Supporting Information for

Oxazaborolidinone-Mediated Asymmetric Bisvinylogous Mukaiyama Aldol Reaction

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General Information

Reactions were carried out using flame-dried glass vessels under argon atmosphere. Dichloromethane was distilled under an inert atmosphere over calcium hydride. Valeronitrile was purified by distillation from P_2O_{10} under nitrogen atmosphere prior to use.
N-Tosyl-L-tryptophan,[1] ethyl (2*E*,4*E*)-2-methylhexa-2,4-dienoate,[2] (*E*)-3-iodo-2-methyl-acrylaldehyde,[3] and 2-butynal dicobalt hexacarbonyl complex[4] were prepared according to literature procedures.

Nuclear Magnetic Resonance Spectroscopy (NMR)

All NMR spectra were recorded at a Bruker DPX-400, AMX-400, Ascend 400 Avance II, DRX-500 or Ascend-600. ^{1}H NMR spectra were calibrated to the residual proton signal of the solvents ($CDCl_3$: 7.26 ppm, C_6D_6: 7.16 ppm). ^{13}C NMR spectra calibrated to the corresponding solvent signal ($CDCl_3$: 77.16 ppm, C_6D_6: 128.06 ppm).

If the samples contained a mixture of two inseparable isomers, distinguishable signals that stem from the minor isomer are marked with an asterisk*. NMR spectra were processed using TopSpin (Bruker) Version 4.0.5.

Chromatography

Thin layer chromatography was performed using silica-coated aluminum TLC-plates by Macherey-Nagel (layer-thickness: 0.20 mm, pore size: 60 A, UV-indicator F_{254}). Substanced were visualized by UV fluorescence extinction (λ_{max} =254 nm) and staining with basic $KMnO_4$, acidic *p*-anisaldehyde or acidic vanillin stain.

Flash column chromatography was performed using silica by Macherey-Nagel (40-63 µm).

High-performance liquid chromatography was performed using a Merck/Hitachi La Chrome®-HPLC-system with L-7150 pump, L-7200 autosampler and L 7400-UV-detection. A Daicel Chiracel® OD-H column and an isocratic *n*-Hexane/*iso*-propanol (99:1) eluent was used; flow rate 1.00 mL/min.

[1] S. Simsek, M. Horzella, M. Kalesse, *Org. Lett.* **2007**, 9, 26, 5637–5639; E. J. Corey, T. P. Loh, *J. Am. Chem. Soc.* **1991**, *113*, 8966-8967.
[2] P. Koukal, M. Kotora, *Chem. Eur. J.* **2015**, *21*, 7408-7412; E. Piers, G. L. Jung, E. H. Ruediger, *Can. J. Chem.* **1987**, *65*, 670-682.
[3] M. T. Gieseler, M. Kalesse, *Org. Lett.* **2011**, *13*, 2430-2432.
[4] S. Simsek, Dissertation, Gottfried Wilhelm Leibniz Universität Hannover, **2009**.

High Resolution Mass Spectrometry

Mass spectra were measured by electron-spray ionization (ESI) at a Waters Micromass LCT (TOF) with lock-spray unit und injection by loop-mode by a Waters Alliance 2695, or electron ionization (EI) at a Agilent 7890 GC system with a 5977B detector (single-quadrupole).

Optical rotation

Optical rotations were measured on a Perkin-Elmer 341 polarimeter at the sodium D-line (λ_{max} = 589.3 nm), with a cell length of d = 1 dm in $CHCl_3$. Concentrations are given in the corresponding experiment. Optical rotations were determined for reaction products with e.r. or d.r. above 5:1.

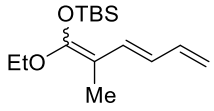
Racemic samples

Racemic samples were synthesized analogously to general procedure 2, substituting *N*-tosyl-L-tryptophan with *N*-tosylglycine.

Compounds were named as suggested by ChemDraw.

General procedure 1: Preparation of ketene silyl acetals

To a solution of DMPU (1.20 equiv) in THF (1.9 M) was added LiHMDS (1.0 M in THF, 1.10 equiv) at –78 °C. After 30 min, the corresponding ester (13.0 mmol, 1.00 equiv) was added and the mixture stirred for 30 min. After addition of the corresponding chlorosilane (14.3 mmol, 1.10 equiv), the reaction mixture was warmed to r.t. immediately and stirred for 2 h. To the resulting orange-yellow solution, *n*-pentane was added until no more lithium salts precipitated. The mixture was transferred to a separation funnel, washed with ice-water (3x 10 mL), dried over Na_2SO_4, and filtered through Celite®. After evaporation of the solvent in vacuo, the so obtained KSAs were directly employed in subsequent bVMARs.



3a

3.44 g, 12.8 mmol, 88%

Prepared according to general procedure 1 starting from 2.24 g of (2*E*,4*E*)-2-methylhexa-2,4-dienoate.

(*E*/*Z* 38:62, asterisk denotes minor component).

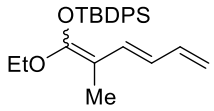
^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 6.67 (d, 1H, *J* = 15.4 Hz), 6.59* (d, 1H, *J* = 15.5 Hz), 6.43 (ddt, 1H, *J* = 0.9 Hz, 10.7 Hz, 16.9 Hz), 6.40* (ddt, 1H, *J* = 0.9 Hz, 10.6 Hz, 16.9 Hz), 5.98 (dd, 1H, *J* = 10.6 Hz, 15.5 Hz), 5.13–5.06 (m, 1H), 4.93–4.89 (m, 1H), 3.86 (q, 2H, *J* = 7.1 Hz), 3.86* (q, 2H, *J* = 7.1 Hz), 1.71* (s, 3H), 1.67 (s, 3H), 1.27 (t, 3H), 0.99* (s, 9H), 0.97 (s, 9H), 0.17 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 153.0, 152.7*, 138.6, 132.2*, 132.0, 124.8*, 124.5, 113.3*, 113.2, 98.3, 97.7*, 77.4, 66.1, 65.4*, 25.82*, 25.77, 18.4*, 18.3, 14.96*, 14.86, 11.5, 11.0*, –4.3, –4.4*.

HRMS due to decomposition in the mass spectrometer not available (ESI+; EI).[5]

Appearance: Orange oil

[5] This is in accordance with observations List et al. made for similar and isomeric ketene silyl acetals. See page 6 in SI: L. Ratjen, P. García-García, F. Lay, M. E. Beck, B. List, Disulfonimide-Catalyzed Asymmetric Vinylogous and Bisvinylogous Mukaiyama Aldol Reactions. *Angew. Chem.* **2011**, *123*, 780‑784; *Angew. Chem. Int. Ed.* **2011**, *50*, 754‑758.



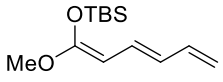
3b R = TES
3c R = TIPS
3d R = TBDPS

Ketene silyl acetals **3b–d** were prepared according to general procedure 1 starting from 600 mg of (2*E*,4*E*)-2-methylhexa-2,4-dienoate. Due to their general instability these compounds were directly applied in the reactions, and used without purification and further characterization.

3b: 1.03 g, 3.85 mmol, 99%, orange oil.

3c: 1.11 g, 3.58 mmol, 92%, orange oil.

3d: 1.40 g, 3.58 mmol, 92%, orange oil.



3e

1.26 g, 5.24 mmol, 80%

Prepared according to general procedure 1 starting from 825 mg of methyl sorbate.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 6.46–6.31 (m, 2H), 5.96 (dd, 1H, *J* = 10.9, 14.9 Hz), 5.01–4.95 (m, 1H), 4.85–4.80 (m, 1H), 4.47 (d, 1H, *J* = 10.7 Hz), 3.58 (s, 3H), 0.95 (s, 9H), 0.17 (s, 6H).
The spectroscopic data match the data reported by List and co-workers.[6]
Appearance: Yellow oil

[6] L. Ratjen, P. García-García, F. Lay, M. E. Beck, B. List, *Angew. Chem.* **2011**, *123*, 780‑784; *Angew. Chem. Int. Ed.*, **2011**, *50*, 754‑758.

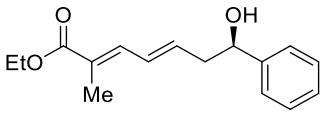
General procedure 2: Bisvinylogous Mukaiyama Aldol Reaction (bVMAR)

To a suspension of *N*-tosyl-L-tryptophan (143 mg, 400 µmol, 1.00 equiv) in dry CH_2Cl_2 (2.0 mL), dichlorophenylborane (52 µL, 400 µmol, 1.00 equiv) was added carefully at r.t. After stirring for 1 h, the solvent was removed under reduced pressure.[7] The resulting solid OXB[8] was dissolved in valeronitrile (2.0 mL) and cooled to –78 °C. The aldehyde (400 µmol, 1.00 equiv) was added, followed by slow addition of the KSA (760 µmol, 1.90 equiv). After 2 h, the reaction was quenched by addition of a mixture of THF/H_2O/2 M HCl (5:1:0.2, 10 mL) and stirred vigorously for 1 h at r.t. To the biphasic mixture was added sat. aq. $NaHCO_3$ solution (5 mL) and EtOAc (20 mL). After phase-separation, the aqueous phase was extracted with EtOAc (3x 10 mL). The combined organic phases were washed with brine (1x 25 ml), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After chromatographic purification the desired ester was obtained.

[7] Solvent was removed at r.t. under high vacuum using a standard Schlenk line with cold trap.

[8] Formation of the OXB could be tracked by ^{11}B-NMR: (128 MHz, CD_2Cl_2) δ [ppm] = 35.9 (broad s). However, this is not necessary since the formation is reliable and fast.

Ethyl (*R*,2*E*,4*E*)-7-hydroxy-2-methyl-7-phenylhepta-2,4-dienoate (5a)



64 mg, 244 µmol, 61%, e.r. 82:18, starting from 42.4 mg of benzaldehyde

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.38–7.34 (m, 4H), 7.33–7.27 (m, 1H), 7.15 (d, 1H, *J* = 11.4 Hz), 6.44 (dd, 1H, *J* = 11.4 Hz, 15.1 Hz), 6.04 (dt, 1H, *J* = 7.4 Hz, 15.1 Hz), 4.80 (t, 1H, *J* = 6.7 Hz), 4.20 (q, 2H, *J* = 7.2 Hz), 2.66 (t, 2H, *J* = 6.7 Hz), 2.00 (br s, 1H), 1.92 (s, 3H), 1.30 (t, 3H, *J* = 7.2 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.7, 143.8, 137.9, 137.6, 129.2, 128.7, 127.9, 126.6, 125.9, 73.8, 60.7, 43.2, 14.5, 12.8.

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{21}O_3$ 261.1491; Found 261.1487.

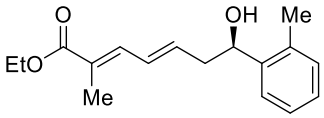
Column chromatography: PE:EtOAc 5:1

R_f = 0.40 (PE:EtOAc 5:1)

$[\alpha]_D^{20}$ = +13.6 (c = 8.8 mg/mL, $CHCl_3$)

Appearance: Yellow oil

Ethyl (*R*,2*E*,4*E*)-7-hydroxy-2-methyl-7-(*o*-tolyl)hepta-2,4-dienoate (5b)



65.9 mg, 240 µmol, 46%, e.r. 65:35, starting from 48.0 mg of 2-methyl benzaldehyde

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.49 (d, 1H, *J* = 7.4 Hz), 7.24–7.12 (m, 4H), 6.45 (dd, 1H, *J* = 11.1 Hz, 15.1 Hz), 6.10 (dt, 1H, *J* = 7.5 Hz, 15.1 Hz), 5.03 (dd, 1H, *J* = 5.5 Hz, 7.0 Hz), 4.20 (q, 2H, *J* = 7.1 Hz), 2.64–2.58 (m, 2H), 2.37 (s, 3H), 1.93−1.92 (m, 3H), 1.30 (t, 3H, *J* = 7.1 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.7, 141.9, 137.9, 134.6, 130.7, 127.8, 126.6, 125.3, 70.1, 60.7, 42.0, 19.2, 14.5, 12.8.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{22}O_3Na$ 297.1467; Found 297.1468.

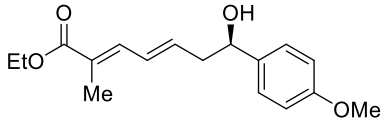
Column chromatography: PE:EtOAc 5:1

R_f = 0.33 (PE:EtOAc 5:1)

$[\alpha]_D^{20}$ = +17.8 (c = 10.0 mg/mL, $CHCl_3$)

Appearance: Yellow oil

Ethyl (*R*,2*E*,4*E*)-7-hydroxy-7-(4-methoxyphenyl)-2-methylhepta-2,4-dienoate (5c)



44.1 mg, 152 µmol, 38%, e.r. 78:22, starting from 54.4 mg of *p*-anisaldehyde, obtained as 3.6:1 mixture of the 2*E* and 2*Z* isomer.[9]

^{1}H NMR (400 MHz, C_6D_6): δ [ppm] = 7.79−7.72 (2*Z*, m, 1H), 7.42−7.36 (2*E*, m, 1H), 7.14−7.09 (m , 2H), 6.81−6.74 (m, 2H), 6.31−6.22 (m, 1H), 5.90−5.80 (2*E*, m, 1H), 5.78−5.70 (2*Z*, m, 1H), 4.47−4.38 (m, 1H), 4.04 (2*Z*, q, 2H, *J* = 7.1 Hz), 4.03 (2*E*, q, 2H, *J* = 7.1 Hz), 3.31 (s, 3H), 2.71−2.62 (2*Z*, m, 1H), 2.61−2.52 (2*Z*, m, 1H), 2.51−2.42 (2*E*, m, 1H), 2.41−2.32 (2*E*, m, 1H), 1.91−1.88 (m, 3H), 1.61 (br s, 1H), 0.99 (2*E*, t, 3H, *J* = 7.1 Hz), 0.98 (2*Z*, t, 3H, *J* = 7.2 Hz).

^{13}C NMR (101 MHz, C_6D_6): δ [ppm] = 168.2 (2*Z*), 168.1 (2*E*), 159.62 (2*E*), 159.60 (2*Z*), 138.4 (2*E*), 138.3 (2*E*), 136.8 (2*E*), 136.7 (2*Z*), 135.3 (2*Z*), 132.9 (2*E*), 128.9 (2*E*), 127.4 (2*Z*), 127.3 (2*E*), 126.6 (2*E*), 126.1 (2*Z*), 114.08 (2*E*), 114.06 (2*Z*), 73.4 (2*Z*), 73.3 (2*E*), 60.6 (2*Z*), 60.5 (2*E*), 54.8 (2*E*), 54.8 (2*Z*), 43.6 (2*E*), 38.2 (2*Z*), 14.36 (2*E*), 14.35 (2*Z*), 12.8 (2*E*), 12.7 (2*Z*).

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{22}O_4Na$ 313.1416; Found 313.1404.

Column chromatography: PE:EtOAc 5:1

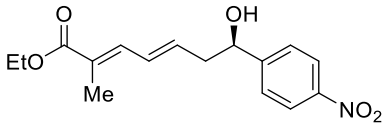
R_f = 0.13 (PE:EtOAc 5:1)

$[\alpha]_D^{20}$ = +8.3 (c = 10.0 mg/mL, $CHCl_3$)

Appearance: Yellow oil

[9] Assignment of *E* and *Z* isomer based on the relative magnitudes of the $^4J_{H,H}$ between the C2 Me group and the olefinic proton at C3. See M. Barfield, R. J. Spear, S. Sternhell, *Chem. Rev.* **1976**, *76*, 593–624.

Ethyl (*R*,2*E*,4*E*)-7-hydroxy-2-methyl-7-(4-nitrophenyl)hepta-2,4-dienoate (5d)



56.1 mg, 184 µmol, 71%, e.r. 86:14, starting from 60.4 mg of *p*-nitro benzaldehyde.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 8.26–8.16 (m, 2H), 7.57-7.50 (m, 2H), 7.13 (d, 1H, *J* = 11.2 Hz), 6.49–6.36 (m, 1H), 6.00 (dt, 1H, *J* = 7.5 Hz, 15.1 Hz), 4.96–4.87 (m, 1H), 4.25-4.15 (m, 2H), 2.70-2.59 (m, 2H), 1.90 (s, 3H), 1.32–1.27 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.6, 151.2, 147.4, 137.5, 136.2, 129.8, 127.1, 126.7, 123.8, 72.5, 60.8, 43.2, 14.4, 12.7.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{19}NO_5Na$ 328.1161; Found 328.1163.

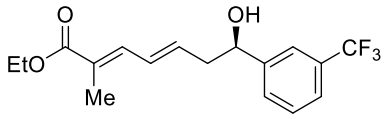
Column chromatography: PE:EtOAc 4:1 to 1:1

R_f = 0.08 (PE:EtOAc 5:1)

$[\alpha]_D^{20}$ = +22.4 (c = 10.0 mg/mL, $CHCl_3$)

Appearance: Orange oil

Ethyl (*R*,2*E*,4*E*)-7-hydroxy-2-methyl-7-(3-(trifluoromethyl)phenyl)hepta-2,4-dienoate (5e)



85.3 mg, 260 µmol, 55%, e.r. 81:19, starting from 69.6 mg of 3-trifluoromethyl benzaldehyde.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.65 (s, 1H), 7.58–7.53 (m, 2H), 7.50–7.45 (m, 1H), 7.17−7.12 (m, 1H), 6.49−6.40 (m, 1H), 6.07−5.99 (m, 1H), 4.86 (dd, 1H, *J* = 5.4 Hz, 5.4 Hz), 4.20 (q, 2H, *J* = 7.1 Hz), 2.68–2.60 (m, 2H), 1.93−1.91 (m, 3H), 1.30 (t, 3H, *J* = 7.1 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.6, 144.7, 137.5, 136.5, 130.9 (q, $J_{C,F}$ = 32.3 Hz), 129.6, 129.2, 129.0, 126.9, 124.6 (q, $J_{C,F}$ = 3.9 Hz), 124.1 (q, $J_{C,F}$ = 272.0 Hz), 122.6 (q, $J_{C,F}$ = 3.9 Hz), 73.0, 60.8, 43.3, 14.4, 12.8.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{19}O_3NaF_3$ 351.1184; Found 351.1184.

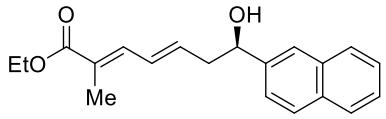
Column chromatography: PE:EtOAc 4:1 to 2:1

R_f = 0.25 (PE:EtOAc 5:1)

$[\alpha]_D^{20}$ = +20.6 (c = 10.0 mg/mL, $CHCl_3$)

Appearance: Yellow oil

Ethyl (*R*,2*E*,4*E*)-7-hydroxy-2-methyl-7-(naphthalen-2-yl)hepta-2,4-dienoate (5f)



51 mg, 184 µmol, 40%, e.r. 80:20, starting from 62.5 mg of 2-naphthaldehyde.

^{1}H NMR (400 MHz, C_6D_6): δ [ppm] = 7.70–7.59 (m, 4H), 7.43–7.37 (m, 1H), 7.34−7.24 (m, 3H), 6.32−6.23 (m, 1H), 5.89−5.80 (m, 1H), 4.55–4.48 (m, 1H), 4.05 (q, 2H, *J* = 7.1 Hz), 2.53–2.36 (m, 2H), 1.91–1.89 (m, 3H), 1.44 (br s, 1H), 0.99 (t, 3H, *J* = 7.1 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.6, 141.1, 137.9, 137.5, 133.4, 133.2, 129.2, 128.5, 128.1, 127.8, 126.6, 126.4, 126.1, 124.7, 124.0, 73.9, 60.7, 43.1, 14.4, 12.7.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{22}O_3Na$ 333.1467; Found 333.1468.

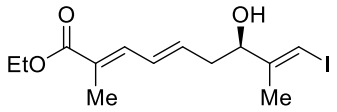
Column chromatography: PE:EtOAc 5:1

R_f = 0.32 (PE:EtOAc 5:1)

$[\alpha]_D^{20}$ = +63.2 (c = 10.0 mg/mL, $CHCl_3$)

Appearance: Waxy solid

Ethyl (*R*,2*E*,4*E*,8*E*)-7-hydroxy-9-iodo-2,8-dimethylnona-2,4,8-trienoate (5g)



91 mg, 260 µmol, 65%, e.r. 89:11, starting from 78.4 mg of 3-iodomethacrolein.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.15 (d, 1H, *J* = 11.4 Hz), 6.48–6.39 (m, 1H), 6.34 (s, 1H), 5.98 (dt, 1H, *J* = 7.4, 14.9 Hz), 4.30–4.25 (m, 1H), 4.21 (q, 2H, *J* = 7.1 Hz), 2.52–2.38 (m, 2H), 1.94 (s, 3H), 1.85 (s, 3H), 1.30 (t, 3H, *J* = 7.1 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.6, 149.1, 137.6, 136.6, 129.3, 126.9, 79.0, 75.8, 60.7, 39.3, 20.3, 14.5, 12.8.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{19}O_3NaI$ 373.0277; Found 373.0275.

Column chromatography: PE:EtOAc 5:1

R_f = 0.44 (PE:EtOAc 5:1)

$[\alpha]_D^{20}$ = −228.6 (c = 10.0 mg/mL, $CHCl_3$)

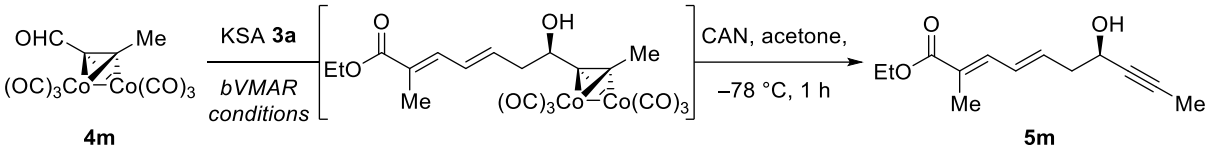
Appearance: Yellow oil

Preparation of protected dicobalt aldehyde 4m and oxidative liberation of bVMAR product 5h:[4]

Preparation of aldehyde **4h:**

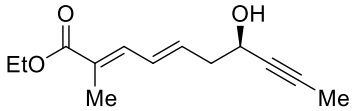
To a solution of dicobalt octacarbonyl (818 mg, 2.39 mmol, 1.00 equiv) in CH_2Cl_2 (48 ml 0.05 M) was slowly added 2-butyne diethyl acetal (380 µl, 2.39 mmol, 1.00 equiv) at rt. After stirring over night at this temperature, the reaction mixture was passed through a short plug of basic aluminium oxide and the filtrate was concentrated under reduced pressure. The residue was then dissolved in acetone (8 ml, 0.3 M) and water (170 µl) and amberlyst 15 (272 mg) were added. After stirring for 3 h at rt, the solution was filtered through Celite® and the filtrate was concentrated under reduced pressure. Purification by column chromatography (PE:MTBE 40:1) yielded aldehyde **4h** (651 mg, 1.84 mmol, 77%) as a red oil, which was used without further purification.

Oxidative liberation of bVMAR product **5h:**



After following General Procedure 2 for the bVMAR of KSA **3a** with aldehyde **4h**, the crude product was passed through a short silica column and the concentrated filtrate was dissolved in acetone (30 ml). To this solution was added ceric ammonium nitrate (1.10 g, 2.00 mmol, 5.00 equiv) in acetone (5 ml) at –78 °C. After 1 h, brine was added and the mixture was warmed to rt. The phases were separated and the aqueous layer was extracted with MTBE (3x 30 ml). The combined organic layers were washed with sat. aq. $NaHCO_3$ solution (1x 75 ml) and brine (1x 75 ml), dried over $MgSO_4$. Purification by flash column chromatography yielded the desired bVMAR product **5h**.

Ethyl (*R*,2*E*,4*E*)-7-hydroxy-2-methyldeca-2,4-dien-8-ynoate (5h)



49 mg, 220 µmol, 55%, e.r. 90:10, starting from 141.6 mg of aldehyde **4h**.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.21–7.15 (m, 1H), 6.50–6.44 (m, 1H), 6.16–6.09 (m, 1H), 4.49–4.40 (m, 1H), 4.20 (q, 2H, *J* = 7.1 Hz), 2.56 (t, 2H, *J* = 6.5 Hz), 1.94 (s, 3H), 1.85 (d, 3H, *J* = 2.1 Hz), 1.30 (t, 3H, 7.1 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.7, 137.9, 136.5, 129.5, 126.7, 82.1, 79.6, 62.0, 60.7, 41.9, 14.4, 12.8, 3.7.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{18}O_3Na$ 245.1154; Found 245.1148.

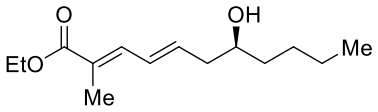
Column chromatography: PE:EtOAc 10:1 to 5:1

R_f = 0.43 (PE:EtOAc 4:1)

$[\alpha]_D^{20}$ = +19.5 (c = 8.2 mg/mL, $CHCl_3$)

Appearance: Colorless oil

Ethyl (*S*,2*E*,4*E*)-7-hydroxy-2-methylundeca-2,4-dienoate (5i)



68 mg, 284 µmol, 71%, e.r. 87:13, starting from 34.4 mg of valeraldehyde.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.20–7.14 (m, 1H), 6.48–6.38 (m, 1H), 6.14–6.04 (m, 1H), 4.20 (q, 2H, *J* = 7.1 Hz), 3.74–3.67 (m, 1H), 2.46–2.38 (m, 1H), 2.35–2.25 (m, 1H), 1.93 (m, 3H), 1.56 (br s, 1H), 1.53–1.27 (m, 9H), 0.94–0.89 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.7, 138.3, 138.0, 129.0, 126.3, 71.2, 60.7, 41.5, 36.9, 28.0, 22.8, 14.5, 14.2, 12.8.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{24}O_3Na$ 263.1623; Found 263.1617.

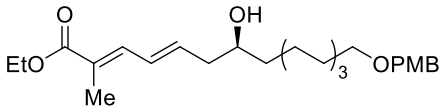
Column chromatography: PE:EtOAc 10:1

R_f = 0.45 (PE:EtOAc 4:1)

$[\alpha]_D^{20}$ = +7.8 (c = 20.6 mg/mL, $CHCl_3$)

Appearance: Yellow oil

Ethyl (S,2E,4E)-7-hydroxy-15-((4-methoxybenzyl)oxy)-2-methylpentadeca-2,4-dienoate (5j)



87 mg, 200 µmol, 50% (75% brsm), e.r. 86:14, starting from 111.4 mg of aldehyde **4j**.

^{1}H NMR (400 MHz, C_6D_6): δ [ppm] = 7.49–7.43 (m, 1H), 7.29–7.24 (m, 2H), 6.85–6.80 (m, 2H), 6.36–6.26 (m, 1H), 5.88–5.78 (m, 1H), 4.38 (s, 2H), 4.09 (q, 2H, *J* = 7.2 Hz), 3.41–3.36 (m, 3H), 3.32 (s, 3H), 2.13–2.00 (m, 2H), 1.97–1.95 (m, 3H), 1.69–1.60 (m, 2H), 1.48–1.18 (m, 12H), 0.89 (br s, 1H), 1.02 (t, 3H, *J* = 7.1 Hz).

^{13}C NMR (101 MHz, C_6D_6): δ [ppm] = 168.1, 159.7, 138.9, 138.4, 131.6, 129.4, 128.7, 126.4, 114.1, 72.8, 70.9, 70.3, 60.5, 54.8, 41.8, 37.5, 30.4, 30.0, 30.0, 29.9, 26.8, 26.0, 14.4, 12.9.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{40}O_5Na$ 455.2773; Found 455.2773.

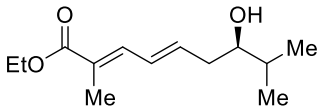
Column chromatography: PE:EtOAc 5:1

R_f = 0.20 (PE:EtOAc 4:1)

$[\alpha]_D^{20}$ = +4.3 (c = 7.0 mg/mL, $CHCl_3$)

Appearance: Amorphous solid

Ethyl (*R*,2*E*,4*E*)-7-hydroxy-2,8-dimethylnona-2,4-dienoate (5k)



59 mg, 261 µmol, 65%, e.r. 95:5, starting from 28.8 mg of isobutyraldehyde.

1.2 mmol scale: 92.7 mg, 0.41 mmol, 34%, e.r. 92:8, starting from 86.4 mg of isobutyraldehyde.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.20–7.15 (m, 1H), 6.49–6.40 (m, 1H), 6.15–6.06 (m, 1H), 4.20 (q, 2H, *J* = 7.1 Hz), 3.50–3.43 (m, 1H), 2.47–2.38 (m, 1H), 2.34–2.24 (m, 1H), 1.95–1.92 (m, 3H), 1.75–1.66 (m, 1H), 1.55 (br s, 1H), 1.30 (t, 3H, *J* = 7.1 Hz), 0.96 (d, 3H, *J* = 2.5 Hz), 0.94 (d, 3H, *J* = 2.5 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] =168.7, 138.9, 138.0, 128.8, 126.2, 75.9, 60.7, 38.4, 33.5, 18.9, 17.5, 14.5, 12.8.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{22}O_3Na$ 249.1467; Found 249.1477.

Column chromatography: PE:EtOAc 10:1

R_f = 0.42 (PE:EtOAc 4:1)

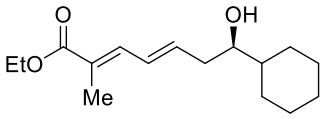
$[\alpha]_D^{20}$ = +12.6 (c = 9.5 mg/mL, $CHCl_3$)

Appearance: Pale-yellow oil

bVMAR with isobutyraldehyde at 1.2 mmol scale:

To a suspension of *N*-tosyl-L-tryptophan (430 mg, 1.20 mmol, 1.00 equiv) in dry CH_2Cl_2 (6.0 mL), dichlorophenylborane (156 µL, 1.20 mmol, 1.00 equiv) was added carefully at r.t. After stirring for 1 h, the solvent was removed under reduced pressure. The resulting solid OXB was dissolved in valeronitrile (6.0 mL) and cooled to –78 °C. Isobutyraldehyde (87 mg, 1.20 mmol, 1.00 equiv) was added, followed by slow addition of the KSA **3a** (611 mg, 2.28 mmol, 1.90 equiv). After 2 h, the reaction was quenched by addition of a mixture of THF/H_2O/2 M HCl (5:1:0.2, 30 mL) and stirred vigorously for 1 h at r.t. To the biphasic mixture was added sat. aq. $NaHCO_3$-solution (15 mL) and EtOAc (60 mL). After phase-separation, the aqueous phase was extracted with EtOAc (3x 30 mL). The combined organic phases were washed with brine (1x 100 ml), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. After chromatographic purification bVMAR product **5k** (92.1 mg, 0.41 mmol, 34%, e.r. 92:8) was obtained as a pale-yellow oil.

Ethyl (*R*,2*E*,4*E*)-7-cyclohexyl-7-hydroxy-2-methylhepta-2,4-dienoate (5l)



47.5 mg, 172 µmol, 45%, e.r. 90:10, starting from 44.9 mg of cyclohexyl carbaldehyde.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.21−7.15 (m, 1H), 6.48−6.39 (m, 1H), 6.15−6.06 (m, 1H), 4.20 (q, 2H, *J* = 7.2 Hz), 3.49−3.43 (m, 1H), 2.48–2.39 (m, 1H), 2.35–2.24 (m, 1H), 1.94−1.92 (m, 3H), 1.88–1.63 (m, 6H), 1.42–0.9 (m, 5H), 1.29 (t, 3H, *J* = 7.2 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.7, 139.1, 138.1, 128.8, 126.1, 75.3, 60.7, 43.4, 38.4, 29.3, 28.1, 26.6, 26.4, 26.2, 14.4, 12.8.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{26}O_3Na$ 289.1780; Found 289.1788.

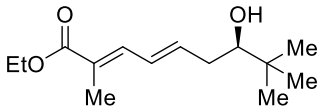
Column chromatography: PE:EtOAc 5:1

R_f = 0.36 (PE:EtOAc 5:1)

$[\alpha]_D^{20}$ = +6.2 (c = 9.2 mg/mL, $CHCl_3$)

Appearance: Yellow oil

Ethyl (*R*,2*E*,4*E*)-7-hydroxy-2,8,8-trimethylnona-2,4-dienoate (5m)



62 mg, 258 µmol, 65%, e.r. 95:5, starting from 34.4 mg of pivaldehyde.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.21–7.15 (m, 1H), 6.49–6.40 (m, 1H), 6.18–6.09 (m, 1H), 4.20 (q, 2H, *J* = 7.1 Hz), 3.33–3.31 (m, 1H), 2.52–2.41 (m, 1H), 2.22–2.11 (m, 1H), 1.93 (s, 3H), 1.53 (br s, 1H), 1.30 (t, 3H, *J* = 7.2 Hz), 0.93 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.7, 140.2, 138.1, 128.6, 126.1, 78.9, 60.7, 36.1, 35.1, 25.8, 14.5, 12.8.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{24}O_3Na$ 263.1623; Found 263.1630.

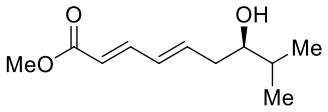
Column chromatography: PE:EtOAc 10:1

R_f = 0.55 (PE:EtOAc 4:1)

$[\alpha]_D^{20}$ = +17.0 (c = 10 mg/mL, $CHCl_3$)

Appearance: Colorless oil

Methyl (*R*,2*E*,4*E*)-7-hydroxy-8-methylnona-2,4-dienoate (5n)



20 mg, 101 µmol, 25%, e.r. 92:8, starting from 28.8 mg of isobutyraldehyde.

^{1}H NMR (400 MHz, C_6D_6): δ [ppm] = 7.42 (dd, 1H, *J* = 15.4 Hz, 10.8 Hz), 5.91–5.82 (m, 2H), 5.76–5.66 (m, 1H), 3.45 (s, 3H), 3.04–2.98 (m, 1H), 1.95–1.85 (m, 2H), 1.44–1.25 (m, 2H), 0.81 (d, 3H, *J* = 6.6 Hz), 0.76 (d, 3H, *J* = 6.8 Hz).

^{13}C NMR (101 MHz, C_6D_6): δ [ppm] = 167.2, 145.0, 141.0, 130.8, 120.0, 75.3, 51.1, 38.3, 33.5, 19.0, 17.2.

HRMS (EI-quadrupole) m/z: $[M–C_4H_8O]^+$ Calcd for $C_7H_{10}O_2$ 126.0681; Found 126.0682[10].

Column chromatography: PE:EtOAc 5:1

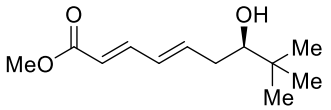
R_f = 0.23 (PE:EtOAc 4:1)

$[\alpha]_D^{20}$ = +17.0 (c = 10 mg/mL, $CHCl_3$)

Appearance: Colorless oil

[10] We suggest that this fragment originates from a McLafferty-like rearrangement, which takes place between the alcohol moiety and the proximal double bond, and results in the formal loss of isobutyraldehyde

Methyl (R,2E,4E)-7-hydroxy-8,8-dimethylnona-2,4-dienoate (5o)



61 mg, 287 µmol, 72%, e.r. 95:5, starting from 34.4 mg of pivaldehyde.

^{1}H NMR (400 MHz, C_6D_6): δ [ppm] = 7.45 (dd, 1H, *J* = 15.4 Hz, 10.8 Hz), 5.92–5.84 (m, 2H), 5.81–5.72 (m, 1H), 3.46 (s, 3H), 2.94–2.87 (m, 1H), 2.03–1.95 (m, 1H), 1.87–1.76 (m, 1H), 1.12 (br s, 1H), 0.81 (s, 9H).

^{13}C NMR (101 MHz, C_6D_6): δ [ppm] = 167.3, 145.1, 142.2, 130.7, 119.9, 78.3, 51.1, 35.9, 34.9, 25.8.

HRMS (EI-quadrupole) m/z: $[M–H_2O]^+$ Calcd for $C_{12}H_{18}O_2$ 194.1307; Found 194.1306.

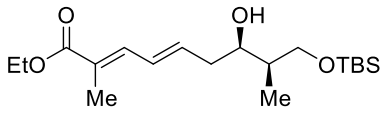
Column chromatography: PE:EtOAc 10:1

R_f = 0.35 (PE:EtOAc 4:1)

$[\alpha]_D^{20}$ = +20.0 (c = 10 mg/mL, $CHCl_3$)

Appearance: Colorless oil

Ethyl (2*E*,4*E*,7*R*,8*R*)-9-((tert-butyldimethylsilyl)oxy)-7-hydroxy-2,8-dimethylnona-2,4-dienoate (5p)



106 mg, 297 µmol, 74%, d.r. ≥95:5, starting from 81.0 mg of aldehyde **4n**.

^{1}H NMR (400 MHz, C_6D_6): δ [ppm] = 7.47−7.42 (m, 1H), 6.39−6.29 (m, 1H), 5.95−5.85 (m, 1H), 4.07 (q, 2H, *J*=7.1 Hz), 3.81−3.74 (m, 1H), 3.50 (d, 2H, *J*=5.0 Hz), 2.34−2.24 (m, 2H), 2.14−2.04 (m, 1H), 1.96−1.93 (m, 3H), 1.57−1.48 (m, 1H), 1.03 (t, 3H, *J*=7.1 Hz), 0.92 (s, 9H), 0.88 (2, 3H, *J*=7.0 Hz), 0.01 (s, 6H);

^{13}C NMR (101 MHz, C_6D_6): δ [ppm] = 168.1, 139.5, 138.5, 126.3, 72.9, 67.7, 60.4, 39.6, 39.1, 26.0, 18.4, 14.4, 12.9, 10.4, −5.4, −5.5;

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{36}O_4SiNa$ 379.2281; Found 379.2280.

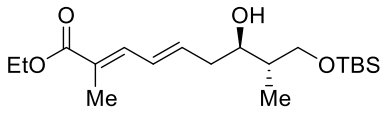
Column chromatography: PE:EtOAc 10:1 to 5:1

R_f = 0.63 (PE:EtOAc 4:1)

$[\alpha]_D^{22}$ = +22.4 (c = 11.7 mg/mL, $CHCl_3$)

Appearance: Yellow oil

Ethyl (2*E*,4*E*,7*R*,8*S*)-9-((tert-butyldimethylsilyl)oxy)-7-hydroxy-2,8-dimethylnona-2,4-dienoate (5q)



70 mg, 196 µmol, 49%, d.r. 90:10, starting from 81.0 mg of aldehyde **4o**.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.22−7.17 (m, 1H), 6.48−6.39 (m, 1H), 6.24−6.16 (m, 1H), 4.20 (q, 2H, *J*=7.1 Hz), 3.94 (d, 1H, *J*=2.9 Hz), 3.80 (dd, 1H, *J*=4.0, 10.1 Hz), 3.70−3.62 (m, 1H), 3.58 (dd, 1H, *J*=7.8, 10.2 Hz), 2.53−2.43 (m, 1H), 2.40−2.29 (m, 1H), 1.94−1.91 (m, 3H), 1.80−1.69 (m, 1H), 1.29 (t, 3H, *J*=7.1 Hz), 0.90 (s, 9H), 0.86 (d, 3H, *J*=7.0 Hz), 0.08 (s, 6H);

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.7, 139.1, 138.4, 128.0, 125.5, 76.2, 68.5, 60.5, 39.2, 39.0, 25.8, 18.1, 14.3, 13.4, 12.6, −5.6, −5.7;

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{36}O_4SiNa$ 379.2281; Found 379.2276.

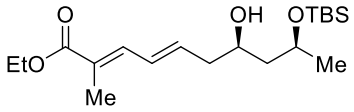
Column chromatography: PE:EtOAc 10:1 to 5:1

R_f = 0.63 (PE:EtOAc 4:1)

$[\alpha]_D^{22}$ = +18.3 (c = 10.9 mg/mL, $CHCl_3$)

Appearance: Yellow oil

Ethyl (2*E*,4*E*,7*R*,9*S*)-9-((tert-butyldimethylsilyl)oxy)-7-hydroxy-2-methyldeca-2,4-dienoate (5r)



107 mg, 301 µmol, 75%, d.r. 93:7, starting from 81.0 mg of aldehyde **4p**.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.20−7.15 (m, 1H), 6.44−6.38 (m, 1H), 6.14−6.07 (m, 1H), 4.22 (q, 2H, *J*=7.1 Hz), 4.11−4.05 (m, 1H), 3.91−3.86 (m, 1H), 3.61 (br s), 2.41−2.30 (m, 2H), 1.94−1.91 (m, 3H), 1.60−1.54 (m, 2H), 1.29 (t, 3H, *J*=7.2 Hz), 1.19 (d, 3H, *J*=6.1 Hz), 0.90 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.7, 138.6, 138.3, 128.5, 126.0, 71.1, 70.3, 60.6, 45.2, 41.5, 25.9, 24.8, 18.0, 14.5, 12.7, −3.7, −4.7.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{36}O_4SiNa$ 379.2281; Found 379.2279.

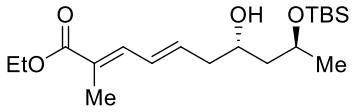
Column chromatography: PE:EtOAc 10:1 to 5:1

R_f = 0.44 (PE:EtOAc 4:1)

$[\alpha]_D^{22}$ = +26.9 (c = 13.0 mg/mL, $CHCl_3$)

Appearance: Yellow oil

Ethyl (2*E*,4*E*,7*R*,9*R*)-9-((tert-butyldimethylsilyl)oxy)-7-hydroxy-2-methyldeca-2,4-dienoate (5s)



78 mg, 220 µmol, 55%, d.r. 47:53[11], starting from 81.0 mg of aldehyde **4p**.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.20−7.15 (m, 1H), 6.45−6.38 (m, 1H), 6.14−6.07 (m, 1H), 4.24−4.21* (m, 1H), 4.22−4.18 (m, 2H, major and minor isomer), 4.11−4.05 (m, 2H, major and minor isomer), 3.91−3.86 (m, 1H), 3.61 (br s, 1H), 3.49* (br s, 1H), 2.42−2.28 (m, 2H), 1.94−1.91 (m, 3H), 1.67* (ddd, 1H, *J*=3.9, 10.2, 14.2 Hz), 1.60−1.55 (m, 2H), 1.52* (ddd, 1H, *J*=2.1, 5.0, 14.3 Hz), 1.30 (t, 3H, *J*=7.1 Hz), 1.23 (d, 3H, *J*=6.7 Hz), 1.18 (d, 3H, *J*=6.0 Hz), 0.90 (s, 9H), 0.89* (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H), 0.09* (s, 3H), 0.085* (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.7, 138.7*, 138.6, 138.3, 128.5, 128.4*, 125.97*, 125.96, 71.1, 70.3, 67.9*, 67.7, 60.6, 45.3, 43.8*, 41.8*, 41.5, 25.94, 25.93*, 24.8, 22.8*, 18.1*,18.0, 14.5, 12.8.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{36}O_4SiNa$ 379.2281; Found 379.2285.

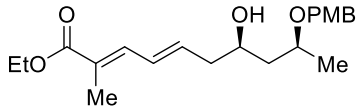
Column chromatography: PE:EtOAc 10:1 to 5:1

R_f = 0.44 (PE:EtOAc 4:1)

Appearance: Yellow oil

[11] The major diastereomer is the *syn*-diastereomer **5r**.

Ethyl (2*E*,4*E*,7*R*,9*S*)-7-hydroxy-9-((4-methoxybenzyl)oxy)-2-methyldeca-2,4-dienoate (5t)



109 mg, 301 µmol, 75%, d.r. 76:24, starting from 83.2 mg of aldehyde **4q**.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.26−7.24 (m, 2H), 7.19−7.13 (m, 1H), 6.90−6.85 (m, 2H), 6.44−6.35 (m, 1H), 6.13−6.03 (m, 1H), 4.60 (d, 1H, *J*=11.2 Hz), 4.56* (d, 1H, *J*=11.3 Hz), 4.38 (d, 1H, *J*=11.3 Hz), 4.34 (d, 1H, *J*=11.0 Hz), 4.22−4.16 (m, 2H), 4.06−3.98* (m, 1H), 3.92−3.83 (m, 1H), 3.82−3.76 (m, 4H), 2.41−2.25 (m, 2H), 1.94−1.90 (m, 3H), 1.73−1.54 (m, 2H), 1.33−1.27 (m, 3H), 1.27* (d, 3H, *J*=6.7 Hz), 1.23 (d, 3H, *J*=6.0 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.74, 168.72*, 159.5, 159.4*, 138.6, 138.3, 138.2*, 130.5*, 130.1, 129.6, 129.5*, 128.5*, 128.4, 126.0*, 125.9, 114.1, 114.0*, 75.9, 72.3*, 71.4, 70.3*, 70.1, 60.64*, 60.61, 55.4, 43.4, 42.4*, 41.51, 41.47, 19.8, 19.2*, 14.5, 12.7.

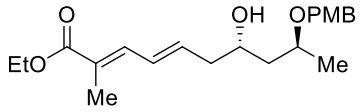
HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{30}O_5Na$ 385.1991; Found 385.1989.

Column chromatography: PE:EtOAc 5:1

R_f = 0.20 (PE:EtOAc 4:1)

Appearance: Yellow oil

Ethyl (2*E*,4*E*,7*R*,9*R*)-7-hydroxy-9-((4-methoxybenzyl)oxy)-2-methyldeca-2,4-dienoate (5u)



59 mg, 164 µmol, 41%, d.r. 84:16, starting from 83.2 mg of aldehyde **4q**.

