Supporting Information

for

STEREOCONTROLLED SYNHTESIS OF NITROGEN-SUBSTITUTED QUATERNARY STEREOGENIC CENTERS: LESSONS FROM A SYNTHTIC ROUTE TO THE CORE STRUCTURE OF SPHINGOFUNGIN E

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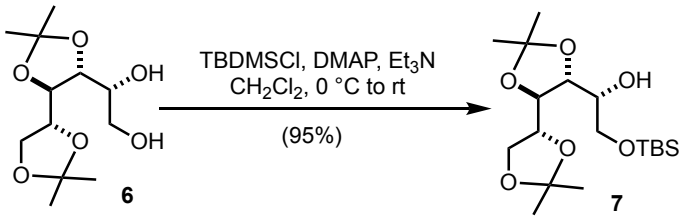
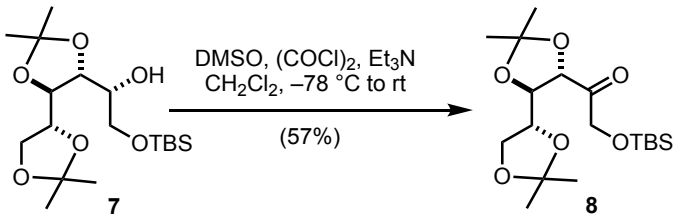
General Experimental

Reactions were run under an inert argon atmosphere when the reactions were sensitive to moisture or oxygen. Dichloromethane, acetonitrile, and toluene were dried over molecular sieves 3 Å. All other commercially available reagents were used as received. Reactions were monitored by thin layer chromatography (TLC) on glass plates 0.25 mm coated with silica gel 60 F_{254} (MERCK 1.05715). Open-column chromatography was carried out with Cica-Reagent Silica gel 60 (particle size 0.063-0.200 mm, 70–230 mesh). Melting points (mp) were recorded on a Yanaco MP-S3 melting point apparatus and were not corrected. Optical rotations were measured on a JASCO DIP-370 digital polarimeter. Infrared spectra (IR) were recorded on a JASCO FT/IR-460 spectrophotometer and were reported in wave number (cm^{-1}). Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on JEOL LA 400 (400 MHz) and JEOL LA 500 (500 MHz) spectrometers. Chemical shifts are expressed in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to residual proton in the NMR solvent ($CHCl_3$ in $CDCl_3$, δ 7.26). Coupling constants (*J*) are given in Hz. Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, br = broadened), coupling constant and integration. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on JEOL LA 400 (100 MHz) and JEOL LA 500 (125 MHz) spectrometers. Chemical shifts are expressed in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonance of the solvent ($CDCl_3$, δ 77.0). High-resolution mass spectra (HRMS), measured on a JEOL JMS-GCMATEII and JEOL JMS-T100CS AccuTOF spectrometers, are reported in *m/z*.

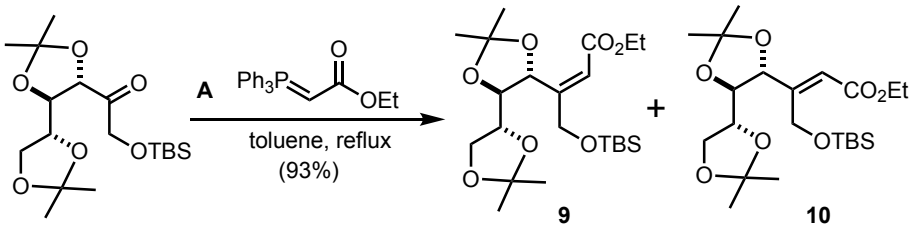
Experimental Section



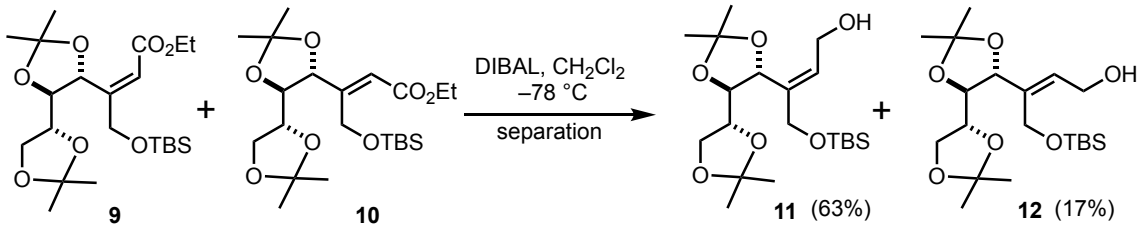
(*R*)-2-((*tert*-butyldimethylsilyl)oxy)-1-((4*R*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)ethan-1-ol (7). To a solution of mannitol derivative **6** (8.62g, 32.9mmol) and triethylamine (26.1 ml, 187 mmol) and DMAP (1.60 g, 13.1 mmol) in CH_2Cl_2 (120 ml) at 0 °C was added *tert*-butylchlorodimethylsilane (6.43 g, 42.7 mmol). After being stirred at room temperature for 1.5 h, the reaction mixture was washed with 1 M $KHSO_4$, saturated $NaHCO_3$, brine, and dried over anhydrous Na_2SO_4. Concentration under reduced pressure provided the crude residue, which was purified by silica gel chromatography (AcOEt/hexane 1:5) to afford TBS ether **7** (11.72 g, 95%) as a colorless oil. $[\alpha]_D^{24}$ +10.9 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 3481, 2954, 2932, 1372 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.10 (s, 6H), 0.91 (s, 9H), 1.36 (s, 3H), 1.37 (s, 3H), 1.38 (s, 3H), 1.45 (s, 3H), 3.13 (d, *J* = 3.5 Hz, 2H), 3.74–3.64 (m, 2H), 3.85 (dd, *J* = 10.0, 3.0 Hz, 1H), 3.87 (t, *J* = 7.0 Hz, 1H), 3.98 (t, *J* = 7.0 Hz, 1H), 4.00 (dd, *J* = 11.0, 9.0 Hz, 1H), 4.14 (dd, *J* = 9.0, 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.0, –3.3, 18.6, 25.4, 25.5, 26.1, 26.6, 26.7, 27.3, 27.4, 27.7, 53.6, 64.5, 66.5, 67.3, 73.1, 76.5, 77.5, 79.4, 79.6, 80.3, 109.8, 110.0; HRMS (ESI): *m/z* calcd for $C_{18}H_{36}O_6NaSi$ $[M+Na]^+$ 399.2179, found 397.2016. HRMS (ESI): *m/z* calcd for $C_{18}H_{37}O_6Si$ $[M+H]^+$ 377.2359, found 399.2182.



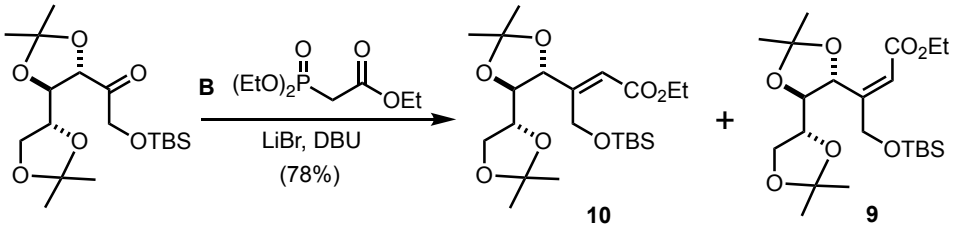
2-((*tert*-Butyldimethylsilyl)oxy)-1-((4*R*,4'*R*,5*S*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)ethan-1-one (8). To a solution of oxalyl chloride (9.62 ml, 113.7 mmol) in CH_2Cl_2 (130 ml) at –78 °C under argon atmosphere was added DMSO (10.7 ml, 152 mmol). After stirring at –78 °C for 20 min, alcohol **7** (14.27 g, 37.9 mmol) in CH_2Cl_2 (10 ml) was added and stirring was continued for 20 min. Triethylamine (26.40 ml, 190 mmol) was introduced, and the reaction mixture was stirred at –78 °C for 5 min, and then allowed to warm to room temperature. The reaction mixture was diluted with CH_2Cl_2, and then washed with 1 M $KHSO_4$, water, saturated $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4. Concentration under reduced pressure provided the crude residue, which was purified by silica gel chromatography (AcOEt/hexane 1:5) to afford **8** (8.07 g, 57%) as a yellow oil. $[\alpha]_D^{24}$ +0.40 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 2932, 1741, 1472, 1373 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.10 (s, 6H), 0.93 (s, 9H), 1.35 (s, 3H), 1.37 (s, 3H), 1.42 (s, 3H), 1.46 (s, 3H), 3.97 (dd, *J* = 7.0, 5.0 Hz, 1H), 4.11 (dd, *J* = 8.0, 6.0 Hz, 1H), 4.22 (dt, *J* = 17.0, 12.0 Hz, 2H), 4.42 (d, *J* = 6.0 Hz, 1H), 4.61 (dd, *J* = 21.0, 18.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.4, 18.4, 25.0, 25.6, 25.7, 26.0, 26.4, 26.8, 30.9, 66.4, 67.7, 76.1, 78.0, 80.0, 109.7, 111.3, 206.4; HRMS (ESI): *m/z* calcd for $C_{18}H_{34}O_6NaSi$ $[M+Na]^+$ 397.2022, found 397.2016.



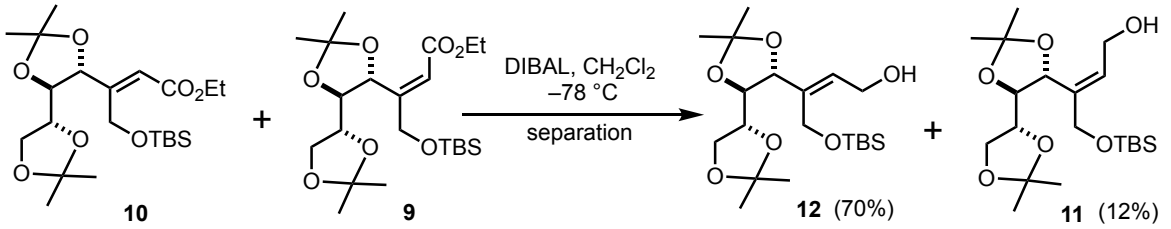
Ethyl (*Z*)-4-((*tert*-butyldimethylsilyl)oxy)-3-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)but-2-enoate (9) and **ethyl (*E*)-4-((*tert*-butyldimethylsilyl)oxy)-3-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)but-2-enoate (10)**. A solution of ketone **8** (7.16 g, 19.1 mmol) and ethyl 2-(triphenylphosphoranylidene)acetate (20.0 g, 57.4 mmol) in toluene (100 mL) was refluxed (oil bath temperature 125 °C) for 3.5 h, and then concentrated under reduced pressure. The resulting crude residue was purified by silica gel chromatography (AcOEt/hexane 1:5) to afford an inseparable 78:22 mixture of **9** and **10** (7.91 g, 93%) as a yellow oil.



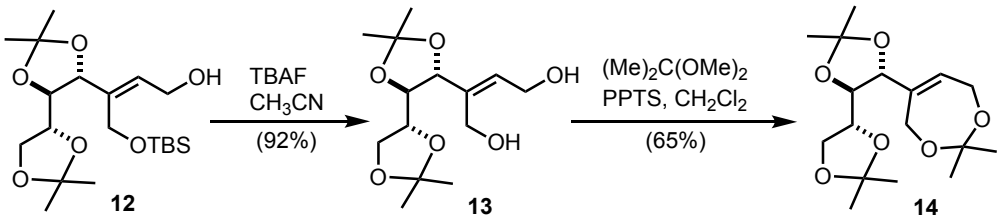
(*Z*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)but-2-en-1-ol (11). To a solution of a mixture of α,β-unsaturated ethyl ester **9** and **10** (7.91 g, 17.8 mmol) in CH_2Cl_2 (90 ml) cooled to –78 °C was added diisobutylaluminum hydride (1 M solution in toluene, 53.4 ml, 53.4 mmol). After stirring at –78 °C for 30 min, the reaction mixture was warmed at 0 °C and treated with H_2O (100 ml) and sodium potassium tartrate (15.0 g, 53.4 mmol). After vigorous stirring at room temperature for 1 h, the separated aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. Concentration under reduced pressure gave the residue, which was purified by silica gel chromatography (AcOEt/hexane 1:8) to afford (*Z*)-allyl alcohol **11** (4.48 g, 63%) and (*E*)-allyl alcohol **12** (1.12 g, 17%) as a colorless oil, respectively. $[\alpha]_D^{26}$ –21.9 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 3397, 2954, 2931, 1713, 1471 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.08 (s, 6H), 0.92 (s, 9H), 1.34 (s, 3H), 1.38 (s, 3H), 1.39 (s, 3H), 1.44 (s, 3H), 4.00–3.90 (m, 2H), 4.03 (dd, *J* = 12.0, 7.0 Hz, 1H), 4.26–4.10 (m, 3H), 4.40–4.28 (m, 3H), 4.97 (d, *J* = 8.0 Hz, 1H), 6.10 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.4, –5.3, 18.3, 25.1, 25.9, 26.4, 26.8, 57.5, 62.0, 67.5, 76.5, 77.1, 78.9, 109.2, 110.1, 128.6, 137.8; HRMS (ESI): *m/z* calcd for $C_{20}H_{38}O_6NaSi$ $[M+Na]^+$ 425.2335, found 425.2318.



Ethyl (*E*)-4-((*tert*-butyldimethylsilyl)oxy)-3-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)but-2-enoate (10) and **ethyl (*Z*)-4-((*tert*-butyldimethylsilyl)oxy)-3-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)but-2-enoate (9).** To a suspension of lithium bromide (2.08 g, 24.0 mmol, dried at 100 °C under reduced pressure just before use) in CH_3CN (30 ml) were added ethyl diethylphosphonoacetate (4.76 ml, 24.0 mmol) and DBU (3.58 ml, 24.0 mmol) at room temperature. The solution was cooled at –45 °C. A solution of ketone **8** (3.0 g, 8.0 mmol) in CH_3CN was added. After stirring at –45 °C for 10 h, the reaction mixture was diluted with EtOAc and washed successively with 1 M aqueous HCl, saturated aqueous $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. Concentration of the solvent gave a residue, which was purified by silica gel column chromatography (AcOEt/hexane 1:5) to provide an inseparable 15:85 mixture of **9** and **10** (2.78 g, 78%) as a colorless oil.

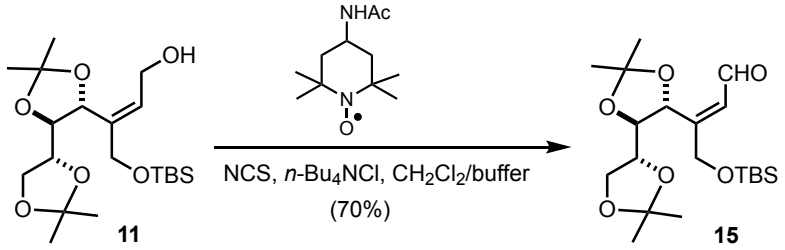


(*E*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)but-2-en-1-ol (12). To a solution of a mixture of α,β-unsaturated ethyl ester **10** and **9** (3.69 g, 8.31 mmol) in CH_2Cl_2 (60 ml) cooled to –78 °C was added diisobutylaluminum hydride (1 M solution in toluene, 25 ml, 25 mmol). After stirring at –78 °C for 25 min, the reaction mixture was warmed at 0 °C and treated with H_2O (50 ml) and sodium potassium tartrate (7.03 g, 24.9 mmol). After vigorous stirring at room temperature for 1 h, the separated aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. Concentration under reduced pressure gave the residue, which was purified by silica gel chromatography (AcOEt/hexane 1:8) to afford (*E*)-allyl alcohol **12** (2.35 g, 70%) and (*Z*)-allyl alcohol **11** (403 mg, 12%) as a colorless oil, respectively. $[\alpha]_D^{24}$ +2.38 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 3446, 2932, 1472, 1372 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.12 (s, 6H), 0.91 (s, 9H), 1.33 (s, 3H), 1.40 (s, 3H), 1.41 (s, 3H), 1.44 (s, 3H), 3.88 (dd, *J* = 8.0, 6.0 Hz, 1H), 3.94 (dd, *J* = 8.0, 5.0 Hz, 1H), 4.06 (dd, *J* = 8.5, 6.0 Hz, 1H), 4.34–4.12 (m, 6H), 4.40 (d, *J* =8.0 Hz, 1H), 6.03 (t, *J* =7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.4, 18.1, 25.1, 25.8, 26.5, 26.9, 27.0, 58.0, 58.9, 66.4, 76.2, 79.5, 82.1, 109.1, 109.5, 132.7, 137.7; HRMS (ESI): *m/z* calcd for $C_{20}H_{38}O_6NaSi$ $[M+Na]^+$ 425.2335, found 425.2316.

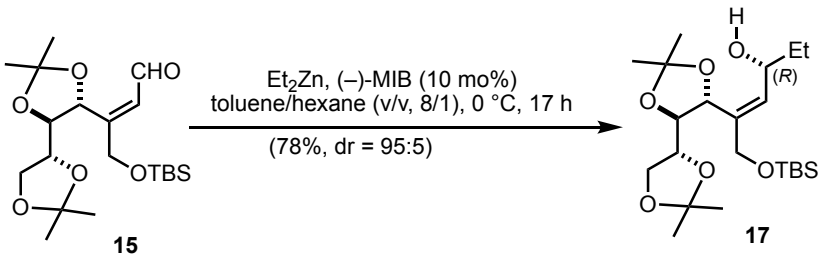


(4*S*,4'*R*,5*R*)-5-(2,2-Dimethyl-4,7-dihydro-1,3-dioxepin-5-yl)-2,2,2',2'-tetramethyl-4,4'-bi (1,3-dioxolane) (14). A solution of tetra-*n*-butylammonium fluoride (1 M solution in THF, 0.40 mL, 0.40 mmol) was added to a solution of (*E*)-allyl alcohol **12** (52 mg, 0.13 mmol) in CH_3CN (1.3 ml). The reaction mixture was stirred at room temperature for 10 min and then concentrated under reduced pressure. Purification of the resulting residue by silica gel chromatography (AcOEt / hexane, 1:1) afforded diol **13** (35 mg, 92%) as a colorless oil.

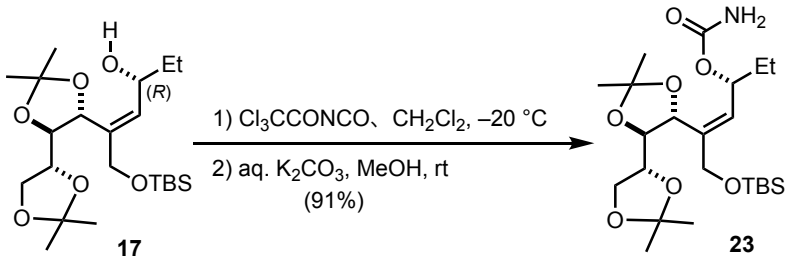
To a solution of the diol **13** (29 mg, 0.10 mmol) dissolved in CH_2Cl_2 (1.0 ml) was added 2,2-dimethoxypropane (0.12 mL, 1.0 mmol) and pyridinium *p*-toluenesulfonate (5 mg, 0.02 mmol). After stirring at room temperature for 30 min, saturated aqueous $NaHCO_3$ was added. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (AcOEt/hexane 1:2) to afford seven-membered ketal **14** (21 mg, 65%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.34 (s, 3H), 1.38 (s, 3H), 1.41 (s, 3H), 1.42 (s, 3H),1.43 (s, 6H), 3.76 (dd, *J* = 7.0, 6.5 Hz, 1H), 3.95 (dd, *J* = 8.5, 5.0 Hz, 1H), 4.06–4.14 (m, 2H), 4.18–4.28 (m, 3H), 4.34 (d, *J* = 7.5 Hz, 1H), 4.40 (brd, *J* = 16.0 Hz, 1H), 5.75 (br, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 24.01, 24.05, 25.4, 26.8, 27.1, 27.2, 60.7, 61.1, 67.0, 76.7, 79.7, 81.7, 102.2, 109.4, 109.8, 128.3, 137.9.



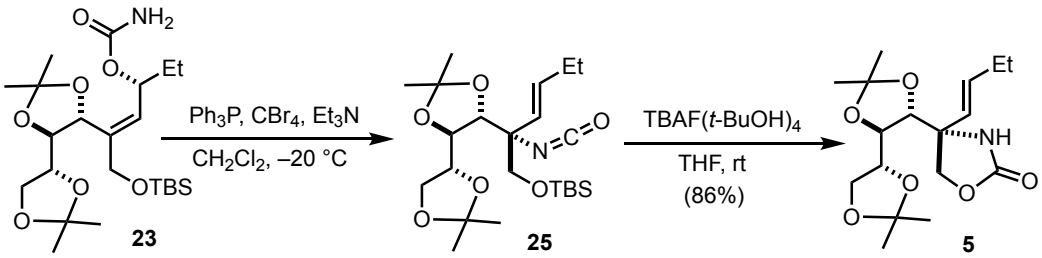
(*Z*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)but-2-enal (15). To a solution of (*Z*)-allyl alcohol **11** (4.42 g, 11.0 mmol) dissolved in a mixture of CH_2Cl_2 (50 ml) and aqueous solution (50 ml) of $NaHCO_3$ (0.5 M) and K_2CO_3 (0.05 M) were added 4-acetamido-TEMPO (468 mg, 2.19 mmol), tetra-*n*-butylammonium chloride (610 mg, 2.19 mmol). After vigorously stirring at room temperature for 10 min, *N*-chlorosuccinimide (5.10 g, 38.4 mmol) was added. After being stirred at room temperature for 2.5 h, the organic layer was separated, and the aqueous phase was extracted with Et_2O. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure. The resulting residue (6.13 g) was purified by silica gel chromatography (AcOEt/hexane 1:3) to afford (*Z*)-α,β-unsaturated aldehyde **15** (3.07 g, 70%) as a colorless oil, which was immediately used for the next step. $[\alpha]_D^{26}$ –31.9 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 2933, 1739, 1681, 1472 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.10 (s, 6H), 0.93 (s, 9H), 1.27 (s, 3H), 1.29 (s, 3H), 1.42 (s, 3H), 1.46 (s, 3H), 3.81 (t, *J* = 8.0 Hz, 1H), 3.95 (dt, *J* = 10.5, 7.0 Hz, 1H), 4.17–4.10 (m, 3H), 4.32 (d, *J* =17.0 Hz, 1H), 4.51 (d, *J* = 17.0 Hz, 1H), 6.32 (d, *J* =8.0 Hz, 1H), 10.18–10.10 (2s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.5, –5.4, 18.3, 25.0, 25.4, 25.8, 26.5, 26.6, 26.7, 61.2, 67.6, 77.3, 80.6, 110.0, 110.4, 126.8, 157.8, 190.4.



(*R*,*Z*)-6-((*tert*-Butyldimethylsilyl)oxy)-5-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)hex-4-en-3-ol (17). To a solution of (*Z*)-α,β-unsaturated aldehyde **15** (613 mg, 1.53 mmol) and (+)-MIB (37 mg, 0.15 mmol) in toluene (24 ml) cooled to 0 °C was added a solution of diethylzinc (1.0 M in hexane, 3.06 ml, 3.06 mmol) dropwise over 5 min. The reaction mixture was kept at 0 °C for 17 h, and then quenched with aqueous 1 M $KHSO_4$. The separated aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The resulting crude product was analyzed by ^1H NMR to determine the diastereoselectivity to be 95:5. Silica gel chromatography of the residue (AcOEt/ hexane 1:5) gave (*R,Z*)-allyl alcohol **17** (515 mg, 78%) as a colorless oil. R_f = 0.56 (eluting with v/v 1:2 AcOEt/hexane). $[\alpha]_D^{25}$ –20.7 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 3476, 2957, 2932, 1462, 1371 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.08 (s, 6H), 0.91 (s, 9H), 0.97 (t, *J* = 7.5 Hz, 3H), 1.32 (s, 3H), 1.36 (s, 3H), 1.38 (s, 3H), 1.42 (s, 3H), 1.60 (quint, *J* = 7.0 Hz, 2H), 4.00–3.86 (m, 2H), 4.14–4.04 (m, 2H), 4.24 (dd, *J* = 22.0, 8.5 Hz 2H), 4.46 (dd, *J* = 13.0, 6.0 Hz, 2H), 5.03 (d, *J* = 8.0 Hz, 1H), 5.81 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.3, –5.2, 9.7, 18.3, 25.2, 25.9, 26.5, 26.8, 26.9, 29.8, 62.2, 67.5, 69.0, 77.2, 79.1, 109.1, 109.7, 132.9, 135.7; HRMS (ESI): *m/z* calcd for $C_{22}H_{42}O_6NaSi$ $[M+Na]^+$ 453.2648, found 453.2642.

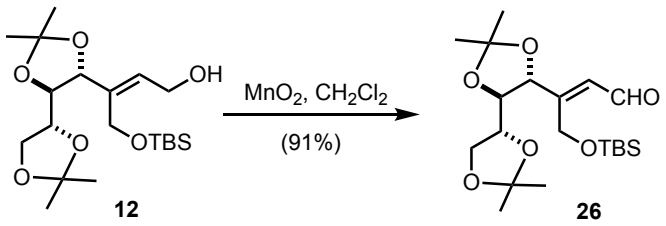


(*R*,*Z*)-6-((*tert*-Butyldimethylsilyl)oxy)-5-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)hex-4-en-3-yl carbamate (23). To a solution of (*R,Z*)-allyl alcohol **17** (612 mg, 1.42 mmol) in CH_2Cl_2 (12.0 ml) cooled to –20 °C was added trichloroacetyl isocyanate (0.51 ml, 4.26 mmol). After being stirred at –20 °C for 15 min, the solvent was removed by evaporation under reduced pressure. The resulting residue was dissolved in a mixture of methanol (1.0 ml) and 2 M aqueous potassium carbonate (12.0 ml), and then was stirred at room temperature for 3.5 h. Methanol was removed by evaporation and the resulting aqueous layer was extracted with Et_2O. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (AcOEt/hexane 1:3) to afford carbamate **23** (610 mg, 91%) as a colorless oil. $[\alpha]_D^{25}$ –13.7 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 3462, 3365, 2933, 1730, 1602 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.06 (s, 6H), 0.91 (s, 9H), 0.95 (t, *J* = 8.0 Hz, 3H), 1.31 (s, 3H), 1.33 (s, 3H), 1.38 (s, 3H), 1.43 (s, 3H), 1.66 (quint, *J* = 7.0Hz, 2H), 3.94–3.86 (m, 2H), 4.15 (dt, *J* = 12.5, 11.0 Hz, 2H) 4.25 (dt, *J* = 20.0, 14.0 Hz, 2H), 4.53 (s, 2H), 5.06 (d, *J* = 9.0 Hz, 1H), 5.47 (dd, *J* = 10.0, 9.5 Hz, 1H), 5.68 (d, *J* = 10.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.4, –5.3, 9.5, 18.3, 25.3, 25.8, 26.5, 26.6, 26.8, 27.5, 61.9, 67.6, 71.5, 77.1, 77.3, 79.3, 109.1, 109.6, 127.4, 137.6, 156.6; HRMS (ESI): *m/z* calcd for $C_{23}H_{43}NO_7NaSi$ $[M+Na]^+$ 496.2707, found 496.2703.

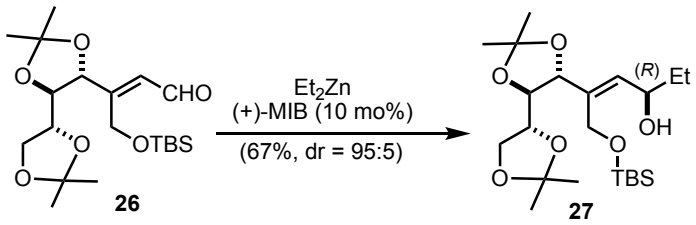


(*R*)-4-((*E*)-But-1-en-1-yl)-4-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)oxazolidin-2-one (5). To a solution of carbamate **23** (300 mg, 0.63 mmol), triphenylphosphine (584 mg, 2.21 mmol) and triethylamine (0.40 ml, 2.91 mmol) in CH_2Cl_2 (4.5 ml) at –20 °C was added a solution of carbon tetrabromide (796 mg, 2.40 mmol) in CH_2Cl_2 (1.8 ml). After being stirred at –20 °C for 15 min, the resulting reaction mixture was diluted with hexane (20 ml). After stirring at room temperature for 10 min, aqueous $KHSO_4$ (1 M, 20 ml) was added. The separated aqueous layer was extracted with hexane. The combined organic layer was washed with water, saturated aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting crude products, containing allyl isocyanate **25** and triphenylphosphine oxide, was diluted with hexane and the precipitated triphenylphosphine oxide was removed by filtration through a pad of Celite. The filter cake was washed with hexane, and the combined filtrate was concentrated under reduced pressure to afford crude **25** (469 mg), which was dissolved in THF (4.0 ml). The resulting solution was cooled to 0 °C and then treated with a solution of tetrabutylammonium tetra(*tert*-butyl alcohol)-coordinated fluoride {$Bu_4NF(t BuOH)_4$}(529 mg, 0.95 mmol) in THF (2.3 ml). After stirring at 0 °C for 20 min, the reaction mixture was concentrated under reduced pressure to afford the crude residue, which was purified by silica gel chromatography (AcOEt/hexane 1:2) to afford C-2 epimeric central core of sphingofungin E **5** (186 mg, 86%) as a white solid. $[\alpha]_D^{21}$ –66.5 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 3356, 2986, 2935, 1772, 1374, 1243 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.01 (t, *J* = 7.5 Hz, 3H), 1.35 (s, 3H), 1.37 (s, 6H), 1.41 (s, 3H), 2.12 (dt, *J* = 14.0, 14.0 Hz, 2H), 3.58 (t, *J* = 8.5 Hz, 1H), 3.88 (d, *J* = 8.0 Hz, 1H), 4.05–3.98 (m, 1H), 4.18–4.08 (m, 2H),

4.47 (d, J = 9.0 Hz, 1H), 5.64 (d, J = 15.0 Hz, 1H), 5.86 (dt, J =15.0, 12.5 Hz, 2H), 6.15 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.3, 25.0, 25.1, 26.4, 26.5, 26.7, 60.3, 67.7, 74.6, 75.7, 77.9, 84.7, 109.1, 110.3, 125.3, 134.3, 158.5; HRMS (ESI): *m/z* calcd for $C_{17}H_{27}NO_6Na$ $[M+Na]^+$ 364.1736, found 364.1736.

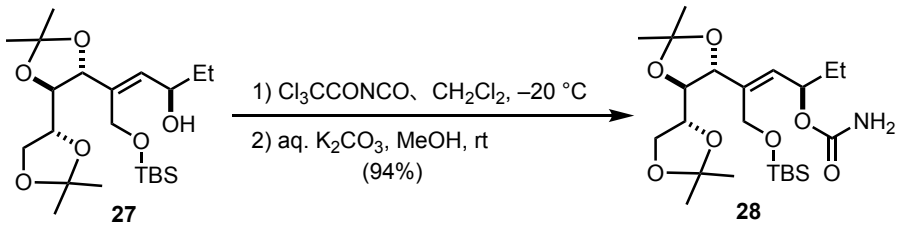


(*E*)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)but-2-enal (26). To a solution of (*E*)-allyl alcohol **12** (400 mg, 1.0 mmol) in CH_2Cl_2 (20 ml) at room temperature was added manganese dioxide (864 mg, 10.0 mmol). After vigorously stirring at room temperature for 15 min, more additional manganese dioxide (177 mg, 2.0 mmol) was added. Six further portions of manganese dioxide (177 mg × 6) were added at fifteen-minute intervals until TLC analysis showed the absence of the starting material. After stirring at room temperature for 25 min, the mixture was filtered through a pad of Celite. The filter cake was washed with AcOEt, and the combined filtrate was concentrated under reduced pressure to afford (*E*)-α,β-unsaturated aldehyde **26** (364 mg, 91%) as a pale yellow oil. $[\alpha]_D^{23}$ +13.5 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 2933, 1734, 1680, 1472 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.11 (s, 6H), 0.91 (s, 9H), 1.33 (s, 3H), 1.36 (s, 3H), 1.41 (s, 3H), 1.44 (s, 3H), 3.81 (t, J = 6.0 Hz, 1H), 4.16–3.89 (m, 4H), 4.51 (d, J =9.5 Hz, 1H), 4.53 (s, 1H), 4.77 (d, J =14.5 Hz, 1H), 6.22 (d, J =8.0 Hz, 1H), 10.34 (2s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.4, 18.2, 25.2, 25.7, 26.6, 26.8, 27.0, 60.0, 67.3, 76.8, 80.8, 81.6, 109.8, 110.2, 128.8, 158.0, 192.4.



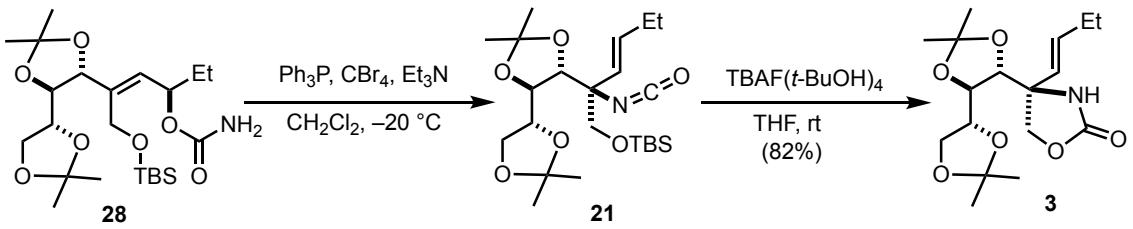
26 **27**

(*R*,*E*)-6-((*tert*-Butyldimethylsilyl)oxy)-5-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)hex-4-en-3-ol (27). To a solution of (*E*)-α,β-unsaturated aldehyde **26** (386 mg, 0.96 mmol) and (+)-MIB (23 mg, 0.09 mmol) in toluene (15.4 ml) cooled to 0 °C was added a solution of diethylzinc (1.0 M in hexane, 1.92 ml, 1.92 mmol) dropwise over 5 min. The reaction mixture was kept at 0 °C for 17 h, and then quenched with aqueous 1 M $KHSO_4$. The separated aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The resulting crude product was analyzed by ^1H NMR to determine the diastereoselectivity to be 95:5. Silica gel chromatography of the residue (AcOEt/hexane 1:5) gave (*R,E*)-allyl alcohol **27** (277 mg, 67%) as a colorless oil. R_f = 0.49 (eluting with v/v 1:2 AcOEt/hexane). $[\alpha]_D^{25}$ +3.63 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 3480, 2957, 2933, 1463, 1379 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.12 (2s, 6H), 0.91 (s, 9H), 0.92 (t, *J* = 8.0 Hz, 3H), 1.33 (s, 3H), 1.40 (s, 6H), 1.44 (s, 3H), 1.72–1.48 (m, 2H), 3.88 (t, *J* = 6.5 Hz, 3H), 3.94 (dd, *J* = 8.0, 5.0 Hz, 1H), 4.06 (t, *J* = 7.5 Hz, 1H), 4.18 (dd, *J* = 13.5, 7.0 Hz, 2H), 4.34 (s, 2H), 4.43–4.35 (m, 2H), 5.84 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.5, –5.4, 9.7, 18.1, 25.1, 25.8, 26.6, 26.9, 27.0, 29.4, 57.9, 66.5, 68.9, 76.3, 79.7, 82.3, 109.1, 109.6, 137.2, 137.5; HRMS (ESI): *m/z* calcd for $C_{22}H_{42}O_6NaSi$ $[M+Na]^+$ 453.2648, found 453.2651.

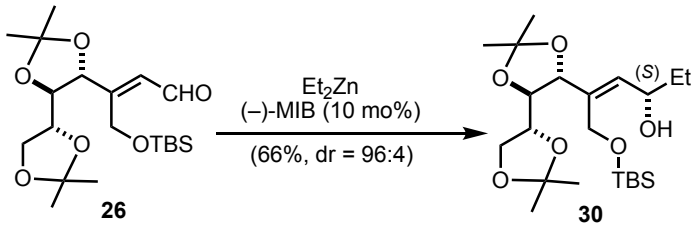


27 **28**

(*R*,*E*)-6-((*tert*-Butyldimethylsilyl)oxy)-5-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)hex-4-en-3-yl carbamate (28). To a solution of (*R,E*)-allyl alcohol **27** (206 mg, 0.48 mmol) in CH_2Cl_2 (5.0 ml) cooled to –20 °C was added trichloroacetyl isocyanate (0.17 ml, 1.44 mmol). After being stirred at –20 °C for 10 min, the solvent was removed by evaporation under reduced pressure. The resulting residue was dissolved in a mixture of methanol (0.5 ml) and 2 M aqueous potassium carbonate (3.0 ml), and then was stirred at room temperature for 3.5 h. Methanol was removed by evaporation and the resulting aqueous layer was extracted with Et_2O. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (AcOEt/hexane 1:3) to afford carbamate **28** (212 mg, 94%) as a colorless oil. $[\alpha]_D^{25}$ –2.81 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 3447, 3362, 2933, 1730, 1605 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.10 (s, 6H), 0.89 (t, *J* = 8.0 Hz, 3H), 0.90 (s, 9H), 1.33 (s, 3H), 1.39 (s, 3H), 1.41 (s, 3H), 1.44 (s, 3H), 1.77–1.52 (m, 2H), 3.93 (t, *J* = 6.5 Hz, 2H), 4.05 (t, *J* = 7.5 Hz, 1H) 4.20 (dd, *J* = 12.5, 6.0 Hz, 1H), 4.31 (dd, *J* = 31.0, 11.5 Hz, 2H), 4.43 (d, *J* = 8.0 Hz, 1H), 5.47 (dd, *J* = 16.0, 7.0 Hz, 1H), 5.67 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.5, –5.3, 9.3, 18.2, 25.2, 25.8, 26.4, 27.0, 28.0, 58.2, 66.3, 72.2, 76.1, 80.4, 80.7, 109.1, 109.4, 129.9, 138.5, 156.2; HRMS (ESI): *m/z* calcd for $C_{23}H_{43}NO_7NaSi$ $[M+Na]^+$ 496.2707, found 496.2715.

