

Supplementary Material
***High Yield Synthesis of Curcumin and Symmetric
Curcuminoids: A “Click” and “Unclick” Chemistry Approach.***

Curcumin synthesis is an art.

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†“In fond memory of our colleague Dr. Xavier Lozoya-Legorreta, d. Nov. 9, 2022”.

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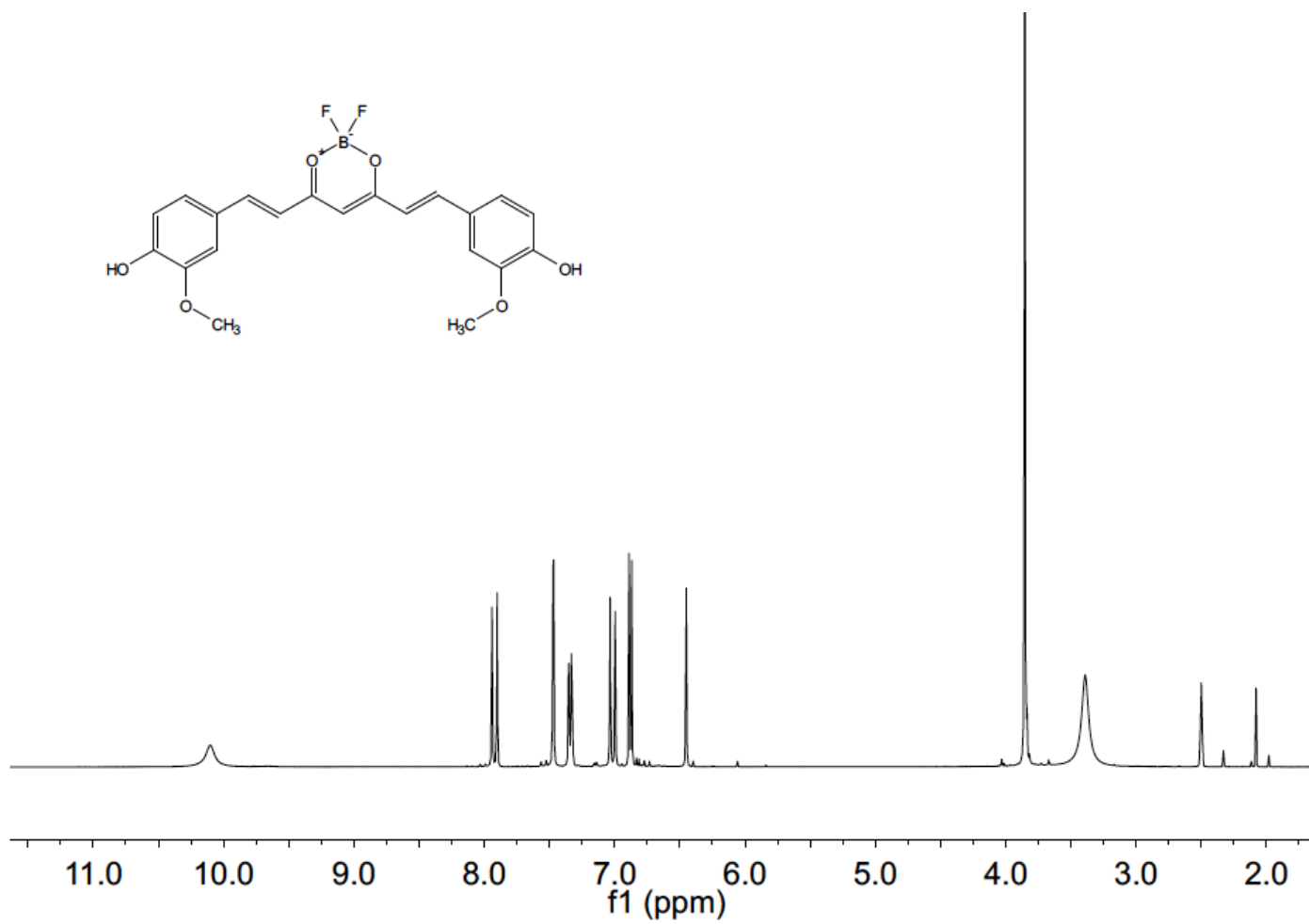


Figure S1. ¹H NMR spectrum of compound 1 (DMSO-*d*₆-400MHz).

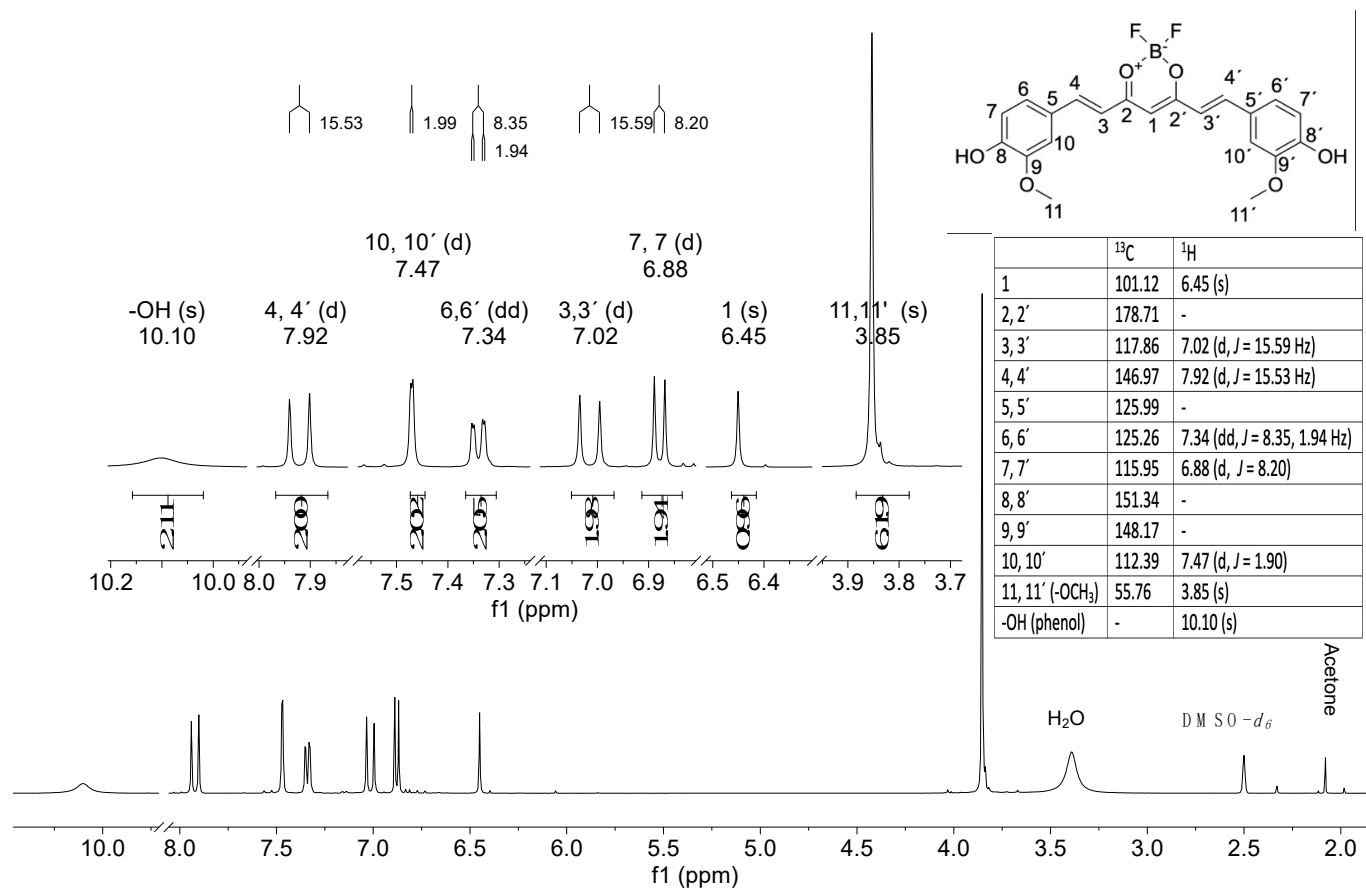


Figure S2. ¹H NMR spectrum of compound 1 (DMSO-*d*₆-400MHz, expansion).

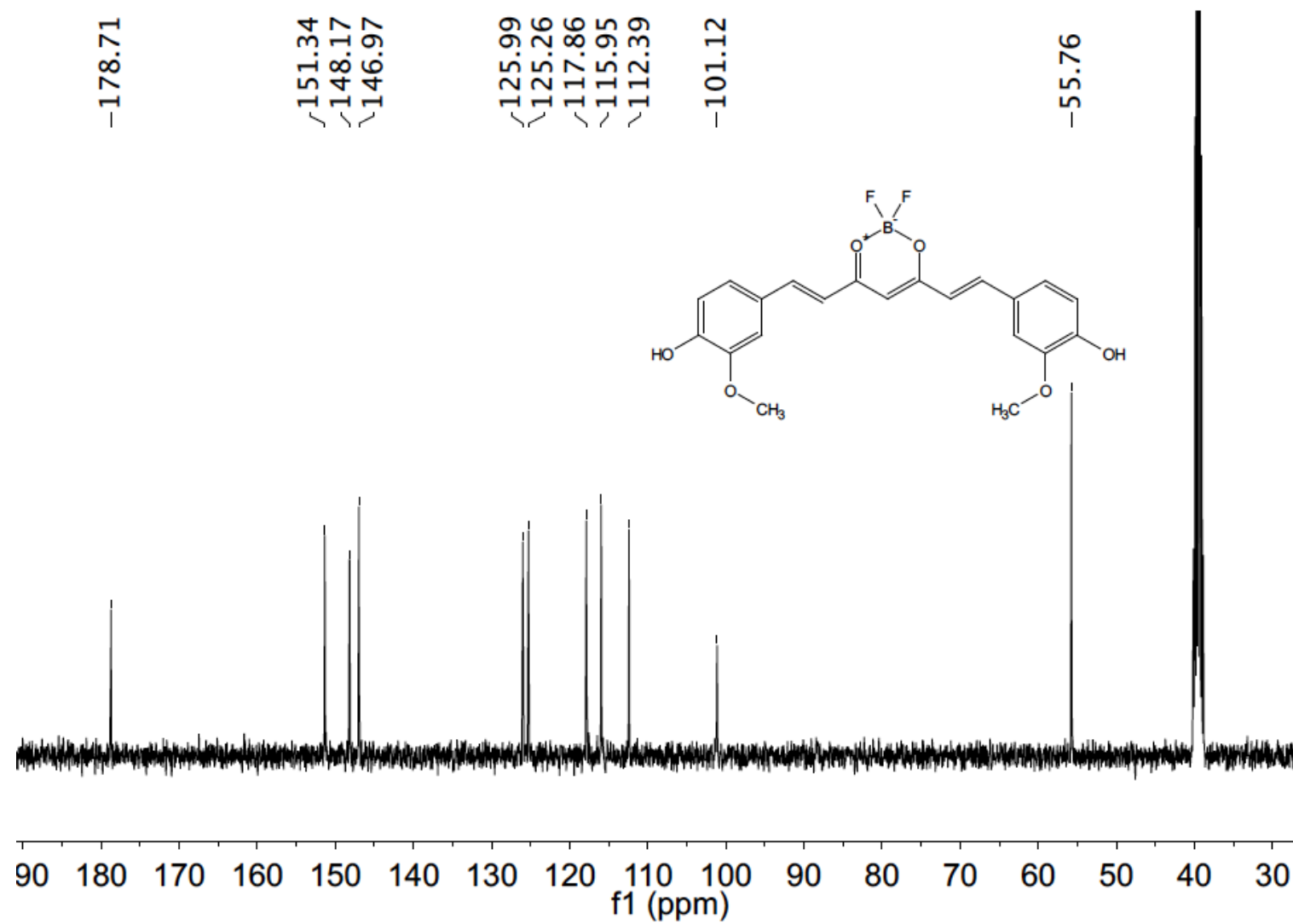


Figure S3. ¹³C NMR spectrum of compound 1 (DMSO-*d*₆-100MHz).

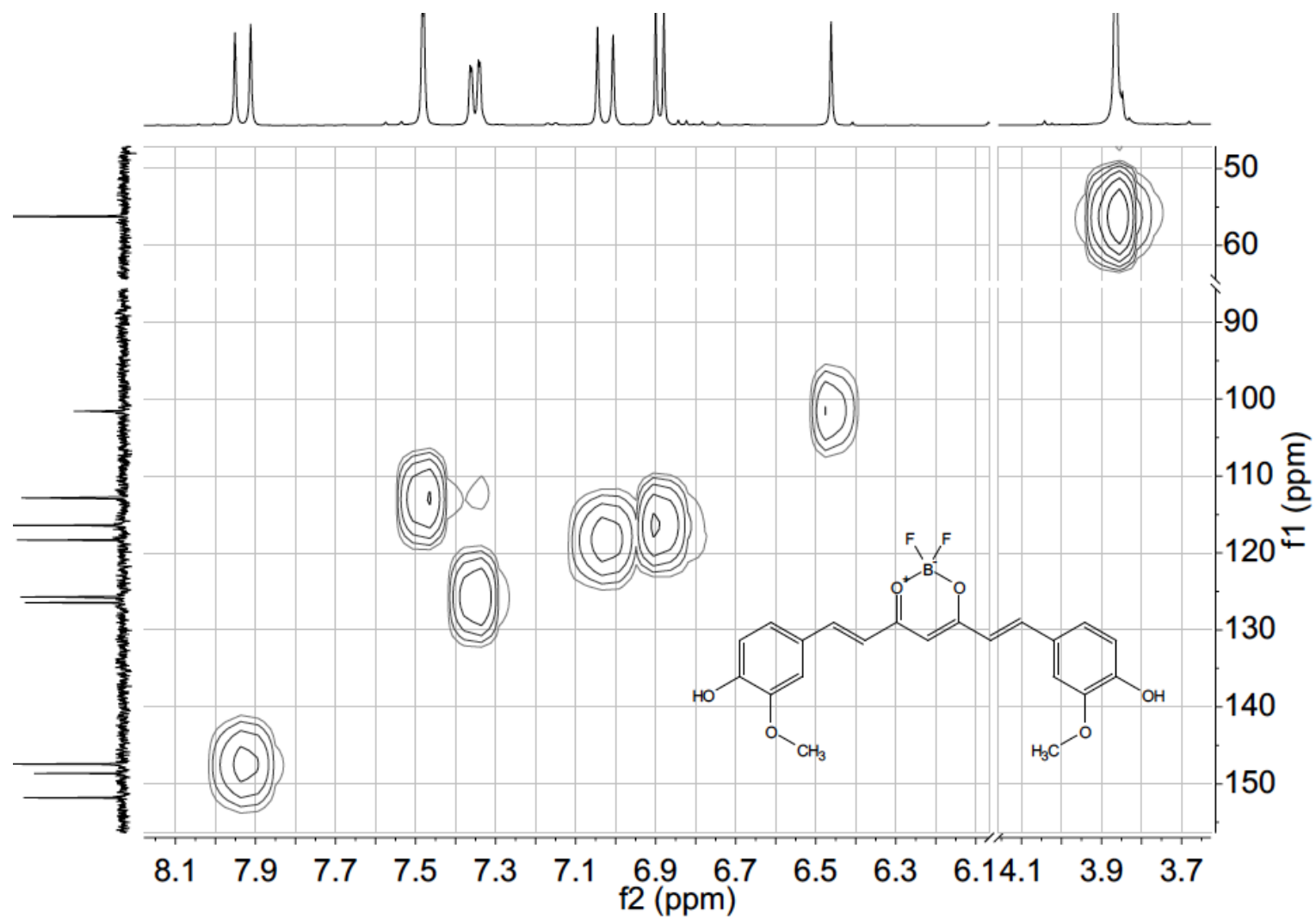


Figure S4. HSQC NMR spectrum of compound 1 (DMSO- d_6 -400MHz).

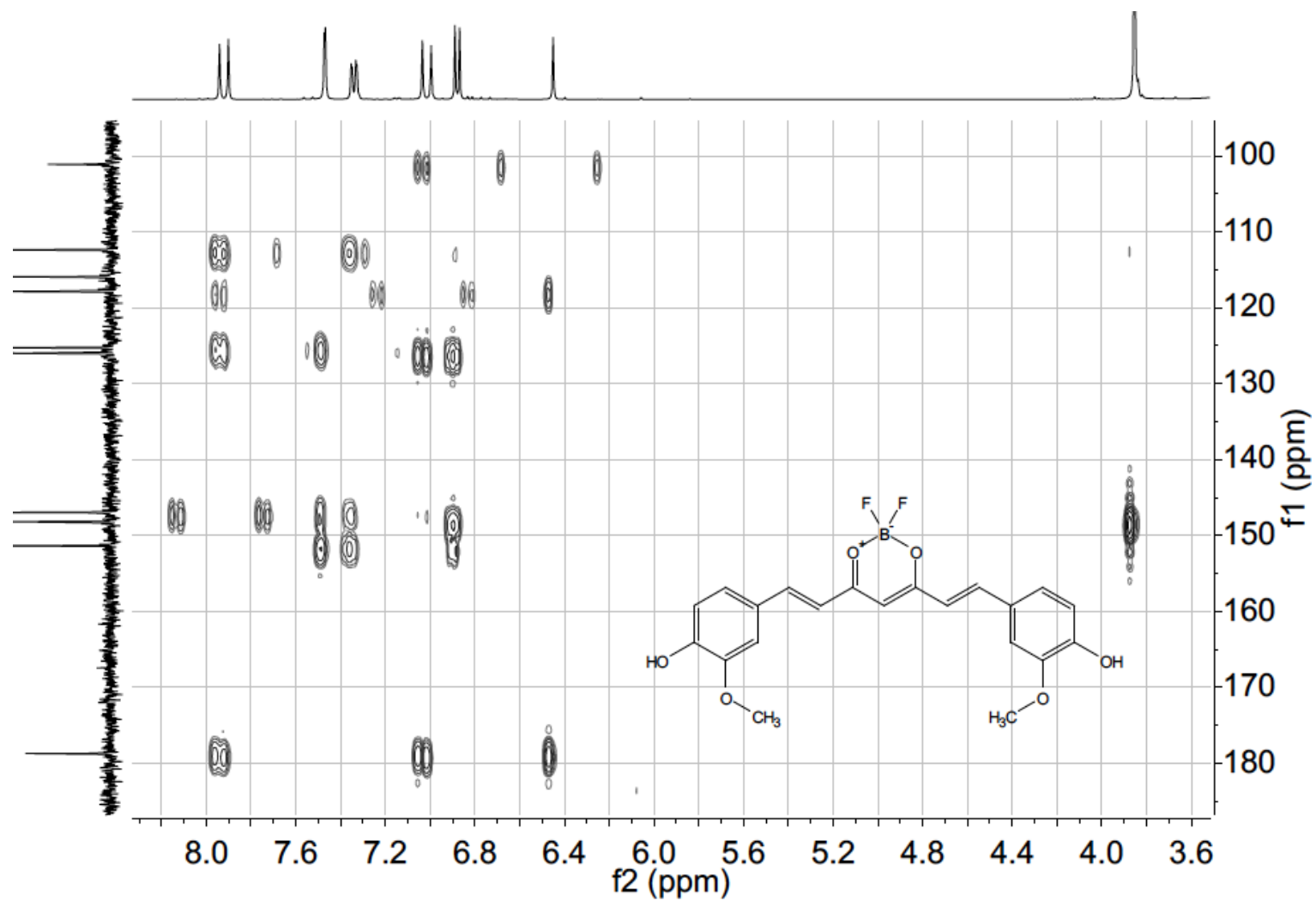


Figure S5. HMBC NMR spectrum of compound 1 (DMSO- d_6 -400MHz).

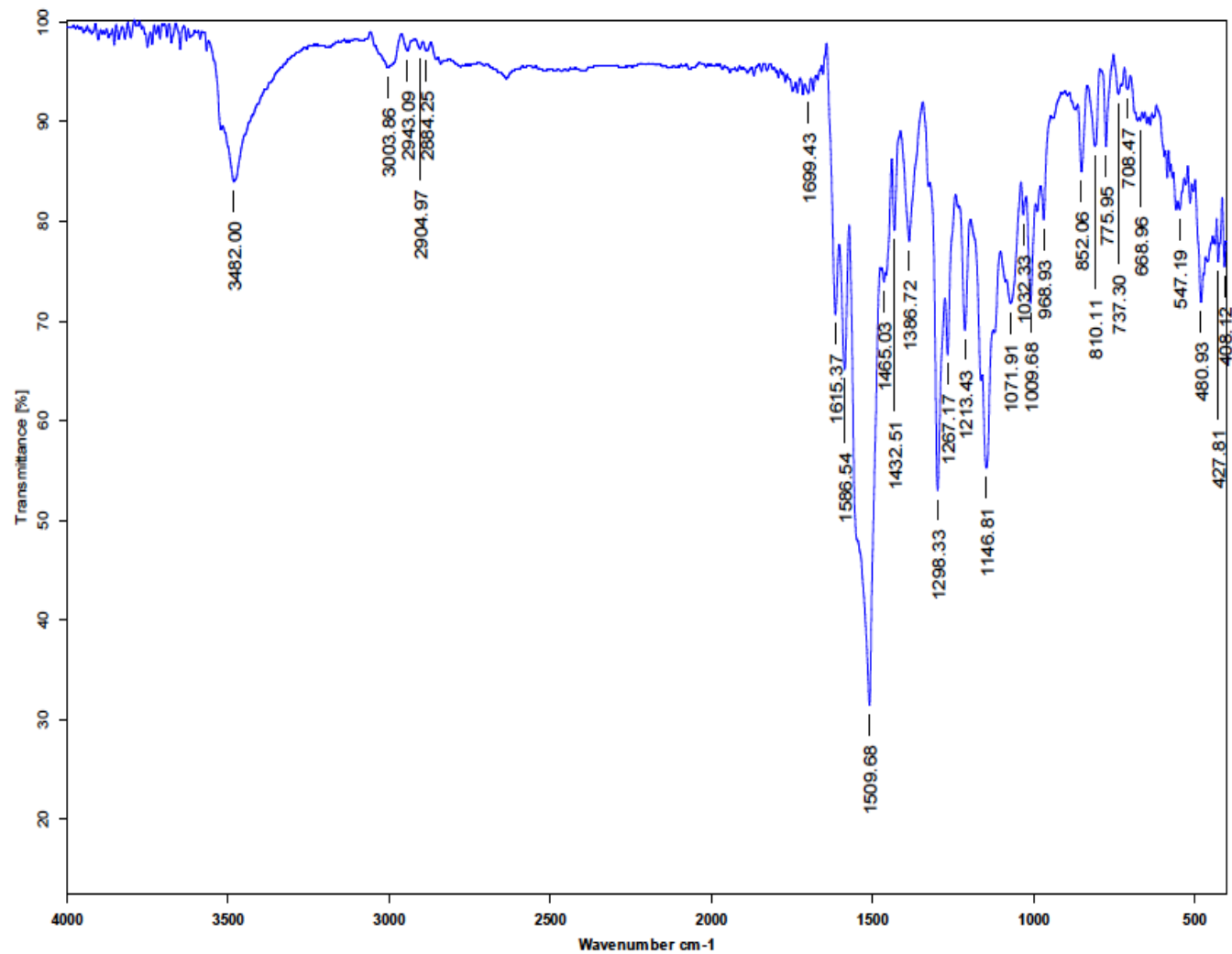


Figure S6. IR spectrum of compound 1.

INSTITUTO DE QUIMICA, UNAM
LABORATORIO DE ESPECTROMETRIA DE MASAS

Acq. Data Name: 1843 CURCU-BF2
Creation Parameters: Average(MS[1] Time:1..2)
Dr Enriquez Raul / Operador: Carmen Garcia

Experiment Date/Time: 11/26/2021 9:35:55 AM
Instrument : JEOL The AccuTOF : JMS-T100LC
Ionization Mode: DART+

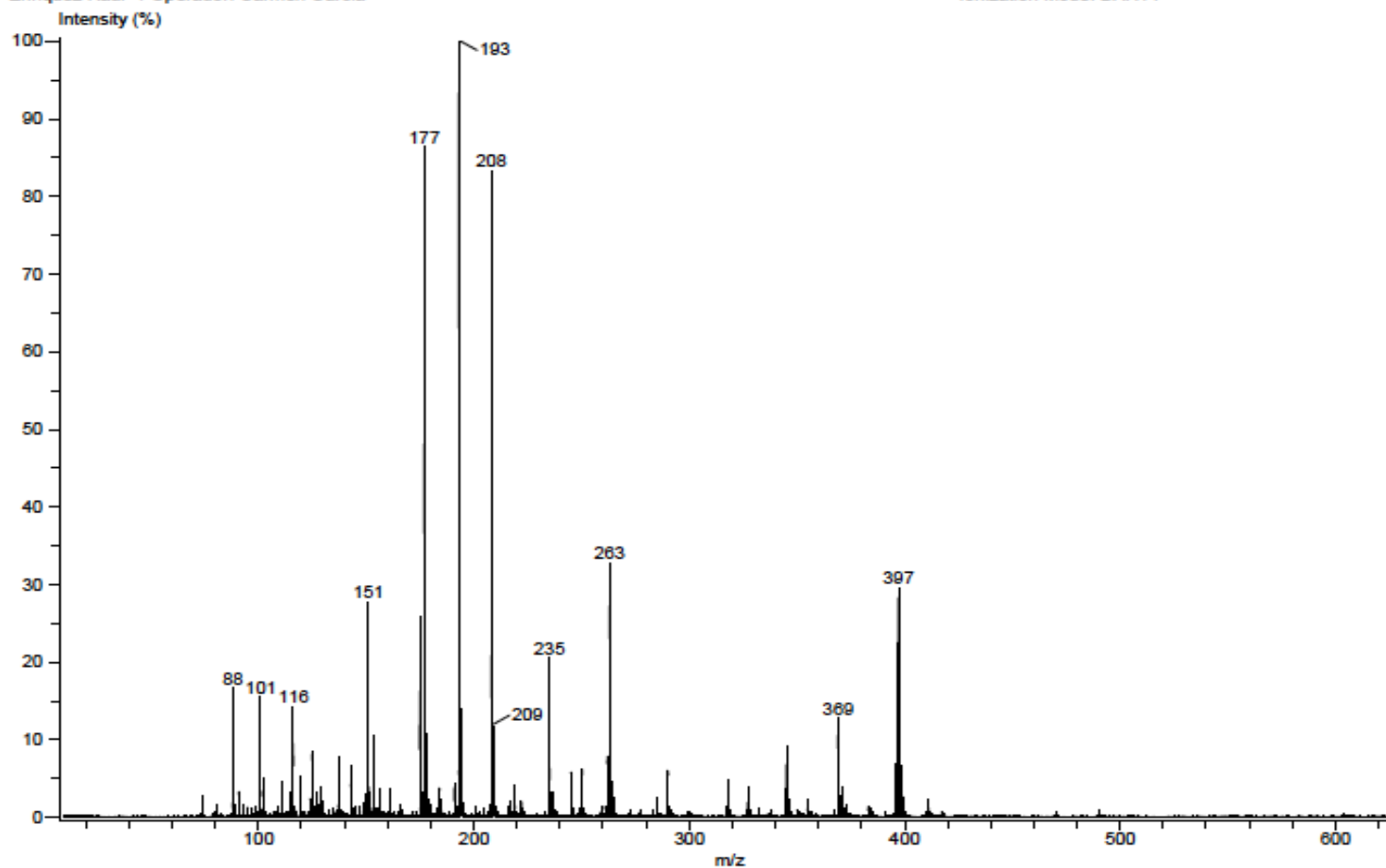


Figure S7. SM of compound 1.

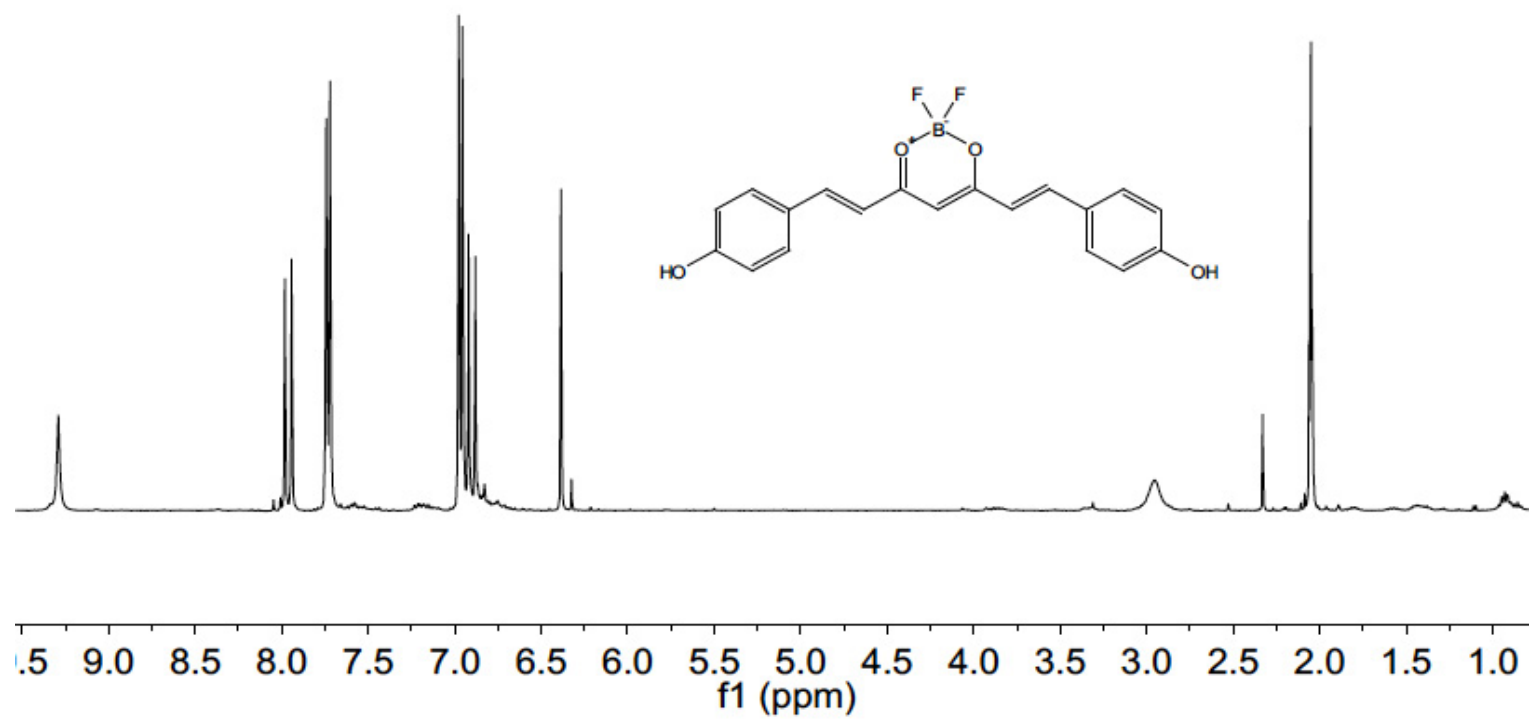


Figure S8. ^1H NMR spectrum of compound **2** ($\text{Acetone-}d_6$ -400MHz).

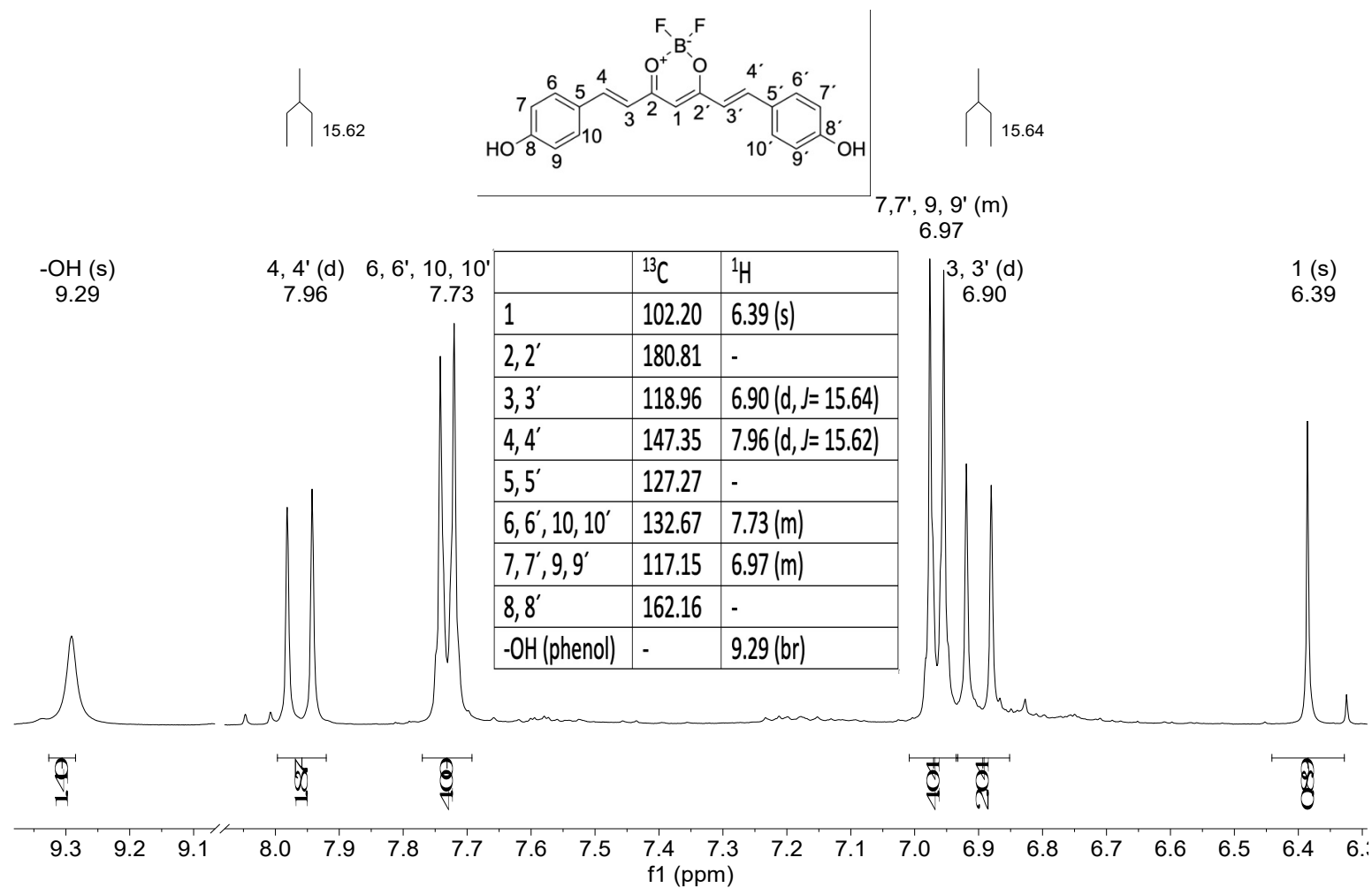


Figure S9. ¹H NMR spectrum of compound 2 (Acetone-*d*₆-400MHz, expansion).

