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REVISED

SUPPORTING INFORMATION

Shortcut Syntheses of Naturally Occuring 5-Alkylresorcinols with DNA Cleaving Properties

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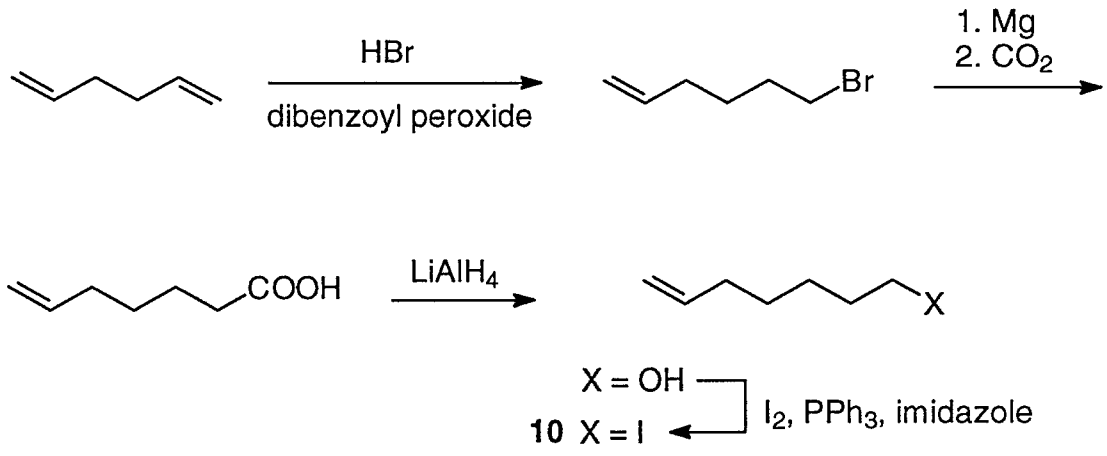
Instrumentation and Spectra Formats. NMR: Spectra were recorded on a Bruker AC 200 spectrometer at 200.2 MHz (^{1}H) and 50.3 MHz (^{13}C) in $CDCl_3$ unless stated otherwise. Chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. The multiplicity in the ^{13}C NMR spectra refers to the geminal protons (DEPT). ^{11}B NMR spectra were recorded on a Bruker AC 200 (64 MHz) with $BF_3 \cdot Et_2O$ as external standard. MS: Finnigan MAT 8200 (70 eV). Melting points: Gallenkamp apparatus (uncorrected) or DSC (Mettler Toledo Star System). Elemental analyses: Dornis & Kolbe, Mülheim. Flash chromatography: Merck silica gel 60 (230-400 mesh).

Large Scale Preparation of 7-Iodo-1-heptene (10)



Scheme 5.

6-Bromo-1-hexene. A three necked flask equipped with a gas inlet and a reflux condenser cooled to -78 °C is charged with 1,5-hexadiene (174.64 g, 2.1 mmol) and dibenzoyl peroxide (0.9 g). HBr gas (8 g) is bubbled into this mixture at -4°C - 0°C, with the HBr up-take being monitored by weighting the gas bomb. Another portion of dibenzoyl peroxide (0.45 g) is then added, followed by condensation of another 8 g of HBr. This portionwise process is repeated 4 times until a total amount of 42 g of HBr and 2.77 g of dibenzoyl peroxide have been introduced into the flask. The resulting solution is stirred at 0°C for 60 min. For work-up the reaction is quenched with water, the organic layer is washed twice with saturated aqueous $NaHCO_3$ and dried (Na_2SO_4), unreacted 1,5-hexadiene is distilled off (125.4 g) through a Vigreux column, followed by distillation of 6-bromo-1-hexene (54.12 g). bp = 41-42 °C (15 torr). The analytical data of the product were identical to that of a commercially available sample.

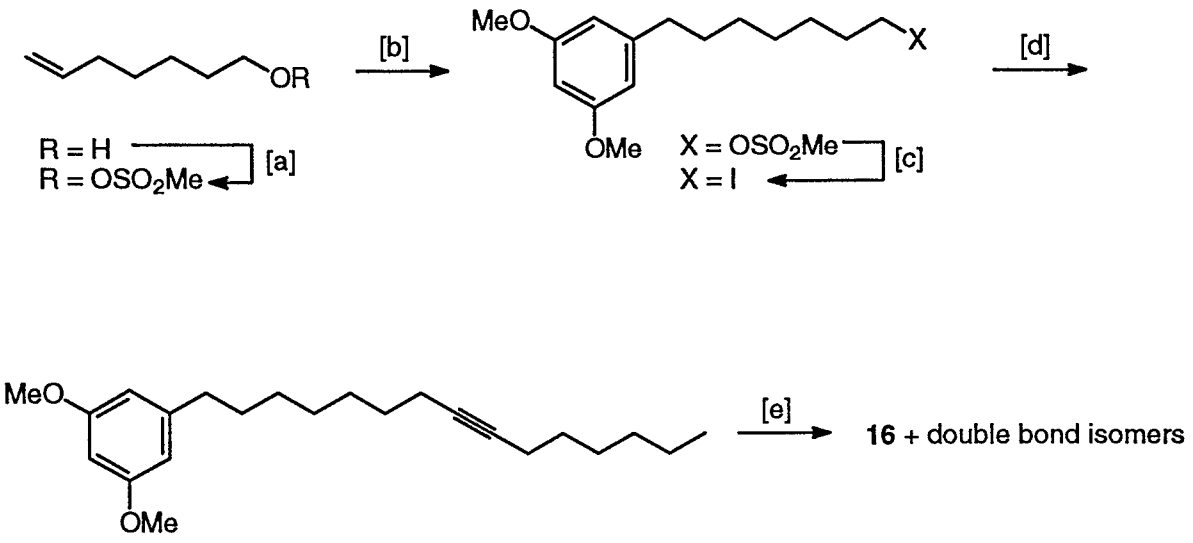
6-Heptenoic Acid. To a suspension of Mg turnings (8.75 g, 360 mmol) activated by a crystal of iodine in Et_2O (250 mL) is added 6-bromo-1-hexene (55.22 g, 339 mmol) at such a rate that the solvent is gently refluxing. Once the addition is complete, the mixture is stirred for

5 h at ambient temperature. Unreacted Mg is filtered off and the resulting solution of 5-hexenylmagnesium bromide is slowly added at -20 °C under an atmosphere of CO_2 to Et_2O (500 mL) saturated with CO_2. The resulting suspension is allowed to warm to ambient temperature, carefully quenched by slowly adding HCl (250 mL, 15% w/w), the organic layer is separated and dried (Na_2SO_4), the solvent is evaporated and the residue purified by distillation using a concentric tube column to afford 6-heptenoic acid (26.2 g, 60%). bp = 95-96 °C/5 torr. The product was identical to a commercially available sample in all analytical respects.

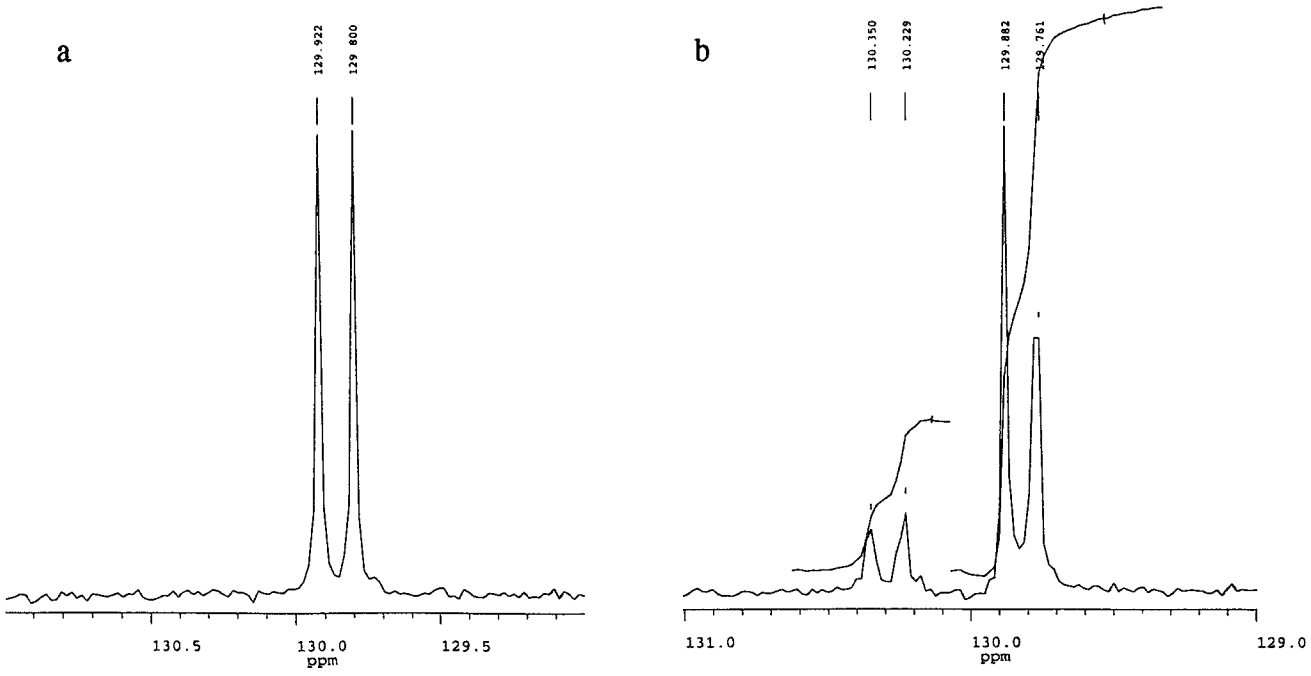
6-Hepten-1-ol. A solution of 6-heptenoic acid (4.66 g, 36 mmol) in Et_2O (20 mL) is slowly added to a suspension of $LiAlH_4$ (1.656 g, 44 mmol) in Et_2O (100 mL) causing the solvent to boil. After complete addition the mixture was refluxed for another 4 h, carefully quenched with crushed ice, the organic layer was separated and dried (Na_2SO_4) and the solvent evaporated *in vacuo*. The resulting product (3.86 g, 93%) was pure enough (GC: 98%) for direct further use. ^{1}H NMR: δ = 5.81 (ddt, 1H), 4.90-5.05 (m, 2H), 3.62 (t, 2H, J = 7), 2.07 (q, 2H, J = 7), 2.01 (br. s, -OH), 1.35-1.60 (m, 6H).- ^{13}C NMR: δ = 138.8, 114.3, 62.7, 33.5, 32.5, 28.6, 25.2.- MS, *m/z* (rel. intensity): 114 (< 1) [M^+], 96 (7), 81 (42), 68 (65), 67 (72), 57 (26), 55 (91), 54 (100), 43 (40), 41 (84), 39 (51), 31 (67), 27 (44).

7-Iodo-1-heptene (**10**). To a rapidly stirred solution of 6-hepten-1-ol (2.75 g, 24 mmol) in toluene (200 mL) are successively added PPh_3 (6.63 g, 25 mmol), imidazole (4.92 g, 72 mmol) and iodine (6.73 g, 53 mmol). The mixture is stirred for 1.5 h at ambient temperature, the solvent is decanted, the residue is washed twice with toluene (50 mL each), the combined fractions are evaporated and the residue is purified by distillation affording the product as a colorless liquid (3.78 g, 70%). bp = 34-35 °C (10^{-2} torr). ^{1}H NMR: δ = 5.80 (ddt, 1H, J = 7, 9, 15), 4.92-5.05 (m, 2H), 3.19 (t, 2H, J = 7), 2.06 (q, 2H, J = 7), 1.84 (quint., 2H, J = 7), 1.41 (m, 4H).- ^{13}C NMR: δ = 138.5, 114.6, 33.5, 33.4, 29.9, 27.8, 7.0.- MS, m/z (rel. intensity): 224 (9) [M^+], 155(3), 97 (40), 69 (8), 55 (100), 41 (27).

Alternative Synthesis of Compound 16



Scheme 6: [a] $MeSO_2Cl$, CH_2Cl_2, Et_3N, 1h, 0°C, 93%; [b] (i) 9-H-9-BBN, THF, 2h, r.t.; (ii) NaOMe, 0.5h, r.t.; (iii) **7**, $PdCl_2$(dppf) (3 mol%), THF, 1h, reflux, 85%; [c] LiI, THF, 3h, r.t., 97%; [d] 1-propynyl lithium, THF, 20h, reflux, 76%; [e] Lindlar catalyst, H_2 (1 atm), hexane, 3h, r.t., 95% (inseparable mixture of isomers, see ^1H and ^{13}C NMR).



Olefinic region in the ^{13}C NMR spectrum of compound **16** prepared (a) by the boron-reaction manifold according to Scheme 2, (b) by Lindlar hydrogenation according to Scheme 6.

