



Title	Modular synthesis of oligoacetylacetones via site-selective silylation of acetylacetone derivatives
Author(s)	Sarkar, Parantap; Inaba, Yuya; Shirakura, Hayato et al.
Citation	Organic & biomolecular chemistry, 18(17), 3297-3302 https://doi.org/10.1039/d0ob00501k
Issue Date	2020-05-07
Doc URL	https://hdl.handle.net/2115/81119
Type	journal article
File Information	Supplement.pdf



Supporting Information

Modular synthesis of oligoacetylacetones *via* site-selective silylation of acetylacetone derivatives

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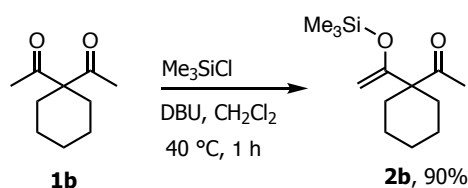
1. General Information

Solvents and reagents were purchased from WAKO Pure Chemical Industries Ltd. and TCI Co., Ltd. and used without further purification unless otherwise mentioned. Compound **1b-d** were prepared by reported procedure.^[1-3] All the ¹H and ¹³C NMR spectra were recorded using a JEOL JMN-ECS400 spectrometer. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane ($\delta = 0.00$ ppm) for ¹H NMR and CDCl₃ ($\delta = 77.16$ ppm) for ¹³C NMR. Infrared spectra were measured using a JASCO Co. FT/IR-4600 spectrometer. Elemental analysis were performed using a CE440 elemental analyzer (Exeter Analytical, Inc.). Elemental analysis for silylated products were not performed as slow hydrolysis were observed for all silylated products and they were quickly utilized for coupling reaction. Thin layered chromatography (TLC) was performed on a silica gel sheet, MERCK silica gel 60 F₂₅₄. Preparative scale separations were carried out using silica gel gravity column chromatography (Wakosil[®] 60 ~ 210 μ m). HPLC chromatograms were recorded using a JASCO MD-2018 photodiode array detector equipped with TSKgel G2000H column (two connected columns of 4.6 ϕ $\times$ 250 mm), a JASCO PU-2089 pump, JASCO AS-2059 sampler, JASCO CO-2060 column thermostat, ADVANTEC CHF 122SC fraction collector. GPC was performed on Japan Analytical Industry LaboACE with JAIGEL-2HR polystyrene columns (two connected columns of 20 ϕ $\times$ 600 mm) with CHCl₃ as mobile phase. ESI-TOF-MS spectra were recorded on a Thermo scientific Exactive spectrometer using MeOH in both positive and negative mode. Single crystal X-ray diffraction data were collected by a Rigaku XtaLAB P200 diffractometer equipped with a PILATUS200K detector using a multi-layer mirror (MoK α radiation $\lambda = 0.71073$ Å). All structures were solved using a dual-space algorithm (SHELXT^[4]) and refined using full-matrix least-squares method (SHELXL^[5]).

2. Synthetic Procedures

2-1 Silylation of acetylacetone monomers **1**

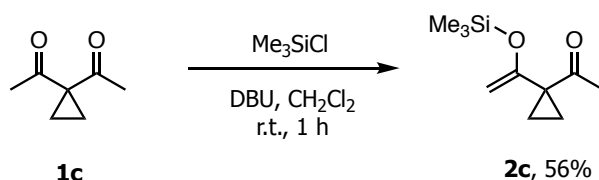
Synthesis of mono-silylated monomer **2b**



To a 50 mL two-necked round bottom flask equipped with a reflux condenser, 1,1-diacetylcyclohexane **1b** (3.36 g, 20 mmol) and degassed dichloromethane (14 mL) were added and cooled to $0\text{ }^\circ\text{C}$ with ice/water bath. To this solution, dropwise addition of trimethylchlorosilane (3.1 mL, 24 mmol) followed by 1,8- diazabicyclo[5.4.0]undec-7-ene (3.9 mL, 26 mmol) were done at $0\text{ }^\circ\text{C}$ while stirring. The ice/water bath was removed, and the mixture was heated to reflux for 1 h. Upon cooling to room temperature, hexane (40 mL) was added to the reaction mixture and the product was extracted with hexane (20 mL x 3) followed by washing with brine (50 mL x 2) and water (50 mL) using an extraction funnel. The organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The crude product was purified by column chromatography through a silica gel column (diameter 2.2 cm, height 10.0 cm) using a mixture of hexane/ ethyl acetate = 25:1 as eluent to obtain mono-silylated monomer (**2b**) as colourless oil (4.3 g) in 90% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 4.29 (d, $J = 2.2$ Hz, 1H, vinyl), 4.23 (d, $J = 2.2$ Hz, 1H, vinyl), 2.12 (s, 3H, acetyl), 1.95 (m, 2H, cyclohexyl), 1.60 (m, 4H, cyclohexyl), 1.39 (m, 4H, cyclohexyl), 0.20 (s, 9H, trimethylsilyl) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 210.1, 160.5, 90.2, 58.3, 31.3, 26.1, 25.3, 22.9, 0.07 ppm; HR-ESI-TOF MS: m/z calculated for $\text{C}_{13}\text{H}_{24}\text{O}_2\text{Si}$: 263.1438 $[\text{M}+\text{Na}]^+$, found 263.1436; $R_f = 0.36$ (eluent: hexane/ethyl acetate = 25:1).

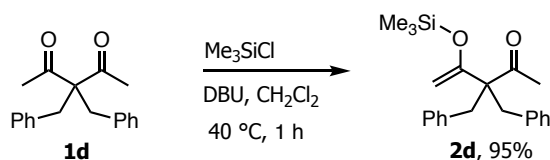
Synthesis of mono-silylated monomer **2c**



In a 50 mL round bottom flask, 1,1-diacetylcyclopropane **1c** (2.01 g, 15.9 mmol) and dichloromethane (10.0 mL) were cooled to 0 °C using ice/water bath. To this solution, dropwise addition of trimethylchlorosilane (2.40 mL, 18.9 mmol) followed by 1,8-diazabicyclo[5.4.0]undec-7-ene (3.00 mL, 20.5 mmol) were done at 0 °C while stirring. The ice/water bath was removed, and the mixture was stirred at room temperature for 1 h. Hexane (10 mL) was added to the reaction mixture and the product was extracted with hexane (5 mL $\times$ 3) followed by washing with brine (5 mL) and water (5 mL) using an extraction funnel. The organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (diameter 4.2 cm, height 6.0 cm) using a mixture of hexane/ ethyl acetate = 20:1 as eluent to obtain mono-silylated monomer (**2c**) as colourless oil (1.73 g) in 56% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 4.29 (d, J = 1.4 Hz, 1H, vinyl), 4.25 (d, J = 1.4 Hz, 1H, vinyl), 2.33 (s, 3H, acetyl), 1.30 (m, 2H, cyclopropyl), 0.98 (m, 2H, cyclopropyl), 0.24 (s, 9H, trimethylsilyl) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 208.0, 158.5, 92.4, 37.7, 28.2, 18.2, 0.13 ppm; HR-ESI-TOF MS: m/z calculated for $\text{C}_{10}\text{H}_{18}\text{O}_2\text{Si}$, 221.0968 $[\text{M}+\text{Na}]^+$, found 221.0971; R_f = 0.38 (eluent: hexane/ethyl acetate = 25:1).

Synthesis of mono-silylated monomer **2d**



To a 250 mL two-necked round bottom flask equipped with a reflux condenser, 3,3-bis(phenylmethyl)-2,4-pentanedione **1d** (26.0 g, 93 mmol) and degassed dichloromethane (60 mL) were added and cooled to $0\text{ }^\circ\text{C}$ with ice/ water bath. To this solution, dropwise addition of trimethylchlorosilane (14.1 mL, 111 mmol) followed by 1,8- diazabicyclo[5.4.0]undec-7-ene (18.1 mL, 121 mmol) were done at $0\text{ }^\circ\text{C}$ while stirring. The ice/water bath was removed, and the mixture was heated to reflux for 1 h. Upon cooling to room temperature, hexane (100 mL) was added to the reaction mixture and the product was extracted with hexane (100 mL x 3) followed by washing with brine (100 mL x 2) and water (100 mL) using an extraction funnel. The organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The crude product was purified by column chromatography through a silica gel column (diameter 8.0 cm, height 9.0 cm) using a mixture of hexane/ ethyl acetate = 20:1 as eluent to obtain mono-silylated monomer (**2d**) as white solid (31.2 g) in 95% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 7.22 (m, 6H, phenyl), 7.11 (m, 4H, phenyl), 4.28 (s, 2H, vinyl), 3.00 (ABq, $\Delta\delta_{\text{AB}} = 0.04$, $J = 15.1$ Hz, 4H, benzyl), 2.20 (s, 3H, acetyl), 0.22 (s, 9H, trimethylsilyl) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 208.8, 158.8, 137.6, 130.5, 128.0, 126.5, 91.1, 63.1, 37.2, 26.6, -0.1 ppm; IR (ATR, neat): 3087 (w), 3053 (w), 3027 (w), 2958 (w), 1715 (s), 1626 (s), 1494 (m), 1451 (s), 1355 (m), 1256 (m), 1252 (s), 1196 (m), 1150 (m), 1086 (m), 1005 (s), 836 (s), 751 (s), 699 (s) cm^{-1} ; mp $51 - 53\text{ }^\circ\text{C}$; HR-ESI-TOF MS: m/z calculated for $\text{C}_{22}\text{H}_{28}\text{O}_2\text{Si}$, 375.1751 $[\text{M}+\text{Na}]^+$, 375.1748; $R_f = 0.31$ (eluent: hexane/ethyl acetate = 20:1).

2-2 Selectivity of mono-silylation of acetylacetone derivatives 1

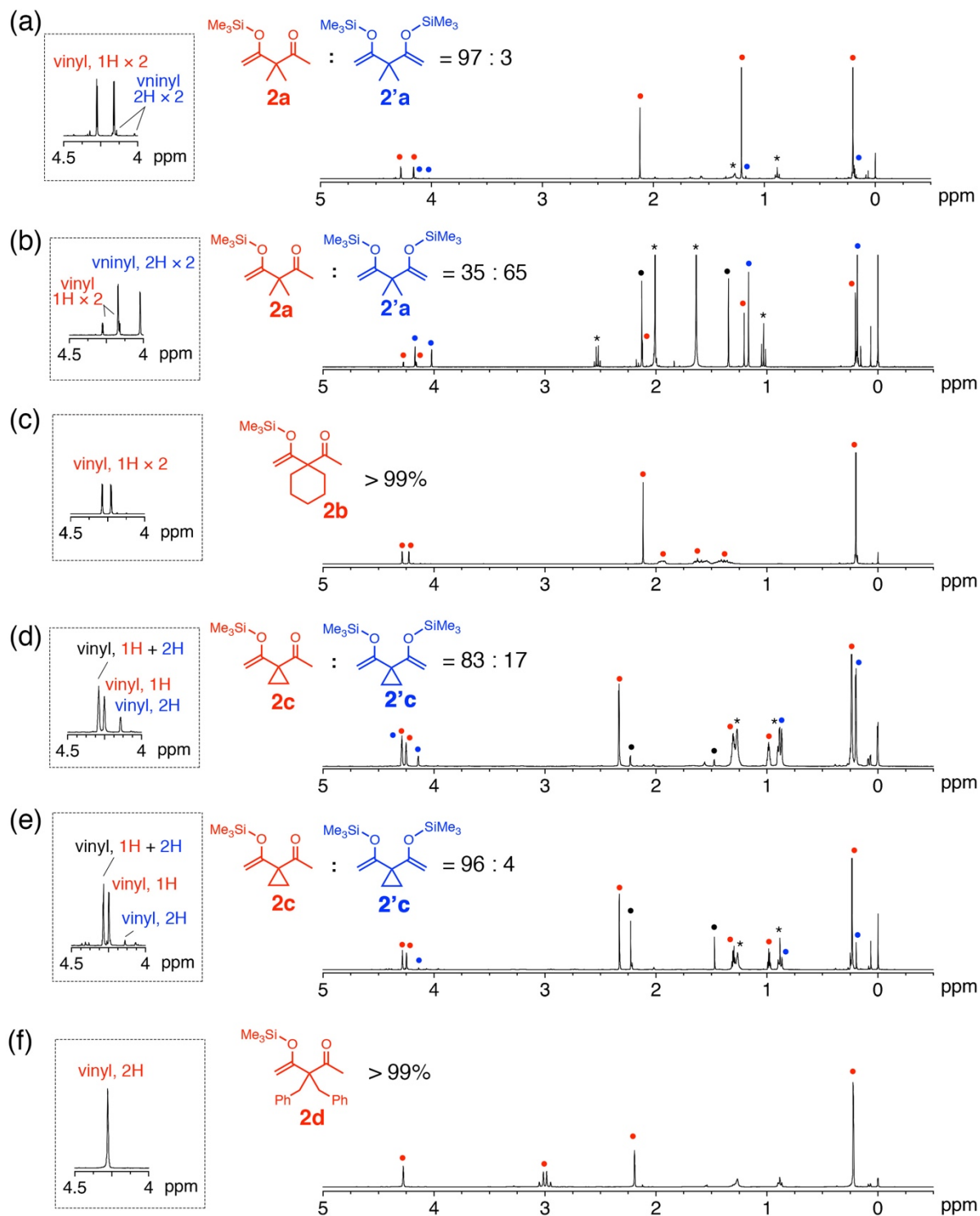
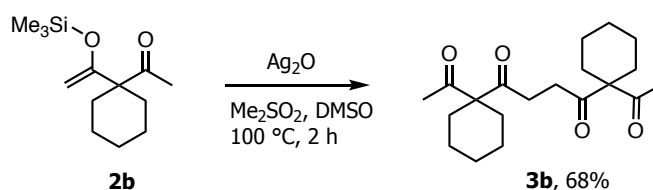


Figure S1. ^1H NMR spectra in CDCl_3 of crude reaction products for the synthesis of (a) **2a** with DBU, (b) **2a** with Et_3N , (c) **2b**, (d) **2c** at reflux, (e) **2c** at room temperature and (f) **2d** (corresponding to Entries 1–6, in Table 1, respectively).

2-3 Synthesis of tetraketones 3

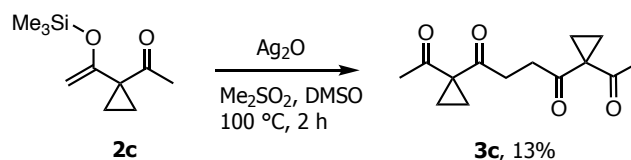
Synthesis of tetraketone 3b



To a 50 mL round bottom flask equipped with a reflux condenser, enol silyl ether **2b** (1.88 g, 7.82 mmol), dimethyl sulfone (2.20 g, 23.5 mmol), dimethyl sulfoxide (111 μ L, 1.6 mmol) and silver(I) oxide (1.09 g, 4.7 mmol) were added, and the reaction mixture was stirred at 100 °C for 2 h. After cooling to room temperature, the reaction mixture was diluted with 20 mL ethyl acetate and filtered through celite pad using additional 50 mL of ethyl acetate. The combined filtrate was washed with brine (50 mL $\times$ 3), dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The crude product was chromatographed through a silica gel column (diameter 2.2 cm, height 9.0 cm) using a mixture of hexane/ethyl acetate/dichloromethane = 5:1:1 as eluent. The resulting solid was then washed in hexane (5 mL) with sonication and then filtered to obtain tetraketone (**3b**) as white solid (890 mg) in 68% yield.

¹H NMR (400 MHz, CDCl₃, 298 K): δ 2.63 (s, 4H, ethylene), 2.12 (s, 6H, acetyl) 1.99 (t, J = 5.7 Hz, 8H, cyclohexyl), 1.47 (m, 8H, cyclohexyl), 1.39 (m, 4H, cyclohexyl) ppm; ¹³C NMR (100 MHz, CDCl₃, 298 K): δ 207.4, 207.3, 68.1, 32.2, 30.5, 26.4, 25.5, 23.0 ppm; IR (ATR, neat): 2926 (m), 2852 (w), 1685 (s), 1454, (w), 1394 (m), 1351 (m), 1182 (m), 1114 (m), 999 (m), 973 (m), 907 (m), 643 (m) cm⁻¹; mp 80 - 82 °C; HR-ESI-TOF MS: m/z calculated for C₂₀H₃₀O₄, 357.2036 [M+Na]⁺, found 357.2034; Elemental analysis (%): calculated for C₂₀H₃₀O₄ (%): C, 71.82; H, 9.04, found C, 71.94; H, 9.09; R_f = 0.33 (eluent: hexane/ethyl acetate/dichloromethane = 5:1:1).

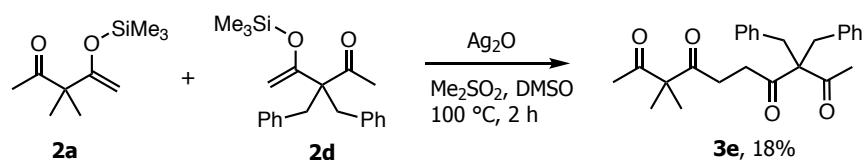
Synthesis of tetraketone **3c**



To a 50 mL round bottom flask equipped with a reflux condenser, enol silyl ether **2c** (3.99 g, 20.0 mmol), dimethyl sulfone (5.67 g, 60.0 mmol), dimethyl sulfoxide (290 μL , 4.0 mmol) and silver(I) oxide (2.78 g, 12.0 mmol) were added, and the reaction mixture was stirred at $100\text{ }^\circ\text{C}$ for 2 h. After cooling to room temperature, the reaction mixture was diluted with 20 mL ethyl acetate and filtered through celite pad using additional 50 mL of ethyl acetate. The combined filtrate was washed with brine (50 mL $\times$ 3), dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The crude product was chromatographed through a silica gel column (diameter 2.2 cm, height 9.0 cm) using a mixture of hexane/ethyl acetate/dichloromethane = 5:1:1 as eluent. The resulting solid was then washed in hexane (5 mL) with sonication and then filtered to obtain tetraketone (**3c**) as colourless oil (325 mg) in 13% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 2.83 (s, 4H, ethylene), 2.21 (s, 6H, acetyl) 1.54 (m, 4H, cyclopropyl), 1.52 (m, 4H, cyclopropyl) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 204.9, 204.2, 43.0, 34.0, 27.6, 17.6 ppm; HR-ESI-TOF MS: m/z calculated for $\text{C}_{14}\text{H}_{18}\text{O}_4$, 273.1097 $[\text{M}+\text{Na}]^+$, found 273.1096; R_f = 0.29 (eluent: hexane/ethyl acetate/dichloromethane = 5:1:1).

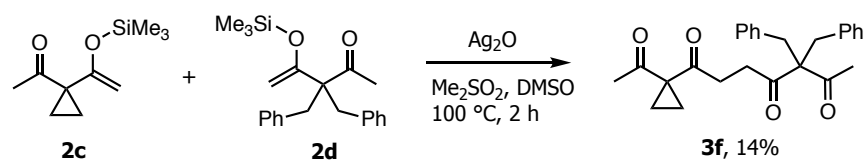
Synthesis of tetraketone **3e**



To a 100 mL round bottom flask equipped with a reflux condenser, enol silyl ethers **2a** (6.61 g, 33 mmol) and **2d** (3.89 g, 11 mmol) were mixed and stirred for 5 min. To this mixture, dimethyl sulfone (12.4 g, 132 mmol), dimethyl sulfoxide (625 μL , 8.8 mmol) and silver(I) oxide (6.20 g, 26.4 mmol) were added and the reaction mixture was stirred at 100°C for 2 h. After cooling to room temperature, the reaction mixture was diluted with 50 mL ethyl acetate and filtered through celite pad using additional 150 mL of ethyl acetate. The combined filtrate was washed with brine (100 mL $\times$ 3), dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The crude product was first chromatographed through a silica gel column (diameter 5.0 cm, height 14.0 cm) using a mixture of hexane/ethyl acetate/dichloromethane = 6:1:4 as eluent and then further purified by GPC. The resulting viscous oil was passed through silica plug using ethyl acetate as eluent to obtain 3,3-bis(phenylmethyl)-8,8-dimethyldecane-2,4,7,9-tetraone (**3e**) as colourless viscous oil (800 mg) in 18% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 7.23 (m, 6H, phenyl), 6.97 (dd, $J = 7.3$ Hz, 1.6 Hz, 4H, phenyl), 3.33 (ABq, $\Delta\delta_{\text{AB}} = 0.04$, $J = 15.1$ Hz, 4H, benzyl), 2.66 (dd, $J = 5.5$ Hz, 4.0 Hz, 2H, ethylene), 2.58 (dd, $J = 5.5$ Hz, 4.0 Hz, 2H, ethylene), 2.24 (s, 3H, acetyl), 2.16 (s, 3H, acetyl), 1.38 (s, 6H, $-\text{C}(\text{CH}_3)_2-$) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 208.3, 207.8, 207.7, 206.5, 136.1, 129.8, 128.6, 127.0, 71.3, 62.3, 37.2, 34.6, 32.0, 28.4, 26.4, 21.6 ppm; HR-ESI-TOF MS: m/z calculated for $\text{C}_{26}\text{H}_{30}\text{O}_4$, 429.2036 $[\text{M}+\text{Na}]^+$, found 429.2039; Elemental analysis (%): calculated for $\text{C}_{26}\text{H}_{30}\text{O}_4$ (%): C, 76.82; H, 7.44, found C, 76.78; H, 7.55; $R_f = 0.43$ (eluent: hexane/ethyl acetate/dichloromethane = 6:1:4).