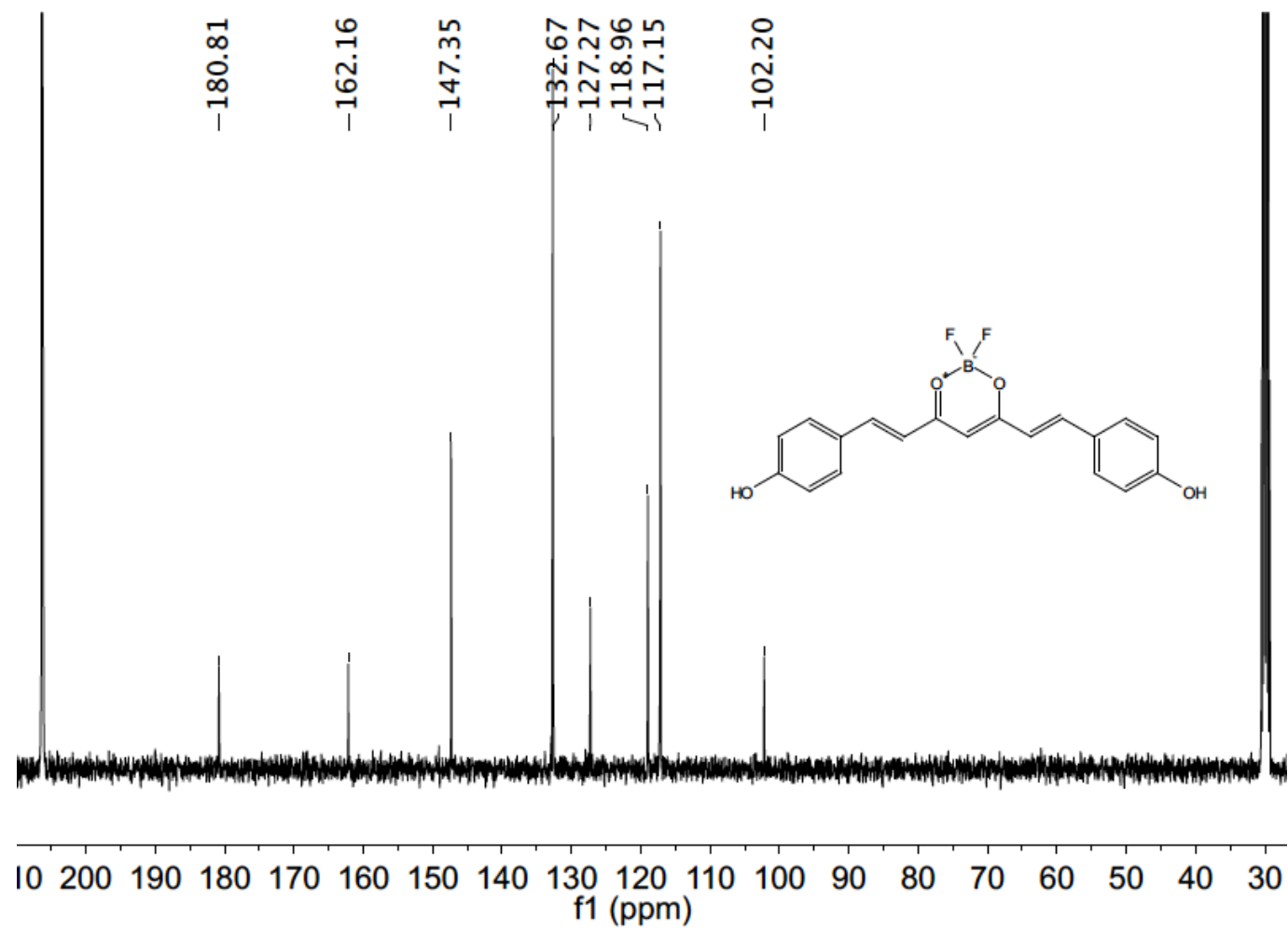


Figure S10. ¹³C NMR spectrum of compound 2 (Acetone-*d*₆-100MHz).

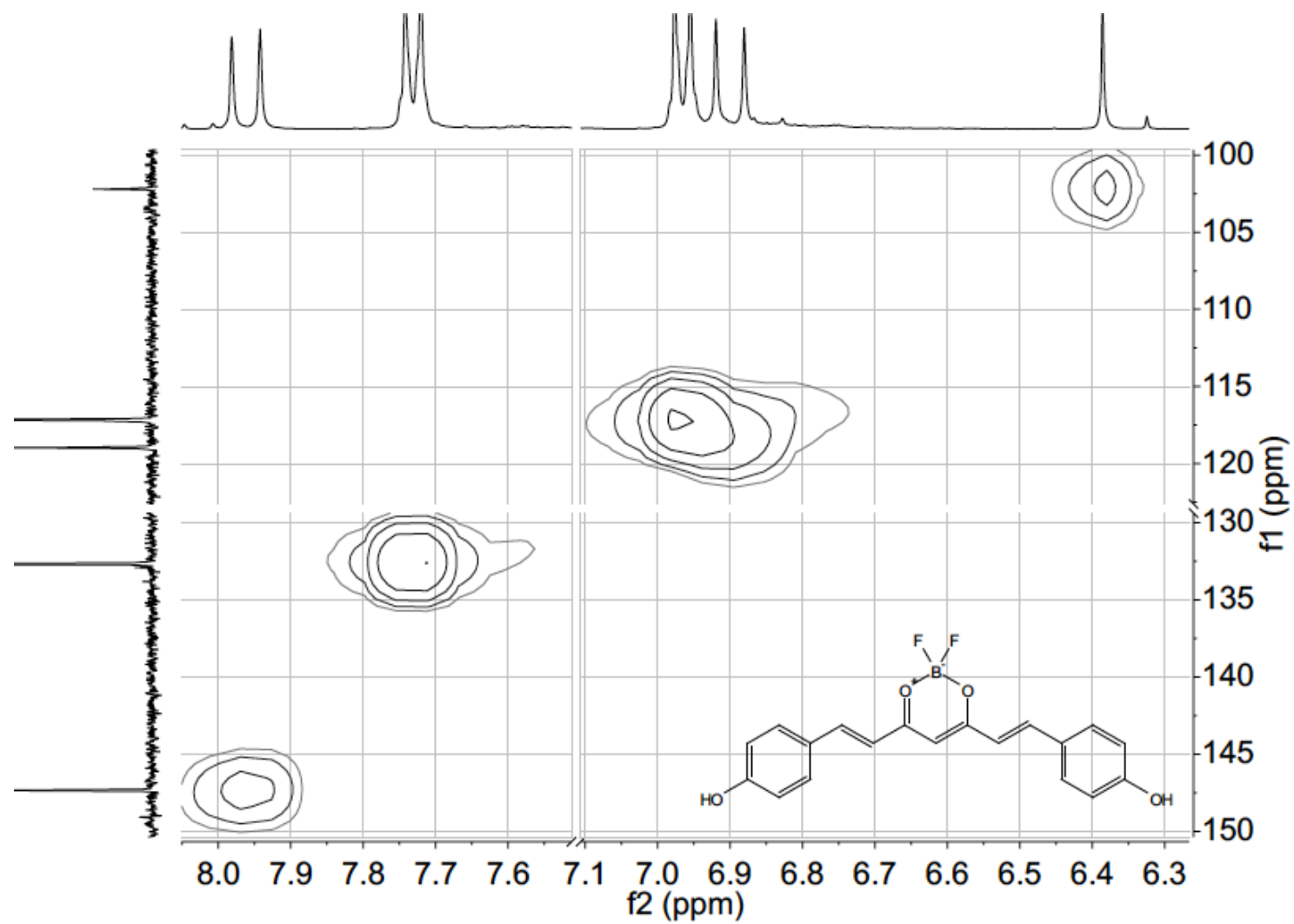


Figure S11. HSQC NMR spectrum of compound 2 (Acetone-*d*₆-400MHz).

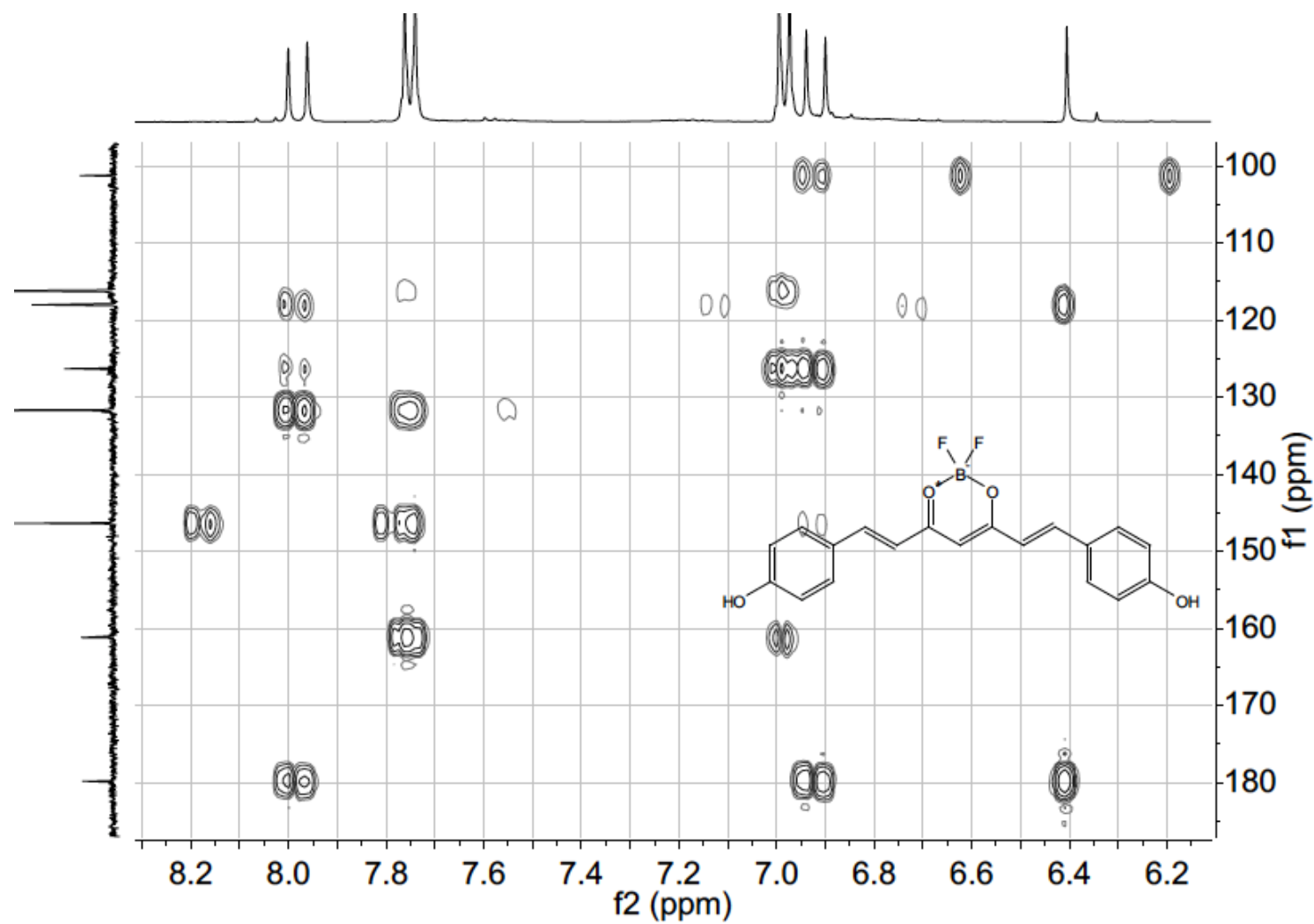


Figure S12. HMBC NMR spectrum of compound **2** (Acetone-*d*₆-400MHz).

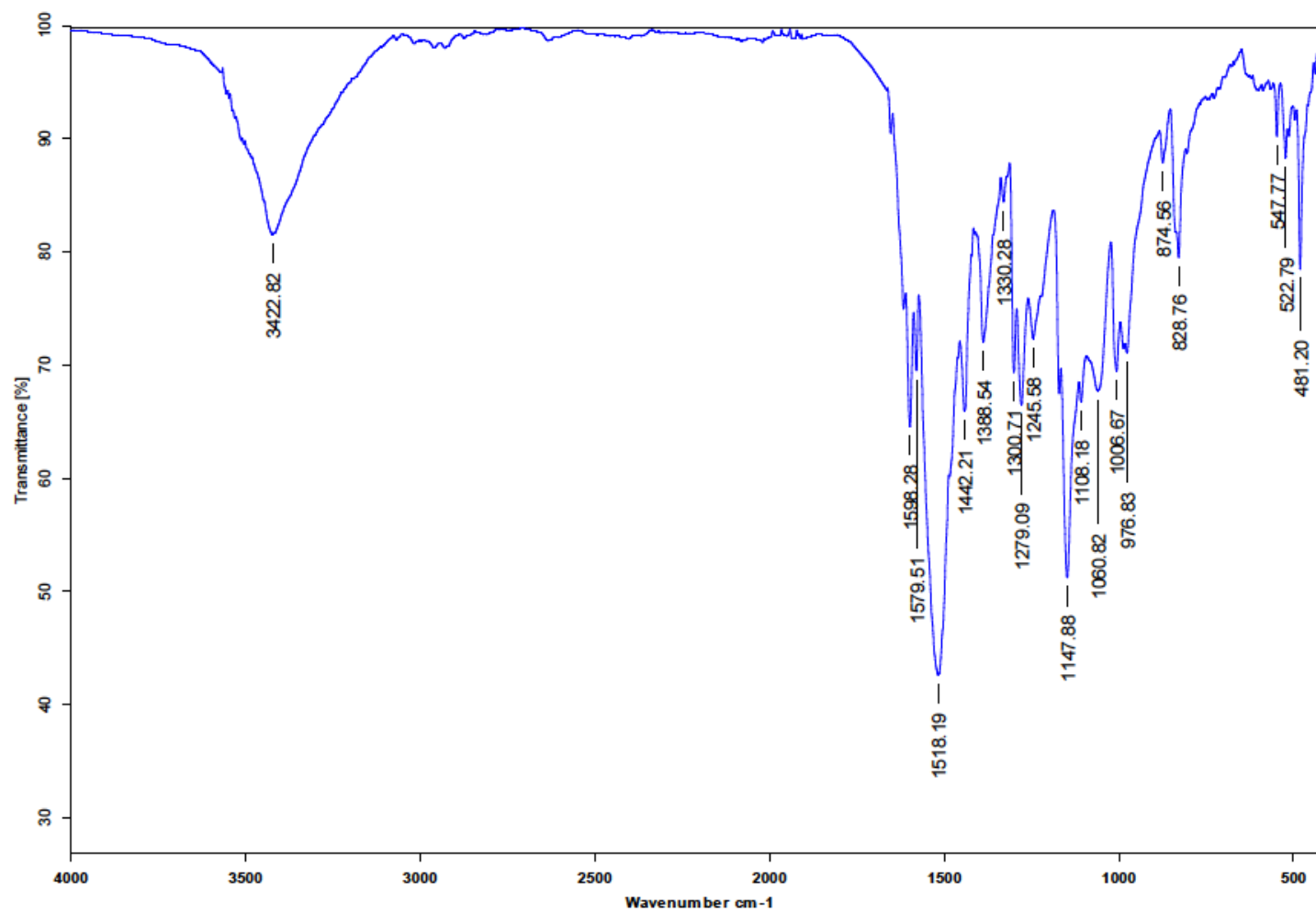


Figure S13. IR spectrum of compound 2.

[Mass Spectrum]
Date : Dr Enriquez Raul-025 Date : 26-May-2022 11:24
Instrument : MStation
Sample : 1665_P-OH-BF2
Note : Operator name: Carmen Garcia
Inlet : Direct Ion Mode : EI+
Spectrum Type : Normal Ion [MF-Linear]
RT : 1.51 min Scan# : (45,47) Temp : 3276.7 deg.C
BP : m/z 43 Int. : 4.19 (43930)
Output m/z range : 0 to 571 Cut Level : 0.00 %

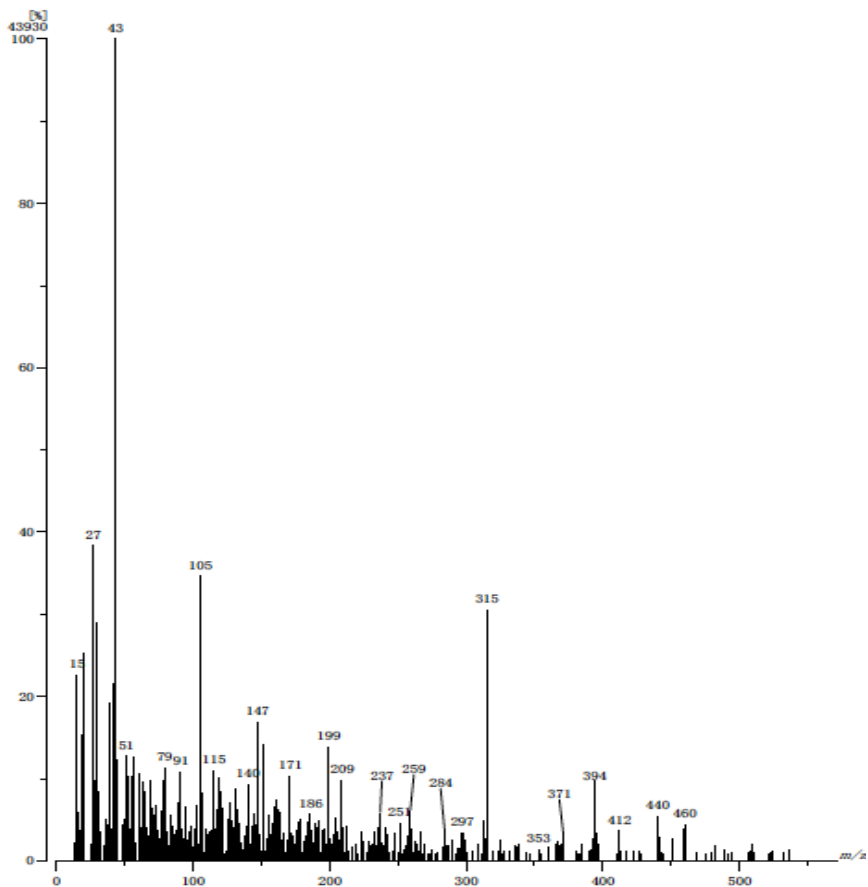


Figure S14. SM of compound 2.

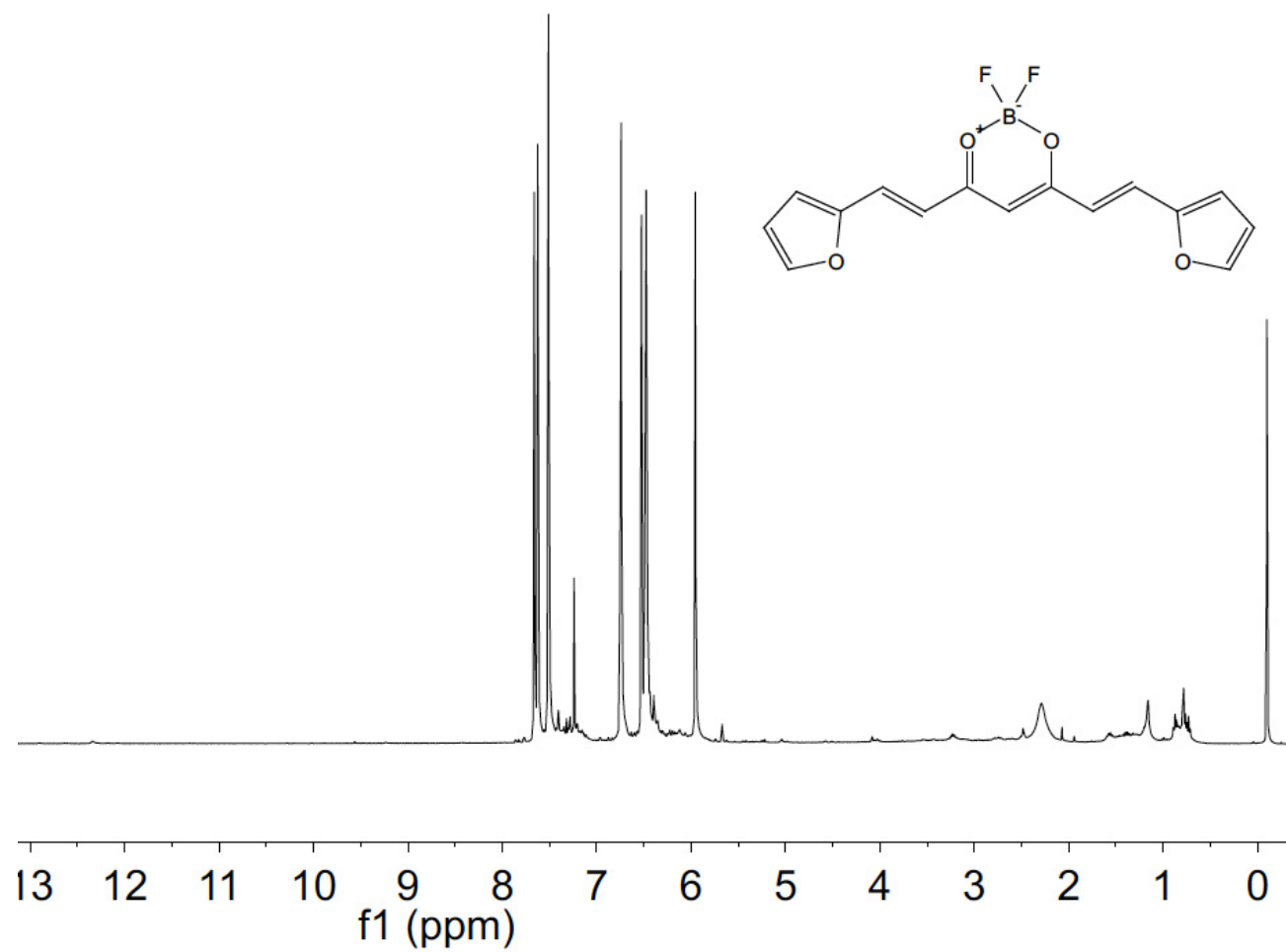


Figure S15. ^1H NMR spectrum of compound 3 (CDCl_3 -400MHz).

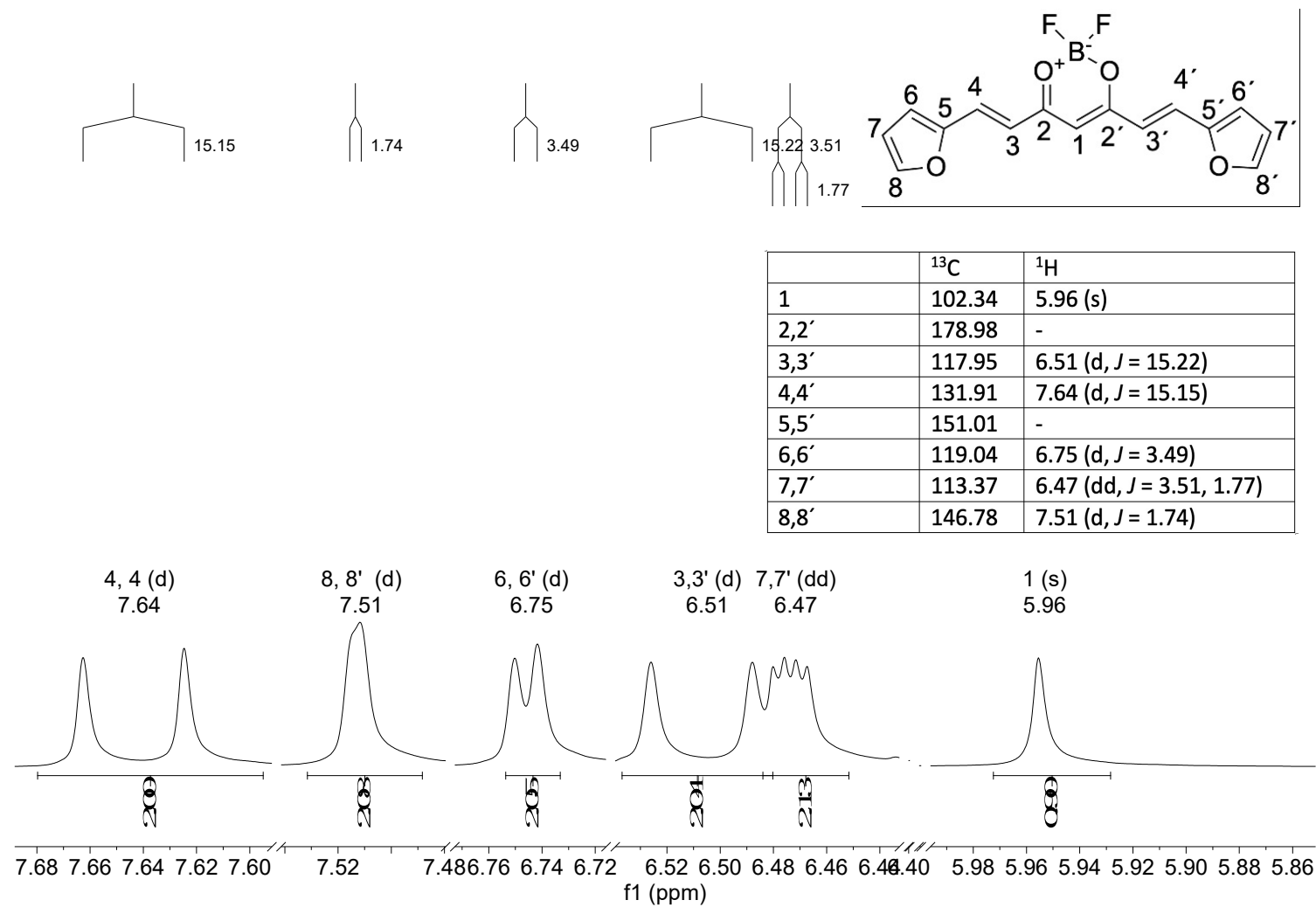


Figure S16. ¹H NMR spectrum of compound 3 (CDCl₃-400MHz, expansion).

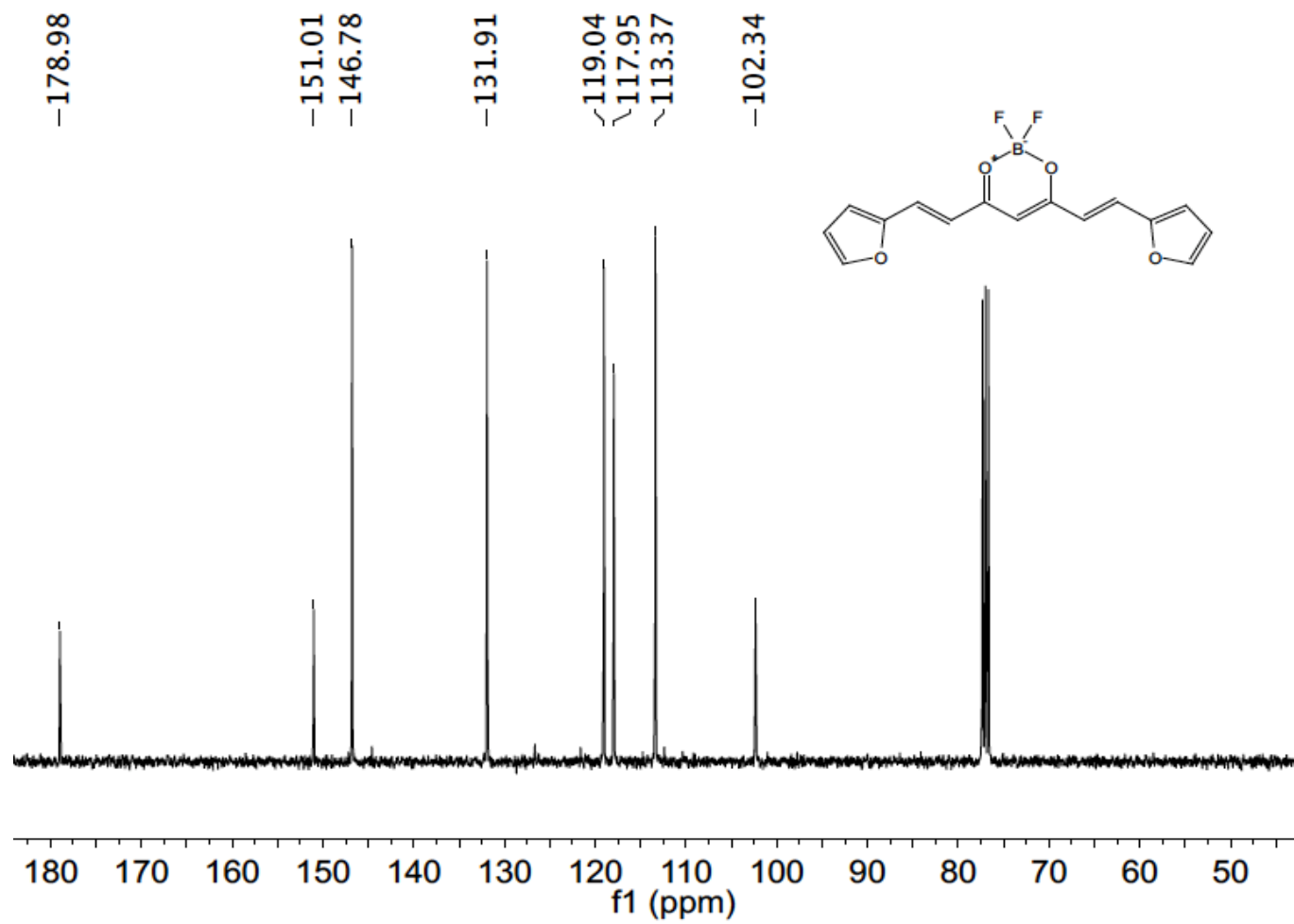


Figure S17. ¹³C NMR spectrum of compound 3 (CDCl₃-100MHz).

