Supporting Information for

Synthesis of the Tricyclic Core of Colchicine via a Dienyne Tandem Ring-Closing Metathesis Reaction

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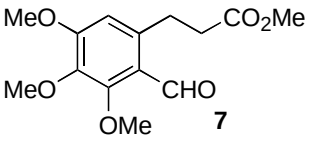
General considerations: Melting points were determined on a Reichert hot stage apparatus. Infrared spectra were recorded on a Perkin-Elmer 1600 FTIR spectrometer or on a Nicolet Avatar 320 FT-IR as neat or in solutions. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 400 NMR spectrometer or on a VARIAN Mercury plus 300 instrument as solutions in $CDCl_3$, using residual protic solvent $C\underline{H}Cl_3$ (δ_H=7.27 ppm) or $\underline{C}DCl_3$ (δ_C=77.0 ppm) as internal reference. Mass spectra were determined on a Hewlett Packard HP 5970B/5890A or on a Micromass (Manchester, United-Kingdom) Quattro LC spectrometer (ESI). All reactions were monitored by TLC carried out on 0.2 mm aluminium silica gel (60 F_{254}) pre-coated plates using UV light and 5% ethanolic phosphomolybdic acid and heat as developing agent. Flash chromatography was performed on 40-63 μm (400-230 mesh) silica gel 60 with ethyl acetate (EtOAc)-petroleum ether (PE) (bp. 40-60°C) or cyclohexane as eluents. Commercially available reagents and solvents were purified and dried when necessary by usual methods. THF and Et_2O were purified by distillation, under nitrogen, from sodium / benzophenone. CH_2Cl_2 was dried by distillation from calcium hydride. Unless otherwise mentioned, all other reagents were purchased from commercial sources and were used without further purification.

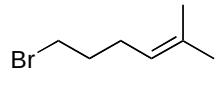


7

$C_{14}H_{18}O_6$
Mol. Wt.: 282,29

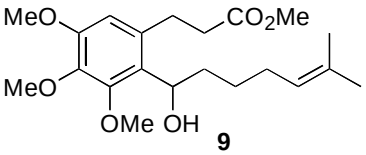
Aldehyde 7: A solution of acid **6** (25 g, 111.6 mmol) in MeOH (265 mL) and conc. HCl (37%) (1.75 mL) was stirred at rt for 24 h. The reaction mixture was neutralized with saturated sodium bicarbonate solution and MeOH evaporated under reduced pressure. The residue was extracted with EtOAc ($3 \times 3\tilde{0}$ mL) and the combined organic extracts washed with brine (200 mL), dried ($MgSO_4$) and evaporated under reduced pressure to furnish the crude methyl ester as a slightly yellow solid (25.8 g, 101.6 mmol, 91%). To a solution of the methyl ester (25.8 g, 101.6 mmol) in CH_2Cl_2 (254 mL) was added at room temperature under argon α,α dichloromethyl methyl ether (27.43 mL, 304.8 mmol). This mixture was cooled to –70°C and neat $SnCl_4$ (11.68 mL, 101.6 mmol) was added dropwise. The resulting yellow reaction mixture was warmed slowly to 0°C (2 h) and water was added dropwise. The mixture was diluted with CH_2Cl_2 (500 mL) and neutralized with saturated sodium bicarbonate solution and solid $NaHCO_3$. The phases were separated and the aqueous layer extracted with CH_2Cl_2 (2×500 mL). The combined organic extracts were washed with brine (500 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The crude product

was purified by chromatography on silica gel (cyclohexane/EtOAc 4:1) to give 27 g (95.7 mmol, 85%) of **7** as a white solid. $\mathbf{R_f}$ 0.4 (cyclohexane/EtOAc 4:1). M.p. 54-55°C. **^{1}H NMR:** δ = 10.36 (s, 1 H), 6.58 (s, 1 H), 3.97 (s, 3 H), 3.91 (s, 3 H), 3.86 (s, 3 H), 3.65 (s, 3 H), 3.22 (t, *J* = 7.5 Hz, 2 H), 2.61 (t, *J* = 7.5 Hz, 2 H). **^{13}C NMR:** δ = 190.6 (CH), 173.4 (C), 158.6 (C), 157.9 (C), 140.2 (C), 140.1 (C), 120.0 (C), 110.2 (CH), 62.3 (CH_3), 60.8 (CH_3), 56.0 (CH_3), 51.4 (CH_3), 35.0 (CH_2), 29.6 (CH_2). **IR** (neat)**:** 2946, 2850, 1735, 1678, 1590 cm^{-1}**. CI MS:** NH_3 *m/z* (%) 283 ($M^{+\cdot}$ + 1) (100), 300 ($M^{+\cdot}$+18) (5). **HMRS** (EI) *m/z* calcd for $C_{14}H_{18}O_3$, 282.11034, found 282.11049.



$C_7H_{13}Br$
Mol. Wt.: 177,08

6-Bromo-2-methyl-hex-2-ene: TsCl (7.49 g, 38.97 mmol) was added portionswise to a solution of 5-methyl-4-hexen-1-ol[1] (4.04 g, 35.43 mmol) an 4-DMAP (45 mg, 0.40 mmol) in anhydrous pyridine (35 mL) at 0°C under argon. The reaction mixture was stirred for 2 h 30 at 0°C poured in a mixture water/ice (100 mL) and the aqueous phase was extracted with Et_2O (3 × 150 mL). The combined organic layers were washed with aq. 10% HCl, sat. aq. $NaHCO_3$, brine, dried over $MgSO_4$ and evaporated under reduced pressure to give 8.32 g (31.0 mmol) of crude tosylate. A solution of this crude tosylate (8.32 g, 31.0 mmol) with LiBr (9.33 g, 107.4 mmol) in acetone (73 mL) was stirred for 1 h at reflux, cooled to room temperature, diluted with pentane (300 mL) and washed with water (100 mL) and brine (100 mL). The organic phase was dried over $MgSO_4$, evaporated under reduced pressure and the residue distilled under vacuum to give the pure 6-Bromo-2-methyl-hex-2-ene (4.827 g, 27.27 mmol, 77% from 5-methyl-4-hexen-1-ol) as a colorless liquid (90°C, 10 mm Hg). **^{1}H NMR:** δ = 5.08 (t, *J* = 7.0 Hz, 1 H), 3.41 (t, *J* = 7.0 Hz, 2 H), 2.14 (q, *J* = 7.0 Hz, 2 H), 1.90 (quin., *J* = 7.0 Hz, 2 H), 1.71 (s, 3 H), 1.64 (s, 3 H). **^{13}C NMR:** δ = 133.1 (C), 122.5 (CH), 33.4 (CH_2), 32.9 (CH_2), 26.5 (CH_2), 25.6 (CH_3), 17.7 (CH_3).



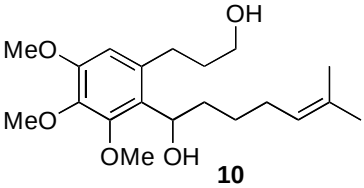
9

$C_{21}H_{32}O_6$
Mol. Wt.: 380,48

Alcool 9: To 680 mg (27.64 mmol) of magnesium turnings in THF (2 mL) was added a solution of 6-bromo-2-methyl-hex-2-ene (4.91 g, 27.72 mmol) in Et_2O (38 mL). At the beginning to initiate the reaction 4 drops of neat 6-bromo-2-methyl-hex-

[1] 5-Methyl-4-hexen-1-ol was prepared according to the procedure of Corey et al (Corey, E. J. ; Cheng, H. ; Baker, C. H. ; Matsuda, S. P. T. ; Li, D. ; Song, X. *J. Am. Chem. Soc*. **1997**, *119*, 1277) from γ-butyrolactone but using isopropyltriphenylphosphonium iodide prepared in our hands by the procedure of Kinney et al. (Kinney, R. J. ; Jones, W. D. ; Bergman, R. G. *J. Am. Chem. Soc*. **1977**, *100*, 7902).

2-ene were added to the mixture and the remainder of the bromide derivative solution was added dropwise over 15 min at a rate sufficient to maintain reflux without heating. The resulting solution of Grignard reagent **8** was stirred under reflux for 2 h, cooled to –10°C and a solution of aldehyde **7** (3.5 g, 12.41 mmol) in THF (73 mL) was added dropwise at this temperature. The reaction mixture was stirred for 2 h at –10°C under argon and quenched with aqueous saturated NH_4Cl (30 mL). The aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified by chromatography on silica gel (EtOAc/cyclohexane 2:8) to give 3.85 g (10.13 mmol, 81%) of **9** as a colorless oil. **R_f** 0.33 (cyclohexane/EtOAc 7:3). **^{1}H NMR:** δ = 6.46 (s, 1 H), 5.46-5.12 (m, 1 H), 4.74-4.68 (m, 1 H), 3.97 (s, 3 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.67 (s, 3 H), 3.42 (d, *J* = 9.9 Hz, 1 H), 2.94-2.82 (m, 2 H), 2.64-2.52 (m, 2 H), 2.05-1.98 (m, 2 H), 1.93-1.81 (m, 1 H), 1.70-1.54 (m, 2 H), 1.66 (s, 3 H), 1.58 (s, 3 H) 1.43-1.30 (m, 1 H). **^{13}C NMR:** δ = 173.1 (C), 152.3 (C), 152.2 (C), 140.7 (C), 133.0 (C), 131.5 (C), 127.9 (C), 124.4 (CH), 108.5 (CH), 70.6 (CH), 61.1 (CH_3), 60.5 (CH_3), 55.9 (CH_3), 51.6 (CH_3), 38.4 (CH_2), 35.7 (CH_2), 28.4 (CH_2), 27.8 (CH_2), 26.8 (CH_2), 25.6 (CH_3), 17.6 (CH_3).



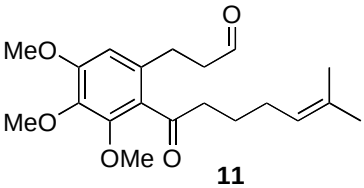
10

$C_{20}H_{32}O_5$

Mol. Wt.: 352,47

Diol 10: A solution of $LiAlH_4$ (1.16 g, 30.52 mmol) in THF (32 mL) was added dropwise under argon to a solution of ester **9** (3.85 g, 10.13 mmol) in THF (152 mL) at –10°C. The reaction mixture was stirred for 30 min at this temperature and quenched by successive addition of H_2O (1.16 mL), 15% aqueous NaOH solution (1.16 mL) and H_2O (3.48 mL) and the mixture stirred for 30 min at room temperature. The solution was filtered and the granular inorganic precipitate rinsed with THF (200 mL). The combined organic layers were evaporated under reduced pressure to give 3.56 g (10.13 mmol, 100%) of crude diol **10** used in the next step without further purification. **R_f** 0.26 (cyclohexane/EtOAc 1:1). **^{1}H NMR:** δ = 6.46 (s, 1 H), 5.08 (tt, *J* = 6.9, 1.5 Hz, 1 H), 4.80 (dd, *J* = 8.4, 5.1 Hz, 1 H), 3.96 (s, 3 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 3.62 (t, *J* = 8.1 Hz, 2 H), 2.74-2.62 (m, 4 H), 2.03-1.97 (m, 2 H), 1.91-1.77 (m, 3 H), 1.71-1.53 (m, 2 H), 1.66 (s, 3 H), 1.58 (s, 3 H) 1.40-1.27 (m, 1 H). **^{13}C NMR:** δ = 152.1 (C), 151.9 (C), 140.1 (C), 134.5 (C), 131.3 (C), 127.5 (C), 124.3 (CH), 108.5 (CH), 70.4 (CH), 61.5 (CH_3), 60.9 (CH_3), 60.4 (CH_3), 55.7 (CH_3), 38.2 (CH_2), 34.2 (CH_2), 29.1 (CH_2), 27.7 (CH_2), 26.6 (CH_2), 25.5 (CH_3),

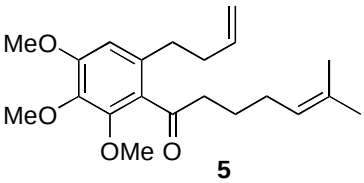
17.5 (CH_3). **IR** (neat)**:** 3376, 2942, 2865, 1598 cm^{-1}**. HMRS** (EI) *m/z* calcd for $C_{20}H_{32}O_5$, 352.22497, found 352.22478.



11

$C_{20}H_{28}O_5$
Mol. Wt.: 348,43

Ketoaldehyde 11: A solution of Dess-Martin reagent (48.3 mL, 14.55 mmol, 0.3 M in CH_2Cl_2) was added dropwise to a solution of crude diol **10** (1.0 g, 2.83 mmol) in CH_2Cl_2 (29 mL) and dry pyridine (88 drops) at –10°C under argon. The reaction mixture was stirred for 2 h at room temperature and cooled for 18 h at 6°C. A mixture of aq. sat. $NaHCO_3$ and aq. sat. $Na_2S_2O_3$ (1:1) (200 mL) was added at the reaction mixture warmed to room temperature and the resulting mixture stirred for 30 min. The aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$) and evaporated under reduced pressure (18 mm Hg and 10^{-1} mm Hg) to give the crude product **11** (0.95 g, 2.72 mmol, 96%) used in the next step without further purification. $\mathbf{R_f}$ 0.60 (cyclohexane/EtOAc 1:1). **^{1}H NMR:** δ = 6.51 (s, 1 H), 5.11 (bt, *J* = 7.8 Hz, 1 H), 3.85 (s, 3 H), 3.84 (s, 3 H), 3.83 (s, 3 H), 2.82-2.70 (m, 5 H), 2.04 (q, *J* = 7.2 Hz, 2 H), 1.74-1.58 (m, 3 H), 1.69 (s, 3 H), 1.60 (s, 3 H). **^{13}C NMR:** δ = 206.8 (C), 201.2 (C), 154.2 (C), 150.8 (C), 140.0 (C), 133.3 (C), 132.1 (C), 128.7 (C), 123.8 (CH), 108.7 (CH), 61.4 (CH_3), 60.8 (CH_3), 56.0 (CH_3), 46.1 (CH_2), 44.5 (CH_2), 27.4 (CH_2), 25.7 (CH_2), 25.6 (CH_3), 24.1 (CH_2), 17.6 (CH_3). **HMRS** (EI) *m/z* calcd for $C_{20}H_{28}O_5$, 348.19367, found 348.19370.

