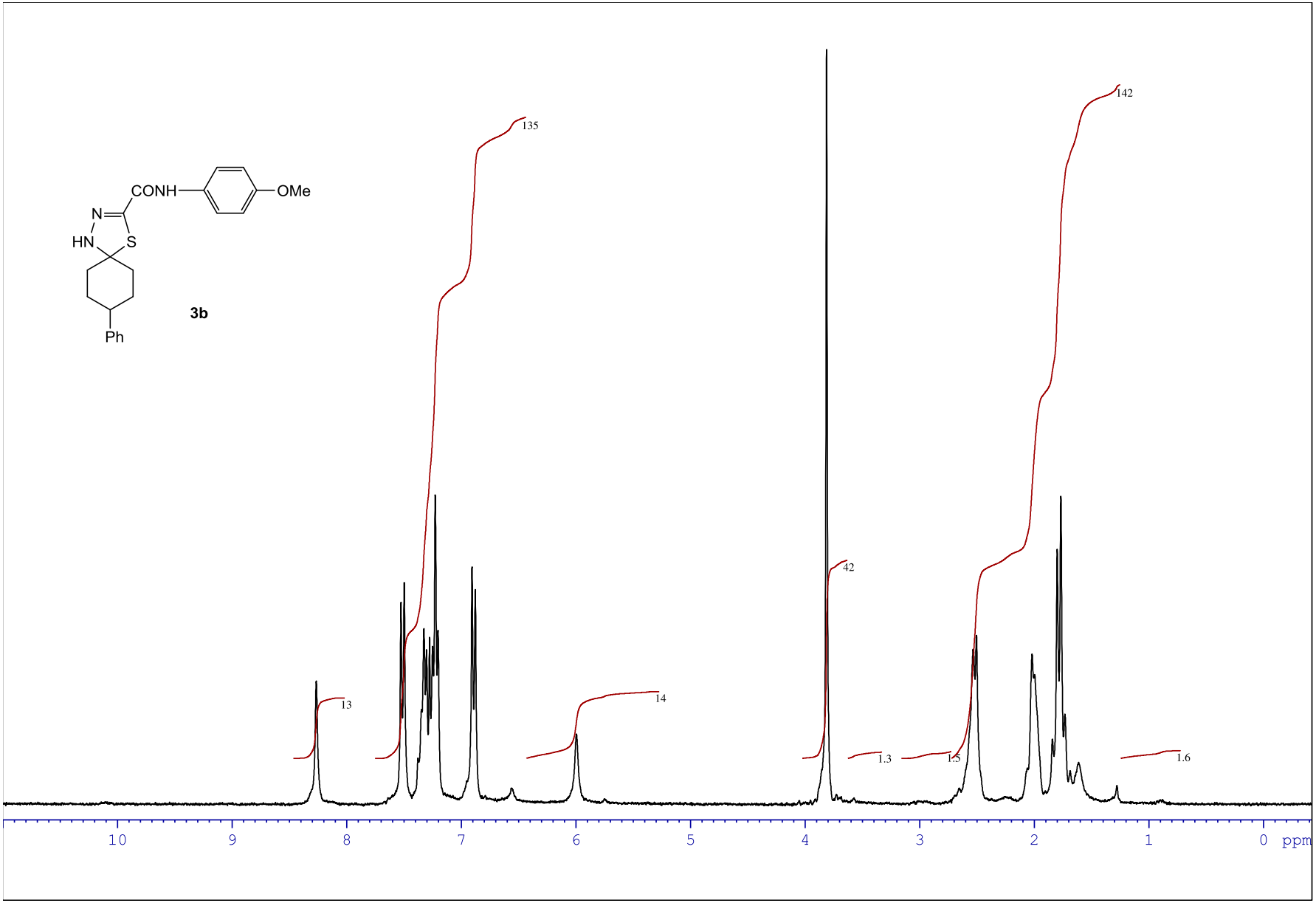


1D ^{1}H NOESY (3.63 ppm) NMR spectrum of **3e** ($CDCl_3$).

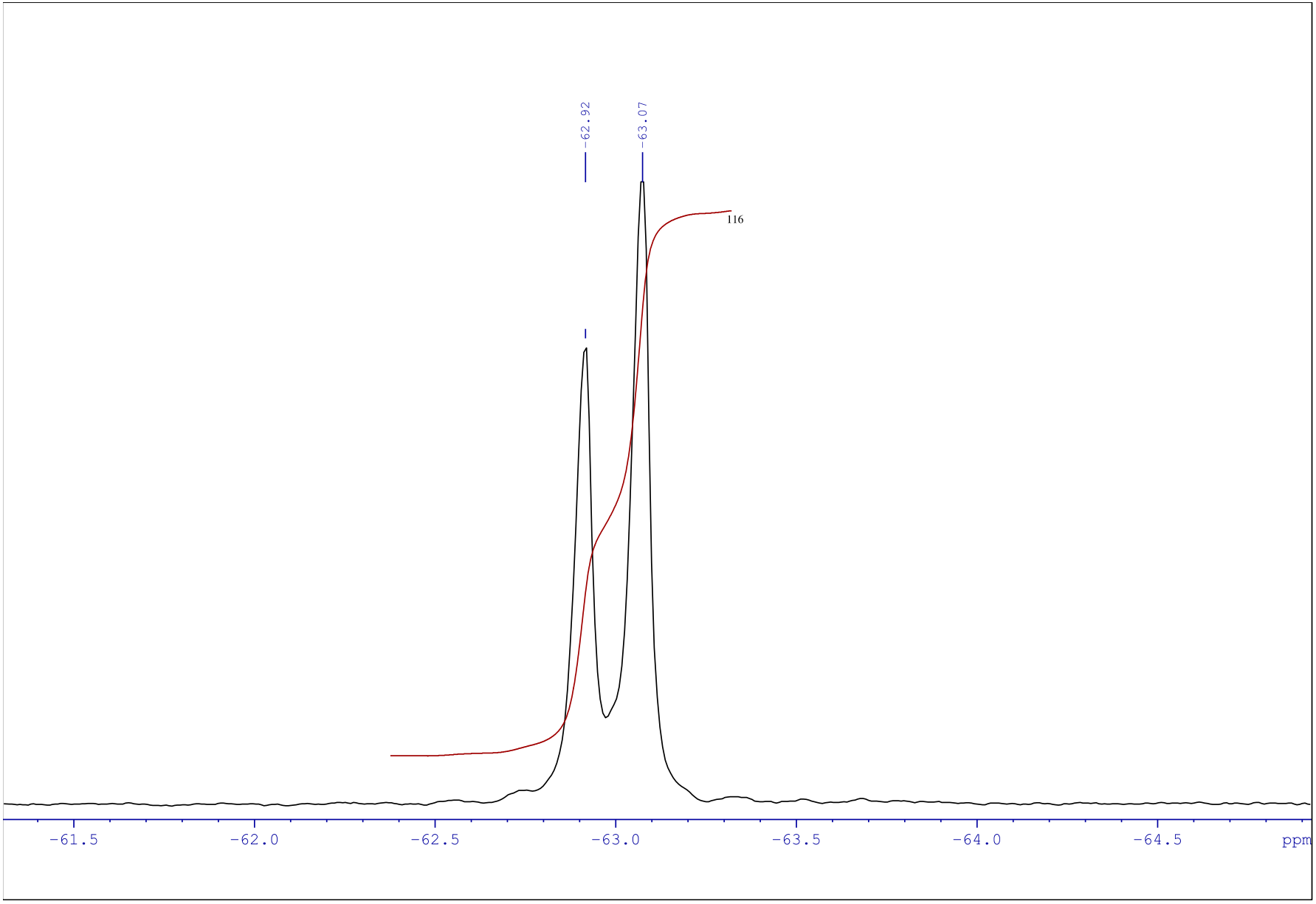


1D ^{1}H NOESY (6.31 ppm) NMR spectrum of **3e** ($CDCl_3$).

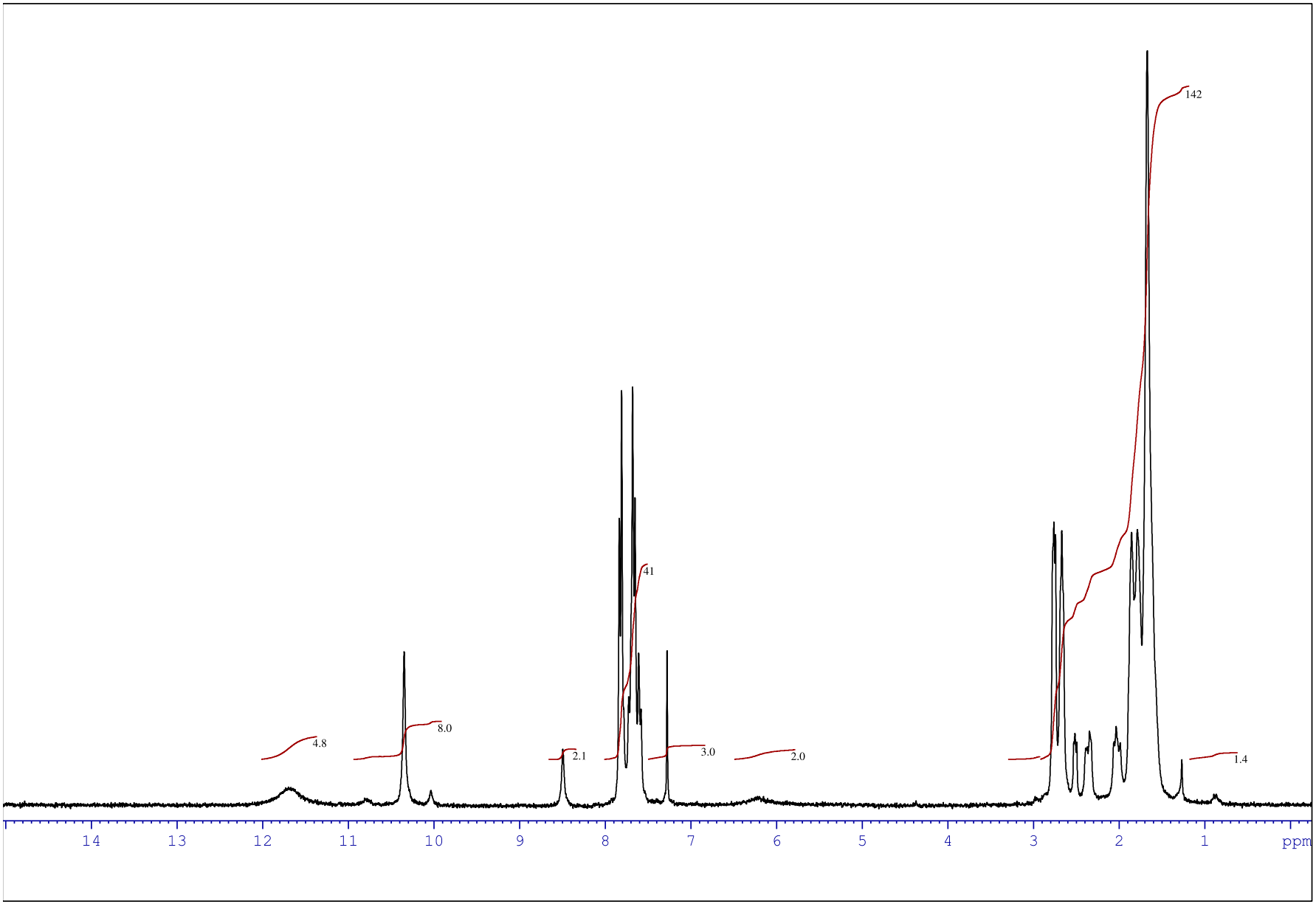
2. NMR spectra (Bruker AM-300)



