Total Synthesis of Ajudazol A by a Modular Oxazole Diversification Strategy

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Supporting Information

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1. Materials and Methods

Solvents and reagents: Unless stated otherwise, solvents were purchased from the central chemical store (ZVE) of the University of Bonn. Cyclohexane (CH) and ethyl acetate (EA) were distilled over a Vigreux column. Dry solvents like dichloromethane, toluene, diethyl ether and acetonitrile were taken out of a solvent purification system MB-SPS 800 from MBraun, Garching. THF was freshly distilled over sodium/benzophenone before use. Reagents were purchased from the following companies: Acros Organics, Geel (Belgium); Alfa-Aesar, Ward Hill, MA (USA); Sigma-Aldrich, St. Louis, MO (USA) and TCI Chemicals, Antwerp (Belgium). Unless stated otherwise all of these chemicals were used without further purification.

The following reagents were prepared according to literature procedures: Andersen's reagent (**12**),[1] IBX.[2]

[1] (a) Andersen, K. K. *Tetrahedron Lett.* **1962**, *3*, 93-95; (b) Solladié, G.; Hutt, J.; Girardin, A. *Synlett* **1987,** 173.
[2] Figero, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537-4538.

Reaction handling: Unless stated otherwise, all non-aqueous reactions were performed in flame-dried glassware under an argon atmosphere. All flasks were equipped with rubber septa or were sealed with a glass stopper and a PTFE-collar. Temperatures above r. t. (23–27 °C) refer to oil bath temperatures, which were controlled by a temperature modulator. The following baths were used for cooling: water/ice (0 °C), acetone/dry ice (–78 °C) and acetone/liquid nitrogen (–90 °C). Reactions were magnetically stirred and monitored by TLC, unless otherwise noted.

Microwave reactions were carried out on a Discover SP-D 80 microwave reactor from CEM in septum-sealed microwave vessels.

Analytical Thin Layer Chomatography (TLC) was carried out with „Polygram® Sil G/UV254“ plastic sheets from Machery-Nagel GmbH & Co. KG, Düren. Detection was carried out using short wave UV-light (254 and 366 nm) and anisaldehyde staining solution (135 mL absolute ethanol, 5 mL concentrated sulfuric acid, 1.5 mL glacial acetic acid and 3.7 mL *p*-anisaldehyde), vanillin staining solution (2 g vanillin in 100 mL EtOH with 1 mL conc. H_2SO_4), potassium permanganate staining solution (1.5 g $KMnO_4$, 10 g K_2CO_3, 1.25 mL 10% aq. NaOH in 200 mL water) or cerium(IV)-sulfate staining solution (5 g ammonium dimolybdate, 200 mL H2O, 16 mL conc. H_2SO_4 with 2 g cerium(IV)-sulfate).

Flash column chromatography was accomplished according to the method introduced by G. Nill[3,4] using silica gel (pore size 60 Å, 0.040 – 0.063 mm) purchased from Merck Millipore, Massachusetts (USA). The given yields refer to the purified products.

Preparative High Performance Liquid Chromatography (PHPLC) was carried out on a Smartline Series instrument from Knauer with a Eurospher II C18P 100-5, 5 µm, 250 x 16 mm column with precolumn (30 x 16.0 mm) from Knauer. Operation and analysis were under control of Knauer ChromGate software (version 3.3.2).

Optical rotations were measured with a MCP 150 polarimeter (Anton Paar) in a 1 dm cuvette using a sodium lamp.

^{1}H-NMR spectra were recorded at room temperature (298 K) on Bruker Avance I spectrometers with a ^{1}H operating frequency of 300, 400 and 500 MHz and Bruker Avance III spectrometers with a ^{1}H operating frequency of 500 MHz and 700 MHz. Unless stated otherwise, all spectra were recorded at room temperature. All chemical shifts are given in δ units relative to the residual protiated solvent residual peak ($CDCl_3$: δH = 7.26 ppm, CD_2Cl_2: δH = 5.32 d_6-acetone: δH = 2.05 ppm).[5] Analyses followed first-order principles and the following abbreviations were used throughout: s = singlet, d =

[3] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923

[4] Helmchen, G.; Nill, G.; Flockerzi, D.; Youssef, M. S. K. *Angew. Chem. Int. Ed.* **1979**, *18*, 63-65.

[5] Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. *Organometallics* **2010**, *29*, 2176-2179.

doublet, t = triplet, q = quartet, m = multiplet, br. = broad. Coupling constants through n bonds (^{n}J) are given in Hertz [Hz].

^{13}C-NMR spectra were recorded at room temperature on Bruker Avance I spectrometers with a ^{13}C operating frequency of 75 and 100 MHz and Bruker Avance III spectrometers with a ^{13}C operating frequency of 125 and 175 MHz. Unless stated otherwise, all spectra were recorded at room temperature. All chemical shifts are given in δ units relative to the residual protiated solvent residual peak ($CDCl_3$: δH = 7.26 ppm, CD_2Cl_2: δC = 53.84 ppm, d_6-acetone: δH = 29.84 ppm).[6]

* chem. shifts associated with the major rotamer are marked with an asterisk

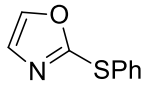
chem. shifts associated with the minor rotamer are marked with an asterisk

Gas-chromatography-Mass spectrometry (GC-MS) were recorded using a GCMS-QP2010 SE from *Shimadzu*, Duisburg (Germany).

Mass spectra (MS) and high-resolution- mass spectra (HR-MS) were recorded on a MAT 95 XL sector field device from Thermo Finnigan (Bremen), mircoTOF-Q from Bruker Daltonik (Bremen) and LTQ Orbitrap XL mass spectrometer from Thermo Fisher Scientific (Bremen). Ionization processes and mol peaks were given in combination with characteristic fragmentations.

2. Selective Oxazole Functionalization

2.1. 2-(Phenylthio)oxazole (8)



8

^{n}BuLi (2.5M in ^{n}hexane, 20.0 mL, 50.0 mmol, 1.20 equiv.) was added dropwise to a stirring solution of oxazole (**6**, 2.66 g, 38.5 mmol, 1.00 equiv.) in dry THF (250 mL) at –78 °C and stirred for 1 h. A solution of diphenyl disulfide (12.8 g, 58.4 mmol, 1.40 equiv.) in dry THF (140 mL) was slowly added and stirred for 1 h. The reaction mixture was allowed to warm to room temperature slowly and stirred for 43 h. Aq. sat. NH_4Cl solution (150 mL) was added and the aqueous phase was extracted with Et_2O (3x 50 mL). All organic phases were combined and washed with aq. sat. $NaHCO_3$ solution (80 mL) and brine (80 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography over silica gel (CH/EA 9:1) gave 2-(phenylthio)oxazole (**8**) as a yellow oil (6.24 g, 35.2 mmol, 91%).

R_f = 0.16 (CH/EA 9:1).

[6]Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. *Organometallics* **2010**, *29*, 2176-2179.

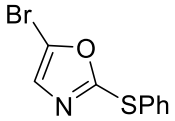
^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 7.67 (d, *J* = 0.9 Hz, 1H), 7.53 – 7.62 (m, 2H), 7.13 (d, *J* = 0.9 Hz, 1H), 7.34 – 7.42 (m, 3H).

^{13}C-NMR (75.0 MHz, $CDCl_3$): δ [ppm] = 141.0, 133.3, 129.6, 129.3, 129.0.

HRMS (ESI, 6.0 eV) m/z: [M+Na$^+$] calcd for [C_7H_9NOS+Na]$^+$ = 200.0141; Found 200.0144.

The experimental data are in agreement with those previously published.[7]

2.2. 5-Bromo-2-(Phenylthio)oxazole (10)



10

^{n}BuLi (2.5M in ^{n}hexane, 1.60 mL, 3.37 mmol, 1.10 equiv.) was slowly added to a stirring solution of (^{i}Pr)$_2$NH (720 µL, 4.28 mmol, 1.40 equiv.) in dry THF (210 mL) at 0 °C. After 0.5 h the reaction mixture was cooled to –78 °C and oxazole **8** (1.6 g, 9.03 mmol, 1.00 equiv.) dissolved in THF (8 mL) was added. The reaction mixture was allowed to stir for 1 h at this temperature. A solution of NBS (600 mg, 3.37 mmol, 1.10 equiv.) in THF (10 mL) was slowly added dropwise and stirred for 0.5 h, before the solution was allowed to warm to room temperature slowly. Aq. sat. NH_4Cl solution (30 mL) was added, the layers were separated and the aqueous phase was extracted with Et_2O (3x 80 mL). All organic phases were combined and washed with brine (200 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography (CH/EA 9:1) gave 5-bromooxazole **10** as an orange-yellowish oil (1.31 g, 5.11 mmol, 57%).

R$_f$ = 0.30 (CH/EA 9:1).

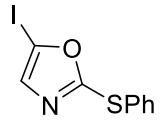
^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 7.60 – 7.51 (m, 2H), 7.43 – 7.36 (m, 3H), 6.99 (s, 1H).

^{13}C-NMR (75.0 MHz, $CDCl_3$): δ [ppm] = 160.1, 133.4, 129.7, 129.6, 129.2, 128.5, 122.9.

HRMS (EI (+), 70.0 eV) m/z: [M$^{+\bullet}$] calcd for $C_7H_8BrNOS^{+\bullet}$ = 286.9353; Found 286.9350.

[7] Williams, D. R.; Fu, L. *Org. Lett.* **2012**, 808-811.

2.3. 5-Iodo-2-(Phenylthio)oxazole (11)



11

^{n}BuLi (2.5M in ^{n}hexane, 9.93 mL, 24.8 mmol, 1.10 equiv.) was slowly added to a stirring solution of (^{i}Pr)$_2$NH (4.45 mL, 31.6 mmol, 1.40 equiv.) in dry THF (210 mL) at 0 °C and stirred for 15 min. The solution was cooled down to –78 °C and a solution of 2-(phenylthio)oxazole (**8**) (3.96 g, 22.3 mmol, 1.00 equiv.) in THF (30 mL) was added dropwise. The resulting yellow cloudy mixture stirred for 1 h at –78 °C and a solution of I_2 (6.83 g, 26.9 mmol, 1.20 equiv.) in dry THF (33 mL) was added slowly. The mixture stirred for 0.5 h before it was quenched with 30% aq. $NaHSO_3$ solution (120 mL) and was allowed to warm to room temperature slowly. The phases were separated and the aqueous layer was extracted with Et_2O (3x 100 mL). All organic extracts were combined and washed with brine (60 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and flash column chromatography over silica gel (CH/EA 9:1) gave 5-iodoxazoole **11** as a white-yellowish powder (6.15 g, 20.3 mmol, 91%).

R$_f$ = 0.30 (CH/EA 9:1).

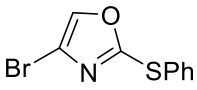
Mp.: 52-53 °C.

^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = δ 7.61 – 7.53 (m, 2H), 7.43 – 7.36 (m, 3H), 7.13 (s, 1H).

^{13}C-NMR (75.0 MHz, $CDCl_3$): δ [ppm] = 163.0, 137.6, 133.5, 129.7, 129.6, 87.7.

HRMS (EI (+), 70.0 eV) m/z: [$M^{+\bullet}$] calcd for $C_7H_8INOS^{+\bullet}$ = 302.9215; Found 302.9215.

2.4. 4-Bromo-2-(phenylthio)oxazole (38)



C_9H_6BrNOS
256.16 g/mol

38

(^{i}Pr)$_2$NH (270 µL, 1.92 mmol,1.40 equiv.) was dissolved in dry THF (11 mL) and cooled to 0 °C, then ^{n}BuLi (2.5M in ^{n}hexane,744 µL, 1.86 mmol, 1.30 equiv.) was added. After 5 min the solution was cooled down to –78 °C and halogenoxazole **10** (350 mg, 1.37 mmol, 1.00 equiv.) in THF (2.5 mL) was added and the reaction stirred for 50 min. Aq. sat. NH_4Cl solution (3 mL) and H_2O (6 mL) were added and the solution was allowed to warm to room temperature. The layers were separated and the aqueous layer was extracted with Et_2O (3x 10 mL) and the combined organic phases were dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash chromatography (CH/EA 9:1) yielded compound **38** as a yellow oil (313 mg, 1.22 mmol, 89%).

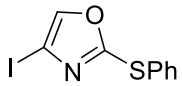
R_f = 0.36 (CH/EA 9:1).

^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.62 (s, 1H), 7.61 – 7.57 (m, 2H), 7.44 – 7.38 (m, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ [ppm] = 159.7, 139.0, 133.8, 129.7, 127.9, 116.8.

HRMS (EI (+), 70.0 eV) m/z: [$M^{+\bullet}$] calcd for $C_7H_8INOS^{+\bullet}$ = 254.9353; Found 254.9350.

