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SUPPORTING INFORMATION

Alkene protection against acid using a bromide substituent: application in a total synthesis of (–)-6,7-dideoxysqualestatin H5

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Table of Contents

5. ^{1}H and ^{13}C NMR Spectra

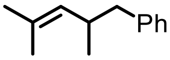
1. General techniques

All reactions requiring anhydrous conditions were carried out in flame–dried glassware under an atmosphere of nitrogen (or argon), the later having been passed through a column of calcium chloride and silica gel. THF, CH_2Cl_2 and DMF were obtained from drying stills.[1] Methanol was dried over activated 4 Å MS under argon. Diisopropylamine, triethylamine and 2,6-lutidine were distilled under nitrogen from CaH_2. A fresh batch of MoOPH was prepared following a slightly modified procedure using molybdic acid[2] instead of molybdenum(VI) oxide,[3] and dried overnight under high vacuum prior use. *n*-BuLi in hexanes was titrated by adding a solution of 2-propanol (1.0 M in toluene with 0.2% of 1,10–phenanthroline) slowly to a solution of *n*-BuLi in toluene until the end-point: a change of colour from clear to red then yellow. MeLi in ether was titrated by adding slowly MeLi to a solution of *N*-benzylbenzamide (100 mg in 5 ml THF) at –20 ºC; the end–point was marked by a colour change from clear to blue. Commercial starting materials were used without further purification, unless otherwise stated. Petrol (petroleum ether) 40–60 °C was used in flash column chromatography, which was carried out using silica gel (VWR chemicals, BDH), and monitored by TLC (Merck 60 F254) plates. TLC plates were viewed using ultraviolet light (λmax = 254/365 nm) and by immersion in $KMnO_4$ or anisaldehyde stains, followed by heating. Infrared spectra were obtained using a PerkinElmer FT–IR spectrometer (Universal ATR Sampling Accessory) with absorption maxima quoted in wavenumbers (cm^{-1}). Peaks are described as broad (br), weak (w), medium (m) and strong (s). Nuclear magnetic resonance (^1H NMR, ^{13}C NMR and ^{19}F NMR) spectra were recorded on Bruker Avance UltraShield AVC 500, AVX 500 and AVF 400, in $CDCl_3$ and CD_3OD, referenced to solvent peaks. Chemical shifts are quoted in parts per million (ppm). The splittings are quoted as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), multiplet (m) and pseudo (p). Proton coupling constants (*J*) are reported to the nearest 0.5 Hz. *E*/*Z* Assignments and stereochemistry of cycloadduct **12** were based on NOE studies. $[\alpha]_D^{25}$ = values are given in 10^{-1} deg cm^2 g^{-1}. Concentrations (c) are given in g/cm^3. Low resolution mass spectra were obtained using electrospray ionisation (ESI). High resolution mass spectra were obtained by ESI using tetraoctylammonium bromide or sodium dodecyl sulfate as the lock mass; values are quoted as ratio of mass to charge (*m*/*z*) in Daltons.

2. Experimental procedures

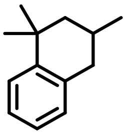
(a) Model studies and methylation cross–coupling optimisation

2,4-Dimethyl-5-phenyl-2-pentene (10)



n-BuLi (1.3 mL, 2.5 M in hexanes, 3.3 mmol) was added dropwise to a solution of isopropyltriphenylphosphonium iodide (1.6 g, 3.7 mmol) in THF (8 mL) at –78 °C. The mixture was warmed to rt, stirred for 30 min, then the dark red solution was re-cooled to –78 °C and a solution of aldehyde *rac*-**17**[4] (0.25 g, 1.69 mmol) in THF (4 mL) was added dropwise. After stirring at rt for 4 h, the mixture was quenched with water (30 mL), extracted with EtOAc (2 x 50 mL). The combined organic layers were washed with brine (30 mL), dried ($MgSO_4$), and evaporated under reduced pressure. Purification of the residue by column chromatography (20% Et_2O in petrol) gave alkene **10**[5] (175 mg, 60%), as a colourless liquid; R_f = 0.71 (20% Et_2O in petrol). ^1H NMR (400 MHz; $CDCl_3$) δ 7.30–7.13 (5H, m, ArH), 4.99 (1H, dquint, *J* = 9, 1.5, C*H*=C(CH_3)$_2$), 2.69–2.48 (3H, m, CHCH_2Ph), 1.67 (3H, d, *J* = 1.5, one CH_3 of =C(CH_3)$_2$), 1.46 (3H, d, *J* = 1.5, second CH_3 of =C(CH_3)$_2$), 0.95 (3H, d, *J* = 6.5, CHC*H*$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 141.4 (Ar*C*), 130.6 (C=*C*H), 130.5 (*C*=CH), 129.4 (Ar*C*H) 128.1 (Ar*C*H), 125.7 (Ar*C*H), 44.2 (*C*H$_2$Ph), 34.8 (*C*HCH$_3$), 25.9 (CH_3), 20.9 (CH*C*H$_3$), 17.9 (CH_3).

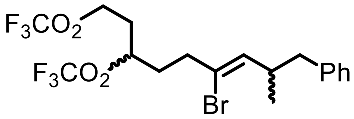
1,1,3-Trimethyl-1,2,3,4-tetrahydronaphthalene (11)



To a solution of alkene **10** (100 mg, 0.57 mmol) in CH_2Cl_2 (4.2 mL) was added TFA (2.1 mL) and H_2O (210 μL). The reaction mixture was heated at 40 °C for 48 h, then cooled to rt, sat. aq. $NaHCO_3$ (5 mL) added and extracted with Et_2O (2 x 15 mL). The combined organic layers were washed with brine (10 mL), dried (K_2CO_3) and evaporated under reduced pressure to give tetralin **11**[6] (94 mg, 95%) as a colourless liquid; R_f = 0.71 (0.5% Et_2O in petrol); ^1H NMR (400 MHz; $CDCl_3$) δ 7.33 (1H, d, *J* = 7.5, ArH), 7.19–7.02 (3H, m, ArH), 2.84–2.74 (1H, m, CH*H*Ar), 2.44–2.34 (1H, m, C*H*HAr), 2.04–1.91 (1H, m, C*H*CH$_3$), 1.67–1.59 (1H, m, C(CH_3)$_2$CH*H*), 1.42–1.32 (4H, m, C(CH_3)$_2$CH*H* and CH_3), 1.25 (3H, s, CH_3), 1.05 (3H, d, *J* = 6.5, CHC*H*$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 145.6 (Ar*C*), 136.3 (Ar*C*), 129.0 (Ar*C*H) 126.7

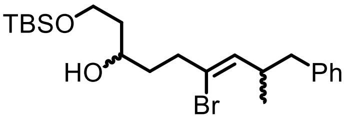
(Ar*C*H), 126.0 (Ar*C*H), 125.4 (Ar*C*H), 48.5 ($C(CH_3)_2\mathit{C}H_2$), 39.9 ($\mathit{C}H_2Ar$), 35.1 ($\mathit{C}(CH_3)_2$), 32.9 (CH_3), 31.9 (CH_3), 25.9 ($\mathit{C}HCH_3$), 22.6 ($CH\mathit{C}H_3$).

(*Z*)-6-Bromo-8-methyl-9-phenylnon-6-ene-1,3-diyl bis(2,2,2-trifluoroacetate) (25)



To a solution of 1,3-diol **22** (100 mg, 0.30 mmol) in CH_2Cl_2 (2.20 mL) were added TFA (1.10 mL) and H_2O (110 μL). The reaction mixture was heated at 40 °C for 48 h. The mixture was then concentrated under reduced pressure to give bistrifluoroacetate **25** (156 mg, quant), as a yellow oil, a 1:1 diastereomeric mixture; R_f = 0.35 (4% EtOAc in petrol); ν_{max}/cm^{-1}(film) 3027 w, 1784 s, 1454 w, 1220 s, 1148 s, 775 m, 731 m, 700 m; ^1H NMR (400 MHz; $CDCl_3$) δ 7.30–7.14 (5H, m, ArH), 5.54–5.49 (1H, m, CH=CBr), 5.15–5.04 (1H, m, $CHOCOCF_3$), 4.41–4.33 (2H, m, CH_2OCOCF_3), 2.94–2.83 (1H, m, $C\mathit{H}CH_3$), 2.71–2.64 (1H, m, CH*H*Ph), 2.59–2.51 (1H, m, C*H*HPh), 2.50–2.40 (2H, m, CH_2CBr), 2.12 (2H, q, *J* = 6, $OCH_2C\mathit{H}_2CHO$), 2.01–1.89 (2H, m, $C\mathit{H}_2CH_2CBr$), 0.97 (3H, d, *J* = 6.5, $CHC\mathit{H}_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 157.3 (2 x q, $J_{C\text{-}F}$ = 42, C=O), 140.0, 140.0 (Ar*C*), 136.2, 136.1 (*C*=CBr), 129.4, 129.3 (Ar*C*H) 128.3, 128.3 (Ar*C*H), 126.2, 126.1 (Ar*C*H), 124.5, 124.4 (C=*C*Br), 114.7 (2 x Q, $J_{C\text{-}F}$ = 286, CF_3), 74.9, 74.7 ($\mathit{C}HOCOCF_3$), 61.6 ($\mathit{C}H_2OCOCF_3$), 42.5 ($\mathit{C}H_2Ph$), 38.1, 38.0 ($\mathit{C}HCH_3$), 37.0, 36.9 ($\mathit{C}H_2CH_2CBr$), 32.5, 32.3, 32.2 ($CH_2\mathit{C}H_2CBr$ and $OCH_2\mathit{C}H_2CHO$), 19.1 ($CH\mathit{C}H_3$); ^{19}F NMR (377 MHz) δ –75.1; HRMS *m/z* ($M+Na^+$) found: 541.0421. $C_{20}H_{21}O_4{}^{79}BrF_6{}^{23}Na$ requires 541.0419.

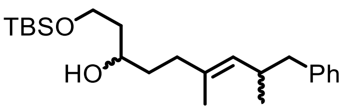
(*Z*)-6-Bromo-1-((*tert*-butyldimethylsilyl)oxy)-8-methyl-9-phenylnon-6-en-3-ol (23)



To a solution of 1,3-diol **22** (0.97 mg, 3.05 mmol) and imidazole (477 mg, 7.01 mmol) in DMF (8 mL) at 0 °C was added a solution of TBSCl (480 mg, 3.2 mmol) in DMF (8 mL). The mixture was stirred for 6 h at 0 °C, then water (5 mL) was added, extracted with Et_2O (2 × 10 mL), washed with brine (5 mL), and dried (Na_2SO_4). Evaporation under reduced pressure followed by column chromatography (20% Et_2O in petrol) gave TBS ether **23** (1.15 g, 86%), as a colourless oil, a 1:1 diastereomeric mixture; R_f = 0.34 (20% Et_2O in petrol); ν_{max}/cm^{-1}(film) 3448 br, 2967 m, 2928 m, 2856 m, 1466 m, 1079 s, 885 m, 625 s; ^1H NMR (400 MHz; $CDCl_3$)

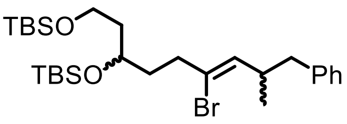
δ 7.29–7.13 (5H, m, ArH), 5.53 (1H, d, *J* = 8.5, CH=CBr), 3.92–3.85 (1H, m, C*H*OH), 3.83–3.66 (2H, m, CH_2OTBS), 3.47 and 3.42 (1H, 2 x s, CHO*H*), 2.95–2.82 (1H, m, C*H*CH_3), 2.73–2.64 (1H, m, CH*H*Ph), 2.61–2.42 (3H, m, C*H*$_2$ and CH*H*Ph), 1.71–1.56 (4H, m, 2 x CH_2), 0.96 (3H, pdd, *J* = 6.5, 4, CHC*H*$_3$), 0.89 (9H, s, OSiCMe$_3$), 0.08 (6H, s, OSi(CH_3)$_2$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 140.3, 140.2 (Ar*C*), 134.2, 134.1 (*C*=CBr), 129.4, 129.3 (Ar*C*H) 128.2 (Ar*C*H), 127.2 (C=*C*Br), 126.0 (Ar*C*H) 71.1, 70.9 (*C*HOH), 63.0 (*C*H$_2$OTBS), 42.7, 42.6 (*C*H$_2$Ph), 38.4, 38.3, 38.0, 37.9, 37.8, 37.7, (all CH_2), 36.1, 35.9 (*C*HCH_3), 26.0 (SiC*Me*$_3$) 19.3, 19.2 (CH*C*H$_3$), 18.2 (Si*C*Me$_3$), -5.4 (OSi(CH_3)$_2$), -5.4 (OSi(CH_3)$_2$); HRMS *m*/*z* (M+H$^+$) found: 441.1822. $C_{22}H_{38}$ $O_2{}^{79}Br^{28}Si$ requires 441.1819.

(*E*)-1-((*tert*-Butyldimethylsilyl)oxy)-6,8-dimethyl-9-phenylnon-6-en-3-ol (27)



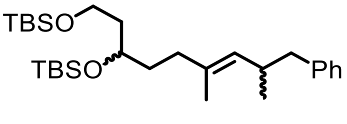
MeLi (112 µL, 1.6 M in Et_2O, 0.18 mmol) was added to a solution of 9-OMe-9BBN (180 µL, 1 M in hexanes, 0.18 mmol) in THF (1 mL). After 10 min, $PdCl_2$(dppf) (11 mg, 10 mol%) and NaOMe (12 mg, 0.22 mmol) were added, followed by a solution of TBS ether **23** (66 mg, 0.15 mmol) in THF (0.5 mL) dropwise. After refluxing for 48 h, the mixture was cooled to rt, added water (1 mL), extracted with Et_2O (2 × 5 mL), washed with brine (2 mL) and dried ($MgSO_4$). Evaporation under reduced pressure followed by column chromatography (5% EtOAc in petrol) gave *E*-alkene **27** (42 mg, 75%), as a colourless oil, a 1:1 diastereomeric mixture; R_f = 0.33 (5% EtOAc in petrol); ν_{max}/cm^{-1}(film) 3386 br, 2955 m, 2925 m, 2856 s, 1495 m, 1254 m, 1083 s, 834 s, 776 s, 698 m, 663 s; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.28–7.10 (5H, m, ArH), 5.00 (1H, d, *J* = 9, C*H*=CCH_3), 3.92–3.85 (1H, m, C*H*OH), 3.83–3.69 (2H, m, CH_2OTBS), 3.37 and 3.35 (1H, 2 x d, *J* = 2.5, CHO*H*), 2.67–2.56 (1H, m, C*H*CH_3), 2.55–2.49 (2H, m, CH_2Ph), 2.13–1.91 (2H, m, CH_2), 1.67–1.44 (4H, m, 2 x CH_2), 1.42 (3H, s, =CCH_3), 0.94 (3H, 2 x d, *J* = 6.5, CHC*H*$_3$), 0.90 (9H, s, OSiCMe$_3$), 0.08 (6H, s, OSi(CH_3)$_2$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 141.3, 141.3 (Ar*C*), 134.1 (*C*=CCH_3), 130.5, 130.5 (C=*C*CH$_3$), 129.4 (Ar*C*H) 128.1, 128.1 (Ar*C*H), 125.7 (Ar*C*H) 72.0, 71.9 (*C*HOH), 63.0 (*C*H$_2$OTBS), 42.1 (*C*H$_2$Ph), 38.4, 38.3, 35.9, 35.8, 35.6, (all CH_2), 34.7 (*C*HCH_3), 26.0 (SiC*Me*$_3$), 21.0, 20.9 (CH*C*H$_3$), 18.2 (Si*C*Me$_3$), 16.2, 16.2 (=C*C*H$_3$), -5.4 (one CH_3 of OSi(CH_3)$_2$), -5.4 (another CH_3 of OSi(CH_3)$_2$). HRMS *m*/*z* (M+H$^+$) found: 377.2876. $C_{23}H_{41}O_2Si$ requires 377.2873.

(*Z*)-5-(3-Bromo-5-methyl-6-phenylhex-3-en-1-yl)-2,2,3,3,9,9,10,10-octamethyl-4,8-dioxa-3,9-disilaundecane (24)



To a solution of TBS ether **23** (50.0 mg, 0.11 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C was added 2,6-lutidine (40 μL, 0.3 mmol) followed by TBSOTf (47 μL, 0.20 mmol). The mixture was stirred for 2 h at 0 °C, then sat. aq. $NaHCO_3$ (2 mL) added, extracted with EtOAc (2 × 5 mL) and the combined organic layers dried ($MgSO_4$) and evaporated under reduced pressure. Purification the residue by column chromatography (5% Et_2O in petrol) gave bis-TBS ether **24** (59 mg, 94%) as a colourless oil, a 1:1 diastereomeric mixture; R_f = 0.65 (5% Et_2O in petrol); ν_{max}/cm^{-1}(film) 3064 w, 2955 s, 2359 w, 1658 w, 1603 w, 1496 m, 1472 m, 1361 m, 1256 s, 1036 m, 1006 m, 836 s, 775 s; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.31–7.16 (5H, m, ArH), 5.49 (1H, d, *J* = 8.5, CH=CBr), 3.87–3.79 (1H, m, CHOTBS), 3.71–3.64 (2H, m, CH_2OTBS), 2.95–2.84 (1H, m, C*H*CH_3), 2.72 (1H, dd, *J* = 13.5, *J* = 6 ,CH*H*Ph), 2.25 (1H, dd, *J* = 13.5, *J* = 8 ,CH*H*Ph), 2.48–1.41 (2H, m, CH_2CBr), 1.76–1.59 (4H, m, C*H*$_2$CH(OTBS)C*H*$_2$), 0.97 (3H, d, *J* = 6.5, CHC*H*$_3$), 0.91 (18H, s, 2 x OSiCMe$_3$), 0.06 (12H, s, 2 x OSi$(CH_3)_2$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 140.2 (Ar*C*), 133.7, (*C*=CBr), 129.4 (Ar*C*H) 128.3 (Ar*C*H), 127.7, 127.6 (C=*C*Br), 126.1 (Ar*C*H) 68.5 (*C*HOTBS), 60.0, 60.0 (*C*H$_2$OTBS), 42.7 (*C*H$_2$Ph), 40.1, 38.0 (2 x CH_2), 37.5, 37.5 (*C*HCH_3), 26.3, 36.2 (CH_2), 26.1, 26.1 (SiC*Me*$_3$), 19.2 ($CHCH_3$), 18.4, 18.3 (Si*C*Me$_3$), -4.3, -4.4 (one CH_3 of OSi$(CH_3)_2$), -5.1, -4.4 (another CH_3 of OSi$(CH_3)_2$); HRMS *m*/*z* (M+H$^+$) found: 555.2672. $C_{28}H_{52}{}^{79}BrO_2{}^{28}Si_2$ requires 555.2684.

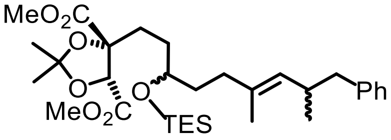
(*E*)-5-(3,5-Dimethyl-6-phenylhex-3-en-1-yl)-2,2,3,3,9,9,10,10-octamethyl-4,8-dioxa-3,9-disilaundecane (28)



Following the procedure to **27** above, but using bis-TBS ether **24** (55 mg, 0.1 mmol), gave after column chromatography (petrol) bis-TBS *E*-alkene **28** (37 mg, 76%), as a colourless oil, a 1:1 diastereomeric mixture; R_f = 0.63 (0.5% Et_2O in petrol); ν_{max}/cm^{-1}(film) 2977s, 2931s, 2861s, 1644 m, 1444 s, 1382s , 1350 s, 1298 m, 1257 m, 1125 br, 1043 m, 837 s, 775 m; ^{1}H NMR

(400 MHz; $CDCl_3$) δ 7.28–7.11 (5H, m, ArH), 4.98 (1H, d, J = 9, C*H*=CCH_3), 3.82–3.74 (1H, m, CHOTBS), 3.72–3.63 (2H, m, CH_2OTBS), 2.67–2.56 (1H, m, C*H*CH_3), 2.55–2.48 (2H, m, CH_2Ph), 2.04–1.87 (2H, m, C*H*$_2$$CCH_3$), 1.66 (2H, q, J = 6.5, C*H*$_2$$CH_2OTBS$), 1.55–1.46 (2H, m, C*H*$_2$$CH_2CCH_3$), 1.42 (3H, d, J = 1, =CCH_3), 0.95 (3H, d, J = 6.5, CHC*H*$_3$), 0.91 (18H, s, 2 x OSiCMe$_3$), 0.06 (12H, s, 2 x OSi(CH_3)$_2$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 141.3 (Ar*C*), 134.4, 134.4 (*C*=CCH_3), 130.2, 130.2 (C=*C*CH_3), 129.4, 129.4 (Ar*C*H) 128.1 (Ar*C*H), 125.7 (Ar*C*H) 69.4 (*C*HOTBS), 60.2, 60.2 (*C*H_2OTBS), 44.2, 44.2 (*C*H_2Ph), 40.2, 40.2, 36.2, 36.1, 35.4, 35.4 (all CH_2), 34.7 (*C*HCH_3), 26.1, 26.1 (SiC*Me*$_3$), 20.9, 20.9 (CH*C*H_3), 18.5, 18.3 (Si*C*Me$_3$), 16.3 (=CCH_3), -4.2, -4.4 (one CH_3 of OSi(CH_3)$_2$), -5.1 (another CH_3 of OSi(CH_3)$_2$); HRMS *m*/*z* (M+H$^+$) found: 491.3734. $C_{29}H_{55}O_2{}^{28}Si_2$ requires 491.3735.

Dimethyl (4*R*,5*R*)-4-((*E*)-6,8-dimethyl-9-phenyl-3-((triethylsilyl)oxy)non-6-en-1-yl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (SI-1)



To a solution of B-OMe-9BBN (93 μL, 1 M in hexane, 0.093 mmol) in THF (400 μL) was added MeLi (78 μL, 1.2 M in Et_2O, 0.093 mmol). Meanwhile, a mixture of $PdCl_2$(dppf) (3 mg, 10 mol%), aq. Cs_2CO_3 (45 mg, 3 M, 0.138 mmol), $AsPh_3$ (4 mg, 30 mol%) and alkylated tartrate **14** (from *rac*-**17**) (30 mg, 0.046 mmol) was prepared in DMF (400 μL) at rt. To the mixture containing **14** and the catalyst system, the borinate complex solution was added dropwise and then the mixture stirred at rt for 40 h. The reaction mixture was then quenched with water (1 mL), extracted with Et_2O (3 × 2 mL), washed with brine (2 mL) and dried ($MgSO_4$). Evaporation under reduced pressure followed by column chromatography (10−30% EtOAc in petrol) gave *E*-alkene tartrate **SI-1** (20 mg, 75%), as a colourless oil, a mixture of 4 diastereoisomers. R_f = 0.53 (20% EtOAc in petrol); ν_{max}/cm^{-1}(film) 3019 s, 2956 s, 2876 m, 1750 m, 1453 m, 1384 m; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.27–7.10 (5H, m, ArH), 4.93 (2H, d, J = 8, C*H*=CCH_3 and C*H*CO_2Me), 3.81 (3H, s, OMe), 3.79 (3H, s, OMe), 3.62–3.53 (1H, m, C*H*OTES), 2.63–2.54 (1H, m, C*H*CH_3), 2.51 (1H, pd, J = 7, CH_2Ph), 2.00–1.74 (4H, m, 2 x CH_2), 1.68–1.59 (5H, m, CH_2 and one Me of CMe$_2$), 1.47–1.41 (5H, m, CH_2 and second Me of CMe$_2$), 1.38 (3H, s, =CCH_3), 0.94 (12H, pq, J = 7.5, OSi(CH_2C*H*$_3$)$_3$ and CHC*H*$_3$), 0.57 (6H, q, J = 7.5, OSi(C*H*$_2$$CH_3$)$_3$); ^{13}C NMR (125 MHz; $CDCl_3$) δ 172.6, 172.5 (*C*O_2Me), 169.0, 168.8

(*C*O$_2$Me), 141.3 (Ar*C*), 134.0, 134.0 (*C*=CCH$_3$), 130.4, 130.4 (C=*C*CH$_3$), 129.4 (Ar*C*H) 128.1, 128.1 (Ar*C*H), 125.7 (Ar*C*H), 112.8, 112.7 (*C*Me$_2$), 86.1, 85.8 (*quat.* C), 80.3, 80.2 (*C*HCO$_2$Me), 71.9, 71.9 (*C*HOTES), 53.0 (OMe), 52.5, 52.4 (OMe), 44.2, 42.1 (*C*H$_2$Ph), 36.0, 35.9, 35.5, 35.4 (all CH$_2$), 34.7, 34.7 (*C*HCH$_3$), 31.4, 31.1, 30.7, 30.2 (all CH$_2$), 27.9, 27.8, 26.2, 26.1 (C(*C*H$_3$)$_2$), 20.9, 20.9 (CH*C*H$_3$), 16.2, 16.2 (=C*C*H$_3$), 7.1 (OSi(CH$_2$*C*H$_3$)$_3$), 5.2, 5.2 (OSi(*C*H$_2$CH$_3$)$_3$); HRMS *m/z* (M+Na$^+$) found: 599.3371. $C_{32}H_{52}O_7{}^{28}Si$ requires 599.3374. [^{1}H and ^{13}C NMR spectra of alkylated tartrate **14** (from *rac*-**17**) are also provided in Section 5 below.]

Table S1: Optimisation of the conditions for methylation cross–coupling with alkylated tartrate **14**.[a]

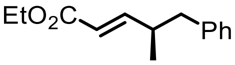
Entry	Base	Ligand (Pd:L; 1:4)	Solvent (5:5:1)	Temp. (°C)	Time (h)	**14**:**SI-1**[b]	Yield (%)[c]
1	-	-	THF	50	48	80:20	-
2	NaOMe	-	THF	rt	48	75:25	-
3	NaOMe	-	THF	50	48	70:30	-
4	Cs_2CO_3	-	THF/DMF	rt	48	25:75	-
5	Cs_2CO_3	-	THF/DMF/H_2O	rt	48	Trace **14**	54
6	Cs_2CO_3	-	THF/DMF/H_2O	50	48	0	45
7	Cs_2CO_3	Ph_3As	THF/DMF/H_2O	rt	40	0	75
8	Cs_2CO_3	Ph_3As	THF/DMF/MeOH	40	8	0	68

[a] Reaction conditions: alkylated tartrate **14** (1 equiv.), B-MeO-9BBN (2 equiv.), MeLi (2 equiv.), PdCl$_2$(dppf) (10 mol%).

[b] Ratio by integration of crude ^{1}H NMR spectra. [c] Isolated yield of **SI-1**.

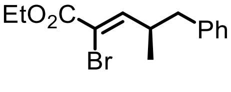
(b) Total synthesis of (–)-6,7-dideoxysqualestatin H5

(−)-(*R*,*E*)-Ethyl 4-methyl-5-phenylpent-2-enoate (18)



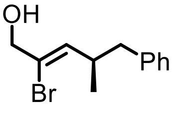
A mixture of ethyl (triphenylphosphoranylidene)acetate (9.5 g, 27 mmol) and (*R*)-2-methyl-3-phenylpropanal **17**[7] (3.7 g, 25 mmol) in CH$_2$Cl$_2$ (23 mL) was stirred for 48 h at rt. The solution was then diluted with hexane (15 mL), filtered through Celite® and evaporated under reduced pressure. The residue was purified by column chromatography (10% EtOAc in petrol) to give *E*-enoate **18**[8] (5.23 g, 96%) as a colourless oil; R_f = 0.78 (10% EtOAc in petrol); $[\alpha]_D^{25} = -52$ (*c*=1.0, CHCl$_3$); ν_{max}/cm^{-1}(film) 3027 w, 2976 s, 2928 m, 1715 s, 1650 m, 1454 m, 1367 w, 1267 m, 1204 w, 1174 s, 1040 m, 745 m, 699 m; ^{1}H NMR (400 MHz; CDCl$_3$) δ 7.25–7.03 (5H, m, ArH), 6.88 (1H, dd, J = 15.5, 6.5, CH=CHCO$_2$), 5.68 (1H, d, J = 15.5, CH=CHCO$_2$), 4.10 (2H, q, J = 7, OCH_2CH$_3$), 2.69 (1H, dd, J = 12, 5, CHHPh), 2.60–2.46 (2H, m, CHHPh and CHCH$_3$), 1.20 (3H, t, J = 7, OCH$_2$CH_3), 0.97 (3H, d, J = 6.5, CHCH_3); ^{13}C NMR (100 MHz; CDCl$_3$) δ 166.9 (CO$_2$Et), 153.6 (CH=CHCO$_2$), 139.7 (ArC), 129.2 (ArCH), 128.4 (ArCH), 126.3 (ArCH), 120.0 (=CHCO$_2$), 60.3 (CO$_2$$CH_2CH_3$), 42.5 ($CH_2$Ph), 38.3 ($CHCH_3$), 18.8 (CH$CH_3$), 14.4 (CO$_2CH_2$$CH_3$); HRMS *m*/*z* (M+H$^+$) found: 219.1380. C$_{14}H_{19}O_2$ requires 219.1379.

(−)-(*R*,*Z*)-Ethyl 2-bromo-4-methyl-5-phenylpent-2-enoate (19)



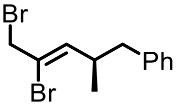
Bromine (1.65 mL, 32.2 mmol) was added dropwise to a stirred solution of *E*-enoate **18** (5.20 g, 23.8 mmol) in CH$_2$Cl$_2$ (46 mL) at 0 °C. After 2 h, the solution was diluted with sat. aq. Na$_2$S$_2$O$_3$ (20 mL), extracted with Et$_2$O (2×30 mL), dried (MgSO$_4$) and concentrated under reduced pressure. Et$_3$N (16.5 mL, 119 mmol) was added to a stirred solution of the residue in CH$_2$Cl$_2$ (46 mL) at rt. After 12 h, the heterogeneous mixture was concentrated under reduced pressure followed by column chromatography (5% EtOAc in petrol) to give *Z*-α-bromoenoate **19** (6.43 g, 91%) as a pale yellow oil; R_f = 0.48 (5% EtOAc in petrol); $[\alpha]_D^{25}$ = −7.6 (*c*=1.0, CHCl$_3$); ν_{max}/cm^{-1}(film) 3028 w, 2961 s, 2872 m, 2360 w, 1731 s, 1625 m, 1454 m, 1367 w, 1249 s, 1094 w, 1035 m, 749 m, 700 m; ^{1}H NMR (400 MHz; CDCl$_3$) δ 7.32–7.14 (6H, m, ArH and CH=CBr), 4.27 (2H, q, J = 7, OCH_2CH$_3$), 3.11–3.00 (1H, m, CHCH$_3$), 2.81 (1H, dd, J = 13.5, 6.5, CHHPh), 2.62 (1H, dd, J = 13.5, 8, CHHPh), 1.33 (3H, t, J = 7, OCH$_2$CH_3), 1.06 (3H, d, J = 6.5, CHCH_3), ^{13}C NMR (100 MHz; CDCl$_3$) δ 162.6 (CO$_2$Et), 150.4 (CH=CBr), 139.1 (ArC), 129.2 (ArCH), 128.5 (ArCH), 126.4 (ArCH), 115.5 (CH=CBr), 62.6 (OCH$_2$CH$_3$), 41.7 (CH$_2$Ph), 38.7 (CHCH$_3$), 18.3 (CHCH$_3$), 14.3 (OCH$_2$$CH_3$); HRMS *m*/*z* (M+NH$_4^+$) found: 314.0752. C$_{14}H_{21}$^{79}BrNO$_2$ requires 314.0750.

(−)-(*R*,*Z*)-2-Bromo-4-methyl-5-phenylpent-2-en-1-ol (SI-2)



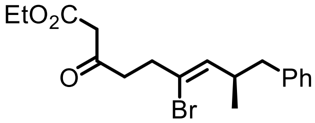
DIBAL–H (60 mL, 1.0 M in hexanes, 62.2 mmol) was added dropwise to a solution of *Z*-α-bromoenoate **19** (6.16 g, 20.7 mmol) in CH$_2$Cl$_2$ (180 mL) at –78 °C. After stirring at –78 °C for 2 h, the mixture was diluted with ether and warmed to 0 °C. Water (2.4 mL) was added dropwise, followed by 15% aq. NaOH (2.4 mL), and then further of water (6 mL). The mixture was stirred for 15 min, dried ($MgSO_4$), and filtered. Evaporation under reduced pressure followed by column chromatography (10% EtOAc in petrol) gave allylic alcohol **SI-2** (4.29 g, 81%), as a yellow oil; R_f = 0.16 (10% EtOAc in petrol); $[\alpha]_D^{23} = -8.0$ (*c*=1.0, $CHCl_3$); ν_{max}/cm^{-1}(film) 3605 s, 3480 br, 3028 s, 2927 s, 2253 s, 1494 m, 1453 s, 1378 s, 1262 m, 1100 m, 907 s; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.30–7.20 (5H, m, ArH), 5.86 (1H, d, *J* = 9, CH=CBr), 4.13 (2H, s, C*H*$_2$OH), 2.92–2.80 (1H, m, C*H*CH$_3$), 2.66 (1H, dd, *J* = 13.5, 6.5, CH*H*Ph), 2.49 (1H, dd, *J* = 13.5, 8, C*H*HPh), 1.79 (1H, br, OH), 0.93 (3H, d, *J* = 6.5, CHC*H*$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 139.8 (Ar*C*), 135.3 (*C*=CBr), 129.3 (Ar*C*H) 128.3 (Ar*C*H), 126.2 (Ar*C*H), 125.8 (C=*C*Br), 68.5 (CH_2OH), 42.4 (*C*H$_2$Ph), 37.5 (*C*HCH$_3$), 19.0 (CH_3); HRMS *m*/*z* ($M+NH_4^+$) found: 272.0642. $C_{12}H_{18}{}^{79}BrNO$ requires 272.0645.

(−)-(*R,Z*)-(4,5-Dibromo-2-methylpent-3-enyl)benzene (20)



To a stirred solution of allylic alcohol **SI-2** (6.32 g, 24.8 mmol) and Ph_3P (24.3 g, 92.6 mmol) in MeCN (400 mL) was added CBr_4 (30.9 g, 93.2 mmol) at 0 °C. After 1 h at 0 °C, the reaction mixture was allowed to warm to rt, and then passed through a short silica gel column using 20% ether in petrol. Evaporation under reduced pressure followed by column chromatography (petrol) gave allylic bromide **20** (8.98 g, quant), as a yellow oil; R_f = 0.47 (petrol); $[\alpha]_D^{23} = -3.8$ (*c*=1.0, $CHCl_3$); ν_{max}/cm^{-1}(film) 3028 m, 2964 m, 2252 s, 1495 m, 1453 s, 1214 s, 908 s; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.31–7.15 (5H, m, ArH), 5.96 (1H, d, *J* = 9, CH=CBr), 4.21 (2H, s, CH_2Br), 2.95–2.83 (1H, m, C*H*CH$_3$), 2.73 (1H, dd, *J* = 13.5, 6.5, CH*H*Ph), 2.57 (1H, dd, *J* = 13.5, 7.5, C*H*HPh), 1.00 (3H, d, *J* = 6.5, CHC*H*$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 139.6 (Ar*C*), 139.4 (*C*=CBr), 129.4 (Ar*C*H) 128.4 (Ar*C*H), 126.3 (Ar*C*H), 121.6 (C=*C*Br), 41.1 (CH_2Ph), 39.0 (CH_2Br), 38.2 (*C*HCH$_3$), 18.7 (CH_3); HRMS *m*/*z* (M^+) found: 315.9465. $C_{12}H_{14}{}^{79}Br_2$ requires 315.9457.

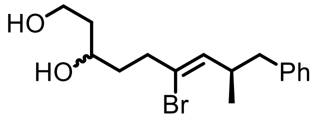
(−)-(*R,Z*)-Ethyl 6-bromo-8-methyl-3-oxo-9-phenylnon-6-enoate (21)



The procedure of Huckin and Weiler[9] was followed with slight modifications. Ethyl acetoacetate (4.20 mL, 33.4 mmol) was added dropwise to a suspension of NaH (1.48 g, 60%

in mineral oil, 37.0 mmol) in THF (250 mL) at 0 °C. The resulting mixture was stirred for 10 min until the solution became clear. *n*-BuLi (13.8 mL, 2.5 M in hexanes, 34.6 mmol) was added dropwise over 30 min and the reaction mixture was stirred at 0 °C for 10 min. A solution of allylic bromide **20** (3.8 g, 11.9 mmol) in THF (20 mL) at 0 °C was then added *via* cannula over 5 min. The reaction mixture was then stirred at 0 °C for 30 min, then at rt for 10 min and quenched with HCl (20 mL, 2M). The mixture was extracted with Et$_2$O (2 x 100 mL). The combined organic layers were washed with water until pH was neutralised (2 x 50 mL), dried (MgSO$_4$) and concentrated under reduced pressure. Purification of the residue by column chromatography (0–20% Et$_2$O in petrol) gave β-ketoester **21** (3.44 g, 79%), as a pale yellow oil; R_f = 0.2 (10% Et$_2$O in petrol); $[\alpha]_D^{23} = -11.4$ (*c*=1.0, CHCl$_3$); ν_{max}/cm^{-1}(film) 2962 m, 2927 m, 1746 s, 1716 s, 1651 m, 1495 m, 1454 m, 1368 m, 1317 s, 1033 s, 746 s, 700 s; ^{1}H NMR (400 MHz; CDCl$_3$) δ (discernable) of major **keto–tautomer**: 7.22–7.06 (5H, m, ArH), 5.49 (1H, d, *J* = 8.5, CH=CBr), 4.13 (2H, q, *J* = 7, OC*H*$_2$CH$_3$), 3.34 (2H, s, CH$_2$(CO)$_2$), 2.83–2.72 (1H, m, *CH*CH$_3$), 2.71–2.56 (5H, m, C*H*$_2$C*H*$_2$CO and CH*H*Ph), 2.46 (1H, dd, *J* = 13.5, 7.5, C*H*HPh), 1.29 (3H, t, *J* = 7, OCH$_2$C*H*$_3$), 0.89 (3H, d, *J* = 6.5, CHC*H*$_3$); ^{13}C NMR (100 MHz; CDCl$_3$) δ (discernable) of major **keto–tautomer**: 201.3 (CH$_2$*C*OCH$_2$), 167.1 (*C*O$_2$Et), 140.0 (Ar*C*), 135.4 (*C*=CBr), 129.4 (Ar*C*H) 128.2 (Ar*C*H), 126.1 (Ar*C*H), 125.0 (C=*C*Br), 61.6 (O*C*H$_2$CH$_3$), 49.6 (CO*C*H$_2$CO), 42.5 (*C*H$_2$Ph), 41.8 and 38.0 (*C*H$_2$*C*H$_2$CO), 35.5 (*C*HCH$_3$), 19.2 (CH*C*H$_3$), 14.3 (OCH$_2$*C*H$_3$); ^{1}H NMR (400 MHz; CDCl$_3$) δ (discernable) of minor **enol–tautomer**: 12.00 (0.1 H, s, CH=CO*H*), 4.91 (0.1 H, s, C*H*=COH); ^{13}C NMR (100 MHz; CDCl$_3$) δ (discernable) of minor **enol–tautomer**: 135.45 (*C*=CBr), 129.3 (Ar*C*H), 90.2 (*C*H=COH), 60.2 (O*C*H$_2$CH$_3$), 42.5 (*C*H$_2$Ph), 39.0 and 38.3 (*C*H$_2$*C*H$_2$CO), 34.1 (*C*HCH$_3$), 19.1 (CH*C*H$_3$), 14.4 (OCH$_2$*C*H$_3$); HRMS *m*/*z* (M+NH$_4^+$) found: 384.1168. C$_{18}$H$_{27}$^{79}BrNO$_3$ requires 384.1169.