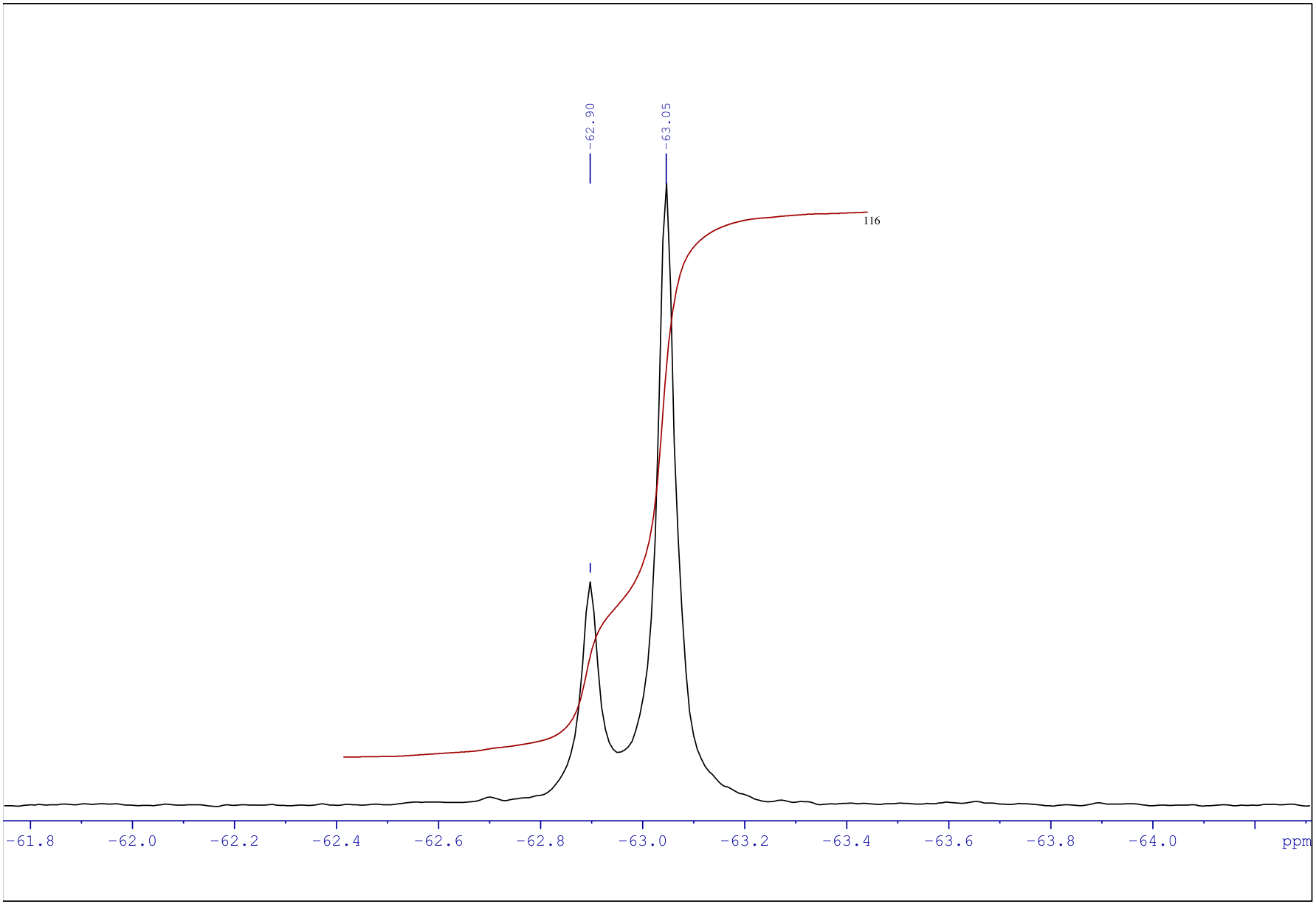
^{1}H NMR spectrum of **3b** ($CDCl_3$)



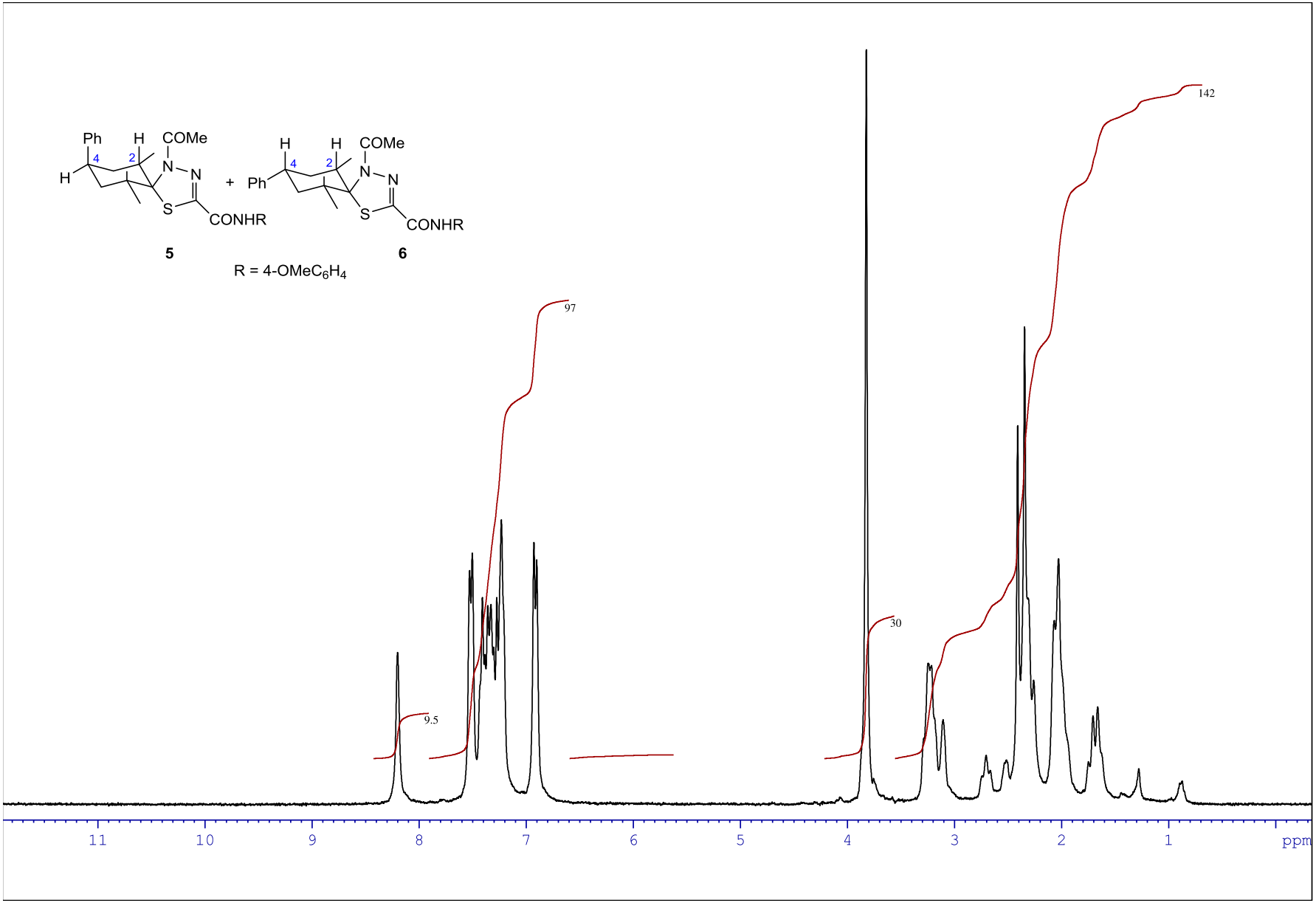
^{19}F NMR spectrum of **3i** ($CDCl_3$).



^{1}H NMR spectrum of **3j** ($CDCl_3$).

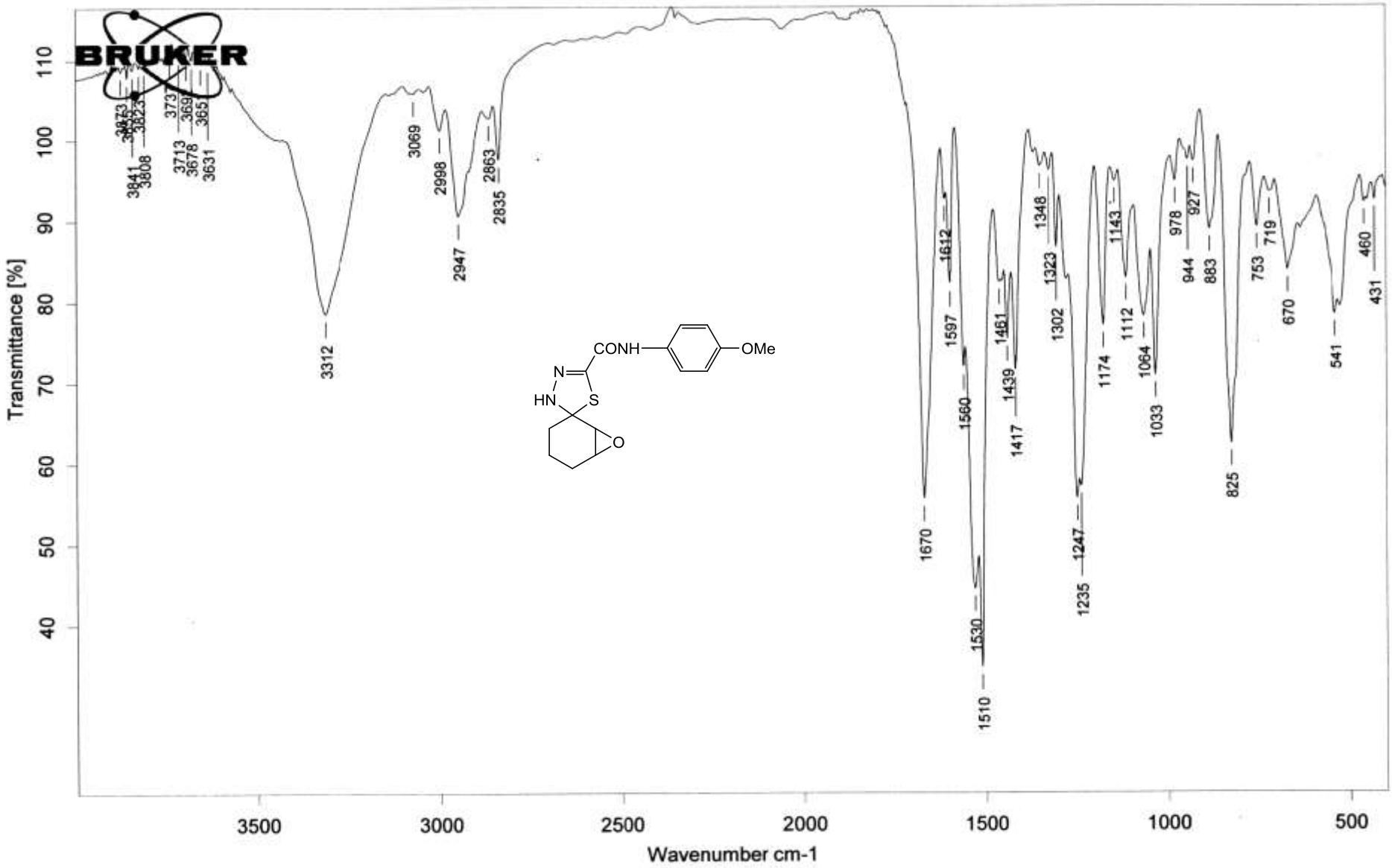


^{19}F NMR spectrum of **3i** ($CDCl_3$).



[1]H NMR spectrum of mixture **5** and **6**.