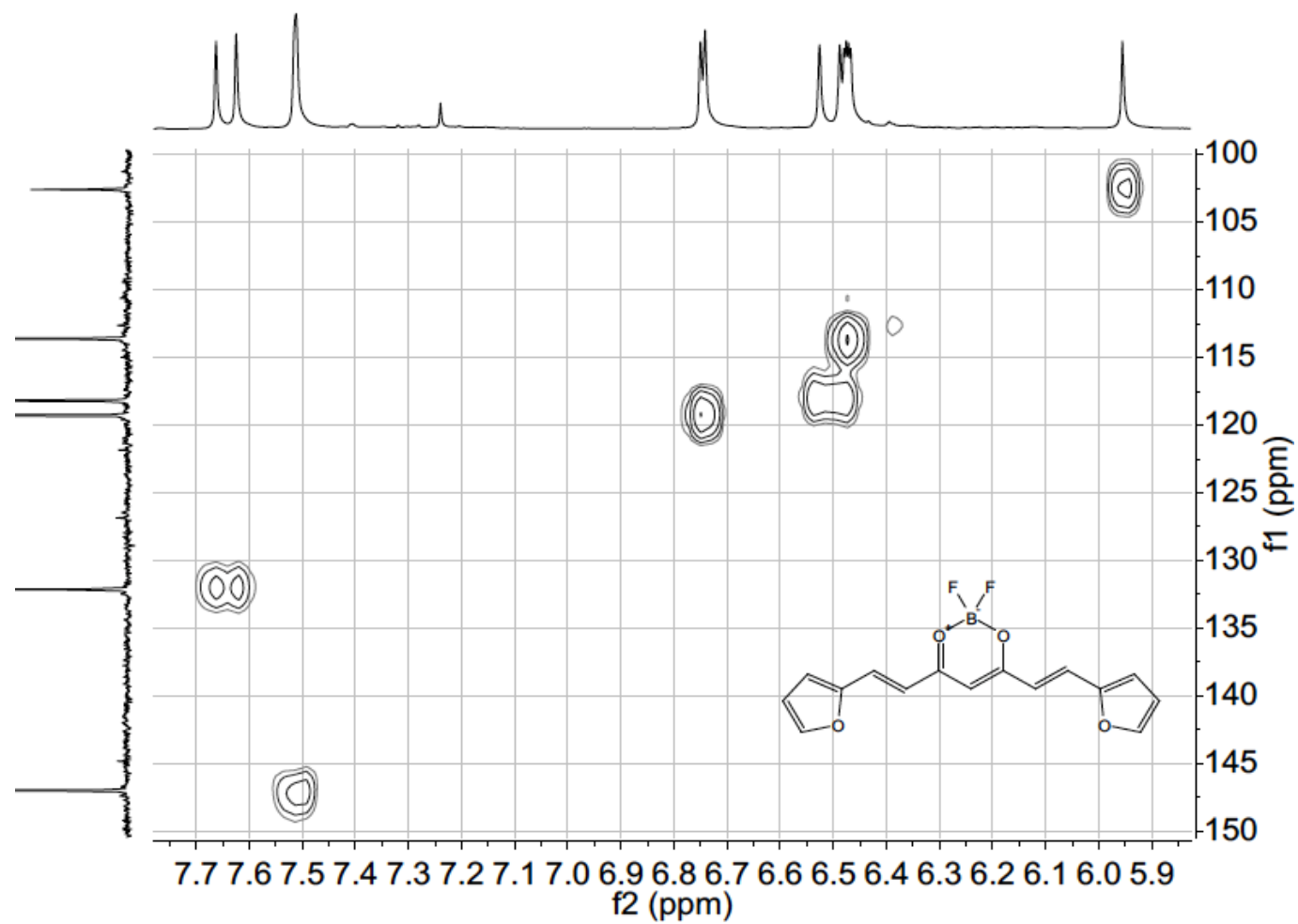


Figure S18. HSQC NMR spectrum of compound 3 (CDCl₃-400MHz).

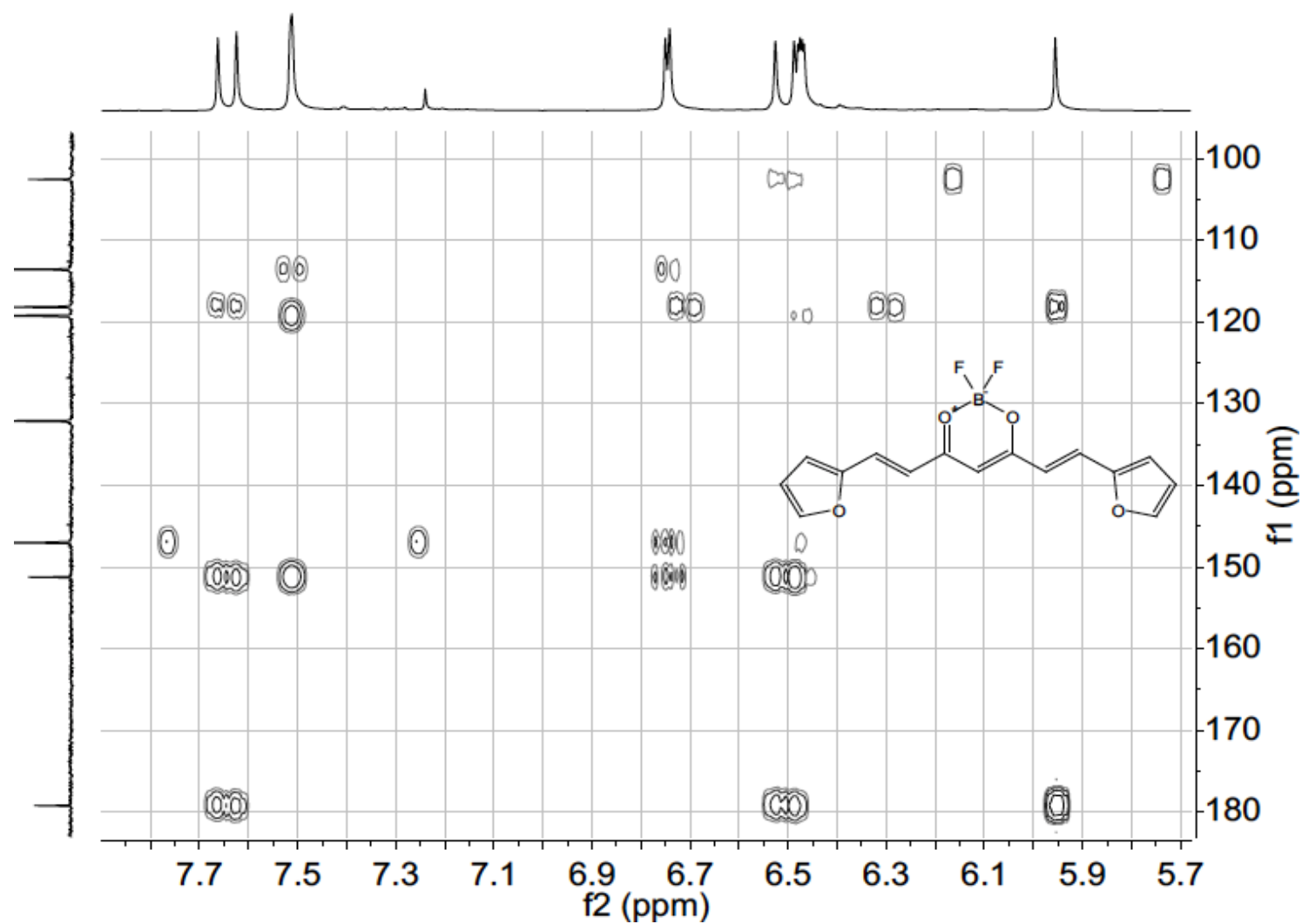


Figure S19. HMBC NMR spectrum of compound 3 (CDCl₃-400MHz).

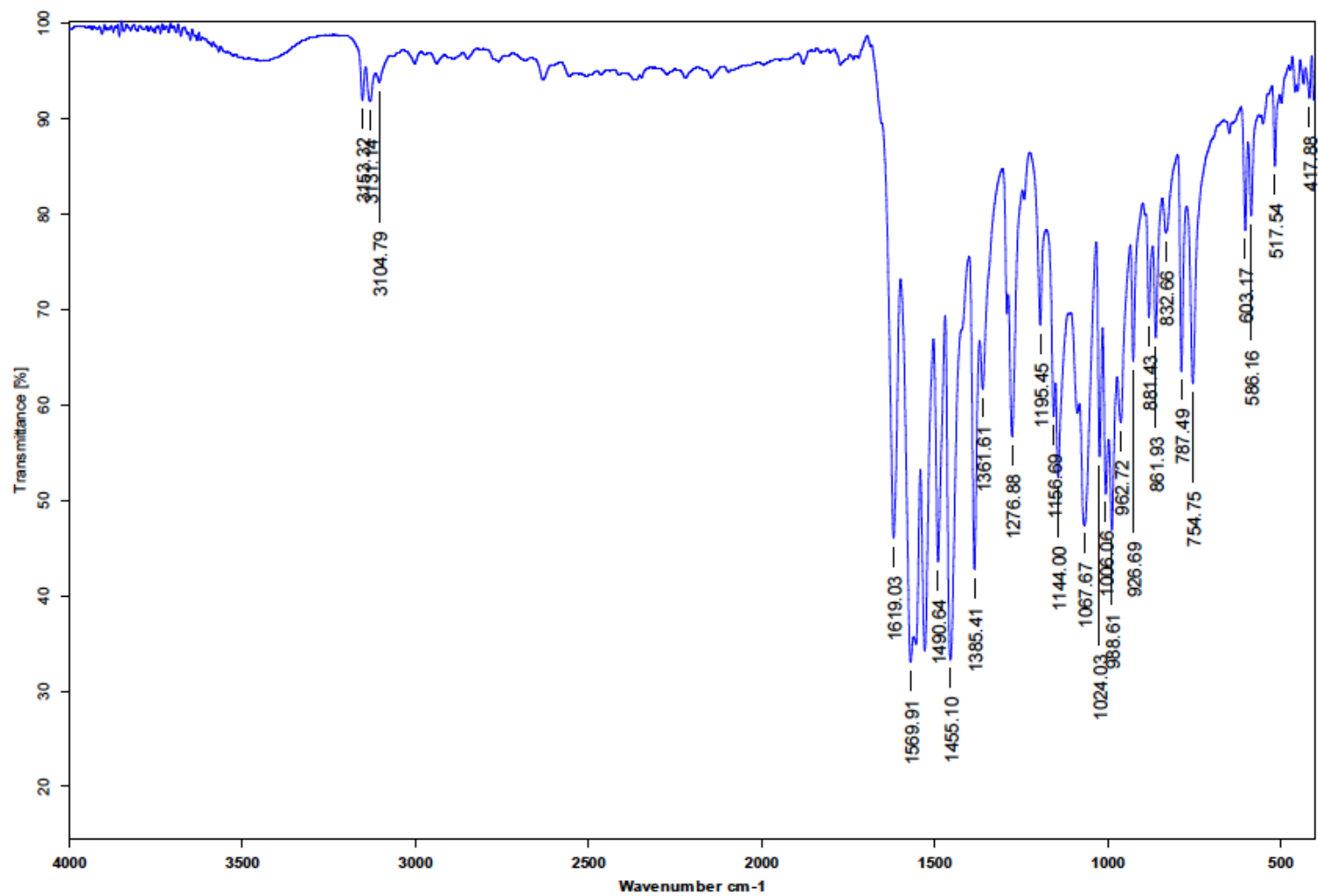


Figure S20. IR spectrum of compound 3.

Acq. Data Name: 1841 FURAN-BF2
Creation Parameters: Average(MS[1] Time:0..0)
Dr. Enriquez Raul / Operador: Carmen Garcia

Experiment Date/Time: 11/26/2021 9:29:13 AM
Instrument : JEOL The AccuTOF : JMS-T100LC
Ionization Mode: DART+

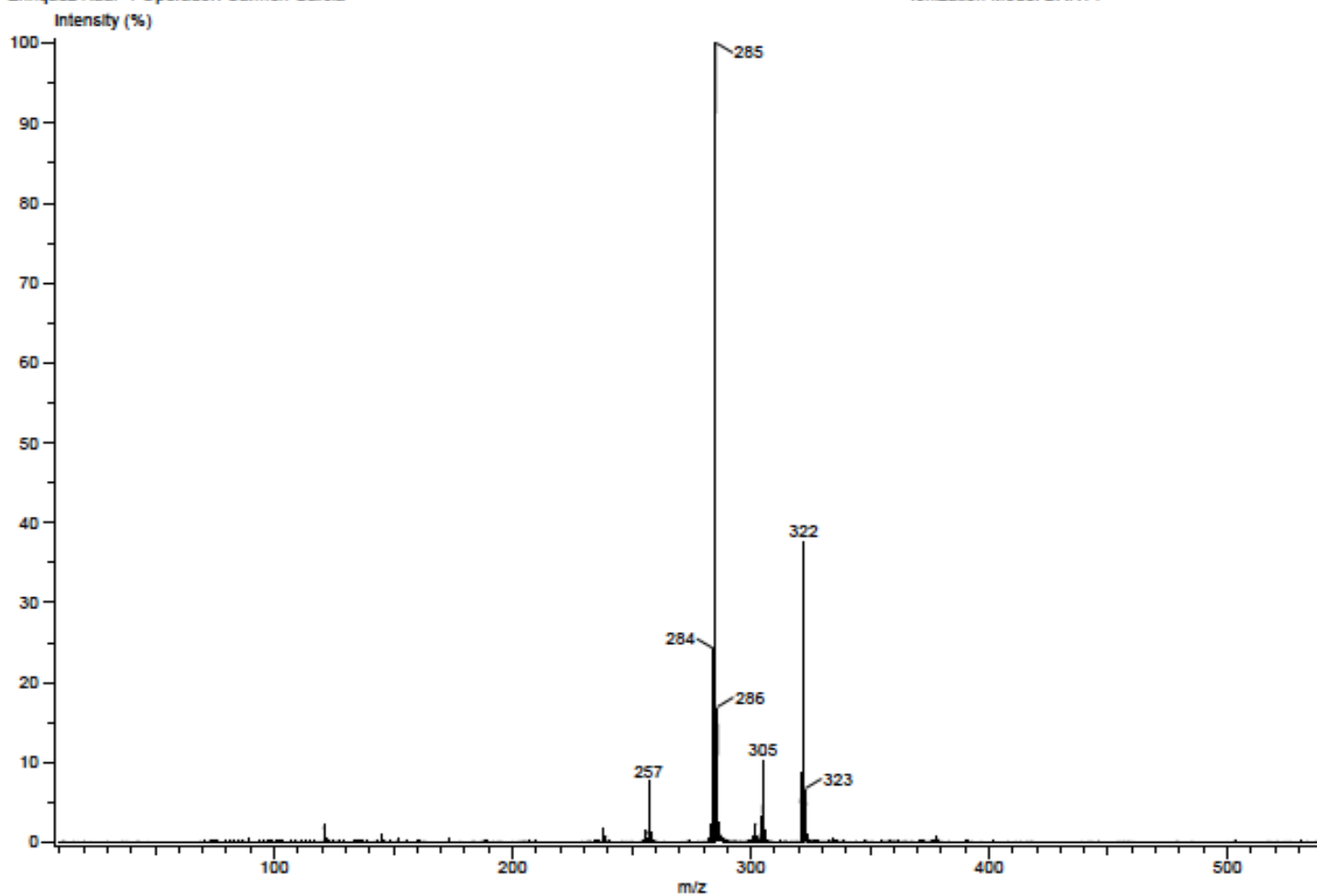


Figure S21. SM of compound 3.

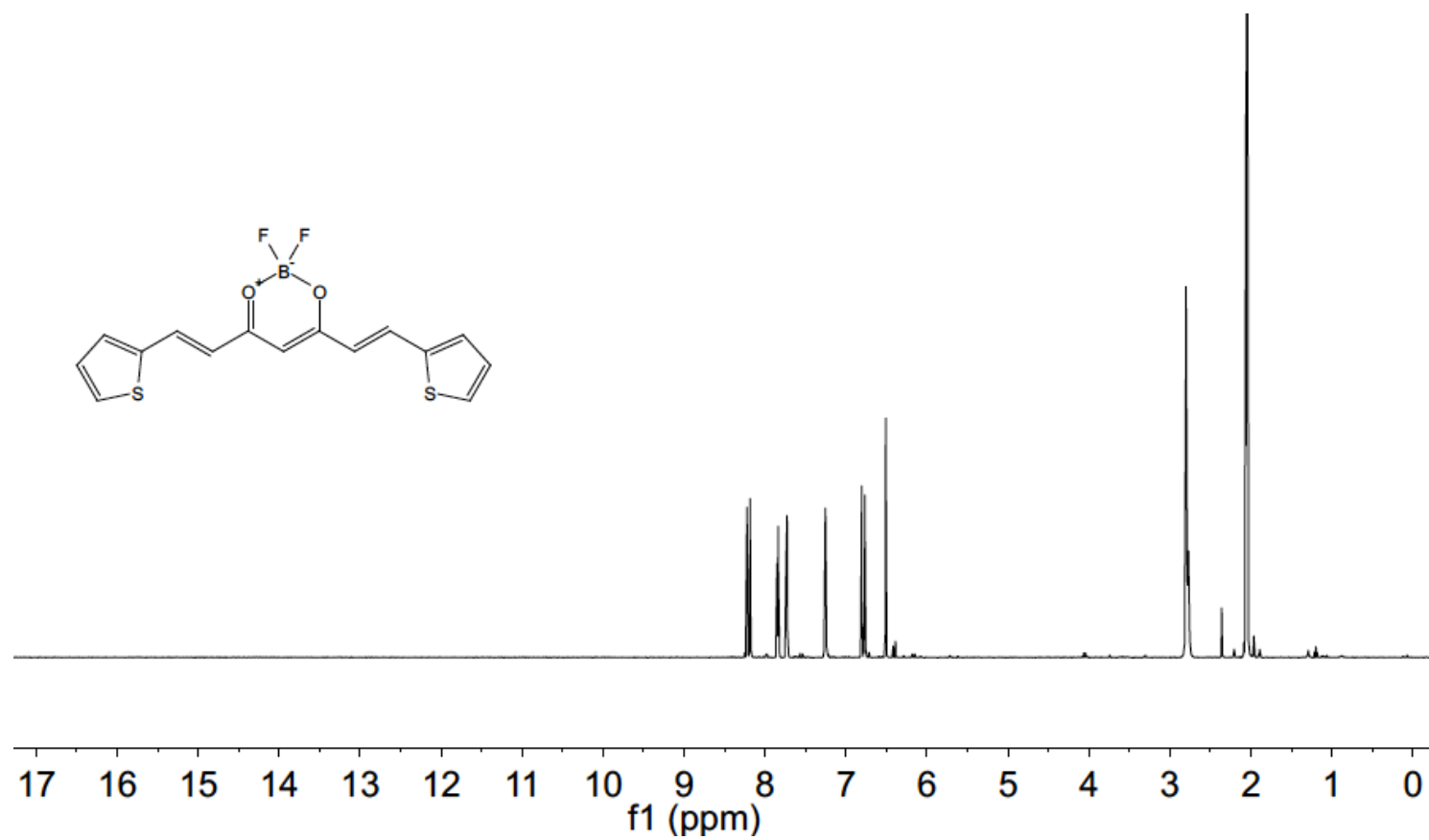


Figure S22. ¹H NMR spectrum of compound 4 (Acetone-*d*₆-400MHz).

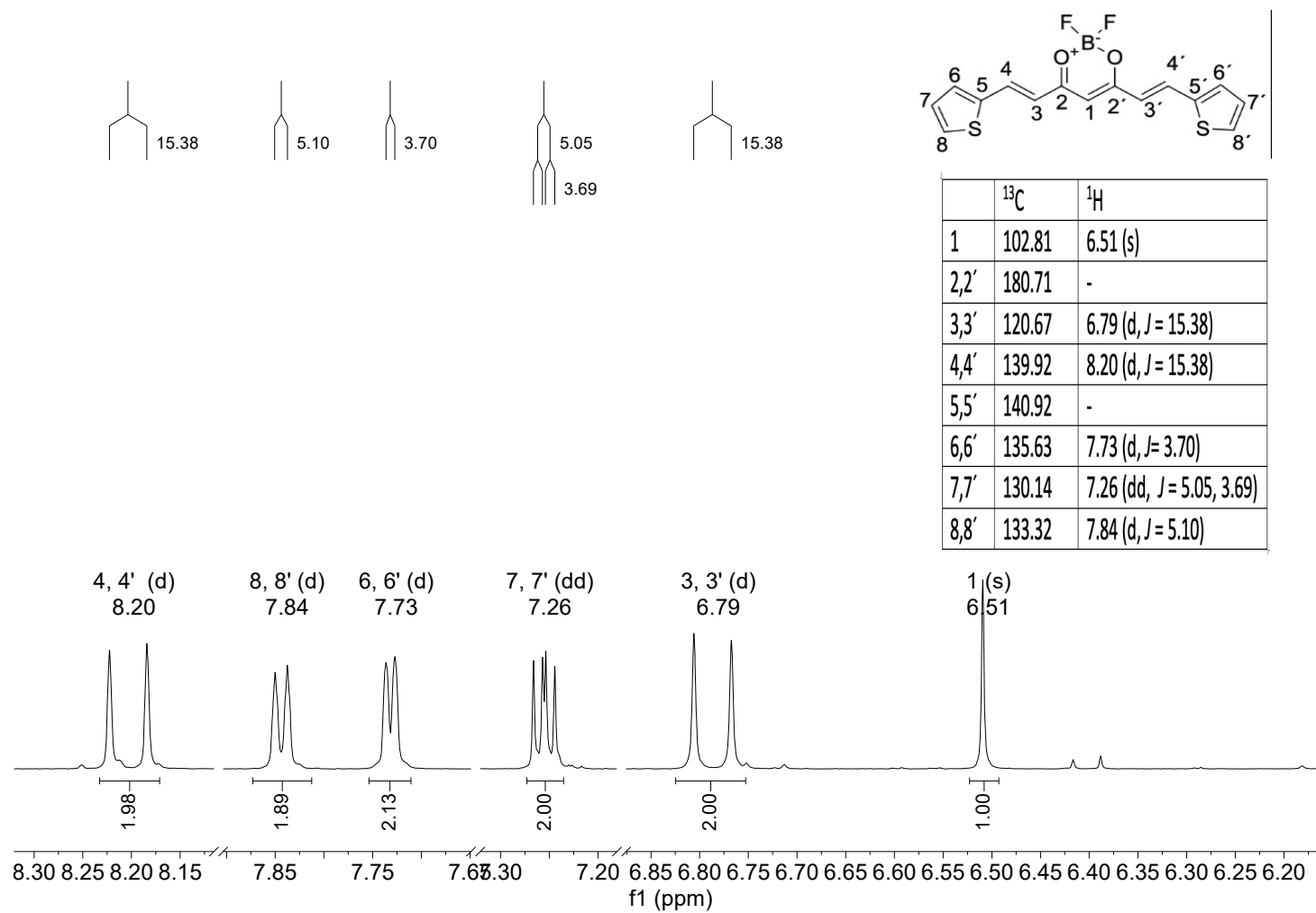


Figure S23. ^1H NMR spectrum of compound 4 (Acetone- d_6 -400MHz, expansion).

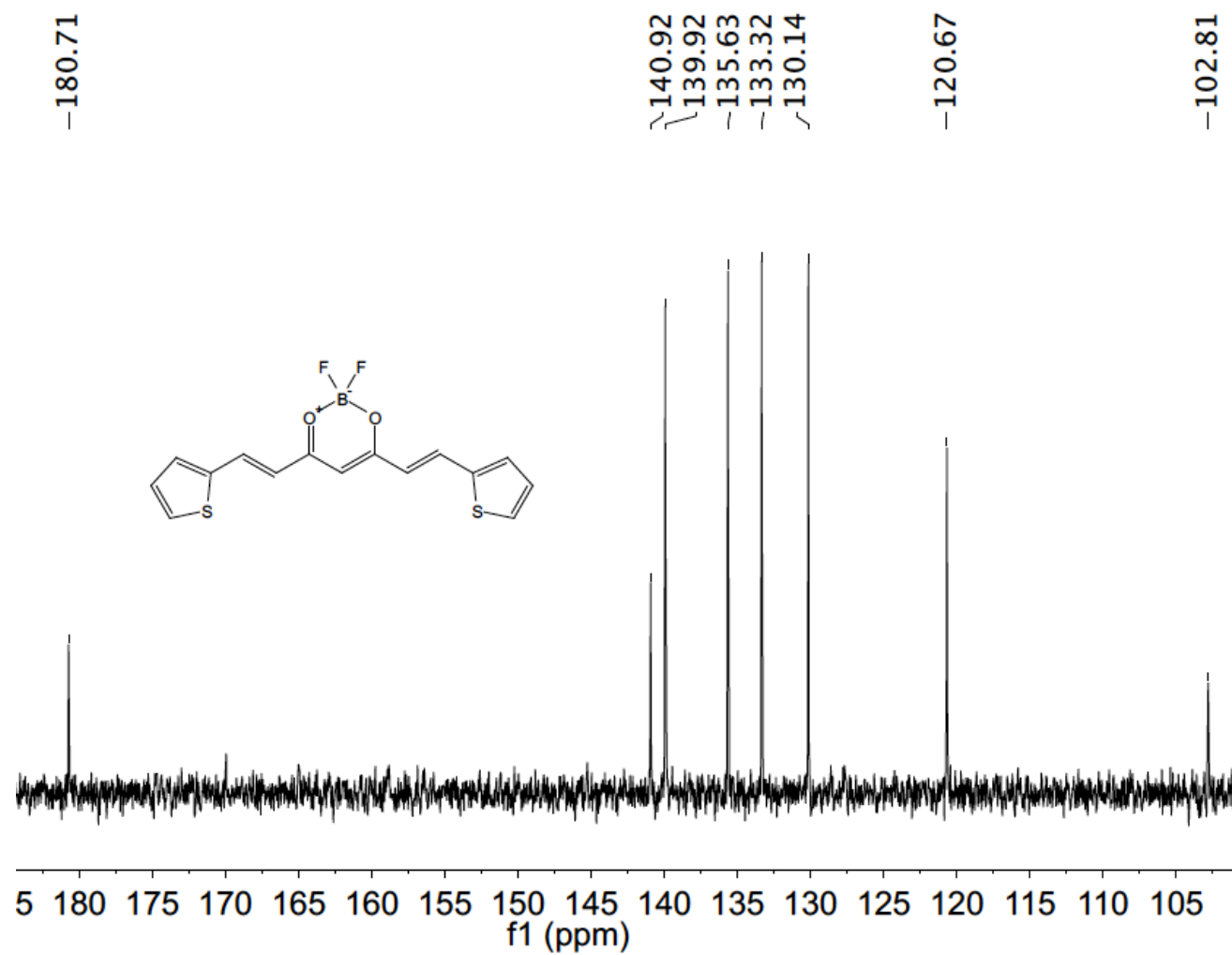


Figure S24. ^{13}C NMR spectrum of compound 4 (Acetone- d_6 -400MHz -100MHz).

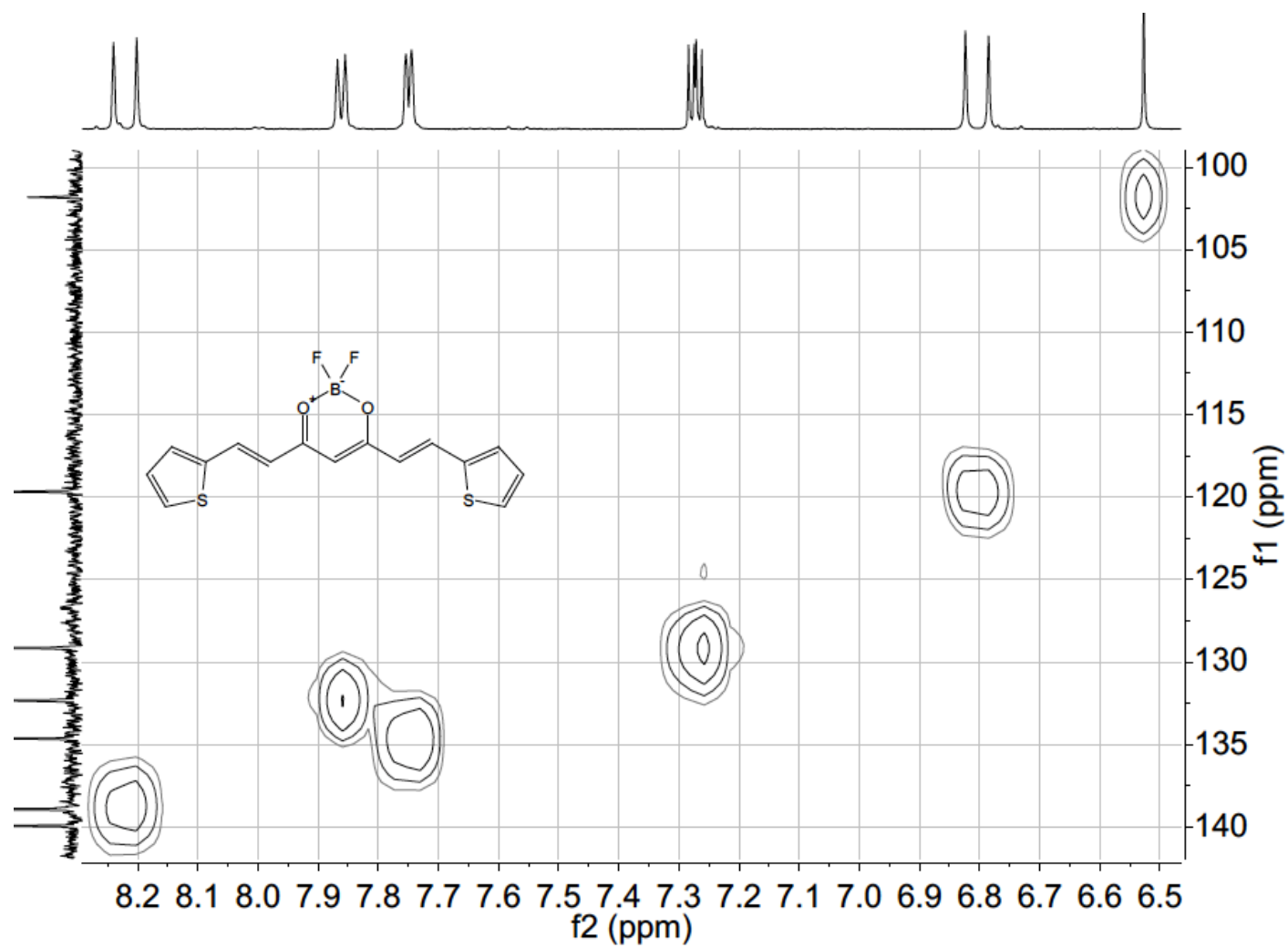


Figure S25. HSQC NMR spectrum of compound 4 (Acetone- d_6 -400MHz 400MHz).

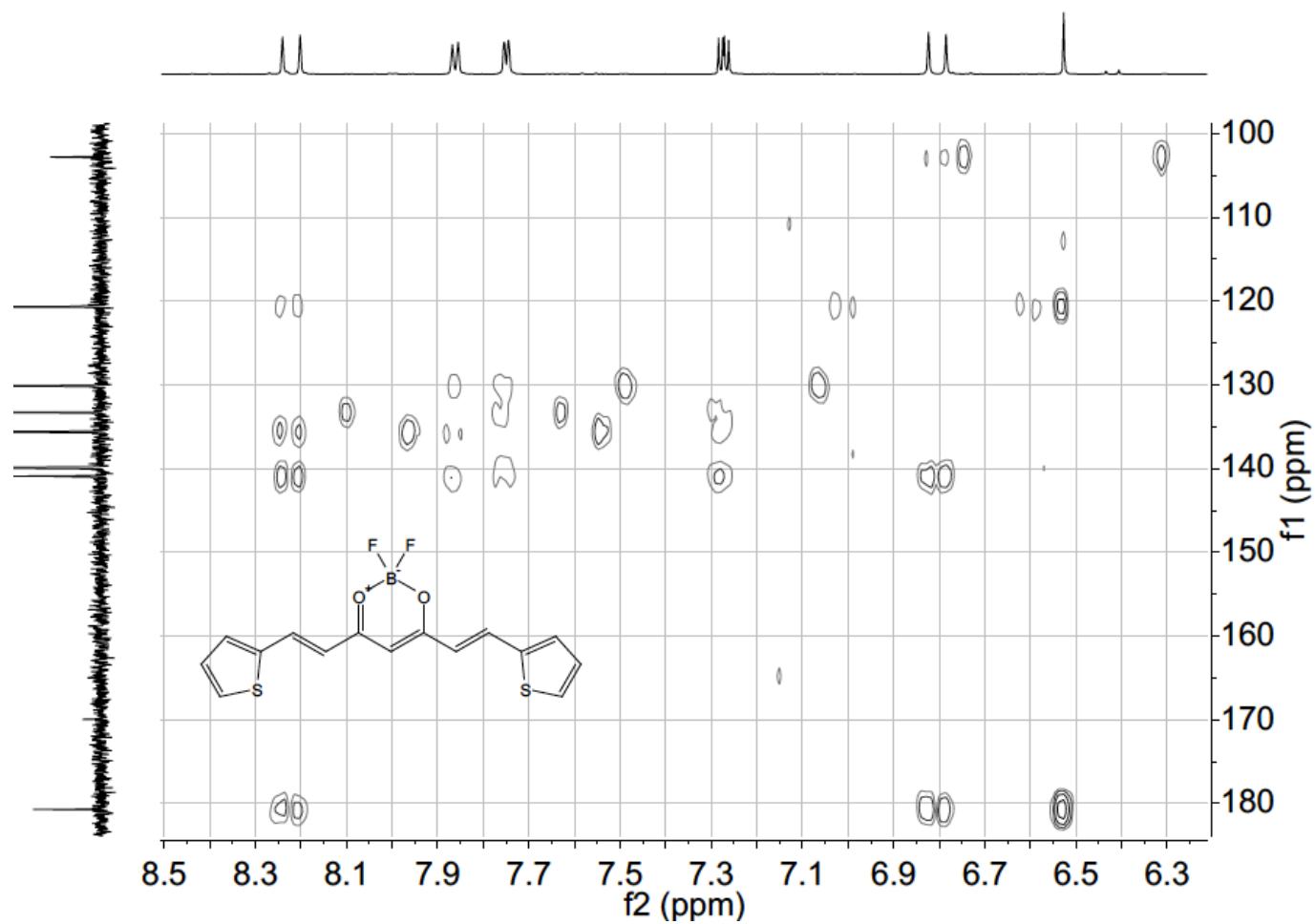


Figure S26. HMBC NMR spectrum of compound **4** (Acetone-*d*₆-400MHz -400MHz).

