

hERG Channel Inhibitory Daphnane Diterpenoid Orthoesters, and Polycephalones A and B with Unprecedented Skeletons from *Gnidia polycephala*

Maria De Mieri,^{†,1} Kun Du,^{‡,1} Markus Neuburger,[§] Priyanka Saxena,[⊥] Pieter C. Zietsman,^{||,▽} Steffen Hering,[⊥] Jan H. van der Westhuizen,[°] and Matthias Hamburger^{†,*}

[†] Division of Pharmaceutical Biology, University of Basel, Klingelbergstrasse 50, CH-4056 Basel, Switzerland

[‡] Department of Chemistry, University of the Free State, Nelson Mandela Avenue, Bloemfontein 9301, South Africa

[§] Division of Inorganic Chemistry, Department of Chemistry, University of Basel, Basel, Switzerland

[⊥] Institute of Pharmacology and Toxicology, University of Vienna, Althanstrasse 14, A-1090 Vienna, Austria

^{||} National Museum, P.O. Box 266, Bloemfontein 9300, South Africa

[▽] Centre for Environmental Management, University of the Free State, P.O. Box 339, Bloemfontein 9301, South Africa

[°] Directorate: Research Development, University of the Free State, Nelson Mandela Avenue, Bloemfontein 9301, South Africa

* Corresponding author. Tel.: +41-61-2671425; fax: +41-61-2671474.

E-mail: matthias.hamburger@unibas.ch

¹ These authors contributed equally to this work

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Table S1. ¹H and ¹³C NMR Spectroscopic Data for Compounds 1 and 2 (CDCl₃, 500 MHz for ¹H, and 125 MHz for ¹³C NMR)

Position	1		2	
	δ_{H} (<i>J</i> in Hz)	δ_{C} , type	δ_{H} (<i>J</i> in Hz)	δ_{C} , type
1	7.50, br s	161.2, CH	7.61, m	161.3, CH
2	-	136.8, C	-	136.8, C
3	-	209.9, C	-	210.0, C
4	-	72.4, C	-	72.4, C
5	4.19, s	71.9, CH	4.25, s	72.0, CH
6	-	60.6, C	-	60.5, C
7	3.36, s	64.2, CH	3.43, s	64.3, CH
8	2.87, br s	36.8, CH	2.93, d (2.5)	36.8, CH
9	-	79.7, C	-	79.7, C
10	3.76, quint ^a (2.5)	48.2, CH	3.81 ^b	48.2, CH
11	2.44, quint ^a (7.0)	35.0, CH	2.49, dq (8.7, 7.0)	35.0, CH
12	2.18 ^b	36.5, CH ₂	2.23, dd (14.3, 8.7)	36.5, CH ₂
	1.59, d (14.0)		1.67, d (14.3)	
13	-	84.5, C	-	84.5, C
14	4.39, br s	82.2, CH	4.42, d (2.5)	82.1, CH
15	-	146.2, C	-	146.2, C
16	4.96, br m	111.5, CH ₂	5.0, br quint (1.4)	111.5, CH ₂
	4.83, br m		4.90, quint (1.4)	
17	1.73, br s	19.1, CH ₃	1.78, t (1.4)	19.1, CH ₃
18	1.10, d (7.0)	20.5, CH ₃	1.17, d (7.0)	20.5, CH ₃
19	1.70 (br s)	10.1, CH ₃	1.80, br s	10.0, CH ₃
20	3.67 and 3.81, ABq (12.2)	65.2, CH ₂	3.82 ^b	65.2, CH ₂
1'	-	116.6, C	-	116.6, C
2'	5.72 (d, 15.0)	125.0, CH	5.70, d (15.4)	122.9, CH
3'	6.95 (dd, 15.0, 10.0)	128.7, CH	6.69, dd (15.4, 10.6)	134.9, CH
4'	5.95 (t, 10.0)	127.2, CH	6.06, br dd (15.0, 10.6)	128.9, CH
5'	5.51 (m)	136.2, CH	5.84, dt (15.0, 7.2)	139.1, CH
6'	2.14 ^b	28.0, CH ₂	2.10, br q (7.2)	32.8, CH ₂
7'	1.33 (m)	29.2, CH ₂	1.39, quint (7.2)	28.9, CH ₂
8'	1.22 ^b	31.5, CH ₂	1.28 ^b	31.4, CH ₂
9'	1.23 ^b	22.6, CH ₂	1.31 ^b	22.6, CH ₂
10'	0.82 (t, 7.0)	14.2, CH ₃	0.88, t (7.0)	14.2, CH ₃

^a apparent; ^b overlapping signals

Table S2. ^1H and ^{13}C NMR Spectroscopic Data for Compound 5 (CDCl_3 , 500 MHz for ^1H , and 125 MHz for ^{13}C NMR)

5

Position	δ_{H} (J in Hz)	δ_{C} , type
1	7.57, m ^a	160.4, CH
2	-	137.0, C
3	-	209.5, C
4	-	72.3, C
5	4.19, s	71.8, CH
6	-	60.8, C
7	3.61, ^a	64.1, CH
8	3.62, d (2.5) ^a	35.9, CH
9	-	78.3, C
10	3.84, quint ^d (2.5) ^a	47.6, CH
11	2.56, q (7.2)	44.2, CH
12	5.23, br s	79.0, CH
13	-	84.0, C
14	4.89, d (2.5)	80.6, CH
15	-	143.0, C
16	5.02, br m	113.8, CH ₂
	4.99, br m	
17	1.87, br s	18.9, CH ₃
18	1.38, d (7.2)	18.5, CH ₃
19	1.76, br m	10.0, CH ₃
20	3.88 and 3.81, ABq (12.4) ^a	64.8, CH ₂
1'	-	117.0, C
2'	5.68, d (15.4)	122.3, CH
3'	6.69, ddd (15.4, 10.6)	135.3, CH
4'	6.06, br dd (15.4, 10.6)	128.7, CH
5'	5.87, br dt (15.4, 7.2)	139.6, CH
6'	2.11 (q, 7.2)	32.8, CH ₂
7'	1.39 ^a	28.8, CH ₂
8'	1.28 ^a	31.4, CH ₂
9'	1.30 ^a	22.6, CH ₂
10'	0.89, t (7.0)	14.2, CH ₃
1''	-	165.4, C
2''	-	129.8, C
3''-7''	7.88, br d (7.5)	129.6, CH
4''-6''	7.43, br t (7.5)	128.7, CH
5''	7.55, br t (7.5) ^a	133.5, CH

^a overlapping signals

Table S3. ¹H and ¹³C NMR Spectroscopic Data for Compounds 6-8 (DMSO-*d*₆ for 6 and 8, CDCl₃ for 7; 500 MHz for ¹H, and 125 MHz for ¹³C NMR)

	6		7		8	
Position	δ_{H} (<i>J</i> in Hz)	$\delta_{\text{C}}^{\text{b}}$, type	δ_{H} (<i>J</i> in Hz)	$\delta_{\text{C}}^{\text{b}}$, type	δ_{H} (<i>J</i> in Hz)	$\delta_{\text{C}}^{\text{b}}$, type
2	-	161.4, C	-	161.5, C	-	161.6, C
3	7.20, s	110.5, CH	6.95, s	112.0, CH	6.67, s	110.6, CH
4	-	177.5, C	-	178.3, C	-	177.2, C
5	8.04, dd (8.0, 1.2)	124.4, CH	8.21, dd (8.0, 1.2)	125.5, CH	7.36, d (3.0)	107.9, CH
6	7.45, t (8.0)	124.8, CH	7.37, t (8.0)	124.9, CH	-	155.4, C
7	7.78, td (8.0, 1.2)	133.7, CH	7.63, td (8.0, 1.2)	133.4, CH	7.24 ^a	123.5, CH
8	7.68, d (8.0)	117.4, CH	7.50, d (8.0)	117.8, CH	7.55, d (7.0)	120.0, CH
9	-	155.6, C	-	155.9, C	-	150.1, C
10	-	123.0, C	-	123.1, C	-	124.8, C
1'	-	117.6, C	-	126.1, C	-	126.2, C
2'	-	147.2, C	-	147.8, C	-	147.0, C
3'	-	148.3, C	-	153.2, C	-	153.7, C
4'	7.12, br d (8.0)	113.8, CH	7.06, br d (8.0)	115.1, CH	7.24 ^a	116.2, CH
5'	6.90, t (8.0)	117.8, CH	7.15, t (8.0)	123.9, CH	7.20, dd (8.0, 7.5)	124.7, CH
6'	7.46, br d (8.0)	119.6, CH	7.33, br d (8.0)	120.6, CH	7.31, dd, (7.5, 1.6)	120.9, CH
2'-OCH ₃	-	-	3.88 ^a	60.7, CH ₃	3.81 ^a	61.0, CH ₃
3'-OCH ₃	3.86, s	55.7, CH ₃	3.88 ^a	55.9, CH ₃	3.87 ^a	56.5, CH ₃

^a overlapping signals; ^b from inverse detected experiments HSQC and HMBC due to low amount of sample

Table S4. ^1H and ^{13}C NMR Spectroscopic Data for Compounds 9 and 10 (CDCl_3 for 9, $\text{DMSO}-d_6$ for 10; 500 MHz for ^1H , and 125 MHz for ^{13}C NMR)

Position	9		10	
	δ_{H} (J in Hz)	$\delta_{\text{C}}^{\text{a}}$, type	δ_{H} (J in Hz)	$\delta_{\text{C}}^{\text{a}}$, type
2	-	160.3, C	-	160.3, C
3	6.31, d (9.5)	113.2, CH	6.36, d (9.5)	113.7, CH
4	7.98, d (9.5)	144.6, CH	7.96, d (9.5)	144.1, CH
5	7.52, s	130.3, CH	7.58, s	121.2, CH
6	-	123.0, C	-	139.9, C
7	-	160.4, C	-	155.0, C
8	7.15, s	100.2, CH	7.29, s	102.1, CH
9	-	155.7, C	-	153.0, C
10	-	112.6, C	-	112.3, C
2'	-	160.3, C	-	160.3, C
3'	6.31, d (9.5)	113.2, CH	6.34, d (9.5)	113.9, CH
4'	7.98, d (9.5)	144.6, CH	8.00, d (9.5)	144.1, CH
5'	7.52, s	130.3, CH	7.67, d (8.6)	130.0, CH
6'	-	123.0, C	6.92, dd (8.6, 2.4)	113.3, C
7'	-	160.4, C	-	161.3, C
8'	7.15, s	100.2, CH	6.84, d (2.4)	103.4, CH
9'	-	155.7, C	-	155.3, C
10'	-	112.6, C	-	114.4, C
7-OCH ₃	3.85, s	57.1, CH ₃	3.85, s	57.1, CH ₃
7'-OCH ₃	3.85, s	57.1, CH ₃	-	-

^aFrom inverse detected experiments HSQC and HMBC

Table S5. ^1H and ^{13}C NMR Spectroscopic Data for Compounds 13 and 14 (CDCl_3 ; 500 MHz for ^1H , and 125 MHz for ^{13}C NMR).

Position	13		14	
	δ_{H} (J in Hz)	δ_{C} , type	δ_{H} (J in Hz)	δ_{C} , type
1	-	51.9, C	-	148.5, C
2	1.87 ^a	35.1, CH_2	5.23, br m	118.9, CH
	1.60, ddd (12.5, 6.5, 2.0)		-	-
3	1.93 ^a	33.3, CH_2	2.53 ^a	41.0, CH_2
	1.39, dddd (12.5, 11.0, 8.5, 6.5)		1.92, br d (16.0) ^a	
4	2.25 ^a	35.0, CH	2.39, sext (7.3)	33.4, CH
5	2.06 ^a	45.8, CH	2.66, m	42.6, CH
6	1.92 ^a	33.6, CH_2	1.97, dd (12.3, 10.5)	32.9, CH_2
	1.51, dd (13.3, 10.6)		1.42, dd (12.3, 8.2)	
7	-	83.2, C	-	83.8, C
8	-	202.3, C	-	220.2, C
9	6.13, br m	127.3 CH	2.53, d (19.0)	47.2, CH_2
			2.06, d (19.0)	
10	-	175.0, C	-	41.6, C
11	2.29, m	43.5, CH	-	49.3, C
12	2.05 ^a	33.0, CH_2	0.84, s	12.4, CH_3
	1.28, ddd (14.5, 4.2, 1.5)		-	-
13	3.46, dd (10.6, 6.2)	65.8, CH_2	3.66 and 3.62, ABq (11.7)	65.5, CH_2
	3.24, dd (10.6, 7.5)		-	-
14	2.02, d (1.0)	23.5, CH_3	1.21, s	16.5, CH_3
15	1.01, d (7.2)	18.8, CH_3	0.87, d (7.3)	17.5, CH_3
7-OH	4.68, br s	-	-	-

^a overlapping signals

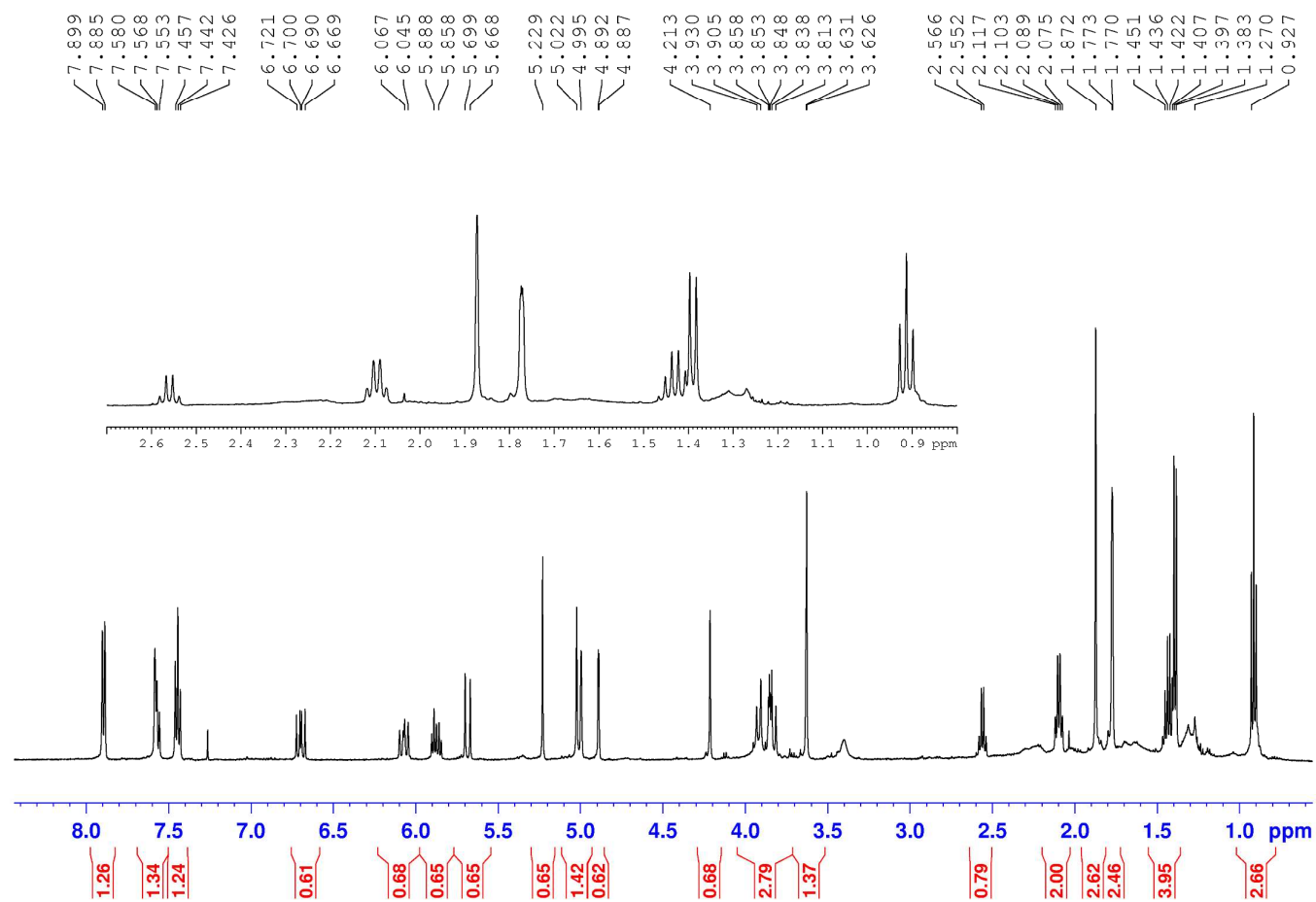


Figure S1. ^1H -NMR spectrum of compound **3** (500 MHz, CDCl_3).