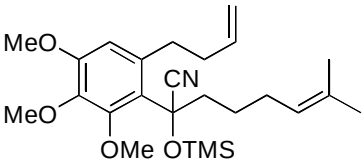


5

$C_{21}H_{30}O_4$
Mol. Wt.: 346,46

Ketone 5: *n*-Butyllithium (2.7 mL, 4.32 mmol, 1.6 M solution in hexane) was added dropwise under argon at room temperature to a solution of methyltriphenylphosphonium bromide (1.6 g, 4.47 mmol) in dry THF (13.5 mL). The resulting yellow-orange solution was stirred for 45 min at room temperature and cooled to 0°C ; a solution of crude aldehyde **11** (950 mg, 2.72 mmol) in dry THF (10 mL) solution was added dropwise under argon to the resulting ylide solution maintained at 15°C. The reaction mixture was stirred for 30 min at room temperature and water (50 mL) added. The biphasic mixture was separated and the aqueous phase extracted with Et_2O (3 × 100 mL). The combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was extracted with pentane (3 × 100 mL), filtered and evaporated under reduced pressure. The crude product was

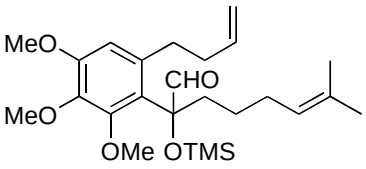
purified by chromatography on silica gel (cyclohexane/EtOAc 95:5 to 8:2) to give 407 mg (1.17 mmol, 41% from alcohol **9**) of ketone **5** as a colorless oil. $\mathbf{R_f}$ 0.75 (cyclohexane/EtOAc 7:3). **^{1}H NMR:** δ = 6.51 (s, 1 H), 5.87-5.79 (m, 1 H), 5.13 (bt, *J* = 7.5 Hz, 1 H), 5.13 (dq, *J* = 17.2, 1.6 Hz, 1 H), 4.98 (dd, *J* = 10.4, 2 Hz, 1 H), 3.87 (s, 6 H), 3.86 (s, 3 H), 2.75 (t, *J* = 7.8 Hz, 2 H), 2.55-2.51 (m, 2 H), 2.34-2.28 (m, 2 H), 2.08-2.02 (m, 2 H), 1.74-1.68 (m, 2 H), 1.69 (s, 3 H), 1.60 (s, 3 H). **^{13}C NMR:** δ = 207.0 (C), 154.0 (C), 150.4 (C), 139.8 (C), 137.8 (CH), 134.4 (C), 132.2 (C), 129.1 (C), 124.0 (CH), 115.2 (CH_2), 108.6 (CH), 61.6 (CH_3), 60.9 (CH_3), 56.0 (CH_3), 44.8 (CH_2), 35.8 (CH_2), 32.6 (CH_2), 27.5 (CH_2), 25.8 (CH_3), 24.1 (CH_2), 17.8 (CH_3). **IR** (neat)**:** 3075, 2935, 2855, 1696, 1640, 1595 cm^{-1}**. HMRS** (EI) *m/z* calcd for $C_{21}H_{30}O_4$, 346.21441, found 346.21407.



$C_{25}H_{39}NO_4Si$ **12**
Mol. Wt.: 445,67

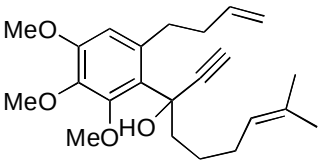
Nitrile 12 : To a solution of ketone **5** (200 mg, 0.57 mmol) in anhydrous CH_2Cl_2 (1.5 mL) was added dropwise TMSCN (550 µL, 4.12 mmol) and ZnI_2[2] (260 mg, 0.81 mmol) at room temperature under argon. The reaction mixture was stirred for 3 h 30 at room temperature, diluted with Et_2O (30 mL) and washed with water (15 mL). The aqueous phase was extracted with Et_2O (2 × 15 mL) and the combined organic layers washed with brine (15 mL), dried ($MgSO_4$), filtered and evaporated under reduced pressure. The residue was purified by purified by chromatography on silica gel (cyclohexane/EtOAc 97.5:2.5 to 95:5) to give 225 mg (0.50 mmol, 87%) of nitrile **12** as a colorless oil. $\mathbf{R_f}$ 0.25 (cyclohexane/EtOAc 95:5). **^{1}H NMR:** δ = 6.48 (s, 1 H), 5.92-5.85 (m, 1 H), 5.09-5.01 (m, 3 H), 4.00 (s, 3 H), 3.86 (s, 3 H), 3.83 (s, 3 H), 3.02-2.93 (m, 2 H), 2.45-2.18 (m, 3 H), 2.10-1.93 (m, 3 H), 1.67 (s, 3 H), 1.57 (s, 3 H) 1.45-1.38 (m, 2 H) , 0.24 (s, 9 H). **^{13}C NMR:** δ = 152.6 (C), 150.5 (C), 139.8 (C), 138.2 (CH), 136.5 (C), 132.0 (C), 123.9 (CH), 123.7 (C), 125.5 (C), 114.8 (CH_2), 110.2 (CH), 73.9 (C), 60.9 (CH_3), 60.4 (CH_3), 55.7 (CH_3), 43.3 (CH_2), 36.5 (CH_2), 32.9 (CH_2), 27.4 (CH_2), 25.7 (CH_3), 24.0 (CH_2), 17.7 (CH_3), 1.2 (Si($\underline{C}H_3$)$_3$). **IR** (neat)**:** 3077, 2939, 2865, 1639, 1592 cm^{-1}**. CI MS:** NH_3 *m/z* (%) 310 (30), 352 (100), 419 (20), 446 ($M^{+\cdot}$+1) (1), 463 ($M^{+\cdot}$+18) (0.5). **HMRS** (EI) *m/z* calcd for $C_{25}H_{39}NO_4Si$, 445.2648, found 445.2651.

[2] ZnI_2 was dried overnight under vacuum (10^{-2} mm Hg).



$C_{25}H_{40}O_5Si$ **13**
Mol. Wt.: 448,67

Aldehyde 13 : To a solution of the nitrile **12** (225 mg, 0.50 mmol) in dry Et_2O (3 mL) cooled at –70 °C and stirred under argon was added dropwise a solution of DIBAL-H 1.0 M in hexane (2.5 mL). After being stirred at this temperature for 1 h 30 min, Et_2O (15 mL) and EtOAc (410 µL) were added, followed by SiO_2 (3.7 g) and the mixture was slowly warmed up 0°C and stirred for 2 h at this temperature. The mixture was filtered and concentrated under reduced pressure. The residue was purified by purified by chromatography on silica gel (cyclohexane/EtOAc 95:5) to give 180 mg (0.40 mmol, 80%) of aldehyde **13** as a colorless oil. $\mathbf{R_f}$ 0.25 (cyclohexane/EtOAc 95:5). **^{1}H NMR:** δ = 9.42 (s, 1 H), 6.57 (s, 1 H), 6.05-5.87 (m, 1 H), 5.14-5.02 (m, 3 H), 3.86 (s, 3 H), 3.79 (s, 3 H), 3.74 (s, 3 H), 3.08-2.92 (m, 2 H), 2.50-2.24 (m, 3 H), 2.10-1.87 (m, 3 H), 1.66 (s, 3 H), 1.57 (s, 3 H) 1.53-1.36 (m, 1 H), 1.15-0.95 (m, 1 H), 0.10 (s, 9 H). **^{13}C NMR:** δ = 193.4 (C), 152.3 (C), 149.6 (C), 138.9 (C), 138.4 (CH), 138.0 (C), 131.7 (C), 126.1 (C), 124.2 (CH), 114.6 (CH_2), 110.5 (CH), 83.4 (C), 60.4 (CH_3), 60.2 (CH_3), 55.8 (CH_3), 37.1 (CH_2), 36.3 (CH_2), 32.1 (CH_2), 28.2 (CH_2), 25.6 (CH_3), 24.4 (CH_2), 17.7 (CH_3), 2.3 (Si($\underline{C}H_3$)$_3$). **IR** (neat)**:** 3077, 2937, 2856, 1729, 1640, 1594 cm^{-1}**. CI MS:** NH_3 *m/z* (%) 355 (100), 420 (10), 449 ($M^{+\cdot}$+1) (5). **HMRS** (EI) *m/z* calcd for $C_{25}H_{40}O_5Si$, 448.2645, found 448.2630.

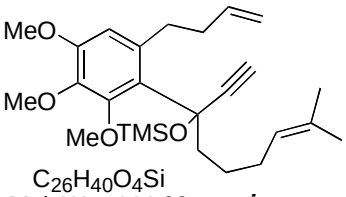


$C_{23}H_{32}O_4$ **14**
Mol. Wt.: 372,50

1-Alkyne 14: To a solution of aldehyde **13** (180 mg, 0.40 mmol) and dimethyl 1-diazo-2-oxopropylphosphonate[3] (112 mg, 0.60 mmol) in anhydrous MeOH (3.2 mL) was added K_2CO_3 (112 mg, 0.81 mmol) and stirring was continued under argon for 3 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with an aq solution of saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic phases washed with brine and dried ($MgSO_4$). Evaporation of the solvents followed by chromatography on silica gel (cyclohexane/EtOAc 9:1) gave 46 mg of 1-alkyne **14** (0.123 mmol, 31%) as a colorless oil. $\mathbf{R_f}$ 0.22 (cyclohexane/EtOAc 9:1). **^{1}H NMR:** δ = 6.53 (s, 1 H), 5.98-5.83 (m, 1 H), 5.87 (s, 1 H, OH), 5.12-5.00 (m, 3 H), 3.96 (s, 3 H), 3.86 (s, 3 H), 3.82 (s, 3 H), 3.14 (ddd, *J* = 16.5, 11.1, 5.4 Hz, 1 H), 2.87 (ddd, *J* = 16.5, 10.8, 5.4 Hz, 1 H), 2.65 (s, 1 H), 2.59-2.46 (m, 1 H), 2.40-2.28 (m, 1 H), 2.06-1.91 (m, 4 H),

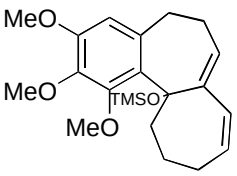
[3] Ohira, S. *Synth. Commun*. **1989**, *19*, 561. For a review see: Eymery, F.; Iorga, B.; Savignac, P. *Synthesis*, **2000**, 185.

1.70-1.53 (m, 2 H), 1.67 (s, 3 H), 1.58 (s, 3 H). **^{13}C NMR:** δ = 152.0 (C), 151.9 (C), 140.4 (C), 138.3 (CH), 135.6 (C), 131.7 (C), 126.3 (C), 124.5 (CH), 114.7 (CH_2), 110.6 (CH), 83.8 (C), 73.8 (C), 72.6 (C), 61.9 (CH_3), 60.7 (CH_3), 55.8 (CH_3), 44.7 (CH_2), 36.8 (CH_2), 33.7 (CH_2), 27.9 (CH_2), 25.8 (CH_3), 24.4 (CH_2), 17.8 (CH_3). **IR** (neat)**:** 3437, 3309, 3076, 2930, 2855, 1639, 1596 cm^{-1}**. CI MS:** NH_3 *m/z* (%) 355 ($M^{+\cdot}$–H_2O+1) (100), 372 ($M^{+\cdot}$+1) (1). **HMRS** (EI) *m/z* calcd for $C_{23}H_{32}O_4$, 372.23006, found 372.22964.



$C_{26}H_{40}O_4Si$
Mol. Wt.: 444,68 ***i***

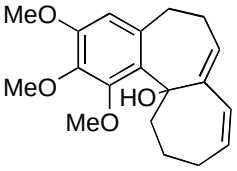
Trimethyl silyl ether *i*: A solution of alcohol **14** (65 mg, 0.174 mmol) in 1-(trimethylsilyl)imidazole (1.6 mL, 10.9 mmol) was stirred at 50°C for 1 h under argon, cooled to room temperature and stirred for 2 h at this temperature. The reaction mixture was diluted with hexane (15 mL), washed with brine (2 × 5 mL), dried over Na_2SO_4, filtered and evaporated under reduced pressure to give 72 mg of trimethyl silyl ether ***i*** (0.162 mmol, 93%) used in the next step without further purification. **R_f** 0.60 (cyclohexane/EtOAc 9:1). **^{1}H NMR:** δ = 6.42 (s, 1 H), 5.98-5.85 (m, 1 H), 5.10-4.98 (m, 3 H), 3.88 (s, 3 H), 3.84 (s, 3 H), 3.81 (s, 3 H), 3.17-3.07 (m, 1 H), 3.03-2.93 (m, 1 H), 2.64 (s, 1 H), 2.45-2.25 (m, 3 H), 2.05-1.84 (m, 1 H), 1.66 (s, 3 H), 1.56 (s, 3 H), 1.50-1.39 (m, 1 H), 1.33-1.15 (m, 1 H), 0.23 (s, 9 H). **^{13}C NMR:** δ = 151.7 (C), 151.5 (C), 140.5 (C), 139.0 (CH), 136.5 (C), 131.3 (C), 127.8 (C), 124.8 (CH), 114.3 (CH_2), 110.6 (CH), 90.0 (C), 74.8 (C), 71.9 (C), 60.6 (CH_3), 60.3 (CH_3), 55.7 (CH_3), 44.4 (CH_2), 36.9 (CH_2), 34.1 (CH_2), 27.8 (CH_2), 25.6 (CH_3), 24.3 (CH_2), 17.7 (CH_3), 2.20 (Si($\underline{C}H_3$)$_3$).



$C_{22}H_{32}O_4Si$ **16**
Mol. Wt.: 388,57

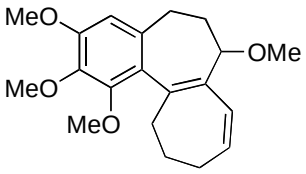
Tricyclic compound 16: A degassed solution of the trimethyl silyl ether ***i*** (72 mg, 0.162 mmol) in dry methylene chloride (150 mL) under argon was treated with Grubbs catalyst **15** (27 mg, 20% mol). The mixture was heated at reflux for 4 h. The solvent was removed and the residue submitted to chromatography on silica gel (cyclohexane/EtOAc 9:1) to isolate the pure tricyclic compound **16** (47 mg, 0.121 mmol, 74%) as a colorless oil. **R_f** 0.46 (cyclohexane/EtOAc 95:5). **^{1}H NMR:** δ = 6.49 (s, 1 H), 5.88 (d, *J* = 12.3 Hz, 1 H), 5.60 (t, *J* = 4.2 Hz, 1 H), 5.39 (dt, *J* = 12.3, 2.0 Hz, 1 H), 4.26 (td, *J* = 13.2, 6.3 Hz, 1 H), 3.85 (s, 3 H), 3.82 (s, 3 H), 3.73 (s, 3 H), 2.98-2.90 (m, 1 H), 2.72-2.62 (m, 1 H), 2.48-2.04 (m, 6 H), 1.76-1.68 (m, 1 H), -0.03 (s, 9 H). **^{13}C NMR:** δ = 151.53 (C), 151.51 (C), 143.6 (C), 141.2 (CH), 137.9 (C), 136.2 (CH), 133.4 (C), 133.2 (CH), 127.0 (CH), 110.7 (CH), 82.7 (C), 61.0 (CH_3),

60.7 (CH_3), 55.9 (CH_3), 39.7 (CH_2), 33.9 (CH_2), 32.1 (CH_2), 29.7 (CH_2), 22.0 (CH_2), 1.88 (Si($\underline{C}H_3$)$_3$). **IR** (neat)**:** 2928, 2852, 1590 cm^{-1}. **HMRS** (EI) *m/z* calcd for $C_{22}H_{32}O_4Si$, 388.2069, found 388.2054.



$C_{19}H_{24}O_4$ **17**
Mol. Wt.: 316,39

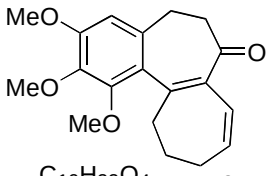
Alcohol 17: A solution of TBAF (400 µL, 0.4 mmol, 1M in THF) was added to a solution of **16** (37 mg, 0.095 mmol) and the mixture was stirred for 3 h at room temperature. The solvent was evaporated under reduced pressure and the residue purified by chromatography on silica gel (cyclohexane/EtOAc 9:1, 8:2 and 7:3) to give the pure alcohol **17** (22 mg, 0.069 mmol, 73%) as a colorless oil. **M.p.** 102-103°C. $\mathbf{R_f}$ 0.33 (cyclohexane/EtOAc 8:2). **^{1}H NMR:** δ = 7.00 (s, 1 H, OH), 6.46 (s, 1 H), 6.07 (br d, *J* = 11.7 Hz, 1 H), 5.81-5.78 (m, 1 H), 5.39 (ddd, *J* = 10.2, 6.3, 3.0 Hz, 1 H), 3.98 (s, 3 H), 3.86 (s, 3 H), 3.83 (s, 3 H), 3.11-3.01 (m, 1 H), 2.60-1.88 (m, 9 H). **^{13}C NMR:** δ = 152.2 (C), 151.5 (C), 142.0 (C), 140.9 (C), 136.4 (C), 133.3 (CH), 131.9 (C), 129.5 (CH), 127.6 (CH), 109.7 (CH), 82.8 (C), 62.3 (CH_3), 60.7 (CH_3), 55.9 (CH_3), 47.3 (CH_2), 36.3 (CH_2), 29.5 (CH_2), 29.0 (CH_2), 25.8 (CH_2). **IR** (neat)**:** 3440, 3010, 2933, 2833, 1664, 1596 cm^{-1}**. ESI MS:** *m/z* (%) 299 (MH^+- H_2O) (100), 339 (MNa^+) (5), 380 (MNa^++ CH_3CN) (10). **HMRS** (EI) *m/z* calcd for $C_{19}H_{24}O_4$, 316.1674, found 316.1686.