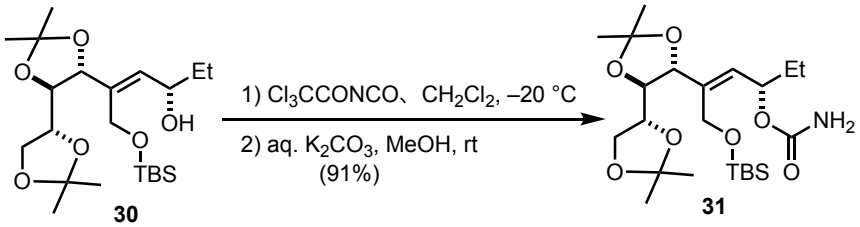


(*S*)-4-((*E*)-But-1-en-1-yl)-4-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)oxazolidin-2-one (3). To a solution of carbamate **28** (240 mg, 0.51 mmol), triphenylphosphine (468 mg, 1.77 mmol) and triethylamine (0.32 ml, 2.33 mmol) in CH_2Cl_2 (3.0 ml) at –20 °C was added a solution of carbon tetrabromide (638 mg, 1.92 mmol) in CH_2Cl_2 (1.5 ml). After being stirred at –20 °C for 25 min, the reaction mixture was diluted with hexane (15 ml). After stirring at room temperature for 10 min, aqueous $KHSO_4$ (1 M, 10 ml) was added. The separated aqueous layer was extracted with hexane. The combined organic layer was washed with water, saturated $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting crude products containing allyl isocyanate **21** and triphenylphosphine oxide, was diluted with hexane and the precipitated triphenylphosphine oxide was removed by filtration through a pad of Celite. The filter cake was washed with hexane, and the combined filtrate was concentrated under reduced pressure to afford the crude **21** (334 mg), which was dissolved in THF (3.5 ml). The resulting solution was cooled to 0 °C and treated with a solution of tetrabutylammonium tetra(*tert*-butyl alcohol)-coordinated fluoride {$Bu_4NF(t BuOH)_4$}(831 mg, 3.18 mmol) in THF (1.5 ml). After stirring at 0 °C for 15 min, the reaction mixture was concentrated under reduced pressure to afford the crude residue, which was purified by silica gel chromatography (AcOEt/hexane 1:2) to afford central core of sphingophangin E **3** (142 mg, 82%) as a white solid.

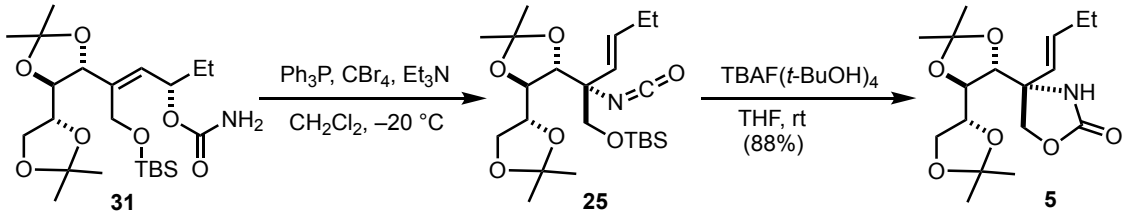


26 30

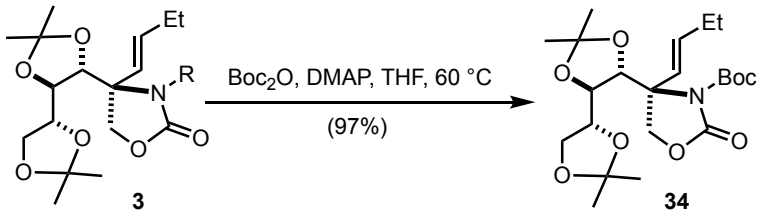
(*S*,*E*)-6-((*tert*-Butyldimethylsilyl)oxy)-5-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)hex-4-en-3-ol (30). To a solution of (*E*)-α,β-unsaturated aldehyde **26** (59 mg, 0.15 mmol) and (–)-MIB (3.5 mg, 0.014 mmol) in toluene (2.4 ml) cooled to 0 °C was added a solution of diethylzinc (1.0 M in hexane, 0.3 ml, 0.3 mmol) dropwise over 5 min. The reaction mixture was kept at 0 °C for 18 h, and then quenched with aqueous 1 M $KHSO_4$. The separated aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The resulting crude product was analyzed by ^1H NMR to determine the diastereoselectivity to be 96:4. Silica gel chromatography of the residue (AcOEt/hexane 1:5) gave (*S,E*)-allyl alcohol **30** (42 mg, 66%) as a colorless oil. R_f = 0.42 (eluting with v/v 1:2 AcOEt/hexane). $[\alpha]_D^{25}$ +2.89 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 3441, 2957, 1693, 1462, 1371 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 0.11 (s, 6H), 0.91 (s, 9H), 0.94 (t, *J* = 7.0 Hz, 3H), 1.33 (s, 3H), 1.39 (s, 3H), 1.41 (s, 3H), 1.44 (s, 3H), 1.70–1.5 (m, 2H), 3.94–3.86 (m, 2H), 4.06 (dd, *J* = 9.0, 7.0 Hz, 1H), 4.18 (dd, *J* = 12.0, 6.0 Hz, 1H), 4.28 (dd, *J* = 14.0, 13.0 Hz, 2H), 4.44–4.38 (m, 3H), 5.78 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.5, –5.4, 9.6, 18.1, 25.1, 25.8, 26.5, 26.9, 27.0, 29.6, 57.5, 66.4, 69.2, 76.1, 79.2, 82.4, 109.0, 109.5, 136.5, 137.5; HRMS (ESI): *m/z* calcd for $C_{22}H_{42}O_6NaSi$ $[M+Na]^+$ 453.2648, found 453.2638.



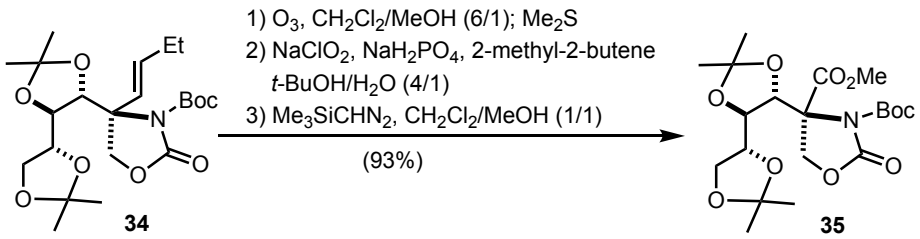
(*S*,*E*)-6-((*tert*-Butyldimethylsilyl)oxy)-5-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)hex-4-en-3-yl carbamate (31). To a solution of (*S,E*)-allyl alcohol **30** (1.11 g, 2.57 mmol) in CH_2Cl_2 (22 ml) cooled to –20 °C was added trichloroacetyl isocyanate (0.92 ml, 7.71 mmol). After being stirred at –20 °C for 30 min, the solution was concentrated under reduced pressure. The resulting residue was dissolved in a mixture of methanol (20 ml) and 2 M aqueous potassium carbonate (10 ml), and then was stirred at room temperature for 3 h. Methanol was removed by evaporation and the resulting aqueous layer was extracted with Et_2O. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure to afford carbamate **31** (1.11 g, 91%), which was used for the next step without further purification. A portion of **31** was purified by silica gel chromatography (AcOEt/ hexane 1:4). $[\alpha]_D^{25}$ +22.1 (*c* 1.00, $CHCl_3$); IR (NaCl) ν_{max} 3460, 3366, 2933, 1730, 1602 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.10 (s, 6H), 0.88 (s, 9H), 0.92 (t, *J* = 8.0 Hz, 3H), 1.33 (s, 3H), 1.40 (s, 6H), 1.43 (s, 3H), 1.74-1.60 (m, 2H), 3.91 (dd, *J* = 7.5, 6.0 Hz, 1H), 4.05 (dd, *J* = 14.0, 7.5 Hz, 2H) 4.26–4.10 (m, 2H), 4.52–4.40 (m, 4H), 5.45 (dd, *J* = 15.5, 7.0 Hz, 1H), 5.65 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ –5.4, 9.4, 18.1, 25.1, 25.8, 26.4, 26.9, 27.0, 27.8, 57.1, 66.3, 72.4, 76.0, 79.4, 81.7, 108.9, 109.5, 132.4, 137.8, 156.3; HRMS (ESI): *m/z* calcd for $C_{23}H_{43}NO_7NaSi$ $[M+Na]^+$ 496.2707, found 496.2711.



(*R*)-4-((*E*)-But-1-en-1-yl)-4-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)oxazolidin-2-one (5). A portion of the carbamate **31** (501 mg, 1.06 mmol), triphenylphosphine (982 mg, 3.71 mmol) and triethylamine (0.68 ml, 4.88 mmol) were dissolved in CH_2Cl_2 (22 ml). The solution was cooed at –20 °C and then treated with a solution of carbon tetrabromide (1.35 g, 4.06 mmol) in CH_2Cl_2 (2.0 ml). After being stirred at –20 °C for 20 min, the resulting reaction mixture was diluted with hexane (14 ml). After stirring at room temperature for 15 min, aqueous $KHSO_4$ (1 M, 5 ml) was added. The separated aqueous layer was extracted with hexane. The combined organic layers were washed with water, saturated $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting crude mixture, containing allyl isocyanate **25** and triphenylphosphine oxide, was diluted with hexane and the precipitated triphenylphosphine oxide was removed by filtration through a pad of Celite. The filter cake was washed with hexane, and the combined filtrate was concentrated under reduced pressure to afford crude **25** (654 mg), which was dissolved in THF (7.0 ml). The resulting solution was cooled to 0 °C and treated with a solution of tetrabutylammonium tetra(*tert*-butyl alcohol)-coordinated fluoride ($Bu_4NF(t\text{BuOH})_4$ 144 mg, 0.26 mmol) in THF (3.0 ml). After stirring at 0 °C for 20 min, the reaction mixture was concentrated under reduced pressure to afford the crude residue, which was purified by silica gel chromatography (AcOEt/hexane 1:2) to afford C-2 epimeric central core of sphingofungin E **5** (316 mg, 88%) as a white solid.

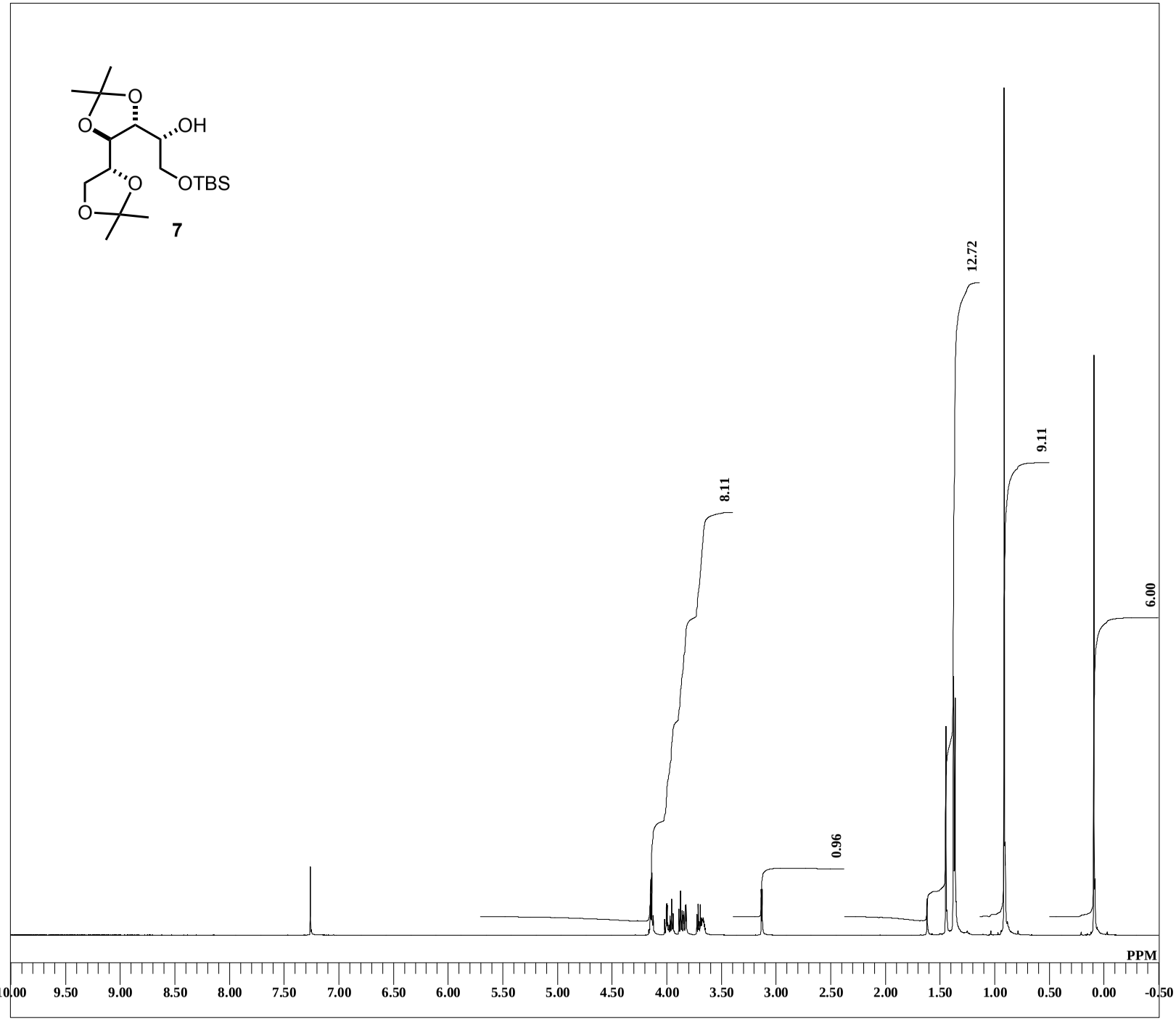


***tert*-Butyl (*S*)-4-((*E*)-but-1-en-1-yl)-2-oxo-4-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)oxazolidine-3-carboxylate (34)**. To a solution of **3** (1.69 g, 4.95 mmol) and 4-dimethylaminopyridine (907 mg, 7.42 mmol) in THF (30 ml) was added di-*tert*-butyl dicarbonate (3.20 ml, 14.9 mmol). After stirring at 60 °C for 40 min, the reaction mixture was diluted with H_2O and aqueous 1 M $KHSO_4$. The separated organic layer was washed with saturated aqueous $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. Concentration under reduced pressure gave the residue, which was purified by silica gel column chromatography (AcOEt/hexane 1:2) to provide imide **34** (2.11 g, 97%) as a white solid. Mp 72–73 °C (recrystallized from hexane); $[\alpha]_D^{24}$ +22.5 (*c* 1.00, $CHCl_3$); IR (KBr) ν_{max} 2974, 1808, 1725, 1457 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.03 (t, *J* = 7.5 Hz, 3H), 1.32 (s, 3H), 1.36 (2s, 6H), 1.42 (s, 3H), 1.51 (s, 9H), 2.13 (dq, *J* = 25.0, 18.0 Hz, 2H), 3.76 (dd, *J* = 9.0, 7.0 Hz, 1H), 4.06–3.92 (m, 3H), 4.15 (dd, *J* = 9.0, 6.5 Hz, 1H), 4.43 (d, *J* = 9.5, 1H), 4.77 (d, *J* = 7.0 Hz, 1H), 5.90–5.78 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.1, 25.3, 25.5, 25.9, 26.8, 28.0, 63.3, 67.7, 69.4, 76.8, 78.9, 81.4, 83.3, 109.1, 110.5, 129.3, 134.4, 148.4, 152.1; HRMS (ESI): *m/z* calcd for $C_{22}H_{35}O_8Na$ $[M+Na]^+$ 464.2260, found 464.2249.



3-(*tert*-Butyl) 4-methyl (*S*)-2-oxo-4-((4*S*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-[4,4'-bi(1,3-dioxolan)]-5-yl)oxazolidine-3,4-dicarboxylate (35). Ozone was passed into a solution of **34** (2.11 g, 4.78 mmol) in a mixture of CH_2Cl_2 (40 mL) and MeOH (6.7 mL) at –78 °C for 20 min. After purging with argon, dimethyl sulfide (1.05 mL, 14.3 mmol) was added at –78 °C. The cooling bath was removed, and the mixture was stirred at room temperature for 1.5 h and then treated with saturated aqueous $NaHCO_3$. The separated aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduce pressure to give aldehyde, which was immediately dissolved in a mixture of *t*-butyl alcohol and water (v/v 4:1 *t*-butyl alcohol/water, 40.0 ml). 2-Methyl-2-butene (2.30 ml, 22.1 mmol), sodium dihydrogenphosphate dihydrate (2.65 g, 22.1 mmol) and sodium chlorite (2.0 g, 22.1 mmol) were added. After stirring at room temperature for 12.5 h, the mixture was diluted with 1 M $NaHSO_3$ and saturated aqueous NH_4Cl. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give carboxylic acid, which was dissolved in a mixture of CH_2Cl_2 and methanol (v/v 1:1 CH_2Cl_2/methanol, 40 ml). The solution was treated with an ether solution of 2.0 M trimethylsilyl diazomethane (7.69 ml, 15.4 mmol) at room temperature. After stirring at room temperature for 15 min, the resulting reaction mixture was concentrated under reduced pressure to give a yellow oil. Purification by silica gel chromatography (AcOEt/hexane 1:2) furnished methyl ester **35** as white crystals (1.93 g, 93% overall yield in three steps). Mp 115–116 °C (recrystallized from AcOEt/hexane); $[\alpha]_D^{24}$ –52.7 (*c* 1.00, $CHCl_3$); IR (KBr) ν_{max} 2983, 2937, 1825, 1760 cm^{-1};

^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.32 (s, 3H), 1.37 (s, 3H), 1.41 (s, 3H), 1.44 (s, 3H), 1.51 (s, 9H), 3.72 (dd, *J* = 8.0, 6.5 Hz, 1H), 3.83 (s, 3H), 3.98 (dd, *J* = 9.0, 6.0 Hz, 1H), 4.06 (ddd, *J* = 9.0, 8.5, 6.0 Hz, 1H), 4.17 (dd, *J* = 8.0, 6.0 Hz, 1H), 4.31 (d, *J* = 9.0, 1H), 4.93 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 25.5, 25.9, 26.6, 27.0, 27.8, 53.1, 65.3, 67.6, 78.9, 79.2, 84.8, 110.3, 110.6, 147.7, 151.3, 169.1. HRMS (ESI): *m/z* calcd for $C_{20}H_{31}NO_{10}$ $[M+H]^+$ 468.1846, found 468.1845.



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SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
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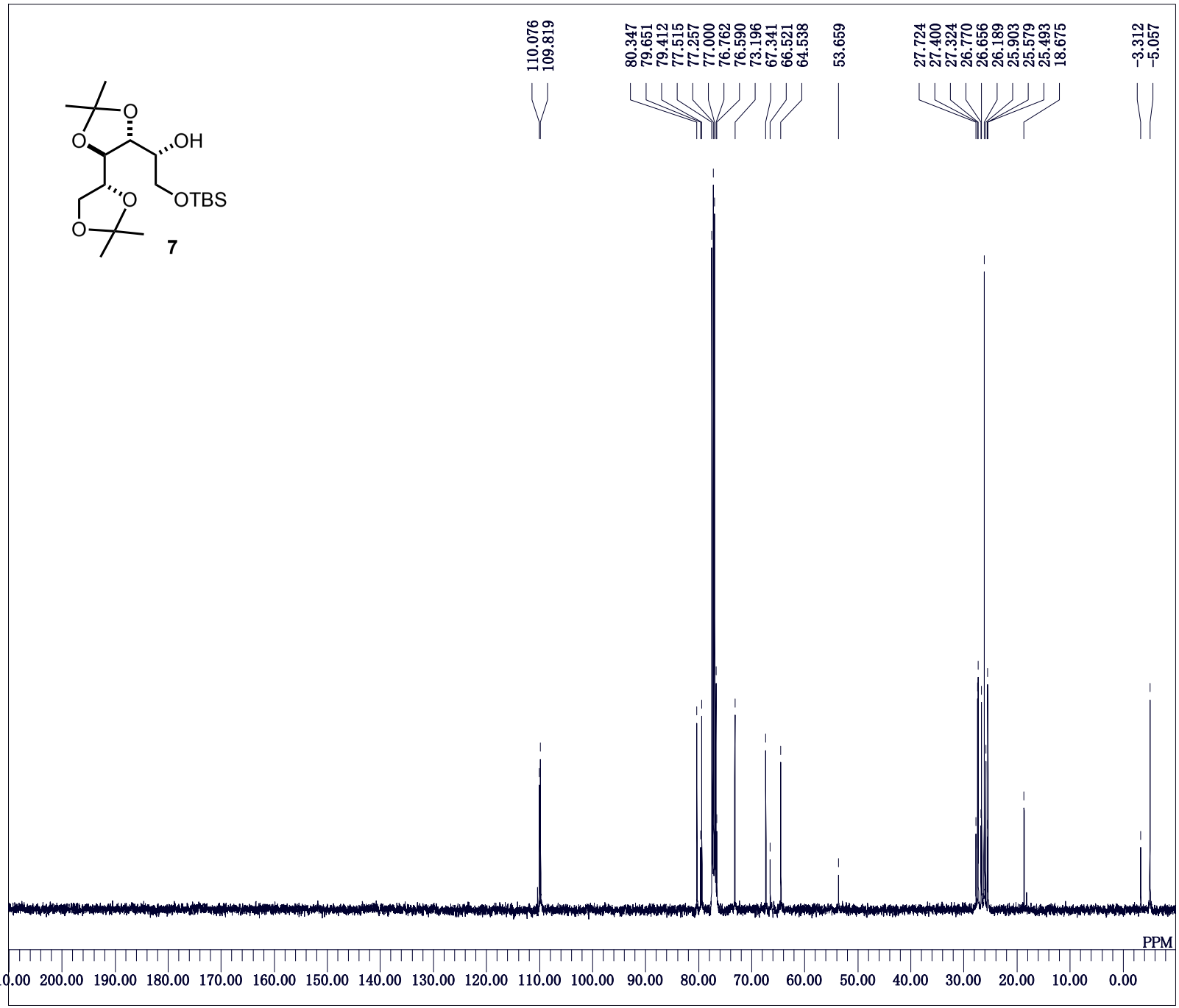
IRNUC	1H
CTEMP	17.4 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50



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FREQU	39308.18 Hz
SCANS	256
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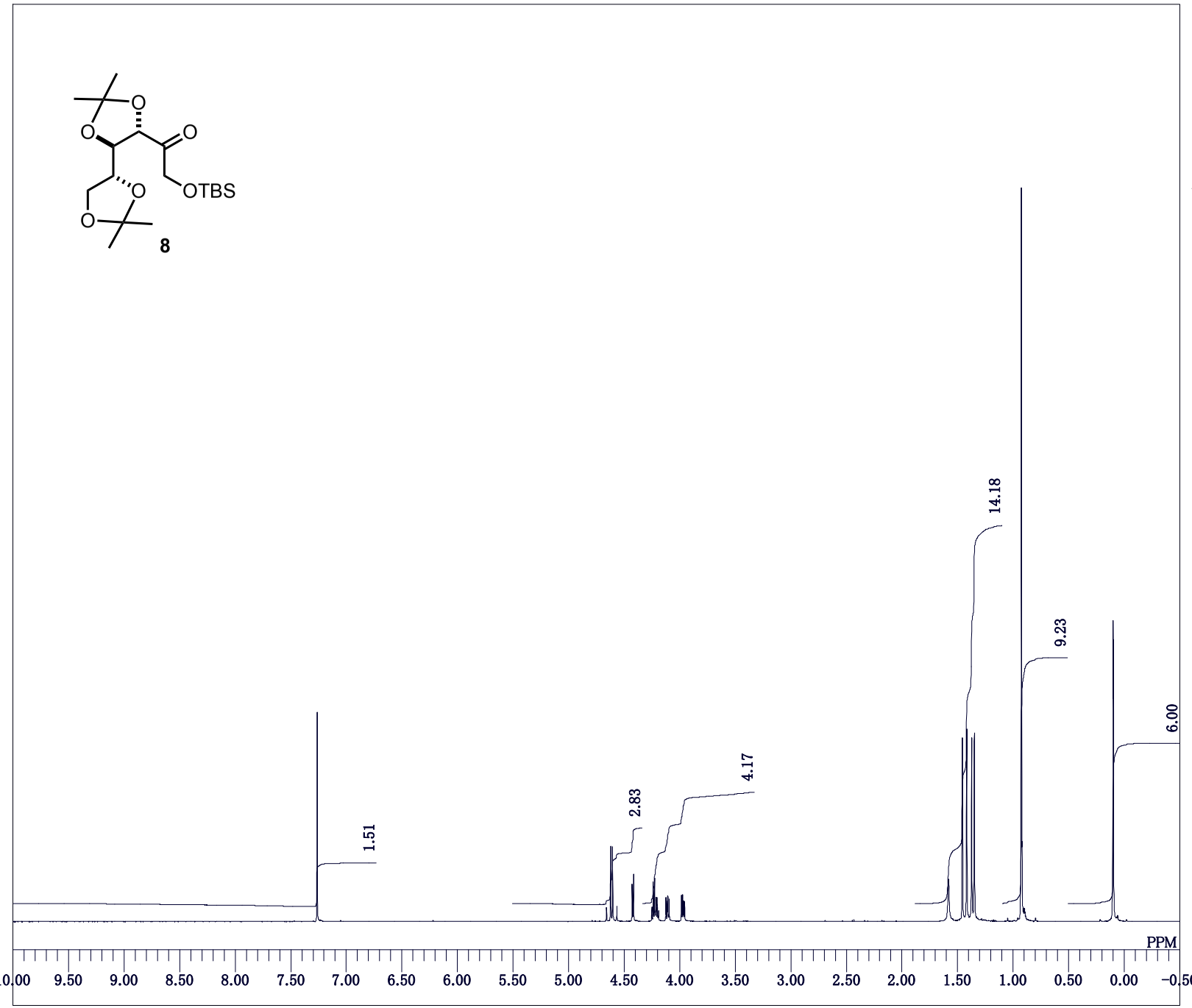
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	23.0 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50



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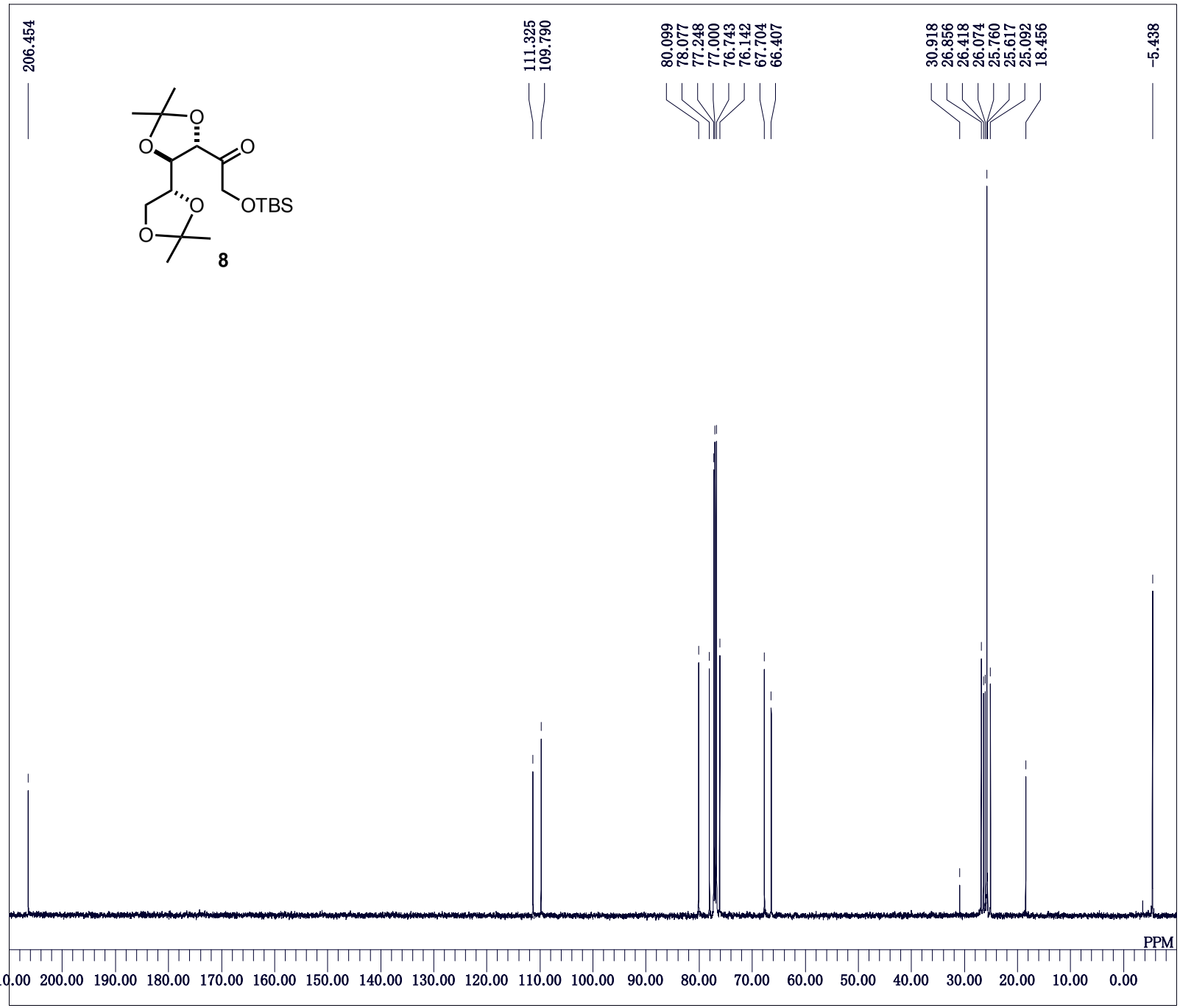
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	17.5 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50



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EXMOD	carbon.jxp
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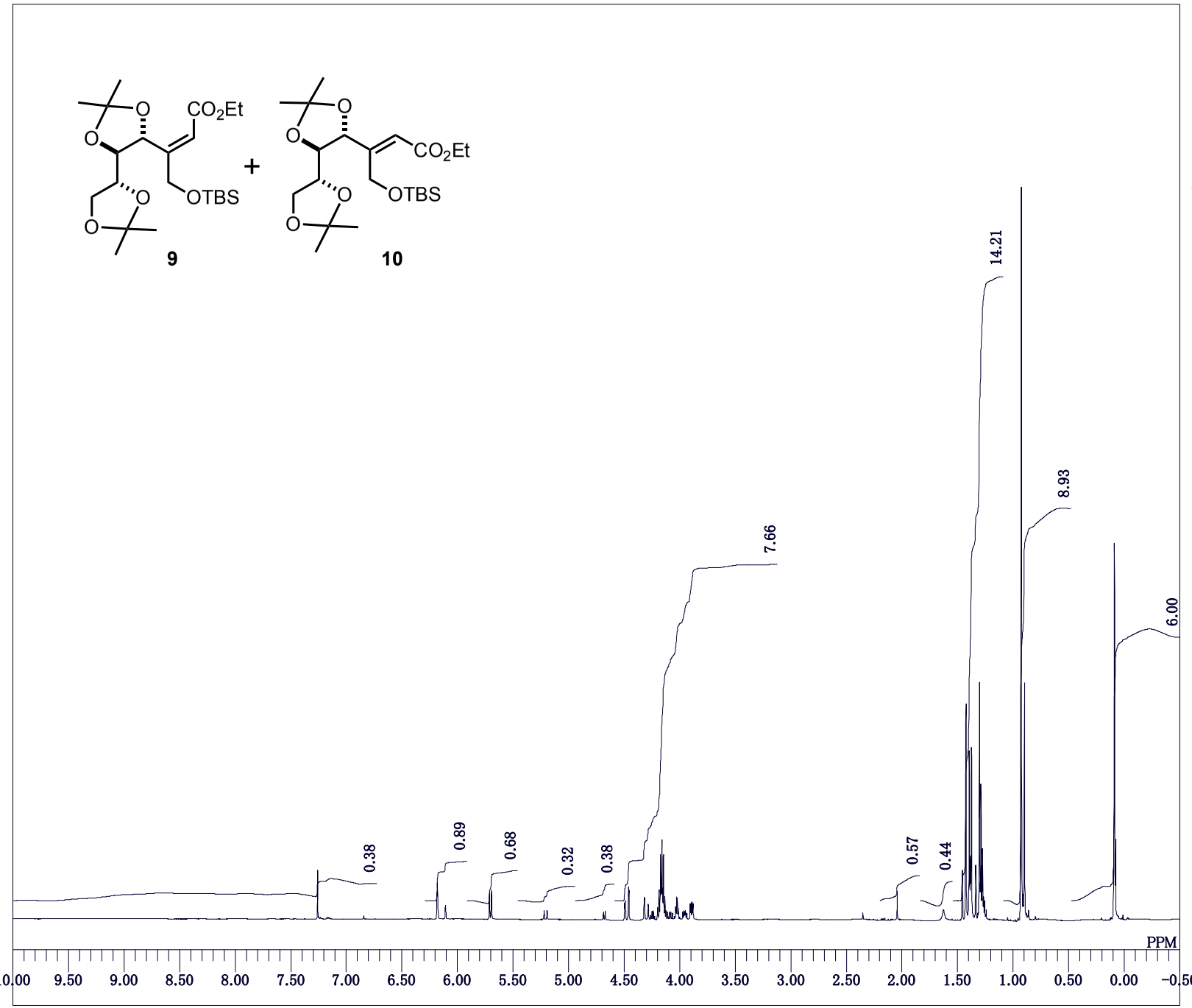
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	17.9 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50


CO2Et
OTBS
9
+
CO2Et
OTBS
10
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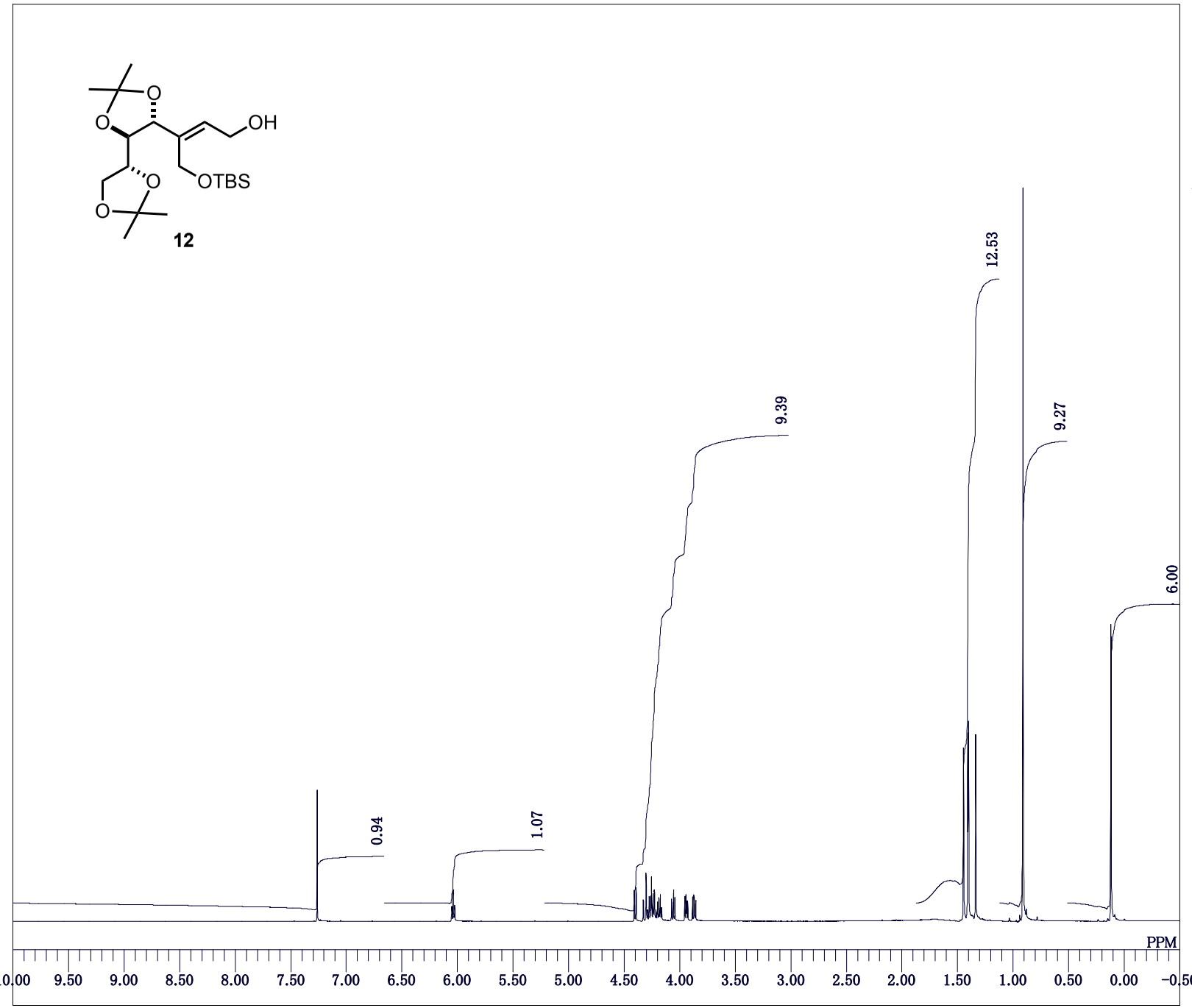
OBSET 2.41 KHz
OBFIN 6.01 Hz
POINT 16400
FREQU 9384.38 Hz
SCANS 8
ACQTM 1.7459 sec
PD 5.0000 sec
PW1 4.68 usec
IRNUC 1H
CTEMP 20.4 c
SLVNT CDCL3
EXREF 12.51 ppm
BF 0.12 Hz
RGAIN 50
0.38
0.89
0.68
0.32
0.38
7.66
0.57
0.44
14.21
8.93
6.00
PPM
10.00 9.50 9.00 8.50 8.00 7.50 7.00 6.50 6.00 5.50 5.00 4.50 4.00 3.50 3.00 2.50 2.00 1.50 1.00 0.50 0.00 -0.50



