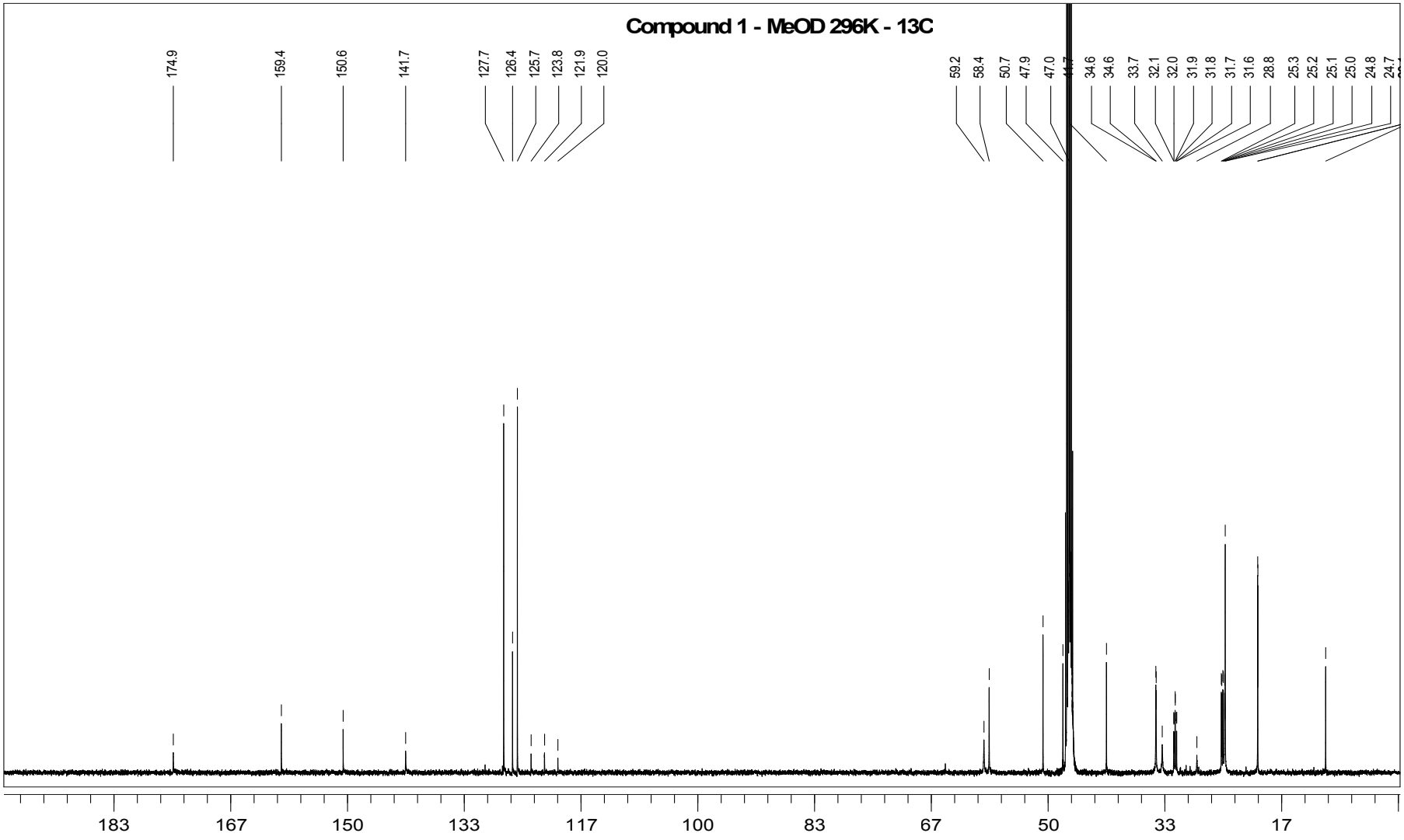
Electronic Supplementary Material (ESI) for MedChemComm.

Diazabicyclo Analogues of Maraviroc: Synthesis, Modeling, NMR Studies and Antiviral Activity

Laura Legnani, Diego Colombo, Lucia Lopalco, Assunta Venuti, Claudia Pastori, Lucio Toma, Matteo Mori, Giovanni Grazioso and Stefania Villa

