Supporting Information

Design and synthesis of cyclopropane congeners of resolvin E2, an endogenous proresolving lipid mediator, as its stable equivalents

Hayato Fukuda, Ryuta Muromoto, Yuuki Takakura, Kohei Ishimura, Ryutaro Kanada, Daichi Fushihara, Makoto Tanabe, Kotaro Matsubara, Toru Hirao, Koki Hirashima, Hiroshi Abe, Mitsuhiro Arisawa, Tadashi Matsuda, and Satoshi Shuto*

Faculty of Pharmaceutical Science, Hokkaido University,

Kita-12, Nishi-6, Kita-Ku, Sapporo 060-0812, Japan

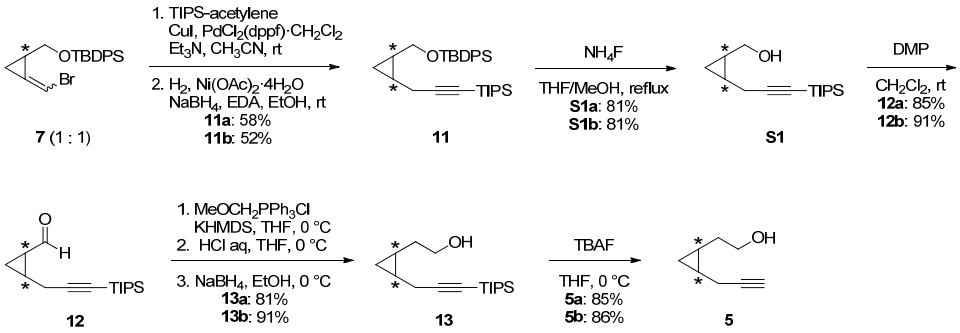
shu@pharm.hokudai.ac.jp

Table of Contents

General procedures

NMR spectra were measured on JEOL ECX400P (400 MHz), JEOL ECS400 (400 MHz) and JEOL ECA500 (500 MHz). Chemical shifts were reported in the δ scale relative to tetramethylsilane (TMS) as 0.00 ppm for ^{1}H ($CDCl_3$) and residual $CHCl_3$ (7.26 ppm for ^{1}H and 77.00 ppm for ^{13}C), DMSO (2.49 ppm for ^{1}H and 39.5 ppm for ^{13}C) as internal reference. Mass spectra (MS) were measured on Thermo Scientific Exactive (ESI). Silica gel column chromatography and flash column chromatography was carried out with Wakogel 60N (Wako Pure Chemical Industries, Ltd., neutral, 63-212 μm) and silica gel (Kishida Chemical Co., Ltd., neutral, 32-63 μm), respectively. Elemental analysis (EA) was measured on Yanaco MT-6 and J-Sience JM10. All reactions were carried out under an argon atmosphere using flame-dried or oven-dried glassware, unless otherwise noted, and monitored with analytical TLC (Merck Ltd., TLC Silica gel 60 F_{254}). Purity of all compounds was determined to be >95% by EA or HPLC (YMC-Pack SIL, 150 x 4.6 mm, UV 254 nm).

Experimental Procedures



tert-Butyldiphenyl(((1*S*,2*S*)-2-(3-(triisopropylsilyl)prop-2-yn-1-yl)cyclopropyl)methoxy)silane (11a)

To a stirred solution of **7a** (600 mg, 1.50 mmol) and triisopropylsilylacetylene (673 μL, 3.00 mmol) in CH_3CN (15 mL) was added Et_3N (416 μL, 3.00 mmol), CuI (57 mg, 300 μmol) and $PdCl_2(dppf)\cdot CH_2Cl_2$ (123 mg, 150 μmol) at room temperature. The mixture was stirred at the same temperature for 2 h, quenched by addition of sat. NH_4Cl aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (hexane) to give crude Sonogashira adduct as a yellow oil.

To a suspension of $Ni(OAc)_2\cdot 4H_2O$ (182 mg, 732 μmol) in EtOH (8 mL) was added $NaBH_4$ (46 mg, 1.22 mmol) and ethylenediamine (280 μL, 4.15 mmol) at room temperature under Ar atmosphere. To the reaction mixture was added a solution of crude Sonogashira adduct in EtOH (4 mL) and the mixture was stirred at the same temperature under H_2 atmosphere for 5 h and filtered with Celite. The filtrate was concerned in reduced pressure. The residue was purified by silica gel column chromatography (hexane) to give **11a** (440 mg, 870 μmol, 58% for 2 steps) as a colorless oil.

11a: $[\alpha]_D^{26}$ –0.6 (*c* 1.19, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (m, 4H), 7.39 (m, 6H), 3.75 (m, 2H), 2.42 (dd, *J* = 18.0, 6.0 Hz, 1H), 2.24 (dd, *J* = 18.0, 6.8 Hz, 1H), 1.12-0.98 (m, 32H), 0.70 (ddd, *J* = 8.4, 8.4, 5.2 Hz, 1H), 0.16 (ddd, *J* = 5.6, 5.6, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.59, 135.56, 134.03, 133.97, 129.5, 127.60, 127.58, 108.6, 80.3, 63.8, 26.9, 19.4, 19.2, 18.6, 18.0, 15.2, 11.3, 9.3; LRMS (ESI) m/z 527 $[M+Na]^+$; Anal. calcd for $C_{32}H_{48}OSi_2$: C, 76.12; H, 9.58; found: C, 75.82; H, 9.64.

tert-Butyldiphenyl(((1*R*,2*R*)-2-(3-(triisopropylsilyl)prop-2-yn-1-yl)cyclopropyl)methoxy)silane (11b)

To a stirred solution of **7b** (2.9 g, 7.20 mmol) and triisopropylsilylacetylene (3.2 mL, 14.4 mmol) in CH_3CN (72 mL) was added Et_3N (2.0 mL, 14.4 mmol), CuI (274 mg, 1.44 mmol) and

$PdCl_2(dppf)\cdot CH_2Cl_2$ (590 mg, 720 μmol) at room temperature. The mixture was stirred at the same temperature for 2 h, quenched by addition of sat. NH_4Cl aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (hexane) to give crude Sonogashira adduct as a yellow oil.

To a suspension of $Ni(OAc)_2\cdot 4H_2O$ (746 mg, 3.0 mmol) in EtOH (42 mL) was added $NaBH_4$ (189 mg, 5.00 mmol) and ethylenediamine (1.1 mL, 16.5 mmol) at room temperature under Ar atmosphere. To the reaction mixture was added a solution of crude Sonogashira adduct (2.5 g, 4.98 mmol) in EtOH (8 mL) and the mixture was stirred at the same temperature under H_2 atmosphere for 5 h and filtered with Celite. The filtrate was concerned in reduced pressure. The residue was purified by silica gel column chromatography (hexane) to give **11b** (1.9 g, 3.77 mmol, 52% for 2 steps) as a colorless oil.

11b: $[\alpha]_D^{26}$ +0.6 (*c* 1.06, $CHCl_3$). ^{1}H NMR spectrum for **11b** agreed with that for **11a**.

((1*S*,2*S*)-2-(3-(Triisopropylsilyl)prop-2-yn-1-yl)cyclopropyl)methanol (S1a)

To a stirred solution of **11a** (1.02 g, 2.03 mmol) in THF (10 mL) and MeOH (10 mL) was added NH_4F (750 mg, 20.3 mmol) at room temperature. The mixture was refluxed for 48 h and cooled to room temperature. The solution was concentrated, added H_2O and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue purified by silica gel column chromatography (AcOEt-hexane = 1:20) to give **S1a** (432 mg, 1.62 mol, 81%) as a colorless oil.

S1a: $[\alpha]_D^{20}$ +74.6 (*c* 0.84, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (m, 1H), 3.42 (ddd, *J* = 12.4, 9.6, 2.4 Hz, 1H), 2.70 (dd, *J* = 18.0, 5.6 Hz, 1H), 2.08 (d, *J* = 5.6 Hz, 1H), 2.05 (dd, *J* = 18.0, 10.4 Hz, 1H), 1.26 (m, 2H), 1.12-1.02 (m, 21H), 0.78 (ddd, *J* = 8.4, 8.4, 5.2 Hz, 1H), 0.11 (ddd, *J* = 5.2, 5.2, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.5, 81.9, 63.2, 19.3, 18.5, 17.8, 15.6, 11.2, 9.7; LRMS (ESI) m/z 289 $[M+Na]^+$; HRMS (ESI) calcd for $C_{16}H_{30}ONaSi$ $[M+Na]^+$ 289.1958, found 289.1959.

((1*R*,2*R*)-2-(3-(Triisopropylsilyl)prop-2-yn-1-yl)cyclopropyl)methanol (S1b)

To a stirred solution of **11b** (607 mg, 1.20 mmol) in THF (6 mL) and MeOH (6 mL) was added NH_4F (669 mg, 18.1 mmol) at room temperature and the mixture was refluxed overnight. Then, additional NH_4F (223 mg, 6.02 mmol) was added to the reaction mixture, which was stirred overnight and cooled to room temperature. The solution was concentrated, added H_2O and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue purified by silica gel column chromatography (AcOEt-hexane = 1:125 to 1:15) to give **S1b** (260 mg, 978 μmol, 81%) as a colorless oil.

S1b: $[\alpha]_D^{25}$ –81.5 (*c* 1.05, $CHCl_3$). ^1H NMR spectrum for **S1b** agreed with that for **S1a**.

(1*S*,2*S*)-2-(3-(Triisopropylsilyl)prop-2-yn-1-yl)cyclopropanecarbaldehyde (12a)

To a stirred solution of **S1a** (432 mg, 1.62 mmol) in DCM (10 mL) was added DMP (1.03 g, 2.44 mmol) at 0 °C. The mixture was stirred at room temperature for 30 min, quenched by addition of $Na_2S_2O_3$ aq and sat. $NaHCO_3$ aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:100 to 1:20) to give **12a** (368 mg, 1.38 mmol, 85%) as a pale yellow oil.

12a: $[\alpha]_D^{25}$ +85.6 (*c* 0.77, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.59 (d, *J* = 4.4 Hz, 1H), 2.65 (dd, *J* = 18.0, 6.0 Hz, 1H), 2.42 (dd, *J* = 18.0, 8.4 Hz, 1H), 2.03 (m, 1H), 1.78 (m, 1H), 1.34 (ddd, *J* = 5.2, 5.2, 5.2 Hz, 1H), 1.26 (ddd, *J* = 8.4, 8.4, 5.2 Hz, 1H), 1.08-1.00 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 106.4, 81.7, 27.0, 23.7, 18.7, 18.4, 14.5, 11.1; LRMS (APCI) m/z 265 $[M+H]^+$; HRMS (APCI) calcd for $C_{16}H_{28}OSi$ $[M+H]^+$ 265.1982, found 265.1982.

(1*R*,2*R*)-2-(3-(Triisopropylsilyl)prop-2-yn-1-yl)cyclopropanecarbaldehyde (12b)

To a stirred solution of **S1b** (447 mg, 1.68 mmol) in DCM (17 mL) was added DMP (1.07 g, 2.52 mmol) at 0 °C. The mixture was stirred at room temperature for 1 h, quenched by addition of $Na_2S_2O_3$ aq and sat. $NaHCO_3$ aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:125) to give **12b** (405 mg, 1.53 mmol, 91%) as a pale yellow oil.

12b: $[\alpha]_D^{24}$ –86.0 (*c* 0.84, $CHCl_3$). ^1H NMR spectrum for **12b** agreed with that for **12a**.

2-((1*R*,2*S*)-2-(3-(Triisopropylsilyl)prop-2-yn-1-yl)cyclopropyl)ethanol (13a)

To a stirred solution of $MeOCH_2PPh_3Cl$ (1.3 g, 3.80 mmol) in THF (7 mL) was added KHMDS (0.5 M in toluene, 7.59 mL, 3.80 mmol) at 0 °C. The resulting solution was stirred at the same temperature for 30 min. After **12a** (334 mg, 1.27 mmol) in THF (3 mL) was added to the reaction mixture, the mixture was stirred at the same temperature for 1 h, quenched by addition of sat. NH_4Cl aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to give crude Wittig product. This material was used without further purification.

To a stirred solution of crude Wittig product in THF (10 mL) was added 12 N HCl aq (3 mL, 36 mmol) at 0 °C. The mixture was stirred at the same temperature for 80 min, quenched by addition of sat. $NaHCO_3$ aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to give crude aldehyde. This material was used without further

purification.

To a stirred solution of crude aldehyde in EtOH (10 mL) was added $NaBH_4$ (72 mg, 1.91 mmol) at 0 °C. The mixture was stirred at the same temperature for 1 h, quenched by addition of sat. NH_4Cl aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:20 to 1:8) to give **13a** (288 mg, 1.03 mmol, 81% for 3 steps) as a colorless oil.

13a: $[\alpha]_D^{25}$ +36.9 (*c* 0.57, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (t, *J* = 6.8 Hz, 1H), 2.43 (dd, *J* = 18.0, 6.0 Hz, 1H), 2.17 (dd, *J* = 18.0, 8.4 Hz, 1H), 1.74 (m, 1H), 1.55 (m, 1H), 1.08-1.00 (m, 22H), 0.86 (m, 1H), 0.72 (ddd, *J* = 8.4, 8.4, 5.2 Hz, 1H), –0.02 (ddd, *J* = 5.2, 5.2, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.4, 80.5, 63.3, 31.4, 19.5, 18.6, 14.7, 12.5, 11.2, 10.3; LRMS (ESI) m/z 303 $[M+Na]^+$; HRMS (ESI) calcd for $C_{17}H_{32}ONaSi$ $[M+Na]^+$ 303.2115, found 303.2115.

2-((1*S*,2*R*)-2-(3-(Triisopropylsilyl)prop-2-yn-1-yl)cyclopropyl)ethanol (13b)

To a stirred solution of $MeOCH_2PPh_3Cl$ (2.25 g, 6.56 mmol) in THF (10 mL) was added KHMDS (0.5 M in toluene, 13.1 mL, 6.56 mmol) at 0 °C. The resulting solution was stirred at the same temperature for 30 min. After **12b** (577 mg, 2.19 mmol) in THF (7 mL) was added to the reaction mixture, the mixture was stirred at the same temperature for 1 h, quenched by addition of sat. NH_4Cl aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to give crude Wittig product. This material was used without further purification.

To a stirred solution of crude Wittig product in THF (17 mL) was added 12 N HCl aq (5 mL, 75 mmol) at 0 °C. The mixture was stirred at the same temperature for 80 min, quenched by addition of sat. $NaHCO_3$ aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to give crude aldehyde. This material was used without further purification.

To a stirred solution of crude aldehyde in EtOH (17 mL) was added $NaBH_4$ (124 mg, 3.29 mmol) at 0 °C. The mixture was stirred at the same temperature for 20 min, quenched by addition of sat. NH_4Cl aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:10 to 1:4) to give **13b** (558 mg, 1.99 mmol, 91% for 3 steps) as a colorless oil.

13b: $[\alpha]_D^{26}$ –38.5 (*c* 1.17, $CHCl_3$). ^{1}H NMR spectrum for **13b** agreed with that for **13a**.

2-((1*R*,2*S*)-2-(Prop-2-yn-1-yl)cyclopropyl)ethanol (5a)

To a stirred solution of **13a** (288 mg, 1.03 mmol) in THF (2 mL) was added TBAF (1.0 M in THF, 8.23 mL, 8.23 mmol) at room temperature. The mixture was stirred at the same temperature for 30 h, added H_2O and extracted with ether. The combined organic extracts were dried (Na_2SO_4), and

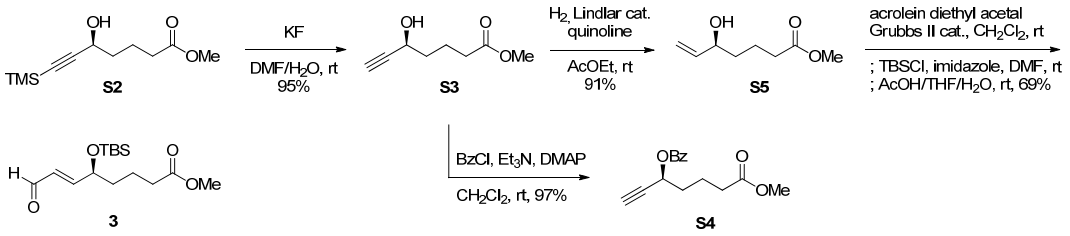
concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:4 to 1:2) to give **5a** (108 mg, 871 μmol, 85%) as a colorless oil.

5a: $[\alpha]_D^{26}$ +58.0 (*c* 0.74, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.72 (t, *J* = 6.8 Hz, 2H), 2.29 (ddd, *J* = 17.6, 6.4, 2.8 Hz, 1H), 2.10 (ddd, *J* = 17.6, 7.6, 2.8 Hz, 1H), 2.04 (s, 1H), 1.99 (t, *J* = 2.8 Hz, 1H), 1.69 (ddt, *J* = 14.0, 6.8, 6.8 Hz, 1H), 1.49 (ddt, *J* = 14.0, 6.8, 6.8 Hz, 1H), 1.03 (m, 1H), 0.84 (m, 1H), 0.72 (ddd, *J* = 8.8, 8.8, 5.2 Hz, 1H), –0.08 (ddd, *J* = 5.2, 5.2, 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 84.1, 68.4, 63.1, 31.4, 18.1, 14.3, 12.4, 10.4; LRMS (APCI) m/z 125 $[M+H]^+$; HRMS (APCI) calcd for $C_8H_{13}O$ $[M+H]^+$ 125.0961, found 125.0961.

2-((1*S*,2*R*)-2-(Prop-2-yn-1-yl)cyclopropyl)ethanol (5b)

To a stirred solution of **13b** (558 mg, 1.99 mmol) in THF (10 mL) was added TBAF (1.0 M in THF, 7.97 mL, 7.97 mmol) at room temperature. The mixture was stirred at the same temperature for 6 h, added H_2O and extracted with ether. The combined organic extracts were dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:8 to 1:2) to give **5b** (213 mg, 1.72 mmol, 86%) as a colorless oil.

5b: $[\alpha]_D^{26}$ –58.2 (*c* 1.21, $CHCl_3$); ^{1}H NMR spectrum for **5b** agreed with that for **5a**.



(*S*)-7-Methoxy-7-oxohept-1-yn-3-yl benzoate (S4)

To a stirred solution of **S2** (3.0 g, 13.2 mmol) in DMF (45 mL) was added a solution of KF (1.53 g, 26.3 mmol) in H_2O (4.5 mL) at room temperature. The mixture was stirred at the same temperature for 1 h. The resulting solution was extracted with Et_2O. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:4) to give **S3** (1.95 g, 12.5 mmol, 95%) as a colorless oil[1].

To a stirred solution of **S3** (13 mg, 83.3 μmol) in CH_2Cl_2 (1 mL) were added Et_3N (116 μL, 833 μmol), BzCl (48 μL, 417 μmol) and DMAP (10 mg, 83.3 μmol) at room temperature. The mixture was stirred at the same temperature for 5 h. The resulting solution was extracted with Et_2O. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. After the residue was added AcOEt and sat. Na_2CO_3 aq, the mixture was stirred at room temperature for 1 h. The resulting solution was extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column

chromatography (AcOEt-hexane = 1:2) to give **S4** (21 mg, 80.8 μmol, 97%, 99% ee) as a colorless oil.

S3: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (m, 2H), 7.58 (m, 1H), 7.46 (m, 2H), 6.65 (td, *J* = 6.2, 2.4 Hz, 1H), 3.68 (s, 3H), 2.51 (d, *J* = 2.4 Hz, 1H), 2.42 (t, *J* = 7.4 Hz, 2H), 2.01-1.88 (m, 2H).

Optical purity of **S4** was determined by chiral HPLC analysis (HPLC conditions: column; CHIRALCEL AS-H, eluent; hexane-*i*-PrOH = 20 : 1, flow rate; 0.5 mL/min, detection; UV 254 nm, retention time; 12.9 min for **S4**)

(*S*)-Methyl 5-hydroxyhept-6-enoate (S5)

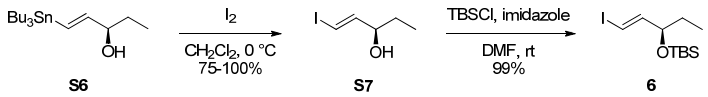
A solution of **S3** (1.46 g, 9.36 mmol), quinoline (5.54 mL, 46.8 mmol) and Lindlar catalyst (146 mg, 10% w/w) in AcOEt (45 mL) was stirred under H_2 atmosphere at room temperature for 1.5 h. The mixture was filtrated through Celite pad and the filtrate was concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:2) to give **S5** (1.35 g, 8.53 mmol, 91%) as a colorless oil.

S5: $[\alpha]_D^{25}$ +8.3 (*c* 0.60, $CHCl_3$), lit. $[\alpha]_D^{25}$ +3.2 (*c* 0.1, $CDCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (ddd, *J* = 17.5, 10.5, 6.5 Hz, 1H), 5.24 (d, *J* = 17.5 Hz, 1H), 5.12 (d, *J* = 10.5 Hz, 1H), 4.12 (dt, *J* = 6.5, 6.5 Hz, 1H), 3.68 (s, 3H), 2.36 (t, *J* = 6.0 Hz, 2H), 1.78-1.67 (m, 3H), 1.57 (m, 2H). Data for **S5** agreed with previous data[1].

(*S*,*E*)-Methyl 5-((*tert*-butyldimethylsilyl)oxy)-8-oxooct-6-enoate (3)

A solution of **S5** (646 mg, 4.09 mmol), acrolein diethyl acetal (1.25 mL, 8.18 mmol) and Grubbs 2nd generation catalyst (G II) (110 mg, 123 μmol) in DCM (20 mL) was stirred at room temperature overnight. Then, additional G II (36 mg, 40 μmol) and acrolein diethyl acetal (300 μL, 1.97 mmol) was added and the reaction mixture was stirred at room temperature for further 4 h. To the solution were added imidazole (1.11 g, 16.4 mmol) and TBSCl (1.23 g, 8.18 mmol) at 0 °C. The mixture was stirred at the room temperature for 3 h. To the solution was added AcOH/THF/H_2O (6 mL/6 mL/6 mL) at room temperature. The mixture was stirred at the same temperature for 6 h, quenched by addition of $NaHCO_3$ and extracted with Et_2O. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:10) to give **3** (852 mg, 2.84 mmol, 69%) as a colorless oil.

$[\alpha]_D^{24}$ +12.2 (*c* 0.99, $CHCl_3$), lit. $[\alpha]_D^{21}$ +16 (*c* 0.91, $CHCl_3$)[2]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.58 (d, *J* = 7.5 Hz, 1H), 6.79 (dd, *J* = 15.5, 4.5 Hz, 1H), 6.28 (dd, *J* = 15.5, 7.5 Hz, 1H), 4.45 (dt, *J* = 4.5, 4.5 Hz, 1H), 3.67 (s, 3H), 2.34 (t, *J* = 7.0 Hz, 2H), 1.71-1.61 (m, 4H), 0.91 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H). Data for **3** agreed with previous data[2].



S6 S7 6

(*R*,*E*)-1-Iodopent-1-en-3-ol (S7)

To a stirred solution of **S6** in CH_2Cl_2 (c.a. 0.3 M) was added I_2 (1.2 eq.) at 0 °C. The mixture was stirred at the same temperature for several min and quenched by addition of sat. $Na_2S_2O_3$ aq and extracted with ether. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane) to give **S7** (75-100%, >97% ee) as a light yellow oil.

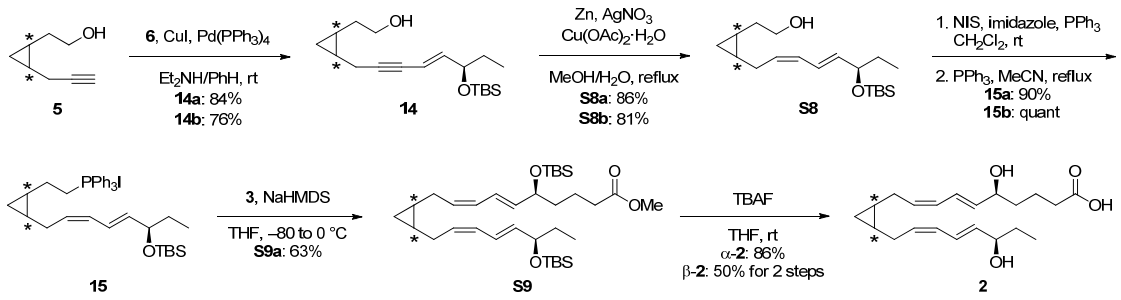
S7: $[\alpha]_D^{18}$ +2.0 (*c* 0.97, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58 (dd, *J* = 15.0, 6.6 Hz, 1H), 6.36 (dd, *J* = 15.0, 1.0 Hz, 1H), 4.04 (m, 1H), 1.61-1.54 (m, 3H), 0.94 (t, *J* = 7.4 Hz, 3H). Data for **S7** agreed with previous data[3].

Optical purity of **S7** was determined by chiral HPLC analysis (HPLC conditions: column; CHIRALCEL AD-H, eluent; hexane-*i*-PrOH = 50:1, flow rate; 0.5 mL/min, detection; UV 250 nm, retention time; 18.0 min for **S7**)

(*R*,*E*)-*tert*-Butyl((1-iodopent-1-en-3-yl)oxy)dimethylsilane (6)

To a stirred solution of **S7** (414 mg, 1.95 mmol) in DMF (6 mL) was added imidazole (532 mg, 7.81 mmol) and TBSCl (589 mg, 3.91 mmol) at room temperature. The mixture was stirred at the same temperature for 1 h and quenched by addition of sat. $NaHCO_3$ aq and extracted with ether. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:10) to give **6** (629 mg, 1.93 mmol, 99%) as a colorless oil.

6: $[\alpha]_D^{20}$ +39.9 (*c* 0.98, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.51 (dd, *J* = 14.8, 6.0 Hz, 1H), 6.19 (dd, *J* = 14.8, 1.4 Hz, 1H), 4.02 (dt, *J* = 6.0, 6.0 Hz, 1H), 1.50 (td, *J* = 7.6, 6.0 Hz, 1H), 0.89 (s, 9H), 0.87 (t, *J* = 7.6 Hz, 3H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 76.2, 75.6, 30.3, 25.8, 18.2, 9.2, –4.6, –4.9; LRMS (EI) m/z 326 $[M]^+$; HRMS (EI) calcd for $C_{11}H_{23}IOSi$ $[M]^+$ 326.0563, found 326.0565.



2-((1*R*,2*S*)-2-((*R*,*E*)-6-((*tert*-Butyldimethylsilyl)oxy)oct-4-en-2-yn-1-yl)cyclopropyl)ethanol (14a)

To a stirred solution of **5a** (108 mg, 871 μmol) and **6** (380 mg, 1.17 mmol) in benzene (5 mL) was added Et_2NH (0.5 ml), CuI (83 mg, 435 μmol) and $Pd(PPh_3)_4$ (101 mg, 87.1 μmol) at room temperature. The mixture was stirred at the same temperature for 1 h, quenched by addition of H_2O and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:8) to give **14a** (235 mg, 730 μmol, 84%) as a yellow oil.

14a: $[\alpha]_D^{26}$ +56.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (dd, *J* = 16.0, 5.2 Hz, 1H), 5.63 (m, 1H), 4.08 (br dt, *J* = 6.0, 5.2 Hz, 1H), 3.77 (m, 2H), 2.45 (ddd, *J* = 18.0, 6.0, 2.0 Hz, 1H), 2.23 (ddd, *J* = 18.0, 8.4, 2.0 Hz, 1H), 1.73 (ddt, *J* = 14.4, 6.8, 6.8 Hz, 1H), 1.58-1.47 (m, 3H), 1.07 (m, 1H), 0.90 (s, 9H), 0.90-0.83 (m, 1H), 0.87 (t, *J* = 7.2 Hz, 3H), 0.75 (ddd, *J* = 8.8, 8.8, 4.8 Hz, 1H), 0.05 (s, 3H), 0.04 (s, 3H), –0.05 (ddd, *J* = 5.6, 5.6, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 108.9, 89.5, 78.9, 73.6, 63.0, 31.4, 30.6, 25.8, 19.1, 18.1, 14.5, 12.4, 10.5, 9.2, –4.6, –5.0; LRMS (ESI) m/z 345 $[M+Na]^+$; HRMS (ESI) calcd for $C_{19}H_{34}O_2NaSi$ $[M+Na]^+$ 345.2220, found 345.2225.

2-((1*S*,2*R*)-2-((*R*,*E*)-6-((*tert*-Butyldimethylsilyl)oxy)oct-4-en-2-yn-1-yl)cyclopropyl)ethanol (14b)

To a stirred solution of **5b** (105 mg, 847 μmol) and **6** (359 mg, 1.10 mmol) in benzene (5 mL) was added Et_2NH (0.5 ml), CuI (81 mg, 423 μmol) and $Pd(PPh_3)_4$ (98 mg, 84.7 μmol) at room temperature. The mixture was stirred at the same temperature for 2 h, quenched by addition of H_2O and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:8) to give **14b** (206 mg, 640 μmol, 76%) as a yellow oil.

14b: $[\alpha]_D^{21}$ –10.7 (*c* 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (dd, *J* = 16.0, 5.6 Hz, 1H), 5.63 (m, 1H), 4.08 (m, 1H), 3.77 (t, *J* = 6.4 Hz, 2H), 2.45 (ddd, *J* = 18.0, 6.4, 2.4 Hz, 1H), 2.23 (ddd, *J* = 18.0, 7.6, 2.1 Hz, 1H), 1.73 (ddt, *J* = 13.4, 6.8, 6.8 Hz, 1H), 1.58-1.47 (m, 3H), 1.07 (m, 1H), 0.90 (s, 9H), 0.90-0.85 (m, 1H), 0.87 (t, *J* = 7.6 Hz, 3H), 0.75 (ddd, *J* = 8.4, 8.4, 4.8 Hz, 1H), 0.05 (s,

3H), 0.04 (s, 3H), –0.05 (ddd, *J* = 5.6, 5.6, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 108.9, 89.6, 79.0, 73.6, 63.3, 31.5, 30.7, 25.8, 19.2, 18.2, 14.5, 12.5, 10.6, 9.3, –4.5, –4.9; LRMS (ESI) m/z 345 $[M+Na]^+$; HRMS (ESI) calcd for $C_{19}H_{34}O_2NaSi$ $[M+Na]^+$ 345.2220, found 345.2221.

2-((1*R*,2*S*)-2-((*R*,2*Z*,4*E*)-6-((*tert*-Butyldimethylsilyl)oxy)octa-2,4-dien-1-yl)cyclopropyl)ethanol (S8a)

To a stirred solution of Zn powder (9.2 g, 141 mmol) in H_2O (35 mL) was added $Cu(OAc)_2 \cdot H_2O$ (920 mg, 4.60 mmol) at room temperature. The mixture was stirred at the same temperature for 15 min. To the mixture was added $AgNO_3$ (920 mg, 5.41 mmol) and stirred at the same temperature for 30 min. To the reaction mixture was added **14a** (230 mg, 714 μmol) in MeOH (35 mL), stirred at reflux for 2 h, filtrated through Celite pad and the filtrate was concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:4) to give **S8a** (199 mg, 614 μmol, 86%) as a yellow oil.

S8a: $[\alpha]_D^{26}$ –22.4 (*c* 1.24, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (dd, *J* = 15.2, 11.2 Hz, 1H), 6.00 (dd, *J* = 11.2, 10.8 Hz, 1H), 5.64 (dd, *J* = 15.2, 6.0 Hz, 1H), 5.50 (dt, *J* = 10.8, 7.2 Hz, 1H), 4.09 (dt, *J* = 6.0, 5.8 Hz, 1H), 3.73 (br t, *J* = 6.6 Hz, 2H), 2.26-2.10 (m, 2H), 1.73 (ddt, *J* = 12.8, 6.0, 6.0 Hz, 1H), 1.55-1.42 (m, 4H), 0.91 (s, 9H), 0.91-0.86 (m, 1H), 0.87 (t, *J* = 7.2 Hz, 3H), 0.81 (m, 1H), 0.69 (ddd, *J* = 8.4, 8.4, 4.4 Hz, 1H), 0.06 (s, 3H), 0.03 (s, 3H), –0.12 (ddd, *J* = 5.4, 5.4, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.8, 130.8, 128.0, 124.3, 74.3, 63.3, 31.8, 31.1, 27.0, 25.9, 18.2, 15.2, 12.3, 10.4, 9.6, –4.4, –4.8; LRMS (ESI) m/z 347 $[M+Na]^+$; HRMS (ESI) calcd for $C_{19}H_{36}O_2NaSi$ $[M+Na]^+$ 347.2377, found 347.2381.

2-((1*S*,2*R*)-2-((*R*,2*Z*,4*E*)-6-((*tert*-Butyldimethylsilyl)oxy)octa-2,4-dien-1-yl)cyclopropyl)ethanol (S8b)

To a stirred solution of Zn powder (8.24 g, 126 mmol) in H_2O (30 mL) was added $Cu(OAc)_2 \cdot H_2O$ (824 mg, 4.13 mmol) at room temperature. The mixture was stirred at the same temperature for 15 min. To the mixture was added $AgNO_3$ (824 mg, 4.85 mmol) and stirred at the same temperature for 30 min. To the reaction mixture was added **14b** (206 mg, 640 μmol) in MeOH (30 mL), stirred at reflux for 2 h, filtrated through Celite pad and the filtrate was concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:10) to give **S8b** (167 mg, 515 μmol, 81%) as a yellow oil.

S8b: $[\alpha]_D^{20}$ –3.9 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (dd, *J* = 15.4, 11.2 Hz, 1H), 6.00 (dd, *J* = 11.2, 10.8 Hz, 1H), 5.65 (dd, *J* = 15.4, 6.0 Hz, 1H), 5.50 (dt, *J* = 10.8, 7.2 Hz, 1H), 4.10 (dt, *J* = 6.0, 6.0 Hz, 1H), 3.73 (t, *J* = 6.6 Hz, 2H), 2.26-2.11 (m, 2H), 1.72 (ddt, *J* = 12.8, 6.4, 6.4 Hz, 1H), 1.55-1.44 (m, 4H), 0.91 (s, 9H), 0.91-0.86 (m, 1H), 0.88 (t, *J* = 7.6 Hz, 3H), 0.84-0.77 (m, 1H), 0.69 (ddd, *J* = 8.4, 8.4, 4.4 Hz, 1H), 0.06 (s, 3H), 0.03 (s, 3H), –0.13 (ddd, *J* = 5.2, 5.2, 5.2 Hz, 1H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 136.9, 130.8, 127.9, 124.2, 74.2, 63.4, 31.8, 31.1, 27.0, 25.9, 18.3, 15.2, 12.3, 10.4, 9.7, –4.4, –4.8; LRMS (ESI) m/z 347 $[M+Na]^+$; HRMS (ESI) calcd for $C_{19}H_{36}O_2NaSi$ $[M+Na]^+$ 347.2377, found 347.2375.

(2-((1*R*,2*S*)-2-((*R*,2*Z*,4*E*)-6-((*tert*-Butyldimethylsilyl)oxy)octa-2,4-dien-1-yl)cyclopropyl)ethyl)iodotriphenylphosphorane (15a)

To a stirred solution of **S8a** (195 mg, 602 μmol), PPh_3 (1.58 g, 6.02 mmol), imidazole (410 mg, 6.02 mmol) in DCM (6 mL) was added NIS (948 mg, 4.21 mmol) at 0 °C under dark. The mixture was stirred at the same temperature for 1 h, quenched by addition of $Na_2S_2O_3$ aq and extracted with DCM. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:30) to give crude iodide as a yellow oil.

To a stirred solution of crude iodide in MeCN (6 mL) was added PPh_3 (316 mg, 1.20 mmol) at room temperature. The mixture was refluxed overnight and cooled to room temperature. The solution was concentrated and purified by silica gel column chromatography (MeOH-$CHCl_3$ = 0:1 to 1:20) to give **15a** (376 mg, 540 μmol, 90% for 2 steps) as an orange amorphous.