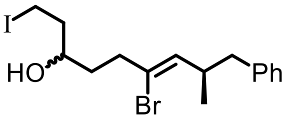
(−)-(8*R*,*Z*)-6-Bromo-8-methyl-9-phenylnon-6-ene-1,3-diol (8*R*-22)



A solution of β-ketoester **21** (3.20 g, 8.71 mmol) in THF (30 mL) was added to a suspension of NaBH$_4$ (1.21 g, 32.0 mmol) in THF (100 mL). The reaction mixture was heated to reflux. MeOH (12 mL) was added dropwise to the refluxing mixture over 10 min and then reflux continued for 1 h. The mixture was then allowed to cool to rt and water (50 mL) was added. The mixture was extracted with Et$_2$O (3 x 100 mL) and the combined organic layers dried (MgSO$_4$). Evaporation under reduced pressure followed by column chromatography (20%

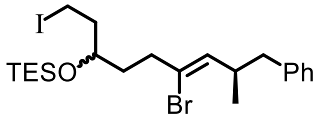
petrol in Et$_2$O) gave 1,3-diol 8*R*-**22** (2.60 g, 91%), as a yellow oil, a 1:1 epimeric mixture at C–3; R_f = 0.19 (20% petrol in Et$_2$O); $[\alpha]_D^{23}$ = −8.1 (*c*=1.0, CHCl$_3$); ν_{max}/cm^{-1}(film) 3351 br, 3027 m, 2925 s, 1654 w, 1602 w, 1495 m, 1453 s, 1059 s, 744 s, 700 s; ^{1}H NMR (400 MHz; CDCl$_3$) δ 7.30–7.15 (5H, m, ArH), 5.53 (1H, d, *J* = 8.5, CH=CBr), 3.89–3.60 (3H, m, C*H*$_2$OH and C*H*OH), 3.01–2.84 (3H, m, C*H*CH$_3$ and 2 x OH), 2.72–2.41 (4H, m, CH$_2$C*H*$_2$CBr and CH$_2$Ph), 1.73–1.58 (4H, m, C*H*$_2$CH(OH)C*H*$_2$), 0.98 (3H, pt, *J* = 6.5, CHC*H*$_3$); ^{13}C NMR (100 MHz; CDCl$_3$) δ 140.3, 140.1 (Ar*C*), 134.4, 134.3 (*C*=CBr), 129.3, 129.2 (Ar*C*H) 128.2 (Ar*C*H), 126.8 (C=*C*Br), 126.1, 126.0 (Ar*C*H) 70.9, 70.5 (*C*HOH), 61.6 (*C*H$_2$OH), 42.6, 42.5 (*C*H$_2$Ph), 38.4, 38.3, 37.9, 37.8, 37.6 (*C*H$_2$*C*H$_2$CH(OH)*C*H$_2$), 36.2, 35.8 (*C*HCH$_3$), 19.4, 19.2 (CH$_3$); HRMS *m*/*z* (M+NH$_4^+$) found: 344.1222. $C_{16}H_{27}{}^{79}BrNO_2$ requires 344.1220.

(−)-(8*R*,*Z*)-6-Bromo-1-iodo-8-methyl-9-phenylnon-6-en-3-ol (SI-3)



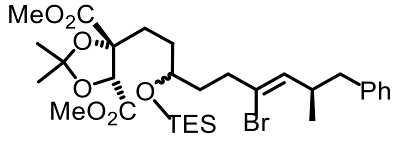
A solution of Ph$_3$P (2.0 g, 7.6 mmol), imidazole (0.9 g, 13 mmol) and I$_2$ (1.0 g, 3.9 mmol) in CH$_2$Cl$_2$ (75 mL) was added dropwise *via* cannula over 30 min to a stirred solution of 1,3-diol 8*R*-**22** (2.2 g, 6.7 mmol) in CH$_2$Cl$_2$ (25 mL) at 0 °C. After a further 1 h at 0 °C, the solution was warmed to rt and stirred overnight. The solution was then re–cooled to 0 °C, and I$_2$ (1.0 g, 3.9 mmol) was added portionwise over 5 min. The suspension was then stirred for 30 min at 0 °C, then filtered through Celite®, washed through with CH$_2$Cl$_2$ (30 mL) and concentrated under reduced pressure. Purification of the residue by column chromatography (3% acetone in petrol) gave iodo alcohol **SI-3** (2.04 g, 70%), as a yellow oil, a 1:1 epimeric mixture at C–3; R_f = 0.24 (3% acetone in petrol); $[\alpha]_D^{23}$ = −32.2 (*c*=1.0, CHCl$_3$); ν_{max}/cm^{-1} (film) 3424 br, 2925 w, 1651 m, 1494 w, 1453 w; ^{1}H NMR (400 MHz; CDCl$_3$) δ 7.31–7.15 (5H, m, ArH), 5.56–5.50 (1H, m, CH=CBr), 3.71–3.63 (0.5H, m, C*H*OH), 3.47–3.39 (0.5H, m, C*H*OH), 3.33–3.16 (2H, m, CH$_2$I), 2.99–2.85 (1H, m, C*H*CH$_3$), 2.72–2.47 (4H, m, CH$_2$ and CH$_2$Ph), 1.99–1.82 (2H, m, CH$_2$), 1.75–1.59 (2H, m, CH$_2$), 1.41 (0.5H, d, *J* = 5.5, CHO*H*), 1.28 (0.5H, d, *J* = 5.5, CHO*H*), 1.03–0.97 (3H, m, CHC*H*$_3$); ^{13}C NMR (100 MHz; CDCl$_3$) δ 140.4, 140.1 (Ar*C*), 134.8, 134.6 (*C*=CBr), 129.3, 129.3 (Ar*C*H) 128.3, 128.3 (Ar*C*H), 126.6, 126.6 (C=*C*Br), 126.1, 126.1 (Ar*C*H), 70.6, 70.2 (*C*HOH), 42.7, 42.6 (*C*H$_2$Ph), 41.2, 40.7, 38.0, 37.9, 37.9, 37.5 (all CH$_2$), 35.6, 34.9 (*C*HCH$_3$), 19.6, 19.3 (CH$_3$), 2.6, 3.0 (CH$_2$I); HRMS *m*/*z* (M+NH$_4^+$) found: 454.0240. $C_{16}H_{26}{}^{79}BrINO$ requires 454.0237.

(−)-(((8*R*,*Z*)-6-Bromo-1-iodo-8-methyl-9-phenylnon-6-en-3-yl)oxy)triethylsilane (16)



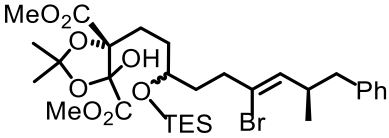
2,6-Lutidine (1.8 mL, 16 mmol) and TESOTf (1.8 mL, 8.2 mmol) were added to a stirred solution of iodo alcohol **SI-3** (2.0 g, 4.5 mmol) in CH_2Cl_2 (140 mL) at −78 °C. After 2 h, the mixture was diluted with sat. aq. $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were washed with HCl (50 mL, 0.1 M), water (2 × 50 mL), brine (2 × 50 mL), dried ($MgSO_4$) and evaporated under reduced pressure. Purification of the residue by column chromatography (10% Et_2O in petrol) gave iodide **16** (2.3 g, 93%), as a colourless oil, a 1:1 epimeric mixture at C–3; R_f = 0.69 (10% Et_2O in petrol); $[\alpha]_D^{23}$ = −26.1 (*c*=1.0, $CHCl_3$); ν_{max}/cm^{-1} (film) 2952 w, 2866 w, 1495 w, 1451 w; ^1H NMR (400 MHz; $CDCl_3$) δ 7.30–7.15 (5H, m, ArH), 5.50 (1H, d, *J* = 8.5, CH=CBr), 3.78–3.69 (1H, m, C*H*OTES), 3.24–3.14 (2H, m, CH_2I), 2.93–2.83 (1H, m, C*H*CH_3), 2.71 (1H, dd, *J* = 13.5, 6.5, CH*H*Ph), 2.53 (1H, dd, *J* = 13.5, 8, C*H*HPh), 2.41 (2H, t, *J* = 7.5, CH_2CBr), 1.98–1.91 (2H, m, CH_2), 1.76–1.59 (2H, m, CH_2), 1.01−0.94 (12H, m, $OSi(CH_2C\mathit{H}_3)_3$ and $CHC\mathit{H}_3$), 0.63 (6H, q, *J* = 7.5, $OSi(C\mathit{H}_2CH_3)_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 140.1 (Ar*C*), 134.2 (*C*=CBr), 129.4 (Ar*C*H) 128.3, 128.3 (Ar*C*H), 126.9 (C=*C*Br), 126.0 (Ar*C*H), 71.2, 71.2 (*C*HOTES), 42.6, 42.6 ($\mathit{C}H_2Ph$), 40.9, 40.8 (CH_2), 38.0 ($\mathit{C}HCH_3$), 37.3, 35.6, 35.5 (all CH_2), 19.2, 19.2 ($CH\mathit{C}H_3$), 7.1 ($OSi(CH_2\mathit{C}H_3)_3$), 5.3 ($OSi(\mathit{C}H_2CH_3)_3$), 3.0, 2.9 ($\mathit{C}H_2I$); HRMS *m*/*z* ($M+NH_4^+$) found: 568.1097. $C_{22}H_{40}{}^{79}BrINOSi$ requires 568.1102.

(−)-Dimethyl (4*R*,5*R*)-4-((8*R*,*Z*)-6-bromo-8-methyl-9-phenyl-3-((triethylsilyl)oxy)non-6-en-1-yl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (8'*R*-14)



A solution of LDA [prepared from *i*-Pr_2NH (300 μL, 2.14 mmol) and *n*-BuLi (1.10 mL, 1.6 M in hexanes, 1.76 mmol)] in THF (10 mL) at −78 ºC, was added dropwise over 3 h to a mixture of dimethyl-2,3-*O*-isopropylidine-*L*-tartrate (**13**) (0.25 mL, 1.36 mmol) and iodide **16** (645 mg, 1.17 mmol) in THF (20 mL) and HMPA (4 mL) at −78 ºC. After 72 h at −78 ºC, the mixture was quenched with sat. aq. NH_4Cl (10 mL) and extracted with Et_2O (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the residue by column chromatography (10% Et_2O in petrol) gave alkylated tartrate 8'*R*-**14** (531 mg, 71%), as a yellow oil, an ~1:1 epimeric mixture at C–3'; R_f = 0.18 (5% Et_2O in petrol); $[\alpha]_D^{23}$ = −42.1 (*c*=1.0, $CHCl_3$); ν_{max}/cm^{-1}(film) 3059 s, 2956 s, 1756 s, 1655 m, 1495 m, 1455 m, 1375 m, 1265 s, 1104 m, 807 s, 743 s, 739 s; ^1H NMR (500 MHz; $CDCl_3$) δ 7.29–7.14 (5H, m, ArH), 5.47 (1H, d, *J* = 8.5, CH=CBr), 4.94 and 4.92 (1H, 2 x s, C*H*(CO_2Me)), 3.82 (3H, s, OMe), 3.80 (3H, s, OMe), 3.65–3.57 (1H, m, C*H*OTES), 2.91–2.82 (1H, m, C*H*CH_3), 2.72–2.67 (1H, m, C*H*HPh), 2.54–2.48 (1H, m, CH*H*Ph), 2.42–2.34 (2H, m, CH_2CBr), 1.97–1.89 (1H, m, C(CO_2Me)C*H*HCH_2CHOTES), 1.81–1.70 (1H, m, C(CO_2Me)CH*H*CH_2CHOTES), 1.64–1.58 (7H, m, C(CO_2Me)CH_2C*H_2*CHOTES, C*H_2*CH_2CBr and one Me of CMe_2), 1.44 (3H, s, one Me of CMe_2), 0.97–0.92 (12H, m, OSi(CH_2C*H_3*$)_3$ and CHC*H_3*), 0.60–0.54 (6H, m, OSi(C*H_2*$CH_3)_3$); ^{13}C NMR (125 MHz; $CDCl_3$) δ 172.6, 172.4 (*C*O_2Me), 169.0, 168.7 (*C*O_2Me), 140.2, 140.2 (Ar*C*), 134.0, 133.9 (*C*=CBr), 129.4 (Ar*C*H) 128.3, 128.3 (Ar*C*H), 127.2 (C=*C*Br), 126.1 (Ar*C*H), 112.9, 112.7 (*C*Me_2), 86.1, 85.7 (*quat.* C), 80.3, 80.3 (*C*HCO_2Me), 71.0, 70.9 (*C*HOTES), 53.0 (OMe), 52.47, 52.45 (OMe), 42.6, 42.6 (*C*H_2Ph), 38.0, 37.5 (*C*HCH_3), 36.1, 36.0, 31.2, 30.9, 30.5, 30.2, 27.9, 27.8 (all CH_2), 26.2, 26.1 (C(*C*$H_3)_2$), 19.2 (CH*C*H_3), 7.1 (OSi(CH_2*C*$H_3)_3$), 5.2 (OSi(*C*$H_2CH_3)_3$); HRMS *m*/*z* ($M+NH_4^+$) found: 658.2766, $C_{31}H_{53}{}^{79}BrNO_7Si$ requires 658.2769.

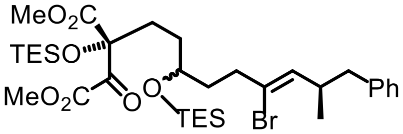
(−)-Dimethyl (4*R*)-4-((8*R*,*Z*)-6-bromo-8-methyl-9-phenyl-3-((triethylsilyl)oxy)non-6-en-1-yl)-5-hydroxy-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (29)



Alkylated tartrate 8'*R*-**14** (1.0 g, 1.55 mmol) in THF (8 mL) at −78 ºC was added over 30 min to a stirred solution of LDA [prepared from *i*-Pr_2NH (0.3 mL, 2.0 mmol) and *n*-BuLi (0.8 mL, 2.5 M in hexanes, 2.0 mmol)] in THF (6 mL) at –78 ºC. After 15 min, MoOPH[2,3] (1.6 g, 3.8 mmol) was added *via* a solid addition tube over 5 min at –78 ºC. The reaction mixture was stirred for additional 30 min, then warmed to −40 ºC. The mixture was stirred at −40 ºC overnight, then warmed to −20 ºC for 1 h before sat. aq. Na_2SO_3 (10 mL) was added. The mixture was then allowed to warm to rt over 1 h, extracted with Et_2O (3 × 20 mL), and the combined organic layers washed with sat. aq. $CuSO_4$ (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the residue by column chromatography (0–50% Et_2O

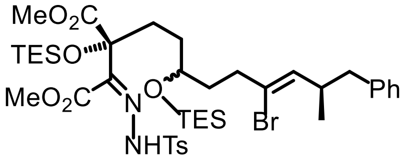
in petrol) gave hydroxy acetonide **29** (726 mg, 71%), as a yellow oil, a mixture of 4 diastereomers; R_f = 0.13 (40% Et_2O in petrol); $[\alpha]_D^{23}$ = −20.1 (*c*=1.0, $CHCl_3$); ν_{max}/cm^{-1}(film) 3426 br, 2963 s, 2086 w, 1752 s, 1644 m, 1421 m, 1264 s, 806 s, 738 s; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.29–7.14 (5H, m, ArH), 5.48–5.43 (1H, m, CH=CBr), 4.06, 4.58, 4.51 and 4.50 (1H, 4 x s, OH), 3.89, 3.80, 3.78 and 3.70 (6H, 4 x s, 2 x OMe), 3.69–3.58 (1H, m, C*H*OTES), 2.90–2.81 (1H, m, C*H*CH_3), 2.72–2.66 (1H, m, C*H*HPh), 2.54–2.47 (1H, m, CH*H*Ph), 2.43–2.35 (2H, m, CH_2CBr), 2.15–1.81 (2H, m, $C(CO_2Me)CH_2CH_2$), 1.78–1.53 (10H, m, CH_2CH_2CBr, $C(CO_2Me)CH_2CH_2$ and CMe_2), 0.98–0.92 (12H, m, $OSi(CH_2CH_3)_3$ and $CHCH_3$), 0.61–0.53 (6H, m, $OSi(CH_2CH_3)_3$); ^{13}C NMR (125 MHz; $CDCl_3$) δ 171.7, 170.3, 170.2, 170.1, 169.3, 169.2 (*C*O_2Me), 140.1, 140.1 (Ar*C*), 134.0, 133.9, 133.8, 133.7 (*C*=CBr), 129.3, 129.3 (Ar*C*H) 128.2, 128.2 (Ar*C*H), 127.3, 127.2, 127.2, 127.1 (C=*C*Br), 126.0, 126.0, 126.0 (Ar*C*H), 114.3, 114.3, 113.6, 113.5 (*C*Me_2), 102.2, 102.0, 101.9, 101.8 (*C*OH), 92.9, 92.7, 91.7, 91.1 (*quat.* C), 70.9, 70.8, 70.7, 70.6 (*C*HOTES), 54.1, 54.1, 54.0, 52.7, 52.5 (OMe), 42.6, 42.6, 42.6, 42.6 (*C*H_2Ph), 38.0, 38.0, 37.9, 37.9 , 37.9, 37.7, 37.5, 37.4, 37.2, 36.0, 35.9, 35.7, 31.9, 31.9, 31.4, 31.3, 31.3, 31.2, 31.2, 30.9 29.3, 29.2, 28.7, 28.6, 28.4, 28.3, 27.5, 27.5, then 19.1, 19.1 (CH*C*H_3), 7.1 ($OSi(CH_2CH_3)_3$), 5.2, 5.2, 5.2, 5.1 ($OSi(CH_2CH_3)_3$); HRMS *m/z* (M+H$^+$) found: 657.2454. $C_{31}H_{50}{}^{79}BrO_8Si$ requires 657.2453.

(−)-Dimethyl (2*R*)-2-((8*R,Z*)-6-bromo-8-methyl-9-phenyl-3-((triethylsilyl)oxy)non-6-en-1-yl)-3-oxo-2-((triethylsilyl)oxy)succinate (30)



A mixture of hydroxy acetonide **29** (302 mg, 0.46 mmol) and H_2SO_4 (40 mL, 0.1 M in MeOH) was stirred at rt. After 24 h, pyridine (1.0 mL, 12.4 mmol) was added, the mixture was concentrated under reduced pressure and the residue was diluted with Et_2O (30 mL) and filtered. The filtrate was concentrated under reduced pressure to give the corresponding lactol which was used in the next step without further purification. To the crude lactol in dry DMF (2 mL) at −10 °C was added TESCl (0.50 mL, 2.98 mmol) and imidazole (272 mg, 4.0 mmol). The reaction mixture was stirred at −10 °C for 24 h, and then at rt for 24 h. The mixture was then concentrated under reduced pressured and purified by chromatography (florisil®, 0−20% Et_2O in petrol) to give bis-TES ether **30** (313 mg, 95%), as a colourless oil, an ~1:1 epimeric mixture at C–3'; R_f = 0.7 (60% Et_2O in petrol); $[\alpha]_D^{23}$ = −18.6 (*c*=1.0, $CHCl_3$); ν_{max}/cm^{-1}(film) 3055 m, 2957 s, 2877 m, 1741 s, 1455 m, 1266 s, 1092 m, 1015 m, 739 s; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.29−7.15 (5H, m, ArH), 5.49 (1H, d, *J* = 8.5, CH=CBr), 3.84 (3H, s, OMe), 3.77 (3H, s, OMe), 3.70−3.63 (1H, m, C*H*OTES), 2.94−2.83 (1H, m, C*H*CH_3), 2.75−2.66 (1H, m, C*H*HPh), 2.57–2.49 (1H, m, CH*H*Ph), 2.41 (2H, t, *J* = 7.5, CH_2CBr), 2.24−1.92 (2H, m, C(CO_2Me)C*H*$_2$$CH_2$), 1.72−1.45 (4H, m, C*H*$_2$$CH_2$CBr and C($CO_2$Me)$CH_2$C*H*$_2$), 1.00−0.91 (21H, m, 2 × OSi(CH_2C*H*$_3$)$_3$ and CHC*H*$_3$), 0.73−0.56 (12H, m, 2 × OSi(C*H*$_2$$CH_3$)$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 190.8 (C=O), 170.0 (*C*O_2Me), 162.9 (*C*O_2Me), 140.0 (ArC), 133.8 (*C*=CBr), 129.2 (ArCH), 128.1 (ArCH), 127.1 (C=*C*Br), 125.9 (ArCH), 84.0, 84.0 (*quat* C), 77.6, 70.5 (*C*HOTES), 52.8, 52.6, 52.6 (2 x OMe), 42.5, 42.5 (*C*H_2Ph), 37.9, 37.8 (*C*HCH_3), 37.4, 37.2, 35.5, 35.3, 32.5, 32.2, 30.1, 29.7 (all CH_2), 19.0, 19.0 (CH*C*H_3), 6.9, 6.8, 6.7, 6.6 (OSi(CH_2*C*H_3)$_3$), 5.8, 5.7, 5.1, 5.0 (OSi(*C*$H_2$$CH_3$)$_3$); HRMS *m*/*z* (M+$NH_4^+$) found: 730.3168. $C_{34}H_{61}{}^{79}BrNO_7Si_2$ requires 730.3164.

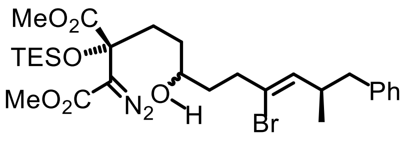
(−)-Dimethyl (*Z*)-2-((8*R*,*Z*)-6-bromo-8-methyl-9-phenyl-3-((triethylsilyl)oxy)non-6-en-1-yl)-3-(2-(*p*-tolyl)hydrazineylidene)-2-((triethylsilyl)oxy)succinate (SI-4)



A mixture of bis-TES ether **30** (90 mg, 0.126 mmol) and $TsNHNH_2$ (35 mg, 0.19 mmol) in THF (1.5 mL) was refluxed for 20 h. The mixture was concentrated under reduced pressure and purified by column chromatography (0−60% Et_2O in petrol) to give *Z*^{10}-hydrazone **SI-4** (52 mg, 47% (58% brsm)), as a pale yellow oil, an ~1:1 epimeric mixture at C–3'; R_f = 0.61 (60% Et_2O in petrol); $[\alpha]_D^{23}$ = −21.5 (*c*=1.0, $CHCl_3$); ν_{max}/cm^{-1}(film) 3180 br, 2956 m, 2932 m, 1752 s, 1704 s, 1496 m, 1053 m; ^{1}H NMR (400 MHz; $CDCl_3$) δ 11.72 , 11.69 (1H, 2 x s, NH), 7.84 (2H, d, *J* = 8.5, 2 x ArCH), 7.32−7.23 (4H, m, 4 x ArCH), 7.30−7.14 (3H, m, 3 x ArCH), 5.52 (1H, d, *J* = 8.5, CH=CBr), 3.75 (3H, s, OMe), 3.67 (3H, s, OMe), 3.65−3.59 (1H, m, C*H*OTES), 2.94−2.83 (1H, m, C*H*CH_3), 2.72 (1H, dd, *J* = 13.5, 6, CH*H*Ph), 2.54−2.47 (1H, m, CH*H*Ph), 2.45−2.36 (3H, s, Ar−*Me* and 2H, m, CH_2CBr), 2.08−1.82 (2H, m, C(CO_2Me) C*H*$_2$$CH_2$CHOTES), 1.71−1.59 (2H, m, CH_2), 1.50−1.37 (1H, m, CH*H*), 1.35−1.24 (1H, m, C*H*H), 1.00−0.93 (12H, m, OSi(CH_2C*H*$_3$)$_3$ and CHC*H*$_3$), 0.80−0.74 (9H, m, OSi(CH_2C*H*$_3$)$_3$), 0.64−0.56 (6H, m, OSi(C*H*$_2$$CH_3$)$_3$), 0.42−0.33 (6H, m, OSi(C*H*$_2$$CH_3$)$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.4, 172.4 (*C*O_2Me), 162.0 (NC*C*O_2Me), 144.6, 140.1 (Ar*C*), 137.1, 137.0

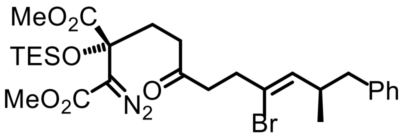
(*C*=CBr), 135.6 (Ar*C*Me), 133.9, 133.9 (N*C*CO$_2$Me), 129.8, 129.3, 128.2, 128.2 , 128.1 128.1(Ar*C*H), 127.5, 127.4 (C=*C*Br), 126.0 (Ar*C*H), 80.9, 80.7 (*quat. C*), 71.3, 71.1 (*C*HOTES), 52.4, 52.3 (OMe), 42.6, 42.6 (*C*H$_2$Ph), 38.0, 38.0, 37.6, 37.3, 36.2, 35.9, 33.7, 33.1, 31.1, 31.0, then 21.7 (Ar−*Me*), 19.1, 19.1 (CH*C*H$_3$), 7.1, 7.1, (OSi(CH$_2$*C*H$_3$)$_3$), 7.0 (OSi(CH$_2$*C*H$_3$)$_3$), 6.3 (OSi(*C*H$_2$CH$_3$)$_3$), 5.3, 5.2 (OSi(*C*H$_2$CH$_3$)$_3$); HRMS *m*/*z* (M+NH$_4^+$) found: 898.3526. $C_{41}H_{69}{}^{79}BrN_3O_8SSi_2$ requires 898.3522.

(−)-Dimethyl 2-((8*R*,*Z*)-6-bromo-3-hydroxy-8-methyl-9-phenylnon-6-en-1-yl)-3-diazo-2-((triethylsilyl)oxy)succinate (SI-5)



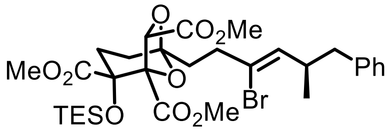
To the *Z*-hydrazone **SI-4** (66 mg, 0.075 mmol) in CH$_2$Cl$_2$ (200 μL) was added Et$_3$N (50 μL, 0.36 mmol) dropwise at rt. After 2 h, the mixture was concentrated to give a (6:4) mixture of diazo bis−TES ether and diazo alcohol **SI-5**; to this mixture in THF (300 μL) was added AcOH (150 μL) and water (150 μL). After 5 h stirring at rt, the mixture was quenched with aq. sat. NaHCO$_3$ (2 mL), extracted with EtOAc (2 x 5 mL), dried (MgSO$_4$) and concentrated under reduced pressure. Purification of the residue by column chromatography (10−30% Et$_2$O in petrol) gave diazo alcohol **SI-5** (42 mg, 92%, from **SI-4**), as a yellow oil, an ~1:1 epimeric mixture at C–3'; R_f = 0.34 (30% Et$_2$O in petrol); $[\alpha]_D^{23} = -23.4$ (*c*=1.0, CHCl$_3$); ν_{max}/cm^{-1} (film) 3518 m, 3027 w, 2955 s, 2877 s, 2098 s, 1747 s, 1707 s, 1495 m, 1437 s, 1315 s, 1141 m, 742 s; ^{1}H NMR (400 MHz; CDCl$_3$) δ 7.29−7.14 (5H, m, ArH), 5.53−5.45 (1H, m, CH=CBr), 3.77−3.71 (6H, m, 2 x OMe), 3.70−3.61 and 3.57−3.49 (1H, m, C*H*OH), 2.98−2.82 (1H, m, C*H*CH$_3$), 2.73−2.34 (4H, m, CH$_2$Ph, and CH$_2$CBr), 2.18−1.84 (2H, m, C(CO$_2$Me)C*H*$_2$CH$_2$), 1.73−1.34 (4H, m, C*H*$_2$CH(OH)C*H*$_2$), 1.02−0.91 (12 H, m, OSi(CH$_2$C*H*$_3$)$_3$ and CHC*H*$_3$), 0.66−0.55 (6H, m, OSi(C*H*$_2$CH$_3$)$_3$); ^{13}C NMR (100 MHz; CDCl$_3$) δ 171.9, 171.8 (*C*O$_2$Me), 165.3 (NC*C*O$_2$Me), 140.4, 140.1 (Ar*C*), 134.5, 134.3 (*C*=CBr), 129.3, 129.3 (Ar*C*H) 128.3, 128.2 (Ar*C*H), 126.9, 126.8 (C=*C*Br), 126.2, 126.0 (Ar*C*H), 76.2, 176.0 (*quat. C*), 70.4, 69.6 (*C*HOH), 64.9 (C=N$_2$), 52.9, 52.8 (OMe), 52.0, 51.9 (OMe), 42.8, 42.6 (*C*H$_2$Ph), 37.9, 37.6 (*C*HCH$_3$), 63.1, 35.3, 34.6, 31.5, 29.8 (all CH$_2$), then 19.5, 19.3 (CH*C*H$_3$), 7.0, 6.7 (OSi(CH$_2$*C*H$_3$)$_3$), 5.9, 5.2 (OSi(*C*H$_2$CH$_3$)$_3$); HRMS *m*/*z* (M+NH$_4^+$) found: 628.2414. $C_{28}H_{47}{}^{79}BrN_3O_6Si$ requires 628.2412.

(−)-Dimethyl 2-((*R,Z*)-6-bromo-8-methyl-3-oxo-9-phenylnon-6-en-1-yl)-3-diazo-2-((triethylsilyl)oxy)succinate (13)



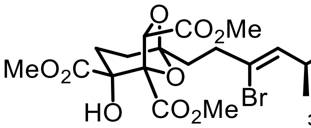
To diazo alcohol **SI-5** (54 mg, 0.088 mmol) in CH_2Cl_2 (2 mL) at rt was added Dess−Martin periodinane (88 mg, 0.21 mmol). After 3 h, the mixture was filtered through Celite® and then purified by column chromatography (10−40% Et_2O in petrol) to give ketone **13** (51 mg, 95%), as a yellow oil; $R_f = 0.57$ (60% Et_2O in petrol); $[\alpha]_D^{23} = -24.9$ (c=1.0, $CHCl_3$); ν_{max}/cm^{-1}(film) 2956 s, 2877 s, 2098 s, 1711 s, 1437 s, 1260 s, 1138 m, 738 s; ^1H NMR (500 MHz; $CDCl_3$) δ 7.28−7.12 (5H, m, ArH), 5.53 (1H, d, J = 8.5, CH=CBr), 3.75 (3H, s, OMe), 3.73 (3H, s, OMe), 2.89−2.79 (1H, m, C*H*CH_3), 2.70−2.49 (7H, m, CH_2Ph, CH*H* and 2 x CH_2), 2.44−2.37 (1H, m, CH*H*) 2.29−2.18 (2H, m, CH_2), 0.97−0.90 (12H, m, $OSi(CH_2CH_3)_3$ and $CHCH_3$), 0.65−0.55 (6H, m, $OSi(CH_2CH_3)_3$); ^{13}C NMR (125 MHz; $CDCl_3$) δ 207.7 (C=O), 171.5 (CO_2Me), 165.2 ($NCCO_2Me$), 140.0 (Ar*C*), 135.1 (*C*=CBr), 129.4 (Ar*C*H) 128.2 (Ar*C*H), 126.1 (Ar*C*H), 125.5 (C=*C*Br), 75.5 (*quat. C*), 64.8 (C=N_2), 53.0 (OMe), 52.1 (OMe), 42.5 (CH_2Ph), 41.7 (CH_2), 38.0 ($CHCH_3$), 37.4 (CH_2), 35.7 (CH_2), 32.3 (CH_2), 19.1 ($CHCH_3$), 7.0 ($OSi(CH_2CH_3)_3$), 5.8 ($OSi(CH_2CH_3)_3$); HRMS *m*/*z* ($M+NH_4^+$) found: 626.2246. $C_{28}H_{45}{}^{79}BrN_3O_6Si$ requires 626.2256.

(−)-Trimethyl (1*S*,2*R*,5*R*,7*S*)-5-((*R*,*Z*)-3-bromo-5-methyl-6-phenylhex-3-en-1-yl)-2-((triethylsilyl)oxy)-6,8-dioxabicyclo[3.2.1]octane-1,2,7-tricarboxylate (12)



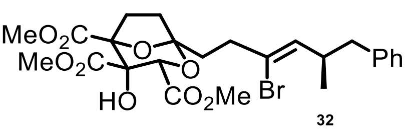
A mixture of ketone **13** (26 mg, 0.043 mmol), freshly distilled methyl glyoxylate[11] (25 mg, 0.28 mmol) and $Rh_2(OAc)_4$ (~1 mg, cat) in toluene (1.5 mL) was refluxed at 110 °C for 2 h. The mixture was then concentrated under reduced pressure and purified by column chromatography (0−20% EtOAc in petrol) to give cycloadduct **12** (19 mg, 66%), as a colourless oil; R_f = 0.39 (60% Et_2O in petrol); $[\alpha]_D^{23} = -13.7$ (c=1.0, $CHCl_3$); ν_{max}/cm^{-1}(film) 2955 s, 2876 s, 1840 s, 1755 s, 1495 s, 1438 s, 1375 m, 1264 s, 1197 m, 1013 s, 738 s; ^1H NMR (500 MHz; $CDCl_3$) δ 7.26−7.15 (5H, m, ArH), 5.59 (1H, d, J = 8.5, CH=CBr), 5.55 (1H, s, C*H*CO_2Me), 3.81 (3H, s, OMe), 3.70 (3H, s, OMe), 3.69 (3H, s, OMe), 2.92−2.83 (1H, m, C*H*CH_3), 2.75−2.65 (3H, m, CH_2CH_2CBr and CH*H*Ph), 2.5 (1H, ddd, J = 13.5, 8, C*H*HPh), 2.40 (1H, ddd, *J* = 14, 12.5, 6, 1H$_{endo}$ of TESOC(CO$_2$Me)CH*H*CH$_2$), 2.17−2.06 (2H, m, CH$_2$CBr), 1.87 (1H, td, *J* = 13, 5.5, 1H$_{endo}$ of TESOC(CO$_2$Me)CH$_2$CH*H*), 1.76 (1H, pdd, *J* = 14, 5, TESOC(CO$_2$Me)CH*H*CH$_2$), 1.66 (1H, pdd, *J* = 13, 5.5, TESOC(CO$_2$Me)CH$_2$CH*H*), 0.97−0.91 (12H, m, OSi(CH$_2$C*H*$_3$)$_3$ and CHC*H*$_3$), 0.69−0.59 (6H, m, OSi(C*H*$_2$CH$_3$)$_3$); ^{13}C NMR (125 MHz; CDCl$_3$) δ 173.4 (*C*O$_2$Me), 169.4 (*C*O$_2$Me), 166.8 (*C*O$_2$Me), 140.2 (Ar*C*), 134.1 (*C*=CBr), 129.4 (Ar*C*H) 128.2 (Ar*C*H), 126.7 (C=*C*Br), 126.0 (Ar*C*H), 111.1 (O−C−O), 90.3 (TESOC*C*CO$_2$Me), 77.5 (*C*HCO$_2$Me), 77.3 (TESO*C*CO$_2$Me), 52.7 (OMe), 52.6 (OMe), 52.5 (OMe), 42.6 (*C*H$_2$Ph), 38.0 (*C*HCH$_3$), 35.9, 35.1, 29.9, 29.8 (4 x CH$_2$), 19.1 (CH*C*H$_3$), 7.2 (OSi(CH$_2$*C*H$_3$)$_3$), 6.7 (OSi(*C*H$_2$CH$_3$)$_3$); HRMS *m*/*z* (M+NH$_4^+$) found: 686.2351. $C_{31}H_{49}{}^{79}BrNO_9Si$ requires 686.2354.