SUPPLEMENTARY MATERIAL (A)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28.8
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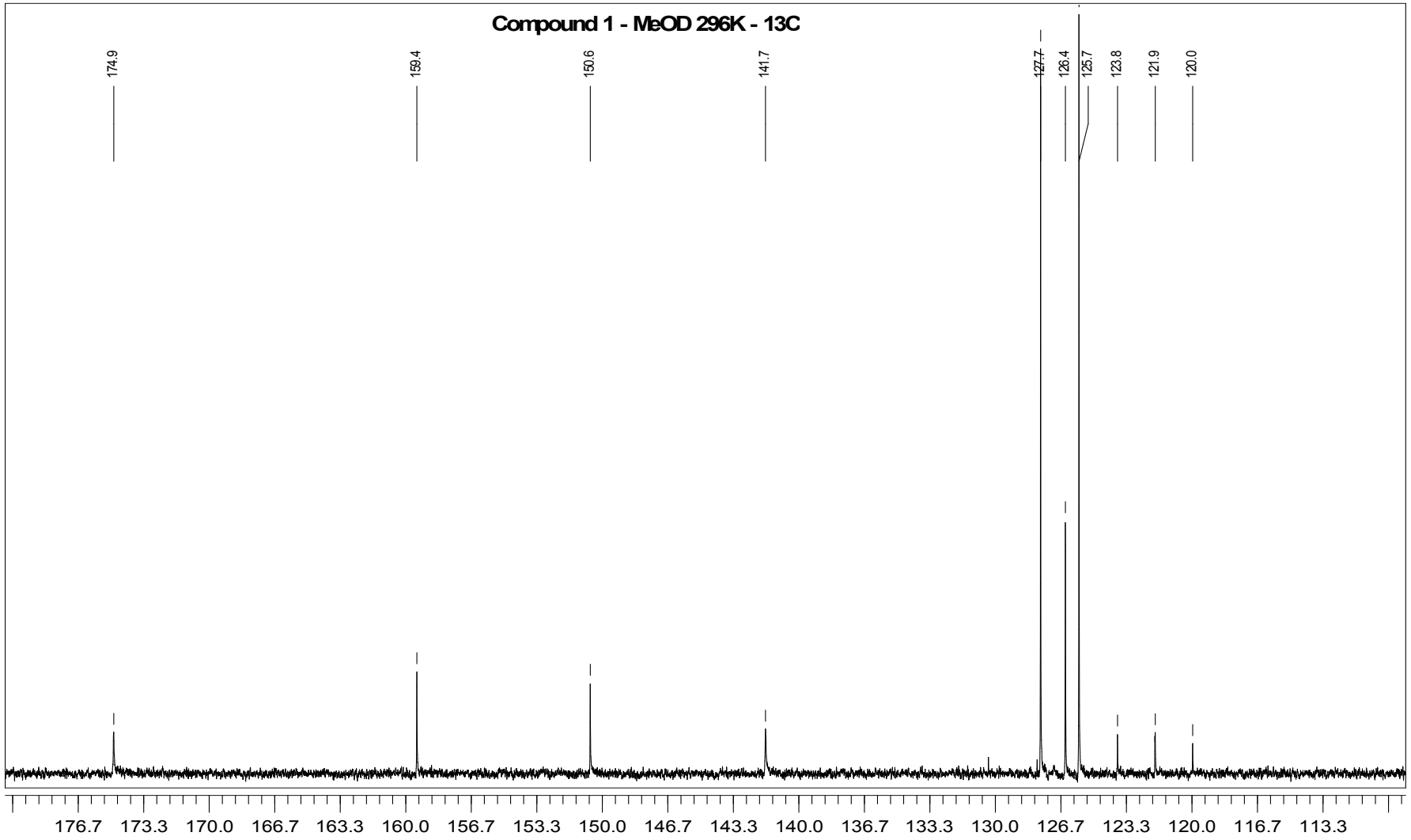
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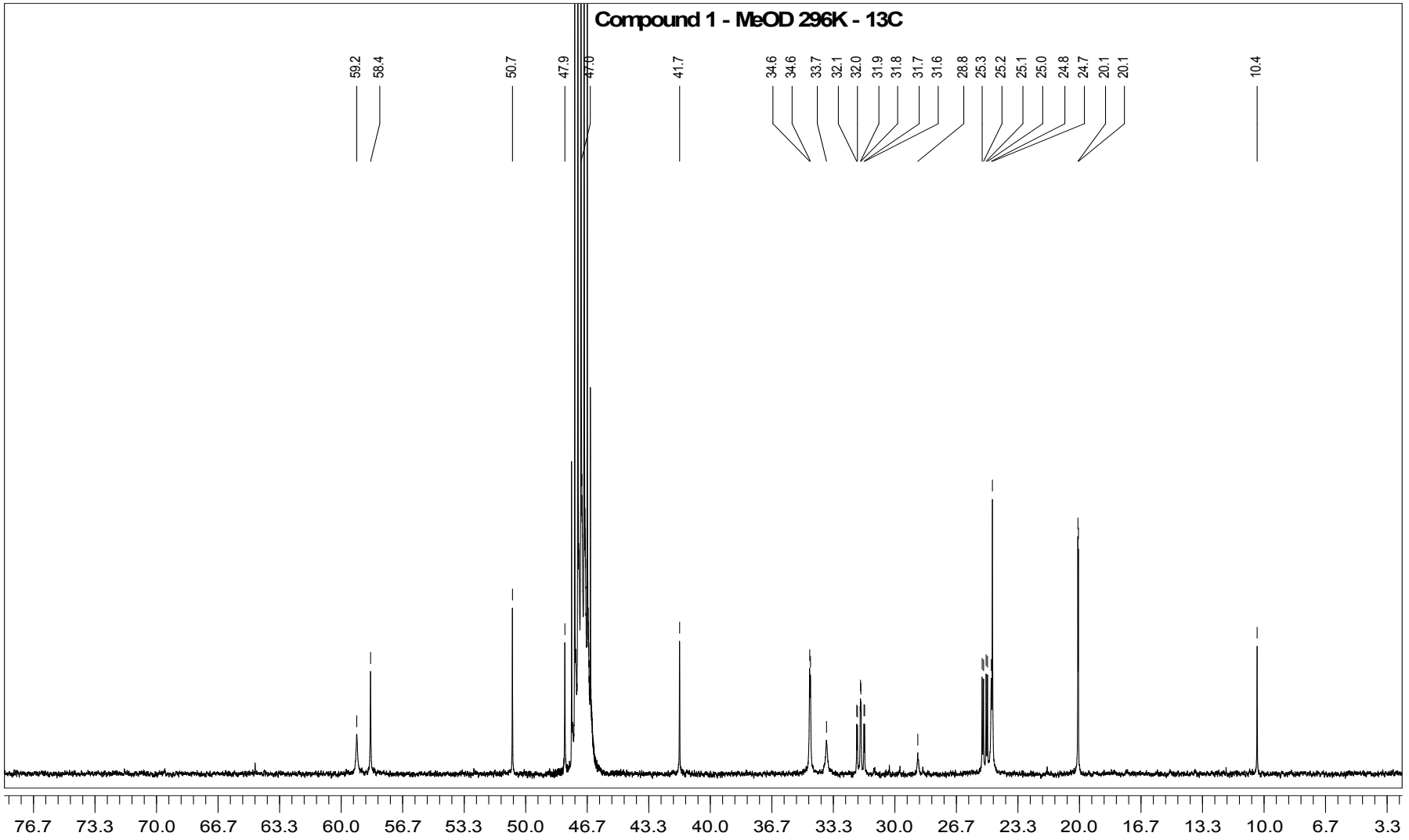
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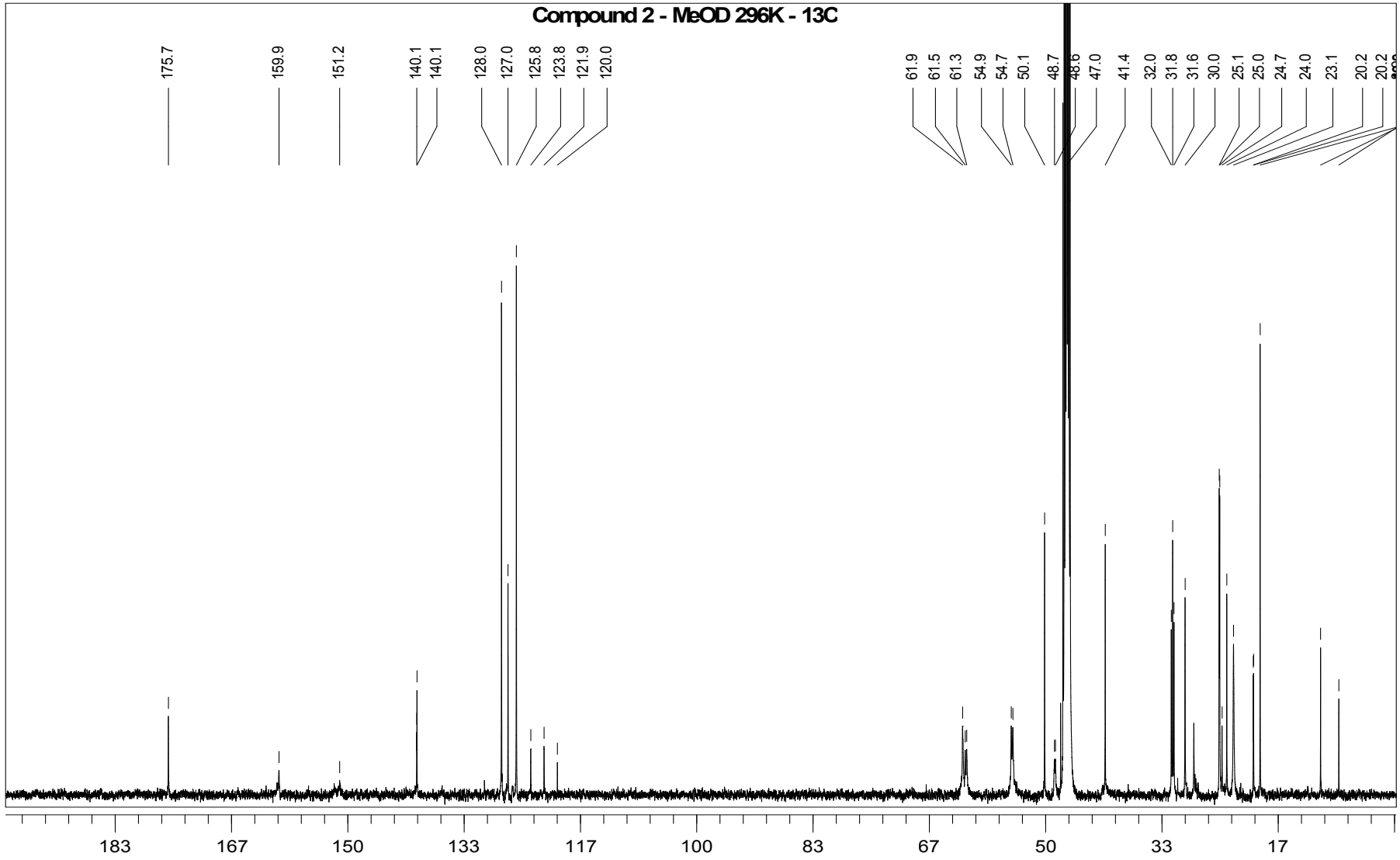
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48.7
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32.0
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25.1