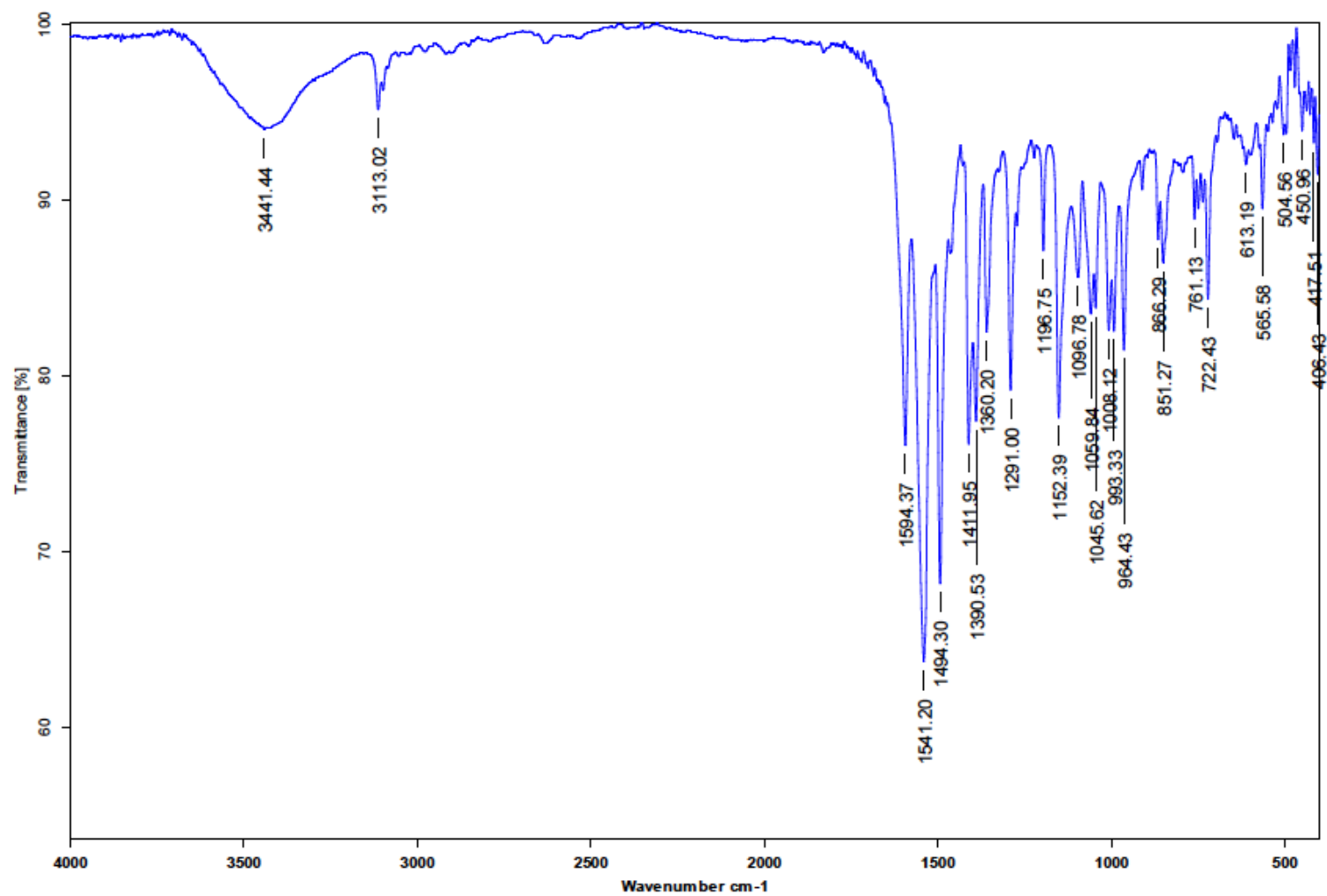


Figure S27. IR spectrum of compound 4.

Acq. Data Name: 1842 TIOFEN-BF2
Creation Parameters: Average(MS[1] Time:0..0)
Dr. Enriquez Raul / Operator: Carmen Garcia

Experiment Date/Time: 11/26/2021 9:31:09 AM
Instrument : JEOL The AccuTOF : JMS-T100LC
Ionization Mode: DART+

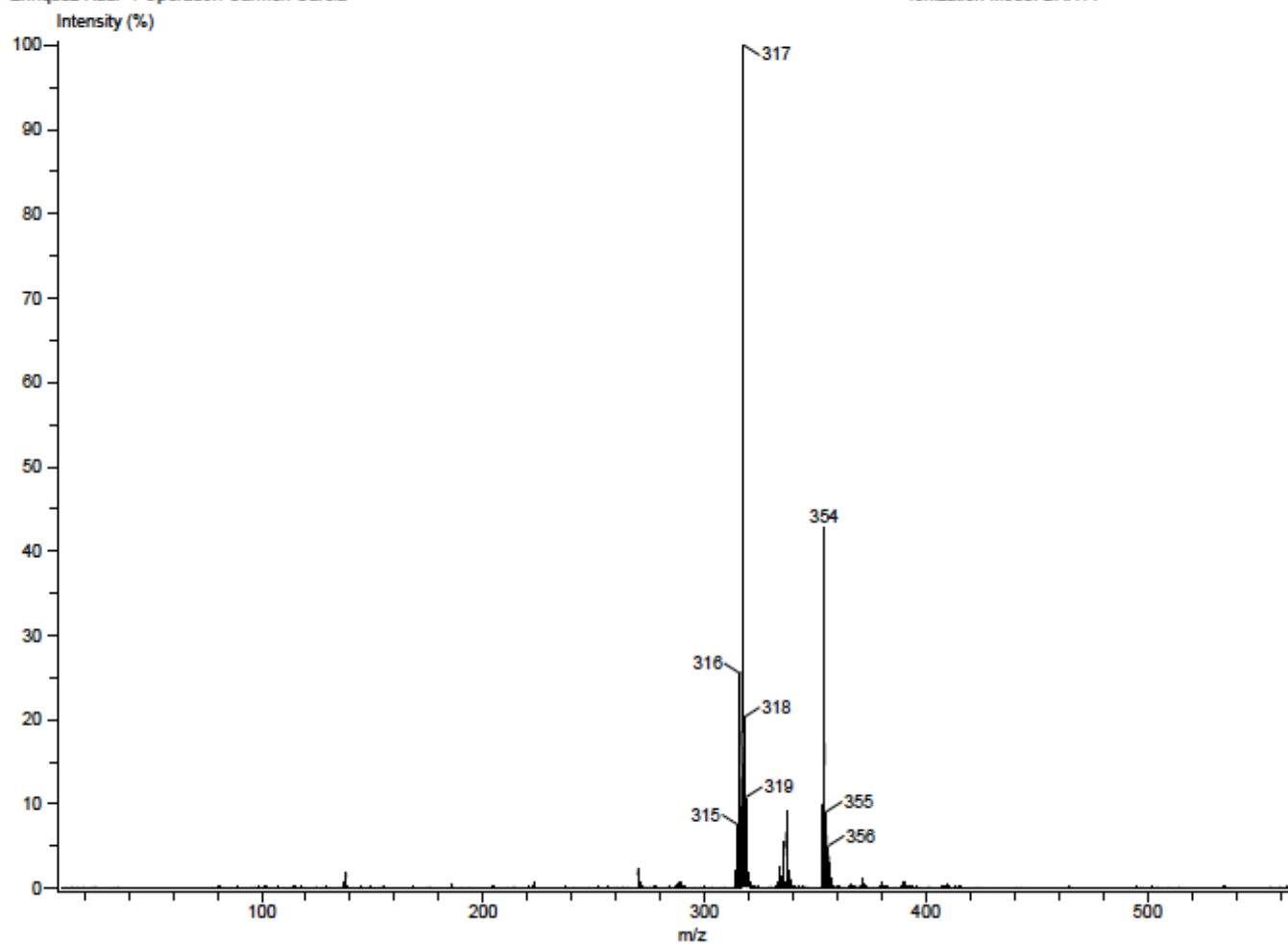


Figure S28. SM of compound 4.

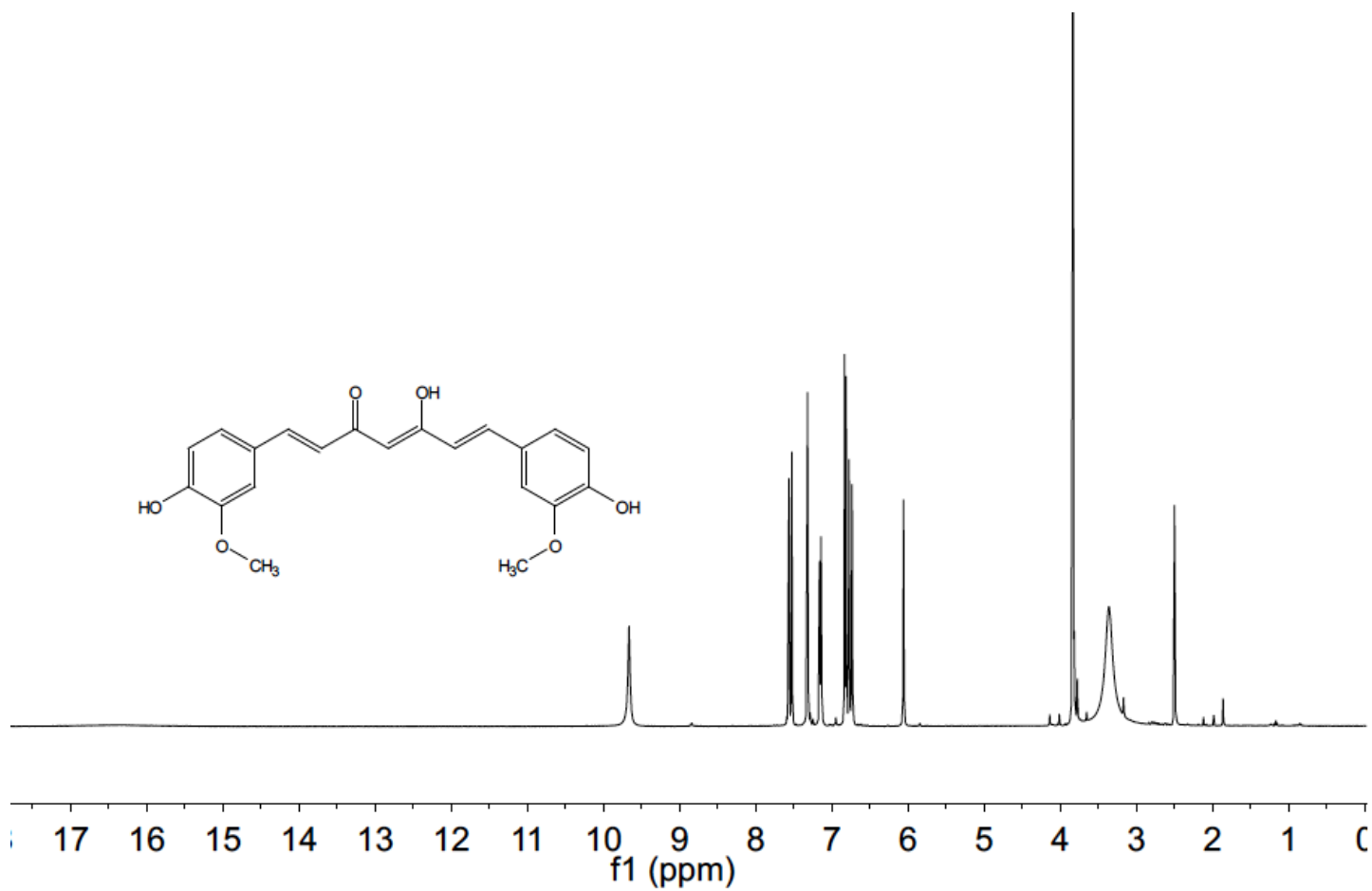


Figure 29. ¹H NMR spectrum of compound 5 (DMSO-*d*₆-400MHz).

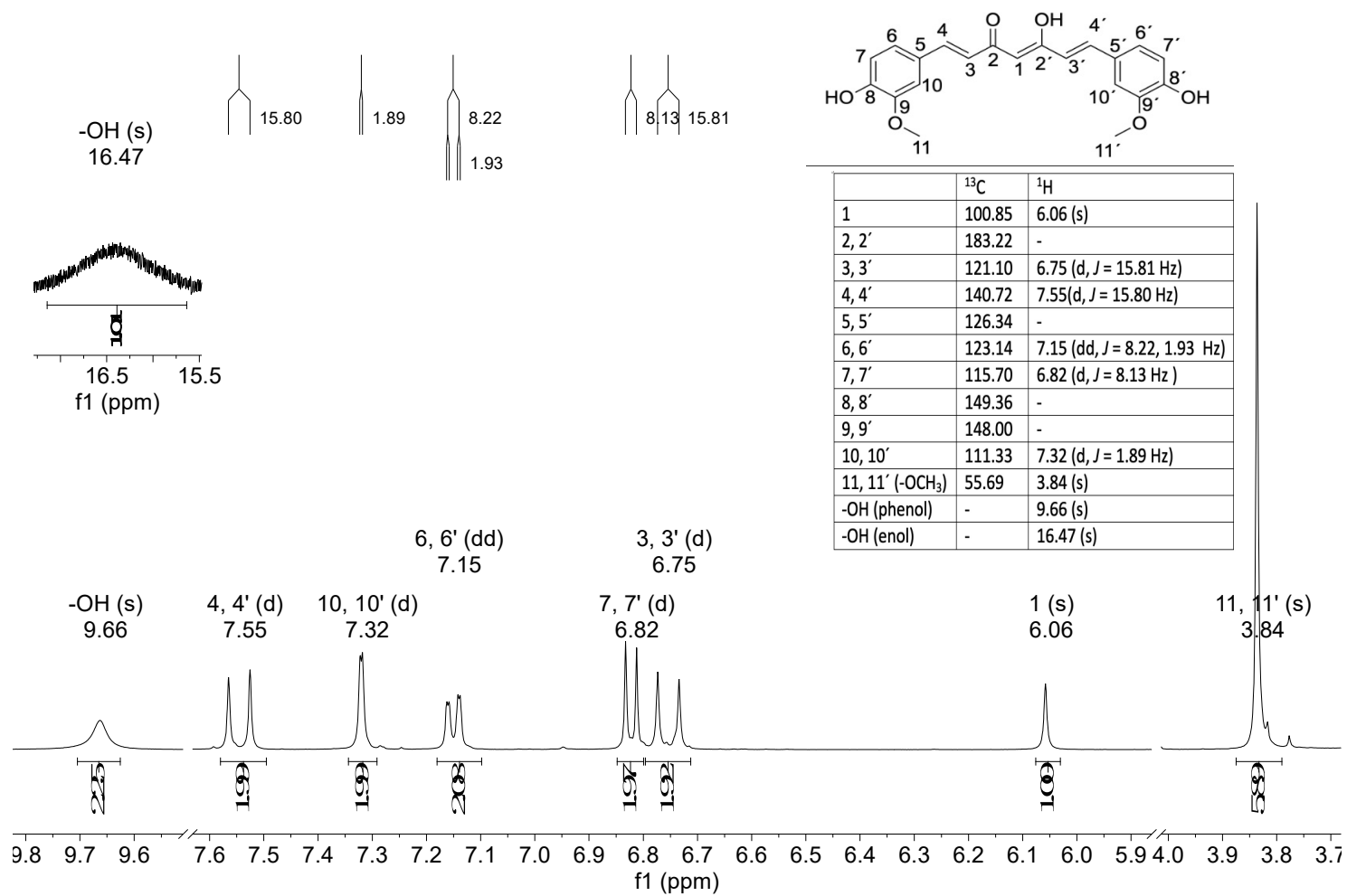


Figure S30. ¹H NMR spectrum of compound 5 (DMSO-*d*₆-400MHz, expansion).

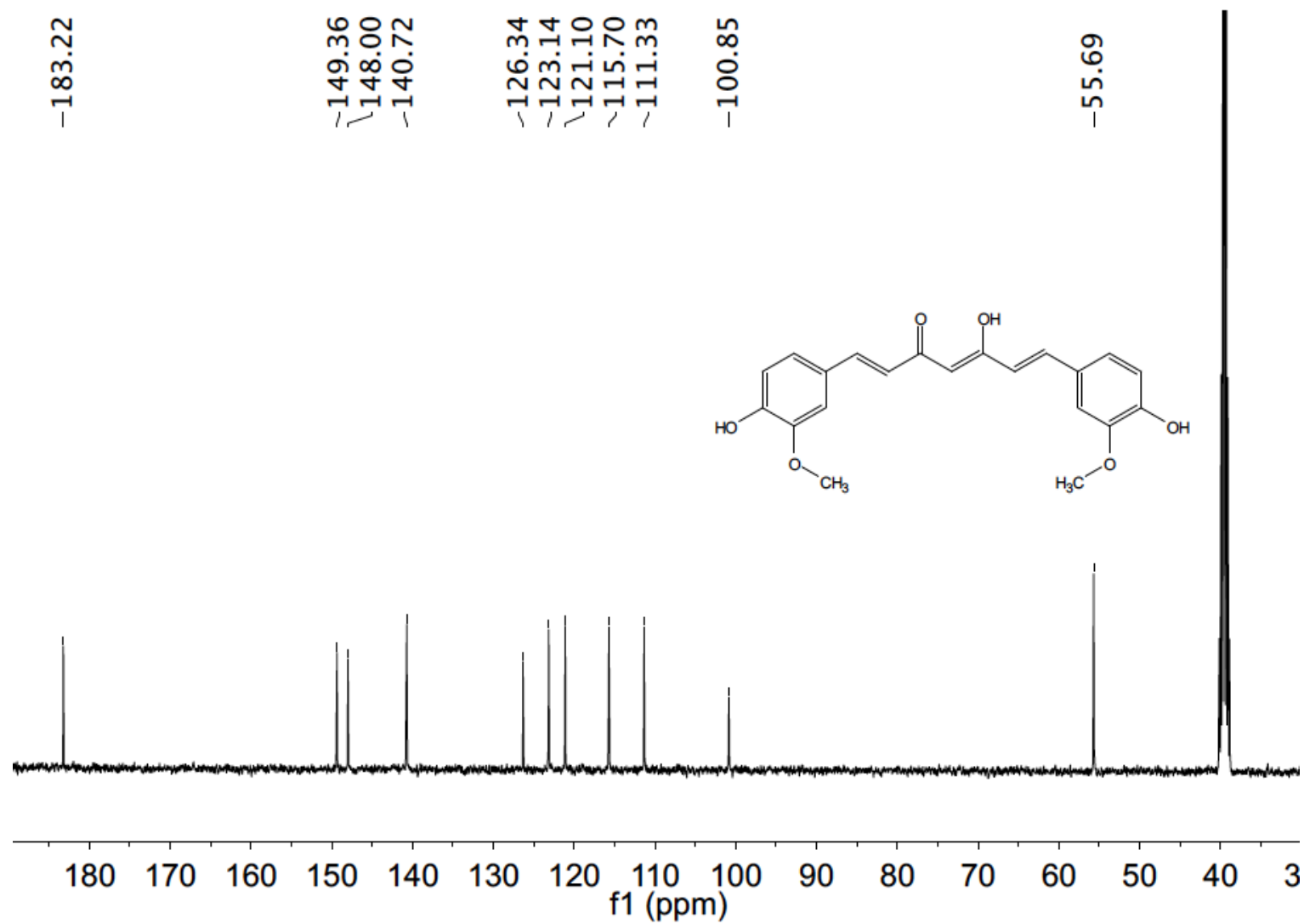


Figure S31. ^{13}C NMR spectrum of compound 5 ($\text{DMSO-}d_6$ -100MHz).

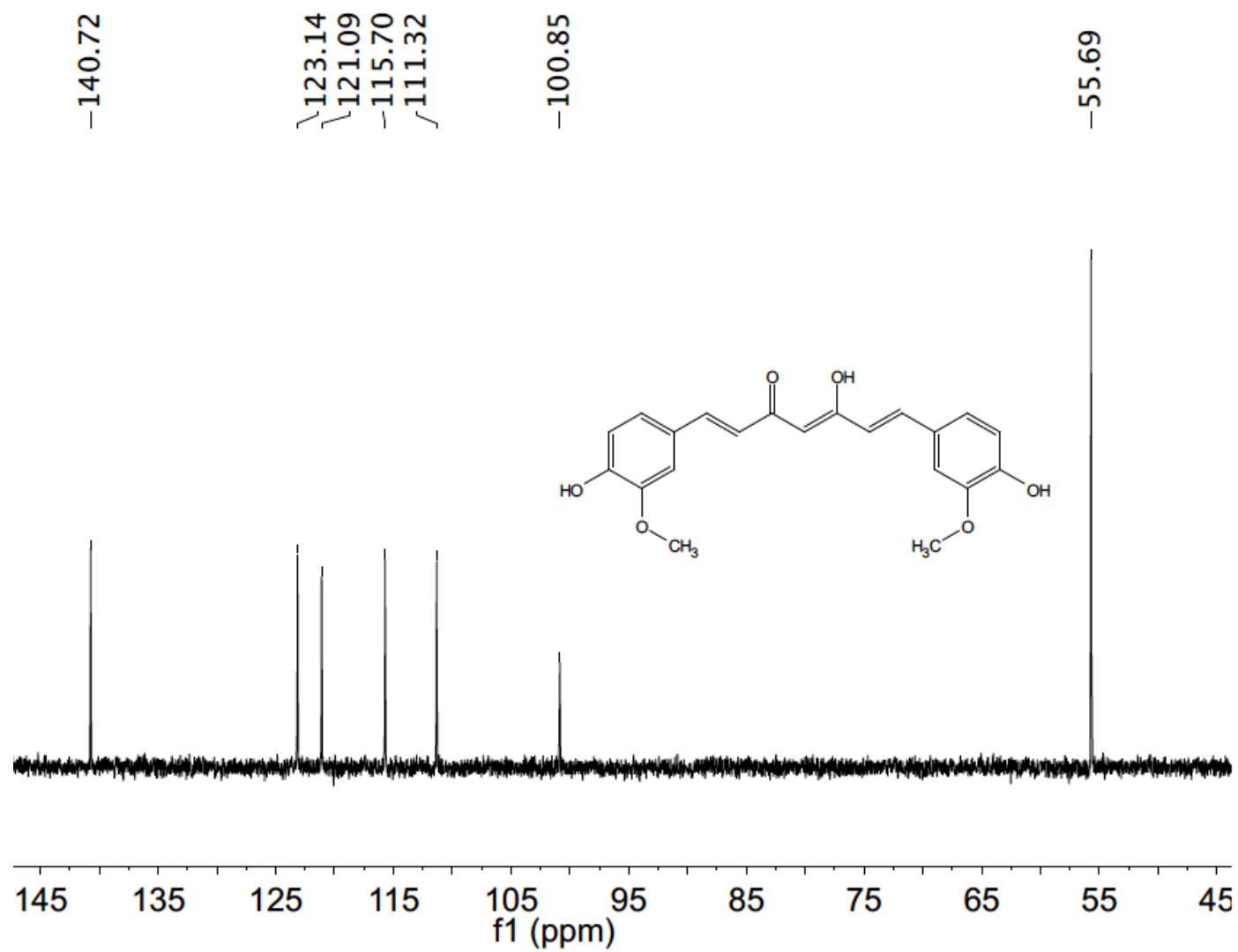


Figure S32. DEPT spectrum of compound 5 (DMSO-*d*₆-100MHz).

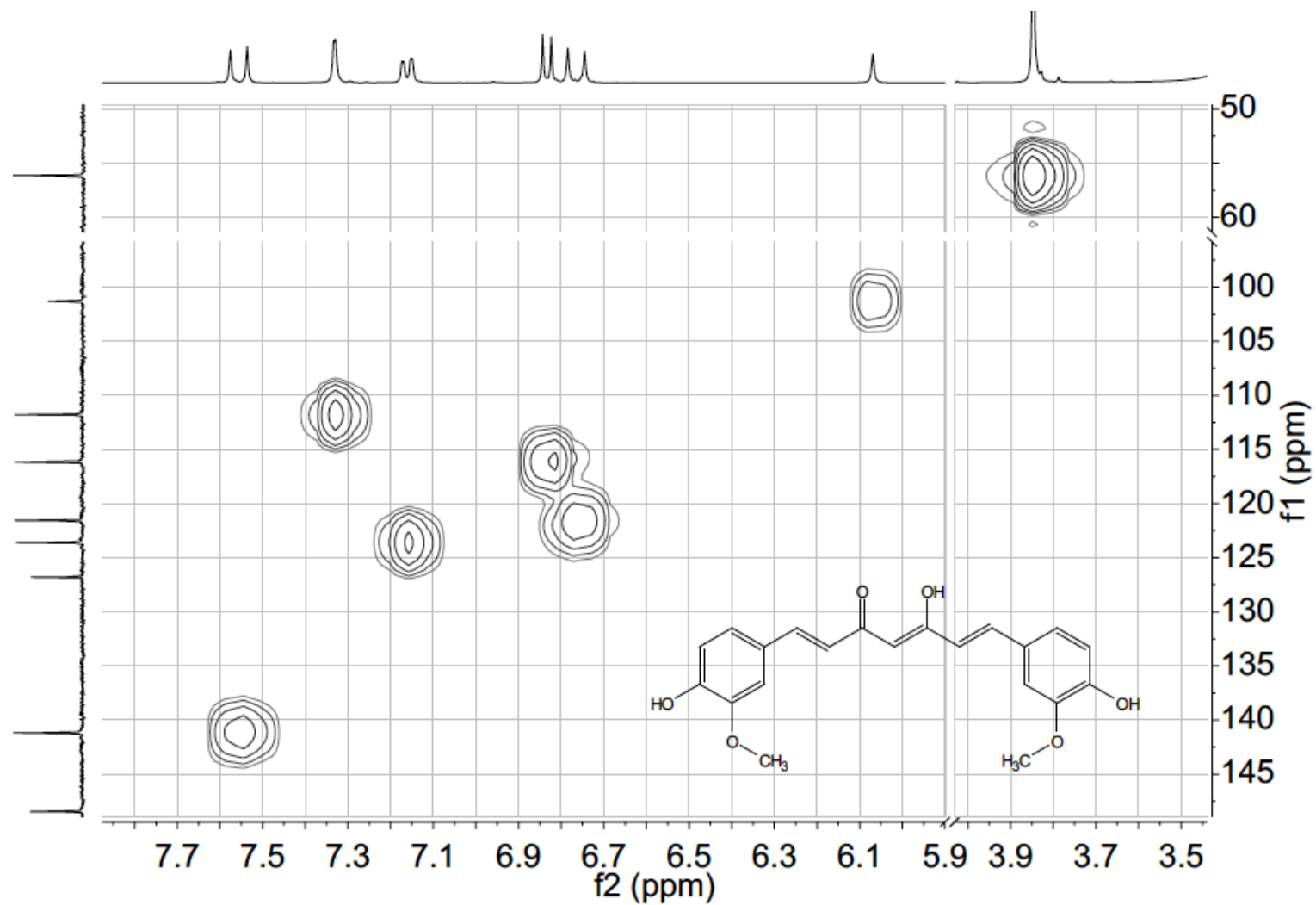


Figure S33. HSQC NMR spectrum of compound 5 (DMSO- d_6 -400MHz).

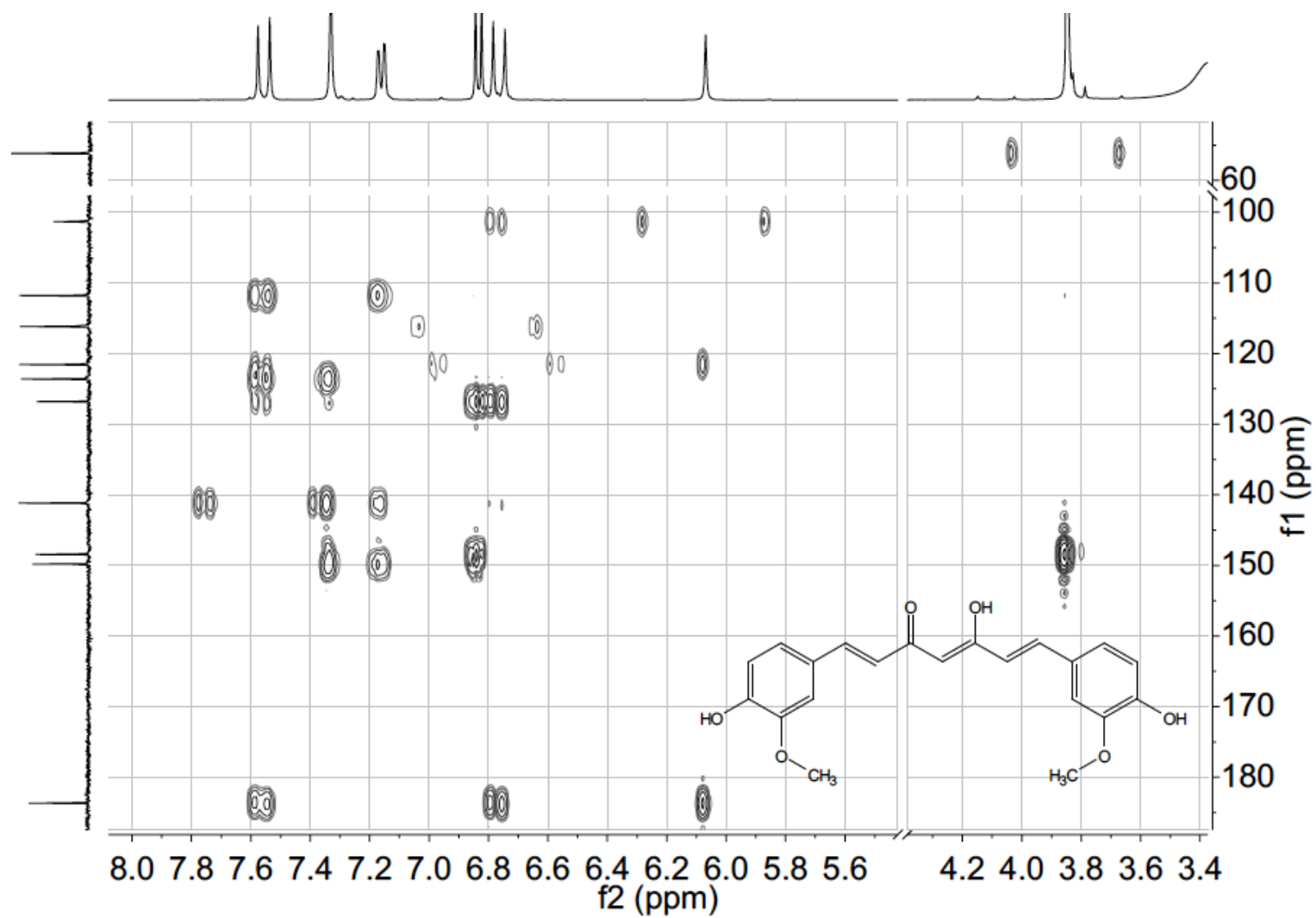


Figure S34. HMBC NMR spectrum of compound 5 (DMSO-*d*₆-400MHz).

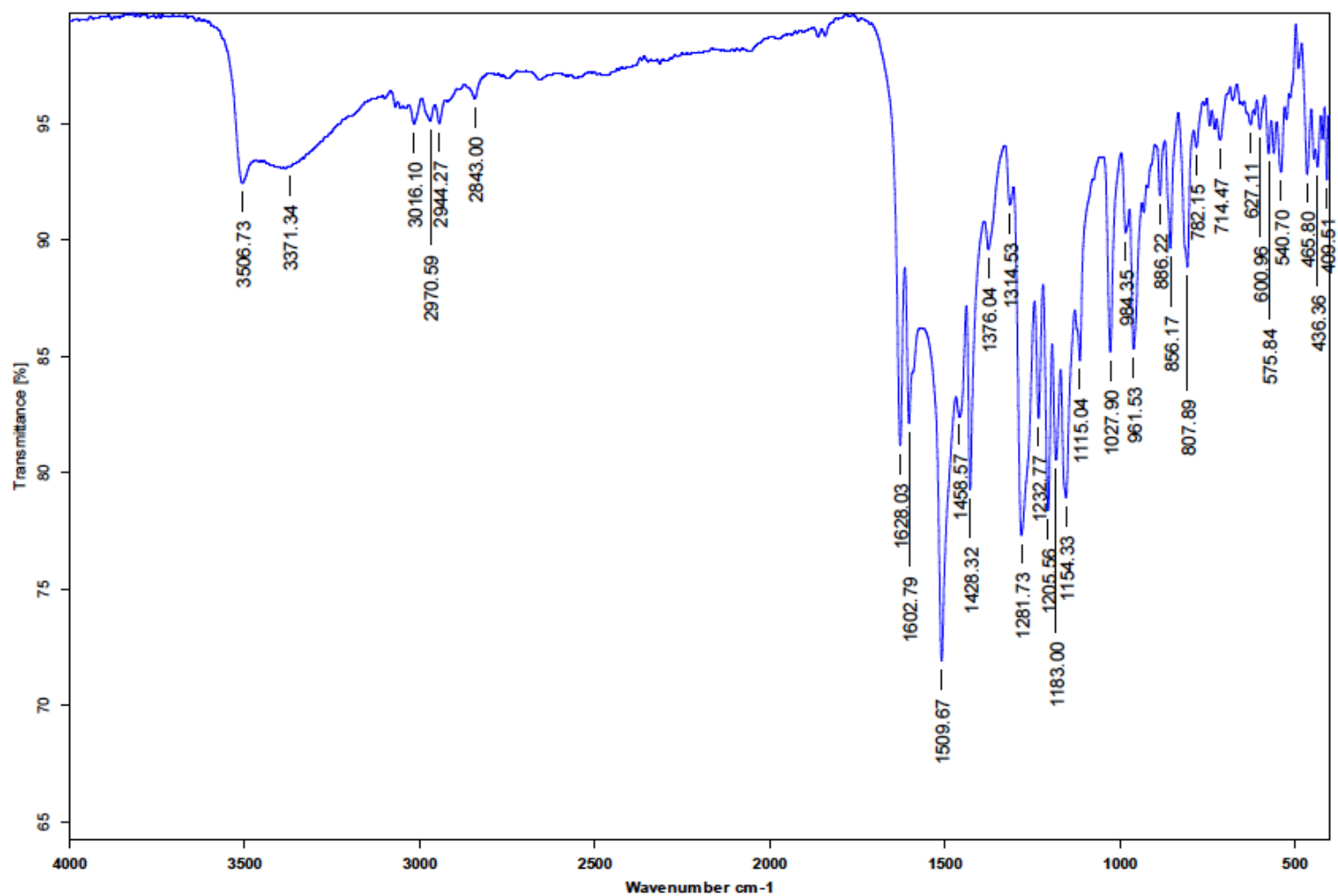


Figure S35. IR spectrum of compound 5.