(−)-Trimethyl (1*S*,2*R*,5*R*,7*S*)-5-((*R*,*Z*)-3-bromo-5-methyl-6-phenylhex-3-en-1-yl)-2-hydroxy-6,8-dioxabicyclo[3.2.1] octane-1,2,7-tricarboxylate (31) and (−)-Trimethyl (1*R*,3*S*,4*S*,5*R*)-1-((*R*,*Z*)-3-bromo-5-methyl-6-phenylhex-3-en-1-yl)-4-hydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (32)



31

and



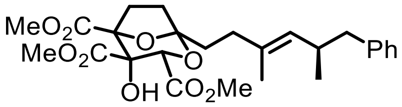
32

To a solution of cycloadduct **12** (19 mg, 0.028 mmol) in CH$_2$Cl$_2$ (210 μL) were added TFA (105 μL) and H$_2$O (10.5 μL). The reaction mixture was heated at 40 °C for 48 h. The mixture was then concentrated under reduced pressure and purified by column chromatography (5−30% EtOAc in petrol). First eluted, cycloadduct alcohol **31** (3 mg, 19%), as a colourless oil; *R$_f$* = 0.48 (100% Et$_2$O in petrol); $[\alpha]_D^{23}$ = −8.2 (*c*=1.0, CHCl$_3$); ν$_{max}$/cm^{-1}(film) 3462 br, 2925 s, 1736 s, 1456 s, 1260 s, 1092 m, 796 s, 737 s; ^{1}H NMR (500 MHz; CDCl$_3$) δ 7.26−7.14 (5H, m, ArH), 5.58 (1H, d, *J* = 8.5, CH=CBr), 5.47 (1H, s, C*H*CO$_2$Me), 3.92 (3H, s, OMe), 3.75 (3H, s, OMe), 3.71 (3H, s, OMe), 2.94−2.83 (1H, m, C*H*CH$_3$), 2.82−2.55 (3H, m, C*H*$_2$CH$_2$CBr and CH*H*Ph), 2.51 (1H, dd, *J* = 13.5, 8, C*H*HPh), 2.36−2.27 (1H, m, TESOC(CO$_2$Me)CH*H*CH$_2$), 2.25−1.92 (4H, m, CH$_2$CBr, TESOC(CO$_2$Me)CH*H*CH$_2$ and TESOC(CO$_2$Me)CH$_2$CH*H*), 1.81−1.73 (1H, m, TESOC(CO$_2$Me)CH$_2$CH*H*), 0.95 (3H, d, *J* = 6.5, CHC*H*$_3$); ^{13}C NMR (125 MHz; CDCl$_3$) δ 173.8 (*C*O$_2$Me), 169.1 (*C*O$_2$Me), 166.9 (*C*O$_2$Me), 140.2 (Ar*C*), 134.3 (*C*=CBr), 129.4 (Ar*C*H) 128.3 (Ar*C*H), 126.7 (C=*C*Br), 126.0 (Ar*C*H), 111.8 (O−C−O), 89.4 (TESOC*C*CO$_2$Me), 77.7 (*C*HCO$_2$Me), 74.1 (TESO*C*CO$_2$Me), 52.9 (OMe), 53.2 (OMe), 52.7 (OMe), 42.6 (*C*H$_2$Ph), 38.0 (*C*HCH$_3$), 35.8, 34.9, 29.9, 29.5 (4 x

CH_2), 19.1 (CH*C*H_3); HRMS *m*/*z* (M+NH_4^+) found: 572.1491. $C_{25}H_{35}{}^{79}BrNO_9$ requires 572.1490.

Second eluted, alkenyl bromide **32** (5.5 mg, 35%) as a colourless oil; R_f = 0.40 (100% Et_2O in petrol); $[\alpha]_D^{23} = -7.3$ (*c*=1.0, $CHCl_3$); ν_{max}/cm^{-1} (film) 3452 br, 2923 s, 1731 s, 1456 s, 1261 s, 1093 m, 795 s, 731 s; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.29−7.14 (5H, m, ArH), 5.58 (1H, d, *J* = 8.5, CH=CBr), 4.79 (1H, s, C*H*CO_2Me), 3.89 (3H, s, OMe), 3.77 (6H, s, 2 x OMe), 3.65 (1H, s, OH), 3.06−2.98 (1H, m, H_{endo} of C(CO_2Me)CH*H*CH_2), 2.95−2.85 (1H, m, C*H*CH_3), 2.71−2.55 (4H, m, CH_2Ph and CH_2), 2.26−2.14 (2H, m, CH_2), 2.05−1.93 (2H, m, CH_2), 1.90−1.82 (1H, m, H_{exo} of C(CO_2Me)CH*H*CH_2), 0.98 (3H, d, *J* = 6.5, CHC*H*$_3$); ^{13}C NMR (125 MHz; $CDCl_3$) δ 170.0 (*C*O_2Me), 168.8 (*C*O_2Me), 167.5 (*C*O_2Me), 140.3 (Ar*C*), 134.8 (*C*=CBr), 129.3 (Ar*C*H) 128.3 (Ar*C*H), 126.4 (C=*C*Br), 126.2 (Ar*C*H), 108.5 (O−*C*−O), 88.0 (*C*CO_2Me), 75.2 (*C*OH), 74.9 (*C*HCO_2Me), 53.5 (OMe), 53.0 (OMe), 52.8 (OMe), 42.7 (*C*H_2Ph), 38.0 (*C*HCH_3), 36.0, 35.4, 31.4, 29.3 (4 x CH_2), 19.5 (CH*C*H_3); HRMS *m*/*z* (M + NH_4^+) found: 572.1490. $C_{25}H_{35}{}^{79}BrNO_9$ requires 572.1490.

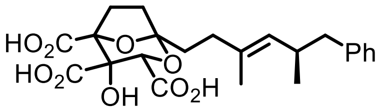
(−)-Trimethyl (1*S*,3*S*,4*S*,5*R*)-1-((*R*,*E*)-3,5-dimethyl-6-phenylhex-3-en-1-yl)-4-hydroxy-2,8-Dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylate (33)



To a solution of 9-MeO-9-BBN (7 µL, 1.0 M in hexane, 0.007 mmol) in THF (30 µL) was added MeLi (6 µL, 1.2 M in Et_2O, 0.007 mmol) and stirred for 5 min at rt. Meanwhile, a mixture of $PdCl_2$(dppf) (0.4 mg, 15 mol%), Cs_2CO_3 (3.5 µL, 3 M in MeOH), Ph_3As (0.4 mg, 40 mol%) and alkenyl bromide **32** (3 mg, 0.0036 mmol) in DMF (30 µL) was prepared at rt. To the mixture containing **32** and the catalyst system, the borinate complex solution was added dropwise and then the reaction mixture was stirred at 40 °C for 6 h. The reaction mixture was then quenched with water (1 mL), extracted with EtOAc (3 × 4 mL), and the combined organic layers washed with brine (2 mL) and dried ($MgSO_4$). Evaporation under reduced pressured followed by column chromatography (0−40% EtOAc in petrol) gave 6,7-dideoxysqualestatin H5 trimethyl ester **33** (0.8 mg, 45%) as a colourless oil, R_f = 0.15 (40% EtOAc in petrol); $[\alpha]_D^{25} = -37.9$ (*c*= 0.53, $CHCl_3$); ν_{max}/cm^{-1} (film) 3078 br, 2956 s, 2925 s, 2854 s, 1768 s, 1739 s, 1439 s, 1266 s; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.24–7.11 (5H, m, ArCH), 5.02 (1H, d, *J* = 9, C*H*=CCH_3), 4.86 (1H, s, C*H*CO_2Me), 3.89 (3H, s, OMe), 3.77 (3H, s, OMe), 3.76 (3H, s, OMe), 3.16–3.05 (1H, m, H_{endo} of C(CO_2Me)CH*H*CH_2), 2.67–2.58 (1H, m, C*H*CH_3), 2.54–

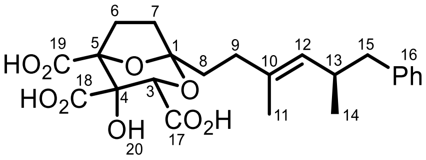
2.48 (2H, m, CH$_2$Ph), 2.21–1.95 (8H, m, H*exo* of C(CO$_2$Me)CH*H*CH$_2$, C(CO$_2$Me)CH$_2$C*H*$_2$, C*H*$_2$C*H*$_2$CMe and OH), 1.46 (3H, d, *J* = 1.5, =CCH$_3$), 0.93 (3H, d, *J* = 6.5, CHC*H*$_3$); ^{13}C NMR (125 MHz; CDCl$_3$) δ 170.1 (*C*O$_2$Me), 168.9 (*C*O$_2$Me), 167.7 (*C*O$_2$Me), 141.3 (*C*=CH), 133.2 (Ar*C*), 130.8 (C=*C*H), 129.4 (Ar*C*H), 128.2 (Ar*C*H), 125.8 (ArCH), 109.3 (O−*C*−O), 88.2 (*C*CO$_2$Me), 75.3 (*C*OH), 75.0 (*C*HCO$_2$Me), 53.5 (OMe), 53.0 (OMe), 52.8 (OMe), 44.1 (*C*H$_2$Ph), 35.2 (*C*HCH$_3$), 34.7, 33.5, 31.3, 29.3 (4 x CH$_2$), 21.0 (CH*C*H$_3$), 16.3 (=C*C*H$_3$); HRMS *m/z* (M+Na$^+$) found 513.2094, $C_{26}H_{34}O_9Na$ requires 513.2095.

(−)-(1*S*,3*S*,4*S*,5*R*)-1-((*R*,*E*)-3,5-Dimethyl-6-phenylhex-3-en-1-yl)-4-hydroxy-2,8-dioxabicyclo [3.2.1]octane-3,4,5-tricarboxylic acid (6,7-dideoxysqualestatin H5) (5)



To a mixture of 6,7–dideoxysqualestatin H5 trimethyl ester **33** (2.0 mg, 0.0041 mmol) and KO*t*-Bu (5.0 mg, 0.045 mmol) was added 1,4–dioxane (0.25 mL) and H$_2$O (0.36 mL) at 0 °C, and then slowly warmed to rt over 1 h and left to stir for 2 h. The reaction mixture was then refluxed at 110 °C overnight. The solvent was evaporated, and H$_2$O (2.5 mL) added. The mixture was washed with Et$_2$O (2 x 2.5 mL), acidified with HCl (1 mL, 0.1 M), extracted with EtOAc (3 x 5 mL) and the combined organic layers washed with brine (2.5 mL). The combined organic layers were evaporated under reduced pressure to give 1.6 mg of material that was re–dissolved in MeOH (0.5 mL). The solution was extracted with *n*-hexane (2 x 0.5 mL), and the methanolic layer was concentrated under reduced pressure to give 6,7-dideoxysqualestatin H5 (**5**) (1.4 mg 78%); $[\alpha]_D^{25} = -12.9$ (*c*= 0.09, MeOH); ν_{max}/cm^{-1}(film) 3437 br, 2956 w, 2530 br, 1730 s, 1452 w, 1050 s, 880 s; ^{1}H NMR (500 MHz; CD$_3$OD) δ 7.23 (2H, t, *J* = 7.5, ArCH), 7.16–7.11 (3H, m, ArCH), 5.04 (1H, d, *J* = 9, C*H*=CCH$_3$), 4.84 (1H, s, C*H*CO$_2$Me), 3.79 (1H, s, OH), 3.23–3.15 (1H, m, H*endo* of C(CO$_2$Me)CH*H*CH$_2$), 2.70–2.62 (1H, m, C*H*CH$_3$), 2.59 (1H, dd, *J* = 13, 6, C*H*HPh), 2.48 (1H, dd, *J* = 13, 8, CH*H*Ph), 2.22–2.10 (2H, m, C(CO$_2$Me)CH$_2$C*H*$_2$), 2.08–1.94 (4H, m, C*H*$_2$C*H*$_2$CCH$_3$), 1.90–1.84 (1H, m, 1H*exo* of C(CO$_2$Me)C*H*HCH$_2$), 1.43 (3H, d, *J* = 1, CC*H*$_3$), 0.96 (3H, d, *J* = 6.5, CHC*H*$_3$); ^{13}C NMR (125 MHz; CD$_3$OD) δ 173.5 (CO$_2$H), 172.5 (CO$_2$H), 171.2 (CO$_2$H), 142.4 (ArC), 135.0 (*C*=CH), 131.7 (C=*C*H), 130.3 (ArCH), 129.0 (ArCH), 126.7 (ArCH), 109.8 (O–C–O), 89.5 (*C*CO$_2$Me), 76.2 (*C*OH), 75.9 (*C*HCO$_2$Me), 45.1 (*C*H$_2$Ph), 36.5 (*C*HCH$_3$), 35.9 (C(CO$_2$Me)*C*H$_2$CH$_2$), 34.7 (C(CO$_2$Me)CH$_2$*C*H$_2$), 32.2 (CH$_2$*C*H$_2$CCH$_3$), 30.3 (*C*H$_2$CH$_2$CCH$_3$), 21.4 (CH*C*H$_3$), 16.1 (C*C*H$_3$); HRMS *m/z* (M+Na$^+$) found: 471.1625, $C_{23}H_{28}O_9Na$ requires 471.1626.

3. NMR data comparison of synthetic 6,7-dideoxysqualestatin H5 (5) with natural isolate[12]



Position*	Natural Isolate[12]		Synthetic	
	^{1}*H NMR*	^{13}*C NMR*	^{1}*H NMR*	^{13}*C NMR*
1		109.8		109.8
3		75.7	4.84 (1H, s, C*H*CO$_2$Me)	75.9
4		76.0		76.2
4-OH			3.79 (1H, s, OH)	
5		89.3		89.5
6	3.18 (1H, m) 1.87 (1H, m)	35.8	3.22–3.15 (1H, m) 1.90–1.84 (1H, m)	35.9
7	2.23–2.09 (2H, m)	34.6	2.22–2.10 (2H, m)	34.7
8	2.0–1.90 (4H, m)	30.3	2.08–1.94 (4H, m)	30.3
9		32.0		32.2
10		142.3		142.4
11	1.44 (3H, d, *J* 1)	21.3	1.43 (3H, d, *J* 1)	21.4
12	5.04 (1H, m)	131.7	5.04 (1H, d, *J* 9)	131.7
13	2.66 (1H, m)	36.3	2.70–2.62 (1H, m)	36.5
14	0.96 (3H, d, *J* 7)	16.0	0.96 (3H, d, *J* 6.5)	16.1
15	2.59 (1H, dd, *J* 13, 6) 2.47 (1H, dd, *J* 13, 8)	45.0	2.59 (1H, dd, *J* 13, 6) 2.48 (1H, dd, *J* 13, 8)	45.1
16 Aromatic ring	7.23 (2H, t, *J* 7) 7.17–7.10 (3H, m)	134.9 130.2 128.9 126.6	7.24–7.20 (2H, m) 7.15–7.12 (3H, m)	135.0 130.3 129.0 126.7
17−19 *C*OOH		173.1 172.1 170.8		173.5 172.5 171.2

*NMR spectra of the natural isolate were recorded on a Bruker AM500, while the synthetic spectra were recorded on a Bruker AVC500 (^{1}H NMR–500 MHz and ^{13}C NMR–125 MHz, CD$_3$OD).

4. References

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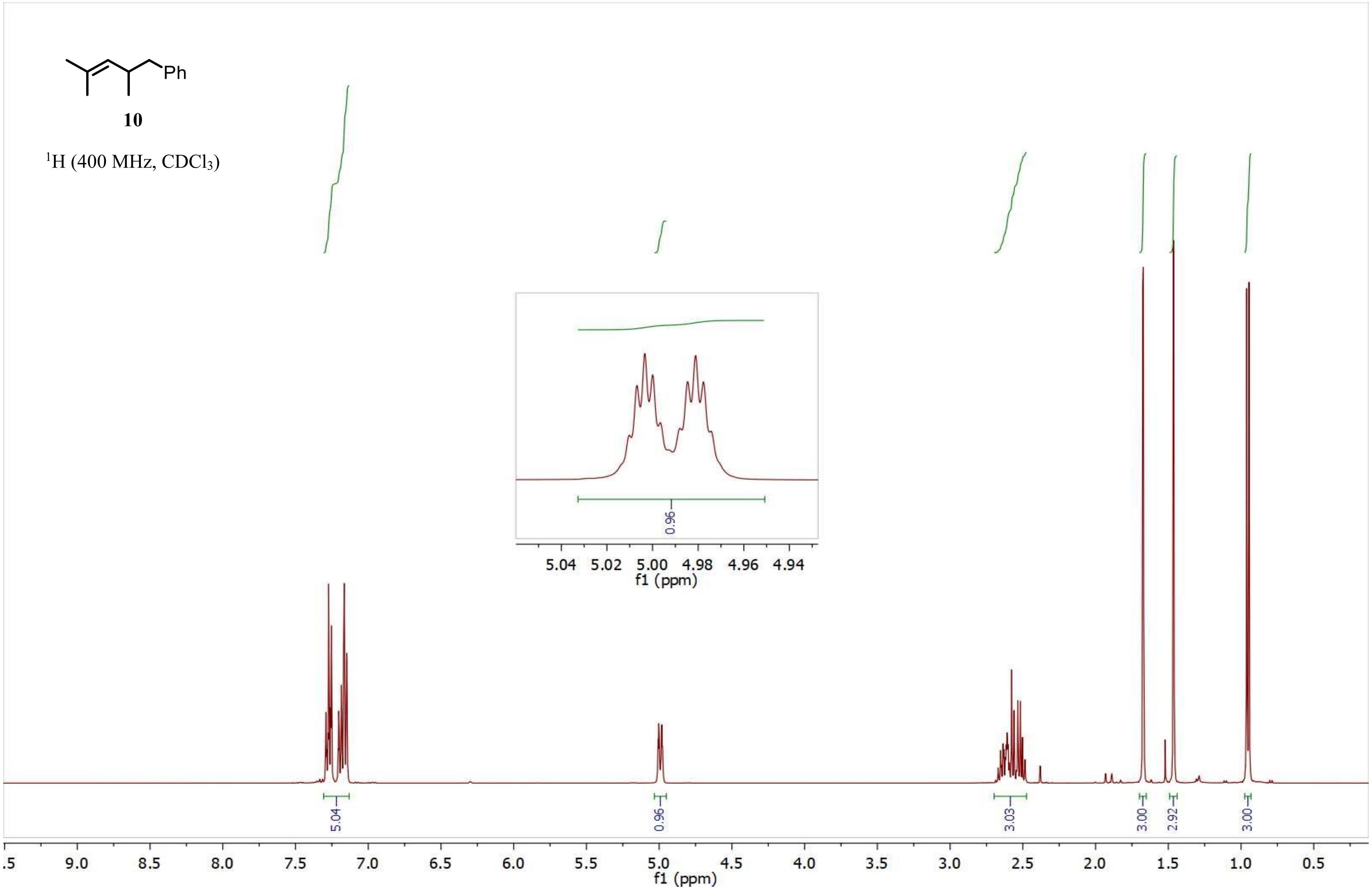
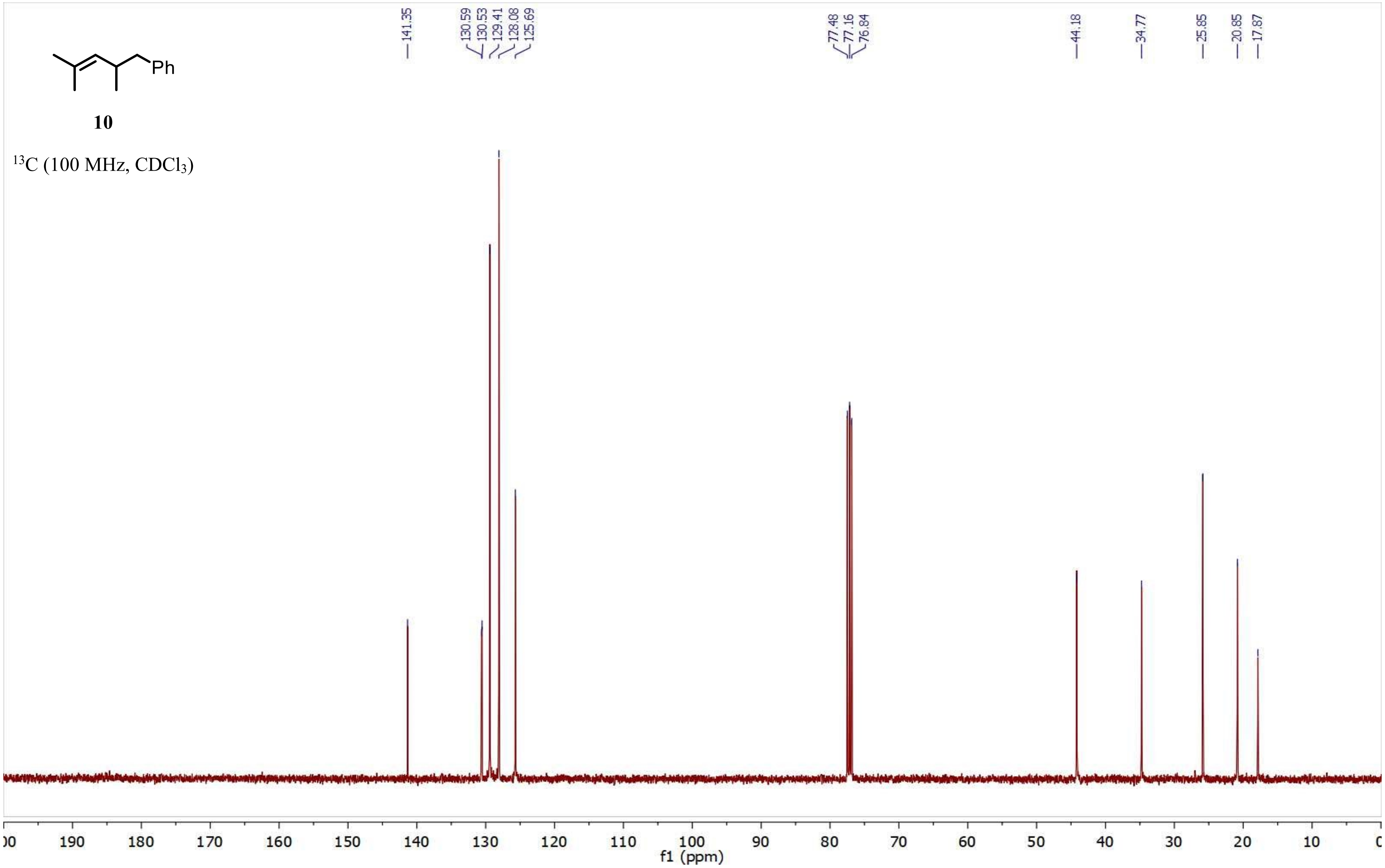
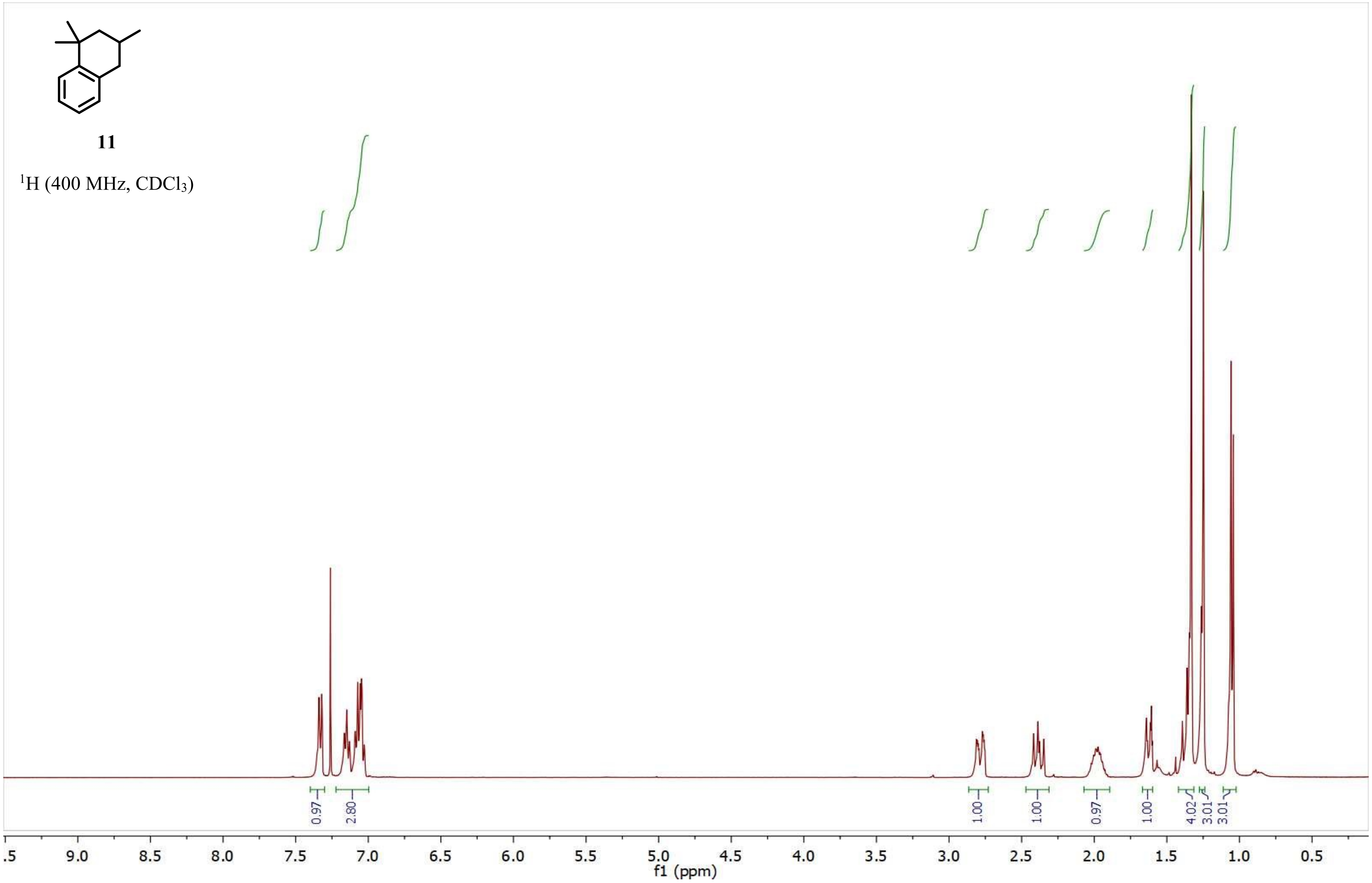
5. ^{1}H and ^{13}C NMR Spectra





10

^{13}C (100 MHz, CDCl$_3$)

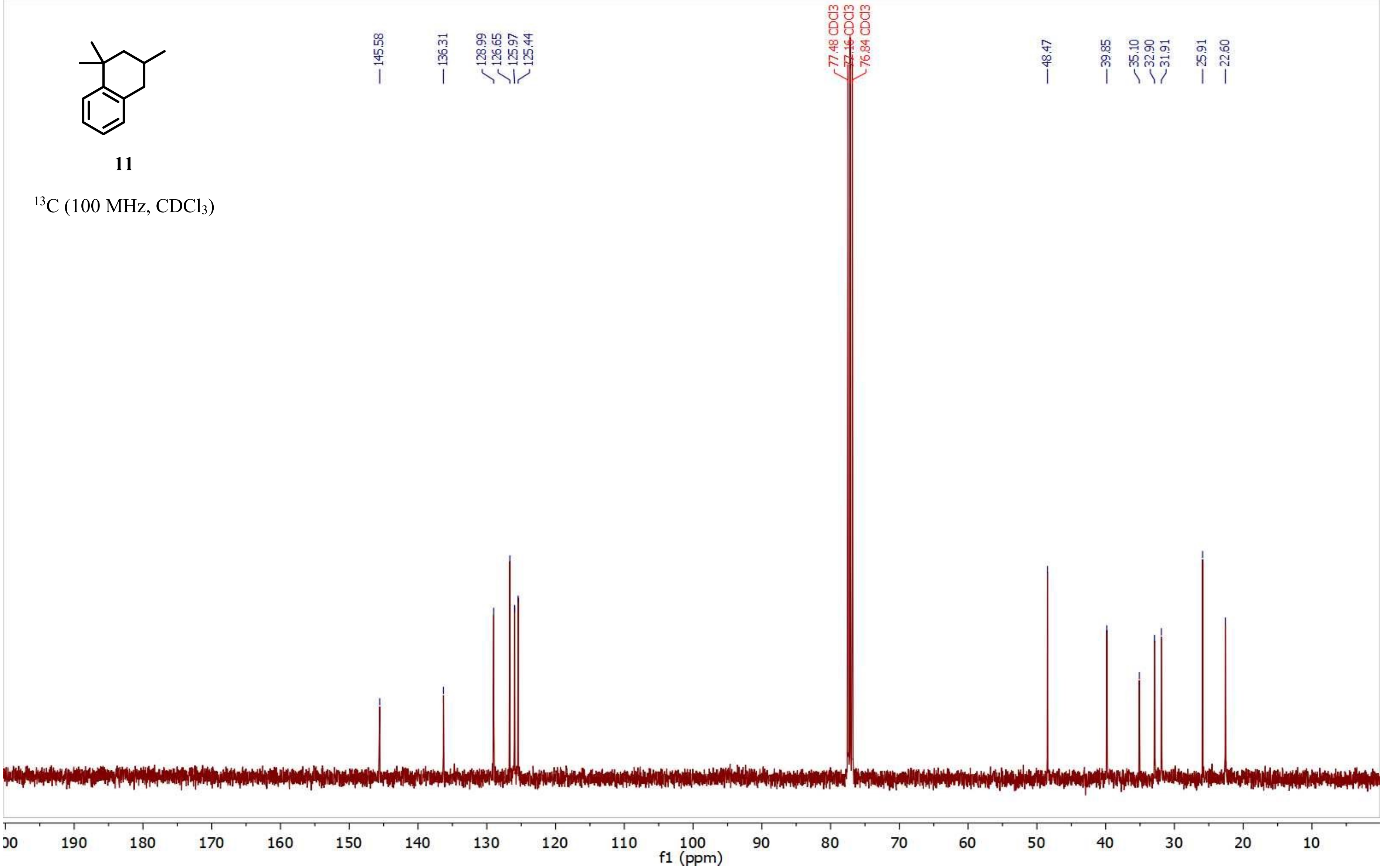


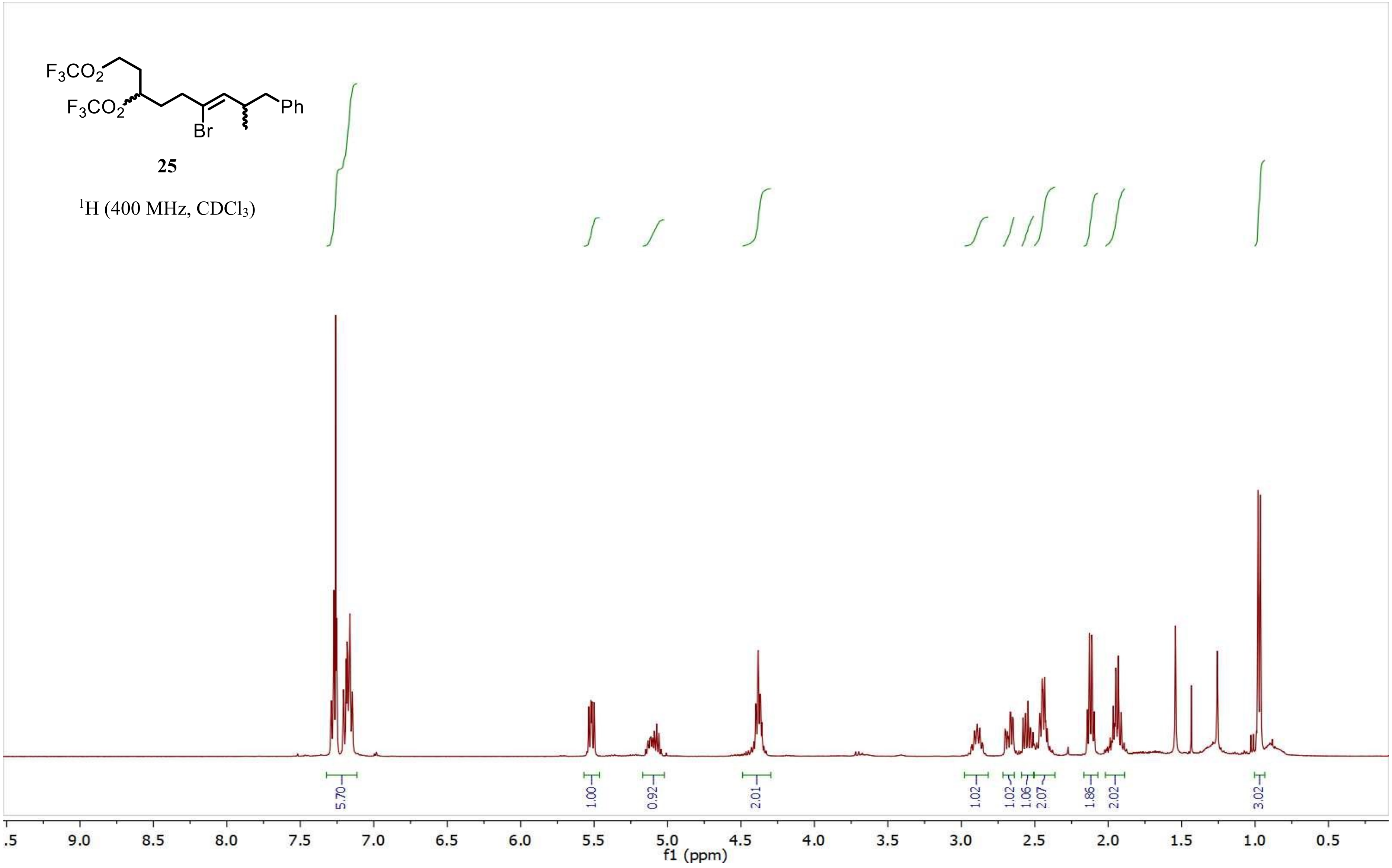
11

^{1}H (400 MHz, CDCl$_3$)

11

^{13}C (100 MHz, $CDCl_3$)



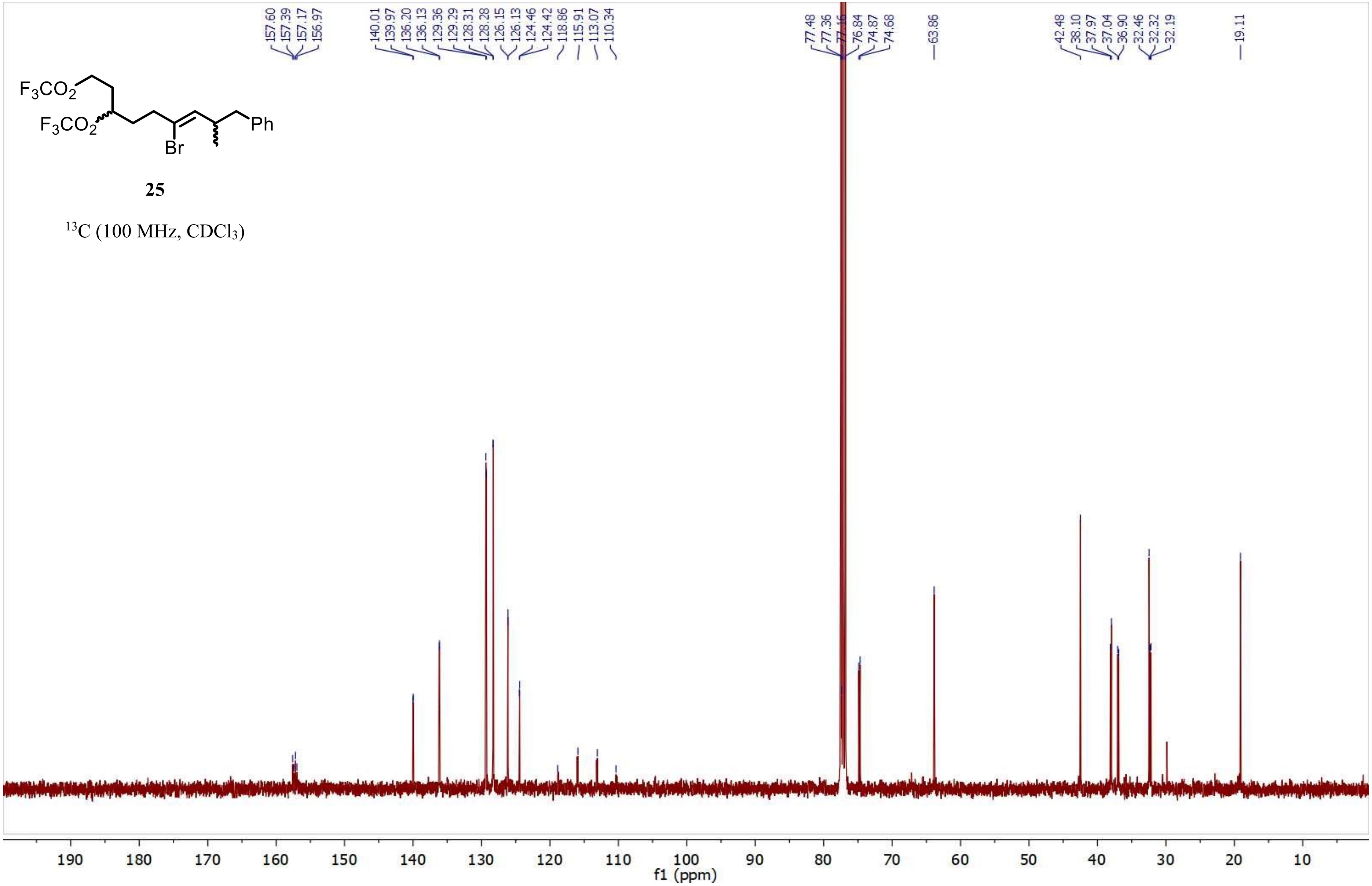


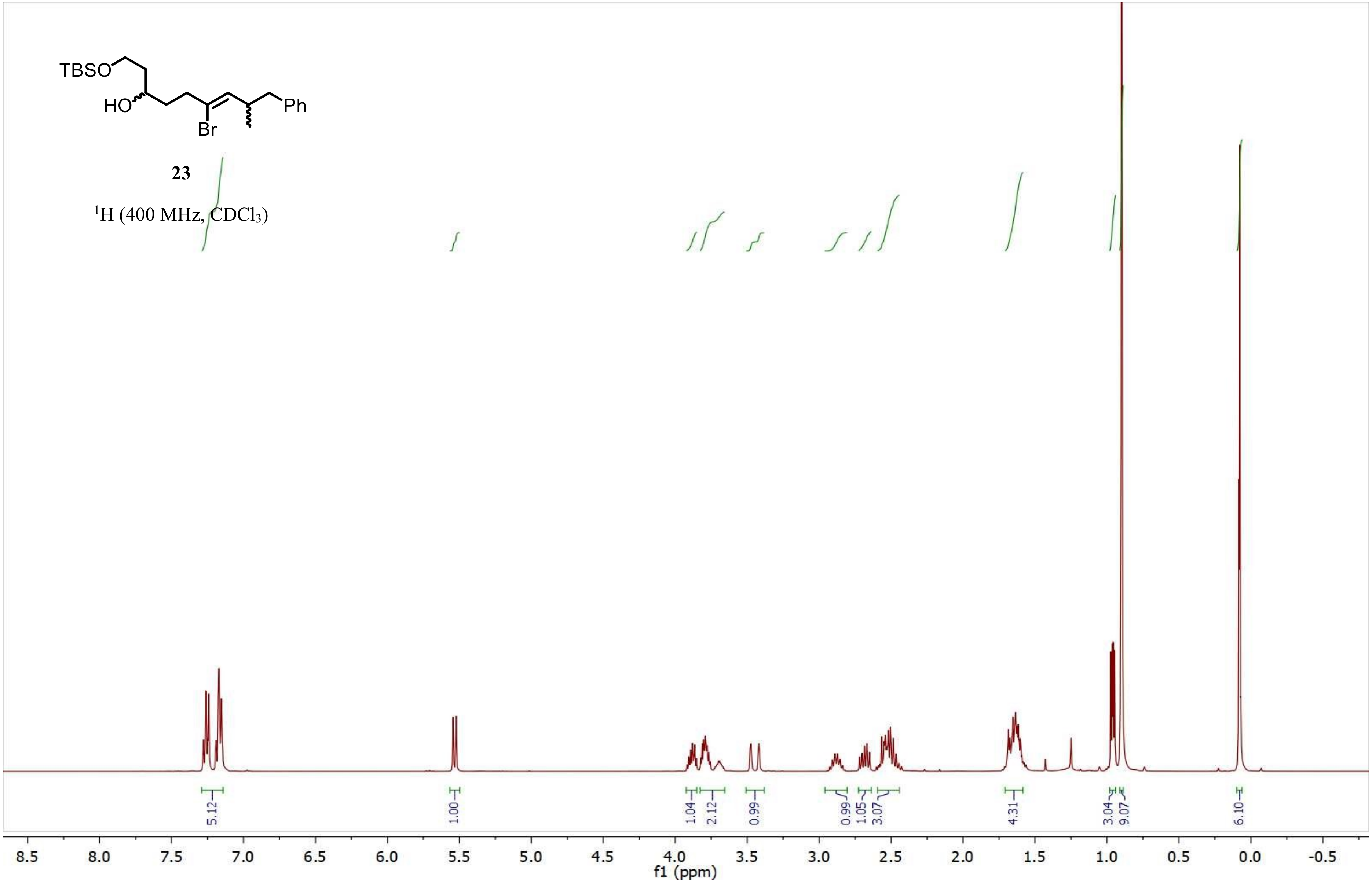
25

^{1}H (400 MHz, CDCl$_3$)