^{1}H NMR (600 MHz, $CDCl_3$): δ [ppm] = 7.27−7.24 (m, 2H), 7.18−7.15 (m, 1H), 6.89−6.86 (m, 2H), 6.42−6.36 (m, 1H), 6.12−6.05 (m, 1H), 4.60* (d, 1H, *J*=10.8 Hz), 4.56 (d, 1H, *J*=11.0 Hz), 4.38 (d, 1H, *J*=11.3 Hz), 4.34* (d, 1H, *J*=11.0 Hz), 4.20 (q, 2H, *J*=7.2 Hz), 4.05−4.00 (m, 1H), 3.92−3.83 (m, 1H), 3.80 (s, 3H), 2.39−2.27 (m, 2H), 1.93−1.91 (m, 3H), 1.71−1.59 (m, 2H), 1.30 (t, 3H, *J*=7.1 Hz), 1.29* (t, 3H, *J*=7.1 Hz), 1.25 (d, 3H, *J*=6.2 Hz), 1.24* (d, 3H, *J*=6.1 Hz).

^{13}C NMR (151 MHz, $CDCl_3$): δ [ppm] = 168.7, 159.4, 138.6, 138.2, 130.5, 129.5, 128.5, 126.0, 114.0, 72.3, 70.3, 68.0, 60.6, 55.4, 42.3, 41.5, 19.2, 14.4, 12.7.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{30}O_5Na$ 385.1991; Found 385.1977.

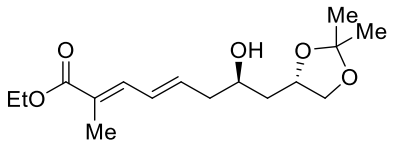
Column chromatography: PE:EtOAc 5:1

R_f = 0.15 (PE:EtOAc 4:1)

$[\alpha]_D^{20}$ = +23.5 (c = 24.4 mg/mL, $CHCl_3$)

Appearance: Yellow oil

Ethyl (*R*,2*E*,4*E*)-8-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)-7-hydroxy-2-methylocta-2,4-dienoate (5v)



64 mg, 215 µmol, 54%, d.r. ≥95:5, starting from 57.7 mg of aldehyde **4r**.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.19−7.13 (m, 1H), 6.49−6.39 (m, 1H), 6.12−6.02 (m, 1H), 4.39−4.31 (m, 1H), 4.20 (q, 2H, *J*=7.1 Hz), 4.09 (dd, 1H, *J*=6.1, 8.1 Hz), 4.01−3.92 (m, 1H), 4.20 (t, 1H, *J*=7.1 Hz), 2.46−2.35 (m, 2H), 1.94−1.92 (m, 3H), 1.80−1.67 (m, 2H), 1.42 (s, 3H), 1.36 (s, 3H), 1.30 (t, 3H, *J*=7.1 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.7, 137.9, 137.7, 129.1, 126.5, 109.1, 73.6, 69.5, 68.4, 60.7, 41.7, 39.6, 27.0, 25.8, 14.5, 12.8.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{26}O_5Na$ 321.1678; Found 321.1668.

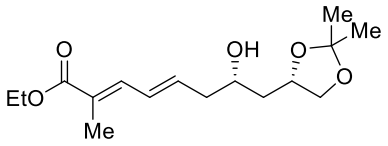
Column chromatography: PE:EtOAc 5:1

R_f = 0.19 (PE:EtOAc 2:1)

$[\alpha]_D^{20}$ = +0.95 (c = 10.5 mg/mL)

Appearance: Yellow oil

Ethyl (*S*,2*E*,4*E*)-8-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)-7-hydroxy-2-methylocta-2,4-dienoate (5w)



43 mg, 144 µmol, 36%, d.r. ≥95:5, starting from 57.7 mg of aldehyde **4r**.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.19–7.13 (m, 1H), 6.46–6.37 (m, 1H), 6.14–6.03 (m, 1H), 4.31–4.23 (m, 1H), 4.19 (q, 2H, *J* = 7.1 Hz), 4.09 (dd, 1 H, *J* = 8.1, 6.0 Hz), 3.98–3.90 (m, 2H), 3.56 (dd, 1H, *J* = 8.1, 7.2 Hz), 2.46–2.30 (m, 2H), 1.92–1.91 (m, 3H), 1.76–1.58 (m, 2H), 1.42 (s, 3H), 1.36 (s, 3H), 1.29 (t, 3H, *J* = 7.1 Hz).

^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 168.7, 138.08, 138.0, 128.7, 126.2, 109.7, 75.9, 70.6, 69.8, 60.7, 41.3, 39.9, 31.0, 27.0, 25.9, 14.4, 12.8.

HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{26}O_5Na$ 321.1678; Found 321.1682.

Column chromatography: PE:EtOAc 5:1

R_f = 0.32 (PE:EtOAc 2:1)

$[\alpha]_D^{20}$ = +4.39 (c = 11.4 mg/mL, $CHCl_3$)

Appearance: Yellow oil

General procedure 3: Synthesis of Mosher esters using the Mosher's acid chloride

4-DMAP (6.00 equiv), Et_3N (10.0 equiv) and (*S*)-MTPA-Cl (6.00 equiv) were added to a solution of the corresponding VMAR-product (usually 20–40 µmol, 1.00 equiv) in CH_2Cl_2 (0.5 mL) at r.t. The reaction mixture was stirred for 10 min, then diluted with MTBE. The solution was washed with NaOH (1 M, 3x), $NaHCO_3$ (3x), $CuSO_4$ (1x) and brine (1x), dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude Mosher esters were used for e.r. determination via ^{19}F-NMR.

Representative Mosher esters for determination of absolute stereochemistry

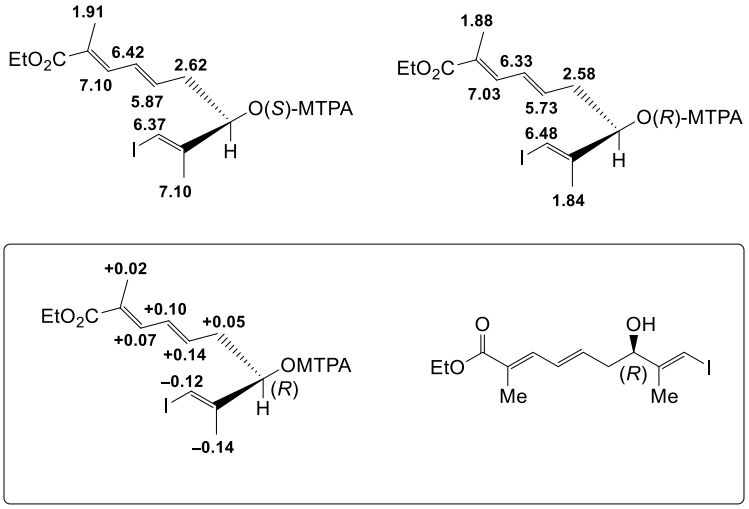


Figure 1. Mosher's ester analysis for the determination of the absolute configuration of bVMAR product **5g**.

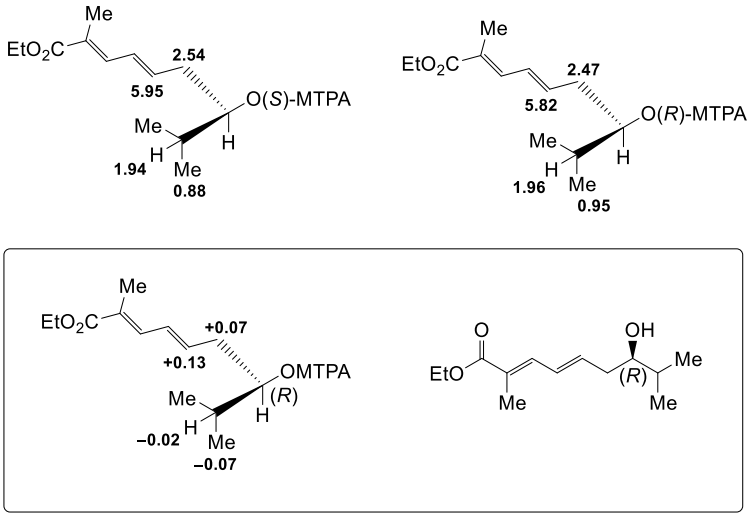


Figure 2. Mosher's ester analysis for the determination of the absolute configuration of bVMAR product **5j**.

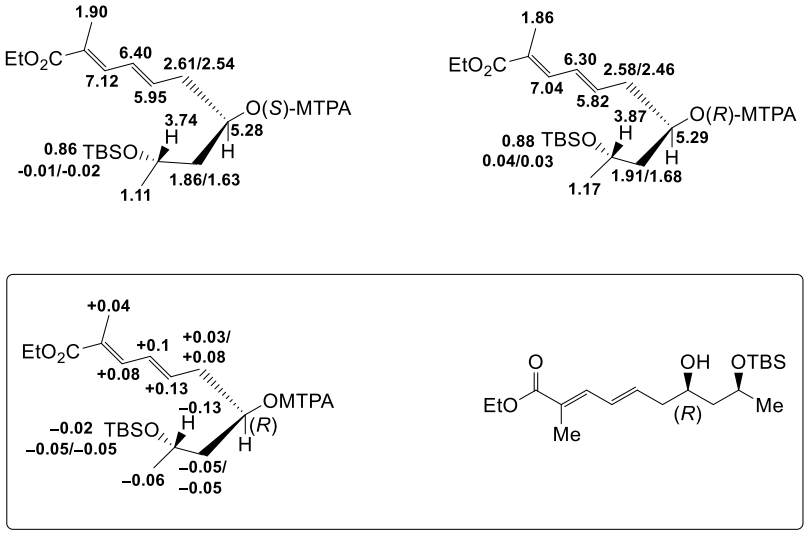


Figure 3. Mosher's ester analysis for the determination of the absolute configuration of bVMAR product **5r**.

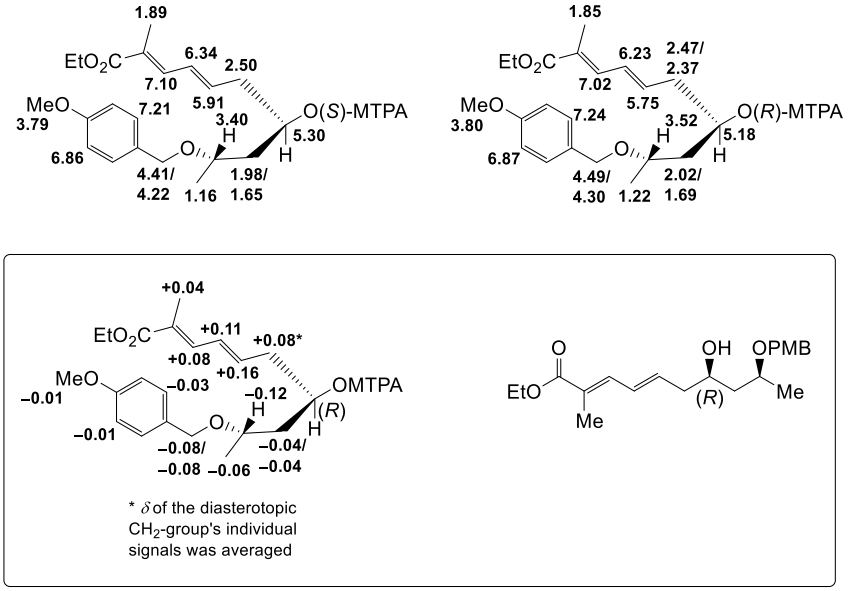


Figure 4. Mosher's ester analysis for the determination of the absolute configuration of bVMAR product **5t**.

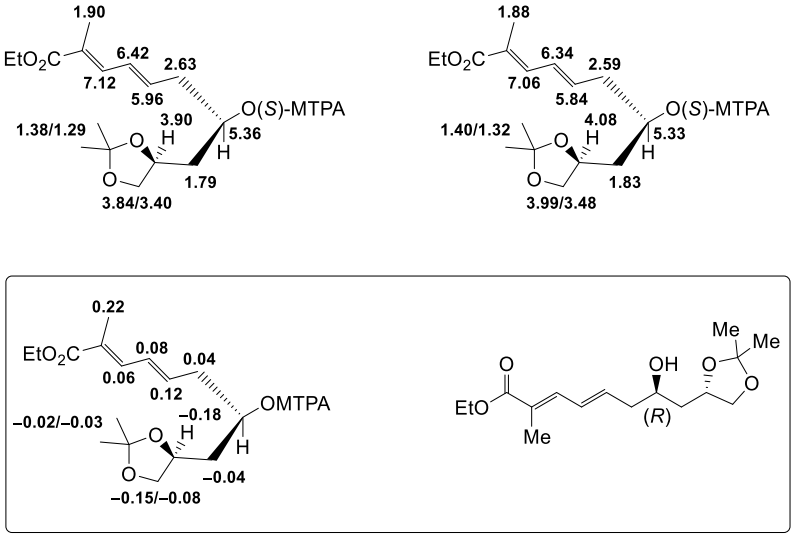
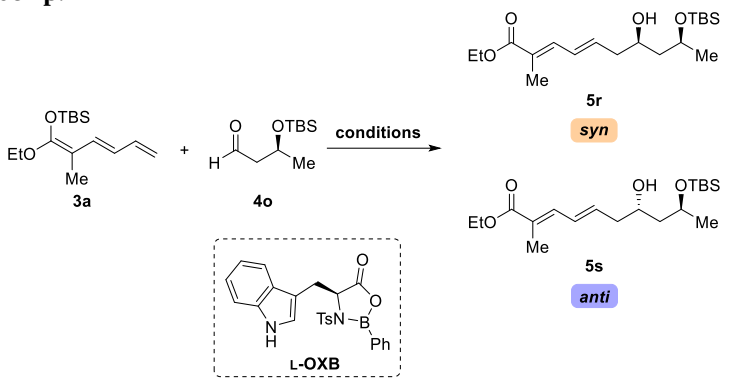


Figure 5. Mosher's ester analysis for the determination of the absolute configuration of bVMAR product **5v**.

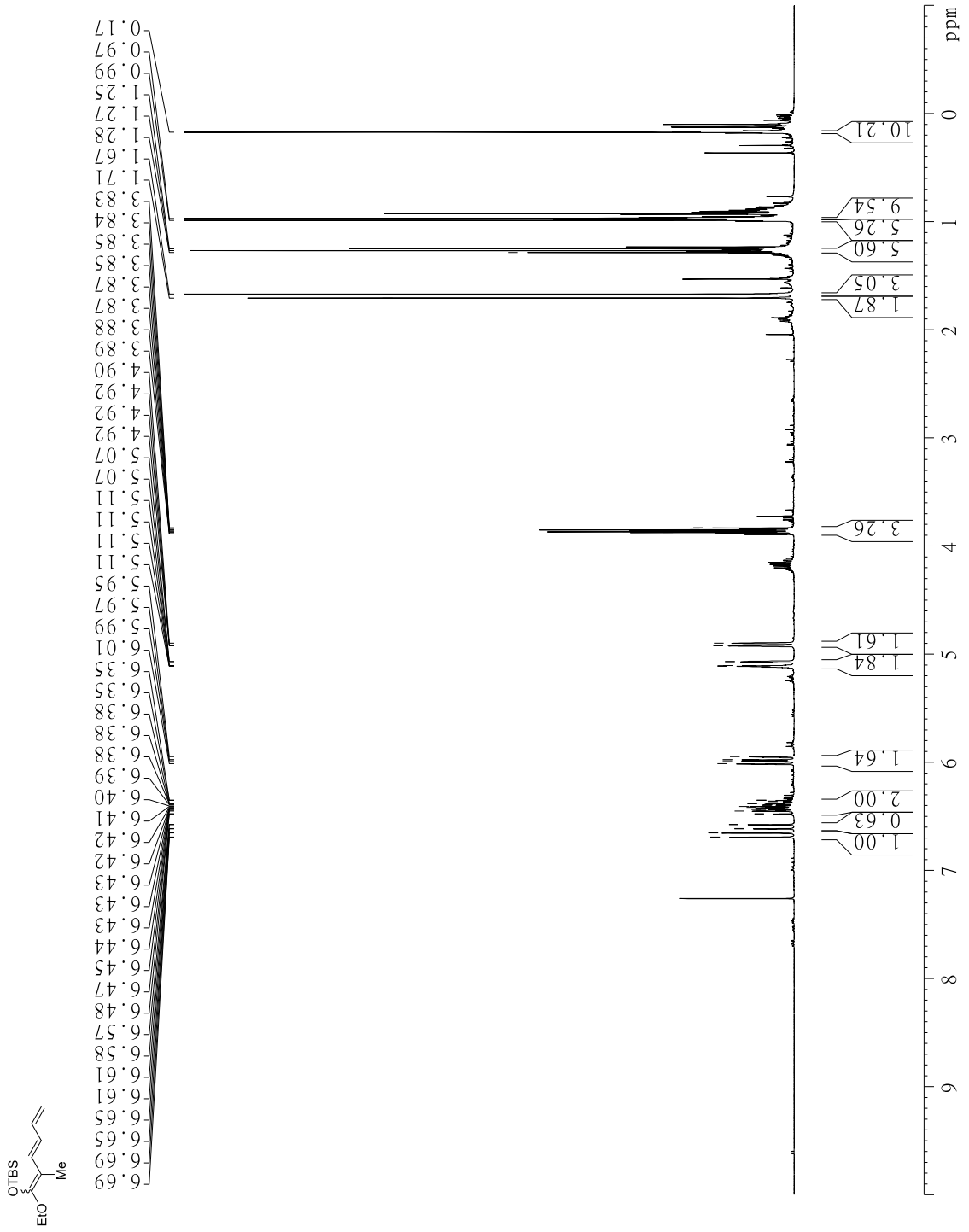
Investigations on the substrate-induced stereocontrol of aldehyde 4p and matched/mismatched cases

Table 1. Lewis acid-dependent distribution *syn*:*anti* product distribution for the bVMAR between ketene acetal **3a** and β-chiral aldehyde **4p**.

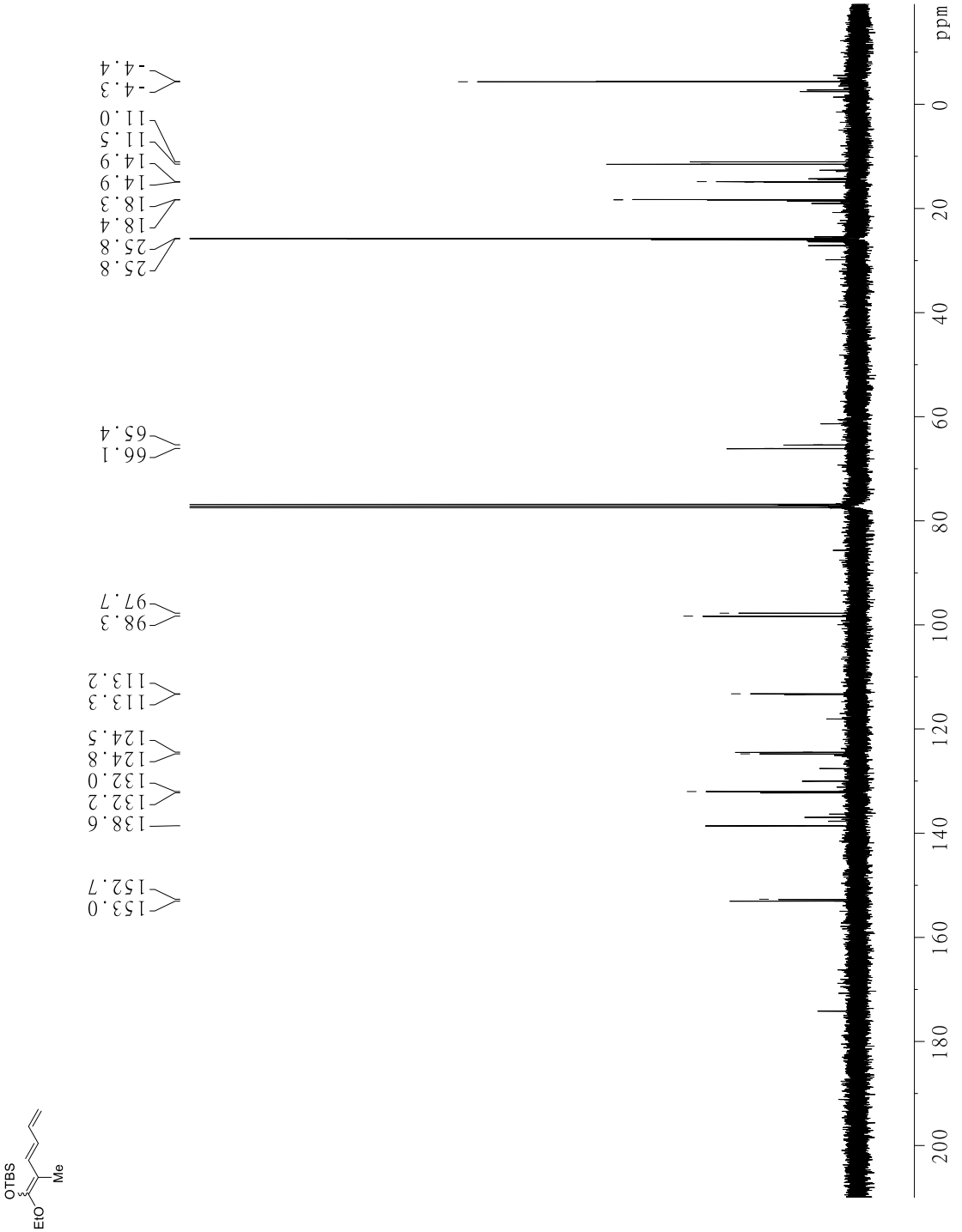


entry	conditions	*syn* : *anti*	yield
1	**L-OXB,** *n*-BuCN, –78°C	93:7 (matched)	75%
2	**D-OXB,** *n*-BuCN, –78°C	53:47 (mismatched)	55%
3	$BF_3 \cdot Et_2O$, CH_2Cl_2, –78 °C	19:81	17%
4	$BF_3 \cdot Et_2O$, *n*-BuCN, –78 °C	27:73	17%
5	$B(C_6F_5)_3 \cdot H_2O$, CH_2Cl_2, –78 °C	≈ 95:5	36%
6	$B(C_6F_5)_3 \cdot H_2O$, *n*-BuCN, –78 °C	—	no reaction

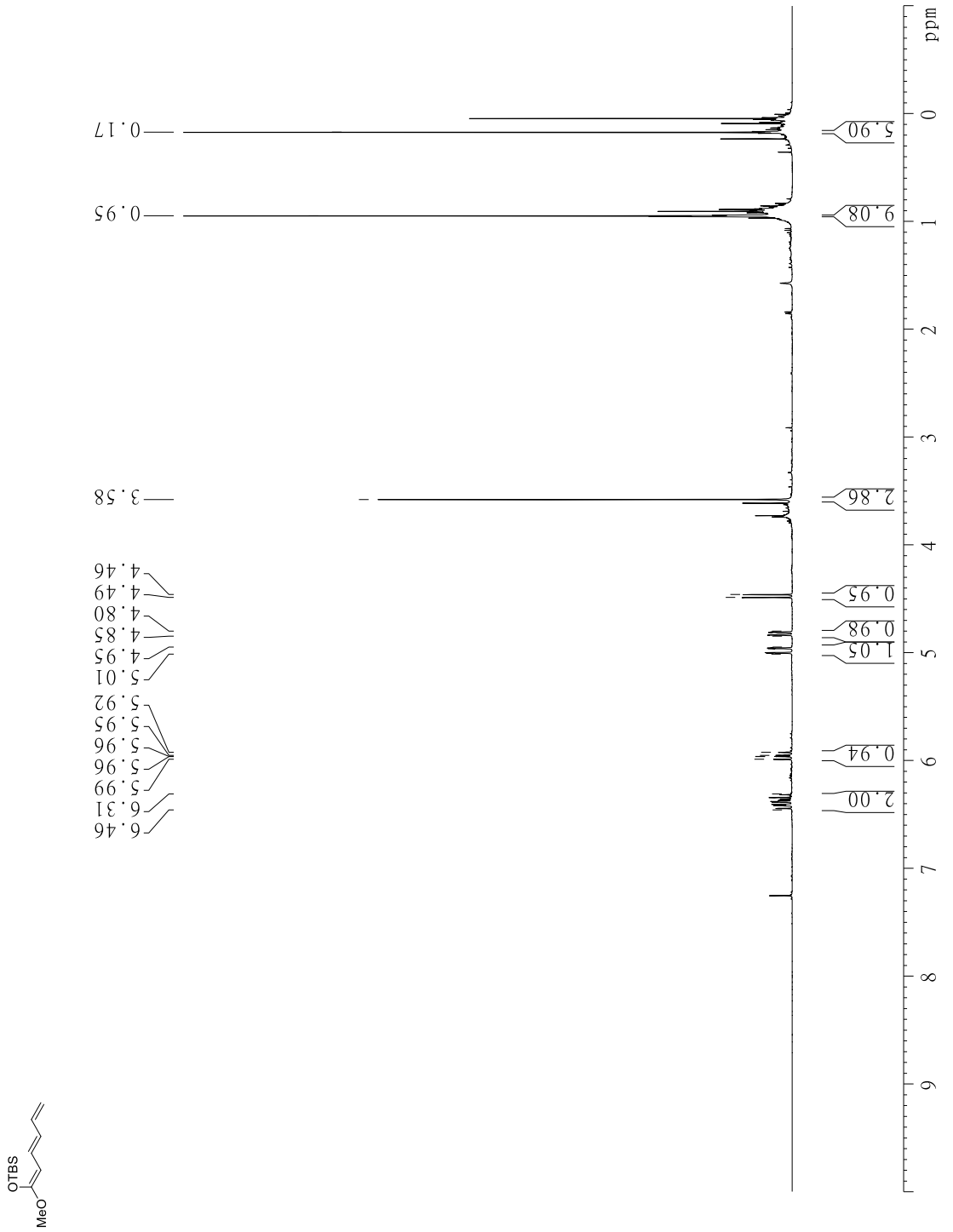
NMR Spectra of new compounds



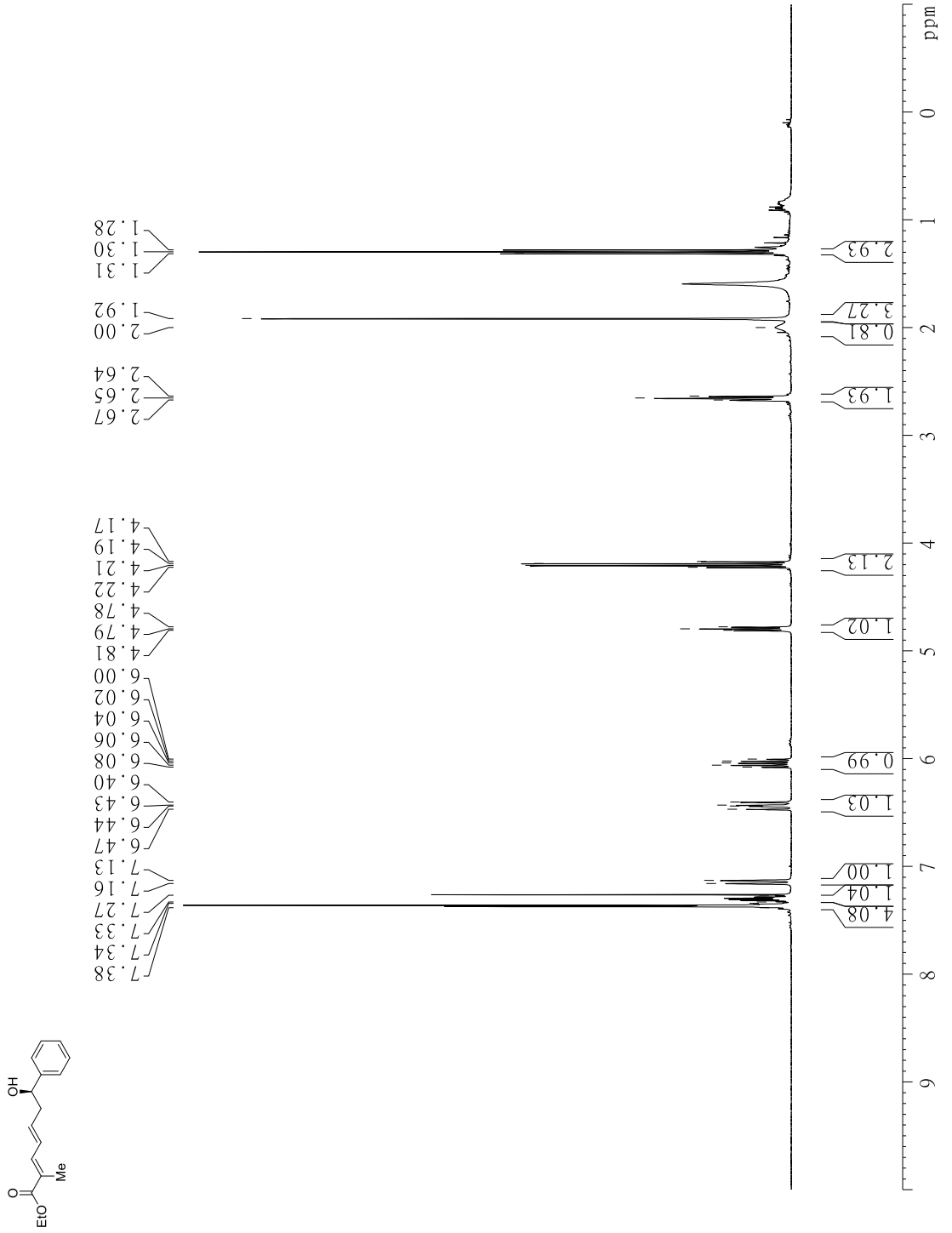
Spectrum 1. ^{1}H spectrum of **3a** measured in $CDCl_3$ at 400 MHz.



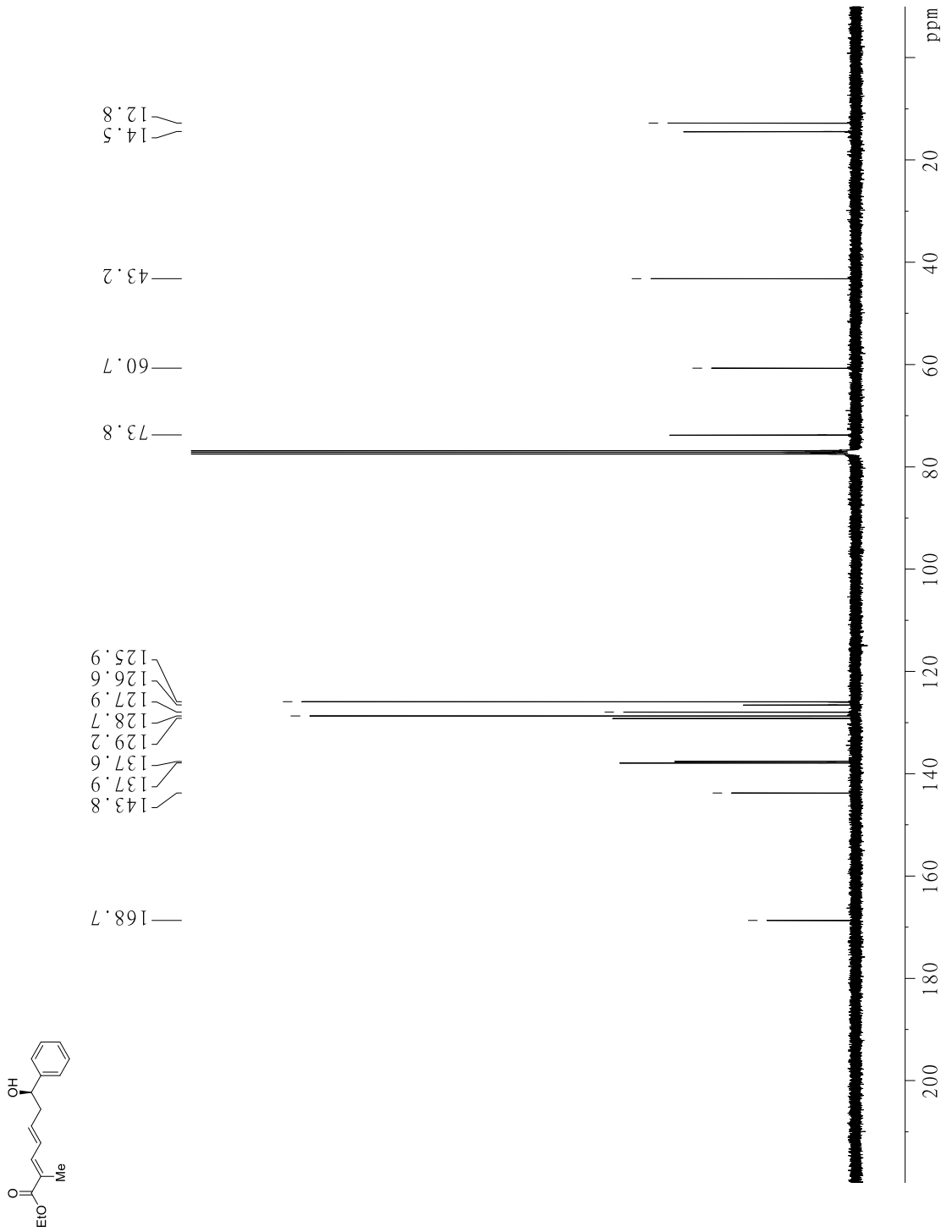
Spectrum 2. ^{13}C spectrum of **3a** measured in $CDCl_3$ at 101 MHz.



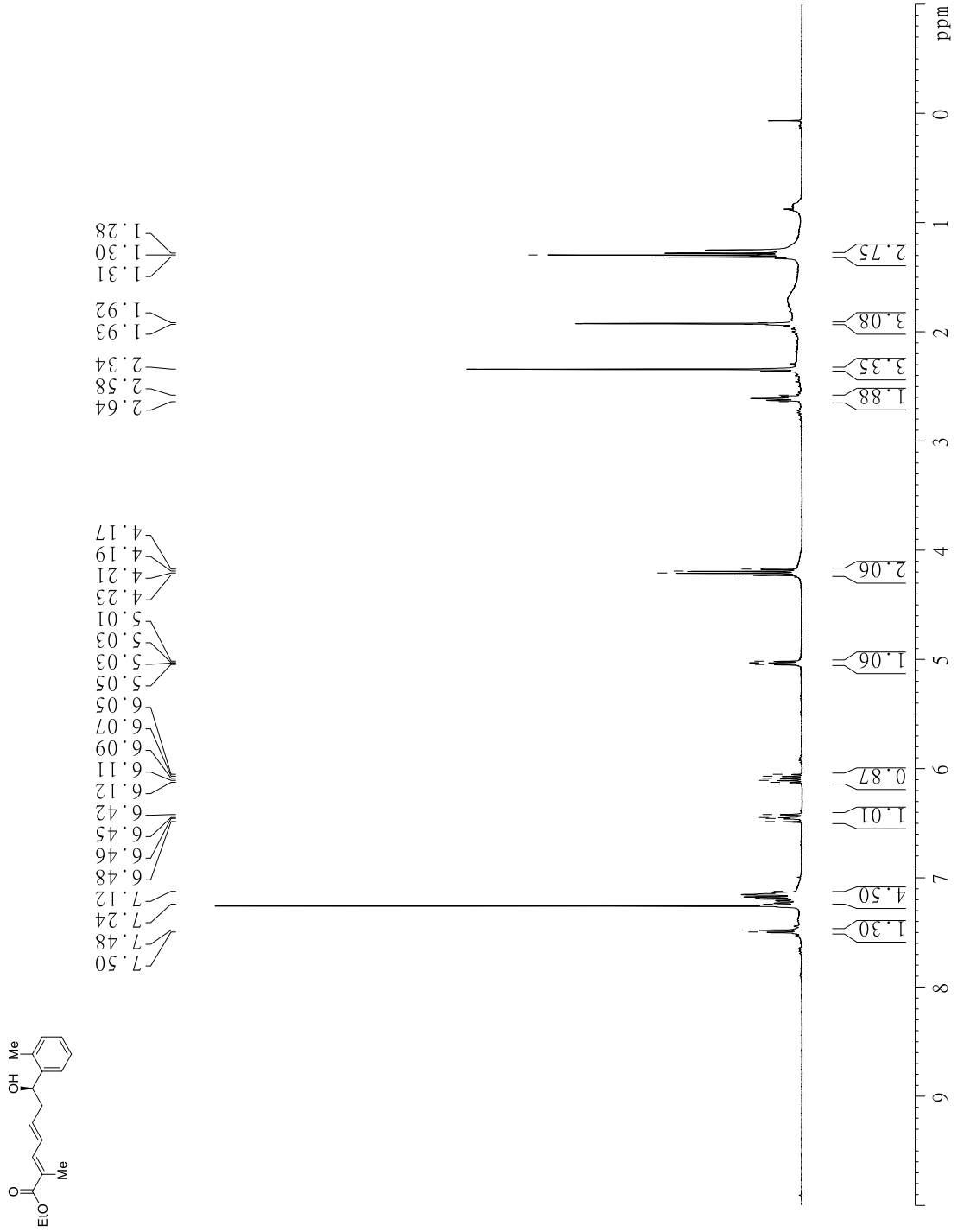
Spectrum 3. ^{1}H spectrum of **3e** measured in $CDCl_3$ at 400 MHz.



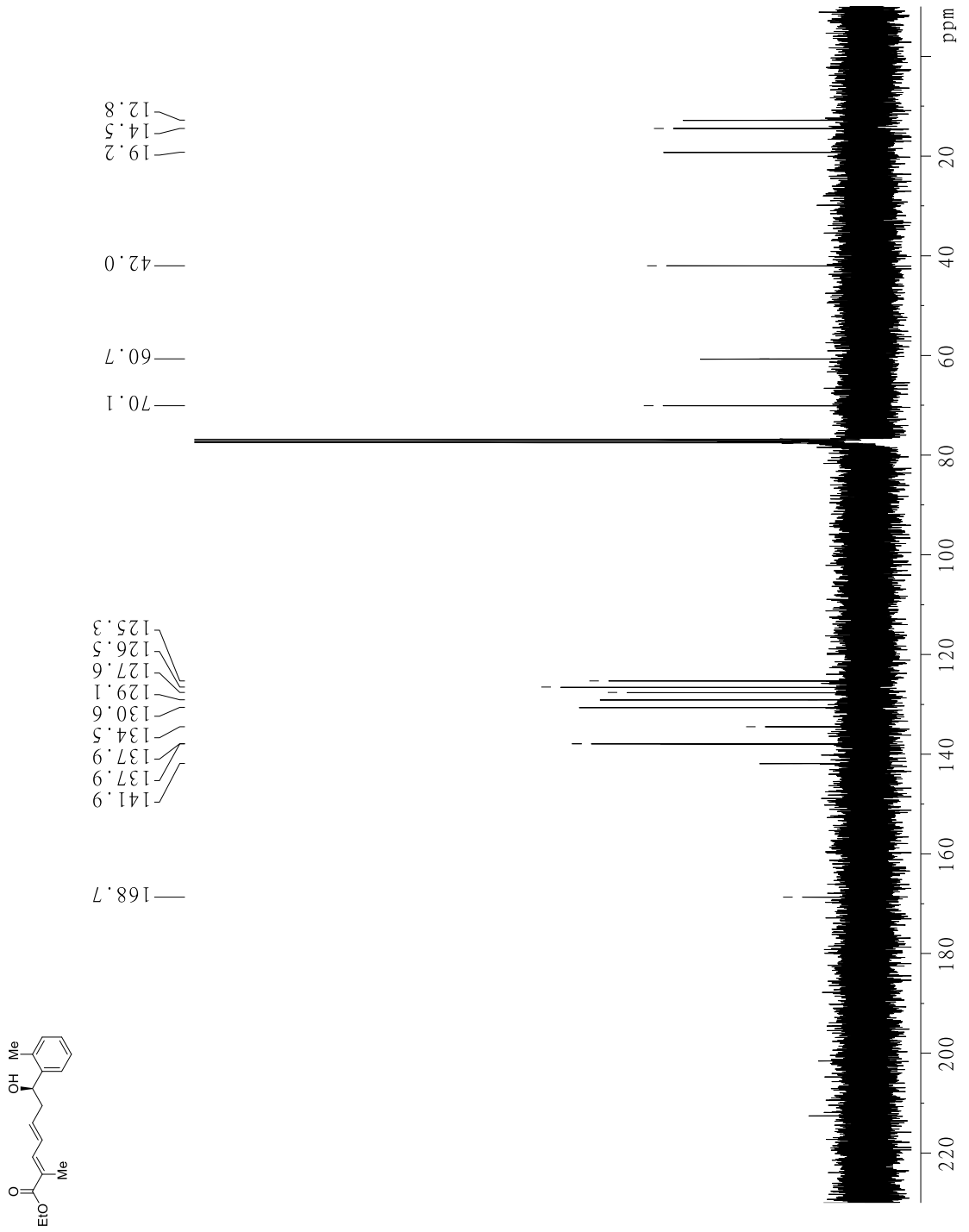
Spectrum 4. ^{1}H spectrum of **5a** measured in $CDCl_3$ at 400 MHz.



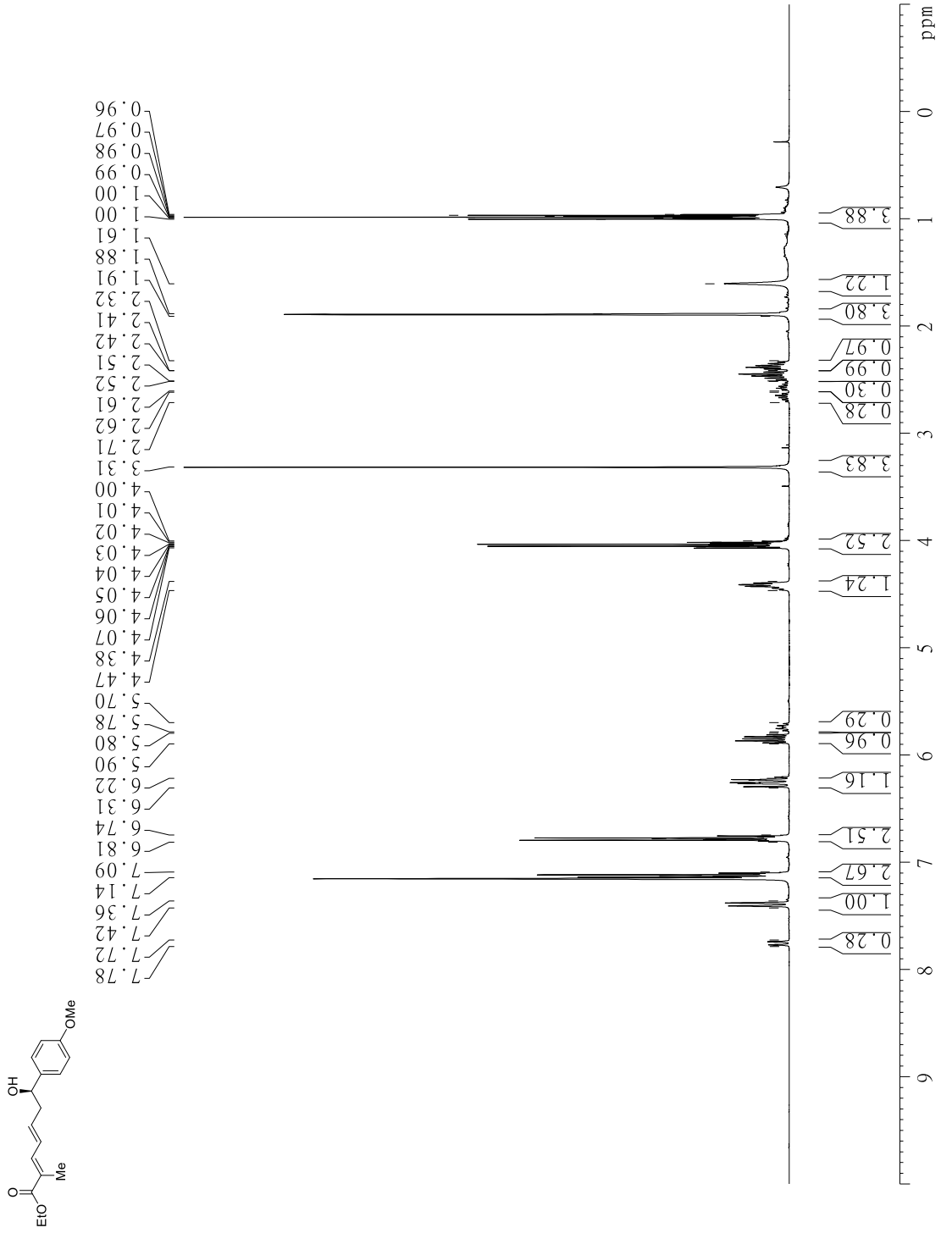
Spectrum 5. ^{13}C spectrum of **5a** measured in $CDCl_3$ at 101 MHz.



