

Hydrogenation of plant polyalkoxybenzene derivatives: convenient access to coenzyme Q₀ analogues

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Experimental

¹H NMR spectra were recorded on a Bruker DRX-500 spectrometer (working frequency 500.13 Hz, DMSO-*d*₆ or CDCl₃, Me₄Si as an internal standard). Low resolution mass spectra were detected on a Finnigan MAT INCOS 50 quadrupole mass spectrometer (direct injection, ionization energy 70 eV). High resolution mass spectra (HRMS) were measured on a Bruker micrOTOF II instrument using electrospray ionization (ESI). Elemental analysis was carried out on a Perkin—Elmer 2400 automated C,H,N microanalyzer. TLC studies were conducted on the Merck 60F254 plates. Silica gel Acros 0.035-0.070 mm 60A was used for preparative chromatography. Melting points were determined on a Boetius heating stage and were not corrected.

Liquid phase hydrogenation was carried out in stainless still reactor partially filled with block highly porous cellular catalyst (Table S1) [S1]. Highly porous ceramic material (α -Al₂O₃) covered by sol γ -Al₂O₃ with pores no less than 70–95% was used as catalyst carrier, readily permeable to air and water. This catalyst carrier was impregnated with Pd(NO₃)₂ and heated at 450 °C to afford PdO-coating catalyst. PdO was hydrogenated to metallic Pd by hydrogen at 50–55 °C, yielding the targeted block highly porous ceramic catalyst with 5%Pd/6% α -Al₂O₃/ γ -Al₂O₃. This type of block catalysts can be repeatedly regenerated by heating at 400-450 °C up to 30–40 times without activity loss [S2].

Table S1 Physical characteristics of the catalyst support.

Density	0.4 g cm ⁻³
Porosity	90%
Specific surface area	350 m ² g ⁻¹
Average pore size	2 μm
Mechanical strength	2 MPa

General procedure for the hydrogenation of allylbenzenes 1a-d and benzaldehydes 3a-e:

A solution of allylbenzene **1a-d** or benzaldehyde **3a-e** (23 mmol) in methanol (100 ml) was loaded into a stainless steel autoclave with fluoroplastic insert and a regenerated block highly porous ceramic catalyst cylinder was fixed. Hydrogenation was carried out at pressure of 20 bar at room temperature for 2–4 h (for allylbenzenes) or 4–8 h (for benzaldehydes). The reaction course was monitored by HPLC and TLC (**3a-e**: $R_f = 0.8$; **4a-e**: $R_f = 0.9$; **1a-d**: $R_f = 0.85$; **5a-d**: $R_f = 0.95$, EtOAc–hexane). After the initial substance disappeared completely, the reaction solution was poured out of the autoclave, the block catalyst was washed with methanol (3×30 ml), and the combined solutions were filtered from mechanical impurities. The solvent was evaporated to afford analytically pure aromatic alkylpolyalkoxybenzenes **4a-e** and **5a-d** (Table S2).

Table S2 Hydrogenation of **1a-d** and **3a-e** (MeOH, 20 atm, substrate conc. 0.25 mol dm⁻³).

Compound	Reaction time, h	Yield, %
4a	5	95
4a*	5	93
4b	6	76
4c	5	93
4d	4	87
4e	4	71
5a	3	97
5b	4	77
5c	2	86
5d	2	85

*Hydrogenation on 30x regenerating catalyst.

4,7-Dimethoxy-5-methyl-1,3-benzodioxole **4a**. Yield 95%. M.p. 39–41 °C (hexane) (lit. [S3] 39–40 °C). Found (%): C, 61.22; H, 6.10. C₁₀H₁₂O₄. Calcd (%): C, 61.23; H, 6.12.

4,5-Dimethoxy-6-methyl-1,3-benzodioxole **4b**. Yield 76%. Yellow oil. Found (%): C, 61.20; H, 6.13. C₁₀H₁₂O₄. Calcd (%): C, 61.23; H, 6.12. ¹H NMR (CDCl₃, δ): 2.2 (s, 3H, Me); 3.77 (s, 3H, OMe); 4.05 (s, 3H, OMe); 5.89 (s, 2H, OCH₂O); 6.37 (s, 1H, H_{Ar}).

1-Methyl-2,3,4,5-tetramethoxybenzene **4c**. Yield 93%. Yellow oil. Found (%): C, 62.24; H, 7.58. C₁₁H₁₆O₄. Calcd (%): C, 62.26; H, 7.55. ¹H NMR (CDCl₃, δ): 2.23 (s, 3H, Me); 3.79, 3.82 (s, 3H, OMe); 3.87, 3.93 (s, 3H, OMe); 6.45 (s, 1H, H_{Ar}).

4-Methoxy-6-methyl-1,3-benzodioxole **4d**. Yield 87%. M.p. 55-56 °C (EtOH, lit. [S4] 60-61 °C). Found (%): C, 65.07; H, 6.01. C₉H₁₀O₃. Calcd (%): C, 65.06; H, 6.02. ¹H NMR (CDCl₃, δ): 2.2 (s, 3H, Me); 3.9 (s, 3H, OMe); 5.88 (s, 2H, OCH₂O); 6.35 (s, 1H, H_{Ar}); 6.4 (s, 1H, H_{Ar}).

1-Methyl-3,4,5-trimethoxybenzene **4e**. Yield 71%. Yellow oil. Found (%): C, 65.92; H, 7.70. C₁₀H₁₄O₃. Calcd (%): C, 65.93; H, 7.69. ¹H NMR (CDCl₃, δ): 2.22 (s, 3H, Me); 3.78 (s, 3H, OMe); 3.82 (s, 3H, OMe); 3.87 (s, 3H, OMe); 6.4 (s, 1H, H_{Ar}), 6.44 (s, 1H, H_{Ar}).

4,7-Dimethoxy-5-propyl-1,3-benzodioxole **5a**. Yield 97%. Yellow oil, slowly crystallized. M.p. 36-37 °C (distillation). Found (%): C, 64.31; H, 7.12. C₁₂H₁₆O₄. Calcd (%): C, 64.29; H, 7.14. ¹H NMR (DMSO-*d*₆, δ): 0.88 (t, *J* = 7.3, 3H, CH₃); 1.46-1.53 (m, 2H, CH₂); 2.44 (t, *J* = 7.5, 2H, CH₂); 3.76 (s, 3H, OMe); 3.79 (s, 3H, OMe); 5.96 (s, 2H, OCH₂O); 6.41 (s, 1H, H_{Ar}). HRMS (ESI/QTOF) *m/z* calcd. for C₁₂H₁₆O₄ + H⁺: 225.2566 [M + H]⁺, found 225.2563; *m/z* calcd. for C₁₂H₁₆O₄ + Na⁺: 246.2386 [M + Na]⁺, found 246.2383.

4,5-Dimethoxy-6-propyl-1,3-benzodioxole **5b**. Yield 77%. Yellow oil. Found (%): C, 64.31; H, 7.13. C₁₂H₁₆O₄. Calcd (%): C, 64.29; H, 7.14. ¹H NMR (CDCl₃, δ): 0.94 (t, *J* = 7.3, 3H, CH₃); 1.5 - 1.62 (m, 2H, CH₂); 2.55 (t, *J* = 7.6, 2H, CH₂); 3.75 (s, 3H, OMe); 4.05 (s, 3H, OMe); 5.89 (s, 2H, OCH₂O); 6.37 (s, 1H, H_{Ar}).

l-Propyl-2,3,4,5-tetramethoxybenzene **5c**: Yield 86%. Yellow oil. Found (%): C, 64.97; H, 8.36. C₁₃H₂₀O₄. Calcd (%): C, 65; H, 8.33. ¹H NMR (CDCl₃, δ): 0.92 (t, *J* = 7.3, 3H, CH₃); 1.54-1.65 (m, 2H, CH₂); 2.51 (t, *J* = 7.5, 2H, CH₂); 3.79, 3.81 (s, 3H, OMe); 3.88, 3.92 (s, 3H, OMe); 6.45 (s, 1H, H_{Ar}). HRMS (ESI/QTOF) *m/z* calcd. for C₁₃H₂₀O₄ + H⁺: 241.2994 [M + H]⁺, found 241.2990; *m/z* calcd. for C₁₃H₂₀O₄ + Na⁺: 262.2814 [M + Na]⁺, found 262.2810.

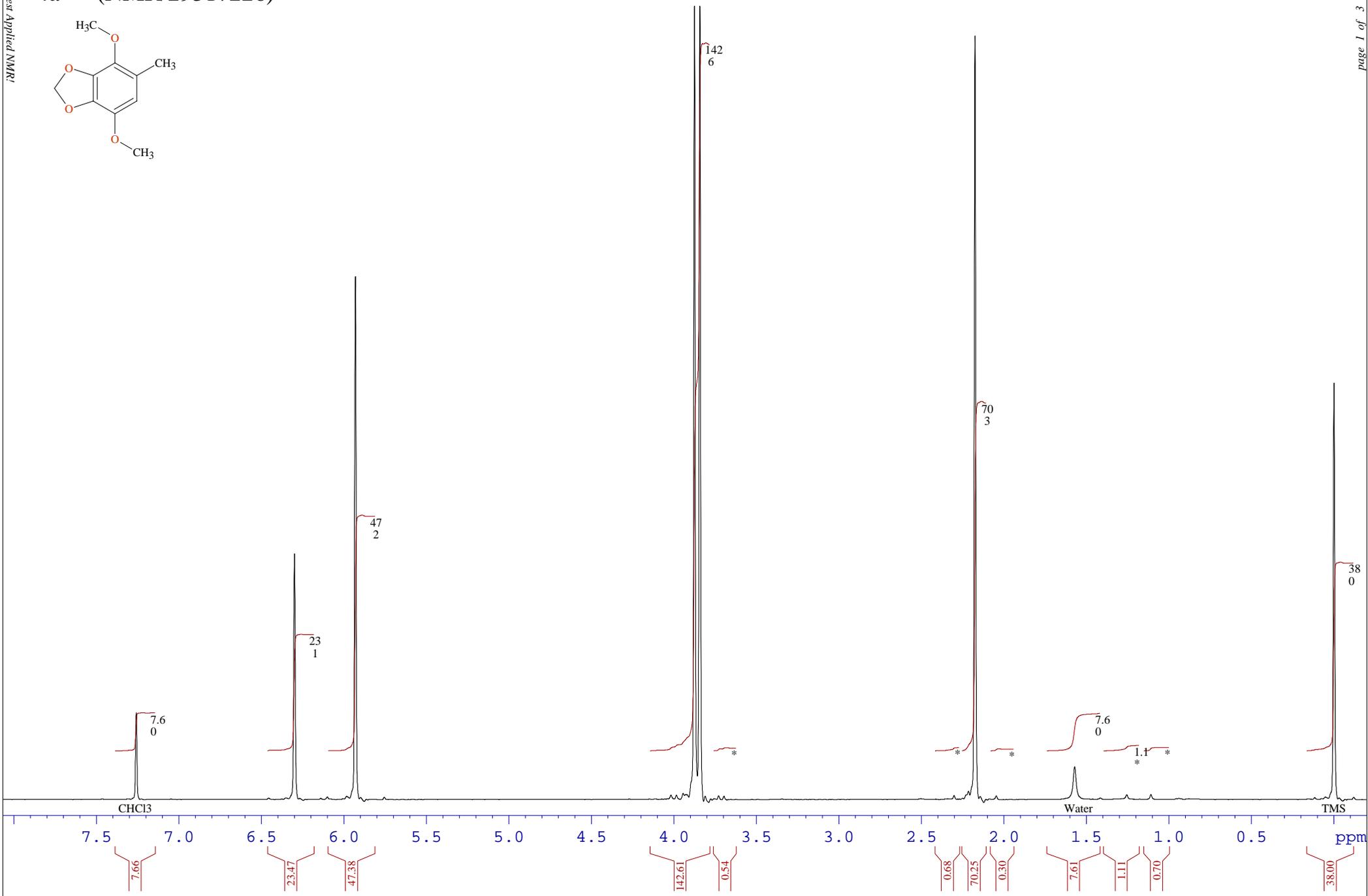
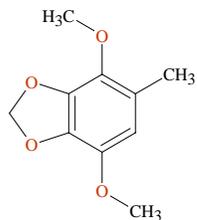
4-Methoxy-6-propyl-1,3-benzodioxole **5d**. Yield 85%. Yellow oil. Found (%): C, 68.06; H, 7.21. C₁₂H₁₄O₃. Calcd (%): C, 68.04; H, 7.22. ¹H NMR, (CDCl₃, δ): 0.92 (t, *J* = 7.3, 3H, CH₃); 1.54-1.66 (m, 2H, CH₂); 2.5 (t, *J* = 7.4, 2H, CH₂); 3.9 (s, 3H, OMe); 5.92 (s, 2H, OCH₂O); 6.34 (s, 1H, H_{Ar}); 6.4 (s, 1H, H_{Ar}).