Sample : 565_CURCU-RC
Note : Operator: Carmen Garcia
Inlet : Direct Ion Mode : EI+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.21 min Scan# : (7.8) Temp : 3276.7 deg.C
BP : m/z 177 Int. : 26.27 (275465)
Output m/z range : 0 to 800 Cut Level : 0.00 %

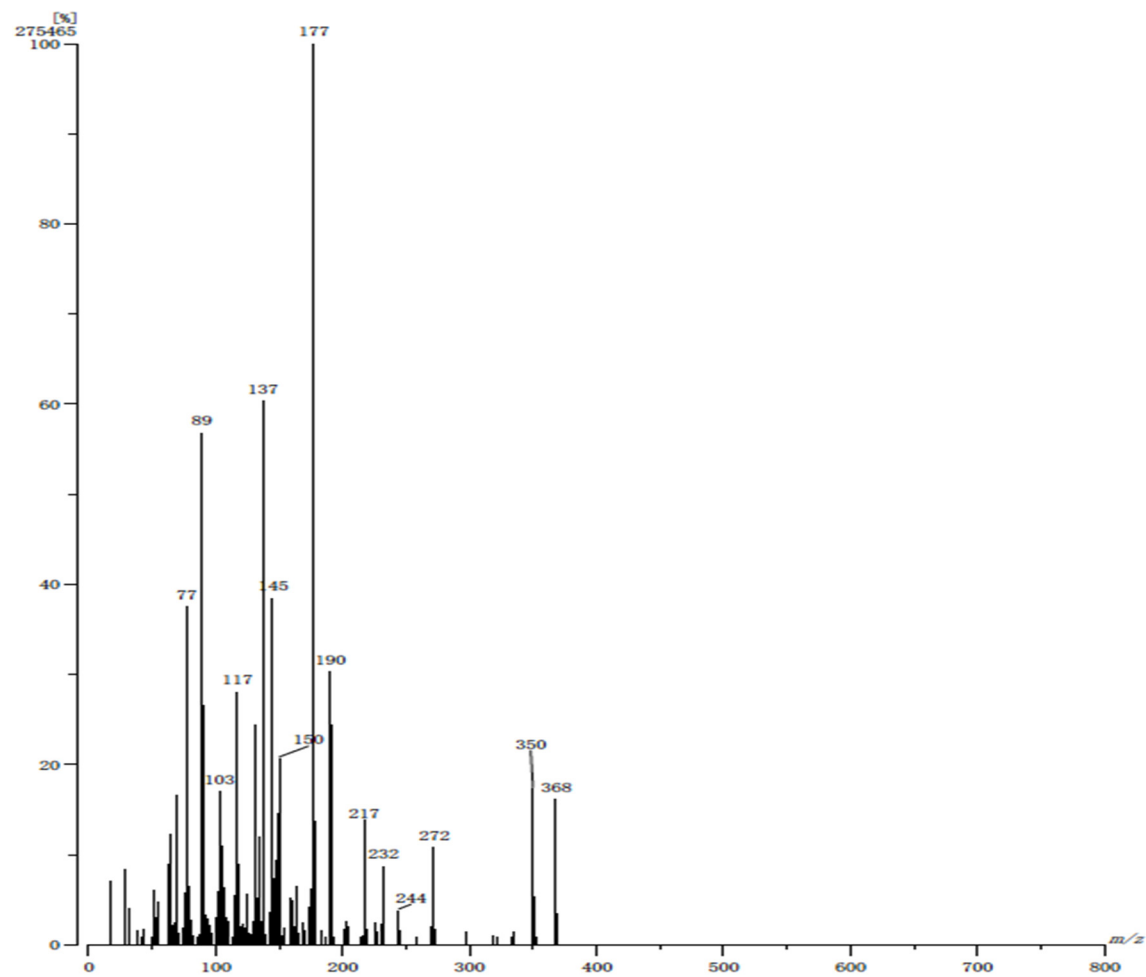


Figure S36. SM of compound 5.

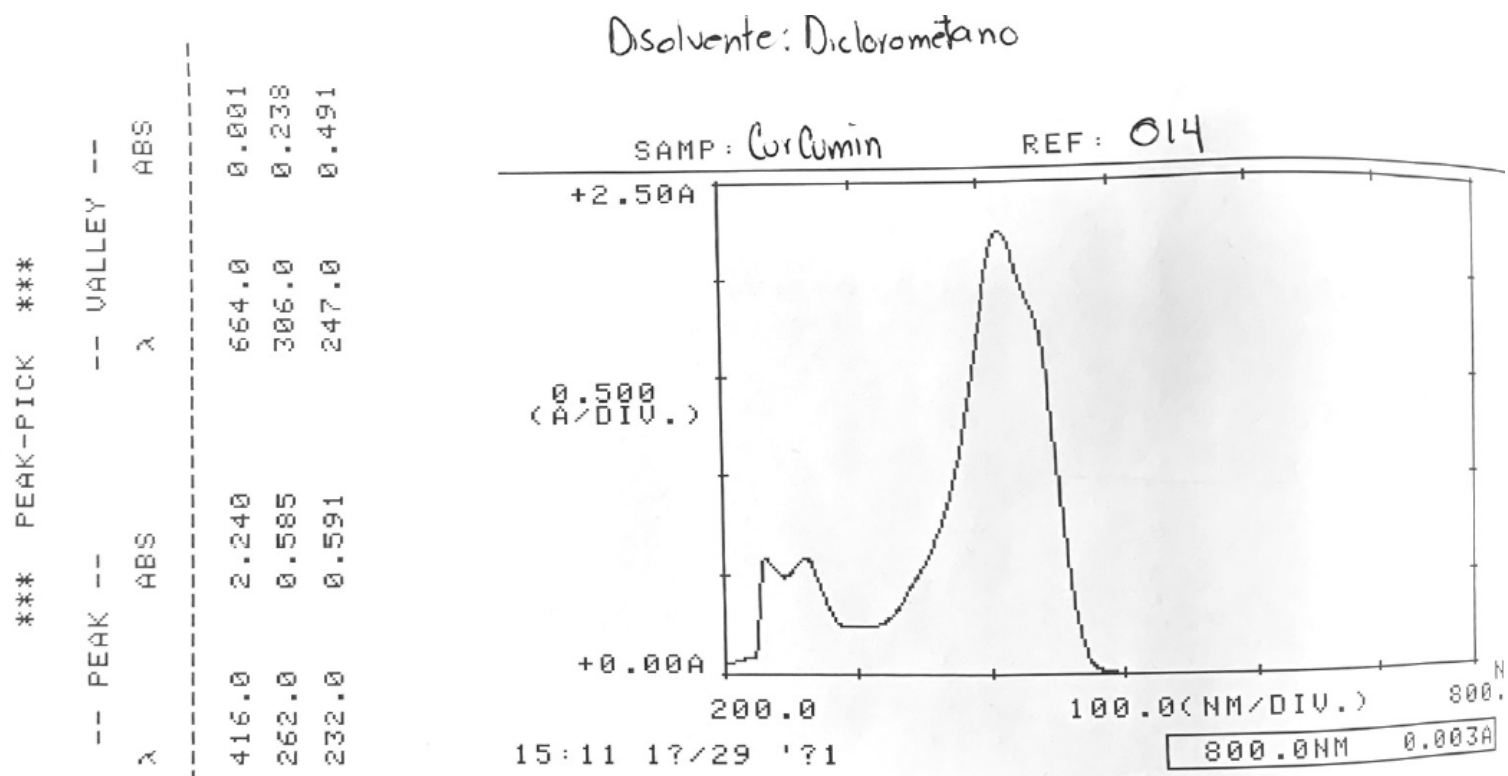
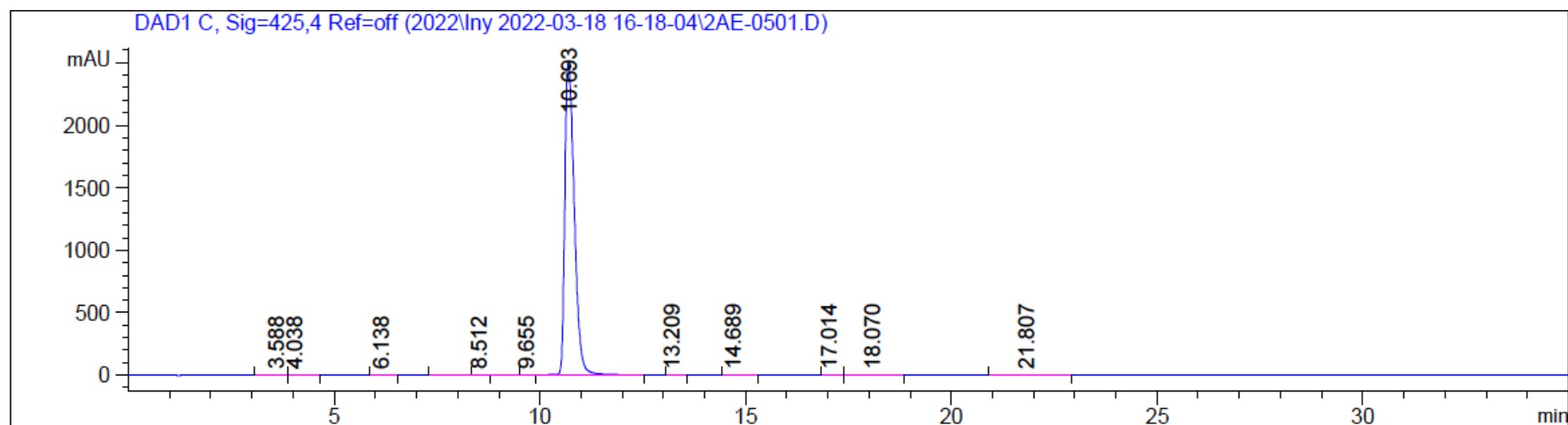


Figure S37. UV-spectrum of compound 5.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.588	BV	0.2152	42.73438	3.01770	0.1064
2	4.038	VB	0.2323	21.86004	1.35418	0.0544
3	6.138	BB	0.2324	16.99524	1.11164	0.0423
4	8.512	BV E	0.2213	11.20550	7.72235e-1	0.0279
5	9.655	VV E	0.1915	11.97119	9.73339e-1	0.0298
6	10.693	VB R	0.2465	3.99483e4	2499.04443	99.4858
7	13.209	BB	0.1857	4.50077	3.33034e-1	0.0112
8	14.689	BB	0.2215	45.94841	3.09032	0.1144
9	17.014	BB	0.2013	7.72818	5.45482e-1	0.0192
10	18.070	VB R	0.2754	18.74504	9.61558e-1	0.0467
11	21.807	BB	0.4521	24.78504	6.98205e-1	0.0617

Totals : 4.01548e4 2511.90213

Figure S38. HPLC of compound 5 (425nm).

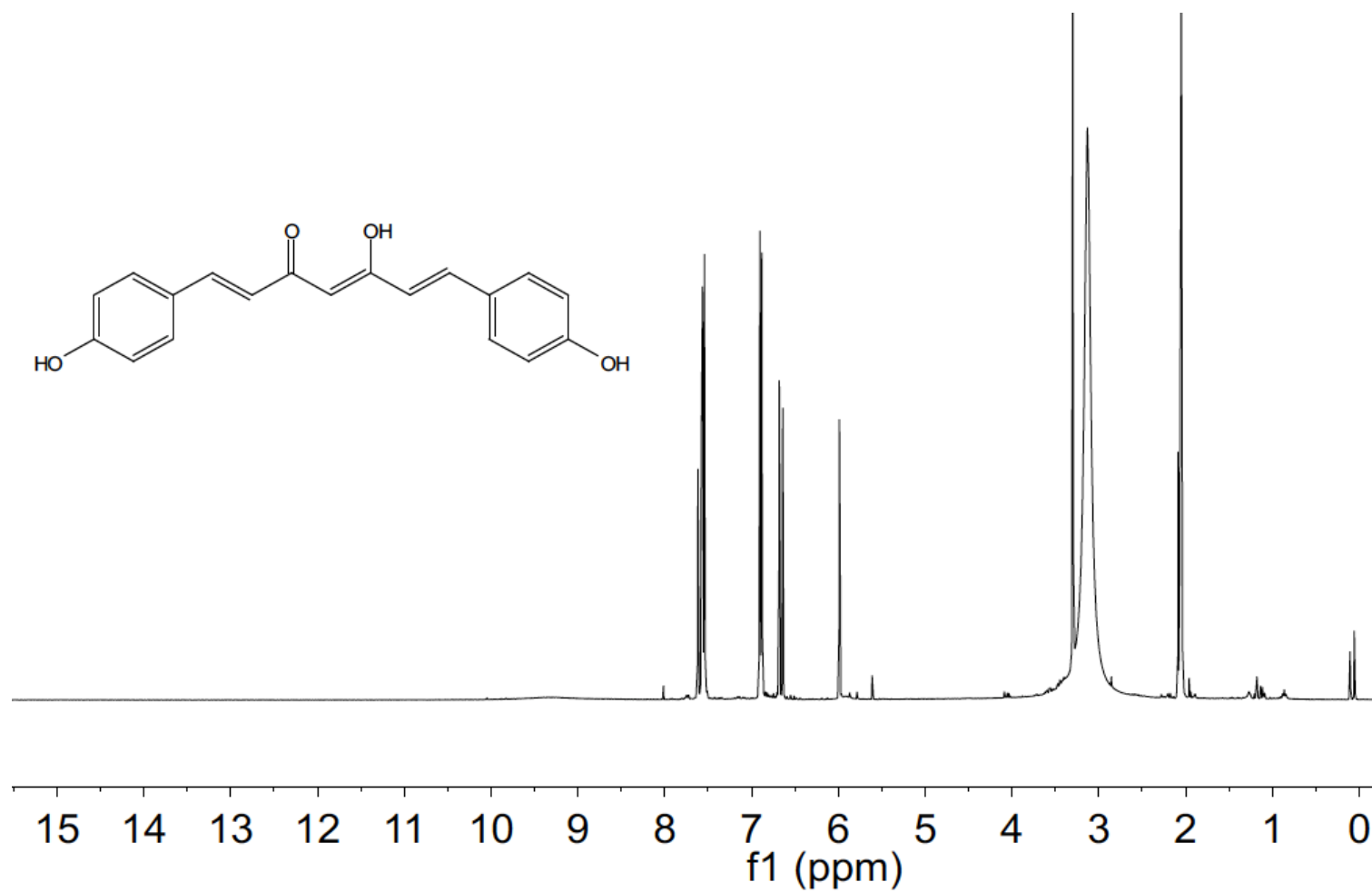


Figure 39. ¹H NMR spectrum of compound 6 (Acetone-*d*₆-400MHz).

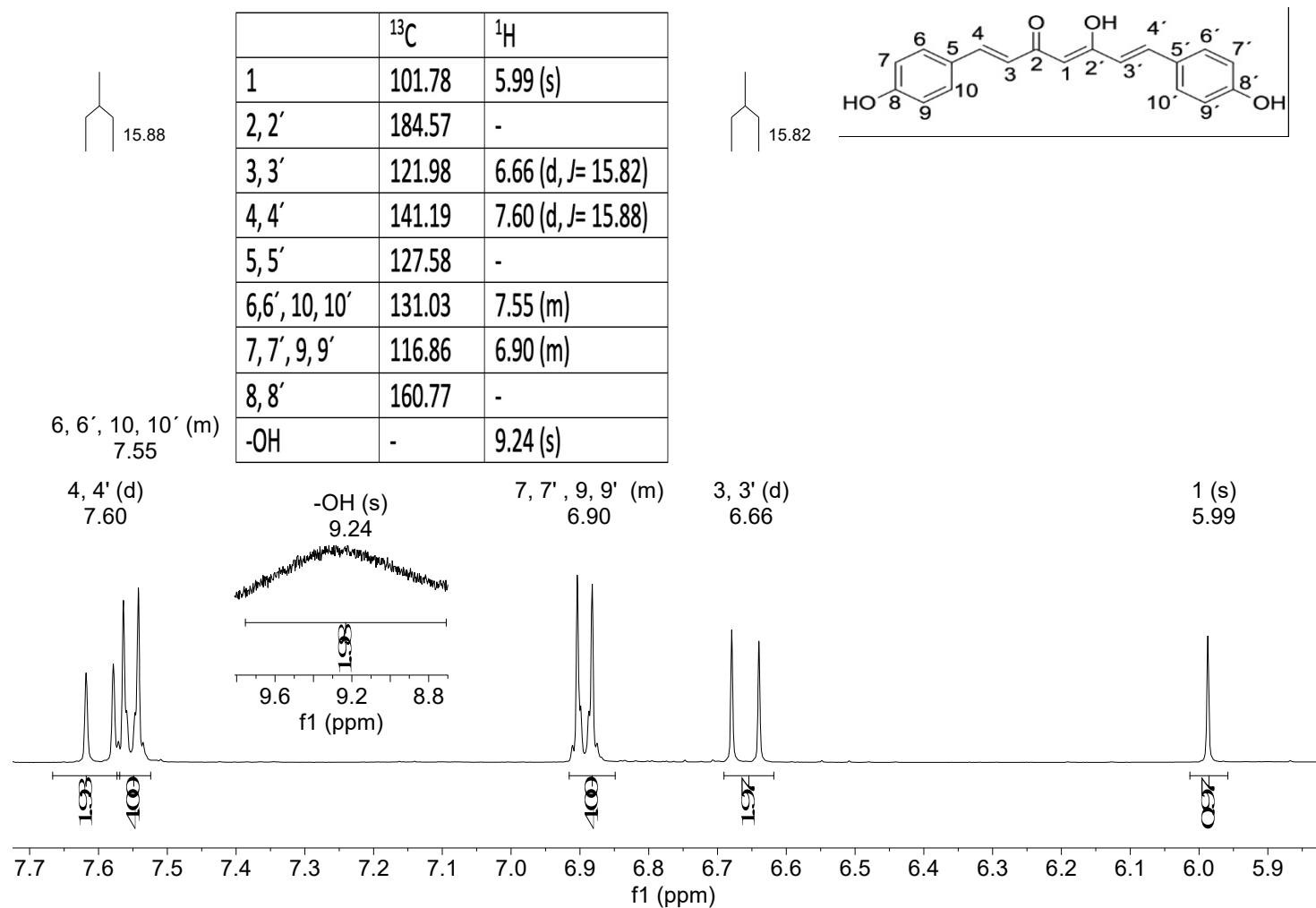


Figure S40. ^1H NMR spectrum of compound 6 (Acetone- d_6 -400MHz, expansion).

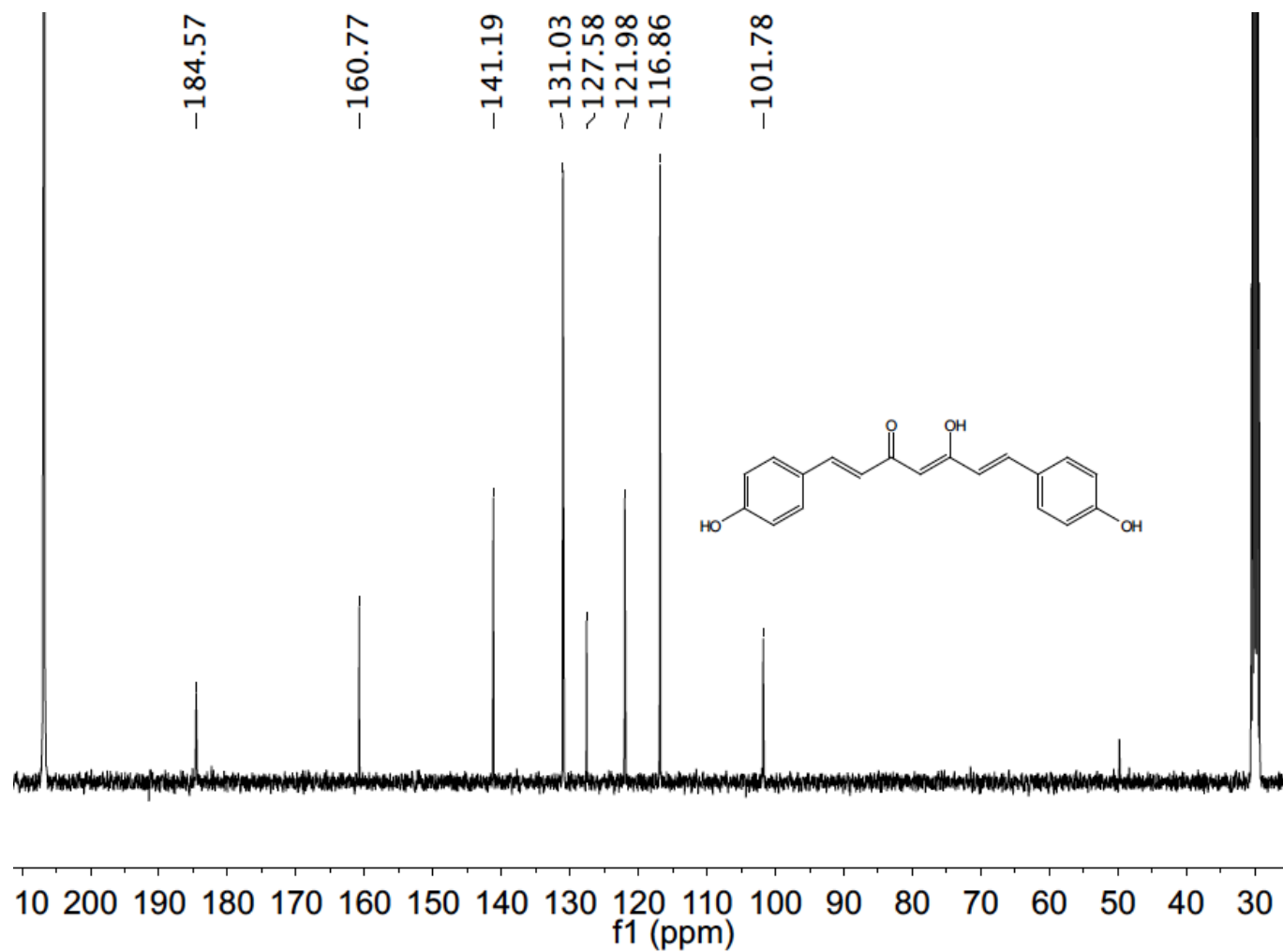


Figure S41. ^{13}C NMR spectrum of compound 6 ($\text{Acetone-}d_6$ -100MHz).

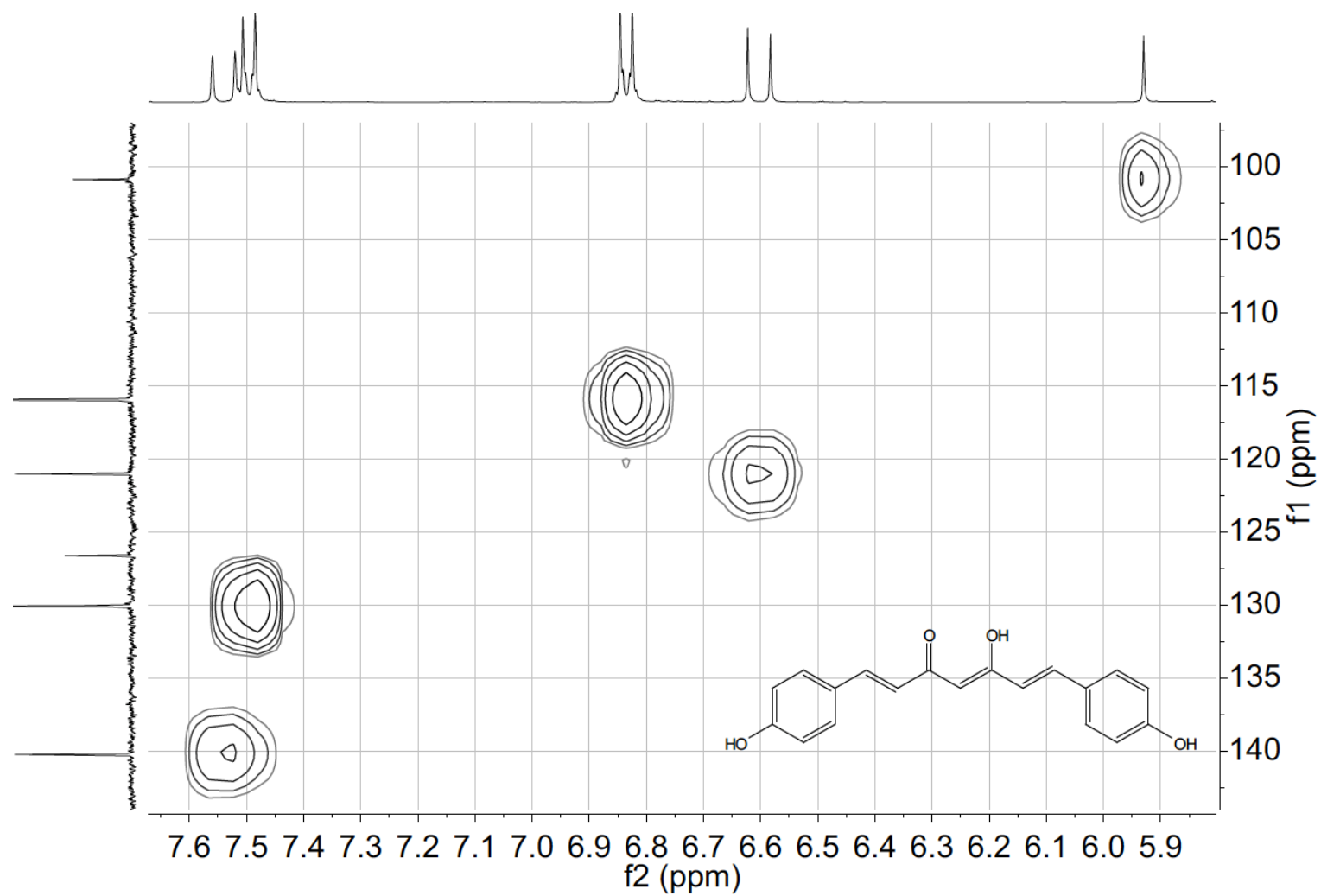


Figure S42. HSQC NMR spectrum of compound 6 (Acetone-*d*₆-400MHz).

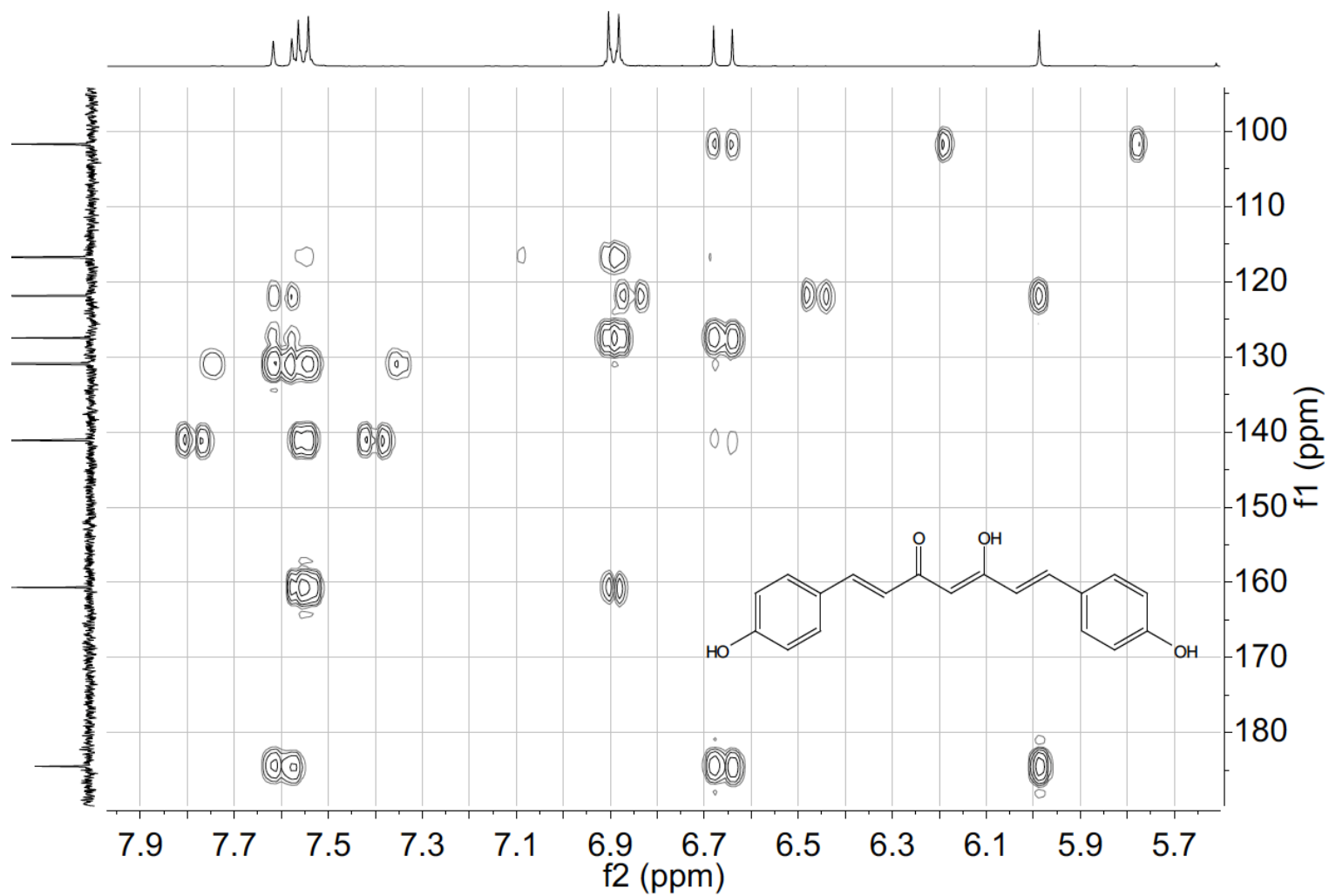


Figure S43. HMBC NMR spectrum of compound 6 (Acetone- d_6 -400MHz).

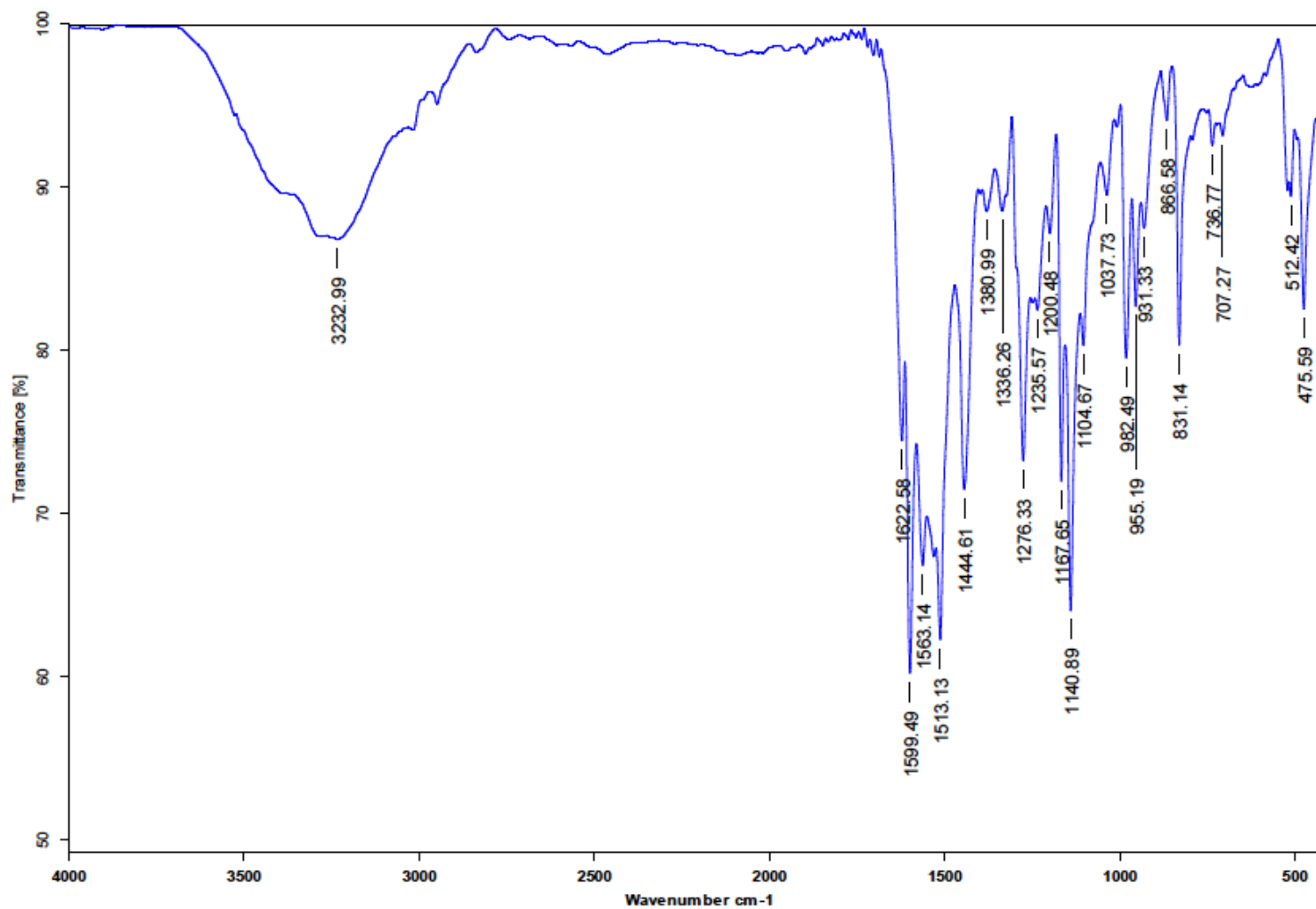


Figure S44. IR spectrum of compound 6.