$C_{20}H_{26}O_4$ **18**
Mol. Wt.: 330,42

Methyl ether 18: A solution of silyl ether **16** (6 mg, 0.015 mmol) and PPTS (2 mg) in a mixture Et_2O/MeOH (1:1, 2 mL) was stirred for 18 h at room temperature. The reaction mixture was diluted with Et_2O (5 mL), washed with water (2 mL), dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by chromatography on silica gel (cyclohexane/EtOAc 95:5 to 9:1) to give 4 mg (0.0123 mmol, 80%) of methyl ether **18** as a colorless oil. $\mathbf{R_f}$ 0.30 (cyclohexane/EtOAc 9:1). **^{1}H NMR:** δ = 6.51 (s, 1 H), 6.25 (d, *J* = 12.0 Hz, 1 H), 6.08 (dt, *J* = 12.0, 4.8 Hz, 1 H), 3.90 (s, 3 H), 3.88 (s, 3 H), 3.84 (s, 3 H), 3.58 (dd, *J* = 12.3, 6.9 Hz, 1 H), 3.20 (s, 3 H), 2.61-1.89 (m, 10 H). **^{13}C NMR:** δ = 152.3 (C), 151.1 (C), 141.1 (C), 136.9 (C), 135.6 (C), 134.5 (C), 134.2 (CH), 128.8 (C), 124.1 (CH), 107.4 (CH), 80.2 (CH), 61.0 (CH_3), 60.7 (CH_3), 57.4 (CH_3), 56.0 (CH_3), 38.7 (CH_2), 34.9 (CH_2), 31.9 (CH_2), 30.7 (CH_2), 30.3 (CH_2). **IR** (neat)**:** 2930,

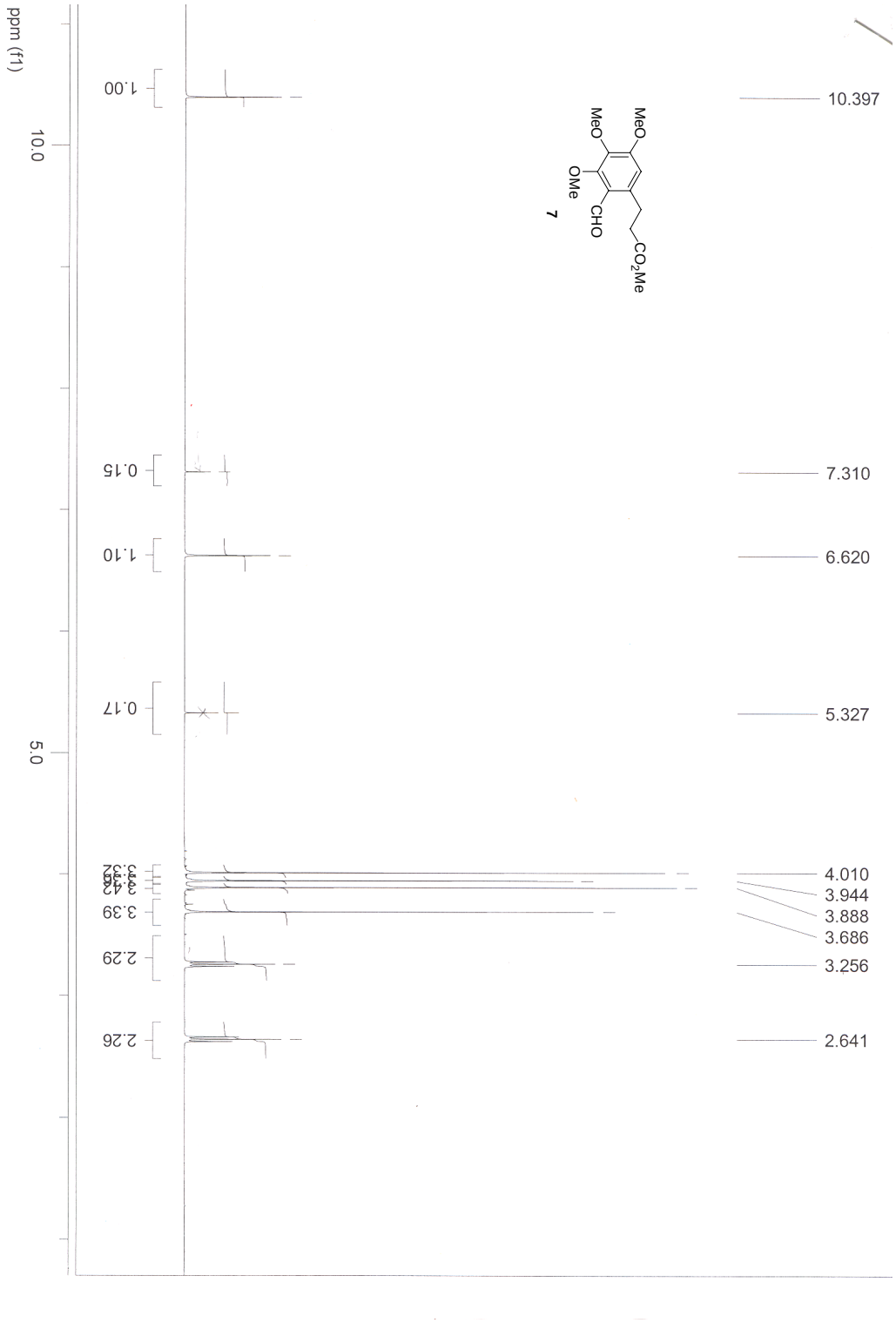
2854, 1595 cm^{-1}**. ESI MS:** *m/z* (%) 353 (MNa^+) (100), 369 (MK^+) (25). **HMRS** (EI) *m/z* calcd for $C_{20}H_{26}O_4$, 330.18311, found 330.18310.



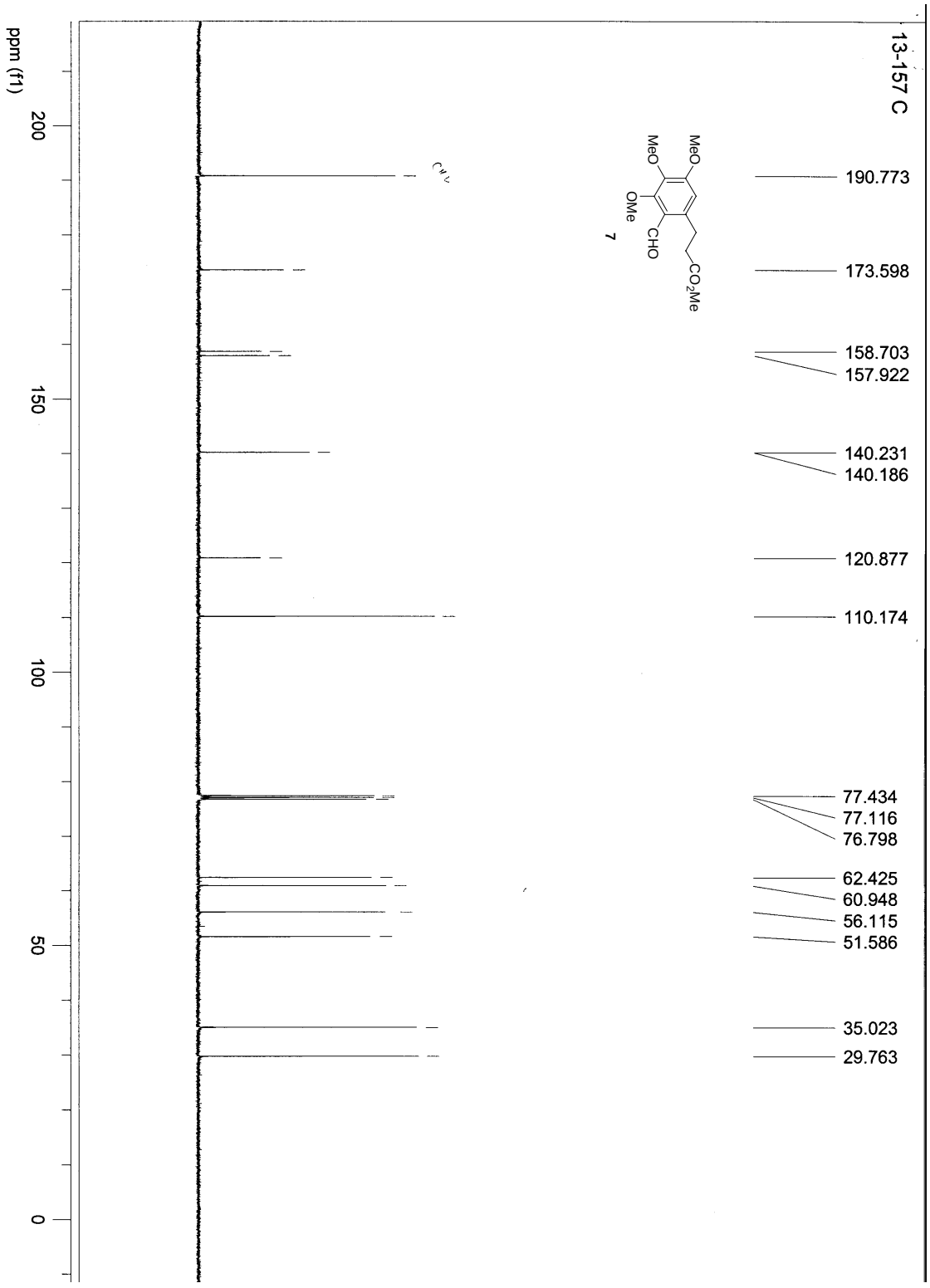
$C_{19}H_{22}O_4$ **19**
Mol. Wt.: 314,38

Ketone 19: A solution of alcohol **17** (8 mg, 0.025 mmol), PCC (10 mg, 2.74 mmol) and molecular sieves 4A (powder) (10 mg) in dry CH_2Cl_2 (500 μL) was stirred at room temperature under argon for 2 h. The reaction mixture was diluted with Et_2O (2 mL) and was purified by chromatography on Florisil® and eluted (cyclohexane/EtOAc 8:2) to give 3 mg (0.0095 mmol, 38%) of ketone **19** as a colorless oil and 1 mg (0.003 mmol, 12%) of epoxides **20** as a colorless oil. **19:** $\mathbf{R_f}$ 0.27 (cyclohexane/EtOAc 8:2). **^{1}H NMR:** δ = 6.52 (s, 1 H), 6.11-6.01 (m, 2 H), 3.88 (s, 3 H), 3.85 (s, 3 H), 3.79 (s, 3 H), 3.18-3.31 (br t, *J* = 11.9 Hz, 1 H), 2.50-2.83 (br m, 5 H), 2.48-2.40 (m, 2 H), 2.20-1.90 (br m, 2 H). **^{13}C NMR:** δ = 208.1 (C), 152.8 (C), 152.5 (C), 145.1 (C), 141.6 (C), 136.6 (C), 135.5 (CH), 135.0 (C), 127.6 (C), 125.2 (CH), 106.6 (CH), 61.0 (2 CH_3), 56.1 (CH_3), 49.1 (CH_2), 36.9 (CH_2), 32.3 (CH_2), 30.3 (CH_2), 29.4 (CH_2). **IR** (neat)**:** 2932, 1680, 1594 cm^{-1}**. ESI MS:** *m/z* (%) 315 (MH^+) (80), 337 (MNa^+) (90), 380 (MK^+) (100). **HMRS** (EI) *m/z* calcd for $C_{19}H_{22}O_4$, 314.1518, found 314.1547.

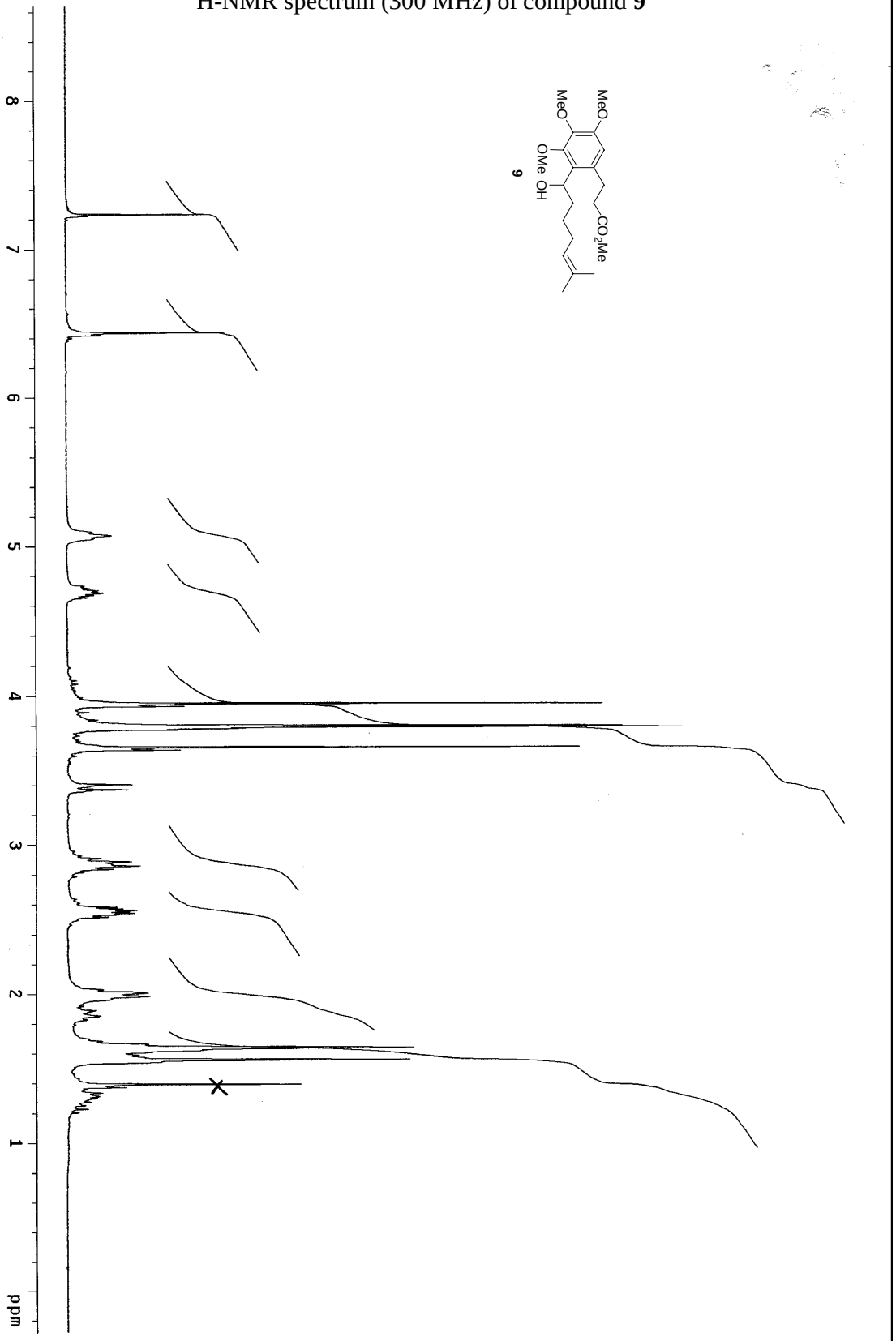
^{1}H-NMR spectrum (400 MHz) of compound **7**