References

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- [S2] V. L. Zbarsky, N. V. Khodov, A. I. Kuimov and A. I. Kozlov, *Patent RU 2333795*, 2008.
- [S3] H. L. Newson, D. A. Wild, S. Y. Yeung, B. W. Skelton, G. R. Flematti, J. E. Allan and M. J. Piggott, *J. Org. Chem.*, 2016, **81**, 3127.
- [S4] H. Sugihara, M. Watanabe, Y. Kawamatsu and H. Morimoto, *Liebigs Ann. Chem.*, 1972, **763**, 109.

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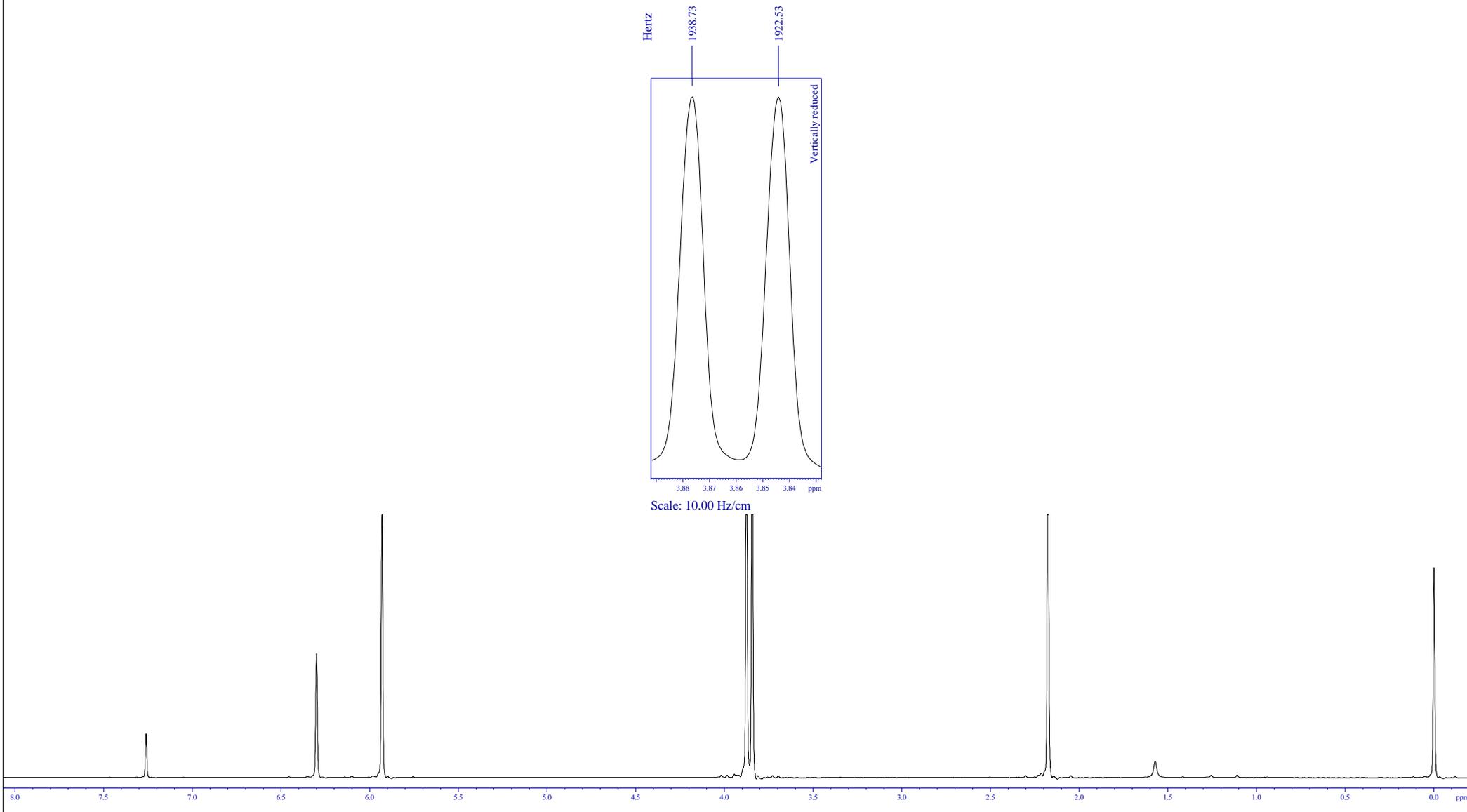
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4a (NMR/29317226)

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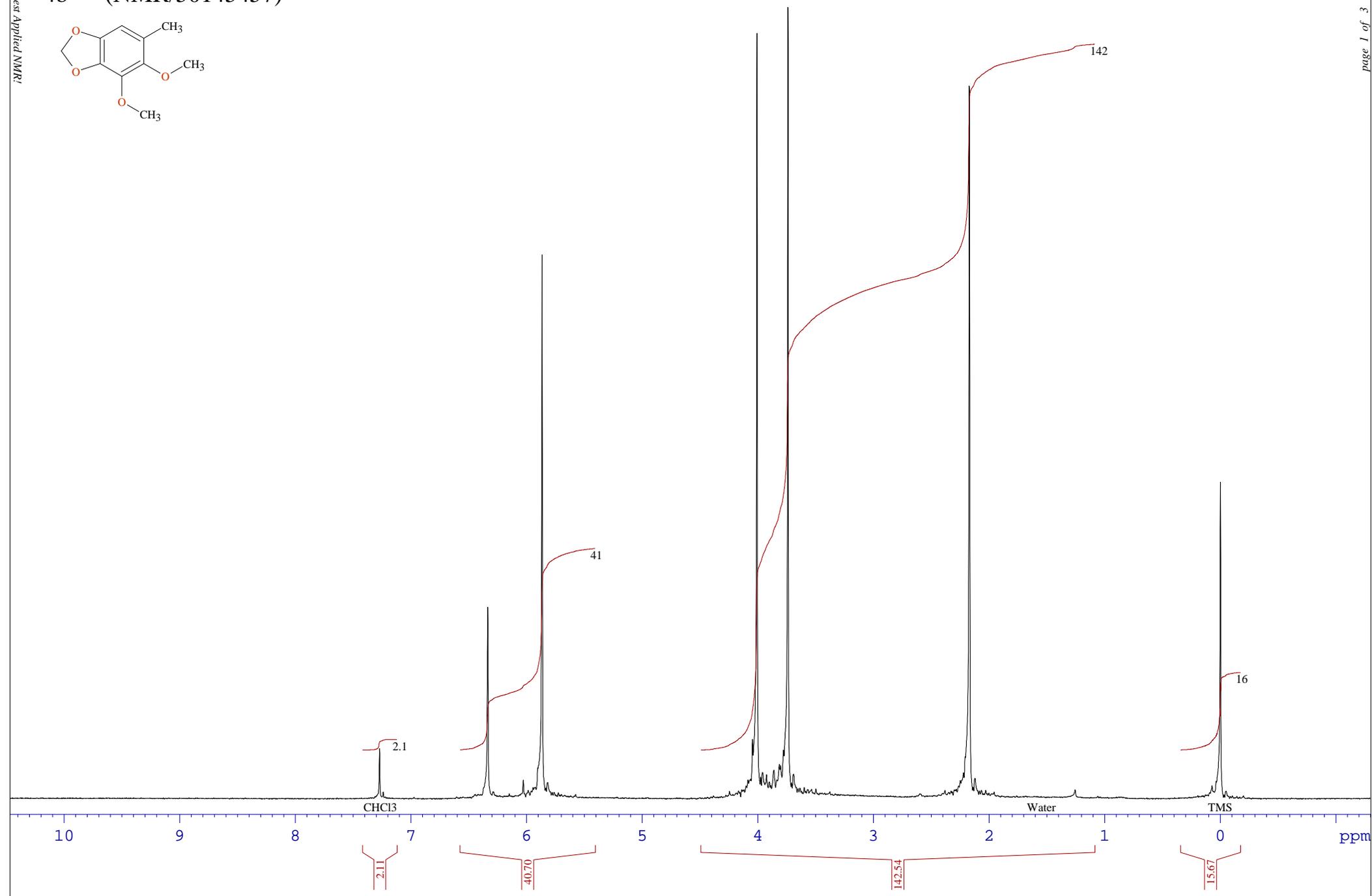
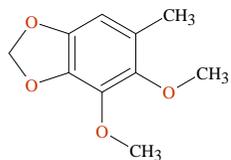


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3	19753.9	2966.509	5.9315	10.51
4	23121.7	1938.734	3.8765	16.00
5	23174.8	1922.534	3.8441	15.97
6	25908.1	1088.389	2.1762	15.34
7	26898.3	786.202	1.5720	0.65
8	29474.5	0.001	0.0000	8.37

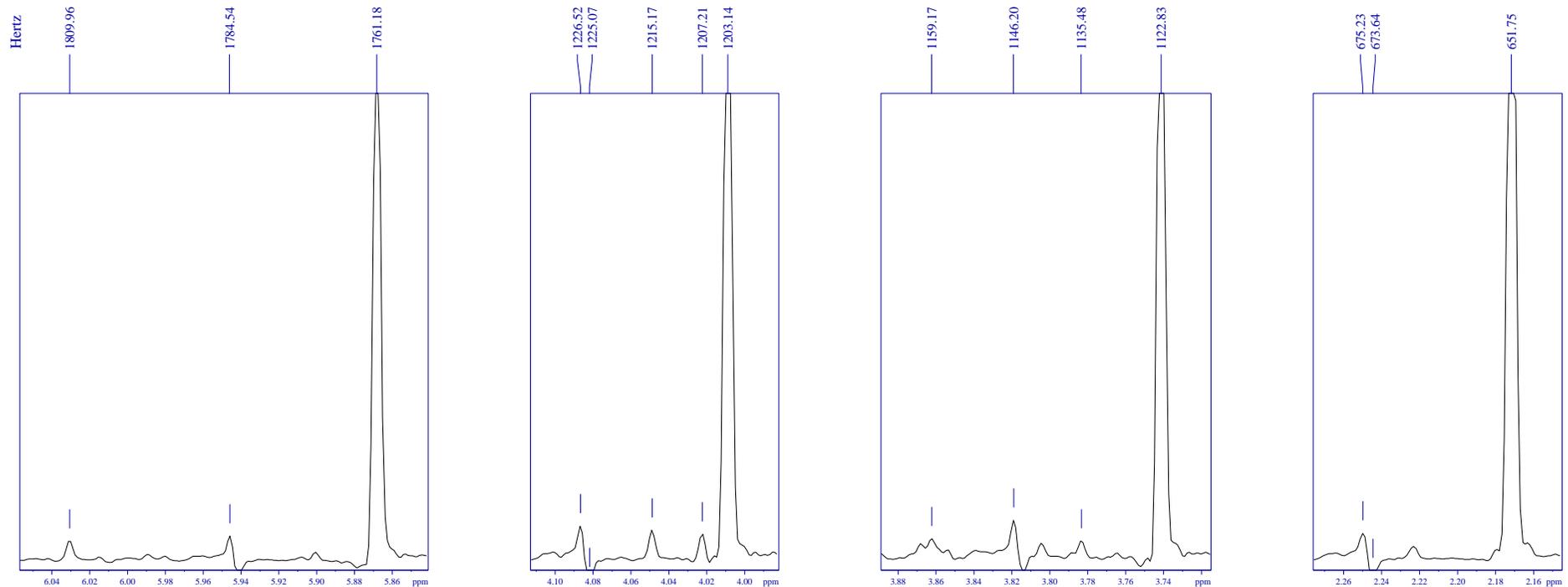
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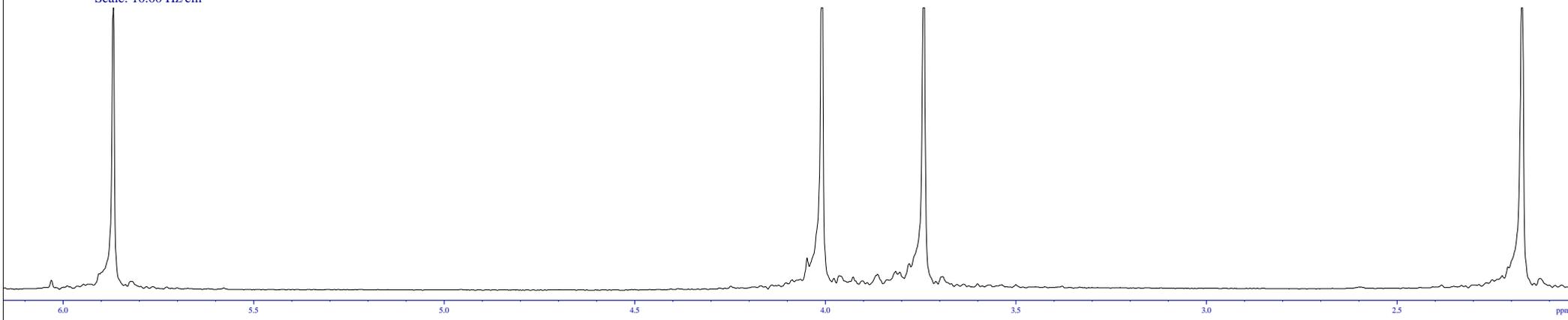
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Scale: 10.00 Hz/cm



