

Supporting Information

Unified Total Synthesis of Madangamines A, C, and E

Takahiro Suto, Yuta Yanagita, Yoshihiro Nagashima, Shinsaku Takikawa, Yasuhiro Kurosu, Naoya Matsuo,
Takaaki Sato* and Noritaka Chida*

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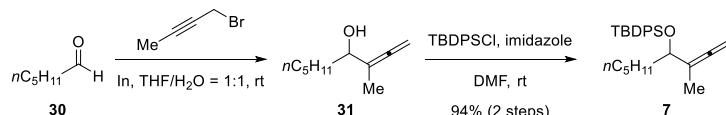
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A. Experimental Procedures

General Details. Reactions were performed in oven-dried glassware fitted with rubber septa under an argon atmosphere. Toluene and DMSO were distilled from CaH₂. DMF and MeOH were distilled from CaSO₄. Pyridine was distilled from sodium hydroxide. Hexamethylphosphoric triamide was distilled from CaO. Toluene, DMSO, DMF, MeOH, pyridine, CH₂Cl₂, MeCN and EtOH were dried over activated 3Å molecular sieves. THF (dehydrated, stabilizer free) and Et₂O (dehydrated, stabilizer free) was purchased from KANTO CHEMICAL CO., INC. Commercial reagents were used without further purification. Thin-layer chromatography was performed on Merck 60 F₂₅₄ precoated silica gel plates, which were visualized by exposure to UV (254 nm) or stained by submersion in *p*-anisaldehyde solution or ethanolic phosphomolybdic acid solution followed by heating on a hot plate. Flash column chromatography was performed on silica gel (Silica Gel 60 N; 63–210 or 40–50 mesh, KANTO CHEMICAL CO., INC.) and basic alumina (Alumina, Activated, about 200 mesh, WAKO PURE CHEMICAL INDUSTRIES, Ltd.). Preparative layer chromatography was performed on Merck PLC silica gel 60 F₂₅₄. ¹H NMR spectra were recorded at 500 MHz with JEOL ECA-500 spectrometer or 400 MHz with JEOL ECS-400 spectrometer. ¹³C NMR spectra were recorded at 125 MHz with JEOL ECA-500 spectrometers. ¹⁹F NMR spectra were recorded at 470 MHz with JEOL ECA-500 spectrometers. Chemical shifts are reported in ppm with reference to solvent signals [¹H NMR: CDCl₃ (7.26), C₆D₆ (7.16); ¹³C NMR: CDCl₃ (77.16), C₆D₆ (128.06); ¹⁹F NMR: C₆F₆ (−164.9)]. Signal patterns are indicated as br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. MPLC was performed on Yamazen, YFLC AI-580. Infrared spectra were recorded using a BRUKER ALPHA FT-IR spectrometer. Mass spectra were measured with Waters, LCT Premier XE (ESI-TOF). Optical rotations were measured with a JASCO P-2100 polarimeter. Melting points were measured with a Yanaco MODEL MP-S3.

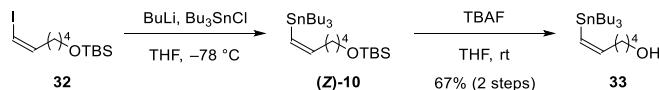
A-1. Stereodivergent Synthesis of Skipped Dienes



Allene (7): 1-Bromobut-2-yne (1.5 mL, 17 mmol) was added to a mixture of indium (3.94 g, 34.3 mmol), hexanal **30** (2.9 mL, 24 mmol) and THF/H₂O (1:1, 40 mL) at room temperature.¹ The mixture was stirred for 12 h at room temperature, and extracted with EtOAc/hexane (1:4, 2x 10 mL). The combined organic extracts were dried over Na₂SO₄, and concentrated to give allenyl alcohol **31**,² which was used in the next step without further purification.

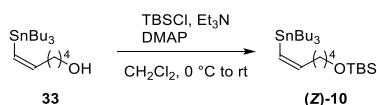
t-Butyldiphenylsilyl chloride (4.9 mL, 19 mmol) was added to a solution of the above allenyl alcohol **31**, imidazole (1.28 g, 18.8 mmol) and DMF (17 mL) at room temperature. The resulting white suspension was stirred at the same temperature for 18 h, quenched with H₂O (10 mL), and extracted with hexane (2x 10 mL). The combined organic extracts were dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane) to afford allene **7** (6.30 g, 94% for 2 steps): a colorless oil; IR (film) 3071, 2956, 2932, 2858, 1960, 1463, 1428, 1111, 1060, 701, 505 cm^{−1}; ¹H NMR (500 MHz, CDCl₃) δ 7.74–7.64 (m, 4H), 7.46–7.32 (m, 6H), 4.42 (dqd, *J* = 9.5, 3.2, 0.9 Hz, 1H), 4.38 (dqd, *J* = 9.5, 3.2, 0.9 Hz,

1H) 4.19 (tdd, $J = 6.9, 0.9, 0.9$ Hz, 1H), 1.64 (dd, $J = 3.2, 3.2$ Hz, 3H), 1.58–1.49 (m, 2H), 1.23–1.03 (m, 4H), 1.07 (s, 9H), 0.81 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 206.6 (C), 136.1 (CH), 136.0 (CH), 134.7 (C), 134.3 (C), 129.6 (CH), 129.5 (CH), 127.5 (CH), 127.4 (CH), 100.0 (C), 75.3 (CH), 73.9 (CH₂), 35.7 (CH₂), 31.6 (CH₂), 27.2 (CH₃), 25.0 (CH₂), 22.6 (CH₂), 19.6 (C), 14.1 (CH₃), 12.6 (CH₃); HRMS (ESI), calcd for $\text{C}_{26}\text{H}_{37}\text{OSi}^+$ ($\text{M}+\text{H}$)⁺ 393.2614, found 393.2601.



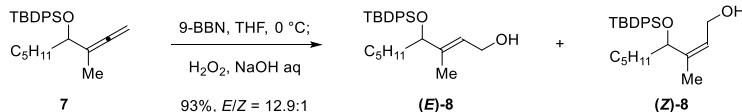
Alcohol (33): Butyllithium (1.6 M in pentane, 2.8 mL, 4.6 mmol) was added dropwise over 5 min to a solution of vinyl iodide **32**³ (1.43 g, 4.19 mmol) and THF (21 mL) at -78°C . After maintaining for 15 min at -78°C , tributyltin chloride (1.3 mL, 4.6 mmol) was added to the solution. The resulting solution was maintained for 10 min at -78°C , quenched with saturated aqueous NH_4Cl (10 mL) at -78°C , and extracted with hexane (2x 10 mL). The combined organic extracts were washed with brine (10 mL) and dried over Na_2SO_4 . The solution was concentrated to give vinylstannane **(Z)-10**,⁴ which was unstable on silica-gel and immediately used in the next reaction without further purification.

Tetrabutylammonium fluoride (1.0 M in THF, 8.4 mL, 8.4 mmol) was added to a solution of above vinylstannane **(Z)-10** and THF (21 mL) at room temperature. This solution was maintained for 6 h and concentrated. The residue was filtrated through a pad of basic alumina to afford alcohol **33** (1.10 g, 67% for 2 steps): a colorless oil; IR (film) 3330, 2957, 2926, 2871, 2855, 1598, 1460, 1376, 1340, 1070, 874, 865, 692, 668, 596, 504 cm⁻¹; ^1H NMR (500 MHz, CDCl_3) δ 6.51 (dt, $J = 12.6, 7.2$ Hz, J (^{117}Sn - and ^{119}Sn -H) = 143.7, 137.2 Hz, 1H), 5.80 (dt, $J = 12.6, 1.2$ Hz, J (^{117}Sn - and ^{119}Sn -H) = 84.2, 59.6 Hz, 1H), 3.66 (td, $J = 6.3, 5.4$ Hz, 2H), 2.06 (tdd, $J = 7.2, 7.2, 1.2$ Hz, 2H), 1.63–1.56 (m, 2H), 1.55–1.41 (m, 8H), 1.31 (qt, $J = 7.5, 7.5$ Hz, 6H), 1.21 (t, $J = 5.4$ Hz, 1H), 1.04–0.74 (m, 15H); ^{13}C NMR (125 MHz, CDCl_3) δ 148.8 (CH), 128.5 (CH), 63.1 (CH₂), 36.9 (CH₂), 32.6 (CH₂), 29.3 (CH₂), 27.5 (CH₂), 26.2 (CH₂), 13.9 (CH₃), 10.4 (CH₂); HRMS (ESI), calcd for $\text{C}_{18}\text{H}_{38}\text{OSnK}^+$ ($\text{M}+\text{K}$)⁺ 429.1582, found 429.1569.

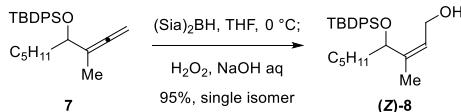


Vinylstannane ((Z)-10): *tert*-Butyldimethylsilyl chloride (253 mg, 1.68 mmol) and DMAP (10.8 mg, 88.5 μmol) were added to a solution of alcohol **33** (689 mg, 1.77 mmol), Et_3N (540 μL , 3.9 mmol) and CH_2Cl_2 (8.9 mL) at 0°C . The solution was allowed to warm to room temperature, maintained for 12 h and quenched with H_2O (4 mL). The resulting mixture was extracted with CH_2CH_2 (2x 2mL). The combined organic extracts were dried over Na_2SO_4 , and concentrated. The residue was filtrated through a pad of basic alumina to afford vinylstannane **(Z)-10** (575 mg, 65%): a colorless oil; IR (film) 2957, 2928, 2857, 1598, 1254, 1104, 836, 775 cm⁻¹; ^1H NMR (500 MHz, CDCl_3) δ 6.50 (dt, $J = 12.3, 7.2$ Hz, J (^{117}Sn - and ^{119}Sn -H) = 144.3, 138.0 Hz, 1H), 5.80 (dt, $J = 12.3, 0.9$ Hz, J (^{117}Sn - and ^{119}Sn -H) = 85.1, 59.9 Hz, 1H), 3.61 (t, $J = 6.6$ Hz, 2H), 2.03 (tdd, $J = 7.2, 7.2, 0.9$ Hz, 2H), 1.58–1.37 (m, 10H), 1.30 (tq, $J = 7.2, 7.2$ Hz, 6H), 0.92–0.85 (m, 6H), 0.89 (s, 9H), 0.89

(t, $J = 7.2$ Hz, 9H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 149.2 (CH), 128.1 (CH), 63.4 (CH_2), 37.1 (CH_2), 32.8 (CH_2), 29.4 (CH_2), 27.5 (CH_2), 26.4 (CH_2), 26.1 (CH_3), 18.5 (C), 13.9 (CH_3), 10.4 (CH_2), -5.1 (CH_3); HRMS (ESI), calcd for $\text{C}_{24}\text{H}_{53}\text{OSiSn}^+ (\text{M}+\text{H})^+$ 505.2888, found 505.2882.



Allylic alcohol ((E)-8): 9-Borabicyclo[3.3.1]nonane (9-BBN, 0.5 M in THF, 460 μL , 230 μmol) was added to a solution of allene **7** (60.1 mg, 153 μmol) and THF (1.5 mL) at room temperature. The solution was maintained at room temperature for 1 h. The reaction was then quenched with 3 M NaOH aq (1 mL) and 30% H_2O_2 aq (1 mL) at 0 °C. The resulting mixture was stirred for 1 h at the same temperature, and extracted with EtOAc (2x 1 mL). The combined organic extracts were washed with brine (1 mL), dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9) to afford a mixture of allylic alcohol **(E)-8** and **(Z)-8** (58.3 mg, 93%, $E/Z = 12.9:1$). For analytical samples, two isomers were separated by HPLC (PEGASIL Silica 120-5, 250×20 mm, UV 254 nm, EtOAc/hexane 1:4, 10 mL/min, **(E)-8**: $T_{\text{R}} = 13.3$ min, **(Z)-8**: $T_{\text{R}} = 11.5$ min). **(E)-8**: a colorless oil; IR (film) 3343, 2956, 2931, 2858, 1465, 1428, 1111, 1063, 999, 702, 504 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.68–7.64 (m, 4H), 7.46–7.31 (m, 6H), 5.17 (t, $J = 6.6$ Hz, 1H), 4.05 (t, $J = 6.6$ Hz, 1H), 4.02–3.89 (m, 2H), 1.62–1.44 (m, 2H), 1.58 (s, 3H), 1.24–1.05 (m, 6H), 1.07 (s, 9H), 0.83 (t, $J = 7.2$ Hz, 3H), 0.67 (brs, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 140.2 (C), 136.2 (CH), 136.1 (CH), 134.7 (C), 134.5 (C), 129.65 (CH), 129.60 (CH), 127.6 (CH), 127.4 (CH), 125.2 (CH), 78.9 (CH), 59.0 (CH₂), 35.7 (CH₂), 31.8 (CH₂), 27.2 (CH₃), 25.0 (CH₂), 22.7 (CH₂), 19.5 (C), 14.1 (CH₃), 11.4 (CH₃); HRMS (ESI), calcd for $\text{C}_{26}\text{H}_{39}\text{O}_2\text{Si}^+ (\text{M}+\text{H})^+$ 411.2719, found 411.2705.

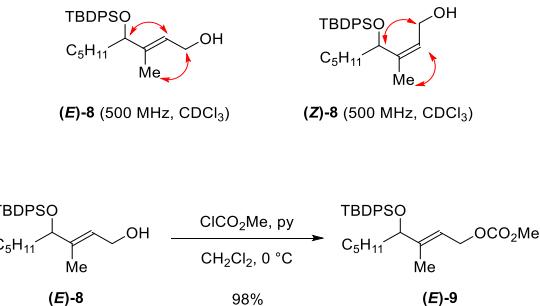


Allylic alcohol ((Z)-8): 2-Methyl-2-butene (600 μL , 5.6 mmol) was added to borane THF complex (0.92 M in THF, 3.0 mL, 2.8 mmol) at 0 °C. The solution was maintained for 1 h at the same temperature to give disiamylborane (calculated as 0.77 M in THF).

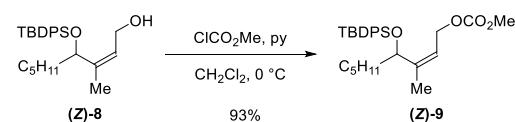
Disiamylborane (0.77 M, 300 μL , 230 μmol) was added to a solution of allene **7** (59.3 mg, 151 μmol) and THF (1.5 mL) at 0 °C. The solution was maintained for 5 min at 0 °C, and quenched with 3 M NaOH aq (1 mL) and 30% H_2O_2 aq (1 mL) at 0 °C. The resulting mixture was stirred for 1 h at the same temperature, and extracted with EtOAc (2x 1 mL). The combined organic extracts were washed with brine (1 mL), dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9) to afford allylic alcohol **(Z)-8** (59.0 mg, 95%, single isomer): **(Z)-8**: a colorless oil; IR (film) 3343, 2956, 2931, 2858, 1463, 1427, 1111, 1061, 1007, 702, 506 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.72–7.67 (m, 2H), 7.67–7.64 (m, 2H), 7.48–7.33 (m, 6H), 5.27–5.20 (m, 1H), 4.43 (dd, $J = 8.3, 5.7$ Hz, 1H), 3.72 (ddd, $J = 12.6, 8.4, 3.5$ Hz, 1H), 3.61 (ddd, $J = 12.6, 7.5, 6.1$ Hz, 1H), 1.77 (d, $J = 0.9$ Hz, 3H), 1.63–1.48 (m, 2H), 1.21–1.04

(m, 4H), 1.06 (s, 9H), 1.01–0.92 (m, 2H), 0.80 (t, J = 7.2 Hz, 3H), 0.55 (dd, J = 7.5, 4.0 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 140.0 (C), 136.15 (CH), 136.08 (CH), 134.33 (C), 134.25 (C), 129.83 (CH), 129.79 (CH), 127.7 (CH), 127.5 (CH), 125.7 (CH), 71.1 (CH), 58.4 (CH₂), 35.9 (CH₂), 31.8 (CH₂), 27.1 (CH₃), 25.1 (CH₂), 22.6 (CH₂), 19.5 (C), 17.9 (CH₃), 14.1 (CH₃); HRMS (ESI), calcd for $\text{C}_{26}\text{H}_{38}\text{O}_2\text{SiNa}^+$ ($M+\text{Na}$)⁺ 433.2539, found 433.2538.

NOESY experiments for (*E*)-8 and (*Z*)-8

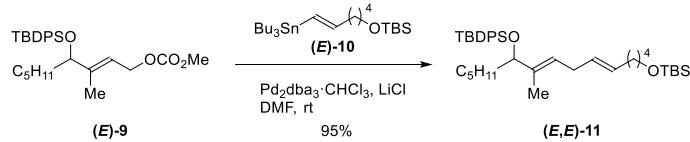


Allylic carbonate ((E)-9): Methyl chloroformate (260 μL , 3.4 mmol) was added to a solution of a mixture of allylic alcohols (*E*)-8 and (*Z*)-8 (933 mg, *E/Z* = 12.9:1, 2.27 mmol), pyridine (280 μL , 3.4 mmol) and CH_2Cl_2 (22 mL) at 0 °C. This solution was maintained for 1 h at 0 °C, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:19) to give a mixture of allylic carbonates (*E*)-9 and (*Z*)-9 (1.04 g, 98%, *E/Z* = 12.2:1). For analytical samples, two isomers were separated by HPLC (PEGASIL Silica 120-5, 250×20 mm, UV 254 nm, EtOAc/hexane 1:19, 10 mL/min, (*E*)-9: T_R = 13.3 min, (*Z*)-9: T_R = 12.8 min). (*E*)-9: a colorless oil; IR (film) 3071, 2931, 2858, 1749, 1589, 1262, 1111, 1064, 702 cm⁻¹; ^1H NMR (500 MHz, CDCl_3) δ 7.68–7.63 (m, 2H), 7.62–7.57 (m, 2H), 7.44–7.31 (m, 6H), 5.30–5.25 (m, 1H), 4.57 (dd, J = 12.3, 7.2 Hz, 1H), 4.52 (dd, J = 12.3, 6.9 Hz, 1H), 4.02 (t, J = 6.3 Hz, 1H), 3.77 (s, 3H), 1.65–1.63 (m, 3H), 1.51–1.40 (m, 2H), 1.21–1.12 (m, 2H), 1.12–0.98 (m, 4H), 1.05 (s, 9H), 0.80 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 155.9 (C), 143.5 (C), 136.1 (CH), 136.0 (CH), 134.6 (C), 134.1 (C), 129.7 (CH), 129.6 (CH), 127.6 (CH), 127.5 (CH), 119.4 (CH), 78.4 (CH), 64.4 (CH₂), 54.8 (CH₃), 35.5 (CH₂), 31.7 (CH₂), 27.2 (CH₃), 24.7 (CH₂), 22.6 (CH₂), 19.5 (C), 14.1 (CH₃), 11.8 (CH₃); HRMS (ESI), calcd for $\text{C}_{28}\text{H}_{40}\text{O}_4\text{SiK}^+$ ($M+\text{K}$)⁺ 507.2333, found 507.2320.



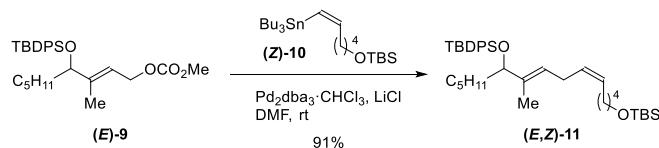
Allylic carbonate ((*Z*)-9): Methyl chloroformate (420 μL , 5.3 mmol) was added to a solution of allylic alcohol (*Z*)-8 (1.46 g, 3.55 mmol), pyridine (430 μL , 5.3 mmol) and CH_2Cl_2 (35 mL) at 0 °C. This solution was maintained for 1 h at 0 °C, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:19) to give allylic carbonate (*Z*)-9 (1.54 g, 93%): a colorless oil; IR (film) 3071, 2956, 2932, 2858, 1750, 1589, 1265, 1111, 702 cm⁻¹; ^1H NMR (500 MHz, CDCl_3) δ 87.69–7.64 (m, 2H), 7.63–7.58 (m, 2H), 7.45–7.32 (m, 6H), 5.29–5.24 (m, 1H), 4.40 (dd, J = 7.8, 6.3 Hz, 1H), 4.24 (ddq, J = 12.1, 6.9, 0.9 Hz, 1H), 4.20 (dd, J = 12.1, 6.9 Hz, 1H), 3.73 (s, 3H), 1.78 (d, J = 0.9 Hz, 3H), 1.57–1.44 (m, 2H),

1.20–1.11 (m, 2H), 1.11–0.90 (m, 4H), 1.05 (s, 9H), 0.79 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 155.8 (C), 143.5 (C), 136.0 (CH), 134.4 (C), 133.9 (C), 129.78 (CH), 129.75 (CH), 128.5 (CH), 127.7 (CH), 127.6 (CH), 119.8 (CH), 71.4 (CH), 63.7 (CH₂), 54.7 (CH₃), 36.0 (CH₂), 31.8 (CH₂), 27.1 (CH₃), 24.9 (CH₂), 22.6 (CH₂), 19.5 (C), 18.2 (CH₃), 14.1 (CH₃); HRMS (ESI), calcd for $\text{C}_{28}\text{H}_{40}\text{O}_4\text{SiNa}^+$ ($\text{M}+\text{Na}$)⁺ 491.2594, found 491.2611.



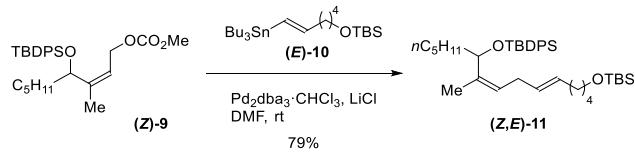
[General Procedure A]

Skipped diene (E,E)-11: In a glove box, a solution of allylic carbonate **(E)-9** (19.9 mg, E/Z = 12.2:1, 42.5 μmol), vinylstannane **(E)-10**⁵ (31.8 mg, 63.1 mmol, 1.5 equiv.) and DMF (4 mL, 10 mM) was added to a mixture of LiCl (18.0 mg, 425 μmol , 10 equiv.) and $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (2.2 mg, 2.1 μmol , 5 mol%) at room temperature. After stirring at room temperature for 12 h, the mixture was quenched with H_2O (4 mL) at 0 °C, and extracted with hexane (3x 2 mL). The combined organic extracts were washed with dried over Na_2SO_4 and concentrated. The residue was purified by preparative thin-layer chromatography (EtOAc/hexane 1:35) to afford an inseparable mixture of skipped dienes **(E,E)-11** (24.5 mg, 95%, $(E,E):(Z,E)$ = 12.0:1). For an analytical sample, **(E,E)-11** was isolated by HPLC (PEGASIL Silica 120-5, 250×20 mm, toluene/hexane 1:9, 10 mL/min, T_R = 20 min): a colorless oil; IR (film) 3071, 2956, 2931, 2858, 1255, 1110, 836, 701 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.69–7.64 (m, 2H), 7.64–7.60 (m, 2H), 7.43–7.29 (m, 6H), 5.33 (dtt, J = 15.2, 6.6, 1.4 Hz, 1H), 5.26 (dtt, J = 15.2, 5.4, 1.2 Hz, 1H), 5.02 (t, J = 7.2 Hz, 1H), 3.98 (t, J = 6.6 Hz, 1H), 3.59 (t, J = 6.6 Hz, 2H), 2.57 (dd, J = 7.2, 6.0 Hz, 2H), 1.97 (td, J = 7.5, 6.6 Hz, 2H), 1.57–1.55 (m, 3H), 1.54–1.42 (m, 4H), 1.40–1.32 (m, 2H), 1.20–1.12 (m, 2H), 1.12–0.97 (m, 4H), 1.04 (s, 9H), 0.89 (s, 9H), 0.79 (t, J = 7.2 Hz, 3H), 0.04 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 136.9 (C), 136.2 (CH), 136.1 (CH), 135.0 (C), 134.6 (C), 130.4 (CH), 129.5 (CH), 129.4 (CH), 128.5 (CH), 127.5 (CH), 127.4 (CH), 124.7 (CH), 79.5 (CH), 63.3 (CH₂), 35.7 (CH₂), 32.51 (CH₂), 32.48 (CH₂), 31.8 (CH₂), 30.7 (CH₂), 27.2 (CH₃), 26.1 (CH₃), 25.9 (CH₂), 25.1 (CH₂), 22.7 (CH₂), 19.5 (C), 18.5 (C), 14.1 (CH₃), 11.0 (CH₃), -5.1 (CH₃); HRMS (ESI), calcd for $\text{C}_{38}\text{H}_{63}\text{O}_2\text{Si}_2^+$ ($\text{M}+\text{H}$)⁺ 607.4367, found 607.4376.

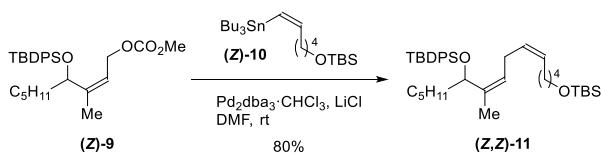


Skipped diene (E,Z)-11: Following the general procedure A, allylic carbonate **(E)-9** (19.6 mg, E/Z = 12.2:1, 41.8 μmol) was converted to skipped diene **(E,Z)-11** (23.0 mg, 91%, $(E,Z):(Z,Z)$ = 12.4:1). For an analytical sample, **(E,Z)-11** was isolated by HPLC (PEGASIL Silica 120-5, 250×20 mm, toluene/hexane 1:9, 10 mL/min, T_R = 20 min): a colorless oil; IR (film) 3072, 2931, 2858, 1255, 1110, 836, 701 cm^{-1} ; ^1H NMR (500 MHz,

CDCl_3) δ 7.70–7.63 (m, 2H), 7.63–7.59 (m, 2H), 7.43–7.29 (m, 6H), 5.33 (dtt, $J = 10.6, 7.2, 1.8$ Hz, 1H), 5.21 (dtt, $J = 10.6, 7.2, 1.4$ Hz, 1H), 4.98 (td, $J = 7.2, 1.2$ Hz, 1H), 3.96 (t, $J = 6.7$ Hz, 2H), 3.61 (t, $J = 6.6$ Hz, 2H), 2.68–2.56 (m, 2H), 2.03 (tdd, $J = 7.5, 7.5, 1.4$ Hz, 2H), 1.59–1.57 (m, 3H), 1.54–1.49 (m, 2H), 1.49–1.43 (m, 2H), 1.42–1.34 (m, 2H), 1.21–1.12 (m, 2H), 1.12–0.94 (m, 4H), 1.04 (s, 9H), 0.89 (s, 9H), 0.79 (t, $J = 7.2$ Hz, 3H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 136.6 (C), 136.2 (CH), 136.1 (CH), 135.0 (C), 134.6 (C), 129.8 (CH), 129.5 (CH), 129.4 (CH), 128.2 (CH), 127.5 (CH), 127.4 (CH), 125.0 (CH), 79.4 (CH), 63.3 (CH₂), 35.7 (CH₂), 32.6 (CH₂), 31.8 (CH₂), 27.2 (CH₃), 27.1 (CH₂), 26.13 (CH₃), 26.07 (CH₂), 25.9 (CH₂), 25.1 (CH₂), 22.6 (CH₂), 19.5 (C), 18.5 (C), 14.1 (CH₃), 11.1 (CH₃), −5.1 (CH₃); HRMS (ESI), calcd for $\text{C}_{38}\text{H}_{63}\text{O}_2\text{Si}_2^+$ ($\text{M}+\text{H}$)⁺ 607.4367, found 607.4337.



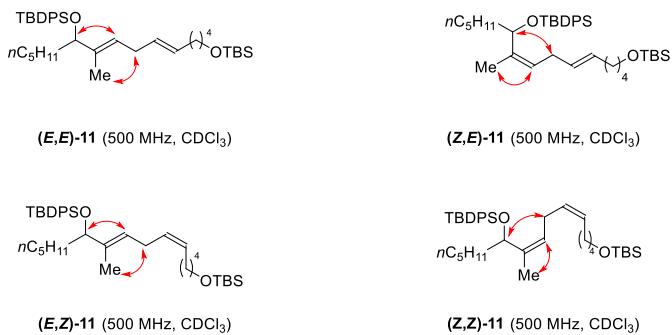
Skipped diene ((Z,E)-11): Following the general procedure A, allylic carbonate **(Z)-9** (22.6 mg, 48.2 μmol) was converted to skipped diene **(Z,E)-11** (23.1 mg, 79%): a colorless oil; IR (film) 3071, 2930, 2857, 1255, 1109, 836, 702 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.70–7.66 (m, 2H), 7.64–7.60 (m, 2H), 7.44–7.30 (m, 6H), 5.21 (dt, $J = 15.2, 6.6$ Hz, 1H), 5.14 (dt, $J = 15.2, 6.3$ Hz, 1H), 5.05 (td, $J = 7.5, 1.2$ Hz, 1H), 4.49 (t, $J = 7.0$ Hz, 1H), 3.58 (t, $J = 6.6$ Hz, 2H), 2.38–2.26 (m, 2H), 1.91 (dt, $J = 7.5, 6.6$ Hz, 2H), 1.75 (d, $J = 1.2$ Hz, 3H), 1.52–1.43 (m, 4H), 1.37–1.28 (m, 2H), 1.18–1.09 (m, 2H), 1.08–1.01 (m, 2H), 1.04 (s, 9H), 1.01–0.93 (m, 2H), 0.89 (s, 9H), 0.78 (t, $J = 7.2$ Hz, 3H), 0.04 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 137.0 (C), 136.1 (CH), 136.0 (CH), 135.0 (C), 134.4 (C), 130.5 (CH), 129.6 (CH), 129.5 (CH), 128.9 (CH), 127.6 (CH), 127.5 (CH), 124.9 (CH), 71.1 (CH), 63.3 (CH₂), 36.0 (CH₂), 32.5 (CH₂), 32.4 (CH₂), 31.9 (CH₂), 30.7 (CH₂), 27.2 (CH₃), 26.1 (CH₃), 25.8 (CH₂), 25.1 (CH₂), 22.6 (CH₂), 19.5 (C), 18.5 (C), 17.9 (CH₃), 14.1 (CH₃), −5.1 (CH₃); HRMS (ESI), calcd for $\text{C}_{38}\text{H}_{63}\text{O}_2\text{Si}_2^+$ ($\text{M}+\text{H}$)⁺ 607.4367, found 607.4343.



Skipped diene ((Z,Z)-11): Following the general procedure A, allylic carbonate **(Z)-9** (19.7 mg, 42.0 μmol) was converted to skipped diene **(Z,Z)-11** (20.4 mg, 80%): a colorless oil; IR (film) 3072, 2931, 2858, 1255, 1109, 836, 701 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.71–7.67 (m, 2H), 7.66–7.60 (m, 2H), 7.44–7.29 (m, 6H), 5.26 (dtt, $J = 10.6, 7.5, 1.7$ Hz, 1H), 5.09 (dtt, $J = 10.6, 7.2, 1.4$ Hz, 1H), 5.01 (td, $J = 7.5, 1.5$ Hz, 1H), 4.50 (dd, $J = 7.5, 6.6$ Hz, 1H), 3.59 (t, $J = 6.6$ Hz, 2H), 2.39 (dddd, $J = 16.1, 7.5, 7.2, 1.7$ Hz, 1H), 2.31 (dddd, $J = 16.1, 7.5, 7.2, 1.7$ Hz, 1H), 1.87 (tdd, $J = 7.5, 7.5, 1.4$ Hz, 2H), 1.74 (d, $J = 1.5$ Hz, 3H), 1.53–1.43 (m, 4H), 1.35–1.28 (m, 2H), 1.20–1.11 (m, 2H), 1.11–1.03 (m, 2H), 1.05 (s, 9H), 1.03–0.95 (m, 2H), 0.90 (s, 9H), 0.79 (t, $J = 7.2$ Hz, 3H), 0.05 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 137.1 (C), 136.1 (CH), 136.0 (CH), 134.9 (C),

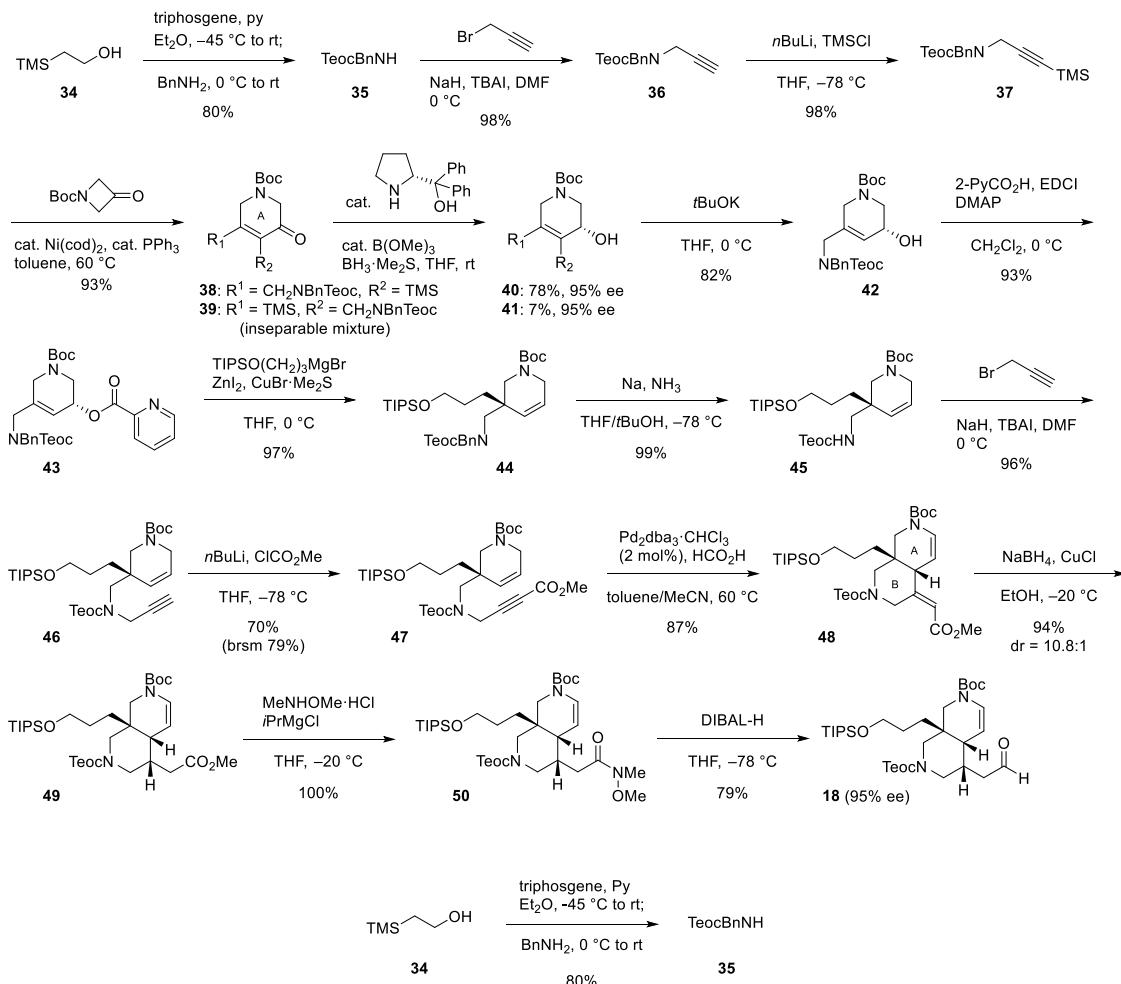
134.4 (C), 129.7 (CH), 129.57 (CH), 129.56 (CH), 128.4 (CH), 127.6 (CH), 127.5 (CH), 125.0 (CH), 71.2 (CH), 63.3 (CH₂), 36.0 (CH₂), 32.6 (CH₂), 31.9 (CH₂), 27.2 (CH₃), 27.0 (CH₂), 26.1 (CH₃), 26.0 (CH₂), 25.7 (CH₂), 25.1 (CH₂), 22.6 (CH₂), 19.5 (C), 18.5 (C), 17.9 (CH₃), 14.1 (CH₃), -5.1 (CH₃); HRMS (ESI), calcd for C₃₈H₆₃O₂Si₂⁺ (M+H)⁺ 607.4367, found 607.4366.

NOESY experiments for skipped deines (*E,E*)-11, (*Z,E*)-11, (*E,Z*)-11 and (*Z,Z*)-11



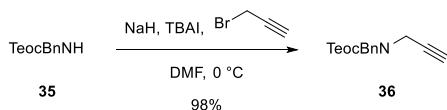
A-2. Enantioselective Synthetic Route to Aldehyde 18

Previously, we reported the racemic synthesis of aldehyde **18** via *N*-Boc-piperidine **47** (*Org. Lett.* **2015**, *17*, 1946). In this communication, we have developed a renewed enantioselective route to aldehyde **18** (95% ee), which was merged to the previous racemic route.

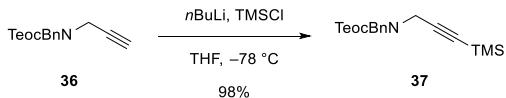


Carbamate (35): 2-Trimethylsilylethanol **34** (7.3 mL, 51 mmol) and pyridine (3.3 mL, 41 mmol) were added to a solution of triphosgene (5.02 g, 16.9 mmol) and Et_2O (250 mL) at -45°C . The reaction mixture was stirred at this temperature for 1 h, then allowed to warm to room temperature, stirred for 3 h, and recooled to 0°C . Benzylamine (11 mL, 100 mmol) was then added dropwise to the mixture at 0°C . The resulting mixture was stirred at 0°C for 30 min, allowed to warm to room temperature, and stirred for 16 h. The resulting mixture was quenched with water (100 mL), and extracted with EtOAc (2x 50 mL). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9) to give carbamate **35** (10.1 g, 80%): a colorless oil; IR (film) 3332, 2953, 1698, 1527, 1250, 1179, 1135, 1060, 1043, 969, 945, 860, 837, 752, 697 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.26 (m, 5H), 5.05–4.65 (m, 1H), 4.37 (d, $J = 5.7$ Hz, 2H), 4.19 (t, $J = 8.6$ Hz, 2H), 0.99 (t, $J = 8.6$ Hz, 2H), 0.04 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 156.9 (C), 138.8 (C), 128.7 (CH), 127.6 (CH), 127.5 (CH), 63.3 (CH₂), 45.1 (CH₂), 17.9 (CH₂), -1.4 (CH₃); HRMS (ESI), calcd for $\text{C}_{13}\text{H}_{21}\text{NO}_2\text{SiK}^+$

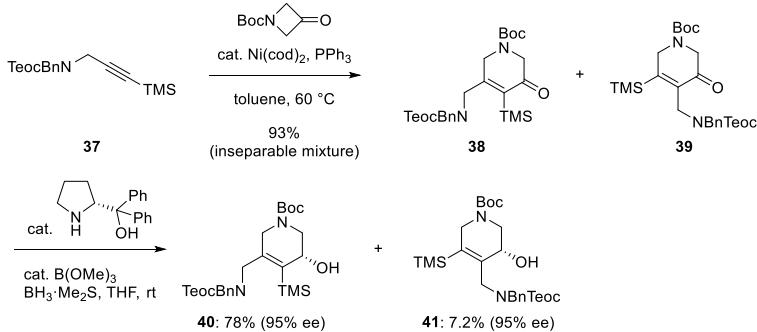
$(M+K)^+$ 290.0979, found 290.0987.



Alkyne (36): Sodium hydride (63% in oil, 874 mg, 23.0 mmol) was added to a solution of carbamate **35** (3.84 g, 15.3 mmol), propargyl bromide (1.4 mL, 1.8 mmol), tetrabutylammonium iodide (565 mg, 1.53 mmol) and DMF (77 mL) at 0 °C. The solution was maintained at this temperature for 1 h, quenched with saturated aqueous NH₄Cl (50 mL), and extracted with hexane (3x 50 mL). The combined organic extracts were washed with brine (30 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:12) to give alkyne **36** (4.35 g, 98%): a colorless oil; IR (film) 2954, 1701, 1496, 1455, 1236, 1177, 1114, 945, 839, 699 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 1:1 mixture of rotamers) δ 7.35–7.26 (m, 5H), 4.60 (s, 2H), 4.29–4.23 (m, 2H), 4.05 (brs, 1H), 3.96 (brs, 1H), 2.22 (t, *J* = 2.6 Hz, 1H), 1.05 (brs, 2H), 0.04 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 156.3 (C), 156.3 (C), 137.1 (C), 137.1 (C), 128.7 (CH), 128.7 (CH), 128.4 (CH), 127.8 (CH), 127.6 (CH), 127.6 (CH), 79.1 (CH), 79.1 (CH), 72.1 (C), 72.0 (C), 64.4 (CH₂), 64.4 (CH₂), 49.3 (CH₂), 49.0 (CH₂), 35.4 (CH₂), 35.1 (CH₂), 17.9 (CH₂), 17.9 (CH₂), -1.4 (CH₃), -1.4 (CH₃); HRMS (ESI), calcd for C₁₆H₂₄NO₂Si⁺ (M+H)⁺ 290.1576, found 290.1571.



TMS alkyne (37): *n*-Butyllithium (1.63 M in hexane, 2.6 mL, 4.2 mmol) was added to a solution of alkyne **36** (1.17 g, 4.04 mmol) and THF (20 mL) at -78 °C. After maintaining for 10 min, chlorotrimethylsilane (620 μL, 4.9 mmol) was added to the solution at the same temperature. The mixture was maintained at -78 °C for 30 min, quenched with saturated aqueous NH₄Cl (5 mL). The resulting mixture was extracted with hexane (2x 10 mL). The combined organic extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:19) to give TMS alkyne **37** (1.43 g, 98%): a colorless oil; IR (film) 2956, 2178, 1704, 1455, 1415, 1250, 1235, 1178, 1114, 1012, 843, 762, 699 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 1:1 mixture of rotamers) δ 7.34–7.25 (m, 5H), 4.59 (s, 2H), 4.25 (t, *J* = 8.6 Hz, 2H), 4.10 (brs, 1H), 3.97 (brs, 1H), 1.08–1.00 (m, 2H), 0.16 (s, 9H), 0.04 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 156.3 (C), 156.3 (C), 137.3 (C), 137.3 (C), 128.6 (CH), 128.6 (CH), 128.4 (CH), 127.9 (CH), 127.5 (CH), 127.5 (CH), 100.9 (C), 100.9 (C), 89.2 (C), 89.0 (C), 64.3 (CH₂), 64.3 (CH₂), 49.4 (CH₂), 48.9 (CH₂), 36.4 (CH₂), 36.3 (CH₂), 17.9 (CH₂), 17.9 (CH₂), 0.0 (CH₃), 0.0 (CH₃), -1.3 (CH₃), -1.3 (CH₃); HRMS (ESI), calcd for C₁₉H₃₂NO₂Si₂⁺ (M+H)⁺ 362.1972, found 362.1979.



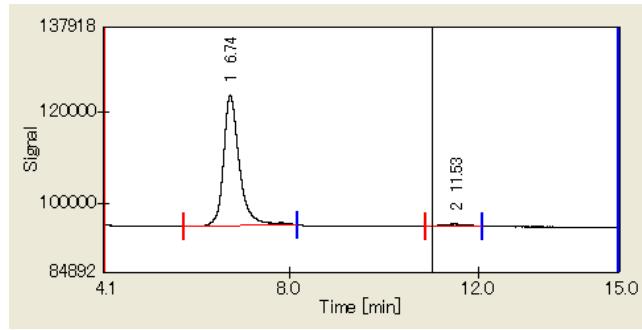
Allylic alcohol (40): In a glove box, $\text{Ni}(\text{cod})_2$ (567 mg, 2.05 mmol) was added to a solution of alkyne **37** (7.41 g, 20.5 mmol), 1-Boc-3-azetidinone (3.51 g, 20.5 mmol), triphenylphosphine (1.07 g, 4.10 mmol) and toluene (210 mL) at room temperature.⁶ The reaction vessel was removed from the glove box. The reaction was stirred at 60 °C for 6 h, and then concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:19 to 1:6) to give an inseparable mixture of enone **38** and **39** (10.1 g, 93%): a colorless oil; IR (film) 2954, 1703, 1670, 1453, 1418, 1366, 1247, 1169, 1115, 843, 767, 699 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C, a mixture of two regioisomers, signals of the major isomer are reported) δ 7.36–7.13 (m, 5H), 4.48 (brs, 2H), 4.35–4.26 (m, 4H), 4.07 (brs, 2H), 3.93 (brs, 2H), 1.49 (s, 9H), 1.06 (t, *J* = 8.6 Hz, 2H) 0.11 (s, 9H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C, a mixture of two regioisomers, signals of the major isomer are reported) δ 197.2 (C), 165.5 (C), 157.1 (C), 154.2 (C), 137.5 (C), 137.0 (C), 128.9 (CH), 127.9 (CH), 127.8 (CH), 80.8 (C), 64.7 (CH₂), 51.6 (CH₂), 50.8 (CH₂), 49.6 (CH₂), 44.7 (CH₂), 28.5 (CH₃), 18.2 (CH₂), 1.4 (CH₃), -1.4 (CH₃); HRMS (ESI), calcd for C₂₇H₄₄N₂O₅Si₂Na⁺ (M+Na)⁺ 555.2686, found 555.2683.

Trimethyl borate (310 μL, 2.80 mmol) was added to a solution of (*R*)-diphenyl(pyrrolidin-2-yl)methanol (595 mg, 2.35 mmol) in THF (39 mL) at room temperature.⁷ The resulting solution was maintained at room temperature for 1 h. Borane-methyl sulfide complex (1.1 mL, 12 mmol) was added to the solution. The solution was maintained for another 1 h. A solution of enone **38** and **39** (6.26 g, 11.7 mmol) and THF (78 mL) was added over 2 h using a syringe pump to the solution of the CBS reagent at room temperature. The resulting solution was maintained for an additional 3 h, and quenched with aqueous HCl (1 N, 50 mL) at 0 °C. The resulting mixture was extracted with EtOAc (2x 50 mL). The combined organic extracts were washed with brine (50 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/toluene 1:19 to 1:4) to afford a mixture of allylic alcohols **40** and **41**. The mixture of **40** and **41** were then separated by MPLC (Yamazen Ultra Pack Column D, 50×300 mm, EtOAc/hexane 11:89 to 32:68, 20 mL/min, **40**: T_R = 62.0 min, **41**: T_R = 58.0 min) to afford allylic alcohol **40** (4.89 g, 78%, 95% ee determined by HPLC (CHIRALPAK AD-H, 250×4.6 mm, UV 210 nm, iPrOH/hexane 1:9 (v/v), 1.0 mL/min, **40**: T_R= 6.7 min, *ent*-**40**: T_R= 11.5 min)) and **41** (452 mg, 7.2%, 95% ee determined by HPLC (CHIRALPAK AD-H, 250×4.6 mm, UV 210 nm, iPrOH/hexane 1:99 (v/v), 1.0 mL/min, **41**: T_R= 26.9 min, *ent*-**41**: T_R= 36.1 min)). Allylic alcohol **40**: a white amorphous solid; mp 34.0–35.5 °C; [α]²¹_D -60.8 (c 1.00, CHCl₃); IR (film) 3444, 2954, 1699, 1453, 1422, 1366, 1250, 1172, 1135, 1062, 838, 766, 697 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.32–7.19 (m, 5H), 4.44 (s, 2H), 4.28–4.10 (m, 6H), 3.93 (d, *J* = 13.5 Hz, 1H), 3.51 (d, *J* = 18.9 Hz, 1H), 2.96 (dd, *J* = 13.5, 2.9 Hz, 1H), 1.49 (s, 9H), 1.04 (t, *J* = 8.1 Hz, 2H), 0.10 (s, 9H), 0.05 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 157.3 (C), 157.0 (C), 155.4 (C), 155.4 (C), 145.3 (C),

144.2 (C), 137.4 (C), 137.4 (C), 135.6 (C), 135.6 (C), 128.7 (CH), 128.7 (CH), 127.6 (CH), 127.4 (CH), 127.4 (CH), 126.9 (CH), 80.1 (C), 80.1 (C), 66.0 (CH), 66.0 (CH), 64.3 (CH₂), 64.3 (CH₂), 49.9 (CH₂), 49.7 (CH₂), 49.7 (CH₂), 49.4 (CH₂), 48.2 (CH₂), 47.2 (CH₂), 44.9 (CH₂), 44.9 (CH₂), 28.5 (CH₃), 28.5 (CH₃), 18.2 (CH₂), 17.9 (CH₂), 0.4 (CH₃), 0.4 (CH₃), -1.4 (CH₃), -1.4 (CH₃); HRMS (ESI), calcd for C₂₇H₄₆N₂O₅Si₂Na⁺ (M+Na)⁺ 557.2843, found 557.2843. Allylic alcohol **41**: a colorless oil; [α]²⁵_D -82.6 (*c* 1.00, CHCl₃); IR (film) 3428, 2954, 1698, 1453, 1422, 1366, 1250, 1172, 1130, 1062, 950, 856, 838, 760, 698 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.35–7.13 (m, 5H), 4.66 (d, *J* = 14.9 Hz, 1H), 4.60 (d, *J* = 16.3 Hz, 1H), 4.30–4.17 (m, 3H), 4.04 (brs, 1H), 3.91 (brs, 2H), 3.79 (d, *J* = 14.9 Hz, 1H), 3.65 (brs, 1H), 3.39 (brs, 1H), 1.49 (s, 9H), 1.00 (t, *J* = 8.3 Hz, 2H), 0.05 (s, 9H), 0.03 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 158.4 (C), 155.1 (C), 143.6 (C), 137.4 (C), 136.1 (C), 128.8 (CH), 127.4 (CH), 126.9 (CH), 80.0 (C), 64.8 (CH₂), 63.2 (CH), 49.5 (CH₂), 48.7 (CH₂), 47.1 (CH₂), 47.1 (CH₂), 28.6 (CH₃), 18.1 (CH₂), 0.1 (CH₃), -1.4 (CH₃); HRMS (ESI), calcd for C₂₇H₄₆N₂O₅Si₂Na⁺ (M+Na)⁺ 557.2843, found 557.2839.

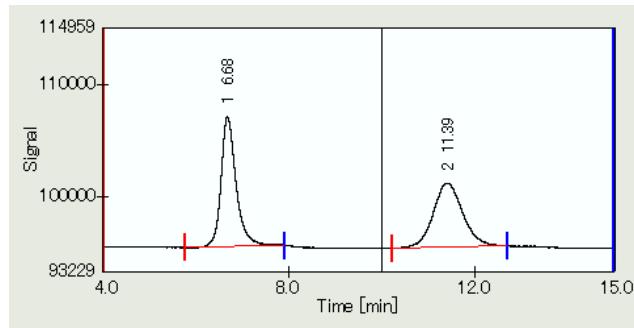
Chiral HPLC chart of **40** (95% ee)

CHIRALPAK AD-H, 250×4.6 mm, UV 210 nm, iPrOH/hexane 1:9 (v/v), 1.0 mL/min



No.	T _R	Area	Height	Area (%)
1	6.74	661336.550	28292	97.5179
2	11.53	16832.500	478	2.4821

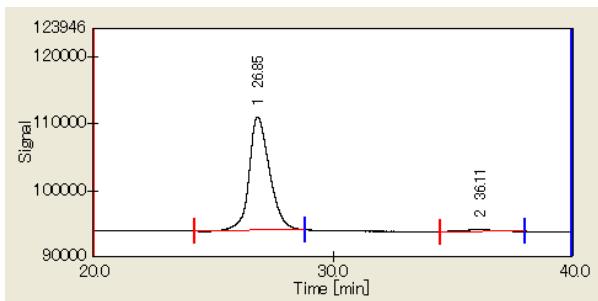
Chiral HPLC chart of *racemic*-**40**



No.	T _R	Area	Height	Area (%)
1	6.68	259498.400	11586	50.8047
2	11.39	251278.000	5701	49.1953

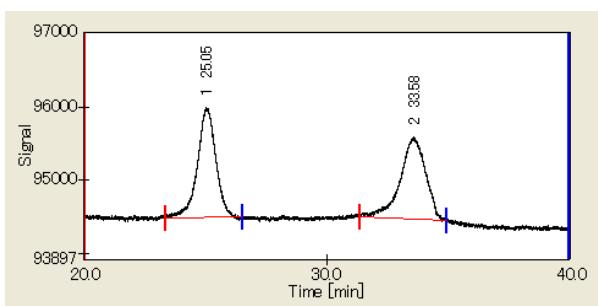
Chiral HPLC chart of **41** (95% ee)

CHIRALPAK AD-H, 250×4.6 mm, UV 210 nm, iPrOH/hexane 1:9 (v/v), 1.0 mL/min



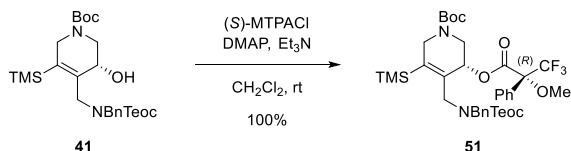
No.	T _R	Area	Height	Area (%)
1	26.85	994061.850	16918	97.6320
2	36.11	24110.150	326	2.3680

Chiral HPLC chart of *racemic*-**41**



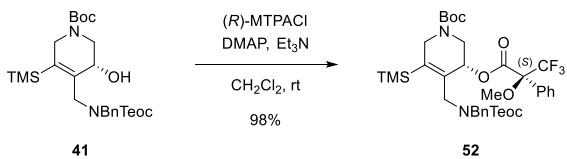
No.	T _R	Area	Height	Area (%)
1	25.05	78236.050	1494	49.3351
2	33.58	80488.300	1118	50.7554

The determination of the absolute stereochemistry of regioisomer **41**



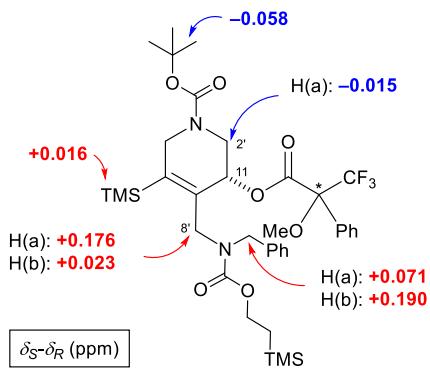
(R)-MTPA ester (51**):** (S)-(+) α -Methoxy- α -trifluoromethylphenylacetyl chloride (31 μ L, 170 μ mol) was added to a solution of alcohol **41** (40.2 mg, 75 μ mol), DMAP (9.7 mg, 113 μ mol), Et₃N (36 μ L, 240 μ mol), and CH₂Cl₂ (1.5 mL) at 0 °C. The solution was allowed to warm to room temperature, maintained for 15 min, and quenched with saturated aqueous NH₄Cl (2 mL). The resulting mixture was extracted with CH₂Cl₂ (2x 2 mL), washed with brine (2 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9 to 1:4) to give (*R*)-MTPA ester **51** (52.0 mg, 100%): a colorless oil; IR (film) 2955, 1746, 1699, 1416, 1366, 1251, 1170, 1133, 1027, 858, 838, 763, 712, 698 cm⁻¹; [α]²⁵_D -48.5 (c 1.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.67–7.58 (m, 2H), 7.43–7.34 (m, 3H), 7.32–7.19 (m, 3H), 7.12–7.04 (m, 2H), 5.45–5.35 (m, 1H), 4.44 (d, *J* = 14.6 Hz, 1H), 4.39–4.31 (m, 1H), 4.28 (dt, *J* = 10.4, 8.6 Hz, 1H), 4.24 (d, *J* = 19.2 Hz, 1H), 4.17 (dt, *J* = 10.4, 7.5 Hz, 1H), 4.14 (d, *J* = 15.2 Hz, 1H), 4.07 (d, *J* = 14.6 Hz, 1H), 4.02 (d, *J* = 15.2 Hz, 1H), 3.66 (d, *J* = 19.2 Hz, 1H), 3.57 (s, 3H), 2.88–2.64 (m, 1H), 1.44 (s, 9H), 1.02 (dd, *J* = 8.6, 7.5 Hz, 2H), 0.06 (s, 9H), 0.04 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 166.3 (C), 157.4 (C), 155.0 (C), 140.9 (C), 138.0 (C), 137.4 (C), 132.5 (C), 129.6 (CH), 128.8 (CH), 128.5 (CH), 128.0 (CH), 127.3 (CH), 127.1 (CH), 123.6 (q, *J* = 287 Hz, CF₃), 85.0 (q, *J* = 27.4 Hz, C-CF₃),

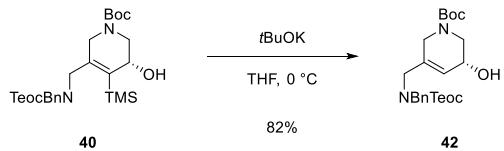
¹H NMR (400 MHz, CDCl₃, 60 °C) δ 80.3 (C), 67.4 (CH), 64.4 (CH₂), 55.5 (CH₃), 49.8 (CH₂), 49.2 (CH₂), 46.3 (CH₂), 44.3 (CH₂), 28.5 (CH₃), 18.2 (CH₂), -0.2 (CH₃), -1.4 (CH₃); ¹⁹F NMR (470 MHz, CDCl₃, 60 °C) δ -74.8 (CF₃); HRMS (ESI), calcd for C₃₇H₅₃N₂O₇F₃Si₂Na⁺ (M+Na)⁺ 773.3241, found 773.3255.



(S)-MTPA ester (52): (*R*)-(−)- α -Methoxy- α -(trifluoromethyl)phenylacetyl chloride (28 μ L, 150 μ mol) was added to a solution of alcohol **41** (36.4 mg, 68.1 μ mol), DMAP (12.5 mg, 102 μ mol), Et₃N (33 μ L, 220 μ mol), and CH₂Cl₂ (1.4 mL) at 0 °C. The solution was allowed to warm to room temperature, maintained for 15 min, and quenched with saturated aqueous NH₄Cl (2 mL). The resulting mixture was extracted with CH₂Cl₂ (2x 2 mL), washed with brine (2 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:4) to give (S)-MTPA ester **52** (45.3 mg, 98%): a colorless oil; IR (film) 2955, 1745, 1699, 1452, 1416, 1366, 1251, 1171, 1133, 1027, 858, 838, 763, 698 cm^{−1}; [α]²⁶_D −59.1 (c 1.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.66–7.56 (m, 2H), 7.43–7.35 (m, 3H), 7.34–7.12 (m, 3H), 7.17–7.10 (m, 2H), 5.46–5.41 (m, 1H), 4.51 (d, *J* = 15.5 Hz, 1H), 4.32 (d, *J* = 15.2 Hz, 1H), 4.28 (dt, *J* = 10.9, 8.6 Hz, 1H), 4.26 (d, *J* = 15.5 Hz, 1H), 4.24–4.18 (m, 1H), 4.21 (d, *J* = 19.2 Hz, 1H), 4.16 (dt, *J* = 10.9, 8.6 Hz, 1H), 4.04 (d, *J* = 15.2 Hz, 1H), 3.66 (d, *J* = 19.2 Hz, 1H), 3.54 (s, 3H), 2.90–2.60 (m, 1H), 1.38 (s, 9H), 0.99 (t, *J* = 8.6 Hz, 2H), 0.08 (s, 9H), 0.02 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 166.2 (C), 157.5 (C), 154.8 (C), 141.3 (C), 138.0 (C), 137.4 (C), 132.3 (C), 129.6 (CH), 128.8 (CH), 128.5 (CH), 128.2 (CH), 127.4 (CH), 127.1 (CH), 123.5 (q, *J* = 286 Hz, CF₃), 85.2 (q, *J* = 28.0 Hz, C-CF₃), 80.2 (C), 67.3 (CH), 64.5 (CH₂), 55.4 (CH₃), 49.8 (CH₂), 49.2 (CH₂), 46.3 (CH₂), 44.2 (CH₂), 28.5 (CH₃), 18.1 (CH₂), −0.2 (CH₃), −1.4 (CH₃); ¹⁹F NMR (470 MHz, CDCl₃, 60 °C) δ −74.8 (CF₃); HRMS (ESI), calcd for C₃₇H₅₃N₂O₇F₃Si₂Na⁺ (M+Na)⁺ 773.3241, found 773.3236.

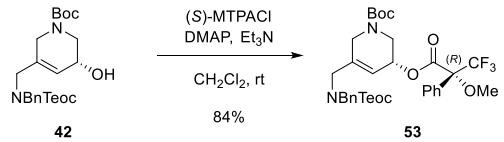
The resulting $\Delta\delta^{SR}$ ($= \delta_S - \delta_R$) values



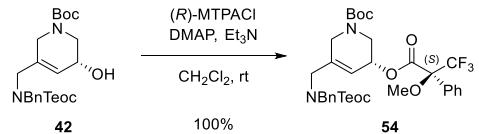


Allylic alcohol (42): Potassium *tert*-butoxide (1.36 g, 12.1 mmol) was added to the solution of **40** (4.30 g, 8.04 mmol) and THF (80 mL) at 0 °C. The solution was maintained at 0 °C for 15 min, 1M HCl was added to the solution until TLC analysis indicated the complete consumption of the TMS ether (total: 30 mL). The resulting mixture was extracted with EtOAc (2x 50 mL). The combined organic extracts were washed with brine (50 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:4) to give allylic alcohol **42** (3.04 g, 82%): a colorless oil; IR (film) 3436, 2954, 1699, 1455, 1419, 1366, 1247, 1166, 1106, 1056, 936, 859, 838, 768, 700 cm⁻¹; [α]²¹_D -26.2 (c 1.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.34–7.20 (m, 5H), 5.67–5.63 (m, 1H), 4.52 (d, *J* = 15.5 Hz, 1H), 4.42 (d, *J* = 15.5 Hz, 1H), 4.30–4.23 (m, 2H), 4.17–4.08 (m, 1H), 3.93–3.84 (m, 2H), 3.82 (d, *J* = 15.8 Hz, 1H), 3.66 (d, *J* = 18.6 Hz, 1H), 3.46 (d, *J* = 4.6 Hz, 2H), 1.48 (s, 9H), 1.08–1.02 (m, 2H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 156.9 (C), 155.2 (C), 137.8 (C), 135.5 (C), 128.7 (CH), 128.1 (CH), 127.5 (CH), 125.7 (CH), 80.3 (C), 64.3 (CH₂), 63.8 (CH), 50.1 (CH₂), 49.4 (CH₂), 47.9 (CH₂), 44.5 (CH₂), 28.6 (CH₃), 18.2 (CH₂), -1.4 (CH₃); HRMS (ESI), calcd for C₂₄H₃₈N₂O₅SiNa⁺ (M+Na)⁺ 485.2448, found 485.2454.

The determination of the absolute stereochemistry of **42**

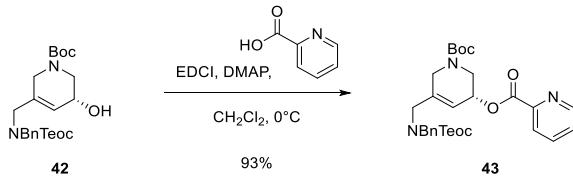
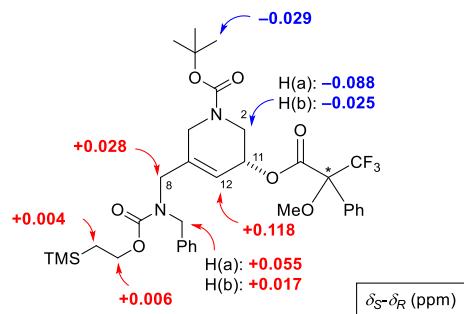


(R)-MTPA ester (53): (S)-(+)*-*α-Methoxy-*α*-trifluoromethylphenylacetyl chloride (25 μL, 140 μmol) was added to a solution of alcohol **42** (52.1 mg, 113 μmol), DMAP (14.0 mg, 113 μmol), Et₃N (35 μL, 250 μmol), and CH₂Cl₂ (2.3 mL) at 0 °C. The solution was allowed to warm to room temperature, maintained for 15 min, and quenched with saturated aqueous NH₄Cl (2 mL). The resulting mixture was extracted with CH₂Cl₂ (2x 2 mL), washed with brine (2 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:4) to give (*R*)-MTPA ester **53** (64.3 mg, 84%): a colorless oil; IR (film) 2954, 1746, 1699, 1453, 1420, 1367, 1239, 1169, 1125, 1081, 1016, 938, 860, 839, 766, 717, 699 cm⁻¹; [α]²⁶_D -44.9 (c 1.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.57–7.51 (m, 2H), 7.42–7.36 (m, 3H), 7.30–7.21 (m, 3H), 7.20–7.12 (m, 2H), 5.70–5.60 (m, 1H), 5.45–5.32 (m, 1H), 4.41 (d, *J* = 15.5 Hz, 1H), 4.34 (d, *J* = 15.5 Hz, 1H), 4.28–4.21 (m, 2H), 4.02–3.88 (m, 2H), 3.88–3.78 (m, 2H), 3.63 (d, *J* = 18.3 Hz, 1H), 3.54 (s, 3H), 3.44 (dd, *J* = 13.7, 3.7 Hz, 1H), 1.44 (s, 9H), 1.06–1.00 (m, 2H), 0.04 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 166.3 (C), 156.9 (C), 154.6 (C), 139.9 (C), 137.4 (C), 132.5 (C), 129.7 (CH), 128.8 (CH), 128.6 (CH), 128.1 (CH), 127.7 (CH), 127.7 (CH), 123.5 (q, *J* = 287 Hz, CF₃), 119.5 (CH), 85.0 (q, *J* = 27.4 Hz, C-CF₃), 80.6 (C), 68.2 (CH), 64.4 (CH₂), 55.5 (CH₃), 49.8 (CH₂), 49.1 (CH₂), 45.0–43.4 (CH₂ x2), 28.5 (CH₃), 18.2 (CH₂), -1.4 (CH₃); ¹⁹F NMR (470 MHz, CDCl₃, 60 °C) δ -74.6 (CF₃); HRMS (ESI), calcd for C₃₄H₄₅N₂O₇F₃SiNa⁺ (M+Na)⁺ 701.2846, found 701.2856.



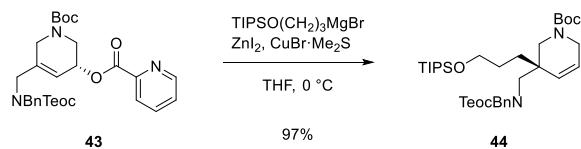
(S)-MTPA ester (54): (R)-(-)- α -Methoxy- α -(trifluoromethyl)phenylacetyl chloride (34 μ L, 180 μ mol) was added to a solution of alcohol **42** (69.2 mg, 150 μ mol), DMAP (18.3 mg, 150 μ mol), Et₃N (46 μ L, 330 μ mol), and CH₂Cl₂ (3.0 mL) at 0 °C. The solution was allowed to warm to room temperature, maintained for 15 min, and quenched with saturated aqueous NH₄Cl (2 mL). The resulting mixture was extracted with CH₂Cl₂ (2x 2 mL), washed with brine (2 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:4) to give (S)-MTPA ester **54** (102 mg, 100%): a colorless oil; $[\alpha]^{26}_D -25.8$ (*c* 1.00, CHCl₃); IR (film) 2953, 1746, 1700, 1453, 1420, 1367, 1238, 1169, 1125, 1016, 938, 859, 839, 716, 699 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.58–7.51 (m, 2H), 7.43–7.36 (m, 3H), 7.34–7.22 (m, 3H), 7.22–7.15 (m, 2H), 5.80–5.74 (m, 1H), 5.44–5.32 (m, 1H), 4.48 (d, *J* = 15.2 Hz, 1H), 4.37 (d, *J* = 15.2 Hz, 1H), 4.30–4.22 (m, 2H), 4.10–3.96 (m, 1H), 3.96–3.78 (m, 2H), 3.83 (dd, *J* = 13.5, 4.6 Hz, 1H), 3.65 (d, *J* = 20.0 Hz, 1H), 3.53 (s, 3H), 3.47–3.35 (m, 1H), 1.48–1.39 (m, 9H), 1.07–1.01 (m, 2H), 0.05 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 166.3 (C), 156.9 (C), 154.5 (C), 140.1 (C), 137.4 (C), 132.5 (C), 129.7 (CH), 128.8 (CH), 128.6 (CH), 128.0 (CH), 127.7 (CH), 127.7 (CH), 123.5 (q, *J* = 287 Hz, CF₃), 119.4 (CH), 84.9 (q, *J* = 28.0 Hz, C-CF₃), 80.5 (C), 68.4 (CH), 64.4 (CH₂), 55.4 (CH₃), 49.9 (CH₂), 49.1 (CH₂), 44.1 (CH₂), 44.1 (CH₂), 28.4 (CH₃), 18.2 (CH₂), -1.4 (CH₃); ¹⁹F NMR (470 MHz, CDCl₃, 60 °C) δ -74.6 (CF₃); HRMS (ESI), calcd for C₃₄H₄₅N₂O₇F₃SiNa⁺ (M+Na)⁺ 701.2846, found 701.2848.

The resulting $\Delta\delta^{SR}$ (= $\delta_S - \delta_R$) values



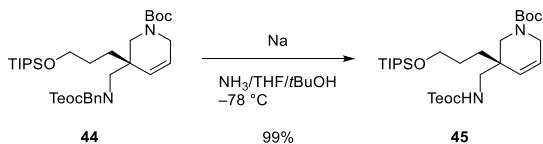
Picolinate (43): 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI, 1.89 g, 9.86 mmol) was added to a solution of alcohol **42** (3.04 g, 6.57 mmol), DMAP (80.3 mg, 657 μ mol), 2-picolinic acid (1.13 g, 9.20 mmol), and CH₂Cl₂ (66 mL) at 0 °C. The solution was maintained at this temperature for 3 h, and quenched with H₂O (30 mL). The resulting mixture was extracted with CH₂Cl₂ (2x 30 mL). The combined extracts were washed with brine (30 mL), dried over Na₂SO₄, and concentrated. The residue was purified by

silica gel column chromatography (EtOAc/hexane 1:3 to 1:1) to give picolinate **43** (3.48 mg, 93%): a colorless oil; $[\alpha]^{21}_D -63.1$ (*c* 1.00, CHCl₃); IR (film) 2954, 1740, 1698, 1454, 1421, 1366, 1245, 1169, 1129, 1044, 939, 858, 839, 750, 702 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 8.77 (d, *J* = 4.3 Hz, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.81 (ddd, *J* = 7.8, 7.8, 1.5 Hz, 1H), 7.45 (dd, *J* = 7.8, 4.3 Hz, 1H), 7.32–7.21 (m, 5H), 5.81 (brs, 1H), 5.49 (brs, 1H), 4.50 (d, *J* = 15.5 Hz, 1H), 4.45 (d, *J* = 15.5 Hz, 1H), 4.29–4.23 (m, 2H), 4.04 (d, *J* = 17.8 Hz, 1H), 3.95 (d, *J* = 16.1 Hz, 1H), 3.89 (dd, *J* = 13.8, 4.6 Hz, 1H), 3.83 (d, *J* = 16.1 Hz, 1H), 3.74 (d, *J* = 17.8 Hz, 1H), 3.60 (dd, *J* = 13.8, 4.6 Hz, 1H), 1.43 (s, 9H), 1.08–1.02 (m, 2H), 0.05 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 164.5 (C), 156.8 (C), 154.6 (C), 150.1 (CH), 148.4 (C), 139.0 (C), 137.5 (C), 136.8 (CH), 128.6 (CH), 128.0 (CH), 127.5 (CH), 126.8 (CH), 125.3 (CH), 120.9 (CH), 80.2 (C), 67.3 (CH), 64.2 (CH₂), 50.0 (CH₂), 49.3 (CH₂), 44.6 (CH₂), 44.3 (CH₂), 28.4 (CH₃), 18.1 (CH₂), −1.5 (CH₃); HRMS (ESI), calcd for C₃₀H₄₁N₃O₆SiNa⁺ (M+Na)⁺ 590.2662, found 590.2673.

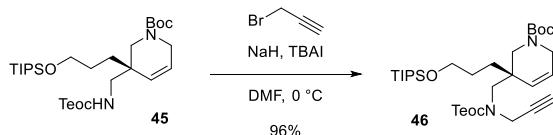


S_N2' product (44): A 100 mL flask equipped with a rubber septa connected to a bubbler was charged with magnesium (turnings, 700 mg, 28.8 mmol) and THF (40 mL). (3-Bromopropoxy)triisopropylsilane (4.5 mL, 16 mmol) was added to the mixture at room temperature over a period of 5 min. The resulting mixture was stirred vigorously for 1 h. The concentration of the Grignard reagent was determined as 0.26 M by titration with 1,10-phenanthroline method.⁸

The above Grignard reagent (0.26 M in THF, 31 mL, 7.5 mmol) was slowly added to a mixture of CuBr·Me₂S (918 mg, 4.46 mmol), ZnI₂ (1.42 g, 4.46 mmol), and THF (25 mL) at 0 °C.⁹ The resulting mixture was stirred at this temperature for 30 min. A solution of picolinate **43** (1.41 g, 2.48 mmol) and THF (25 mL) was added dropwise to the mixture dropwise at 0 °C. The mixture was stirred for 30 min, and quenched with saturated aqueous NH₄Cl (50 mL). The resulting mixture was extracted with hexane (2x 50 mL). The combined organic extracts were washed with brine (50 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9) and MPLC (Yamazen Ultra Pack Column B, 26×300 mm, EtOAc/hexane 18:82, 20 mL/min, **44**: T_R = 28.5 min) to afford S_N2' product **44** (1.58 g, 97%): a colorless oil; $[\alpha]^{21}_D +18.0$ (*c* 1.00, CHCl₃); IR (film) 2945, 2866, 1699, 1464, 1419, 1365, 1249, 1175, 1144, 1103, 882, 858, 838, 770 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.31–7.14 (m, 5H), 5.70 (d, *J* = 10.9 Hz, 1H), 5.64 (d, *J* = 10.9 Hz, 1H), 4.56 (d, *J* = 15.8 Hz, 1H), 4.51 (d, *J* = 15.8 Hz, 1H), 4.19 (dt, *J* = 10.6, 7.2 Hz, 2H), 3.85 (brs, 2H), 3.65 (t, *J* = 5.5 Hz, 2H), 3.54–3.25 (m, 4H), 1.60–1.41 (m, 13H), 1.12–1.04 (m, 21H), 1.05–0.96 (m, 2H), 0.04 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 157.9 (C), 155.4 (C), 138.4 (C), 132.8 (CH), 128.6 (CH), 127.6 (CH), 127.3 (CH), 124.4 (CH), 79.8 (C), 64.2 (CH₂), 63.9 (CH₂), 52.7 (CH₂), 52.0 (CH₂), 48.1 (CH₂), 43.5 (CH₂), 41.4 (C), 33.4 (CH₂), 28.6 (CH₃), 27.6 (CH₂), 18.2 (CH₃), 18.1 (CH₂), 12.3 (CH), −1.4 (CH₃); HRMS (ESI), calcd for C₃₆H₆₄N₂O₅Si₂Na⁺ (M+Na)⁺ 683.4252, found 683.4232.

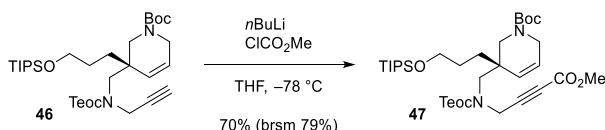


Tetrahydropyridine (45): Sodium (1.10 g, 47.8 mmol) was added to a solution of **44** (1.58 g, 2.39 mmol), *t*BuOH (0.7 mL), and NH₃/THF (25:24, 34 mL) at -78 °C. The resulting mixture was stirred for 15 min at -78 °C, quenched with solid NH₄Cl (3.84 g, 71.7 mmol), allowed to warm to room temperature, and diluted with water (20 mL). The resulting mixture was extracted with hexane (2x 20 mL). The combined organic extracts were washed with brine (10 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:19 to 1:9) to give tetrahydropyridine **45** (1.34 g, 99%): a colorless oil; [α]²¹_D -11.5 (*c* 1.00, CHCl₃); IR (film) 3350, 2945, 2866, 1724, 1701, 1518, 1425, 1249, 1104, 860, 837, 681 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.72 (d, *J* = 10.1 Hz, 1H), 5.58 (d, *J* = 10.1 Hz, 1H), 4.92 (m, 1H), 4.15 (t, *J* = 8.3 Hz, 2H), 4.00 (d, *J* = 18.3 Hz, 1H), 3.74 (d, *J* = 18.3 Hz, 1H), 3.67 (dt, *J* = 9.8, 6.3 Hz, 1H), 3.64 (dt, *J* = 9.8, 6.3 Hz, 1H), 3.55 (brs, 1H), 3.27 (dd, *J* = 13.8, 7.8 Hz, 1H), 3.09 (brs, 1H), 3.02–2.90 (m, 1H), 1.64–1.45 (m, 2H), 1.48 (s, 9H), 1.45–1.39 (m, 2H), 1.14–1.01 (m, 21H), 0.98 (t, *J* = 8.3 Hz, 2H), 0.04 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 157.1 (C), 157.1 (C), 155.4 (C), 154.7 (C), 131.7 (CH), 131.0 (CH), 126.0 (CH), 125.3 (CH), 80.2 (C), 80.0 (C), 63.9 (CH₂), 63.9 (CH₂), 63.1 (CH₂), 62.9 (CH₂), 47.5 (CH₂), 46.4 (CH₂), 46.2 (CH₂), 46.2 (CH₂), 44.1 (CH₂), 43.1 (CH₂), 40.1 (C), 40.1 (C), 31.3 (CH₂), 31.2 (CH₂), 28.5 (CH₃), 28.5 (CH₃), 27.3 (CH₂), 27.3 (CH₂), 18.2 (CH₃), 18.2 (CH₃), 17.8 (CH₂), 17.8 (CH₂), 12.1 (CH), 12.1 (CH), -1.4 (CH₃), -1.4 (CH₃); HRMS (ESI), calcd for C₂₉H₅₉N₂O₅Si₂⁺ (M+H)⁺ 571.3963, found 571.3991.

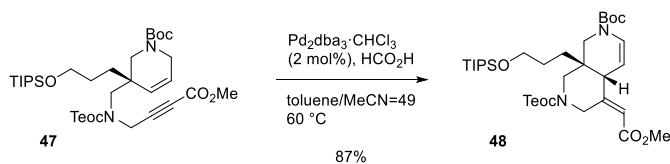


Eneyne (46): Sodium hydride (257 mg, 6.75 mmol) was added to a solution of tetrahydropyridine **45** (2.57 g, 4.50 mmol), propargyl bromide (510 μL, 6.8 mmol), tetrabutylammonium iodide (166 mg, 450 μmol) and DMF (45 mL) at 0 °C. This solution was maintained at this temperature for 4 h, quenched with saturated aqueous NH₄Cl (25 mL), and extracted with EtOAc/hexane = 1/3 (3x 25 mL). The combined organic extracts were washed with brine (15 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:29 to 1:12) to give enyne **46** (2.63 g, 96%): a colorless oil; [α]²¹_D +10.5 (*c* 1.00, CHCl₃); IR (film) 3313, 2945, 2866, 1702, 1418, 1249, 1175, 1147, 1105, 839 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.74–5.66 (m, 1H), 5.63 (ddd, *J* = 10.3, 2.0, 2.0 Hz, 1H), 4.25–4.17 (m, 2H), 4.10 (brs, 2H), 3.88 (d, *J* = 18.1 Hz, 1H), 3.82 (d, *J* = 18.1 Hz, 1H), 3.65 (t, *J* = 6.0 Hz, 2H), 3.48–3.36 (m, 1H), 3.43 (d, *J* = 14.9 Hz, 1H), 3.39 (d, *J* = 14.9 Hz, 1H), 3.33–3.24 (m, 1H), 2.17 (brs, 1H), 1.64–1.44 (m, 4H), 1.48 (s, 9H), 1.14–1.00 (m, 23H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 157.1 (C), 157.1 (C), 155.3 (C), 155.2 (C), 132.3 (CH), 131.9 (CH), 125.1 (CH), 124.6 (CH), 80.2–79.2 (C x4), 72.2–71.3 (CH x2), 64.3 (CH₂), 64.3 (CH₂), 63.9 (CH₂), 63.9 (CH₂), 52.8 (CH₂), 52.1 (CH₂), 48.0 (CH₂), 46.8 (CH₂), 43.7 (CH₂), 42.9 (CH₂), 41.2–40.4 (C x2), 38.4 (CH₂), 38.4 (CH₂), 32.8 (CH₂), 32.5 (CH₂), 28.6 (CH₃),

28.6, (CH₃), 27.4 (CH₂), 27.4 (CH₂), 18.2 (CH₃), 18.2 (CH₃), 17.9 (CH₂), 17.8 (CH₂), 12.1 (CH), 12.1 (CH), -1.4 (CH₃), -1.4 (CH₃); HRMS (ESI), calcd for C₃₂H₆₁N₂O₅Si₂⁺ (M+H)⁺ 609.4119, found 609.4130.

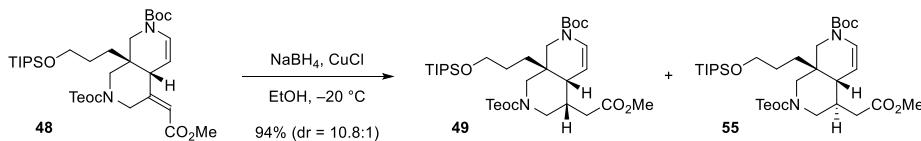


Methyl ynoate (47): *n*-Butyllithium (1.6 M in hexane, 1.3 mL, 2.2 mmol) was added to a solution of alkyne **46** (1.27 g, 2.09 mmol) and THF (21 mL) at -78 °C. After the solution was maintained for 15 min, methyl chloroformate (240 µL, 3.1 mmol) was added at the same temperature. The solution was maintained for 30 min, and quenched with saturated aqueous NH₄Cl (10 mL) at -78 °C. The resulting mixture was extracted with EtOAc (2x 10 mL). The combined organic extracts were washed with brine (10 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:5) to give a mixture of methyl ynoate **47** and alkyne **46**. The mixture was then separated by MPLC (Yamazen Ultra Pack Column B, 26×300 mm, EtOAc/hexane 24:76, 20 mL/min, **47**: T_R = 30.0 min, **46**: T_R = 28.0 min) to afford methyl ynoate **47** (969 mg, 70%, brsm 79%) and alkyne **46** (140 mg, 11%). **47**: a colorless oil; [α]²⁵_D +12.3 (*c* 1.00, CHCl₃); IR (film) 2945, 2866, 2239, 1702, 1462, 1423, 1250, 1175, 1104, 839 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.76–5.69 (m, 1H), 5.60 (d, *J* = 10.3 Hz, 1H), 4.28–4.17 (m, 4H), 3.94–3.86 (m, 1H), 3.84–3.76 (m, 1H), 3.75 (s, 3H), 3.65 (t, *J* = 6.1 Hz, 2H), 3.56–3.32 (m, 1H), 3.42 (d, *J* = 14.9 Hz, 1H), 3.35 (d, *J* = 14.9 Hz, 1H), 3.25 (brs, 1H), 1.62–1.45 (m, 4H), 1.48 (s, 9H), 1.13–1.00 (m, 23H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 156.9 (C), 156.9 (C), 155.4 (C), 155.2 (C), 153.8 (C), 153.8 (C), 132.1 (CH), 131.7 (CH), 125.6 (CH), 125.2 (CH), 84.3 (C), 84.3 (C), 83.8 (C), 83.8 (C), 80.1 (C), 80.1 (C), 64.7 (CH₂), 64.7 (CH₂), 63.9 (CH₂), 63.9 (CH₂), 52.8 (CH₃), 52.8 (CH₃), 52.7 (CH₂), 52.7 (CH₂), 48.0 (CH₂), 46.7 (CH₂), 43.7 (CH₂), 43.0 (CH₂), 40.9 (C), 40.6 (C), 38.6 (CH₂), 38.5 (CH₂), 32.9 (CH₂), 32.1 (CH₂), 28.6 (CH₃), 28.6 (CH₃), 27.4 (CH₂), 27.4 (CH₂), 18.2 (CH₃), 18.2 (CH₃), 18.0 (CH₂), 17.9 (CH₂), 12.1 (CH), 12.1 (CH), -1.4 (CH₃), -1.4 (CH₃); HRMS (ESI), calcd for C₃₄H₆₃N₂O₇Si₂⁺ (M+H)⁺ 667.4174, found 667.4173.



Unsaturated methyl ester (48): Tris(dibenzylidenacetone)dipalladium chloroform adduct (39.4 mg, 38.1 µmol) was added to a solution of methyl ynoate **47** (1.27 g, 1.90 mmol), HCO₂H (350 µL, 9.5 mmol) and PhMe/MeCN = 49 (190 mL).¹⁰ The solution was heated to 60 °C, maintained for 1 h, quenched with saturated aqueous NaHCO₃ (50 mL) at room temperature, and extracted with EtOAc (3x 50 mL). The combined organic extracts were washed with brine (50 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:19) to give unsaturated methyl ester **48** (1.10 g, 87%): a colorless oil; [α]²⁵_D +62.0 (*c* 1.00, CHCl₃); IR (film) 2947, 2866, 1708, 1649, 1369, 1249, 1167, 1107, 858,

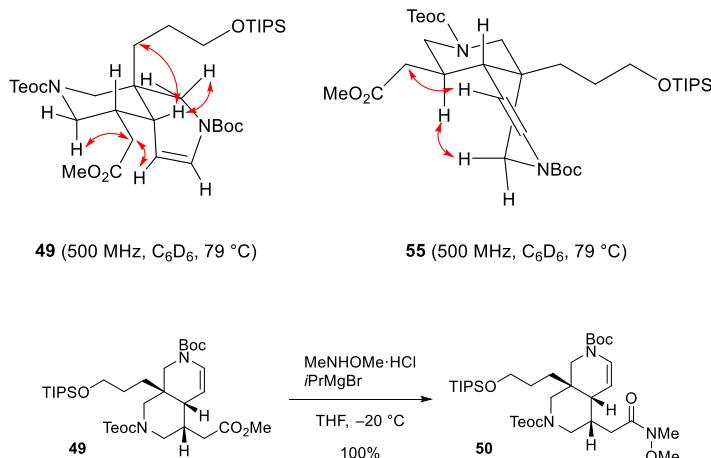
838 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.07–6.77 (m, 1H), 5.76 (s, 1H), 5.01 (brs, 1H), 4.57 (brs, 1H), 4.40–4.12 (m, 1H), 4.19 (t, *J* = 8.6 Hz, 2H), 3.84–3.56 (m, 4H), 3.73 (s, 3H), 3.30 (d, *J* = 9.2 Hz, 1H), 2.88 (d, *J* = 13.8 Hz, 1H), 2.66 (brs, 1H), 1.68–1.36 (m, 4H), 1.50 (s, 9H), 1.12–0.99 (m, 23H), 0.04 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 166.1 (C), 166.1 (C), 156.6 (C), 156.4 (C), 155.9 (C), 155.9 (C), 152.7 (C), 152.2 (C), 127.0 (CH), 126.8 (CH), 118.4 (CH), 118.0 (CH), 103.3 (CH), 103.3 (CH), 81.5 (C), 81.5 (C), 63.9 (CH₂), 63.9 (CH₂), 63.7 (CH₂), 63.7 (CH₂), 51.4 (CH₃), 51.4 (CH₃), 46.7 (CH₂), 46.3 (CH₂), 46.0 (CH), 46.0 (CH₂), 45.6 (CH), 45.4 (CH₂), 44.2 (CH₂), 44.2 (CH₂), 37.4 (C), 37.2 (C), 32.0 (CH₂), 31.7 (CH₂), 28.3 (CH₃), 28.3 (CH₃), 26.7 (CH₂), 26.7 (CH₂), 18.1 (CH₃), 18.1 (CH₃), 18.0 (CH₂), 17.9 (CH₂), 12.0 (CH), 12.0 (CH), -1.4 (CH₃), -1.4 (CH₃); HRMS (ESI), calcd for C₃₄H₆₂N₂O₇Si₂Na⁺ (M+Na)⁺ 689.3993, found 689.3984.



Methyl ester (49): Copper (I) chloride (264 mg, 2.67 mmol) and NaBH₄ (101 mg, 2.67 mmol) were added to a solution of unsaturated methyl ester **48** (1.78 g, 2.67 mmol) and EtOH (27 mL) at -20 °C.¹¹ Copper (I) chloride (264 mg, 2.67 mmol) and NaBH₄ (101 mg, 2.67 mmol) were added to the mixture every 15 min until TLC analysis indicated the complete consumption of unsaturated methyl ester **48** (total: CuCl 3.0 equiv., NaBH₄ 3.0 equiv.). The mixture was quenched with saturated aqueous NH₄Cl (10 mL), and extracted with EtOAc (3x 10 mL). The combined organic extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was filtered through a pad of silica gel (EtOAc/hexane 1:19). Two diastereomers were then separated by MPLC (Yamazen Ultra Pack Column D, 50×300 mm, EtOAc/hexane 9:91 to 30:70, 45 mL/min, **49**: T_R = 38.0 min, **55**: T_R = 42.0 min) to afford methyl esters **49** (1.54 g, 86%) and **55** (142 mg, 7.9%). methyl ester **49**: a colorless oil; [α]²⁵_D -10.3 (c 1.00, CHCl₃); IR (film) 2946, 2865, 1742, 1703, 1652, 1436, 1367, 1250, 1168, 1110 cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 79 °C) δ 7.20–6.90 (m, 1H), 4.43 (d, *J* = 8.3 Hz, 1H), 4.29 (t, *J* = 8.3 Hz, 2H), 4.12–3.96 (m, 1H), 3.94–3.72 (m, 2H), 3.64–3.54 (m, 2H), 3.38 (s, 3H), 2.92 (d, *J* = 13.2 Hz, 1H), 2.87 (d, *J* = 13.5 Hz, 1H), 2.52–2.40 (m, 2H), 2.23 (brs, 1H), 2.07 (dd, *J* = 16.0, 7.2 Hz, 1H), 2.02 (dd, *J* = 15.8, 6.6 Hz, 1H), 1.65–1.49 (m, 4H), 1.42 (s, 9H), 1.17–1.05 (m, 21H), 1.02–0.95 (m, 2H), -0.02 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 172.4 (C), 172.2 (C), 156.0 (C), 156.0 (C), 152.9 (C), 152.4 (C), 127.0 (CH), 126.8 (CH), 101.8 (CH), 101.4 (CH), 81.3 (C), 81.3 (C), 63.8 (CH₂), 63.7 (CH₂), 63.7 (CH₂), 63.6 (CH₂), 51.9 (CH₃), 51.9 (CH₃), 48.9 (CH₂), 47.9 (CH₂), 45.5 (CH₂), 45.1 (CH₂), 44.2 (CH₂), 43.9 (CH₂), 38.2 (CH), 37.5 (CH), 35.2 (CH₂), 35.0 (CH₂), 34.0 (C), 34.0 (C), 31.7 (CH), 31.4 (CH), 30.7 (CH₂), 30.5 (CH₂), 28.4 (CH₃), 28.4 (CH₃), 26.4 (CH₂), 26.4 (CH₂), 18.2 (CH₃), 18.2 (CH₃), 17.9 (CH₂), 17.9 (CH₂), 12.1 (CH), 12.1 (CH), -1.4 (CH₃), -1.4 (CH₃); HRMS (ESI), calcd for C₃₄H₆₂N₂O₇Si₂Na⁺ (M+Na)⁺ 691.4150, found 691.4172. methyl ester **55**: a colorless oil; [α]²⁷_D +30.6 (c 1.00, CHCl₃); IR (film) 2947, 2866, 1741, 1705, 1649, 1369, 1249, 1173, 1136, 1110 cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 79 °C) δ 7.10–6.80 (m, 1H), 4.67 (dd, *J* = 7.2, 7.2 Hz, 1H), 4.41–4.20 (m, 3H), 4.13 (d, *J* = 13.5 Hz, 1H), 4.00–3.75 (m, 1H), 3.61–3.52 (m, 2H), 3.37 (s, 3H), 3.28 (d, *J* = 13.8 Hz, 1H), 2.71 (d, *J* = 13.2 Hz, 1H),

2.45 (dd, $J = 12.9$, 12.9 Hz, 1H), 2.30 (d, $J = 12.1$ Hz, 1H), 2.02–1.88 (m, 2H), 1.62–1.46 (m, 2H), 1.44–1.38 (m, 1H), 1.42 (s, 9H), 1.36–1.17 (m, 2H), 1.15–1.03 (m, 21H), 1.01–0.95 (m, 2H), –0.03 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3 , 1:1 mixture of rotamers) δ 172.6 (C), 172.6 (C), 155.6 (C), 155.6 (C), 153.0 (C), 152.4 (C), 125.4 (CH), 125.0 (CH), 104.2 (CH), 103.7 (CH), 81.1 (C), 81.1 (C), 63.8 (CH_2), 63.8 (CH_2), 63.7 (CH_2), 51.8 (CH_3), 51.8 (CH_3), 50.5 (CH_2), 50.5 (CH_2), 48.5 (CH_2), 48.3 (CH_2), 44.3 (CH_2), 43.6 (CH_2), 42.0 (CH), 41.8 (CH), 38.5 (CH), 38.5 (CH), 36.0 (CH_2), 35.8 (CH_2), 34.4 (C), 34.3 (C), 32.1 (CH_2), 32.1 (CH_2), 28.4 (CH_3), 28.4 (CH_3), 26.8 (CH_2), 26.7 (CH_2), 18.1 (CH_3), 18.1 (CH_3), 17.9 (CH_2), 17.9 (CH_2), 12.0 (CH), 12.0 (CH), –1.3 (CH_3), –1.3 (CH_3); HRMS (ESI), calcd for $\text{C}_{34}\text{H}_{65}\text{N}_2\text{O}_7\text{Si}_2^+$ ($\text{M}+\text{H}$)⁺ 669.4330, found 669.4363.