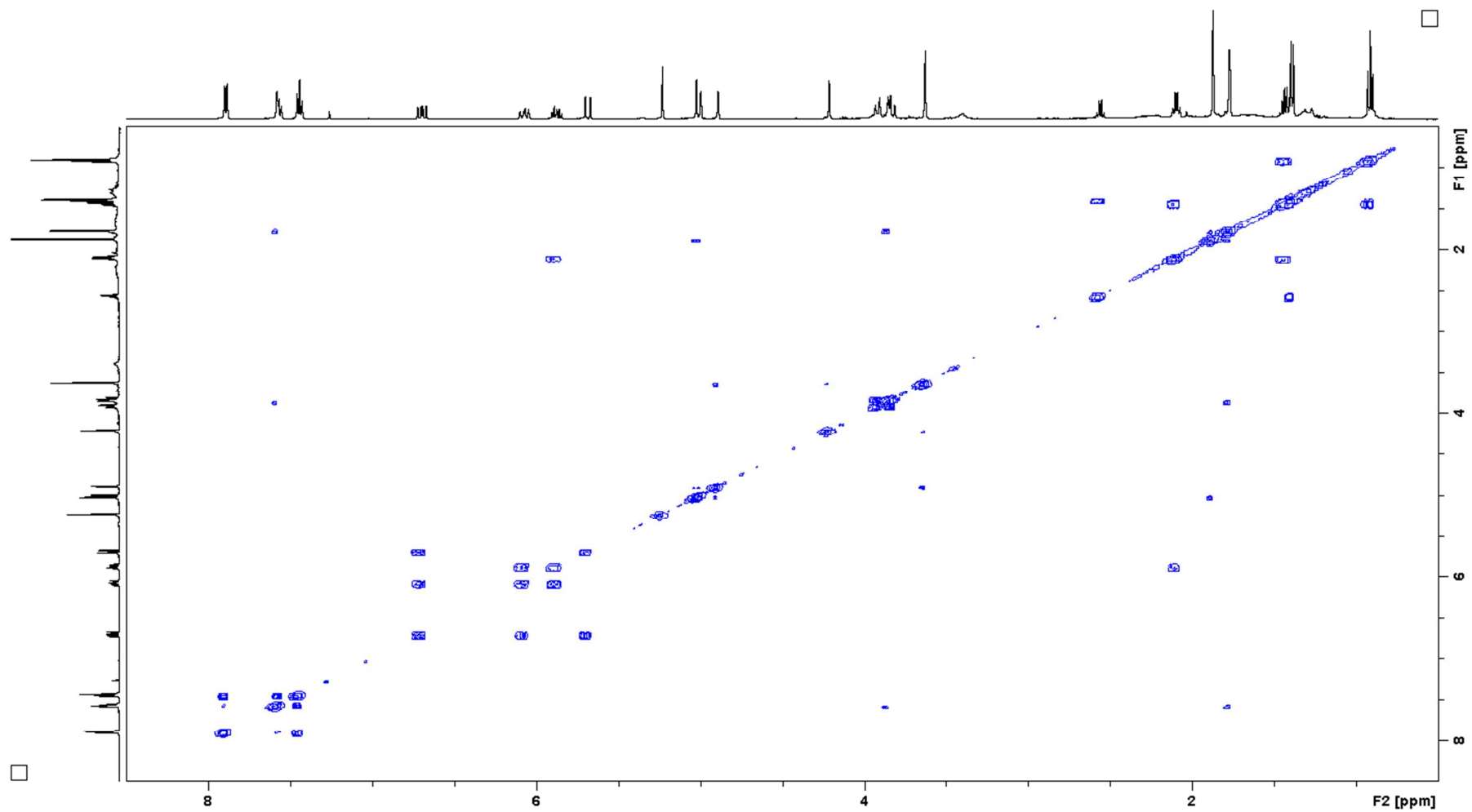


Figure S2. ^1H - ^1H COSY spectrum of compound **3** (500 MHz, CDCl_3).

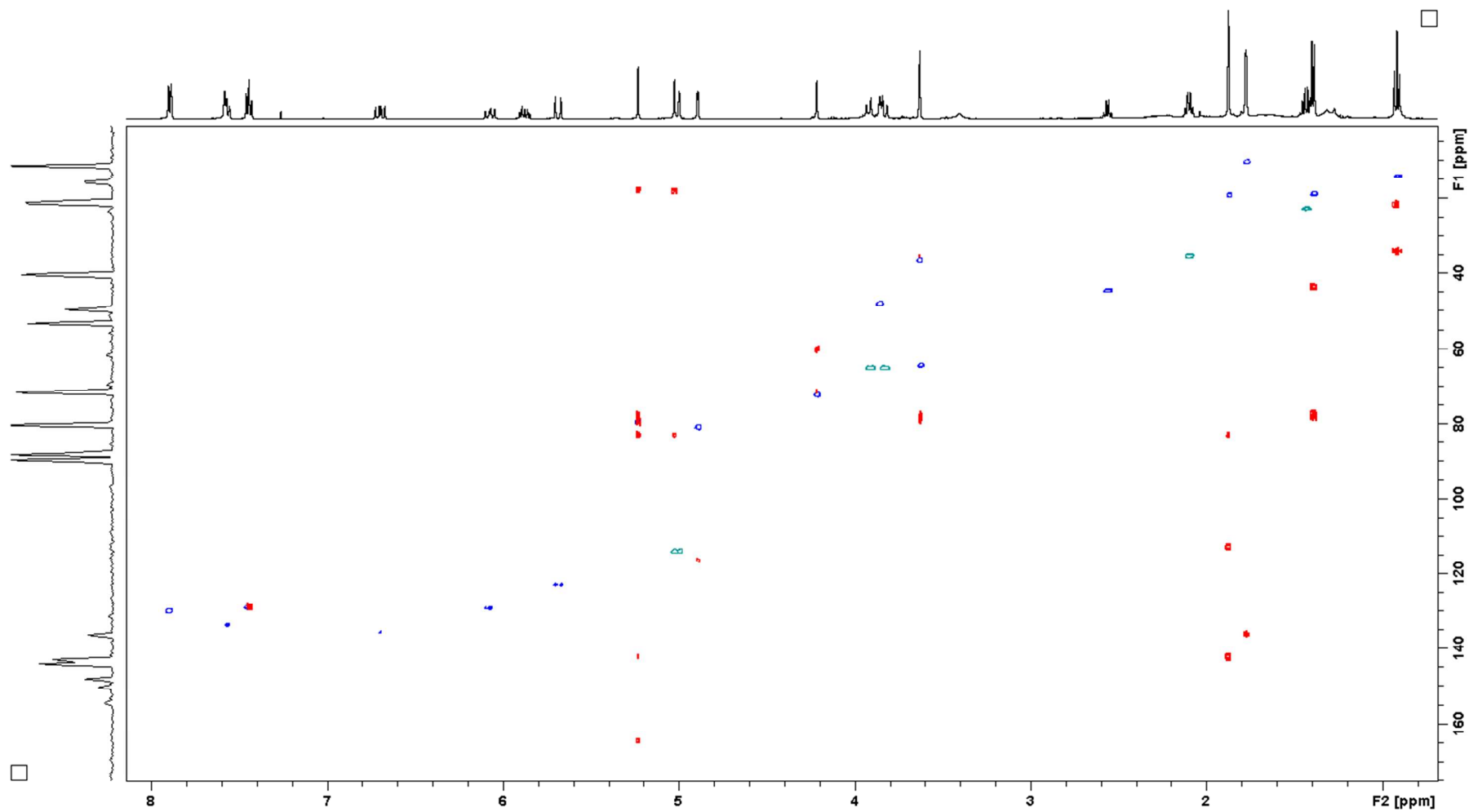


Figure S3. Overlay of HSQC-DEPT (blue/light green) and HMBC (red) spectra of compound **3** (500 MHz, CDCl₃).

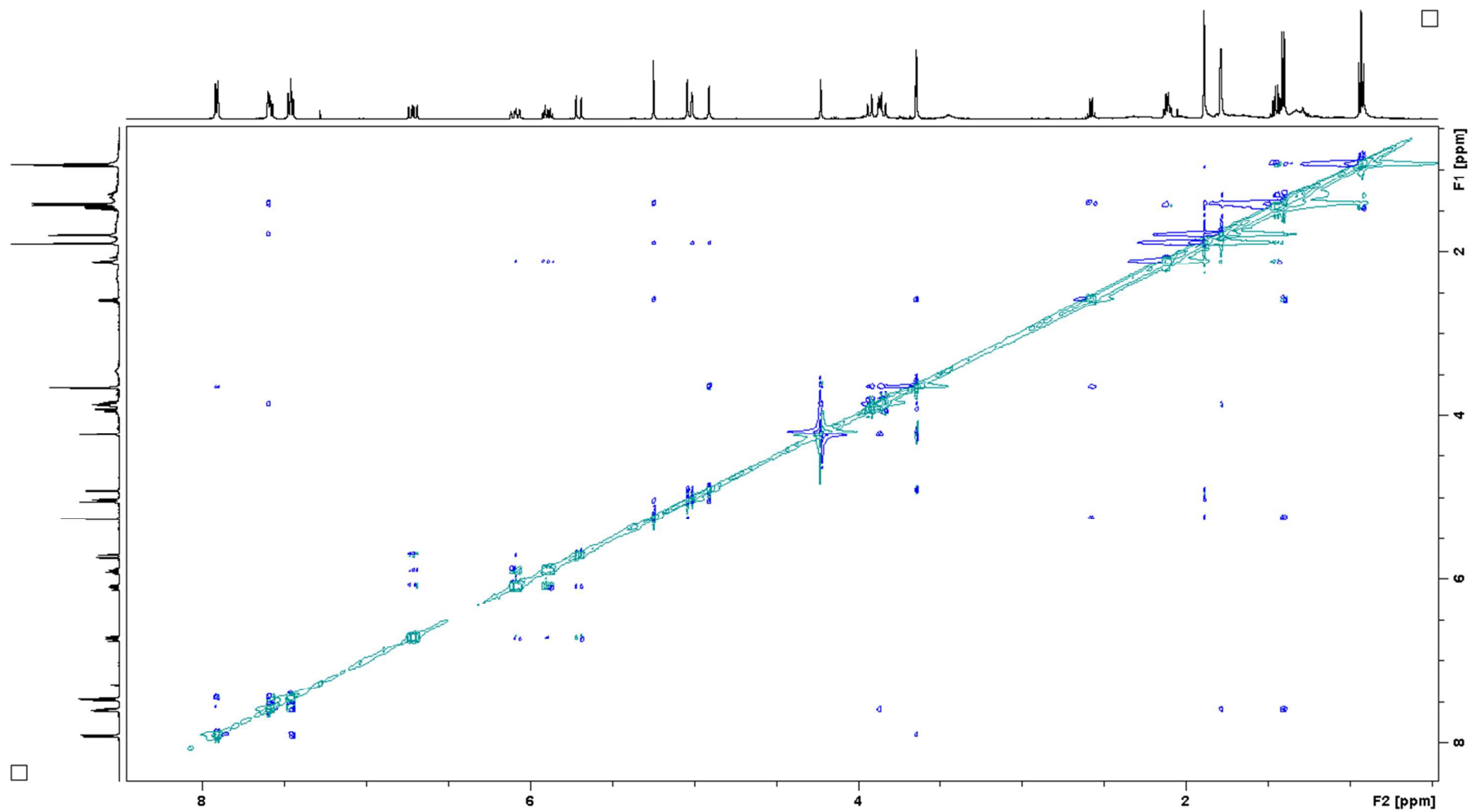


Figure S4. 2D ^1H - ^1H ROESY spectrum of compound **3** (500 MHz, CDCl_3).

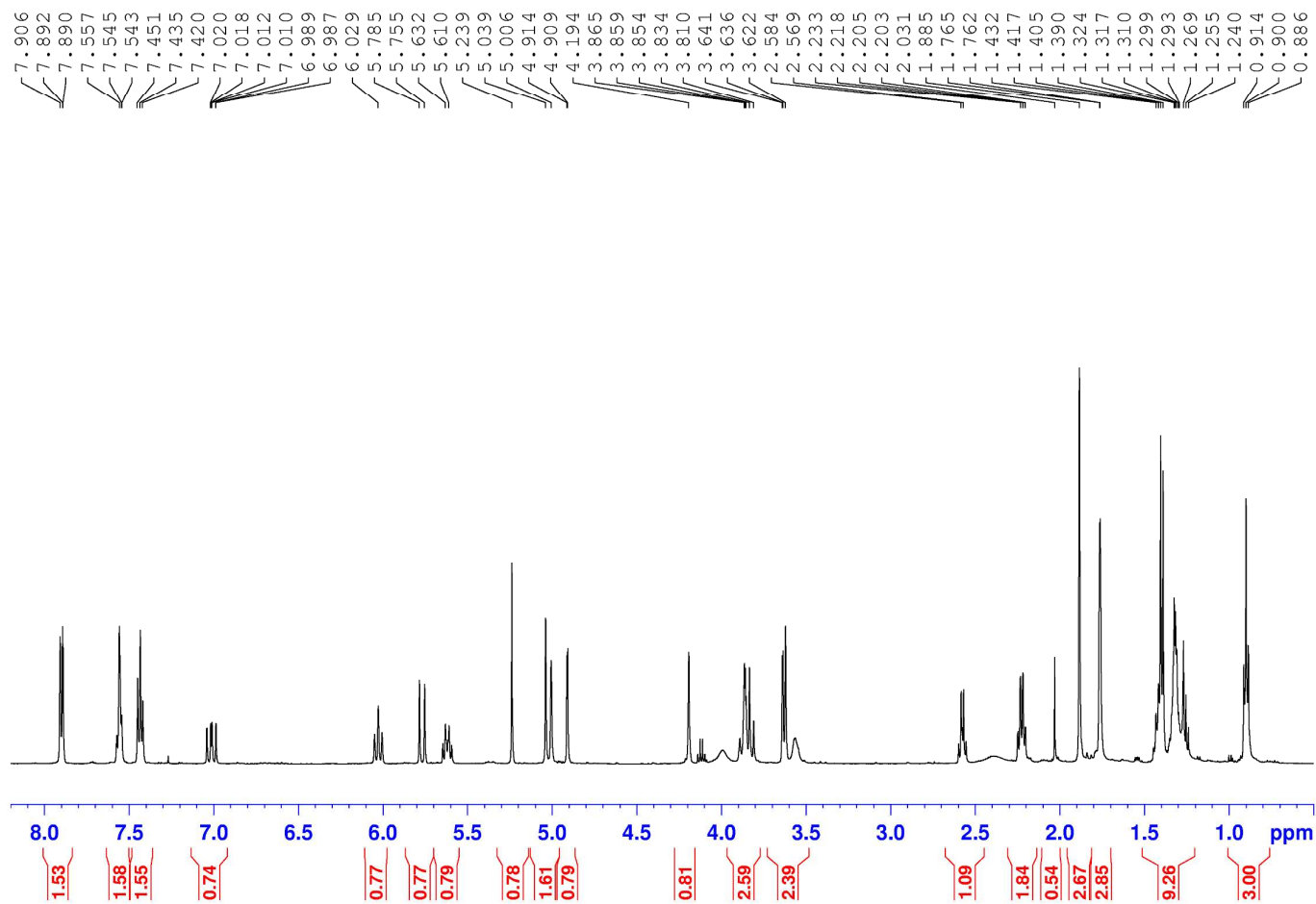


Figure S5. ¹H-NMR spectrum of compound **4** (500 MHz, CDCl₃).

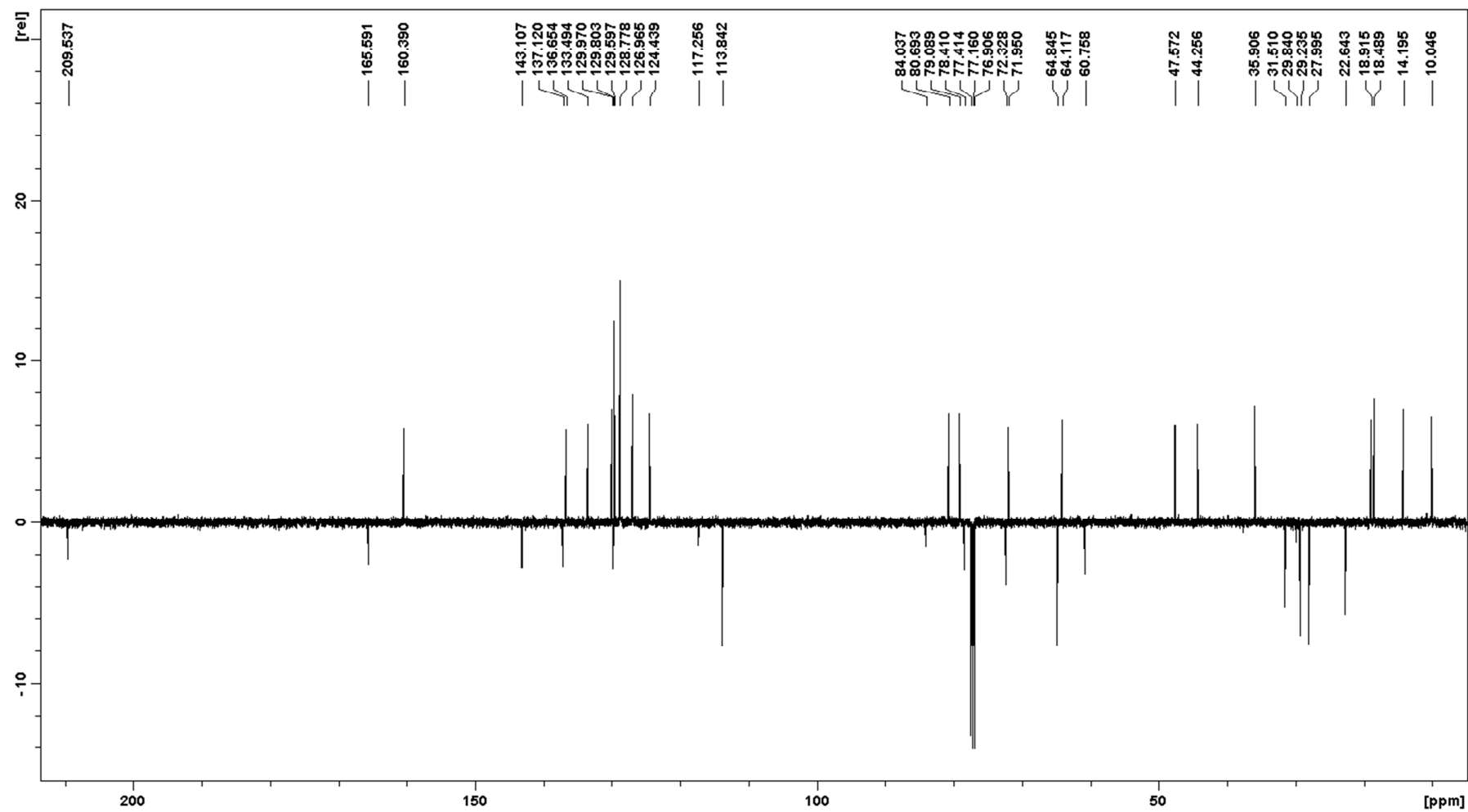


Figure S6. DEPTQ spectrum of compound 4 (500 MHz, CDCl₃).