3. IR spectra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Transmittance [%]
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2000
1500
1000
500
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1670
1612
1597
1560
1530
1510
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1439
1417
1348
1323
1302
1247
1235
1174
1143
1112
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460
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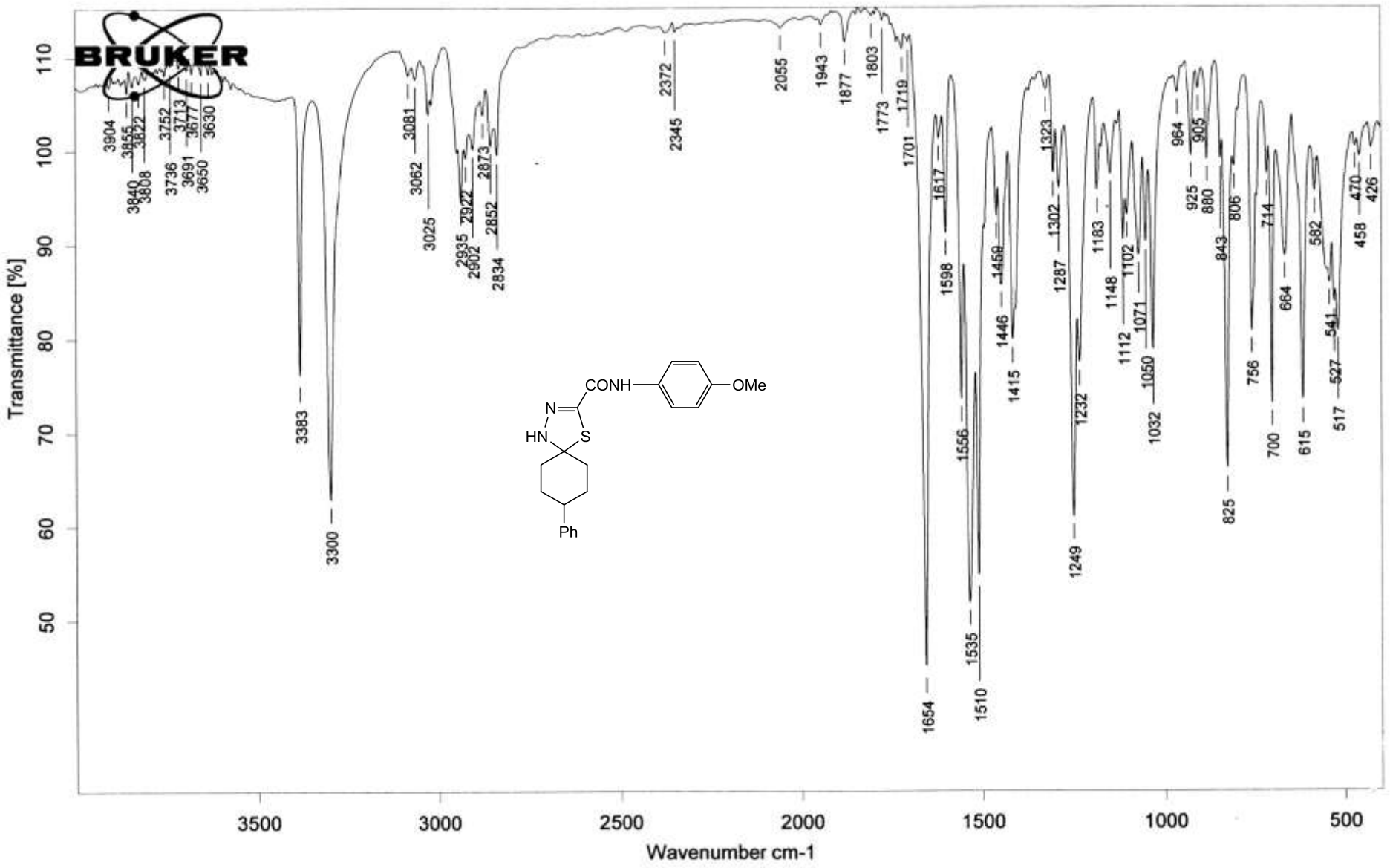
OMe
HN
S
O


BRUKER
Transmittance [%]
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3808
3840
3752
3736
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3691
3677
3650
3630
3383
3300
3081
3062
3025
2935
2922
2902
2873
2852
2834
2372
2345
2055
1943
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1719
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1535
1510
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1446
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1050
1032
964
925
905
880
843
825
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CONH
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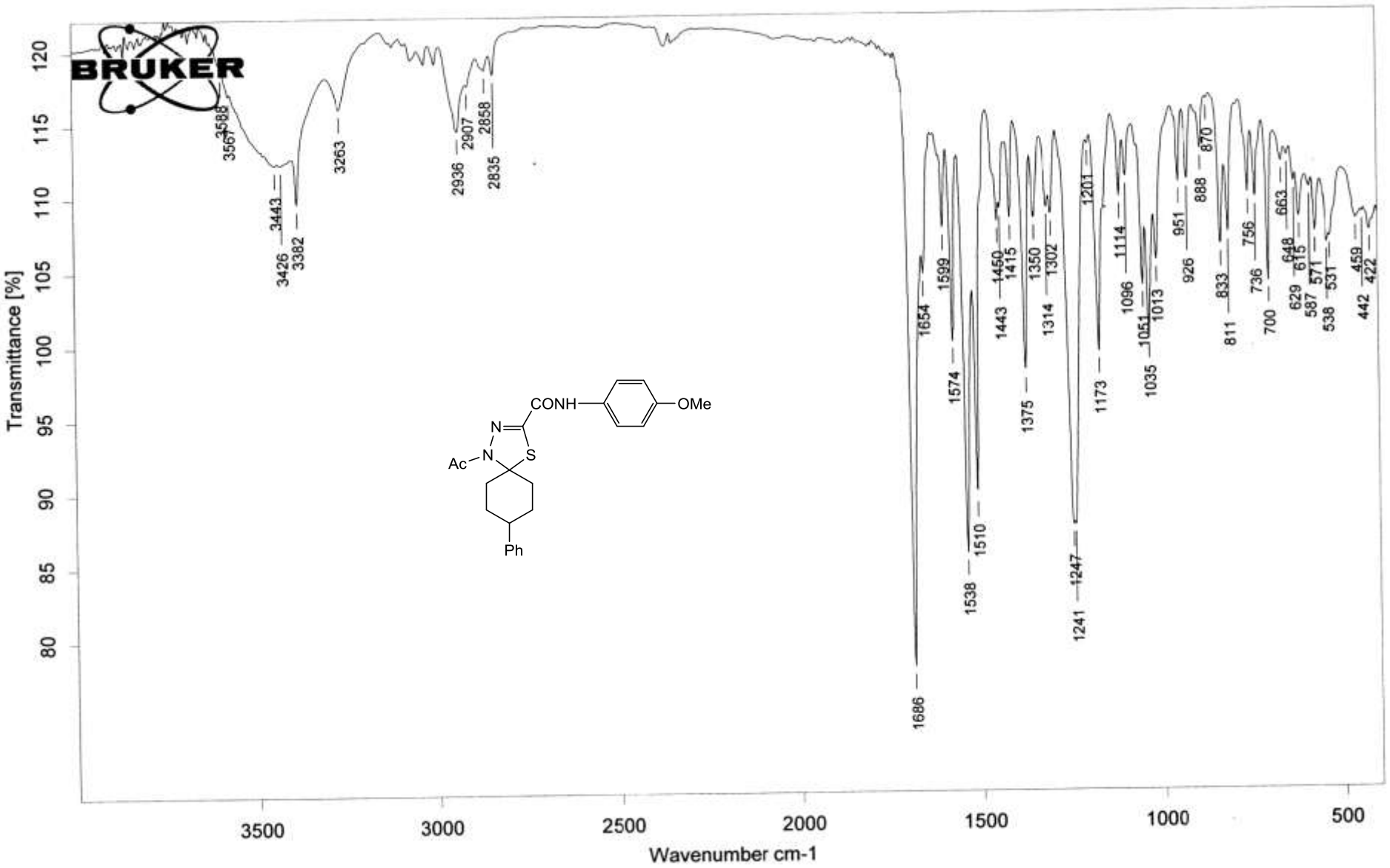
N
HN
S
Ph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Transmittance [%]
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110
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100
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90
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80
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2000
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1000
500
Wavenumber cm-1
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1443
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1302
1247
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1201
1173
1114
1096
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1035
1013
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CONH
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N
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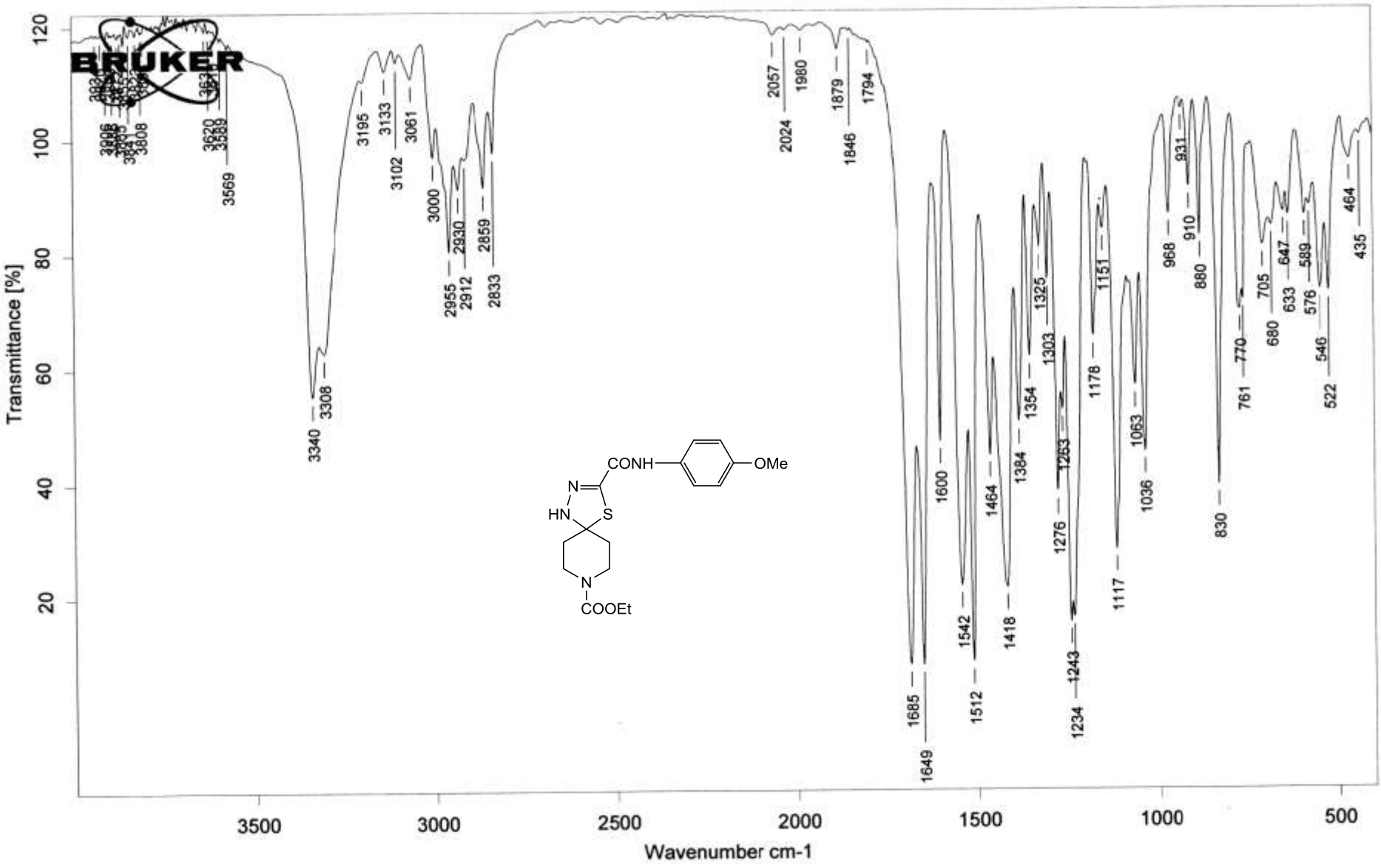
Ph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Transmittance [%]
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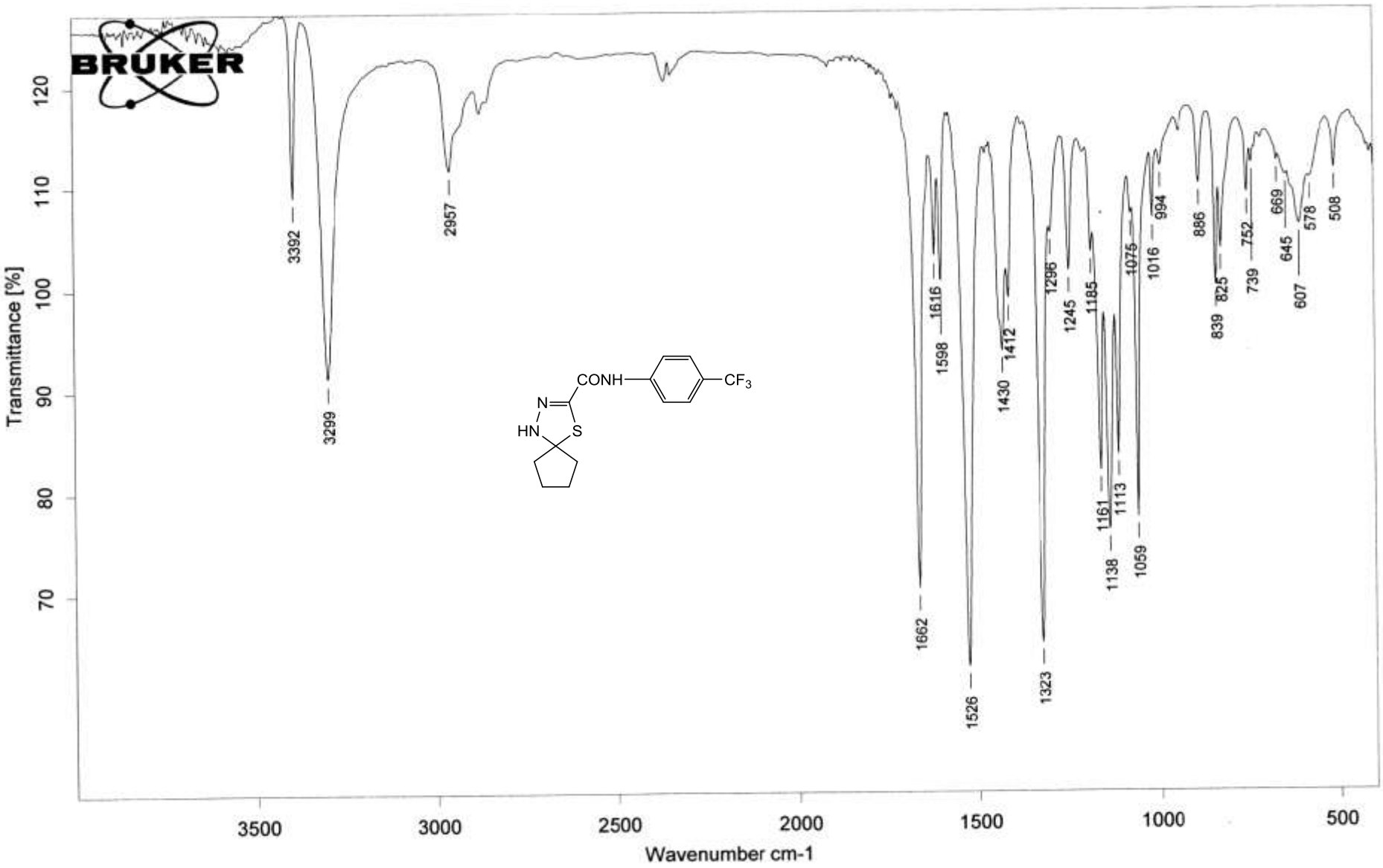
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1016
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839
825
752
739
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HN
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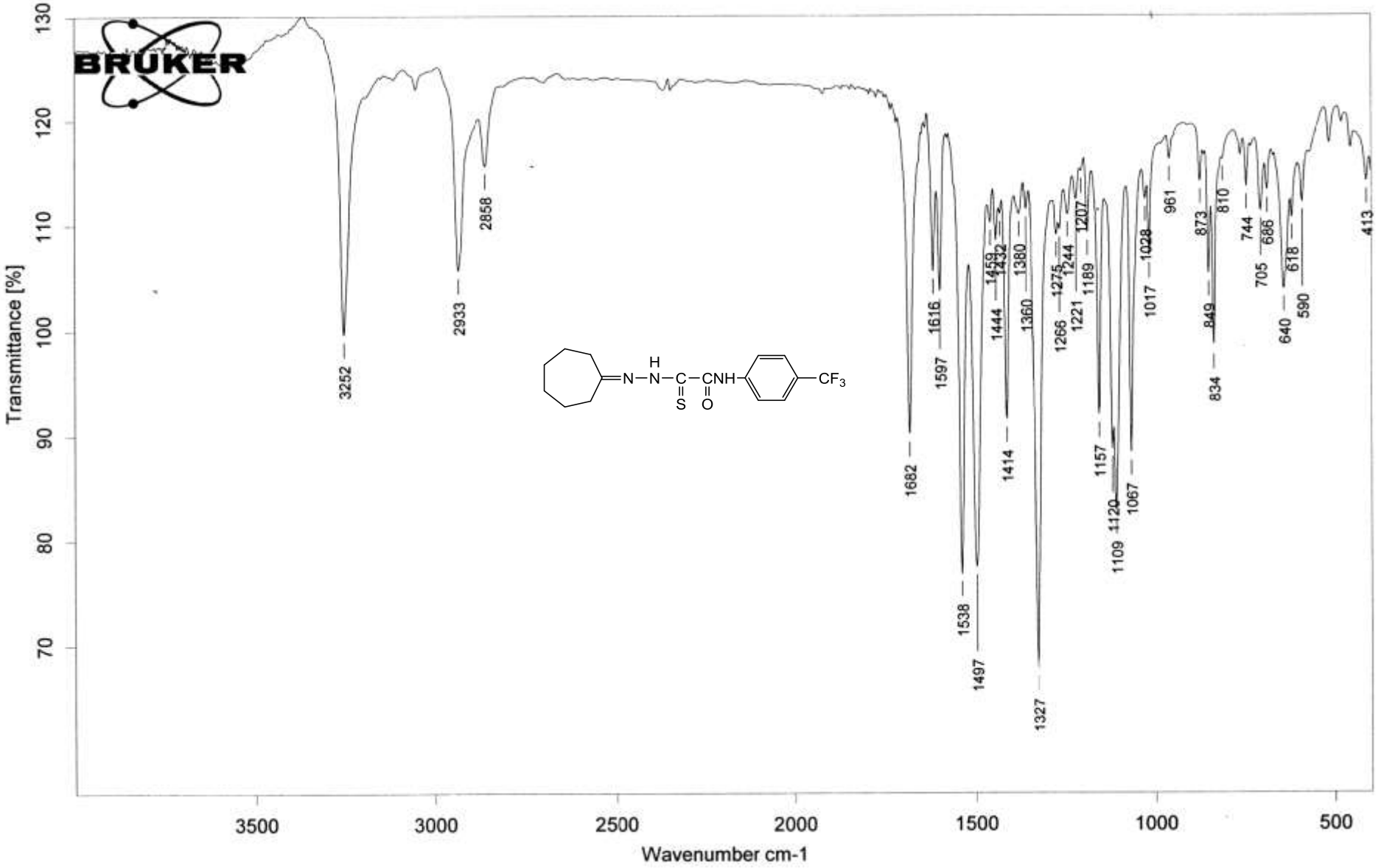
Wavenumber cm-1