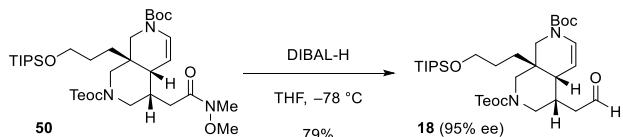
NOESY experiments for 49 and 55



Weinreb amide (50): A 200 mL flask equipped with a rubber septa connected to a bubbler was charged with magnesium (turnings, 751 mg, 30.9 mmol) and THF (47 mL). 1,2-Dibromoethane (12 μ L, 140 μ mol) and 2-bromopropane (2.64 mL, 28.2 mmol) were added to the mixture at room temperature over a period of 5 min. The resulting mixture was stirred vigorously for 1 h. The concentration of the resulting isopropylmagnesium bromide was determined as 0.38 M by titration with 1,10-phenanthroline method.⁸

Isopropylmagnesium bromide (0.38 M in THF, 24 mL, 9.2 mmol) was added to a mixture of methyl ester **49** (1.53 g, 2.29 mmol), MeNHOMe·HCl (447 mg, 4.58 mmol), and THF (12 mL) at -20 °C. The mixture was stirred for 15 min, quenched with saturated aqueous NH₄Cl (5 mL), and extracted with EtOAc (2x 10 mL). The combined organic extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:3) to give Weinreb amide **50** (1.60 g, 100%): a colorless oil; [α]²⁷_D -3.9 (*c* 1.00, CHCl₃); IR (film) 2944, 2866, 1703, 1670, 1367, 1250, 1170, 1110 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.02–6.72 (m, 1H), 4.70 (brs, 1H), 4.17 (t, *J* = 8.4 Hz, 2H), 3.94–3.84 (m, 1H), 3.84–3.50 (m, 4H), 3.69 (s, 3H), 3.18 (s, 3H), 3.09–2.91 (m, 1H), 2.80 (d, *J* = 14.0 Hz, 1H), 2.60–2.42 (m, 3H), 2.41–2.30 (m, 2H), 1.63–1.46 (m, 4H), 1.49 (s, 9H), 1.13–1.03 (m, 21H), 1.00 (m, 2H), 0.04 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 172.5 (C), 172.2 (C), 156.1 (C), 156.1 (C), 153.0 (C), 152.5 (C), 126.7 (CH), 126.6 (CH), 102.4 (CH), 102.1 (CH), 81.2 (C), 81.2 (C), 63.9 (CH₂), 63.6 (CH₂), 63.6 (CH₂), 63.6 (CH₂), 61.4 (CH₃), 61.4 (CH₃), 49.0 (CH₂), 47.9 (CH₂), 45.4 (CH₂), 45.2 (CH₂), 44.4 (CH₂), 44.3 (CH₂), 38.8–37.0 (CH x4), 34.1 (C), 34.0 (C), 32.8–32.0 (CH₃ x2),

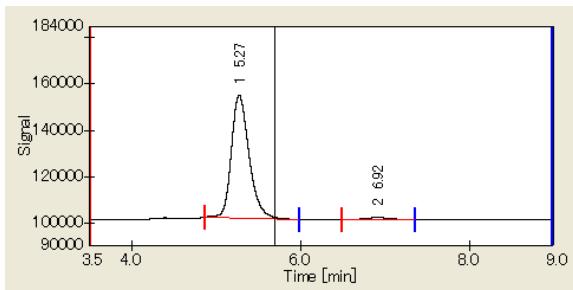
CH_2 x2), 31.0 (CH), 30.9 (CH), 30.7 (CH₂), 30.5 (CH₂), 28.4 (CH₃), 28.4 (CH₃), 26.5 (CH₂), 26.5 (CH₂), 18.1 (CH₃), 18.1 (CH₃), 17.9 (CH₂), 17.9 (CH₂), 12.0 (CH), 12.0 (CH), -1.4 (CH₃), -1.4 (CH₃); HRMS (ESI), calcd for $\text{C}_{35}\text{H}_{68}\text{N}_3\text{O}_7\text{Si}_2^+$ ($\text{M}+\text{H}$)⁺ 698.4596, found 698.4590.



Aldehyde (18): Diisobutylaluminium hydride (1.0 M in hexane, 3.4 mL, 3.4 mmol) was added to a solution of Weinreb amide **50** (1.60 g, 2.29 mmol) and THF (23 mL) at -78 °C. This solution was maintained at this temperature for 1 h, and quenched with saturated aqueous (+)-potassium sodium tartrate (50 mL). The resulting mixture was allowed to warm to room temperature, stirred for 1 h, and extracted with EtOAc (2x 50 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:4) to give aldehyde **18** (1.46 g, 79%, 95% ee by HPLC (CHIRALPAK AD-H, 250×4.6 mm, UV 210 nm, *i*PrOH/hexane 1:19 (v/v), 1.0 mL/min, **18**: $T_{\text{R}}=5.3$ min, *ent*-**18**: $T_{\text{R}}=6.9$ min)): a colorless oil; $[\alpha]^{27}_{\text{D}}=-7.6$ (*c* 1.00, CHCl_3); IR (film) 2945, 2866, 2723, 1703, 1367, 1250, 1169, 1111, 838 cm^{-1} ; ¹H NMR (500 MHz, CDCl_3 , 60 °C) δ 9.79 (s, 1H), 7.02–6.72 (m, 1H), 4.60(brs, 1H), 4.17 (t, $J=8.6$ Hz, 2H), 3.91–3.77 (m, 1H), 3.75–3.55 (m, 4H), 3.09–2.94 (m, 1H), 2.83 (d, $J=14.3$ Hz, 1H), 2.63–2.49 (m, 2H), 2.45 (dd, $J=17.8, 5.2$ Hz, 1H), 2.38 (dd, $J=17.8, 6.9$ Hz, 1H), 2.32 (brs, 1H), 1.63–1.52 (m, 2H), 1.51–1.45 (m, 2H), 1.50 (s, 9H), 1.14–1.03 (m, 21H), 1.00 (m 2H), 0.05 (s, 9H); ¹³C NMR (125 MHz, CDCl_3 , 60 °C) δ 200.0 (CH), 156.1 (C), 152.7 (C), 127.4 (CH), 101.4 (CH), 81.4 (C), 63.82 (CH₂), 63.78 (CH₂), 49.3–47.5 (CH₂, broad), 45.7 (CH₂), 44.5 (CH₂), 44.3 (CH₂), 38.5 (CH), 34.3 (C), 31.1 (CH₂), 29.5 (CH), 28.5 (CH₃), 26.6 (CH₂), 18.2 (CH₃), 18.1 (CH₂), 12.3 (CH), -1.3 (CH₃); HRMS (ESI), calcd for $\text{C}_{33}\text{H}_{63}\text{N}_2\text{O}_6\text{Si}_2^+$ ($\text{M}+\text{H}$)⁺ 639.4225, found 639.4222.

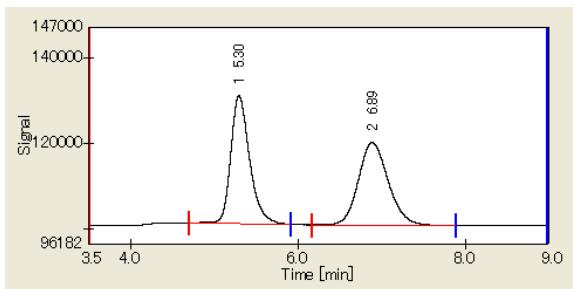
Chiral HPLC chart of **18** (95% ee)

CHIRALPAK AD-H, 250×4.6 mm, UV 210 nm, *i*-PrOH/hexane 1:19 (v/v), 1.0 mL/min



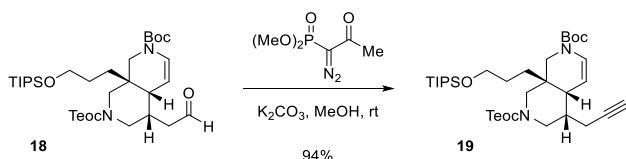
No.	T _R	Area	Height	Area (%)
1	5.27	768844.050	52766	97.5153
2	6.92	19589.900	927	2.4847

Chiral HPLC chart of *racemic*-**18**

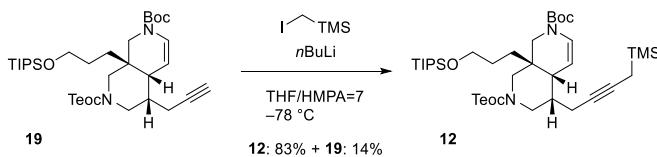


No.	T _R	Area	Height	Area (%)
1	5.30	475248.250	30065	49.6683
2	6.89	481596.300	19410	50.3317

A-3. Synthesis of Common Intermediate 17

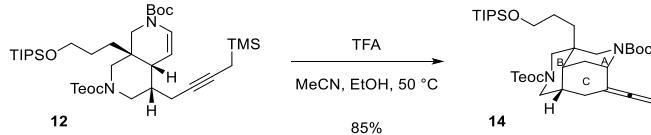


Alkyne (19): Ohira-Bestmann reagent (410 μ L, 2.7 mmol) was added to a mixture of aldehyde **18** (1.15 g, 1.80 mmol), K_2CO_3 (498 mg, 3.60 mmol), and MeOH (18 mL) at room temperature. The mixture was stirred for 3 h, and quenched with saturated aqueous NH_4Cl (10 mL) at 0 °C. The resulting mixture was extracted with hexane (2x 10 mL). The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9) to give alkyne **19** (1.07 g, 94%): a colorless oil; $[\alpha]^{27}_D -16.4$ (*c* 1.00, $CHCl_3$); IR (film) 3313, 2945, 2866, 1704, 1652, 1465, 1435, 1412, 1366, 1250, 1169, 1146, 1111, 883, 859, 839, 766, 722, 683 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$, 60 °C) δ 6.84 (brs, 1H), 4.65 (brs, 1H), 4.17 (t, *J* = 8.3 Hz, 2H), 3.99 (brs, 1H), 3.81 (brs, 1H), 3.74–3.52 (m, 3H), 3.08–2.92 (m, 1H), 2.76 (d, *J* = 13.2 Hz, 1H), 2.52–2.42 (m, 2H), 2.28–2.08 (m, 3H), 1.99 (m, 1H), 1.60–1.48 (m, 4H), 1.49 (s, 9H), 1.09–1.04 (m, 21H), 1.00 (t, *J* = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, 60 °C) δ 156.1 (C), 152.7 (C), 127.1 (CH), 101.5 (CH), 81.4 (C), 81.2 (C), 70.2 (CH), 63.9 (CH₂), 63.6 (CH₂), 49.6–47.8 (br, CH₂), 45.6 (CH₂), 44.2 (CH₂), 37.8 (CH), 34.3 (C), 34.2 (CH), 30.8 (CH₂), 28.5 (CH₃), 26.6 (CH₂), 19.9 (CH₂), 18.2 (CH₃), 18.1 (CH₂), 12.3 (CH), –1.3 (CH₃); HRMS (ESI), calcd for $C_{34}H_{63}N_2O_5Si_2^+$ ($M+H$)⁺ 635.4276, found 635.4271.

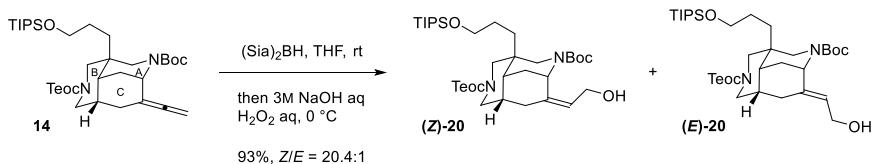


Propargylsilane (12): *n*-Butyllithium (1.6 M in hexane, 1.1 mL, 1.8 mmol) was added to a solution of alkyne **19** (1.07 g, 1.68 mmol) and THF (15 mL) at -78 °C. After maintaining for 15 min, (iodomethyl)trimethylsilane (300 µL, 2.0 mmol) and HMPA (2 mL) were added to the solution at -78 °C. The mixture was stirred for 30 min at -78 °C, quenched with saturated aqueous NH₄Cl (10 mL) at the same temperature, and extracted with hexane (2x 5 mL). The combined organic extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9) to give a mixture of propargylsilane **12** and alkyne **19**. The mixture was then separated by MPLC (Yamazen Ultra Pack Column B, 26×300 mm, EtOAc/hexane 7:93 to 30:70, 20 mL/min, **12**: T_R = 25.5 min, **19**: T_R = 28.5 min) to afford propargylsilane **12** (1.01 g, 83%) and alkyne **19** (149 mg, 14%). Propargylsilane **12**: a colorless oil; [α]²⁵_D -21.1 (*c* 1.00, CHCl₃); IR (film) 2953, 2866, 1705, 1465, 1435, 1366, 1250, 1170, 1110, 946, 854, 765, 722, 681 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.00–8.68 (m, 1H), 4.80–4.60 (m, 1H), 4.16 (t, *J* = 8.0 Hz, 2H), 4.00–3.90 (m, 1H), 3.83 (brs, 1H), 3.74–3.56 (m, 3H), 2.98 (brs, 1H), 2.74 (d, *J* = 13.5 Hz, 1H), 2.48 (brs, 1H), 2.42 (t, *J* = 11.8 Hz, 1H), 2.26–2.16 (m, 1H), 2.16–2.00 (m, 2H), 1.60–1.48 (m, 4H), 1.50 (s, 9H), 1.43 (m, 2H), 1.10–1.04 (m, 21H), 1.00 (t, *J* = 8.9 Hz, 2H), 0.10 (s, 9H),

0.05 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3 , 60 °C) δ 156.2 (C), 152.8 (C), 126.8 (CH), 102.3 (CH), 81.2 (C), 79.6 (C), 75.5 (C), 64.0 (CH₂), 63.6 (CH₂), 49.8–47.6 (br, CH₂), 45.6 (CH₂), 44.5 (CH₂), 38.0 (CH), 34.6 (CH), 34.3 (C), 30.9 (CH₂), 28.5 (CH₃), 26.7 (CH₂), 20.5 (CH₂), 18.22 (CH₃), 18.19 (CH₂), 12.3 (CH), 7.3 (CH₂), –1.3 (CH₃), –1.8 (CH₃); HRMS (ESI), calcd for $\text{C}_{38}\text{H}_{73}\text{N}_2\text{O}_5\text{Si}_3^+$ ($\text{M}+\text{H}$)⁺ 721.4827, found 721.4825.



Tricyclic core (14): Trifluoroacetic acid (33 μL , 430 μmol) was added to a solution of propargylsilane **12** (208 mg, 288 μmol) and MeCN/EtOH = 9 (29 mL). The solution was heated to 50 °C, maintained for 5h, quenched with Et_3N (80 μL , 580 μmol) at room temperature, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:14) and MPLC (Yamazen Ultra Pack Column B, 26×300 mm, EtOAc/hexane 7:93 to 30:70, 20 mL/min, **14**: T_R = 23.0 min) to afford tricyclic core **14** (158 mg, 85%): a colorless oil; $[\alpha]^{25}_D$ +40.8 (*c* 1.00, CHCl_3); IR (film) 3449, 2945, 2865, 1958, 1696, 1463, 1437, 1365, 1250, 1174, 1105, 839, 765, 682 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 60 °C) δ 5.00–4.55 (m, 3H), 4.19 (t, *J* = 8.6 Hz, 2H), 4.09–3.95 (m, 1H), 3.92–3.75 (m, 1H), 3.73–3.58 (m, 3H), 3.13 (d, *J* = 13.5 Hz, 1H), 2.87 (d, *J* = 12.3 Hz, 1H), 2.63 (d, *J* = 13.2 Hz, 1H), 2.62–2.50 (m, 1H), 2.35 (dd, *J* = 15.8, 6.6 Hz, 1H), 2.15 (ddd, *J* = 13.2, 3.2, 3.2 Hz, 1H), 2.00 (brs, 1H), 1.70–1.66 (m, 1H), 1.55–1.40 (m, 14H), 1.11–1.05 (m, 21H), 1.01 (t, *J* = 8.6 Hz, 2H), 0.06 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3 , 60 °C) δ 205.5 (C), 156.8 (C), 155.8 (C), 99.6 (C), 79.7 (C), 74.0 (CH₂), 63.93 (CH₂), 63.88 (CH₂), 51.1 (CH₂), 49.3 (CH), 49.1 (CH₂), 47.4 (CH₂), 36.0–34.9 (br, C x1, CH x1), 34.8 (CH), 33.0 (CH₂), 29.9 (CH₂), 29.5 (CH₂), 28.6 (CH₃), 27.0 (CH₂), 18.2 (CH₃), 18.1 (CH₂), 12.3 (CH), –1.3 (CH₃); HRMS (ESI), calcd for $\text{C}_{35}\text{H}_{65}\text{N}_2\text{O}_5\text{Si}_2^+$ ($\text{M}+\text{H}$)⁺ 649.4432, found 649.4434.

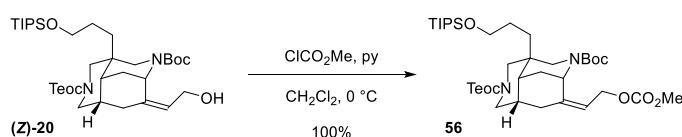
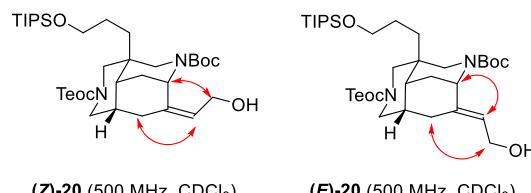


Z-Allylic alcohol ((Z)-20): 2-Methyl-2-butene (1.7 mL, 16 mmol) was added to borane THF complex (0.92 M in THF, 8.0 mL, 7.4 mmol) at 0 °C. The solution was maintained at this temperature for 1 h to give disiamylborane (calculated as 0.76 M in THF).

Disiamylborane (0.76 M, 6.0 mL, 4.6 mmol) was added to a solution of allene **14** (1.48 g, 2.28 mmol) and THF (23 mL) at room temperature. The solution was maintained for 15 min at room temperature, and quenched with 1M NaOH aq (10 mL) and 30% H_2O_2 aq (10 mL) at 0 °C. The resulting mixture was maintained for 1h at 0 °C, and extracted with EtOAc (2x 30 mL). The combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:4) to give *Z*-allylic alcohol **(Z)-20** (1.34 g, 88%) and *E*-allylic alcohol **(E)-20** (65.7 mg, 4%). **(Z)-20:** a colorless oil; $[\alpha]^{27}_D$ +4.3 (*c* 1.00, CHCl_3); IR (film) 3450, 2945, 2866, 1688, 1463, 1437, 1415, 1250, 1175, 1132, 1105, 838, 765, 681 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 60 °C) δ

5.68–5.38 (m, 1H), 5.18–4.90 (m, 1H), 4.46–4.33 (m, 1H), 4.30–4.12 (m, 2H), 4.01 (d, $J = 12.3$ Hz, 1H), 3.92–3.76 (m, 2H), 3.74–3.63 (m, 2H), 3.58 (d, $J = 14.1$ Hz, 1H), 3.38 (brs, 1H), 3.10 (d, $J = 14.1$ Hz, 1H), 2.86 (d, $J = 12.3$ Hz, 1H), 2.63 (d, $J = 13.5$ Hz, 1H), 2.51 (dd, $J = 13.2, 13.2$ Hz, 1H), 2.28 (dd, $J = 16.3, 6.9$ Hz, 1H), 2.15 (ddd, $J = 13.5, 3.5, 3.5$ Hz, 1H), 1.99–1.91 (m, 1H), 1.70–1.65 (m, 1H), 1.58–1.35 (m, 14H), 1.12–1.04 (m, 21H), 1.01 (t, $J = 8.3$ Hz, 2H), 0.06 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3 , 60 °C) δ 156.8 (C), 156.7 (C), 140.4 (C), 125.2 (CH), 80.7 (C), 63.9 (CH_2), 63.9 (CH_2), 57.1 (CH_2), 51.1 (CH_2), 49.1 (CH_2), 48.1 (CH_2), 44.3 (CH), 35.9 (CH), 35.6 (CH), 35.4 (CH_2), 35.0 (C), 33.4 (CH_2), 29.5 (CH_2), 28.7 (CH_3), 27.0 (CH_2), 18.2 (CH_3), 18.1 (CH_2), 12.3 (CH), –1.3 (CH_3); HRMS (ESI), calcd for $\text{C}_{35}\text{H}_{66}\text{N}_2\text{O}_6\text{Si}_2\text{Na}^+$ ($\text{M}+\text{Na}$)⁺ 689.4357, found 689.4359. **(E)-20:** a colorless oil; $[\alpha]^{27}\text{D} +11.1$ (c 1.00, CHCl_3); IR (film) 3461, 2944, 2866, 1693, 1463, 1437, 1414, 1366, 1250, 1175, 1132, 1104, 838, 765, 681 cm^{–1}; ^1H NMR (500 MHz, CDCl_3 , 60 °C) δ 5.80–5.40 (m, 1H), 4.80–4.35 (m, 1H), 4.26–4.13 (m, 3H), 4.09 (dd, $J = 12.9, 5.7$ Hz, 1H), 4.08–3.96 (m, 1H), 3.84 (d, $J = 11.8$ Hz, 1H), 3.74–3.57 (m, 3H), 3.13–2.95 (m, 1H), 2.87 (d, $J = 12.6$ Hz, 1H), 2.70–2.54 (m, 2H), 2.24 (dd, $J = 15.5, 12.9$ Hz, 1H), 2.13 (ddd, $J = 13.5, 3.8, 3.8$ Hz, 1H), 1.98–1.86 (m, 1H), 1.72–1.65 (m, 1H), 1.60–1.38 (m, 14H), 1.12–1.04 (m, 21H), 1.01 (t, $J = 8.3$ Hz, 2H), 0.06 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3 , 1:1 mixture of rotamers) δ 156.8 (C), 156.8 (C), 155.7 (C), 155.4 (C), 139.1 (C), 138.5 (C), 126.6 (CH), 125.5 (CH), 79.7 (C), 79.7 (C), 63.9 (CH_2), 63.9 (CH_2), 63.8 (CH_2), 63.7 (CH_2), 58.4 (CH_2), 58.4 (CH_2), 53.0 (CH), 51.8 (CH), 50.9 (CH_2), 50.7 (CH_2), 49.0 (CH_2), 48.8 (CH_2), 47.1 (CH_2), 47.1 (CH_2), 35.8 (CH), 35.8 (CH), 35.1 (C), 35.0 (CH), 34.8 (CH), 34.7 (C), 32.8 (CH_2), 32.4 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 28.6 (CH_2), 28.6 (CH_3), 28.6 (CH_3), 28.5 (CH_2), 26.8 (CH_2), 26.8 (CH_2), 18.1 (CH_3), 18.1 (CH_3), 17.9 (CH_2), 17.9 (CH_2), 12.0 (CH), 12.0 (CH), –1.3 (CH_3), –1.3 (CH_3); HRMS (ESI), calcd for $\text{C}_{35}\text{H}_{66}\text{N}_2\text{O}_6\text{Si}_2\text{Na}^+$ ($\text{M}+\text{Na}$)⁺ 689.4357, found 689.4354.

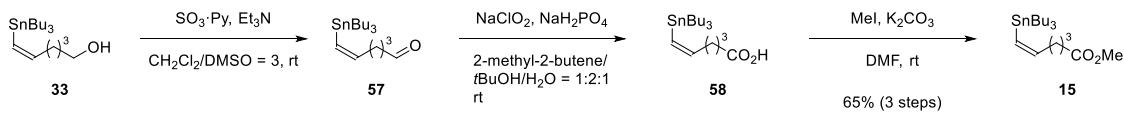
NOESY experiments for **(Z)-20** and **(E)-20**



Allylic carbonate (56): Methyl chloroformate (140 μL , 1.8 mmol) was added to a solution of allylic alcohol **(Z)-20** (614 mg, 920 μmol), pyridine (150 μL , 1.8 mmol) and CH_2Cl_2 (9.0 mL) at 0 °C. This solution was maintained for 2 h at 0 °C, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:4) to give allylic carbonate **56** (670 mg, 100%): a colorless oil; $[\alpha]^{28}\text{D} +49.6$ (c 1.00, CHCl_3); IR (film) 2926, 2865, 1750, 1695, 1463, 1440, 1366, 1266, 1252, 1175, 1131, 945, 838, 682 cm^{–1}; ^1H NMR (500 MHz, CDCl_3 , 60 °C) δ 5.40 (t, $J = 6.9$ Hz, 1H), 5.22–4.90 (m, 2H), 4.78–4.46 (m, 1H), 4.25–4.12 (m,

2H), 4.09–3.94 (m, 1H), 3.90–3.79 (m, 1H), 3.77 (s, 3H), 3.74–3.56 (m, 3H), 3.07 (d, J = 14.4 Hz, 1H), 2.85 (d, J = 12.3 Hz, 1H), 2.63 (d, J = 12.6 Hz, 1H), 2.63–2.50 (m, 1H), 2.32 (dd, J = 16.3, 6.3 Hz, 1H), 2.16 (ddd, J = 13.5, 3.4, 3.4 Hz, 1H), 2.02–1.91 (m, 1H), 1.72–1.66 (m, 1H), 1.60–1.35 (m, 14H), 1.12–1.04 (m, 21H), 1.01 (t, J = 8.3 Hz, 2H), 0.06 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3 , 1:1 mixture of rotamers) δ 156.8 (C), 156.8 (C), 155.8 (C), 155.8 (C), 155.3 (C), 155.2 (C), 143.6 (C), 142.9 (C), 119.7 (CH), 118.6 (CH), 80.4 (C), 79.8 (C), 64.2 (CH_2), 64.1 (CH_2), 63.9 (CH_2), 63.8 (CH_2), 63.8 (CH_2), 63.7 (CH_2), 54.8 (CH_3), 54.7 (CH_3), 50.8 (CH_2), 50.7 (CH_2), 48.8 (CH_2), 48.6 (CH_2), 47.3 (CH_2), 47.1 (CH_2), 45.1 (CH), 43.9 (CH), 35.6 (CH), 35.5 (CH), 35.4 (CH), 35.1 (CH_2), 35.1 (CH_2), 34.9 (C), 34.8 (CH), 34.7 (C), 32.8 (CH_2), 32.7 (CH_2), 29.8 (CH_2), 29.3 (CH_2), 28.6 (CH_3), 28.5 (CH_3), 26.8 (CH_2), 26.8 (CH_2), 18.1 (CH_3), 18.1 (CH_3), 17.9 (CH_2), 17.9 (CH_2), 12.0 (CH), 12.0 (CH), –1.3 (CH_3), –1.3 (CH_3); HRMS (ESI), calcd for $\text{C}_{37}\text{H}_{68}\text{N}_2\text{O}_8\text{Si}_2\text{Na}^+$ ($\text{M}+\text{Na}$)⁺ 747.4412, found 747.4404.

Synthesis of Z-vinylstannane 15

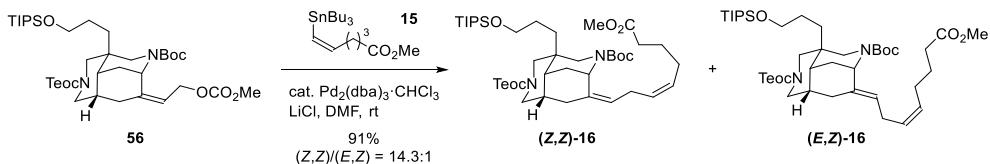


Vinylstannane (15): Sulfur trioxide pyridine complex (2.51 g, 15.8 mmol) was added to a solution of alcohol **33** (2.23 g, 5.73 mmol), Et_3N (4.4 mL, 32 mmol), DMSO (7.5 mL) and CH_2Cl_2 (23 mL) at room temperature. The resulting solution was maintained for 1 h, quenched with saturated aqueous NH_4Cl (30 mL), and extracted with hexane (2x 30 mL). The combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4 , and concentrated to give the corresponding aldehyde **57**, which was unstable and immediately used in the next reaction without further purification.

A solution of sodium chlorite (4.15 g, 45.8 mmol), sodium phosphate monobasic (2.75 g, 22.9 mmol) and H_2O (14 mL) was added to a solution of the crude aldehyde **57**, 2-methyl-2-butene (14 mL) and *t*BuOH (28 mL) at room temperature. The reaction mixture was vigorously stirred for 2 h, quenched with saturated aqueous NH_4Cl (30 mL), and extracted with EtOAc (2x 30 mL). The combined organic extracts were washed with brine (30 mL), and dried over Na_2SO_4 . The solution was concentrated to give the corresponding carboxylic acid **58** which was immediately used in the next reaction without further purification.

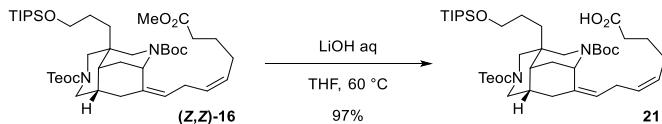
Methyl iodide (1.4 mL, 23 mmol) was added to a mixture of the crude carboxylic acid **58**, potassium carbonate (2.38 g, 17.2 mmol) and DMF (28 mL) at room temperature. The resulting mixture was stirred for 2 h at room temperature, quenched with saturated aqueous NH_4Cl (20 mL) at 0 °C, and extracted with hexane (2x 20 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4 and concentrated. The residue was filtrated through a pad of basic alumina to afford Z-vinylstannane **15** (1.55 g, 65 % for 3 steps): a colorless oil; IR (film) 2957, 2926, 2872, 2853, 1744, 1598, 1459, 1436, 1376, 1246, 1197, 1173, 1142, 1071, 1001, 873, 864, 692, 596, 504 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 6.47 (dt, J = 12.3, 7.2 Hz, J (^{117}Sn - and ^{119}Sn -H) = 142.0, 135.7 Hz, 1H), 5.83 (dt, J = 12.3, 1.2 Hz, J (^{117}Sn - and ^{119}Sn -H) = 82.8, 57.9 Hz, 1H), 3.67 (s, 3H), 2.32 (t, J = 7.4 Hz, 2H), 2.06 (tdd, J = 7.2, 7.2, 1.2 Hz, 2H), 1.72 (tt, J = 7.4, 7.2 Hz, 2H), 1.56–1.40 (m, 6H), 1.30 (qt, J = 7.4, 7.4 Hz, 6H), 0.97–0.81 (m, 15H); ^{13}C NMR (125 MHz, CDCl_3)

δ 174.1 (C), 147.8 (CH), 129.4 (CH), 51.6 (CH₃), 36.4 (CH₂), 33.7 (CH₂), 29.3 (CH₂), 27.5 (CH₂), 25.1 (CH₂), 13.8 (CH₃), 10.4 (CH₂); HRMS (ESI), calcd for C₁₉H₃₈O₂SnK⁺ (M+K)⁺ 457.1531, found 457.1534.

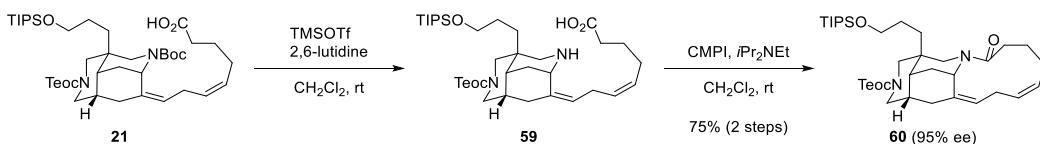


Skipped diene ((Z,Z)-16): A solution of allylic carbonate **56** (667 mg, 920 μ mol), vinylstannane **15** (960 mg, 2.30 mmol) and DMF (9.2 mL) was added to a mixture of LiCl (195 mg, 4.60 mmol) and Pd₂(dba)₃·CHCl₃ (47.6 mg, 46.0 μ mol) at room temperature. After stirring at room temperature for 1 h, the mixture was quenched with KF aq (1 M, 5 mL) at 0 °C, stirred for 1 h at room temperature, and extracted with hexane (3x 10 mL). The combined organic extracts were washed with brine (5 mL), dried over Na₂SO₄ and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:19 to 1:14) to afford a mixture of skipped dienes **(Z,Z)-16** and **(E,Z)-16**. Two skipped dienes were then separated by MPLC (Yamazen Ultra Pack Column B, 26×300 mm, Et₂O/hexane 1:4 to 2:3, 20 mL/min, **(Z,Z)-16**: T_R = 32.0 min, **(E,Z)-16**: T_R = 36.0 min) to afford skipped diene **(Z,Z)-16** (611 mg, 85%) and skipped diene **(E,Z)-16** (42.6 mg, 6%). Skipped diene **(Z,Z)-16**: a colorless oil; $[\alpha]^{26}_D$ +26.5 (*c* 1.00, CHCl₃); IR (film) 2946, 2866, 1741, 1692, 1463, 1436, 1414, 1250, 1175, 1131, 859, 839, 765, 682 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.40–5.27 (m, 2H), 5.23–4.90 (m, 2H), 4.25–4.10 (m, 2H), 4.10–3.91 (m, 1H), 3.91–3.78 (m, 1H), 3.77–3.55 (m, 6H), 3.12 (d, *J* = 14.0 Hz, 1H), 3.05–2.90 (m, 2H), 2.84 (d, *J* = 13.2 Hz, 1H), 2.61 (d, *J* = 12.6 Hz, 1H), 2.55 (d, *J* = 13.7, 13.7 Hz, 1H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.26 (dd, *J* = 13.7, 6.9 Hz, 1H), 2.16–2.07 (m, 3H), 1.98–1.89 (m, 1H), 1.70 (tt, *J* = 7.5, 7.5 Hz, 2H), 1.78–1.63 (m, 1H), 1.60–1.40 (m, 13H), 1.35–1.26 (m, 1H), 1.13–1.04 (m, 21H), 1.00 (t, *J* = 8.3 Hz, 2H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 174.3 (C), 174.1 (C), 156.8 (C), 156.8 (C), 155.4 (C), 155.2 (C), 136.8 (C), 136.1 (C), 129.4 (CH), 129.3 (CH), 129.0 (CH), 128.8 (CH), 124.9 (CH), 123.9 (CH), 79.8 (C), 79.4 (C), 63.9 (CH₂), 63.9 (CH₂), 63.8 (CH₂), 63.8 (CH₂), 51.6 (CH₃), 51.5 (CH₃), 50.9 (CH₂), 50.7 (CH₂), 49.0 (CH₂), 48.7 (CH₂), 47.2 (CH₂), 47.2 (CH₂), 45.2 (CH), 44.0 (CH), 35.9 (CH), 35.7 (CH), 35.6 (CH₂), 35.6 (CH), 35.3 (CH₂), 35.22 (C), 35.18 (CH), 34.9 (C), 33.60 (CH₂), 33.56 (CH₂), 32.8 (CH₂), 32.5 (CH₂), 30.2 (CH₂), 29.7 (CH₂), 28.63 (CH₃), 28.57 (CH₃), 26.9 (CH₂), 26.9 (CH₂), 26.7 (CH₂), 26.6 (CH₂), 26.1 (CH₂), 26.0 (CH₂), 25.0 (CH₂), 24.9 (CH₂), 18.2 (CH₃), 17.9 (CH₂), 17.9 (CH₂), 12.1 (CH), 12.1 (CH), -1.3 (CH₃), -1.3 (CH₃); HRMS (ESI), calcd for C₄₂H₇₆N₂O₇Si₂Na⁺ (M+Na)⁺ 799.5089, found 799.5090. Skipped diene **(E,Z)-16**: a colorless oil; $[\alpha]^{24}_D$ +2.1 (*c* 1.00, CHCl₃); IR (film) 2946, 2866, 1741, 1694, 1463, 1436, 1414, 1366, 1318, 1250, 1175, 1131, 882, 860, 839, 765, 687 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.54–5.06 (m, 3H), 4.78–4.36 (m, 1H), 4.25–4.10 (m, 2H), 4.12–3.94 (m, 1H), 3.92–3.76 (m, 1H), 3.74–3.56 (m, 5H), 3.61 (d, *J* = 14.4 Hz, 1H), 3.16–2.94 (m, 1H), 2.87 (d, *J* = 13.5 Hz, 1H), 2.77 (ddd, *J* = 16.1, 6.3, 6.3 Hz, 1H), 2.70–2.50 (m, 3H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.26–2.16 (m, 1H), 2.16–2.05 (m, 3H), 1.98–1.85 (m, 1H), 1.70 (tt, *J* = 7.5, 7.5 Hz, 2H), 1.74–1.64 (m, 1H), 1.60–1.37 (m, 14H), 1.13–1.04 (m, 21H), 1.01 (t, *J* = 8.3 Hz, 2H), 0.06 (s, 9H), ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 174.1 (C), 174.1 (C), 156.8 (C), 156.8 (C), 155.9 (C), 155.3 (C),

136.6 (C), 135.9 (C), 129.1 (CH), 129.0 (CH), 128.91 (CH), 128.87 (CH), 126.1 (CH), 124.8 (CH), 79.5 (C), 79.5 (C), 63.9 (CH₂), 63.8 (CH₂), 63.8 (CH₂), 63.7 (CH₂), 53.3 (CH), 52.0 (CH), 51.6 (CH₃), 51.6 (CH₃), 50.9 (CH₂), 50.7 (CH₂), 49.1 (CH₂), 48.9 (CH₂), 47.2 (CH₂), 47.0 (CH₂), 36.0 (CH), 35.5 (CH), 35.2 (C), 35.1 (CH), 34.74 (CH), 34.69 (C), 33.5 (CH₂), 33.5 (CH₂), 32.8 (CH₂), 32.3 (CH₂), 29.7 (CH₂), 29.6 (CH₂), 28.6 (CH₃), 28.6 (CH₃), 28.4 (CH₂), 28.4 (CH₂), 26.8 (CH₂), 26.8 (CH₂), 26.7 (CH₂), 26.7 (CH₂), 25.5 (CH₂), 25.4 (CH₂), 24.8 (CH₂), 24.8 (CH₂), 18.1 (CH₃), 18.1 (CH₃), 17.9 (CH₂), 17.9 (CH₂), 12.0 (CH), 12.0 (CH), -1.3 (CH₃), -1.3 (CH₃); HRMS (ESI), calcd for C₄₂H₇₆N₂O₇Si₂Na⁺ (M+Na)⁺ 799.5089, found 799.5094.



Carboxylic acid (21): Aqueous LiOH (1 M, 2.6 mL) was added to a solution of (Z,Z)-16 (611 mg, 786 μmol) and THF (5.3 mL). The mixture was heated to 60 °C, maintained for 10 h at 60 °C, quenched with saturated aqueous NH₄Cl (5 mL) at room temperature, and extracted with EtOAc (2x 10 mL). The combined organic extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:4) to give carboxylic acid 21 (583 mg, 97%): a colorless oil; [α]²⁹_D +26.1 (*c* 1.00, CHCl₃); IR (film) 3158, 2944, 2866, 1736, 1691, 1463, 1438, 1415, 1366, 1321, 1250, 1175, 1132, 882, 858, 839, 765, 681 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.42–5.25 (m, 2H), 5.25–4.90 (m, 2H), 4.30–4.10 (m, 2H), 4.10–3.90 (m, 1H), 3.90–3.77 (m, 1H), 3.77–3.58 (m, 3H), 3.13 (d, *J* = 12.9 Hz, 1H), 3.05–2.74 (m, 2H), 2.84 (d, *J* = 12.3 Hz, 1H), 2.70–2.46 (m, 2H), 2.36 (t, *J* = 7.5 Hz, 2H), 2.32–2.20 (m, 1H), 2.20–2.06 (m, 3H), 1.98–1.86 (m, 1H), 1.72 (tt, *J* = 7.5, 7.2 Hz, 2H), 1.70–1.63 (m, 1H), 1.60–1.36 (m, 13H), 1.36–1.25 (m, 1H), 1.13–1.03 (m, 21H), 1.01 (t, *J* = 8.4 Hz, 2H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 1:1 mixture of rotamers) δ 179.0 (C), 178.7 (C), 156.9 (C), 156.9 (C), 155.3 (C), 155.3 (C), 136.8 (C), 136.0 (C), 129.6 (CH), 129.4 (CH), 128.9 (CH), 128.8 (CH), 125.1 (CH), 123.9 (CH), 79.9 (C), 79.7 (C), 63.9 (CH₂), 63.9 (CH₂), 63.8 (CH₂), 63.8 (CH₂), 50.9 (CH₂), 50.7 (CH₂), 49.0 (CH₂), 48.7 (CH₂), 47.1 (CH₂), 47.1 (CH₂), 45.2 (CH), 44.1 (CH), 35.9 (CH), 35.7 (CH), 35.5 (CH₂), 35.5 (CH), 35.3 (C), 35.2 (CH₂), 35.1 (CH), 34.9 (C), 33.5 (CH₂), 33.5 (CH₂), 32.7 (CH₂), 32.5 (CH₂), 30.1 (CH₂), 29.7 (CH₂), 28.61 (CH₃), 28.58 (CH₃), 26.8 (CH₂), 26.8 (CH₂), 26.7 (CH₂), 26.5 (CH₂), 26.0 (CH₂), 26.0 (CH₂), 24.73 (CH₂), 24.67 (CH₂), 18.1 (CH₃), 18.1 (CH₃), 17.9 (CH₂), 17.9 (CH₂), 12.0 (CH), 12.0 (CH), -1.3 (CH₃), -1.3 (CH₃); HRMS (ESI), calcd for C₄₁H₇₄N₂O₇Si₂Na⁺ (M+Na)⁺ 785.4932, found 785.4937.



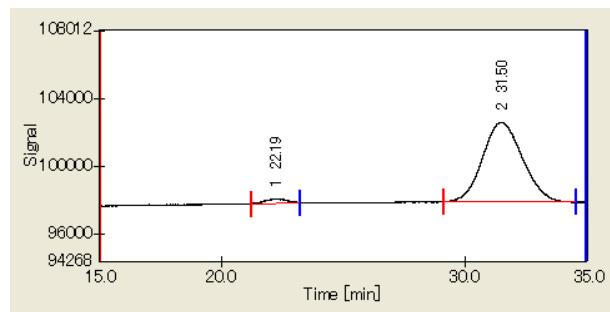
Tetracyclic core (60): 2,6-Lutidine (74 μ L, 640 μ mol) and TMSOTf (58 μ L, 320 μ mol) were added to a solution of carboxylic acid 21 (122 mg, 160 μ mol) and CH₂Cl₂ (1.6 mL) at room temperature. 2,6-Lutidine (7.4 μ L, 64 μ mol) and TMSOTf (5.8 μ L, 32 μ mol) were added to the solution every 15 min until TLC analysis indicated the complete consumption of carboxylic acid 21 (total: 2,6-lutidine 5.6 equiv., TMSOTf 2.8

equiv.). The resulting solution was quenched with Et₃N (76 µL, 550 µmol) and concentrated. The residue was filtrated through a pad of silica gel (CHCl₃/MeOH 29:1) to give amino acid **59**, which was immediately used in the next reaction without further purification.

2-Chloro-1-methylpyridinium iodide (CMPI, 204 mg, 800 µmol) was added to a solution of the above amino acid **59**, DIPEA (140 µL, 800 µmol) and CH₂Cl₂ (160 mL) at room temperature. The solution was maintained for 16 h at room temperature, quenched with saturated aqueous NH₄Cl (50 mL), and extracted with CH₂Cl₂ (2x 50 mL). The combined organic extracts were washed with brine (50 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:4) to give tetracyclic core **60** (77.0 mg, 75% for 2 steps, 95% ee by HPLC (CHIRALPAK AD-H, 250×4.6 mm, UV 210 nm, iPrOH/hexane 1:20 (v/v), 1.0 mL/min, **60**: T_R= 31.5 min, *ent*-**60**: T_R= 22.2 min)): a colorless oil; [α]²⁸_D +87.0 (c 1.00, CHCl₃); IR (film) 2944, 2865, 1697, 1633, 1438, 1249, 1103, 923, 882, 859, 764, 731, 681 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.62–5.48 (m, 1H), 5.48–5.34 (m, 1H), 5.34–5.10 (m, 1H), 5.10–4.90 (m, 1H), 4.38–4.08 (m, 3H), 4.08–3.92 (m, 1H), 3.94–3.75 (m, 1H), 3.74–3.52 (m, 2H), 3.22–3.02 (m, 1H), 3.00–2.77 (m, 2H), 2.76–2.35 (m, 4H), 2.35–1.88 (m, 6H), 1.88–1.66 (m, 2H), 1.64–1.23 (m, 6H), 1.12–0.98 (m, 23H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 173.5 (C), 156.8 (C), 137.2 (C), 129.2 (CH), 128.0 (CH), 125.5 (CH), 63.91 (CH₂), 63.86 (CH₂), 50.9 (CH₂), 49.1 (CH₂), 48.1 (CH), 45.2 (CH₂), 36.3 (C), 35.8 (CH), 35.1 (CH), 34.5 (CH₂), 32.9 (CH₂), 32.5 (CH₂), 30.6 (CH₂), 27.8 (CH₂), 26.9 (CH₂), 26.5 (CH₂), 25.8 (CH₂), 18.2 (CH₃), 18.2 (CH₂), 12.3 (CH), -1.3 (CH₃); HRMS (ESI), calcd for C₃₆H₆₅N₂O₄Si₂⁺ (M+H)⁺ 645.4483, found 645.4487.

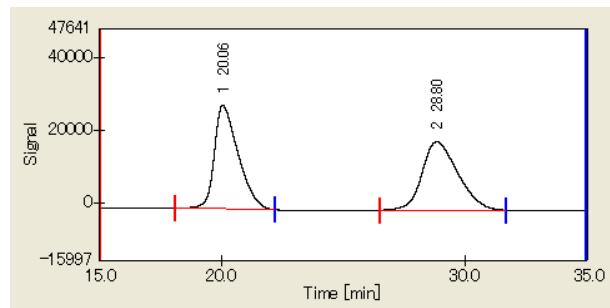
Chiral HPLC chart of **60** (95% ee)

CHIRALPAK AD-H, 250×4.6 mm, UV 210 nm, iPrOH/hexane 1:20 (v/v), 1.0 mL/min

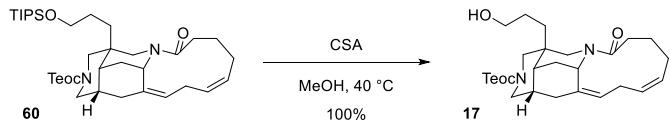


No.	T _R	Area	Height	Area (%)
1	22.19	14216.700	254	2.5995
2	31.50	532685.700	4726	97.4005

Chiral HPLC chart of *racemic*-**60**

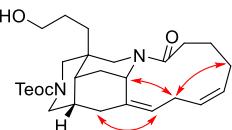


No.	T _R	Area	Height	Area (%)
1	20.06	1927767.200	28426	50.2559
2	28.80	1908134.050	18767	49.7441



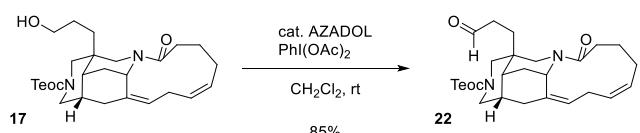
Common intermediate (17): 10-Camphorsulfonic acid (CSA, 55.3 mg, 238 µmol) was added to a solution of tetracyclic core **60** (77.0 mg, 119 µmol) and MeOH (2.4 mL) at room temperature. The solution was heated to 40 °C, maintained for 1 h at 40 °C, quenched with Et₃N (66 µL, 480 µmol) at room temperature, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/MeOH 19:1) to give common intermediate **17** (58.2 mg, 100%): a white amorphous solid; mp 45.0–47.0 °C; [α]²⁶_D +43.1 (c 1.00, CHCl₃); IR (film) 3413, 2950, 2921, 1693, 1613, 1438, 1249, 1059, 936, 859, 839, 754, 698 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.70–5.50 (m, 1H), 5.46–5.32 (m, 1H), 5.32–5.15 (m, 1H), 5.12–4.94 (m, 1H), 4.39–4.26 (m, 1H), 4.25–4.15 (m, 2H), 4.10–3.80 (m, 2H), 3.70–3.60 (m, 1H), 3.55–3.45 (m, H), 3.10 (ddd, *J* = 14.9, 9.5, 9.5 Hz, 1H), 2.94–2.76 (m, 2H), 2.76–2.64 (m, 1H), 2.64–2.40 (m, 3H), 2.35–1.90 (m, 6H), 1.90–1.74 (m, 1H), 1.74–1.53 (m, 4H), 1.53–1.36 (m, 2H), 1.22–1.09 (m, 1H), 1.02 (t, *J* = 8.3 Hz, 2H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 173.8 (C), 156.8 (C), 136.8 (C), 129.0 (CH), 128.1 (CH), 126.4 (CH), 63.9 (CH₂), 62.9 (CH₂), 50.9 (CH₂), 49.2 (CH₂), 48.4 (CH), 43.5 (CH₂), 37.1 (CH), 36.8 (C), 34.9 (CH), 33.9 (CH₂), 32.6 (CH₂), 31.8 (CH₂), 30.6 (CH₂), 27.8 (CH₂), 26.5 (CH₂), 26.3 (CH₂), 25.7 (CH₂), 18.2 (CH₂), –1.3 (CH₃); HRMS (ESI), calcd for C₂₇H₄₅N₂O₄Si⁺ (M+H)⁺ 489.3149, found 489.3153.

NOESY experiment for 17

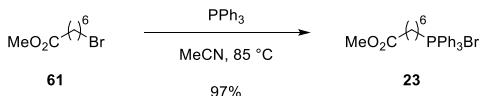


17 (500 MHz, CDCl₃, 60 °C)

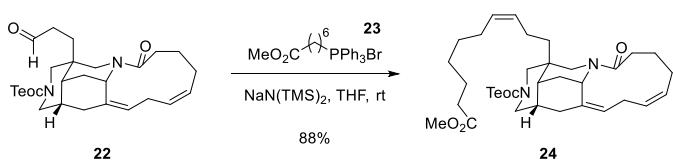
A-4. Total Synthesis of Madangamine C



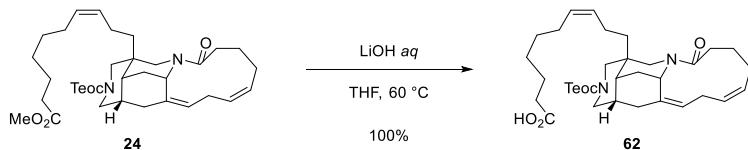
Aldehyde (22): AZADOL® (1.8 mg, 11.9 µmol) and PhI(OAc)₂ (57.5 mg, 179 µmol) were added to a solution of alcohol **17** (58.2 mg, 119 µmol) and CH₂Cl₂ (2.4 mL) at room temperature. The solution was maintained for 17 h, quenched with saturated aqueous Na₂S₂O₃ (2 mL), and extracted with CH₂Cl₂ (2x 2 mL). The combined organic extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:2 to EtOAc) to give aldehyde **22** (49.2 mg, 85%): a colorless oil; [α]_D²⁶ +121.6 (*c* 1.00, CHCl₃); IR (film) 2951, 2919, 1724, 1693, 1626, 1439, 1248, 1087, 1044, 936, 859, 839, 761, 697 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 9.73 (s, 1H), 5.70–5.48 (m, 1H), 5.46–5.31 (m, 1H), 5.30–5.14 (m, 1H), 5.12–4.92 (m, 1H), 4.34–4.10 (m, 3H), 4.08–3.75 (m, 2H), 3.09 (ddd, *J* = 14.9, 9.5, 9.2 Hz, 1H), 2.96–2.75 (m, 2H), 2.75–2.41 (m, 5H), 2.33 (ddd, *J* = 17.2, 11.2, 5.2 Hz, 1H), 2.28–1.93 (m, 6H), 1.91–1.72 (m, 2H), 1.71–1.57 (m, 1H), 1.50–1.32 (m, 3H), 1.00 (t, *J* = 8.6 Hz, 2H), 0.05 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 201.1 (CH), 173.4 (C), 156.6 (C), 136.6 (C), 129.0 (CH), 128.0 (CH), 126.4 (CH), 64.0 (CH₂), 50.8 (CH₂), 49.2 (CH₂), 48.2 (CH), 43.1 (CH₂), 38.3 (CH₂), 37.1 (CH), 36.3 (C), 34.8 (CH), 34.0 (CH₂), 32.5 (CH₂), 30.6 (CH₂), 27.8 (CH₂), 27.6 (CH₂), 26.3 (CH₂), 25.7 (CH₂), 18.2 (CH₂), -1.3 (CH₃); HRMS (ESI), calcd for C₂₇H₄₃N₂O₄Si⁺ (M+H)⁺ 487.2992, found 487.2991.



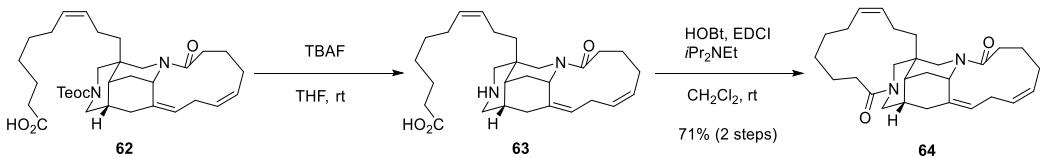
Phosphonium salt (23): Triphenylphosphine (451 mg, 1.72 mmol) was added to a solution of bromide **61**¹² (192 mg, 861 µmol) and MeCN (1.1 mL) at room temperature. The resulting solution was heated to 85 °C, maintained for 35 h at 85 °C, and concentrated. The residue was purified by silica gel column chromatography (MeOH/CHCl₃ 1:39 to 1:19) to give phosphonium salt **23** (407 mg, 97%): a colorless oil; IR (film) 2937, 2865, 1729, 1626, 1439, 1201, 1113, 997, 751, 724, 692, 535, 510 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.91–7.82 (m, 6H), 7.83–7.75 (m, 3H), 7.73–7.66 (m, 6H), 3.93–3.81 (m, 2H), 3.62 (s, 3H), 2.26 (t, *J* = 9.2 Hz, 2H), 1.75–1.49 (m, 6H), 1.32 (tt, *J* = 7.6, 7.3 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 174.0 (C), 135.0 (d, *J* = 2.4 Hz, CH), 133.5 (d, *J* = 10.1 Hz, CH), 130.5 (d, *J* = 12.5 Hz, CH), 118.1 (d, *J* = 85.3 Hz, C), 51.4 (CH₃), 33.7 (CH₂), 29.9 (d, *J* = 16.1 Hz, CH₂), 28.4 (CH₂), 24.2 (CH₂), 22.6 (d, *J* = 49.5 Hz, CH₂), 22.3 (d, *J* = 4.2 Hz, CH₂); HRMS (ESI), calcd for C₂₆H₃₀O₂P⁺ (M–Br)⁺ 405.1983, found 405.1980.



Methyl ester (24): In a glove box, sodium hexamethyldisilazide (25.1 mg, 137 μmol) was added to a mixture of phosphonium salt **23** (67.9 mg, 140 μmol) and THF (1.0 mL) at room temperature. After stirring for 5 min, a solution of aldehyde **22** (19.6 mg, 40.3 μmol) and THF (1.0 mL) was added to the mixture of the ylide. The reaction vessel was removed from the glove box, and stirred at room temperature for 1h. The mixture was quenched with saturated aqueous NH_4Cl (2 mL), and extracted with EtOAc (2x 5 mL). The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9 to 1:3) to give methyl ester **24** (21.8 mg, 88%): a colorless oil; $[\alpha]^{26}_D +92.0$ (*c* 1.00, CHCl_3); IR (film) 2926, 2856, 1738, 1695, 1631, 1437, 1249, 859, 839 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 60 °C) δ 5.62–5.47 (m, 1H), 5.47–5.10 (m, 4H), 5.10–4.88 (m, 1H), 4.30–4.10 (m, 3H), 4.10–3.76 (m, 2H), 3.66 (s, 3H), 3.12 (dt, *J* = 14.4, 9.5 Hz, 1H), 3.00–2.76 (m, 2H), 2.76–2.38 (m, 3H), 2.64 (d, *J* = 13.5 Hz, 1H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.34–1.86 (m, 10H), 1.85–1.52 (m, 5H), 1.50–1.18 (m, 7H), 1.01 (t, *J* = 8.3 Hz, 2H), 0.05 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3 , 60 °C) δ 174.2 (C), 173.4 (C), 156.8 (C), 137.1 (C), 130.3 (CH), 129.5 (CH), 129.2 (CH), 128.0 (CH), 125.7 (CH), 63.9 (CH₂), 51.4 (CH₃), 50.9 (CH₂), 49.2 (CH₂), 48.1 (CH), 44.7 (CH₂), 36.7 (C), 36.3 (CH₂), 36.1 (CH), 35.1 (CH), 34.4 (CH₂), 34.2 (CH₂), 32.9 (CH₂), 30.7 (CH₂), 29.5 (CH₂), 29.0 (CH₂), 27.8 (CH₂), 27.2 (CH₂), 26.5 (CH₂), 25.8 (CH₂), 25.1 (CH₂), 21.3 (CH₂), 18.2 (CH₂), -1.3 (CH₃); HRMS (ESI), calcd for $\text{C}_{35}\text{H}_{57}\text{N}_2\text{O}_5\text{Si}^+$ ($\text{M}+\text{H}$)⁺ 613.4037, found 613.4037.

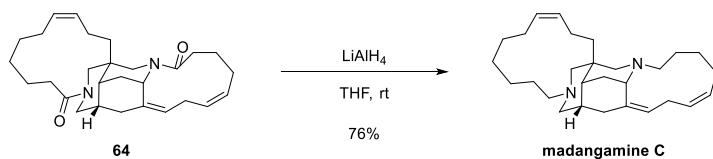


Carboxylic acid (62): Aqueous LiOH (1M, 0.6 mL) was added to a solution of ester **24** (21.8 mg, 35.6 μmol) and THF (1.2 mL). The mixture was heated to 60 °C, maintained for 5 h at that temperature, quenched with saturated aqueous NH_4Cl (1 mL) at room temperature, and extracted with EtOAc (2x 5 mL). The combined organic extracts were washed with brine (2 mL), dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:1) to give carboxylic acid **62** (21.3 mg, 100%): a colorless oil; $[\alpha]^{26}_D +104.1$ (*c* 1.00, CHCl_3); IR (film) 3141, 2925, 2855, 1696, 1631, 1590, 1439, 1249, 932, 859, 839 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , 60 °C) δ 5.66–5.48 (m, 1H), 5.48–5.10 (m, 4H), 5.10–4.90 (m, 1H), 4.34–4.10 (m, 3H), 4.10–3.74 (m, 2H), 3.11 (dt, *J* = 14.0, 9.2 Hz, 1H), 3.00–2.77 (m, 2H), 2.77–2.40 (m, 3H), 2.63 (d, *J* = 13.2 Hz, 1H), 2.38–2.25 (m, 3H), 2.24–1.86 (m, 9H), 1.86–1.56 (m, 5H), 1.54–1.15 (m, 7H), 1.02 (t, *J* = 8.3 Hz, 2H), 0.06 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3 , 60 °C) δ 176.7 (C), 173.9 (C), 156.9 (C), 136.8 (C), 130.4 (CH), 129.5 (CH), 129.2 (CH), 128.0 (CH), 126.0 (CH), 64.0 (CH₂), 51.0 (CH₂), 49.2 (CH₂), 48.2 (CH), 44.7 (CH₂), 36.8 (C), 36.3 (CH), 36.2 (CH₂), 35.1 (CH), 34.3 (CH₂), 34.1 (CH₂), 32.9 (CH₂), 30.7 (CH₂), 29.1 (CH₂), 28.7 (CH₂), 27.8 (CH₂), 27.1 (CH₂), 26.5 (CH₂), 25.8 (CH₂), 24.8 (CH₂), 21.3 (CH₂), 18.2 (CH₂), -1.3 (CH₃); HRMS (ESI), calcd for $\text{C}_{34}\text{H}_{55}\text{N}_2\text{O}_5\text{Si}^+$ ($\text{M}+\text{H}$)⁺ 599.3880, found 599.3878.



Pentacyclic bislactam (64): Tetrabutylammonium fluoride (1.0 M in THF, 160 μ L, 160 μ mol) was added to a solution of carboxylic acid **62** (23.4 mg, 39.1 μ mol) and THF (3.9 mL) at room temperature. This solution was maintained for 5 h, and concentrated to give amino acid **63**, which was immediately used in the next reaction without further purification.

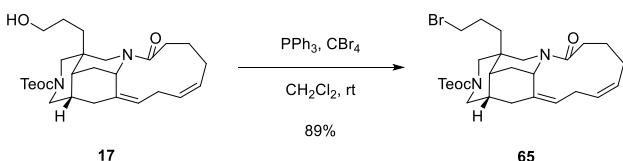
1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI, 37.5 mg, 196 μ mol) was added to a solution of the above amino acid **63**, *i*Pr₂EtN (67 μ L, 390 μ mol), HOBr (26.6 mg, 196 μ mol), and CH₂Cl₂ (39 mL) at room temperature. The solution was maintained for 24 h, quenched with saturated aqueous NH₄Cl (20 mL), and extracted with CH₂Cl₂ (2x 20 mL). The combined organic extracts were washed with brine (10 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:1 to 3:1) to pentacyclic bislactam **64** (12.1 mg, 71% for 2 steps): a colorless oil; $[\alpha]^{26}_D$ +143.6 (*c* 1.00, CHCl₃); IR (film) 2925, 2856, 1628, 1446, 1270, 1247, 923, 730 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.60 (t, *J* = 7.8 Hz, 1H), 5.50 (td, *J* = 10.6, 4.3 Hz, 1H), 5.45–5.30 (m, 2H), 5.20 (td, *J* = 9.8, 4.3 Hz, 1H), 4.98 (brs, 1H), 4.45 (d, *J* = 13.8 Hz, 1H), 4.26 (d, *J* = 13.2 Hz, 1H), 3.59 (d, *J* = 13.7 Hz, 1H), 3.17 (dt, *J* = 14.6, 10.1 Hz, 1H), 2.93 (d, *J* = 13.7 Hz, 1H), 2.81 (d, *J* = 13.8 Hz, 1H), 2.76–2.66 (m, 2H), 2.59–2.21 (m, 7H), 2.20–1.48 (m, 13H), 1.48–1.10 (m, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 174.0 (C), 173.8 (C), 136.2 (C), 129.7 (CH), 129.5 (CH), 128.3 (CH), 128.0 (CH), 126.8 (CH), 52.5 (CH₂), 48.0 (CH), 46.4 (CH₂), 43.6 (CH₂), 39.7 (CH), 36.6 (C), 34.43 (CH), 34.36 (CH₂), 34.1 (CH₂), 33.7 (CH₂), 32.5 (CH₂), 30.3 (CH₂), 28.2 (CH₂), 26.0 (CH₂), 25.9 (CH₂), 25.5 (CH₂), 25.0 (CH₂), 23.3 (CH₂), 22.9 (CH₂), 21.7 (CH₂); HRMS (ESI), calcd for C₂₈H₄₁N₂O₂⁺ (M+H)⁺ 437.3168, found 437.3167.



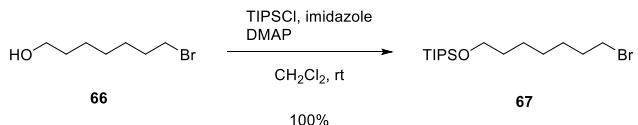
Madangamine C: In a glove box, LiAlH₄ (1.0 M in THF, 140 μ L, 140 μ mol) was added to a solution of pentacyclic bislactam **64** (6.3 mg, 14 μ mol) and THF (1.4 mL) at room temperature. The reaction vessel was removed from the glove box, stirred at room temperature for 6 h, cooled to 0 °C, and quenched with a few drops of distilled water. The resulting suspension was dried over Na₂SO₄, and filtrated. The solid was washed with Et₂O (3 mL). The resulting solution was then concentrated. The residue was purified by silica gel column chromatography (Et₂O/hexane 1:19 to 1:5) to give madangamine C (4.5 mg, 76%): a colorless oil; $[\alpha]^{26}_D$ +132.9 (*c* 0.09, EtOAc); IR (film) 2928, 2857, 1458, 1438, 1126, 722, 685, 497 cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 65 °C) δ 5.49–5.35 (m, 3H), 5.20 (dt, *J* = 11.5, 3.2 Hz, 1H), 5.23–5.13 (m, 1H), 3.72 (t, *J* = 3.2 Hz, 1H), 3.42 (dd, *J* = 12.1, 1.2 Hz, 1H), 3.35 (dt, *J* = 13.5, 11.5 Hz, 1H), 3.13 (ddt, *J* = 16.3, 12.1, 3.2 Hz, 1H), 2.83 (ddd, *J* = 13.8, 11.8, 5.2 Hz, 1H), 2.74 (dd, *J* = 12.1, 1.7 Hz, 1H), 2.73 (ddd, *J* = 12.0, 3.7, 2.0 Hz, 1H), 2.68 (d,

J = 12.1 Hz, 1H), 2.60 (td, *J* = 13.8, 4.3 Hz, 1H), 2.36 (dt, *J* = 12.6, 3.2 Hz, 1H), 2.33 (d, *J* = 10.9 Hz, 1H), 2.36–2.01 (m, 9H), 2.16 (dd, *J* = 10.9, 3.5 Hz, 1H), 1.89–1.78 (m, 2H), 1.76–1.57 (m, 3H), 1.57–1.07 (m, 10H), 1.53 (d, *J* = 12.1 Hz, 1H), 1.27 (dt, *J* = 12.6, 3.2 Hz, 1H), 0.90 (ddt, *J* = 12.0, 9.5, 1.7 Hz, 1H); ^{13}C NMR (125 MHz, C₆D₆, 65 °C) δ 139.2 (C), 133.8 (CH), 129.2 (CH), 129.2 (CH), 129.1 (CH), 122.0 (CH), 63.4 (CH₂), 62.7 (CH₂), 56.2 (CH₂), 55.6 (CH₂), 53.7 (CH₂), 51.6 (CH), 40.0 (CH), 38.6 (CH₂), 38.2 (C), 37.4 (CH), 36.3 (CH₂), 32.1 (CH₂), 30.2 (CH₂), 28.0 (CH₂), 26.9 (CH₂), 26.4 (CH₂), 26.0 (CH₂), 25.5 (CH₂), 25.0 (CH₂), 24.9 (CH₂), 24.6 (CH₂), 23.4 (CH₂); HRMS (ESI), calcd for C₂₈H₄₅N₂⁺ (M+H)⁺ 409.3583, found 409.3585.

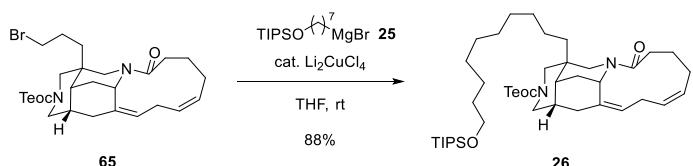
A-5. Total Synthesis of Madangamine E



Bromide (65): Carbon tetrabromide (17.6 mg, 531 μmol) was added to a solution of alcohol **17** (17.3 mg, 35.4 μmol), PPh₃ (13.9 mg, 53.1 μmol) and CH₂Cl₂ (1.2 mL) at room temperature. The solution was maintained for 1 h, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9 to 1:3) to give bromide **65** (17.4 mg, 89%): a colorless oil; [α]²²_D +86.7 (*c* 1.00, CHCl₃); IR (film) 2950, 2916, 1693, 1627, 1438, 1248, 858, 838 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.65–5.50 (m, 1H), 5.48–5.33 (m, 1H), 5.33–5.15 (m, 1H), 5.14–4.94 (m, 1H), 4.30–4.10 (m, 3H), 4.08–3.95 (m, 1H), 3.94–3.80 (m, 1H), 3.45–3.35 (m, 1H), 3.33–3.25 (m, 1H), 3.12 (ddd, *J* = 14.6, 9.8, 9.2 Hz, 1H), 2.96–2.78 (m, 2H), 2.76–2.64 (m, 1H), 2.64–2.40 (m, 3H), 2.36–1.64 (m, 10H), 1.59–1.34 (m, 4H), 1.02 (t, *J* = 8.3 Hz, 2H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 173.4 (C), 156.7 (C), 136.8 (C), 129.1 (CH), 128.0 (CH), 126.1 (CH), 64.0 (CH₂), 50.9 (CH₂), 49.2 (CH₂), 48.1 (CH), 44.2 (CH₂), 36.6 (C), 36.5 (CH), 34.9 (CH), 34.8 (CH₂), 34.23 (CH₂), 34.17 (CH₂), 32.7 (CH₂), 30.6 (CH₂), 27.8 (CH₂), 26.8 (CH₂), 26.4 (CH₂), 25.7 (CH₂), 18.2 (CH₂), -1.3 (CH₃); HRMS (ESI), calcd for C₂₇H₄₄N₂O₃SiBr⁺ (*M*+H)⁺ 551.2305, found 551.2304.



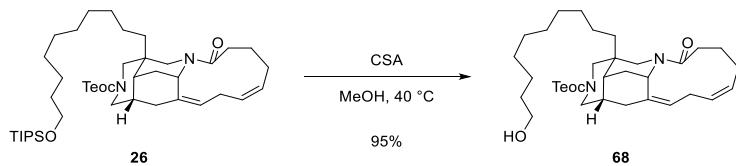
(7-Bromoheptyl)oxytriisopropylsilane (67): *N,N*-Dimethyl-4-aminopyridine (DMAP, 213 mg, 1.74 mmol) was added to a solution of alcohol **66** (3.40 g, 17.4 mmol), imidazole (3.55 g, 52.2 mmol), TIPSCl (4.1 mL, 19 mmol) and CH₂Cl₂ (87 mL) at room temperature. The solution was maintained at room temperature for 2 h, and quenched with saturated aqueous NH₄Cl (50 mL). The resulting mixture was extracted with CH₂Cl₂ (2x 50 mL). The combined extracts were washed with brine (50 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane to EtOAc/hexane 1:19) to give bromide **67** (6.12 g, 100%): a colorless oil; IR (film) 2939, 2865, 1462, 1108, 883, 681 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 3.67 (t, *J* = 6.6 Hz, 2H), 3.41 (t, *J* = 6.9 Hz, 2H), 1.86 (tt, *J* = 7.2, 6.9 Hz, 2H), 1.54 (tt, *J* = 6.9, 6.9 Hz, 2H), 1.44 (tt, *J* = 8.0, 6.9 Hz, 2H), 1.40–1.30 (m, 4H), 1.15–1.00 (m, 21H); ¹³C NMR (125 MHz, CDCl₃) δ 63.5 (CH₂), 34.0 (CH₂), 33.0 (CH₂), 32.9 (CH₂), 28.7 (CH₂), 28.3 (CH₂), 25.8 (CH₂), 18.2 (CH₃), 12.2 (CH); HRMS (ESI), calcd for C₁₆H₃₆OSiBr⁺ (M+H)⁺ 351.1719, found 351.1705.



Alkylation product (26): A 30 mL flask equipped with a rubber septa connected to a bubbler was charged

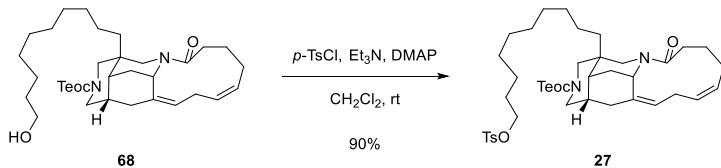
with magnesium (turnings, 41.5 mg, 1.71 mmol) and THF. ((7-Bromoheptyl)oxy)triisopropylsilane **67** (333 mg, 948 μ mol) was added to the mixture at room temperature over a period of 5 min. The resulting mixture was stirred vigorously for 1 h. The concentration of the resulting Grignard reagent **25** was determined as 0.26 M by titration with 1,10-phenanthroline method.⁸

A 20 mL flask was charged with copper (II) chloride (2.1 mg, 16 μ mol) and LiCl (1.3 mg, 32 μ mol). The reagent was heated under reduced pressure until blue copper (II) chloride became orange. A solution of bromide **65** (17.4 mg, 31.5 μ mol) and THF (3.2 mL) was added to the solids via cannula at room temperature. The solution of Grignard reagent **25** (0.26 M in THF, 910 μ L, 240 μ mol) was then added to the resulting solution at room temperature. The solution was maintained for 30 min at room temperature, and quenched with saturated aqueous NH₄Cl (3 mL). The resulting mixture was extracted with EtOAc (2x 5 mL). The combined extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:19 to 1:12) to give alkylation product **26** (20.5 mg, 88%): a colorless oil; $[\alpha]^{23}_D +85.8$ (*c* 1.00, CHCl₃); IR (film) 2927, 2863, 1698, 1633, 1462, 1438, 1249, 1105, 859, 838 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.60–5.48 (m, 1H), 5.48–5.35 (m, 1H), 5.35–5.12 (m, 1H), 5.10–4.90 (m, 1H), 4.25–4.10 (m, 3H), 4.06–3.92 (m, 1H), 3.92–3.75 (m, 1H), 3.69 (t, *J* = 6.6 Hz, 2H), 3.13 (ddd, *J* = 13.6, 10.5, 9.2 Hz, 1H), 2.96–2.77 (m, 2H), 2.77–2.65 (m, 1H), 2.61 (d, *J* = 13.2 Hz, 1H), 2.64–2.37 (m, 2H), 2.36–2.23 (m, 1H), 2.23–1.90 (m, 5H), 1.87–1.75 (m, 1H), 1.75–1.66 (m, 1H), 1.54 (tt, *J* = 6.9, 6.6 Hz, 2H), 1.50–1.14 (m, 18H), 1.12–1.05 (m, 21H), 1.02 (t, *J* = 8.6 Hz, 2H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 173.5 (C), 156.8 (C), 137.2 (C), 129.2 (CH), 128.0 (CH), 125.6 (CH), 63.9 (CH₂), 63.7 (CH₂), 51.0 (CH₂), 49.2 (CH₂), 48.1 (CH), 45.1 (CH₂), 36.6 (C), 36.4 (CH₂), 36.0 (CH), 35.2 (CH), 34.4 (CH₂), 33.3 (CH₂), 32.9 (CH₂), 30.7 (CH₂), 30.6 (CH₂), 29.8 (CH₂), 29.71 (CH₂), 29.66 (CH₂), 29.62 (CH₂), 27.8 (CH₂), 26.5 (CH₂), 26.0 (CH₂), 25.8 (CH₂), 23.2 (CH₂), 18.2 (CH₃, CH₂), 12.4 (CH), -1.3 (CH₃); HRMS (ESI), calcd for C₄₃H₇₉N₂O₄Si₂⁺ (M+H)⁺ 743.5578, found 743.5580.

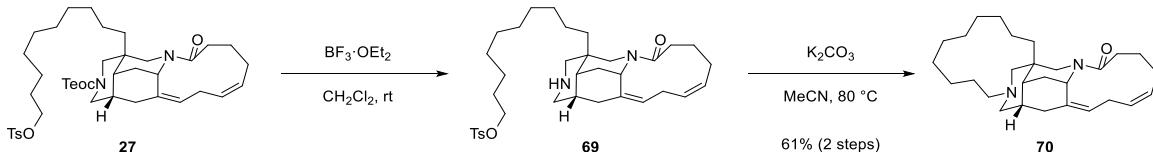


Alcohol (68): 10-Camphorsulfonic acid (CSA, 17.6 mg, 75.9 μ mol) was added to a solution of alkylation product **26** (28.2 mg, 37.9 μ mol) and MeOH (1.3 mL) at room temperature. The solution was heated to 40 °C, maintained for 1 h at 40 °C, quenched with Et₃N (21 μ L, 150 μ mol) at room temperature, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9 to 1:1) to give alcohol **68** (21.1 mg, 95%): a colorless oil; $[\alpha]^{27}_D +90.4$ (*c* 1.00, CHCl₃); IR (film) 3421, 2927, 2854, 1695, 1616, 1437, 1248, 859, 838, 760 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.64–5.46 (m, 1H), 5.46–5.34 (m, 1H), 5.34–5.12 (m, 1H), 5.08–4.84 (m, 1H), 4.26–4.10 (m, 3H), 4.08–3.92 (m, 1H), 3.92–3.74 (m, 1H), 3.63 (t, *J* = 6.6 Hz, 2H), 3.12 (ddd, *J* = 13.5, 10.1, 9.7 Hz, 1H), 2.98–2.76 (m, 2H), 2.76–2.64 (m, 1H), 2.60 (d, *J* = 13.5 Hz, 1H), 2.64–2.36 (m, 2H), 2.35–2.22 (m, 1H), 2.22–1.90 (m, 5H), 1.87–1.74 (m, 1H), 1.73–1.64 (m, 1H), 1.57 (tt, *J* = 7.2, 6.6 Hz, 2H), 1.45–1.10 (m, 18H), 1.02 (t, *J* = 8.3 Hz, 2H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 173.5 (C), 156.8 (C), 137.2 (C), 129.2 (CH), 128.0 (CH), 125.6 (CH), 63.9 (CH₂), 63.7 (CH₂), 51.0 (CH₂), 49.2 (CH₂), 48.1 (CH), 45.1 (CH₂), 36.6 (C), 36.4 (CH₂), 36.0 (CH), 35.2 (CH), 34.4 (CH₂), 33.3 (CH₂), 32.9 (CH₂), 30.7 (CH₂), 30.6 (CH₂), 29.8 (CH₂), 29.71 (CH₂), 29.66 (CH₂), 29.62 (CH₂), 27.8 (CH₂), 26.5 (CH₂), 26.0 (CH₂), 25.8 (CH₂), 23.2 (CH₂), 18.2 (CH₃, CH₂), 12.4 (CH), -1.3 (CH₃); HRMS (ESI), calcd for C₄₃H₇₉N₂O₄Si₂⁺ (M+H)⁺ 743.5578, found 743.5580.

CDCl_3 , 60 °C) δ 173.5 (C), 156.8 (C), 137.1 (C), 129.2 (CH), 128.0 (CH), 125.6 (CH), 63.9 (CH_2), 63.1 (CH_2), 51.0 (CH_2), 49.1 (CH_2), 48.1 (CH), 45.0 (CH_2), 36.6 (C), 36.3 (CH_2), 36.1 (CH), 35.1 (CH), 34.5 (CH_2), 33.0 (CH_2), 32.9 (CH_2), 30.6 (CH_2), 30.4 (CH_2), 29.6 (CH_2), 29.52 (CH_2), 29.52 (CH_2), 29.46 (CH_2), 27.8 (CH_2), 26.5 (CH_2), 25.9 (CH_2), 25.8 (CH_2), 23.2 (CH_2), 18.2 (CH_2), -1.3 (CH_3); HRMS (ESI), calcd for $\text{C}_{34}\text{H}_{59}\text{N}_2\text{O}_4\text{Si}^+$ ($\text{M}+\text{H}$)⁺ 587.4244, found 587.4244.



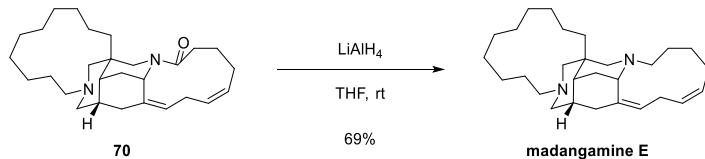
Tosylate (27): *p*-Toluenesulfonyl chloride (13.7 mg, 71.8 μ mol) was added to a solution of alcohol **68** (21.1 mg, 35.9 μ mol), Et₃N (20 μ L, 140 μ mol), DMAP (0.9 mg, 7.2 μ mol) and CH₂Cl₂ (1.2 mL) at room temperature. The solution was maintained at room temperature for 15 h, and quenched with saturated aqueous NH₄Cl (3 mL). The resulting mixture was extracted with CH₂Cl₂ (2x 5 mL). The combined extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:12 to 1:1) to give tosylate **27** (23.9 mg, 90%): a colorless oil; $[\alpha]^{25}_D +84.9$ (*c* 1.00, CHCl₃); IR (film) 2927, 2856, 1693, 1612, 1441, 1358, 1249, 1176, 925, 838, 664 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 5.62–5.46 (m, 1H), 5.46–5.33 (m, 1H), 5.33–5.10 (m, 1H), 5.10–4.84 (m, 1H), 4.25–4.10 (m, 3H), 4.03 (t, *J* = 6.6 Hz, 2H), 4.06–3.91 (m, 1H), 3.90–3.72 (m, 1H), 3.12 (ddd, *J* = 13.8, 9.8, 9.2 Hz, 1H), 3.00–2.76 (m, 2H), 2.76–2.64 (m, 1H), 2.59 (d, *J* = 13.5 Hz, 1H), 2.64–2.48 (m, 2H), 2.44 (s, 3H), 2.34–2.21 (m, 1H), 2.21–1.90 (m, 5H), 1.86–1.73 (m, 1H), 1.72–1.67 (m, 1H), 1.63 (tt, *J* = 6.9, 6.6 Hz, 2H), 1.45–1.10 (m, 18H), 1.01 (t, *J* = 8.3 Hz, 2H), 0.05 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 173.5 (C), 156.8 (C), 144.6 (C), 137.2 (C), 134.0 (C), 129.9 (CH), 129.2 (CH), 128.0 (CH), 128.0 (CH), 125.6 (CH), 70.8 (CH₂), 63.9 (CH₂), 51.0 (CH₂), 49.2 (CH₂), 48.1 (CH), 45.0 (CH₂), 36.6 (C), 36.3 (CH₂), 36.1 (CH), 35.1 (CH), 34.5 (CH₂), 32.9 (CH₂), 32.9 (CH₂), 30.6 (CH₂), 30.5 (CH₂), 29.55 (CH₂), 29.45 (CH₂), 29.09 (CH₂), 29.05 (CH₂), 27.8 (CH₂), 26.5 (CH₂), 25.8 (CH₂), 25.5 (CH₂), 23.2 (CH₂), 21.7 (CH₃), 18.2 (CH₂), -1.3 (CH₃); HRMS (ESI), calcd for C₄₁H₆₅N₂O₆SiS⁺ (M+H)⁺ 741.4333, found 741.4329.



Macrocyclic amine (70): Boron trifluoride ethyl ether complex (10 μ L, 76 μ mol) was added to a solution of tosylate **27** (11.2 mg, 15.1 μ mol) and CH₂Cl₂ (1.5 mL) at room temperature. The solution was maintained for 30 min, quenched with Et₃N (21 μ L, 150 μ mol) at room temperature. The solution was concentrated to give the corresponding amine **69**, which was immediately used in the next step without further purification.

Potassium carbonate (10.4 mg, 75.5 μ mol) was added to a solution of the above amine **69** and MeCN (15

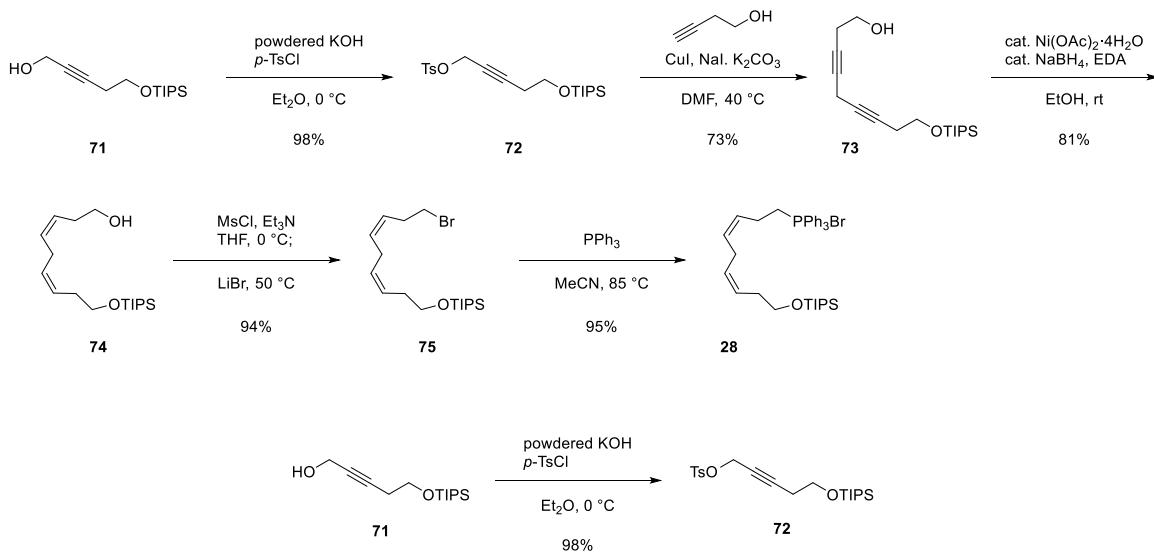
mL) at room temperature. The resulting solution was heated to 80 °C, maintained for 80 h at 80 °C, and concentrated. The residue was purified by silica gel column chromatography (Et₂O/hexane 1:9 to 1:2) to give macrocyclic amine **70** (3.9 mg, 61% for 2 steps): a colorless oil; $[\alpha]^{27}_D -9.1$ (*c* 0.50, EtOAc); IR (film) 2925, 2856, 1629, 1447, 678 cm⁻¹; ¹H NMR (500 MHz, C₆D₆, 1.4:1 mixture of rotamers) δ 5.87–5.79 (m, 5/12H), 5.44–5.17 (m, 3H), 4.74–4.67 (m, 7/12H), 4.55 (d, *J* = 14.0 Hz, 7/12H), 3.40 (ddd, *J* = 14.9, 10.6, 10.0 Hz, 5/12H), 3.23 (d, *J* = 14.0 Hz, 7/12H), 3.16 (d, *J* = 13.5 Hz, 5/12H), 3.13–3.02 (m, 5/12H), 2.81 (ddd, *J* = 14.6, 9.5, 8.9 Hz, 7/12H), 2.69 (d, *J* = 13.5 Hz, 5/12H), 2.72–2.61 (m, 7/12H), 2.50–1.10 (m, 36H); ¹³C NMR (125 MHz, C₆D₆, mixture of two rotamers) δ 172.1 (C), 169.7 (C), 138.9 (C), 137.4 (C), 129.3 (CH), 129.0–127.0 (CH x3), 126.4 (CH), 124.8 (CH), 60.4 (CH₂), 59.4 (CH₂), 59.3 (CH₂), 58.8 (CH₂), 57.5 (CH₂), 57.2 (CH₂), 52.2 (CH₂), 48.6 (CH), 46.3 (CH₂), 44.9 (CH), 36.9 (C), 36.7 (C), 35.9 (CH₂), 35.8 (CH₂), 35.2 (CH), 35.0 (CH₂), 34.6 (CH), 33.0 (CH₂), 32.7 (CH), 31.7 (CH₂), 30.1 (CH₂), 28.8 (CH₂), 28.4 (CH), 27.9 (CH₂), 27.6 (CH₂), 27.5 (CH₂), 27.14 (CH₂), 27.08 (CH₂), 26.4 (CH₂), 26.1 (CH₂), 26.0 (CH₂), 25.8 (CH₂), 25.7 (CH₂), 25.6 (CH₂), 25.4 (CH₂), 25.1 (CH₂), 25.04 (CH₂), 24.97 (CH₂), 24.87 (CH₂), 24.65 (CH₂), 24.56 (CH₂), 24.4 (CH₂), 23.7 (CH₂), 23.2 (CH₂), 22.1 (CH₂), 20.7 (CH₂); HRMS (ESI), calcd for C₂₈H₄₅N₂O⁺ (M+H)⁺ 425.3532, found 425.3532.



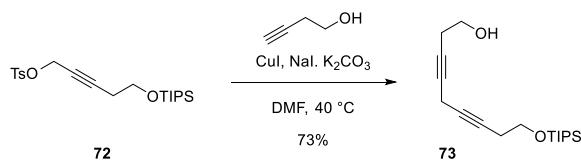
Madangamine E: In a glove box, LiAlH₄ (1.0 M in THF, 74 μL, 74 μmol) was added to a solution of macrocyclic amine **70** (6.3 mg, 15 μmol) and THF (1.5 mL) at room temperature. The reaction vessel was removed from the glove box, stirred at room temperature for 8 h, cooled to 0 °C, and quenched with a few drops of distilled water. The resulting suspension was dried over Na₂SO₄, and filtrated. The solid was washed with Et₂O (3 mL). The resulting solution was then concentrated. The residue was purified by silica gel column chromatography (Et₂O/hexane 1:19 to 1:5) to give madangamine E (4.2 mg, 69%): a colorless oil; $[\alpha]^{22}_D +90.9$ (*c* 0.40, EtOAc); IR (film) 2925, 2853, 1458, 1445, 1350, 1129, 1116, 923, 862, 722 cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 5.46 (td, *J* = 10.9, 4.3 Hz, 1H), 5.41 (tdd, *J* = 10.9, 6.3, 1.4 Hz, 1H), 5.20 (dt, *J* = 11.5, 2.6 Hz, 1H), 3.71 (t, *J* = 2.9 Hz, 1H), 3.34 (dt, *J* = 13.5, 11.5 Hz, 1H), 3.30 (d, *J* = 12.1 Hz, 1H), 3.02 (ddt, *J* = 15.8, 12.6, 2.6 Hz, 1H), 2.85 (ddd, *J* = 13.7, 11.7, 5.4 Hz, 1H), 2.63 (m, 1H), 2.58 (d, *J* = 12.0 Hz, 1H), 2.70–2.56 (m, 1H), 2.46 (d, *J* = 12.1 Hz, 1H), 2.36 (dt, *J* = 12.0, 2.9 Hz, 1H), 2.25 (m, 1H), 2.39–2.20 (m, 4H), 2.12 (ddd, *J* = 12.9, 4.6, 3.7 Hz, 1H), 1.95–1.74 (m, 4H), 1.83 (d, *J* = 12.0 Hz, 1H), 1.72–1.61 (m, 1H), 1.61–1.09 (m, 21H); ¹³C NMR (125 MHz, C₆D₆) δ 139.1 (C), 129.1 (CH), 129.0 (CH), 122.1 (CH), 62.3 (CH₂), 60.1 (CH₂), 57.4 (CH₂), 56.3 (CH₂), 55.3 (CH₂), 51.8 (CH), 39.0 (CH₂), 37.0 (C), 36.6 (CH), 36.5 (CH), 35.4 (CH₂), 32.2 (CH₂), 27.3 (CH₂), 27.1 (CH₂), 26.8 (CH₂), 26.1 (CH₂), 25.7 (CH₂), 25.4 (CH₂), 25.11 (CH₂), 25.09 (CH₂), 24.81 (CH₂), 24.76 (CH₂), 24.2–23.4 (CH₂, br), 22.8 (CH₂); HRMS (ESI), calcd for C₂₈H₄₇N₂⁺ (M+H)⁺ 411.3739, found 411.3743.