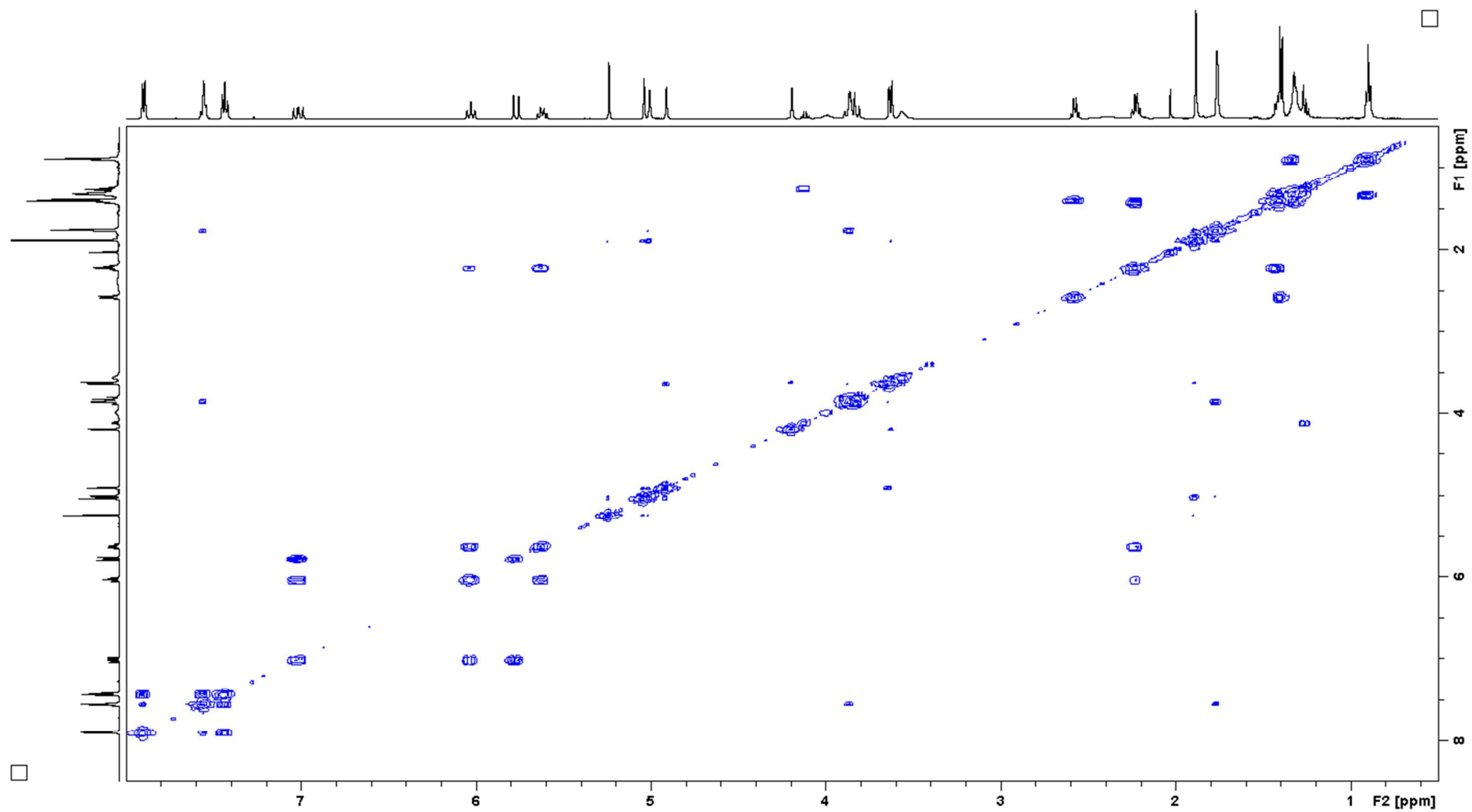


Figure S7. ^1H - ^1H COSY spectrum of compound **4** (500 MHz, CDCl_3).

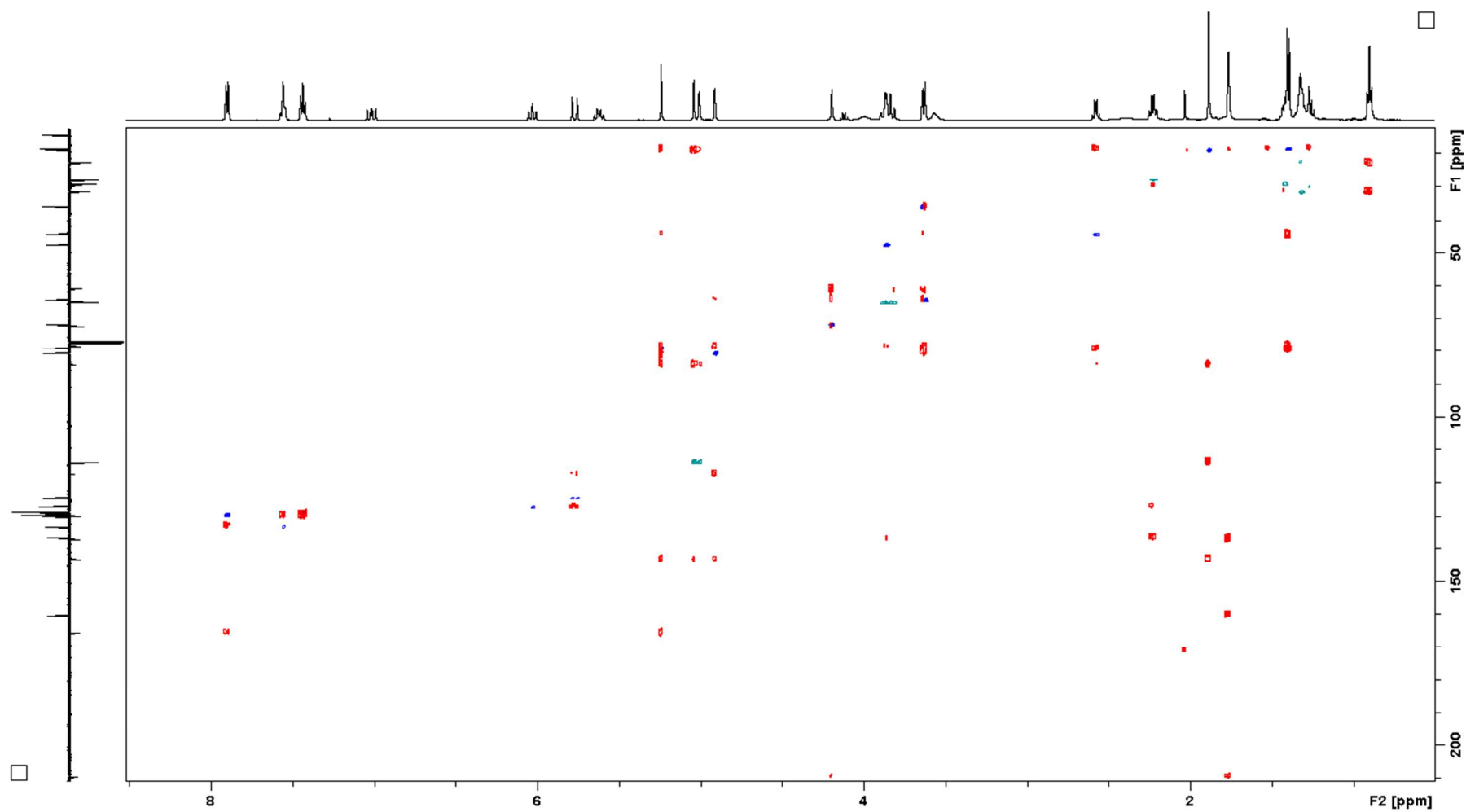


Figure S8. Overlay of HSQC-DEPT (blue/light green) and HMBC spectra of compound **4** (500 MHz, CDCl₃).

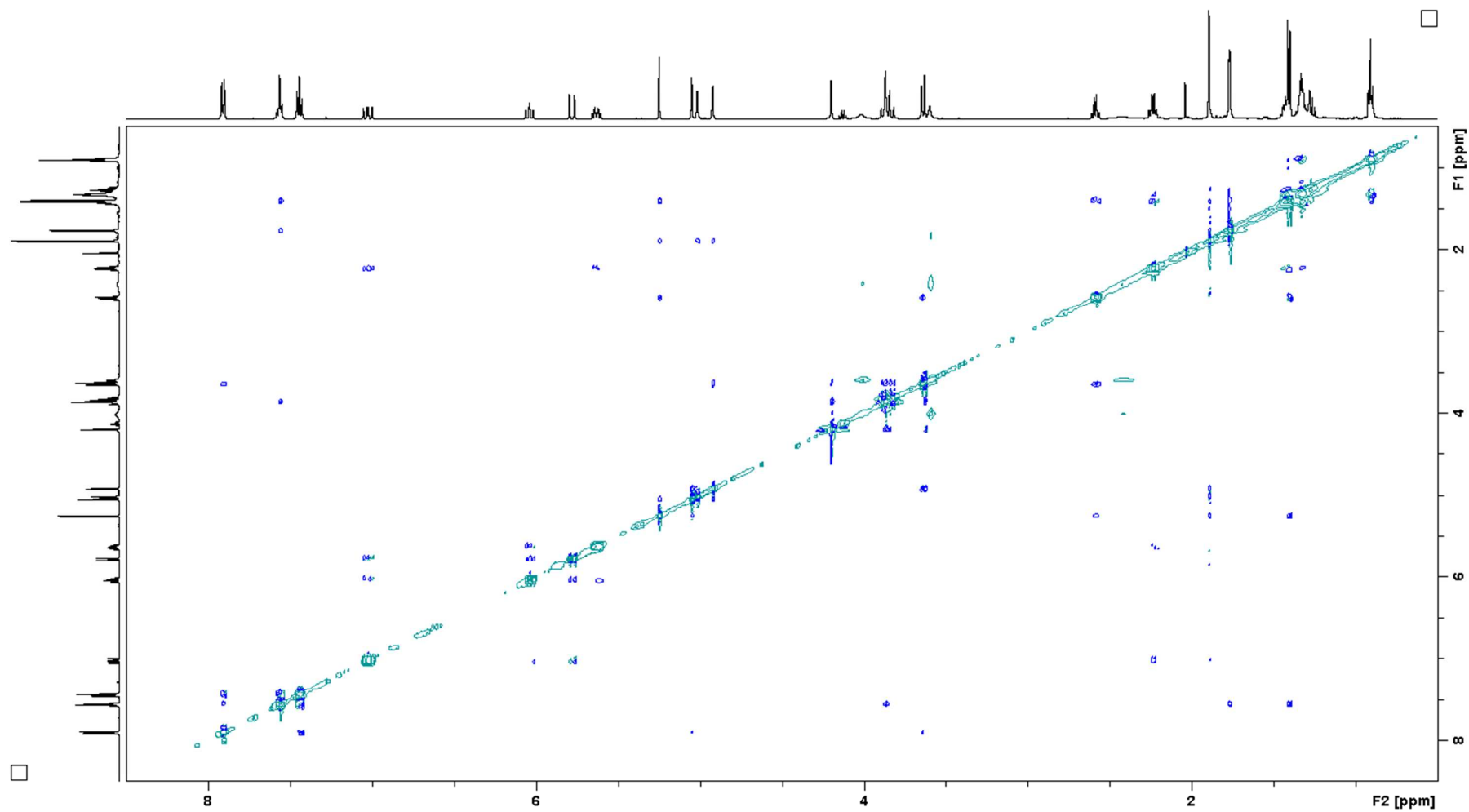


Figure S9. 2D ^1H - ^1H ROESY spectrum of compound **4** (500 MHz, CDCl_3).

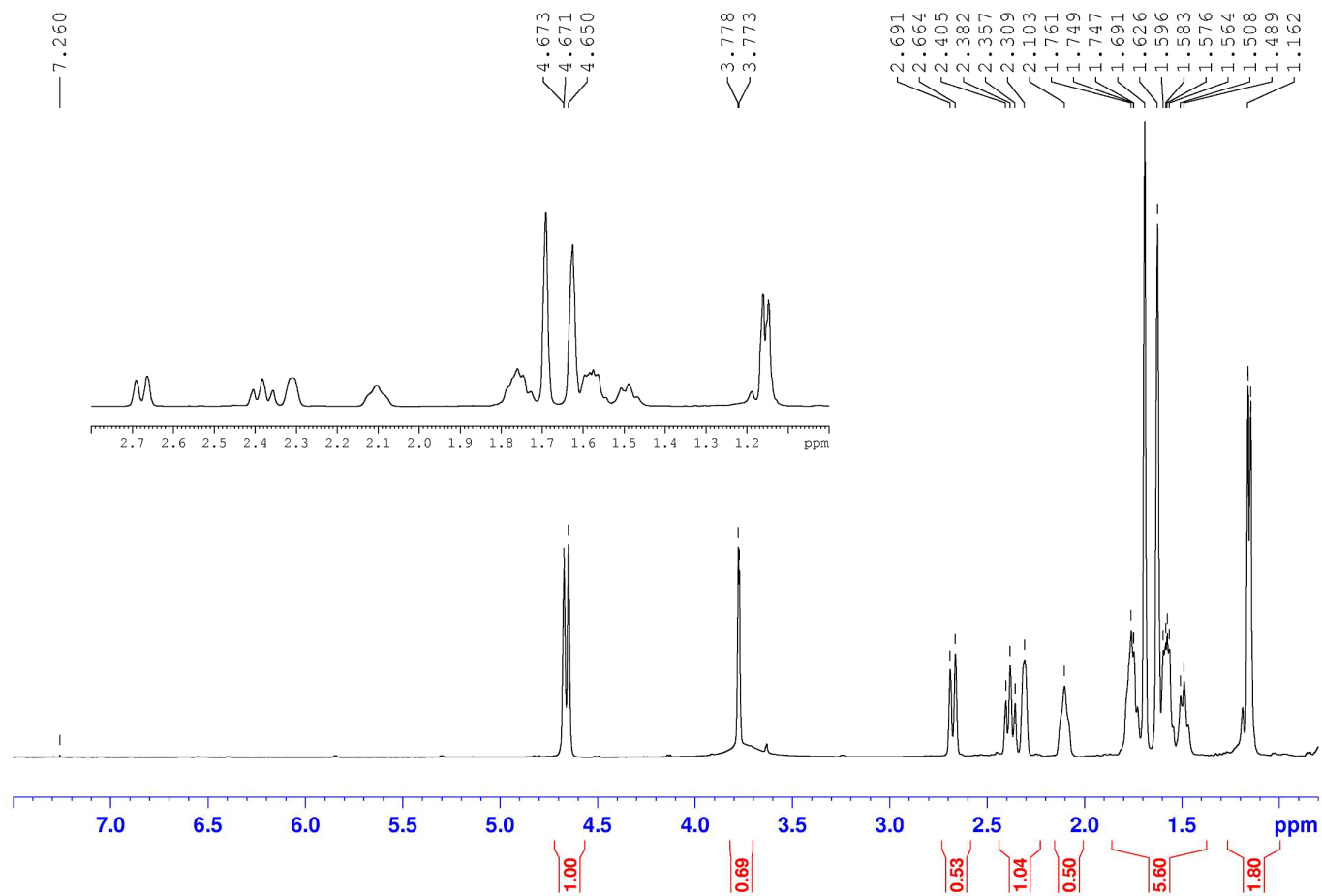


Figure S10. ^1H -NMR spectrum of compound **11** (500MHz, CDCl_3).

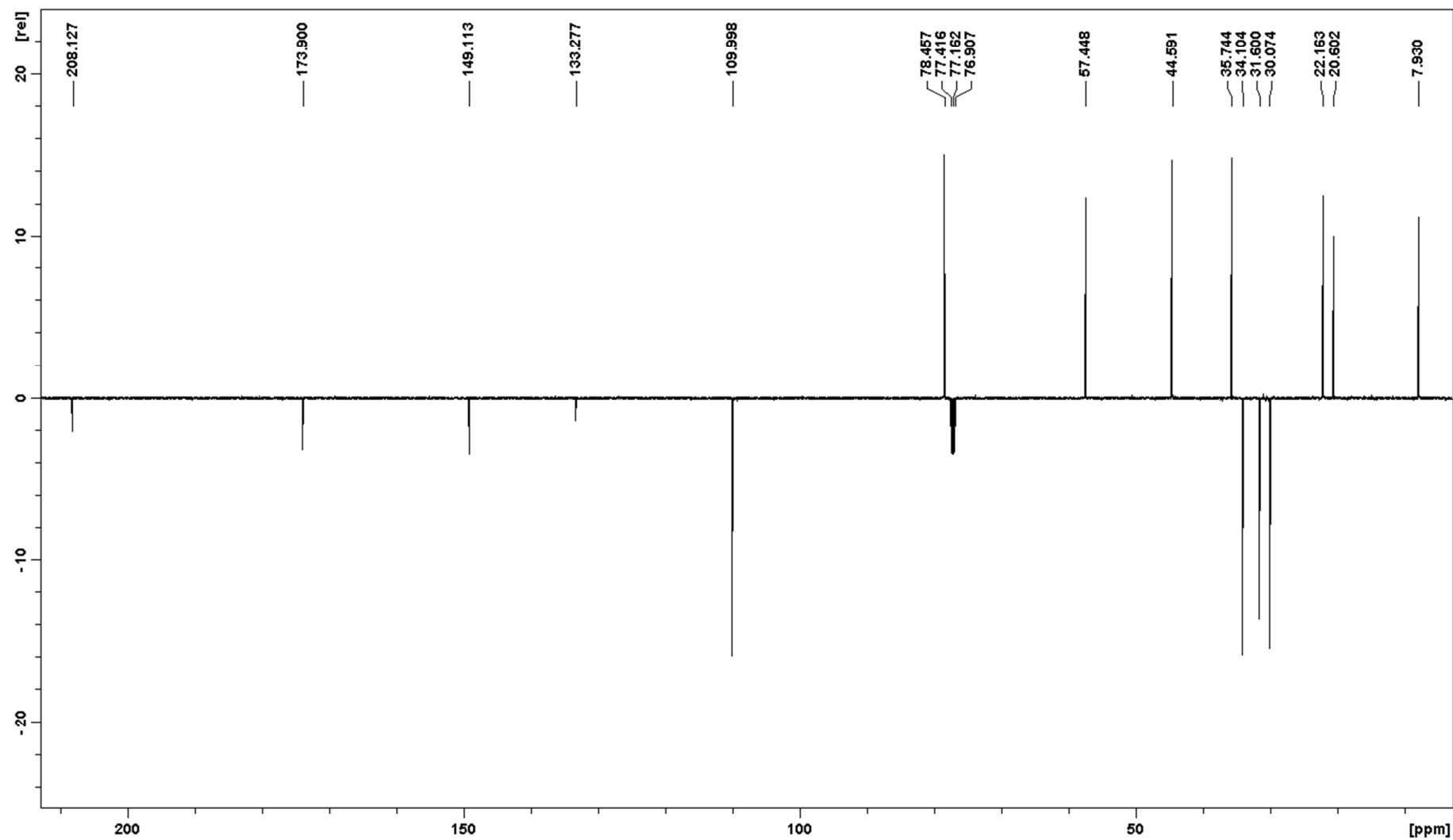


Figure S11. DEPTQ spectrum of compound **11** (500 MHz, CDCl₃).