BRUKER
Transmittance [%]
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500
Wavenumber cm-1
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1459
1444
1432
1414
1380
1360
1327
1275
1266
1244
1221
1207
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1120
1109
1067
1028
1017
961
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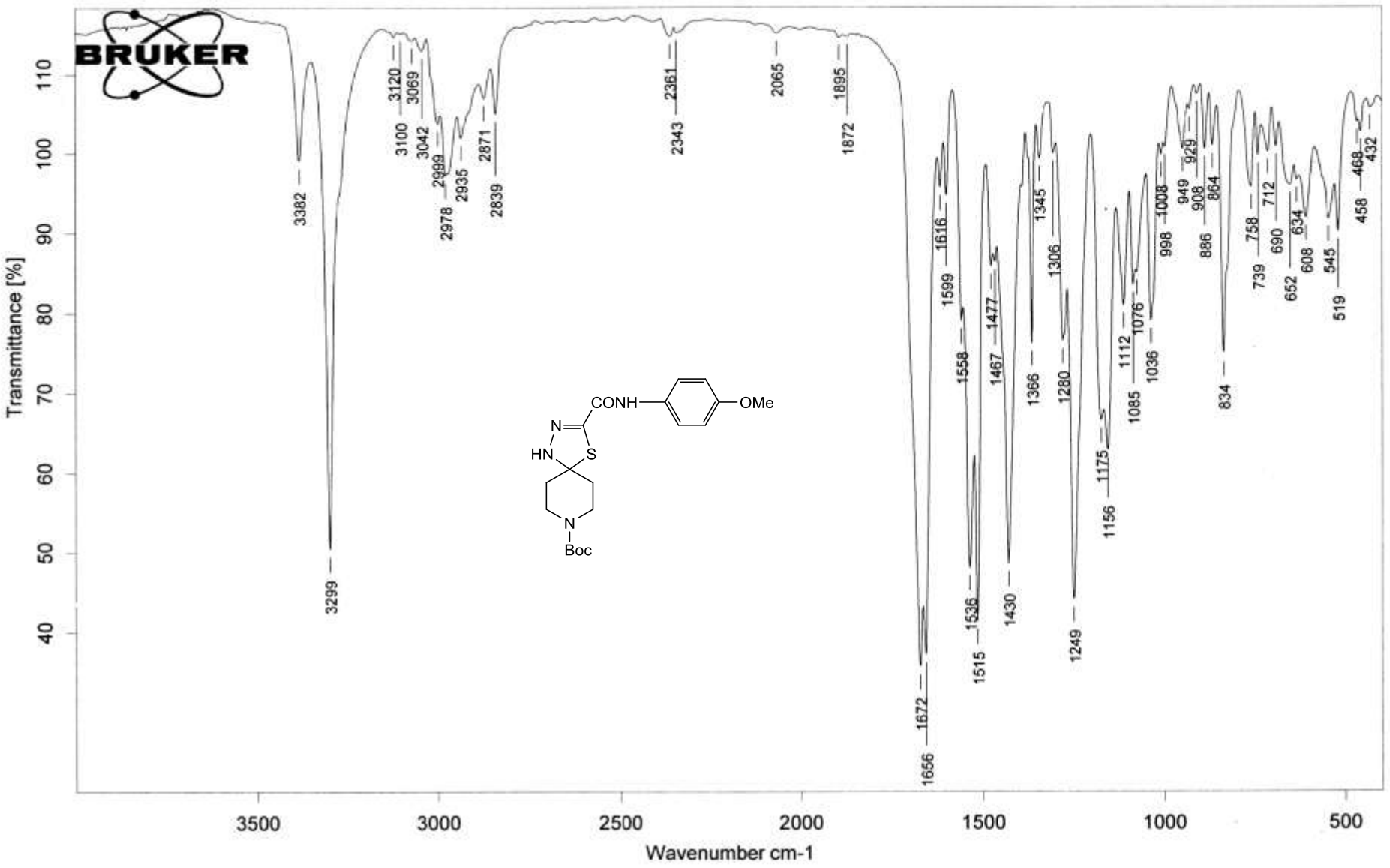
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Transmittance [%]
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864
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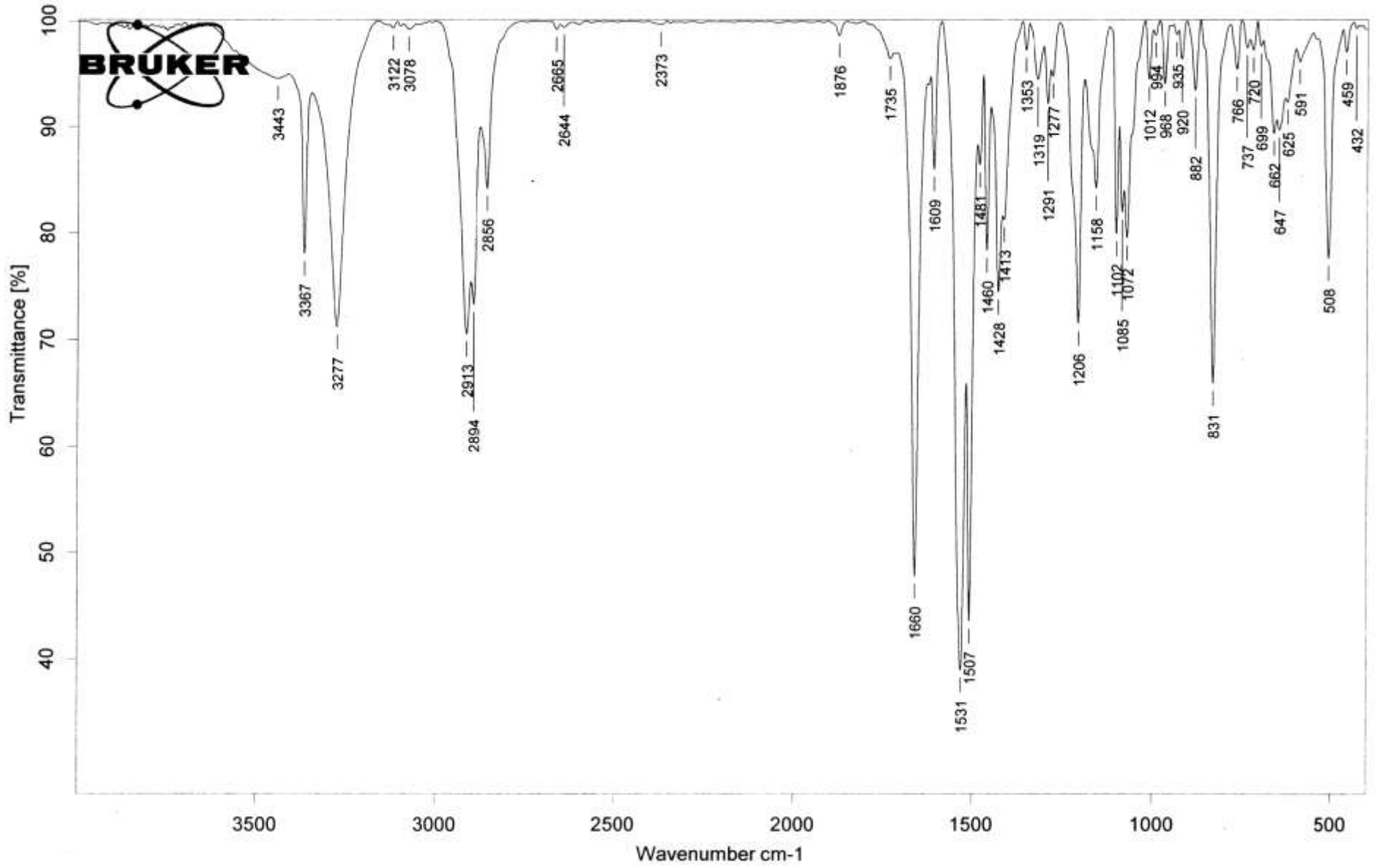
BRUKER
Transmittance [%]
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1000
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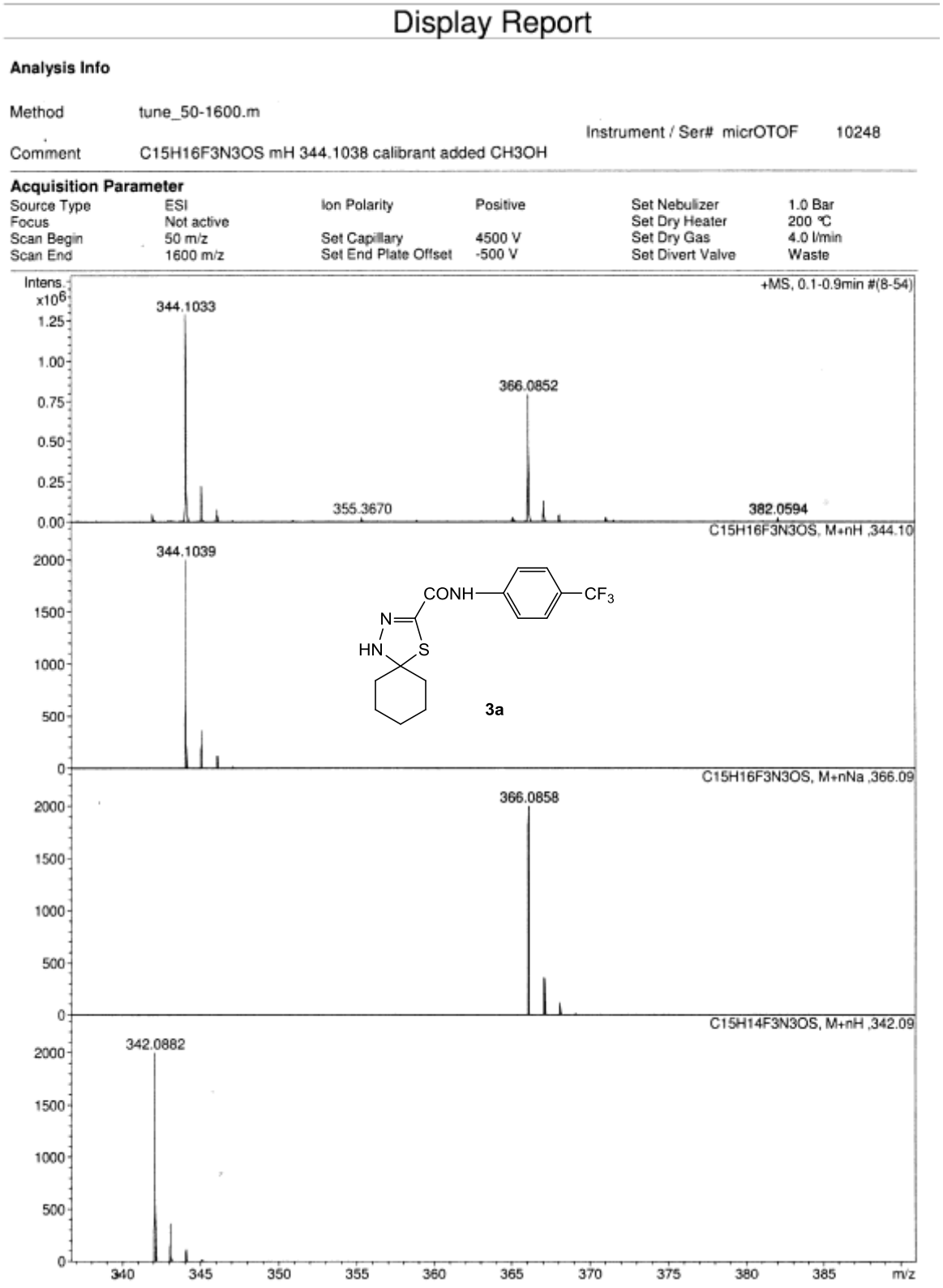
Wavenumber cm-1