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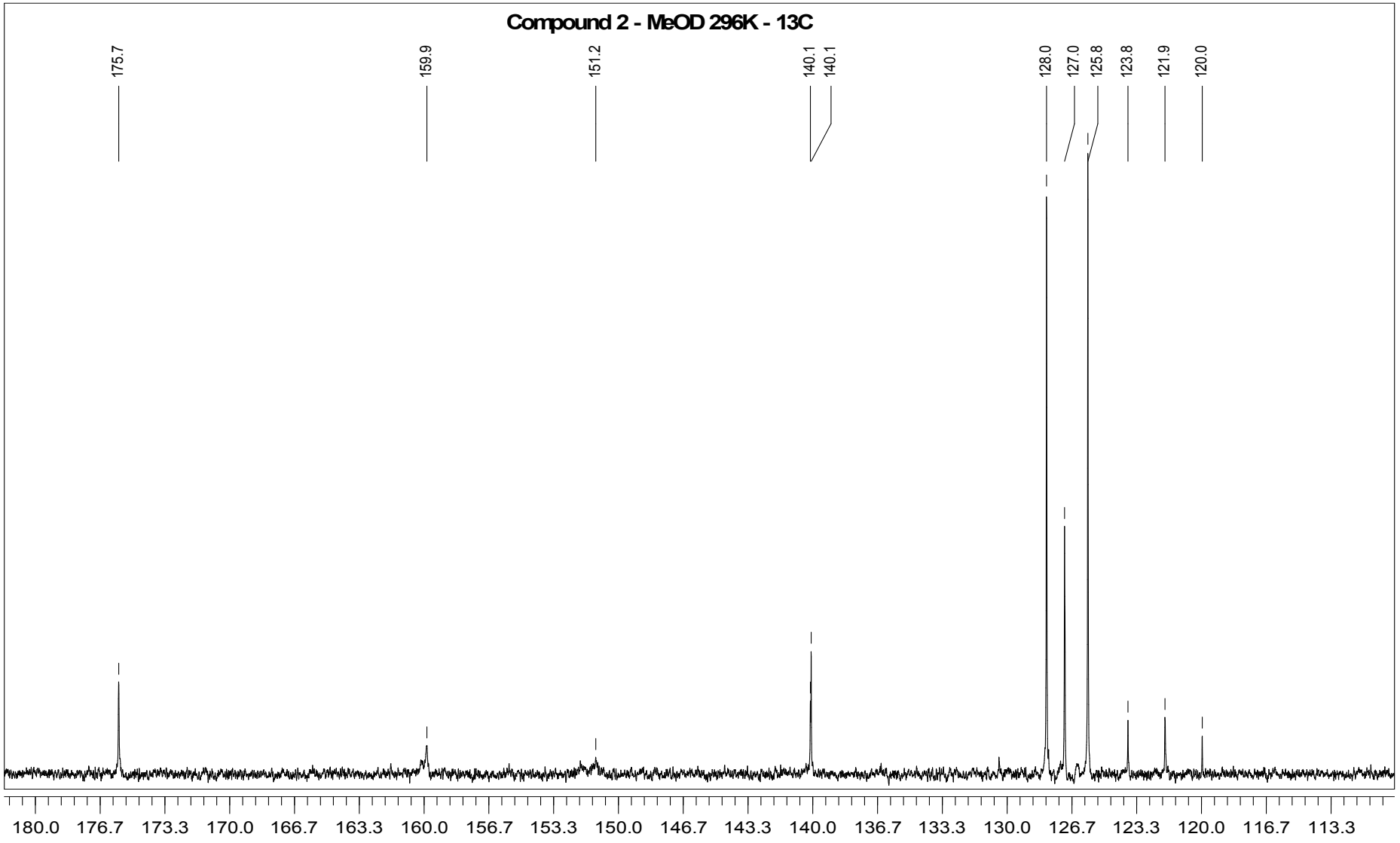
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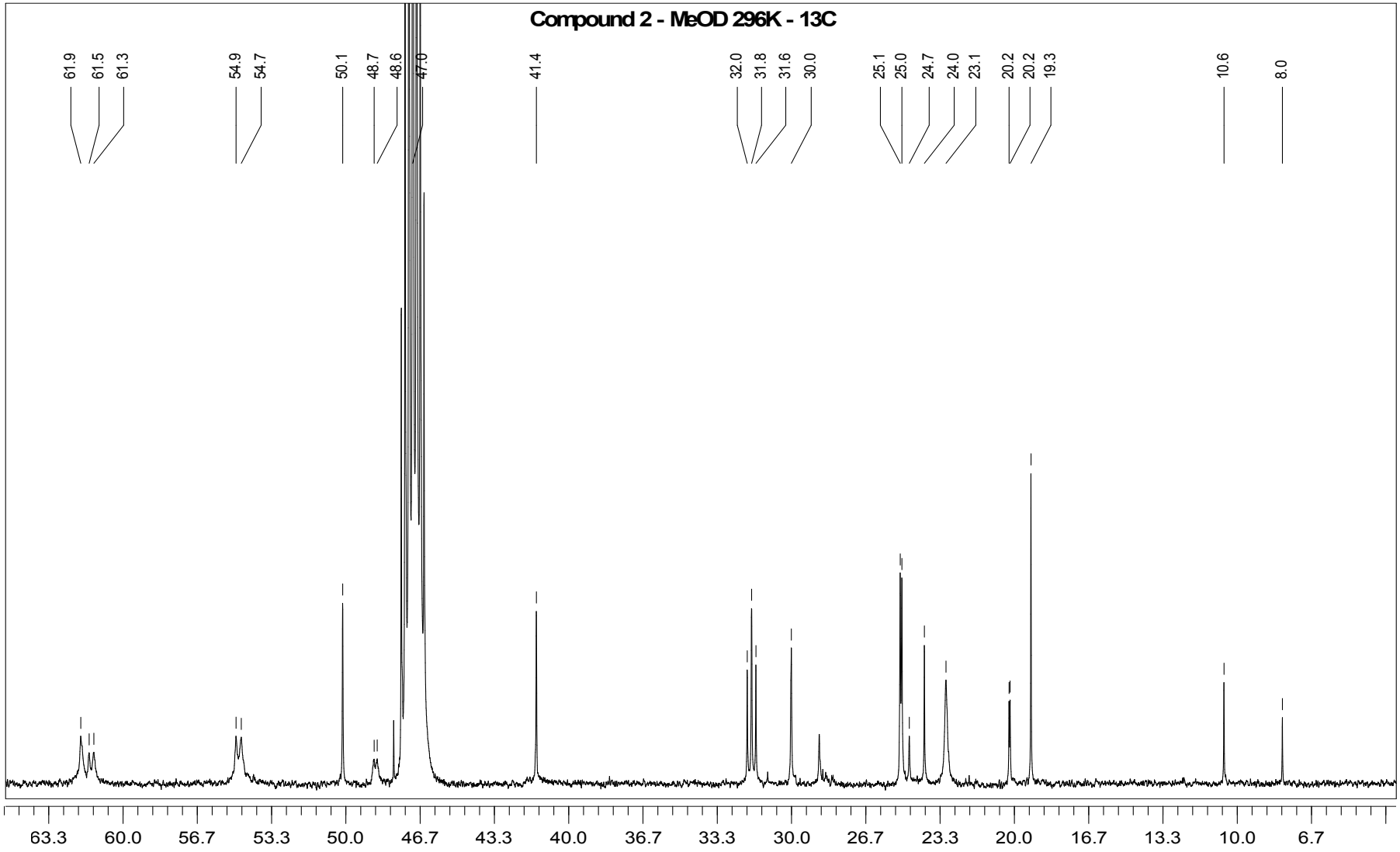
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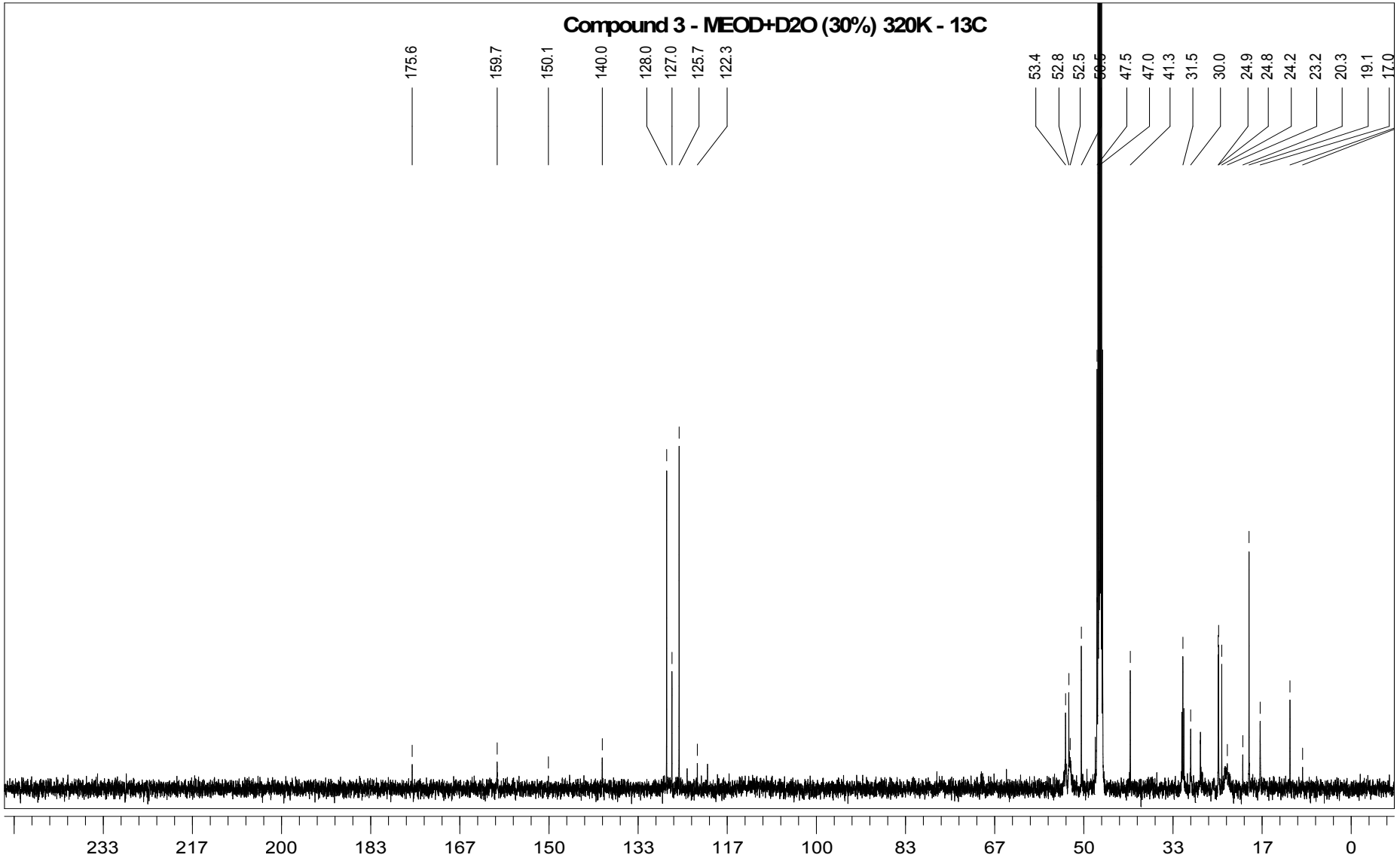
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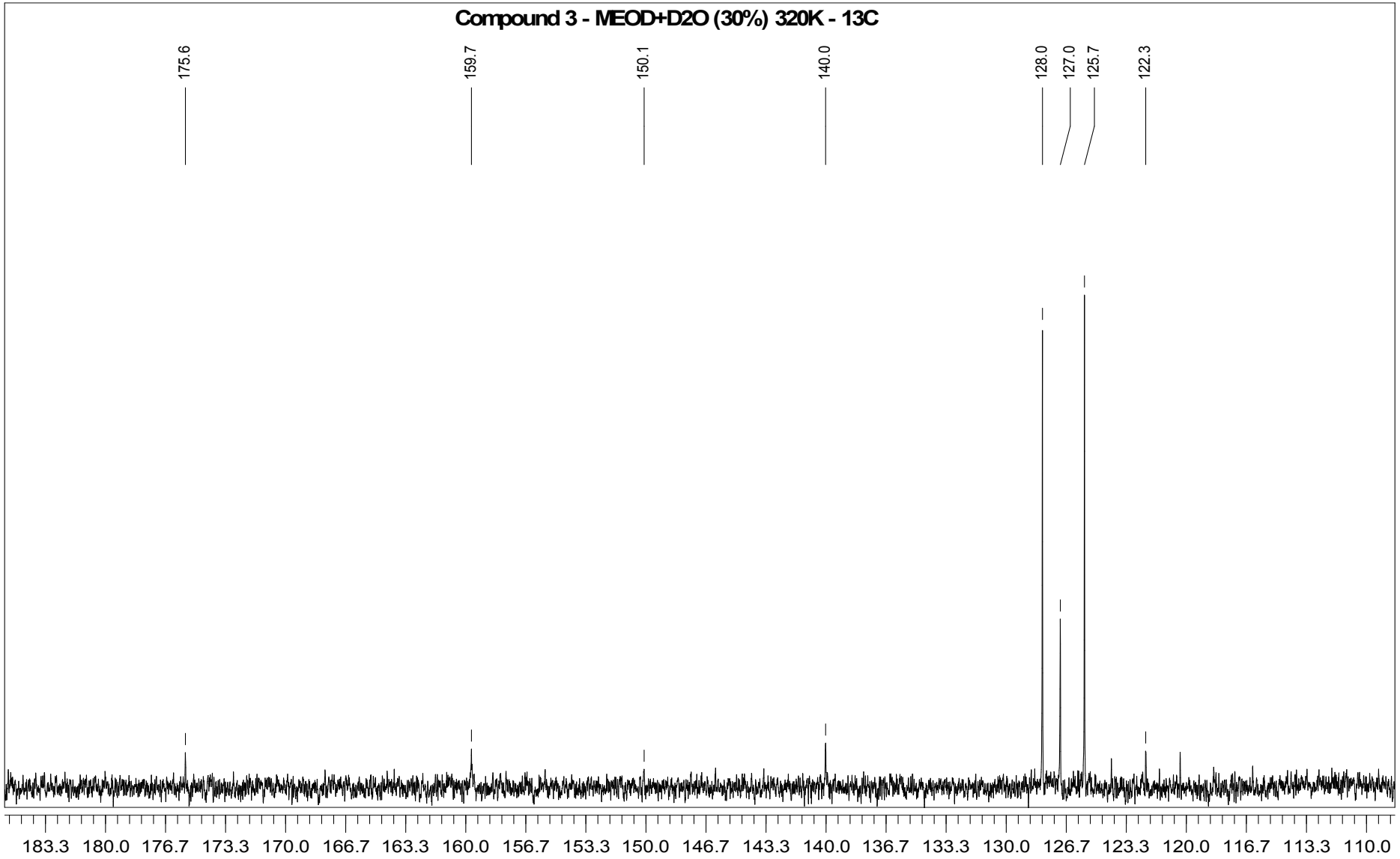
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140.0
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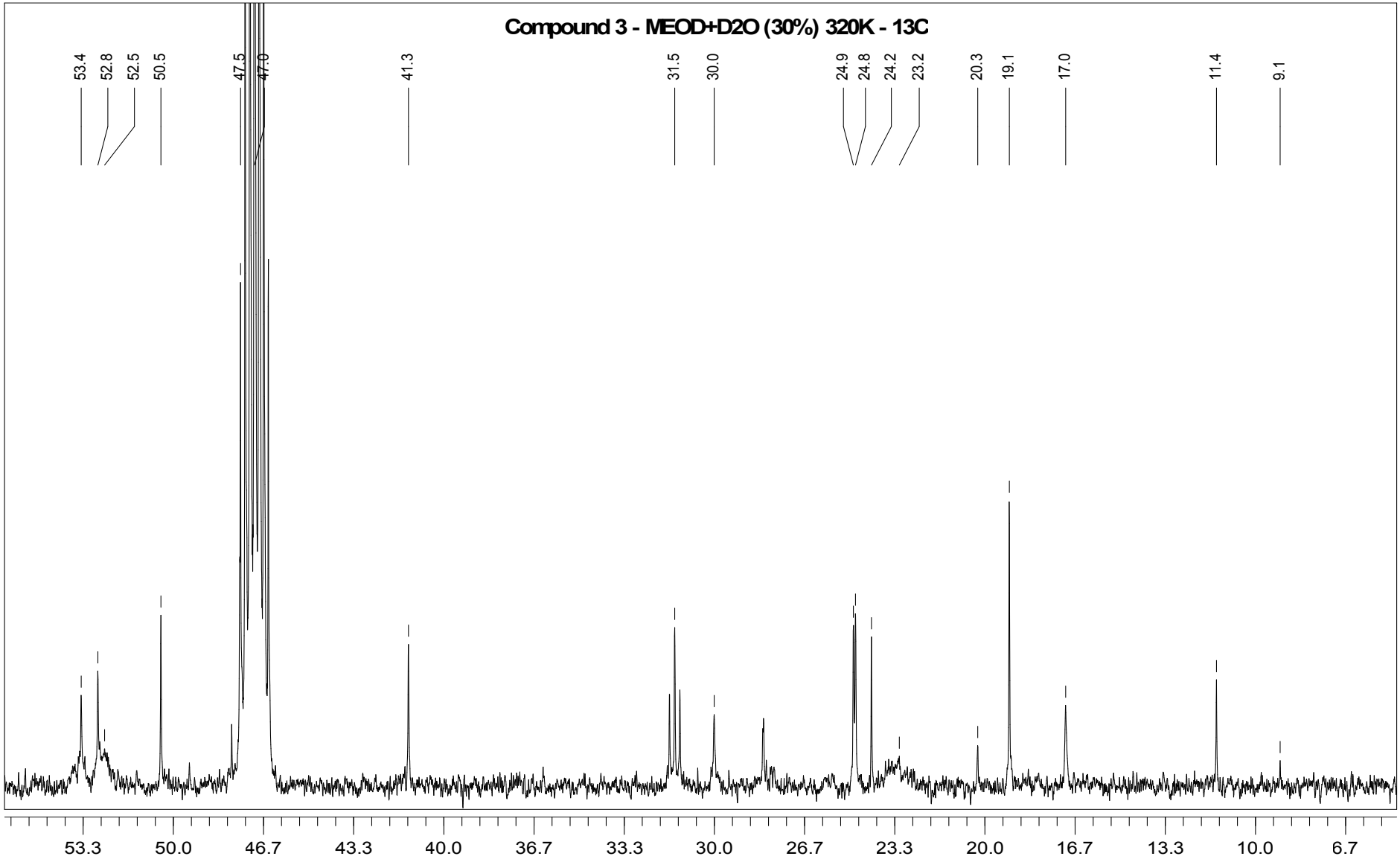
125.7
122.3