2.5. 4-Iodo-2-(phenylthio)oxazole (12)



12

A stirring solution of (^{i}Pr)$_2$NH (282 µL, 2.01 mmol, 2.00 equiv.) in dry THF (12 mL) was cooled to 0 °C and ^{n}BuLi (2.5M in ^{n}hexane, 720 µL, 1.81 mmol, 1.80 equiv.) was added. The solution was allowed to stir for 5 min at this temperature, before it was cooled to –78 °C. 5-Bromooxazole **10** (25.7 mg, 100 µmol, 0.10 equiv.) and 5-iodooxazole **11** (304 mg, 1.00 mmol, 1.00 equiv.) were solved in THF (6 mL) and cooled to –78 °C. The LDA solution was slowly transferred dropwise *via* cannula into the oxazole solution (addition time: 61 min) and stirred for 2 min. Aq. sat. NH_4Cl solution (3 mL) and water (3 mL) were added and the reaction was allowed to warm to r.t. slowly. The layers were separated and the aqueous phase was extracted with Et_2O (3x 15 mL). All organic extracts were combined and dried dried over $MgSO_4$. Concentration of the crude product *in vacuo* and purification of the residue by flash column chromatography (CH/EA 9:1) afforded 4-iodooxazole **12** as an orange oil containing 8% impurities of 4-bromooxazole **38** (268 mg, 884 µmol, 88%).[8]

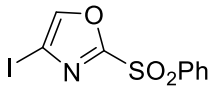
R_f = 0.36 (CH/EA 9:1).

^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.65 (s, 1H), 7.56–7.59 (m, 2H), 7.38–7.42 (m, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ [ppm] = 160.3, 144.8, 133.7, 129.7 (2C), 129.6, 128.1.

HRMS (EI (+), 70.0 eV) m/z: [$M^{+\bullet}$] calcd for $C_7H_8INOS^{+\bullet}$ = 254.9353; Found 254.9350.

2.6. 4-Iodo-2-Phenylsulfonyloxazole (13)



13

Ammonium molybdate tetrahydrate (5.99 g, 4.84 mmol, 2.20 equiv.) was dissolved in aq. hydrogen peroxide solution (30% *v/v*, 25 mL, 2.20 equiv.) at 0 °C and stirred for 15 min. The resulting yellow

[8] measured by GC-MS analysis

solution was added dropwise to a solution of thiooxazole **12** (673 mg, 2.22 mmol, 1.00 equiv.) in EtOH (36 mL) and the reaction was allowed to warm to r.t. and stirred over night (18 h). Et_2O (50 mL) was added, the layers were separated and the aqueous phase was extracted with Et_2O (3x 80 mL). All organic extracts were combined and washed with brine (20 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography (CH/EA 3:2) gave sulfonyloxazole **13** as white needles (744 mg, 2.22 mmol, quant.).

R_f = 0.38 (CH:EA 3:2).

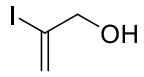
Mp.: 73 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 8.14 – 8.06 (m, 2H), 7.78 (s, 1H), 7.76 – 7.69 (m, 1H), 7.67 – 7.59 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ [ppm] = 159.9, 145.9, 137.5, 135.4, 129.9, 129.2, 83.61.

HRMS (EI (+), 70.0 eV) m/z: [$M^{+\bullet}$] calcd for $C_7H_8INO_3S^{+\bullet}$ = 334.9113, Found 334.9105.

2.7. 2-Iodoprop-2-en-1-ol (39)



39

TMSCl (44 mL, 346 mmol, 2.00 equiv.), water (3.12 mL, 173 mmol, 1.00 equiv.) and propargyl alcohol (10 mL, 173 mmol, 1.00 equiv.) were added to a stirring solution of NaI (51.9 g, 346 mmol, 2.00 equiv.) in CH_3CN (430 mL) at 0 °C and stirred for 1.5 h. Water (150 ml) was added, the layers were separated and the aqueous phase was extracted with Et_2O (3x 150 mL). All organic phases were combined and washed with aq. sat. $NaSO_3$ solution (200 mL) and brine (200 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography over silica gel (CH/EA 5:1) yielded allyl alcohol **39** as an orange liquid (14.8 g, 80.4 mmol, 46%).

R$_f$ = 0.26 (CH/EA 5:1).

^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 6.39 (q, *J* = 1.7 Hz, 1H), 5.86 (q, *J* = 1.4 Hz, 1H), 4.18 (s, 2H), 2.07 (br. s, 1H).

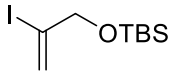
^{13}C-NMR (100 MHz, $CDCl_3$): δ [ppm] = ^{13}C NMR (101 MHz, Chloroform-*d*) δ 124.6, 110.6, 71.2.

GC-MS (EI (+), 70.0 eV) m/z: $[M]^{\bullet+}$ calcd for $C_3H_5IO^{\bullet+}$ = 183.94; Found 183.85.

The experimental data are in agreement with those previously published.[9]

[9] Kamiya, N.; Chikami, Y.; Ishii, Y. *Synlett* **1990**, *11*, 375-676.

2.8. *tert*-Butyl((2-iodoallyl)oxy)dimethylsilane (15)



15

TBSOTf (6.37 mL, 27.7 mmol, 1.20 equiv.) was added dropwise to a solution of allyl alcohol **39** (4.25 g, 21.1 mmol, 1.00 equiv.) and 2,6-lutidine (6.44 mL, 55.4 mmol, 2.40 equiv.) in dry CH_2Cl_2 (83 mL) at 0 °C. The reaction was allowed to warm to r.t. and stirred for 1.5 h. Water (80 mL) was added, the phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3x 50 mL). All organic phases were combined and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash column chromatography (CH/EA 99:1) yielded TBS ether **15** as a clear liquid (6.34 g, 21.3 mmol, 92%).

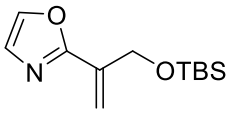
$\boldsymbol{R_f}$ = 0.48 (CH/EA 99:1).

^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 6.42 (q, *J* = 1.8 Hz, 1H), 5.81 (q, *J* = 1.7 Hz, 1H), 4.17 (t, *J* = 1.8 Hz, 2H), 0.92 (s, 9H), 0.09 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ [ppm] = 123.1 , 109.9, 71.2, 26.0, 18.5, –5.2.

HRMS (EI (+), 70.0 eV) m/z: $[M]^+$ calcd for $[C_9H_{19}IOSi^{\bullet+}-{}^tBu^{\bullet}]^+$ = 241.1223 Found 241.1211.

2.9. 2-(3-((*tert*-Butyldimethylsilyl)oxy)prop-1-en-2-yl)oxazole (16)



16

$ZnCl_2$ (12.0 g, 87.9 mmol, 1.40 equiv.) was heated under vacuum until free-flowing, recooled to r.t. and suspended in dry THF (44 mL). ^{n}BuLi (2.5M in ^{n}hexane, 19.7 mL, 49.2 mmol, 1.68 equiv.) was added dropwise to a stirring solution of oxazole (**6**, 100 µL, 1.52 mmol, 1.40 equiv.) in dry THF (190 mL) at −78 °C and stirred for 0.5 h. The solution was transferred *via* cannula to the $ZnCl_2$ suspension and was allowed to warm up to r.t. over a period of 15 min. A solution of iodoalkene **15** (8.74 g, 29.3 mmol, 1.00 equiv.) in dry THF (8.0 mL) was slowly added, followed by addition of $Pd(PPh_3)_4$ (847 mg, 733 µmol, 2.5mol-%). The reaction was sealed, heated to 60 °C and stirred for 19 h and was concentrated *in vacuo*. EtOAc (150 mL) and aq. sat. NH_4Cl solution (100 mL). were added, the layers were separated and the aqueous layer was extracted with EtOAc (3x 100 mL). All organic phases were combined and washed with brine (150 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography (CH/EA 19:1) yielded oxazole **16** as a colourless liquid (2.97 g, 12.4 mmol, 42%).

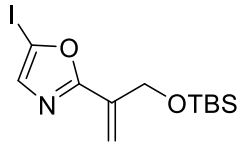
R$_f$ = 0.18 (CH/EA 19:1).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 7.60 (d, *J* = 0.8 Hz, 1H), 7.12 (d, *J* = 0.8 Hz, 1H), 6.08 (q, *J* = 1.9 Hz, 1H), 5.77 (td, *J* = 2.1, 1.4 Hz, 1H), 4.62 (t, *J* = 2.1 Hz, 2H), 0.95 (s, 9H), 0.12 (s, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 160.7, 138.3, 135.4, 127.9, 116.0, 61.7, 27.1, 26.1, 18.5,–5.3.

HRMS (EI (+), 70.0 eV): $[M]^+$ calcd for $[C_{12}H_{21}NO_2Si^{\bullet+}-CH_3^{\bullet}]^+$ = 224.1101; Found 224.1106.

2.10. 2-(3-((*tert*-Butyldimethylsilyl)oxy)prop-1-en-2-yl)-5-iodooxazole (17)



17

^{n}BuLi (2.5M in ^{n}hexane, 5.15 mL, 12.9 mmol, 1.10 equiv.) was slowly added to a solution of ^{i}Pr$_2$NH (2.30 mL, 16.4 mmol, 1.40 equiv.) in dry THF (110 mL) at 0 °C and stirred for 15 min. A solution of oxazole **16** (2.80 g, 11.7 mmol, 1.00 equiv.) in dry THF (12 mL) was added at −78 °C and stirred for 1 h. I_2 (3.27 g, 12.9 mmol, 1.10 equiv.) in dry THF (33 mL) was slowly added dropwise and the reaction stirred for additional 30 min. The solution was poured into a separating funnel with aq. sat. NH_4Cl solution (100 mL) and aq. sat. Na_2SO_3 solution (100 mL) and was shaken vigorously until decolouration. The layers were separated and the aqueous phase was extracted with EtOAc (3x 100 mL). All organic phases were combined and washed with brine (150 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography (CH/EA 19:1) yielded 5-iodooxazole **17** as a yellow liquid (3.62 g, 9.92 µmol, 85%).

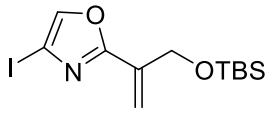
R$_f$ = 0.36 (CH/EA 19:1).

^{1}H-NMR (700 MHz, CD_2Cl_2): δ [ppm] = 7.62 (s, 1H), 6.09 (q, *J* = 1.8 Hz, 1H), 5.80 (td, *J* = 2.2, 1.3 Hz, 1H), 4.58 (t, *J* = 2.1 Hz, 2H), 0.94 (s, 9H), 0.11 (s, 6H).

^{13}C-NMR (175 MHz, CD_2Cl_2): δ [ppm] = 165.2, 136.5, 134.7, 116.9, 86.9, 61.4, 26.0, 18.5, –2.60, –5.3.

HRMS (EI (+), 70.0 eV): $[M^+]$ calcd for $[C_{12}H_{20}INO_2Si^{\bullet+}-CH_3^{\bullet}]^+$ = 350.0068; Found 350.0072.

2.11. 2-(3-((*tert*-Butyldimethylsilyl)oxy)prop-1-en-2-yl)-4-iodooxazole (18)



18

A stirring solution of (^{i}Pr)$_2$NH (700 µL, 4.97 mmol, 1.80 equiv.) in dry THF (30 mL) was cooled to 0 °C and ^{n}BuLi (2.5M in ^{n}hexane, 1.77 mL, 4.42 mmol, 1.60 equiv.) was added. The solution was allowed to stir for 15 min at this temperature, before it was cooled to –78 °C. 5-bromooxazole **10** (70.1 mg, 274 µmol, 0.10 equiv.) and 5-iodooxazole **17** (1.01 g, 2.76 mmol, 1.00 equiv.) were solved in THF (14 mL) and cooled to –78 °C. The LDA solution was transferred dropwise *via* a syringe pump into the oxazole solution over a period of 1 h and stirred for additional 2 min. Aq. sat. NH_4Cl solution (40 mL) was added and the reaction was allowed to warm to r.t. The layers were separated and the aqueous phase was extracted with Et_2O (3x 15 mL). All organic phases were combined and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash column chromatography over silica gel (CH/EA 50:1) afforded 4-iodooxazole **18** as an orange liquid (875 mg, 2.39 mmol, 87%).

$\boldsymbol{R}_f$ = 0.33 (CH/EA 50:1).

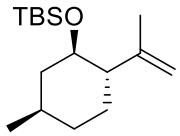
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 7.62 (s, 1H), 6.09 (q, *J* = 1.8 Hz, 1H), 5.80 (td, *J* = 2.2, 1.3 Hz, 1H), 4.58 (t, *J* = 2.1 Hz, 2H), 0.94 (s, 9H), 0.11 (s, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 161.9, 142.2, 134.8, 117.1, 82.7, 61.5, 26.0, 18.5, –5.2.

HRMS (EI (+), 70.0 eV): [M$^+$] calcd for [$C_{12}H_{20}INO_2Si^{\bullet+}$–$CH_3^{\bullet}$]$^+$ = 350.0068; Found 350.0072.

3. sp^3-sp^2-oxazole cross coupling studies

3.1. *tert*-Butyldimethyl(((*1R,2S,5R*)-5-methyl-2-(prop-1-en-2-yl)cyclohexyl)oxy)silane (40)



40

TBSCl (2.58 g, 17.1 mmol, 1.50 equiv.) was added slowly to a solution of (–)-isopulegol (**19**, 2.02 g, 13.1 mmol, 1.00 equiv.) and imidazole (1.34 g, 19.7 mmol, 1.50 equiv.) in dry CH_2Cl_2 (20 mL) at 0 °C. The solution was allowed to warm to r.t. and stirred for 16 h. Water (10 mL) was added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 20 mL). All organic phases were combined and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the

residue by flash chromatography over silica gel (CH/EA 99:1) yielded TBS ether **40** as a colourless liquid (3.52 g, 13.1 mmol, quant.).