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OBFIN	6.01 Hz
POINT	16400
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SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
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CTEMP	17.6 c
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EXREF	12.51 ppm
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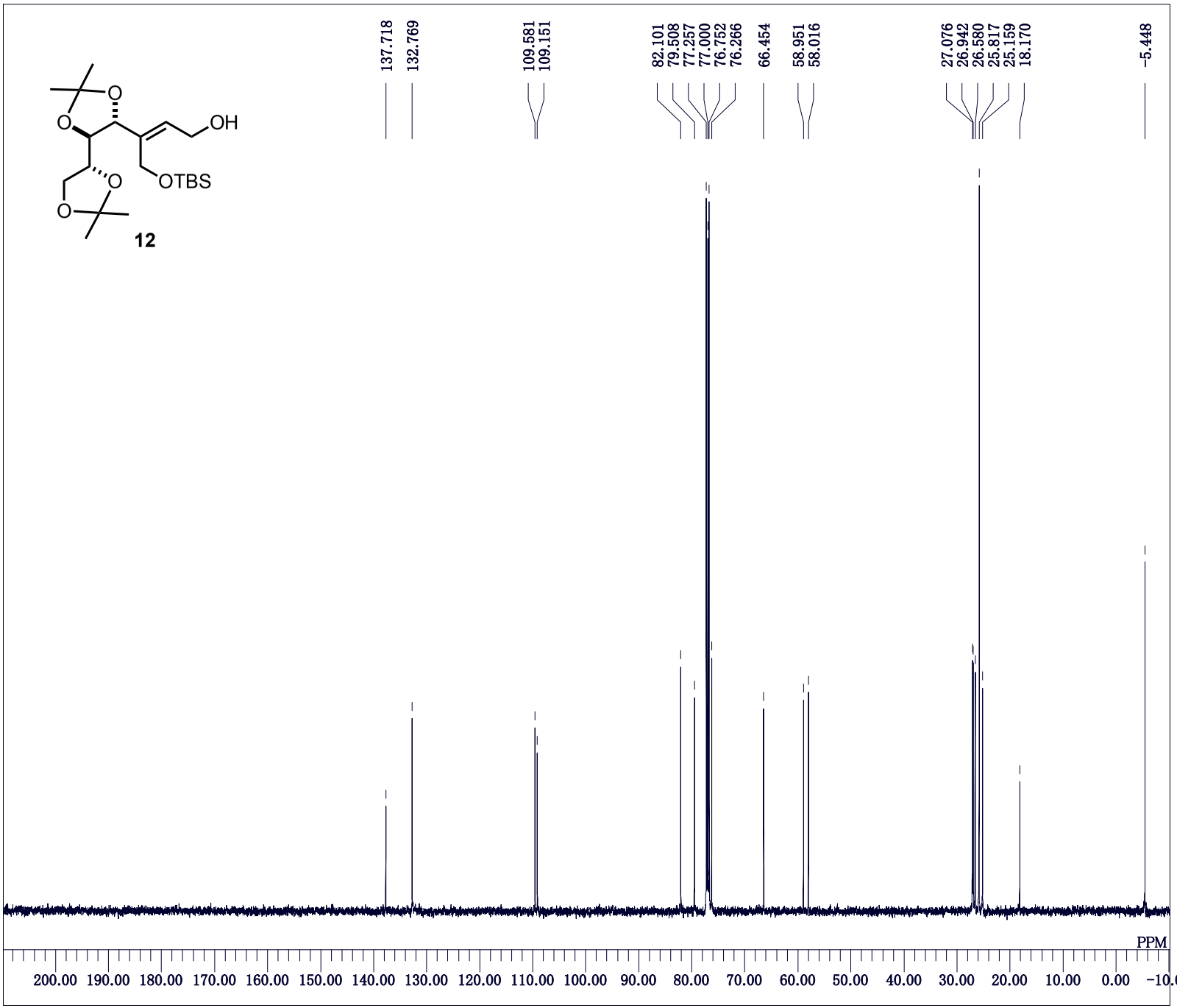
RGAIN	50



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EXMOD	carbon.jxp
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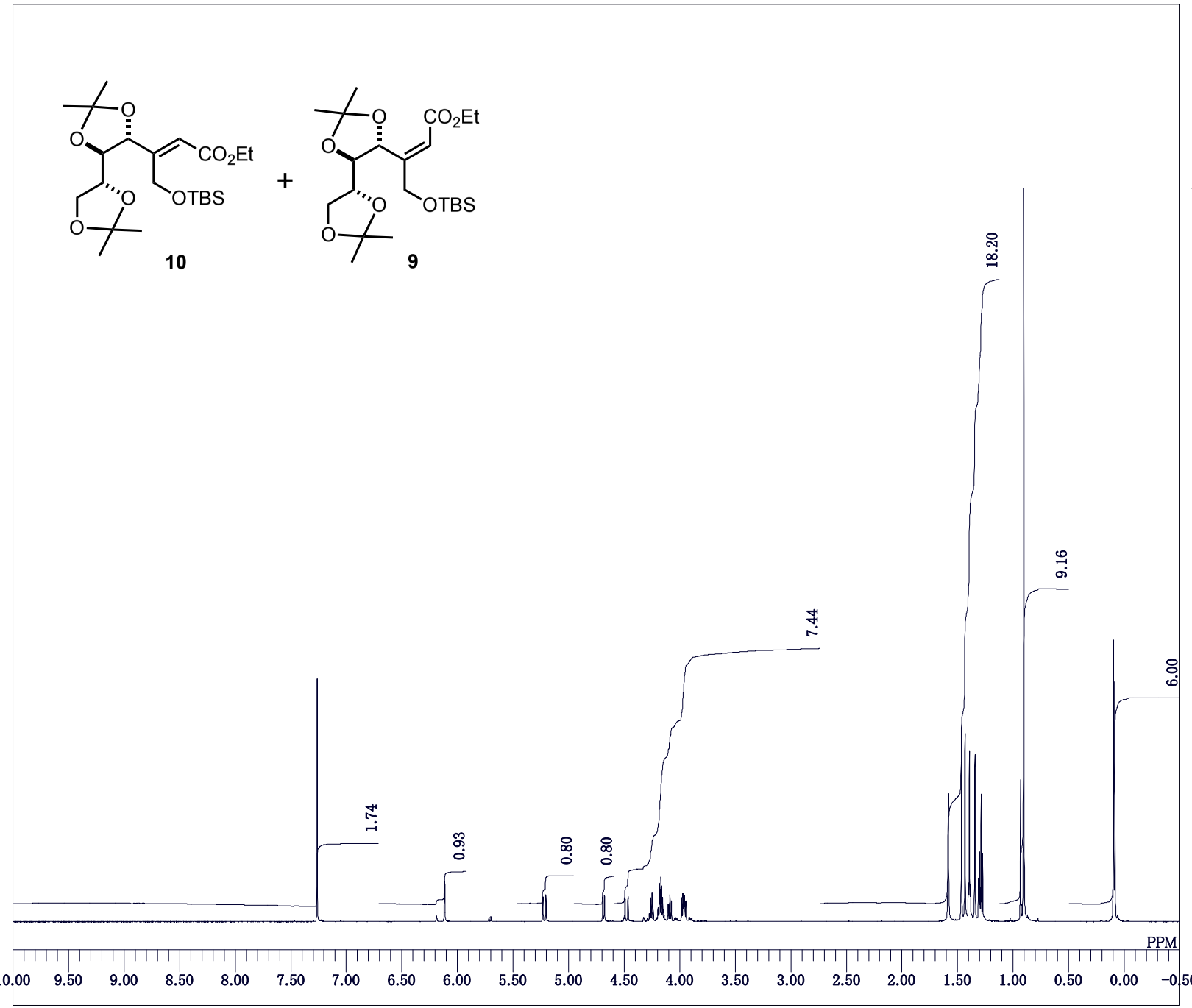
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	17.9 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50



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EXMOD	proton.jxp
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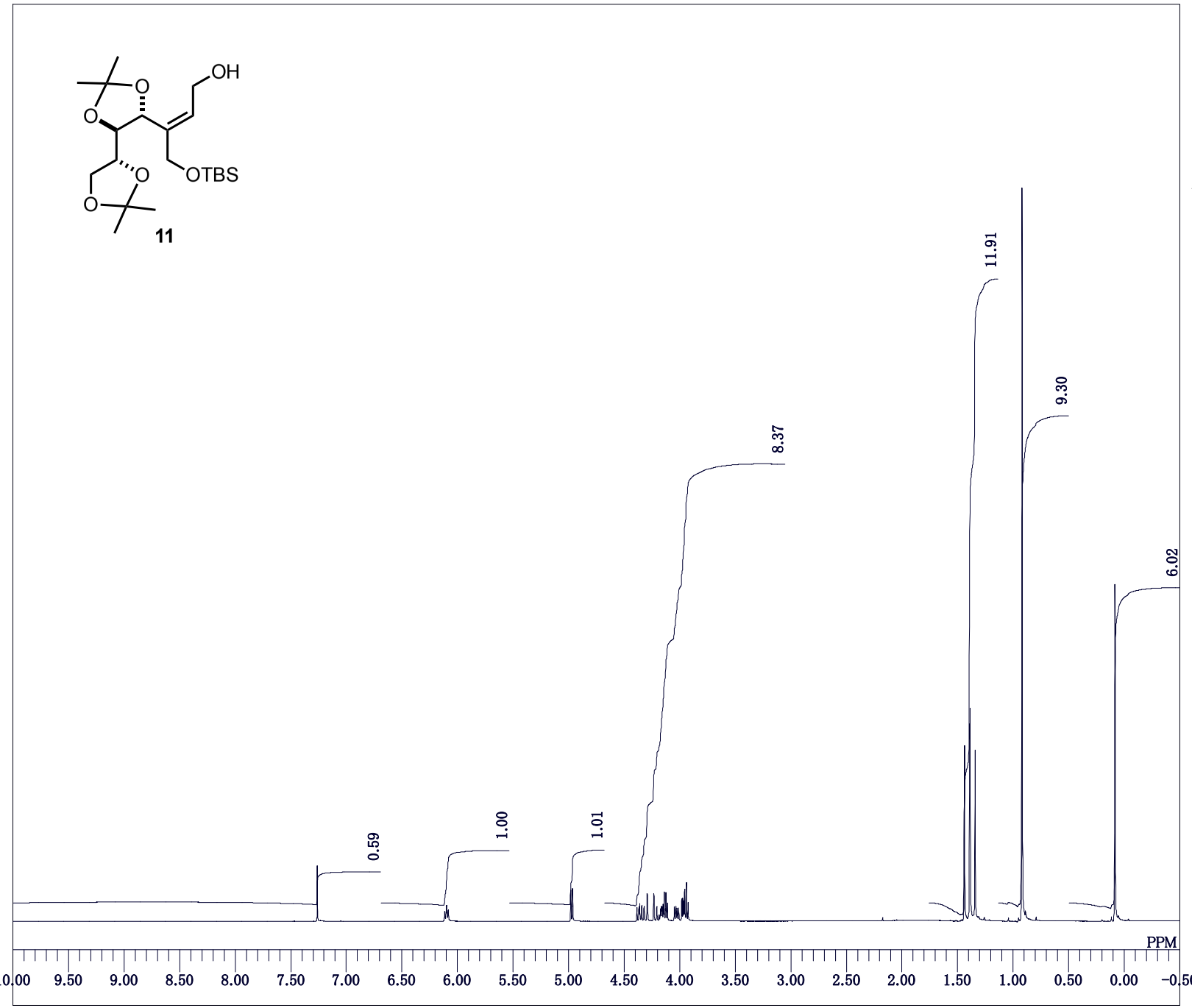
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	17.5 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50



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EXMOD	proton.jxp
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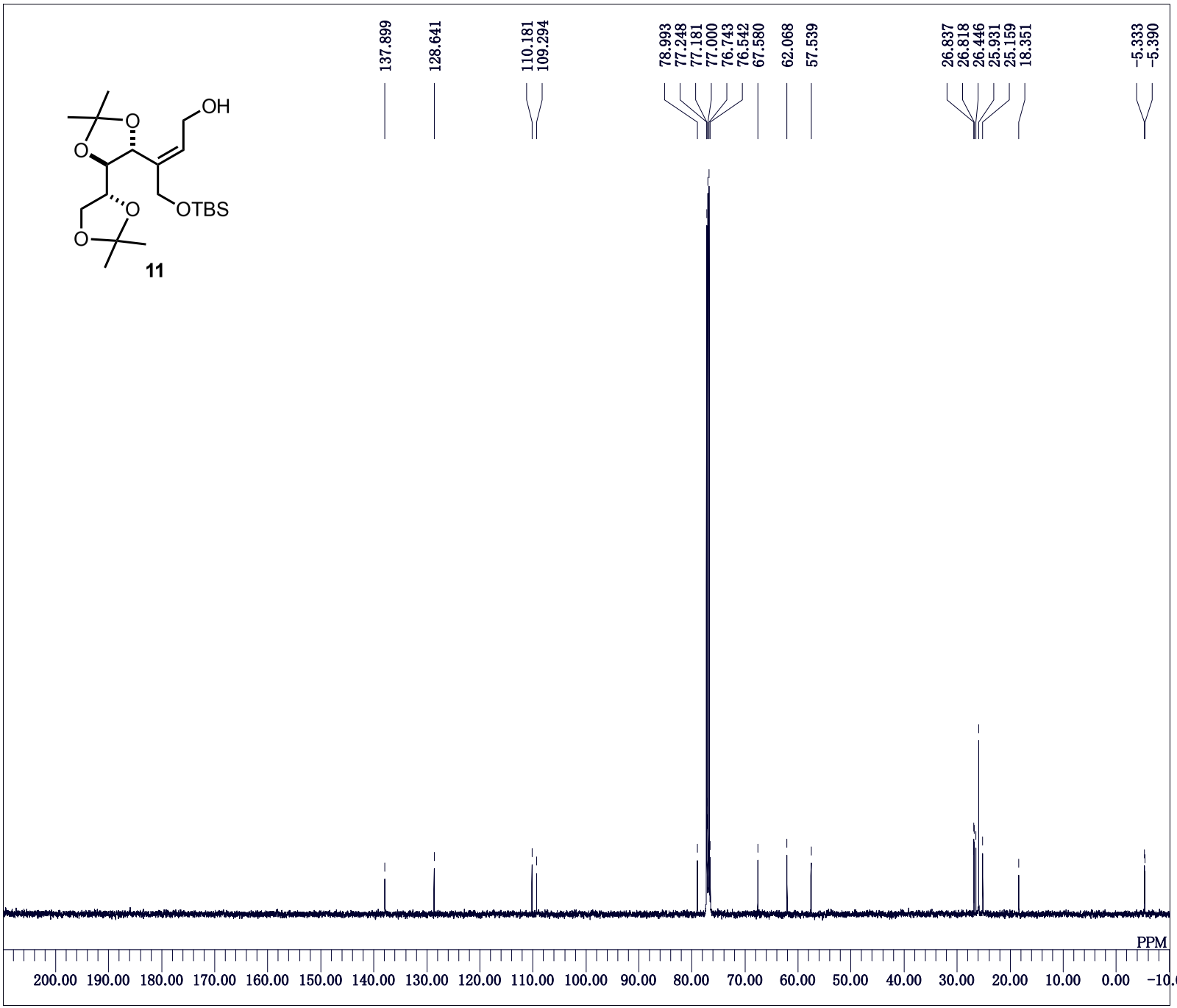
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	24.2 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50



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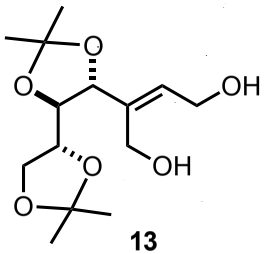
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	512
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	24.7 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

single_pulse

C:¥DOCUME~1¥ADMINI~1.WIN¥LOCALS~1¥Tem ﾃﾝﾎﾟﾗﾘ ﾌｧｲﾙ¥KIN3127_proton-1-1.jdf



13

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PD	5.0000 sec
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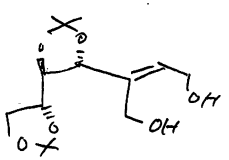
RGAIN	50



3127

33

single_pulse

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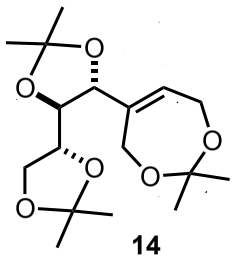

14

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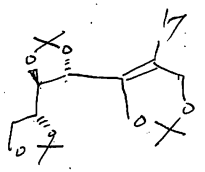
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	22.9 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	1.00 Hz
RGAIN	50



3128 product

single pulse decoupled gated NOE

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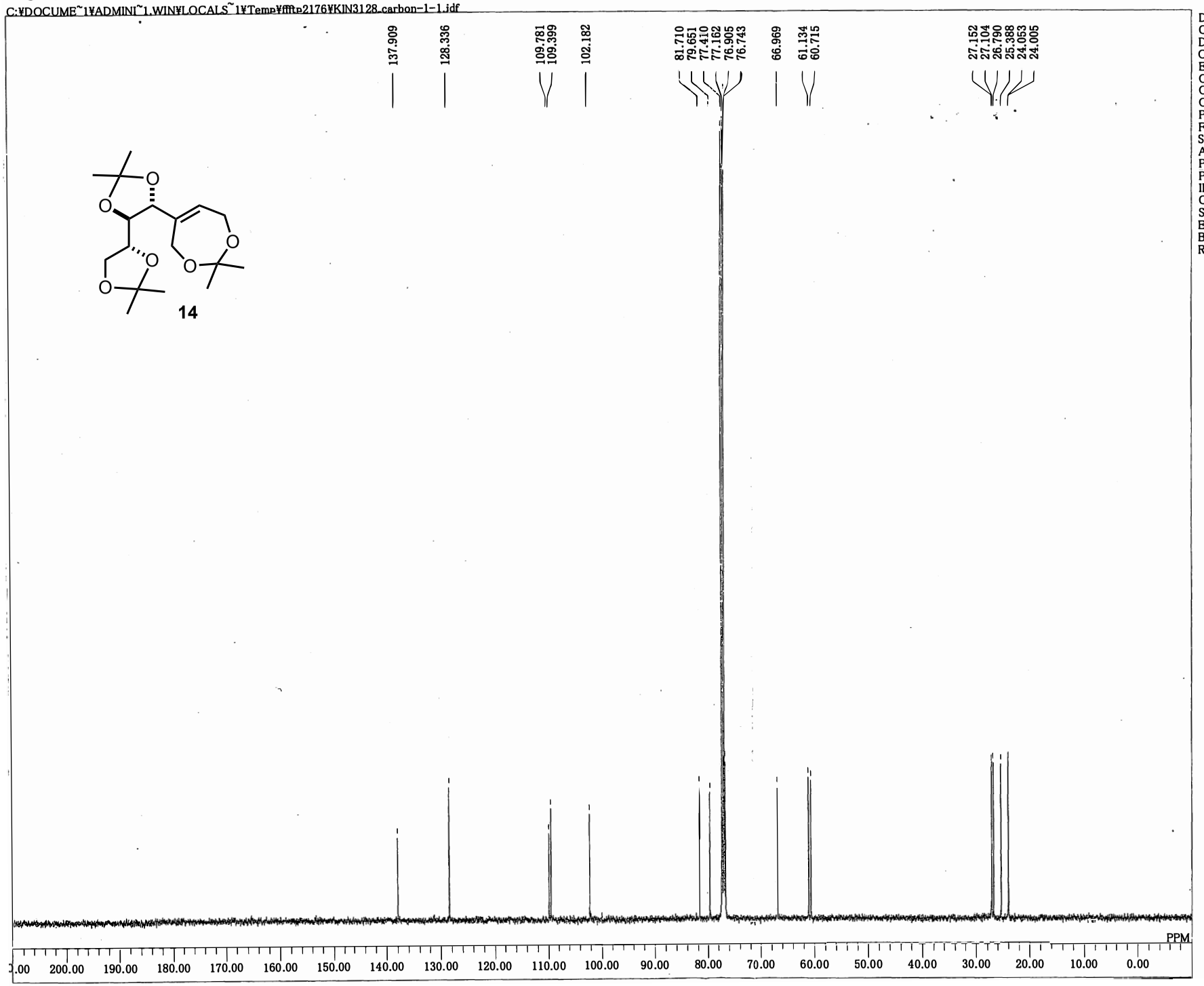

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OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	512
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	23.5 c
SLVNT	CDCL3
EXREF	225.02 ppm
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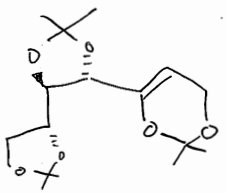
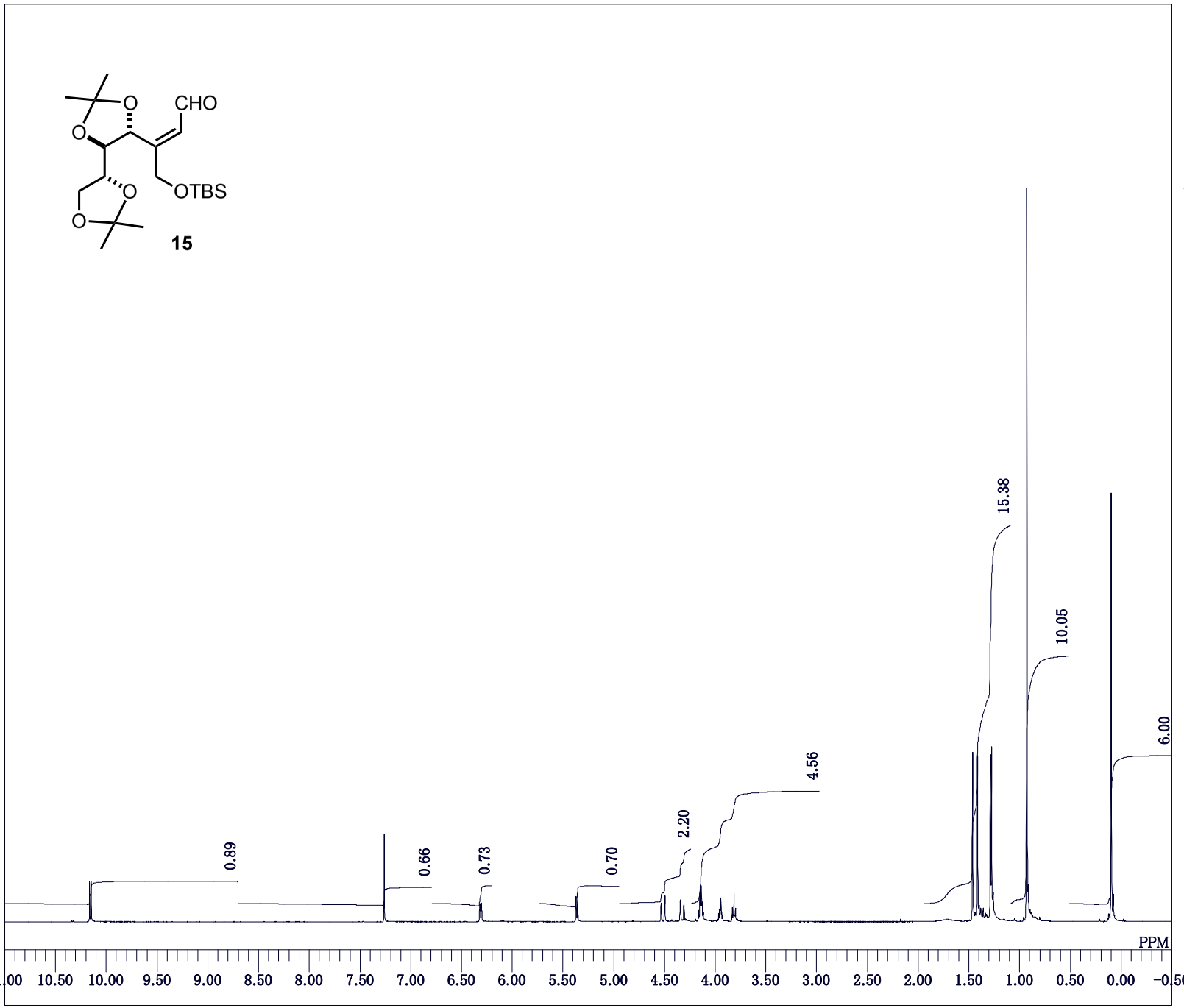
RGAIN	50



3128 product



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OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
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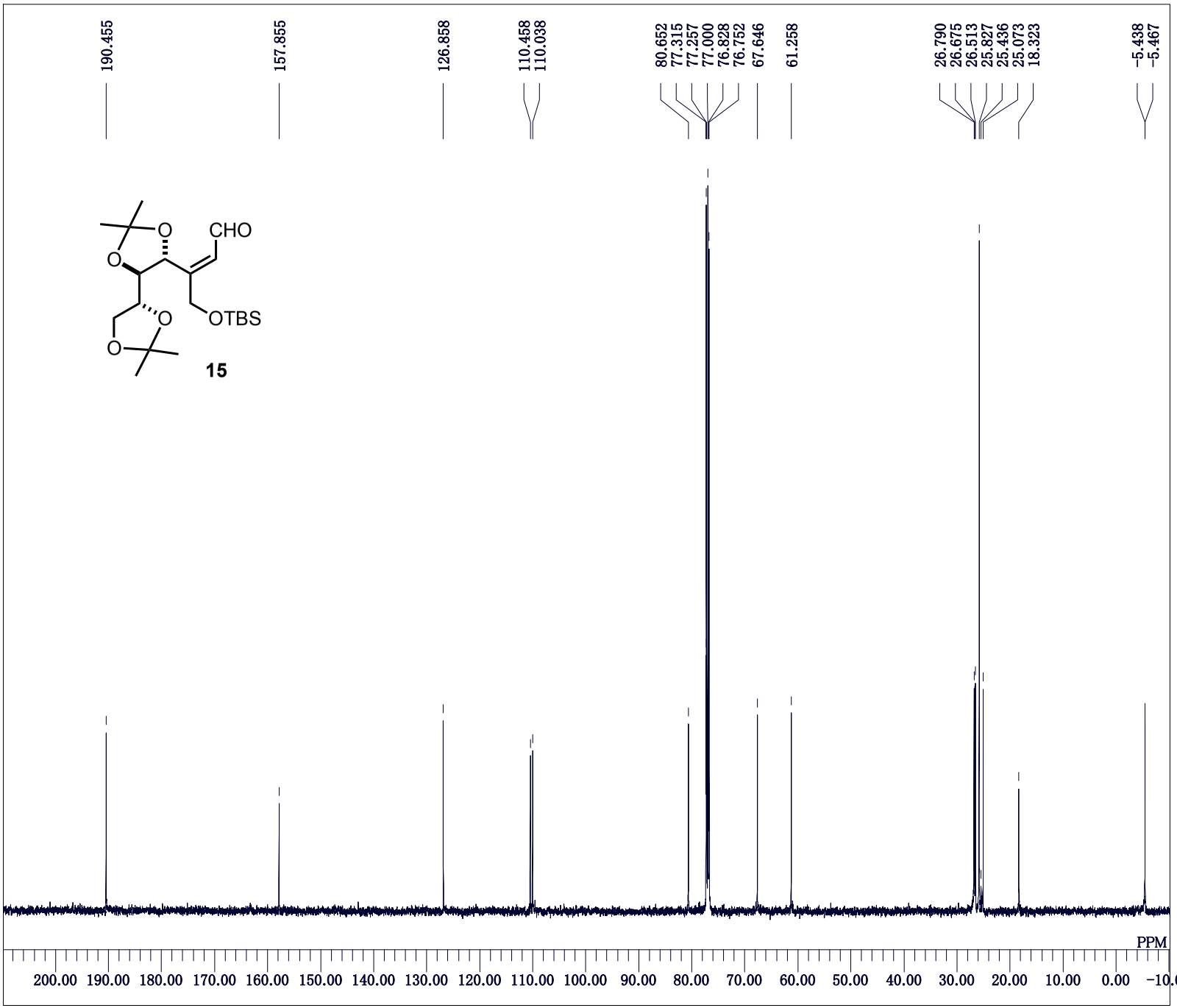
IRNUC	1H
CTEMP	23.0 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50



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EXMOD carbon.jxp
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OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 32780
FREQU 39308.18 Hz
SCANS 256
ACQTM 0.8336 sec
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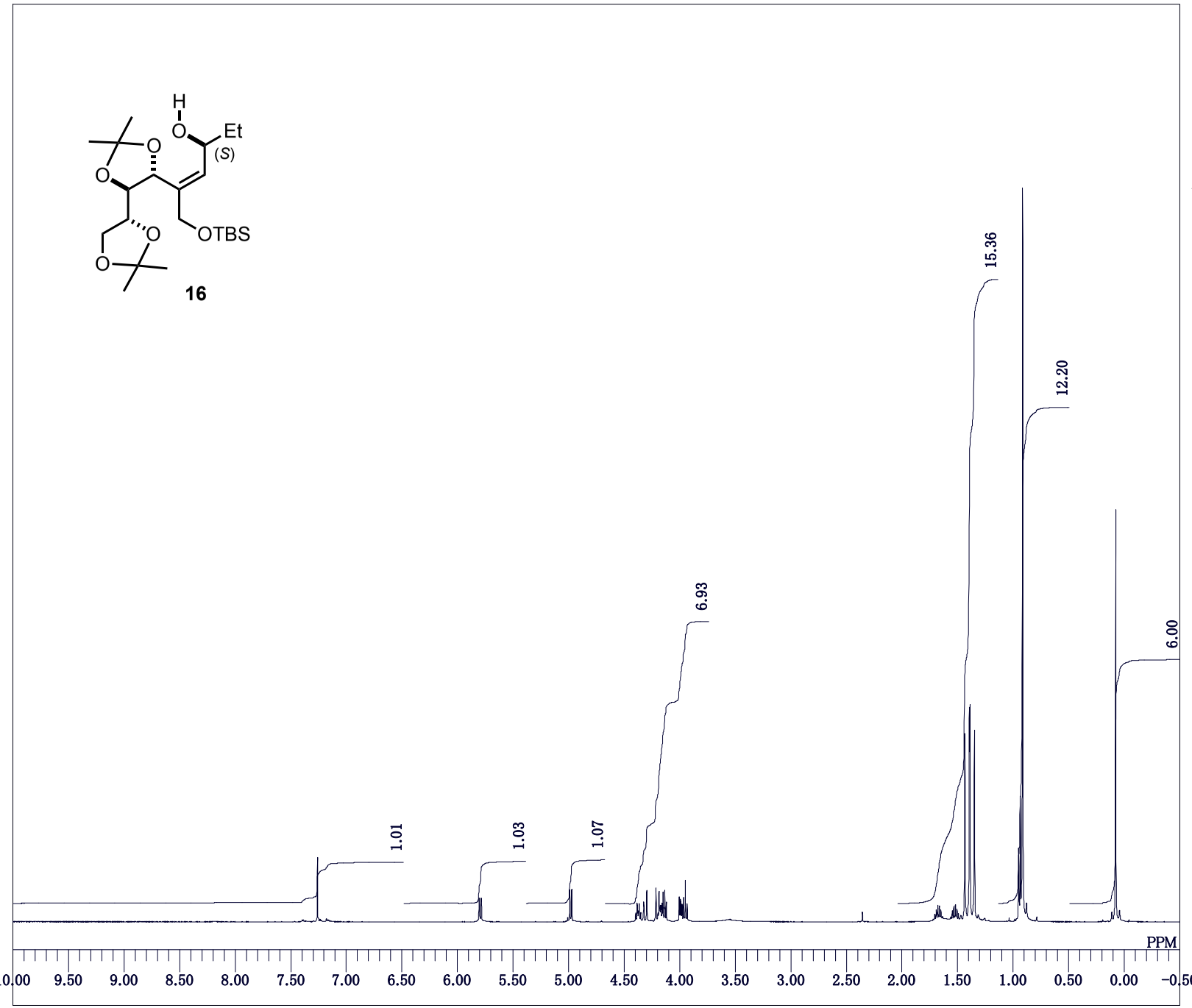
PW1 2.72 usec
IRNUC 1H
CTEMP 17.8 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 50



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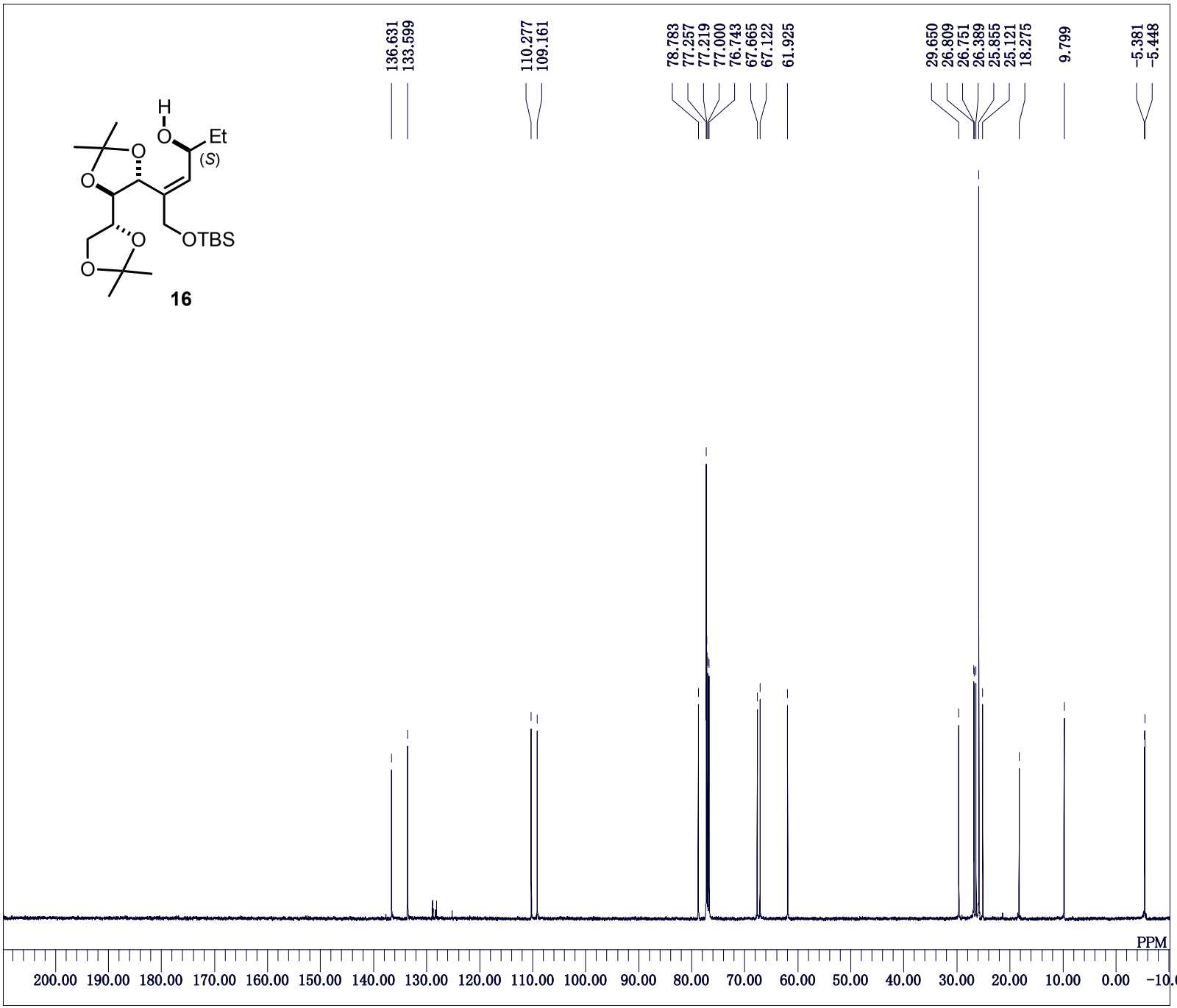
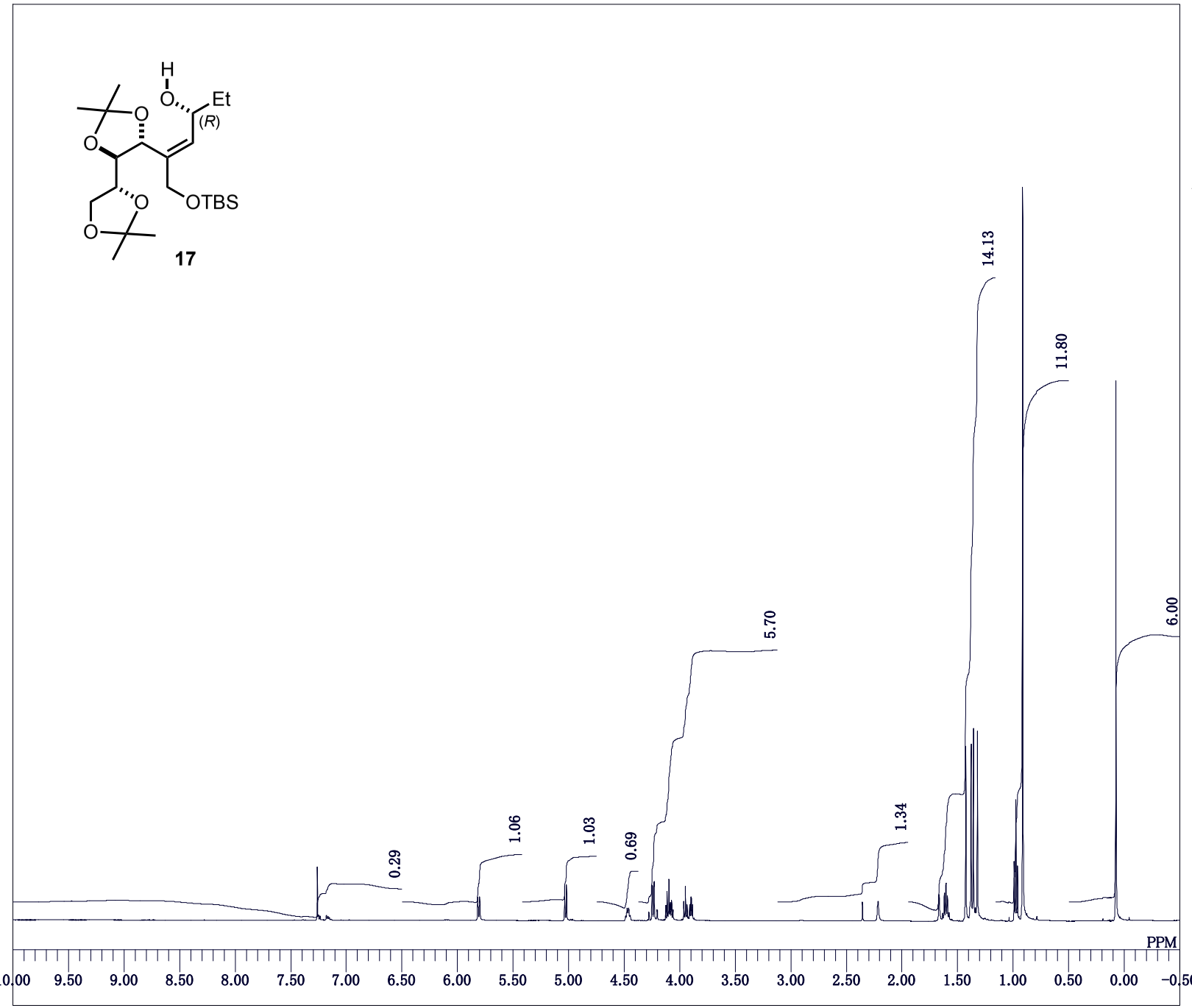
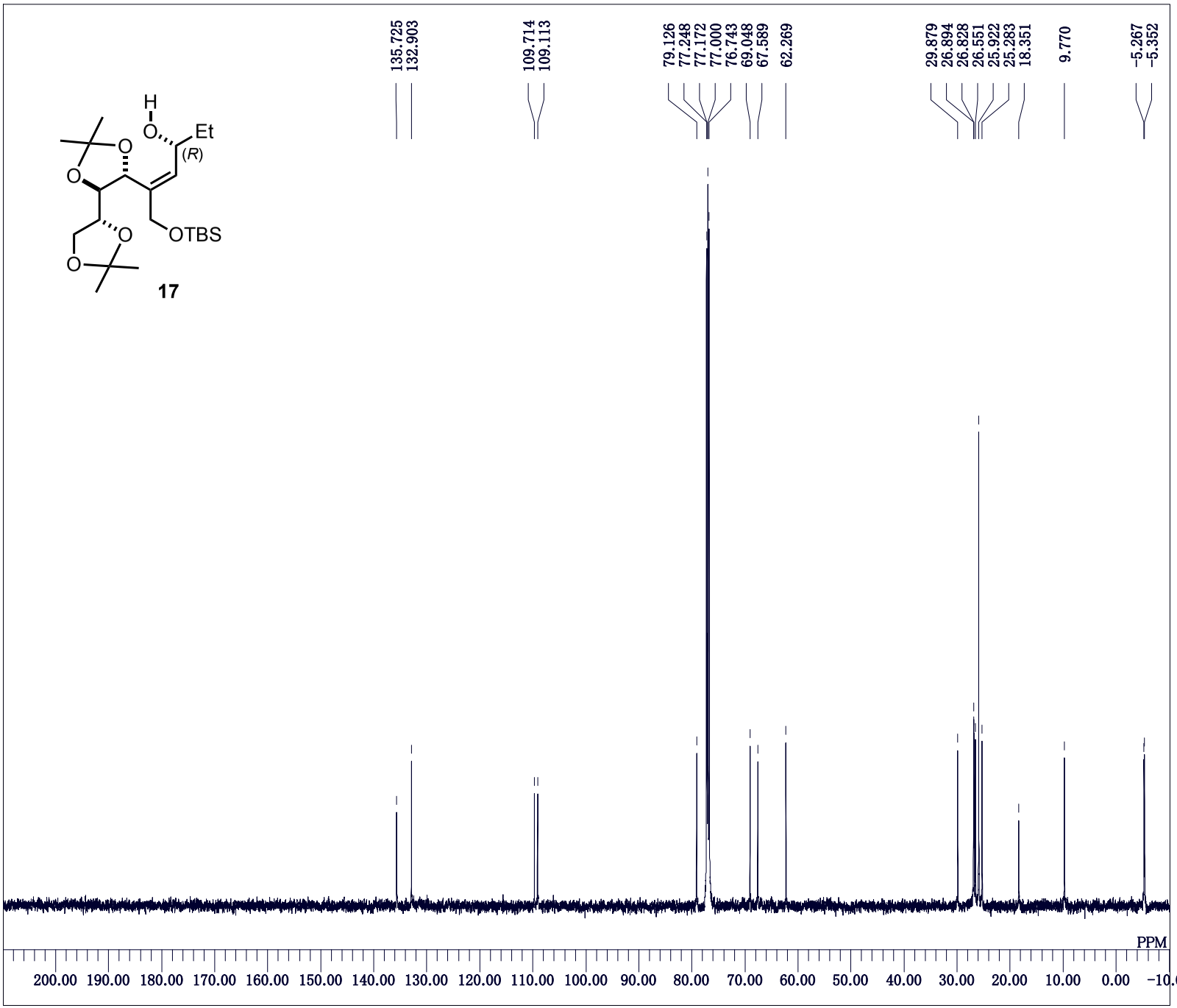
COMNT	single_pulse
DATIM	2013-06-03 15:49:21
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	20.6 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50