183.3 180.0 176.7 173.3 170.0 166.7 163.3 160.0 156.7 153.3 150.0 146.7 143.3 140.0 136.7 133.3 130.0 126.7 123.3 120.0 116.7 113.3 110.0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24.8
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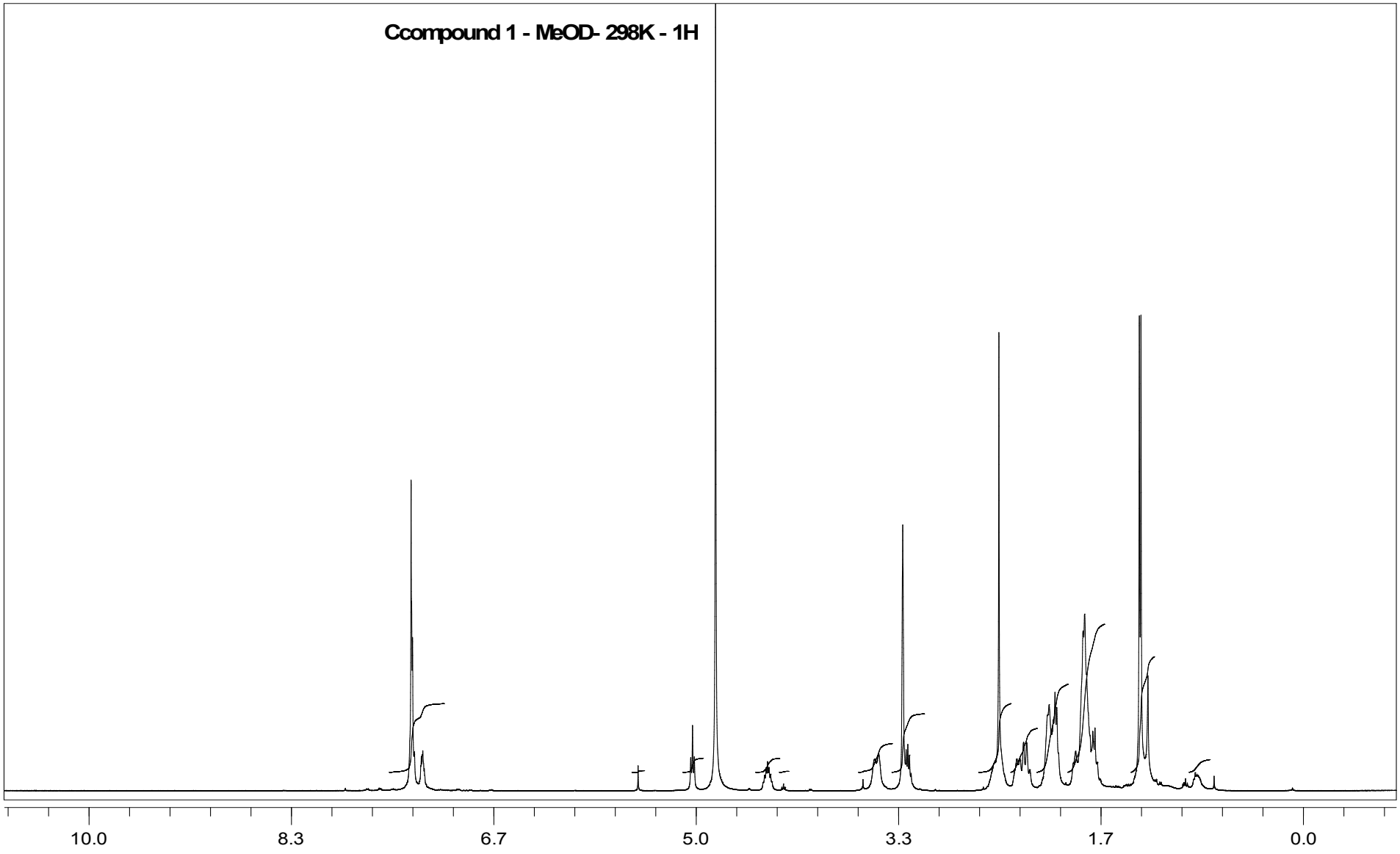
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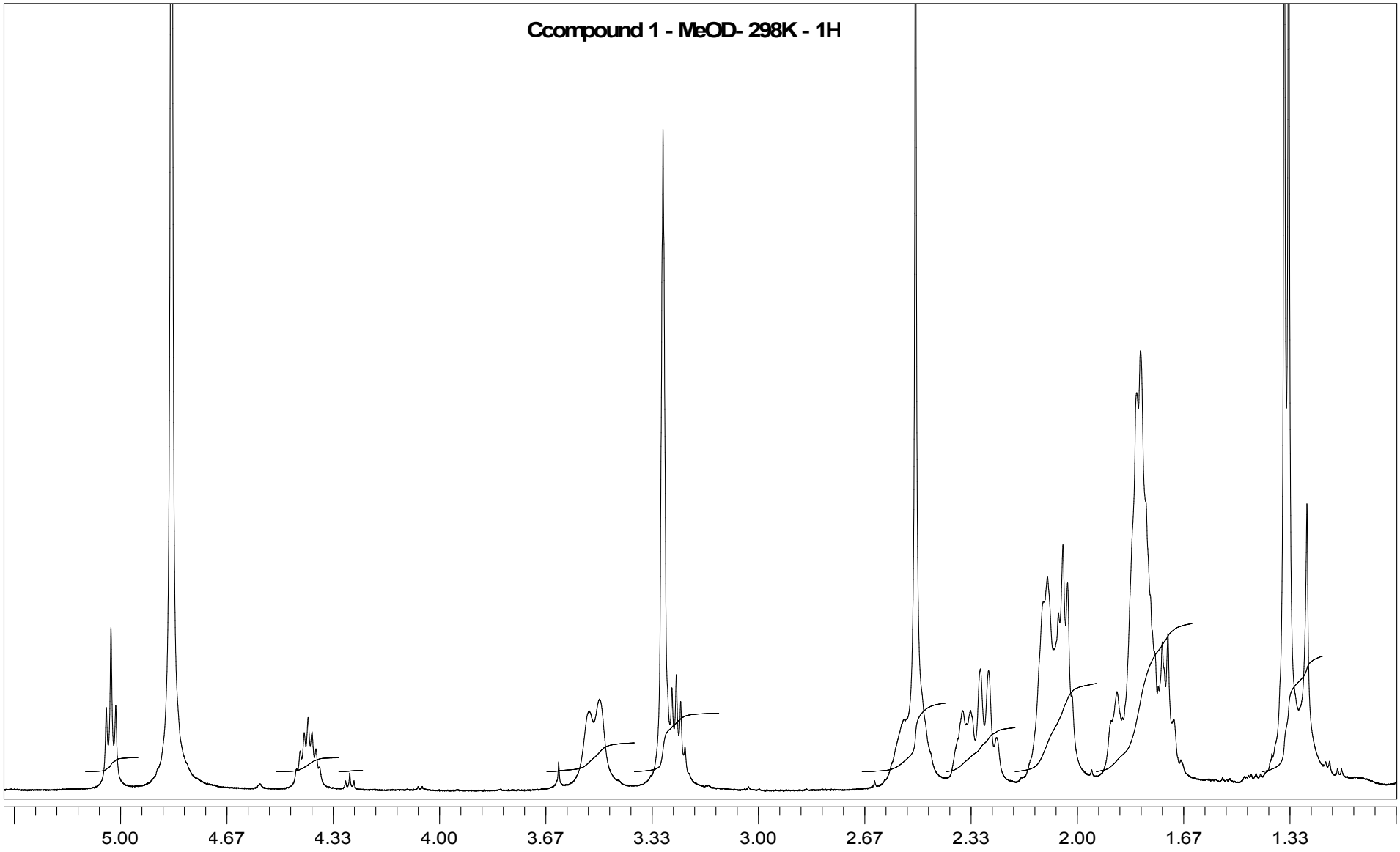
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4.00
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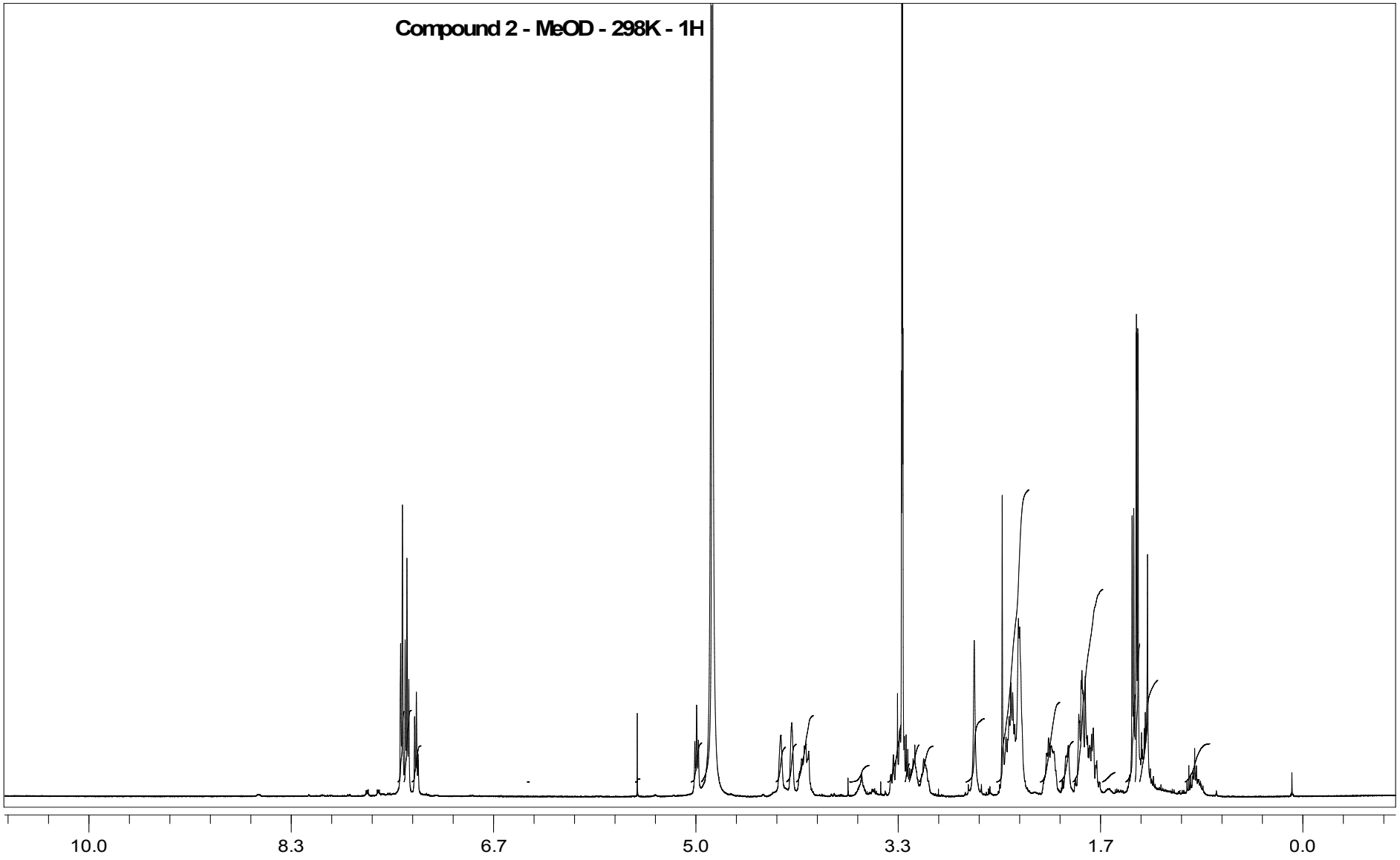
3.33
3.00
2.67
2.33
2.00
1.67