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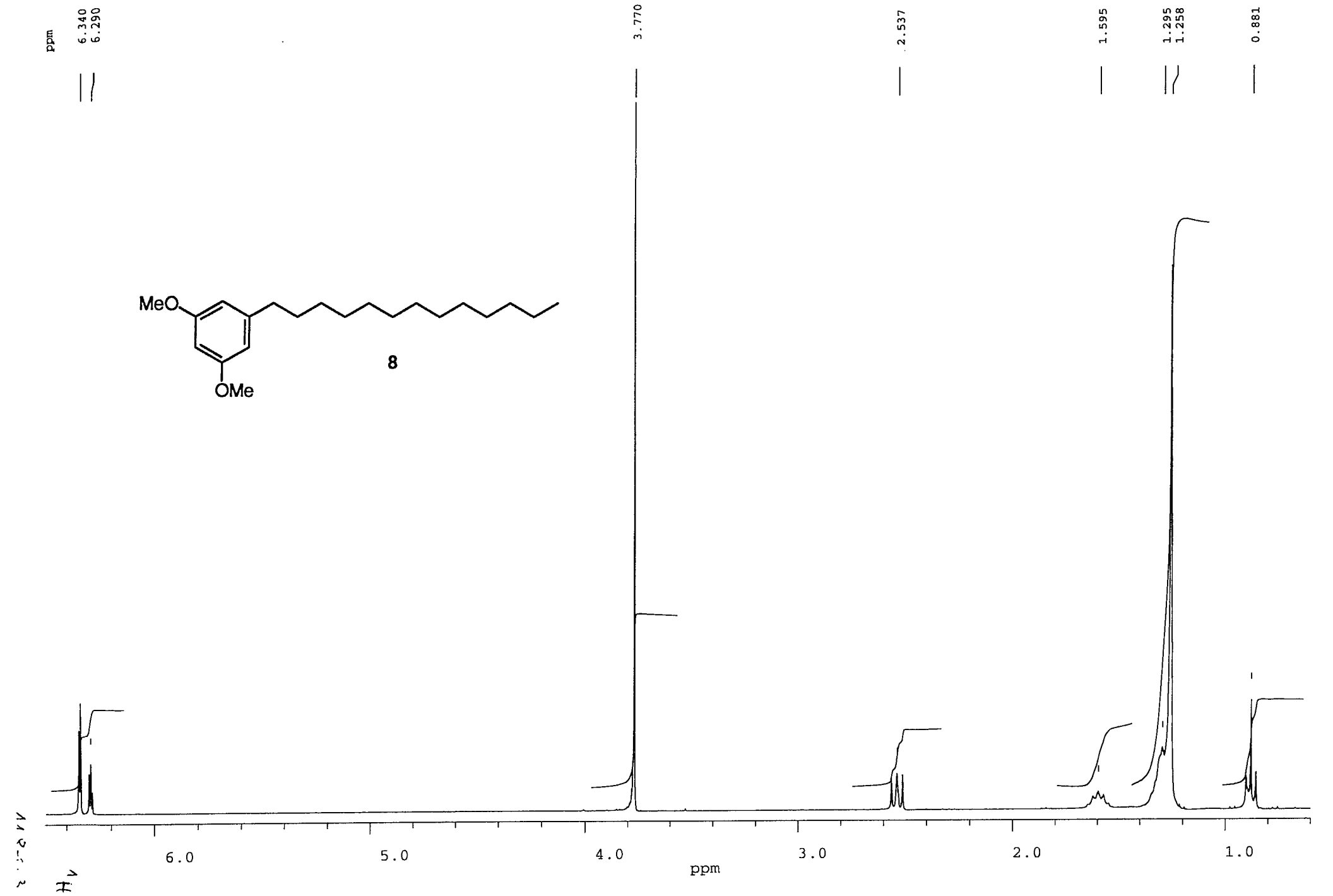
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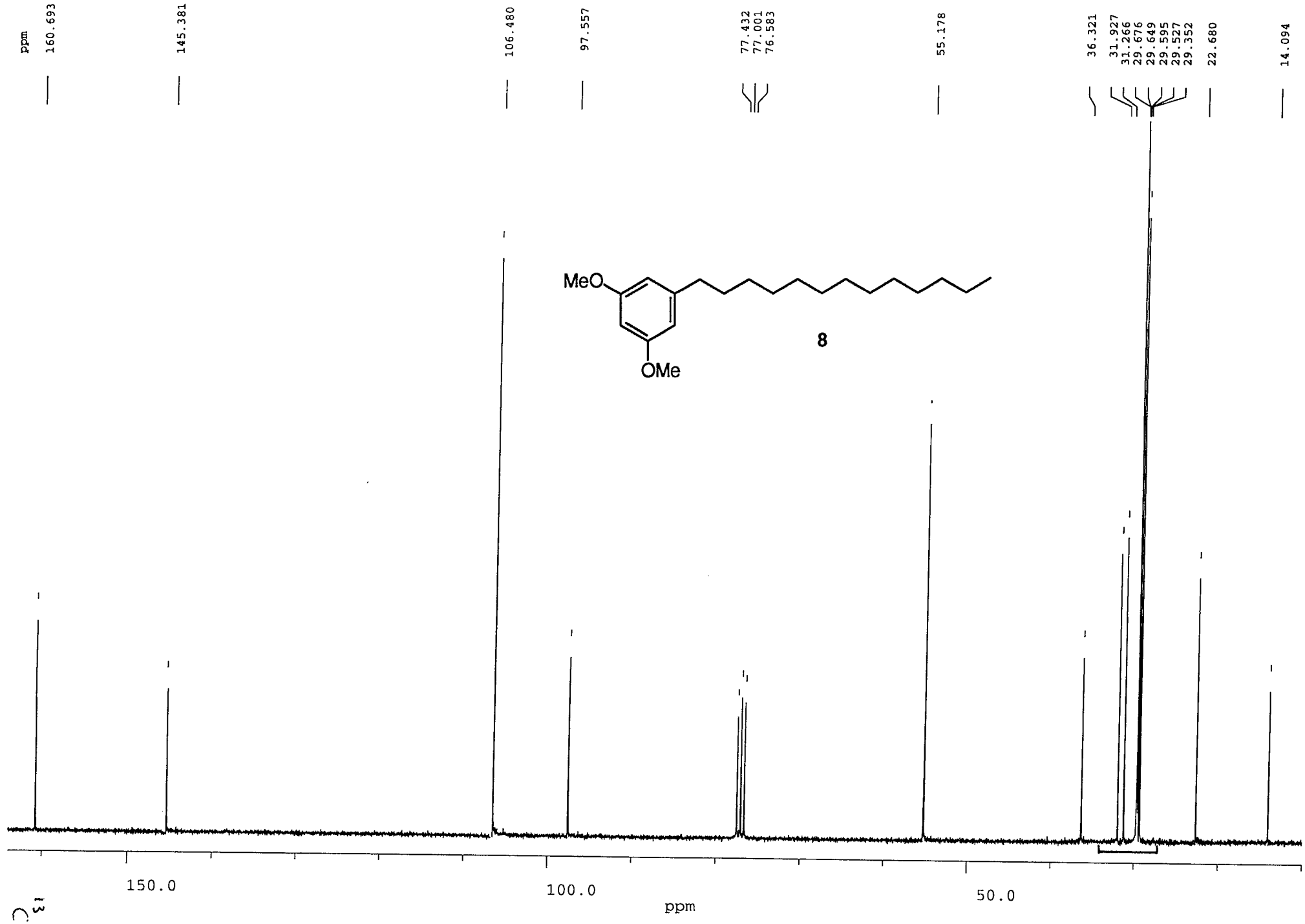
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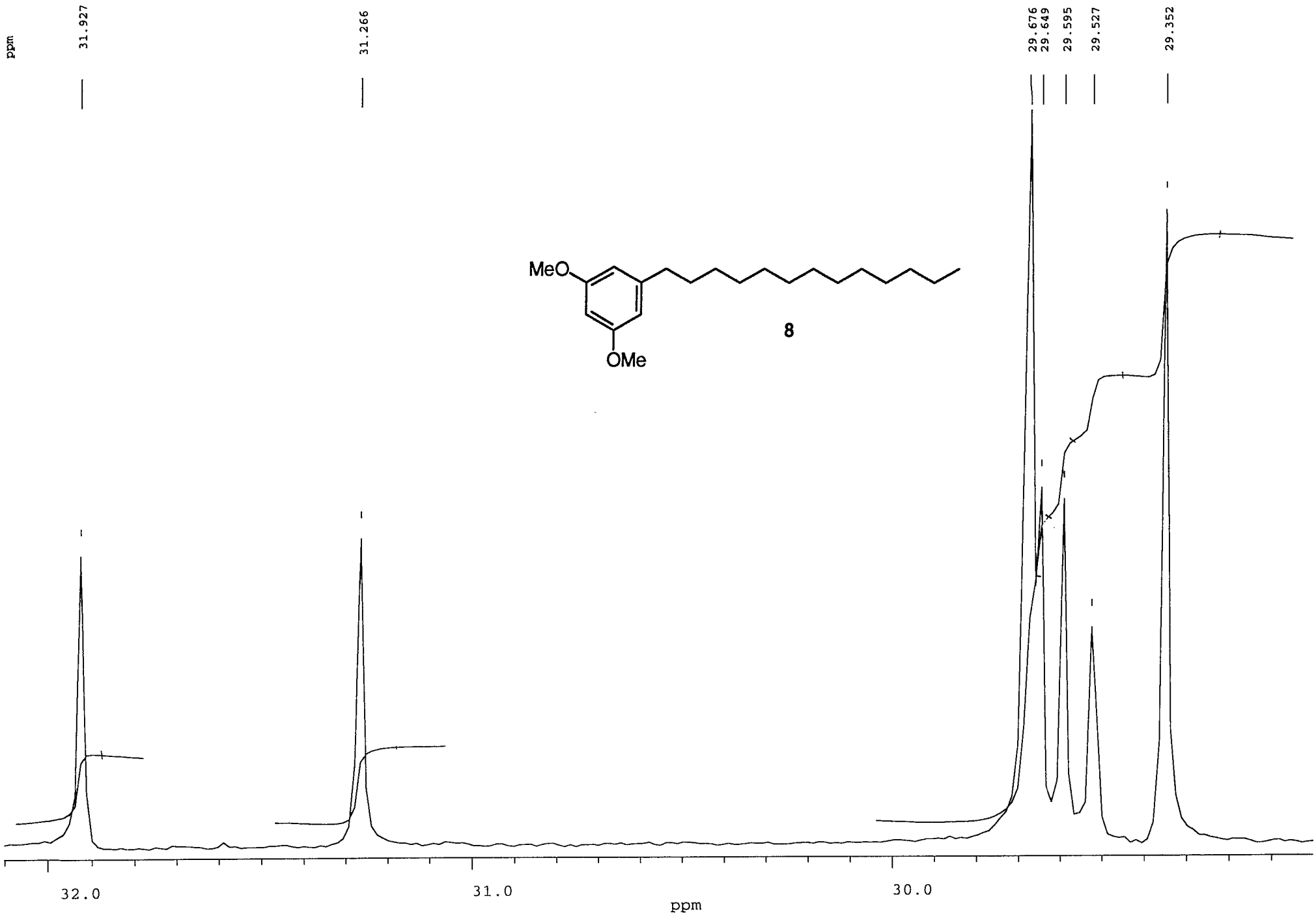
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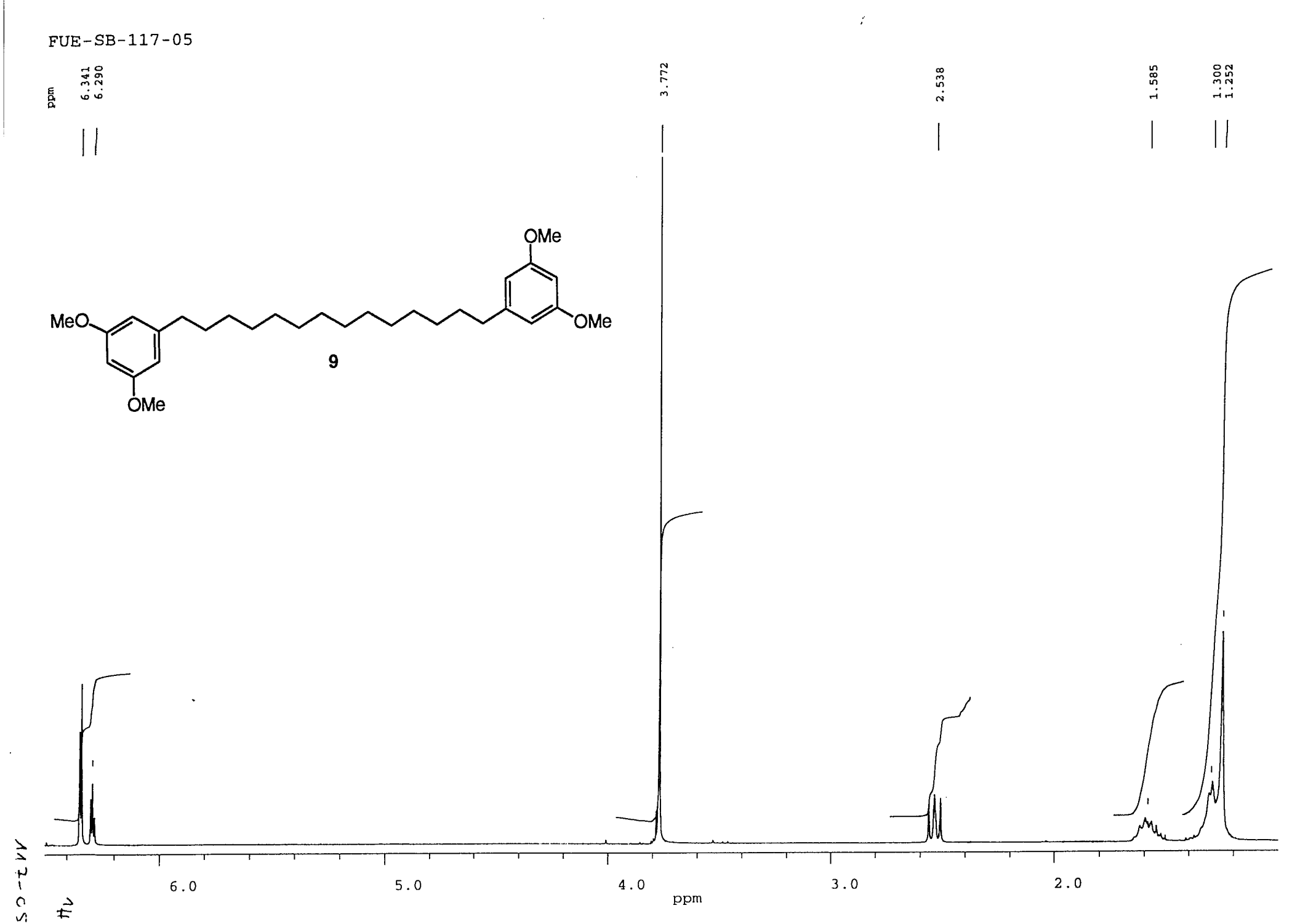
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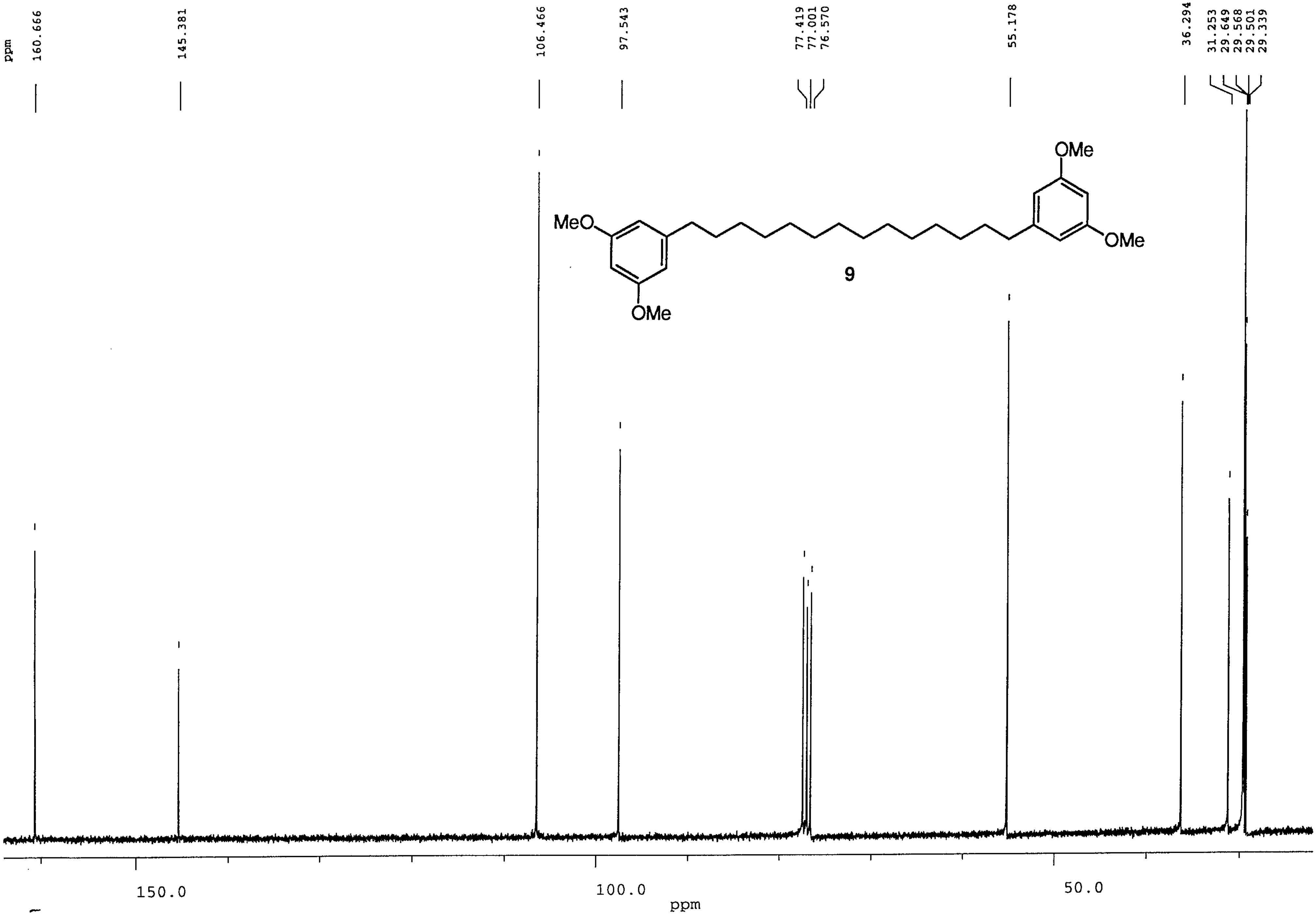