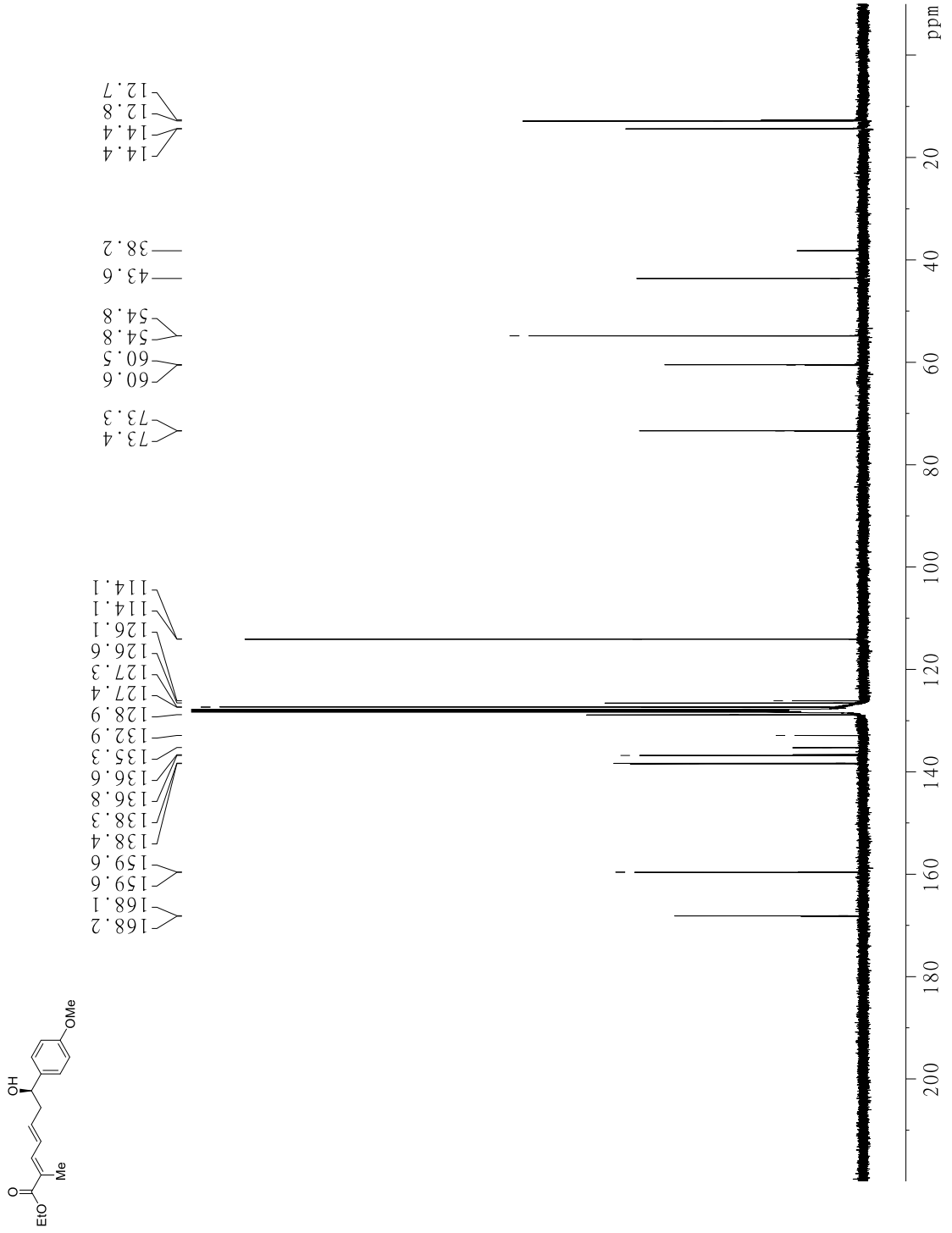
Spectrum 6. ^{1}H spectrum of **5b** measured in $CDCl_3$ at 400 MHz.



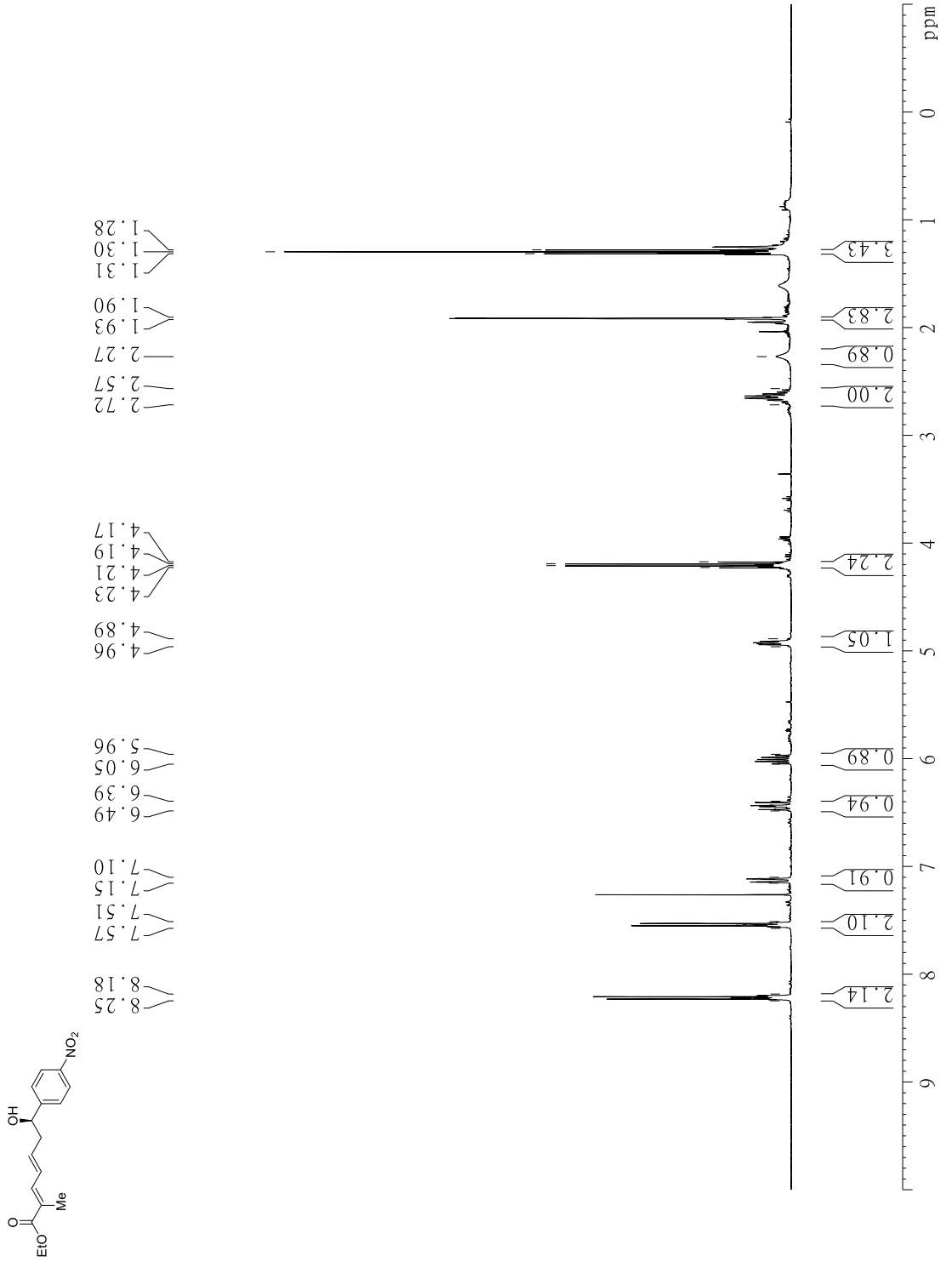
Spectrum 7. ^{13}C spectrum of **5b** measured in $CDCl_3$ at 101 MHz.



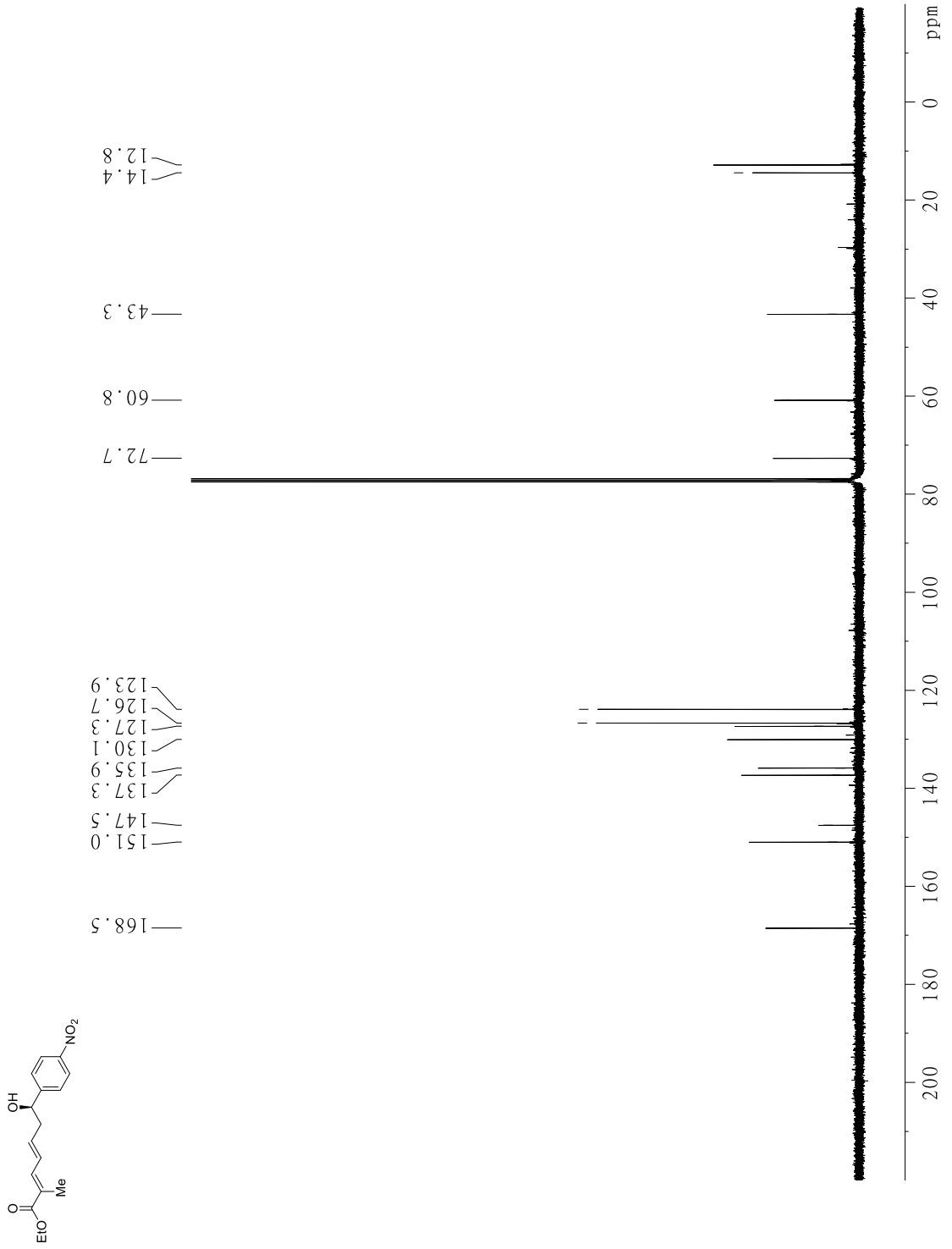
Spectrum 8. ^{1}H spectrum of **5c** measured in C_6D_6 at 400 MHz.



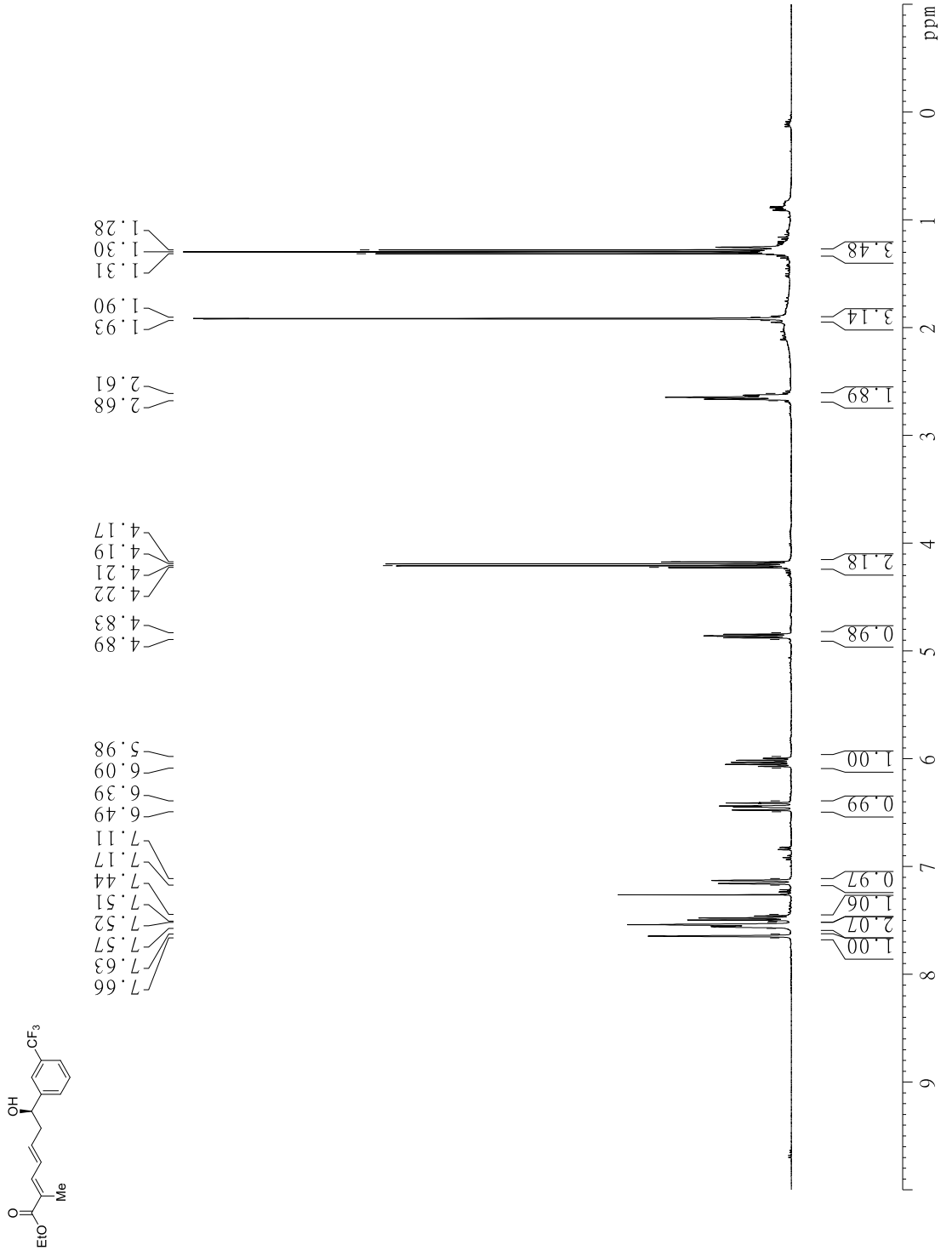
Spectrum 9. ^{13}C spectrum of **5c** measured in C_6D_6 at 101 MHz.



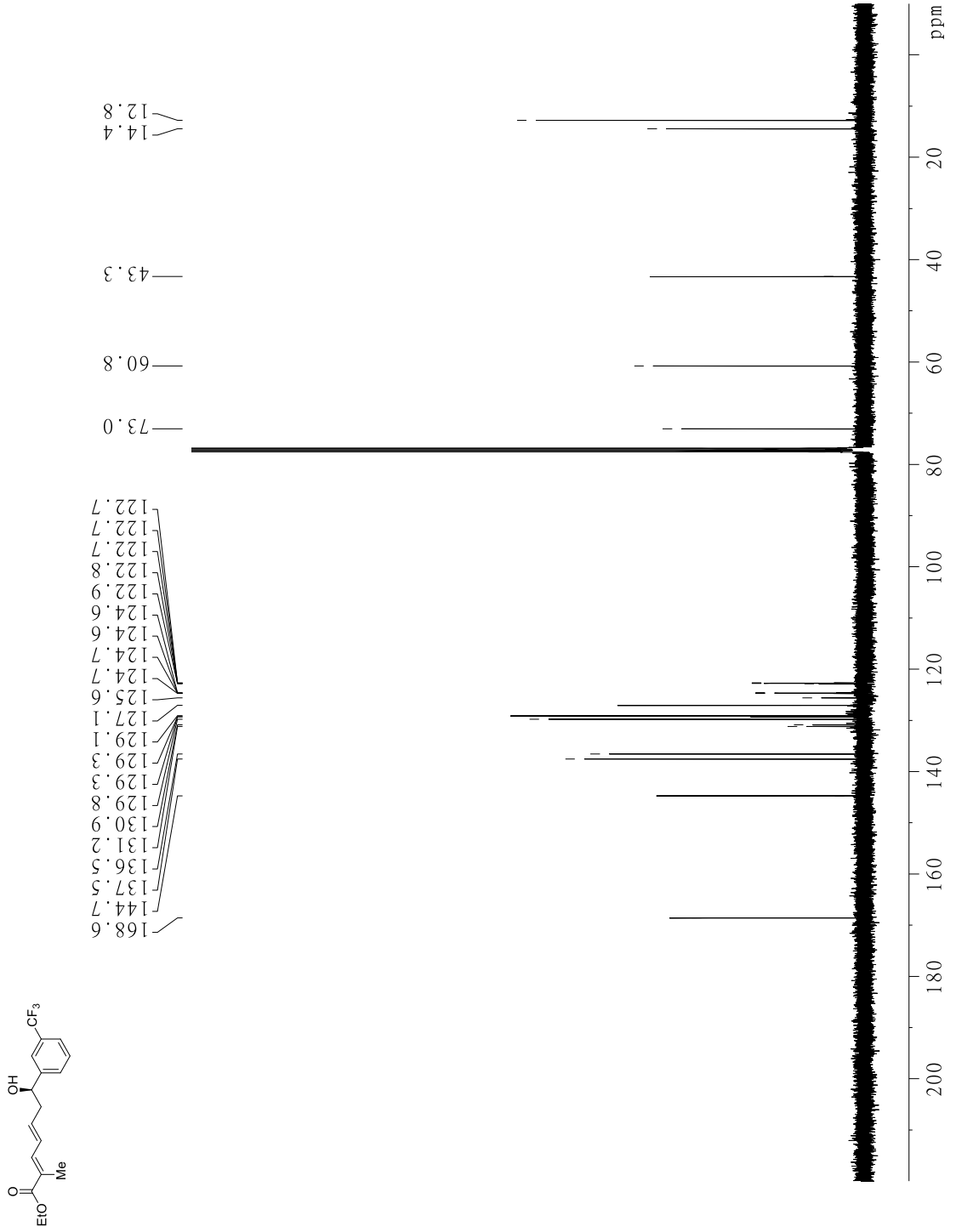
Spectrum 10. ^{1}H spectrum of **5d** measured in $CDCl_3$ at 400 MHz.



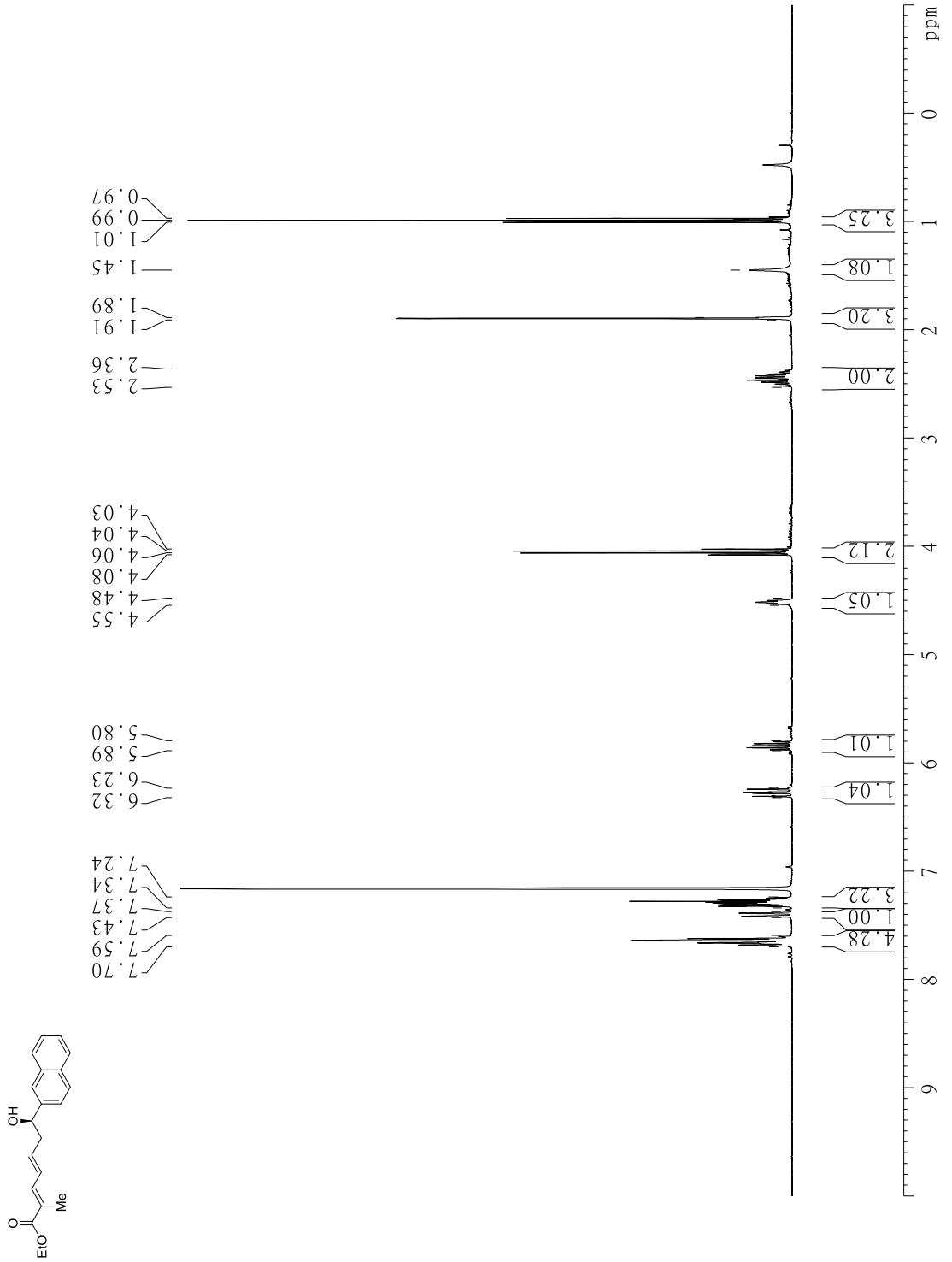
Spectrum 11. ^{13}C spectrum of **5d** measured in $CDCl_3$ at 101 MHz.



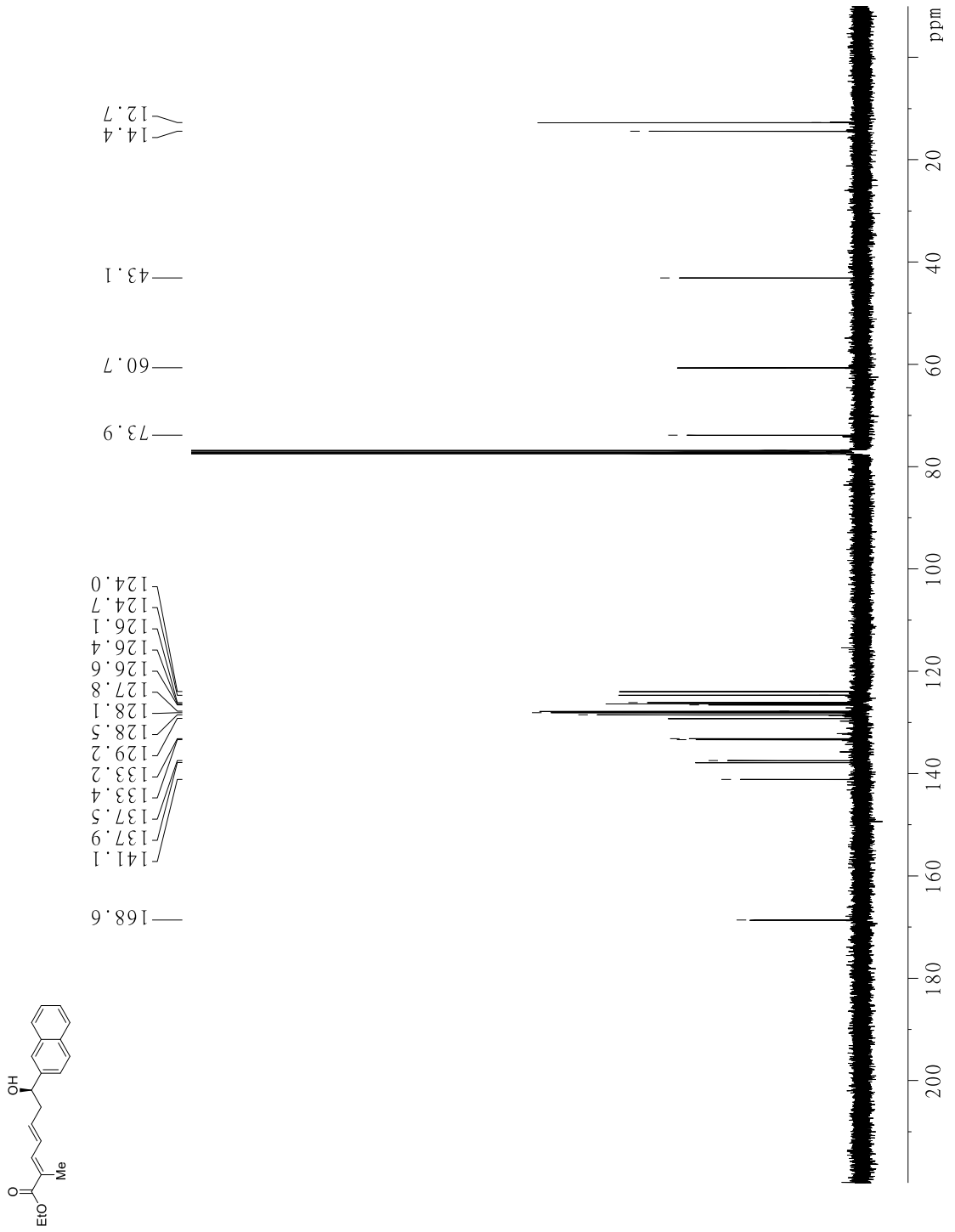
Spectrum 12. ^{1}H spectrum of **5e** measured in $CDCl_3$ at 400 MHz.



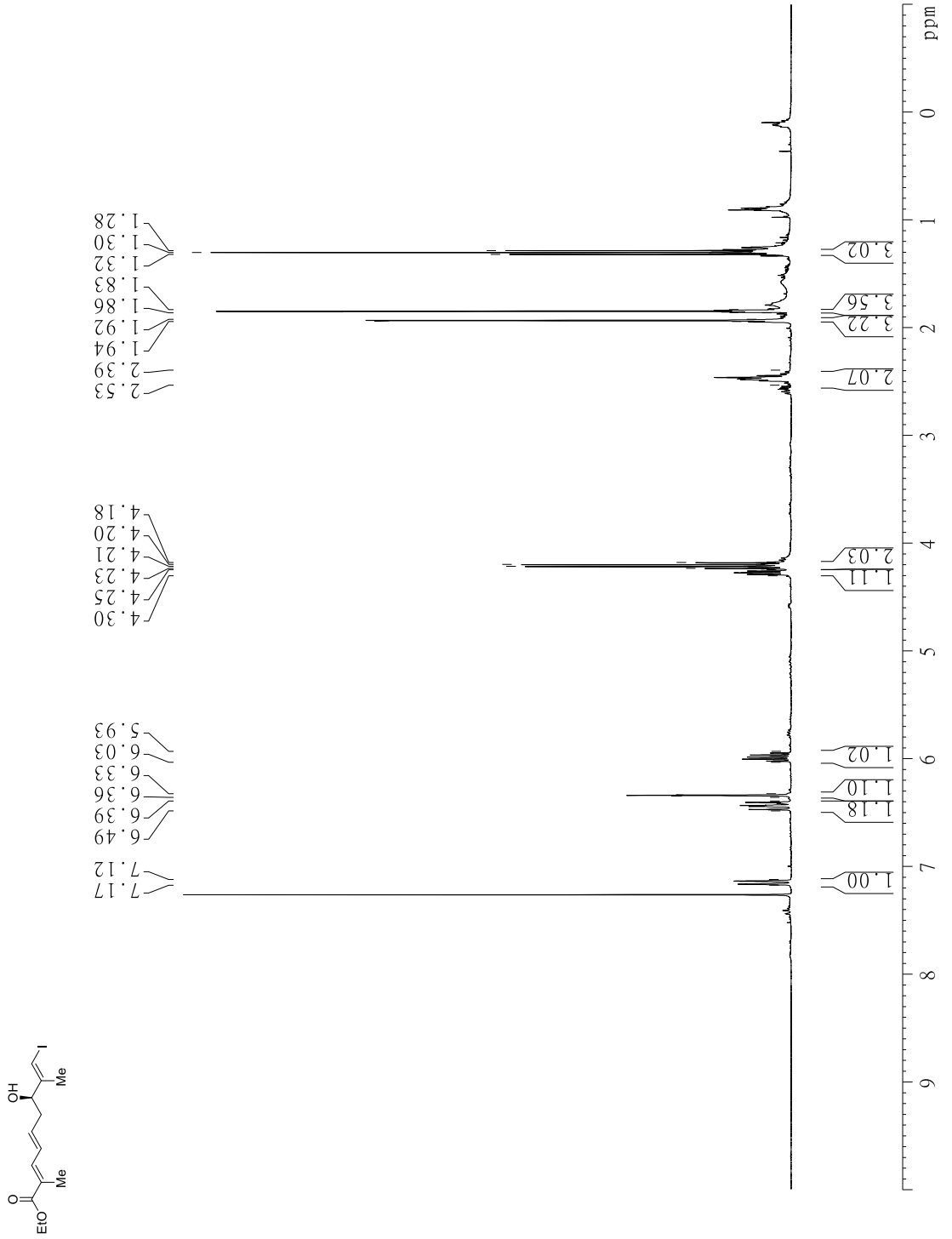
Spectrum 13. ^{13}C spectrum of **5e** measured in $CDCl_3$ at 101 MHz.



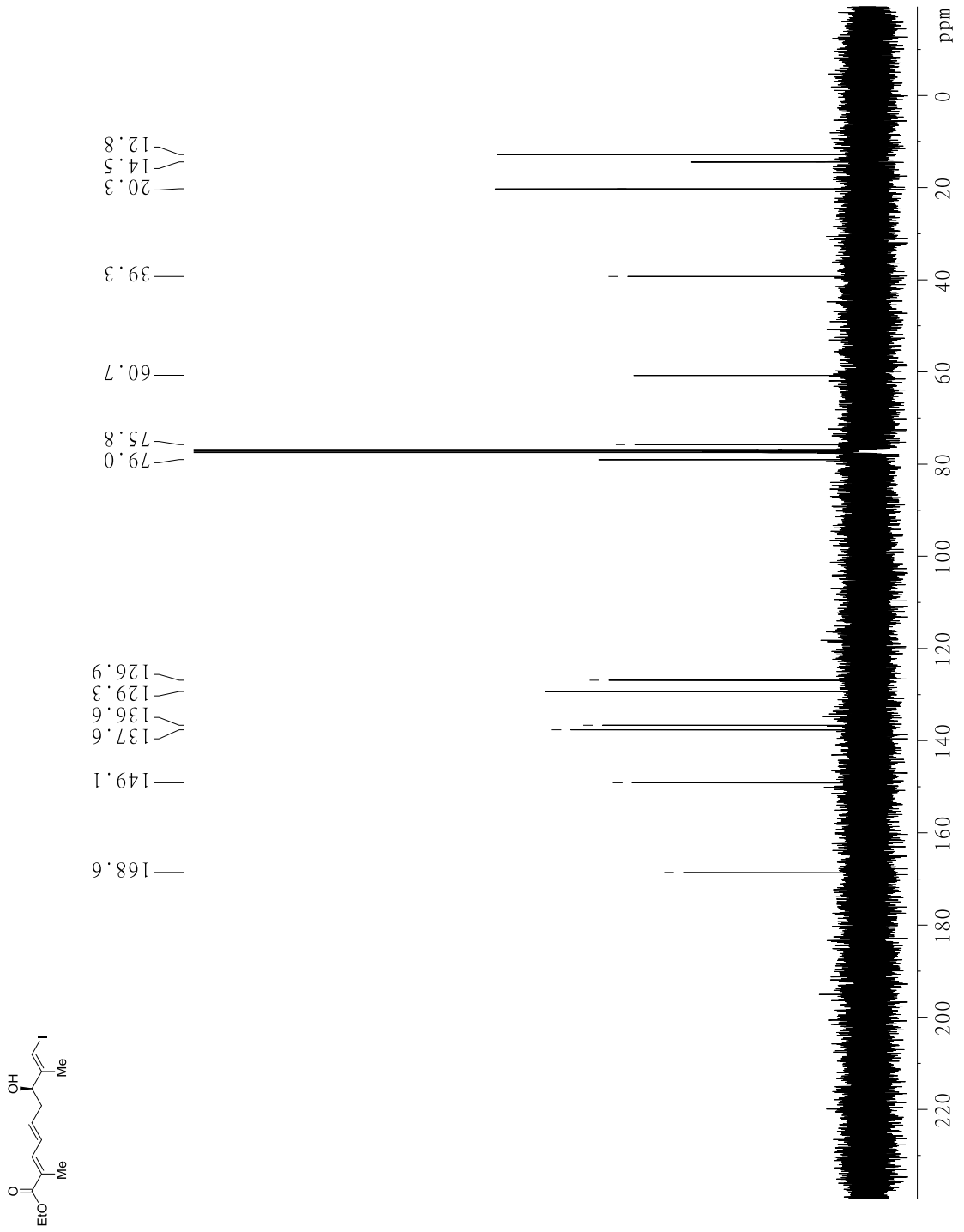
Spectrum 14. ^{1}H spectrum of **5f** measured in C_6D_6 at 400 MHz.



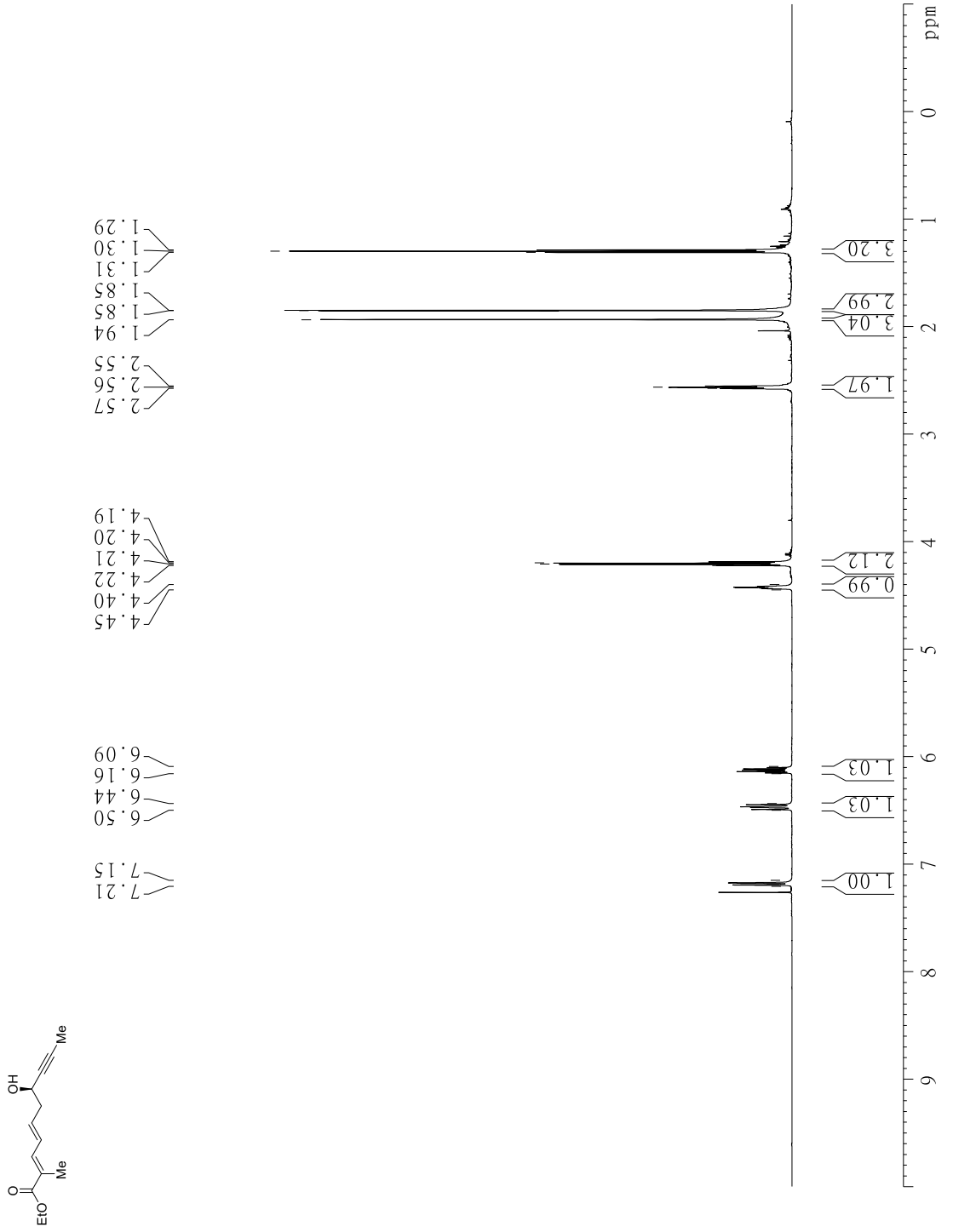
Spectrum 15. ^{13}C spectrum of **5f** measured in $CDCl_3$ at 101 MHz.



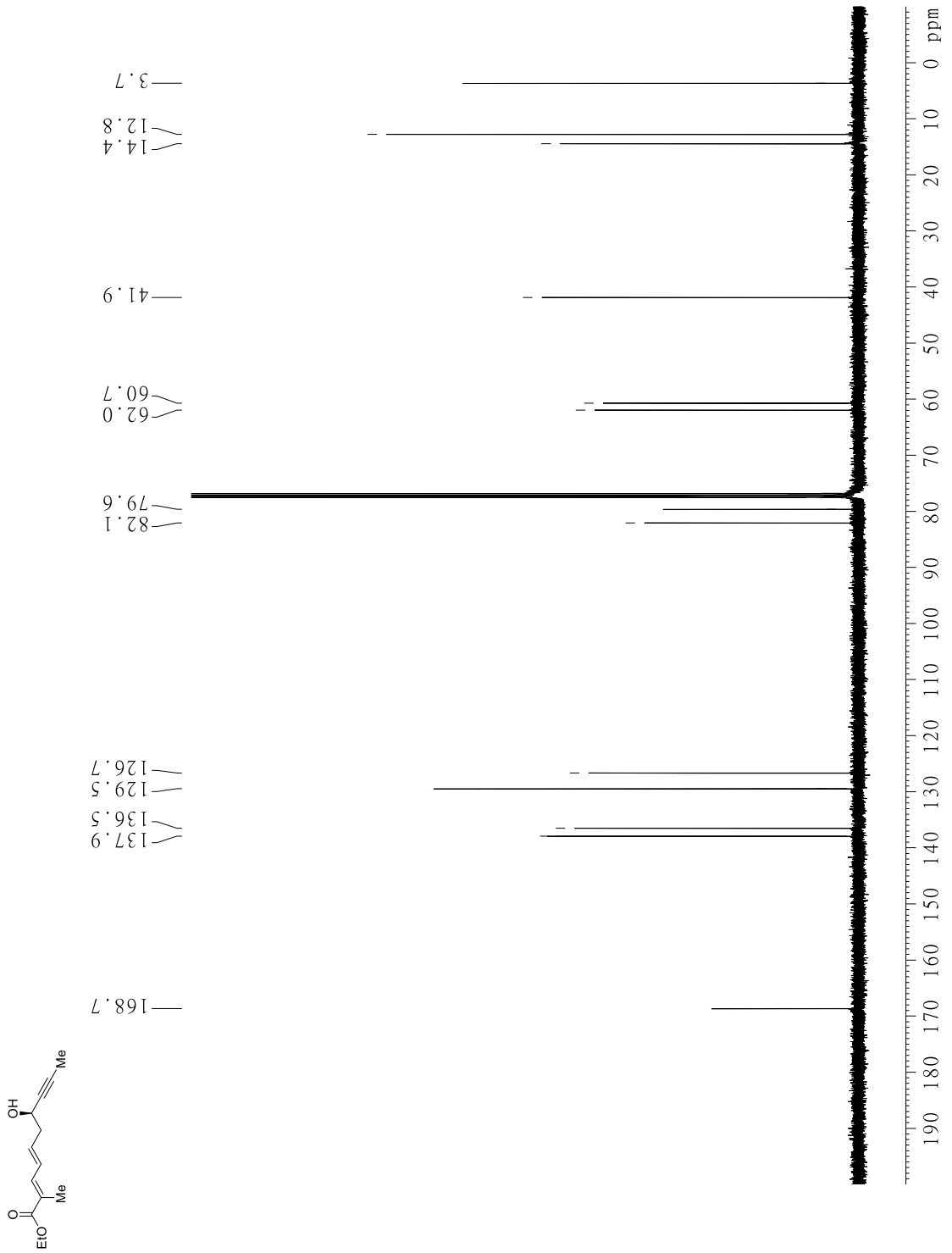
Spectrum 16. ^{1}H spectrum of **5g** measured in $CDCl_3$ at 400 MHz.



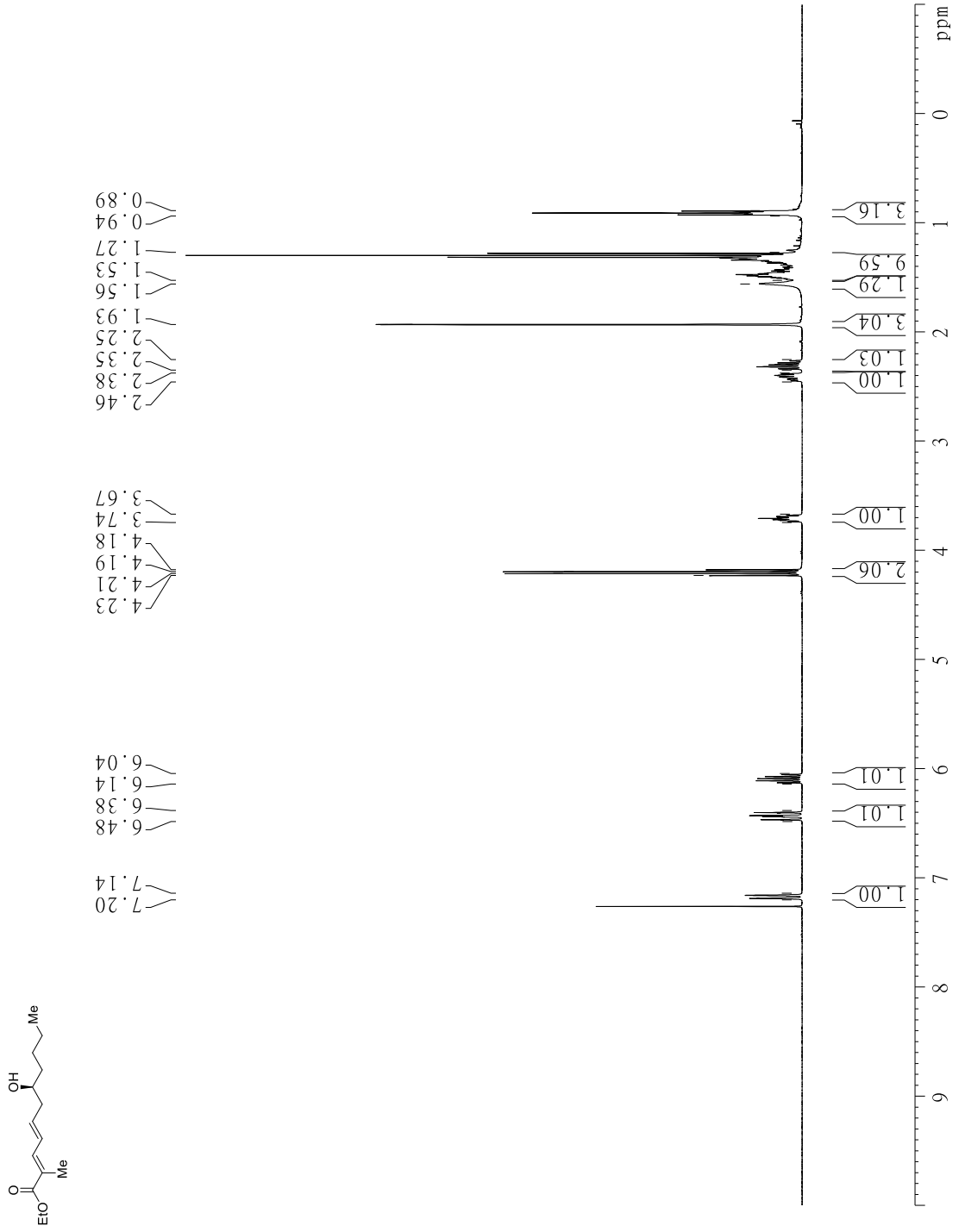
Spectrum 17. ^{13}C spectrum of **5g** measured in $CDCl_3$ at 101 MHz.