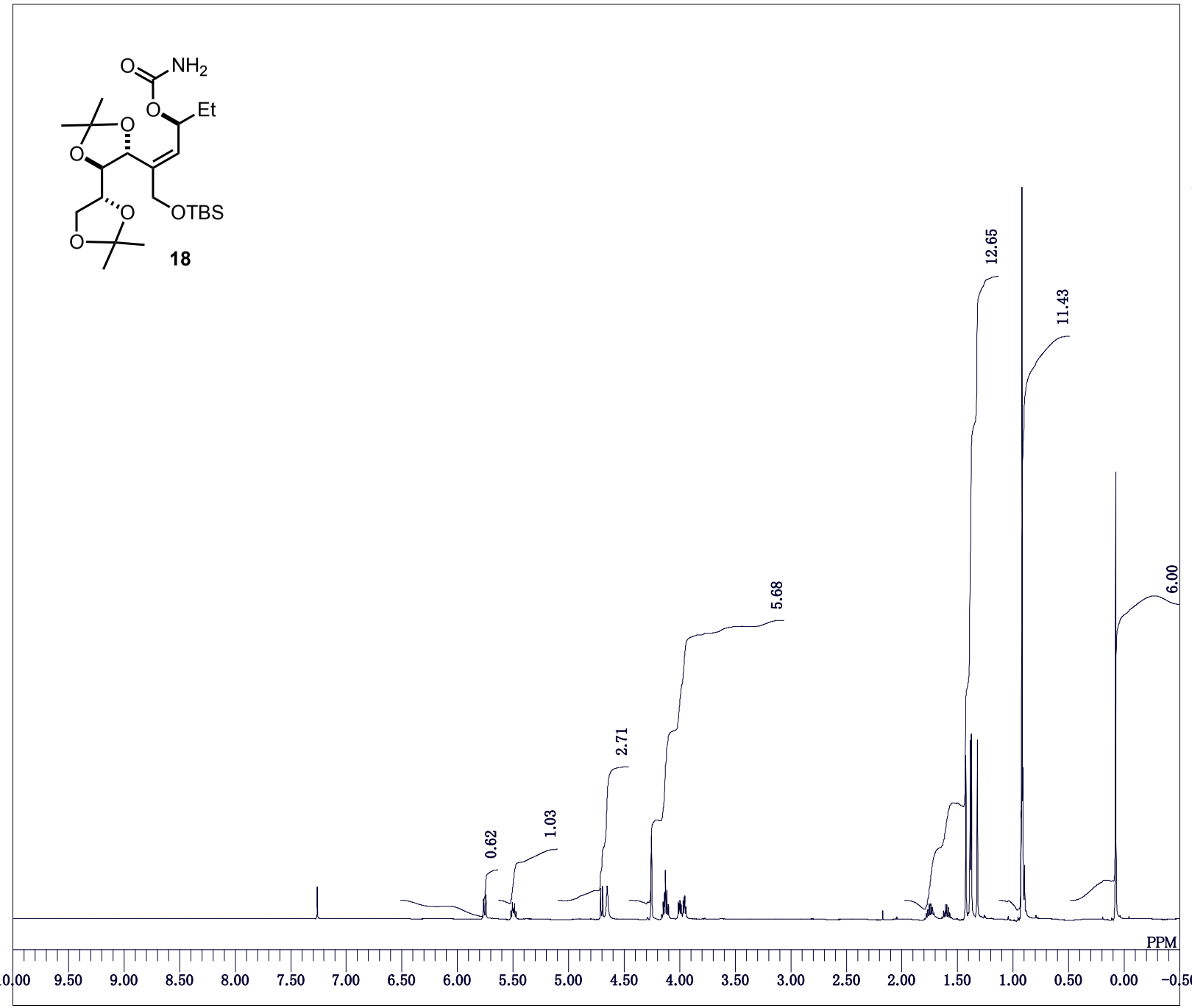
DFILE	KIN3100carbon_Carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2013-06-03 16:00:16
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	21.0 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50



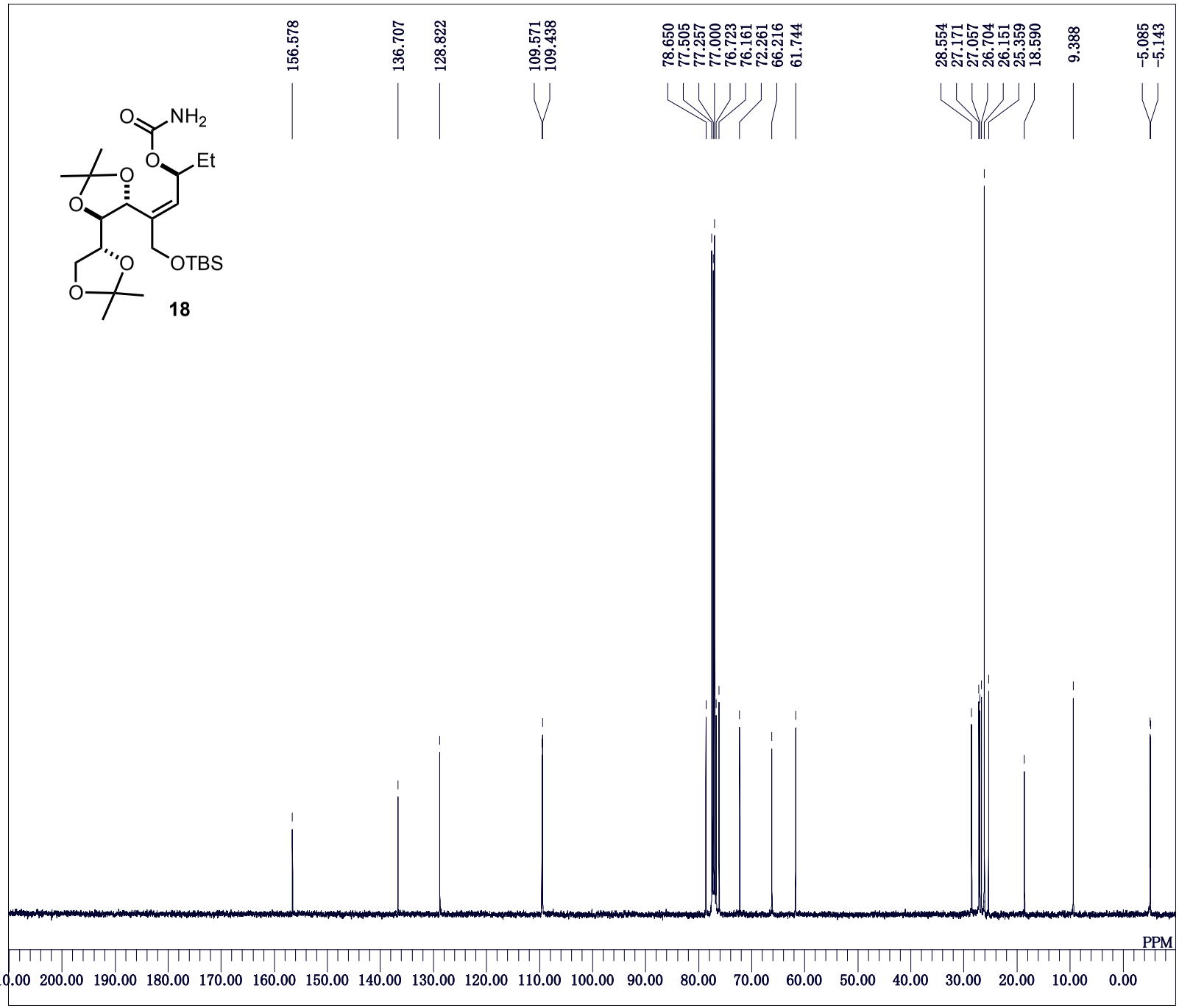
DFILE	KIN2113product_proton-1-1.jdf
COMNT	single_pulse
DATIM	2012-06-01 21:34:53
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	18.8 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50



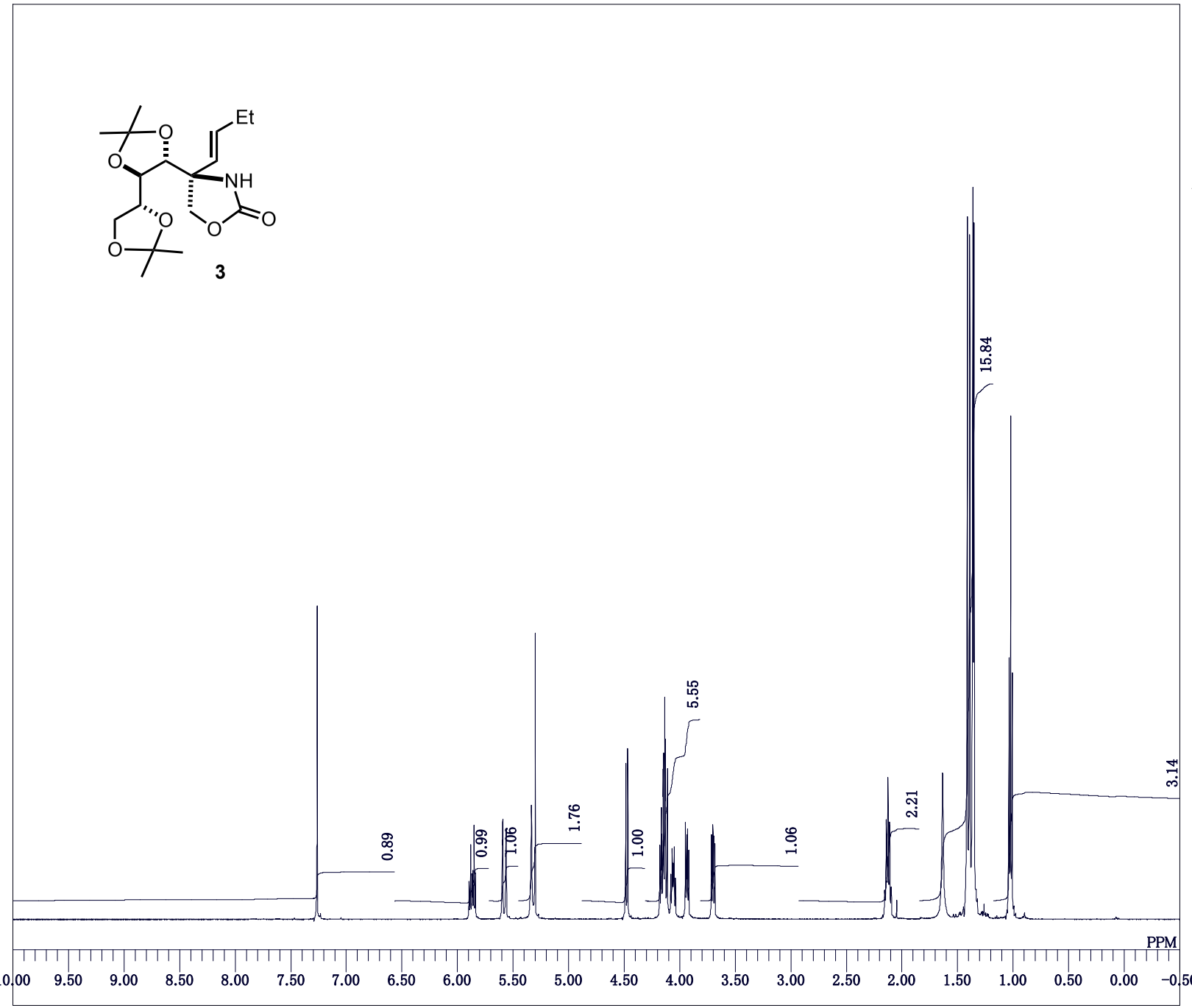
DFILE	KIN4007_carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2013-12-12 18:04:15
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	22.7 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50



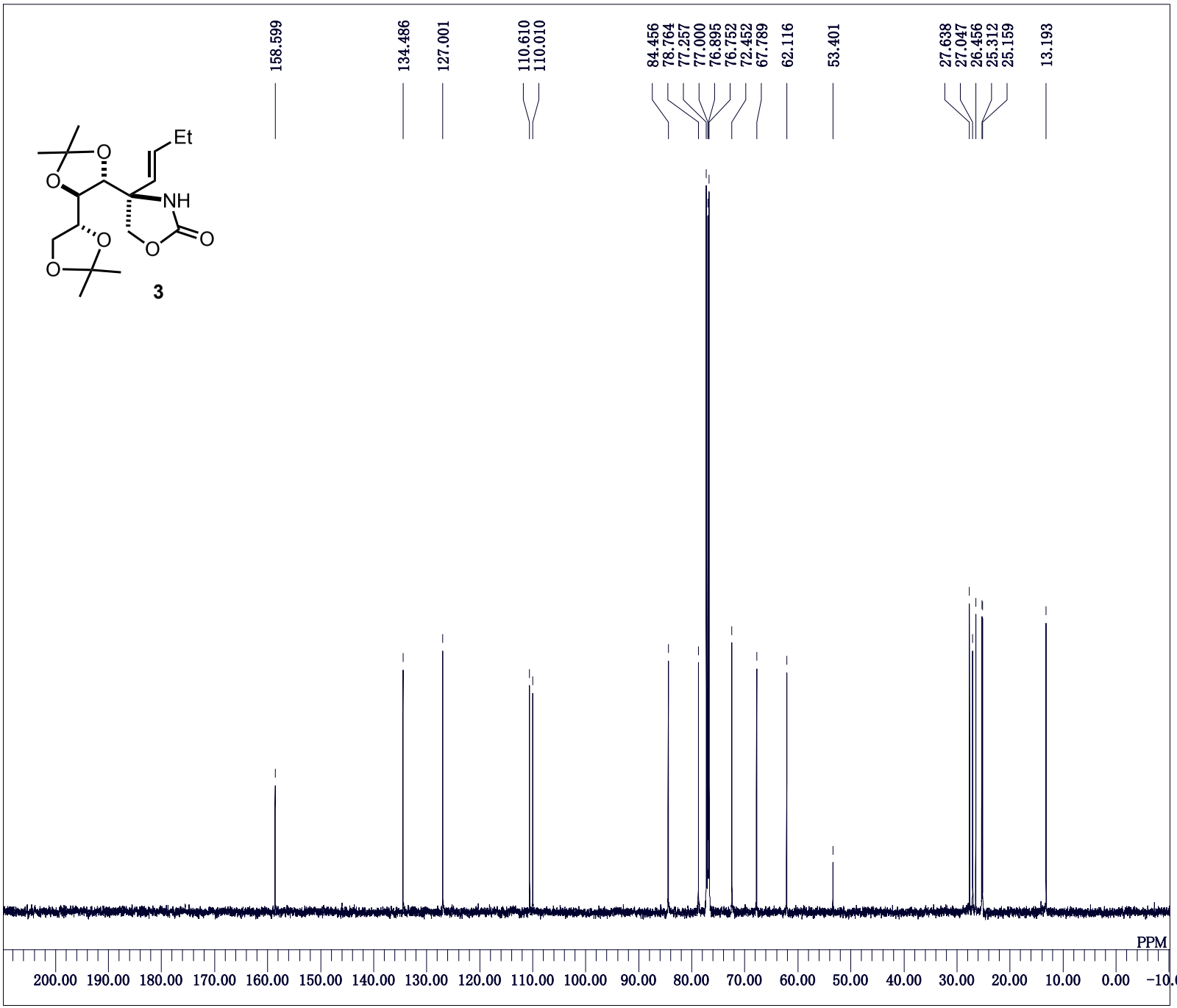
DFILE	KIN3107_proton-2-1.jdf
COMNT	single_pulse
DATIM	2013-06-29 16:21:35
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	22.5 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50



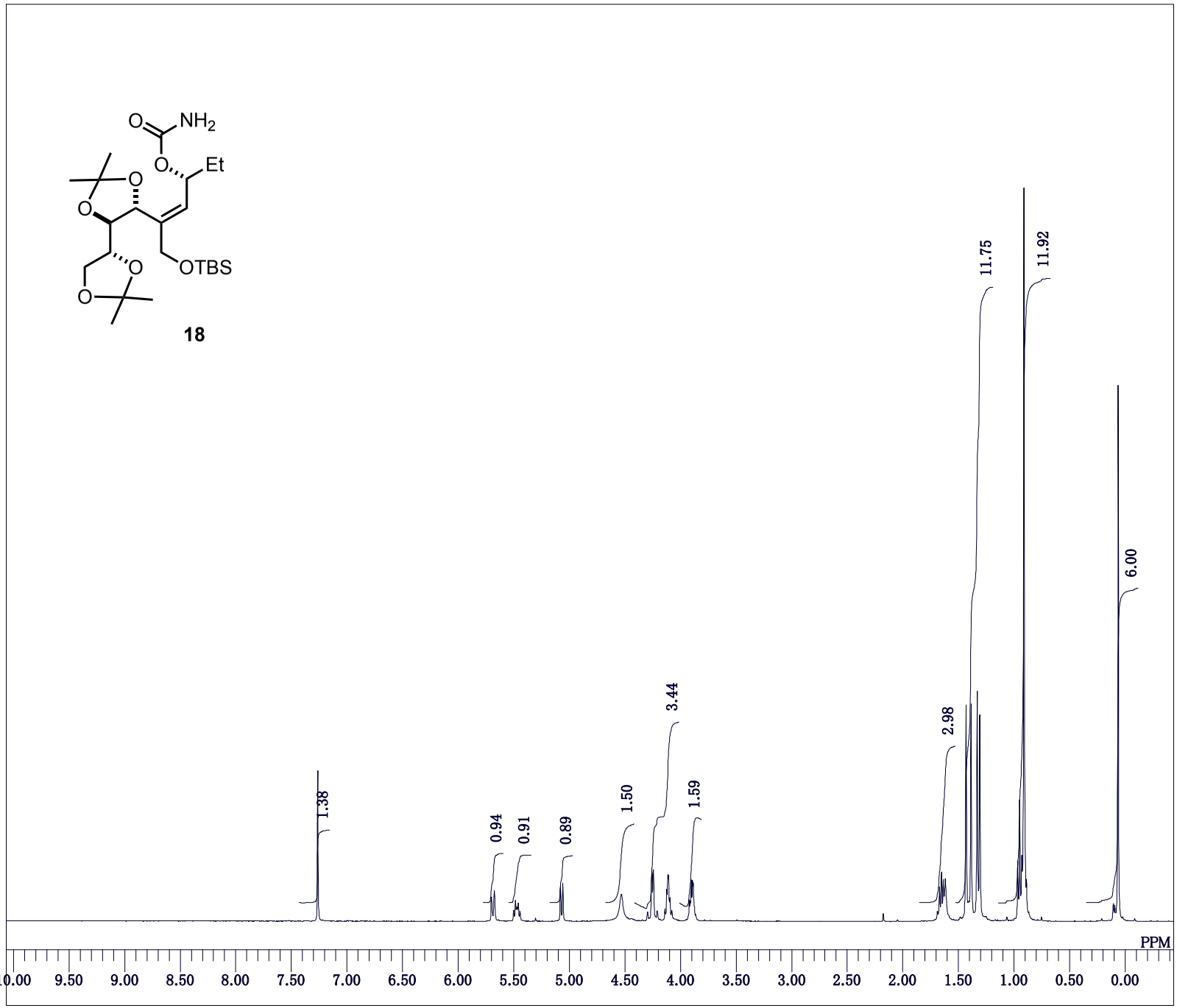
DFILE	KIN3107pro_carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2013-06-29 15:20:52
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	512
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	22.8 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50



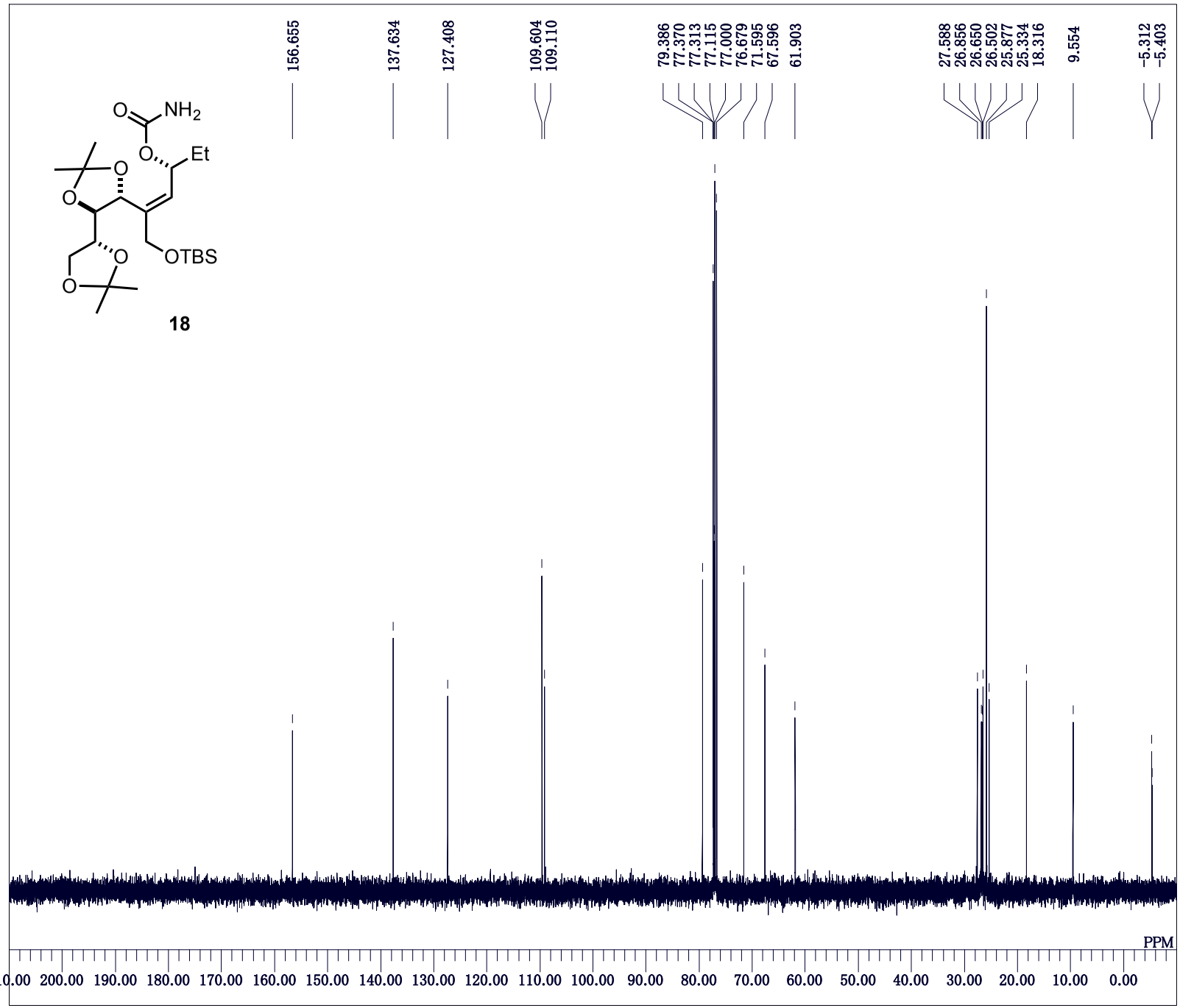
DFILE	KIN3112product_proton-1-1.jdf
COMNT	single_pulse
DATIM	2013-07-04 16:26:54
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	22.8 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50



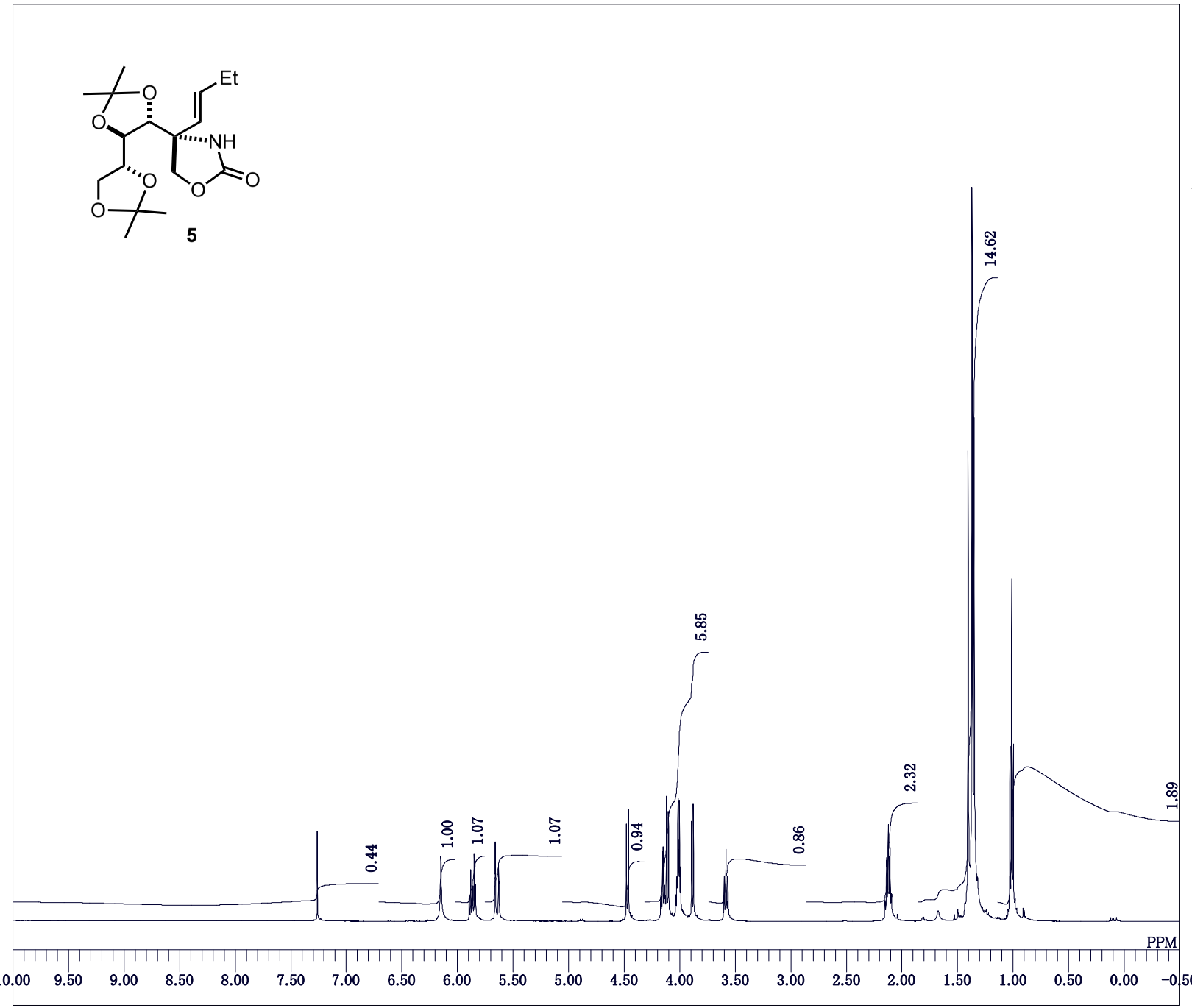
DFILE	KIN3112product_carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2013-07-04 16:34:19
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	23.3 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50



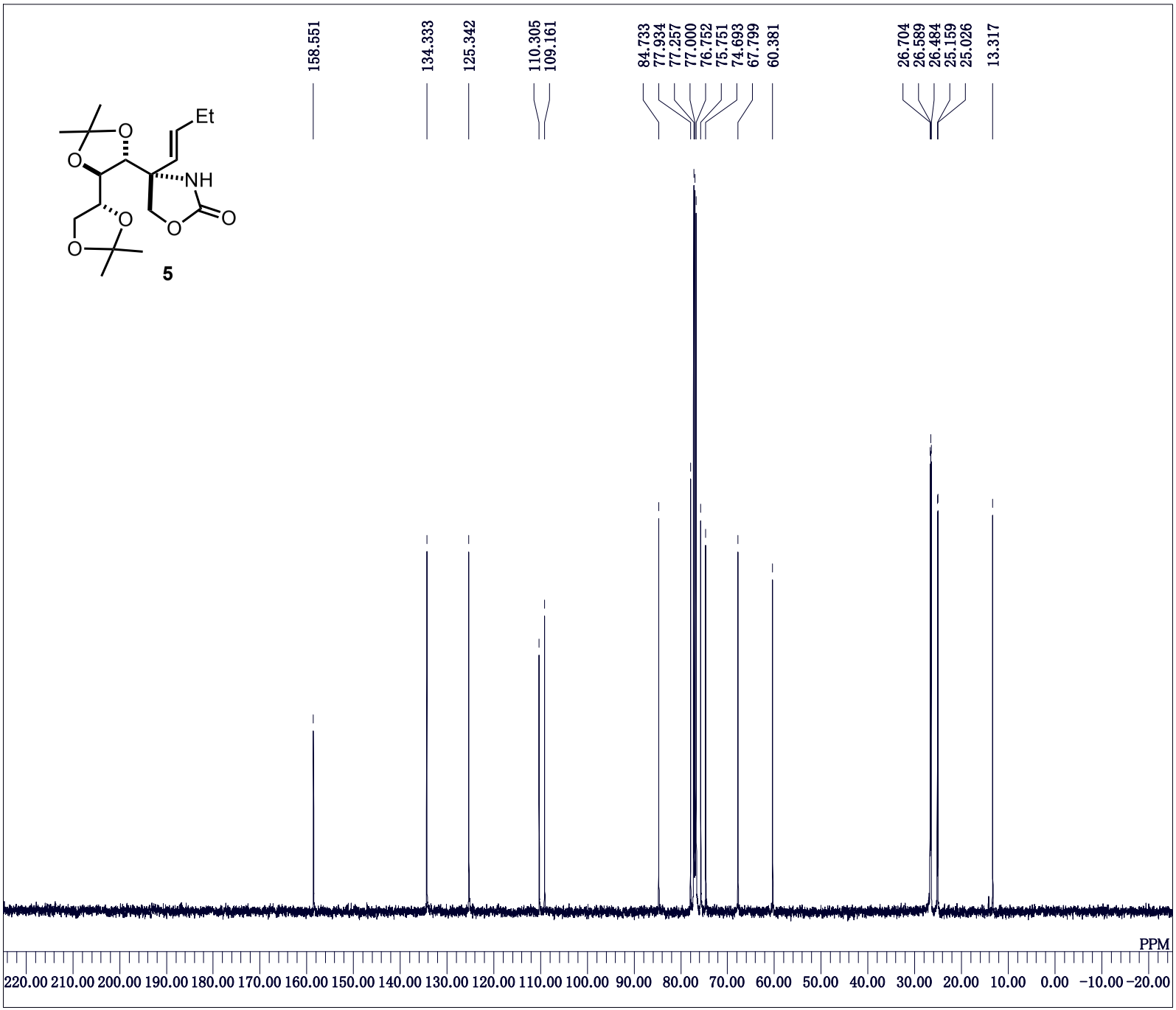
DFILE	KIN4013product.als
COMNT	
DATIM	Sun Dec 15 17:53:00 2013
OBNUC	1H
EXMOD	non
OBFRQ	399.65 MHz
OBSET	0.00 KHz
OBFIN	134300.00 Hz
POINT	8192
FREQU	7993.60 Hz
SCANS	8
ACQTM	1.0248 sec
PD	5.9752 sec
PW1	5.50 usec
IRNUC	1H
CTEMP	16.7 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	1.20 Hz
RGAIN	22