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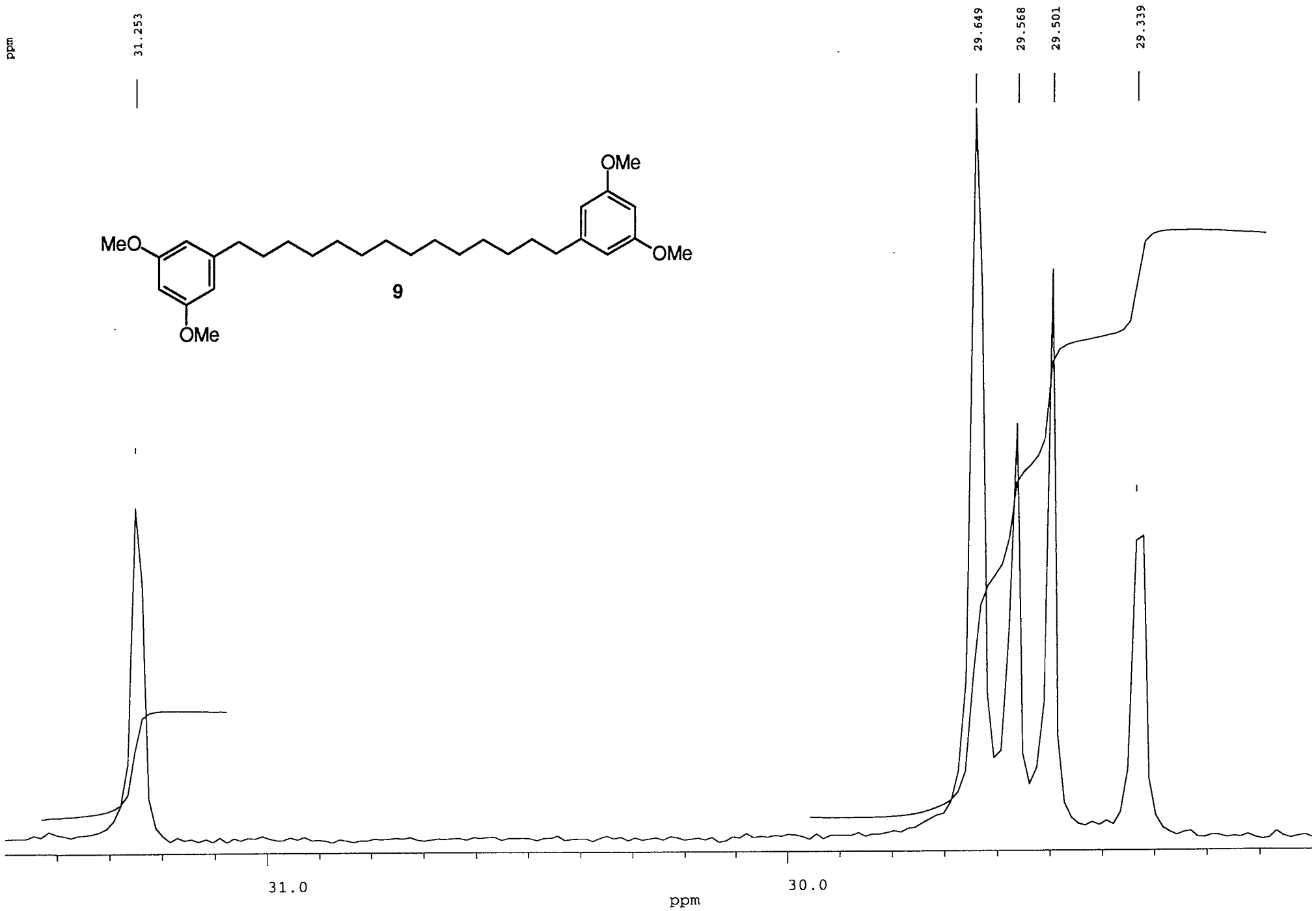
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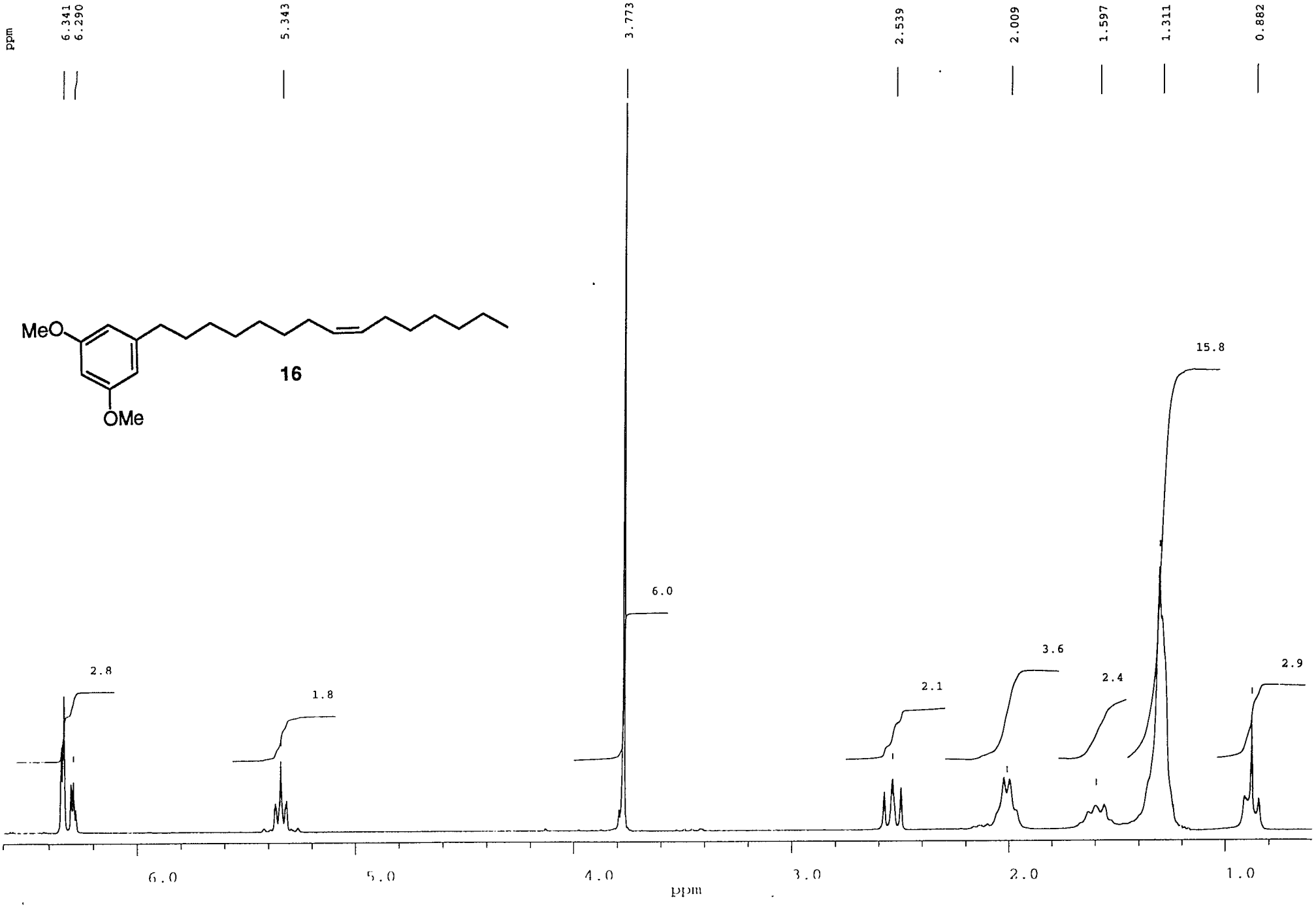
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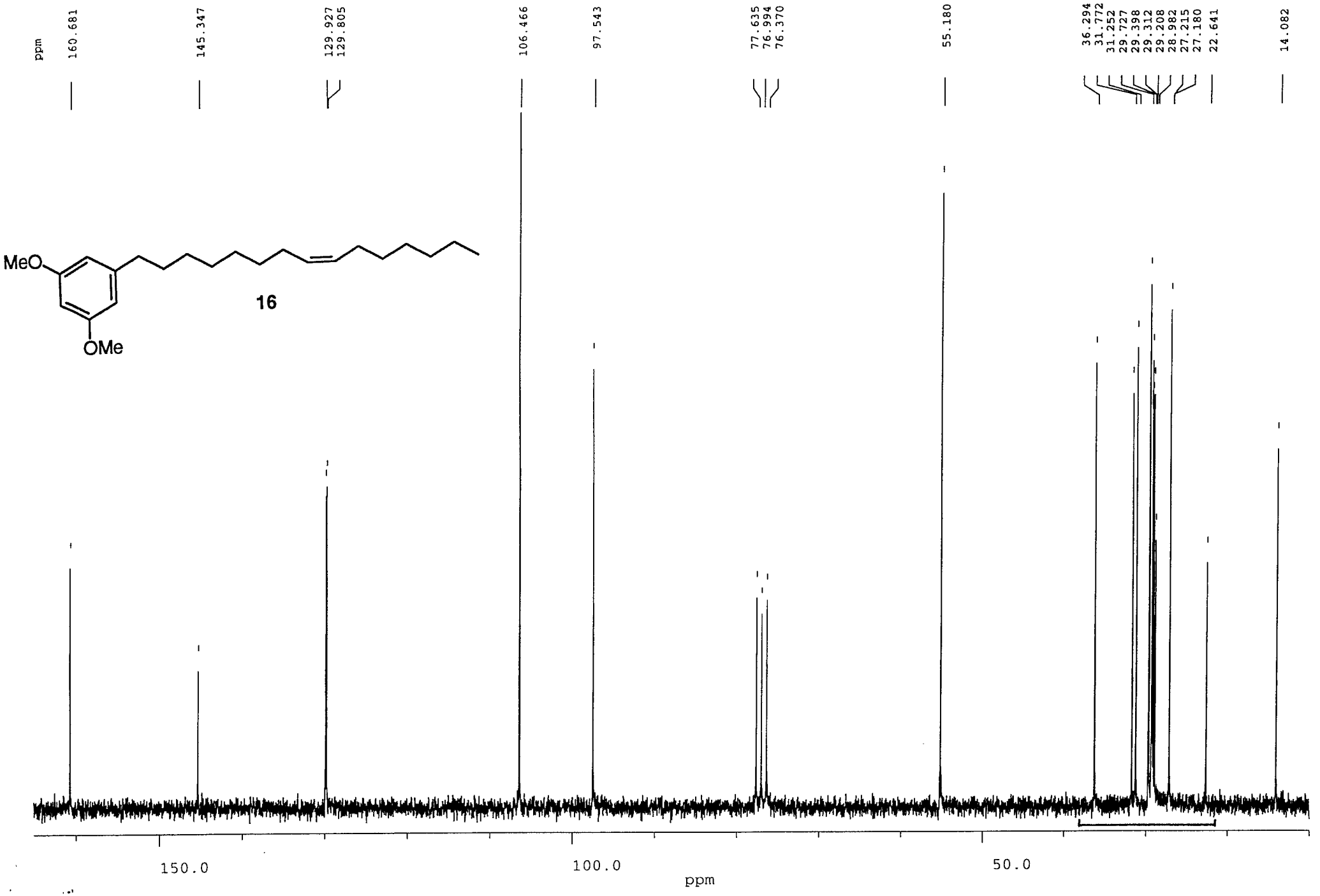
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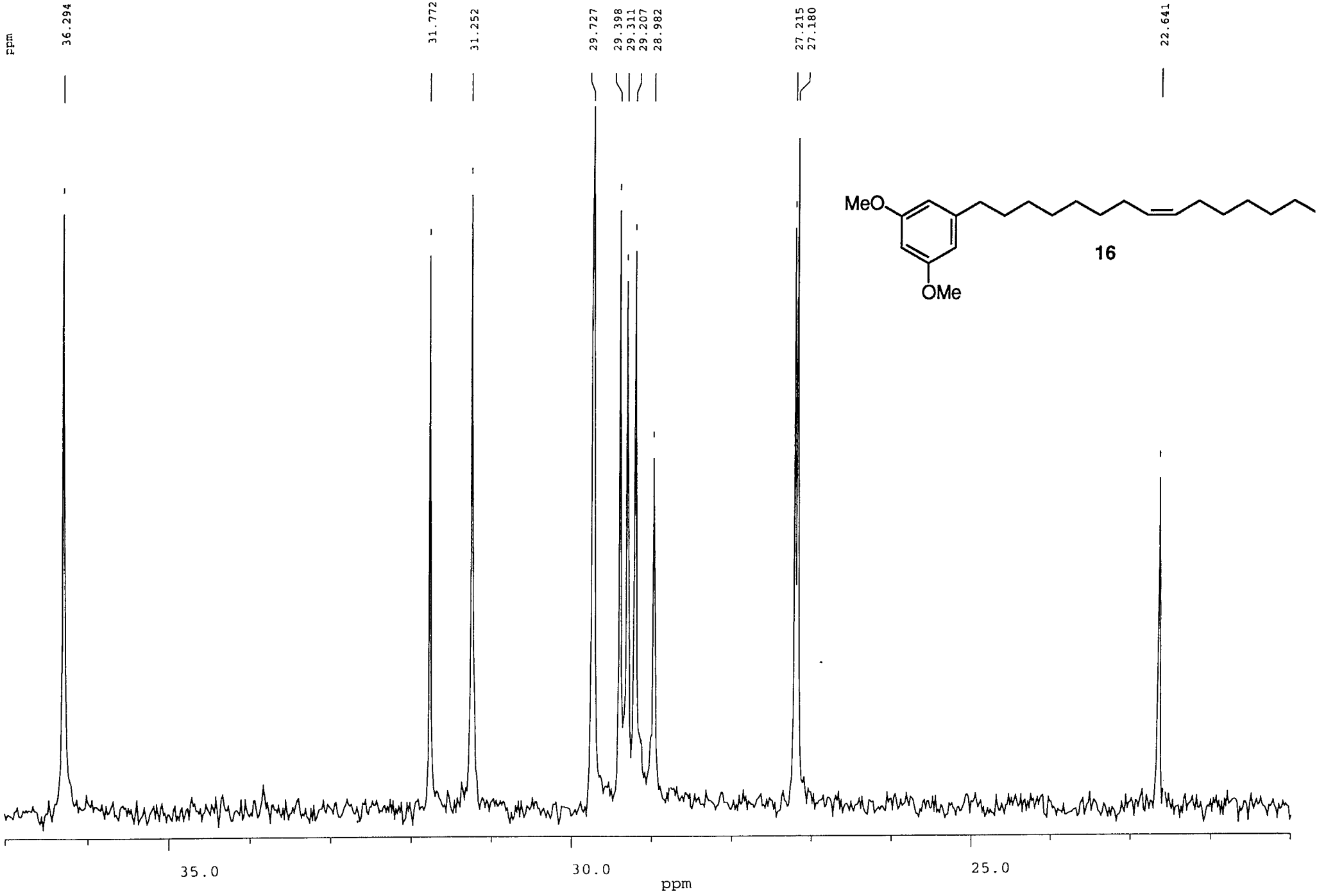
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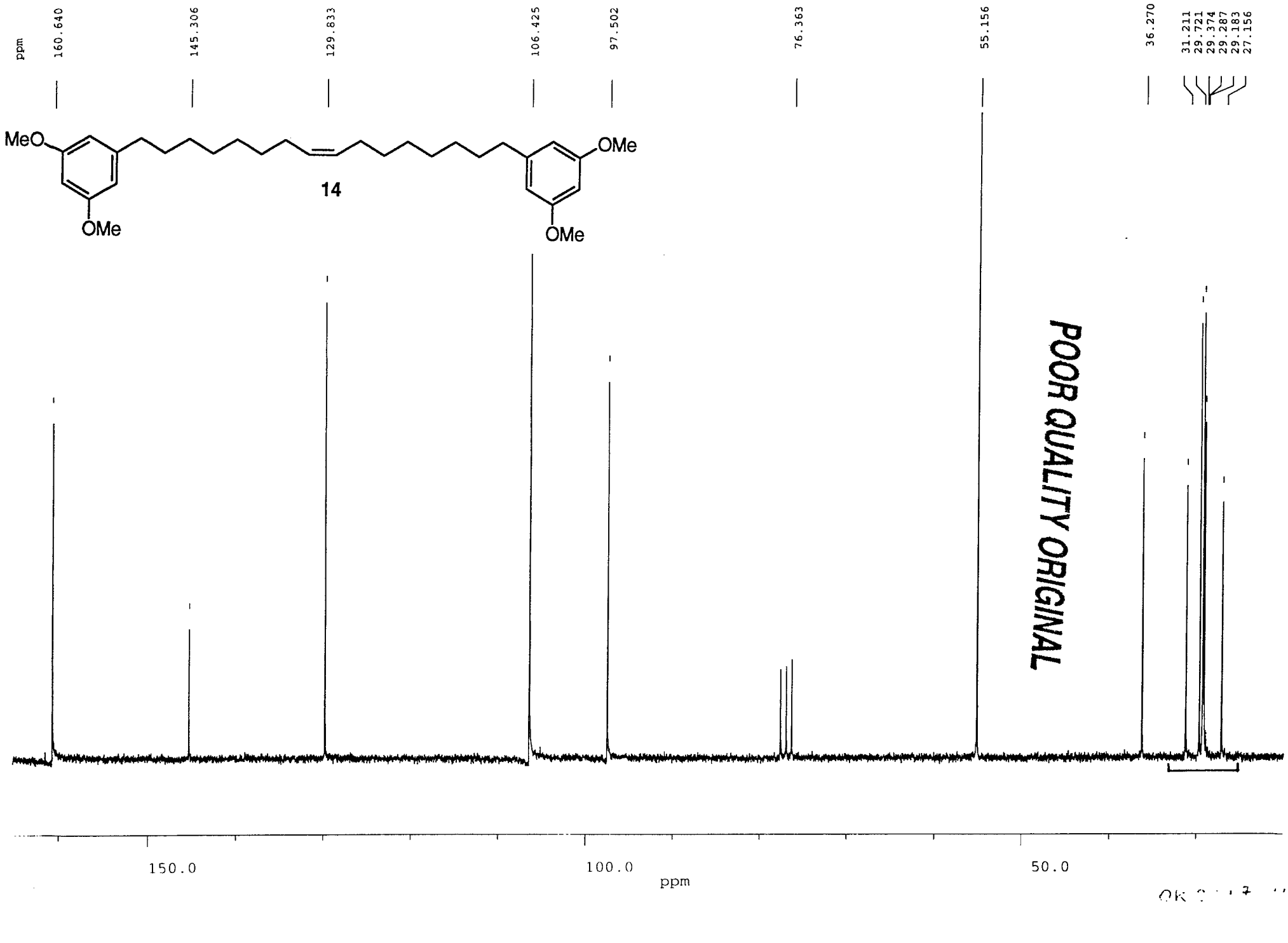