15a: $[\alpha]_D^{25}$ +3.1 (*c* 0.89, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.80 (m, 9H), 7.74-7.70 (m, 6H), 6.28 (dd, *J* = 15.2, 11.2 Hz, 1H), 5.94 (dd, *J* = 11.2, 11.2 Hz, 1H), 5.63 (dd, *J* = 15.2, 6.0 Hz, 1H), 5.36 (dt, *J* = 11.2, 7.2 Hz, 1H), 4.09 (dt, *J* = 6.0, 6.0 Hz, 1H), 3.93 (m, 1H), 3.76 (m, 1H), 2.09 (ddd, *J* = 15.0, 7.6, 7.2 Hz, 1H), 1.89 (ddd, *J* = 15.0, 7.8, 7.2 Hz, 1H), 1.80-1.72 (m, 1H), 1.66-1.58 (m, 1H), 1.53-1.46 (m, 2H), 1.29 (m, 1H), 0.92-0.83 (m, 1H), 0.87 (s, 9H), 0.87 (t, *J* = 7.2 Hz, 3H), 0.75 (ddd, *J* = 8.4, 8.4, 4.4 Hz, 1H), 0.04 (s, 3H), 0.00 (s, 3H), –0.17 (ddd, *J* = 5.6, 5.6, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.0, 134.98, 134.95, 133.4, 133.3, 130.4, 130.3, 129.8, 128.1, 123.8, 118.1, 117.3, 73.9, 30.8, 26.4, 25.6, 23.7, 23.2, 21.94, 21.90, 18.0, 16.4, 16.35, 16.25, 11.1, 9.4, –4.6, –5.0; LRMS (ESI) m/z 569 $[M-I]^+$; Anal. calcd for $C_{37}H_{50}IOPSi$: C, 63.78; H, 7.23; found: C, 63.59; H, 7.27.

(2-((1*S*,2*R*)-2-((*R*,2*Z*,4*E*)-6-((*tert*-Butyldimethylsilyl)oxy)octa-2,4-dien-1-yl)cyclopropyl)ethyl)iodotriphenylphosphorane (15b)

To a stirred solution of **S8b** (167 mg, 515 μmol), PPh_3 (1.35 g, 5.15 mmol), imidazole (351 mg, 5.15 mmol) in DCM (5 mL) was added NIS (812 mg, 3.61 mmol) at 0 °C under dark. The mixture was stirred at the same temperature for 1 h, quenched by addition of $Na_2S_2O_3$ aq and extracted with DCM. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:30) to give crude iodide as a yellow oil.

To a stirred solution of crude iodide in MeCN (5 mL) was added PPh_3 (270 mg, 1.03 mmol) at room

temperature. The mixture was refluxed overnight and cooled to room temperature. The solution was concentrated and purified by silica gel column chromatography (MeOH-$CHCl_3$ = 0:1 to 1:10) to give **15b** (359 mg, 516 μmol, quant for 2 steps) as an orange amorphous.

15b: $[\alpha]_D^{19}$ –9.5 (*c* 0.95, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85-7.80 (m, 9H), 7.75-7.70 (m, 6H), 6.31 (dd, *J* = 15.2, 11.2 Hz, 1H), 5.95 (dd, *J* = 11.2, 11.2 Hz, 1H), 5.64 (dd, *J* = 15.2, 6.0 Hz, 1H), 5.37 (dt, *J* = 11.2, 6.8 Hz, 1H), 4.09 (dt, *J* = 6.0, 6.0 Hz, 1H), 3.90 (m, 1H), 3.71 (m, 1H), 2.00 (m, 2H), 1.72 (m, 1H), 1.63 (m, 1H), 1.49 (dq, *J* = 7.2, 7.2 Hz, 2H), 1.29 (m, 1H), 0.91-0.84 (m, 1H), 0.87 (s, 9H), 0.87 (t, *J* = 7.2 Hz, 3H), 0.74 (ddd, *J* = 8.4, 8.4, 5.2 Hz, 1H), 0.05 (s, 3H), 0.00 (s, 3H), –0.17 (ddd, *J* = 5.6, 5.6, 5.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.2, 135.04, 135.02, 133.5, 133.4, 130.5, 130.4, 129.8, 128.3, 123.7, 118.2, 117.5, 73.8, 30.9, 26.5, 25.7, 23.7, 23.3, 22.07, 22.04, 18.1, 16.46, 16.44, 16.3, 11.2, 9.6, –4.6, –4.9; LRMS (ESI) m/z 569 $[M-I]^+$; HRMS (ESI) calcd for $C_{37}H_{50}IOPSi$ $[M-I]^+$ 569.3363, found 569.3355.

(*S*,6*E*,8*Z*)-Methyl 5-((*tert*-butyldimethylsilyl)oxy)-10-((1*R*,2*S*)-2-((*R*,2*Z*,4*E*)-6-((*tert*-butyldimethylsilyl)oxy)octa-2,4-dien-1-yl)cyclopropyl)deca-6,8-dienoate (S9a)

To a stirred solution of **15a** (70 mg, 101 μmol) in THF (0.2 mL) was added NaHMDS (1.0 M in toluene, 96 μL, 96 μmol) at –80 °C. The resulting solution was stirred at –80 °C for 1 h. After **3** (15.1 mg, 50.3 μmol) in THF (0.3 mL) was added to the reaction mixture, the mixture was stirred at –80 °C for 1 h. The reaction mixture was warmed to room temperature overnight, quenched by addition of sat. NH_4Cl aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:20) to give **S9a** (18.7 mg, 31.7 μmol, 63%) as a colorless oil.

S9a: $[\alpha]_D^{25}$ –5.2 (*c* 0.94, $CHCl_3$); 1H-NMR (400 MHz, $CDCl_3$) δ 6.42 (dd, *J* = 15.2, 12.0 Hz, 2H), 5.99 (dd, *J* = 11.2, 10.8 Hz, 1H), 5.98 (dd, *J* = 11.2, 11.2 Hz, 1H), 5.63 (dd, *J* = 15.2, 6.4 Hz, 1H), 5.61 (dd, *J* = 15.2, 6.4 Hz, 1H), 5.51 (m, 2H), 4.18 (dt, *J* = 6.0, 6.0 Hz, 1H), 4.09 (dt, *J* = 6.0, 6.0 Hz, 1H), 3.66 (s, 3H), 2.31 (t, *J* = 7.6 Hz, 2H), 2.28-2.11 (m, 2H), 1.72-1.56 (m, 2H), 1.54-1.47 (m, 4H), 0.90 (s, 18H), 0.87 (t, *J* = 7.6 Hz, 3H), 0.80 (m, 2H), 0.67 (ddd, *J* = 8.4, 8.4, 4.8 Hz, 1H), 0.05 (s, 6H), 0.03 (s, 3H), 0.02 (s, 3H), –0.12 (ddd, *J* = 5.2, 4.8, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 136.8, 136.4, 131.4, 131.0, 127.9, 127.8, 124.7, 124.4, 74.4, 72.8, 51.4, 37.7, 34.0, 31.2, 27.0, 25.88, 25.86, 20.7, 18.3, 18.2, 15.90, 15.88, 10.7, 9.7, –4.3, –4.4, –4.76, –4.80; LRMS (ESI) m/z 613 $[M+Na]^+$; HRMS (ESI) calcd for $C_{34}H_{62}O_4NaSi_2$ $[M+Na]^+$ 613.4079, found 613.4084.

(*S*,6*E*,8*Z*)-Methyl 5-((*tert*-butyldimethylsilyl)oxy)-10-((1*S*,2*R*)-2-((*R*,2*Z*,4*E*)-6-((*tert*-butyldimethylsilyl)oxy)octa-2,4-dien-1-yl)cyclopropyl)deca-6,8-dienoate (S9b)

To a stirred solution of **15b** (55 mg, 79 μmol) in THF (0.2 mL) was added NaHMDS (2.0 M in toluene, 36 μL, 74 μmol) at –80 °C. The resulting solution was stirred at –80 °C for 1 h. After **3**

(15.8 mg, 52.7 μmol) in THF (0.3 mL) was added to the reaction mixture, the mixture was stirred at –80 °C for 1 h. The reaction mixture was warmed to room temperature overnight, quenched by addition of sat. NH_4Cl aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 0:1 to 1:50) to give crude **S9b** as a colorless oil.

(*S*,6*E*,8*Z*)-5-Hydroxy-10-((1*R*,2*S*)-2-((*R*,2*Z*,4*E*)-6-hydroxyocta-2,4-dien-1-yl)cyclopropyl)deca-6,8-dienoic acid (α-CP-RvE2, α-2)

To a stirred solution of **S9a** (4.5 mg, 7.63 μmol) in THF (1 mL) was added TBAF (1.0 M in THF, 61 μL, 61 μmol) at room temperature. The mixture was stirred at the same temperature for 14 h. After the reaction was completed, the mixture was added H_2O and extracted with ether. The combined organic extracts were dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (MeOH-$CHCl_3$ = 1:20) to give α-CP-RvE2, α-**2** (2.3 mg, 6.61 μmol, 87%) as a colorless oil.

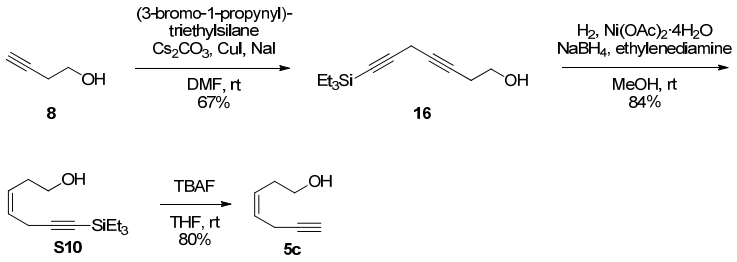
α-CP-RvE2, α-**2**: $[\alpha]_D^{19}$ –4.3 (*c* 0.30, MeOH); IR (neat) ν 3357, 2961, 2927, 1723, 985, 951 cm^{-1}; ^{1}H-NMR (500 MHz, CD_3OD) δ 6.51 (dd, *J* = 15.3, 11.3 Hz, 1H), 6.50 (dd, *J* = 15.3, 11.3 Hz, 1H), 5.98 (dd, *J* = 11.5, 11.0 Hz, 2H), 5.63 (dd, *J* = 15.0, 6.5 Hz, 1H), 5.62 (dd, *J* = 15.0, 6.5 Hz, 1H), 5.52 (m, 2H), 4.10 (dt, *J* = 6.5, 6.5 Hz, 1H), 4.00 (dt, *J* = 6.5, 6.5 Hz, 1H), 2.30 (t, *J* = 7.3 Hz, 2H), 2.26-2.17 (m, 4H), 1.72-1.47 (m, 6H), 0.90 (t, *J* = 7.5 Hz, 3H), 0.81 (m, 2H), 0.66 (ddd, *J* = 8.5, 8.5, 4.7 Hz, 1H), –0.10 (ddd, *J* = 5.3, 5.3, 4.7 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 177.5, 137.18, 137.15, 132.7, 132.5, 128.99, 128.94, 126.7, 74.7, 73.0, 37.8, 34.8, 31.2, 28.0, 22.2, 17.0, 11.2, 10.2; LRMS (ESI) m/z 371 $[M+Na]^+$; HRMS (ESI) calcd for $C_{21}H_{32}O_4Na$ $[M+Na]^+$ 371.2193, found 371.2193.

(*S*,6*E*,8*Z*)-5-Hydroxy-10-((1*S*,2*R*)-2-((*R*,2*Z*,4*E*)-6-hydroxyocta-2,4-dien-1-yl)cyclopropyl)deca-6,8-dienoic acid (β-CP-RvE2, β-2)

To a stirred solution of crude **S9b** in THF (1 mL) was added TBAF (1.0 M in THF, 132 μL, 132 μmol) at room temperature. The mixture was stirred at the same temperature for 10 h. Then, additional TBAF (1.0 M in THF, 132 μL, 132 μmol) was added to the reaction mixture, which was stirred overnight. The mixture was added H_2O and extracted with ether. The combined organic extracts were dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (MeOH-$CHCl_3$ = 1:50 to 1:10) to give β-CP-RvE2, β-**2** (9.2 mg, 26.4 μmol, 50% for 2 steps) as a colorless oil.

β-CP-RvE2, β-**2**: $[\alpha]_D^{18}$ –9.8 (*c* 0.46, MeOH); IR (neat) ν 3357, 2962, 2927, 1712, 984, 952 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 6.52 (dd, *J* = 15.6, 10.8 Hz, 1H), 6.50 (dd, *J* = 15.6, 10.8 Hz, 1H), 5.99 (dd, *J* = 11.2, 10.8 Hz, 2H), 5.64 (dd, *J* = 15.6, 6.6 Hz, 1H), 5.63 (dd, *J* = 15.6, 6.6 Hz, 1H), 5.52 (m,

2H), 4.10 (dt, *J* = 6.4, 6.4 Hz, 1H), 4.01 (dt, *J* = 6.4, 6.4 Hz, 1H), 2.30 (t, *J* = 7.4 Hz, 2H), 2.30-2.15 (m, 4H), 1.72-1.48 (m, 6H), 0.90 (t, *J* = 7.6 Hz, 3H), 0.81 (m, 2H), 0.66 (ddd, *J* = 8.4, 8.4, 4.8 Hz, 1H), –0.10 (ddd, *J* = 5.4, 5.4, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 177.5, 137.19, 137.17, 132.7, 132.5, 129.02, 128.97, 126.6, 74.7, 72.9, 37.8, 34.8, 31.2, 28.0, 22.2, 17.0, 11.2, 10.2; LRMS (ESI) m/z 347 [M-H]; HRMS (ESI) calcd for $C_{21}H_{31}O_4$ [M-H] 347.2228, found 347.2233.



(*Z*)-7-(Triethylsilyl)hept-3-en-6-yn-1-ol (S10)

To a stirred solution of CuI (3.68 g, 19.3 mmol), Cs_2CO_3 (6.29 g, 19.3 mmol) and NaI (2.89 g, 19.3 mmol) was added **8** (1.45 mL, 19.3 mmol) in DMF (20 mL) at room temperature. The mixture was stirred at the same temperature for 20 min and added the solution of (3-bromo-1-propynyl)triethylsilane (3.07 g, 16.1 mmol) in DMF (12 mL). The reaction mixture was stirred overnight. The resulting solution was quenched by addition of sat. NH_4Cl aq and extracted with Et_2O. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:20) to give **16** (2.30 g, 10.4 mmol, 64%) as a colorless oil.

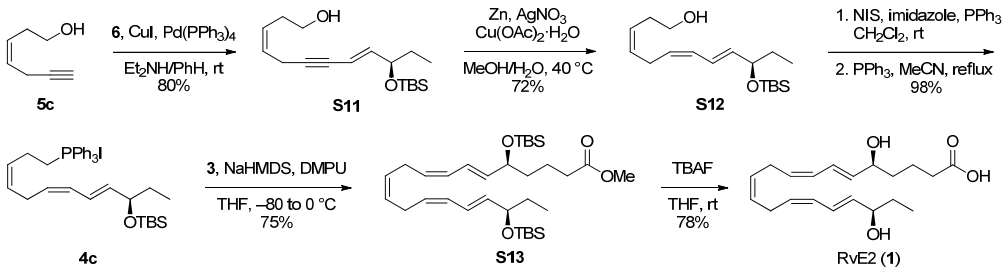
To a suspension of $Ni(OAc)_2 \cdot 4H_2O$ (3.16 g, 12.7 mmol) in MeOH (90 mL) was added $NaBH_4$ (798 mg, 21.1 mmol) and ethylenediamine (4.8 mL, 71.9 mmol) at room temperature under Ar atmosphere. To the reaction mixture was added a solution of **16** (9.37 g, 42.2 mmol) in MeOH (16 mL) and the mixture was stirred at the same temperature under H_2 atmosphere overnight and filtered with Celite. The filtrate was concerned in reduced pressure. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:25 to 1:4) to give **S10** (7.87 g, 35.5 mmol, 84%) as a colorless oil.

S10: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.67-5.61 (m, 1H), 5.53-5.47 (m, 1H), 3.68 (t, *J* = 6.4 Hz, 2H), 2.99 (d, *J* = 7.2 Hz, 2H), 2.36 (dt, *J* = 6.8, 6.4 Hz, 2H), 0.98 (t, *J* = 8.0 Hz, 1H), 0.57 (q, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 127.4, 127.3, 106.0, 81.7, 62.0, 30.7, 18.5, 7.4, 4.4; LRMS (ESI) m/z 247 $[M+Na]^+$; HRMS (ESI) calcd for $C_{13}H_{24}ONaSi$ $[M+Na]^+$ 247.1489, found 247.1491.

(*Z*)-Hept-3-en-6-yn-1-ol (5c)

To a stirred solution of **S9** (703 mg, 3.14 mmol) in THF (10 mL) was added TBAF (1.0 M in THF, 1.57 mL, 1.57 mmol) at room temperature. The mixture was stirred at the same temperature. After the reaction was completed, the mixture was quenched by addition of sat. NH_4Cl aq and extracted with ether. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:10) to give **5c** (276 mg, 2.51 mmol, 80%) as a colorless oil.

5c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.67-5.61 (m, 1H), 5.56-5.50 (m, 1H), 3.68 (t, *J* = 6.4 Hz, 2H), 2.99 (br d, *J* = 6.8 Hz, 2H), 2.36 (dt, *J* = 13.8, 6.8 Hz, 2H), 2.00 (t, *J* = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 127.8, 126.5, 82.5, 68.2, 61.7, 30.6, 16.9; LRMS (EI) m/z 109 $[M+H]^+$; HRMS (EI) calcd for C_7H_9O $[M+H]^+$ 109.0653, found 109.0652.



(*R*,3*Z*,8*E*)-10-((*tert*-Butyldimethylsilyl)oxy)dodeca-3,8-dien-6-yn-1-ol (S11)

To a stirred solution of **5c** (66 mg, 600 μmol) and **6** (196 mg, 600 μmol) in benzene (4 mL) was added Et_2NH (0.4 mL), CuI (57 mg, 300 μmol) and $Pd(PPh_3)_4$ (69 mg, 60 μmol) at room temperature. The mixture was stirred at the same temperature for 1.5 h, quenched by addition of H_2O and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:10) to give **S11** (148 mg, 481 μmol, 80%) as a yellow oil.

S11: $[\alpha]_D^{19}$ +28.2 (*c* 0.53, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (dd, *J* = 16.0, 5.6 Hz, 1H), 5.68-5.59 (m, 2H), 5.54-5.48 (m, 1H), 4.07 (dt, *J* = 5.6, 5.6 Hz, 1H), 3.68 (td, *J* = 6.4, 6.0 Hz, 2H), 3.10 (br d, *J* = 6.8 Hz, 2H), 2.36 (dt, *J* = 6.8, 6.4 Hz, 2H), 1.49 (qd, *J* = 7.6, 5.6 Hz, 2H), 1.41 (t, *J* = 6.0 Hz, 1H), 0.90 (s, 9H), 0.86 (t, *J* = 7.6 Hz, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 127.3, 108.8, 87.9, 78.8, 73.6, 61.9, 30.7, 25.8, 18.2, 17.9, 9.3, –4.6, –4.9; LRMS (ESI) m/z 331 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{32}O_2NaSi$ $[M+Na]^+$ 331.2064, found 331.2063.

(*R*,3*Z*,6*Z*,8*E*)-10-((*tert*-Butyldimethylsilyl)oxy)dodeca-3,6,8-trien-1-ol (S12)

To a stirred solution of Zn powder (4.52 g, 69.1 mmol) in H_2O (25 mL) was added $Cu(OAc)_2 \cdot H_2O$ (452 mg, 2.26 mmol) at room temperature. The mixture was stirred at the same temperature for 15

min. To the mixture was added $AgNO_3$ (452 mg, 2.66 mmol) and stirred at the same temperature for 30 min. To the reaction mixture was added **S11** (113 mg, 367 μmol) in MeOH (25 mL), stirred at 40 °C for 24 h, filtrated through Celite pad and the filtrate was concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:8) to give **S12** (82 mg, 265 μmol, 72%) as a colorless oil and **S11** (12 mg, 39 μmol, 11%) as a colorless oil.

S12: $[\alpha]_D^{19}$ –16.1 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.46 (dd, *J* = 15.6, 11.6 Hz, 1H), 6.00 (dd, *J* = 11.2, 11.2 Hz, 1H), 5.66 (dd, *J* = 15.6, 6.0 Hz, 1H), 5.60-5.53 (m, 1H), 5.46-5.40 (m, 1H), 5.38-5.32 (m, 1H), 4.11 (dt, *J* = 6.4, 6.0 Hz, 1H), 3.66 (br t, *J* = 6.8 Hz, 2H), 3.01-2.92 (m, 2H), 2.37 (dt, *J* = 7.0, 6.8 Hz, 2H), 1.56-1.48 (m, 2H), 0.91 (s, 9H), 0.88 (t, *J* = 7.6 Hz, 3H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 130.6, 128.8, 128.3, 125.9, 124.0, 74.2, 62.1, 31.1, 30.8, 26.1, 25.8, 18.2, 9.6, –4.4, –4.8; LRMS (ESI) m/z 333 $[M+Na]^+$; HRMS (ESI) calcd for $C_{18}H_{34}O_2NaSi$ $[M+Na]^+$ 333.2220, found 333.2221.

((*R*,3*Z*,6*Z*,8*E*)-10-((*tert*-Butyldimethylsilyl)oxy)dodeca-3,6,8-trien-1-yl)iodotriphenylphosphorane (4c)

To a stirred solution of **S12** (76 mg, 245 μmol), PPh_3 (643 mg, 2.45 mmol), imidazole (167 mg, 2.45 mmol) in DCM (2 mL) was added NIS (386 mg, 1.72 mmol) at 0 °C under dark. The mixture was stirred at room temperature for 1 hr, quenched by addition of $Na_2S_2O_3$ aq and extracted with $CHCl_3$. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:20) to give crude iodide as a brown oil.

To a stirred solution of crude iodide in MeCN (6 mL) was added PPh_3 (193 mg, 735 μmol) at room temperature. The mixture was refluxed overnight and cooled to room temperature. The solution was concentrated and purified by silica gel column chromatography (MeOH-$CHCl_3$ = 0:1 to 1:6) to give **4c** (164 mg, 240 μmol, 98% for 2 steps) as an orange amorphous.

4c: $[\alpha]_D^{21}$ –6.0 (*c* 0.30, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.80 (m, 9H), 7.74-7.70 (m, 6H), 6.30 (dd, *J* = 15.6, 11.6 Hz, 1H), 5.94 (dd, *J* = 11.2, 10.8 Hz, 1H), 5.67-5.62 (m, 2H), 5.44-5.37 (m, 1H), 5.66 (dt, *J* = 10.8, 7.6 Hz, 1H), 4.08 (dt, *J* = 6.0, 6.0 Hz, 1H), 3.88-3.81 (m, 2H), 2.71 (dd, *J* = 7.6, 7.2 Hz, 2H), 2.53-2.45 (m, 2H), 1.50 (dq, *J* = 7.2, 7.2 Hz, 1H), 0.88 (s, 9H), 0.87 (t, *J* = 7.2 Hz, 3H), 0.04 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 134.90, 134.86, 133.3, 133.2, 130.3, 130.2, 129.8, 128.5, 127.5, 126.4, 126.2, 123.3, 117.8, 117.0, 77.2, 73.7, 30.7, 25.51, 25.46, 23.1, 22.6, 20.0, 19.9, 17.8, 9.3, –4.7, –5.1; LRMS (ESI) m/z 555 $[M-I]^+$; HRMS (ESI) calcd for $C_{36}H_{48}OPSi$ $[M-I]^+$ 555.3212, found 555.3207.

(5*S*,6*E*,8*Z*,11*Z*,14*Z*,16*E*,18*R*)-Methy l5,18-bis((*tert*-butyldimethylsilyl)oxy)icosa-6,8,11,14,16-pentaenoate (S13)

To a stirred solution of **4c** (37 mg, 54.3 μmol) and DMPU (44 μL, 362 μmol) in THF (0.2 mL) was added NaHMDS (1.9 M in toluene, 27 μL, 50.6 μmol) at –80 °C. The resulting solution was stirred at –80 °C for 1 h. After **3** (10.9 mg, 36.2 μmol) in THF (0.3 mL) was added to the reaction mixture, the mixture was stirred at –80 °C for 1 h. The reaction mixture was warmed to room temperature overnight, quenched by addition of sat. NH_4Cl aq and extracted with AcOEt. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (AcOEt-hexane = 1:20) to give **S13** (15.8 mg, 27.4 μmol, 75%) as a colorless oil.

S13: $[\alpha]_D^{20}$ –2.4 (*c* 0.79, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (dd, *J* = 15.6, 11.6 Hz, 2H), 6.00 (dd, *J* = 11.6, 11.2 Hz, 1H), 5.99 (dd, *J* = 11.6, 11.2 Hz, 1H), 5.65 (dd, *J* = 15.6, 6.8 Hz, 1H), 5.64 (dd, *J* = 15.6, 6.8 Hz, 1H), 5.41-5.32 (m, 4H), 4.19 (dt, *J* = 6.4, 5.8 Hz, 1H), 4.10 (dt, *J* = 6.0, 6.0 Hz, 1H), 3.66 (s, 3H), 2.97-2.94 (m, 4H), 2.32 (t, *J* = 7.6 Hz, 2H), 1.72-1.61 (m, 2H), 1.55-1.48 (m, 4H), 0.91 (s, 9H), 0.90 (s, 9H), 0.88 (t, *J* = 8.0 Hz, 3H), 0.058 (s, 3H), 0.056 (s, 3H), 0.037 (s, 3H), 0.031 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 137.3, 136.9, 129.3, 128.9, 128.4, 128.25, 128.19, 128.1, 124.4, 124.1, 74.3, 72.7, 51.5, 37.6, 34.0, 31.1, 26.0, 25.88, 25.86, 20.7, 18.3, 18.2, 9.7, –4.3, –4.4, –4.77, –4.80; LRMS (ESI) m/z 599 $[M+Na]^+$; HRMS (ESI) calcd for $C_{33}H_{60}O_4NaSi_2$ $[M+Na]^+$ 599.3922, found 599.3924.

(5*S*,6*E*,8*Z*,11*Z*,14*Z*,16*E*,18*R*)-5,18-Dihydroxyicosa-6,8,11,14,16-pentaenoic acid (RvE2, 1)

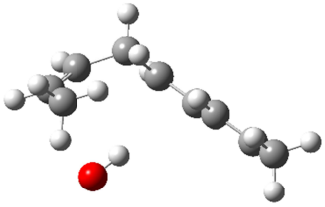
To a stirred solution of **S12** (10 mg, 17.4 μmol) in THF (1 mL) was added TBAF (1.0 M in THF, 104 μL, 104 μmol) at room temperature. The mixture was stirred at the same temperature. After the reaction was completed, the mixture was added H_2O and extracted with ether. The combined organic extracts were dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (MeOH-$CHCl_3$ = 1:80) to give RvE2, **1** (4.5 mg, 13.5 μmol, 78%) as a colorless oil.

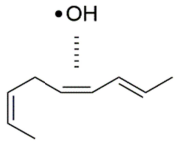
1: $[\alpha]_D^{18}$ –6.5 (*c* 0.79, MeOH); IR (neat) ν 3347, 2962, 2926, 1710, 984, 953 cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD) δ 6.56 (dd, *J* = 15.0, 11.0 Hz, 1H), 6.55 (dd, *J* = 15.0, 11.0 Hz, 1H), 6.00 (dd, *J* = 11.0, 11.0 Hz, 2H), 5.66 (dd, *J* = 15.0, 6.5 Hz, 1H), 5.65 (dd, *J* = 15.0, 6.5 Hz, 1H), 5.42-5.34 (m, 4H), 4.12 (dt, *J* = 6.5, 6.5 Hz, 1H), 4.02 (dt, *J* = 6.5, 6.5 Hz, 1H), 3.00-2.97 (m, 4H), 2.31 (t, *J* = 7.3 Hz, 2H), 1.72-1.48 (m, 6H), 0.91 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 177.5, 137.70, 137.67, 130.6, 130.5, 129.45, 129.39, 129.10, 129.08, 126.4, 74.7, 72.9, 37.7, 34.8, 31.2, 27.0, 22.2, 10.2; LRMS (ESI) m/z 357 $[M+Na]^+$; HRMS (ESI) calcd for $C_{20}H_{30}O_4Na$ $[M+Na]^+$ 357.2036, found 357.2039.

Computational calculation

All geometries were optimized in the gas phase without any constraint by The UB3LYP/6-31G*, followed by the UBHandHLYP/6-311G+(d,p) at final step using Gaussin09W software. Frequency analysis was performed after the optimization to transition states (only one imaginary frequency). Final single point energies in the gas phase were calculated by UBHandHLYP/6-311G+(d,p) method using same basis sets above. All energies in figure 3 were corrected by zero-point energy.

Intermediate **A**





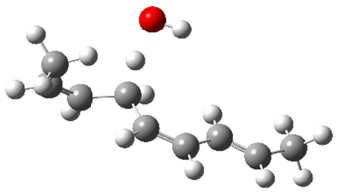
Electronic Energy = -426.845589 a.u.

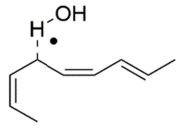
Zero-point Energy = 0.221513 a.u.

Lowest Frequency Vibration = 18.9836 cm^{-1}

C	-2.83366900	0.59586700	-0.17503200
H	-3.76013000	0.68895500	0.37421200
C	-2.36461100	-0.63599800	-0.35876600
H	-2.93761100	-1.45490800	0.05476900
C	-1.09423000	-1.04017700	-1.05665700
H	-0.61442700	-0.18655300	-1.51925800
H	-1.34465500	-1.73069400	-1.86476500
C	-0.16040200	-1.74186800	-0.11035300
H	-0.55865900	-2.63887900	0.34382200
C	1.08030700	-1.37922300	0.23233300
H	1.60623100	-2.00925800	0.93691900
C	1.82686100	-0.22361800	-0.24285300
H	1.34747100	0.43840900	-0.94882400
C	3.06885500	0.05527300	0.15308800
H	3.54725000	-0.60976100	0.86105300
C	3.87298300	1.22642100	-0.30215700
H	3.32023700	1.83923300	-1.00826800
H	4.15914500	1.85375600	0.54074700
H	4.79610200	0.90359800	-0.78135800
C	-2.23921900	1.88957700	-0.63051200
H	-2.93908000	2.42573800	-1.26933900
H	-2.03209300	2.52603200	0.22686100
H	-1.31455400	1.76168700	-1.18237800
O	-1.19507200	0.48042300	2.30088000
H	-0.65589800	-0.12826500	1.77423100

Transition state **A'**





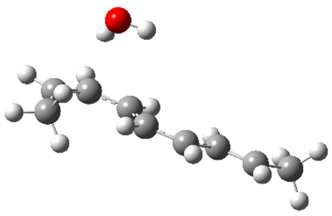
Electronic Energy = -426.834739 a.u.

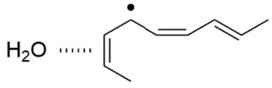
Zero-point Energy = 0.217337 a.u.

Imaginary Frequency Vibration = -641.0181 cm^{-1}

C	3.30250700	-0.69702600	0.48086900
H	4.10608000	-1.25406600	0.94289900
C	2.10903000	-0.75824900	1.06490300
H	2.01788600	-1.34502700	1.96818100
C	0.84532100	-0.10171600	0.59989700
H	1.11237000	0.99367700	0.30143100
H	0.16128900	0.02859400	1.43148800
C	0.18733100	-0.74192300	-0.56613000
H	0.85193300	-1.19902300	-1.28337300
C	-1.13003300	-0.78135100	-0.81929400
H	-1.45019600	-1.27891900	-1.72406300
C	-2.19097600	-0.21900100	-0.00513900
H	-1.91906000	0.27347900	0.91735500
C	-3.48213900	-0.27537400	-0.34130100
H	-3.75338300	-0.76712800	-1.26693900
C	-4.60433800	0.28915800	0.46291700
H	-4.24480300	0.76486000	1.37071000
H	-5.16295800	1.02790500	-0.11014200
H	-5.31220000	-0.48926000	0.74430600
C	3.67050000	0.06681700	-0.75070500
H	4.54161400	0.69070400	-0.56011000
H	3.94320600	-0.61508200	-1.55591100
H	2.87255500	0.71290300	-1.09721700
O	1.20746000	2.40948100	-0.04872700
H	0.33276500	2.49251300	-0.44490400

Intermediate **A”**





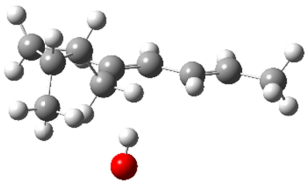
Electronic Energy = -426.908424 a.u.

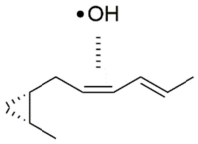
Zero-point Energy = 0.220711 a.u.

Lowest Frequency Vibration = 18.5441 cm^{-1}

C	-3.10368500	-0.89807500	-0.37504900
H	-4.01087700	-1.08165800	-0.93089600
C	-1.96181100	-0.82442600	-1.11154100
H	-2.08735800	-0.99341200	-2.17167200
C	-0.61174000	-0.57927900	-0.72155800
H	-2.49870100	1.66576400	-0.68527700
H	0.11108500	-0.70187100	-1.51316100
C	-0.13166600	-0.17502300	0.52440500
H	-0.84490800	0.00562700	1.30984200
C	1.19700300	0.04526600	0.85838400
H	1.39676800	0.38195500	1.86519100
C	2.33807100	-0.12838300	0.01731200
H	2.18404500	-0.48020100	-0.99277400
C	3.60158100	0.11922000	0.41551200
H	3.76379400	0.46935100	1.42672300
C	4.81441500	-0.05448500	-0.43372000
H	4.55798300	-0.40863600	-1.42806900
H	5.35812700	0.88380600	-0.53771900
H	5.50605800	-0.76830200	0.01227000
C	-3.25615400	-0.78387500	1.10844700
H	-4.23553200	-1.13557400	1.41624300
H	-2.50796900	-1.37156400	1.63575800
H	-3.16252000	0.24868700	1.44544100
O	-2.42027400	2.53463900	-0.29402200
H	-1.48388300	2.68327200	-0.19287900

Intermediate **B**





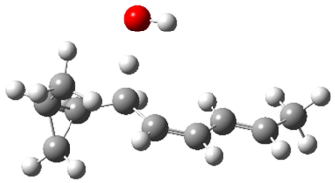
Electronic Energy = -466.126499 a.u.

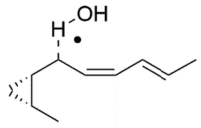
Zero-point Energy = 0.251713 a.u.

Lowest Frequency Vibration = 13.9091 cm^{-1}

C	3.34783200	-0.85180200	0.20064000
C	2.00800400	-0.74025300	-0.47024900
C	0.86983400	0.07891000	0.10053000
H	1.26841800	0.97369300	0.57702700
H	0.36673400	-0.48551300	0.88128100
C	-0.09342700	0.49528500	-0.96984300
H	0.34889100	1.04473200	-1.78967300
C	-1.40650400	0.24427900	-1.03583900
H	-1.94311200	0.61298900	-1.89980800
C	-2.21538800	-0.48152700	-0.06645700
H	-1.72135500	-0.89734600	0.79934600
C	-3.53134200	-0.65291500	-0.19633700
H	-4.02433700	-0.23240900	-1.06378700
C	-4.40070200	-1.38728800	0.76817000
H	-3.82758200	-1.77731700	1.60427500
H	-5.17988400	-0.73730800	1.16348800
H	-4.90439900	-2.22156900	0.28208200
C	3.67710800	-0.16435400	1.50119300
H	3.25396000	0.83430000	1.55569300
H	3.30489300	-0.72990000	2.35320500
H	4.75441400	-0.06476900	1.61440800
O	-1.44422500	3.18393400	0.63745400
H	-1.33348800	2.34982700	0.15238800
C	3.21174000	-0.07488400	-1.07643600
H	3.63005700	-0.47740700	-1.98494500
H	3.27063300	1.00138800	-1.00301100
H	3.81429200	-1.82139600	0.09924100
H	1.67272600	-1.63618200	-0.97307100

Transition State **B'**





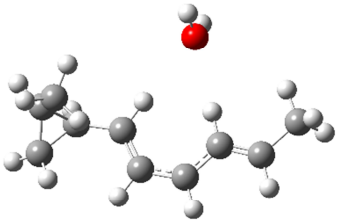
Electronic Energy = -466.111658 a.u.

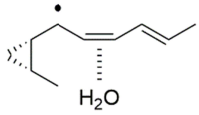
Zero-point Energy = 0.248182 a.u.

Imaginary Frequency Vibration = -503.2186 cm^{-1}

C	-3.21900500	-0.21070000	-0.28405500
H	-4.05952900	0.02687500	-0.92038500
C	-1.93153200	-0.42543800	-1.03525500
H	-2.03620000	-0.32573100	-2.10477200
C	-0.57440000	0.05237400	-0.56734900
H	-0.69254000	1.19123000	-0.37643600
H	0.11426600	0.02718100	-1.40540900
C	0.04042700	-0.55827600	0.63475400
H	-0.62499200	-0.92112200	1.40095400
C	1.35557100	-0.66580800	0.87995100
H	1.65411100	-1.12035200	1.81434300
C	2.44284600	-0.22838000	0.02420400
H	2.19512100	0.22492400	-0.92460400
C	3.73043000	-0.35159600	0.35552300
H	3.97758500	-0.80157000	1.30882400
C	4.87993900	0.08467800	-0.48898600
H	4.54401200	0.52504900	-1.42323500
H	5.49146900	0.81938800	0.03297500
H	5.53206600	-0.75539900	-0.72395500
C	-3.27578500	0.48074900	1.05374700
H	-4.20934800	0.24567800	1.56058600
H	-2.46541800	0.17903700	1.70962500
H	-3.21242300	1.55898700	0.93435100
O	-0.69085300	2.66253500	-0.17500200
H	0.07493400	2.68222000	0.41014100
C	-2.67279000	-1.59538000	-0.44072200
H	-3.15927000	-2.28145100	-1.11574200
H	-2.25122700	-2.06856700	0.43187600

Intermediate **B”**





Electronic Energy = -466.180374 a.u.