25

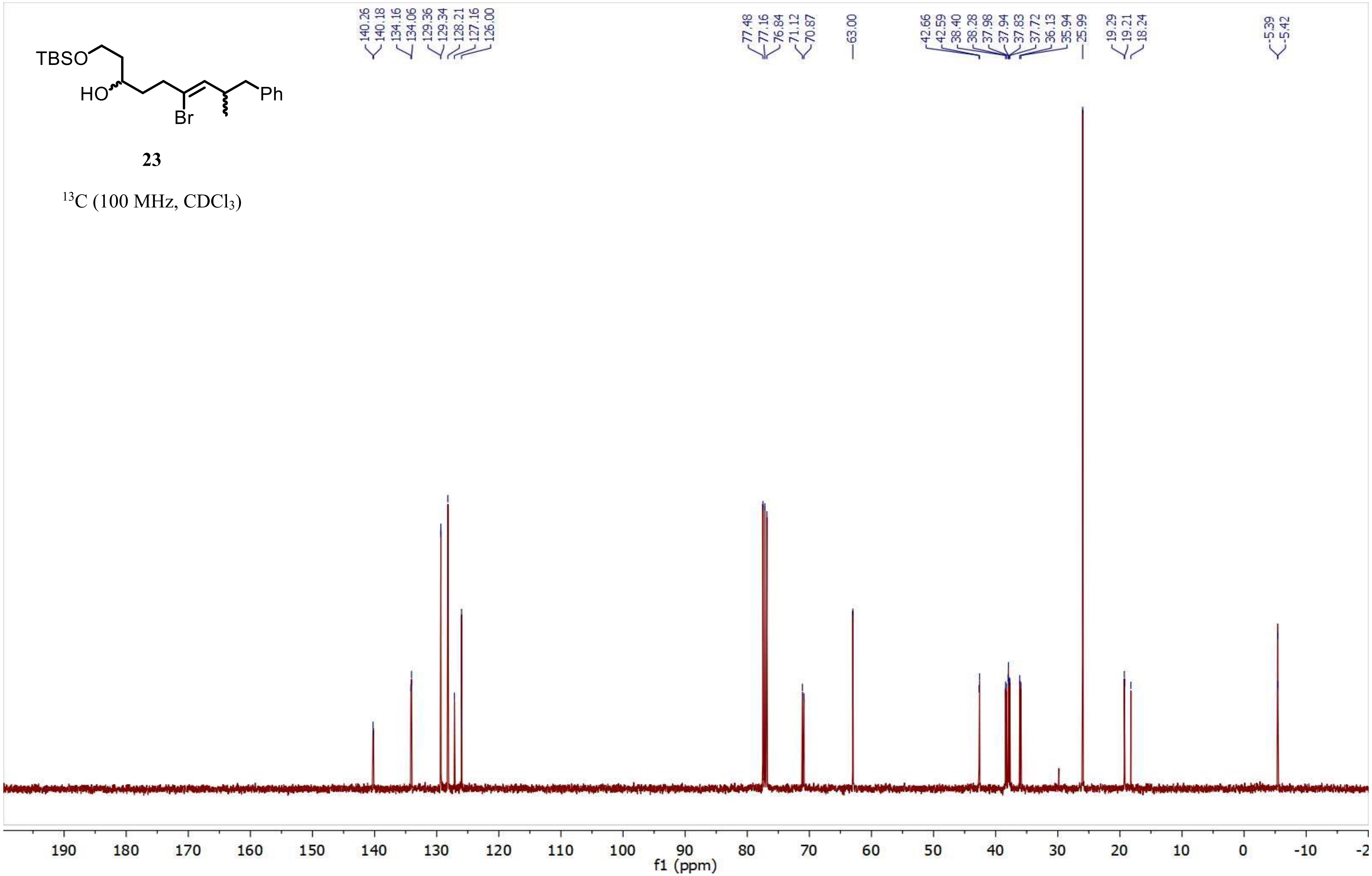
^{13}C (100 MHz, $CDCl_3$)





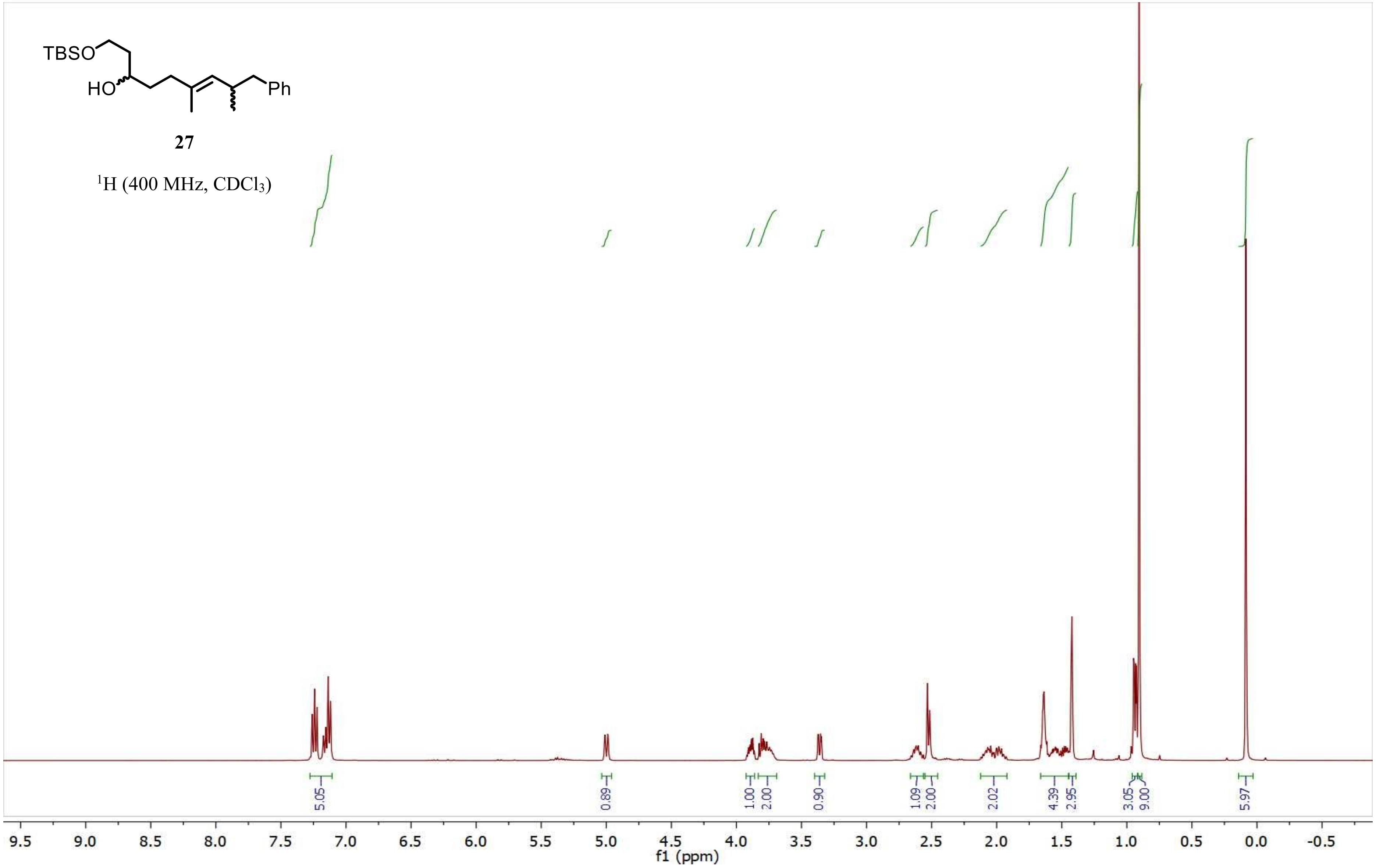
23

^{1}H (400 MHz, CDCl$_3$)



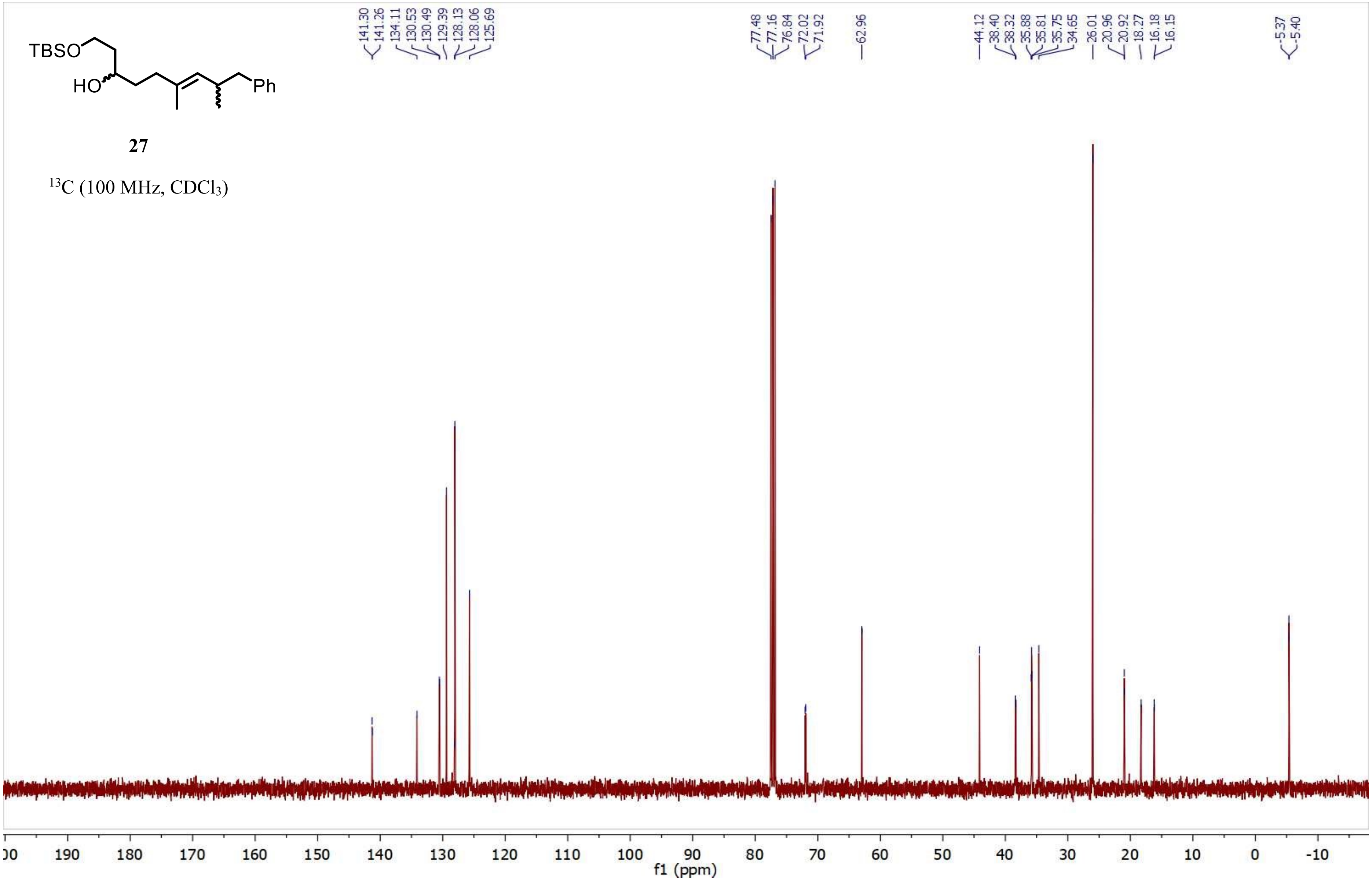
23

^{13}C (100 MHz, CDCl$_3$)



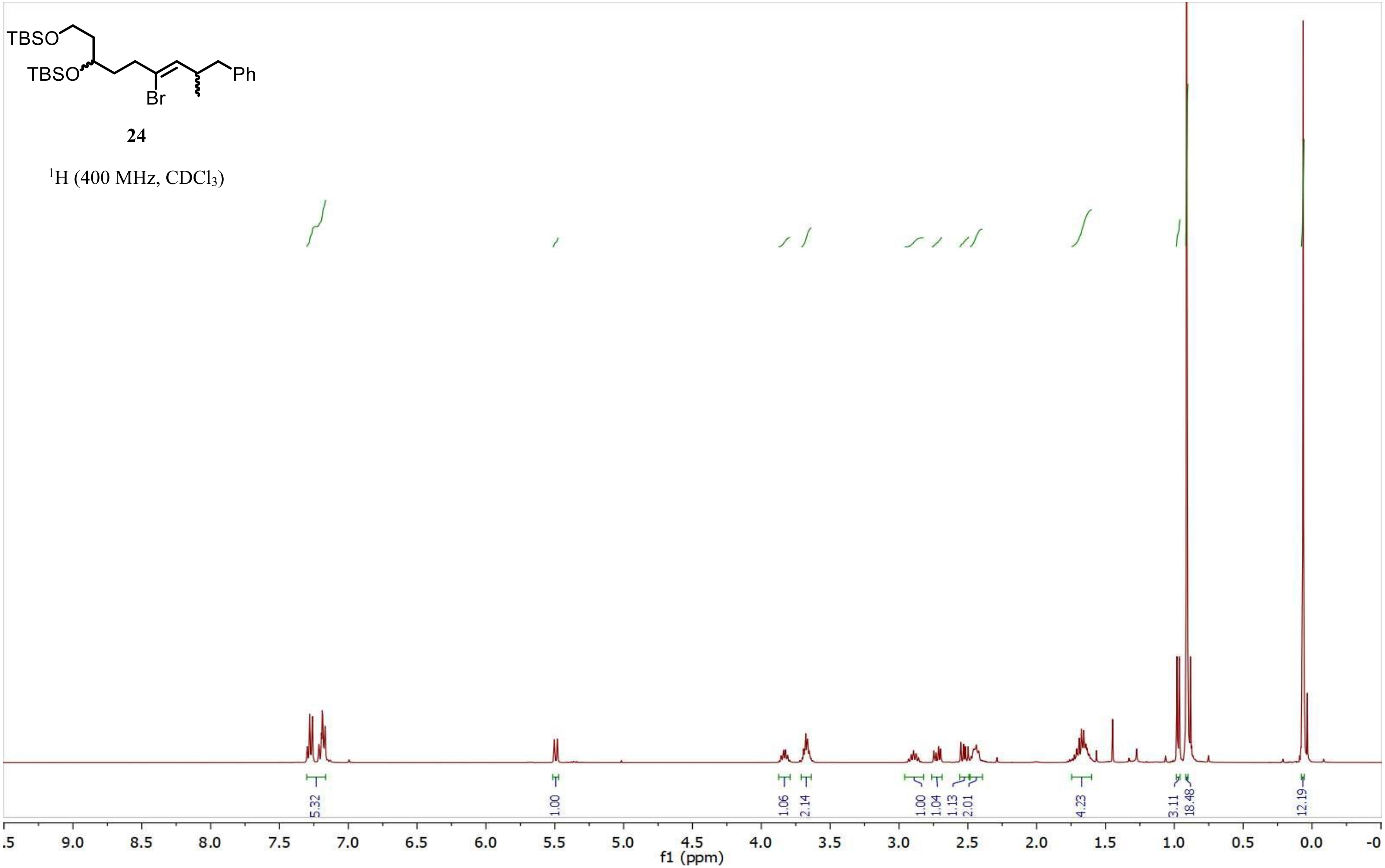
27

^{1}H (400 MHz, CDCl$_3$)



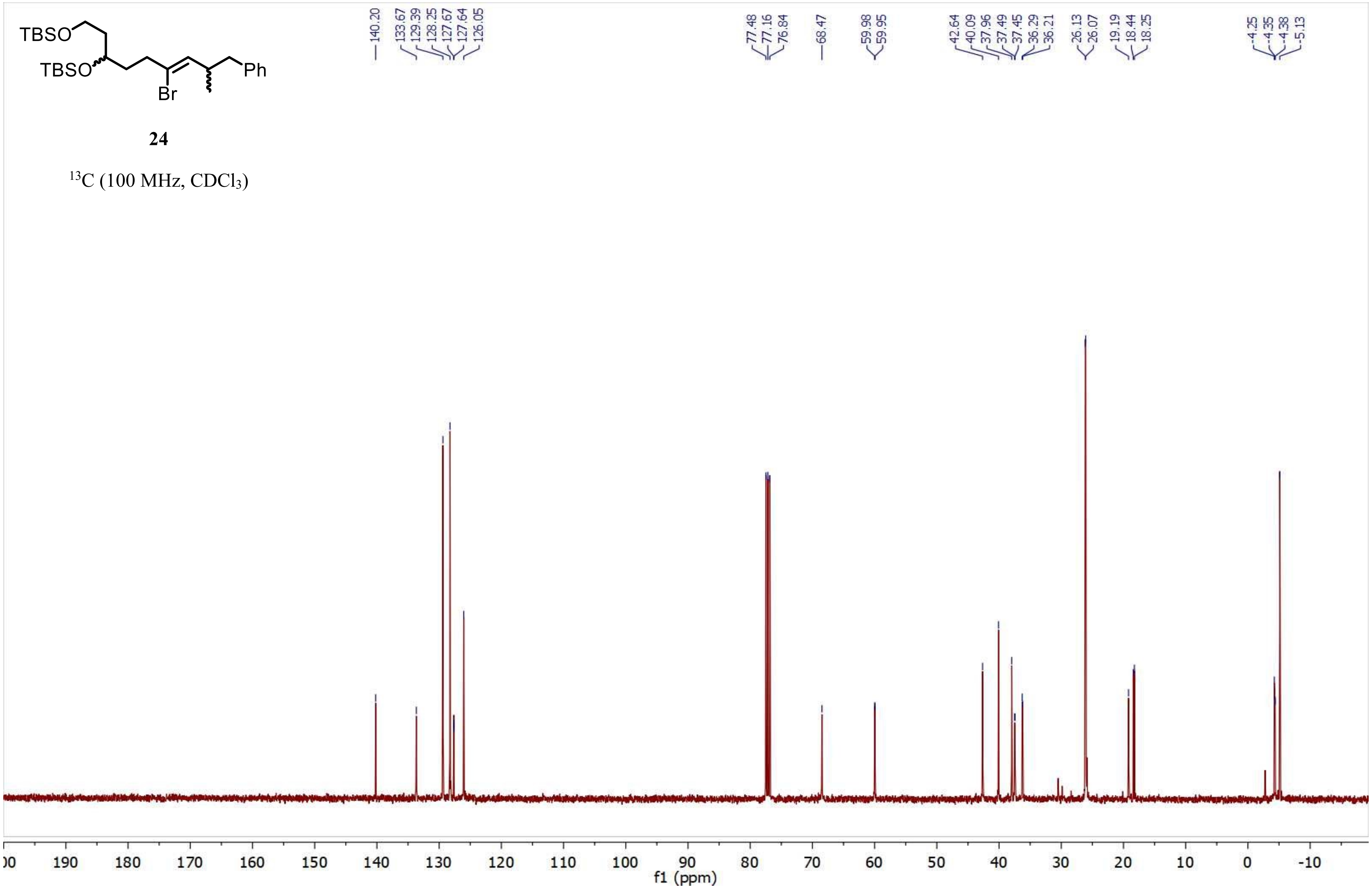
27

^{13}C (100 MHz, CDCl$_3$)



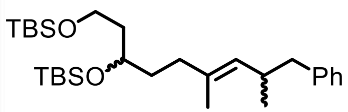
24

^1H (400 MHz, $CDCl_3$)



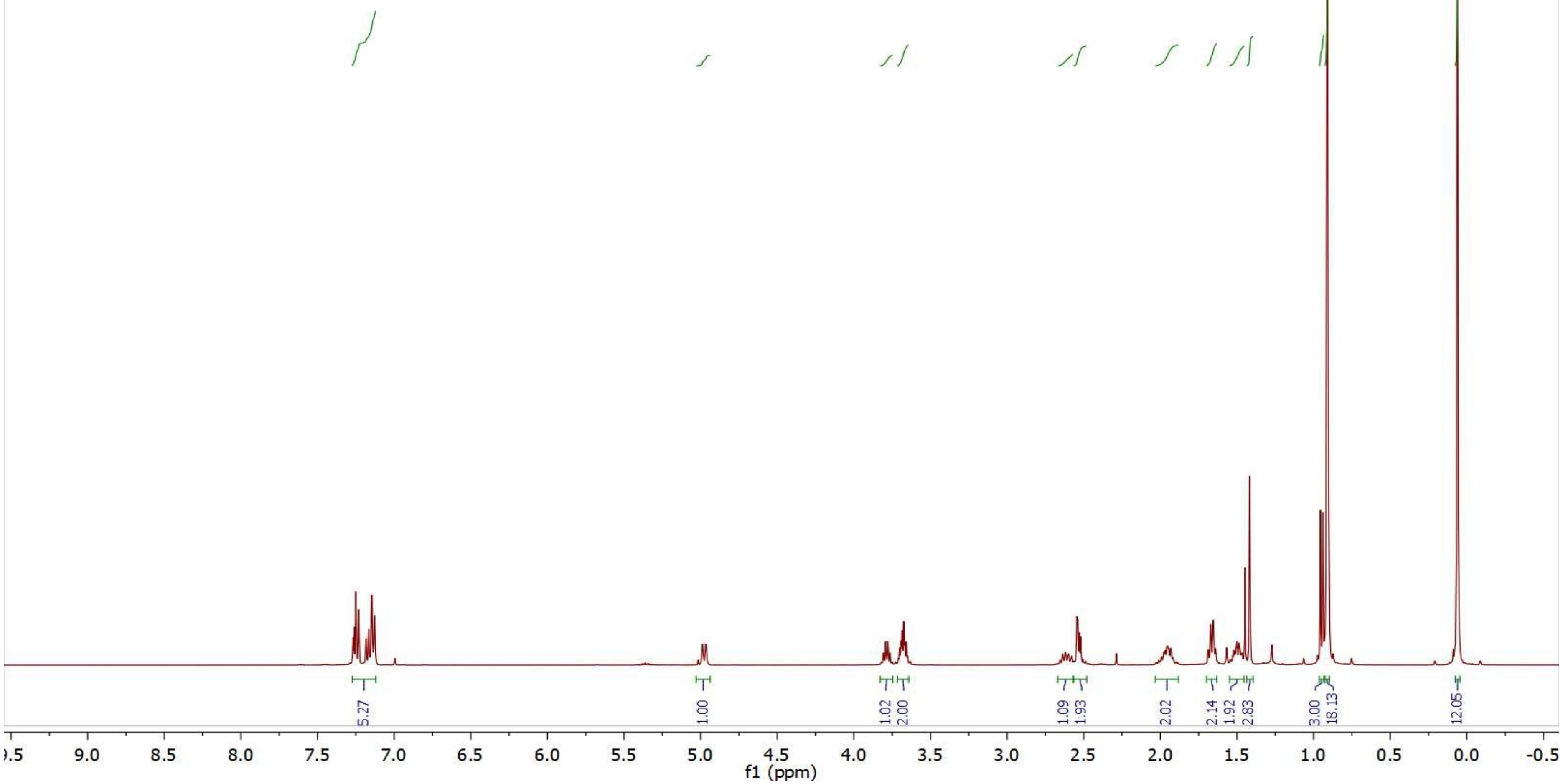
24

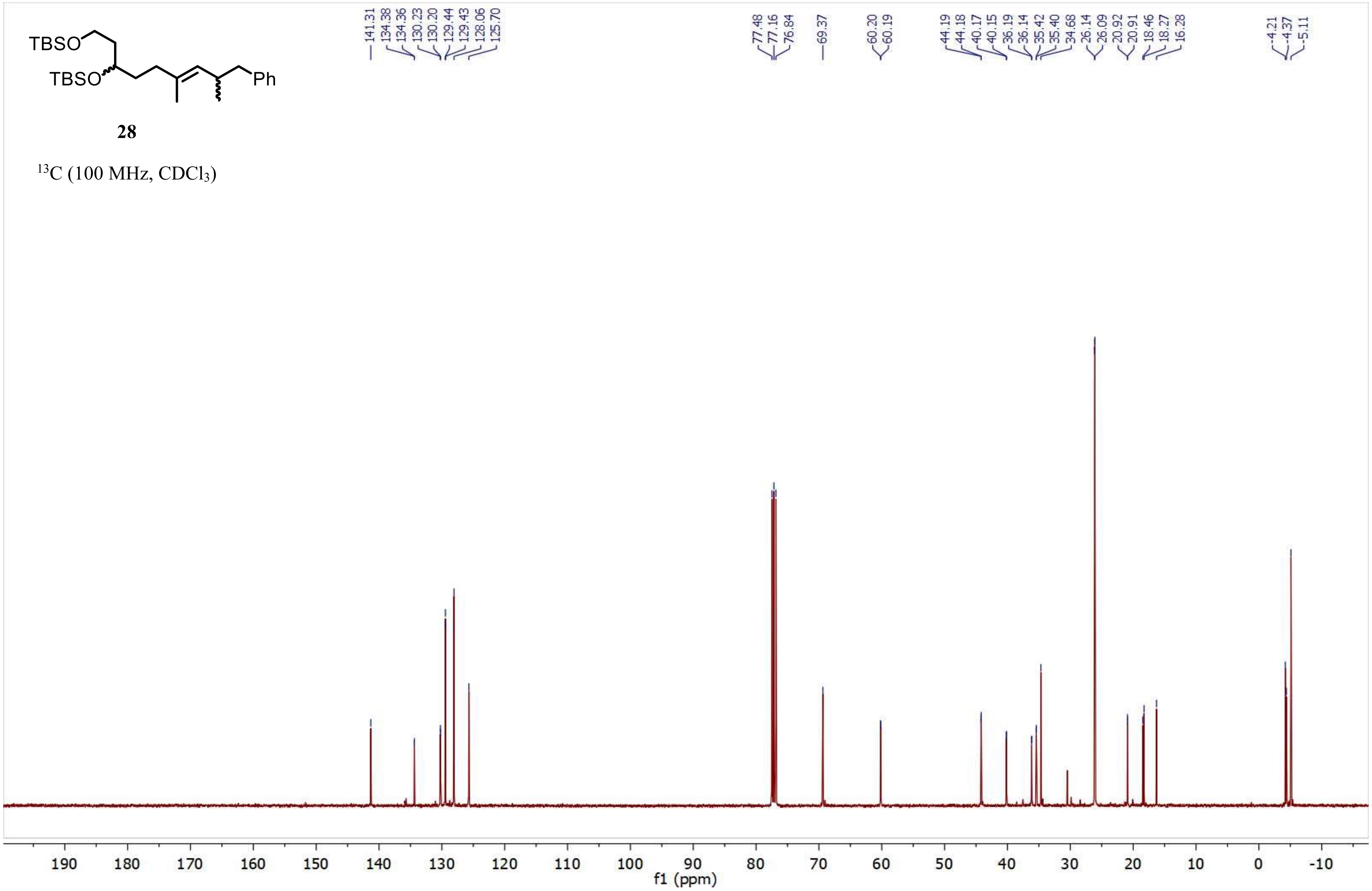
^{13}C (100 MHz, CDCl$_3$)



28

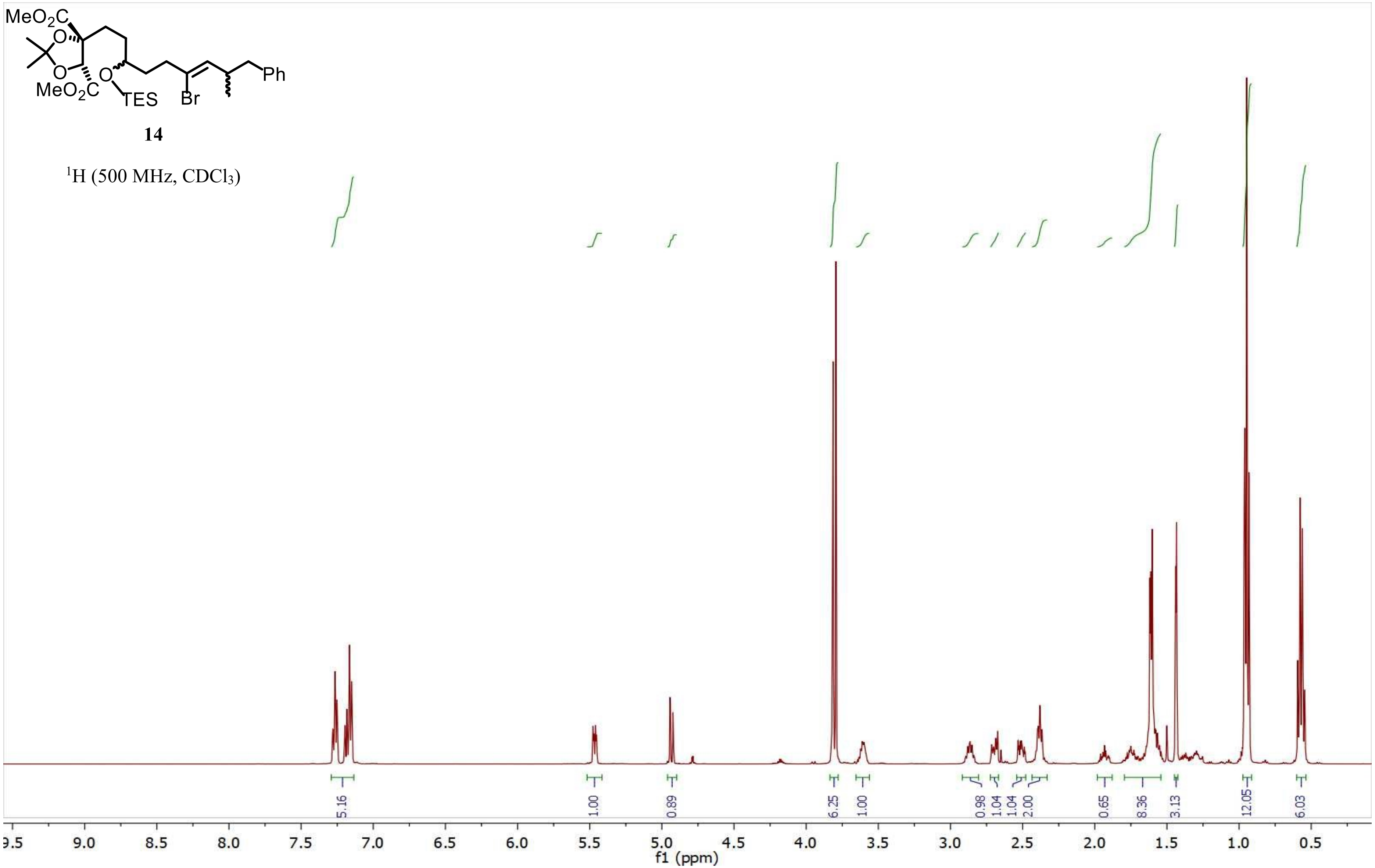
^1H (400 MHz, $CDCl_3$)





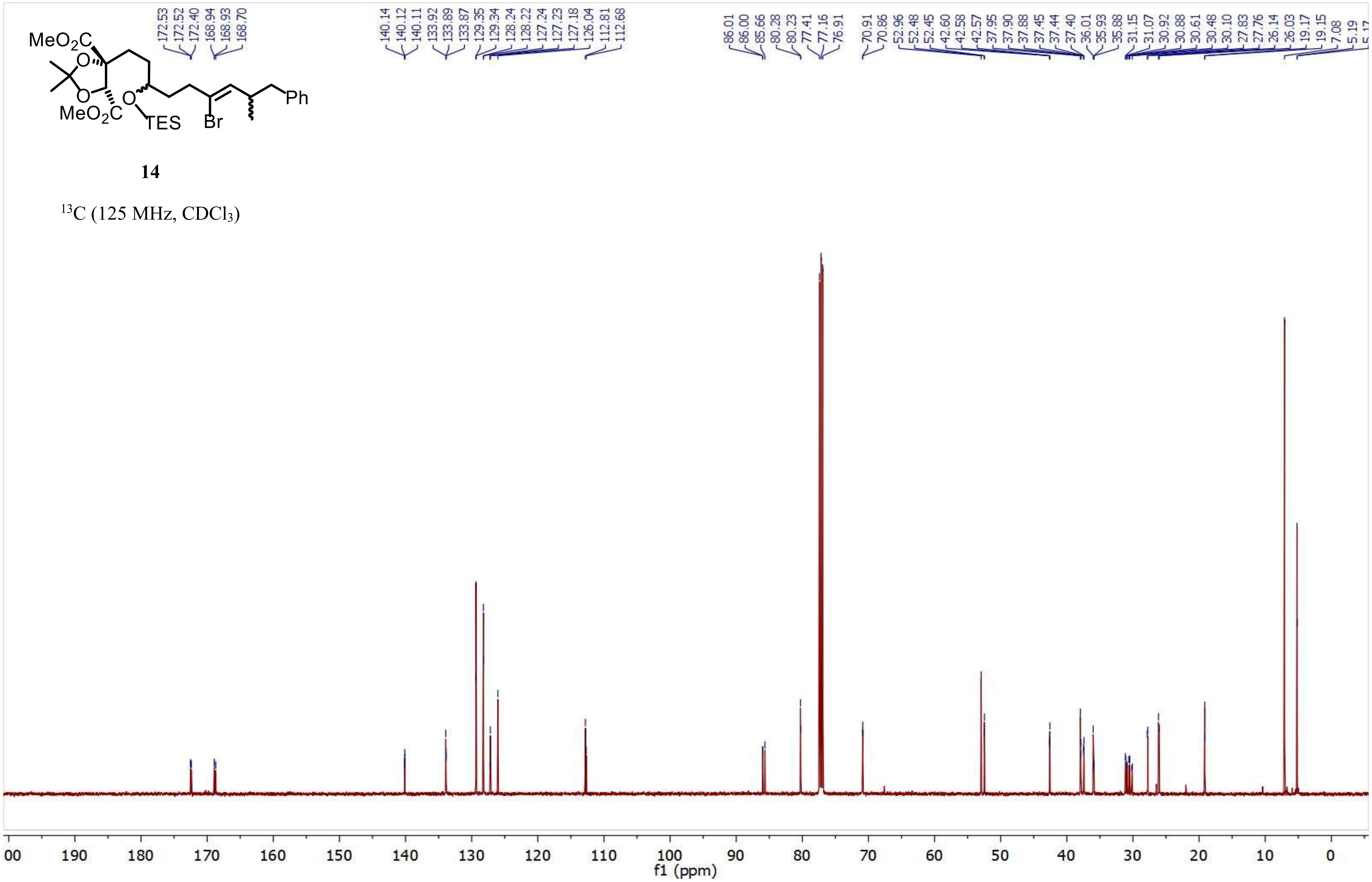
28

^{13}C (100 MHz, CDCl$_3$)