A-6. Total Synthesis of Madangamine A

Synthesis of phosphonium salt 30

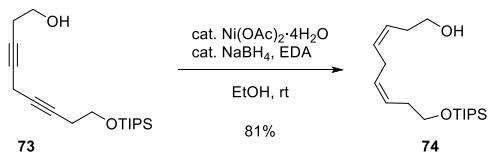


Tosylate (72): Powdered KOH (85wt%, 1.38 g, 20.9 mmol) was added to a solution of propargyl alcohol **71**¹³ (1.07 g, 4.18 mmol), *p*-toluenesulfonyl chloride (956 mg, 5.02 mmol) and Et₂O (21 mL) at 0 °C. The mixture was stirred for 2 h at 0 °C, quenched with saturated aqueous NH₄Cl (5 mL), and extracted with EtOAc (2x 5 mL). The combined organic extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (hexane to EtOAc/hexane 1:19) to give tosylate **72** (1.68 g, 98%): a colorless oil; IR (film) 2943, 2866, 2241, 1371, 1189, 1178, 1110, 1098, 942, 664 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.81 (d, *J* = 8.6 Hz, 2H), 7.34 (d, *J* = 8.6 Hz, 2H), 4.68 (t, *J* = 2.0 Hz, 2H), 3.68 (t, *J* = 7.2 Hz, 2H), 2.45 (s, 3H), 2.33 (tt, *J* = 7.2, 2.0 Hz, 2H), 1.11–0.97 (m, 21H); ¹³C NMR (125 MHz, CDCl₃) δ 145.0 (C), 133.4 (C), 129.8 (CH), 128.2 (CH), 87.6 (C), 73.0 (C), 61.6 (CH₂), 58.7 (CH₂), 23.3 (CH₂), 21.7 (CH₃), 18.0 (CH₃), 12.0 (CH); HRMS (ESI), calcd for C₂₁H₃₅O₄SiS⁺ (M+H)⁺ 411.2025, found 411.2022.

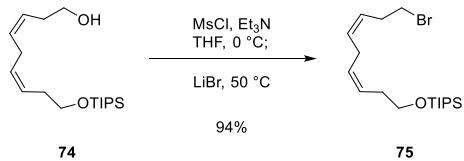


1,4-Diyne (73): Potassium carbonate (259 mg, 1.88 mmol) was added to a mixture of tosylate **72** (515 mg, 1.25 mmol), 3-butyn-1-ol (95 µL, 1.3 mmol), CuI (238 mg, 1.25 mmol), NaI (187 mg, 1.25 mmol) and DMF (6.3 mL) at room temperature. The mixture was heated to 40 °C, stirred for 12 h at this temperature, and quenched with saturated aqueous NH₄Cl (5 mL). The resulting mixture was filtrated through a pad of Celite®. After the organic layer was separated, the resulting aqueous layer was extracted with Et₂O (2x 10 mL). The combined organic extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:19 to 1:4) to give 1,4-diyne **73** (281 mg, 73%): a colorless oil; IR (film) 3372, 2942, 2866, 2216, 1462, 1106, 1056, 882, 681 cm⁻¹; ¹H NMR (500 MHz,

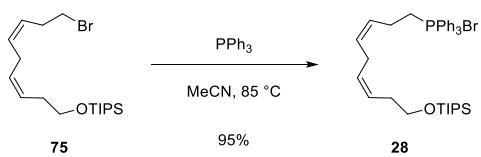
CDCl_3) δ 3.78 (t, $J = 7.5$ Hz, 2H), 3.70 (t, $J = 6.0$ Hz, 2H), 3.13 (tt, $J = 2.3, 2.3$ Hz, 2H), 2.45 (tt, $J = 6.0, 2.3$ Hz, 2H), 2.41 (tt, $J = 7.5, 2.3$ Hz, 2H), 1.14–0.97 (m, 21H); ^{13}C NMR (125 MHz, CDCl_3) δ 77.7 (C), 77.0 (C), 76.6 (C), 75.3 (C), 62.3 (CH_2), 61.1 (CH_2), 23.24 (CH_2), 23.15 (CH_2), 18.0 (CH_3), 12.1 (CH), 9.8 (CH_2); HRMS (ESI), calcd for $\text{C}_{18}\text{H}_{33}\text{O}_2\text{Si}^+$ ($\text{M}+\text{H}$)⁺ 309.2250, found 309.2249.



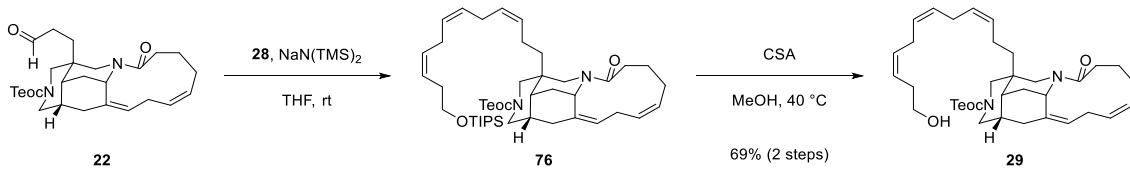
1,4-Diene (74): Sodium borohydride (48.9 mg, 1.29 mmol) was added to a mixture of nickel (II) acetate tetrahydrate (134 mg, 538 μmol) and EtOH (8.5 mL) at room temperature. After stirring for 30 min at room temperature, ethylene diamine (420 μL , 6.20 mmol) was added to the mixture. The mixture was stirred for additional 30 min. A solution of 1,4-diyne **73** (518 mg, 1.68 mmol) and EtOH (8.5 mL) were then added to the mixture. The resulting mixture was stirred under hydrogen for 1 h, and filtrated through a pad of Celite®. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:19 to 1:7) to give 1,4-diene **74** (423 mg, 81%): a colorless oil; IR (film) 3328, 2941, 2865, 1461, 1100, 1049, 881, 679, 657 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.54 (dtt, $J = 10.6, 7.5, 1.5$ Hz, 1H), 5.49–5.36 (m, 3H), 3.69 (t, $J = 6.9$ Hz, 2H), 3.66 (td, $J = 6.3, 5.5$ Hz, 2H), 2.85 (dd, $J = 6.6, 6.6$ Hz, 2H), 2.36 (td, $J = 7.2, 6.3$ Hz, 2H), 2.33 (td, $J = 6.9, 6.0$ Hz, 2H), 1.38 (t, $J = 5.5$ Hz, 1H), 1.14–0.97 (m, 21H); ^{13}C NMR (125 MHz, CDCl_3) δ 131.3 (CH), 129.4 (CH), 126.6 (CH), 125.7 (CH), 63.2 (CH_2), 62.3 (CH_2), 31.4 (CH_2), 30.9 (CH_2), 26.0 (CH_2), 18.1 (CH_3), 12.1 (CH); HRMS (ESI), calcd for $\text{C}_{18}\text{H}_{37}\text{O}_2\text{Si}^+$ ($\text{M}+\text{H}$)⁺ 313.2563, found 313.2563.



Bromide (75): Methanesulfonyl chloride (210 μL , 2.7 mmol) was added to a solution of 1,4-diene **74** (423 mg, 1.35 mmol), Et_3N (380 μL , 2.7 mmol) and THF (14 mL) at 0 °C. After the solution was maintained for 1 h at 0 °C, lithium bromide (1.17 g, 13.5 mmol) was added to the solution. The resulting mixture was then heated to 50 °C, maintained for 3 h at this temperature. The mixture was cooled to room temperature, quenched with saturated aqueous NaHCO_3 , and extracted with hexane (2x 5 mL). The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4 , and concentrated. The residue was purified by silica gel column chromatography (hexane to EtOAc/hexane 1:19) to give bromide **75** (475 mg, 94%): a colorless oil; IR (film) 2943, 2866, 1463, 1107, 882, 681 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.52 (dtt, $J = 10.6, 7.5, 1.5$ Hz, 1H), 5.49–5.36 (m, 3H), 3.69 (t, $J = 7.2$ Hz, 2H), 3.38 (t, $J = 7.2$ Hz, 2H), 2.82 (ddd, $J = 7.5, 6.6, 0.6$ Hz, 2H), 2.65 (tddt, $J = 7.2, 7.2, 1.5, 0.6$ Hz, 2H), 2.33 (td, $J = 7.2, 6.9$ Hz, 2H), 1.14–1.00 (m, 21H); ^{13}C NMR (125 MHz, CDCl_3) δ 131.2 (CH), 129.0 (CH), 126.8 (CH), 126.3 (CH), 63.1 (CH_2), 32.4 (CH_2), 31.4 (CH_2), 30.9 (CH_2), 26.1 (CH_2), 18.1 (CH_3), 12.1 (CH); HRMS (ESI), calcd for $\text{C}_{18}\text{H}_{36}\text{OBrSi}^+$ ($\text{M}+\text{H}$)⁺ 375.1719, found 375.1723.



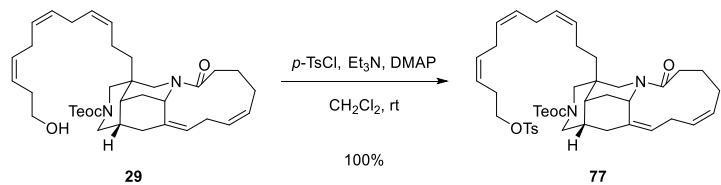
Phosphonium salt (28): Triphenylphosphine (3.32 g, 12.7 mmol) was added to a solution of bromide **75** (475 mg, 1.27 mmol) and MeCN (4.2 mL) at room temperature. The resulting solution was heated to 85 °C, maintained for 15 h at 85 °C, cooled to room temperature, and concentrated. The residue was purified by silica gel column chromatography (MeOH/CHCl₃ 1:39 to 1:19) to give phosphonium salt **28** (770 mg, 95%): a colorless oil; IR (film) 3403, 2942, 2865, 1438, 1112, 883, 746, 723, 689 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.93–7.84 (m, 6H), 7.82–7.76 (m, 3H), 7.74–7.67 (m, 6H), 5.64 (dtt, *J* = 10.6, 6.9, 1.7 Hz, 1H), 5.40–5.33 (m, 2H), 5.24 (dtt, *J* = 10.9, 7.2, 1.5 Hz, 1H), 4.04–3.95 (m, 2H), 3.62 (t, *J* = 6.9 Hz, 2H), 2.55 (dd, *J* = 7.2, 7.2 Hz, 2H), 2.52–2.43 (m, 2H), 2.15 (tdd, *J* = 6.9, 6.9, 1.5 Hz, 2H), 1.11–0.97 (m, 21H); ¹³C NMR (125 MHz, CDCl₃) δ 135.0 (d, *J* = 2.4 Hz, CH), 133.5 (d, *J* = 10.1 Hz, CH), 130.5 (d, *J* = 12.5 Hz, CH), 130.3 (CH), 128.3 (CH), 126.7 (CH), 126.4 (d, *J* = 14.3 Hz, CH), 117.9 (d, *J* = 85.3 Hz, C), 62.8 (CH₂), 31.1 (CH₂), 25.6 (CH₂), 22.8 (d, *J* = 48.9 Hz, CH₂), 20.3 (d, *J* = 3.0 Hz, CH₂), 17.9 (CH₃), 11.8 (CH); HRMS (ESI), calcd for C₃₆H₅₀OSiP⁺ (M+H)⁺ 557.3367, found 557.3369.



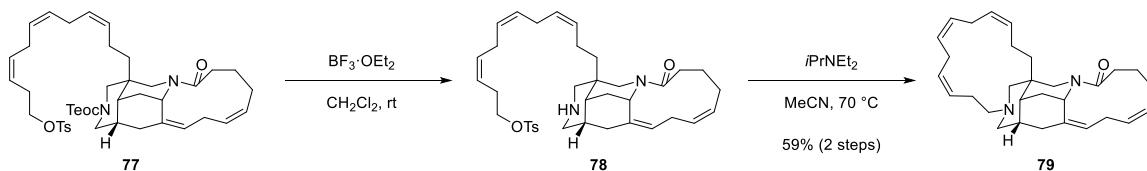
Alcohol (29): In a glove box, sodium hexamethyldisilazide (21.1 mg, 115 µmol) was added to a mixture of phosphonium salt **28** (75.4 mg, 118 µmol) and THF (1.0 mL) at room temperature. After stirring for 5 min, a solution of aldehyde **22** (12.7 mg, 26.1 µmol) and THF (2.0 mL) was added to the mixture of the ylide. The reaction vessel was then removed from the glove box, and stirred at room temperature for 1h. The mixture was quenched with saturated aqueous NH₄Cl (2 mL), and extracted with EtOAc (2x 5 mL). The combined organic extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:19 to 1:5) to give triene **76**, which was immediately used in the next reaction without further purification.

10-Camphorsulfonic acid (CSA, 10.6 mg, 45.8 µmol) was added to a solution of triene **76** and MeOH (1.1 mL) at room temperature. The solution was heated to 40 °C, maintained for 1 h at 40 °C, quenched with Et₃N (13 µL, 92 µmol) at room temperature, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9 to 1:2) to give alcohol **29** (10.9 mg, 69% for 2 steps): a colorless oil; $[\alpha]^{23}_D +109$ (*c* 1.00, CHCl₃); IR (film) 3426, 2949, 2921, 1694, 1611, 1440, 1248, 1049, 858, 839 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 5.60–5.48 (m, 2H), 5.46–5.20 (m, 7H), 5.10–4.90 (m, 1H), 4.36–4.12 (m, 3H), 4.10–3.80 (m, 2H), 3.65 (t, *J* = 6.6 Hz, 2H), 3.12 (ddd, *J* = 13.8, 10.3, 9.8 Hz, 1H), 2.87 (dd, *J* = 6.3, 6.0 Hz, 2H), 2.95–2.75 (m, 4H), 2.73–2.60 (m, 1H), 2.63 (d, *J* = 13.5 Hz, 1H), 2.60–2.42 (m, 2H), 2.38 (dt, *J* =

6.9, 6.9 Hz, 2H), 2.30–2.22 (m, 1H), 2.22–1.90 (m, 7H), 1.86–1.74 (m, 1H), 1.74–1.65 (m, 1H), 1.62–1.47 (m, 2H), 1.45–1.36 (m, 1H), 1.30–1.16 (m, 1H), 1.02 (t, J = 8.6 Hz, 2H), 0.06 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3 , 60 °C) δ 173.6 (C), 156.8 (C), 137.0 (C), 130.9 (CH), 129.8 (CH), 129.2 (CH), 128.5 (CH), 128.5 (CH), 128.38 (CH), 128.0 (CH), 126.1 (CH), 125.9 (CH), 64.0 (CH_2), 62.4 (CH_2), 51.0 (CH_2), 49.2 (CH_2), 48.1 (CH), 44.4 (CH_2), 36.8 (C), 36.6 (CH), 36.2 (CH_2), 35.2 (CH), 34.4 (CH_2), 32.9 (CH_2), 31.4 (CH_2), 30.7 (CH_2), 27.8 (CH_2), 26.5 (CH_2), 26.1 (CH_2), 25.9 (CH_2), 25.8 (CH_2), 21.4 (CH_2), 18.2 (CH_2), -1.3 (CH_3); HRMS (ESI), calcd for $\text{C}_{36}\text{H}_{57}\text{N}_2\text{O}_4\text{Si}^+$ ($\text{M}+\text{H}$)⁺ 609.4088, found 609.4081.



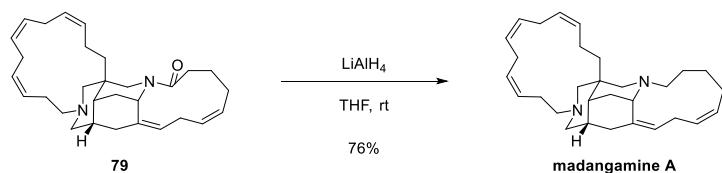
Tosylate (77): *p*-Toluenesulfonyl chloride (27.9 mg, 146 µmol) was added to a solution of alcohol **29** (44.5 mg, 73.1 µmol), Et₃N (41 µL, 290 µmol), DMAP (1.8 mg, 15 µmol) and CH₂Cl₂ (1.5 mL) at room temperature. The solution was maintained at room temperature for 15 h, and quenched with saturated aqueous NH₄Cl (1 mL). The resulting mixture was extracted with CH₂Cl₂ (2x 5 mL). The combined extracts were washed with brine (5 mL), dried over Na₂SO₄, and concentrated. The residue was purified by silica gel column chromatography (EtOAc/hexane 1:9 to 1:2) to give tosylate **77** (55.7 mg, 100%): a colorless oil; [α]²⁷_D +86.5 (c 1.00, CHCl₃); IR (film) 2951, 2921, 1693, 1627, 1439, 1361, 1248, 1176, 959, 913, 859, 838 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, 60 °C) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 5.62–5.18 (m, 9H), 5.10–4.90 (m, 1H), 4.30–4.11 (m, 3H), 4.04 (t, *J* = 6.9 Hz, 2H), 4.07–3.94 (m, 1H), 3.94–3.76 (m, 1H), 3.12 (ddd, *J* = 14.6, 9.8, 9.2 Hz, 1H), 2.96–2.80 (m, 2H), 2.80–2.72 (m, 4H), 2.72–2.60 (m, 1H), 2.64 (d, *J* = 13.8 Hz, 1H), 2.60–2.50 (m, 3H), 2.44 (s, 3H), 2.50–2.37 (m, 1H), 2.32–2.21 (m, 1H), 2.20–1.86 (m, 7H), 1.85–1.75 (m, 1H), 1.74–1.62 (m, 1H), 1.51–1.37 (m, 2H), 1.36–1.20 (m, 2H), 1.01 (t, *J* = 8.6 Hz, 2H), 0.06 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, 60 °C) δ 173.4 (C), 156.8 (C), 144.8 (C), 137.0 (C), 134.0 (C), 131.9 (CH), 130.02 (CH), 129.95 (CH), 129.3 (CH), 128.9 (CH), 128.3 (CH), 128.1 (CH), 128.1 (CH), 127.8 (CH), 125.8 (CH), 123.6 (CH), 69.7 (CH₂), 63.9 (CH₂), 50.9 (CH₂), 49.2 (CH₂), 48.1 (CH), 44.7 (CH₂), 36.7 (C), 36.1 (CH), 36.1 (CH), 35.1 (CH), 34.4 (CH₂), 32.9 (CH₂), 30.7 (CH₂), 27.8 (CH₂), 27.5 (CH₂), 26.5 (CH₂), 25.94 (CH₂), 25.8 (CH₂), 21.7 (CH₃), 21.4 (CH₂), 18.2 (CH₂), -1.3 (CH₃); HRMS (ESI), calcd for C₄₃H₆₃N₂O₆SiS⁺ (M+H)⁺ 763.4176, found 763.4177.



Macrocyclic amine (79): Boron trifluoride ethyl ether complex (18 μ L, 140 μ mol) was added to a solution of tosylate **77** (21.4 mg, 28.0 μ mol) and CH₂Cl₂ (2.8 mL) at room temperature. The solution was maintained for 30 min, and quenched with *N,N*-diisopropylethylamine (48 μ L, 280 μ mol) at room temperature. The solution

was concentrated to give the corresponding amine **78**, which was immediately used in the next step without further purification.

N,N-Diisopropylethylamine (24 μ L, 140 μ mol) was added to a solution of the above amine **78** and MeCN (28 mL) at room temperature. The resulting solution was heated to 70 °C, maintained for 20 h at this temperature, and then concentrated. The residue was purified by silica gel column chromatography (Et₂O/hexane 1:9 to 1:2) to give macrocyclic amine **79** (7.4 mg, 59% for 2 steps): a colorless oil; $[\alpha]^{28}_D +80.3$ (*c* 1.00, EtOAc); IR (film) 2918, 1627, 1446, 1417, 701 cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 5.70–5.59 (m, 1H), 5.53–5.12 (m, 8H), 4.73 (brs, 1H), 4.70 (d, *J* = 14.1 Hz, 1H), 3.26 (d, *J* = 14.1 Hz, 1H), 3.20–2.78 (m, 6H), 2.74 (d, *J* = 11.2 Hz, 1H), 2.70–2.54 (m, 1H), 2.54–1.84 (m, 13H), 1.91 (ddd, *J* = 13.2, 3.5, 3.5 Hz, 1H), 1.82–1.50 (m, 3H), 1.58 (d, *J* = 11.2 Hz, 1H), 1.50–1.20 (m, 1H), 1.20–1.14 (m, 1H), 1.10 (d, *J* = 13.2 Hz, 1H), 0.94–0.82 (m, 1H); ¹³C NMR (125 MHz, C₆D₆) δ 172.2 (C), 138.8 (C), 131.9 (CH), 129.2 (CH), 129.1 (CH), 128.8 (CH), 128.5–127.6 (CH x3), 127.2 (CH), 124.7 (CH), 60.8 (CH₂), 58.7 (CH₂), 58.4 (CH₂), 48.0 (CH), 44.6 (CH₂), 38.9 (CH), 36.8 (C), 36.1 (CH), 35.8 (CH), 35.4 (CH₂), 32.6 (CH₂), 30.8 (CH₂), 28.1 (CH₂), 26.5 (CH₂), 26.5 (CH₂), 26.3 (CH₂), 26.0 (CH₂), 25.2 (CH₂), 23.0 (CH₂); HRMS (ESI), calcd for C₃₀H₄₃N₂O⁺ (M+H)⁺ 447.3375, found 447.3375.

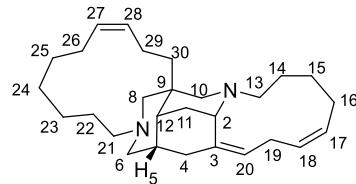


Madangamine A: In a glove box, LiAlH₄ (1.0 M in THF, 160 µL, 160 µmol) was added to a solution of macrocyclic amine **79** (14.0 mg, 31.3 µmol) and THF (1.6 mL) at room temperature. The reaction vessel was removed from the glove box, stirred at room temperature for 6 h, cooled to 0 °C, and quenched with a few drops of distilled water. The resulting suspension was dried over Na₂SO₄, and filtrated. The solid was washed with Et₂O (3 mL). The resulting solution was then concentrated. The residue was purified by silica gel column chromatography (Et₂O/hexane 1:19 to 1:5) to give madangamine A (10.3 mg, 76%): a colorless oil; [α]²⁴_D +142 (*c* 0.500, EtOAc); IR (film) 3005, 2912, 2873, 2853, 2792, 2758, 1459, 1440, 1128, 1091, 923, 917, 723, 675 cm⁻¹; ¹H NMR (500 MHz, C₆D₆) δ 5.58 (m, 1H), 5.45 (td, *J* = 10.9, 4.3 Hz, 1H), 5.42–5.30 (m, 6H), 5.18 (dt, *J* = 11.8, 2.9 Hz, 1H), 3.72 (t, *J* = 3.2 Hz, 1H), 3.36 (dt, *J* = 13.2, 11.2 Hz, 1H), 3.19–3.05 (m, 2H), 3.13 (d, *J* = 12.3 Hz, 1H), 3.08 (t, *J* = 16.3 Hz, 1H), 2.84 (ddd, *J* = 13.8, 11.8, 5.8 Hz, 1H), 2.73 (dd, *J* = 10.9, 0.9 Hz, 1H), 2.70–2.20 (m, 5H), 2.66 (brt, *J* = 13.4 Hz, 1H), 2.60 (m, 1H), 2.54 (ddd, *J* = 10.3, 3.2, 3.2 Hz, 1H), 2.48 (dt, *J* = 11.8, 5.2 Hz, 1H), 2.48 (d, *J* = 11.8 Hz, 1H), 2.42 (ddd, *J* = 12.4, 4.6, 3.2 Hz, 1H), 2.32 (d, *J* = 10.6 Hz, 1H), 2.24 (dd, *J* = 16.3, 7.7 Hz, 1H), 2.15 (ddd, *J* = 11.8, 5.5, 3.7 Hz, 1H), 2.11 (dd, *J* = 10.6, 3.2 Hz, 1H), 1.98–1.89 (m, 2H), 1.89–1.77 (m, 2H), 1.71 (m, 1H), 1.45 (m, 1H), 1.38 (d, *J* = 10.9 Hz, 1H), 1.29 (ddd, *J* = 12.4, 3.2, 2.6 Hz, 1H), 1.26–1.13 (m, 2H), 1.15 (m, 1H), 1.01 (dddd, *J* = 10.3, 7.5, 2.0, 1.7 Hz, 1H); ¹³C NMR (125 MHz, C₆D₆) δ 139.4 (C), 132.9 (CH), 129.2 (CH), 129.1 (CH), 129.0 (CH), 128.7–127.6 (CH x2), 127.5 (CH), 125.9 (CH), 121.9 (CH), 61.6 (CH₂), 59.4 (CH₂), 57.7 (CH₂), 55.7 (CH₂), 52.4 (CH₂), 51.8 (CH), 39.1 (CH), 38.4 (CH₂), 37.1 (CH), 37.0 (C), 36.1 (CH₂), 32.4 (CH₂), 26.9 (CH₂), 26.7 (CH₂), 26.6 (CH₂), 25.9

(CH₂), 25.5 (CH₂), 25.4 (CH₂), 23.9–22.9 (CH₂, br), 22.7 (CH₂); HRMS (ESI), calcd for C₃₀H₄₅N₂⁺ (M+H)⁺ 433.3583, found 433.3582.

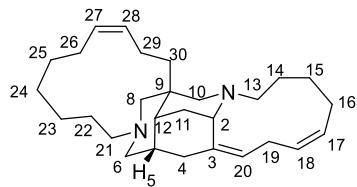
B. Comparison of Spectral Data of Madangamine Alkaloids

Comparison of ^1H NMR of madangamine C



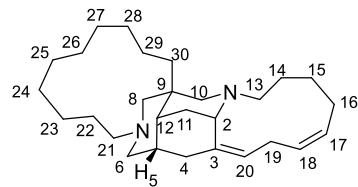
	our synthetic sample	natural sample
Proton	^1H NMR (500 MHz, C_6D_6 , 65 °C)	^1H NMR (500 MHz, C_6D_6 , 65 °C)
28, 18, 17	5.49–5.35 (m, 3H)	5.44 (1H), 5.43 (1H), 5.39 (1H)
20	5.20 (dt, $J = 11.5, 3.2$ Hz, 1H)	5.19 (dt, $J = 11.7, 3.3$ Hz, 1H)
27	5.23–5.13 (m, 1H)	5.16 (m, 1H)
2	3.72 (t, $J = 3.2$ Hz, 1H)	3.70 (t, $J = 3.2$ Hz, 1H)
10ax	3.42 (dd, $J = 12.1, 1.2$ Hz, 1H)	3.40 (dd, $J = 11.9, 1.6$ Hz, 1H)
19a	3.35 (dt, $J = 13.5, 11.5$ Hz, 1H)	3.33 (dt, $J = 13.4, 11.1$ Hz, 1H)
4ax	3.13 (ddt, $J = 16.3, 12.1, 3.2$ Hz, 1H)	3.11 (ddt, $J = 16.4, 11.7, 3.2$ Hz, 1H)
13a	2.83 (ddd, $J = 13.8, 11.8, 5.2$ Hz, 1H)	2.82 (ddd, $J = 13.8, 11.7, 5.4$ Hz, 1H)
8eq	2.74 (dd, $J = 12.1, 1.7$ Hz, 1H)	2.73 (dd, $J = 11.8, 1.8$ Hz, 1H)
30a	2.73 (ddd, $J = 12.0, 3.7, 2.0$ Hz, 1H)	2.70 (ddd, $J = 12.0, 3.7, 2.0$ Hz, 1H)
10eq	2.68 (d, $J = 12.1$ Hz, 1H)	2.67 (d, $J = 11.9$ Hz, 1H)
13b	2.60 (td, $J = 13.8, 4.3$ Hz, 1H)	2.59 (td, $J = 13.8, 4.5$ Hz, 1H)
11a	2.36 (dt, $J = 12.6, 3.2$ Hz, 1H)	2.34 (dt, $J = 12.5, 3.4$ Hz, 1H)
6eq	2.33 (d, $J = 10.9$ Hz, 1H)	2.32 (brd, $J = 10.7$ Hz, 1H)
19b, 21a, 29a		2.31 (1H), 2.31 (1H), 2.25 (1H)
16a, 4eq, 26a	2.36–2.01 (m, 9H)	2.24 (1H), 2.23 (1H), 2.20 (m, 1H)
21b, 29b, 26b		2.18 (1H), 2.09 (m, 1H), 2.06 (m, 1H)
6ax	2.16 (dd, $J = 10.9, 3.5$ Hz, 1H)	2.15 (dd, $J = 10.7, 3.4$ Hz, 1H)
16b, 14a	1.89–1.78 (m, 2H)	1.84 (1H), 1.82 (1H)
5, 22a, 24a	1.76–1.57 (m, 3H)	1.71 (m, 1H), 1.68 (m, 1H), 1.62 (m, 1H)
8ax	1.53 (d, $J = 12.1$ Hz, 1H)	1.52 (d, $J = 11.8$ Hz, 1H)
25a, 14b, 22b		1.49 (m, 1H), 1.43 (1H), 1.43 (m, 1H)
25b, 24b, 15a	1.57–1.07 (m, 10H)	1.39 (m, 1H), 1.27 (m, 1H), 1.22 (1H)
23a, 12, 23b		1.22 (1H), 1.20 (m, 1H), 1.15 (m, 1H)
15b		1.12 (m, 1H)
11b	1.27 (dt, $J = 12.6, 3.2$ Hz, 1H)	1.26 (dt, $J = 12.5, 2.9$ Hz, 1H)
30b	0.90 (ddt, $J = 12.0, 9.5, 1.7$ Hz, 1H)	0.89 (ddt, $J = 12.0, 9.2, 1.9$ Hz, 1H)

Comparison of ^{13}C NMR of madangamine C



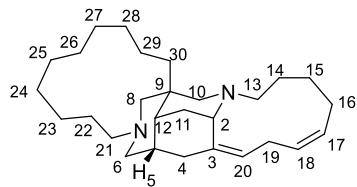
	our synthetic sample	natural sample
	^{13}C NMR (125 MHz, C ₆ D ₆ , 65 °C)	^{13}C NMR (125 MHz, C ₆ D ₆ , 65°C)
C-3	139.2 (C)	139.2 (C)
C-28	133.8 (CH)	133.7 (CH)
C-17	129.2 (CH)	129.1 (CH)
C-27	129.2 (CH)	129.1 (CH)
C-18	129.1 (CH)	129.0 (CH)
C-20	122.0 (CH)	122.0 (CH)
C-8	63.4 (CH ₂)	63.3 (CH ₂)
C-6	62.7 (CH ₂)	62.6 (CH ₂)
C-13	56.2 (CH ₂)	56.2 (CH ₂)
C-21	55.6 (CH ₂)	55.6 (CH ₂)
C-10	53.7 (CH ₂)	53.8 (CH ₂)
C-2	51.6 (CH)	51.6 (CH)
C-12	40.0 (CH)	39.9 (CH)
C-4	38.6 (CH ₂)	38.6 (CH ₂)
C-9	38.2 (C)	38.2 (C)
C-5	37.4 (CH)	37.4 (CH)
C-30	36.3 (CH ₂)	36.2 (CH ₂)
C-11	32.1 (CH ₂)	32.1 (CH ₂)
C-22	30.2 (CH ₂)	30.1 (CH ₂)
C-25	28.0 (CH ₂)	28.0 (CH ₂)
C-19	26.9 (CH ₂)	26.8 (CH ₂)
C-16	26.4 (CH ₂)	26.4 (CH ₂)
C-24	26.0 (CH ₂)	26.0 (CH ₂)
C-15	25.5 (CH ₂)	25.5 (CH ₂)
C-26	25.0 (CH ₂)	25.0 (CH ₂)
C-23	24.9 (CH ₂)	24.9 (CH ₂)
C-14	24.6 (CH ₂)	24.5 (CH ₂)
C-29	23.4 (CH ₂)	23.3 (CH ₂)

Comparison of ^1H NMR of madangamine E



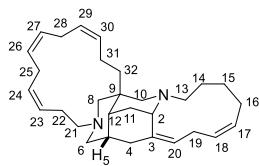
	our synthetic sample	natural sample <i>* ^1H NMR was reported as an inseparable mixture of madangamines D and E</i>
Proton	^1H NMR (500 MHz, C_6D_6)	^1H NMR (500 MHz, C_6D_6)
18	5.46 (td, $J = 10.9, 4.3$ Hz, 1H)	5.48 (1H)
17	5.41 (tdd, $J = 10.9, 6.3, 1.4$ Hz, 1H)	5.38 (1H)
20	5.20 (dt, $J = 11.5, 2.6$ Hz, 1H)	5.20 (brt, 1H)
2	3.71 (t, $J = 2.9$ Hz, 1H)	3.69 (brs, 1H)
19a	3.34 (dt, $J = 13.5, 11.5$ Hz, 1H)	3.34 (1H)
10ax	3.30 (d, $J = 12.1$ Hz, 1H)	3.25 (1H)
4ax	3.02 (ddt, $J = 15.8, 12.6, 2.6$ Hz, 1H)	3.00 (1H)
13a	2.85 (ddd, $J = 13.7, 11.7, 5.4$ Hz, 1H)	2.81 (1H)
13b	2.63 (m, 1H)	2.61 (1H)
8eq	2.58 (d, $J = 12.0$ Hz, 1H)	2.55 (1H)
21a	2.70–2.56 (m, 1H)	2.30 (1H)
10eq	2.46 (d, $J = 12.1$ Hz, 1H)	2.45 (1H)
11ax	2.36 (dt, $J = 12.0, 2.9$ Hz, 1H)	2.30 (1H)
4eq	2.25 (m, 1H)	2.21 (1H)
19b, 6eq, 6ax, 16a	2.39–2.20 (m, 4H)	2.34 (1H), 2.29 (1H), 2.24 (1H), 2.19 (1H)
21b	2.12 (ddd, $J = 12.9, 4.6, 3.7$ Hz, 1H)	2.15 (1H)
14a, 5, 16b, 30a	1.95–1.74 (m, 4H)	1.85 (1H), 1.8 (1H), 1.80 (m, 1H) 30a was not reported
8ax	1.83 (d, $J = 12.0$ Hz, 1H)	1.77 (1H)
22a	1.72–1.61 (m, 1H)	not reported
11b, 14b, 15a, 15b, 12, 22b, 23–29, 30b	1.61–1.09 (m, 21H)	1.42 (1H), 1.30 (1H), 1.19 (1H) 1.19 (1H), 1.18 (1H) 22b, 23–29, 30b were not reported

Comparison of ^{13}C NMR of madangamine E



	our synthetic sample	natural sample * ^{13}C NMR was reported as an inseparable mixture of madangamines D and E
	^{13}C NMR (125 MHz, C_6D_6)	^{13}C NMR (125 MHz, C_6D_6)
C-3	139.1 (C)	139.5 (C)
C-18, C-17	129.1 (CH), 129.0 (CH)	129.2 (CH), 129.0 (CH)
C-20	122.1 (CH)	122.0 (CH)
C-8	62.3 (CH_2)	62.0 (CH_2)
C-6	60.1 (CH_2)	60.0 (CH_2)
C-21	57.4 (CH_2)	57.2 (CH_2)
C-13	56.3 (CH_2)	56.0 (CH_2)
C-10	55.3 (CH_2)	58.2 (CH_2)
C-2	51.8 (CH)	51.8 (CH)
C-4	39.0 (CH_2)	39.0 (CH_2)
C-9	37.0 (C)	37.0 (C)
C-5	36.6 (CH)	36.5 (CH)
C-12	36.5 (CH)	40.1 (CH)
C-30	35.4 (CH_2)	not reported
C-11	32.2 (CH_2)	32.2 (CH_2)
C-19	26.8 (CH_2)	27.1 (CH_2)
C-16	26.1 (CH_2)	25.8 (CH_2)
C-15	27.3 (CH_2), 27.1 (CH_2), 25.7 (CH_2),	25.2 (CH_2)
C-14	25.4 (CH_2), 25.11 (CH_2), 25.09 (CH_2), 24.81 (CH_2), 24.76 (CH_2),	23.2 (CH_2)
C-22–C-29	24.2–23.4 (CH_2 , br), 22.8 (CH_2)	not reported

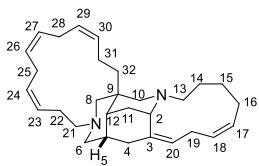
Comparison of ^1H NMR of madangamine A



	our synthetic sample	natural sample
Proton	^1H NMR (500 MHz, C_6D_6)	^1H NMR (500 MHz, C_6D_6)
30	5.58 (m, 1H)	5.55 (m, 1H)
18	5.45 (td, $J = 10.9, 4.3$ Hz, 1H)	5.43 (td, $J = 10.7, 4.1$ Hz, 1H)
17, 23, 24, 26, 27, 29	5.42–5.30 (m, 6H)	5.38 (m, 1H), 5.36 (m, 1H), 5.36 (m, 1H), 5.35 (m, 1H), 5.35 (m, 1H), 5.31 (m, 1H)
20	5.18 (dt, $J = 11.8, 2.9$ Hz, 1H)	5.16 (dt, $J = 11.5, 2.8$ Hz, 1H)
2	3.72 (t, $J = 3.2$ Hz, 1H)	3.69 (brs, 1H)
19a	3.36 (dt, $J = 13.2, 11.2$ Hz, 1H)	3.34 (dt, $J = 13.3, 11.3$ Hz, 1H)
28a, 25a	3.19–3.05 (m, 2H)	3.12 (1H), 3.07 (1H)
10ax	3.13 (d, $J = 12.3$ Hz, 1H)	3.10 (d, $J = 12.0$ Hz, 1H)
4a	3.08 (t, $J = 16.3$ Hz, 1H)	3.07 (t, $J = 16.5$ Hz, 1H)
13a	2.84 (ddd, $J = 13.8, 11.8, 5.8$ Hz, 1H)	2.81 (ddd, $J = 13.5, 11.9, 5.8$ Hz, 1H)
8eq	2.73 (dd, $J = 10.9, 0.9$ Hz, 1H)	2.72 (d, $J = 11.2$ Hz, 1H)
28b, 22a, 19b, 31a, 16b	2.70–2.20 (m, 5H)	2.56 (brd, $J = 16.5$ Hz, 1H), 2.40 (m, 1H) 2.32 (dd, $J = 13.3, 3.0$ Hz, 1H) 2.25 (1H), 2.24 (1H)
13b	2.66 (brt, $J = 13.4$ Hz, 1H)	2.63 (brt, $J = 13.5$ Hz, 1H)
25b	2.60 (m, 1H)	2.60 (brd, $J = 16.9$ Hz, 1H)
32a	2.54 (ddd, $J = 10.3, 3.2, 3.2$ Hz, 1H)	2.50 (ddd, $J = 13.0, 10.5, 3.0$ Hz, 1H)
21a	2.48 (dt, $J = 11.8, 5.2$ Hz, 1H)	2.47 (td, $J = 11.0, 5.9$ Hz, 1H)
10eq	2.48 (d, $J = 11.8$ Hz, 1H)	2.45 (d, $J = 12.0$ Hz, 1H)
11ax	2.42 (ddd, $J = 12.4, 4.6, 3.2$ Hz, 1H)	2.40 (dt, $J = 12.4, 3.4$ Hz, 1H)
6eq	2.32 (d, $J = 10.6$ Hz, 1H)	2.31 (bd, $J = 10.8$ Hz, 1H)
4eq	2.24 (dd, $J = 16.3, 7.7$ Hz, 1H)	2.21 (dd, $J = 16.5, 7.7$ Hz, 1H)
21b	2.15 (ddd, $J = 11.8, 5.5, 3.7$ Hz, 1H)	2.14 (ddd, $J = 11.0, 5.5, 3.3$ Hz, 1H)
6ax	2.11 (dd, $J = 10.6, 3.2$ Hz, 1H)	2.11 (dd, $J = 10.8, 3.1$ Hz, 1H)
22b, 31b	1.98–1.89 (m, 2H)	1.94 (1H), 1.93 (1H)
14a, 16b	1.89–1.77 (m, 2H)	1.81 (1H), 1.80 (1H)
5	1.71 (m, 1H)	1.70 (m, 1H)
14b	1.45 (m, 1H)	1.42 (m, 1H)
8ax	1.38 (d, $J = 10.9$ Hz, 1H)	1.38 (d, $J = 11.2$ Hz, 1H)

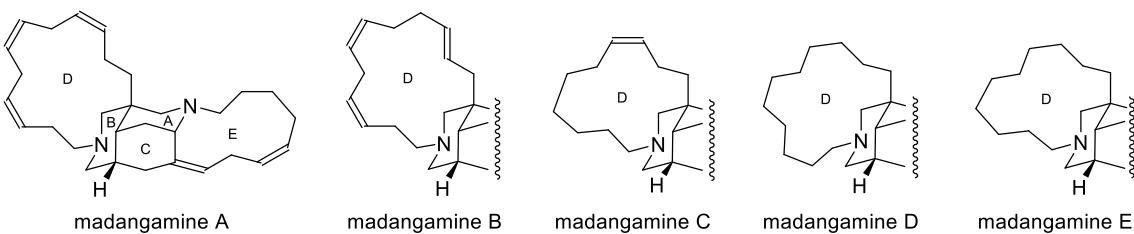
11eq	1.29 (ddd, $J = 12.4, 3.2, 2.6$ Hz, 1H)	1.27 (dt, $J = 12.4, 2.6$ Hz, 1H)
15a, 15b	1.26–1.13 (m, 2H)	1.19 (1H), 1.19 (1H)
12	1.15 (m, 1H)	1.14 (m, 1H)
32b	1.01 (dddd, $J = 10.3, 7.5, 2.0, 1.7$ Hz, 1H)	1.00 (bdd, $J = 13.0, 7.2$ Hz, 1H)

Comparison of ^{13}C NMR of madangamine A



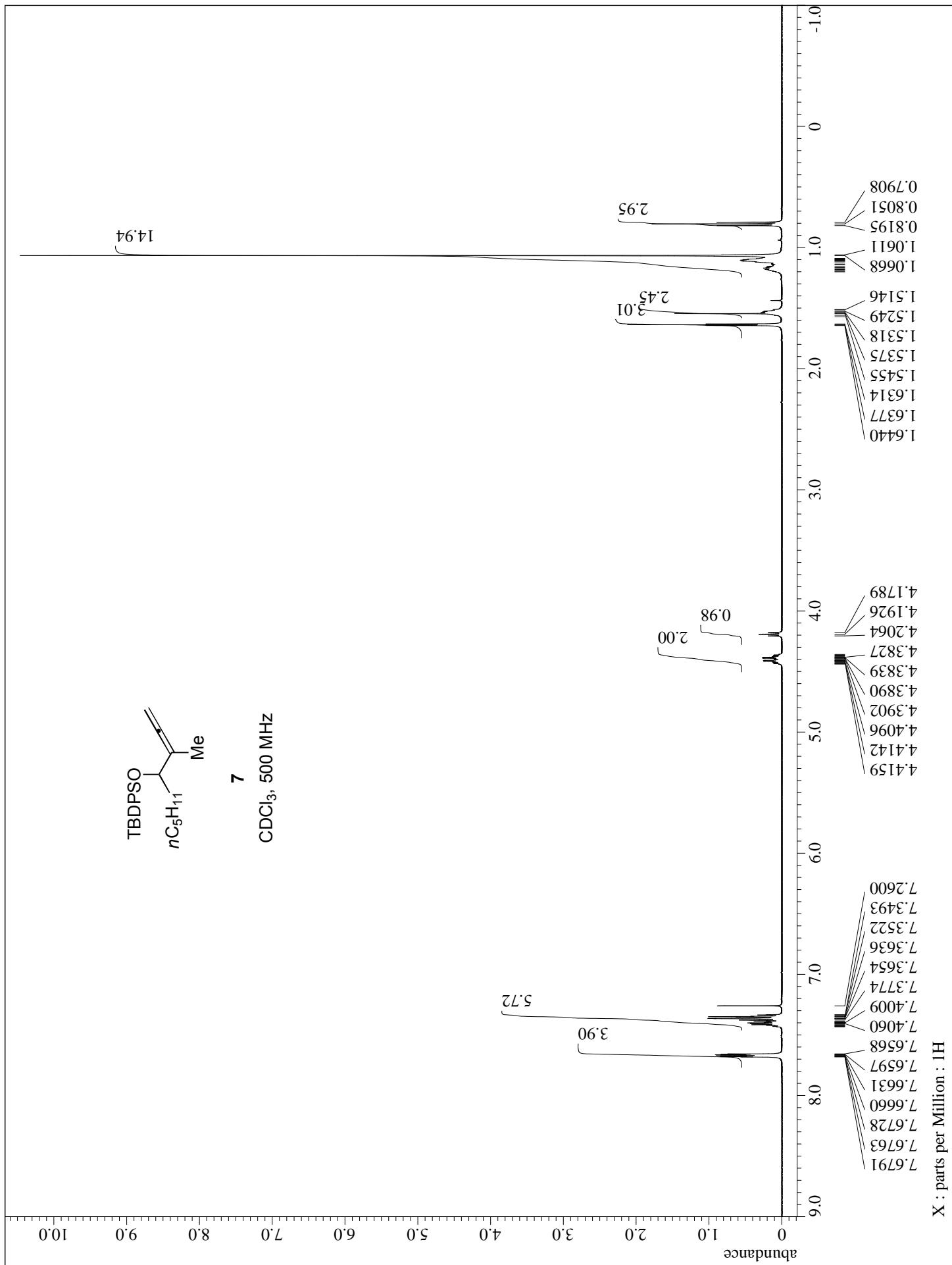
	our synthetic sample	natural sample
	^{13}C NMR (125 MHz, C_6D_6)	^{13}C NMR (125 MHz, C_6D_6)
C-3	139.4 (C)	139.3 (C)
C-30	132.9 (CH)	132.8 (C)
C-23	129.2 (CH)	129.2 (C)
C-17	129.1 (CH)	129.0 (CH)
C-18	129.0 (CH)	129.0 (CH)
C-27	128.7–127.6 (CH x2)	128.3 (CH)
C-24	(These peaks were overlapped with C_6D_6)	128.0 (CH)
C-26	127.5 (CH)	127.5 (CH)
C-29	125.9 (CH)	125.9 (CH)
C-20	121.9 (CH)	121.8 (CH)
C-6	61.6 (CH_2)	61.6 (CH_2)
C-8	59.4 (CH_2)	59.4 (CH_2)
C-21	57.7 (CH_2)	57.7 (CH_2)
C-13	55.7 (CH_2)	55.6 (CH_2)
C-10	52.4 (CH_2)	52.4 (CH_2)
C-2	51.8 (CH)	51.8 (CH)
C-12	39.1 (CH)	39.1 (CH)
C-4	38.4 (CH_2)	38.3 (CH_2)
C-5	37.1 (CH)	37.1 (CH)
C-9	37.0 (C)	37.0 (C)
C-32	36.1 (CH_2)	36.1 (CH_2)
C-11	32.4 (CH_2)	32.4 (CH_2)
C-19	26.9 (CH_2)	26.8 (CH_2)
C-28	26.7 (CH_2)	26.7 (CH_2)
C-25	26.6 (CH_2)	26.6 (CH_2)
C-16	25.9 (CH_2)	25.8 (CH_2)
C-22	25.5 (CH_2)	25.5 (CH_2)
C-15	25.4 (CH_2)	25.4 (CH_2)
C-14	23.9–22.9 (CH_2 , br)	23.2 (CH_2)
C-31	22.7 (CH_2)	22.7 (CH_2)

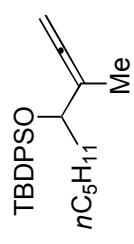
Comparison of the optical rotation



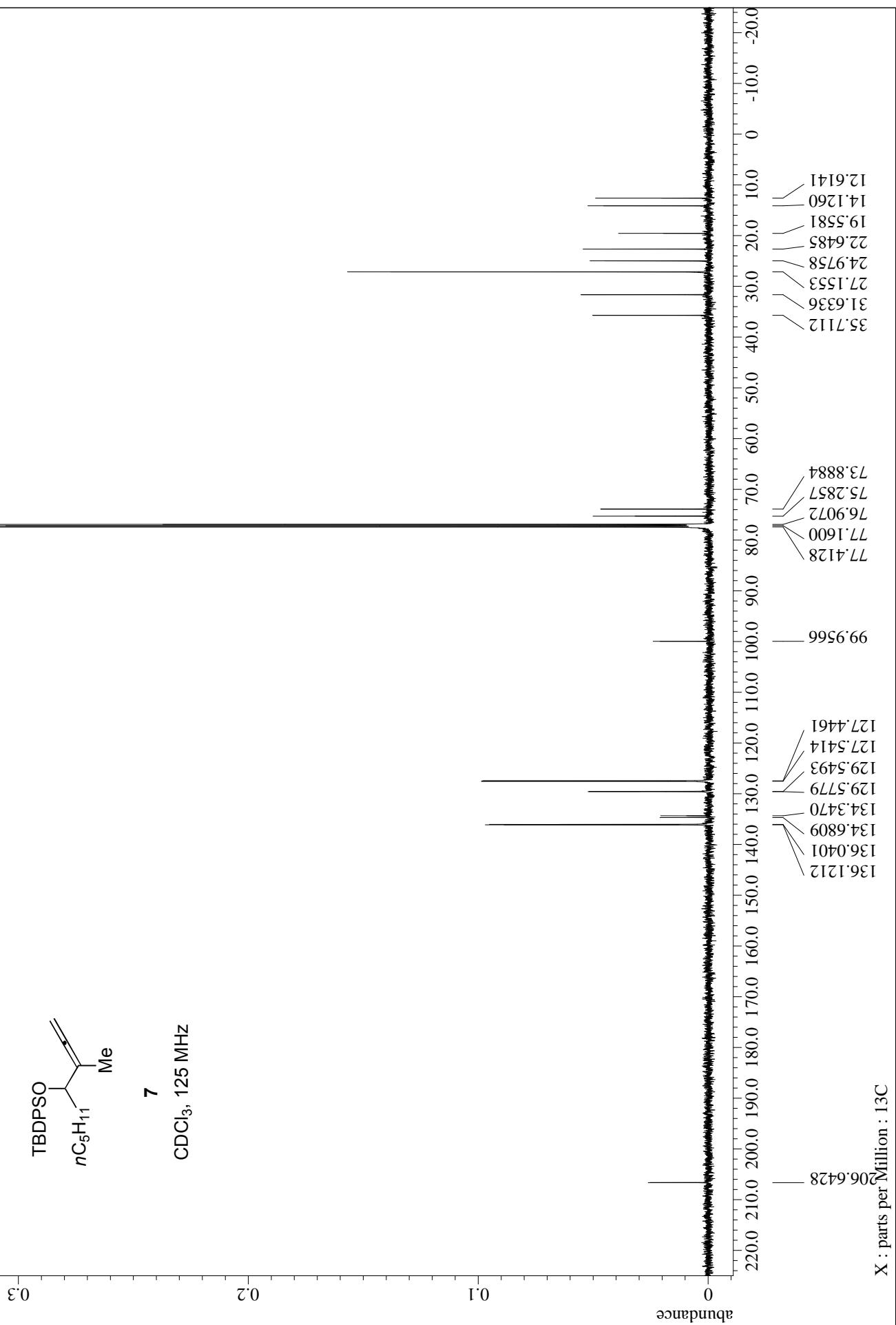
	Natural product	Amat's sample	Our synthetic sample
madangamine A	$[\alpha]_D +319$ (<i>c</i> 1.00, EtOAc) ¹⁴⁾	-	$[\alpha]^{24}_D +142$ (<i>c</i> 0.50, EtOAc, 95% ee)
			$[\alpha]^{23}_D +146$ (<i>c</i> 0.10, EtOAc, 95% ee)
madangamine B	$[\alpha]_D +150.7$ (<i>c</i> 0.09, EtOAc) ¹⁵⁾	-	-
madangamine C	$[\alpha]_D +140.8$ (<i>c</i> 0.09, EtOAc) ¹⁵⁾	-	$[\alpha]^{26}_D +132$ (<i>c</i> 0.09, EtOAc, 95% ee)
madangamine D	not reported	$[\alpha]_D +101.3$ (<i>c</i> 0.29, CHCl ₃) ¹⁶⁾	-
madangamine E	not reported	-	$[\alpha]^{22}_D +90.9$ (<i>c</i> 0.40, EtOAc, 95% ee)

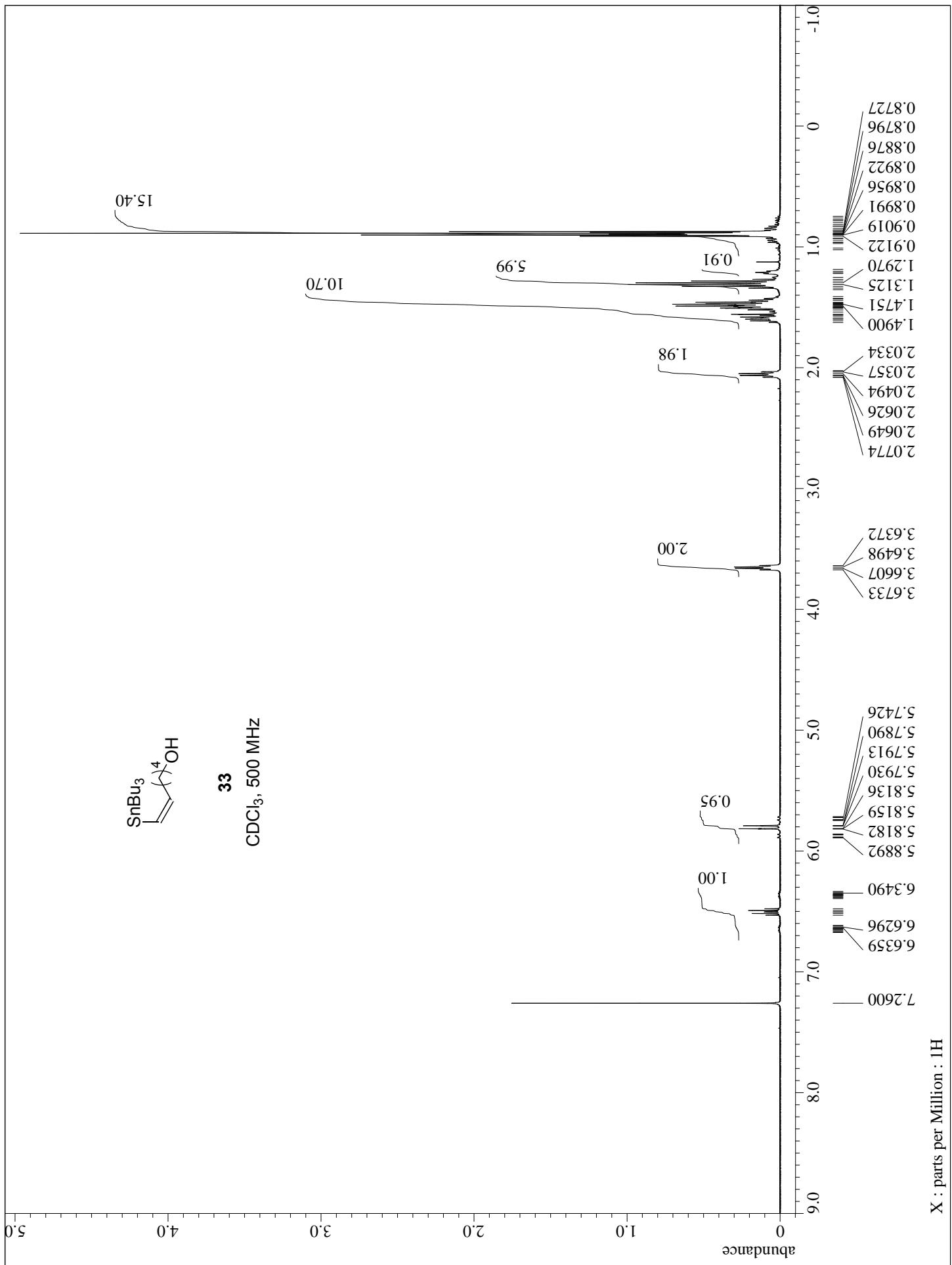
Our synthetic madangamine A was found to be indistinguishable from a natural sample based on ¹H NMR, ¹³C NMR, HRMS and IR except for its optical rotation. Although we measured the optical rotaion of the synthetic sample by changing the pH, concentration and temperature, it did not solve the case. Unfortunately, the natural sample of madangamine A does not exist anymore in the Andersen's group.





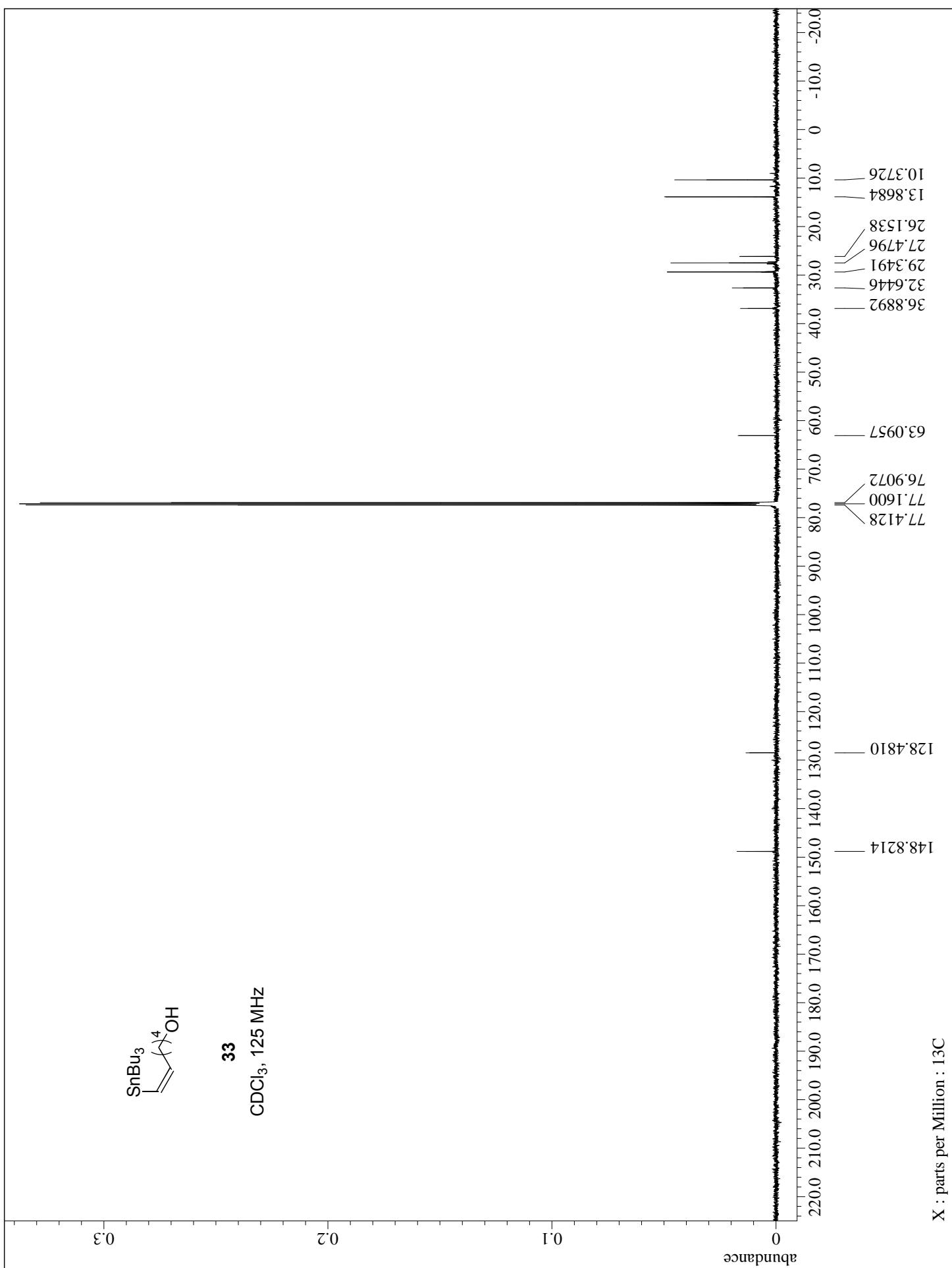
7
 CDCl_3 , 125 MHz

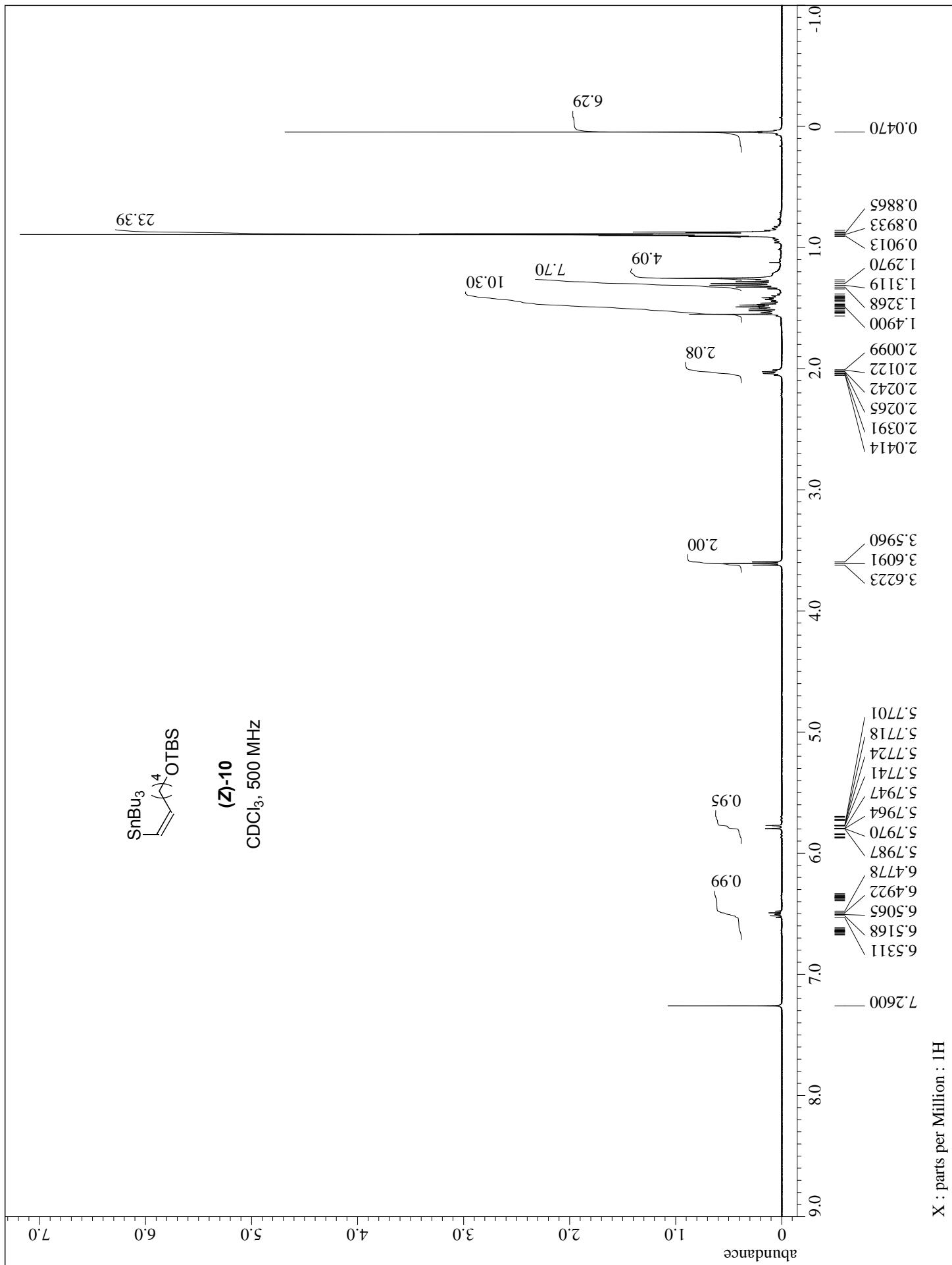


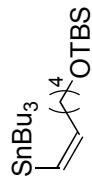




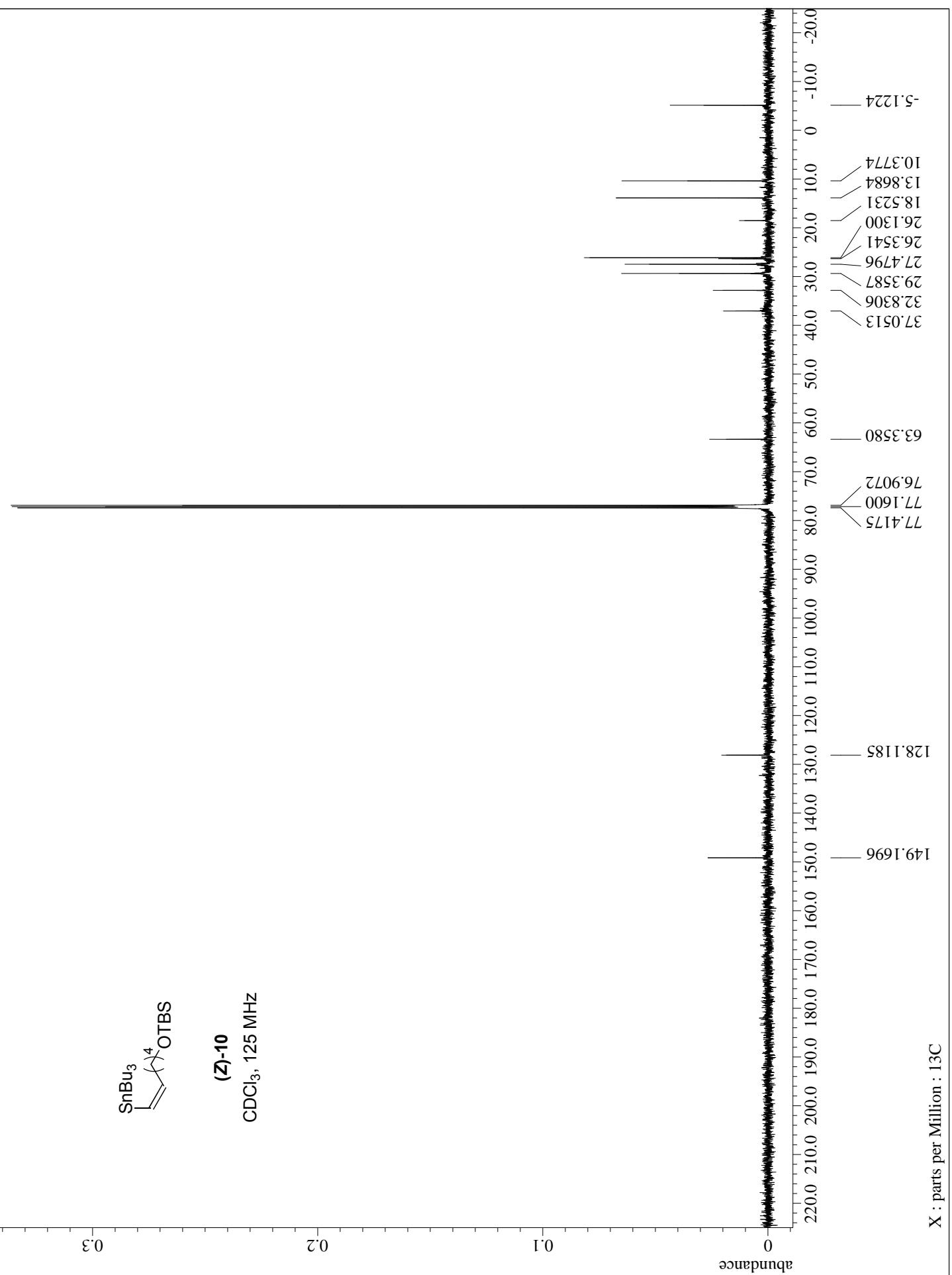
33
 CDCl_3 , 125 MHz

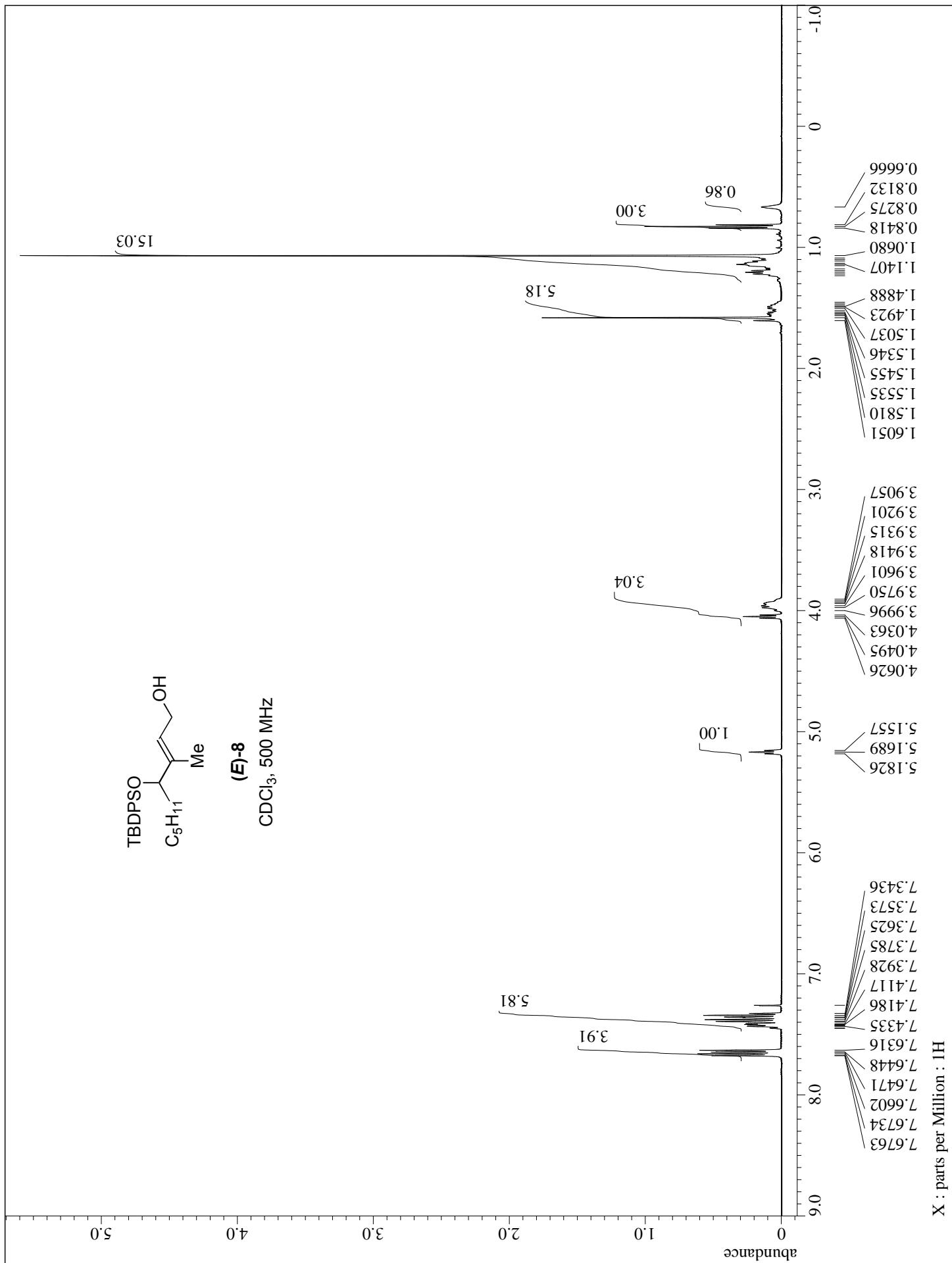


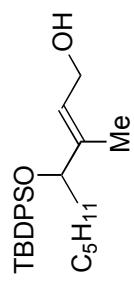




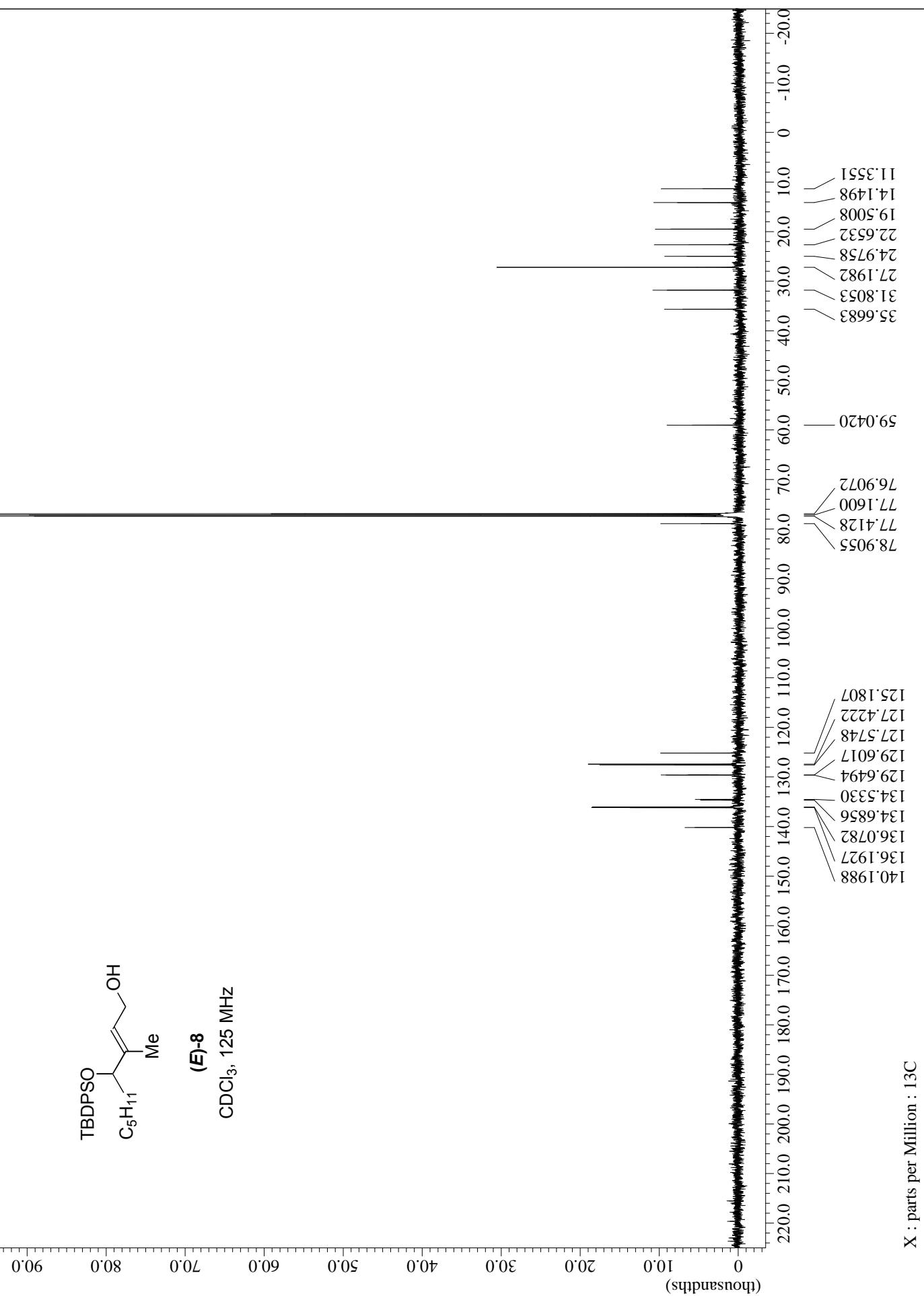
(Z)-10
 CDCl_3 , 125 MHz

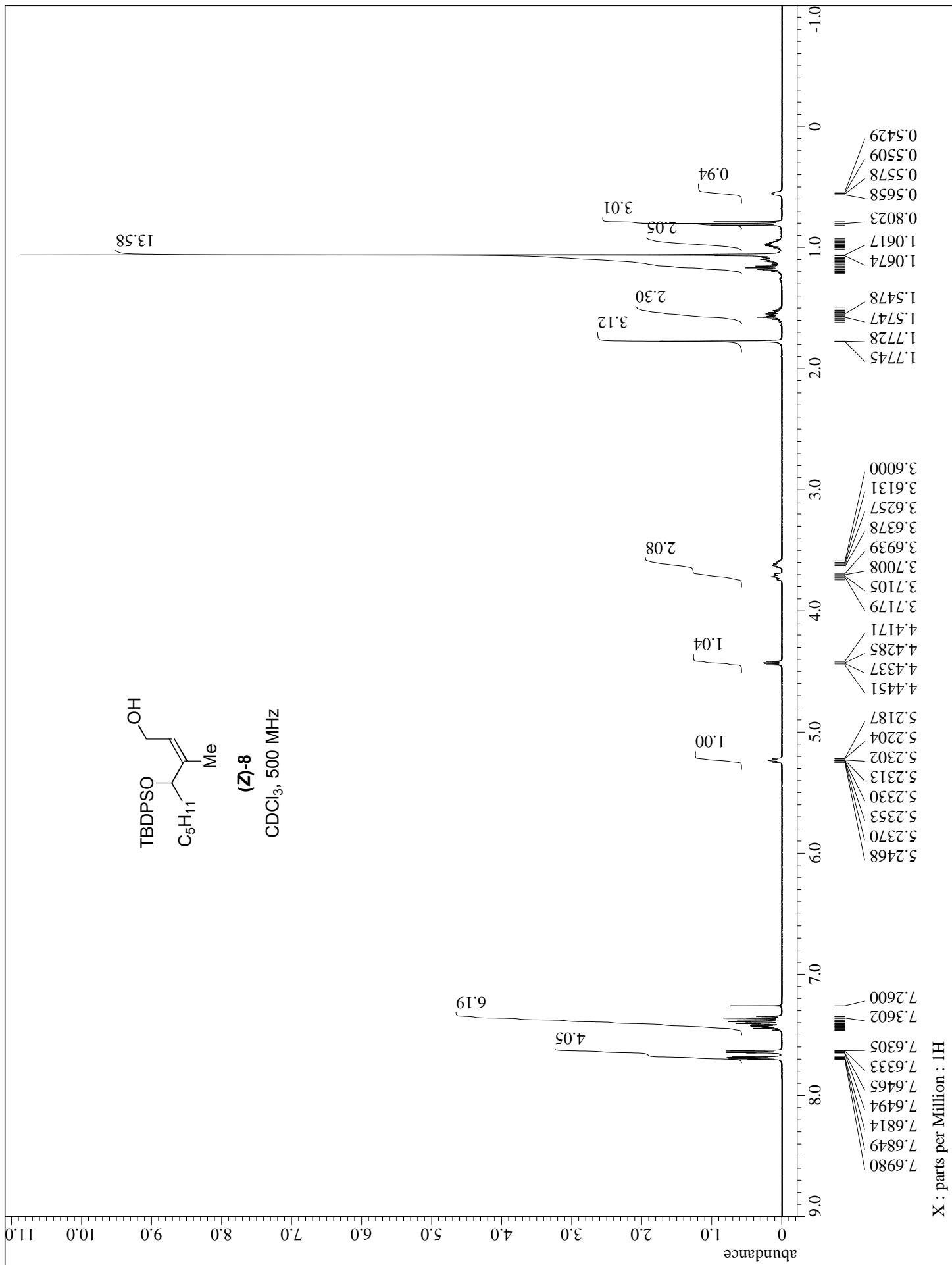


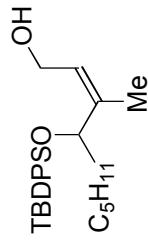




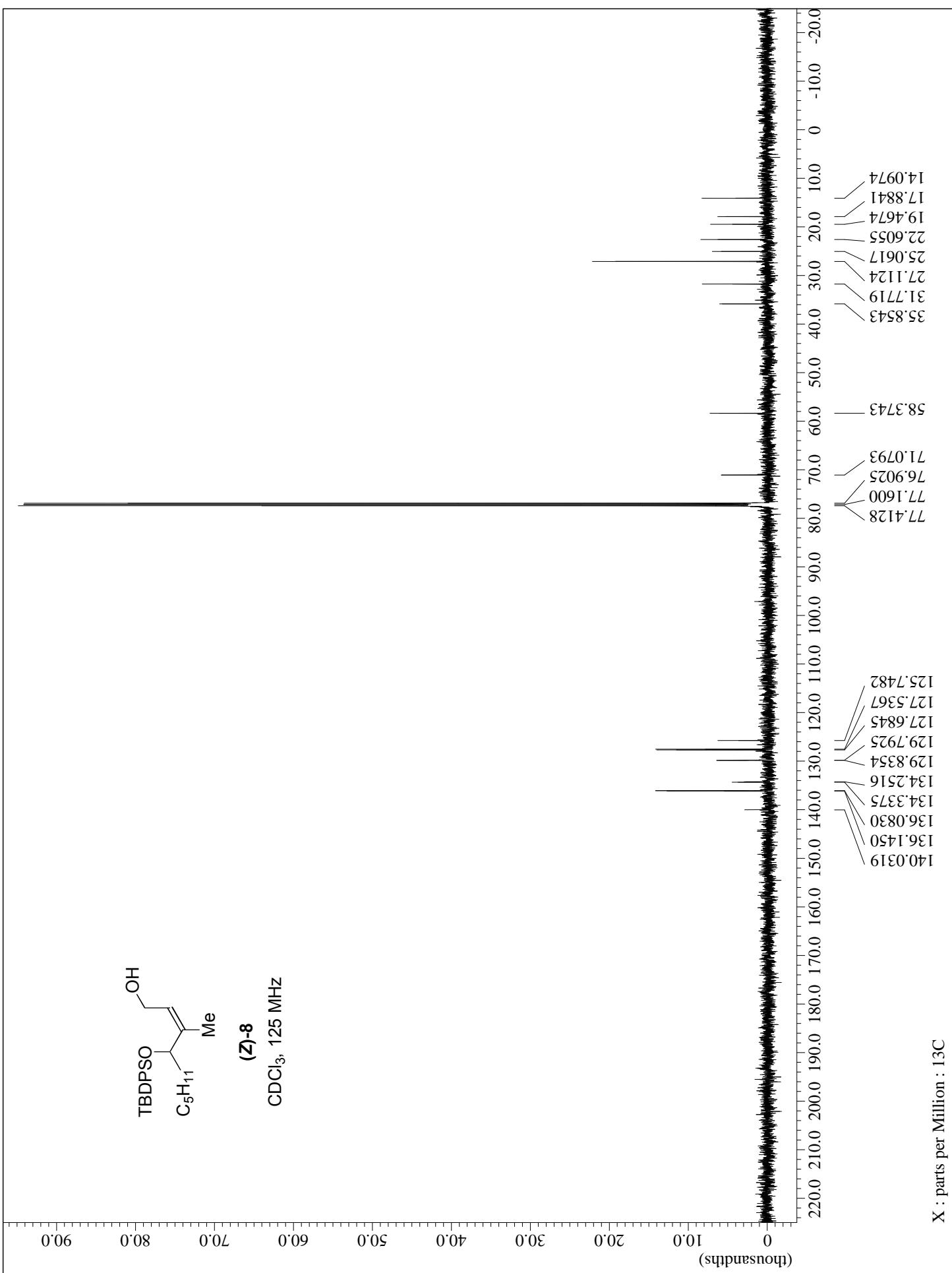
(E) -8
 $\text{CDCl}_3, 125 \text{ MHz}$