1.33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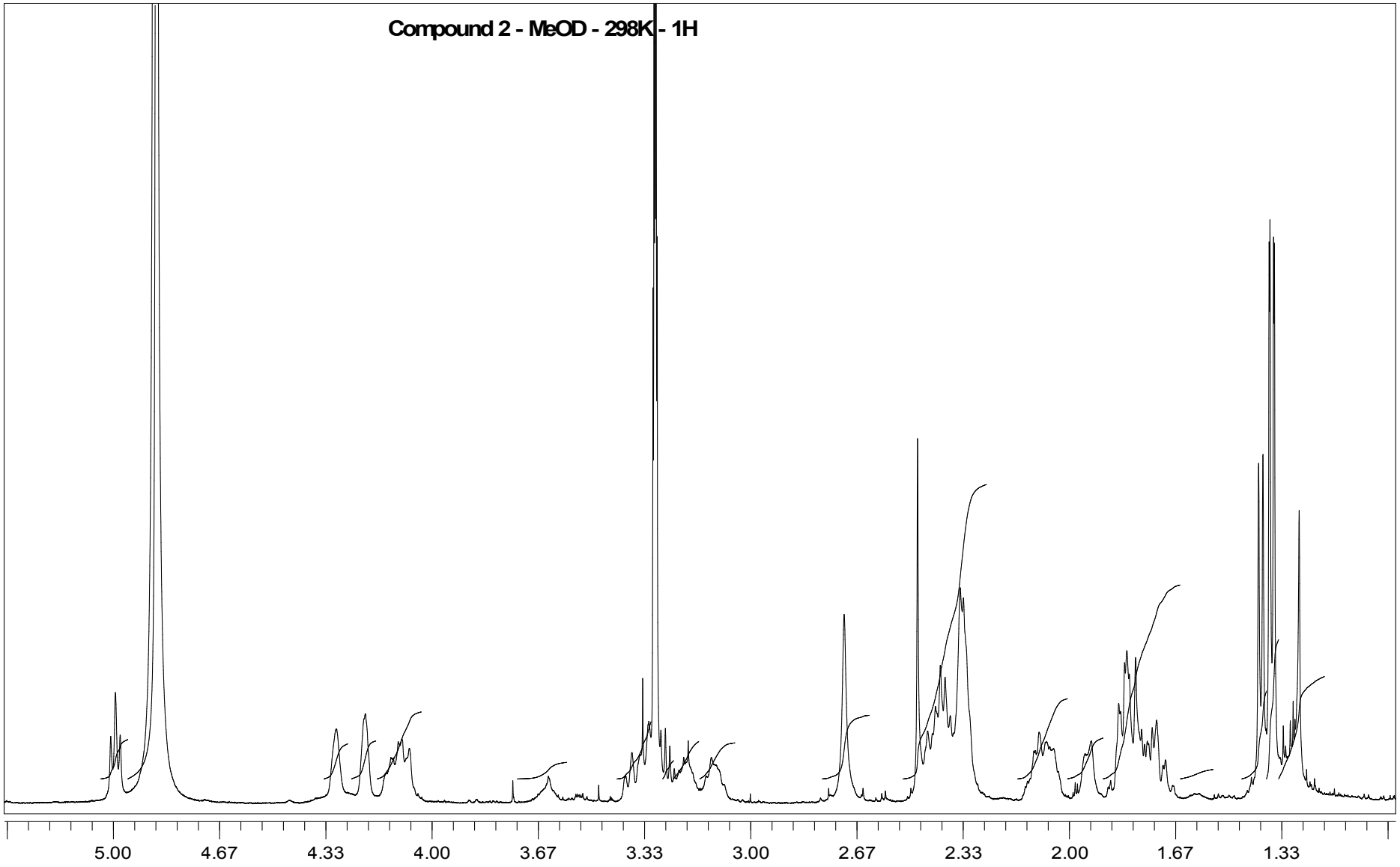
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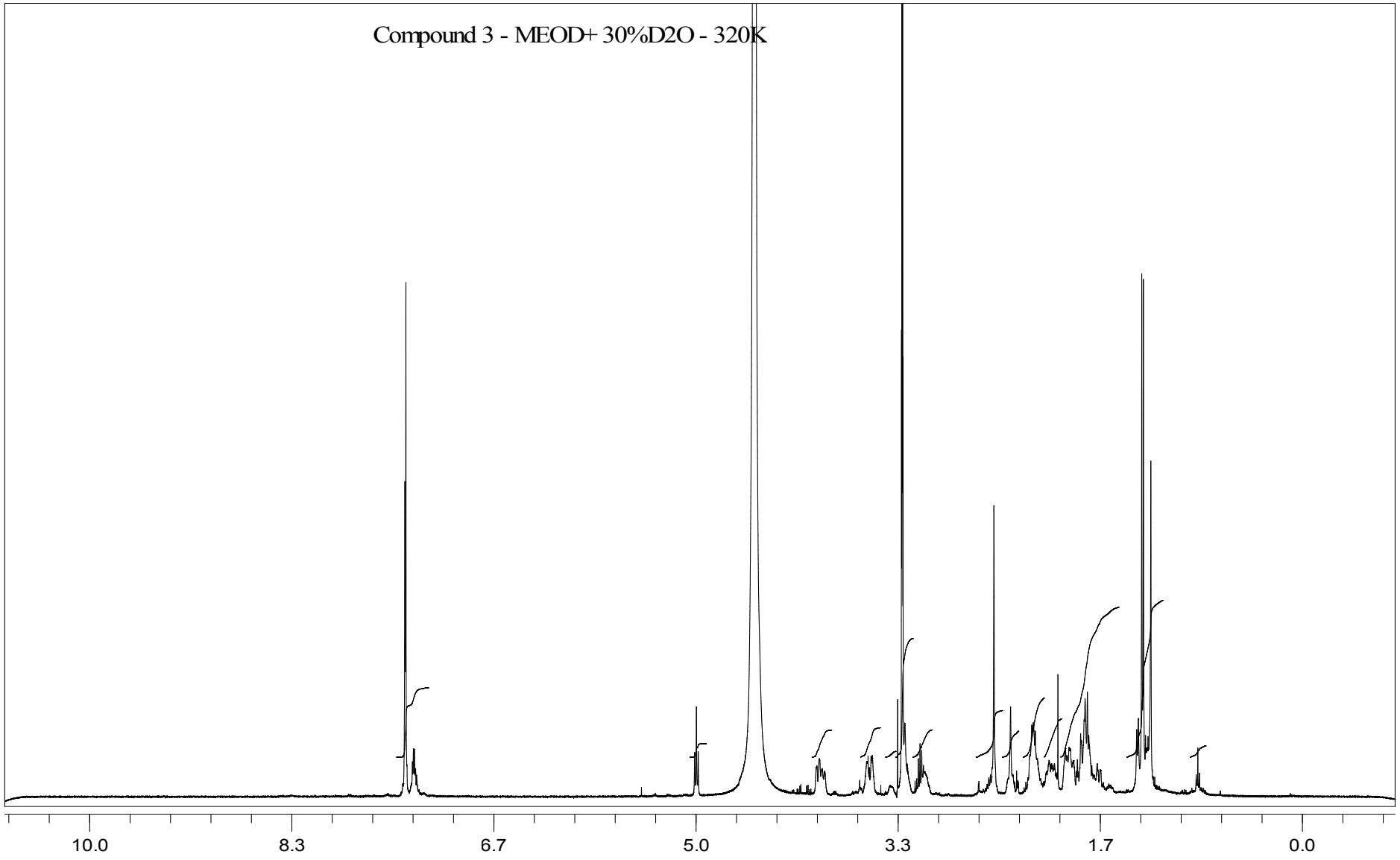
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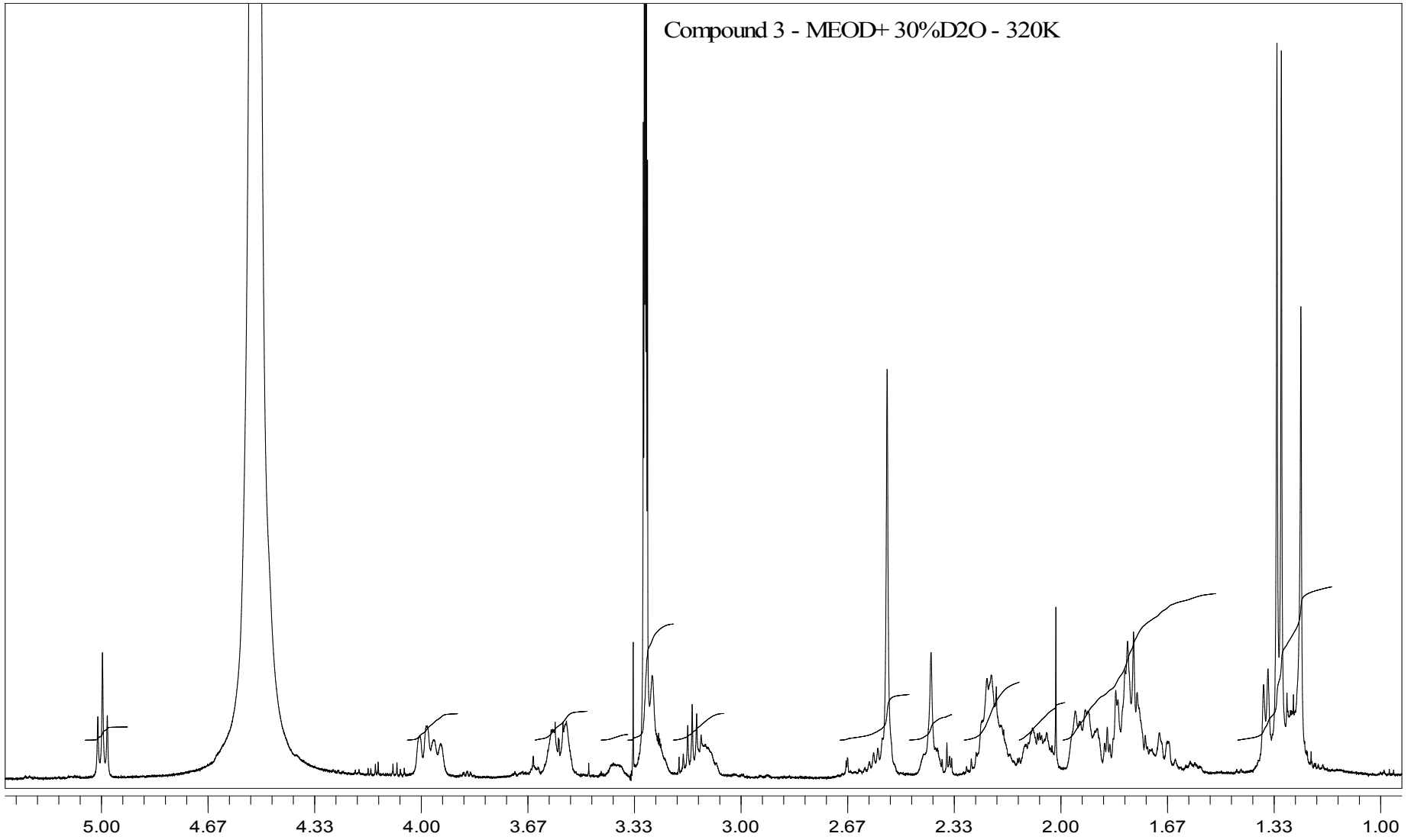
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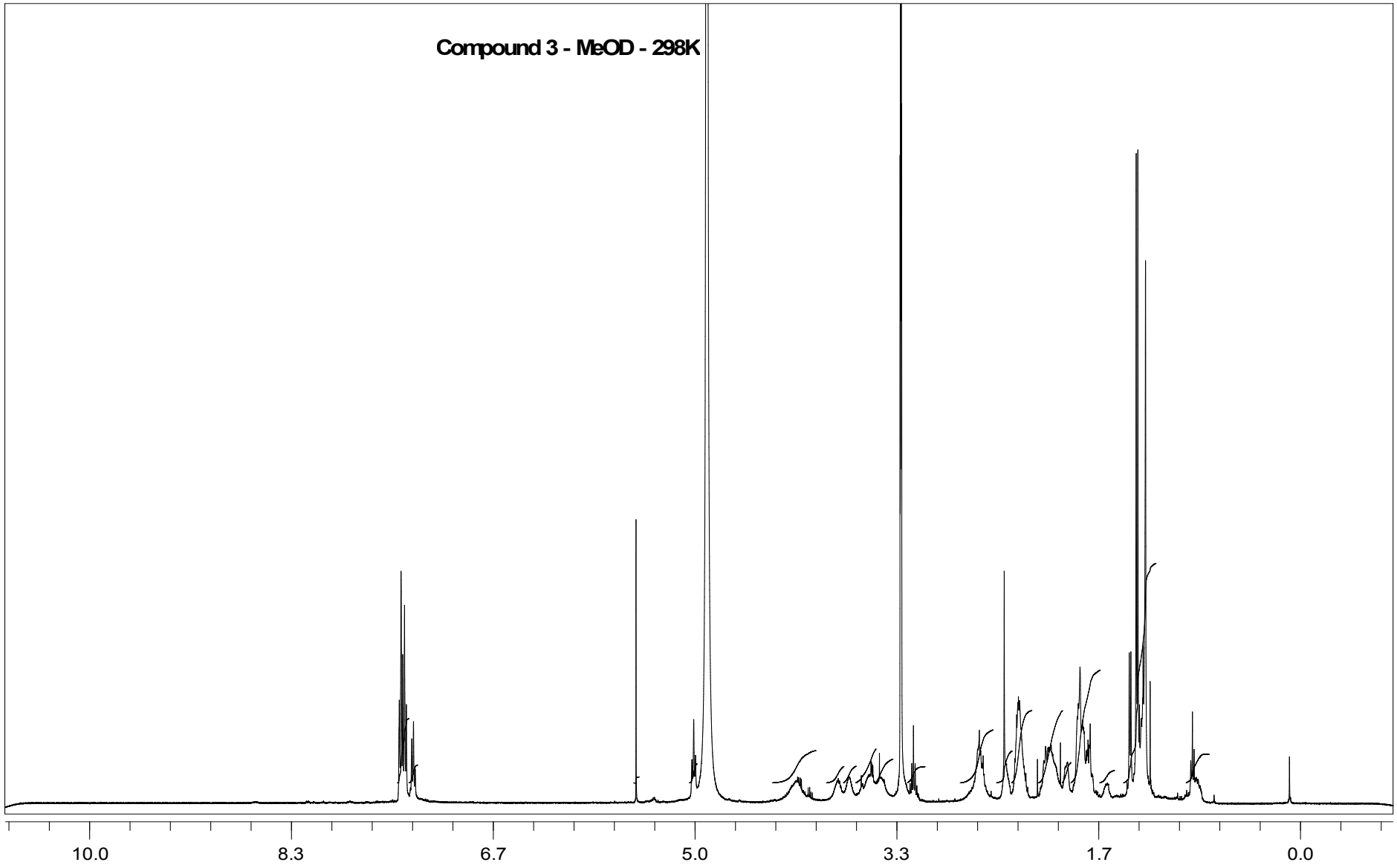
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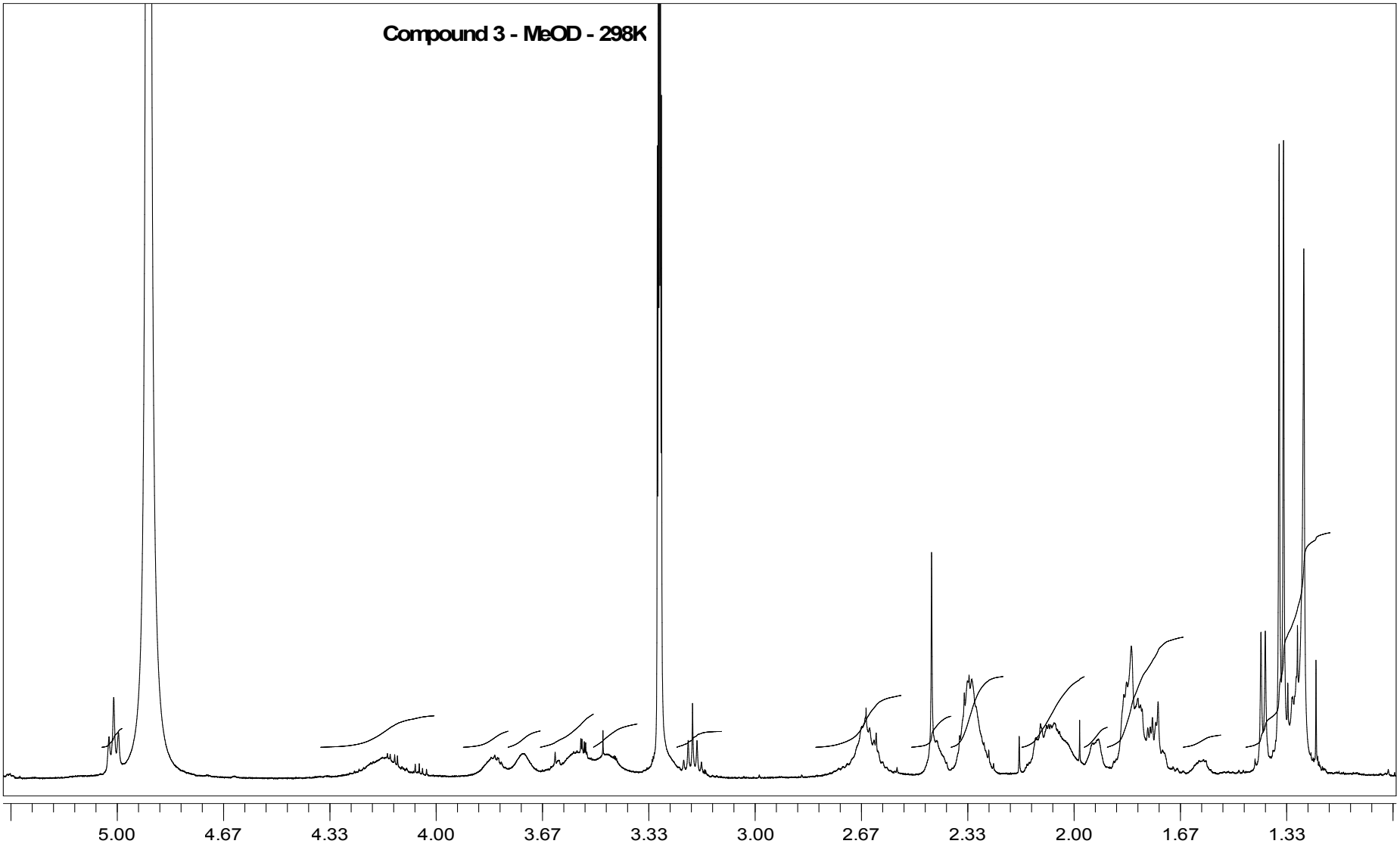
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3.67
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2.00
1.67
1.33