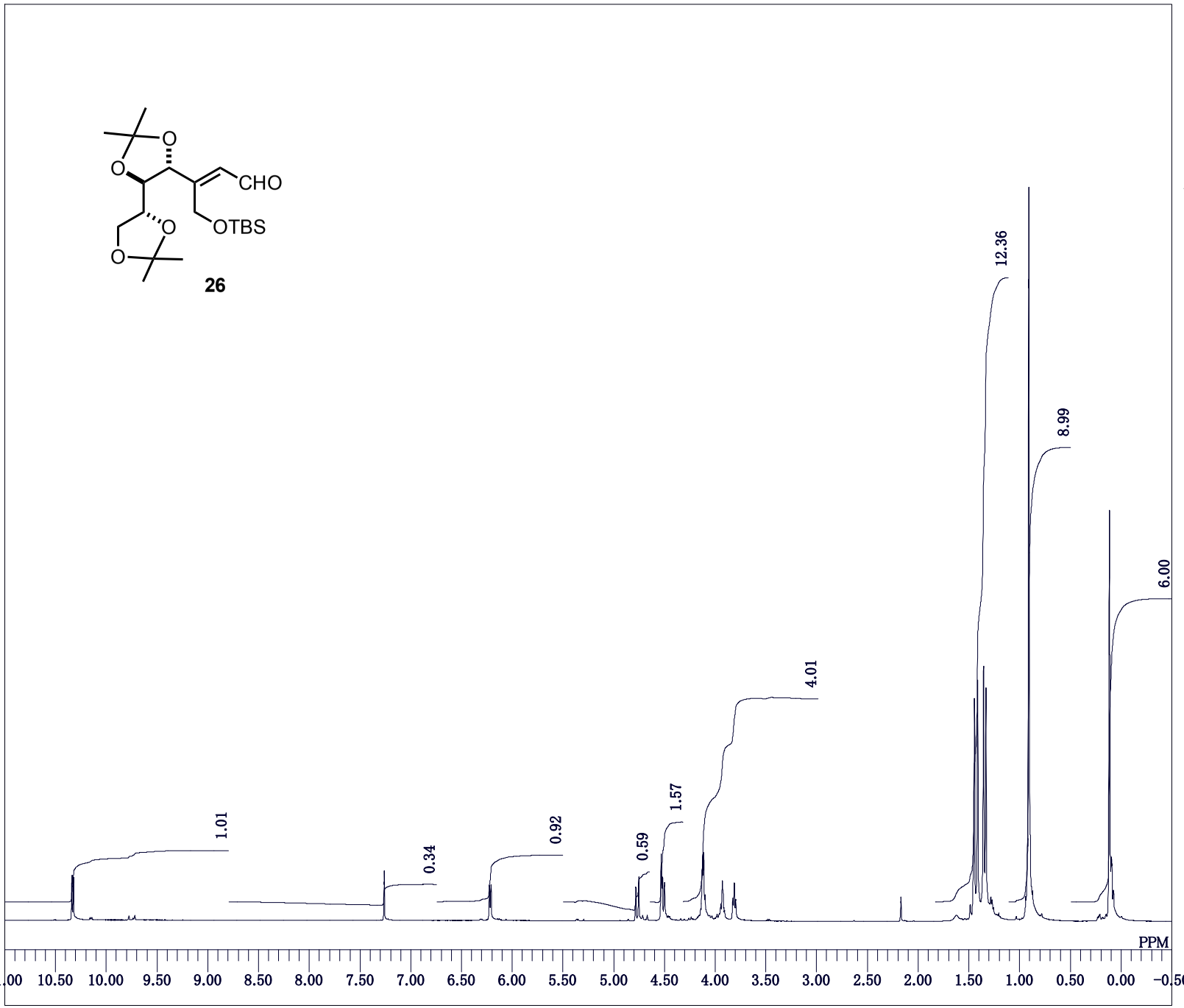
DFILE	KIN4013.als
COMNT	
DATIM	Fri Dec 13 22:16:38 2013
OBNUC	13C
EXMOD	bcm
OBFRQ	100.40 MHz
OBSET	0.00 KHz
OBFIN	135500.00 Hz
POINT	32768
FREQU	27100.27 Hz
SCANS	256
ACQTM	1.2091 sec
PD	1.7909 sec
PW1	5.75 usec
IRNUC	1H
CTEMP	18.0 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	29



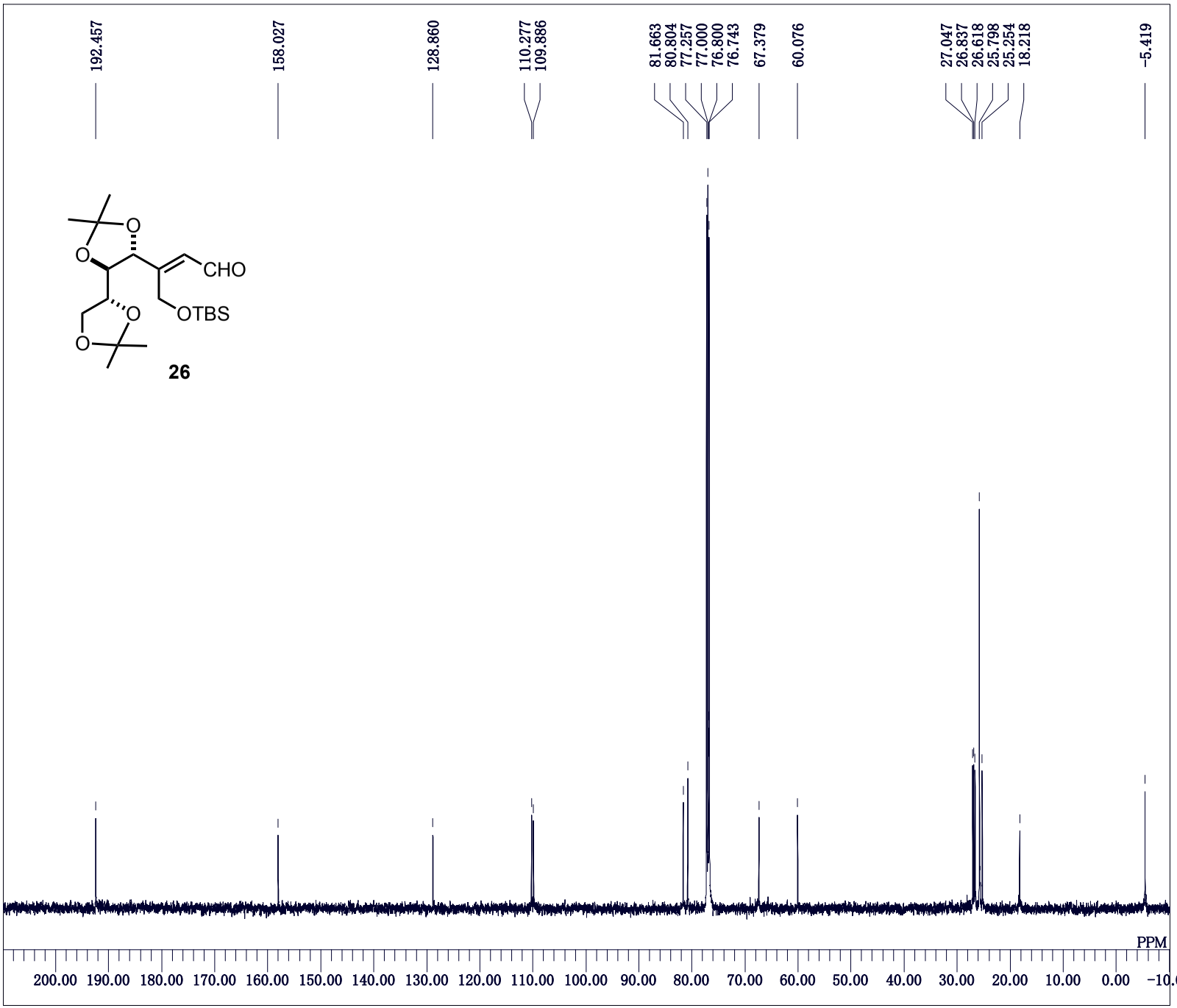
DFILE	KIN4016pro_proton-1-1.jdf
COMNT	single_pulse
DATIM	2013-12-16 16:49:36
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	19.2 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50



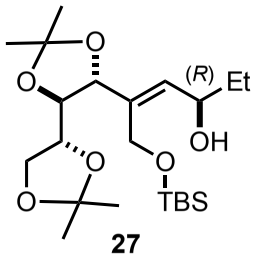
DFILE	KIN4030_carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2014-01-15 23:02:21
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	21.8 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50



DFILE	KIN4039_proton-1-1.jdf
COMNT	single_pulse
DATIM	2014-01-29 16:57:29
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	24.0 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50

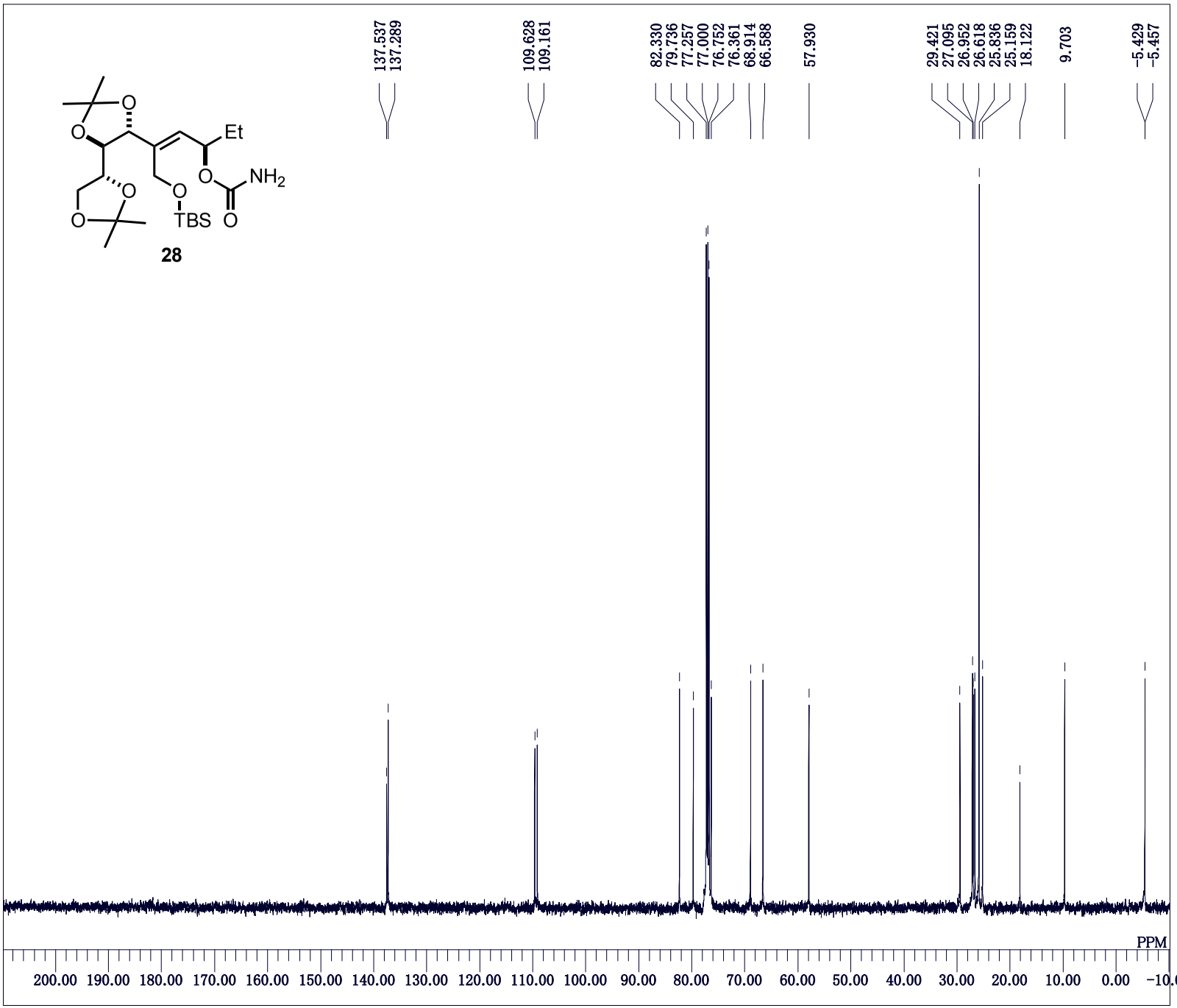


DFILE	KIN4039_carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2014-01-29 16:39:52
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	24.2 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

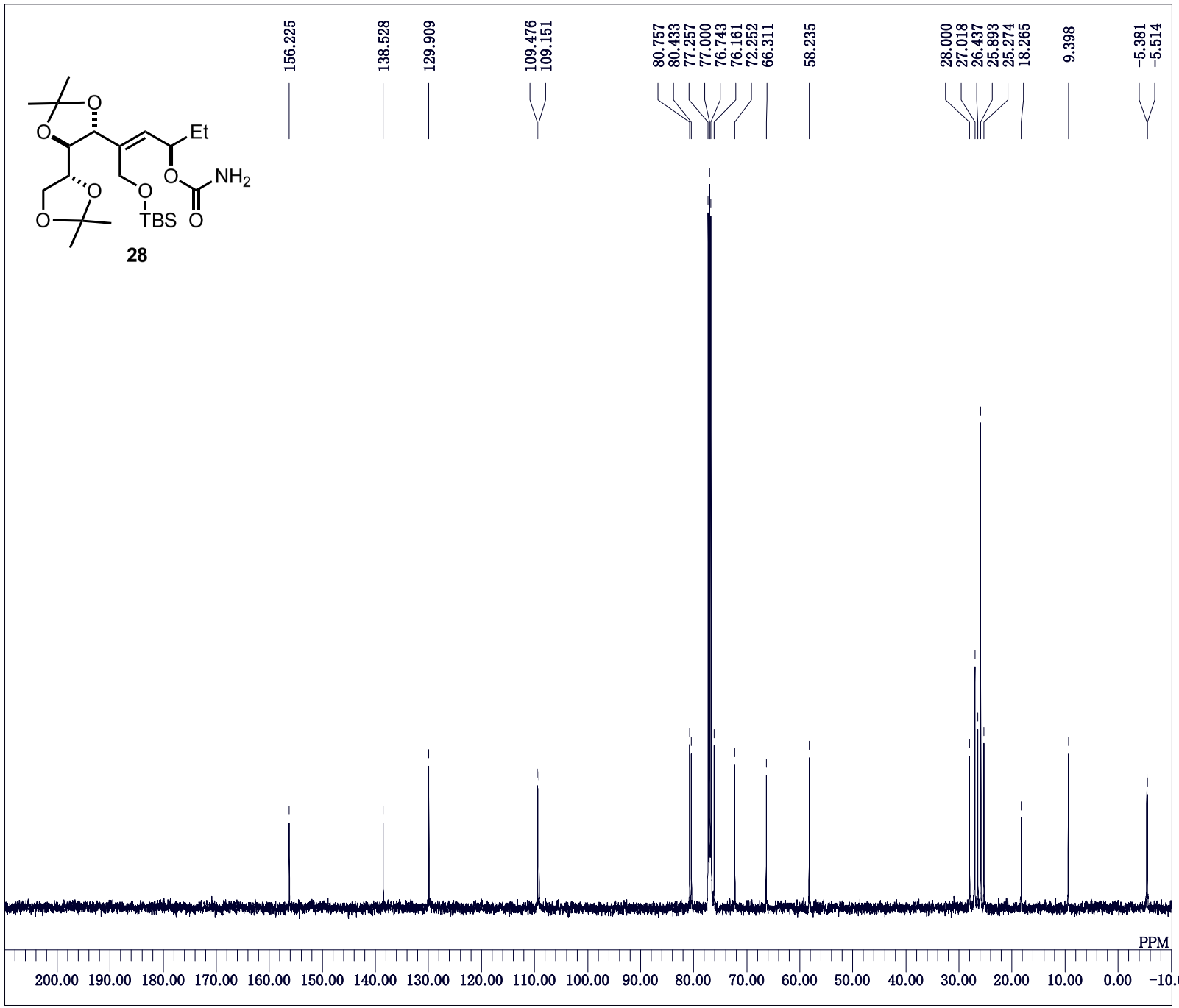


27

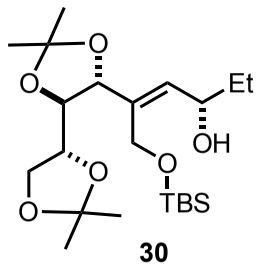
DFILE	KIN3198product.als
COMNT	
DATIM	Sun Dec 15 17:40:04 2013
OBNUC	1H
EXMOD	non
OBFRQ	399.65 MHz
OBSET	0.00 KHz
OBFIN	134300.00 Hz
POINT	8192
FREQU	7993.60 Hz
SCANS	8
ACQTM	1.0248 sec
PD	5.9752 sec
PW1	5.50 usec
IRNUC	1H
CTEMP	16.3 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	1.20 Hz
RGAIN	23



DFILE KIN3198product_carbon-1-1.jdf
COMNT single pulse decoupled gated NOE
DATIM 2013-12-05 22:25:09
OBNUC 13C
EXMOD carbon.jxp
OBFRQ 125.77 MHz
OBSET 7.87 KHz
OBFIN 4.21 Hz
POINT 32780
FREQU 39308.18 Hz
SCANS 256
ACQTM 0.8336 sec
PD 2.0000 sec
PW1 2.72 usec
IRNUC 1H
CTEMP 18.5 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 1.20 Hz
RGAIN 50



DFILE	KIN4009_carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2013-12-10 11:33:56
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	24.1 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	50



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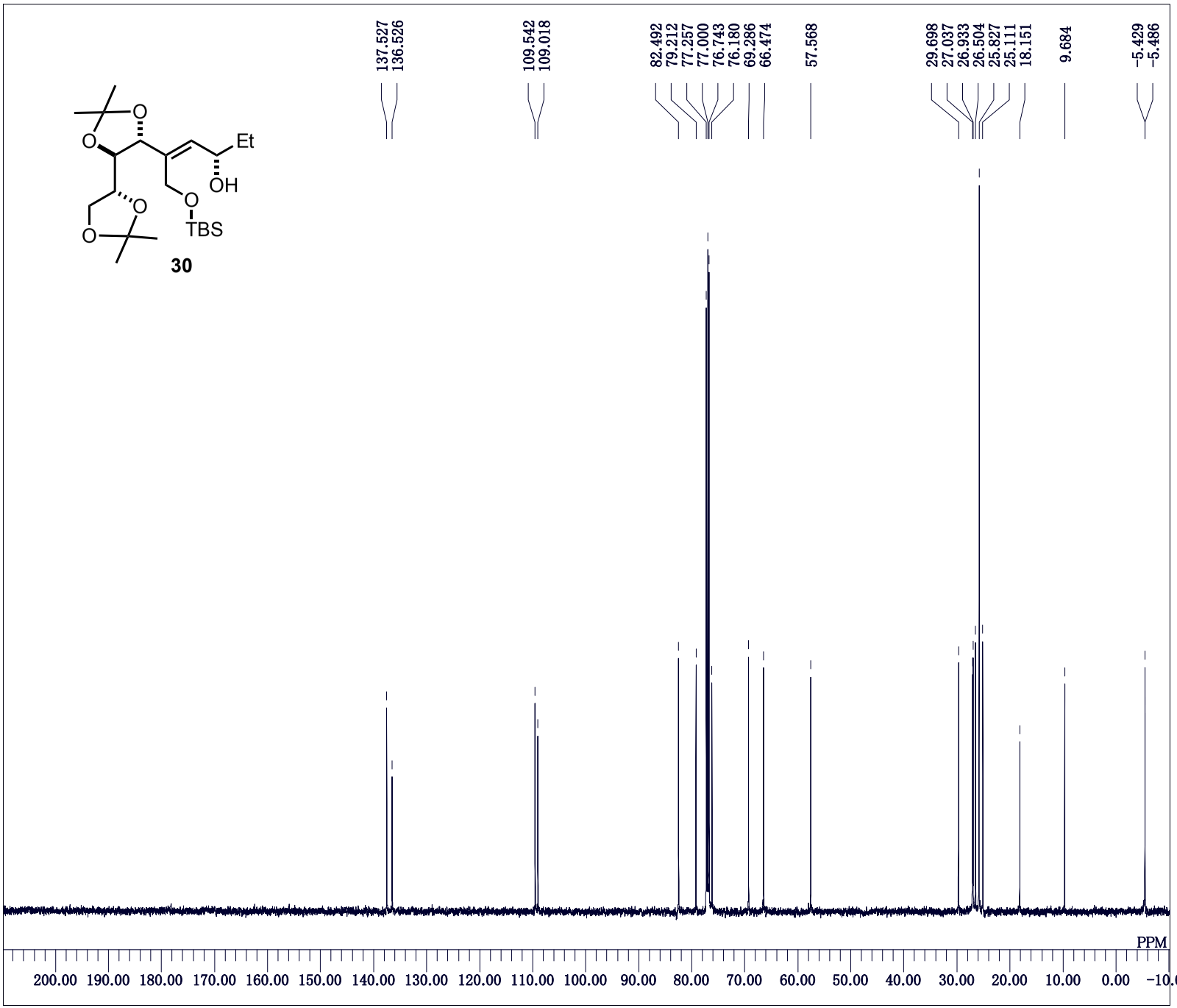
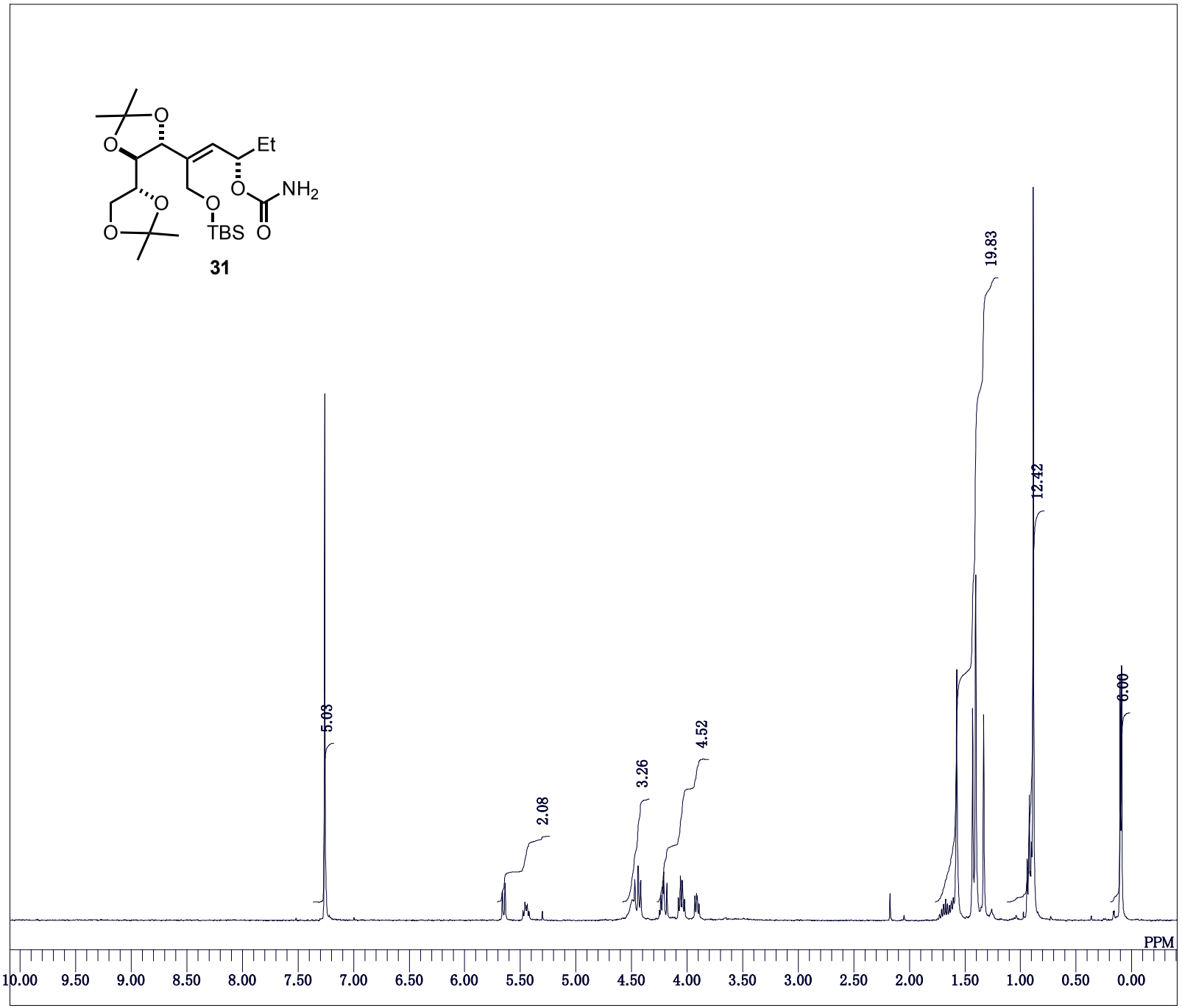
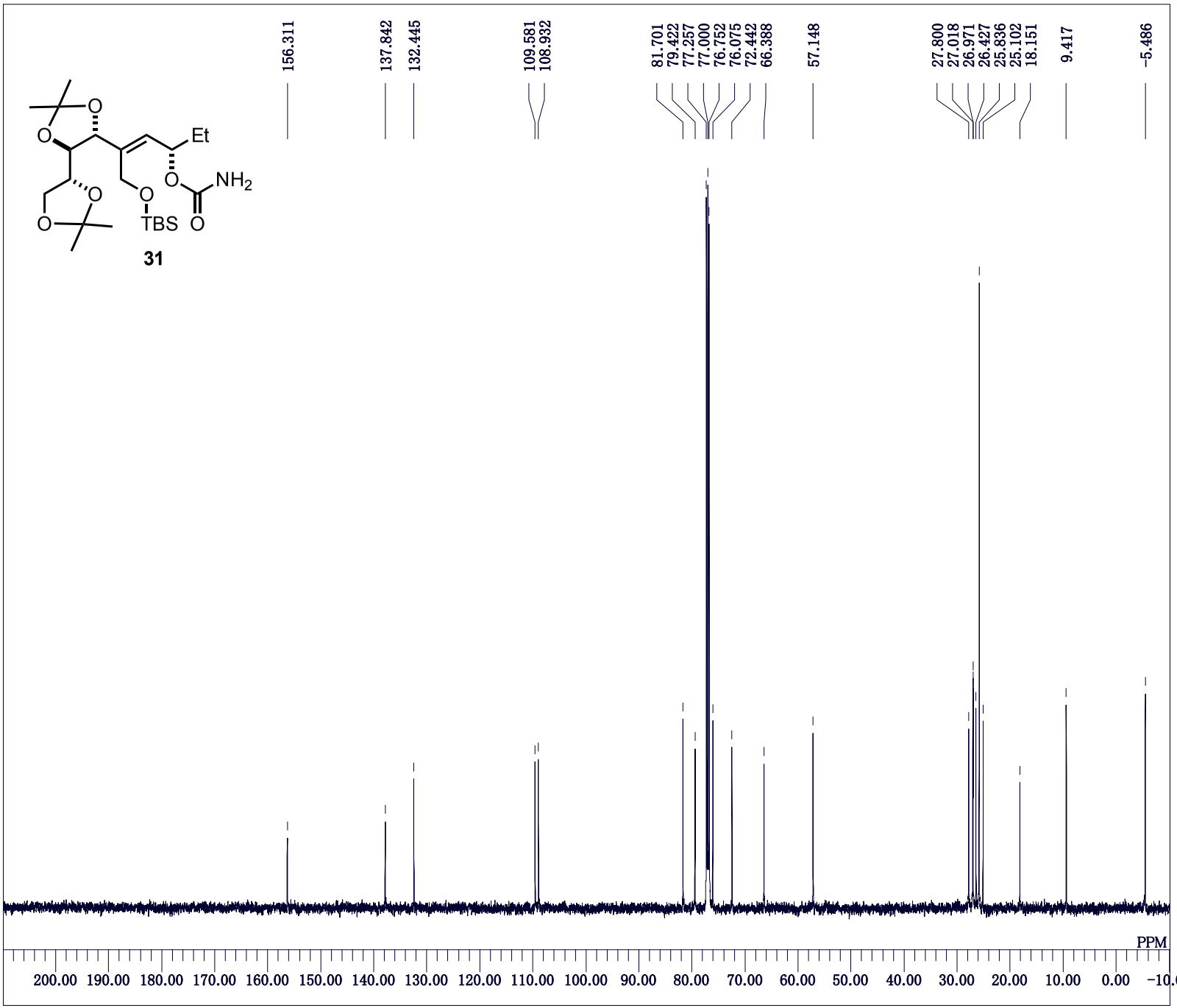
DFILE	KIN3197product_proton-1-1.jdf
COMNT	single_pulse
DATIM	2013-12-01 21:04:45
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	17.3 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	1.20 Hz
RGAIN	50



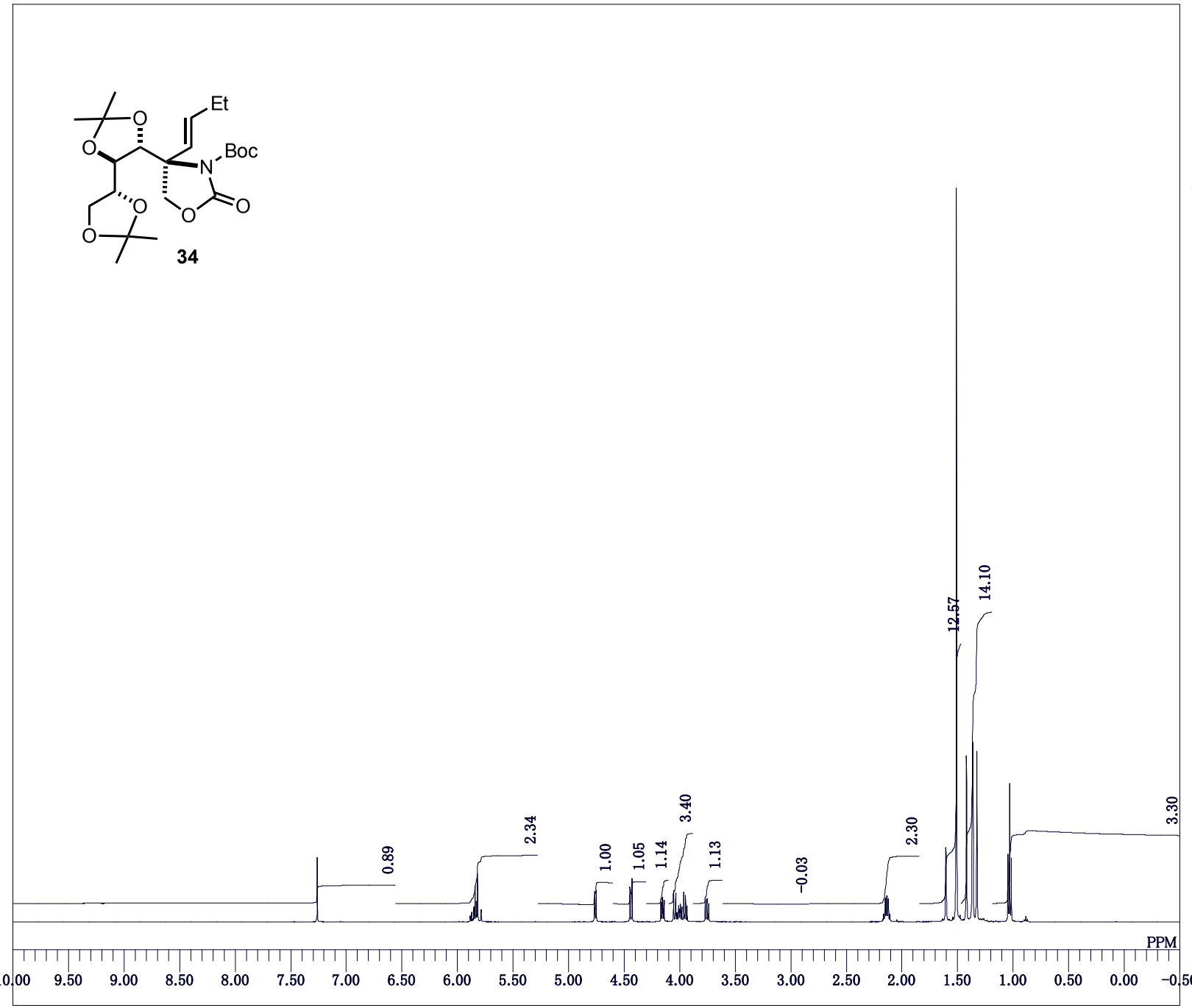
DFILE	KIN3197carbon_carbon-2-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2013-12-03 20:58:58
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	17.7 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	50



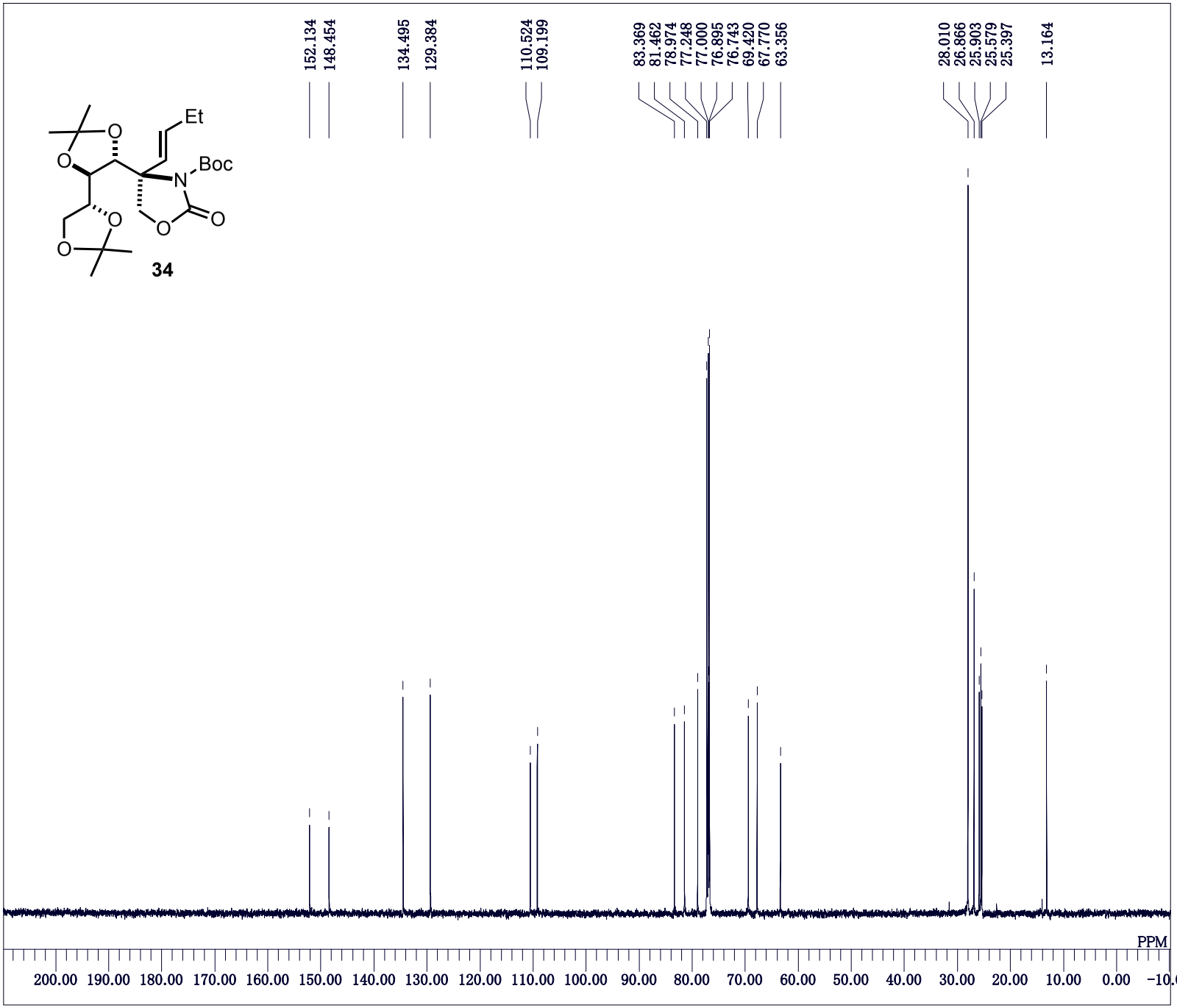
DFILE KIN4001pro.als
COMNT
DATIM Sun Dec 15 17:44:42 2013
OBNUC 1H
EXMOD non
OBFRQ 399.65 MHz
OBSET 0.00 KHz
OBFIN 134300.00 Hz
POINT 8192
FREQU 7993.60 Hz
SCANS 8
ACQTM 1.0248 sec
PD 5.9752 sec
PW1 5.50 usec
IRNUC 1H
CTEMP 16.5 c
SLVNT CDCL3
EXREF 7.26 ppm
BF 1.20 Hz
RGAIN 27



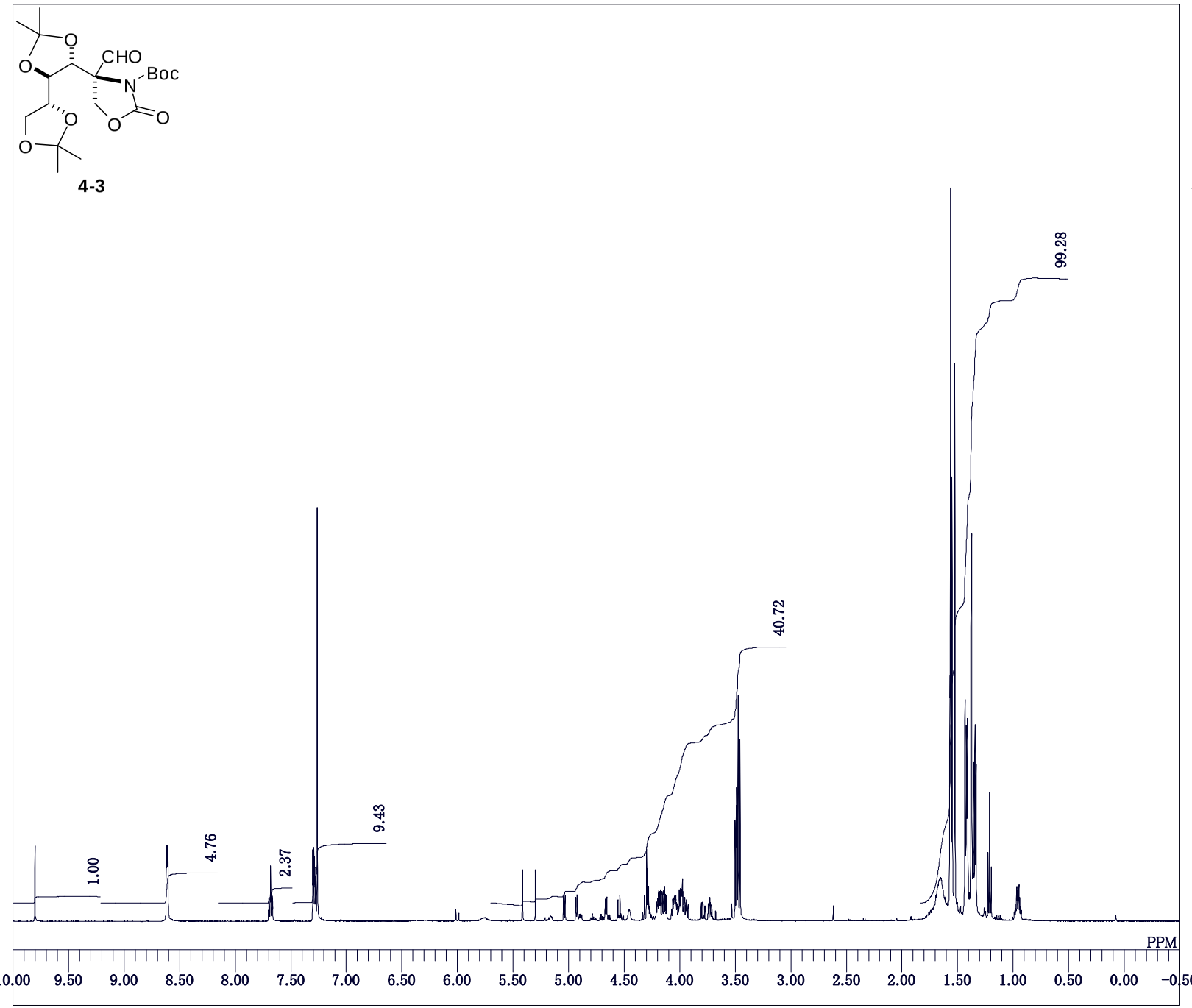
DFILE	KIN4001_carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2013-12-09 16:51:25
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	24.2 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	50