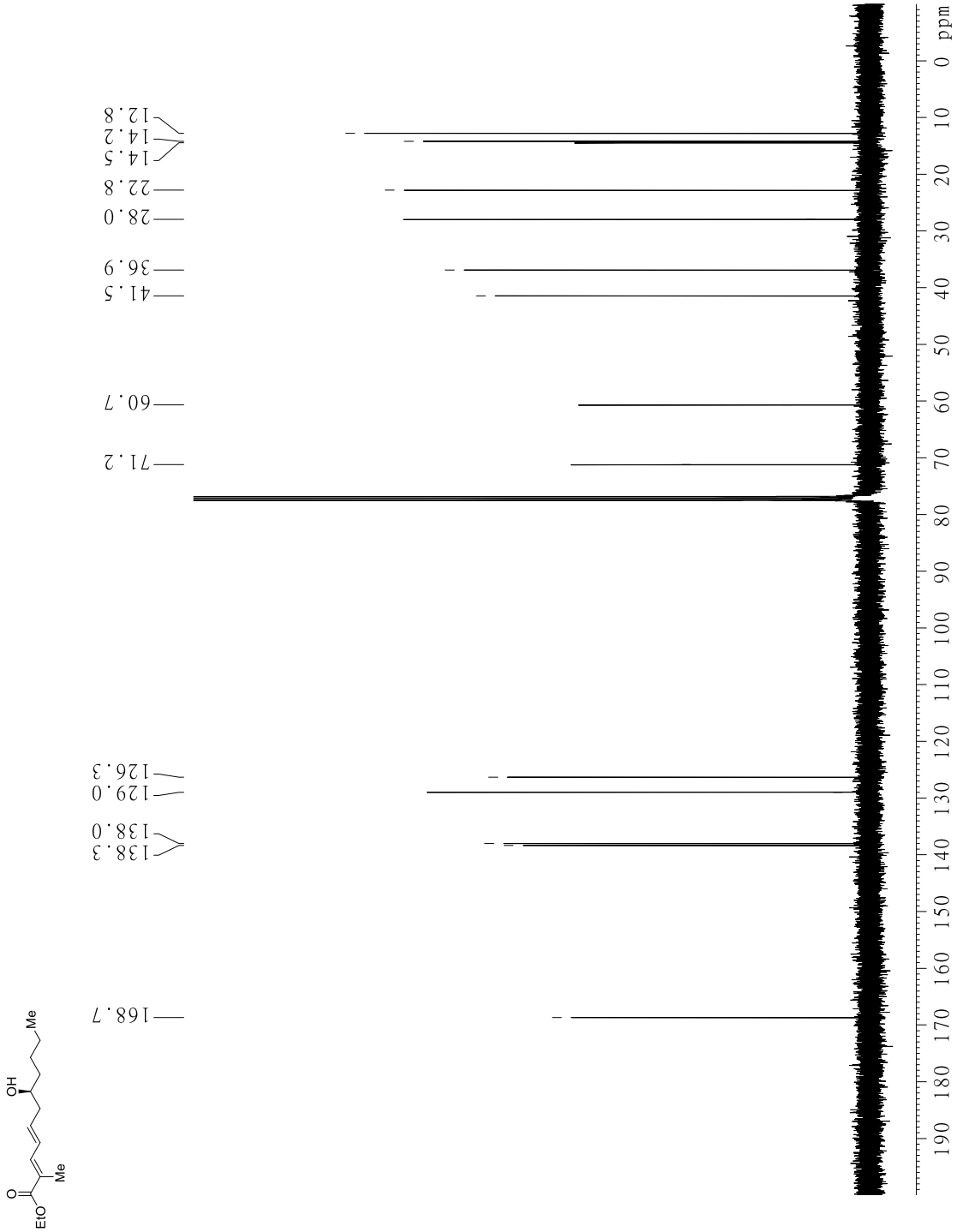
Spectrum 18. ^{1}H spectrum of **5h** measured in $CDCl_3$ at 600 MHz.



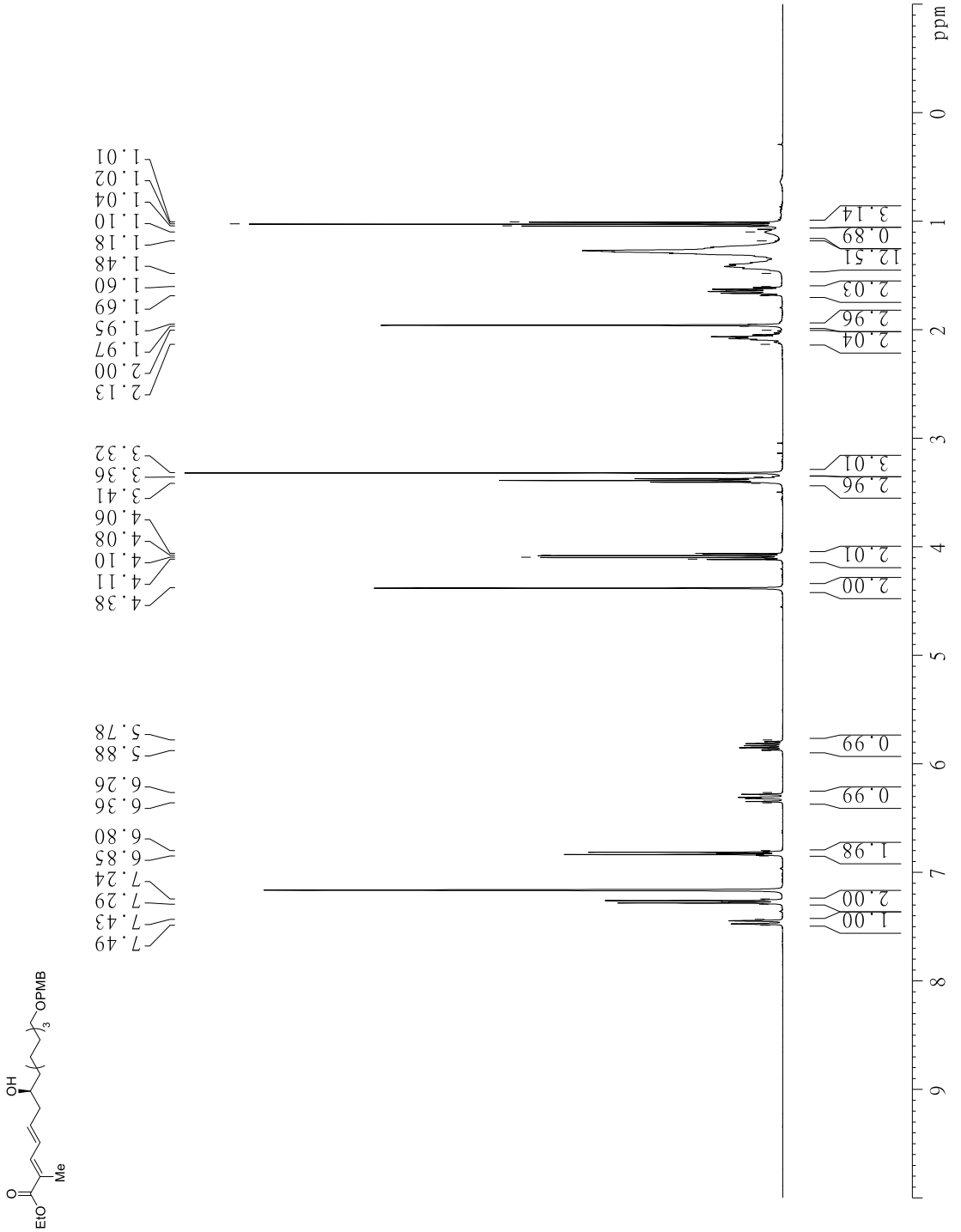
Spectrum 19. ^{13}C spectrum of **5h** measured in $CDCl_3$ at 151 MHz.



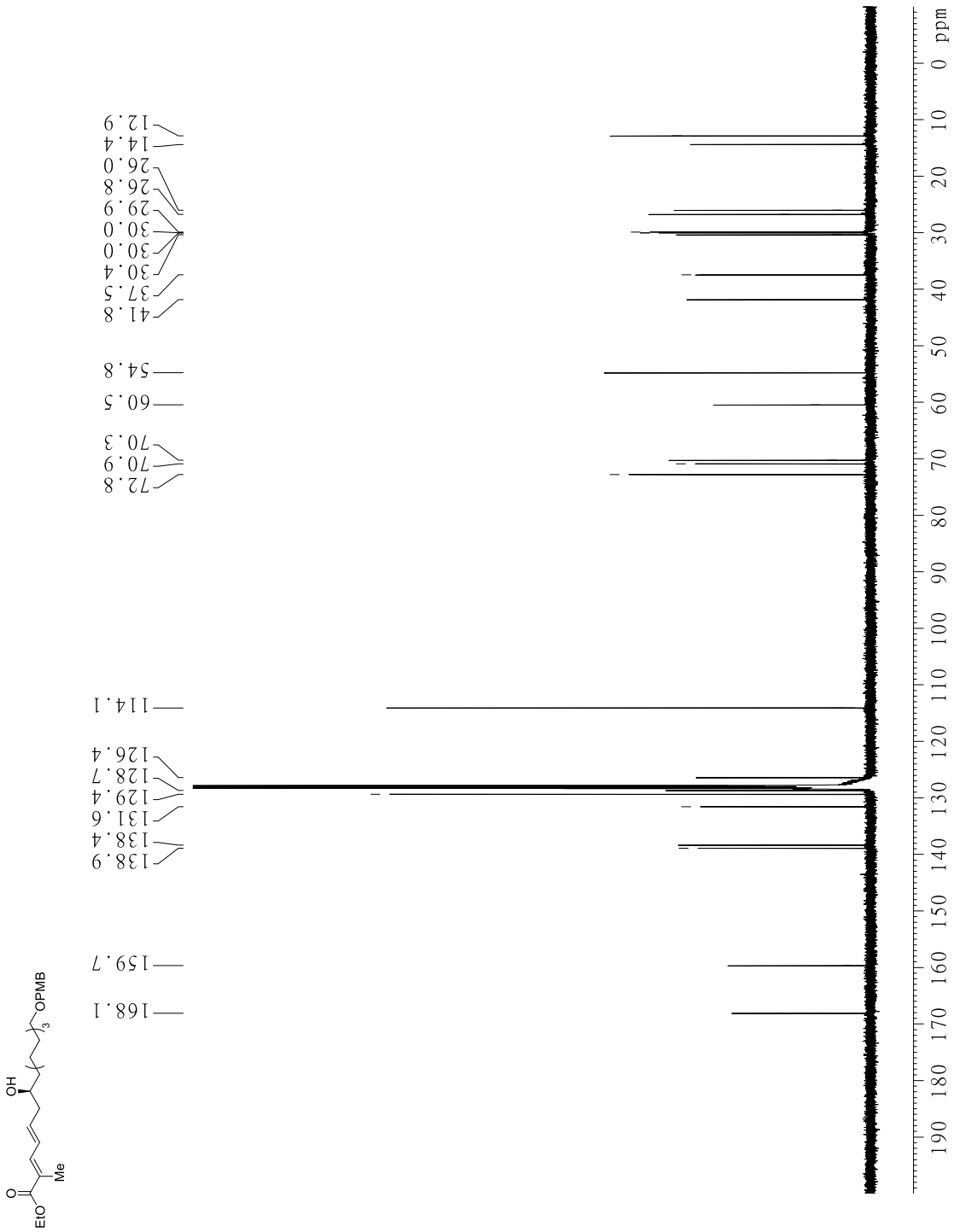
Spectrum 20. ^{1}H spectrum of **5i** measured in $CDCl_3$ at 400 MHz.



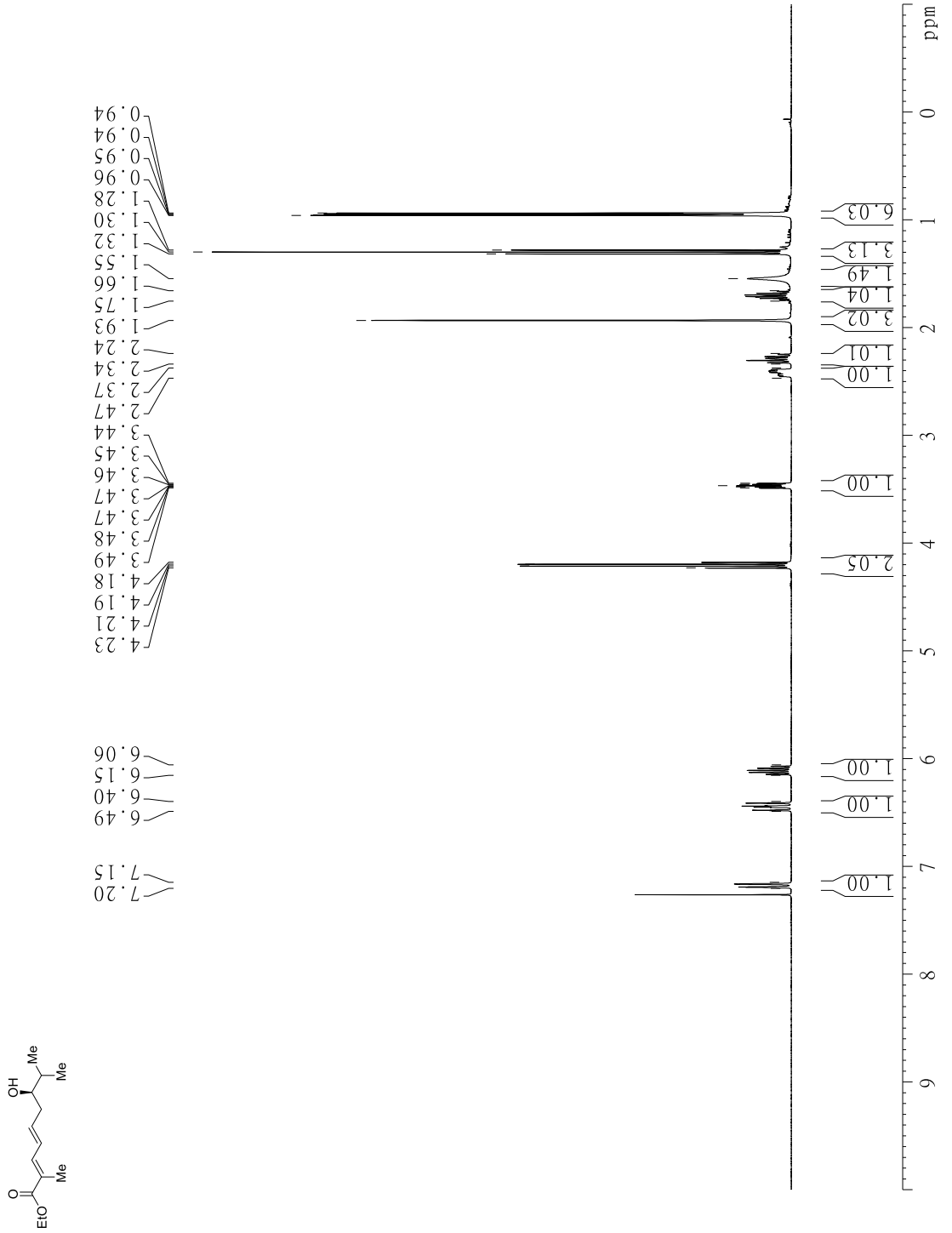
Spectrum 21. ^{13}C spectrum of **5i** measured in $CDCl_3$ at 101 MHz.



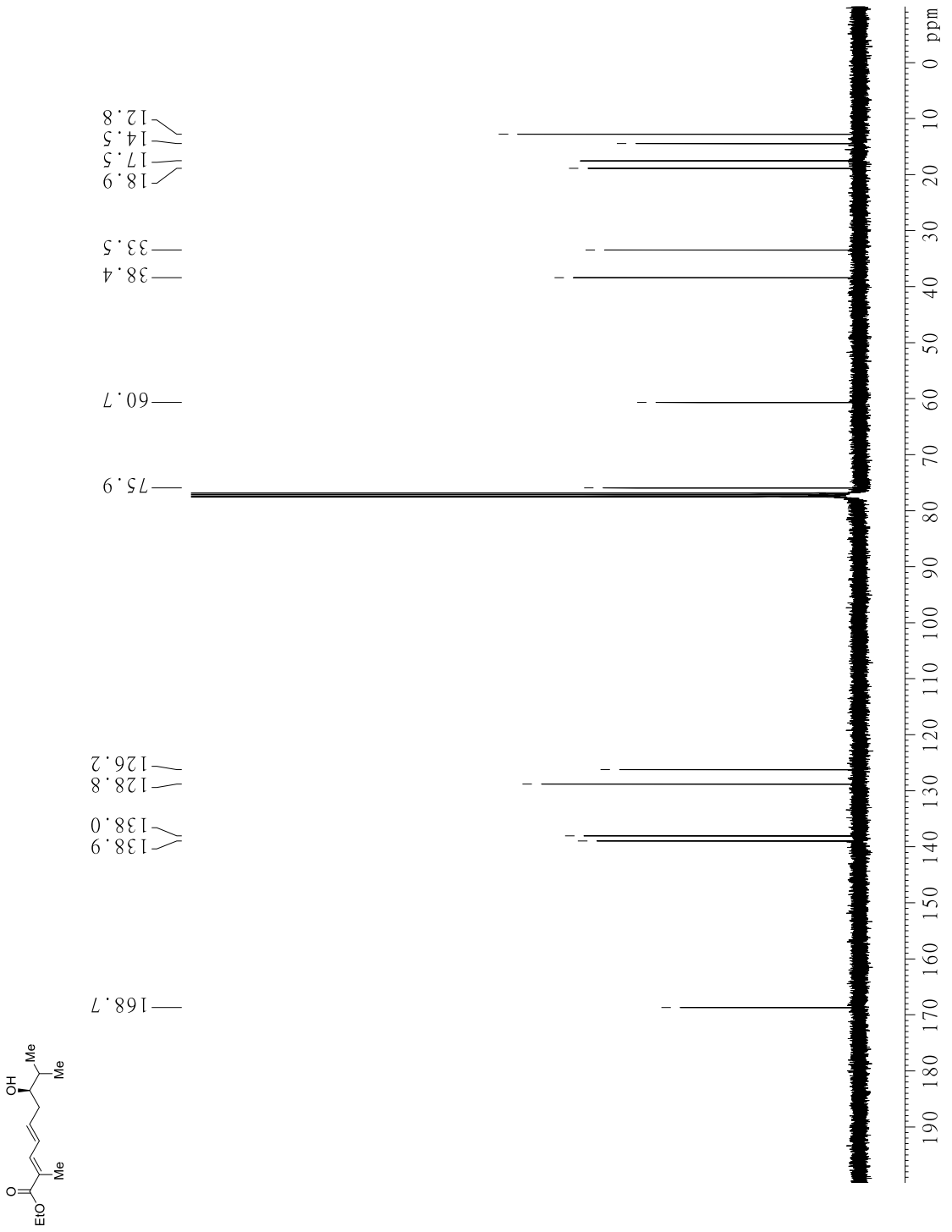
Spectrum 22. ^{1}H spectrum of **5j** measured in C_6D_6 at 400 MHz.



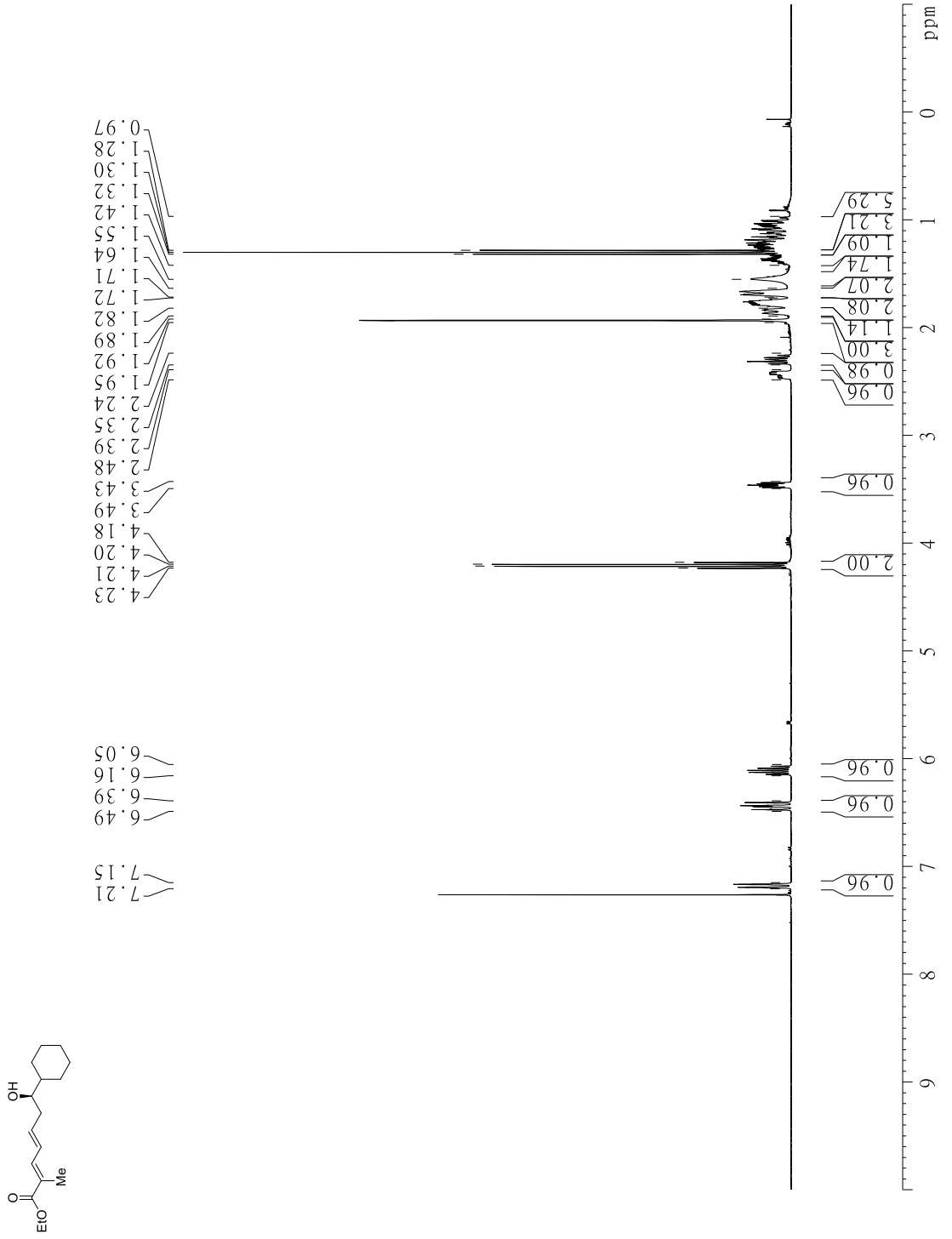
Spectrum 23. ^{13}C spectrum of **5j** measured in C_6D_6 at 101 MHz.



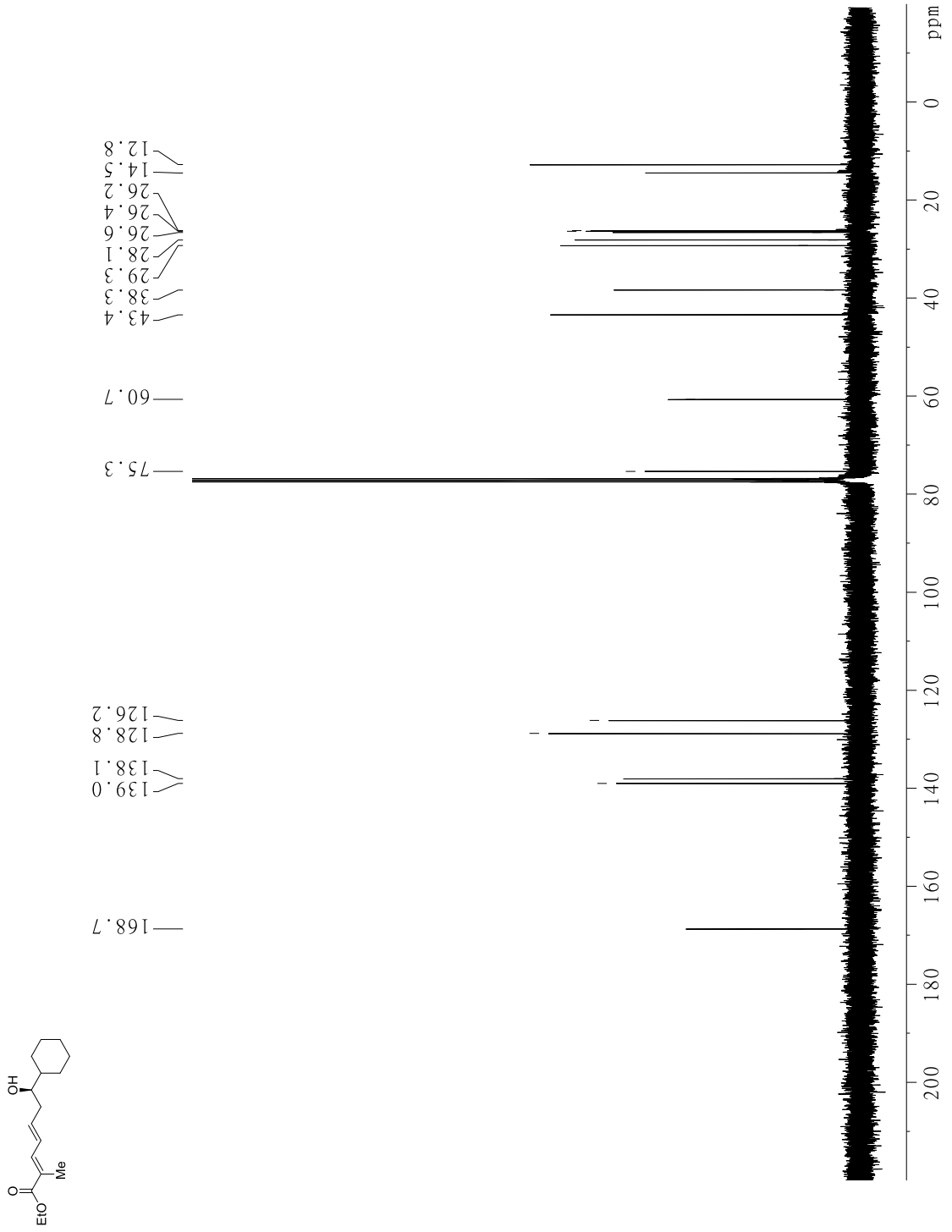
Spectrum 24. ^{1}H spectrum of **5k** measured in $CDCl_3$ at 400 MHz.



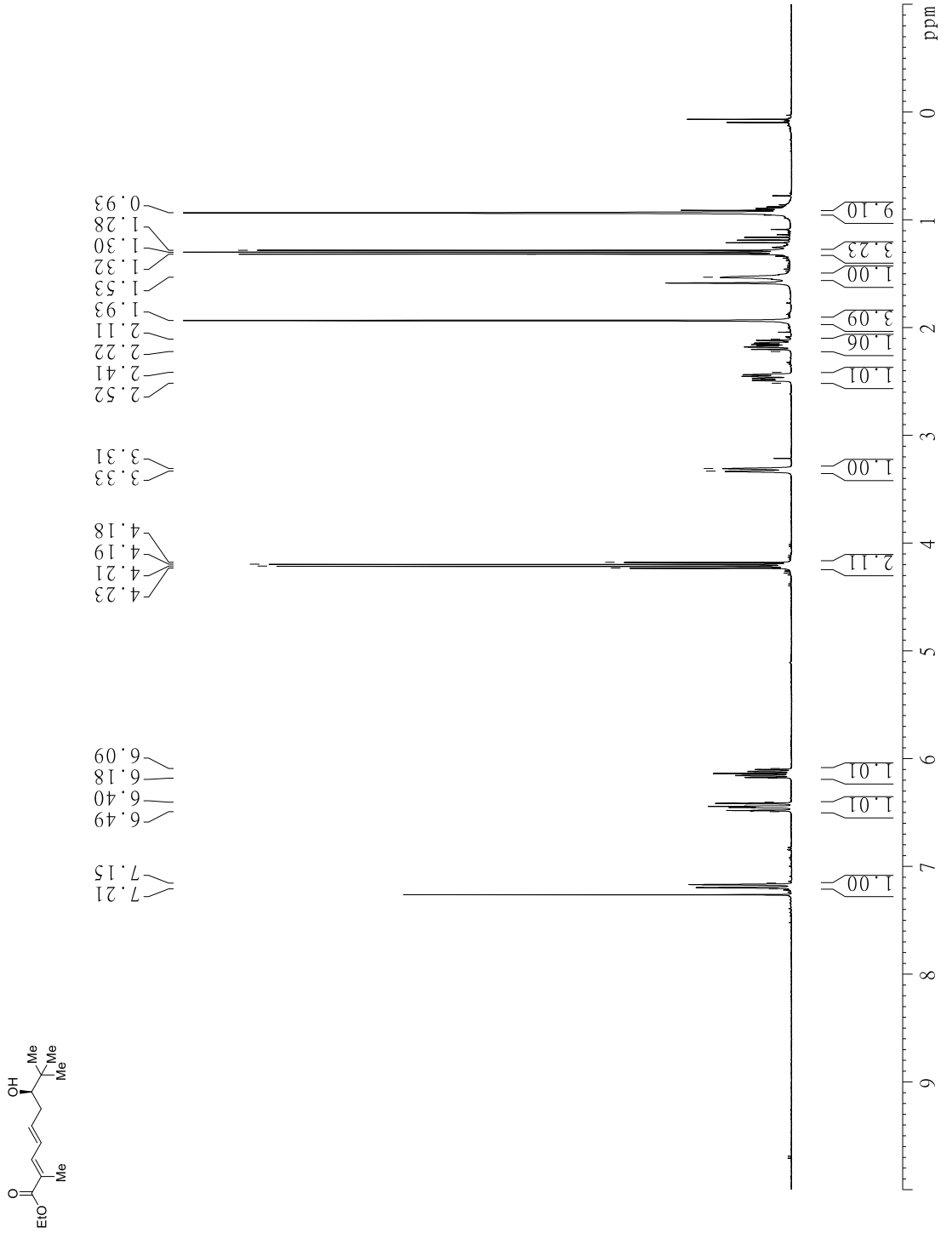
Spectrum 25 ^{13}C spectrum of **5k** measured in $CDCl_3$ at 101 MHz.



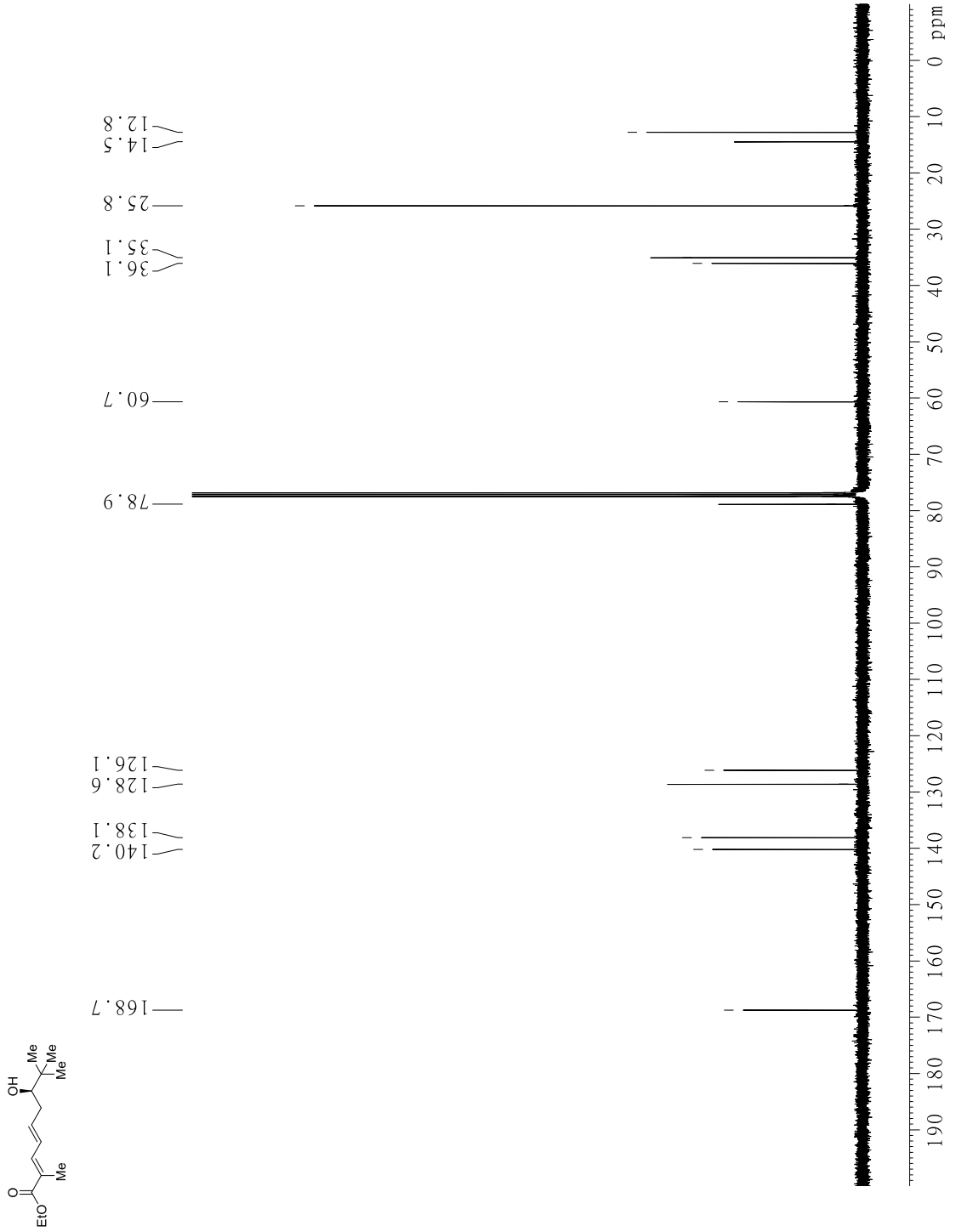
Spectrum 26. ^{1}H spectrum of **5l** measured in $CDCl_3$ at 400 MHz.



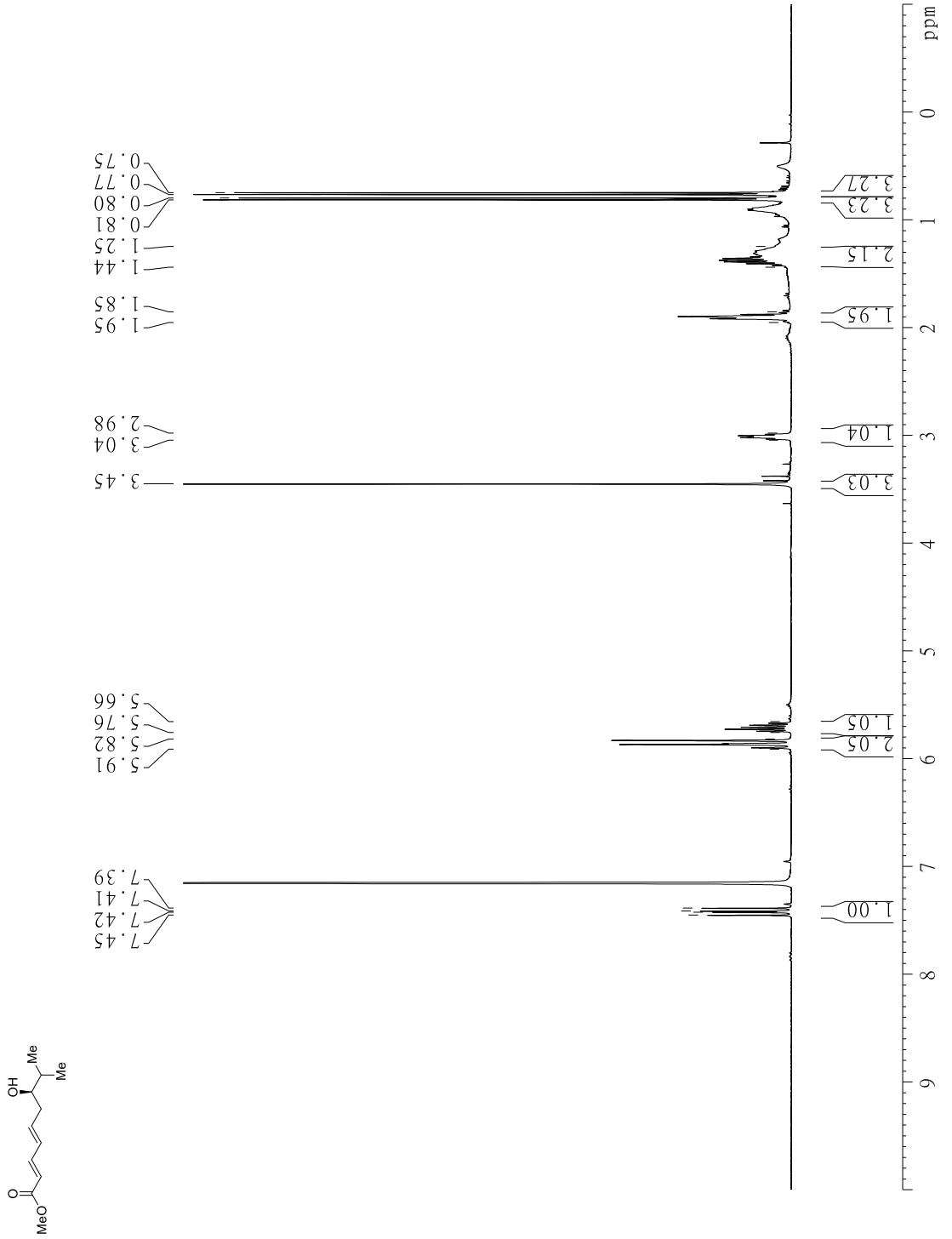
Spectrum 27. ^{13}C spectrum of **5l** measured in $CDCl_3$ at 101 MHz.



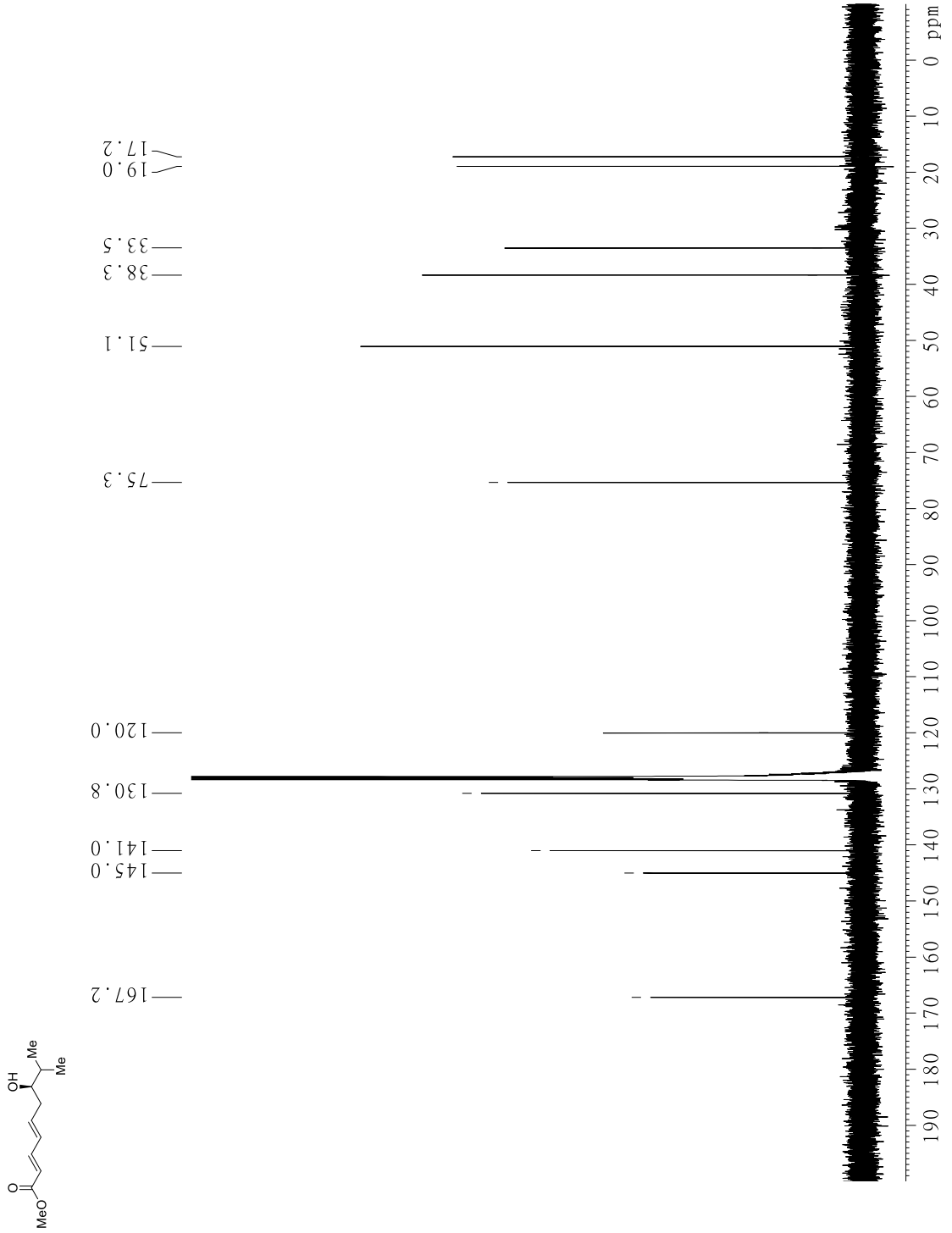
Spectrum 28. ^{1}H spectrum of **5m** measured in $CDCl_3$ at 400 MHz.



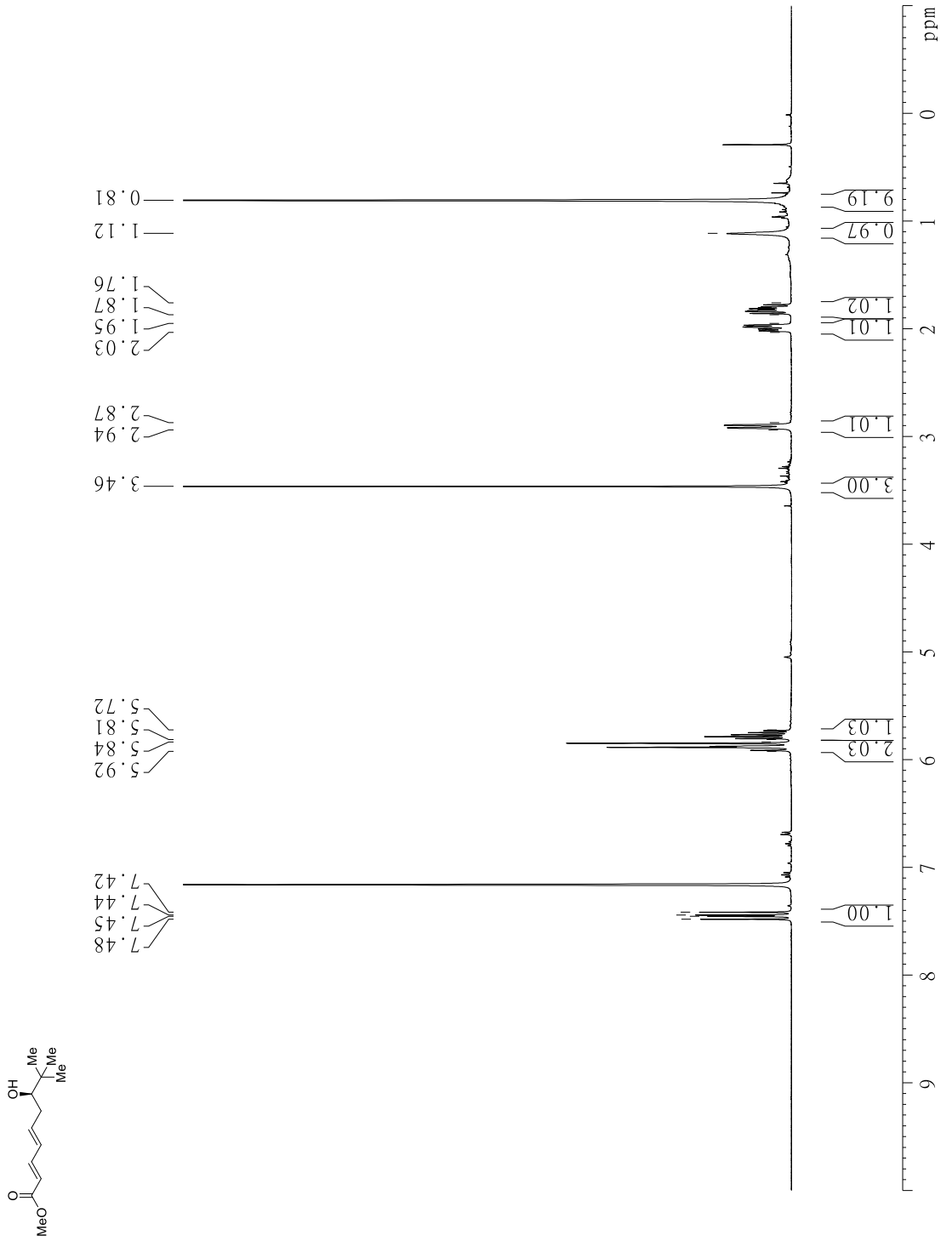
Spectrum 29. ^{13}C spectrum of **5m** measured in $CDCl_3$ at 101 MHz.