Assignments of the axial and equatorial protons of 1-3

Equatorial H-2/H-4 of compound 1 were given at 1.81 ppm due to their NOESY cross peaks with H-3 (4.41 ppm); consequently the axial H-2/H-4 were assigned at 2.29 ppm. Similar correlations were observed between equatorial H-2/H-4 at 3.32 and 3.35 ppm and H-6/H-7 at 2.34 of compound 2 and between equatorial H-2/H-4 at 3.29 and equatorial H-6/H-8 at 1.95 ppm of compound 3.

Table S1. Relative energies (kcal/mol), equilibrium percentages at 298 K, and significant torsional angles[a] (°) of significantly populated conformers (P_i > 1%) of compound **1**.

	E_{rel} (kcal/mol)	P_i(%)	τ_1 (°)[a]	τ_2 (°)[b]	τ_3 (°)[c]	τ_4 (°)[d]	τ_5 (°)[e]	τ_6 (°)[e]	τ_7 (°)[g]	τ_8 (°)[h]
1A	0.00	39.3	-4	-164	67	165	-60	-168	-112	41
1B	0.12	32.3	-4	-165	67	165	-60	-168	-125	-41
1C	0.92	8.4	-3	-164	68	168	-60	-167	64	2
1D	1.13	5.8	-2	-162	77	105	-63	-65	63	7
1E	1.38	3.8	-1	-162	77	103	-64	-65	-112	41
1F	1.52	3.0	-2	-162	77	103	-64	-66	-127	-41
1G	1.67	2.3	37	-162	67	174	-61	-76	-123	-41
1H	1.81	1.8	24	-162	67	173	-61	-76	-108	40

[a] τ_1: H-C1”-C1’’a-N; τ_2: C1’’a-N-C8c-C1’; τ_3: C1’-C8c-C8b-C8a; τ_4: C8c-C8b-C8a-N8; τ_5: N-C8c-C1’- C2’; τ_6: C8b-C8a-N8-C5; τ_7: C4-C3-N1’’’-C5’’’ ; τ_8: N1’’’-C5’’’-C5’’’a-H.

Figure S1. 3D-plots of conformers **C-H** of compound **1**.

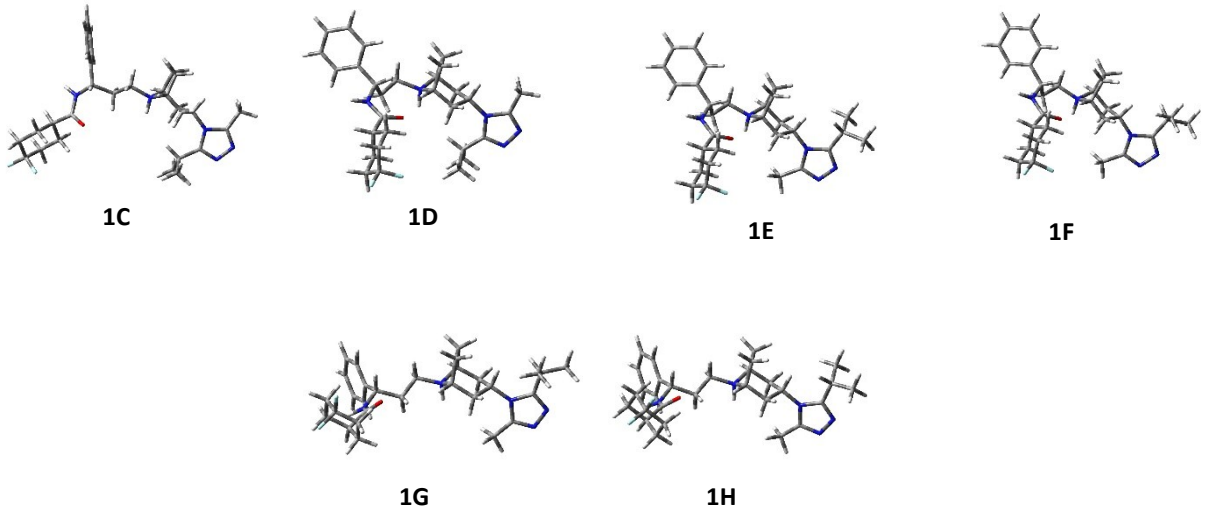
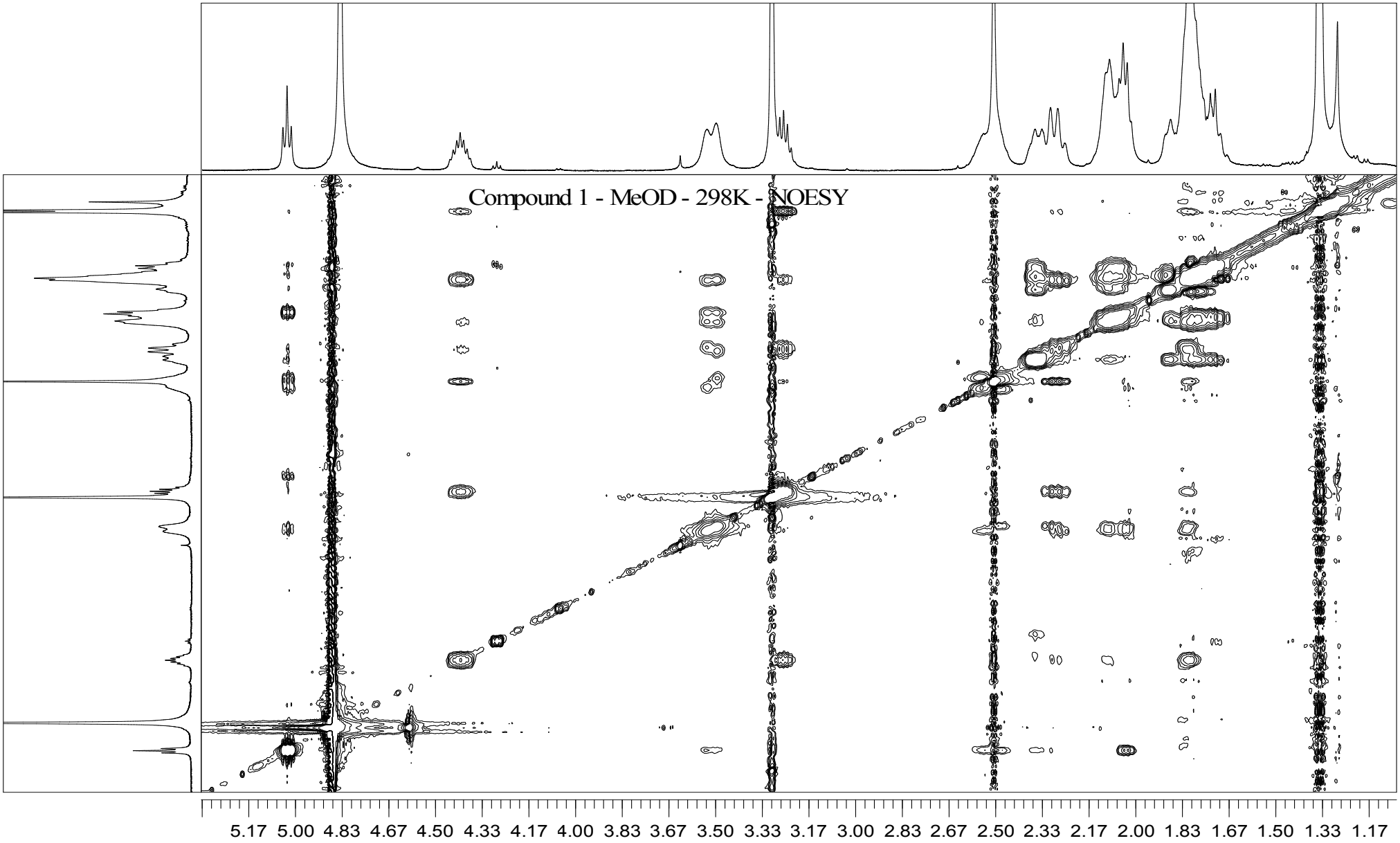


Table S2. Relative energies (kcal/mol), equilibrium percentages at 298 K, and torsional angles[a] (°) of significantly populated conformers (P_i > 1%) of compounds **2** and **3**.

	E_{rel} (kcal/mol)	P_i(%)	τ_1 (°)[a]	τ_2 (°)[b]	τ_3 (°)[c]	τ_4 (°)[d]	τ_5 (°)[e]	τ_6 (°)[f]	τ_7 (°)[g]	τ_8 (°)[h]
2A	0.37	21.1	7	-163	66	169	-60	-169	-111	29
2B	0.20	28.0	7	-163	67	168	-60	-169	-114	-31
2C	0.00	39.3	-2	-164	68	165	-60	-168	68	11
2D	1.47	3.3	-2	-162	77	103	-63	-66	68	9
2E	1.79	1.9	-3	-162	78	102	-63	-67	-112	31
2F	1.68	2.3	0	-162	78	101	-63	-67	-115	-31
3A	0.88	7.0	7	-163	69	168	-60	-161	-110	37
3B	0.62	11.0	7	-163	65	165	-60	-166	-118	-36
3C	0.00	31.2	-1	-164	66	160	-61	-167	67	-11
3D	0.10	26.1	7	-163	67	175	-60	-71	67	-3
3E	0.73	9.1	8	-163	67	178	-61	-69	-110	36
3F	0.76	8.7	9	-163	69	-179	-60	-67	-118	-36
3I	1.51	2.4	4	-163	66	174	-60	-167	67	8

[a] τ1: H-C1”-C1’’a-N; τ2: C1’’a-N-C8c-C1’ for **2**, C1’’a-N-C9c-C1’ for **3**; τ3: C1’-C8c-C8b-C8a for **2**, C1’-C9c-C9b-C9a for **3**; τ4: C8c-C8b-C8a-N8 for **2**, C9c-C9b-C9a-N9 for **3**; τ5: N-C8c-C1’- C2’ for **2**, τ5: N-C9c-C1’- C2’ for **3**; τ6: C8b-C8a-N8-C5 for **2**, C9b-C9a-N9-C5 for **3**; τ7: C4-C3-N1’’’-C5’’’; τ8: N1’’’-C5’’’-C5’’’a-H.