Zero-point Energy = 0.250158 a.u.

Lowest Frequency Vibration = 17.6480 cm^{-1}

C	-3.28775200	0.44135900	0.22844600
H	-4.03404200	1.17318500	-0.04642200
C	-2.28895500	0.11828400	-0.86603100
H	-2.46707600	0.66895900	-1.78076300
C	-0.85188100	-0.10171100	-0.59288400
H	1.06461800	3.40136200	0.26783600
H	-0.23611000	0.78602900	-0.60695300
C	-0.27143800	-1.31490800	-0.35701800
H	-0.91155600	-2.18526200	-0.38196500
C	1.09140700	-1.56869000	-0.09019900
H	1.37591700	-2.60090400	0.05487200
C	2.12212200	-0.60056900	0.00429300
H	1.86157000	0.43938500	-0.13285900
C	3.41897400	-0.90318300	0.25900200
H	3.69262300	-1.94126200	0.39835900
C	4.51604200	0.10229200	0.36414800
H	4.14096300	1.11024300	0.21075100
H	4.99600300	0.06415800	1.34222200
H	5.29746700	-0.08499700	-0.37256800
C	-2.88674900	0.48475800	1.67869800
H	-3.73950100	0.27228600	2.32055600
H	-2.11269200	-0.24533200	1.89593700
H	-2.50030800	1.46511200	1.95105500
O	1.27009300	2.79643600	-0.44020500
H	1.44049700	3.33037400	-1.21178800
C	-3.36087200	-0.86545900	-0.50088200
H	-3.07122900	-1.74658200	0.04981700
H	-4.16328100	-1.03128800	-1.20188900

Oxidative stability

1, α-**2**, and β-**2** in ethanol (1 mg/mL) were sampled and evaporated. Then, the compounds (10-20 μg) were stayed while exposing to air in Eppendorf Tubes® and analyzed by HPLC at various time points.

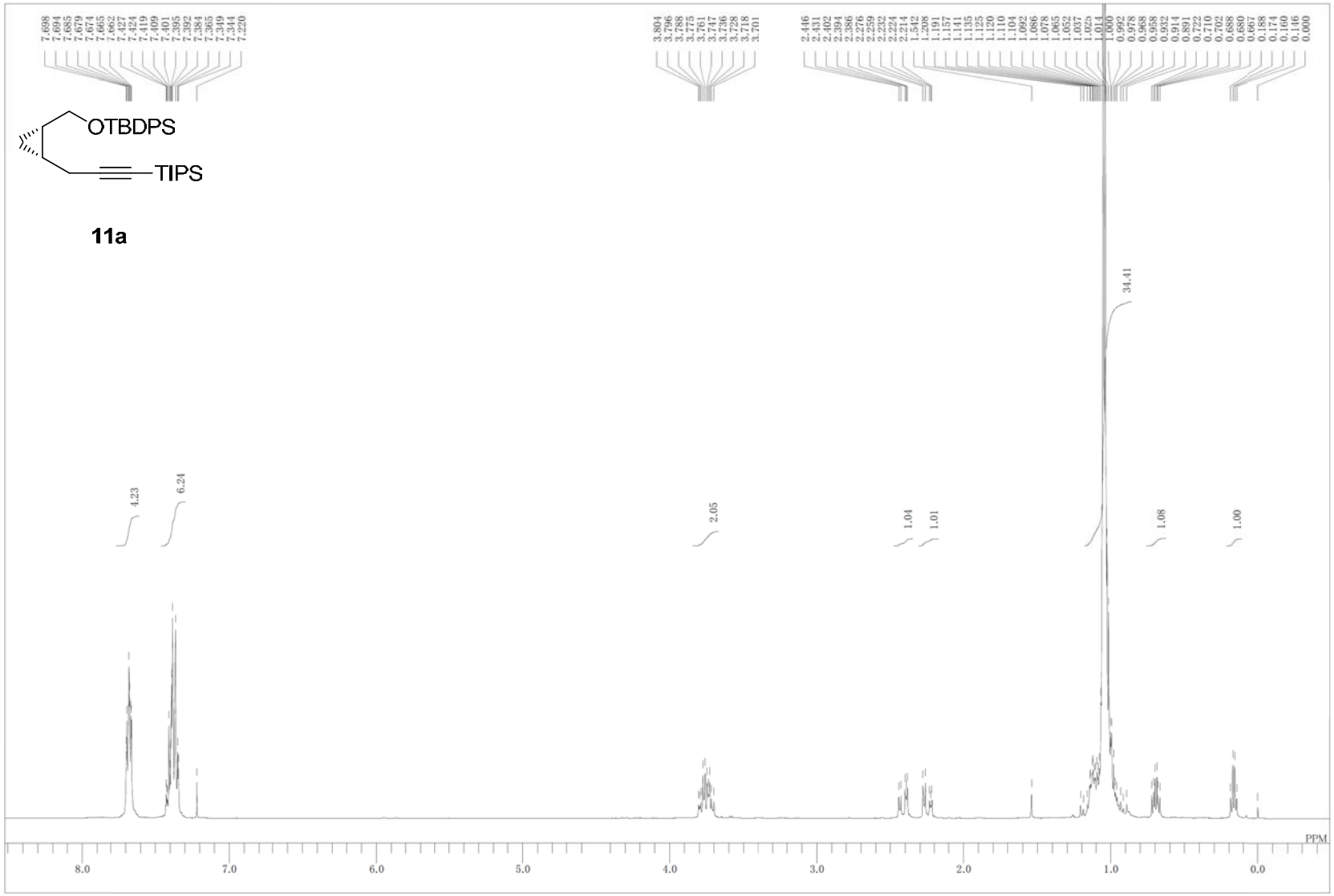
HPLC conditions: column; Mightysil RP-8 GP, eluent; MeOH : H_2O : AcOH = 65 : 35 : 0.01, flow rate; 1.0 mL/min, detection; UV 250 nm, retention time; 14.2 min for **1**, 20.3 min for α-**2**, and 20.9 min for β-**2**.

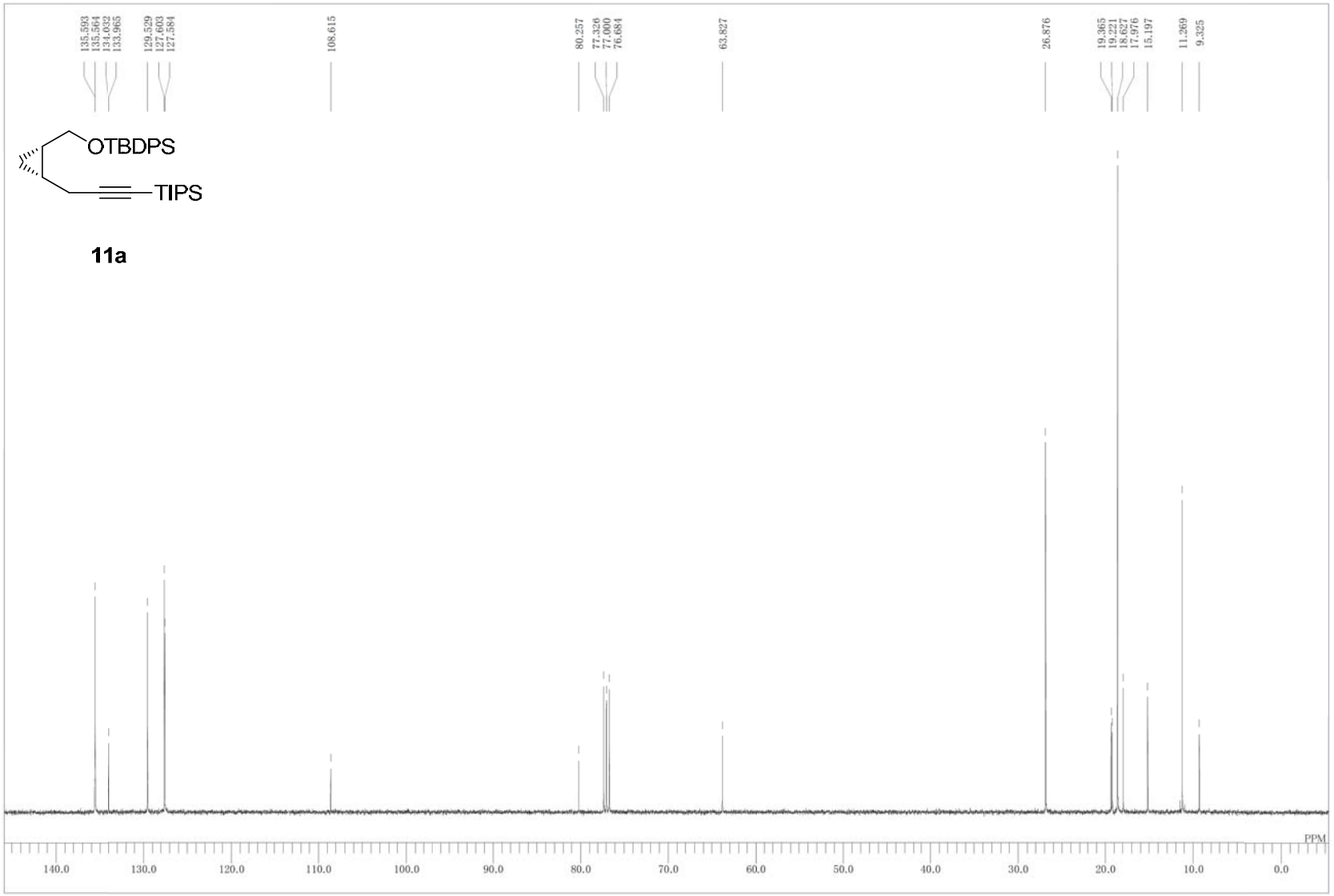
Murine peritonitis evaluation

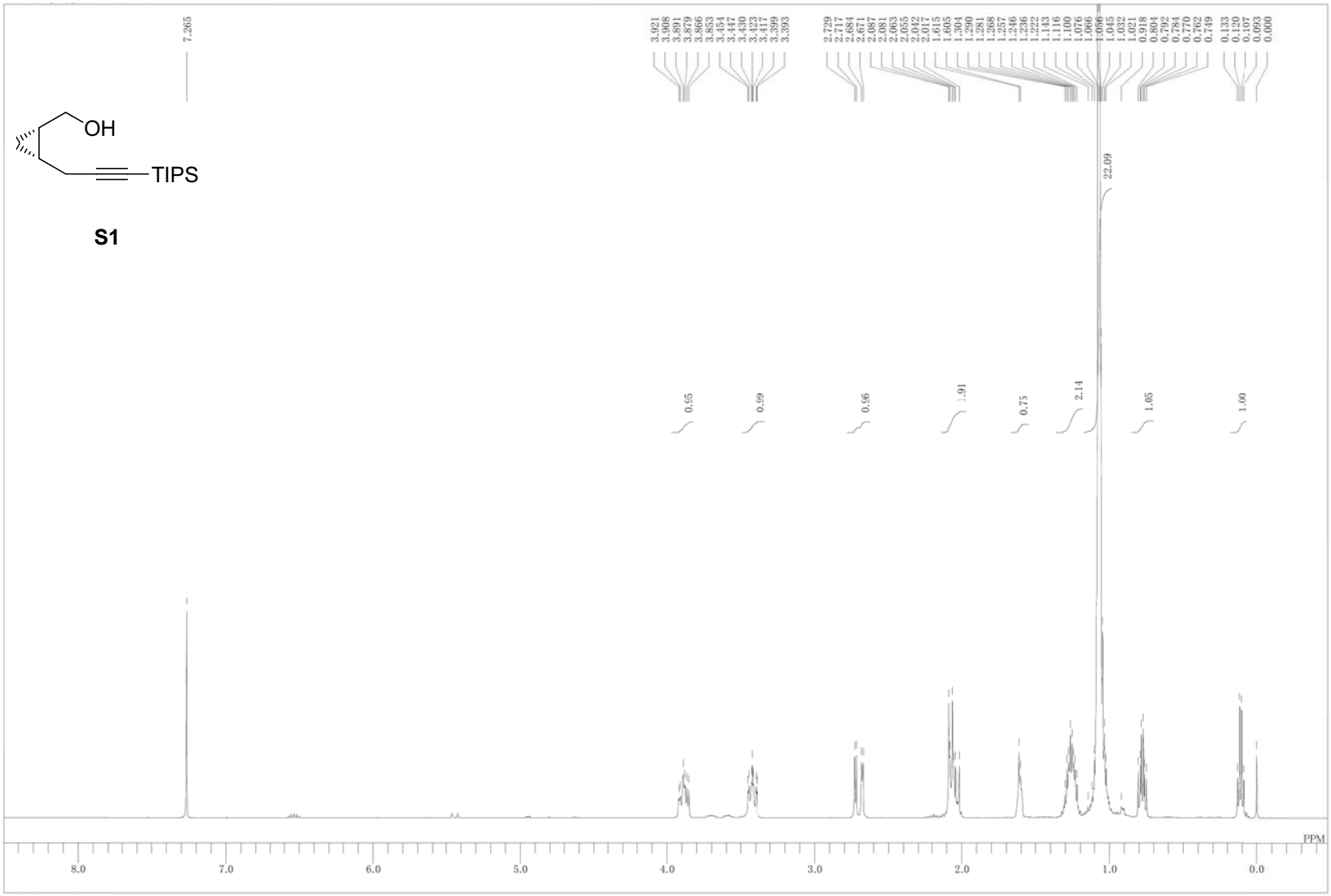
Male BALB/c mice (6–7 weeks; Japan SLC, Shizuoka, Japan) were used. Heat-killed *Propionibacterium acnes* (*P. acnes*; 500 μg per mouse) was injected intraperitoneally. At 12 h after *P.acnes* injection, three different doses (300 fg, 30 pg or 3 ng per mouse) of RvE2, α-CP-RvE2, β-CP-RvE2 or vehicle alone was administered intraperitoneally. At 24 h after *P. acnes* injection, peritoneal exudate cells (PECs) were collected and counted. Results were expressed as percentage inhibition of *P. acnes*-induced increase in the number of PECs compared with vehicle alone. All animal procedures were conducted in accordance with the Hokkaido University animal ethics committee.

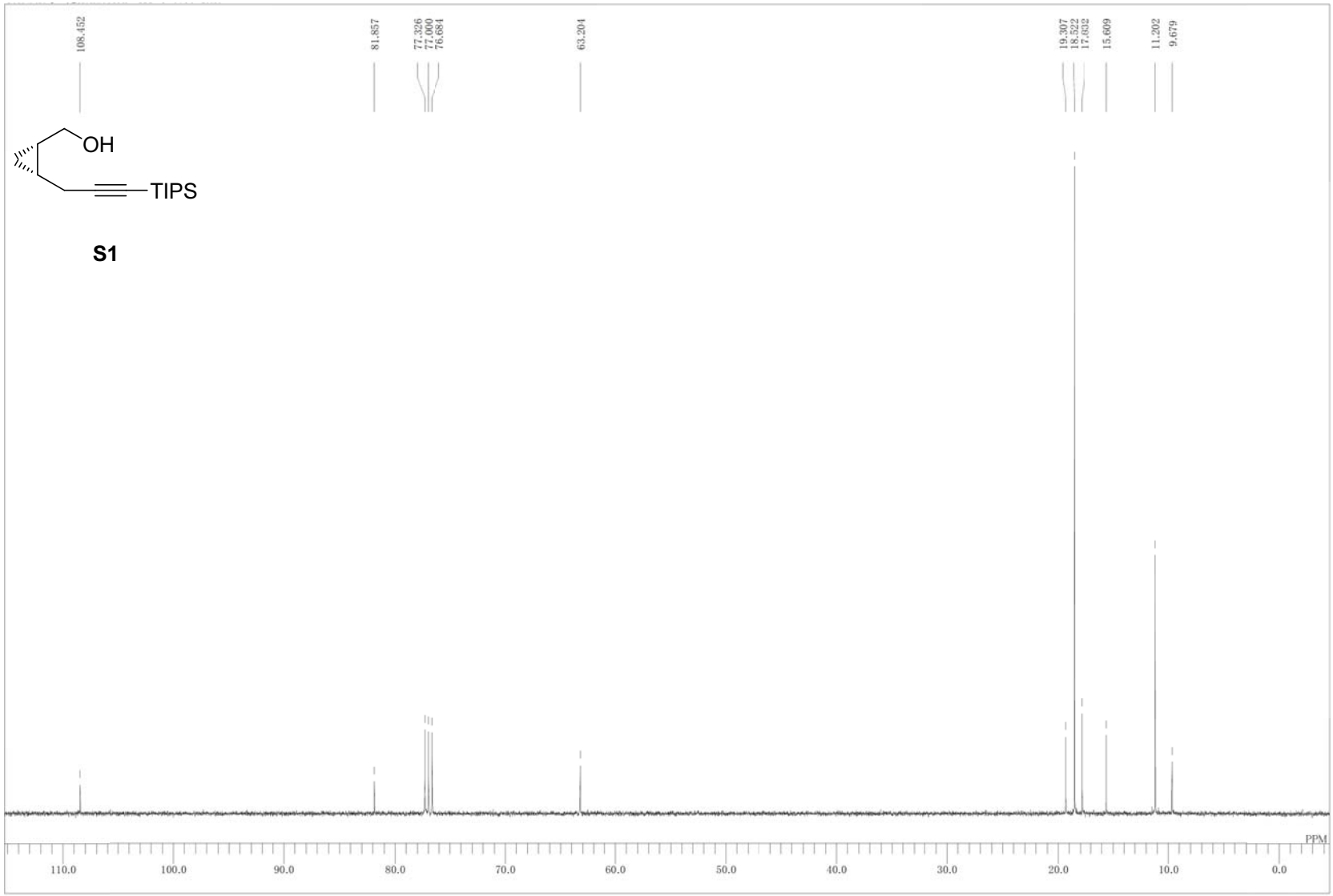
References

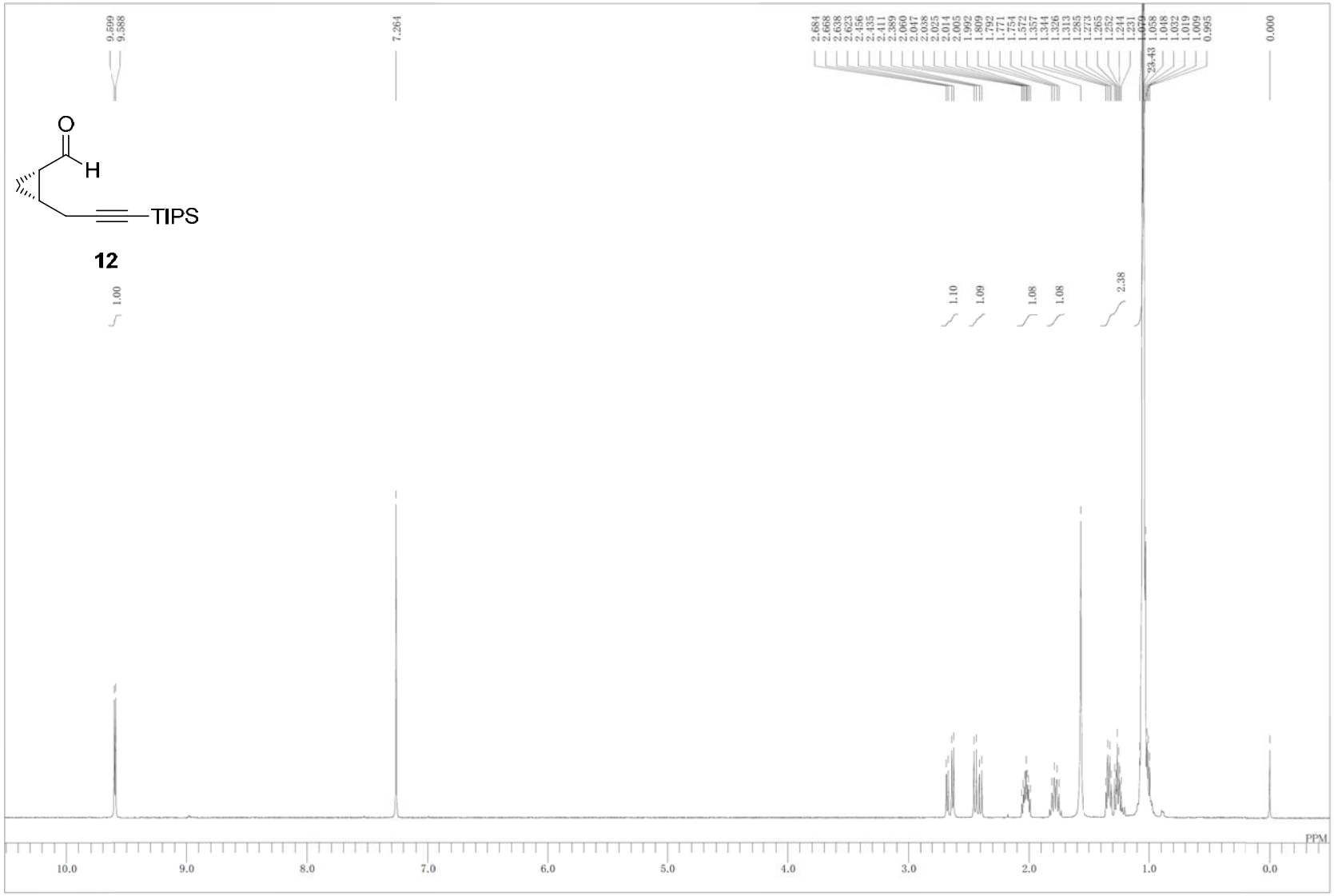
1. K. Götz, J. C. Liermann, E. Thines, H. Anke, T. Opatz, *Org. Biomol. Chem*. **2010**, *8*, 2123-2130.
2. Y. Kosaki, N. Ogawa, Y. Kobayashi, *Tetrahedron Lett.* **2010**, *51*, 1856-1859.
3. M. Allard, K. Barnes, X. Chen, Y.-Y. Cheung, B. Duffy, C. Heap, J. Inthavongsay, M. Johnson, R. Krishnamoorthy, C. Manley, S. Steffke, D. Varughese, R. Wang, Y. Wang, C. E. Schwartz, *Tetrahedron Lett*. **2011**, *52*, 2623-2626.

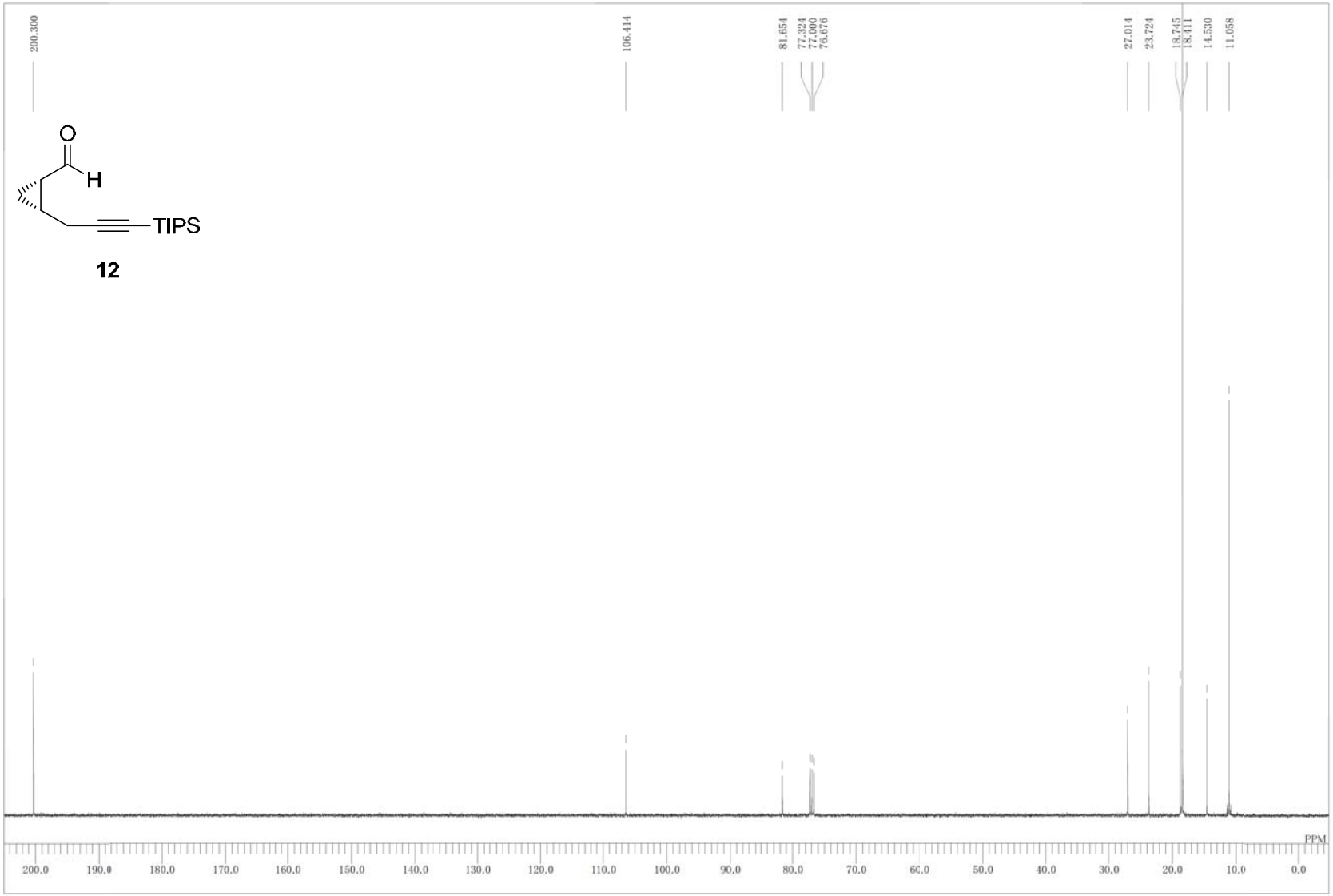

OTBDPS
TIPS
11a
PPM

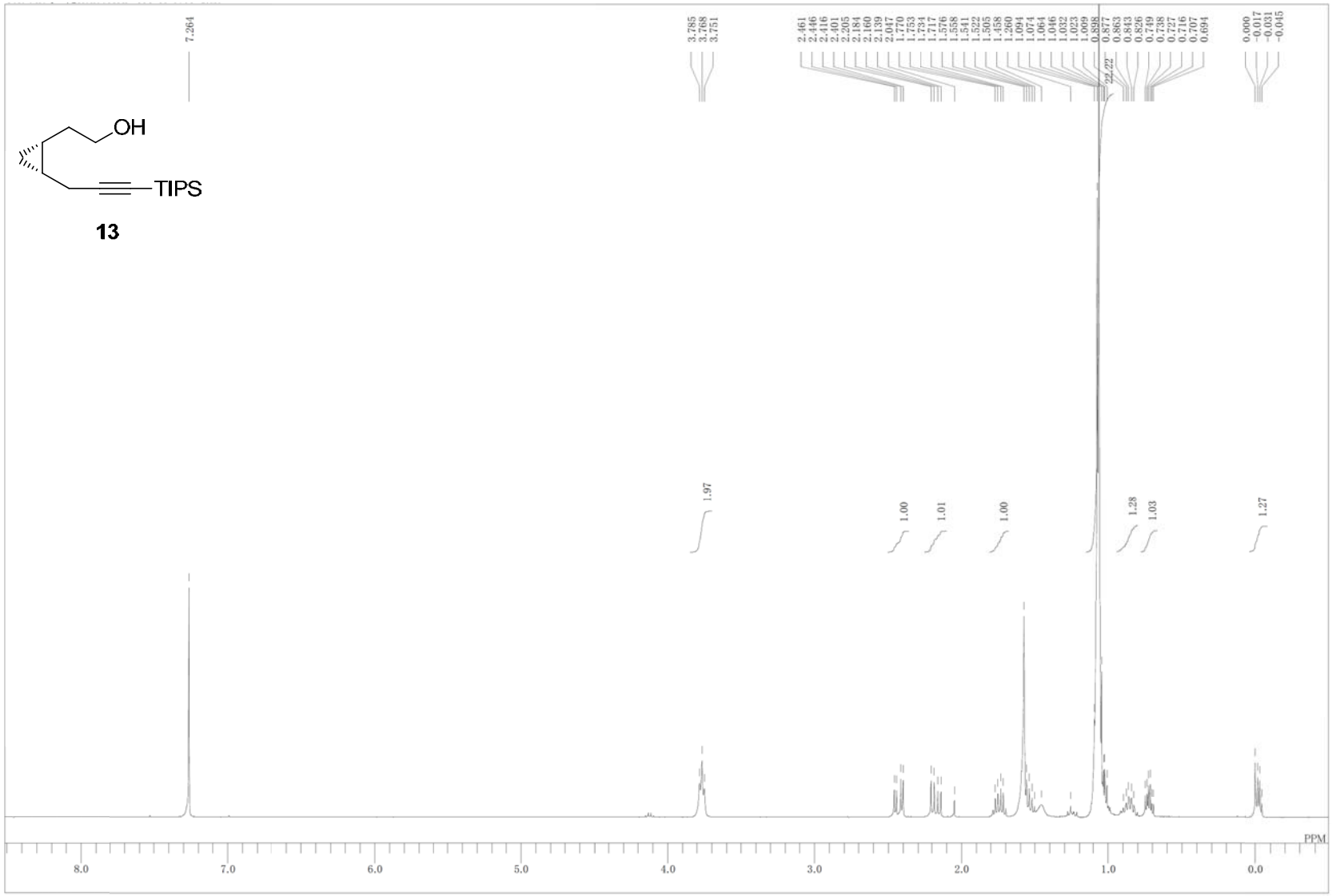

135.593
135.564
134.032
133.965
129.529
127.603
127.584
108.615
80.257
77.326
77.000
76.684
63.827
26.876
19.365
19.221
18.627
17.976
15.197
11.269
9.325
OTBDPS
TIPS
11a
PPM
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

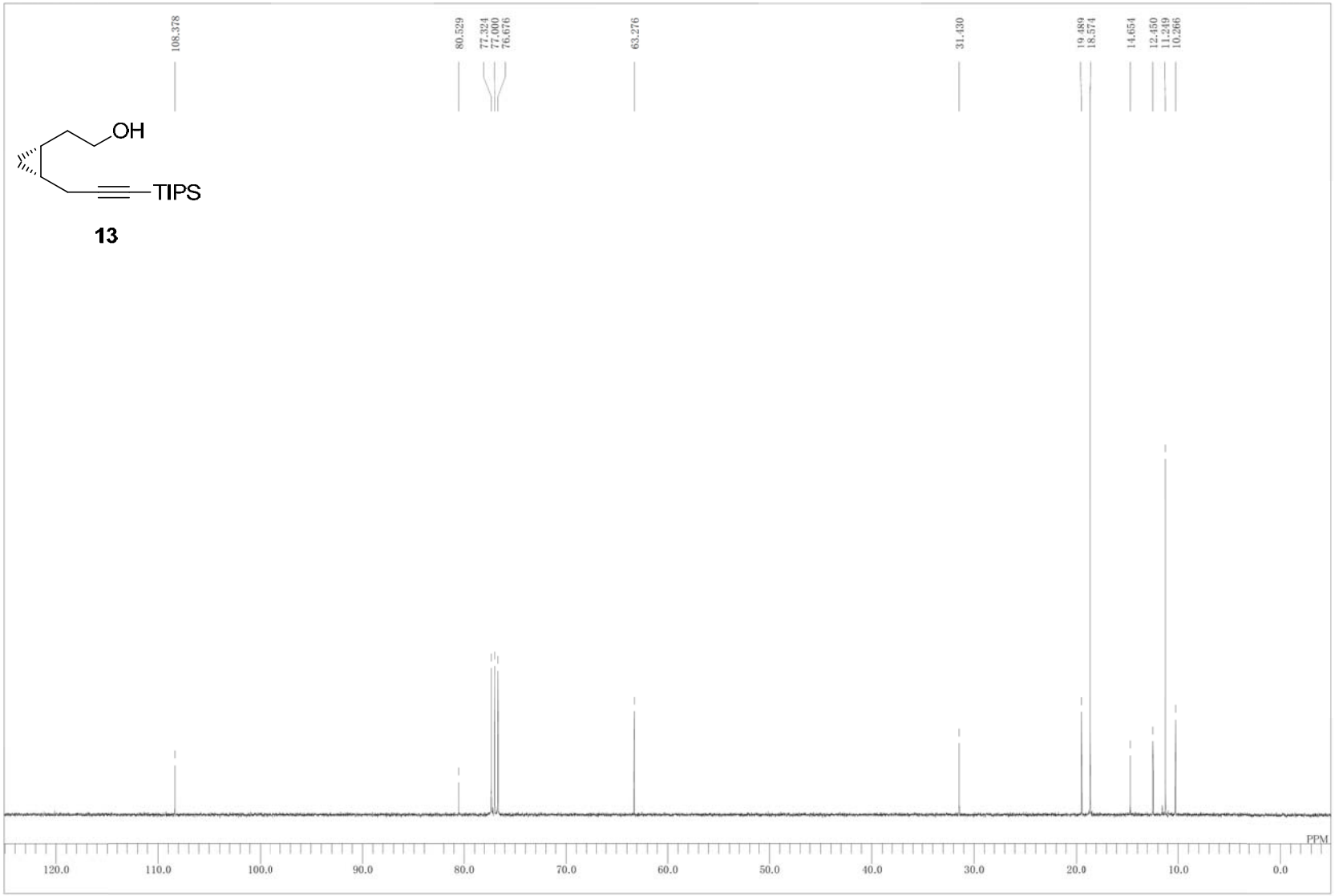

OH
TIPS
S1
7.265
3.921
3.908
3.891
3.879
3.866
3.853
3.454
3.447
3.430
3.423
3.417
3.399
3.393
2.729
2.717
2.684
2.671
2.087
2.081
2.063
2.055
2.042
2.017
1.615
1.605
1.304
1.290
1.281
1.268
1.257
1.246
1.236
1.222
1.143
1.116
1.100
1.076
1.066
1.045
1.032
1.021
0.918
0.804
0.792
0.784
0.770
0.762
0.749
0.133
0.120
0.107
0.093
0.000
22.09
0.55
0.89
0.96
1.91
0.75
2.14
1.05
1.00
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

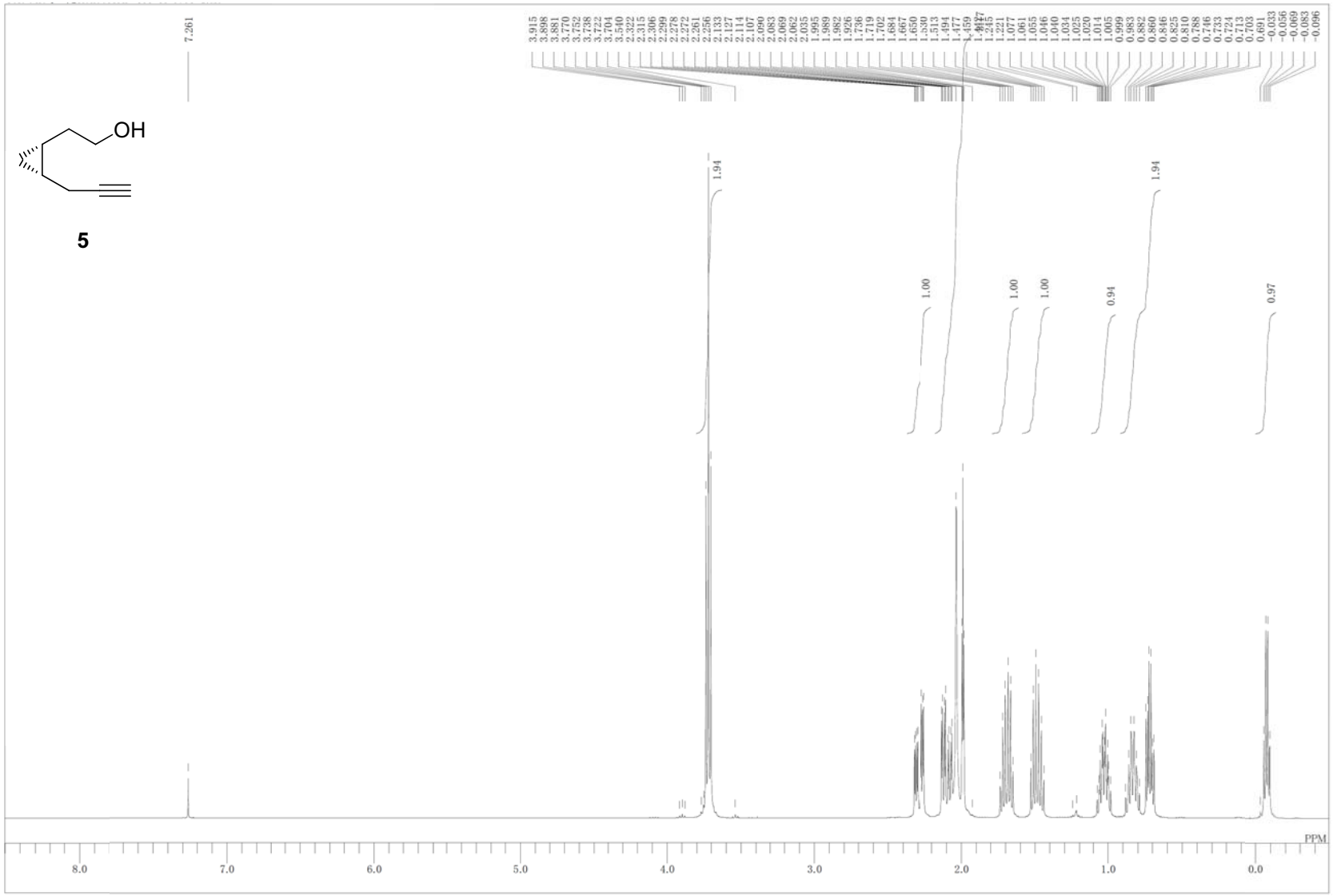

108.452
81.857
77.326
77.000
76.684
63.204
19.307
18.822
17.632
15.609
11.202
9.679
OH
TIPS
S1
PPM
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