Synthesis of tetraketone **3f**

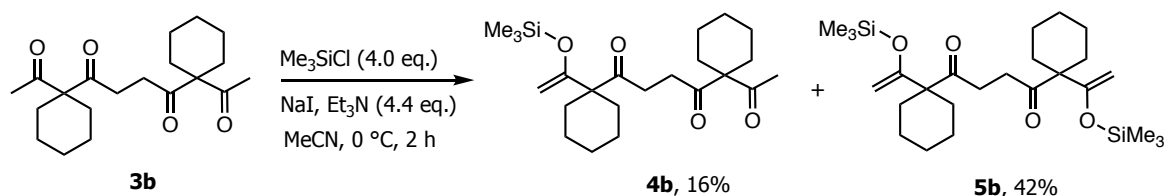


Synthesis of tetraketone **3f** was performed similarly as described previously for **3e** with enol silyl ethers **2c** (2.58 g, 13.0 mmol) and **2d** (2.30 g, 6.5 mmol), dimethyl sulfone (5.50 g, 58.5 mmol), dimethyl sulfoxide (277 μL , 3.9 mmol) and silver(I) oxide (2.71 g, 11.7 mmol). Tetraketone (**3f**) was obtained as colourless viscous oil (365 mg) in 14% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 7.23 (m, 6H, phenyl), 6.97 (dd, $J = 7.3$ Hz, 1.6 Hz, 4H, phenyl) 3.32 (ABq, $\Delta\delta_{\text{AB}} = 0.04$, $J = 15.1$ Hz, 4H, benzyl), 2.73 (m, 2H, ethylene), 2.68 (m, 2H, ethylene), 2.22 (s, 3H, acetyl), 2.21 (s, 3H, acetyl), 1.55 (m, 2H, cyclopropyl), 1.50 (m, 2H, cyclopropyl) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 208.0, 206.5, 204.6, 204.2, 136.2, 129.8, 128.6, 127.0, 71.3, 43.1, 37.2, 34.9, 33.8, 28.4, 27.6, 17.7 ppm; HR-ESI-TOF MS: m/z calculated for $\text{C}_{26}\text{H}_{28}\text{O}_4$, 427.1880 $[\text{M}+\text{Na}]^+$, found 427.1886; Elemental analysis (%): calculated for $\text{C}_{26}\text{H}_{28}\text{O}_4$ (%): C, 77.20; H, 6.98, found C, 77.15; H, 7.08; $R_f = 0.33$ (eluent: hexane/ethyl acetate/dichloromethane = 6:1:4).

2-4 Silylation of acetylacetone tetraketones 3

Synthesis of 4b and 5b

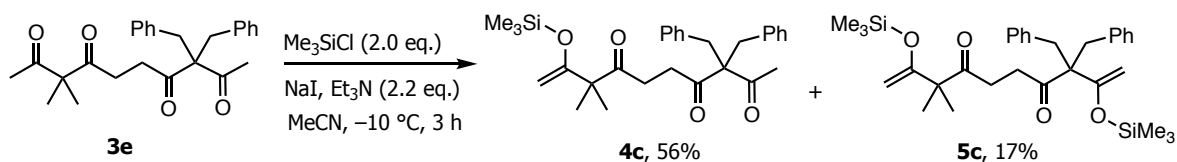


To a 50 mL round bottom flask, tetraketone **3b** (760 mg, 2.27 mmol), sodium iodide (1.36 g, 9.10 mmol), triethylamine (1.4 mL, 10.0 mmol) and degassed acetonitrile (4 mL) were added. The resulting suspension was cooled to $0\text{ }^\circ\text{C}$ with an ice/water bath while stirring. To this mixture, trimethylchlorosilane (1.2 mL, 9.1 mmol) were added slowly *via* syringe keeping the temperature at $0\text{ }^\circ\text{C}$. After additional stirring for 2 h at $0\text{ }^\circ\text{C}$, the reaction was quenched by addition of water (10 mL) and the product mixture were extracted with hexane ($50\text{ mL} \times 3$). The combined organic layer was washed with water (50 mL), dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The residue was chromatographed through silica gel column (diameter 3.0 cm, height 17.0 cm) using a mixture of hexane/ethyl acetate = 19:1 as eluent to obtain bis-silylated product **5b** (450 mg, 42%) as the first fraction followed by mono-silylated product **4b** (150 mg, 16%) as colourless oils, along with recovery of **3b** (290 mg, 38%) in the last fraction.

4b: ^1H NMR (400 MHz, CDCl_3 , 298 K): δ 4.30 (d, $J = 1.8\text{ Hz}$, 1H, vinyl), 4.24 (d, $J = 1.8\text{ Hz}$, 1H, vinyl), 2.80 (dd, $J = 6.0\text{ Hz}$, 4.6 Hz, 2H, ethylene), 2.58 (dd, $J = 6.0\text{ Hz}$, 4.6 Hz, 2H, ethylene), 2.13 (s, 3H, acetyl), 2.00 (t, $J = 6.0\text{ Hz}$, 4H, cyclohexyl), 1.93 (m, 2H, cyclohexyl), 1.66 (m, 2H, cyclohexyl), 1.56–1.36 (m, 12H, cyclohexyl), 0.20 (s, 9H, trimethylsilyl) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 210.1, 207.9, 207.4, 160.1, 90.6, 68.2, 57.7, 32.4, 31.4, 31.0, 30.5, 26.5, 26.0, 25.5, 23.0, 22.8, 0.04 ppm; HR-ESI-TOF MS: m/z calculated for $\text{C}_{23}\text{H}_{38}\text{O}_4\text{Si}$, 429.2432 $[\text{M}+\text{Na}]^+$, found 429.2429; $R_f = 0.23$ (eluent: hexane/ethyl acetate = 19:1).

5b: ^1H NMR (400 MHz, CDCl_3 , 298 K): δ 4.30 (d, $J = 1.8\text{ Hz}$, 2H, vinyl), 4.23 (d, $J = 1.8\text{ Hz}$, 2H, vinyl), 2.74 (s, 4H, ethylene), 1.96 (m, 4H, cyclohexyl), 1.66 (m, 4H, cyclohexyl), 1.56–1.34 (m, 12H, cyclohexyl), 0.20 (s, 18H, trimethylsilyl) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 210.9, 160.3, 90.5, 57.9, 31.4, 26.1, 22.9, 0.09 ppm; HR-ESI-TOF MS: m/z calculated for $\text{C}_{26}\text{H}_{46}\text{O}_4\text{Si}_2$, 501.2827 $[\text{M}+\text{Na}]^+$, found 501.2845; $R_f = 0.40$ (eluent: hexane/ethyl acetate = 19:1).

Synthesis of **4c** and **5c**

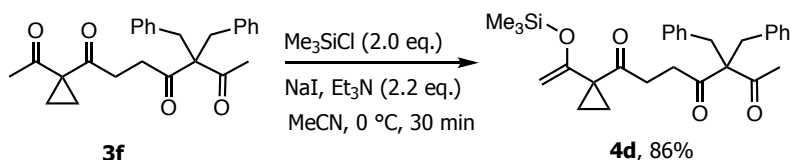


To a 50 mL round bottom flask, tetraketone **3e** (1.54 g, 3.79 mmol), sodium iodide (1.14 g, 7.58 mmol), triethylamine (1.2 mL, 8.33 mmol) and degassed acetonitrile (8 mL) were added. The resulting suspension was cooled to -10°C using cooling bath while stirring. To this mixture, trimethylchlorosilane (1.0 mL, 7.58 mmol) were added slowly *via* syringe keeping the temperature at -10°C . After additional stirring for 3 h at -10°C , the reaction was quenched by addition of water (20 mL) and the product mixture were extracted by hexane (50 mL $\times$ 3). The combined organic layer was washed with water (50 mL), dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The residue was chromatographed through silica gel column (diameter 3.0 cm, height 17.0 cm) using a mixture of hexane/ethyl acetate = 9:1 as eluent to obtain bis-silylated product **5c** (370 mg, 17%) as the first fraction followed by mono-silylated product **4c** (1.02 g, 56%) as colourless oils, along with recovery of **3e** (310 mg, 20%) in the last fraction.

4c: ^1H NMR (400 MHz, CDCl_3 , 298 K): δ 7.23 (m, 6H, phenyl), 6.97 (dd, $J = 7.3$ Hz, 1.6 Hz, 4H, phenyl), 4.32 (d, $J = 1.8$ Hz, 1H, vinyl), 4.19 (d, $J = 1.8$ Hz, 1H, vinyl), 3.32 (ABq, $\Delta\delta_{\text{AB}} = 0.04$, $J = 15.1$ Hz, 4H, benzyl), 2.74 (dd, $J = 6.4$ Hz, 6.0 Hz, 2H, ethylene), 2.63 (dd, $J = 6.4$ Hz, 6.0 Hz, 2H, ethylene), 2.23 (s, 3H, acetyl), 1.23 (s, 6H, $-\text{C}(\text{CH}_3)_2-$), 0.20 (s, 9H, trimethylsilyl) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 211.2, 207.9, 206.7, 162.0, 136.3, 129.8, 128.6, 126.9, 89.1, 71.4, 53.7, 37.2, 34.8, 30.8, 28.5, 23.1, 0.1 ppm; HR-ESI-TOF MS: m/z calculated for $\text{C}_{29}\text{H}_{38}\text{O}_4\text{Si}$, 501.2432 $[\text{M}+\text{Na}]^+$, found 501.2433; $R_f = 0.40$ (eluent: hexane/ethyl acetate = 9:1).

5c: ^1H NMR (400 MHz, CDCl_3 , 298 K): δ 7.20 (m, 6H, phenyl), 7.08 (m, 4H, phenyl), 4.31 (d, $J = 1.6$ Hz, 1H, vinyl), 4.29 (s, 2H, vinyl), 4.20 (d, $J = 1.8$ Hz, 1H, vinyl), 3.02 (s, 4H, benzyl), 2.85 (dd, $J = 6.4$ Hz, 5.0 Hz, 2H, ethylene), 2.71 (dd, $J = 6.4$ Hz, 5.0 Hz, 2H, ethylene), 1.23 (s, 6H, $-\text{C}(\text{CH}_3)_2-$), 0.23 (s, 9H, trimethylsilyl), 0.19 (s, 9H, trimethylsilyl) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 211.4, 209.9, 162.2, 158.8, 137.5, 130.5, 128.0, 126.4, 91.3, 89.1, 62.5, 53.8, 37.2, 33.2, 31.4, 23.1, 0.1, 0.0 ppm; HR-ESI-TOF MS: m/z calculated for $\text{C}_{32}\text{H}_{46}\text{O}_4\text{Si}_2$, 573.2827 $[\text{M}+\text{Na}]^+$, found 573.2831; $R_f = 0.50$ (eluent: hexane/ethyl acetate = 9:1).

Synthesis of **4d**

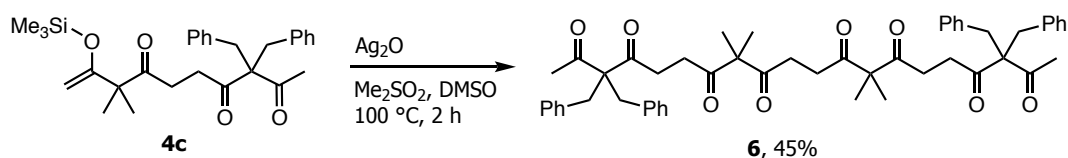


Synthesis of **4d** was performed similarly as described previously for **4c** with tetraketone **3f** (340 mg, 0.84 mmol), sodium iodide (252 mg, 1.68 mmol), triethylamine (0.26 mL, 1.84 mmol), degassed acetonitrile (2 mL) and trimethylchlorosilane (0.21 mL, 1.68 mmol) at $0\text{ }^\circ\text{C}$ for 30 minutes. The product was purified by silica gel column chromatography (diameter 3.0 cm, height 5.0 cm) using a mixture of hexane/ethyl acetate = 9:1 as eluent to obtain mono-silylated product **4d** (343 mg) in 86% yield as colourless oil.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 7.23 (m, 6H, phenyl), 6.98 (dd, $J = 7.3\text{ Hz}$, 1.9 Hz , 4H, phenyl), 4.35 (d, $J = 1.4\text{ Hz}$, 1H, vinyl), 4.30 (d, $J = 1.4\text{ Hz}$, 1H, vinyl), 3.32 (ABq, $\Delta\delta_{\text{AB}} = 0.04$, $J = 15.1\text{ Hz}$, 4H, benzyl), 2.98 (dd, $J = 6.4\text{ Hz}$, 6.0 Hz , 2H, ethylene), 2.65 (dd, $J = 6.4\text{ Hz}$, 6.0 Hz , 2H, ethylene), 2.22 (s, 3H, acetyl), 1.31 (m, 2H, cyclopropyl), 1.00 (m, 2H, cyclopropyl), 0.25 (s, 9H, trimethylsilyl) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 207.9, 207.8, 206.7, 157.9, 136.3, 129.8, 128.5, 126.9, 93.2, 71.4, 37.4, 37.1, 34.7, 33.8, 28.4, 18.3, 0.2 ppm; HR-ESI-TOF MS: m/z calculated for $\text{C}_{29}\text{H}_{36}\text{O}_4\text{Si}$, 499.2275 $[\text{M}+\text{Na}]^+$, found 499.2282; $R_f = 0.55$ (eluent: hexane/ethyl acetate = 9:1).

2-5 Synthesis of octaketones

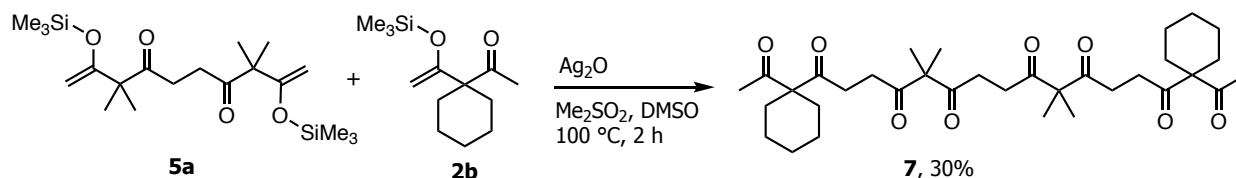
Synthesis of octaketone 6



To a 50 mL round bottom flask equipped with a reflux condenser, enol silyl ether **4c** (1.00 g, 2.1 mmol) dimethyl sulfone (593 mg, 6.3 mmol), dimethyl sulfoxide (30 μL , 0.42 mmol) and silver(I) oxide (292 mg, 1.26 mmol) were added and the reaction mixture was stirred at 100°C for 2 h. After cooling to room temperature, the reaction mixture was diluted with 50 mL dichloromethane and filtered through celite pad using additional 150 mL of dichloromethane. The combined filtrate was washed with brine (100 mL $\times$ 3), dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The crude product was first chromatographed through a silica gel column (diameter 2.2 cm, height 17.0 cm) using a mixture of hexane/ethyl acetate/dichloromethane = 6:1:2 as eluent and then further purified by GPC. The resulting viscous oil was passed through silica plug using ethyl acetate as eluent to obtain 3,3,18,18-tetra(phenylmethyl)-8,8,13,13-tetramethyl-icosane-2,4,7,9,12,14,17,19-octaone (**6**) as colourless viscous oil (380 mg) in 45% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 7.24 (m, 12H, phenyl), 6.97 (dd, $J = 7.3$ Hz, 1.9 Hz, 8H, phenyl) 3.31 (ABq, $\Delta\delta_{\text{AB}} = 0.04$, $J = 15.1$ Hz, 8H, benzyl), 2.75 (s, 4H, central ethylene) 2.70 (dd, $J = 5.0$ Hz, 4.5 Hz, 4H, terminal ethylene), 2.62 (dd, $J = 5.0$ Hz, 4.5 Hz, 4H, terminal ethylene), 2.23 (s, 6H, acetyl), 1.41 (s, 12H, $-\text{C}(\text{CH}_3)_2-$) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 208.4, 208.2, 207.8, 206.5, 136.2, 129.8, 128.6, 126.9, 71.3, 61.9, 37.2, 34.6, 32.3, 32.1, 28.4, 21.8 ppm; HR-ESI-TOF MS: m/z calculated for $\text{C}_{52}\text{H}_{58}\text{O}_8$, 833.4024 $[\text{M}+\text{Na}]^+$, found 833.4016; Elemental analysis (%): calculated for $\text{C}_{52}\text{H}_{58}\text{O}_8$ (%): C, 77.01; H, 7.21, found C, 76.75; H, 7.36; $R_f = 0.14$ (eluent: hexane/ethyl acetate/dichloromethane = 6:1:2).

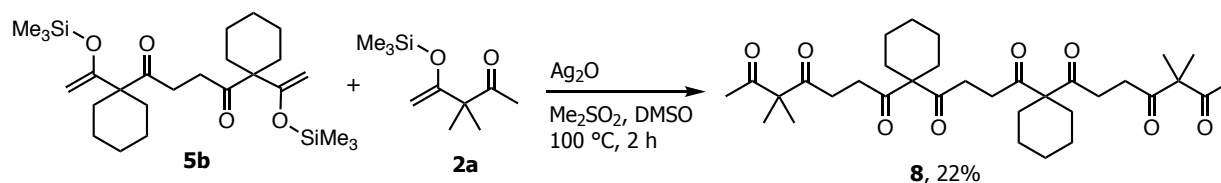
Synthesis of octaketone **7**



To a 50 mL round bottom flask equipped with a reflux condenser, enol silyl ethers **5a** (666 mg, 1.67 mmol) and **2b** (4.0 g, 16.6 mmol) were mixed and stirred for 5 min. To this mixture, dimethyl sulfone (5.2 g, 54.9 mmol), dimethyl sulfoxide (260 μL , 3.66 mmol) and silver(I) oxide (2.55 g, 11.0 mmol) were added and the reaction mixture was stirred at 100°C for 2 h. After cooling to room temperature, the reaction mixture was diluted with 50 mL dichloromethane and filtered through celite pad using additional 150 mL of dichloromethane. The combined filtrate was washed with brine (100 mL $\times$ 3), dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The crude product was first chromatographed through a silica gel column (diameter 5.0 cm, height 9.0 cm) using a mixture of hexane/ethyl acetate/dichloromethane = 6:1:2 as eluent and then further purified by GPC. The resulting solid was passed through silica plug using ethyl acetate as eluent and precipitated by addition of hexane to obtain octaketone (**7**) as white solid (290 mg) in 30% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 2.73 (s, 4H, central ethylene), 2.69 (m, 8H, terminal ethylene), 2.12 (s, 6H, acetyl), 1.99 (broad t, $J = 5.5$ Hz, 8H, cyclohexyl), 1.47 (m, 8H, cyclohexyl), 1.39 – 1.37 (m, 4H, cyclohexyl), 1.39 (s, 12H, $-\text{C}(\text{CH}_3)_2-$) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 208.3, 208.1, 207.6, 207.2, 68.0, 61.8, 32.3, 32.2, 32.1, 30.4, 26.4, 25.4, 22.9, 21.8 ppm; IR (ATR, neat): $\tilde{\nu} = 2994$ (w), 2930 (m), 2862 (w), 1687 (s), 1465 (m), 1452 (m), 1391 (m), 1363 (m), 1345 (m), 1296 (w), 1179 (m), 1066 (m), 1015 (m), 968 (m), 803 (m) cm^{-1} ; mp $83 - 85^\circ\text{C}$; HR-ESI-TOF MS: m/z calculated for $\text{C}_{34}\text{H}_{50}\text{O}_8$, 609.3398 $[\text{M}+\text{Na}]^+$, found 609.3414; Elemental analysis (%): calculated for $\text{C}_{34}\text{H}_{50}\text{O}_8$ (%): C, 69.60; H, 8.59, found C, 69.55; H, 8.57; $R_f = 0.15$ (eluent: hexane/ethyl acetate/dichloromethane = 6:1:2).

Synthesis of octaketone **8**



The synthesis of the octaketone **8** was performed similarly as described previously for **7** with enol silyl ethers **5b** (450 mg, 0.94 mmol) and **2a** (1.88 g, 9.4 mmol), dimethyl sulfone (2.80 g, 30.0 mmol), dimethyl sulfoxide (147 μL , 2.1 mmol) and silver(I) oxide (1.44 g, 6.2 mmol). After purification, octaketone (**8**) was obtained as white solid (290 mg) in 30% yield.

^1H NMR (400 MHz, CDCl_3 , 298 K): δ 2.71 (m, 4H, terminal ethylene), 2.67 (m, 4H, terminal ethylene), 2.66 (s, 4H, central ethylene), 2.16 (s, 6H, acetyl) 2.02 (broad t, $J = 5.5$ Hz, 8H, cyclohexyl), 1.47 (m, 8H, cyclohexyl), 1.39 (m, 4H, cyclohexyl), 1.37 (s, 12H, $-\text{C}(\text{CH}_3)_2-$) ppm; ^{13}C NMR (100 MHz, CDCl_3 , 298 K): δ 208.7, 207.8, 207.7, 207.4, 67.7, 62.3, 32.32, 32.29, 30.6, 26.5, 25.5, 23.0, 21.6 ppm; IR (ATR, neat): $\tilde{\nu} = 2995$ (w), 2935 (m), 2858 (w), 1687 (s), 1451 (w), 1444 (m), 1394 (m), 1346 (m), 1304 (m), 1206 (m), 1116 (m), 1066 (m), 1028 (m), 998 (m), 962 (m), 756 (m), 693 (m) cm^{-1} ; mp $164 - 166^\circ\text{C}$; HR-ESI-TOF MS: m/z calculated for $\text{C}_{34}\text{H}_{50}\text{O}_8$, 585.3433 $[\text{M}-\text{H}]^-$, found 585.3446; Elemental analysis (%): calculated for $\text{C}_{34}\text{H}_{50}\text{O}_8$ (%): C, 69.60; H, 8.59, found C, 69.41; H, 8.57; $R_f = 0.13$ (eluent: hexane/ethyl acetate/dichloromethane = 6:1:2).