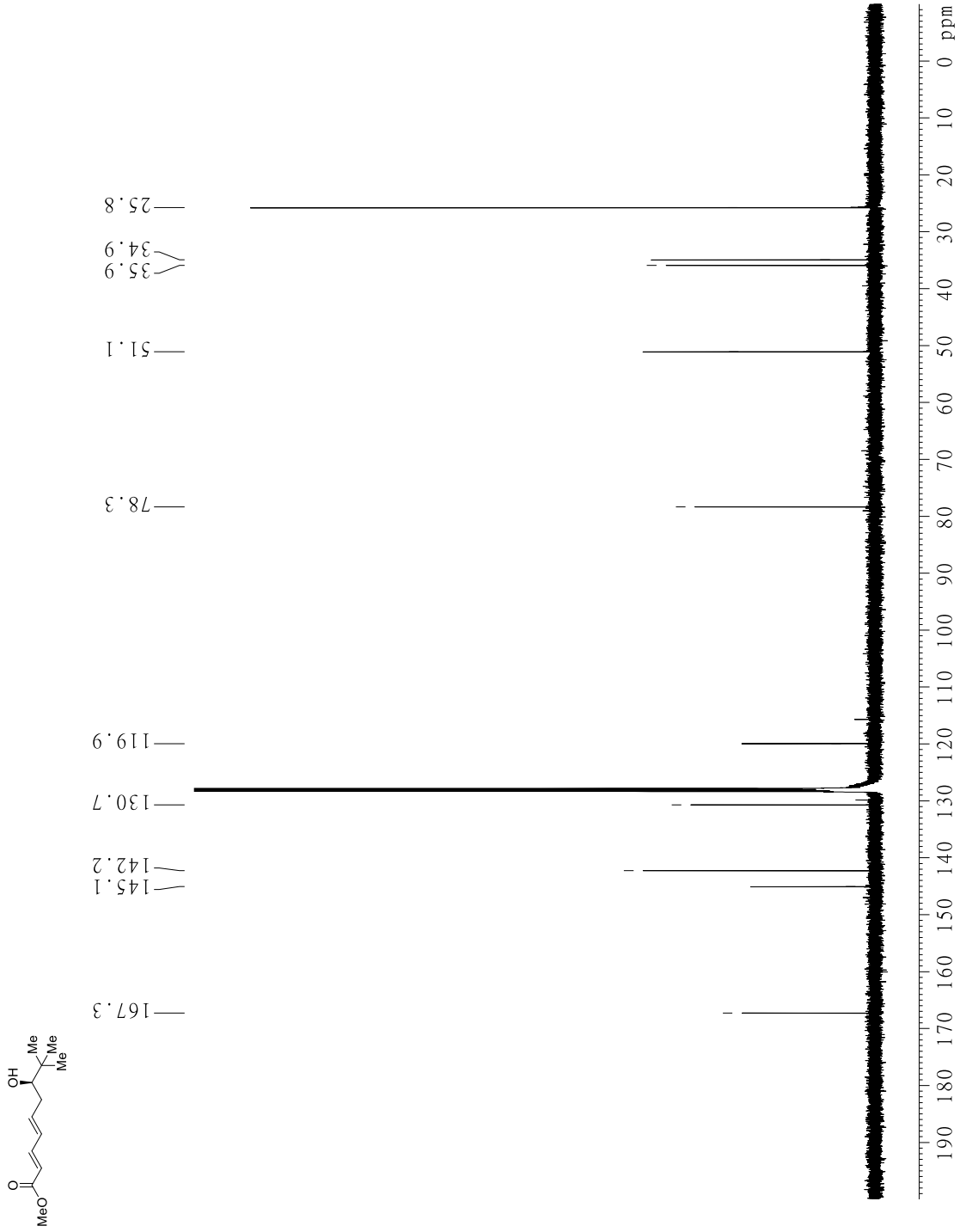
Spectrum 30. ^{1}H spectrum of **5n** measured in C_6D_6 at 400 MHz.



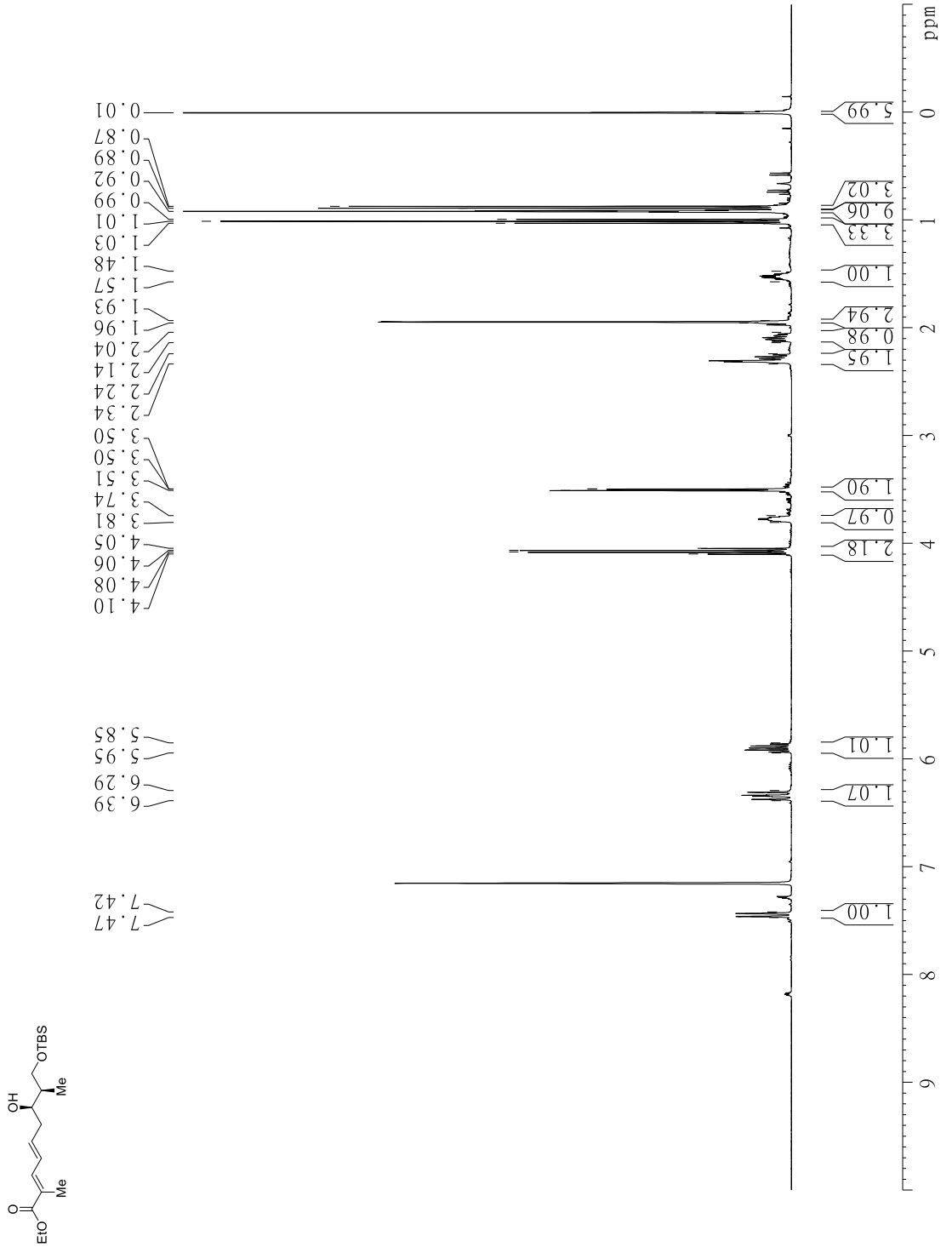
Spectrum 31. ^{13}C spectrum of **5n** measured in C_6D_6 at 101 MHz.



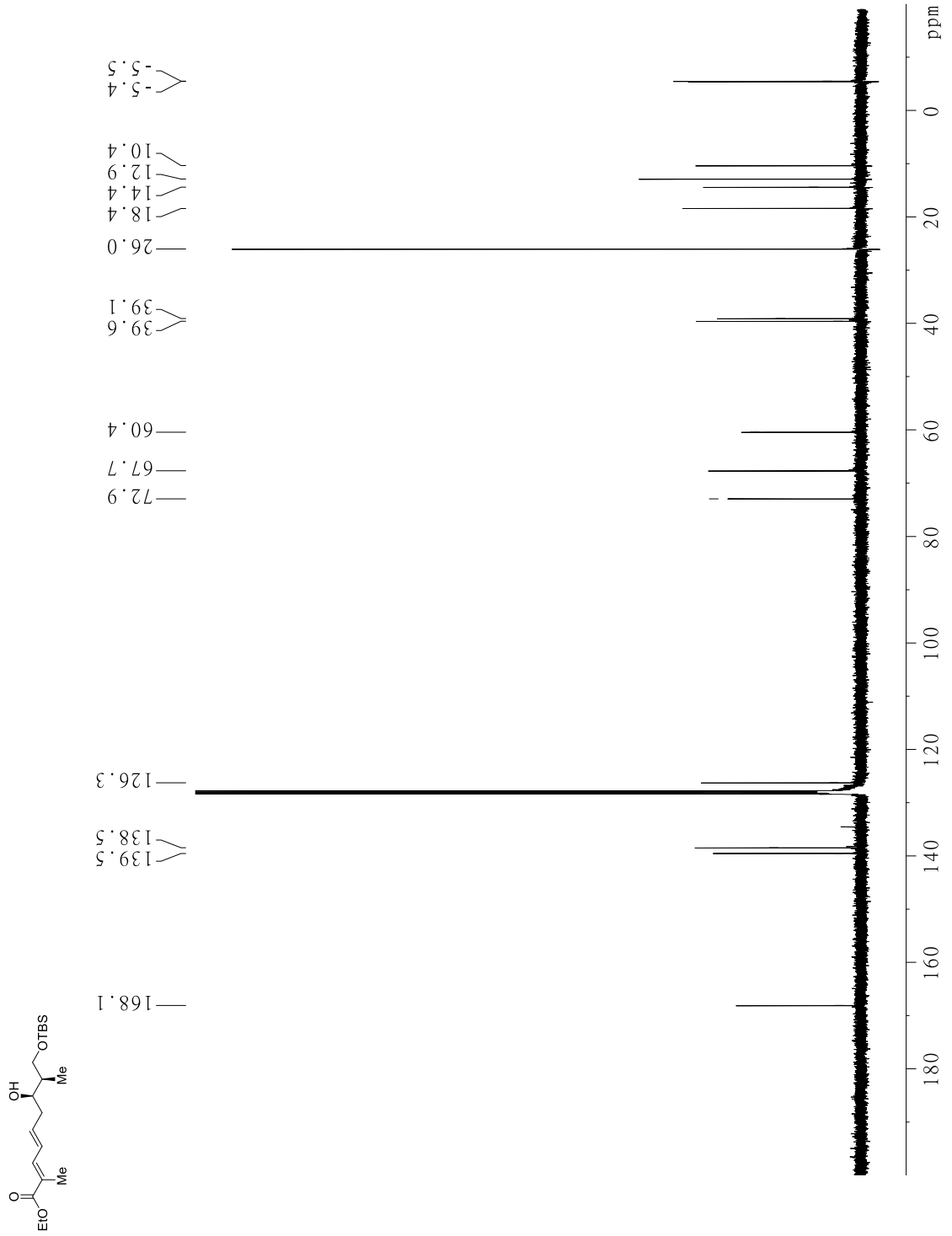
Spectrum 32. ^{1}H spectrum of **5o** measured in C_6D_6 at 400 MHz.



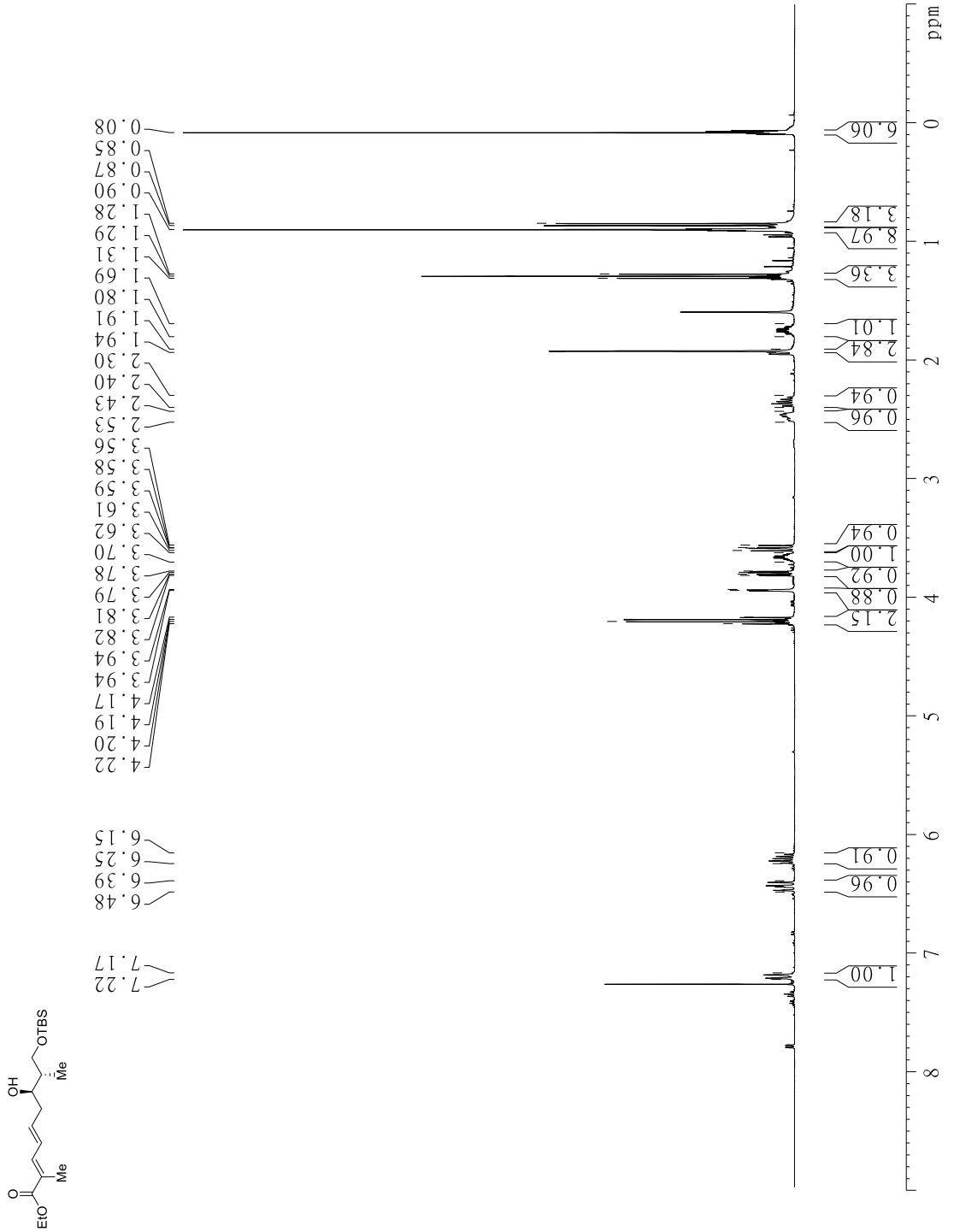
Spectrum 33. ^{13}C spectrum of **5o** measured in C_6D_6 at 101 MHz.



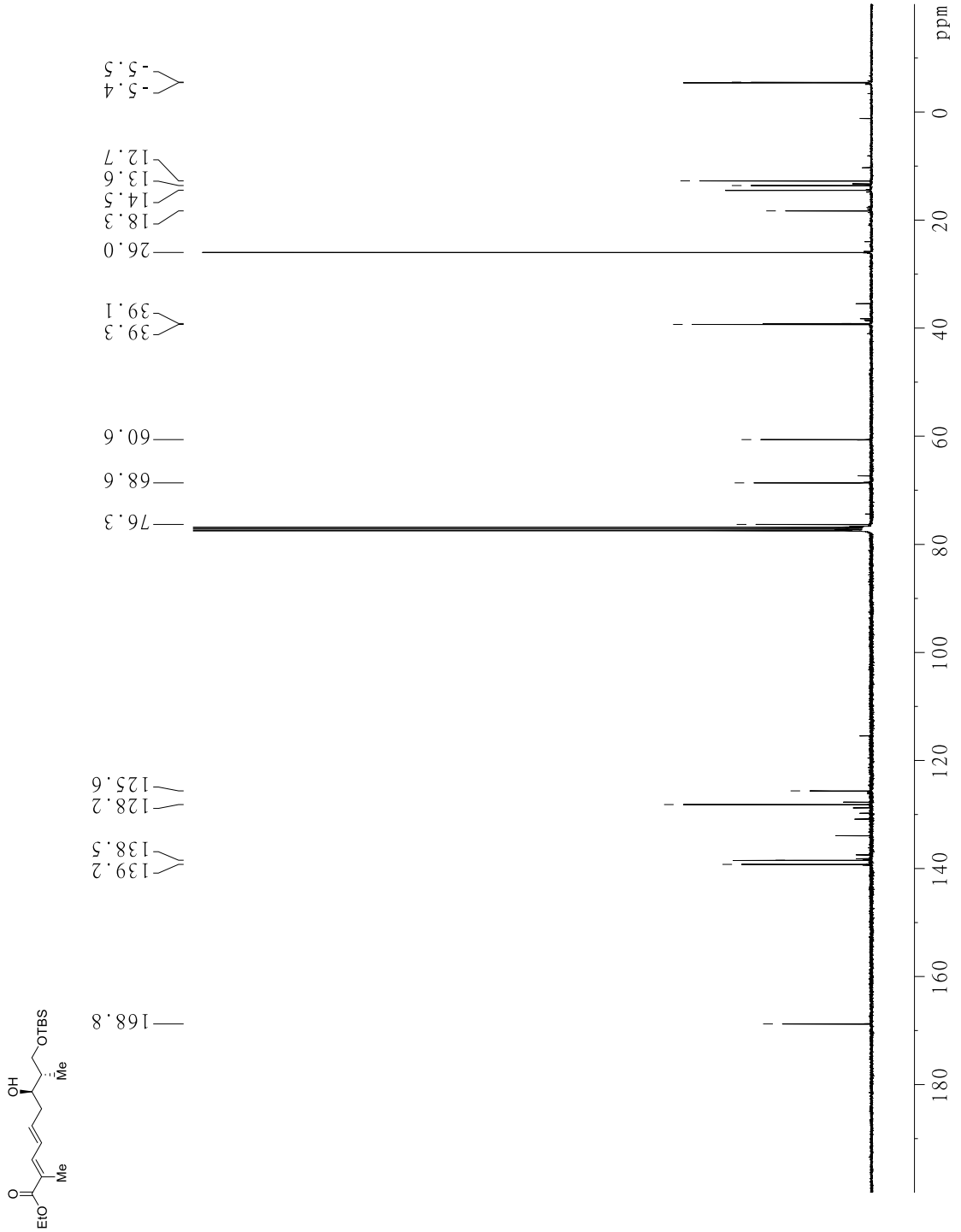
Spectrum 34. ^{1}H spectrum of **5p** measured in C_6D_6 at 400 MHz.



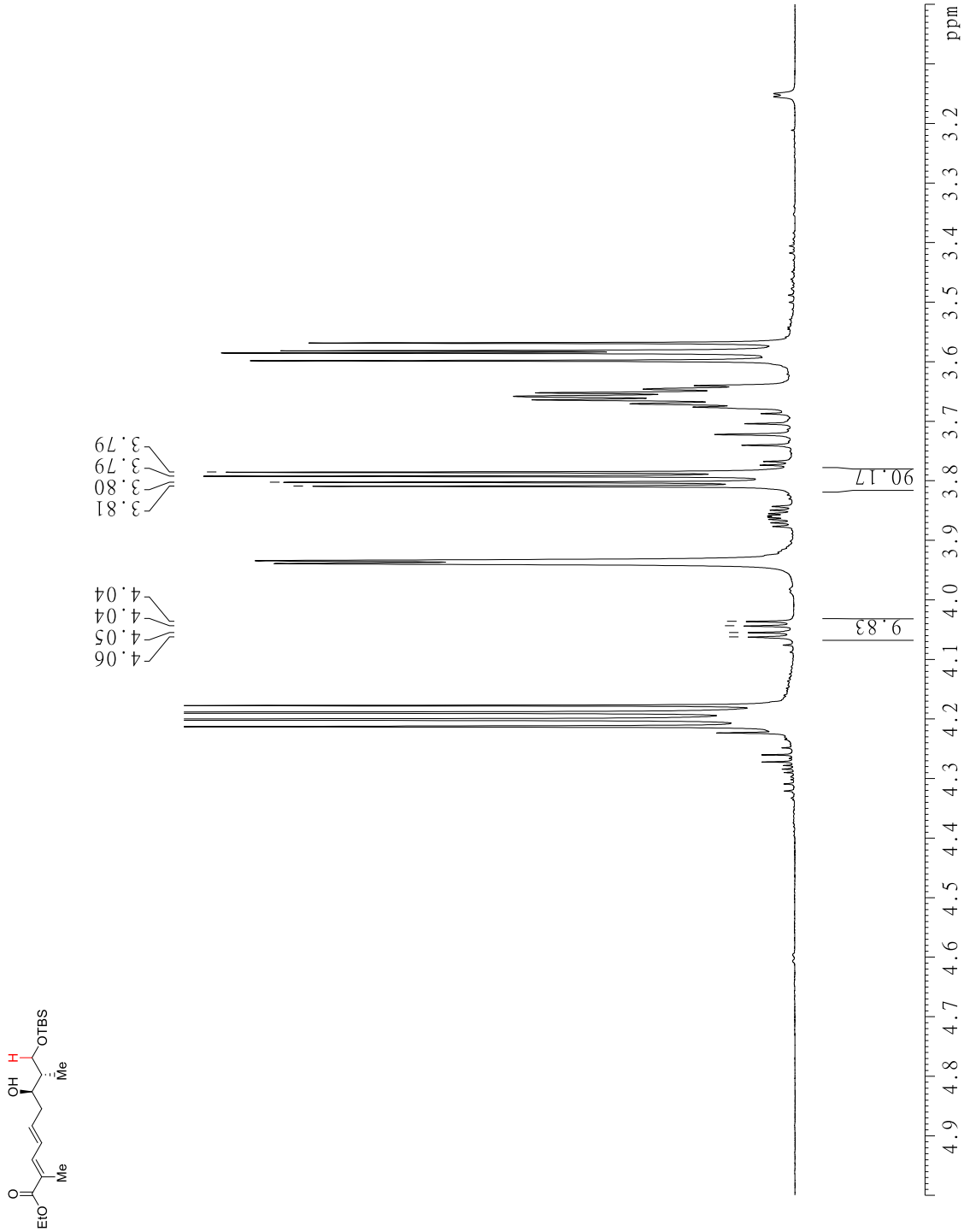
Spectrum 35. ^{13}C spectrum of **5p** measured in C_6D_6 at 101 MHz.



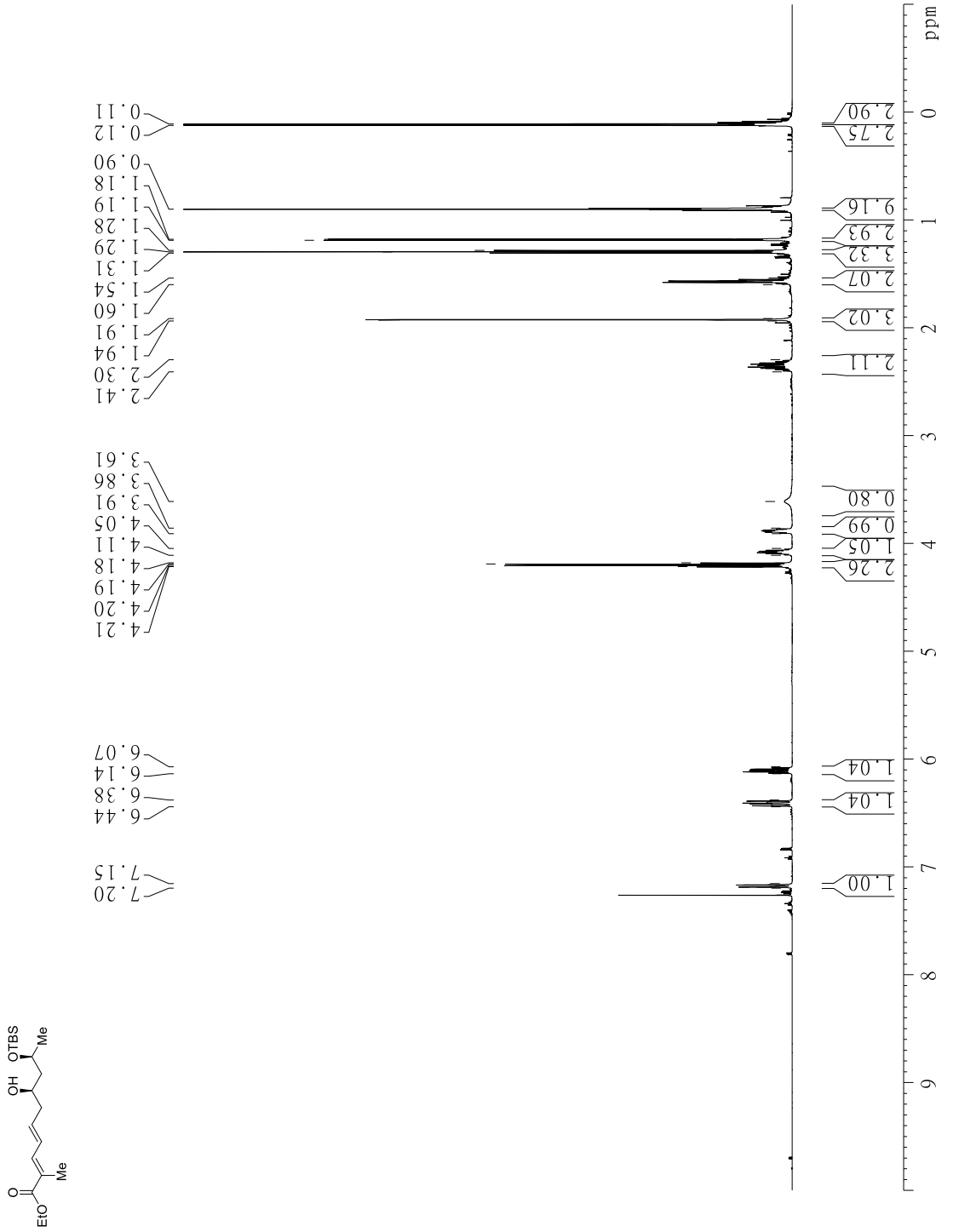
Spectrum 36. ^{1}H spectrum of **5q** measured in $CDCl_3$ at 600 MHz.



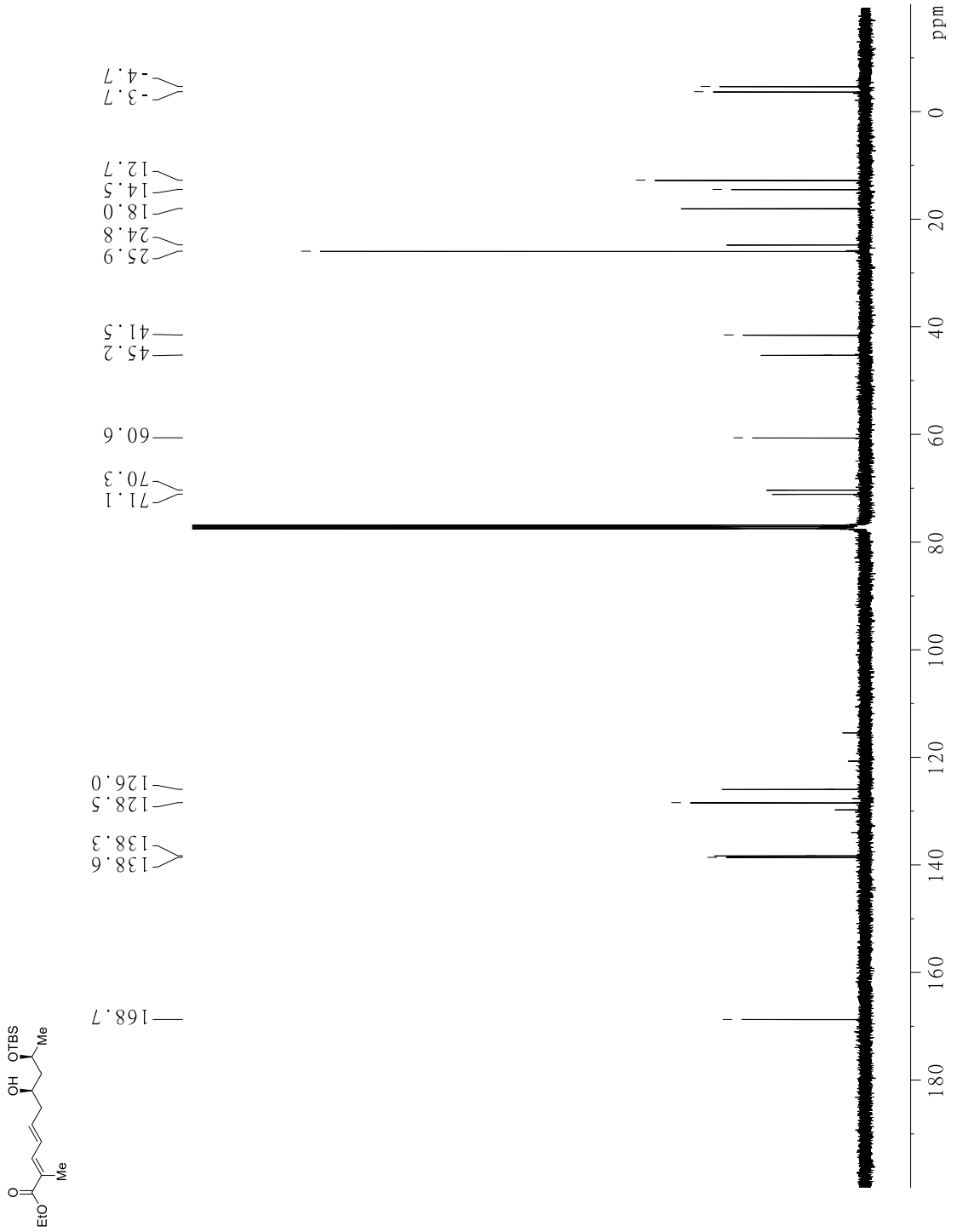
Spectrum 37. ^{13}C spectrum of **5q** measured in $CDCl_3$ at 151 MHz.



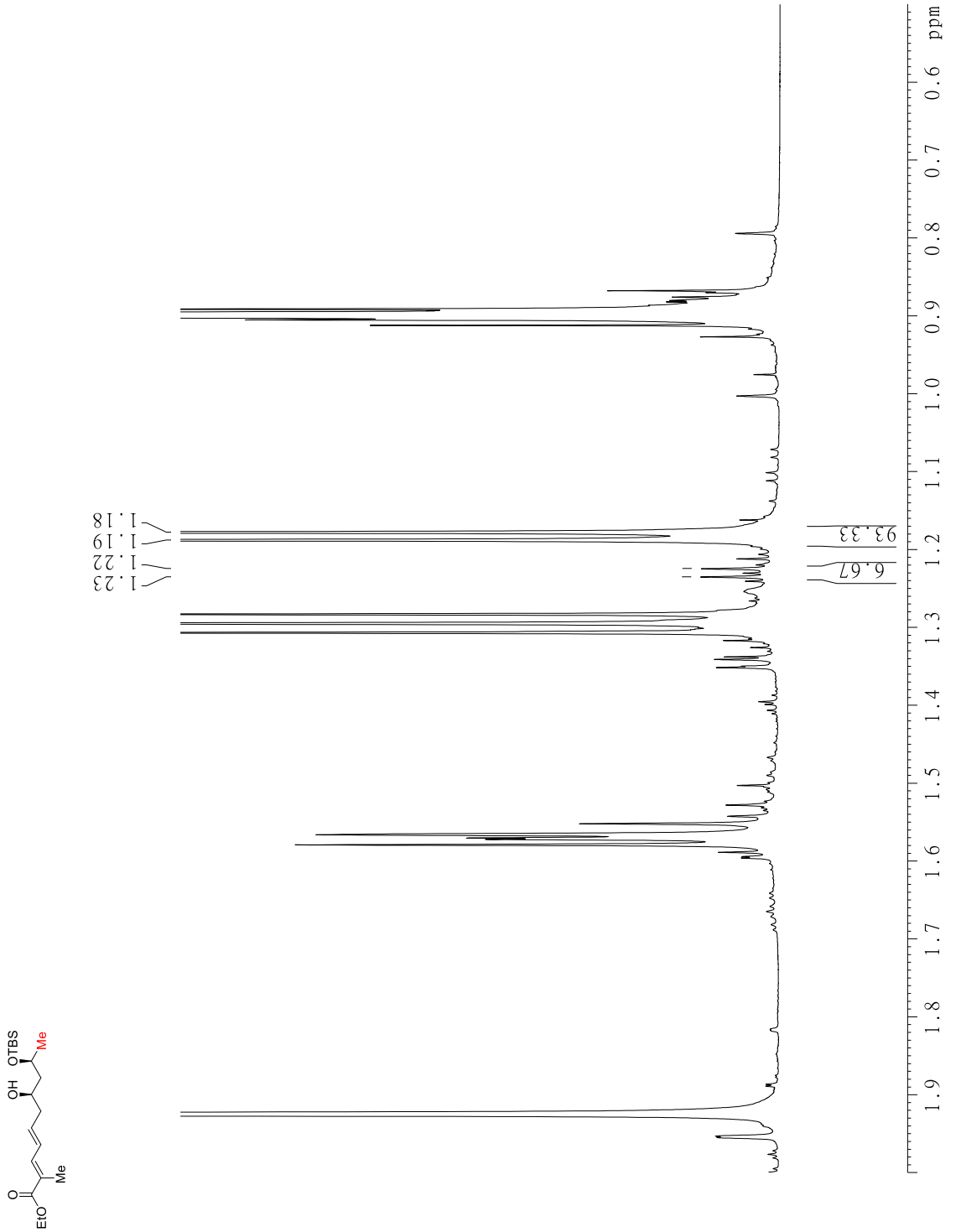
Spectrum 38. Enlarged view of the ^{1}H spectrum of **5q** for the determination of the diastereomeric ratio; the spectrum was measured in $CDCl_3$ at 600 MHz.



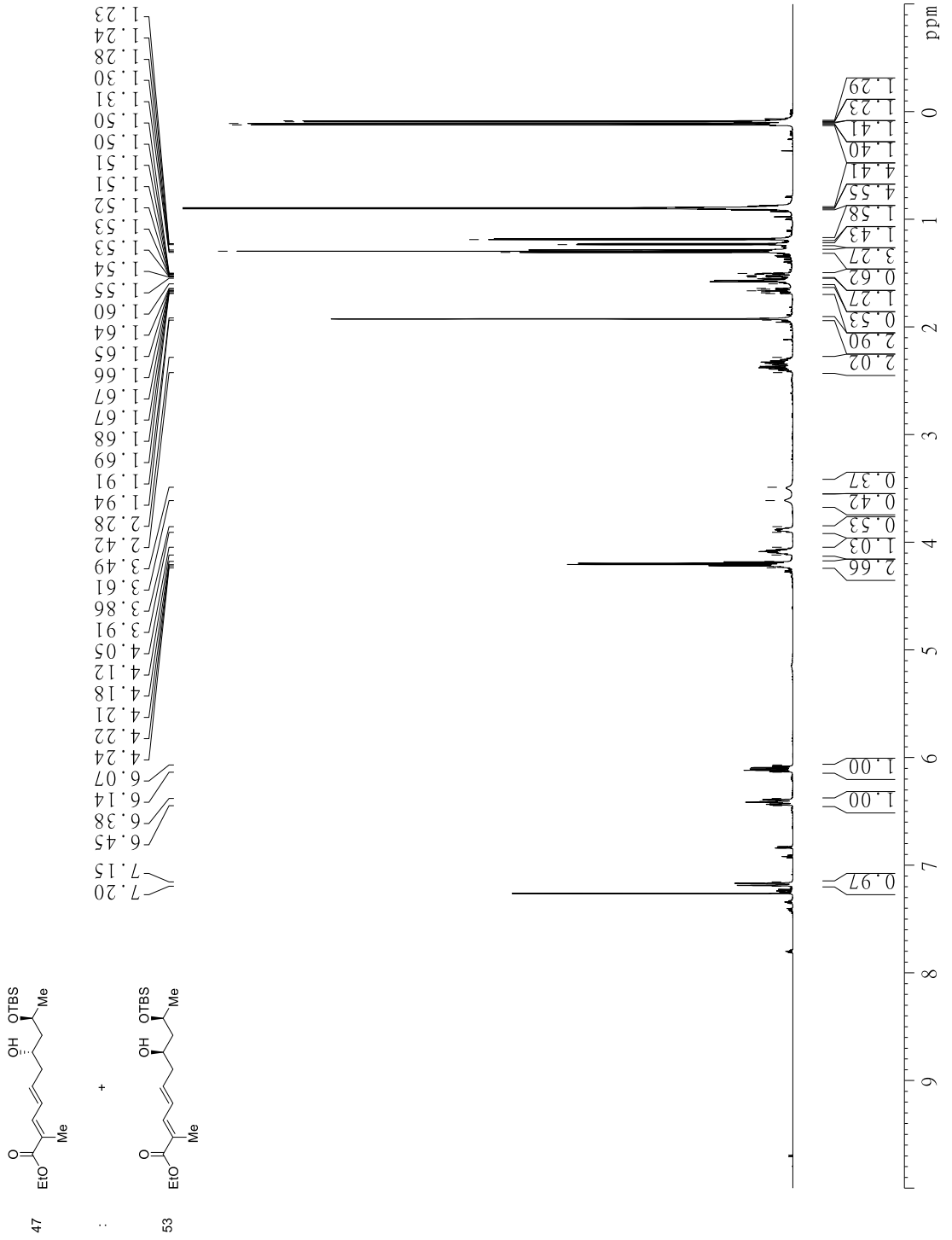
Spectrum 39. ^{1}H spectrum of **5r** measured in $CDCl_3$ at 400 MHz.



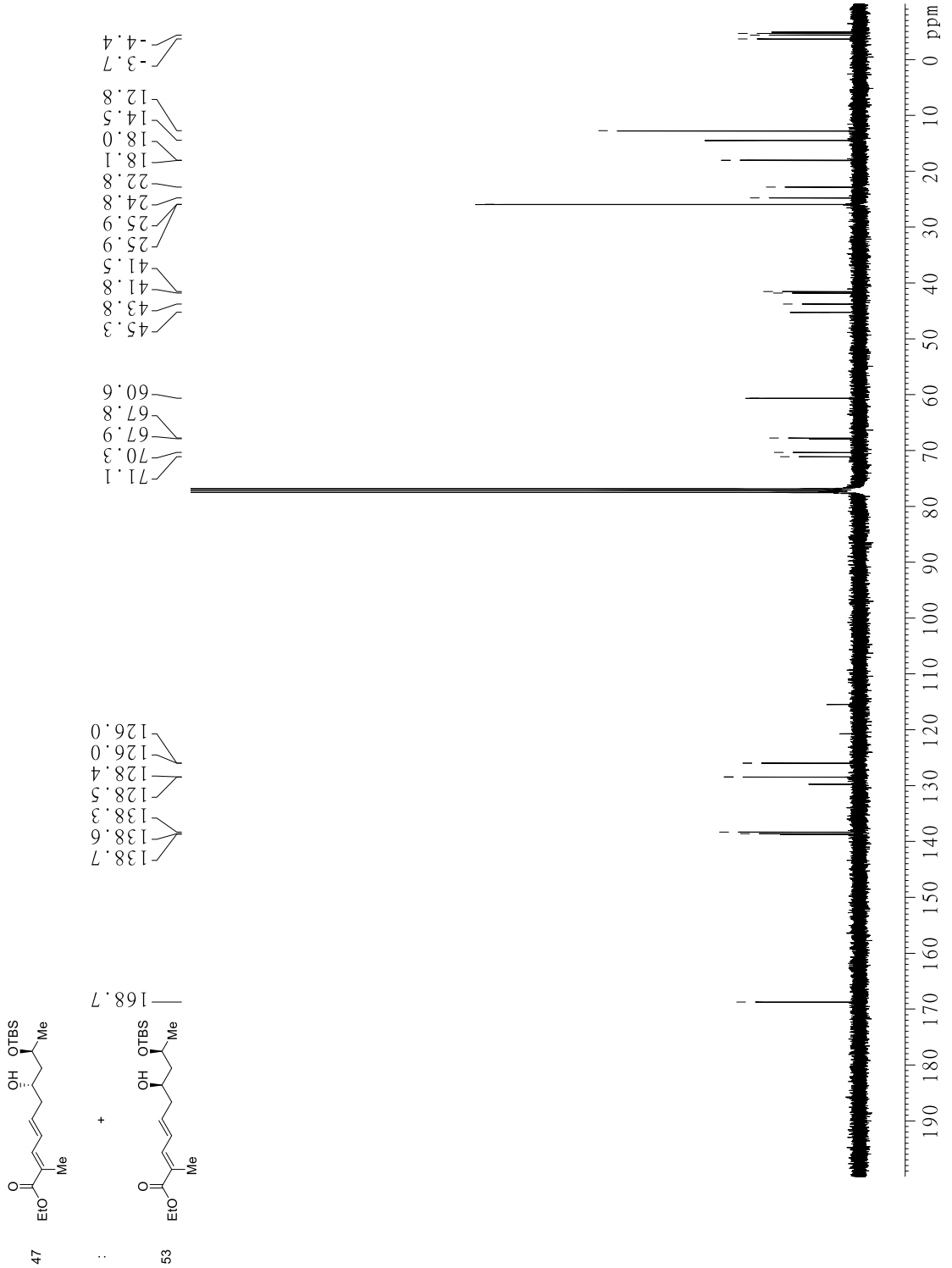
Spectrum 40. ^{13}C spectrum of **5r** measured in $CDCl_3$ at 101 MHz.



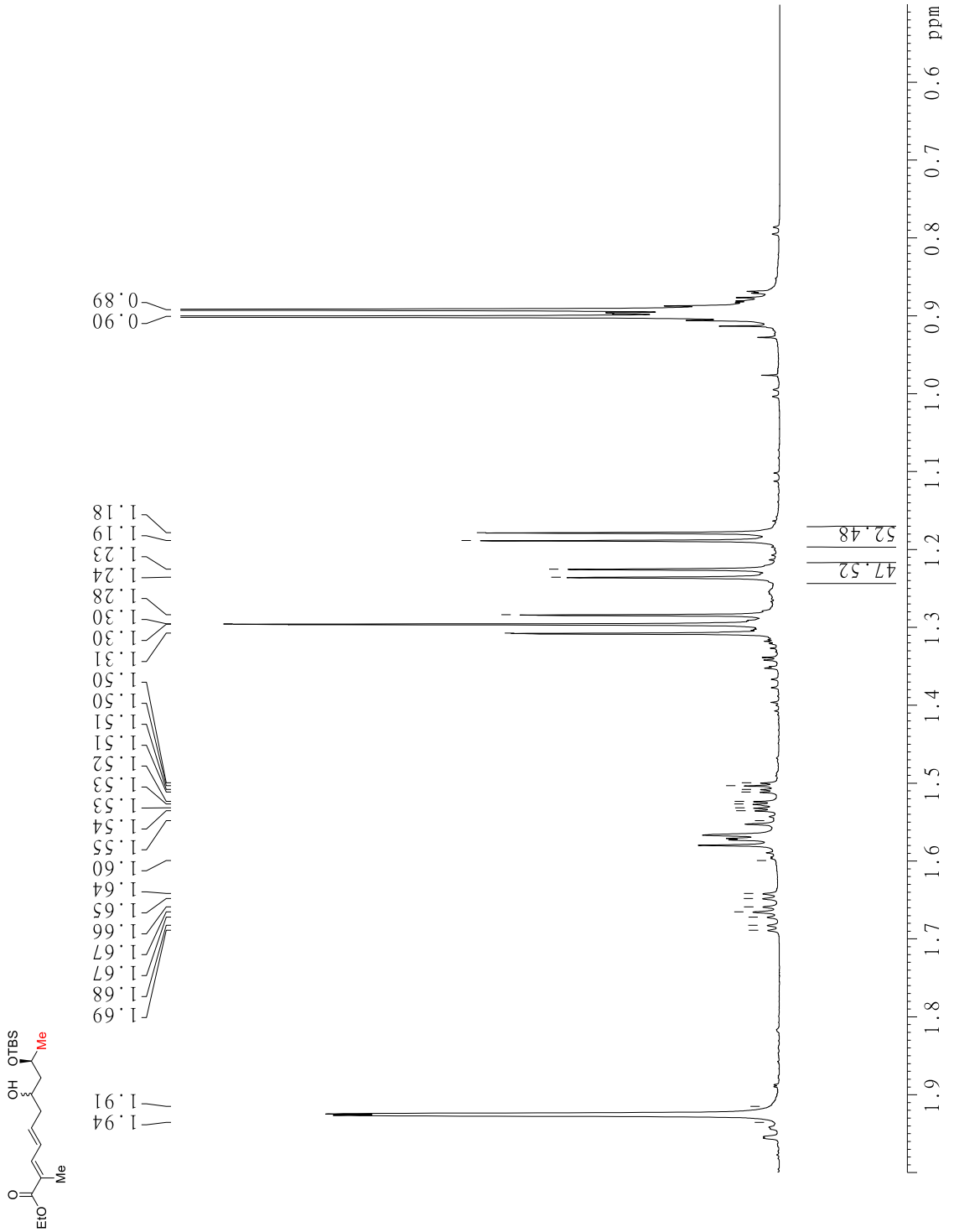
Spectrum 41. Enlarged view of the ^{1}H spectrum of **5r** for the determination of the diastereomeric ratio; the spectrum was measured in $CDCl_3$ at 600 MHz.