R$_f$ = 0.55 (CH/EA 99:1).

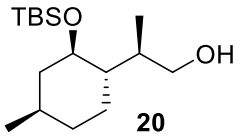
[α]$_D^{23}$ = –31.1° ($CHCl_3$, c = 1.0).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 4.74 (dt, *J* = 3.0, 1.4 Hz, 1H), 4.72 (td, *J* = 1.4, 0.7 Hz, 1H), 3.47 (ddd, *J* = 10.6, 9.8, 4.4 Hz, 1H), 1.87 (d, *J* = 22.5 Hz, 2H), 1.68 (t, *J* = 1.2 Hz, 3H), 1.64 – 1.57 (m, 2H), 1.49 – 1.37 (m, 1H), 1.37 – 1.23 (m, 1H), 1.00 (td, *J* = 12.3, 10.6 Hz, 1H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.85 (s, 9H), 0.02 (s, 3H), –0.01 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 148.1, 111.2, 73.5, 53.6, 45.3, 34.5, 31.8, 30.7, 26.0, 22.5, 21.0, 18.3,–3.7, –4.7.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{16}H_{32}OSi+H]^+$ = 269.2295; Found 269.2290.

3.2. *(R)*-2-((*1S,2R,4R*)-2-((*tert*-Butyldimethylsilyl)oxy)-4-methylcyclohexyl)propan-1-ol (20)



20

BH_3 (1.0m in THF, 39 mL, 39 mmol, 1.50 equiv.) was slowly added to a stirring solution of protected alcohol **40** (9.39 g, 35.0 mmol, 1.0 equiv.) in dry THF (244 mL) at 0 °C and stirred for 3 h. Water (9 mL) was added, followed by careful addition of aq. NaOH solution (7.5m, 14 mL, 3.00 equiv.) and H_2O_2 (30 vol% in water, 13 mL, 3.00 equiv.). The reaction was allowed to warm to r.t. and stirred for 30 min. The layers were separated and the aqueous phase was extracted with Et_2O (3x 200 mL). All organic phases were combined and washed with brine (200 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography over silica gel (CH/EA 12:1) gave alcohol **20** as a colourless oil (8.82 g, 30.8 mmol, 88%, *dr* = 12:1).***R***$_f$ = 0.22 (CH/EA 12:1).

[α]$_D^{20}$ = −17.9 ($CHCl_3$, c = 1.0).

Major epimer: **^{1}H-NMR (700 MHz, $CDCl_3$):** δ [ppm] = 3.63 (dd, *J* = 10.6, 5.8 Hz, 1H), 3.54 (td, *J* = 10.3, 4.2 Hz, 1H), 3.46 – 3.42 (m, 1H), 2.04 (dqd, *J* = 12.9, 7.2, 2.3 Hz, 1H), 1.92 – 1.86 (m, 1H), 1.77 (s, 1H), 1.65 – 1.59 (m, 2H), 1.41 – 1.33 (m, 2H), 1.11 – 1.03 (m, 1H), 1.01 – 0.96 (m, 1H), 0.94 (dd, *J* = 7.2, 0.9 Hz, 3H), 0.91 – 0.88 (m, 12H), 0.88 – 0.79 (m, 1H), 0.09 (d, *J* = 1.2 Hz, 6H).

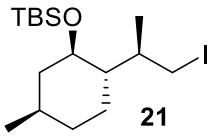
^{13}C-NMR (175 MHz, $CDCl_3$): δ [ppm] = 72.7, 66.2, 48.1, 45.7, 36.5, 34.9, 31.7, 27.4, 26.2, 22.4, 18.3, 14.3, –3.4, d –4.1.

Minor epimer: **^{1}H-NMR (700 MHz, $CDCl_3$):** δ [ppm] = 3.50 – 3.47 (m, 2H), 3.42 (td, *J* = 10.3, 4.3 Hz, 1H), 2.21 (hd, *J* = 7.1, 2.6 Hz, 1H), 1.88 (dtd, *J* = 12.4, 3.9, 2.0 Hz, 1H), 1.62 (dp, *J* = 12.7, 3.2 Hz, 1H), 1.52 (dq, *J* = 13.3, 3.4 Hz, 1H), 1.44 – 1.33 (m, 2H), 1.00 (dddd, *J* = 18.8, 13.0, 9.3, 3.4 Hz, 2H), 0.90 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.77 (dt, *J* = 7.0, 0.8 Hz, 3H), 0.07 (s, 3H), 0.06 (s, 3H).

^{13}C-NMR (175 MHz, $CDCl_3$): δ [ppm] = 72.1, 67.5, 45.5, 45.4, 34.5, 34.1, 31.7, 27.1, 23.8, 22.5, 18.2, 11.1, –3.6, –4.6.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{16}H_{34}O_2Si+H]^+$= 287.2401; Found 287.2409.

3.3. *tert*-Butyl(((1*R*,2*S*,5*R*)-2-((*R*)-1-iodopropan-2-yl)-5-methylcyclohexyl)oxy)dimethylsilane (21)



I_2 (1.46 g, 5.76 mmol, 1.50 equiv.) was added to a stirring solution of triphenylphosphine (1.71 g, 6.53 mmol, 1.70 equiv.) and imidazole (784 mg, 11.5 mmol, 3.00 equiv.) in dry CH_2Cl_2 at 0 °C and stirred for 15 min. A solution of alcohol **20** (1.13 g, 4.10 mmol, 1.00 equiv.) in dry CH_2Cl_2 (84 mL) was added slowly and the reaction was allowed to warm to r.t. and stirred for 2.5 h. Aq. pH 7-buffer solution (7 mL) and aq. sat. Na_2SO_3 solution (7 mL) were added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 35 mL). All organic phases were combined and washed with brine (60 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 99:1) yielded alkyl iodide **21** as a colourless liquid (1.10 g, 2.78 mmol, 68%).

***R*$_f$** = 0.55 (CH/EA 99:1).

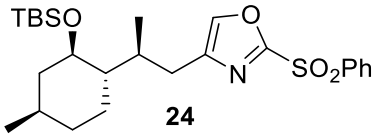
$[\alpha]_D^{20}$ = −51.4 ($CHCl_3$, c = 0.5).

^{1}H-NMR (700 MHz, $CDCl_3$): δ [ppm] = 3.47 (td, *J* = 10.3, 4.2 Hz, 1H), 3.34 (dd, *J* = 9.4, 3.5 Hz, 1H), 2.93 (dd, *J* = 11.0, 9.3 Hz, 1H), 2.32 (tp, *J* = 11.0, 7.4, 4.0 Hz, 1H), 1.91 – 1.84 (m, 1H), 1.63 (ddt, *J* = 13.2, 9.8, 3.2 Hz, 2H), 1.35 (td, *J* = 11.0, 10.3, 4.0 Hz, 2H), 1.09 (d, *J* = 7.0 Hz, 3H), 1.04 – 0.94 (m, 2H), 0.89 (d, *J* = 2.5 Hz, 12H), 0.88 – 0.79 (m, 1H), 0.09 (d, *J* = 13.9 Hz, 6H).

^{13}C-NMR (175 MHz, $CDCl_3$): δ [ppm] = 72.3, 50.5, 45.5, 36.0, 34.6, 31.7, 26.2, 24.7, 22.4, 18.8, 18.2, 13.1, –3.4, –4.4.

HRMS (EI (+), 70.0 eV): $[M^+]$ calcd for $[C_{16}H_{33}OISi^{\bullet+}-{}^tBu^{\bullet}]^+$= 339.0641; Found 339.0640.

3.4. 4-((*S*)-2-((1*S*,2*R*,4*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-4-methylcyclohexyl)propyl)-2-(phenylsulfonyl)oxazole (24)



24

9-BBN-OMe (1.0M in ^{n}hexane, 74 µL, 73.8 µmol, 1.50 equiv.) was added to a stirring solution of alkyl iodide **21** at −78 °C. ^{t}BuLi (1.7M in ^{n}pentane, 80 µL, 134 µmol, 2.80 equiv.) was added and the solution was allowed to warm to room temperature and stirred for 1 h. Aq. Cs_2CO_3 solution (3.0M in water, 43 µL, 2.74 equiv.) was added to a solution of iodoxazole **13** (15.7 mg, 46.9 µmol, 1.00 equiv.), $AsPh_3$ (4.31 mg, 14.1µmol, 0.30 equiv.) and Pd(dtpbpf)Cl_2 (3.06 mg, 4.69 µmol, 0.10 equiv.) in dry THF (280 µL). The solution was degassed *via* freeze-pump-thaw cycles (3x) and the reaction was sealed and covered in aluminium foil and was allowed to stir for 20 h at r.t. Water (2 mL) and Et_2O (4 mL) were added, the layers were separated and the aqueous phase was extracted with Et_2O (3x 3 mL). All organic phases were combined and washed with aq. sat. $NaHCO_3$ solution (4 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/CH_2Cl_2 1:1) yielded alkyl oxazole **24** as a yellow oil (15.6 mg, 31.2 µmol, 69%).

R_f = 0.38 (CH:EA, 3:2).

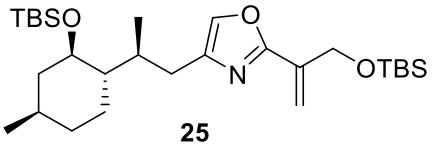
$[\alpha]_D^{20}$ = –20.0° ($CHCl_3$, c = 0.3)

^{1}H-NMR (700 MHz, d_6-acetone): δ [ppm] = 8.08 – 8.04 (m, 2H), 7.94 (dd, *J* = 1.3, 0.7 Hz, 1H), 7.87 – 7.82 (m, 1H), 7.75 – 7.71 (m, 2H), 2.62 (ddd, *J* = 14.7, 3.4, 1.3 Hz, 1H), 2.46 – 2.38 (m, 1H), 2.24 (ddd, *J* = 14.6, 11.4, 0.7 Hz, 1H), 1.99 – 1.93 (m, 1H), 1.69 – 1.63 (m, 2H), 1.45 (ddt, *J* = 12.0, 6.9, 3.5 Hz, 1H), 1.26 – 1.20 (m, 1H), 1.11 – 1.03 (m, 1H), 1.01 – 0.93 (m, 1H), 0.91 – 0.89 (m, 3H), 0.88 (s, 10H), 0.83 (d, *J* = 7.0 Hz, 3H), 0.08 (s, 3H), 0.06 (s, 3H).

^{13}C-NMR (175 MHz, $CDCl_3$): δ [ppm] = 158.7, 144.2, 140.2, 139.4, 136.0, 130.7, 129.4, 72.5, 51.4, 46.5, 35.4, 32.2, 31.0, 28.4, 27.5, 26.5, 24.9, 22.6, 18.6, 18.1, –3.33, –4.3.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ cald for $[C_{25}H_{39}NO_4SSi+H]^+$= 500.2261; Found 500.2267.

3.5. 4-((*S*)-2-((1*S*,2*R*,4*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-4-methylcyclohexyl)propyl)-2-(3-((*tert*-butyldimethylsilyl)oxy)prop-1-en-2-yl)oxazole (25)



25

Anhydrous LiCl (12.7 mg, 300 µmol, 4.20 equiv.) was heated under vacuum at 150–170 °C for 5 min. Zinc powder (325 mesh, 9.15 mg, 140 µmol, 1.96 equiv.) was added and dried again under vacuum at 150–170 °C for 5 min. The reaction flask was flushed with argon (3x) and dry THF (160 µL) was added. $C_2H_4Br_2$ (0.2 g/mL in dry THF, 6 µL, 5.00 µmol, 0.07 equiv.) and TMSCl (7.5 mg/mL in dry THF, 16 µL, 1.00 µmol, 1.40 mol-%) were added to the stirring suspension and the reaction was heated to 50 °C for 10 min. A solution of alkyl iodide **21** (39.6 mg, 100 µmol, 1.40 equiv.) in dry THF (540 µL) was added and stirred for 2 h. The solution was allowed to cool down to r.t. and a solution of Pd(dtpbf)Cl_2 (12.6 mg, 19.3 µmol, 0.05 equiv.) in dry NMP (690 µL), a solution of $AsPh_3$ (35.4 mg, 116 µmol, 0.30 equiv) and iodooxazole **18** (26.1 mg, 71.4 µmol, 1.00 equiv.) in dry THF (690 µL) were added. The flask was covered in aluminium foil and the reaction was allowed to stir for 2 h. EtOAc (2 mL) and aq. sat. NH_4Cl solution (2 mL) were added, the layers were separated and the aqueous phase was extracted with EtOAc (3x 5 mL). All organic phases were combined, washed with water (2x 15mL) and brine (5 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography over silica gel (CH 100%→CH/EA 50:1) yielded alkyl oxazole **25** as a yellow oil (18.5 mg, 36.4 µmol, 51%).$\boldsymbol{R_f}$ = 0.38 (CH/EA 50:1).