2-6 NMR analysis of homo-coupling reaction of 2c

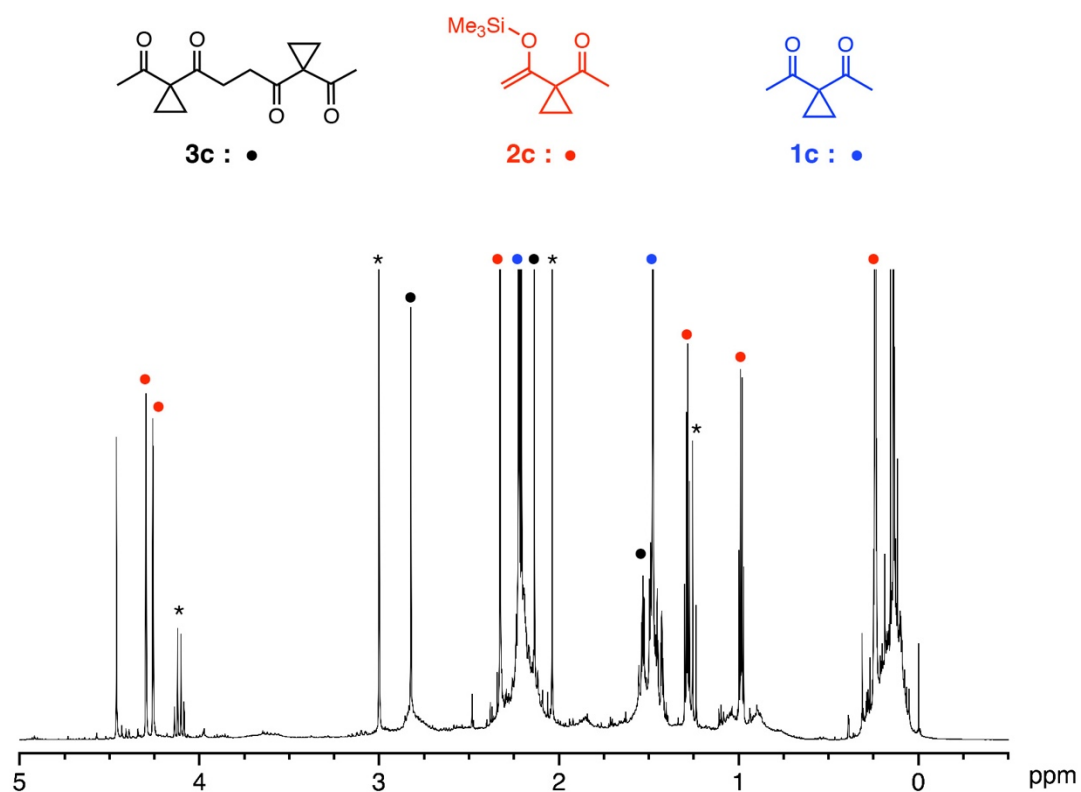
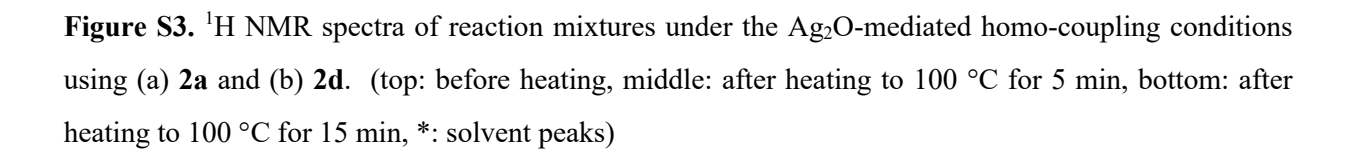


Figure S2. ¹H NMR spectrum (blow-up of the aliphatic region in CDCl₃) of crude products obtained from coupling reaction of 2c (Table 2, for the synthesis of 3c).



3. X-ray Crystallographic Analysis

Single crystal X-ray diffraction data for (2d)

Single crystals of **2d** were grown by slow evaporation of the solution in hexane at 0 °C. Colourless needle-like crystal of approximate size $0.40 \times 0.20 \times 0.06 \text{ mm}^3$, was used for data collection. $\text{C}_{22}\text{H}_{28}\text{O}_2\text{Si}$, $M_{\text{w}} = 352.53$, Monoclinic, space group $C2$, $a = 19.7751(7) \text{ \AA}$, $b = 7.6977(3) \text{ \AA}$, $c = 13.7091(5) \text{ \AA}$, $\beta = 104.859(4)^\circ$, $V = 2017.05(13) \text{ \AA}^3$, $Z = 4$, $T = 123(2) \text{ K}$, $\mu = 0.128 \text{ mm}^{-1}$, $D_{\text{calc}} = 1.161 \text{ g/cm}^3$, $2.286^\circ \leq \theta \leq 24.998^\circ$, 3240 unique reflections out of 3316 with $I > 2\sigma(I)$, GOF = 1.082, $R_1 = 0.0268$, $wR_2 = 0.0720$. CCDC deposit number: 1987581.

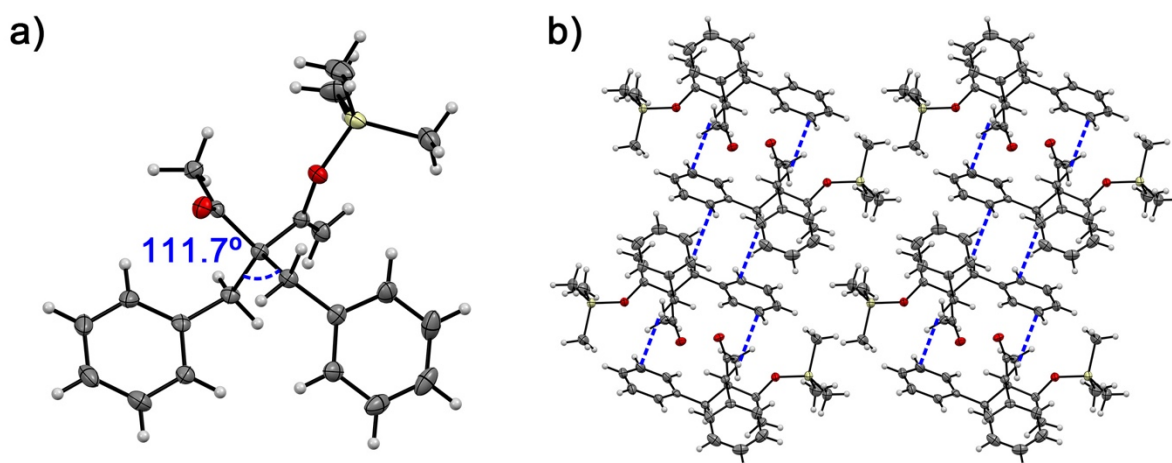


Figure S4. a) Crystal structure of mono-silylated monomer **2d**. Thermal ellipsoid are set at 50% probability b) crystal packing for mono-silylated monomer **2d** viewing along *b*-axis. Blue-dashed lines indicate presence of intermolecular CH- π interaction.

4. 1D and 2D NMR Spectra

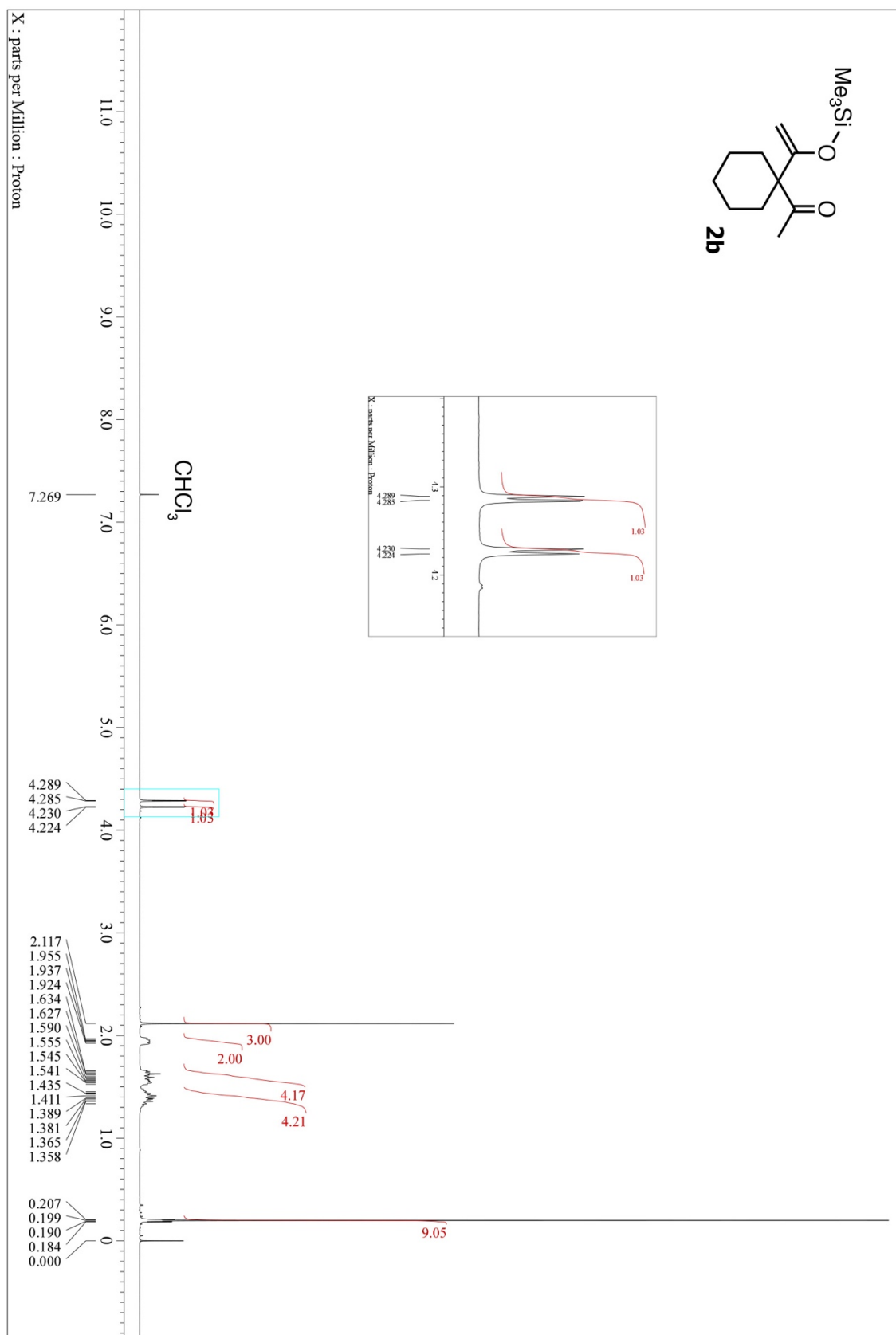


Figure S5. ¹H NMR spectrum of **2b** in CDCl₃ at 25 °C.

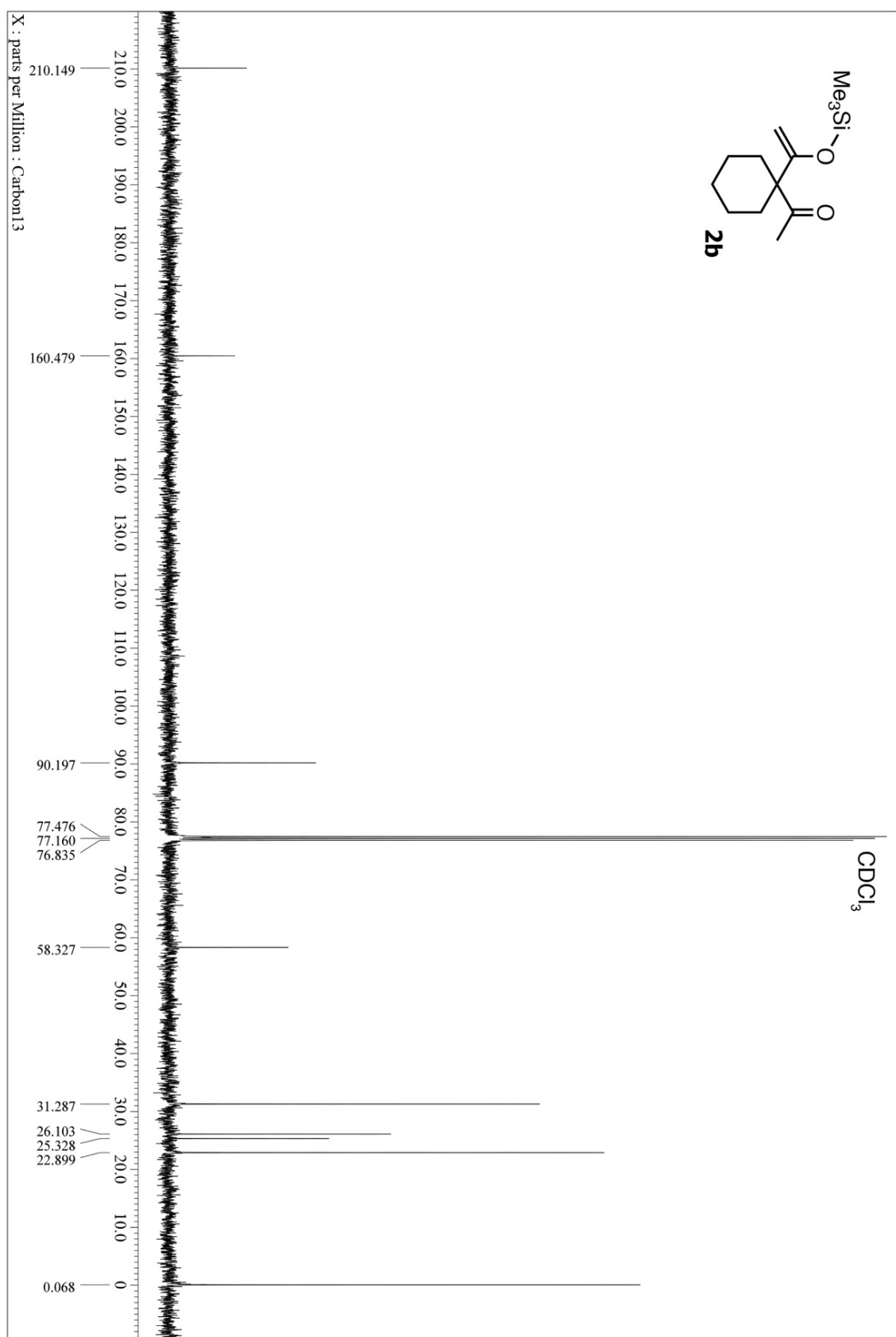


Figure S6. ^{13}C NMR spectrum of **2b** in CDCl_3 at 25 °C.

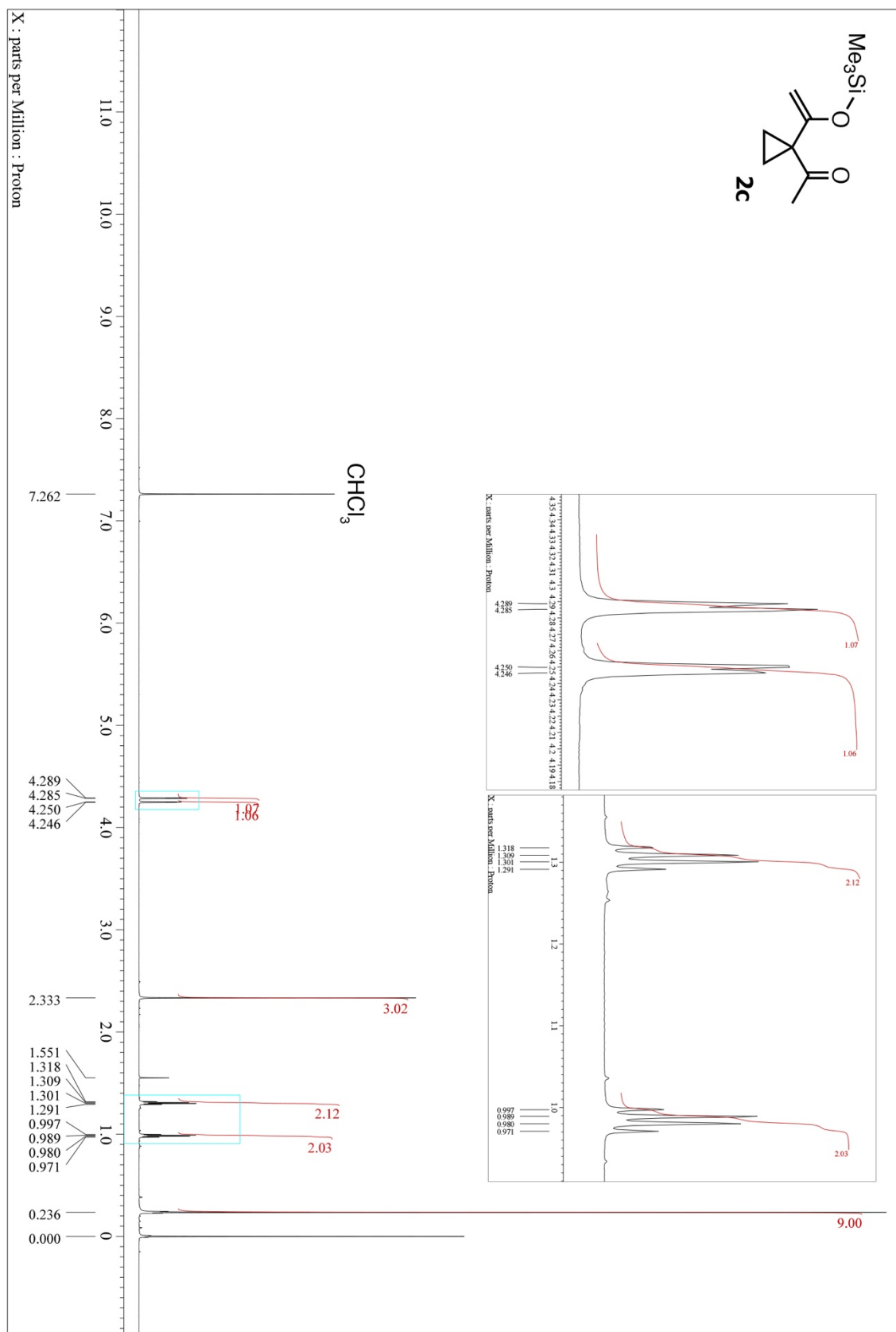


Figure S7. ¹H NMR spectrum of **2c** in CDCl₃ at 25 °C.

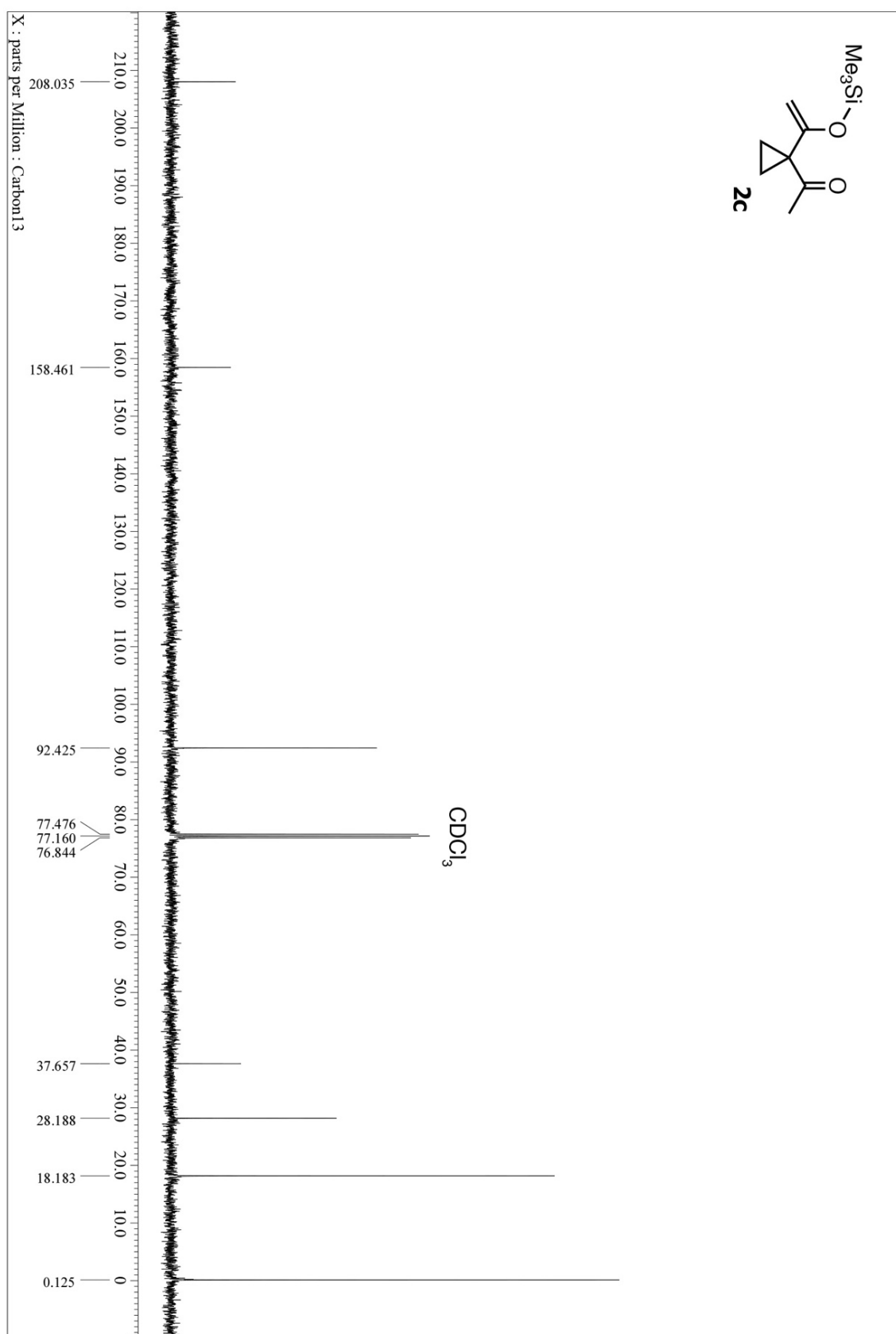


Figure S8. ^{13}C NMR spectrum of **2c** in CDCl_3 at 25 °C.