Sample : 930 B-DESME-C
Note :
Inlet : Direct Ion Mode : EI+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.88 min Scan# : (27,32) Temp : 3276.7 deg.C
BP : m/z 31 Int. : 80.48 (843877)
Output m/z range : 0 to 330 Out Level : 0.00 %

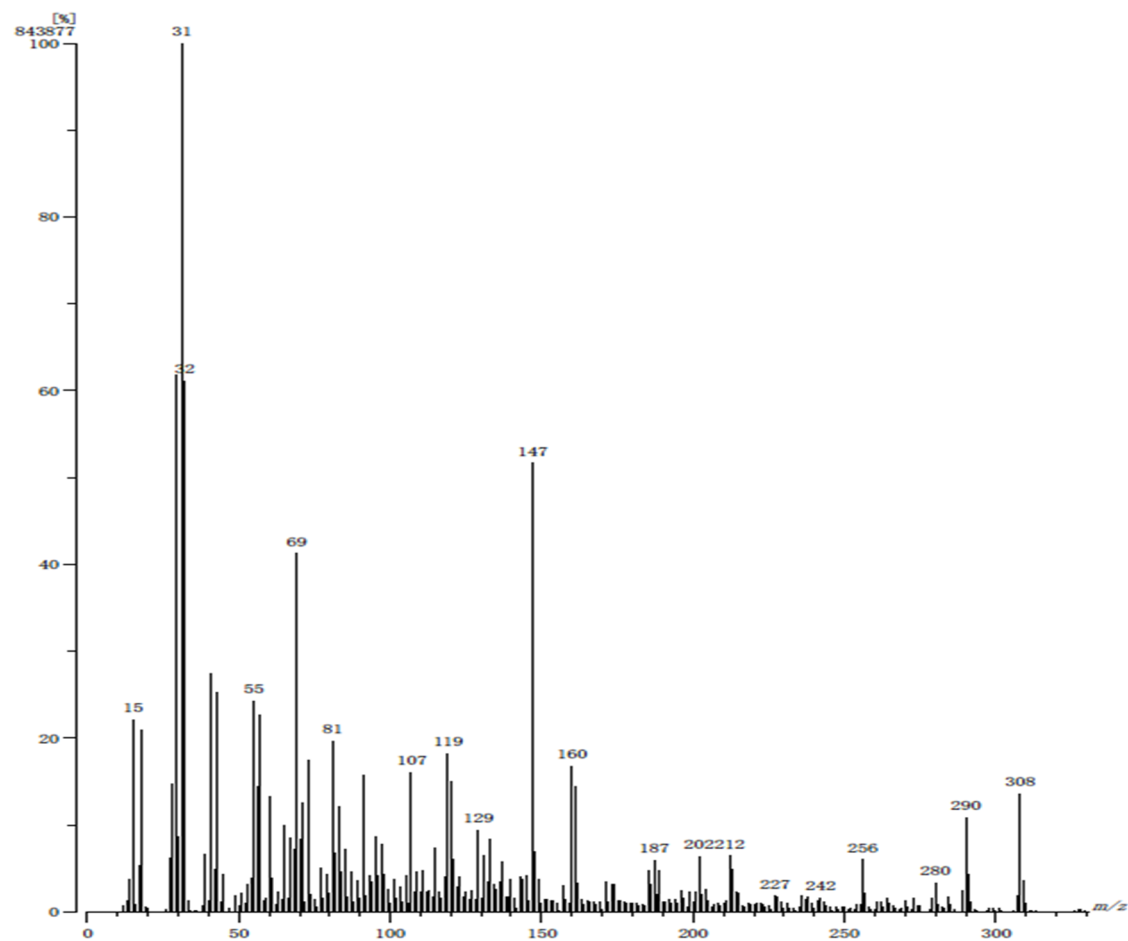


Figure S45. SM of compound 6.

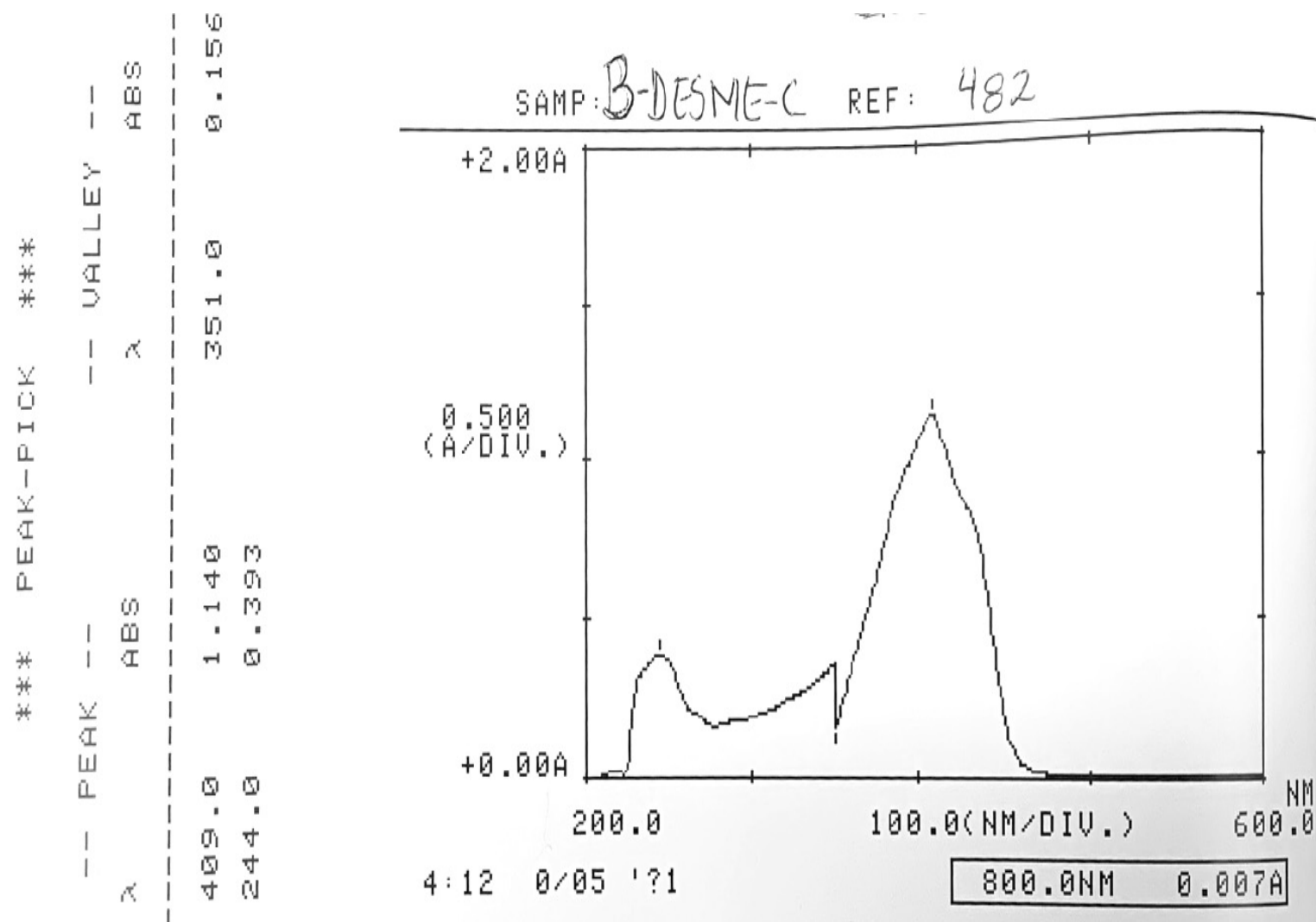
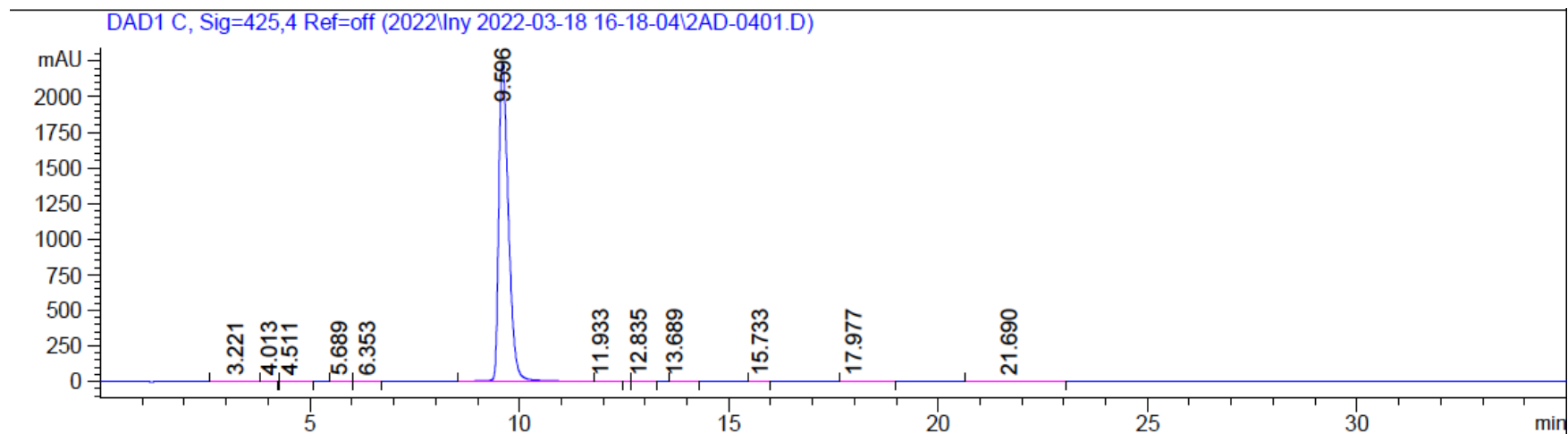


Figure S46. UV-spectrum of compound 6.



Signal 2: DAD1 C, Sig=425,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.221	VV R	0.2575	48.88575	2.62117	0.1351
2	4.013	VB E	0.1681	1.97942	1.53853e-1	5.472e-3
3	4.511	BV R	0.2440	9.65700	6.05775e-1	0.0267
4	5.689	BV	0.2274	11.49994	7.47740e-1	0.0318
5	6.353	VB	0.2731	8.18628	3.68578e-1	0.0226
6	9.596	BV R	0.2500	3.59731e4	2232.55737	99.4504
7	11.933	VB E	0.2525	3.43527	1.70917e-1	9.497e-3
8	12.835	BB	0.1994	6.59981	4.60051e-1	0.0182
9	13.689	BB	0.3211	1.85606	7.05078e-2	5.131e-3
10	15.733	BB	0.1821	5.40276	4.43434e-1	0.0149
11	17.977	BB	0.2585	19.91590	1.11436	0.0551
12	21.690	BB	0.5418	81.36864	1.91462	0.2250

Totals : 3.61718e4 2241.22838

Figure S47. HPLC of compound **6** (425nm).

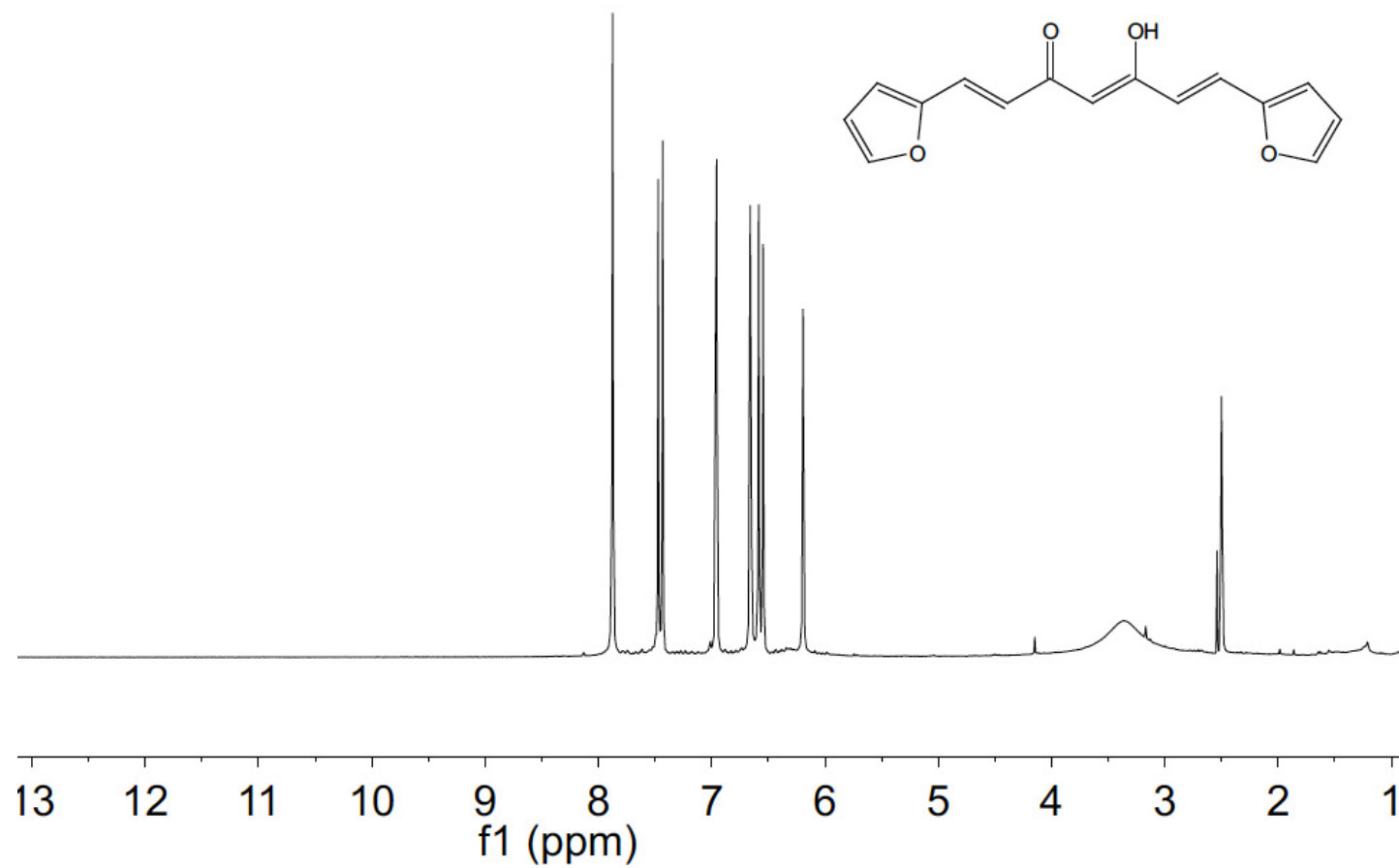


Figure 48. ^1H NMR spectrum of compound 7 ($\text{DMSO-}d_6$ -400MHz).

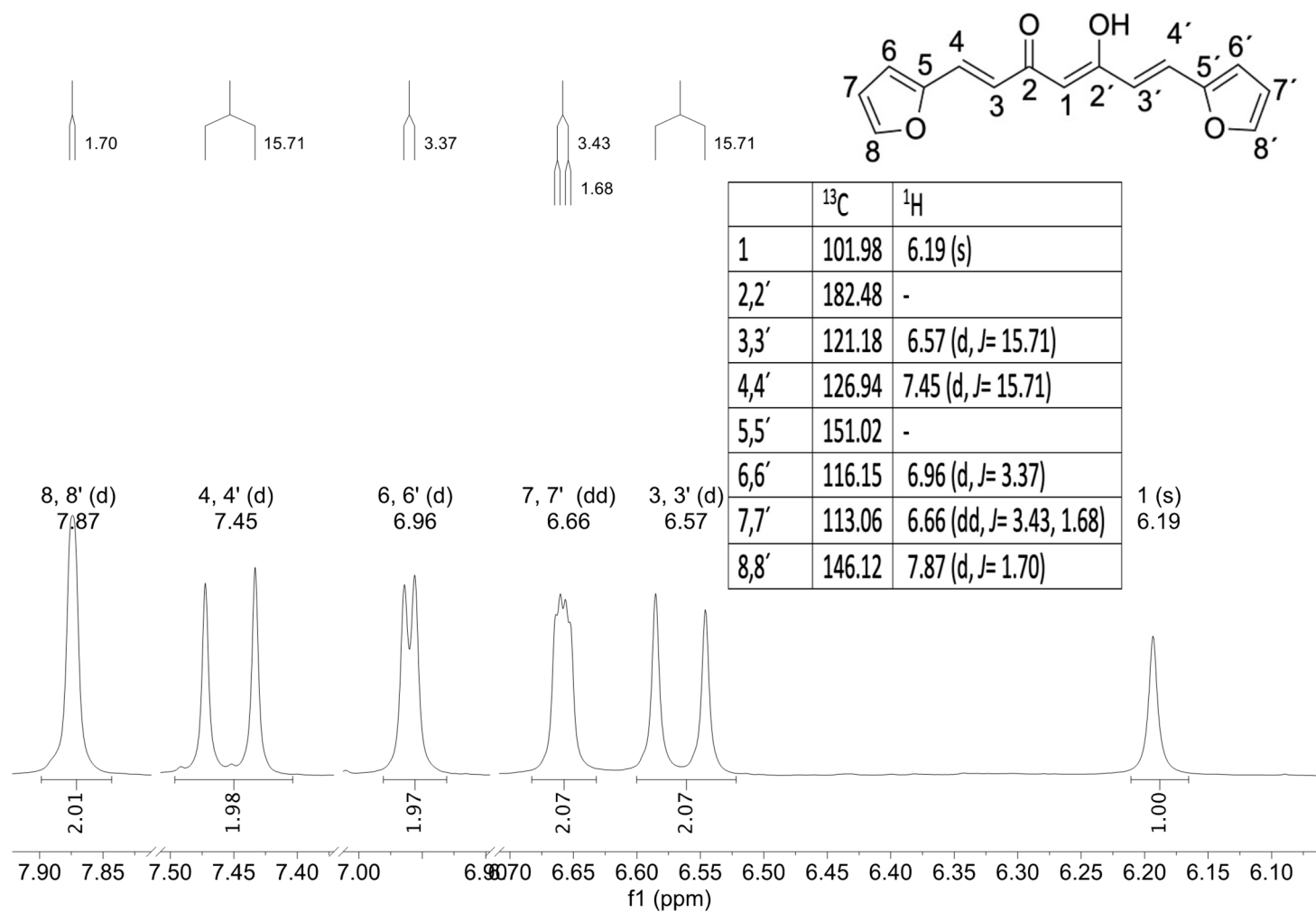


Figure S49. ¹H NMR spectrum of compound **7** (DMSO-*d*₆-400MHz, expansion).

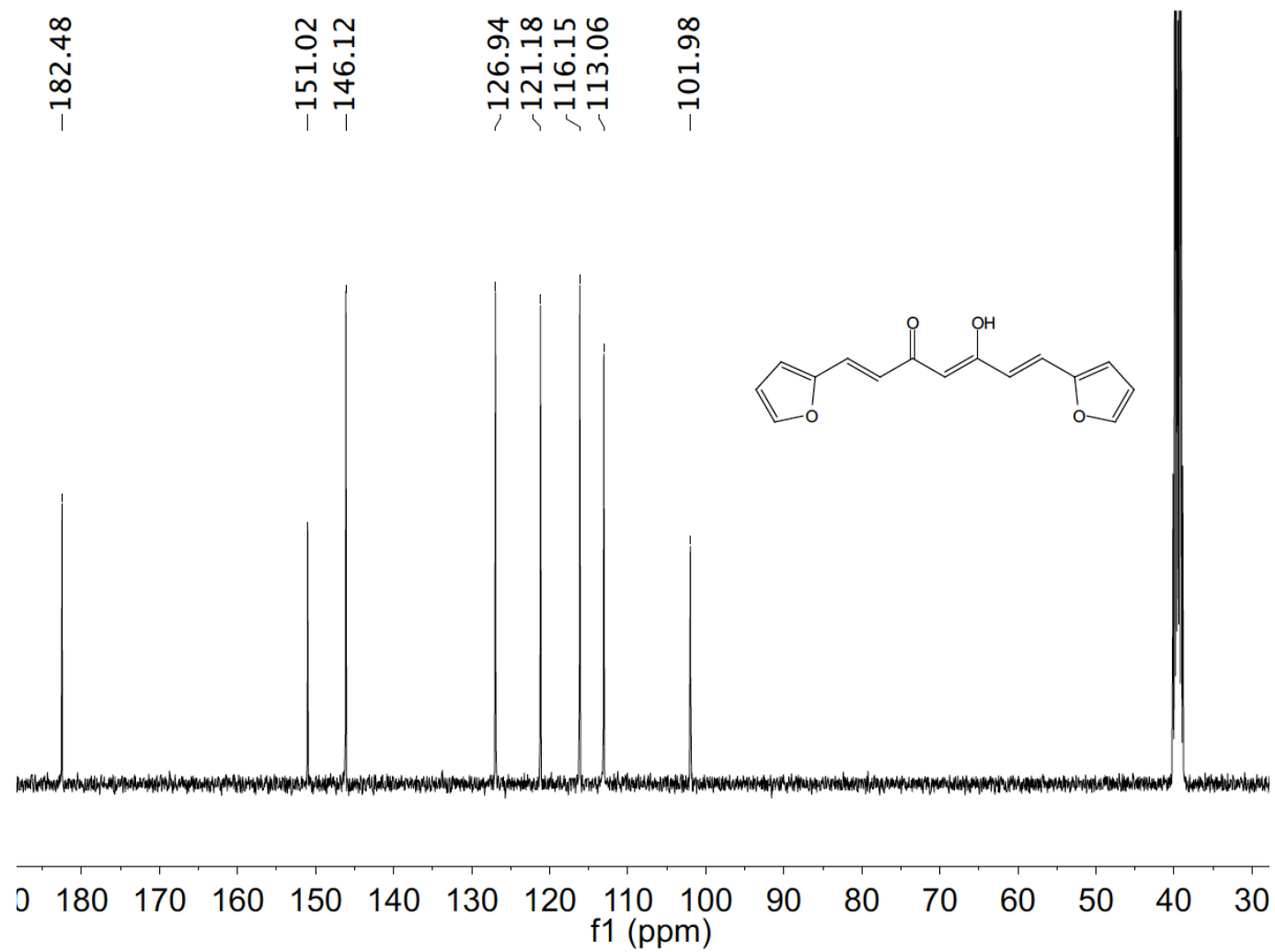


Figure S50. ^{13}C NMR spectrum of compound 7 (DMSO- d_6 -100MHz).

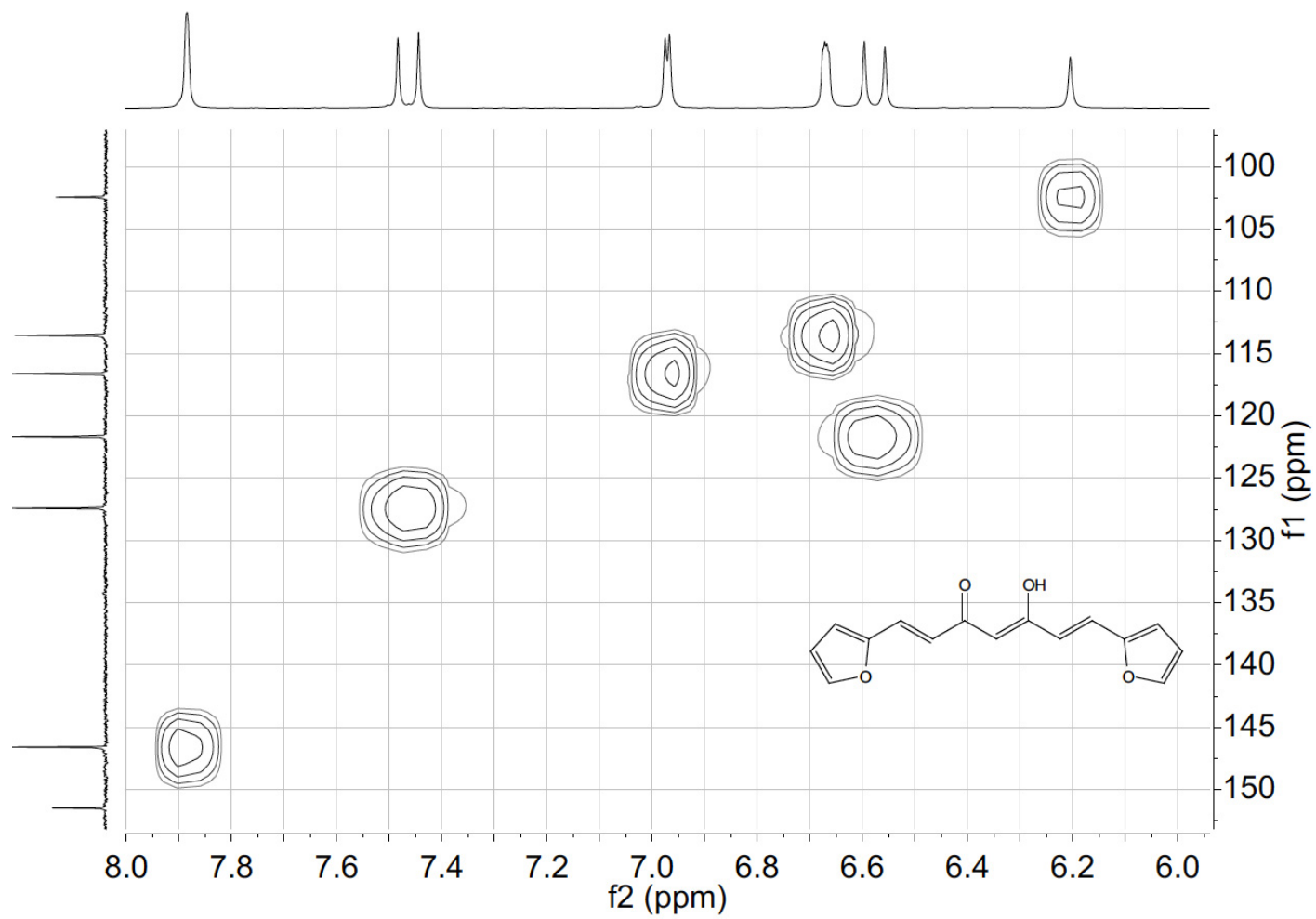


Figure S51. HSQC NMR spectrum of compound 7 (DMSO-*d*₆-400MHz).

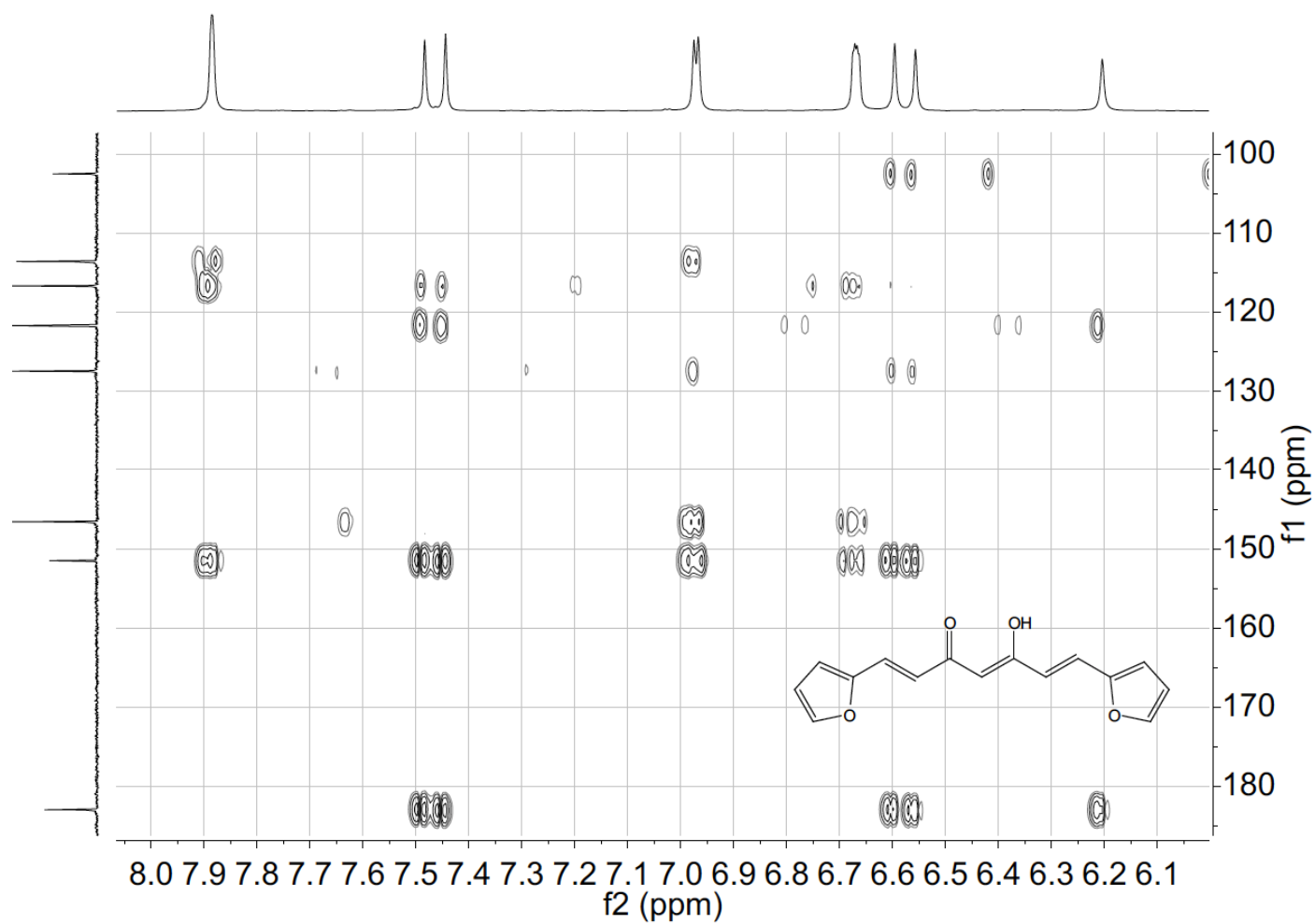


Figure S52. HMBC NMR spectrum of compound **7** (DMSO-*d*₆-400MHz).

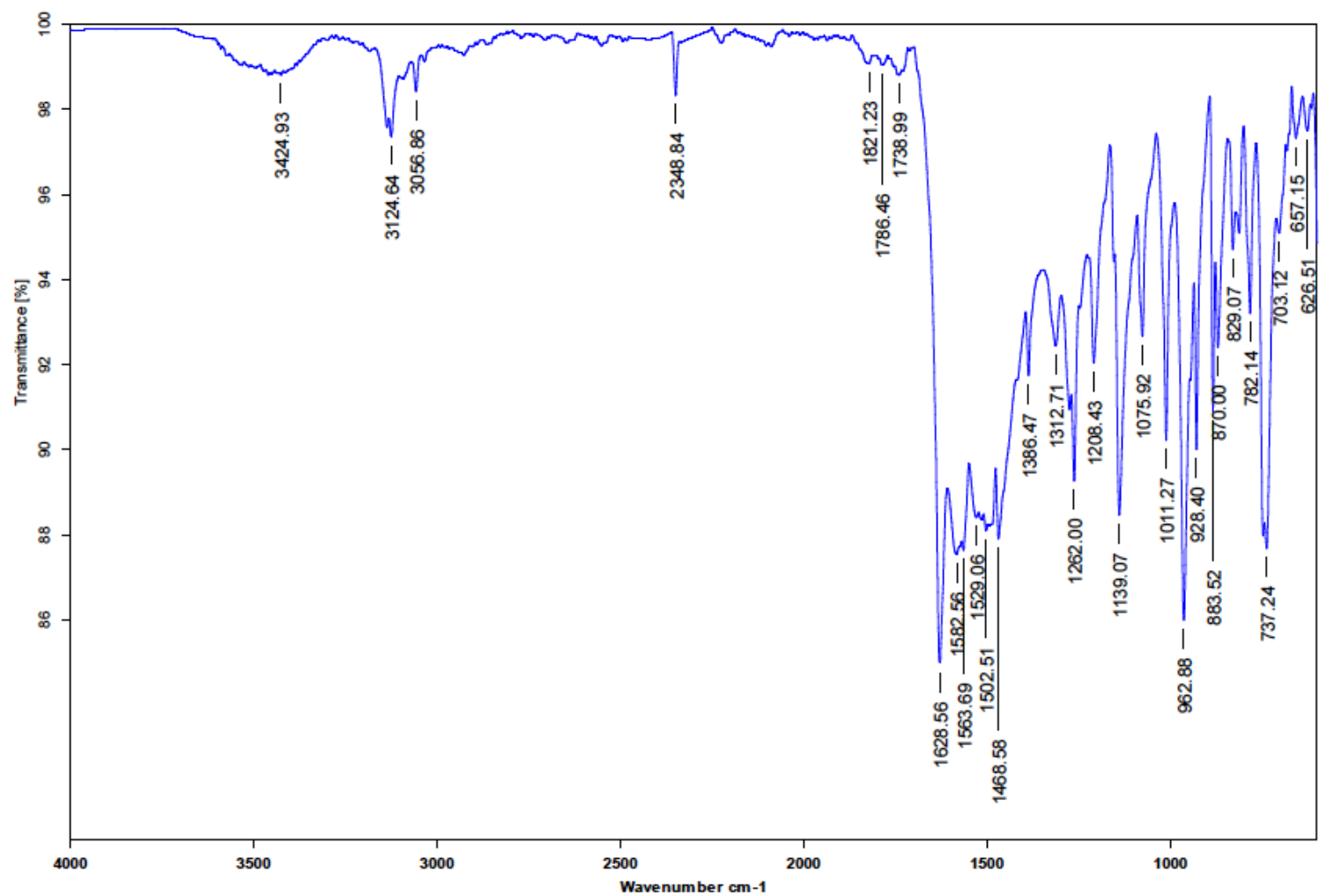


Figure S53. IR spectrum of compound 7.

