

Supplementary Materials

In Vivo Hepatoprotective and Nephroprotective Activity of Acylated Iridoid Glycosides from *Scrophularia Hepericifolia*

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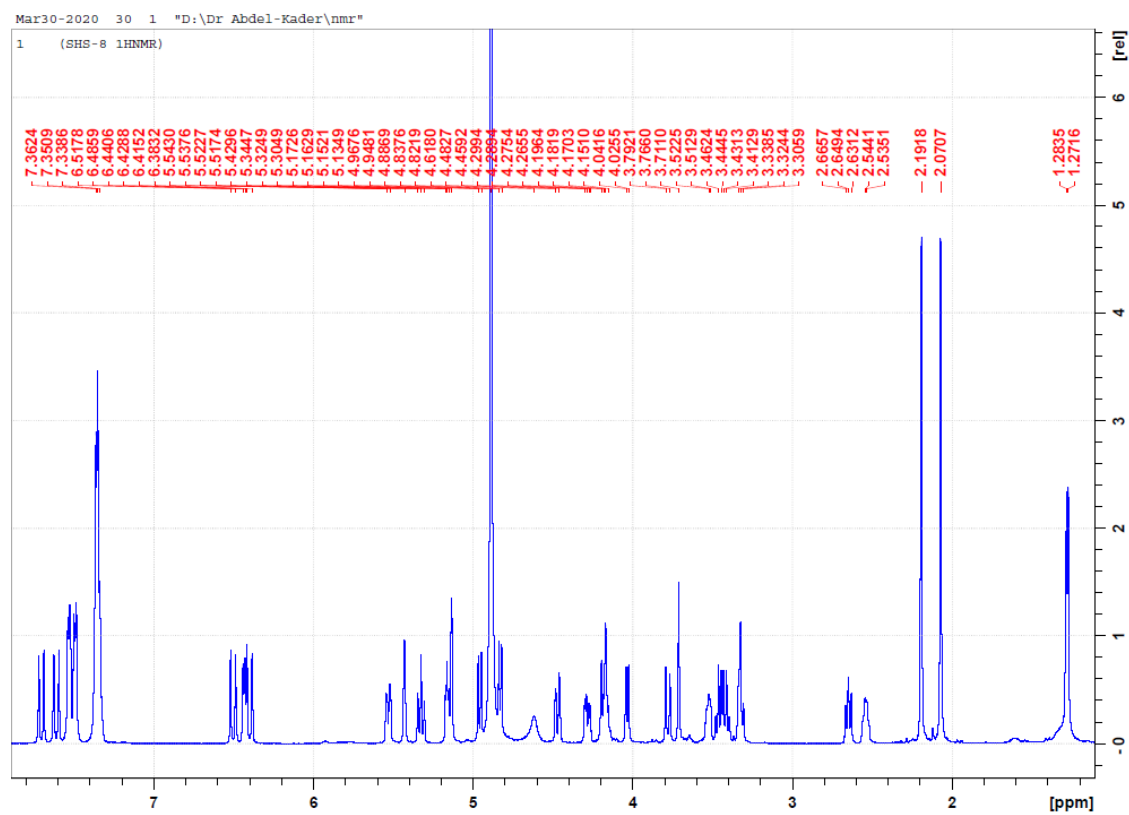


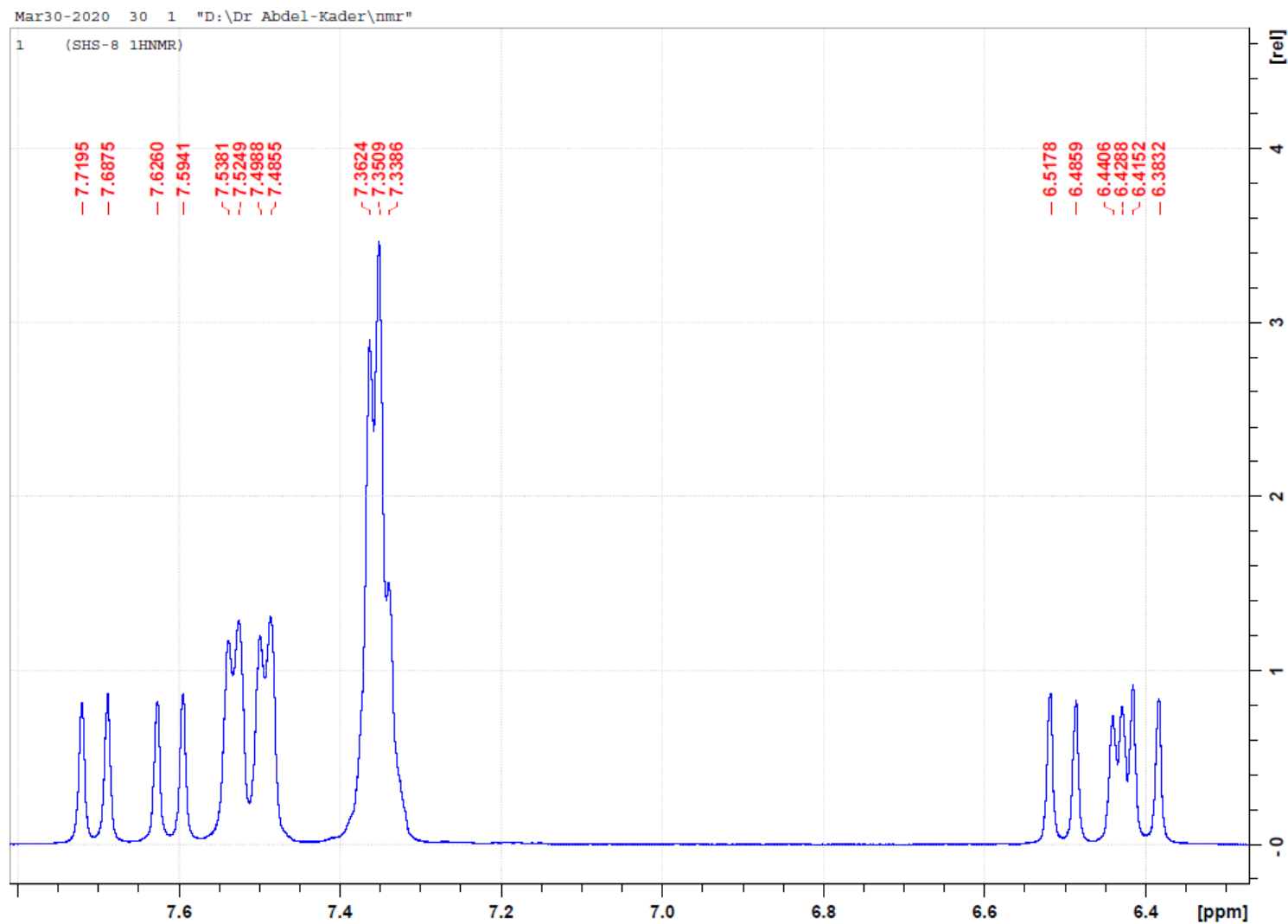
Figure S1. ¹HNMR spectrum of compound 1.

Figure S2. ¹HNMR spectrum of compound 1 (Expansion).

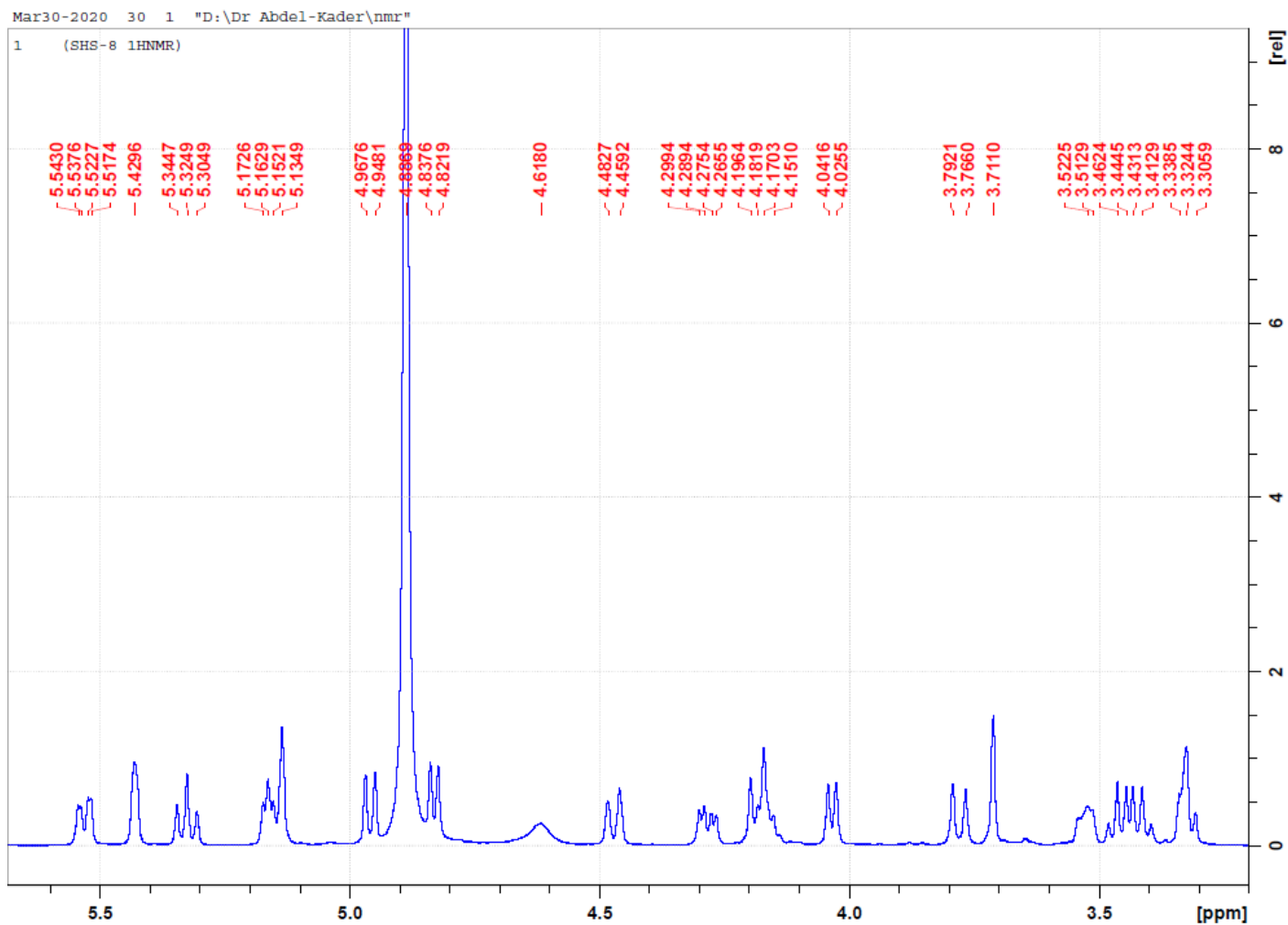


Figure S3. ¹HNMR spectrum of compound 1 (Expansion).

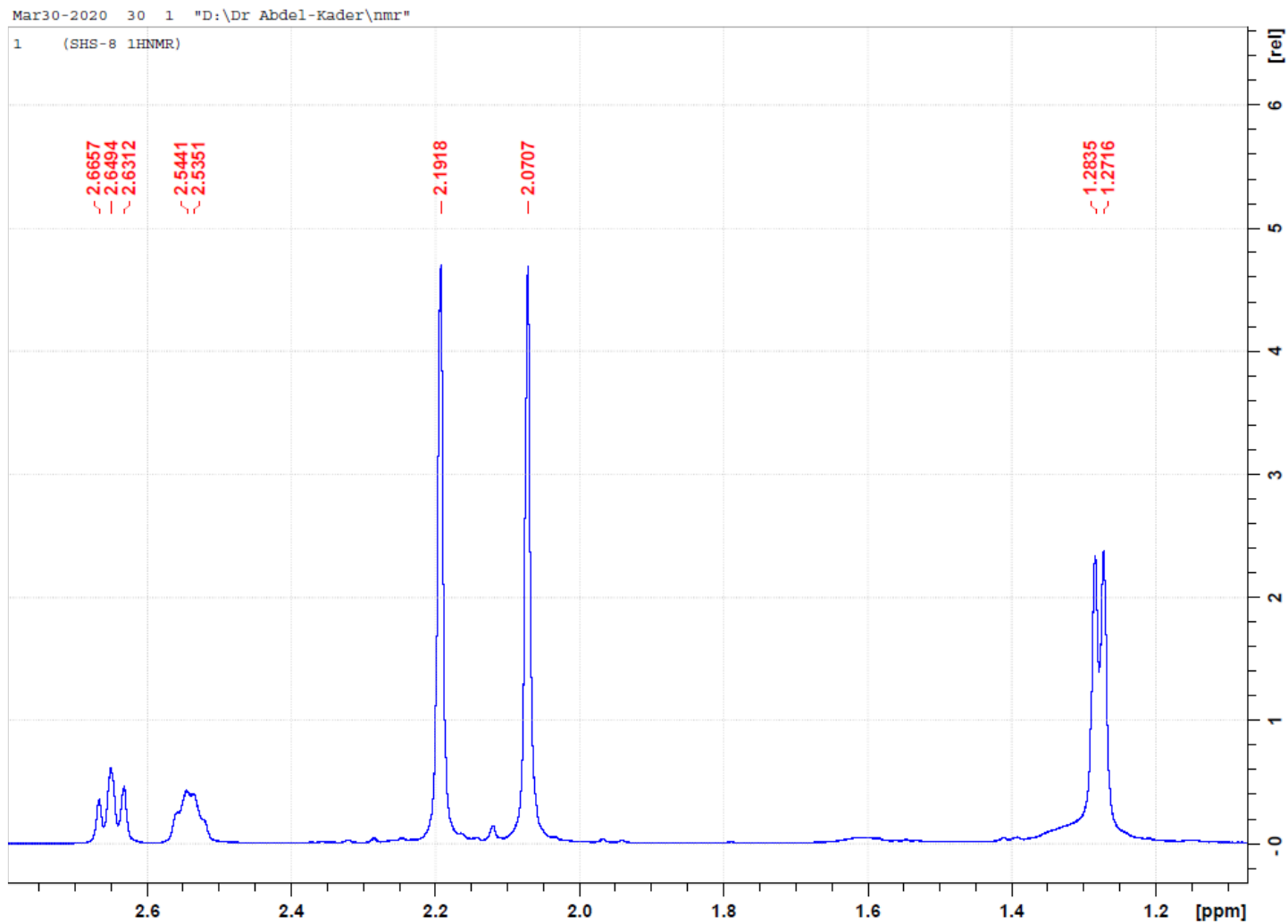


Figure S4. ¹H NMR spectrum of compound 1 (Expansion).

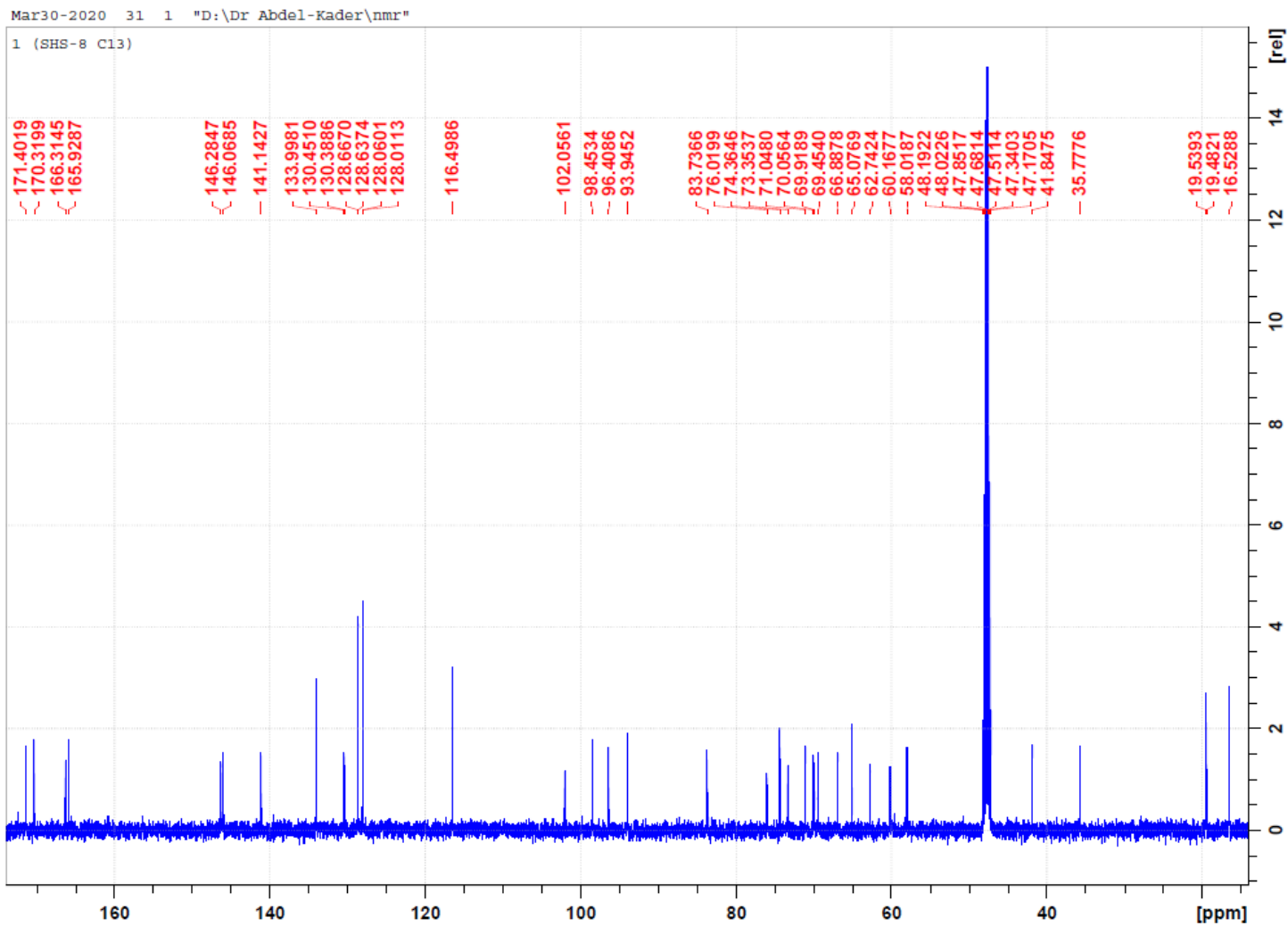


Figure S5. ¹³CNMR spectrum of compound 1.

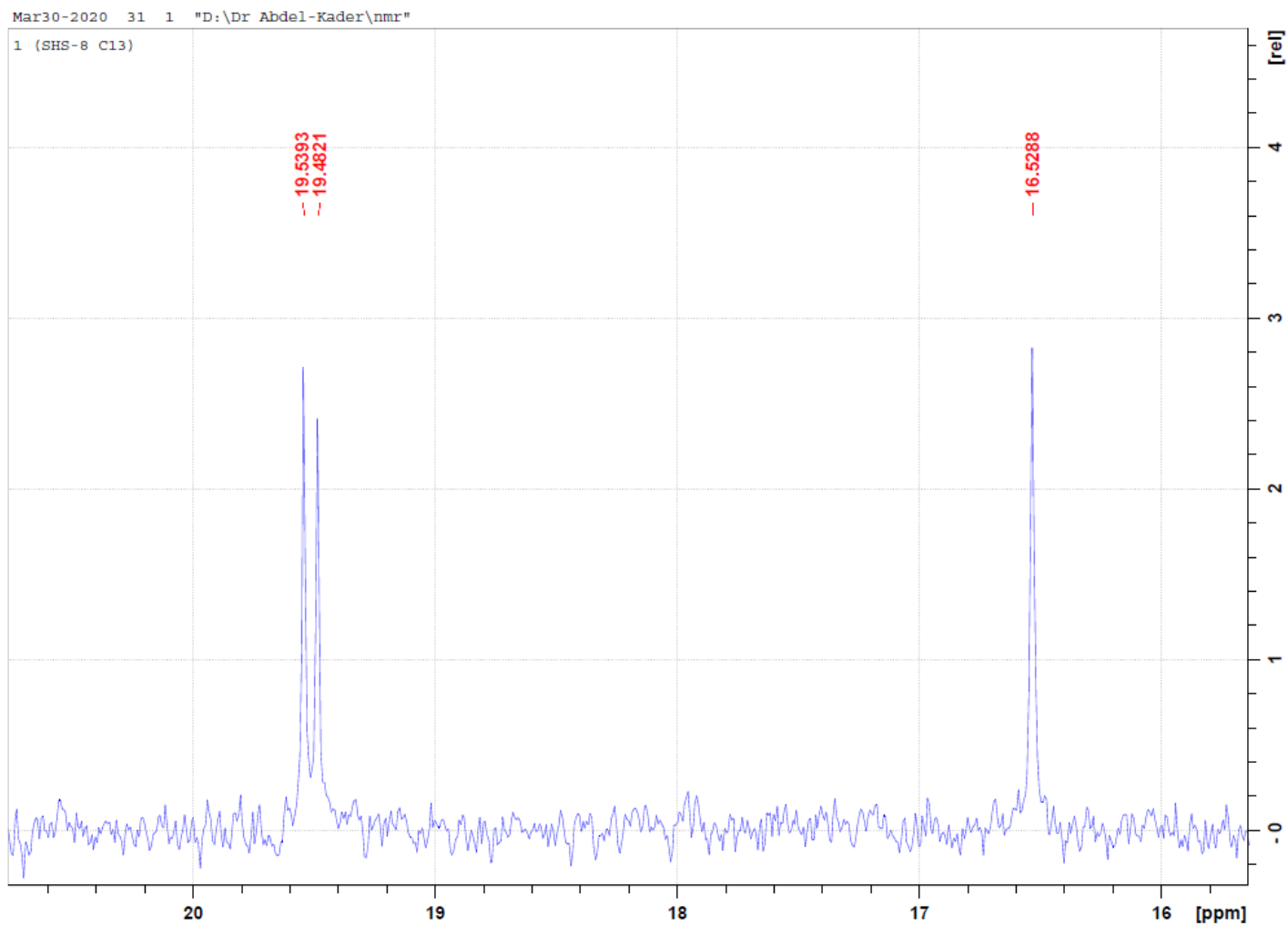


Figure S6. ¹³CNMR spectrum of compound 1 (Expansion).

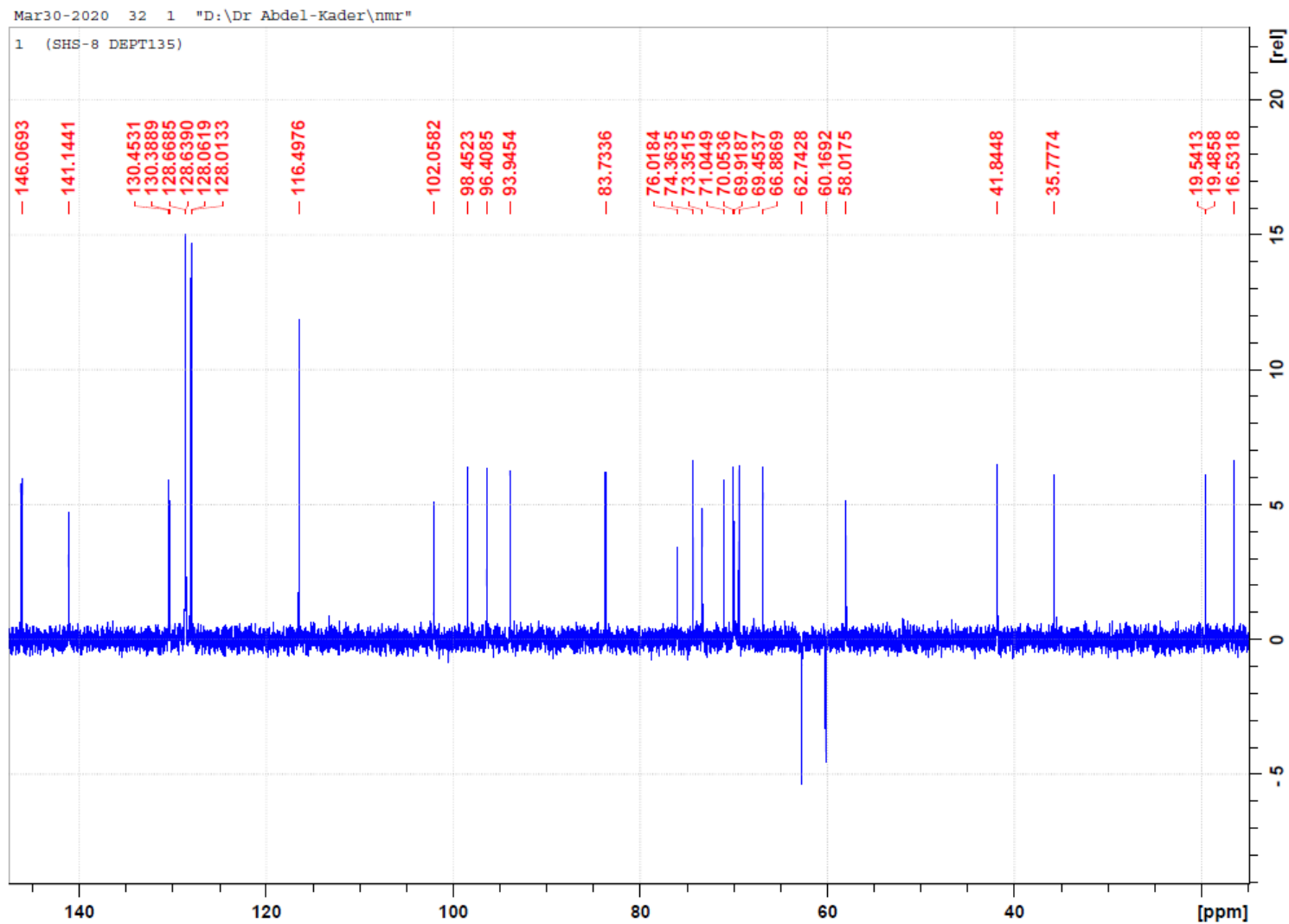


Figure S7. DEPT135 spectrum of compound 1.

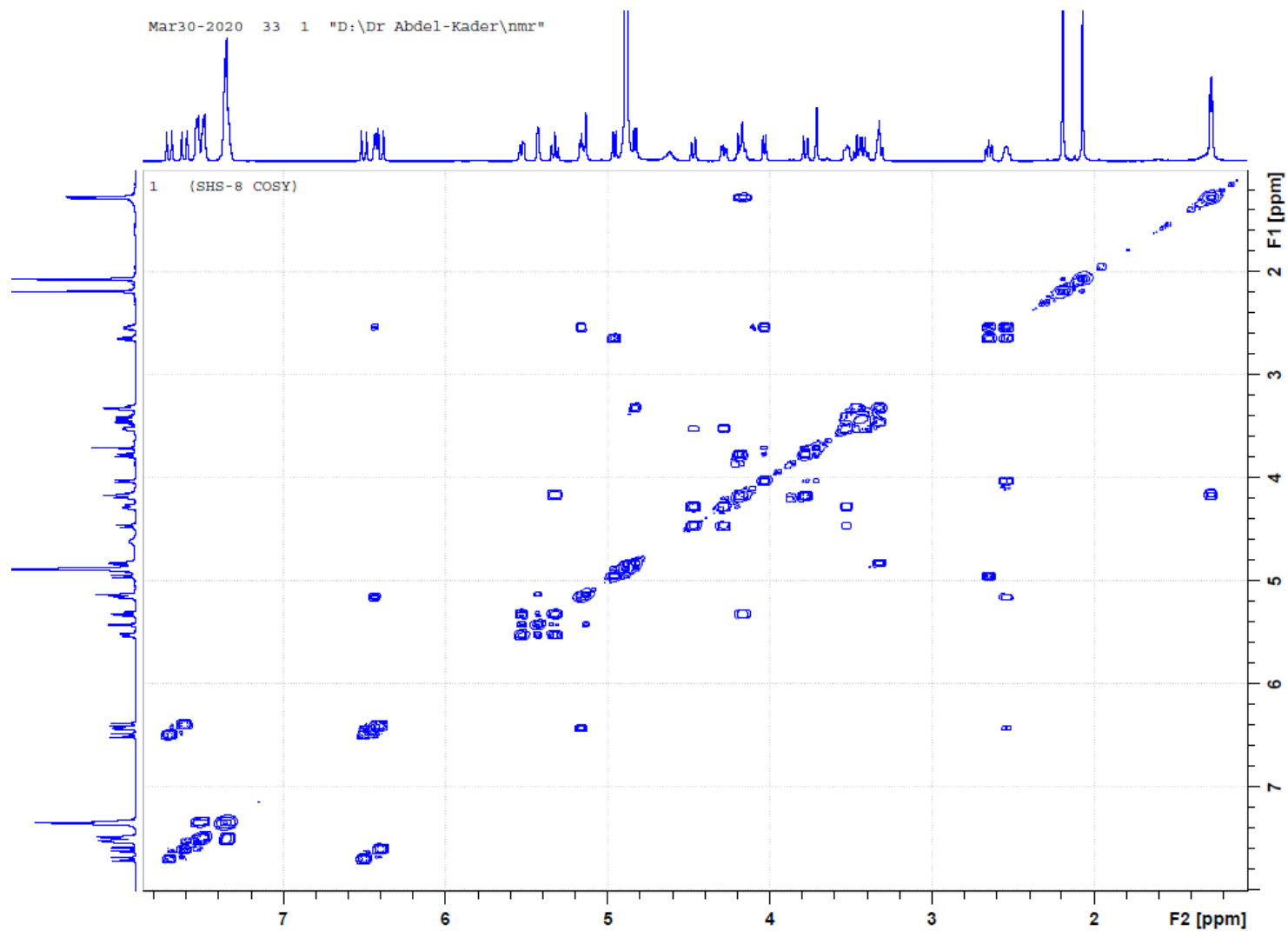


Figure S8. COSY spectrum of compound 1.

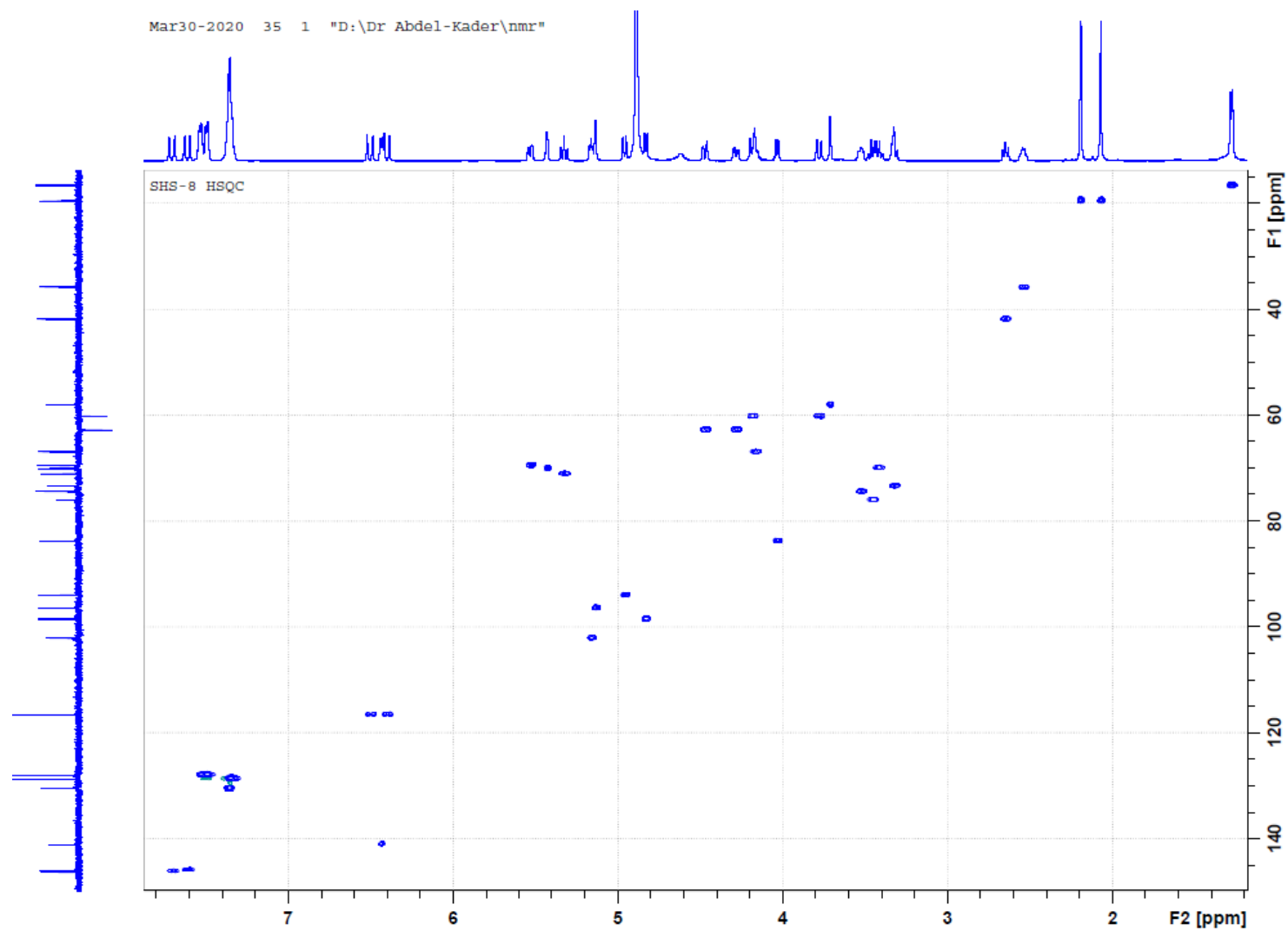


Figure S9. HSQC spectrum of compound 1.

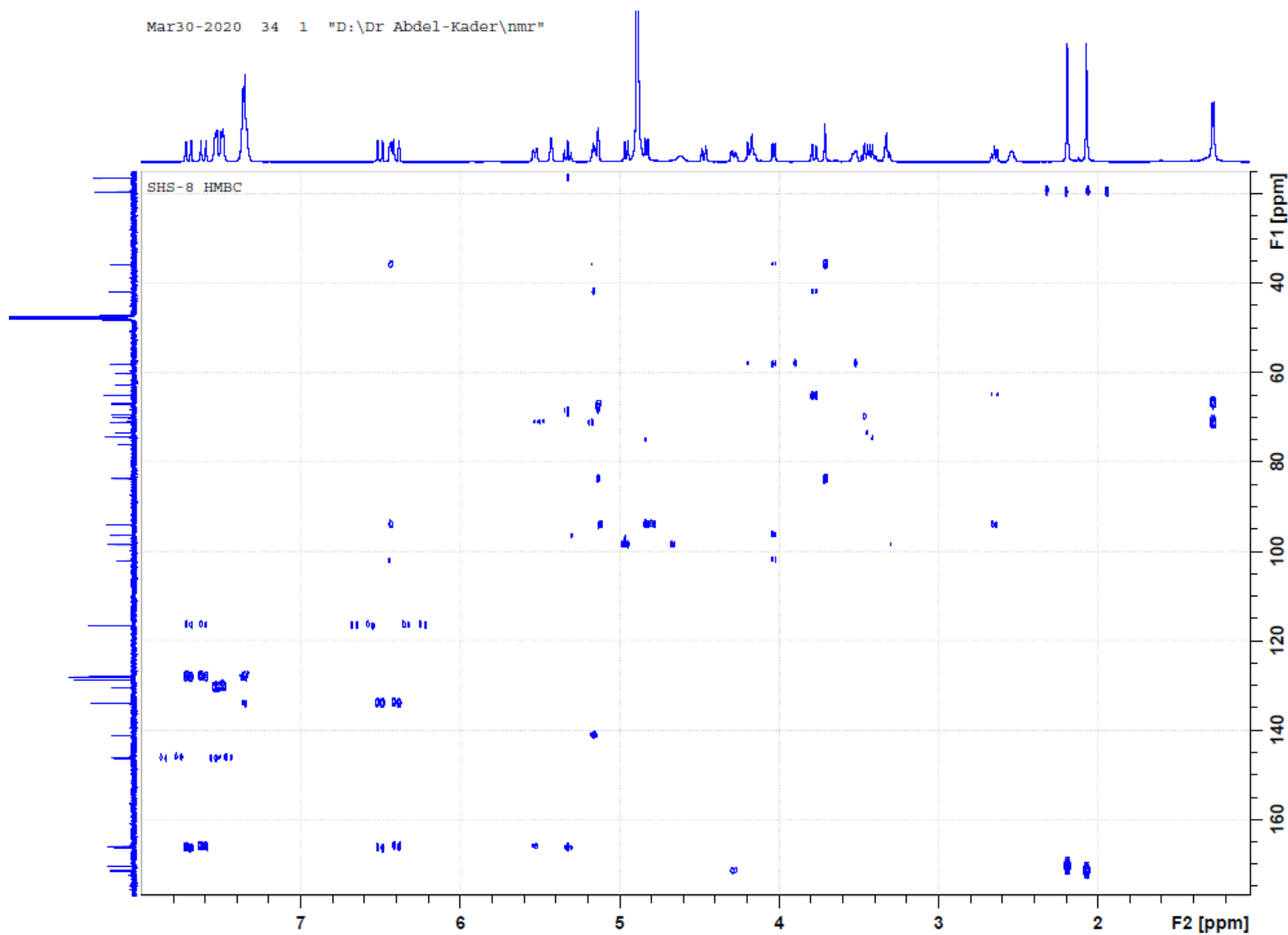


Figure S10. HMBC spectrum of compound 1.

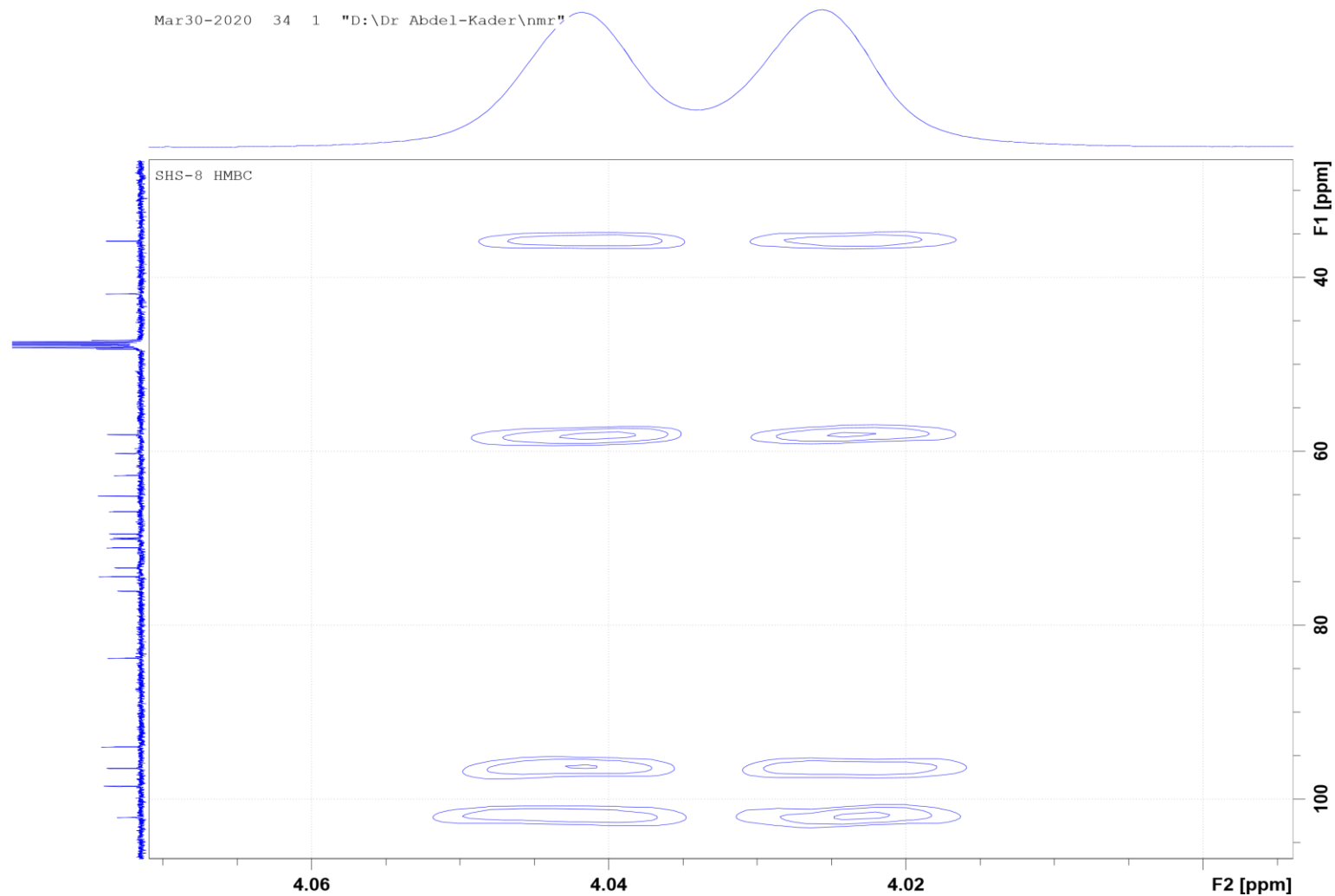


Figure S11. HMBC spectrum of compound 1 (Expansion).

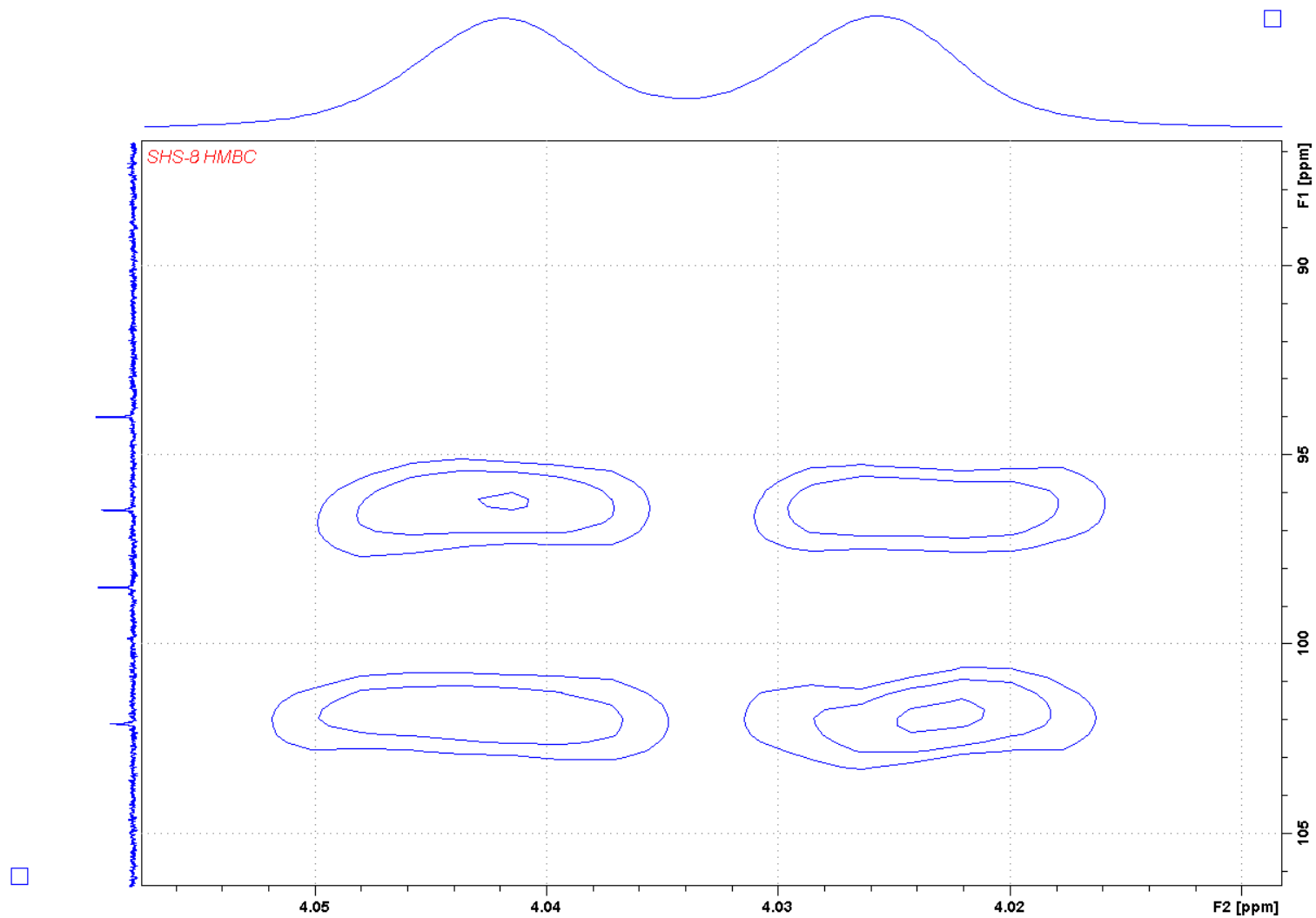


Figure S12. HMBC spectrum of compound 1 (Expansion).

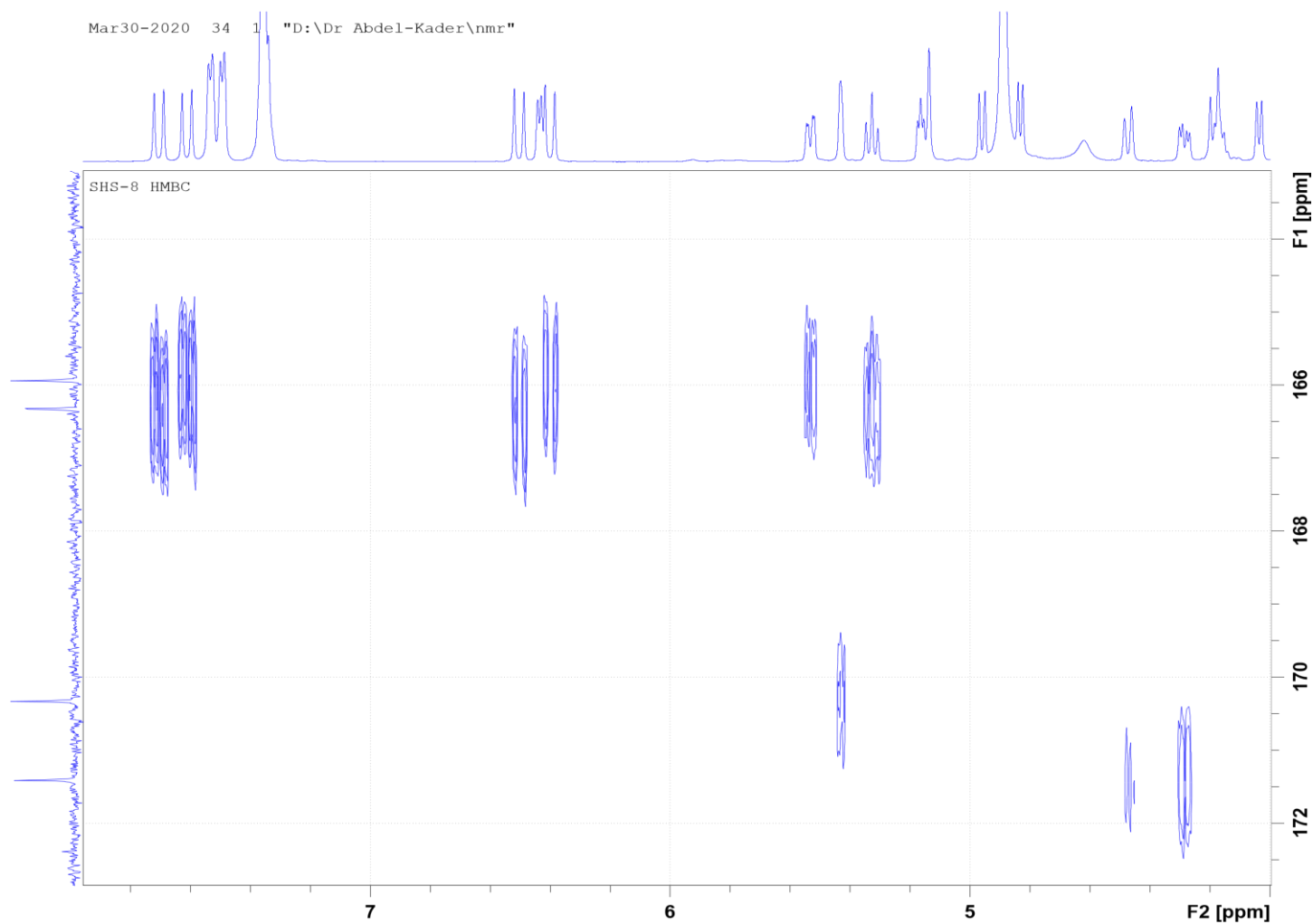


Figure S13. HMBC spectrum of compound 1 (Expansion).