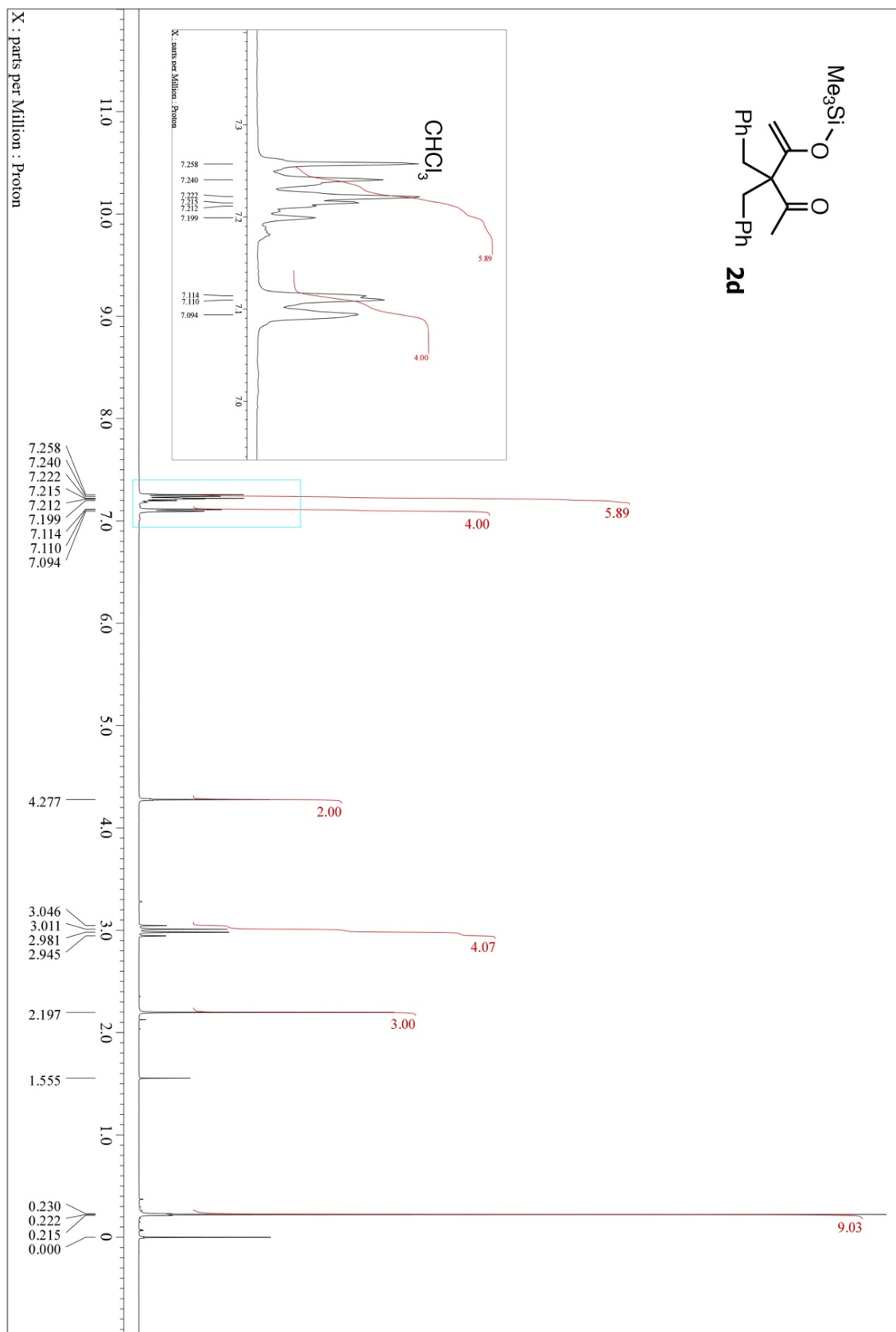


Figure S9. ^1H NMR spectrum of **2d** in CDCl_3 at $25\text{ }^\circ\text{C}$.

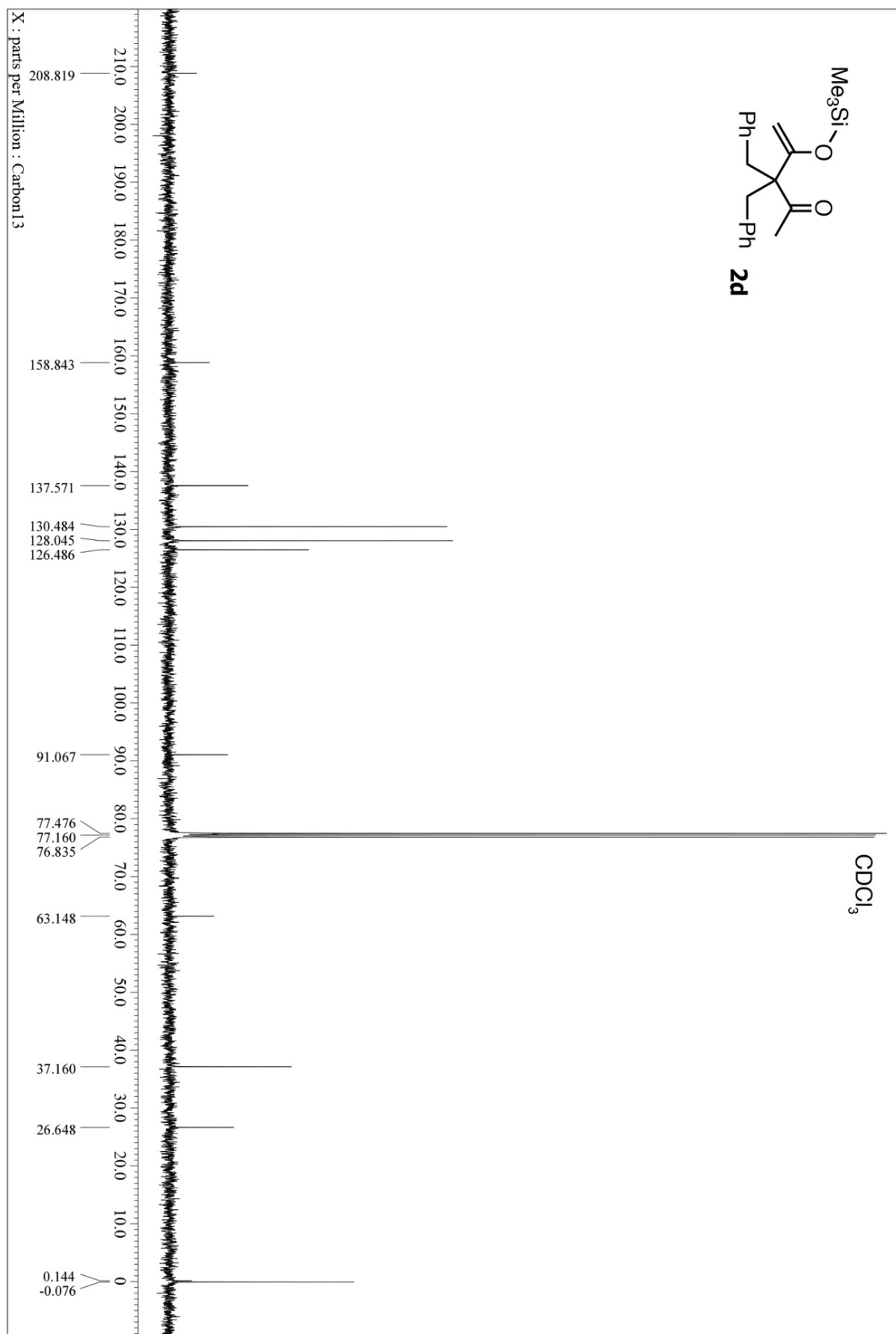


Figure S10. ^{13}C NMR spectrum of **2d** in CDCl_3 at 25 °C.

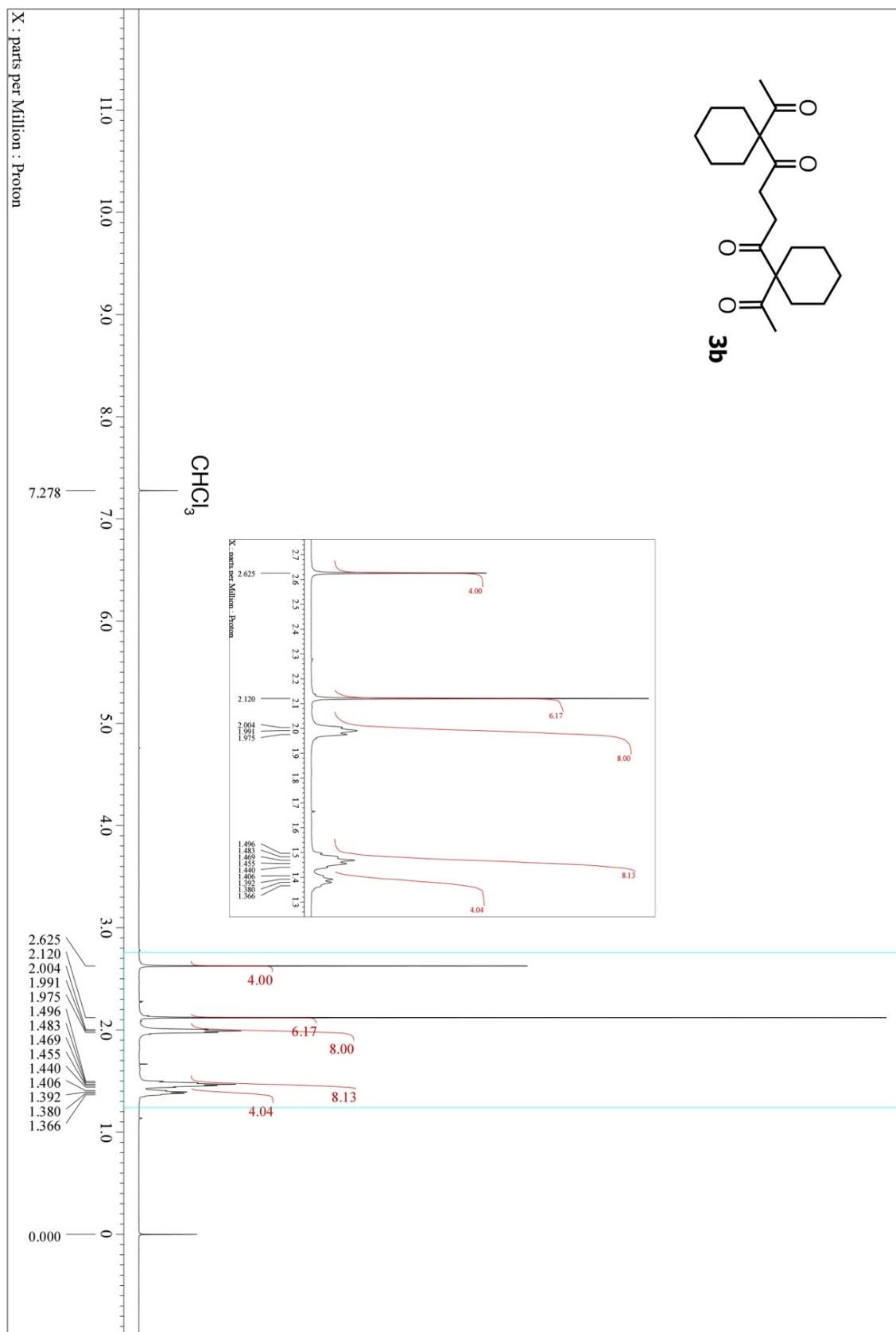


Figure S11. ^1H NMR spectrum of **3b** in CDCl_3 at 25 °C.

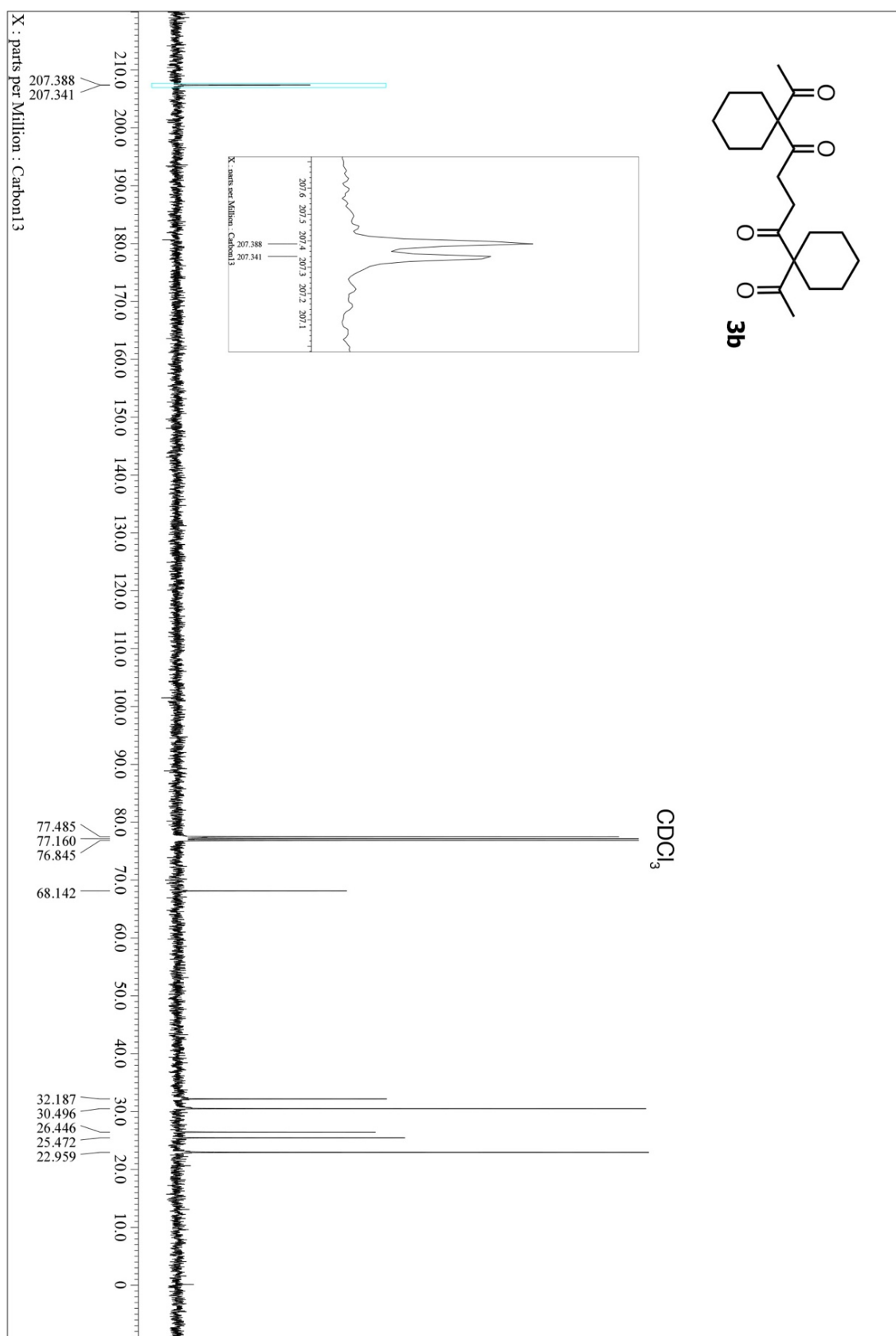


Figure S12. ^{13}C NMR spectrum of **3b** in CDCl_3 at 25 °C.

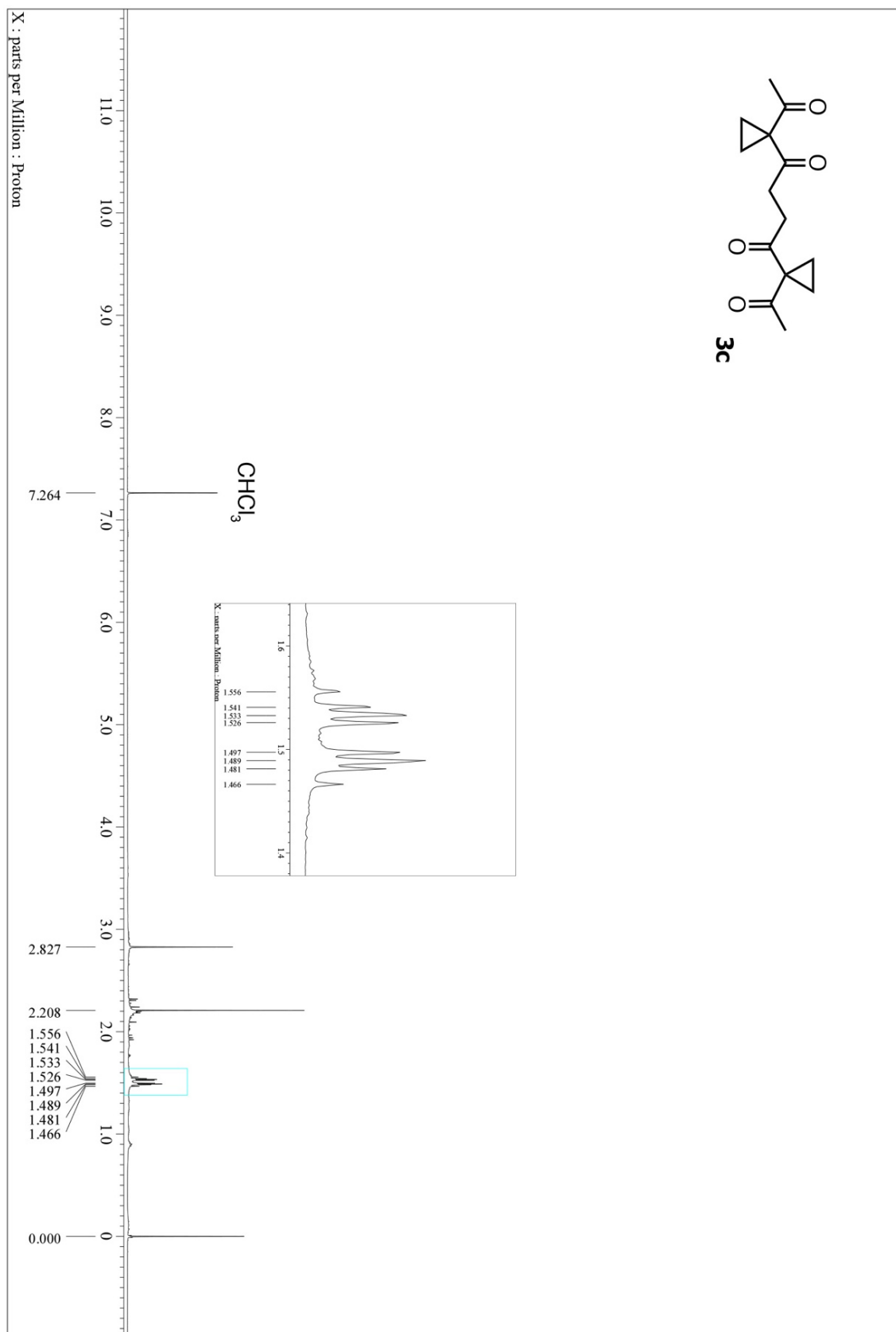


Figure S13. ^1H NMR spectrum of **3c** in CDCl_3 at 25 °C.

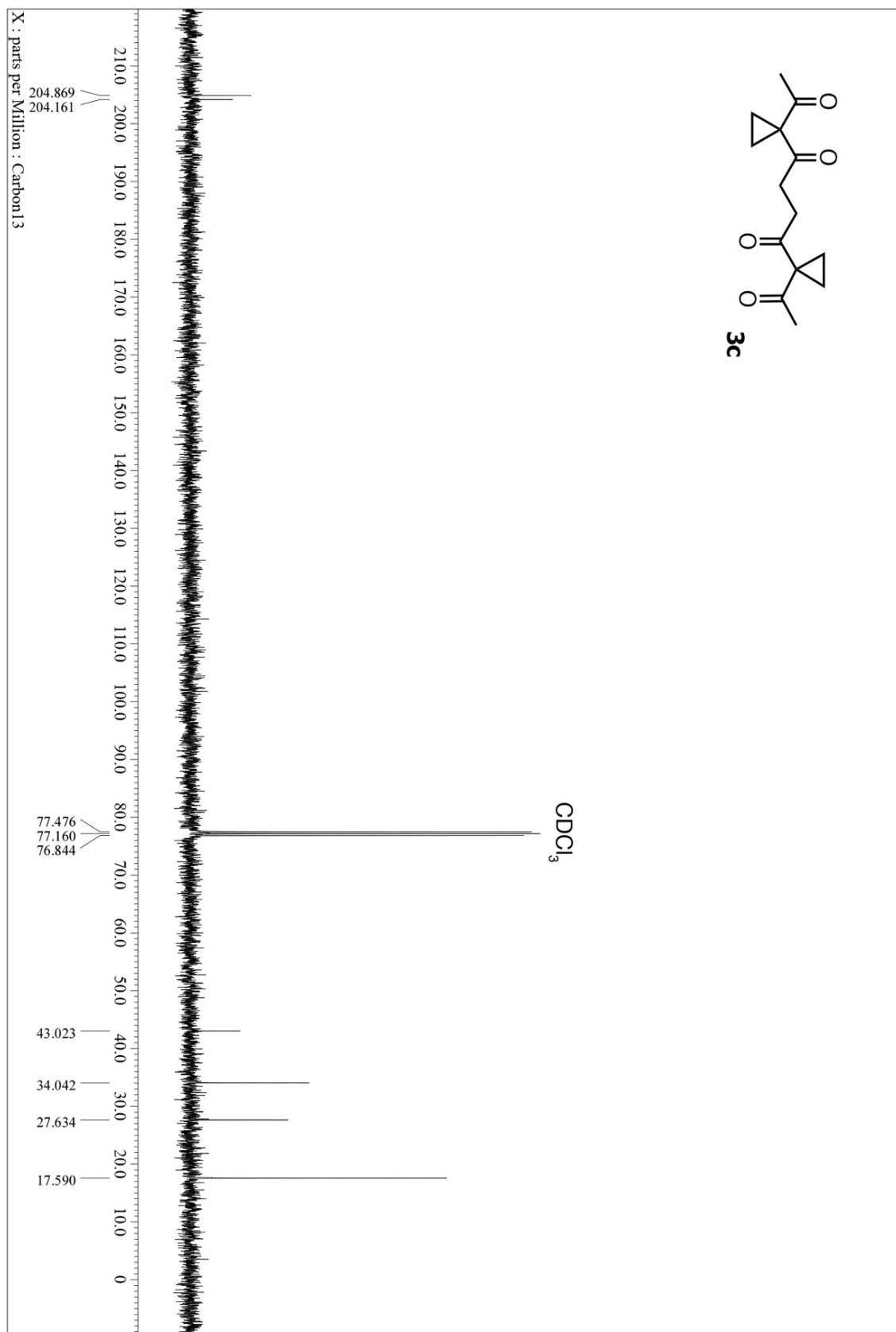


Figure S14. ^{13}C NMR spectrum of **3c** in CDCl_3 at 25 °C.