Sample : 566_FURAN-RC
Note : Operator: Carmen Garcia
Inlet : Direct Ion Mode : EI+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.48 min Scan# : (15,16) Temp : 3276.7 deg.C
BP : m/z 18 Int. : 32.27 (338424)
Output m/z range : 0 to 800 Out Level : 0.00 %

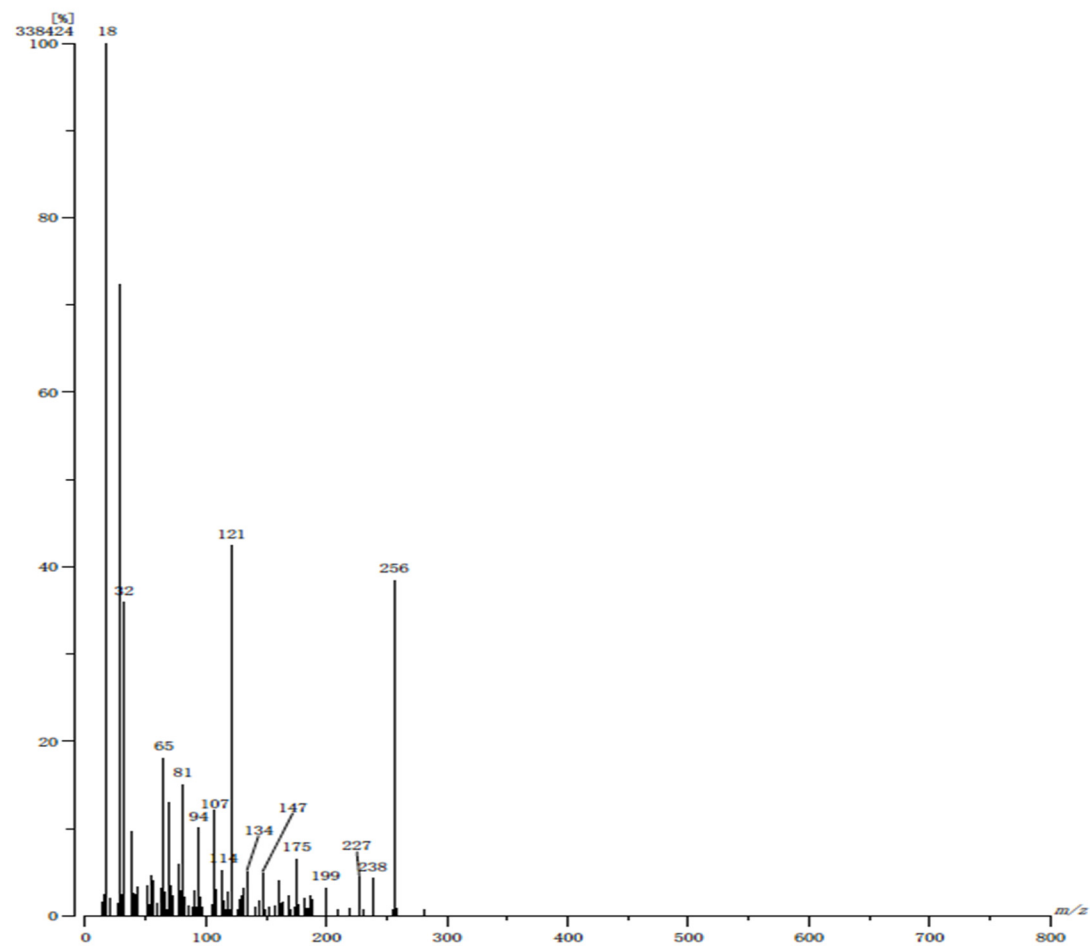


Figure S54. SM of compound 7.

*** PEAK-PICK ***					
-- PEAK --		-- VALLEY --			
λ	ABS	λ	ABS	λ	ABS
416.0	2.030	704.0	0.001		
256.0	0.311	285.0	0.203		
231.0	0.316	242.0	0.293		

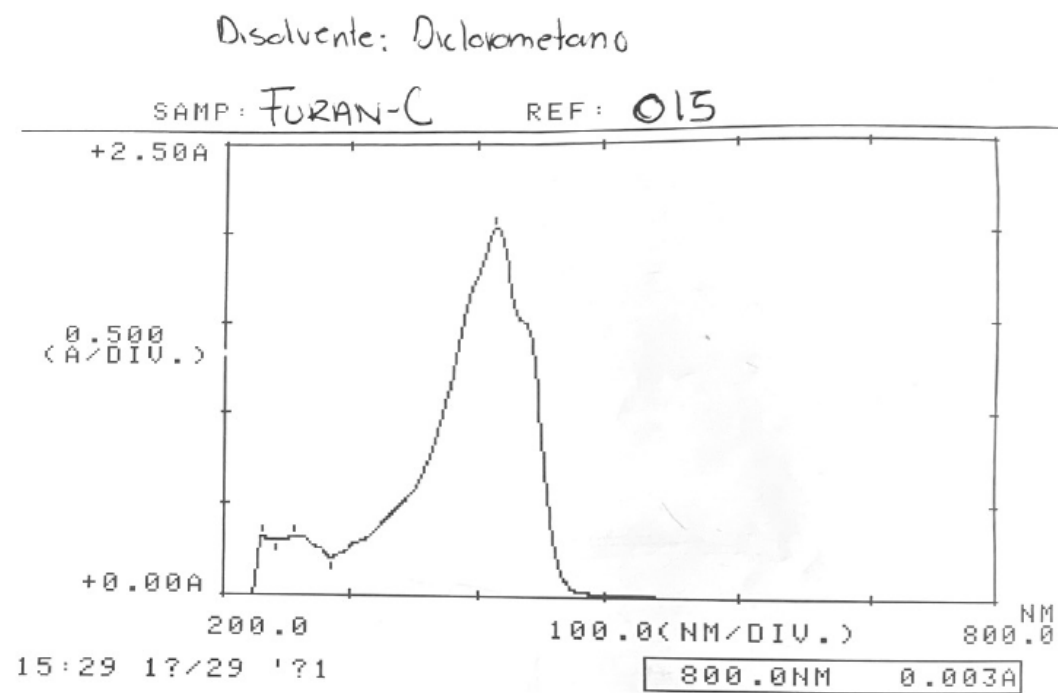
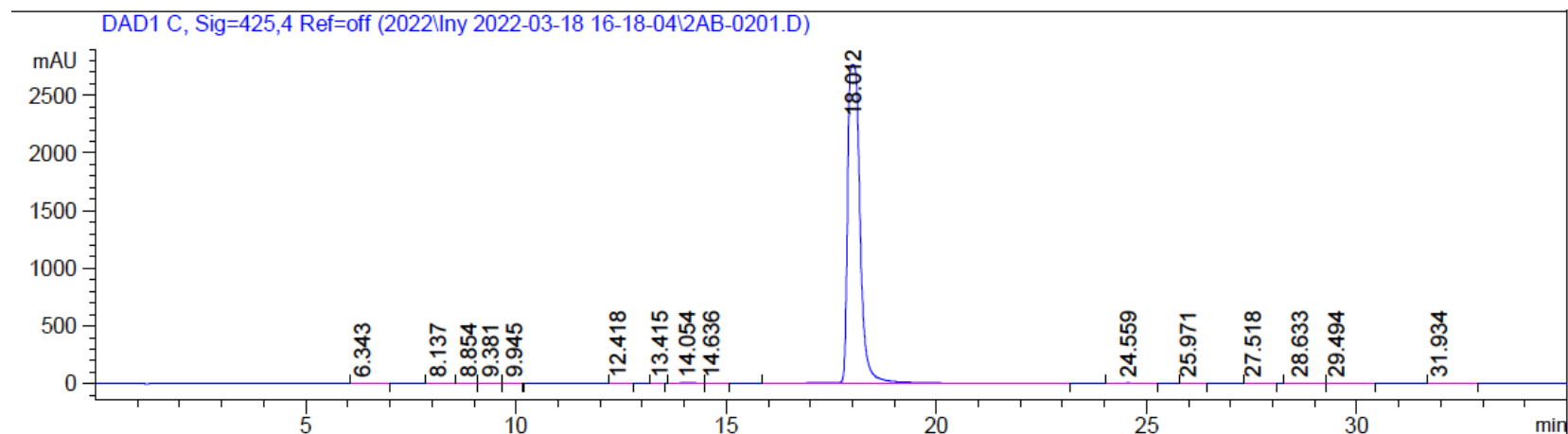


Figure S55. UV-spectrum of compound 7.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.343	BB	0.2932	12.61454	6.10135e-1	0.0219
2	8.137	BV R	0.2770	63.40073	3.34631	0.1103
3	8.854	VV E	0.2257	2.36512	1.25611e-1	4.114e-3
4	9.381	VV E	0.2726	5.15727	2.25721e-1	8.972e-3
5	9.945	VB E	0.2618	2.34206	1.07646e-1	4.074e-3
6	12.418	BV R	0.1774	4.07692	2.98304e-1	7.092e-3
7	13.415	BB	0.1595	1.87429	1.50328e-1	3.261e-3
8	14.054	BV	0.3764	139.91582	5.47125	0.2434
9	14.636	VB	0.2270	40.73635	2.62541	0.0709
10	18.012	BV R	0.3212	5.71032e4	2761.48315	99.3367
11	24.559	VB R	0.2489	68.03589	4.04835	0.1184
12	25.971	BB	0.1819	5.99880	4.79577e-1	0.0104
13	27.518	BB	0.2614	3.39260	1.62647e-1	5.902e-3
14	28.633	BV	0.2917	8.84350	3.97265e-1	0.0154
15	29.494	VV R	0.2347	17.05420	1.03259	0.0297
16	31.934	BV R	0.2554	5.46527	2.90593e-1	9.507e-3

Totals : 5.74845e4 2780.85491

Figure S56. HPLC of compound 7 (425nm).

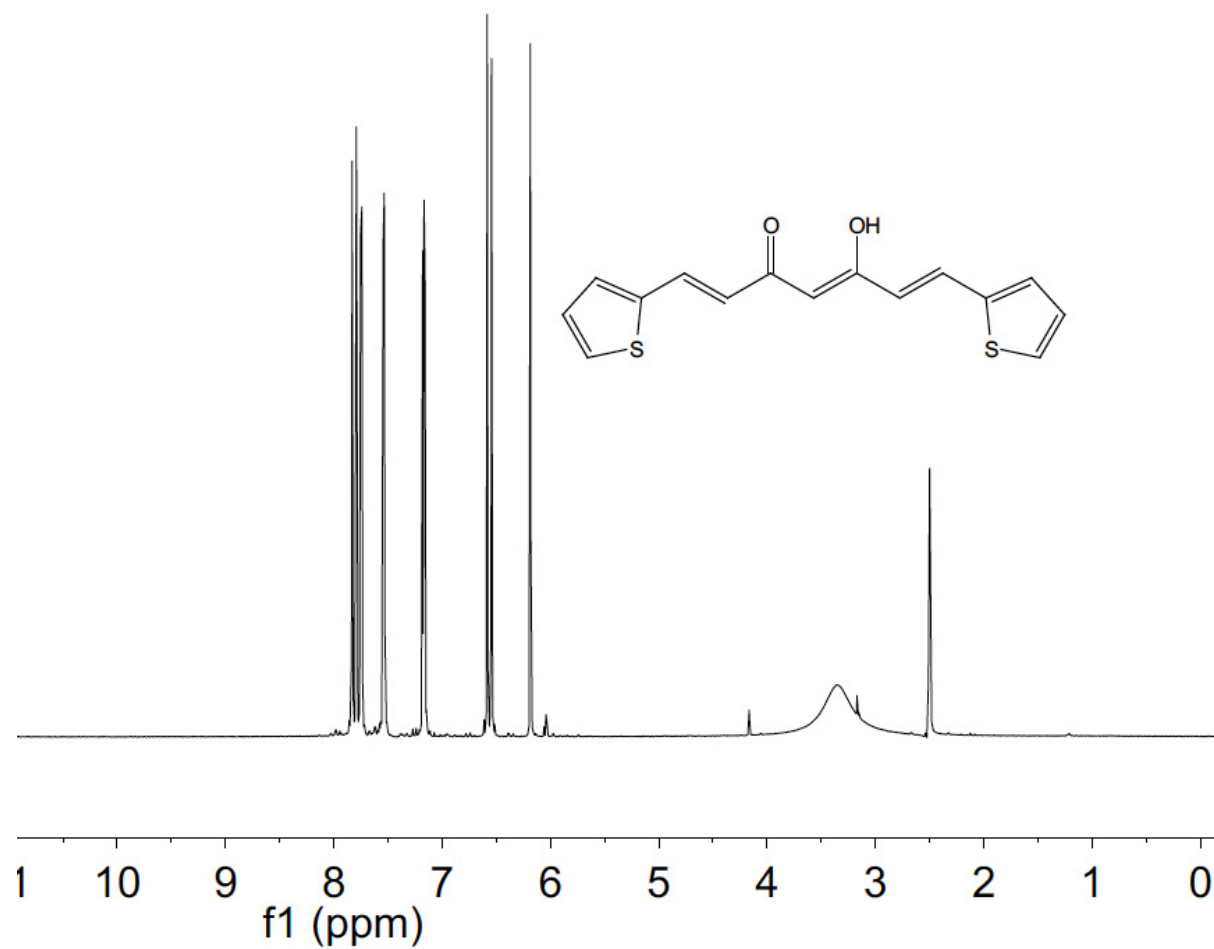


Figure 57. ^1H NMR spectrum of compound 8 ($\text{DMSO-}d_6$ -400MHz).

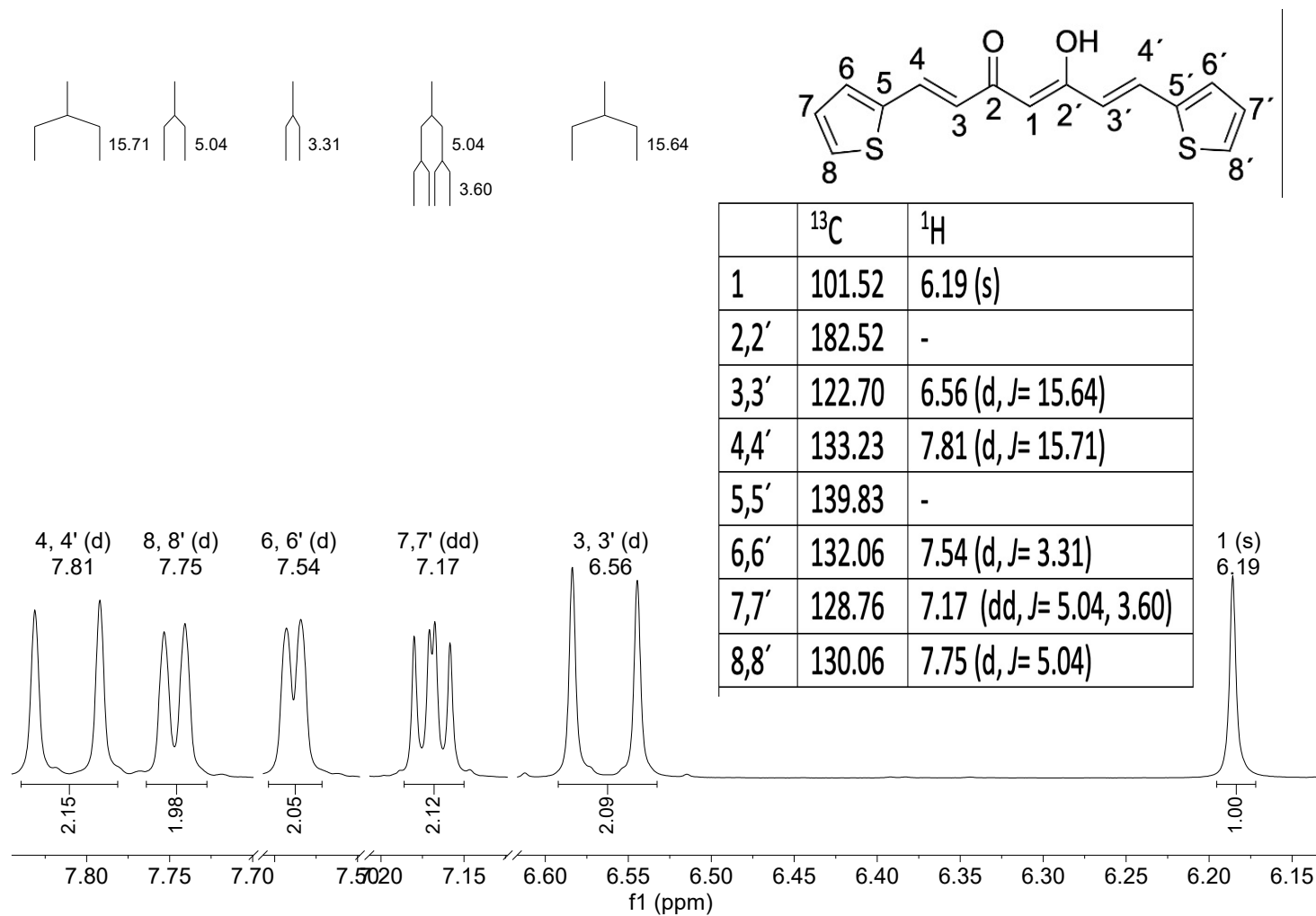


Figure S58. ^1H NMR spectrum of compound 8 (DMSO- d_6 -400MHz, expansion).

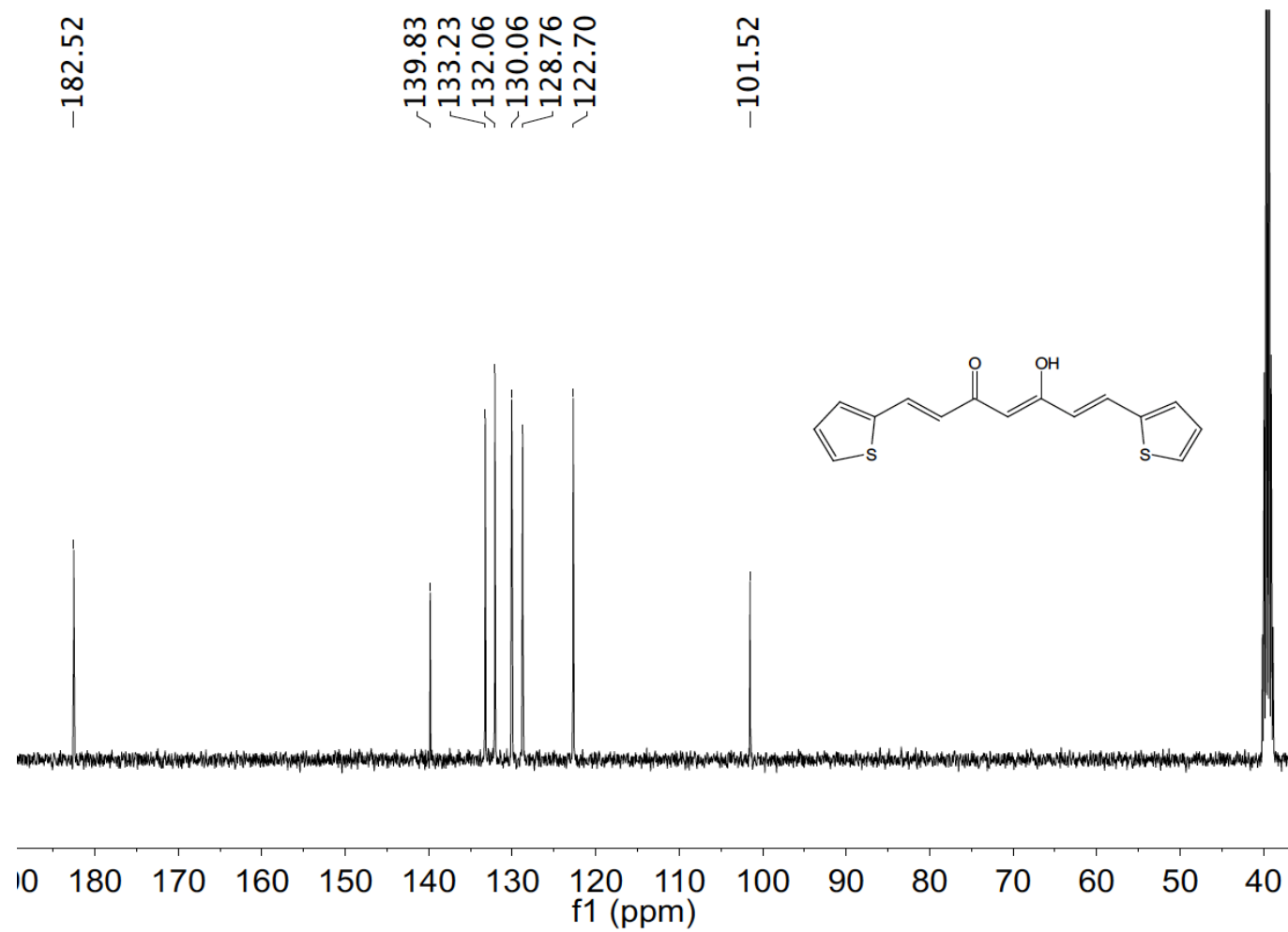


Figure S59. ^{13}C NMR spectrum of compound 8 ($\text{DMSO-}d_6$ -100MHz).

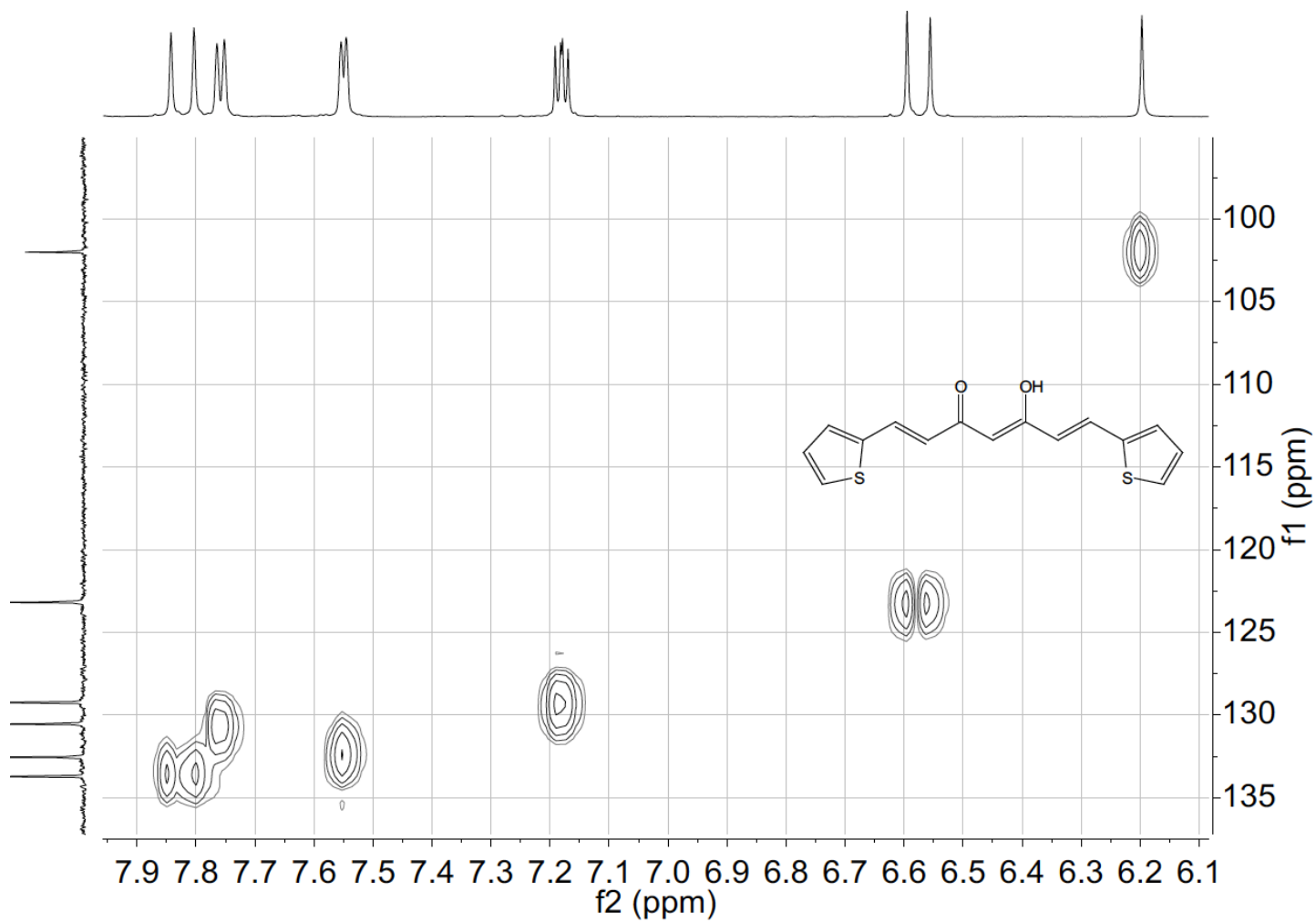


Figure S60. HSQC NMR spectrum of compound 8 (DMSO- d_6 -400MHz).

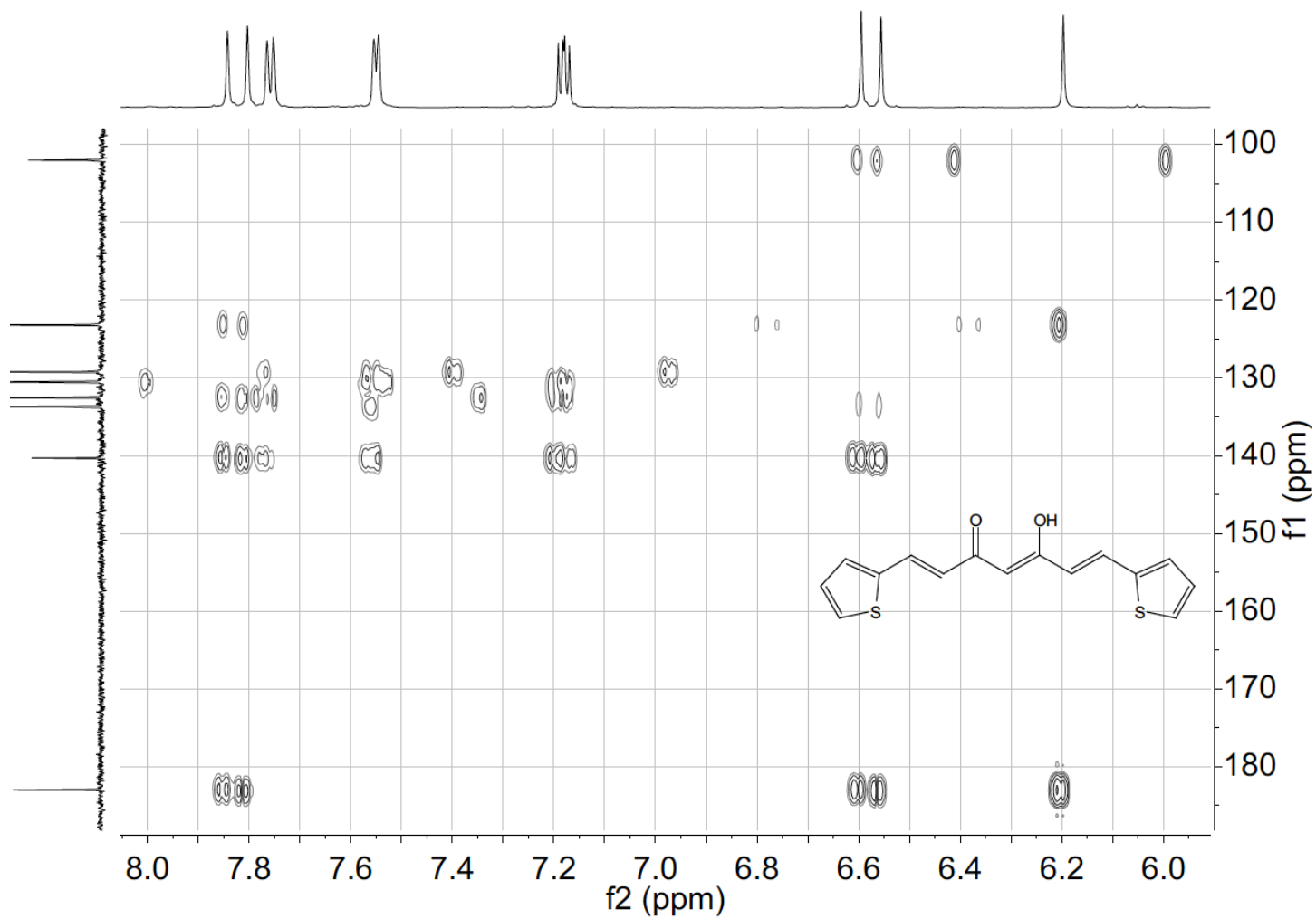


Figure S61. HMBC NMR spectrum of compound 8 (DMSO-*d*₆-400MHz).

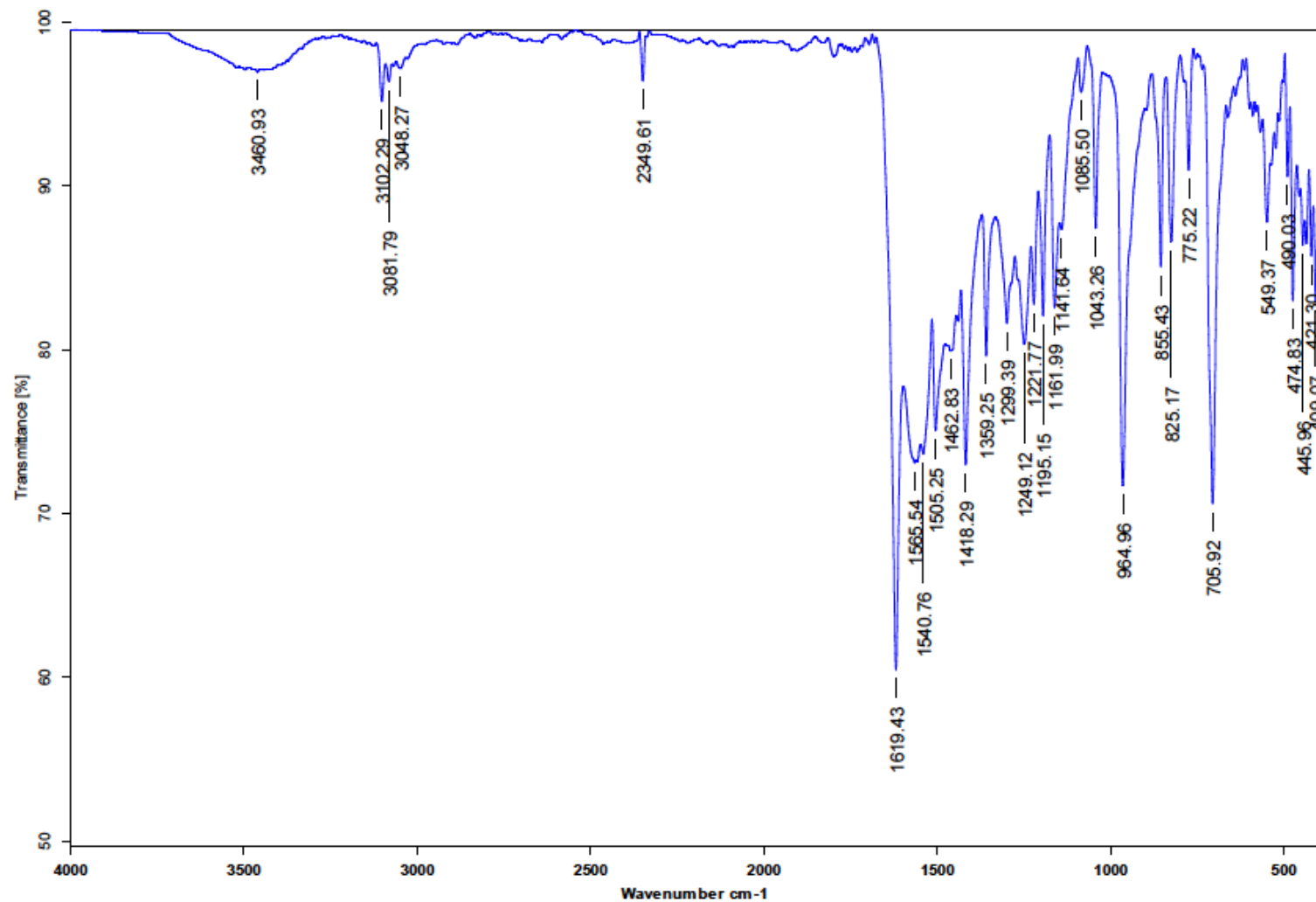


Figure S62. IR spectrum of compound 8.