$[\alpha]_D^{20}$ = –24.4° (CH_2Cl_2, c = 0.9).

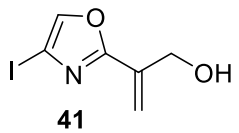
^{1}H-NMR (700 MHz, CD_2Cl_2): δ [ppm] = 7.31 (q, *J* = 0.6 Hz, 1H), 5.96 (q, *J* = 1.9 Hz, 1H), 5.66 (q, *J* = 2.0 Hz, 1H), 4.62 (t, *J* = 2.0 Hz, 0H), 4.56 (t, *J* = 2.0 Hz, 2H), 3.56 (td, *J* = 10.2, 4.4 Hz, 1H), 2.54 (dd, *J* = 14.4, 3.3 Hz, 1H), 2.44 – 2.37 (m, 1H), 2.11 (dd, *J* = 14.1, 11.5 Hz, 1H), 1.96 – 1.91 (m, 1H), 1.71 – 1.63 (m, 2H), 1.41 (tqt, *J* = 16.6, 6.5, 3.4 Hz, 1H), 1.28 – 1.22 (m, 1H), 1.08 – 0.99 (m, 1H), 1.00 – 0.97 (m, 1H), 0.97 – 0.92 (m, 12H), 0.91 (s, 9H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.12 (s, 3H), 0.11 (s, 6H), 0.10 (s, 3H).

^{13}C-NMR (125 MHz, CD_2Cl_2): δ [ppm] = 160.1, 142.0, 136.5, 134.7, 114.8, 72.4, 62.3, 51.0, 46.2, 32.2, 30.7, 28.5, 27.5, 26.4, 26.2, 24.9, 22.6, 18.8, 18.5, 18.1, 1.3, –3.3, –4.2, –5.14.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ cald for $[C_{28}H_{53}NO_3Si_2+H]^+$ = 508.3637; Found 508.3642.

3.6. Additional Suzuki cross coupling studies

3.6.1. 2-(4-iodooxazol-2-yl)prop-2-en-1-ol (41)



41

(+)-CSA (27.8 mg, 120 µmol, 0.10 equiv.) was added to a solution of TBS Ether **18** (440 mg, 1.20 mmol, 1.00 equiv.) in CH_2Cl_2/MeOH (2:1, 7.2 mL) at r.t. and stirred for 4 h. NEt_3 (500 µL) was added and the solvent was removed *in vacuo*. Purification of the residue by flash column chromatography over silica gel (CH/EA 3:1) yielded allyl alcohol **41** as a yellowish oil (256 mg, 1.02 mmol, 85%).

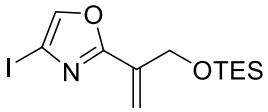
$\boldsymbol{R_f}$ = 0.24 (CH/EA 3:1).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 7.63 (s, 1H), 6.06 (t, *J* = 0.8 Hz, 1H), 5.67 (td, *J* = 1.3, 0.6 Hz, 1H), 4.52 (ddd, *J* = 6.8, 1.4, 0.7 Hz, 2H), 2.75 (t, *J* = 6.8 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 162.2, 142.5, 134.5, 119.1, 82.6, 63.2.

HRMS (ESI (+), 6.0 eV): $[M+Na]^+$ calcd for $[C_6H_6INO_2+Na]^+$ = 273.9335; Found 273.9344.

3.6.2. 4-Iodo-2-(3-((triethylsilyl)oxy)prop-1-en-2-yl)oxazole (26)



26

TESCl (200 µL, 1.20 mmol, 1.20 equiv.) was added to a solution of alcohol **41** (250 mg, 996 µmol, 1.00 equiv.) and imidazole (163 mg, 2.48 mmol, 2.50 equiv.) in dry CH_2Cl_2 (8 mL) at 0 °C. The solution was allowed to warm to r.t. and stirred for 3 h. Water (10 mL) was added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 4 mL). All organic phases were combined and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 50:1) yielded TES ether **26** as a yellow liquid (305 mg, 834 µmol, 84%).

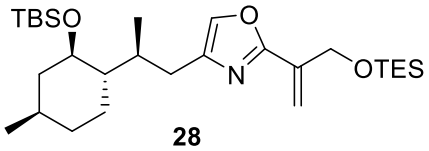
$\boldsymbol{R_f}$ = 0.33 (CH/EA 50:1).

^{1}H-NMR (400 MHz, CD_2Cl_2): δ [ppm] = 7.70 (s, 1H), 6.11 (q, *J* = 1.7 Hz, 1H), 5.91 – 5.75 (m, 1H), 4.60 (t, *J* = 2.0 Hz, 2H), 1.01 (q, *J* = 8.3 Hz, 9H), 0.71 (q, *J* = 7.9 Hz, 6H).

^{13}C-NMR (175 MHz, CD_2Cl_2): δ [ppm] = 161.7, 142.3, 134.8, 116.7, 82.5, 61.1, 6.5, 4.3.

HRMS (EI (+), 70.0 eV): $[M]^+$ calcd for $[C_{12}H_{20}INO_2Si^{\bullet+}-Et^{\bullet}]^+$ = 335.9917; Found 335.9910.

3.6.3. 4-((*S*)-2-((1*S*,2*R*,4*R*)-2-((*tert*-butyldimethylsilyl)oxy)-4-methylcyclohexyl)propyl)-2-(3-((triethylsilyl)oxy)prop-1-en-2-yl)oxazole (28)



9-BBN-OMe (1.0M in ^{n}hexane, 24 µL, 73.8 µmol, 1.50 equiv.) was added to a stirring solution of alkyl iodide **21** at −78 °C. ^{t}BuLi (1.7M in ^{n}pentane, 26 µL, 43.9 µmol, 2.80 equiv.) was added and the solution was allowed to warm to room temperature and stirred for 1 h. A solution of Pd(dtbpf)Cl_2 (997 µg, 1.53 µmol, 0.10 equiv.) in dry DMF (28 µL), a solution of iodooxazole **26** (5.60 mg, 15.3 µmol, 1.00 equiv.) and $AsPh_3$ (1.41 mg, 4.60 µmol, 0.30 equiv.) were added, followed by addition of aq. Cs_2CO_3 solution (3.0m, 43 µL, 2.74 equiv.). The solution was degassed *via* freeze-pump-thaw cycles (3x), sealed and the flask was covered in aluminium foil. The reaction stirred overnight (20 h). Water (400 µL) and CH_2Cl_2 (600 µL) were added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 400 µL). All organic phases were combined and washed with aq. sat. $NaHCO_3$ solution (400 µL) and brine (400 µL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 100:0→50:1) yielded alkyl oxazole **28** as a yellow oil (5.80 mg, 11.4 µmol, 75%).

R_f = 0.28 (CH/EA 50:1).

$[\alpha]_D^{23}$ = –15.7° (CH_2Cl_2, c = 1.0).

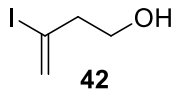
^{1}H-NMR (700 MHz, CD_2Cl_2): δ [ppm] = 7.32 – 7.30 (m, 1H), 5.96 (q, *J* = 1.8 Hz, 1H), 5.69 (q, *J* = 2.0 Hz, 1H), 4.56 (t, *J* = 2.0 Hz, 2H), 3.56 (td, *J* = 10.2, 4.4 Hz, 1H), 2.54 (ddd, *J* = 14.4, 3.3, 1.3 Hz, 1H), 2.44 – 2.37 (m, 1H), 2.11 (dd, *J* = 14.4, 11.5 Hz, 1H), 1.97 – 1.90 (m, 1H), 1.71 – 1.62 (m, 2H), 1.41 (tdt, *J* = 11.8, 6.6, 3.4 Hz, 1H), 1.29 – 1.22 (m, 1H), 1.08 – 1.01 (m, 1H), 0.98 (td, *J* = 8.0, 1.4 Hz, 9H), 0.91 (s, 9H), 0.90 – 0.88 (m, 3H), 0.89 – 0.81 (m, 4H), 0.67 (q, *J* = 8.0 Hz, 6H), 0.13 (s, 3H), 0.10 (s, 3H).

^{13}C-NMR (175 MHz, CD_2Cl_2): δ [ppm] = 160.1, 142.9, 142.0, 136.5, 134.7, 117.3, 114.8, 72.4, 61.9, 51.0, 46.2, 35.3, 32.2, 30.7, 28.5, 26.4, 24.9, 22.6, 18.5, 18.1, 7.1, 5.0, –3.3, –4.2.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{28}H_{53}NO_3Si_2+H]^+$ = 508.3637; Found 508.3634.

4. Implementation of previous protocols for analog synthesis of ajudazol A

4.1. 3-Iodobut-3-en-1-ol (42)



42

TMSCl (78 mL), 616 mmol, 2.00 equiv.), water (5.55 mL), 308 mmol, 1.00 equiv,) and 3-butyn-1-ol (20 mL, 308 mmol, 1.00 equiv.) were added to a stirring solution of NaI (92.4 g, 616 mmol, 2.00 equiv.) in CH_3CN (590 mL) at 0 °C and stirred for 1.5 h. Aq. sat. Na_2SO_3 solution (150 mL) was added, the layers were separated and the aqueous phase was extracted with Et_2O (3x 200 mL). All organic phases were combined and washed with brine (400 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography over silica gel (CH/EA 4:1) yielded alcohol **42** as an orange liquid (14.8 g, 80.4 mmol, 46%).

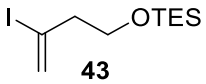
$\boldsymbol{R}_f$ = 0.22 (CH/EA 4:1).

^{1}H-NMR (700 MHz, d$_6$-acetone): δ [ppm] = 6.16 (q, *J* = 1.4 Hz, 1H), 5.76 (dt, *J* = 1.3, 0.6 Hz, 1H), 3.77 – 3.58 (m, 3H), 2.60 (tdd, *J* = 6.4, 1.3, 0.6 Hz, 2H).

^{13}C-NMR (175 MHz, d$_6$-acetone): δ [ppm] = 127.9, 109.0, 61.4, 49.2.

HRMS (EI (+), 70.0 eV): $[M]^{\bullet+}$ calcd for $[C_4H_7IO]^{\bullet+}$ = 283.0015; Found 283.0013.

4.2. Triethyl((3-iodobut-3-en-1-yl)oxy)silane (43)



43

TESCl (3.61 mL, 21.5 mmol, 1.40 equiv.) was added dropwise to a stirring solution of alcohol **42** (3.04 g, 15.4 mmol, 1.00 equiv.) and imidazole (2.93 g, 93.8 mmol, 2.80 equiv.) in dry CH_2Cl_2 (55 mL) at 0 °C. The reaction was allowed to warm to r.t. and stirred for 2 h. Water (40 mL) was added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 40 mL). All organic phases were combined and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash column chromatography over silica gel (CH/EA 99:1) yielded TES ether **43** as a yellow liquid (9.27 g, 31.1 mmol, quant.).

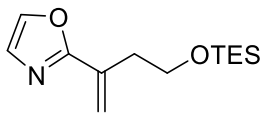
$\boldsymbol{R}_f$ = 0.43 (CH/EA 99:1).

^{1}H-NMR (700 MHz, d$_6$-acetone): δ [ppm] = 6.17 (q, *J* = 1.4 Hz, 1H), 5.78 (d, *J* = 1.4 Hz, 1H), 3.76 (t, *J* = 6.2 Hz, 2H), 2.60 (td, *J* = 6.2, 1.3 Hz, 2H), 1.02 – 0.91 (m, 9H), 0.62 (qd, *J* = 8.0, 1.2 Hz, 6H).

^{13}C-NMR (175 MHz, d$_6$-acetone): δ [ppm] = 127.3, 107.8, 61.2, 48.2, 6.1, 4.1.

HRMS (EI (+), 70.0 eV): $[M]^{\bullet+}$ calcd for $[C_{10}H_{21}IOSi]^{\bullet+}$ = 283.0015; Found 283.0013.

4.3. 2-(4-((Triethylsilyl)oxy)but-1-en-2-yl)oxazole (44)



44

$ZnCl_2$ (5.94 g, 43.6 mmol, 1.40 equiv.) was heated under vacuum until free-flowing, recooled to r.t. and suspended in dry THF (22 mL). ^{n}BuLi (2.5M in ^{n}hexane, 9.77 mL, 24.4 mmol, 1.68 equiv.) was added dropwise to a stirring solution of oxazole (**6**, 1.34 mL, 20.4 mmol, 1.40 equiv.) in dry THF (80 mL) at −78 °C and stirred for 30 min. The solution was transferred via cannula to the $ZnCl_2$ suspension and was allowed to warm up to r.t. over a period of 15 min. A solution of iodoalkene **43** (4.54 g, 14.5 mmol, 1.00 equiv.) in dry THF (8.0 mL) was slowly added, followed by addition of $Pd(PPh_3)_4$ (420 mg, 360 µmol, 2.5mol-%). The reaction was sealed and heated to 60 °C, stirred for 2 h and was concentrated *in vacuo*. EtOAc (50 mL) and aq. sat. NH_4Cl solution (50 mL) were added, the layers were separated and the aqueous phase was extracted with EtOAc (3x 50 mL). All organic phases were combined and washed with brine (50 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography (CH/EA 19:1) yielded oxazole **44** as a colourless liquid (2.66 g, 10.5 mmol, 72%).