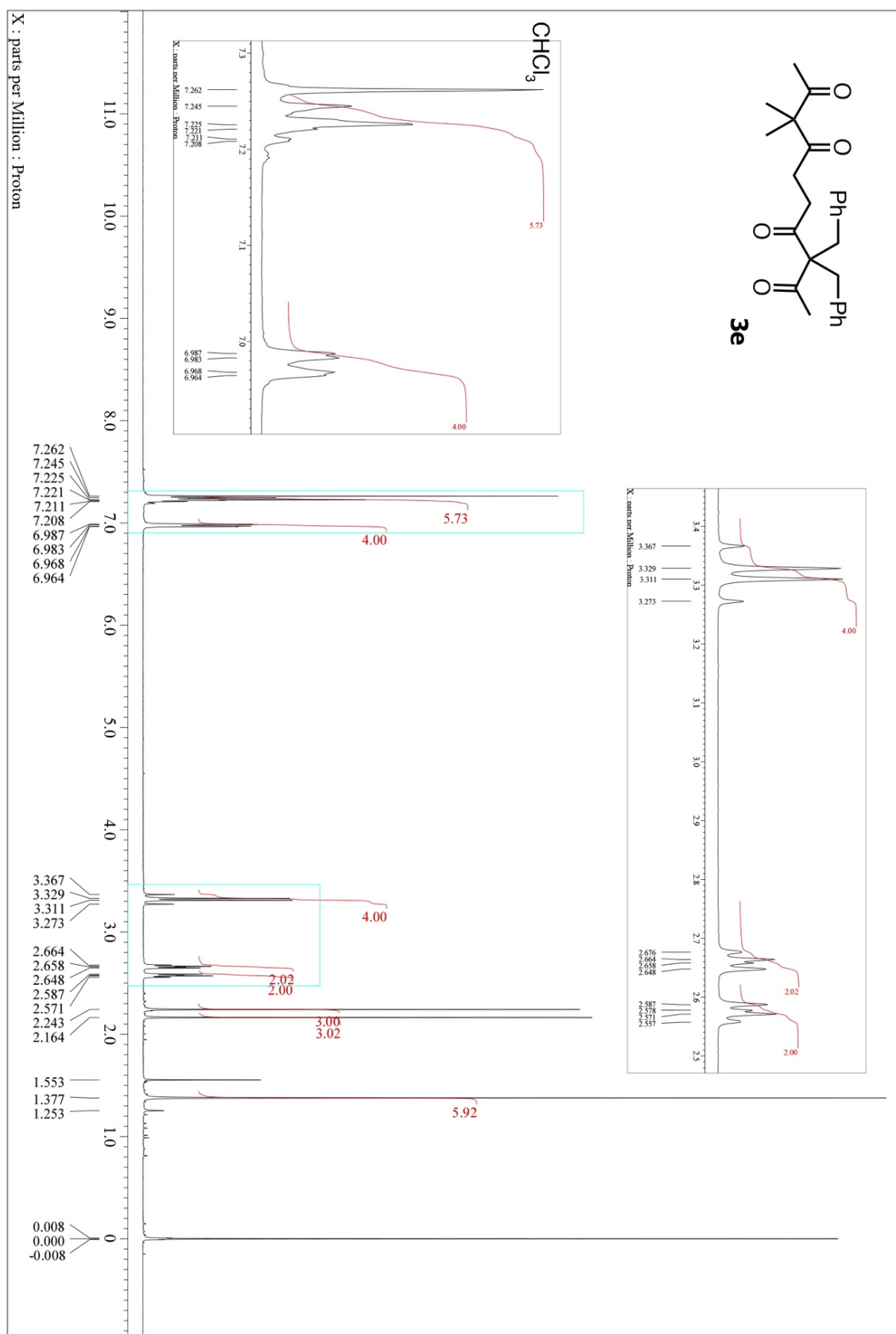


Figure S15. ¹H NMR spectrum of **3e** in CDCl₃ at 25 °C.

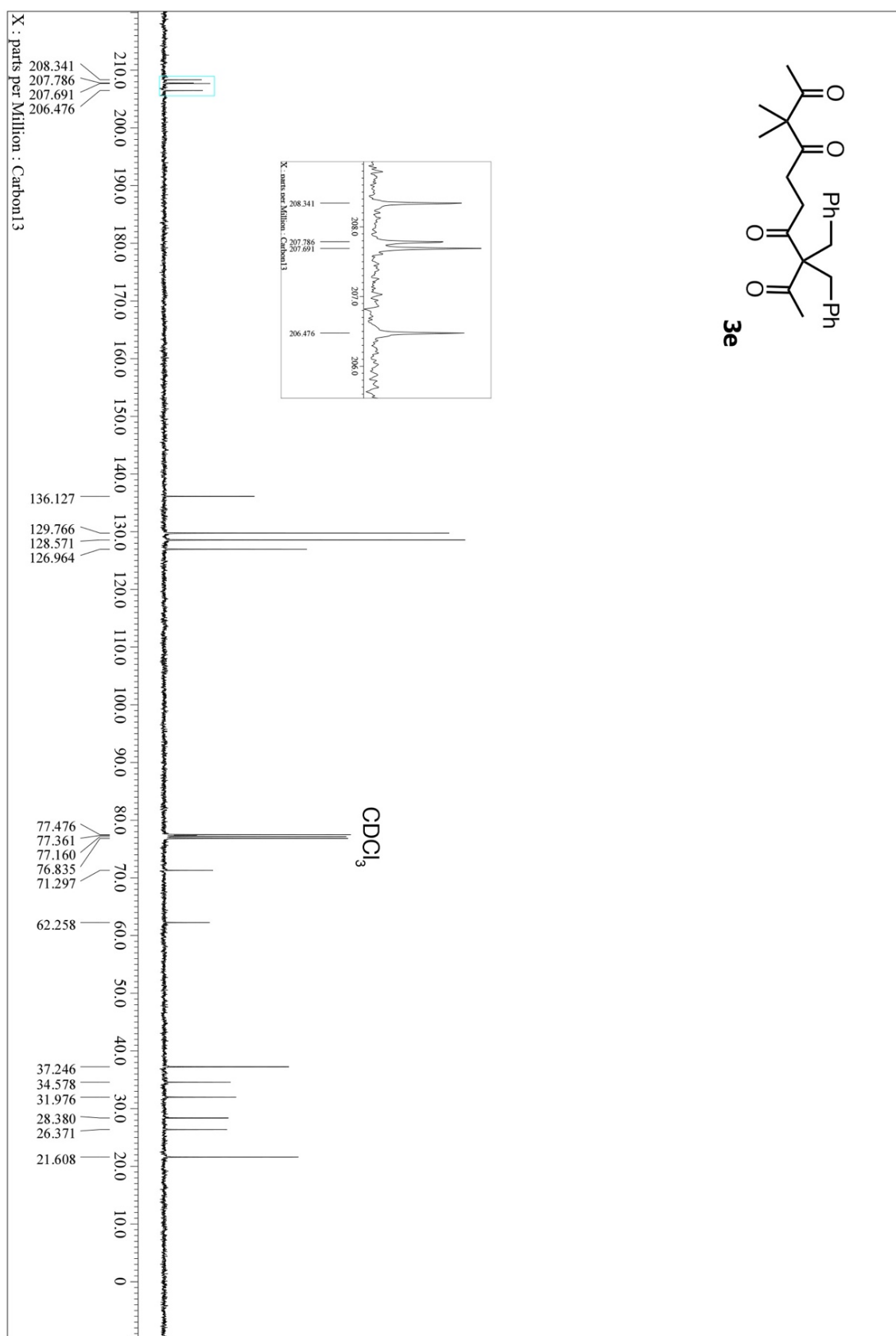


Figure S16. ^{13}C NMR spectrum of **3e** in CDCl_3 at 25 °C.

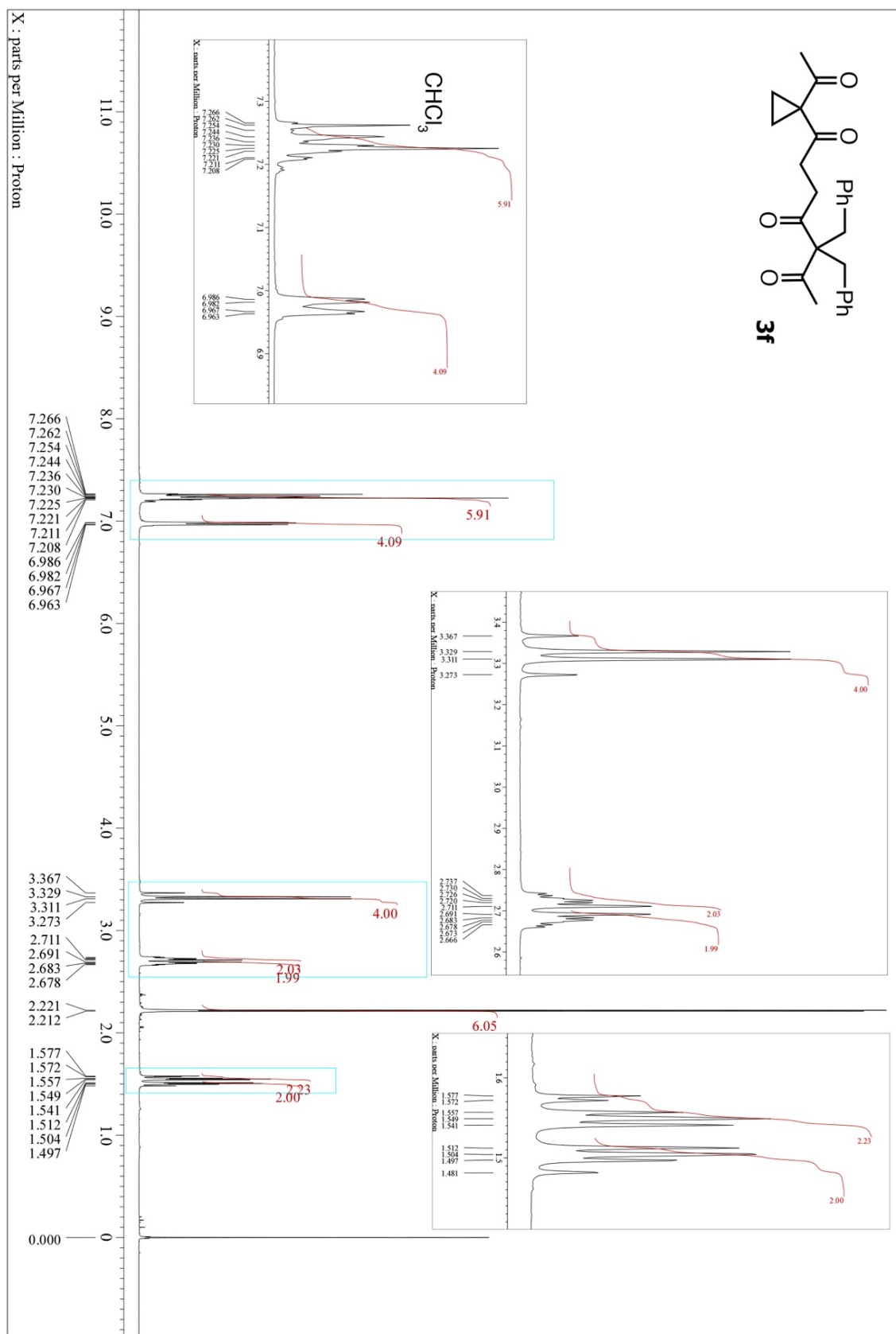


Figure S17. ¹H NMR spectrum of **3f** in CDCl₃ at 25 °C.

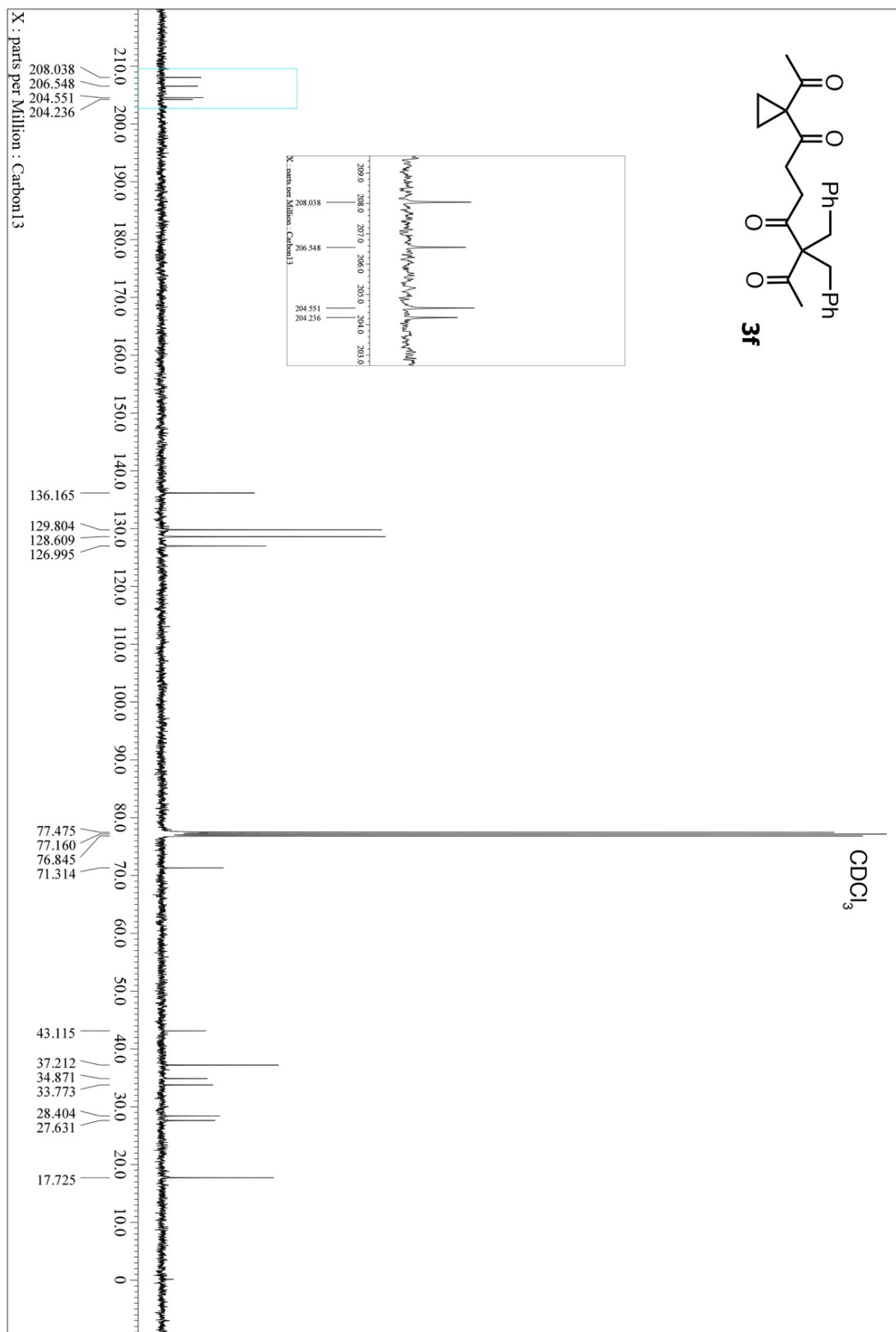


Figure S18. ^{13}C NMR spectrum of **3f** in CDCl_3 at 25 °C.

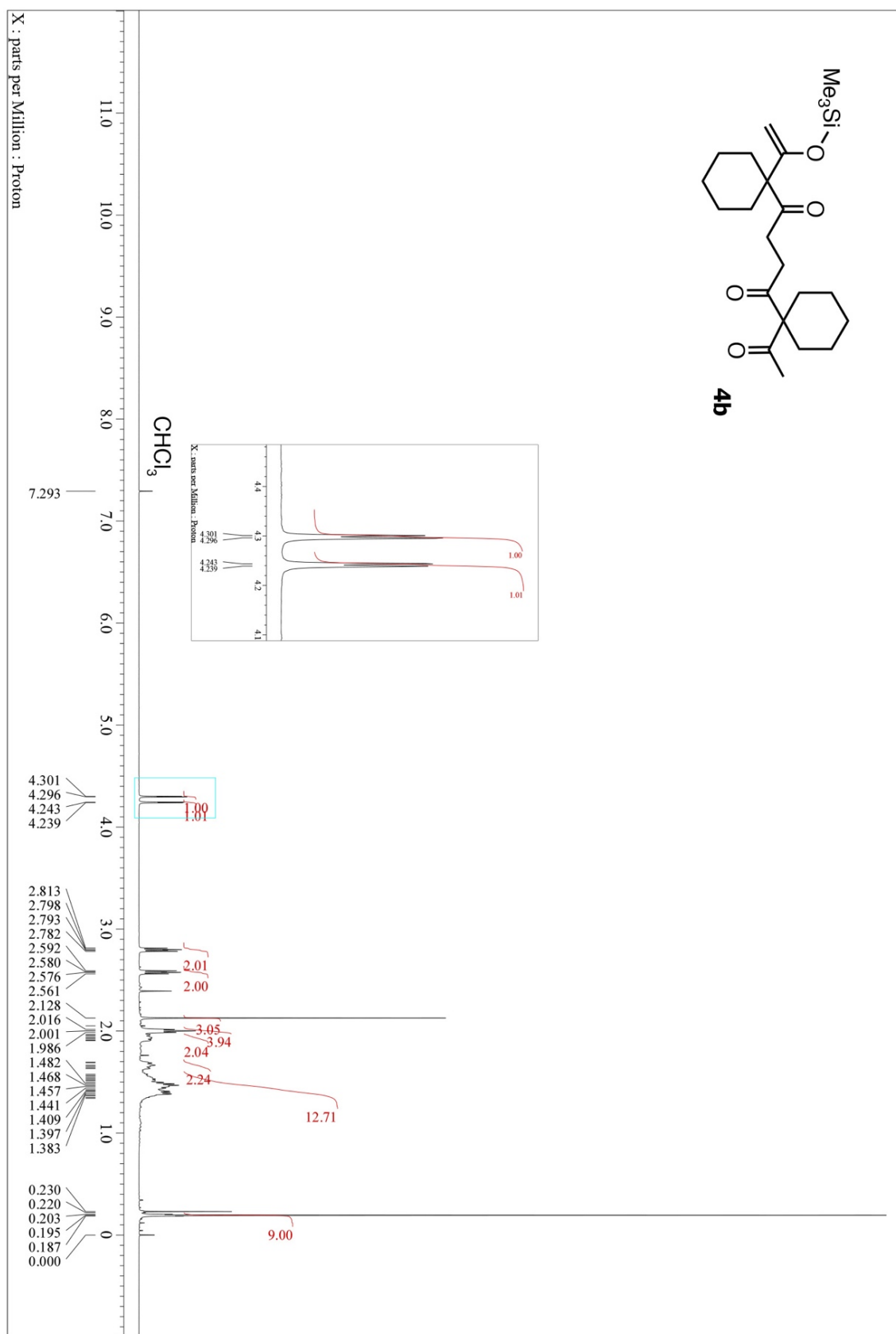


Figure S19. ^1H NMR spectrum of **4b** in CDCl_3 at 25 °C.

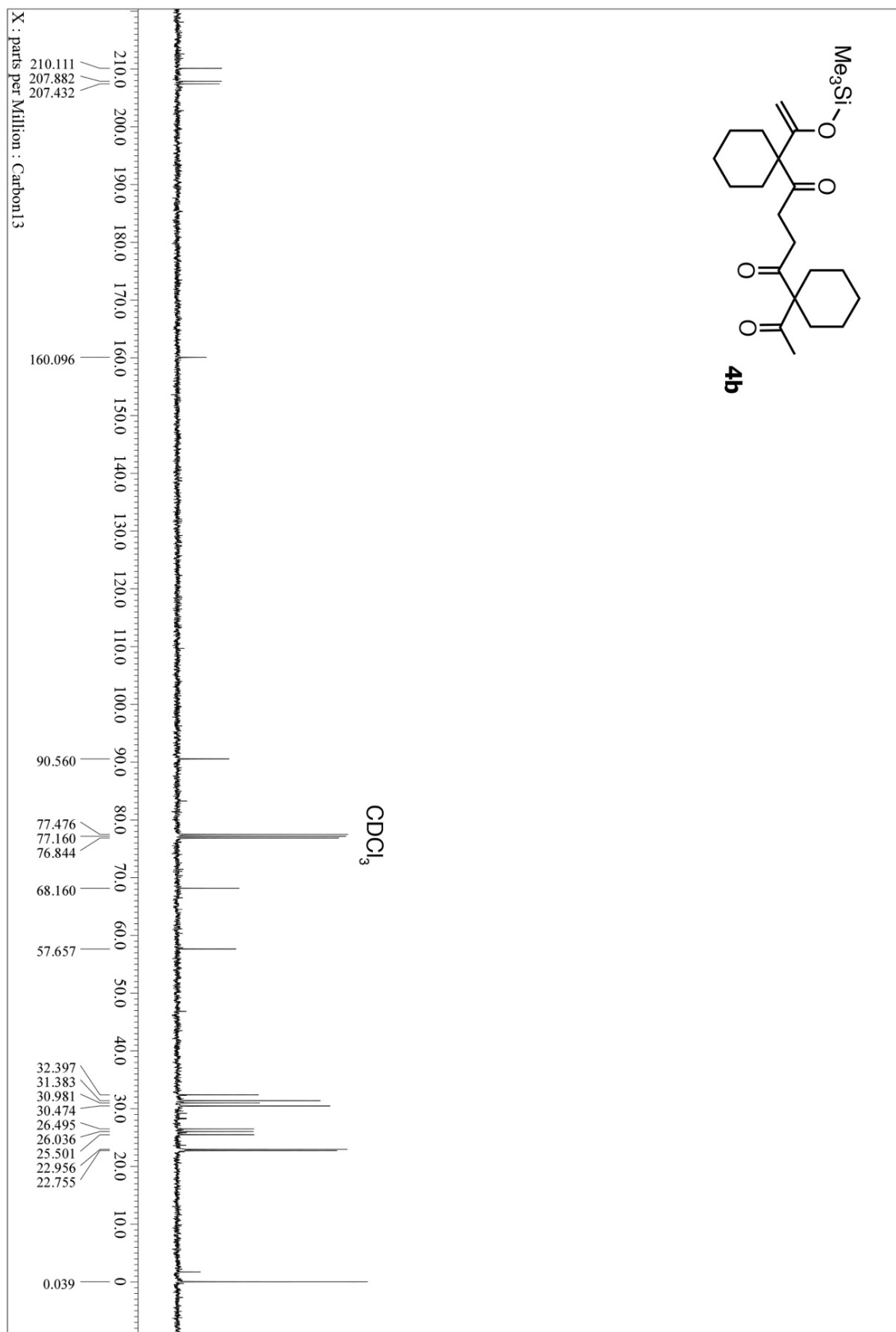


Figure S20. ^{13}C NMR spectrum of **4b** in CDCl_3 at 25 °C.