4. Mass spectra



Mass-spectra of **3a**.

Display Report

Analysis Info

Method tune_50-1600.m

Instrument / Ser# micrOTOF 10248

Comment C21H23N3O2S mH 382.1583 calibrant added, CH3OH

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
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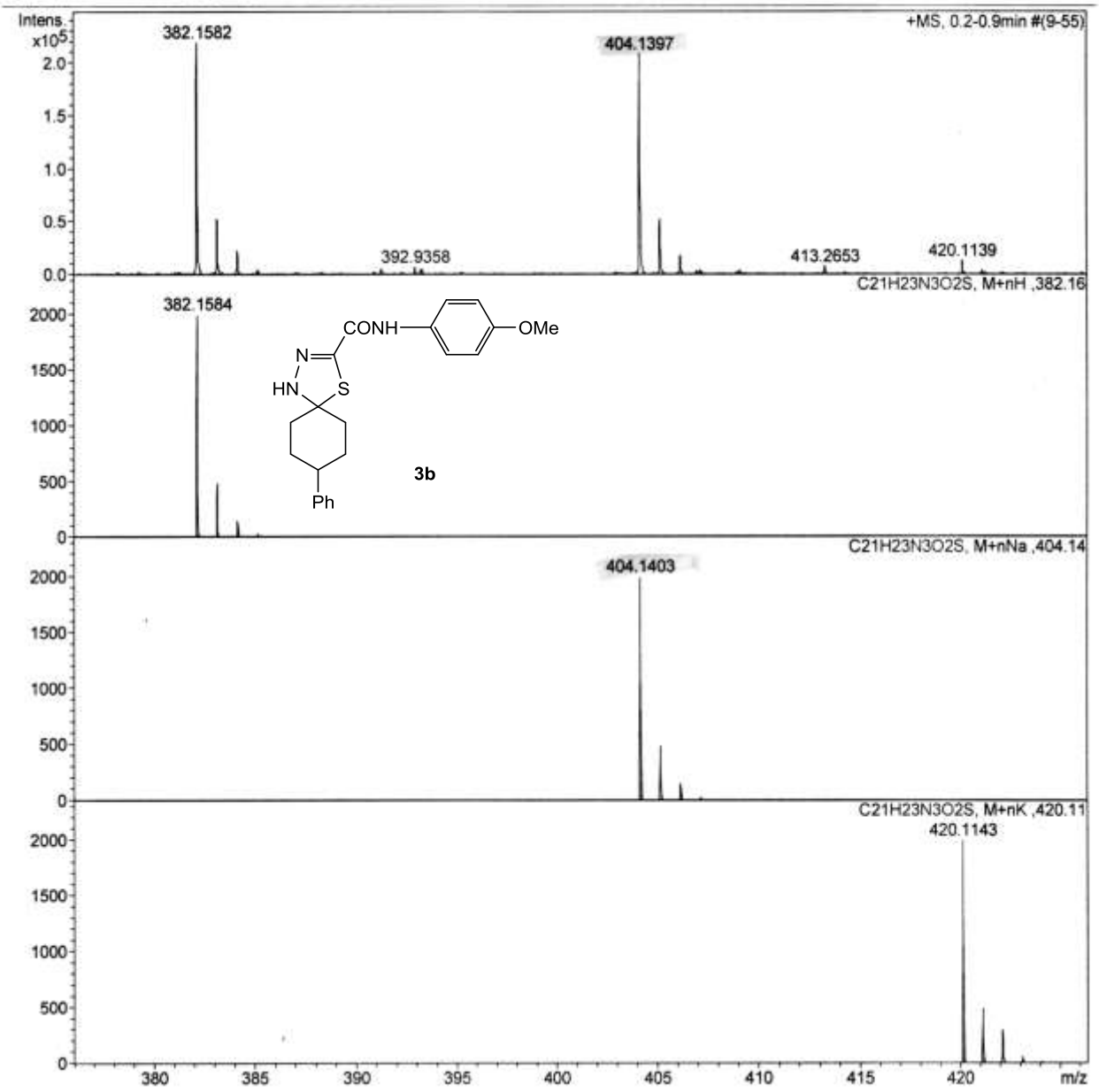

Mass-spectra of **3b**.

Mass-spectra of **3c**.