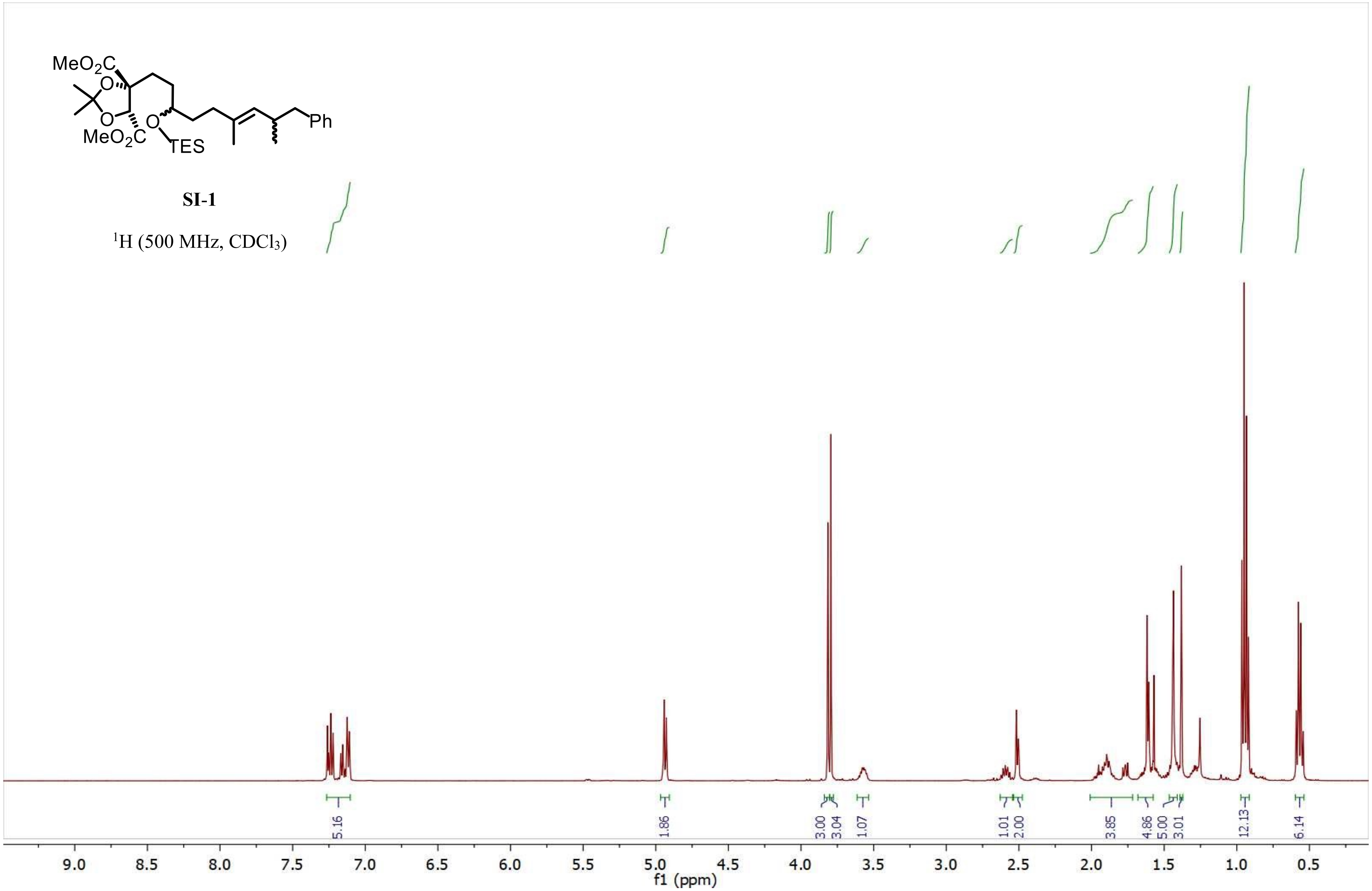
14

^{1}H (500 MHz, CDCl$_3$)



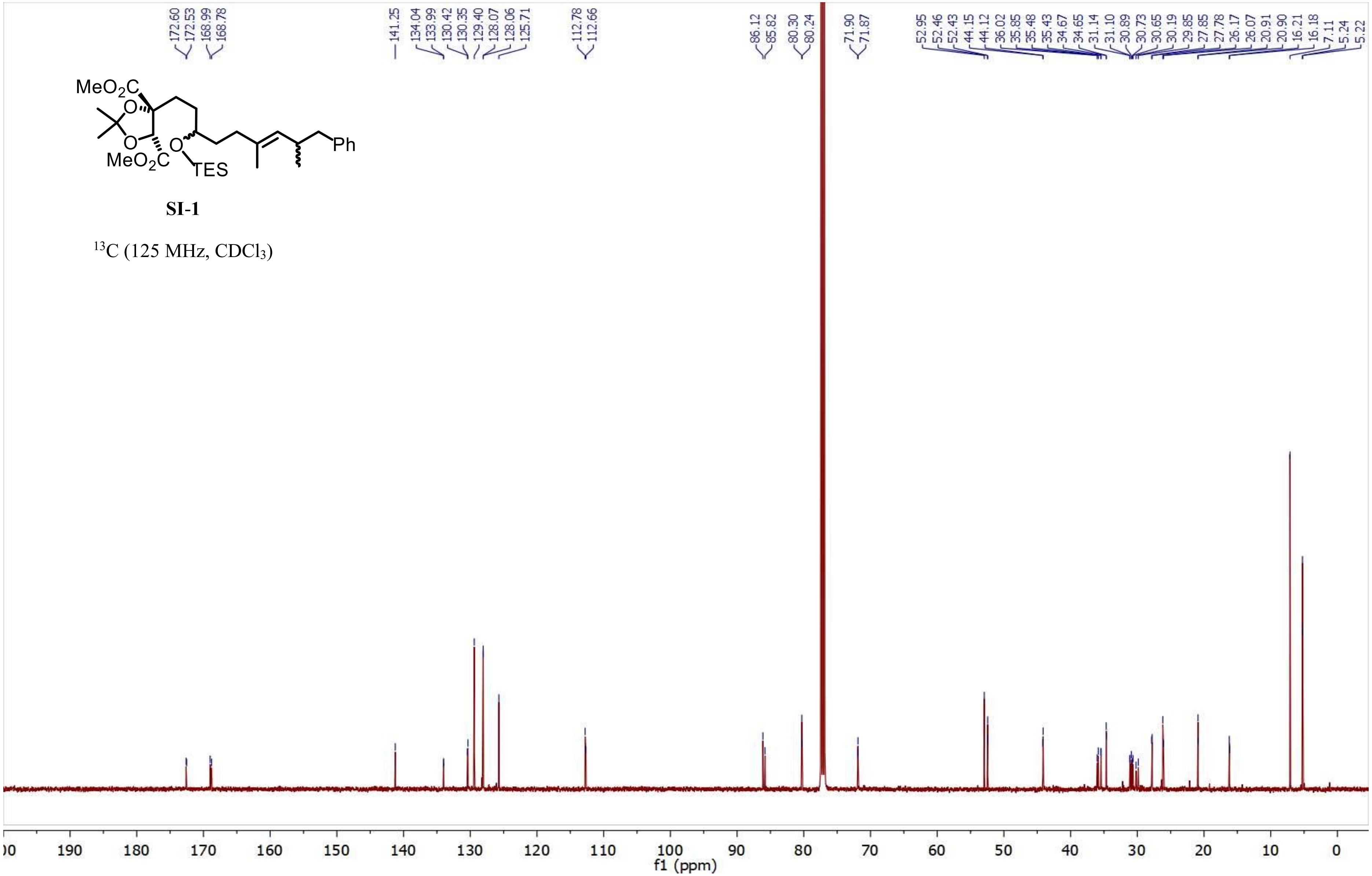
14

^{13}C (125 MHz, CDCl$_3$)



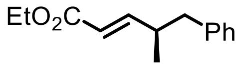
SI-1

^{1}H (500 MHz, $CDCl_3$)



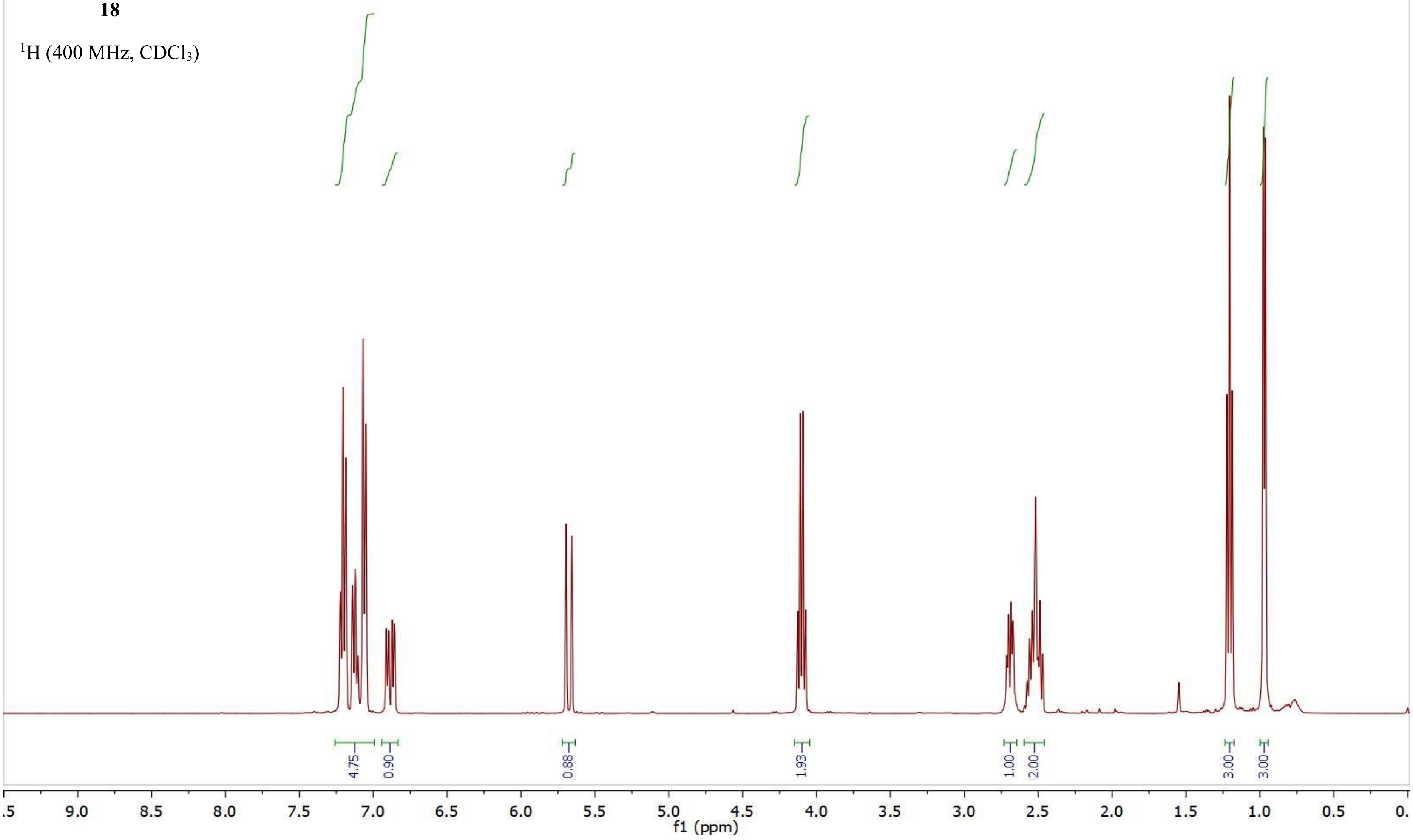
SI-1

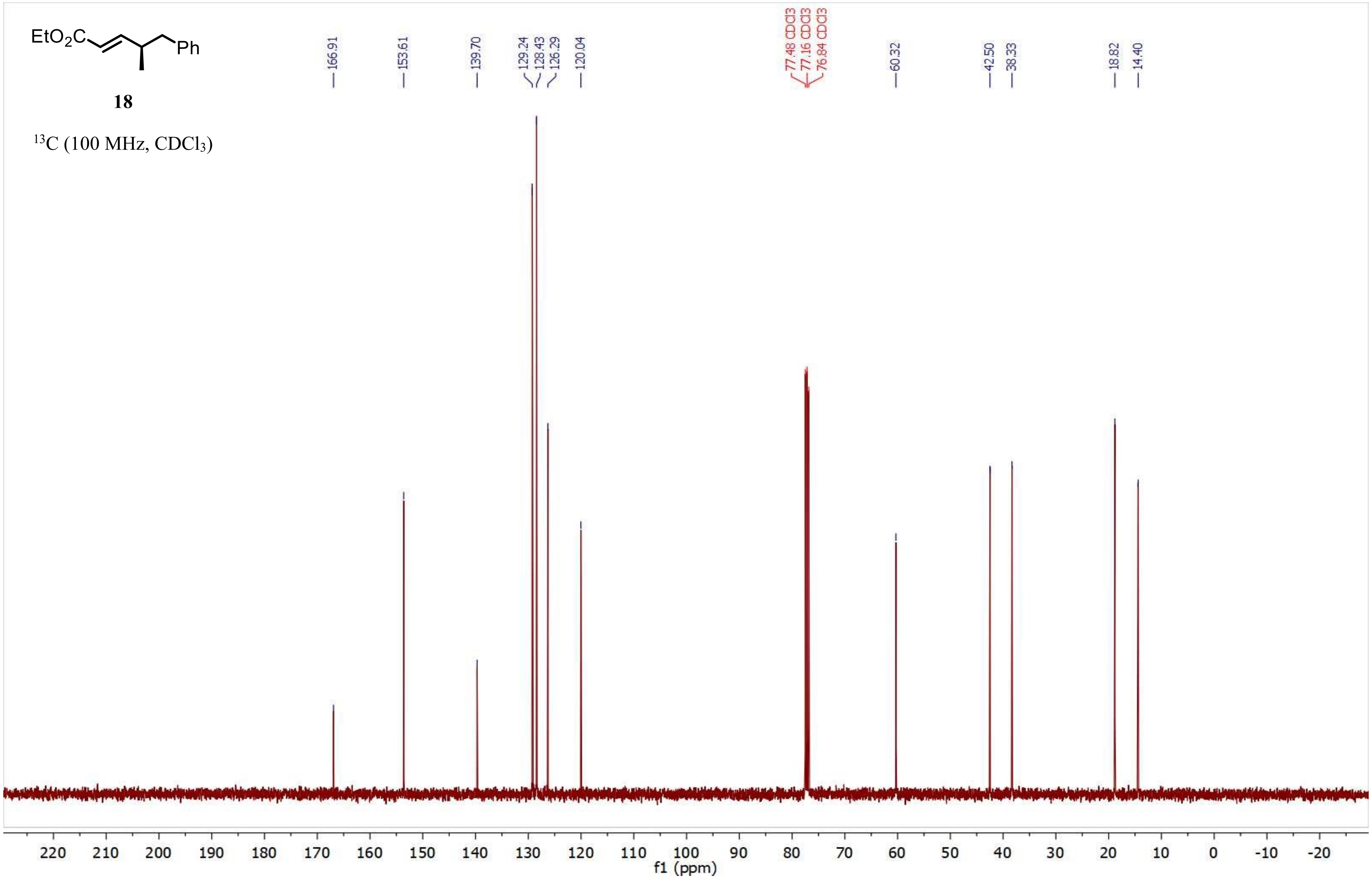
^{13}C (125 MHz, CDCl$_3$)



18

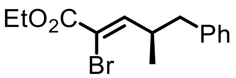
^{1}H (400 MHz, CDCl$_3$)





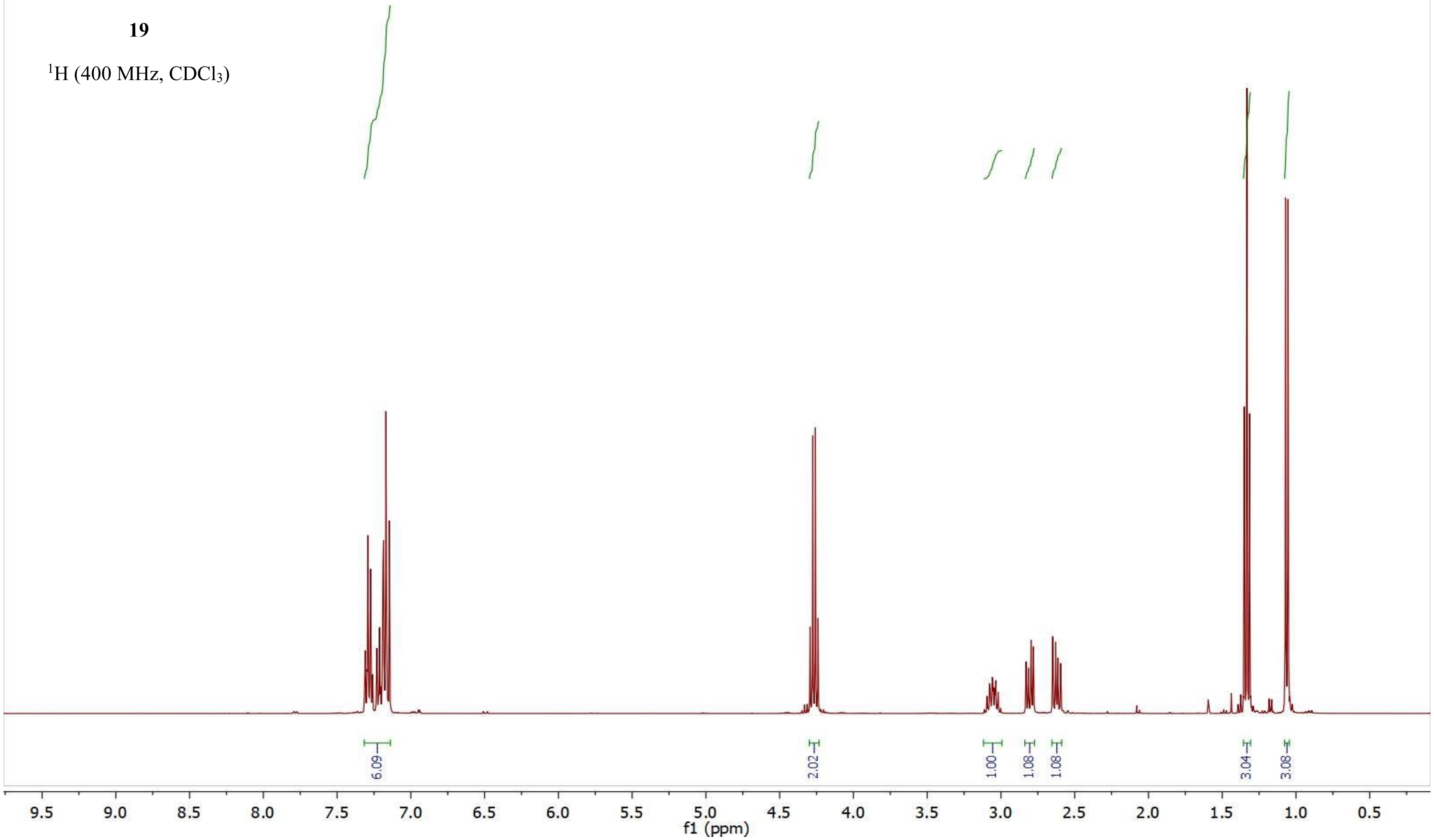
18

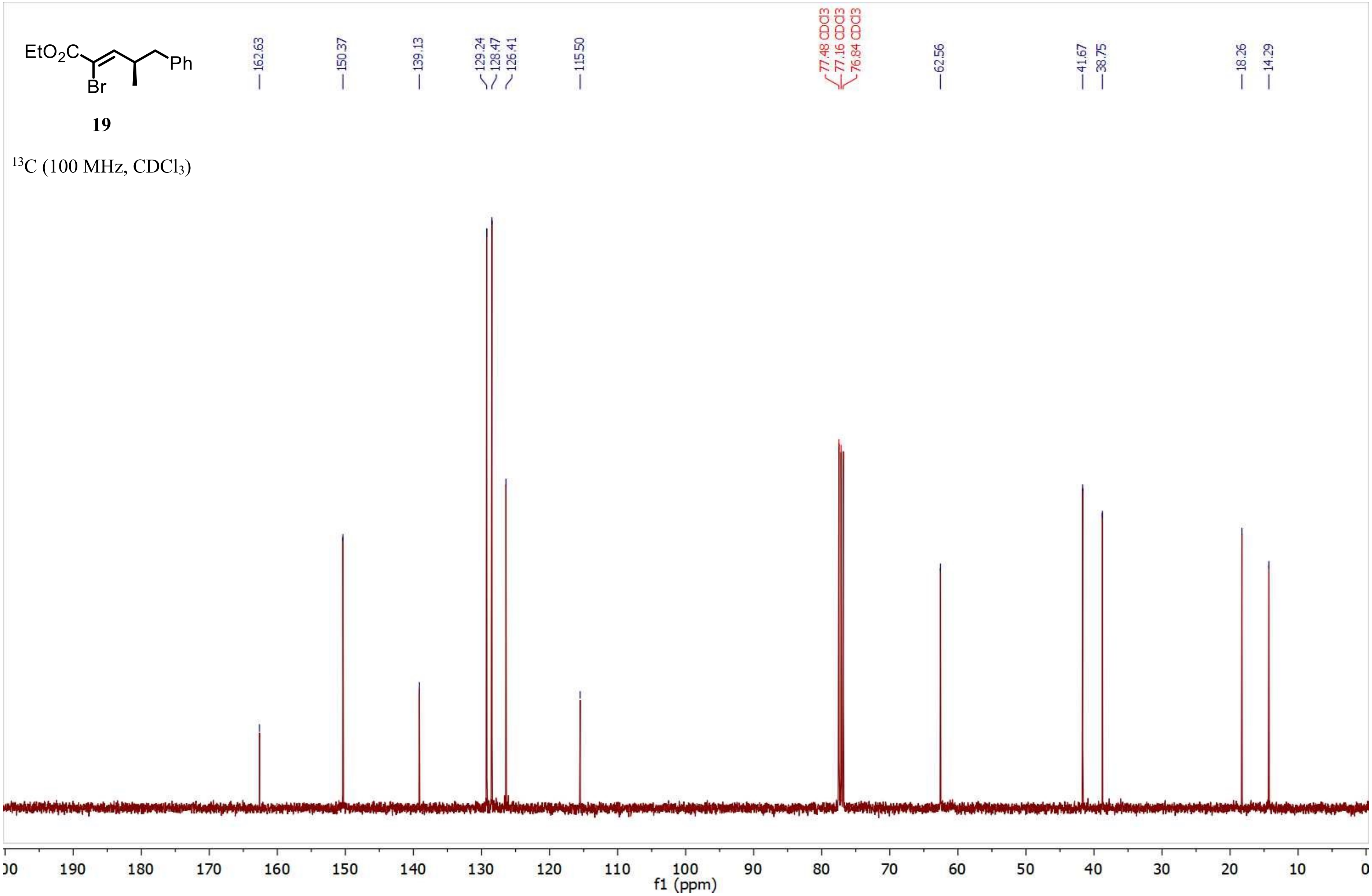
^{13}C (100 MHz, $CDCl_3$)



19

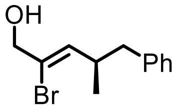
^{1}H (400 MHz, CDCl$_3$)





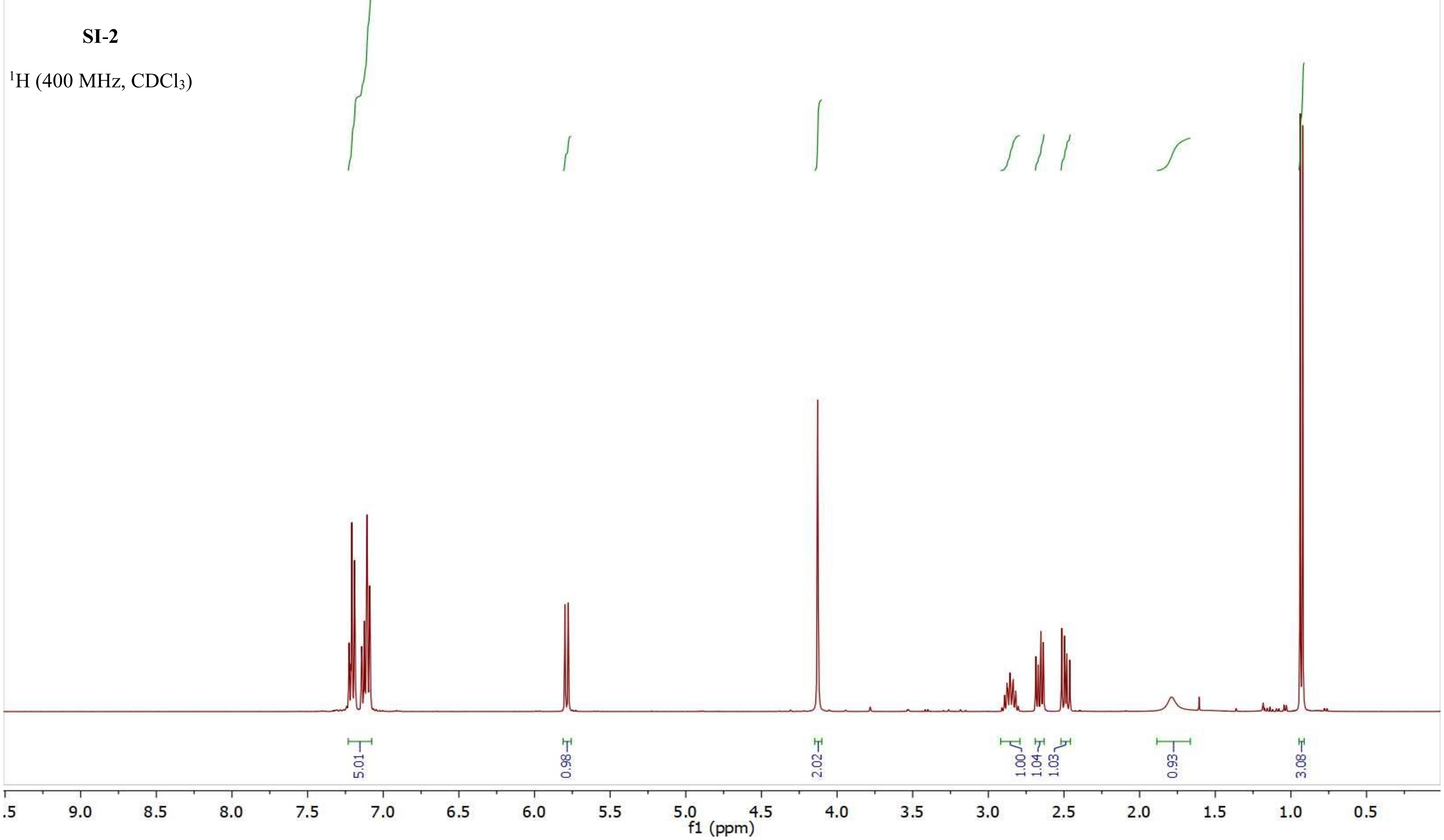
19

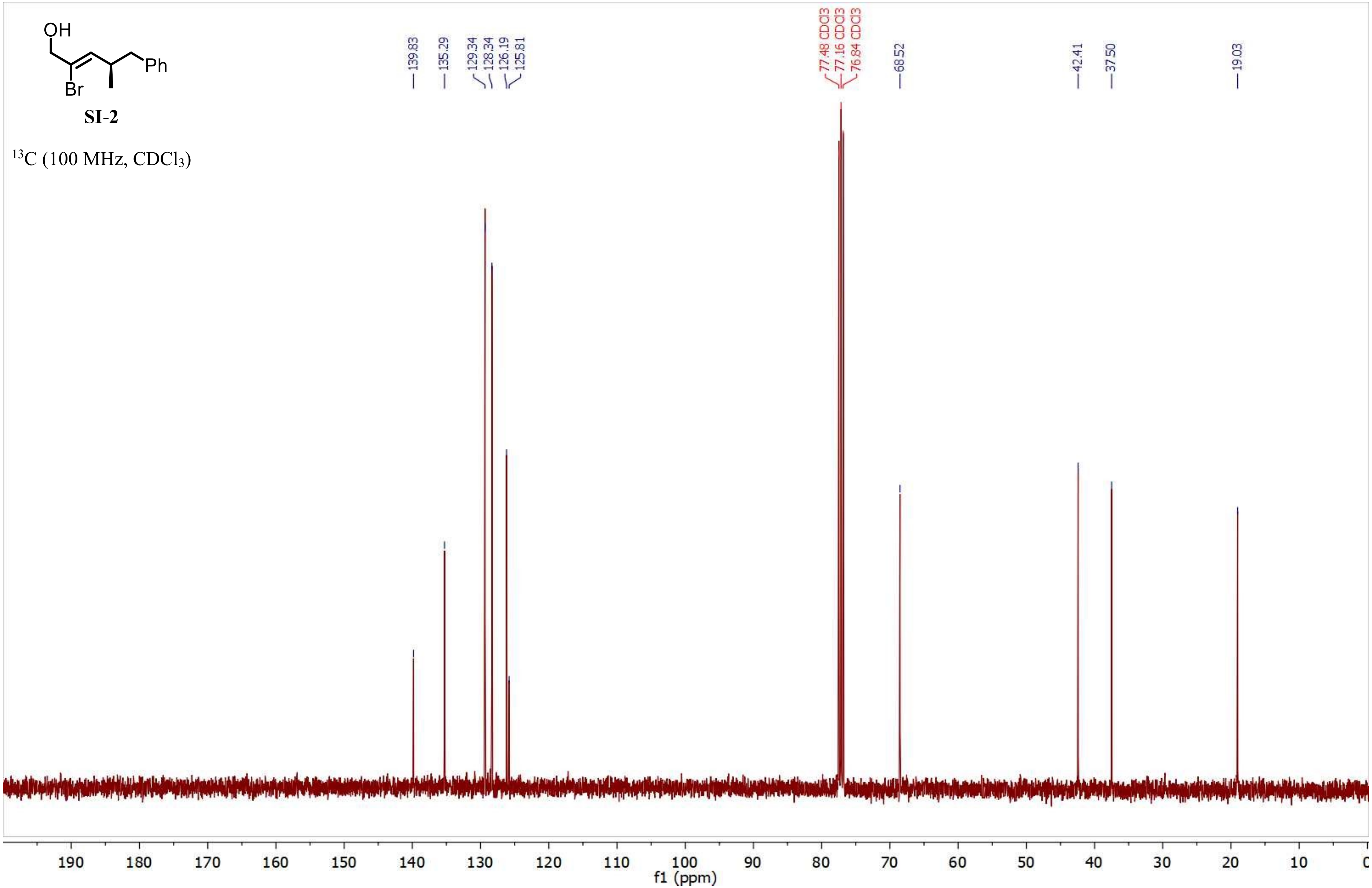
^{13}C (100 MHz, $CDCl_3$)



SI-2

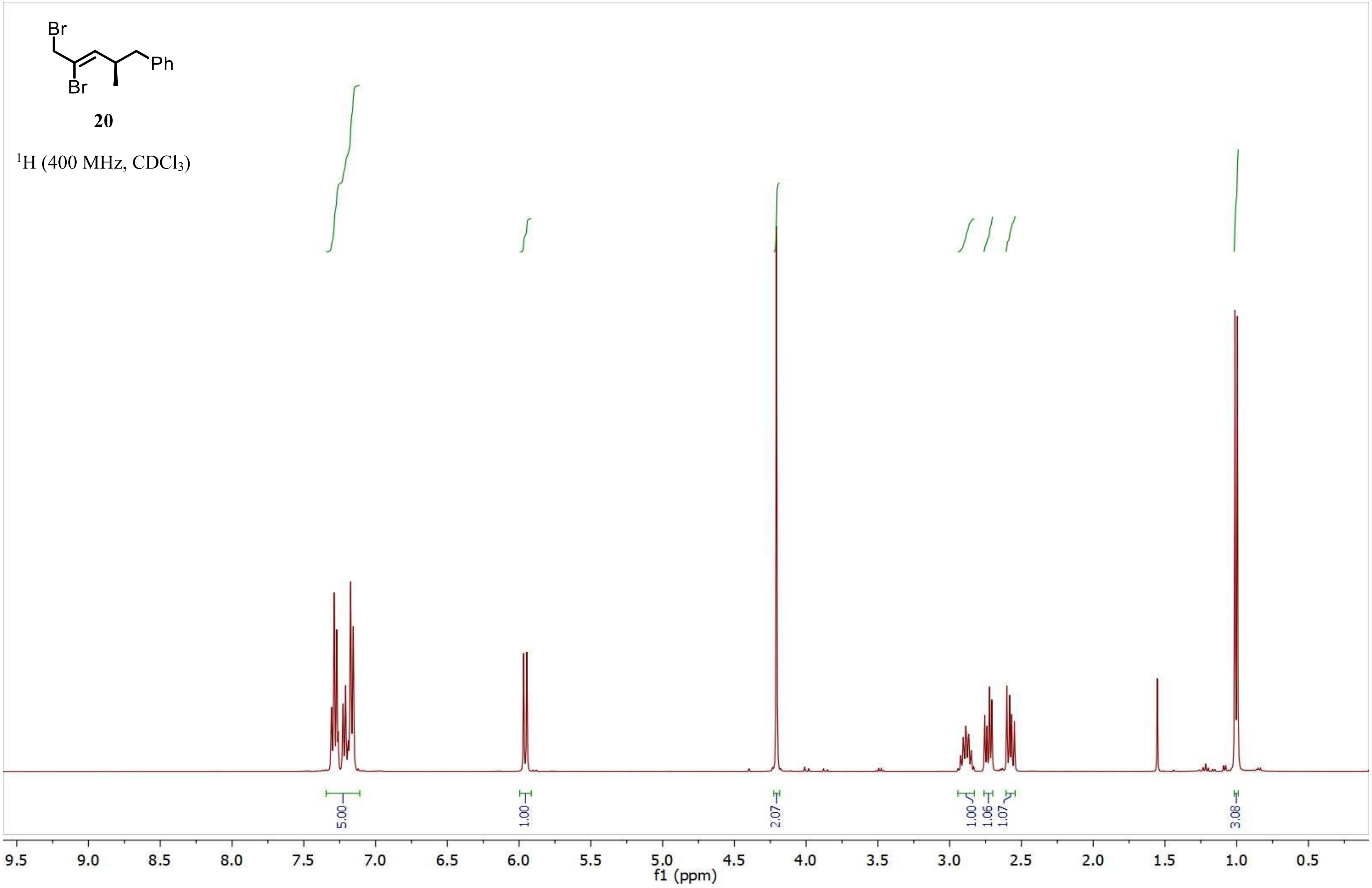
^{1}H (400 MHz, CDCl$_3$)

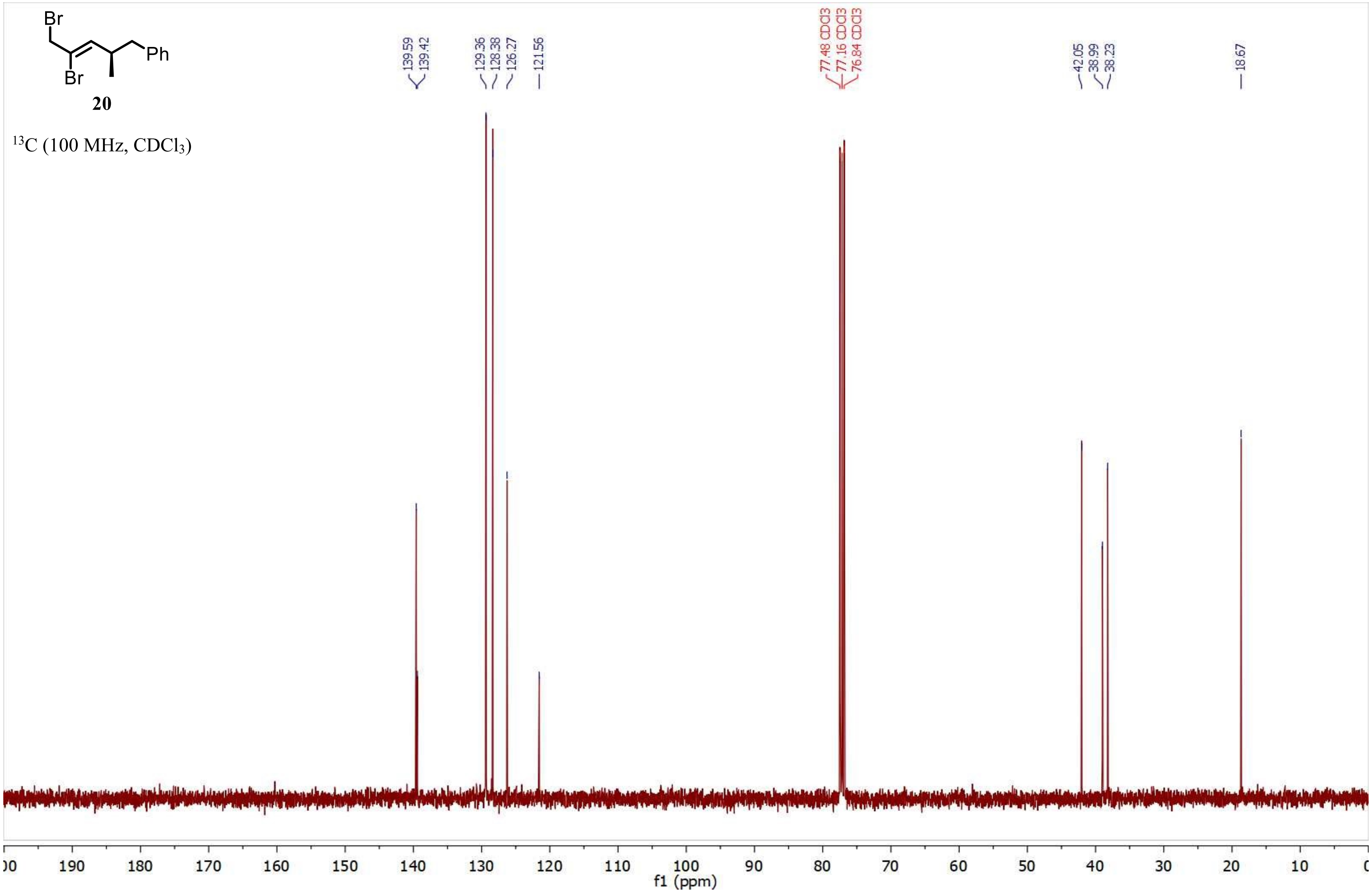




SI-2

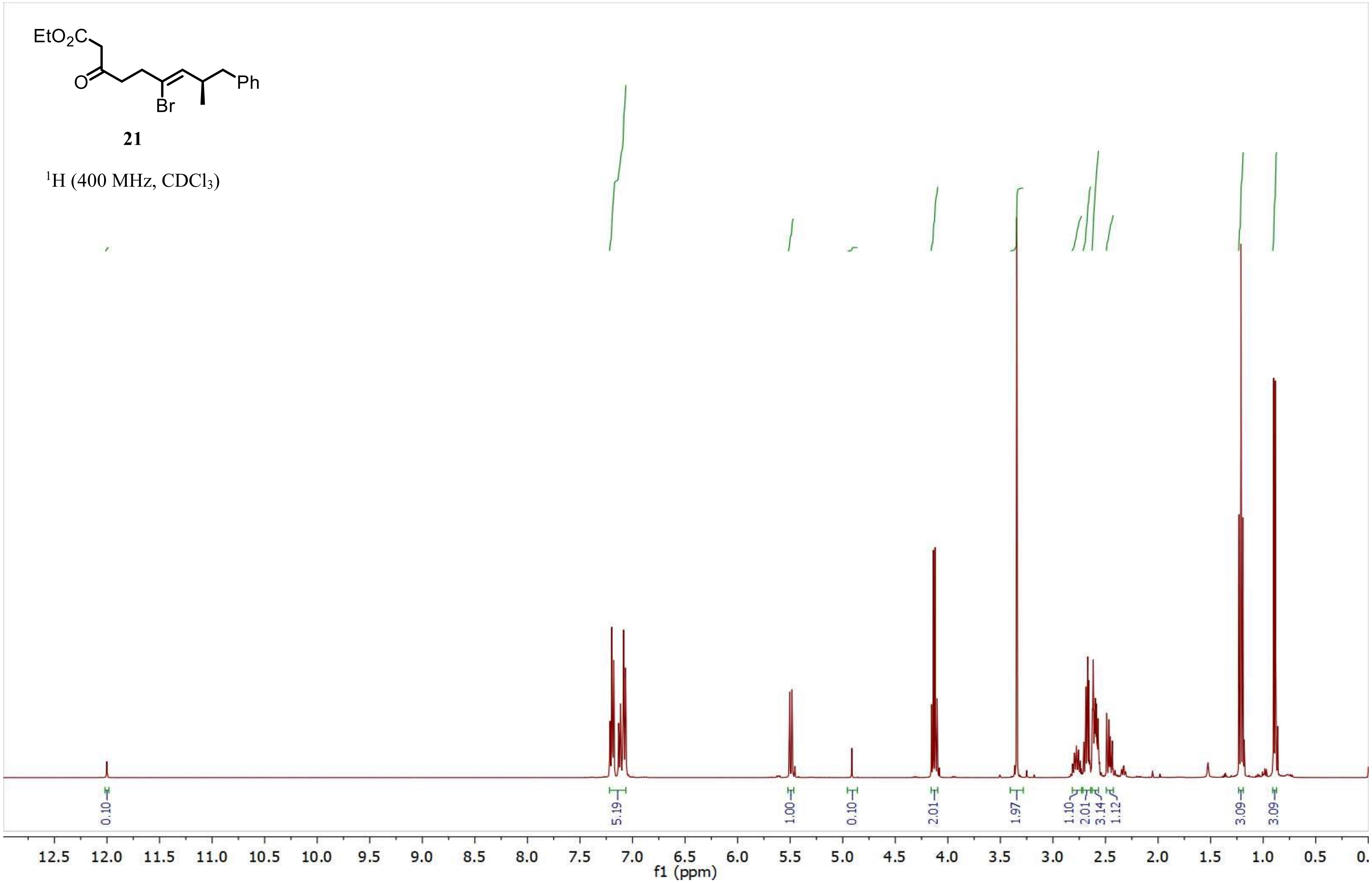
^{13}C (100 MHz, $CDCl_3$)