Sample : 567_TIOFEN-RC
Note : Operator: Carmen Garcia
Inlet : Direct Ion Mode : EI+
Spectrum Type : Normal Ion [MF-Linear]
RT : 0.54 min Scan# : (17,18) Temp : 3276.7 deg.C
BP : m/z 137 Int. : 57.49 (602836)
Output m/z range : 0 to 800 Out Level : 0.00 %

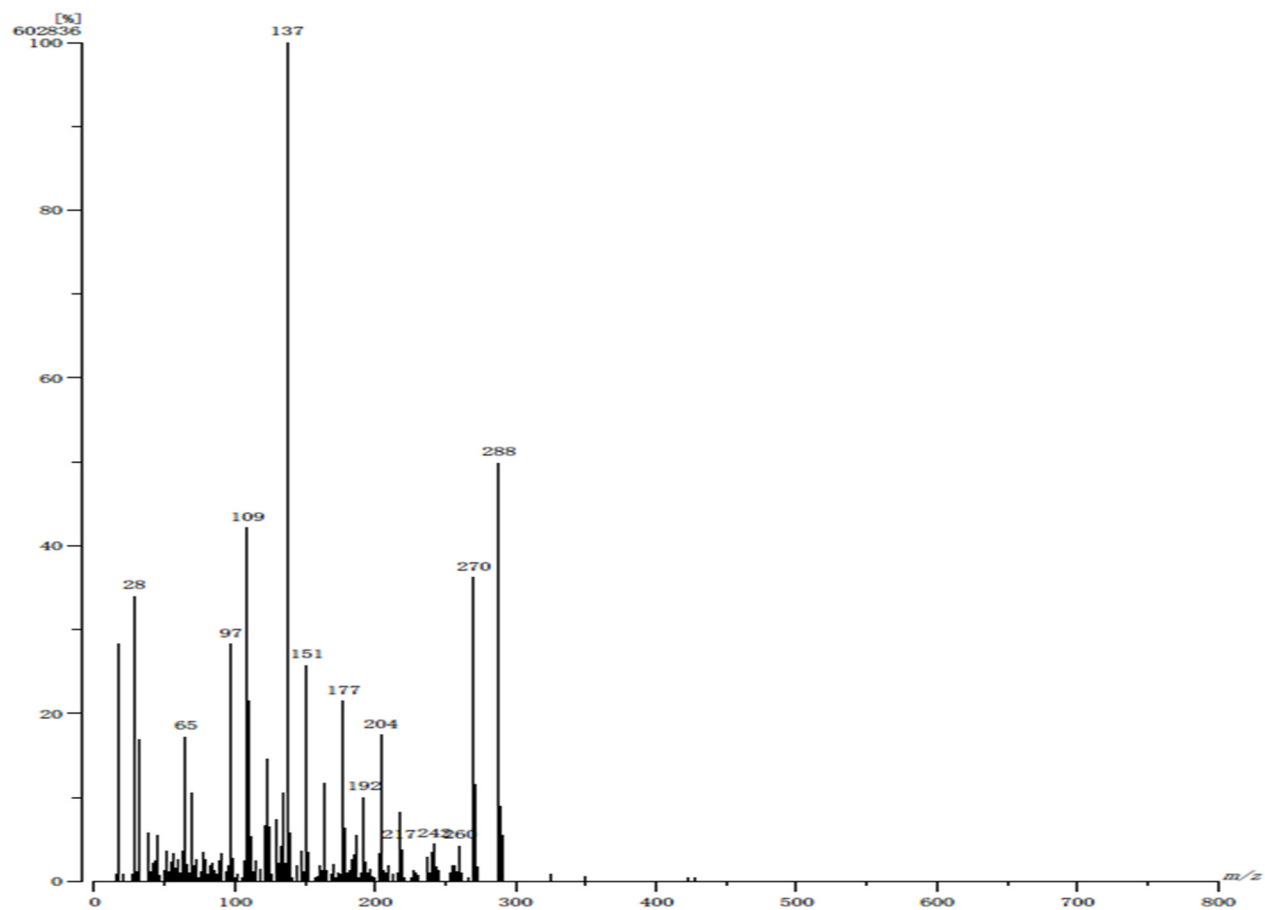


Figure S63. SM of compound 8.

*** PEAK-PICK ***			
-- PEAK --		-- VALLEY --	
λ	ABS	λ	ABS
419.0	2.245	301.0	0.247
273.0	0.316	248.0	0.154
231.0	0.282		

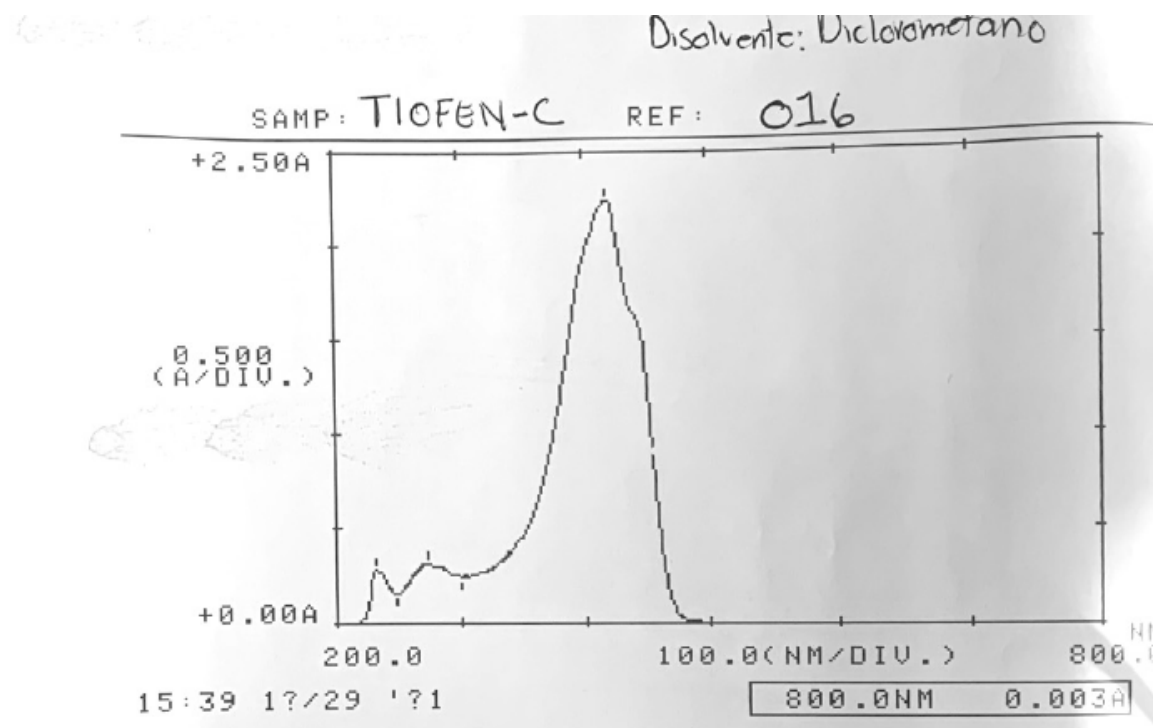
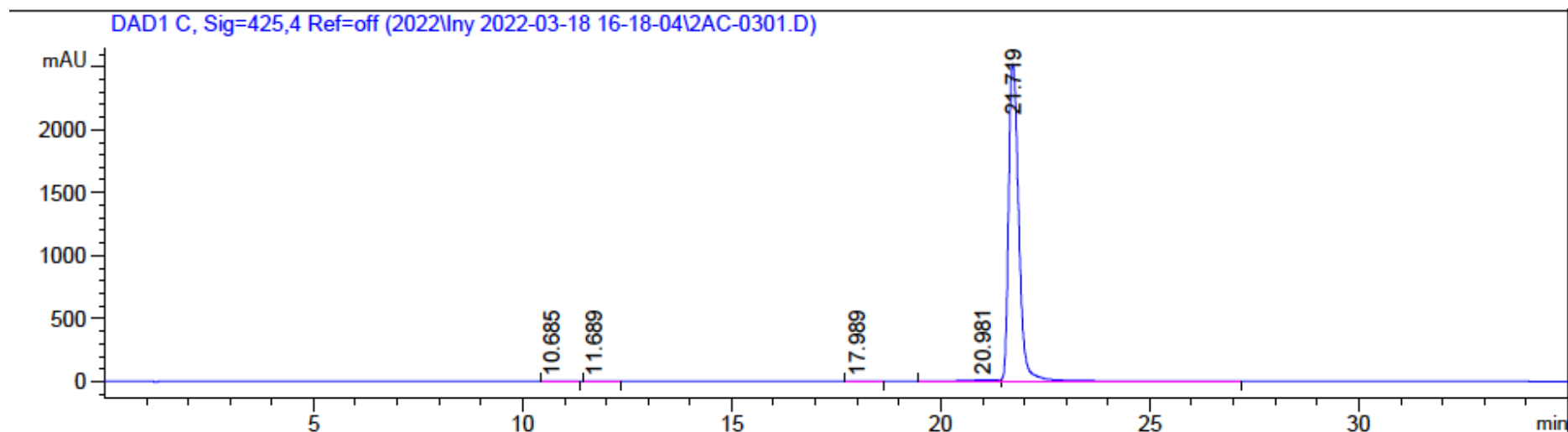


Figure S64. UV-spectrum of compound 8.



Signal 2: DAD1 C, Sig=425,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.685	BV R	0.2321	11.45039	6.74358e-1	0.0263
2	11.689	BB	0.2776	32.45408	1.70894	0.0745
3	17.989	BB	0.2627	28.49121	1.65650	0.0654
4	20.981	BV E	0.5686	502.61679	11.52888	1.1535
5	21.719	VB R	0.2651	4.29988e4	2520.15991	98.6804

Totals : 4.35738e4 2535.72859

Figure S65. HPLC of compound 8 (425nm).

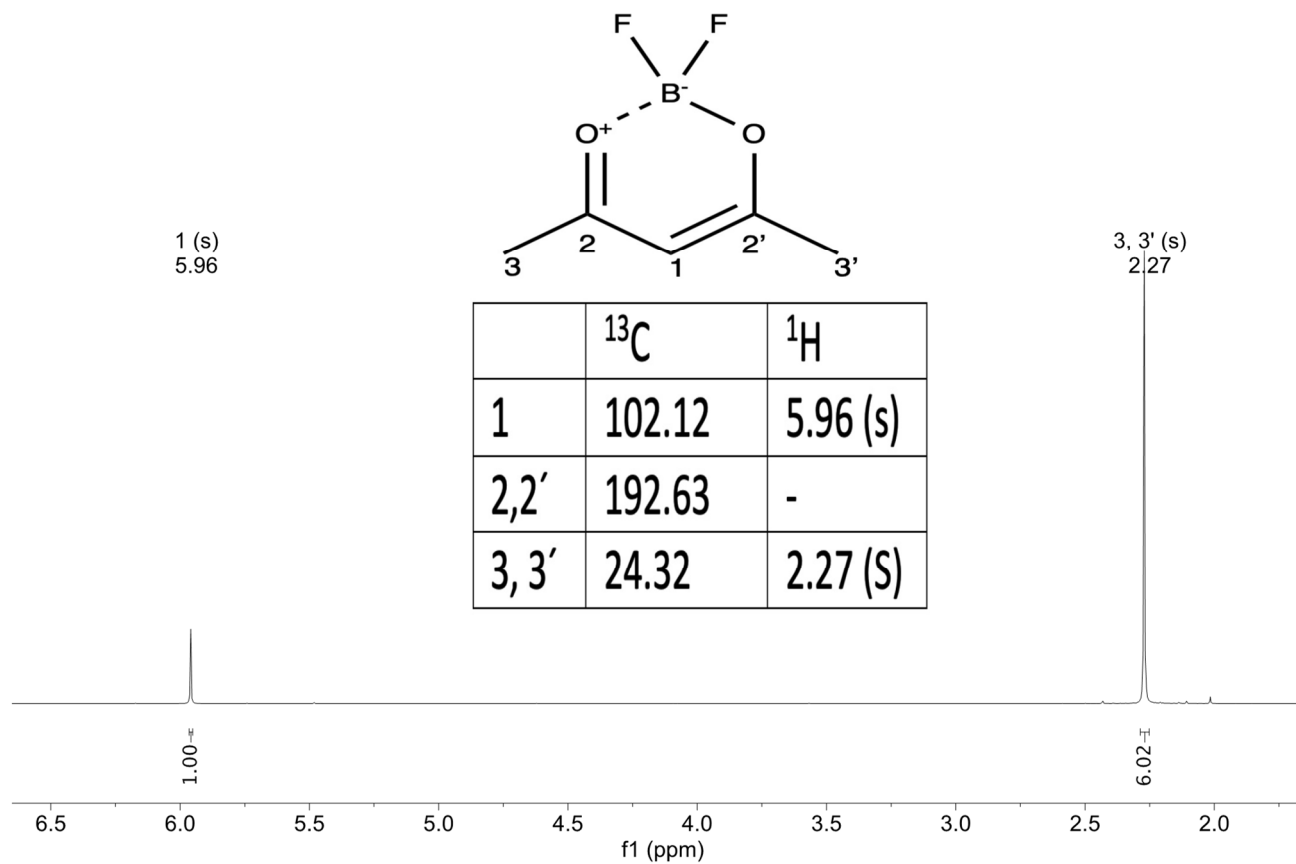


Figure 66. ^1H NMR spectrum of *synthon I* (CDCl_3 -400MHz).

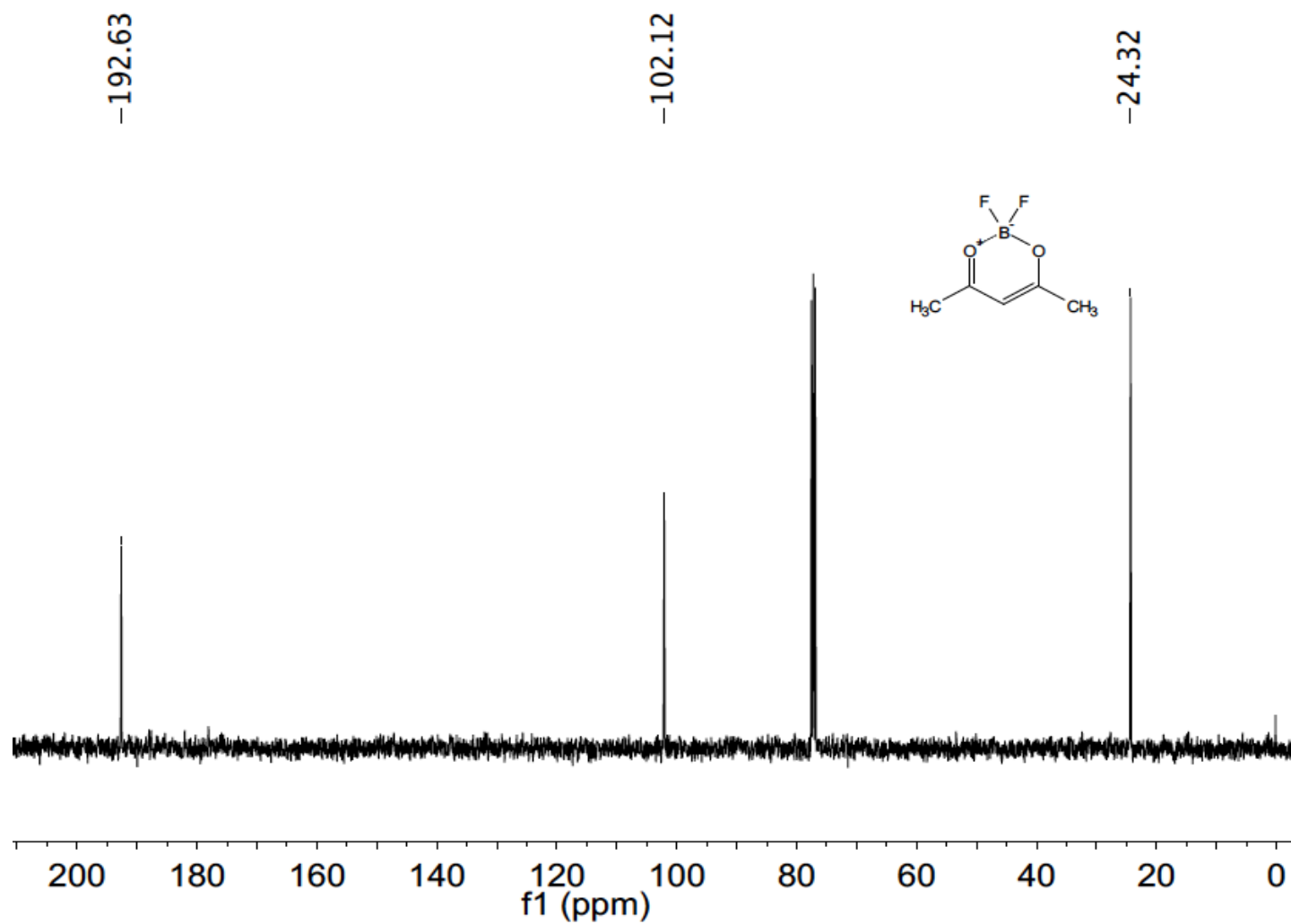


Figure S67. ^{13}C NMR spectrum of *synthon I* (CDCl_3 -100MHz).

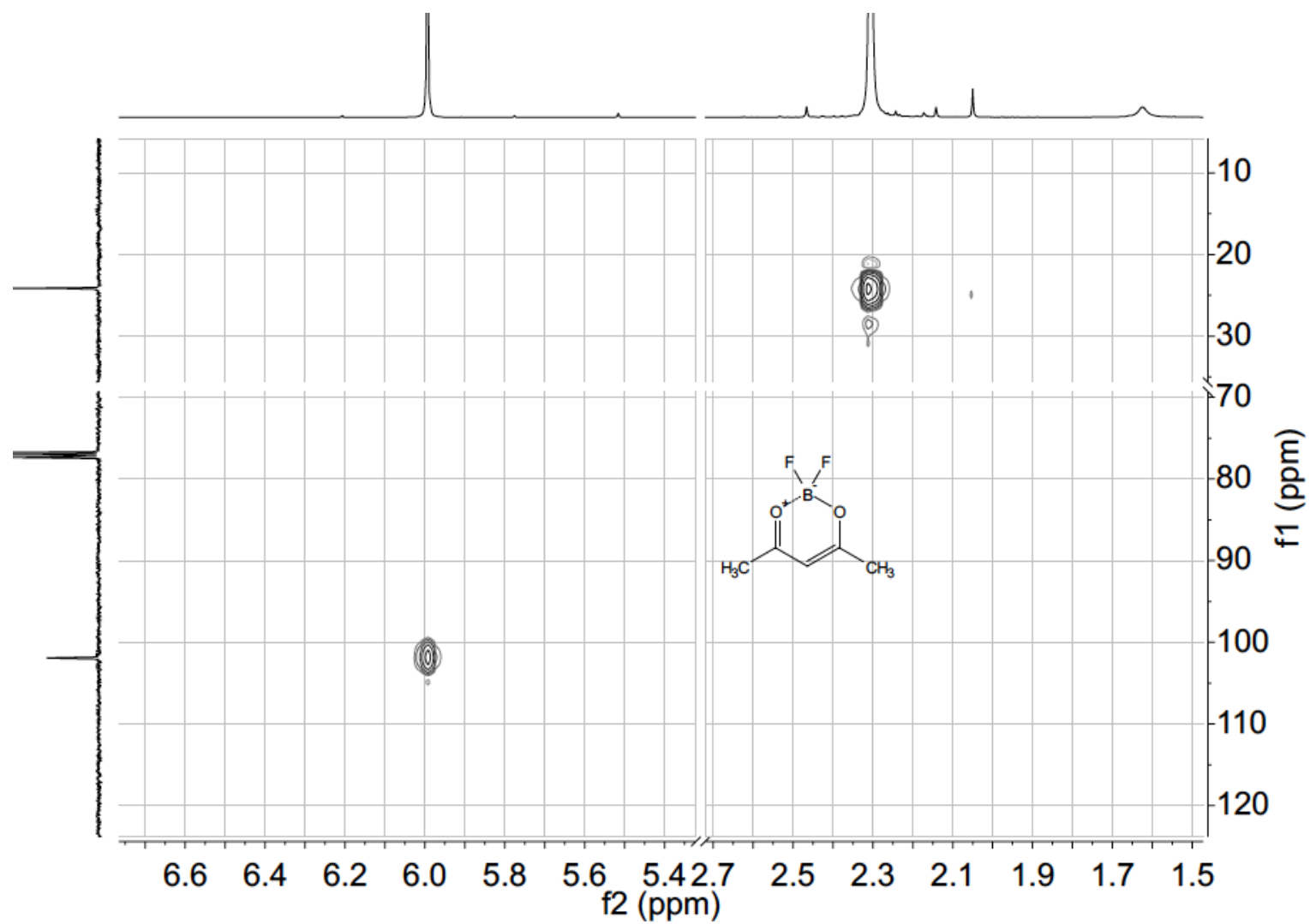


Figure S68. HSQC NMR spectrum of *synthon I* (CDCl_3 -400MHz).

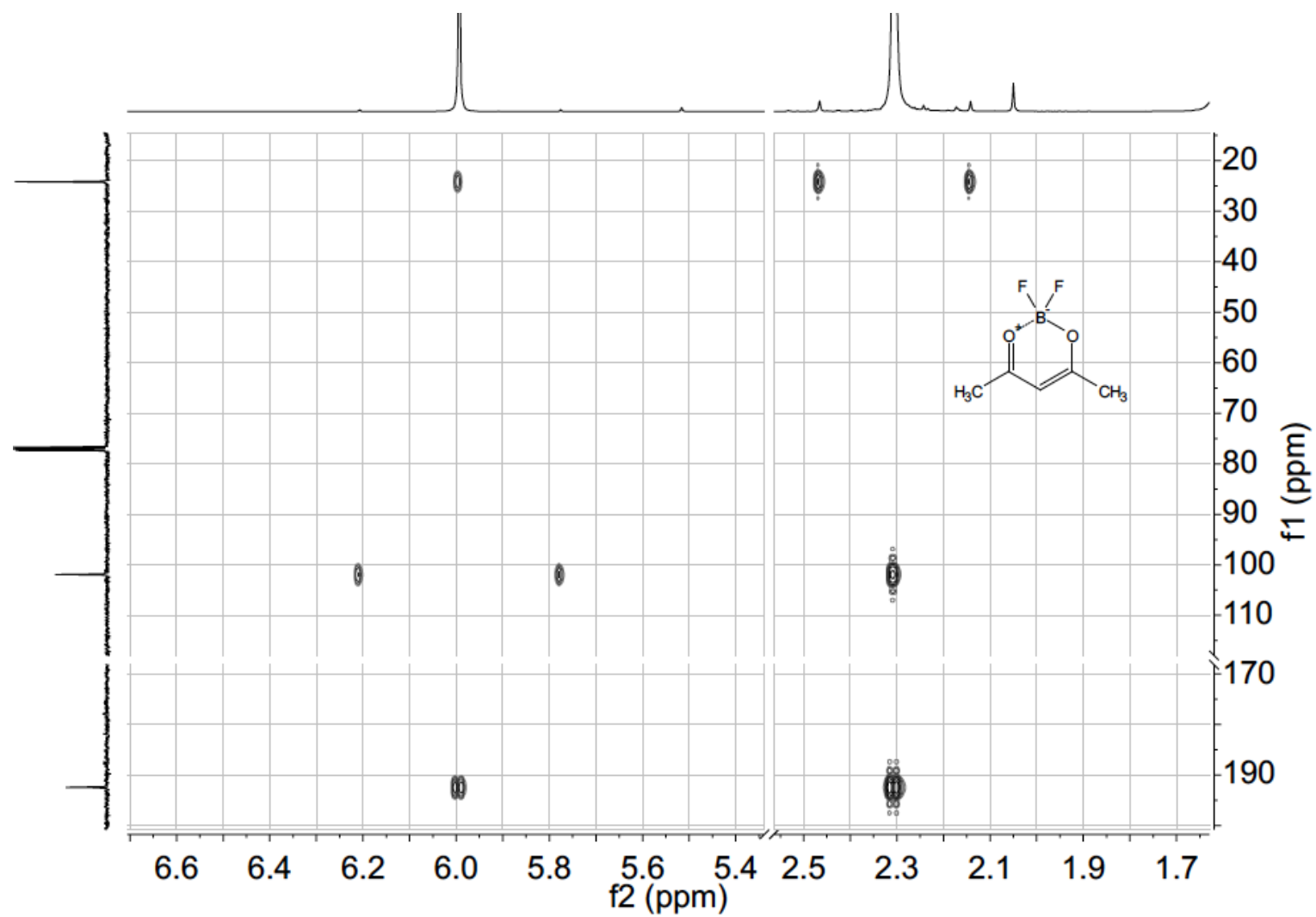


Figure S69. HMBC NMR spectrum of synthon I (CDCl_3 -400MHz).

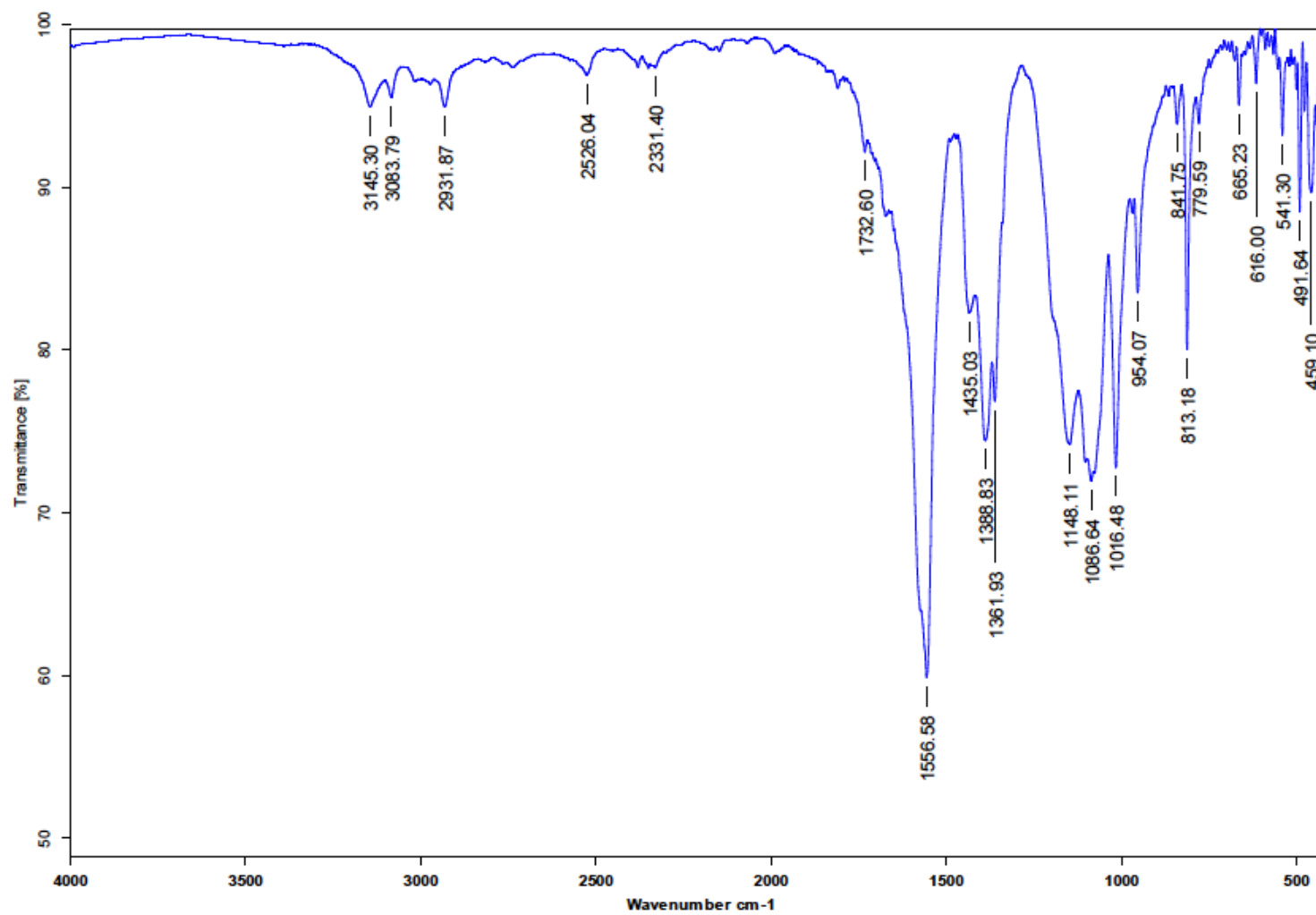


Figure S70. IR spectrum of *synthon I*.

Acq. Data Name: 1840 PENTANOBF2-THF
Creation Parameters: Average(MS[1] Time:0.0)
Dr Enriquez Raul / Operador: Carmen Garcia

Experiment Date/Time: 11/26/2021 9:26:29 AM
Instrument : JEOL The AccuTOF : JMS-T100LC
Ionization Mode: DART+

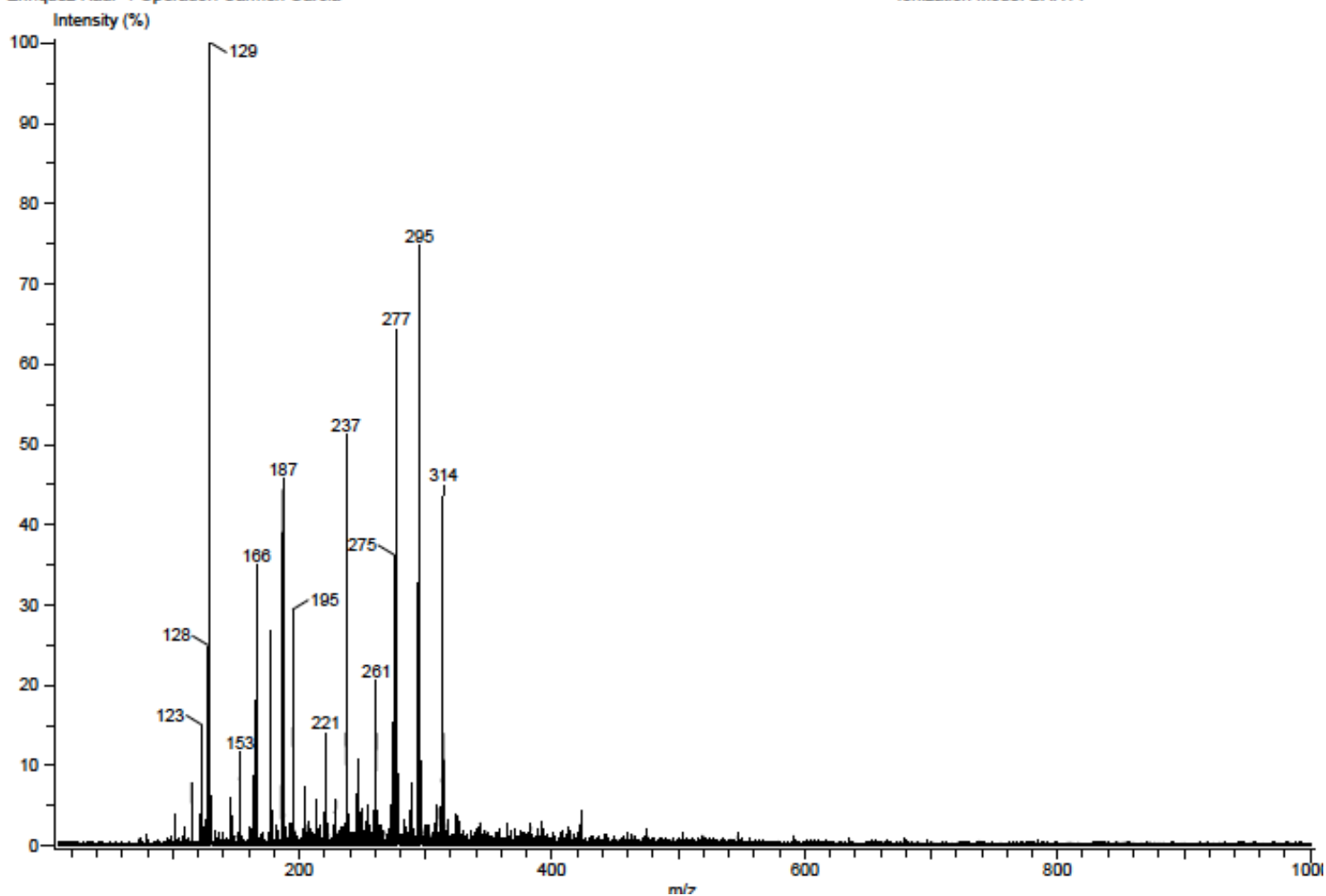


Figure S71. SM of *synthon I*.