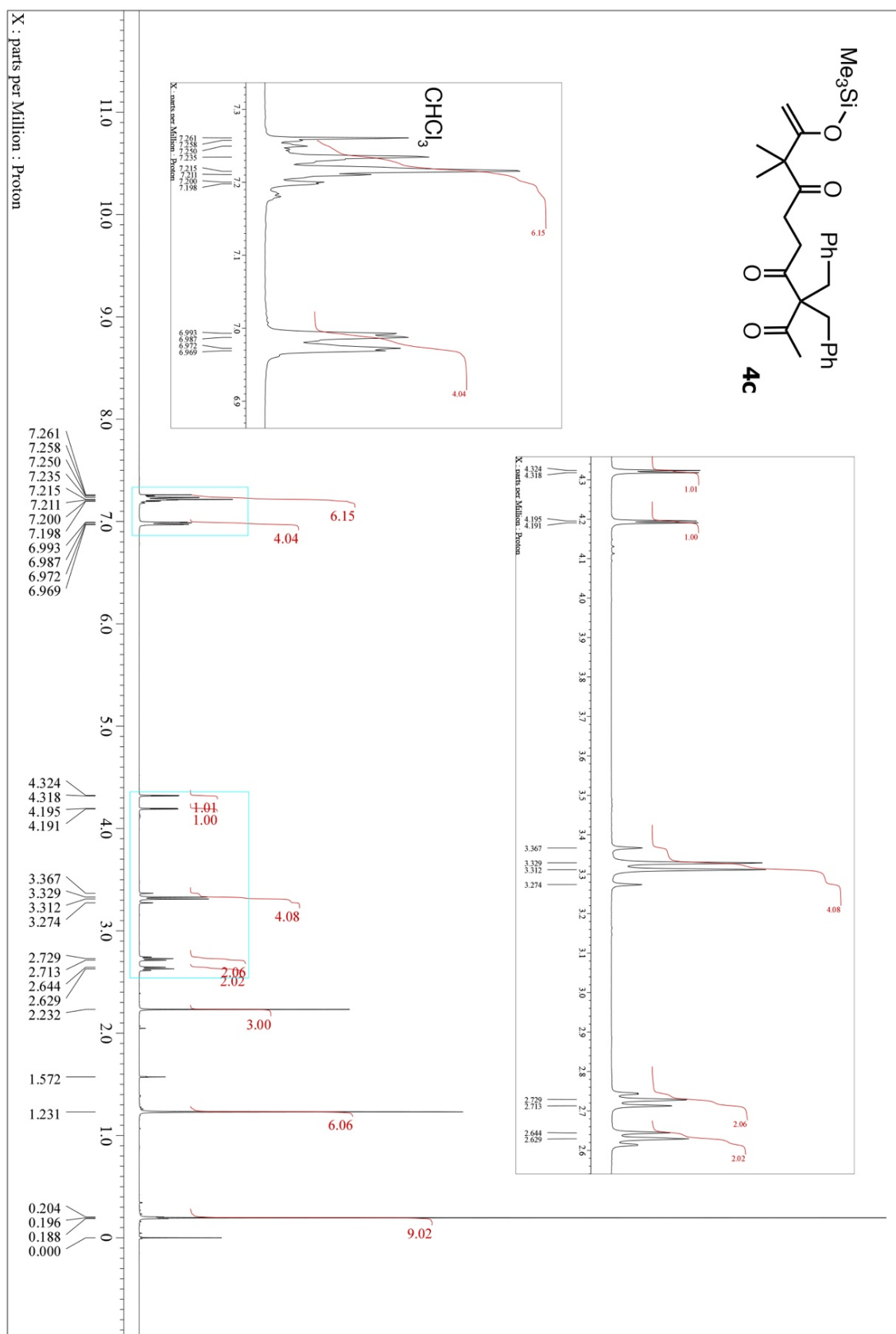


Figure S21. ^1H NMR spectrum of **4c** in CDCl_3 at 25 °C.

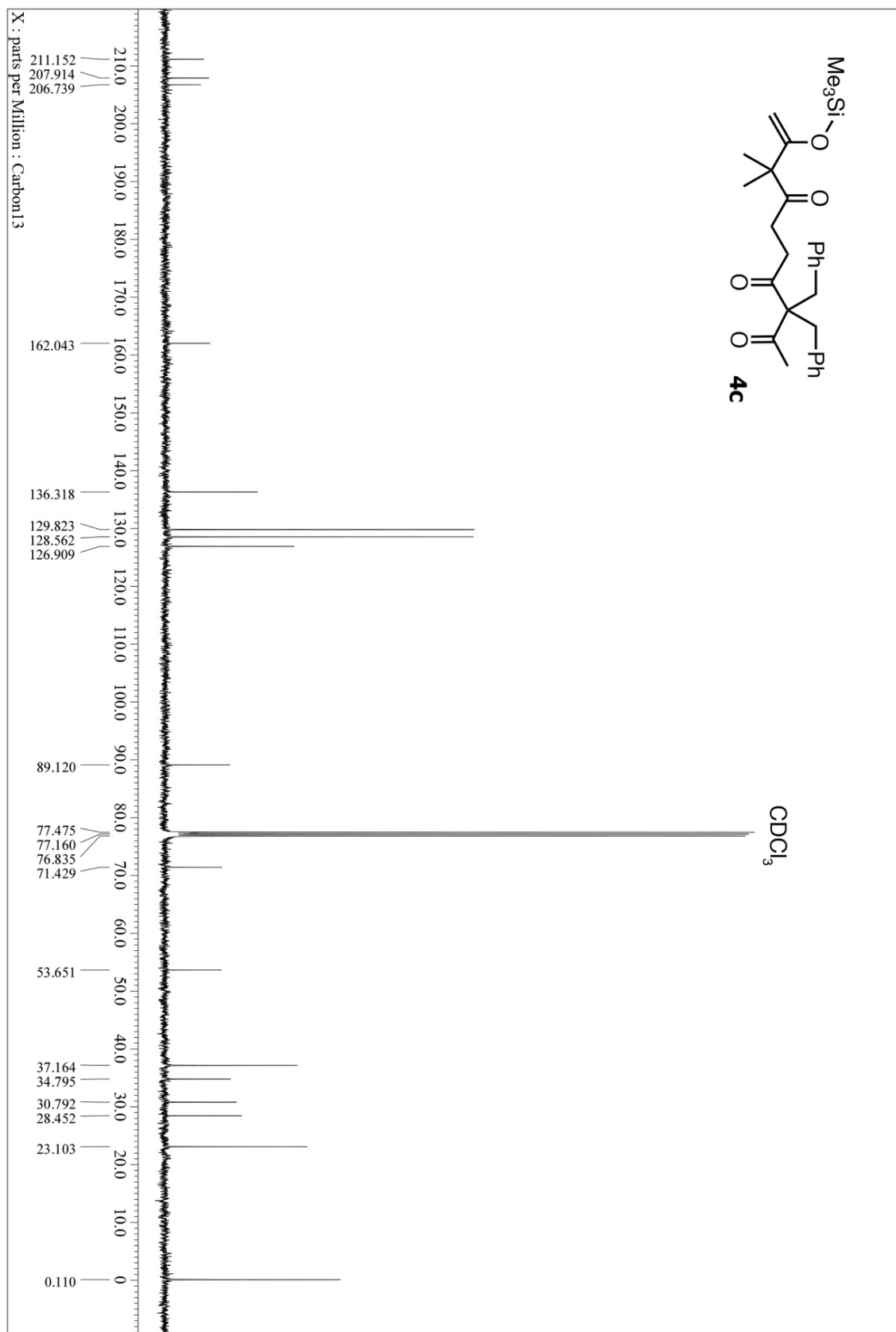


Figure S22. ^{13}C NMR spectrum of **4c** in CDCl_3 at 25 °C.

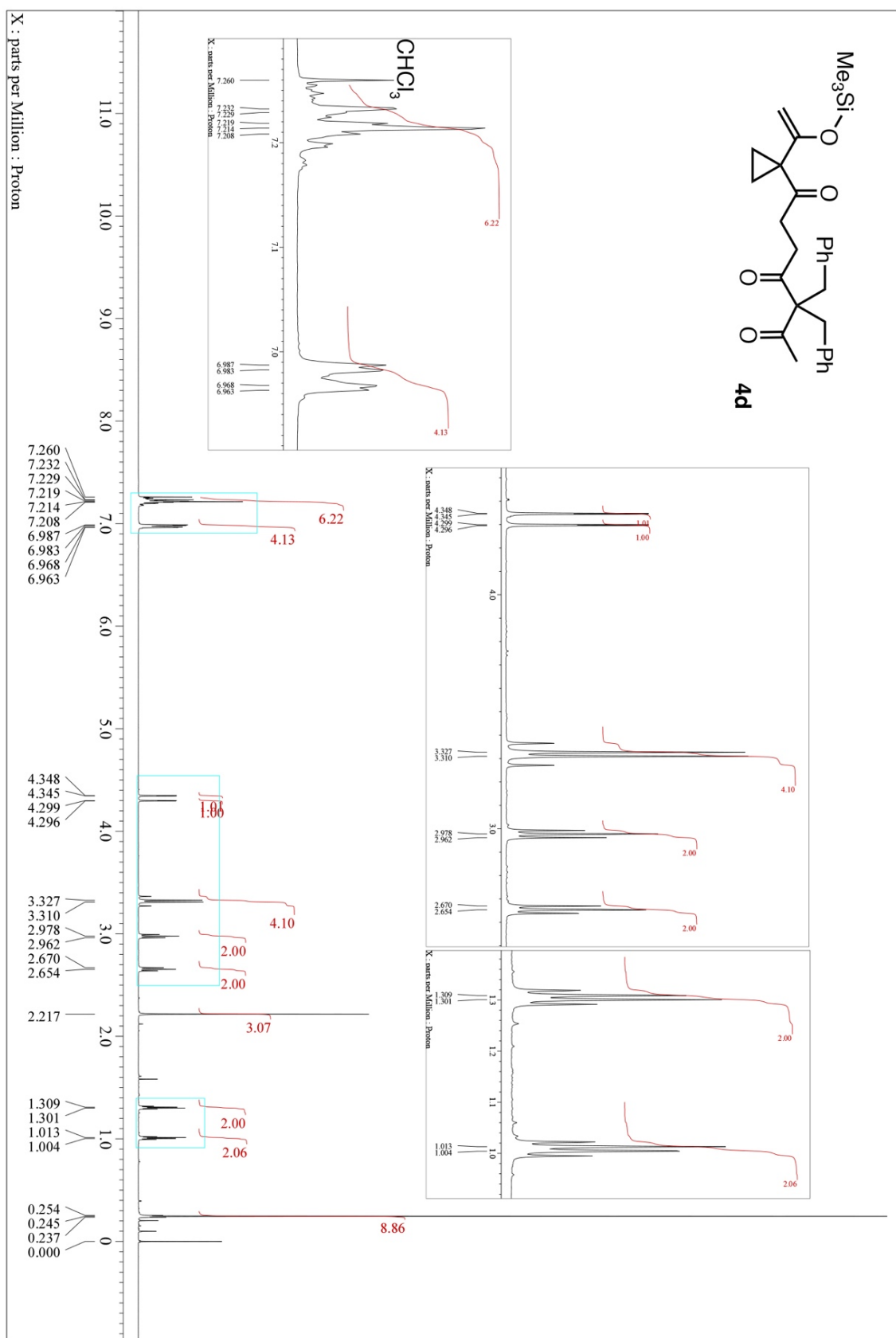


Figure S23. ¹H NMR spectrum of **4d** in CDCl₃ at 25 °C.

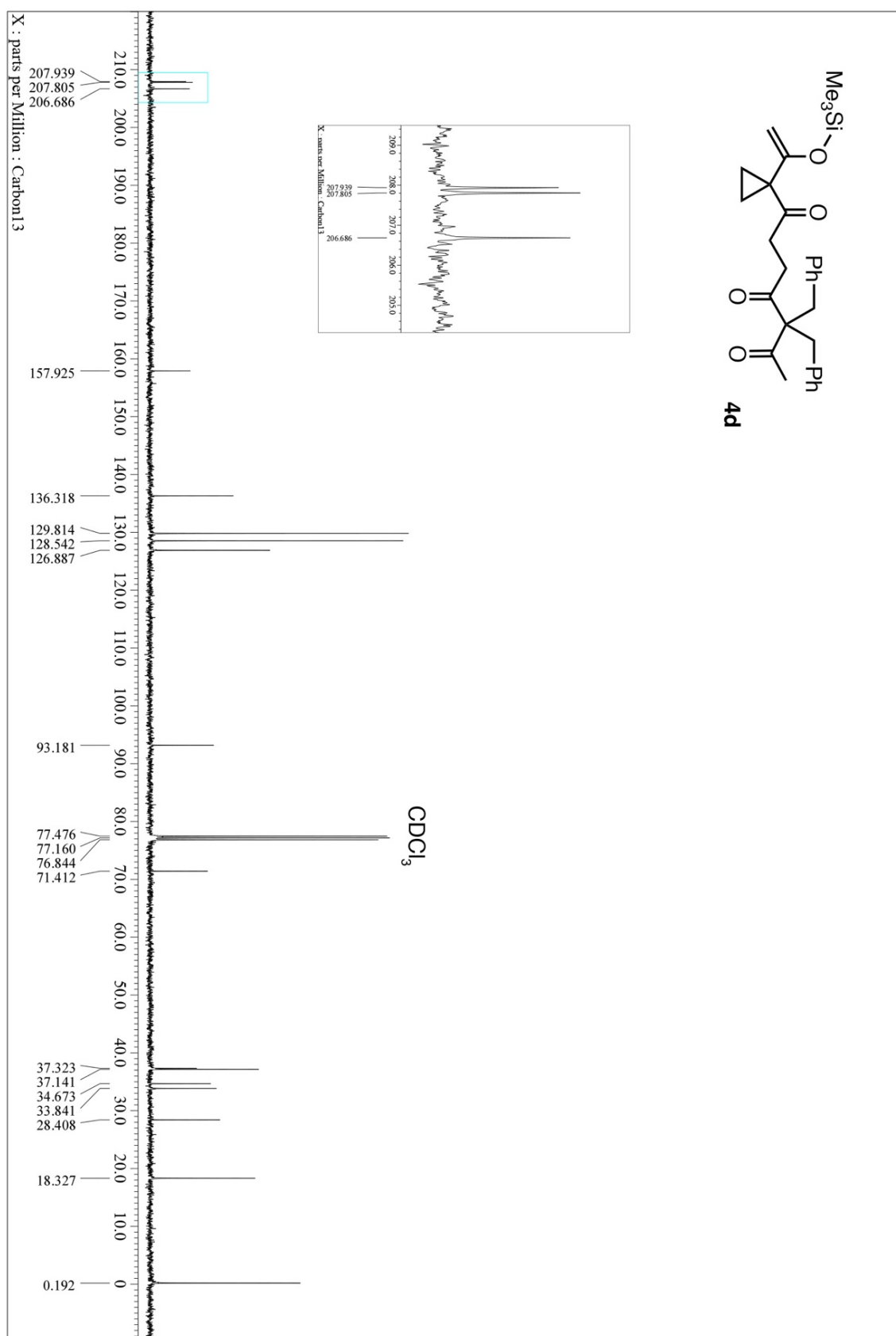


Figure S24. ^{13}C NMR spectrum of **4d** in CDCl_3 at 25 °C.

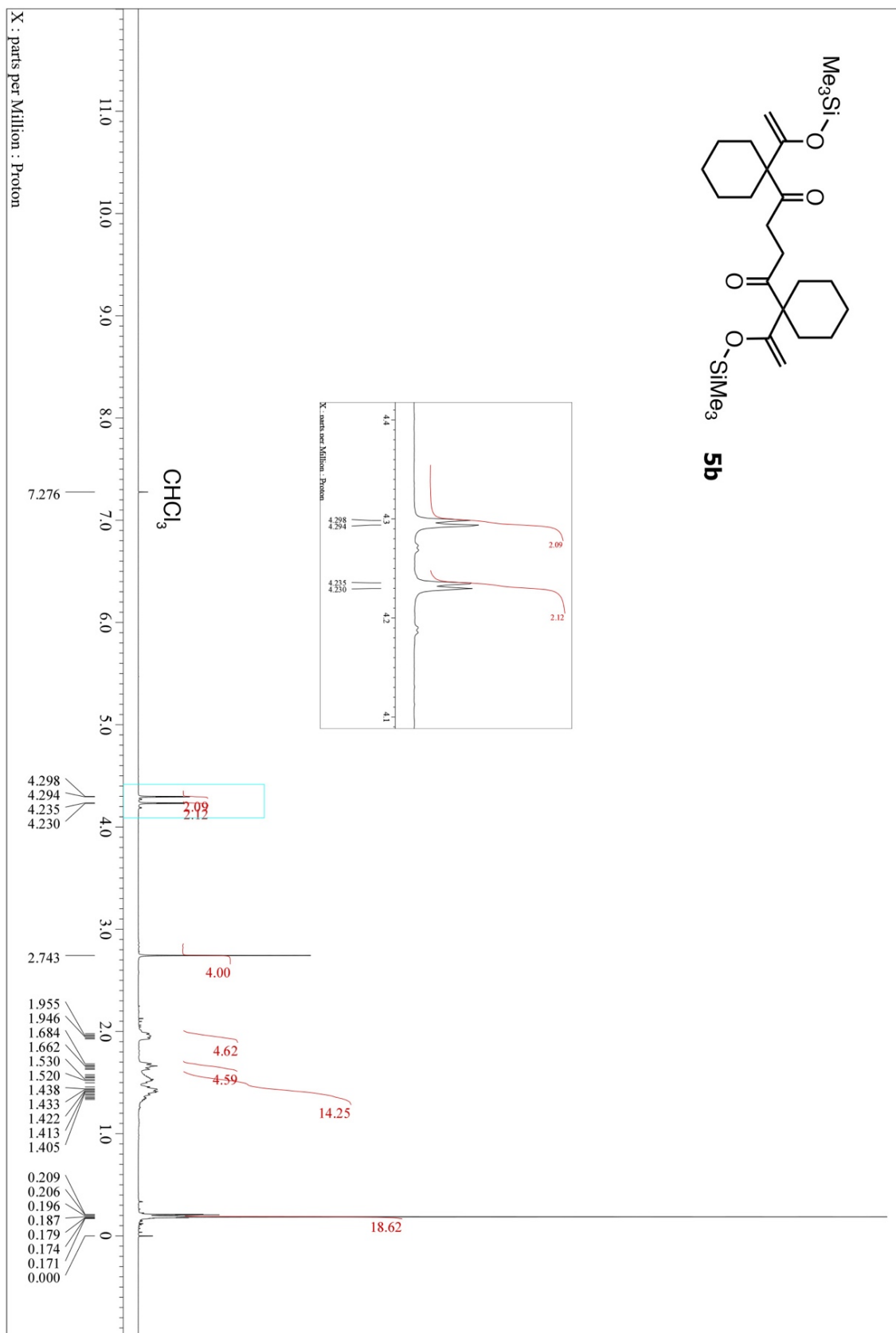


Figure S25. ^1H NMR spectrum of **5b** in CDCl_3 at 25 °C.

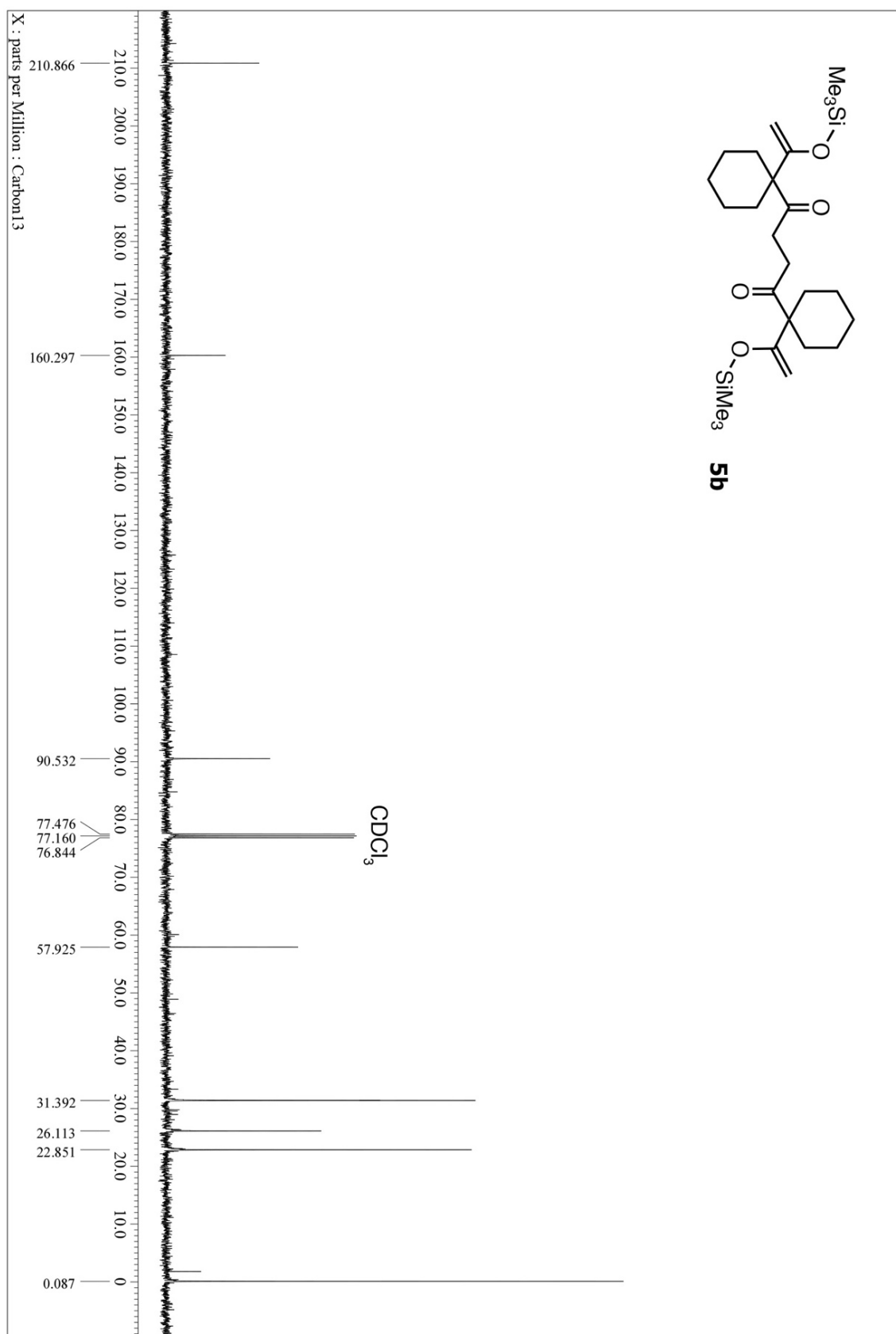


Figure S26. ^{13}C NMR spectrum of **5b** in CDCl_3 at 25 °C.