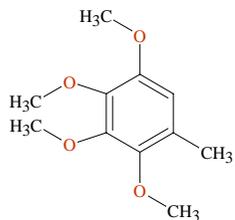
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2	9547.1	1902.188	6.3379	2.99
3	9798.5	1809.957	6.0306	0.31
4	9867.8	1784.537	5.9459	0.37
5	9931.5	1761.179	5.8681	10.58
6	11389.1	1226.522	4.0866	0.53
7	11393.1	1225.074	4.0818	-0.39
8	11420.1	1215.172	4.0488	0.46
9	11441.8	1207.215	4.0223	0.41
10	11452.9	1203.136	4.0087	15.43
11	11572.7	1159.175	3.8622	0.33
12	11608.1	1146.197	3.8190	0.61
13	11637.3	1135.483	3.7833	0.30
14	11671.8	1122.833	3.7412	16.00
15	12892.1	675.233	2.2498	0.42
16	12896.5	673.642	2.2445	-0.34
17	12956.1	651.748	2.1716	12.71
18	14733.0	0.001	0.0000	6.57

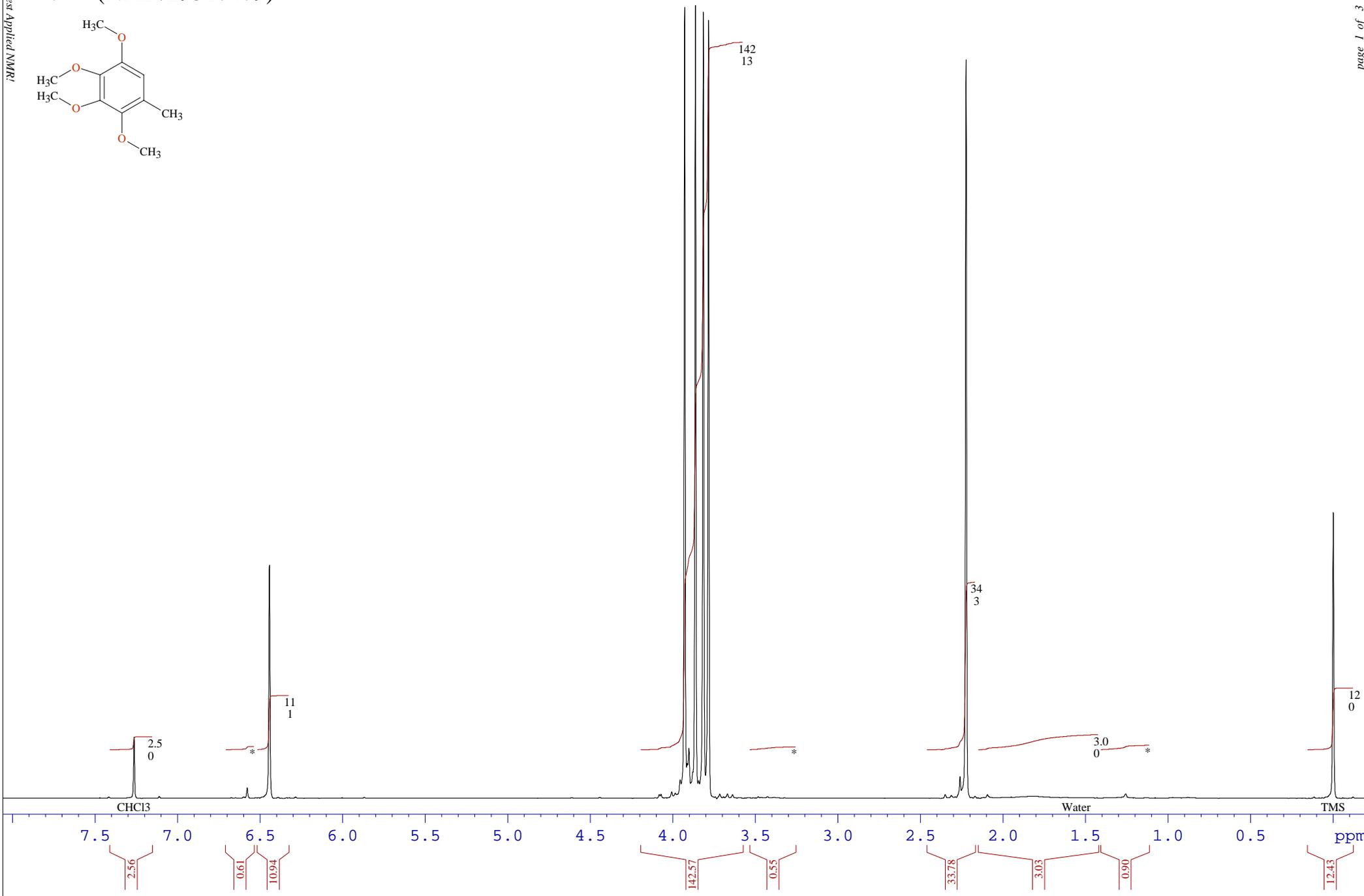
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4c (NMR/29317479)



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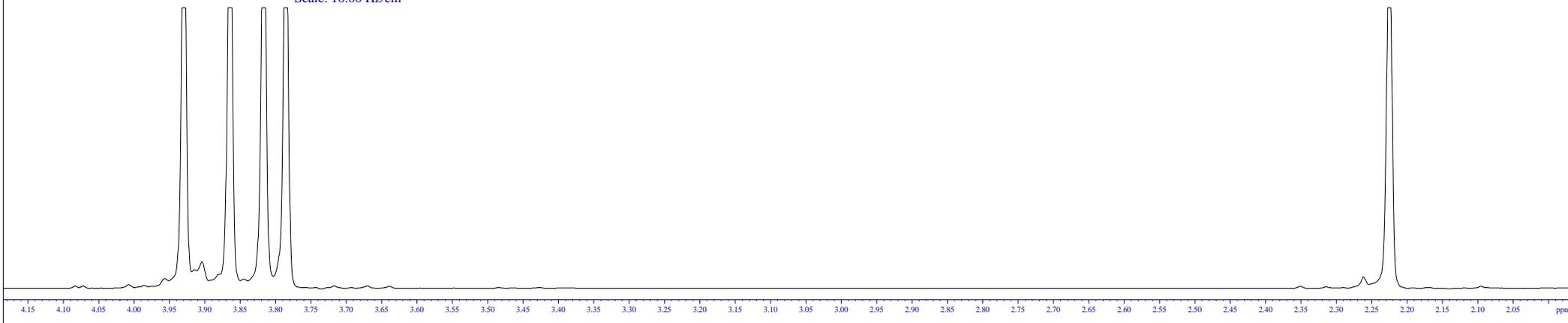
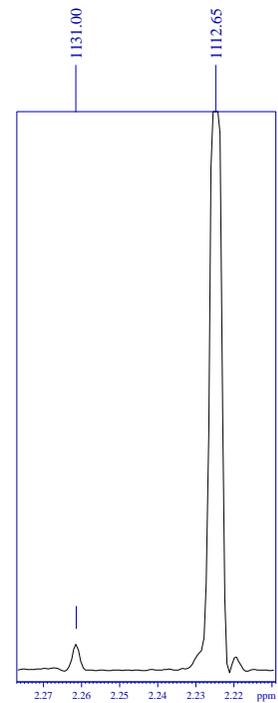
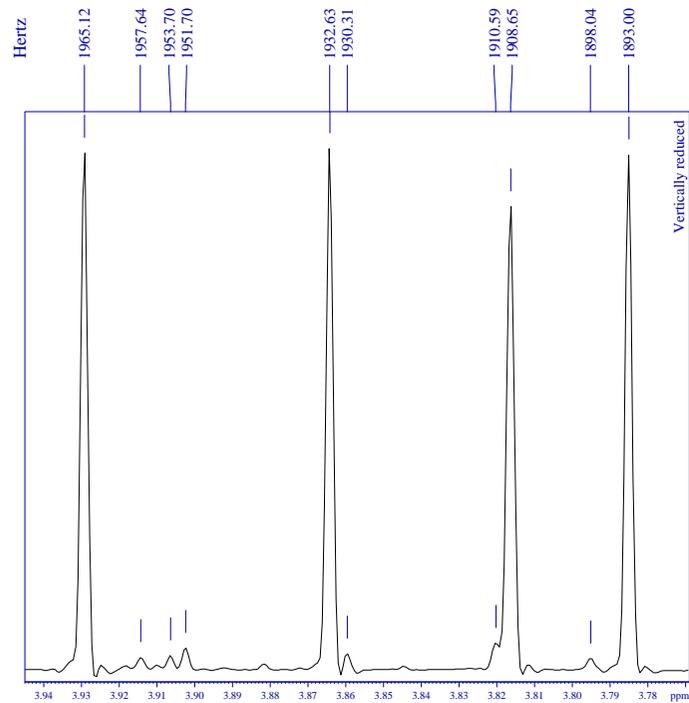
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4c (NMR/29317479)