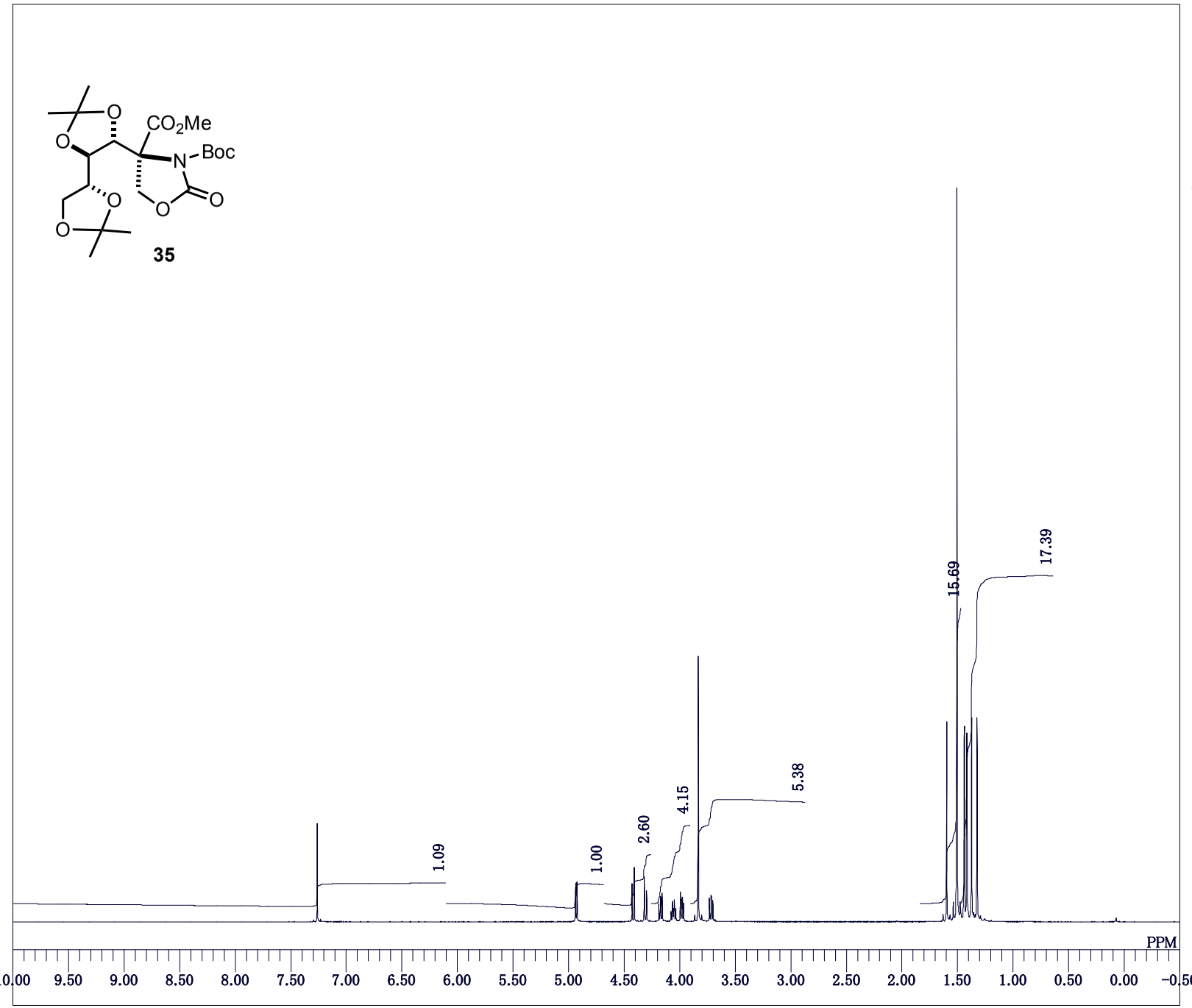
DFILE	KIN3113_proton-1-1.jdf
COMNT	single_pulse
DATIM	2013-07-05 16:34:48
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	23.2 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	1.20 Hz
RGAIN	50



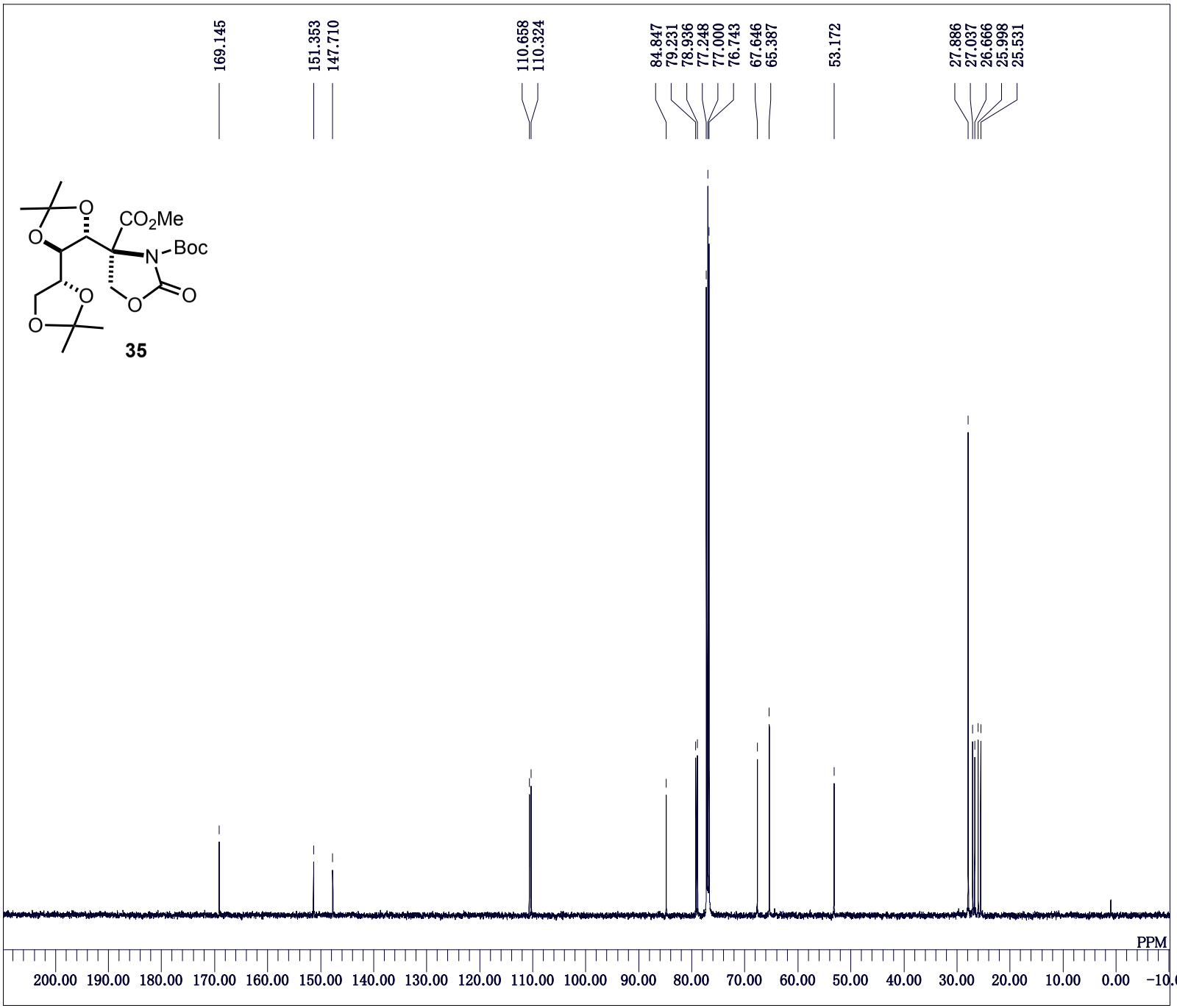
DFILE	KIN3113_carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2013-07-05 16:43:29
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	23.9 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	50



DFILE	KIN3131_proton-1-1.jdf
COMNT	single_pulse
DATIM	2013-09-13 18:14:02
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	24.3 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50

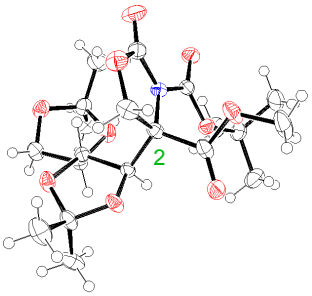


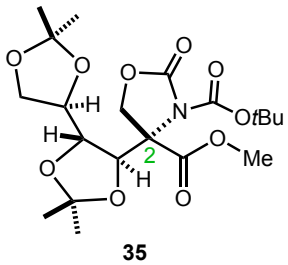
DFILE	KIN3135product_proton-1-1.jdf
COMNT	single_pulse
DATIM	2013-09-17 10:07:08
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	21.2 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	1.20 Hz
RGAIN	50



DFILE	KIN3135product_carbon-2-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2013-09-21 11:07:24
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	512
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	22.8 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	50

X-ray crystallographic structure of **35**





35

CCDC 1991095

A. Crystal Data

Empirical Formula	$C_{20}H_{31}NO_{10}$
Formula Weight	445.47
Crystal Color, Habit	colorless, block
Crystal Dimensions	0.600 X 0.600 X 0.300 mm
Crystal System	orthorhombic
Lattice Type	Primitive
Lattice Parameters	a = 26.2424(5) Å b = 8.65281(17) Å c = 10.17301(19) Å V = 2309.99(8) Å^3
Space Group	$P2_12_12_1$ (#19)
Z value	4
D_{calc}	1.281 g/cm^3
F_{000}	952.00
m(CuKa)	8.740 cm^{-1}

B. Intensity Measurements

Diffractometer	R-AXIS RAPID
Radiation	CuKa (l = 1.54187 Å) graphite monochromated
Voltage, Current	50kV, 100mA
Temperature	23.0°C
Detector Aperture	460.0 x 256.0 mm
Data Images	90 exposures
w oscillation Range (c=54.0, f=0.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
w oscillation Range (c=54.0, f=105.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
w oscillation Range (c=54.0, f=180.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
w oscillation Range (c=54.0, f=270.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
w oscillation Range (c=0.0, f=0.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2q_{max}$	136.4°

No. of Reflections Measured	Total: 26496 Unique: 4232 (R_{int} = 0.0597) Parsons quotients (Flack x parameter): 1750
Corrections	Lorentz-polarization Absorption (trans. factors: 0.562 - 0.769)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SHELXT Version 2014/4)
Refinement	Full-matrix least-squares on F^2
Function Minimized	S w $(Fo^2 - Fc^2)^2$
Least Squares Weights	w = 1/ [$s^2(Fo^2)$ + $(0.0573 \cdot P)^2$ + 0.3984 · P] where P = (Max(Fo^2,0) + 2Fc^2)/3
$2q_{max}$ cutoff	136.4°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	4232
No. Variables	280
Reflection/Parameter Ratio	15.11
Residuals: R1 (I>2.00s(I))	0.0343
Residuals: R (All reflections)	0.0349
Residuals: wR2 (All reflections)	0.0901

Goodness of Fit Indicator	1.054
Flack parameter (Parsons' quotients = 1750)	-0.01(4)
Max Shift/Error in Final Cycle	0.001
Maximum peak in Final Diff. Map	0.22 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.29 $e^-/Å^3$

IV. Determination of the diastereoselectivity in the enantioselective addition of diethylzinc

Enantioselective addition of Et_2Zn to the (*Z*)-aldehyde **15** using 10 mol% (–)-MIB or (+)-MIB provided the (*S,Z*)-allyl alcohol **16** or (*R,Z*)-allyl alcohol **17** predominantly. The ^{1}HNMR spectrum of the crude reaction mixture contains well resolved resonances corresponding to (*S,Z*)-allyl alcohol **16** (δ 4.98, d, *J* = 8 Hz, 1H) and (*R,Z*)-allyl alcohol **17** (δ 5.03, d, *J* = 8 Hz, 1H), which were used to determine the respective diastereomer ratios of >98:2 and 95:5.

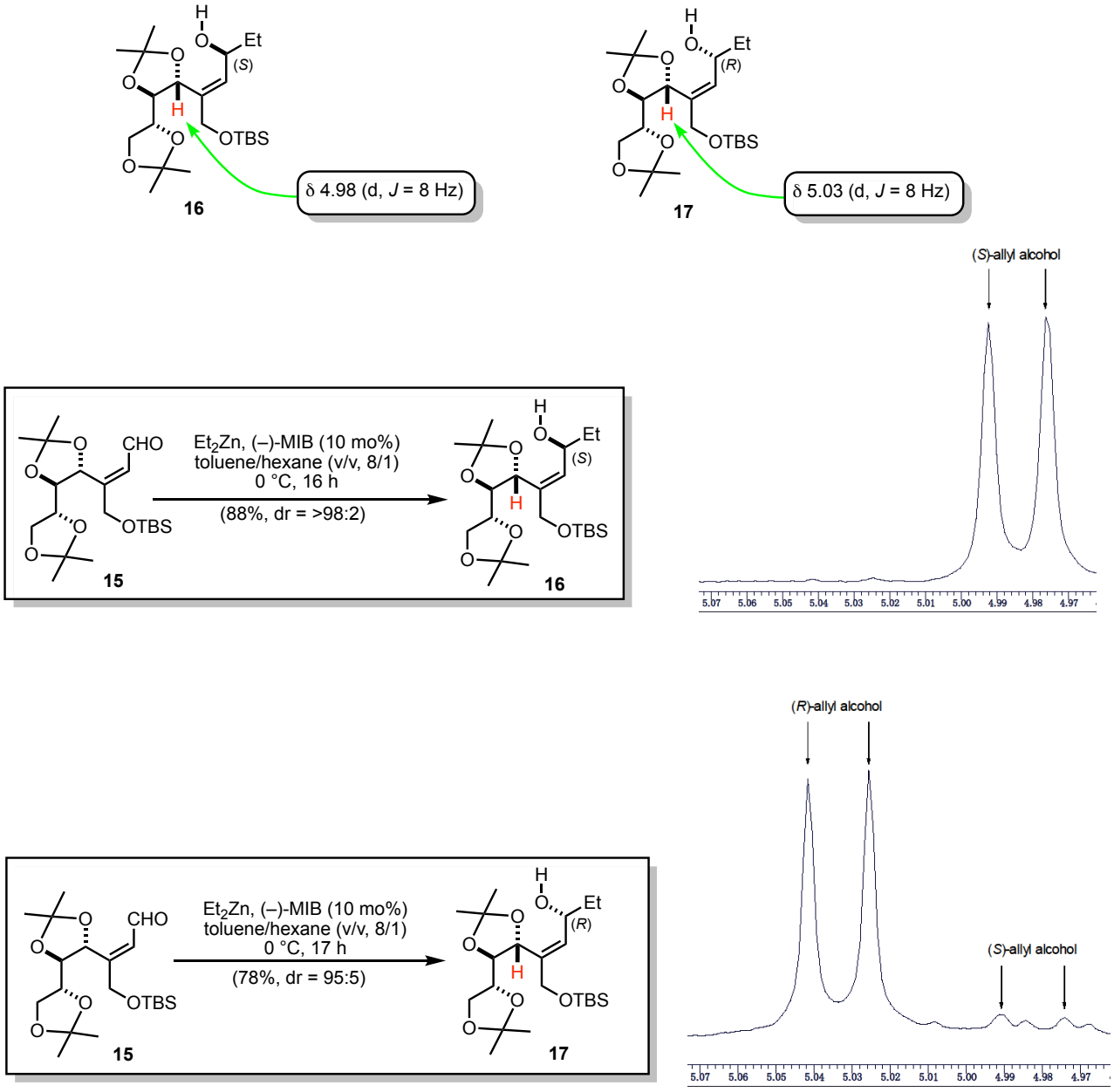


Figure S1. ^{1}H NMR spectra of the crude product mixture of **16** and **17**

Enantioselective addition of Et_2Zn to the (*E*)-aldehyde **25** using 10 mol% (+)-MIB or (–)-MIB provided the (*R,E*)-allyl alcohol **26** or (*S,E*)-allyl alcohol **29** as a major product respectively. ^{1}HNMR analysis of the crude reaction mixture of (*R,E*)-allyl alcohol **26** and (*S,E*)-allyl alcohol **29** reveals that well resolved peaks are observed around 5.77–5.86 ppm. Diagnostic vinyl proton signals of **26** (δ 5.79, d, *J* = 8 Hz, 1H) and **29** (δ 5.84, d, *J* = 8 Hz,1H) were used to determine the respective diastereomer ratios of 95:5 and 96:4.

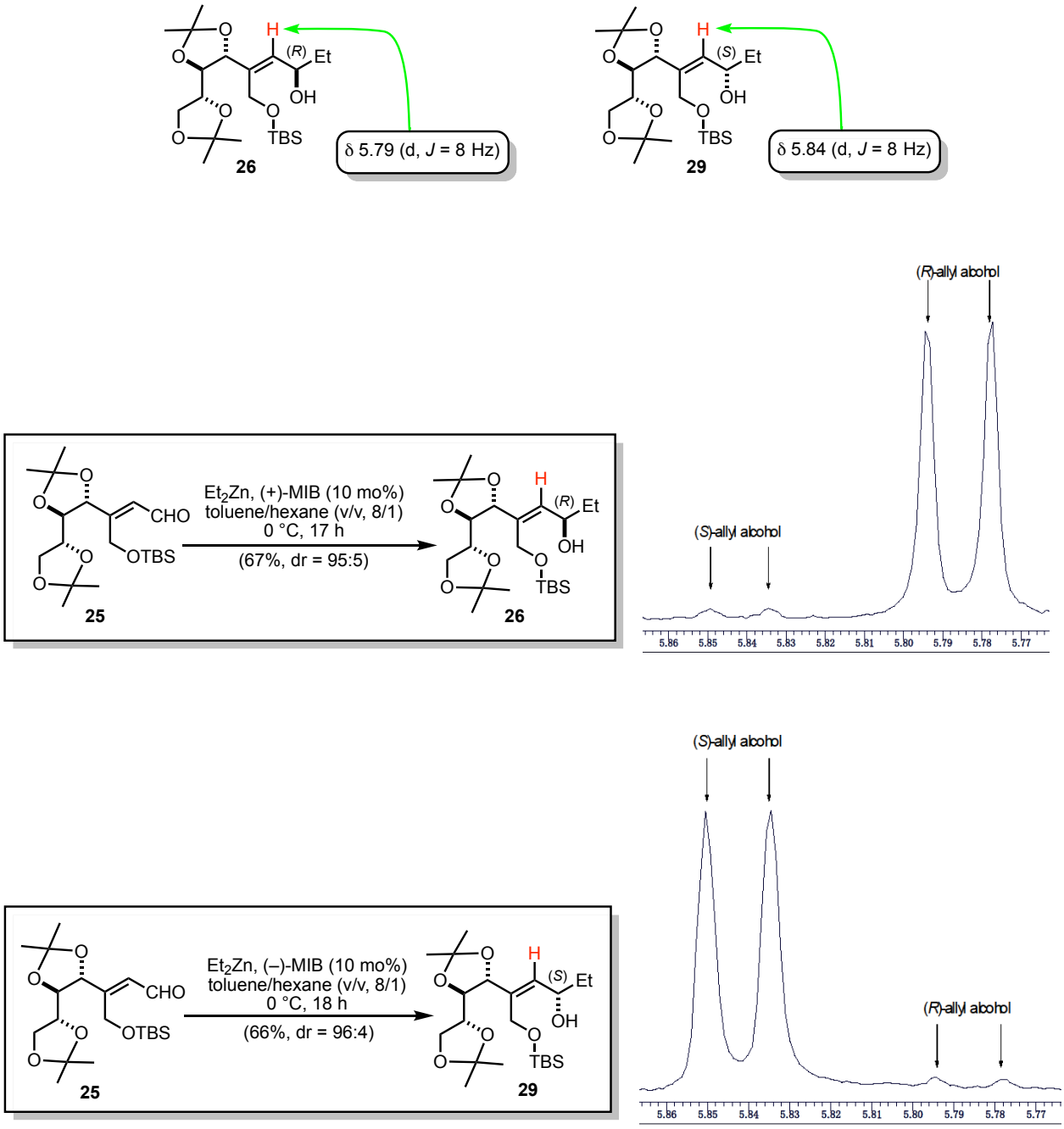


Figure S2 [1] ^{1}H NMR spectra of the crude product mixtures of **26** and **29**

V. Determination of the selectivity in the allyl cyanate-to-isocyanate rearrangement

Dehydration of (*S,Z*)-allyl carbamate **18** followed by sigmatropic rearrangement produced allyl cyanate **21**, which was successively treated with tetrabutylammonium tetra(*tert*-butyl alcohol)-coordinated fluoride {TBAF(*t*-BuOH)$_4$} in THF to produce carbamate **3**. The ^{1}HNMR spectrum of the crude reaction mixture around 5.52–5.70 ppm is shown below. Similarly, (*S,Z*)-allyl carbamate **23** was transformed to the carbamate **5** and the ^{1}HNMR spectrum of the crude products is represented below. In each case, the peak corresponding to an isomer was not detected, indicating the level of [1,3]-chirality transfer in the rearrangement is almost quantitative.

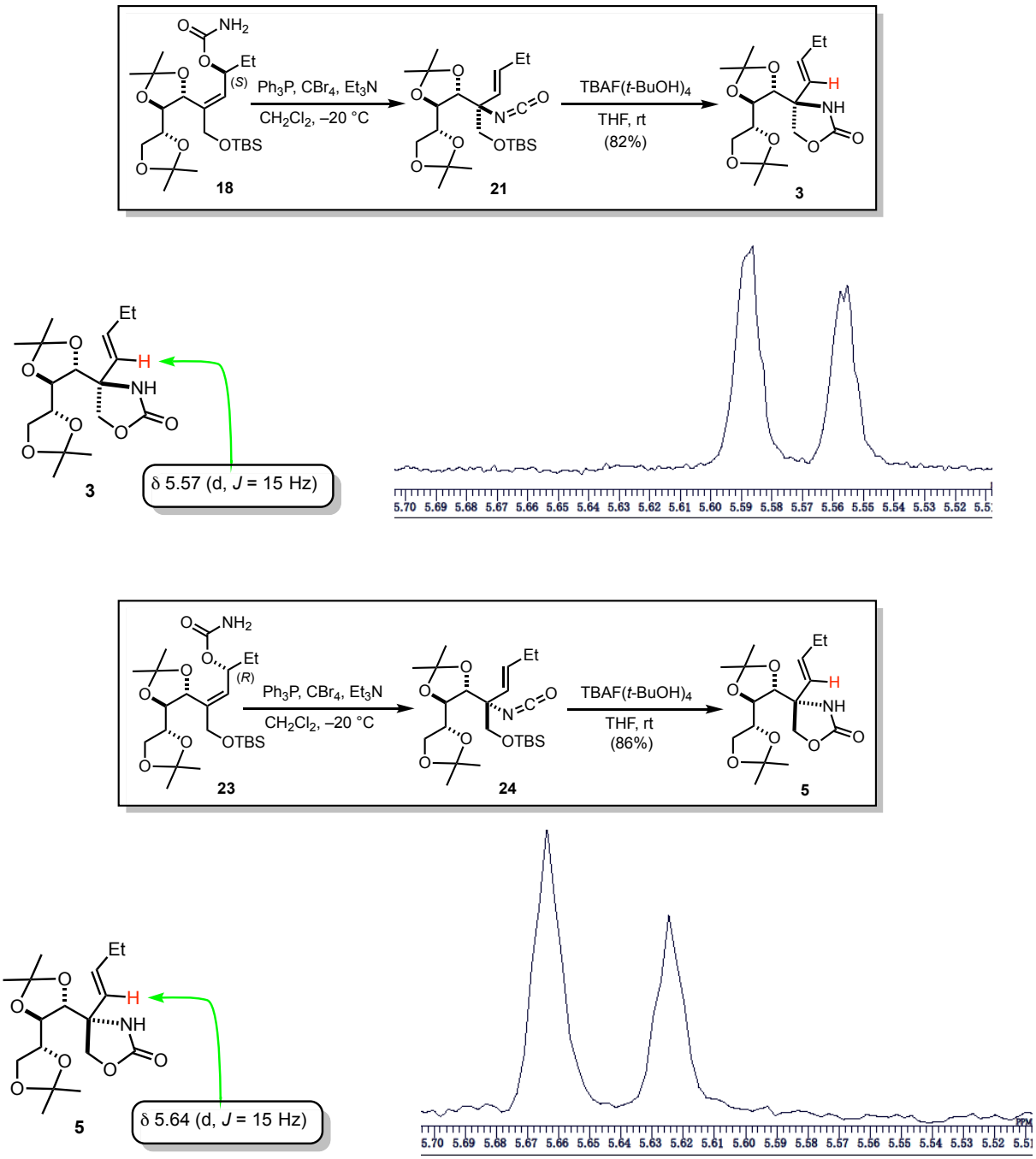
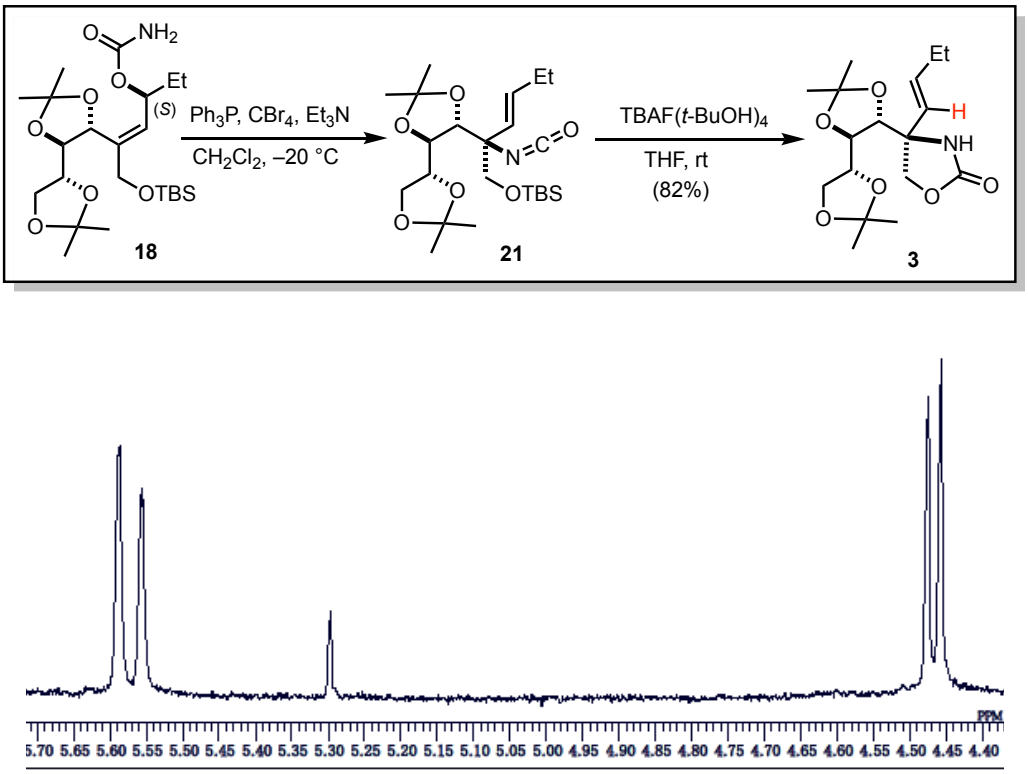


Figure S3 ^{1}H NMR spectra of the crude product mixtures of **3** prepared from **18** and **5** prepared from **23**



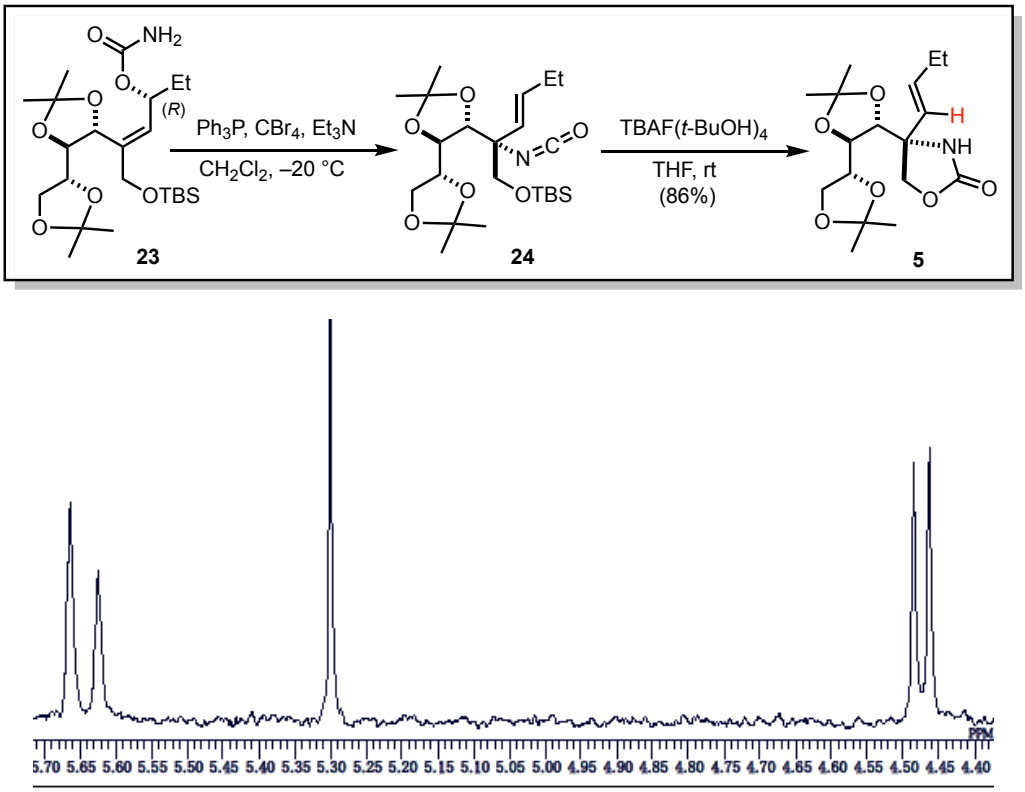


Figure S4 ^{1}H NMR spectra of the crude product mixtures of **3** prepared from **18** and **5** prepared from **23**

The [1]HNMR spectrum region around 5.52–5.70 ppm of the crude reaction mixtures of **3** prepared from (*R,E*)-allyl carbamate **27** and **5** prepared from (*S,E*)-allyl carbamate **30** are shown below. In each case, the peaks associated with isomers are not detected, indicating the level of [1,3]-chirality transfer is almost quantitative.

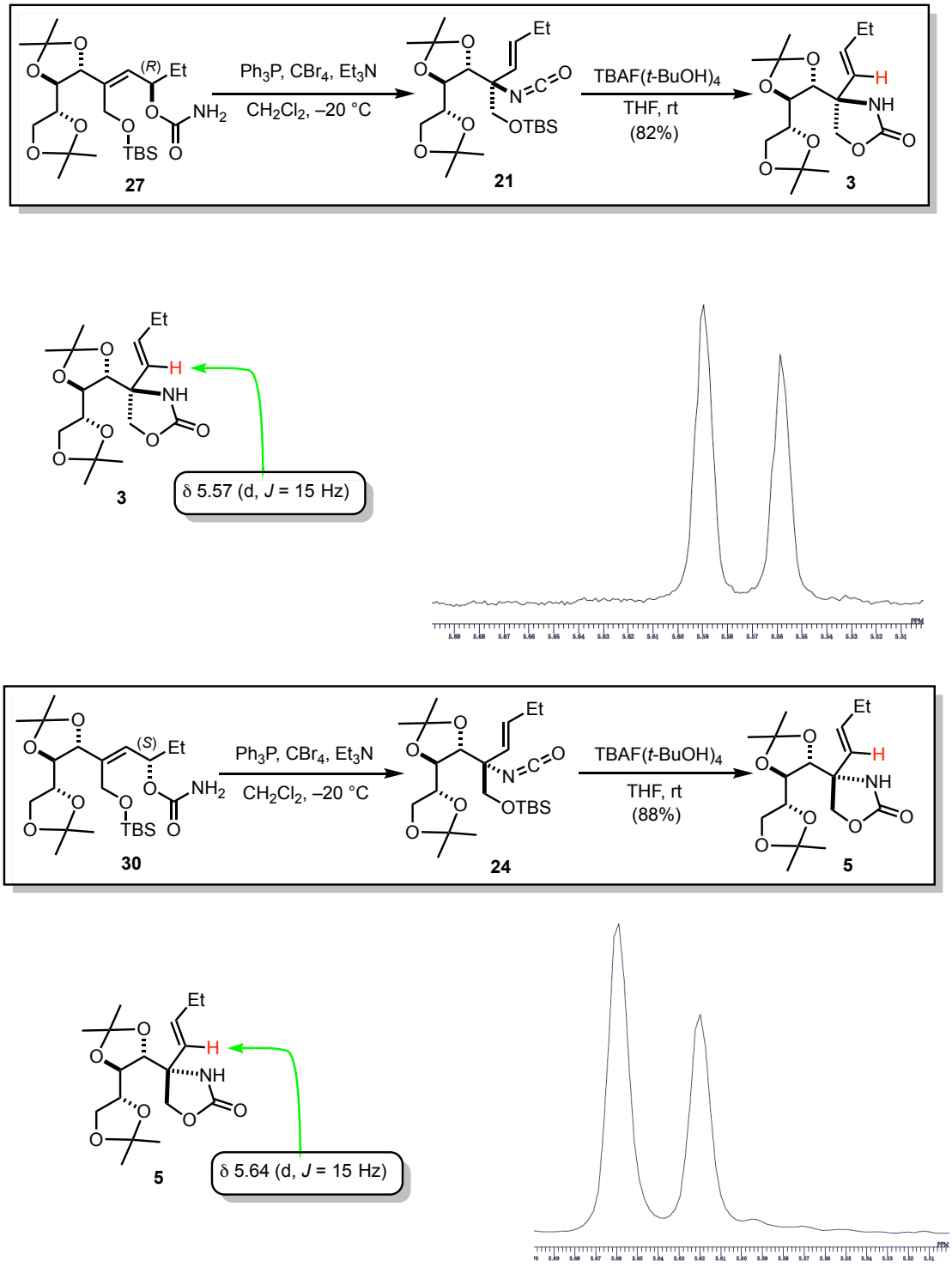
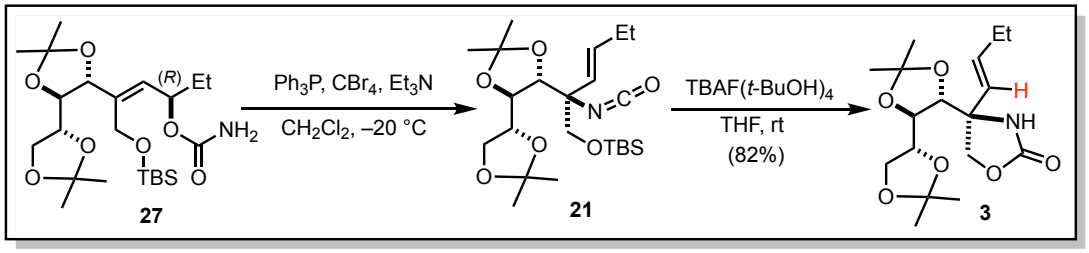
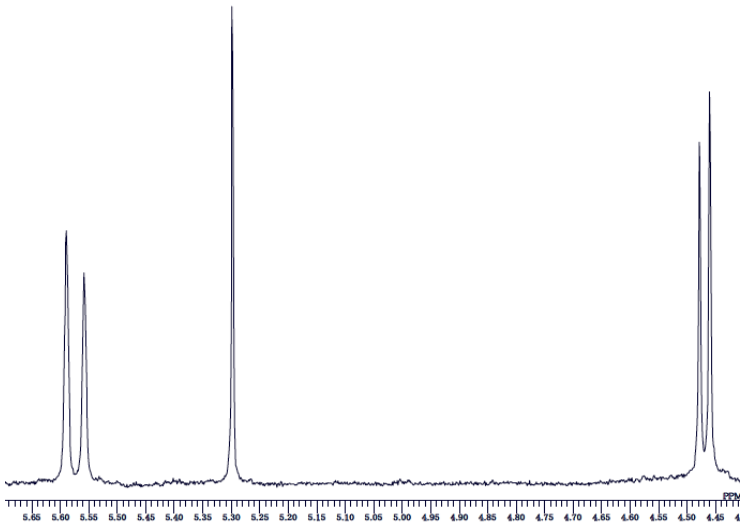
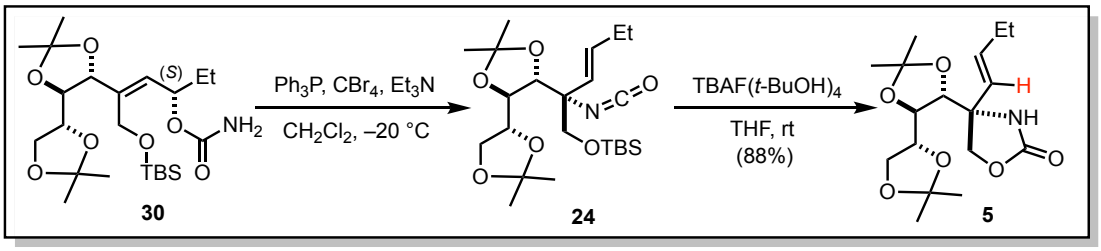