Br
Br
Ph
20
^{1}H (400 MHz, CDCl$_3$)
5.00
1.00
2.07
1.00
1.06
1.07
3.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)



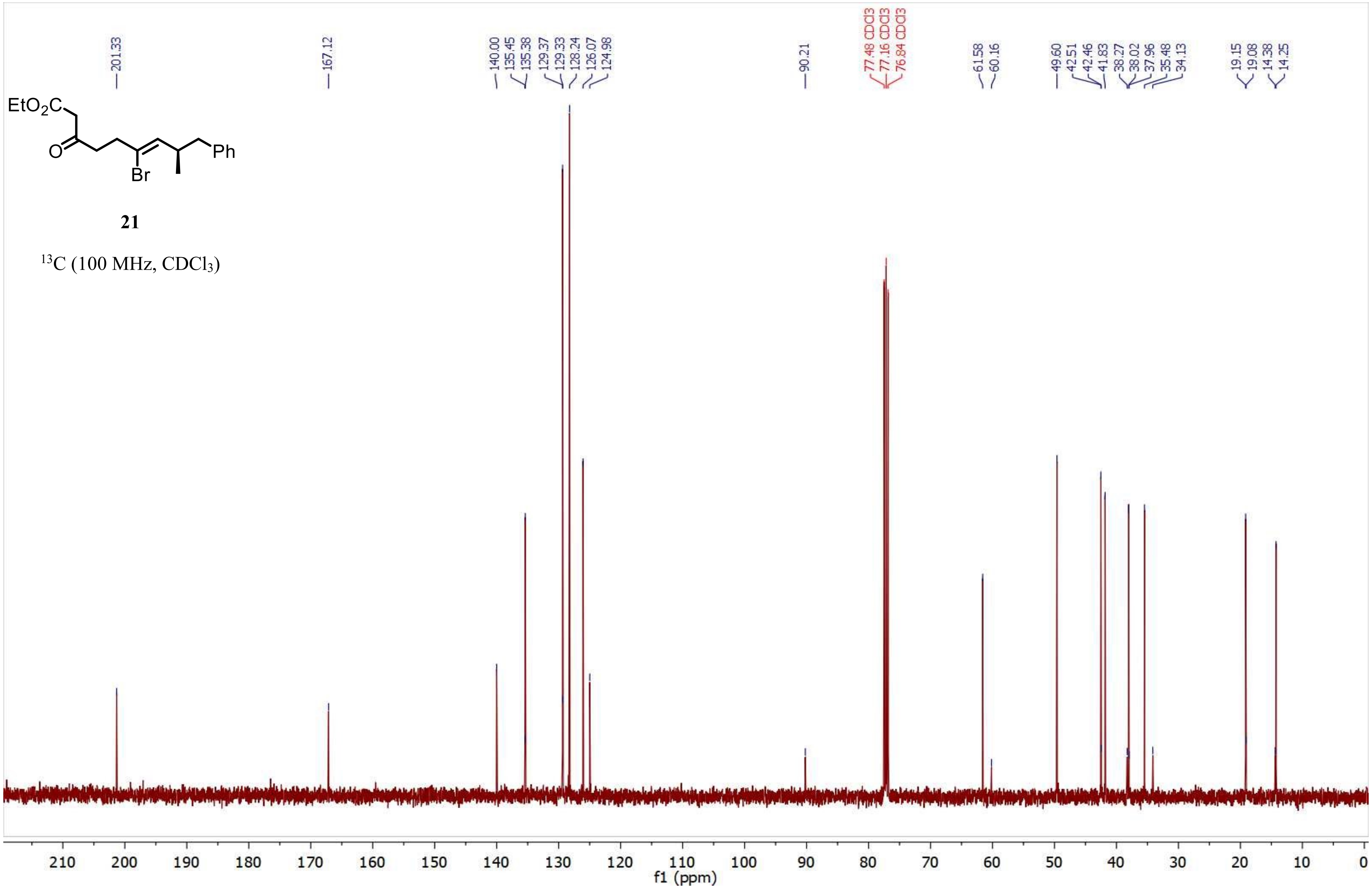
20

^{13}C (100 MHz, CDCl$_3$)



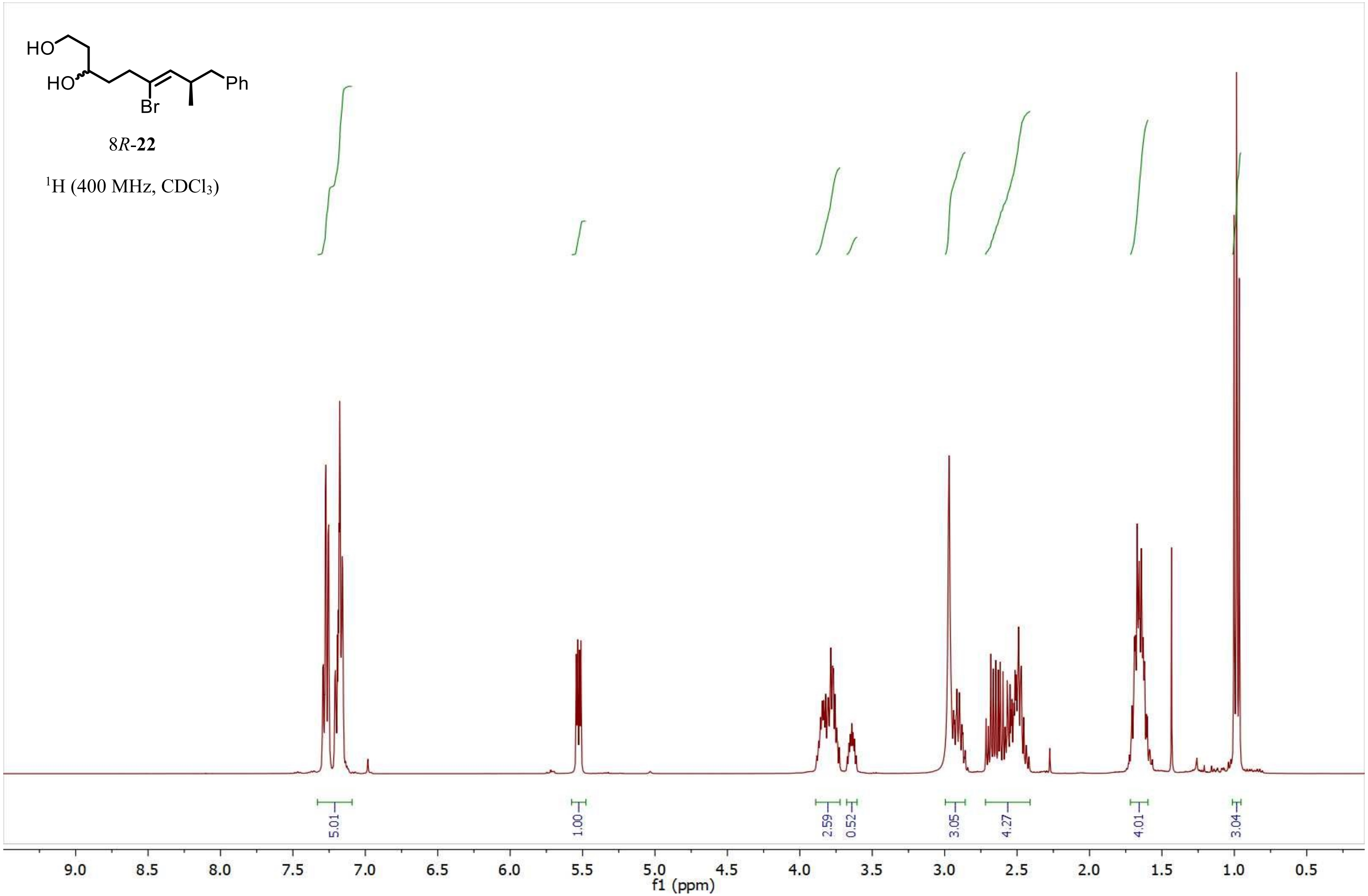
21

^{1}H (400 MHz, CDCl$_3$)



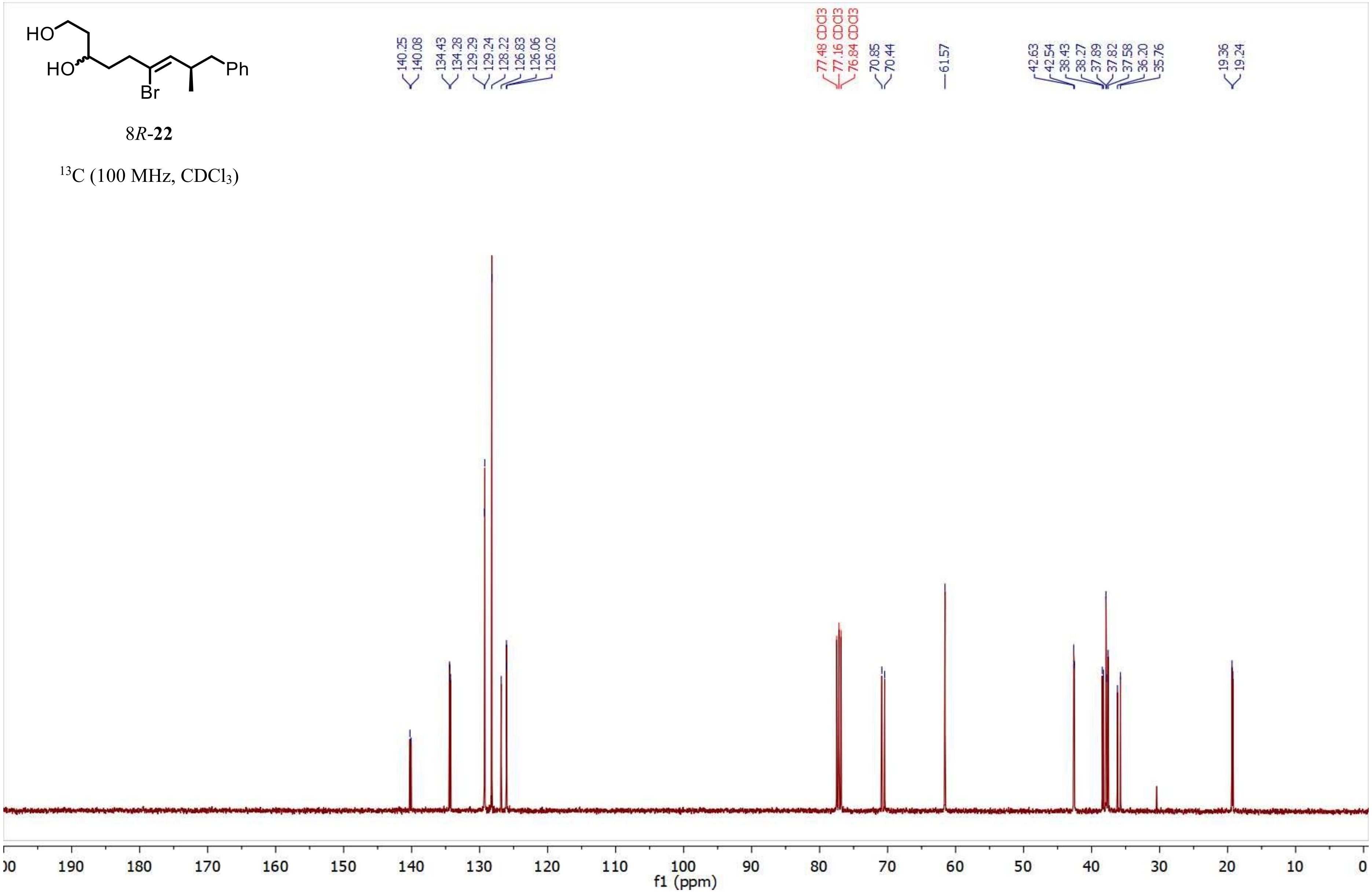
21

^{13}C (100 MHz, $CDCl_3$)



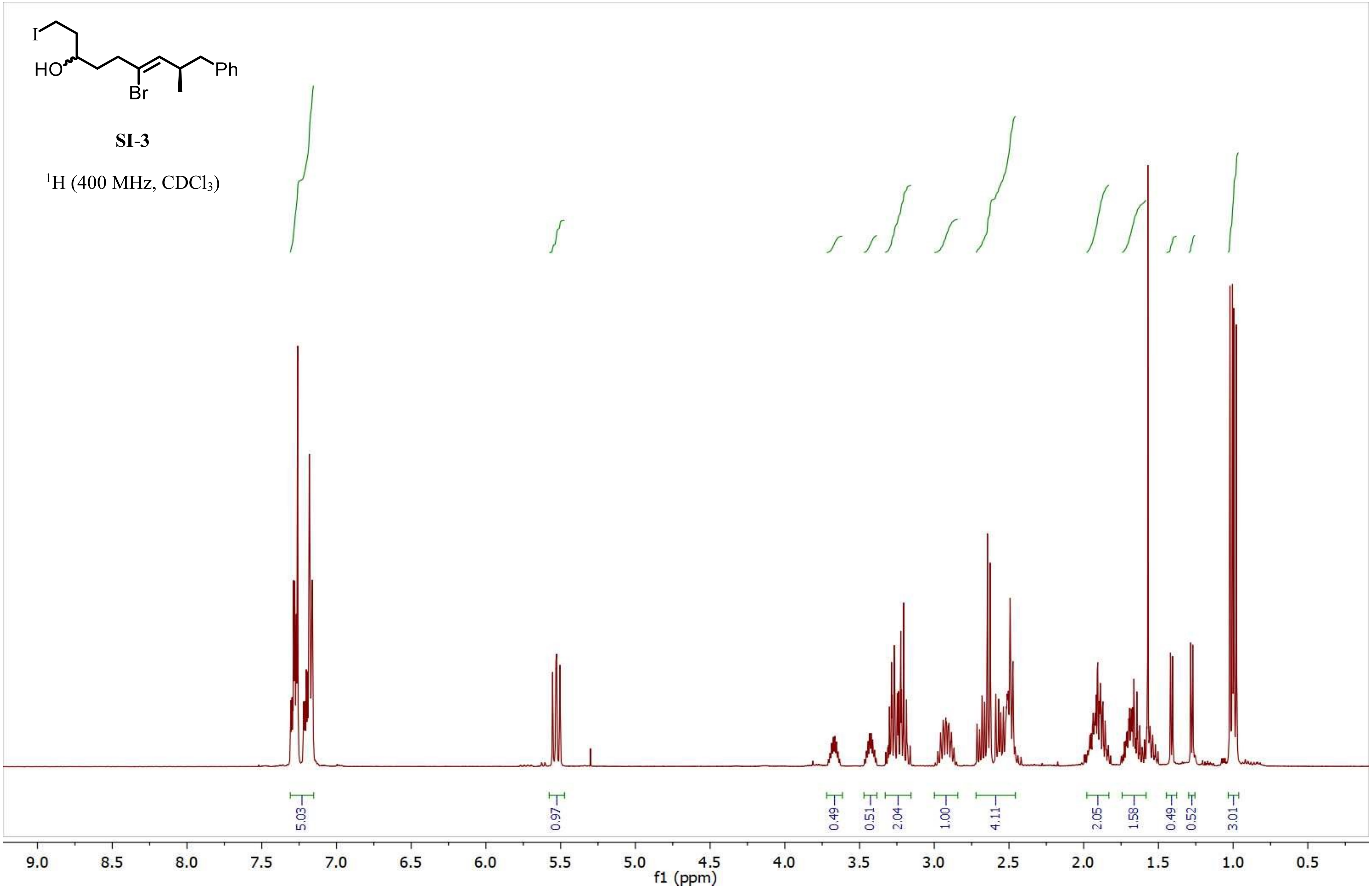
8*R*-**22**

^{1}H (400 MHz, CDCl$_3$)



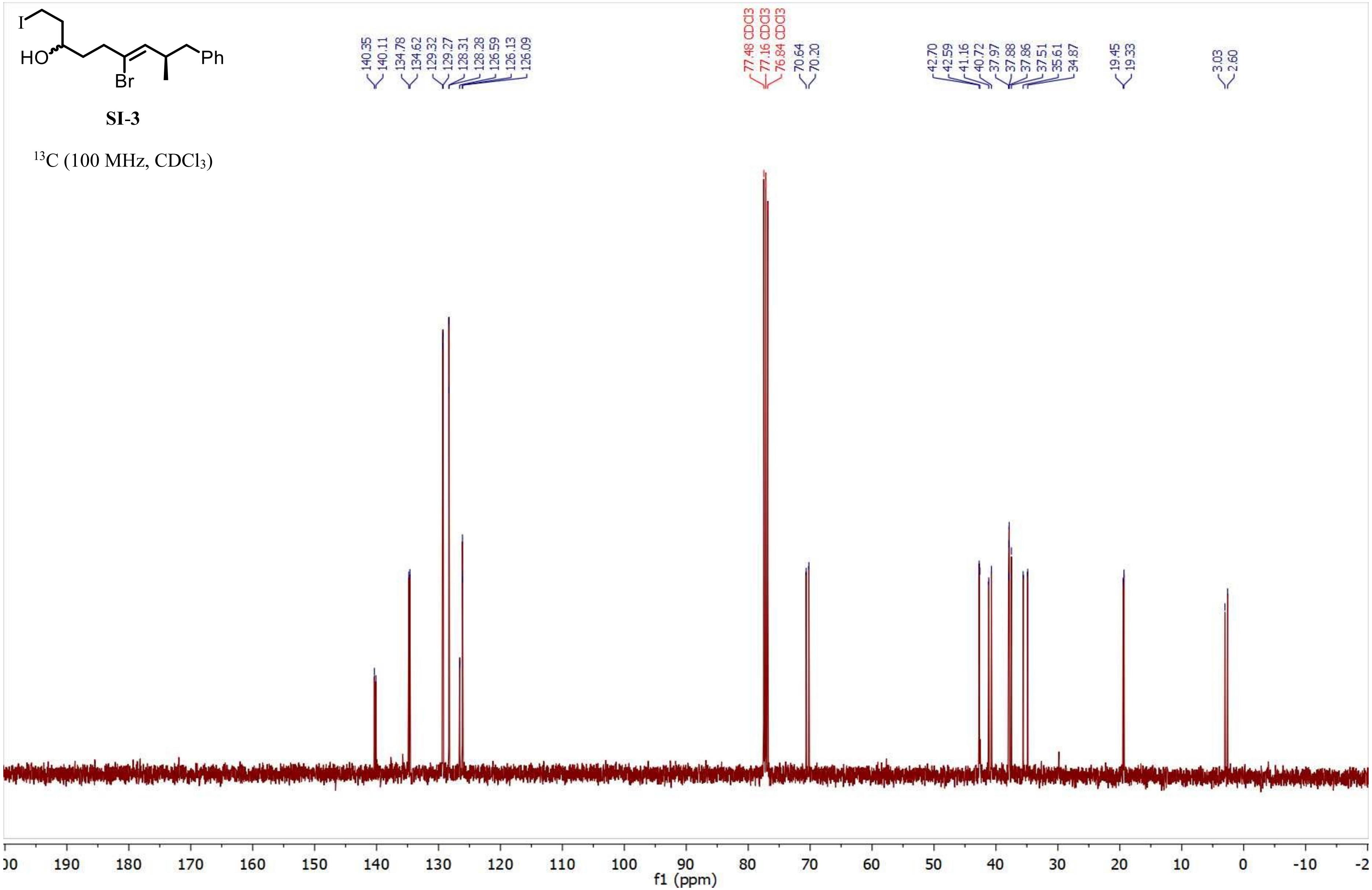
8*R*-**22**

^{13}C (100 MHz, CDCl$_3$)



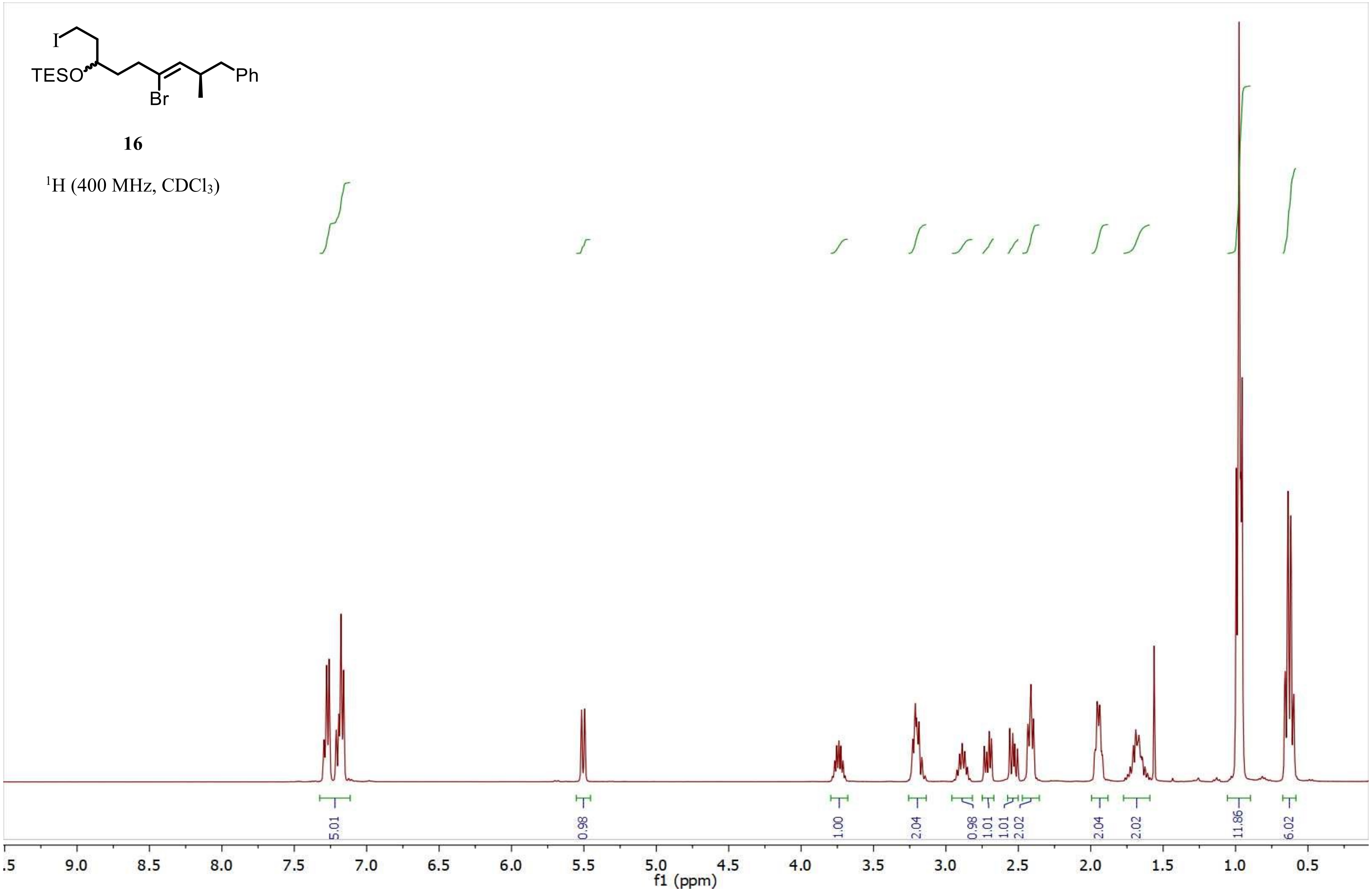
SI-3

^{1}H (400 MHz, CDCl$_3$)



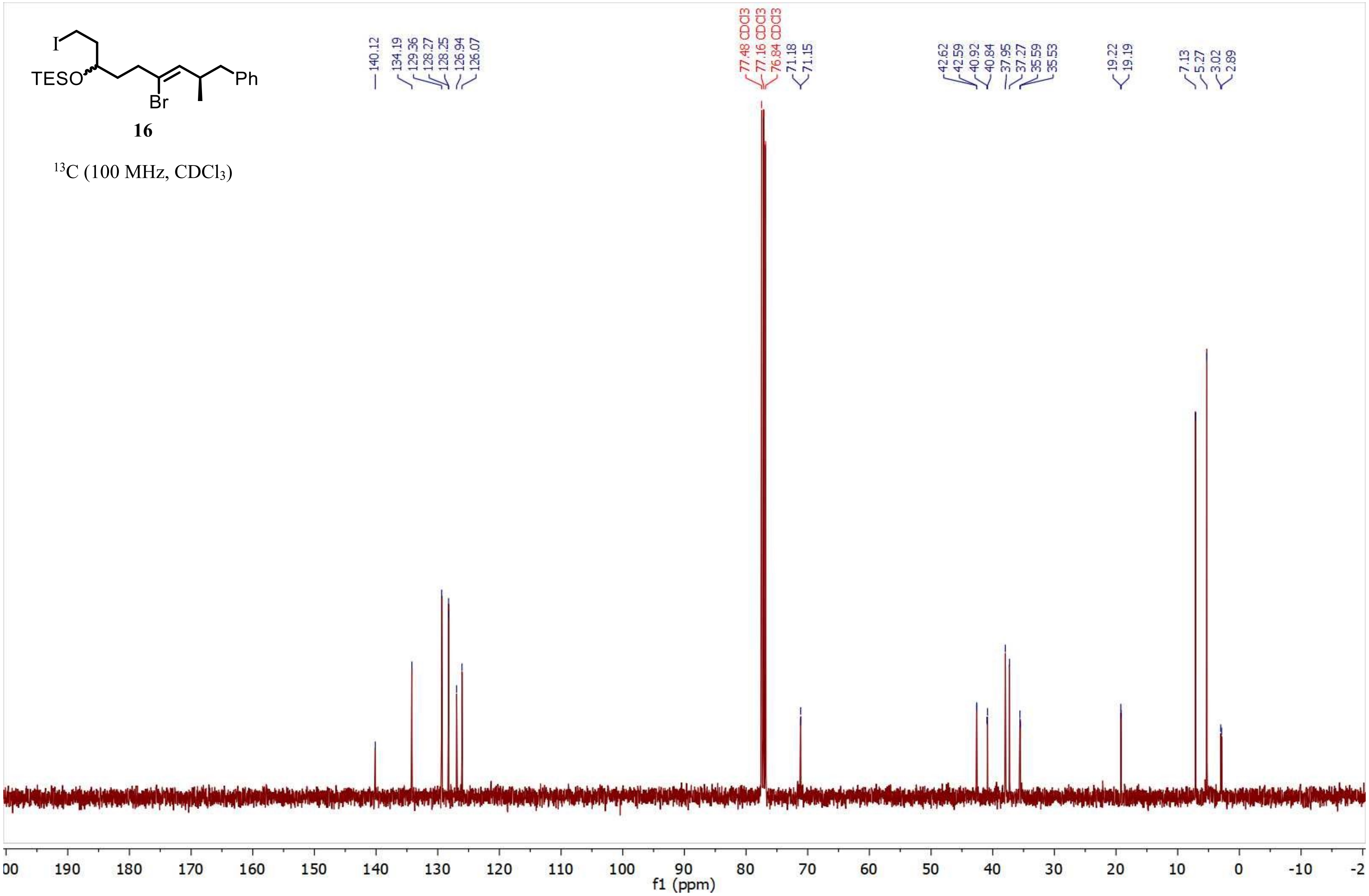
SI-3

^{13}C (100 MHz, CDCl$_3$)



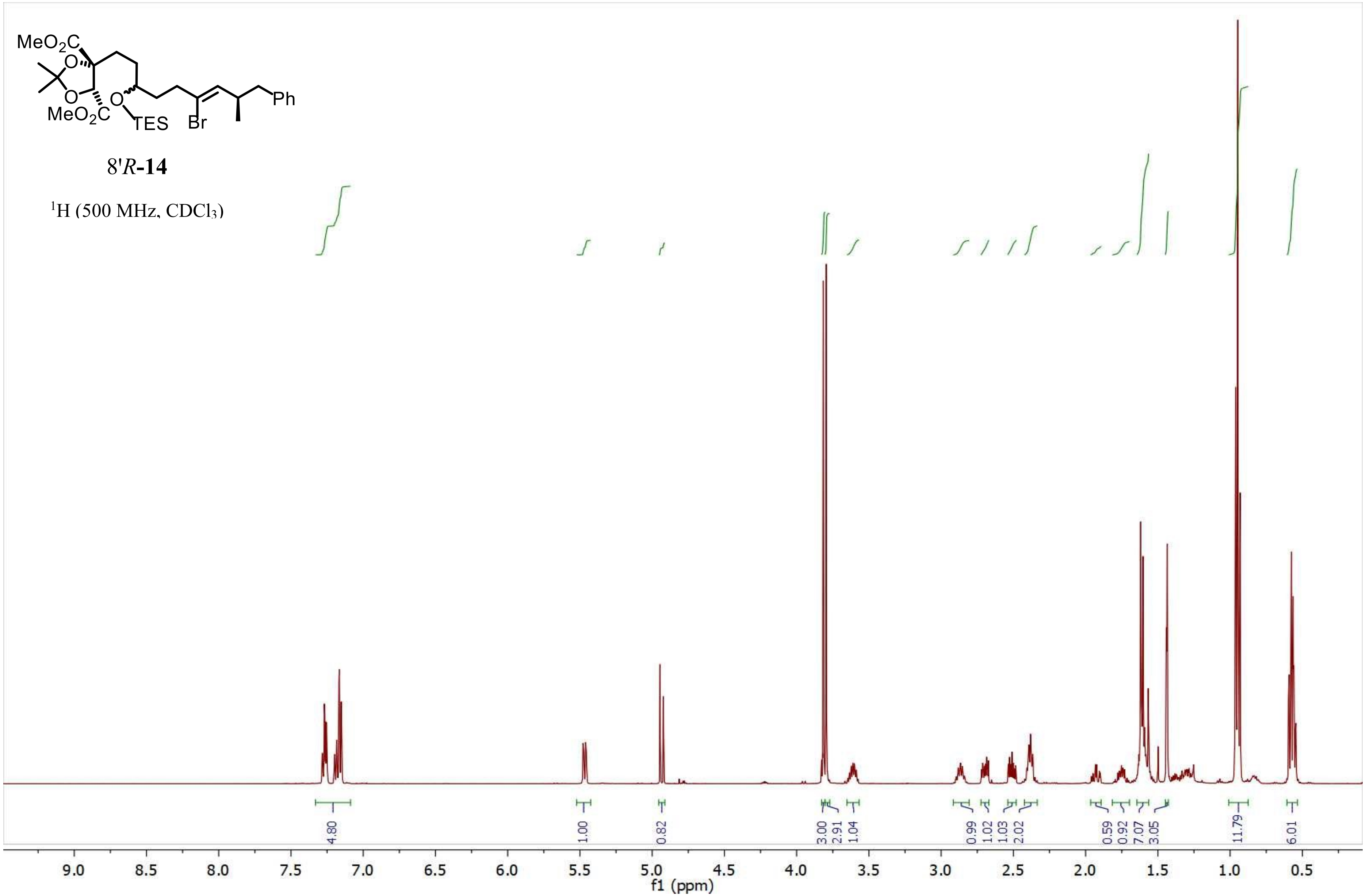
16

^{1}H (400 MHz, $CDCl_3$)



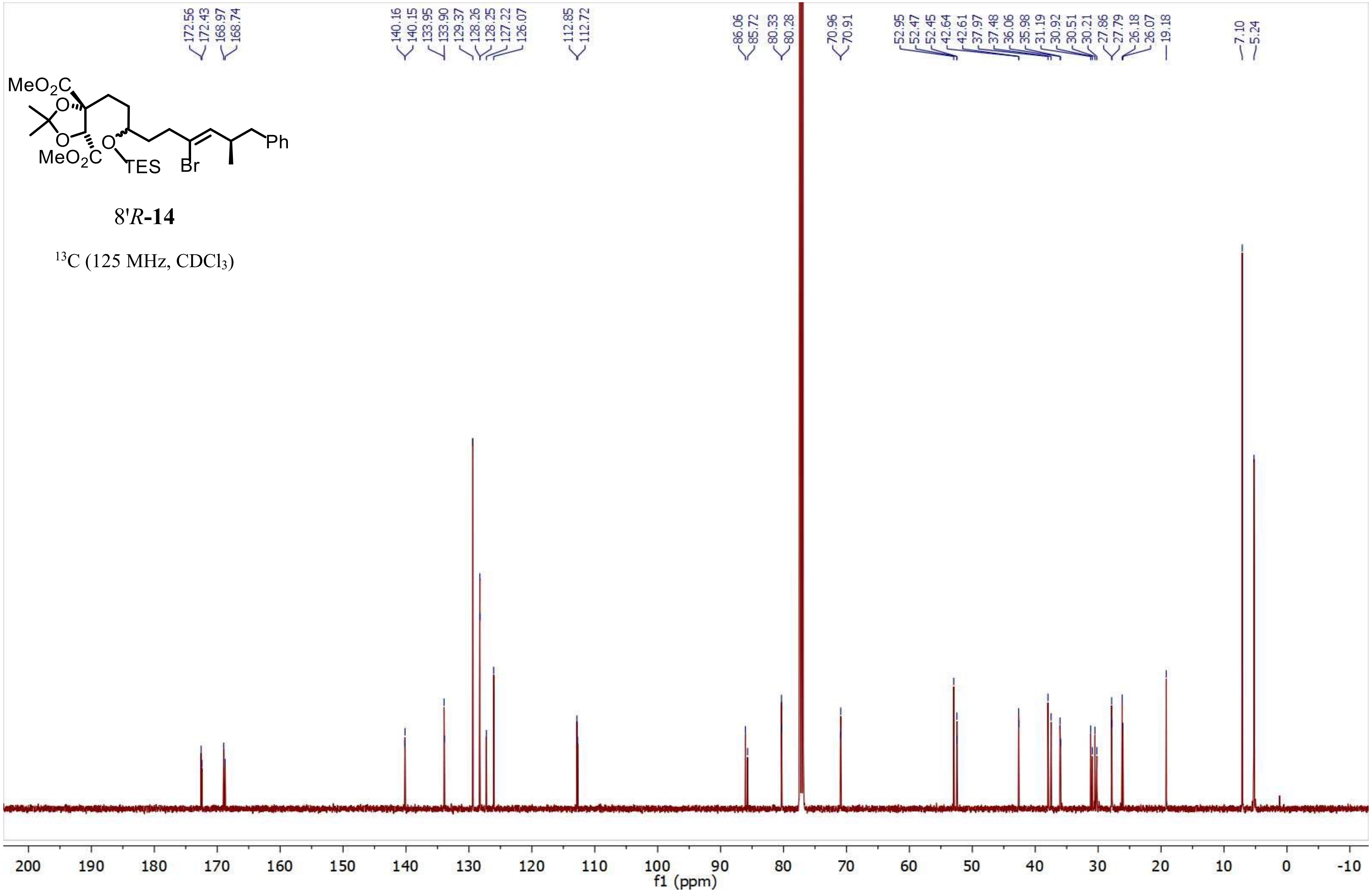
16

^{13}C (100 MHz, CDCl$_3$)