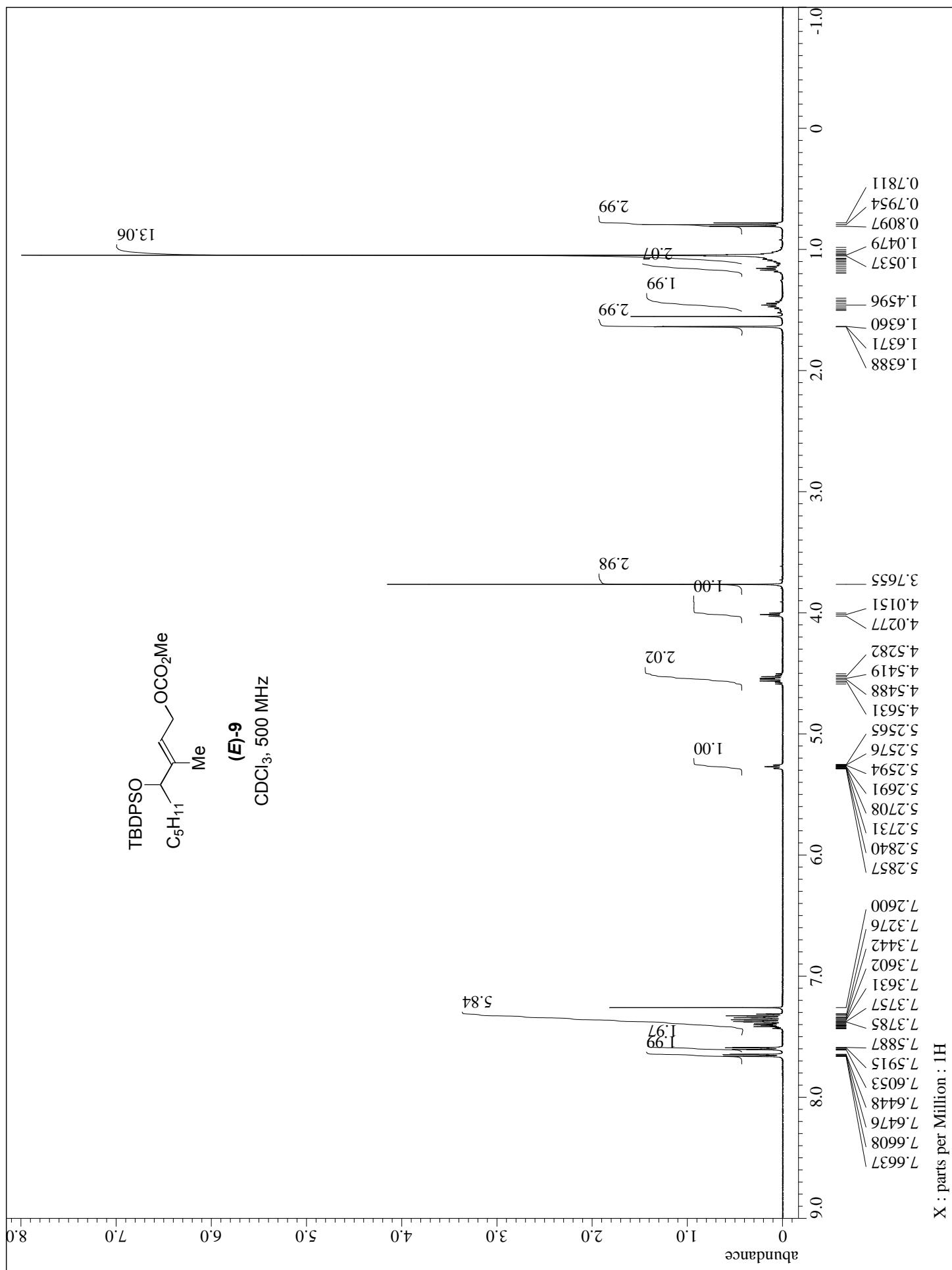


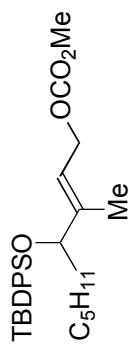




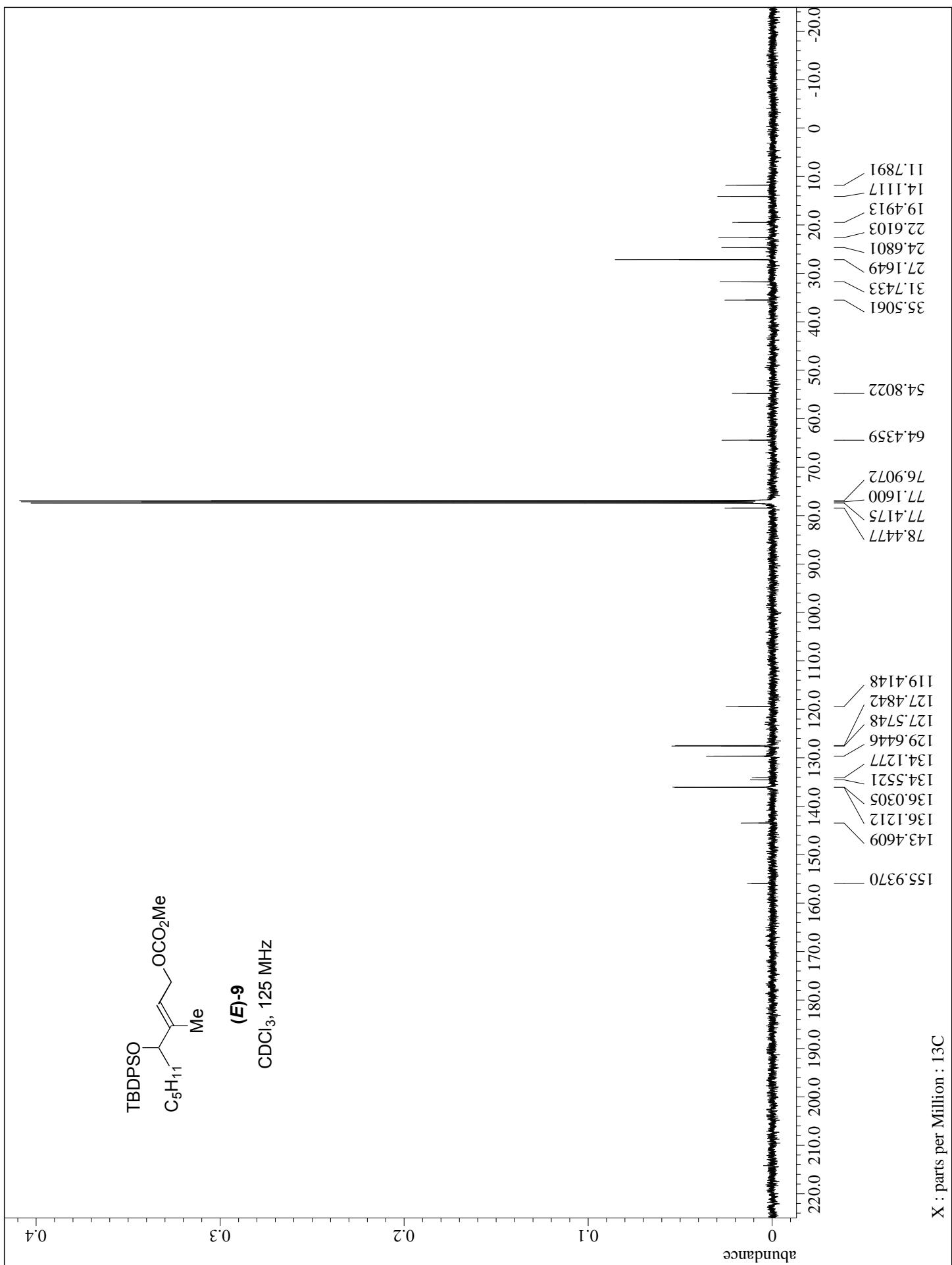
(Z)-8
 $\text{CDCl}_3, 125 \text{ MHz}$

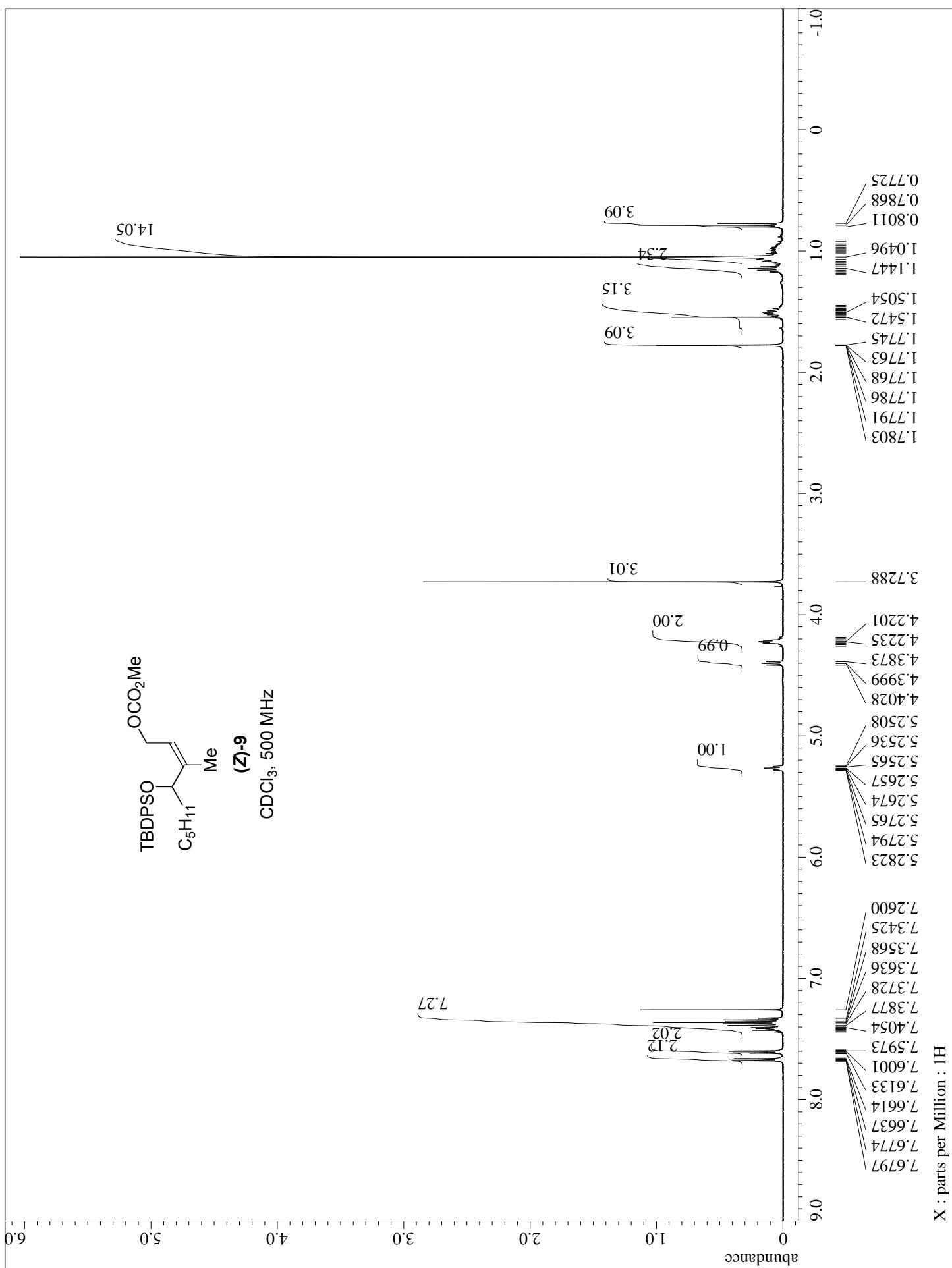




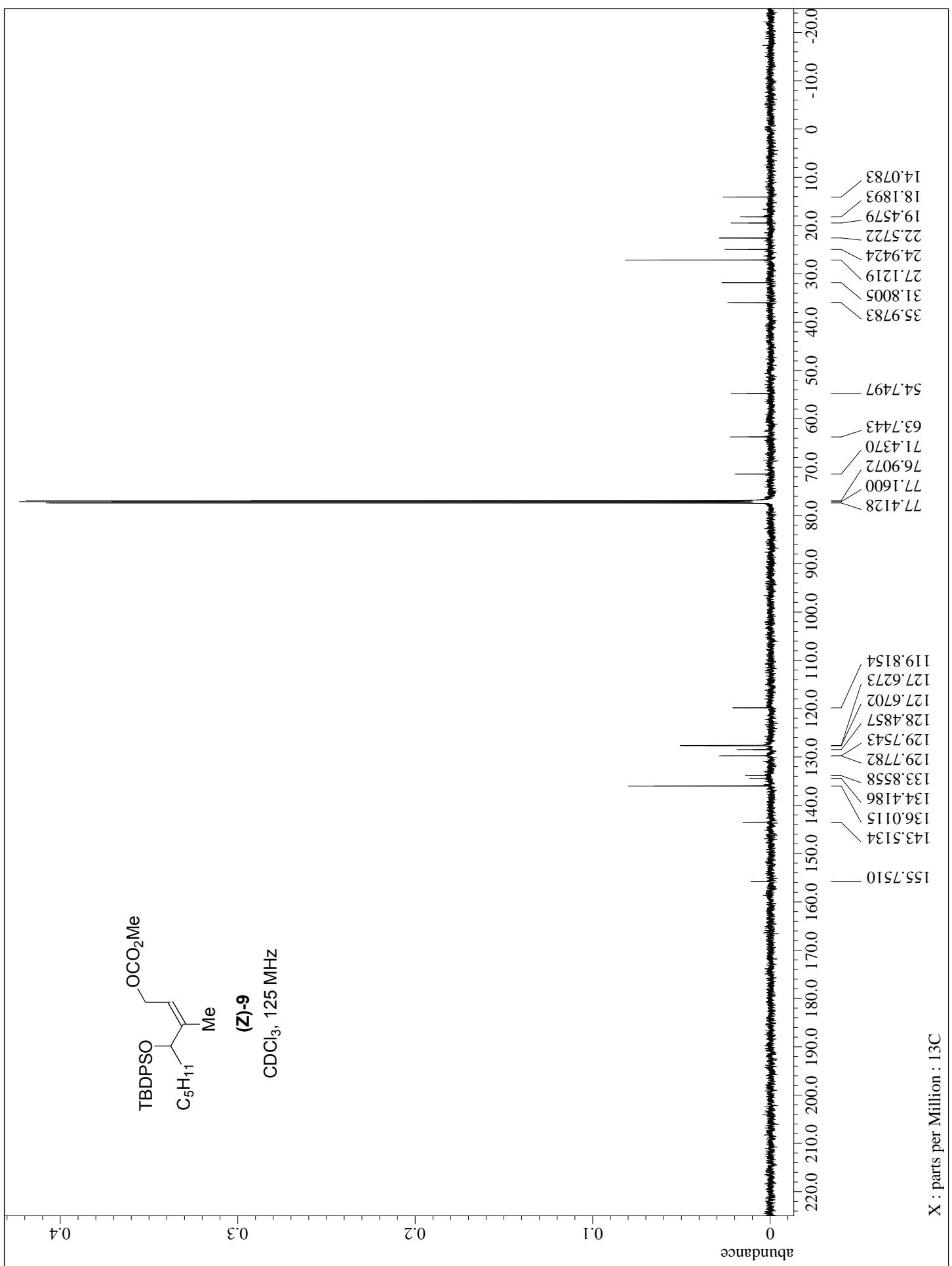


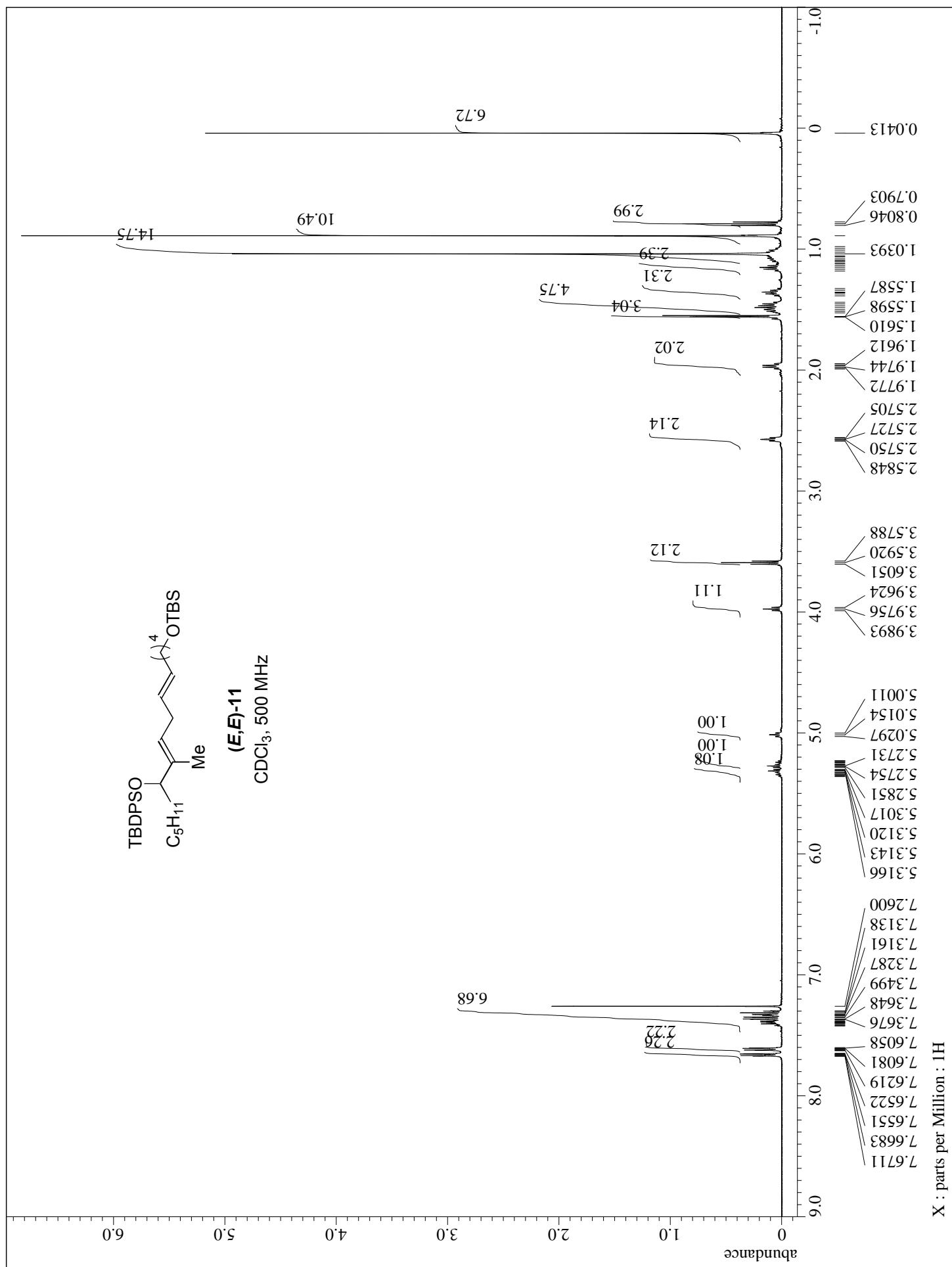
(E)-9
 $\text{CDCl}_3, 125 \text{ MHz}$

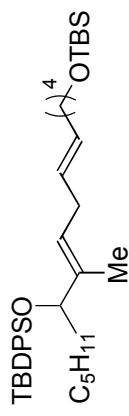




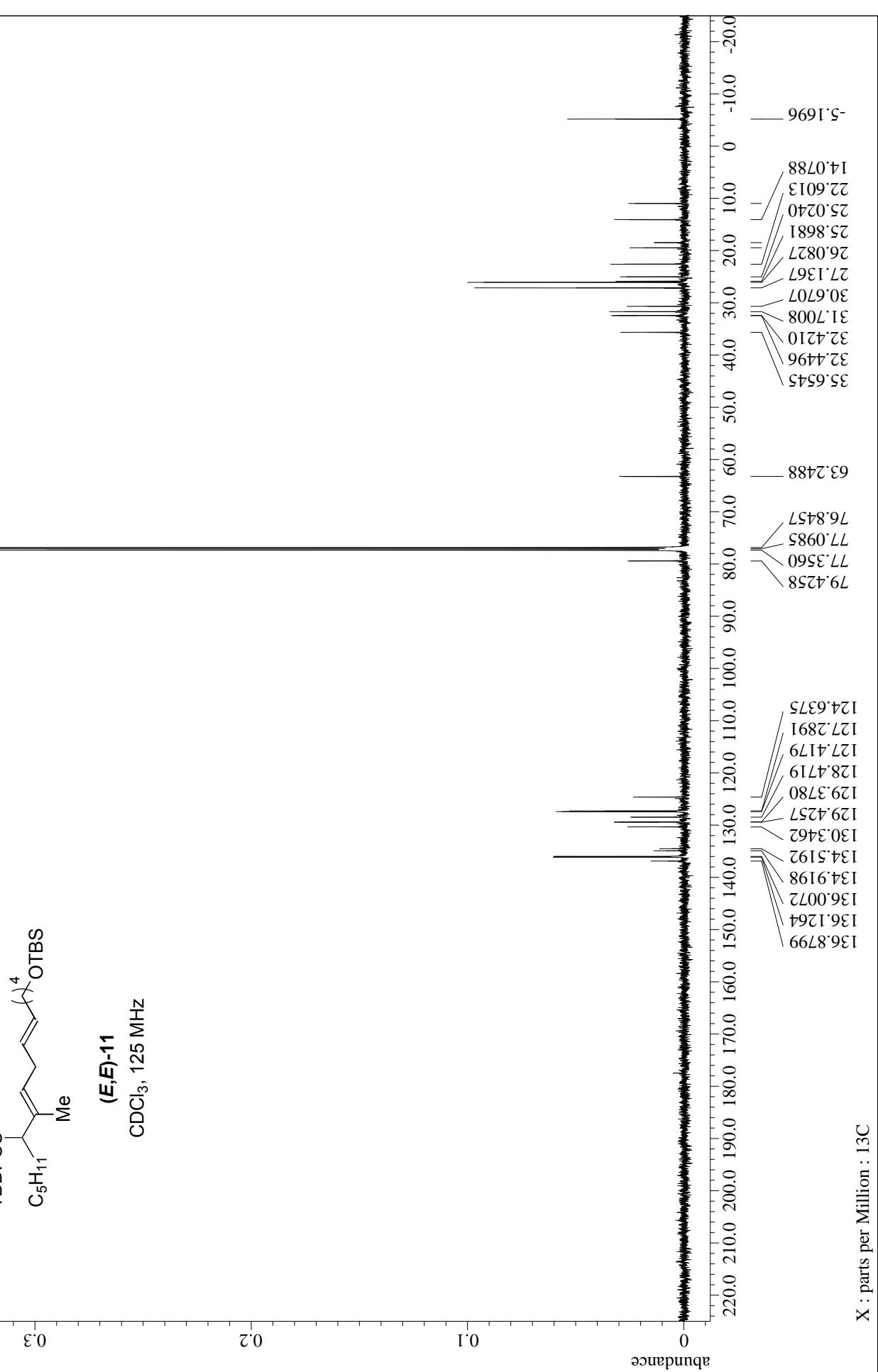
X : parts per Million : 13C



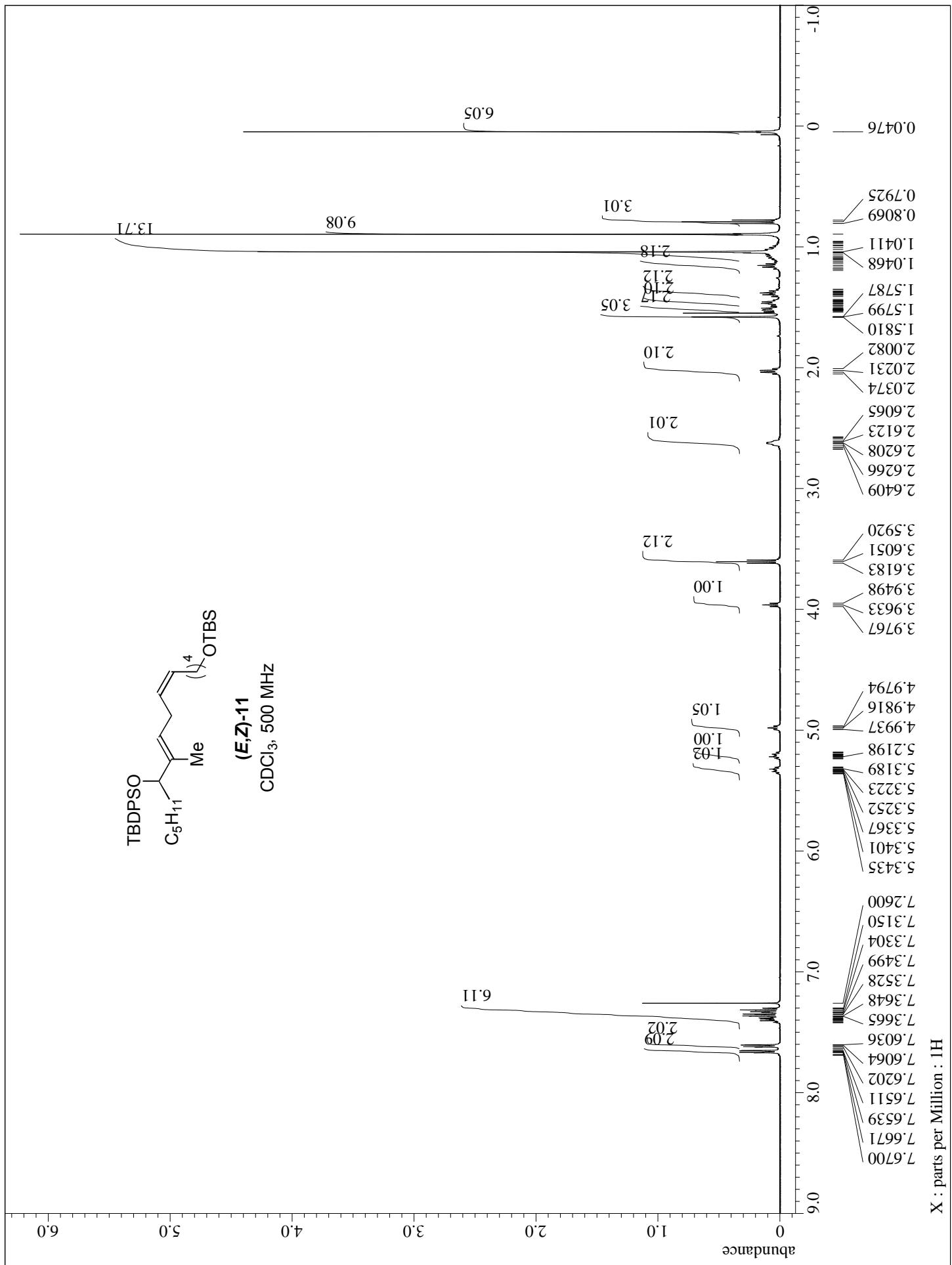


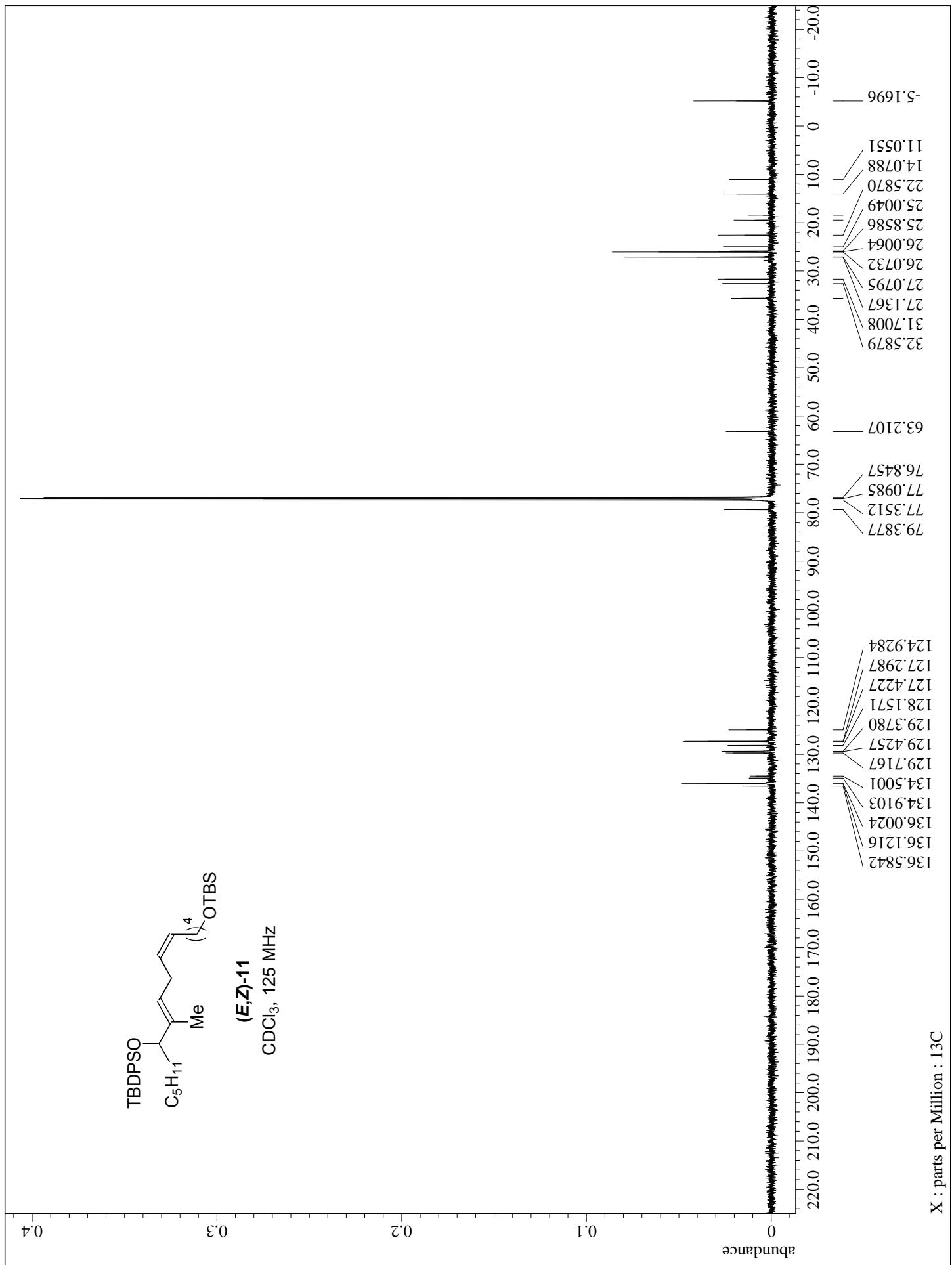


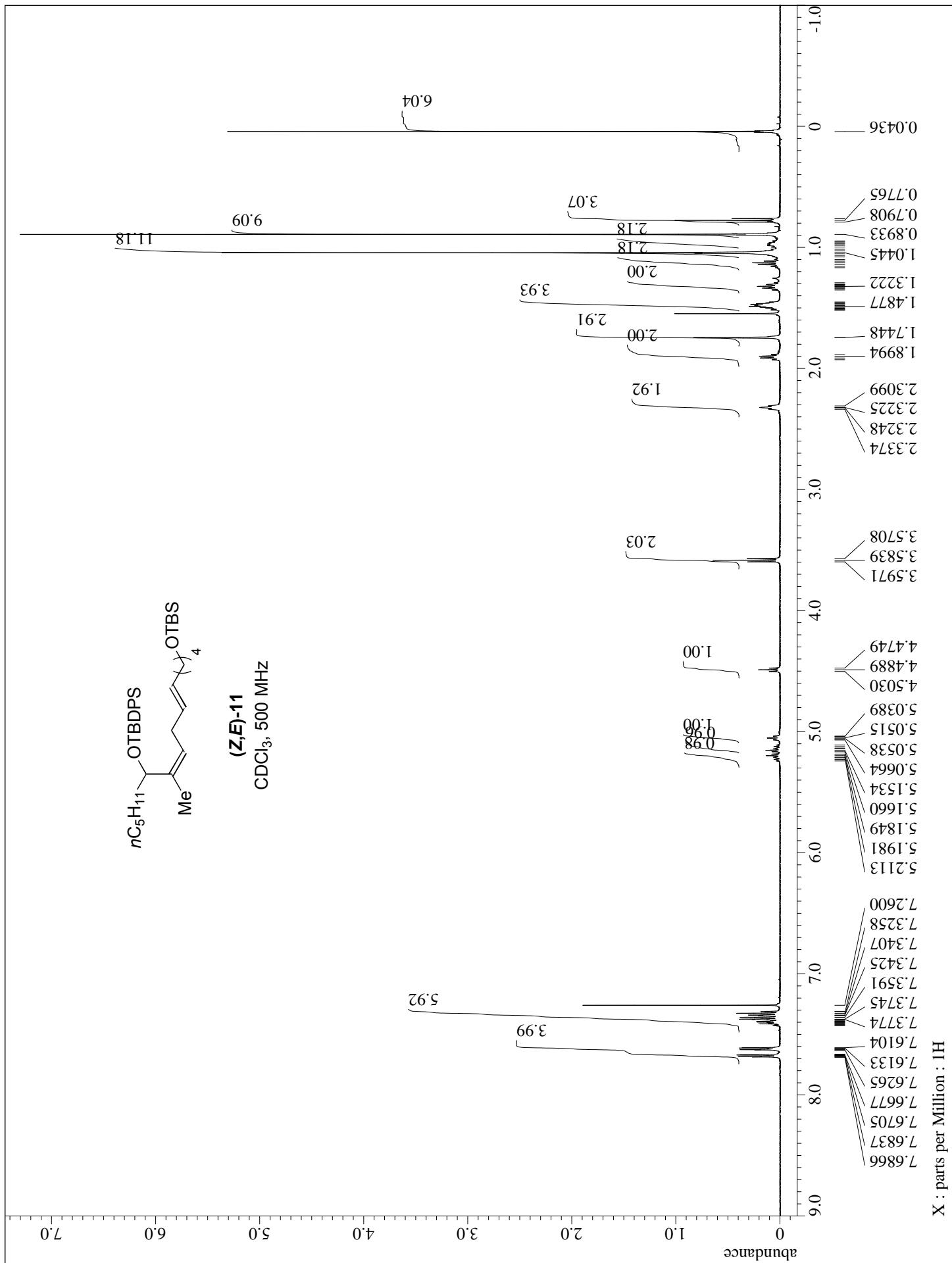
(E,E) -11
 $\text{CDCl}_3, 125 \text{ MHz}$

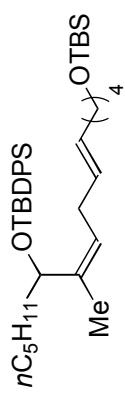


X : parts per Million : ^{13}C

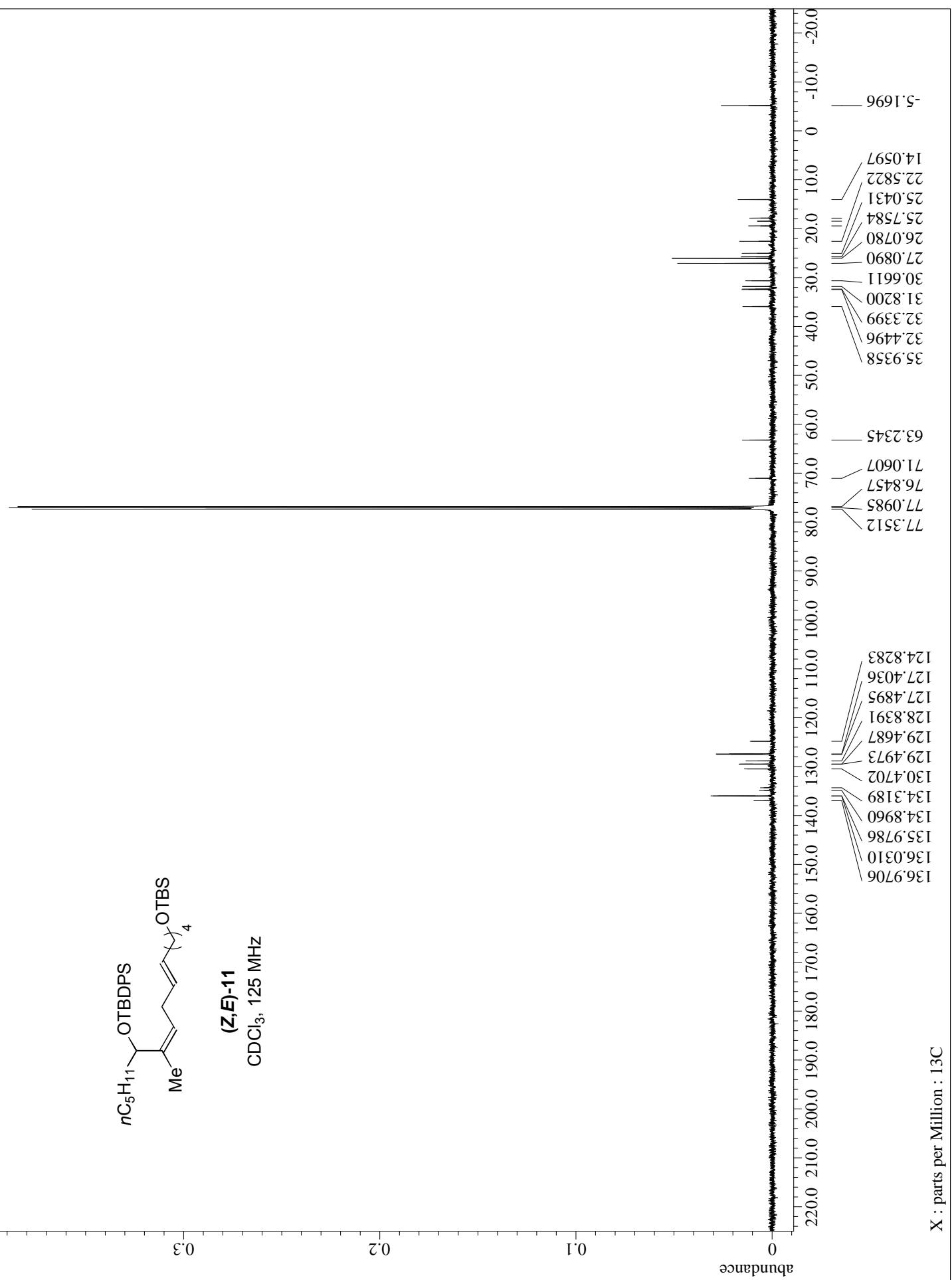


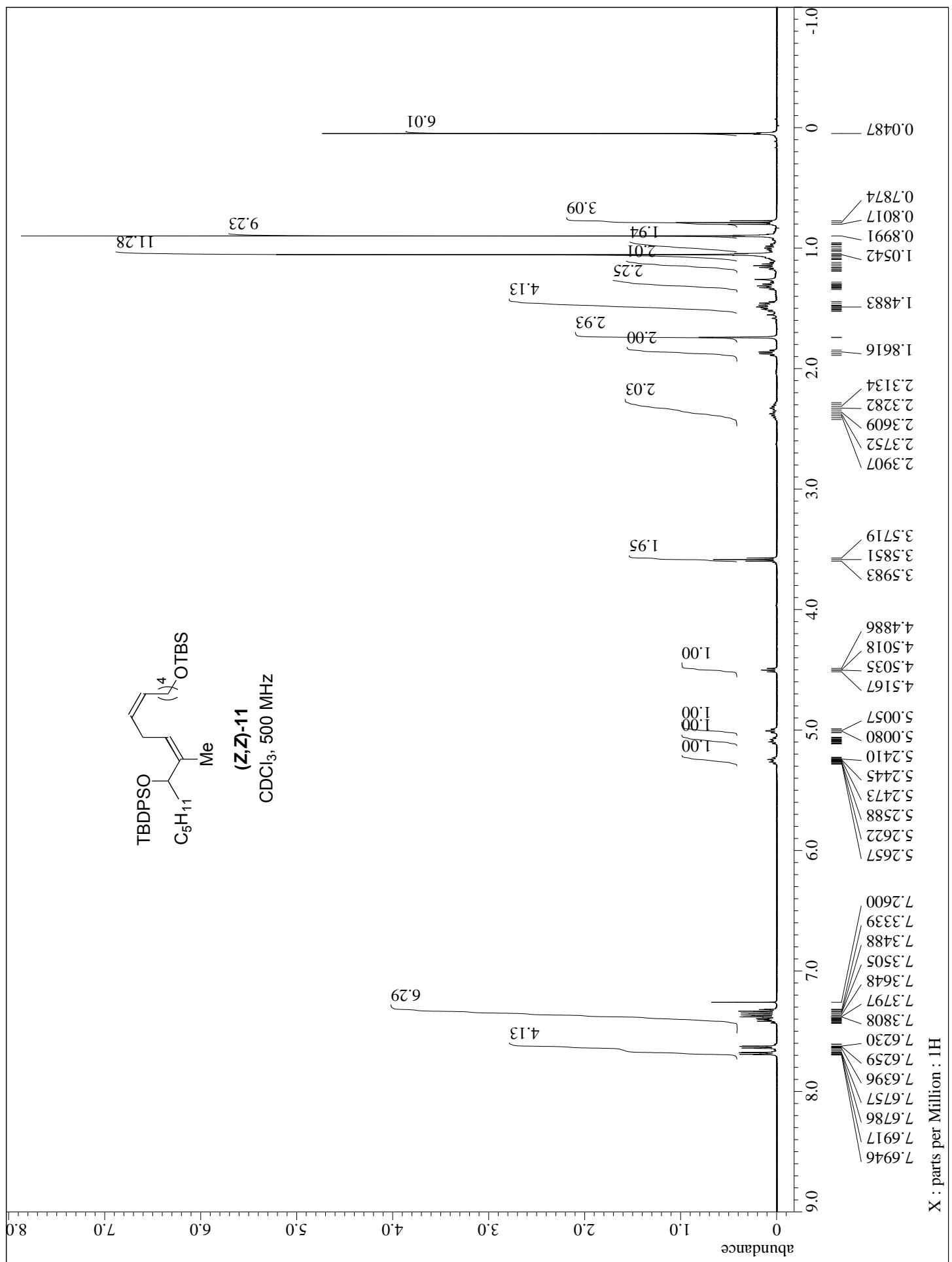


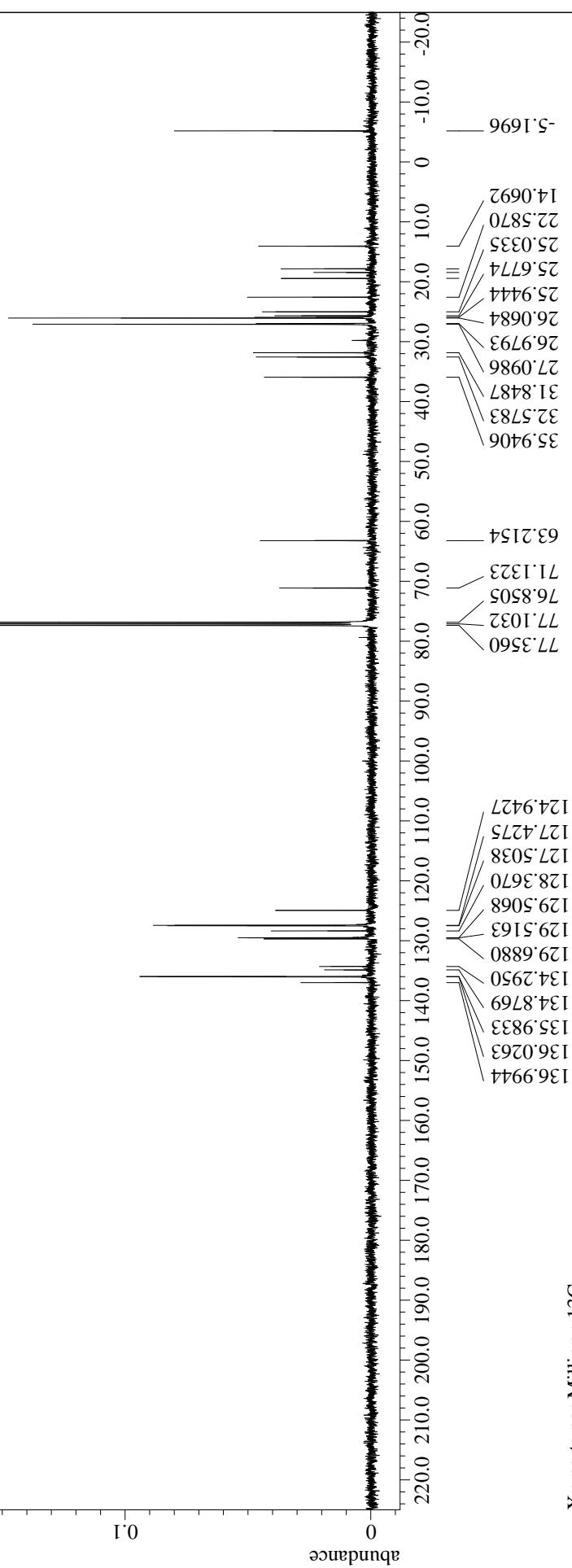
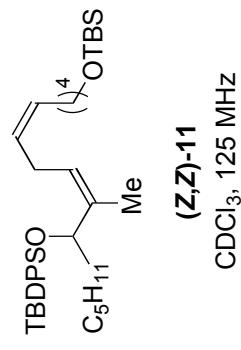


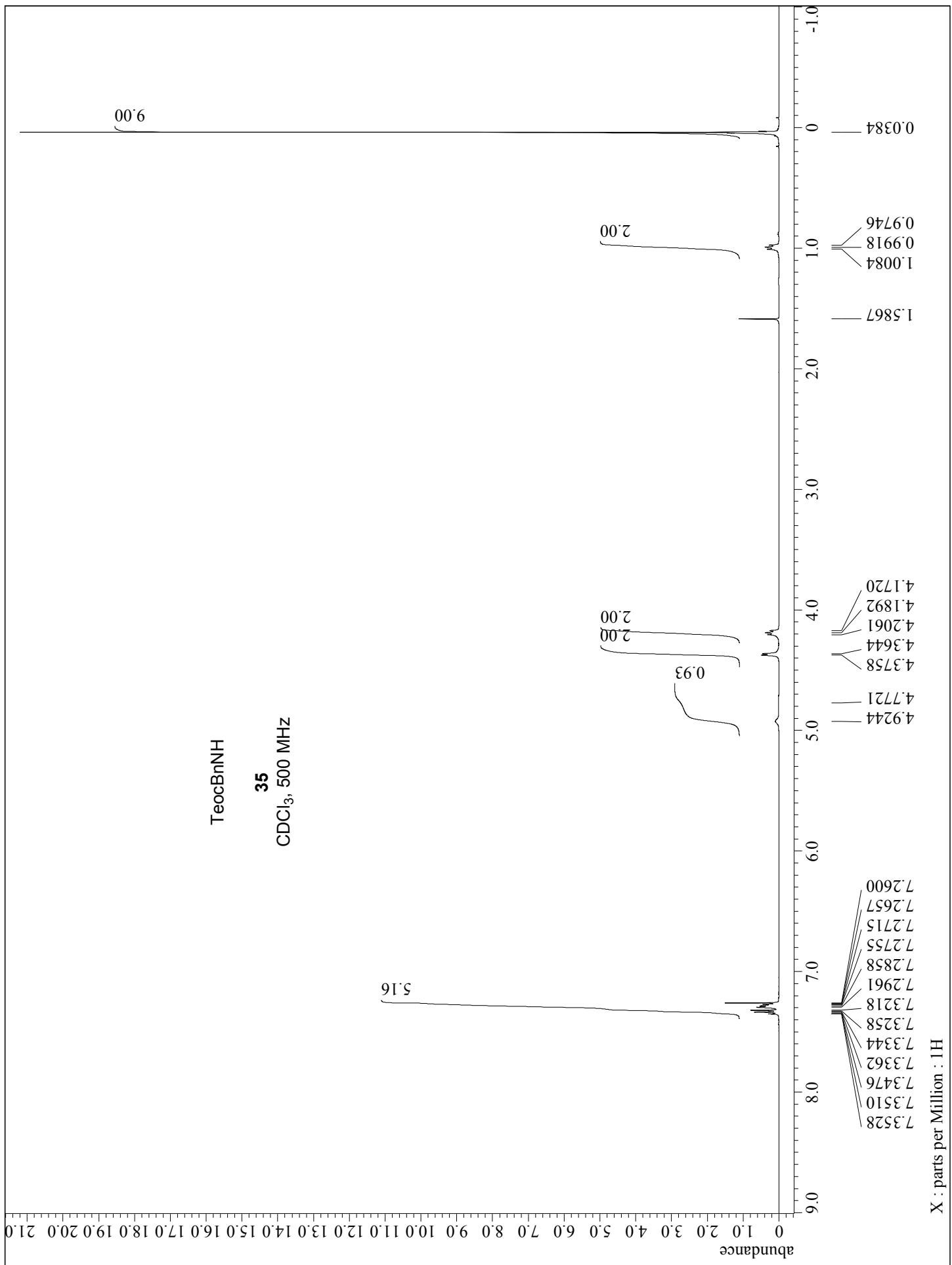


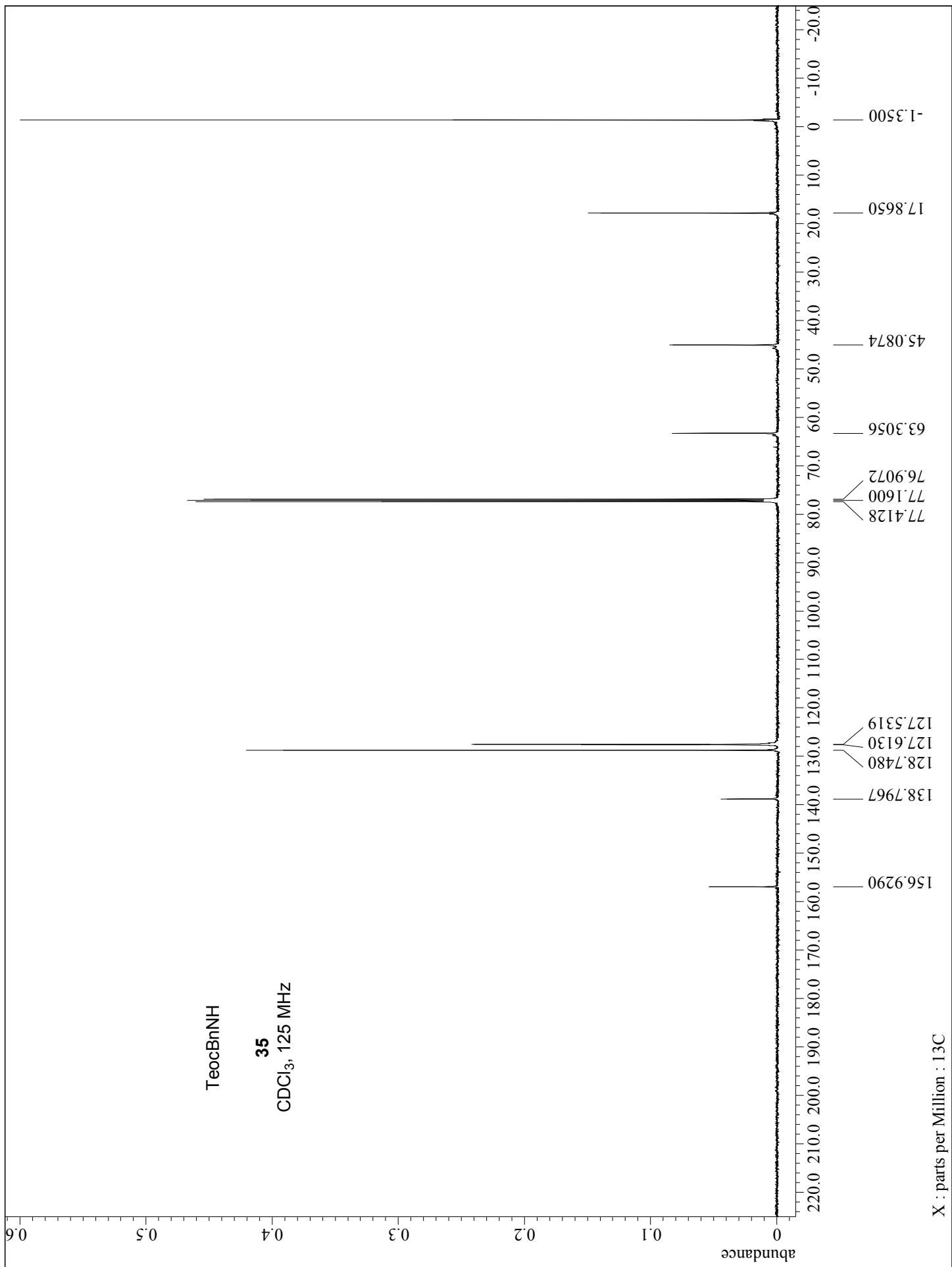
(Z,E)-11
 CDCl_3 , 125 MHz

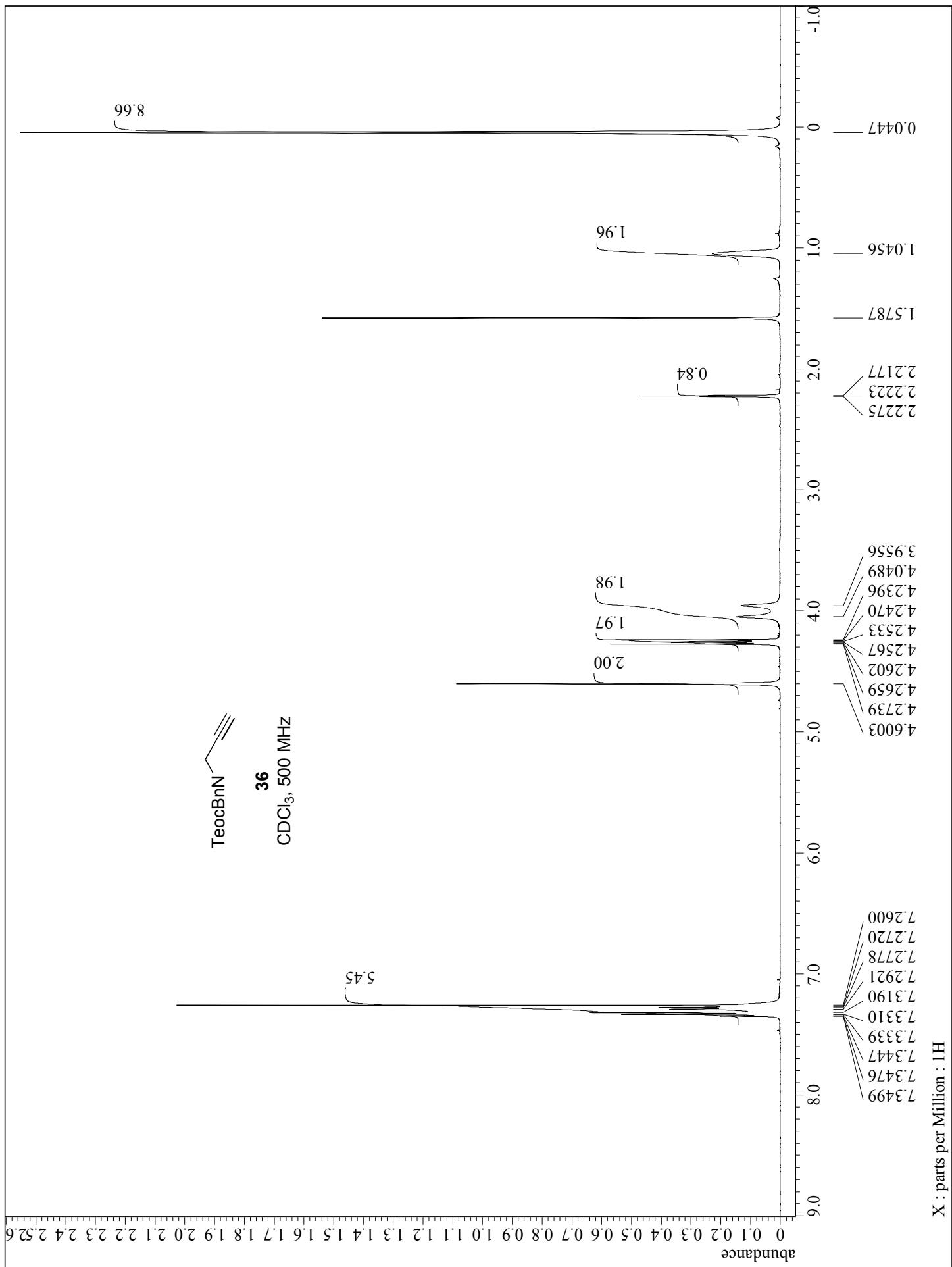


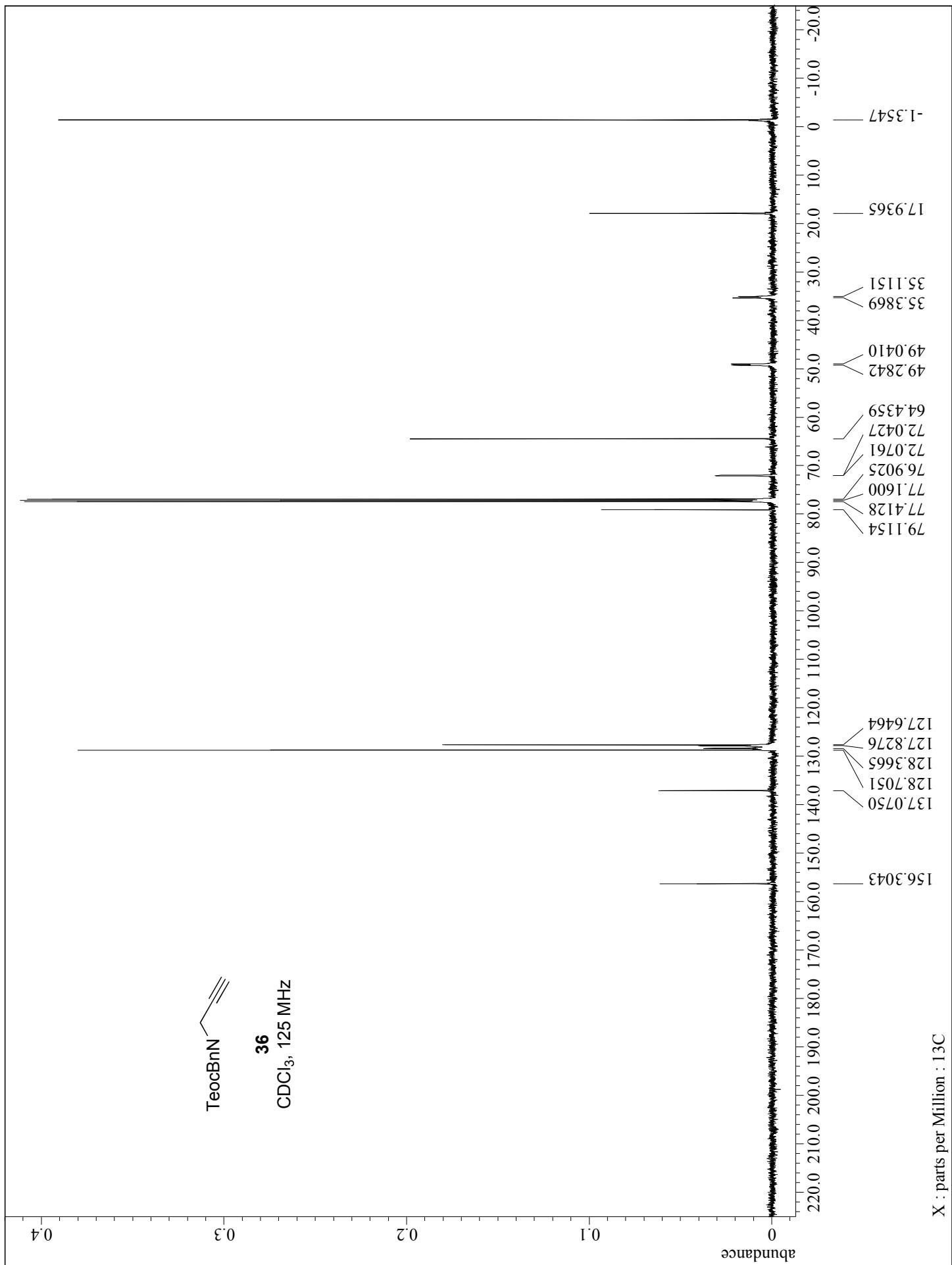














$\text{CDCl}_3, 500 \text{ MHz}$

9.00
9.01

2.06

0.0442
0.1564

1.5696
1.0370

2.00

3.9733
4.0987
4.2293
4.2464

2.06

4.2630
4.5929

2.10

4.2241
4.53218

2.00

4.53356
7.3407

1.06

7.3348
7.3356

1.02

7.2812
7.3098

1.00

7.2669
7.2600

0.96

7.2537

0.92

7.2537

0.88

7.2537

0.84

7.2537

0.80

7.2537

0.76

7.2537

0.72

7.2537

0.68

7.2537

0.64

7.2537

0.60

7.2537

0.56

7.2537

0.52

7.2537

0.48

7.2537

0.44

7.2537

0.40

7.2537

0.36

7.2537

0.32

7.2537

0.28

7.2537

0.24

7.2537

0.20

7.2537

0.16

7.2537

0.12

7.2537

0.08

7.2537

0.04

7.2537

0.00

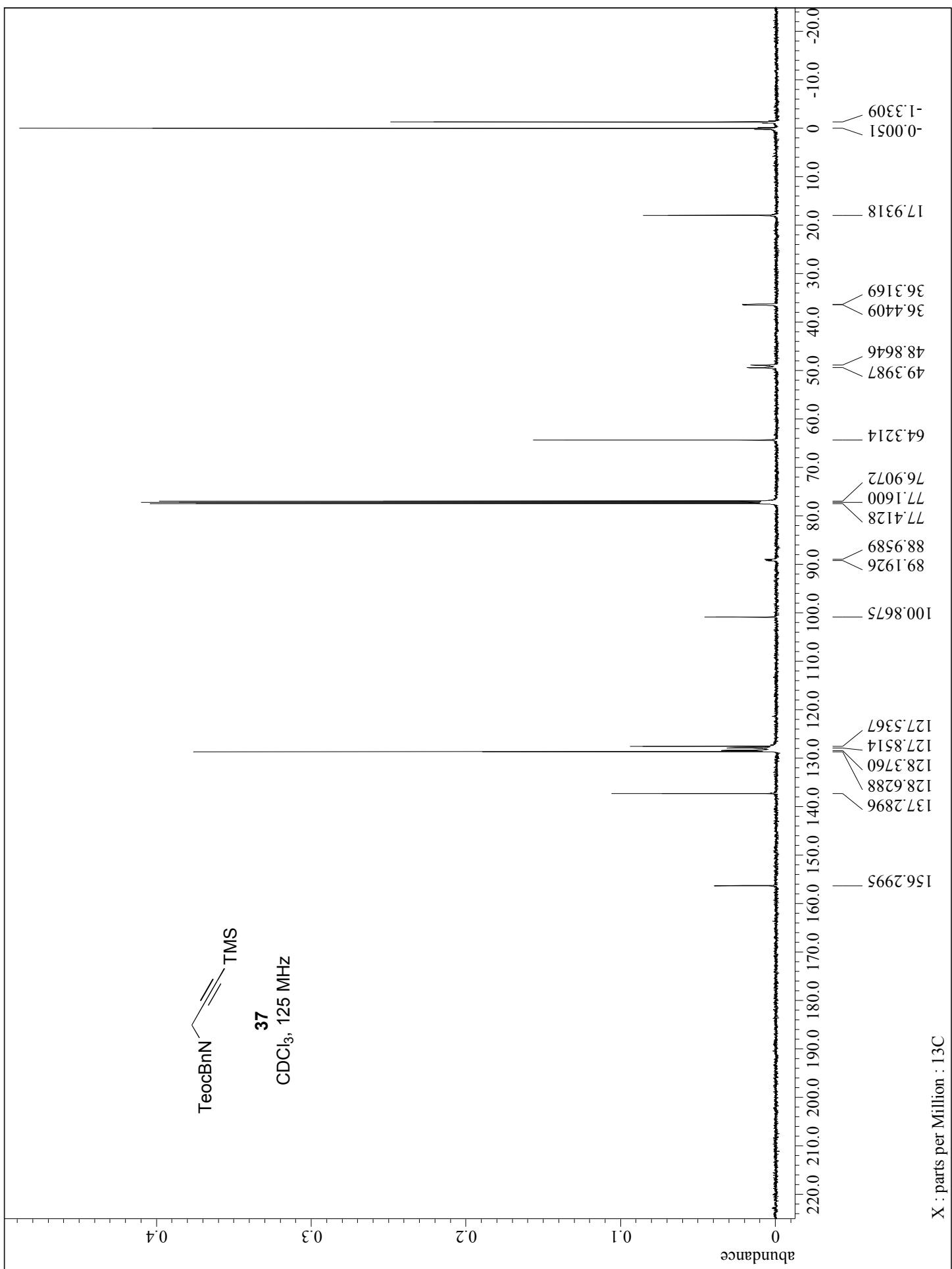
7.2537

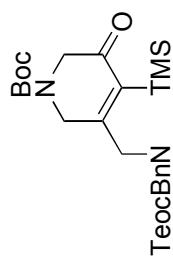
abundance

X : parts per Million : IH

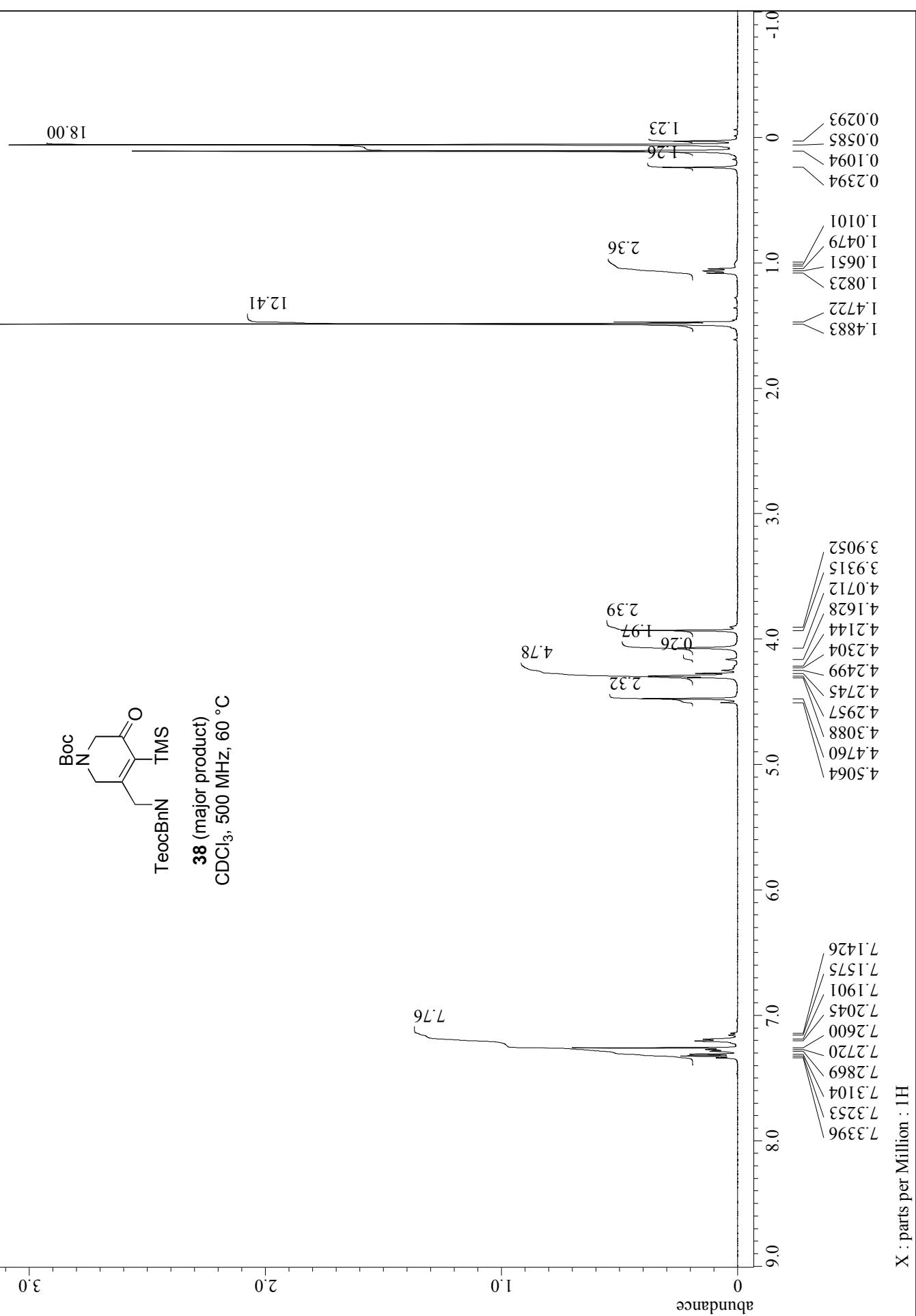


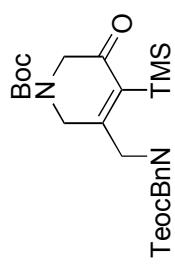
37
 CDCl_3 , 125 MHz



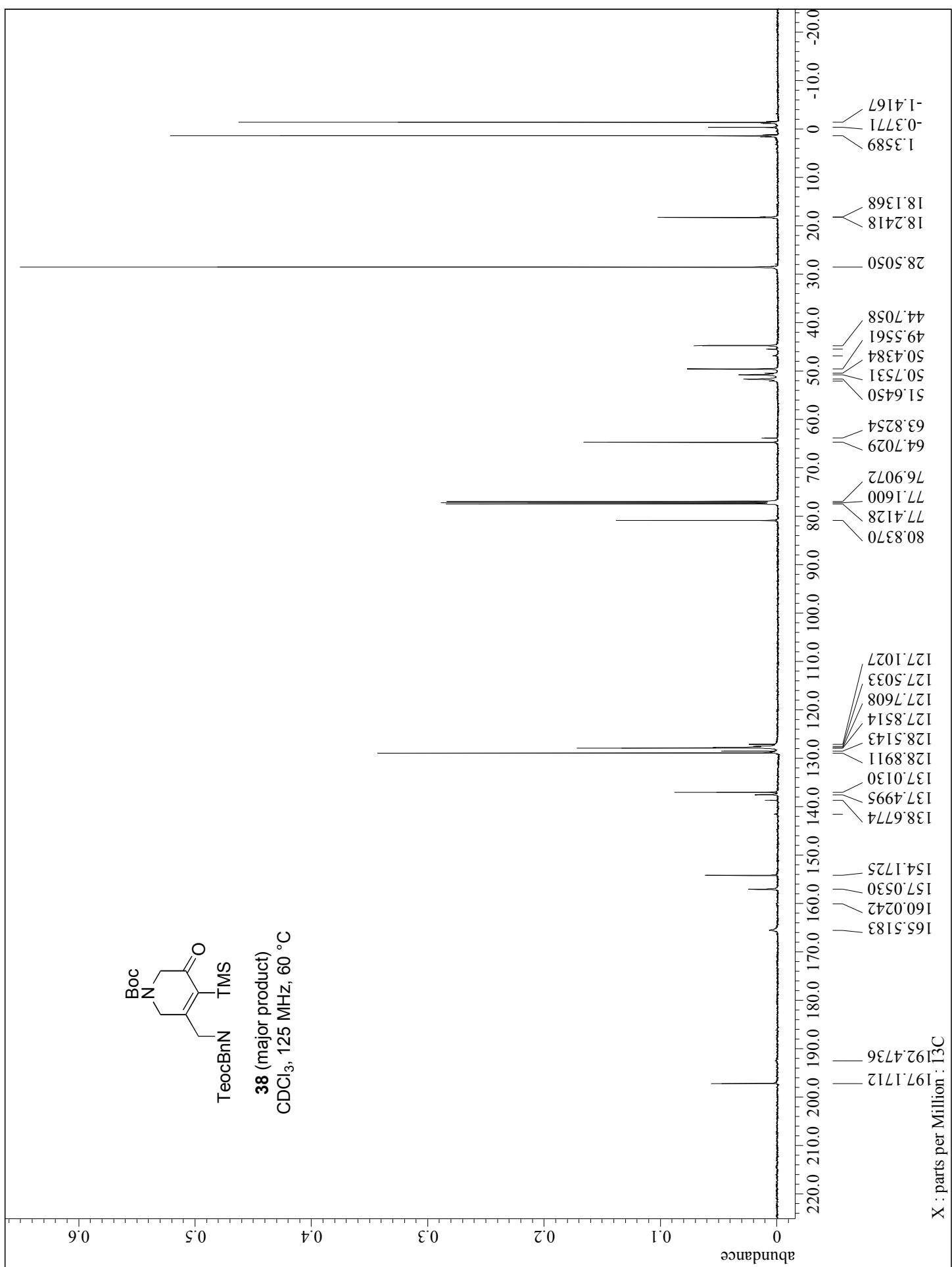


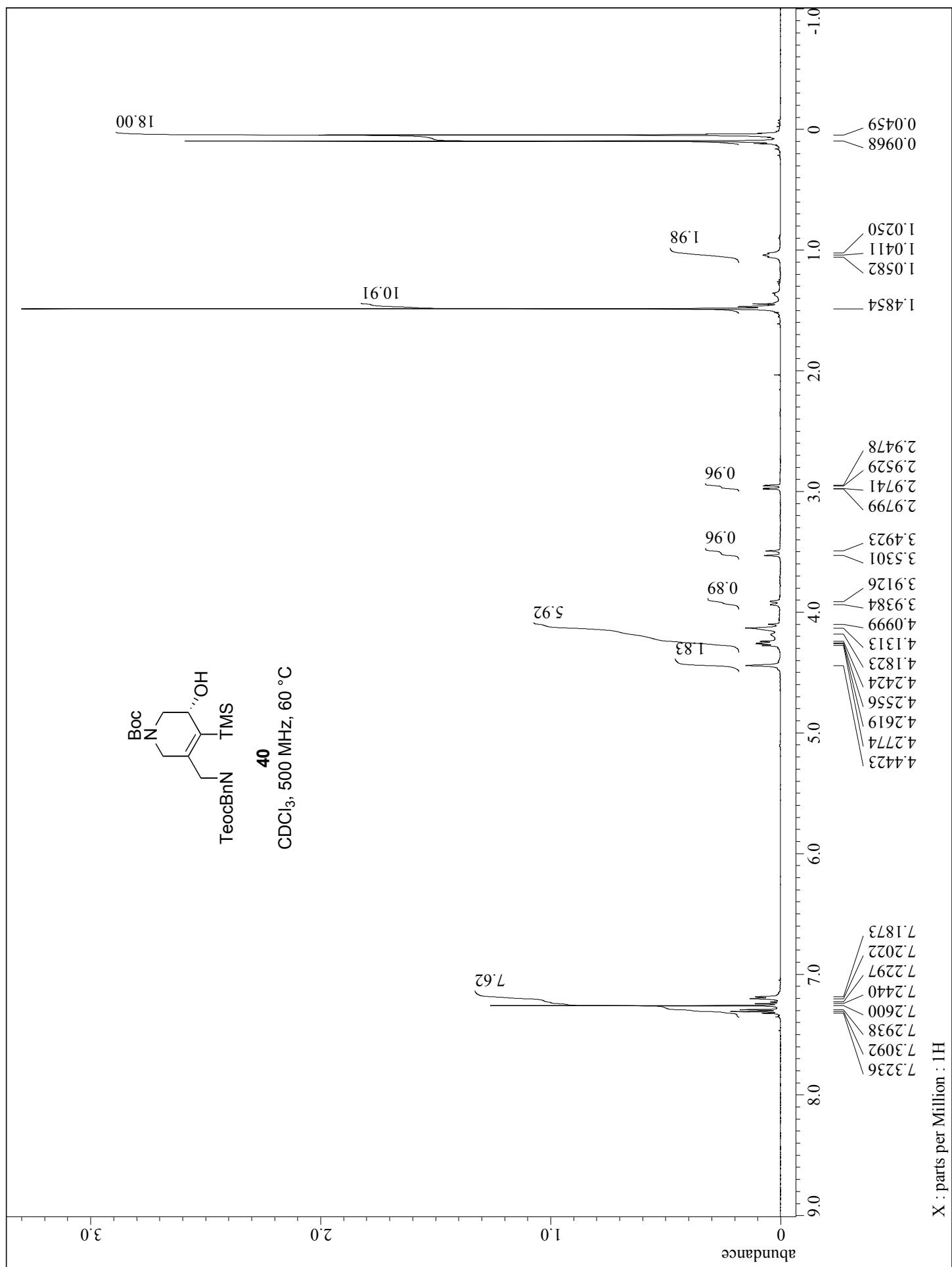
CDCl_3 , 500 MHz, 60 °C

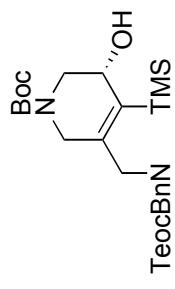




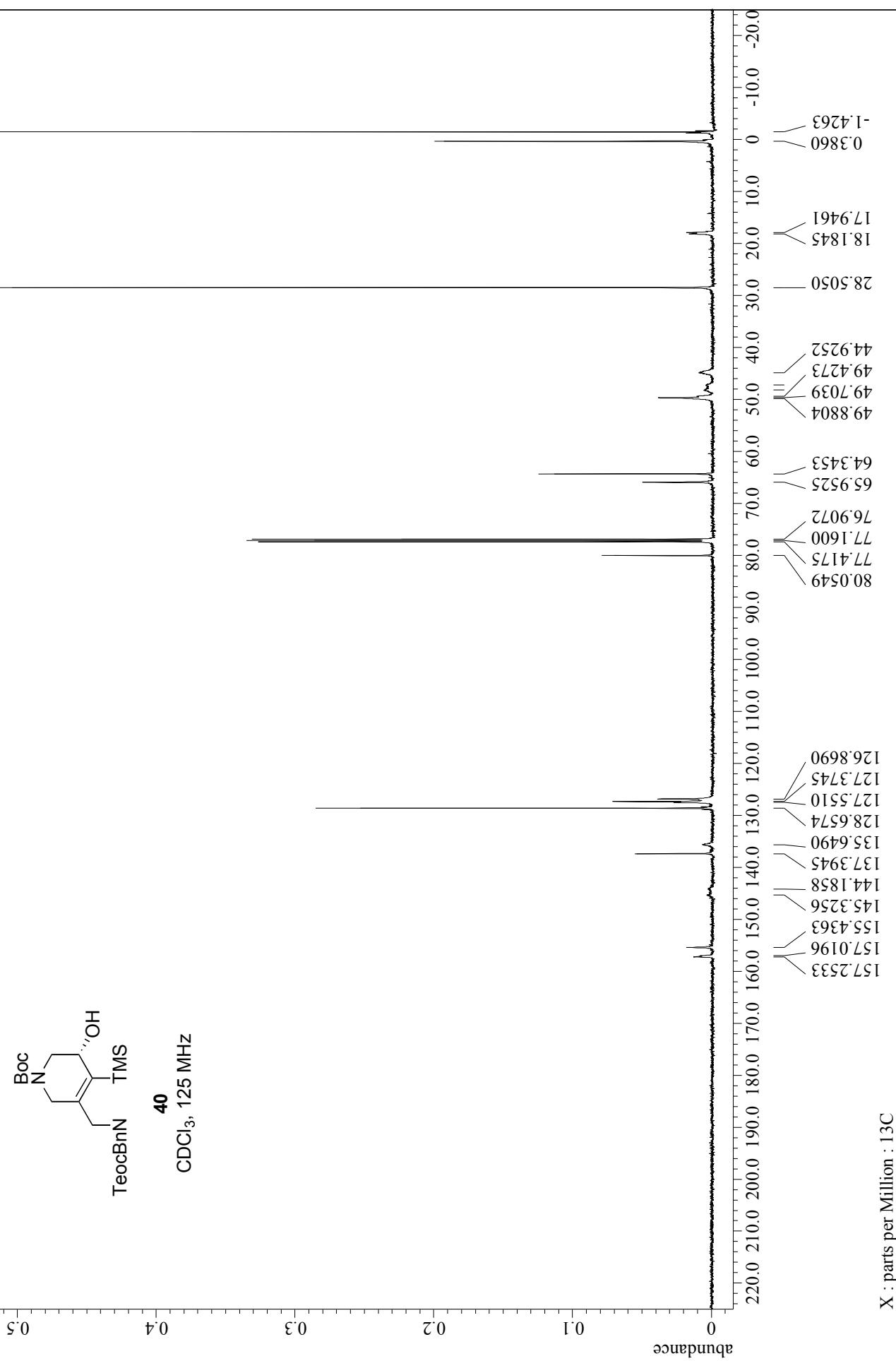
38 (major product)
 CDCl_3 , 125 MHz, 60 °C

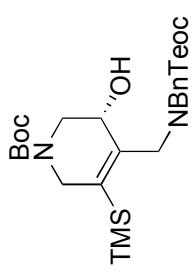




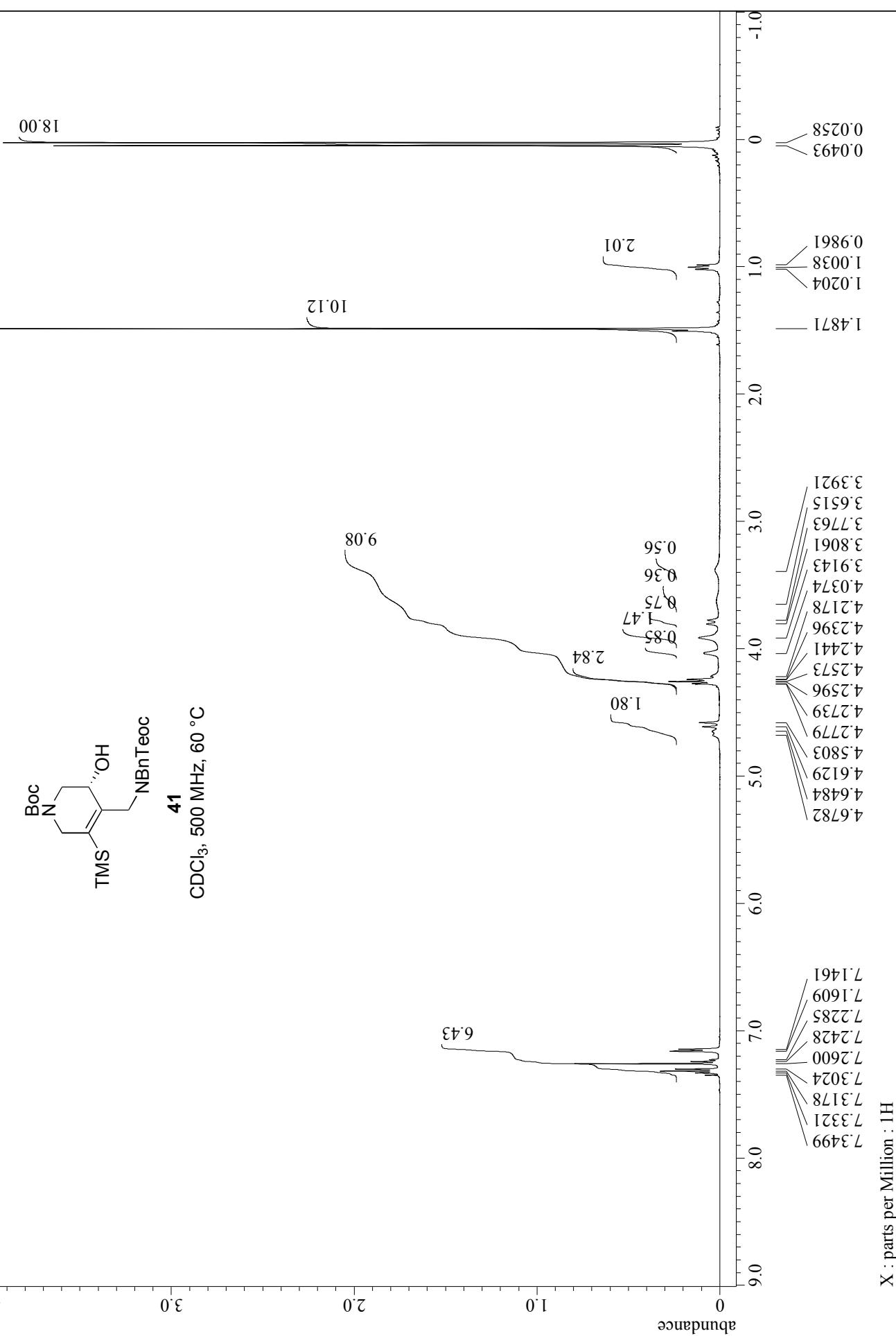


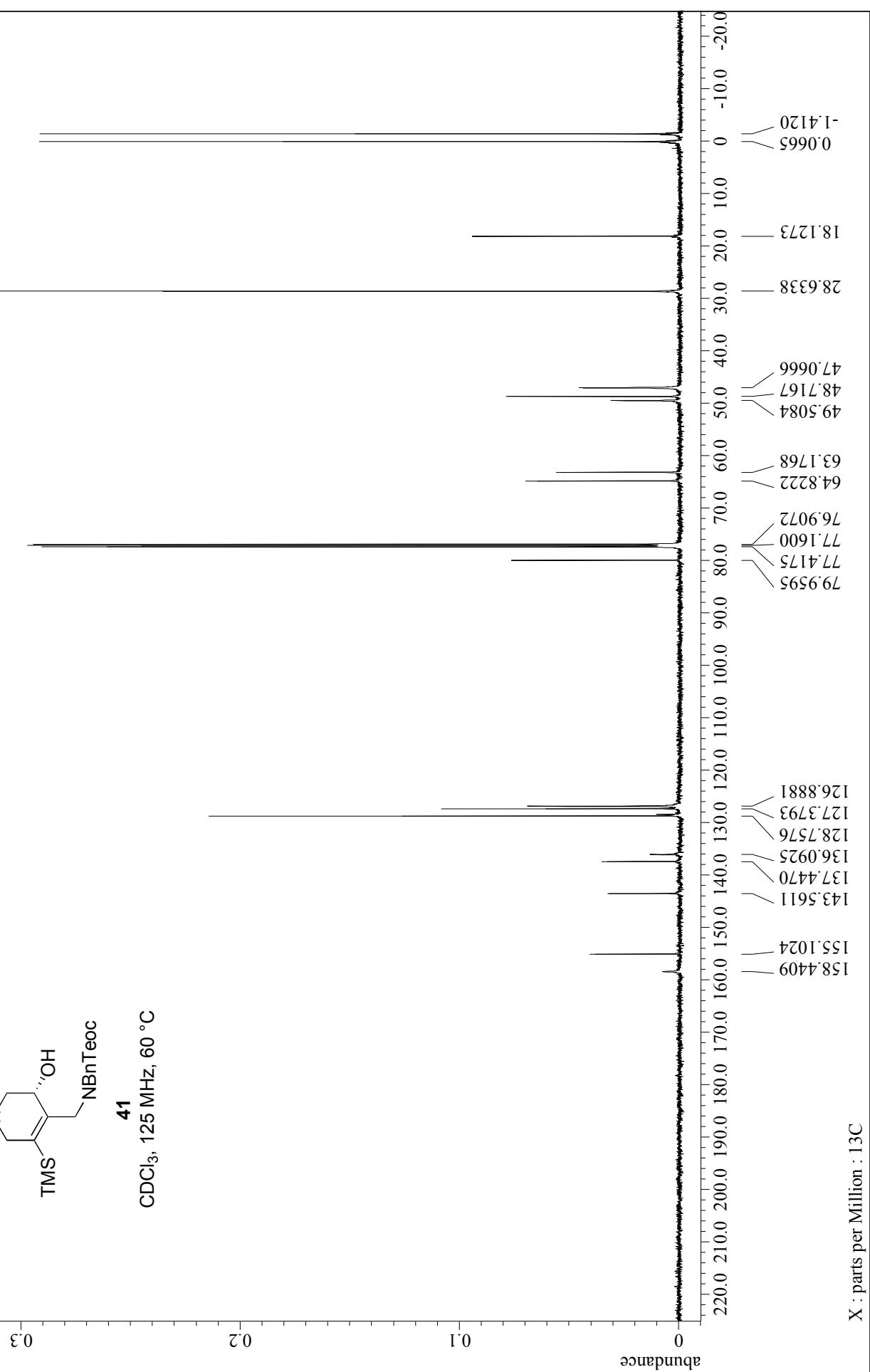
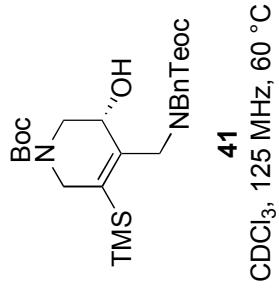
CDCl_3 , 125 MHz

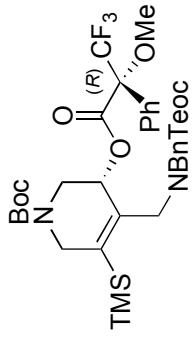




41
 CDCl_3 , 500 MHz, 60 °C







CDCl_3 , 500 MHz, 60 °C

18.00

10.65

4.06

8.13

0.94

1.75
4.23

1.86

2.88

3.0

2.0

1.0

abundance

-1.0

0.0362
0.0642

0.9981
1.0156
1.0325
1.0325

1.4430
1.4757

2.7737

3.5702
3.6446
3.6830
4.0002

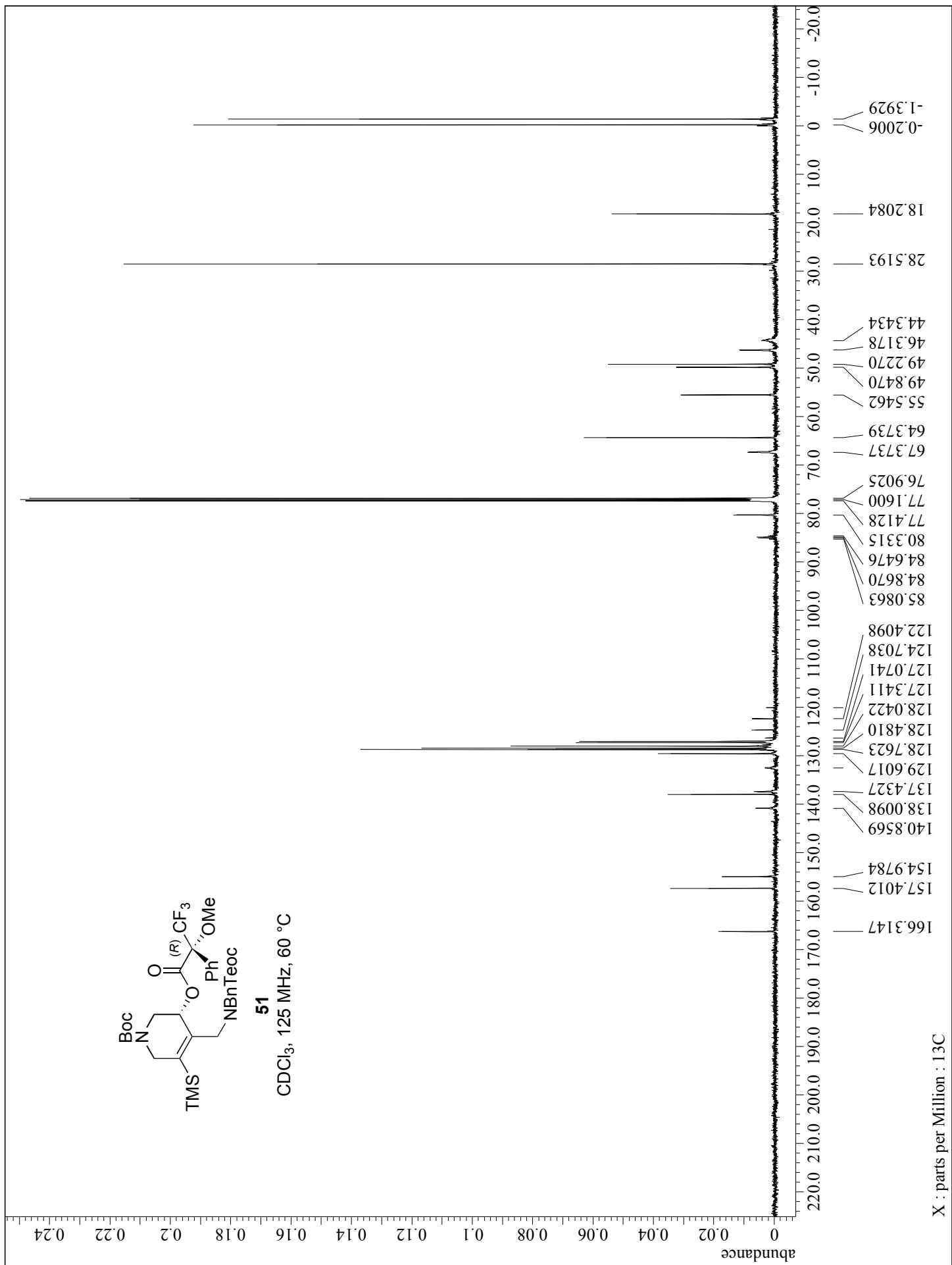
4.1617
4.2253
4.1794

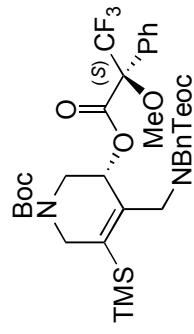
5.4008

7.0716
7.0859

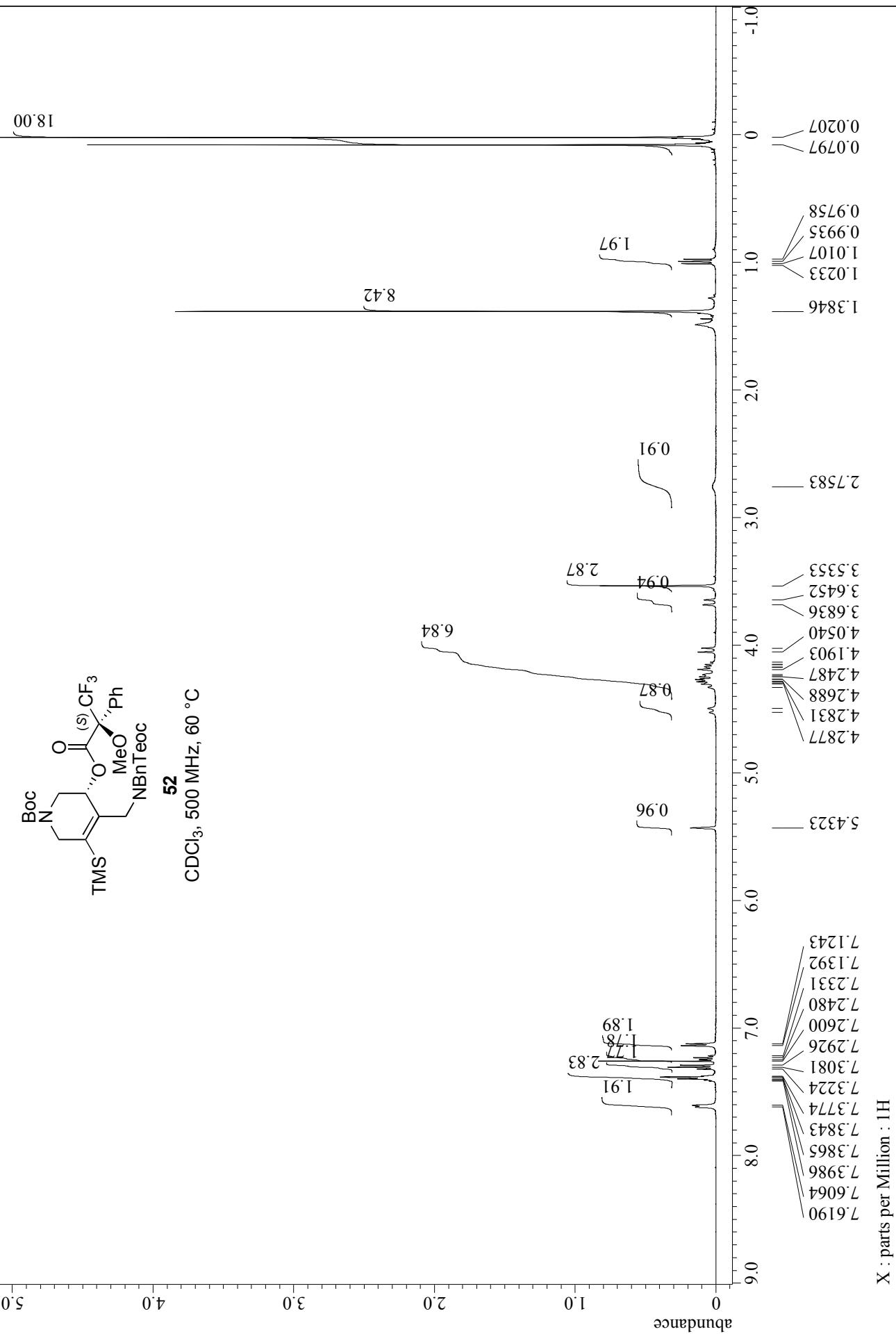
7.2600
7.2778
7.2932
7.3785
7.3940
7.6184
7.6333