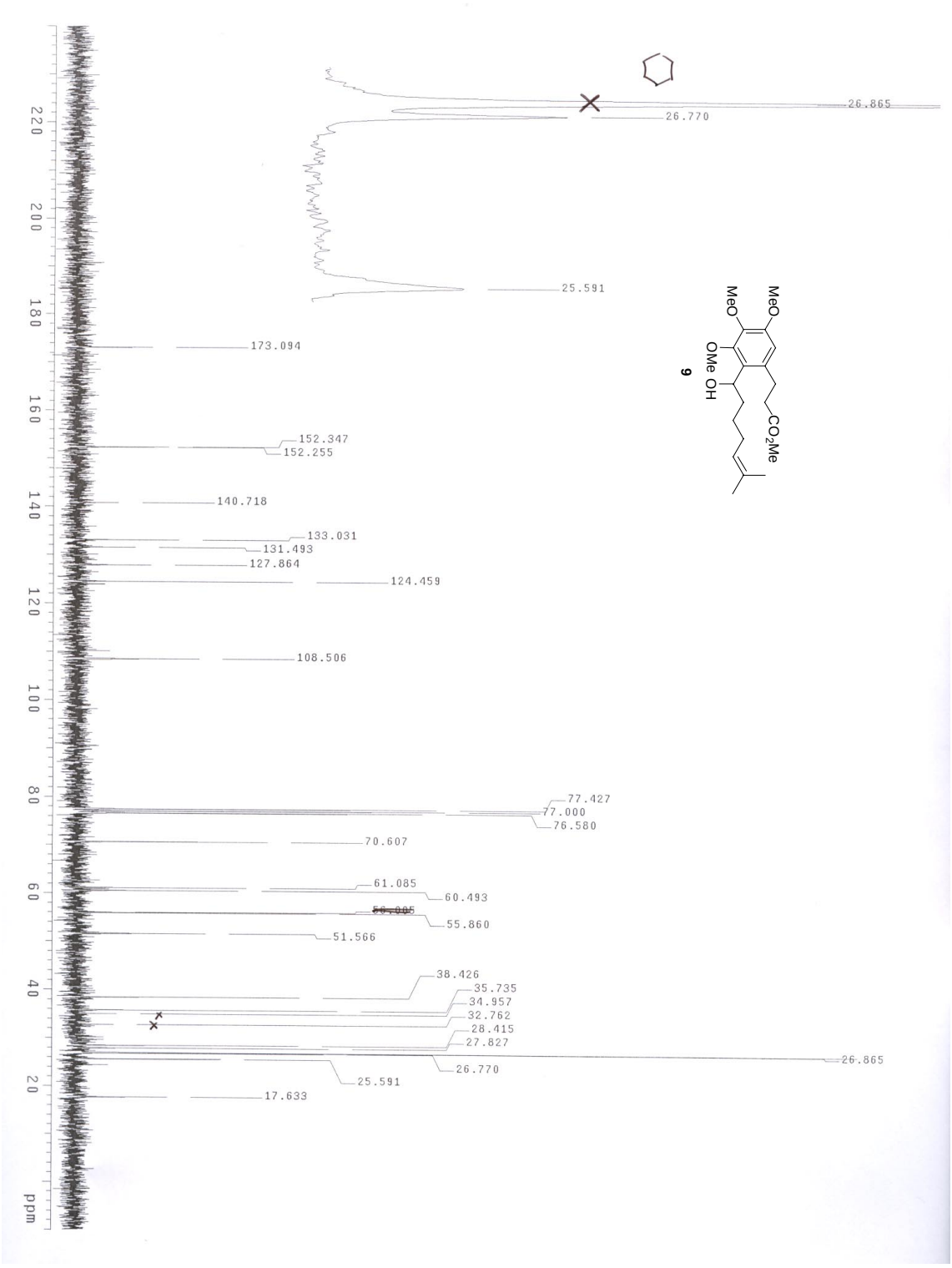
^{13}C-NMR spectrum (100 MHz) of compound **7**



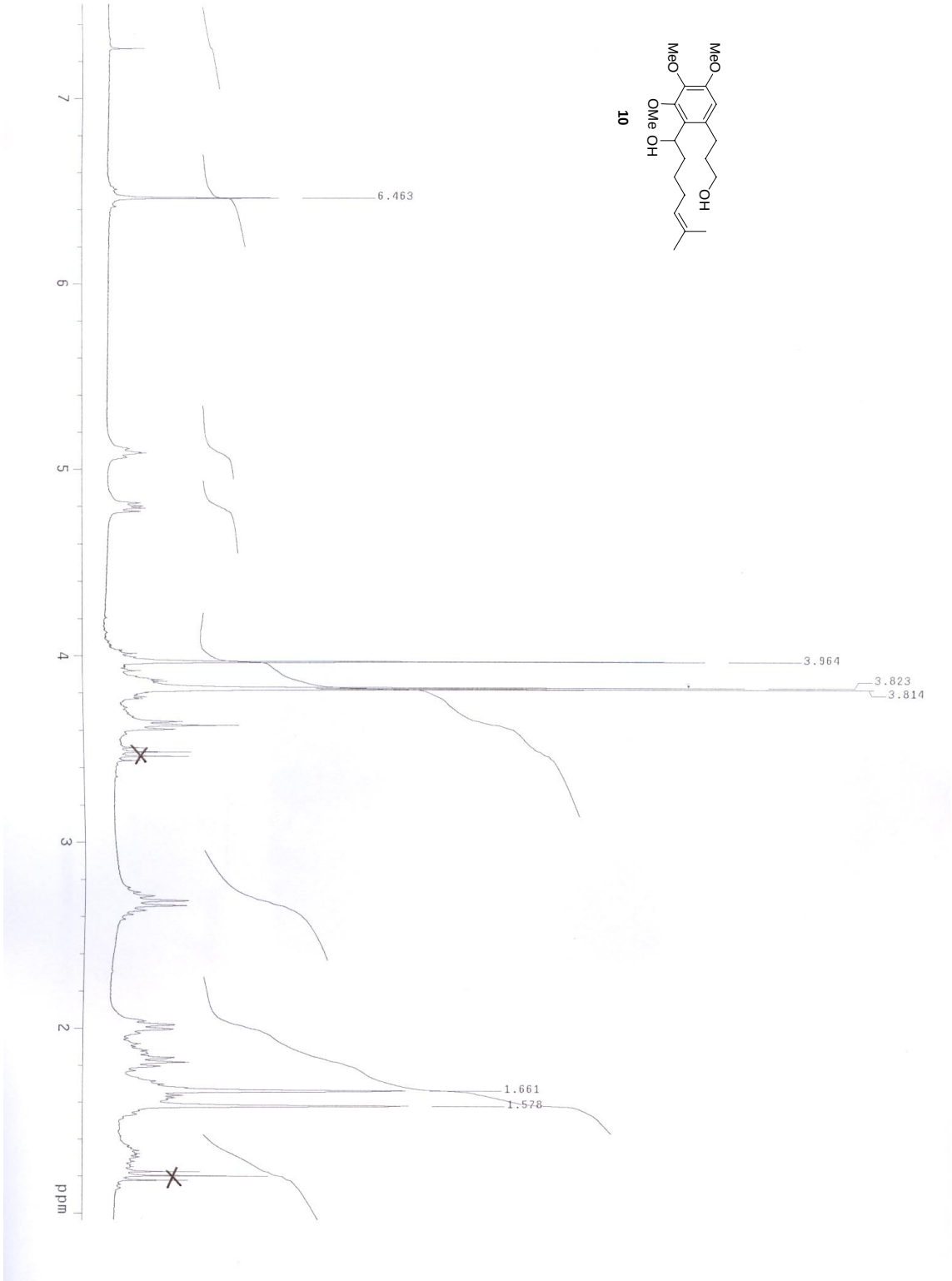
^{1}H-NMR spectrum (300 MHz) of compound **9**



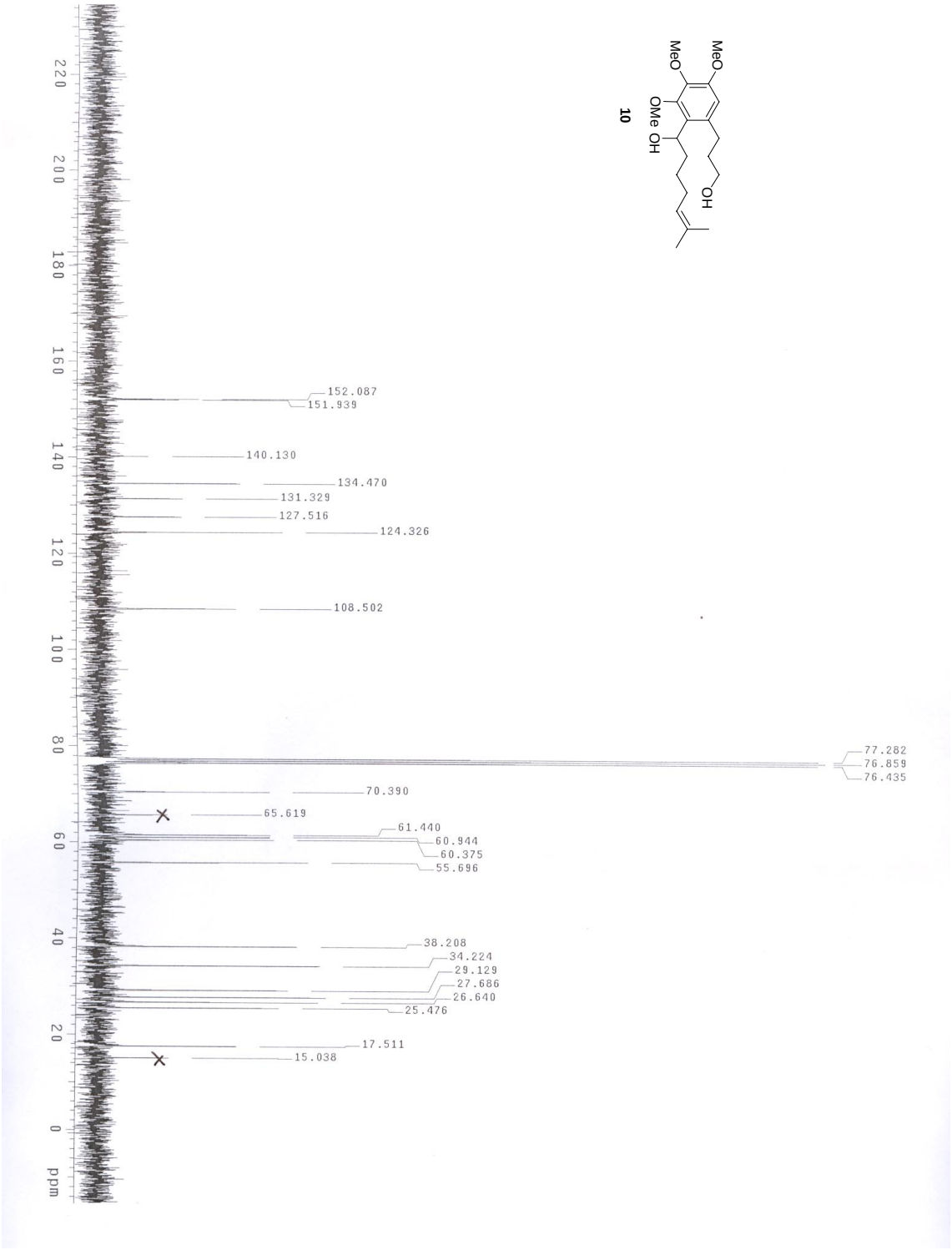
^{13}C-NMR spectrum (75 MHz) of compound **9**



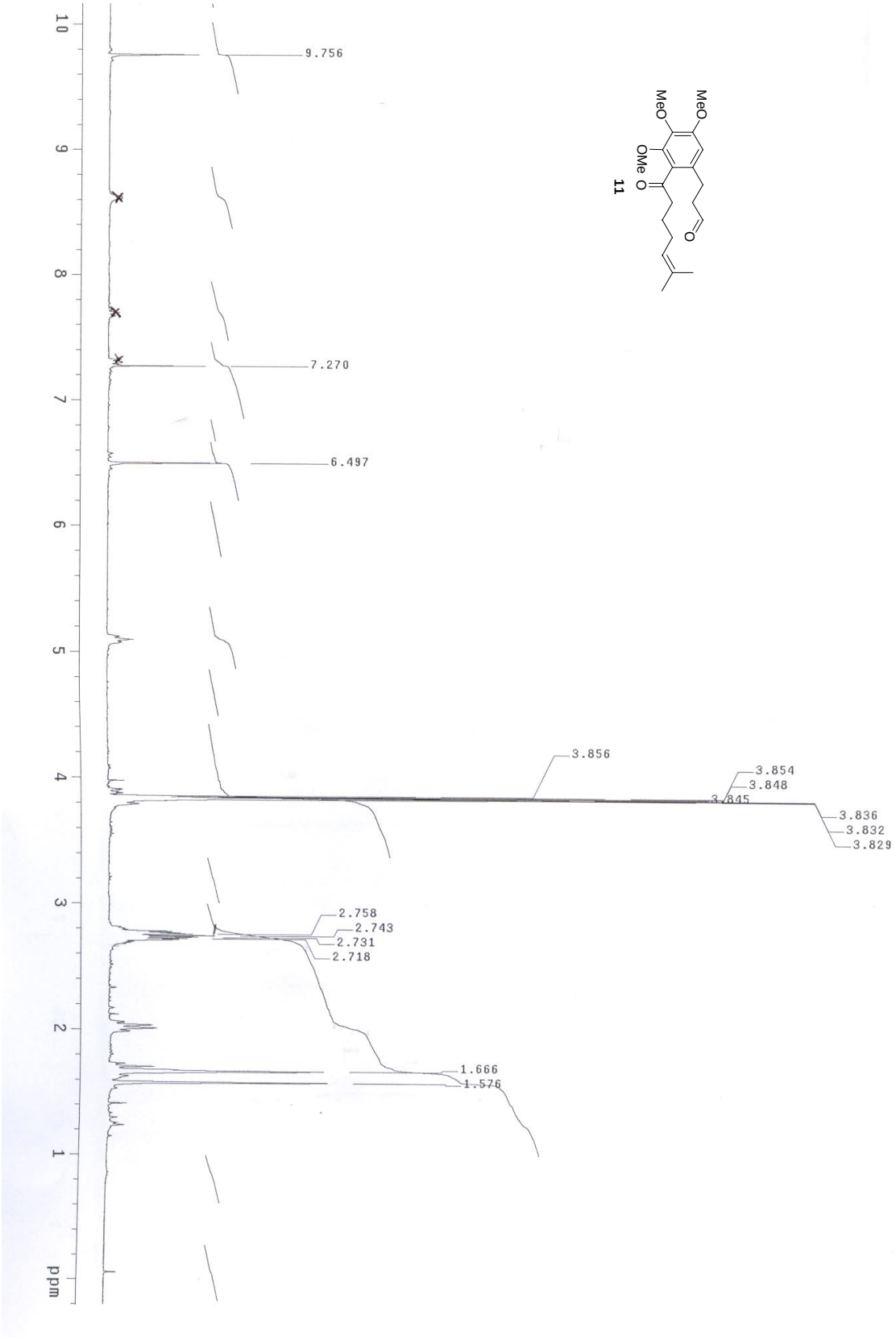
^{1}H-NMR spectrum (300 MHz) of compound **10**