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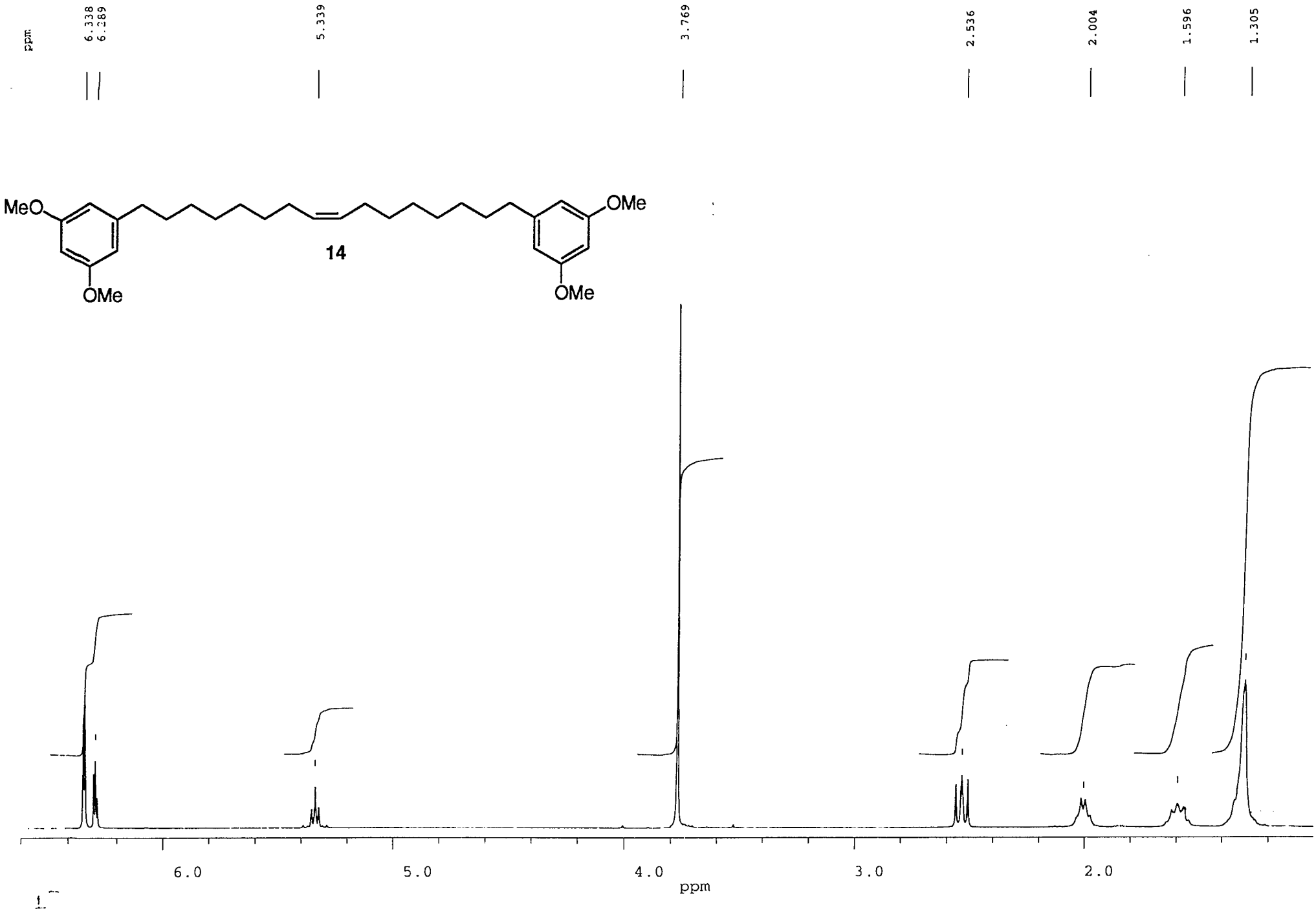
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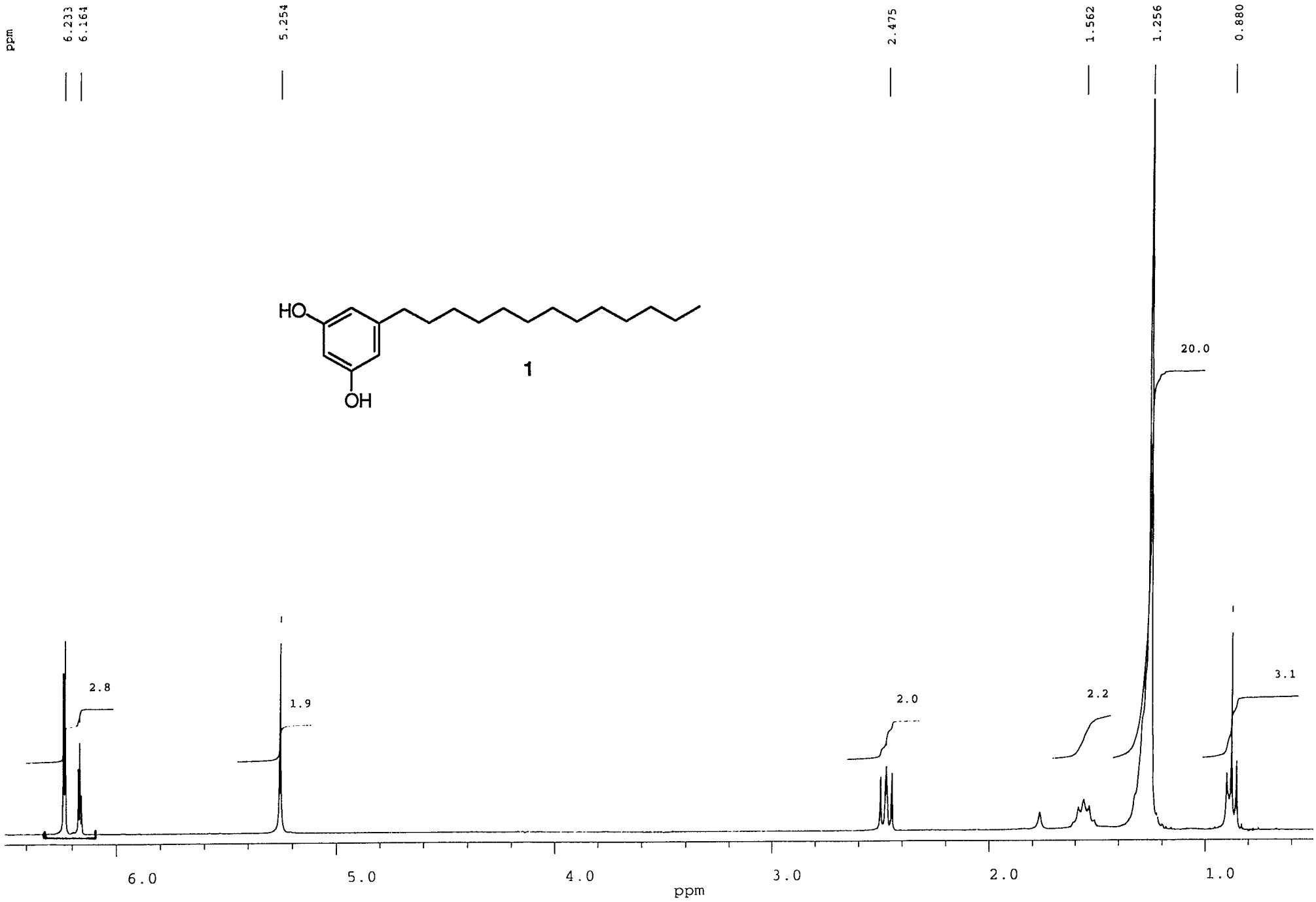
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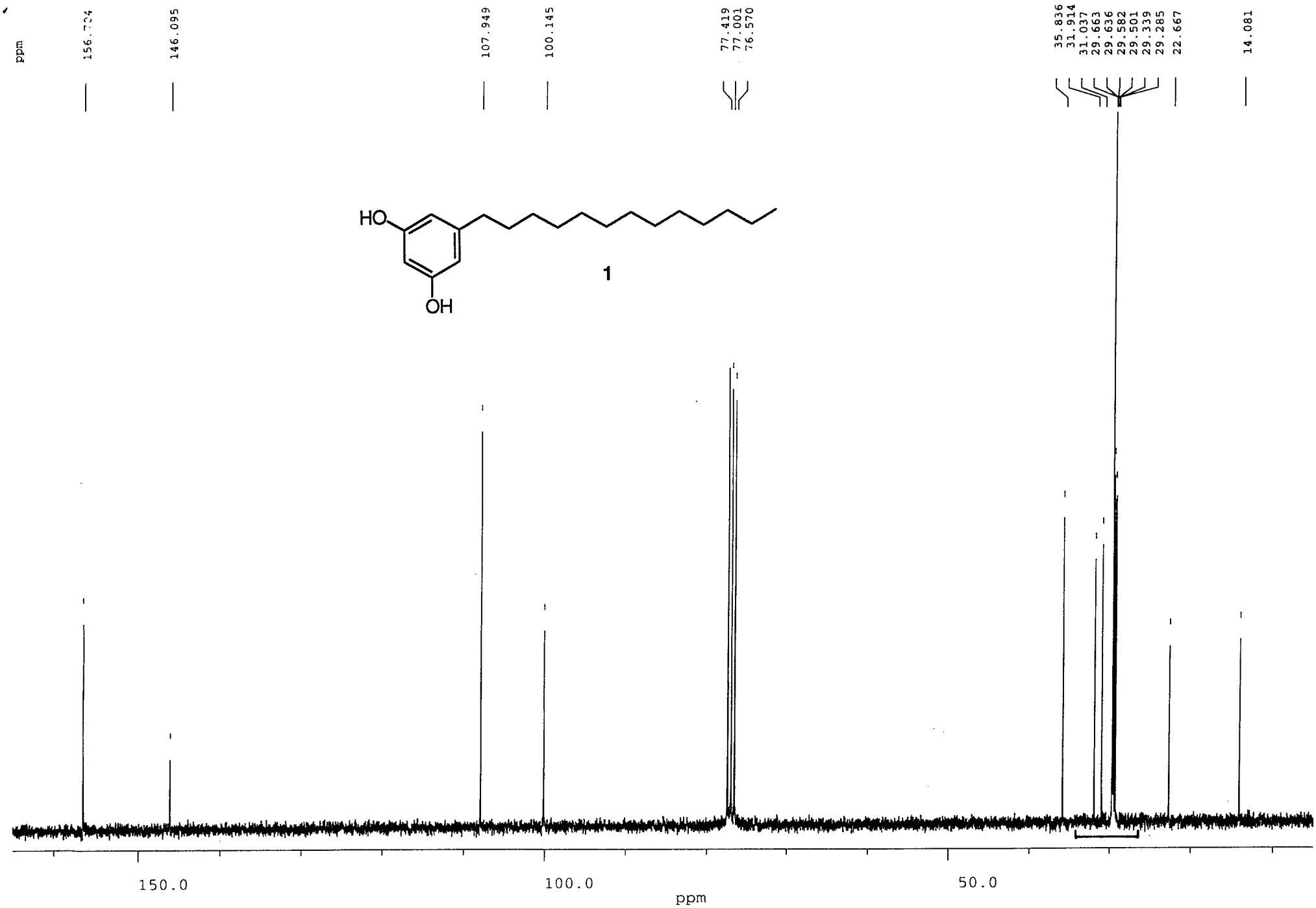
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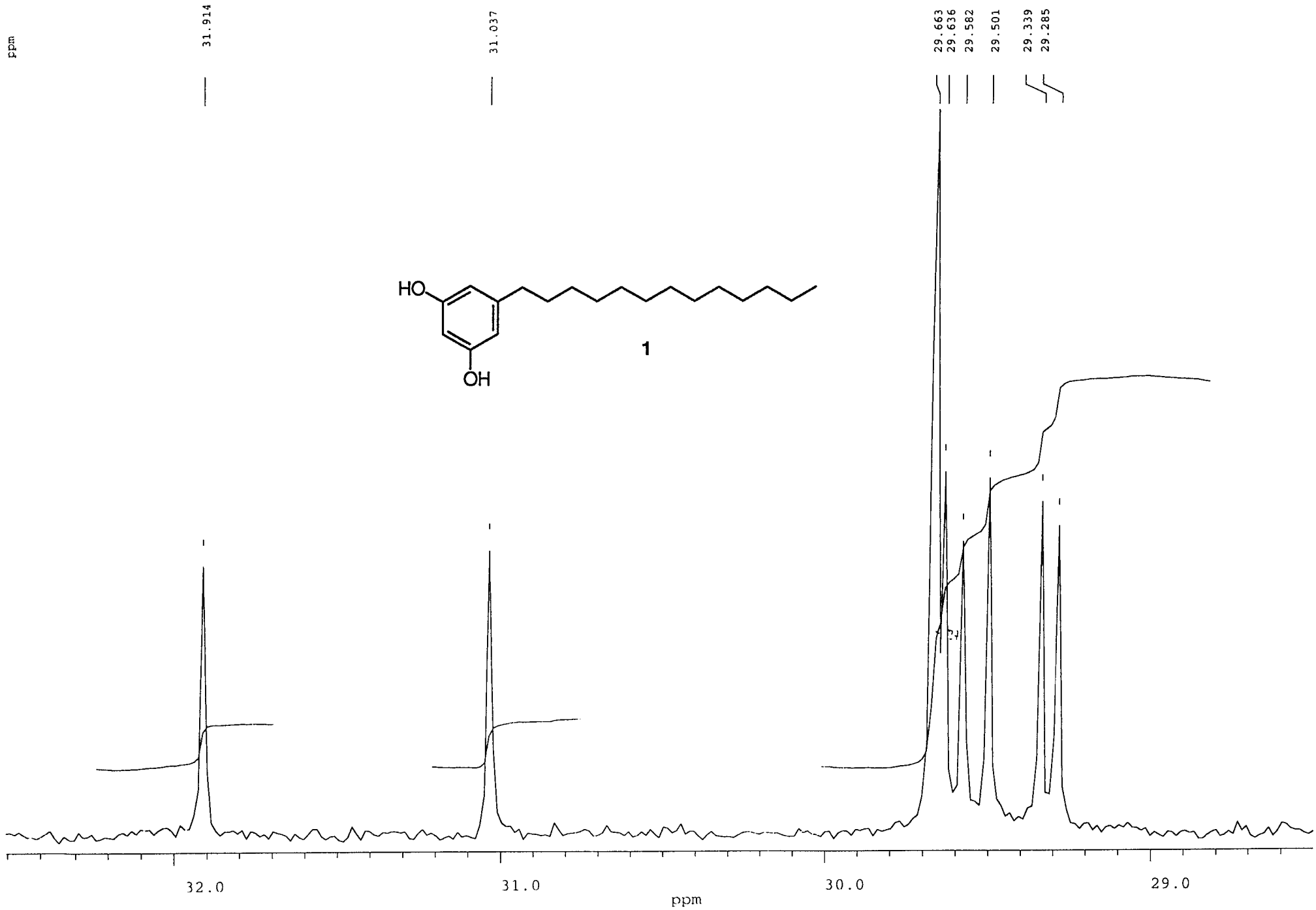
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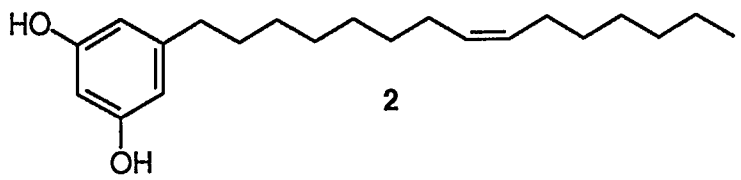