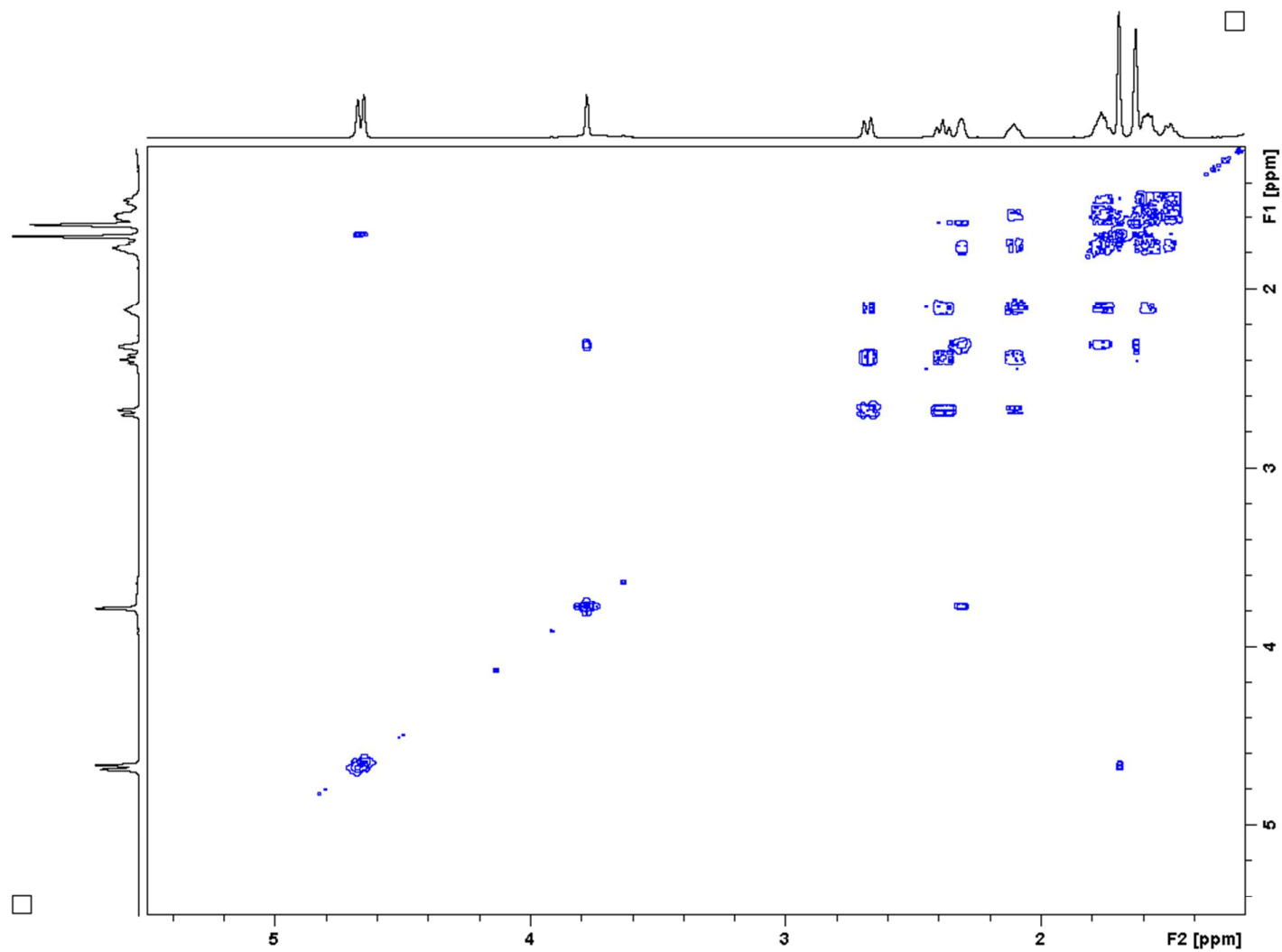


Figure S12. ^1H - ^1H COSY spectrum of compound **11** (500 MHz, CDCl_3).

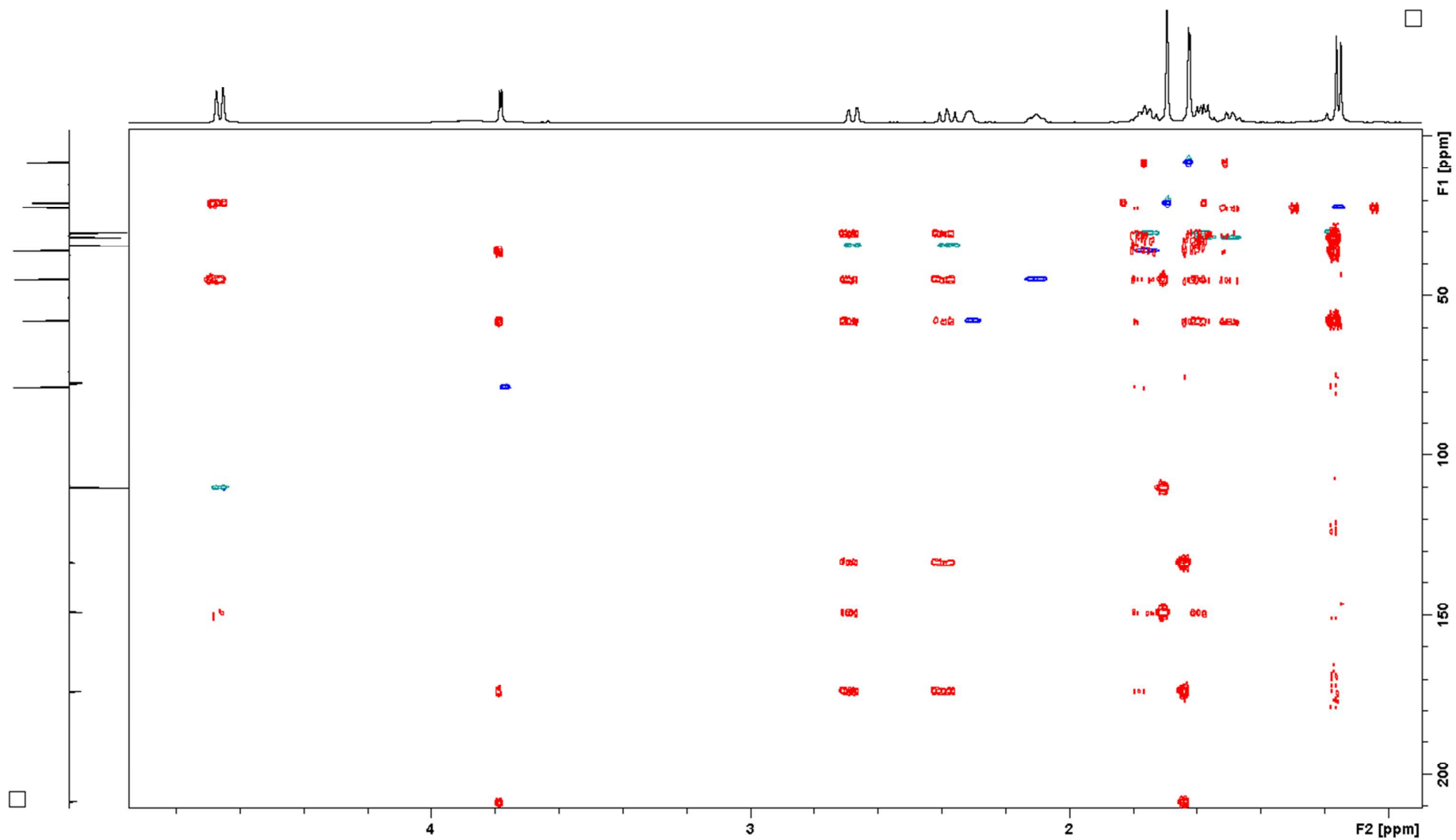


Figure S13. Overlay of HSQC-DEPT (blue/light green) and HMBC spectra of compound **11** (500 and 125 MHz, CDCl₃).

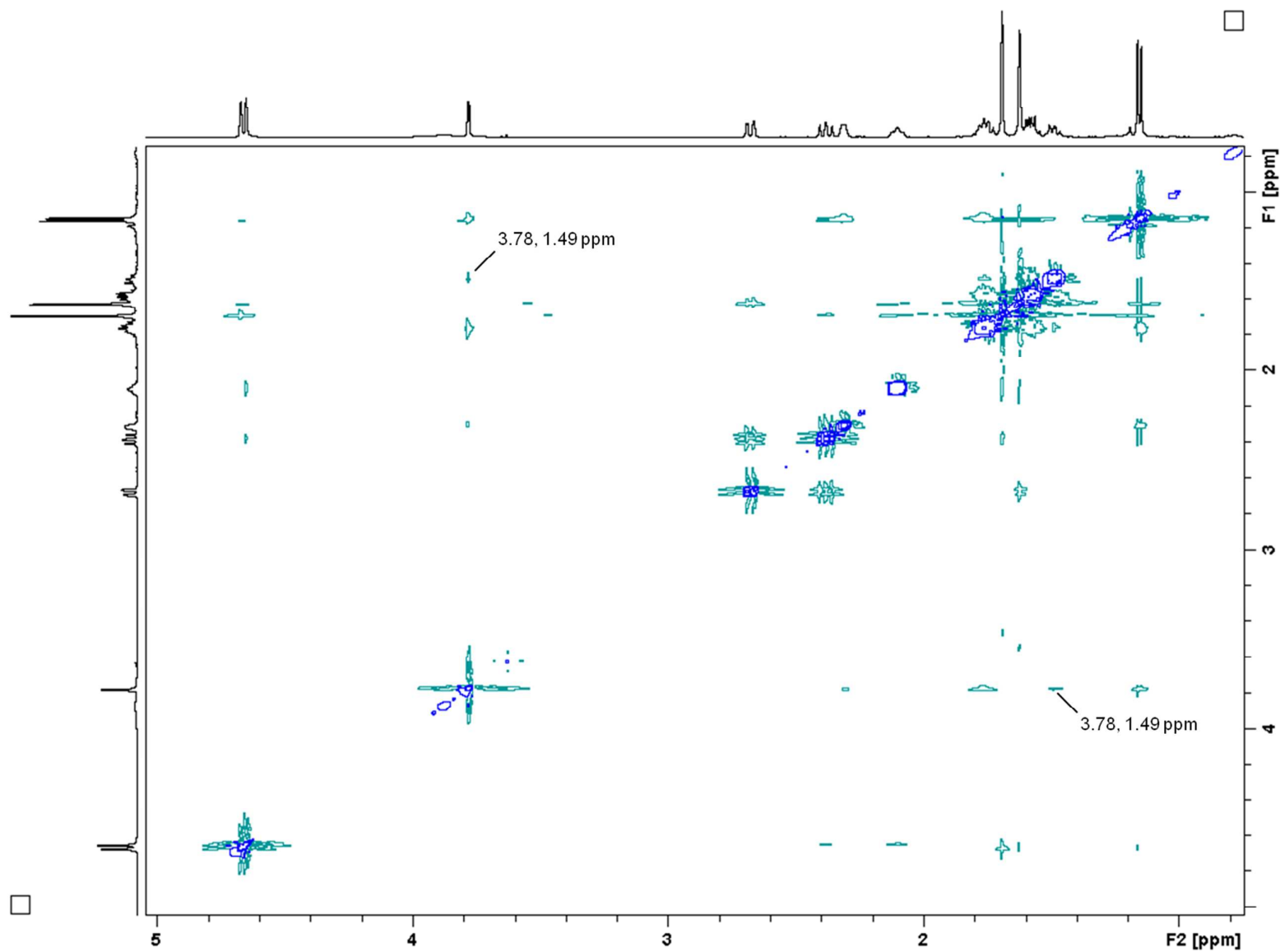


Figure S14. 2D ^1H - ^1H NOESY spectrum of compound **11** (500 MHz, CDCl_3).

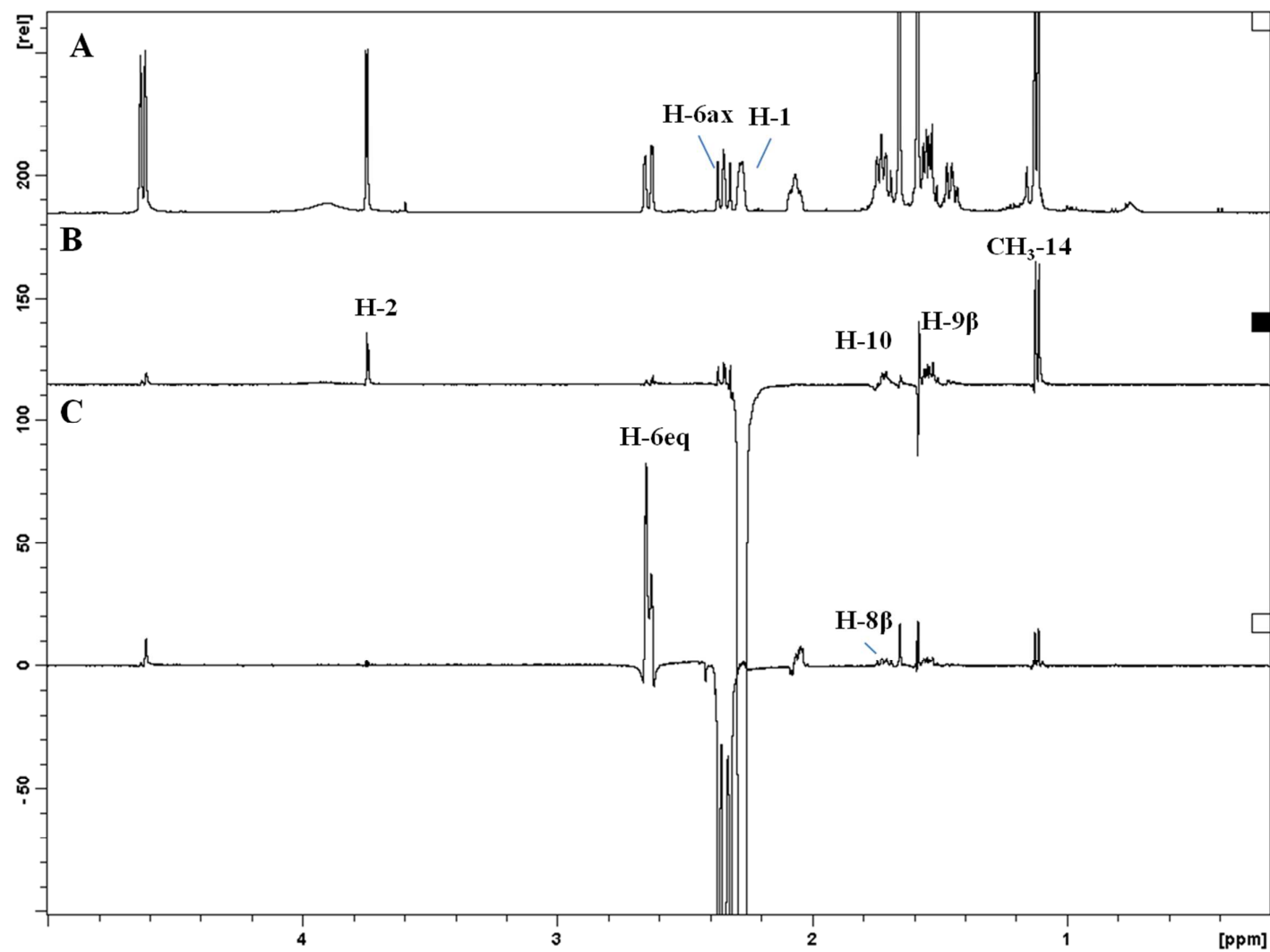


Figure S15. 1D Selective NOESY spectra of compound **11** (500 MHz, CDCl_3 ; $D_8 = 0.5$ sec)

(A) Full ^1H NMR spectrum (B-C) Selective irradiations of H-1 and H-6, respectively.