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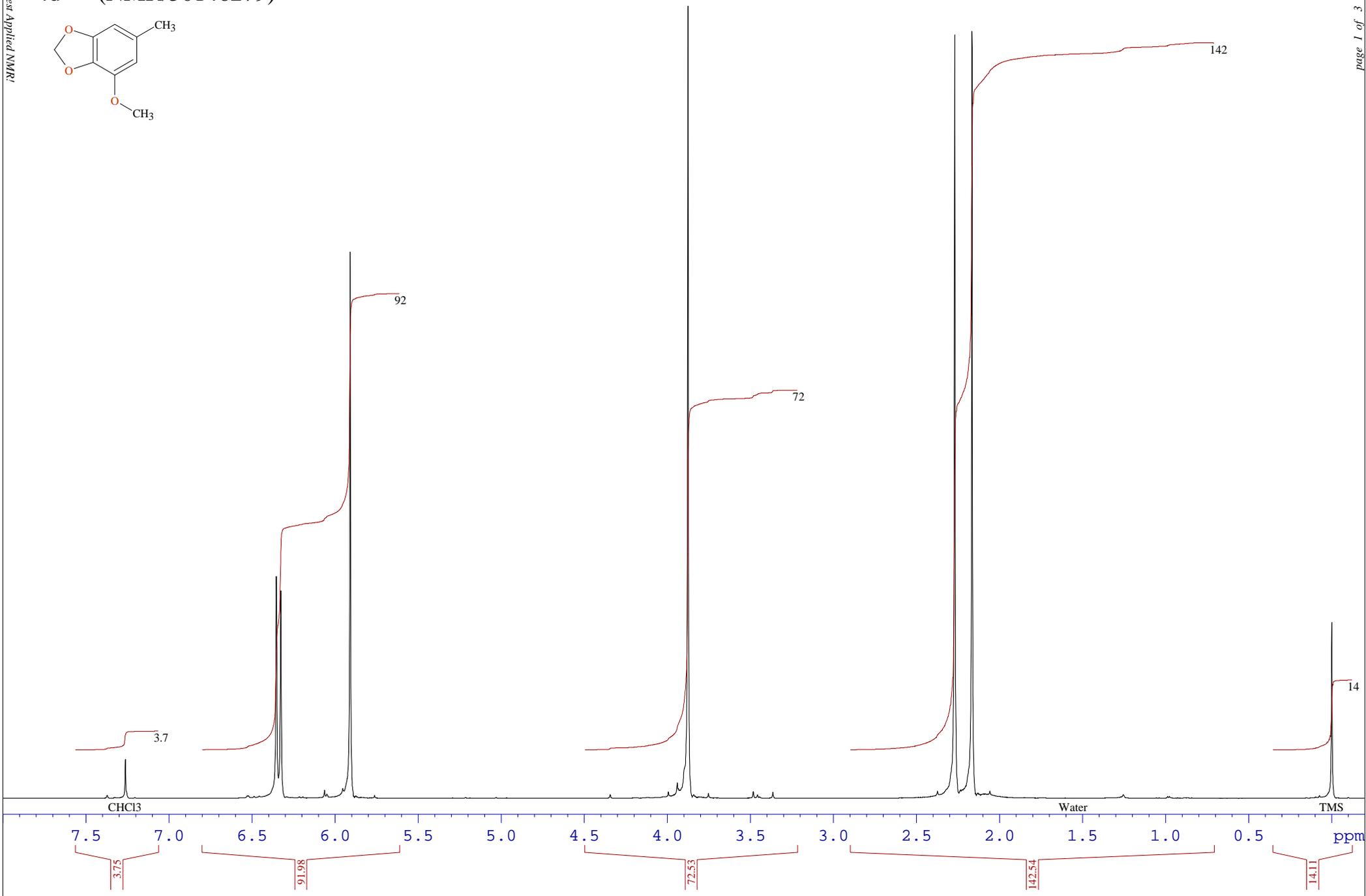
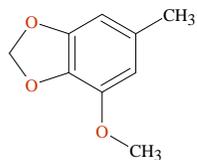


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2	18922.8	3223.342	6.4450	2.79
3	23045.7	1965.119	3.9292	16.00
4	23070.2	1957.640	3.9143	0.41
5	23083.1	1953.696	3.9064	0.46
6	23089.7	1951.698	3.9024	0.70
7	23152.2	1932.626	3.8642	15.95
8	23159.8	1930.312	3.8596	0.52
9	23224.4	1910.585	3.8202	0.86
10	23230.7	1908.651	3.8163	14.26
11	23265.5	1898.044	3.7951	0.37
12	23282.0	1893.003	3.7850	15.66
13	25779.0	1130.998	2.2614	0.35
14	25839.1	1112.654	2.2247	11.30
15	29485.0	0.002	0.0000	5.85

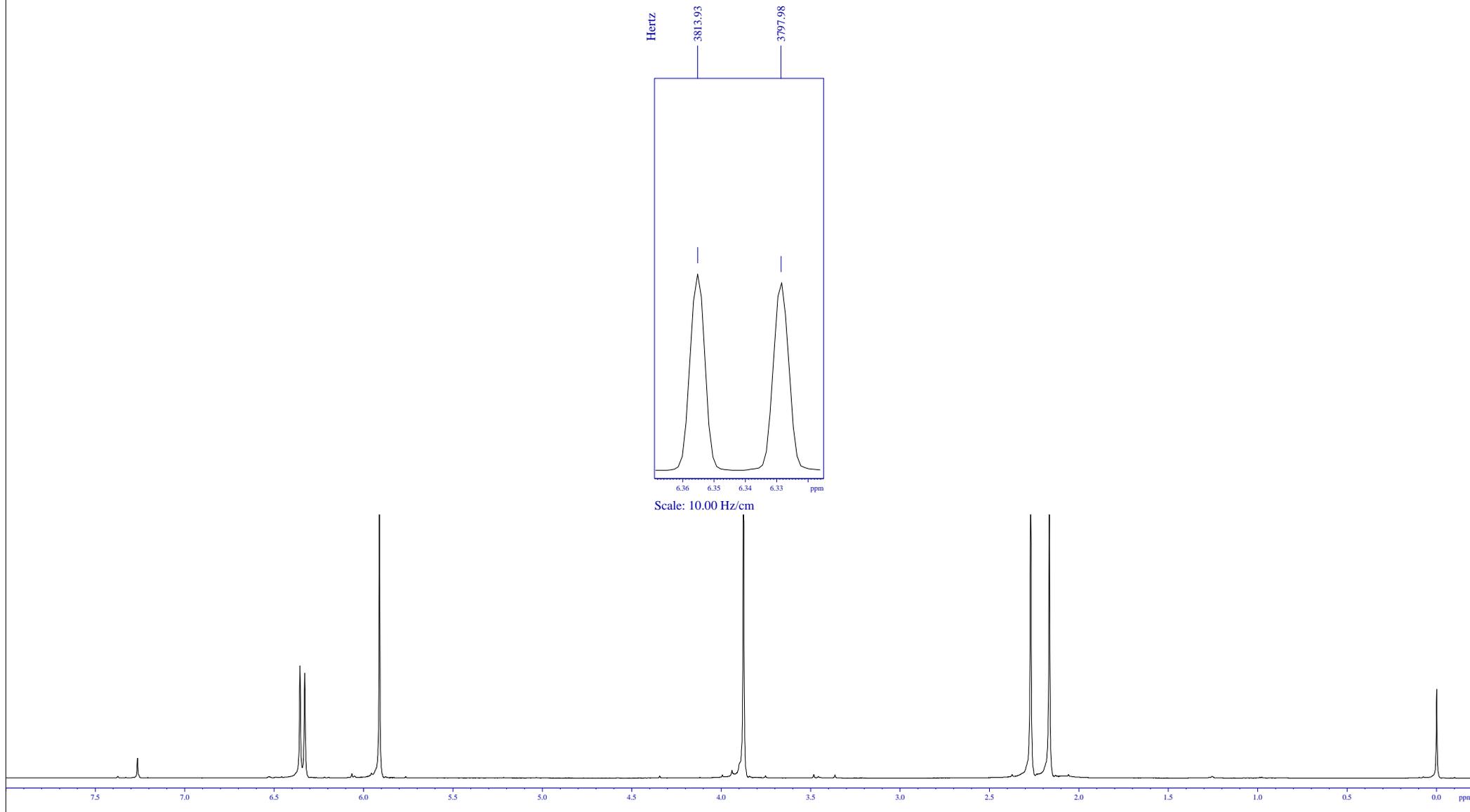
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4d (NMR/50146279)

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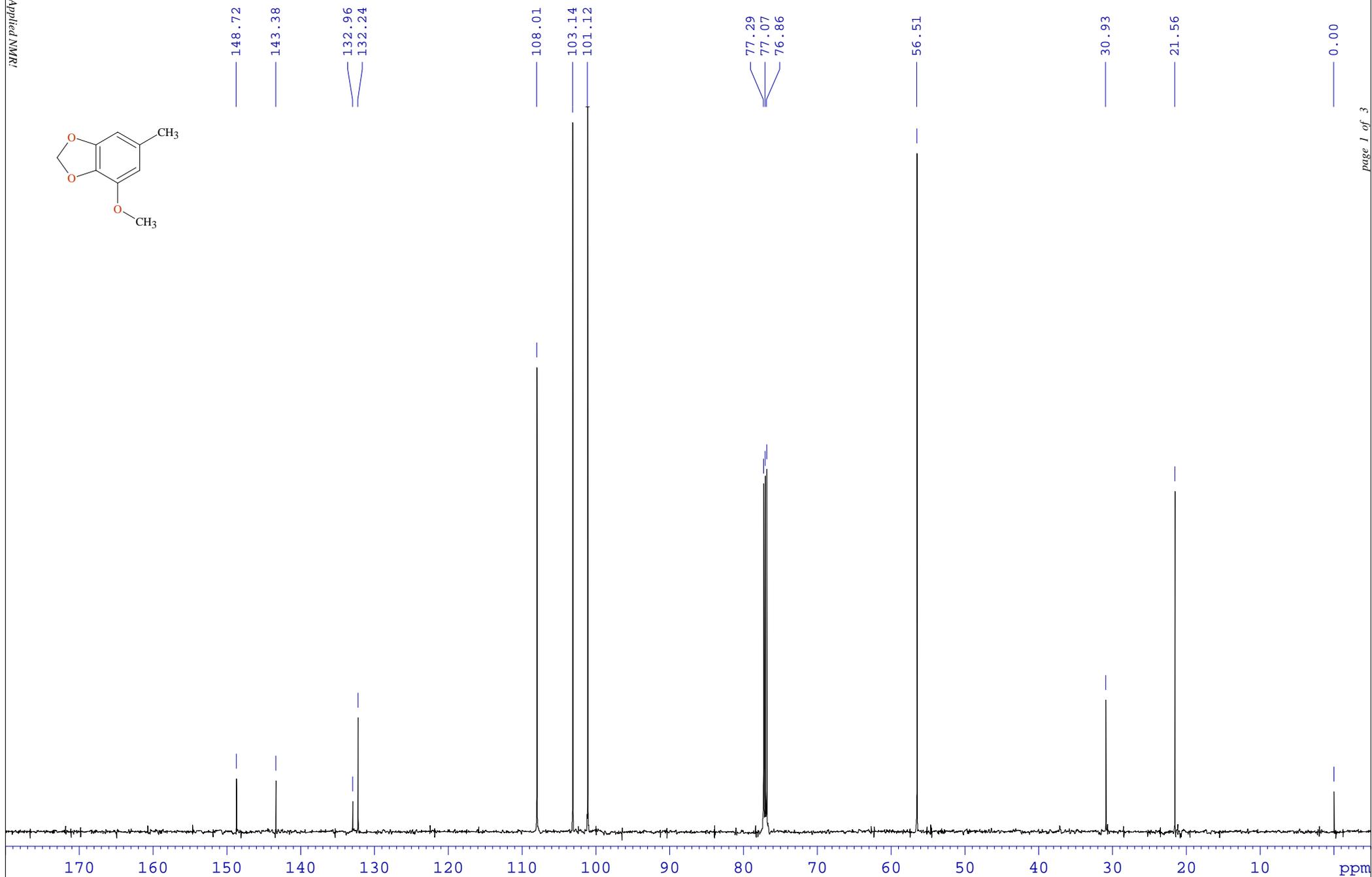
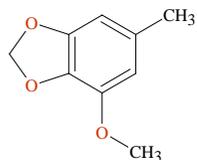


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2	9554.8	3797.979	6.3286	3.43
3	9896.8	3547.096	5.9105	10.87
4	11560.7	2326.491	3.8766	16.00
5	12874.4	1362.737	2.2707	13.97
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7	14732.0	0.002	0.0000	3.47