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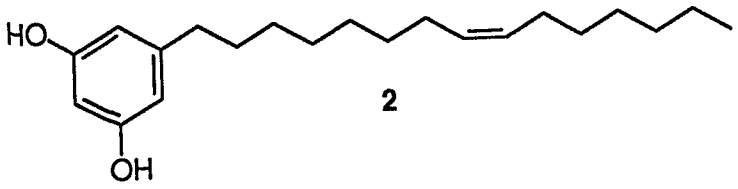
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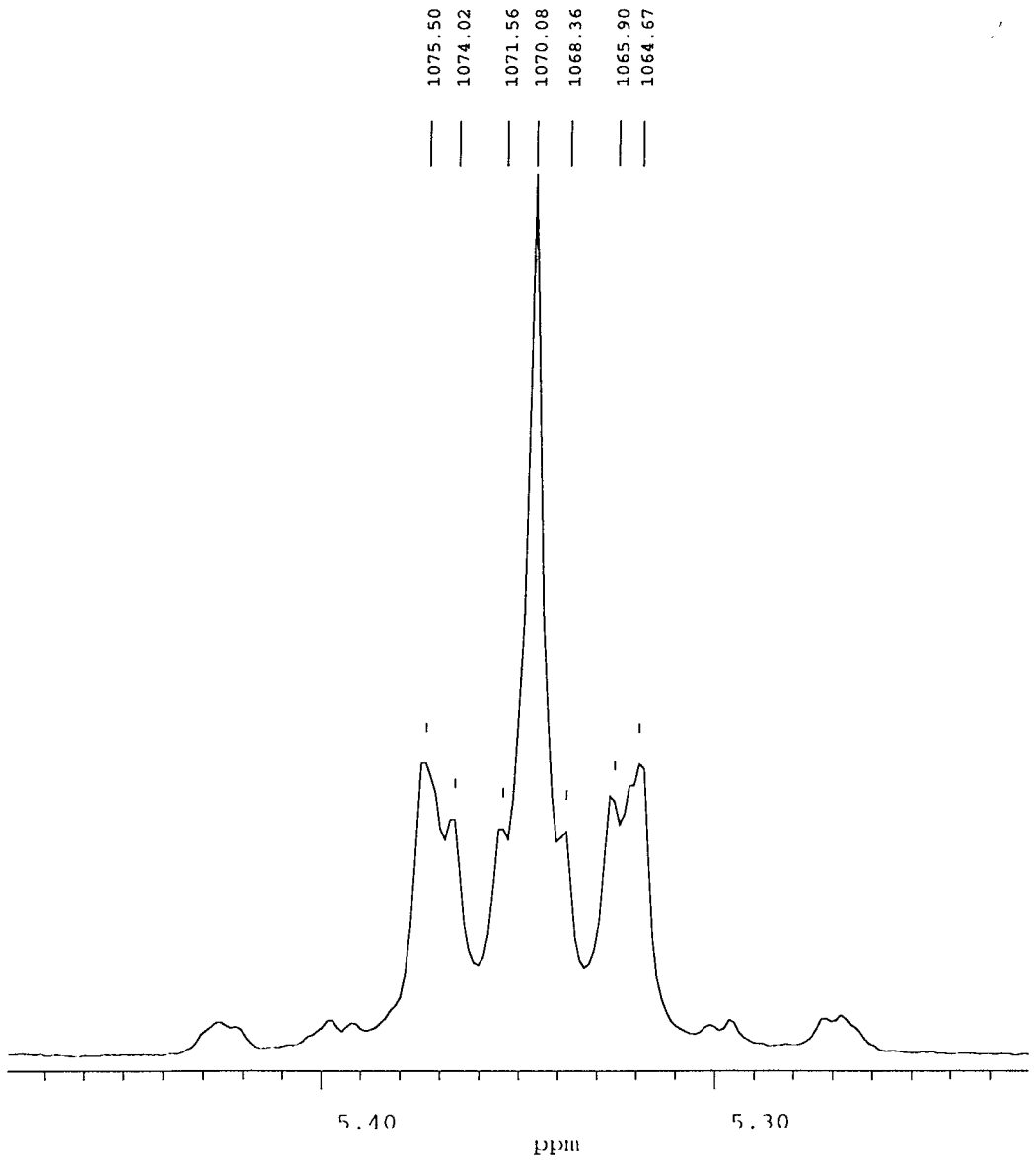
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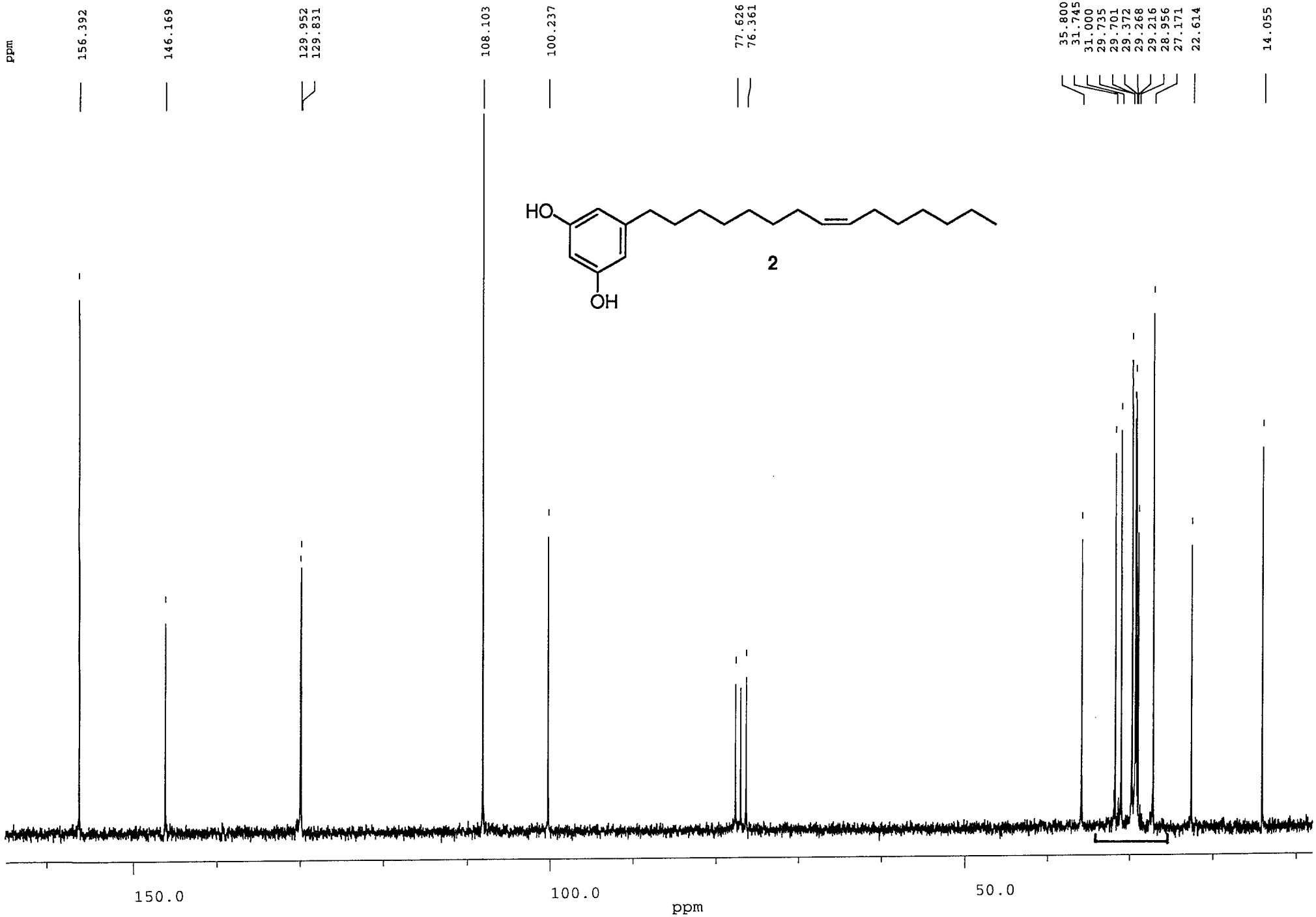
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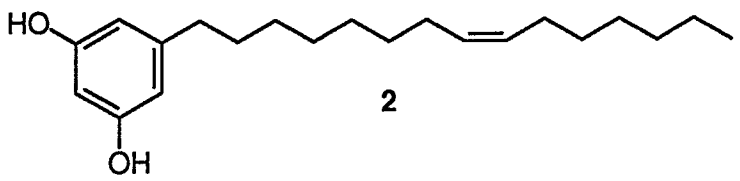