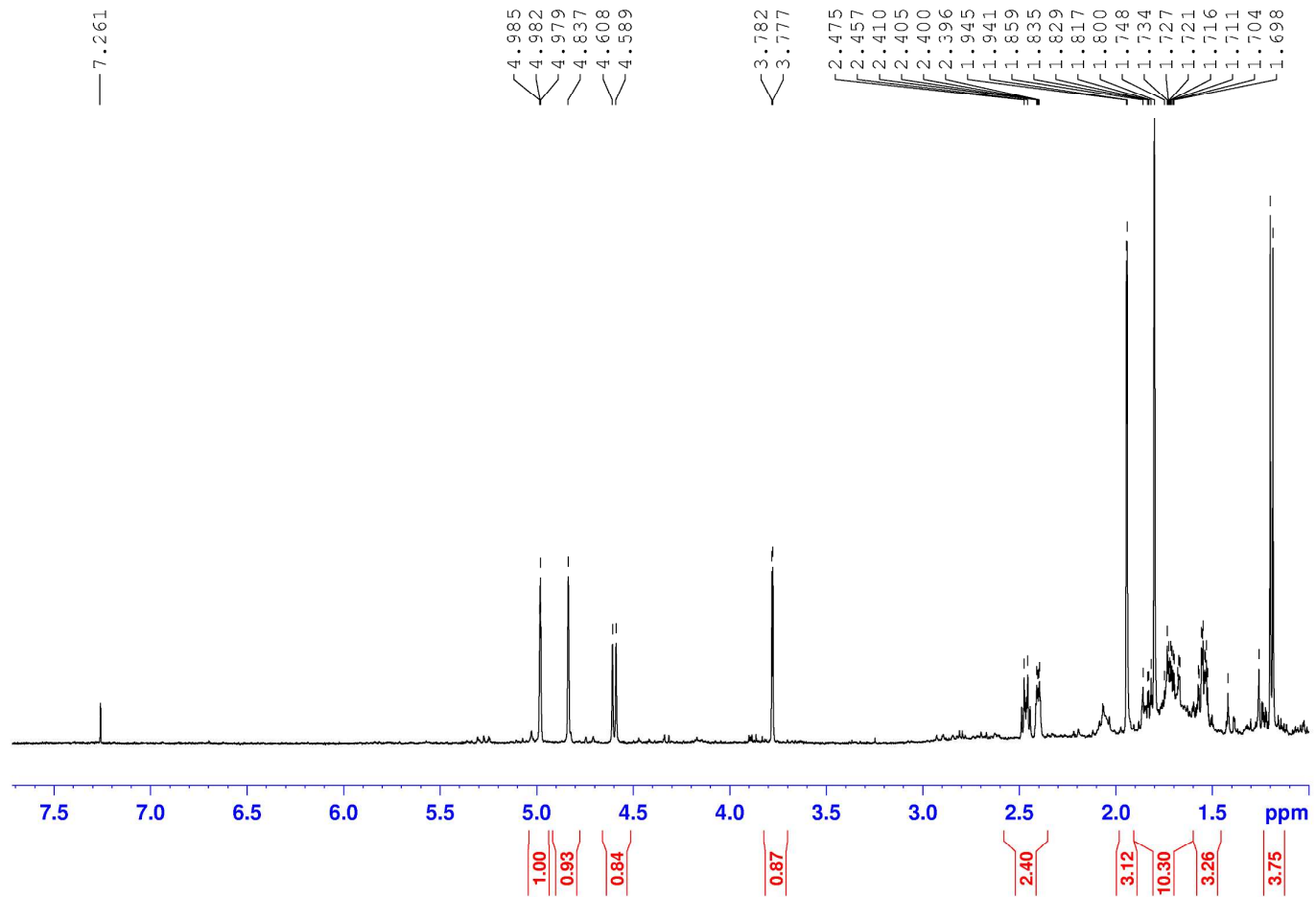


Figure S16. ^1H -NMR spectrum of compound **12** (500 MHz, CDCl_3).

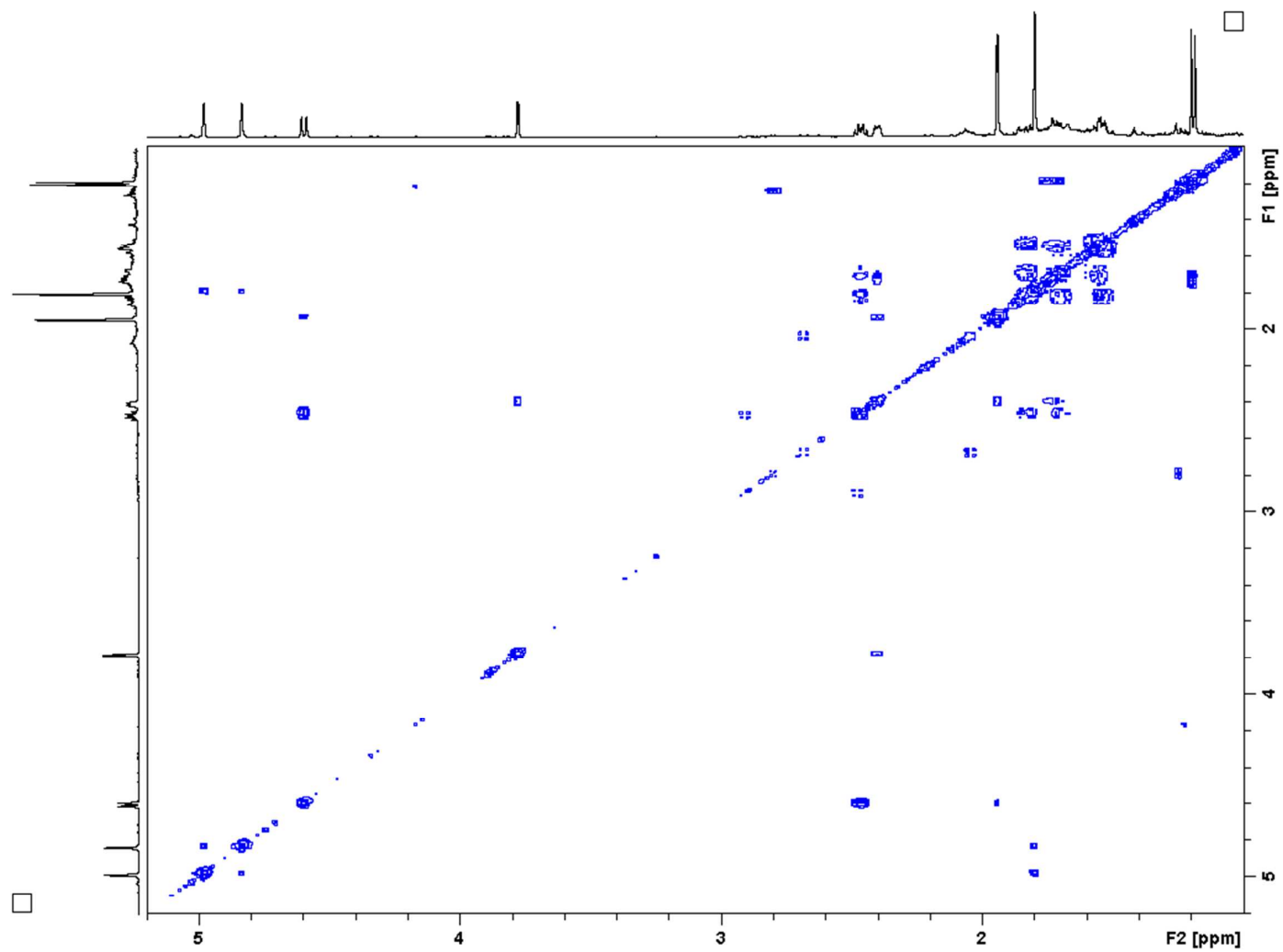


Figure S17. ^1H - ^1H COSY spectrum of compound **12** (500 MHz, CDCl_3).

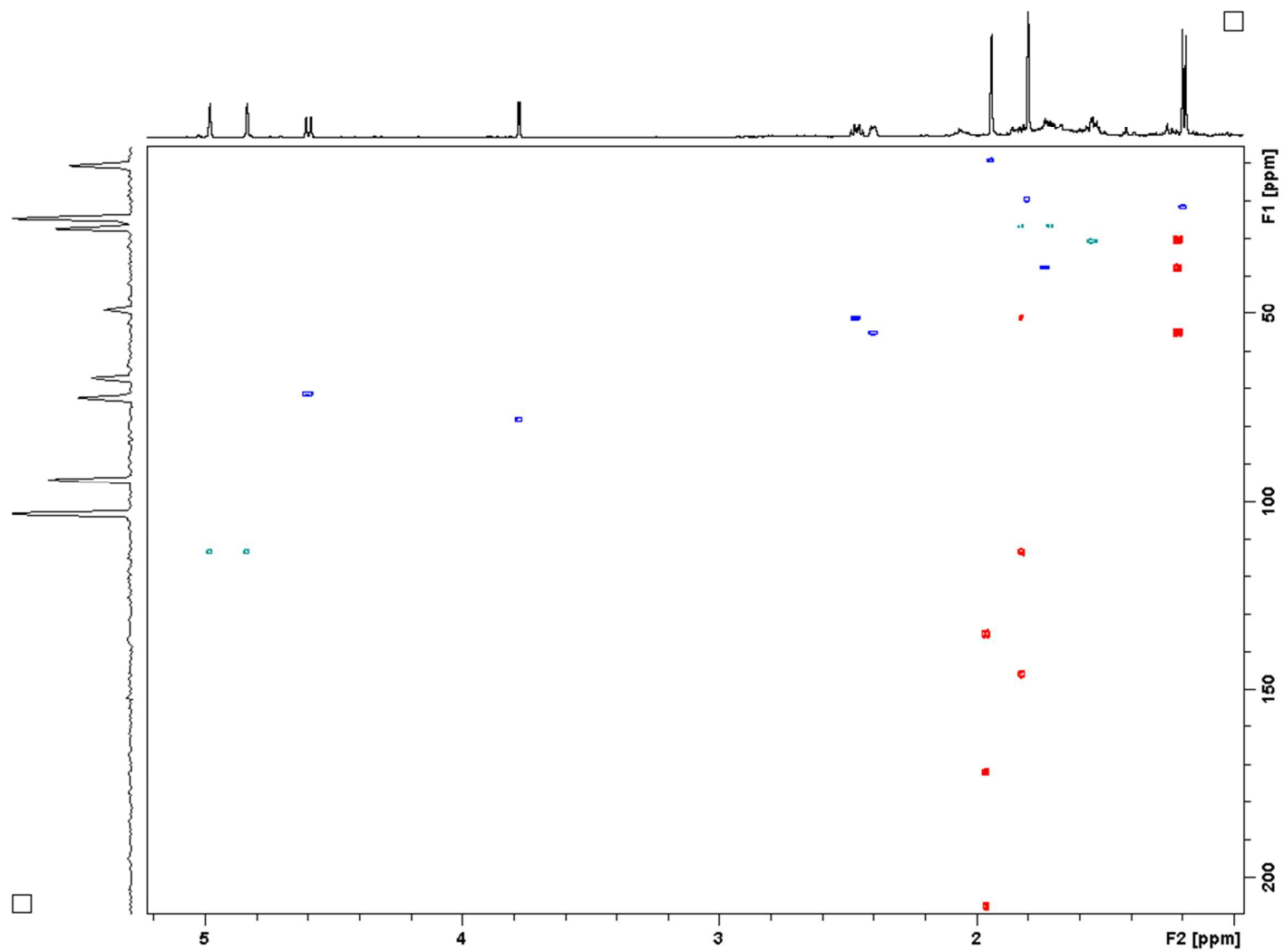


Figure S18. Overlay of HSQC-DEPT (blue/light green) and HMBC spectra of compound **12** (500 MHz, CDCl₃)

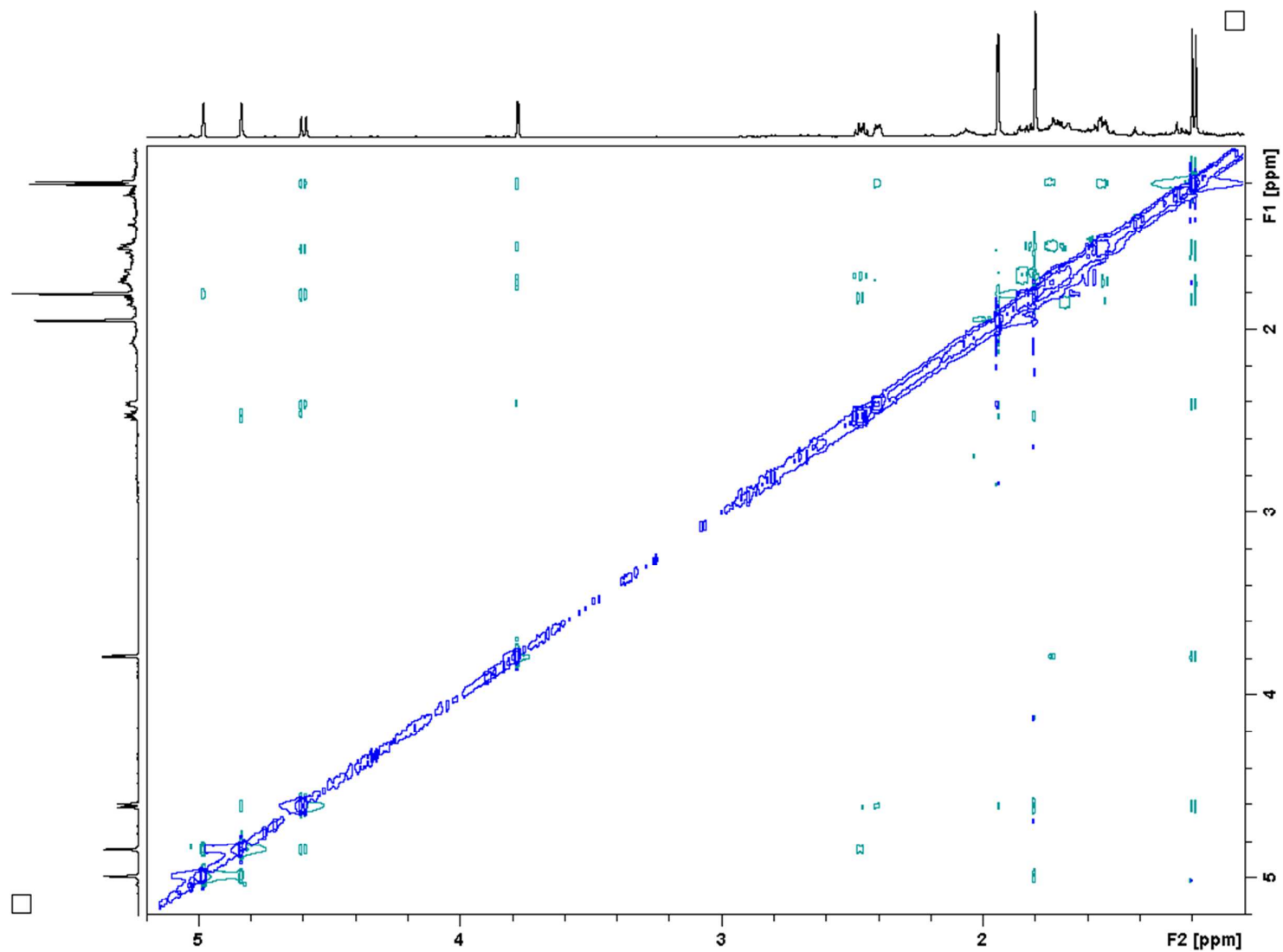


Figure S19. 2D ^1H - ^1H NOESY spectrum of compound **12** (500 MHz, CDCl_3).

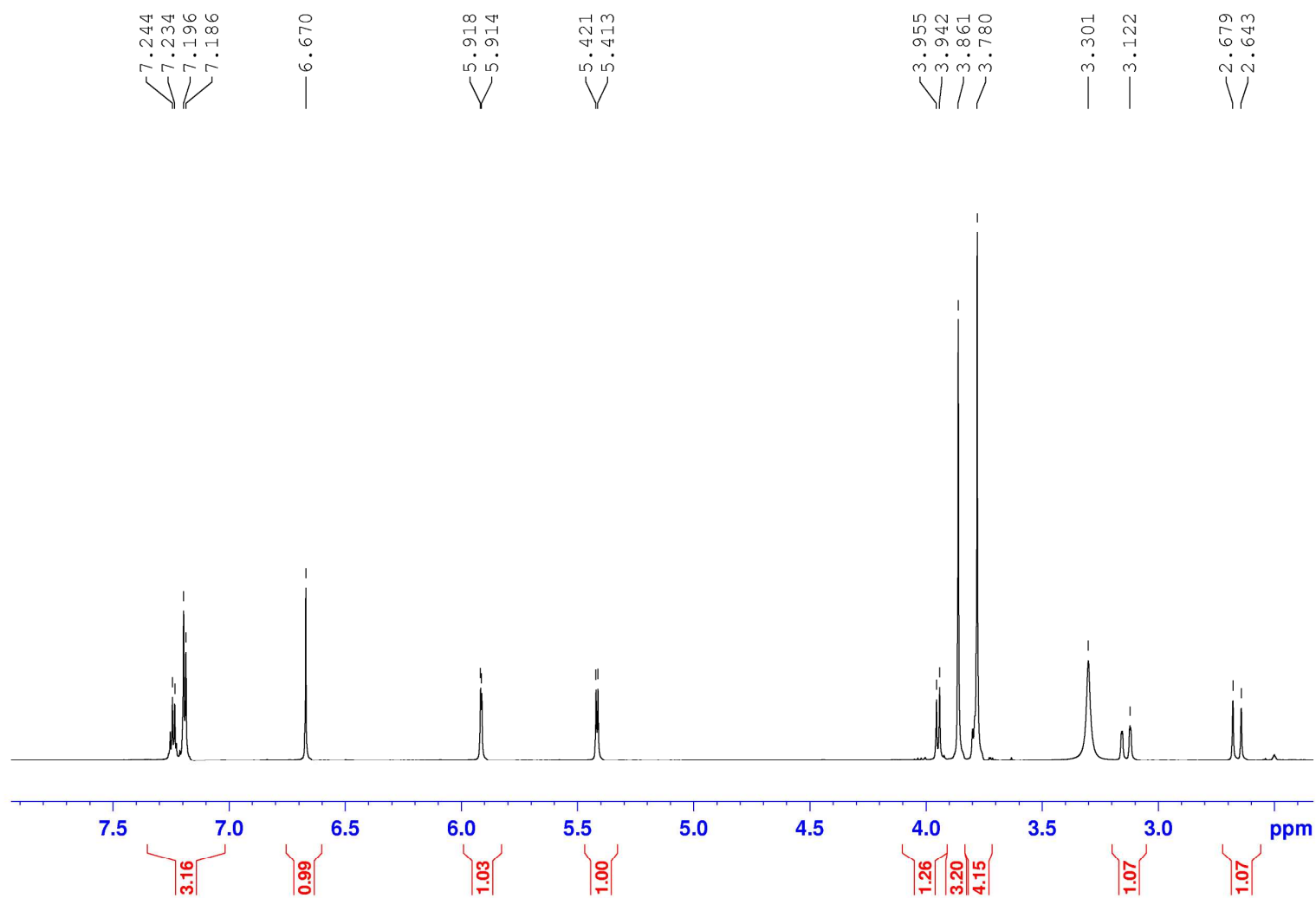


Figure S20. ^1H -NMR spectrum of compound **15** (500 MHz, $\text{DMSO}-d_6$).