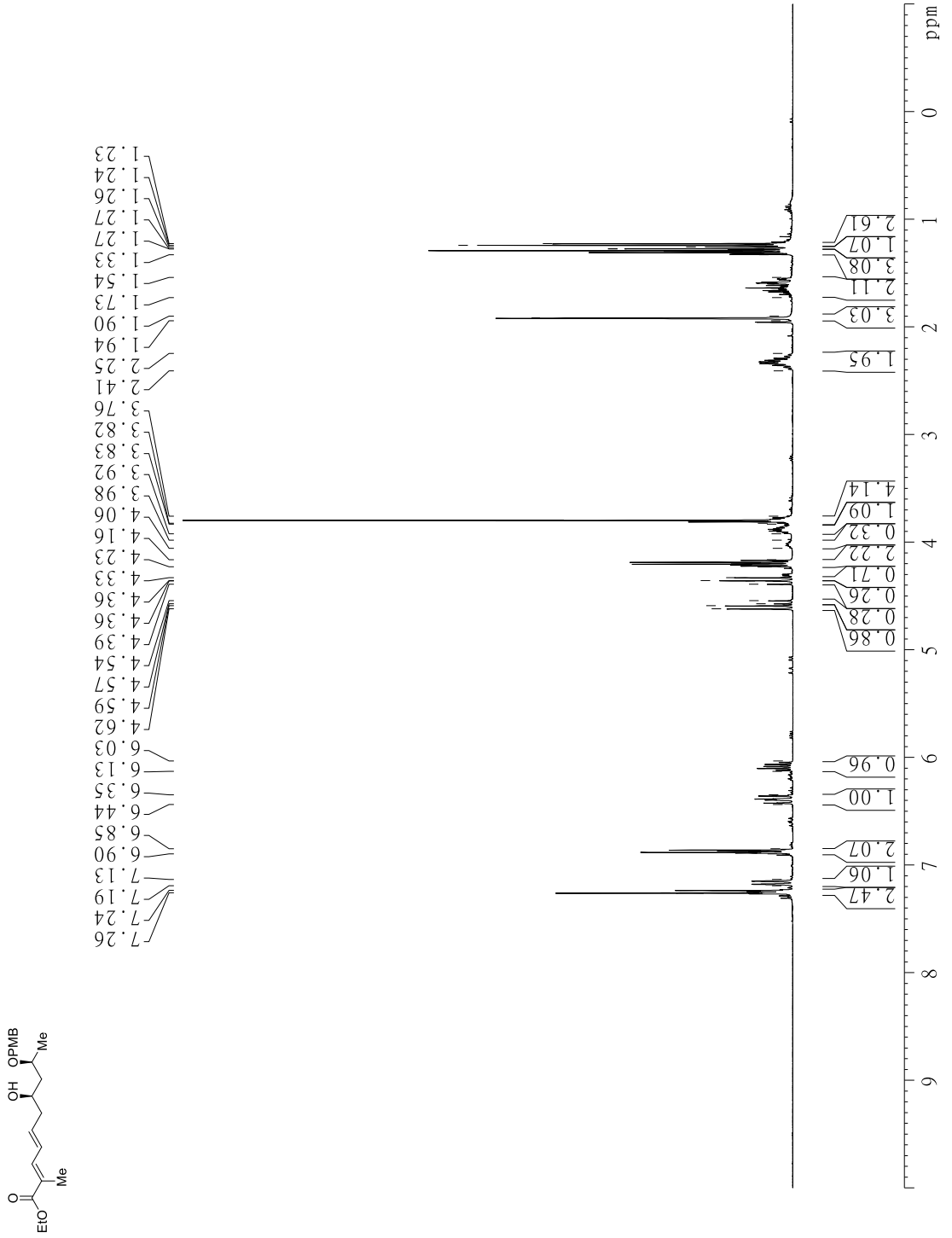
Spectrum 42. ^{1}H spectrum of **5s** measured in $CDCl_3$ at 400 MHz. **5s** was obtained as a mixture with its diastereomer **5r**.



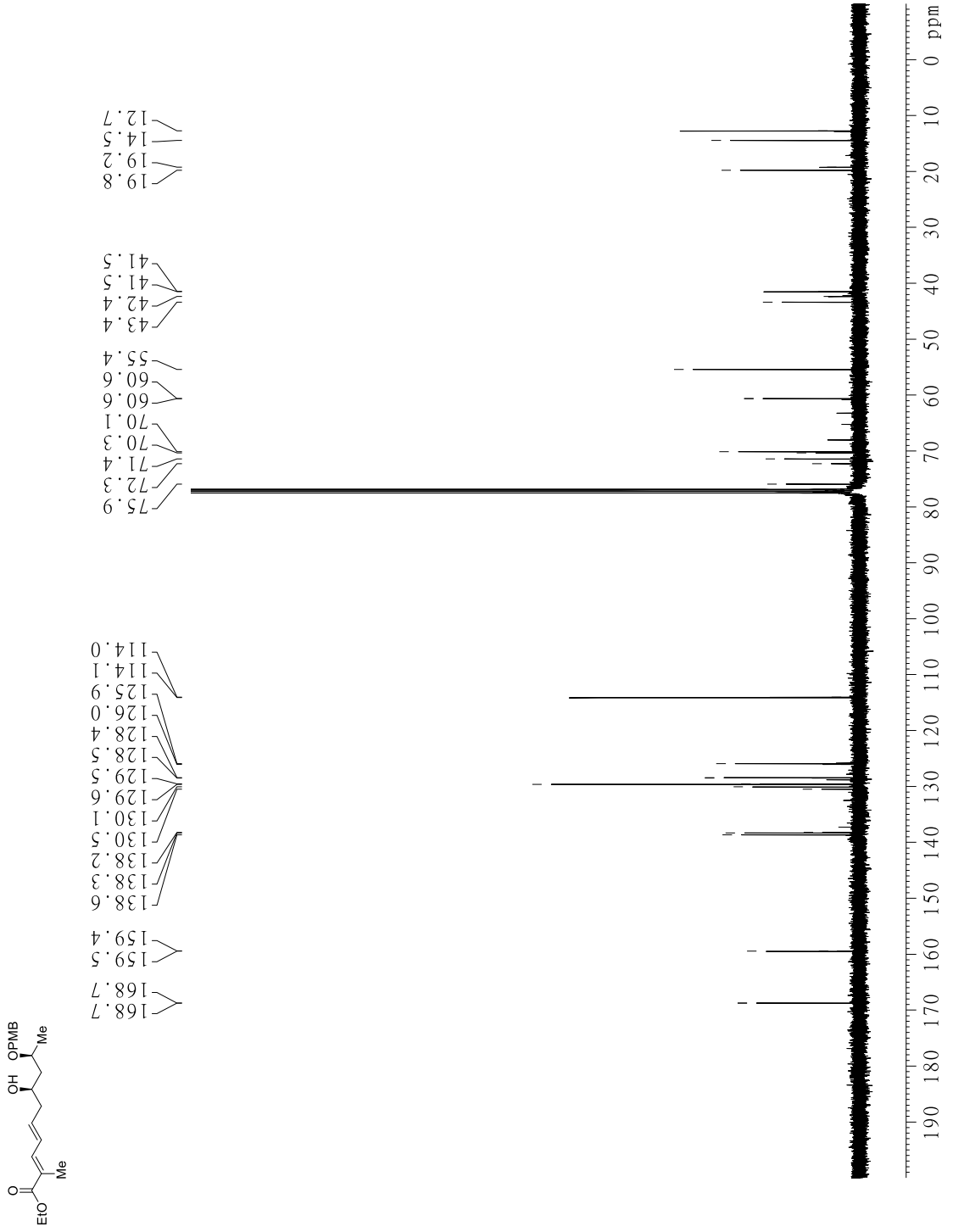
Spectrum 43. ^{13}C spectrum of **5s** measured in $CDCl_3$ at 101 MHz. **5s** was obtained as a mixture with its diastereomer **5r**.



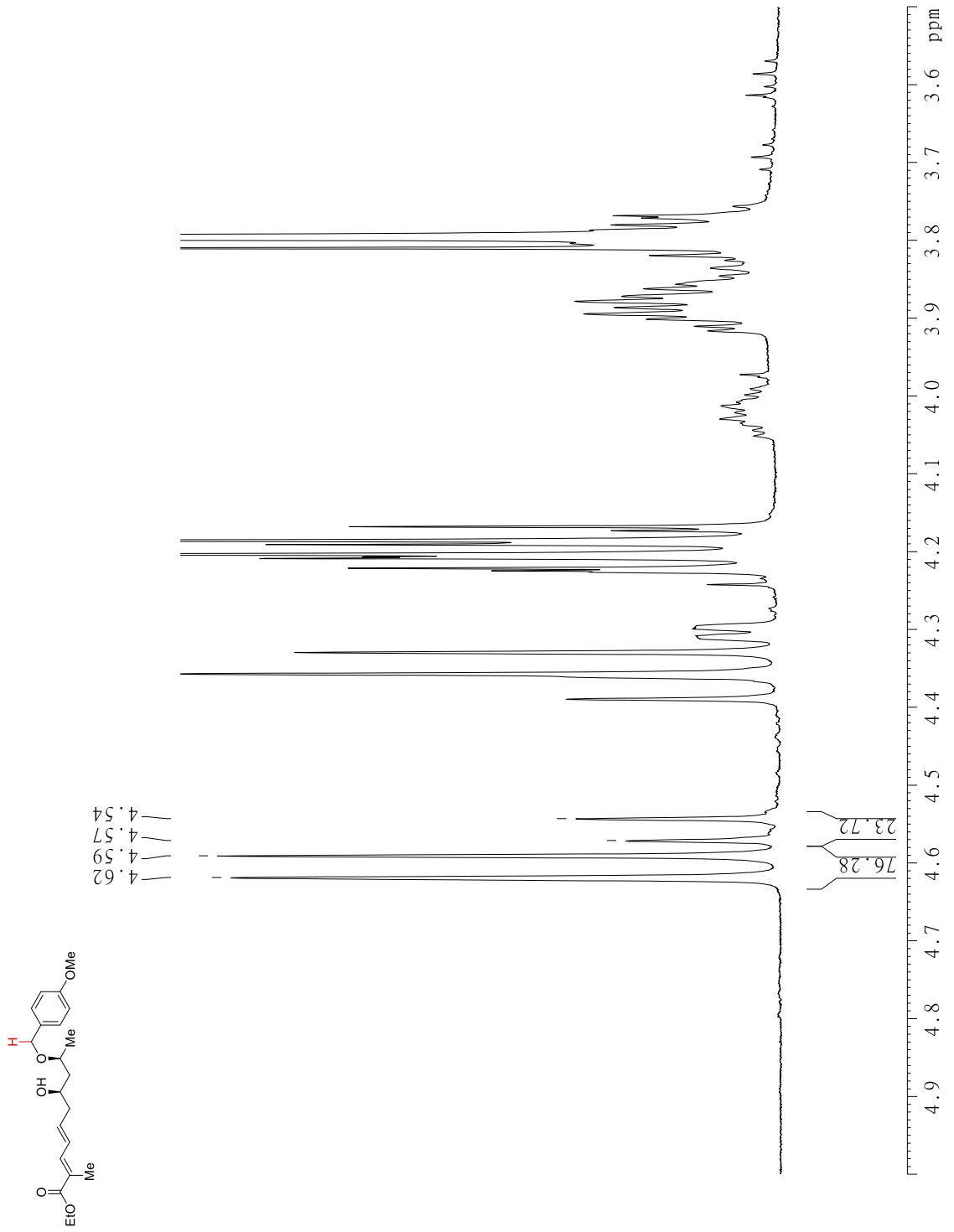
Spectrum 44. Enlarged view of the ^{1}H spectrum of **5s** for the determination of the diastereomeric ratio; the spectrum was measured in $CDCl_3$ at 600 MHz.



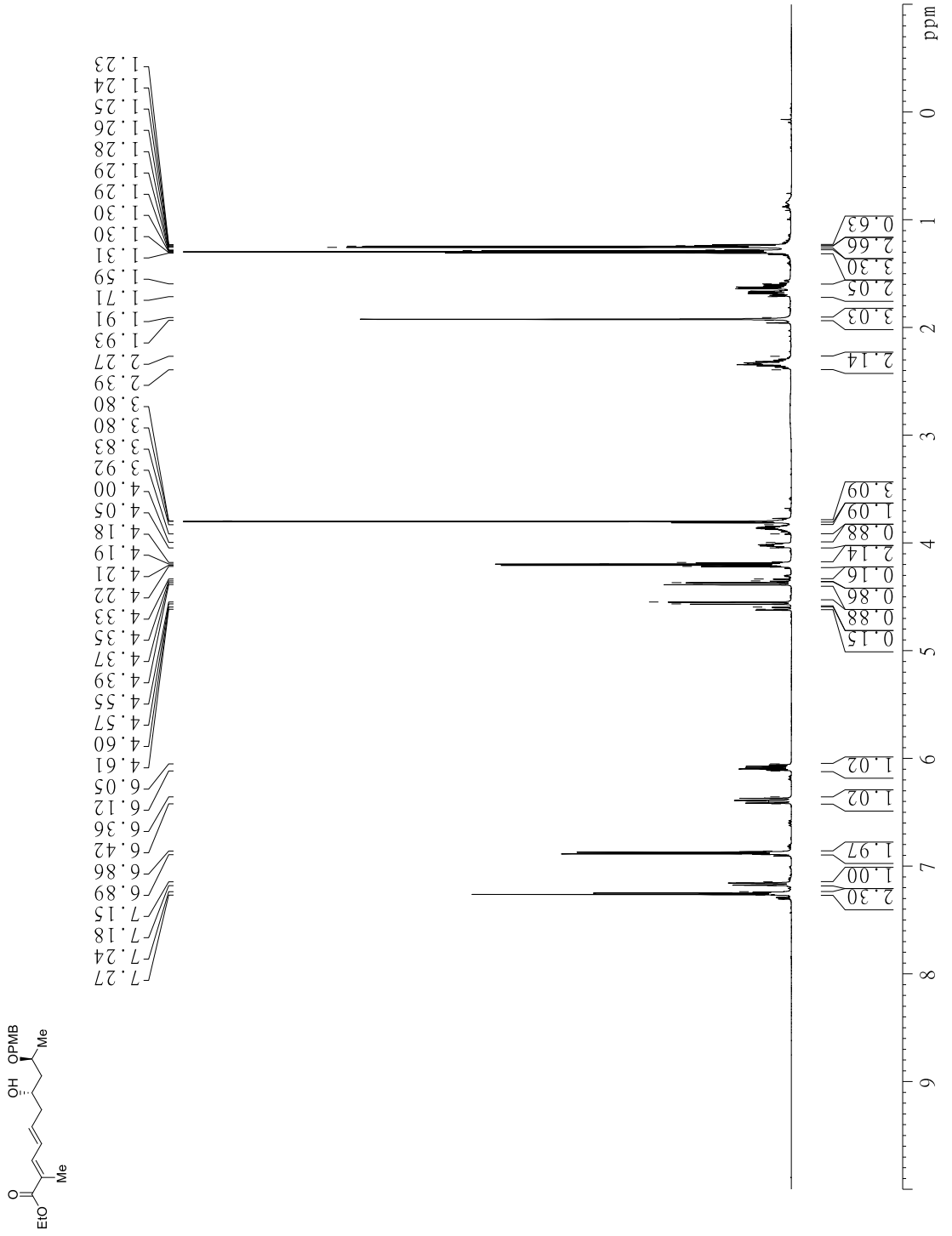
Spectrum 45. ^{1}H spectrum of **5t** measured in $CDCl_3$ at 400 MHz.



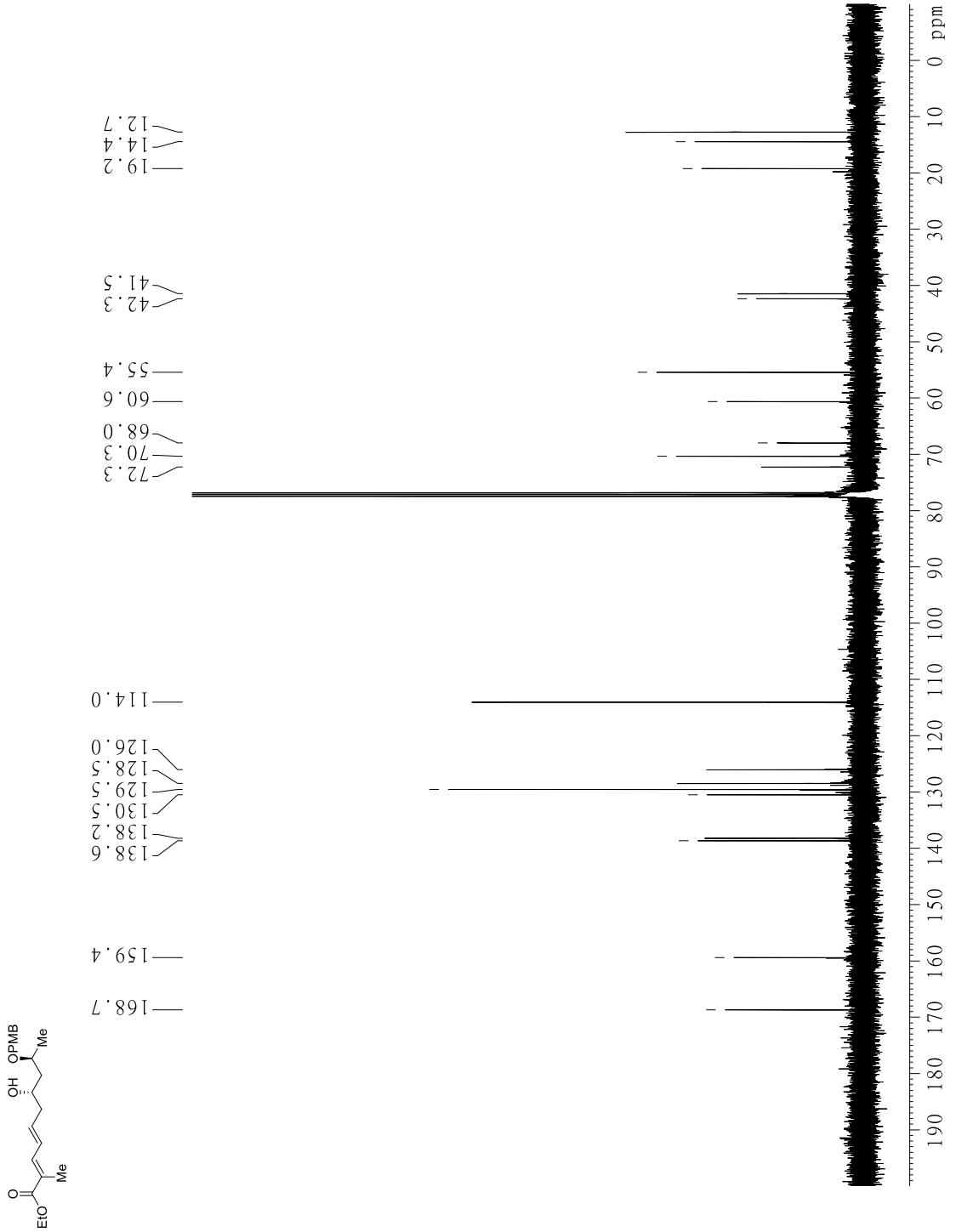
Spectrum 46. ^{13}C spectrum of **5t** measured in $CDCl_3$ at 101 MHz.



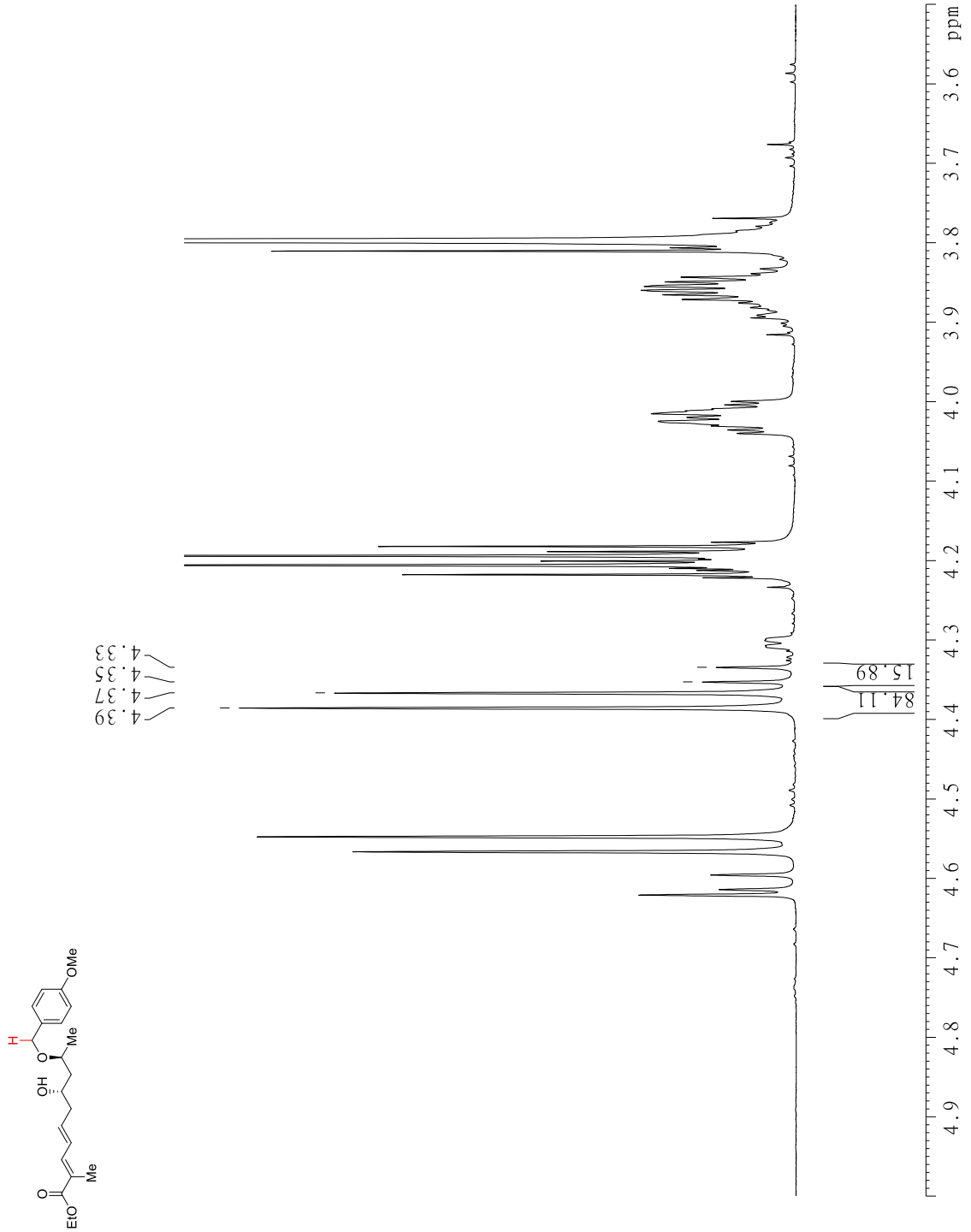
Spectrum 47. Enlarged view of the ^{1}H spectrum of **5t** for the determination of the diastereomeric ratio; the spectrum was measured in $CDCl_3$ at 400 MHz.



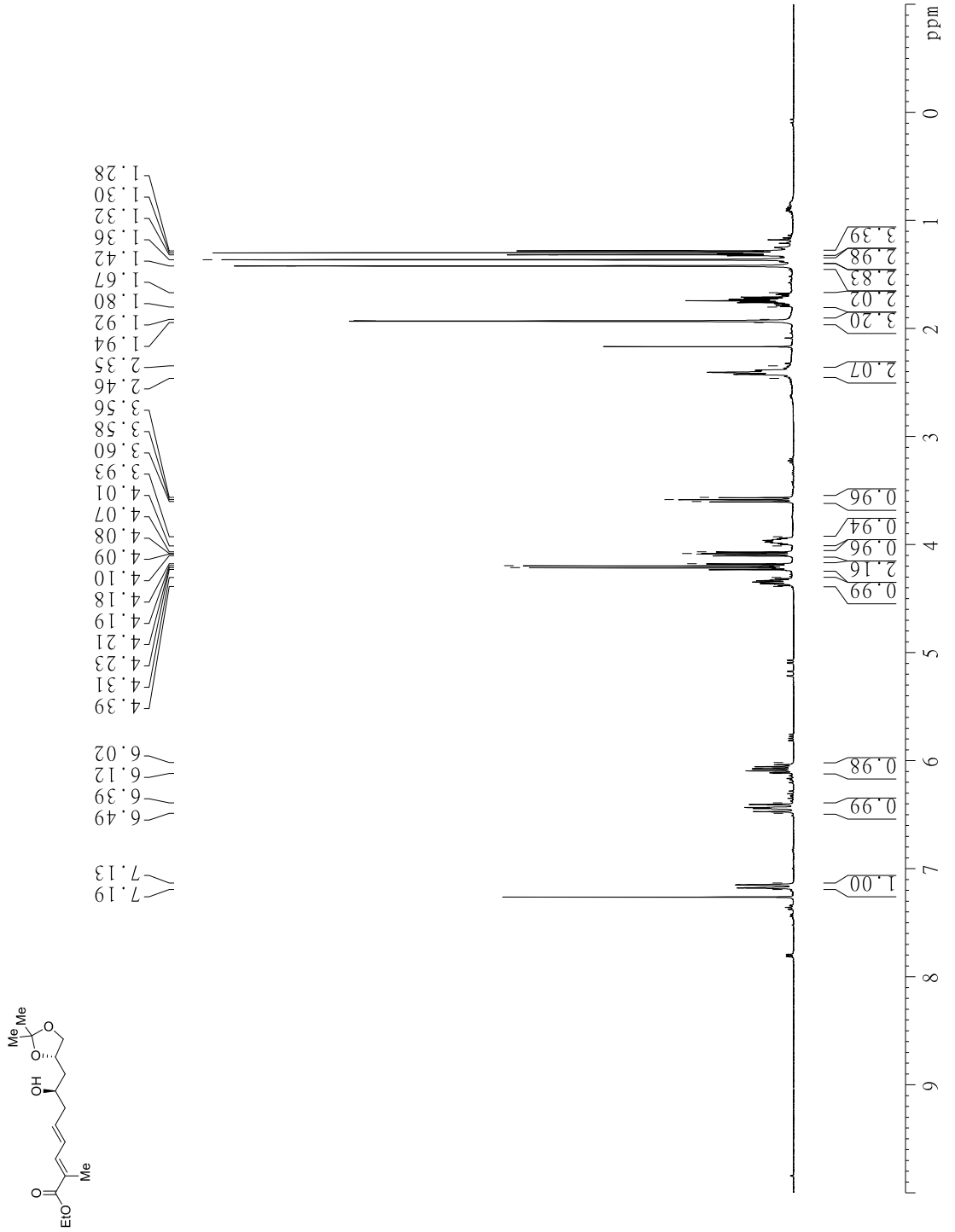
Spectrum 48. ^{1}H spectrum of **5u** measured in $CDCl_3$ at 600 MHz.



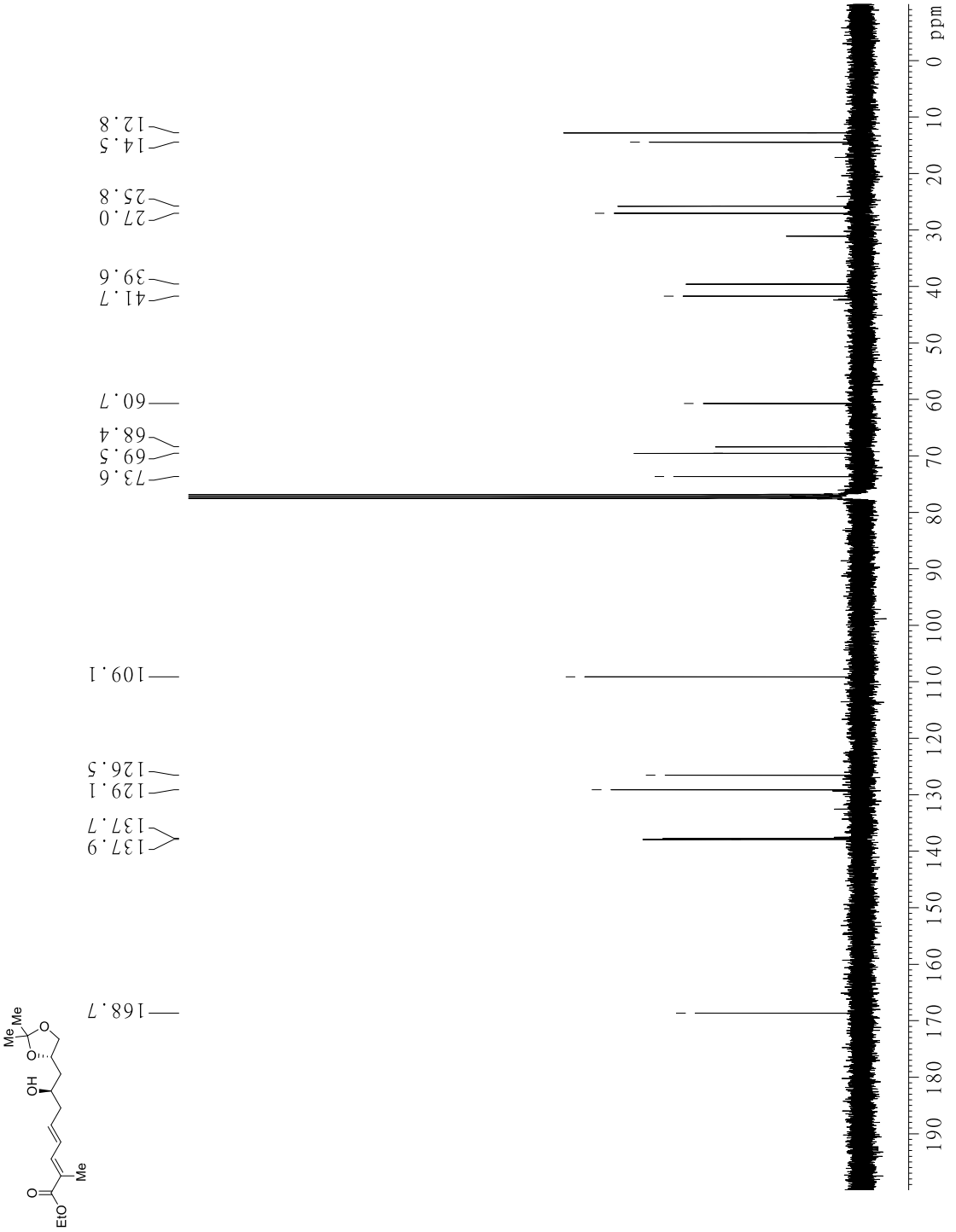
Spectrum 49. ^{13}C spectrum of **5u** measured in $CDCl_3$ at 101 MHz.



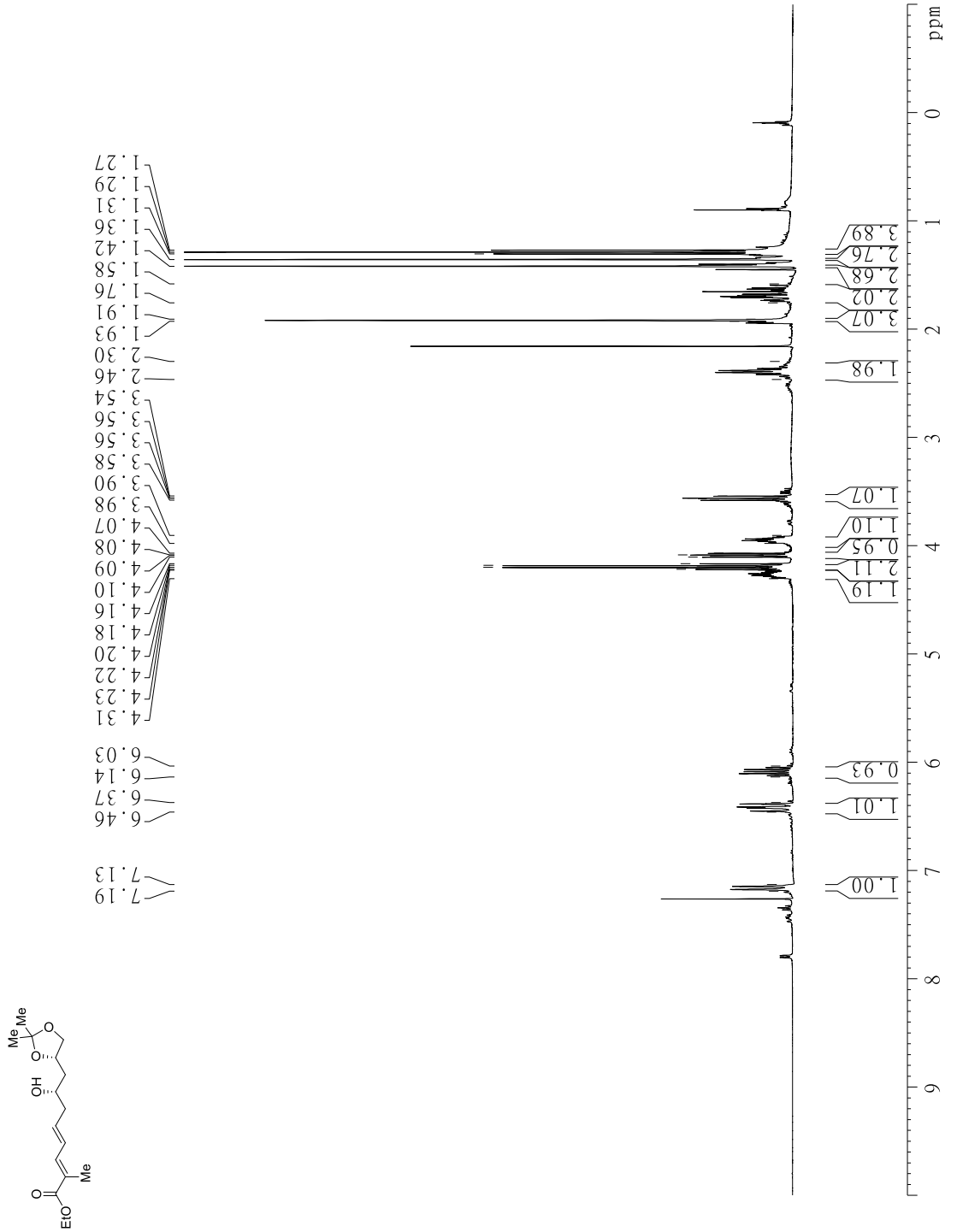
Spectrum 50. Enlarged view of the ^{1}H spectrum of **5u** for the determination of the diastereomeric ratio; the spectrum was measured in $CDCl_3$ at 600 MHz.



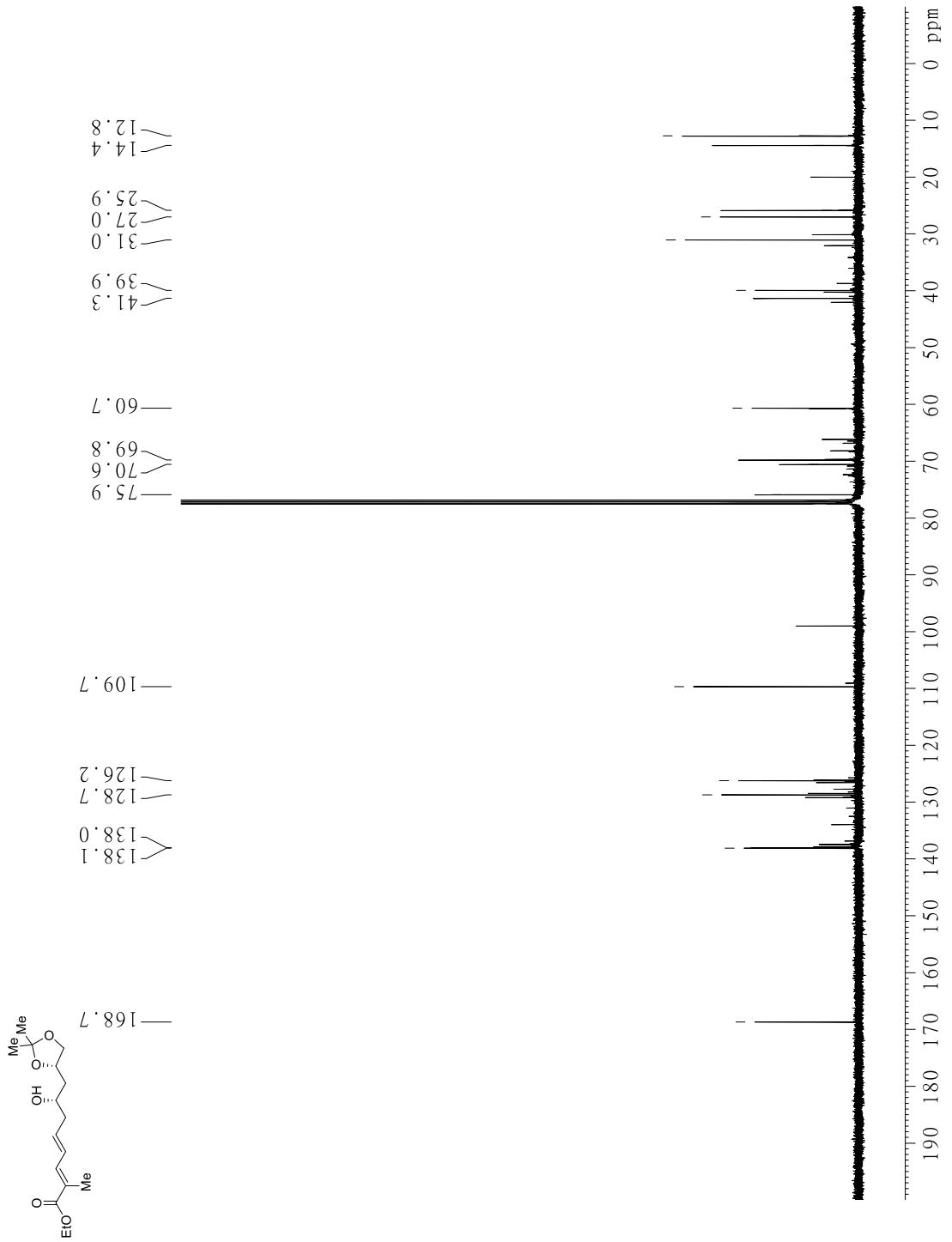
Spectrum 51. ^{1}H spectrum of **5v** measured in $CDCl_3$ at 400 MHz.



Spectrum 52. ^{13}C spectrum of **5v** measured in $CDCl_3$ at 101 MHz.

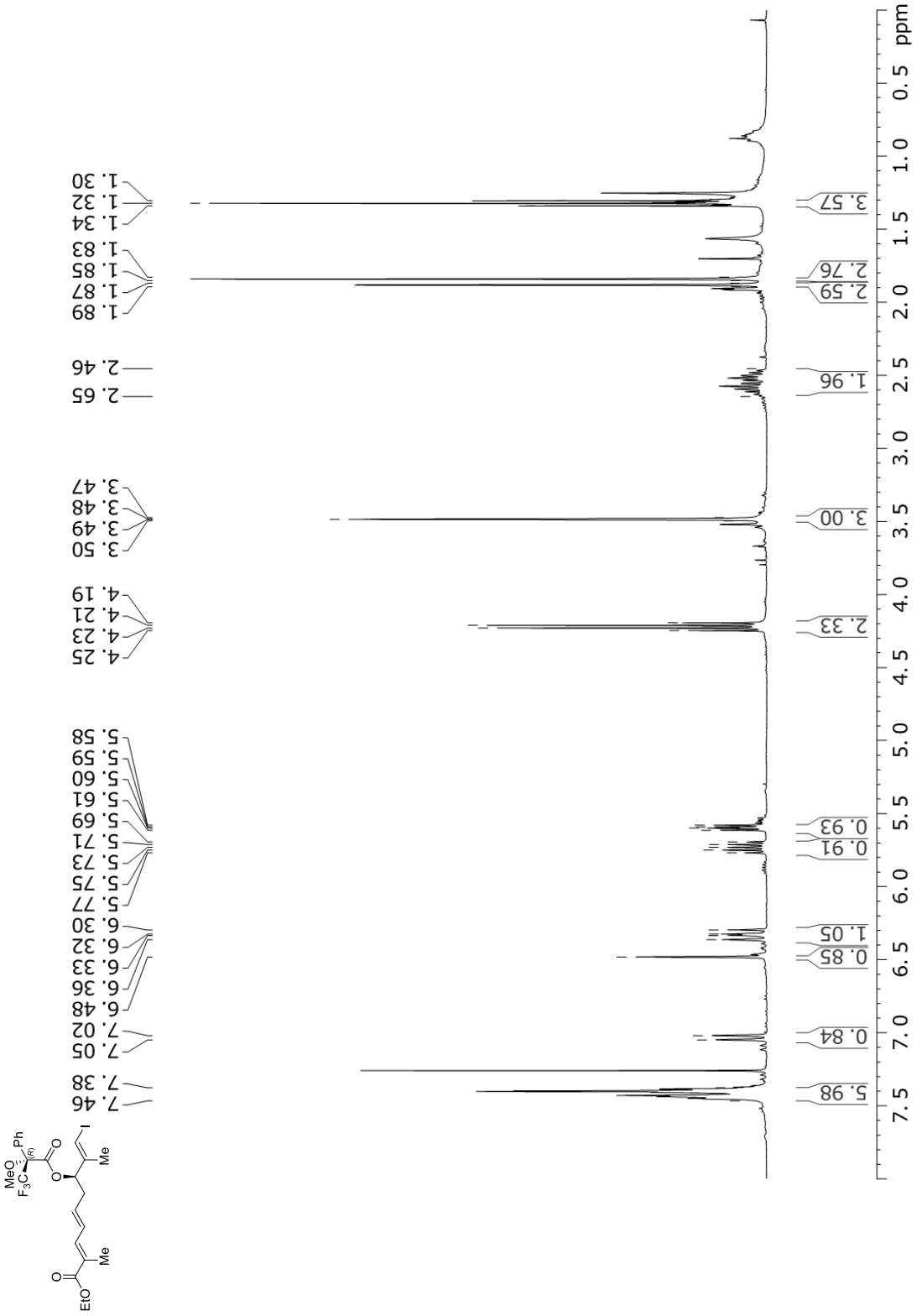


Spectrum 53. ^{1}H spectrum of **5w** measured in $CDCl_3$ at 400 MHz.

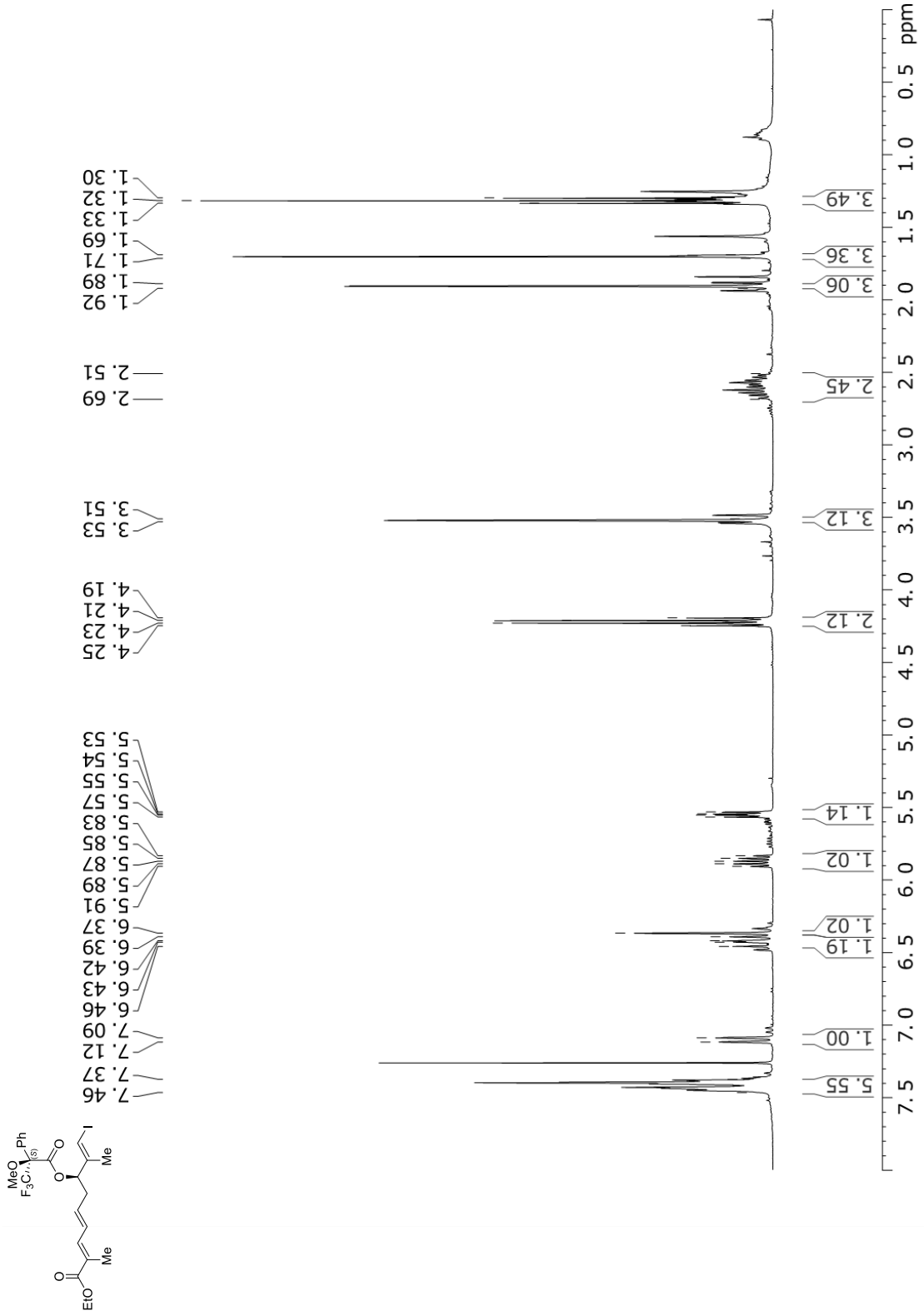


Spectrum 54. ^{13}C spectrum of **5w** measured in $CDCl_3$ at 101 MHz.