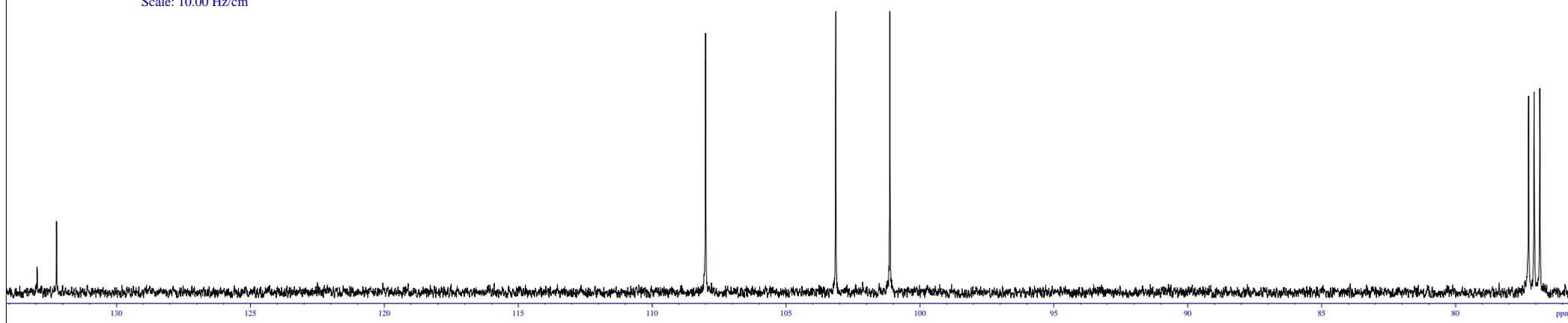
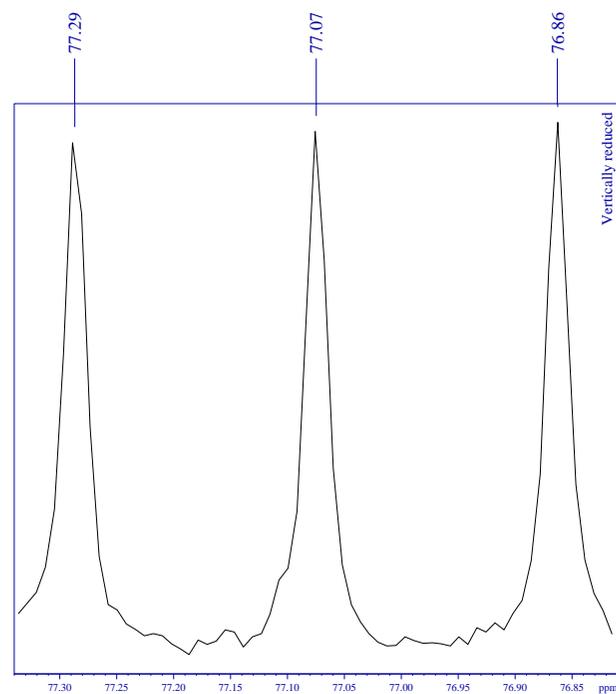
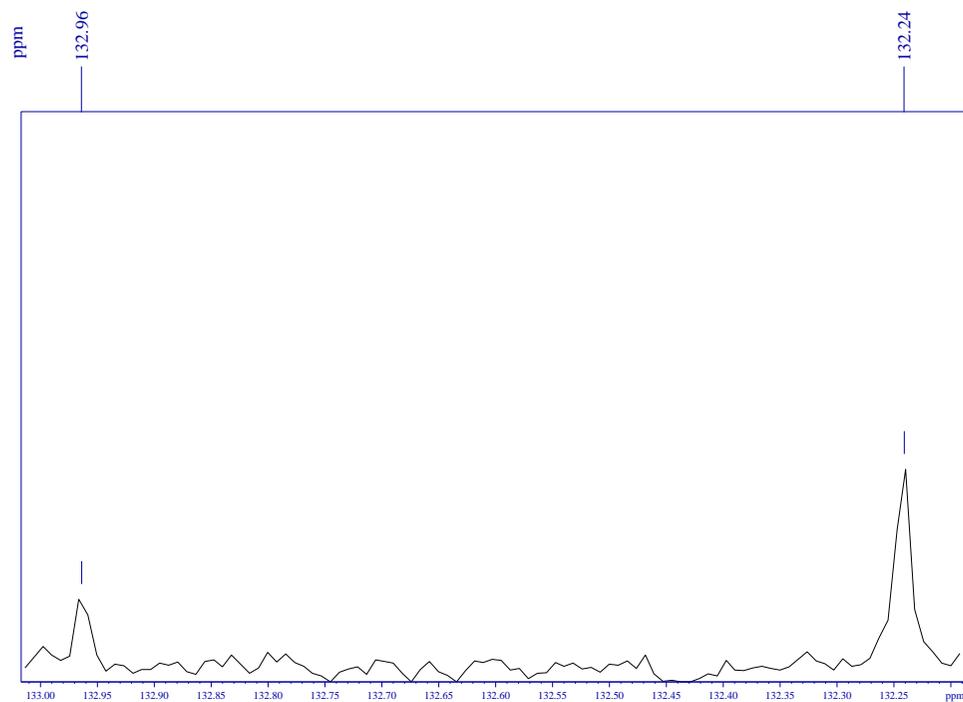
4d (NMR/50146279)



4d (NMR/50146279)

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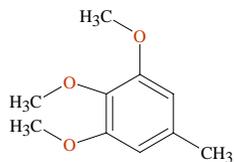


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Peaks List

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		[Hz]	[ppm]	
1	12635.1	22441.877	148.7174	1.39
2	13310.7	21636.539	143.3806	1.40
3	14629.3	20064.615	132.9638	0.96
4	14720.8	19955.521	132.2409	2.66
5	17788.7	16298.362	108.0057	9.80
6	18404.1	15564.743	103.1442	14.41
7	18659.8	15259.836	101.1236	16.00
8	21677.2	11662.793	77.2868	7.35
9	21704.1	11630.791	77.0747	7.40
10	21730.9	11598.775	76.8626	7.51
11	24307.9	8526.780	56.5051	13.82
12	27545.5	4667.345	30.9295	3.12
13	28732.0	3252.827	21.5558	7.10
14	31460.7	0.001	0.0000	1.15

4e (NMR/50146281)



153.94
153.68

136.46
134.63
134.25

106.65
105.25
104.39

78.19
77.98
77.76
75.50

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56.64

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22.47

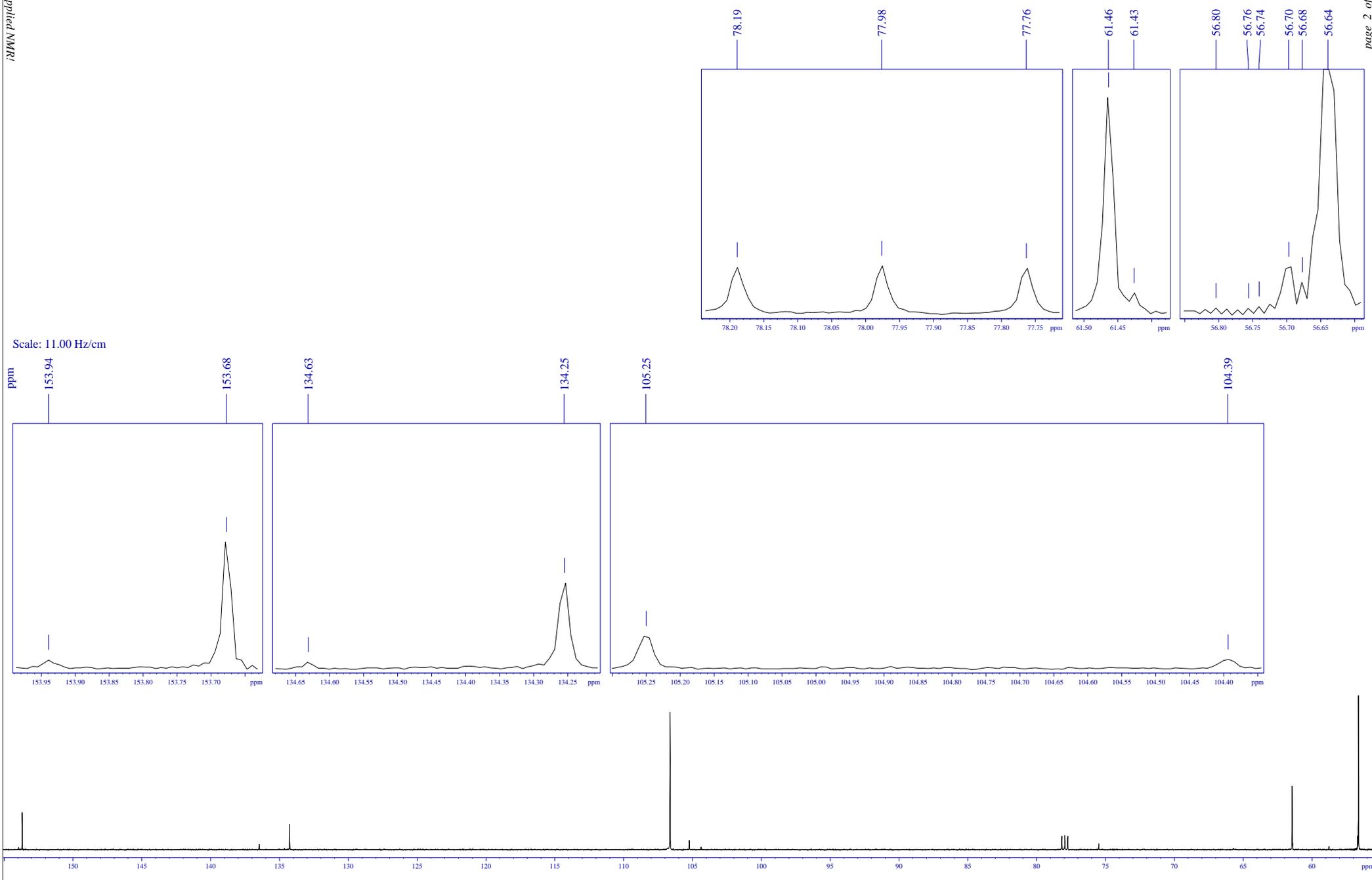
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0.65



4e (NMR/50146281)