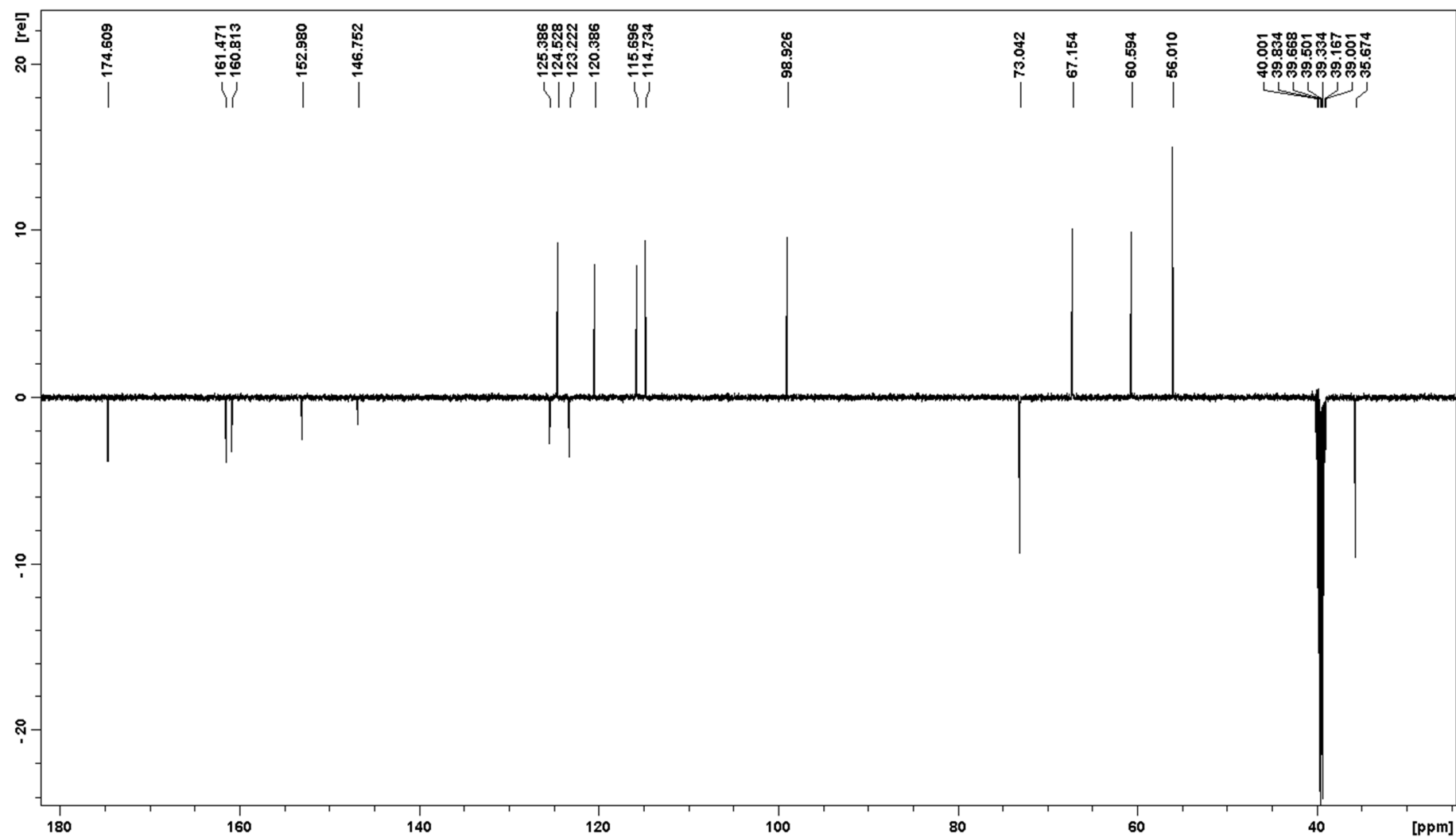


Figure S21. ¹³C spectrum of compound **15** (125 MHz, DMSO-*d*₆).

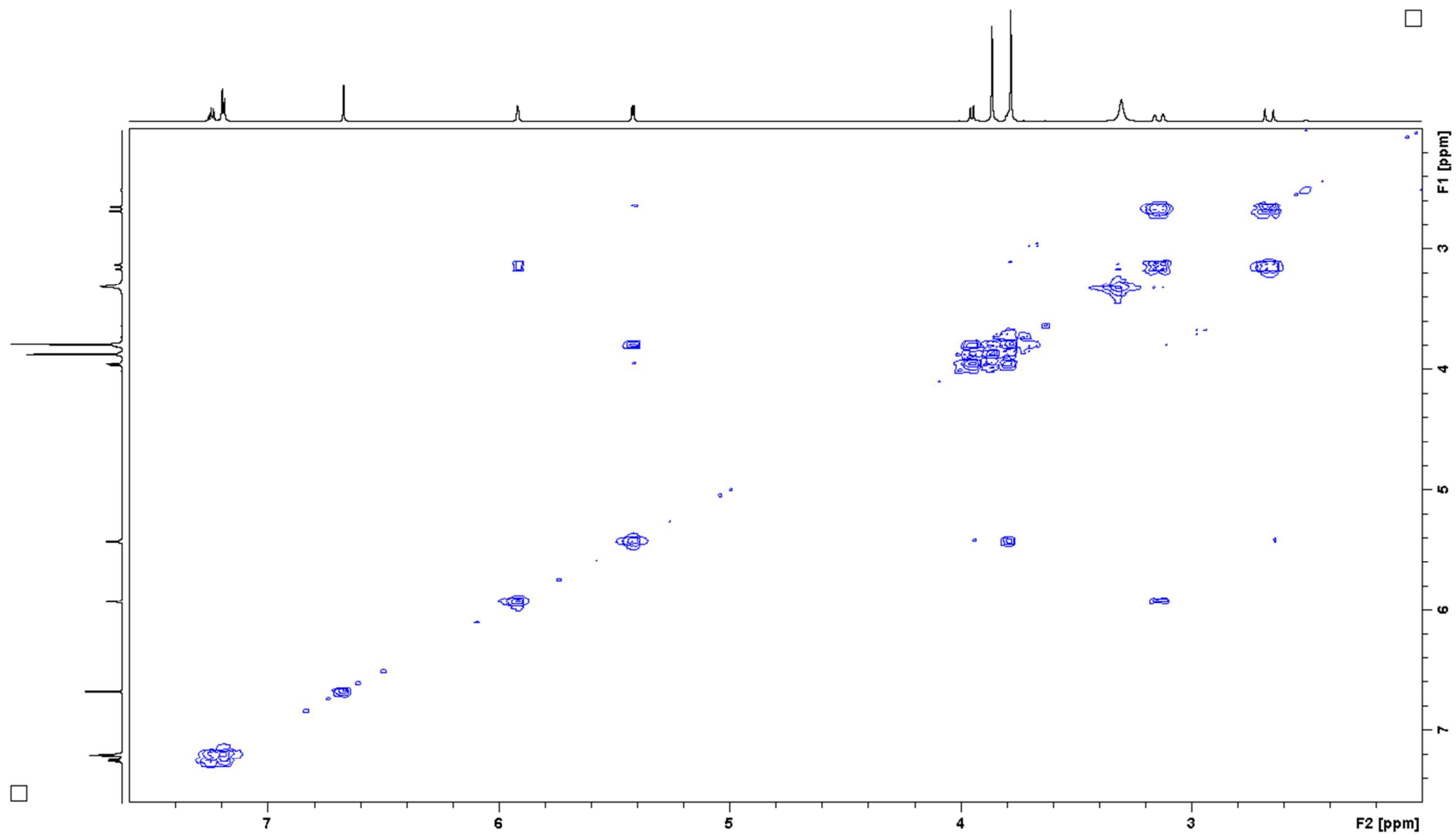


Figure S22. ^1H - ^1H COSY spectrum of compound **15** (500 MHz, $\text{DMSO}-d_6$)

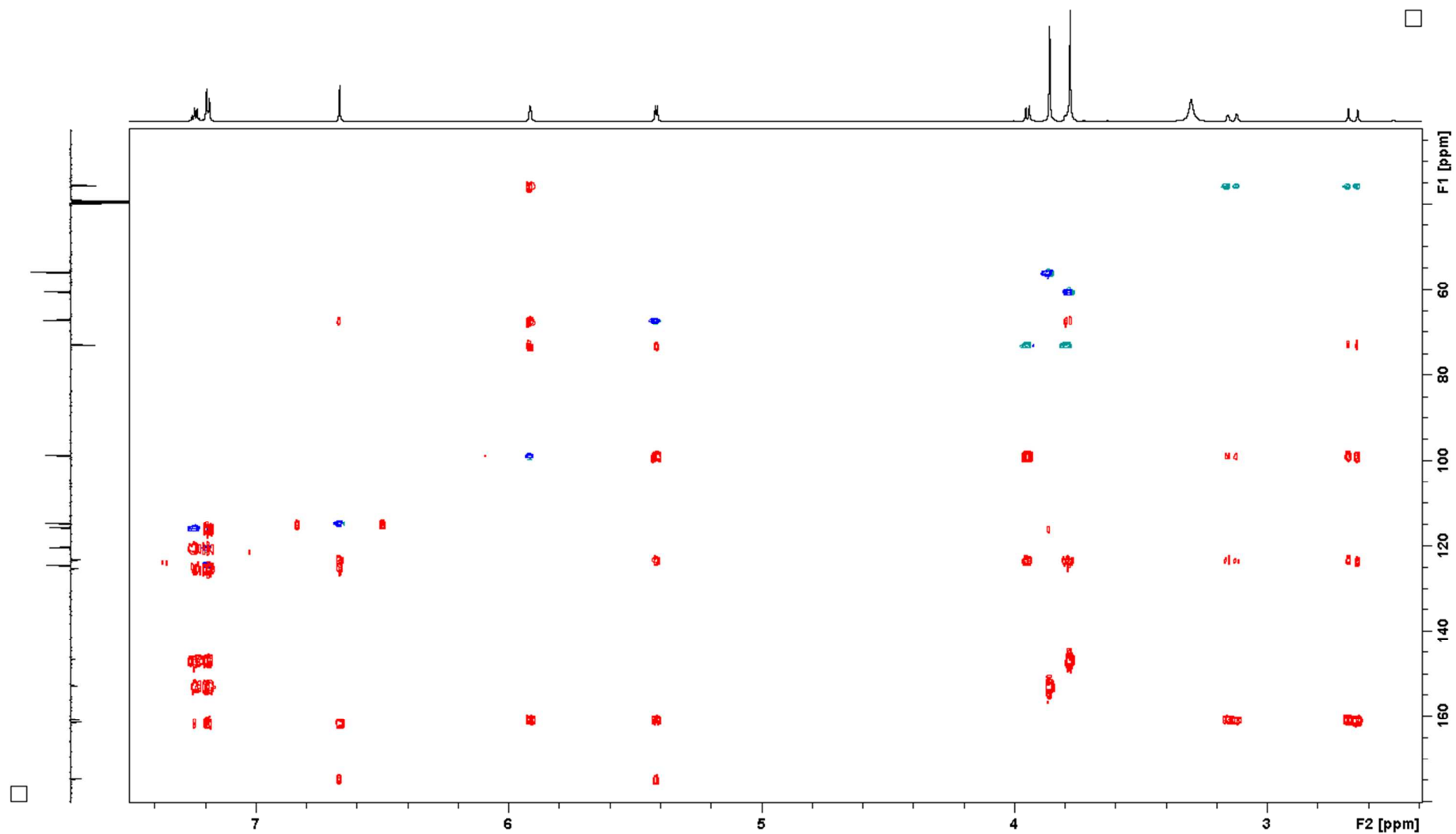


Figure S23. Overlay of HSQC-DEPT (blue/light green) and HMBC spectra of compound **15** (500 MHz, DMSO-*d*₆).

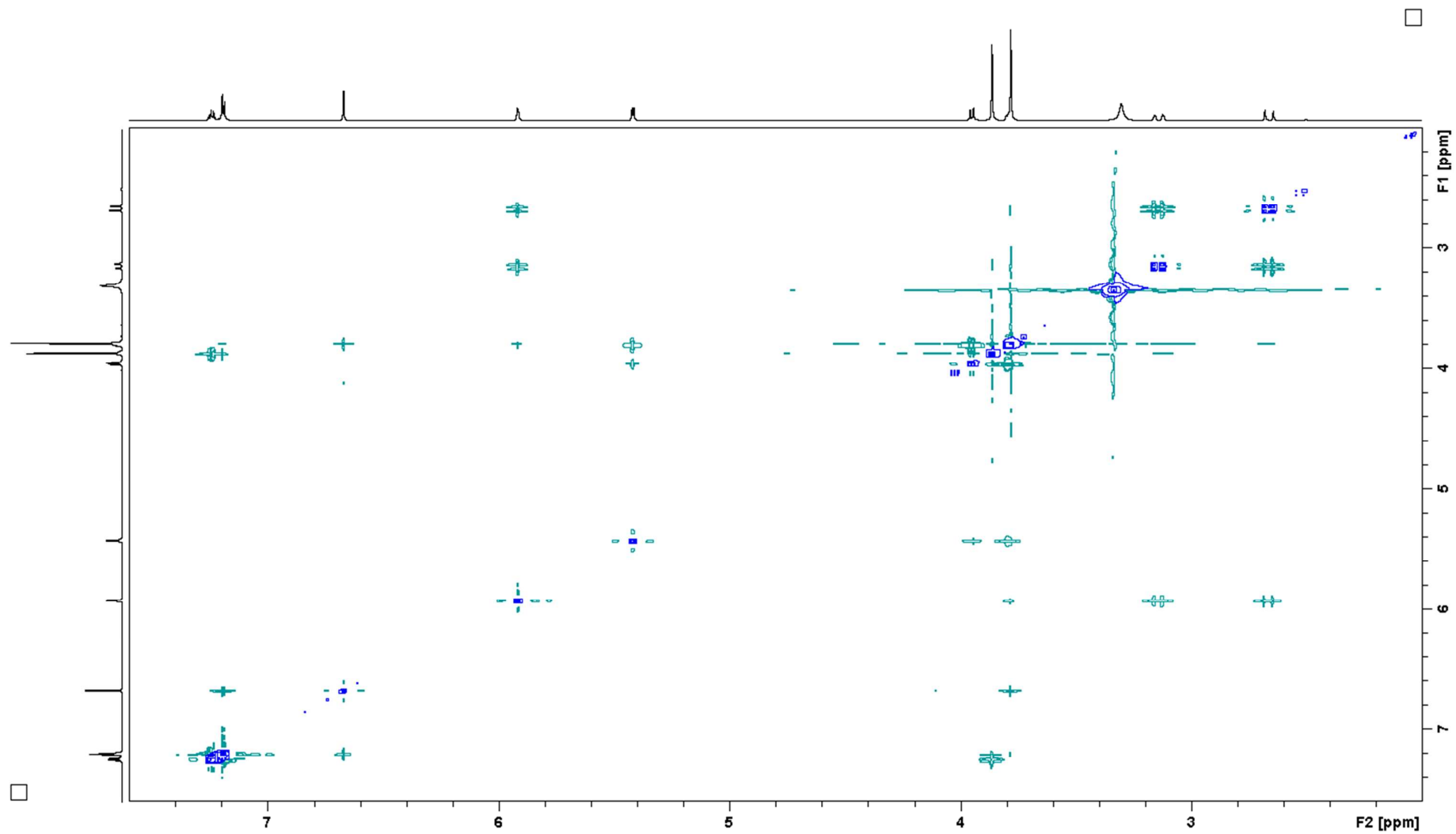


Figure S24. 2D ^1H - ^1H NOESY spectrum of compound **15** (500 MHz, $\text{DMSO-}d_6$).