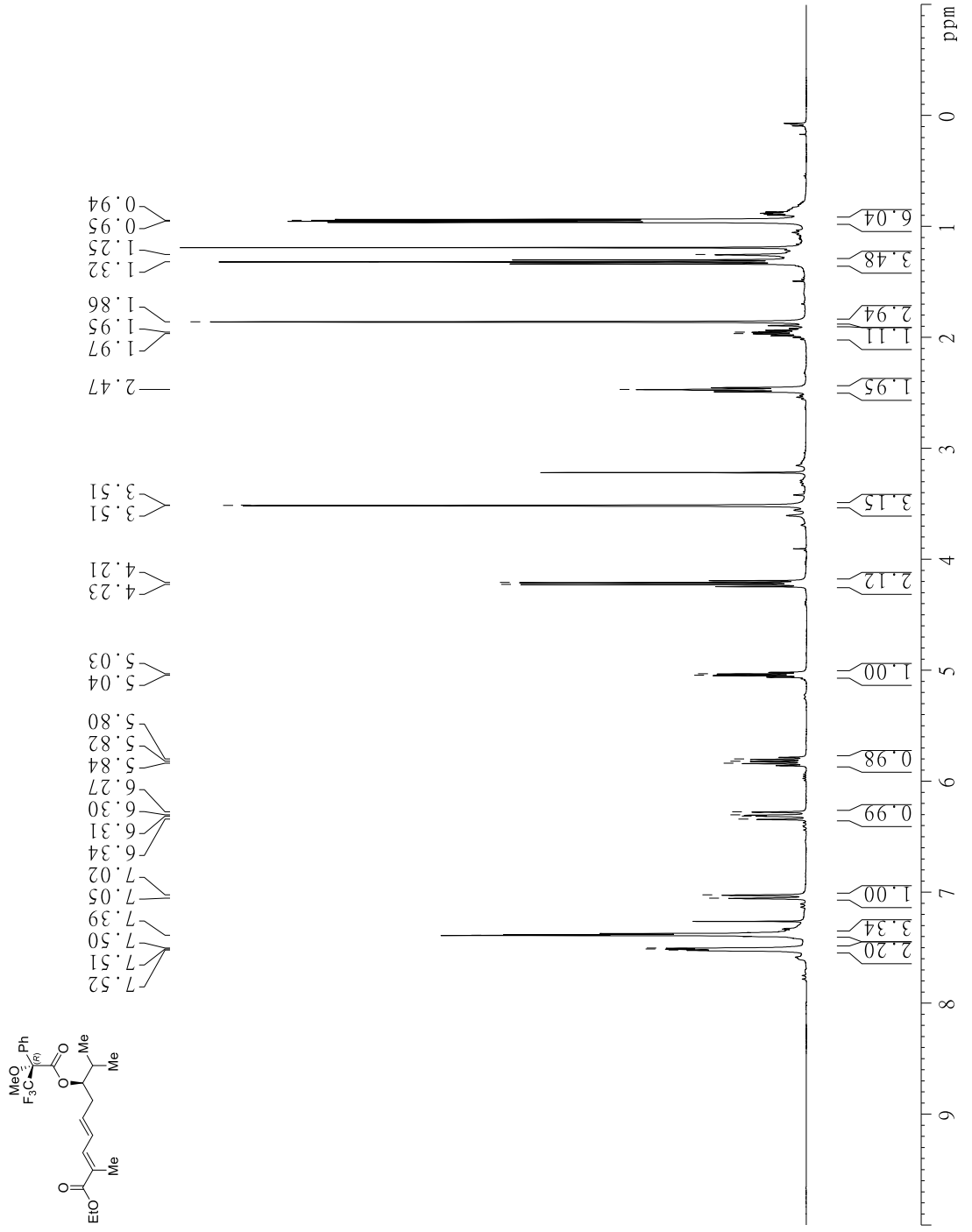
NMR spectra of the Mosher esters for determination of the absolute configuration



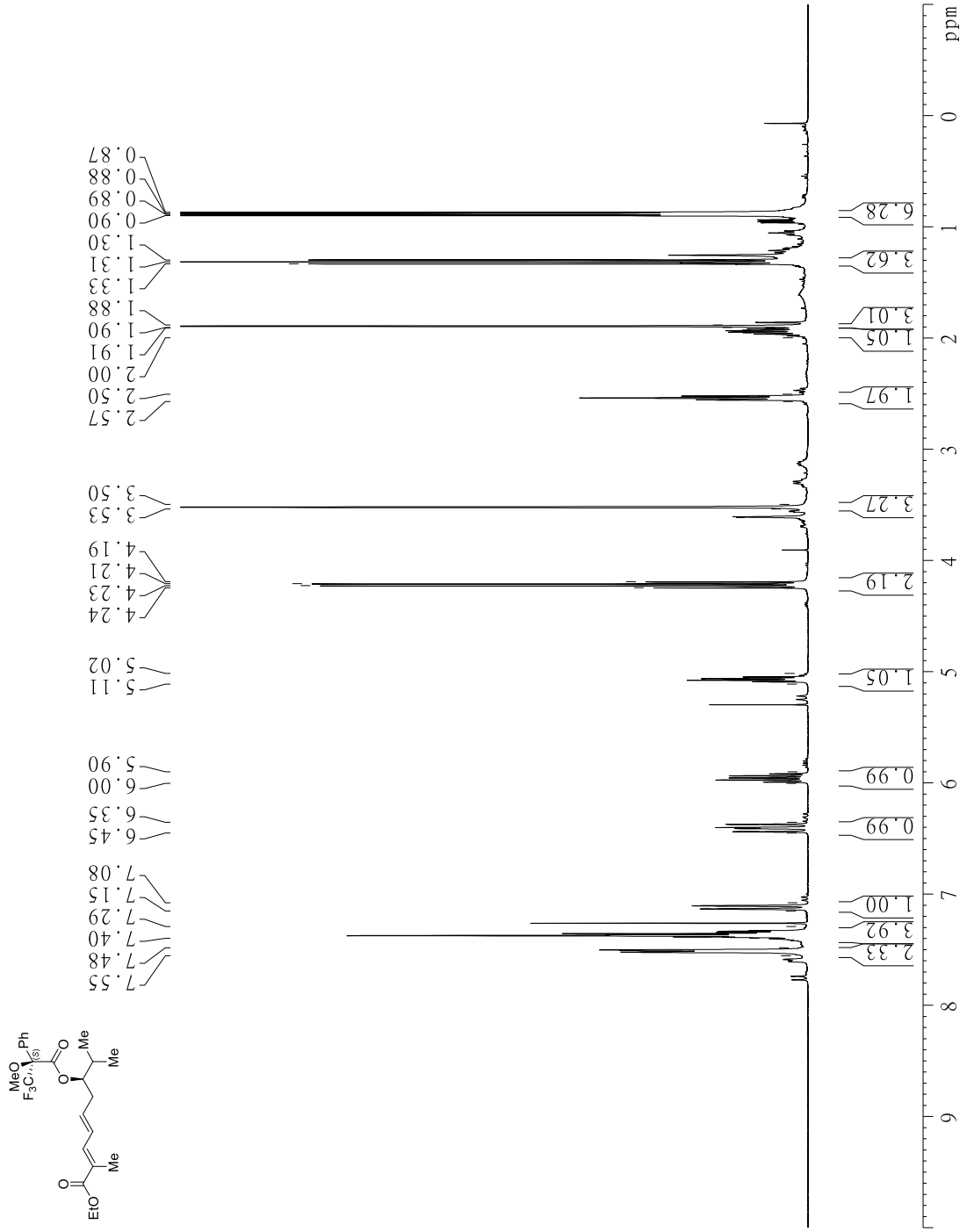
Spectrum 55. ^{1}H spectrum of the (*R*)-Mosher's ester of bVMAR product **5g** measured in $CDCl_3$ at 400 MHz.



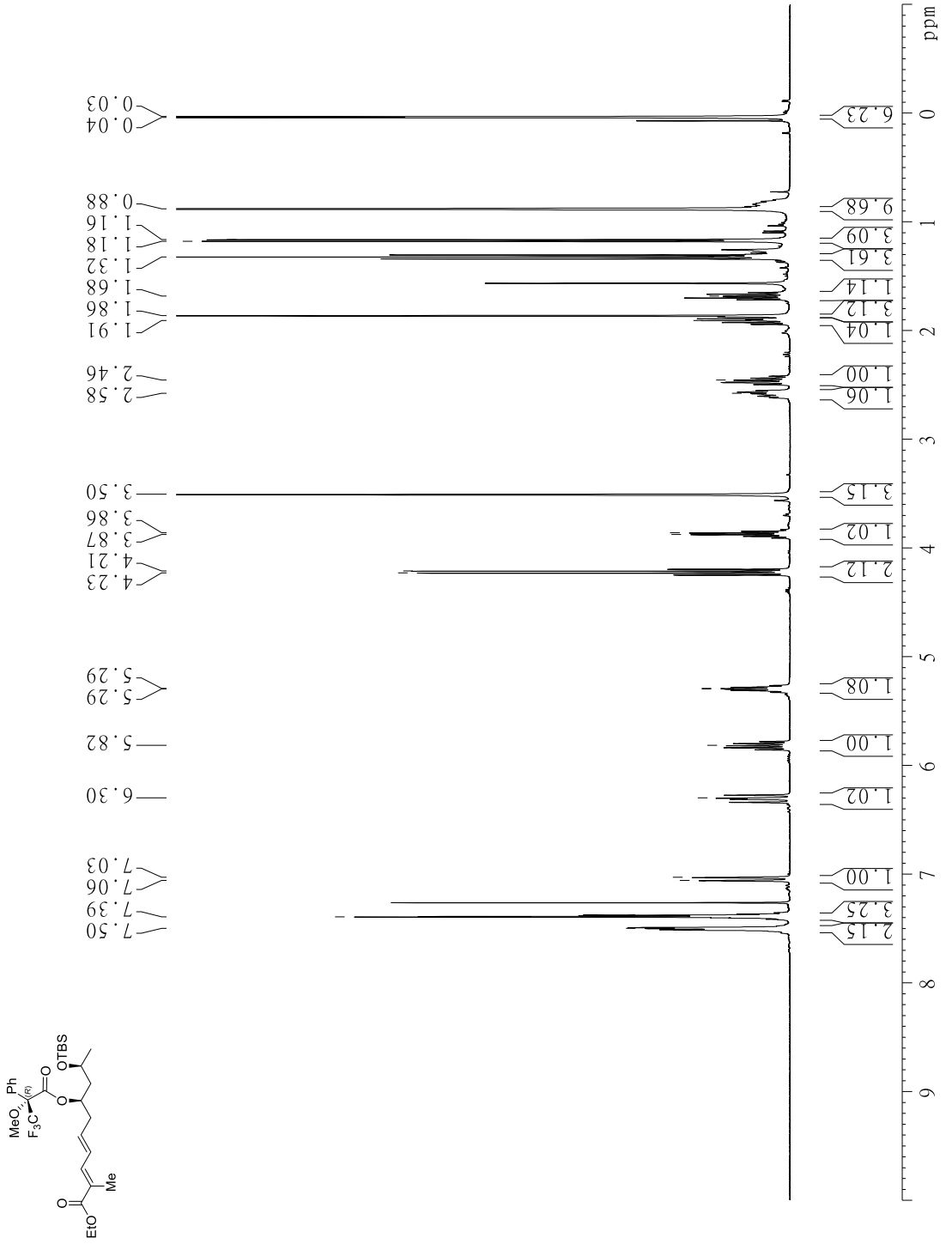
Spectrum 56. [1]H spectrum of the (*S*)-Mosher's ester of bVMAR product **5g** measured in $CDCl_3$ at 400 MHz.



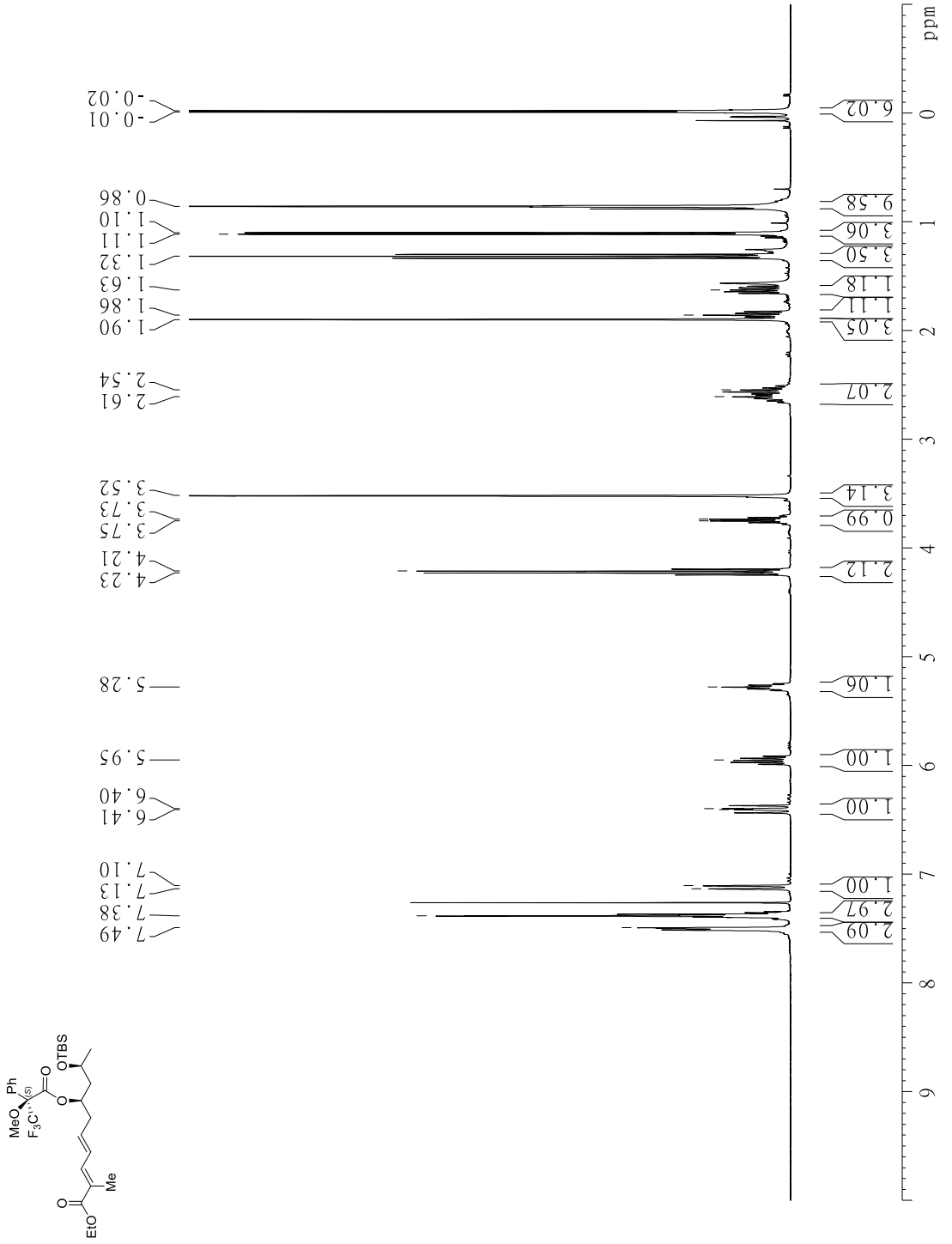
Spectrum 57. ^{1}H spectrum of the (*R*)-Mosher's ester of bVMAR product **5k** measured in $CDCl_3$ at 400 MHz.



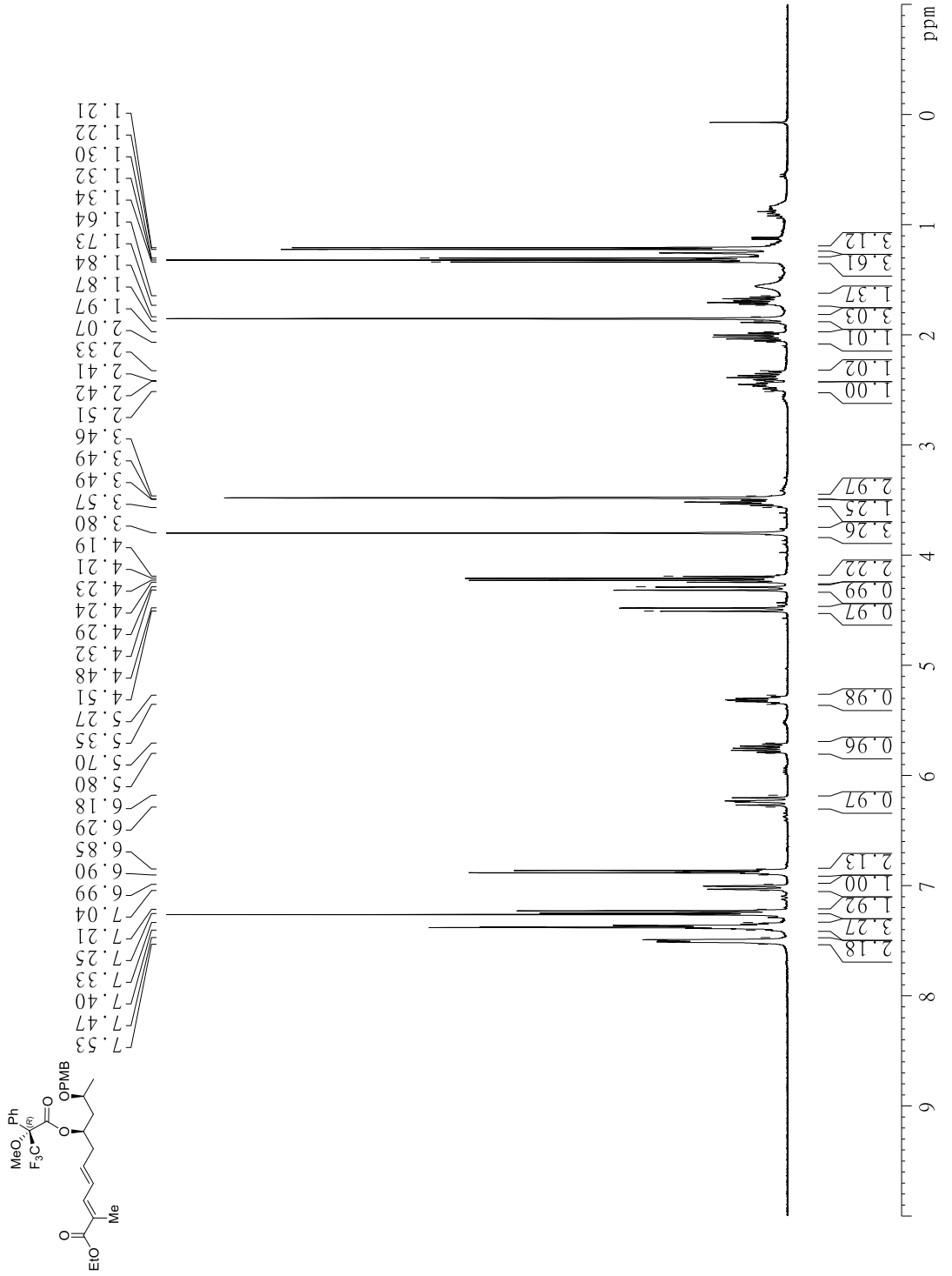
Spectrum 58. [1]H spectrum of the (*S*)-Mosher's ester of bVMAR product **5k** measured in $CDCl_3$ at 400 MHz.



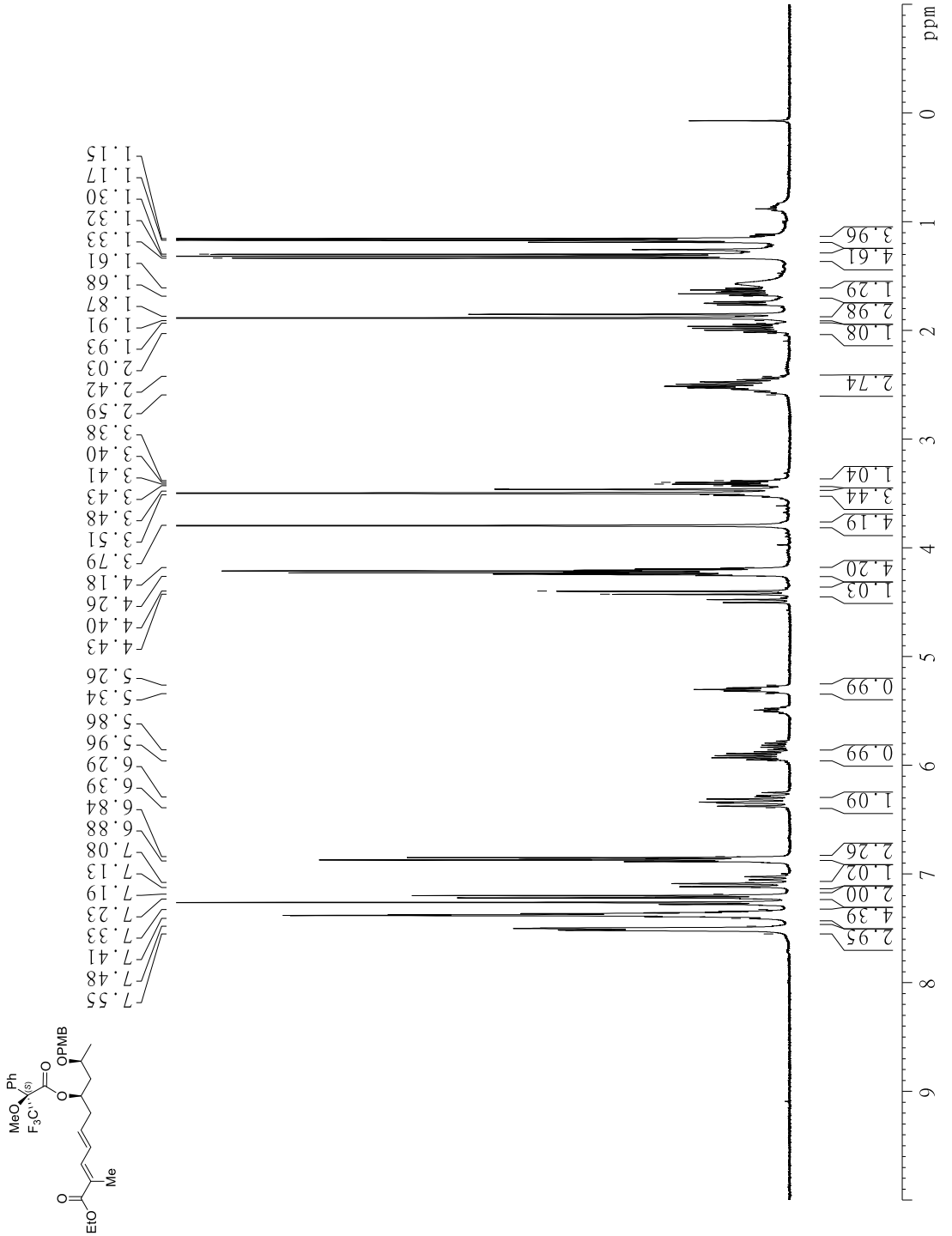
Spectrum 59. ^{1}H spectrum of the (*R*)-Mosher's ester of bVMAR product **5r** measured in $CDCl_3$ at 400 MHz.



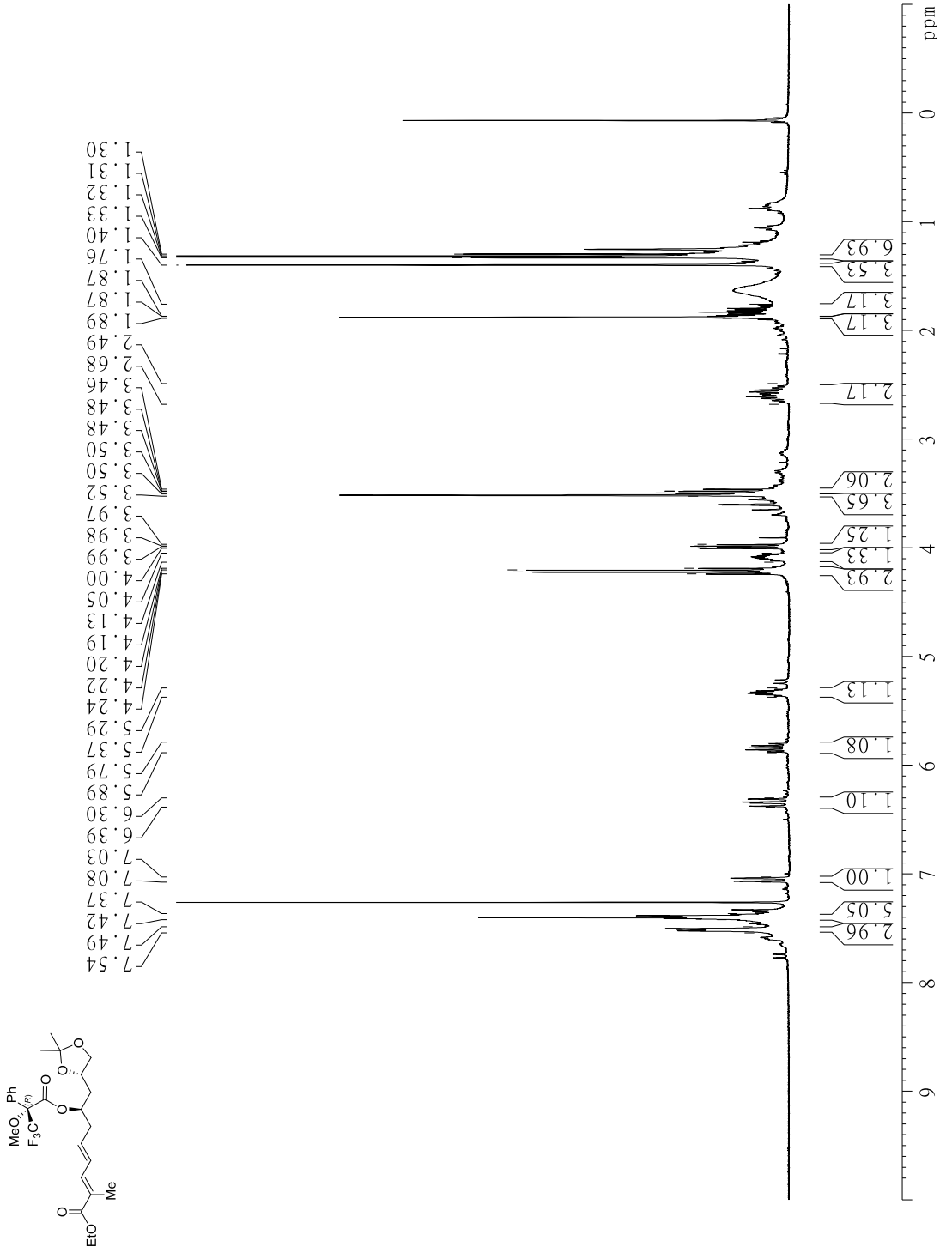
Spectrum 60. [1]H spectrum of the (*S*)-Mosher's ester of bVMAR product **5r** measured in $CDCl_3$ at 400 MHz.



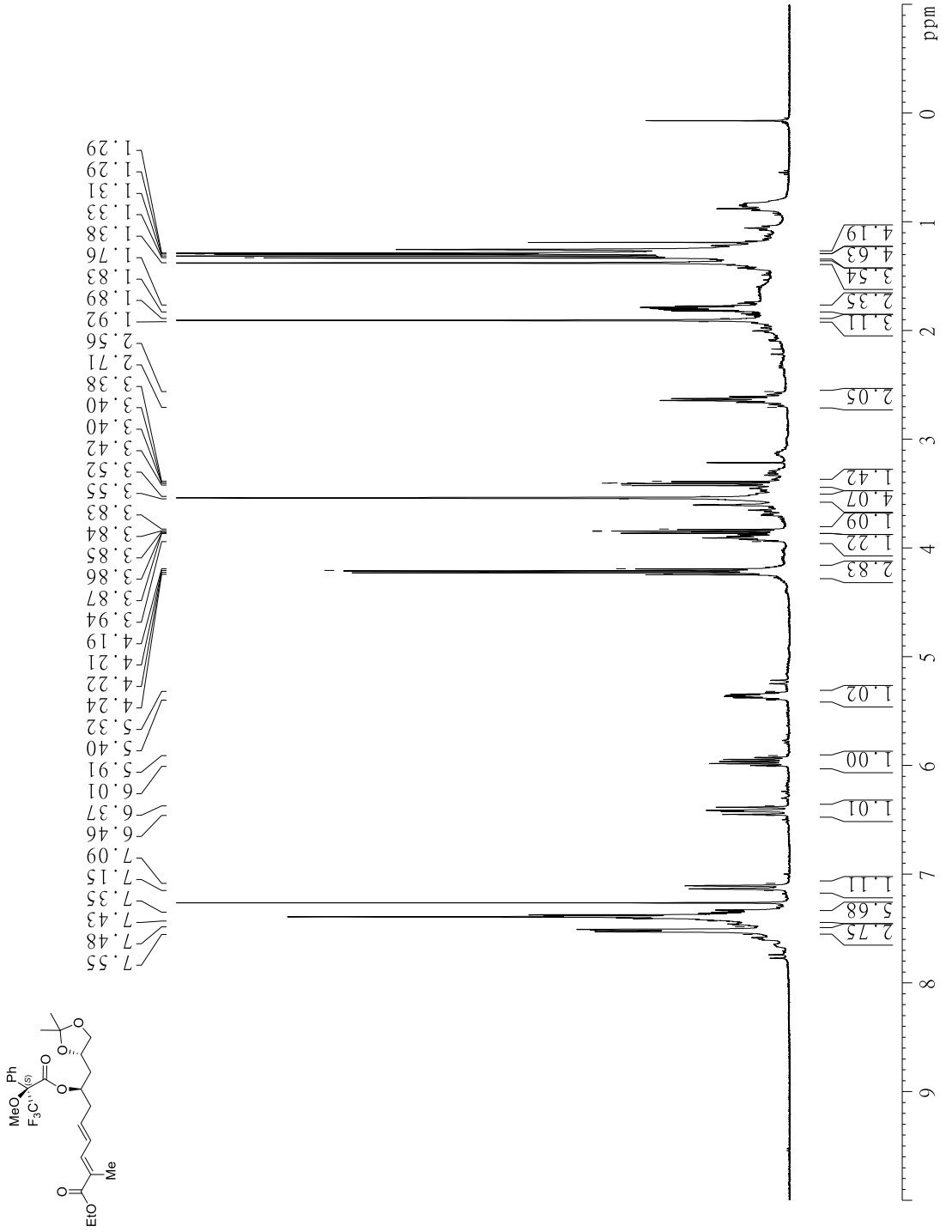
Spectrum 61. [1]H spectrum of the (*R*)-Mosher's ester of bVMAR product **5t** measured in $CDCl_3$ at 400 MHz.



Spectrum 62. [1]H spectrum of the (*S*)-Mosher's ester of bVMAR product **5t** measured in $CDCl_3$ at 400 MHz.

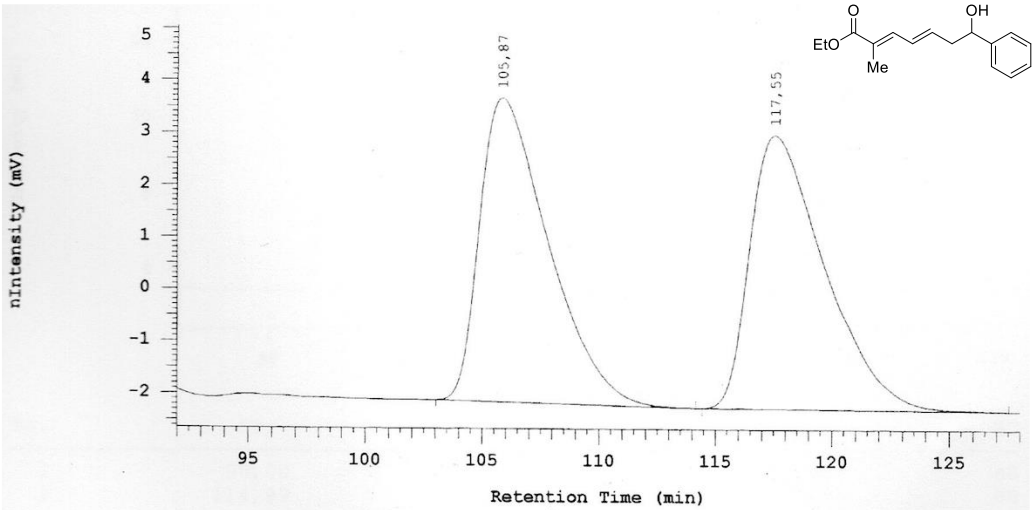


Spectrum 63. [1]H spectrum of the (*R*)-Mosher's ester of bVMAR product **5v** measured in $CDCl_3$ at 400 MHz.



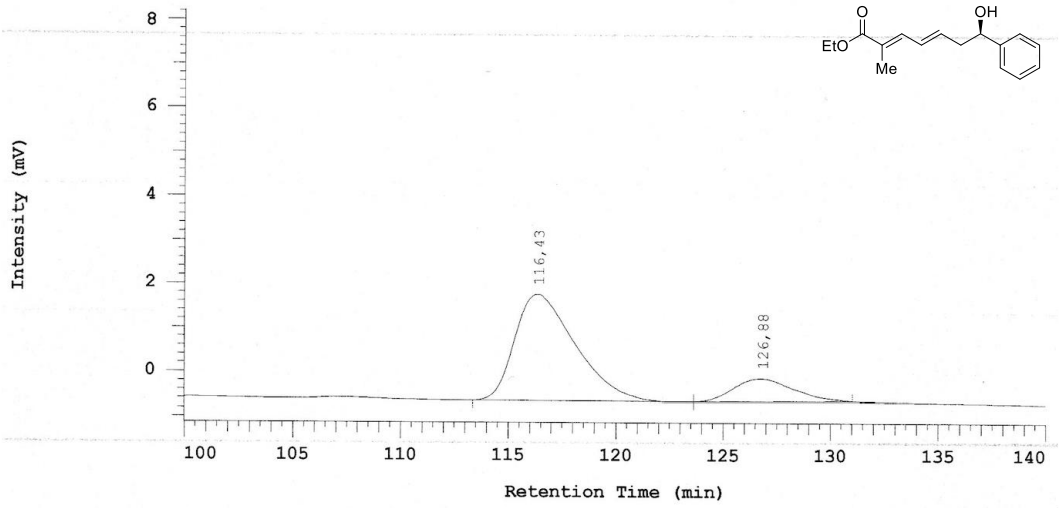
Spectrum 64. [1]H spectrum of the (*S*)-Mosher's ester of bVMAR product **5v** measured in $CDCl_3$ at 400 MHz.

***ee*-determination – part 1: chiral HPLC**



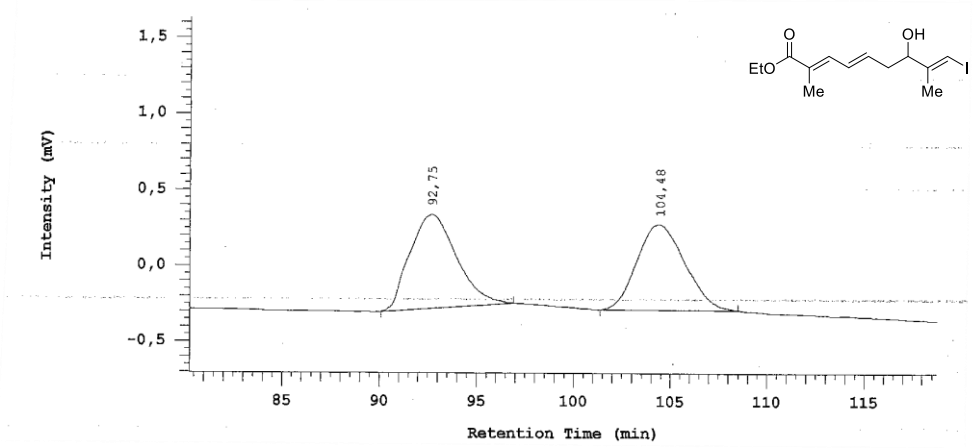
No.	RT	Area	Conc 1	BC
1	105,87	1189636	50,442	BB
2	117,55	1168780	49,558	BB
		2358416	100,000	

Chromatogram 1. Racemic sample of bVMAR product **5a.**



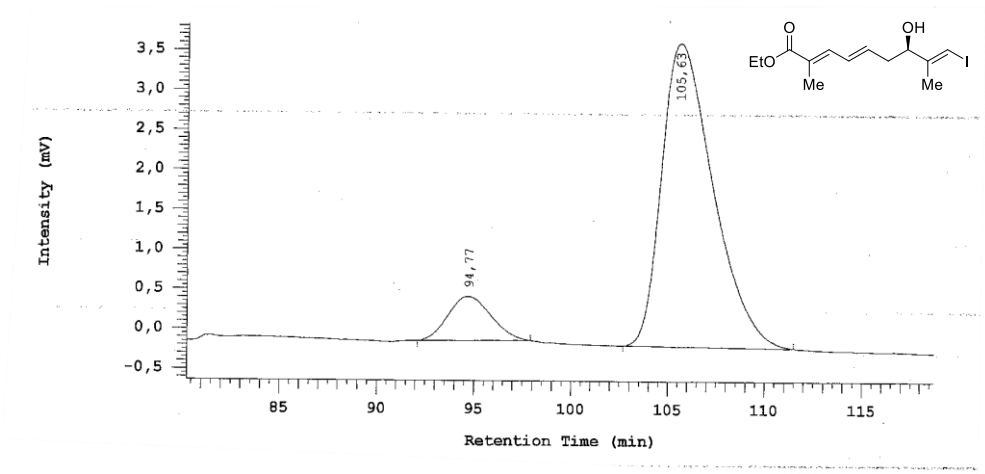
No.	RT	Area	Conc 1	BC
1	116,43	471902	82,180	BB
2	126,88	102331	17,820	BB
		574233	100,000	

Chromatogram 2. Enantiomerically enriched sample of bVMAR product **5a**.



No.	RT	Area	Conc 1	BC
1	92,75	103284	51,262	MC
2	104,48	98200	48,738	MC
		201484	100,000	

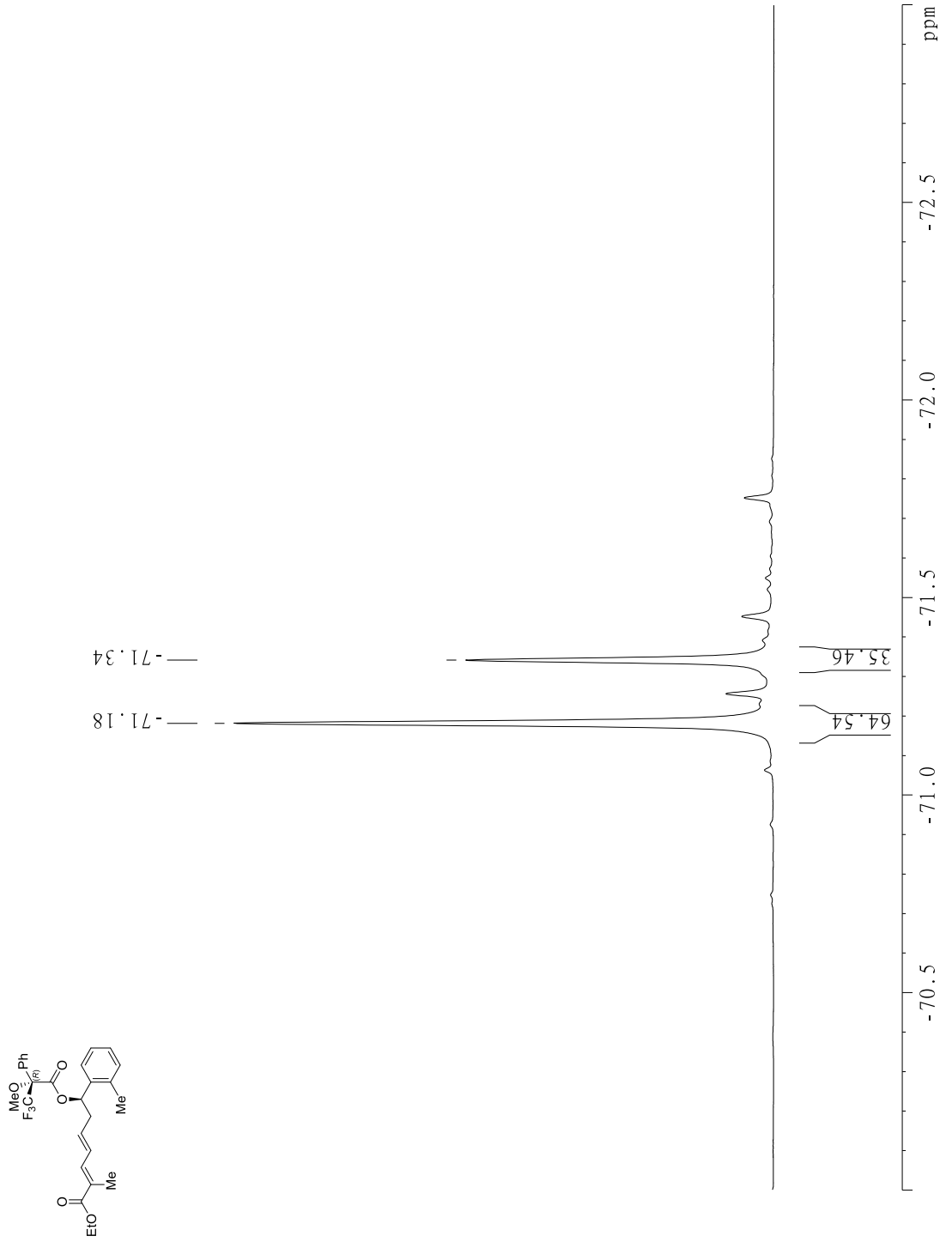
Chromatogram 3. Racemic sample of bVMAR product **5g**.



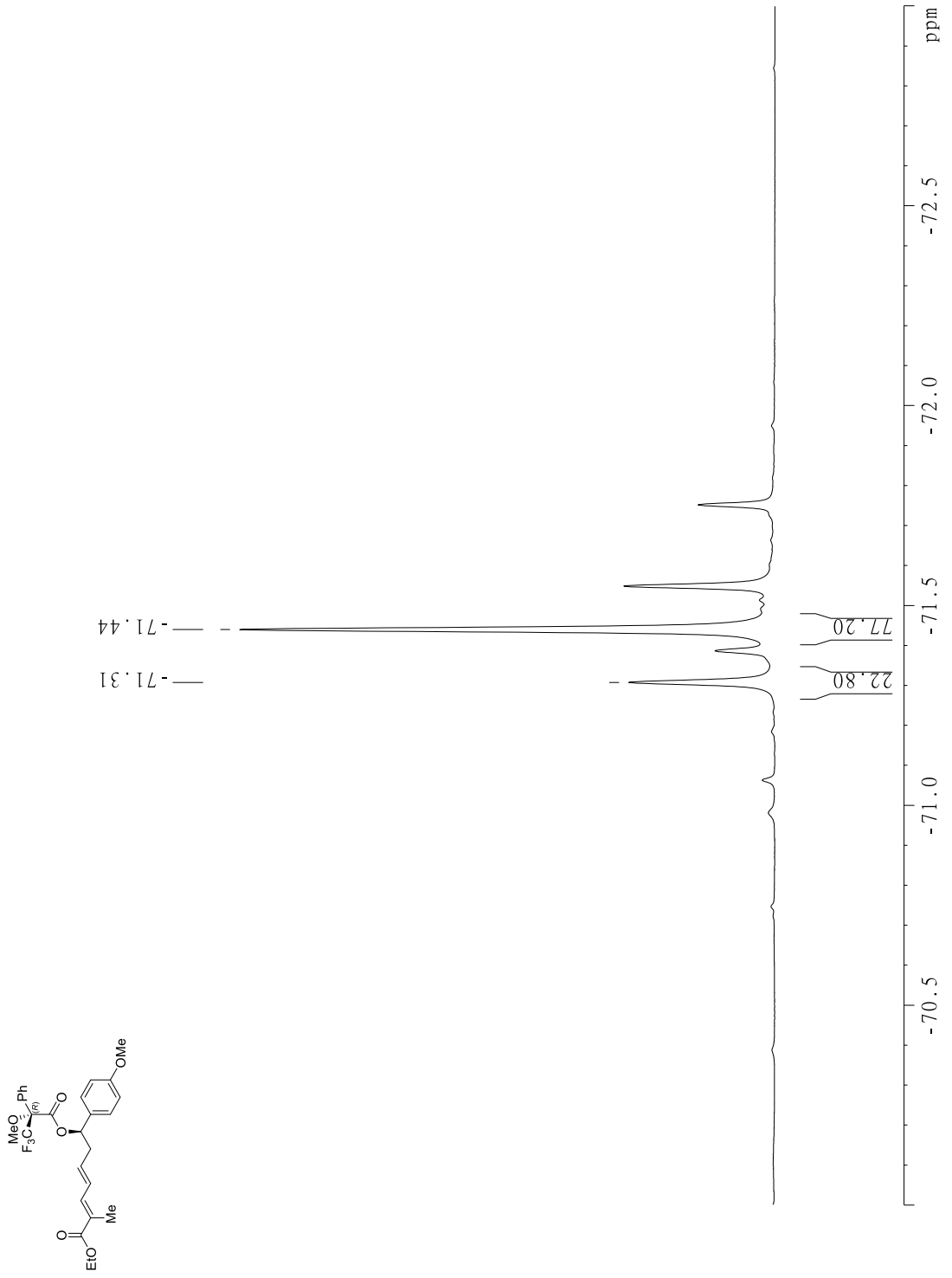
No.	RT	Area	Conc 1	BC
1	94,77	84928	10,670	MC
2	105,63	710995	89,330	BB
		795923	100,000	

Chromatogram 4. Enantiomerically enriched sample of bVMAR product **5g**.