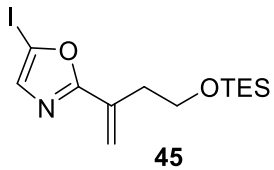
$\boldsymbol{R_f}$ = 0.18 (CH/EA 19:1).

^{1}H-NMR (500 MHz, CD_2Cl_2): δ [ppm] = 7.61 (d, *J* = 0.8 Hz, 1H), 7.12 (d, *J* = 0.8 Hz, 1H), 6.00 (d, *J* = 1.3 Hz, 1H), 5.43 (q, *J* = 1.2 Hz, 1H), 3.83 (t, *J* = 6.7 Hz, 2H), 2.74 (td, *J* = 6.7, 1.2 Hz, 2H), 0.93 (t, *J* = 8.0 Hz, 9H), 0.57 (q, *J* = 7.7 Hz, 6H).

^{13}C-NMR (125 MHz, CD_2Cl_2): δ [ppm] = 162.8, 138.9, 133.7, 128.5, 119.3, 62.0, 36.9, 7.1, 4.9.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{13}H_{23}NO_2Si+H]^+$ = 254.1571; Found 254.1563.

4.4. 5-Iodo-2-(4-((triethylsilyl)oxy)but-1-en-2-yl)oxazole (45)



45

^{n}BuLi (2.5M in ^{n}hexane, 4.36 mL, 10.9 mmol, 1.10 equiv.) was slowly added to a solution of ^{i}Pr$_2$NH (1.96 mL, 13.9 mmol, 1.40 equiv.) in dry THF (100 mL) at 0 °C and stirred for 15 min. The solution was

cooled to −78 °C and oxazole **44** (2.51 g, 9.90 mmol, 1.00 equiv.) in dry THF (11 mL) was added and the reaction stirred for 1 h. A solution of I_2 (3.27 g, 12.9 mmol, 1.10 equiv.) in dry THF (28 mL) was slowly added and the reaction stirred for additional 0.5 h. Aq. sat. NH_4Cl solution (30 mL) and aq. sat. Na_2SO_3 solution (30 mL) were added and the reaction was allowed to warm up to r.t. The layers were separated and aqueous phase was extracted with EtOAc (3x 80 mL). All organic phases were combined and washed with brine (80 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography (CH/EA 19:1) yielded 5-iodooxazole **45** as an orange solid (3.07 g, 8.09 mmol, 82%).

R$_f$ = 0.39 (CH/EA 19:1).

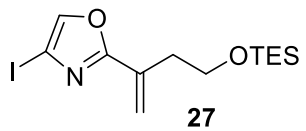
Mp.: 39-41 °C

^{1}H-NMR (500 MHz, CD_2Cl_2): δ [ppm] = 7.15 (s, 1H), 5.99 (d, *J* = 1.0 Hz, 1H), 5.44 (q, *J* = 1.2 Hz, 1H), 3.81 (t, *J* = 6.7 Hz, 2H), 2.71 (td, *J* = 6.7, 1.2 Hz, 2H), 0.93 (t, *J* = 7.9 Hz, 9H), 0.57 (q, *J* = 7.9 Hz, 6H).

^{13}C-NMR (125 MHz, CD_2Cl_2): δ [ppm] = 167.4, 137.2, 133.0, 120.2, 87.1, 61.9, 36.6, 7.1, 4.9.

HRMS (EI (+), 70.0 eV): $[M]^+$ calcd for $[C_{13}H_{22}INO_2Si^{\bullet+}-Et^{\bullet}]^+$ = 350.0068; Found 350.0076.

4.5. 4-Iodo-2-(4-((triethylsilyl)oxy)but-1-en-2-yl)oxazole (27)



27

A stirring solution of $(^iPr)_2NH$ (1.90 mL, 13.4 mmol, 1.80 equiv.) in dry THF (80 mL) was cooled to 0 °C and ^{n}BuLi (2.5M in ^{n}hexane, 4.78 mL, 11.9 mmol, 1.60 equiv.) was added. The solution was allowed to stir for 15 min, before it was cooled to –78 °C. 5-bromooxazole **10** (191 mg, 746 µmol, 0.10 equiv.) and 5-iodooxazole **45** (2.83 g, 7.46 mmol, 1.00 equiv.) were solved in THF (37 mL) and cooled to –78 °C. The LDA solution was transferred dropwise *via* a syringe pump into the oxazole solution over a period of 1 h and was allowed to stir for additional 2 min. Aq. sat. NH_4Cl (80 mL) was added and the solution was allowed to warm to r.t. slowly. The layers were separated and the aqueous phase was extracted with EtOAc (3x 60 mL). All organic phases were combined and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash column chromatography over silica gel (CH/EA 50:1) afforded 4-iodooxazole **27** as an orange liquid (2.44 g, 6.43 mmol, 86%).

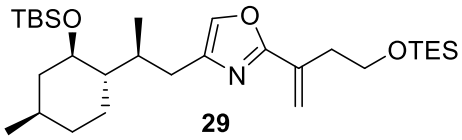
R$_f$ = 0.22 (CH/EA 50:1).

^{1}H-NMR (500 MHz, CD_2Cl_2): δ [ppm] = 7.64 (s, 1H), 6.03 (d, *J* = 0.9 Hz, 1H), 5.48 (q, *J* = 1.2 Hz, 1H), 3.82 (t, *J* = 6.6 Hz, 2H), 2.71 (td, *J* = 6.6, 1.2 Hz, 2H), 0.93 (t, *J* = 7.9 Hz, 9H), 0.57 (q, *J* = 7.9 Hz, 6H).

^{13}C-NMR (125 MHz, CD_2Cl_2): δ [ppm] = 164.1, 142.9, 132.9, 130.2, 120.6, 83.2, 61.8, 36.6, 7.1, 4.9.

HRMS (EI (+), 70.0 eV): $[M]^+$ calcd for $[C_{13}H_{22}INO_2Si^{\bullet+}-Et^{\bullet}]^+$ = 350.0068; Found 350.0074.

4.6. 4-((*S*)-2-((1*S*,2*R*,4*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-4-methylcyclohexyl)propyl)-2-(4-((triethylsilyl)oxy)but-1-en-2-yl)oxazole (29)



29

Anhydrous LiCl (159 mg, 3.75 mmol, 4.20 equiv.) was heated under vacuum at 150–170 °C for 5 min. Zinc powder (325 mesh, 114 mg, 1.75 mmol, 1.96 equiv.) was added and dried also under vacuum at 150–170 °C for 5 min. The reaction flask was flushed with argon (3x) and dry THF (360 µL) was added. $C_2H_4Br_2$ (6 µL, 62.5 µmol, 0.07 equiv.) and TMSCl (0.07m in dry THF, 180 µL, 13.8 µmol, 1.40 mol%) were added to the stirring suspension and the reaction was heated to 50 °C for 10 min. A solution of alkyl iodide **21** (495 mg, 1.25 mmol, 1.40 equiv.) in dry THF (540 µL) was added and stirred for 2 h. The solution was allowed to cool down to r.t. and a solution of Pd(dtpbf)Cl_2 (29.1 mg, 44.7 µmol, 0.05 equiv.) in dry NMP (1.1 mL), followed by a solution of $AsPh_3$ (82.1 mg, 268 µmol, 0.30 equiv) and iodooxazole **27** (339 mg, 893 µmol, 1.00 equiv.) in dry THF (1.1 mL) were added. The flask was covered in aluminium foil and was allowed to stir for 2 h. EtOAc (4 mL) and aq. sat. NH_4Cl solution (4 mL) were added, the layers were separated and the aqueous phase was extracted with EtOAc (3x 9 mL). All organic phases were combined and washed with brine (10 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography over silica gel (CH/EA 50:1) yielded alkyl oxazole **29** as a yellow oil (321 mg, 615 µmol, 69%).$\boldsymbol{R_f}$ = 0.26 (CH/EA 50:1).

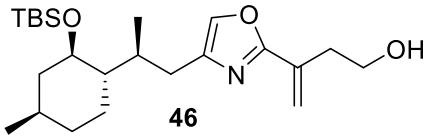
$\mathbf{[\alpha]_D^{20}}$ = −27.0 (MeOH, c = 1.0).

^{1}H-NMR (700 MHz, d_6-acetone): δ [ppm] = 7.55 (d, *J* = 0.8 Hz, 1H), 5.93 (d, *J* = 1.4 Hz, 1H), 5.42 (q, *J* = 1.3 Hz, 1H), 3.87 (td, *J* = 6.6, 2.1 Hz, 2H), 3.66 (td, *J* = 10.2, 4.4 Hz, 1H), 2.73 (tdd, *J* = 6.6, 2.3, 1.1 Hz, 2H), 2.59 (ddd, *J* = 14.2, 3.4, 1.3 Hz, 1H), 2.56 – 2.49 (m, 1H), 2.19 – 2.12 (m, 1H), 1.99 (dddd, *J* = 12.2, 4.3, 3.4, 2.0 Hz, 1H), 1.73 – 1.65 (m, 2H), 1.47 (dddt, *J* = 15.3, 8.9, 6.6, 3.3 Hz, 1H), 1.27 (ddd, *J* = 11.9, 10.0, 3.7 Hz, 1H), 1.11 (qd, *J* = 14.5, 13.8, 4.1 Hz, 1H), 1.00 (td, *J* = 12.2, 10.5 Hz, 1H), 0.96 – 0.89 (m, 21H), 0.90 – 0.87 (m, 1H), 0.87 (d, *J* = 7.0 Hz, 3H), 0.57 (q, *J* = 7.9 Hz, 6H), 0.18 (s, 3H), 0.12 (s, 3H).

^{13}C-NMR (175 MHz, d_6-acetone): δ [ppm] = 162.1, 142.4, 135.7, 134.3, 118.6, 72.5, 62.2, 51.5, 46.6, 37.3, 35.5, 32.3, 30.8, 28.3, 26.5, 24.9, 22.6, 18.7, 18.3, 7.1, 5.1, -3.3, –4.2.

HRMS (ESI (+), 5.0 eV): $[M+H]^+$ calcd for $[C_{29}H_{55}NO_3Si_2+H]^+$ = 522.3793; Found 522.3791.

4.7. 3-(4-((*S*)-2-((1*S*,2*R*,4*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-4-methylcyclohexyl)propyl)-oxazol-2-yl)but-3-en-1-ol (46)



46

HCO_2H (5 wt-% in MeOH, 4 mL, 12.0 equiv.) was added to a stirring solution of TES ether **29** (215 mg, 413 µmol, 1.00 equiv.) in CH_2Cl_2 (2 mL) at 0°C and stirred for 1.5 h. Aq. sat. $NaHCO_3$ solution (9 mL) was added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 5 mL). All organic phases were combined, washed with brine (9 mL) and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash column chromatography (CH/EA 4:1) yielded alcohol **46** as a colourless oil (146 mg, 358 µmol, 87%).

$\boldsymbol{R_f}$ = 0.31 (CH/EA 4:1).

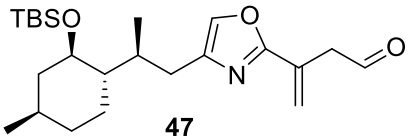
$\mathbf{[\alpha]_D^{20}}$ = −32.0 (MeOH, c = 1.0).

^{1}H-NMR (700 MHz, d$_6$-acetone): δ [ppm] = 0.12 (s, 3H), 0.17 (s, 3H), 0.87 (d, *J* = 7.1 Hz, 4H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.92 (s, 9H), 1.00 (td, *J* = 12.2, 10.5 Hz, 1H), 1.11 (qd, *J* = 14.4, 13.7, 4.1 Hz, 1H), 1.26 (tdd, *J* = 9.9, 3.2, 2.2 Hz, 1H), 1.47 (dddt, *J* = 15.3, 8.8, 6.6, 3.3 Hz, 1H), 1.65 – 1.73 (m, 2H), 1.99 (dddd, *J* = 12.3, 4.3, 3.4, 2.0 Hz, 1H), 2.12 – 2.19 (m, 1H), 2.46 – 2.54 (m, 1H), 2.59 (ddd, *J* = 14.3, 3.4, 1.3 Hz, 1H), 2.73 (tdd, *J* = 6.4, 4.9, 1.1 Hz, 2H), 3.66 (dd, *J* = 10.1, 4.6 Hz, 1H), 3.72 – 3.82 (m, 2H), 5.43 (q, *J* = 1.3 Hz, 1H), 5.92 (d, *J* = 1.3 Hz, 1H), 7.56 (dd, *J* = 1.4, 0.6 Hz, 1H).

^{13}C-NMR (175 MHz, d$_6$-acetone): δ [ppm] = 162.4, 142.4, 135.7, 134.8, 118.5, 72.5, 61.5, 61.4, 51.5, 46.6, 37.4, 35.5, 32.3, 30.8, 28.4, 26.5, 24.9, 22.6, 18.3, –3.4, –4.2.

HRMS (ESI (+), 5.0 eV): $[M+H]^+$ calcd for $[C_{23}H_{41}NO_3Si+H]^+$ = 408.2928; Found 408.32924.