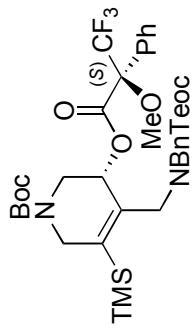
X : parts per Million : IH



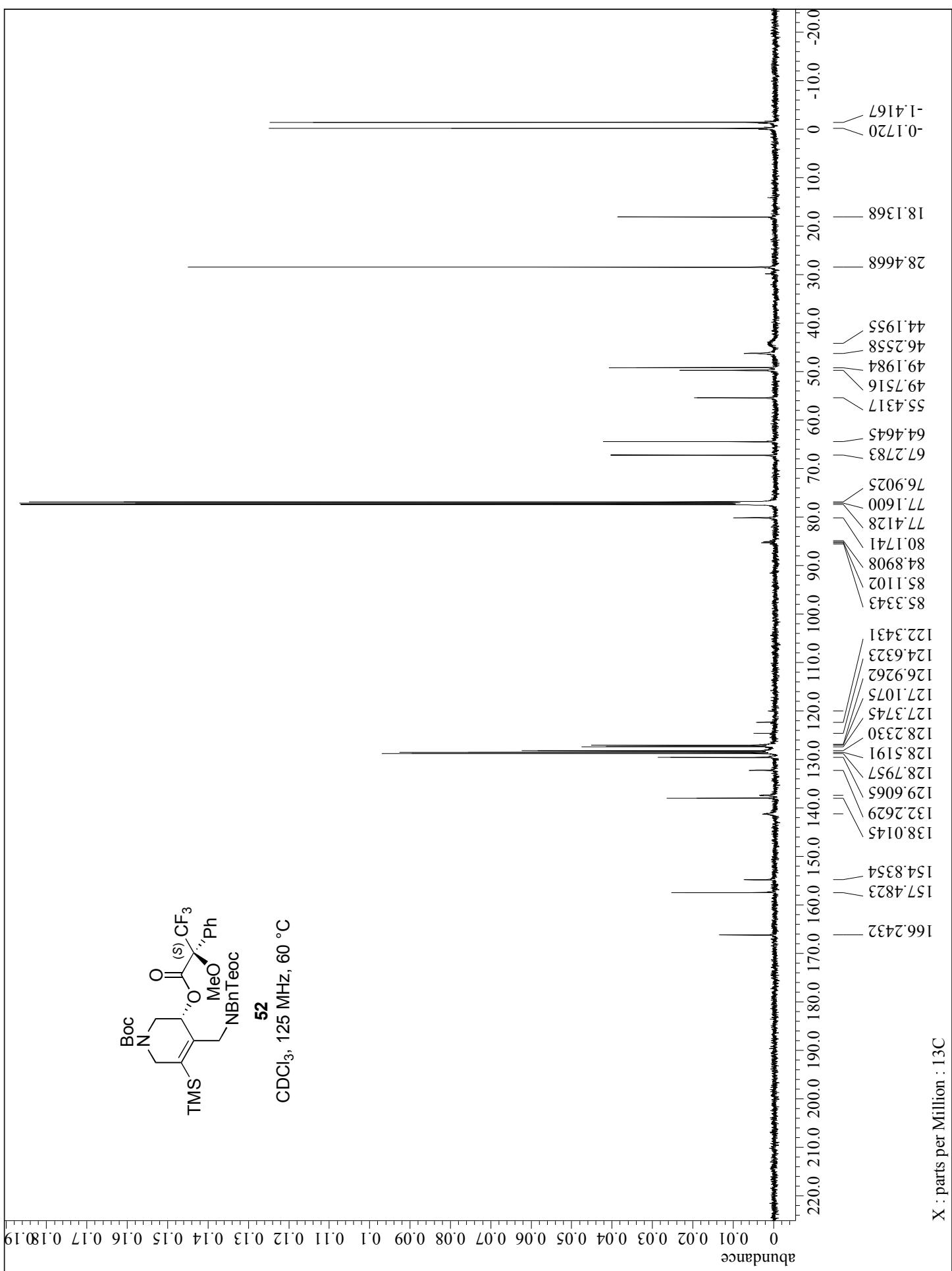


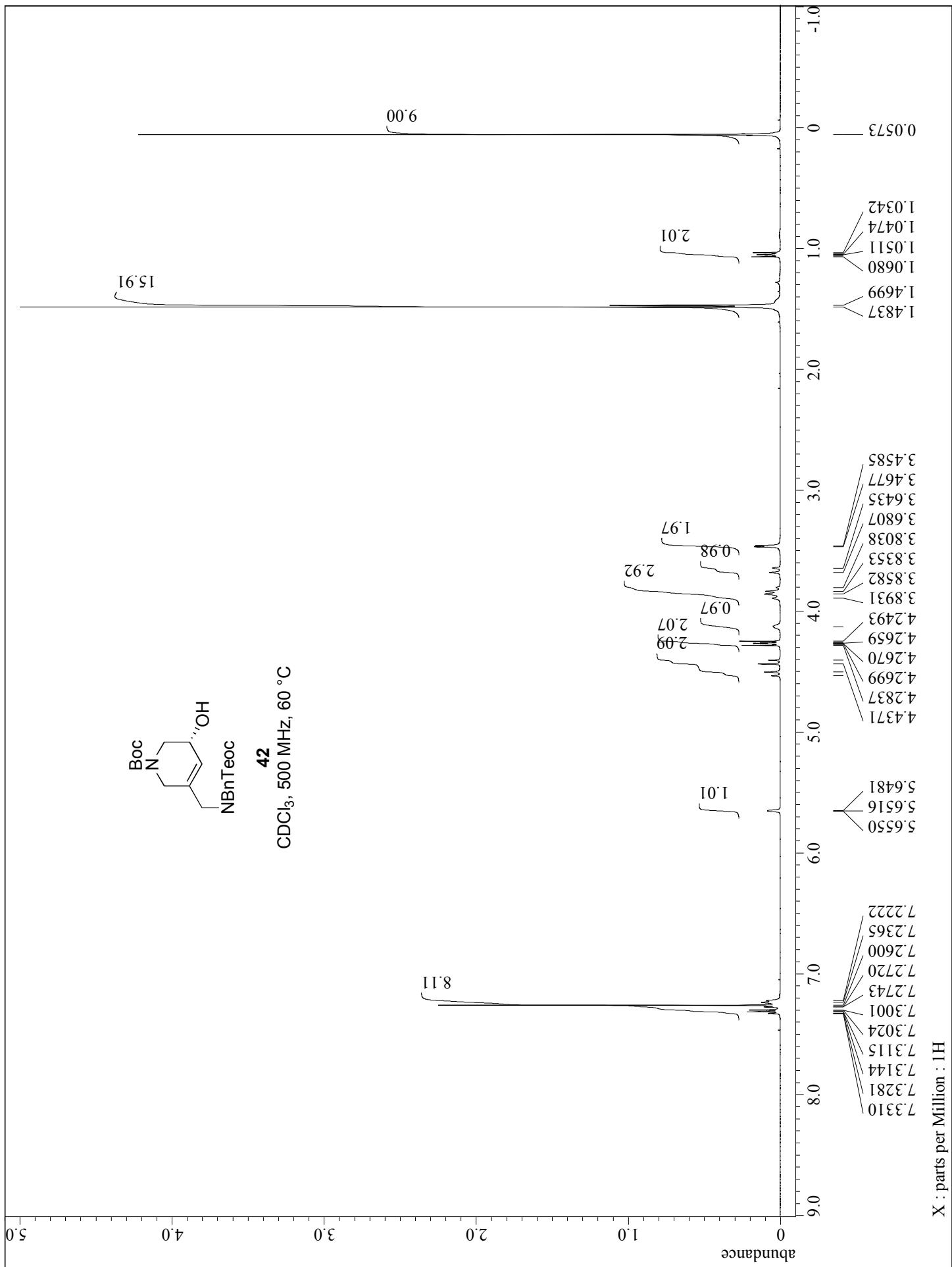
52
 $\text{CDCl}_3, 500 \text{ MHz}, 60^\circ\text{C}$

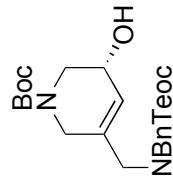




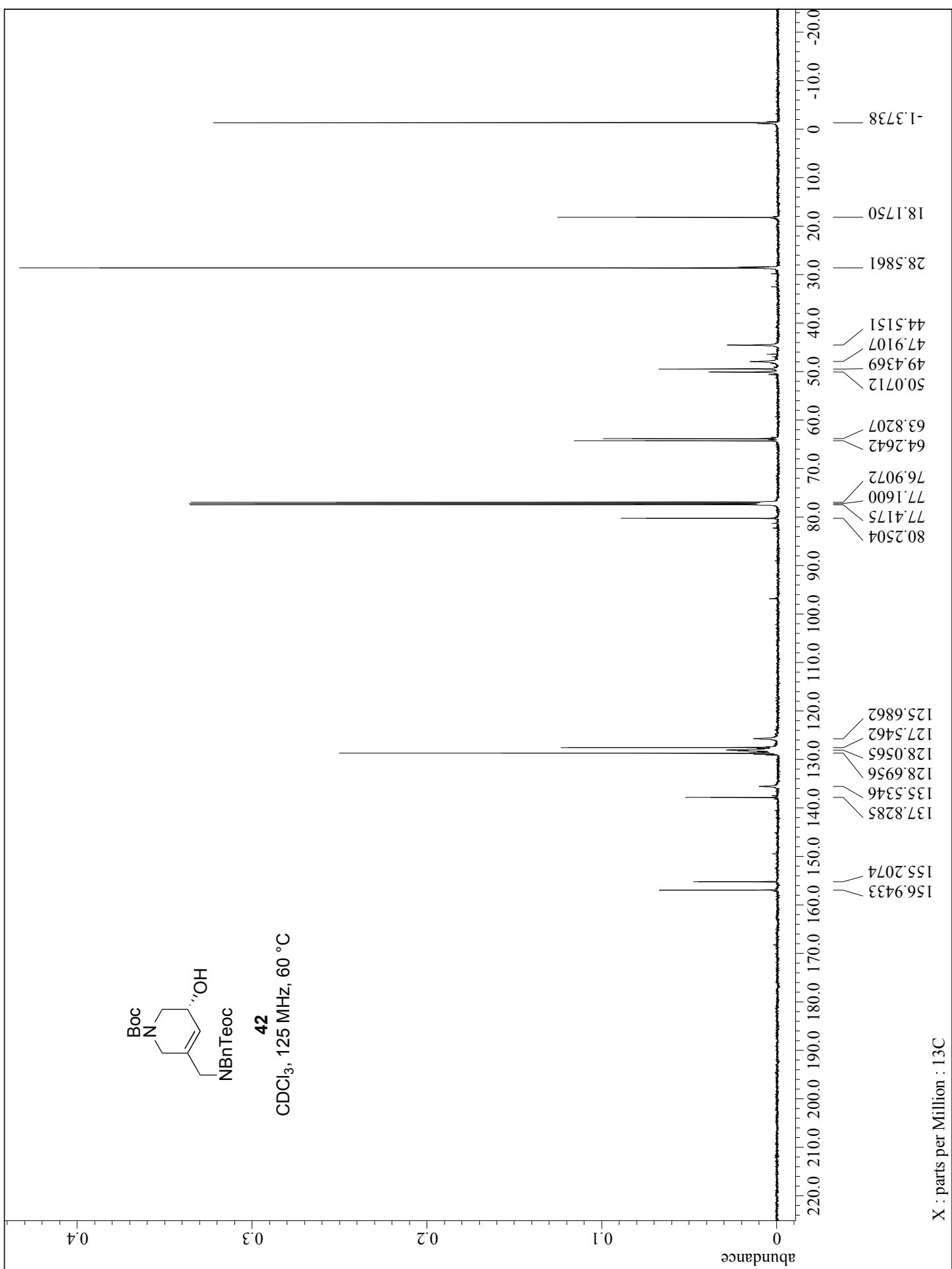
CDCl_3 , 125 MHz, 60 °C



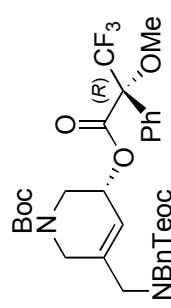




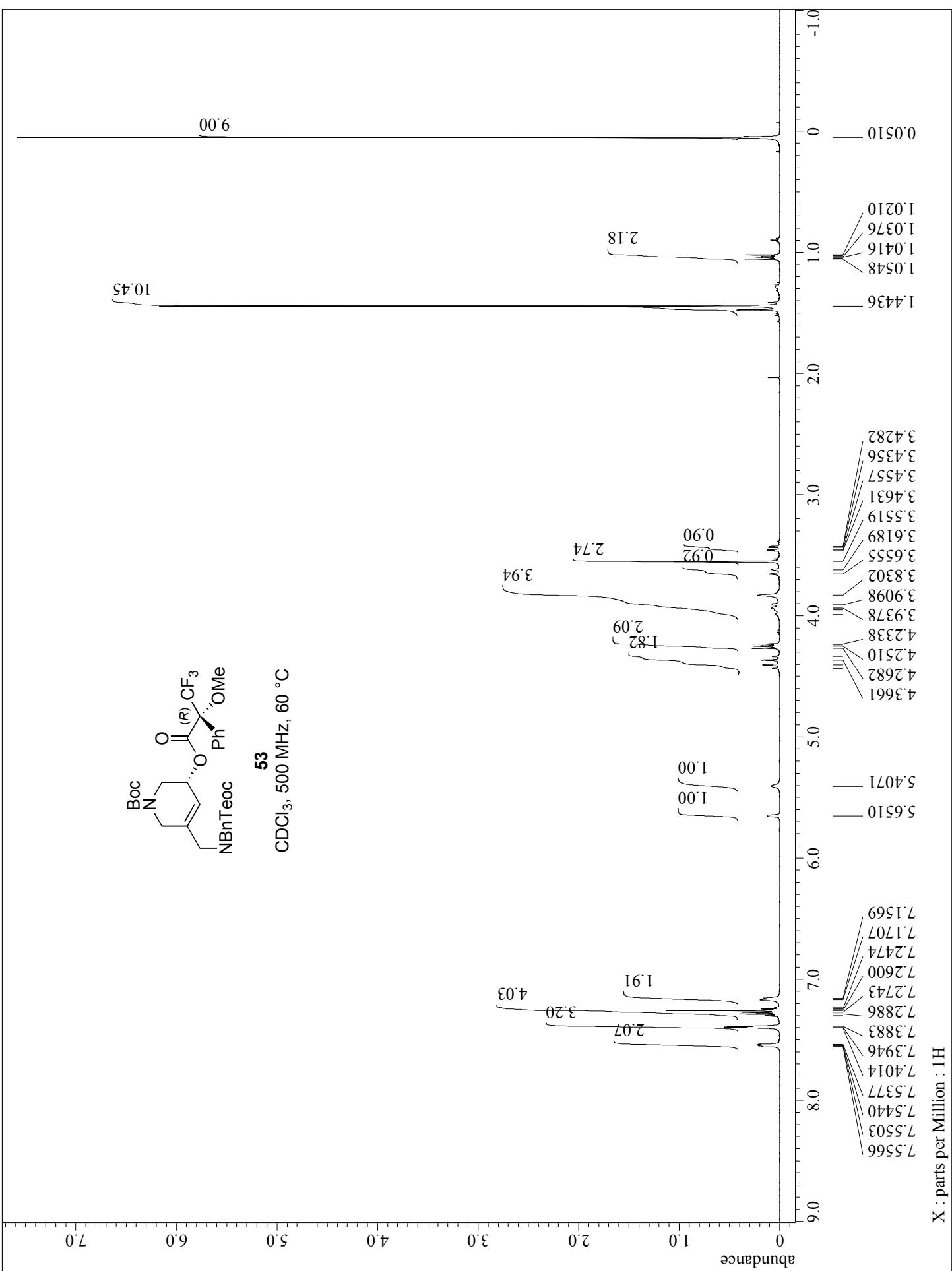
42
 $\text{CDCl}_3, 125 \text{ MHz}, 60^\circ\text{C}$

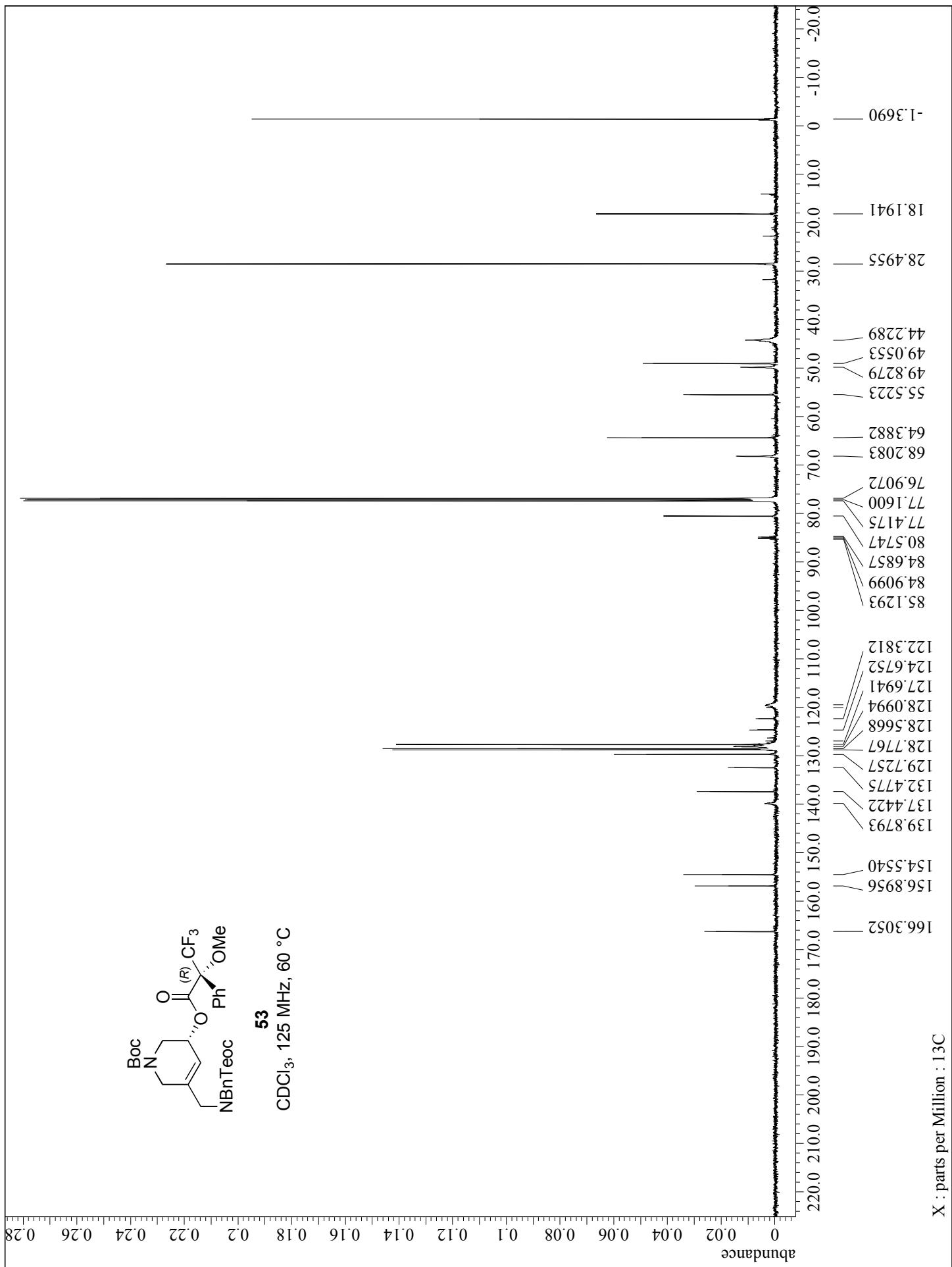


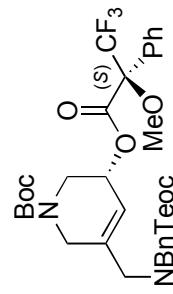
X : parts per Million : ^{13}C



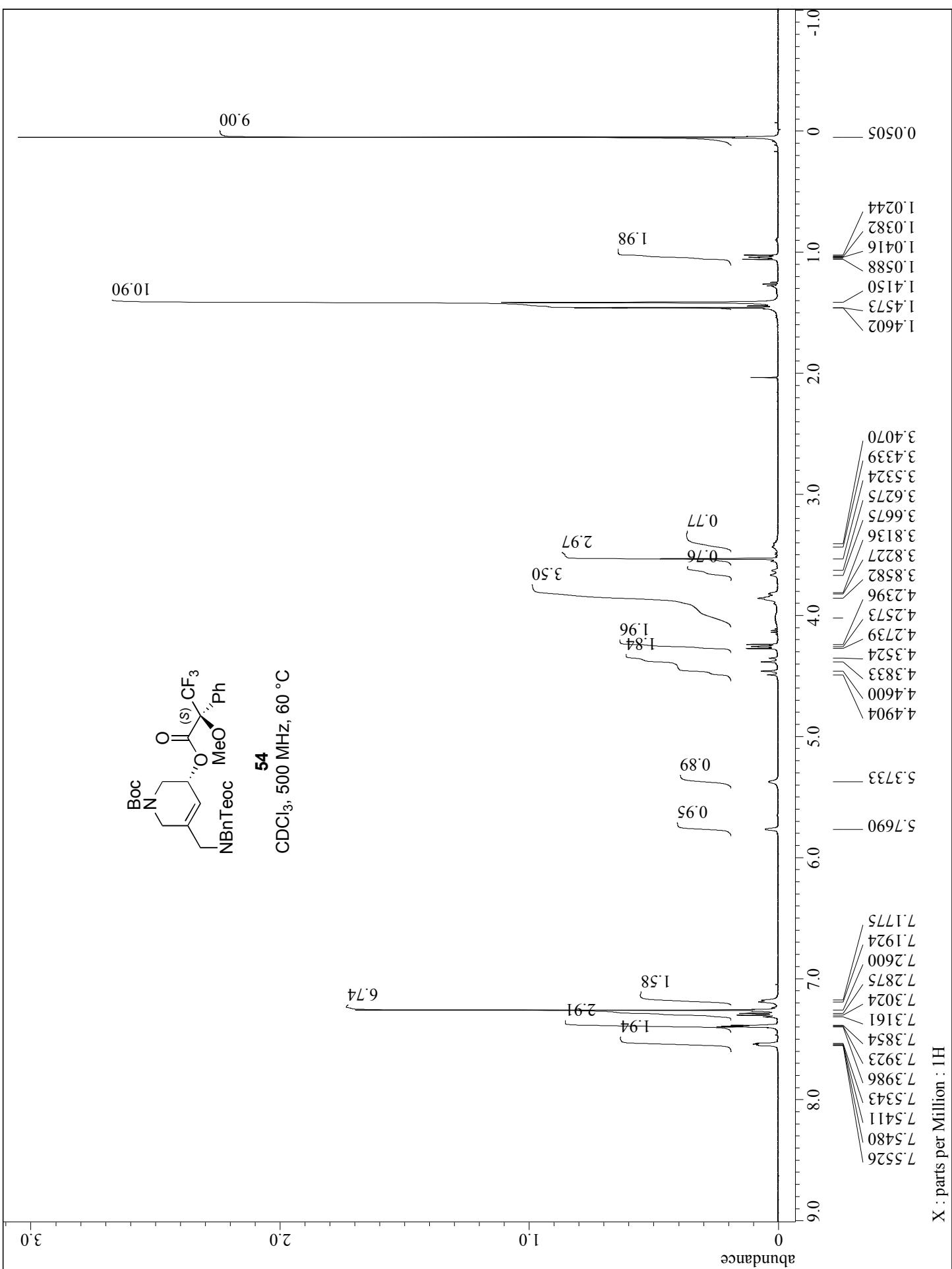
CDCl_3 , 500 MHz, 60 °C

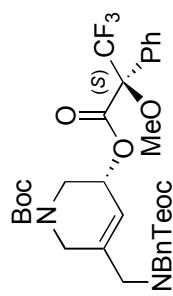




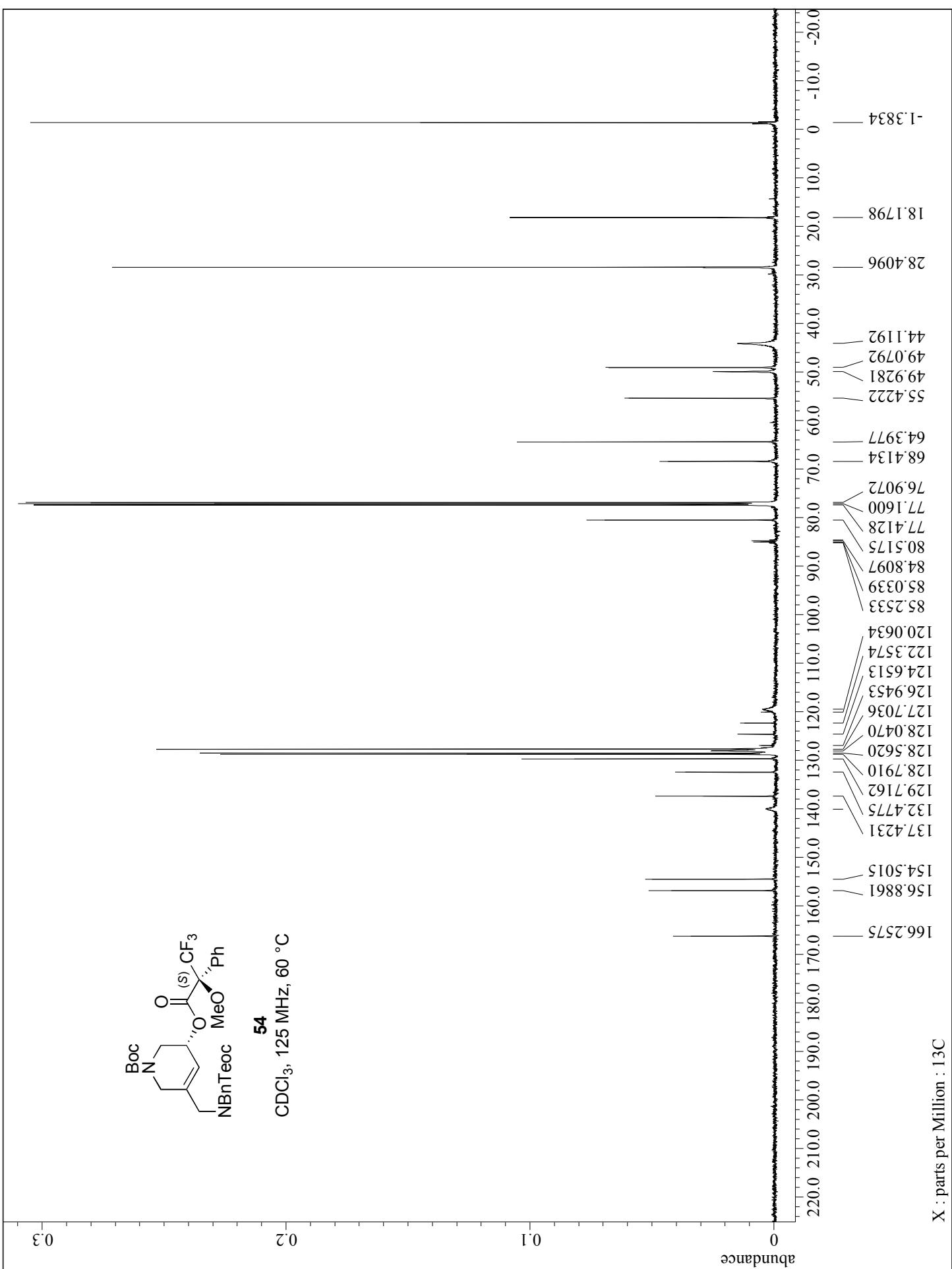


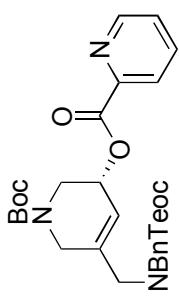
54
 CDCl_3 , 500 MHz, 60 °C



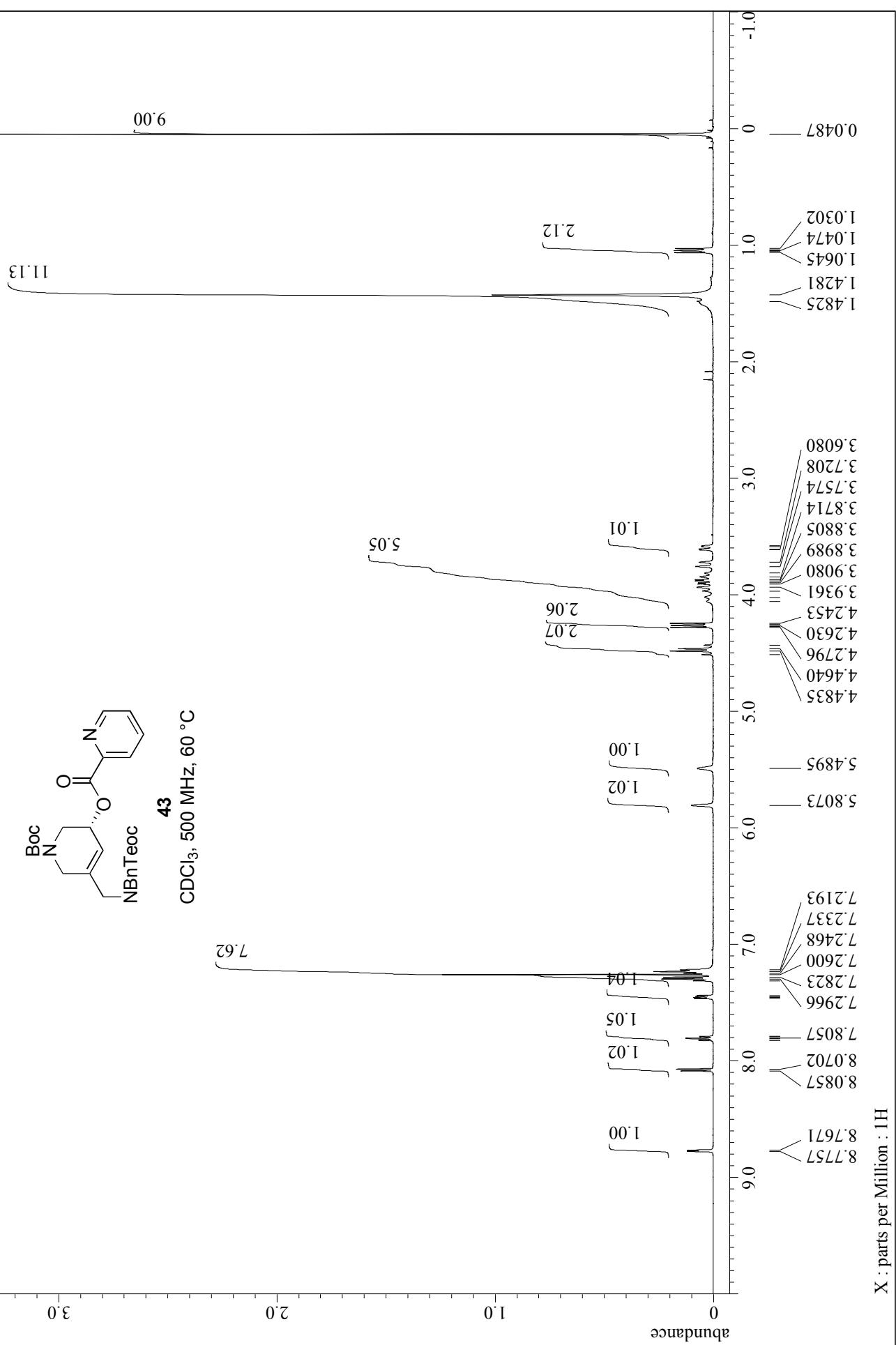


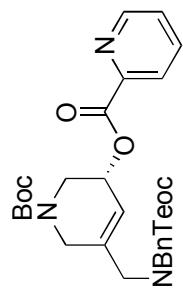
54
 $\text{CDCl}_3, 125 \text{ MHz}, 60^\circ\text{C}$



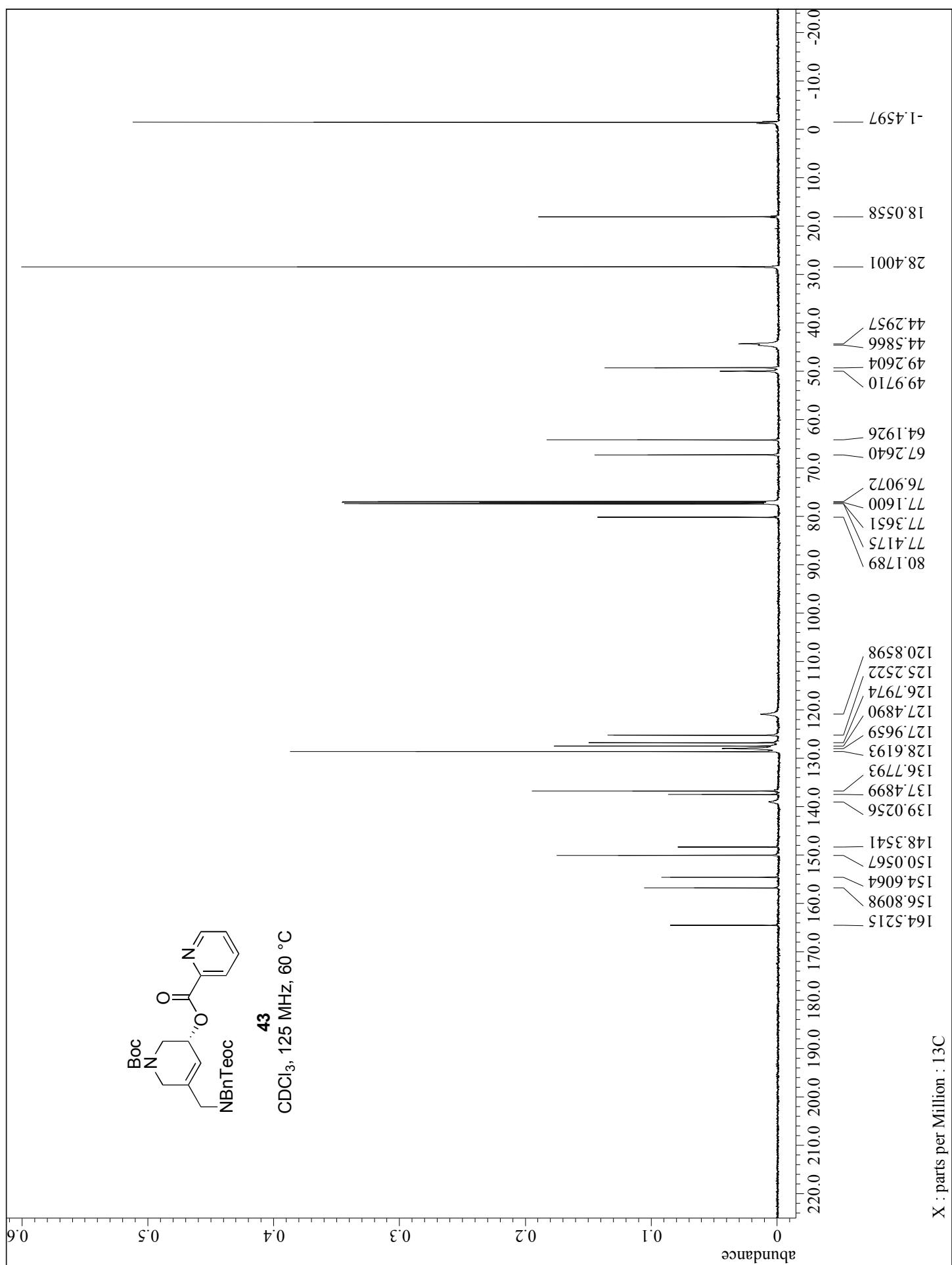


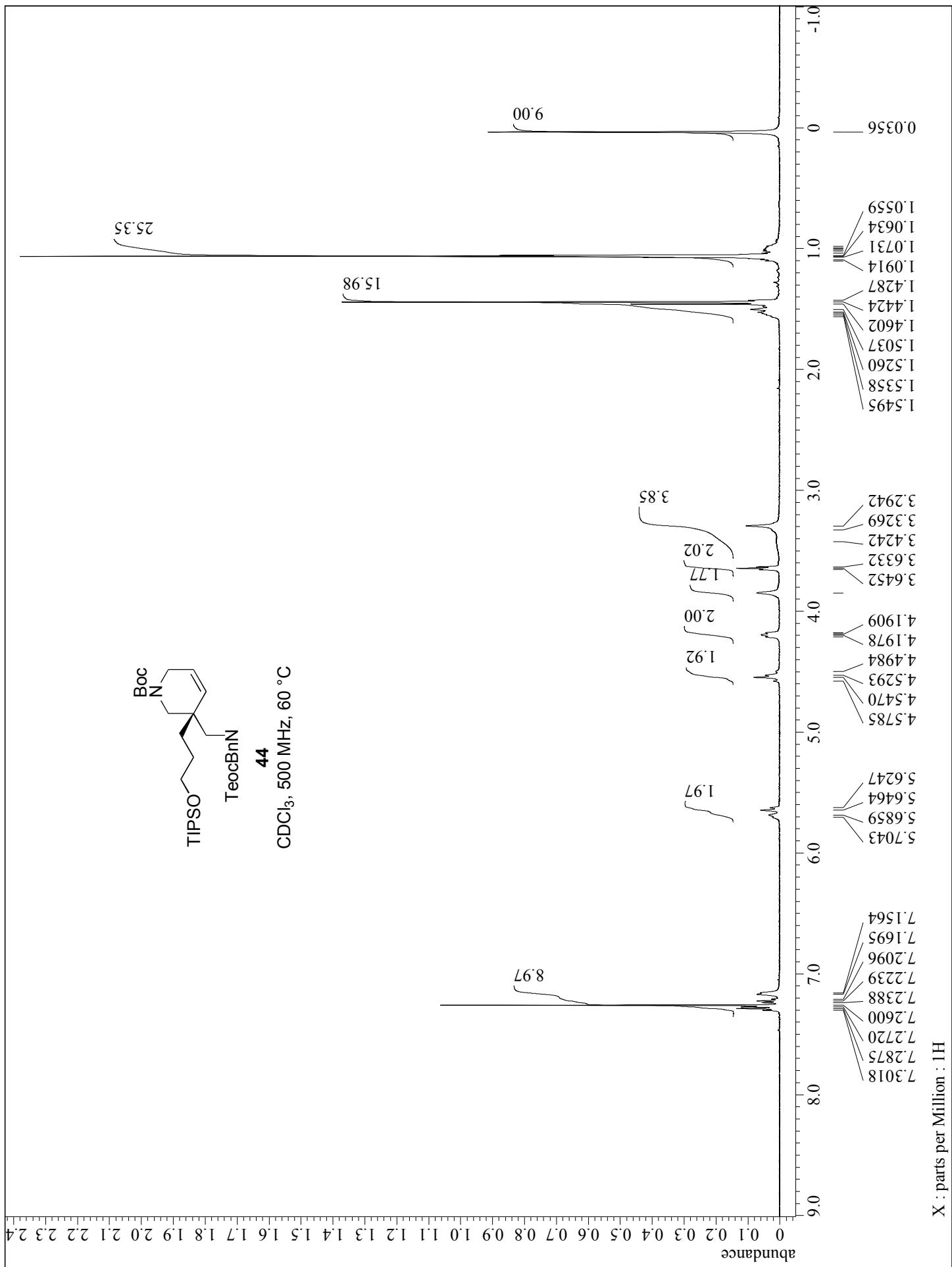
43
 $\text{CDCl}_3, 500 \text{ MHz}, 60^\circ\text{C}$

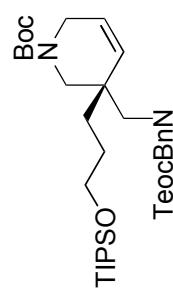




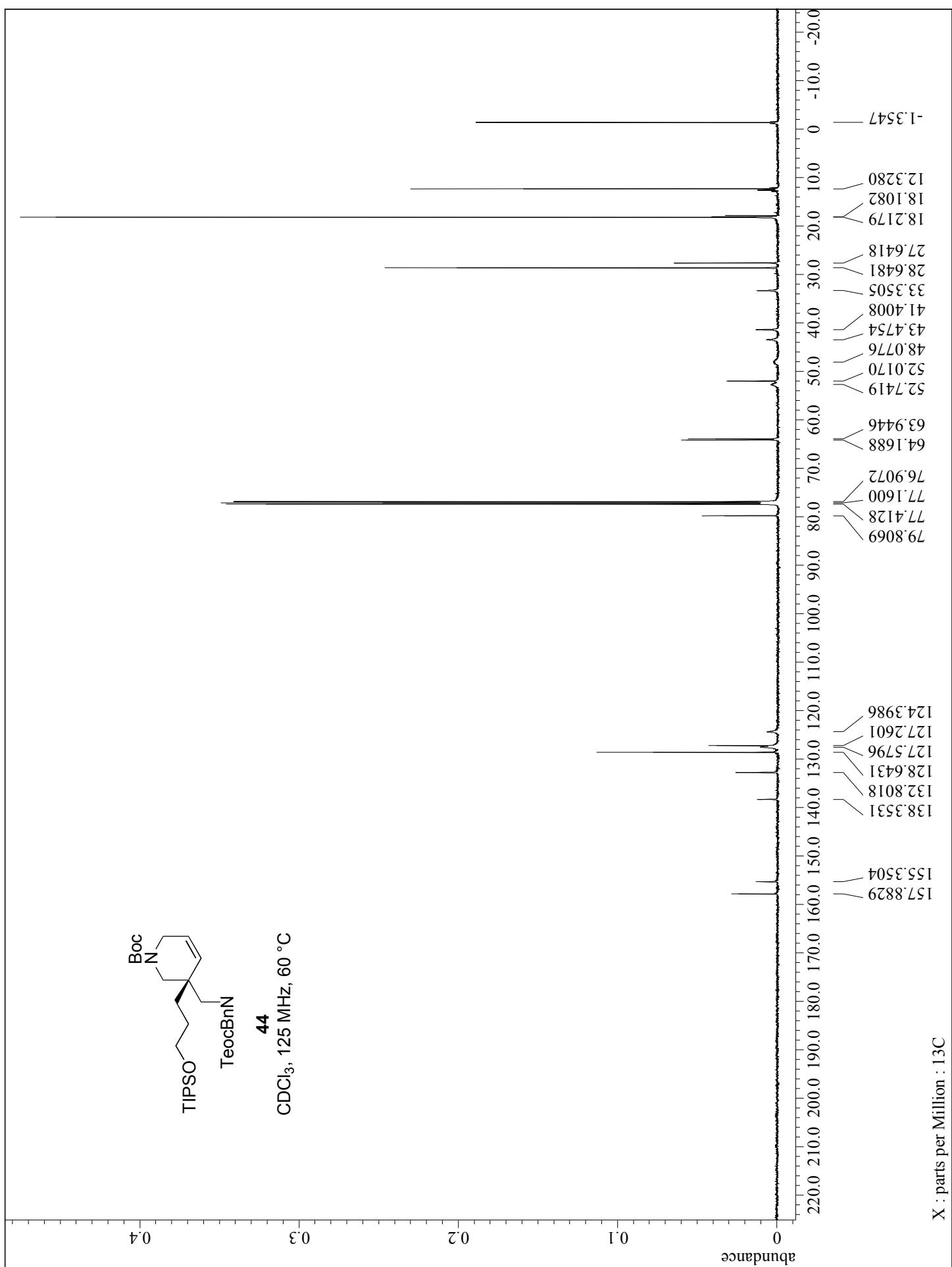
CDCl_3 , 125 MHz, 60 °C

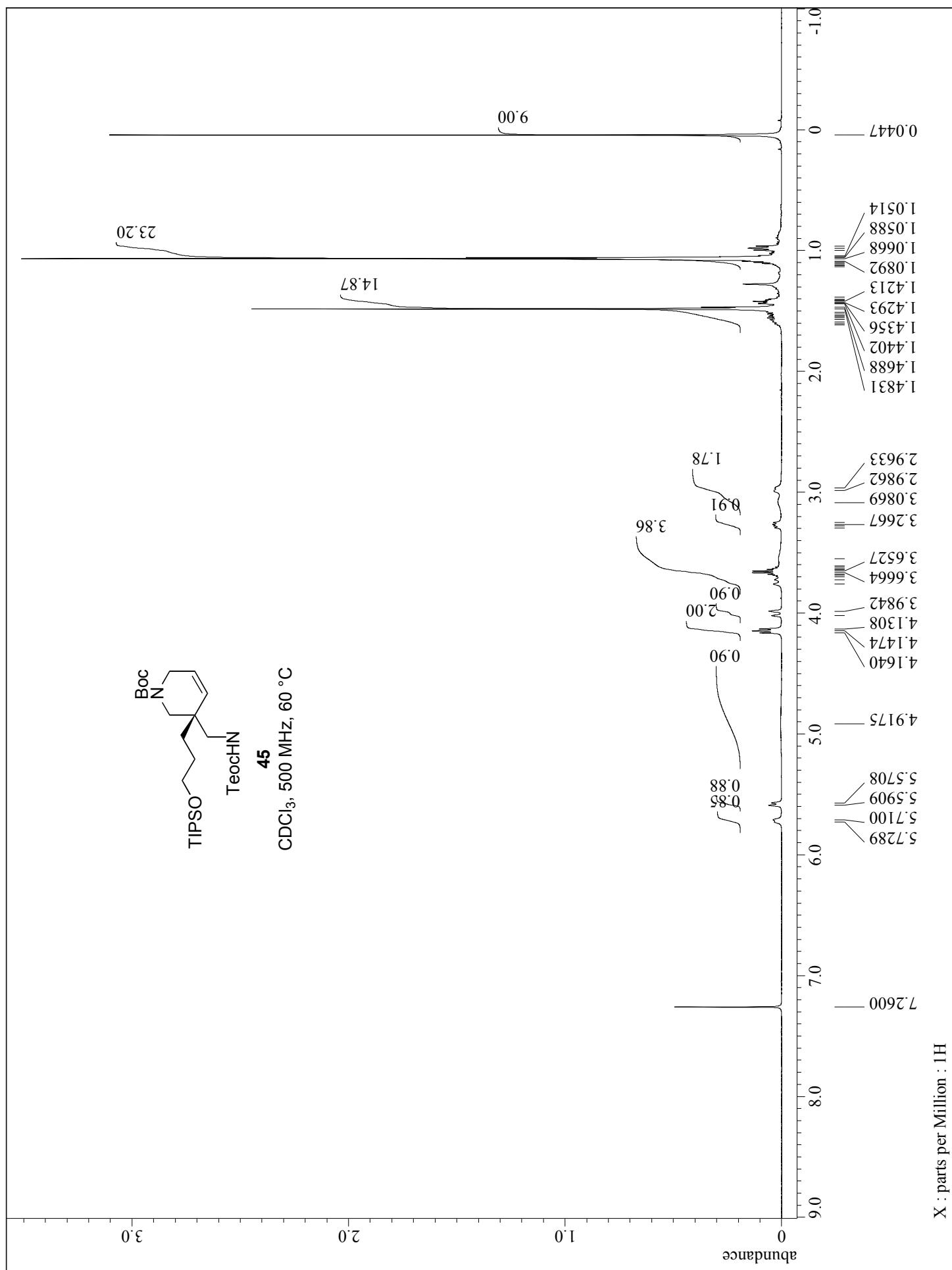


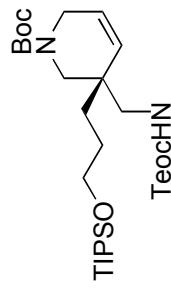




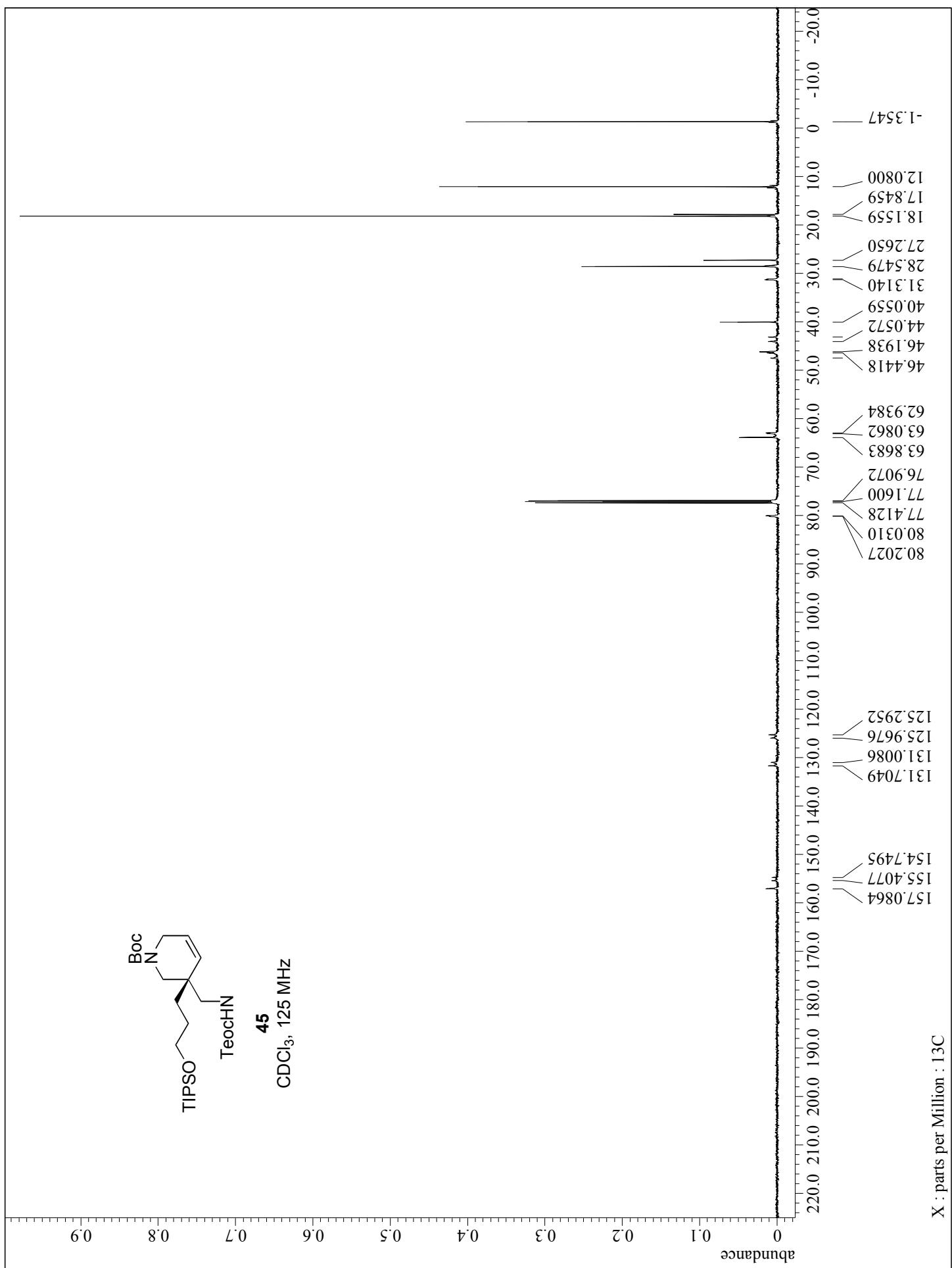
CDCl_3 , 125 MHz, 60 °C

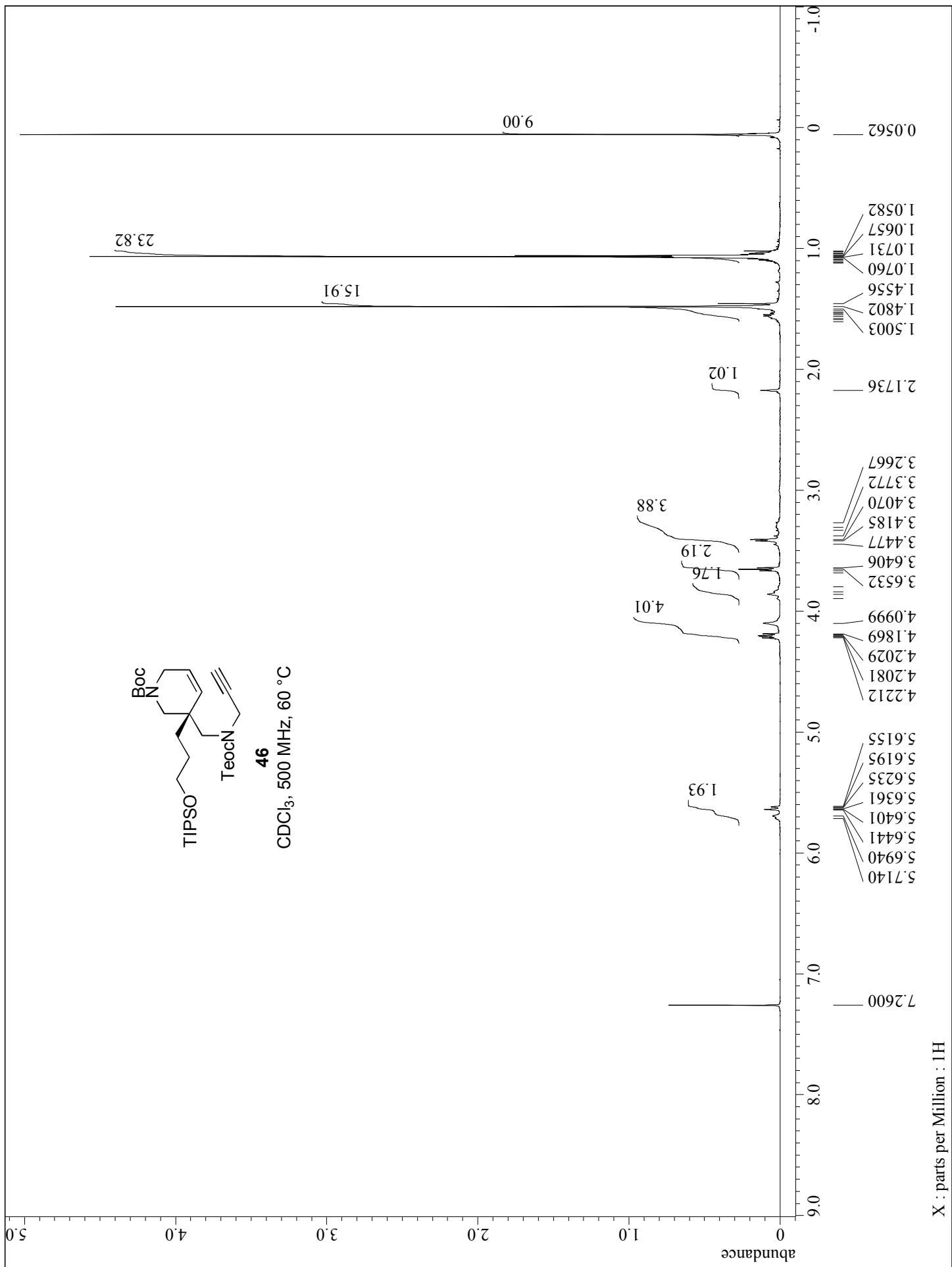


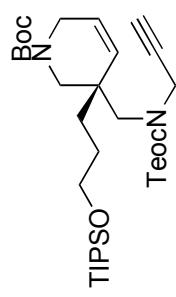




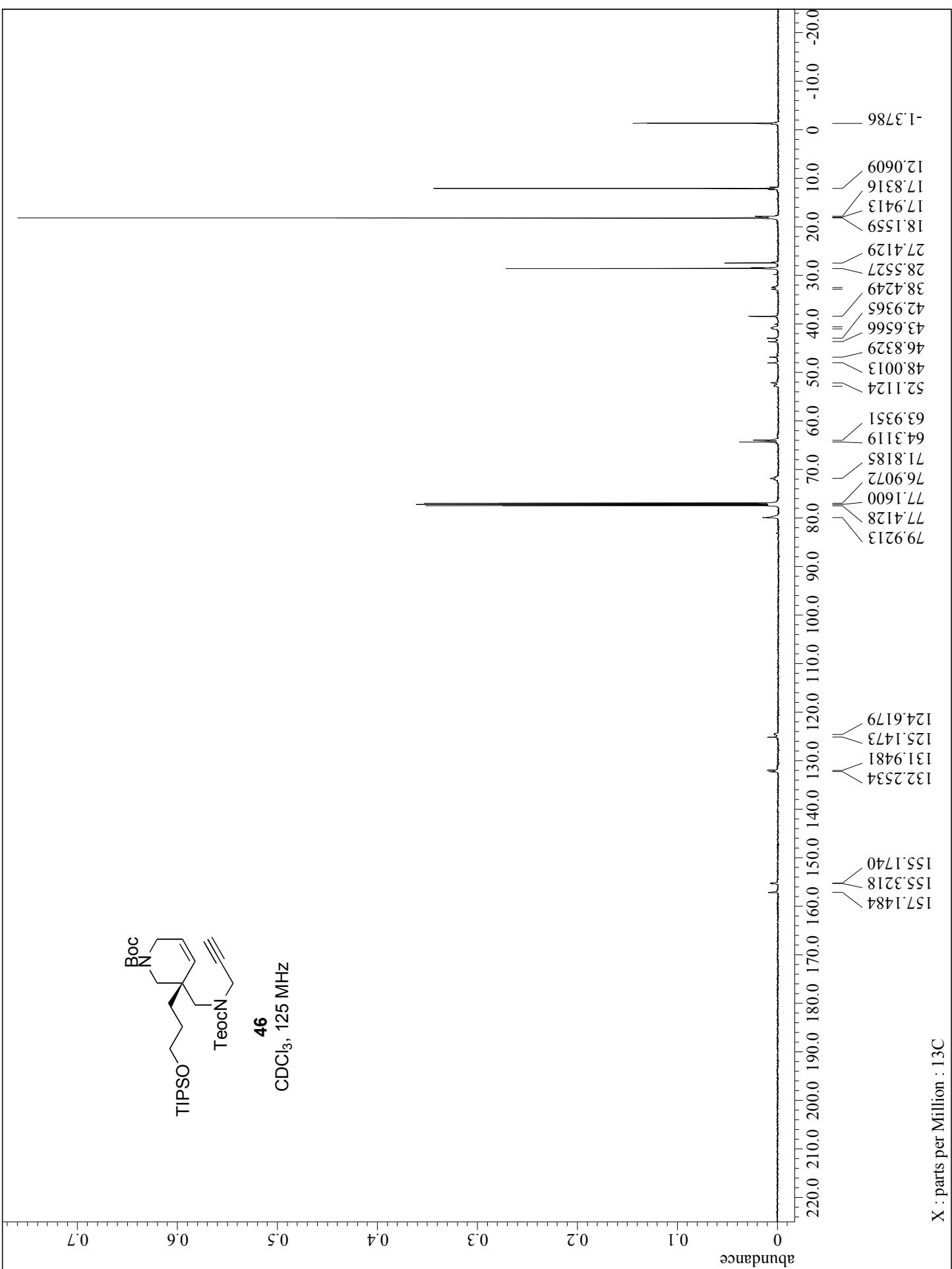
CDCl_3 , 125 MHz

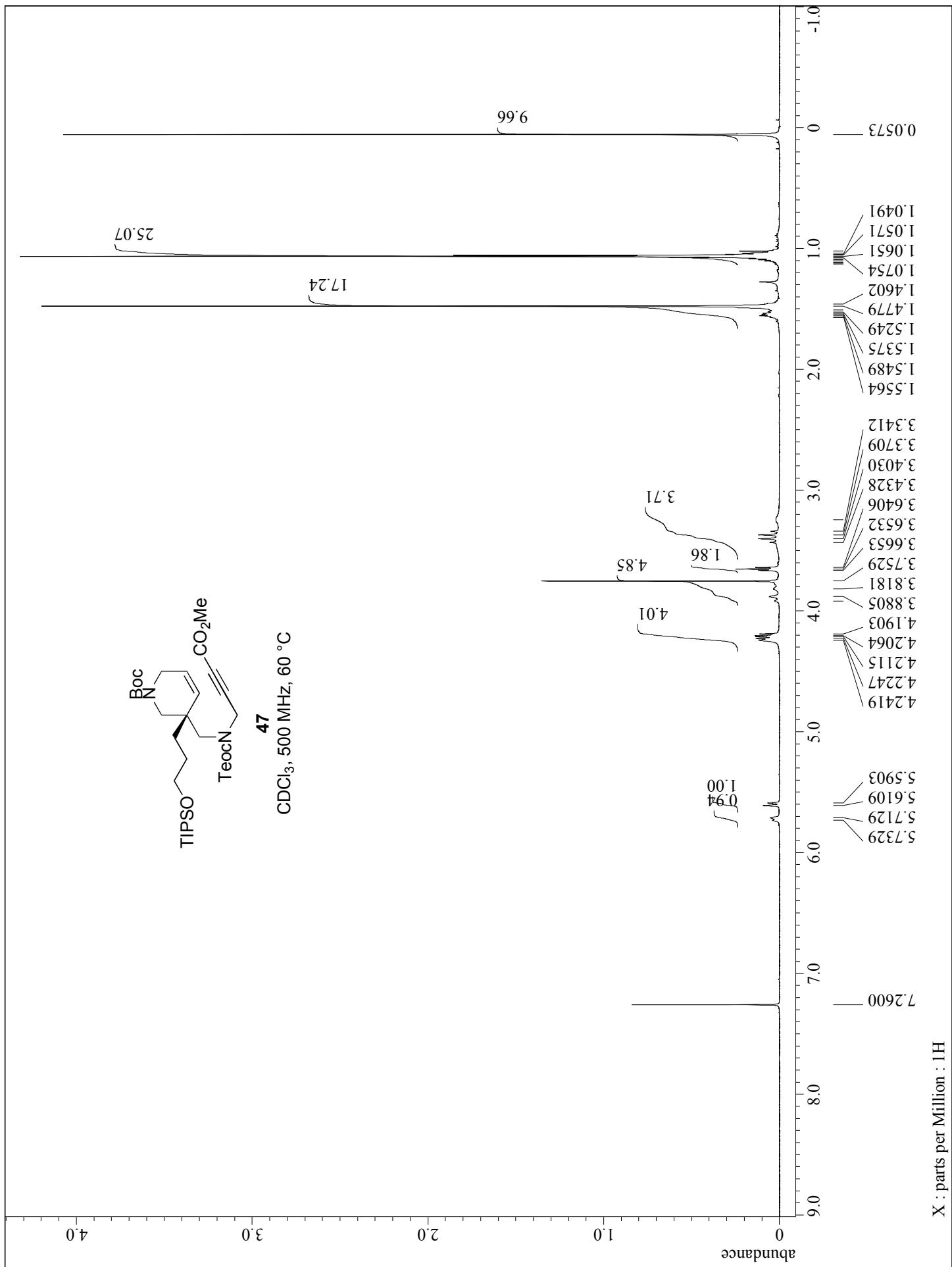


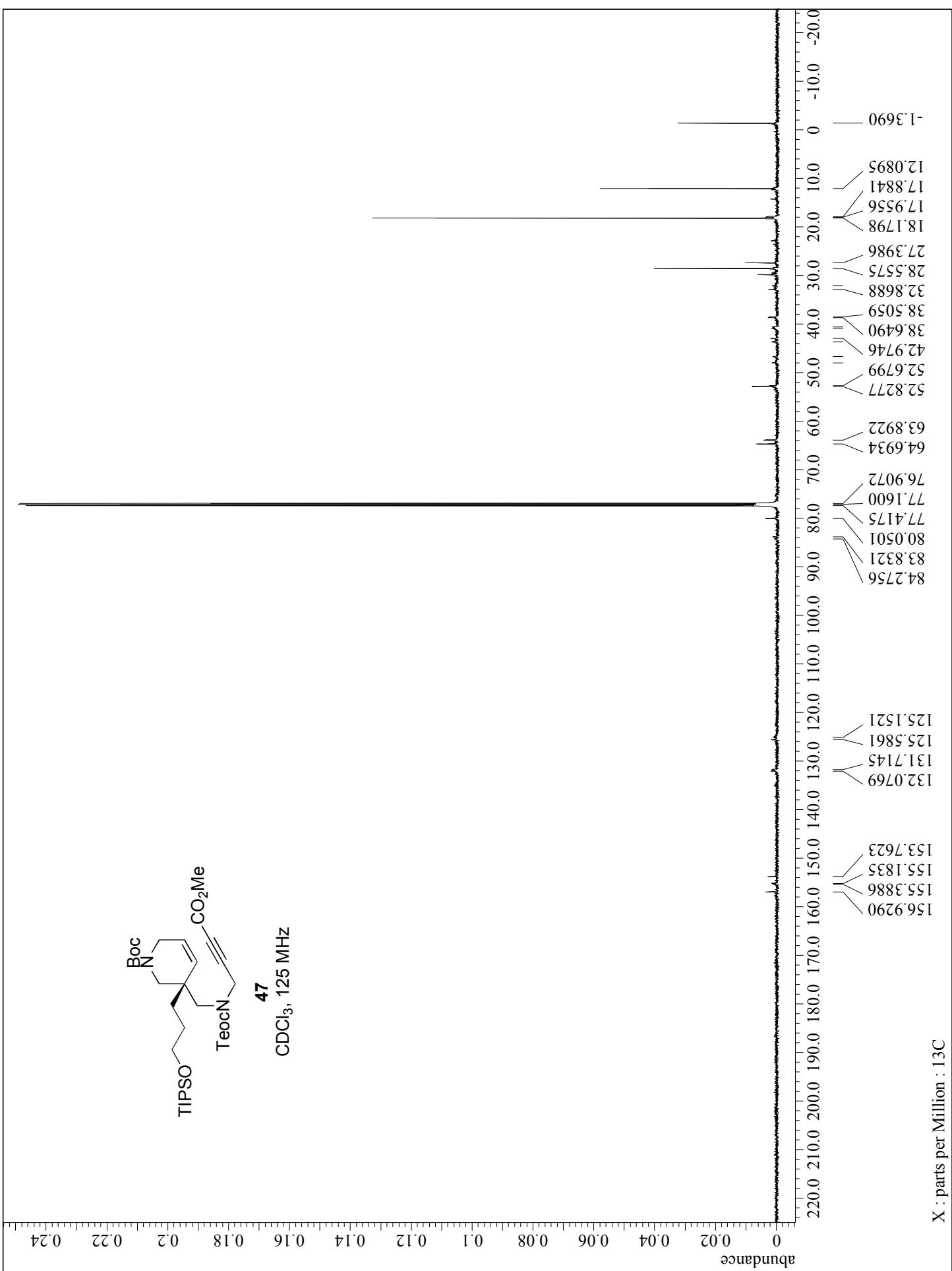
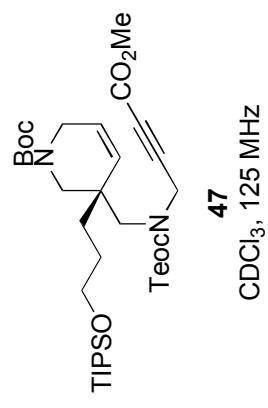


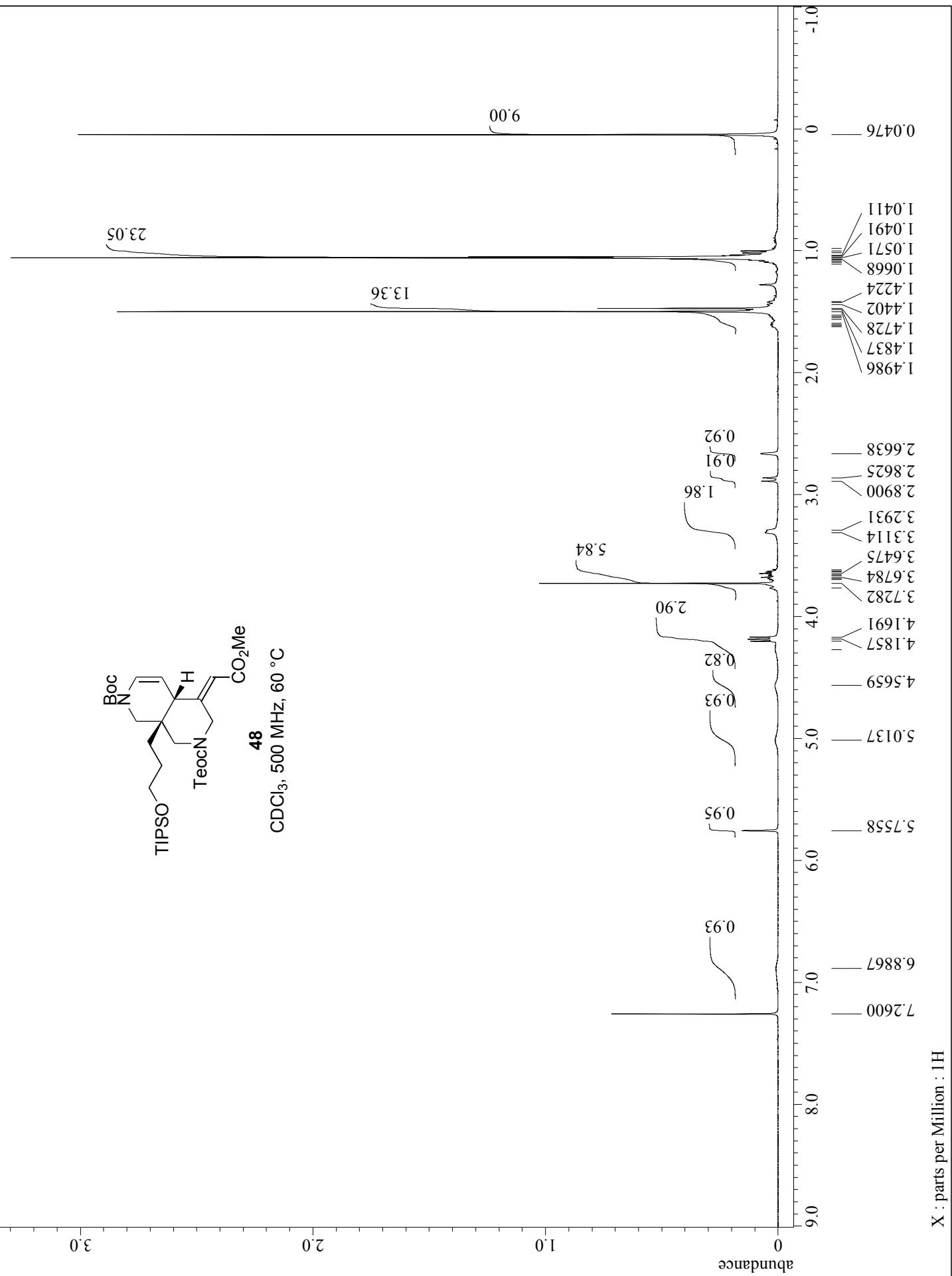
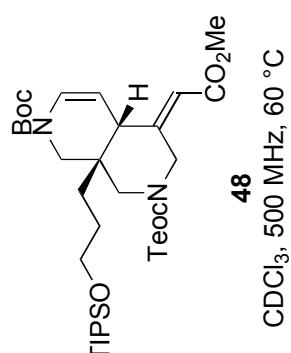


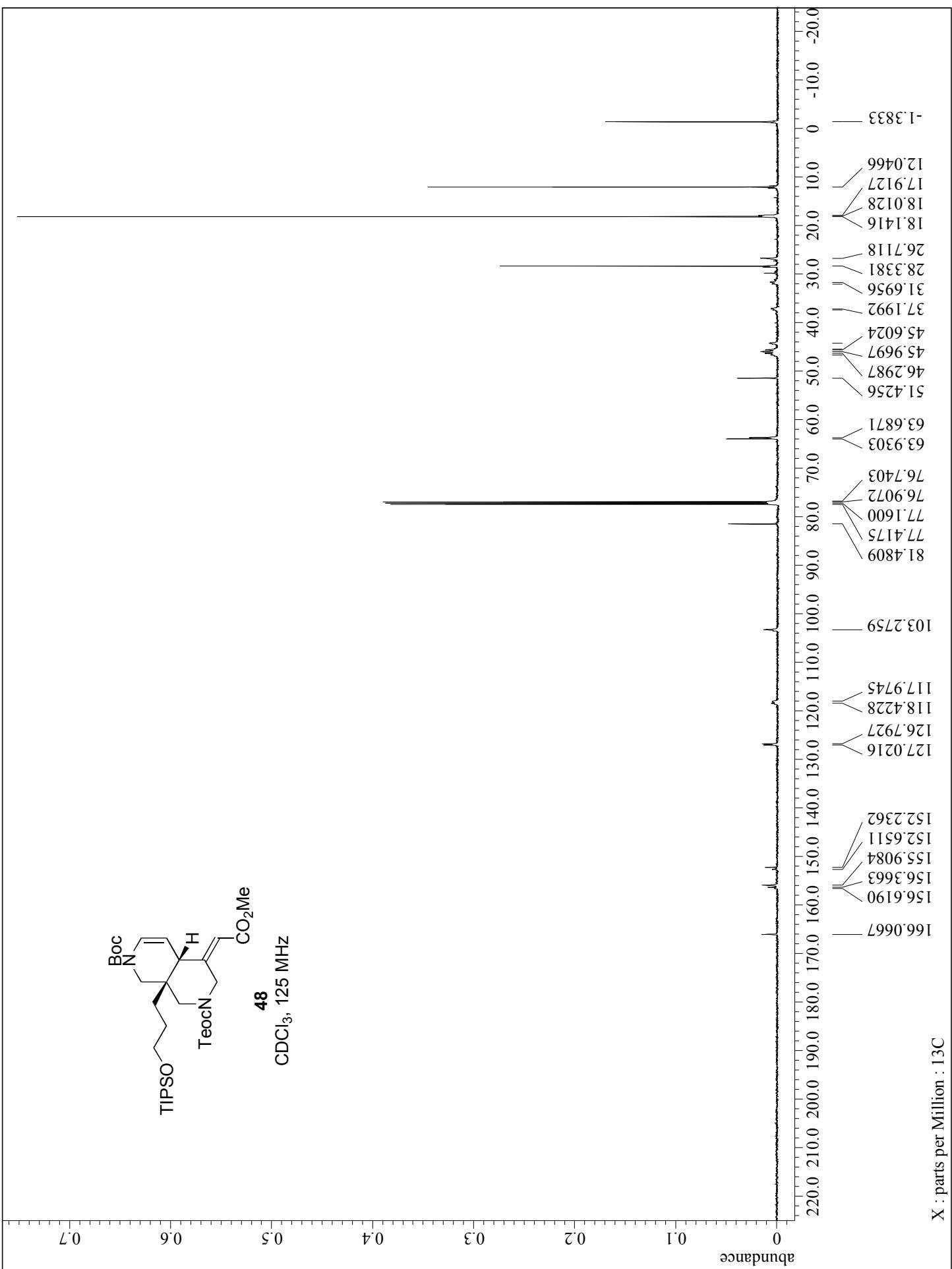
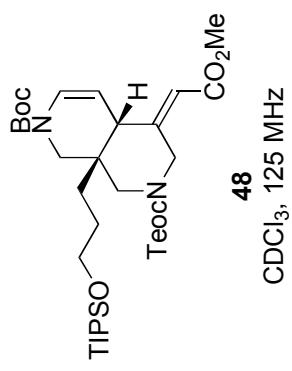
CDCl_3 , 125 MHz

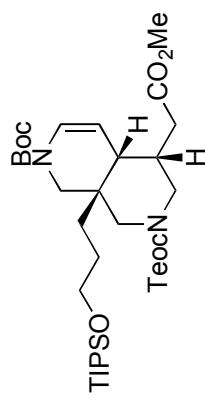




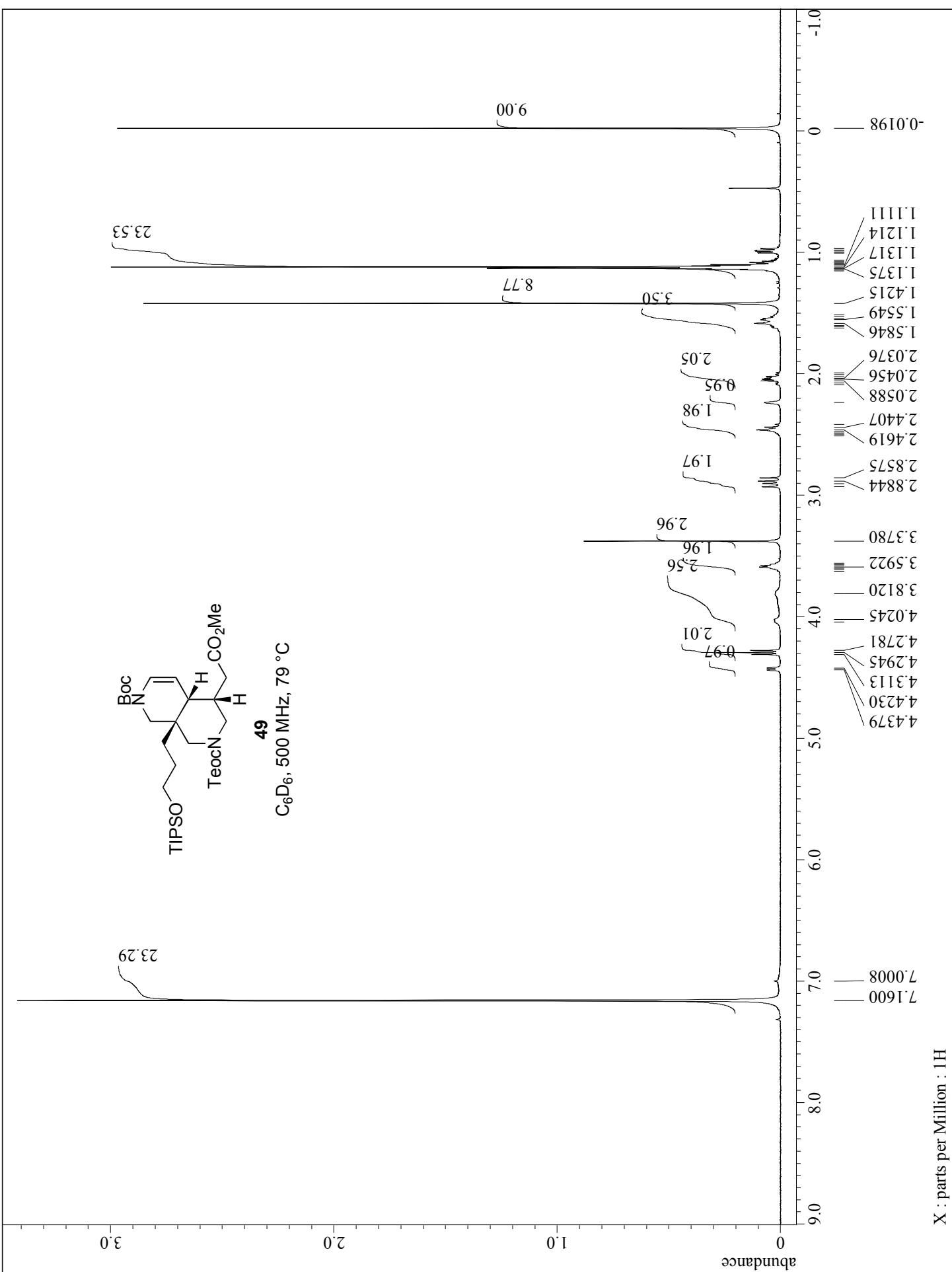


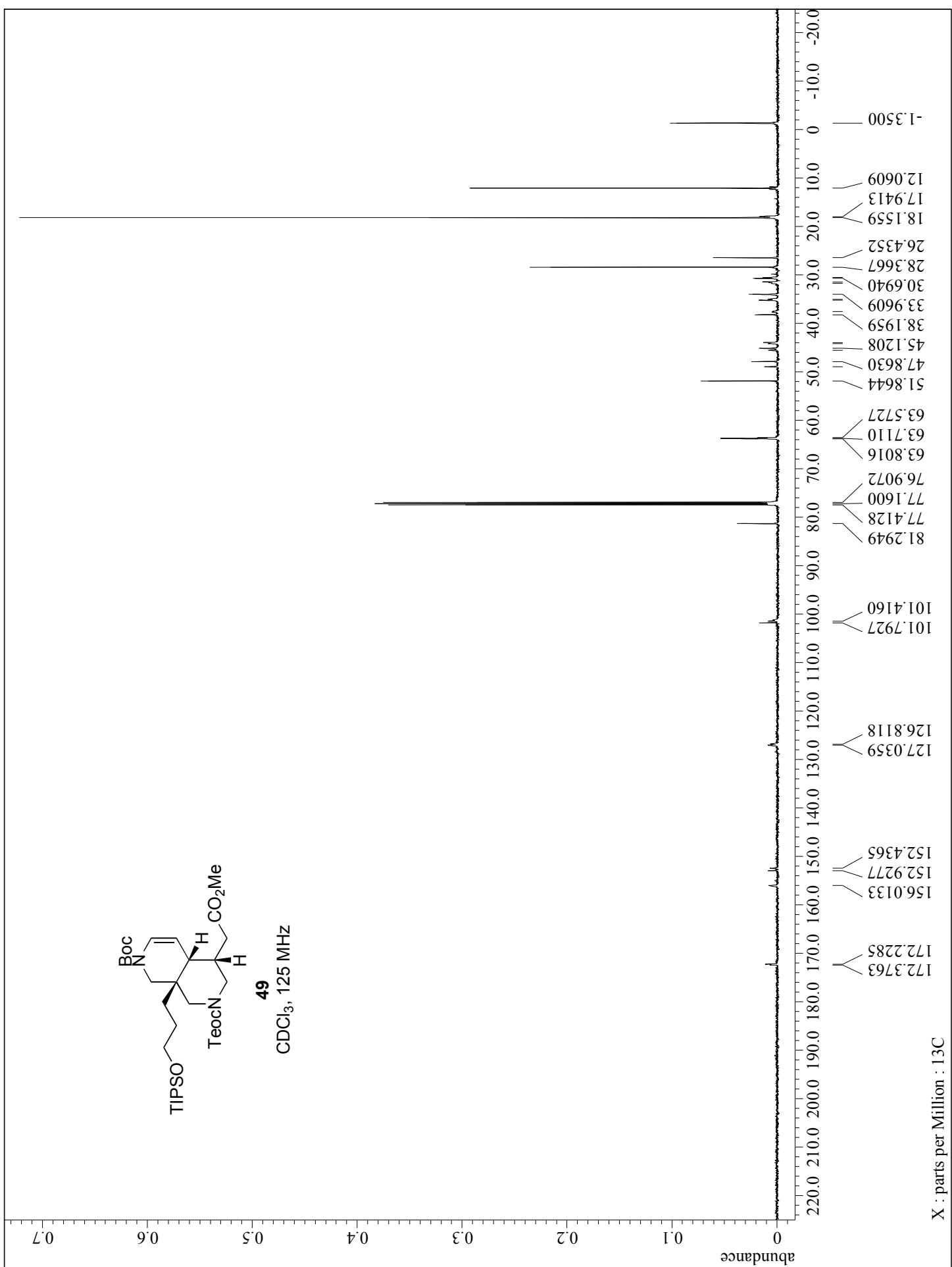
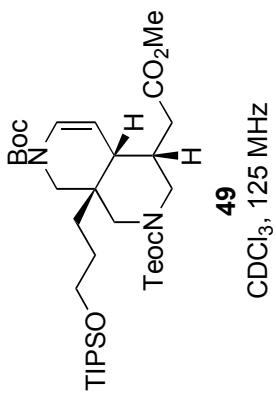


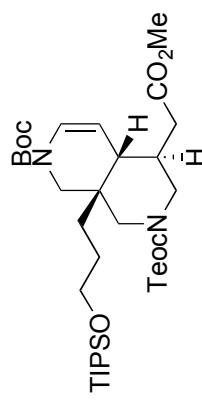




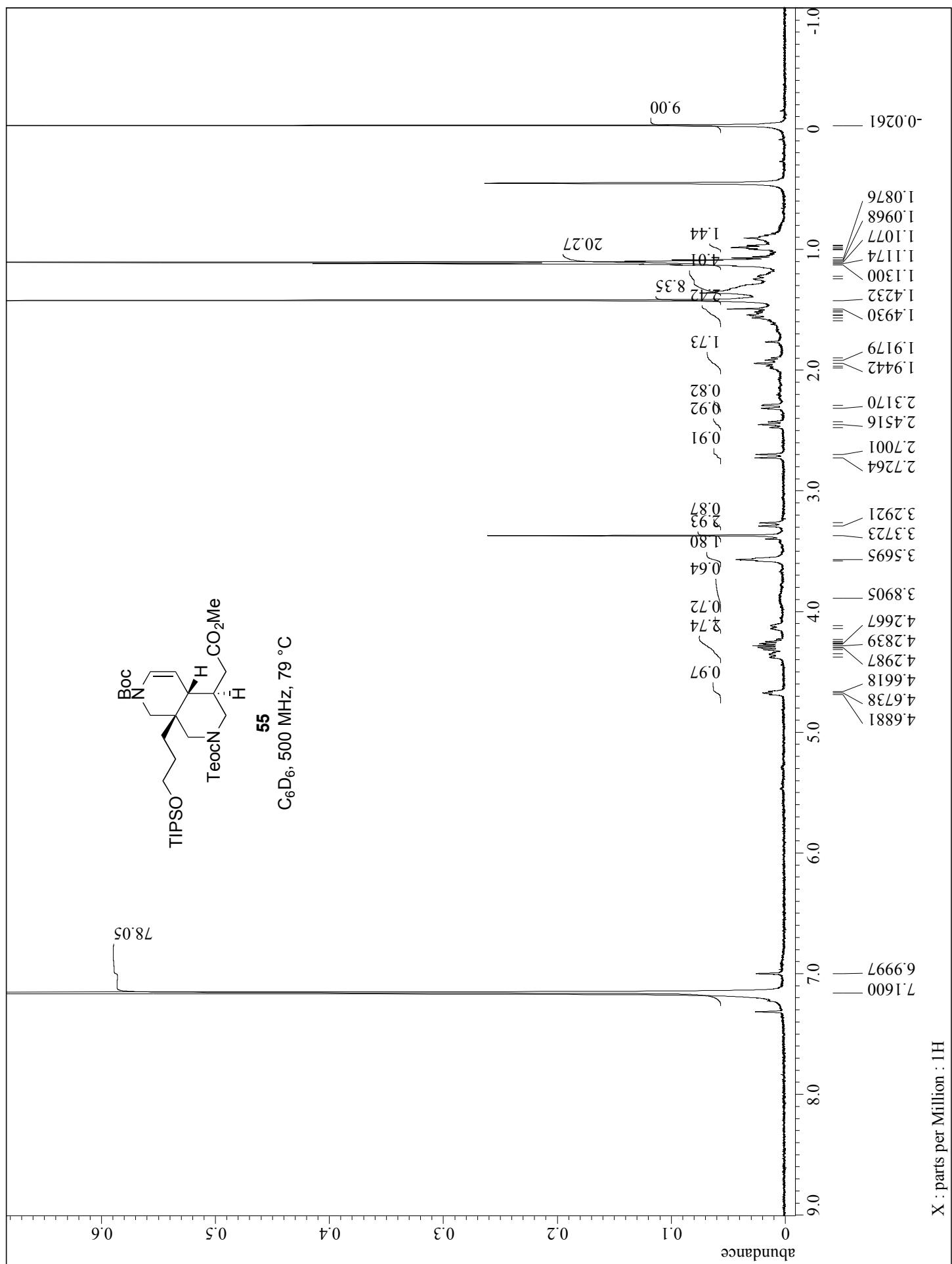
C₆D₆, 500 MHz, 79 °C

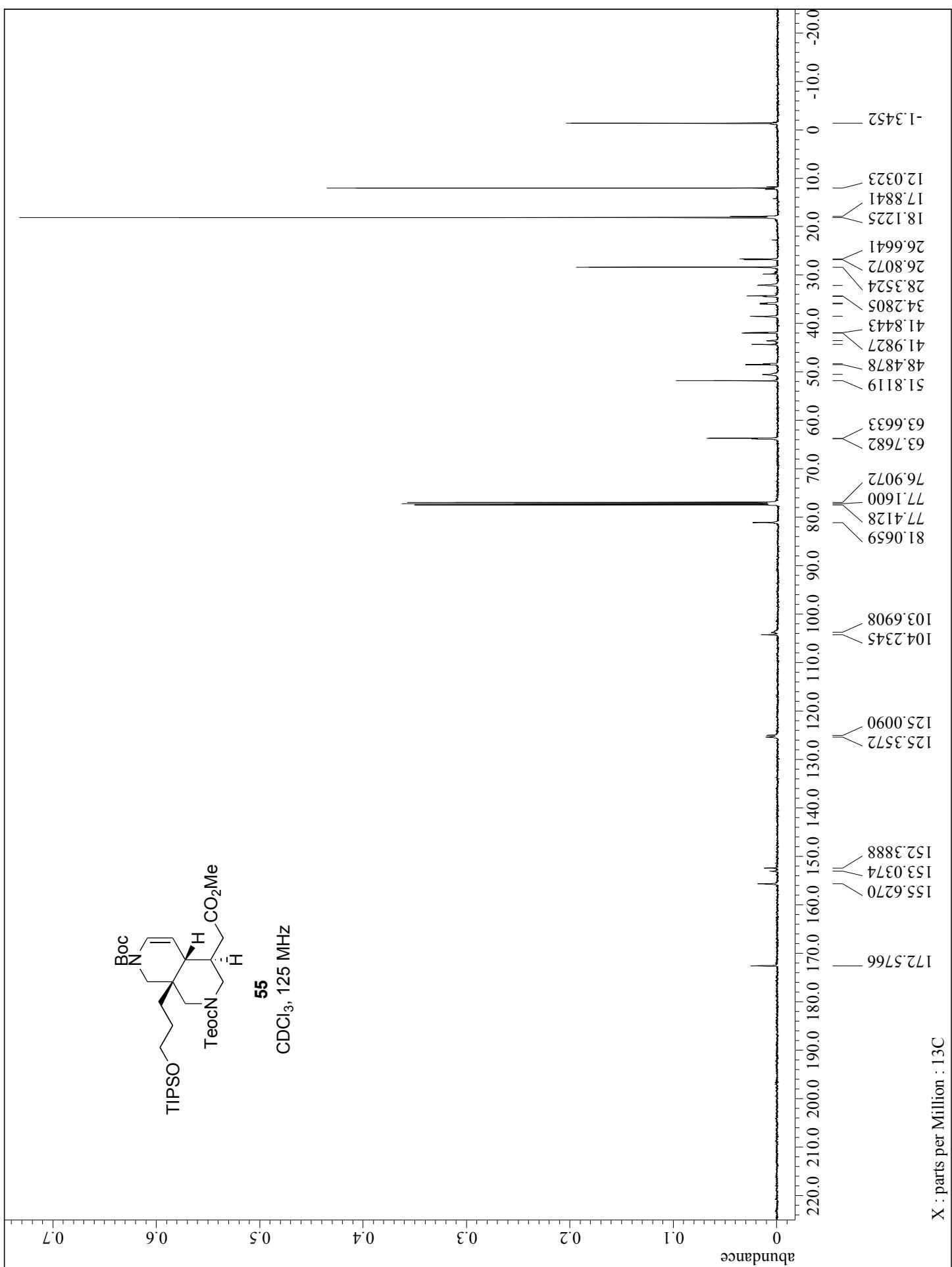
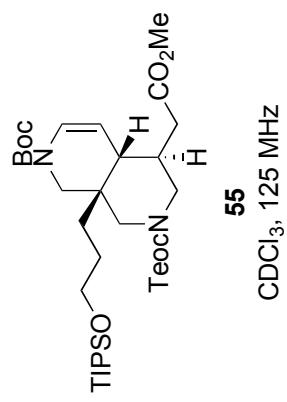