Compound 1 - MeOD - 298K - NOESY
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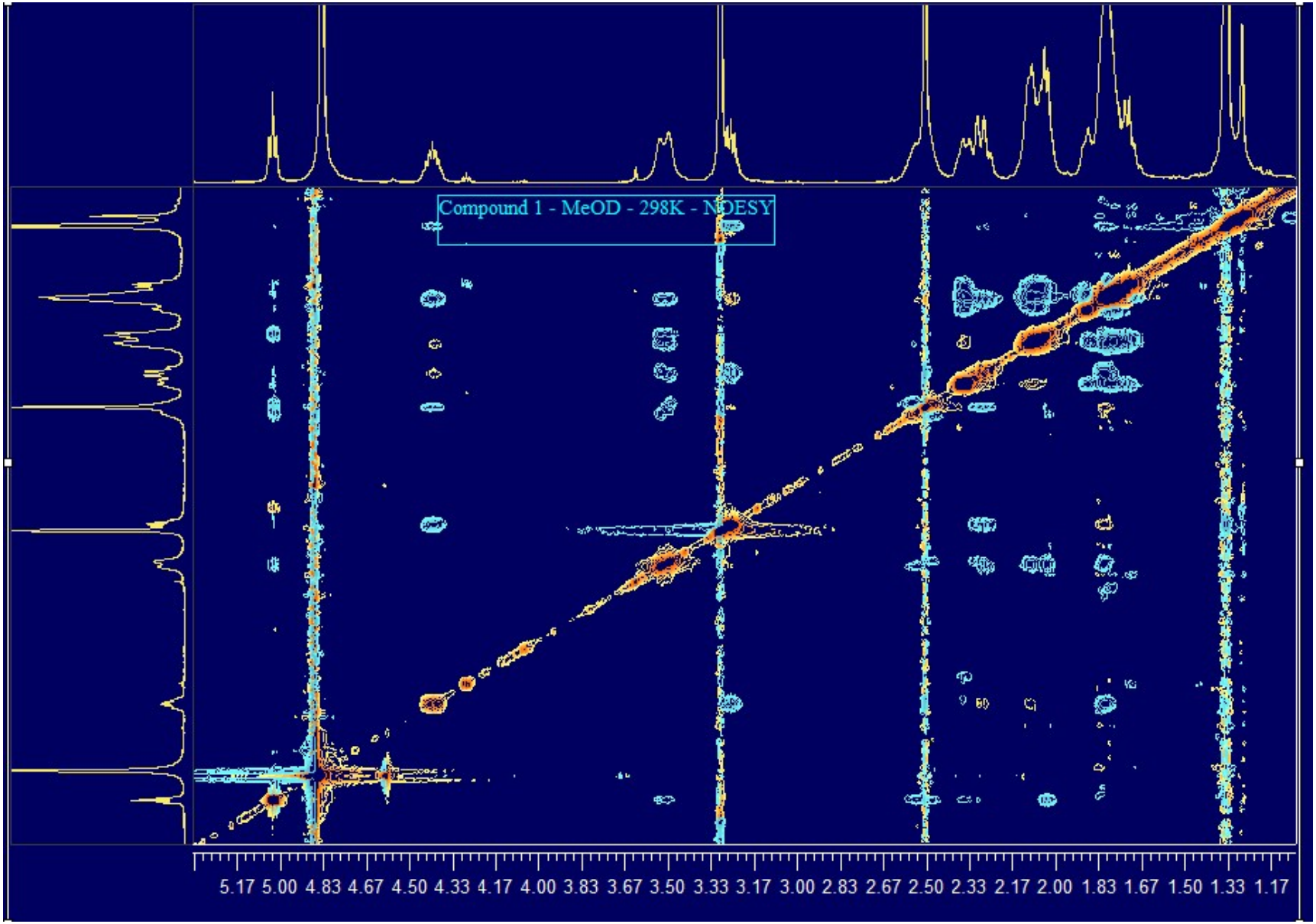
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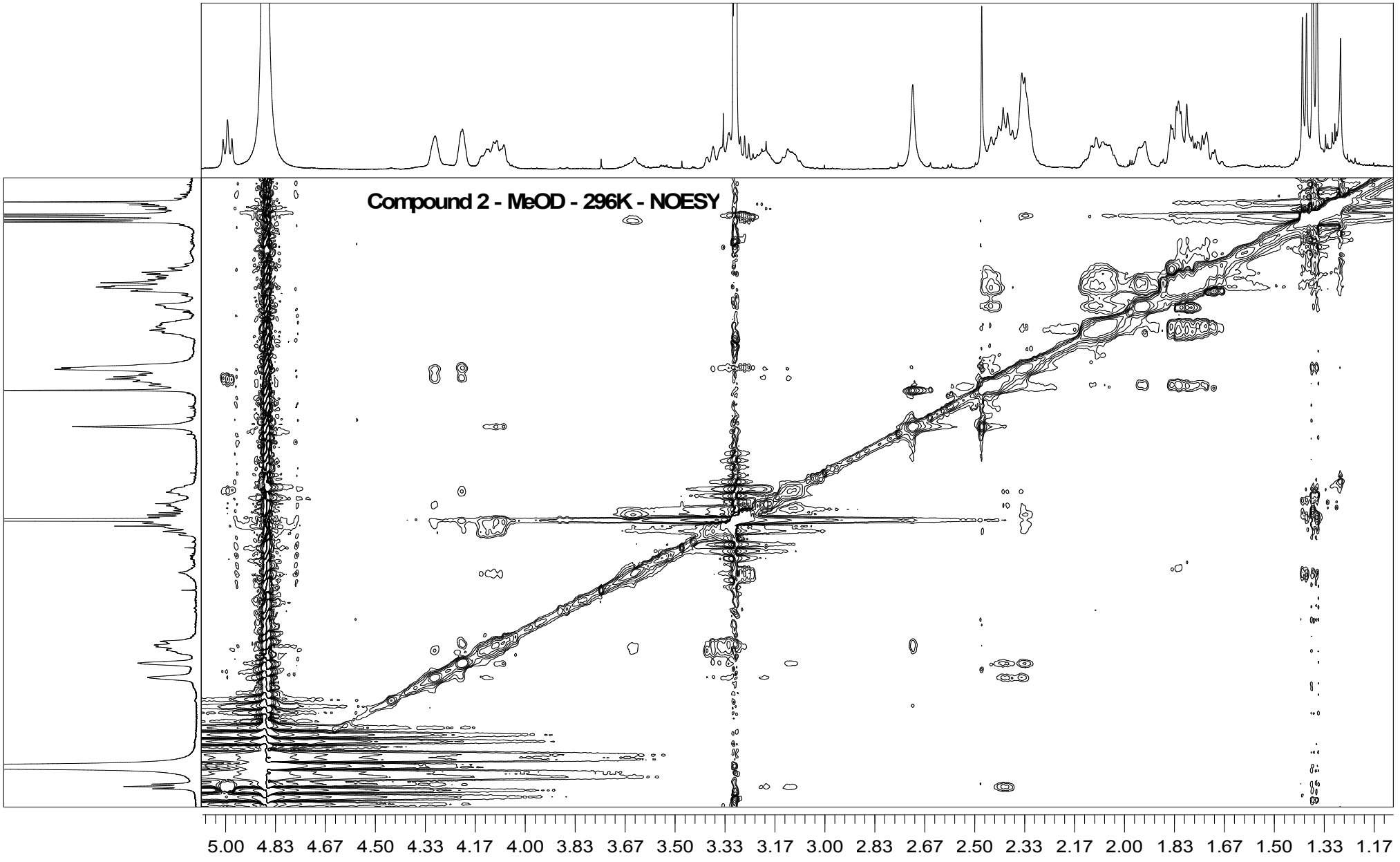
Compound 2 - MeOD - 296K - NOESY
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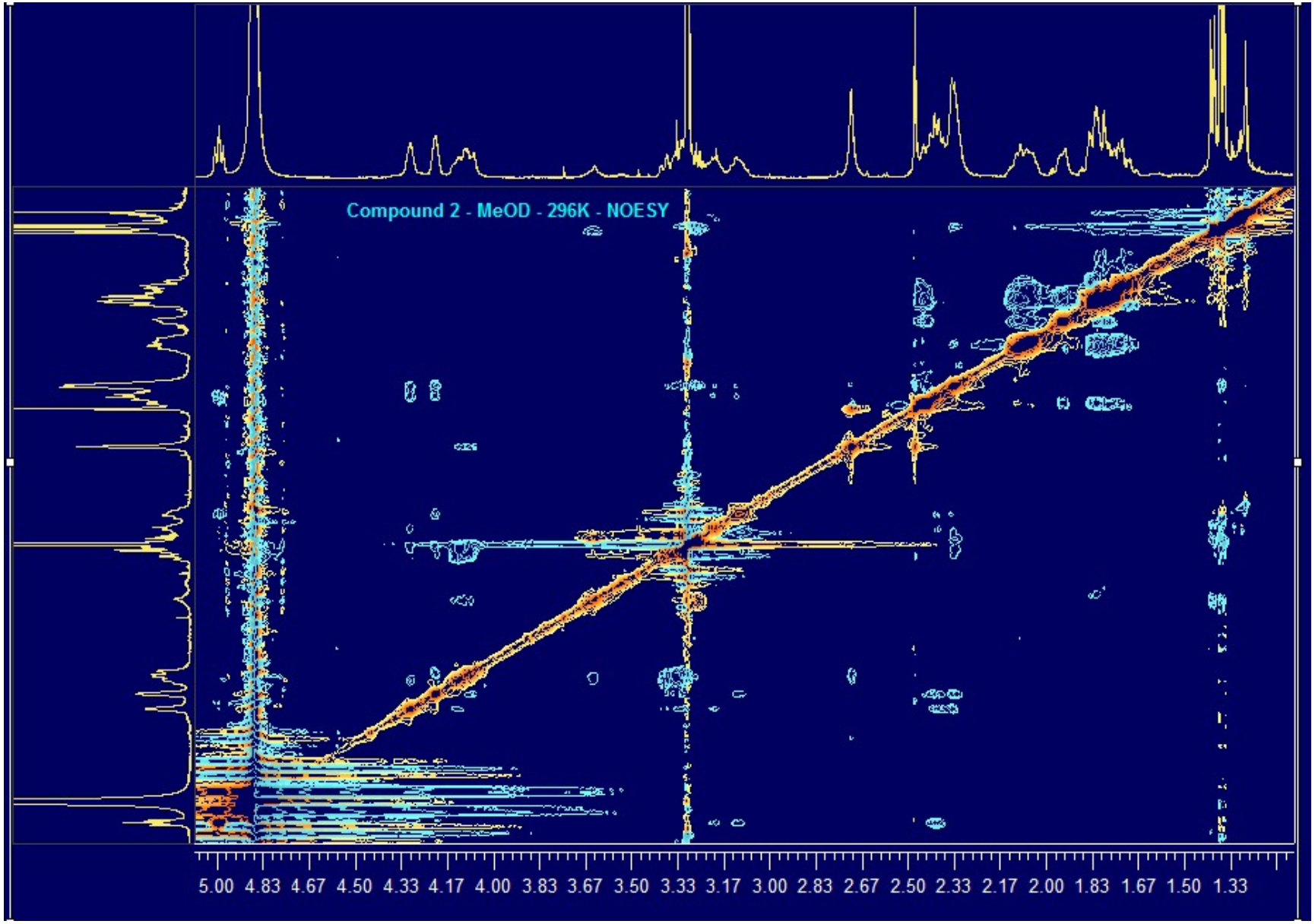
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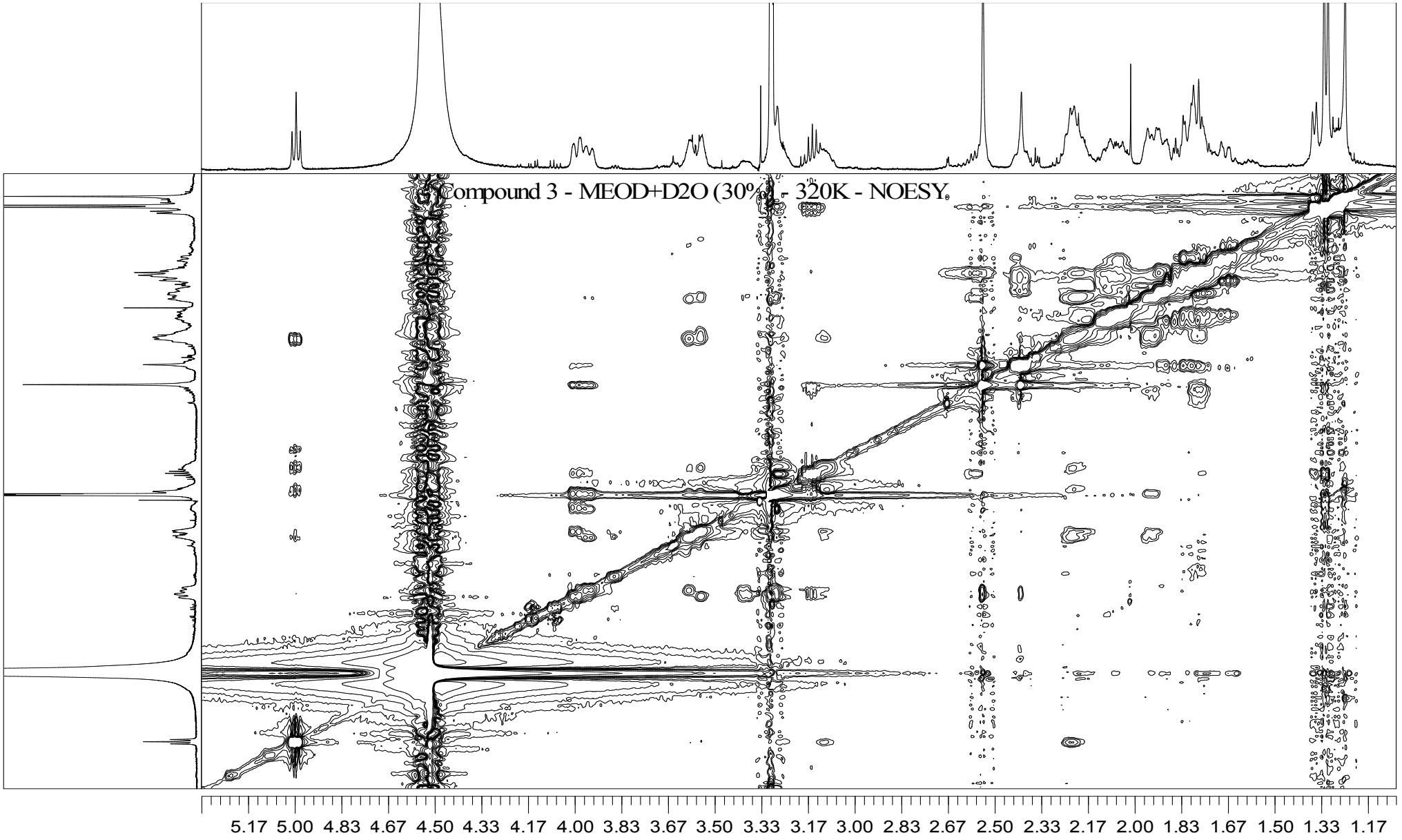
Compound 3 - MEOD+D2O (30%) - 320K - NOESY
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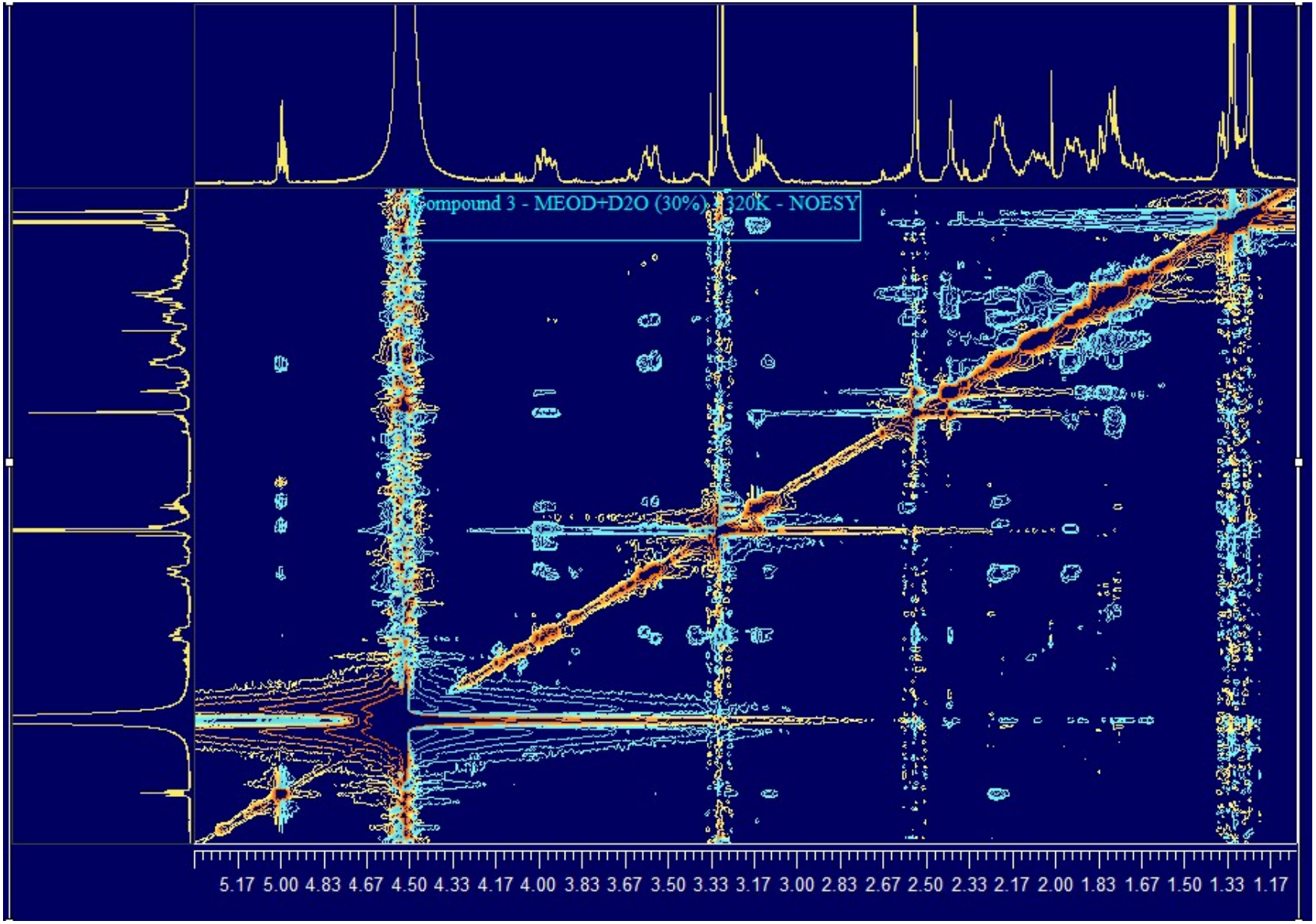
ompound 3 - MEOD+D2O (30%), 320K - NOESY
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^{1}H-NMR spectra of **2** recorded at increasing temperatures