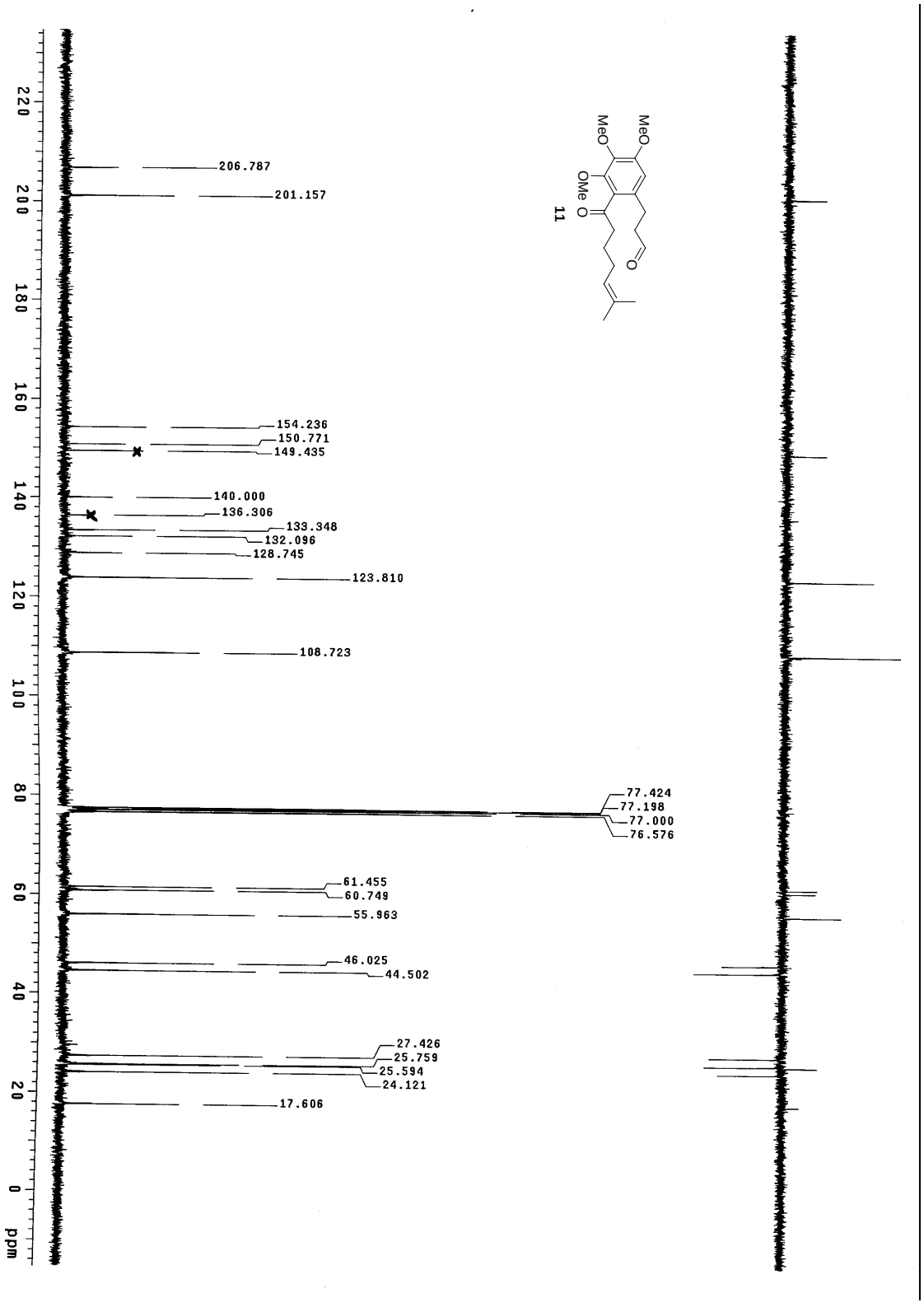
^{13}C-NMR spectrum (75 MHz) of compound **10**



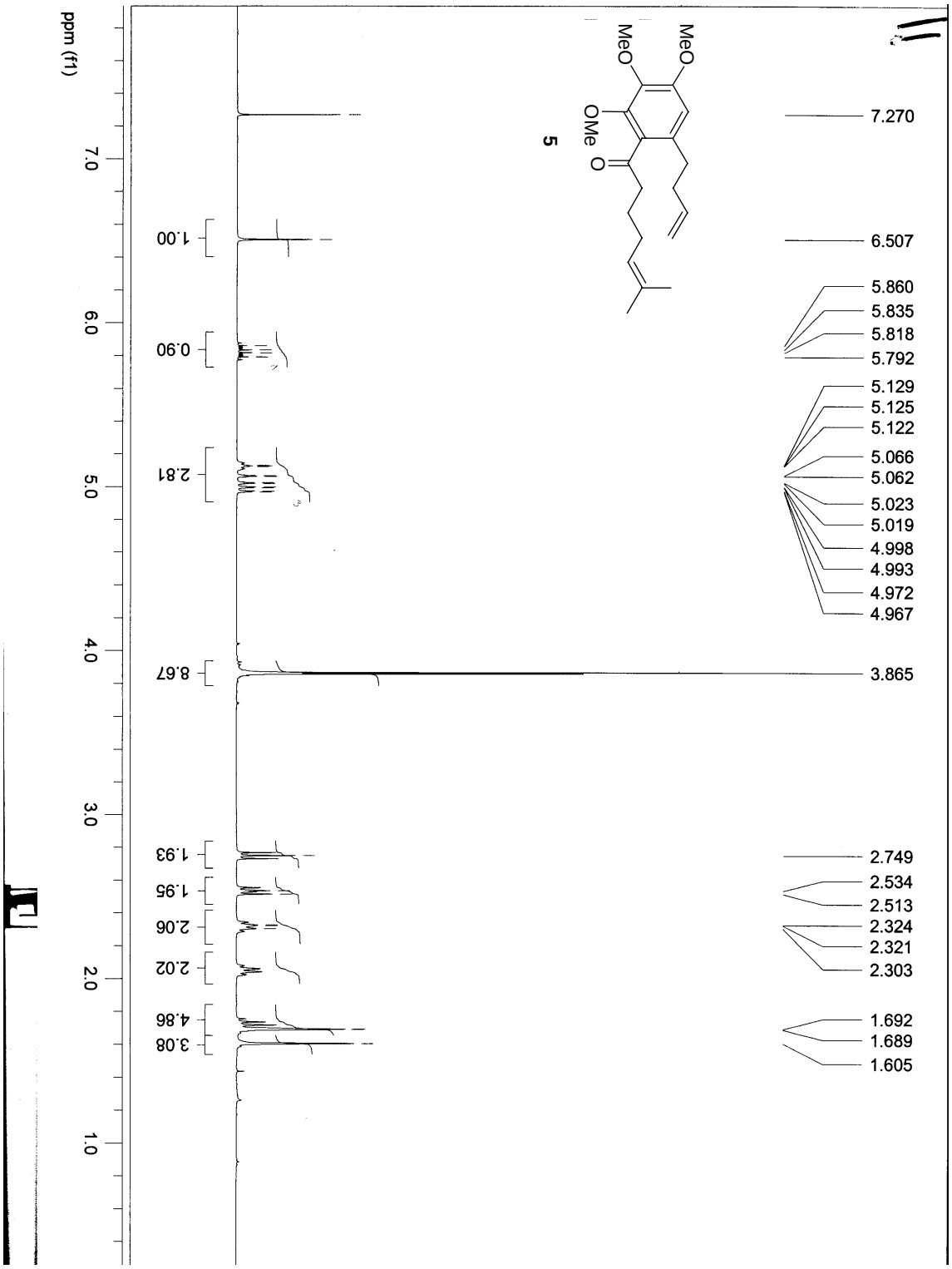
^{1}H-NMR spectrum (300 MHz) of compound **11**



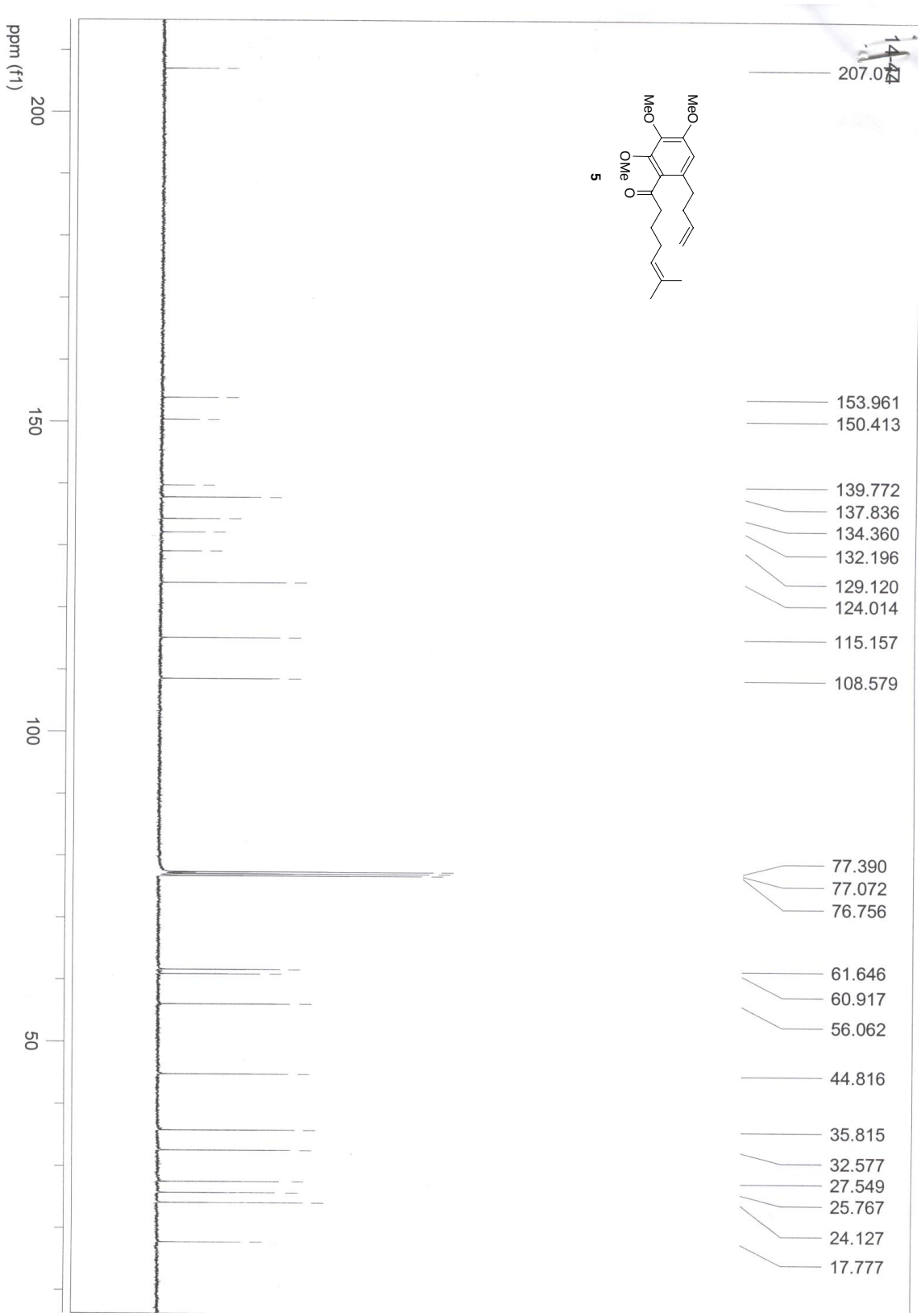
^{13}C-NMR spectrum (75 MHz) of compound **11**



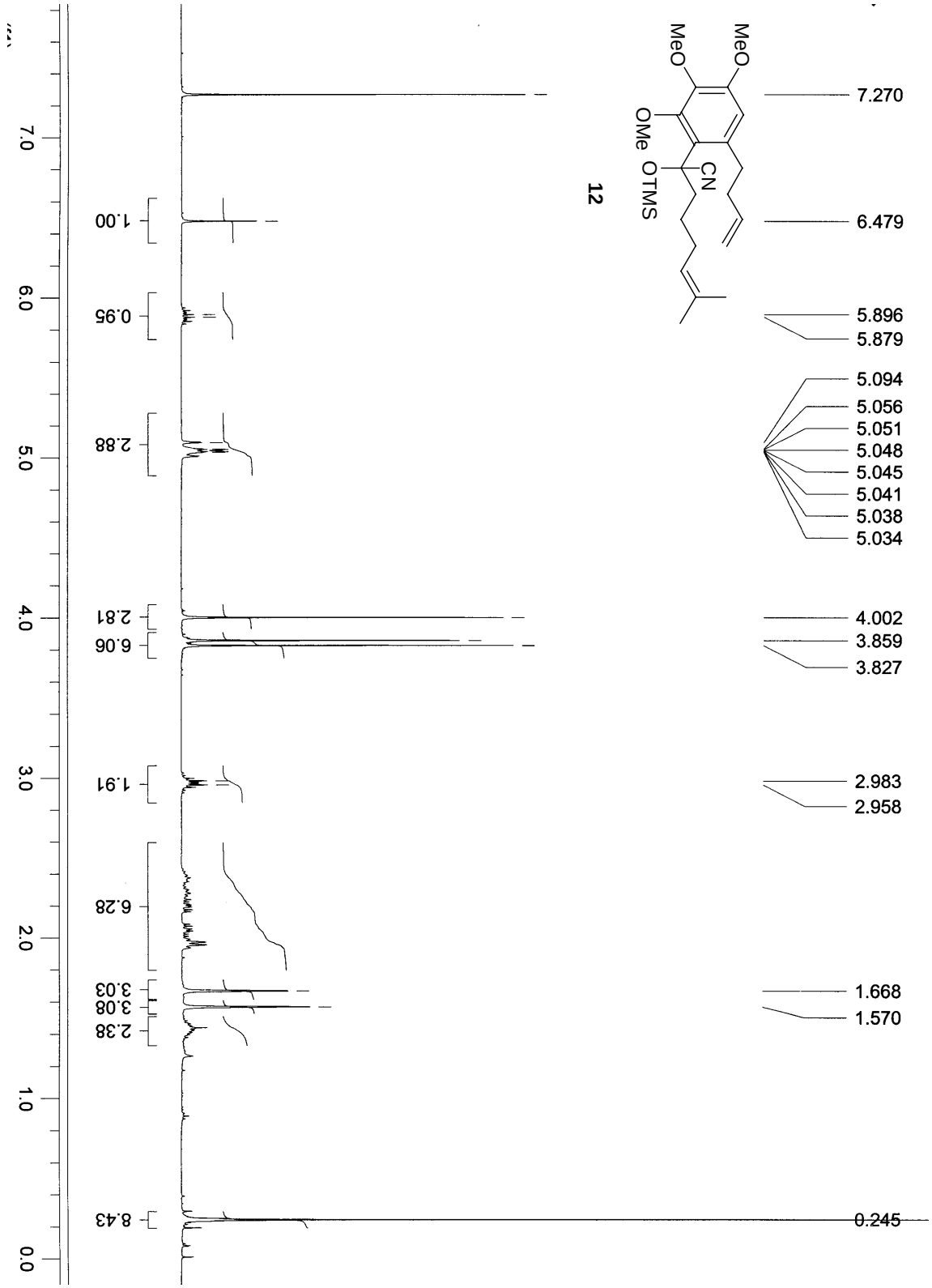
^{1}H-NMR spectrum (400 MHz) of compound **5**