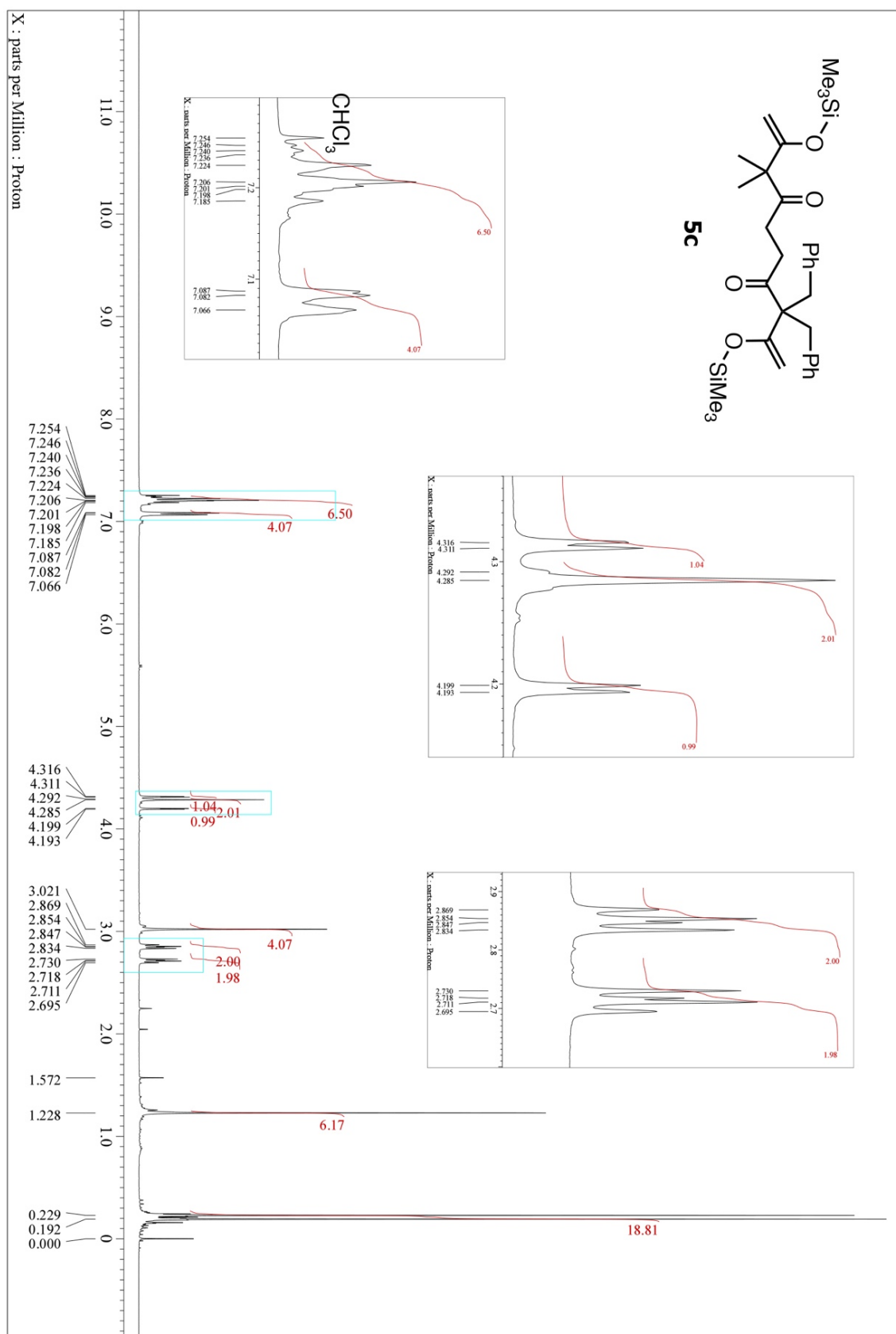


Figure S27. ¹H NMR spectrum of **5c** in CDCl₃ at 25 °C.

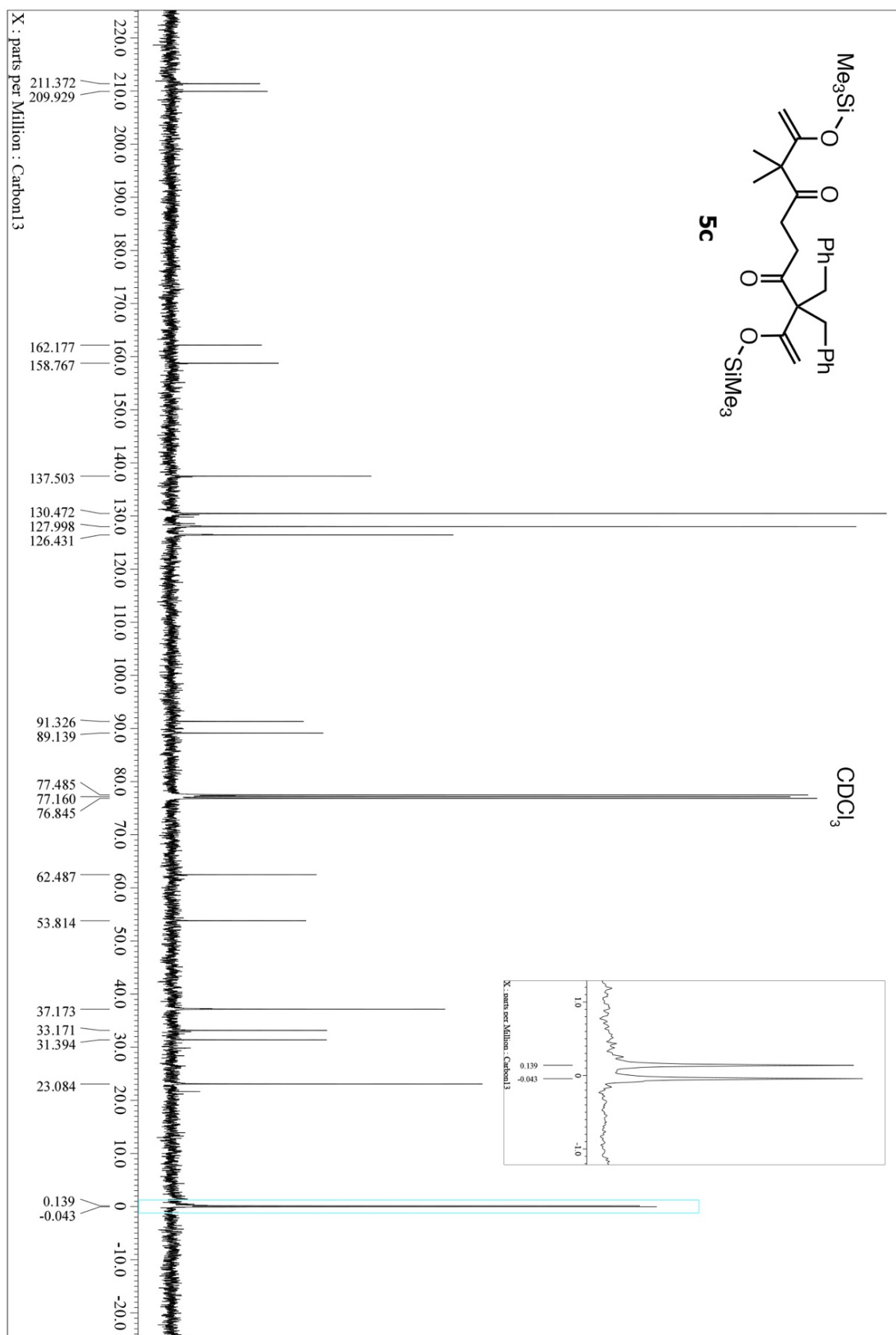


Figure S28. ¹³C NMR spectrum of **5c** in CDCl₃ at 25 °C.

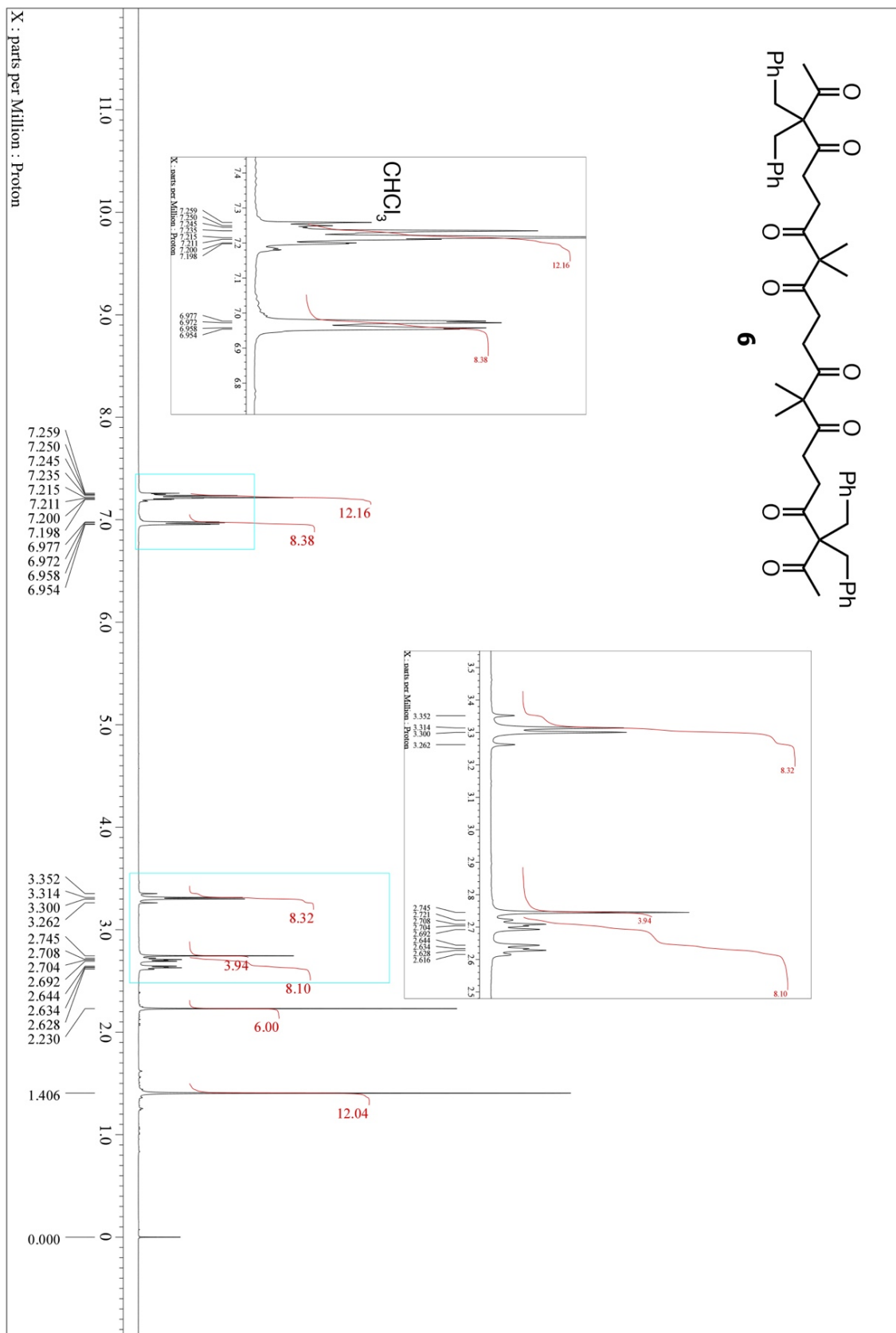


Figure S29. ¹H NMR spectrum of **6** in CDCl₃ at 25 °C.

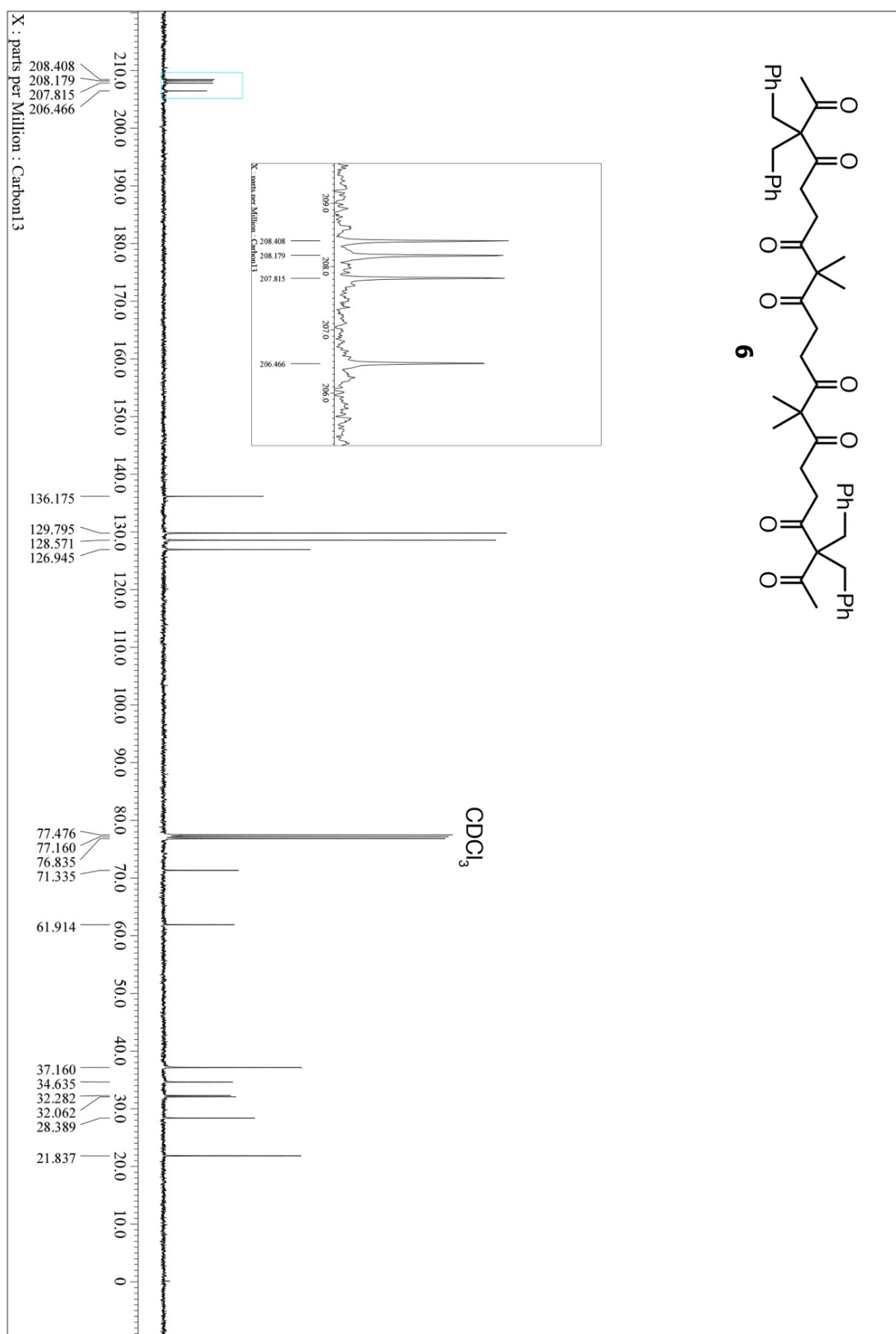


Figure S30. ¹³C NMR spectrum of **6** in CDCl₃ at 25 °C.

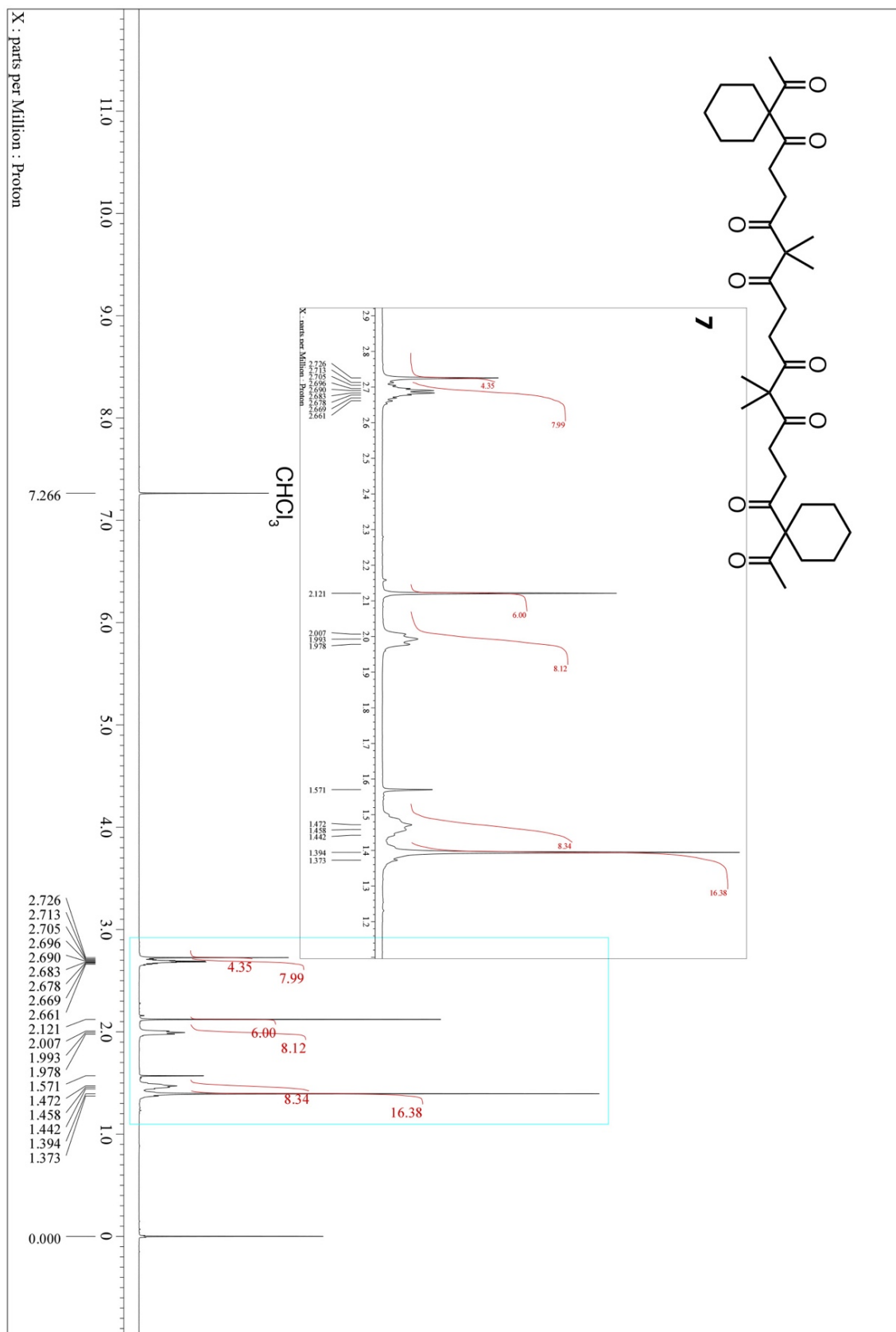


Figure S31. ¹H NMR spectrum of **7** in CDCl₃ at 25 °C.

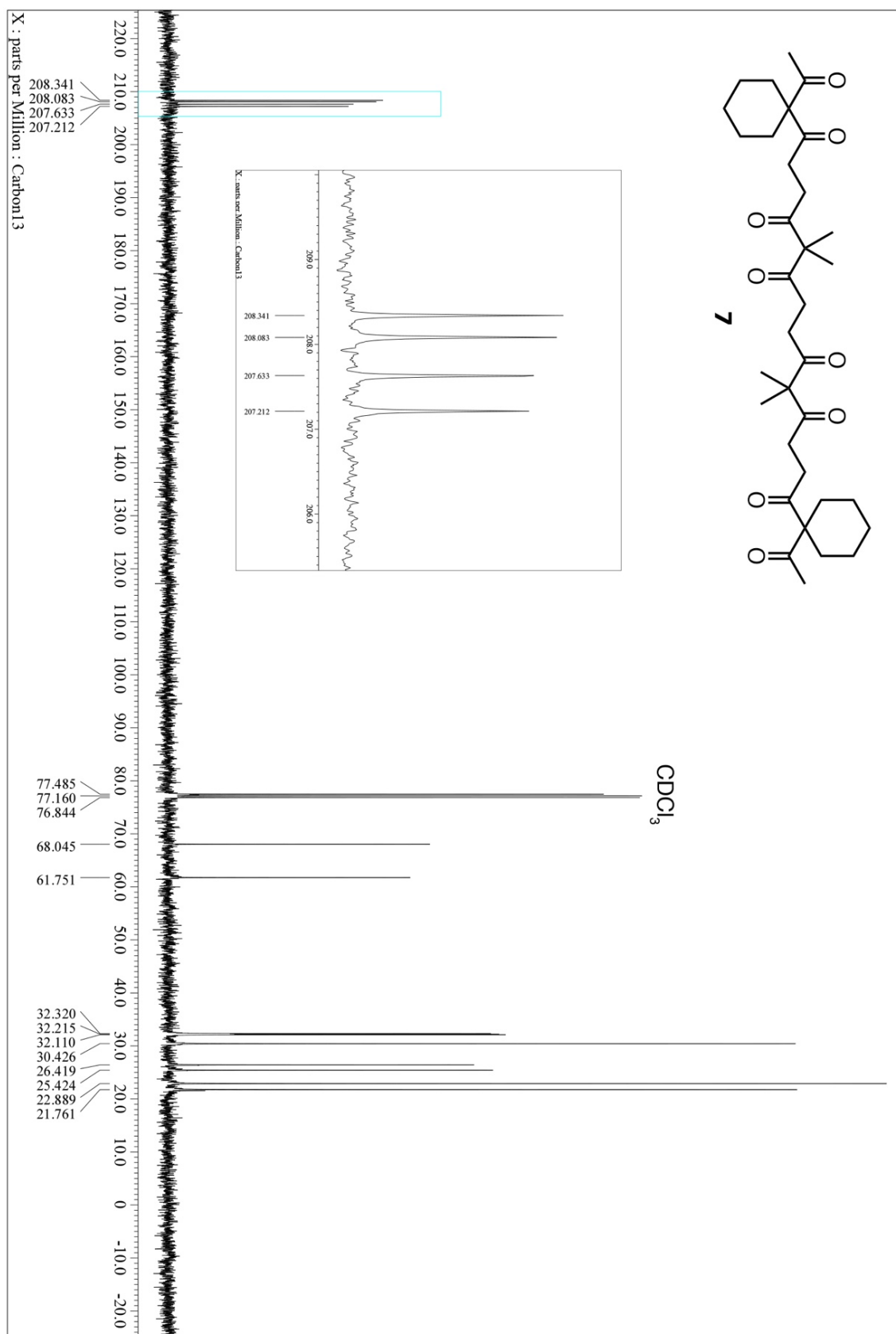


Figure S32. ^{13}C NMR spectrum of **7** in CDCl_3 at 25 °C.