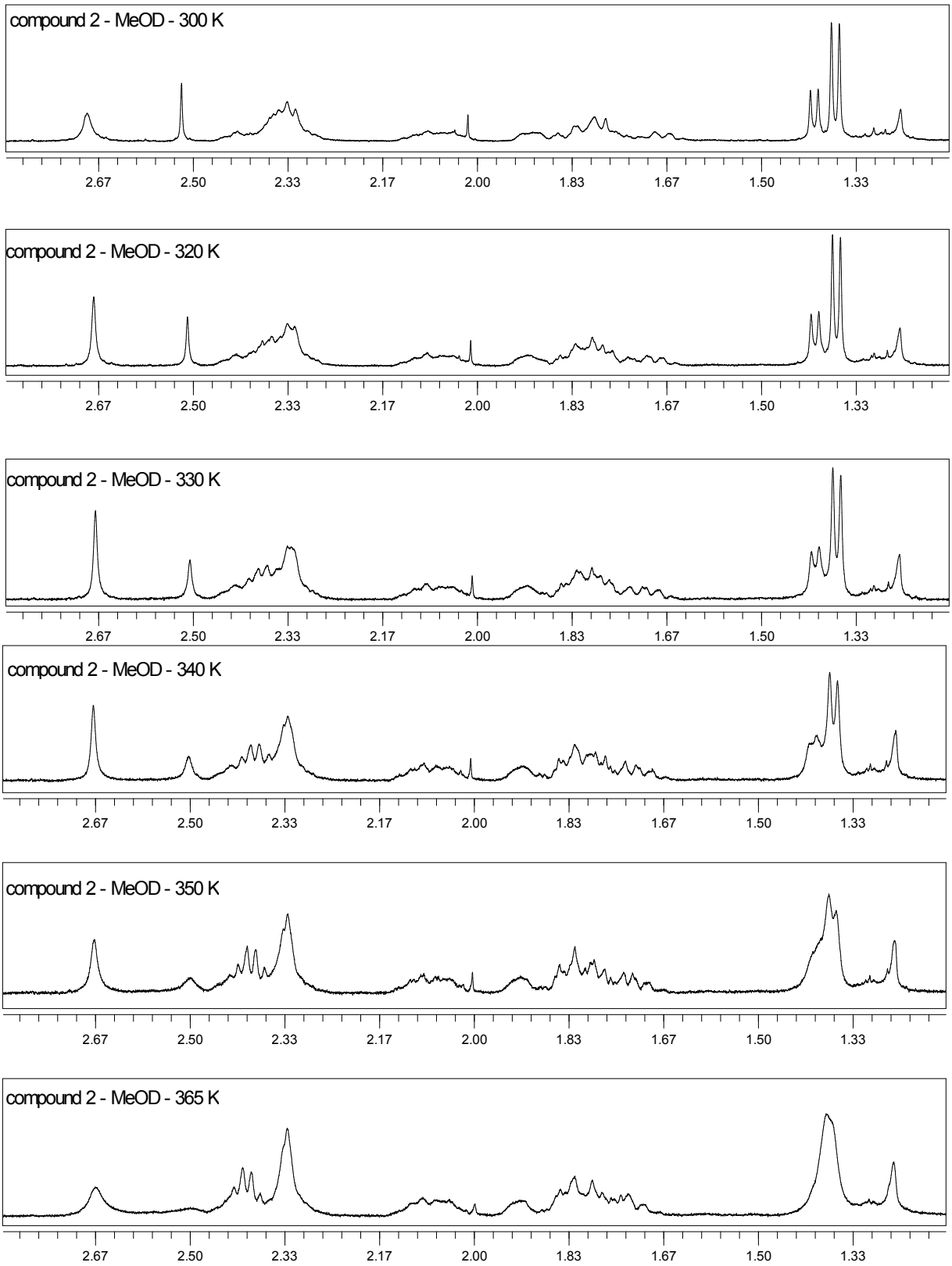

Table S3. ^{1}H NMR chemical shift (δ) of compounds **1**-**3**.

^{1}H position	δ(ppm)		
	(**1**) [a] Exp	(**2**) [a] Exp	(**3**) [b] Exp
1 (5)	3.50	4.30	3.59
2-ax (4-ax)	2.29	4.11	3.99
2-eq (4-eq)	1.81	3.32	3.29
3	4.41	-	-
4-ax (2-ax)	2.29	4.11	3.95
4-eq (2-eq)	1.81	3.35	3.29
5 (1)	3.53	4.21	3.55
6-ax	2.10	2.34	2.20
6-eq	2.10	2.34	1.95
7-ax	2.10	2.34	2.58
7-eq	2.10	2.34	1.79
8-ax	-	-	2.20
8-eq	-	-	1.95
8a (9a)	2.54	3.11	3.11
8a (9a)	2.54	3.19	3.26
8b (9b)	2.03	2.35	2.24
8b (9b)	2.03	2.42	2.24
8c (9c)	5.03	4.99	4.99
1″	2.35	2.45	2.40
2″,3″,5″,6″	1.68-2.18	1.65-2.15	1.64-2.13
2'-6'	7.23-7.34	7.27-7.45	7.27-7.43
2C*H*$_3$(*i*Pr)	1.35	1.36	1.32
2C*H*$_3$(*i*Pr)	-	1.40	1.36
C*H*$_3$	2.51	2.70	2.54
C*H*$_3$	-	2.47	2.40
5‴a	3.26	3.26	3.15
5‴a	-	3.63	3.29

[a] CD_3OD, 298 K

[b] CD_3OD:D_2O 70:30, 320 K