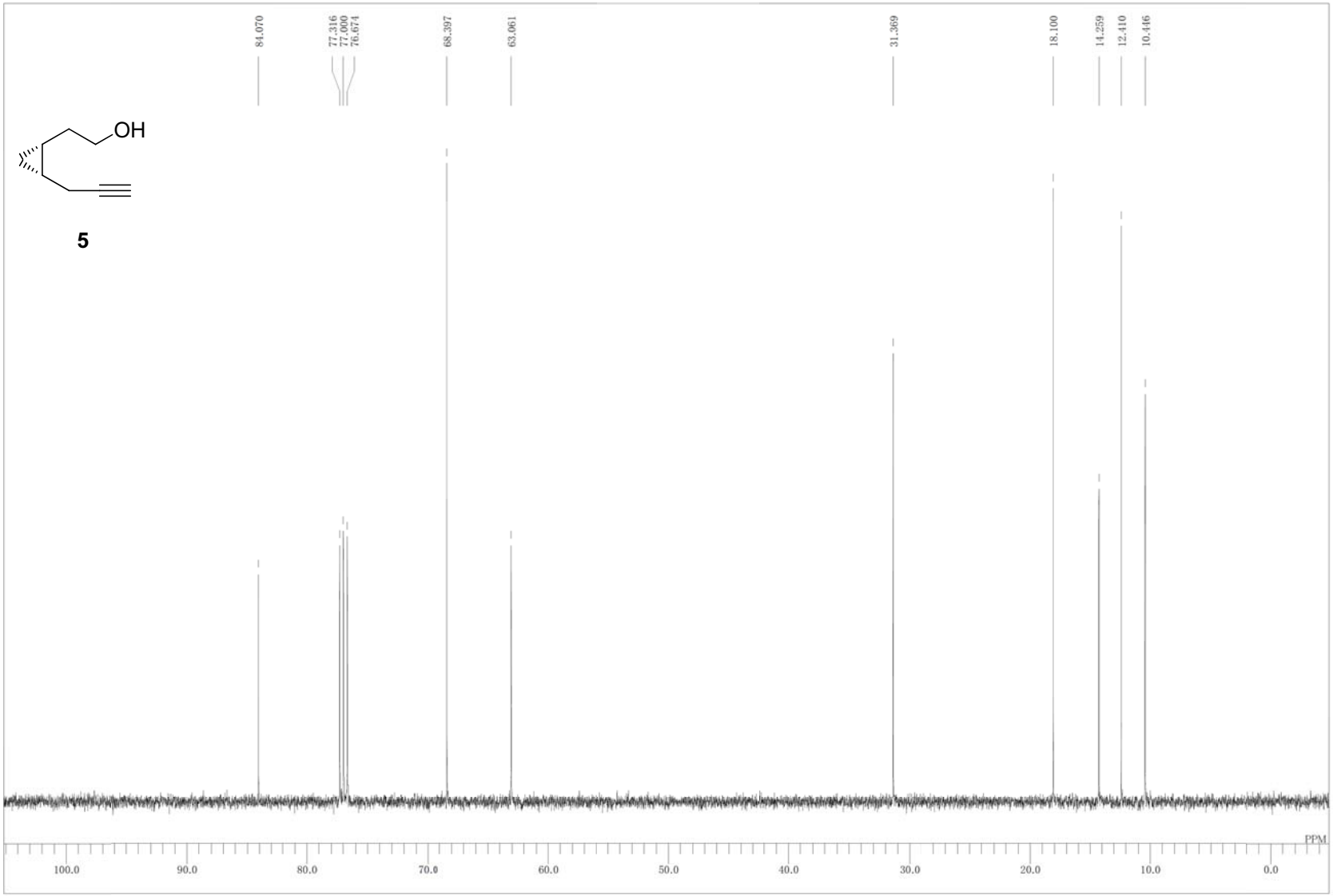

O
H
TIPS
12
9.599
9.588
7.264
2.684
2.668
2.638
2.623
2.456
2.435
2.411
2.389
2.060
2.047
2.038
2.025
2.014
2.005
1.992
1.809
1.792
1.771
1.754
1.572
1.357
1.344
1.326
1.313
1.285
1.273
1.265
1.252
1.244
1.231
1.059
1.058
1.048
1.032
1.019
1.009
0.995
0.000
1.00
1.10
1.09
1.08
1.08
2.38
23.43
PPM
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

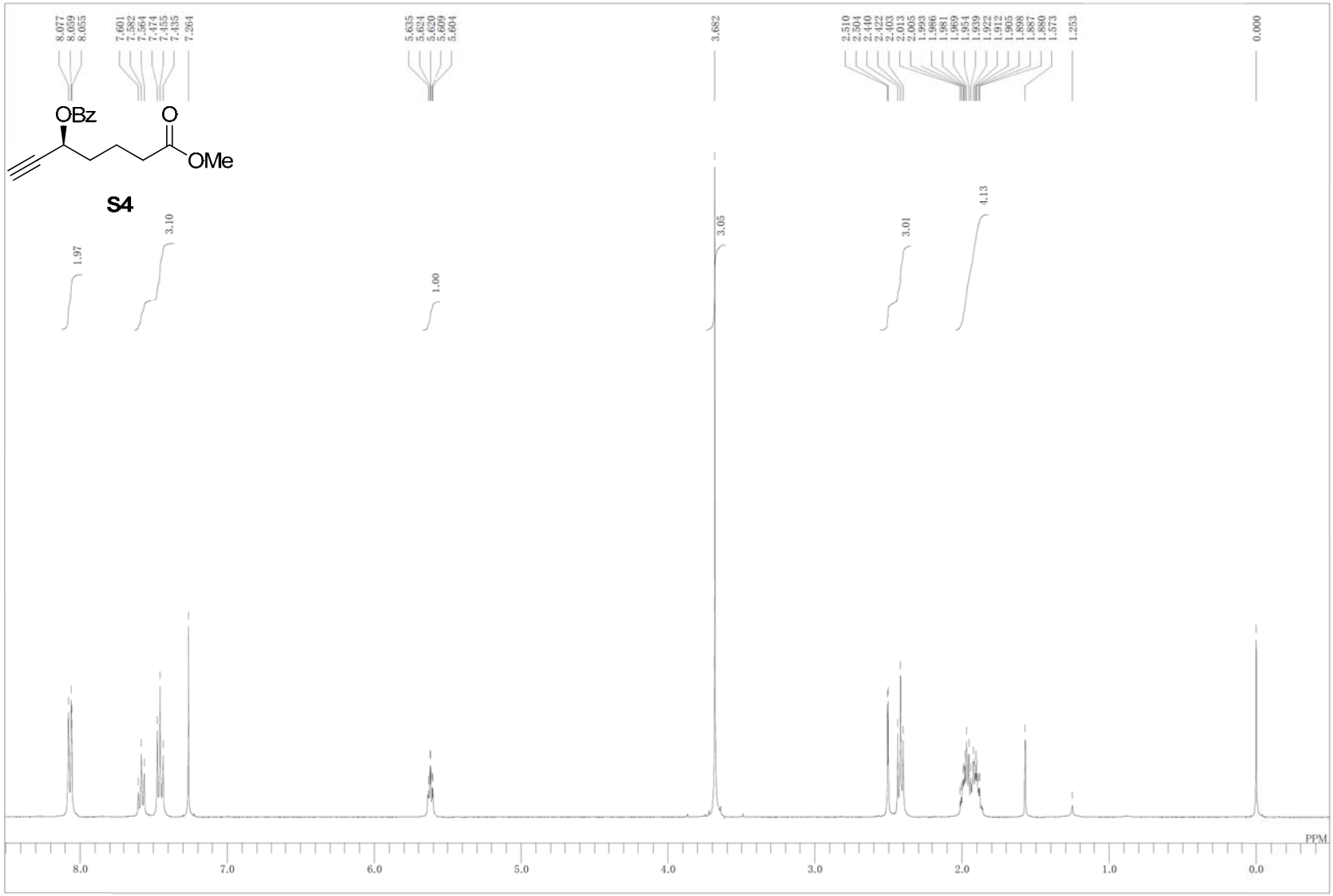

200.300
106.414
81.654
77.324
77.000
76.676
27.014
23.724
18.745
18.411
14.530
11.058
O
H
TIPS
12
PPM
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

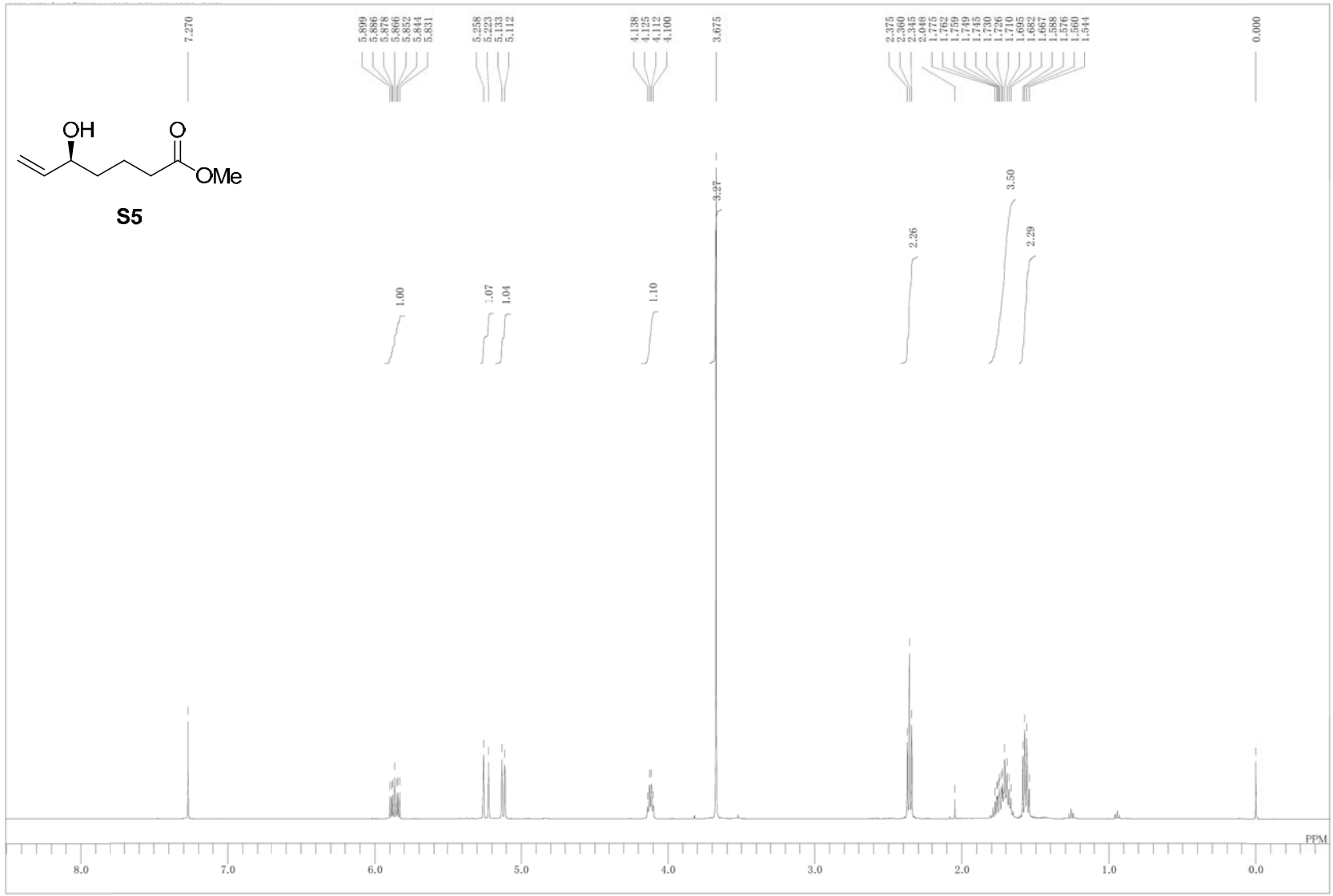

OH
TIPS
13
7.264
3.785
3.768
3.751
2.461
2.446
2.416
2.401
2.205
2.184
2.160
2.139
2.047
1.770
1.753
1.734
1.717
1.576
1.558
1.541
1.522
1.505
1.458
1.260
1.094
1.074
1.064
1.046
1.032
1.023
1.009
0.898
0.877
0.863
0.843
0.836
0.749
0.738
0.727
0.716
0.707
0.694
22.22
0.000
−0.017
−0.031
−0.045
1.97
1.00
1.01
1.00
1.28
1.03
1.27
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

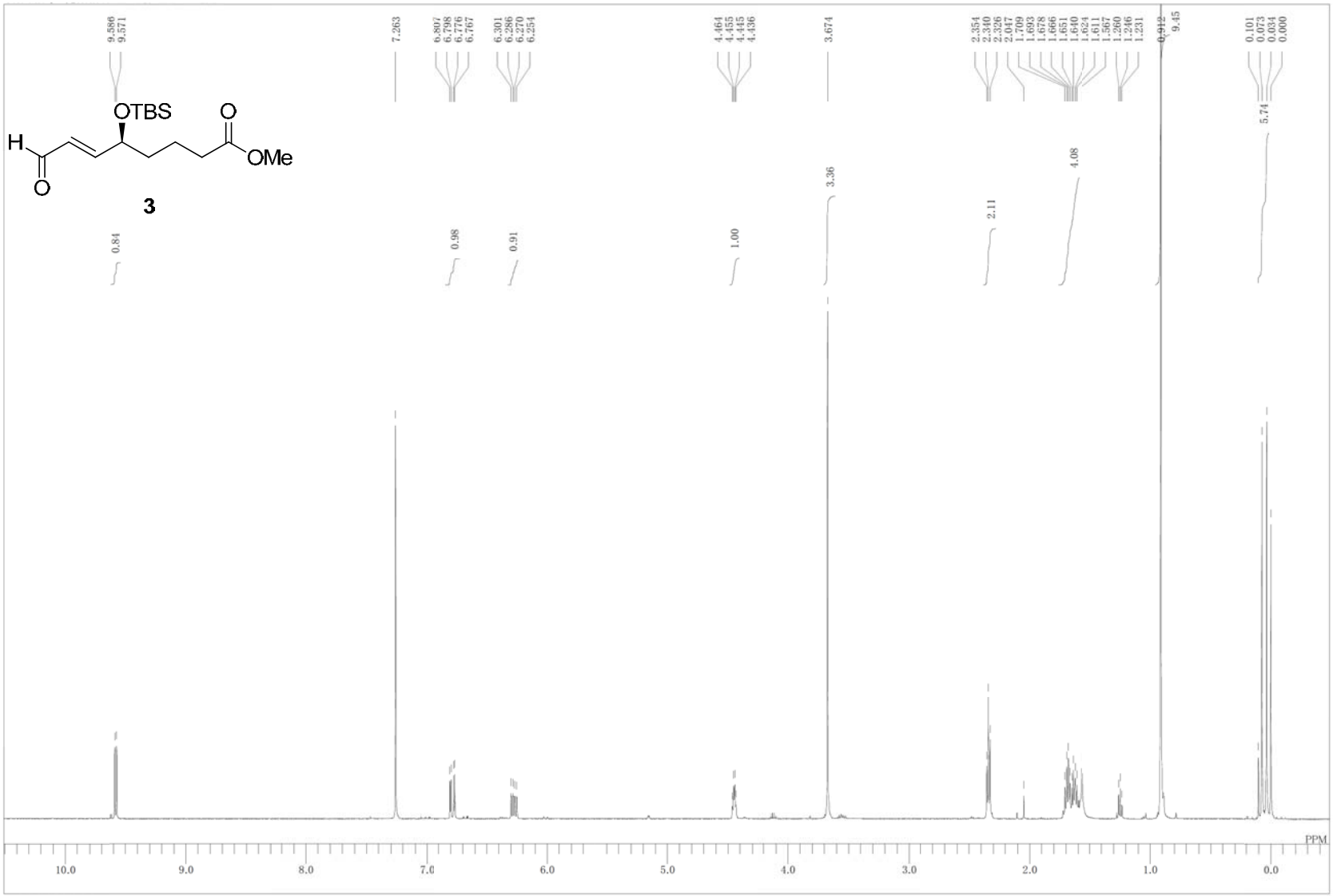

108.378
80.529
77.324
77.000
76.676
63.276
31.430
19.489
18.574
14.654
12.450
11.249
10.266
OH
TIPS
13
PPM
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

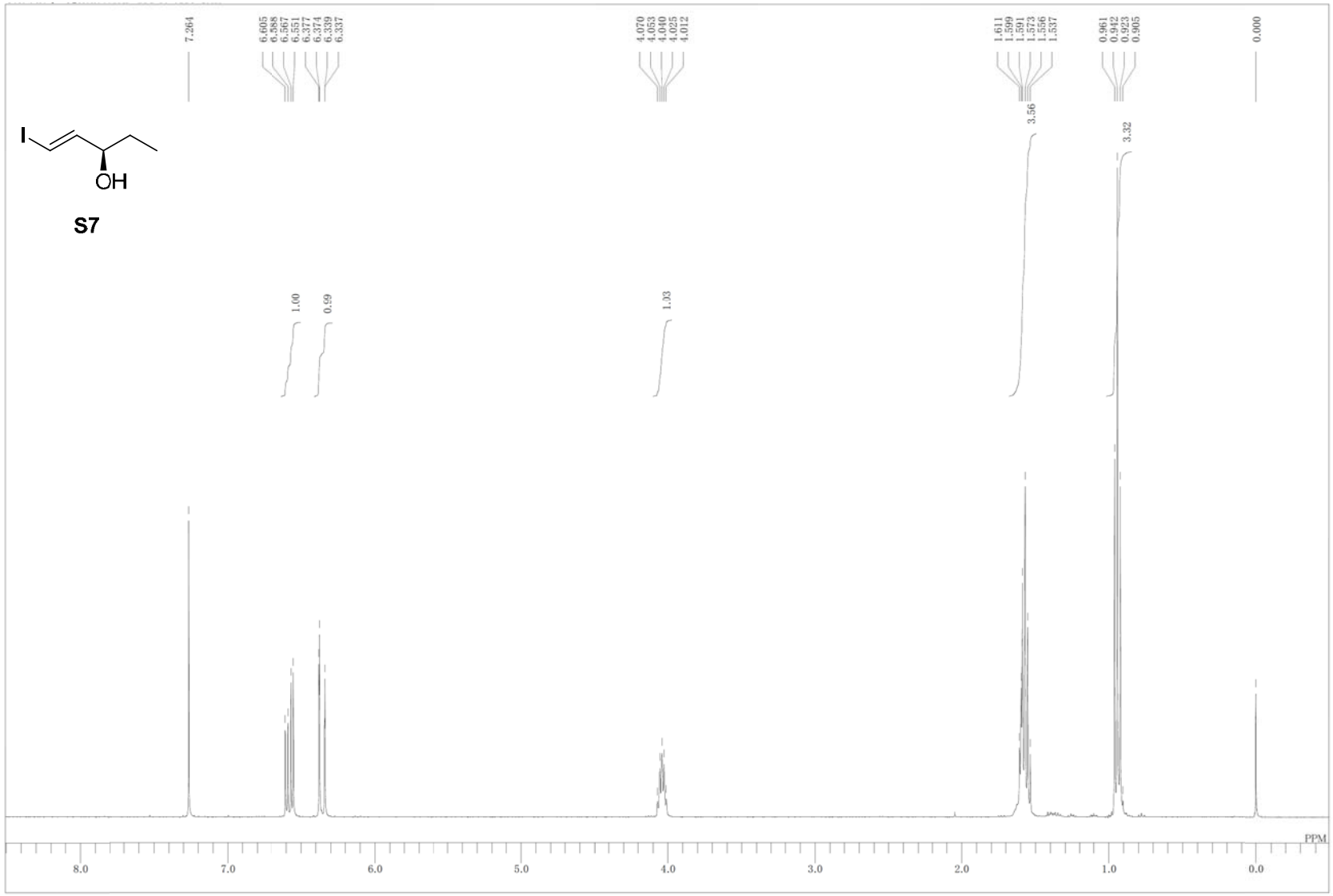

OH
5
7.261
1.94
1.00
1.00
1.00
0.94
1.94
0.97
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

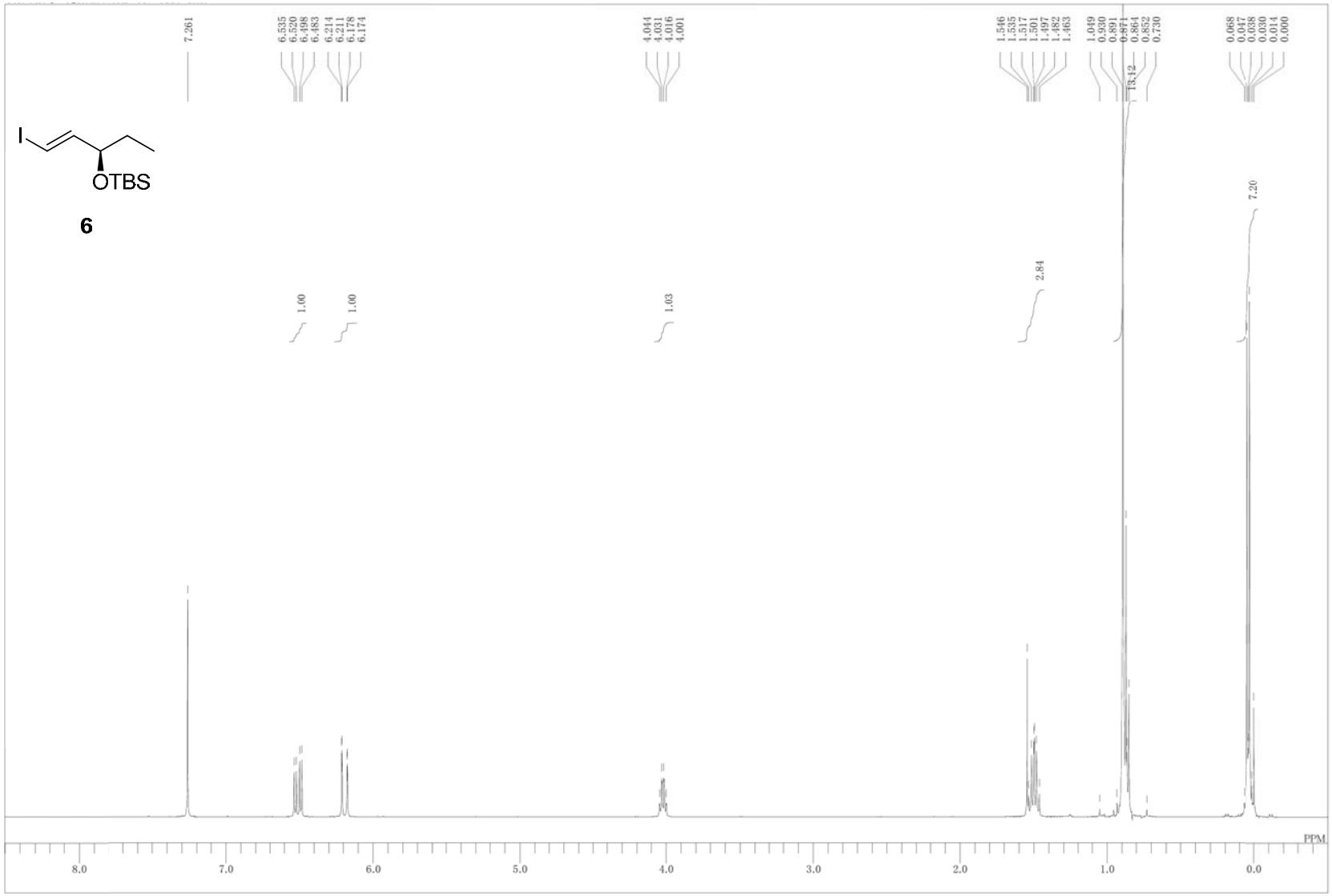

84.070
77.316
77.000
76.674
68.397
63.061
31.369
18.100
14.259
12.410
10.446
OH
5
PPM
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

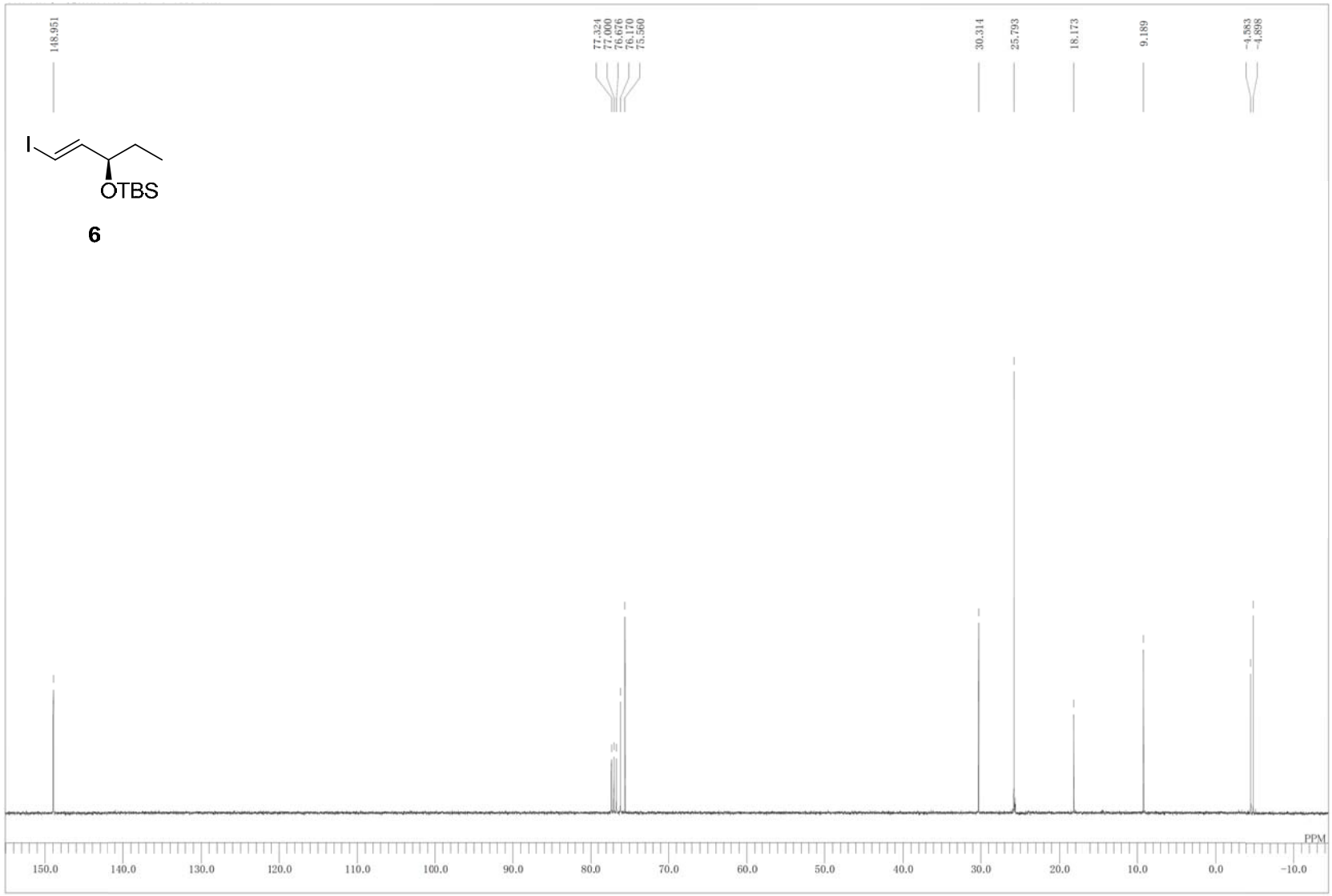

8.077
8.059
8.055
7.601
7.582
7.564
7.474
7.455
7.435
7.264
5.635
5.624
5.620
5.609
5.604
3.682
2.510
2.504
2.440
2.422
2.403
2.013
2.005
1.993
1.986
1.981
1.969
1.954
1.939
1.922
1.912
1.905
1.898
1.887
1.880
1.573
1.253
0.000
OBz
O
OMe
S4
1.97
3.10
1.00
3.05
3.01
4.13
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

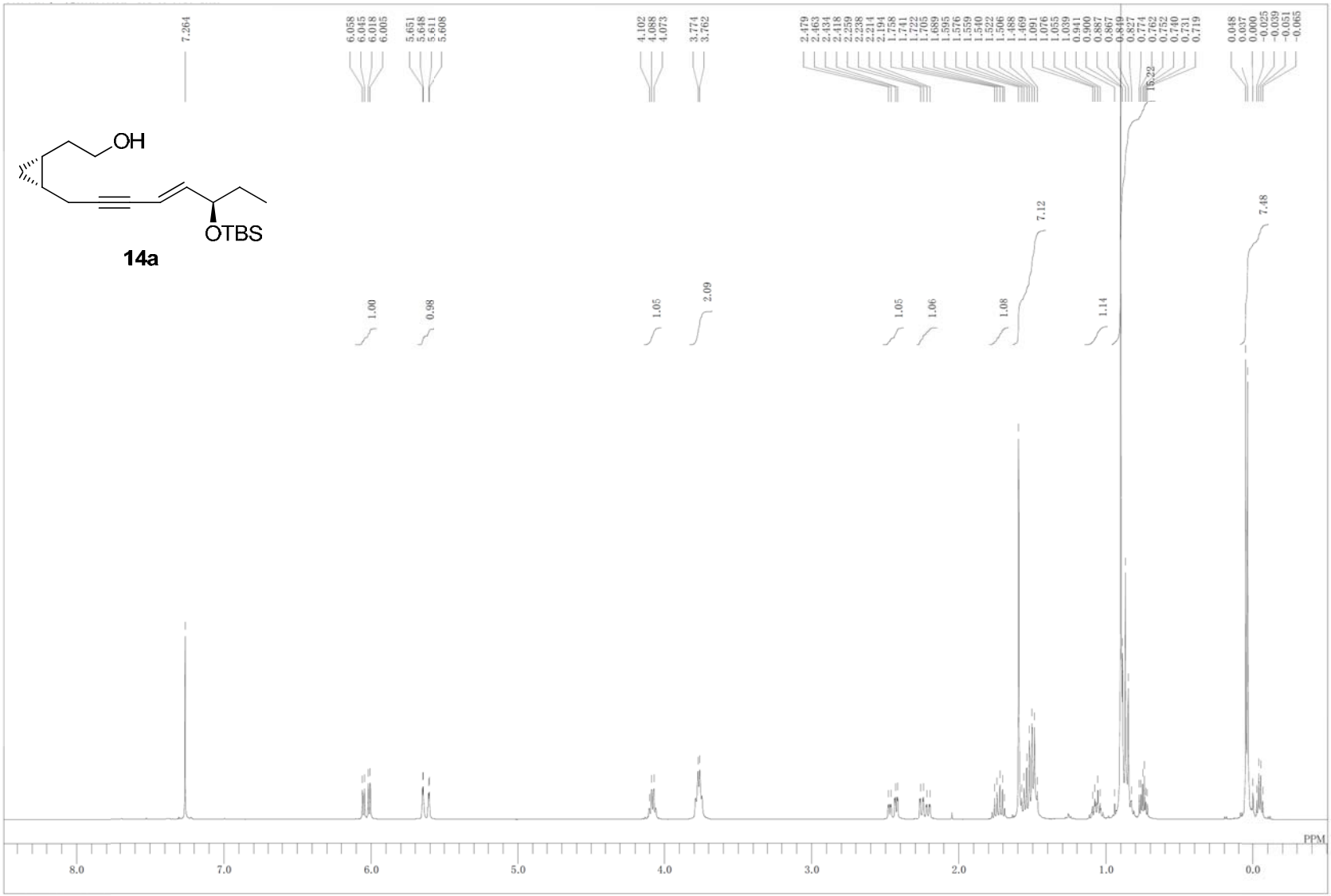

OH
O
OMe
S5
7.270
5.899
5.886
5.878
5.866
5.852
5.844
5.831
5.258
5.223
5.133
5.112
4.138
4.125
4.112
4.100
3.675
2.375
2.360
2.345
2.048
1.775
1.762
1.759
1.749
1.745
1.730
1.726
1.710
1.695
1.682
1.667
1.588
1.576
1.560
1.544
0.000
1.00
1.07
1.04
1.10
3.27
2.26
3.50
2.29
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

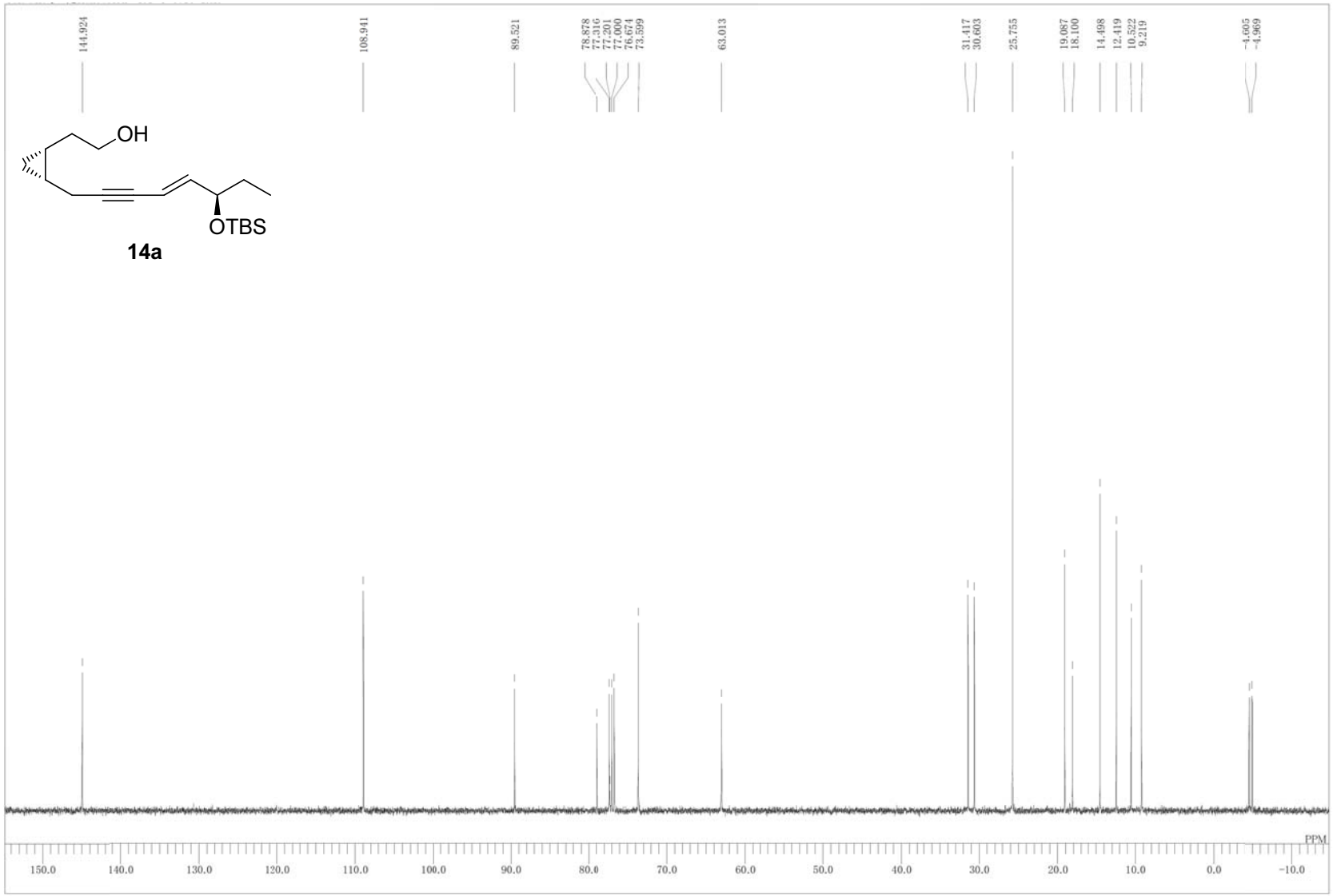

OTBS
O
H
OMe
O
3
9.586
9.571
7.263
6.807
6.798
6.776
6.767
6.301
6.286
6.270
6.254
4.464
4.455
4.445
4.436
3.674
2.354
2.340
2.326
2.047
1.709
1.693
1.678
1.666
1.651
1.640
1.624
1.611
1.567
1.260
1.246
1.231
0.912
9.45
0.101
0.073
0.034
0.000
5.74
4.08
3.36
2.11
1.00
0.98
0.91
0.84
PPM
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