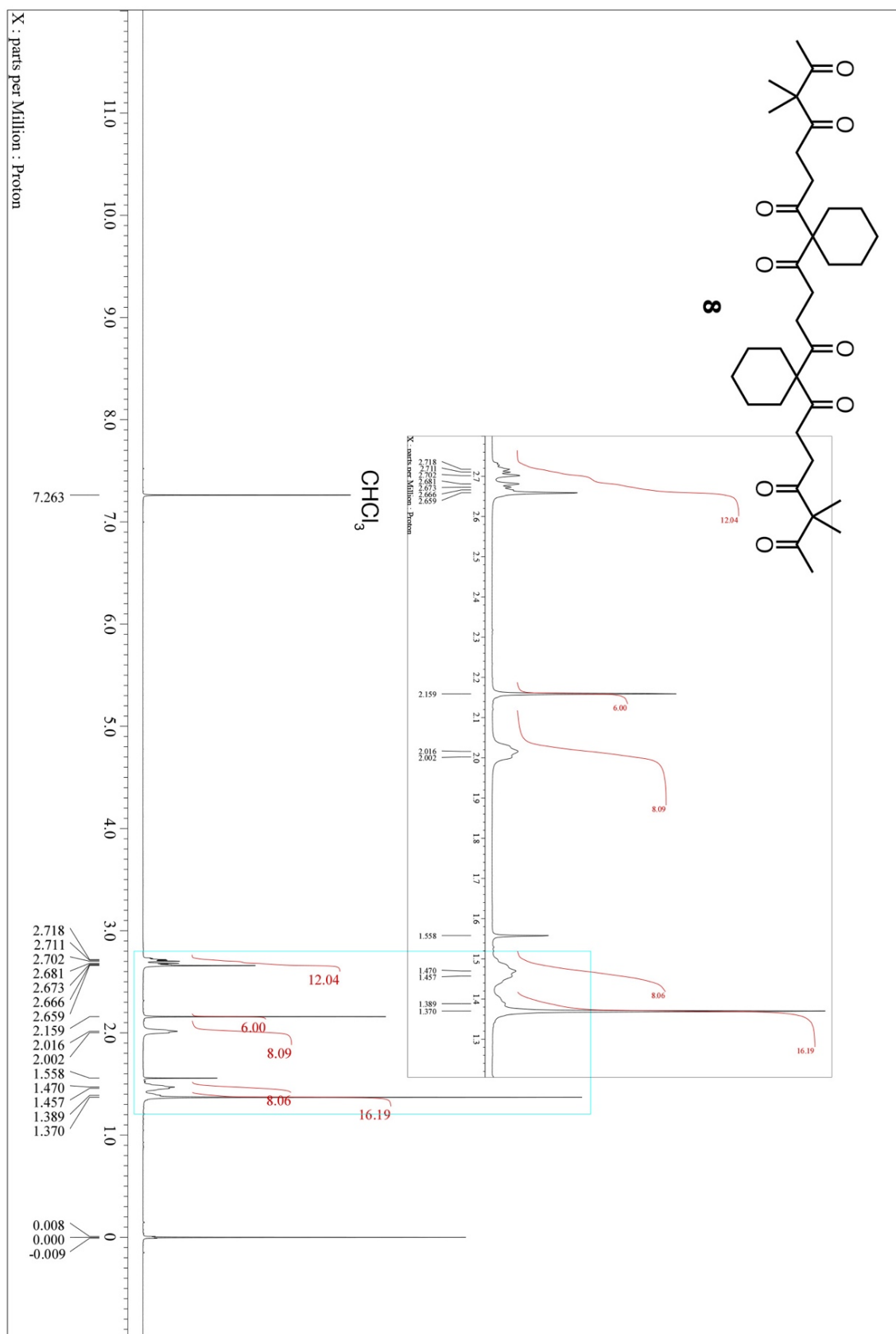


Figure S33. ^1H NMR spectrum of **8** in CDCl_3 at 25 °C.

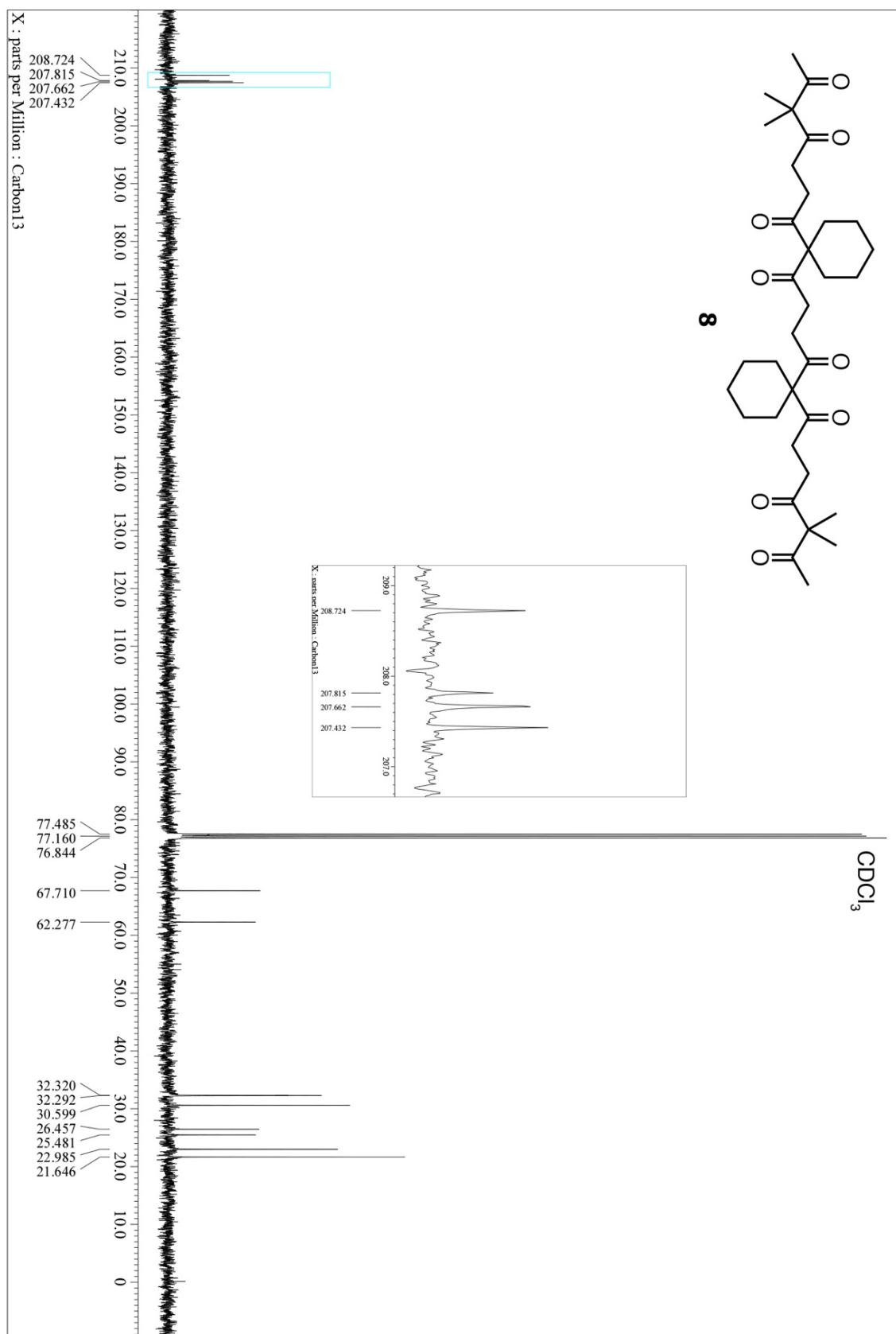


Figure S34. ^{13}C NMR spectrum of **8** in CDCl_3 at 25 °C.

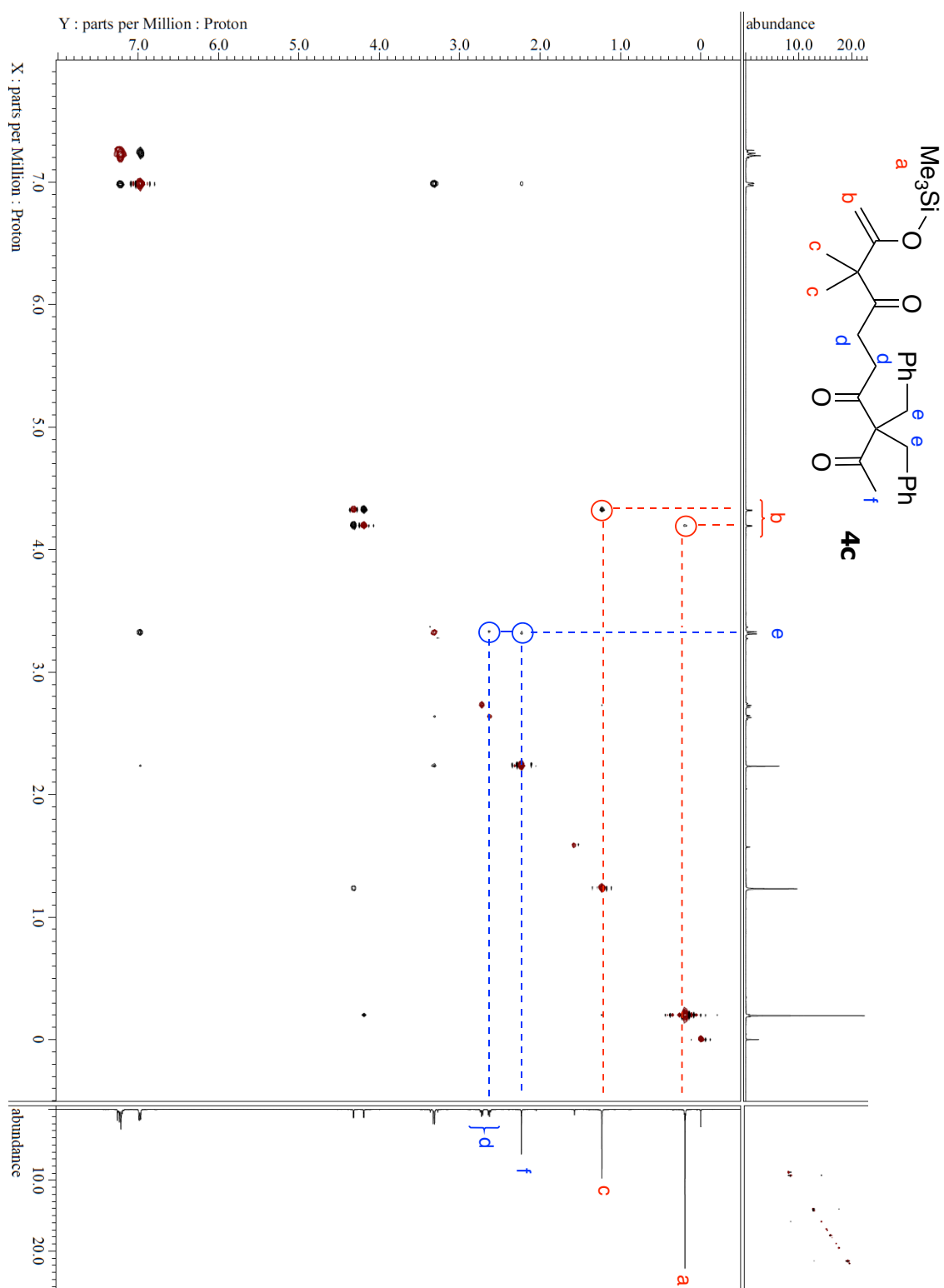


Figure S35. NOESY spectrum of **4c** in in CDCl₃ at 25 °C. The NOE correlated protons are indicated in same colour (red and blue).

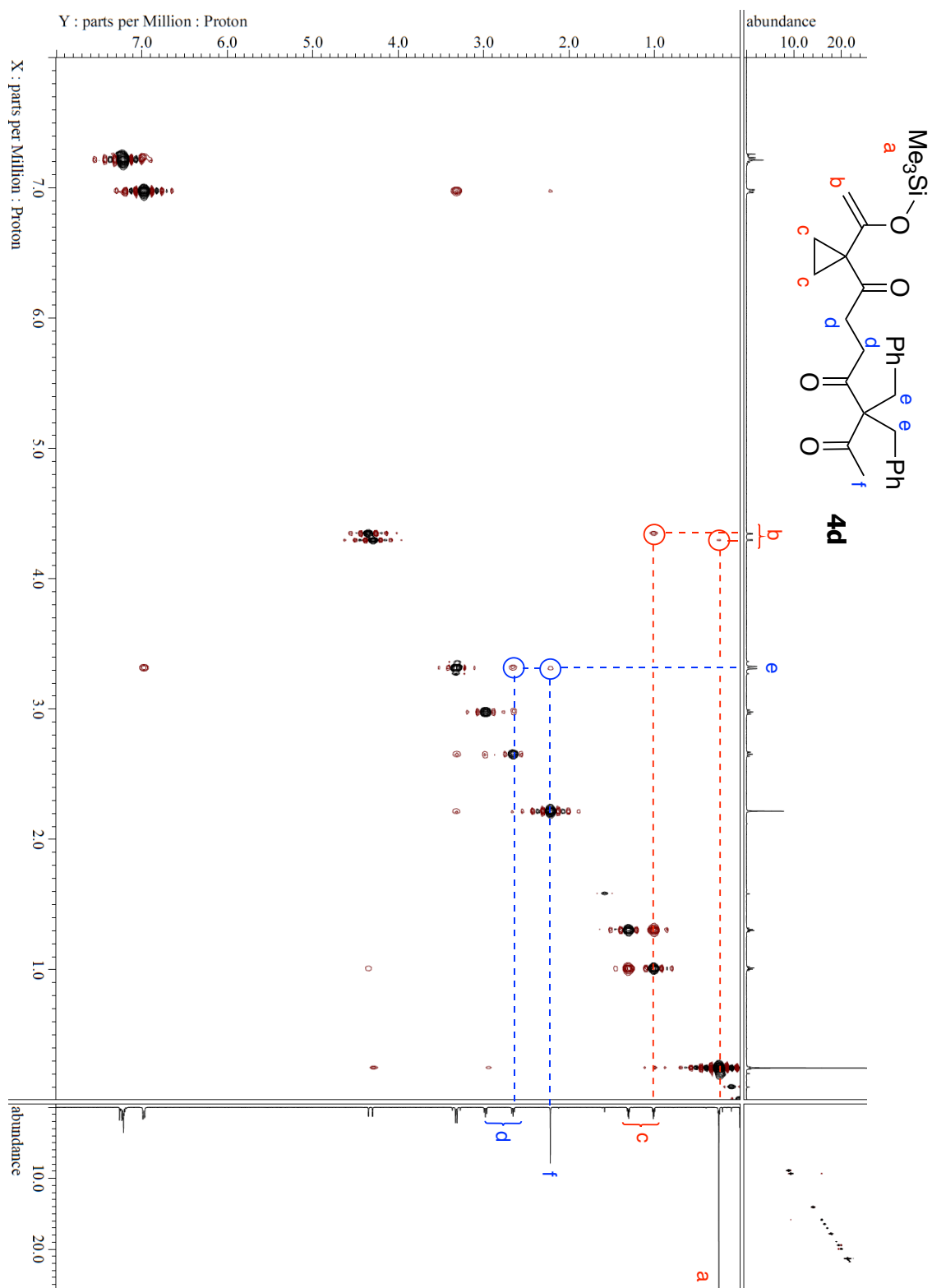


Figure S36. NOESY spectrum of **4d** in CDCl_3 at 25 °C. The NOE correlated protons are indicated in same colour (red and blue).

5. ESI-TOF MS Spectra of Octaketones

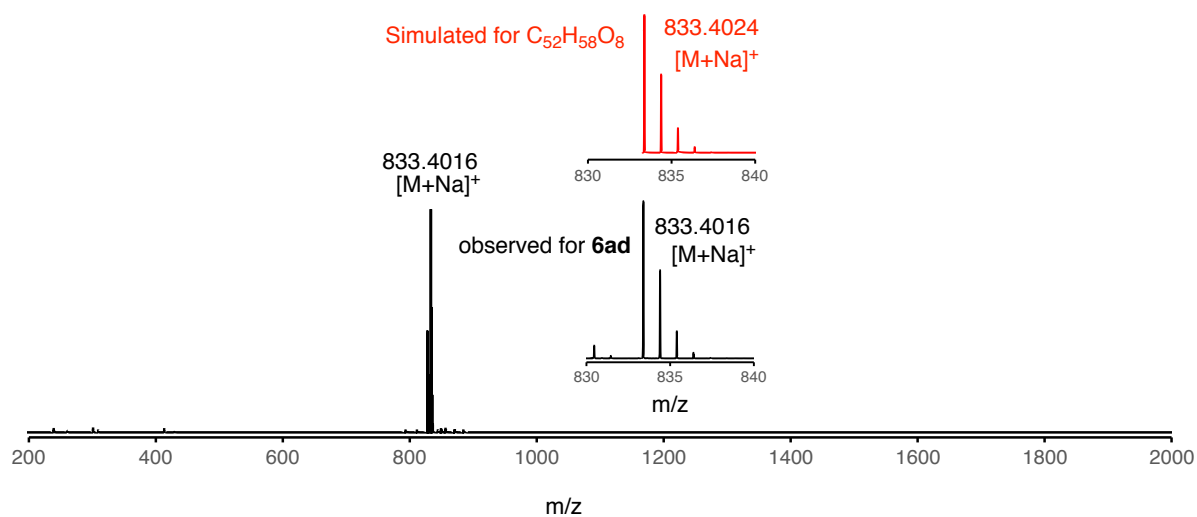


Figure S37. ESI-TOF MS spectrum of **6** with observed and simulated isotopic pattern for $[M+Na]^+$.

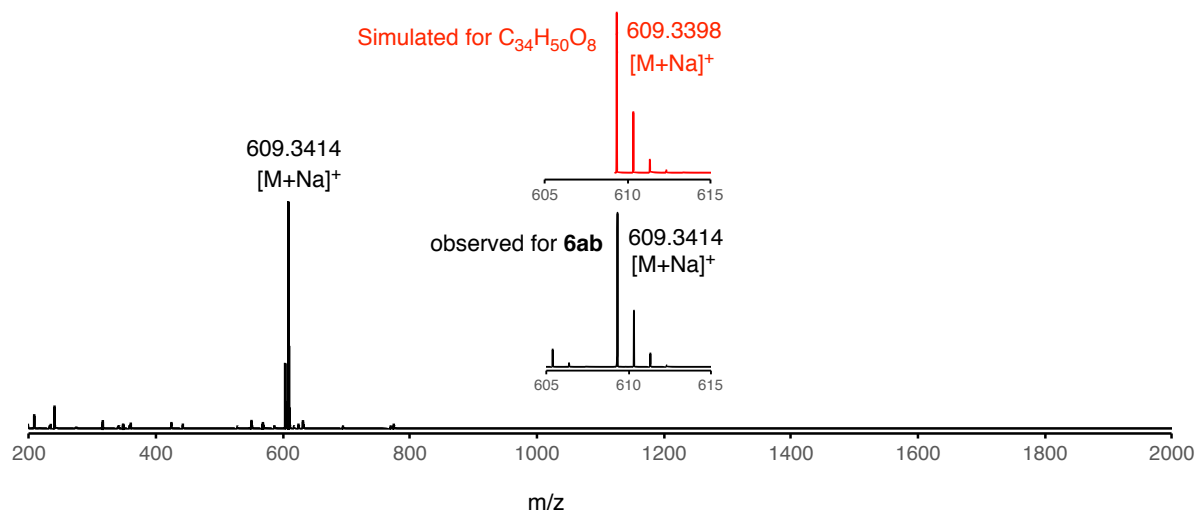


Figure S38. ESI-TOF MS spectrum of **7** with observed and simulated isotopic pattern for $[M+Na]^+$.

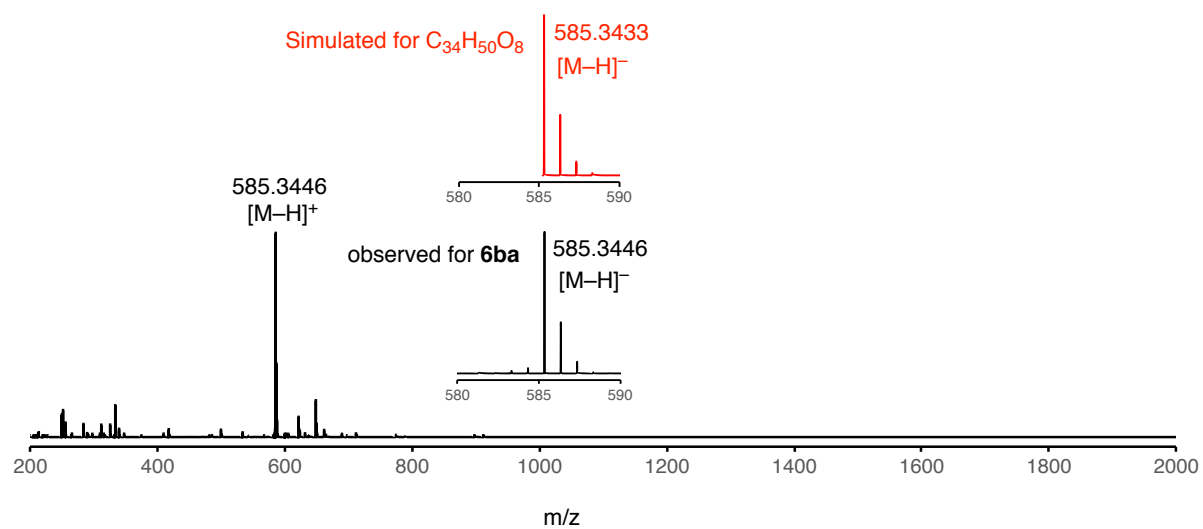


Figure S39. ESI-TOF MS spectrum of **8** with observed and simulated isotopic pattern for $[M-H]^-$.

6. References

1. K. Beck, S. Hunig, *Chem. Ber.*, 1987, **20**, 477.
2. D. S. Siegel, G. Piizzi, G. Piersanti, M. Movassaghi, *J. Org. Chem.*, 2009, **74**, 9292.
3. U. Sankar, C. Raju, R. Uma, *Curr. Chem. Lett.* 2012, **1**, 123.
4. G. M. Sheldrick, *Acta Crystallogr. Sect. A*, 2015, **71**, 3.
5. G. M. Sheldrick, *Acta Crystallogr. Sect. C*, 2015, **71**, 3.