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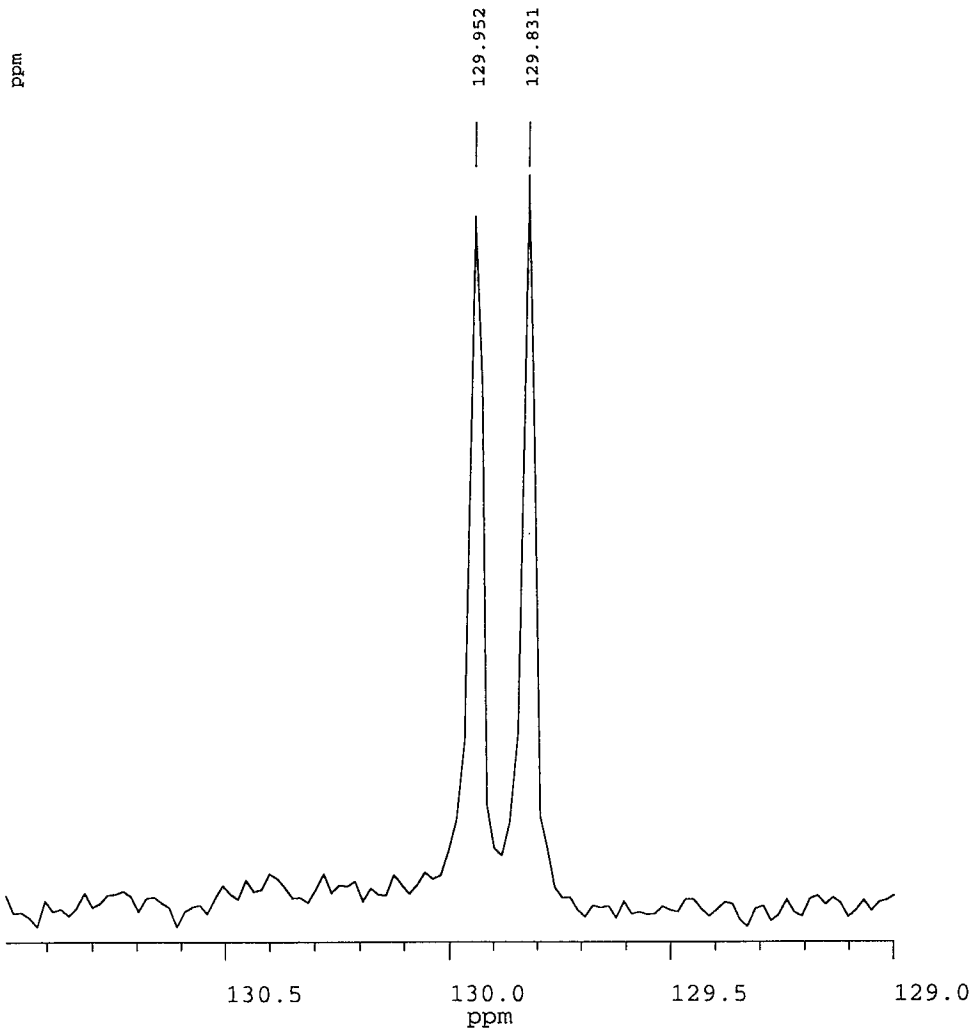