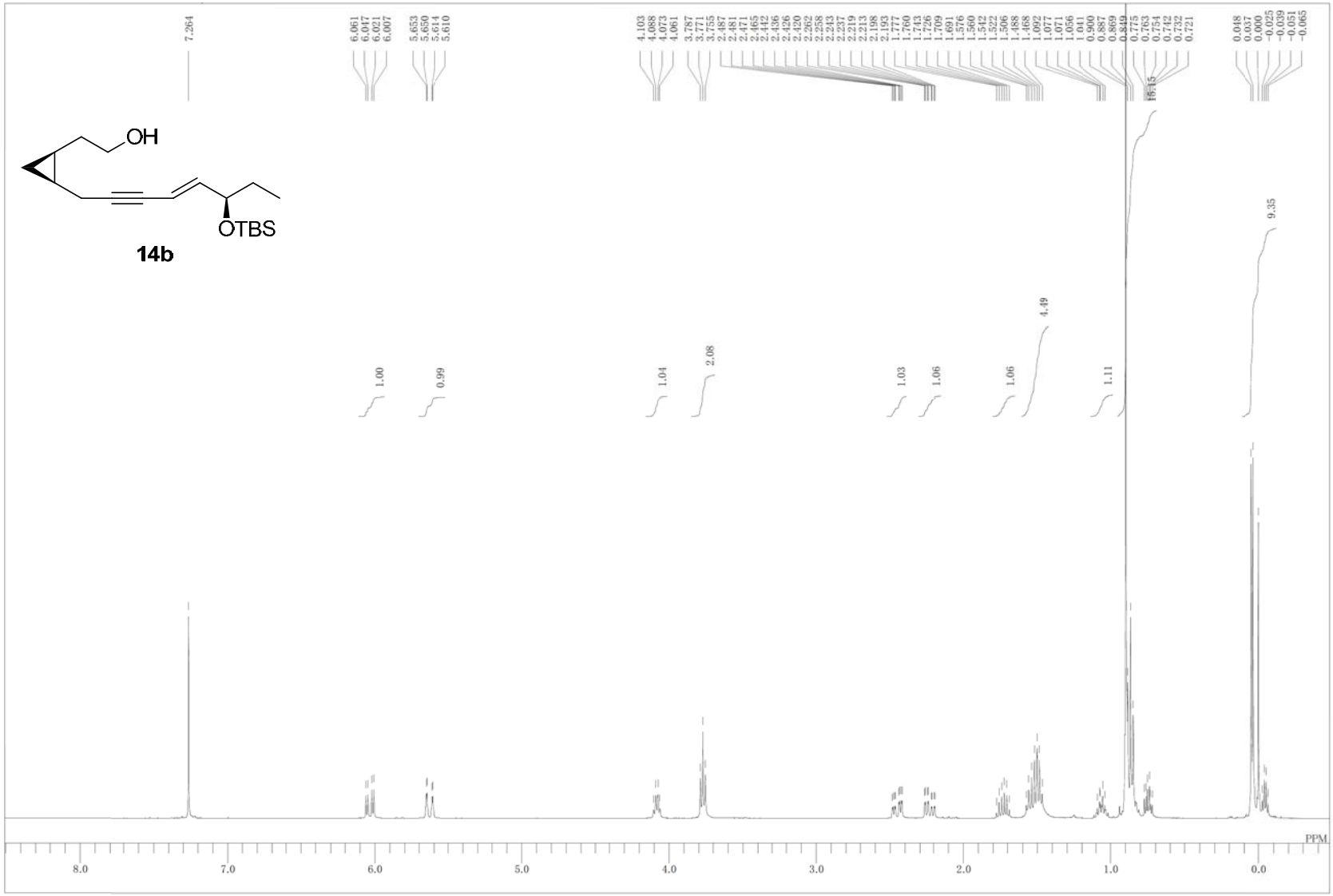

7.264
6.605
6.588
6.567
6.551
6.377
6.374
6.339
6.337
4.070
4.053
4.040
4.025
4.012
1.611
1.599
1.591
1.573
1.556
1.537
0.961
0.942
0.923
0.905
0.000
3.56
3.32
1.00
0.99
1.03
I
OH
S7
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

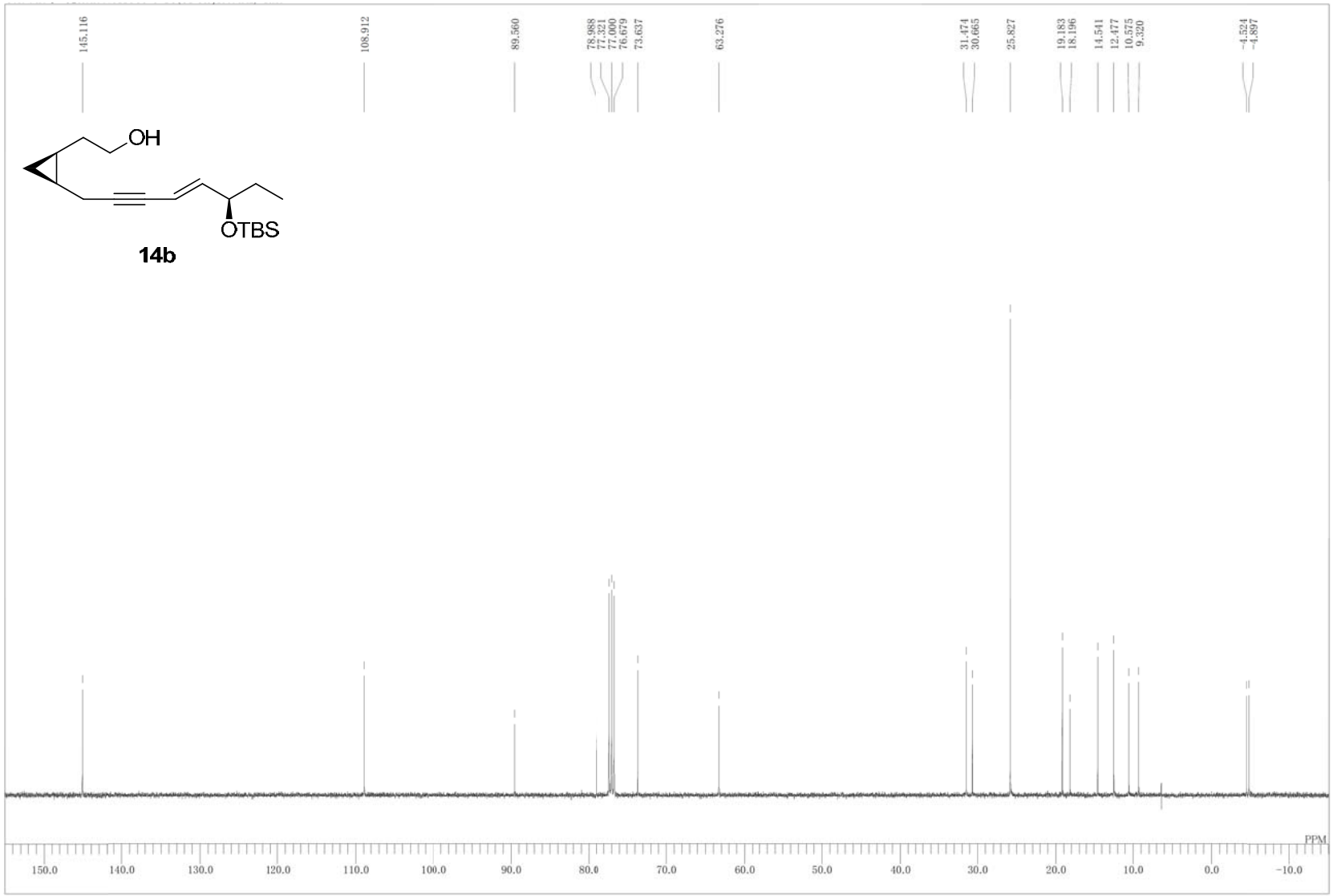

I
OTBS
6
7.261
6.535
6.520
6.498
6.483
6.214
6.211
6.178
6.174
4.044
4.031
4.016
4.001
1.546
1.535
1.517
1.501
1.497
1.482
1.463
1.049
1.930
0.891
0.871
0.864
0.852
0.730
0.068
0.047
0.038
0.030
0.014
0.000
13.12
7.20
2.84
1.00
1.00
1.03
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

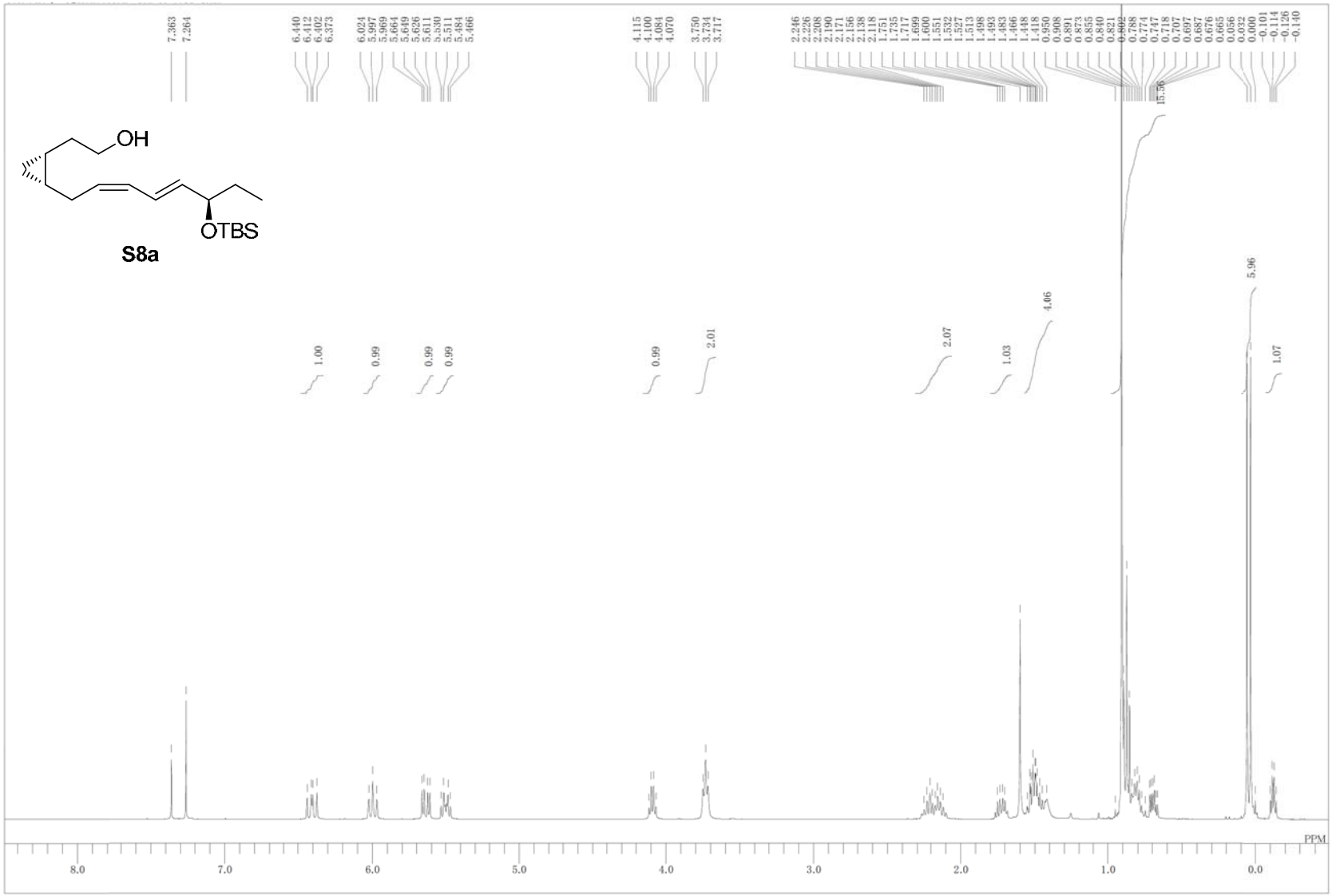

148.951
77.324
77.000
76.676
76.170
75.560
30.314
25.793
18.173
9.189
-4.583
-4.898
I
OTBS
6
PPM
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0

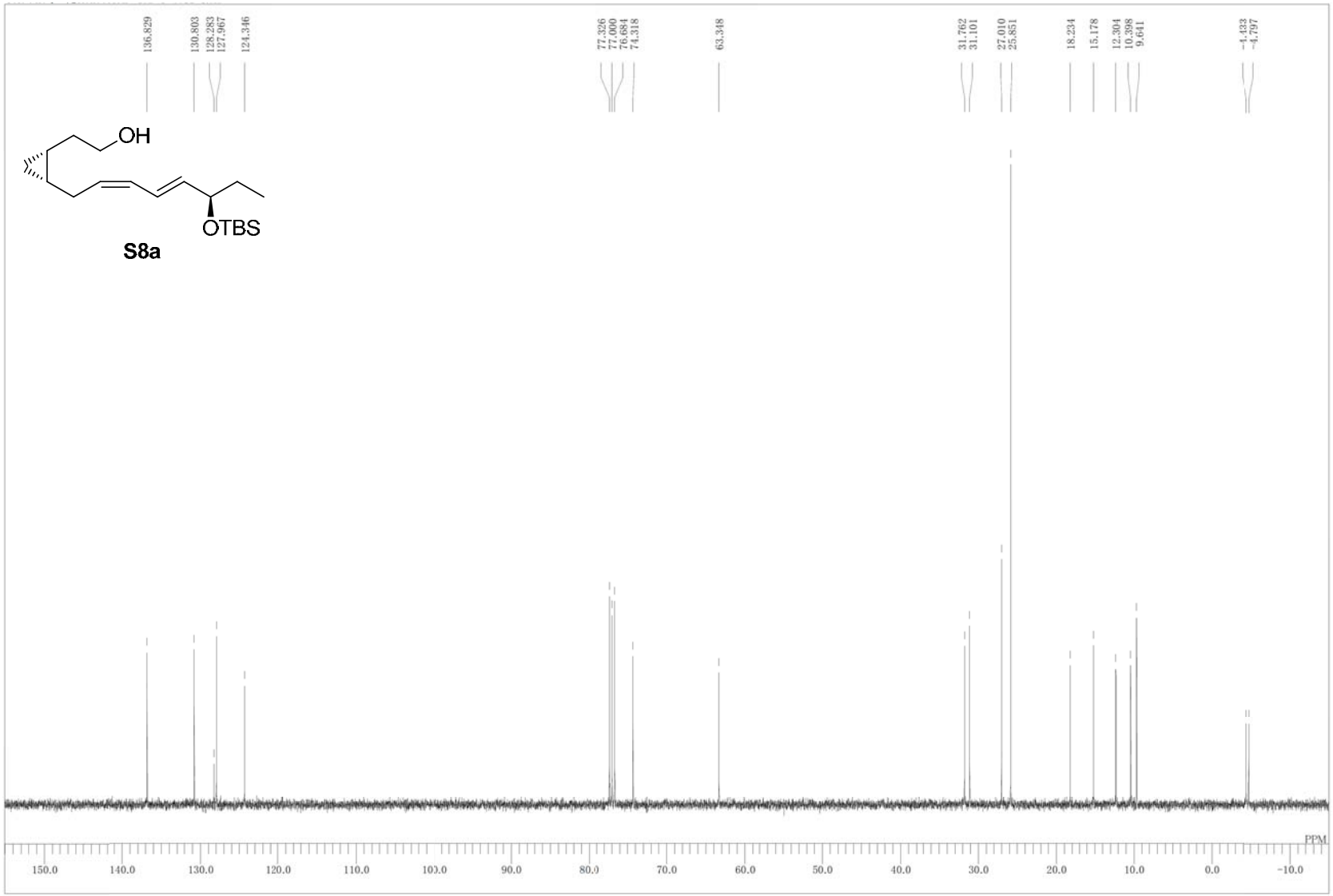

OH
OTBS
14a
7.264
6.058
6.045
6.018
6.005
5.651
5.648
5.611
5.608
4.102
4.088
4.073
3.774
3.762
2.479
2.463
2.434
2.418
2.259
2.238
2.214
2.194
1.758
1.741
1.722
1.705
1.689
1.595
1.576
1.559
1.540
1.522
1.506
1.488
1.469
1.091
1.076
1.055
1.039
0.941
0.900
0.887
0.867
0.849
0.827
0.774
0.762
0.752
0.740
0.731
0.719
16.29
0.048
0.037
0.000
-0.025
-0.039
-0.051
-0.065
1.00
0.98
1.05
2.09
1.05
1.06
1.08
7.12
1.14
7.48
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

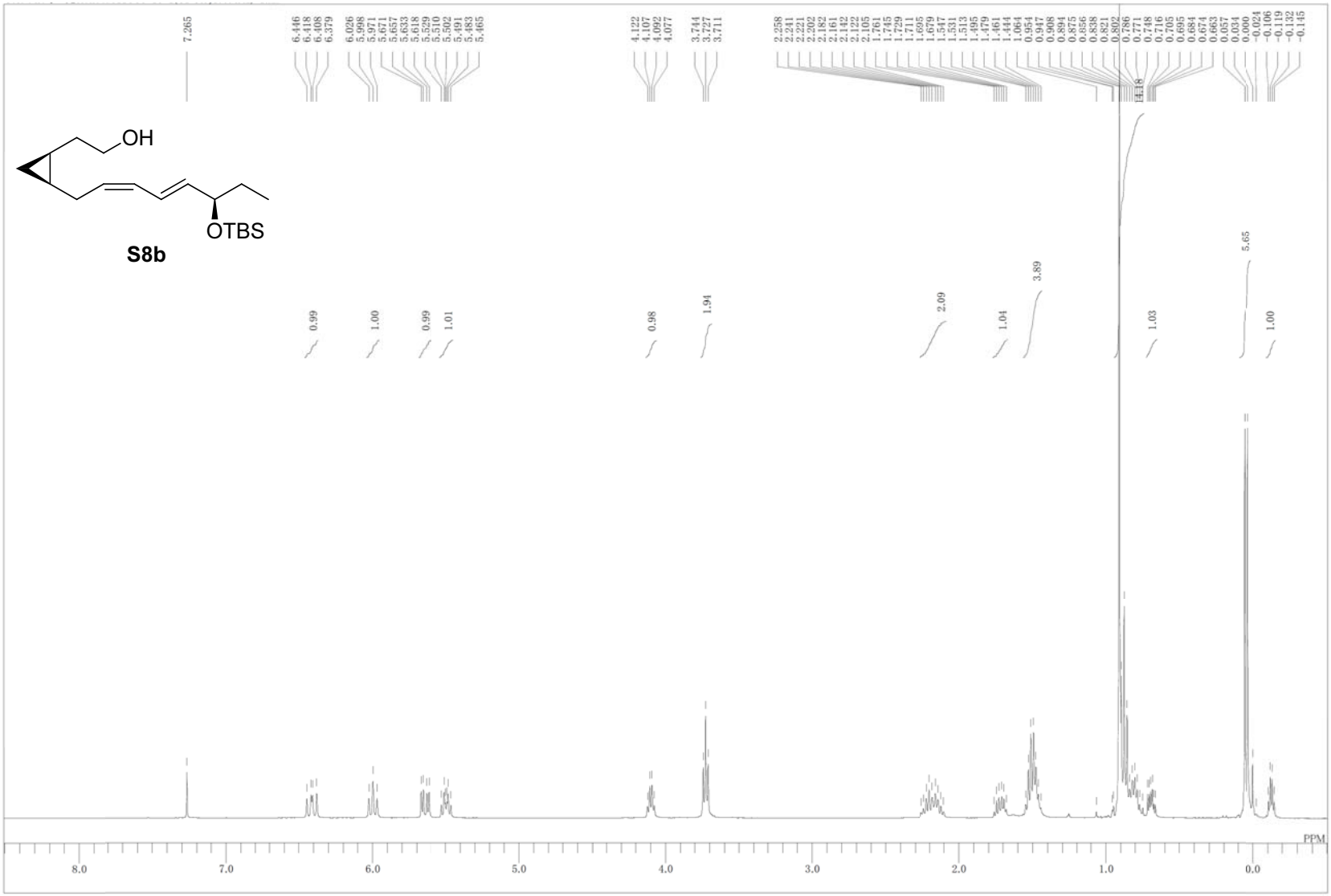

144.924
108.941
89.521
78.878
77.316
77.201
77.000
76.674
73.599
63.013
31.417
30.603
25.755
19.087
18.100
14.498
12.419
10.522
9.219
-4.605
-4.969
OH
OTBS
14a
PPM
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0

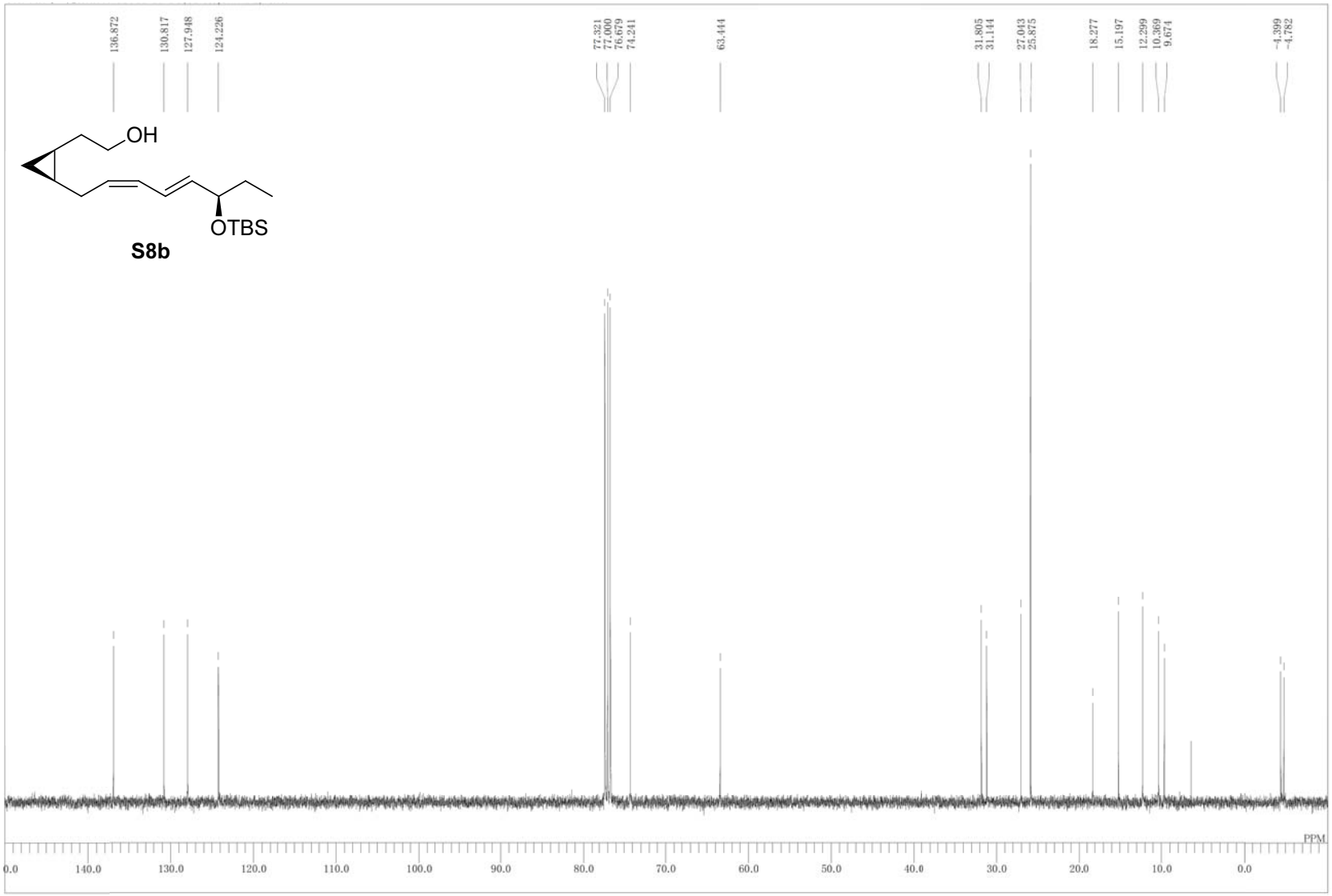

OH
OTBS
14b
7.264
6.061
6.047
6.021
6.007
5.653
5.650
5.614
5.610
4.103
4.088
4.073
4.061
3.787
3.771
3.755
2.487
2.481
2.471
2.465
2.442
2.436
2.426
2.420
2.262
2.258
2.243
2.237
2.219
2.213
2.198
2.193
1.777
1.760
1.743
1.726
1.709
1.691
1.576
1.560
1.542
1.522
1.506
1.488
1.468
1.092
1.077
1.071
1.056
1.041
0.900
0.887
0.869
0.849
0.775
0.763
0.754
0.742
0.732
0.721
0.048
0.037
0.000
−0.025
−0.039
−0.051
−0.065
15.15
9.35
4.49
2.08
1.00
0.99
1.04
1.03
1.06
1.06
1.11
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

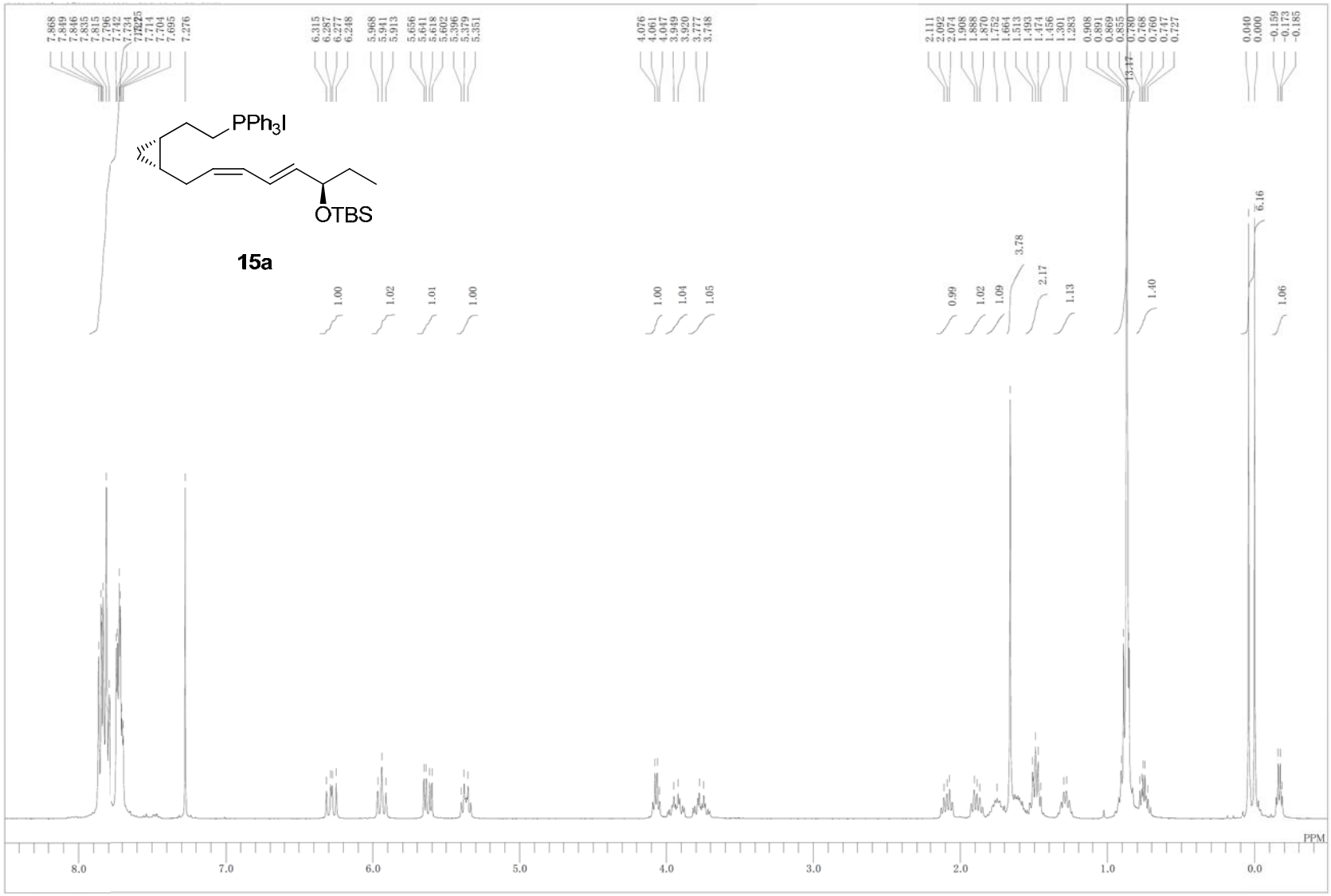

145.116
108.912
89.560
78.988
77.321
77.000
76.679
73.637
63.276
31.474
30.665
25.827
19.183
18.196
14.541
12.477
10.575
9.320
-4.524
-4.897
OH
OTBS
14b
PPM
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0

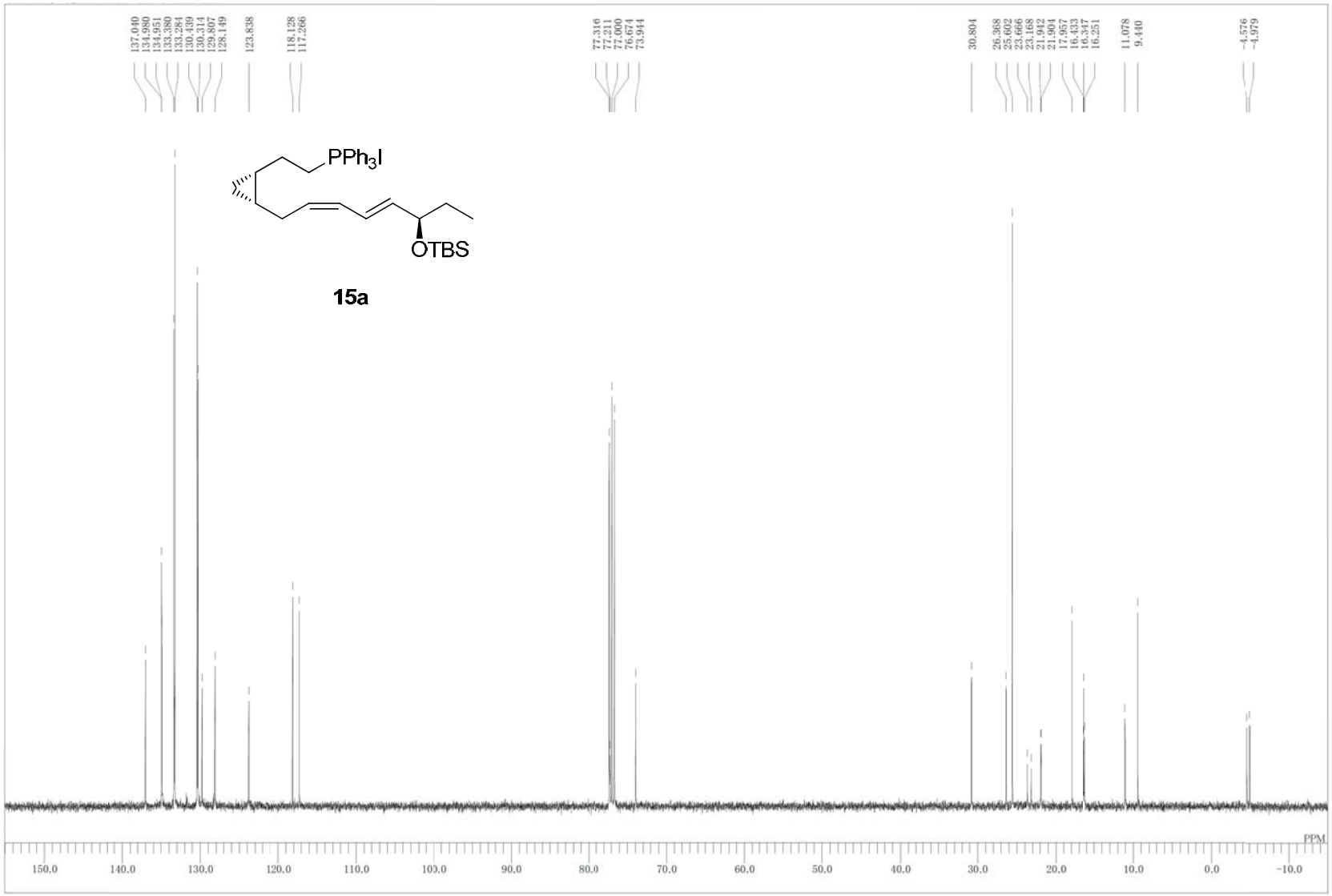

OH
OTBS
S8a
7.363
7.264
6.440
6.412
6.402
6.373
6.024
5.997
5.969
5.664
5.649
5.626
5.611
5.530
5.511
5.484
5.466
4.115
4.100
4.084
4.070
3.750
3.734
3.717
2.246
2.226
2.208
2.190
2.171
2.156
2.138
2.118
1.751
1.735
1.717
1.699
1.660
1.551
1.522
1.507
1.513
1.493
1.483
1.466
1.448
1.418
0.950
0.908
0.891
0.873
0.855
0.840
0.821
0.802
0.788
0.774
0.747
0.718
0.707
0.697
0.687
0.676
0.665
0.056
0.032
0.000
-0.101
-0.114
-0.126
-0.140
15.56
1.00
0.99
0.99
0.99
0.99
2.01
2.07
1.03
4.06
5.96
1.07
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