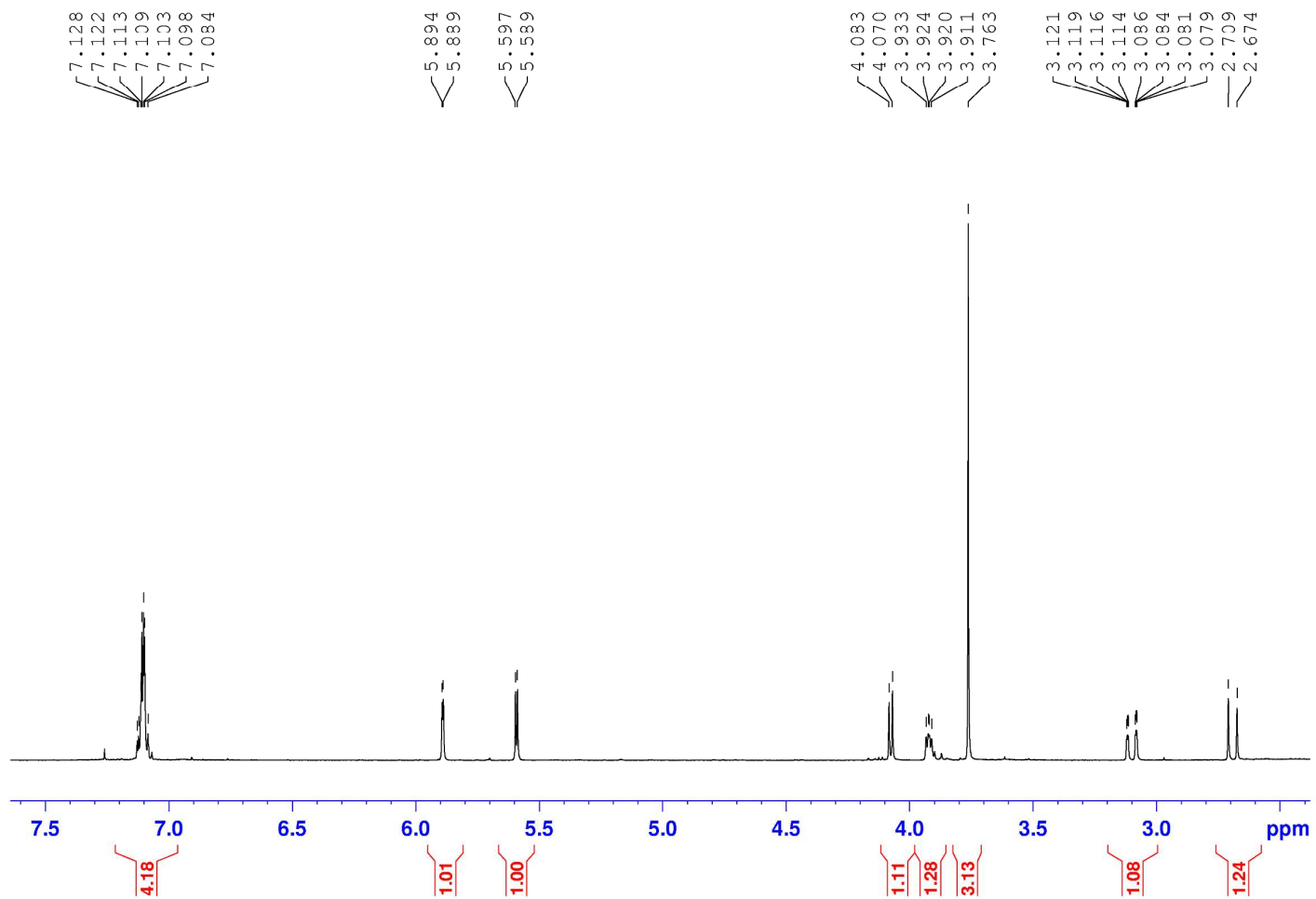


Figure S25. ¹H-NMR spectrum of compound **16** (500 MHz, CDCl₃).

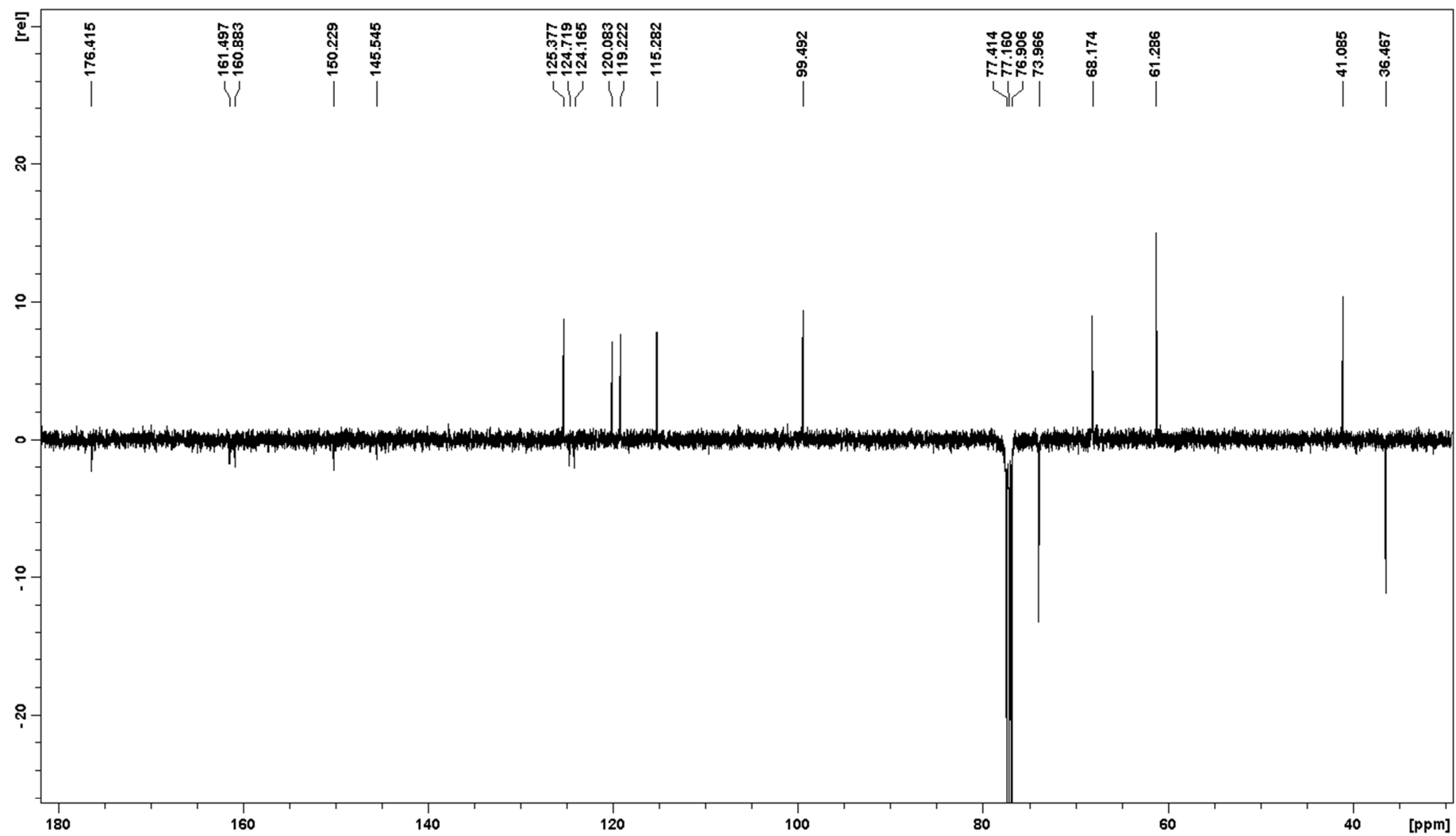


Figure S26. ¹³C spectrum of compound **16** (125 MHz, CDCl₃).

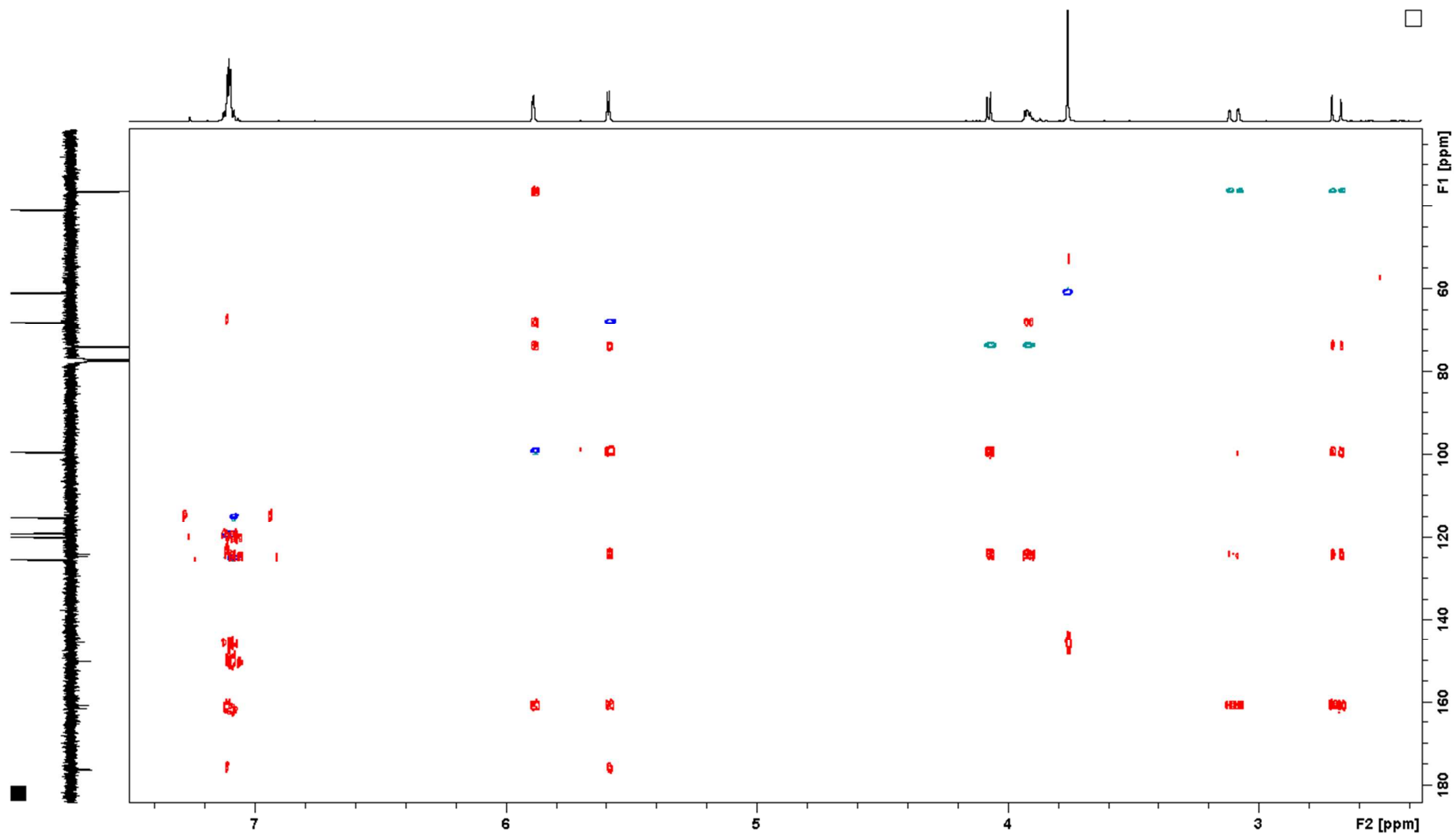


Figure S28. Overlay of HSQC-DEPT (blue/light green) and HMBC spectra of compound **16** (500 MHz, CDCl₃).

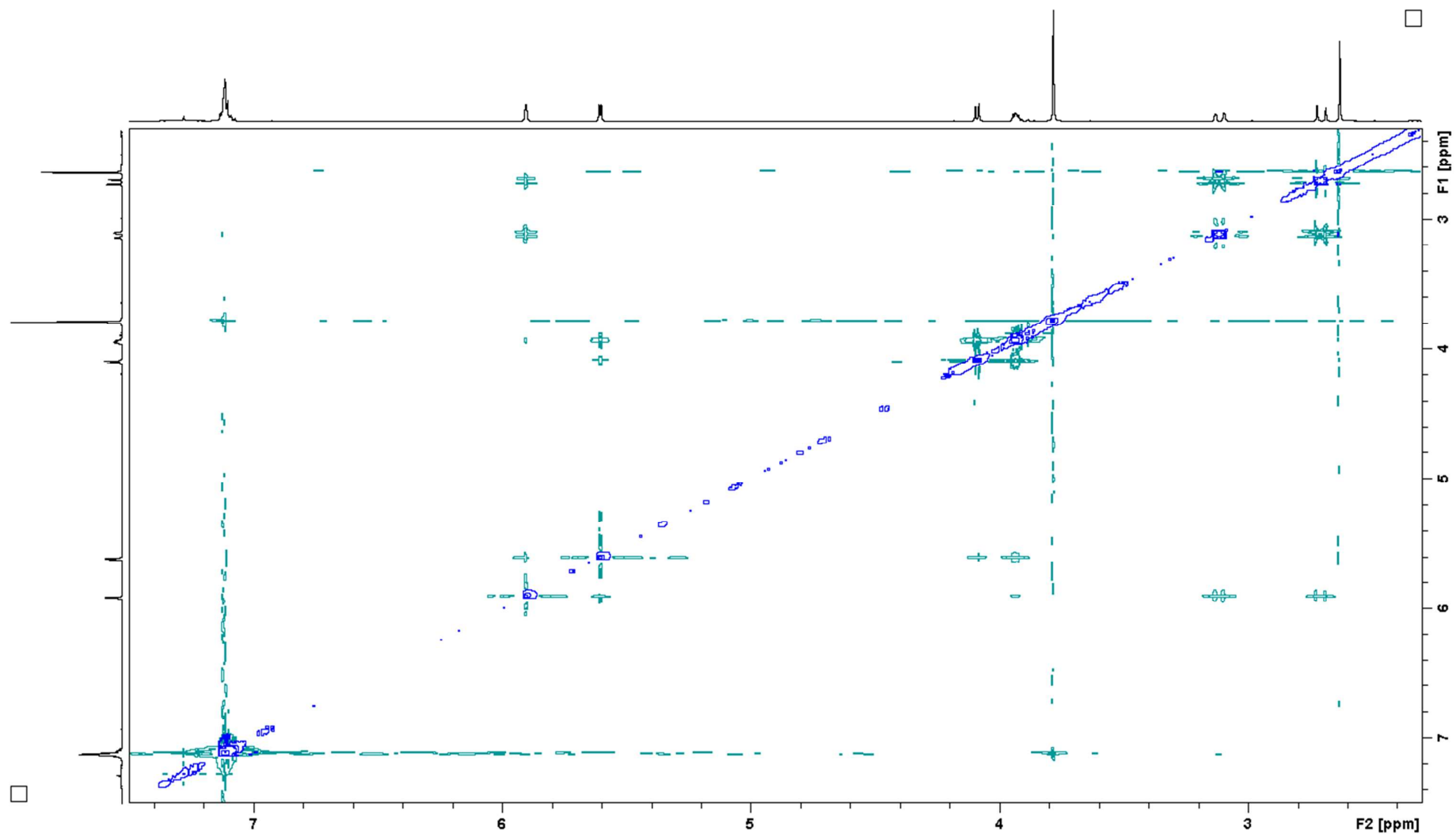


Figure S29. 2D ^1H - ^1H NOESY spectrum of compound **16** (500 MHz, CDCl_3).

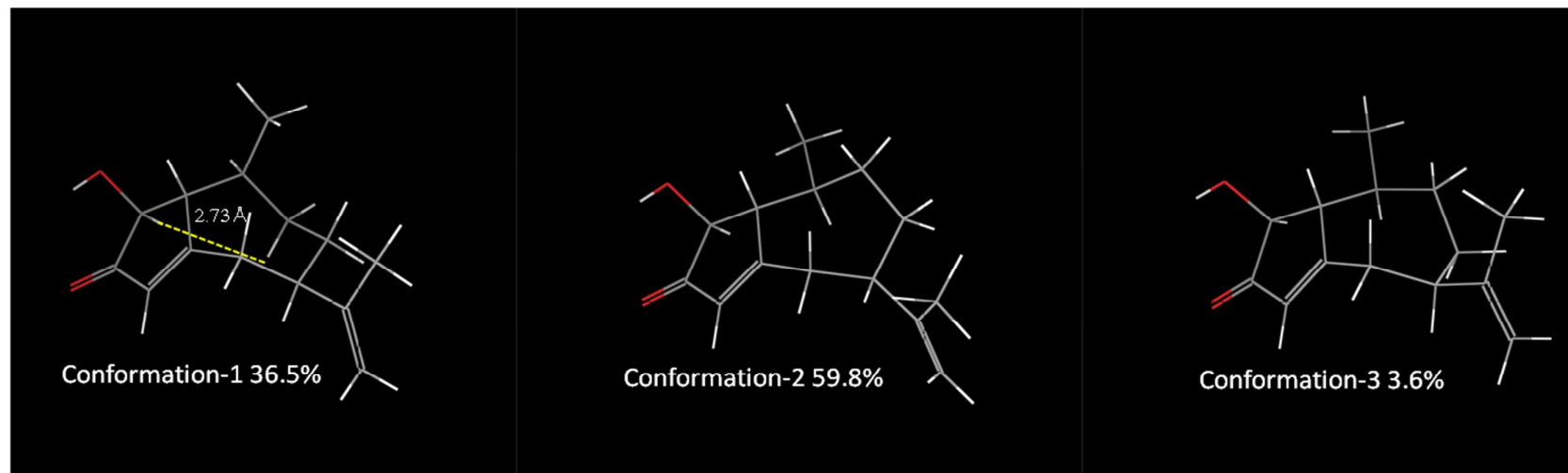


Figure S30. Major conformers of compound **11**, according to their weight in the Boltzmann distribution after geometrical optimization (b3lyp/6-31g(d,p)) in gas phase.

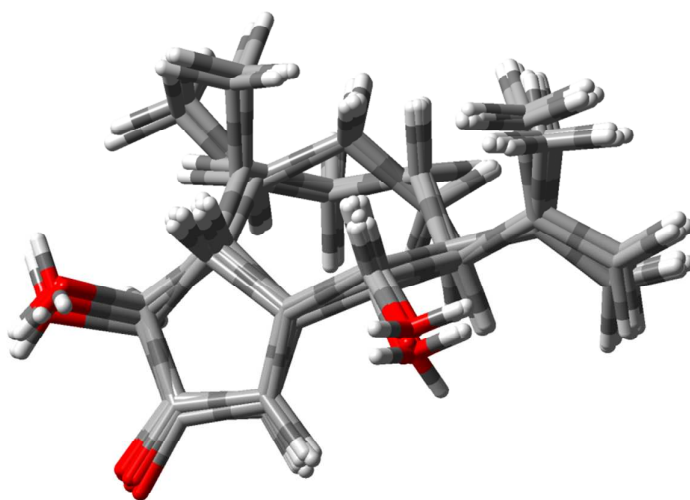


Figure S31. Superimposed conformers of compound **11** found within 2 Kcal/mol from the global minimum (Schrödinger MacroModel 9.8; OPLS2005 in water).