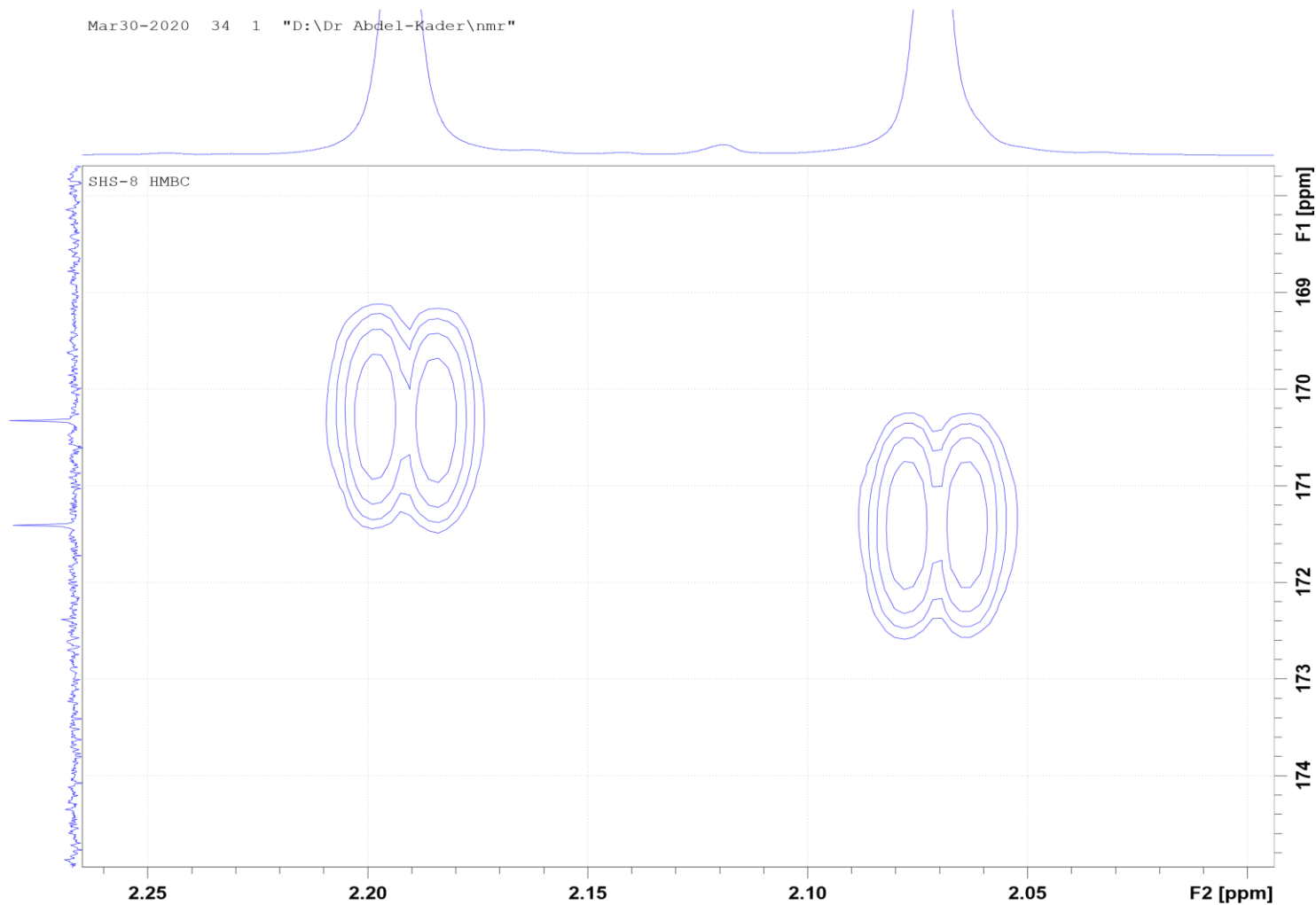


Figure S14. HMBC spectrum of compound 1 (Expansion).

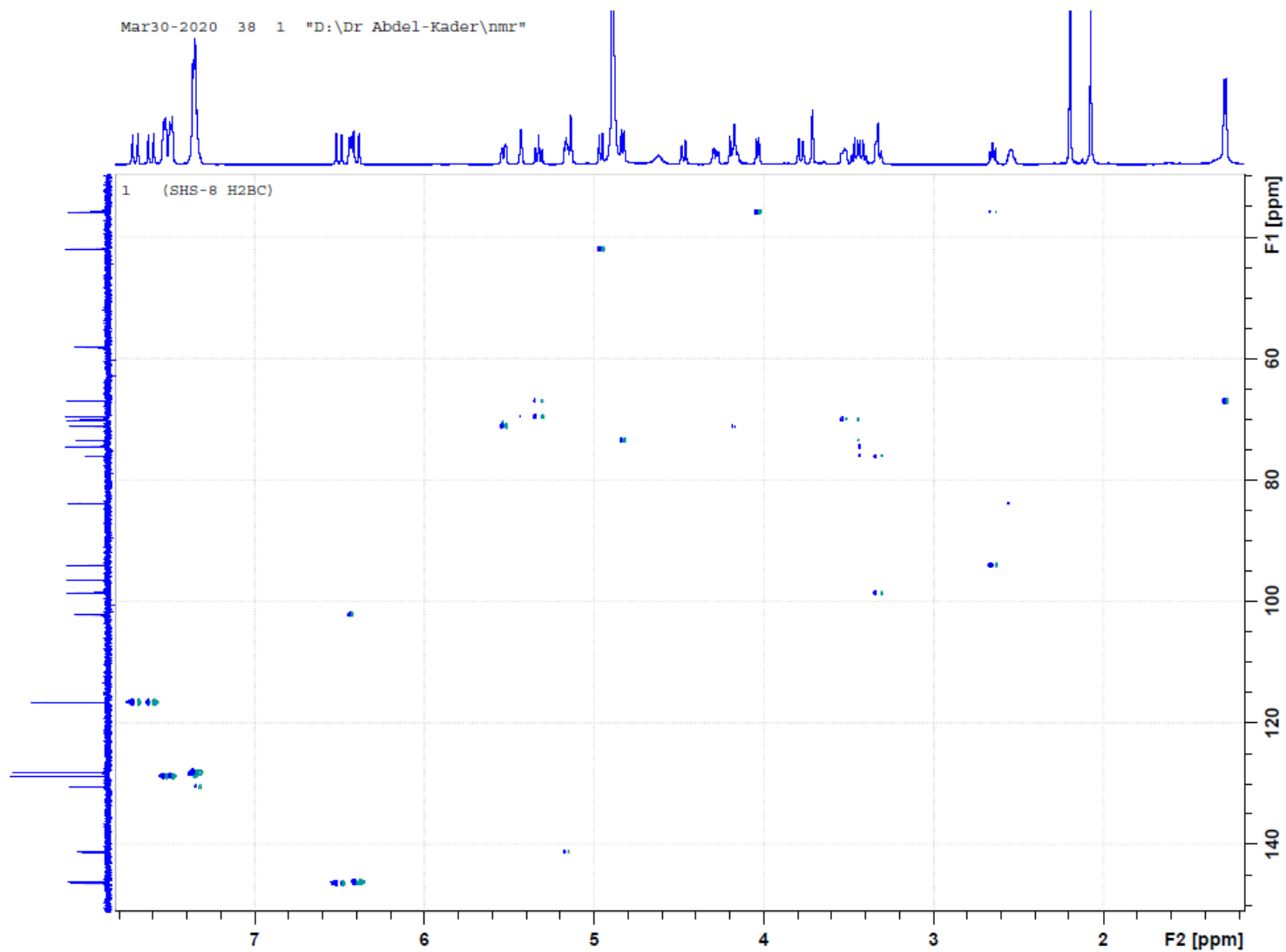


Figure S15. H2BC spectrum of compound 1.

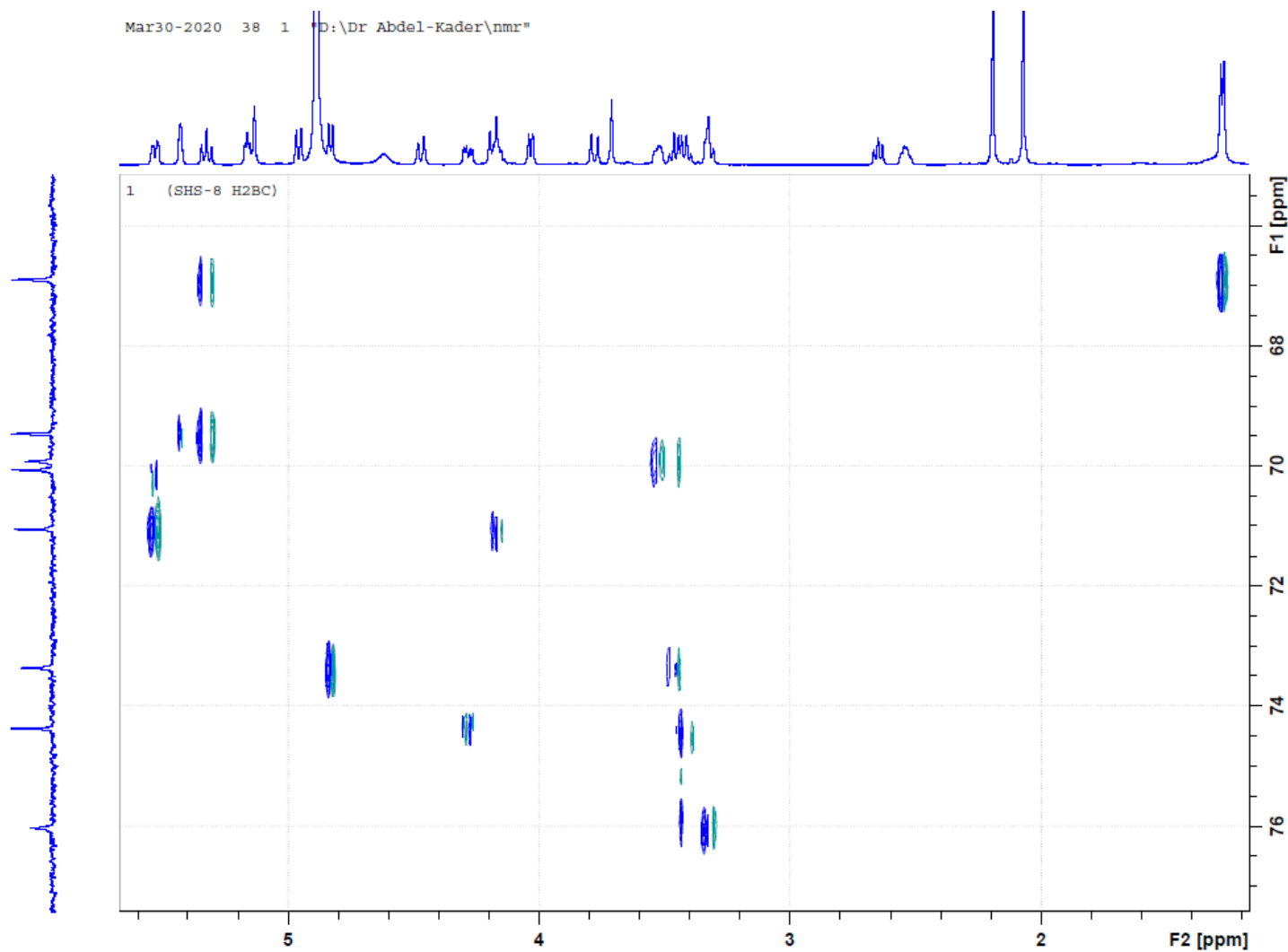


Figure S16. H2BC spectrum of compound 1 (Expansion).

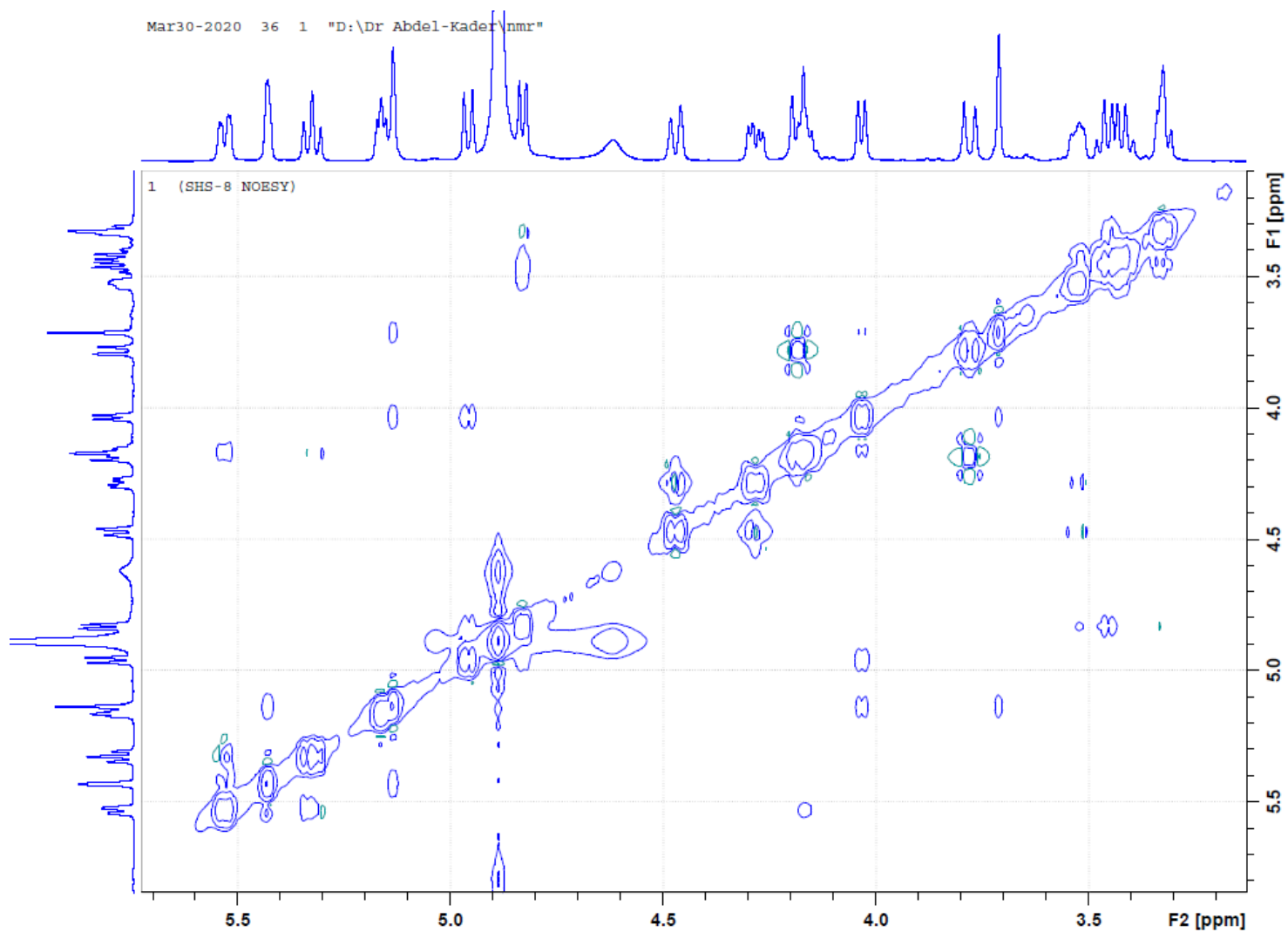


Figure S17. NOESY spectrum of compound 1 (Expansion).

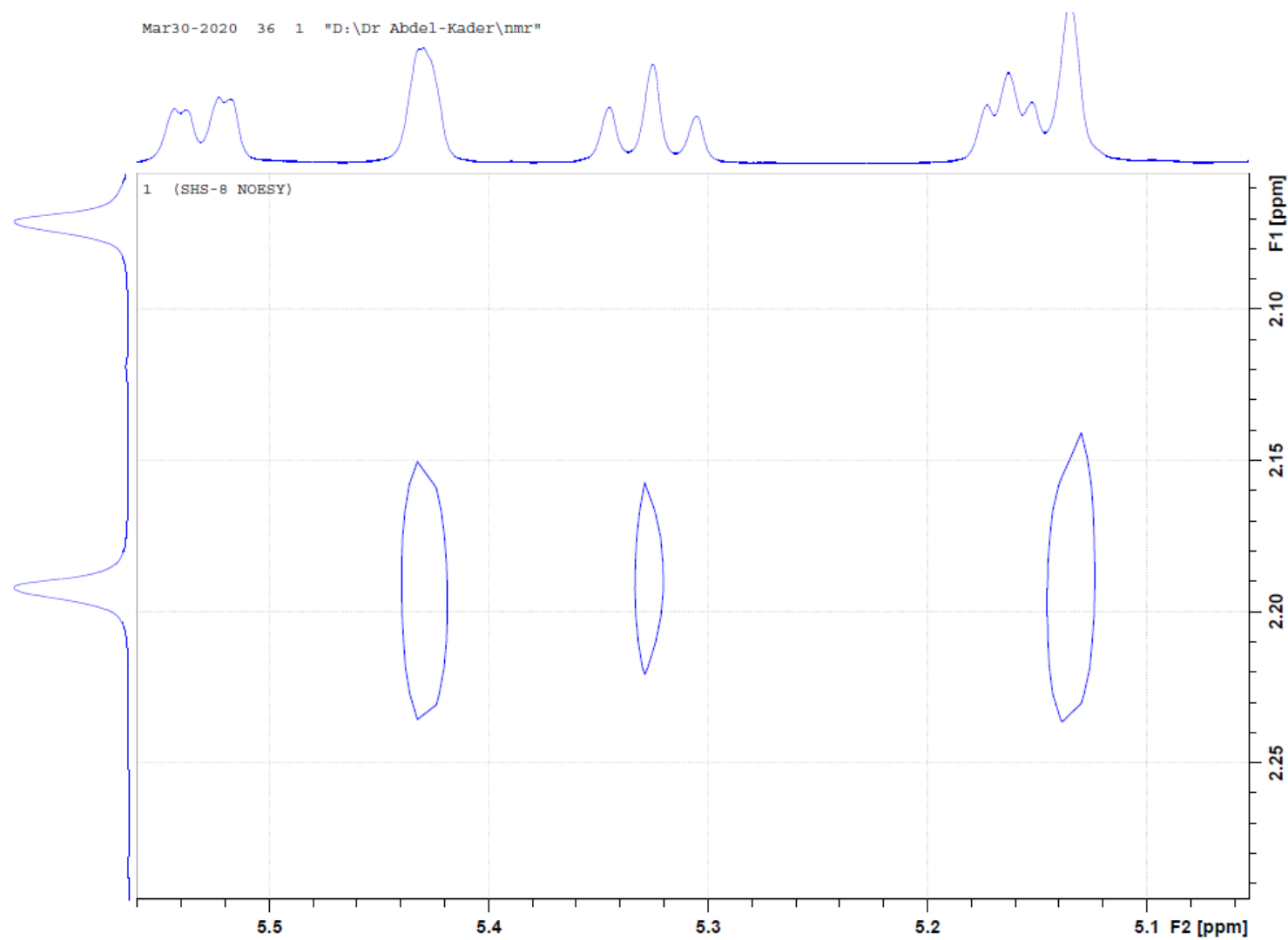


Figure S18. NOESY spectrum of compound 1 (Expansion).

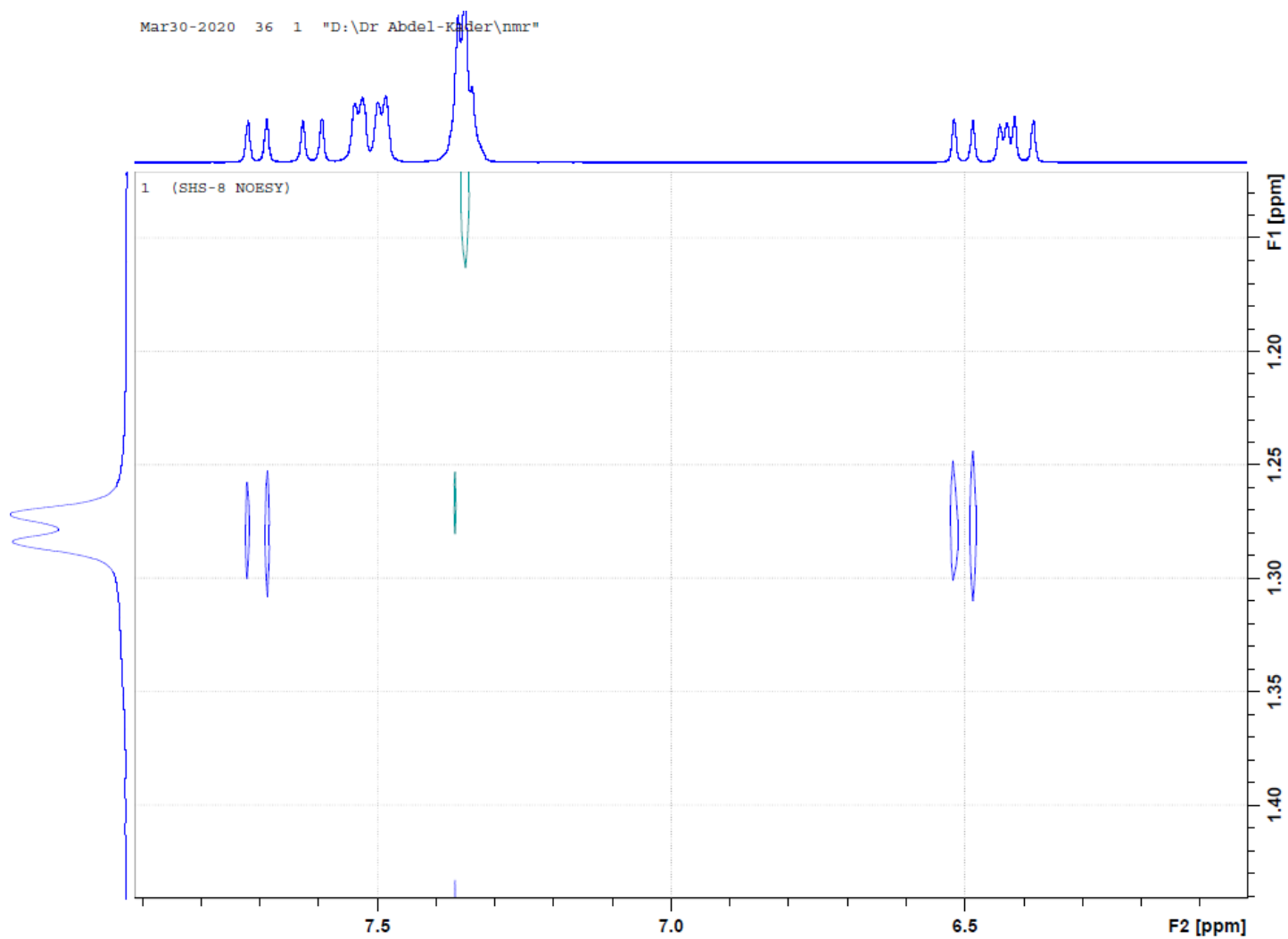


Figure S19. NOESY spectrum of compound 1 (Expansion).

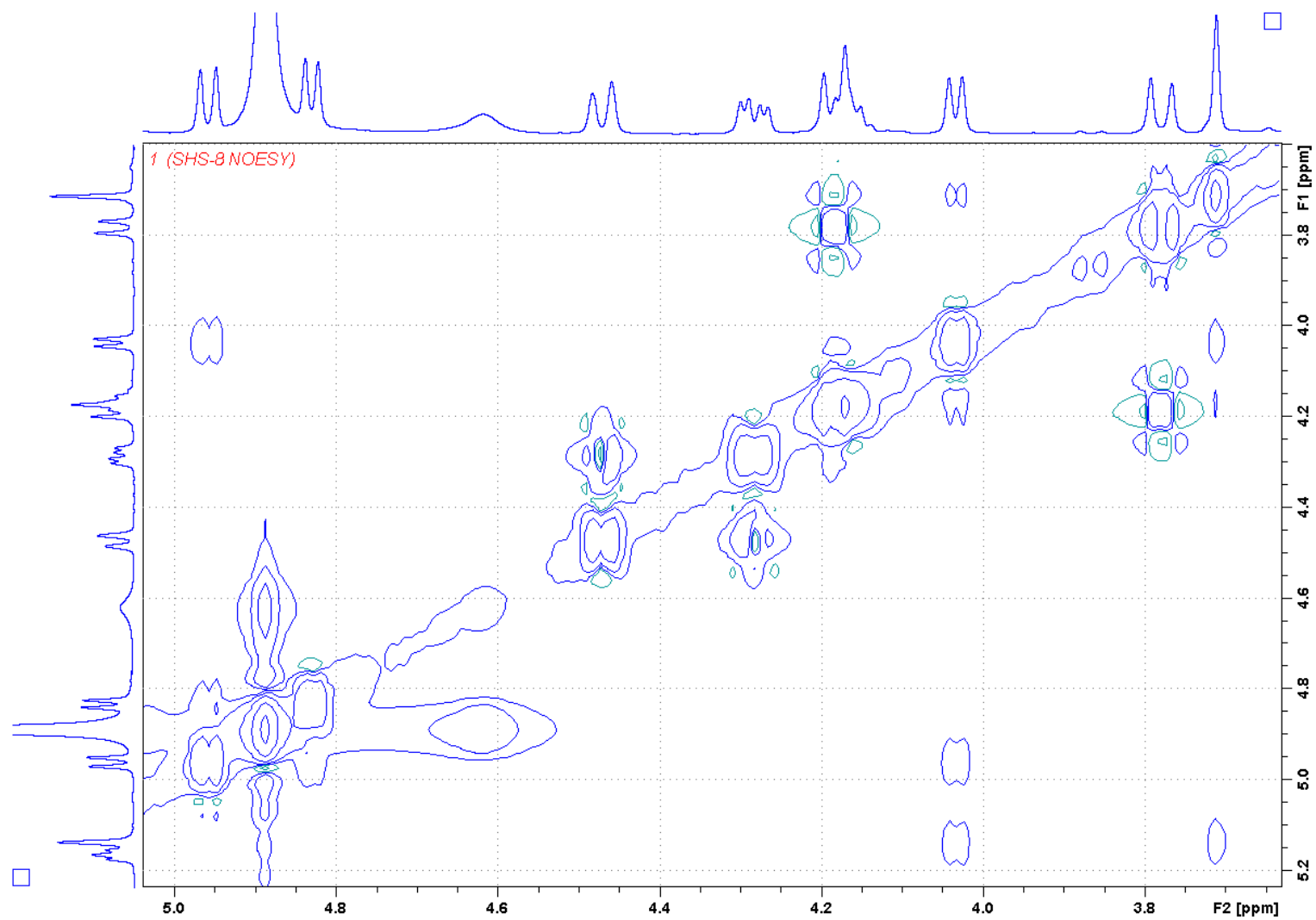


Figure S20. NOESY spectrum of compound 1 (Expansion).

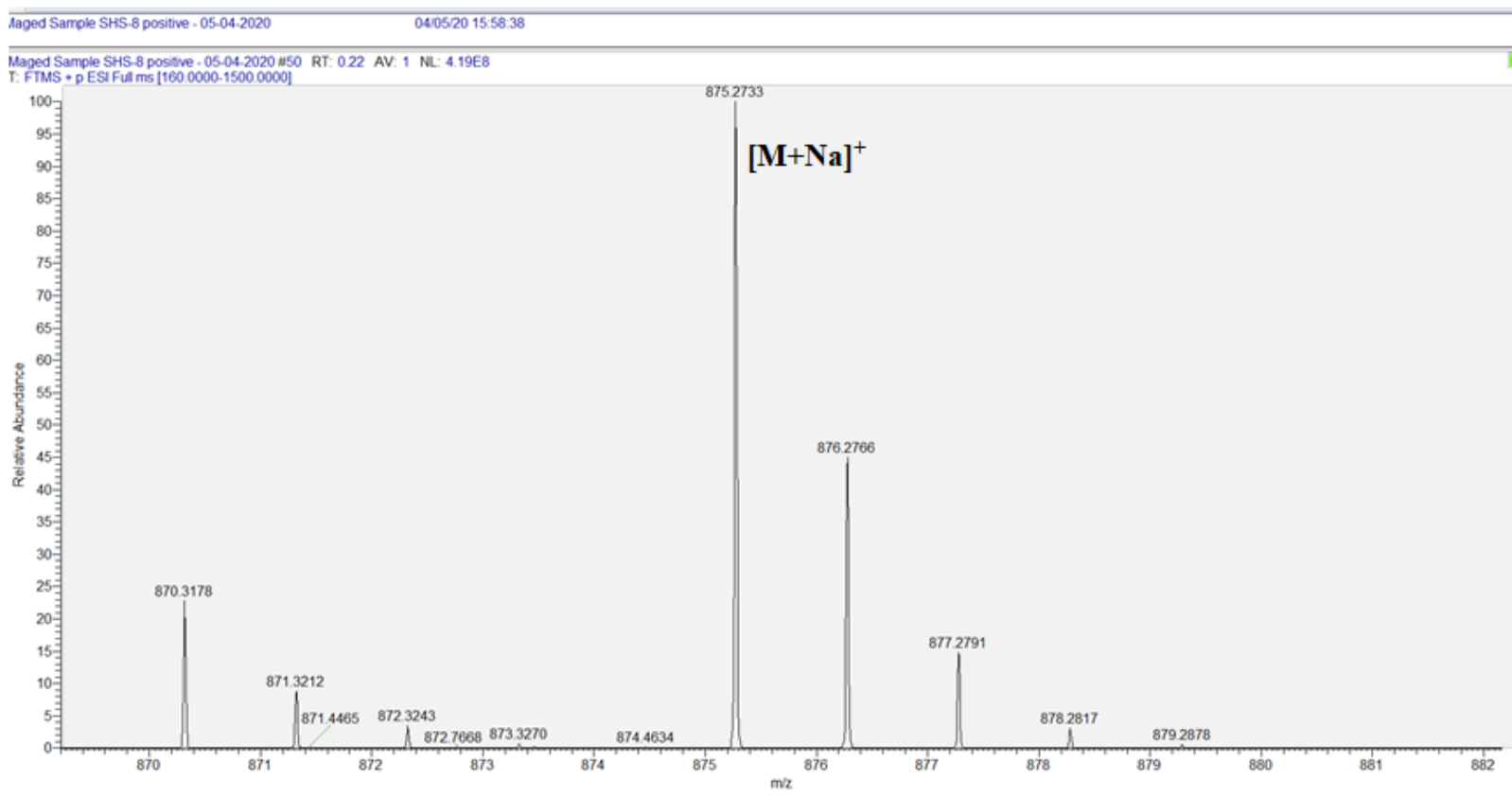


Figure S21. HRESIMS of compound 1 (positive mode).

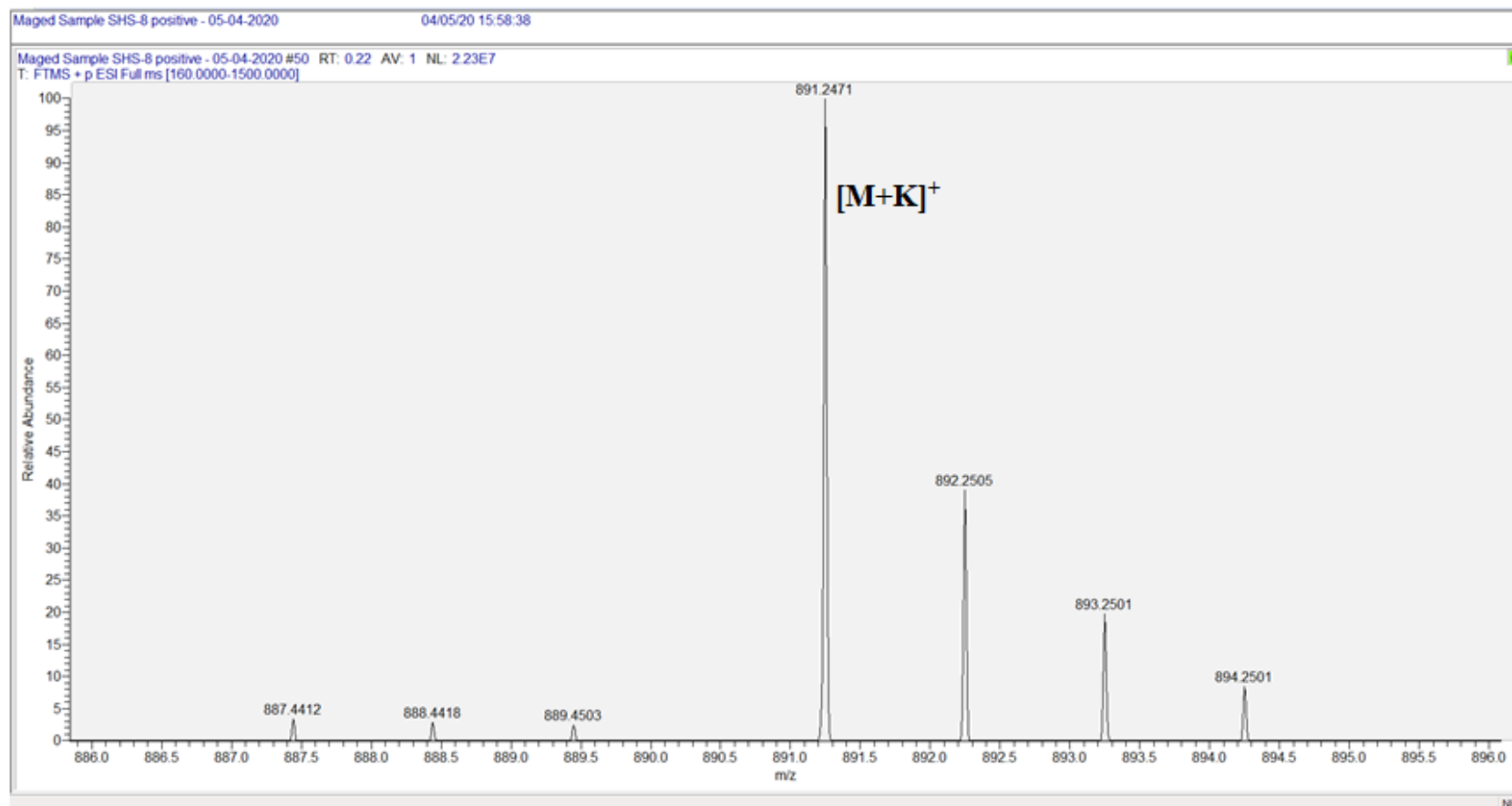


Figure S22. HRESIMS of compound 1 (positive mode).

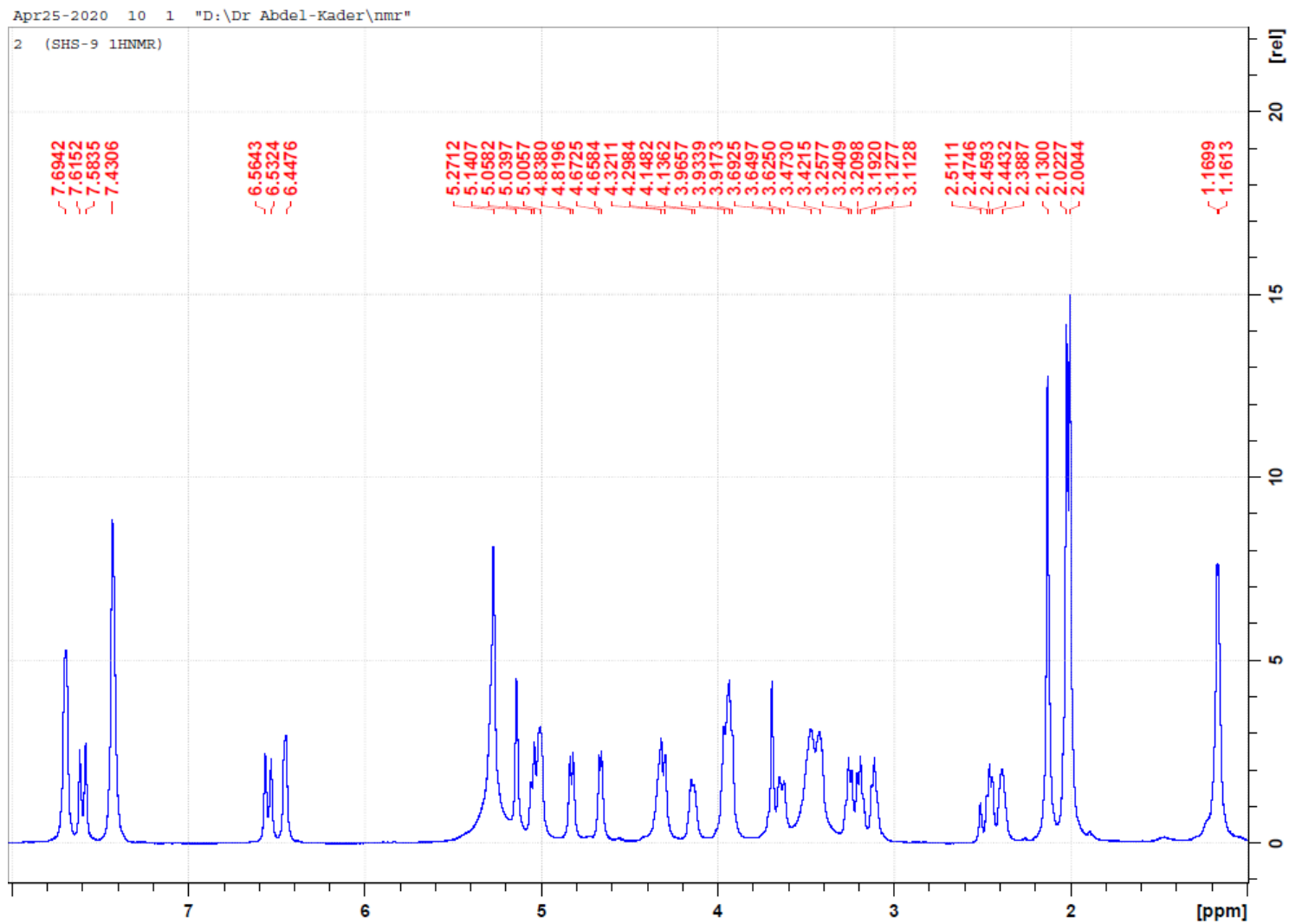


Figure S23. ¹H NMR spectrum of compound 2.

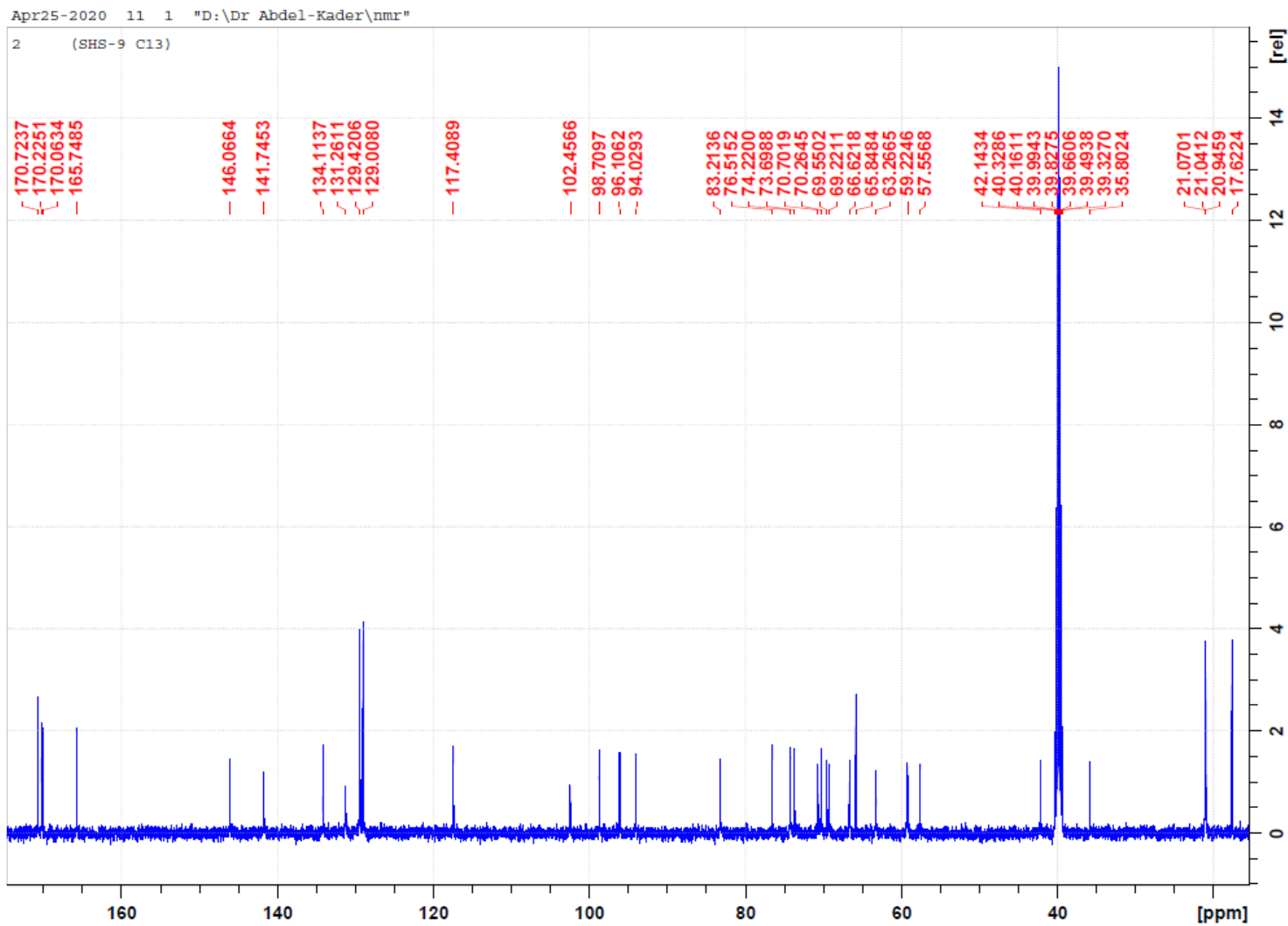


Figure S24. ¹³CNMR spectrum of compound 2.

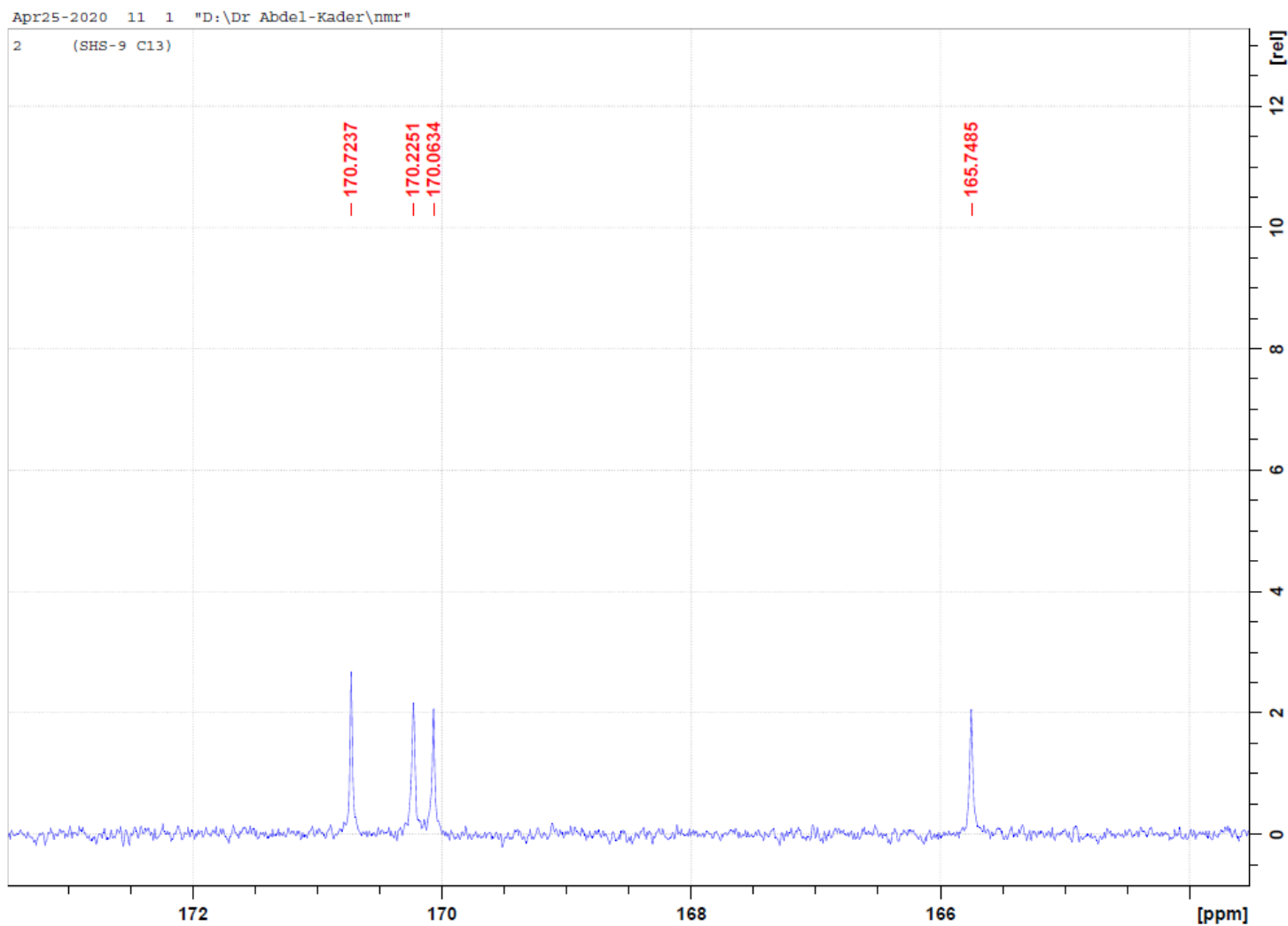


Figure S25. ^{13}C NMR spectrum of compound 2 (Expansion).

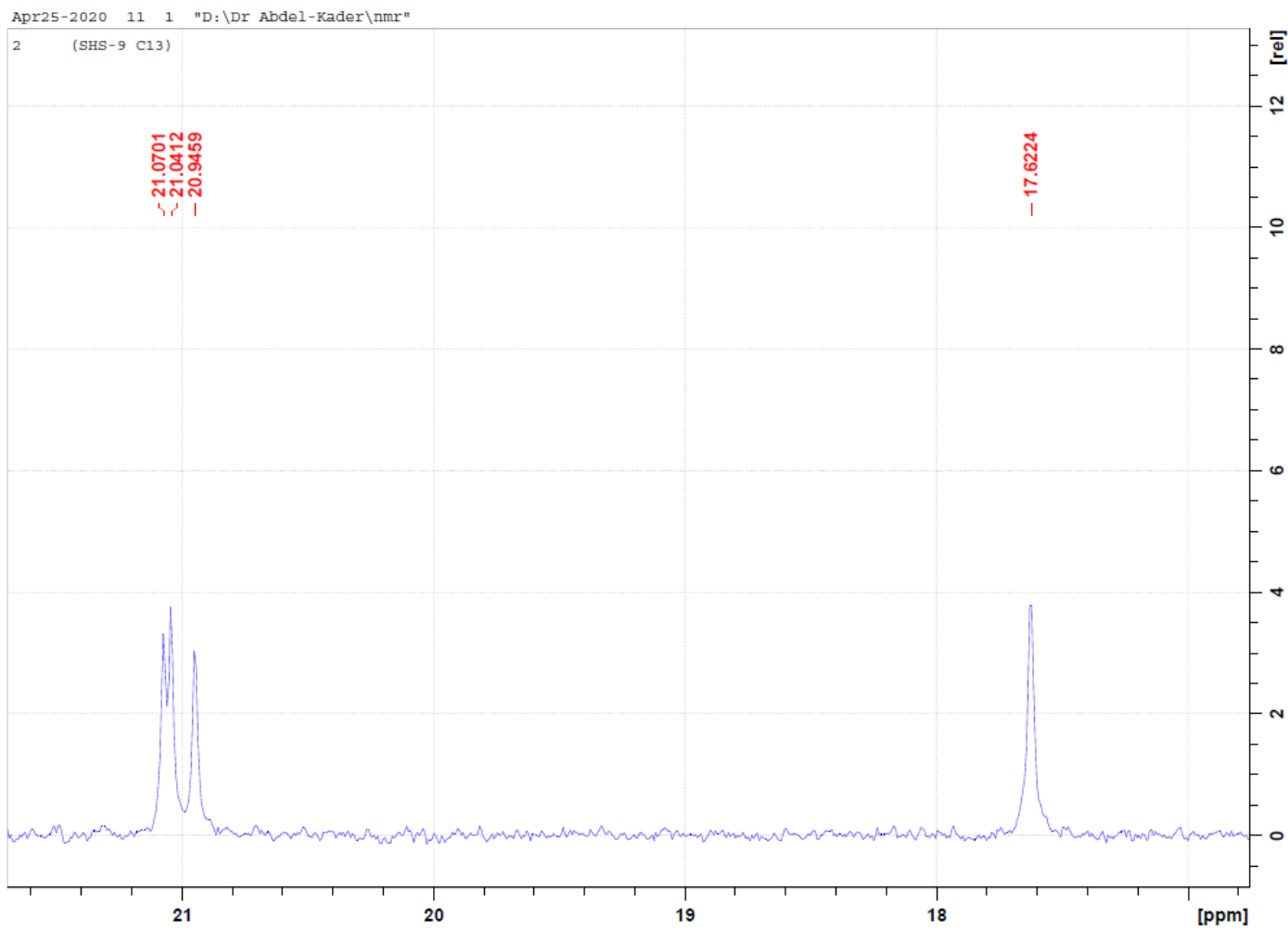


Figure S26. ¹³CNMR spectrum of compound 2 (Expansion).

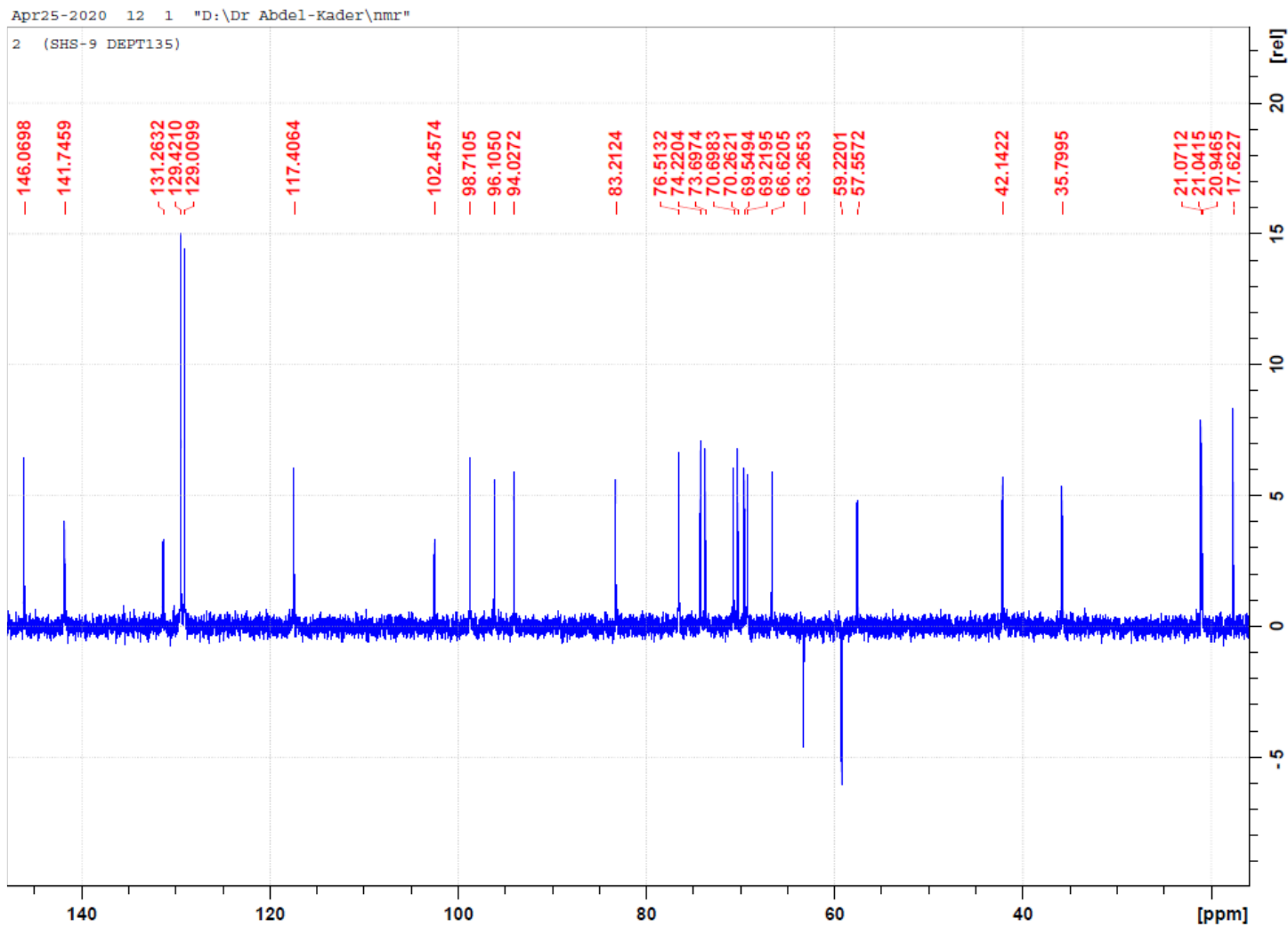


Figure S27. DEPT135 spectrum of compound 2.