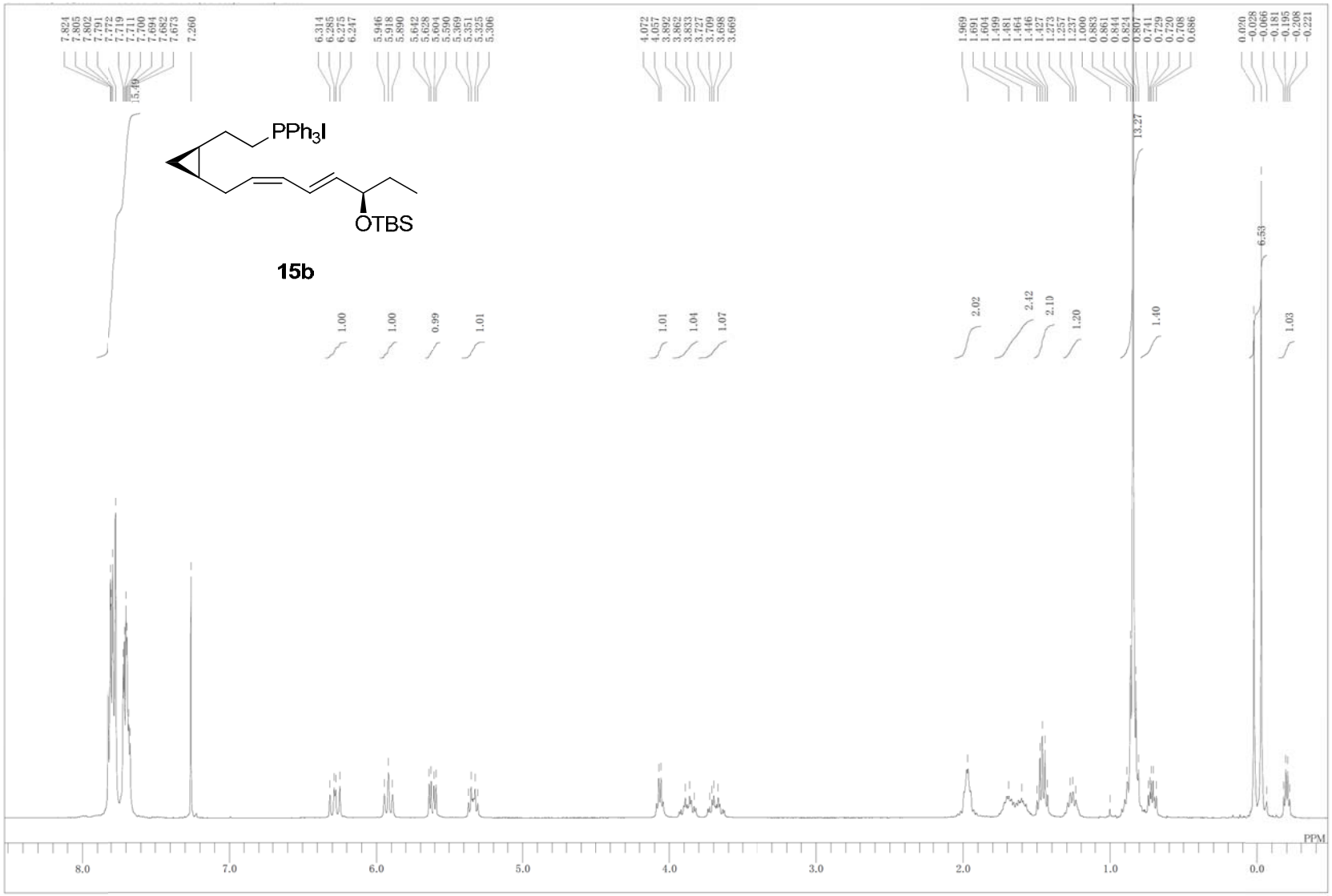

136.829
130.803
128.283
127.967
124.346
77.326
77.000
76.684
74.318
63.348
31.762
31.101
27.010
25.851
18.234
15.178
12.304
10.398
9.641
-4.433
-4.797
OH
OTBS
S8a
PPM
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0

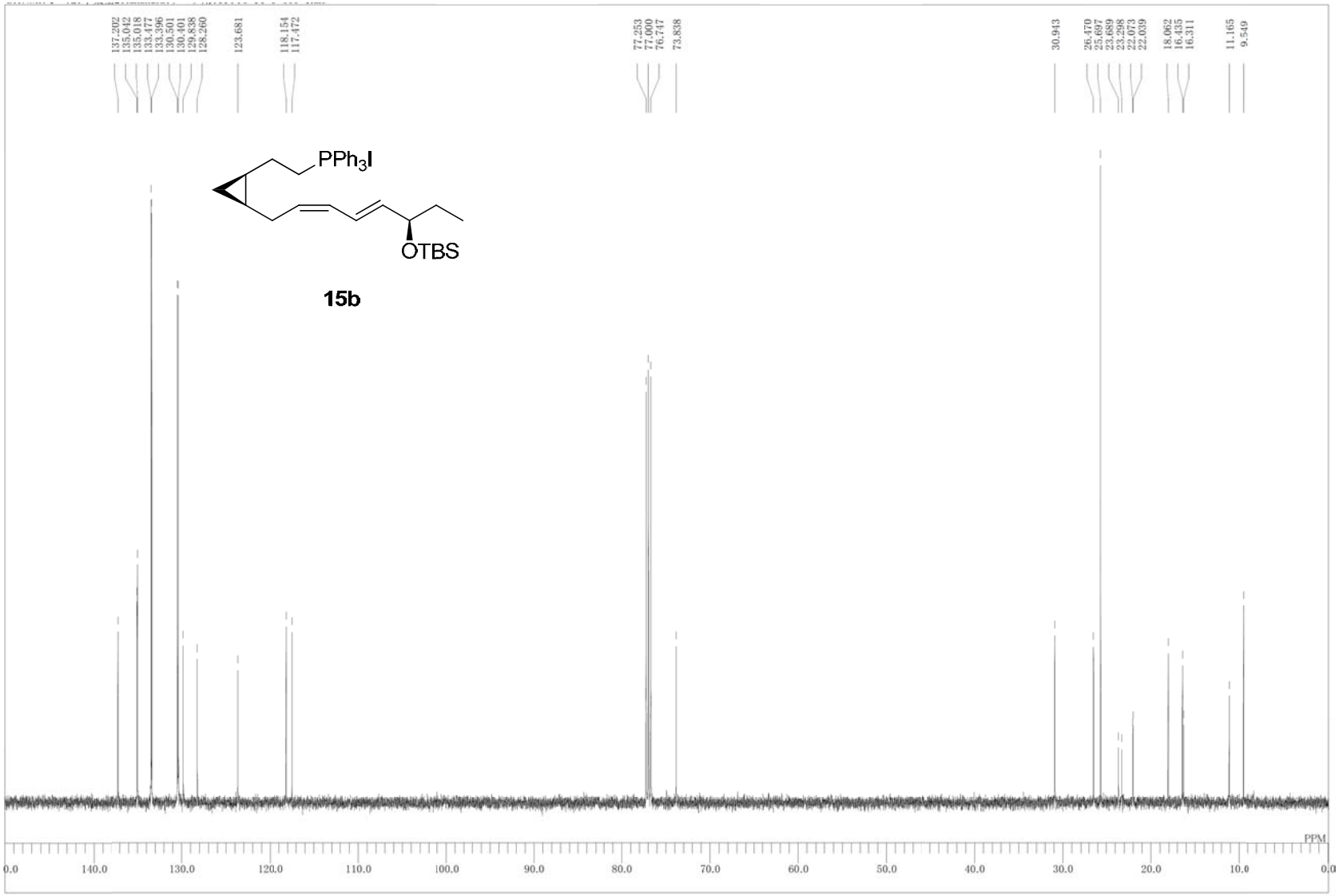

OH
OTBS
S8b
7.265
6.446
6.418
6.408
6.379
6.026
5.998
5.971
5.671
5.657
5.633
5.618
5.529
5.510
5.502
5.491
5.483
5.465
4.122
4.107
4.092
4.077
3.744
3.727
3.711
2.258
2.241
2.221
2.202
2.182
2.161
2.142
2.122
2.105
1.761
1.745
1.729
1.711
1.695
1.679
1.547
1.531
1.513
1.495
1.479
1.461
1.444
1.064
0.954
0.947
0.908
0.894
0.875
0.855
0.838
0.821
0.802
0.786
0.771
0.748
0.716
0.705
0.695
0.684
0.674
0.663
0.057
0.034
0.000
-0.024
-0.106
-0.119
-0.132
-0.145
0.99
1.00
0.99
1.01
0.98
1.94
2.09
1.04
3.89
1.03
5.65
1.00
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

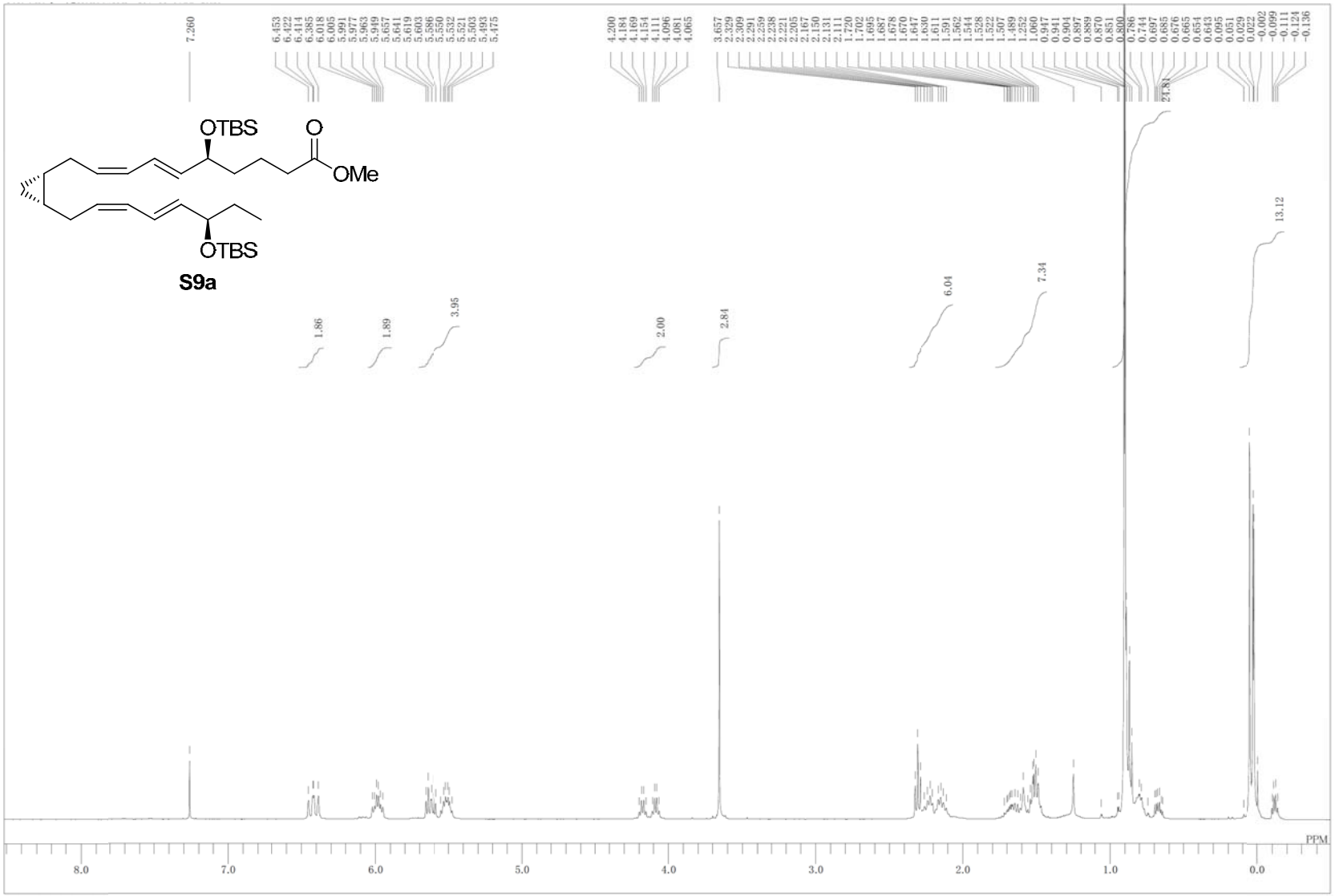

136.872
130.817
127.948
124.226
77.321
77.000
76.679
74.241
63.444
31.805
31.144
27.043
25.875
18.277
15.197
12.299
10.369
9.674
-4.399
-4.782
OH
OTBS
S8b
PPM
0.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

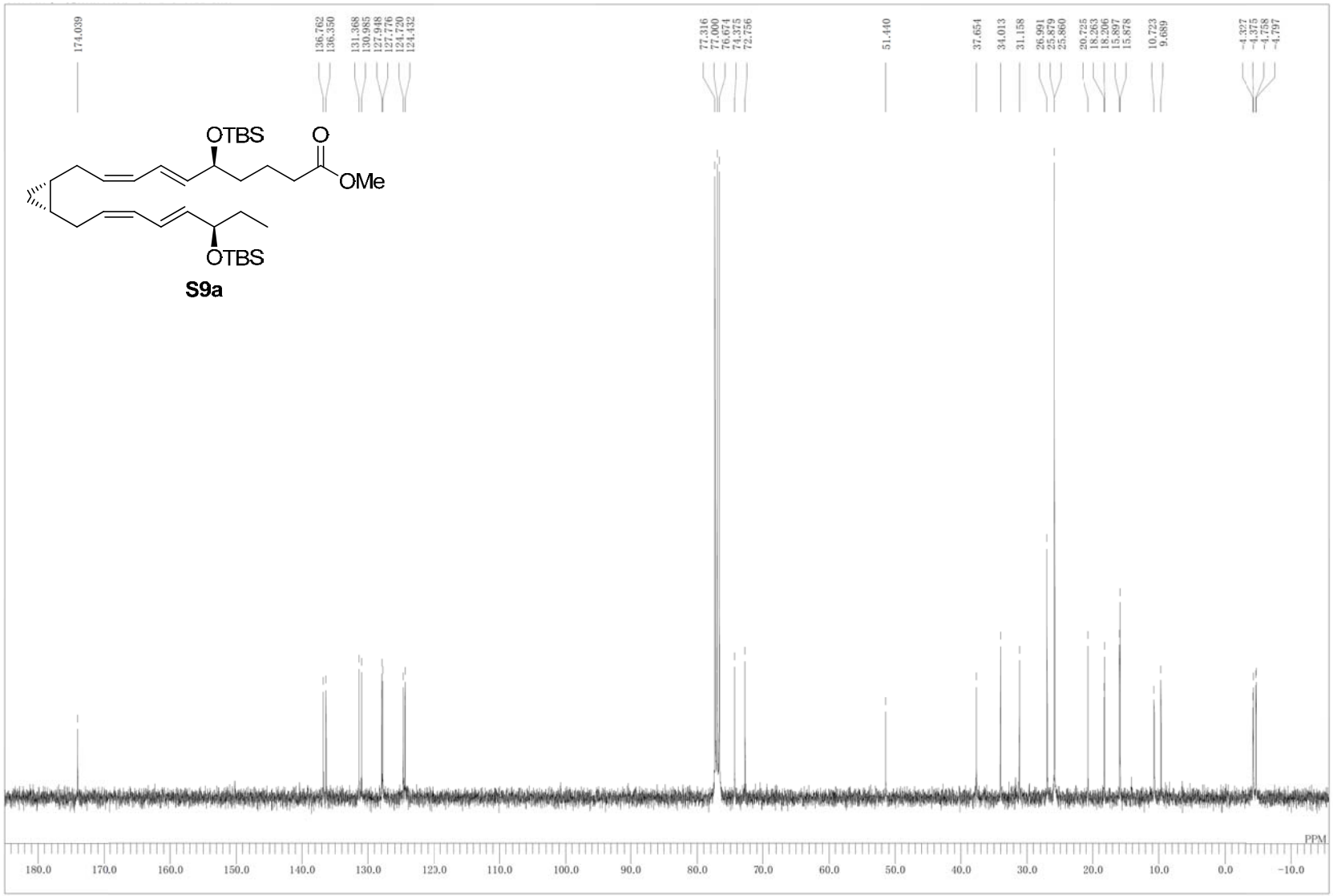

PPh3I
OTBS
15a
PPM

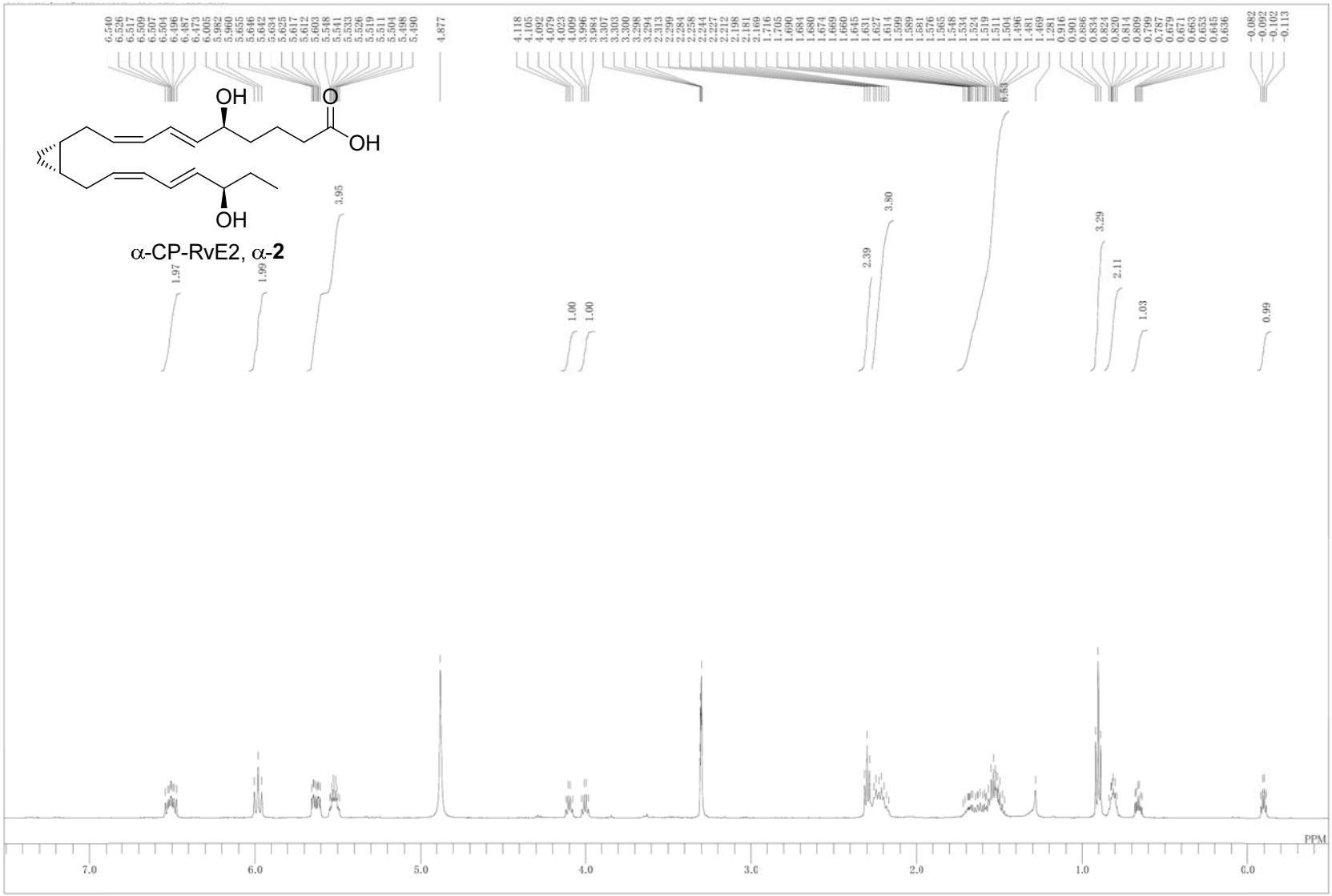

137.040
134.980
134.951
133.380
133.284
130.439
130.314
129.867
128.149
123.838
118.128
117.266
77.316
77.211
77.000
76.674
73.944
30.804
26.368
25.602
23.666
23.168
21.942
21.904
17.957
16.433
16.347
16.251
11.078
9.440
-4.576
-4.979
PPh3I
OTBS
15a
PPM
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0

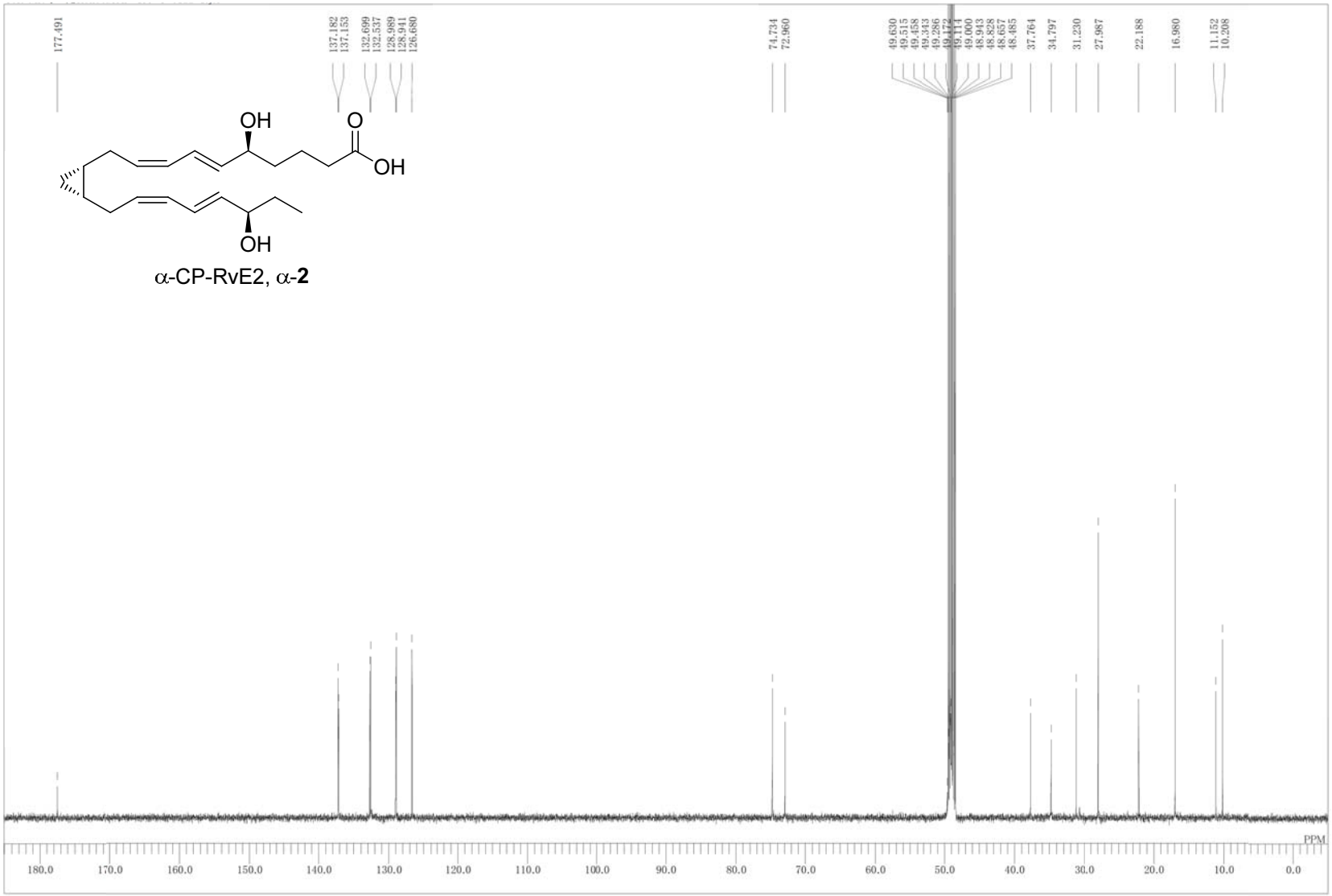

PPh3I
OTBS
15b
PPM


137.202
135.042
135.018
133.477
133.396
130.501
130.401
129.838
128.260
123.681
118.154
117.472
77.253
77.000
76.747
73.838
30.943
26.479
25.697
23.689
23.298
22.673
22.039
18.062
16.435
16.311
11.165
9.549
PPh3I
OTBS
15b
PPM
0.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

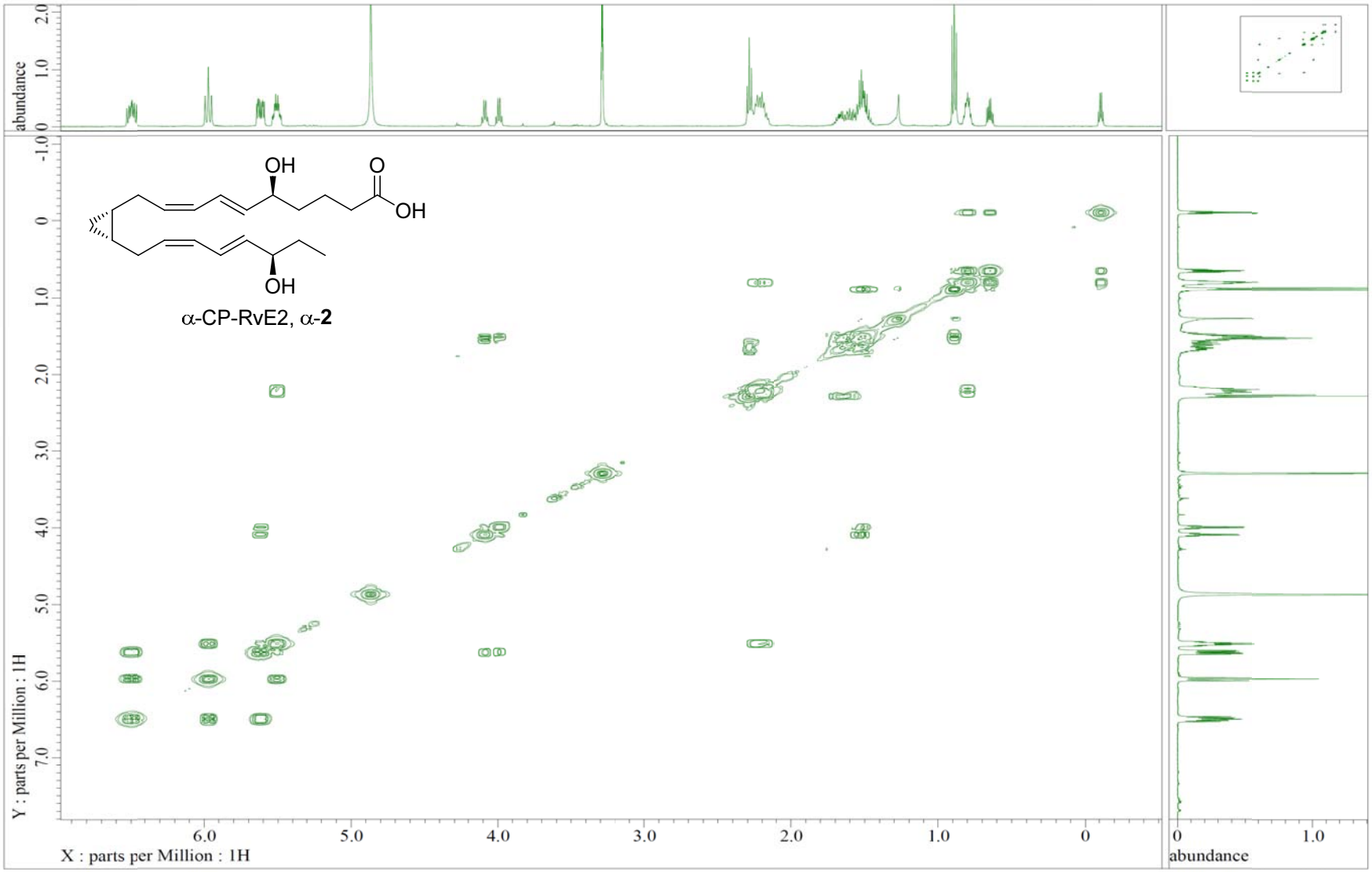

OTBS
O
OMe
OTBS
S9a
7.260
6.453
6.422
6.414
6.385
6.018
6.005
5.991
5.977
5.963
5.949
5.657
5.641
5.619
5.603
5.586
5.550
5.532
5.521
5.503
5.493
5.475
4.200
4.184
4.169
4.154
4.111
4.096
4.081
4.065
3.657
2.329
2.309
2.291
2.259
2.238
2.221
2.205
2.167
2.150
2.131
2.111
1.720
1.702
1.695
1.687
1.678
1.670
1.647
1.639
1.611
1.591
1.562
1.544
1.528
1.522
1.507
1.489
1.252
1.060
0.947
0.941
0.904
0.897
0.889
0.870
0.851
0.800
0.786
0.744
0.697
0.685
0.676
0.665
0.654
0.643
0.095
0.051
0.029
0.022
-0.002
-0.099
-0.111
-0.124
-0.136
24.81
1.86
1.89
3.95
2.00
2.84
6.04
7.34
13.12
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

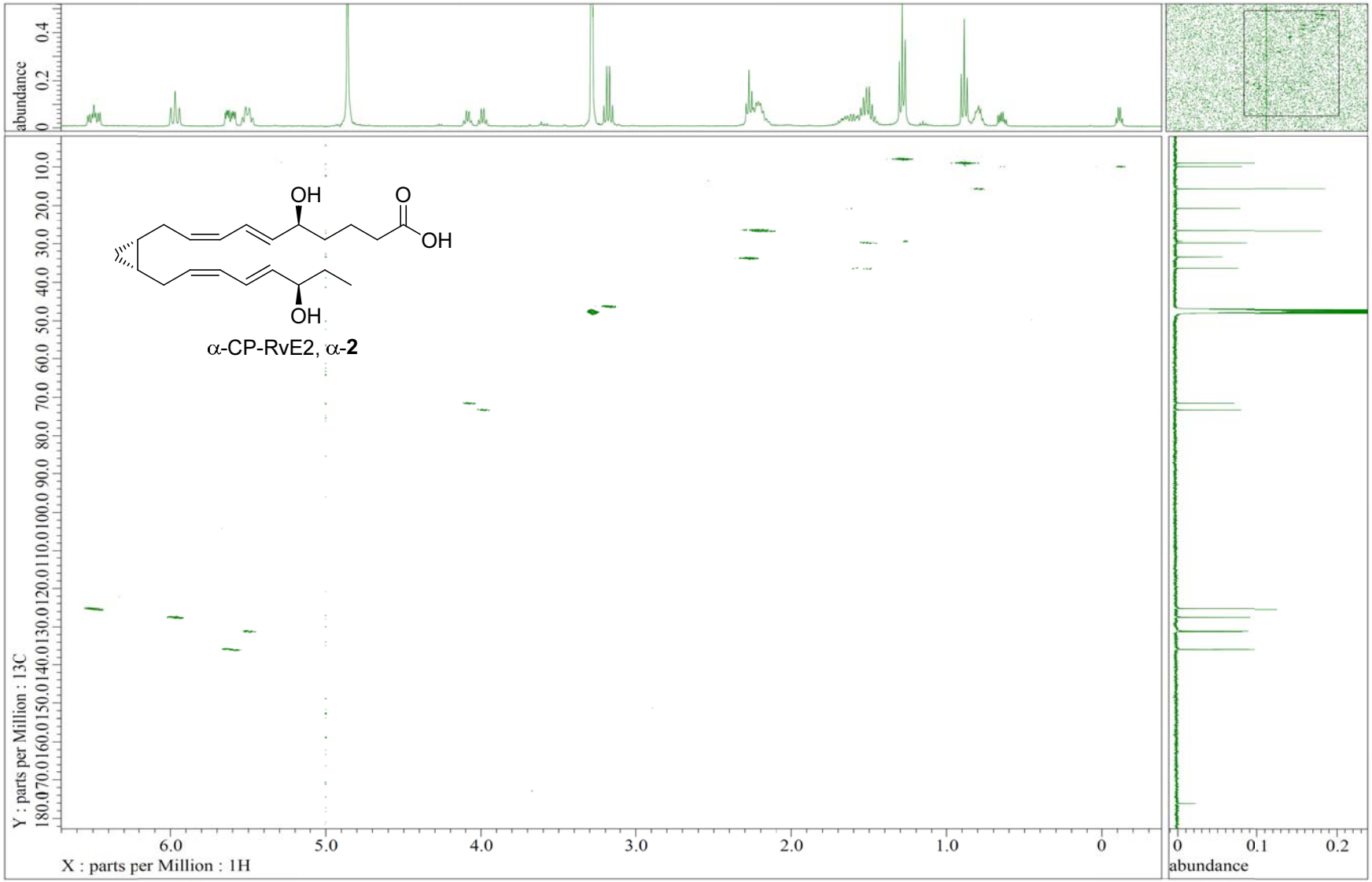

174.039
136.762
136.350
131.368
130.985
127.948
127.776
124.720
124.432
77.316
77.000
76.674
74.375
72.756
51.440
37.654
34.013
31.158
26.991
25.879
25.860
20.725
18.263
18.206
15.897
15.878
10.723
9.689
-4.327
-4.375
-4.758
-4.797
OTBS
O
OMe
OTBS
S9a
PPM
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0

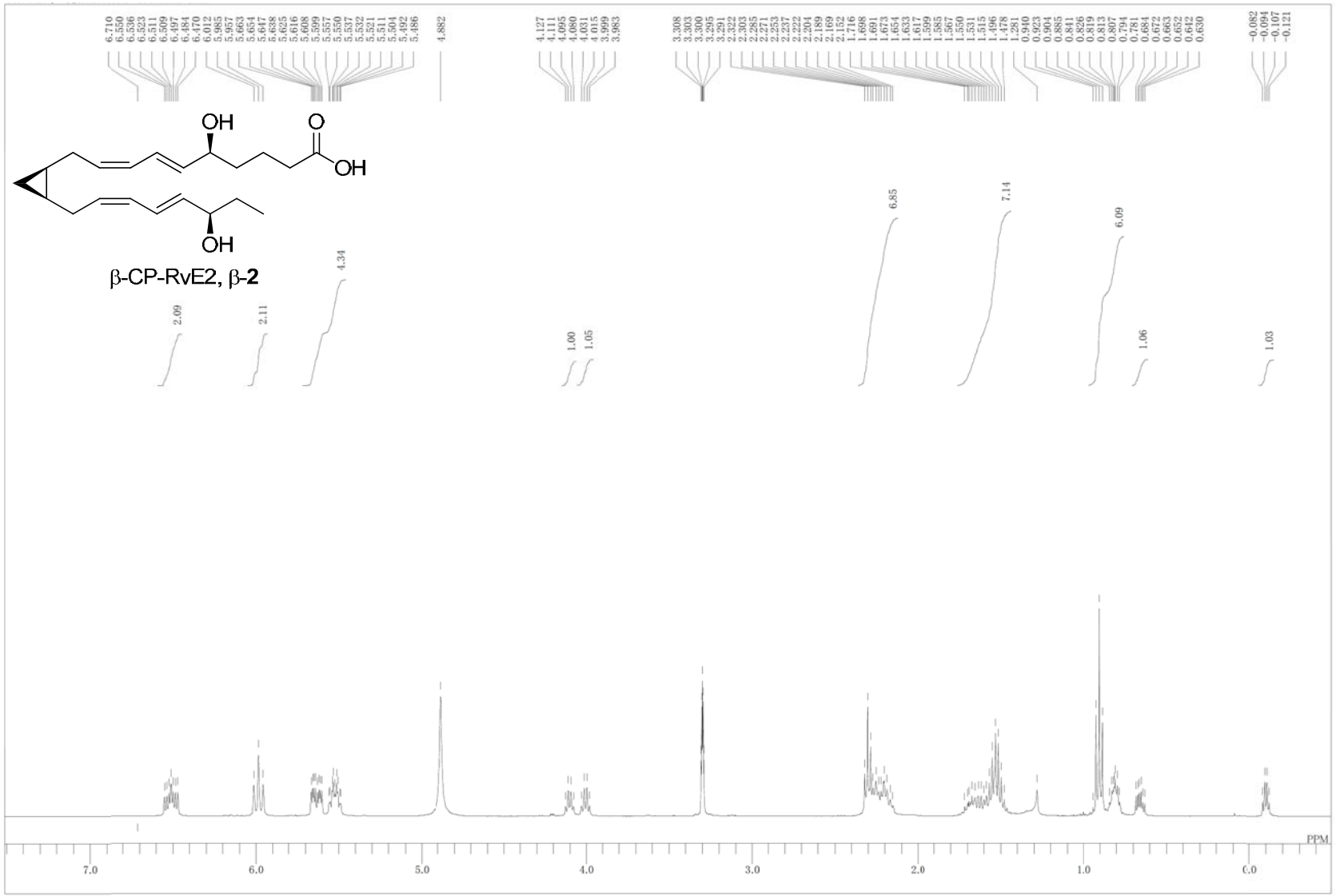

OH
O
OH
OH
α-CP-RvE2, α-2
PPM
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