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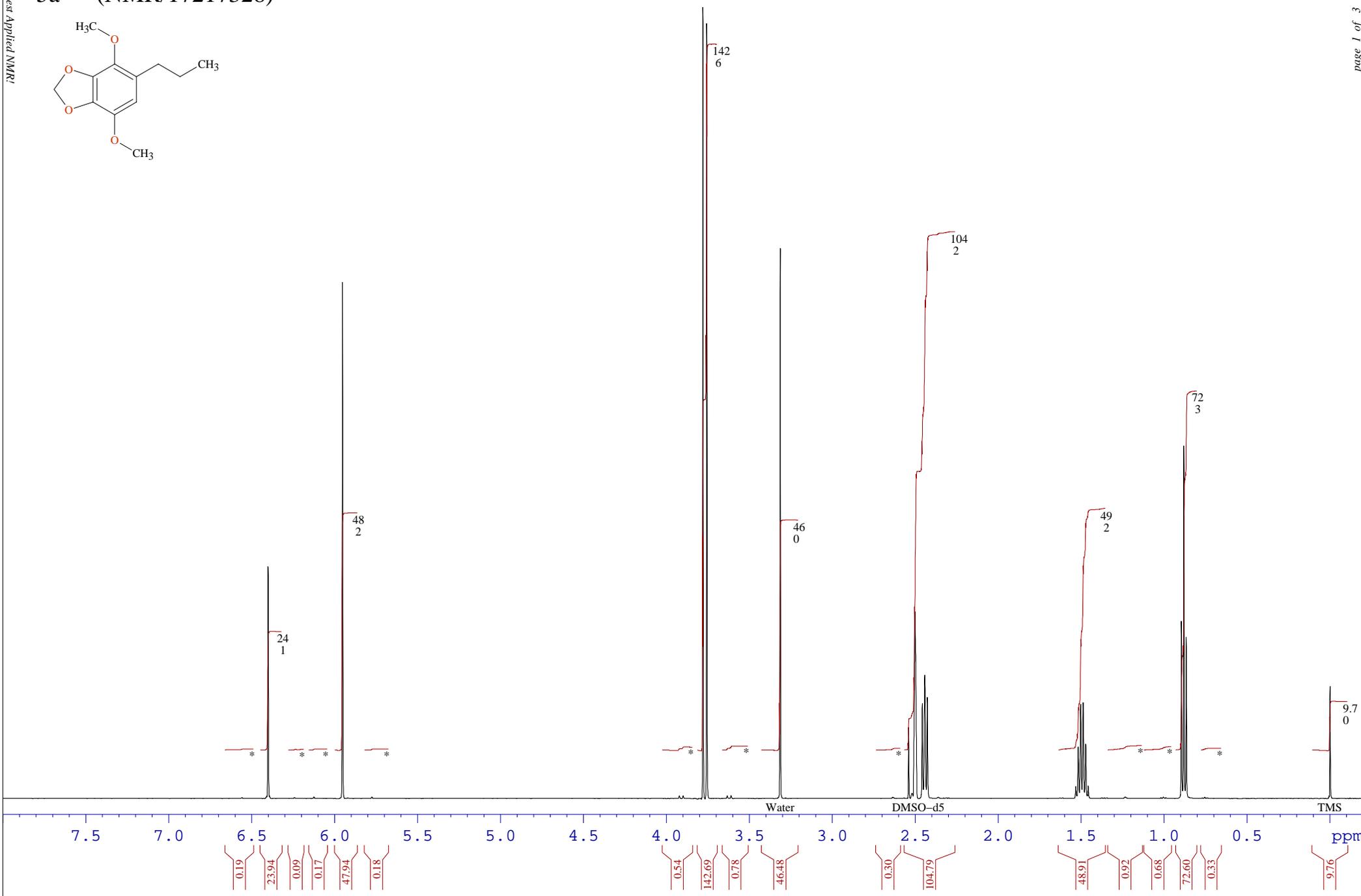
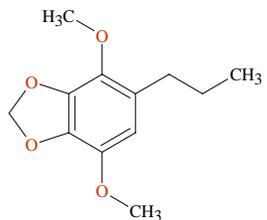
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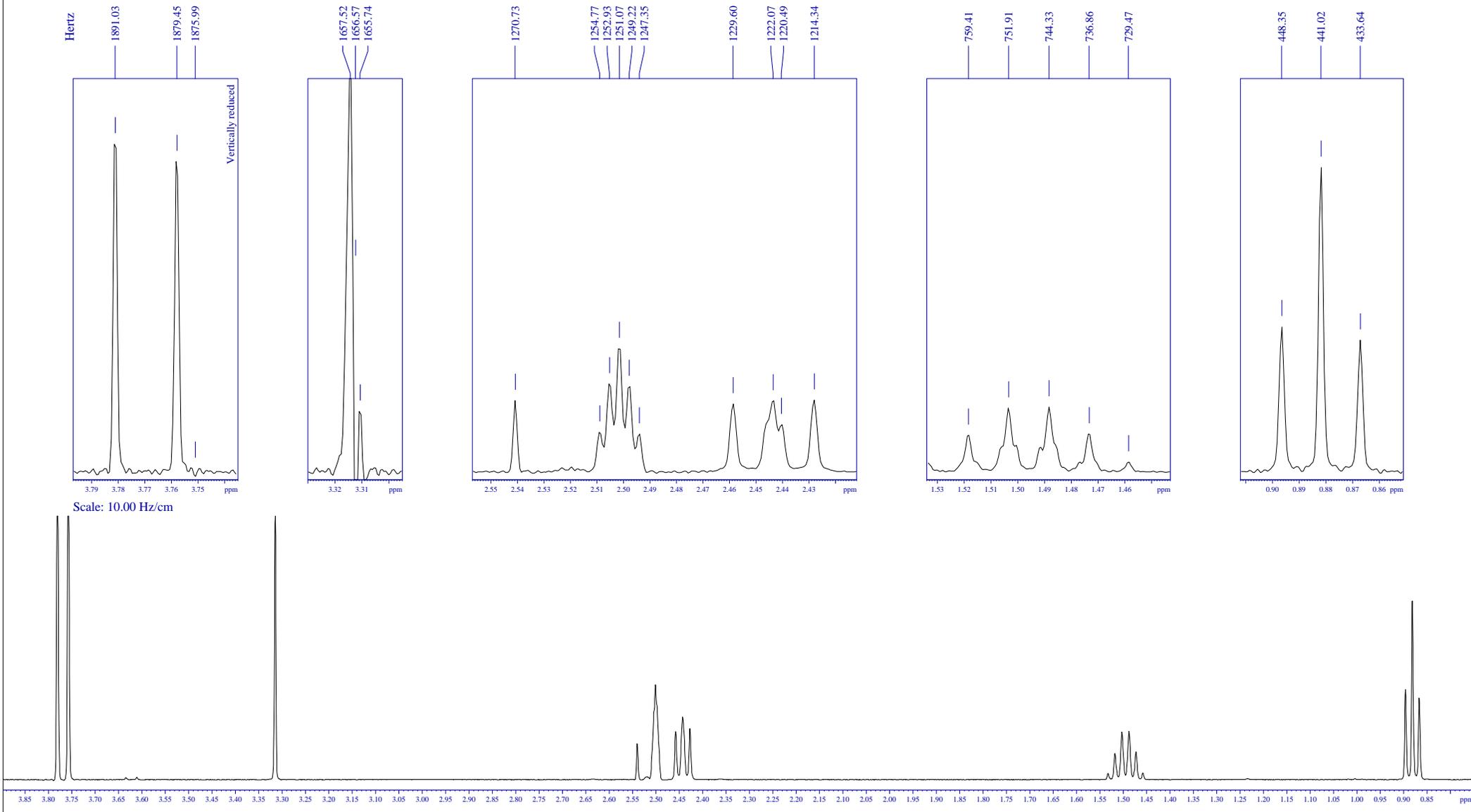
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3	14274.6	20592.242	136.4604	0.38
4	14506.1	20316.234	134.6313	0.12
5	14553.8	20259.402	134.2547	1.72
6	18048.6	16093.265	106.6466	9.56
7	18225.4	15882.513	105.2500	0.65
8	18333.8	15753.283	104.3936	0.17
9	21650.9	11798.969	78.1892	0.92
10	21677.9	11766.829	77.9763	0.96
11	21704.8	11734.698	77.7633	0.91
12	21991.2	11393.268	75.5008	0.41
13	23227.1	9919.991	65.7377	0.11
14	23768.1	9275.075	61.4639	4.31
15	23772.9	9269.359	61.4261	0.42
16	24107.2	8870.847	58.7852	0.24
17	24358.0	8571.910	56.8042	0.11
18	24364.1	8564.648	56.7561	0.11
19	24366.0	8562.322	56.7407	0.15
20	24371.5	8555.722	56.6969	1.01
21	24374.1	8552.699	56.6769	0.63
22	24378.9	8546.984	56.6390	16.00
23	26324.0	6228.249	41.2733	1.08
24	28704.0	3391.077	22.4719	3.70
25	29669.8	2239.674	14.8418	0.14
26	31465.9	98.589	0.6533	0.12

5a (NMR/17217328)

Found protons = 16 impurity* < 0.1 %



5a (NMR/17217328)



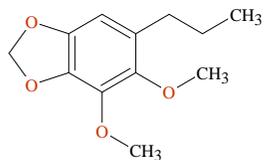
5a (NMR/17217328)

Peaks List

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2	19721.2	2977.844	5.9541	9.43
3	23282.5	1891.031	3.7811	16.00
4	23320.4	1879.455	3.7579	14.86
5	23331.8	1875.992	3.7510	-0.21
6	24047.7	1657.516	3.3142	10.46
7	24050.7	1656.574	3.3123	-4.09
8	24053.5	1655.743	3.3106	1.46
9	25315.1	1270.735	2.5408	1.44
10	25367.4	1254.773	2.5089	0.82
11	25373.4	1252.931	2.5052	1.81
12	25379.5	1251.074	2.5015	2.57
13	25385.6	1249.223	2.4978	1.77
14	25391.7	1247.349	2.4940	0.77
15	25449.8	1229.603	2.4586	1.37
16	25474.5	1222.069	2.4435	1.45
17	25479.7	1220.493	2.4404	0.96
18	25499.9	1214.340	2.4280	1.44
19	26990.6	759.411	1.5184	0.75
20	27015.2	751.908	1.5034	1.29
21	27040.0	744.325	1.4883	1.30
22	27064.5	736.858	1.4733	0.78
23	27088.7	729.473	1.4586	0.20
24	28009.9	448.349	0.8965	2.93
25	28033.9	441.016	0.8818	6.14
26	28058.0	433.643	0.8671	2.65
27	29479.0	0.002	0.0000	2.37

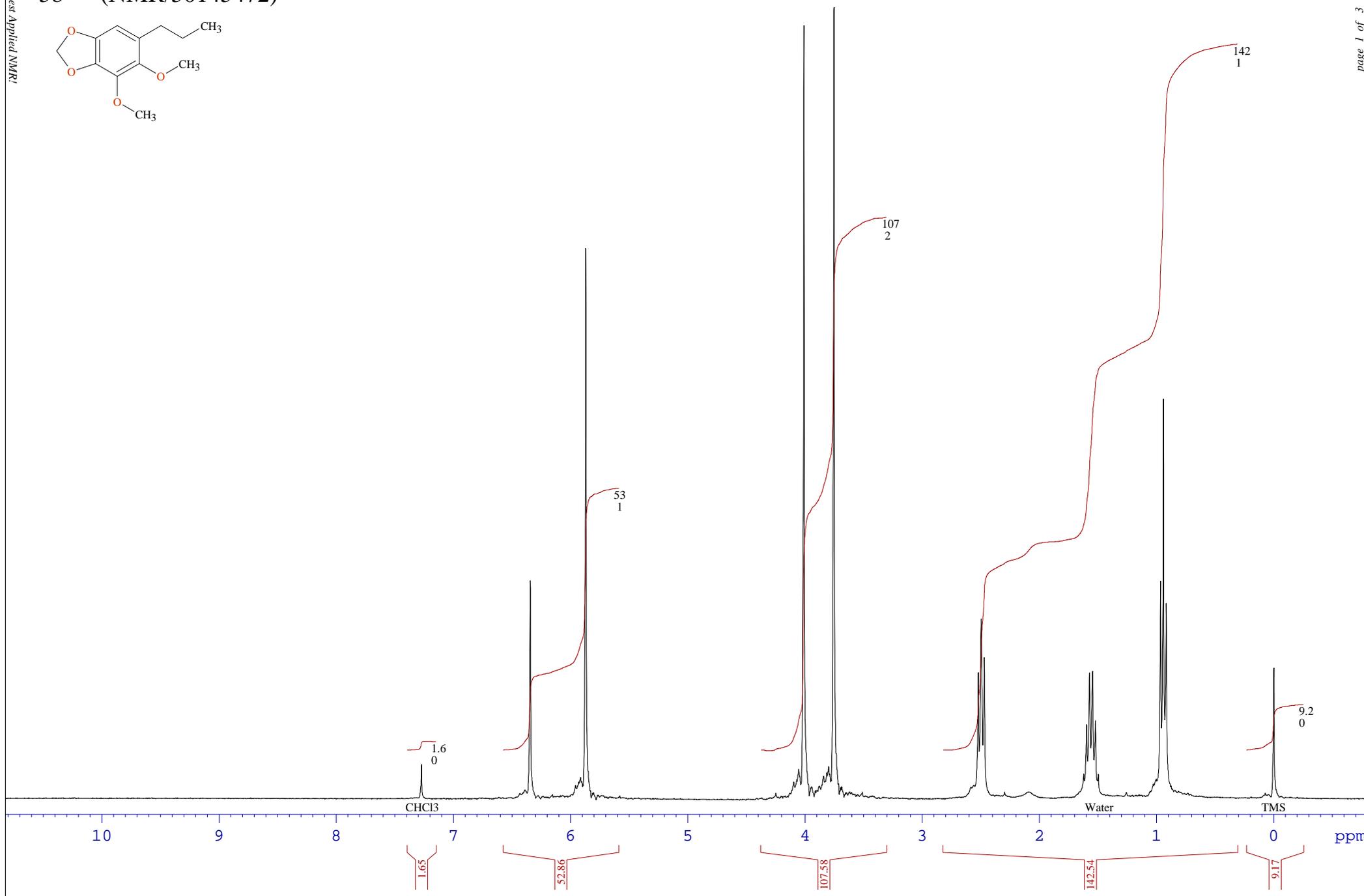
5b (NMR/50145472)

Found protons = 4 impurity* < 0.1 %



The Best Applied NMR!