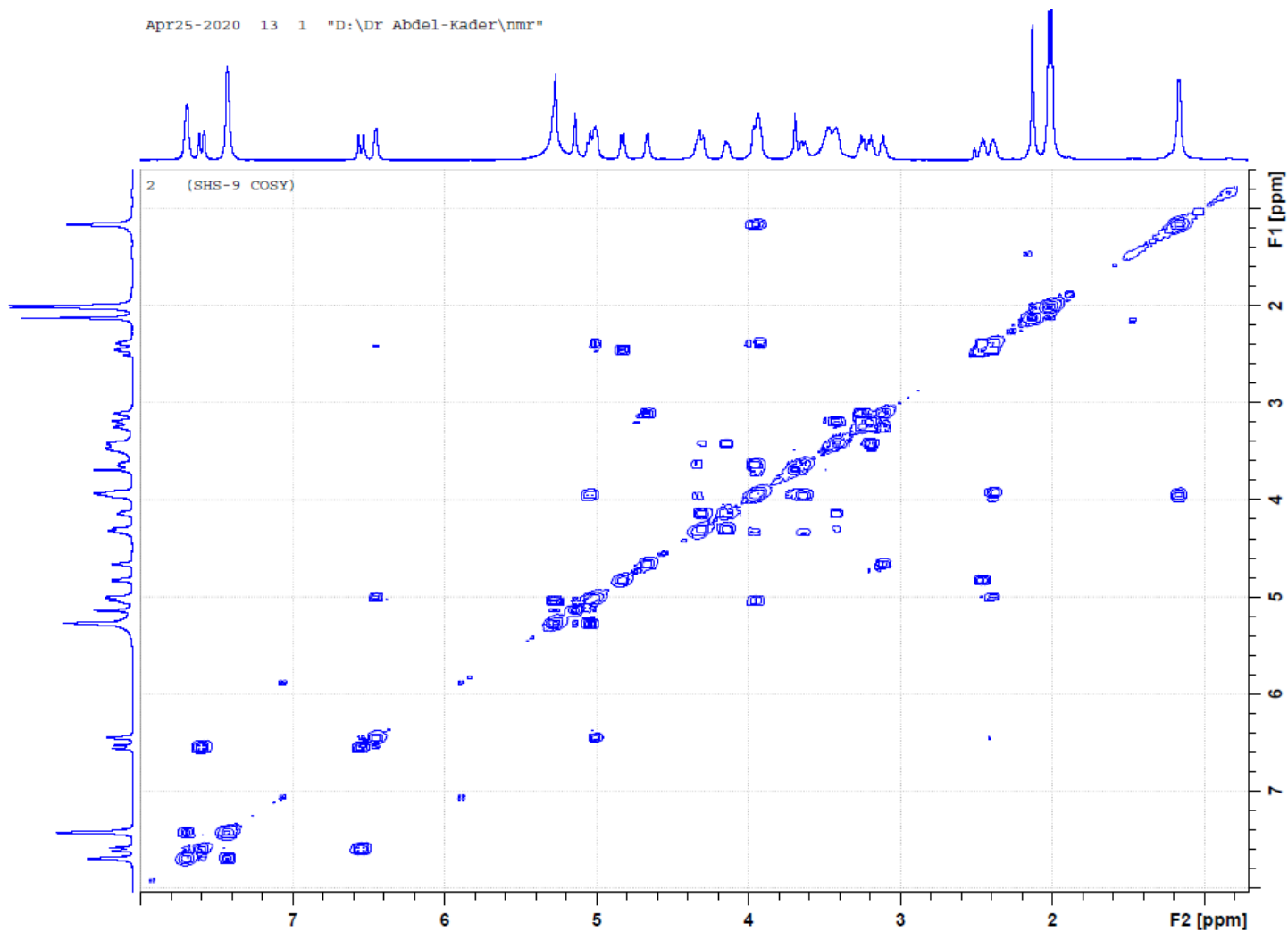


Figure S28. COSY spectrum of compound 2.

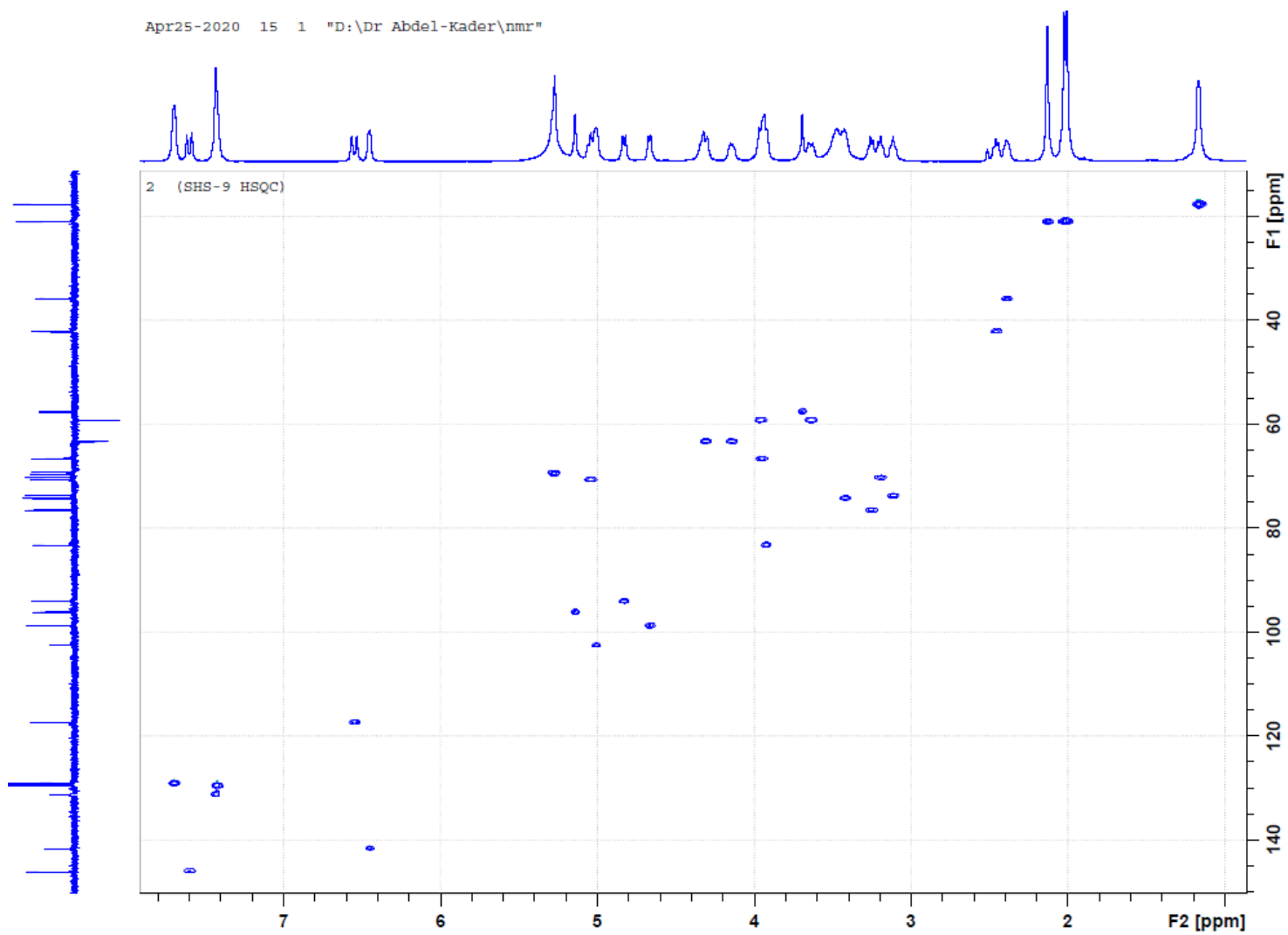


Figure S29. HSQC spectrum of compound 2.

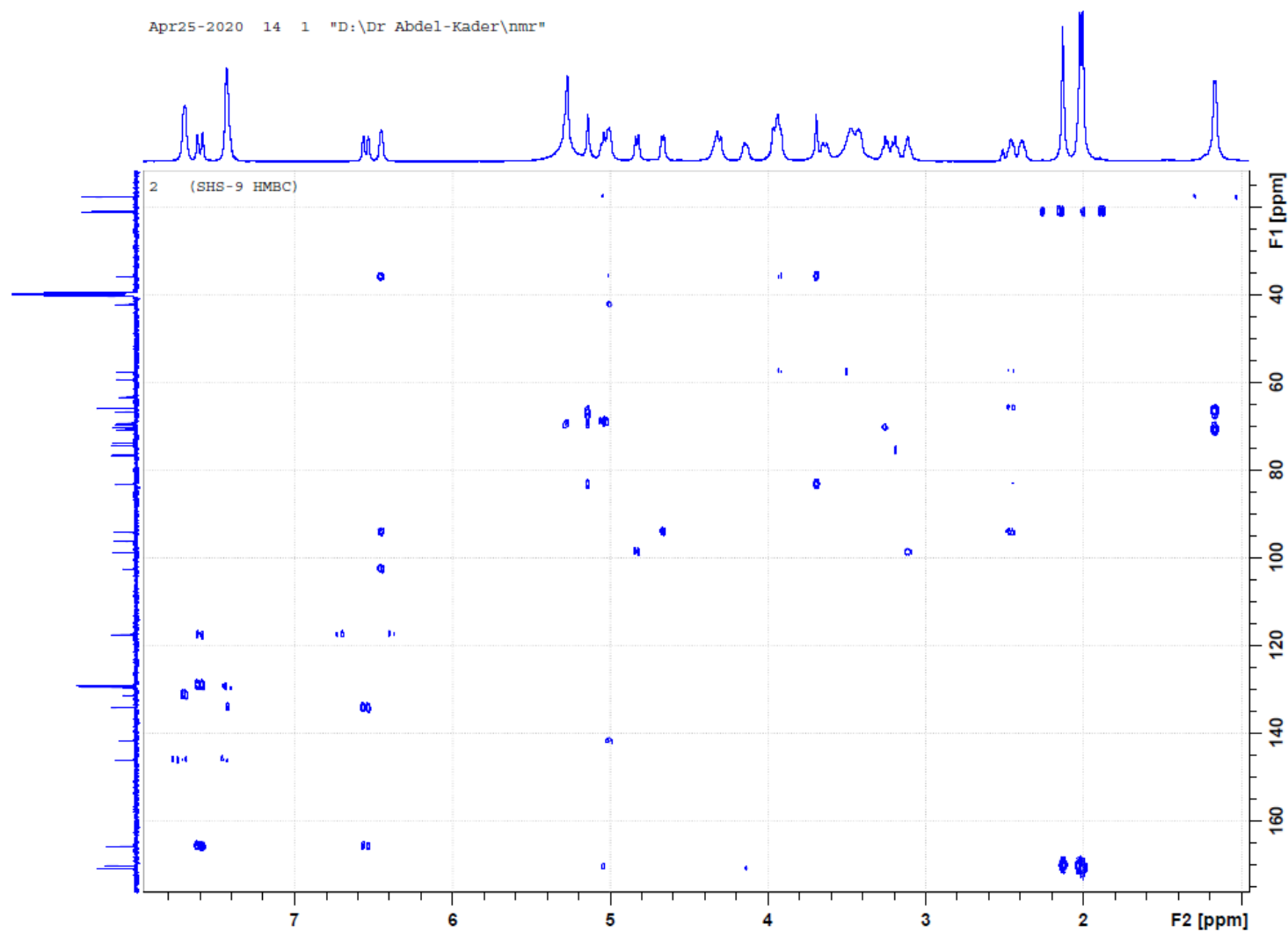


Figure S30. HMBC spectrum of compound 2.

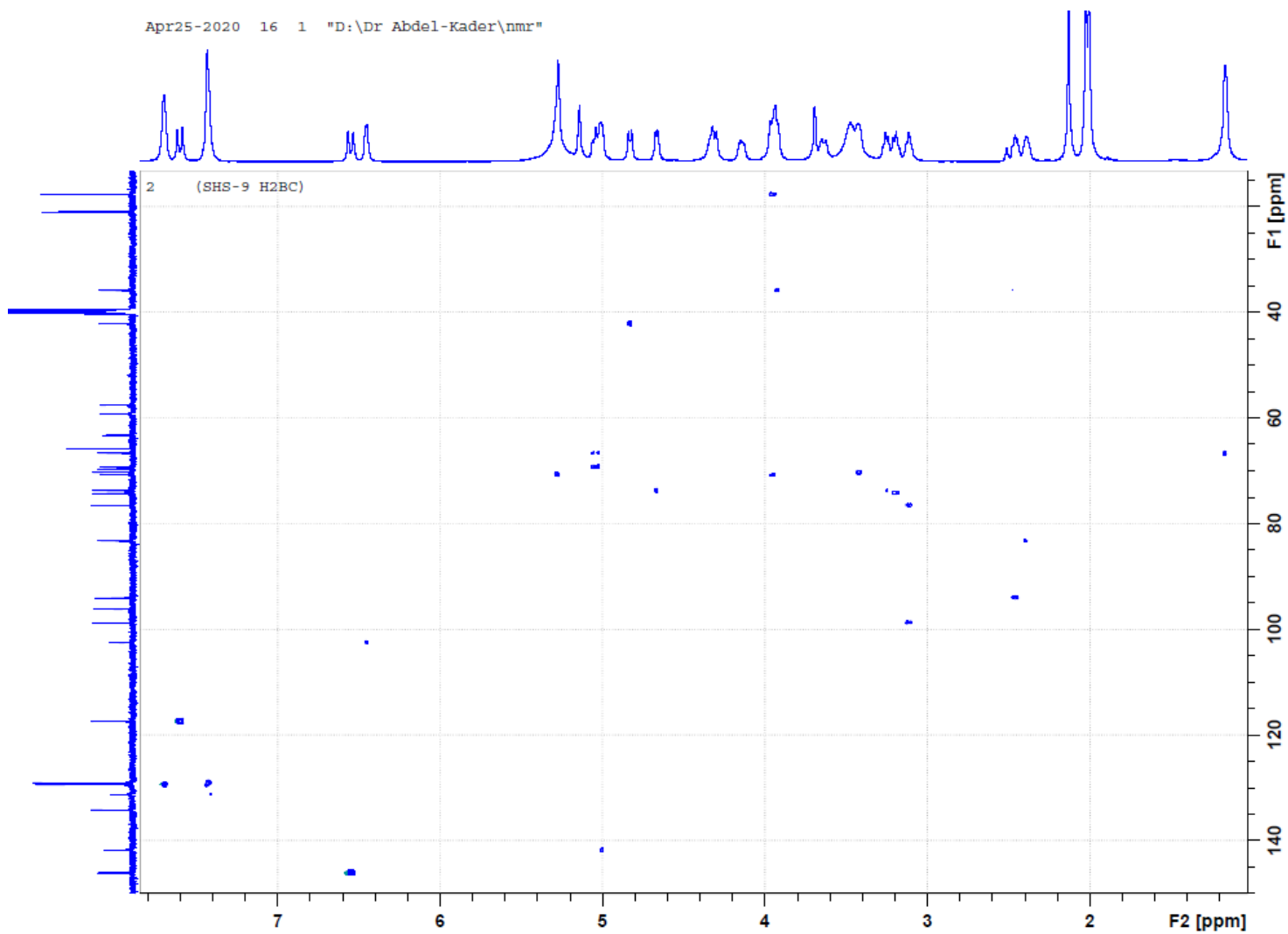


Figure S31. H2BC spectrum of compound 2.

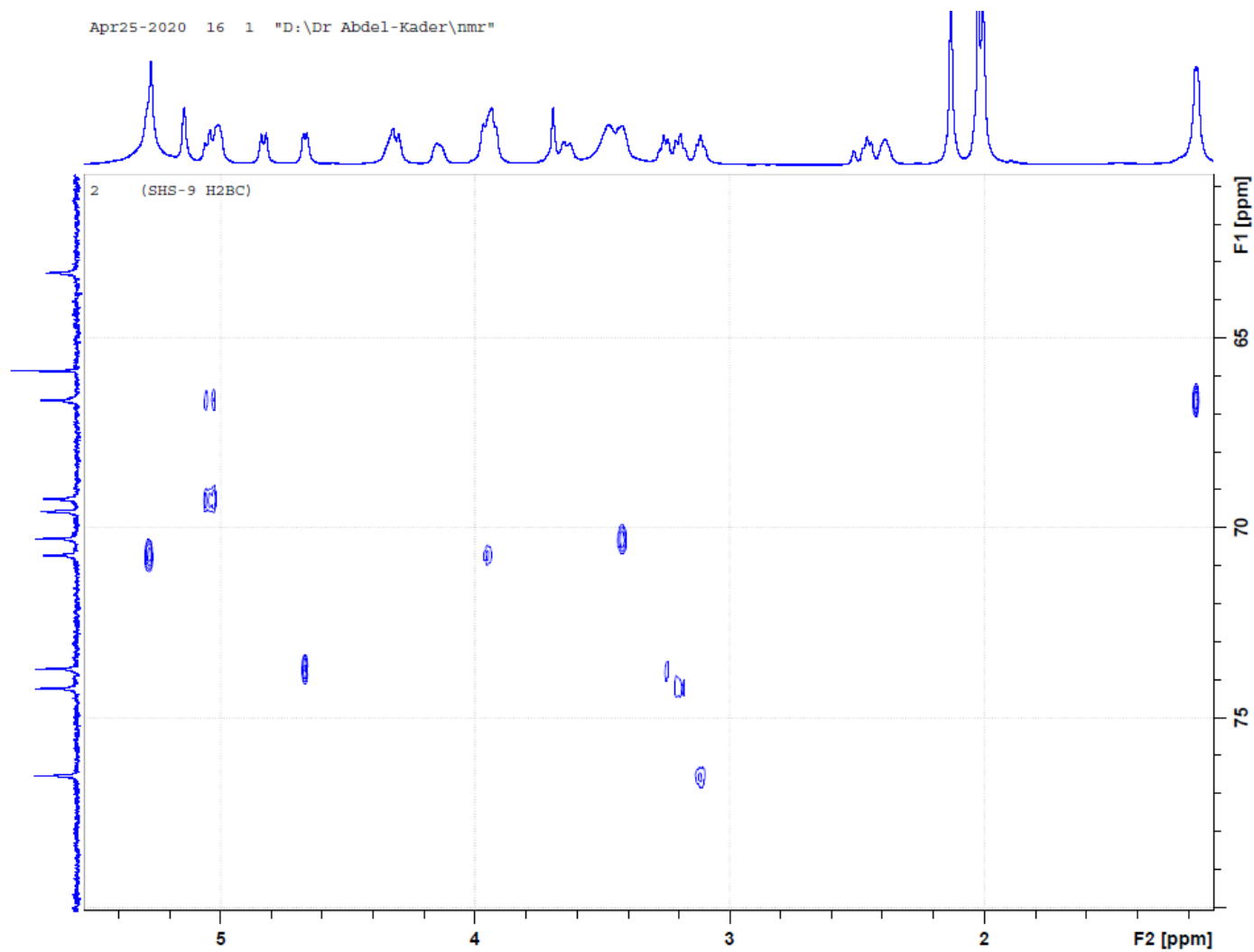


Figure S32. H2BC spectrum of compound 2 (expansion).

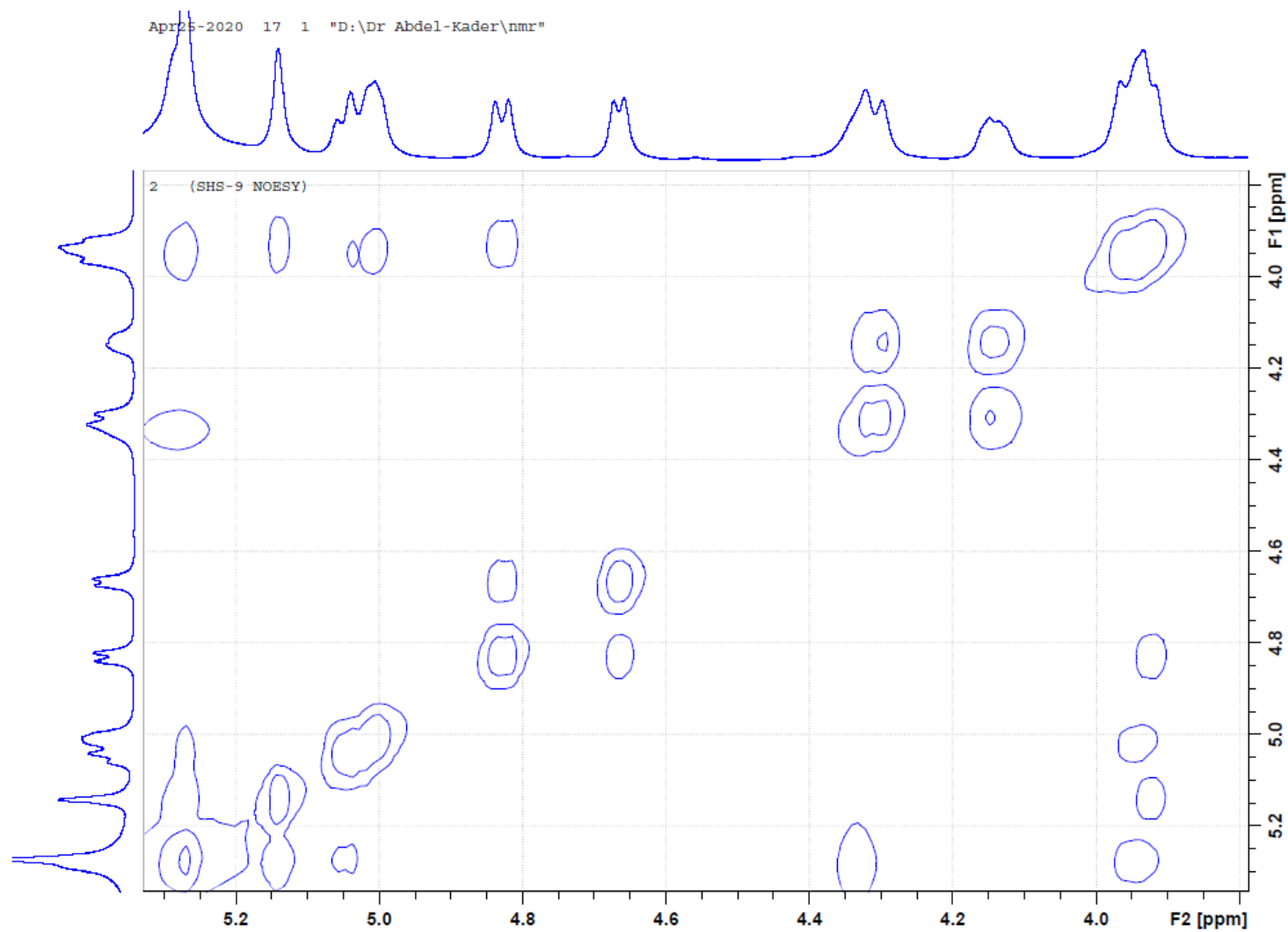


Figure S33. NOESY spectrum of compound 2 (Expansion).

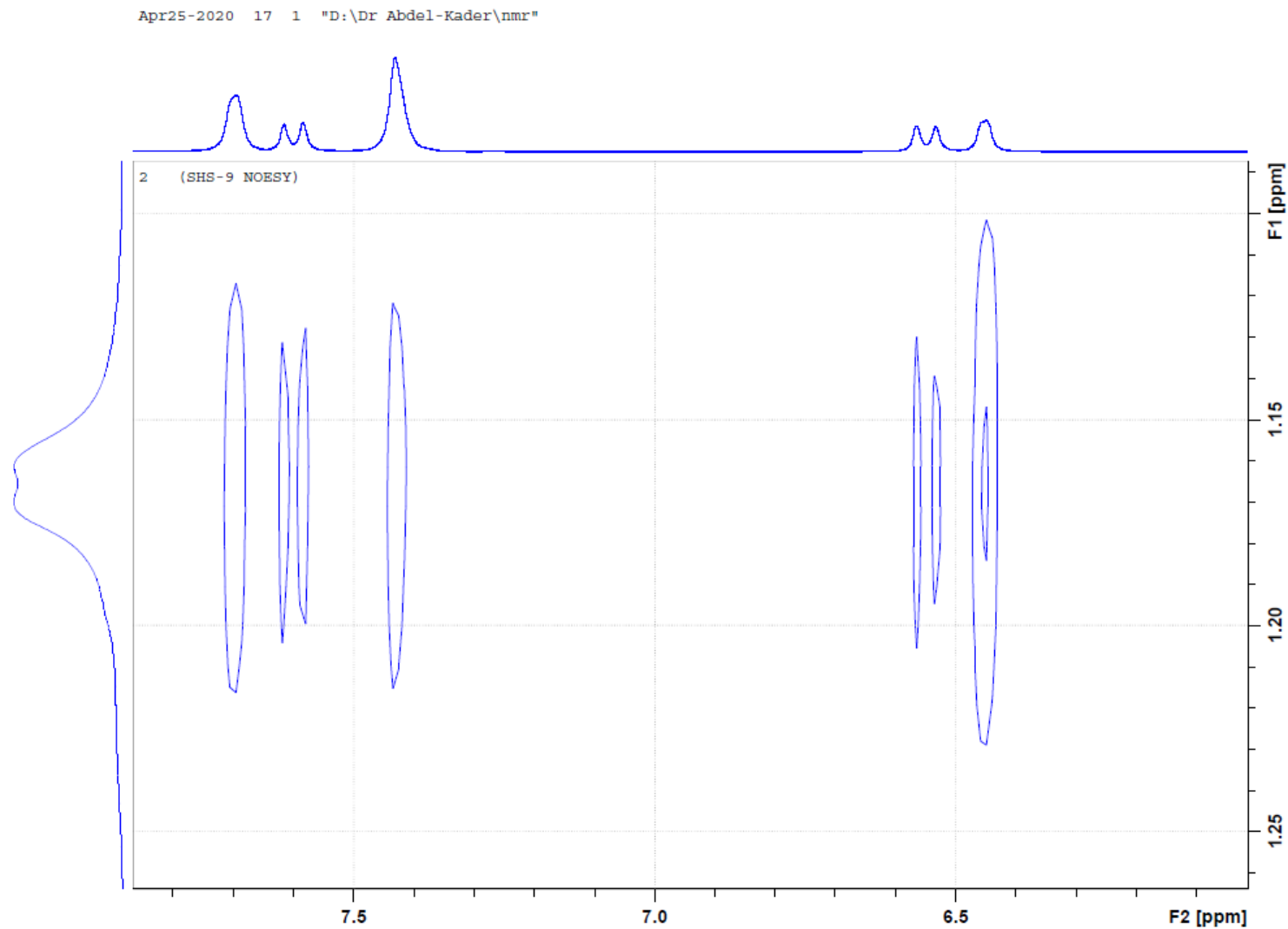


Figure S34. NOESY spectrum of compound 2 (Expansion).

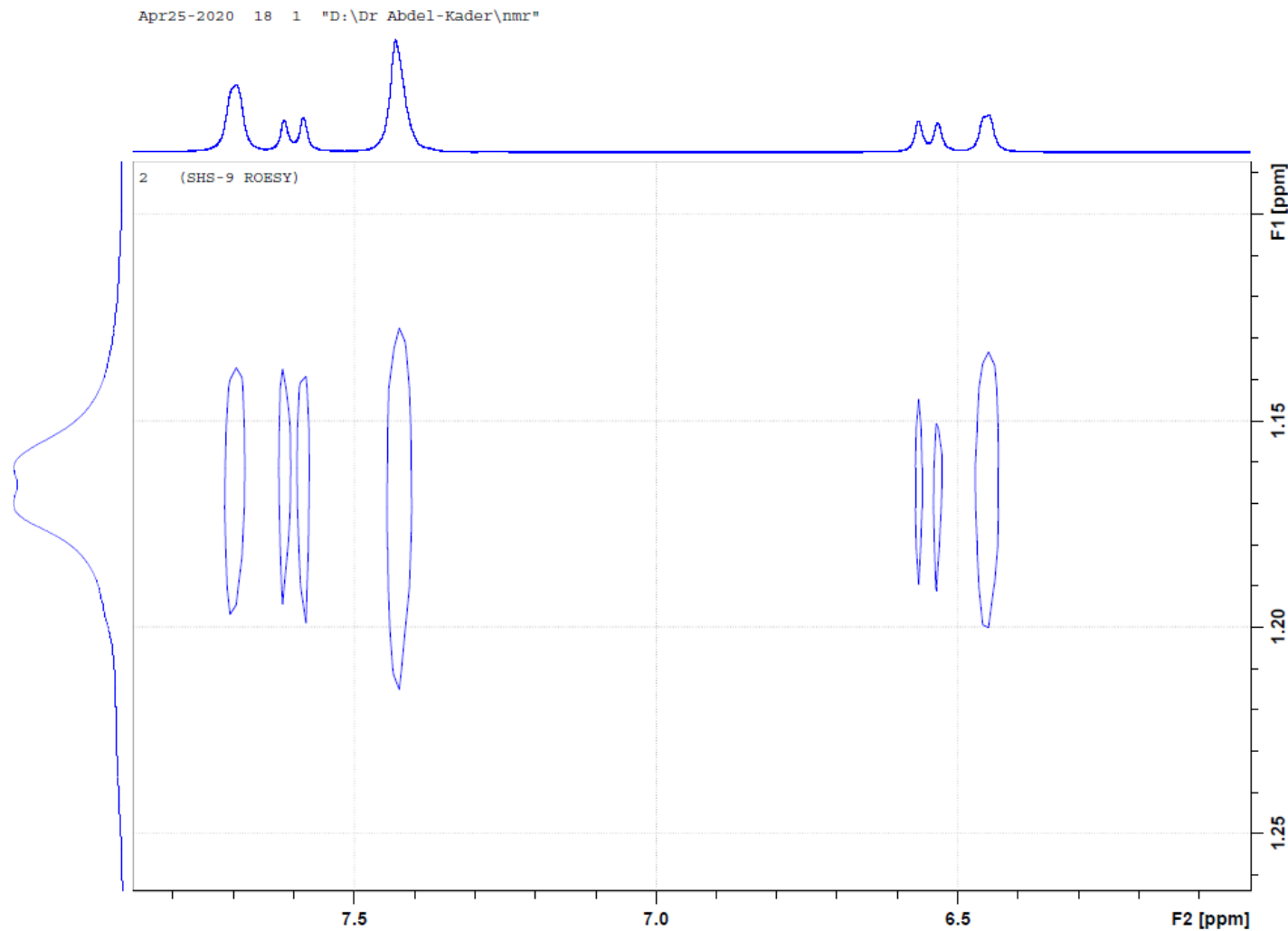


Figure S35. ROESY spectrum of compound 2 (Expansion).

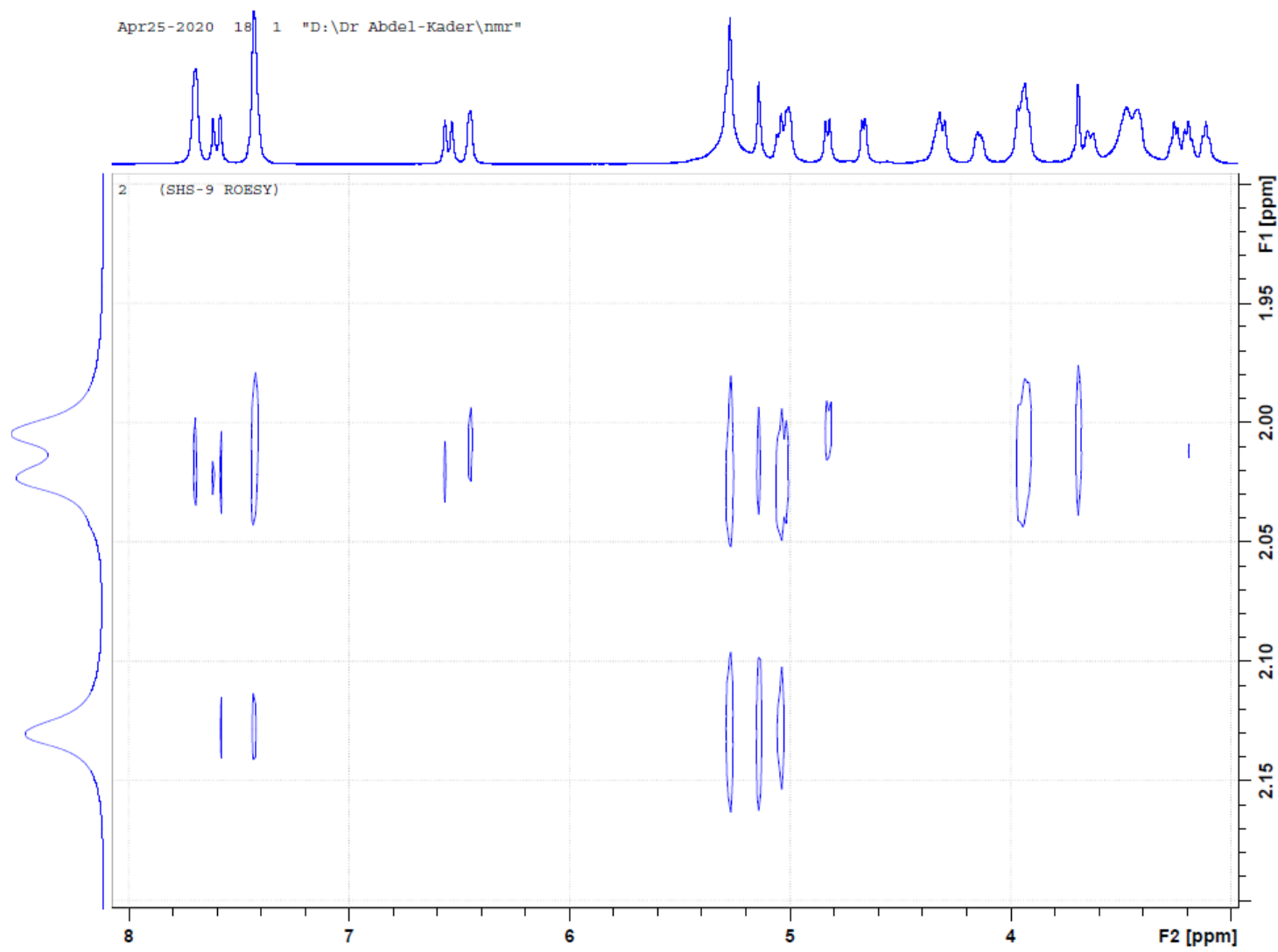


Figure S36. ROESY spectrum of compound 2 (Expansion).

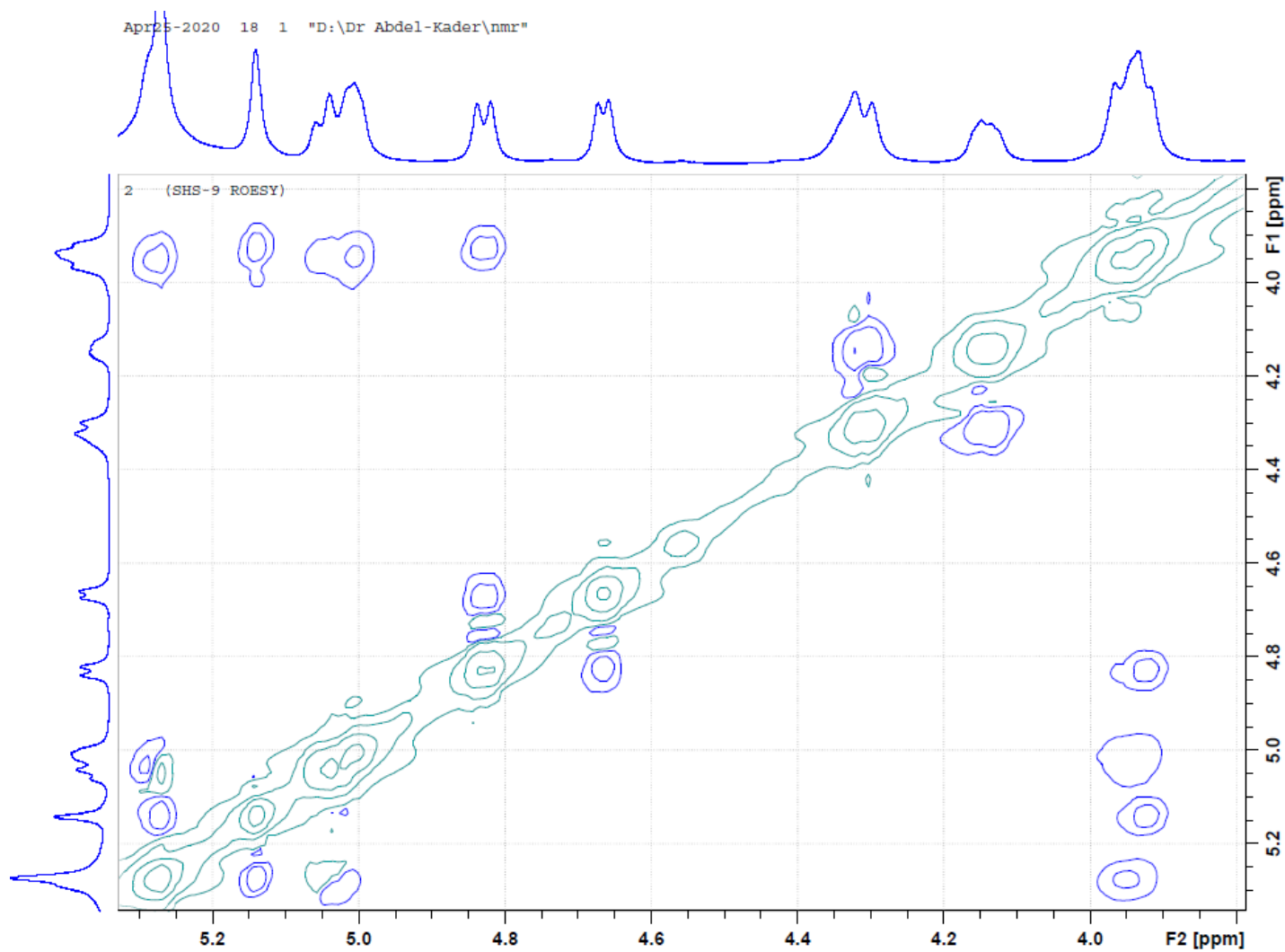


Figure S37. ROESY spectrum of compound 2 (Expansion).

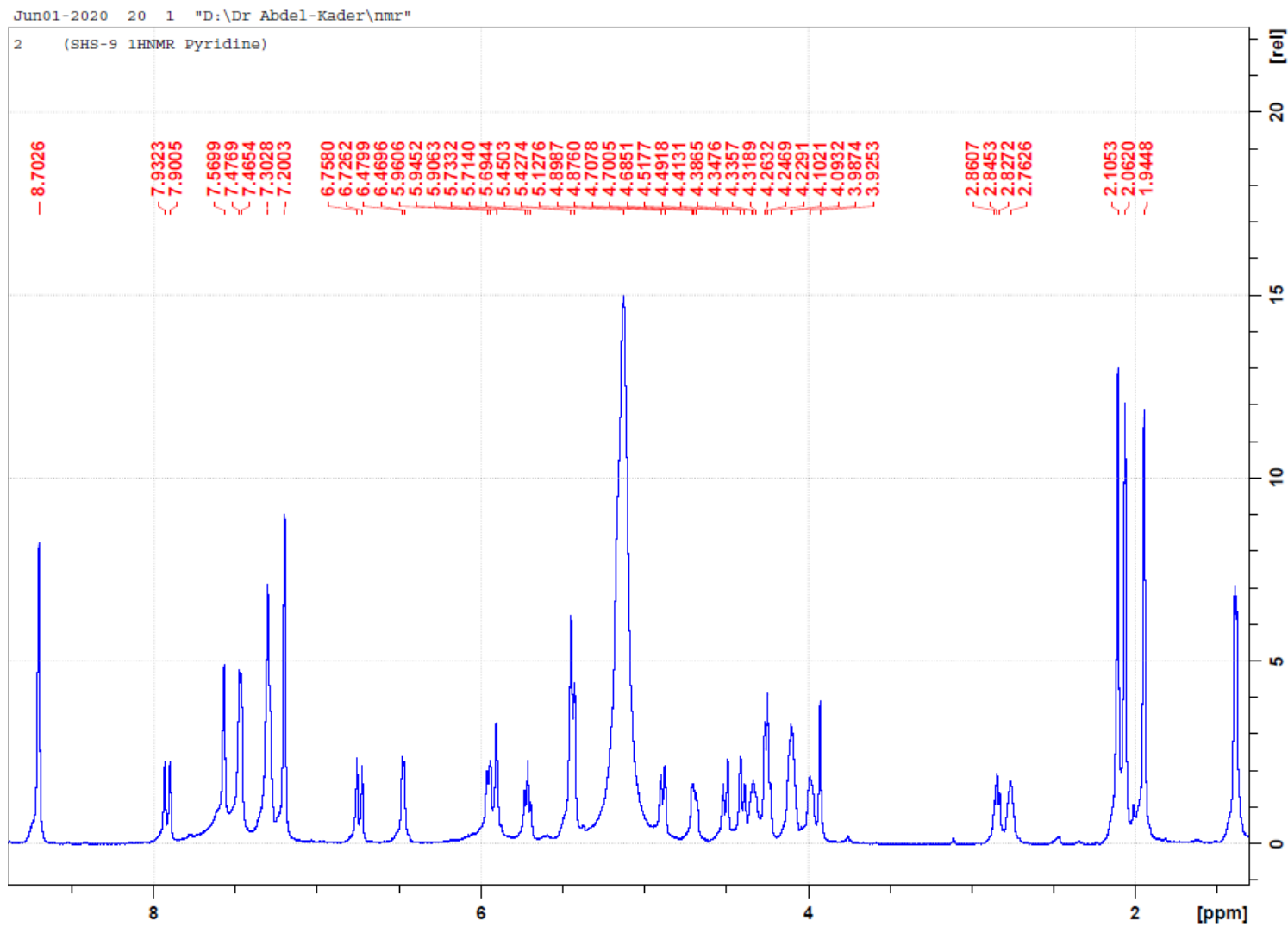


Figure S38. ¹H NMR spectrum of compound 2 in Pyridine.

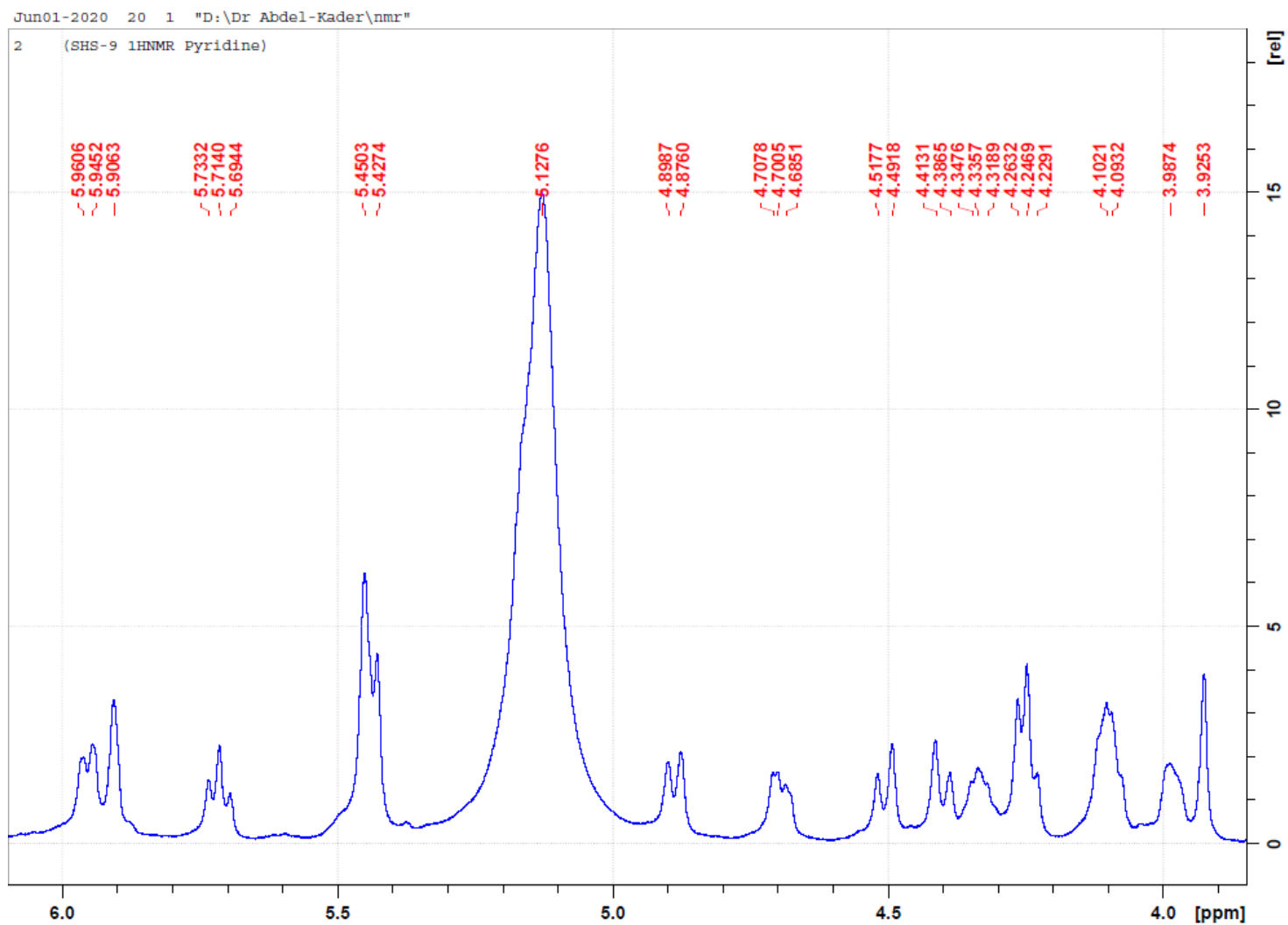


Figure S39. ¹H NMR spectrum of compound 2 in Pyridine (expansion).

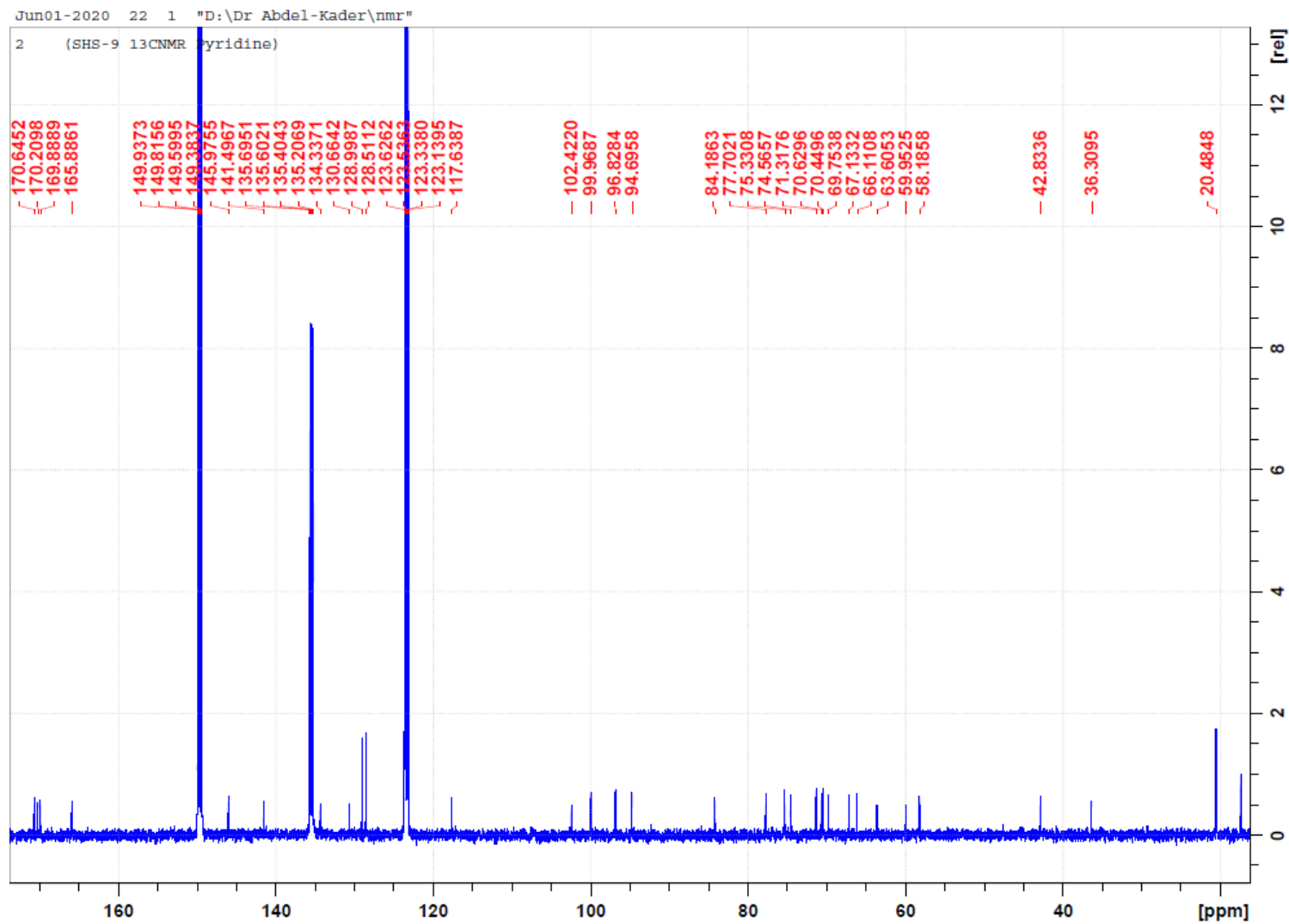


Figure S40. ¹³CNMR spectrum of compound 2 in Pyridine.