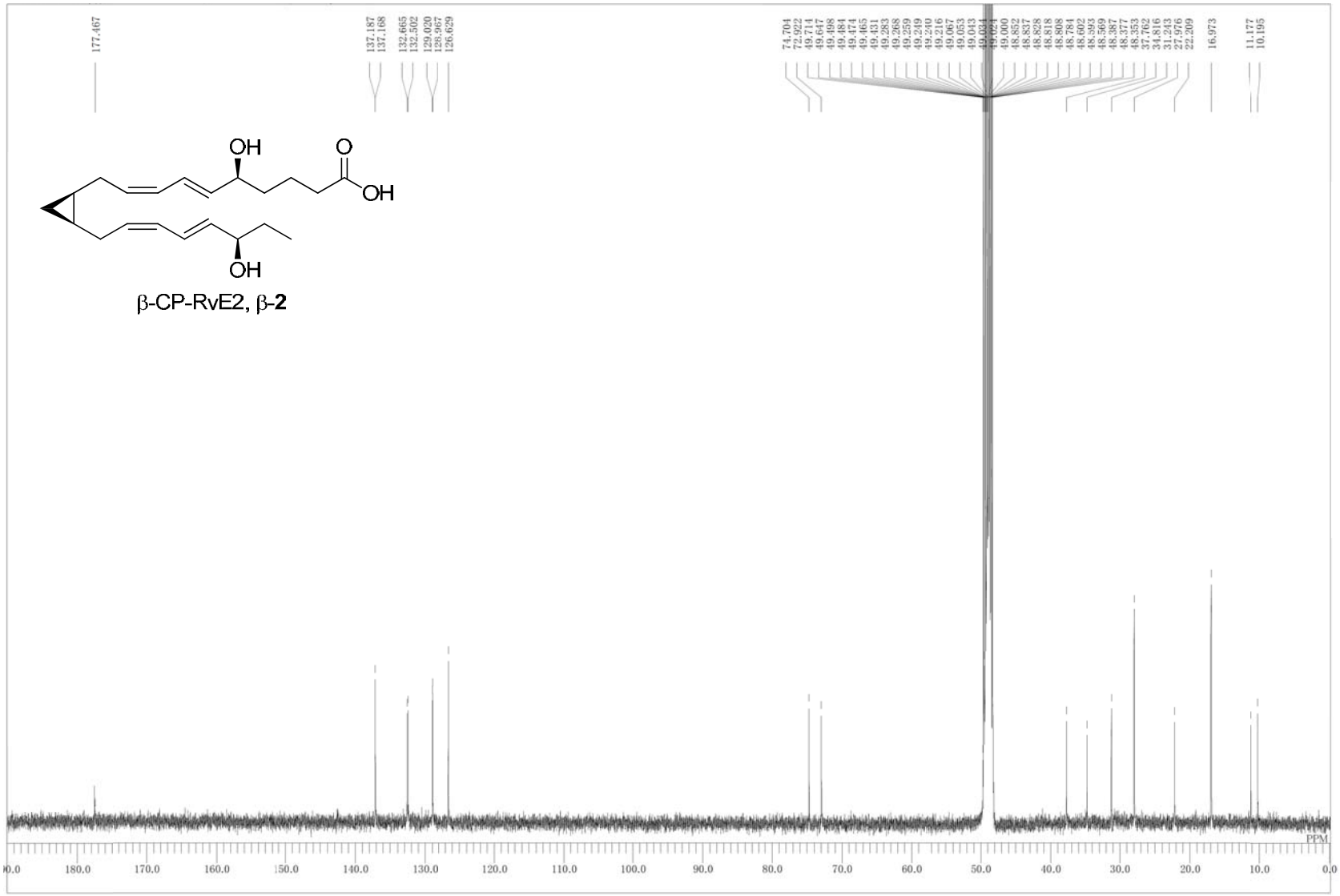

177.491
137.182
137.153
132.699
132.537
128.989
128.941
126.680
74.734
72.960
49.630
49.515
49.458
49.343
49.286
49.172
49.114
49.000
48.943
48.828
48.657
48.485
37.764
34.797
31.230
27.987
22.188
16.980
11.152
10.208
OH
O
OH
OH
PPM
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

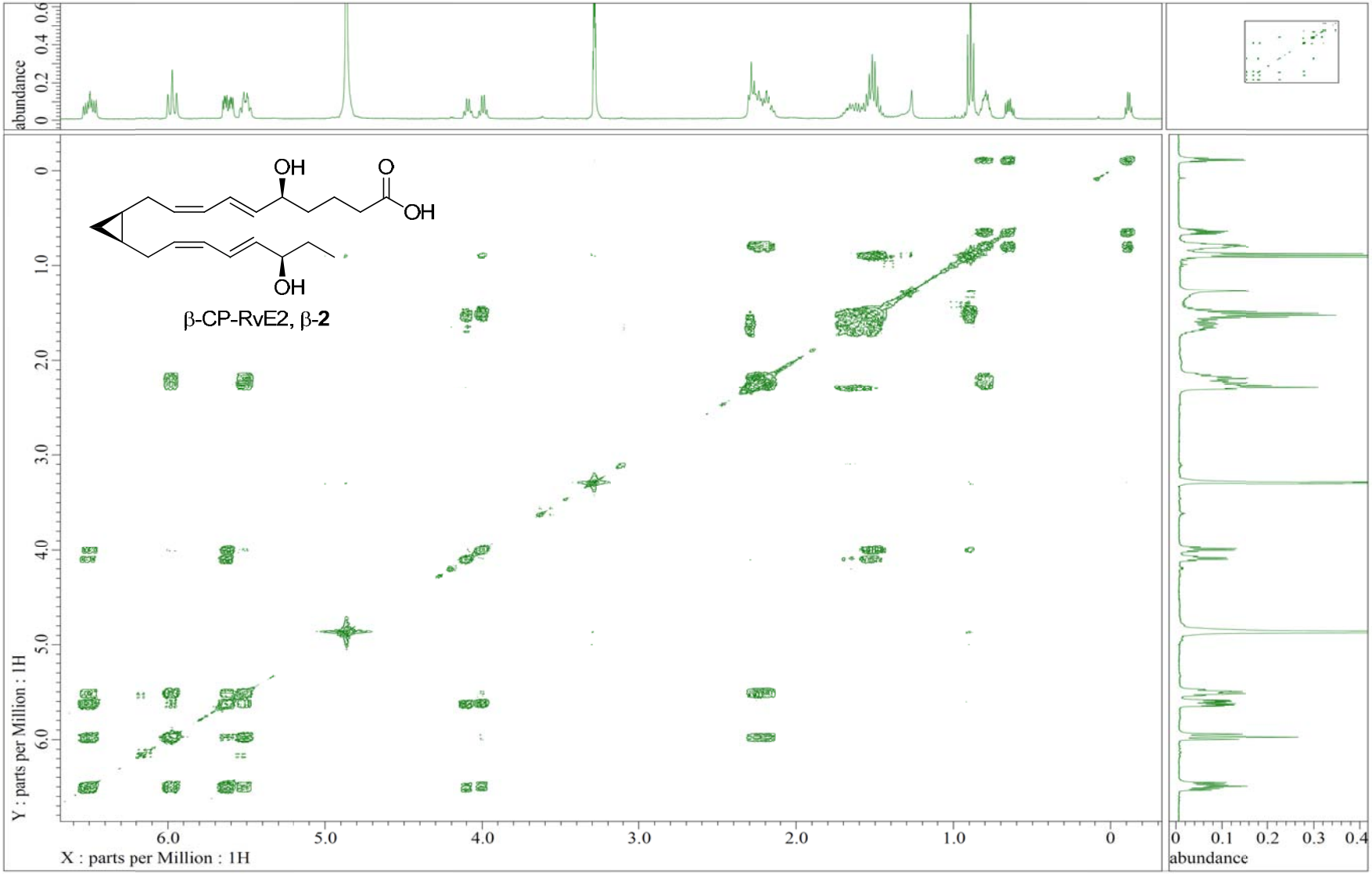
α-CP-RvE2, α-**2**

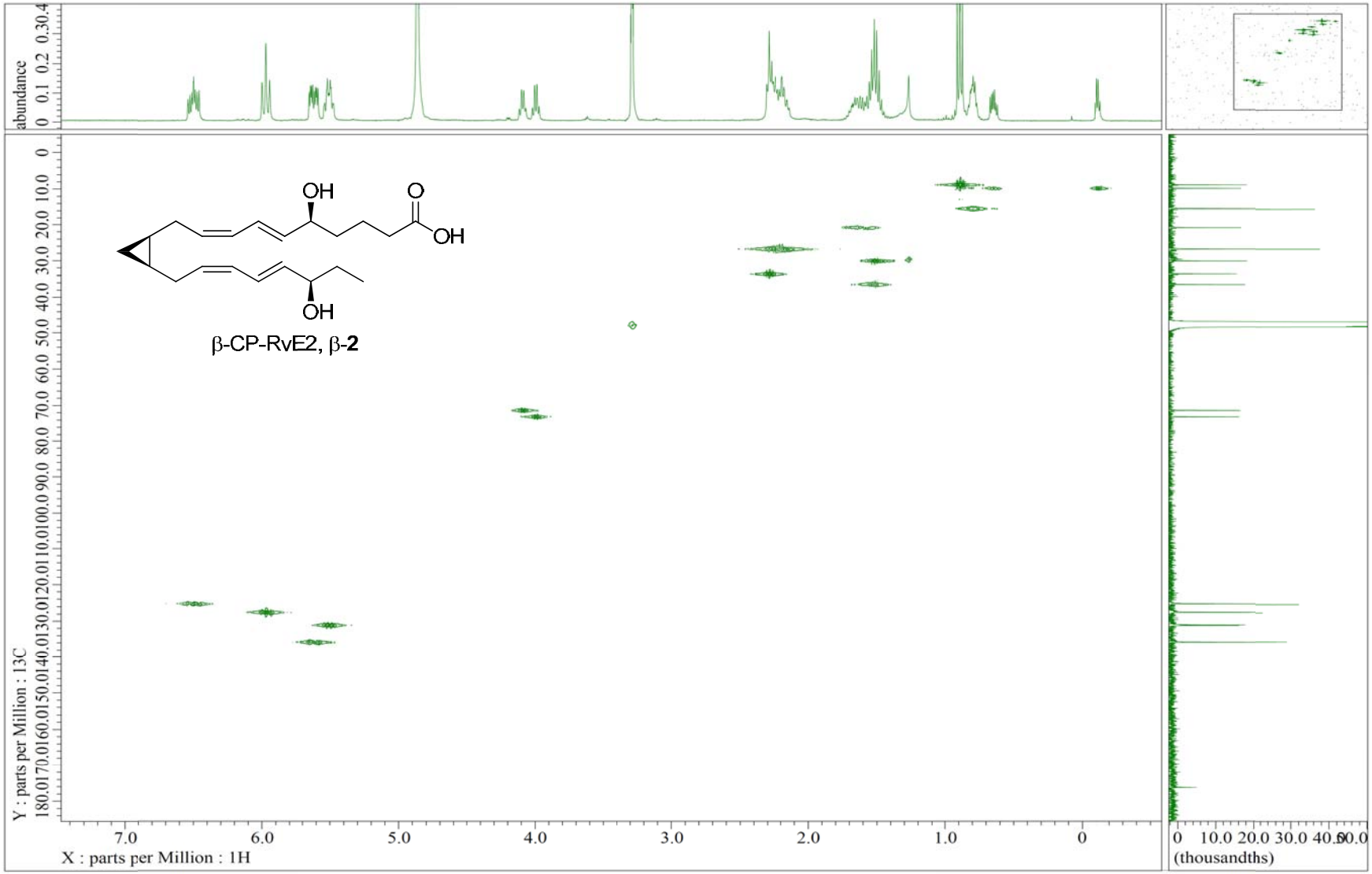

abundance
OH
O
OH
OH
α-CP-RvE2, α-2
Y : parts per Million : 1H
X : parts per Million : 1H
abundance

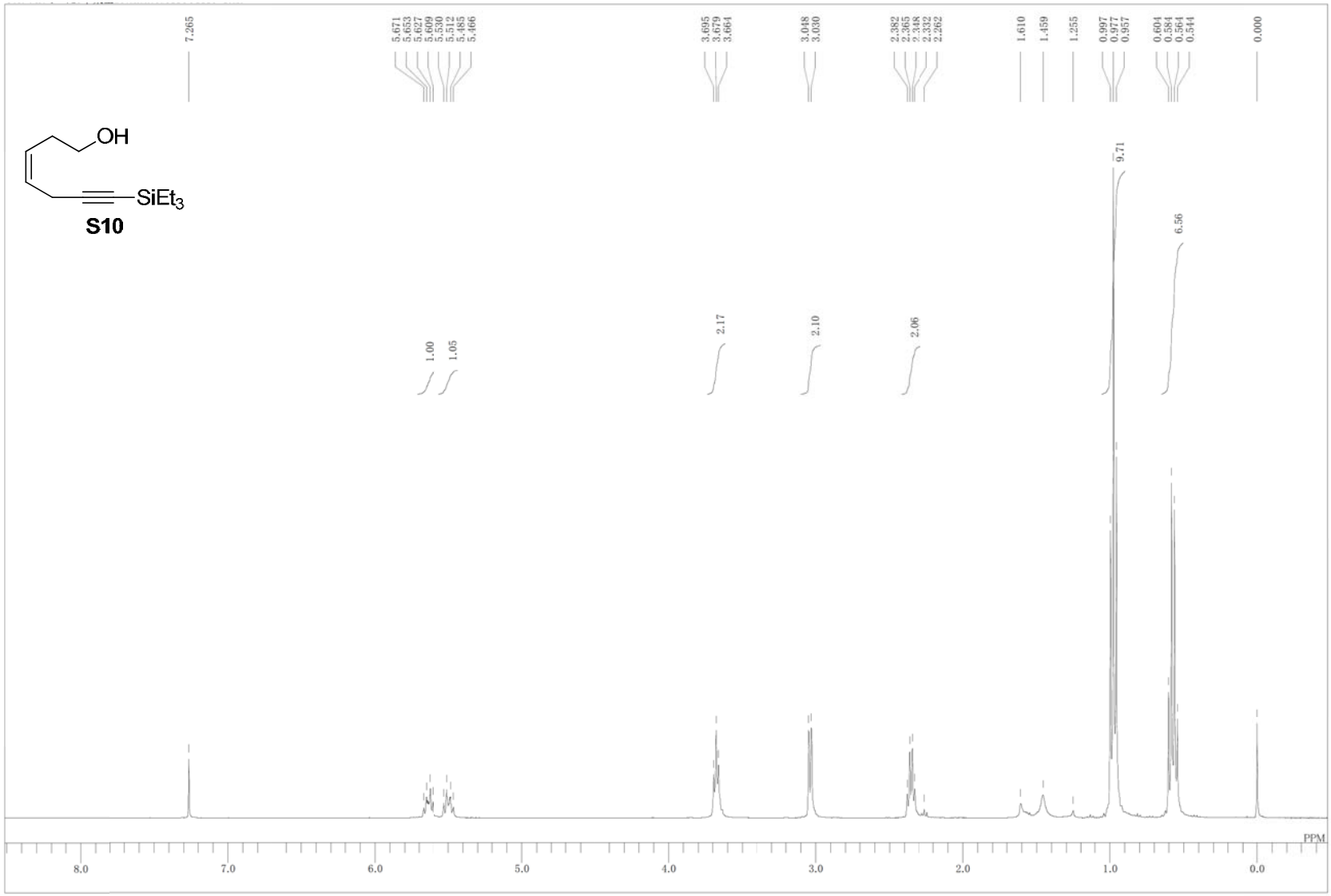

abundance
0
0.2
0.4
OH
O
OH
OH
α-CP-RvE2, α-2
Y : parts per Million : 13C
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
180.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H
0
0.1
0.2
abundance

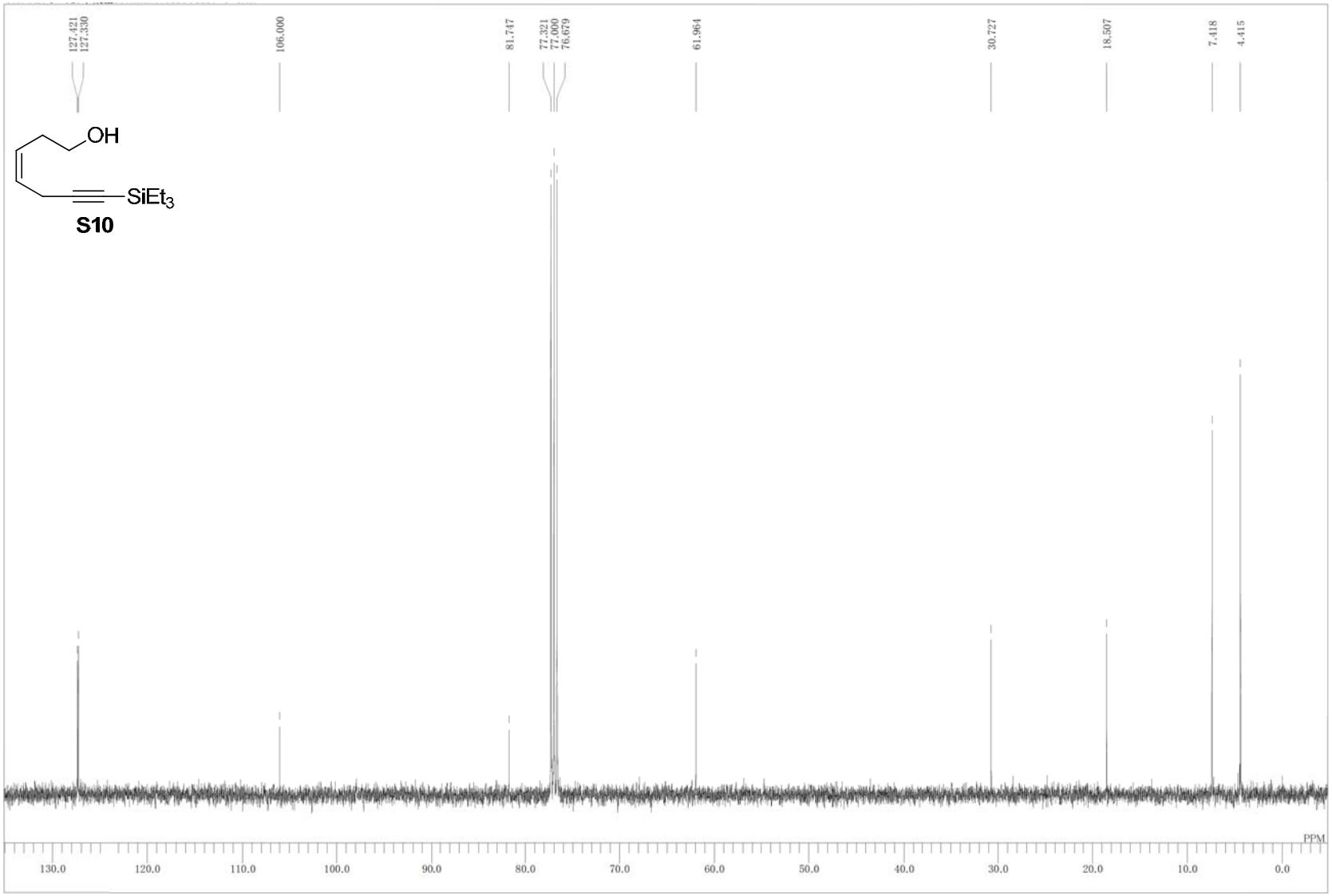

OH
O
OH
OH
β-CP-RvE2, β-2
6.85
7.14
6.09
4.34
2.09
2.11
1.00
1.05
1.06
1.03
PPM
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

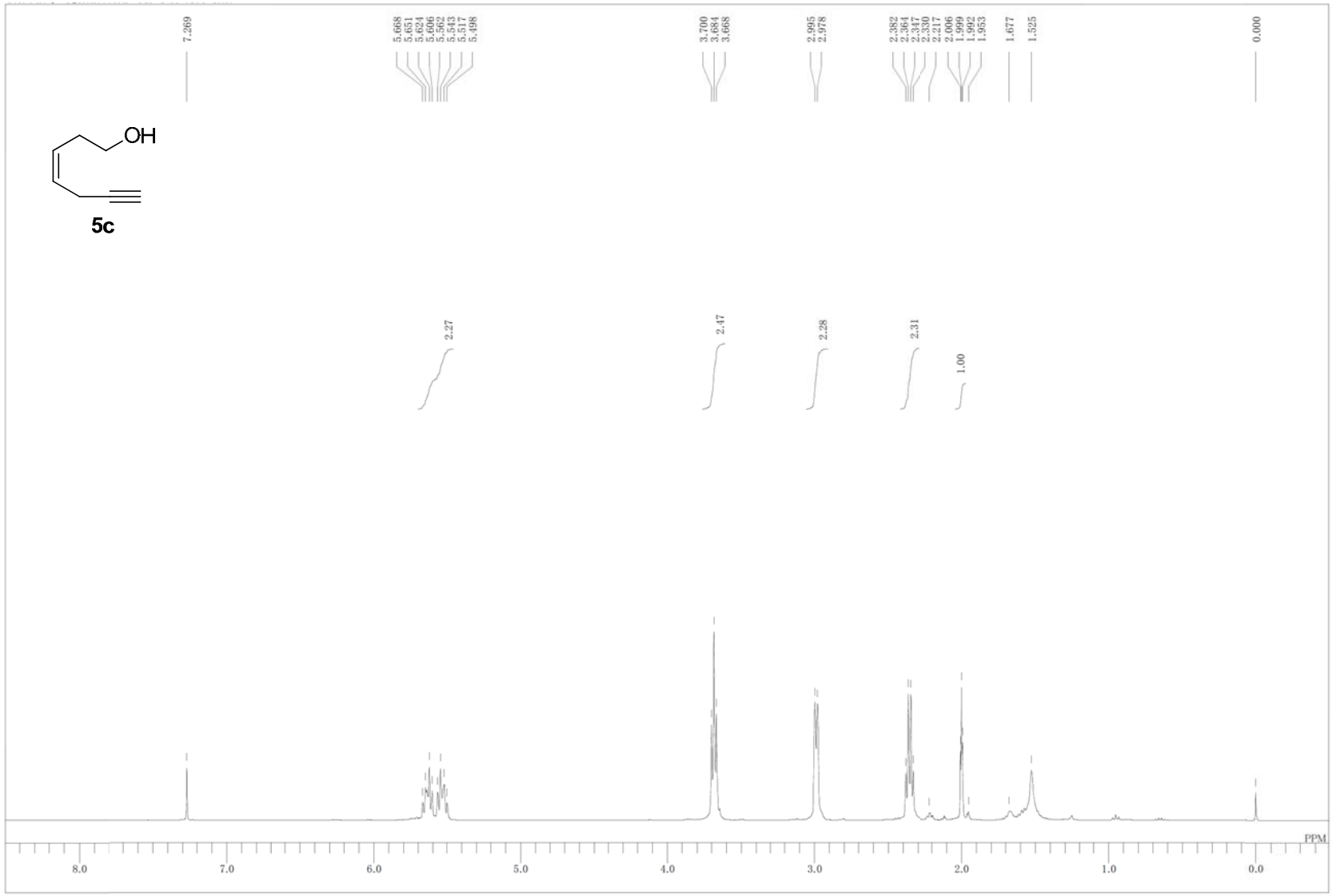

177.467
137.187
137.168
132.665
132.502
129.020
126.657
126.629
74.704
72.922
49.711
49.647
49.498
49.484
49.471
49.465
49.431
49.283
49.268
49.259
49.249
49.240
49.216
49.067
49.053
49.043
49.034
49.021
49.000
48.852
48.837
48.828
48.818
48.808
48.784
48.602
48.593
48.569
48.387
48.377
48.353
37.762
34.816
31.243
27.976
22.209
16.973
11.177
10.195
OH
O
OH
OH
β-CP-RvE2, β-2
PPM
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

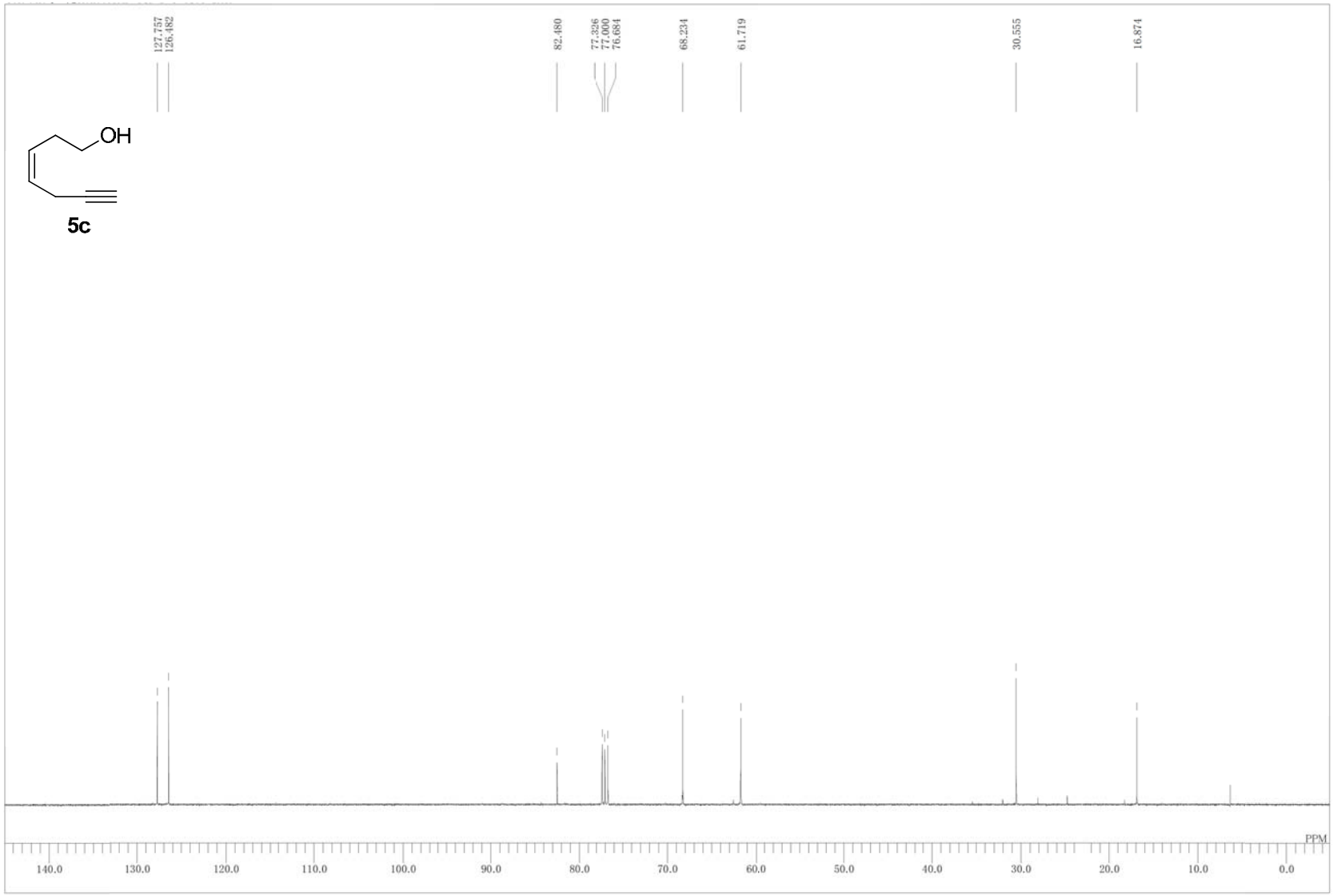

abundance
0
0.2
0.4
0.6
OH
O
OH
OH
β-CP-RvE2, β-2
Y : parts per Million : 1H
X : parts per Million : 1H
6.0
5.0
4.0
3.0
2.0
1.0
0
0.1
0.2
0.3
0.4
abundance

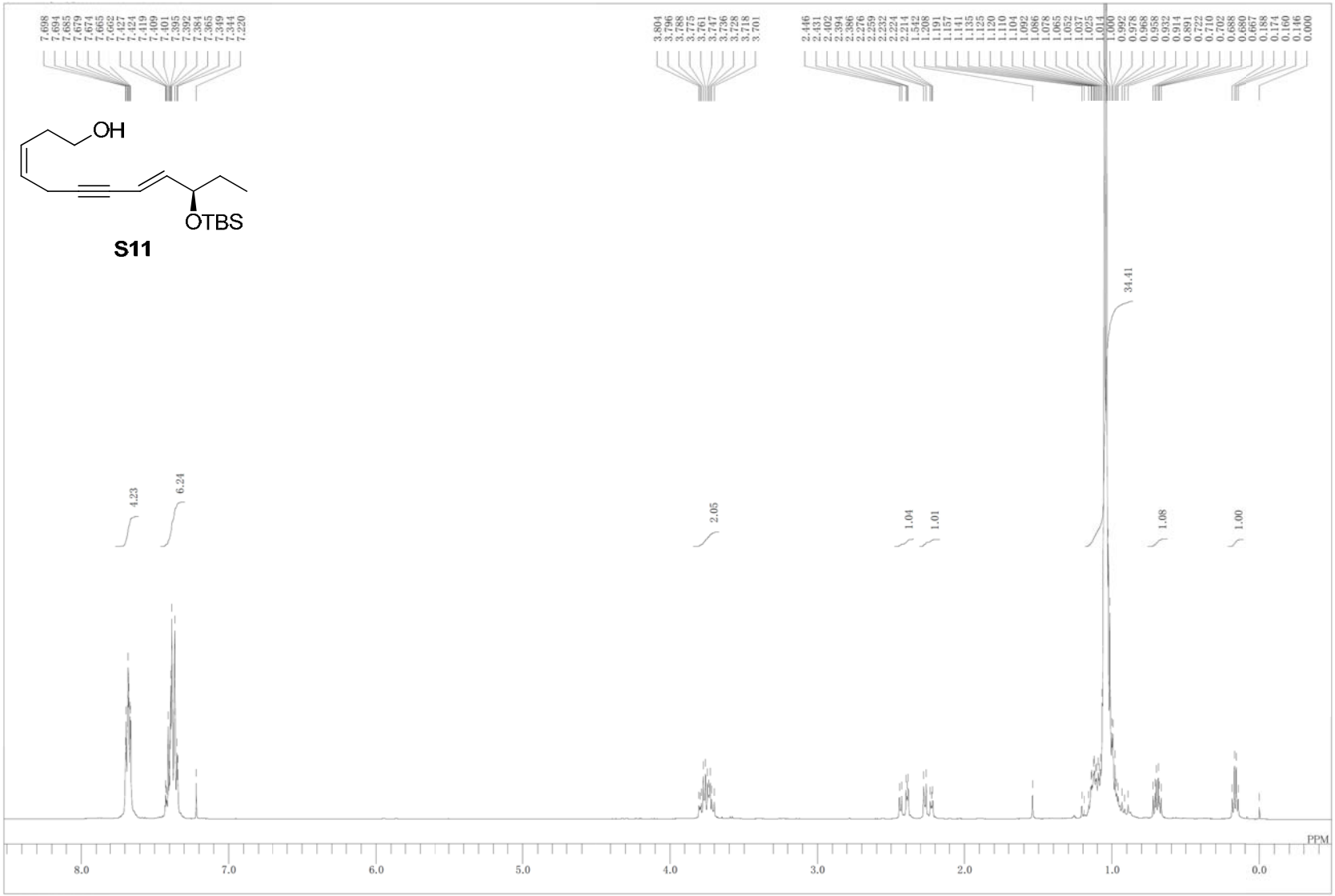

abundance
0 0.1 0.2 0.3 0.4
OH
O
OH
OH
β-CP-RvE2, β-2
Y : parts per Million : 13C
0 10.0 20.0 30.0 40.0 50.0 60.0 70.0 80.0 90.0 100.0 110.0 120.0 130.0 140.0 150.0 160.0 170.0 180.0
7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
X : parts per Million : 1H
0 10.0 20.0 30.0 40.0 50.0
(thousandths)

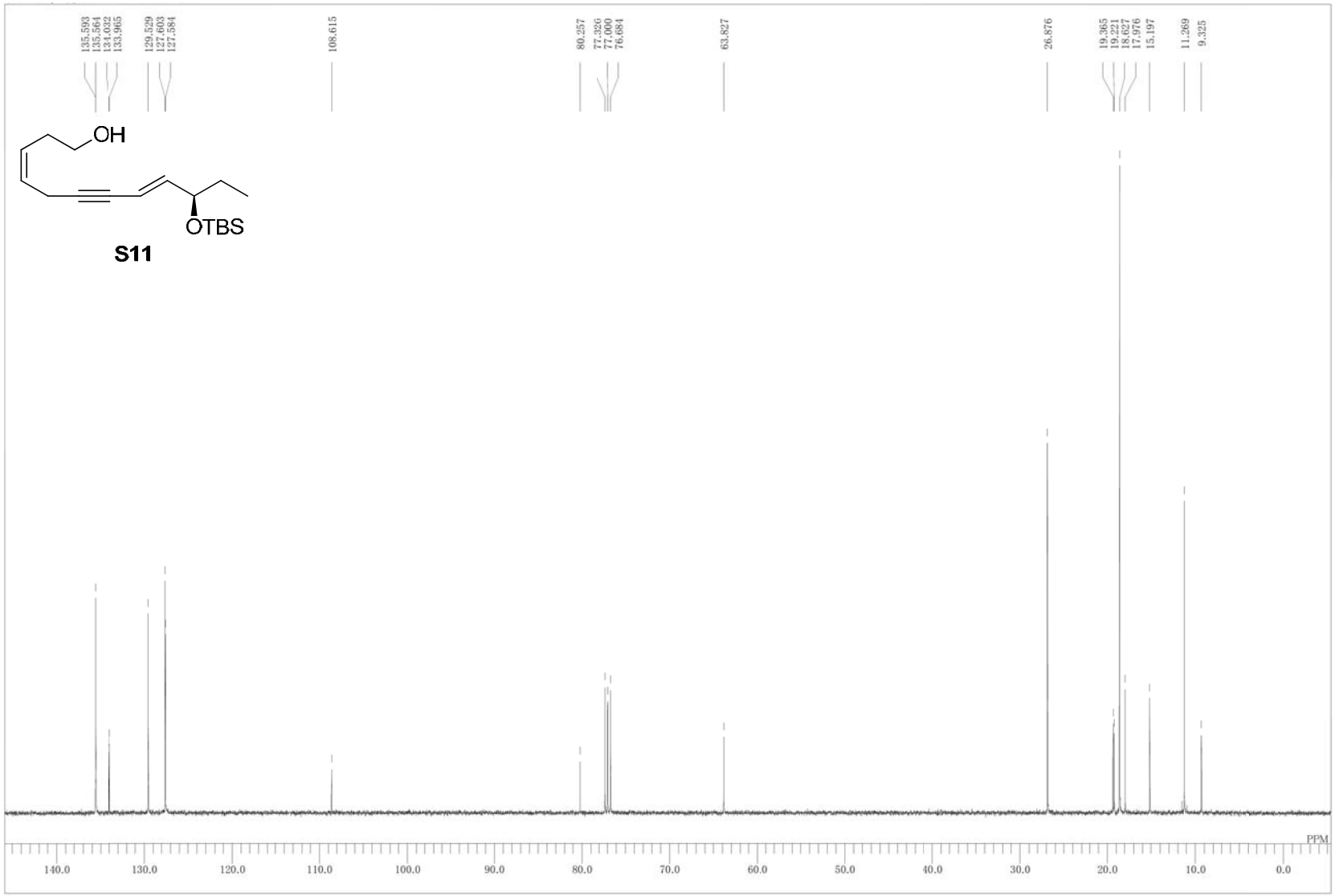

7.265
5.671
5.653
5.627
5.609
5.530
5.512
5.485
5.466
3.695
3.679
3.664
3.048
3.030
2.382
2.365
2.348
2.332
2.262
1.610
1.459
1.255
0.997
0.977
0.957
0.604
0.584
0.564
0.544
0.000
OH
SiEt3
S10
9.71
6.56
1.00
1.05
2.17
2.10
2.06
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

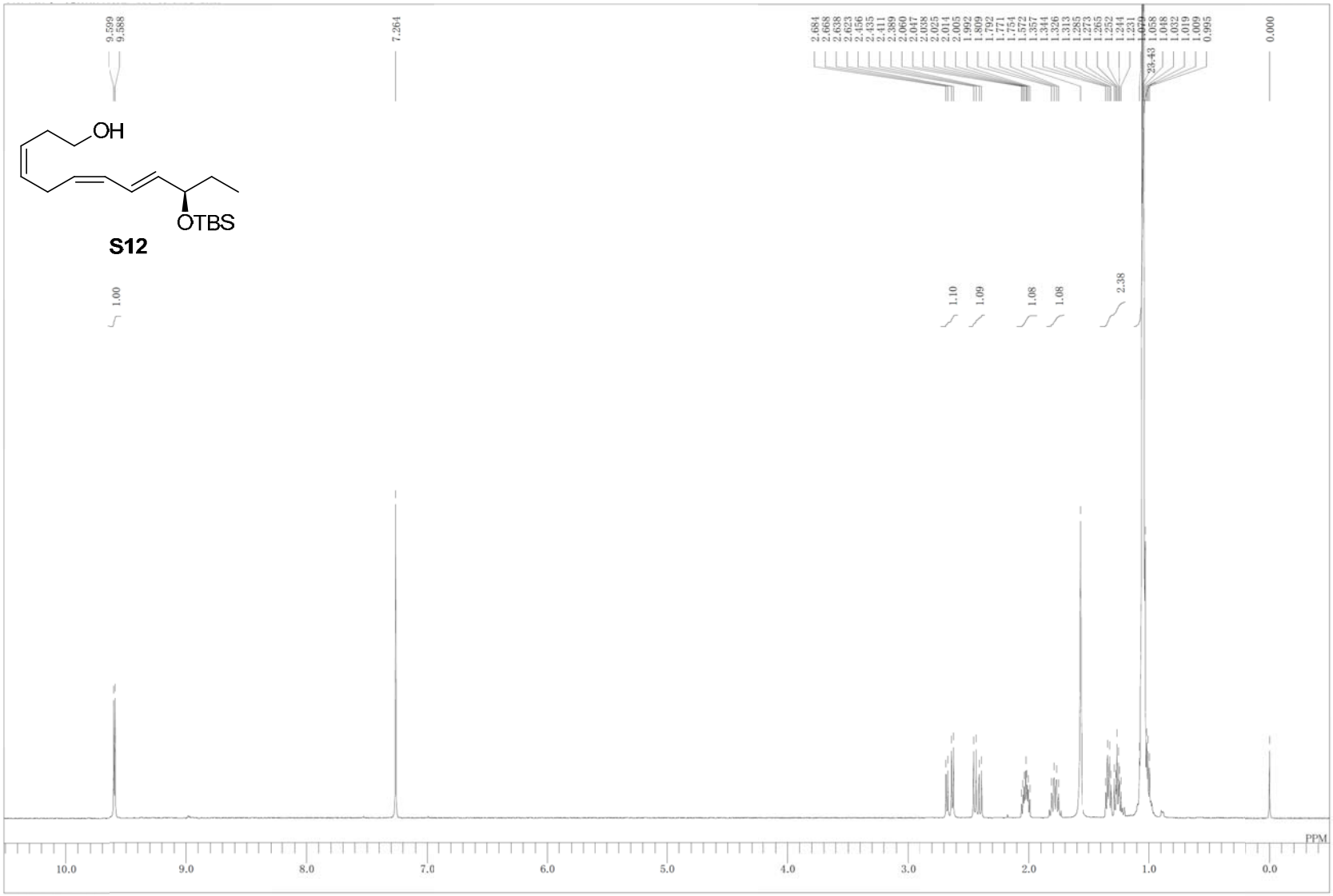

127.421
127.330
106.000
81.747
77.321
77.000
76.679
61.964
30.727
18.507
7.418
4.415
OH
SiEt3
S10
PPM
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