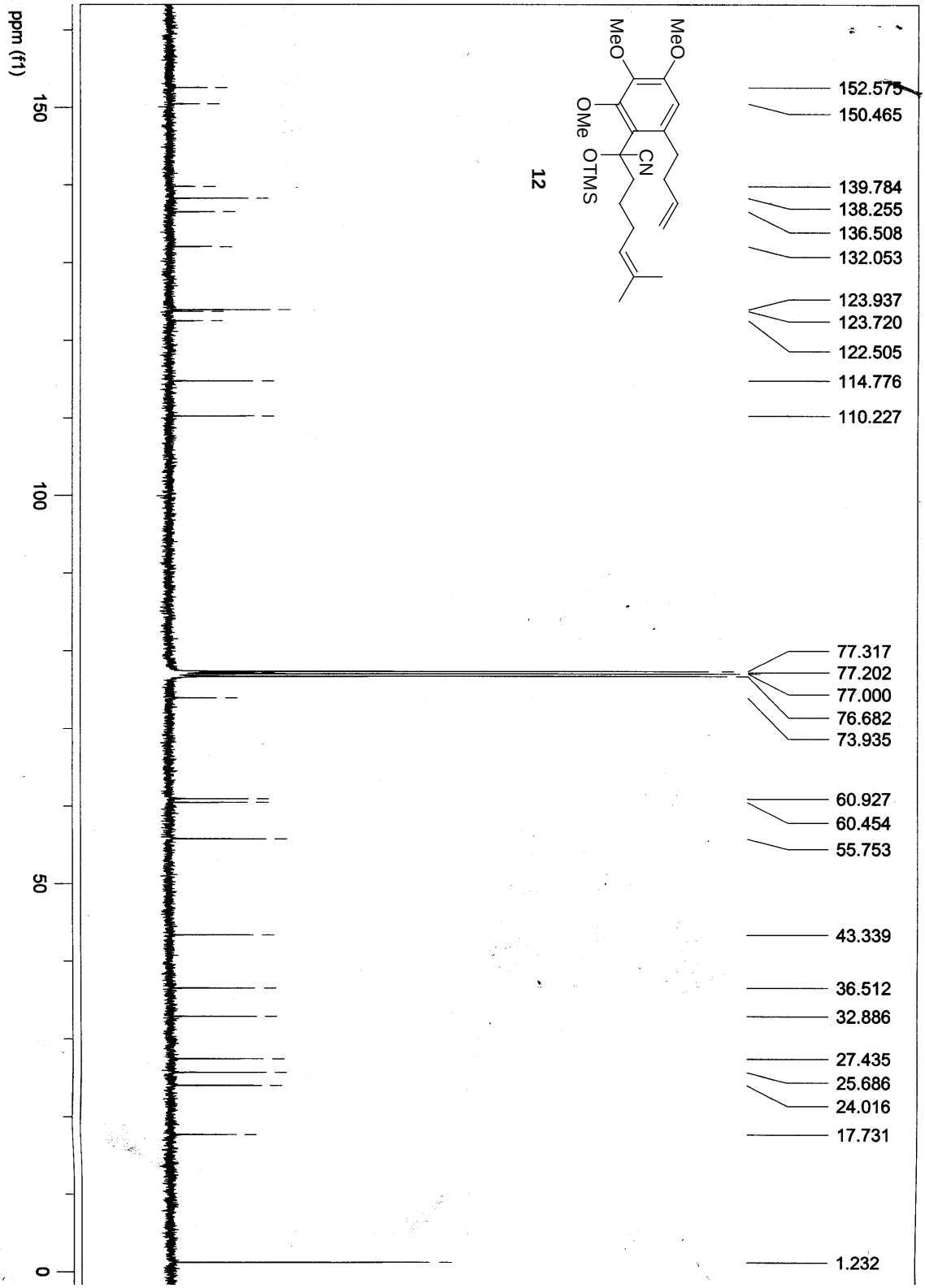
^{13}C-NMR spectrum (100 MHz) of compound **5**



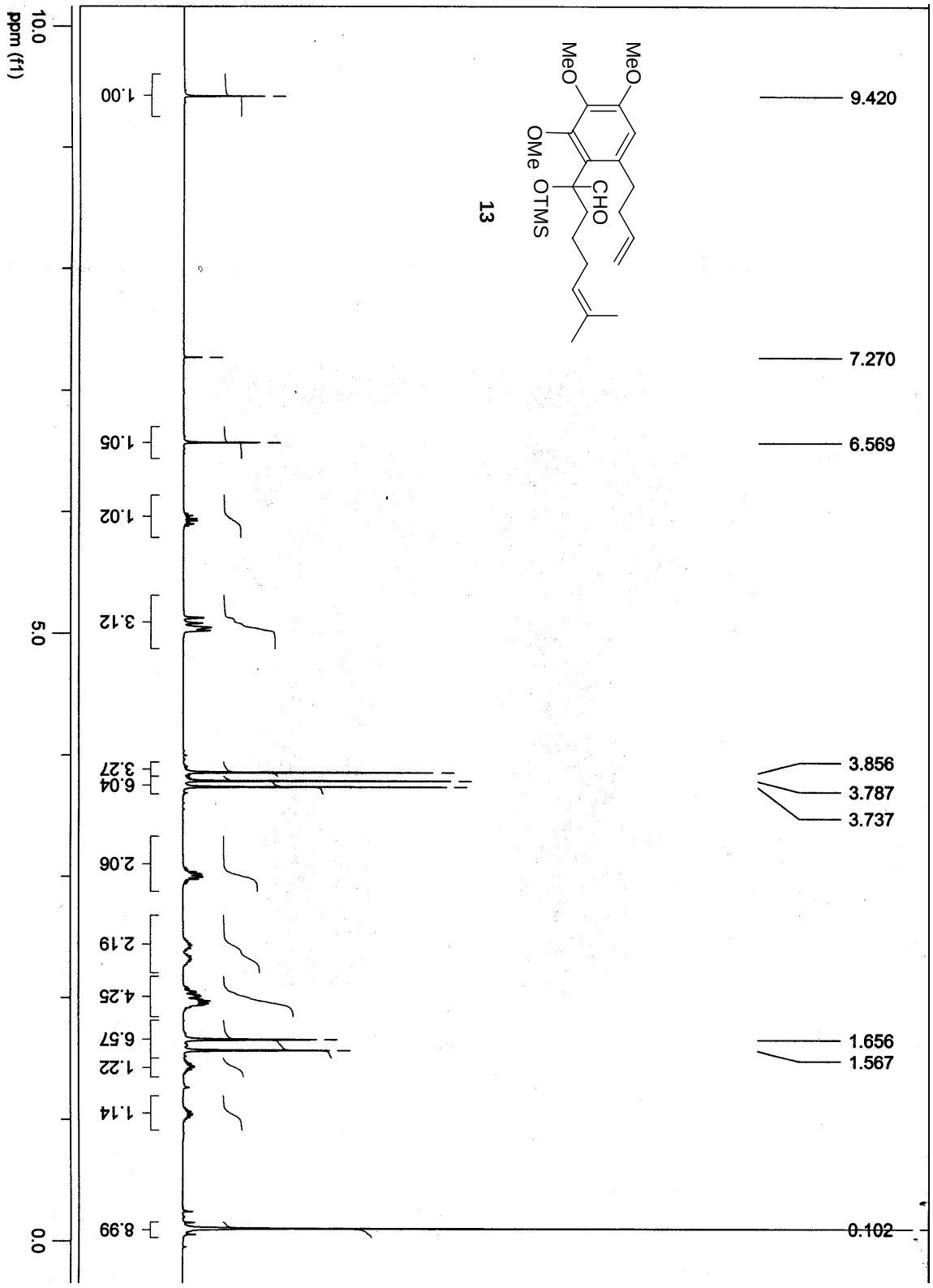
^{1}H-NMR spectrum (400 MHz) of compound **12**



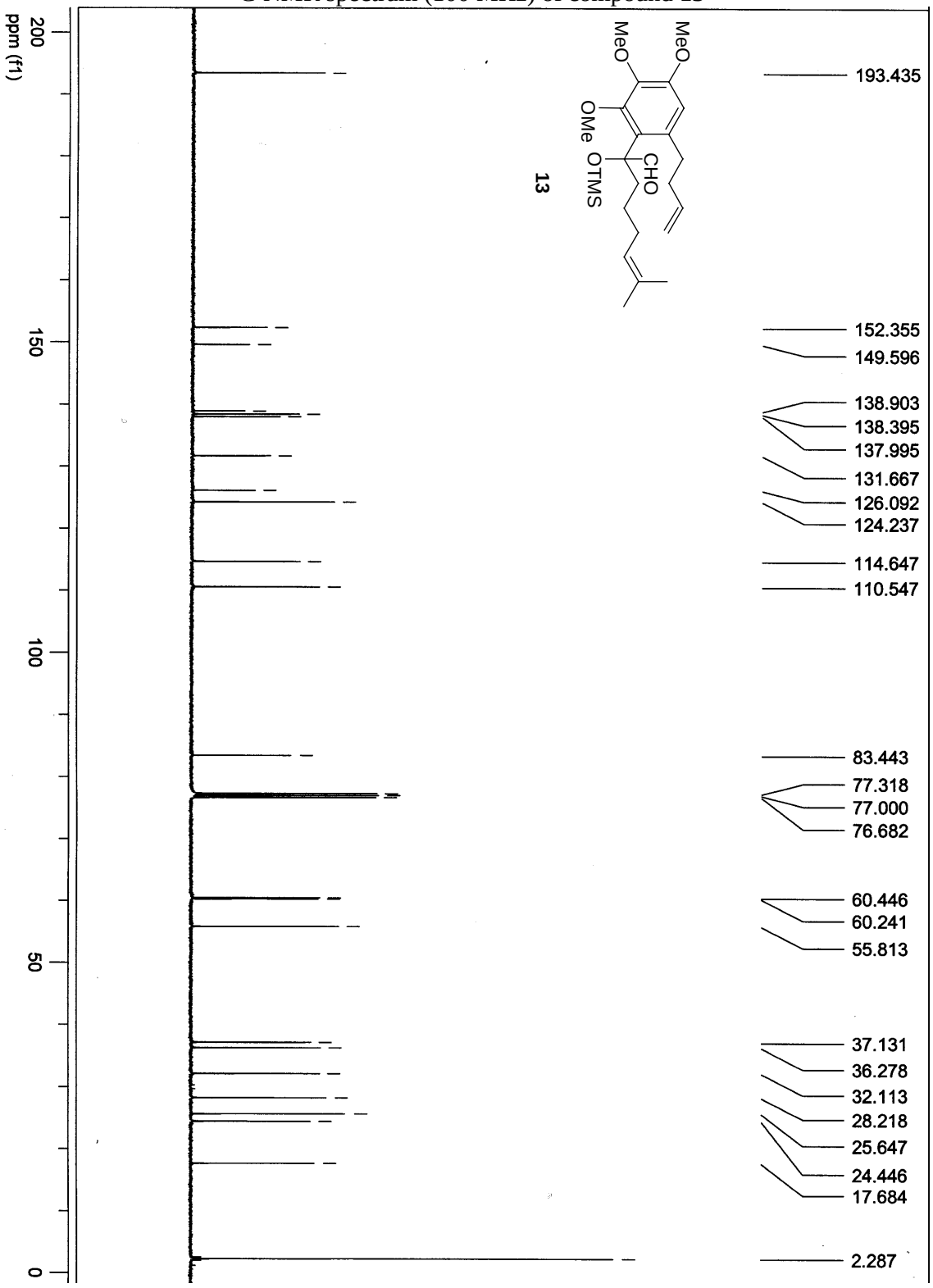
^{13}C-NMR spectrum (100 MHz) of compound **12**



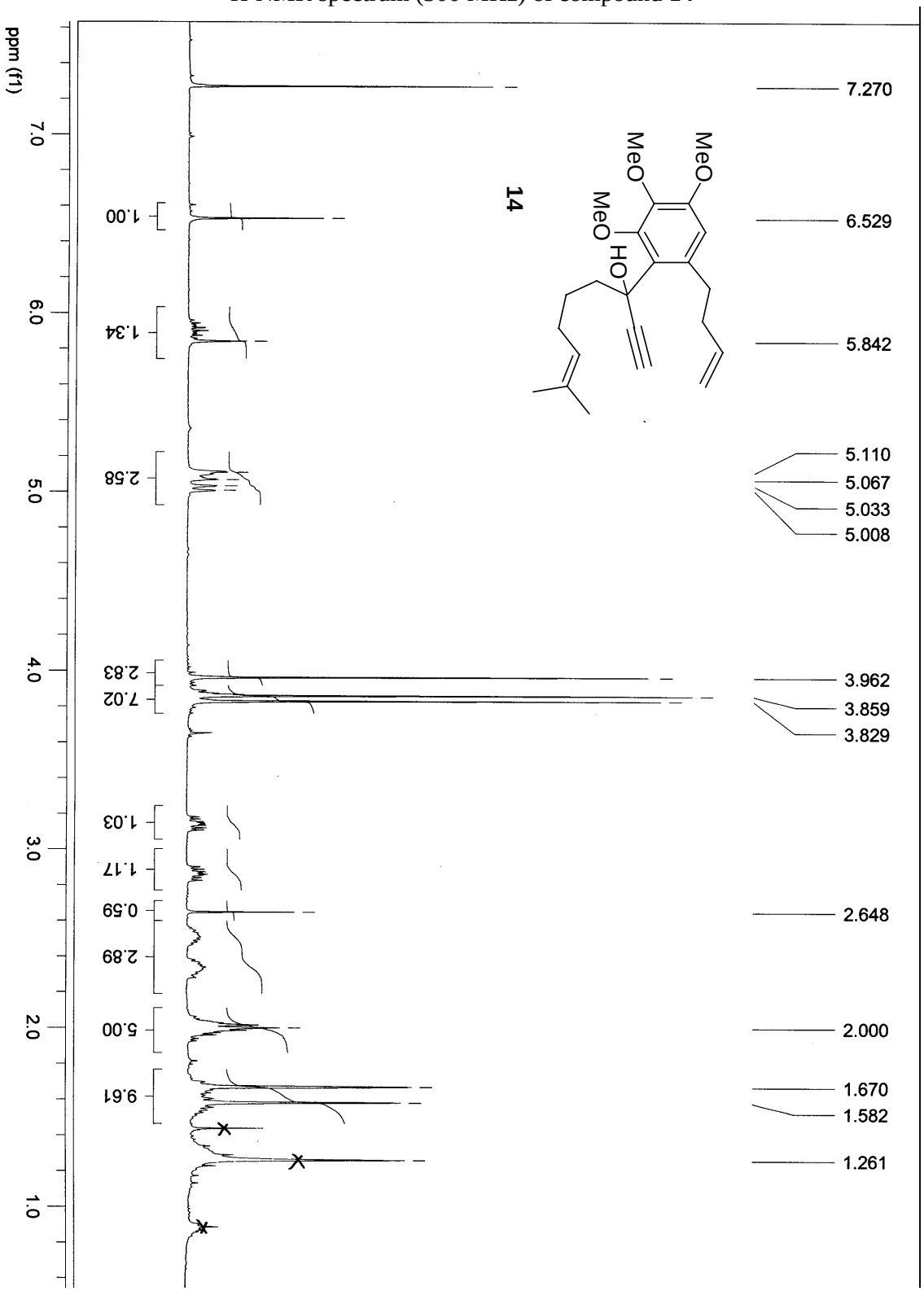
^{1}H-NMR spectrum (400 MHz) of compound **13**