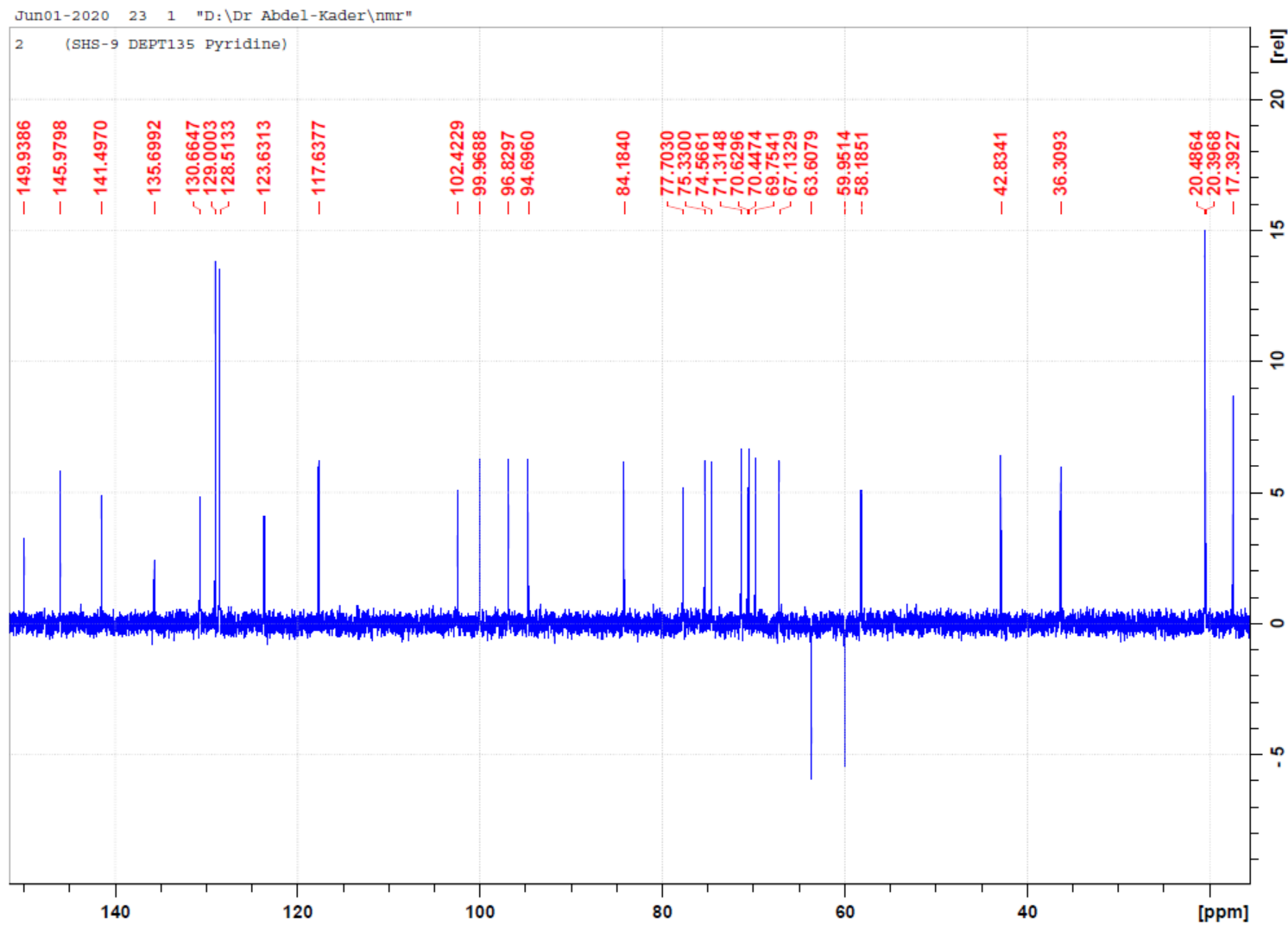


Figure S41. DEPT135 spectrum of compound 2 in Pyridine.

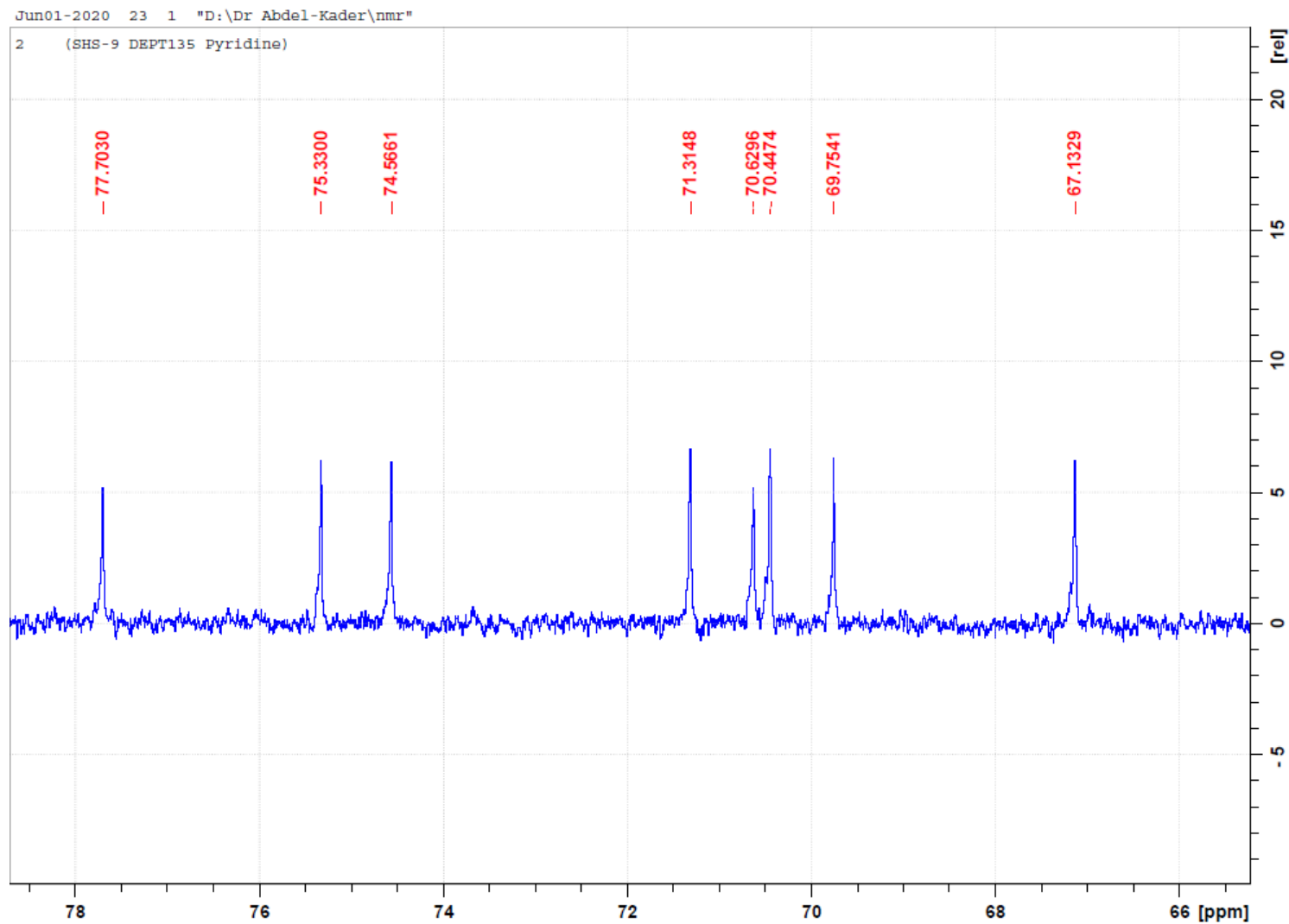


Figure S42. DEPT135 spectrum of compound 2 in Pyridine (expansion).

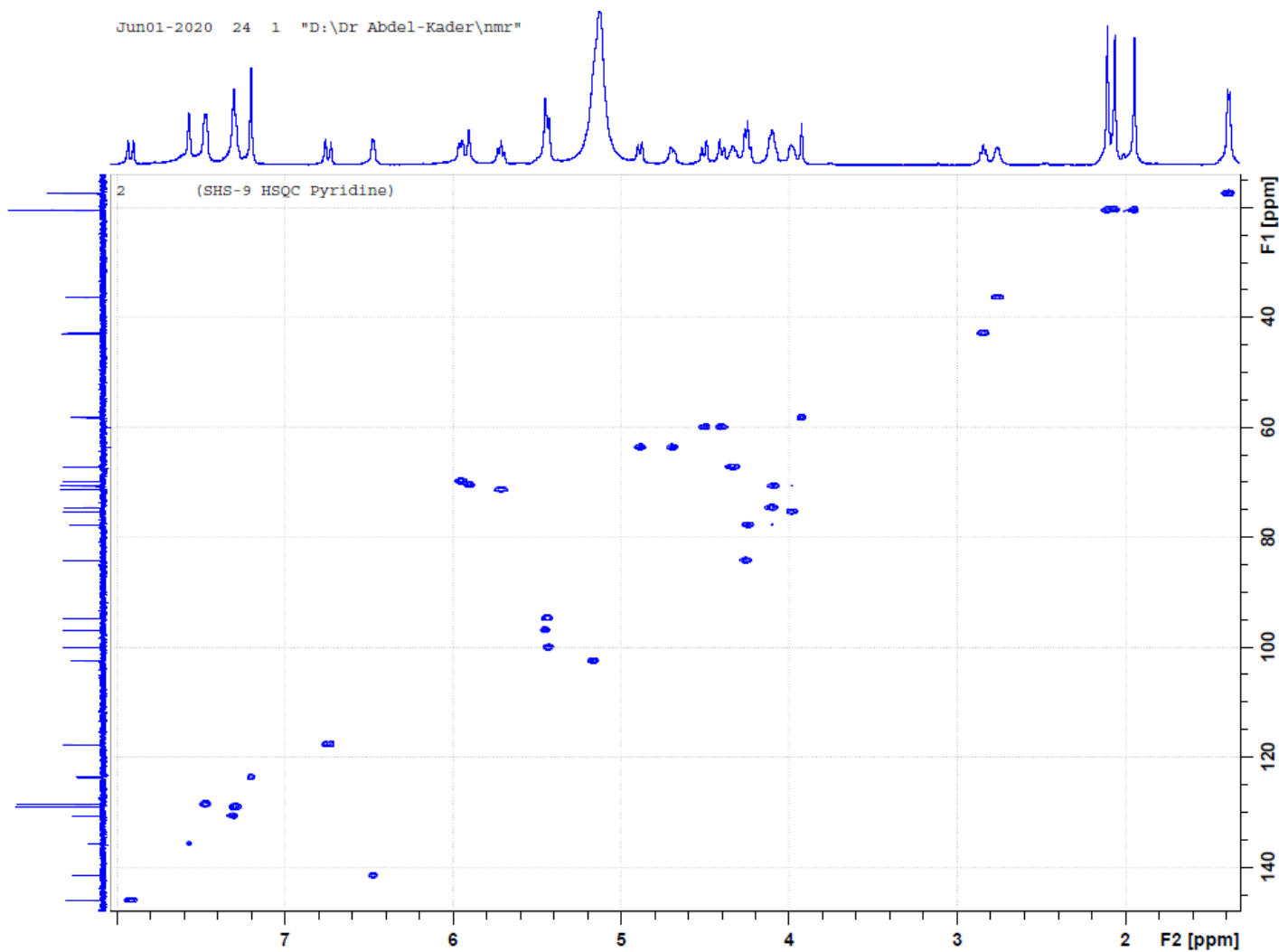


Figure S43. HSQC spectrum of compound 2 in Pyridine.

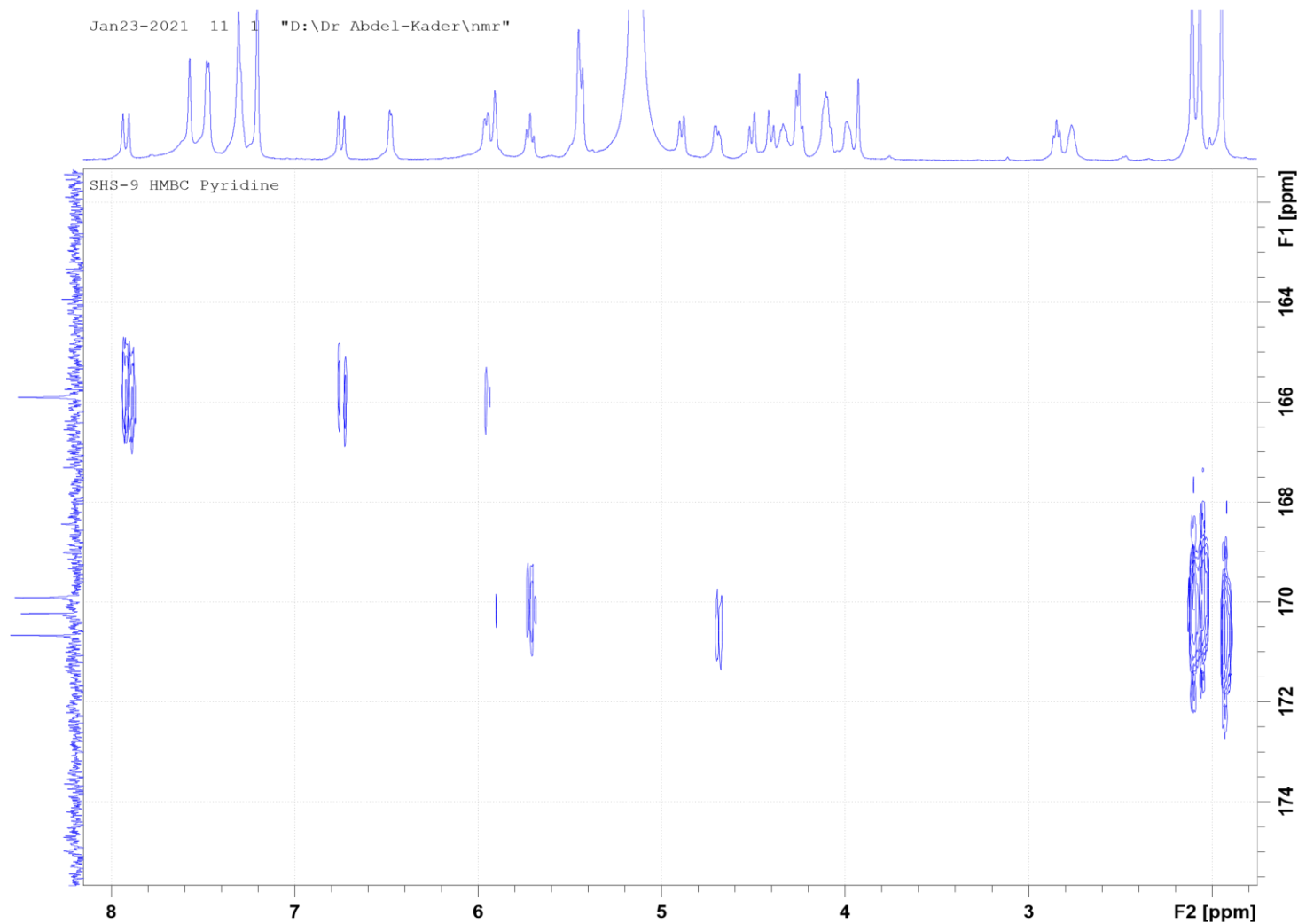


Figure S44. HMBC spectrum of compound 2 in Pyridine (expansion).

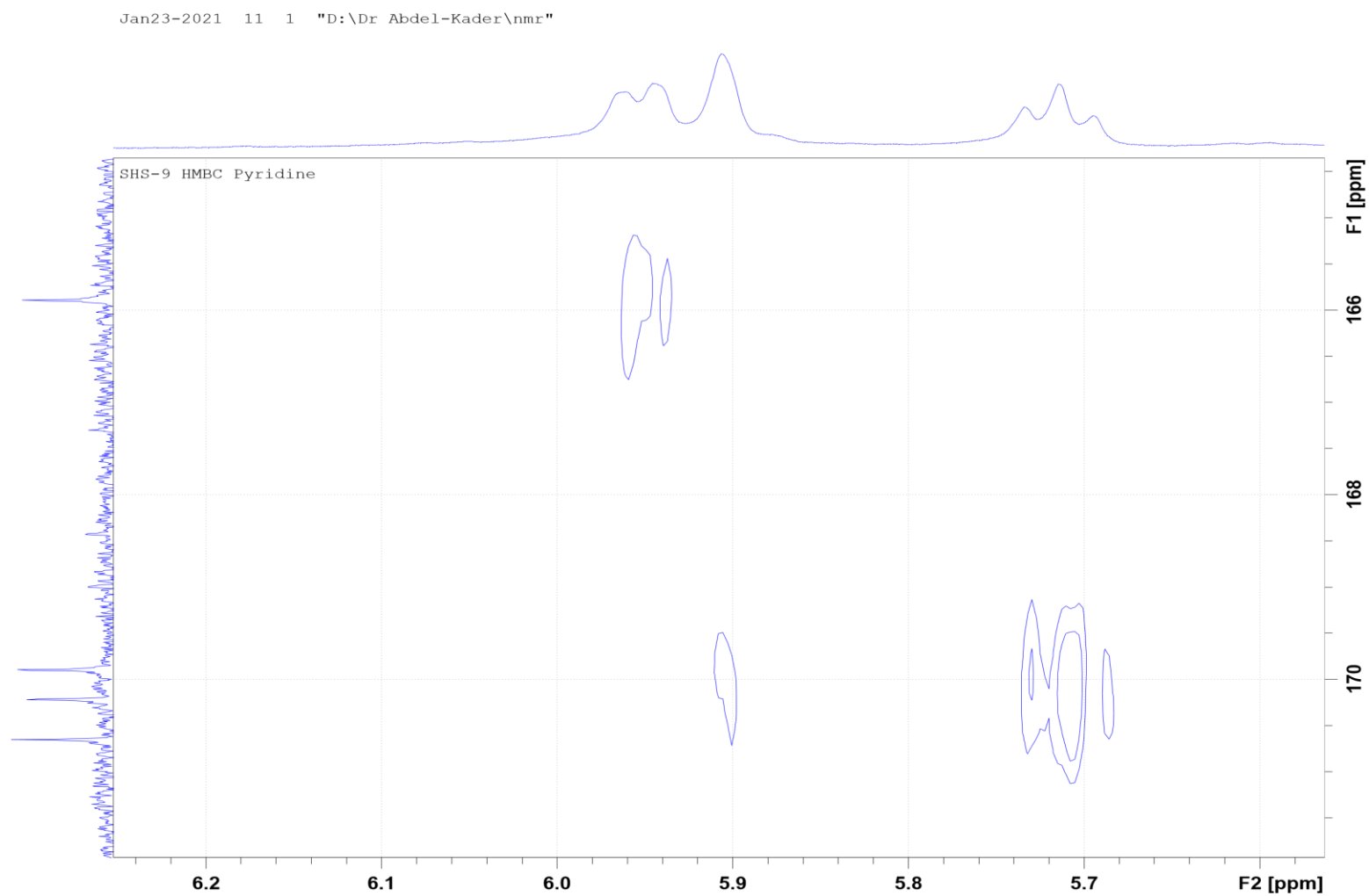


Figure S45. HMBC spectrum of compound 2 in Pyridine (expansion).

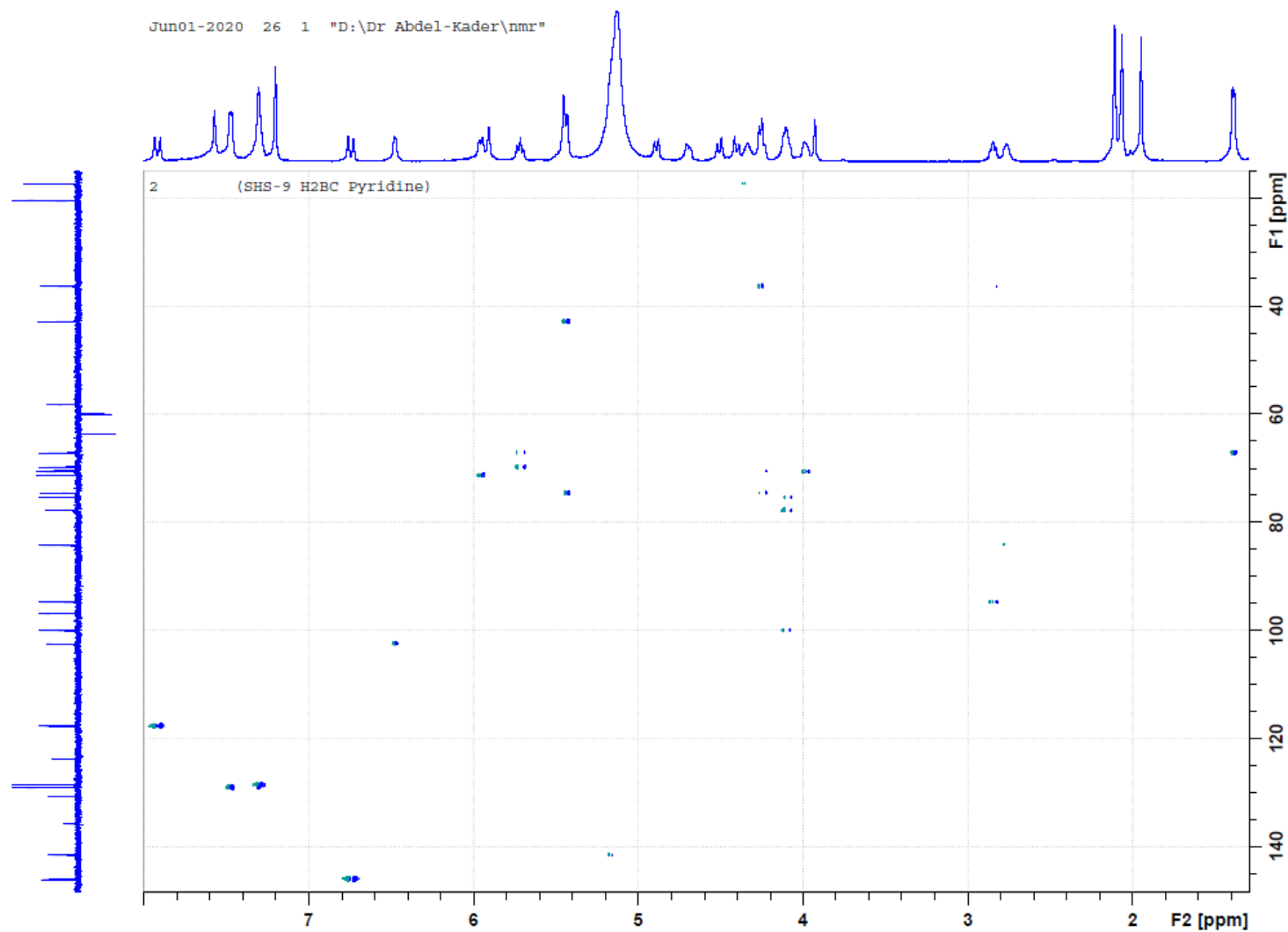


Figure S46. H2BC spectrum of compound 2 in Pyridine.

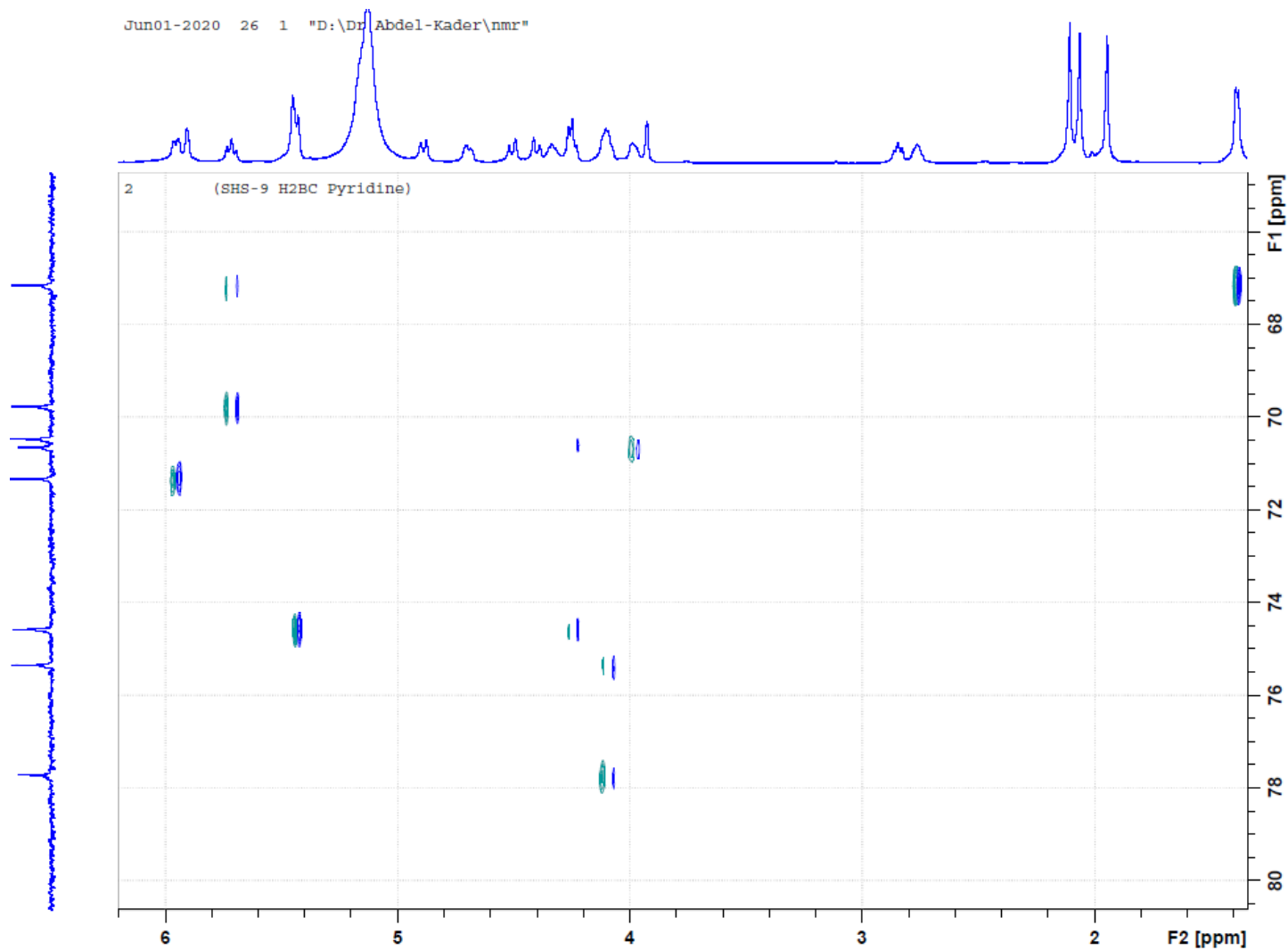


Figure S47. H2BC spectrum of compound 2 in Pyridine (expansion).

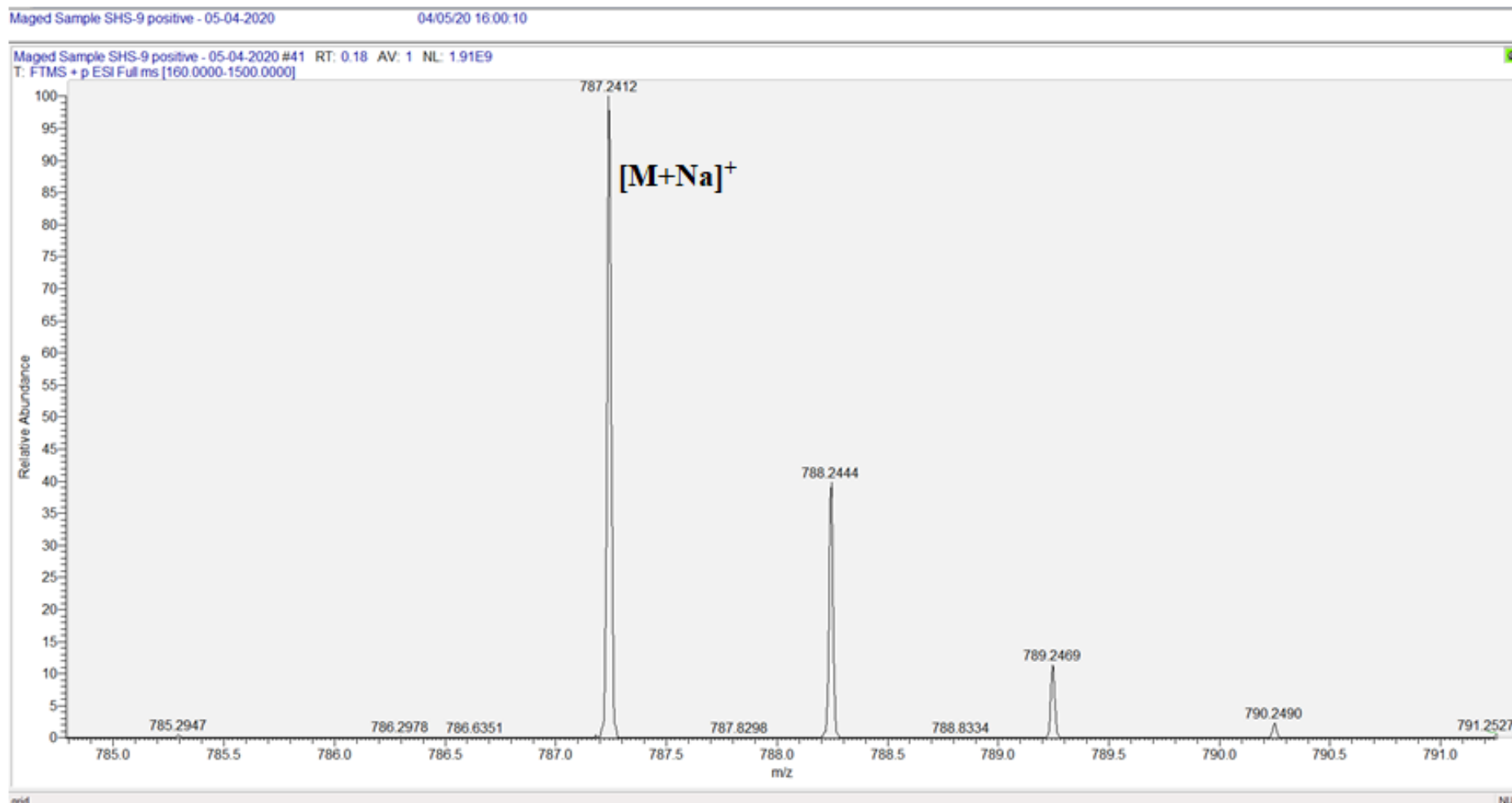


Figure S48. HRESIMS of compound 2 (positive mode).

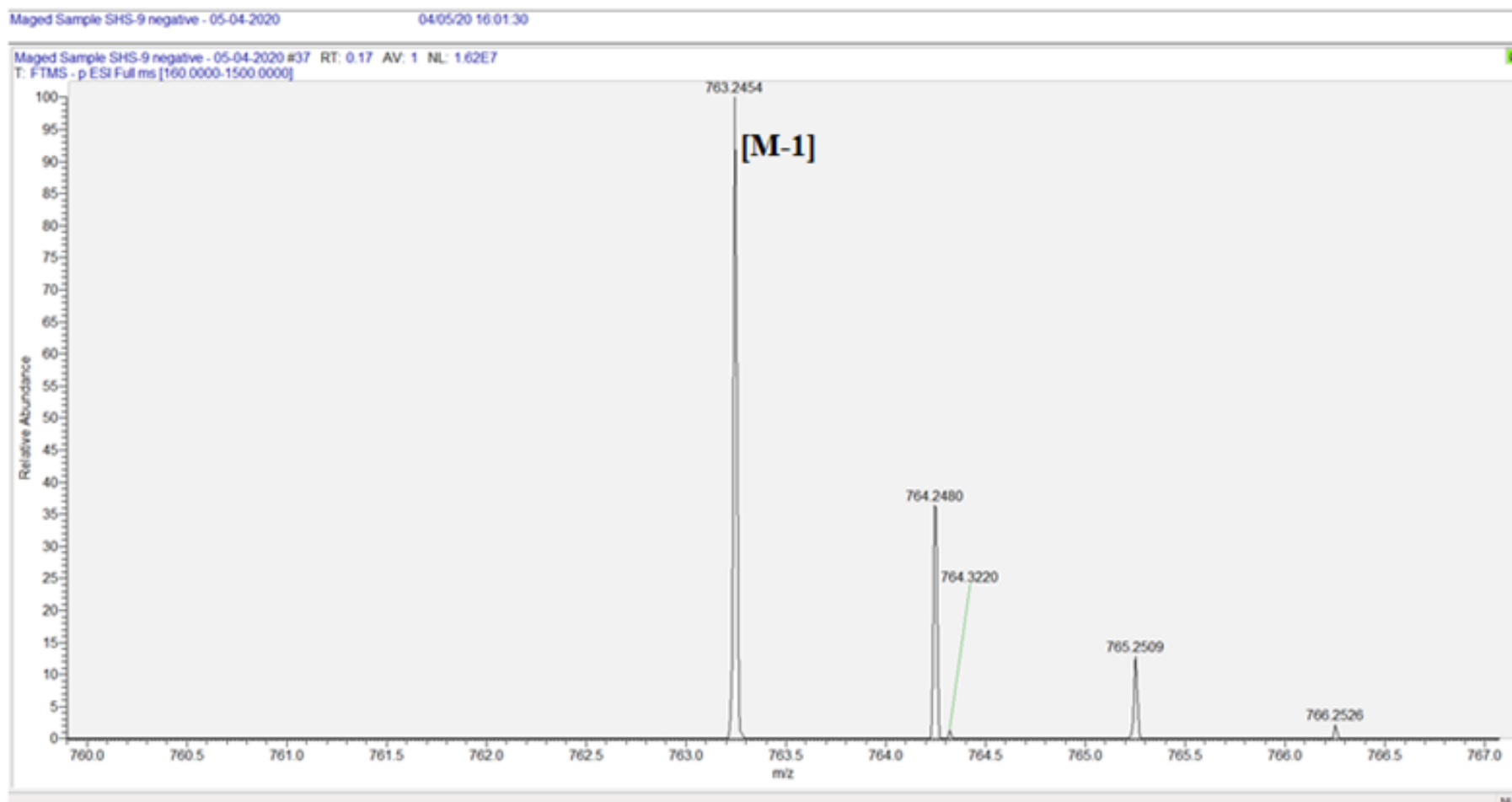


Figure S49. HRESIMS of compound 2 (negative mode).

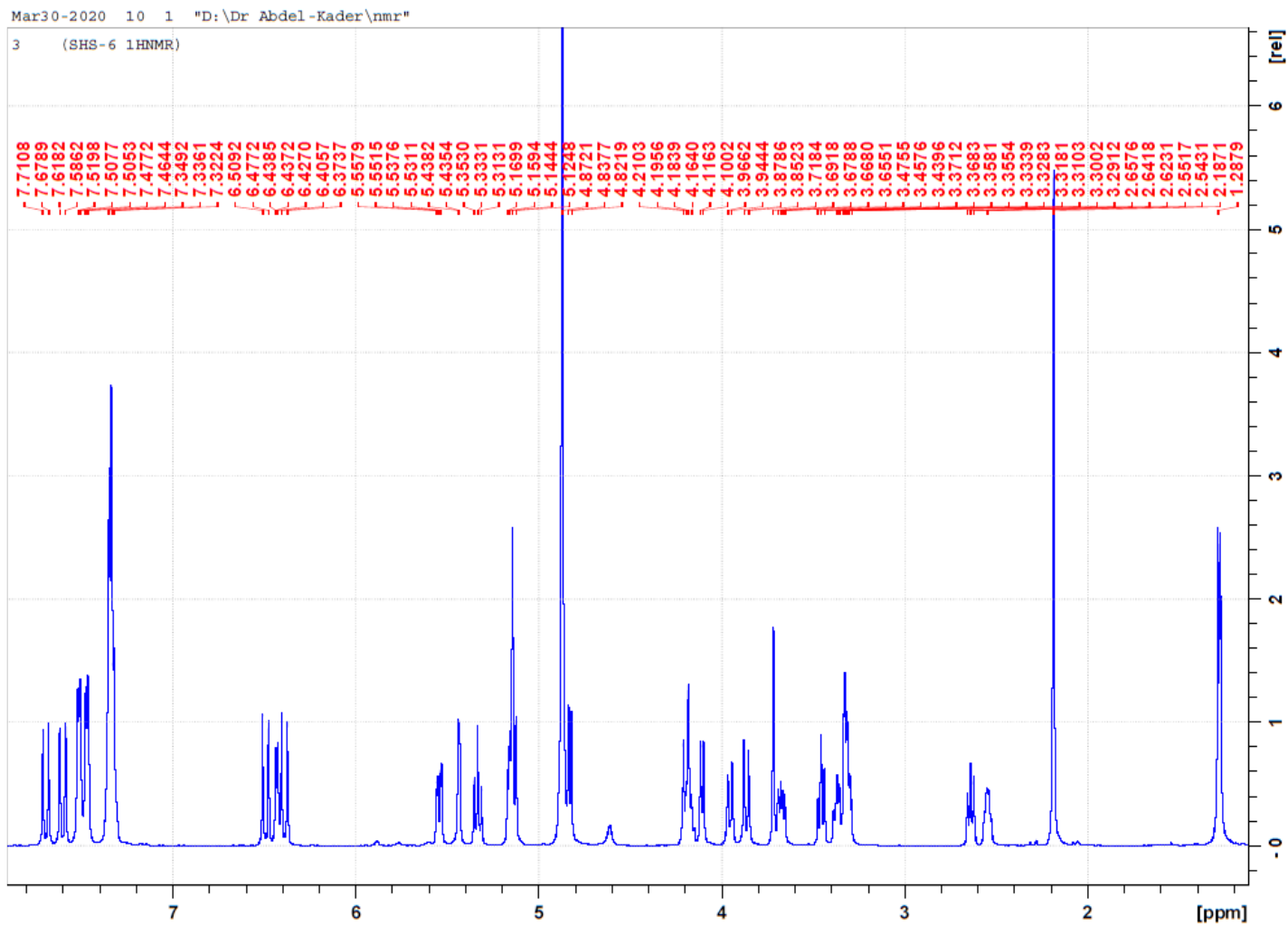


Figure S50. ¹H NMR spectrum of compound 3.

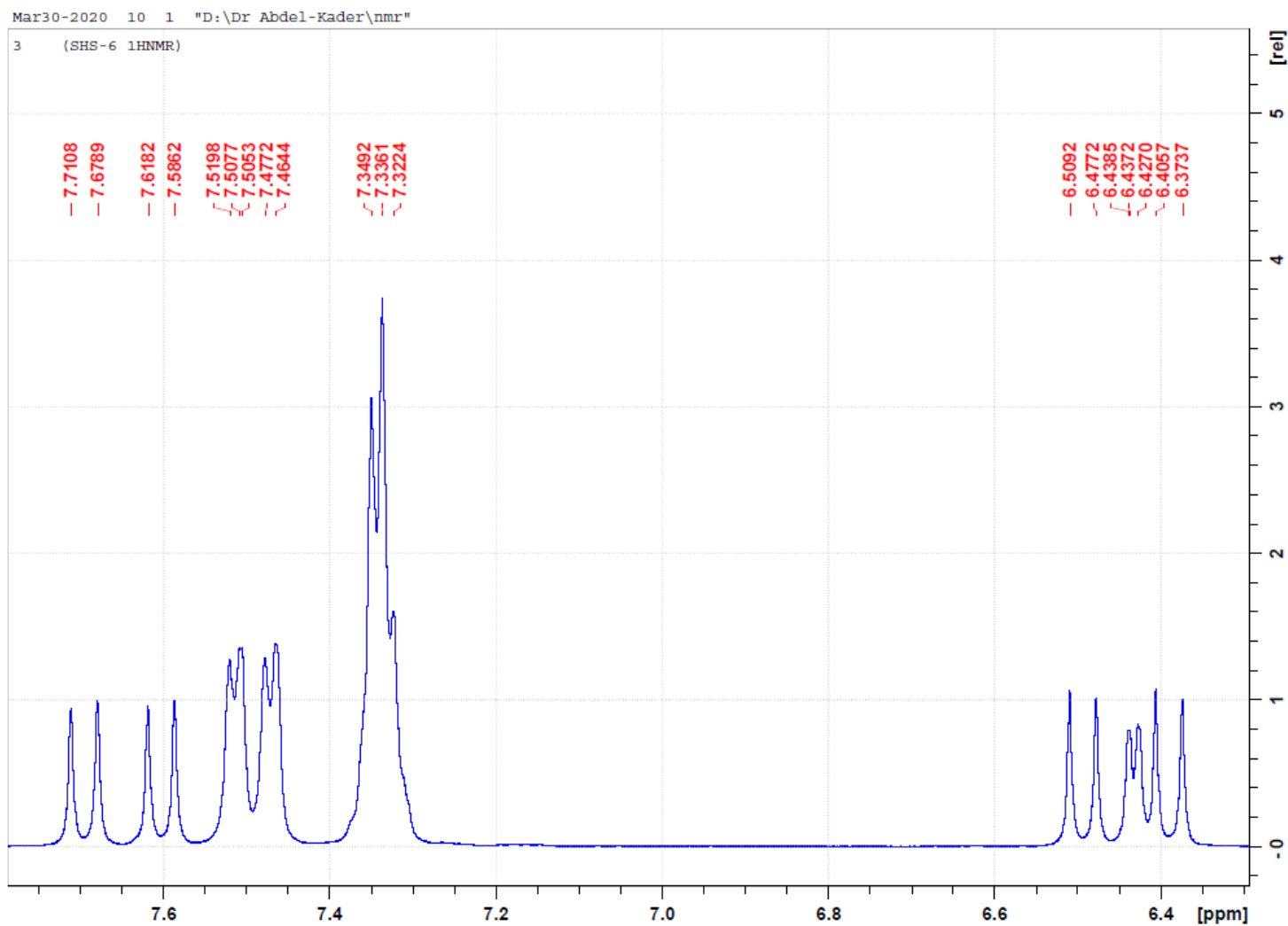


Figure S51. ¹HNMR spectrum of compound 3 (expansion).

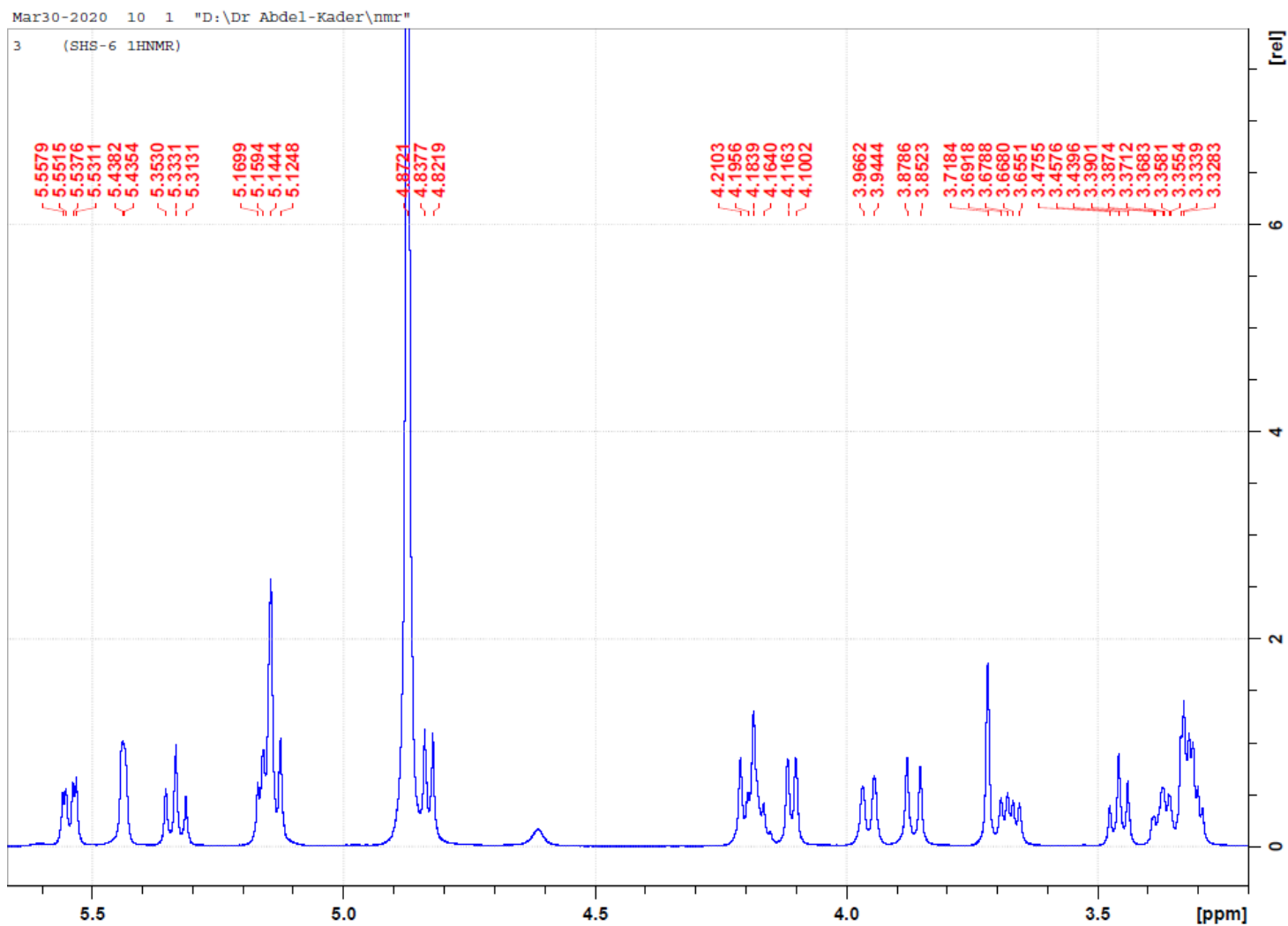


Figure S52. ¹HNMR spectrum of compound 3 (expansion).

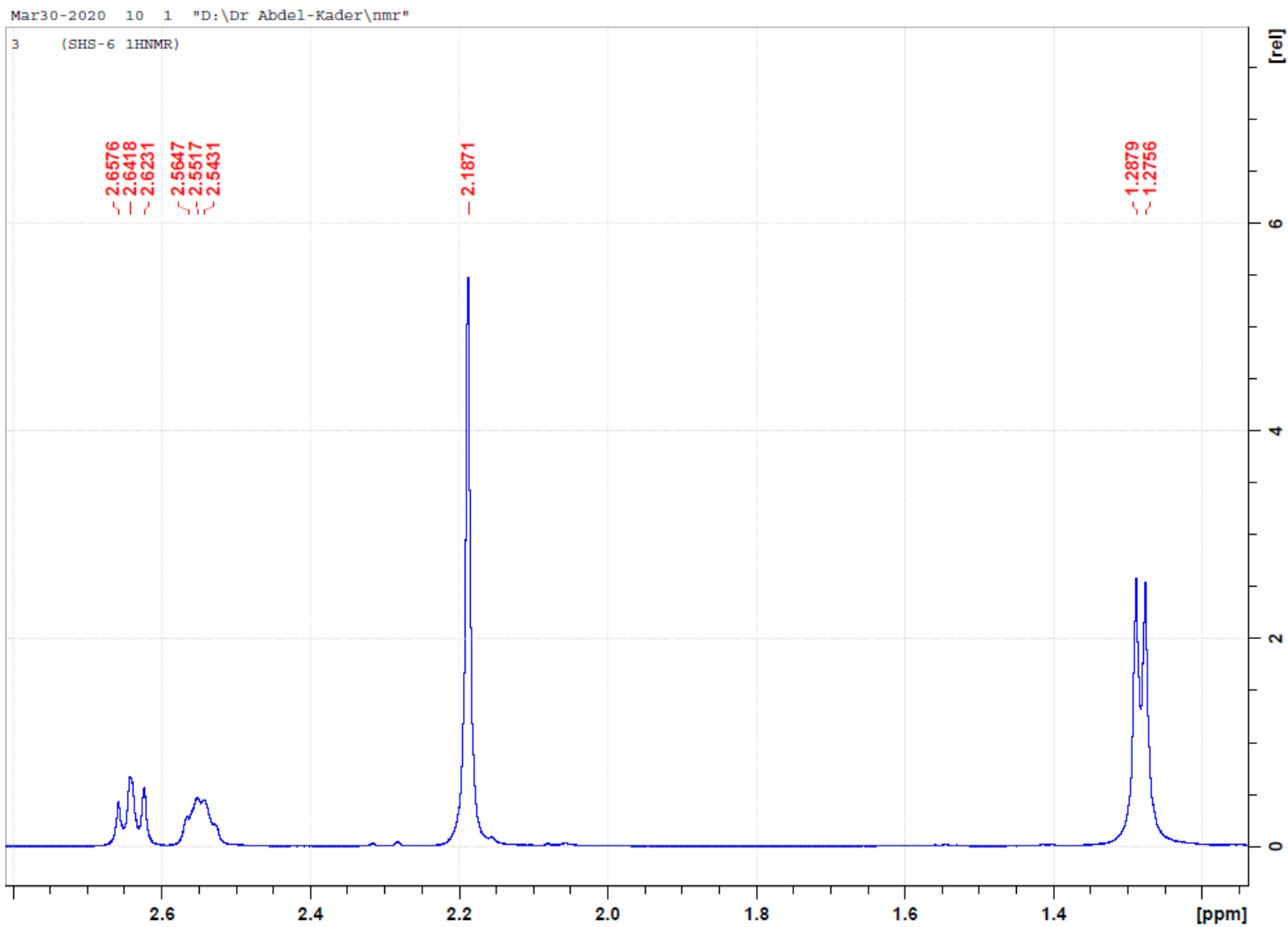


Figure S53. ¹H NMR spectrum of compound 3 (expansion).