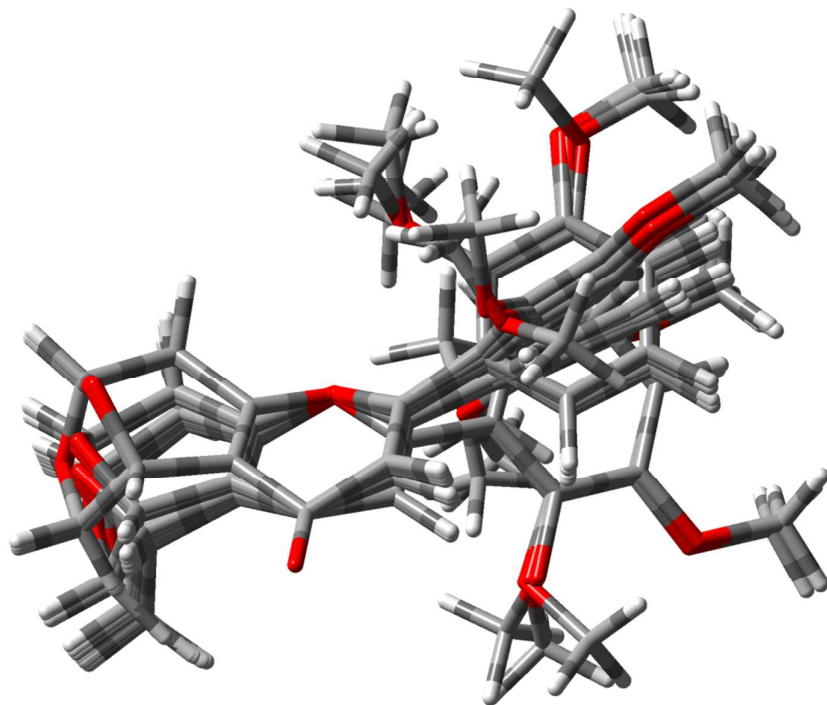


Figure S32. Superimposed conformers of compound **15** found within 2 Kcal/mol from the global minimum (Schrödinger MacroModel 9.8 ;OPLS2005 in water)

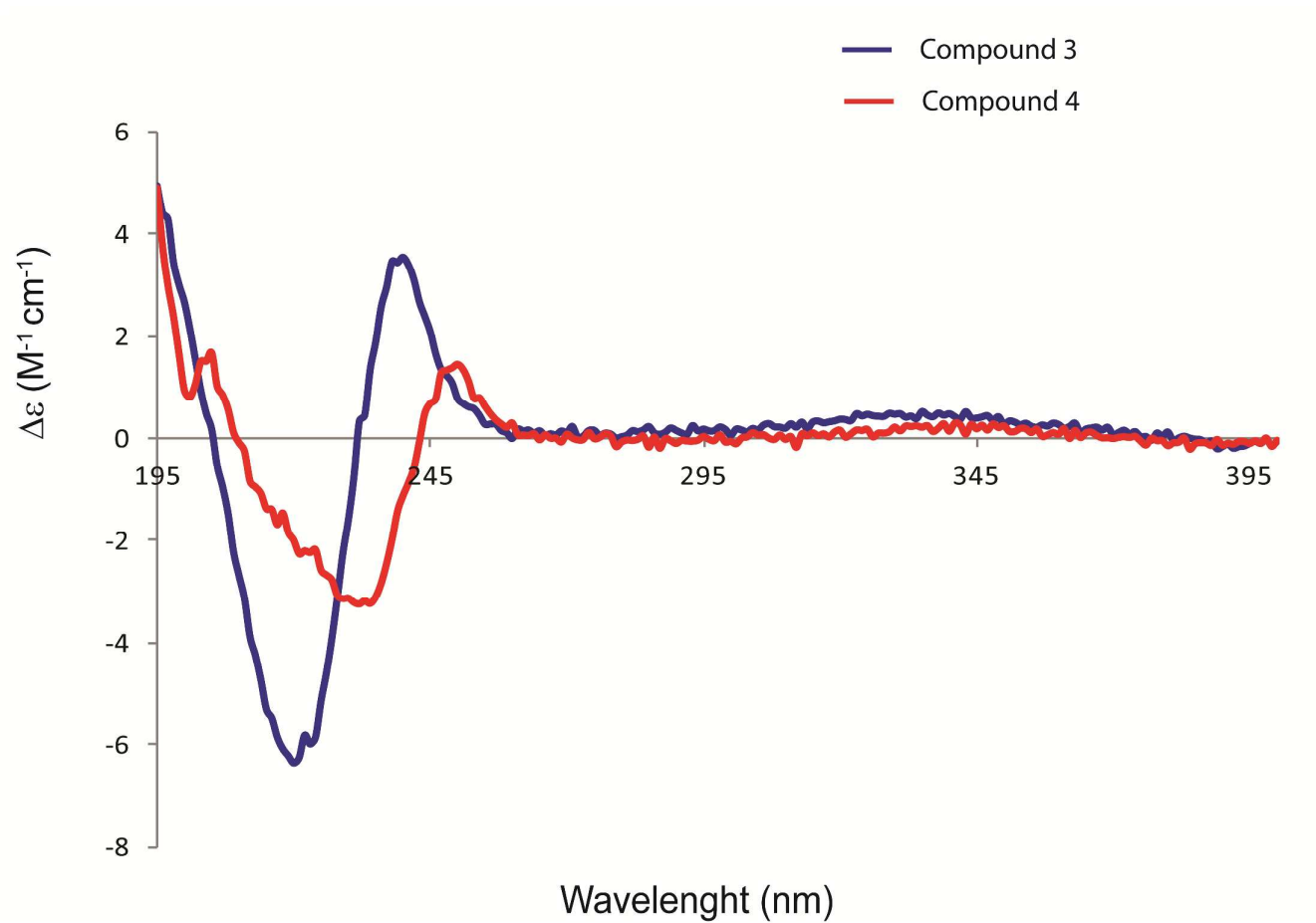


Figure S33. ECD spectra of compounds **3** and **4** in MeOH.

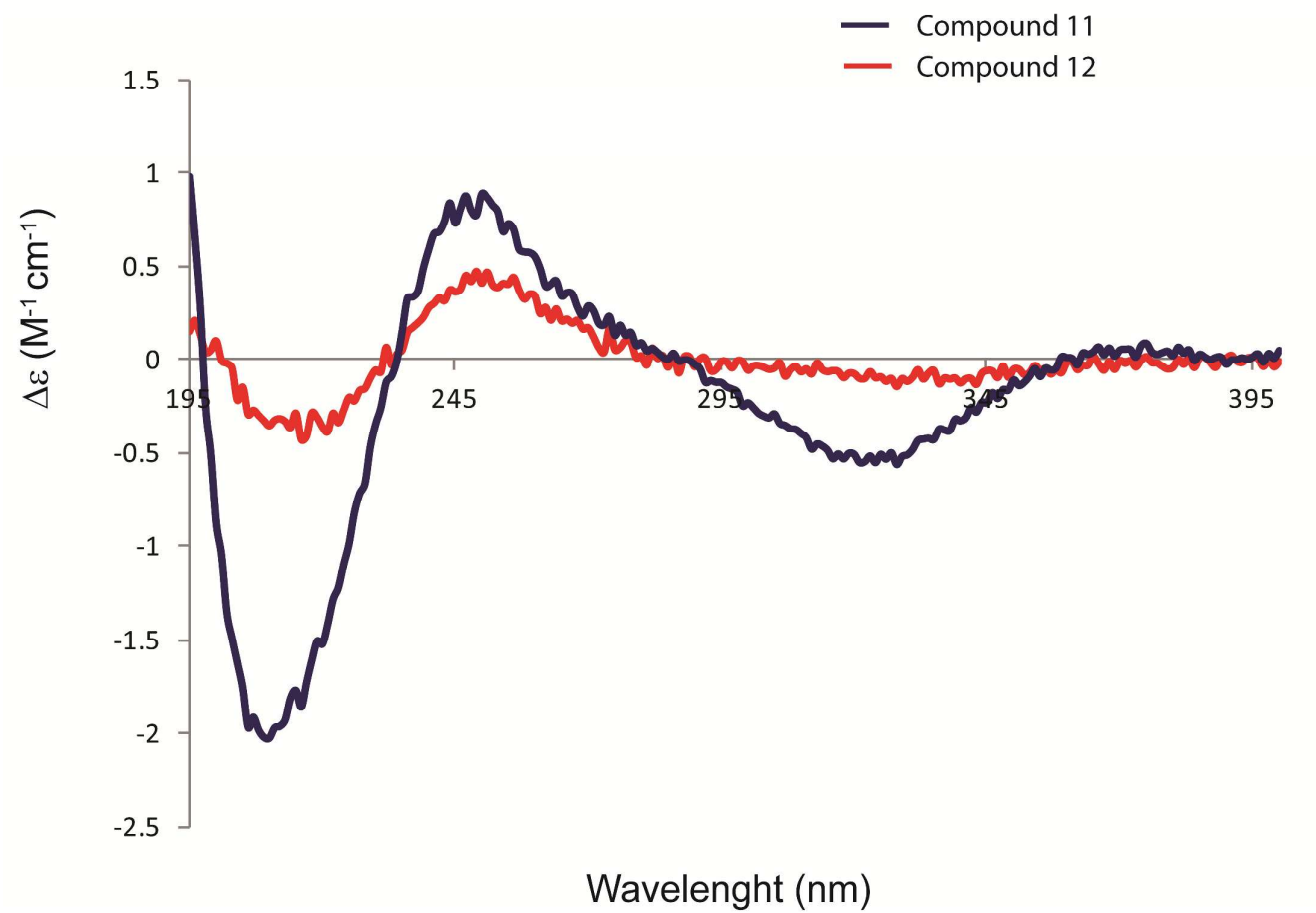


Figure S34. ECD spectra of compounds **11** and **12** in MeOH.

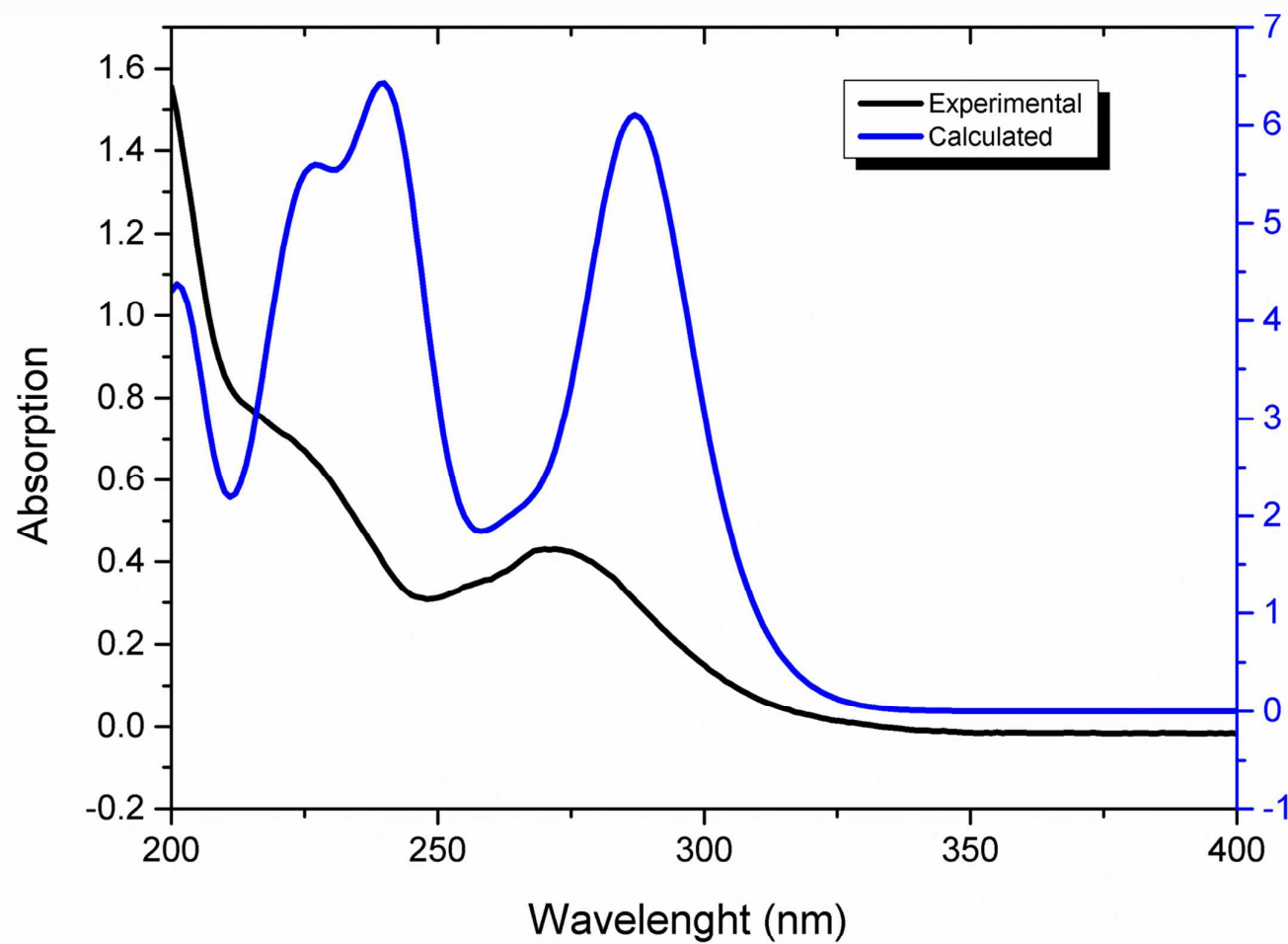


Figure S35. Experimental and calculated (cam-b3lyp/6-31g(d,p) UV spectra for the 5*R*,7*S* stereoisomer of compound **15** in MeOH.

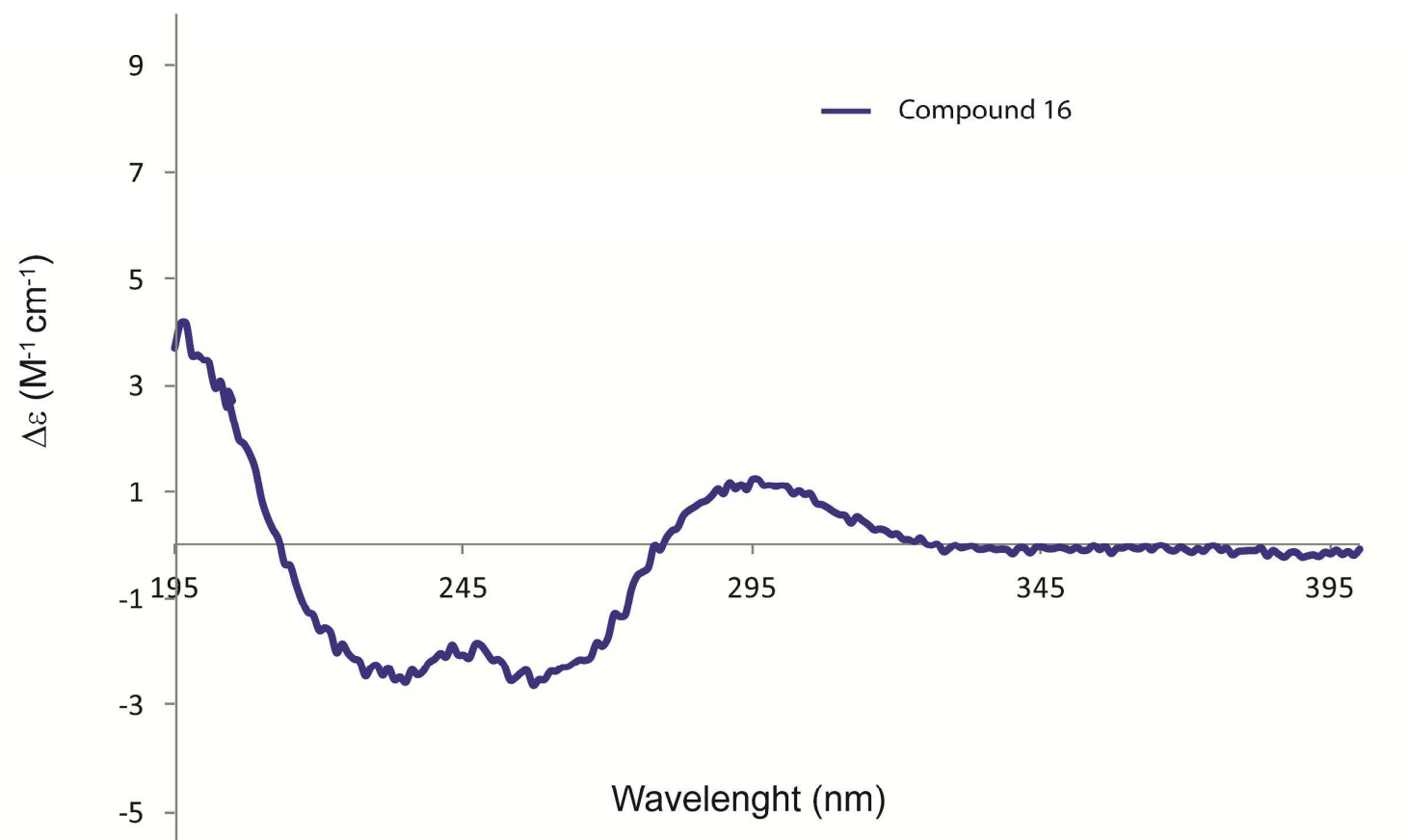


Figure S36. ECD spectra of compound **16** in MeOH.