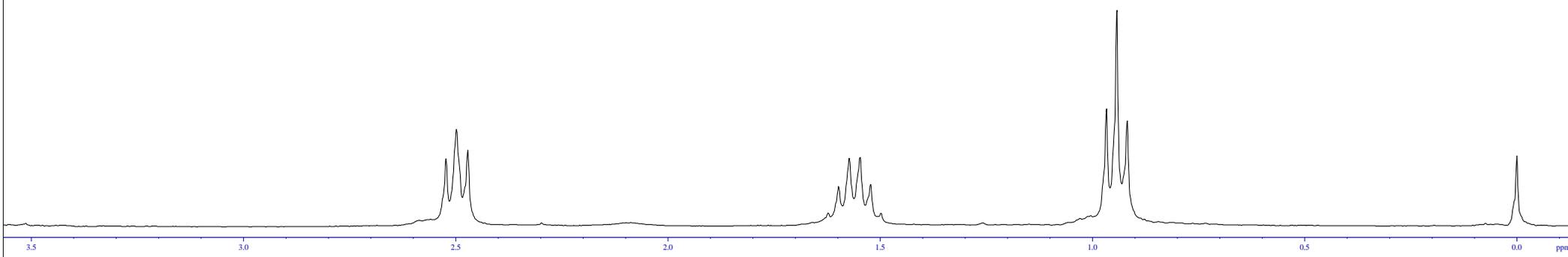
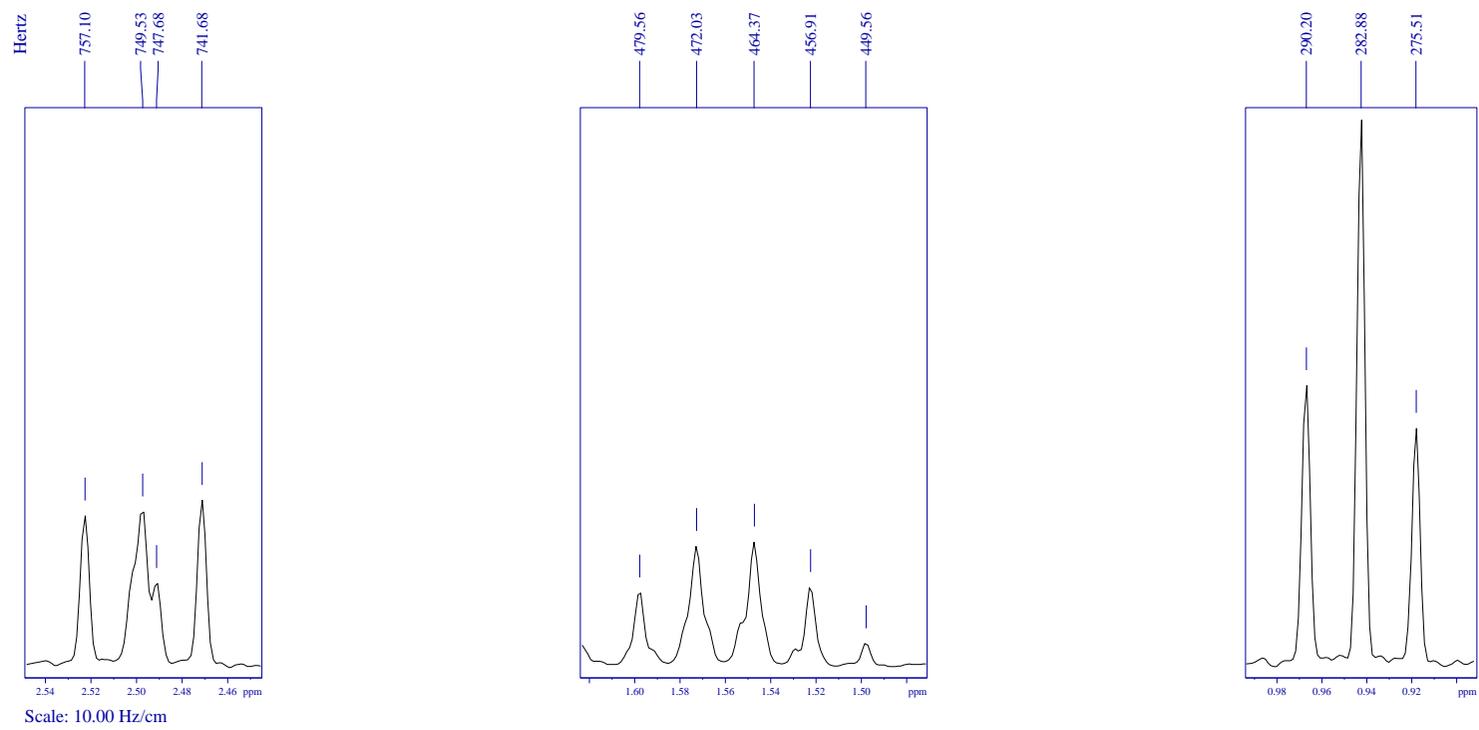
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5b (NMR/50145472)

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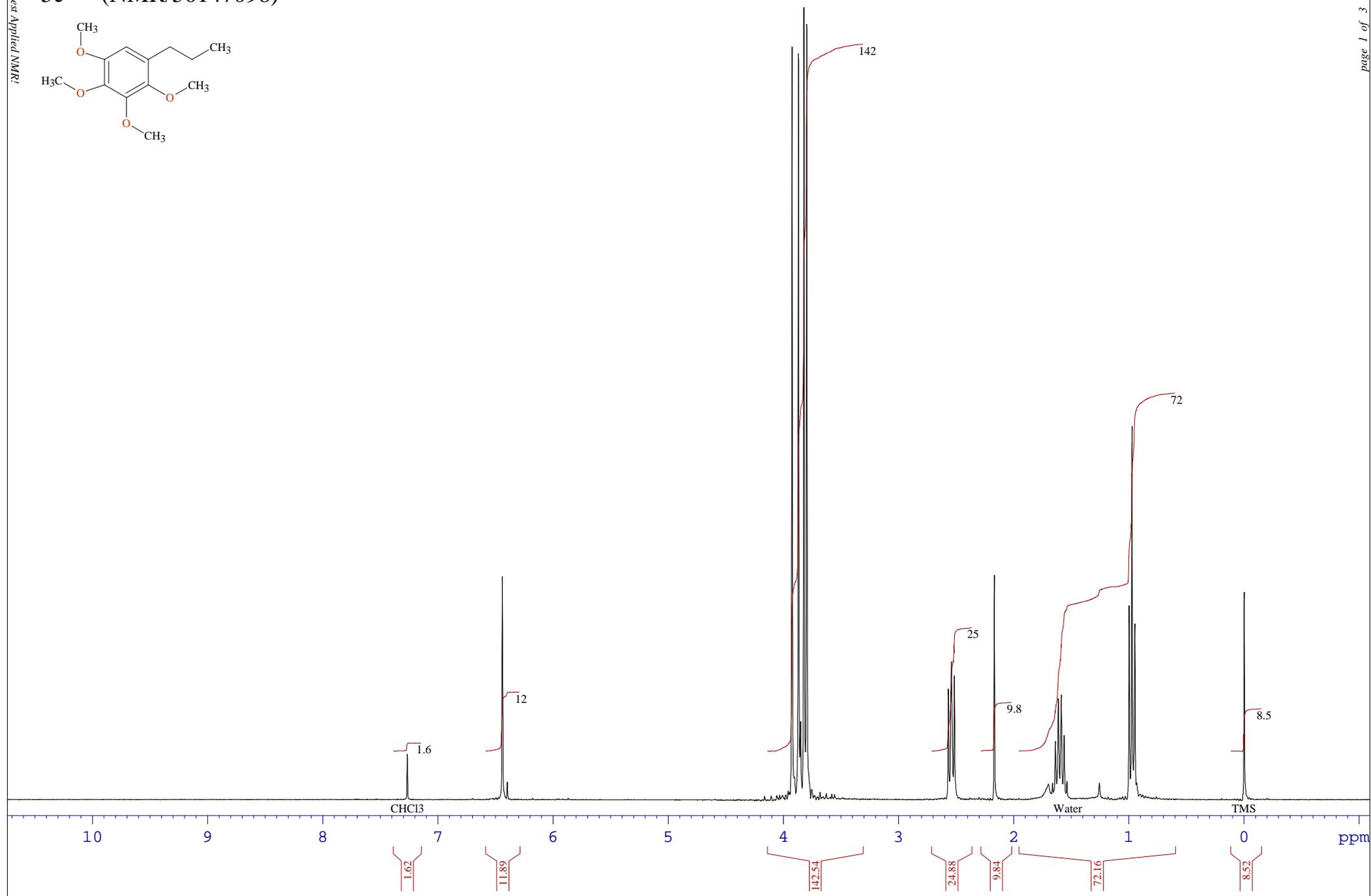
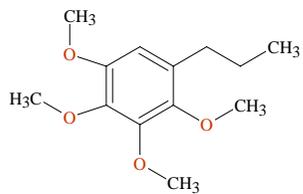


5b (NMR/50145472)

Peaks List

#	Address [points]	Frequency		Intensity [cm]
		[Hz]	[ppm]	
1	8777.9	2183.207	7.2742	0.71
2	9537.6	1904.578	6.3458	3.71
3	9925.2	1762.381	5.8721	10.63
4	11448.0	1203.814	4.0110	15.51
5	11657.8	1126.881	3.7546	16.00
6	12665.9	757.095	2.5226	1.92
7	12686.6	749.529	2.4973	2.02
8	12691.6	747.680	2.4912	1.09
9	12707.9	741.684	2.4712	2.12
10	13422.6	479.562	1.5978	0.97
11	13443.1	472.028	1.5727	1.53
12	13464.0	464.369	1.5472	1.59
13	13484.3	456.914	1.5224	1.03
14	13504.4	449.562	1.4979	0.30
15	13938.8	290.204	0.9669	3.60
16	13958.8	282.876	0.9425	7.03
17	13978.9	275.514	0.9180	3.05
18	14730.0	-0.000	-0.0000	2.65

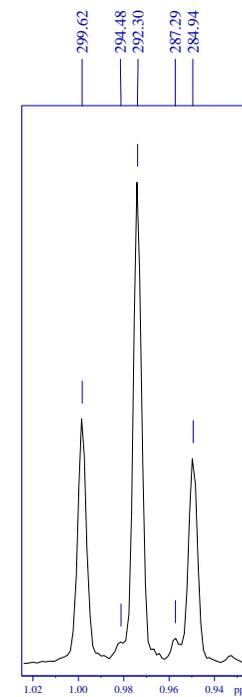
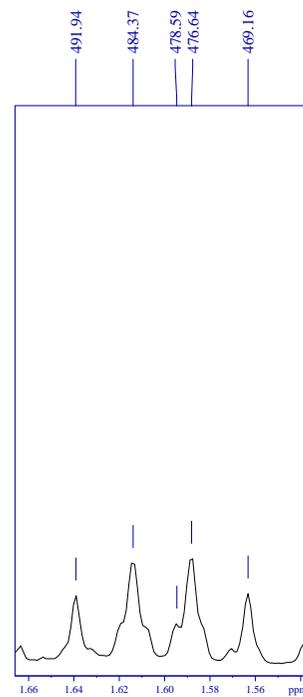
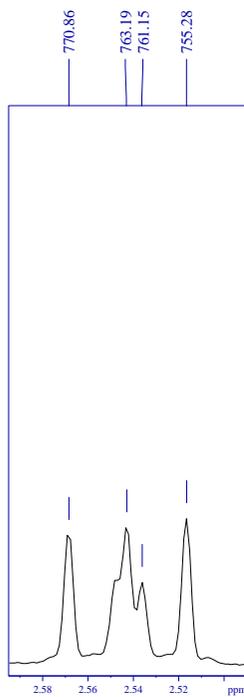
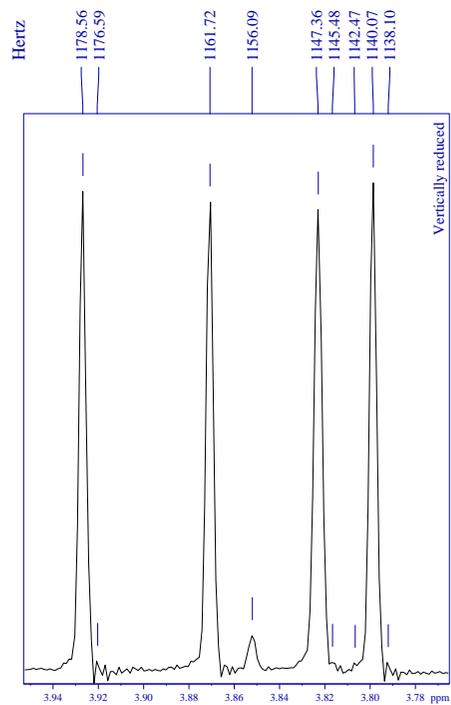
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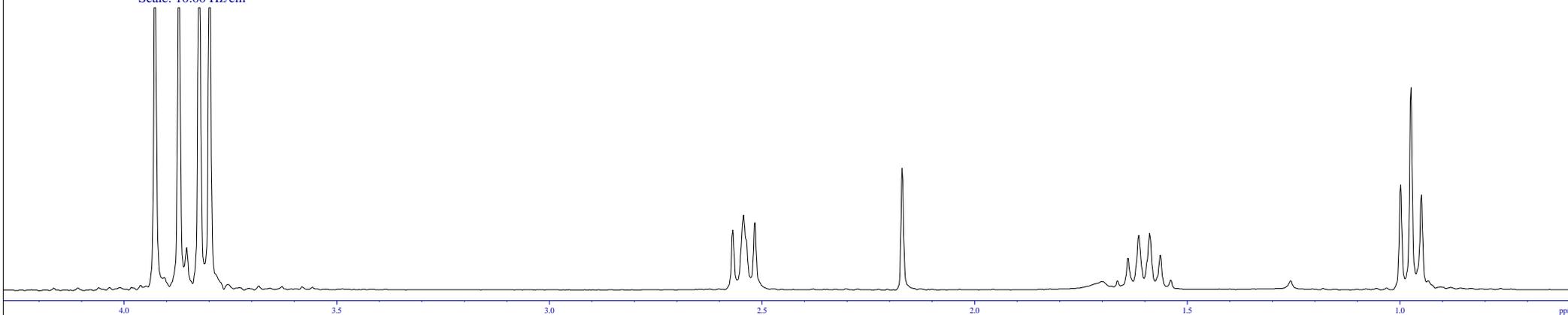
5c (NMR/50147098)