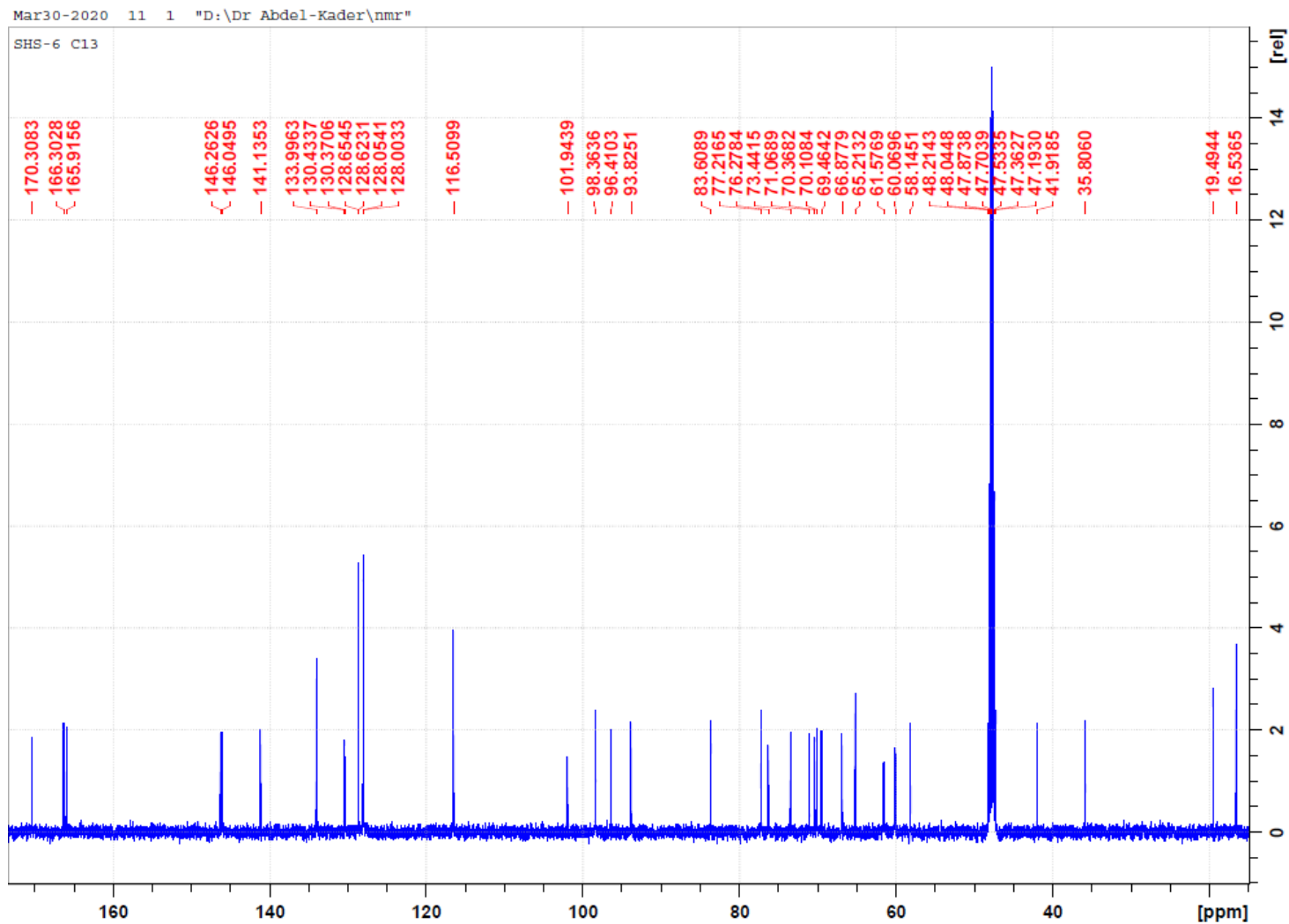


Figure S54. ¹³CNMR spectrum of compound 3.

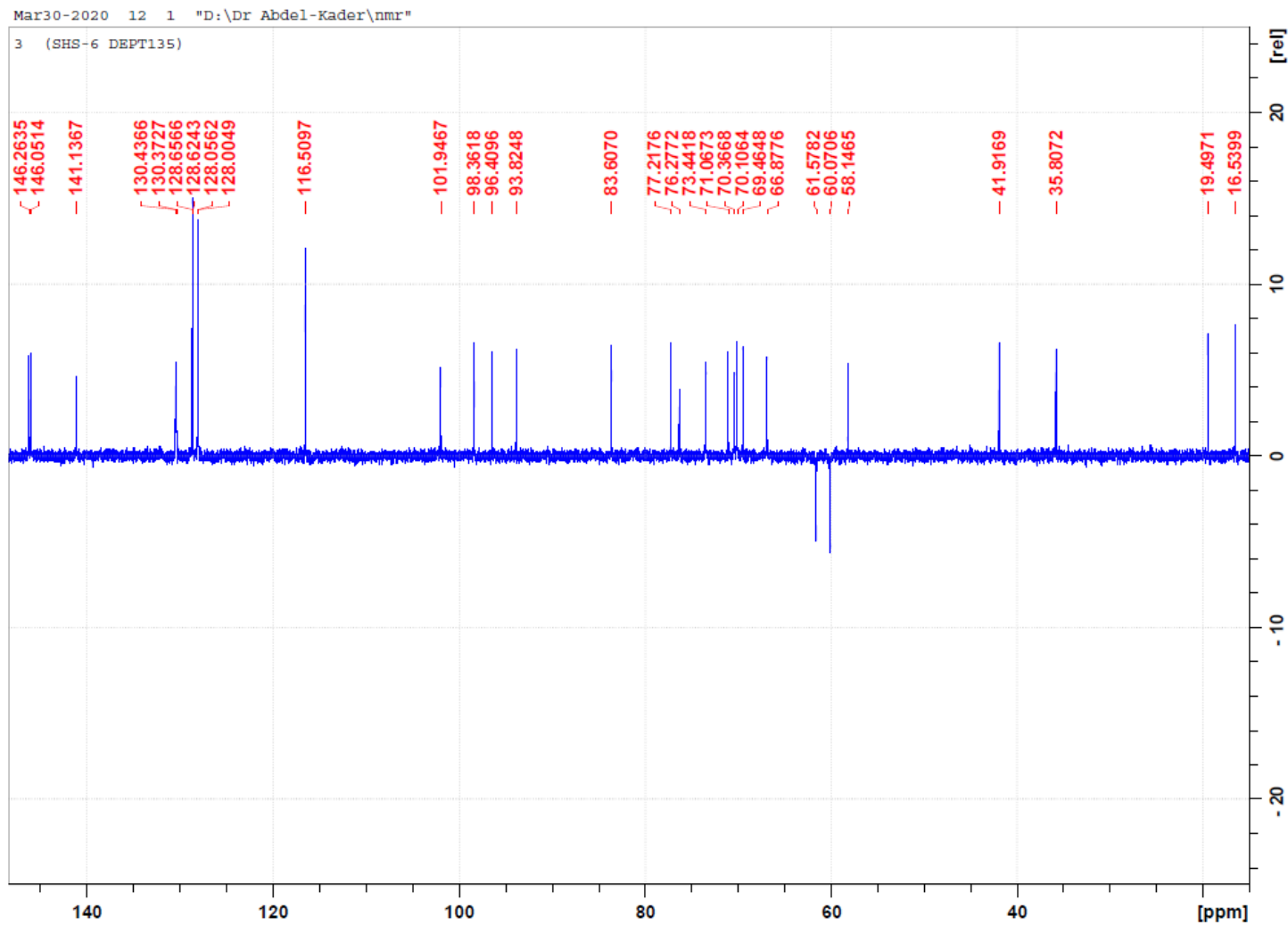


Figure S55. DEPT135 spectrum of compound 3.

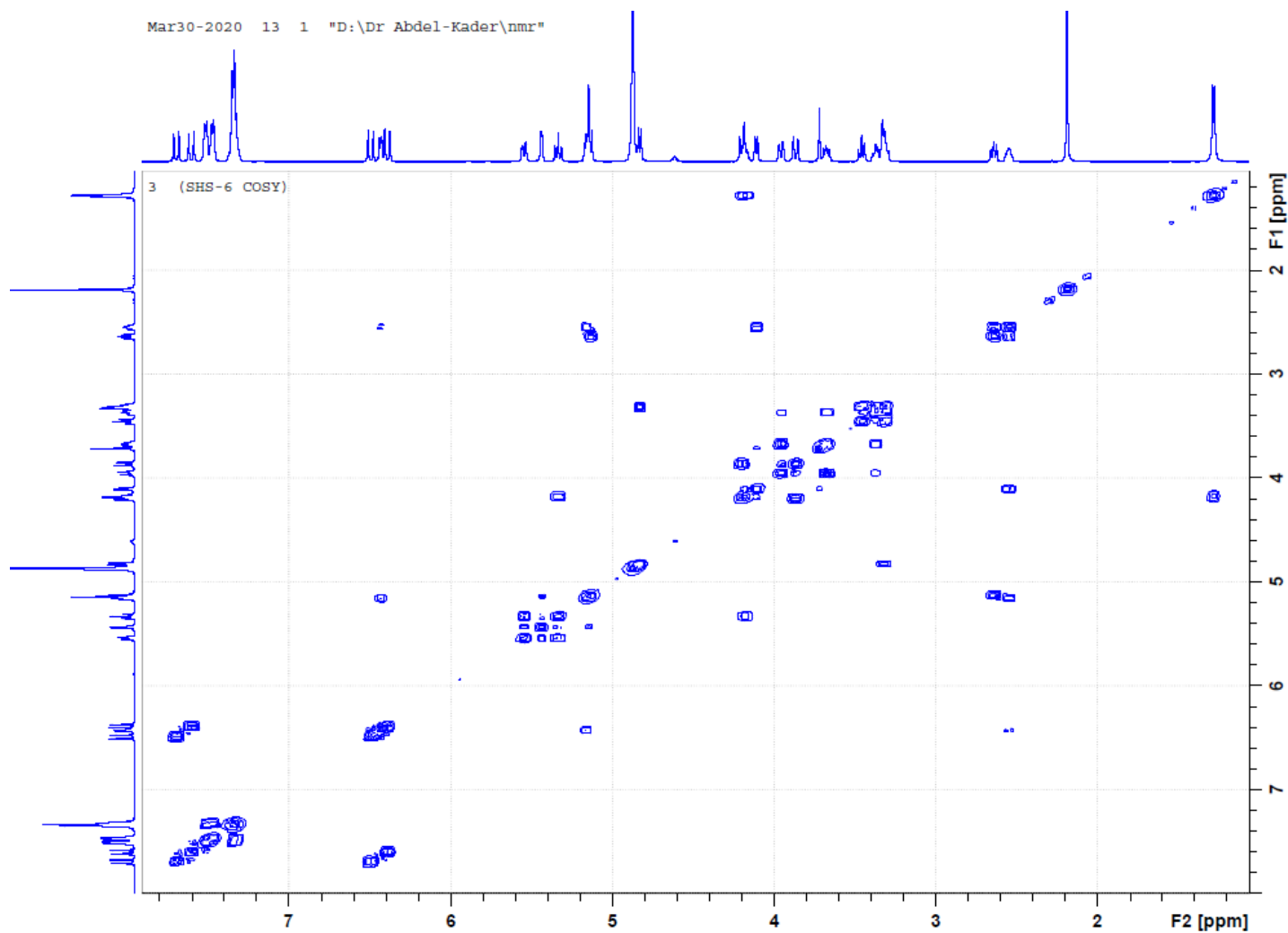


Figure S56. COSY spectrum of compound 3.

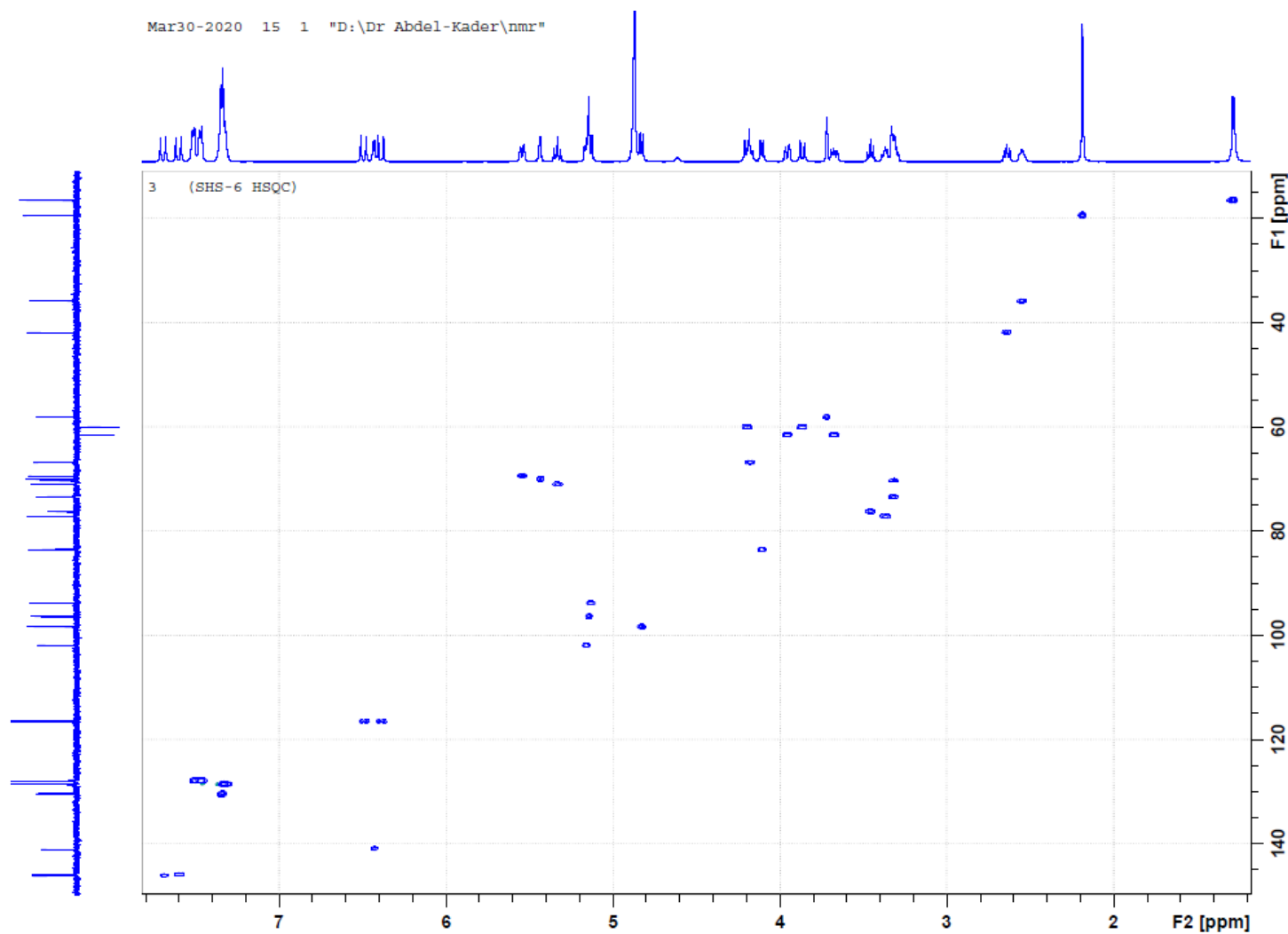


Figure S57. HSQC spectrum of compound 3.

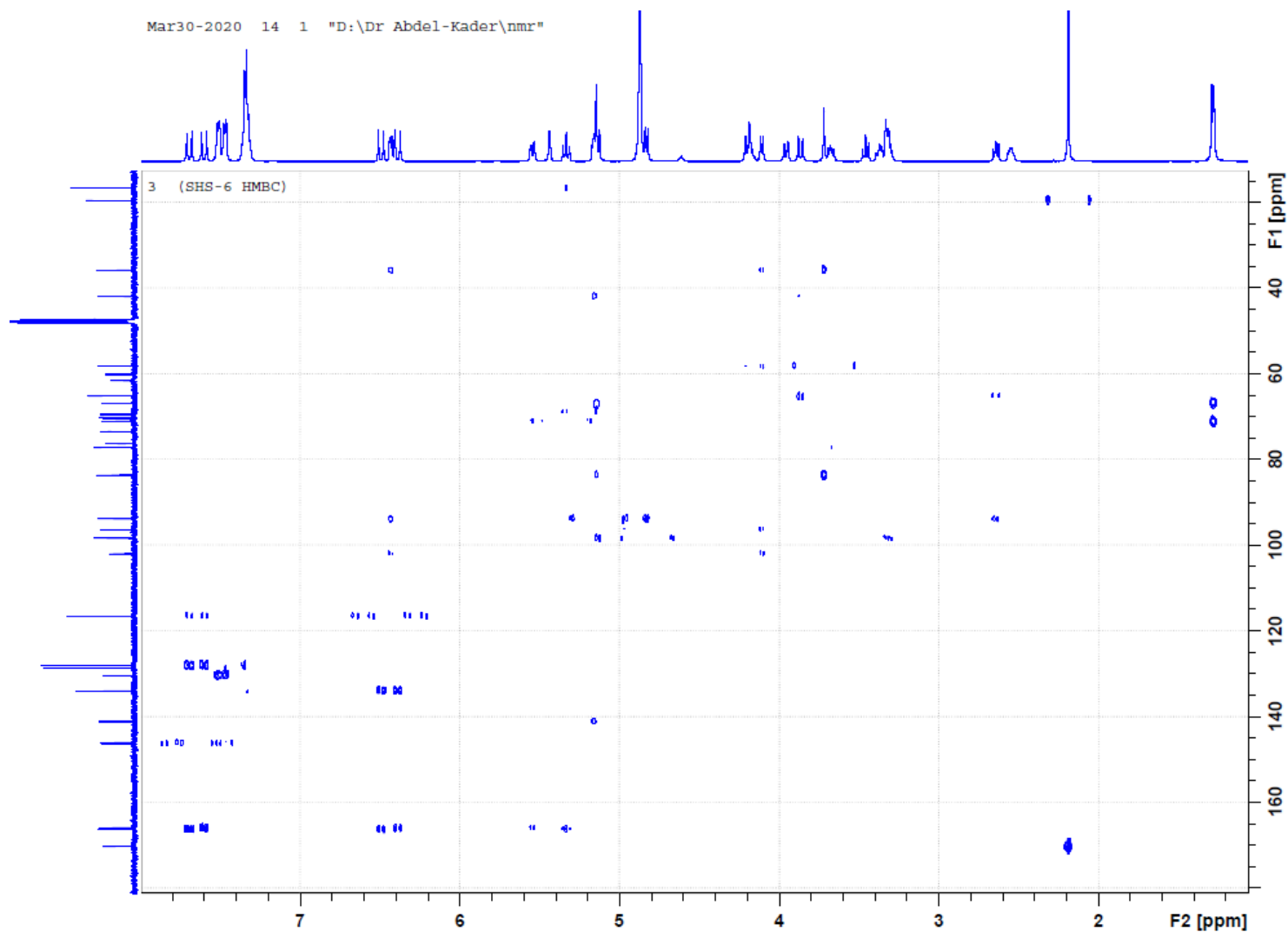


Figure S58. HMBC spectrum of compound 3.

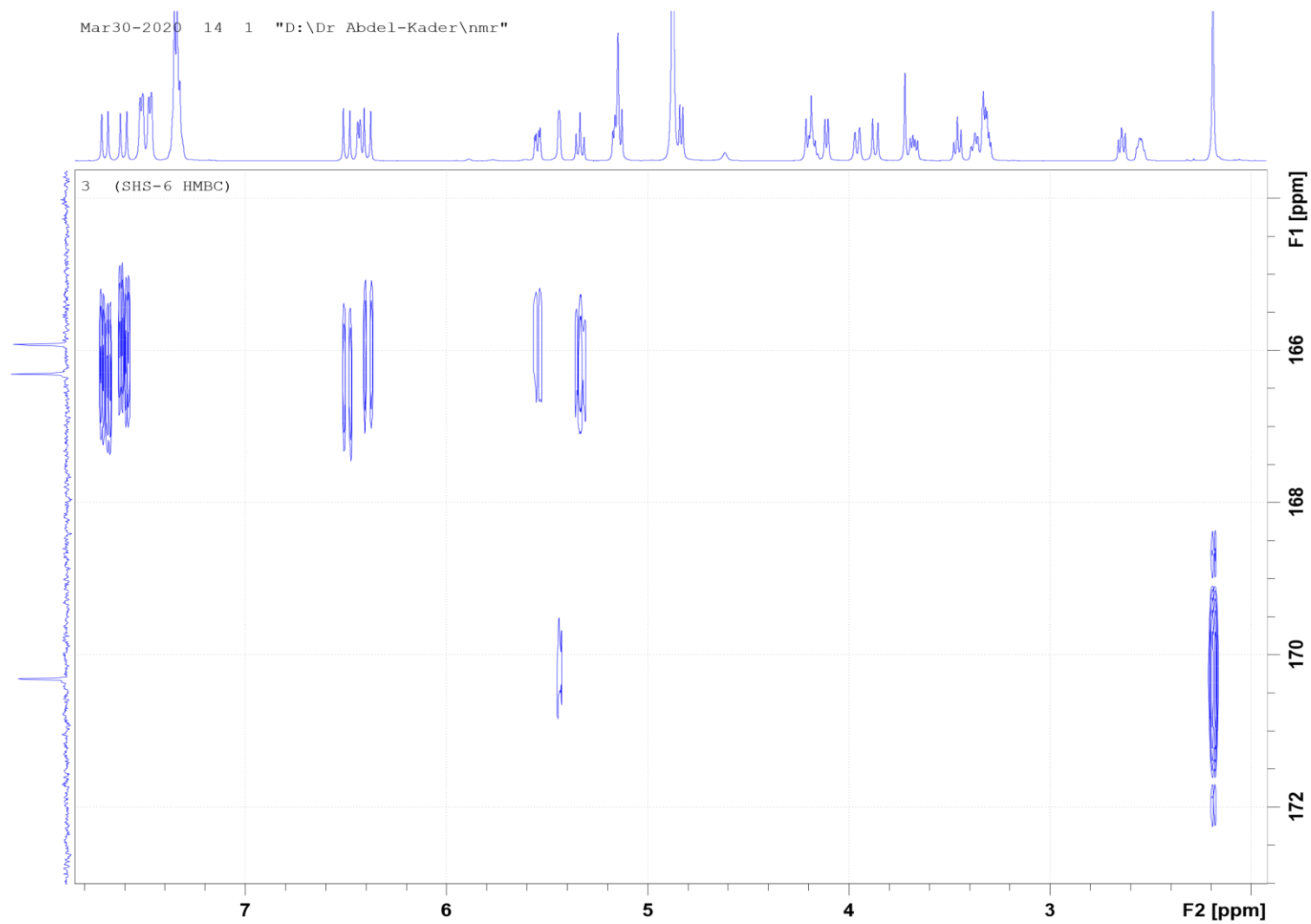


Figure S59. HMBC spectrum of compound 3 (expansion).

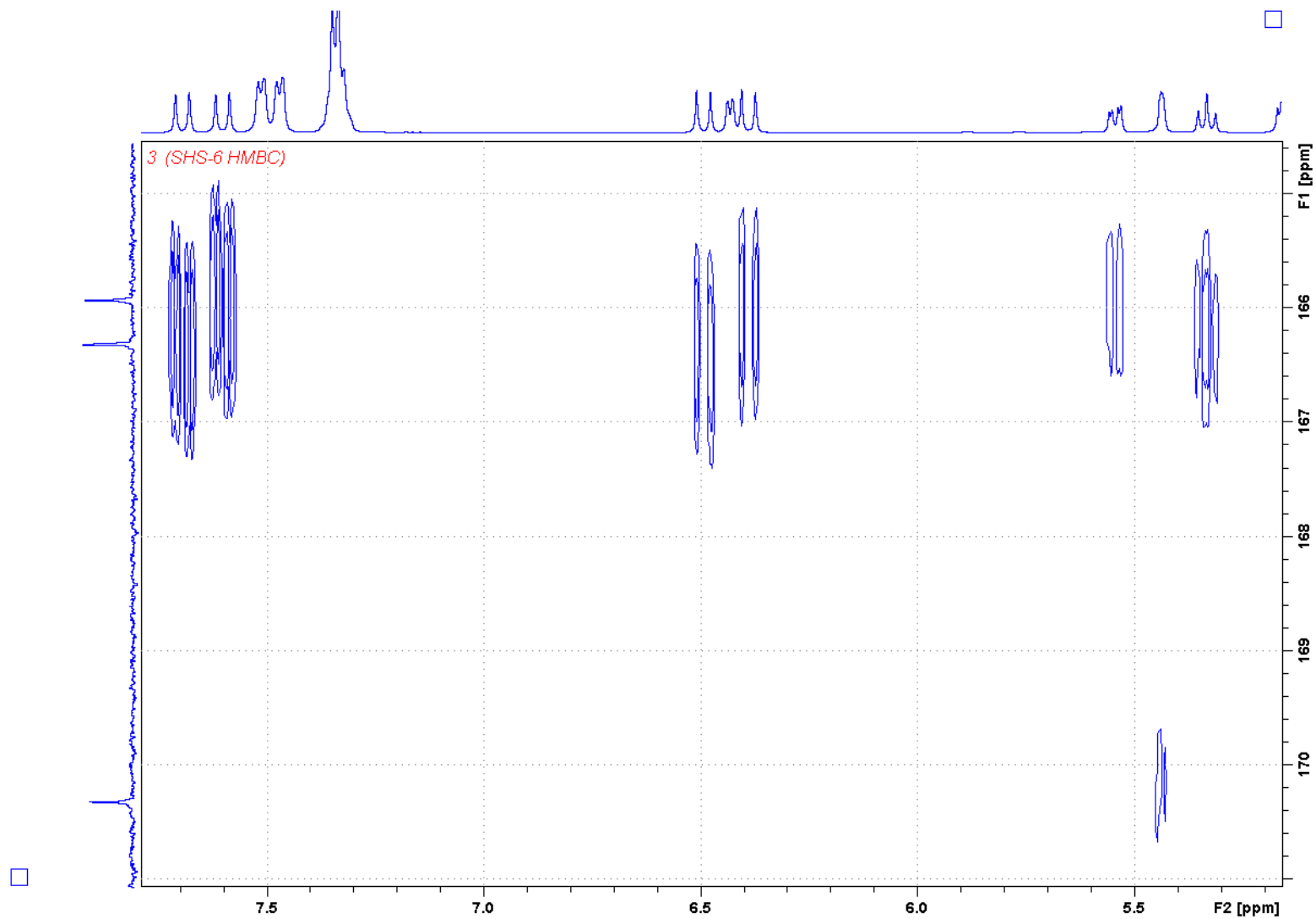


Figure S60. HMBC spectrum of compound 3 (expansion).

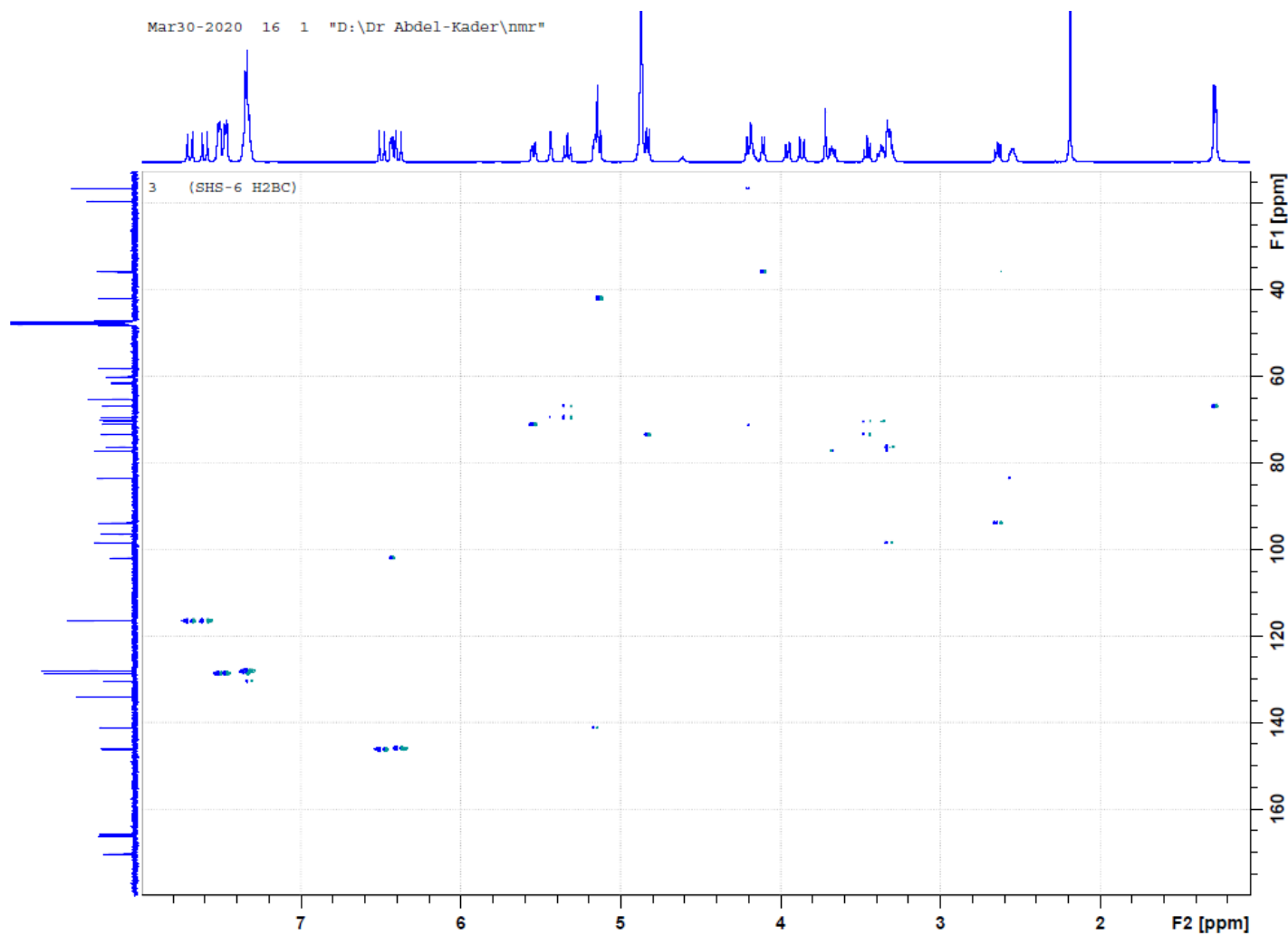


Figure S61. H2BC spectrum of compound 3.

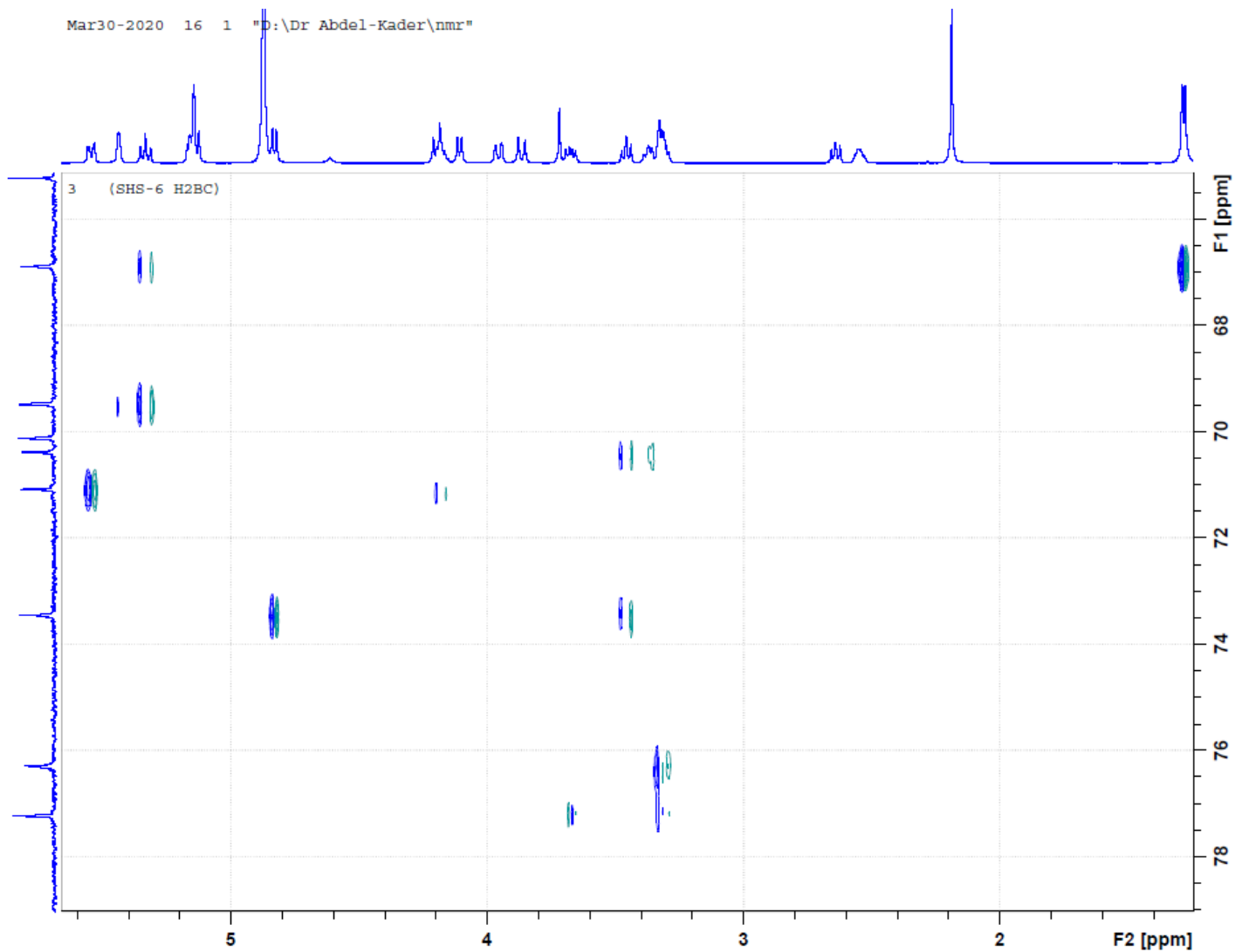


Figure S62 H2BC spectrum of compound 3 (expansion).

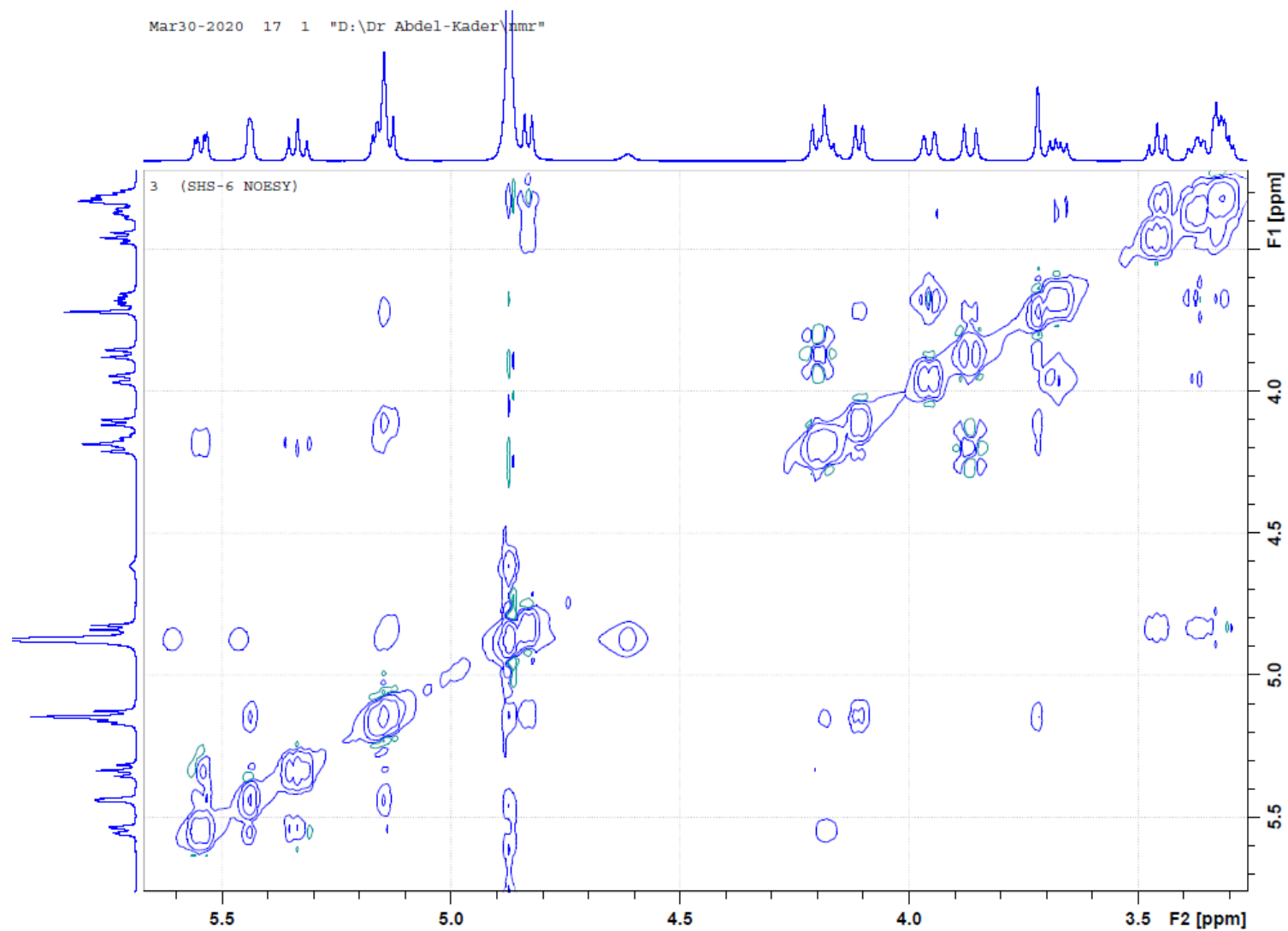


Figure S63. NOESY spectrum of compound 3 (expansion).

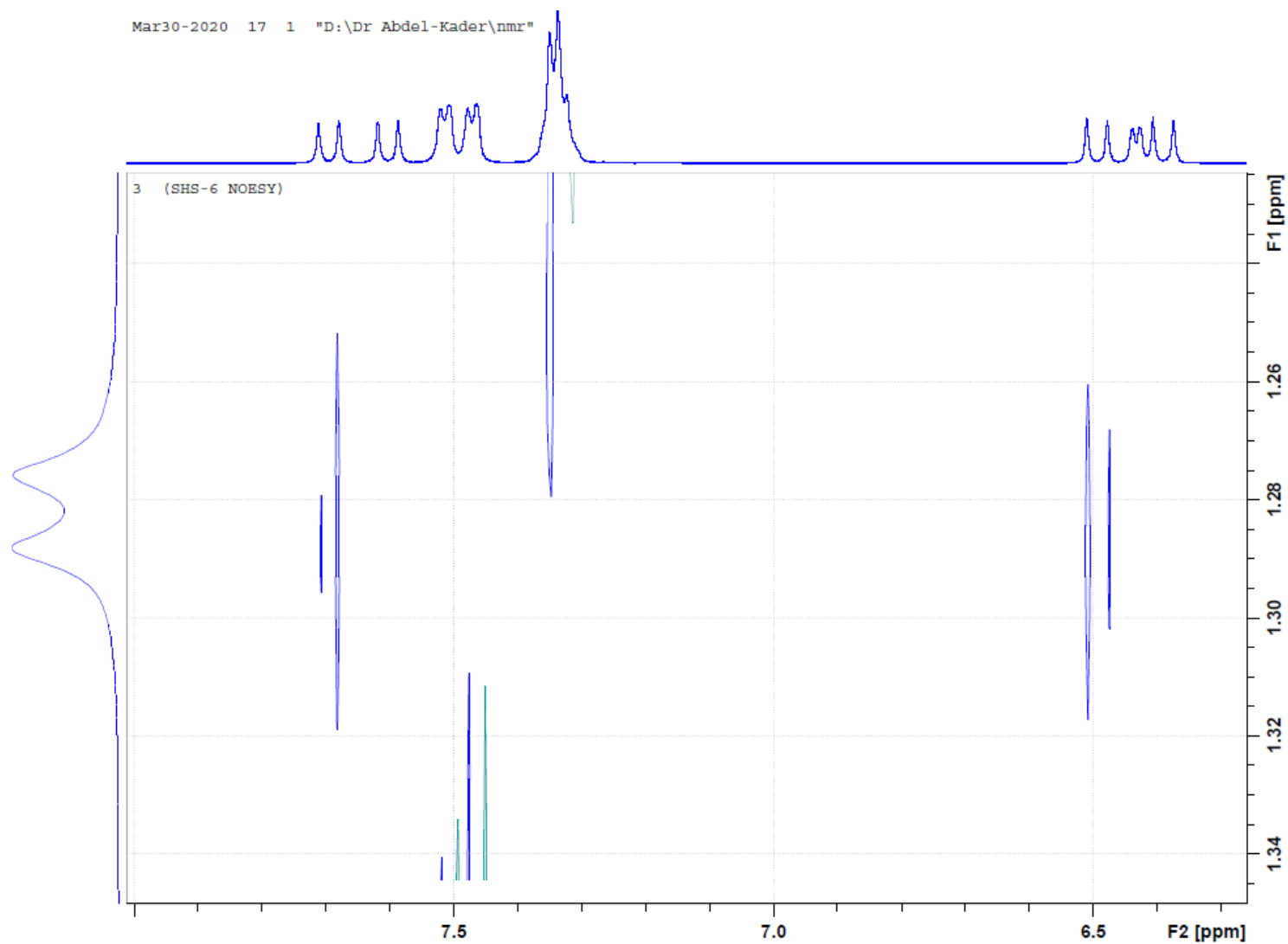


Figure S64. NOESY spectrum of compound 3 (expansion).

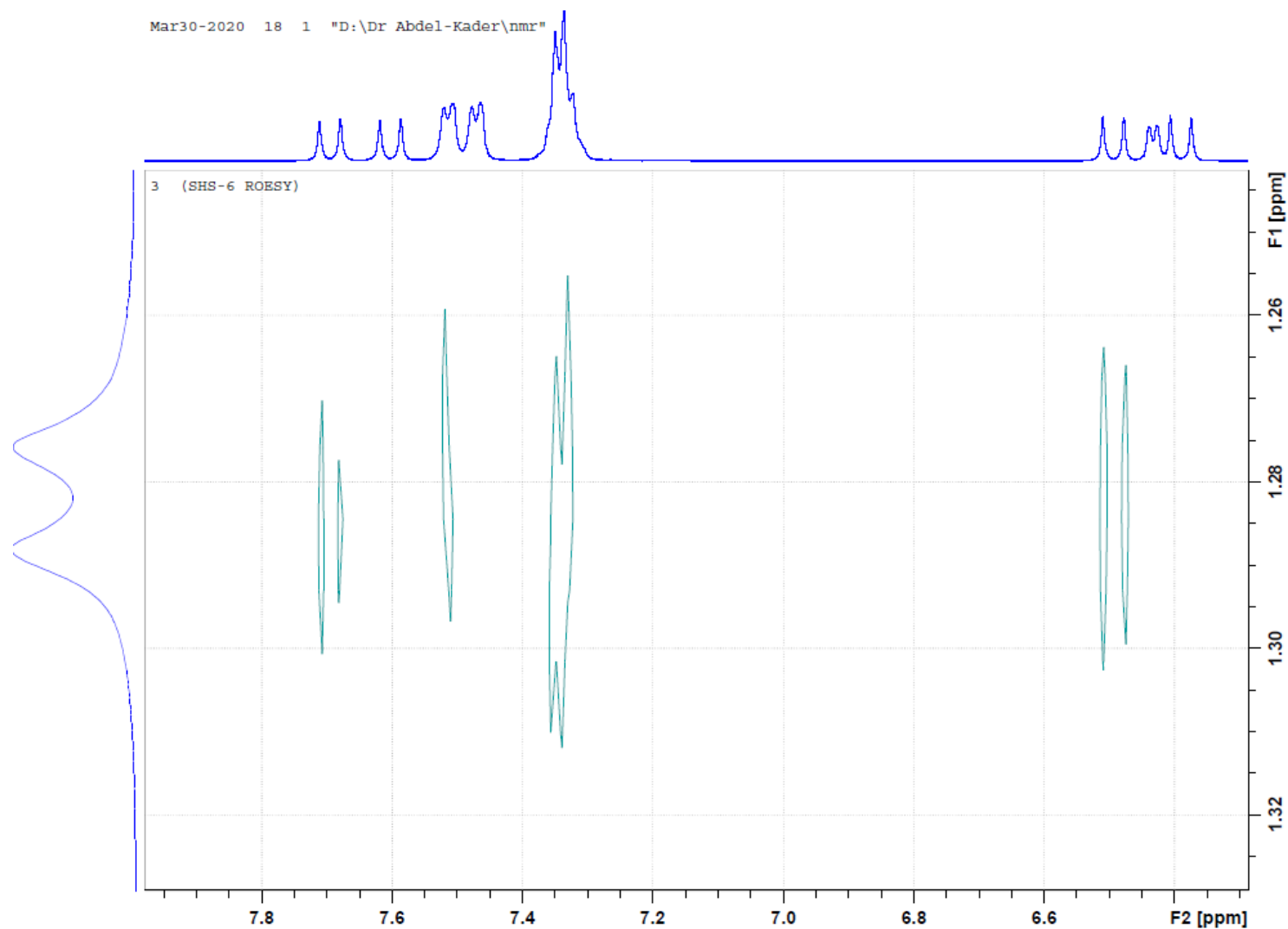


Figure S65. ROESY spectrum of compound 3 (expansion).

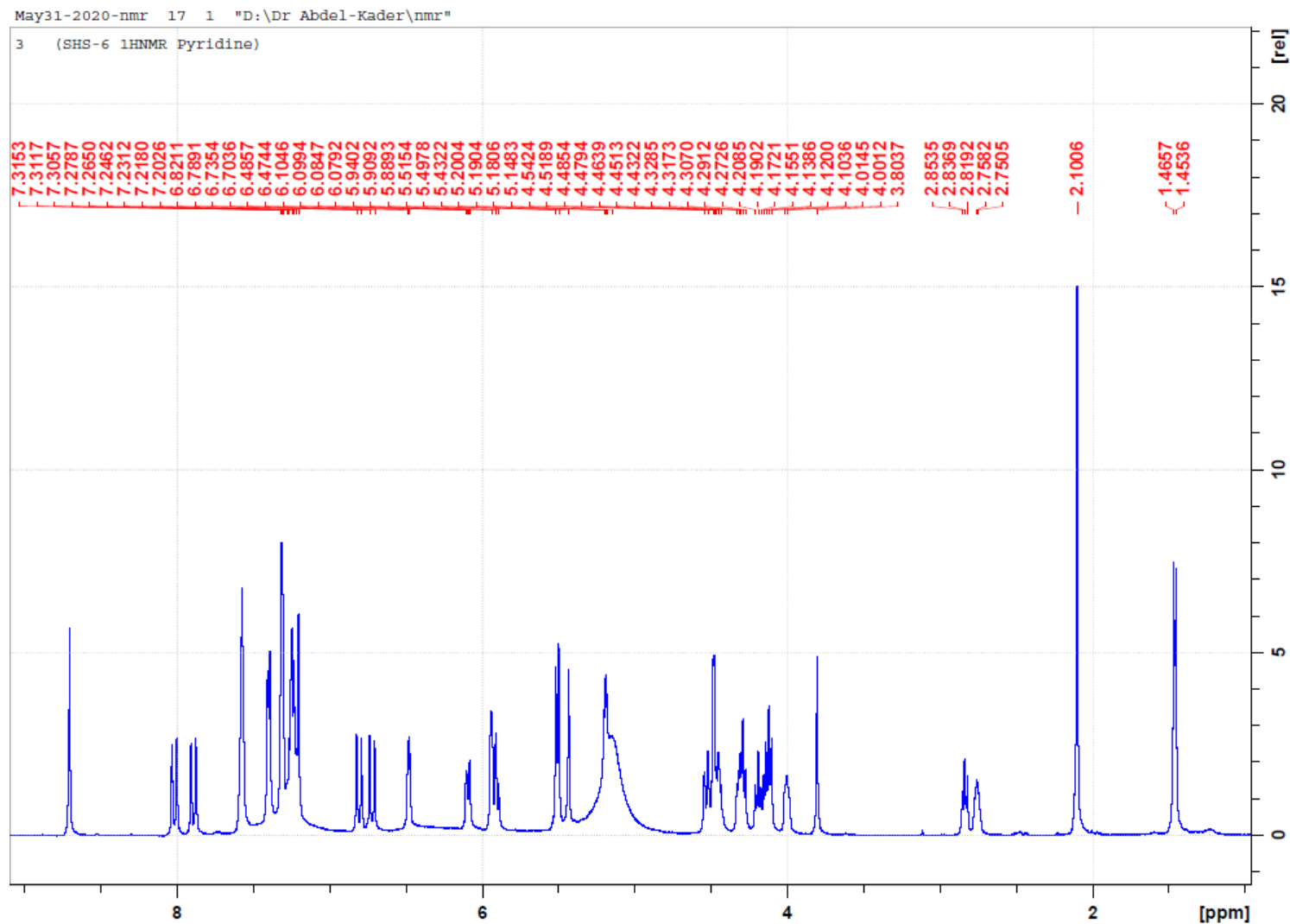


Figure S66. ¹HNMR spectrum of compound 3 in Pyridine.