4.8. 3-(4-((*S*)-2-((1*S*,2*R*,4*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-4-methylcyclohexyl)propyl)oxazol-2-yl)but-3-enal (47)



47

IBX (309 mg, 1.10 mmol, 3.00 equiv.) was added to a stirring solution of alcohol **46** (149.8 mg, 368 µmol, 1.00 equiv.) in EtOAc (3.7 mL) and refluxed for 4 h. The precipitate was filtered off over a plug of silica gel and rinsed with EtOAc. Concentration of the filtrate *in vacuo* yielded aldehyde **47** as a yellow oil (143 mg, 352 µmol, 96%).

R_f = 0.26 (CH/EA 15:1).

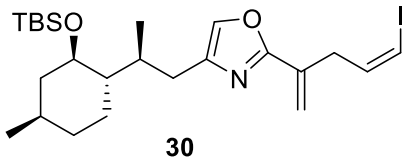
$[\alpha]_D^{20}$ = −32.5 (MeOH, c = 0.4).

^{1}H-NMR (400 MHz, d_6-acetone): δ [ppm] = 9.73 (t, *J* = 1.6 Hz, 1H), 7.60 (d, *J* = 1.3 Hz, 1H), 6.10 (d, *J* = 0.9 Hz, 1H), 5.56 (q, *J* = 1.1 Hz, 1H), 3.67 – 3.62 (m, 1H), 3.61 (dt, *J* = 7.6, 1.4 Hz, 2H), 2.57 (ddd, *J* = 14.2, 3.3, 1.4 Hz, 1H), 2.54 – 2.44 (m, 2H), 2.15 (dd, *J* = 14.2, 11.5 Hz, 1H), 1.98 (dtd, *J* = 12.2, 4.1, 1.9 Hz, 2H), 1.74 – 1.64 (m, 3H), 1.47 (ddddd, *J* = 16.4, 14.2, 11.2, 7.3, 3.9 Hz, 1H), 1.29 – 1.22 (m, 1H), 1.20 (td, *J* = 7.2, 1.8 Hz, 1H), 1.10 (qd, *J* = 14.2, 13.6, 3.9 Hz, 1H), 1.03 – 0.93 (m, 2H), 0.93 – 0.90 (m, 15H), 0.91 – 0.86 (m, 1H), 0.85 – 0.83 (m, 3H), 0.15 (s, 3H), 0.11 (s, 3H).

^{13}C-NMR (175 MHz, d_6-acetone): δ [ppm] = 199.0, 161.7, 142.6, 136.3, 129.9, 120.7, 72.5, 51.5, 47.7, 46.6, 35.5, 32.3, 30.7, 28.2, 26.5, 24.8, 22.6, 18.7, 18.3, –3.4, –4.2.

HRMS (APCI (+), 5.0 eV): $[M+H]^+$ calcd for for $[C_{23}H_{39}NO_3Si+H]^+$ = 406.2772; Found 406.2772.

4.9. 4-((*S*)-2-((1*S*,2*R*,4*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-4-methylcyclohexyl)propyl)-2-((*Z*)-5-iodopenta-1,4-dien-2-yl)oxazole (30)



30

NaHMDS (1.0m in THF, 60 µL, 1.30 equiv.) was added to a stirring suspension of (iodomethyl)triphenylphosphonium iodide (31.9 mg, 60.3 mmol, 1.30 equiv.) in dry THF (200 µL) at r.t. and stirred for 5 min. The suspension was cooled to −78 °C and a solution of aldehyde **47** (18.8 mg, 46.3 µmol, 1.00 equiv.) was added, followed by addition of dry DMI (50 µL). The reaction stirred for 40 min before it was allowed to warm up to r.t. and stirred for additional 20 min. Cyclohexane (1 mL) and aq. sat. NH_4Cl solution (1 mL) were added, the layers were separated and the aqueous phase was extracted with cyclohexane (3x 1.5 mL). All organic phases were combined, washed with brine (1.5 mL) and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 50:1) yielded vinyl iodide **30** as a yellow oil (13.9 mg, 26.3 µmol, 57%).

R_f = 0.39 (CH/EA 50:1).

$[\alpha]_D^{20}$ = −26.7 (MeOH, c = 0.2).

^{1}H-NMR (500 MHz, d_6-acetone): δ [ppm] = 7.60 (d, *J* = 1.2 Hz, 1H), 6.55 (dt, *J* = 7.4, 1.2 Hz, 1H), 6.49 (dt, *J* = 7.4, 6.7 Hz, 1H), 5.94 (q, *J* = 1.0 Hz, 1H), 5.44 (q, *J* = 1.3 Hz, 1H), 3.66 (td, *J* = 10.2, 4.4 Hz, 1H), 3.42 – 3.31 (m, 2H), 2.64 – 2.56 (m, 1H), 2.55 – 2.50 (m, 2H), 2.20 – 2.12 (m, 1H), 1.99 (dq, *J* = 12.2, 4.3, 3.4, 2.0 Hz, 1H), 1.75 – 1.64 (m, 3H), 1.47 (dddd, *J* = 15.3, 12.1, 6.7, 3.4 Hz, 0H), 1.33 – 1.21 (m,

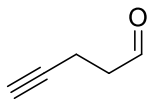
3H), 1.11 (qd, *J* = 14.0, 13.4, 3.8 Hz, 1H), 1.00 (td, *J* = 12.2, 10.4 Hz, 1H), 0.93 (s, 8H), 0.91 (d, *J* = 6.7 Hz, 6H), 0.89 (d, *J* = 3.7 Hz, 0H), 0.87 (d, *J* = 7.0 Hz, 3H), 0.19 (s, 3H), 0.12 (s, 3H).

^{13}C-NMR (125 MHz, d_6-acetone): δ [ppm] = 161.8, 142.5, 139.0, 136.1, 134.0, 117.4, 85.1, 72.5, 51.6, 46.6, 38.6, 35.5, 32.3, 30.7, 28.3, 24.8, 22.6, 18.3.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{24}H_{40}INO_2Si+H^+]$ = 530.1946; Found 530.1944.

4.10. Synthesis of Eastern fragment (31)

4.10.1. Pent-4-ynal (48)



48

A solution of DMSO (13.9 mL, 195 mmol, 2.50 equiv.) in dry CH_2Cl_2 (29 mL) was added slowly dropwise to a stirring solution of $(COCl)_2$ (7.16 mL, 83.4 mmol, 1.15 equiv) in dry CH_2Cl_2 (250 mL) at −78 °C and stirred for 0.5 h. A solution of 4-pentyn-1-ol in dry CH_2Cl_2 (21 mL) was slowly added and stirred for 1 h. NEt_3 (40.0 mL, 290 mmol, 4.00 equiv.) was added and the solution stirred for 0.5 h before it was allowed to warm to r.t. over a period of 0.5 h. Water (200 mL) was added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 100 mL). All organic phases were combined, washed with brine (2x 100 mL) and dried over $MgSO_4$. The crude product was concentrated *in vacuo*, the precipitate was filtered over a plug of silica gel and rinsed with CH_2Cl_2. Removal of the solvent yielded aldehyde **48** as a yellow liquid (5.11 g, 62.2 mmol, 86%).

R_f = 0.5 (CH/EA 9:1).

^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 9.80 (t, *J* = 1.1 Hz, 1H), 2.70 (tt, *J* = 7.1, 0.8 Hz, 2H), 2.51 (tdd, *J* = 7.1, 2.7, 0.7 Hz, 2H), 1.99 (t, *J* = 2.7 Hz, 1H).

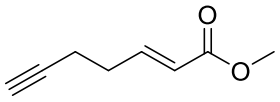
^{13}C-NMR (100 MHz, $CDCl_3$): δ [ppm] = 200.2, 82.4, 69.4, 42.5, 11.8.

MS (EI (+), 70.0 eV): $[M]^+$ calcd for $[C_5H_6O^{\bullet+}-H^\bullet]^+$ = 81.0; Found 81.0.

The experimental data are in agreement with those previously published.[10]

[10] (a) Essig, S.; Bretzke, S.; Müller, R.; Menche, D. *J. Am. Chem. Soc.* **2012**, *134*, 19362–19365. (b) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (c) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

4.10.2. Methyl (*E*)-hept-2-en-6-ynoate (49)



49

Methyl(triphenylphosphoranylidene)acetate (23.8 g, 71.2 mmol, 1.20 equiv.) was added to a stirring solution of aldehyde **48** (4.87 g, 59.3 mmol, 1.00 equiv.) at room temperature and stirred for 16 h. Sat. aq. NH_4Cl (60 mL) was added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 70 mL). All organic phases were combined and washed with brine (60 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 15:1) yielded acrylate **49** as a colourless liquid (4.95 g, 35.8 mmol, 60%).

R_f = 0.24 (CH/EA 15:1)

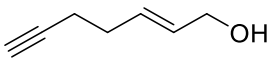
^{1}H-NMR (700 MHz, $CDCl_3$): δ [ppm] = 6.98 (dt, *J* = 15.6, 6.8 Hz, 1H), 5.90 (dt, *J* = 15.7, 1.6 Hz, 1H), 3.74 (s, 3H), 2.46 – 2.40 (m, 2H), 2.36 (tdd, *J* = 7.0, 2.7, 0.9 Hz, 2H), 2.00 (t, *J* = 2.6 Hz, 1H).

^{13}C-NMR (175 MHz, $CDCl_3$): δ [ppm] = 166.9, 146.8, 122.3, 82.8, 69.6, 51.7, 31.2, 17.6.

MS (EI (+), 70.0 eV): $[M]^{\bullet+}$ calcd for $[C_8H_{10}O_2]^{\bullet+}$ = 138.0675; Found 183.0660.

The experimental data are in agreement with those previously published.[21]

4.10.3. (*E*)-Hept-2-en-6-yn-1-ol (50)



50

DIBALH (1.0M in CH_2Cl_2, 32.2 mL, 32.2 mmol, 2.50 equiv.) was added to a solution of ester **49** (1.78 g, 12.9 mmol, 1.00 equiv.) in dry CH_2Cl_2 (6.3 mL) at −78 °C. The reaction was allowed to warm up to r.t. and stirred for 1 h. Et_2O (40 mL) was added, the solution was poured into sat. aq. Rochelle-salt solution (100 mL) and stirred vigorously until two phases were formed. The layers were separated and the aqueous phase was extracted with Et_2O (3x 100 mL). All organic phases were combined and dried over $MgSO_4$. Removal of the solvent *in vacuo* yielded alcohol **50** as a colourless liquid, which was used in the next step without further purification (1.43 g, 12.9 mmol, quant.).

R_f = 0.12 (CH/EA 5:1).

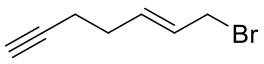
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 5.80 – 5.66 (m, 2H), 4.12 (d, *J* = 4.3 Hz, 2H), 2.28 (t, *J* = 2.1 Hz, 4H), 1.97 (d, *J* = 2.5 Hz, 1H), 1.30 (s, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 130.8, 130.6, 83.9, 68.9, 63.7, 31.3, 18.6.

HRMS (ESI (+), 6.0 eV): $[M+Na]^+$ calcd for $[C_7H_{10}O+Na]^+$ = 133.0624; Found 130.0620.

The experimental data are in agreement with those previously published. [11]

4.10.4. (*E*)-7-Bromohept-5-en-1-yne (51)



51

PPh_3 (1.94 g, 7.41 mmol, 1.20 equiv.) was added in several portions to a solution of CBr_4 (2.46 g, 7.41 mmol, 1.20 equiv.) and alcohol **50** (680 mg, 6.18 mmol, 1.00 equiv.) in dry CH_2Cl_2 (45 mL) was added at 0 °C. The solution was allowed to warm up to r.t. and stirred for 1.5 h. Silica gel was added, the solvent was removed carefully *in vacuo* and the crude product was purified by flash chromatography over silica gel (^{n}Pentane/CH_2Cl_2 90:1) to afford allyl bromide **51** as a colourless oil (759 mg, 4.39 mmol, 71%).

R$_f$ = 0.21 (^{n}Pentane/CH_2Cl_2 90:1).

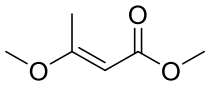
^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 5.91 – 5.70 (m, 2H), 3.95 (d, *J* = 6.5 Hz, 2H), 2.36 – 2.23 (m, 4H), 2.00 – 1.94 (m, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ [ppm] = 134.0, 127.9, 83.5, 69.1, 33.0, 31.1, 18.3.

HRMS (EI (+), 70.0 eV): $[M]^{\bullet+}$ calcd for $[C_7H_9Br]^{\bullet+}$ = 171.9888; Found 171.9833.

The experimental data are in agreement with those previously published.[22]

4.10.5. Methyl (*E*)-3-methoxybut-2-enoate (52)



52

Conc. H_2SO_4 (9 drops) was added to a stirring solution of methyl acetoacetate (28 mL, 260 mmol, 1.00 equiv.) and trimethyl orthoformate (28.5 mL, 260 mmol, 1.00 equiv.) at r.t. and stirred for 24 h. Quinoline (18 drops) was added and the crude product was purified by vacuum destillation (110 °C, 47 mbar) to afford ester **52** as a colourless liquid (33.1 g, 254 mmol, 98%).