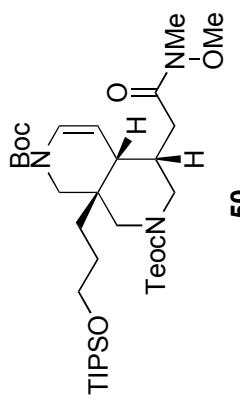




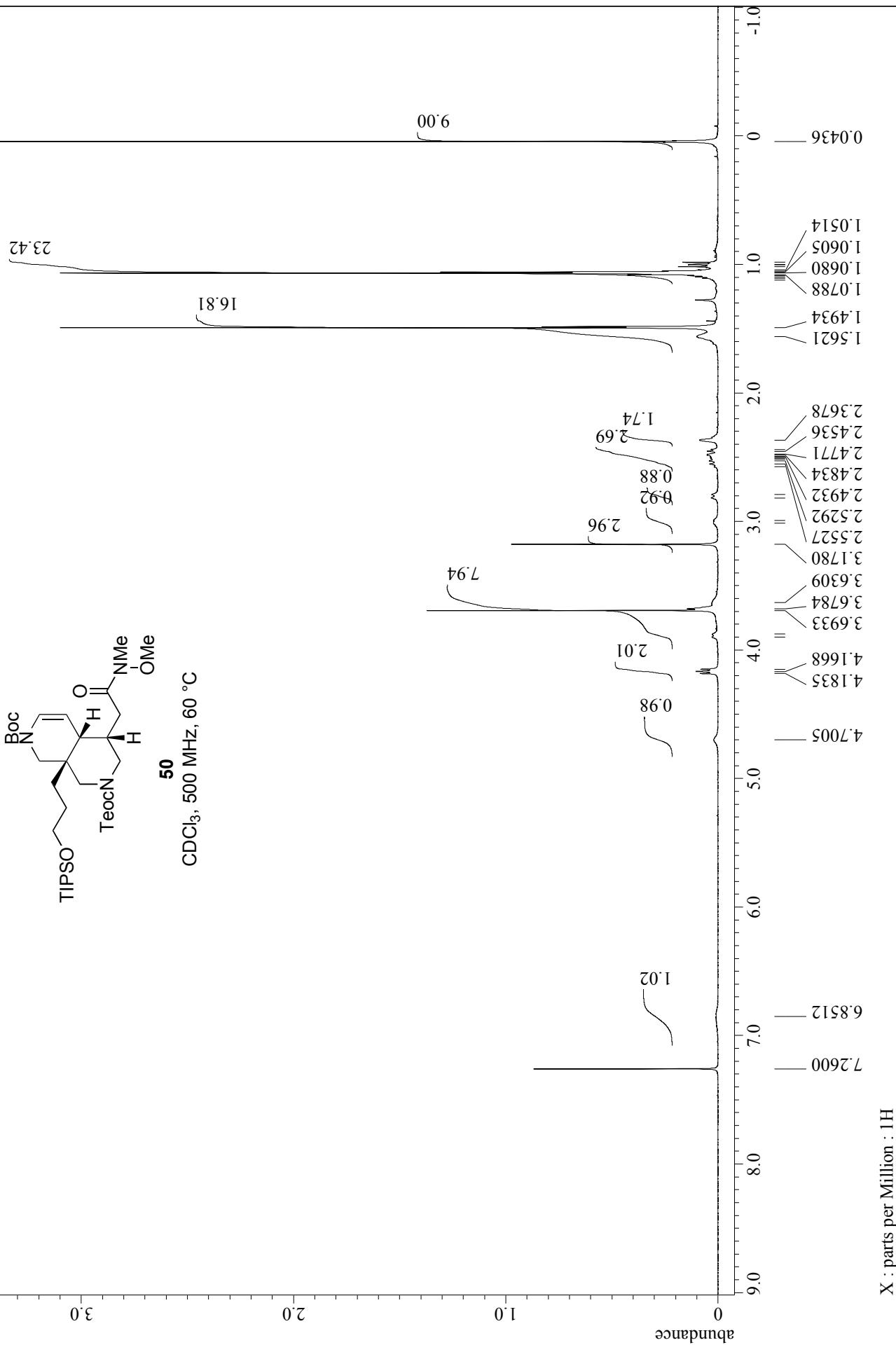
C_6D_6 , 500 MHz, 79 °C



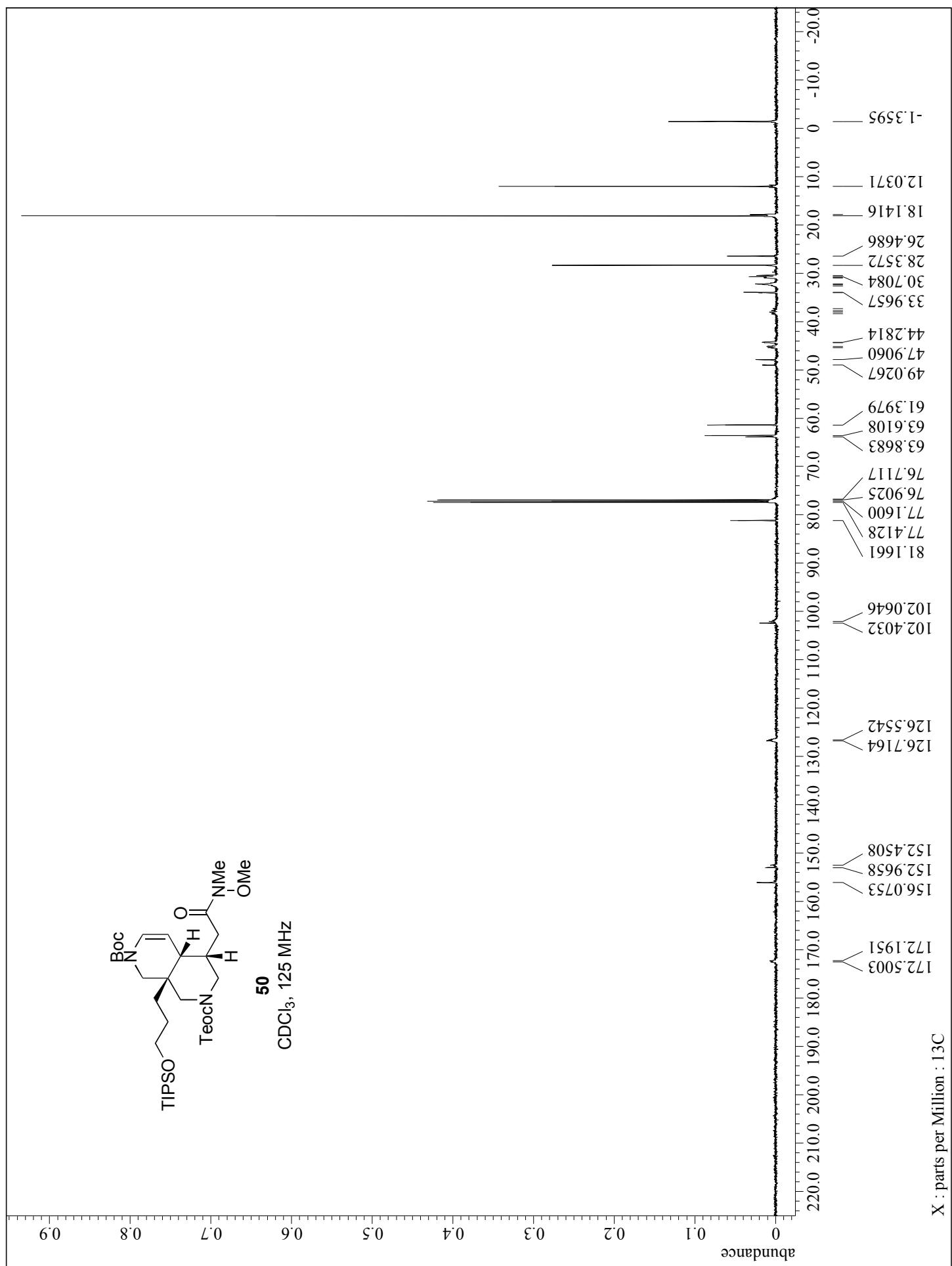
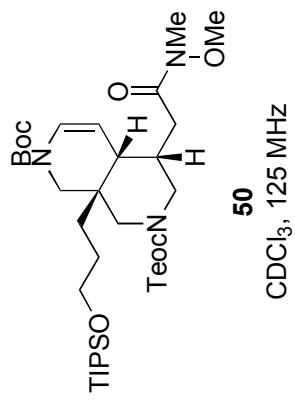


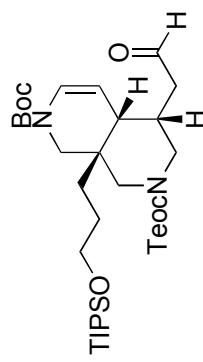


CDCl_3 , 500 MHz, 60 °C

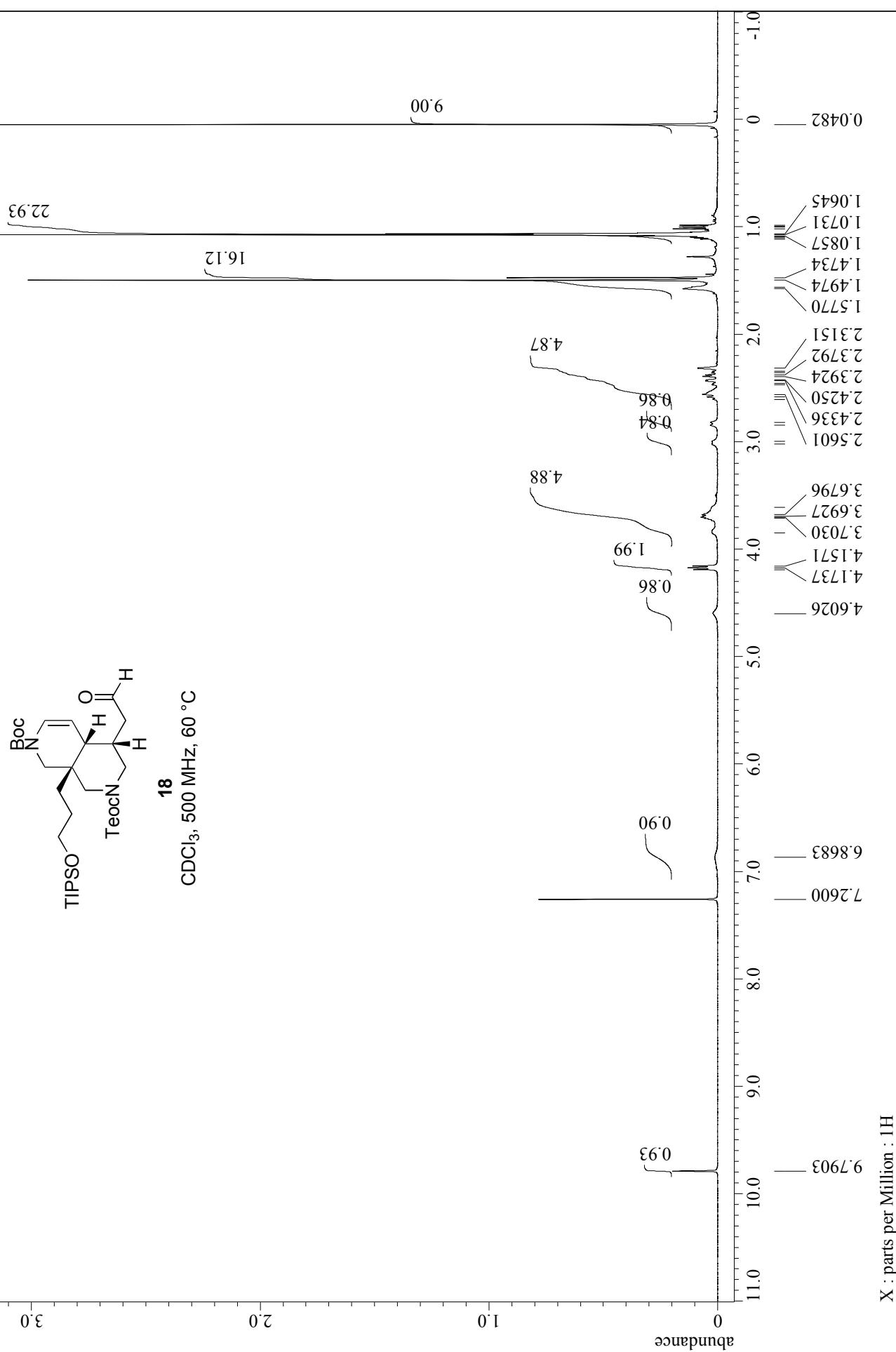


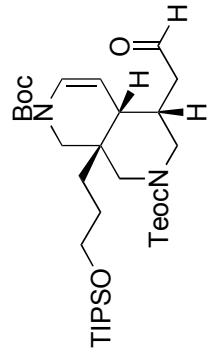
X : parts per Million : IH



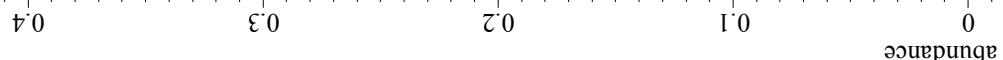


CDCl_3 , 500 MHz, 60 °C





CDCl_3 , 125 MHz, 60 °C



X : parts per Million : ^{13}C

156.1278

152.7083

127.3698

101.3826

63.7777

63.8206

76.9025

77.1600

77.4128

81.3855

44.5437

44.3148

38.5012

34.3043

31.1137

29.5017

28.4573

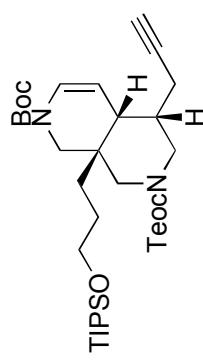
26.6498

18.2036

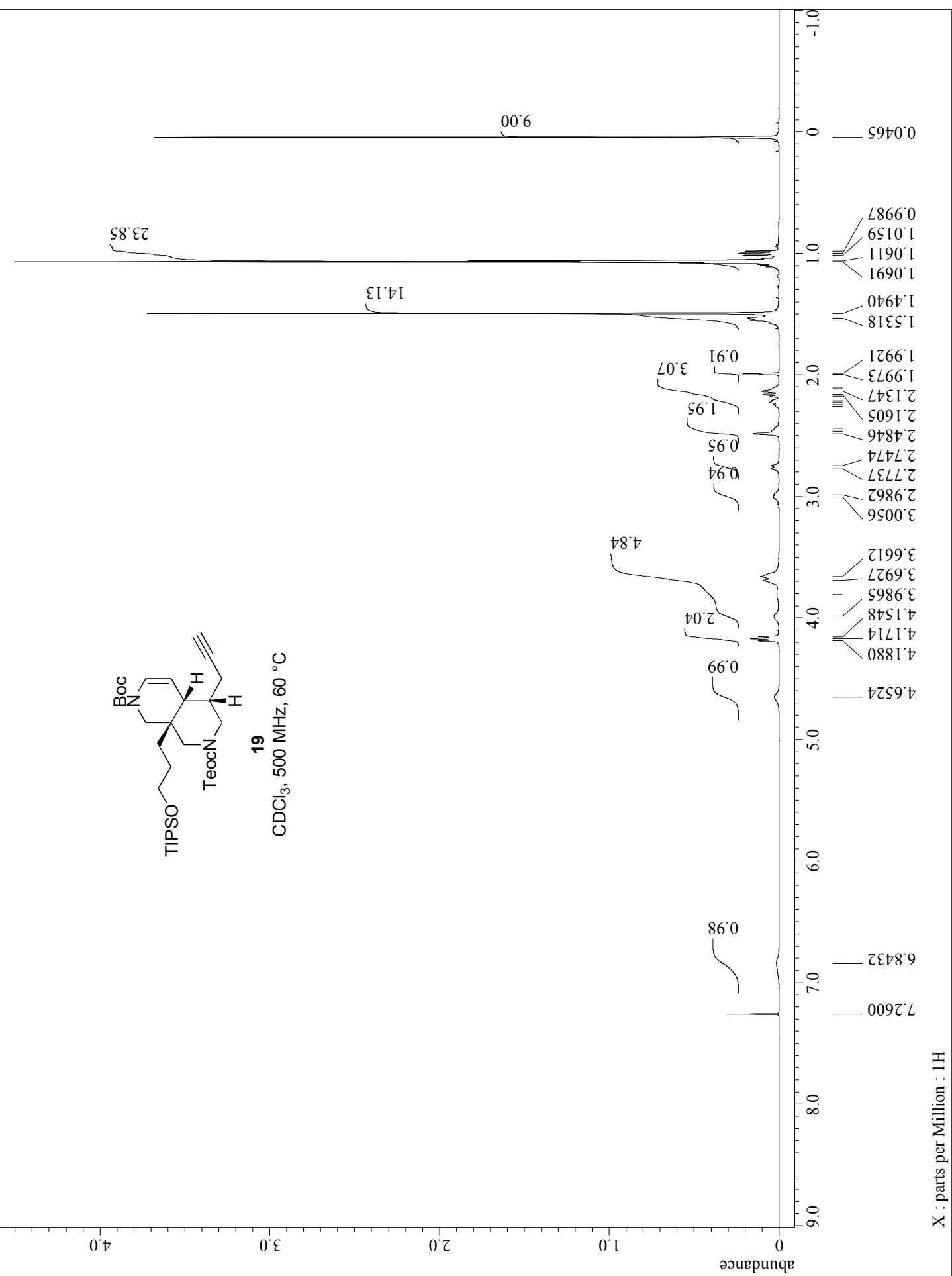
18.1273

12.3041

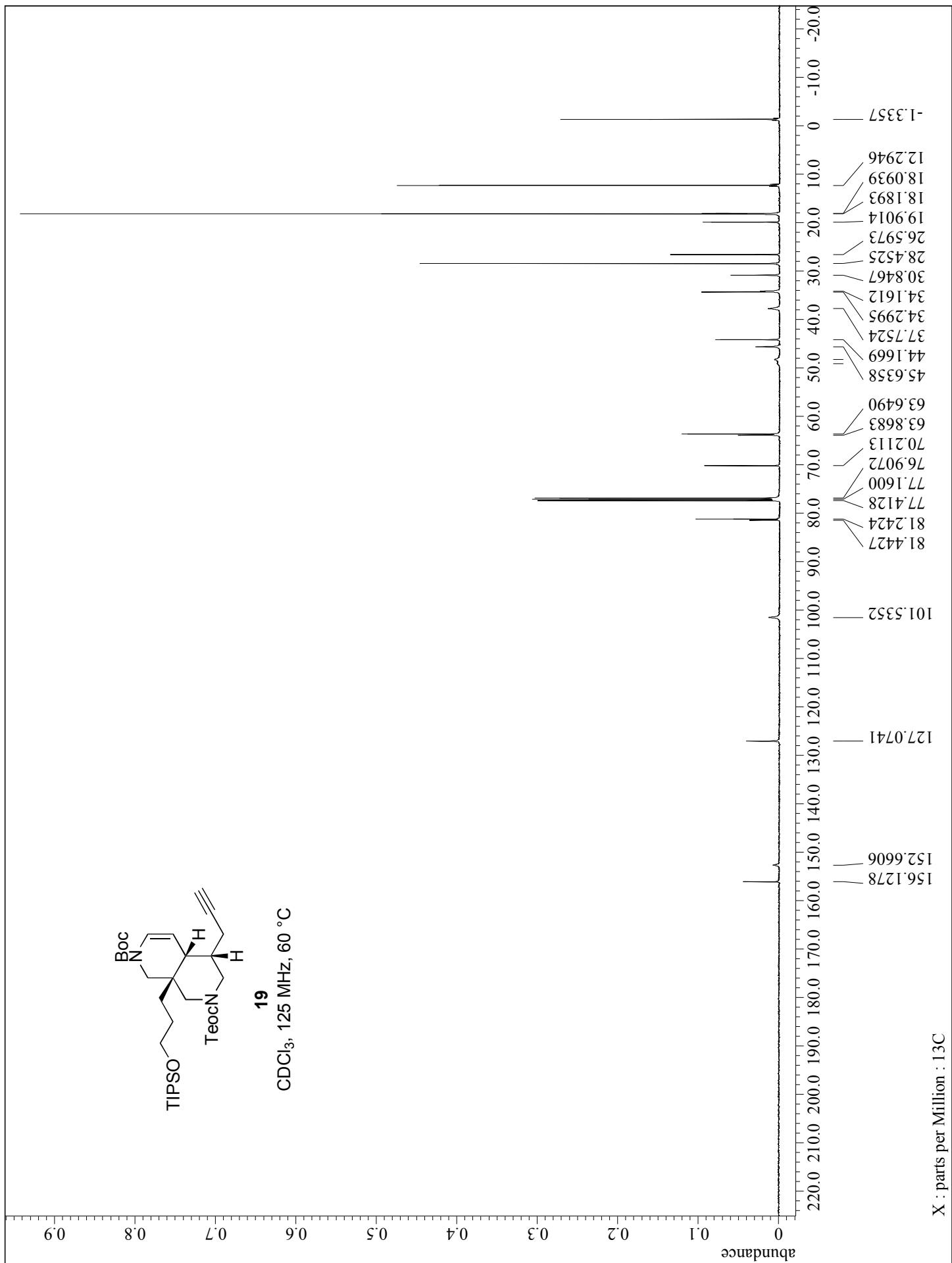
-1.3452

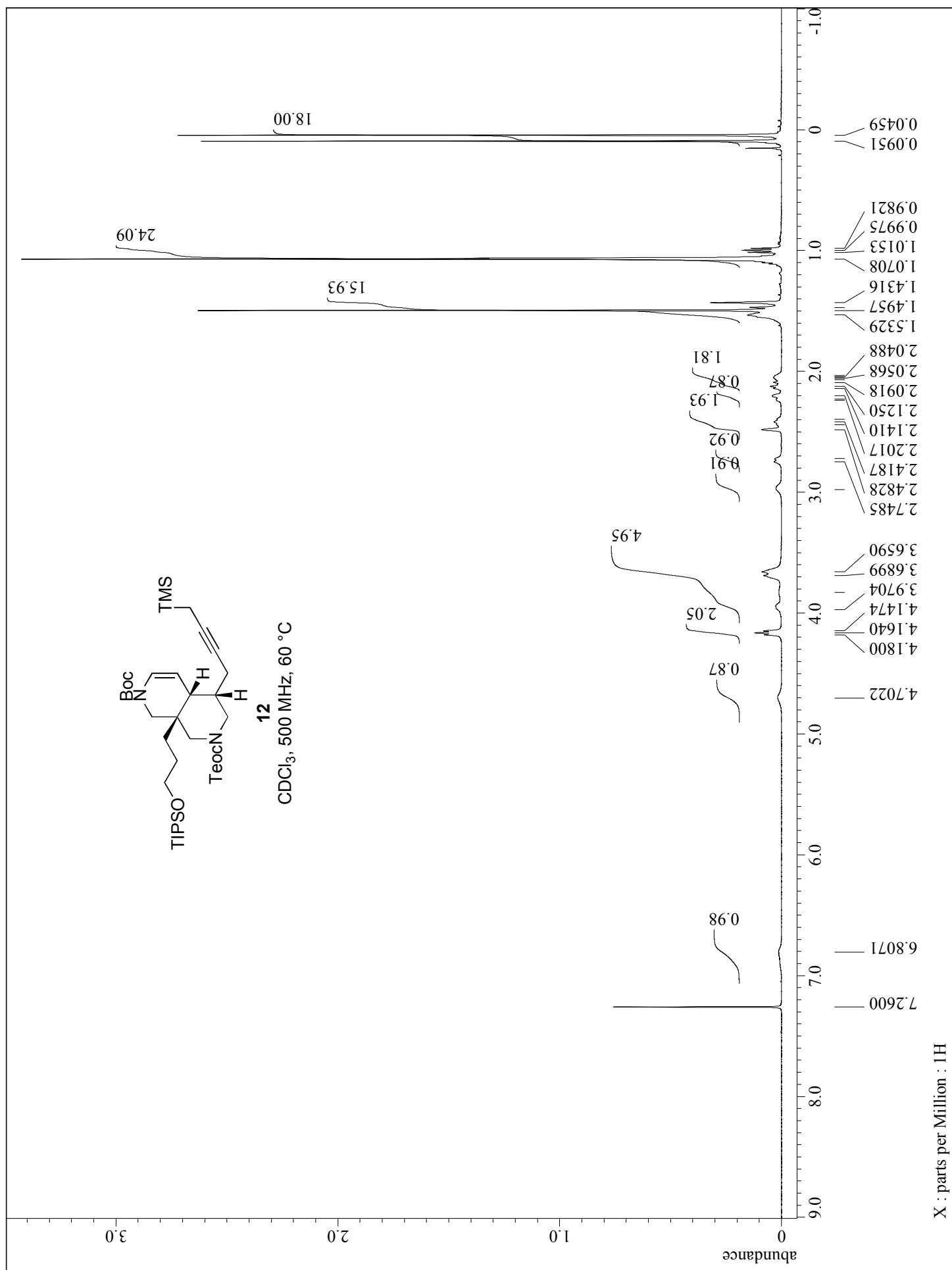


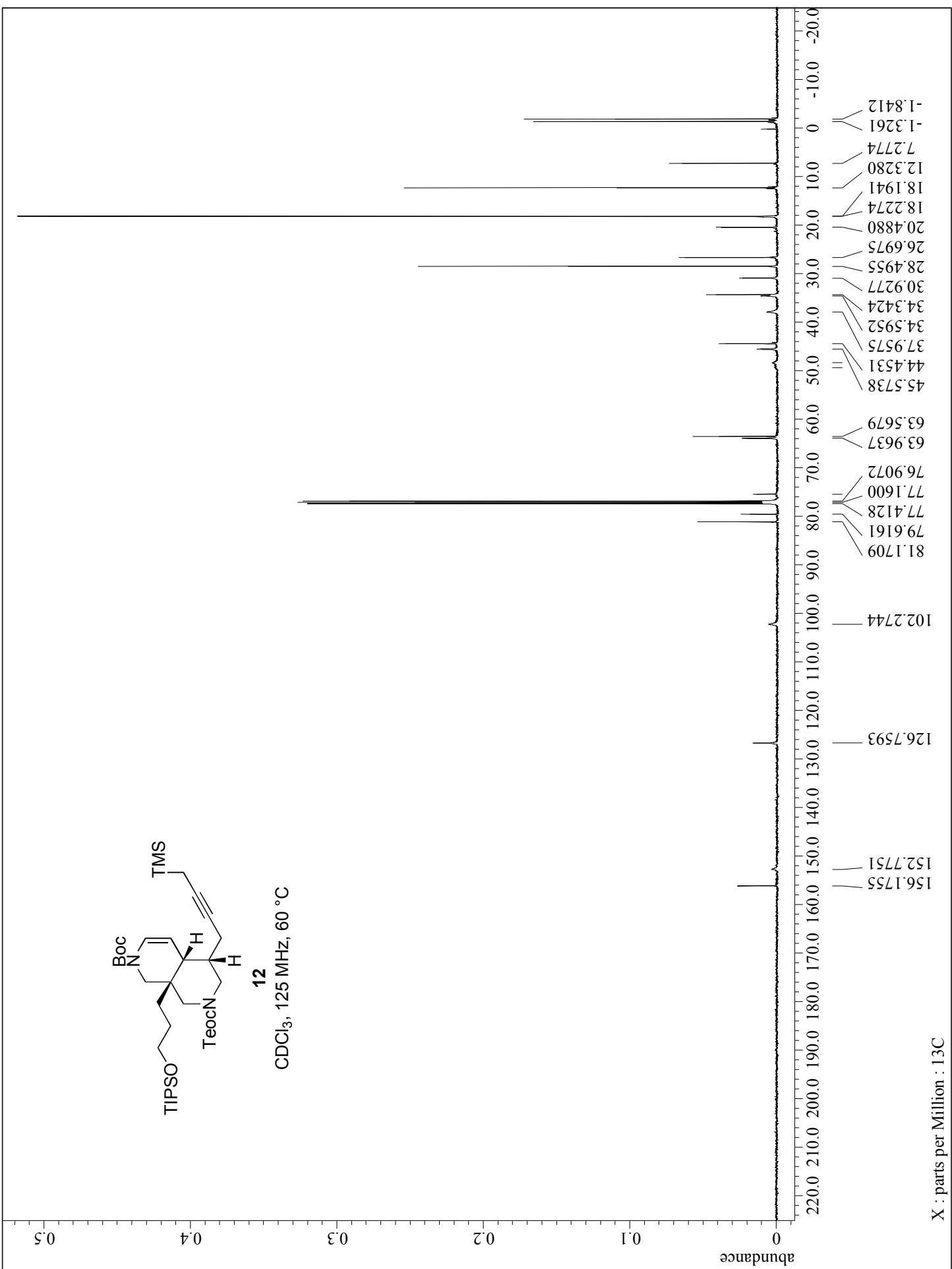
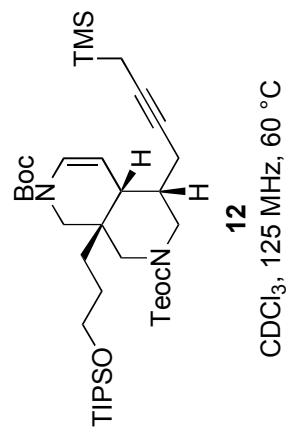
19
 $\text{CDCl}_3, 500 \text{ MHz}, 60^\circ\text{C}$

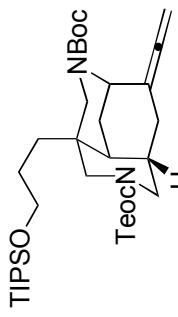


X : parts per Million : IH

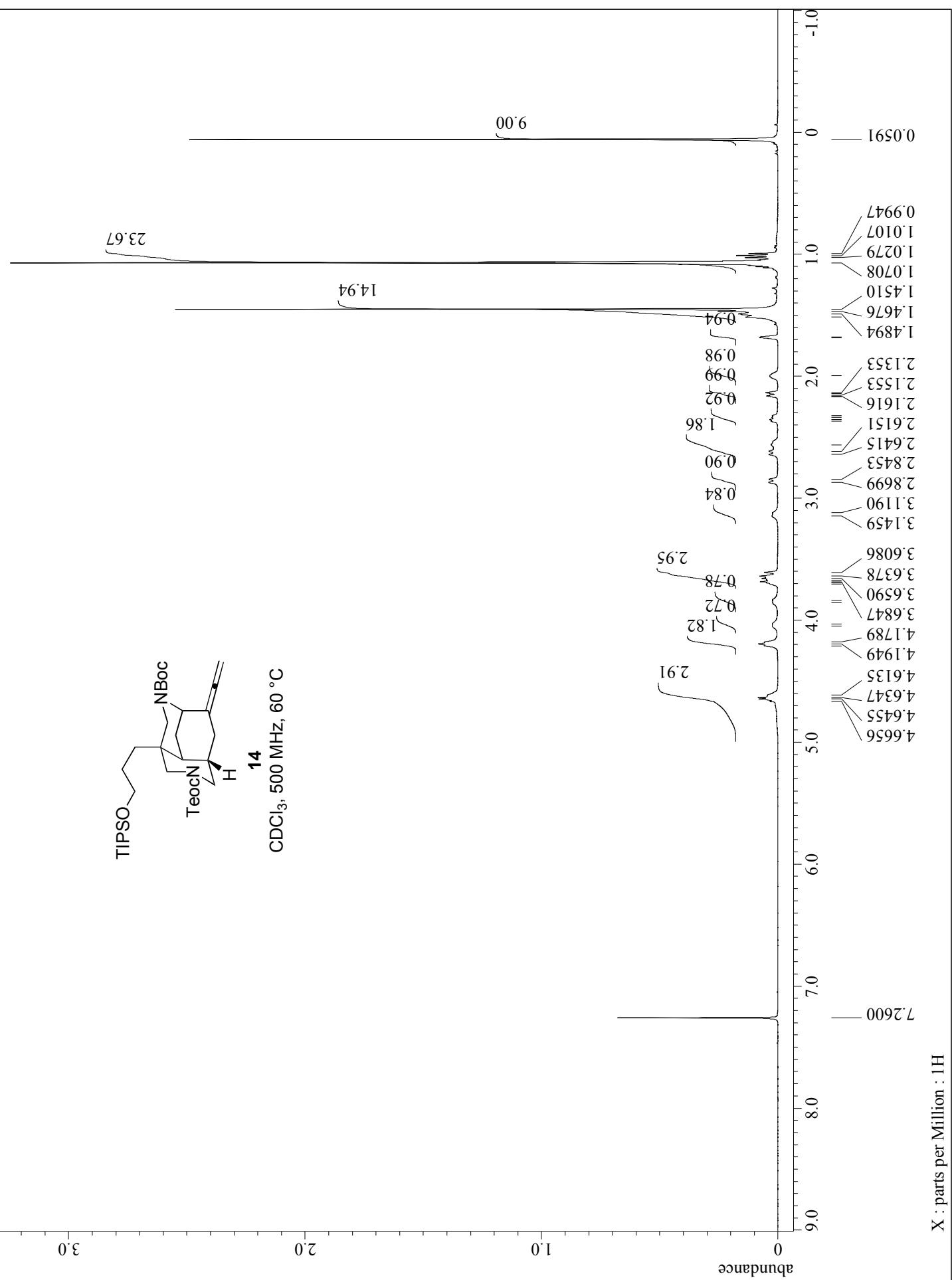




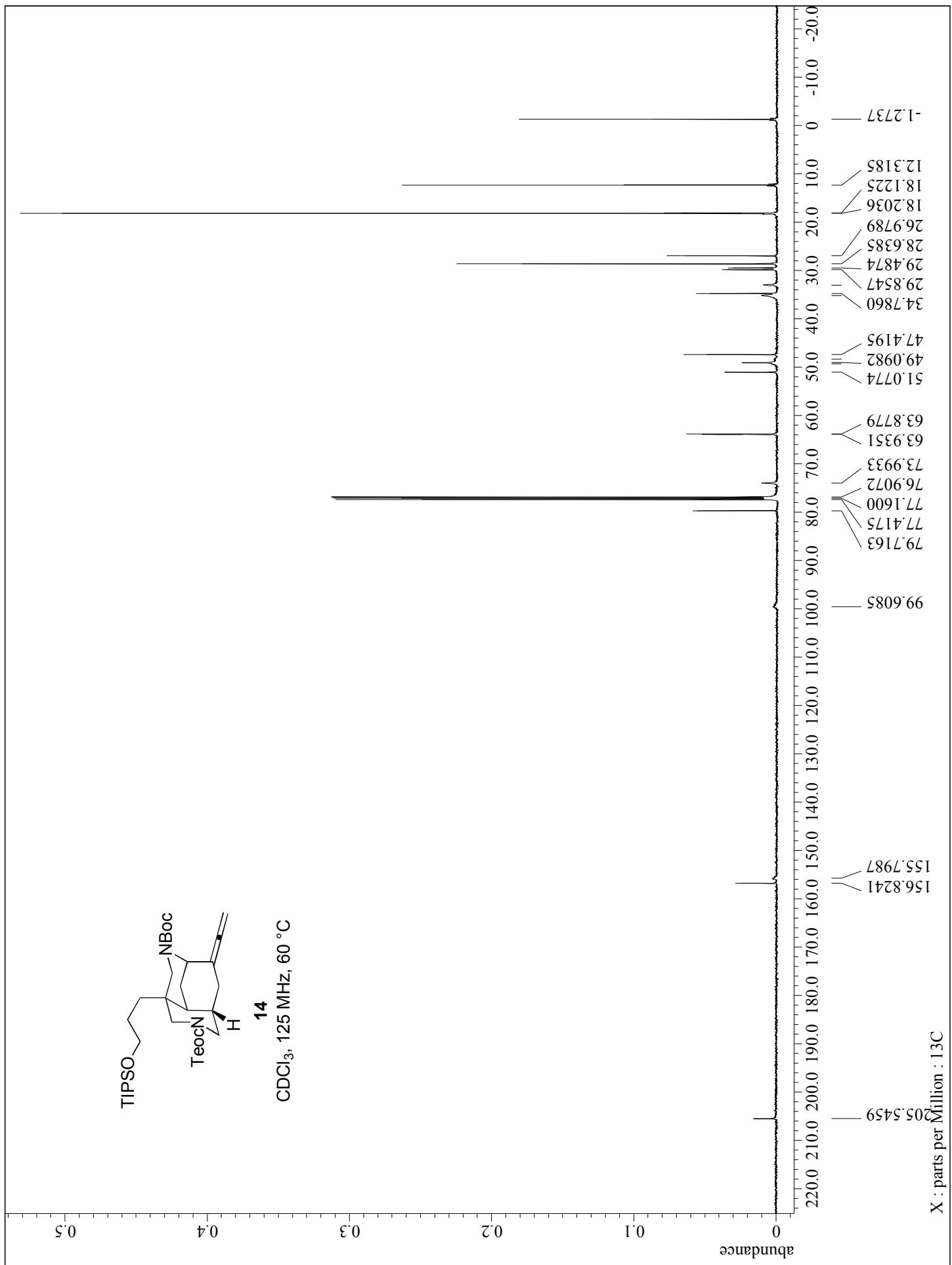


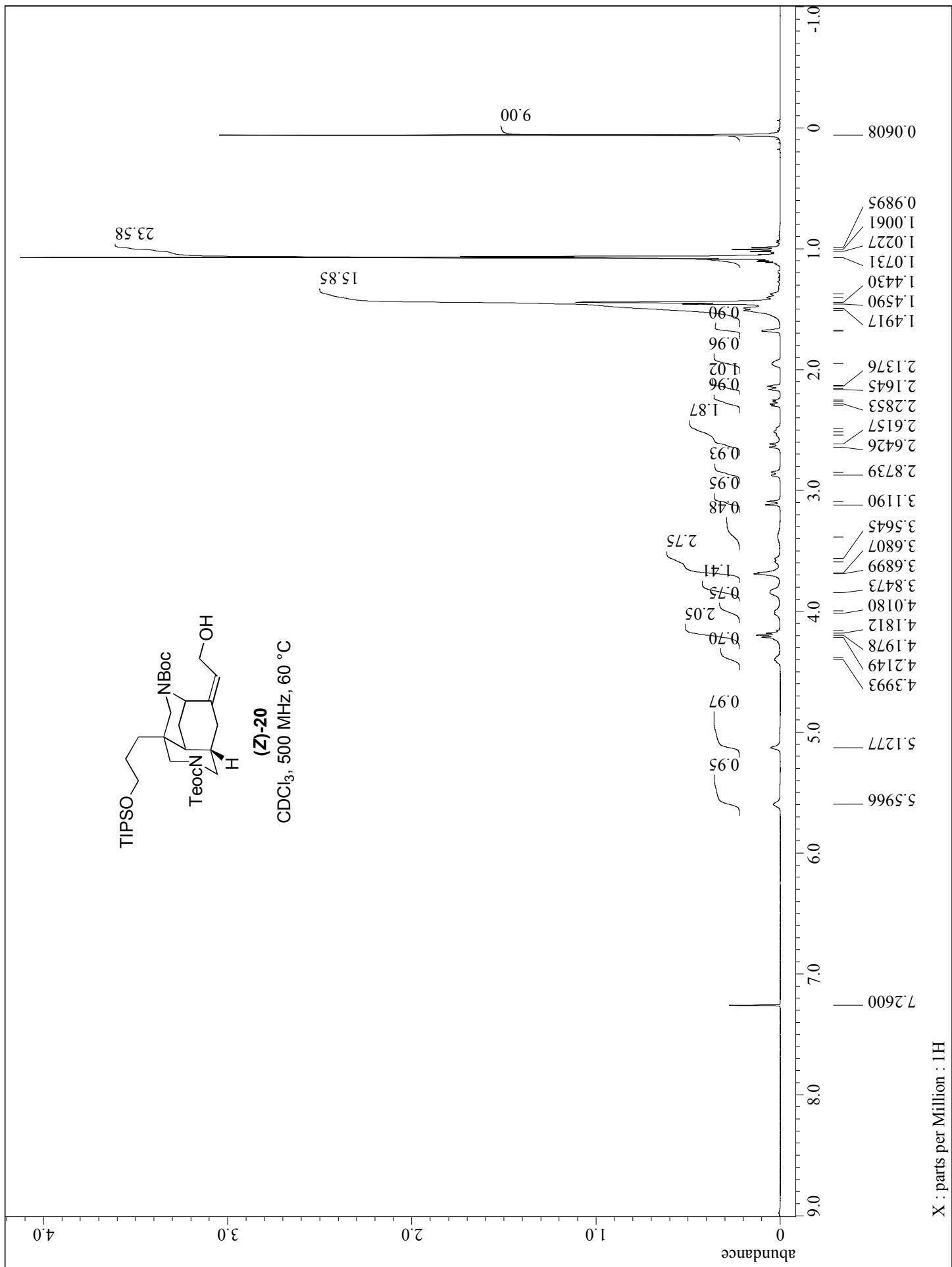


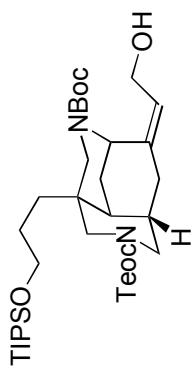
14
 $\text{CDCl}_3, 500 \text{ MHz}, 60^\circ\text{C}$



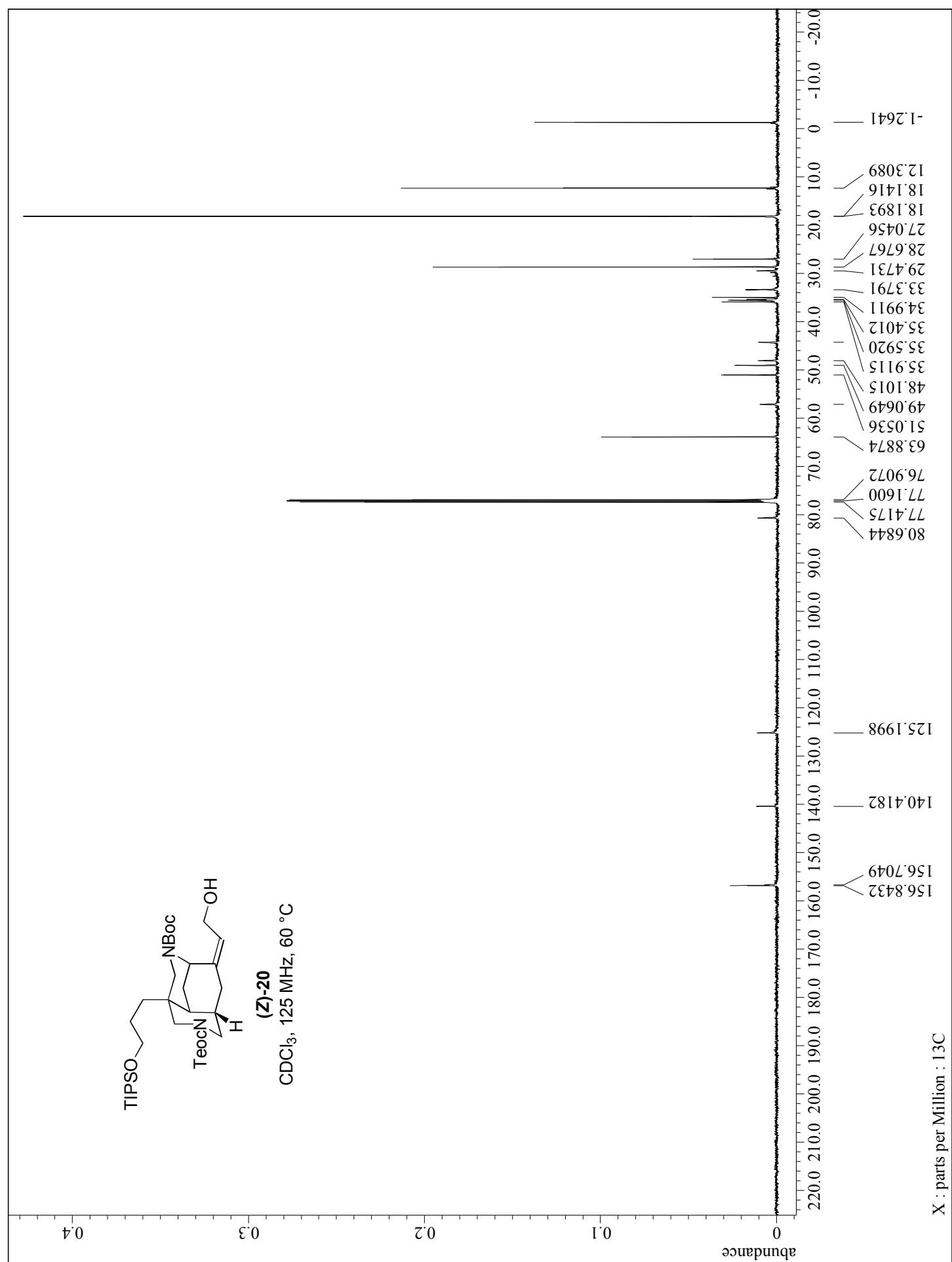
X : parts per Million : IH

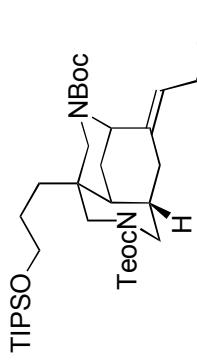




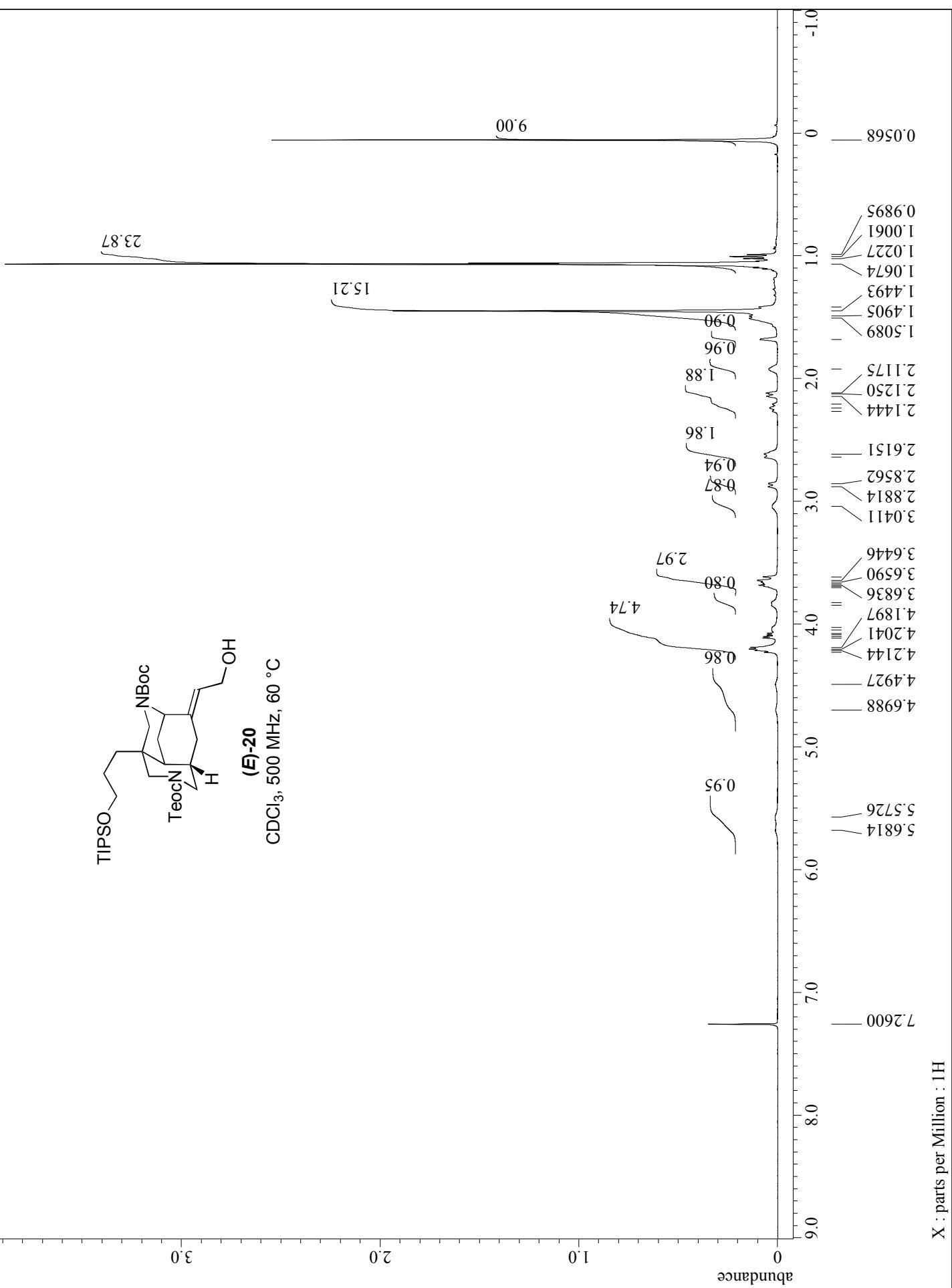


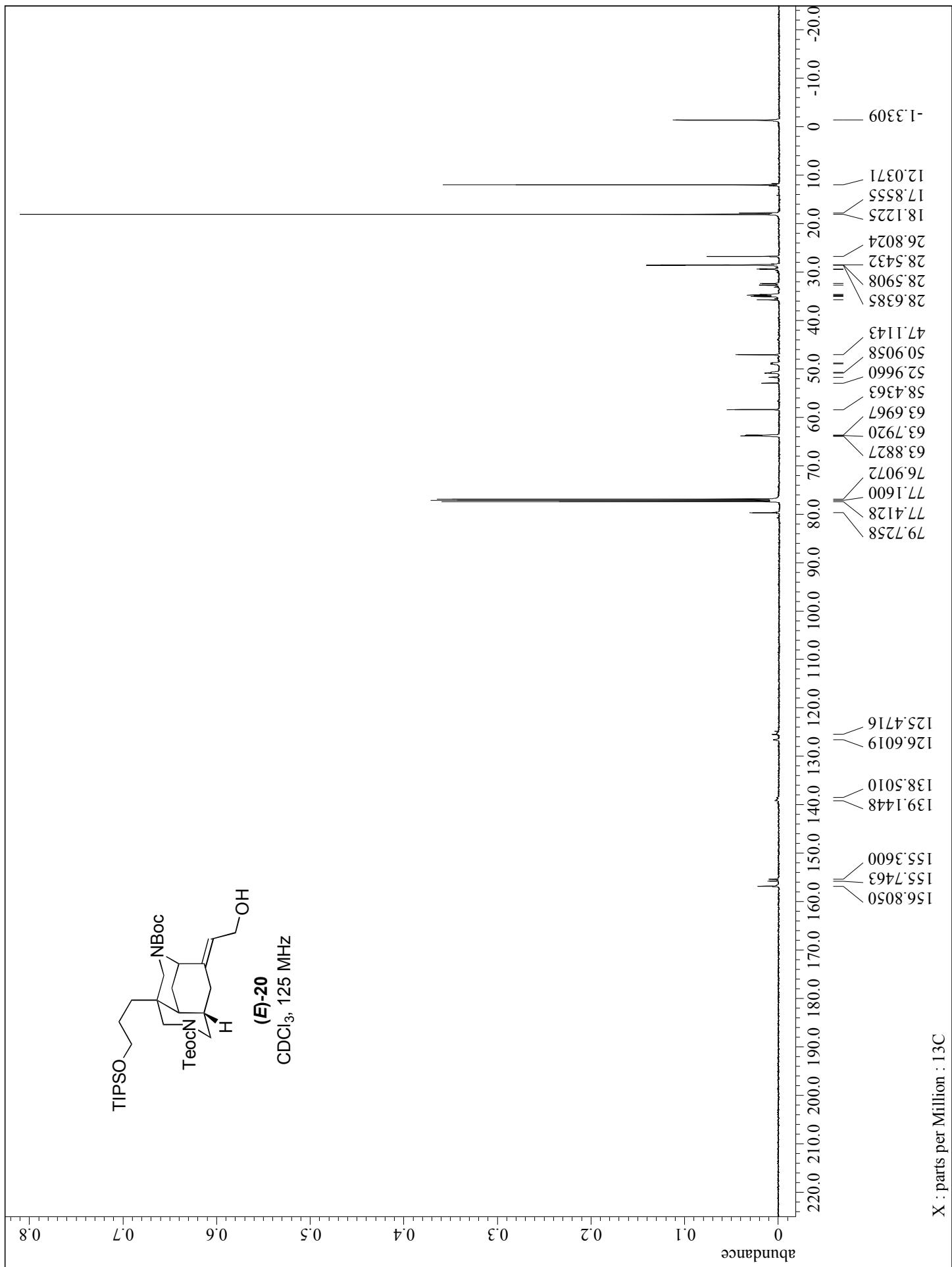
CDCl_3 , 125 MHz, 60 °C

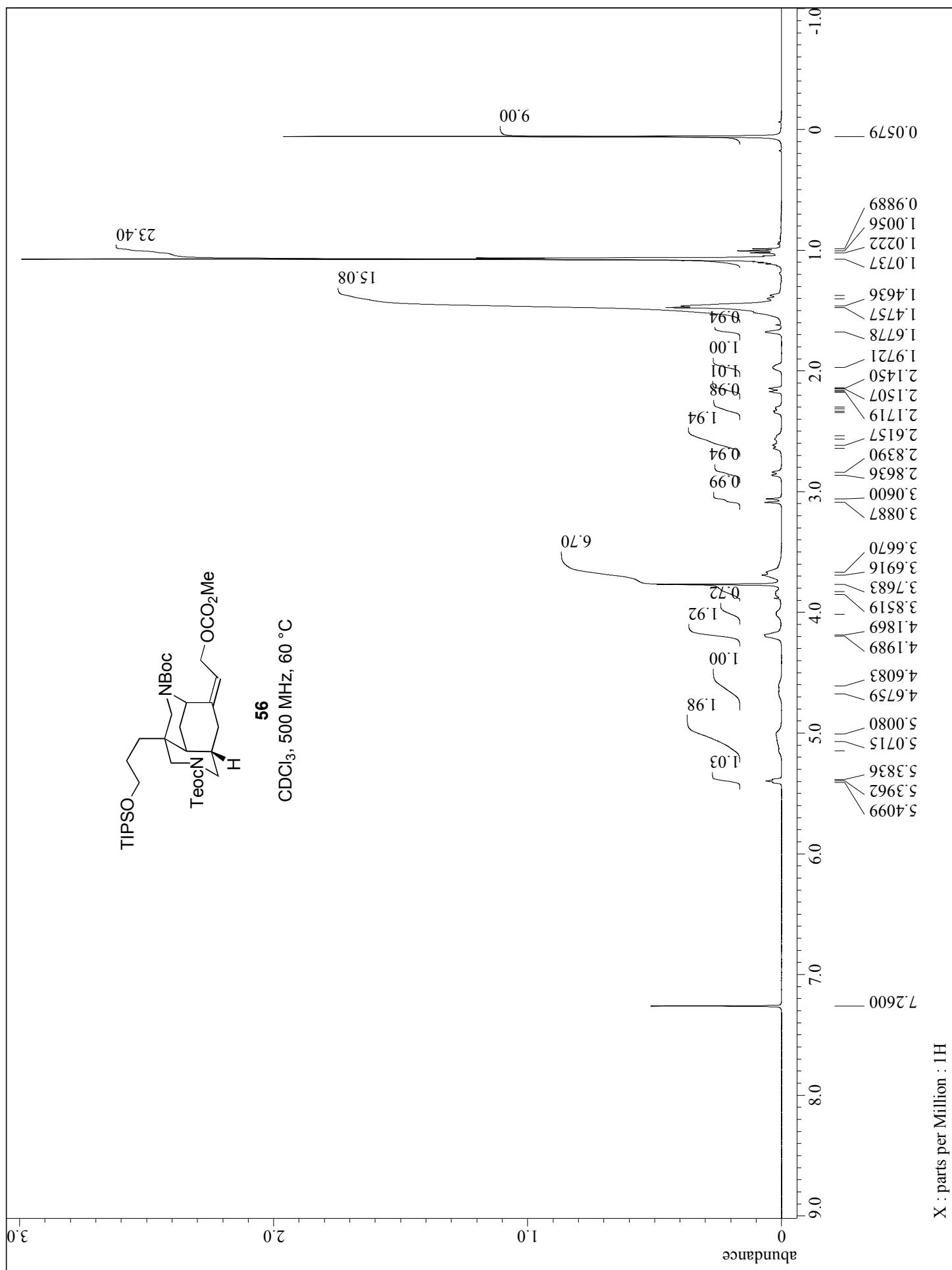


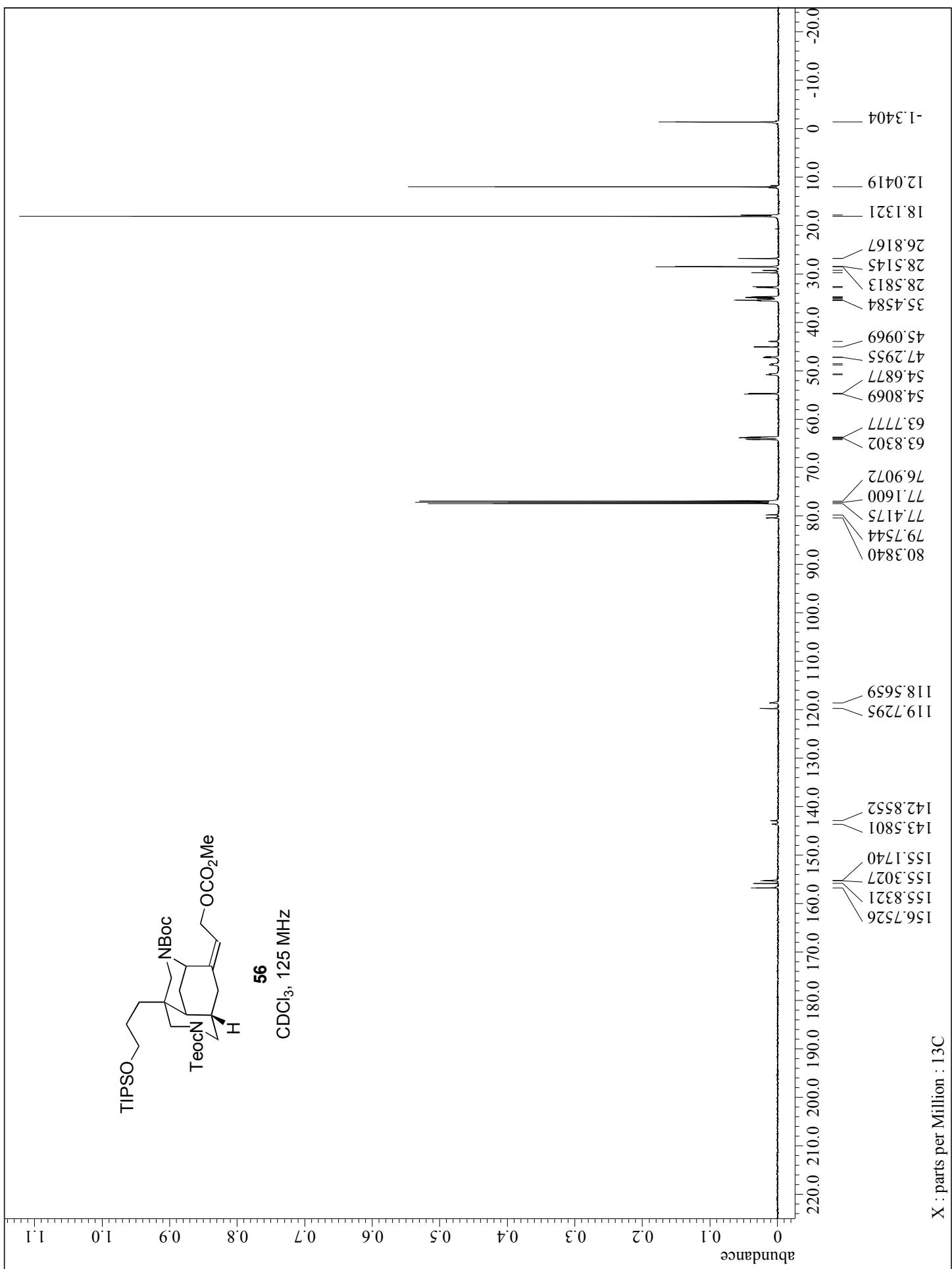
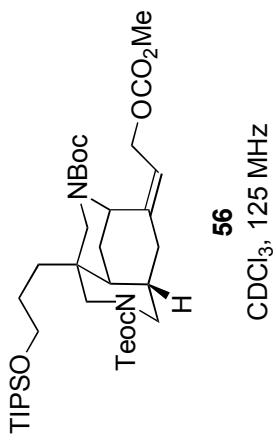


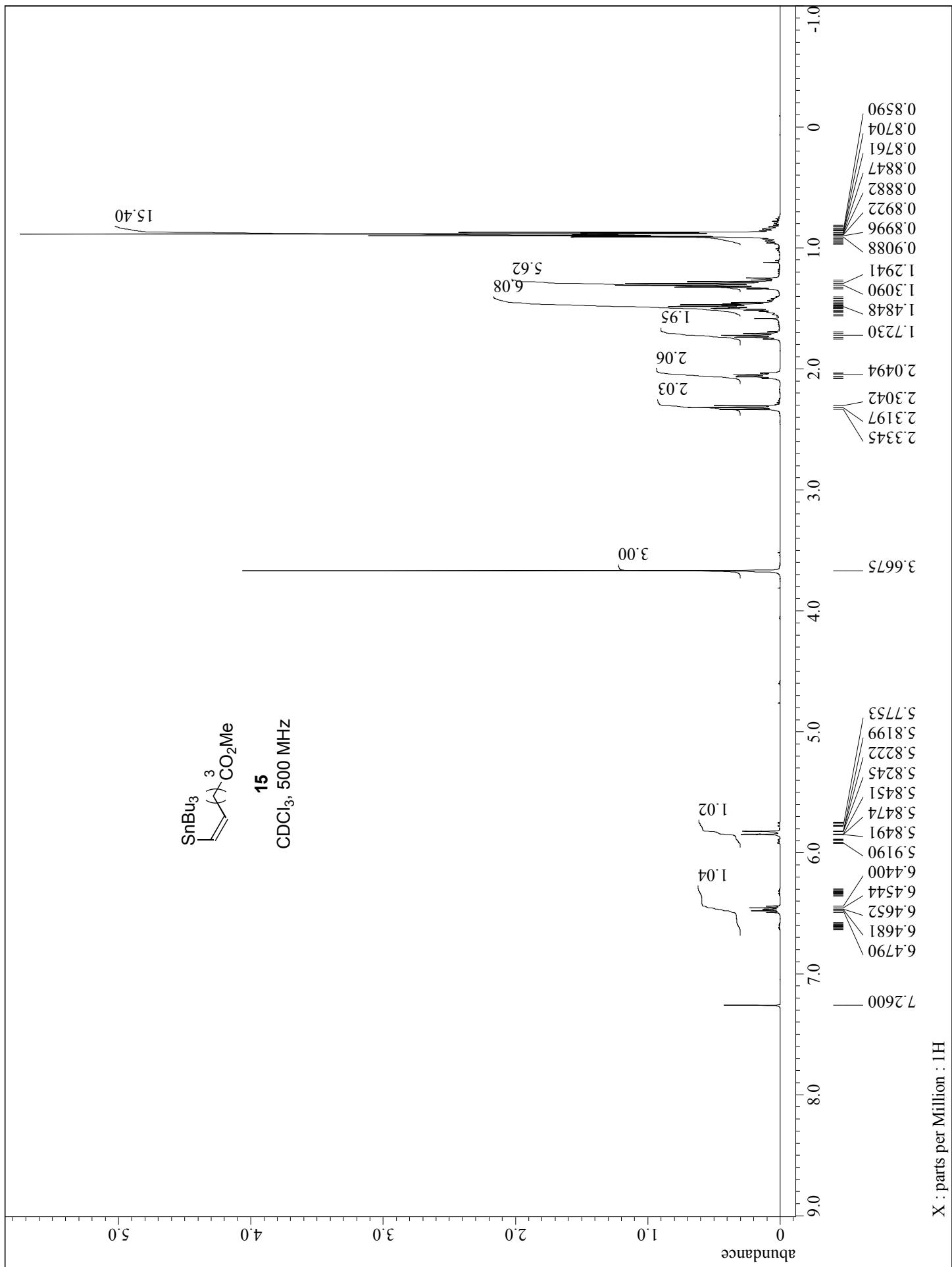
CDCl₃, 500 MHz, 60 °C

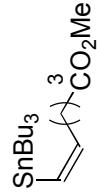




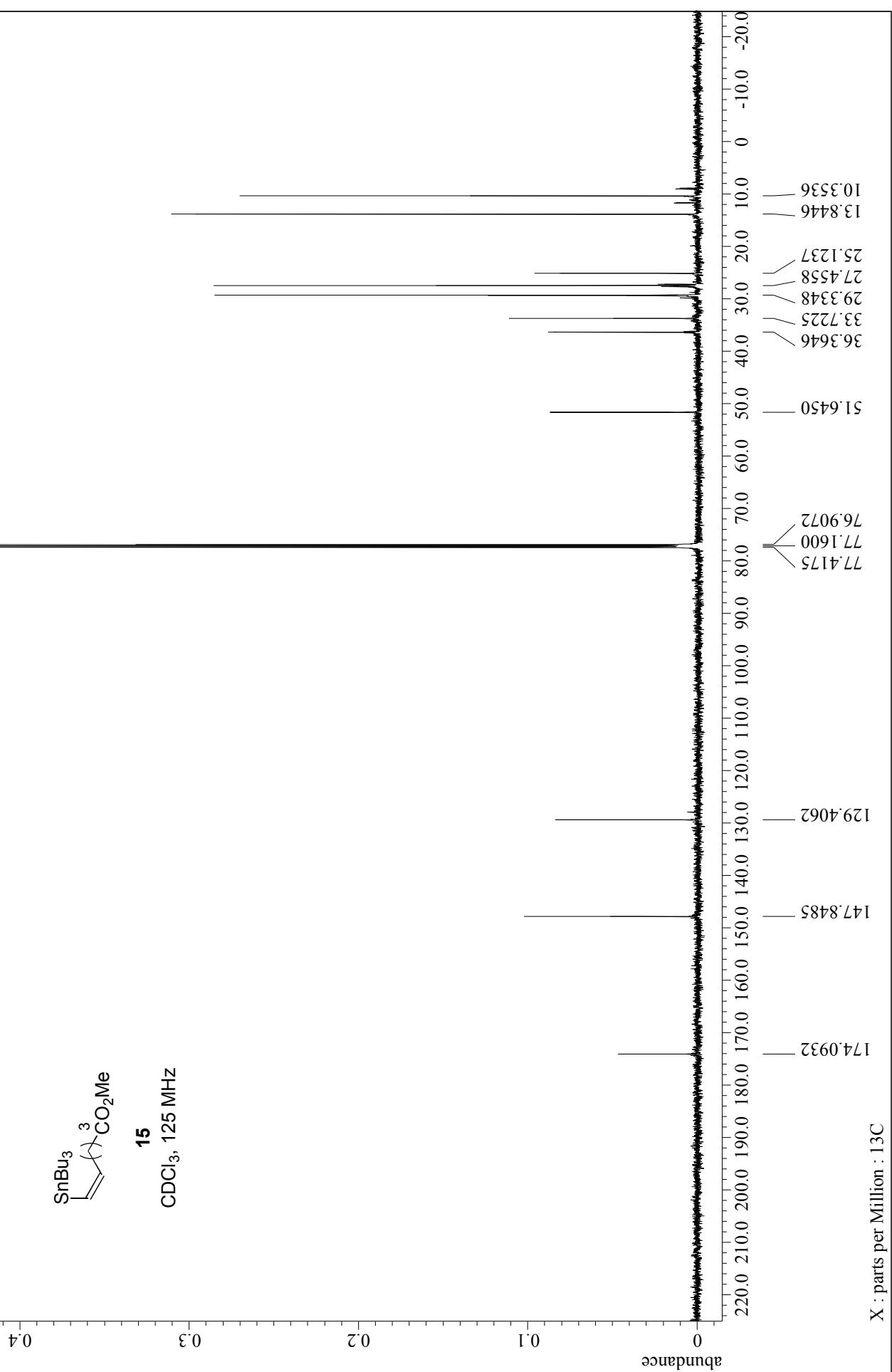


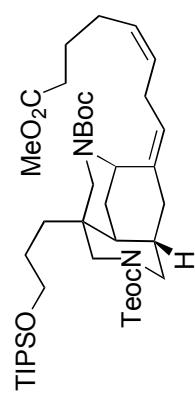




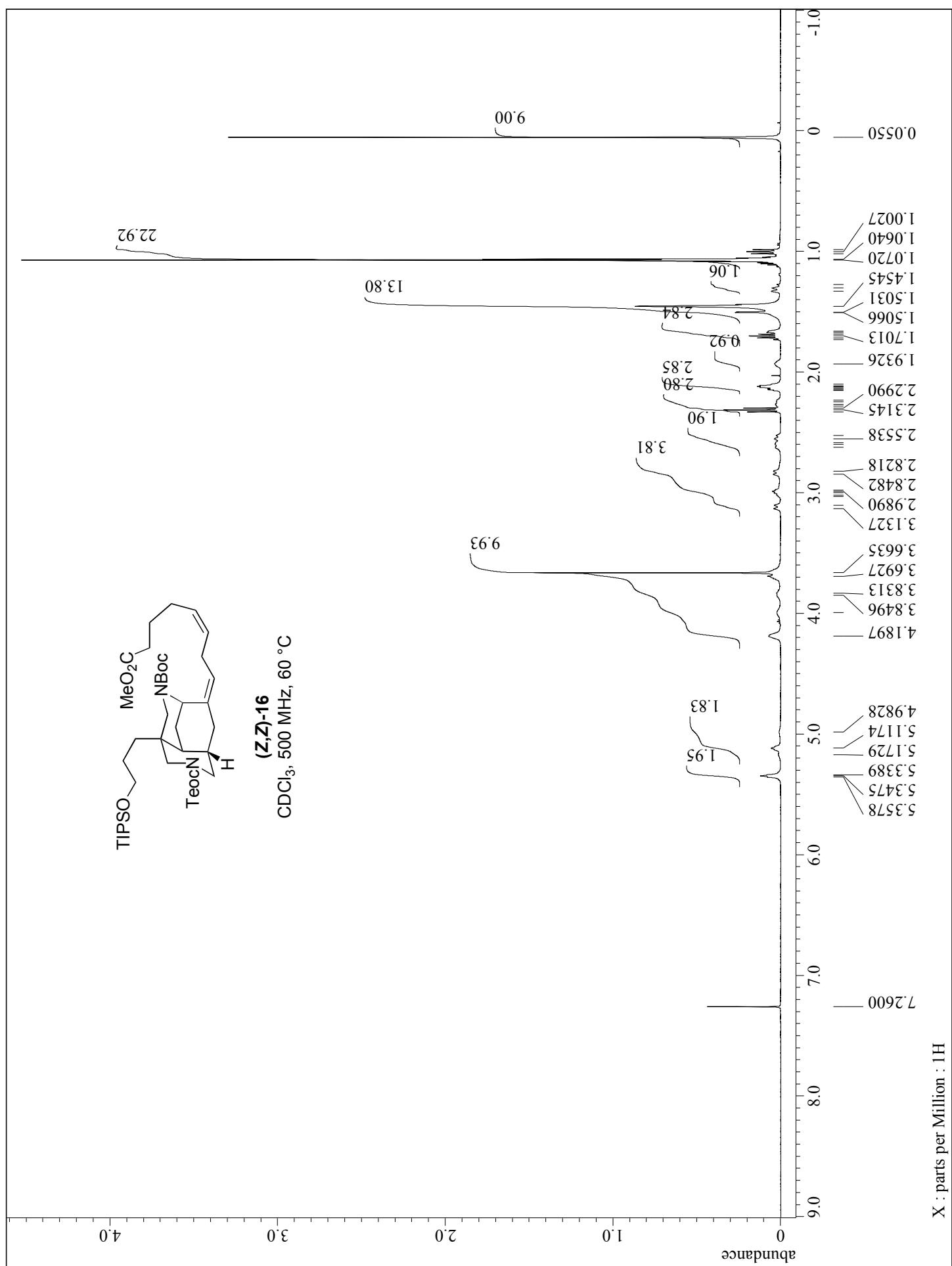


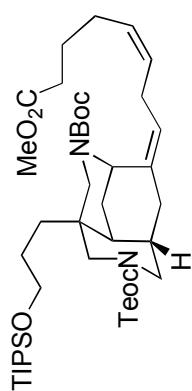
CDCl_3 , 125 MHz



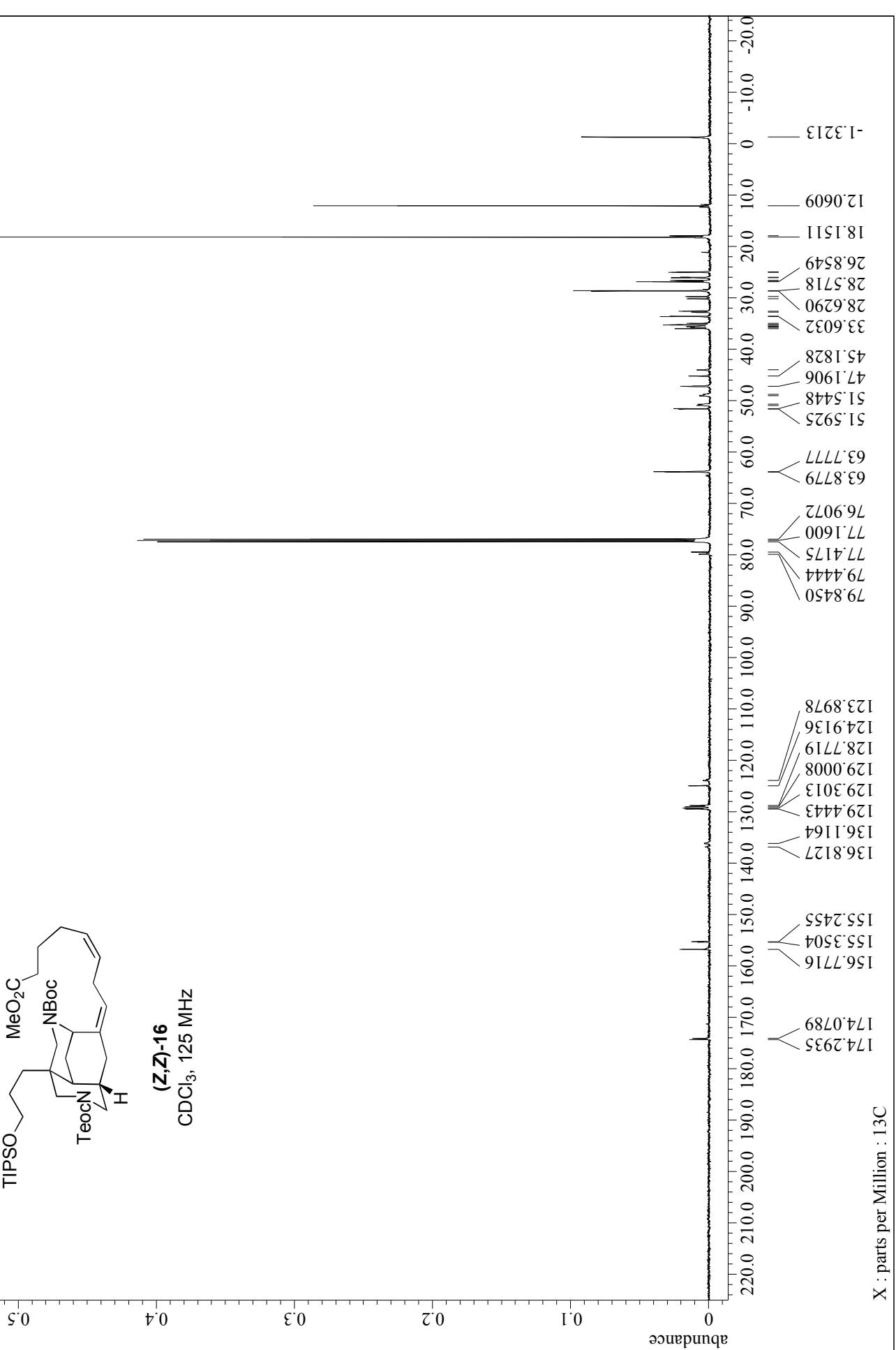


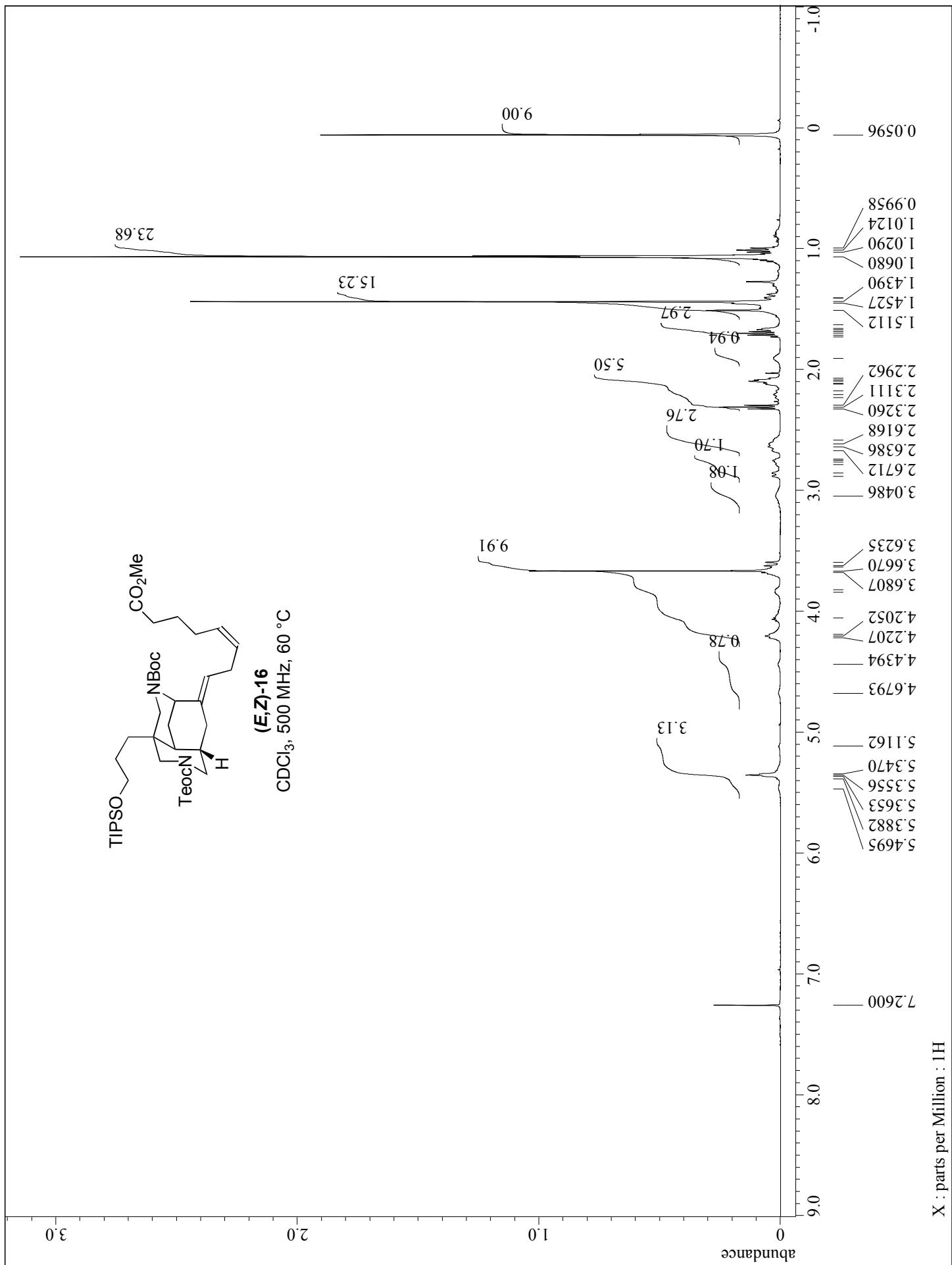
CDCl_3 , 500 MHz, 60 °C

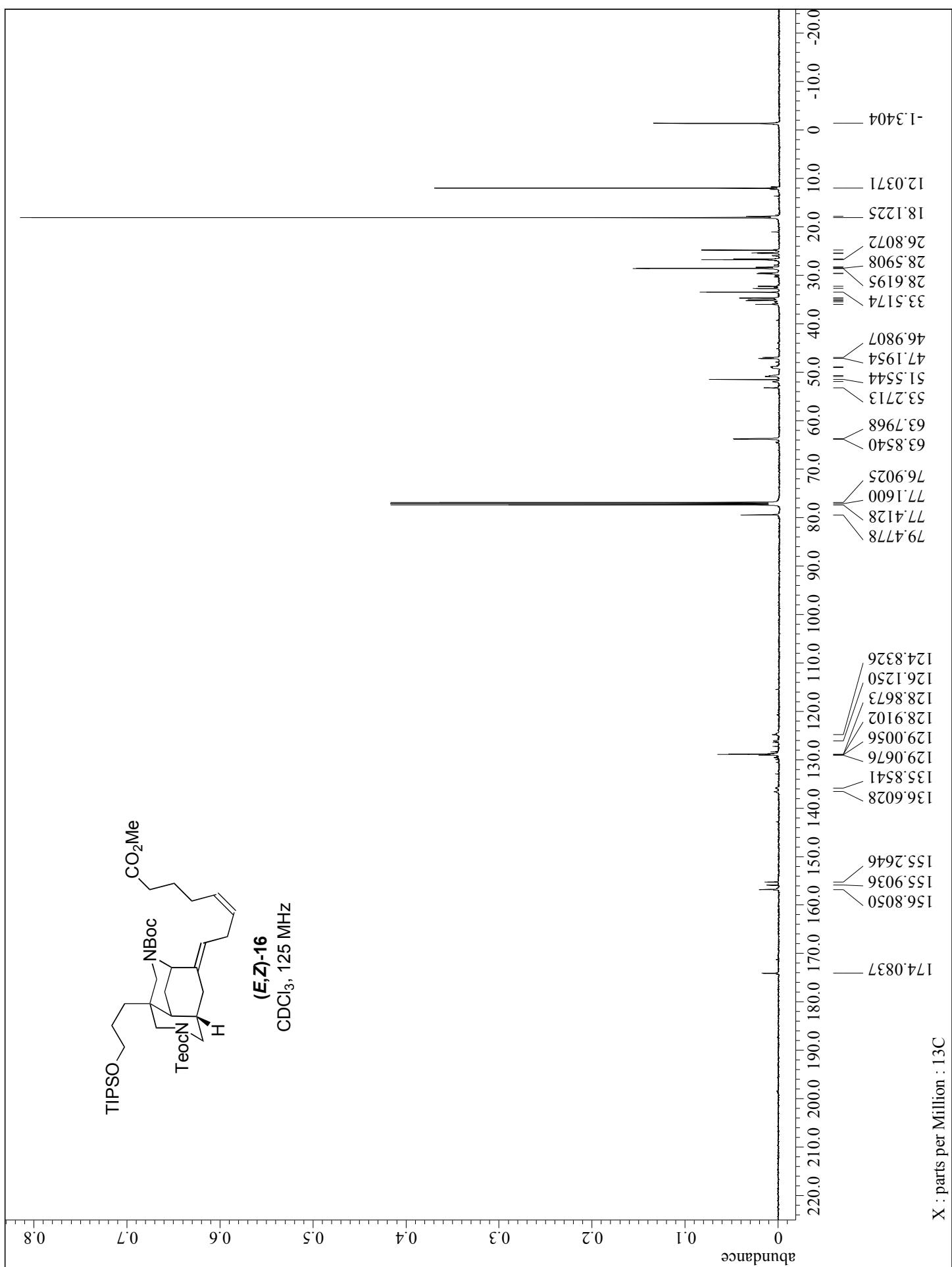
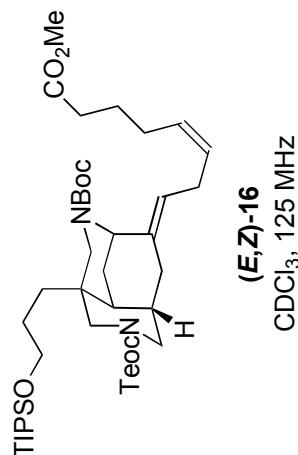