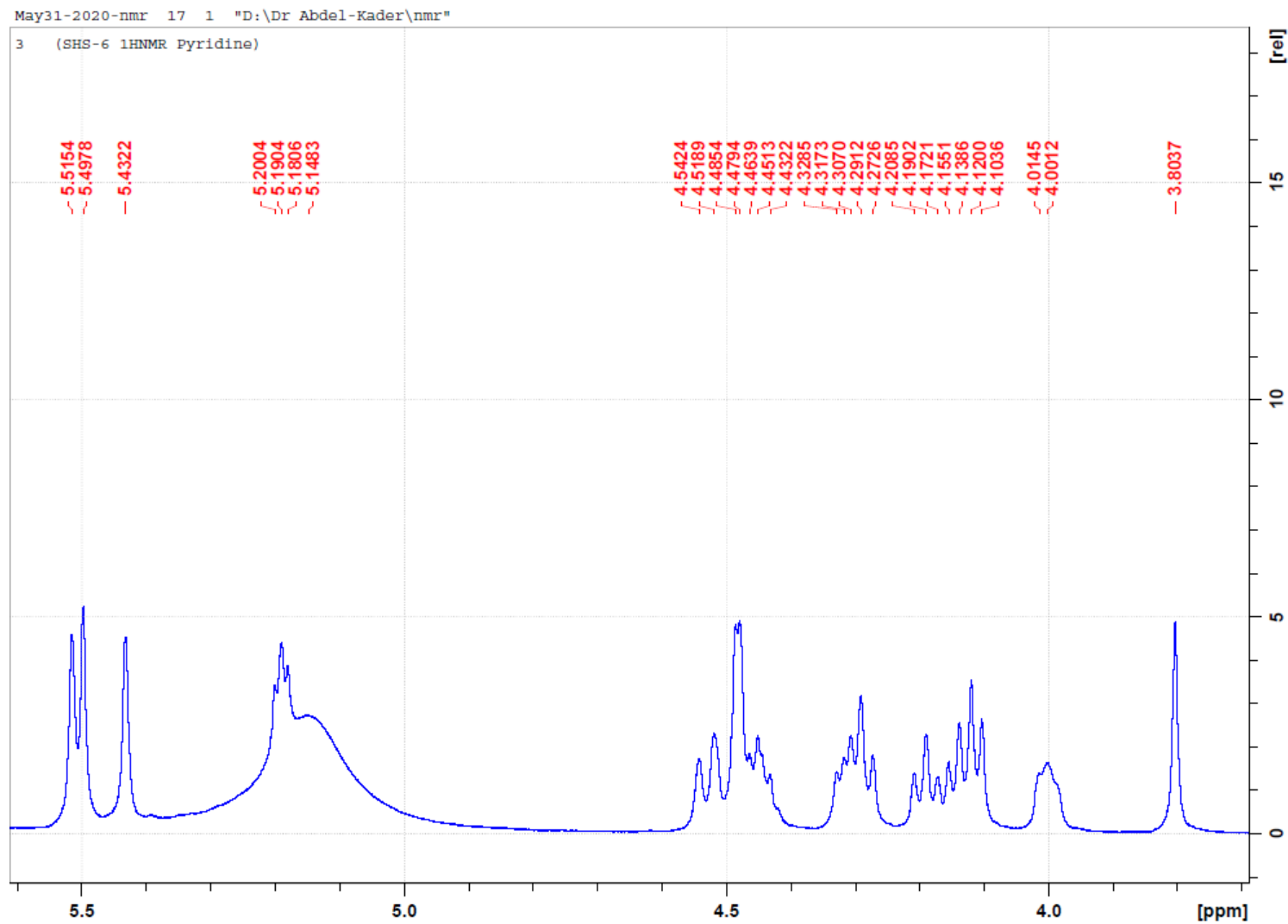


Figure S67. ¹HNMR spectrum of compound 3 in Pyridine (expansion).

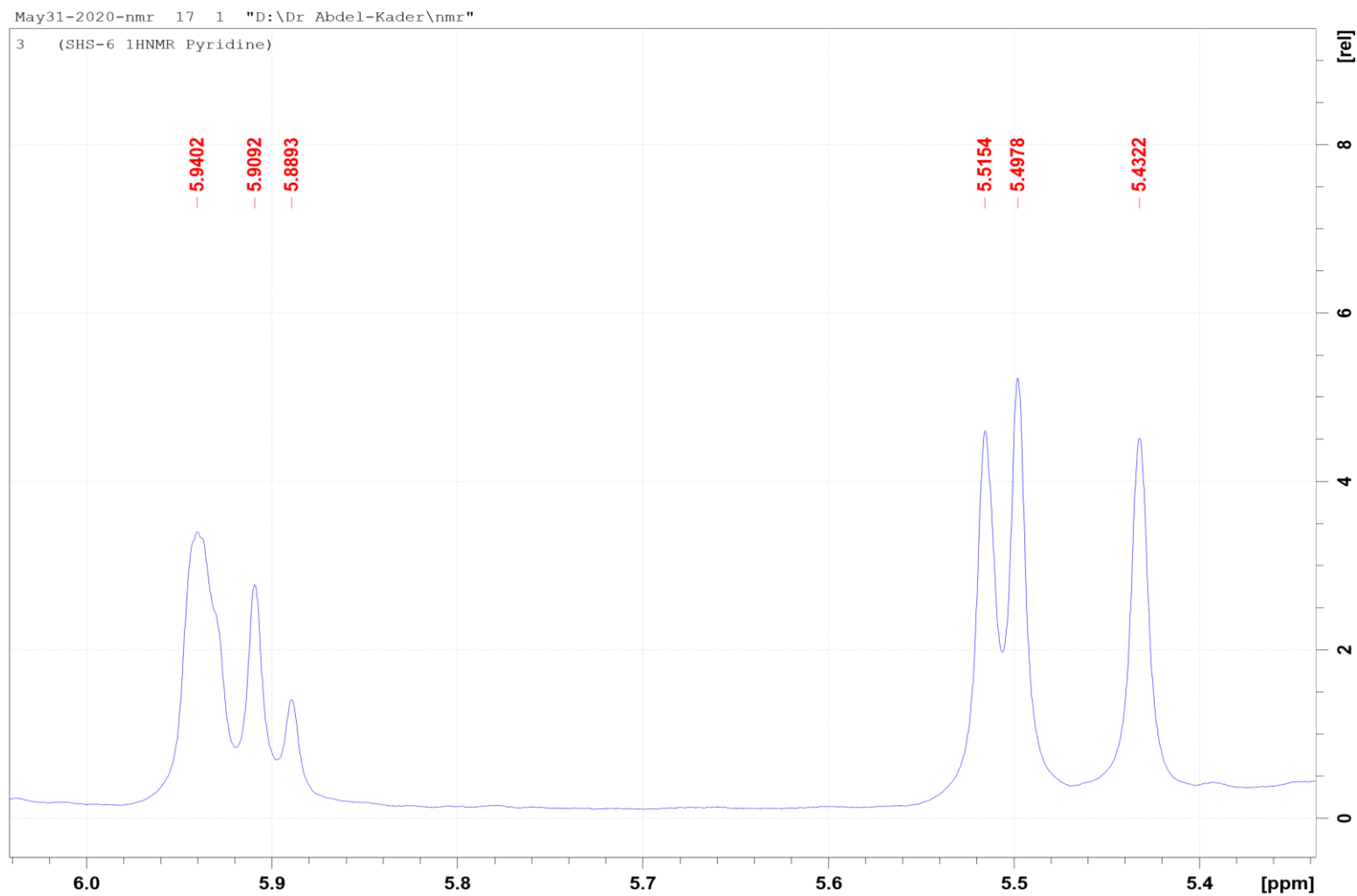


Figure S68. ^1H NMR spectrum of compound 3 in Pyridine (expansion).

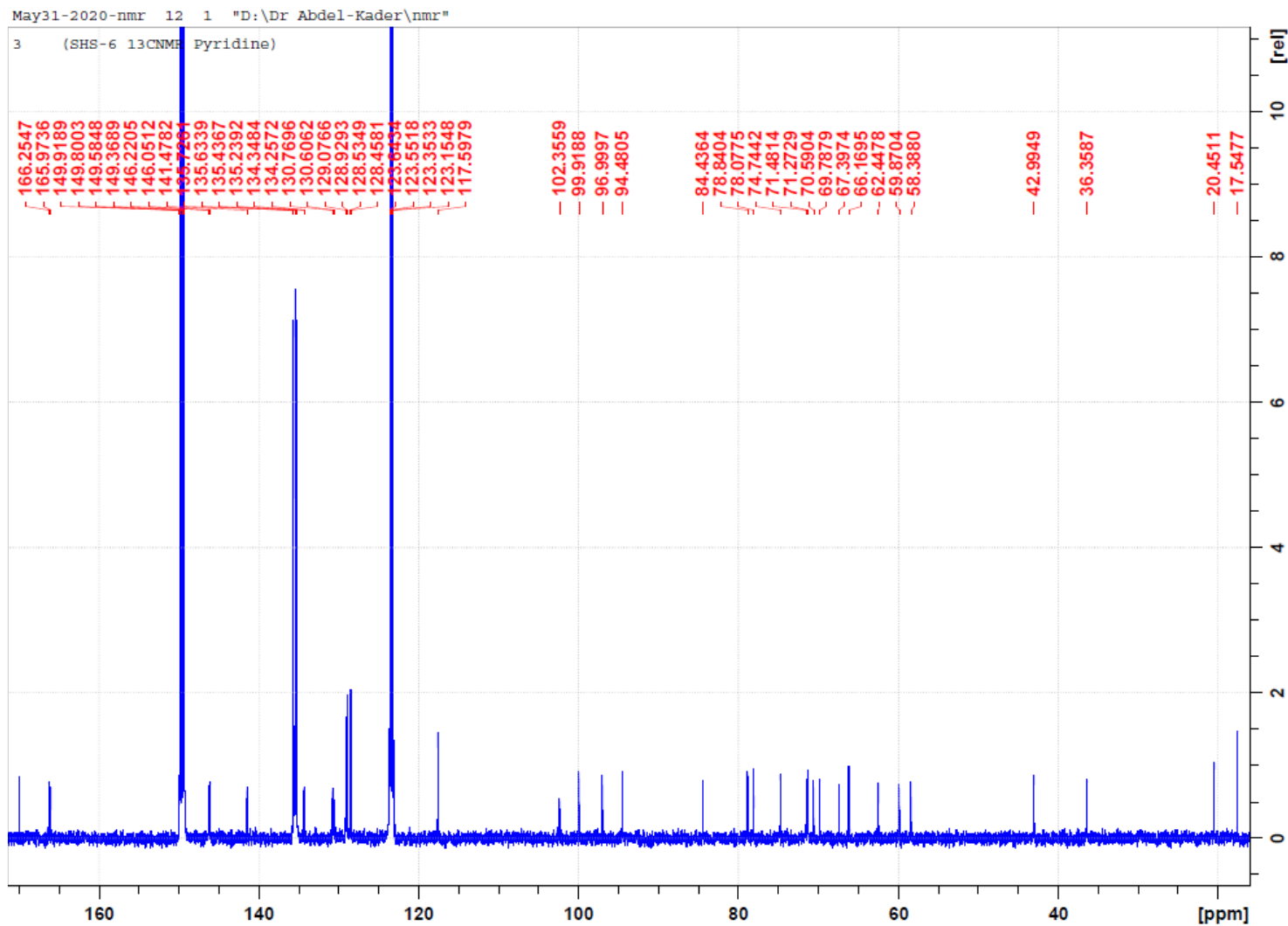


Figure S69. ¹³CNMR spectrum of compound 3 in Pyridine.

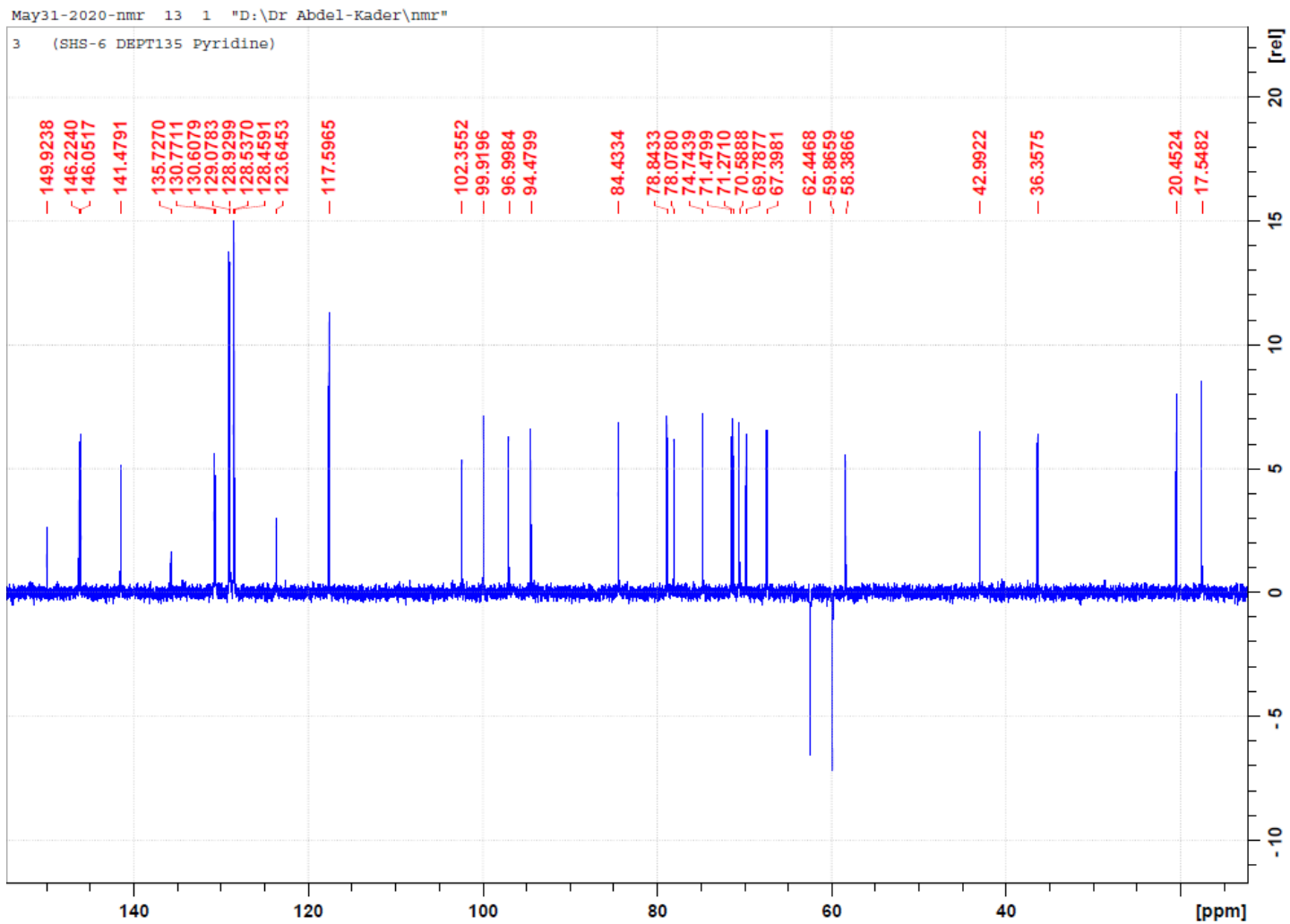


Figure S70. DEPT135 spectrum of compound 3 in Pyridine.

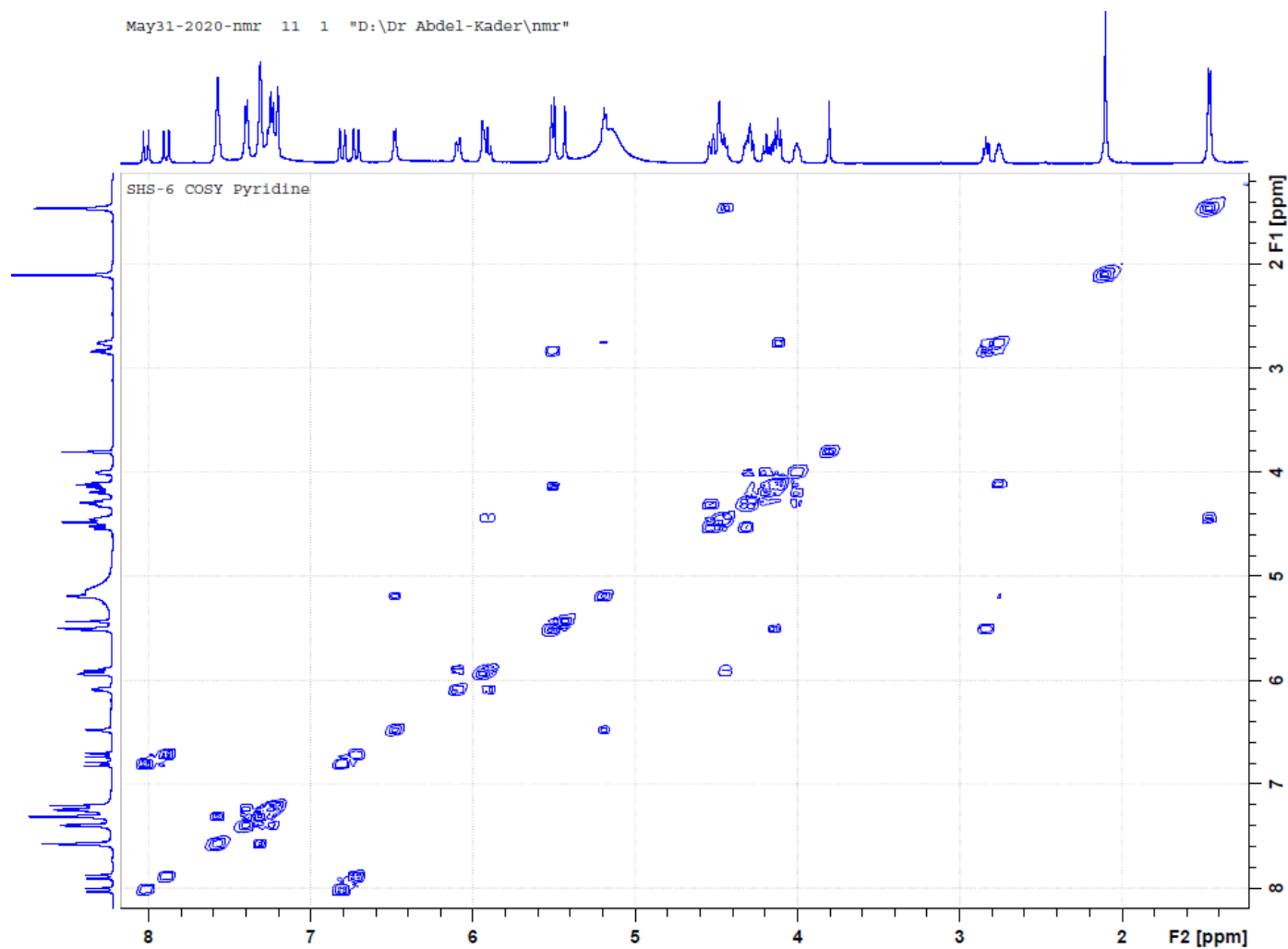


Figure S71. COSY spectrum of compound 3 in Pyridine.

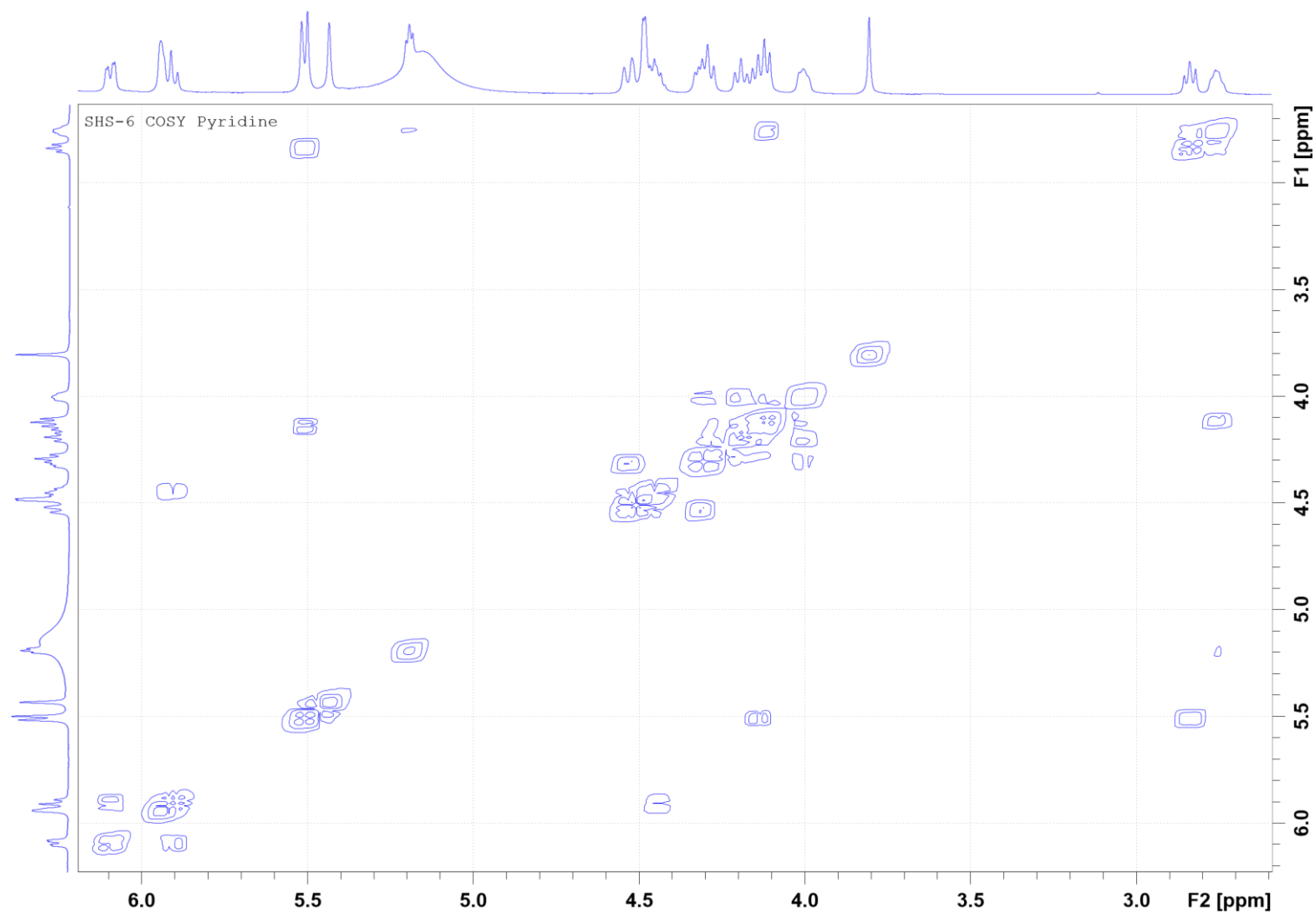


Figure S72. COSY spectrum of compound 3 in Pyridine (expansion).

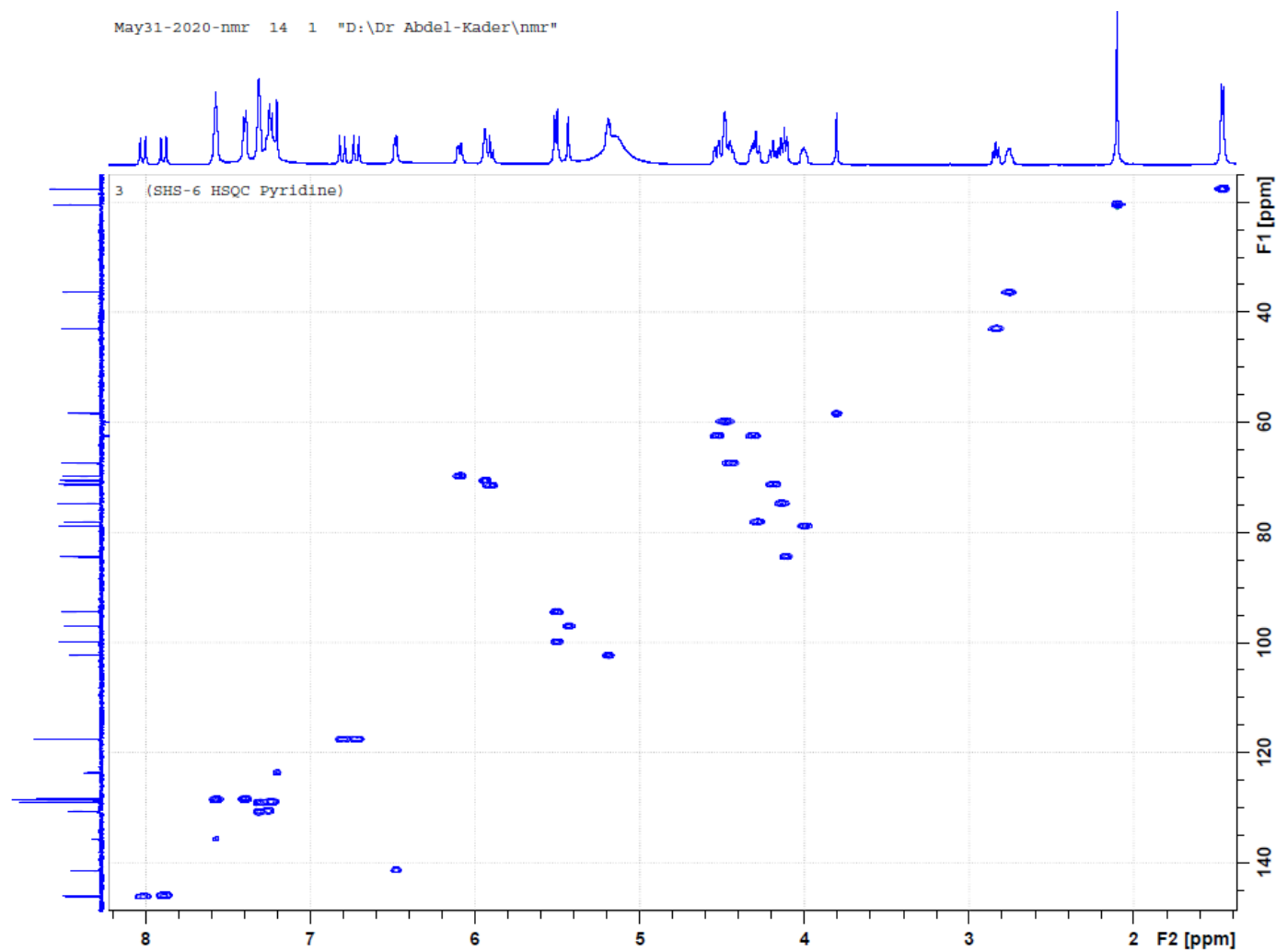


Figure S73. HSQC spectrum of compound 3 in Pyridine.

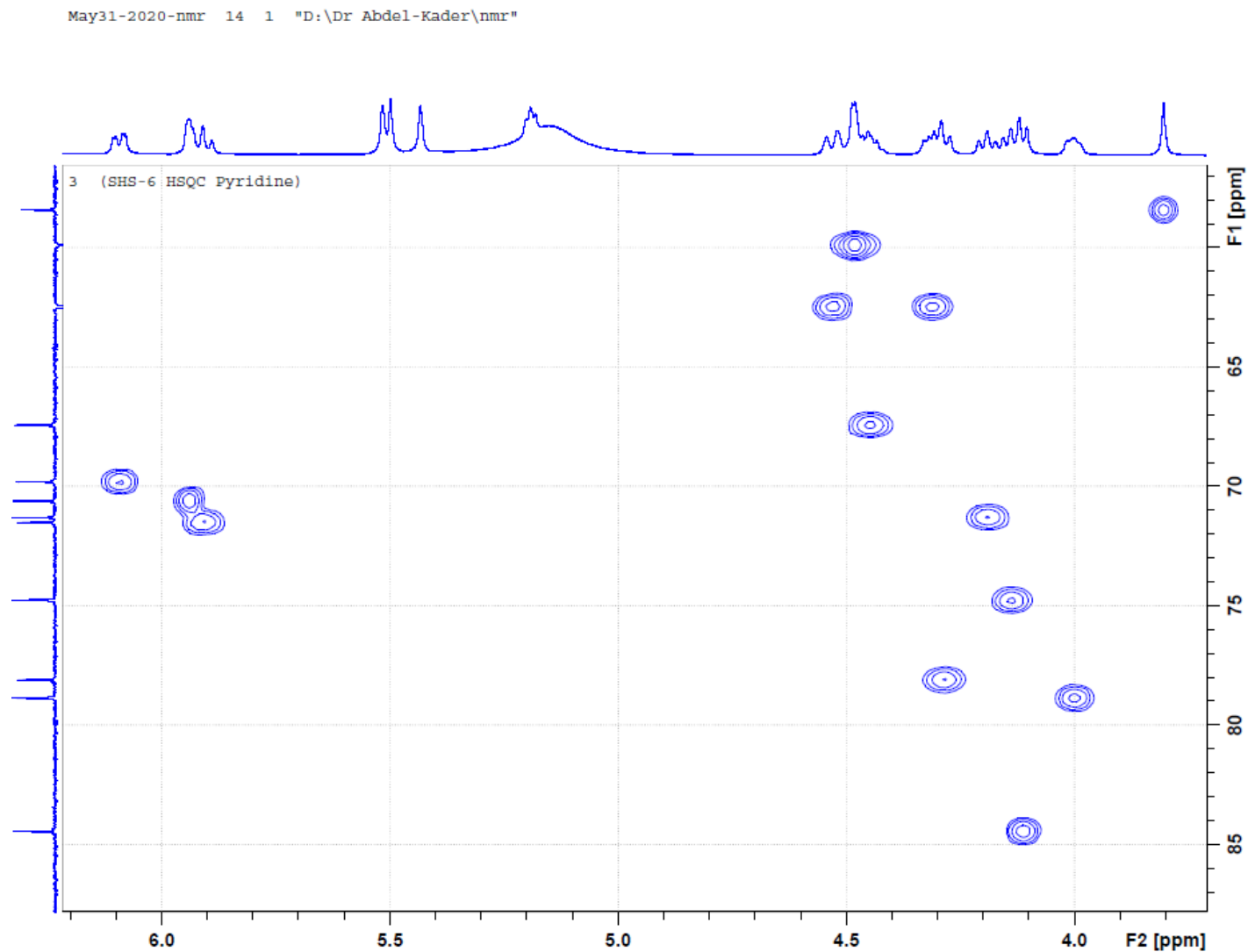


Figure S74. HSQC spectrum of compound 3 in Pyridine (expansion).

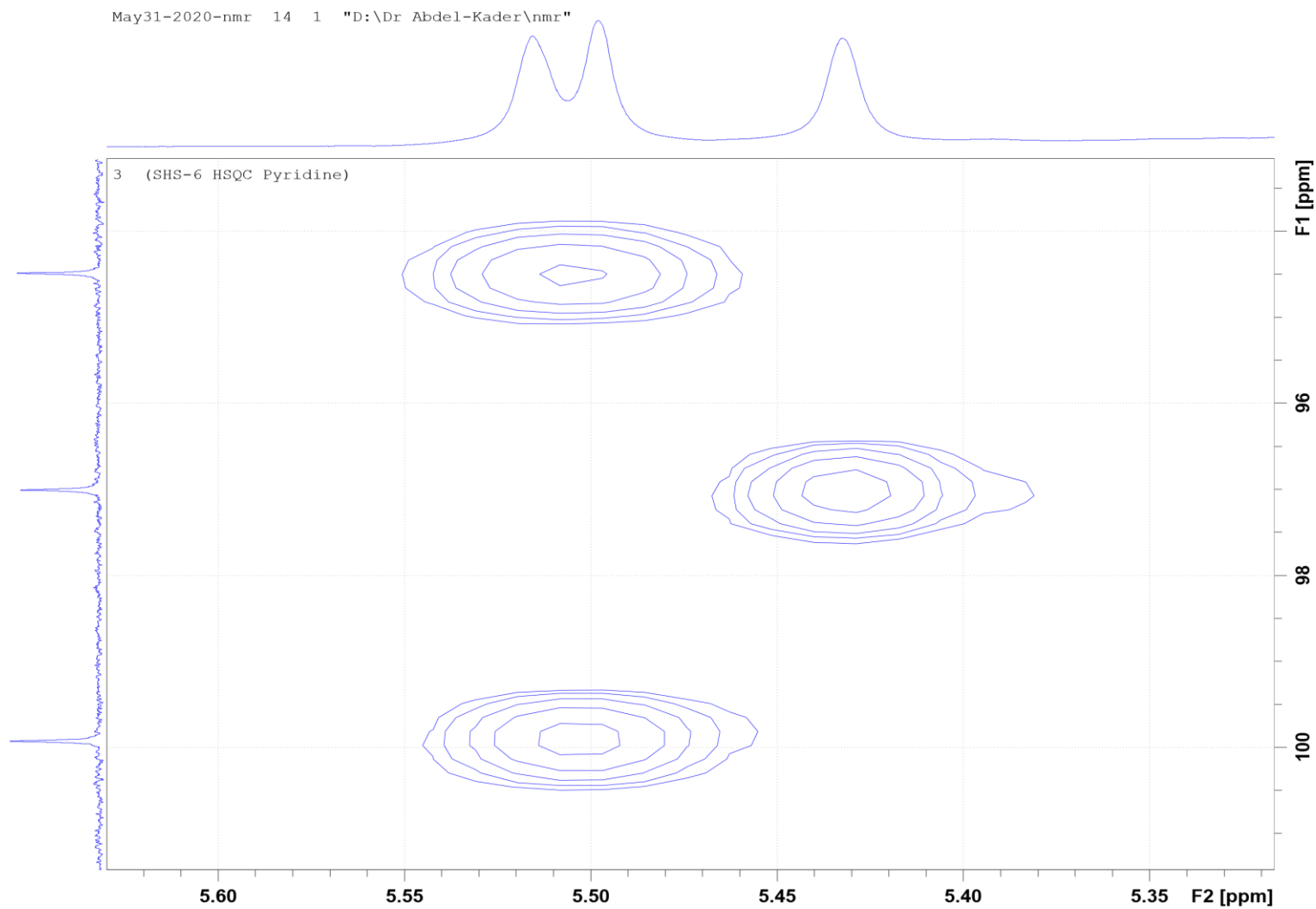


Figure S75. HSQC spectrum of compound 3 in Pyridine (expansion).

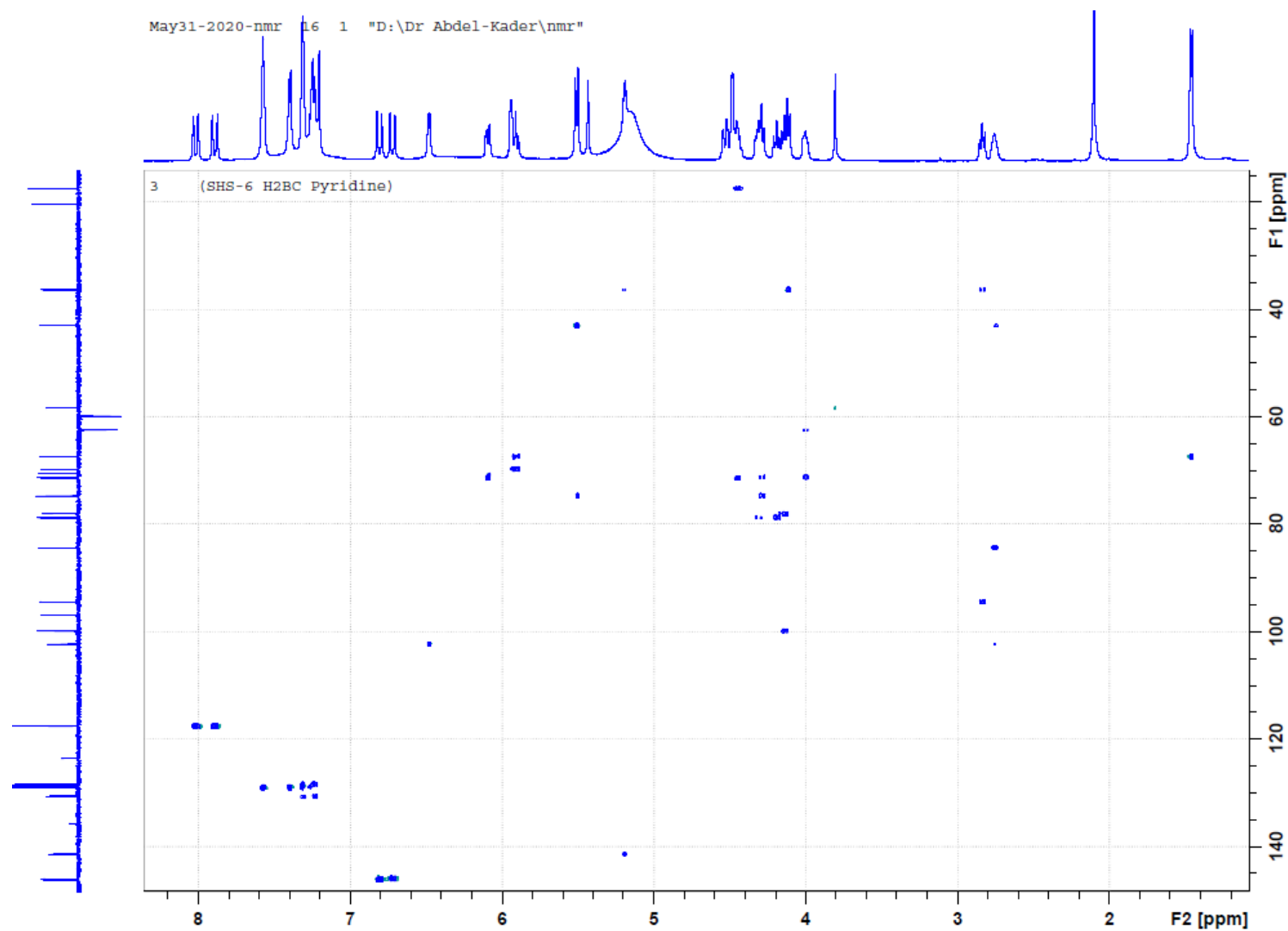


Figure S76. H2BC spectrum of compound 3 in Pyridine.

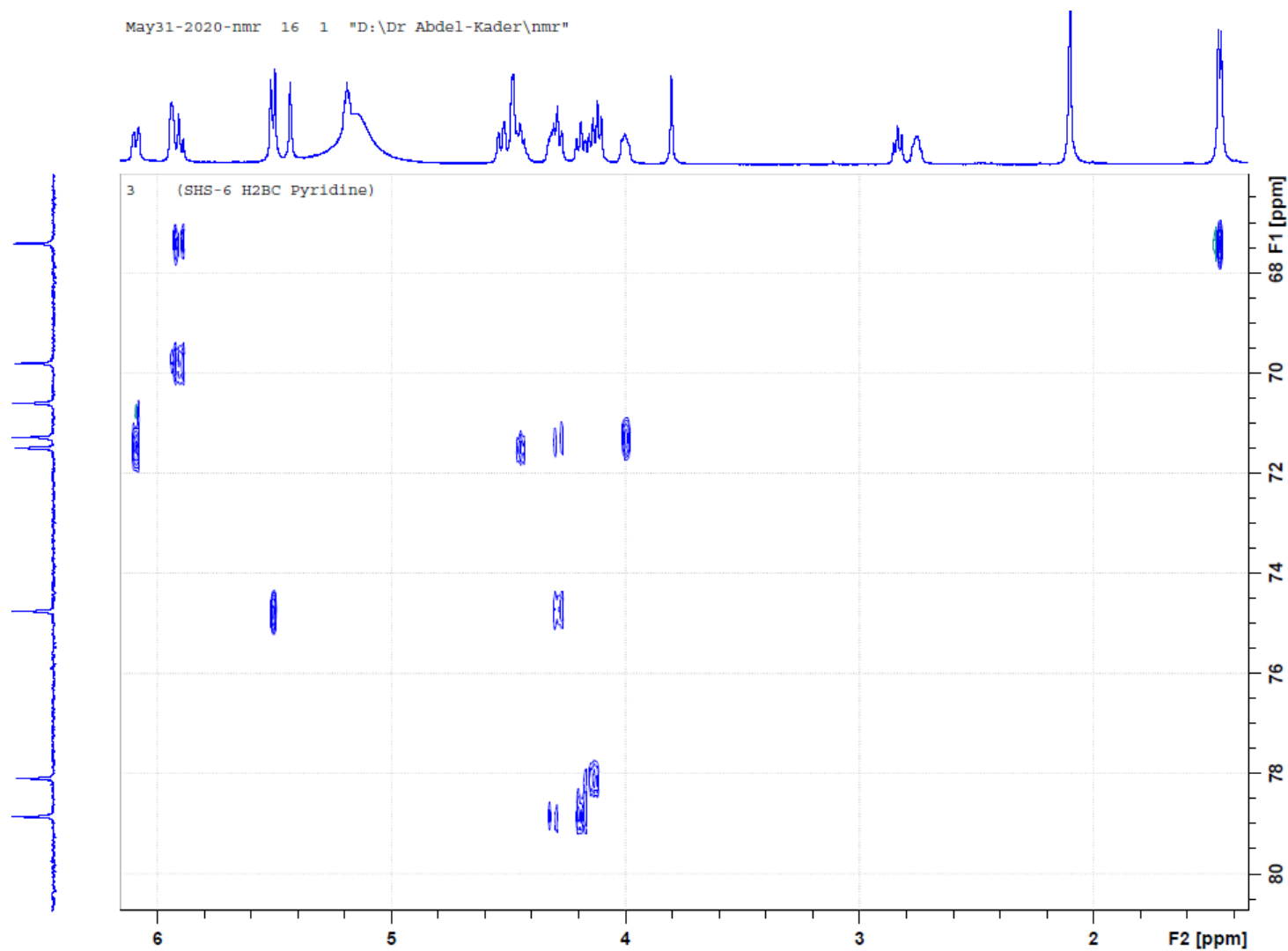


Figure S77. H2BC spectrum of compound 3 in Pyridine (expansion).

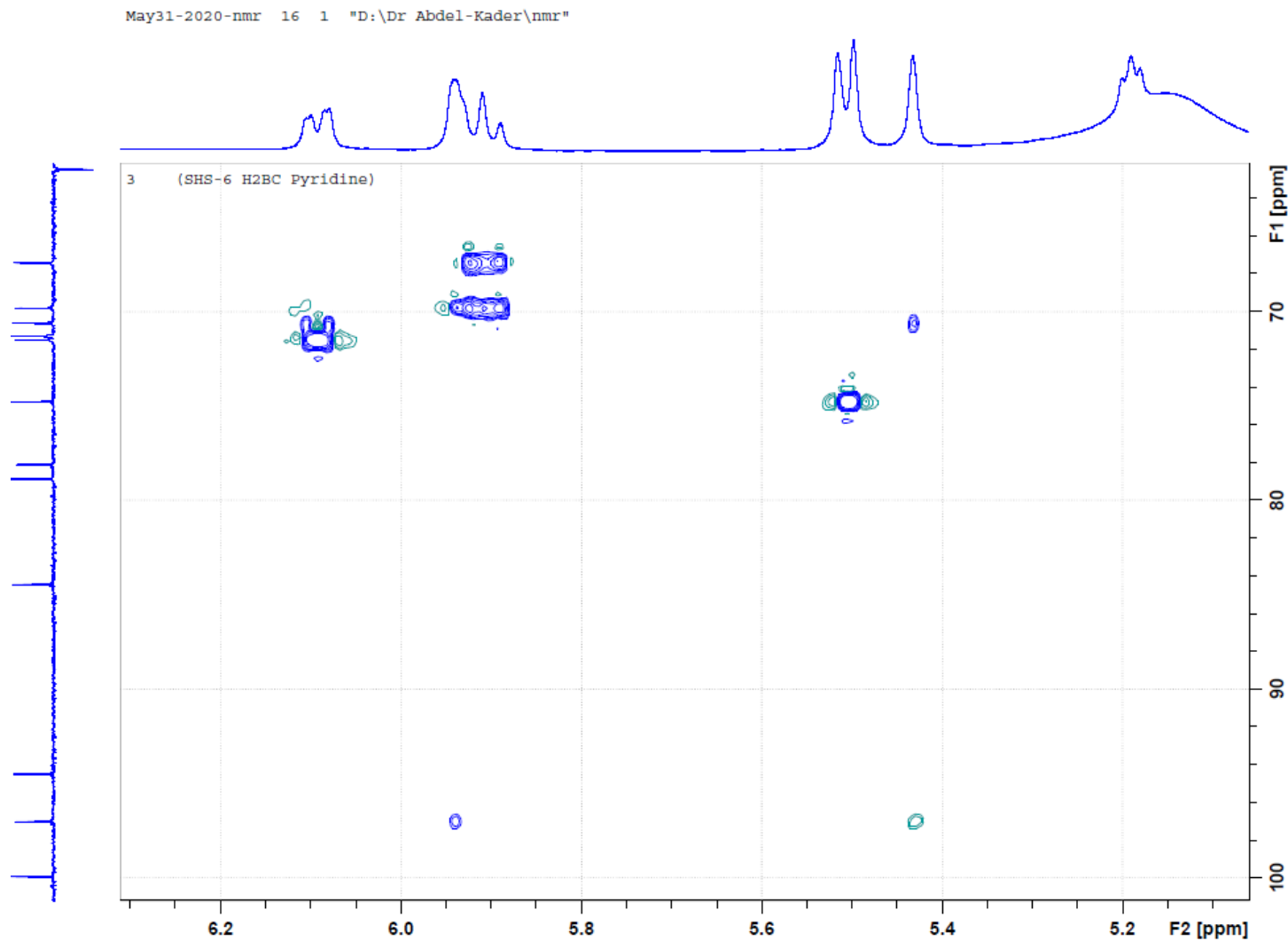


Figure S78. H2BC spectrum of compound 3 in Pyridine (expansion).

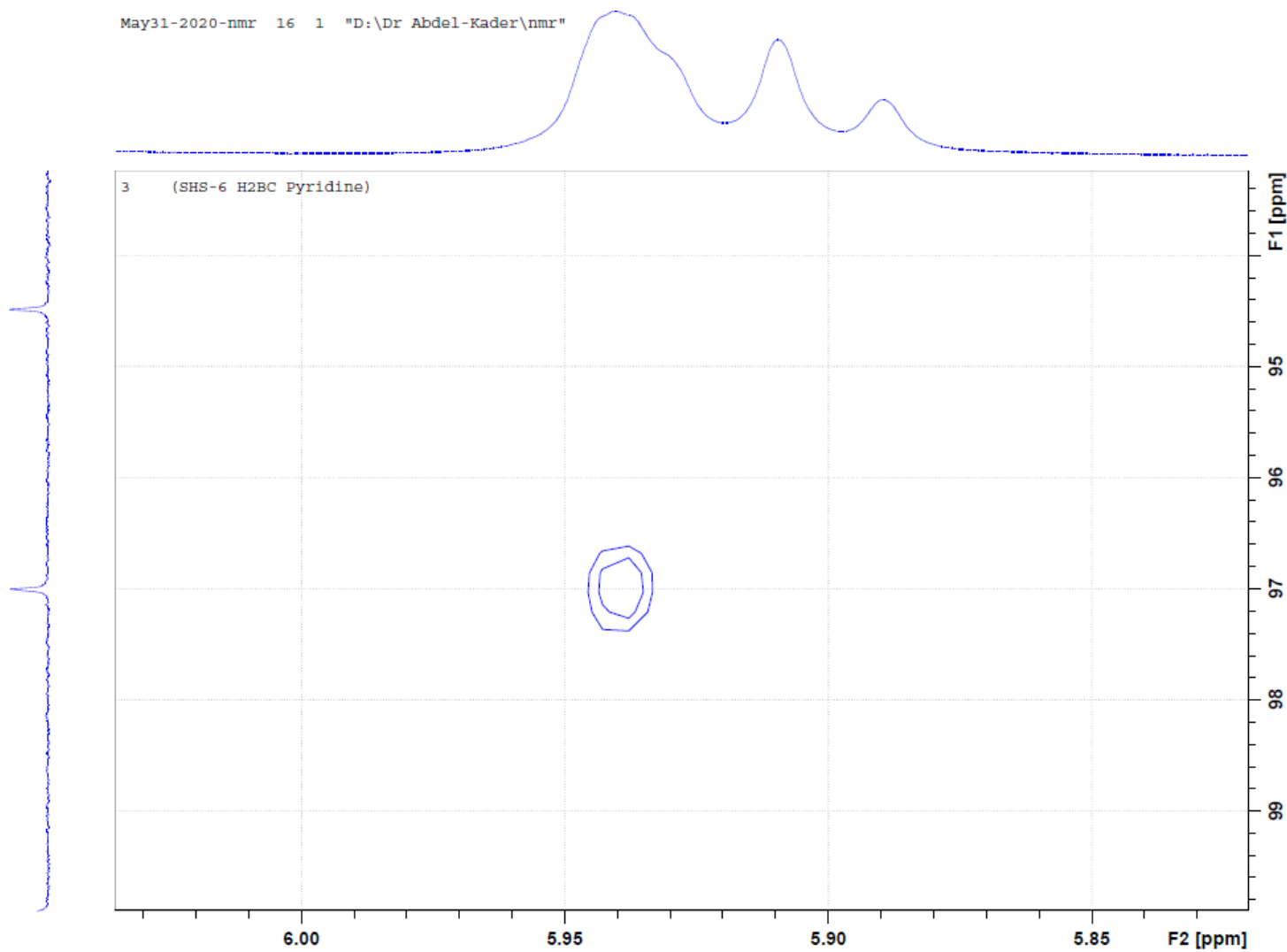


Figure S79. H2BC spectrum of compound 3 in Pyridine (expansion).

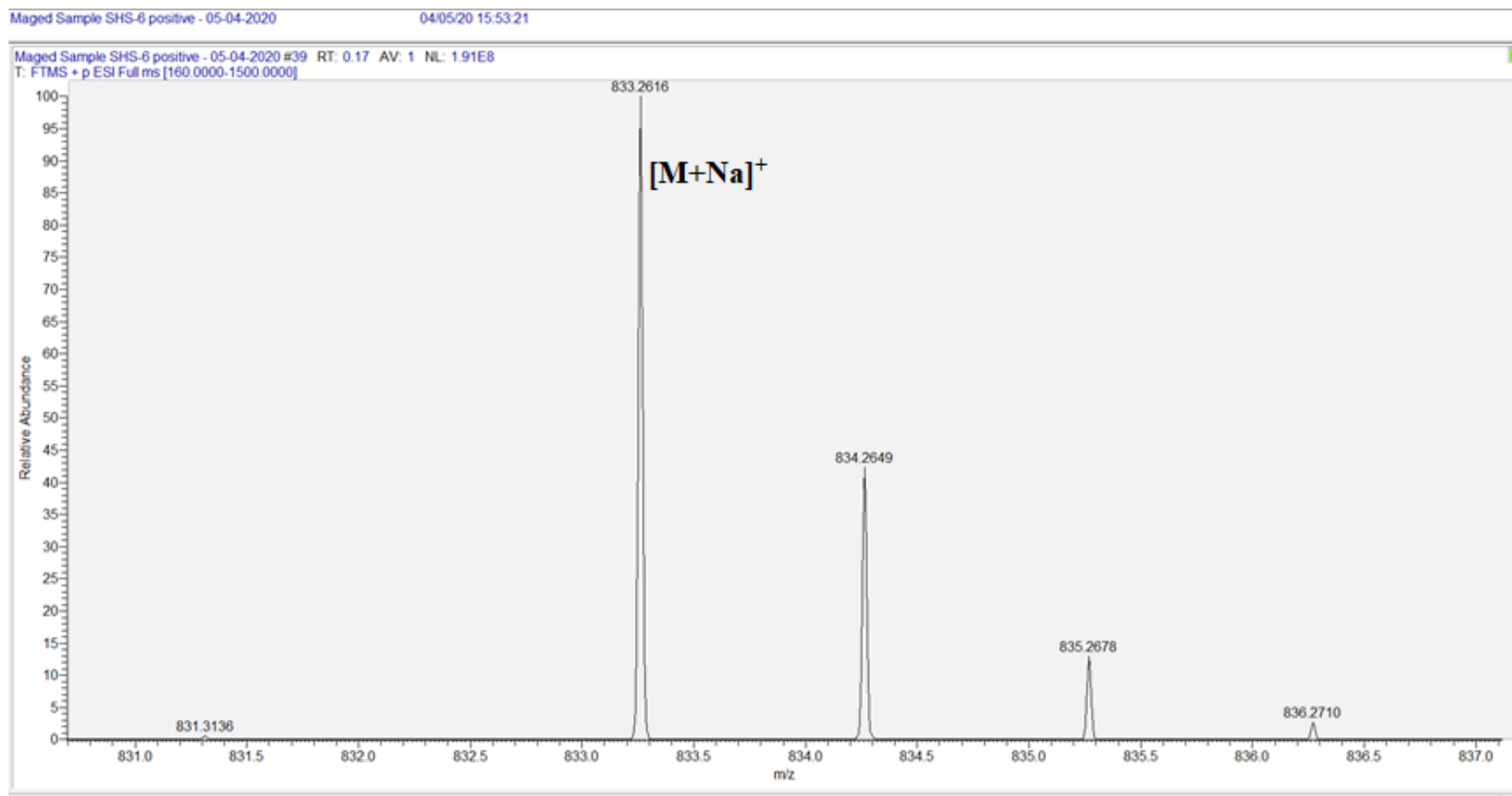


Figure S80. HRESIMS of compound 3 (positive mode).