Display Report

Analysis Info

Method	tune_50-1600.m		
Comment	C17H22N4O4S mH 379.1434 calibrant added	Instrument / Ser#	micrOTOF 10248

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
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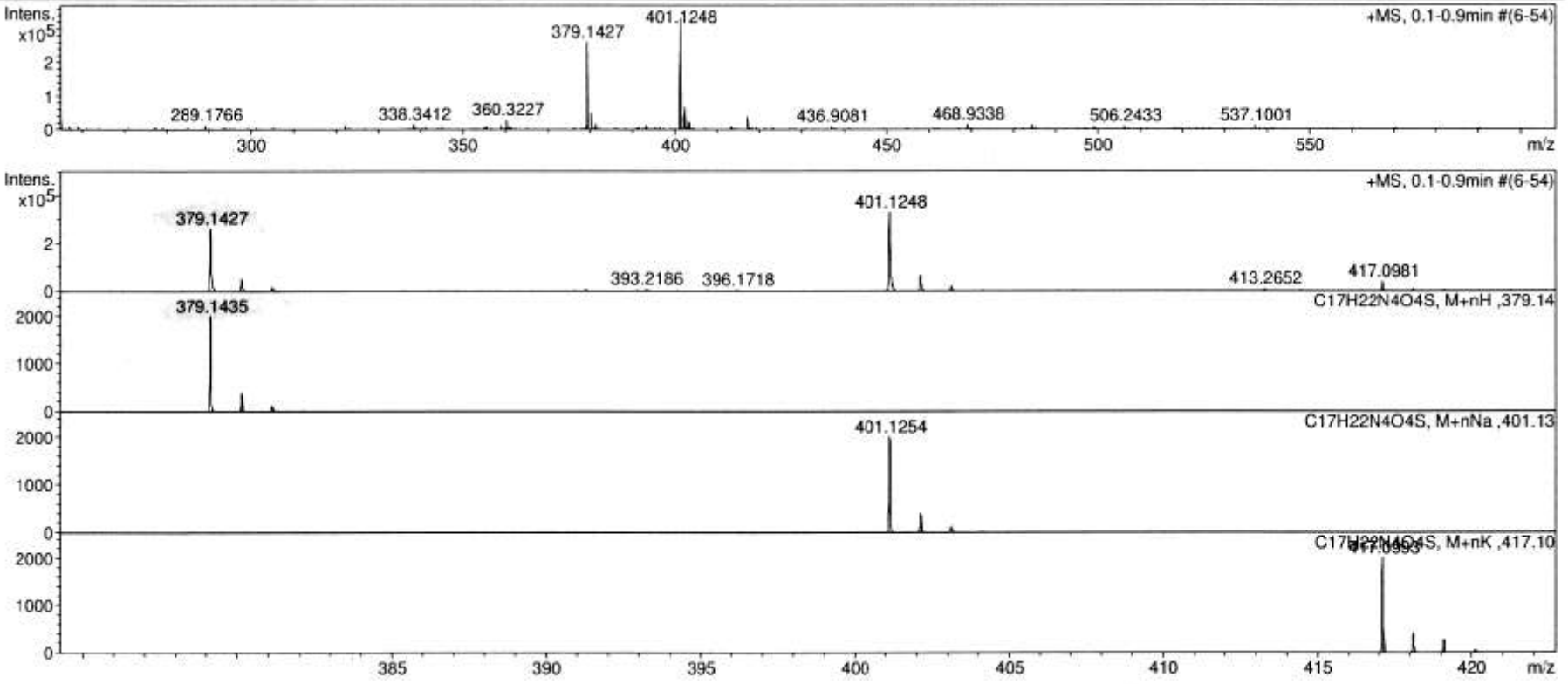
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



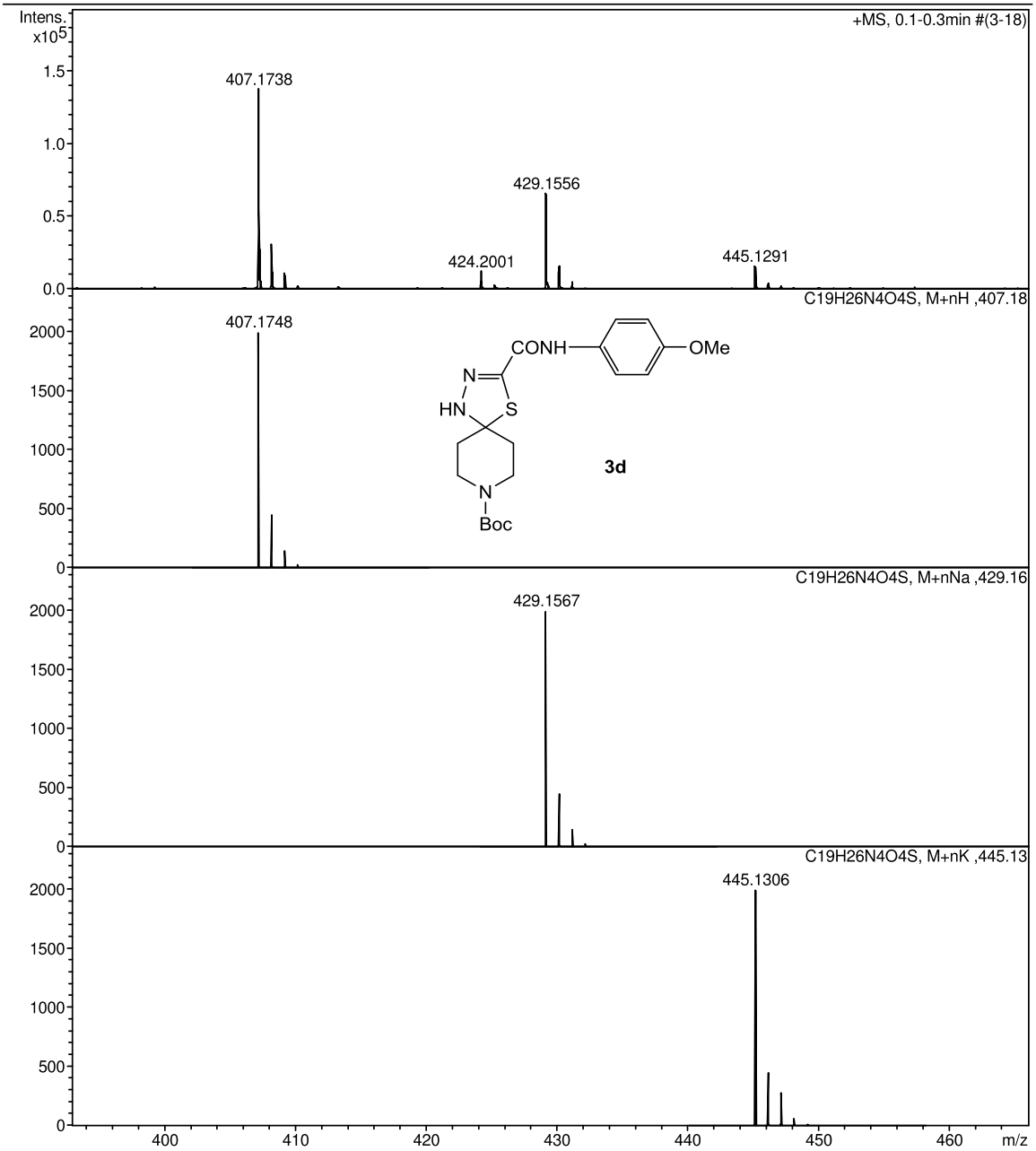
Display Report

Analysis Info

Method	tune_50-1600.m		
		Instrument / Ser#	micrOTOF 10248
Comment	C19H26N4O4S mH 407.1757 clb added CH3OH		

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Mass-spectra of **3d**.

Display Report

Analysis Info

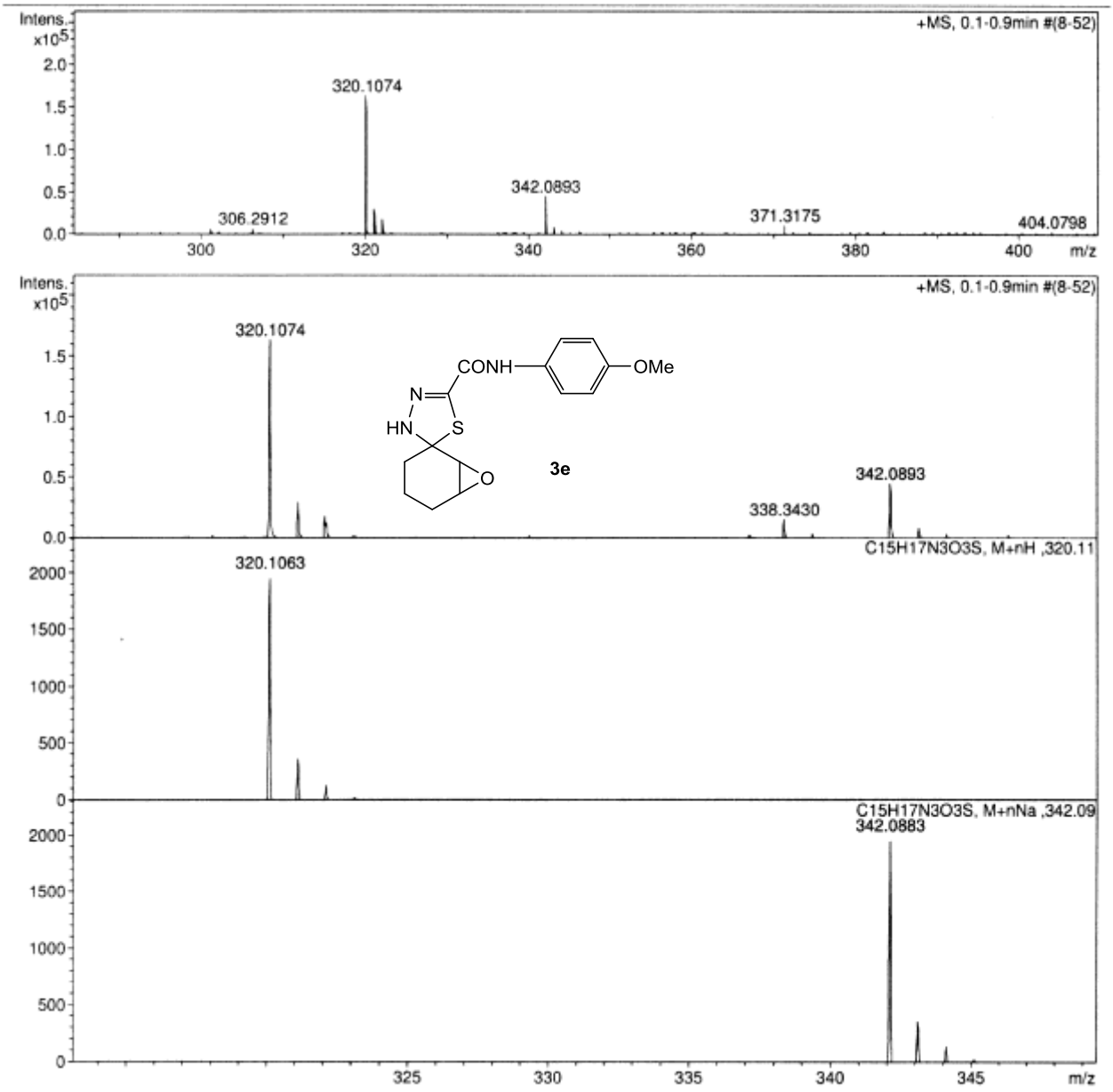
Method tune_50-1600.m

Instrument / Ser# micrOTOF 10248

Comment C15H17N3O3S mH 320.1063 clb added,

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Mass-spectra of **3e**.