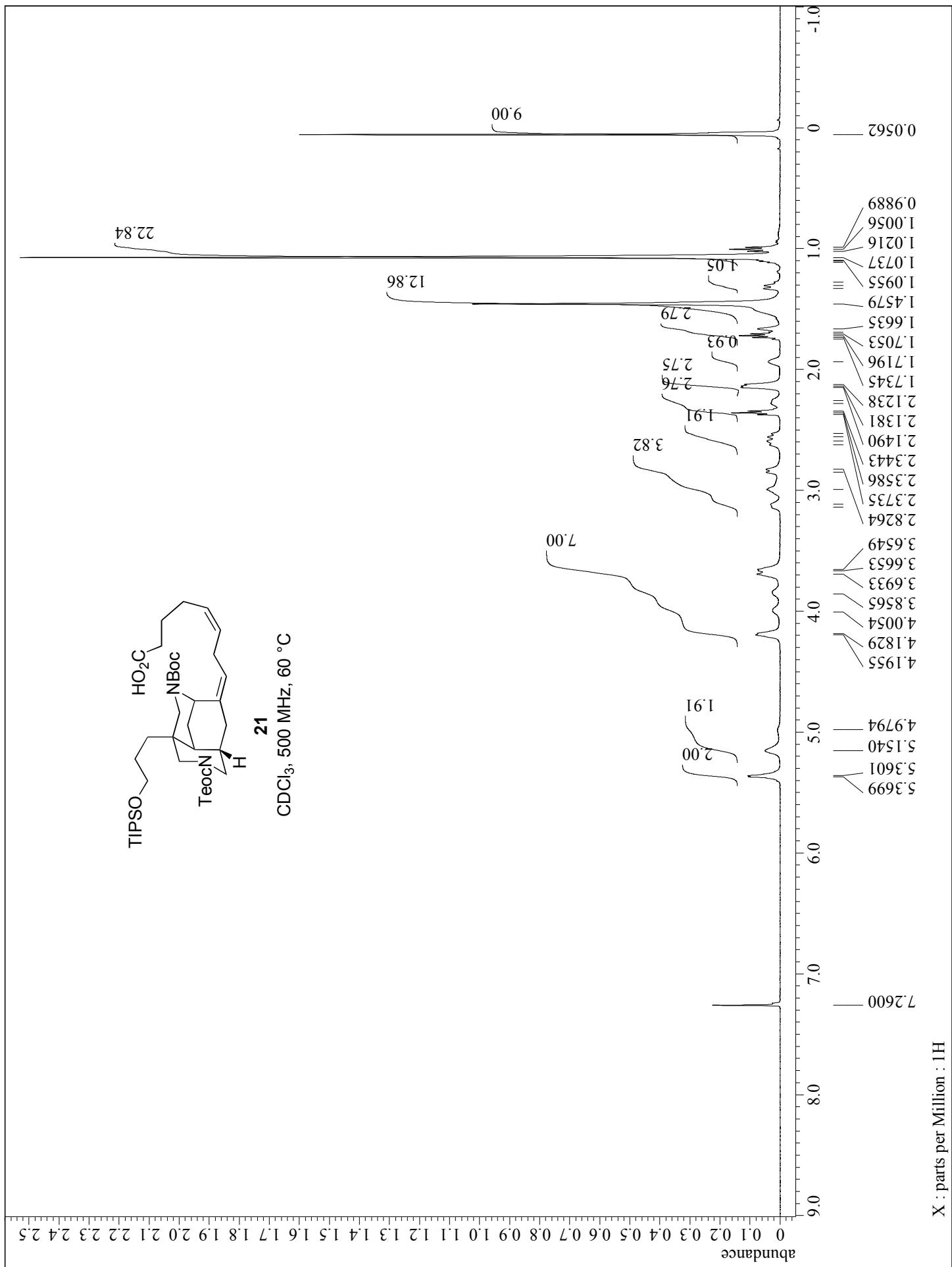


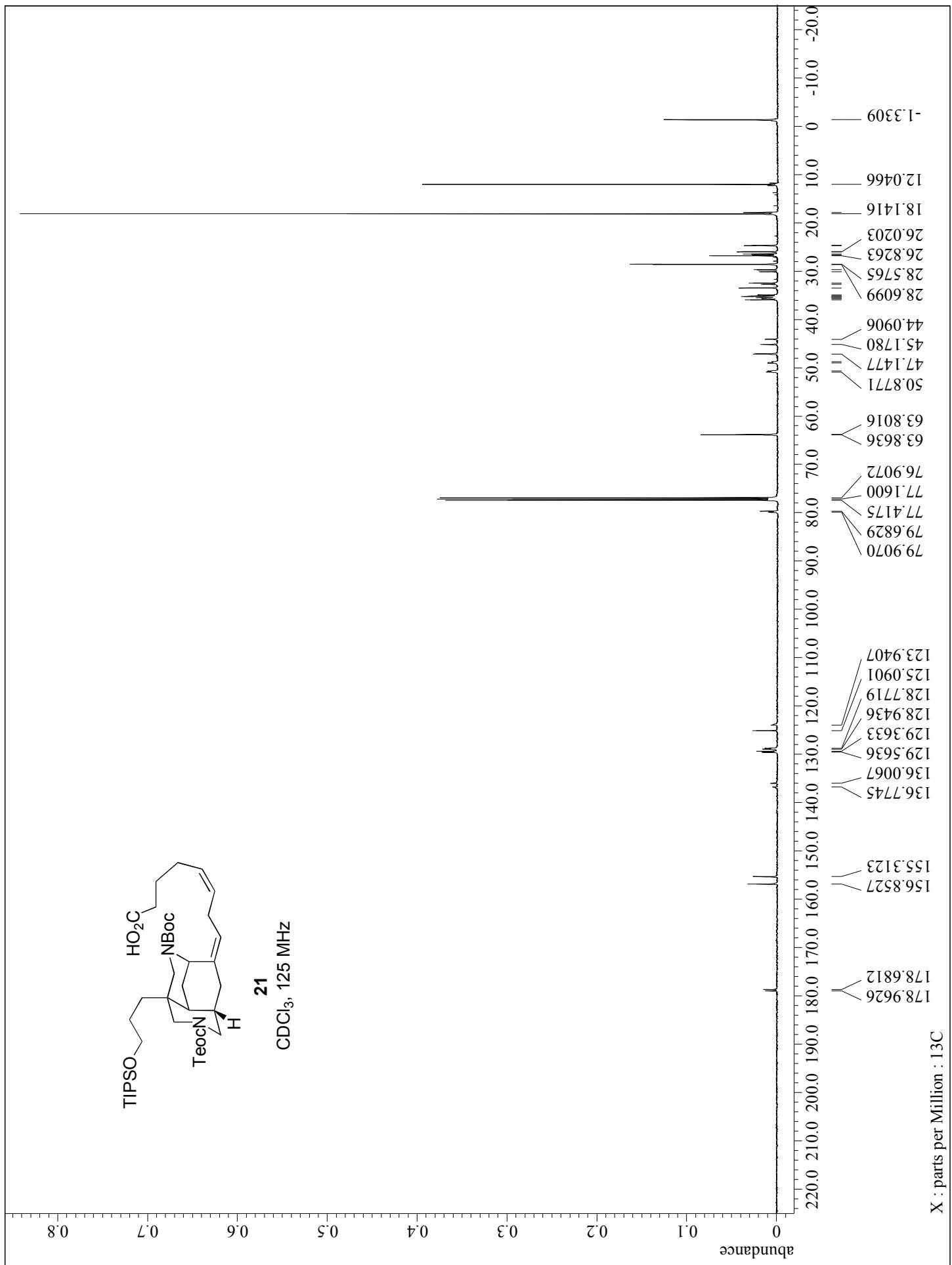
CDCl_3 , 125 MHz

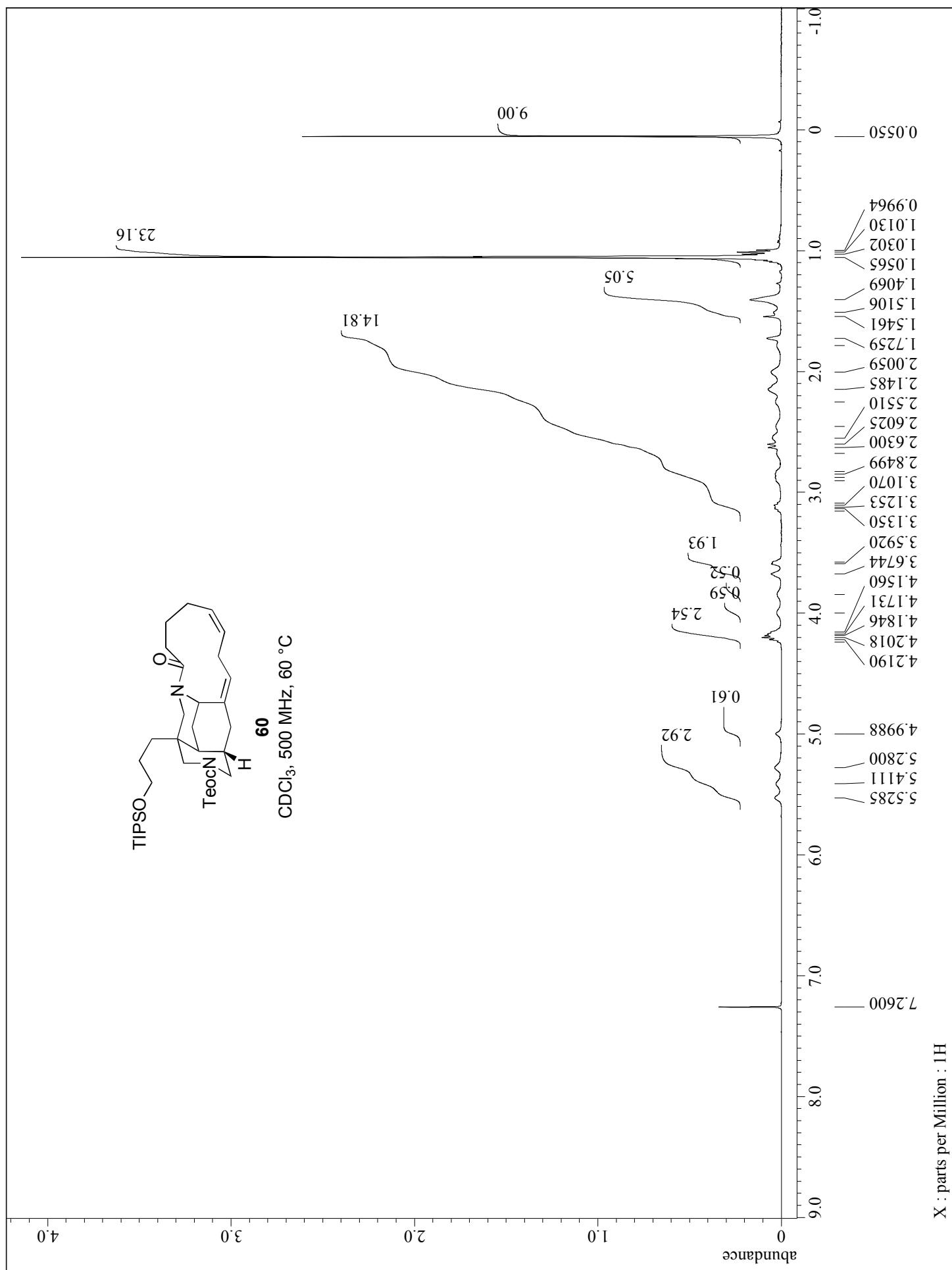


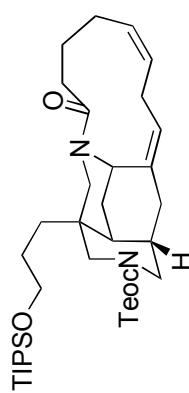




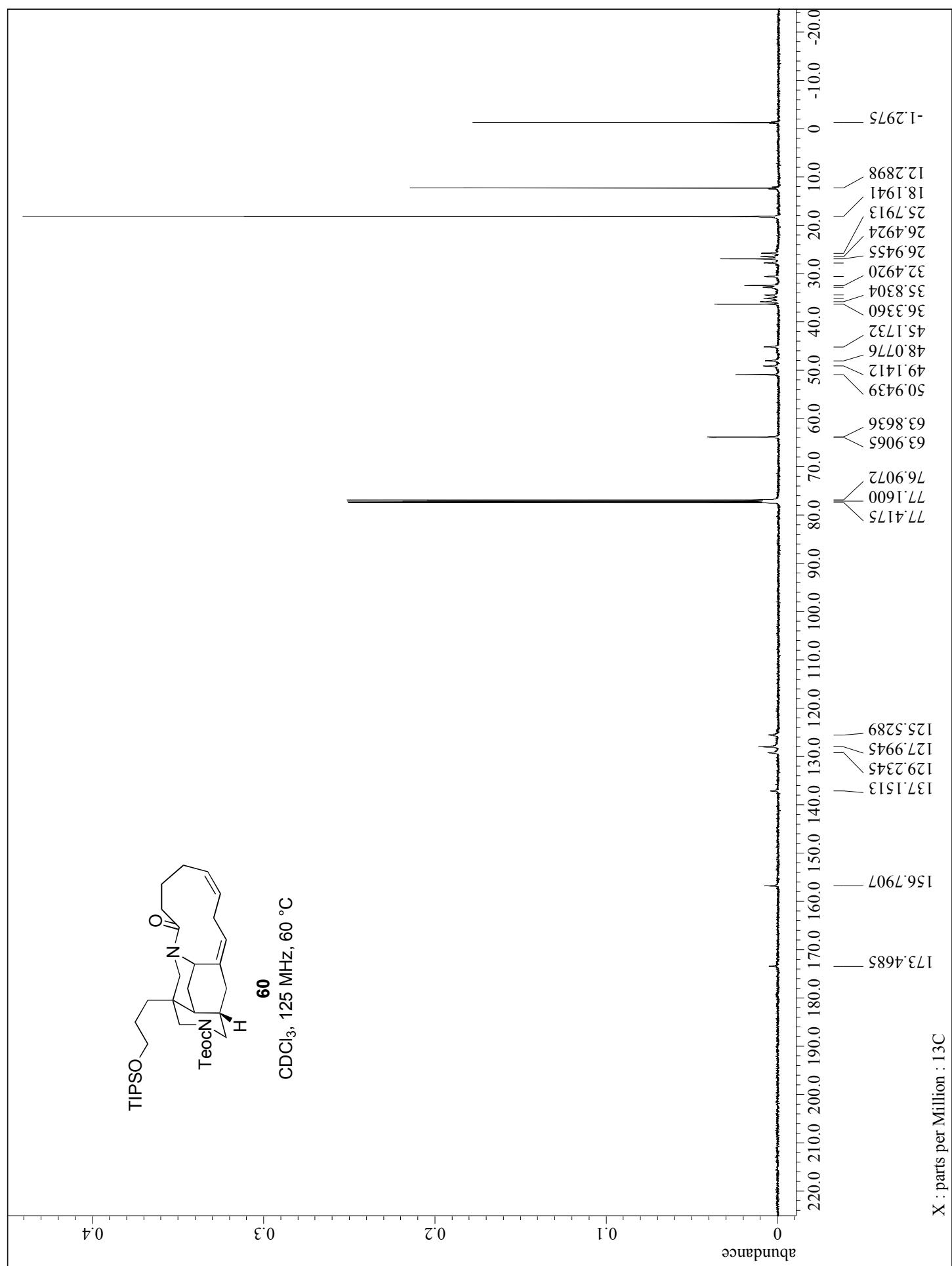


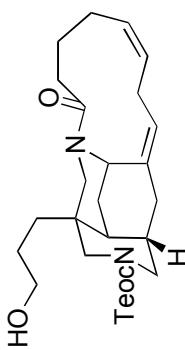




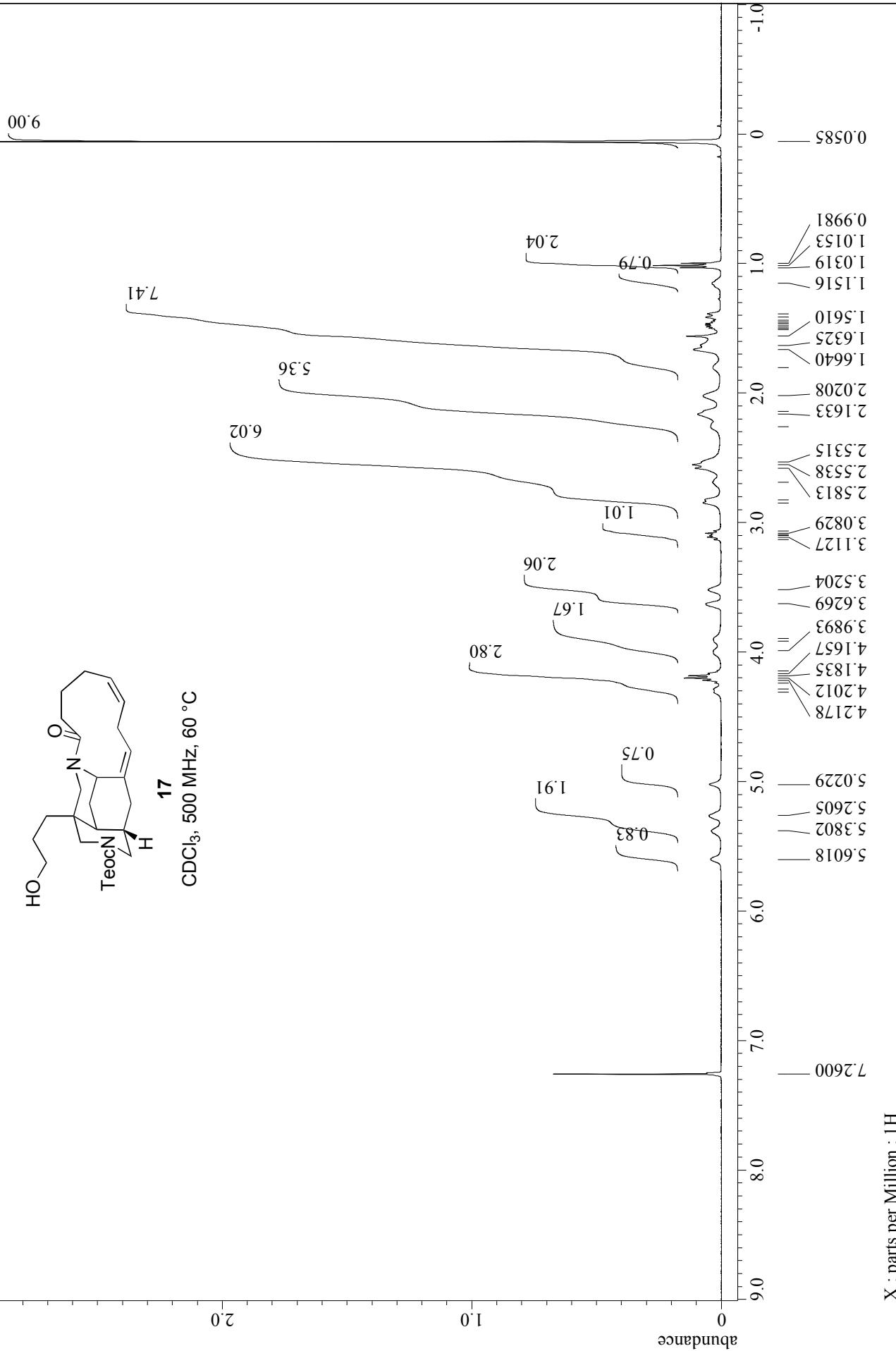


CDCl_3 , 125 MHz, 60 °C

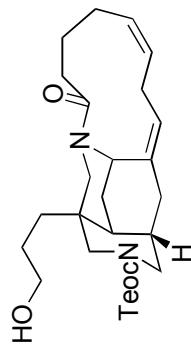




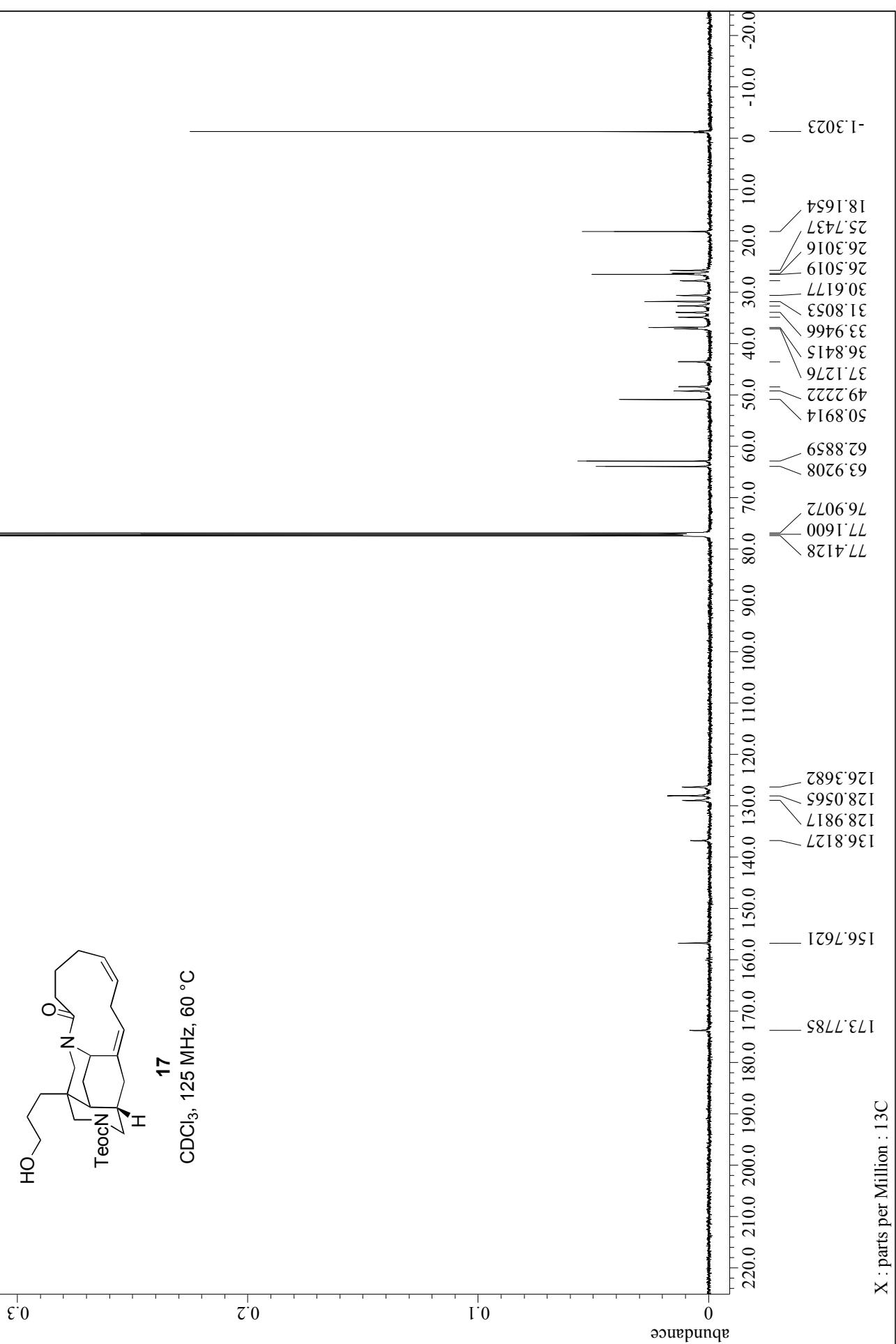
CDCl_3 , 500 MHz, 60 °C

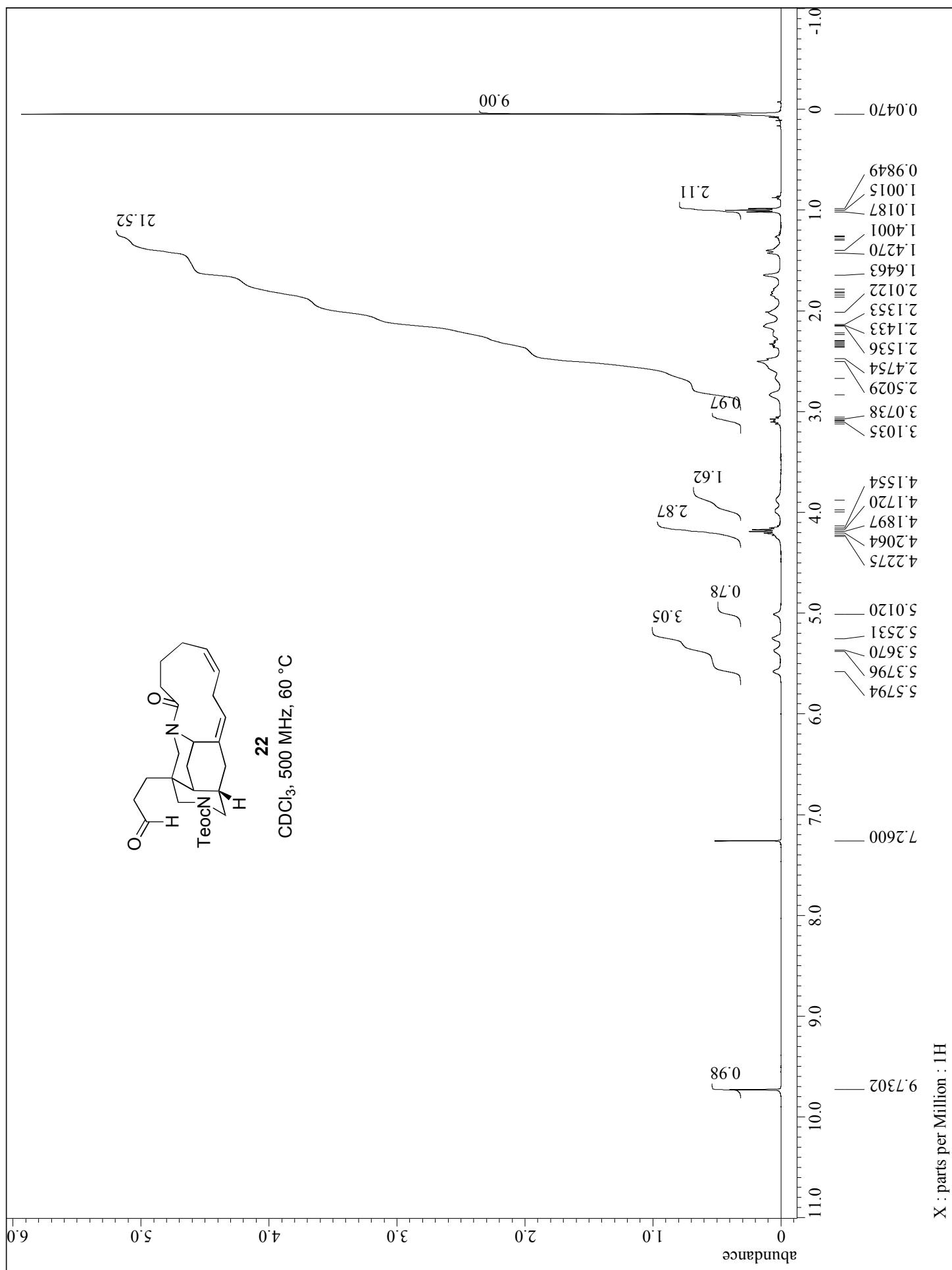


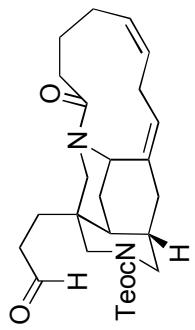
X : parts per Million : Hz



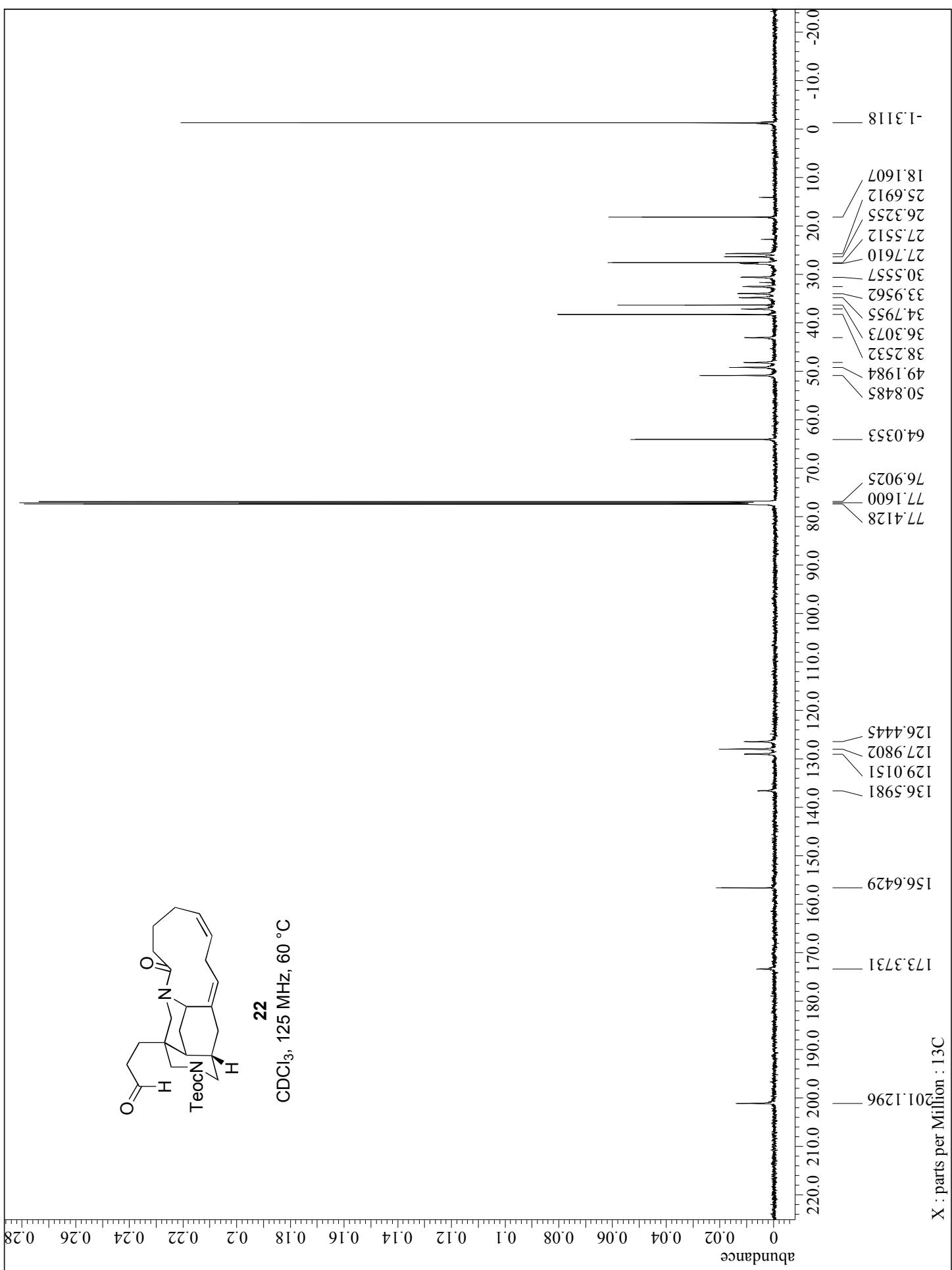
CDCl_3 , 125 MHz, 60 °C

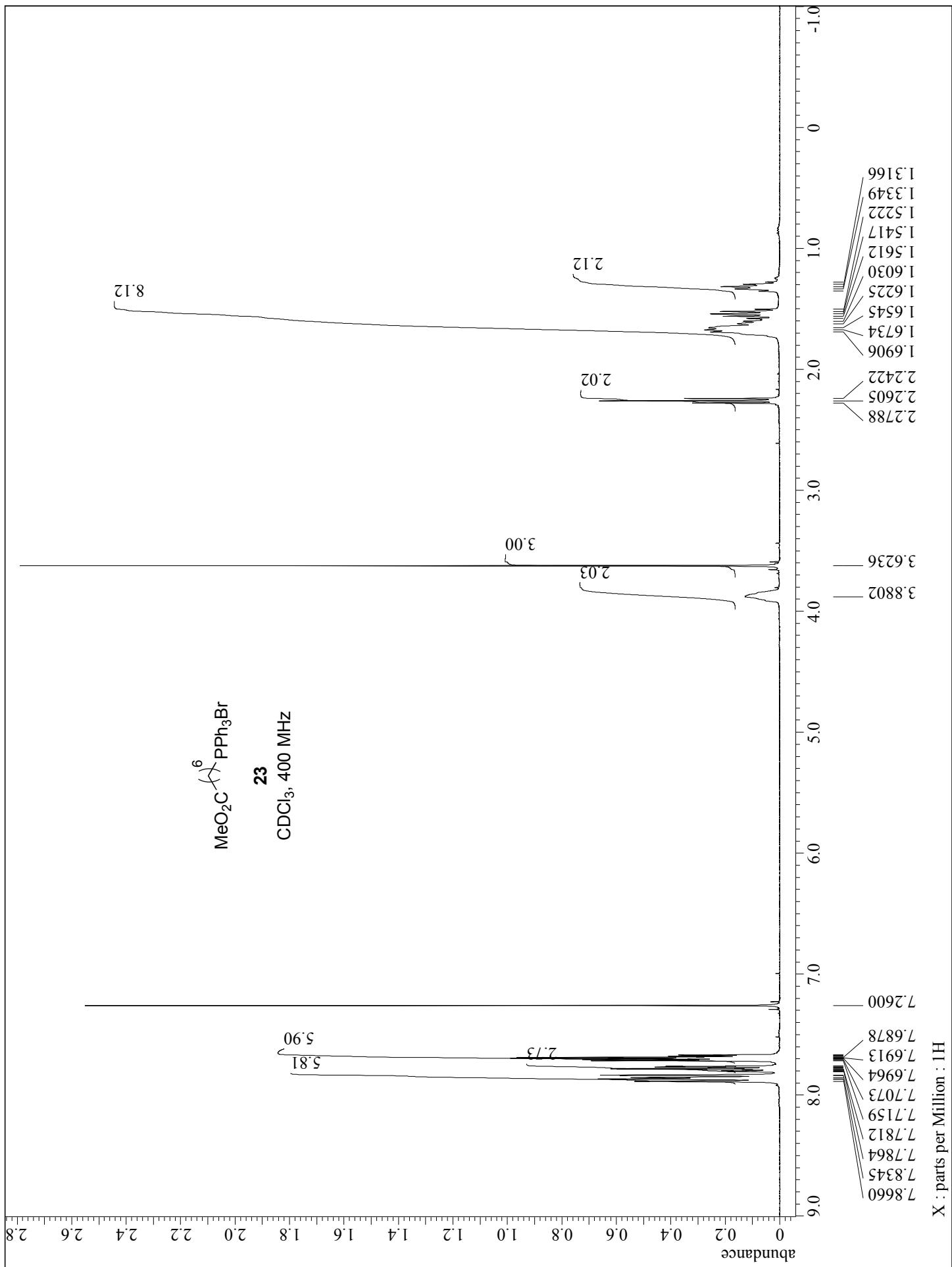


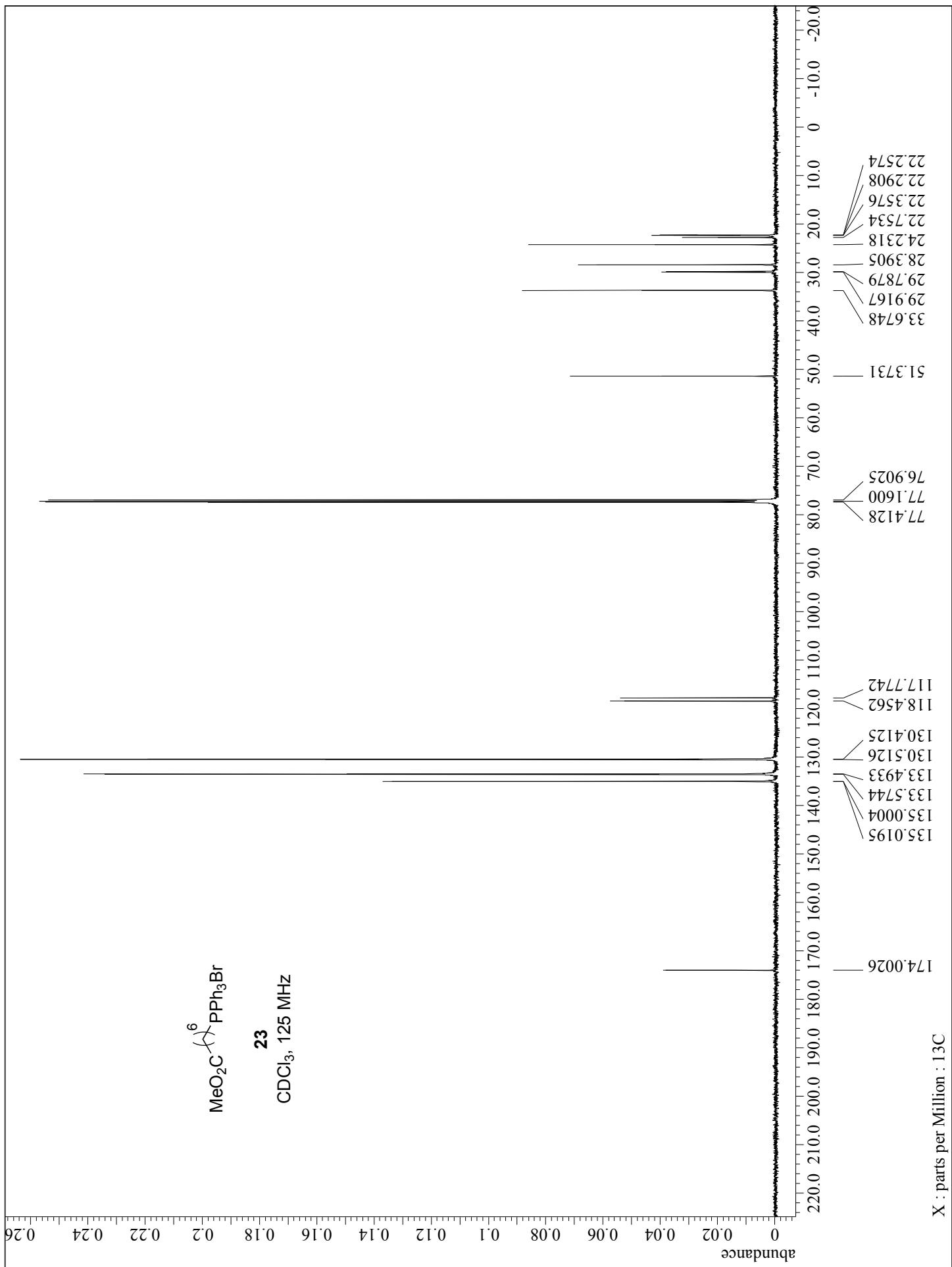


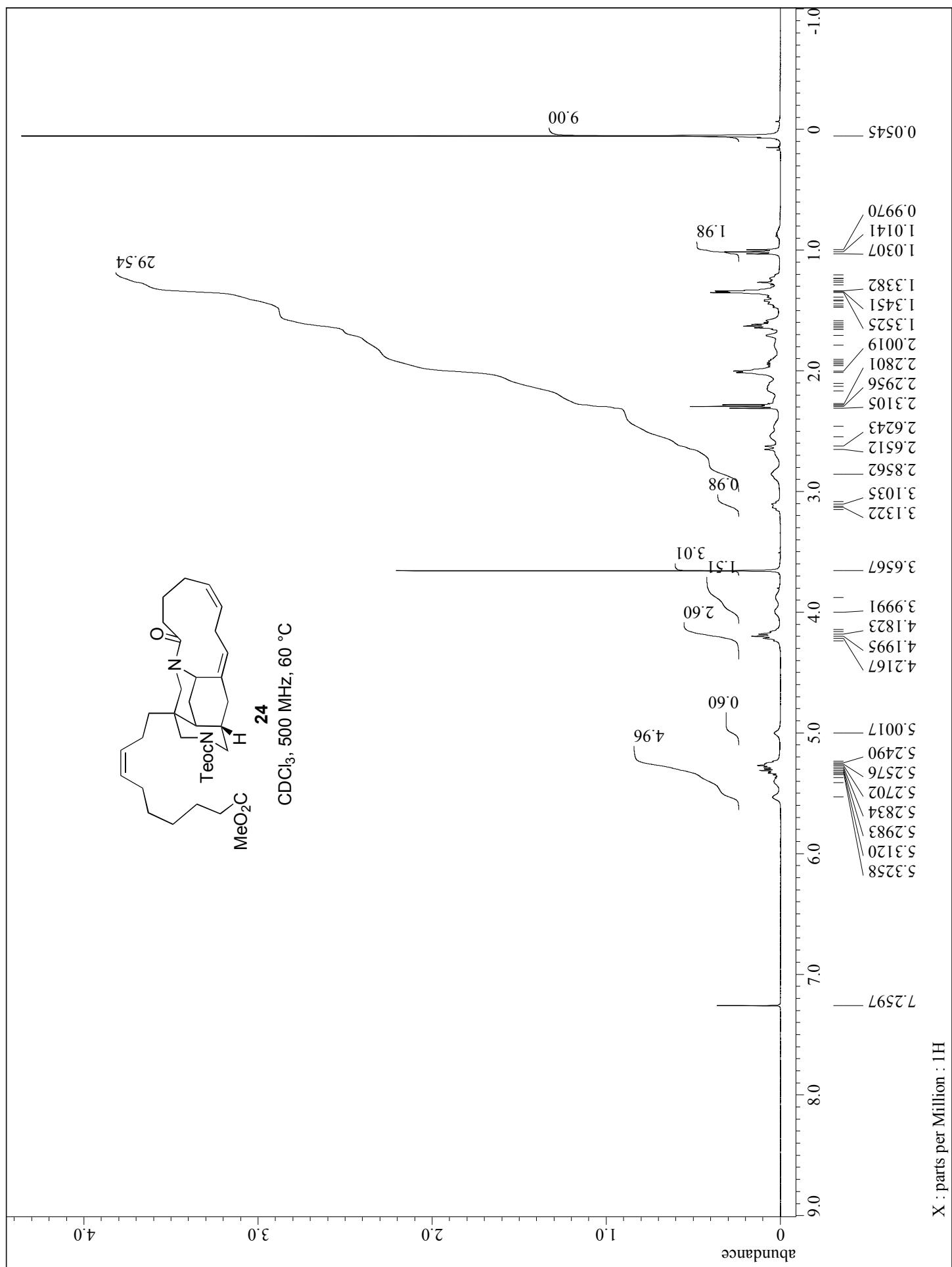


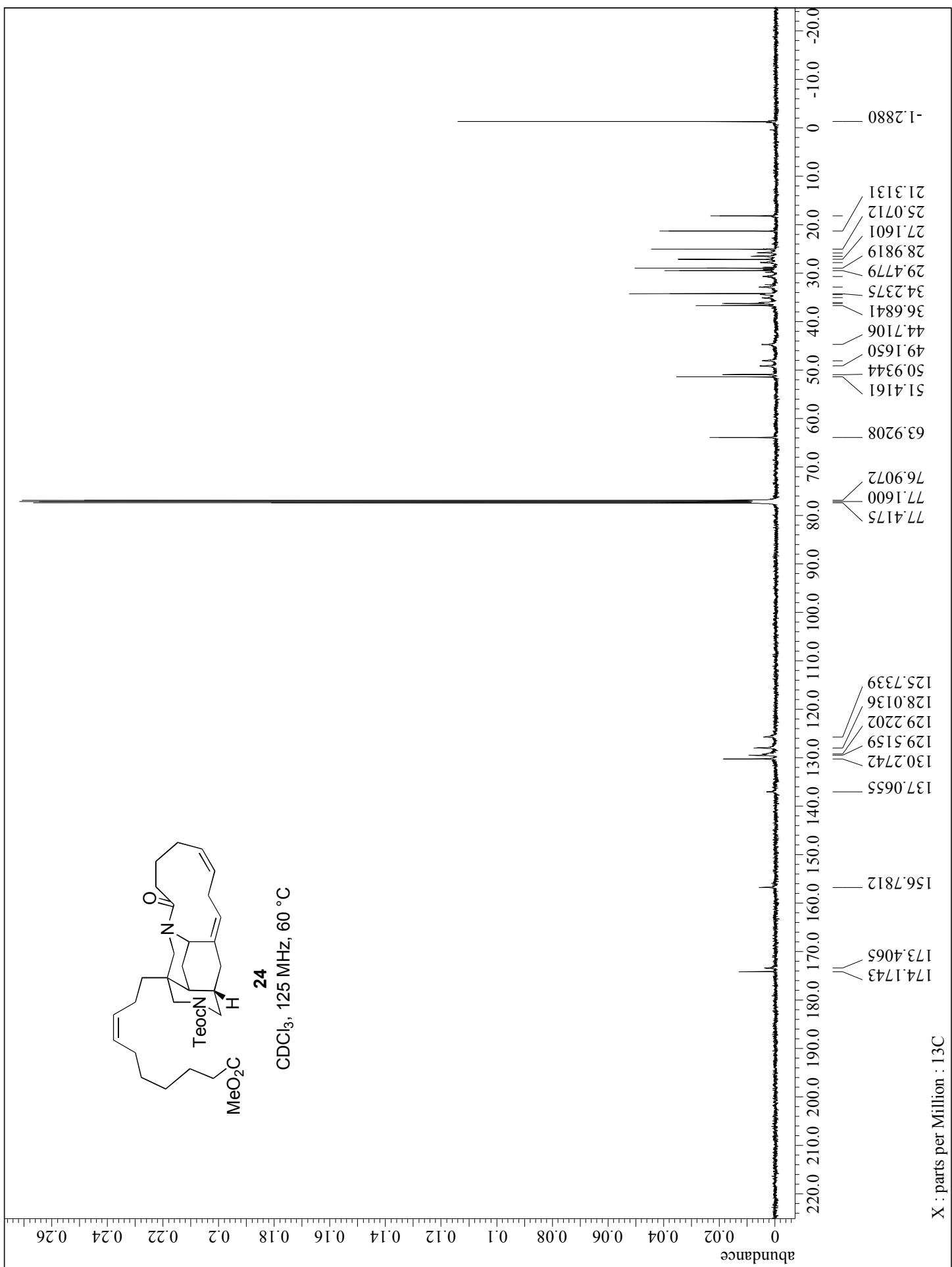
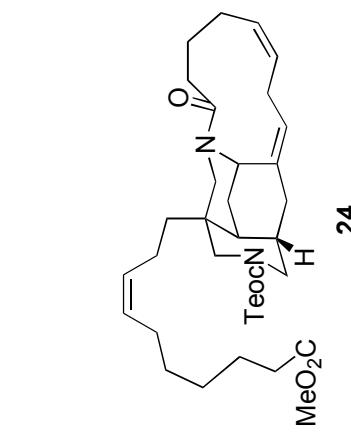
22
 $\text{CDCl}_3, 125 \text{ MHz}, 60^\circ\text{C}$