Figure S5 [1]H NMR spectra of the crude product mixtures of **3** prepared from **27** and **5** prepared from **30**







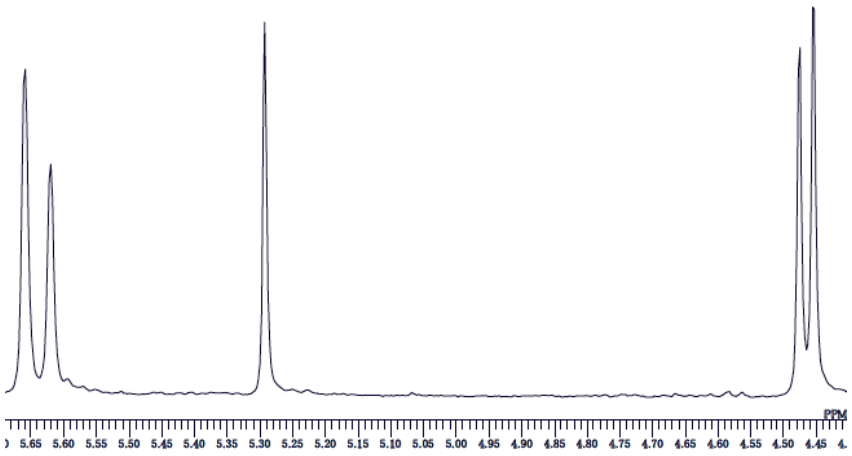
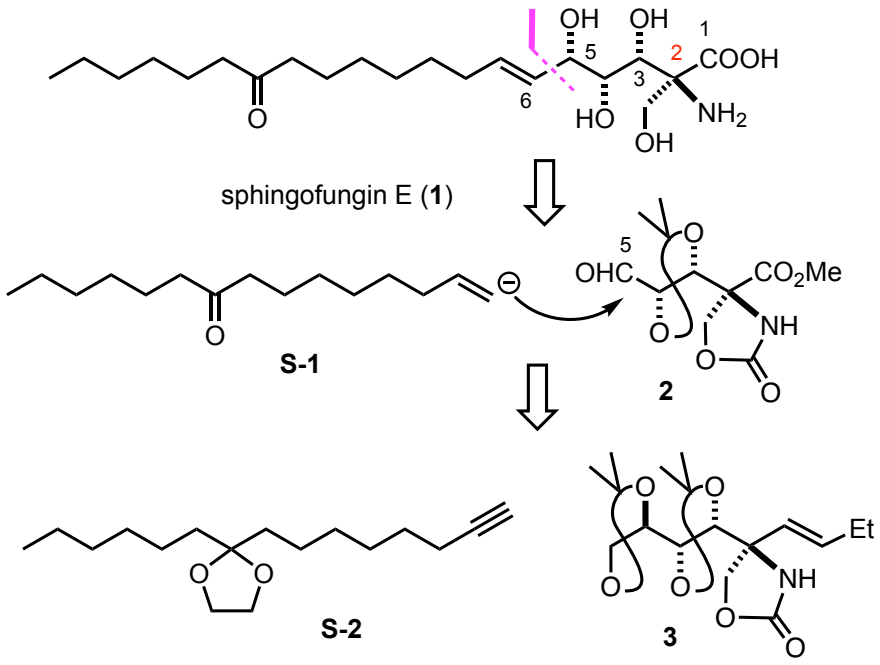


Figure S6 ^{1}H NMR spectra of the crude product mixtures of **3** prepared from **27** and **5** prepared from **30**

VI. Detailed retrosynthetic analysis and final elaboration to the synthesis of sphingophangin E

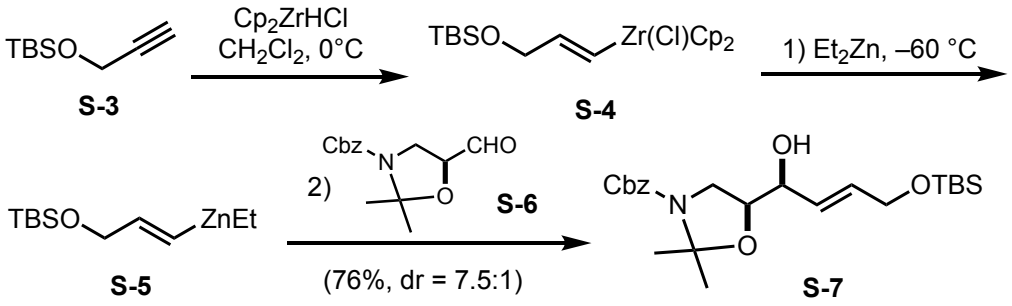
The retrosynthetic analysis of sphingophangin E (**1**) commences with the disconnection of the C–C bond between C-5 and C-6 (Scheme S1), which leads to the two building blocks including the left-hand segment **S-1** and the right-hand segment **2**. We speculated that the absolute stereochemistry at C-5 could be accessed through addition of vinyl anion equivalent **S-1** to an aldehyde **2**. Further functional group conversion led us to the core structure of sphingophangin E **3** and protected terminal alkyne intermediate **S-2**.



Scheme S1. Detailed retrosynthesis of sphingophangin E

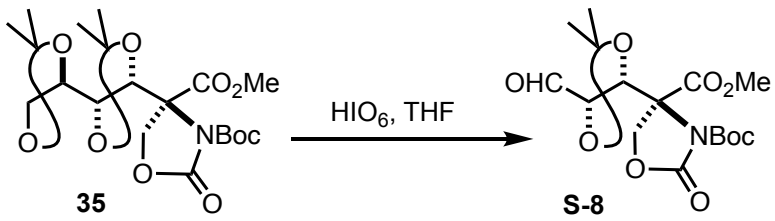
The synthesis plan represented in Scheme S1 is guided by the instructive observation of Li and his coworkers[1] (Scheme S2). Following a procedure reported by Wipf,[2] hydrozirconation of alkyne **S-3** with zirconocene hydrochloride (Cp_2ZrHCl) provided alkenylzirconocene complex **S-4**. Transmetalation of **S-4** to the alkenylzinc intermediate **S-5** was accomplished by in situ treatment of **S-4** with diethylzinc at –60 °C. Subsequent

addition of the Cbz-protected (*S*)-isoserinal acetonide **S-6** afforded *syn*-isomer **S-7** predominately in 76% yield with good diastereoselectivity (dr = 7.5:1). In addition to this *syn*-selectivity, we noticed a high functional group compatibility of the addition reaction of zinc reagents to aldehydes, which would guarantee to tolerate the acetonide, carbamate and ester functional groups found in our intermediate **2**.



Scheme S2. Instructive sequence reported by Li

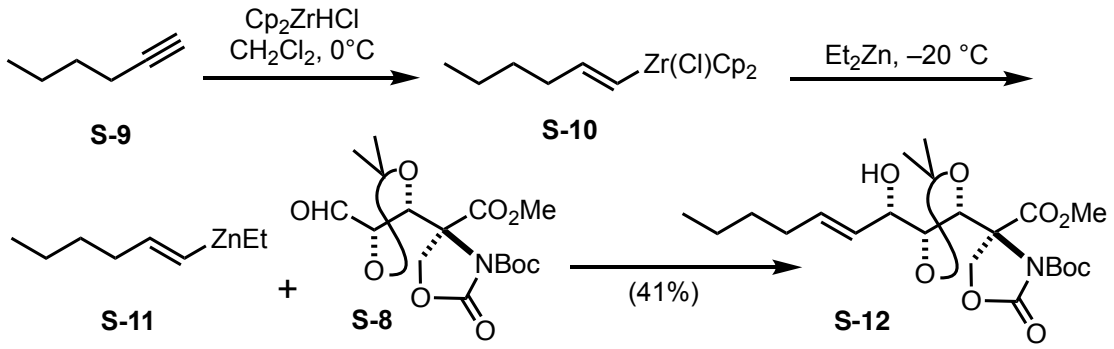
Final elaboration for the synthesis of sphingophangin E would follow the plan represented in Scheme S1. Selective hydrolysis of the terminal isopropylidene acetal in **35** and subsequent glycol cleavage was performed by treatment of an ether solution of **35** with periodic acid[3] (equation 1). The aldehyde **S-8** was subsequently used for the next step without further purification.



(1)

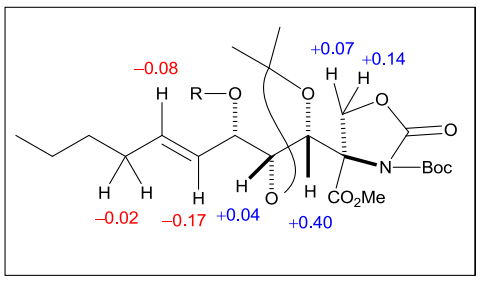
Using 1-hexyne (**S-9**) as a model compound, we initially focused on the assessment of the diastereoselectivity in the addition reaction of the vinylzinc segment to the aldehyde **S-8** (Scheme S3). Hydrozirconation of **S-9** with Cp_2ZrHCl generated (*E*)-alkenylzirconocene

S-10, which was directly treated with diethylzinc to lead to the zirconocene→zinc transmetalation. Treatment of the aldehyde **S-8** with a solution of the zinc reagent **S-11** provided **S-12** predominantly in 41% overall yield from **35**.

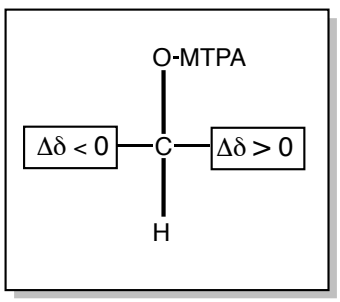


Scheme S3. Model reaction to assess the diastereoselectivity

The structure for **S-12**, initially assigned by the analogy of Li, was confirmed using a modified Mosher-Kusumi MTPA ester analysis[4] (Fig. S7). Thus, the product **S-12** was transformed into the corresponding (*S*)- and (*R*)-MTPA esters (**S-13a** and **S-13b**), and their chemical shift differences (Δδ values: $\Delta\delta = \delta_S - \delta_R$) were calculated. The protons with positive Δδ are placed on the right side in the configurational correlation model and those with negative Δδ are set into the left side. This procedure elucidates the absolute stereochemistry of secondary alcohol moiety in **S-12** to be in the *S* configuration.



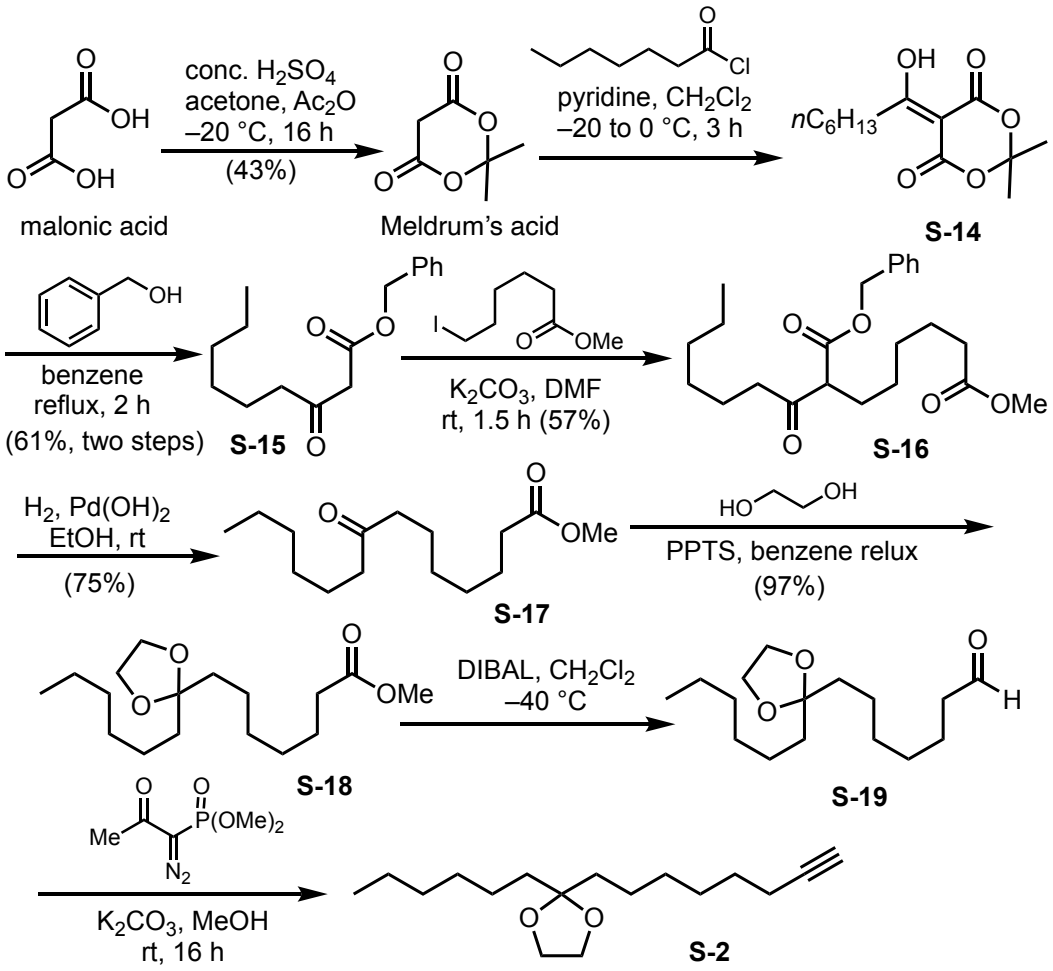
S-12: R = H
S-13a: R = (*S*)-MTPA
S-13b: R = (*R*)-MTPA
(*R*)- or (*S*)-MTPACl
DMAP, Et_3N, CH_2Cl_2



Configurational Correlation Model

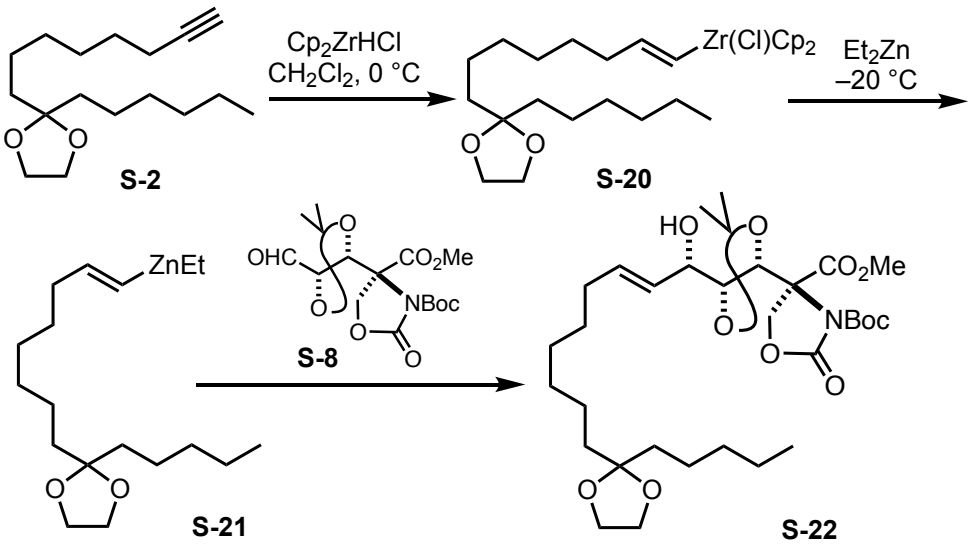
Figure S7. Mosher-Kusumi MTPA ester analysis of the secondary alcohol **S-12**

Encouraged by the results of the model reactions, the alkyne **S-2** for a synthetic equivalent of left-hand segment was prepared starting with malonic acid (Scheme S4). Treatment of malonic acid with acetic anhydride and acetone in the presence of conc. sulfuric acid provided Meldrum's acid. Following a procedure for the synthesis of β-keto esters reported by Yonemitsu,[5] acylation of Meldrum's acid with heptanoyl chloride followed by refluxing a benzene solution of the resulting acyl Meldrum's acid **S-14** containing about three equiv. of benzyl alcohol generated the β-keto benzyl ester **S-15**. Alkylation of **S-15** with 6-iodohexanoic acid methyl ester[6] and potassium carbonate in DMF provided **S-16** in 57% yield. The moderate yield in this process is due to the difficulty to avoid formation of the dialkylated byproduct. Dealkoxycarbonylation of the β-keto ester **S-16** was achieved by a two-step procedure involving hydrogenolysis of benzyl ester in **S-16** and ensuing decarboxylation of the resulting β-keto acid to furnish **S-17** in 75% yield. Protection of the ketone in **S-17** with ethylene glycol and pyridinium *p*-toluenesulfonate in refluxing benzene and diisobutylaluminum hydride reduction of the terminal methyl ester in **S-18** then generated the aldehyde **S-19**. Conversion of the aldehyde **S-19** to the terminal alkyne **S-2** by a one-carbon chain extension using 1-diazo-2-oxopropynylphosphonate (the Bestmann-Ohira reagent) [7] completed the synthesis of the left-hand segment **S-2**.



Scheme S4. Synthesis of a left-hand segment equivalent **S-2** starting with malonic acid

With the synthetic equivalent of left-hand segment **S-2** in hand, we explored the coupling of the left-hand segment and right-hand segment **S-8** (Scheme S5). Using conditions similar to those depicted in S3, hydrozirconation of alkyne **S-2** with Cp_2ZrHCl generated (*E*)-alkenylzirconocene **S-20**, which was transformed to vinyl zinc reagent **S-21** by treatment with diethylzinc. Reaction of **S-21** with aldehyde **S-8** gave rise to **S-22** predominantly in modest yield (41% overall yield from **35**).



Scheme S5. Coupling reaction of the left-hand segment and the right-hand segment

The absolute configuration at C-5 in **S-22** determined using Mosher-Kusumi MTPA ester method is *S* stereochemistry (Fig. S8). As a result, synthesis of fully protected sphingophangin E was accomplished.

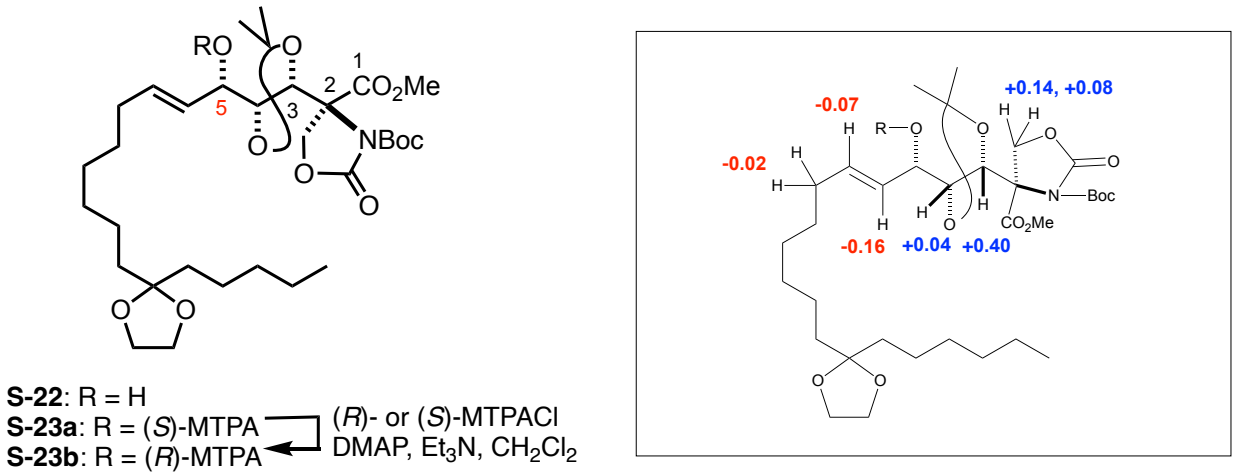
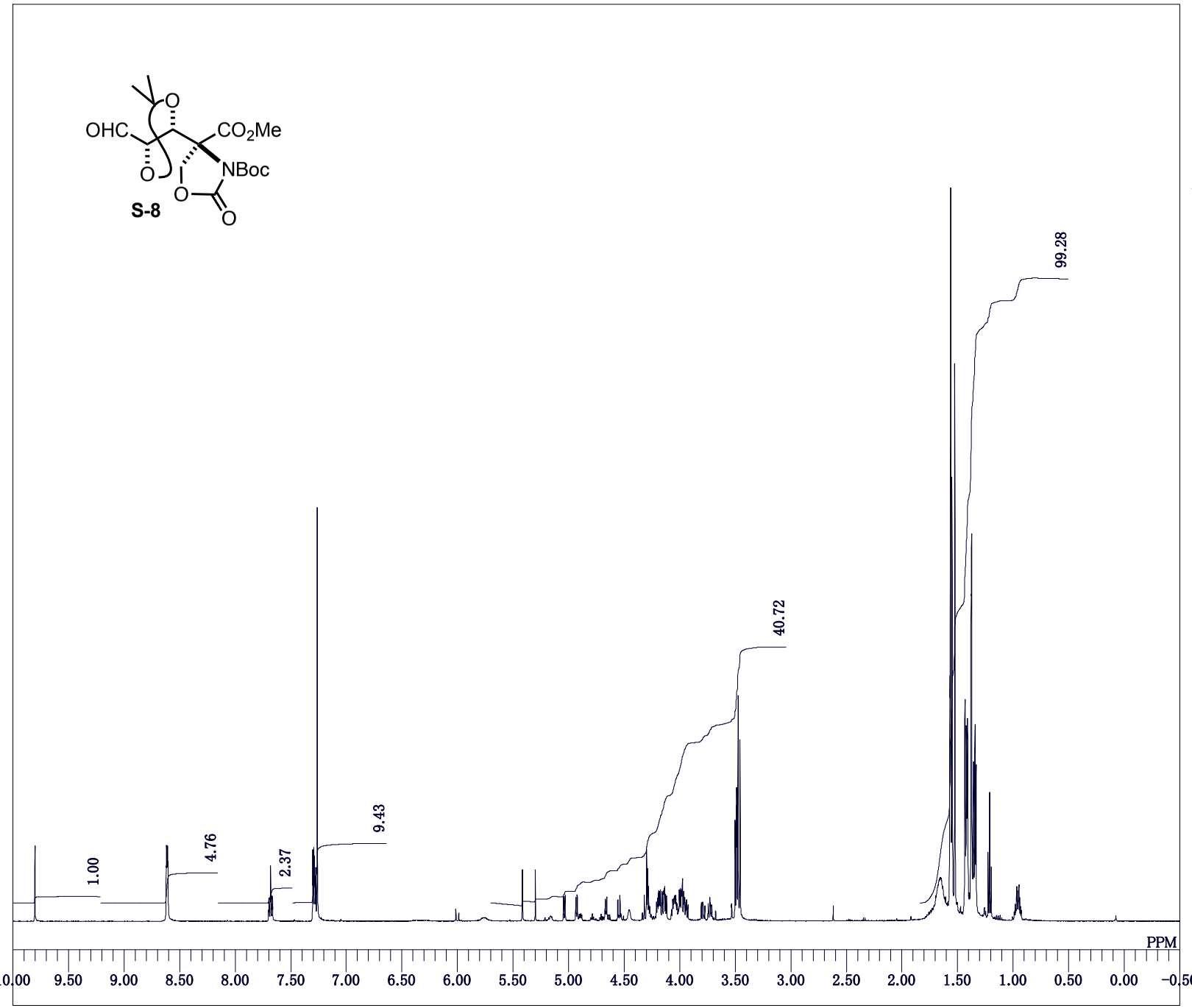


Figure S8. Mosher-Kusumi MTPA ester analysis of the secondary alcohol **S-22**



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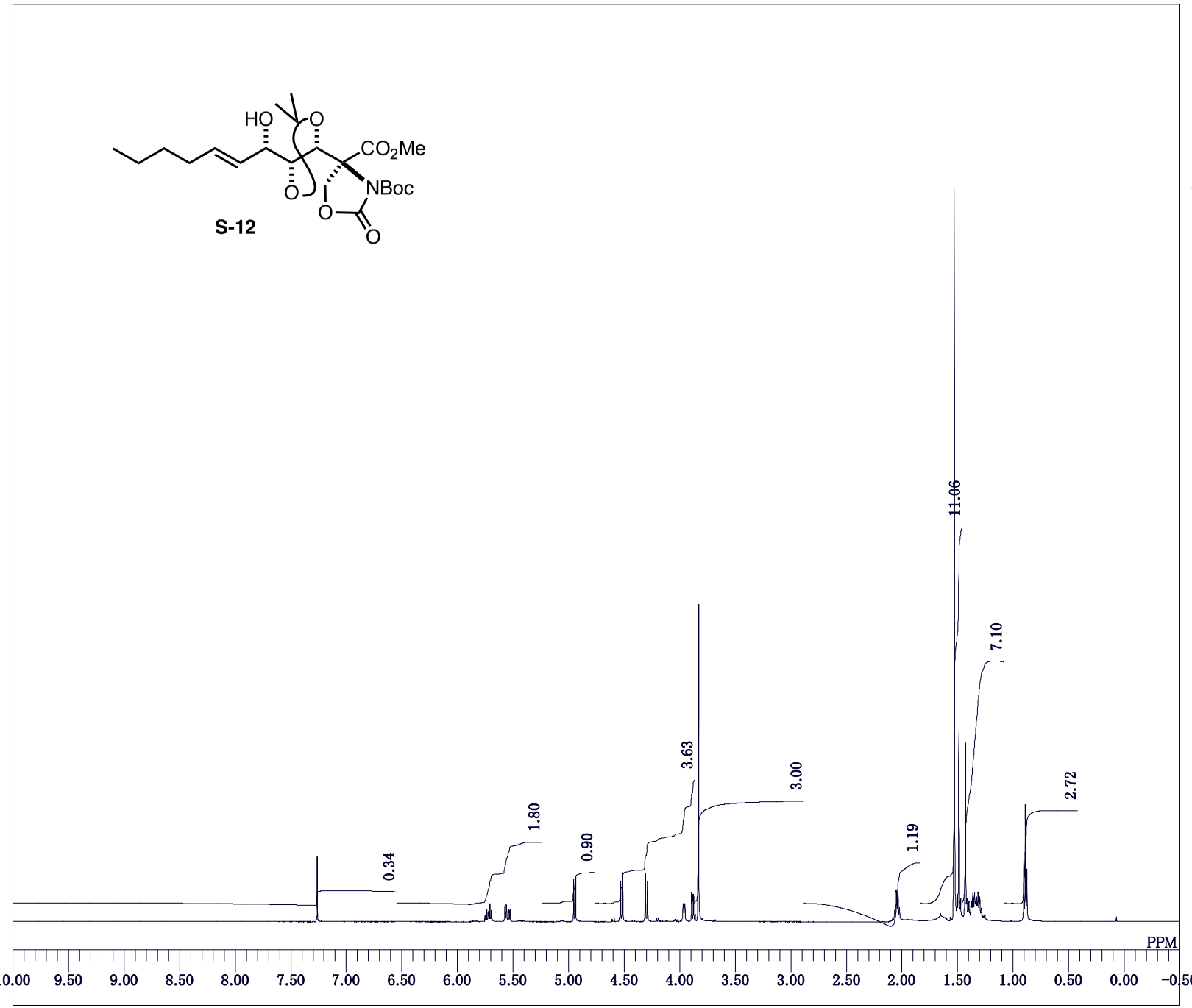

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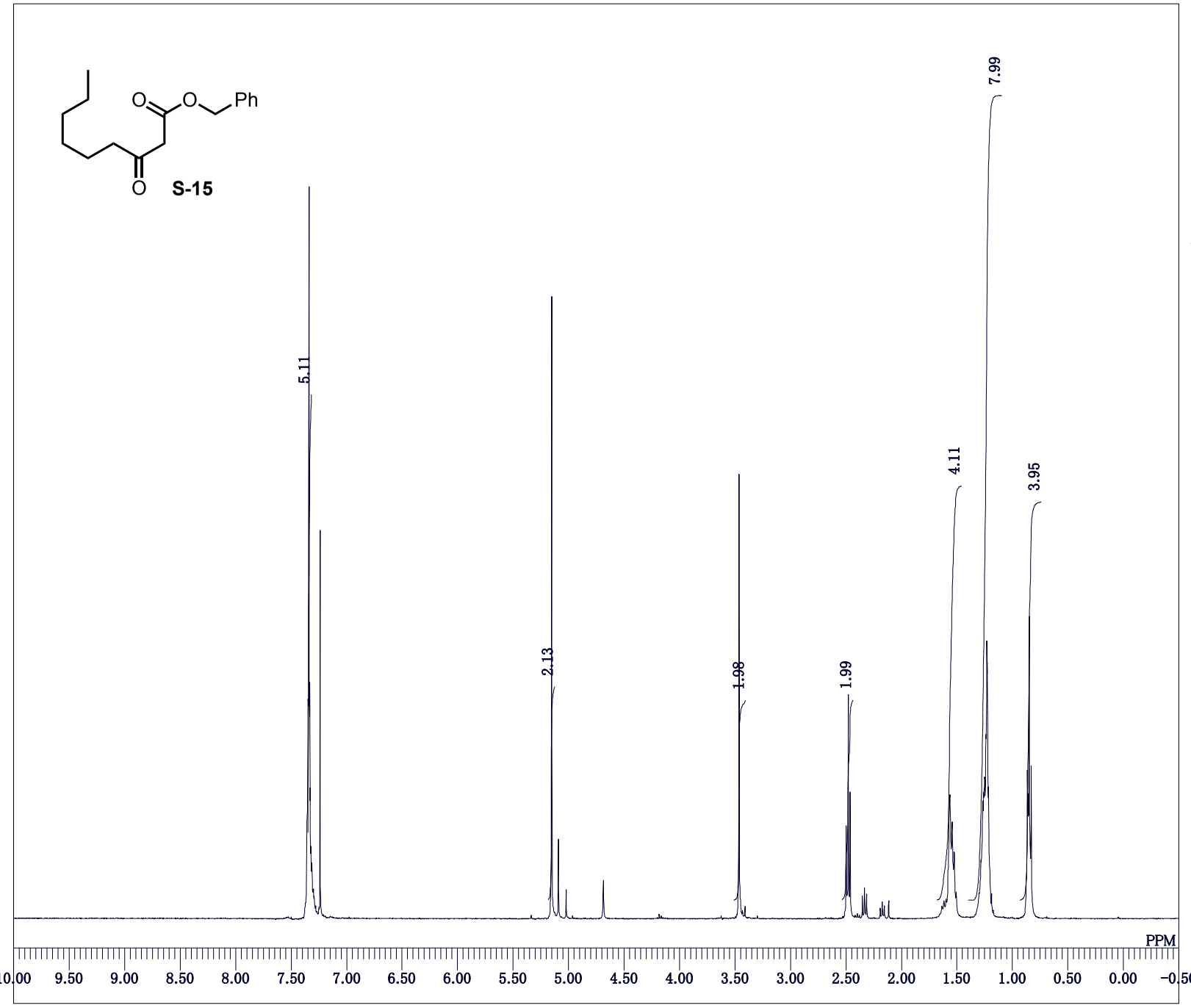
RGAIN	50



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CTEMP	18.2 c
SLVNT	CDCL3
EXREF	7.24 ppm
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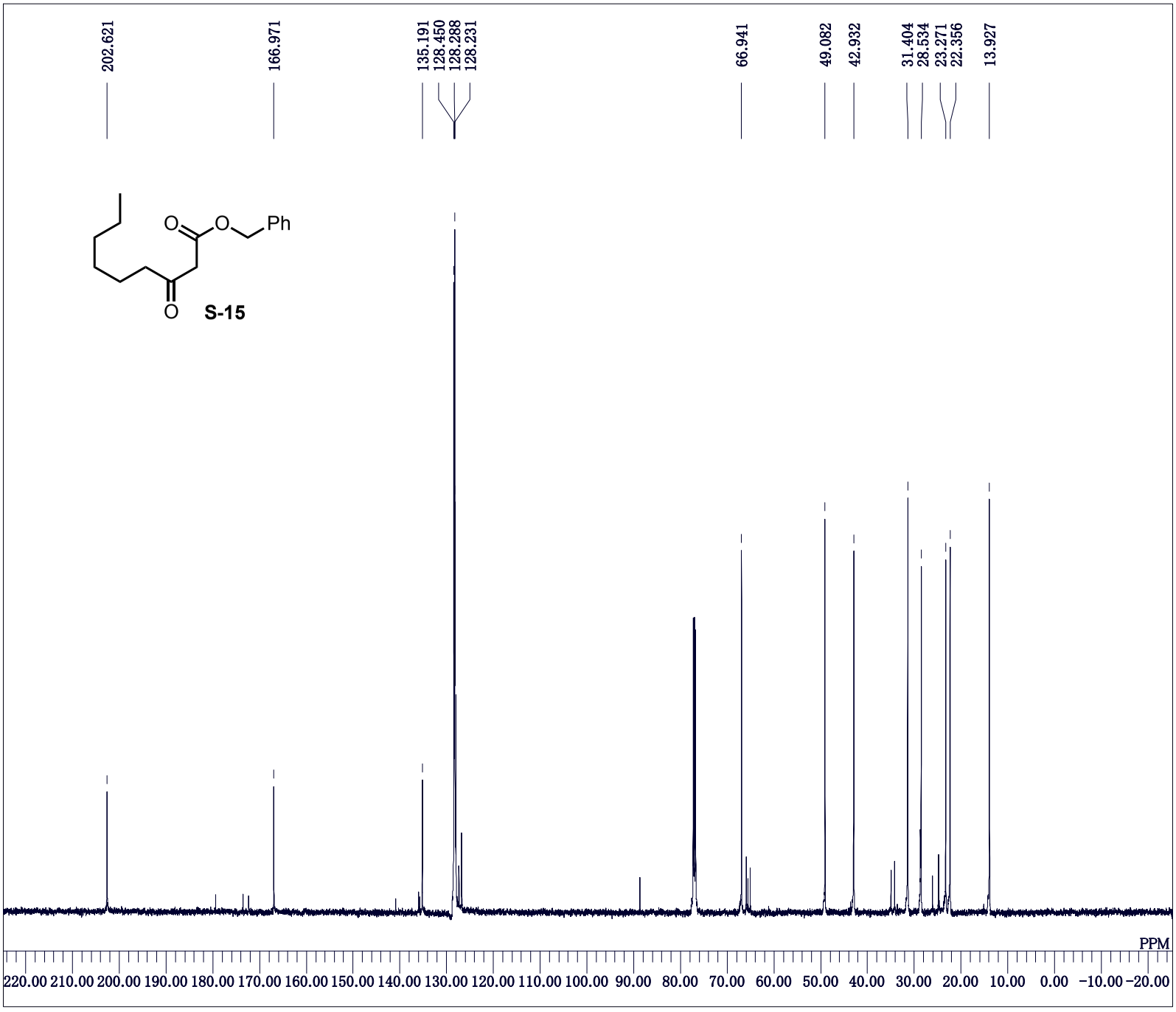
RGAIN	23



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PD	2.0000 sec
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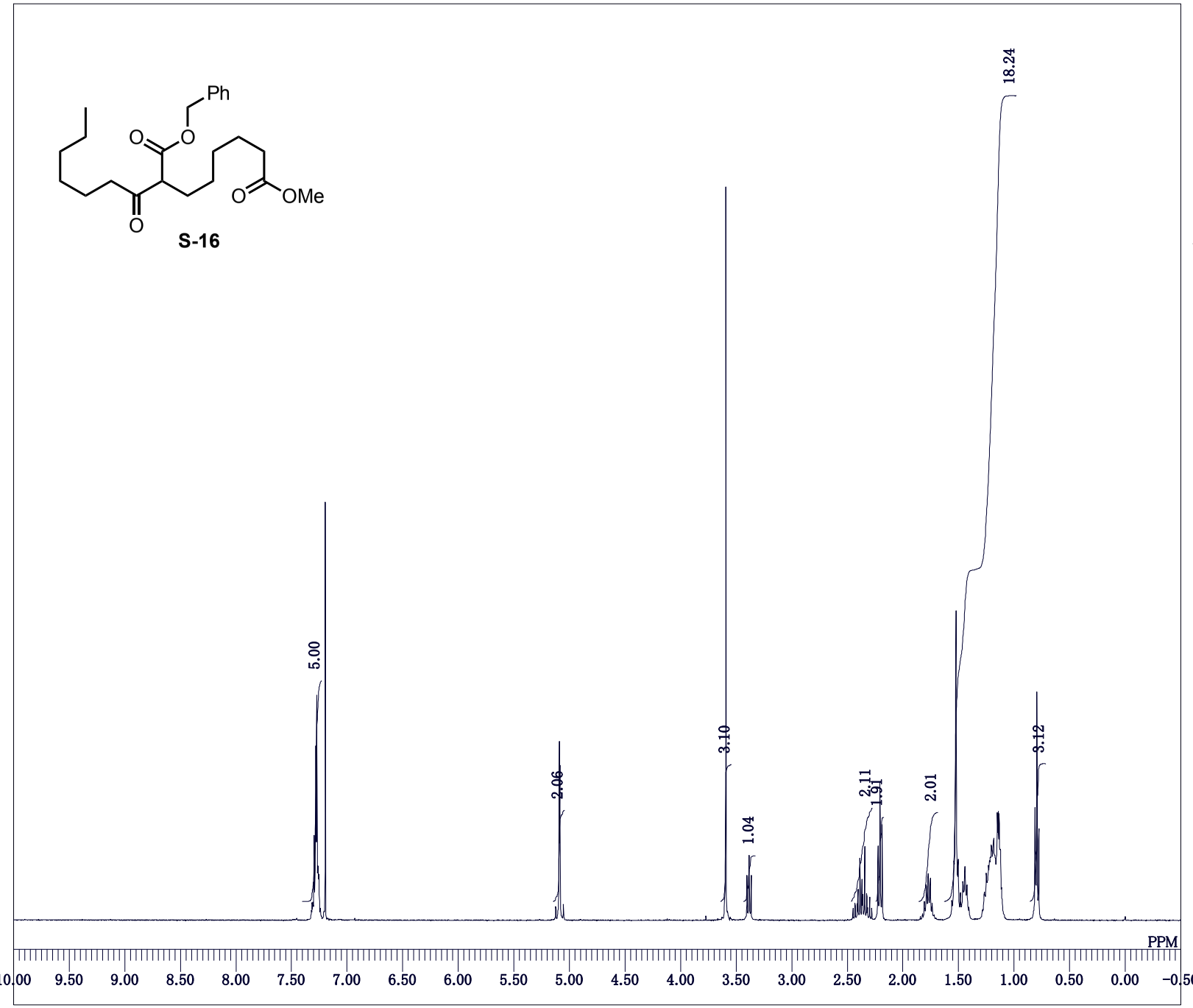