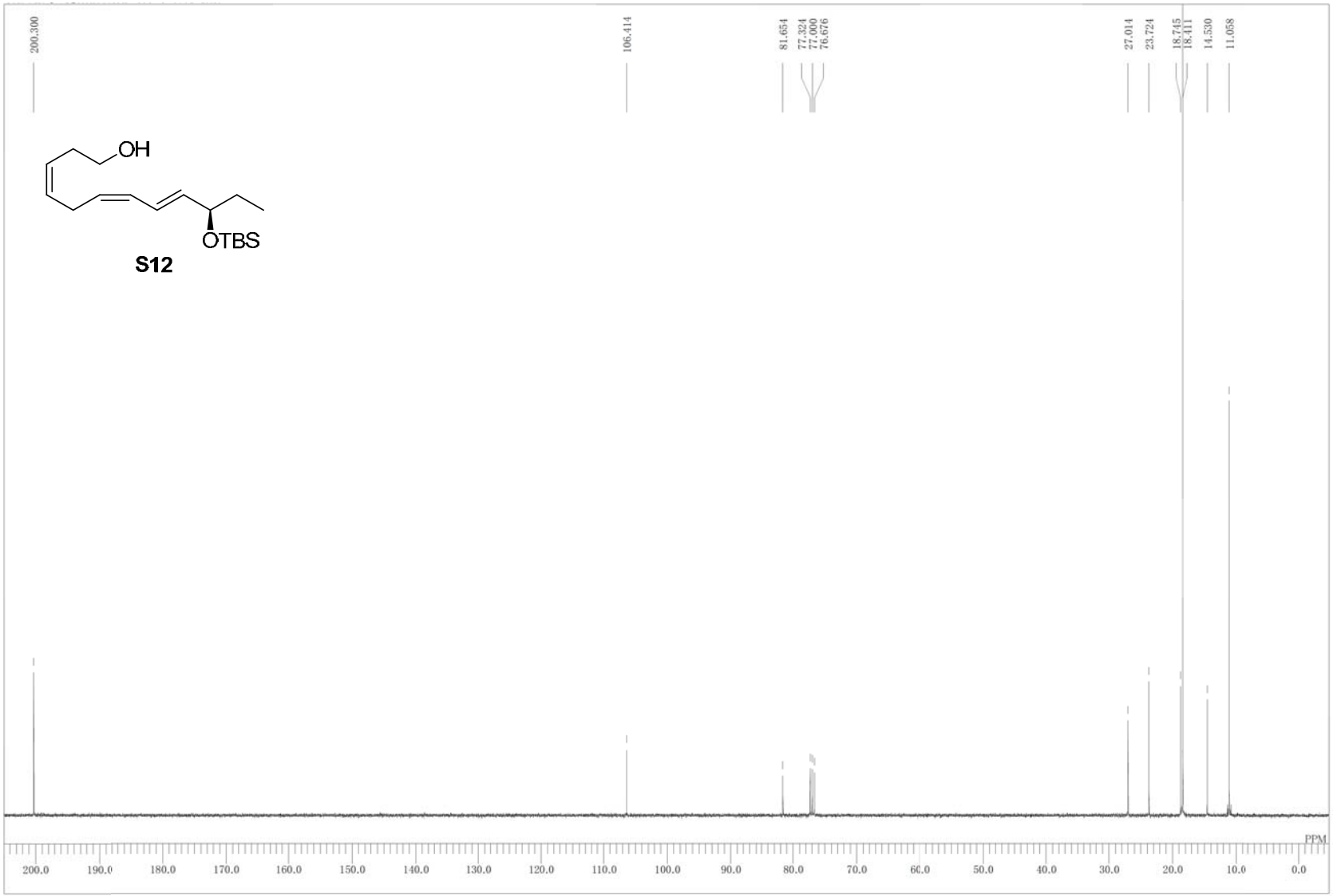

7.269
5.668
5.651
5.624
5.606
5.562
5.543
5.517
5.498
3.700
3.684
3.668
2.995
2.978
2.382
2.364
2.347
2.330
2.217
2.006
1.999
1.992
1.953
1.677
1.525
0.000
OH
5c
2.27
2.47
2.28
2.31
1.00
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

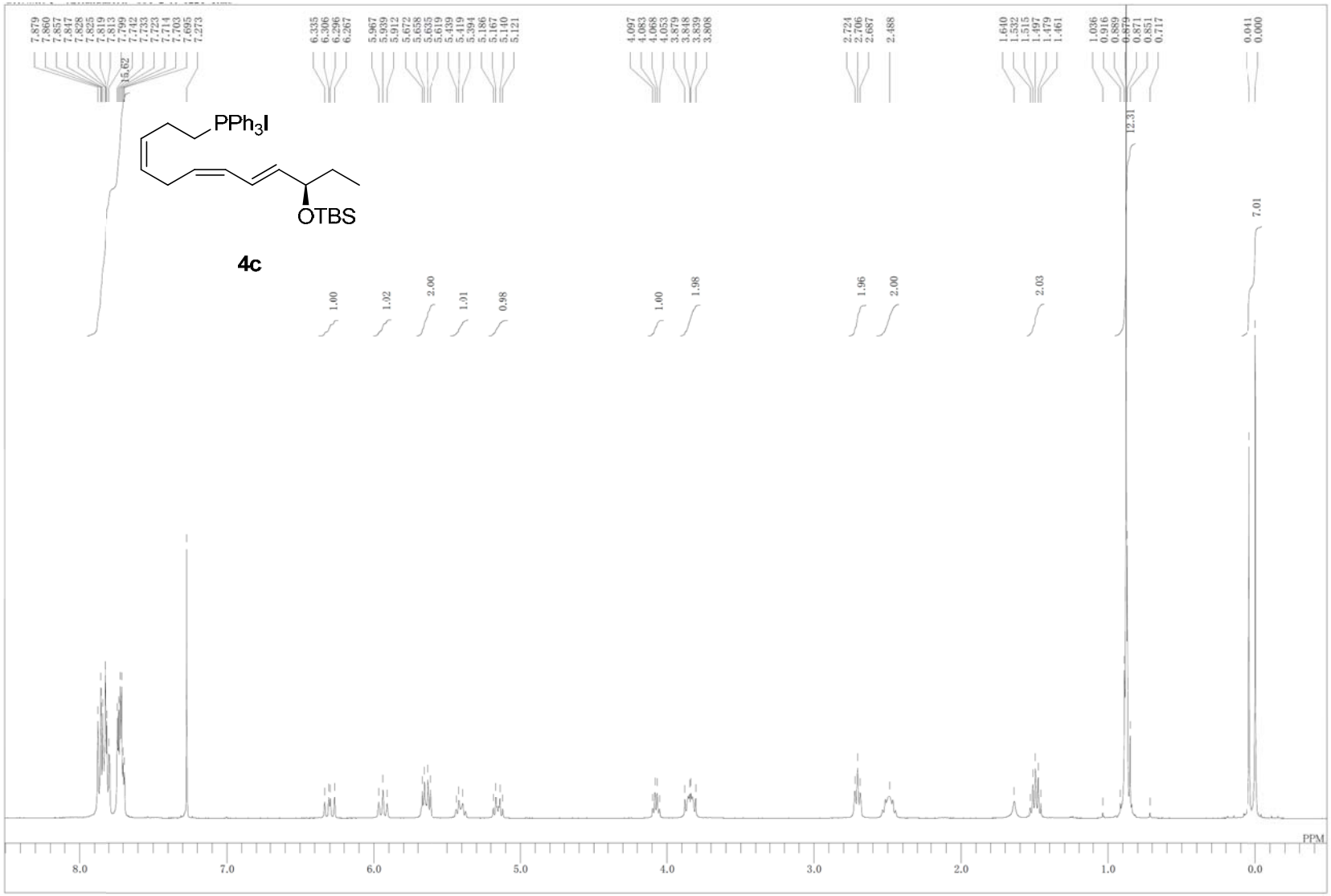

127.757
126.482
82.480
77.326
77.000
76.684
68.234
61.719
30.555
16.874
OH
5c
PPM
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

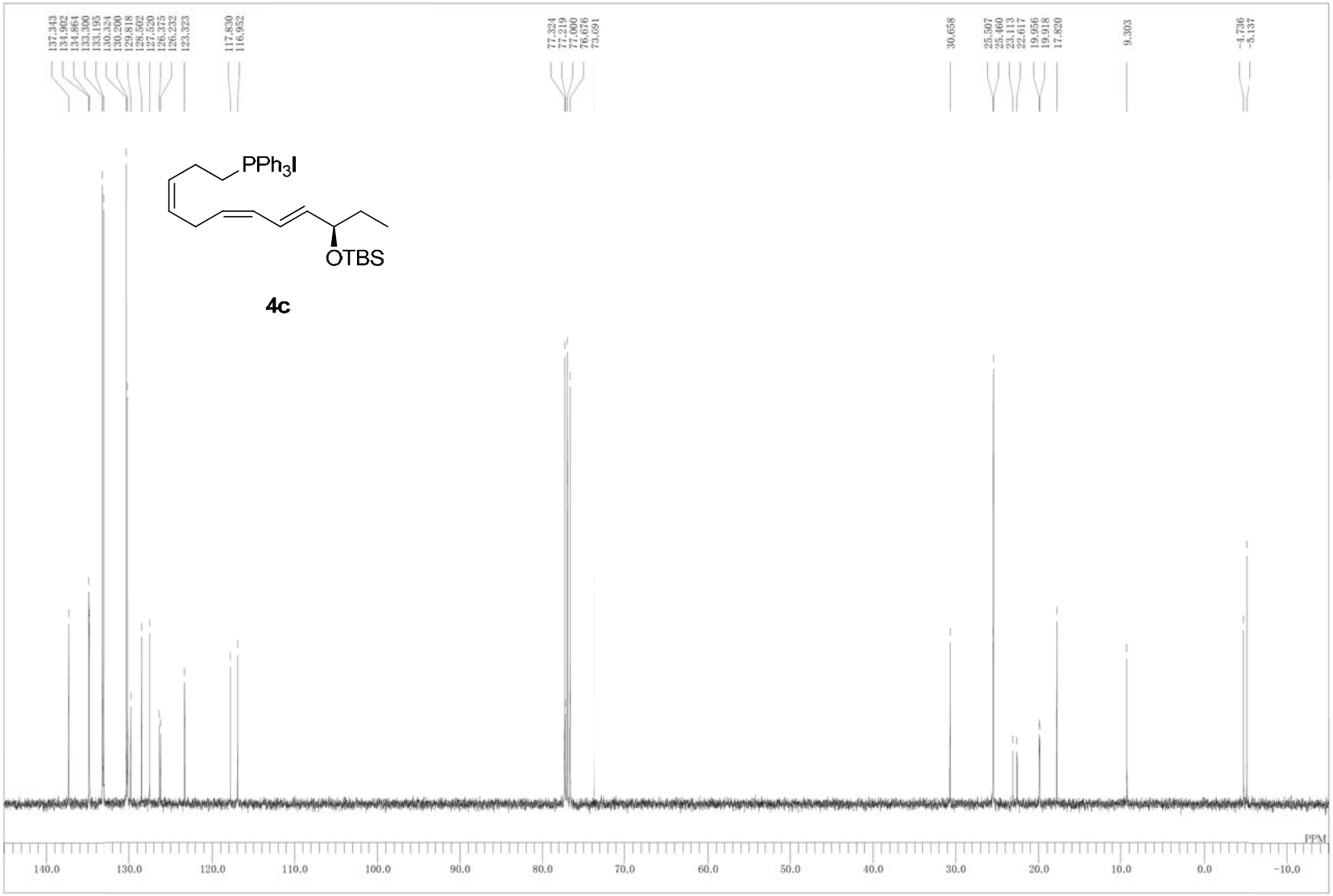

OH
OTBS
S11
7.698 7.694 7.685 7.679 7.674 7.665 7.662 7.427 7.424 7.419 7.409 7.401 7.395 7.392 7.384 7.365 7.349 7.344 7.220
3.804 3.796 3.788 3.775 3.761 3.747 3.736 3.728 3.718 3.701
2.446 2.431 2.402 2.394 2.386 2.276 2.259 2.252 2.224 2.214 2.142 1.208 1.191 1.157 1.141 1.135 1.125 1.120 1.110 1.104 1.092 1.086 1.078 1.065 1.052 1.037 1.025 1.014 1.000 0.992 0.978 0.968 0.958 0.932 0.914 0.891 0.722 0.710 0.702 0.688 0.680 0.667 0.198 0.174 0.160 0.146 0.000
4.23
6.24
2.05
1.04
1.01
34.41
1.08
1.00
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

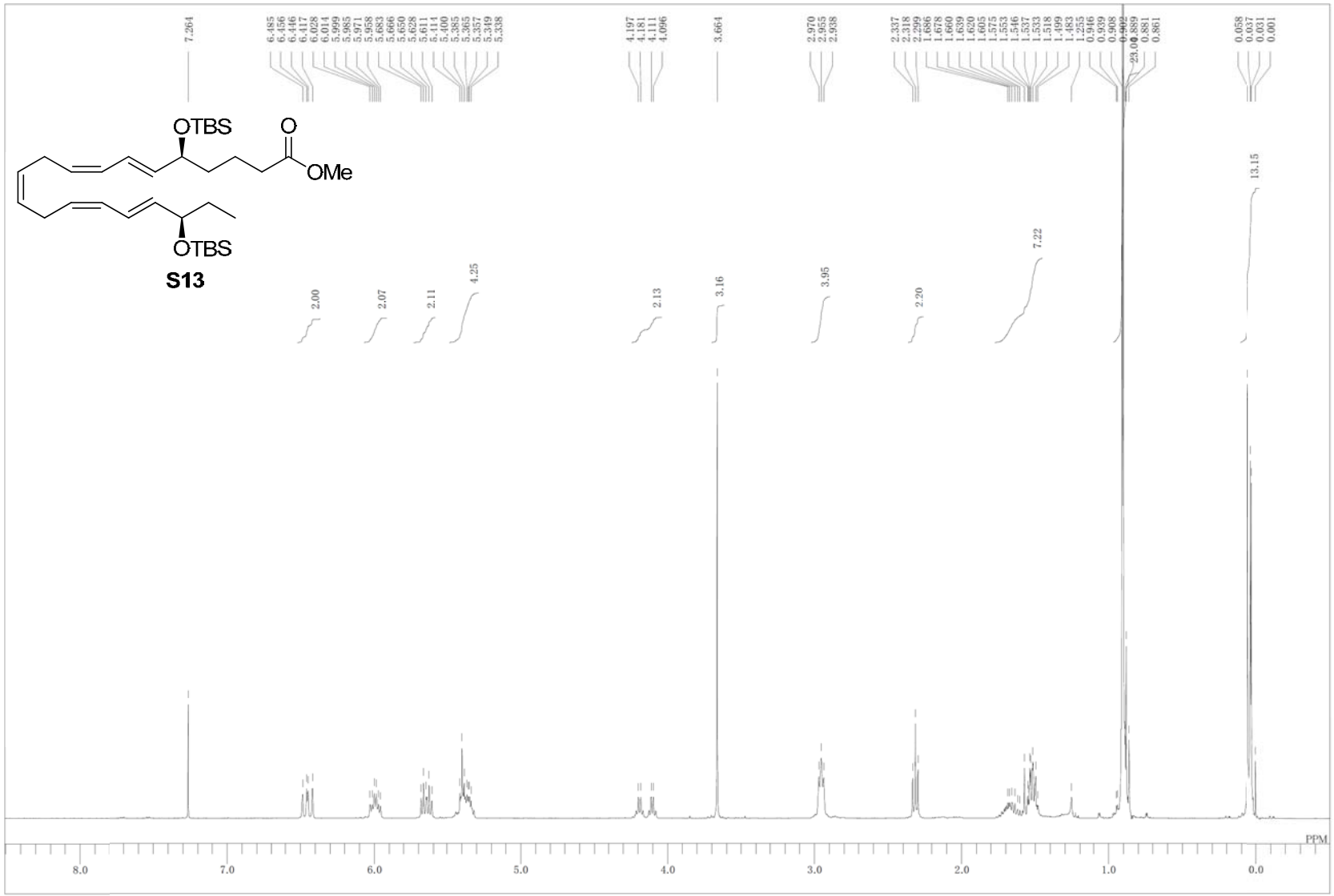

135.593
135.564
134.032
133.965
129.529
127.603
127.584
108.615
80.257
77.326
77.000
76.684
63.827
26.876
19.365
19.221
18.627
17.976
15.197
11.269
9.325
OH
OTBS
S11
PPM
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

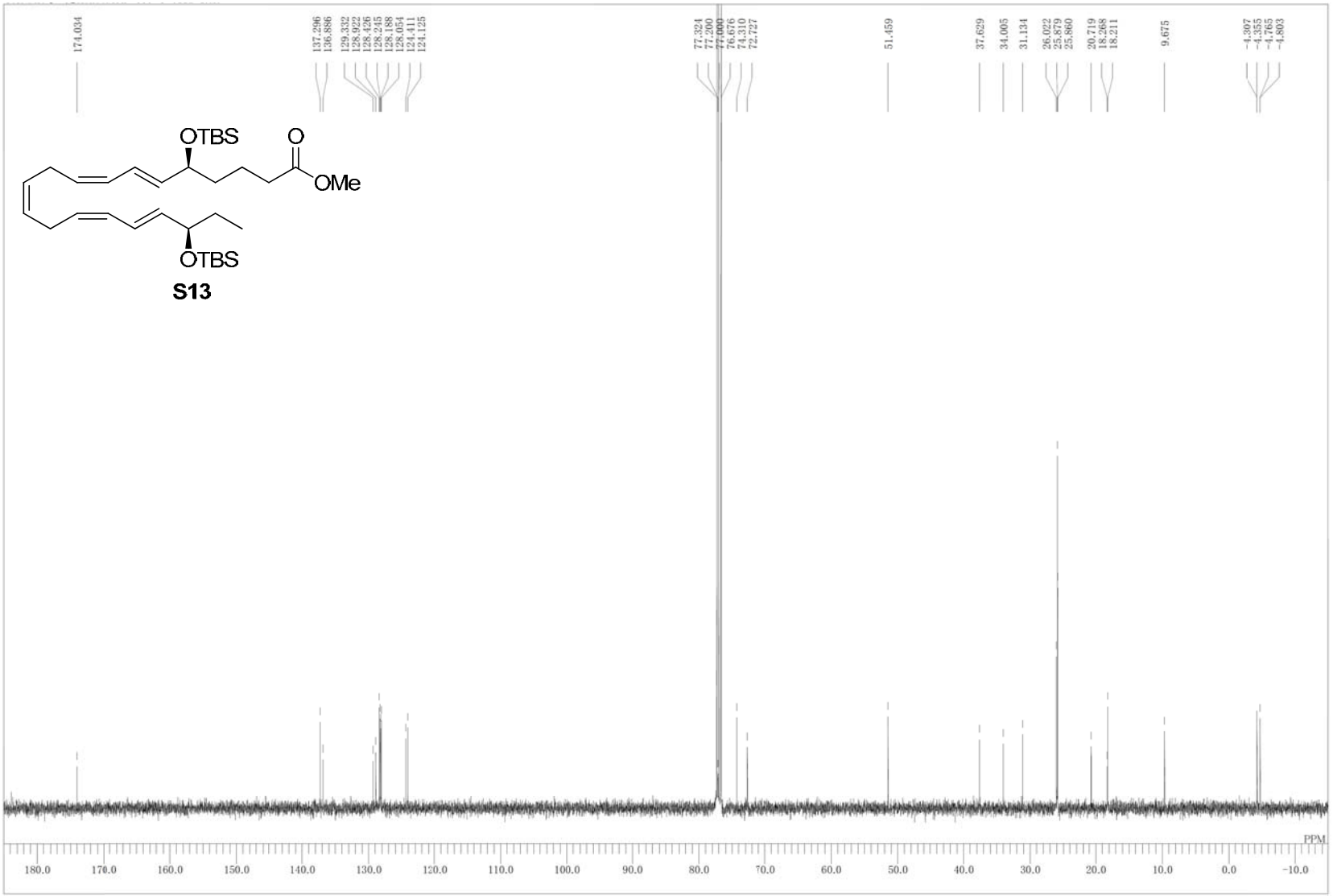

OH
OTBS
S12
9.599
9.588
7.264
2.684
2.668
2.658
2.623
2.456
2.435
2.411
2.389
2.060
2.047
2.038
2.025
2.014
2.005
1.992
1.809
1.792
1.771
1.754
1.572
1.357
1.344
1.326
1.313
1.285
1.273
1.265
1.252
1.244
1.231
1.079
1.058
1.048
1.032
1.019
1.009
0.995
0.000
1.00
1.10
1.09
1.08
1.08
2.38
28.43
PPM
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

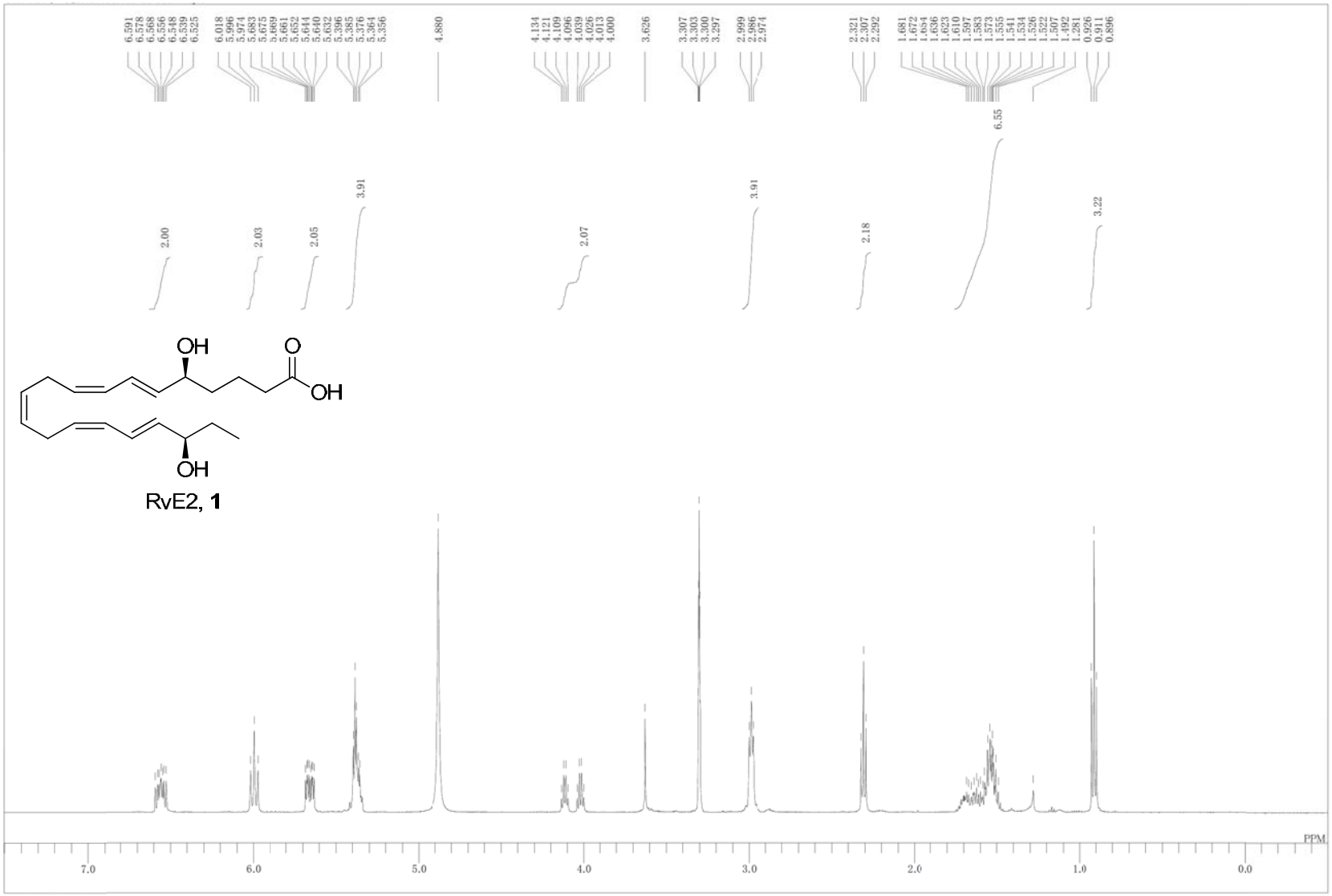

200.300
106.414
81.654
77.324
77.000
76.676
27.014
23.724
18.745
18.411
14.530
11.058
OH
OTBS
S12
PPM
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0


PPh3I
OTBS
4c
PPM

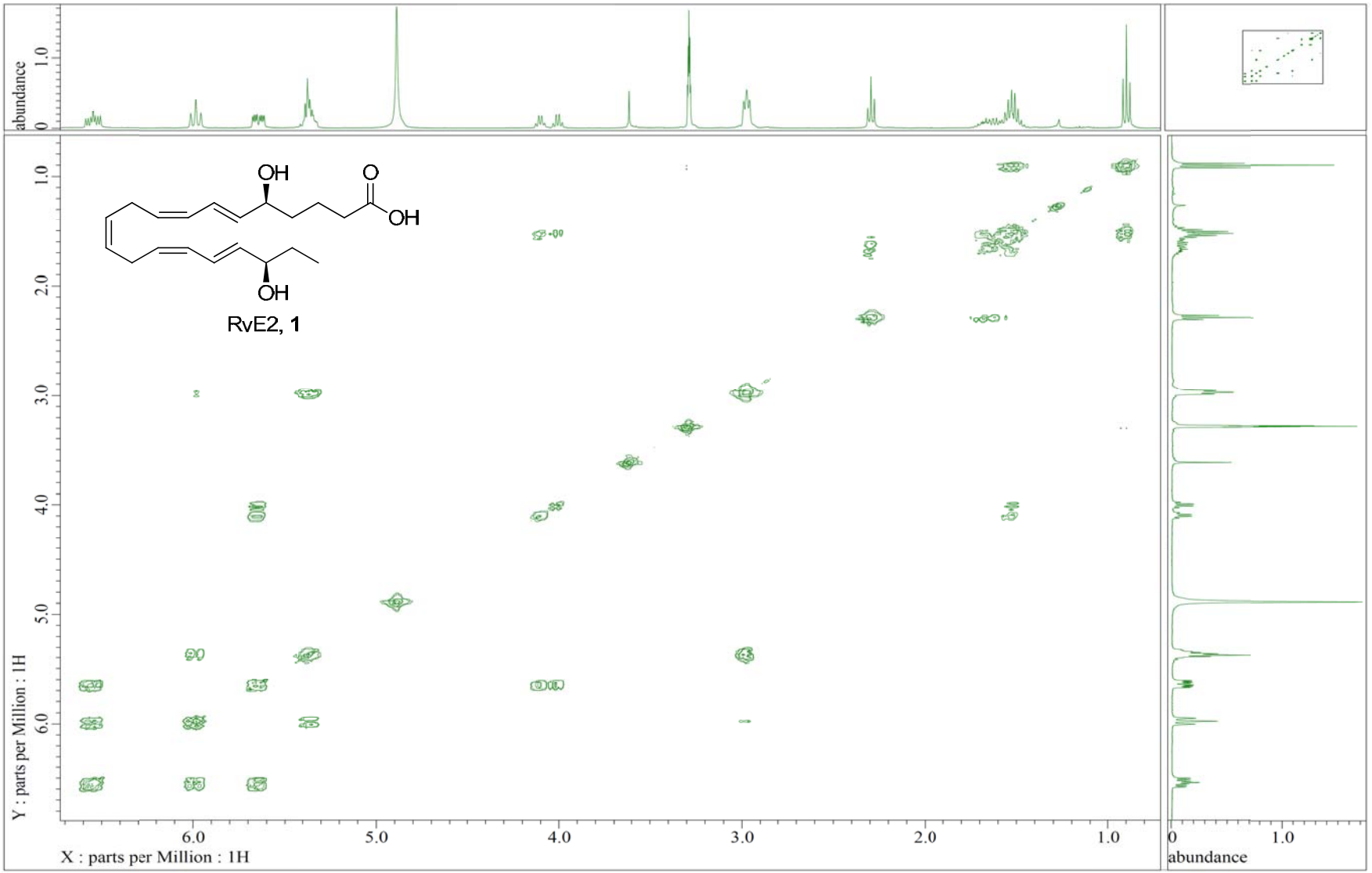

137.343
134.902
134.864
133.300
133.195
130.324
130.200
129.818
128.562
127.520
126.375
126.232
123.323
117.830
116.952
77.324
77.219
77.000
76.676
73.091
30.658
25.507
25.460
23.113
22.617
19.956
19.918
17.820
9.303
-4.736
-5.137
PPh3I
OTBS
4c
PPM
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0

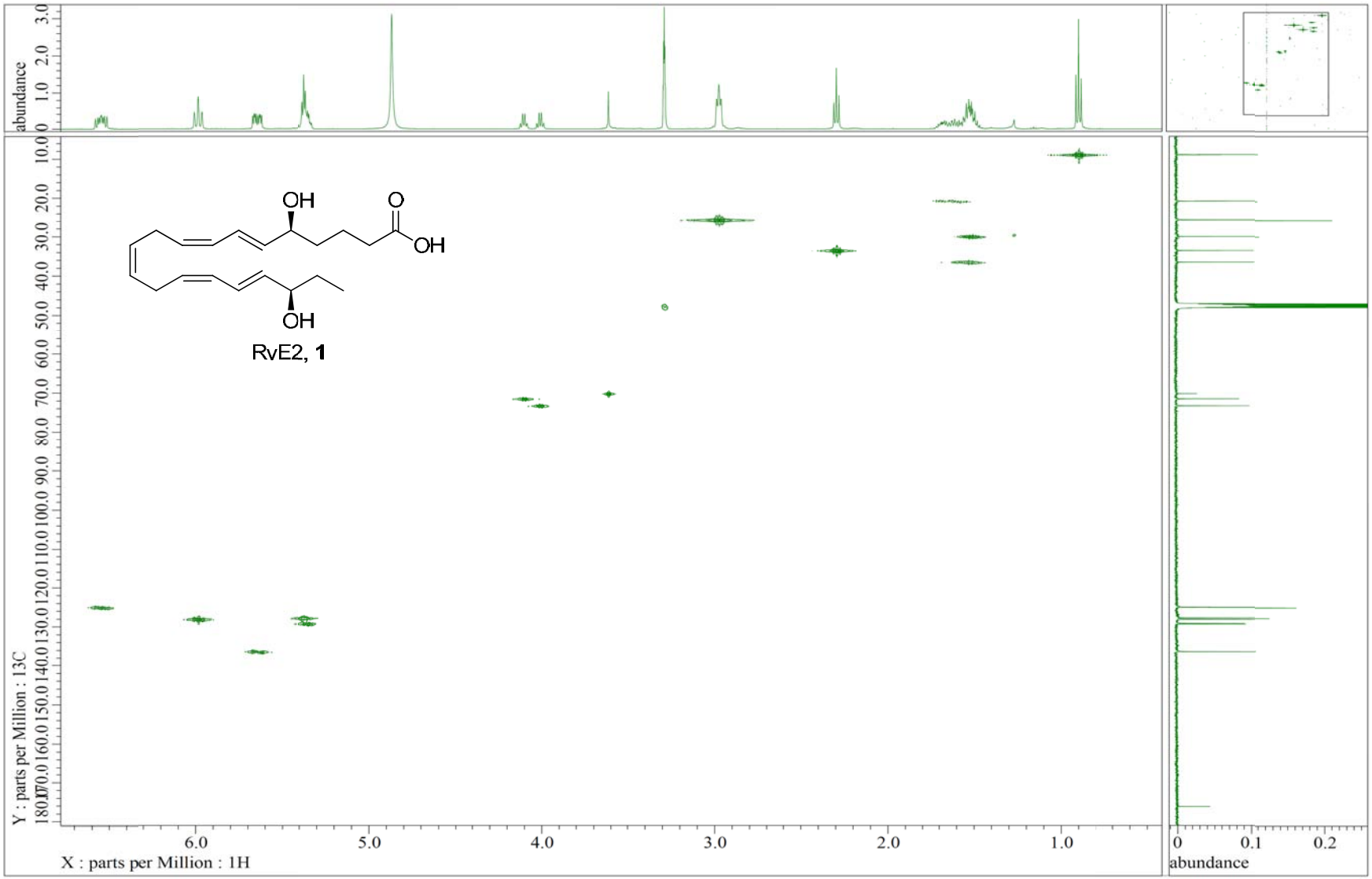

OTBS
O
OMe
OTBS
S13
7.264
6.485
6.456
6.446
6.417
6.028
6.014
5.999
5.985
5.971
5.958
5.683
5.666
5.650
5.628
5.611
5.111
5.100
5.385
5.365
5.357
5.349
5.338
4.197
4.181
4.111
4.096
3.664
2.970
2.955
2.938
2.337
2.318
2.299
1.678
1.660
1.639
1.620
1.605
1.575
1.553
1.546
1.537
1.533
1.518
1.499
1.483
1.255
0.946
0.939
0.908
0.889
0.881
0.861
0.058
0.037
0.031
0.001
2.00
2.07
2.11
4.25
2.13
3.16
3.95
2.20
7.22
13.15
PPM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


OTBS
O
OMe
OTBS
S13
174.034
137.296
136.886
129.332
128.922
128.426
128.245
128.188
126.054
124.411
124.125
77.324
77.200
77.000
76.676
74.310
72.727
51.459
37.629
34.005
31.134
26.022
25.879
25.860
20.719
18.268
18.211
9.675
-4.307
-4.355
-4.765
-4.803
PPM
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0


6.591
6.578
6.568
6.556
6.548
6.539
6.525
6.018
5.996
5.974
5.683
5.675
5.669
5.661
5.652
5.644
5.640
5.632
5.396
5.385
5.376
5.364
5.356
4.880
4.134
4.121
4.109
4.096
4.039
4.026
4.013
4.000
3.626
3.307
3.303
3.300
3.297
2.999
2.986
2.974
2.321
2.307
2.292
1.681
1.672
1.654
1.636
1.623
1.610
1.597
1.583
1.573
1.555
1.541
1.534
1.526
1.522
1.507
1.492
1.281
0.926
0.911
0.896
2.00
2.03
2.05
3.91
2.07
3.91
2.18
6.55
3.22
OH
O
OH
OH
RvE2, 1
PPM
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


177.472
137.697
137.668
130.648
130.476
129.446
129.389
129.103
129.084
126.365
74.687
72.903
49.630
49.515
49.458
49.343
49.286
49.172
49.114
49.000
48.943
48.828
48.657
48.494
37.726
34.778
31.211
26.976
22.188
10.198
OH
O
OH
OH
RvE2, 1
PPM
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0


abundance
1.0
0
OH
O
OH
OH
RvE2, 1
Y : parts per Million : 1H
X : parts per Million : 1H
6.0
5.0
4.0
3.0
2.0
1.0
0
abundance


abundance
OH
O
OH
OH
RvE2, 1
Y : parts per Million : 13C
X : parts per Million : 1H
abundance