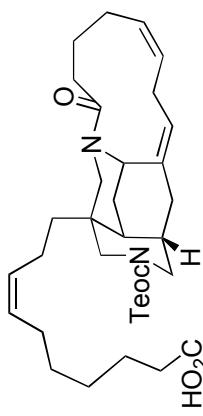




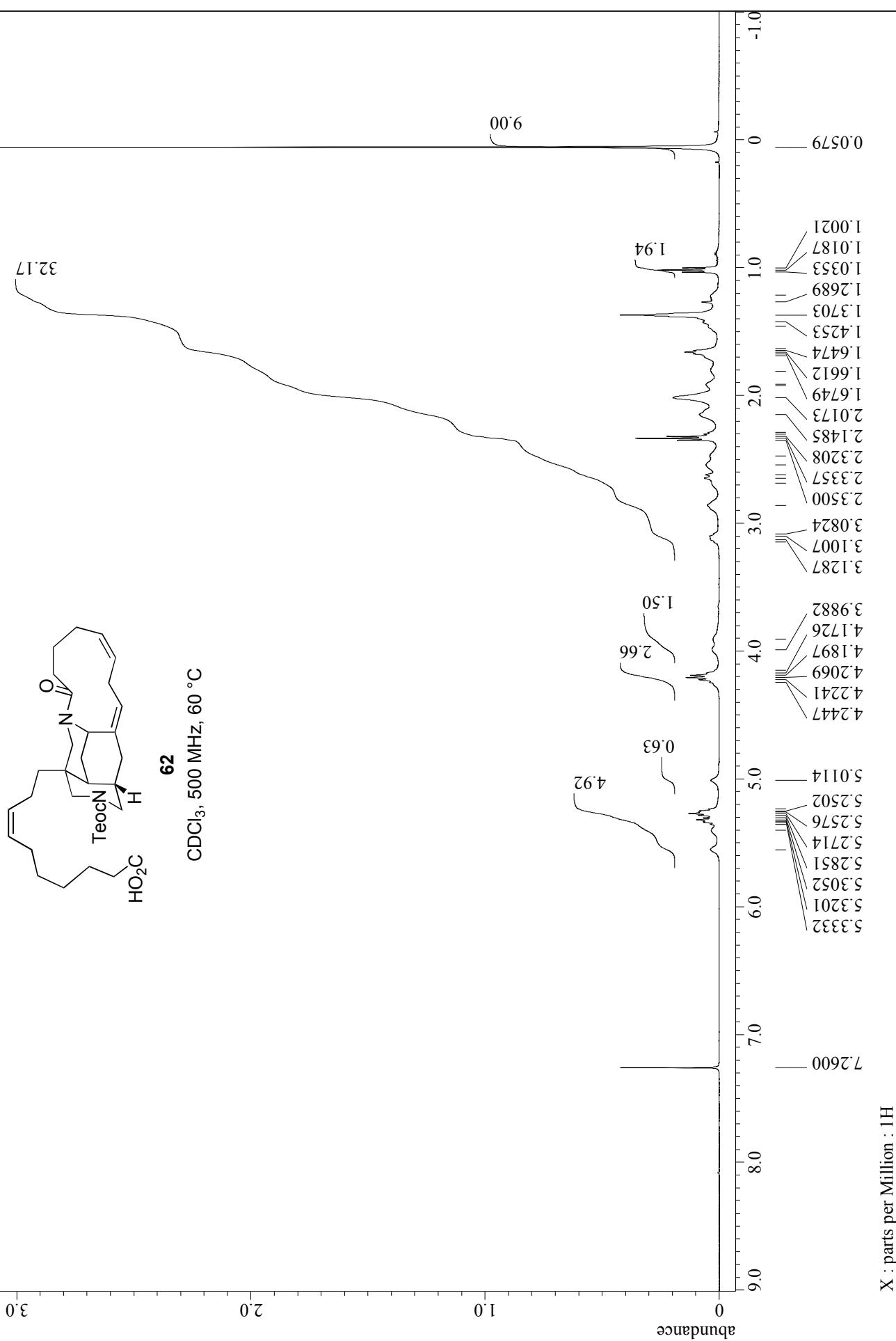




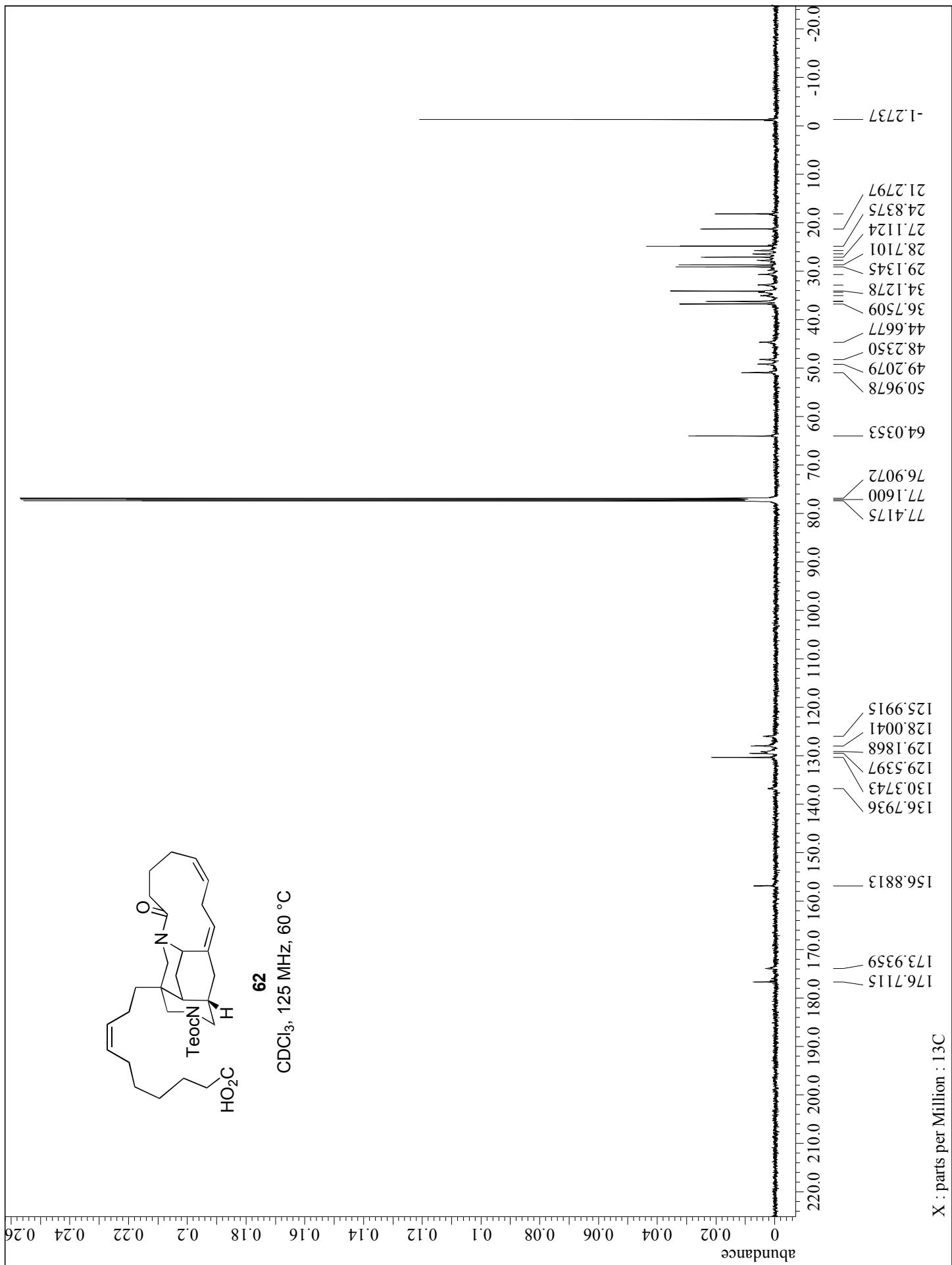


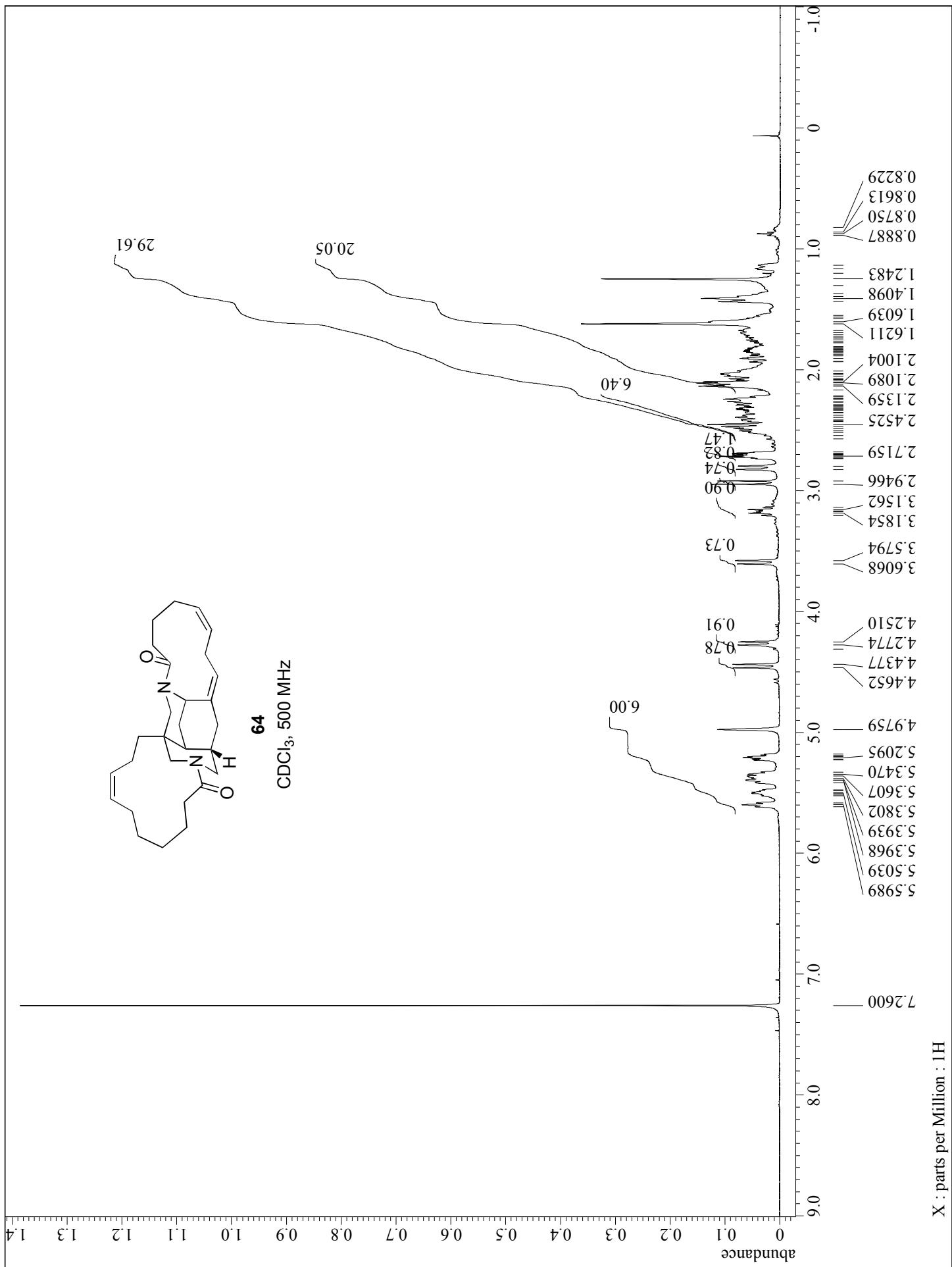


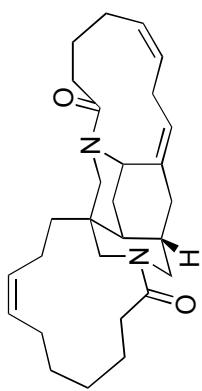
CDCl_3 , 500 MHz, 60 °C



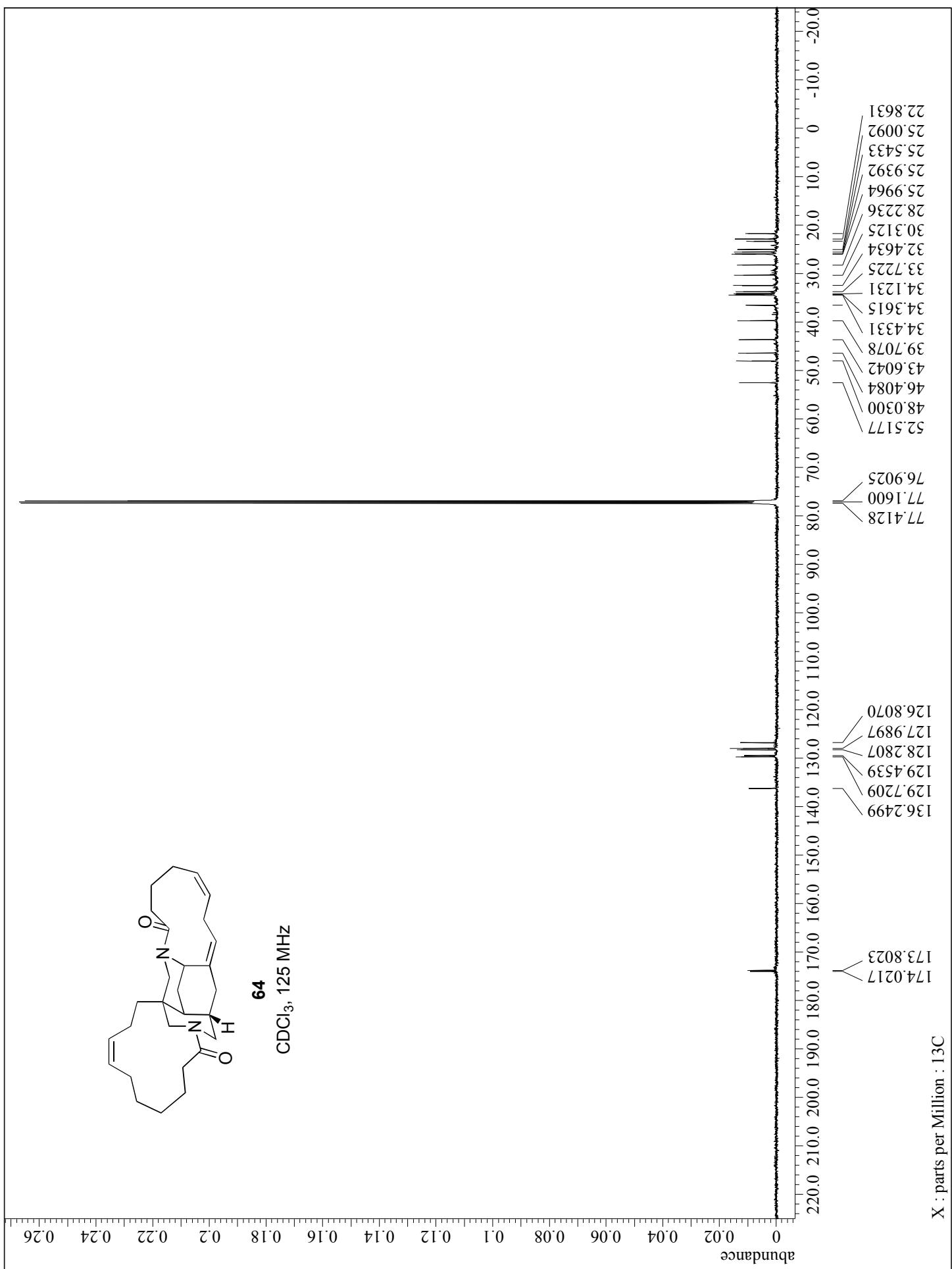
X : parts per Million : IH

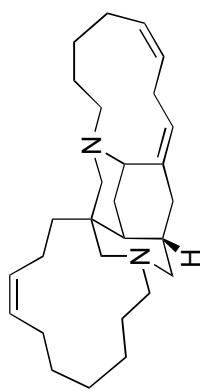




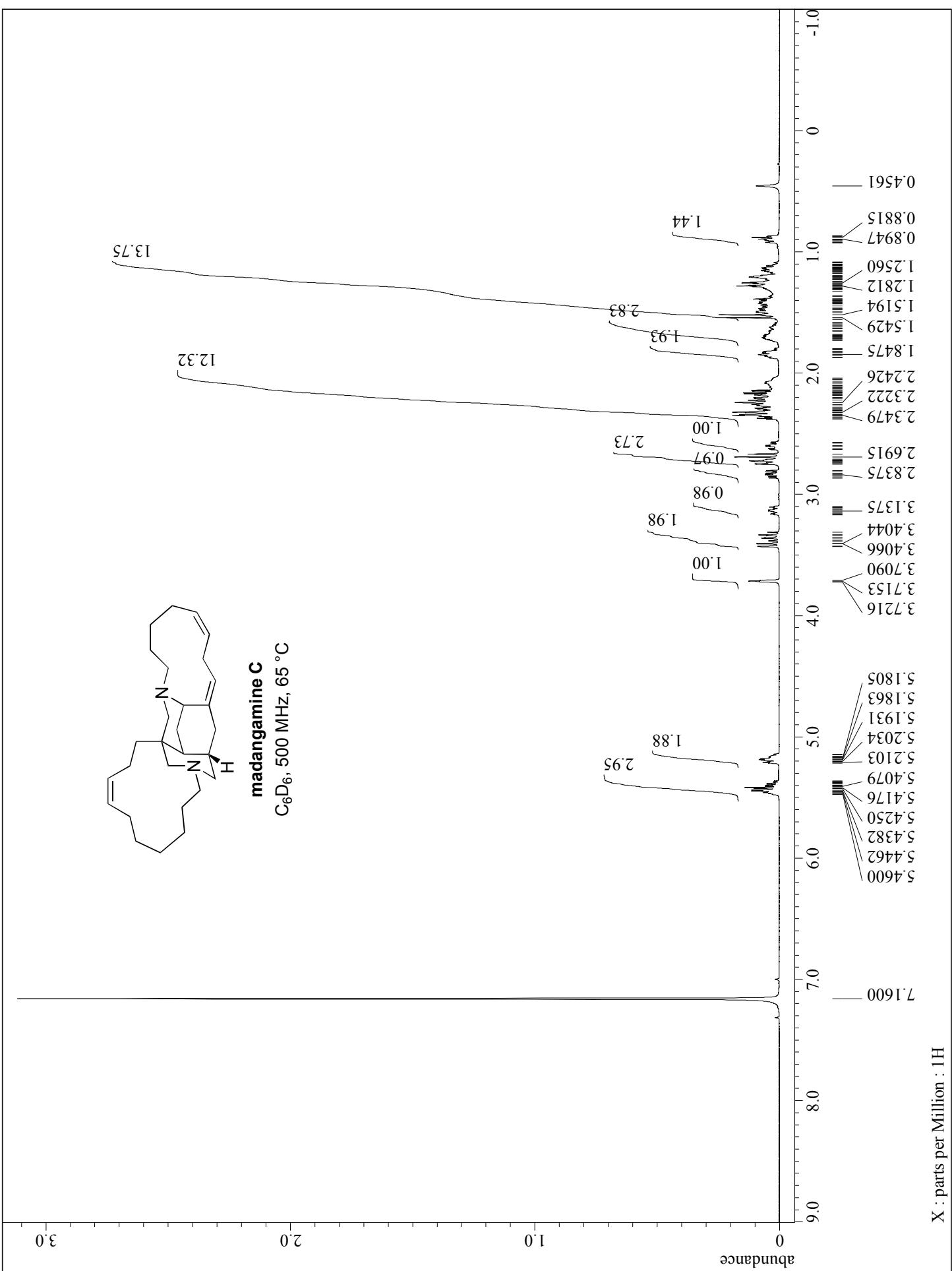


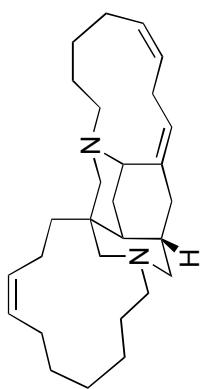
64
 $\text{CDCl}_3, 125 \text{ MHz}$



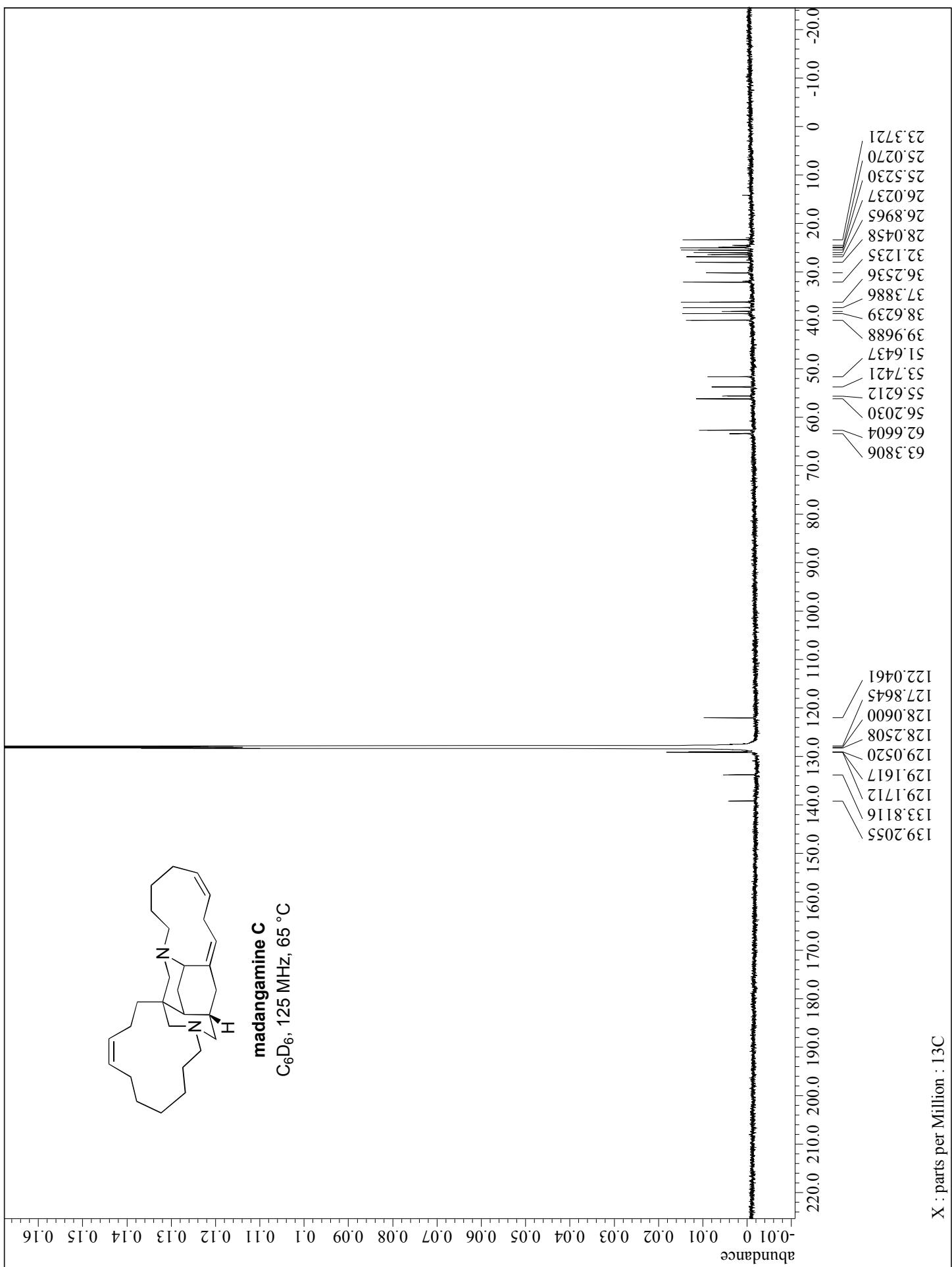


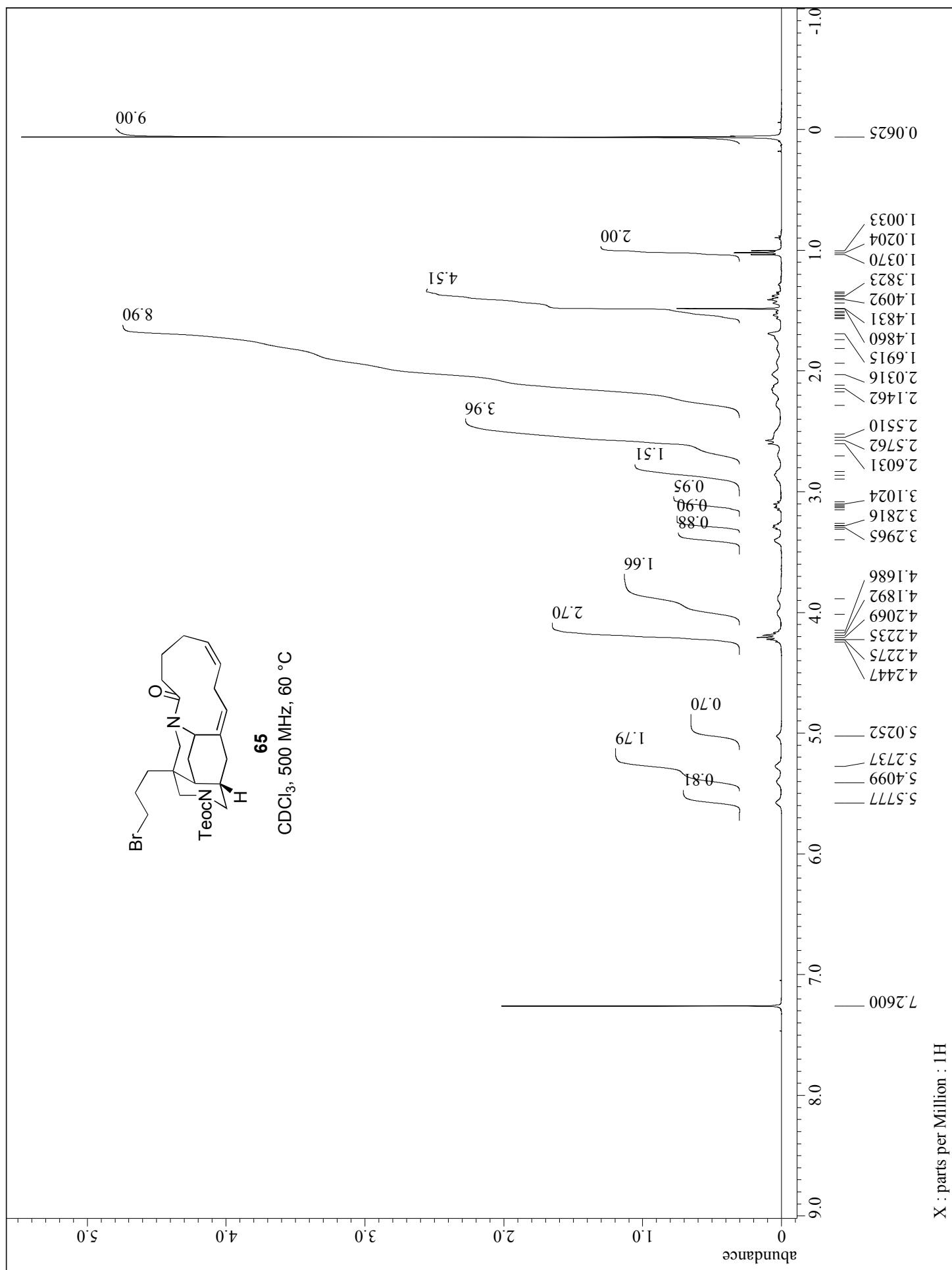
madangamine C
 C_6D_6 , 500 MHz, 65 °C

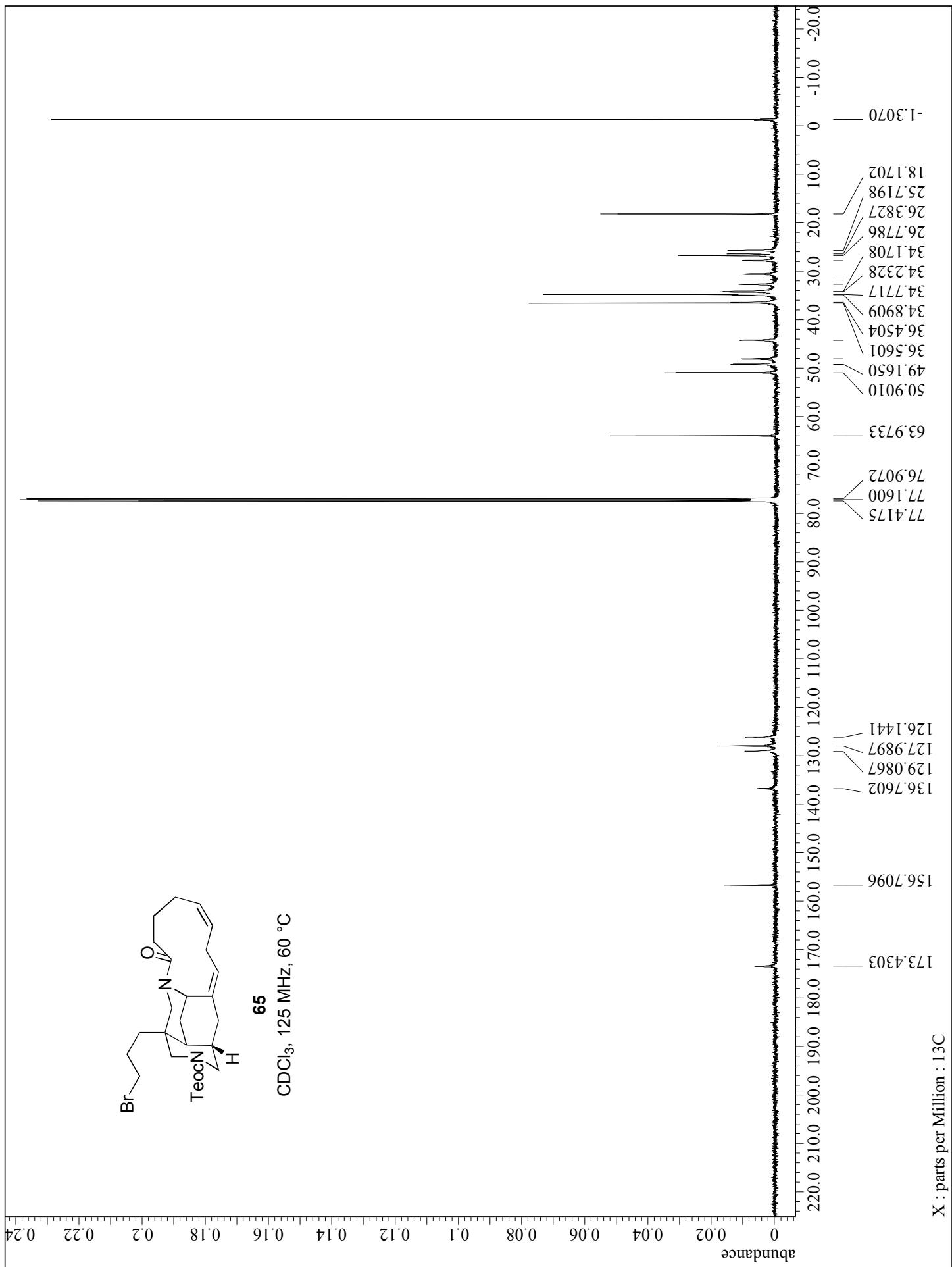


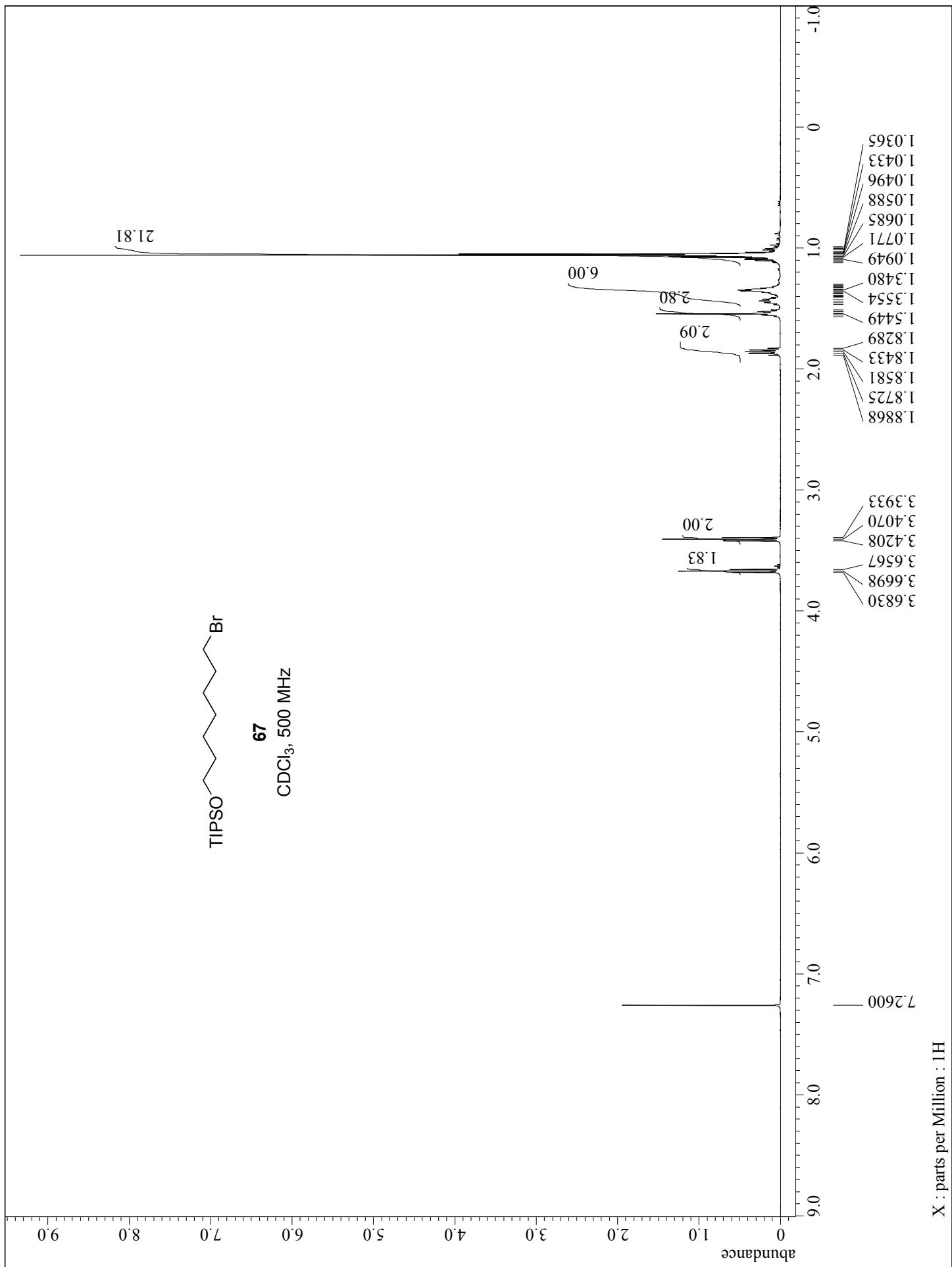


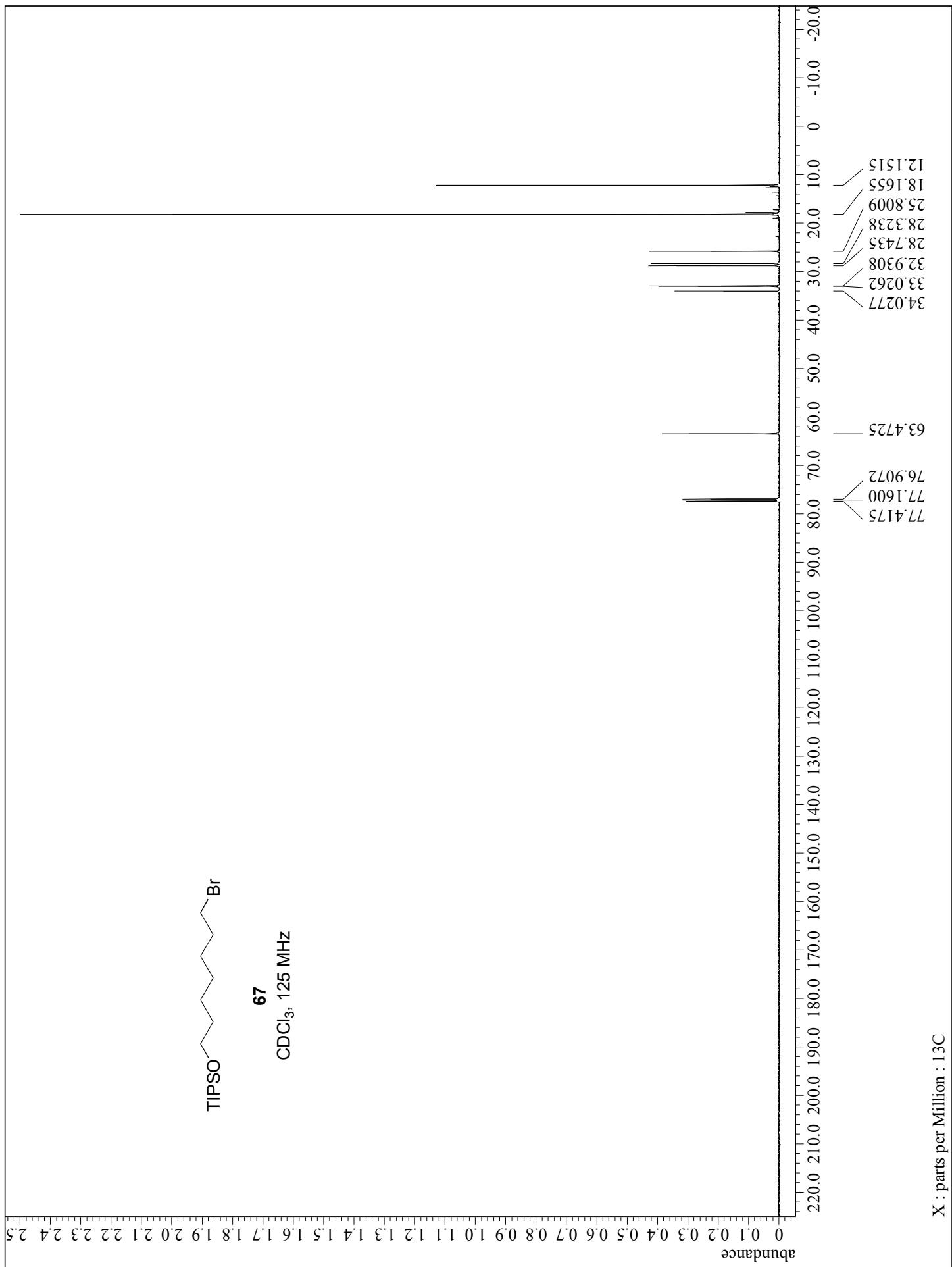
madangamine C
 C_6D_6 , 125 MHz, 65 °C

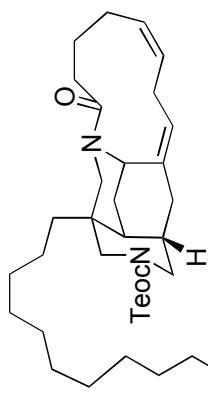




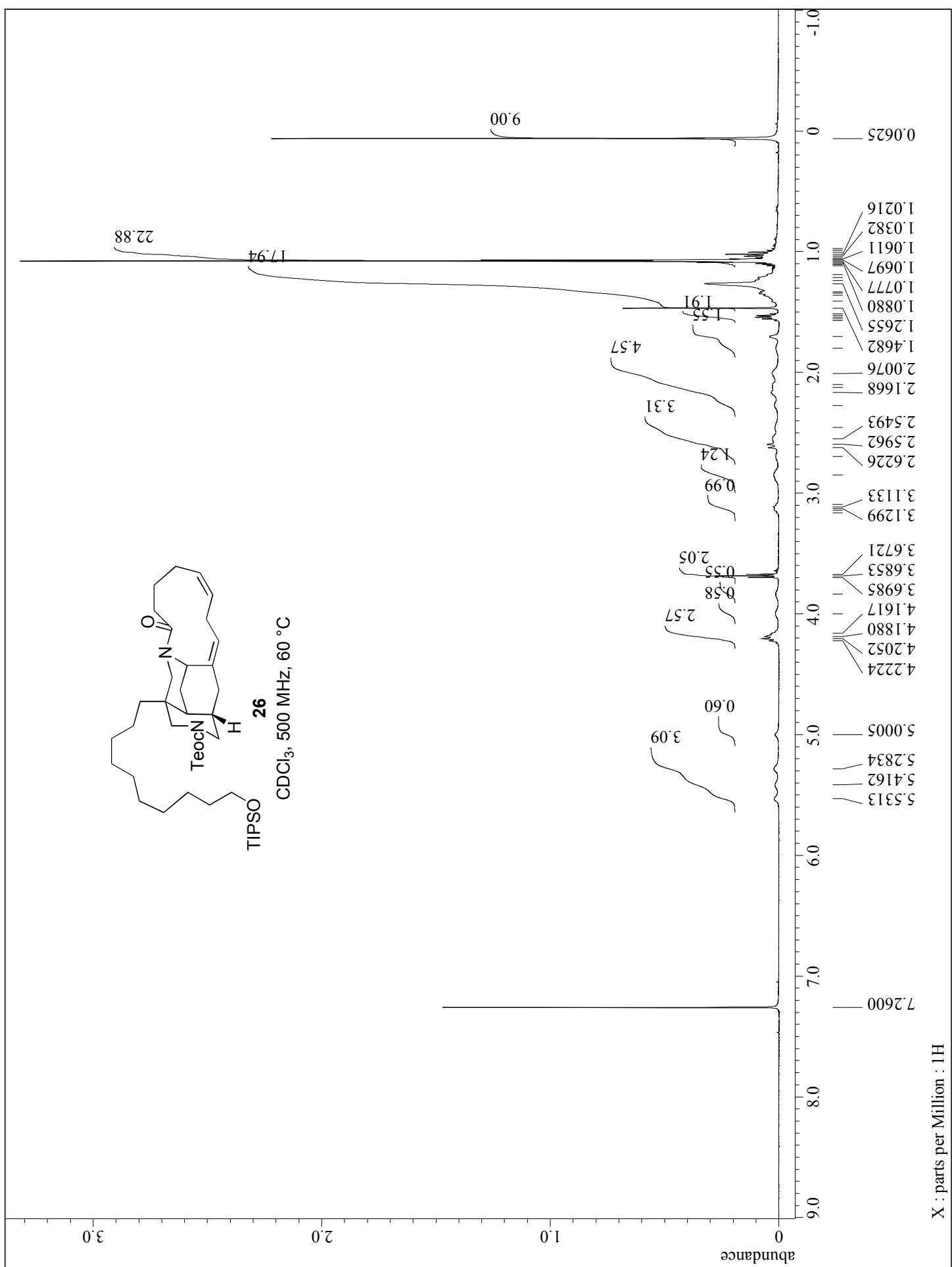


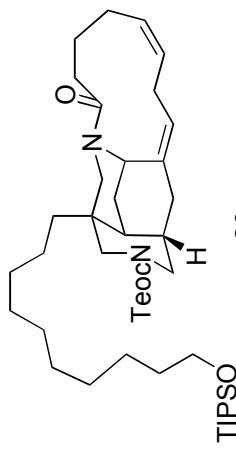




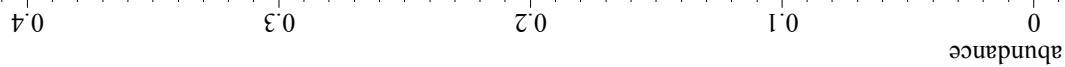


26
 $\text{CDCl}_3, 500 \text{ MHz}, 60^\circ\text{C}$

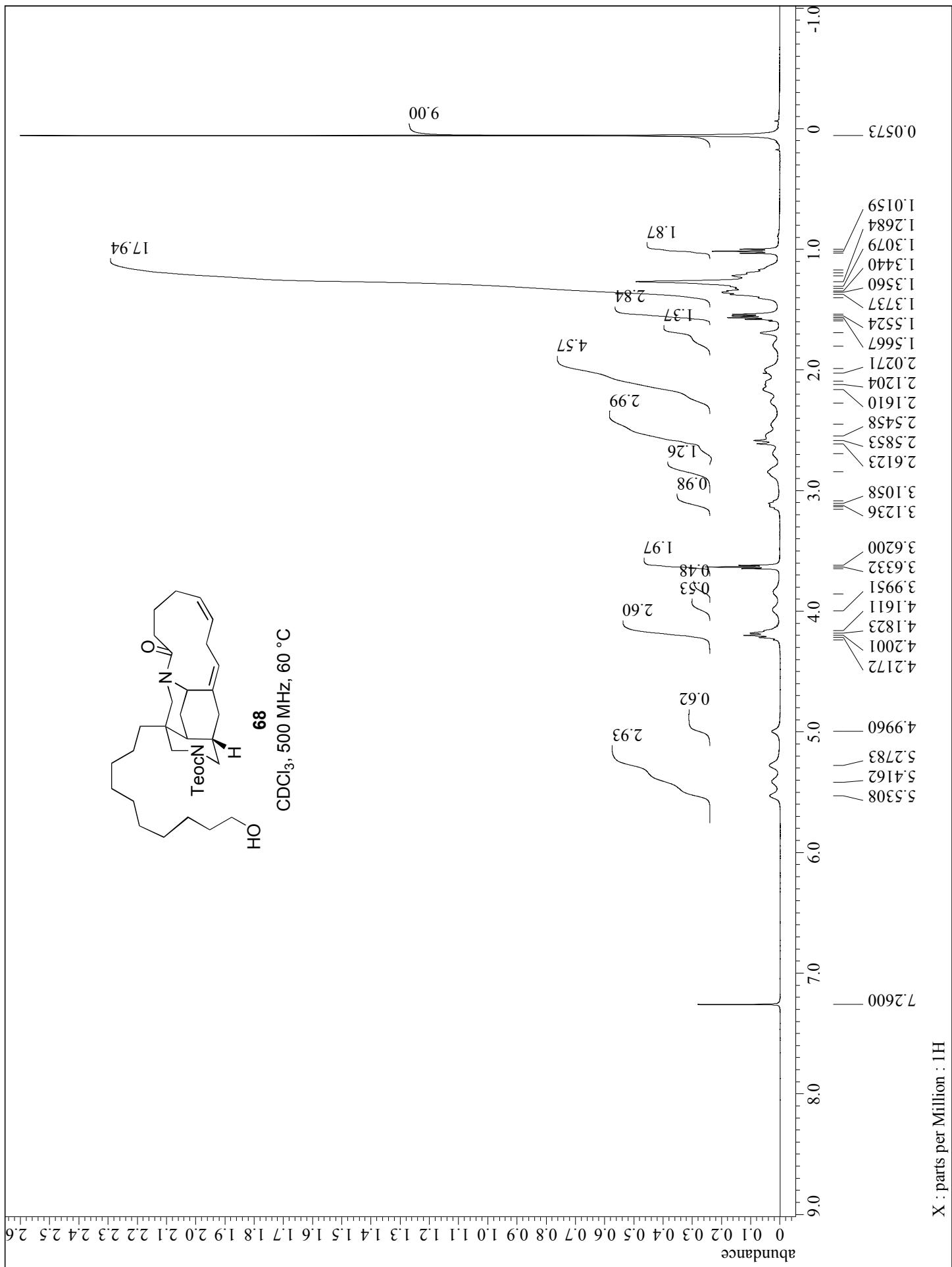


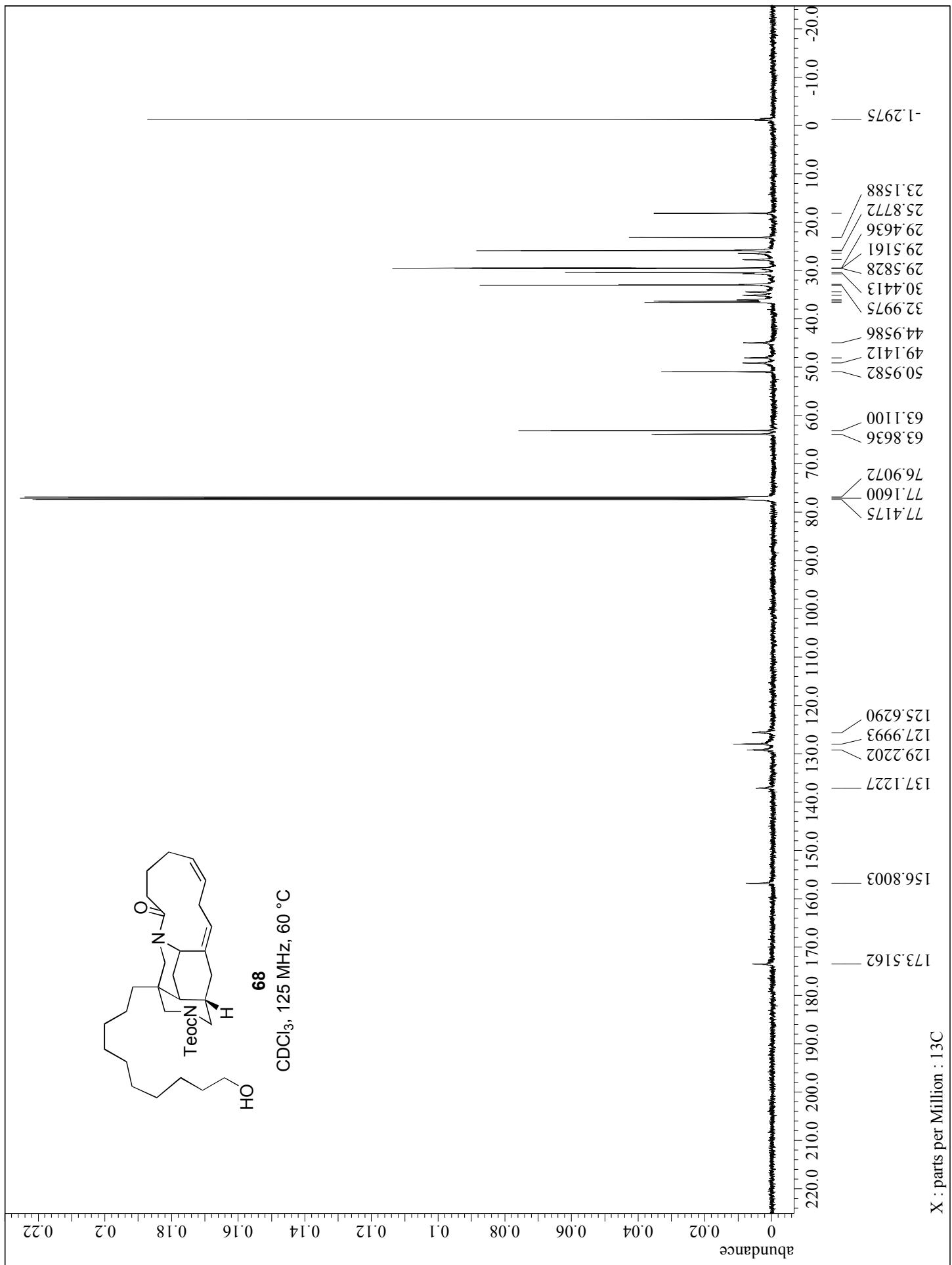


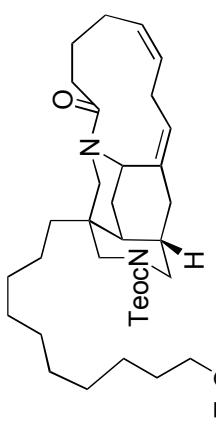
CDCl_3 , 125 MHz, 60 °C



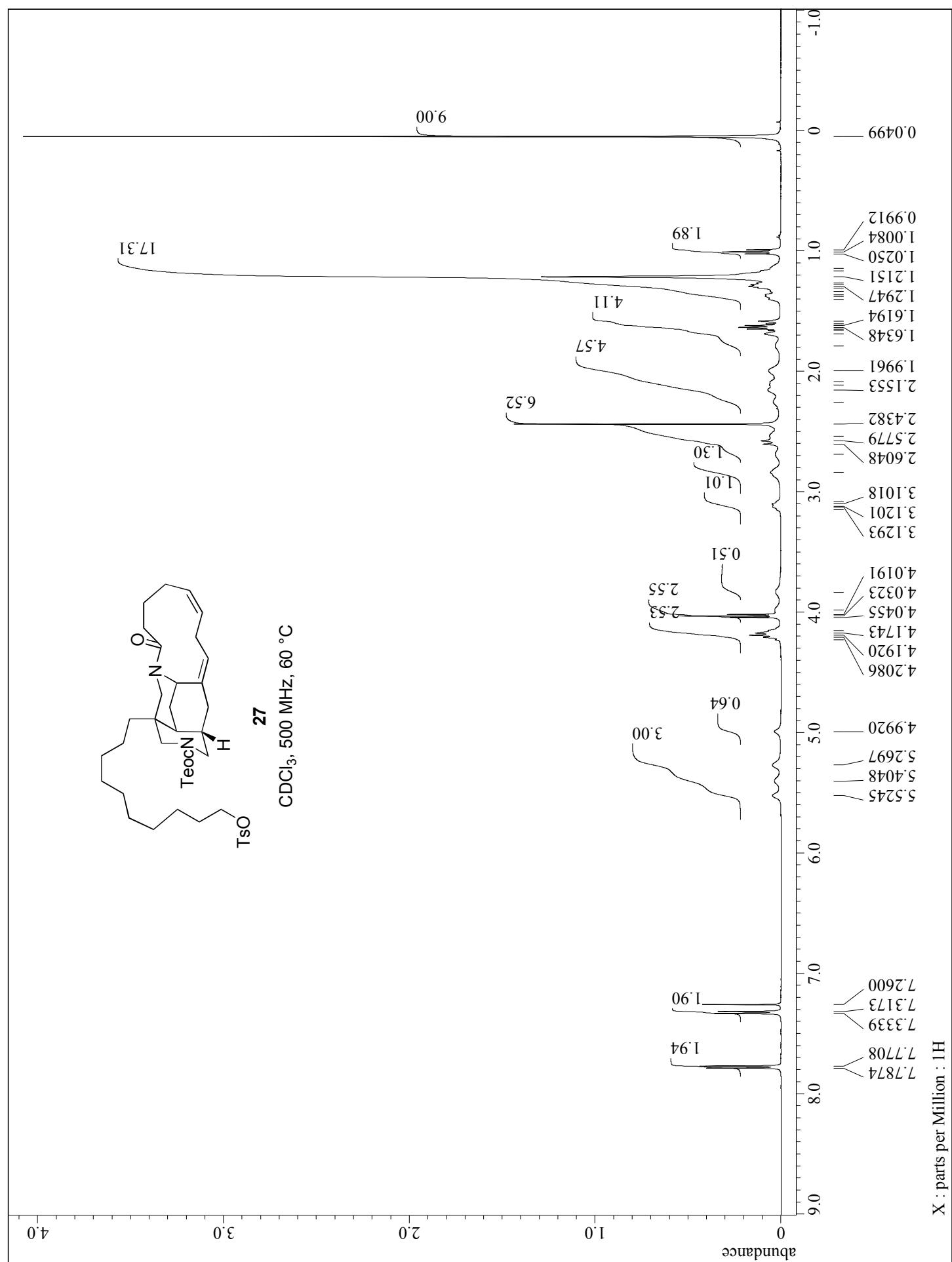
X : parts per Million : ^{13}C

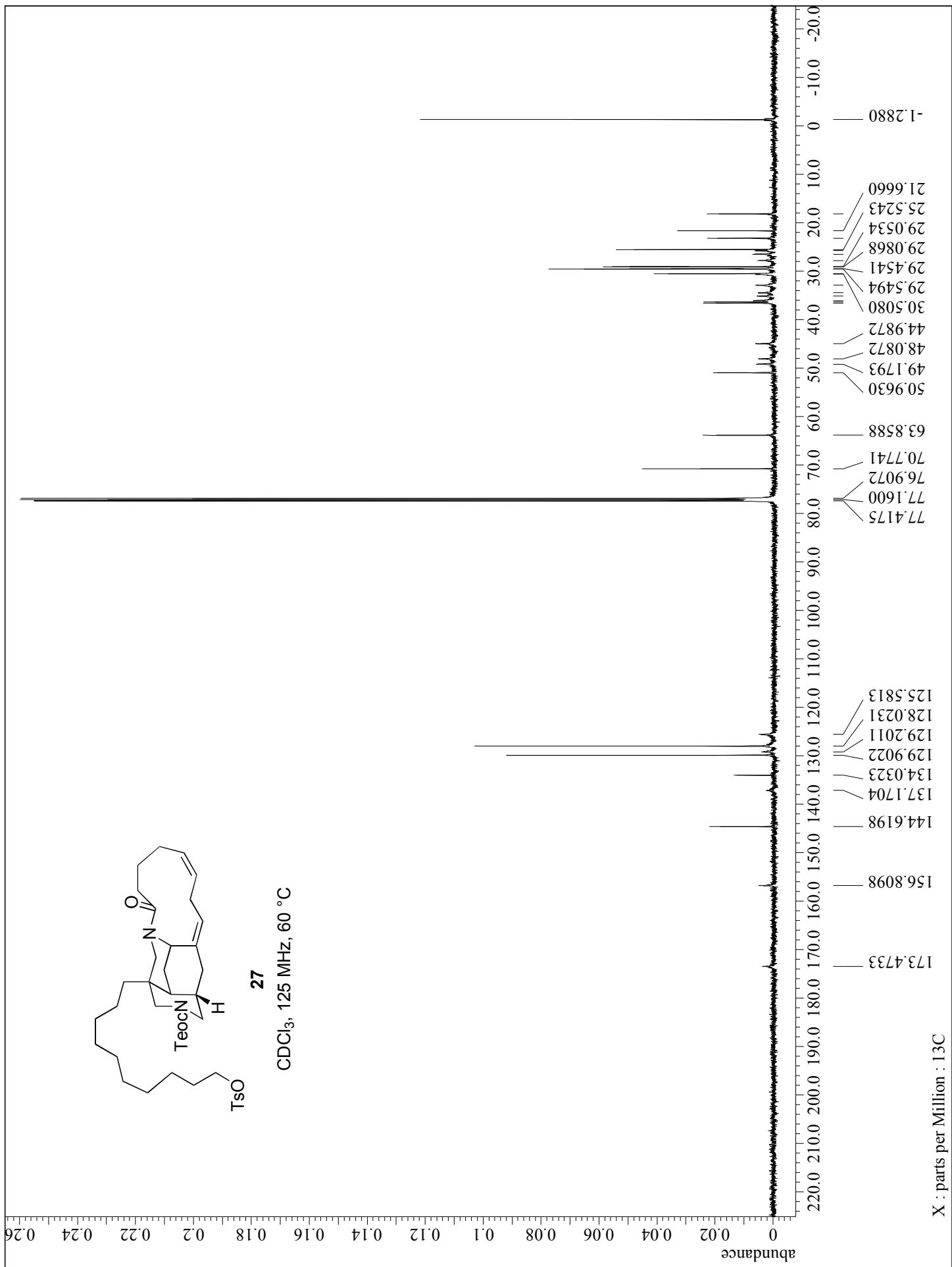


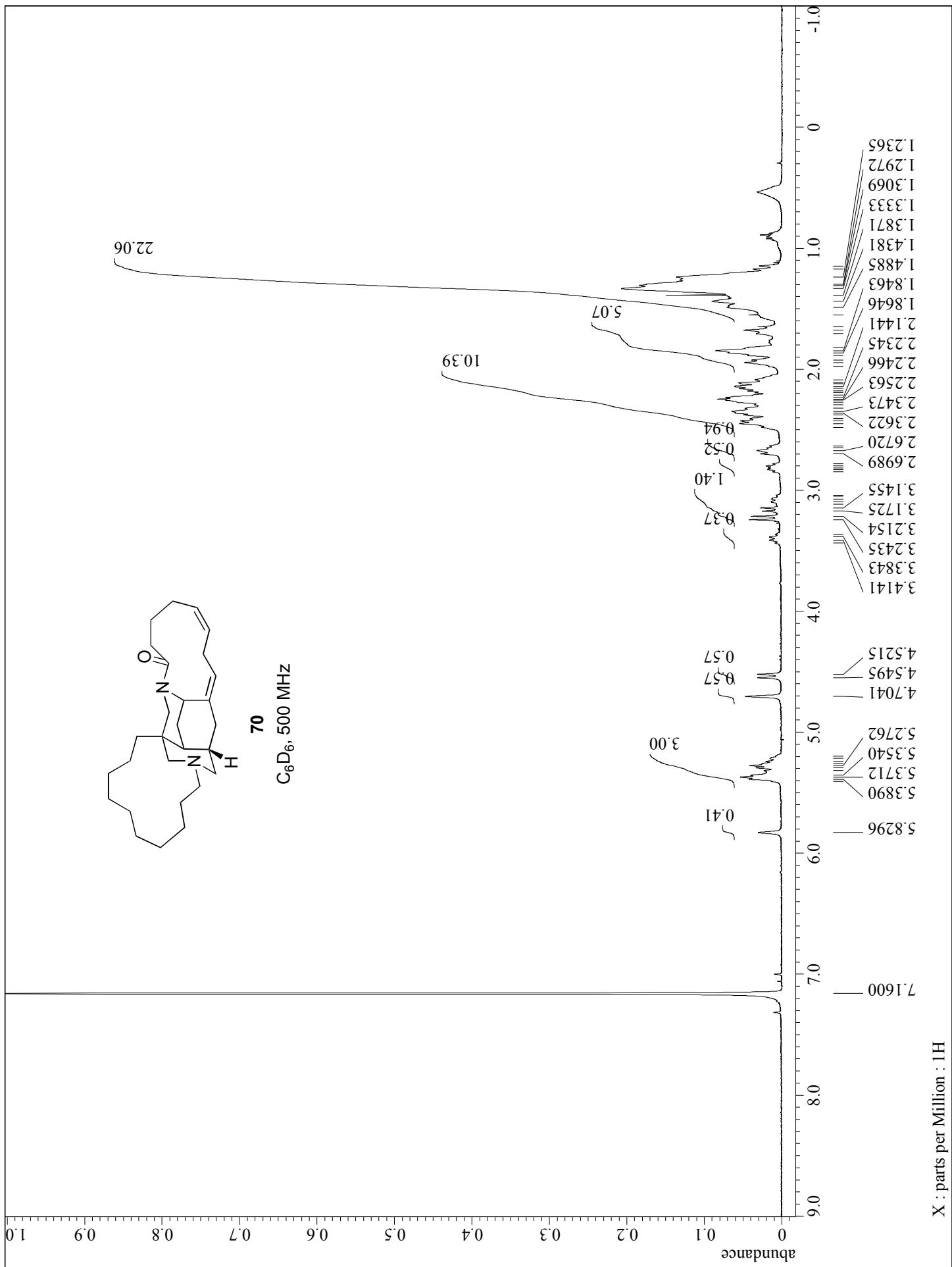


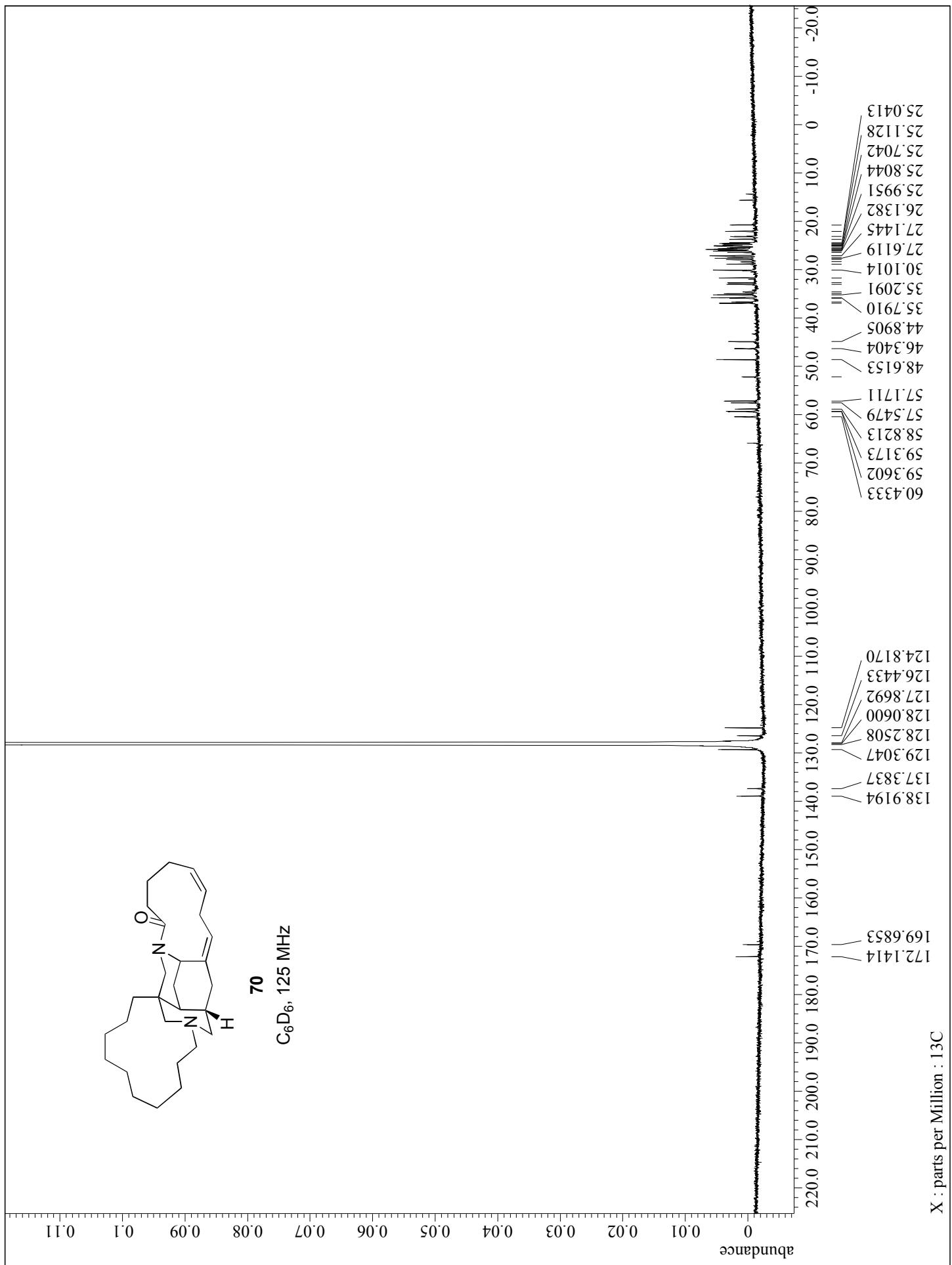


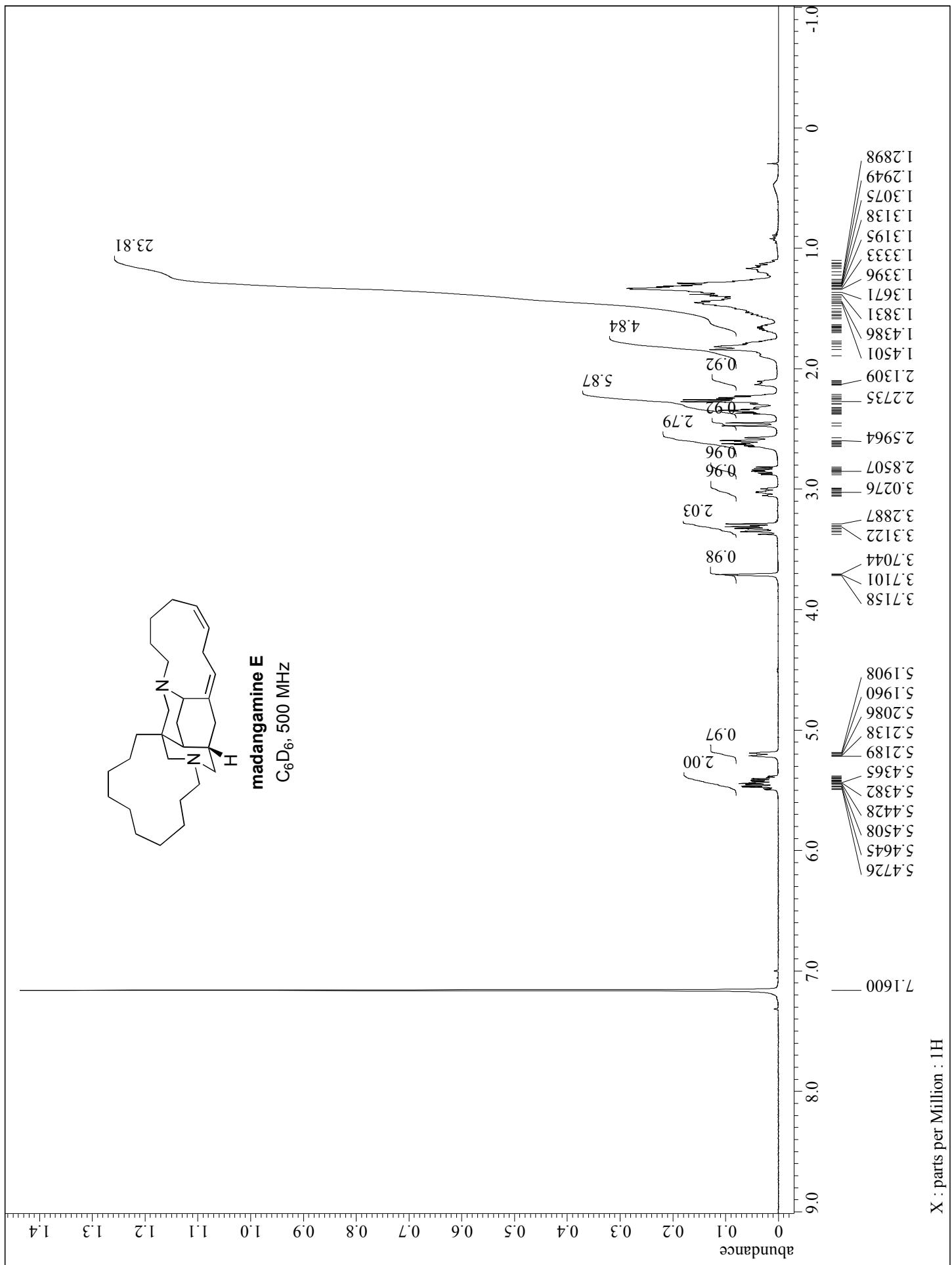
CDCl_3 , 500 MHz, 60 °C

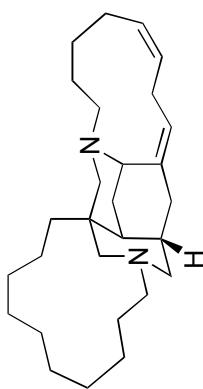




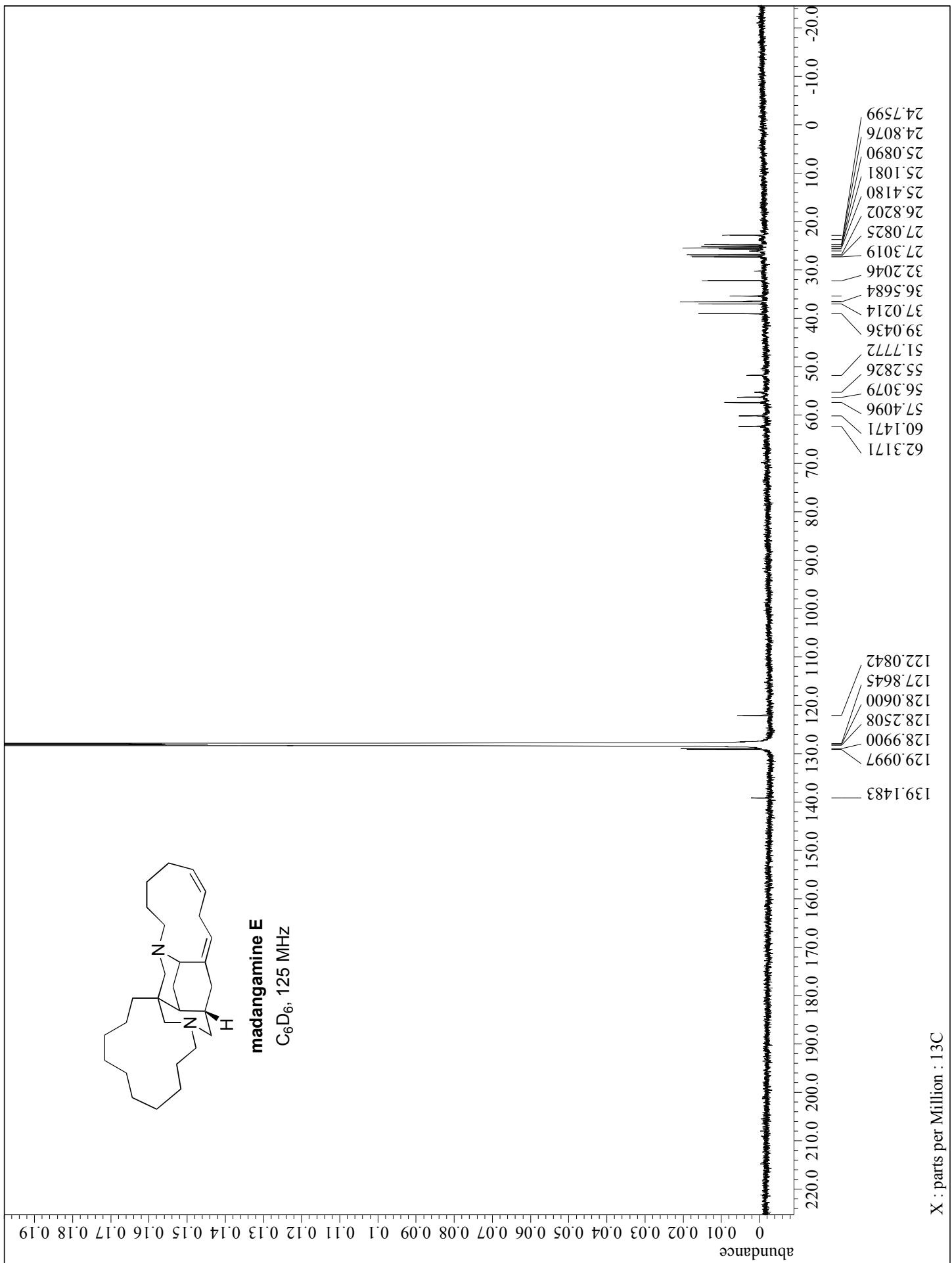


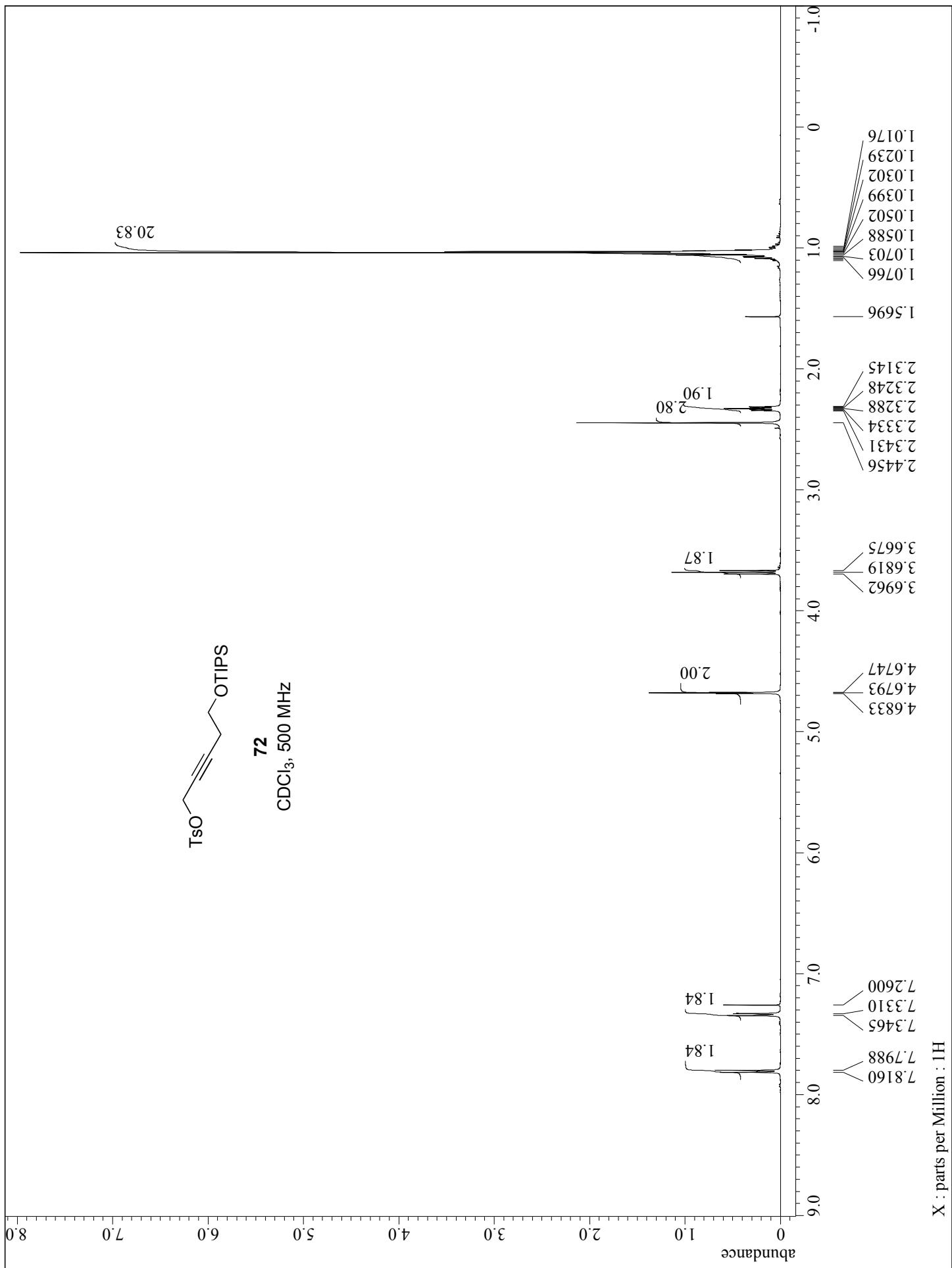






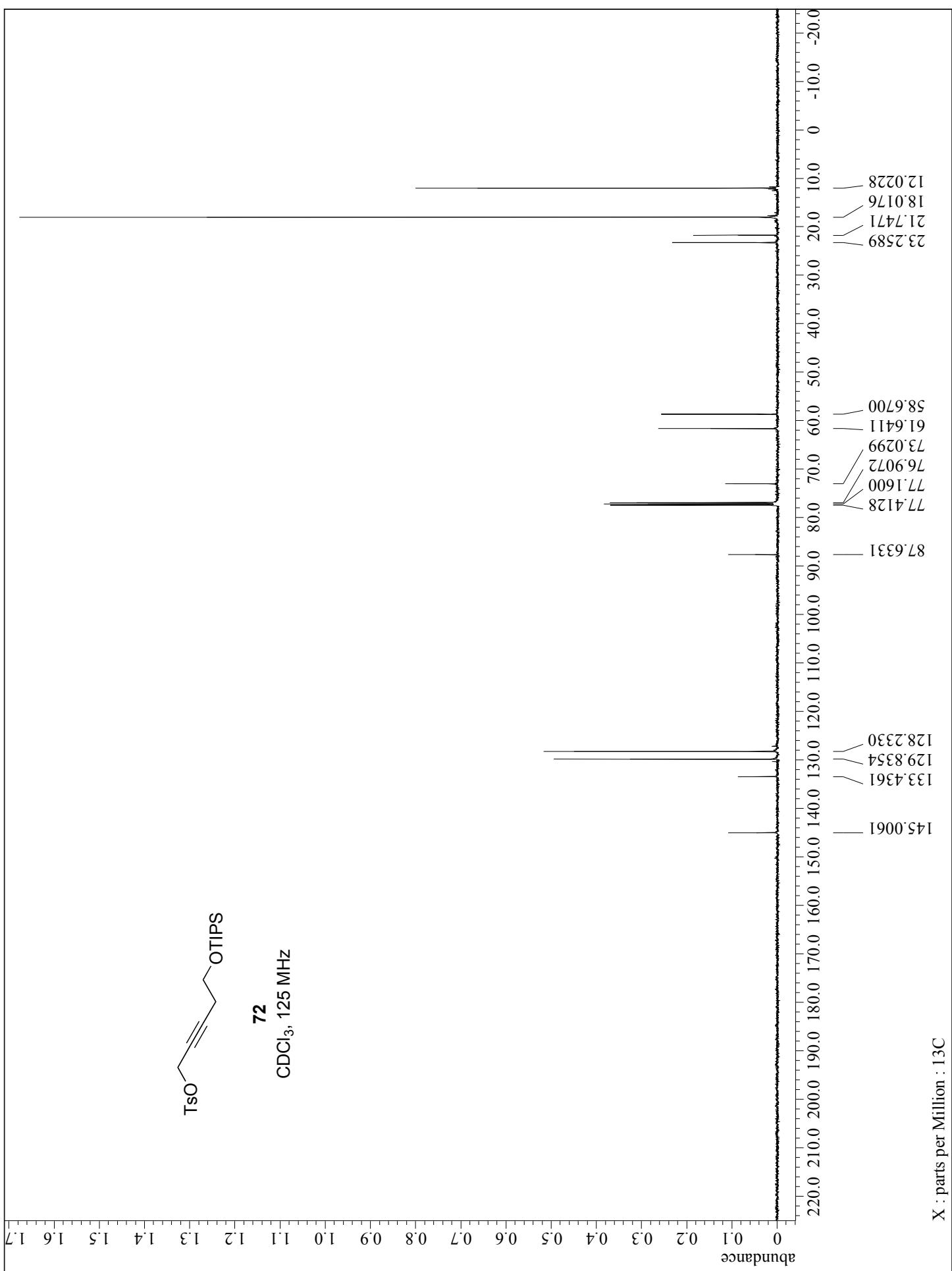
madangamine E
 C_6D_6 , 125 MHz

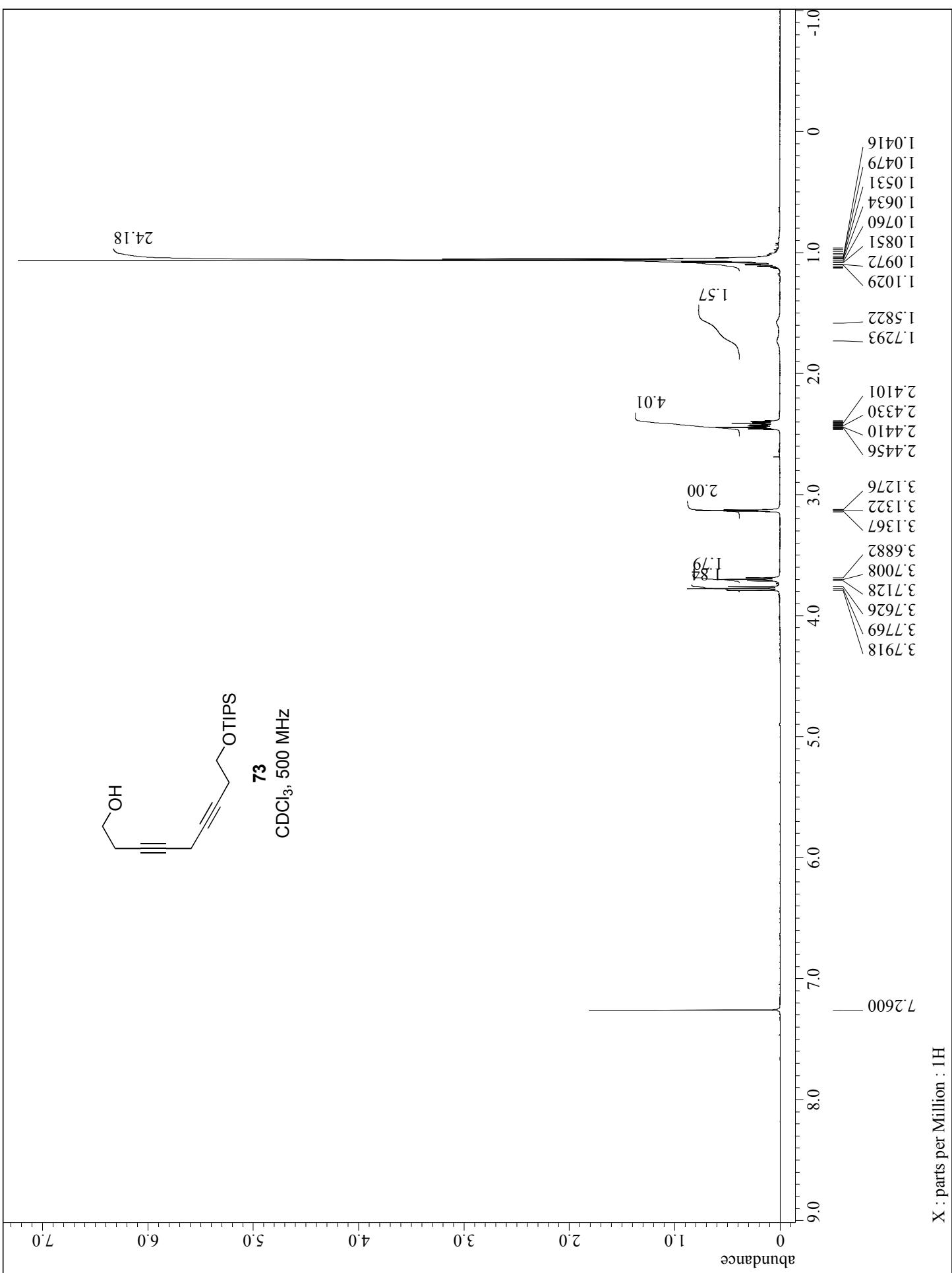
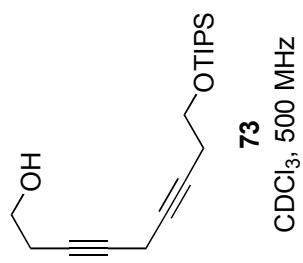


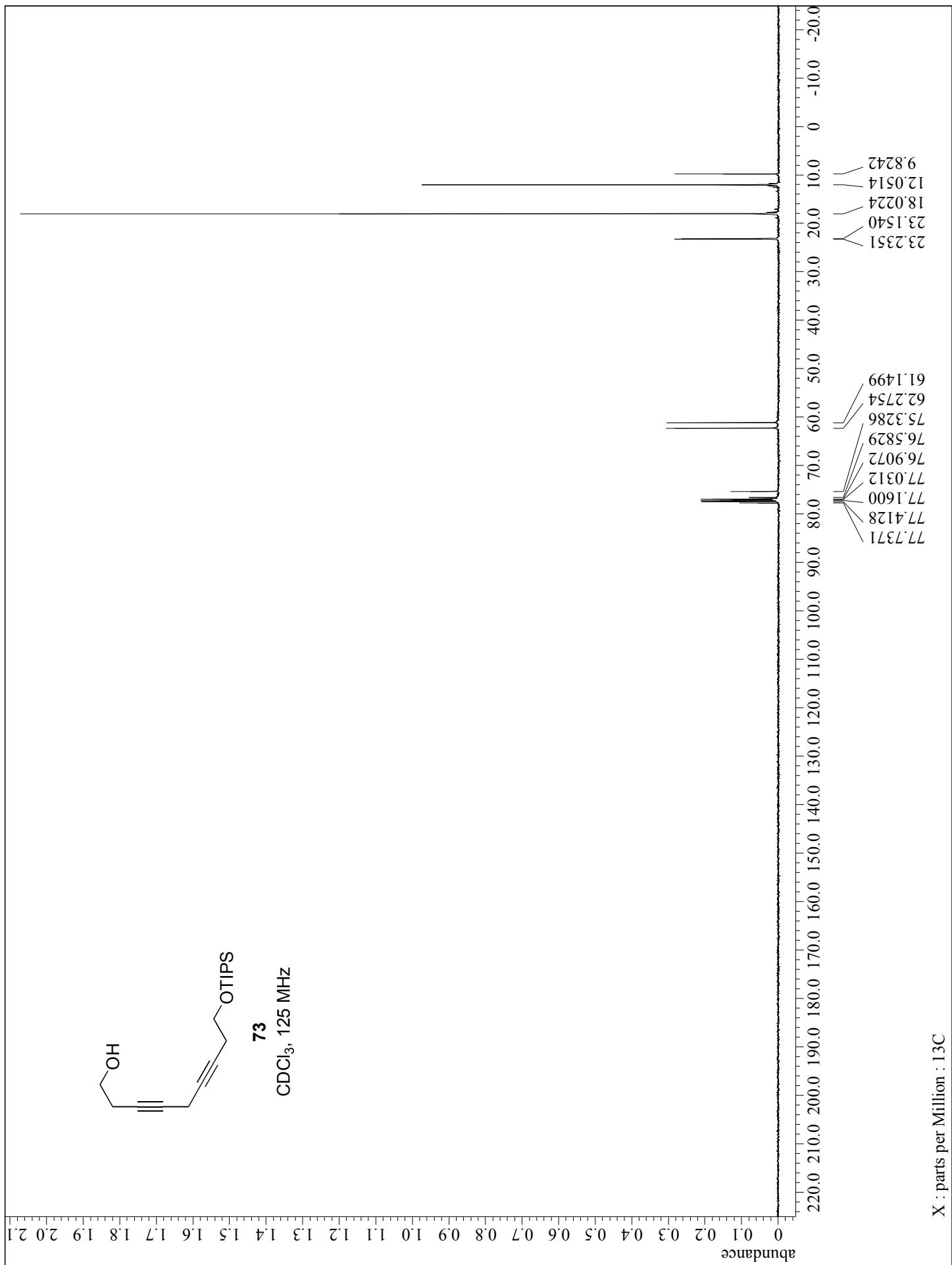


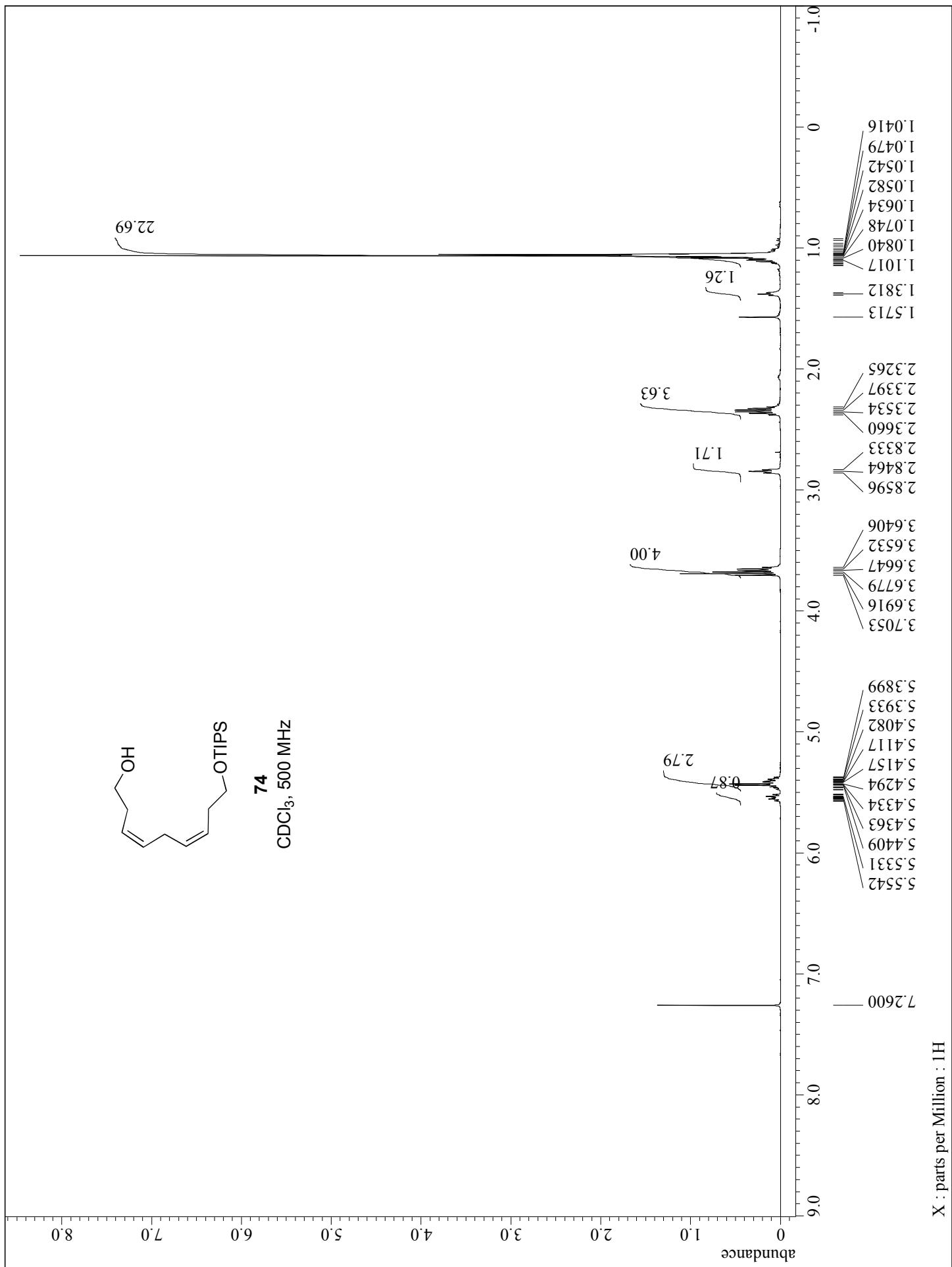


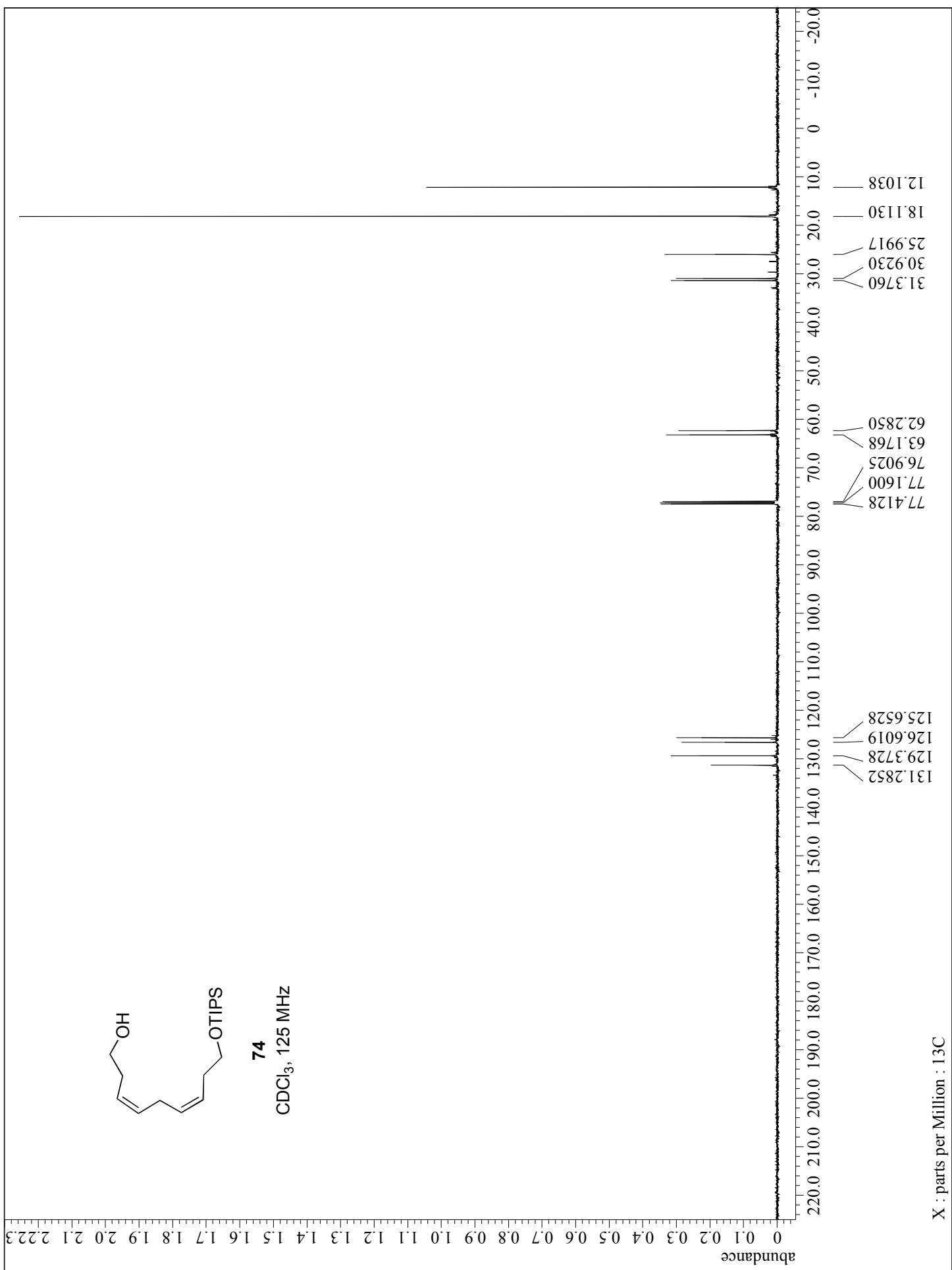
72
 $\text{CDCl}_3, 125 \text{ MHz}$

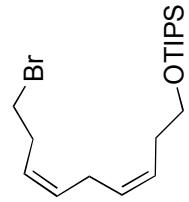




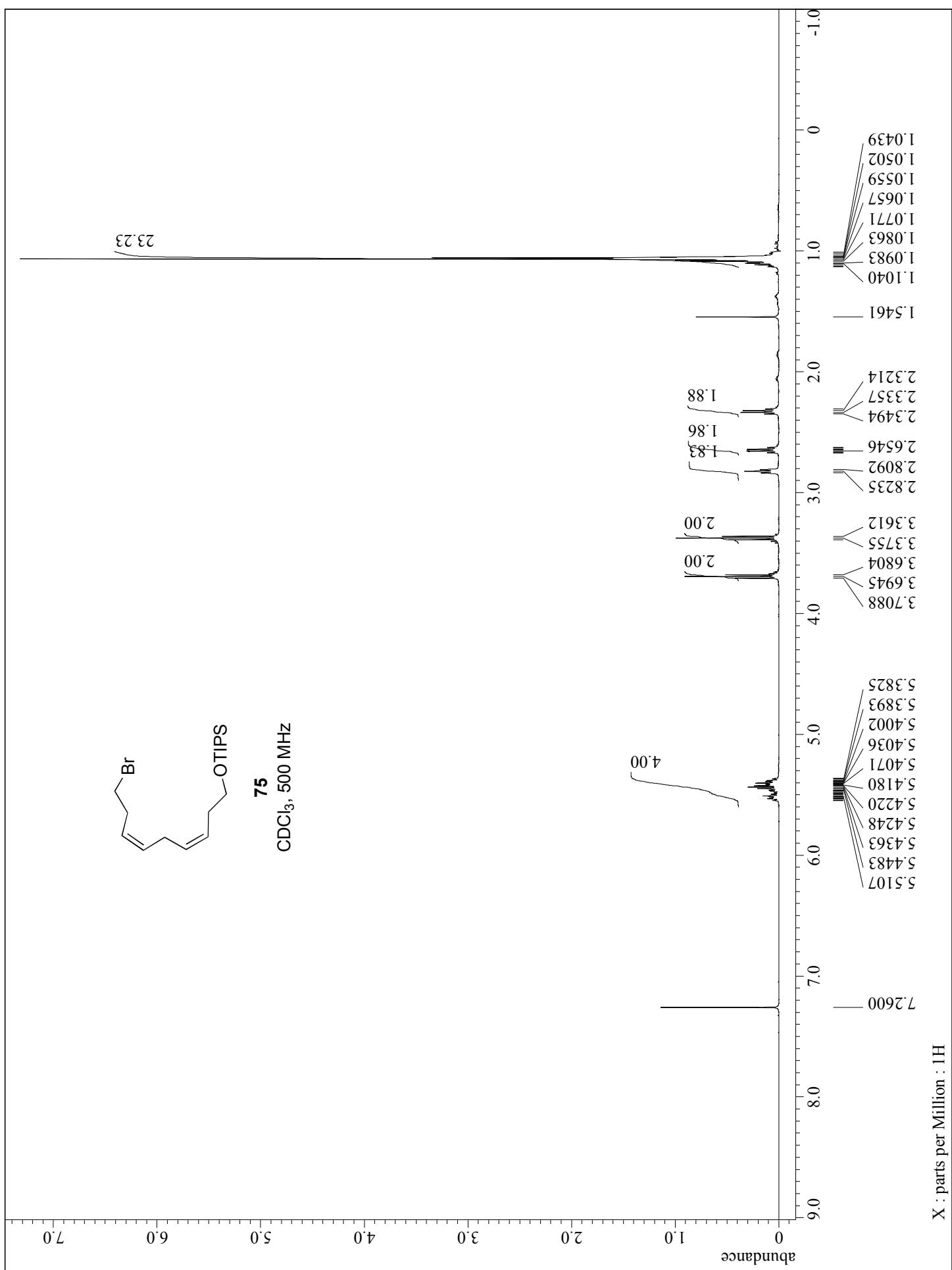


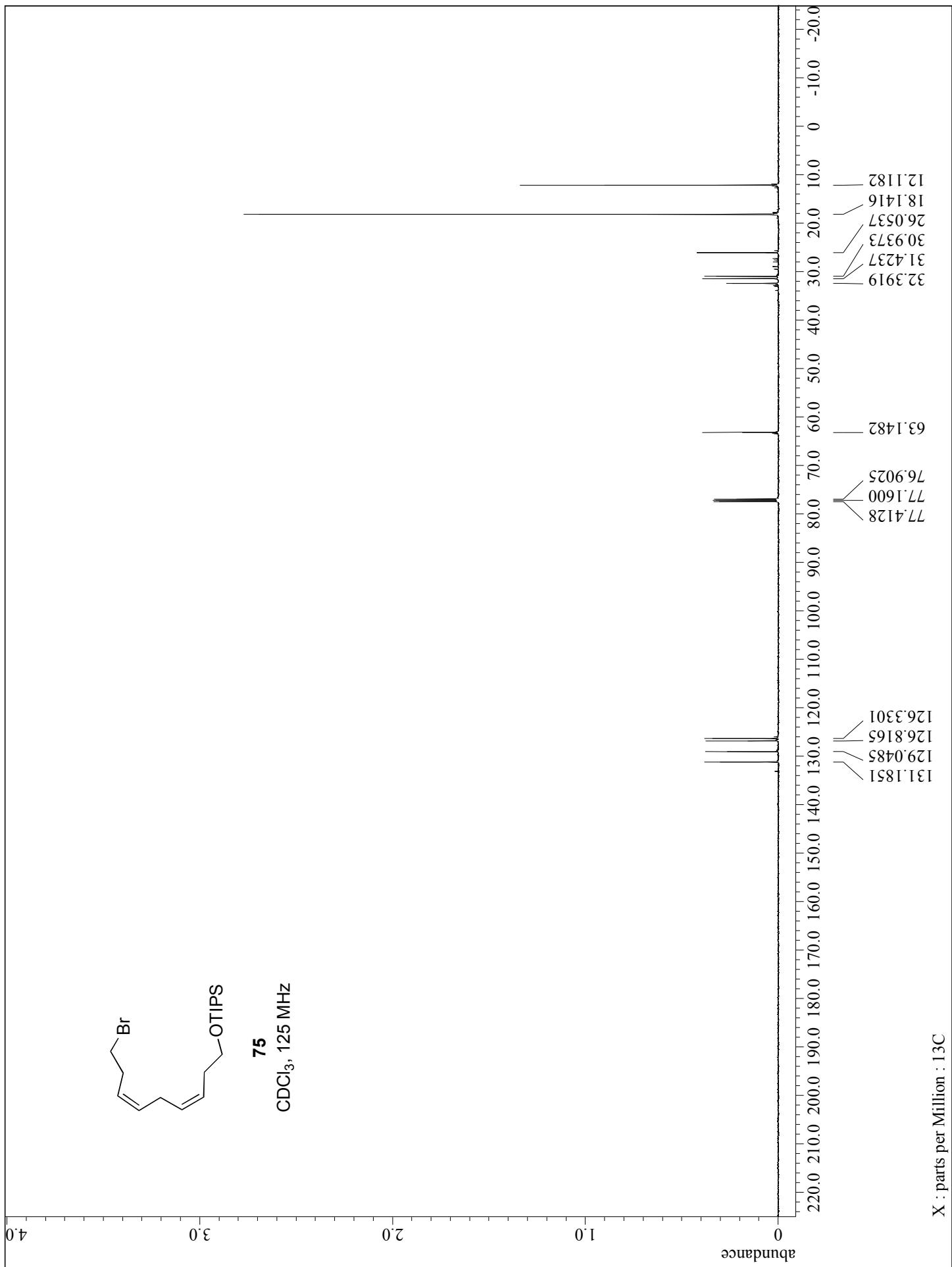


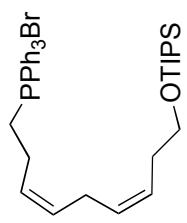




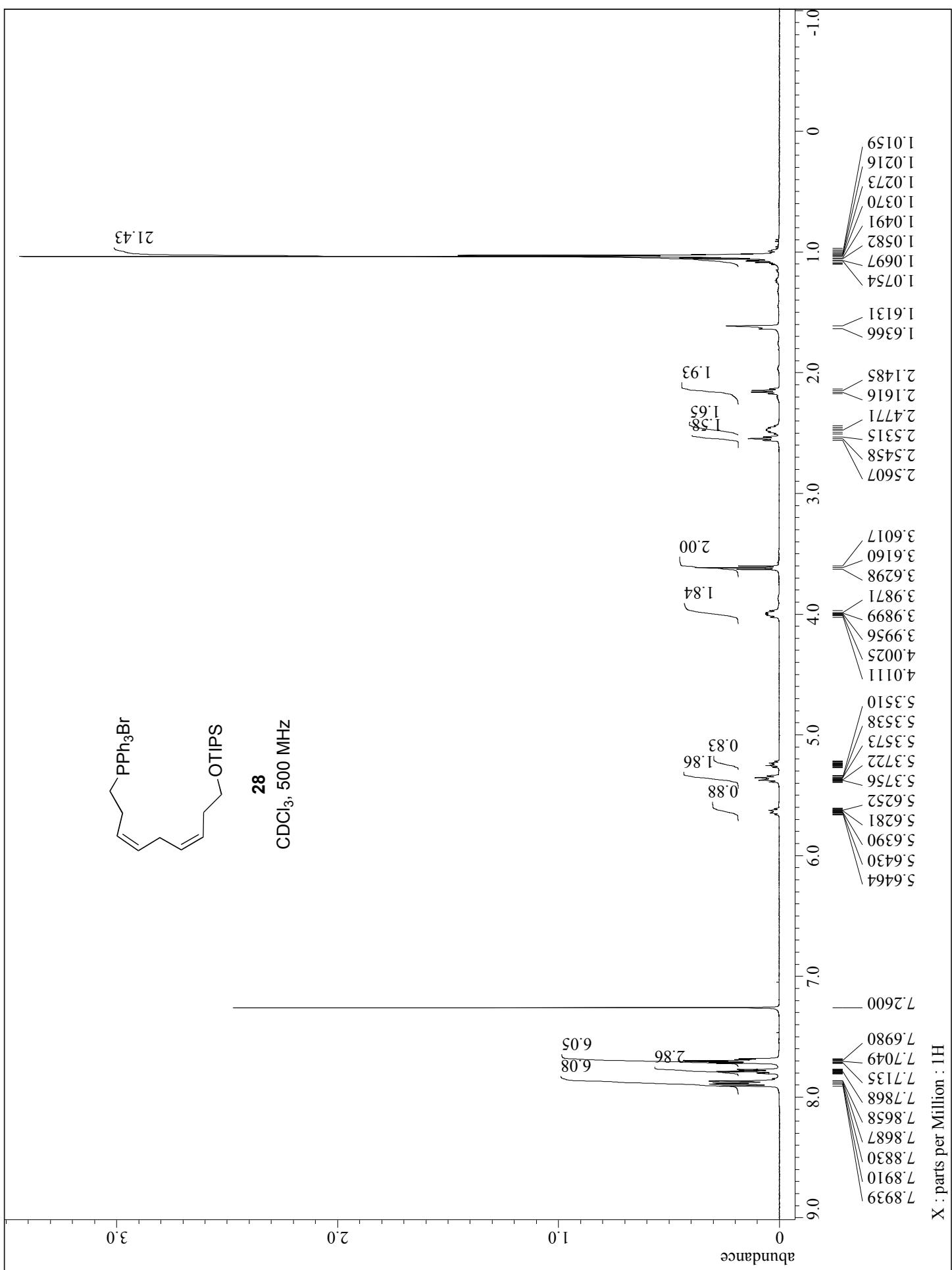
75
CDCl₃, 500 MHz

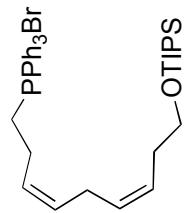




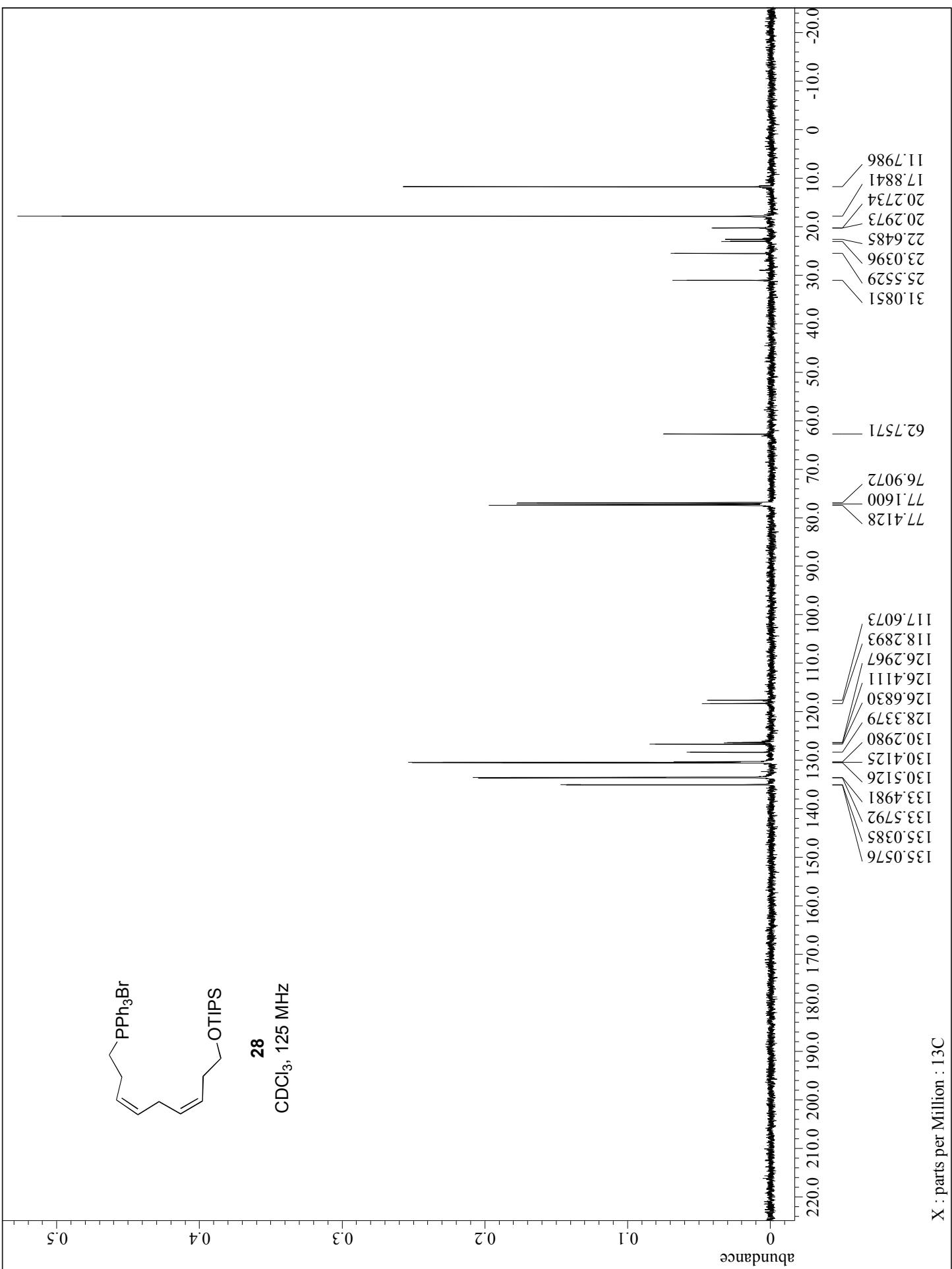


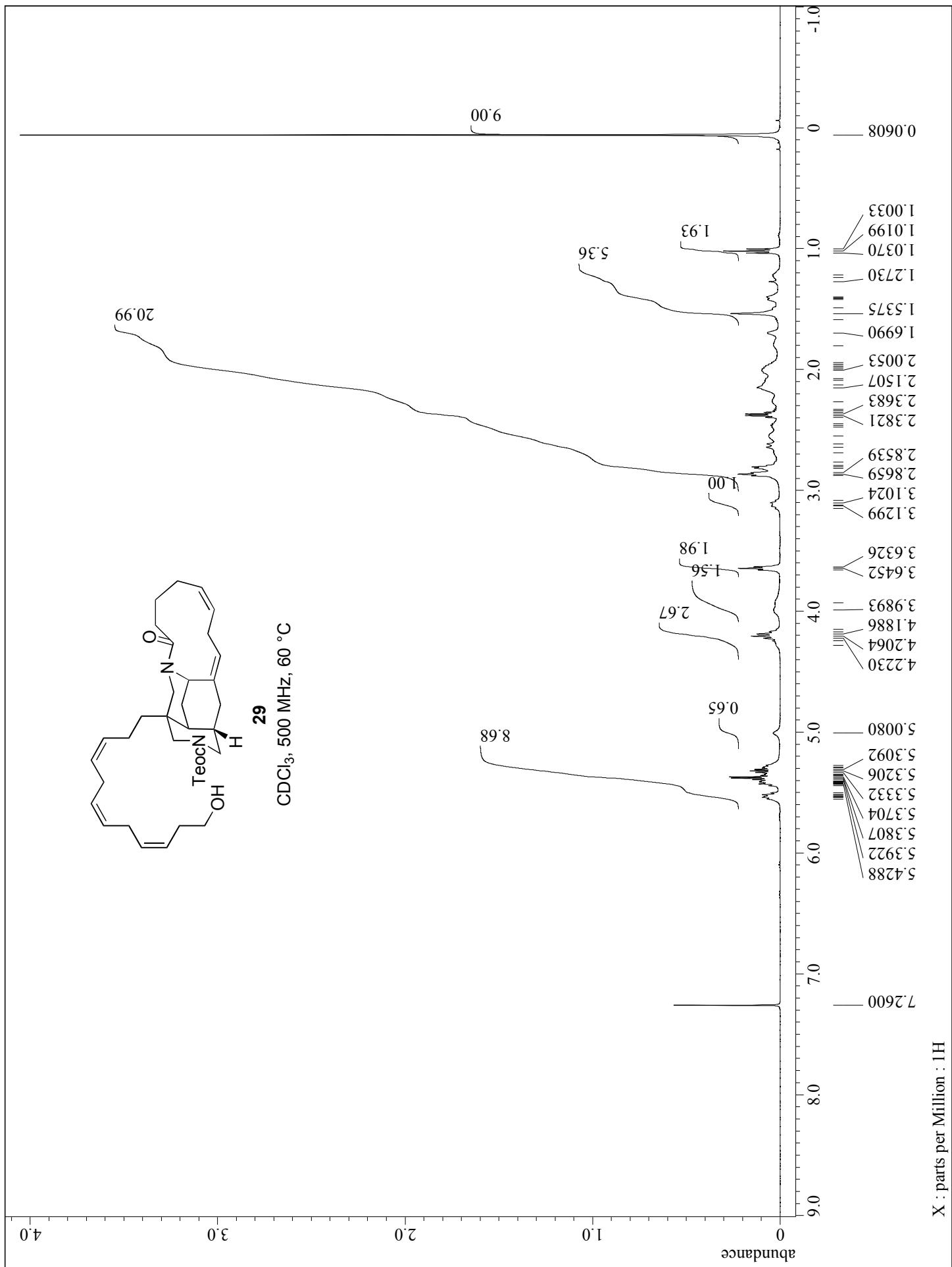
CDCl_3 , 500 MHz

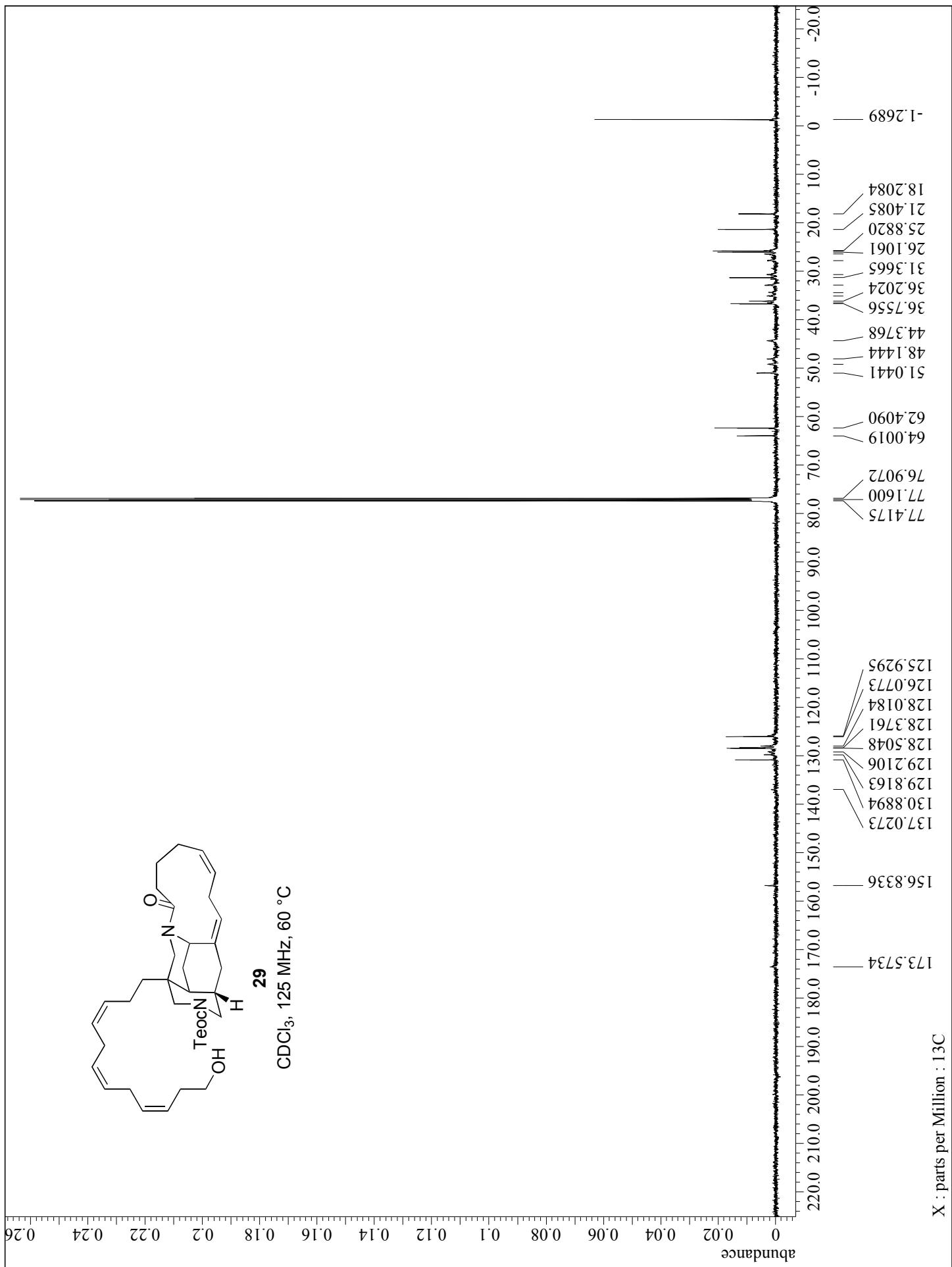


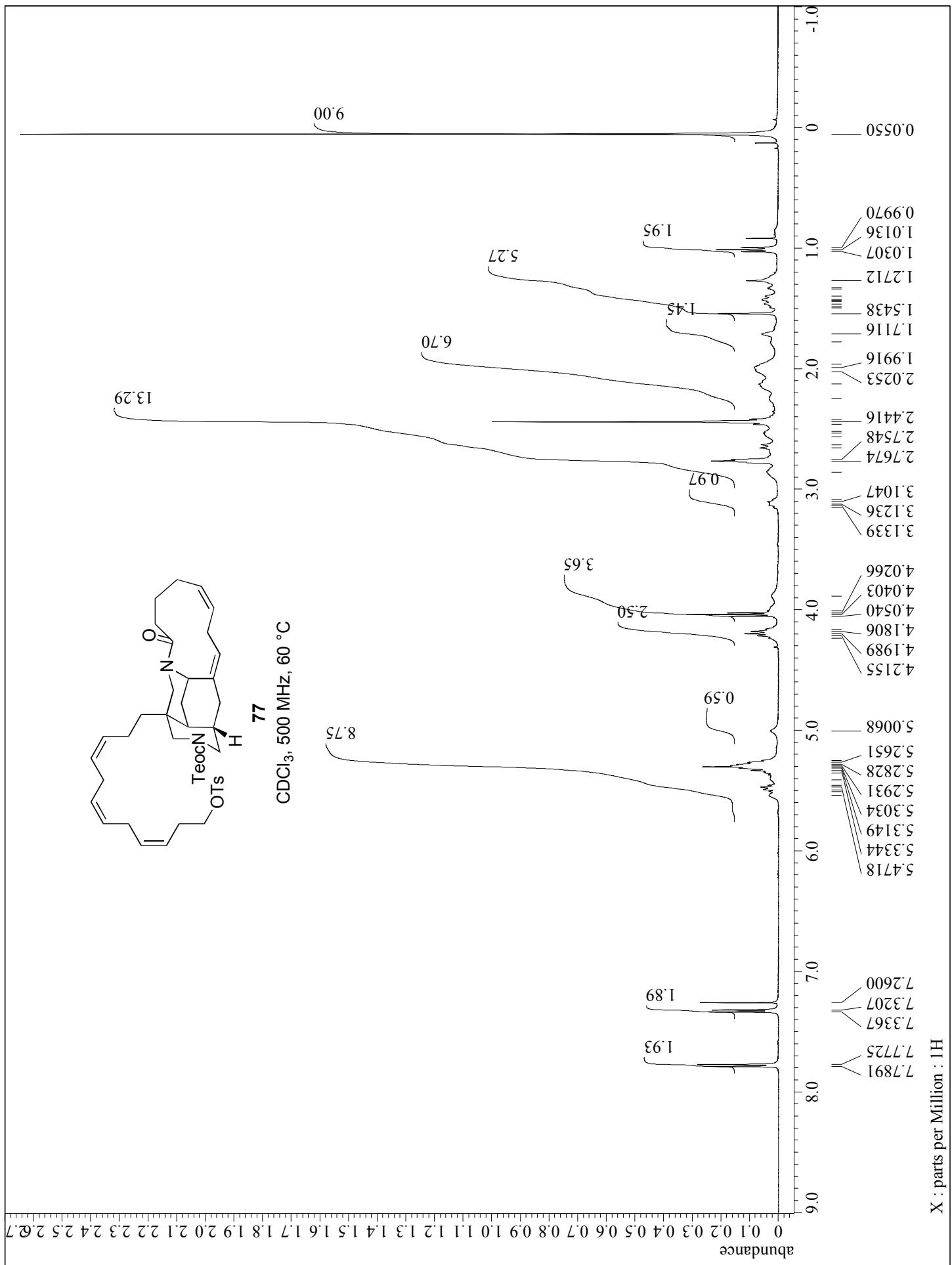


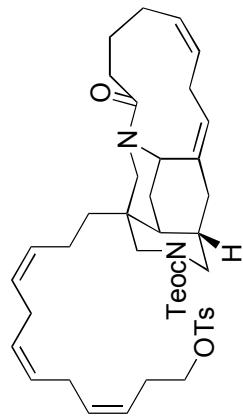
CDCl_3 , 125 MHz



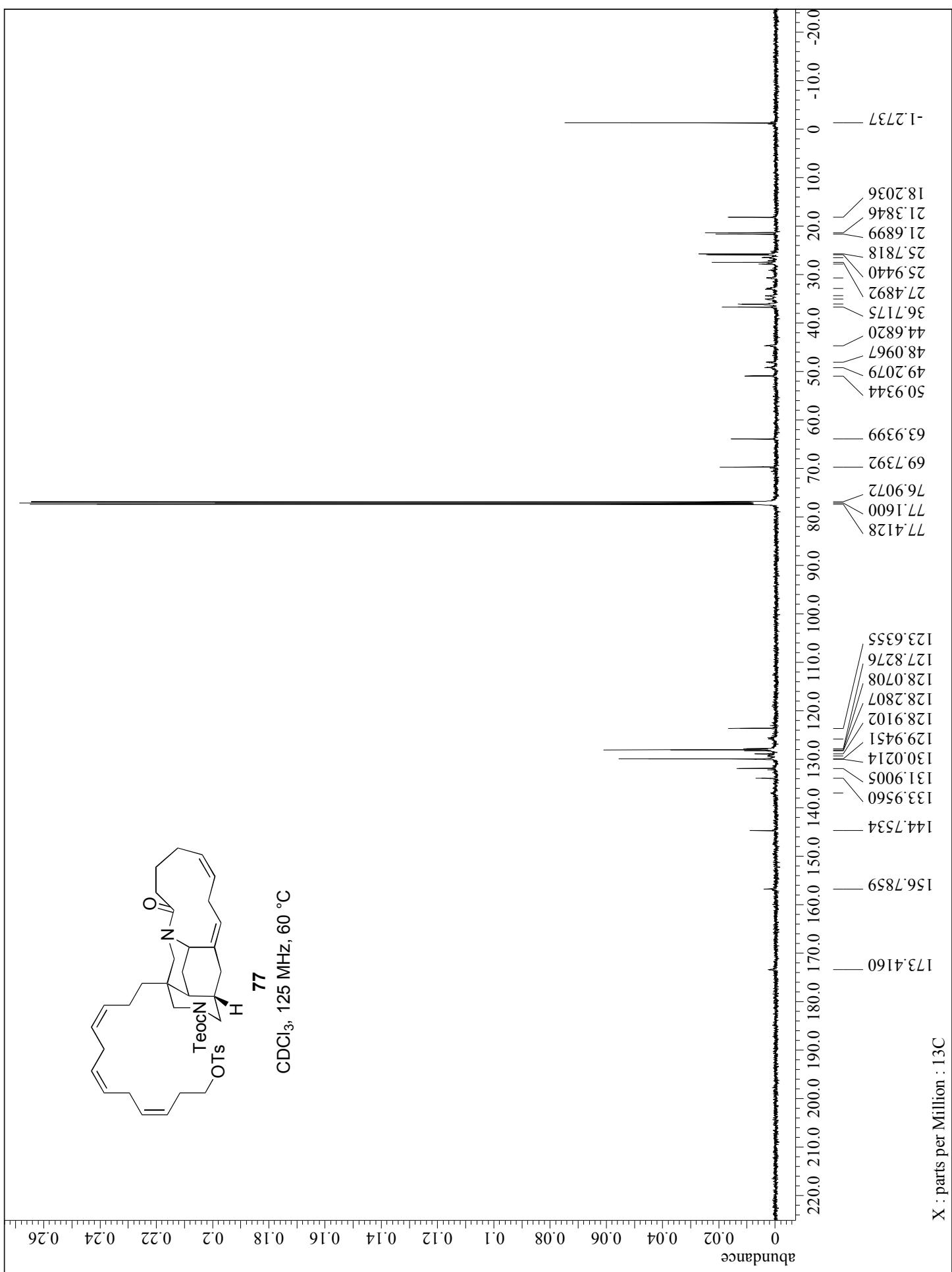


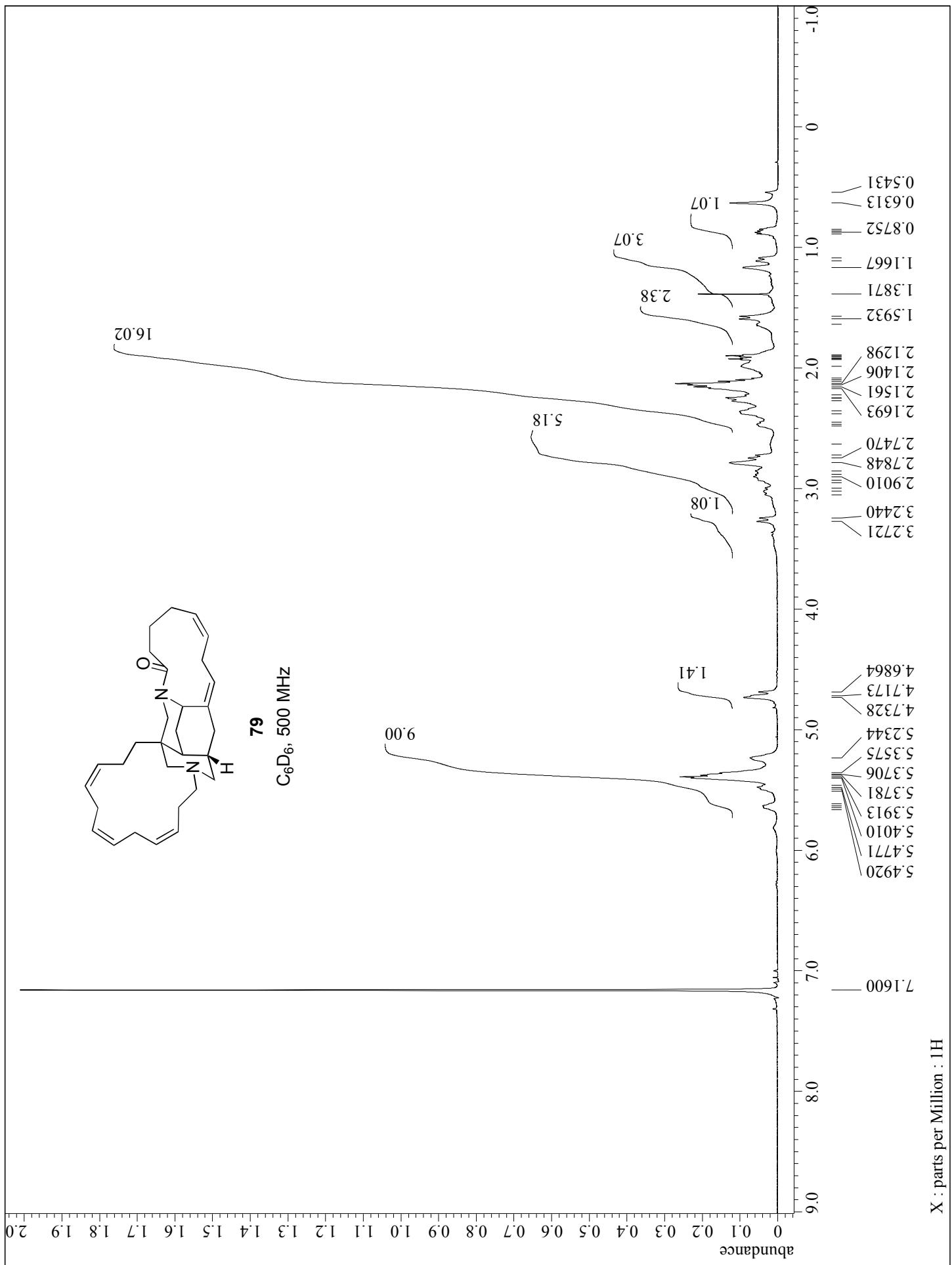


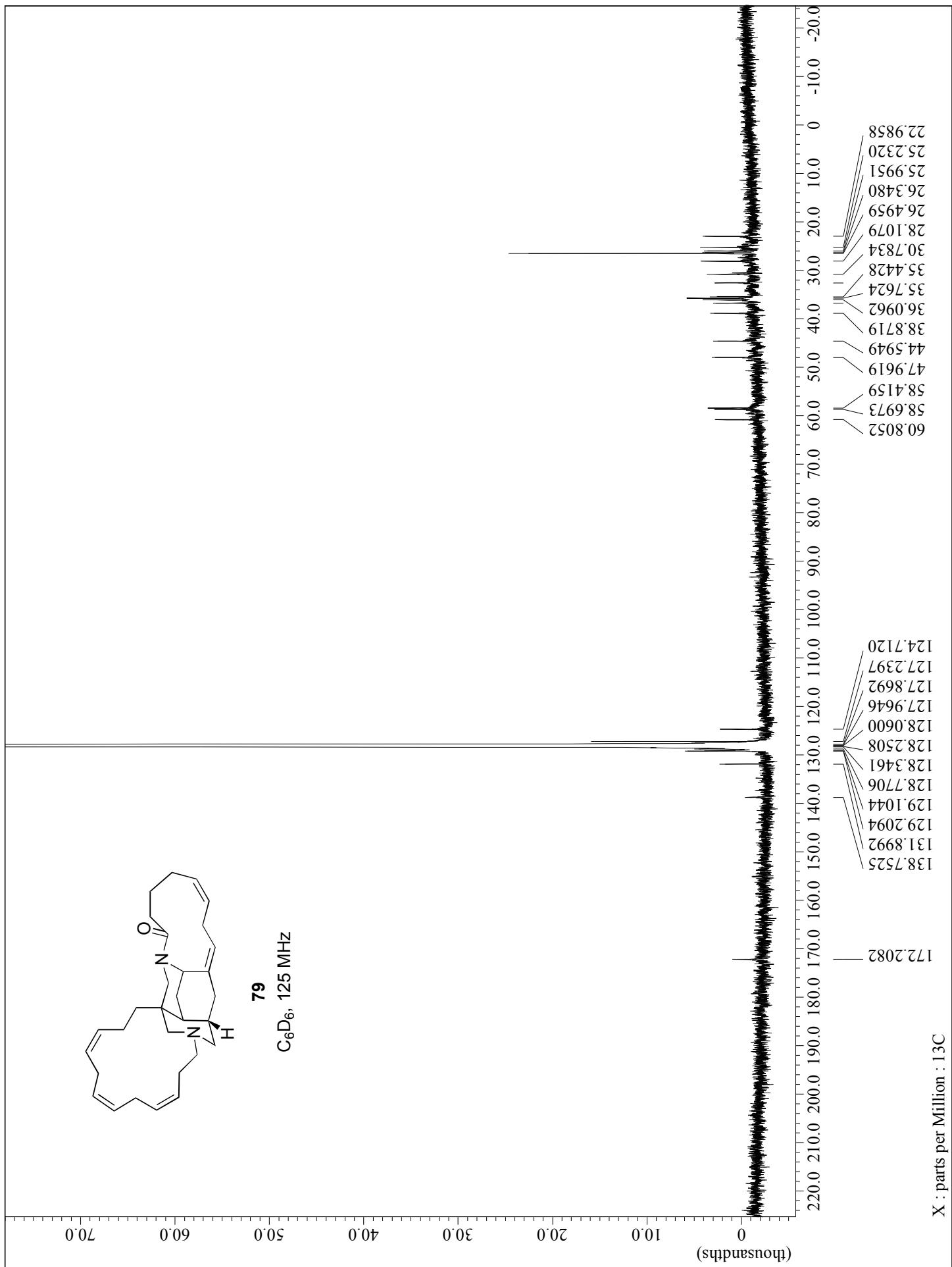


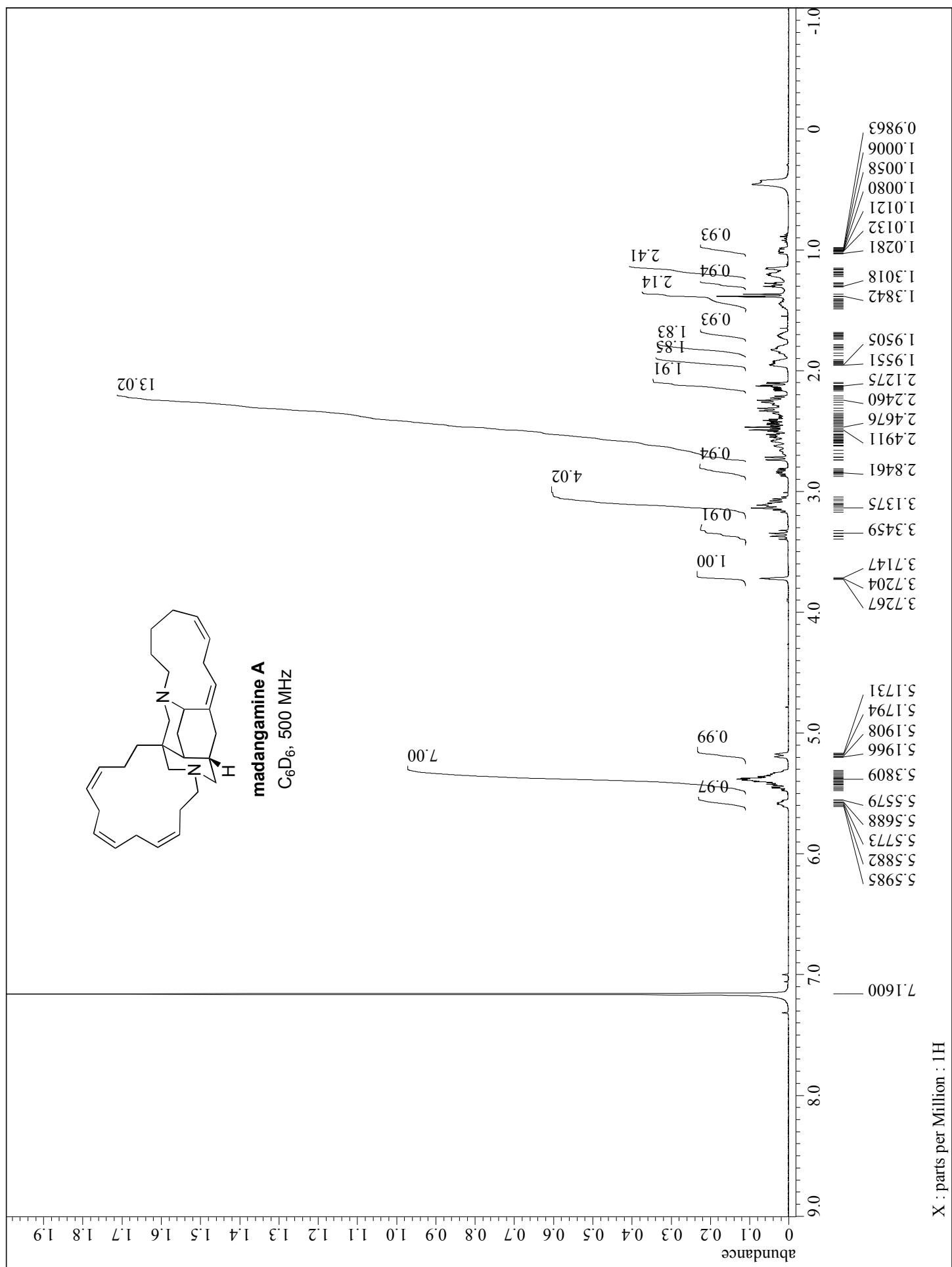


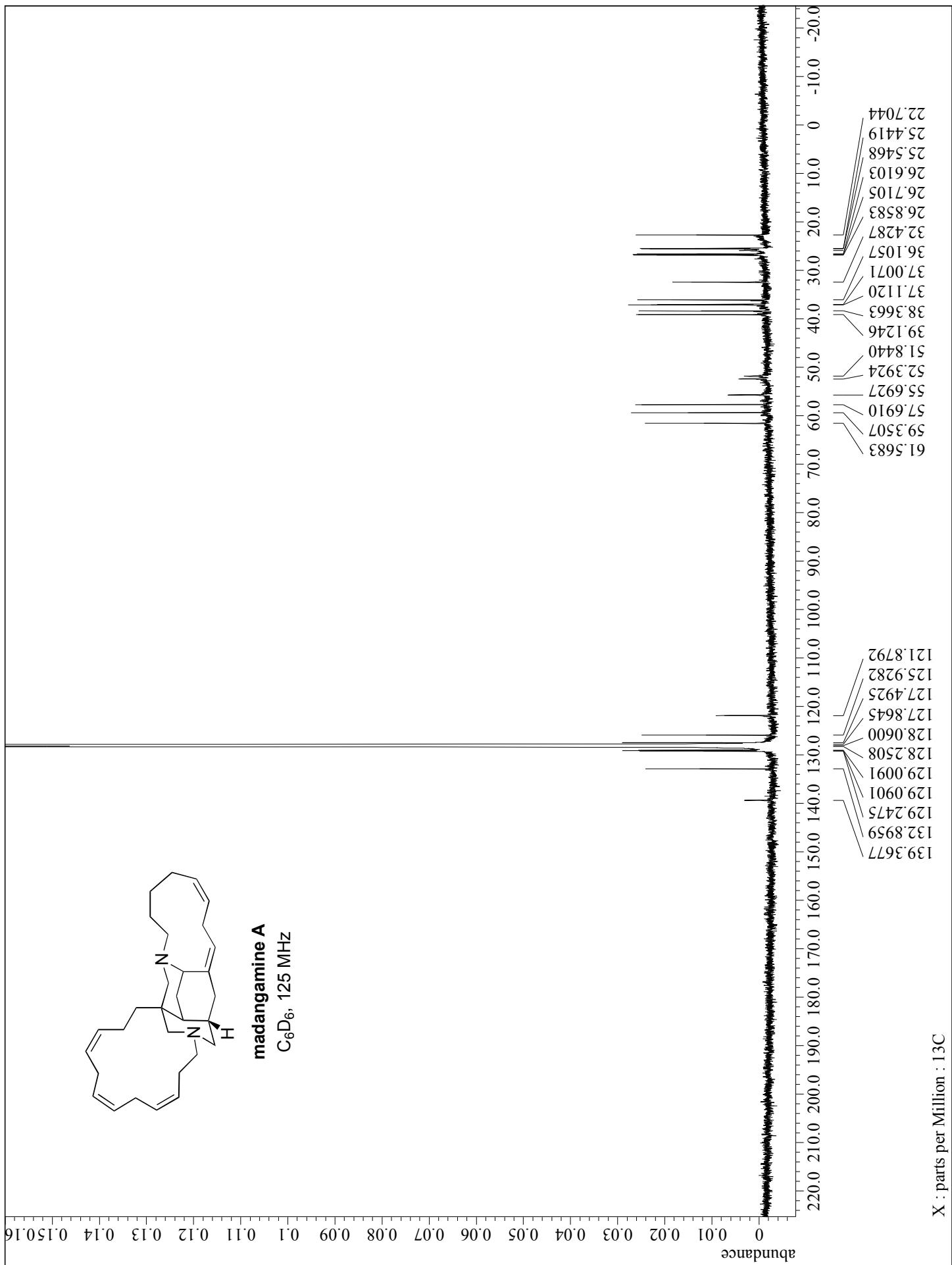
CDCl_3 , 125 MHz, 60 °C











D. References

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