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Scale: 10.00 Hz/cm



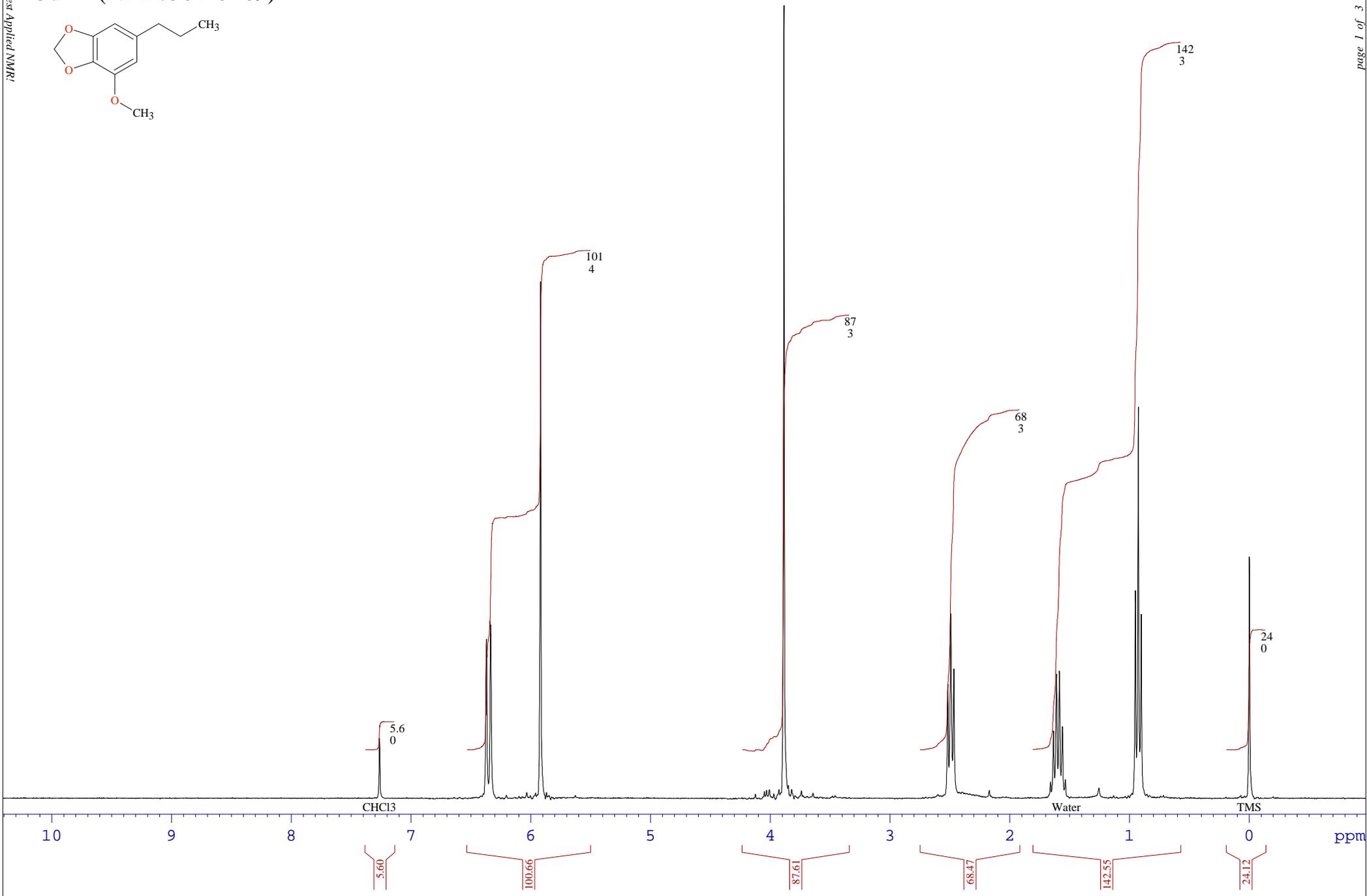
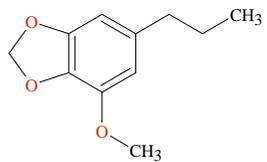
5c (NMR/50147098)

Peaks List

#	Address [points]	Frequency		Intensity [cm]
		[Hz]	[ppm]	
1	8780.8	2181.064	7.2671	1.18
2	9455.6	1933.547	6.4424	3.78
3	11513.9	1178.562	3.9268	15.65
4	11519.3	1176.592	3.9203	0.40
5	11559.8	1161.716	3.8707	15.41
6	11575.2	1156.089	3.8520	1.21
7	11598.9	1147.364	3.8229	15.01
8	11604.1	1145.476	3.8166	0.34
9	11612.3	1142.471	3.8066	0.32
10	11618.8	1140.067	3.7986	16.00
11	11624.2	1138.096	3.7920	0.35
12	12625.4	770.860	2.5684	1.88
13	12646.3	763.193	2.5429	1.97
14	12651.9	761.146	2.5361	1.17
15	12667.9	755.279	2.5165	2.08
16	12951.3	651.339	2.1702	4.43
17	13385.8	491.939	1.6391	0.98
18	13406.5	484.369	1.6139	1.47
19	13422.2	478.594	1.5946	0.58
20	13427.5	476.643	1.5881	1.54
21	13447.9	469.156	1.5632	1.01
22	13910.1	299.618	0.9983	3.50
23	13924.2	294.476	0.9812	0.32
24	13930.1	292.299	0.9739	6.86
25	13943.8	287.287	0.9572	0.38
26	13950.2	284.937	0.9494	2.94
27	14727.0	-0.001	-0.0000	4.46

Found protons = 13 impurity* = 0.9 %

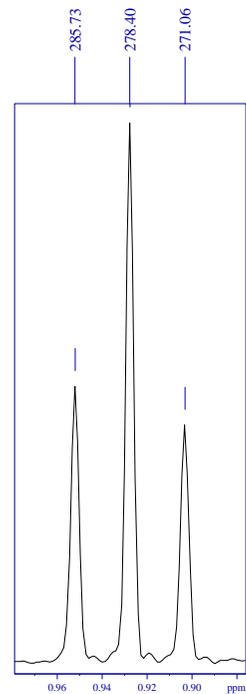
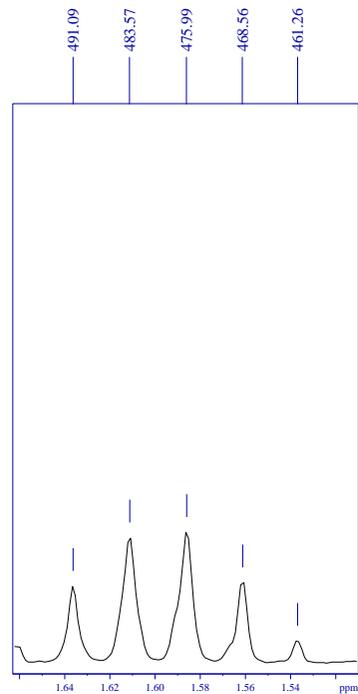
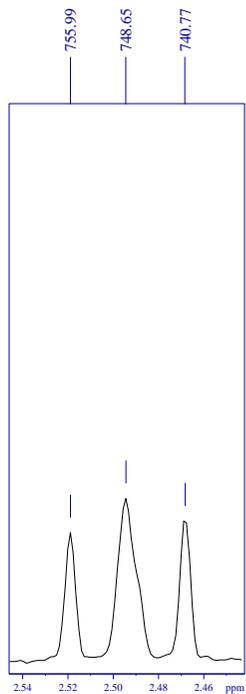
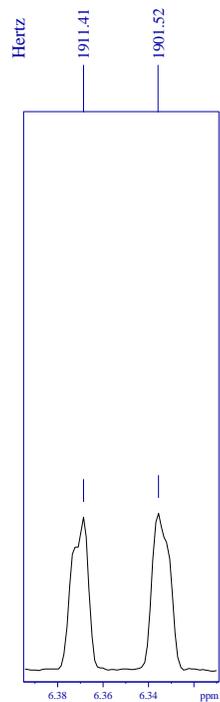
5d (NMR/50145469)



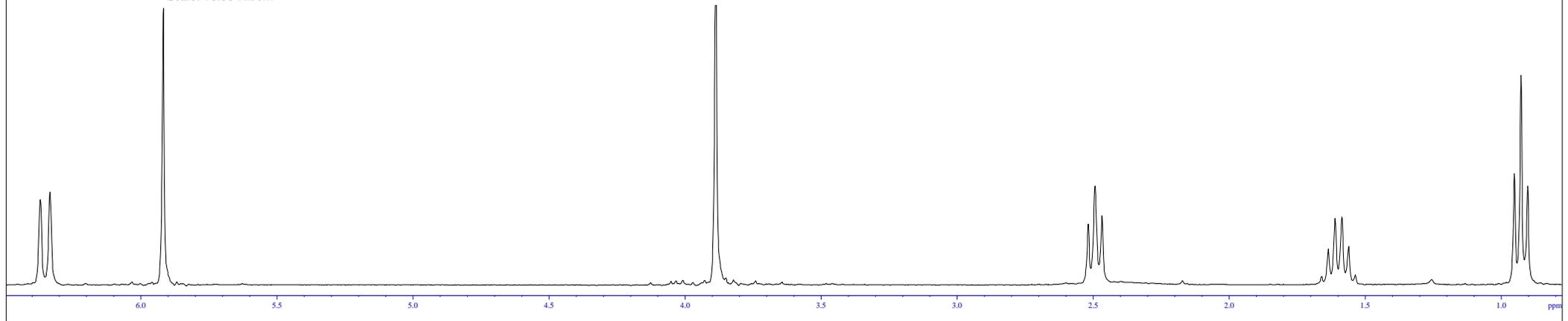
5d (NMR/50145469)

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Scale: 10.00 Hz/cm



5d (NMR/50145469)

Peaks List

#	Address [points]	Frequency [Hz]	Frequency [ppm]	Intensity [cm]
1	8780.5	2179.684	7.2625	1.24
2	9511.9	1911.412	6.3686	2.10
3	9538.9	1901.516	6.3356	2.16
4	9880.5	1776.228	5.9182	10.58
5	11541.6	1166.933	3.8881	16.00
6	12661.9	755.993	2.5189	1.78
7	12682.0	748.647	2.4944	2.25
8	12703.4	740.768	2.4682	1.99
9	13384.2	491.088	1.6363	1.05
10	13404.7	483.567	1.6112	1.74
11	13425.3	475.993	1.5860	1.81
12	13445.6	468.557	1.5612	1.13
13	13465.5	461.261	1.5369	0.31
14	13944.0	285.729	0.9520	3.79
15	13964.0	278.405	0.9276	7.40
16	13984.0	271.061	0.9031	3.26
17	14723.0	0.001	0.0000	5.09