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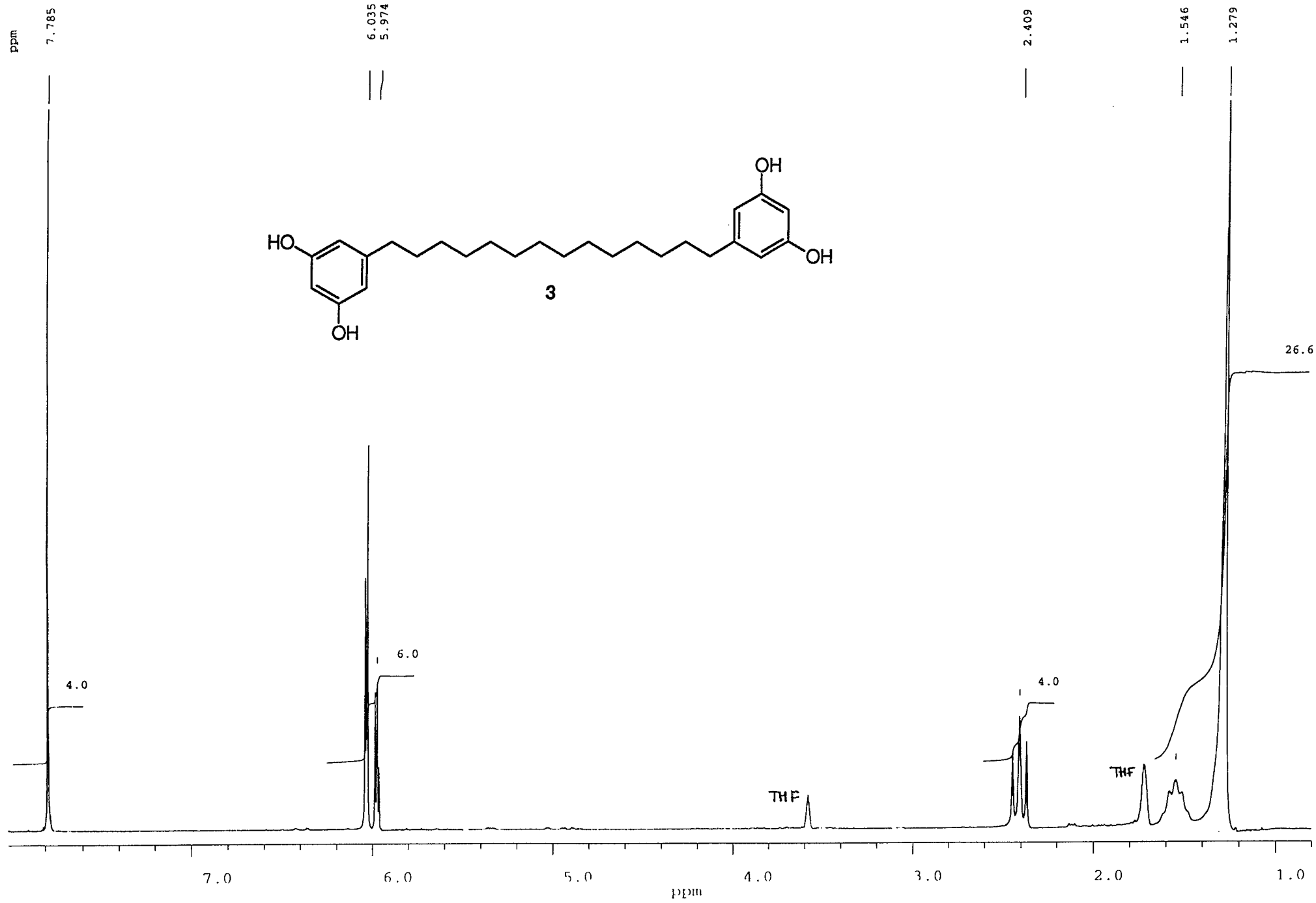
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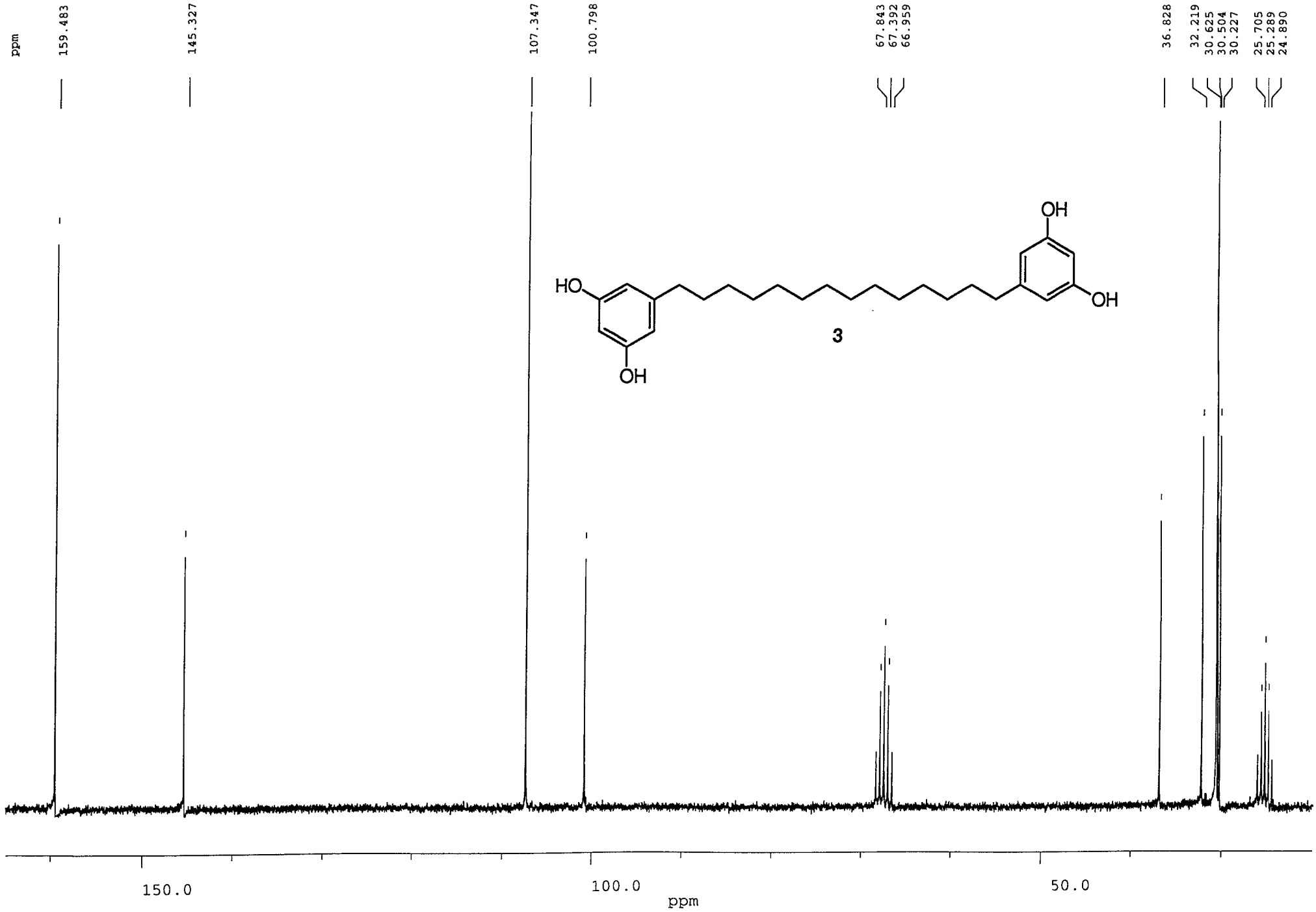
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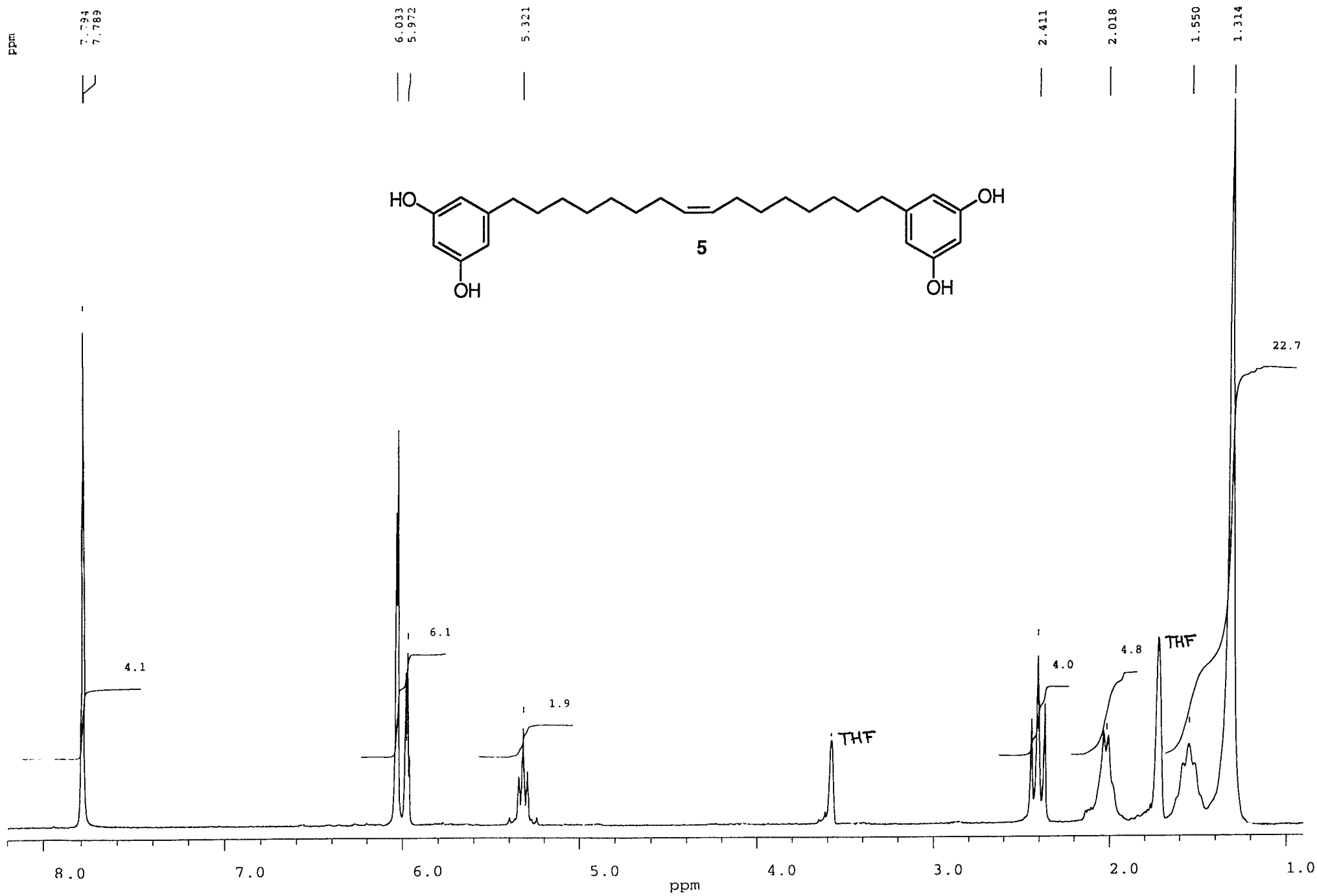
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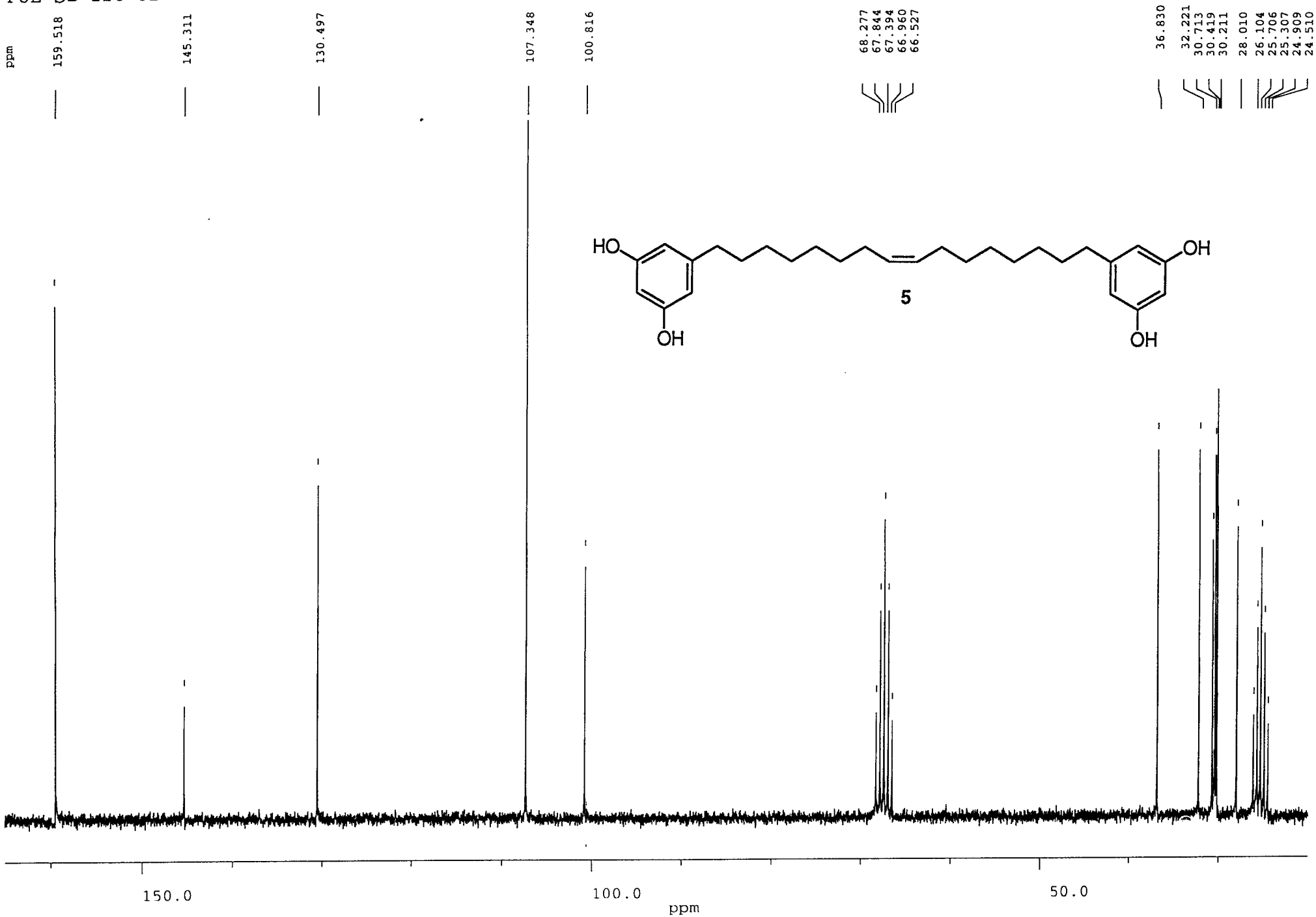
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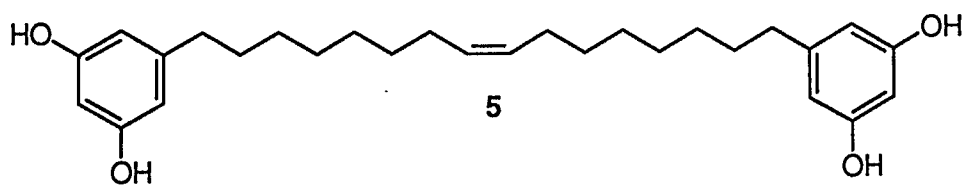
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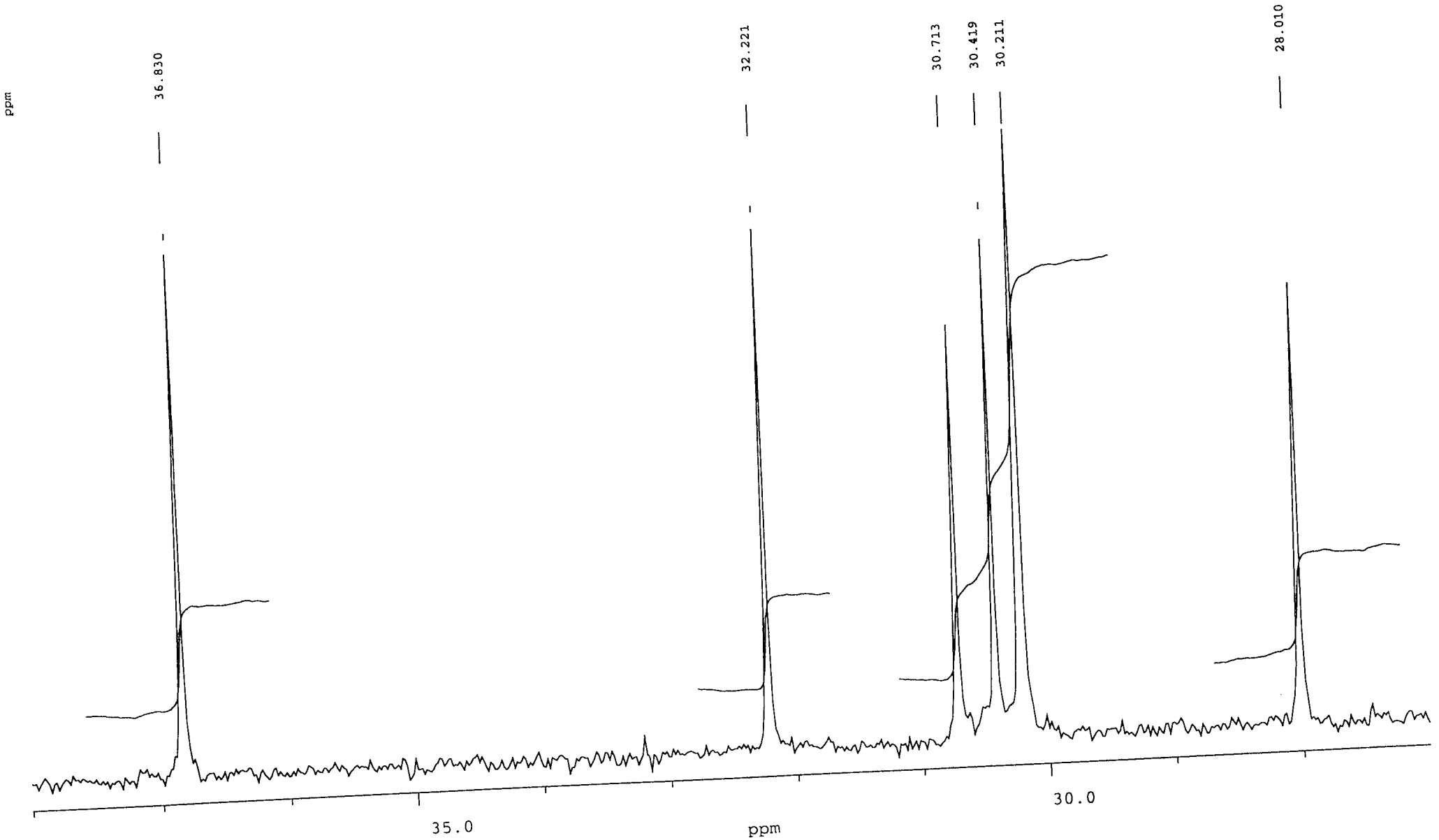
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^exo FUE-SB-227-02 11.12.1996 09:02:2