R$_f$ = 0.26 (CH/EA, 15:1).

^{1}H-NMR (500 MHz, d_6-acetone): δ [ppm] = 5.05 (s, 1H), 3.66 (s, 3H), 3.60 (s, 3H), 2.23 (d, *J* = 0.5 Hz, 3H).

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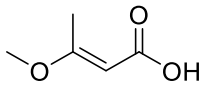
[11] (a) Essig, S.; Bretzke, S.; Müller, R.; Menche, D. *J. Am. Chem. Soc.* **2012**, *134*, 19362–19365. (b) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (c) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

^{13}C-NMR (125 MHz, d_6-acetone): δ [ppm] = 173.6, 168.4, 91.1, 56.0, 50.7, 18.8.

MS (EI (+), 70.0 eV): $[M]^{\bullet+}$ calcd for $[C_6H_{10}O_3]^{\bullet+}$ = 130.0624; Found 130.0630.

The experimental data are in agreement with those previously published.[12

4.10.6. (*E*)-3-Methoxybut-2-enoic acid (53)



53

$LiOH{\cdot}H_2O$ (19.1 g, 456 µmol, 6.90 equiv.) was added to a stirring solution of ester **52** (8.60 g, 66.1 mmol, 1.00 equiv.) in THF/H_2O (3:1, 427 mL) and heated to reflux for 26 h. The solution was acidified with aq. conc. HCl (37 wt-%) to pH = 3. The layers were separated and the aqueous phase was extracted with Et_2O (3x 200 mL). All organic phases were combined and washed with brine (200 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and recrystallization of the residue in ^{n}hexane/Et_2O (1:1) gave carboxylic acid **53** as a white powder (4.13 g, 35.5 mmol, 54%).

R$_f$ = 0.22 (CH/EA, 2:1).

Mp.: 128-130 °C.

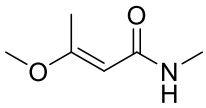
^{1}H-NMR (700 MHz, $CDCl_3$): δ [ppm] = 11.42 (br. s, 1H), 5.04 (s, 1H), 3.66 (s, 3H), 2.30 (s, 3H).

^{13}C-NMR (175 MHz, $CDCl_3$): δ [ppm] = 175.4, 173.1, 90.5, 55.8, 19.4.

HRMS (APCI (+), 5.0 eV): $[M+H]^+$ calcd for $[C_5H_8O_3+H]^+$ = 117.0546; Found 117.0550.

The experimental data are in agreement with those previously published.[13

4.10.7. (*E*)-3-Methoxy-*N*-methylbut-2-enamide (54)



54

EDC·HCl (2.56 g, 13.4 mmol, 1.25 equiv.) was added in several portions to a solution of carboxylic acid **53** (1.24 g, 10.7 mmol, 1.00 equiv.) in dry THF (21 mL) at 0 °C. A solution of $MeNH_2$ (2.0M in THF, 8 mL, 16.0 mmol, 1.50 equiv.) was added and the suspension was allowed to warm to room temperature and stirred for 20 h.Water (10 mL) and EtOAc (15 mL) were added, the layers were separated and the aqueous phase was extracted with EtOAc (3x 20 mL). All organic phases were

[12] (a) Smissman, E. E.; Voldeng, A. N. *J. Org. Chem.* **1964**, *29*, 3161-3165. (b) Krebs, O.; Taylor, R. J. K. *Org. Lett.* **2005**, *7*, 1063-1066.

[13]. (b) Krebs, O.; Taylor, R. J. K. *Org. Lett.* **2005**, *7*, 1063-1066.

combined and washed with brine (10 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (EtOAc 100%) yielded amide **54** as a white solid (947 mg, 7.47 mmol, 70%).

***R*$_f$** = 0.26 (EtOAc 100%).

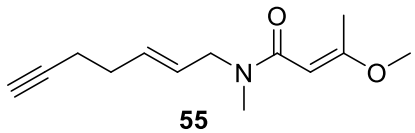
Mp.: 40 °C.

^{1}H-NMR (500 MHz, d$_6$-acetone): δ [ppm] = 6.71 (br. s, 1H), 5.11 (s, 1H), 3.54 (s, 3H), 2.70 (d, *J* = 4.7 Hz, 3H), 2.24 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ [ppm] = 168.2, 167.9, 94.5, 55.1, 25.9, 18.1.

HRMS (ESI-(+), 5.0 eV): $[M+H]^+$ calcd for $[C_6H_{11}NO_2+H]^+$ = 130.0784; Found 130.0860.

4.10.8. (*E*)-*N*-((*E*)-Hept-2-en-6-yn-1-yl)-3-methoxy-*N*-methylbut-2-enamide (55)



55

A solution of Amide **54** (150 mg, 1.16 mmol, 1.20 equiv.) in dry DMF (800 µL) was slowly added dropwise to a stirring suspension of NaH (60 wt-% in paraffin liquid, 162 mg, 4.06 mmol, 3.50 equiv) in dry DMF (3.4 mL) at 0 °C. The reaction was allowed to warm to r.t. and stirred for 1.5 h before the mixture was recooled to 0 °C. A solution of bromide **51** (168 mg, 968 µmol, 1.00 equiv.) in dry DMF (800 µL) was slowly added dropwise and stirred for 1.5 h. Water (4 mL) was carefully added, the layers were separated and the aqueous phase was extracted with EtOAc (3x 6 mL). All organic phases were combined and washed with brine (6 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography (CH/EA 1:1) yielded amide **55** as a yellow liquid (146 mg, 659 µmol, 68%).

***R*$_f$** = 0.21 (CH/EA 1:1).

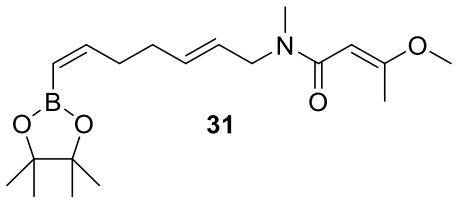
^{1}H-NMR (700 MHz, d$_6$-acetone): δ [ppm] = 5.67 (dd, *J* = 15.4, 6.4 Hz, 1H), 5.60 – 5.43 (m, 1H), 5.36 (s, 1H)*, 5.34 (s, 1H)$^\#$, 3.97 – 3.93 (m, 2H), 3.66 – 3.57 (m, 3H), 2.97 (s, 1H)$^\#$, 2.86 (s, 2H)*, 2.36 – 2.32 (m, 1H), 2.29 – 2.21 (m, 4H), 2.14 (s, 3H).

^{13}C-NMR (175 MHz, d$_6$-acetone): δ [ppm] = 168.2, 167.8, 132.2$^\#$, 131.5*, 128.2$^\#$, 127.9*, 92.3, 84.4, 70.4, 55.4, 52.5*, 49.2$^\#$, 33.4$^\#$, 32.1*, 30.4, 19.2, 18.8.

HRMS (APCI (+), 5.0 eV): $[M+H]^+$ calcd for $[C_{13}H_{19}NO_2+H]^+$ = 221.1416; Found 221.1416.

The experimental data are in agreement with those previously published.[14]

4.10.9. (*E*)-3-Methoxy-*N*-methyl-*N*-((2*E*,6Z)-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hepta-2,6-dien-1-yl)but-2-enamide (31)



31

P^iPr_3 (16 µL, 82.6 µmol, 0.14 equiv.), NEt_3 (410 µL, 2.95 mmol, 5.00 equiv.) and pinacolborane (86 µL, 590 µmol, 1.00 equiv.) were added to a stirring solution of $[Rh(COD)Cl]_2$ (8.73 mg, 17.7 µmol, 0.03 equiv.) in dry cyclohexane (1.7 mL) at r.t. and stirred for 0.5 h. A solution of alkyne **55** (150 mg, 678 µmol, 1.15 equiv.) in dry cyclohexane (1.15 mL) was added and the reaction was allowed to stir for 3 h. MeOH (0.5 mL) was added and the solvent was removed *in vacuo*. Purification of the residue by flash chromatography over silica gel (CH/EA 1:1) yielded vinyl boronate **31** as a red oil (126 mg, 360 µmol, 61%, *Z*:*E* > 9:1).

***R*$_f$** = 0.21 (CH/EA 1:1).

^{1}H-NMR (500 MHz, d$_6$-acetone): δ [ppm] = 6.40 (dt, *J* = 14.2, 7.5 Hz, 1H), 5.67 – 5.55 (m, 1H), 5.54 – 5.38 (m, 1H), 5.34 (s, 1H), 5.29 (dt, *J* = 13.5, 1.4 Hz, 1H), 3.92 (dd, *J* = 5.9, 1.4 Hz, 2H), 3.61 (s, 3H), 2.95 (s, 3H)$^{\#}$, 2.85 (s, 3H)*, 2.50 (qd, *J* = 7.4, 1.3 Hz, 2H), 2.14 (s, 5H), 1.24 (s, 12H).

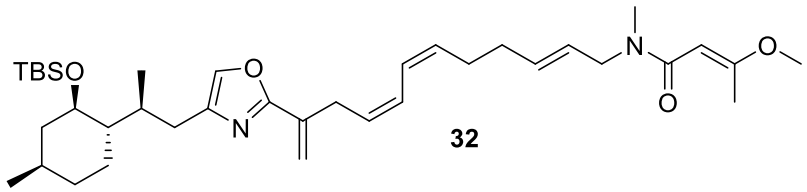
^{13}C-NMR (125 MHz, d$_6$-acetone): δ [ppm] = 168.8$^{\#}$, 168.5*, 168.0*, 167.6$^{\#}$, 154.5, 133.5$^{\#}$, 132.8*, 127.0$^{\#}$, 126.7$^{\#}$, 120.0– 118.2 (m), 92.2, 83.5, 55.3, 52.5*, 49.2$^{\#}$, 35.0$^{\#}$, 33.3*, 32.9, 32.5, 25.2, 25, 18.7.

HRMS (EI (+), 70.0 eV): $[M]^{\bullet+}$ calcd for $[C_{19}H_{32}BNO_4]^{\bullet+}$ = 221.1416; Found 221.1416.

The experimental data are in agreement with those previously published.[24]

[14] (a) Essig, S.; Bretzke, S.; Müller, R.; Menche, D. *J. Am. Chem. Soc.* **2012**, *134*, 19362–19365. (b) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (c) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

4.11. *N*-((2*E*,6*Z*,8*Z*)-11-(4-((*S*)-2-((1*S*,2*R*,4*R*)-2-((*tert*-butyldimethylsilyl)oxy)-4-methylcyclohexyl)propyl)oxazol-2-yl)dodeca-2,6,8,11-tetraen-1-yl)-3-methoxy-*N*-methylbutanamide (32)



To a solution of (*Z*)-Vinylboronate **31** (36.2 mg, 104 µmol, 1.50 equiv.) and Cs_2CO_3 (113 mg, 346 µmol, 5.00 equiv.) in H_2O (50 µL, 50.0 equiv.) was added a solution of Pd(dppf)Cl_2 (7.61 mg, 10.4 µmol, 0.15 equiv.) in dry DMF (170 µL) and a solution of (*Z*)-Vinyliodide **30** (36.6 mg, 69.0 µmol, 1.00 equiv.) in dry THF (520 µL) subsequently. The solution was degassed by freeze-pump-thaw-cycles (3x), the flask was covered in aluminium foil and the reaction stirred for 20 h. Et_2O (2 mL) and aq. sat. $NaHCO_3$ solution (2 mL) were added, the layers were separated and the aqueous phase was extracted with Et_2O (3x 4 mL). All organic extracts were combined and washed with aq. sat. $NaHCO_3$ solution (4 mL), water (2x 4 mL) and brine (4 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue yielded (*Z*,*Z*)-diene **32** as an orange oil (25.7 mg, 41.1 µmol, 60%).

R_f = 0.12 (CH/EA, 4:1).

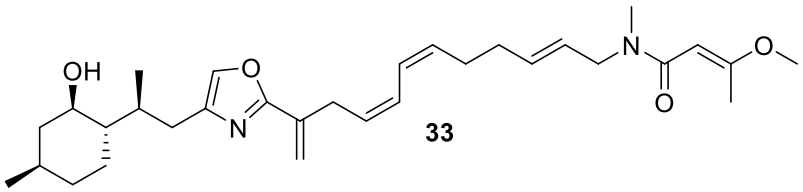
$[\alpha]_D^{20}$ = −14.0 (MeOH, c = 0.5).

^{1}H-NMR (700 MHz, d_6-acetone): δ [ppm] = 7.58 (s, 1H), 6.45 – 6.36 (m, 1H), 5.91 (d, *J* = 1.1 Hz, 1H), 5.68 – 5.58 (m, 2H), 5.55 – 5.47 (m, 2H), 5.47 – 5.39 (m, 1H), 5.38 (q, *J* = 1.4 Hz, 1H), 5.33 (s, 1H), 3.92 (dq, *J* = 6.0, 1.3 Hz, 2H), 3.66 (td, *J* = 10.2, 4.4 Hz, 1H), 3.64 – 3.56 (m, 3H), 3.41 (dt, *J* = 7.5, 1.4 Hz, 2H), 2.95 (s, 1H), 2.85 (s, 2H), 2.59 (ddd, *J* = 14.1, 3.3, 1.3 Hz, 1H), 2.56 – 2.50 (m, 1H), 2.31 (q, *J* = 7.4 Hz, 2H), 2.18 – 2.15 (m, 2H), 2.15 – 2.12 (m, 5H), 1.99 (dddd, *J* = 12.2, 4.3, 3.3, 1.9 Hz, 1H), 1.74 – 1.64 (m, 1H), 1.47 (dddd, *J* = 15.3, 8.8, 6.7, 3.4 Hz, 1H), 1.29 – 1.23 (m, 1H), 1.11 (qd, *J* = 12.6, 12.2, 3.0 Hz, 1H), 1.00 (td, *J* = 12.2, 10.5 Hz, 1H), 0.93 (s, 9H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.90 – 0.83 (m, 4H), 0.19 (s, 3H), 0.12 (s, 3H).