Display Report

Analysis Info

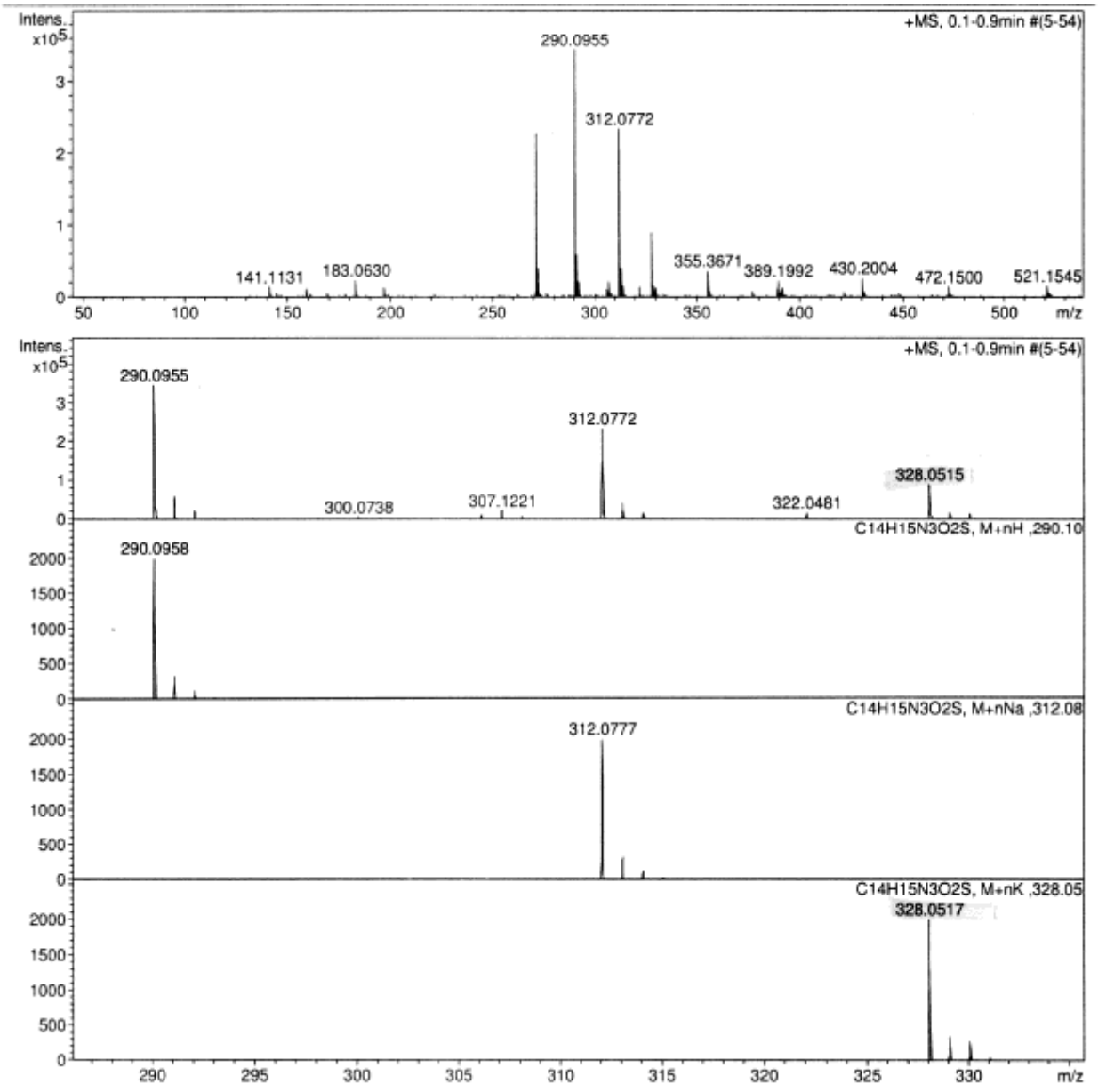
Method tune_50-1600.m

Instrument / Ser# micrOTOF 10248

Comment C14H15N3O2S mH 290.0957 calibrant added

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Mass-spectra of **3f**.

Display Report

Analysis Info

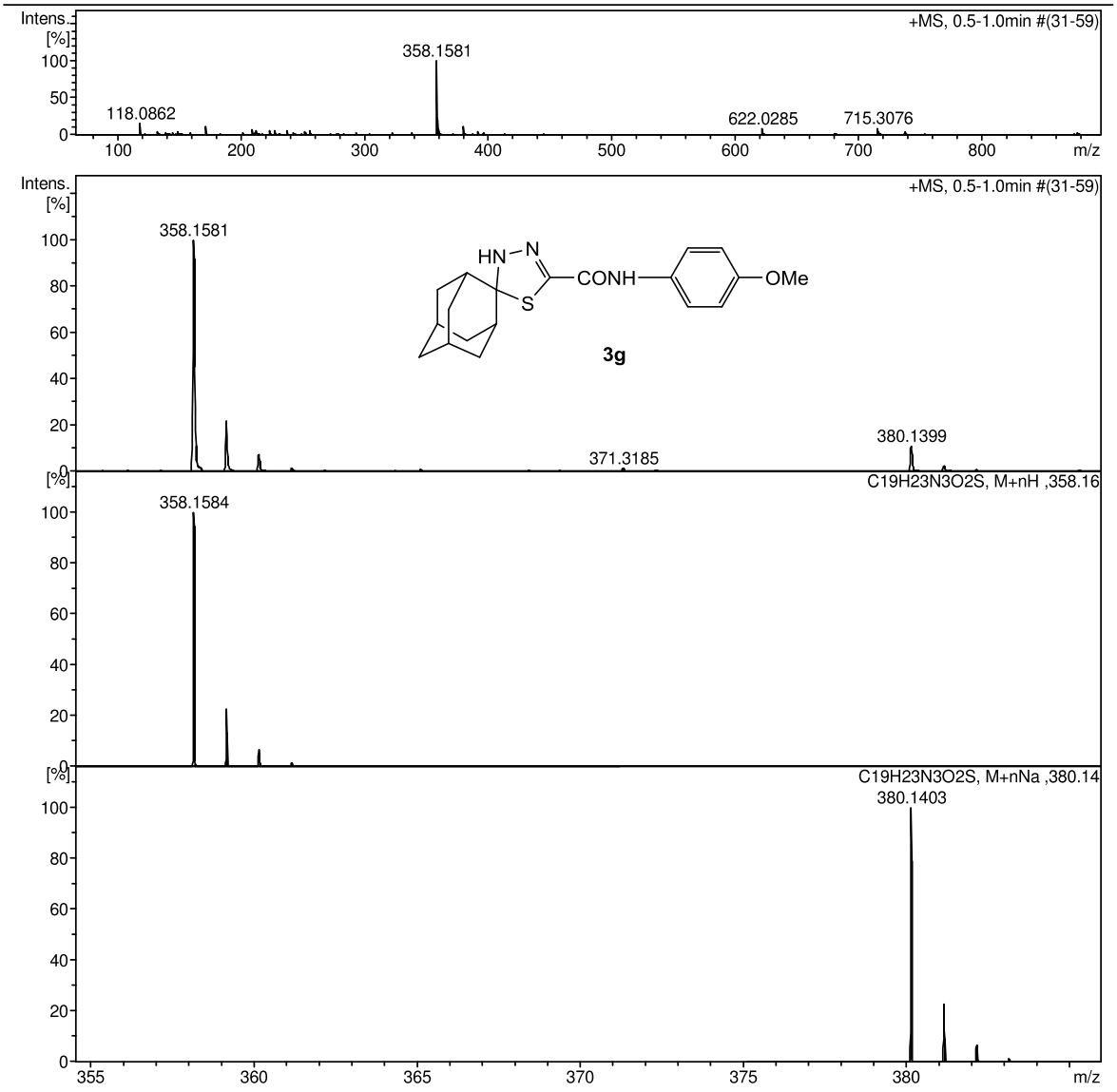
Method tune_low.m

Instrument / Ser# micrOTOF 10248

Comment C19H25N3O2S mH 360.1740 calibrant added CH3CN

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active			Set Dry Heater	180 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Mass-spectra of **3g**.

Display Report

Analysis Info

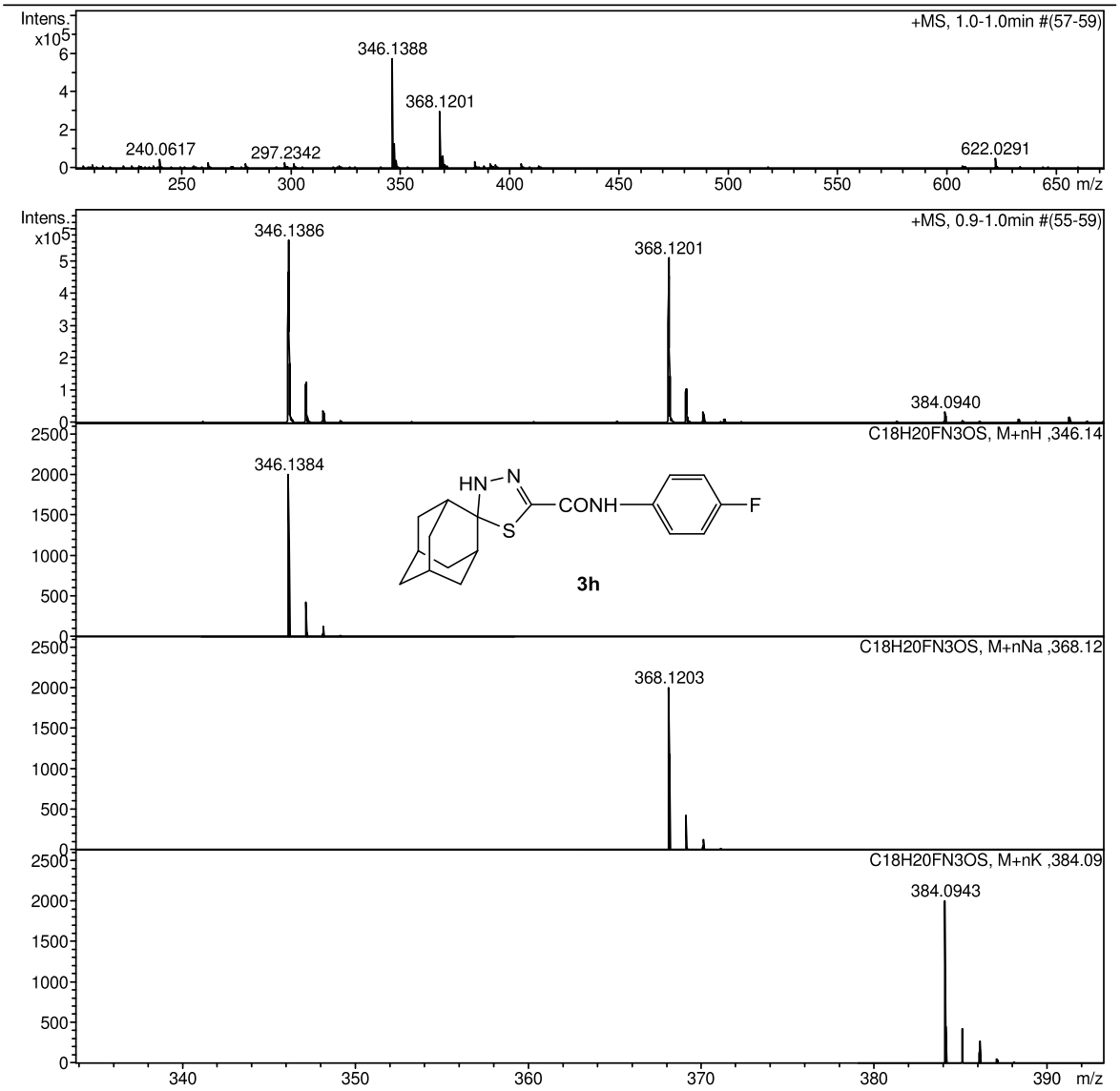
Method tune_low.m

Instrument / Ser# micrOTOF 10248

Comment C18H20FN3OS mH 346.1383 calibrant added CH3OH

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active			Set Dry Heater	180 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	3000 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Mass-spectra of **3h**.