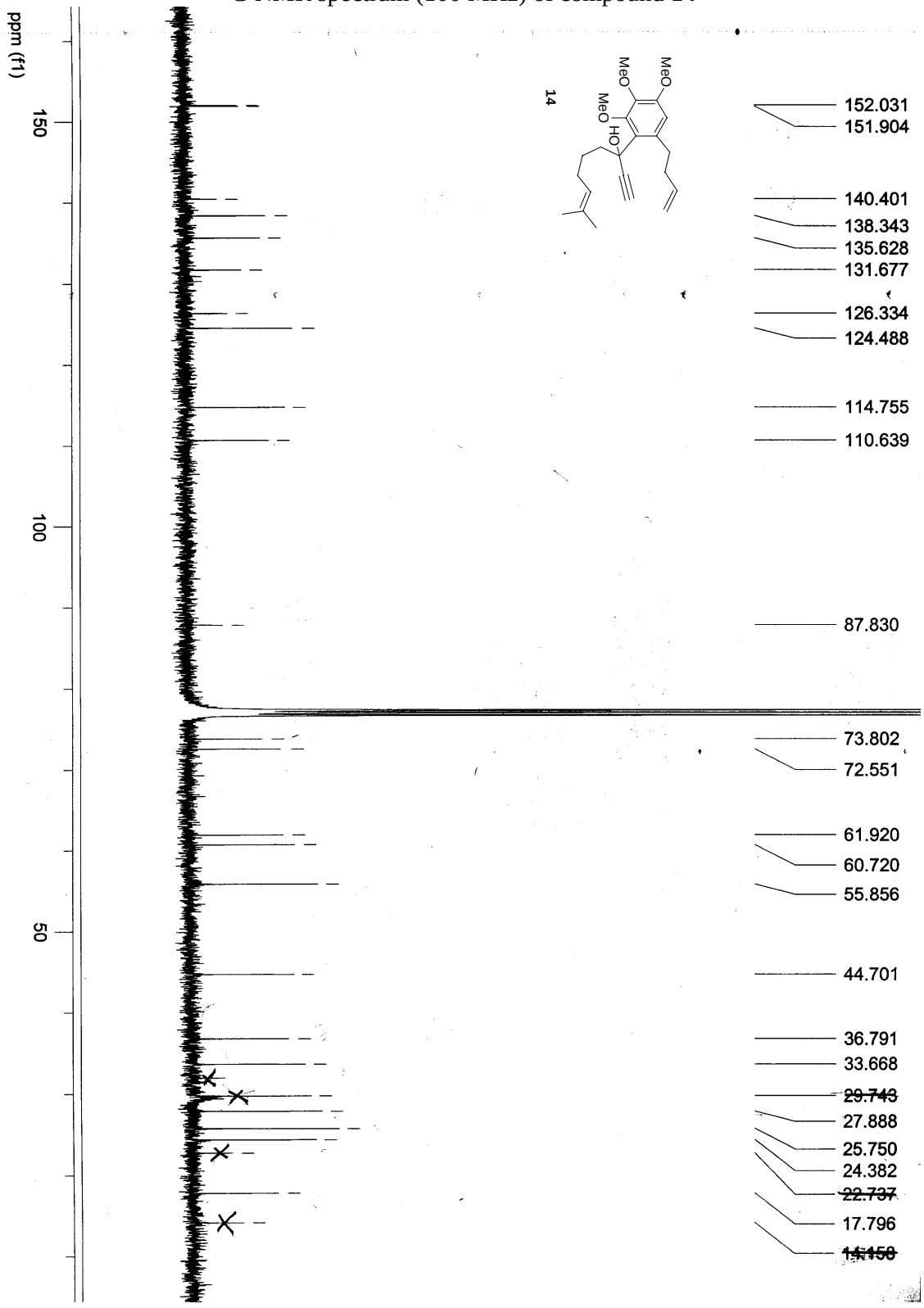
^{13}C-NMR spectrum (100 MHz) of compound **13**



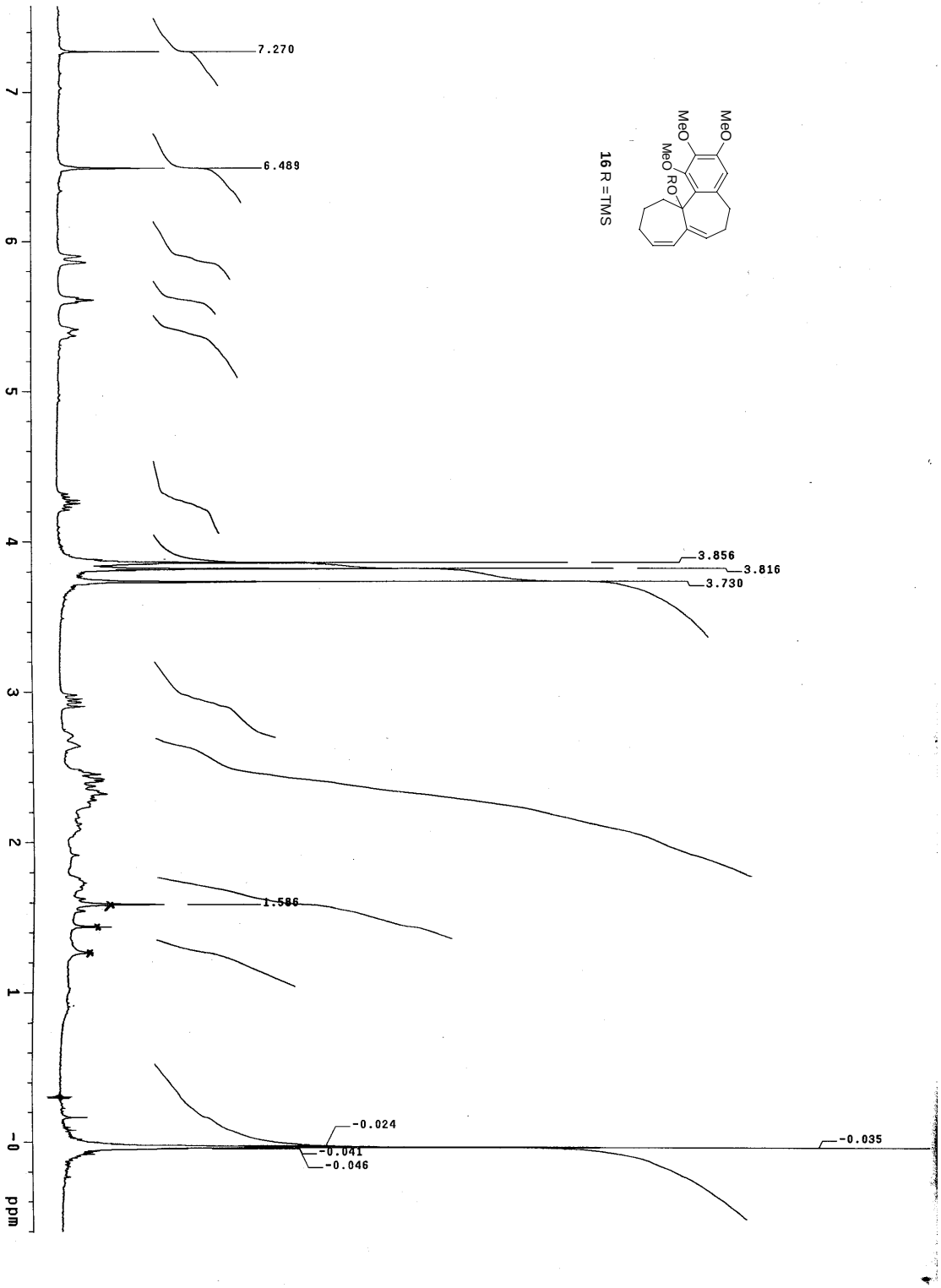
^{1}H-NMR spectrum (300 MHz) of compound **14**



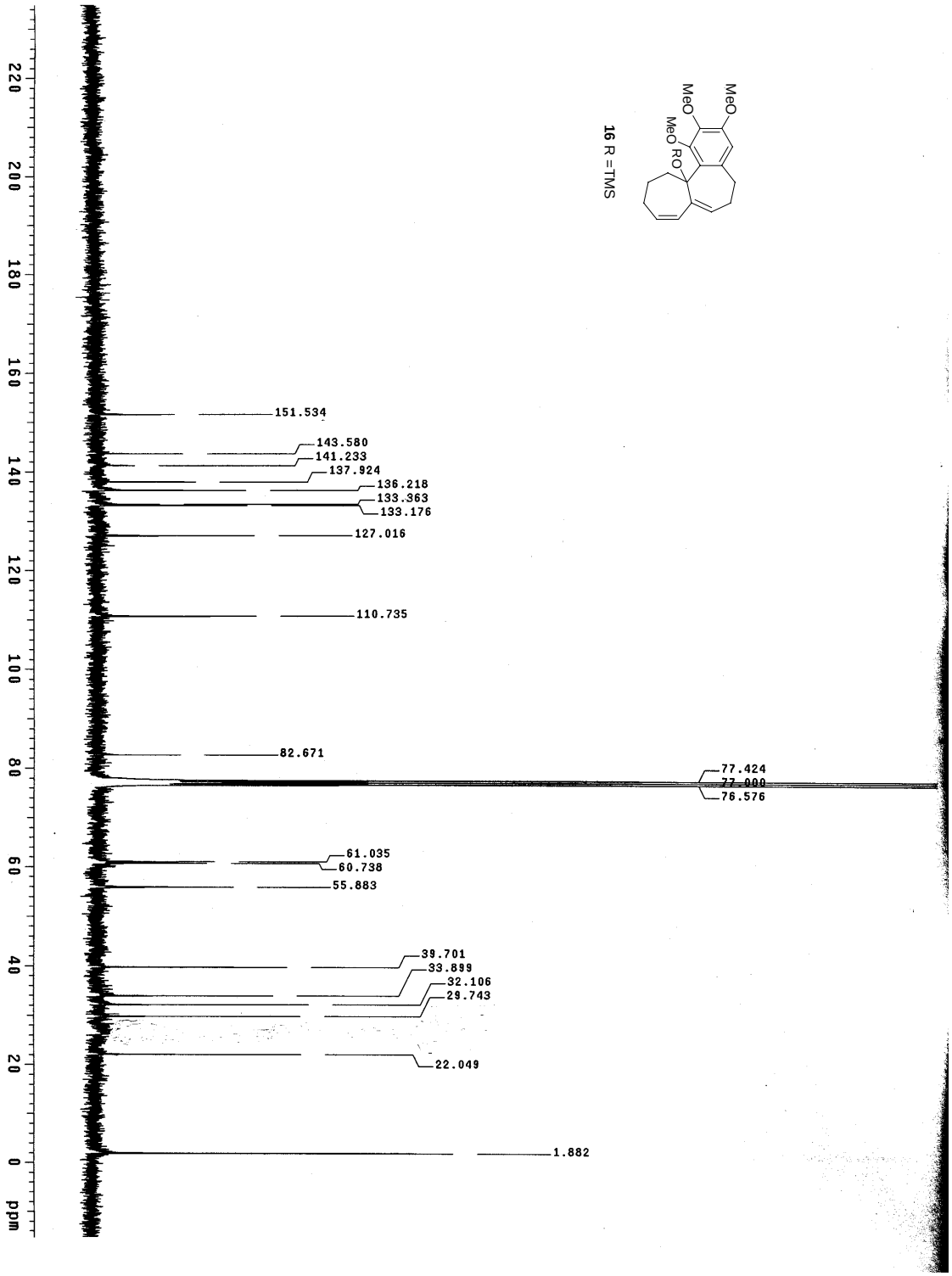
^{13}C-NMR spectrum (100 MHz) of compound **14**



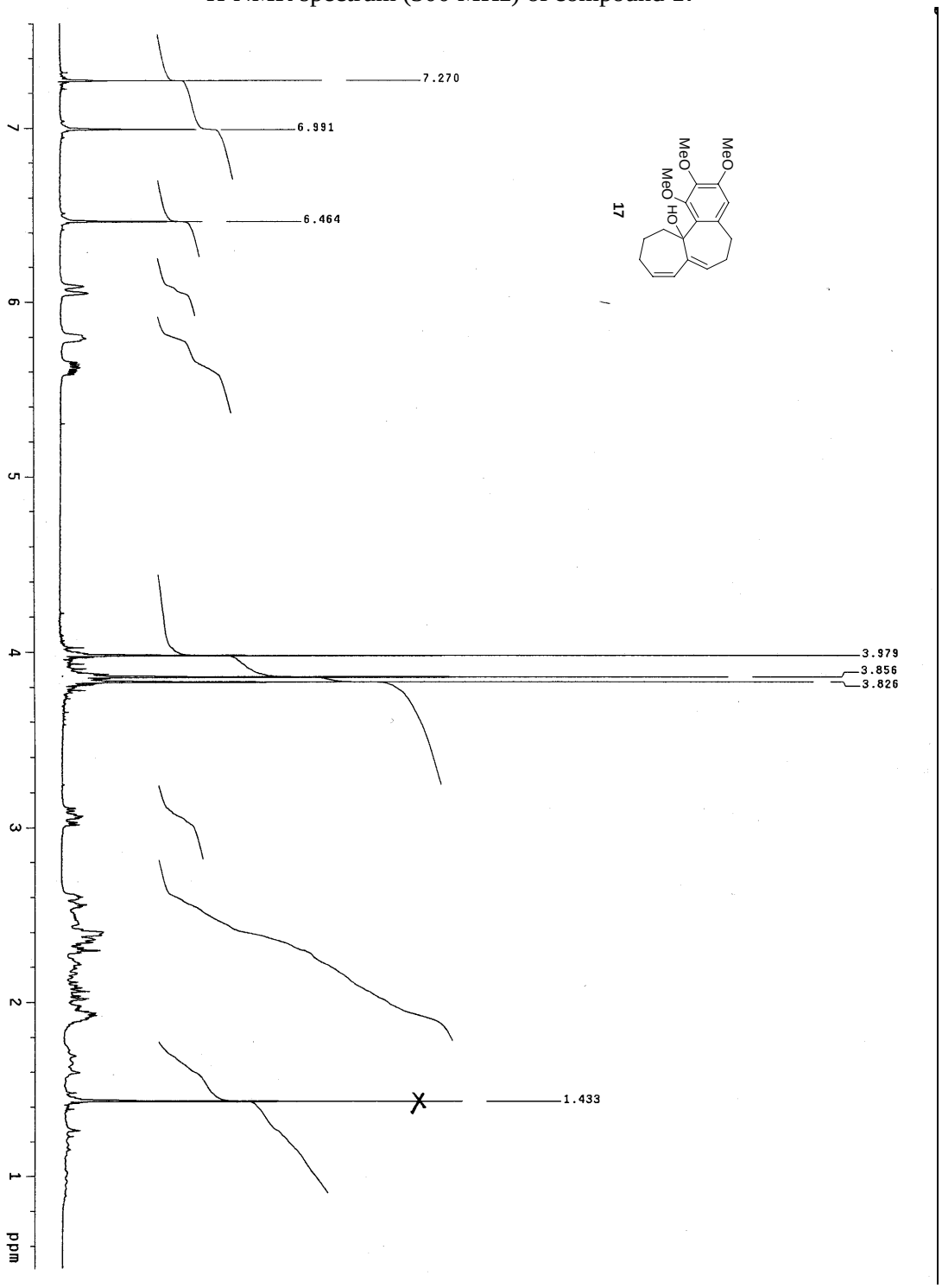
^{1}H-NMR spectrum (300 MHz) of compound **16**