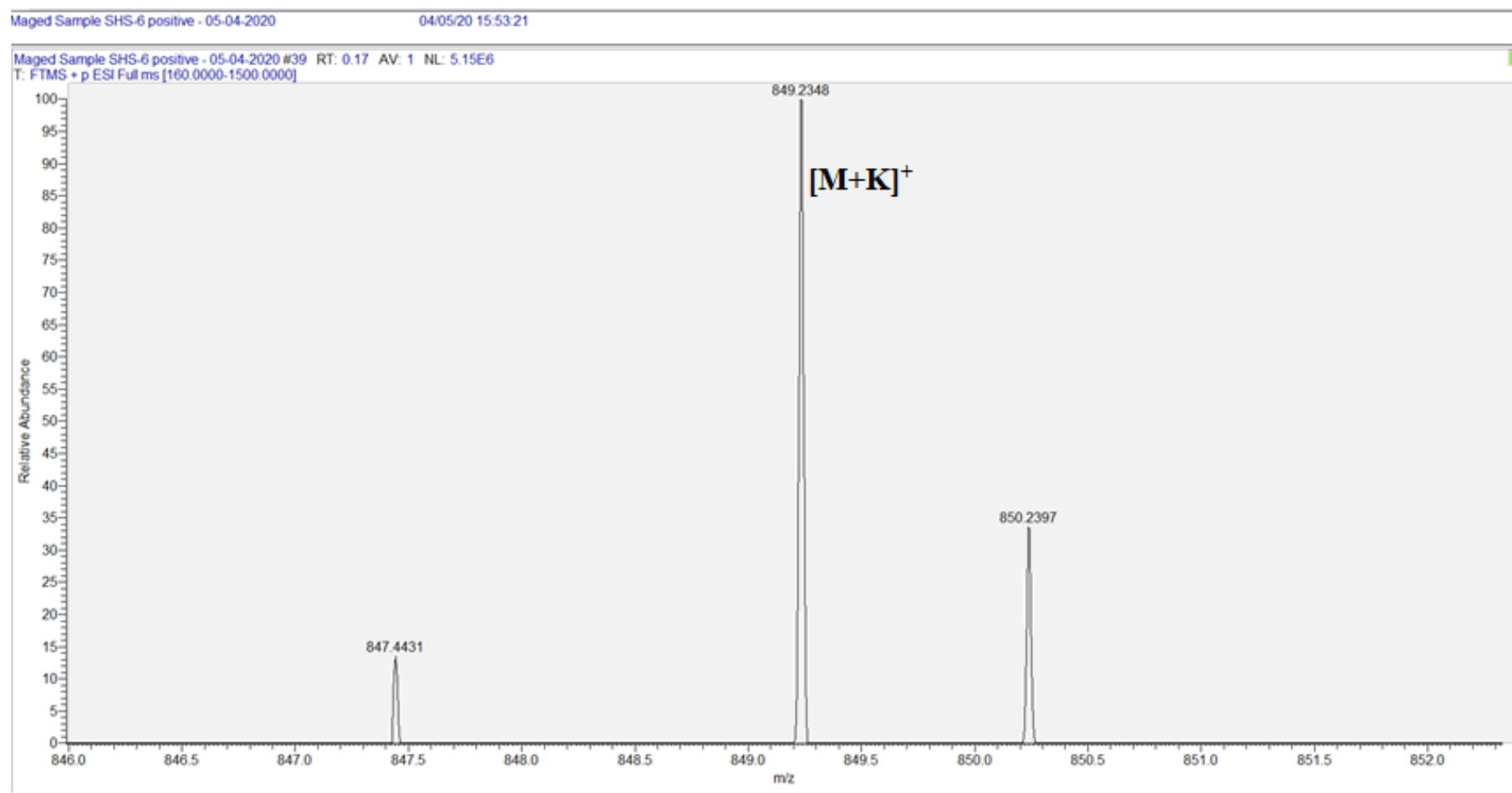


Figure S81. HRESIMS of compound 3 (positive mode).

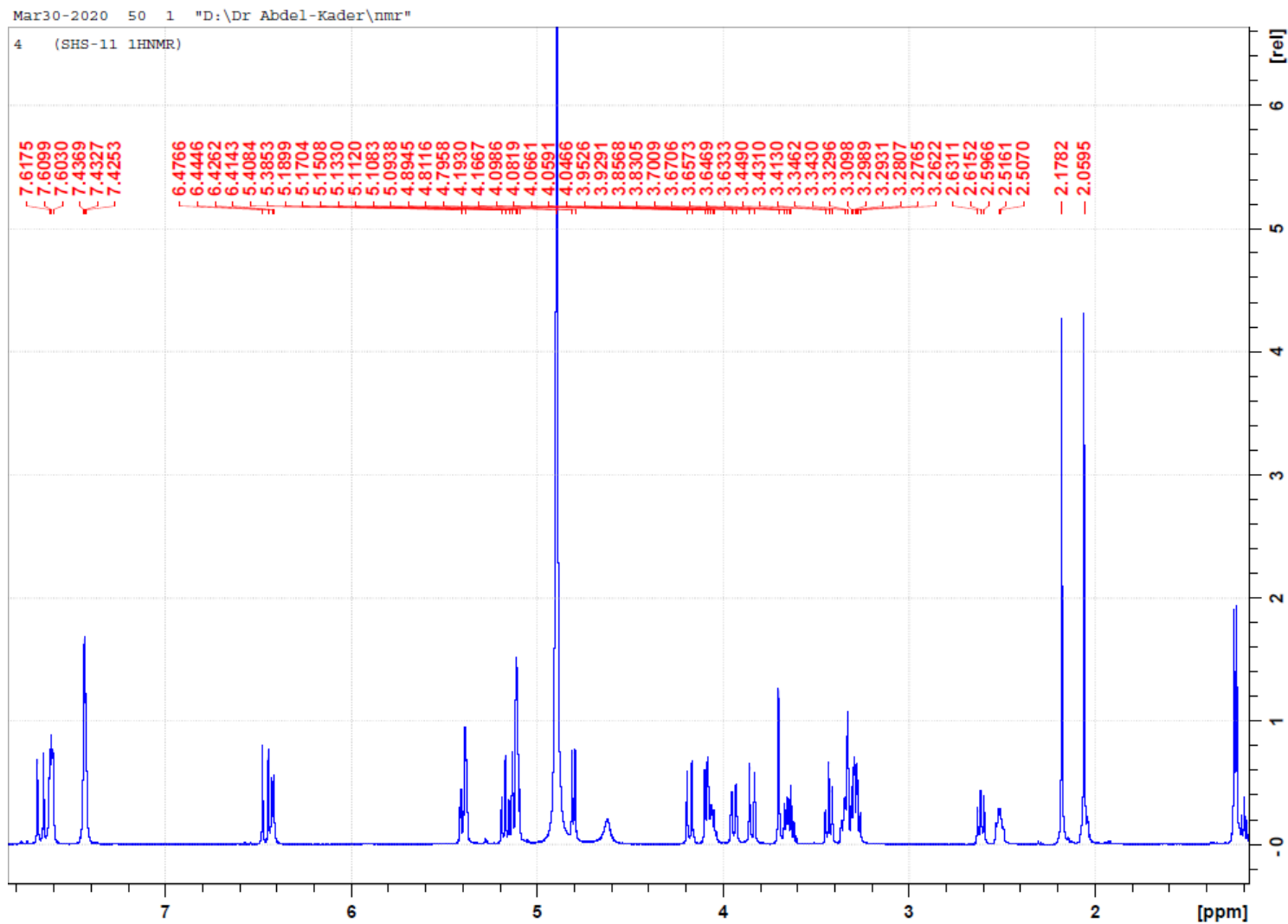


Figure S82. ¹H NMR spectrum of compound 4.

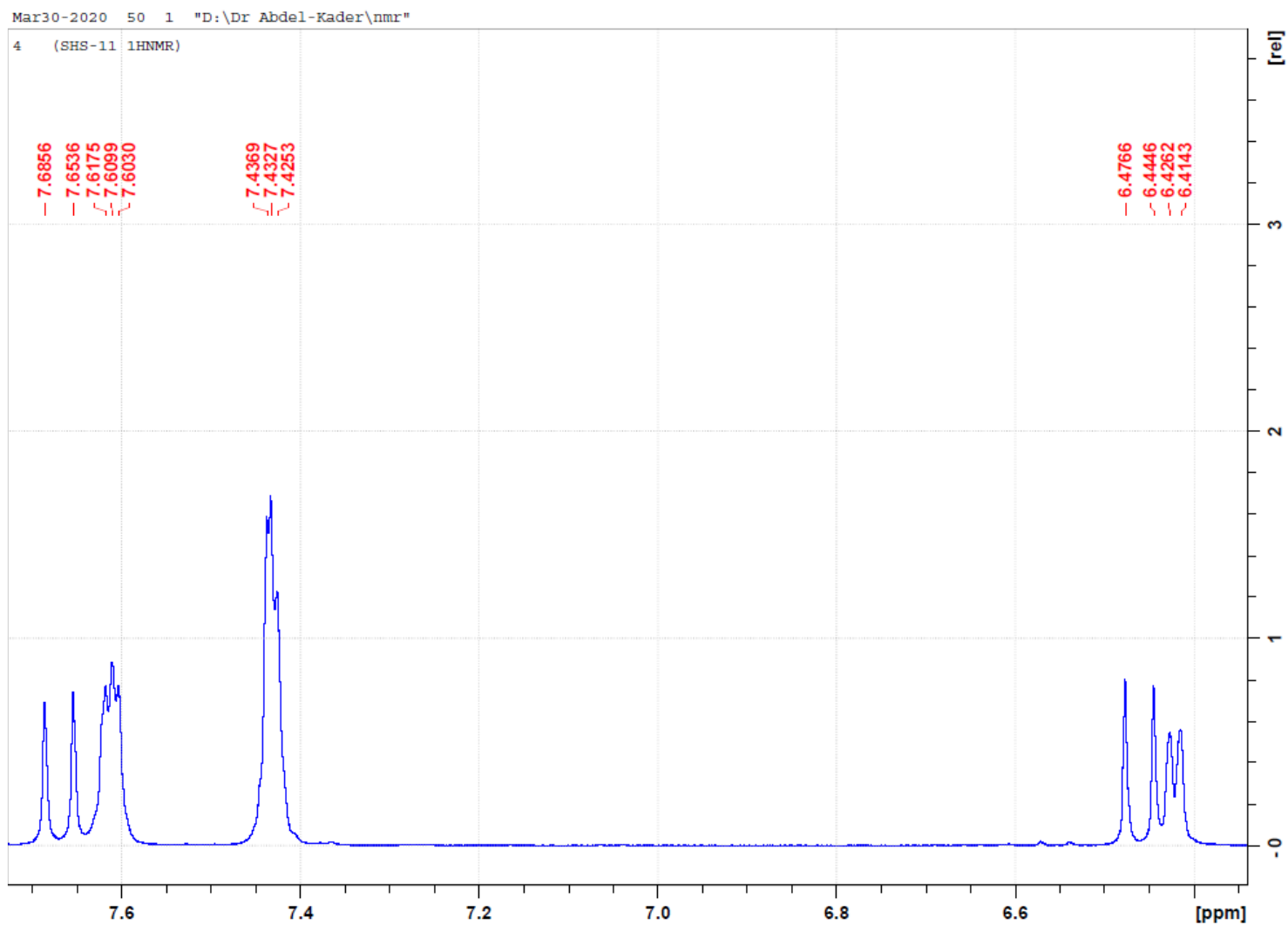


Figure S83. ¹HNMR spectrum of compound 4 (expansion).

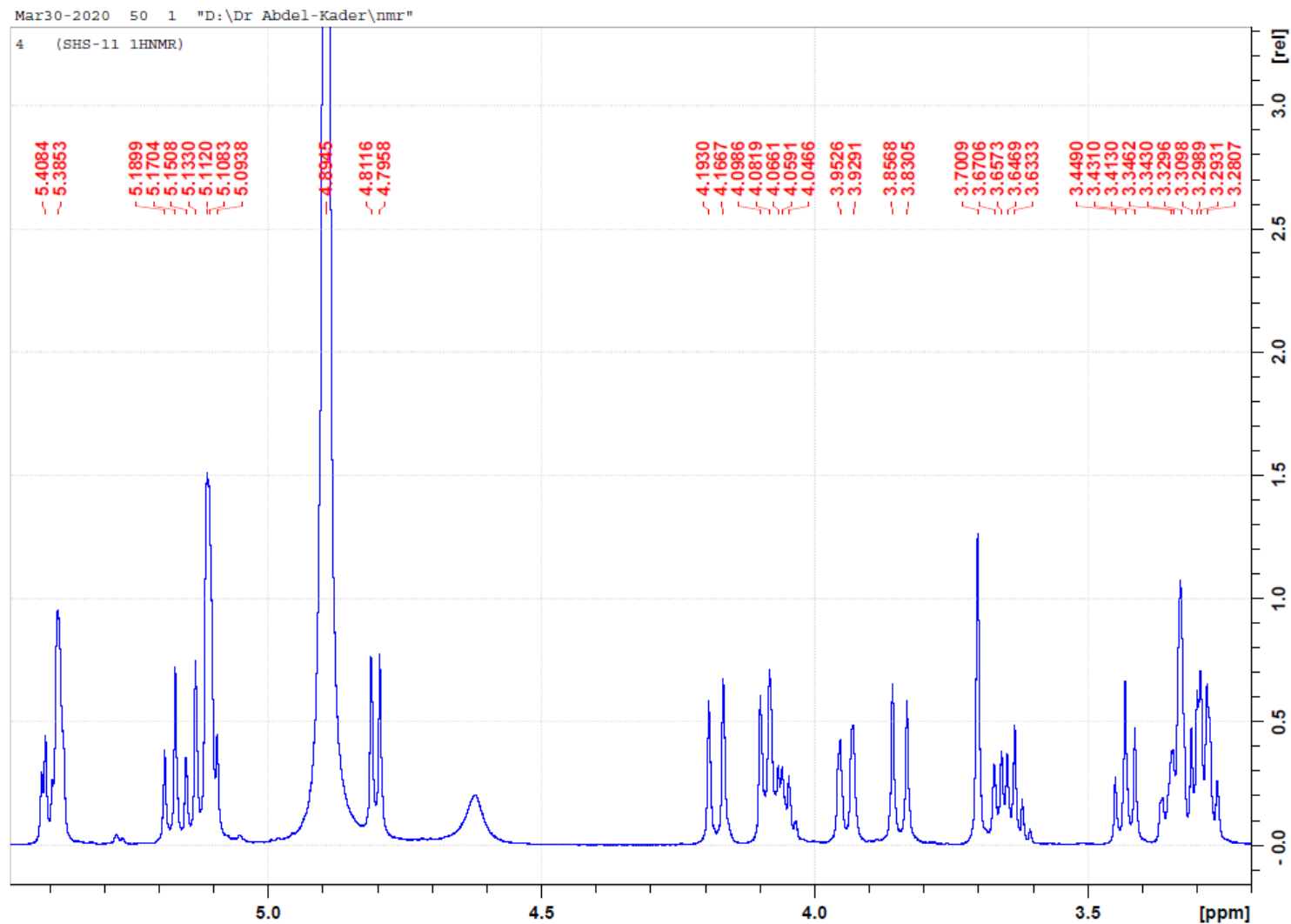


Figure S84. ¹HNMR spectrum of compound 4 (expansion).

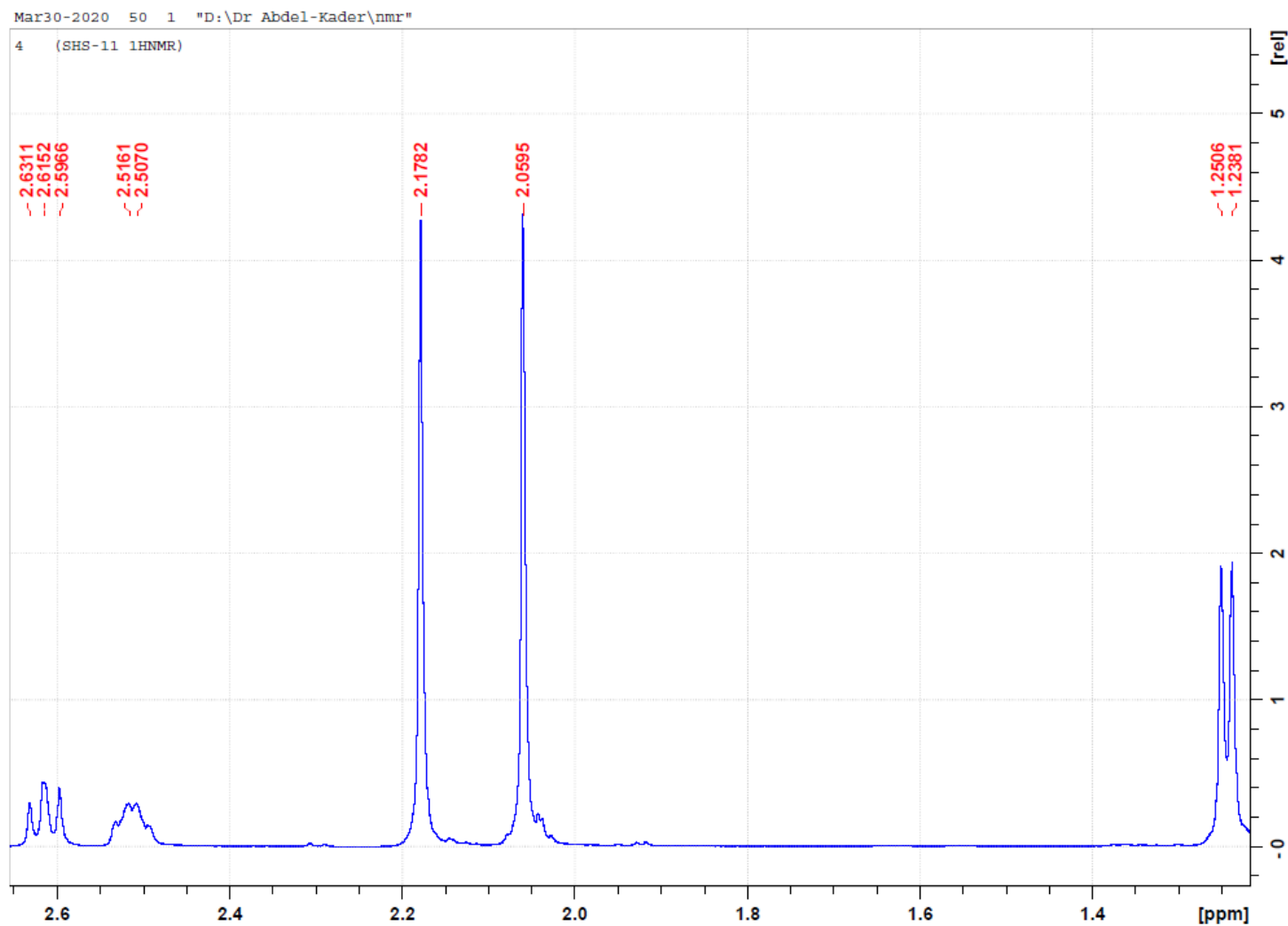


Figure S85. ¹HNMR spectrum of compound 4 (expansion).

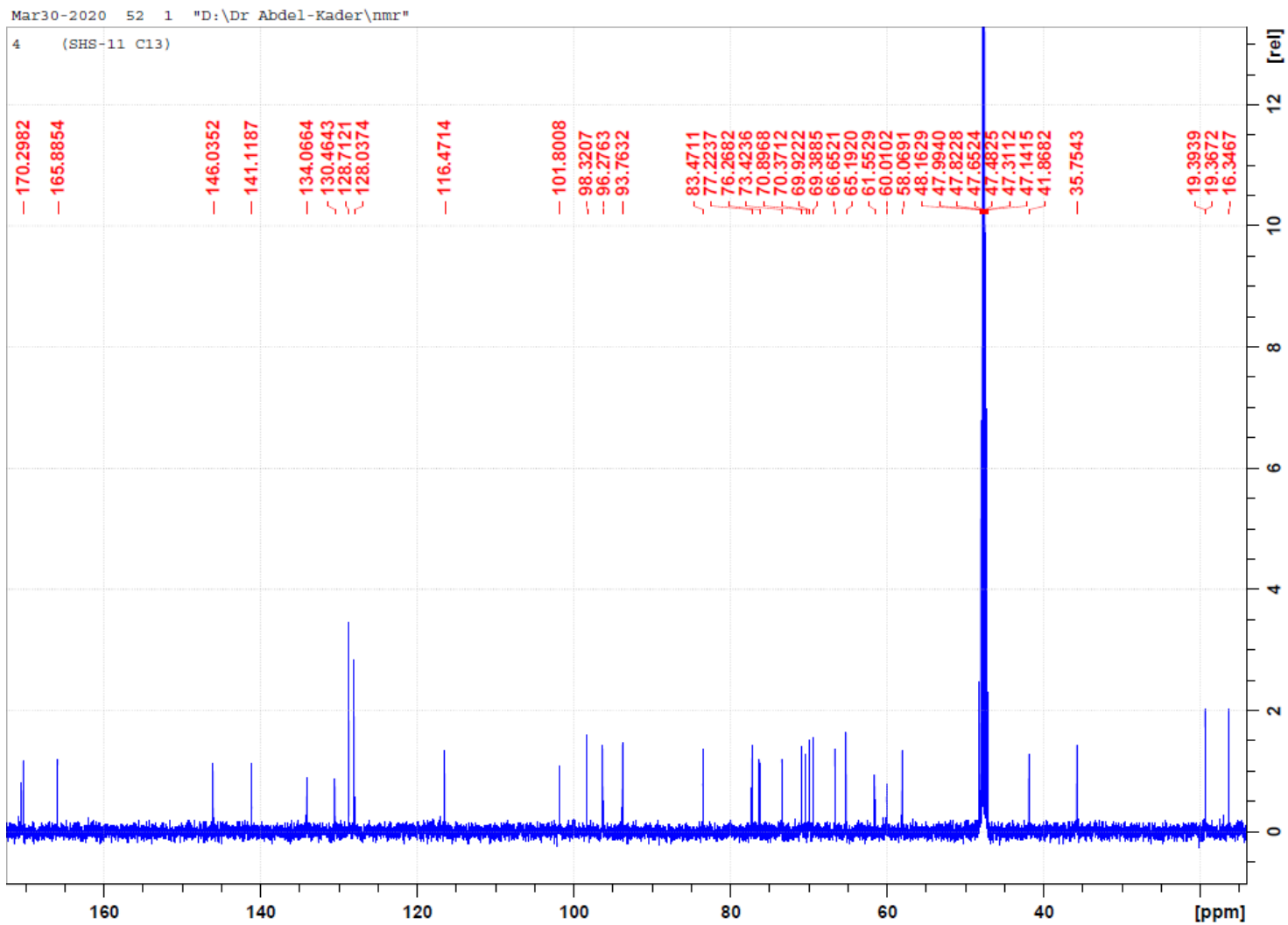


Figure S86. ¹³CNMR spectrum of compound 4.

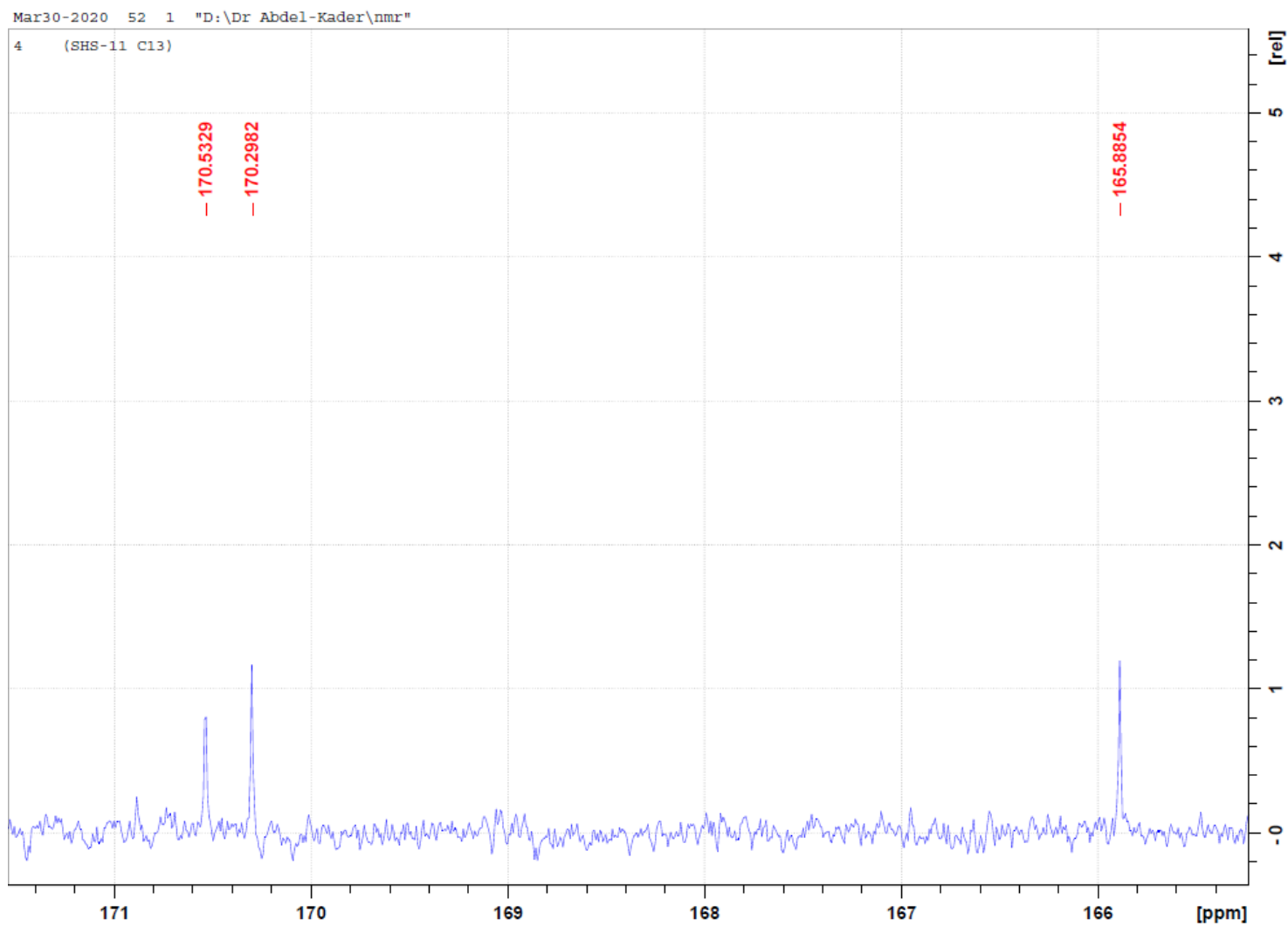


Figure S87. ^{13}C NMR spectrum of compound 4 (expansion).

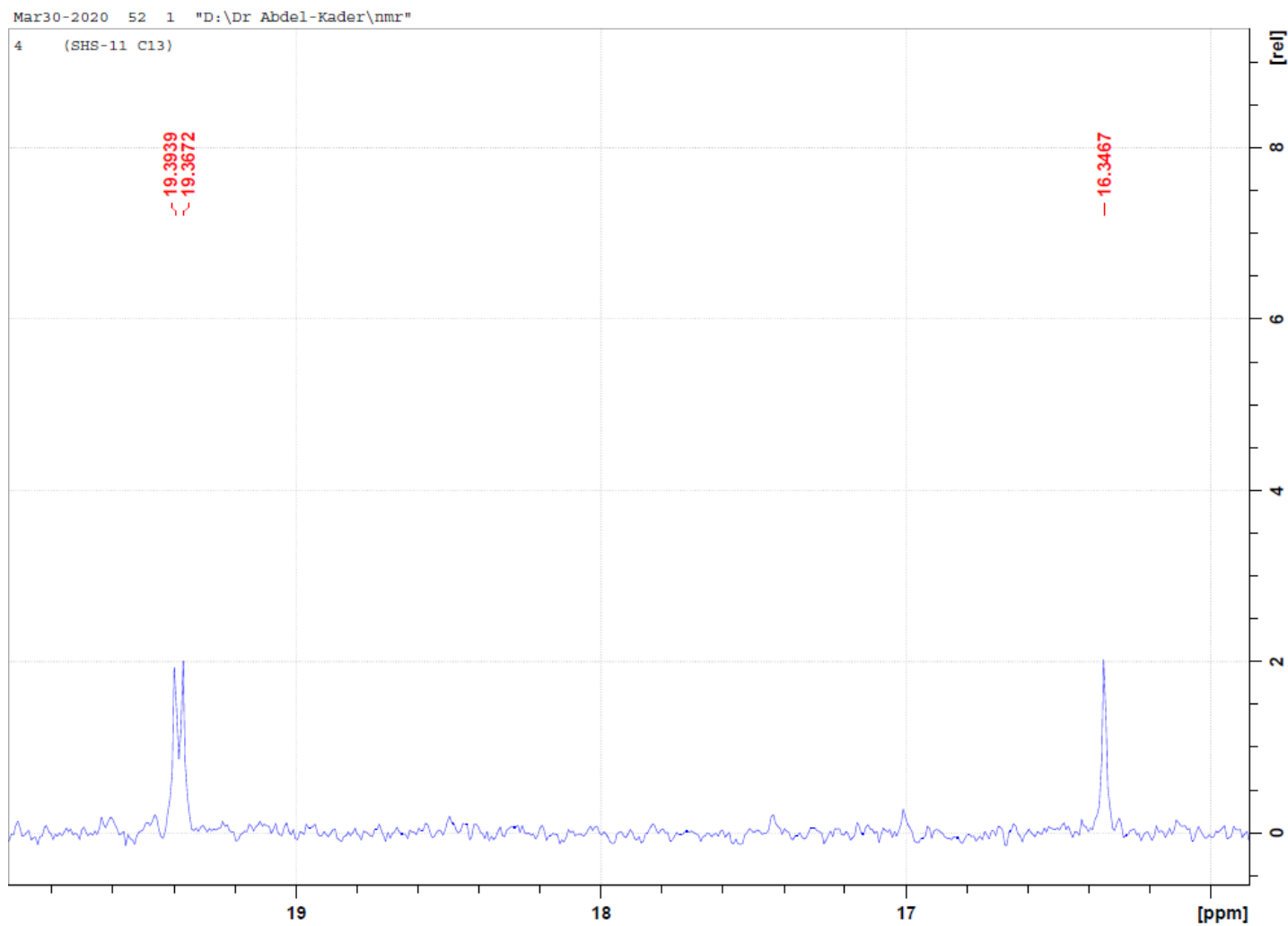


Figure S88. ^{13}C NMR spectrum of compound 4 (expansion).

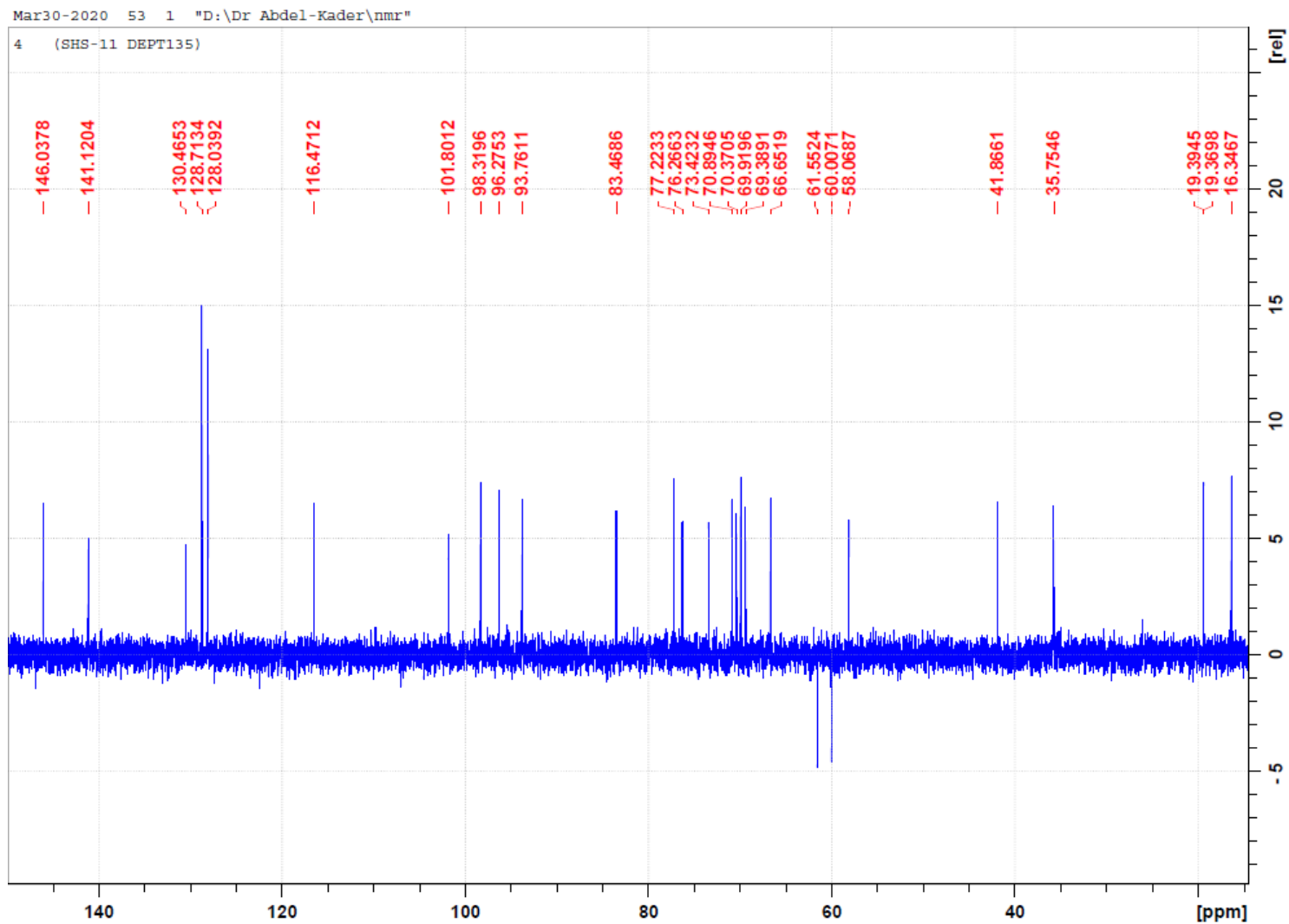


Figure S89. DEPT135 spectrum of compound 4.

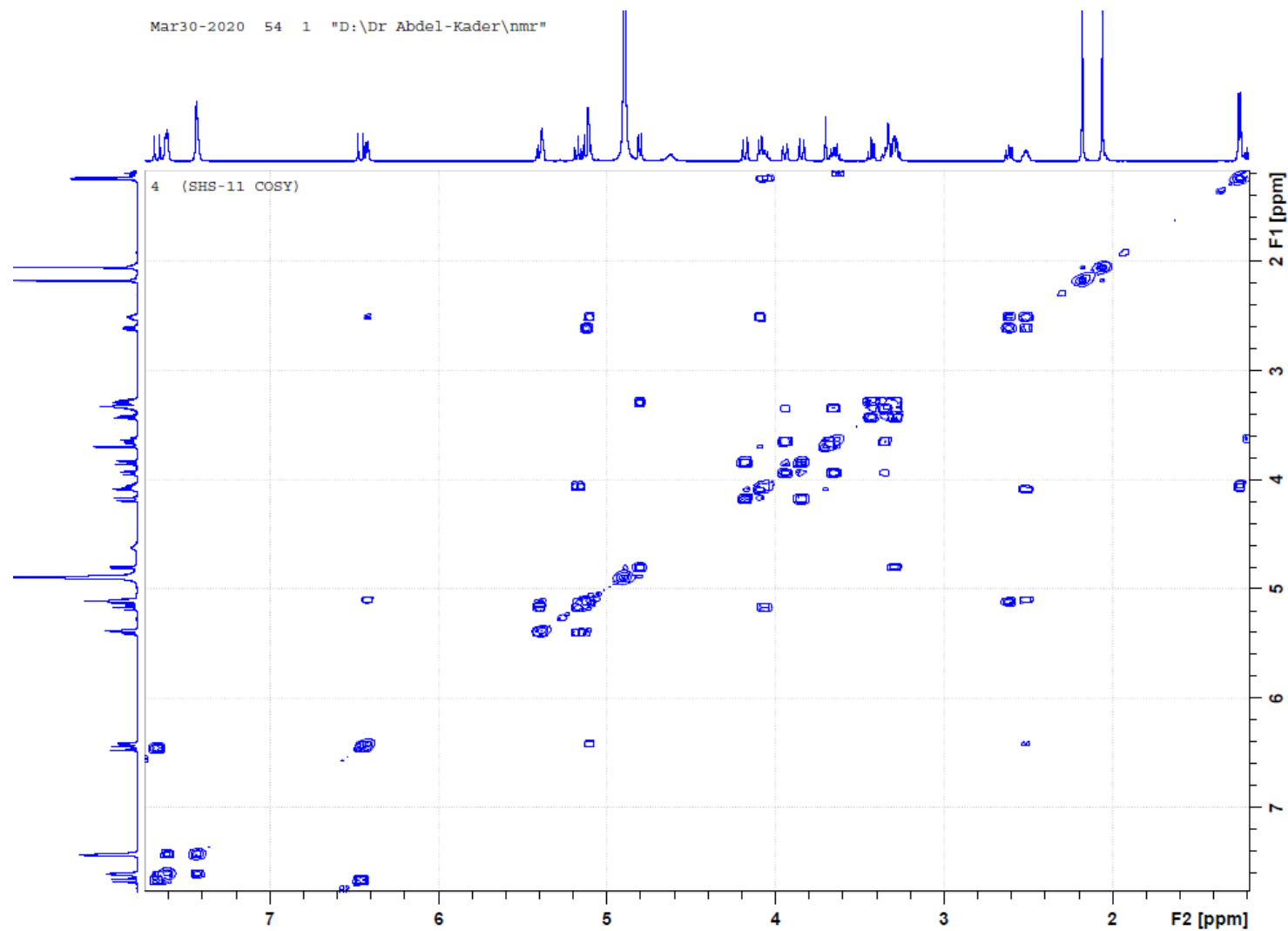


Figure S90. COSY spectrum of compound 4.

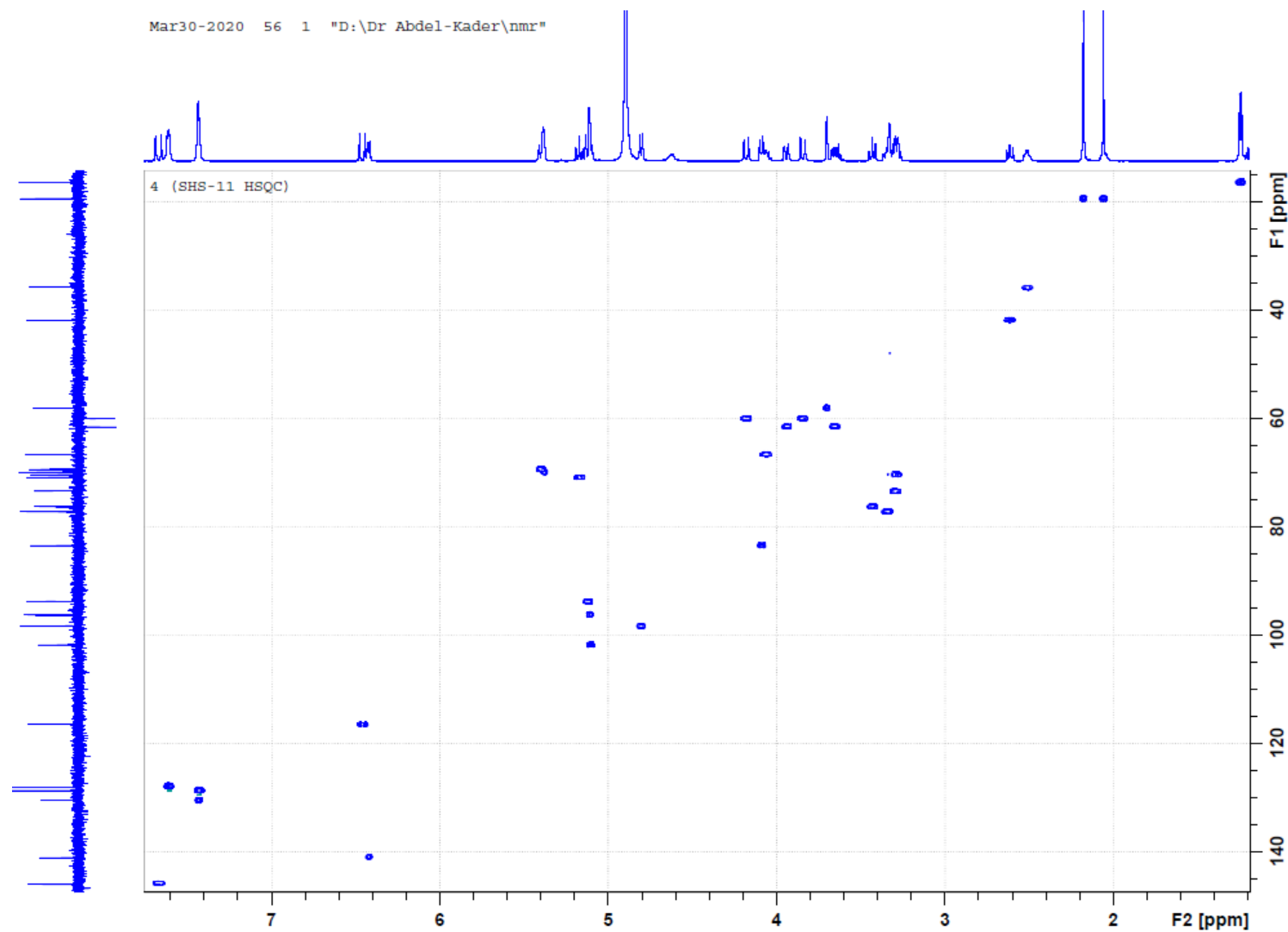


Figure S91. HSQC spectrum of compound 4.

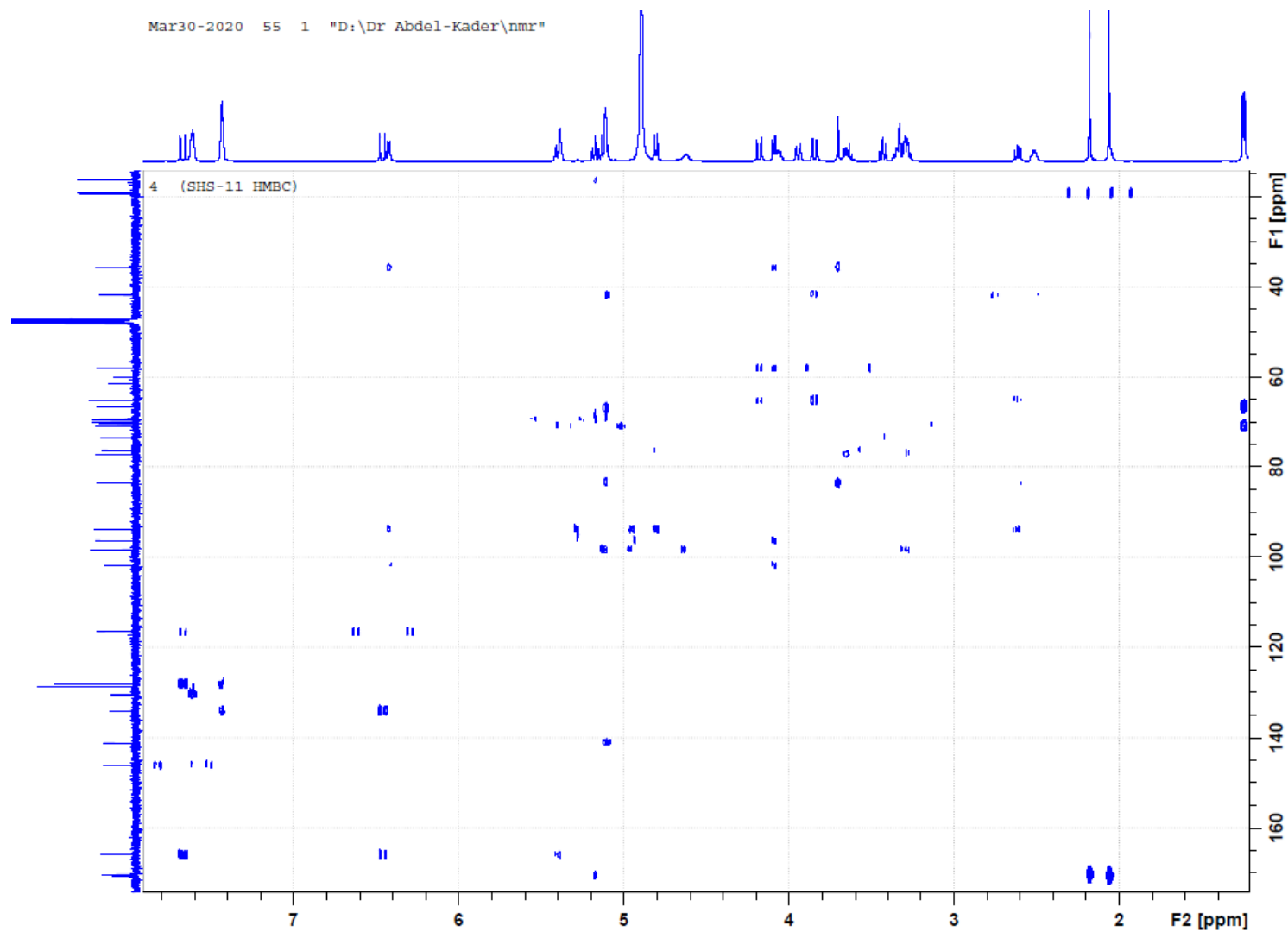


Figure S92. HMBC spectrum of compound 4.

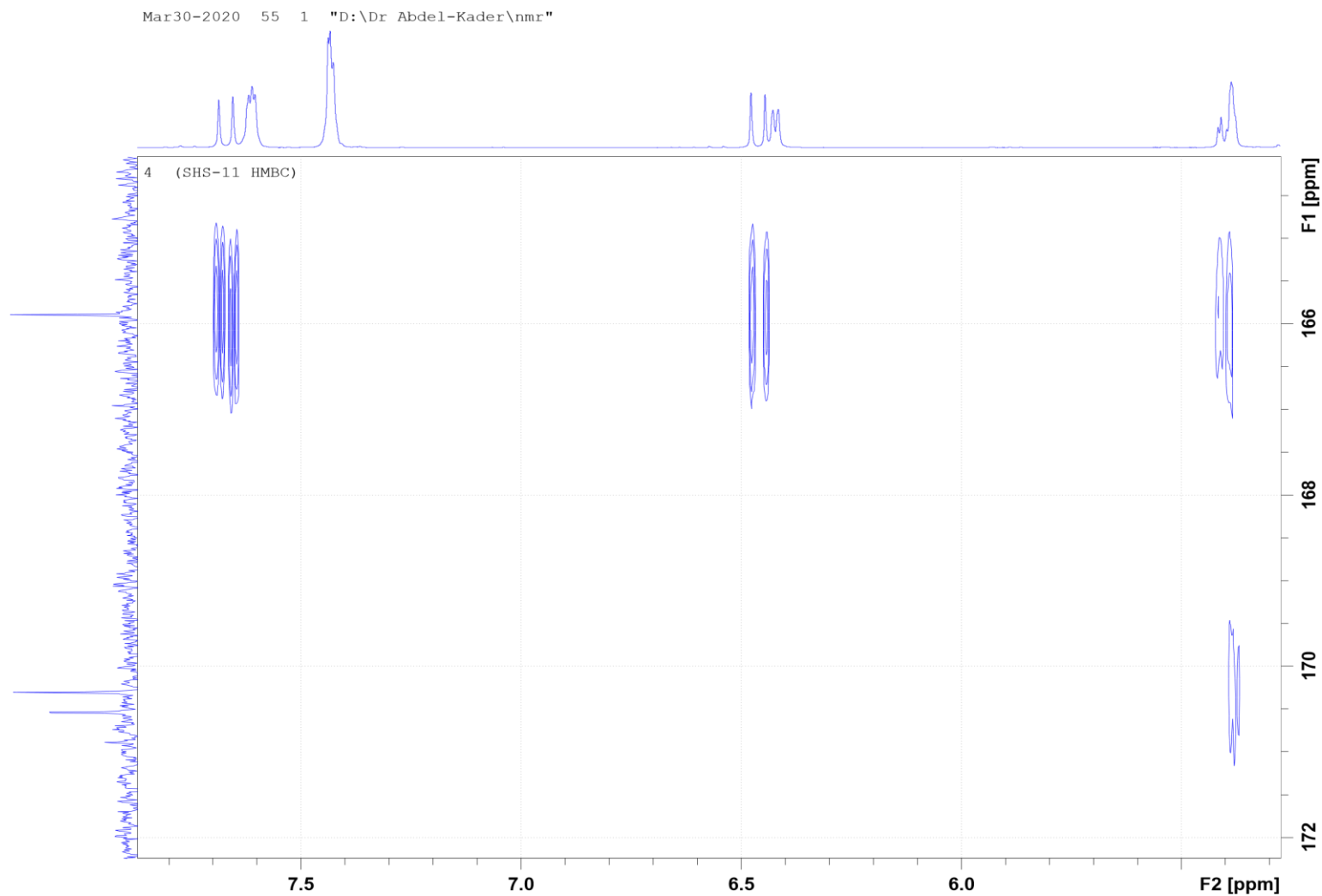


Figure S93. HMBC spectrum of compound 4 (expansion).