Display Report

Analysis Info

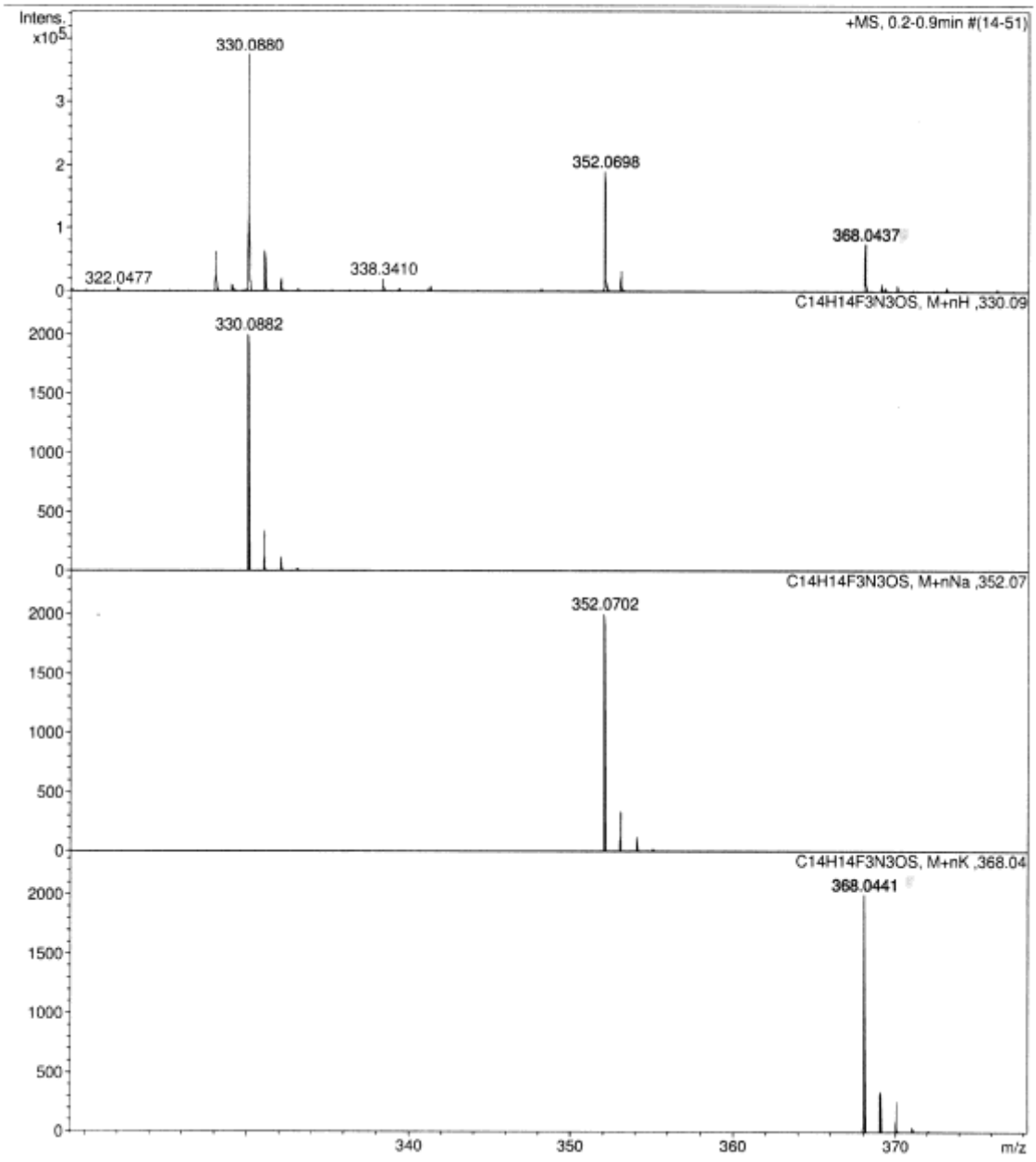
Method tune_50-1600.m

Instrument / Ser# micrOTOF 10248

Comment C14H14F3N3OS mH 330.0882 calibrant added

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Mass-spectra of **3i**.

Display Report

Analysis Info

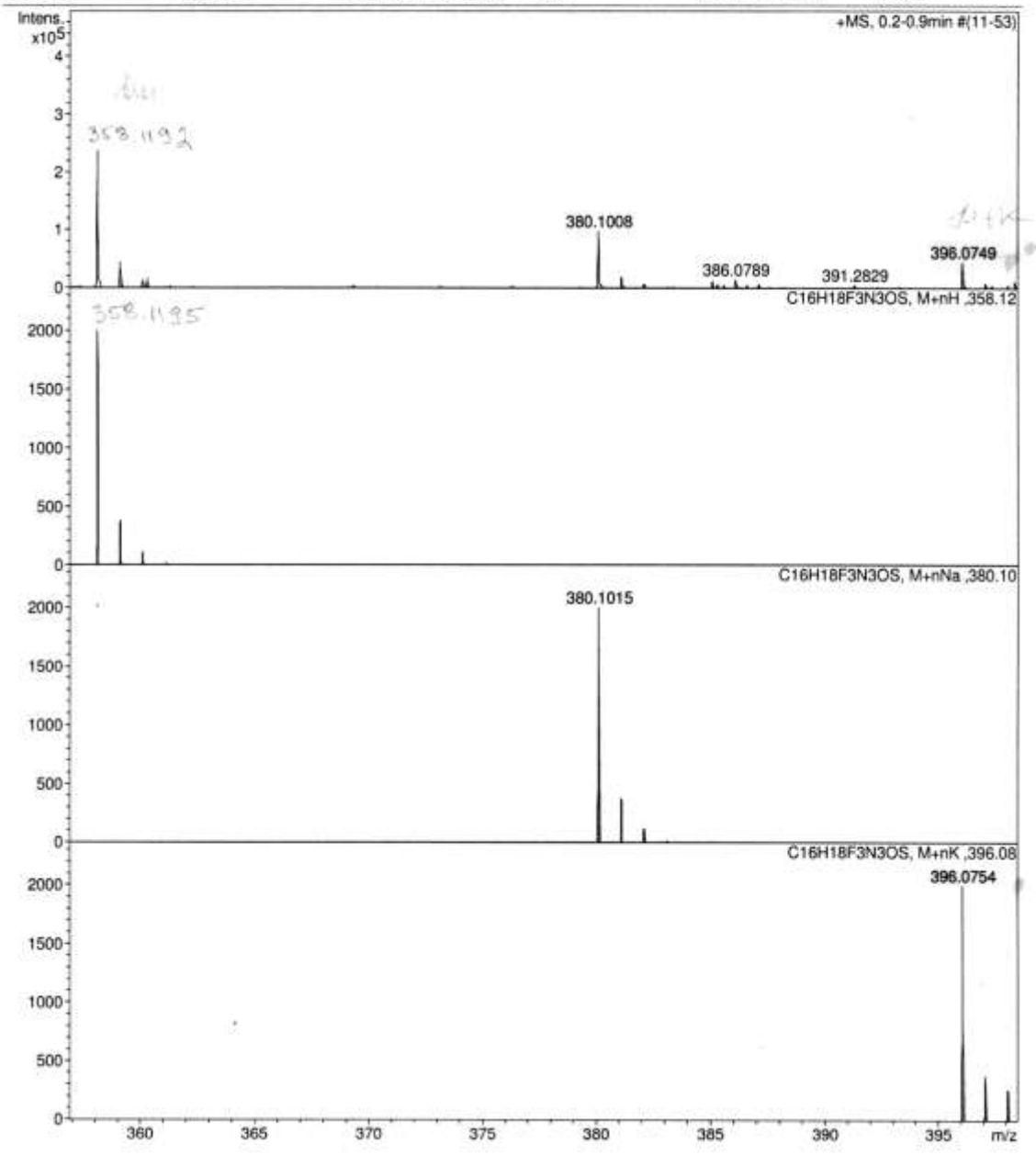
Method tune_50-1600.m

Instrument / Ser# micrOTOF 10248

Comment C16H18F3N3OS mH 358.1195 calibrant added

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Mass-spectra of **3j-4j**.

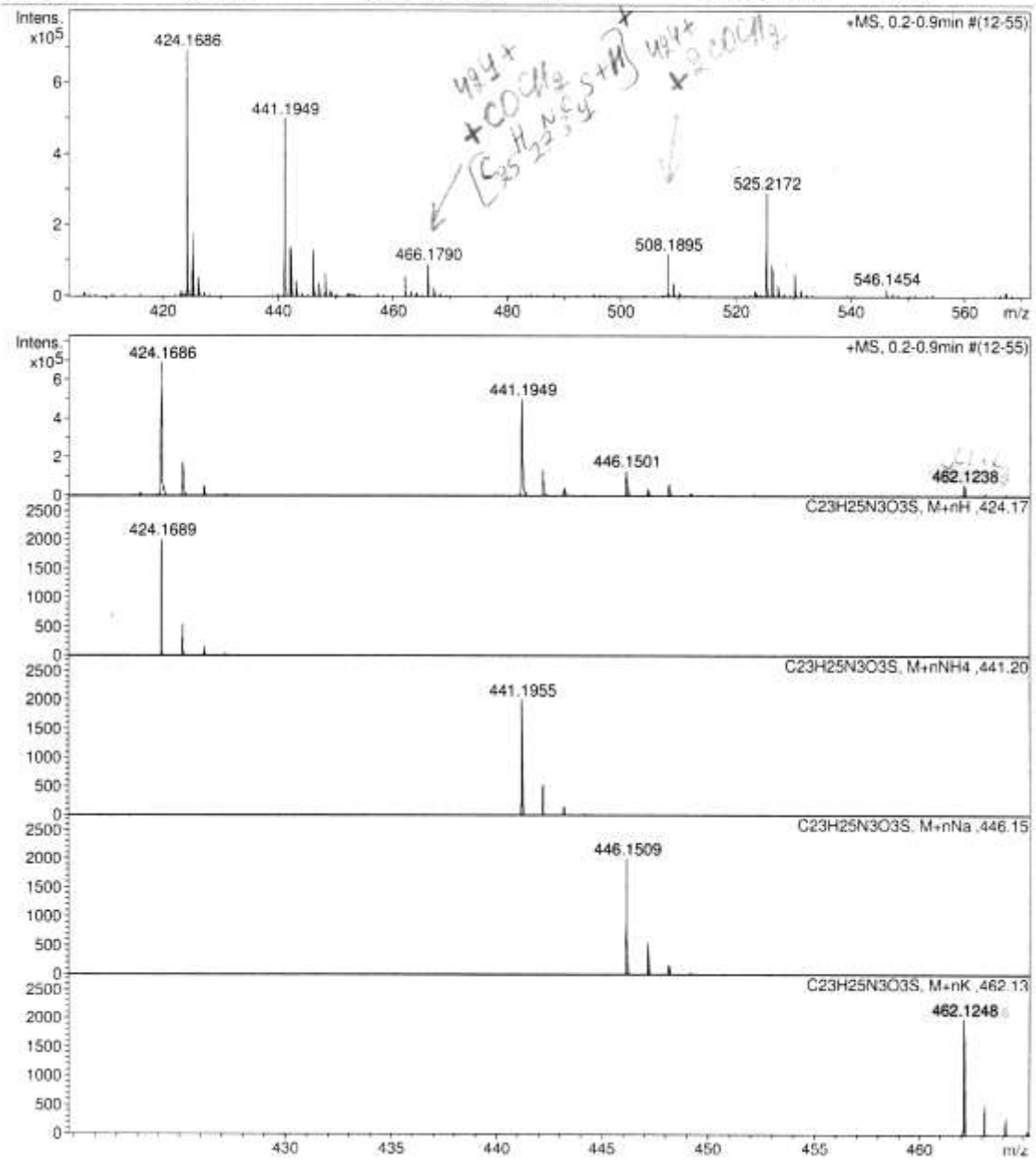
Display Report

Analysis Info

Method	tune 50-1600.m		
Comment	C23H25N3O3S mH 424.1689 calibrant added	Instrument / Ser#	micrOTOF 10248

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.0 Bar
Focus	Not active			Set Dry Heater	200 °C
Scan Begin	50 m/z	Set Capillary	4500 V	Set Dry Gas	4.0 l/min
Scan End	1600 m/z	Set End Plate Offset	-500 V	Set Divert Valve	Waste



Mass-spectra of **5**/**6**.