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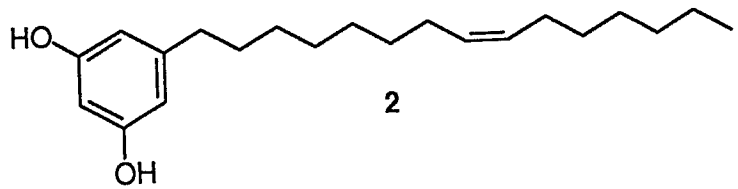
FUE-SB-227-02, 4.5500 mg

Methodenname: 0-80°C/5°C/MIN_



2

2
mW

22°C

32°C

Integral	-82.28 mJ
normalis.	-18.08 Jg^-1
Onset	15.64 °C
Peakhöhe	0.99 mW
Peak	22.18 °C
Extrapol. Peak	22.01 °C
Peakweite	16.47 °C

Integral	-167.74 mJ
normalis.	-36.87 Jg^-1
Onset	25.42 °C
Peakhöhe	2.12 mW
Peak	31.97 °C
Extrapol. Peak	32.30 °C
Peakweite	7.28 °C

0 10 20 30 40 50 60 70 °

L: Dreier

METTLER TOLEDO STAR^{e} Syste

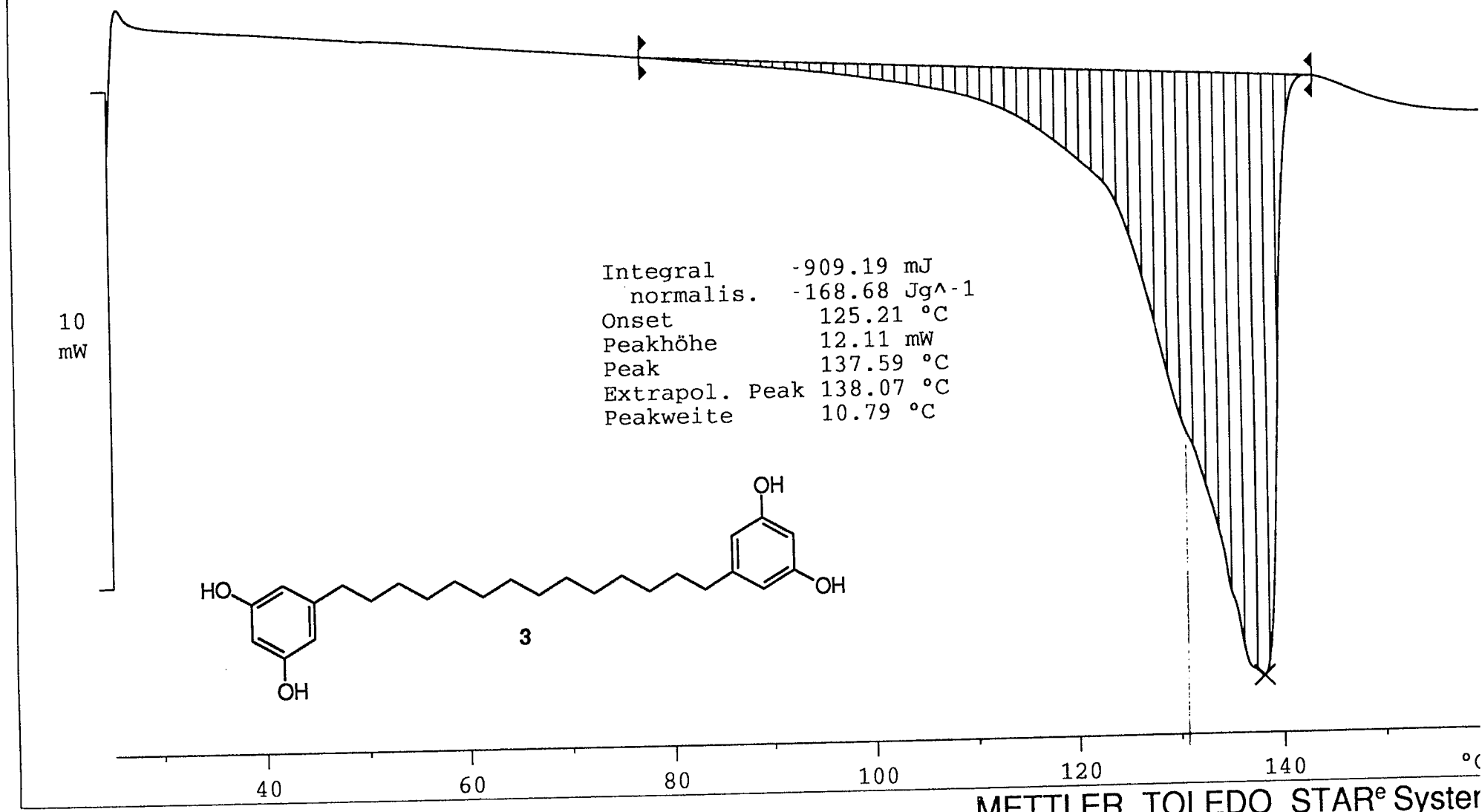
^exo

FUE-SA-224-01/VIRGIN

27.11.1996 09:16:19

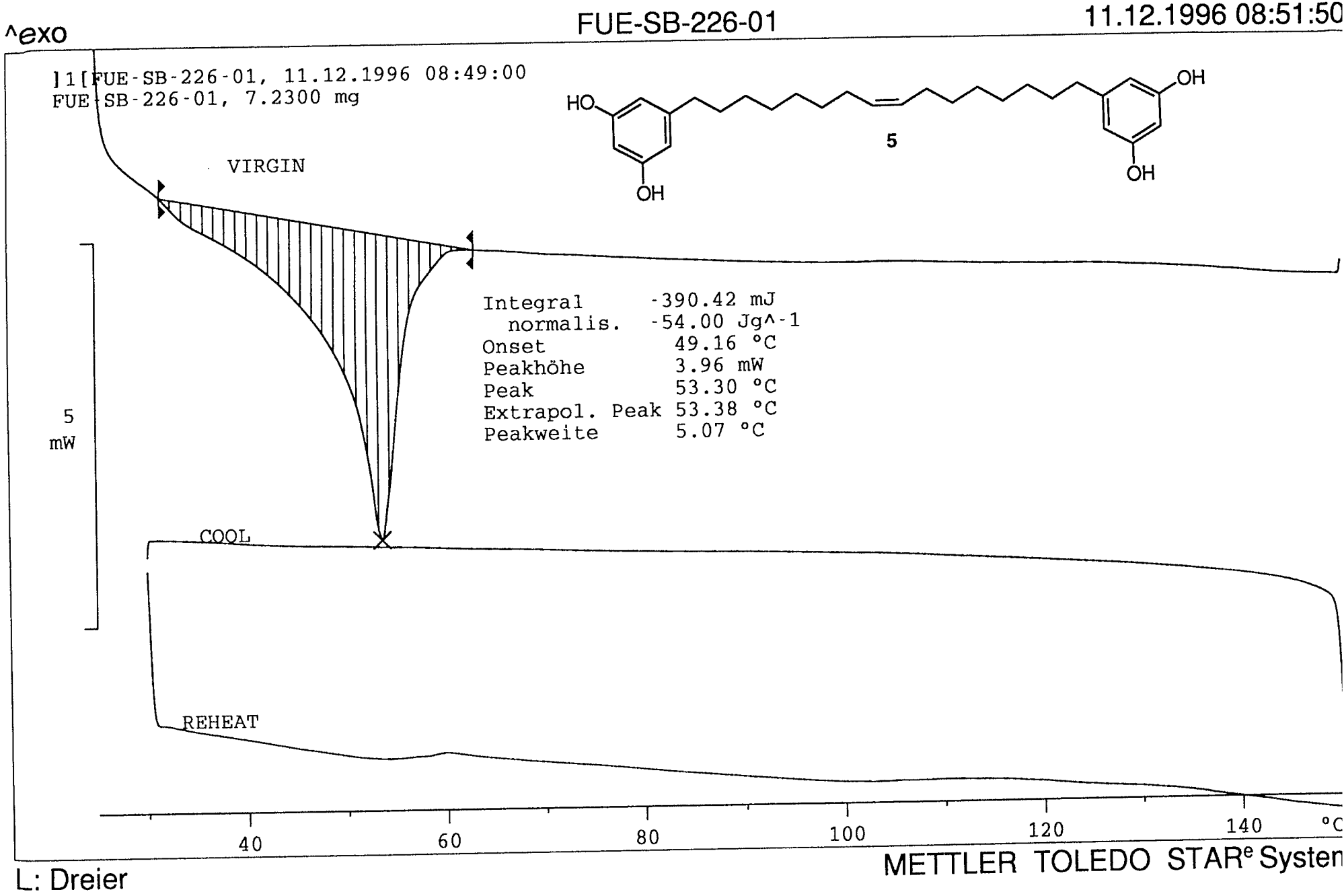
FUE-SB-224-01, 27.11.1996 08:15:03
FUE-SB-224-01, 5.3900 mg

Methodenname: 25>160°C_10°C/MIN
Bemerkungen: C26H38O4



METTLER TOLEDO STAR^{e} Syster

L: Dreier


^exo
FUE-SB-226-01
11.12.1996 08:51:50
]1[FUE-SB-226-01, 11.12.1996 08:49:00
FUE-SB-226-01, 7.2300 mg
HO
OH
OH
OH
5
VIRGIN
Integral -390.42 mJ
normalis. -54.00 Jg^-1
Onset 49.16 °C
Peakhöhe 3.96 mW
Peak 53.30 °C
Extrapol. Peak 53.38 °C
Peakweite 5.07 °C
5
mW
COOL
REHEAT
40
60
80
100
120
140
°C
METTLER TOLEDO STARe System
L: Dreier