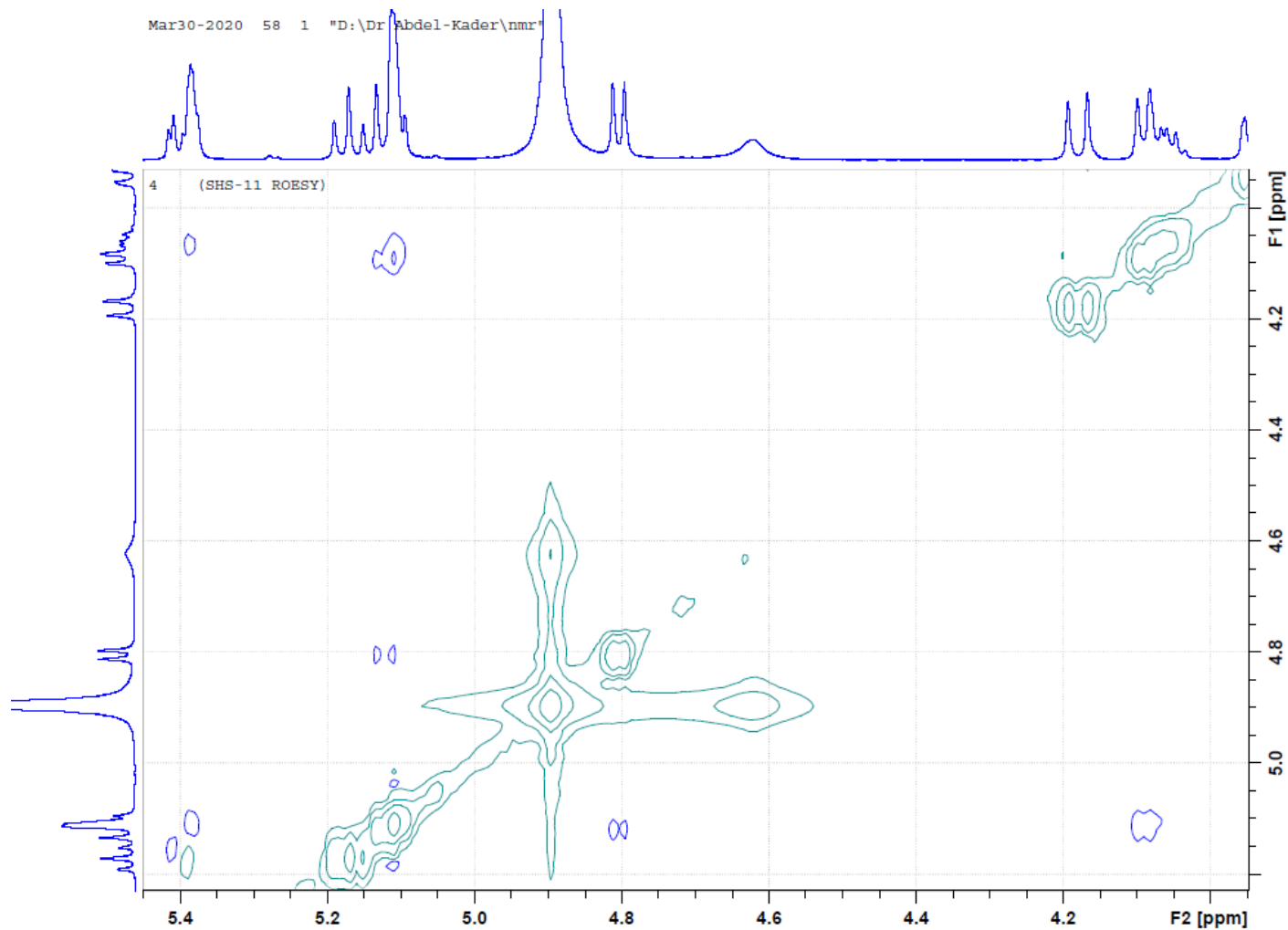


Figure S94. ROESY spectrum of compound 4 (expansion).

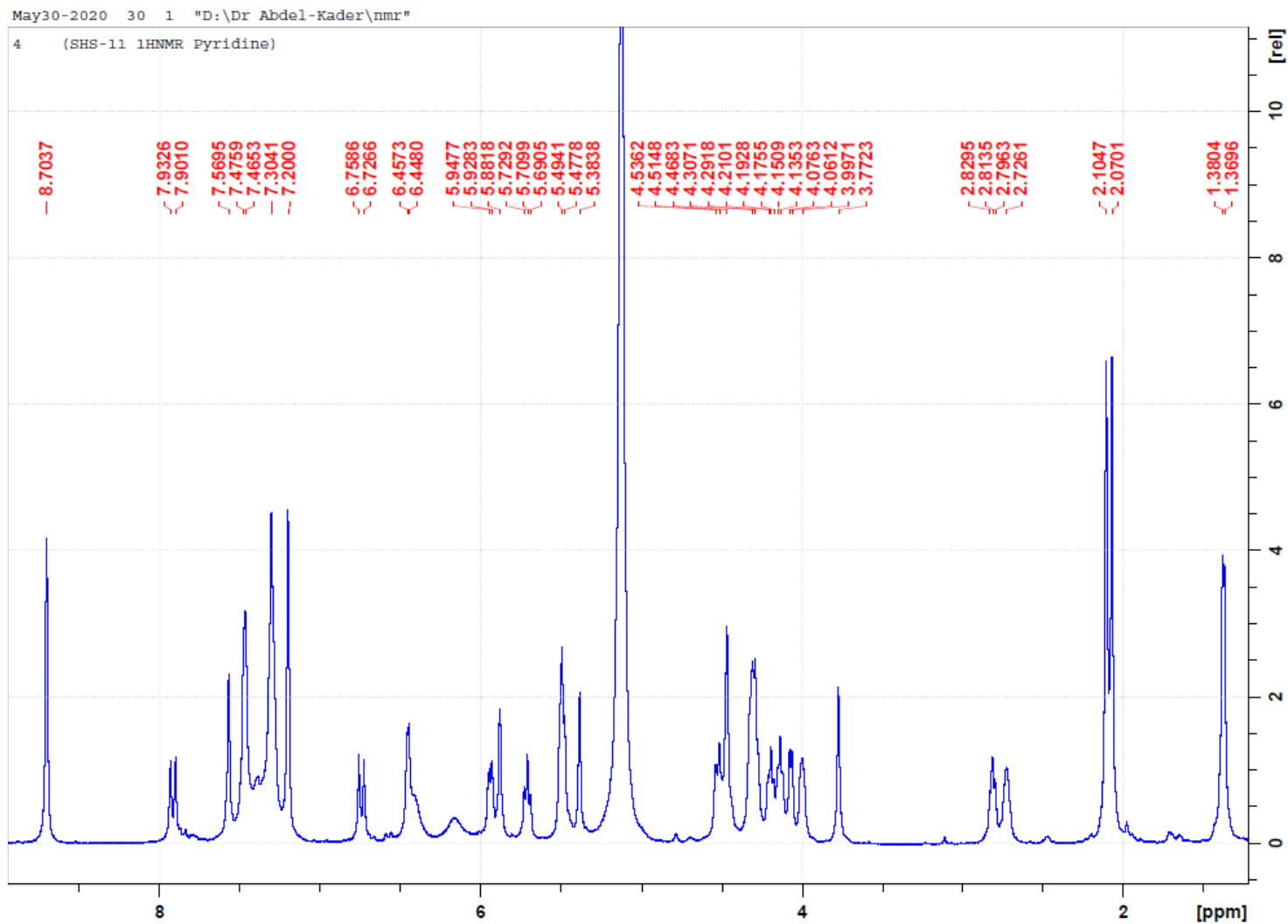


Figure S95. ¹HNMR spectrum of compound 4 in Pyridine.

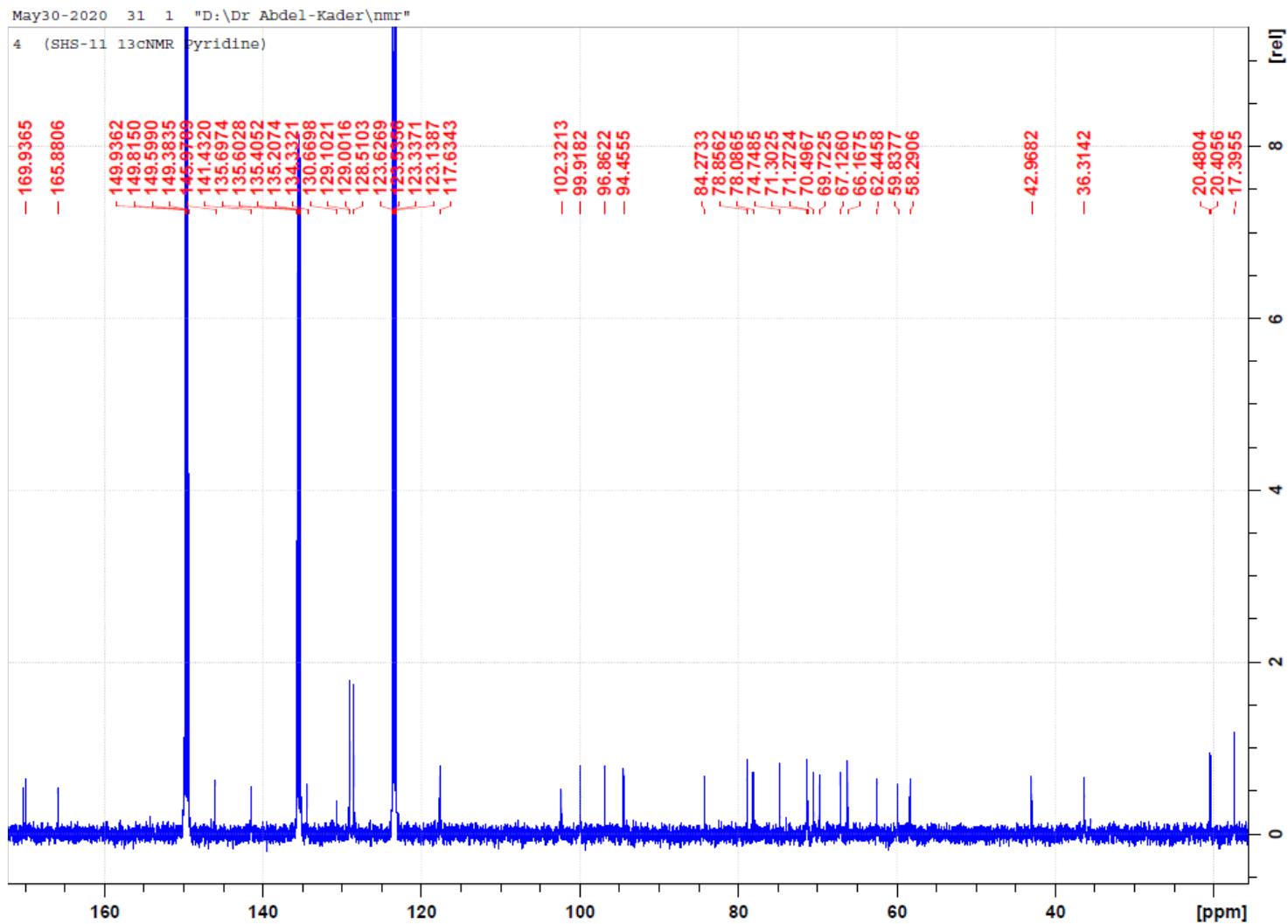


Figure S96. ¹³CNMR spectrum of compound 4 in Pyridine.

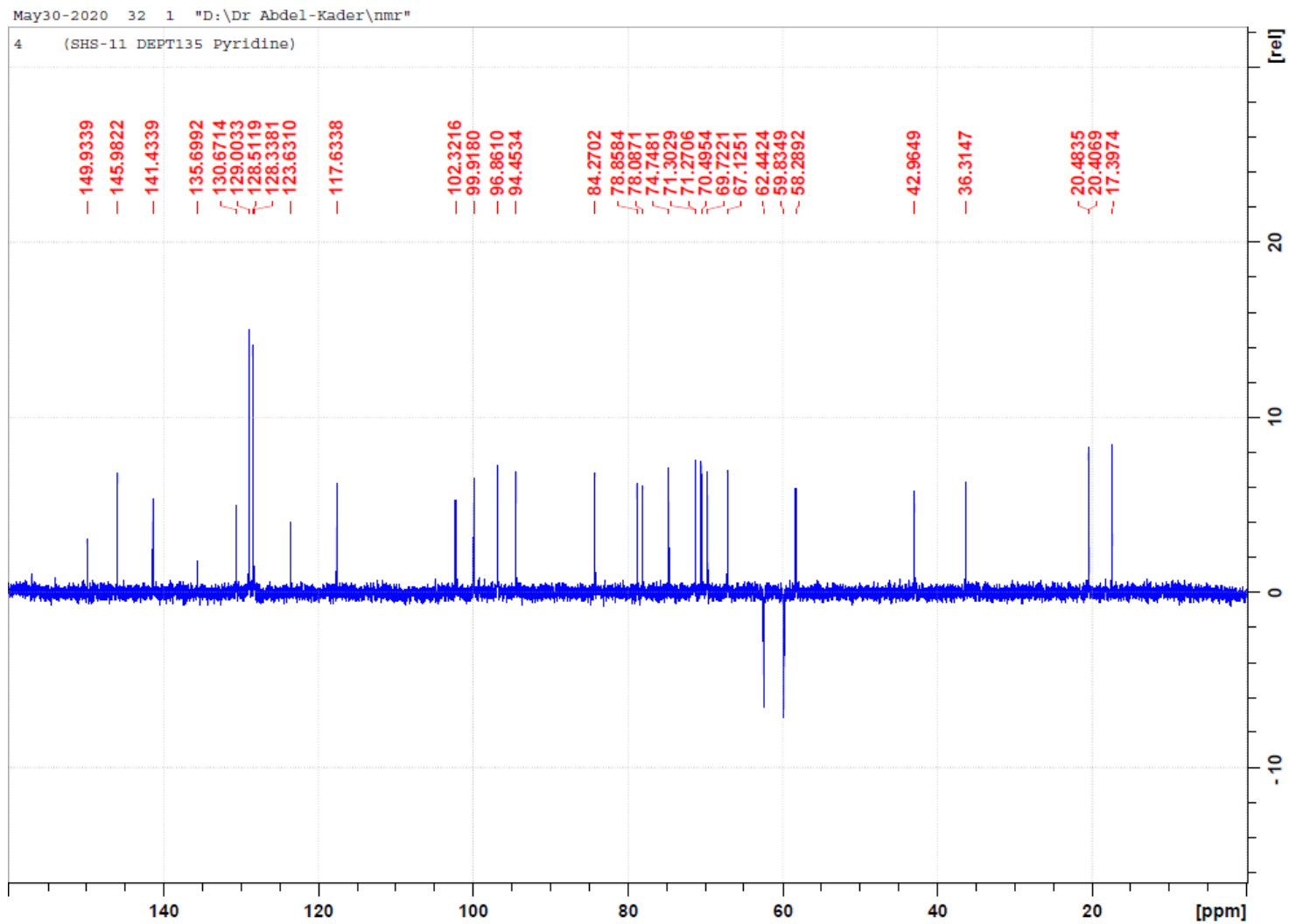


Figure S97. DEPT135 spectrum of compound 4 in Pyridine.

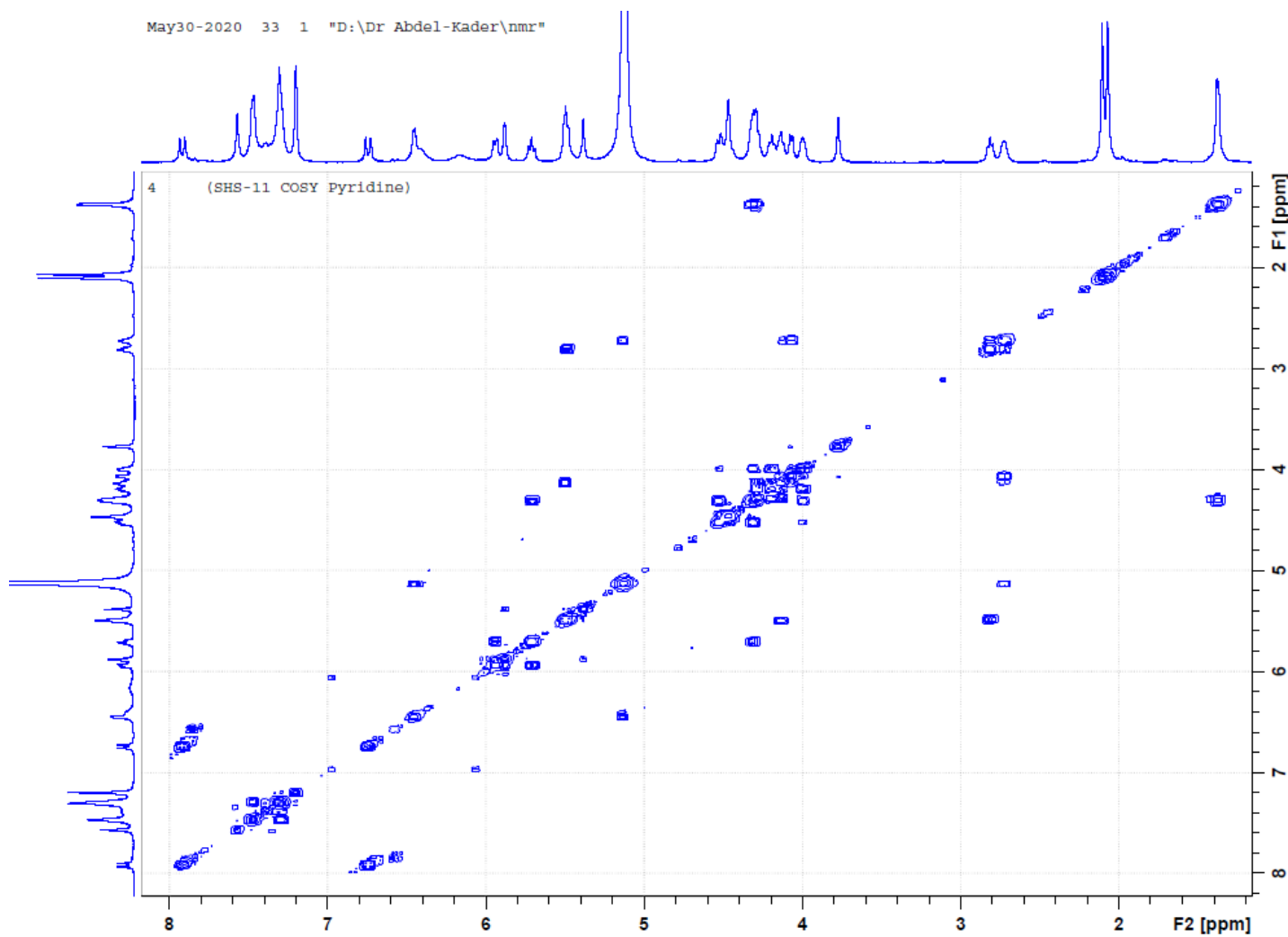


Figure S98. COSY spectrum of compound 4 in Pyridine.

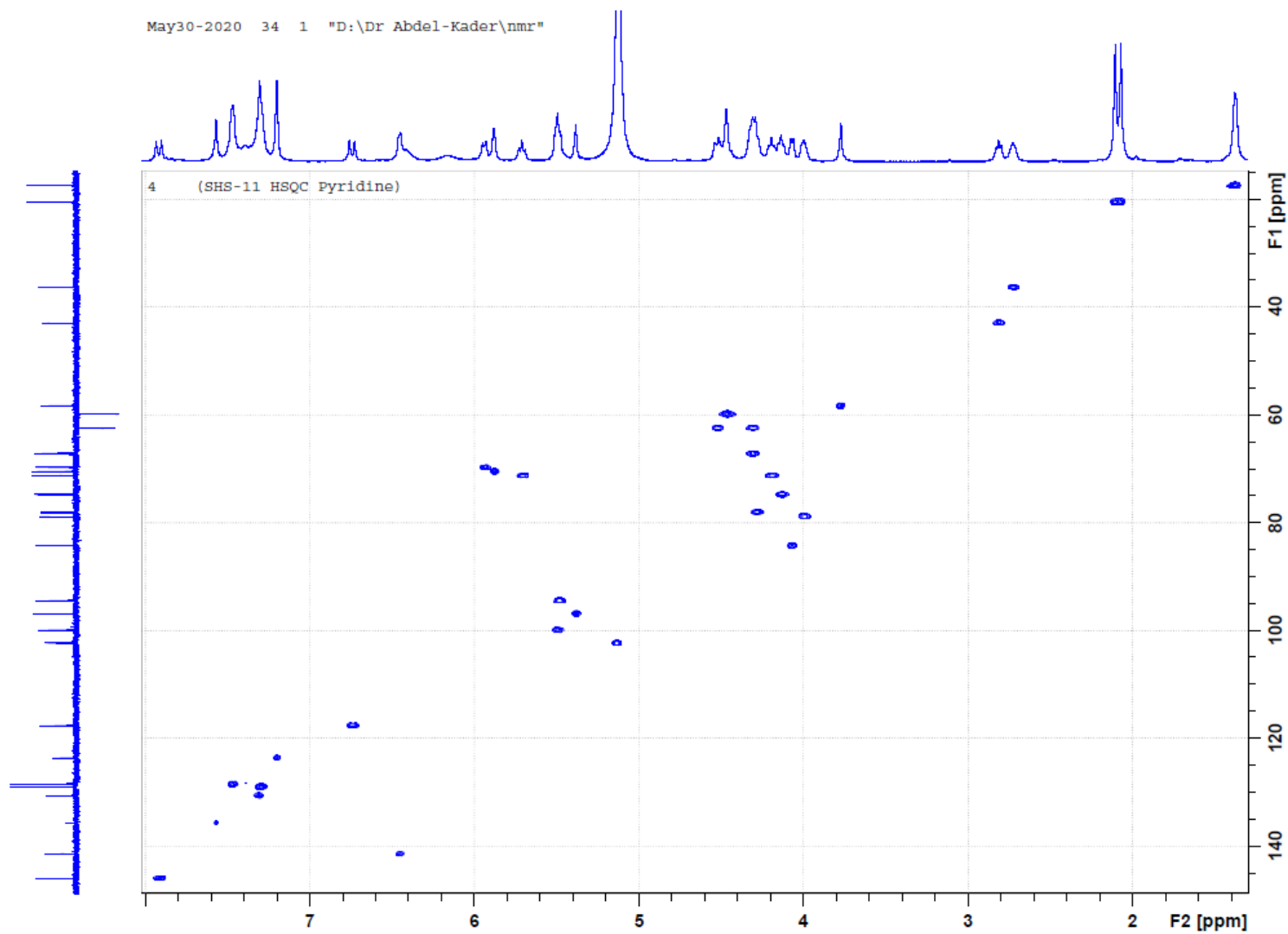


Figure S99. HSQC spectrum of compound 4 in Pyridine.

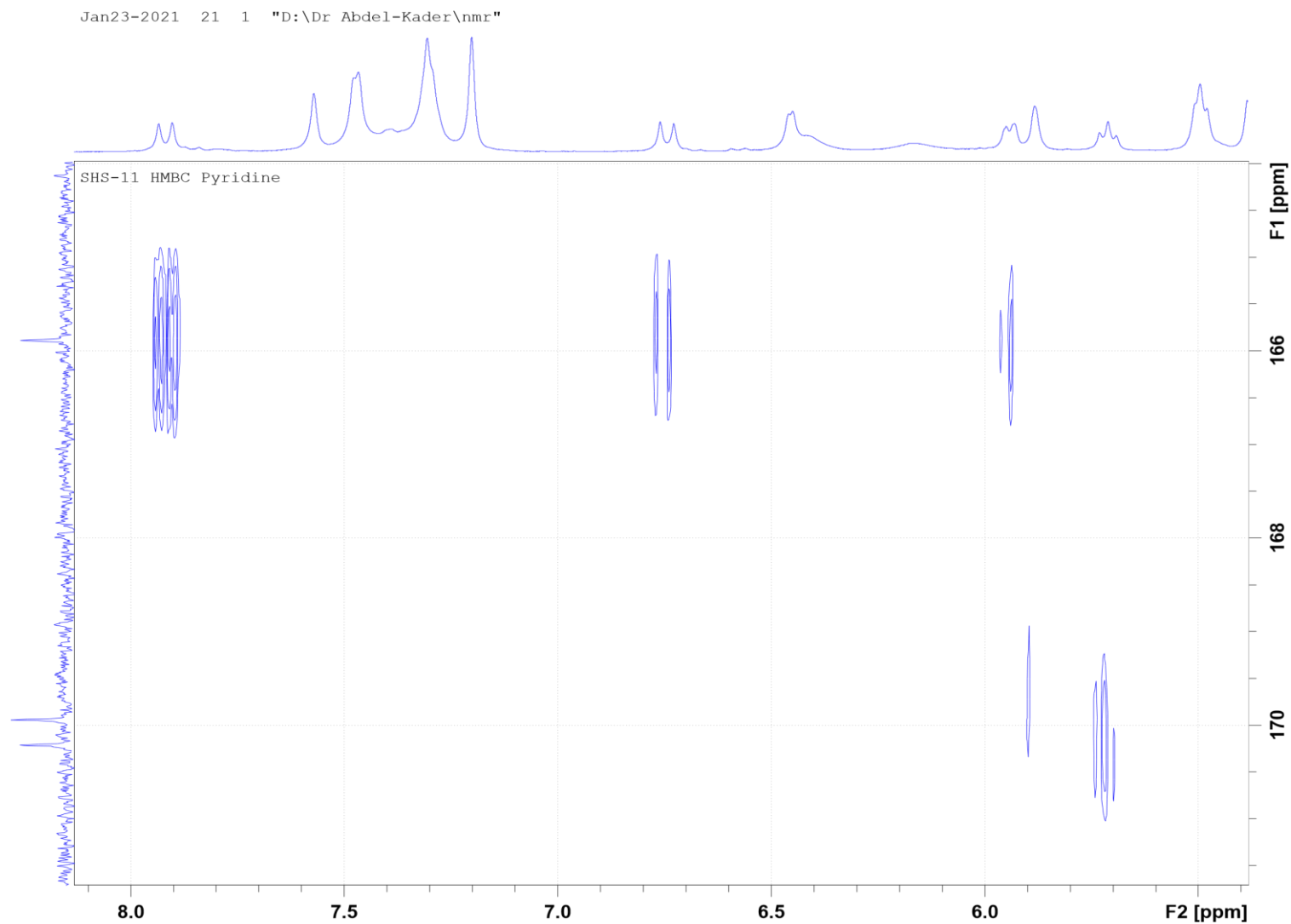


Figure S100. HMBC spectrum of compound 4 in Pyridine (expansion).

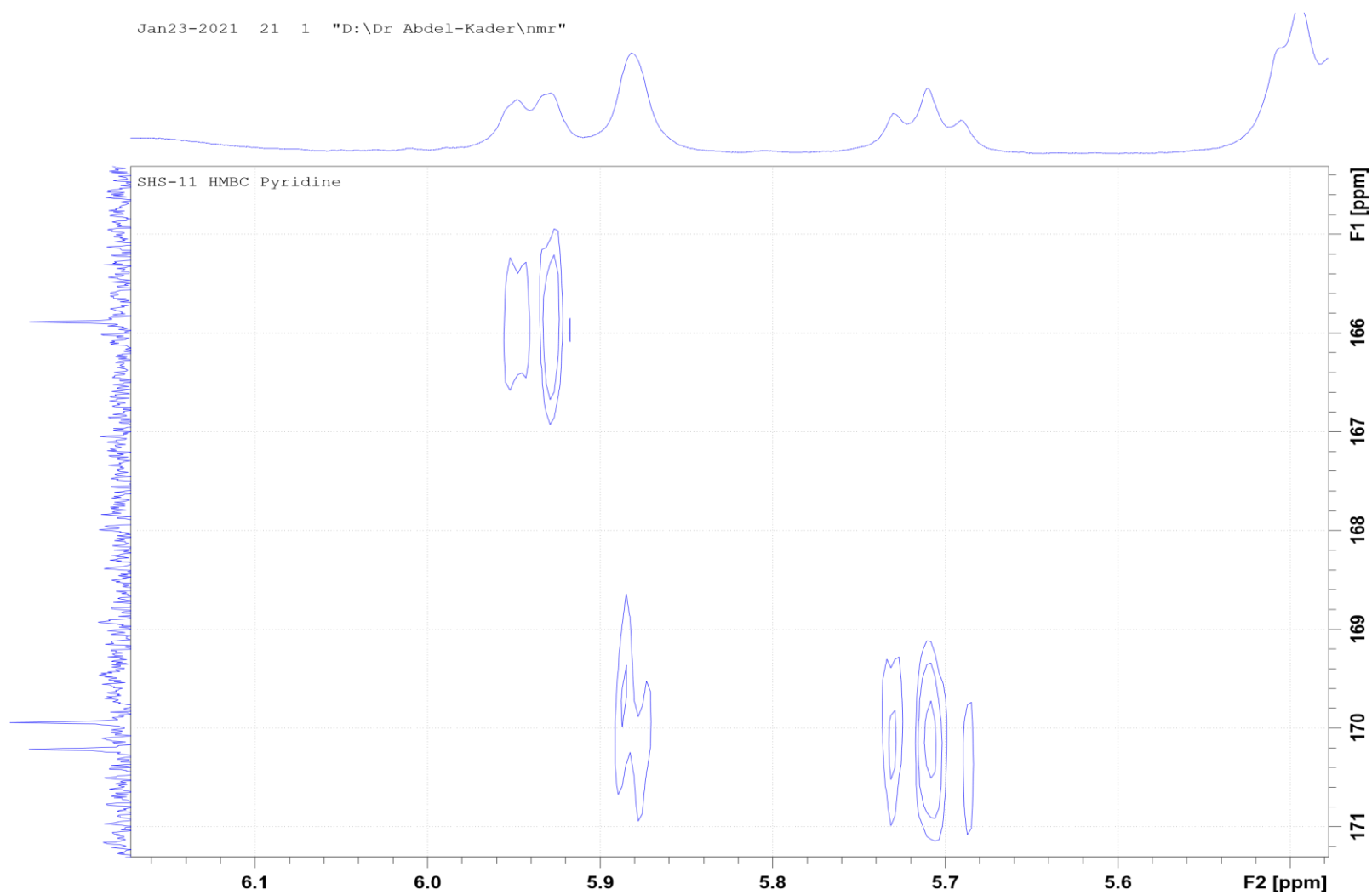


Figure S101. HMBC spectrum of compound 4 in Pyridine (expansion).

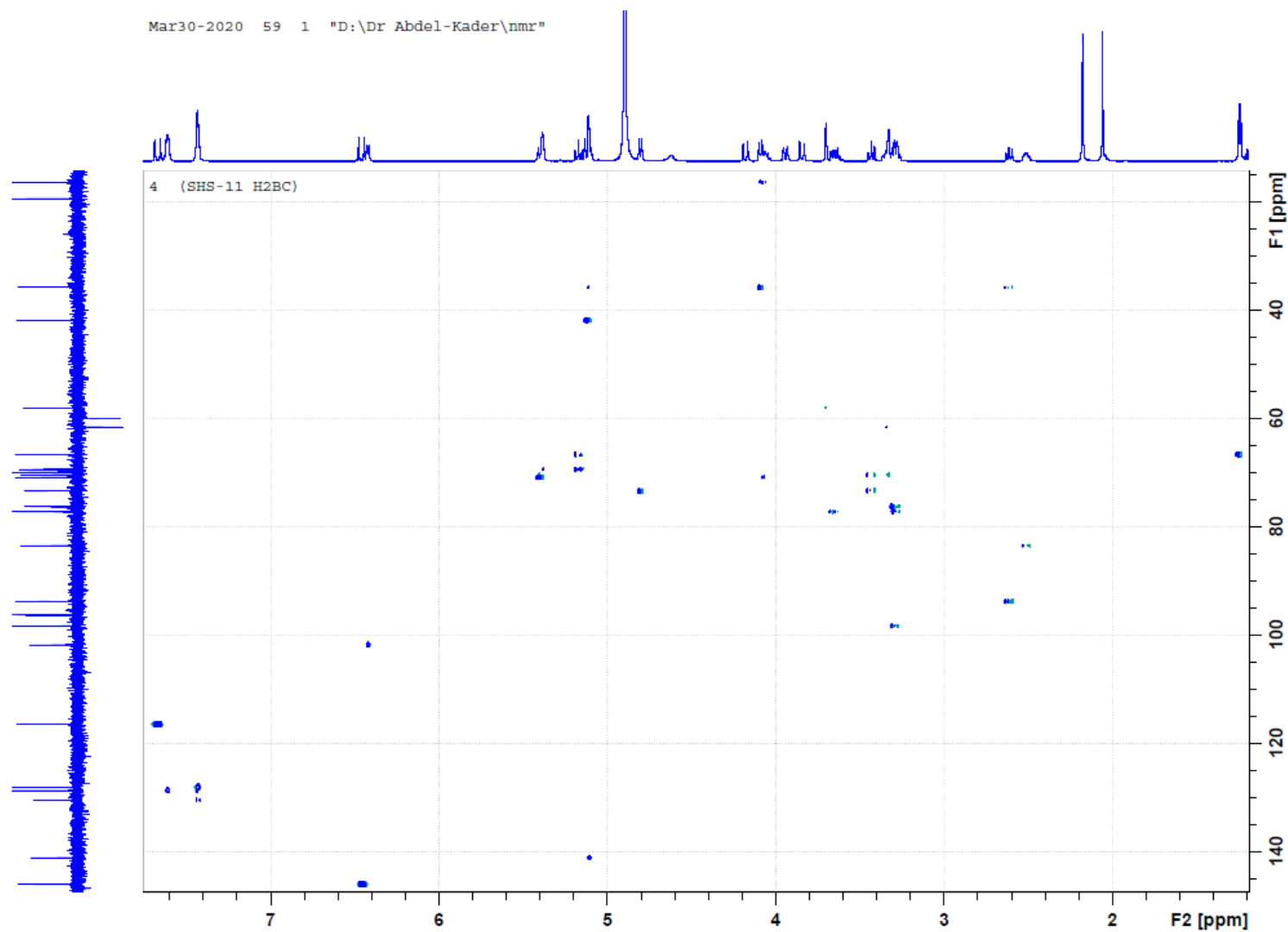


Figure S102. H2BC spectrum of compound 4 in Pyridine.

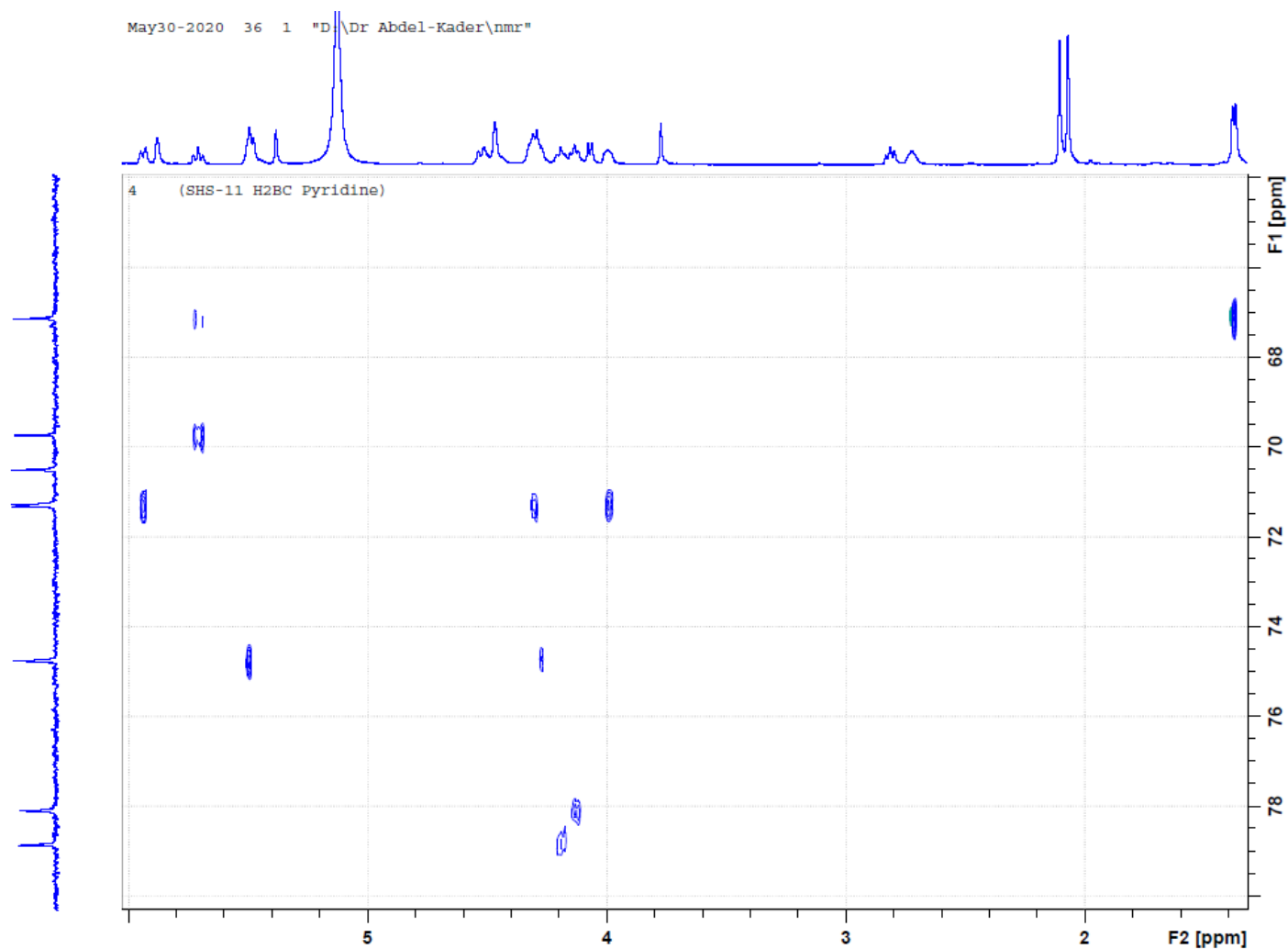


Figure S103. H2BC spectrum of compound 4 in Pyridine (expansion).

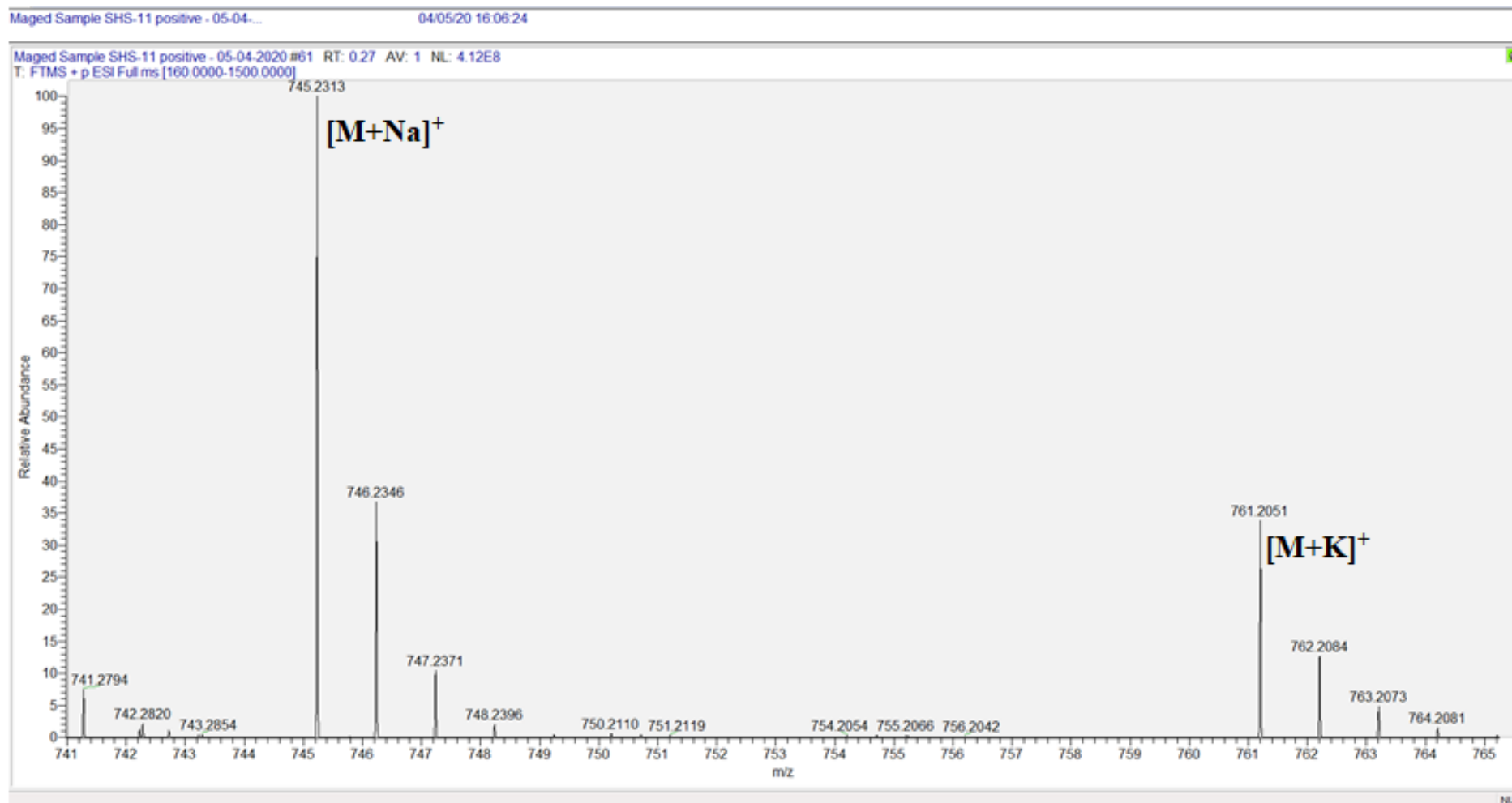


Figure S104. HRESIMS of compound 4 (positive mode).

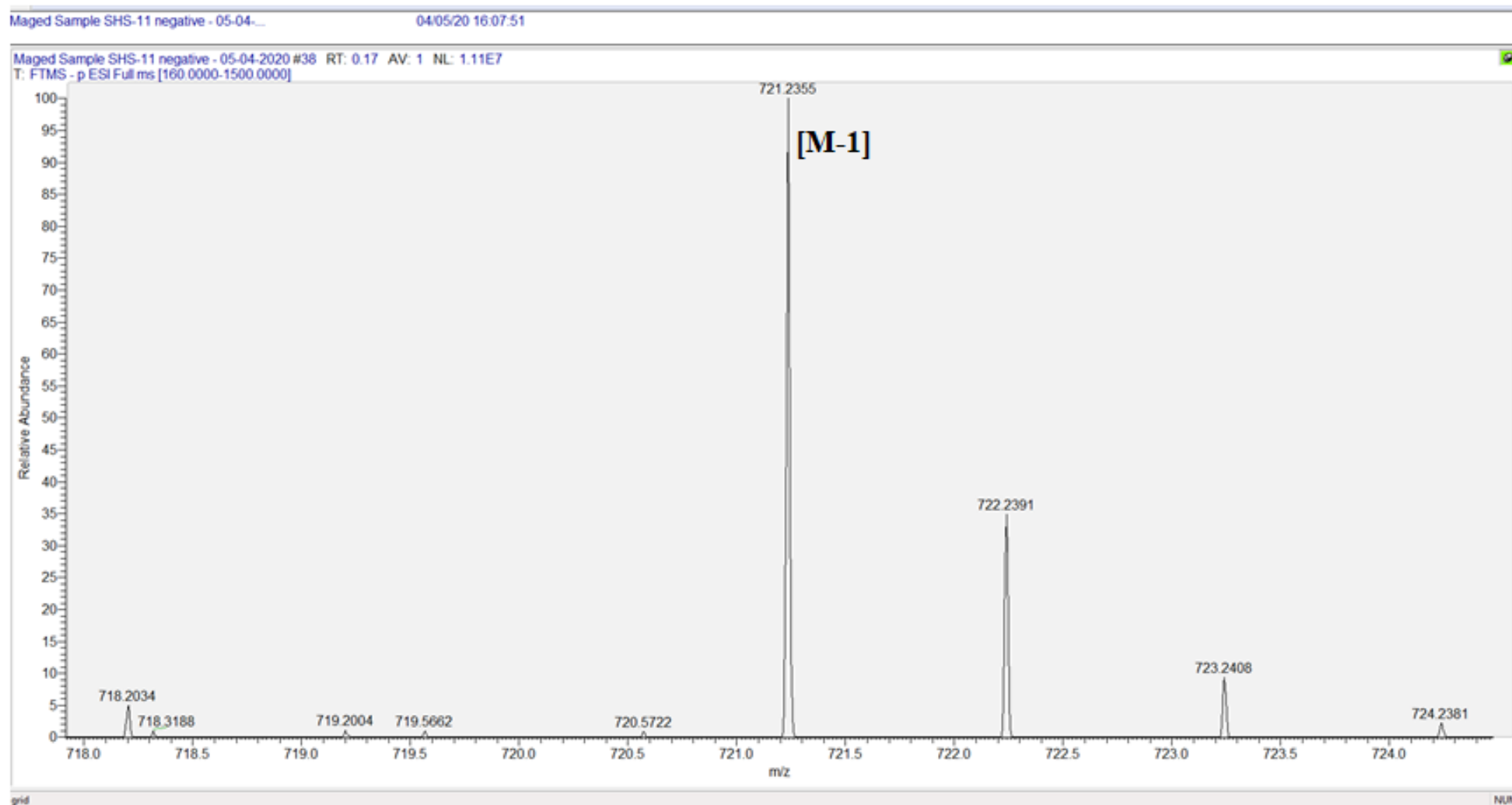


Figure S105. HRESIMS of compound 4 (negative mode).

Table S1. Effect of compounds 2-4, 6 on liver Serum Biochemical Parameters.

Treatment (n = 5)	AST(u/l)		ALT(u/l)		GGT(u/l)		ALP(u/l)		Bilirubin(mg/dl)	
	(Mean ±S.E.)	% change	(Mean ± S.E.)	% change	(Mean ± S.E.)	% change	(Mean ± S.E.)	% change	(Mean ± S.E.)	% change
Normal	84.66±2.76		23.31±1.84		3.75±0.31		326.00±16.23		0.5±0.03	
Pa[§]	242.83±12.56*** ^a		205.66±15.09*** ^a		12.03±0.89*** ^a		566.83±11.13*** ^a		2.40±0.13*** ^a	
Sil[§]	151.16±13.54*** ^b	37.74	116.35±8.40*** ^b	43.29	7.51±0.44*** ^b	37.53	412.00±14.01*** ^b	27.31	1.10±0.12*** ^b	54.15
2 + Pa[§]	212.66±7.27 ^b	12.42	192.33±10.58 ^b	6.25	10.75±0.59 ^b	10.66	526.33±14.75* ^b	7.14	2.31±0.06** ^b	3.87
3 + Pa[§]	186.33±7.24** ^b	23.26	136.00±7.11** ^b	33.71	7.46±0.30*** ^b	37.95	472.33±11.87*** ^b	16.67	1.74±0.09** ^b	27.70
4 + Pa[§]	209.16±5.68* ^b	13.86	150.33±6.75** ^b	26.72	7.68±0.19*** ^b	36.14	487.50±9.68*** ^b	13.99	1.80±0.06** ^b	25.00
6 + Pa[§]	208.33±7.05* ^b	14.20	188.33±11.74 ^b	7.96	9.36±0.27* ^b	22.16	518.33±13.04* ^b	8.55	2.19±0.13 ^b	8.79

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.00$ ^a as compared to control group ^b As compared to Pa group [§]Doses: Pa (500 mg/kg), Sil, 2-4, 6 (20.7 μ mole/kg).

Table S2. Effect of compounds 2-4, 6 on liver and kidney TP and NP-SH.

Treatment (n = 5)	Liver		Kidney	
	TP (g/l)	NP-SH(nmol/g)	TP (g/l)	NP-SH(nmol/g)
Normal	77.93±2.55	3.91±0.09	91.87±7.95	0.81±0.02
Pa[§]	24.31±1.96*** ^a	1.45±0.14*** ^a	26.55±3.40*** ^a	0.26±0.02*** ^a
Sil[§]	73.04±6.63*** ^b	3.37±0.28*** ^b	60.54±5.17*** ^b	0.74±0.03*** ^b
2 + Pa[§]	26.15±3.14 ^b	1.44±0.19 ^b	30.55±2.30 ^b	0.36±0.06 ^b
3 + Pa[§]	37.36±3.72* ^b	3.43±0.30*** ^b	46.25±2.73*** ^b	0.74±0.06*** ^b
4 + Pa[§]	36.82±3.72* ^b	2.72±0.20*** ^b	43.04±2.44** ^b	0.52±0.05* ^b
6 + Pa[§]	36.08±2.55** ^b	2.54±0.28** ^b	39.80±4.04* ^b	0.48±0.05 ^b

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.00$ ^a as compared to control group ^b As compared to Pa group [§]Doses: Pa (500 mg/kg), Sil, 2-4, 6 (20.7 μ mole/kg).

Table S3. Effect of compounds **2-4, 6** on kidney Serum Biochemical Parameters.

Treatment (n = 5)	Urea(mg/dl)		Creatinine(mg/dl)		Sodium(mmol/l)		Potassium(mmol/l)	
	(Mean ±)	% change	(Mean ±)	% change	(Mean ±)	% change	(Mean ±)	% change
Normal	52.05±3.35		2.48±0.21		63.91±7.51		6.10±0.36	
Pa [§]	142.00±5.92*** a		13.93±1.00*** a		191.83±9.41*** a		14.51±0.82*** a	
Sil [§]	85.38±5.10*** b	39.87	6.98±0.26*** b	49.88	81.60±9.52*** b	57.46	7.83±0.36*** b	46.03
2 + Pa [§]	132.83±5.17 ^b	6.45	11.31±0.27* ^b	18.77	185.50±14.02 ^b	3.30	12.66±0.62 ^b	12.47
3 + Pa [§]	107.05±5.86** ^b	24.61	8.91±0.19*** ^b	36.00	126.83±5.27*** ^b	33.88	9.36±0.44*** ^b	35.47
4 + Pa [§]	116.66±5.54* ^b	17.84	9.31±0.30** ^b	33.13	152.16±7.24* ^b	20.67	9.93±0.30*** ^b	31.57
6 + Pa [§]	121.66±4.12* ^b	14.31	10.93±0.39* ^b	21.53	181.16±6.93 ^b	5.56	10.06±0.46** ^b	30.65

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.00$ ^a as compared to control group ^b As compared to Pa group [§]Doses: Pa (500 mg/kg), Sil, **2-4, 6** (20.7 μ mole/kg).