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EXREF	0.00 ppm
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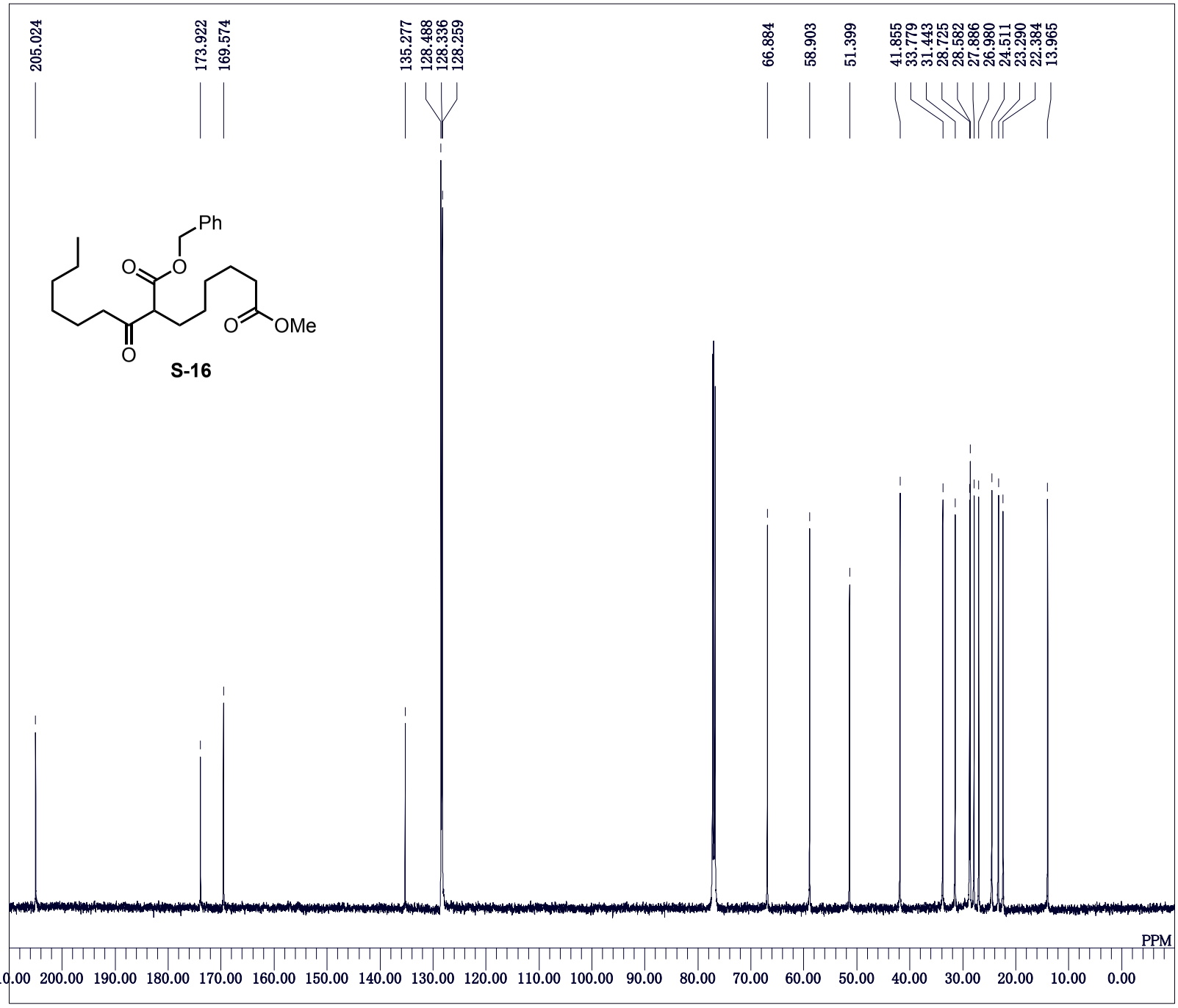
RGAIN	23



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OBFIN	4.21 Hz
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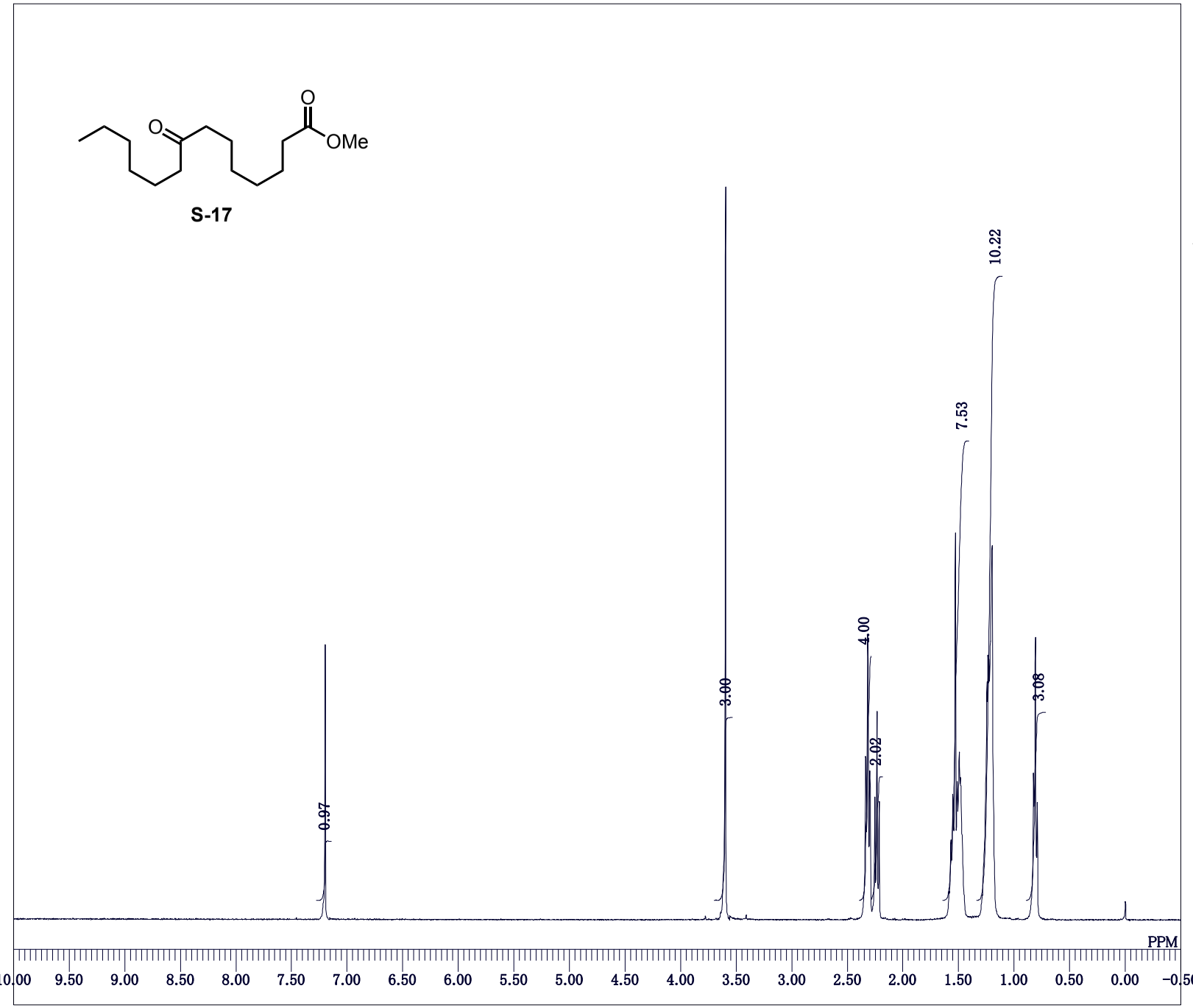
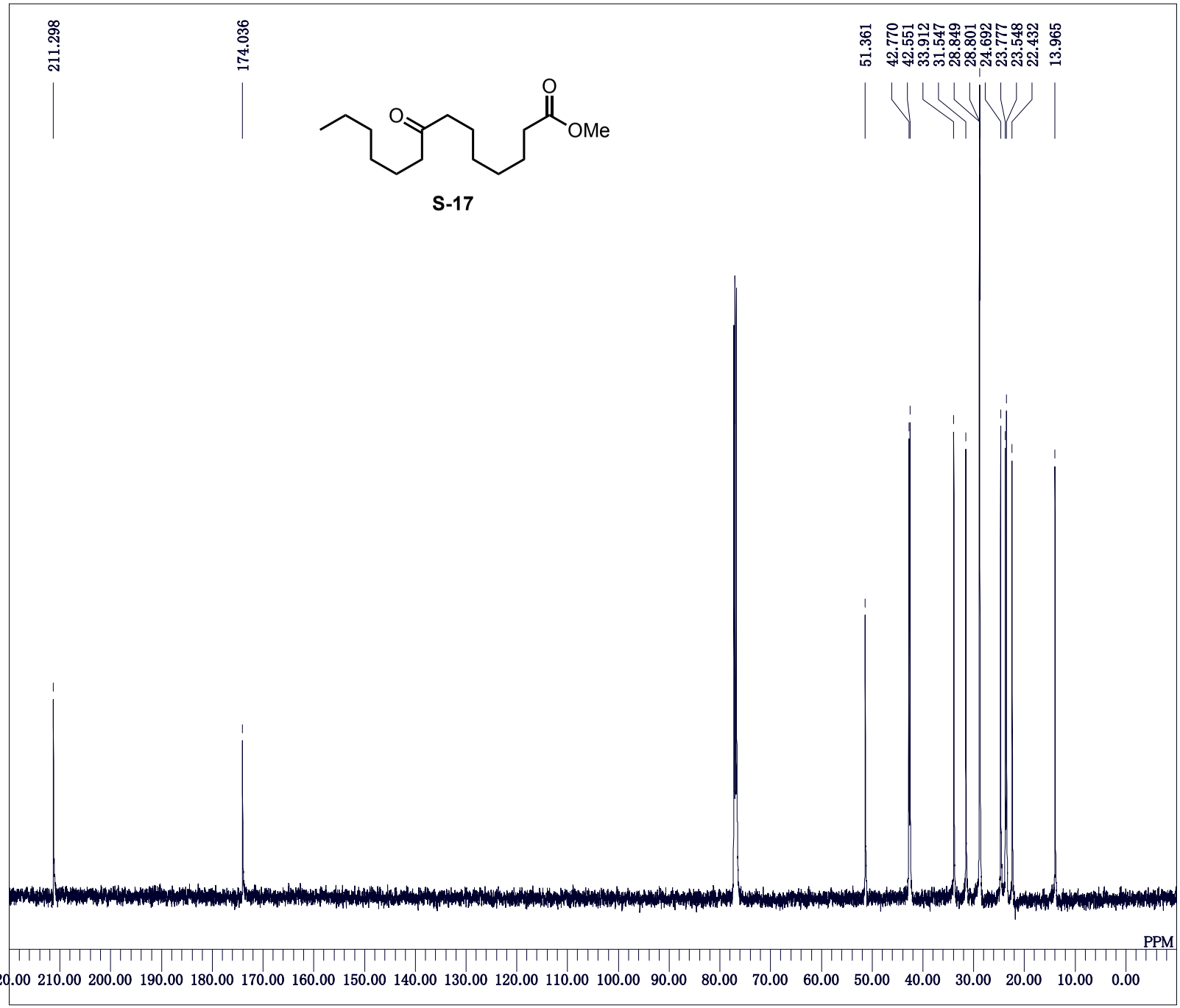
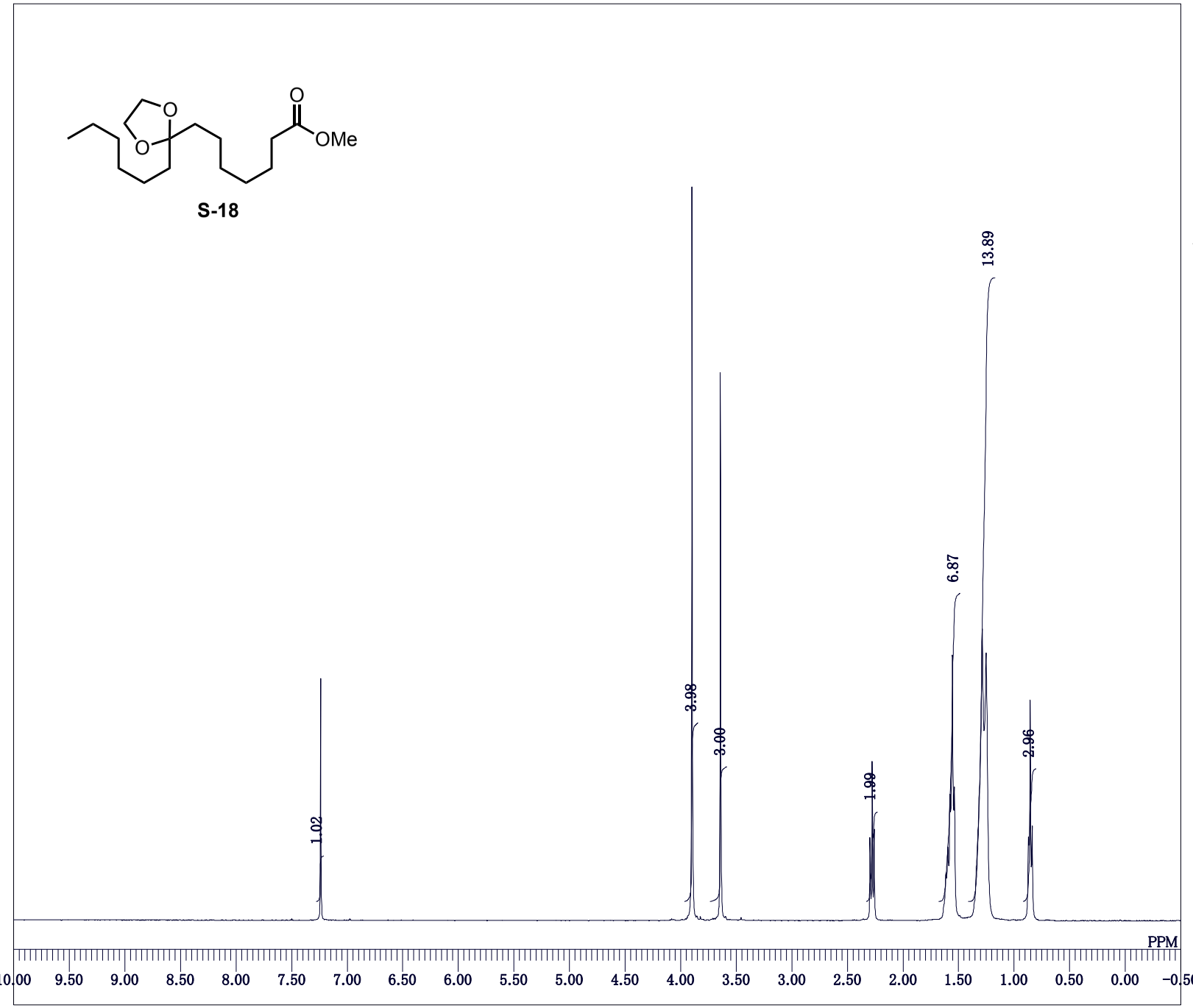
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	19.4 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

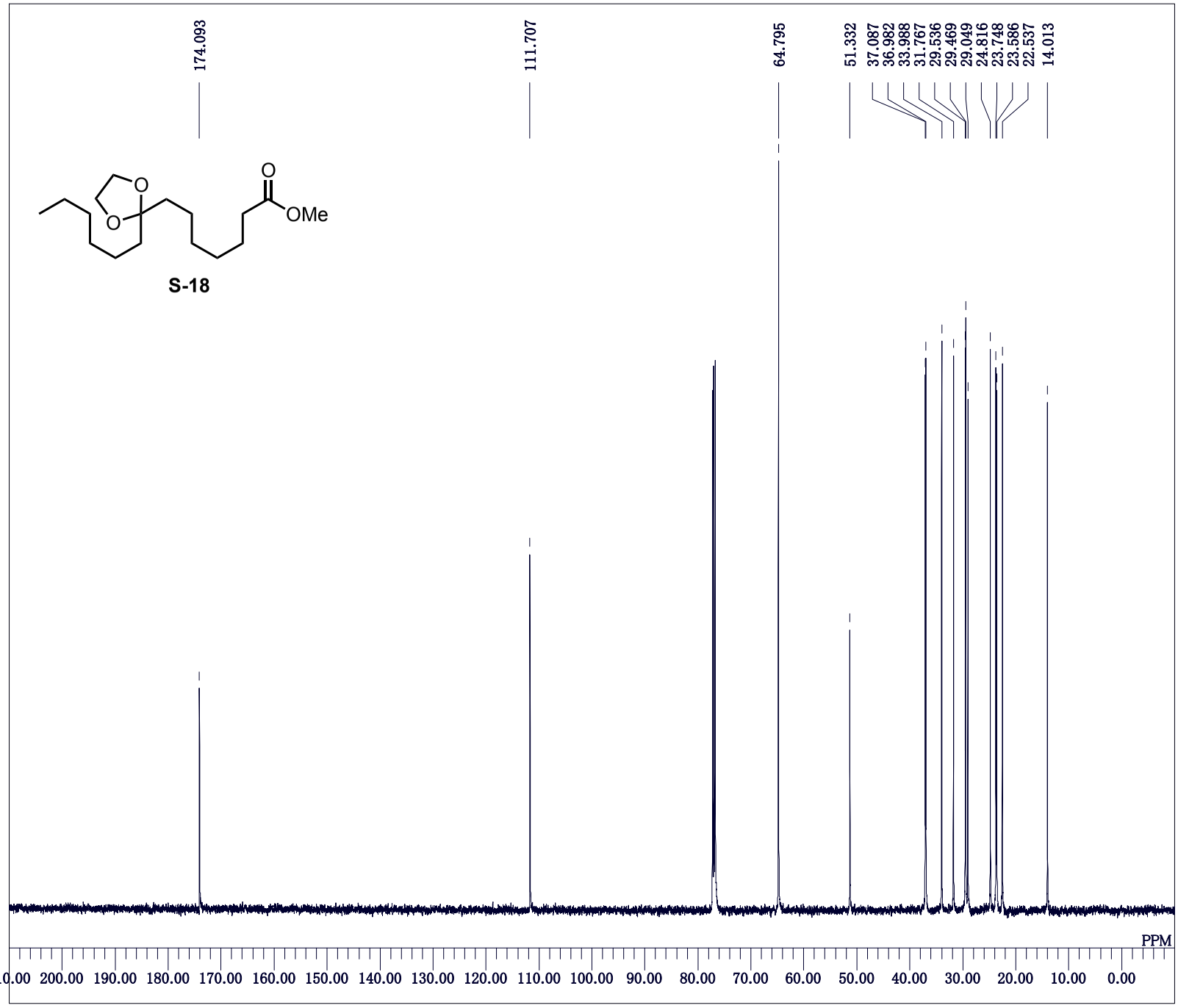


DFILE	YOS1114C-H.als
COMNT	
DATIM	Fri Jan 17 16:08:53 2014
OBNUC	1H
EXMOD	non
OBFRQ	399.65 MHz
OBSET	0.00 KHz
OBFIN	134300.00 Hz
POINT	8192
FREQU	7993.60 Hz
SCANS	8
ACQTM	1.0248 sec
PD	5.9752 sec
PW1	5.50 usec
IRNUC	1H
CTEMP	17.4 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	23

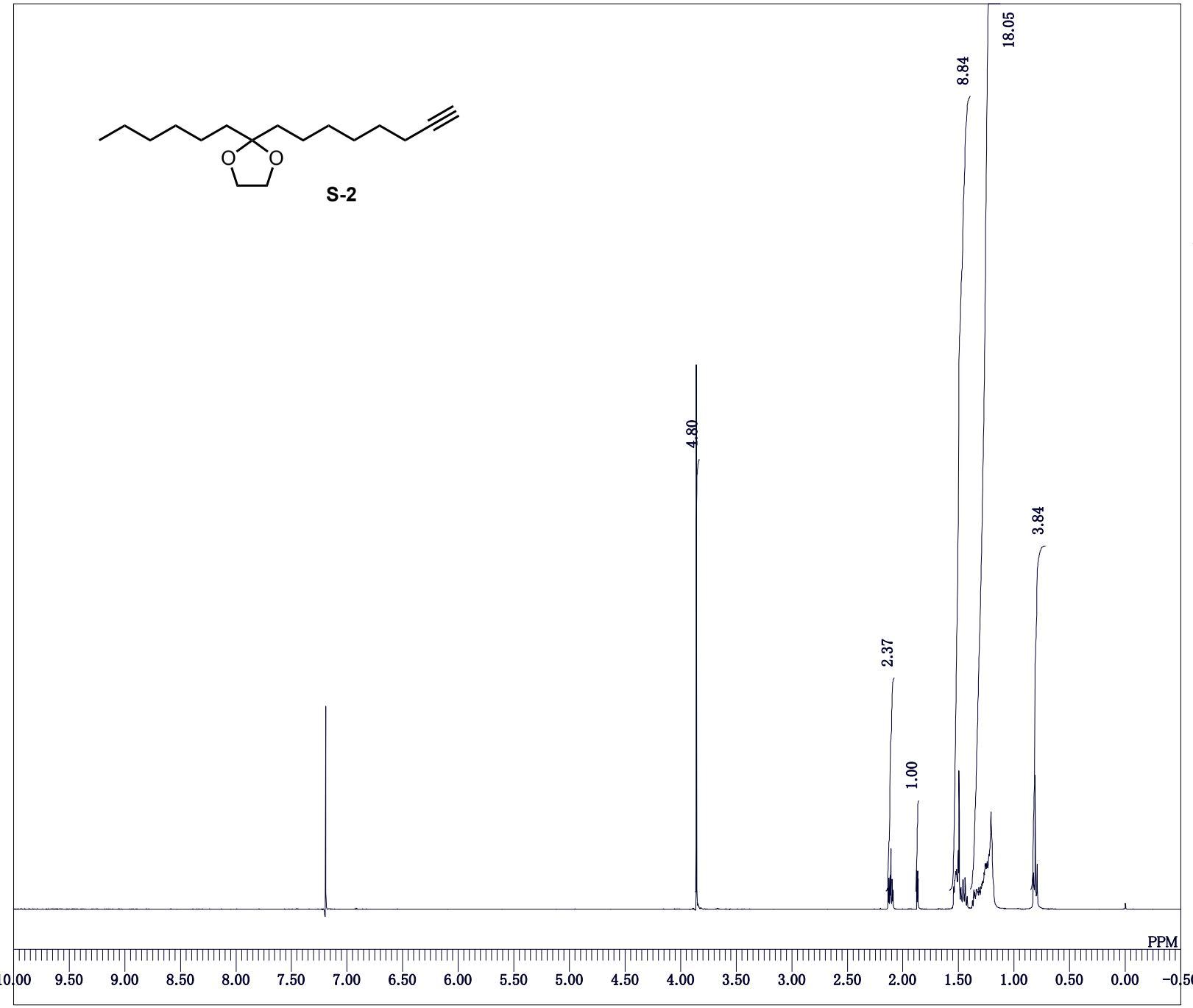


DFILE	YOS1114_carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2014-01-17 19:17:18
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	23.4 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

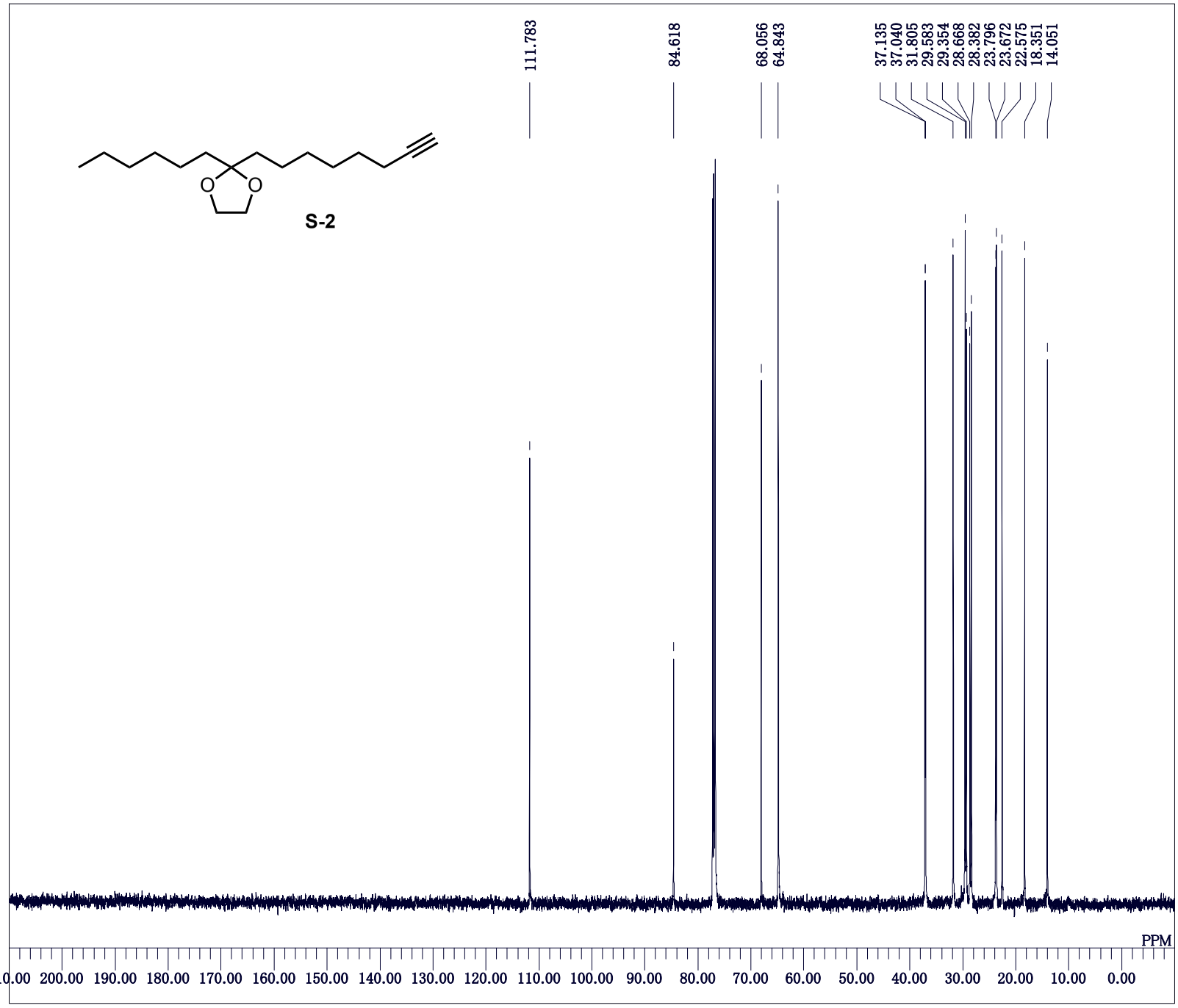

S-18
DFILE YOS1117-2.als
COMNT
DATIM Tue Jan 28 21:22:21 2014
OBNUC 1H
EXMOD non
OBFRQ 399.65 MHz
OBSET 0.00 KHz
OBFIN 134300.00 Hz
POINT 8192
FREQU 7993.60 Hz
SCANS 8
ACQTM 1.0248 sec
PD 5.9752 sec
PW1 5.50 usec
IRNUC 1H
CTEMP 19.1 c
SLVNT CDCL3
EXREF 7.24 ppm
BF 1.20 Hz
RGAIN 22
1.02
3.98
3.00
1.99
6.87
13.89
2.06
PPM
10.00 9.50 9.00 8.50 8.00 7.50 7.00 6.50 6.00 5.50 5.00 4.50 4.00 3.50 3.00 2.50 2.00 1.50 1.00 0.50 0.00 -0.50



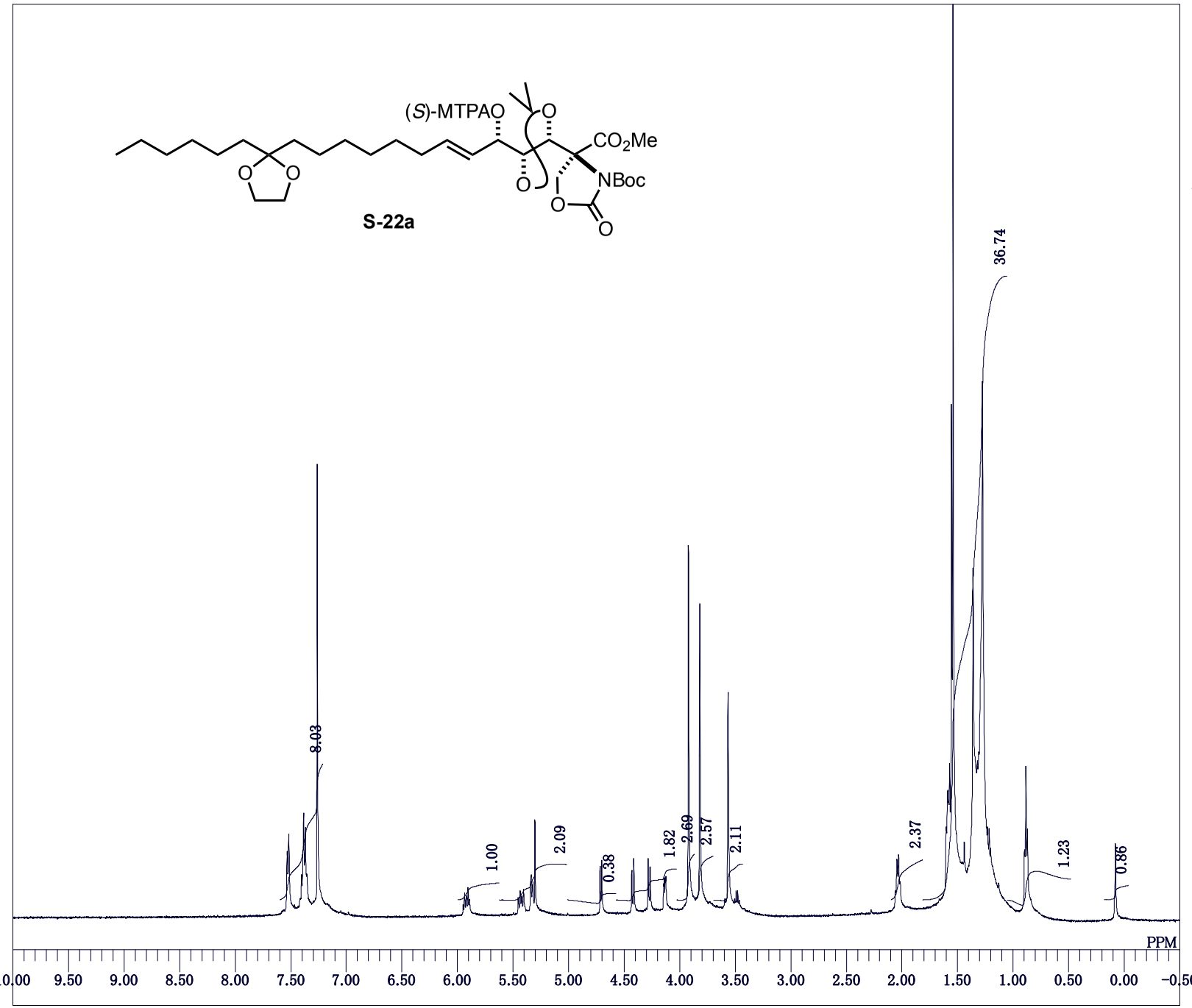
DFILE	YOS1117_carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2014-01-28 23:03:20
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	23.9 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50



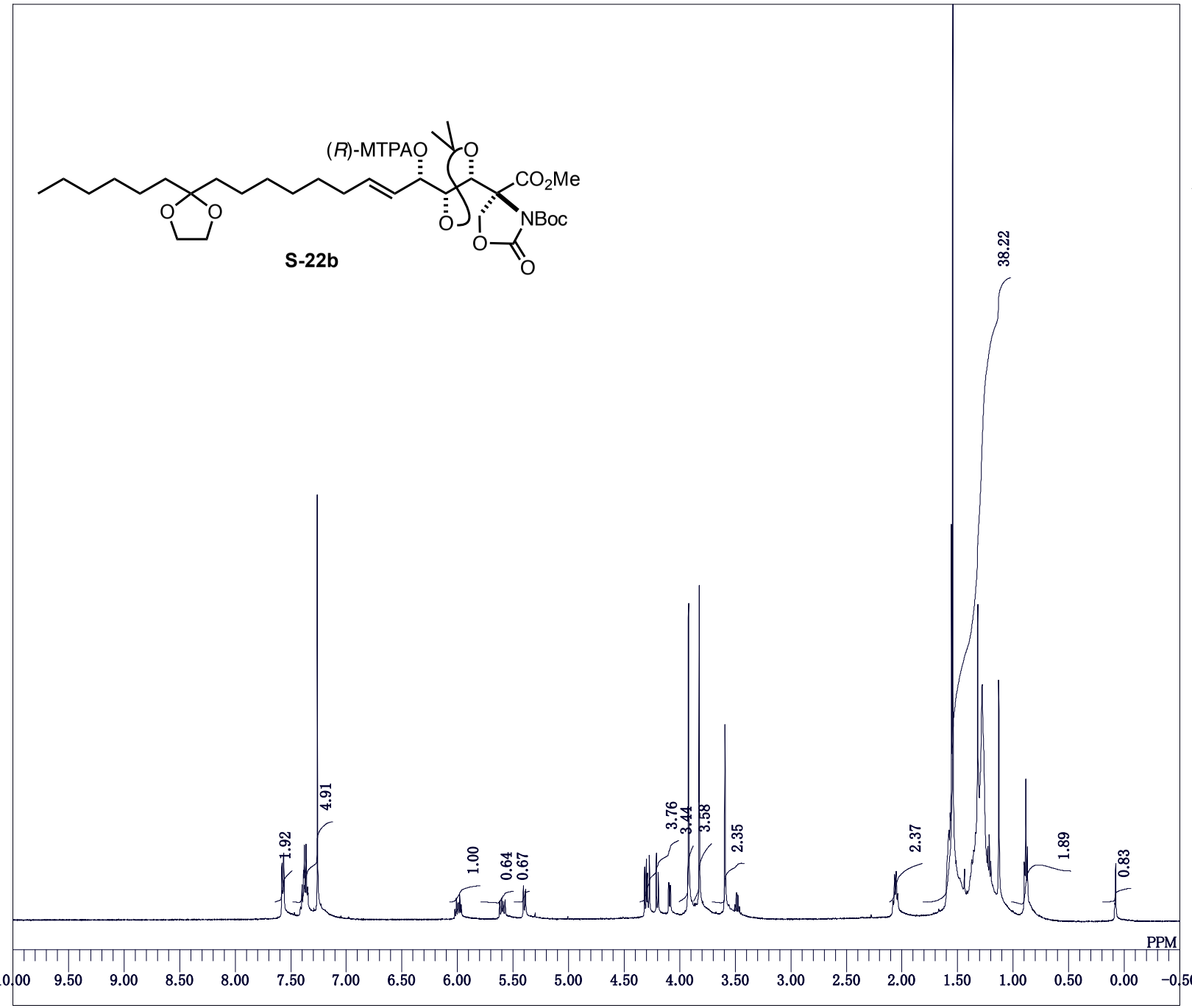
DFILE	YOS1121.als
COMNT	
DATIM	Mon Feb 03 16:41:00 2014
OBNUC	1H
EXMOD	non
OBFRQ	399.65 MHz
OBSET	0.00 KHz
OBFIN	134300.00 Hz
POINT	8192
FREQU	7993.60 Hz
SCANS	8
ACQTM	1.0248 sec
PD	5.9752 sec
PW1	5.50 usec
IRNUC	1H
CTEMP	20.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	22



DFILE	YOS1121_carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2014-02-04 20:40:09
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32780
FREQU	39308.18 Hz
SCANS	256
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	26.6 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50



DFILE	KIN4058_proton-1-1.jdf
COMNT	single_pulse
DATIM	2014-03-08 19:23:31
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	16
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	23.9 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50



DFILE	KIN4057_proton-1-1.jdf
COMNT	single_pulse
DATIM	2014-03-08 16:10:12
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16400
FREQU	9384.38 Hz
SCANS	16
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	23.9 c
SLVNT	CDCL3
EXREF	12.51 ppm
BF	0.12 Hz
RGAIN	50

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