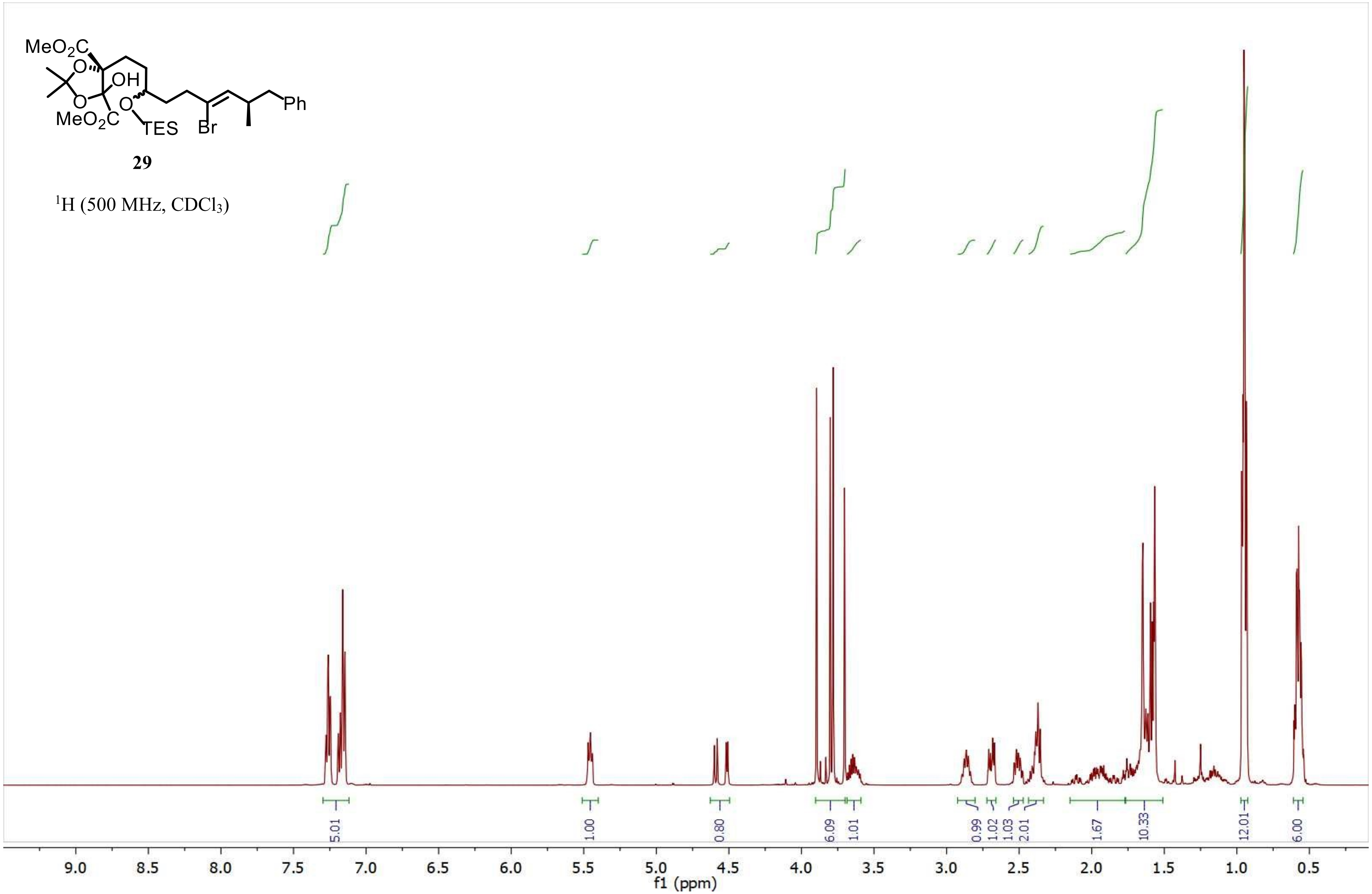
8'*R*-**14**

^{1}H (500 MHz, CDCl$_3$)



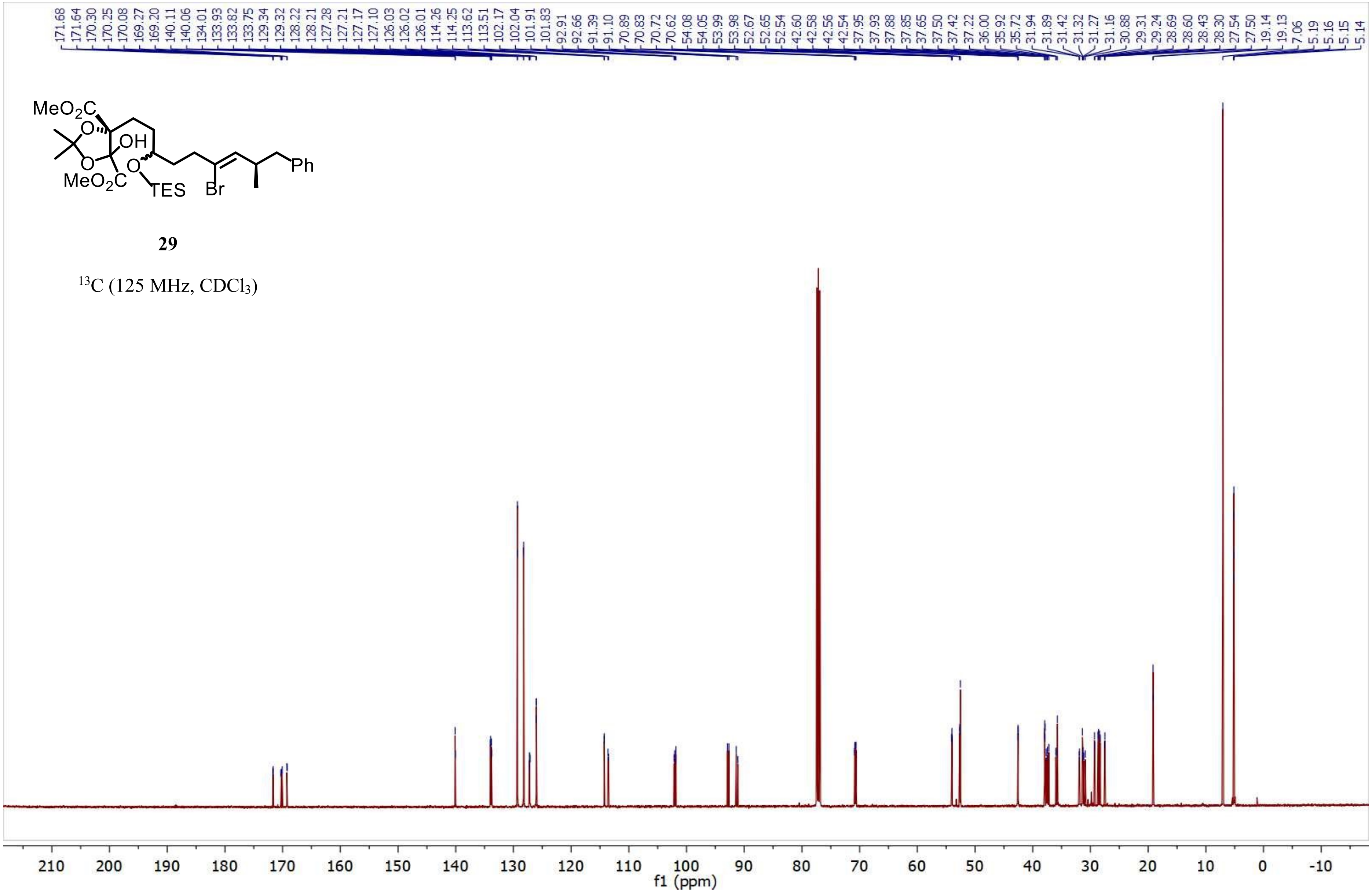
8'*R*-**14**

^{13}C (125 MHz, $CDCl_3$)



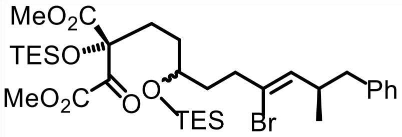
29

^{1}H (500 MHz, CDCl$_3$)



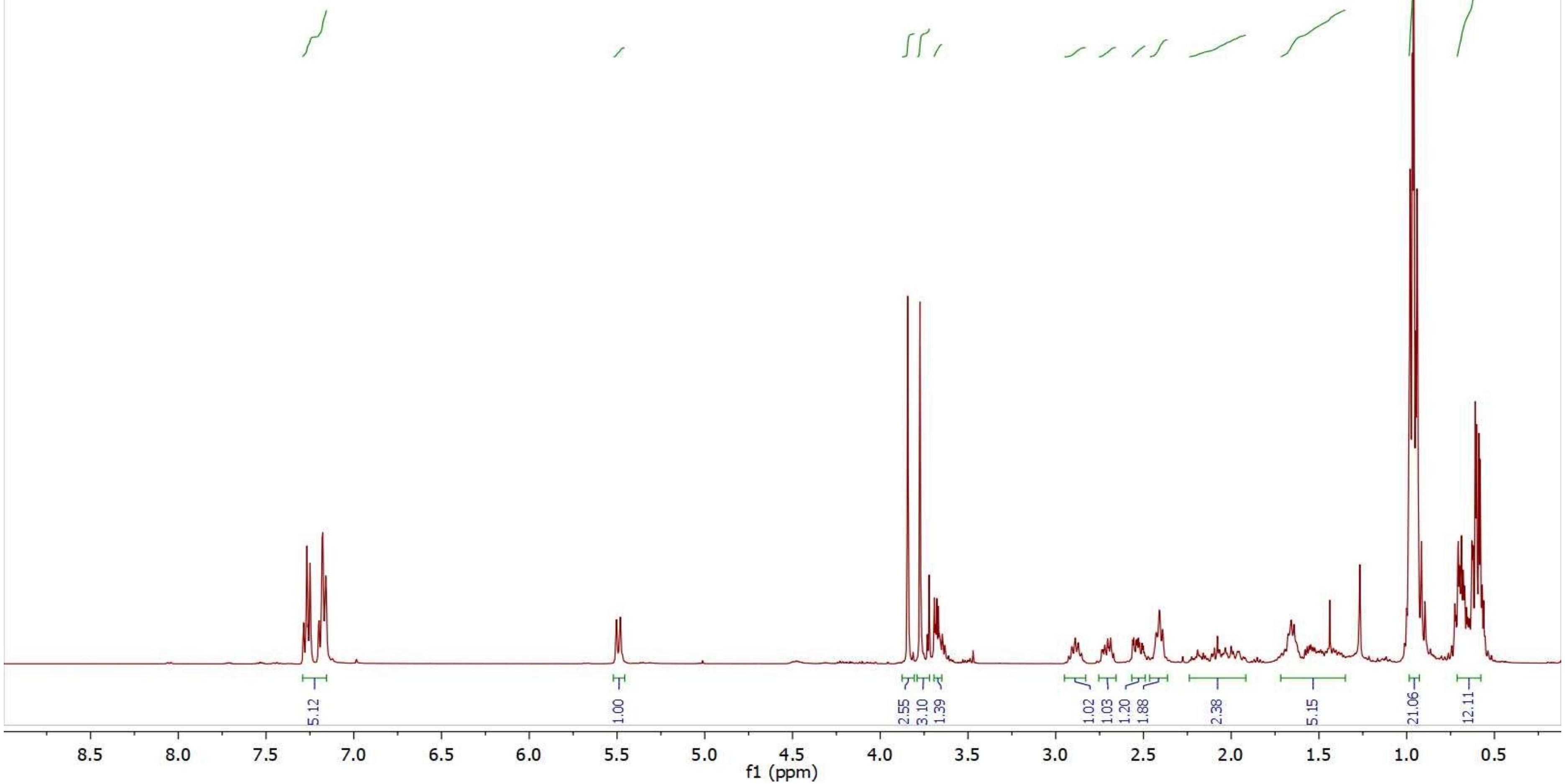
29

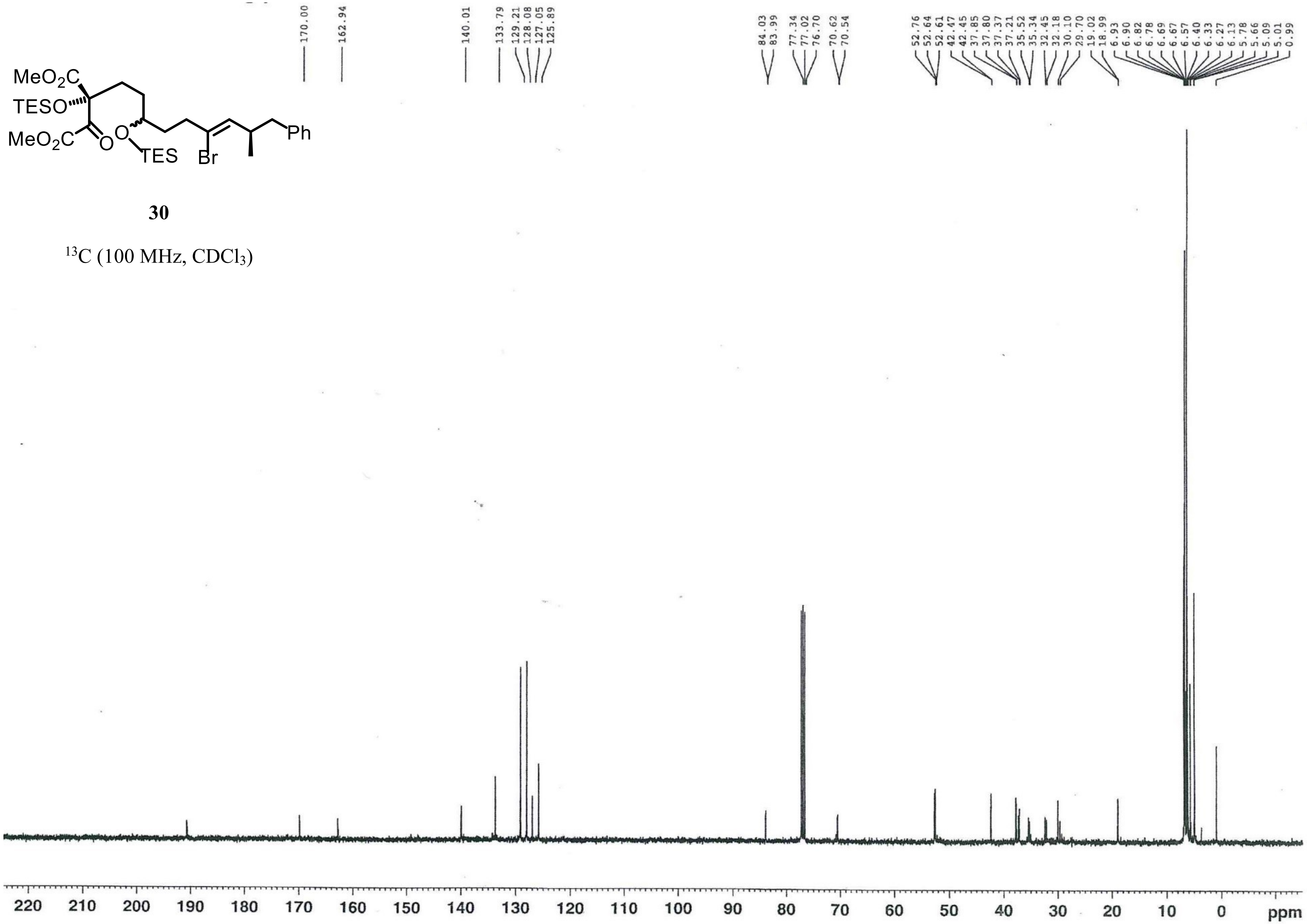
^{13}C (125 MHz, CDCl$_3$)



30

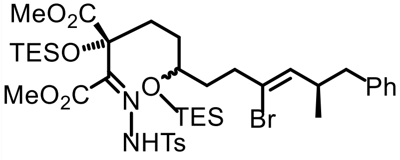
^{1}H (400 MHz, CDCl$_3$)





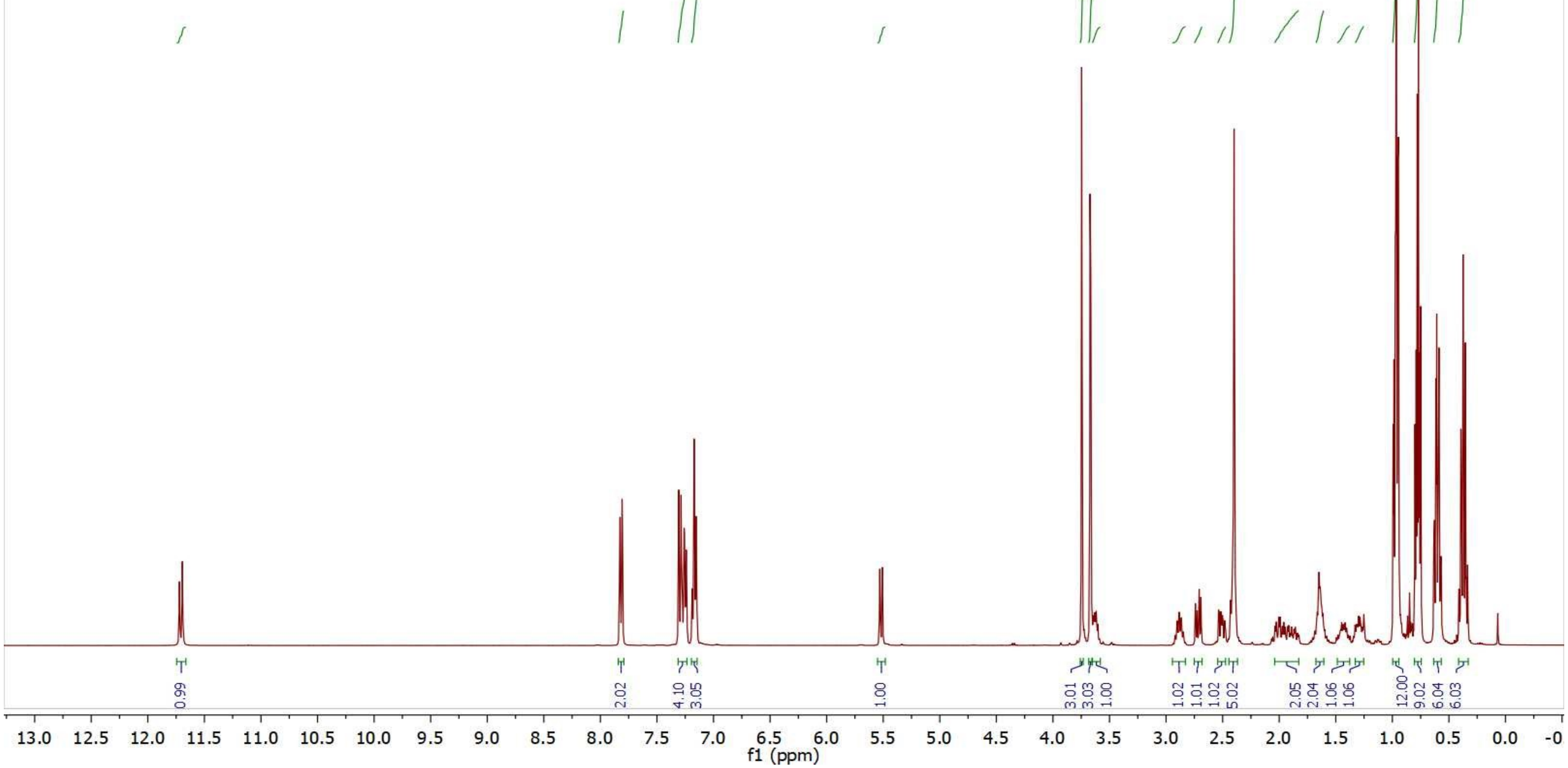
30

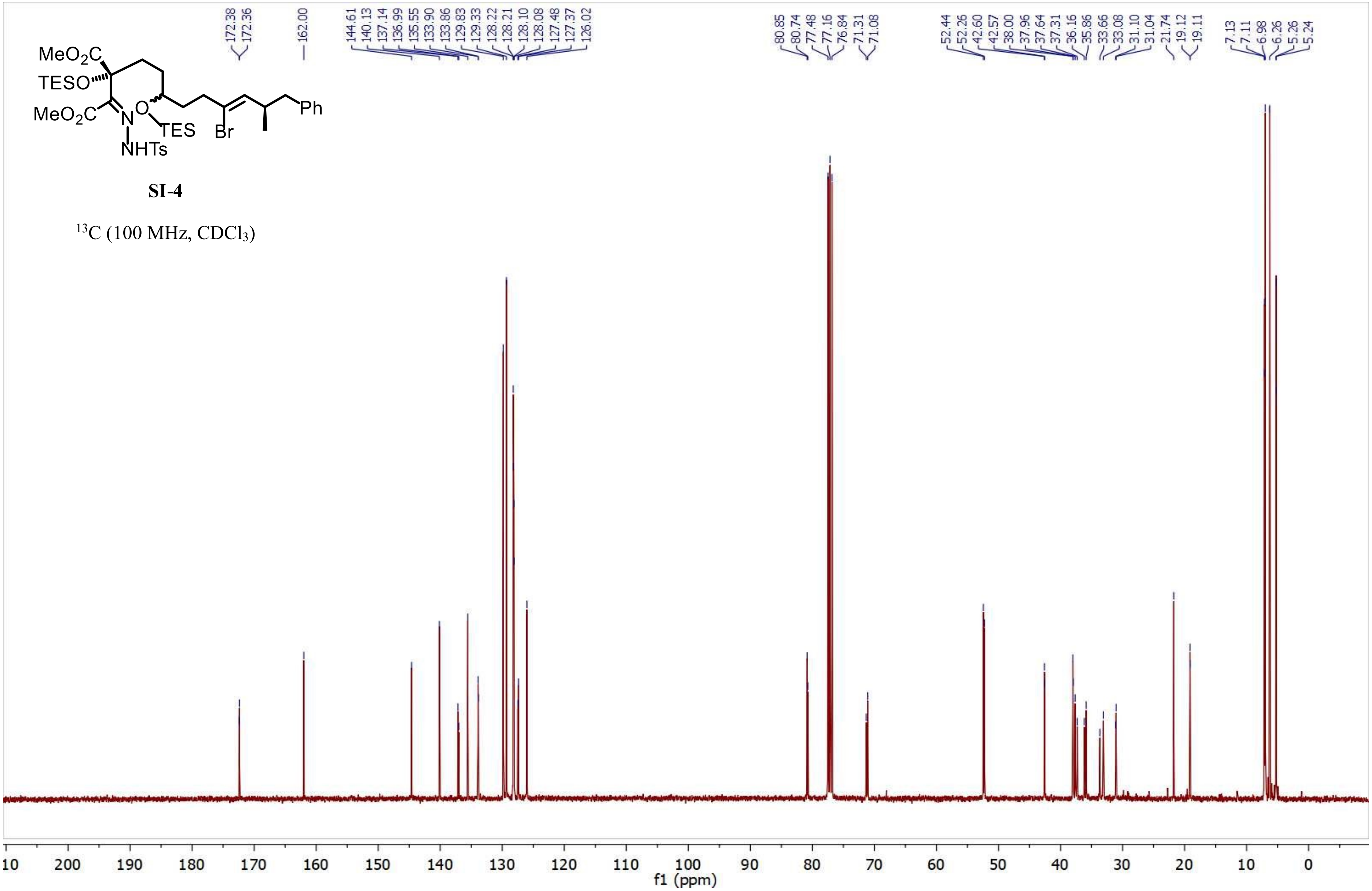
^{13}C (100 MHz, CDCl$_3$)



SI-4

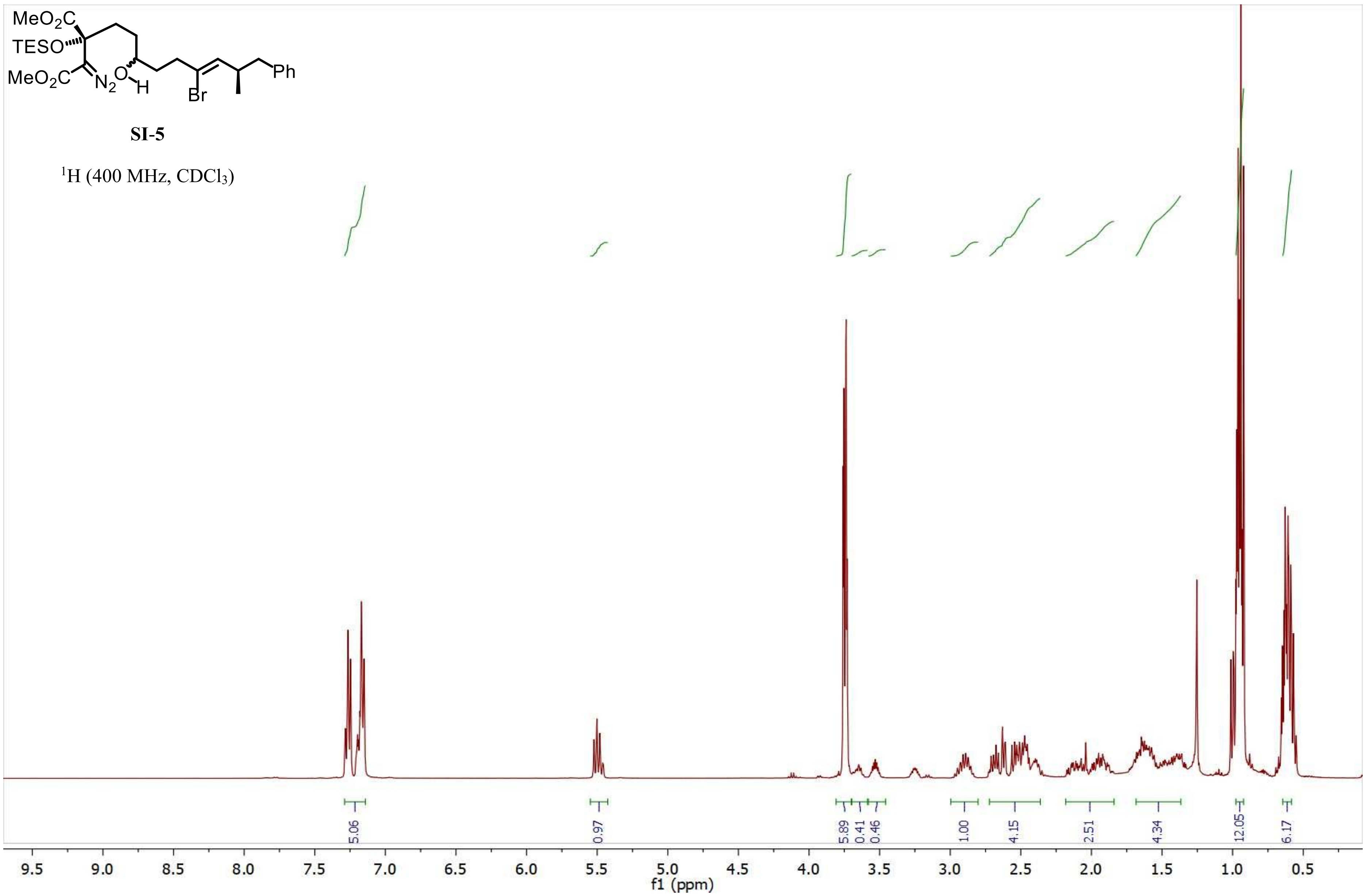
^1H (400 MHz, $CDCl_3$)





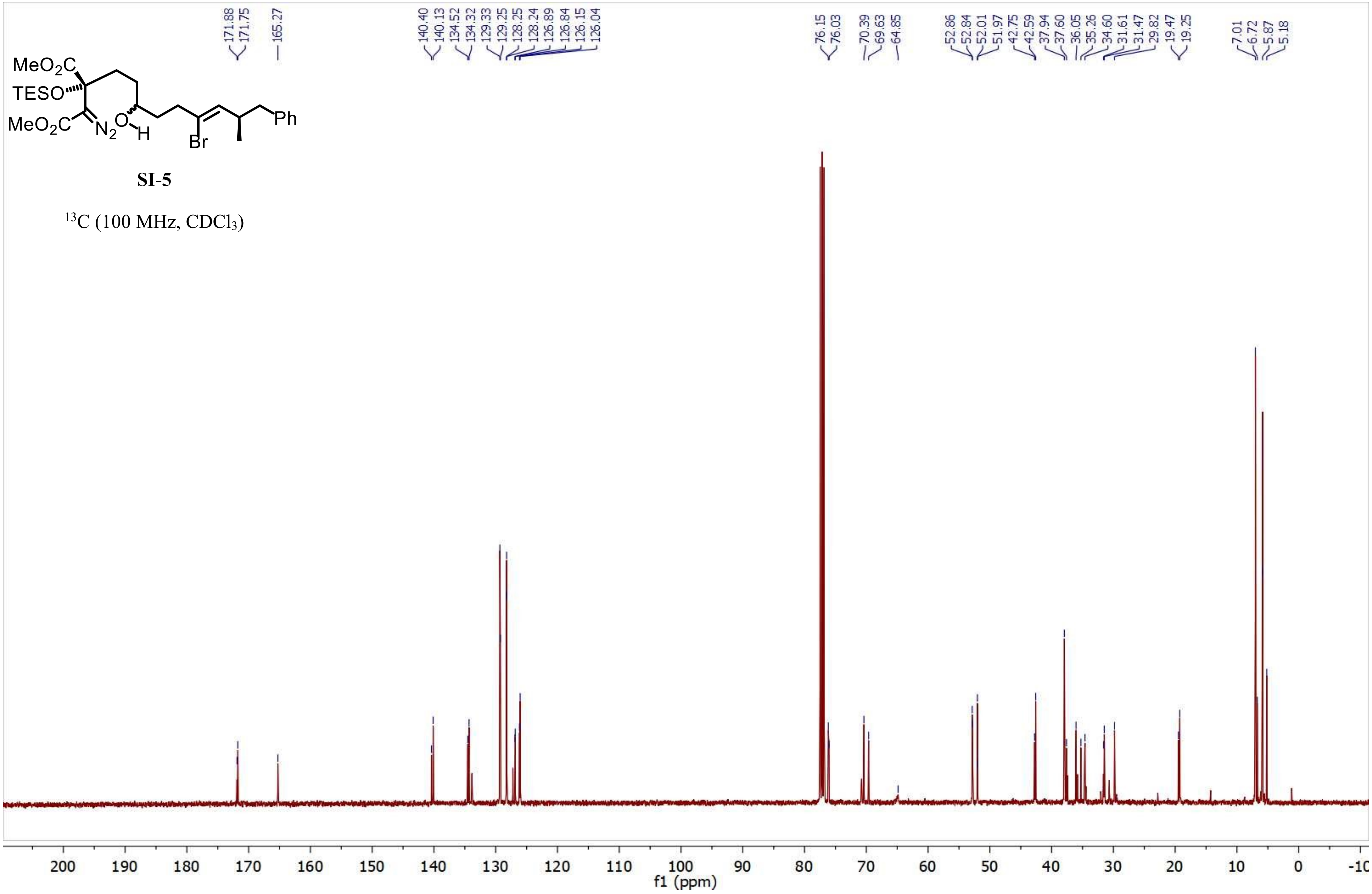
SI-4

^{13}C (100 MHz, CDCl$_3$)



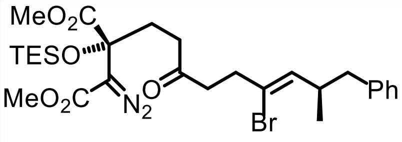
SI-5

^{1}H (400 MHz, CDCl$_3$)



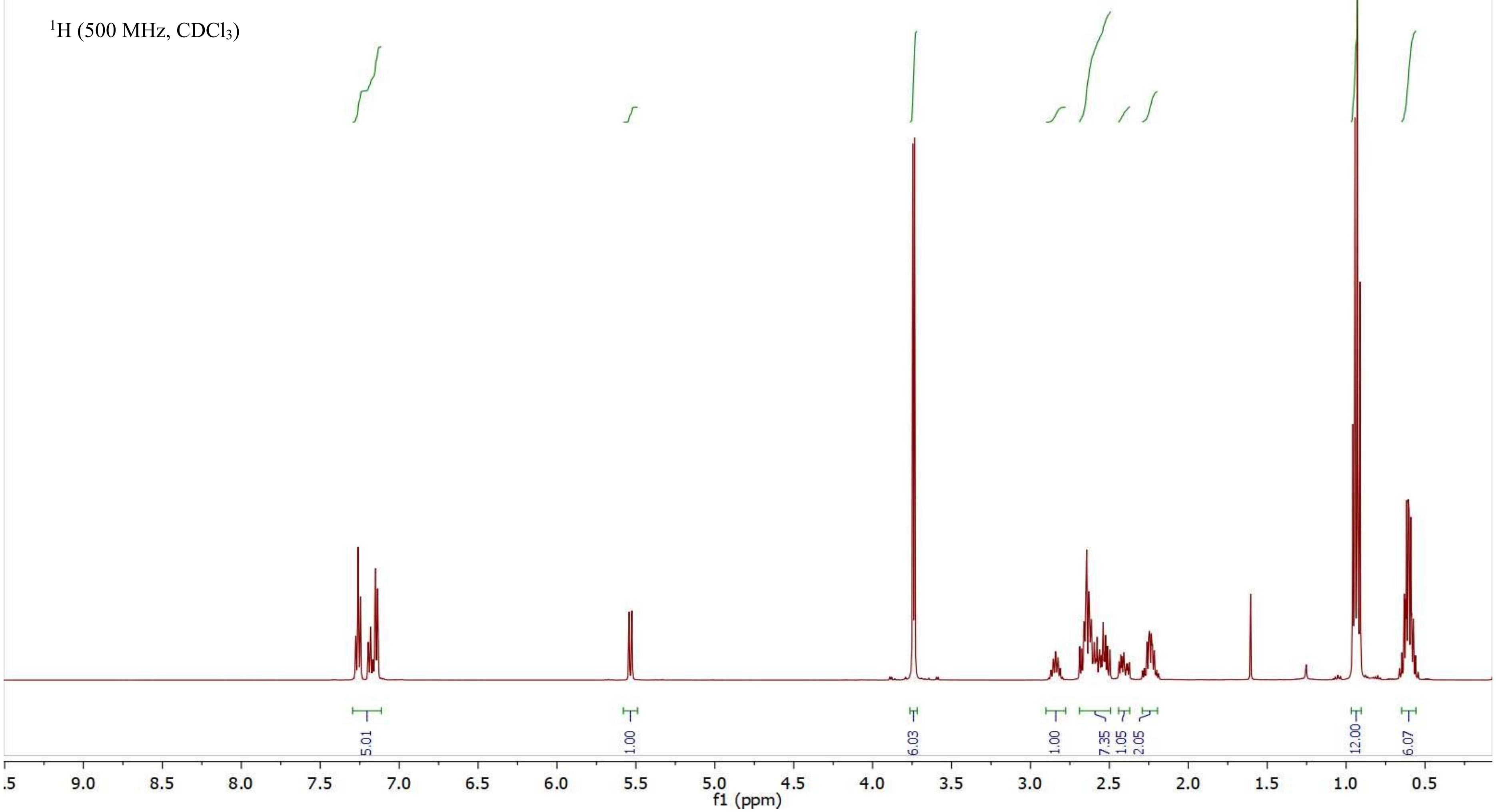
SI-5

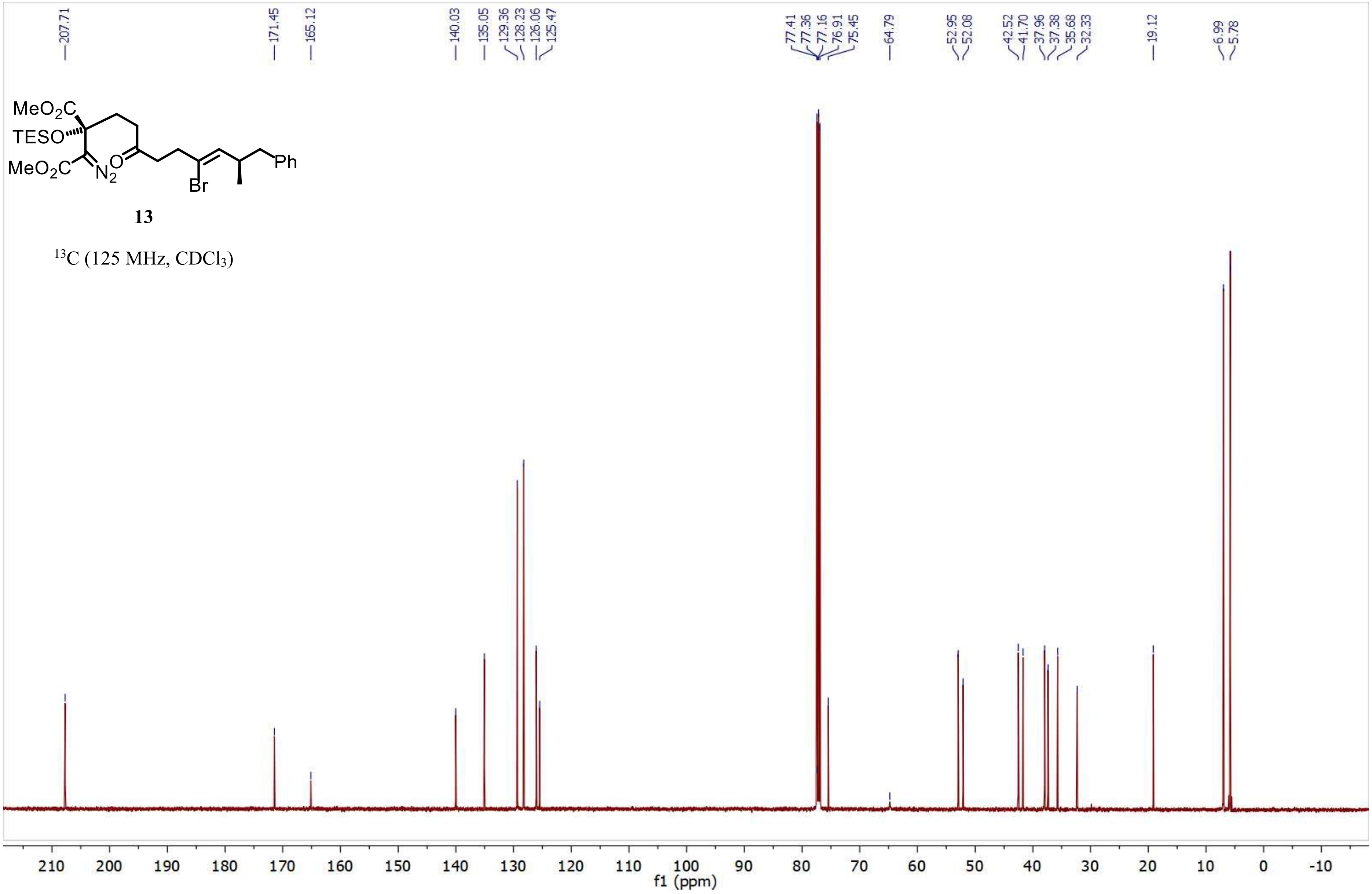
^{13}C (100 MHz, CDCl$_3$)