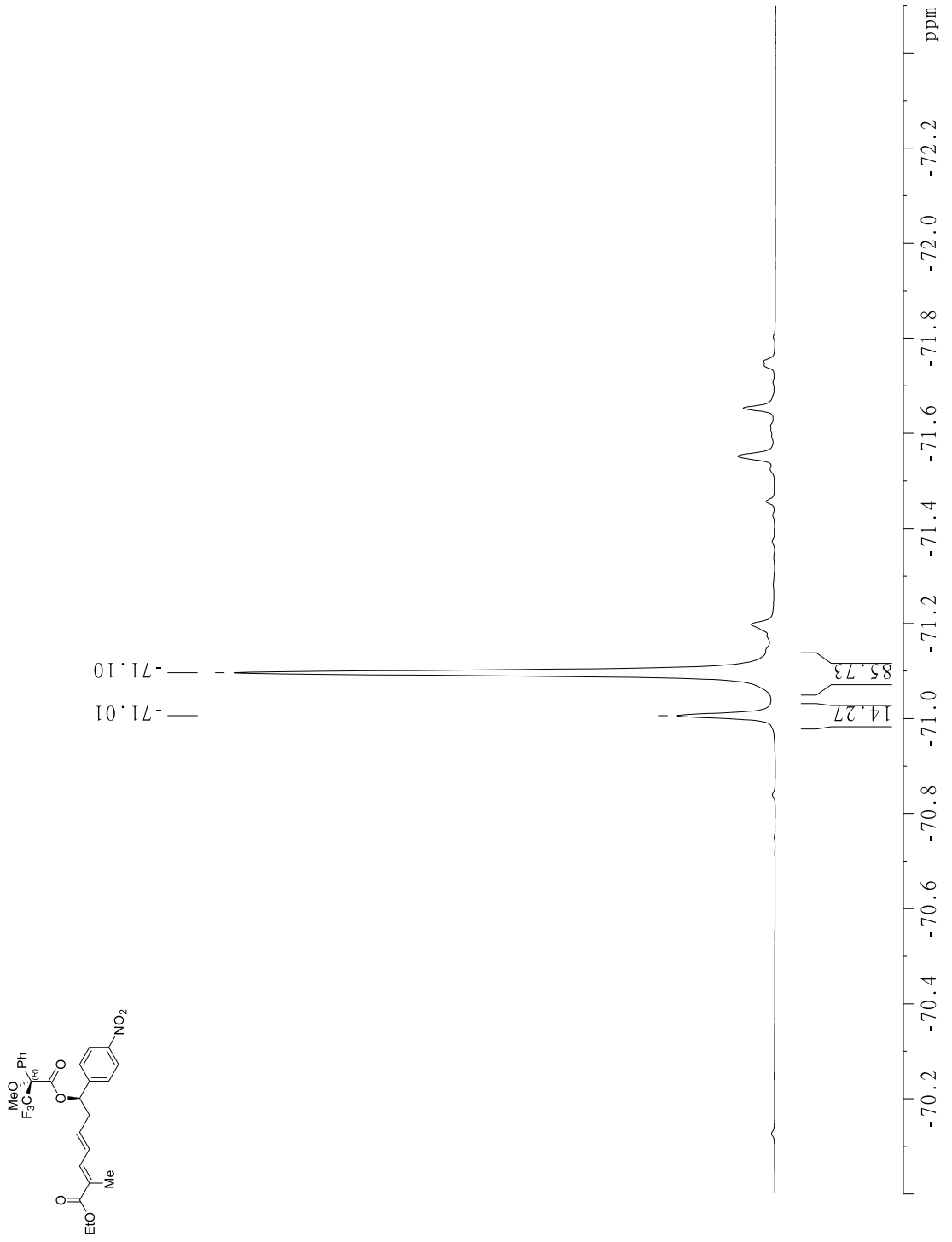
***ee*-determination – part 2: ^{19}F-NMR-data of the corresponding MTPAtes**



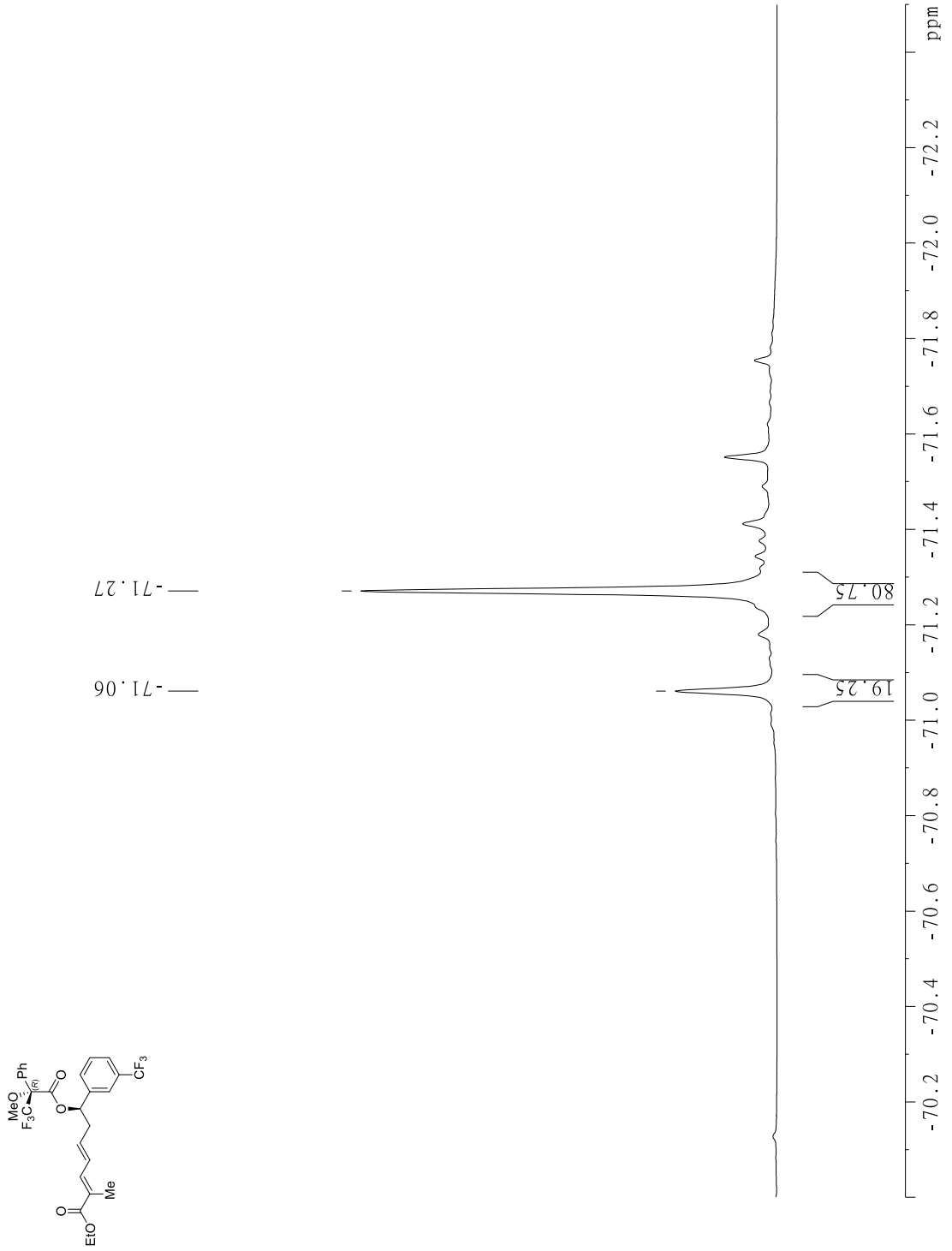
Spectrum 65. ^{19}F spectrum of the (*R*)-Mosher ester of **5b** measured in $CDCl_3$ at 376 MHz.



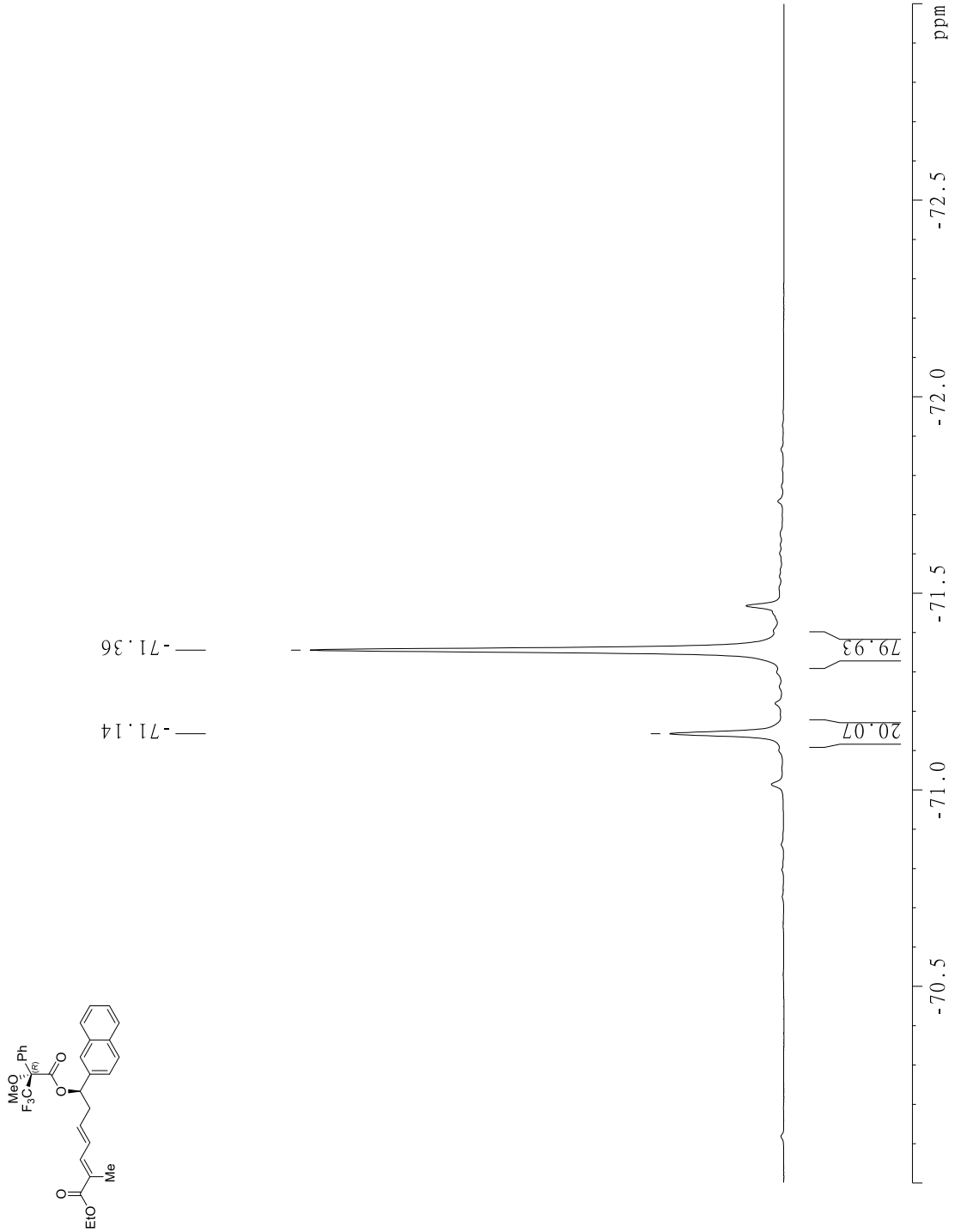
Spectrum 66. ^{19}F spectrum of the (*R*)-Mosher ester of **5c** measured in $CDCl_3$ at 376 MHz.



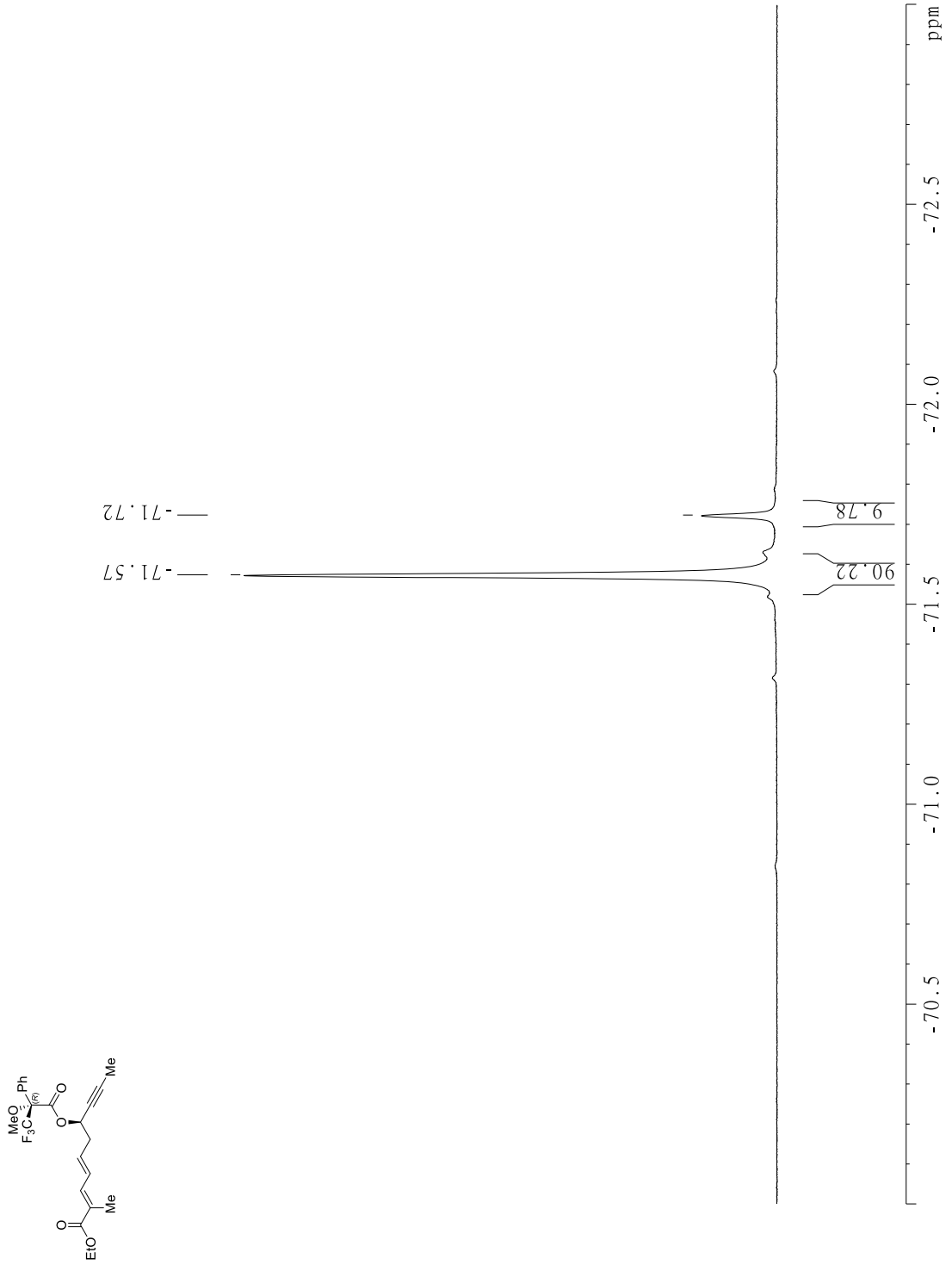
Spectrum 67. ^{19}F spectrum of the (*R*)-Mosher ester of **5d** measured in $CDCl_3$ at 376 MHz.



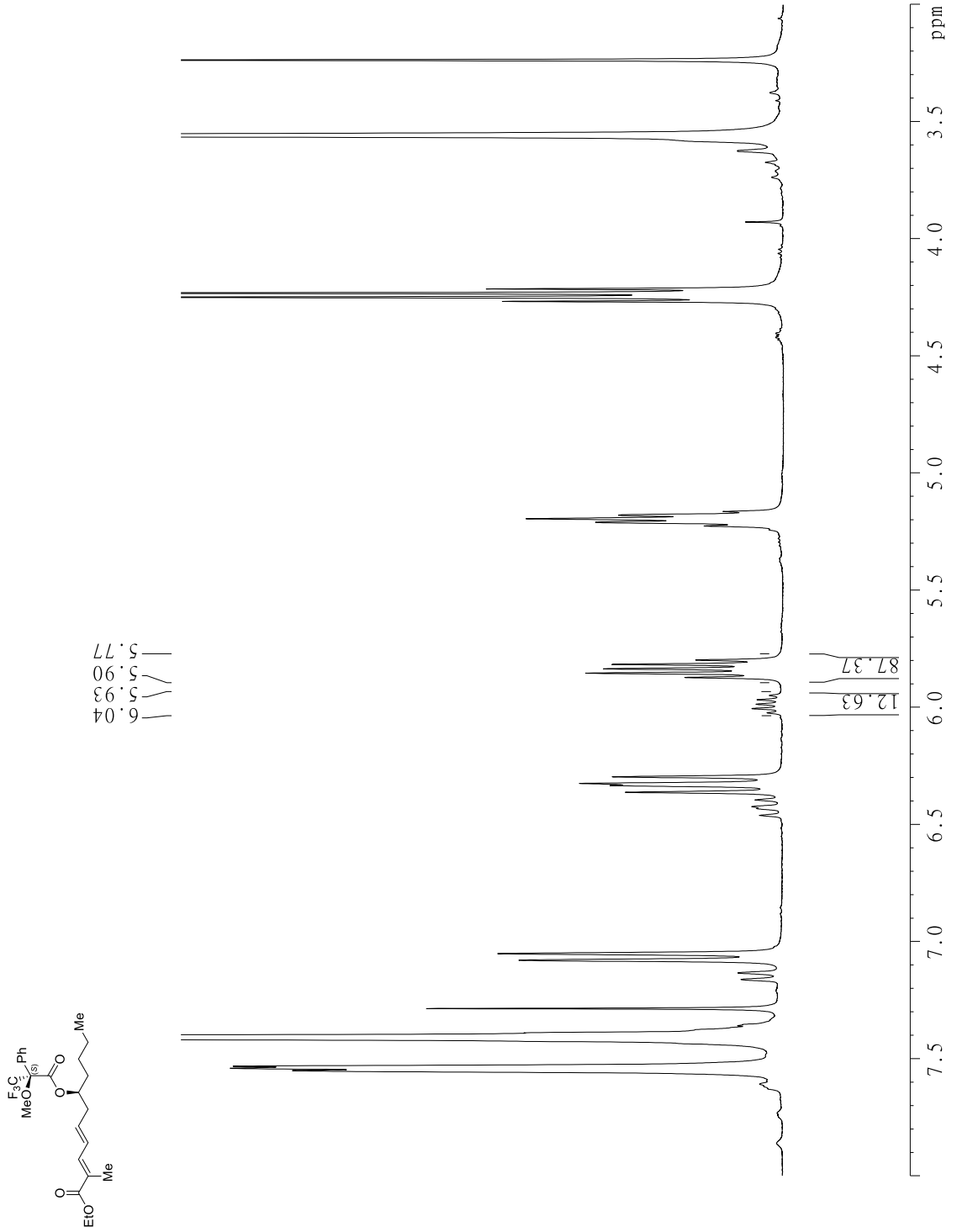
Spectrum 68. ^{19}F spectrum of the (*R*)-Mosher ester of **5e** measured in $CDCl_3$ at 376 MHz.



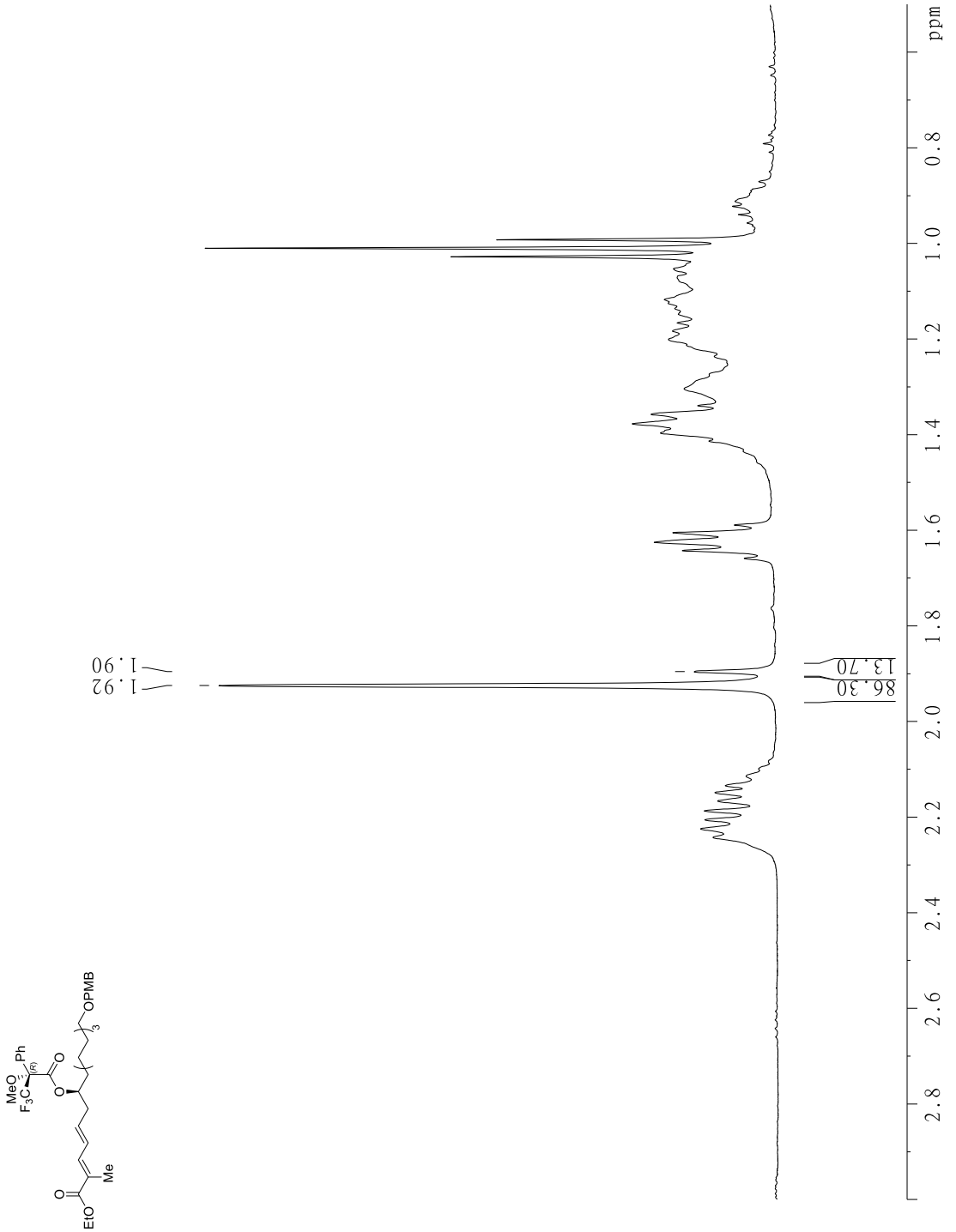
Spectrum 69. ^{19}F spectrum of the (*R*)-Mosher ester of **5f** measured in $CDCl_3$ at 376 MHz.



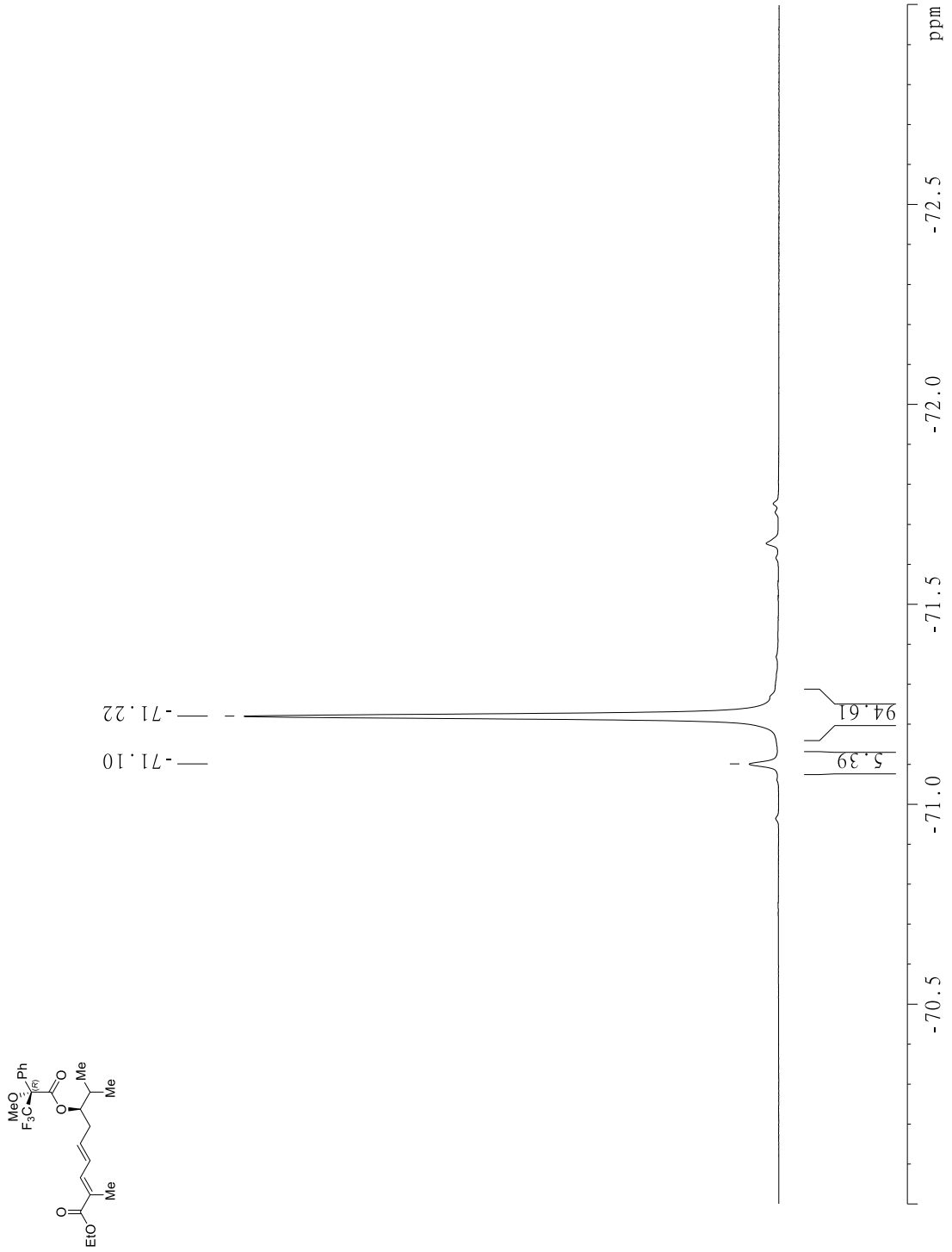
Spectrum 70. ^{19}F spectrum of the (*R*)-Mosher ester of **5h** measured in $CDCl_3$ at 376 MHz.



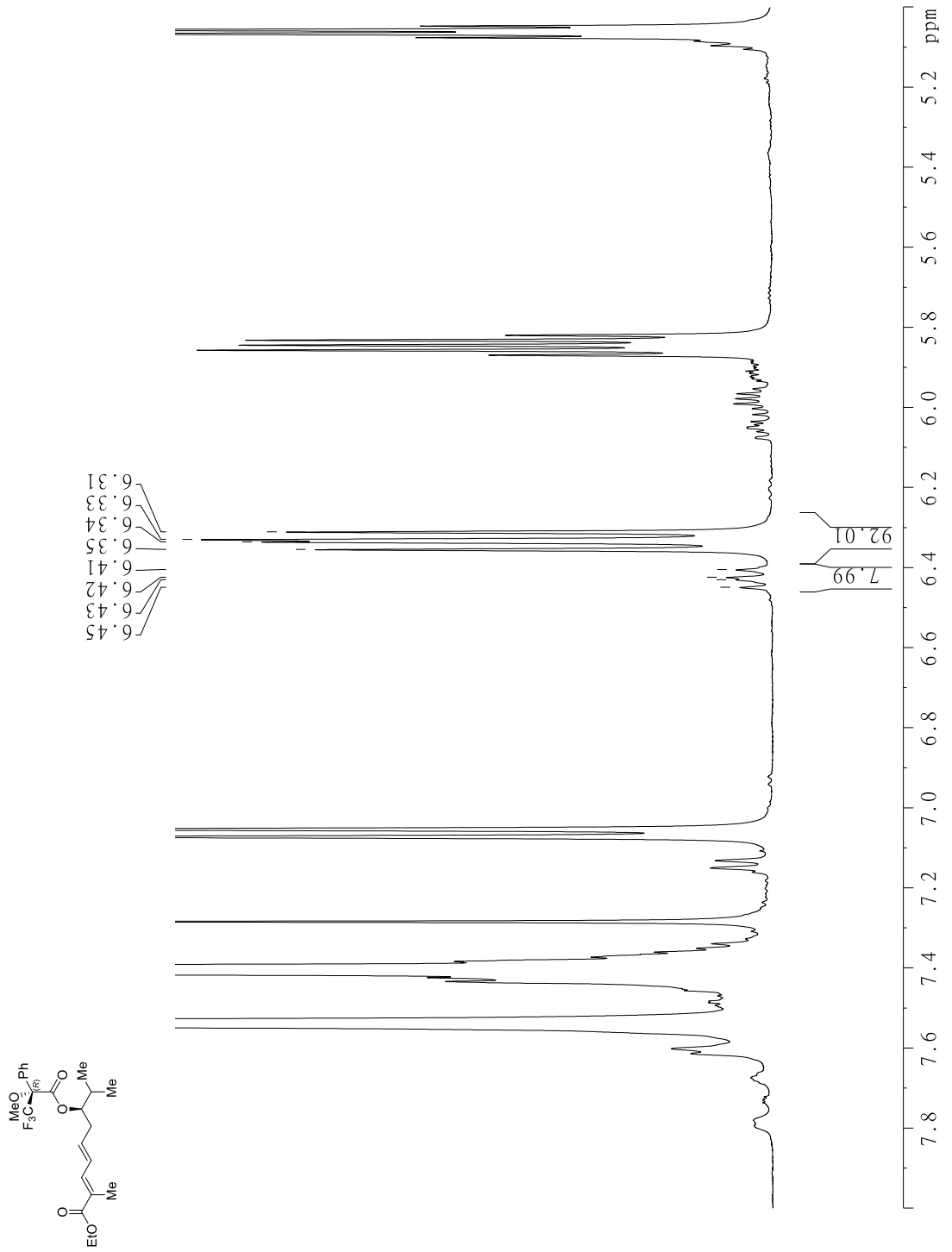
Spectrum 71. Enlarged view of the ^{1}H spectrum of the (*S*)-Mosher ester of **5i** for the determination of the enantiomeric ratio; the spectrum was measured in $CDCl_3$ at 400 MHz.



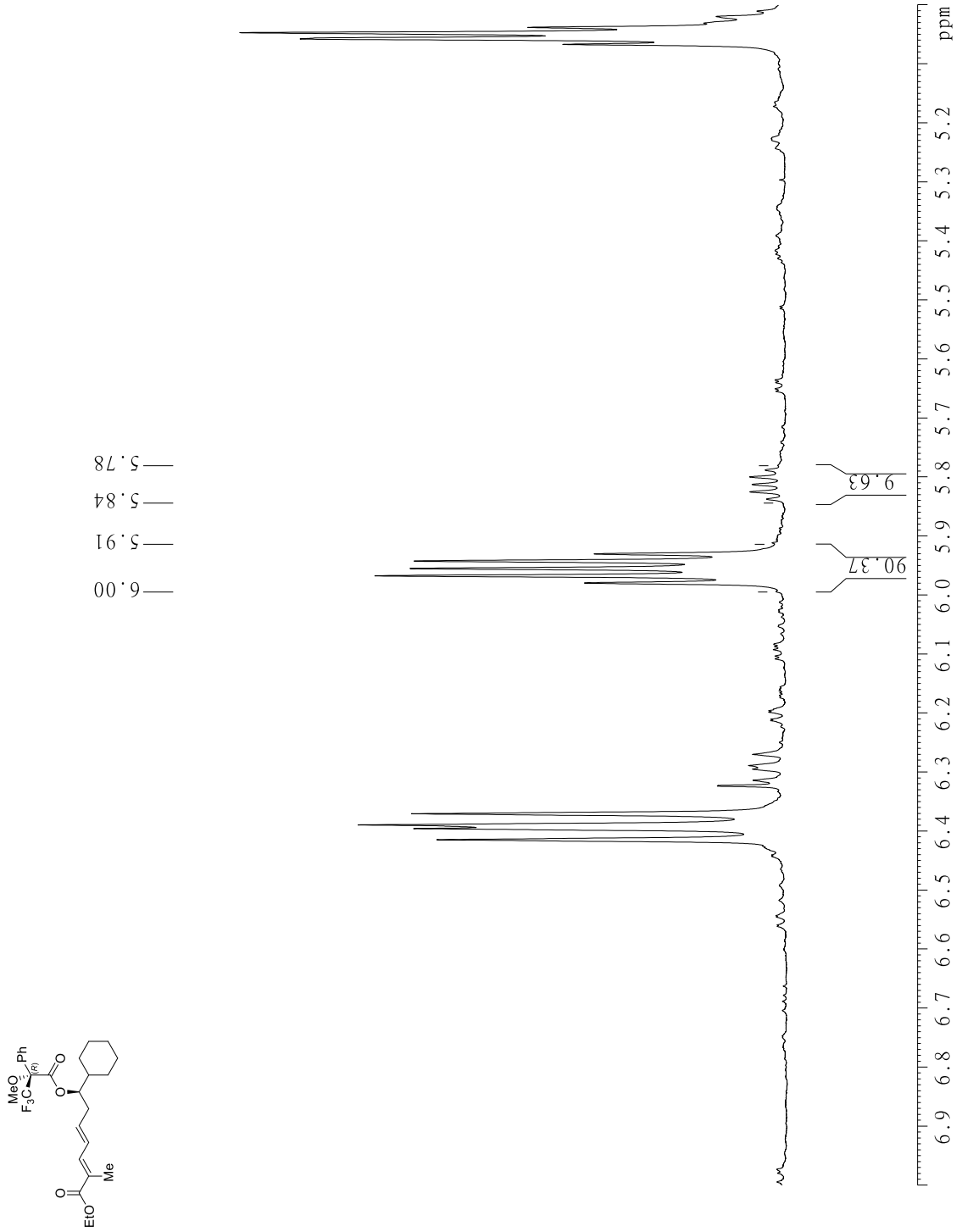
Spectrum 72. Enlarged view of the ^{1}H spectrum of the (*R*)-Mosher ester of **5j** for the determination of the enantiomeric ratio; the spectrum was measured in C_6D_6 at 400 MHz.



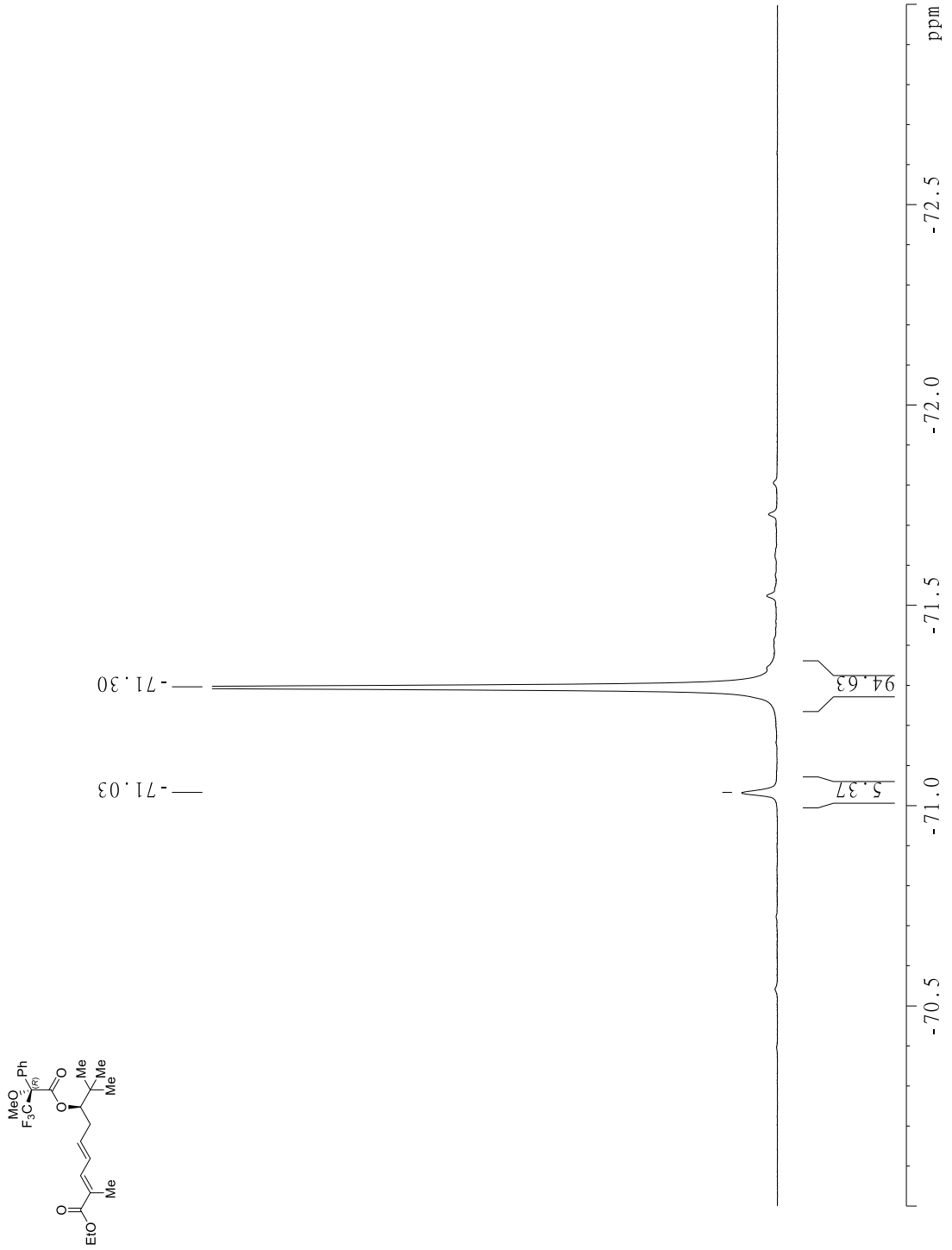
Spectrum 73. ^{19}F spectrum of the (*R*)-Mosher ester of **5k** measured in $CDCl_3$ at 376 MHz.



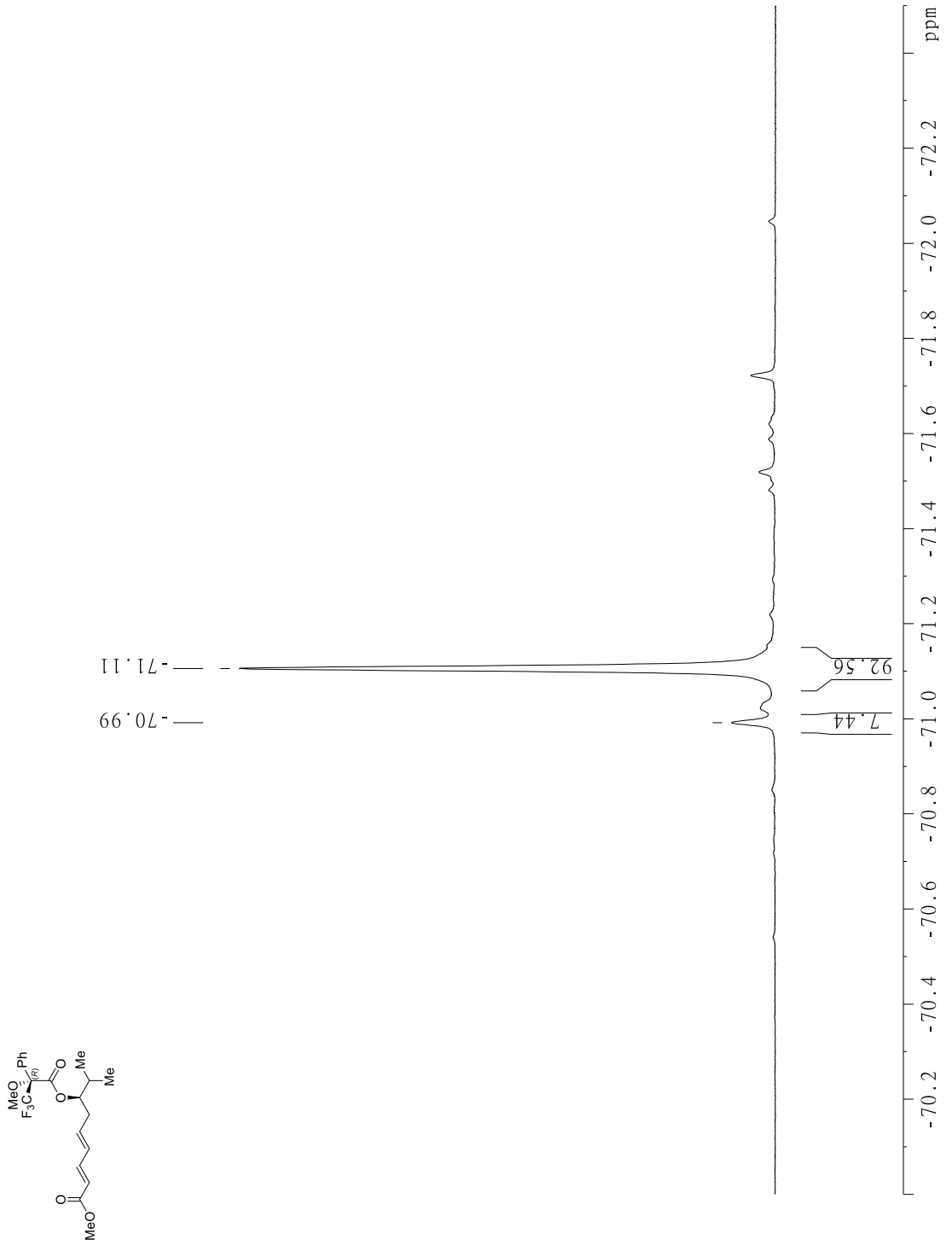
Spectrum 74. Enlarged view of the ^{1}H spectrum of the (*R*)-Mosher ester of **5k** (obtained from the bVMAR reaction at a 1.2 mmol scale) for the determination of the enantiomeric ratio; the spectrum was measured in $CDCl_3$ at 600 MHz.



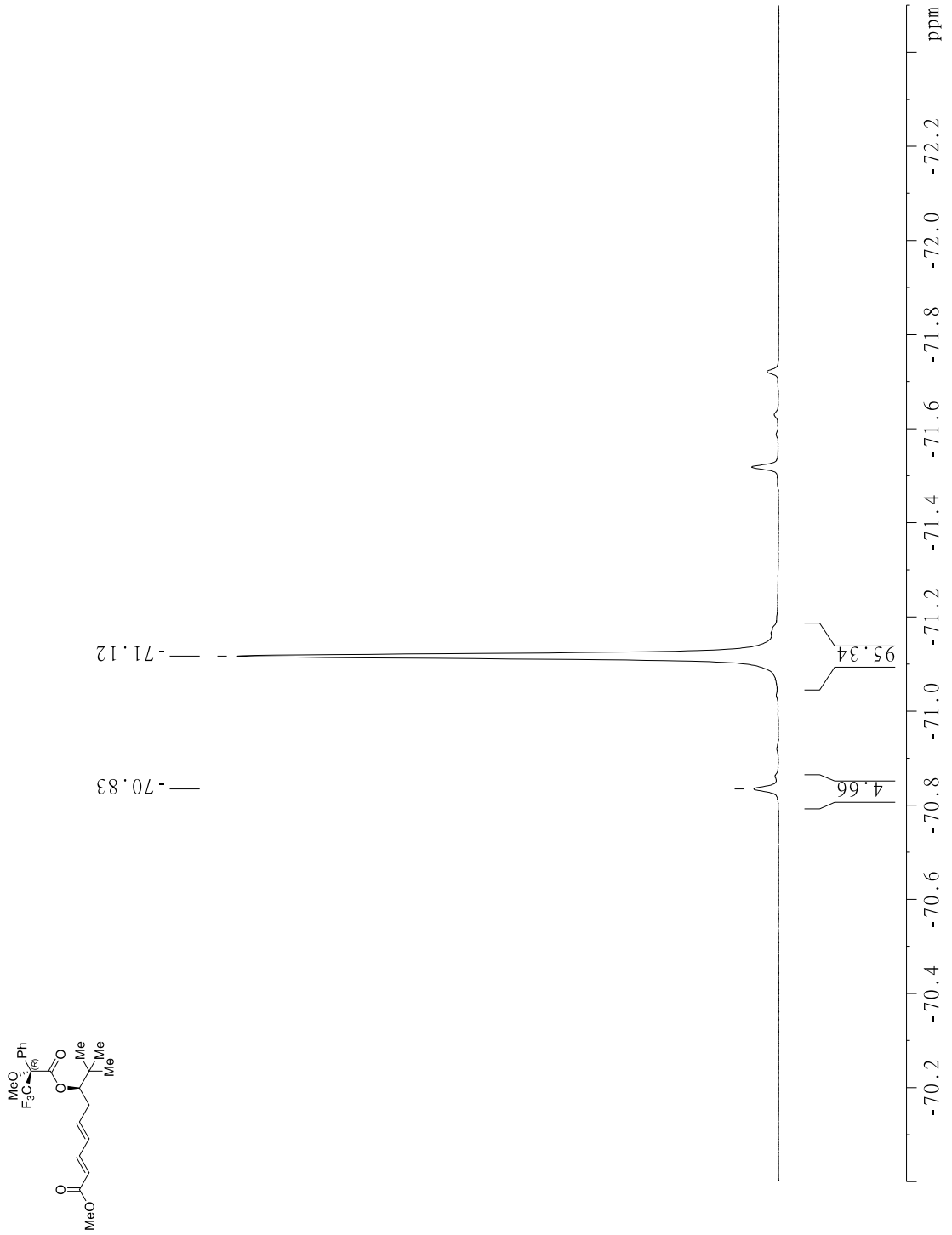
Spectrum 75. Enlarged view of the ^{1}H spectrum of the (*R*)-Mosher ester of **5l** for the determination of the enantiomeric ratio; the spectrum was measured in $CDCl_3$ at 600 MHz.



Spectrum 76. ^{19}F spectrum of the (*R*)-Mosher ester of **5m** measured in $CDCl_3$ at 376 MHz.



Spectrum 77. ^{19}F spectrum of the (*R*)-Mosher ester of **5n** measured in $CDCl_3$ at 376 MHz.



Spectrum 78. ^{19}F spectrum of the (*R*)-Mosher ester of **5o** measured in $CDCl_3$ at 376 MHz.