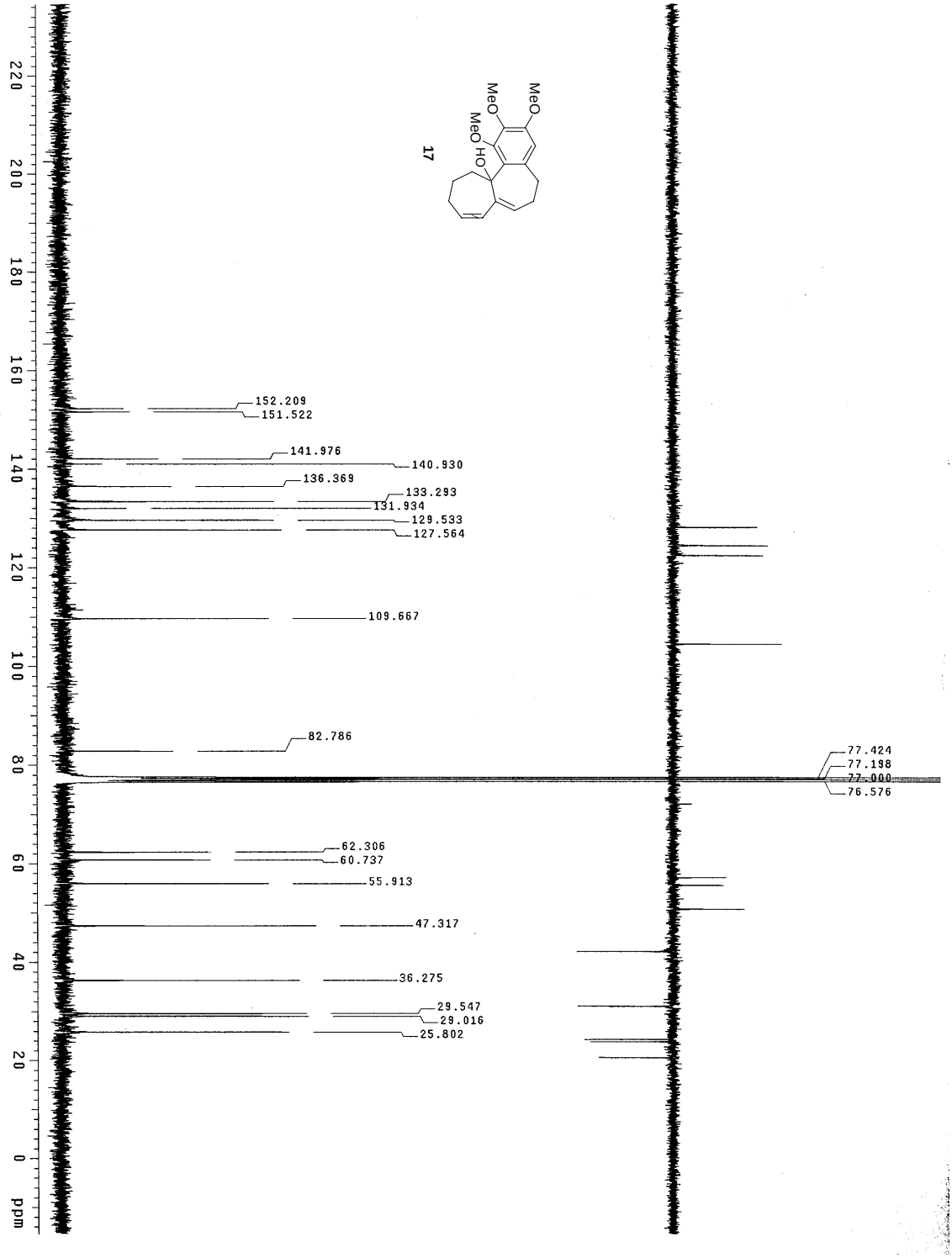
^{13}C-NMR spectrum (75 MHz) of compound **16**



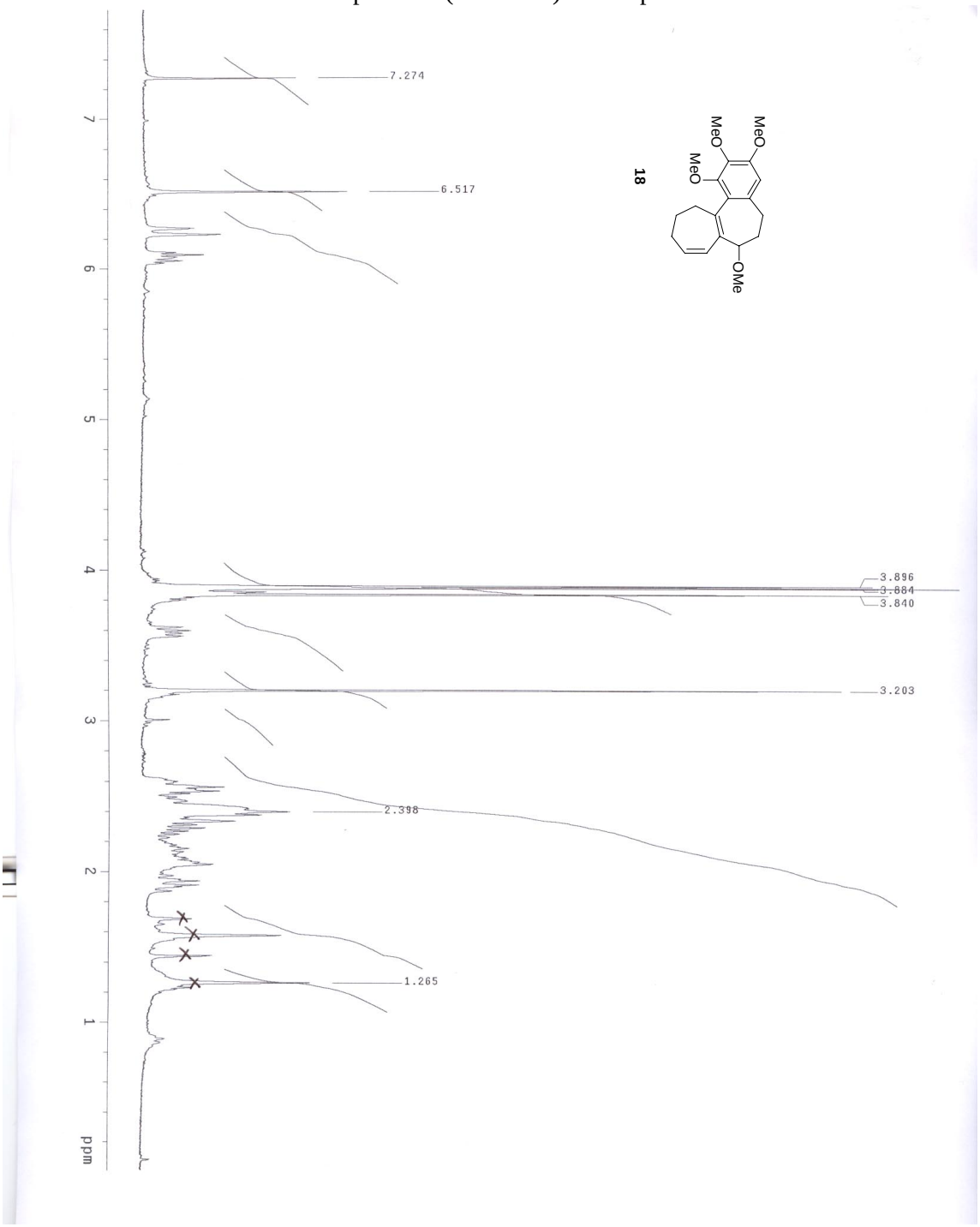
^{1}H-NMR spectrum (300 MHz) of compound **17**



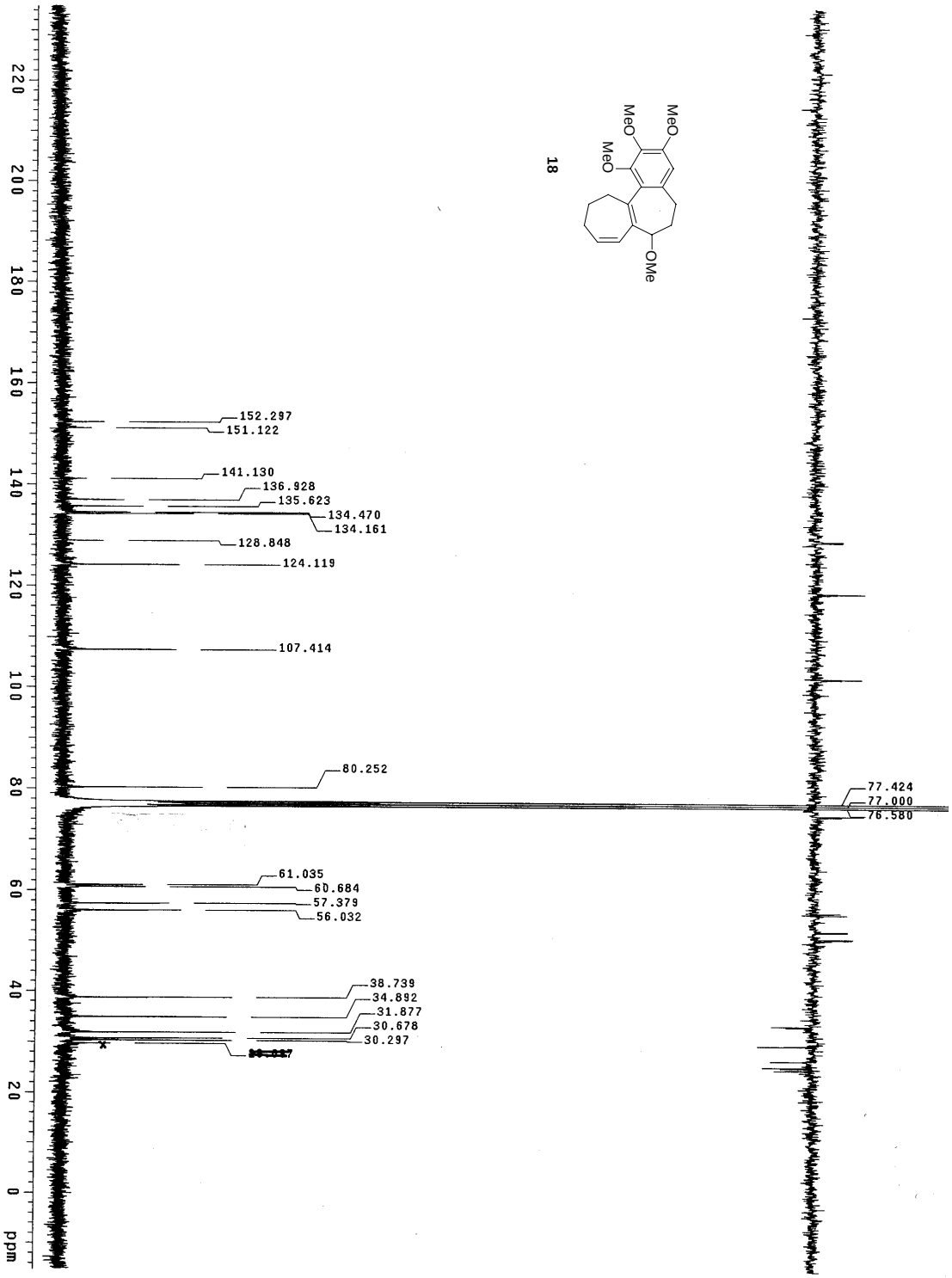
^{13}C-NMR spectrum (75 MHz) of compound **17**



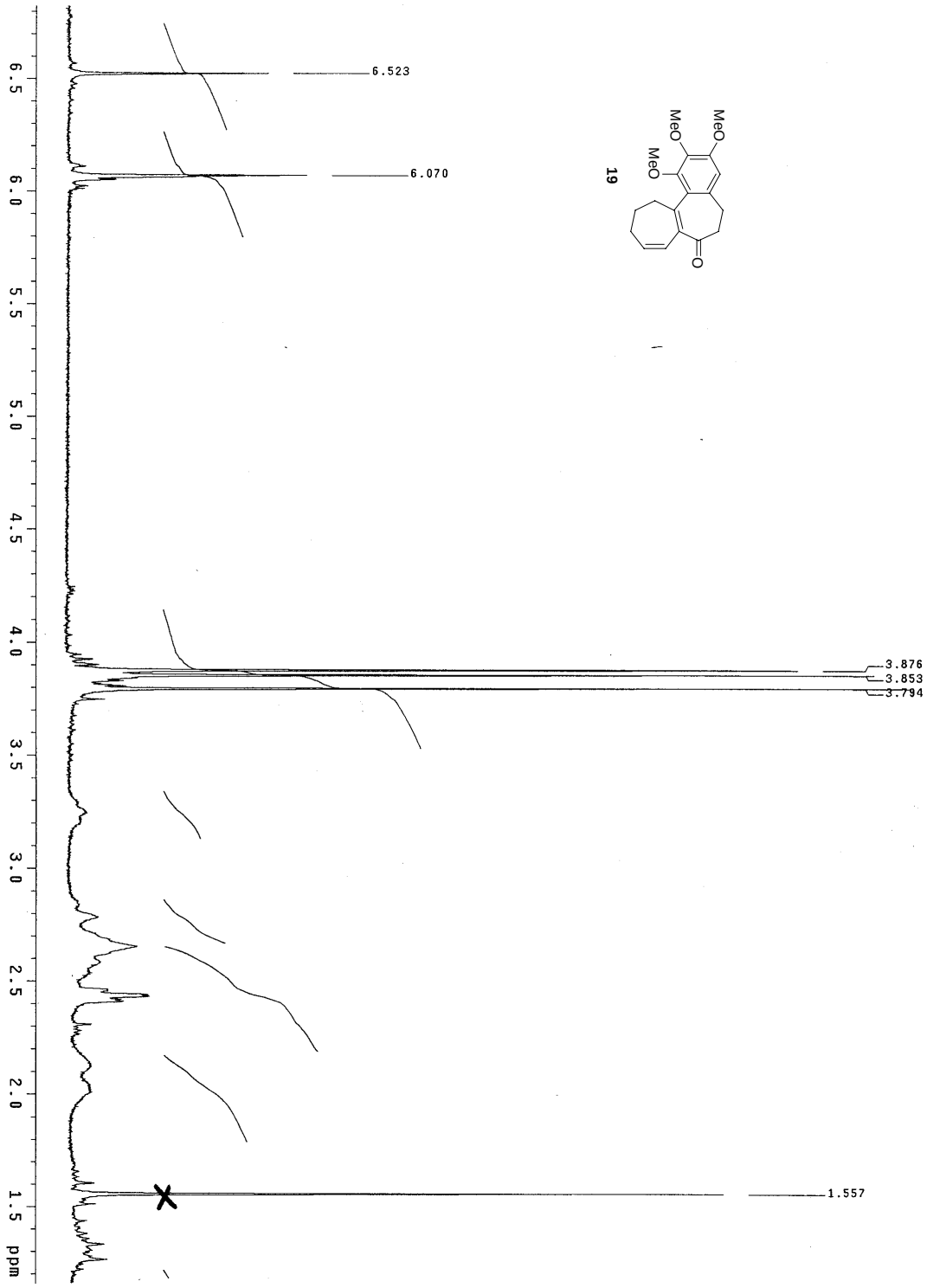
^{1}H-NMR spectrum (300 MHz) of compound **18**



^{13}C-NMR spectrum (75 MHz) of compound **18**



^{1}H-NMR spectrum (300 MHz) of compound **19**



^{13}C-NMR spectrum (75 MHz) of compound **19**