13

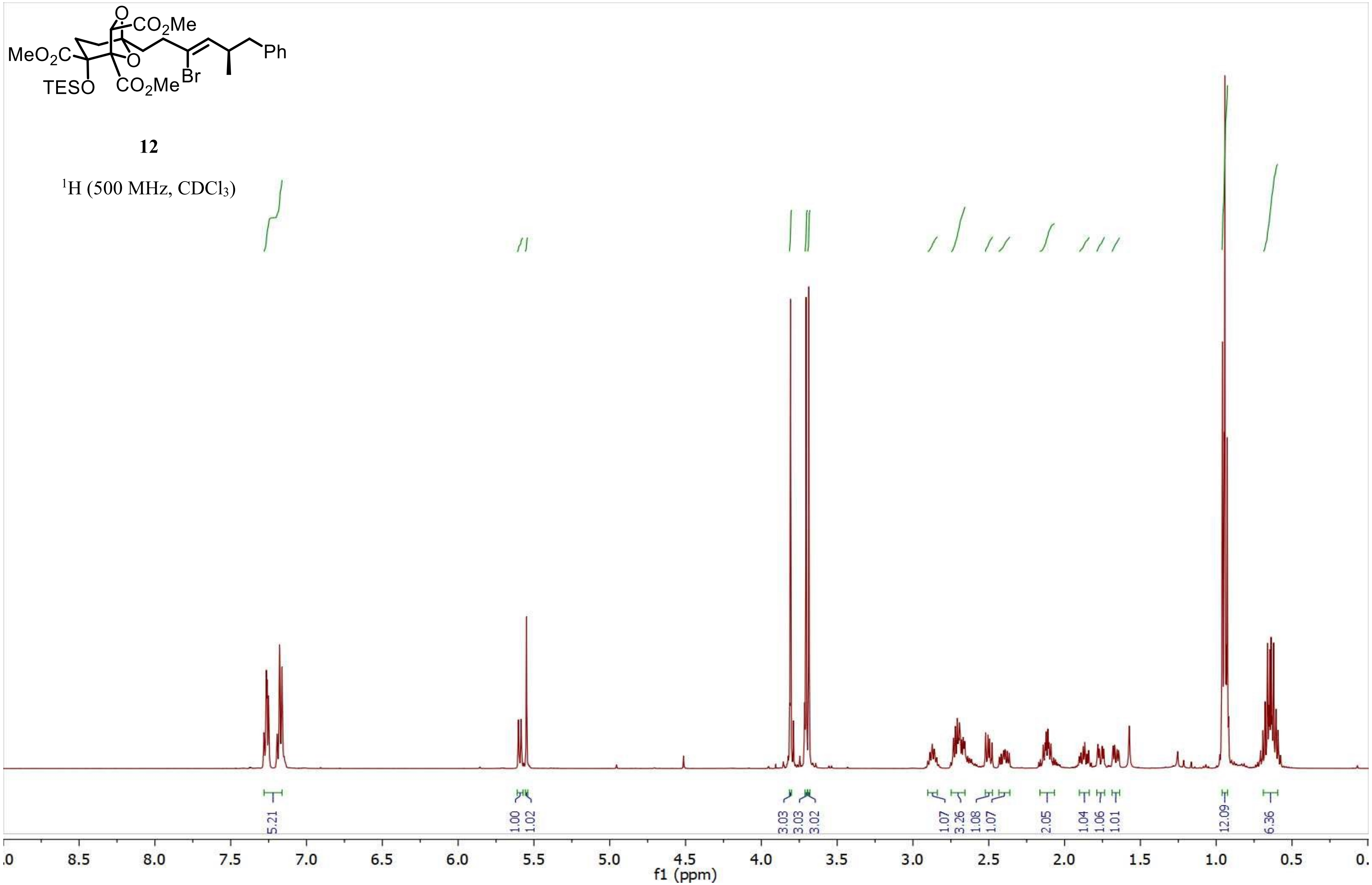
^{1}H (500 MHz, CDCl$_3$)





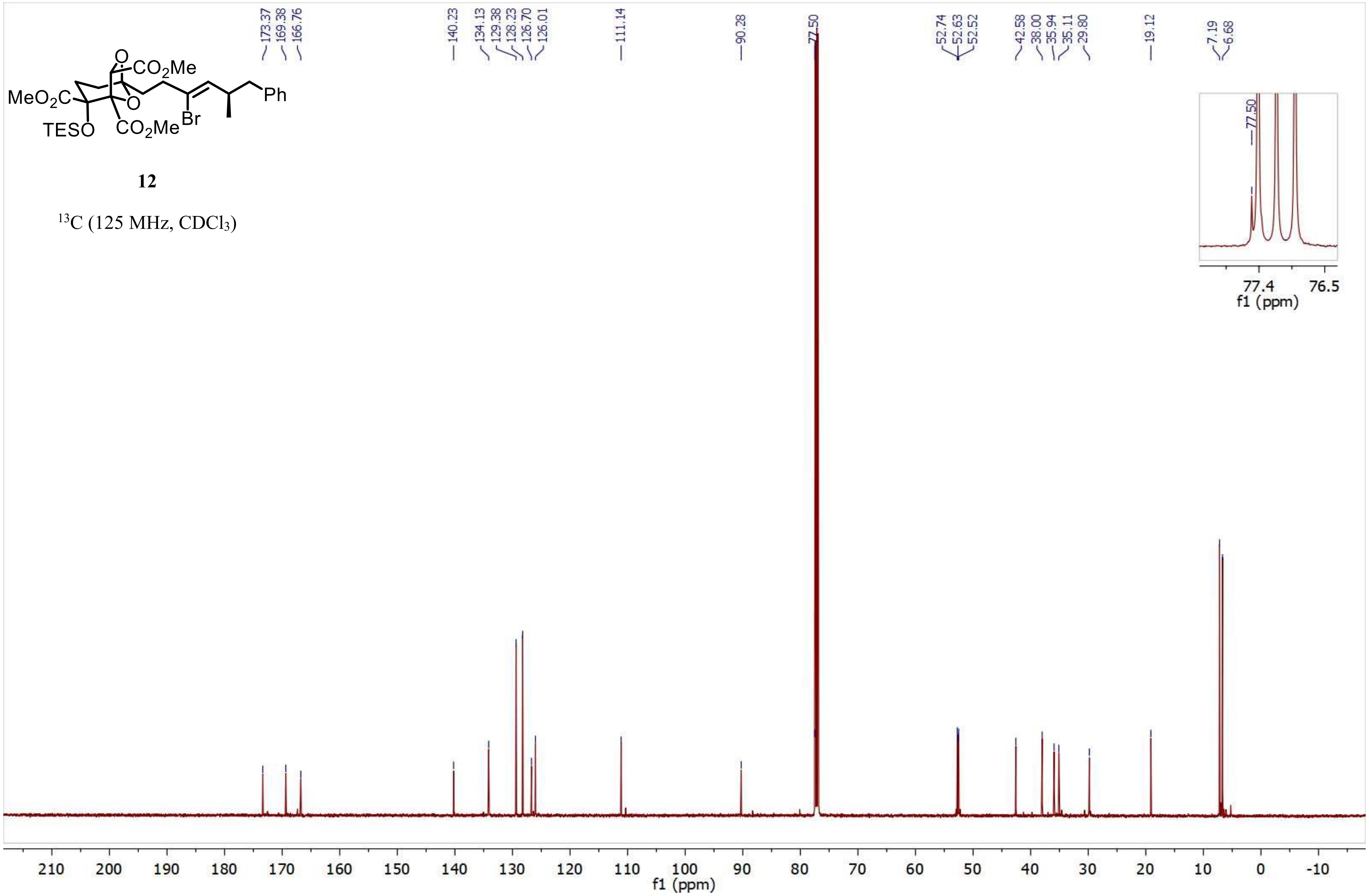
13

^{13}C (125 MHz, CDCl$_3$)



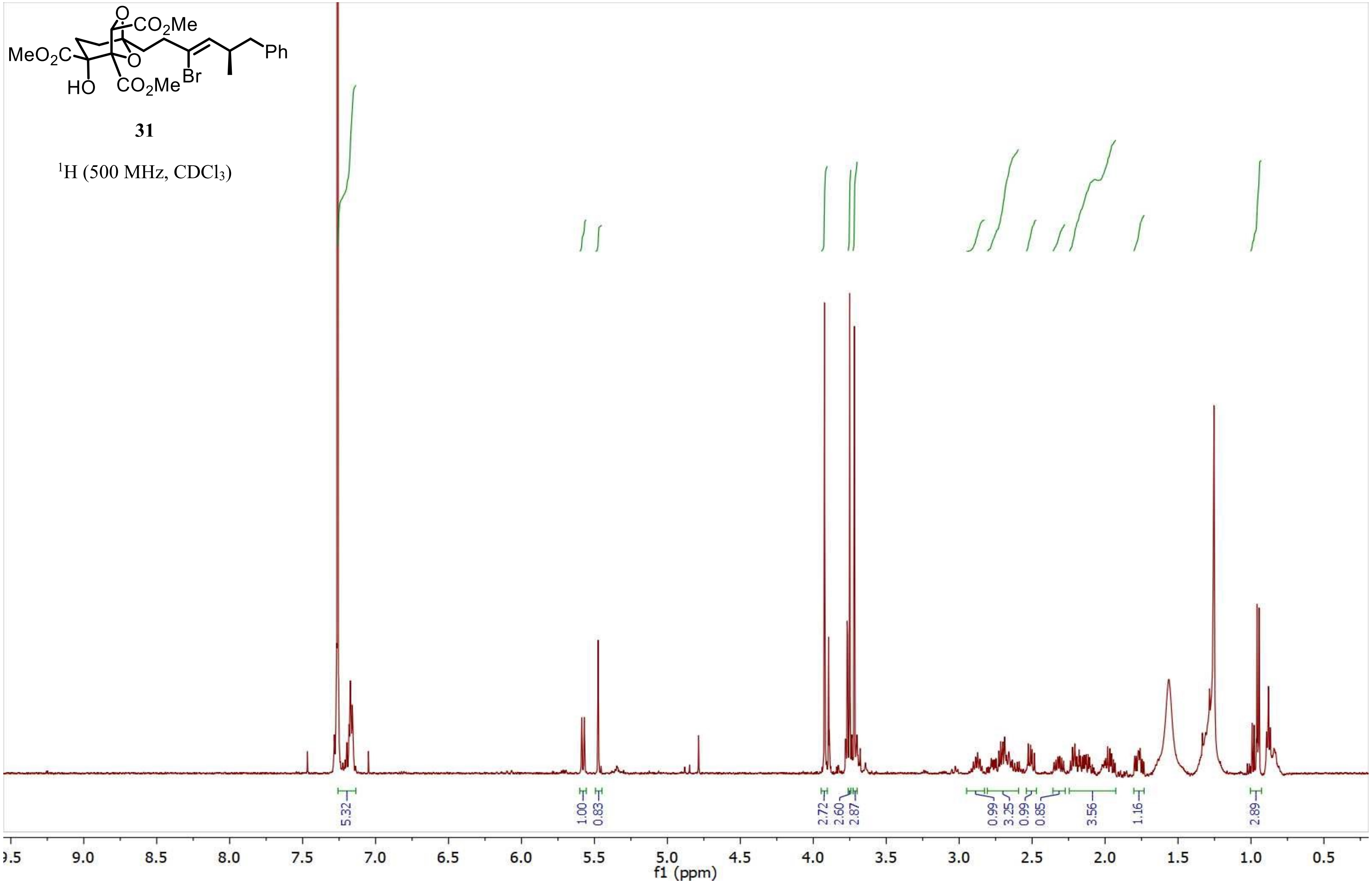
12

^{1}H (500 MHz, CDCl$_3$)



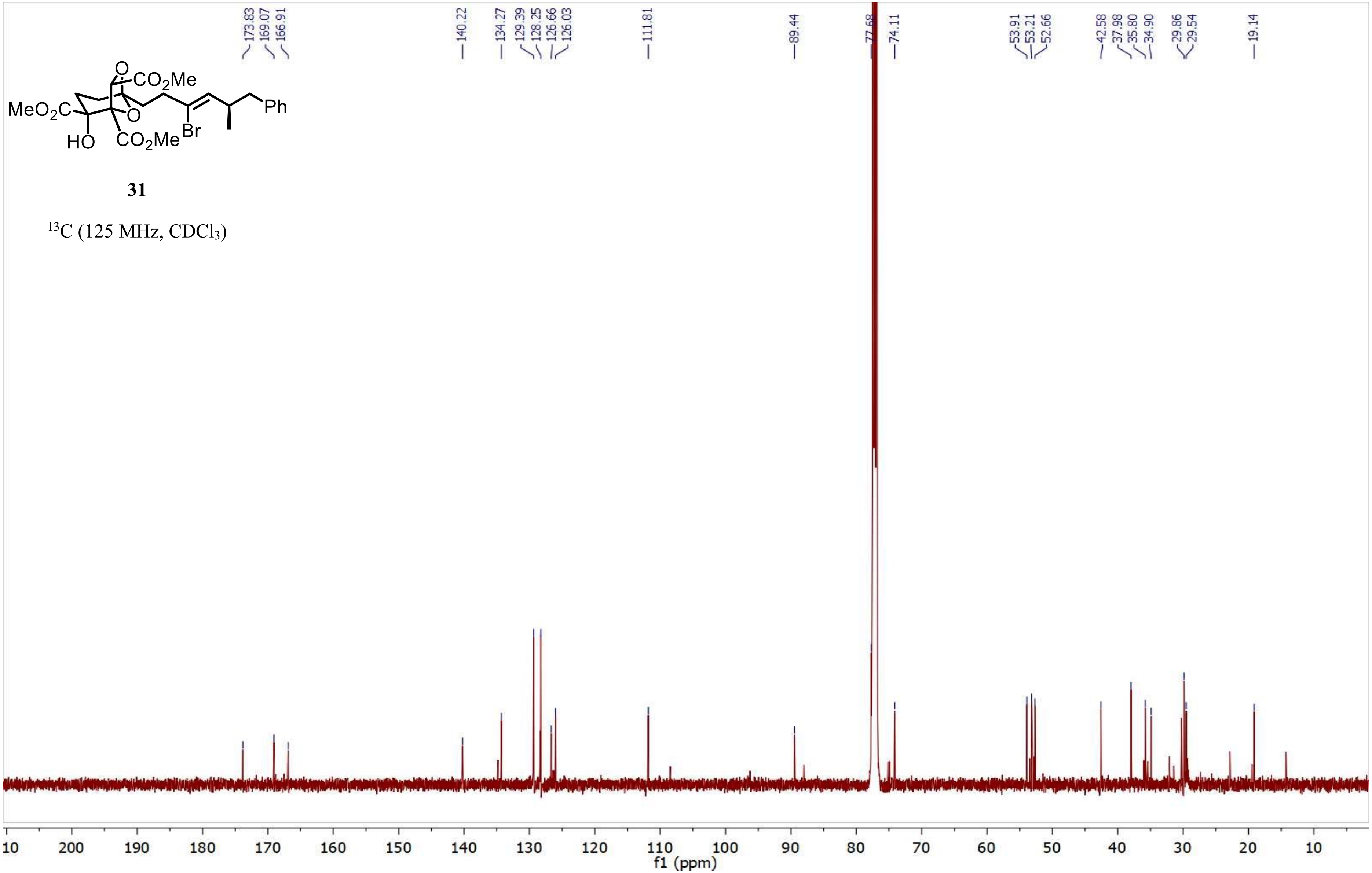
12

^{13}C (125 MHz, CDCl$_3$)



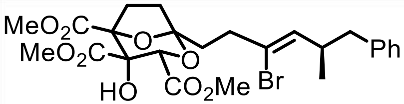
31

^{1}H (500 MHz, CDCl$_3$)



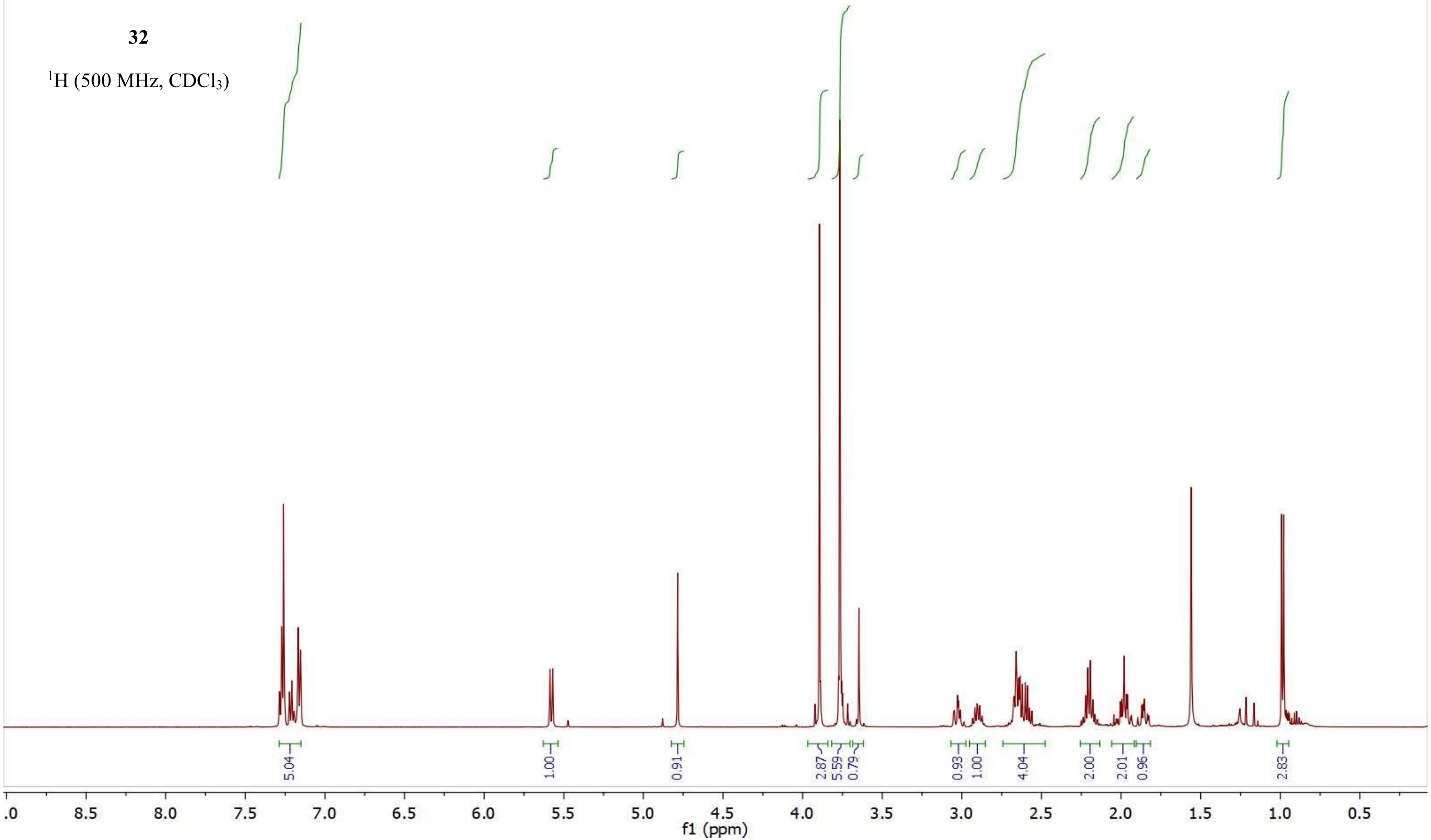
31

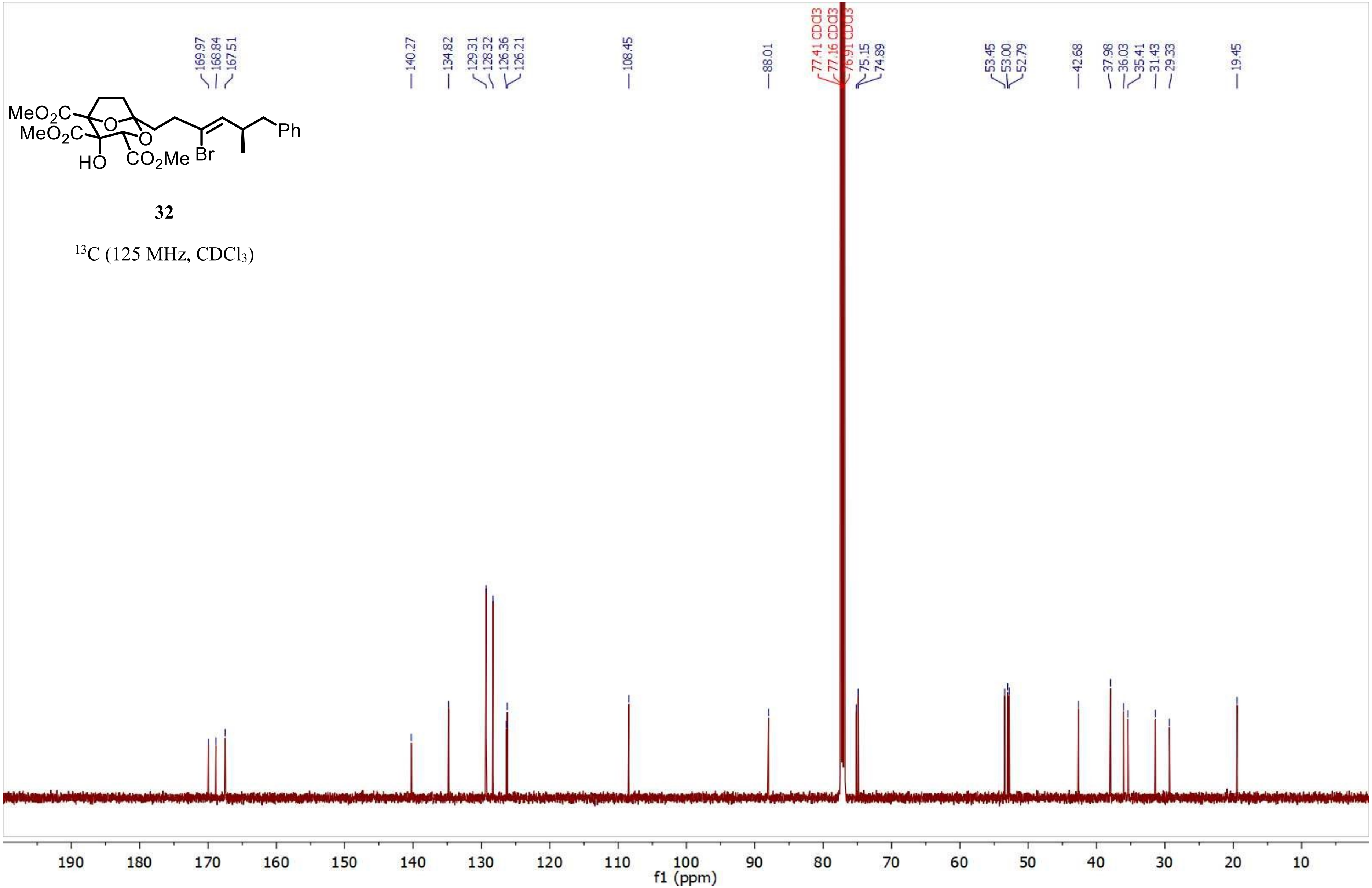
^{13}C (125 MHz, $CDCl_3$)



32

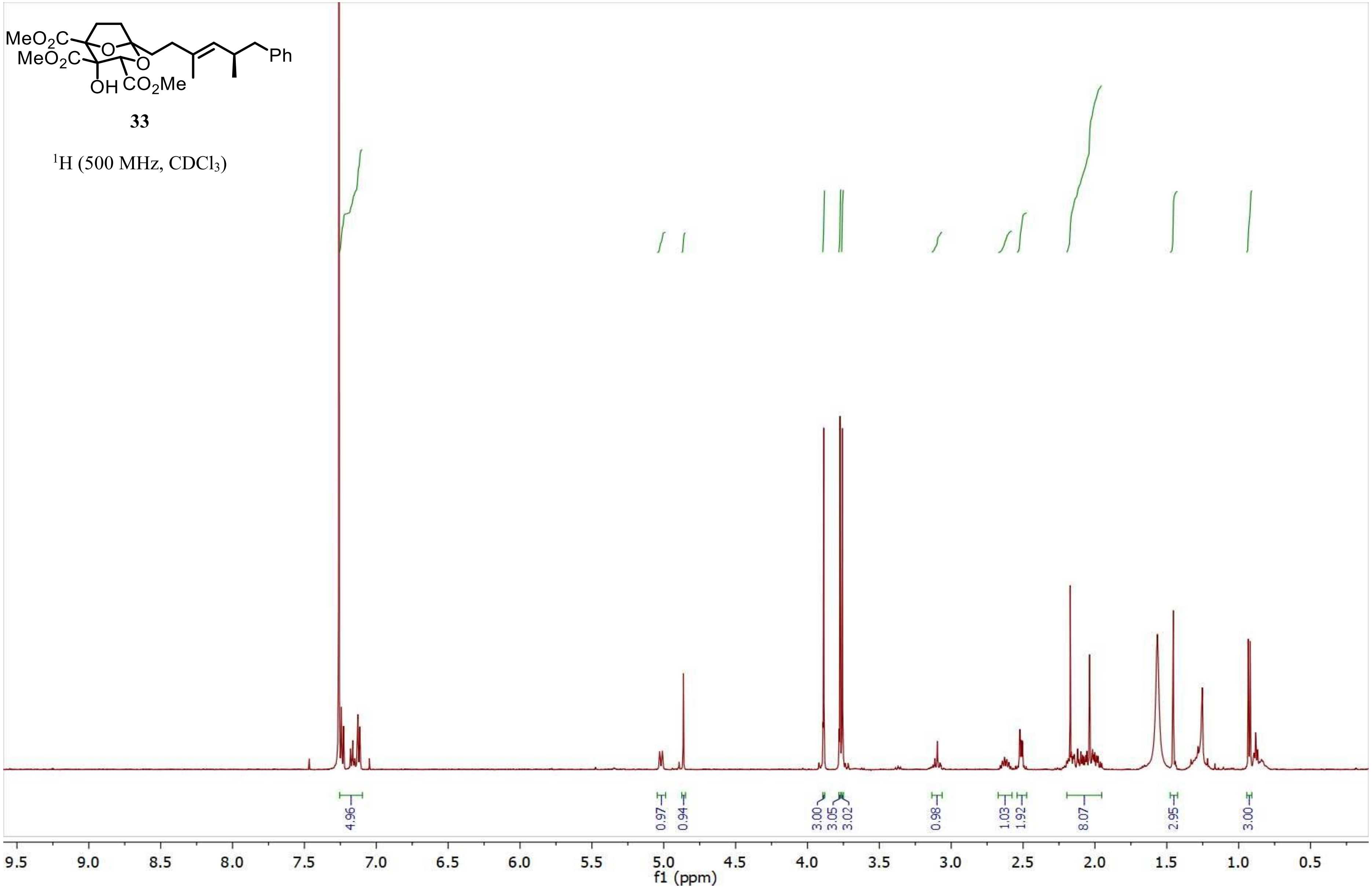
^{1}H (500 MHz, CDCl$_3$)





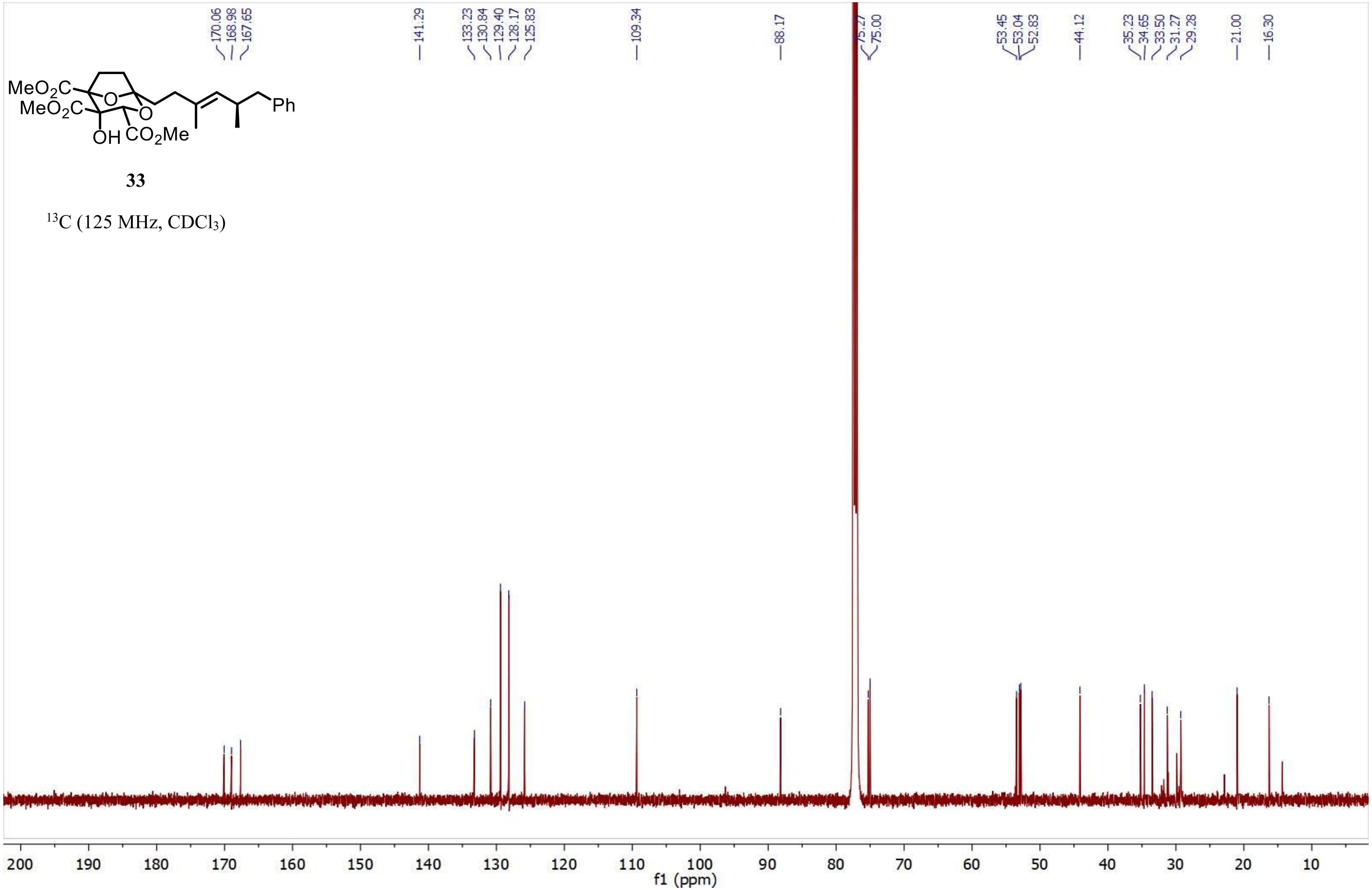
32

^{13}C (125 MHz, CDCl$_3$)



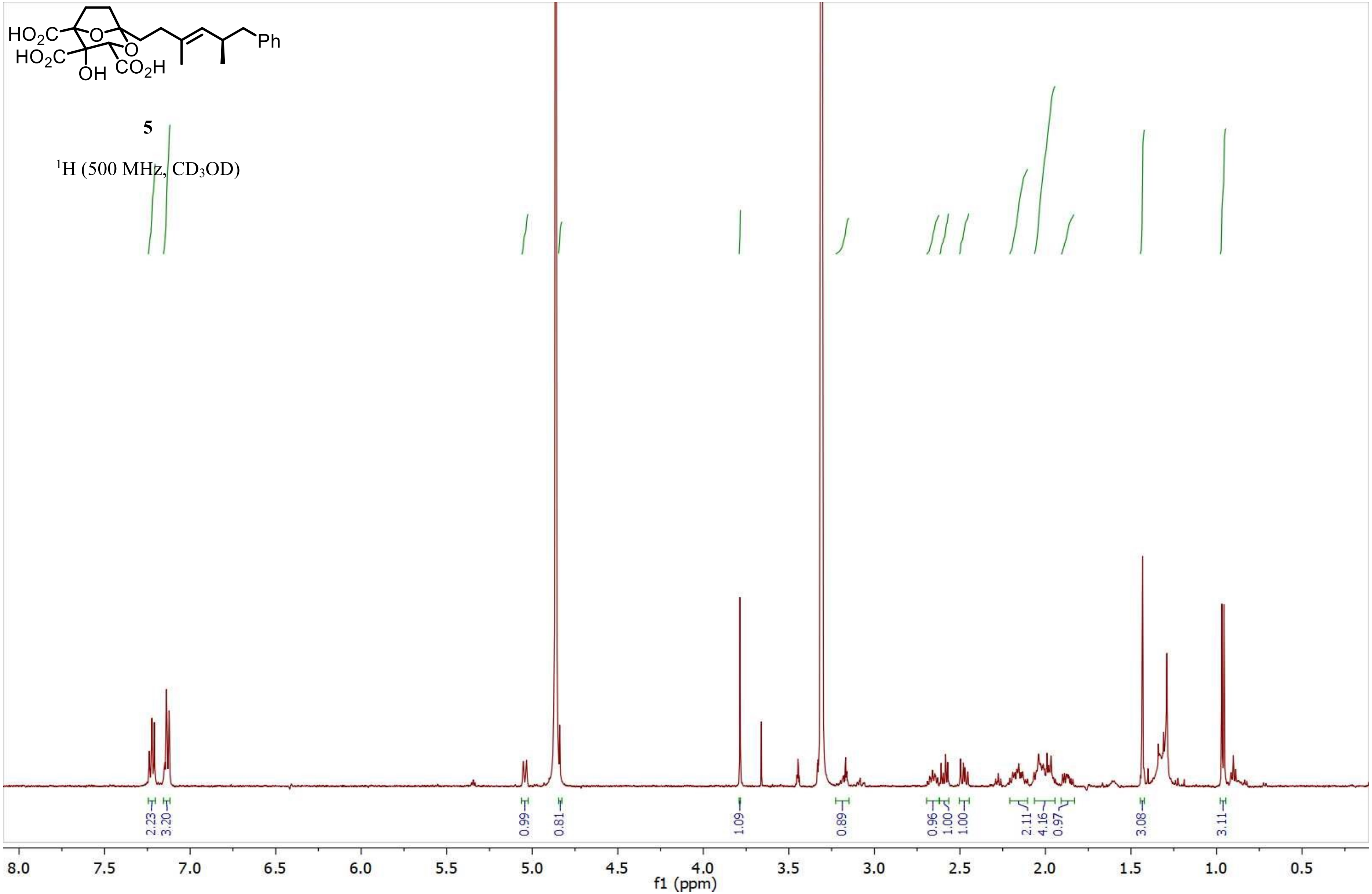
33

^{1}H (500 MHz, CDCl$_3$)



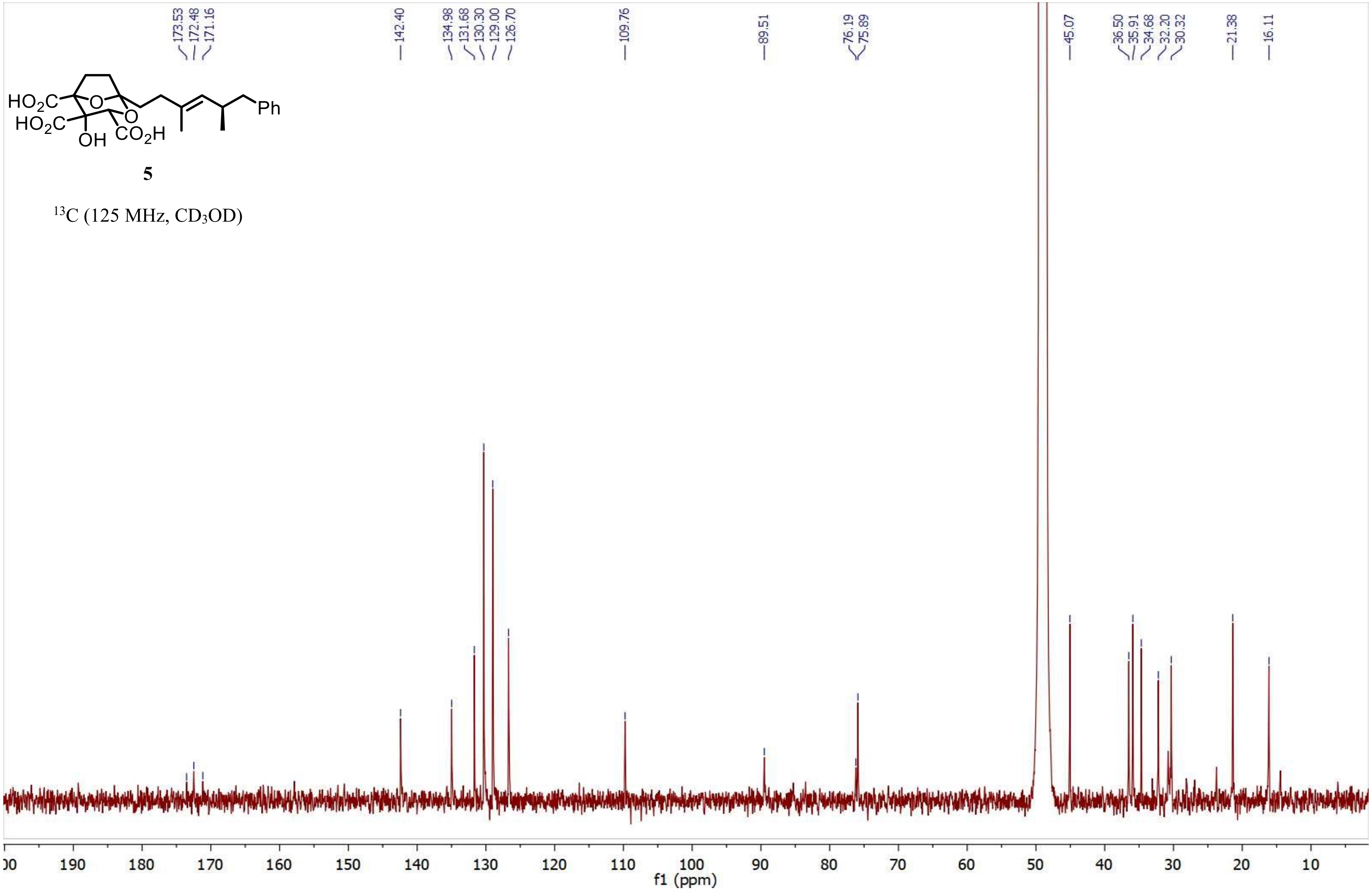
33

^{13}C (125 MHz, CDCl$_3$)



5

^1H (500 MHz, CD_3OD)



5

^{13}C (125 MHz, CD$_3$OD)