^{13}C-NMR (125 MHz, d_6-acetone): δ [ppm] = 162.1, 142.5, 136.1, 135.9, 133.3, 132.7, 128.7, 126.9, 126.8, 126.1, 124.6, 116.9, 92.2, 72.5, 55.3, 52.5, 51.6, 49.2, 46.6, 35.5, 35.0, 33.3, 32.8, 32.3, 31.0, 30.7, 28.4, 27.5, 26.6, 24.8, 22.7, 18.7 (2x), 18.3, –3.3, –4.2.

HRMS (ESI-(+), 6.0 eV): $[M+H]^+$ calcd for $[C_{37}H_{62}N_2O_4Si+H]^+$ = 625.4395; Found 625.4399.

4.12. (*E*)-*N*-((2*E*,6*Z*,8*Z*)-11-(4-((*S*)-2-((1*S*,2*R*,4*R*)-2-Hydroxy-4-methylcyclohexyl)propyl)oxazol-2-yl)dodeca-2,6,8,11-tetraen-1-yl)-3-methoxy-*N*-methylbut-2-enamide (33)



To an ice-cooled solution of silyl ether **32** (25.7 mg, 41.1 µmol, 1.00 equiv.) in dry THF (1.7 mL) were added dry pyridine (760 µL) and HF·pyridine (500 µL). The solution was allowed to warm to r.t. and stirred for 3 h. Aq. pH 7 buffer solution (8 mL) and EtOAc (6 mL) were added at 0 °C, the layers were separated, the aqueous phase was extracted with EtOAc (3x 10 mL). All organic extracts were combined and washed with aq. pH 7 buffer solution(2x 8 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography (CH/EA 1:1) yielded alcohol **33** as a yellow oil (14.6 mg, 24.7 µmol, 53%).

R_f = 0.12 (CH/EA 1:1).

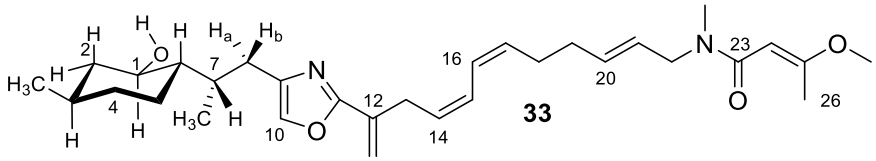
$[\alpha]_D^{20}$ = −33.3 (MeOH, c = 0.6).

^{1}H-NMR (700 MHz, d$_6$-acetone): δ [ppm] = 7.60 (t, *J* = 1.0 Hz, 1H), 6.42 (ddt, *J* = 9.2, 3.4, 1.6 Hz, 2H), 5.91 (dd, *J* = 2.2, 1.2 Hz, 1H), 5.68 – 5.57 (m, 2H), 5.55 – 5.49 (m, 1H), 5.50 – 5.40 (m, 0H), 5.39 (q, *J* = 1.4 Hz, 1H), 5.33 (s, 1H), 3.95 – 3.91 (m, 2H), 3.62 (s, 1H), 3.60 (s, 2H), 3.55 (d, *J* = 20.6 Hz, 1H), 3.45 (td, *J* = 10.4, 4.2 Hz, 1H), 3.40 (d, *J* = 7.6 Hz, 2H), 2.95 (s, 1H), 2.87 – 2.77 (m, 5H), 2.71 (ddd, *J* = 14.0, 4.4, 1.4 Hz, 1H), 2.36 (dddd, *J* = 9.2, 6.7, 4.5, 2.3 Hz, 0H), 2.33 – 2.27 (m, 2H), 2.18 – 2.16 (m, 1H), 2.16 – 2.12 (m, 4H), 1.93 (dtd, *J* = 12.1, 3.9, 2.0 Hz, 1H), 1.69 – 1.60 (m, 2H), 1.43 (dddt, *J* = 15.4, 11.9, 6.7, 3.3 Hz, 1H), 1.25 (ddt, *J* = 12.6, 10.1, 2.4 Hz, 1H), 1.14 (qd, *J* = 12.6, 3.1 Hz, 1H), 1.04 – 0.94 (m, 1H), 0.93 (dd, *J* = 6.9, 1.8 Hz, 3H), 0.89 (dd, *J* = 6.6, 1.8 Hz, 3H), 0.88 – 0.81 (m, 1H).

^{13}C-NMR (125 MHz, d$_6$-acetone): δ [ppm] = 167.5, 167.4, 162.1, 142.8, 136.0, 135.8, 133.3 , 132.8, 132.6, 128.7, 128.5, 127.3, 126.9, 124.7, 117.2, 92.2, 71.0, 55.3, 55.0, 52.5, 50.4, 49.3, 46.4, 35.7, 35.1, 33.2, 33.0, 32.8, 31.0, 30.3, 28.0, 26.6, 22.6, 18.7, 17.7.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{31}H_{46}N_2O_4+H]^+$ = 511.3530; Found 511.43531.

Table 1. NMR-Data of compound **33** (d_6-acetone, 700/175 MHz, r.t.).



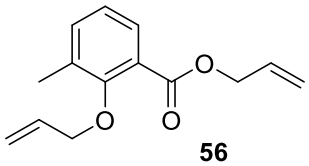
Atom	δ_H [ppm]	m	*J* [Hz]	δ_C [ppm]
1	3.45	td	10.4, 4.2	71.04
2_{ax}	0.96	m	–	46.40
2_{eq}	1.93	dtd	12.1, 3.9, 2.0	
3	1.43	dddt	15.4, 11.9, 6.7, 3.3	32.40
3-CH_3	0.93	dd	6.9, 1.80	33.21
4_{ax}	0.85	m	–	35.66
4_{eq}	1.65	m	–	
5_{ax}	1.14	qd	12.6, 3.14	26.61
5_{eq}	1.65	m	–	
6	1.25	ddt	12.6, 10.1, 2.4	50.35
7	2.36	dddd	9.2, 6.7, 4.5, 2.3	31.02
7-CH_3	0.89	dd	6.6, 1.8	17.69
8_a	2.14	m	–	30.31
8_b	2.71	ddd	14.1, 4.4, 1.4	
9	–	–	–	142.81
10	7.60	s	–	135.79
11	–	–	–	162.09
12	–	–	–	135.98
12-CH_a	5.91	dd	2.2, 1.2	117.16[a]
12-CH_b	5.39	q	1.4	
13	3.40	d	7.6	29.84
14	5.62	m	–	128.60[a]
15	6.42	ddt	9.2, 3.4, 1.6	124.66[a]
16	5.52	m	–	126.87[a]
17	5.46	m	–	132.70[a]
18	2.31	m	–	27.96
19	2.17	m	–	32.83
20	5.62	m	–	133.25[a]
21	5.52	m	–	127.26[a]
22	3.92	m	–	52.45/49.26
22-NCH_3	2.95/2.83	s	br	35.07[a]/33.02
23	–	–	–	168.80[a,b]/168.55[b]
24	5.34/5.33	s	br	92.20
25	–	–	–	167.49/167.39
25-OCH_3	3.62/3.60	s	br	55.28/54.97
26	2.14	m	br	18.72

[a] broad signals. [b] Reconstruction by HMBC-Correlations.

5. Total synthesis of ajudazol A

5.1. Synthesis of Western Part 34

5.1.1. Allyl-2-(allyloxy)-3-methylbenzoate (56)



56

NaH (60% suspension in paraffin liquid, 11.4 g, 284 mmol, 2.40 equiv.) was added in six portions over 30 min to a stirring solution of 3-methylsalicylic acid (18.0 g, 118 mmol, 1.00 equiv.) in dry DMF (240 mL) at 0 °C and stirred for 1.5 h. Allyl bromide (30.7 mL, 355 mmol, 3.00 equiv.) was slowly added dropwise,. the reaction was allowed to warm to r.t. and stirred for 1 h. Water (300 mL) and Et_2O (250 mL) were added, the layers were separated and the aqueous phase was extracted with Et_2O (3x 100 mL). All organic phases were combined and dried over $MgSO_4$. Removal of the solvent *in vacuo* yielded allyl benzoate **56** as a yellow liquid, which was used in the next step without further purification (25.3 g, 109 mmol, 92%).

$\boldsymbol{R_f}$ = 0.33 (CH/EA 9:1).

^{1}H NMR (700 MHz, $CDCl_3$): δ [ppm] = 7.66 (ddd, *J* = 7.8, 1.8, 0.7 Hz, 1H), 7.34 (ddq, *J* = 7.5, 1.5, 0.8 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.11 (ddt, *J* = 17.2, 10.4, 5.7 Hz, 1H), 6.04 (ddt, *J* = 17.2, 10.5, 5.8 Hz, 1H), 5.40 (ddq, *J* = 17.6, 16.1, 1.6 Hz, 2H), 5.26 (ddq, *J* = 26.5, 10.4, 1.3 Hz, 2H), 4.81 (dt, *J* = 5.8, 1.4 Hz, 2H), 4.44 (dt, *J* = 5.7, 1.4 Hz, 2H), 2.32 (d, *J* = 0.6 Hz, 3H).

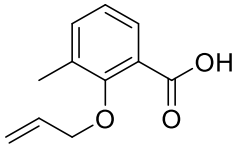
^{13}C NMR (175 MHz, $CDCl_3$): δ [ppm] = 166.3, 157.2, 135.3, 134.0, 133.1, 132.3, 129.3, 125.1, 123.7, 118.7, 117.7, 75.1, 65.9, 16.5.

HRMS (ESI (+), 6.0 eV): $[M+Na]^+$ calcd for $[C_{14}H_{16}O_3+Na]^+$ = 255.099; Found 255.099.

The experimental data are in agreement with those previously published.[15]

[15] (a) Essig, S.; Bretzke, S.; Müller, R.; Menche, D. *J. Am. Chem. Soc.* **2012**, *134*, 19362–19365. (b) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (c) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

5.1.2. 2-(Allyloxy)-3-methylbenzoic acid (57)



57

To a stirring solution of ester **56** (28.2 g, 121 mmol, 1.00 equiv.) in MeOH (400 mL) was added aq. NaOH (6.0m, 103 mL, 6.00 equiv.) and the reaction was heated to reflux for 4 h. The solvent was removed *in vacuo*, the residue was diluted with water (300 mL) and acidified with aq. H_2SO_4 (1.0M) to pH = 2–3. Et_2O (100 mL) was added, the layers were separated and the aqueous phase was extracted with Et_2O (3x 150 mL). All organic phases were combined and washed with water (150 mL). Drying over $MgSO_4$ and removal of the solvent *in vacuo* yielded carboxylic acid **57** as a white solid (23.3 g, 121 mmol, quant.), which was used in the next step without further purification.

***R*$_f$** = 0.19 (CH/EA 5:1).

Mp.: 52-54 °C.

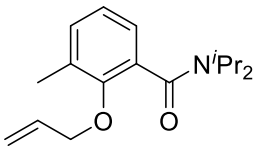
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 11.16 (br. s, 1H), 7.97 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.48 – 7.41 (m, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 6.11 (ddt, *J* = 16.7, 10.3, 6.0 Hz, 1H), 5.48 (dq, *J* = 17.1, 1.4 Hz, 1H), 5.39 (dq, *J* = 10.4, 1.1 Hz, 1H), 4.51 (dt, *J* = 6.0, 1.2 Hz, 2H), 2.37 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 166.0, 156.2, 137.1, 131.7, 131.6, 130.9, 125.3, 122.7, 120.7, 76.2, 16.3.

HRMS (ESI (+), 6.0 eV): calculated for $[M-H^+]^-$: 191.071; Found 191.08.

The experimental data are in agreement with those previously published. [16]

5.1.3. 2-(Allyloxy)-*N*,*N*-diisopropyl-3-methylbenzamide (58)



58

To a stirring solution of carboxylic acid **57** (4.83 g, 20.8 mmol, 1.00 equiv.) in dry CH_2Cl_2 (50 mL) was added $SOCl_2$ (4.52 mL, 62.4 mmol, 3.00 equiv.) and the reaction was heated to reflux for 5.5 h. Excess $SOCl_2$ was removed *in vacuo* (80 °C, 20 mbar) and the residue was dissolved in dry CH_2Cl_2 (50 mL). A

[16] (a) Essig, S.; Bretzke, S.; Müller, R.; Menche, D. *J. Am. Chem. Soc.* **2012**, *134*, 19362–19365. (b) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (c) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

solution of $^{i}Pr_2NH$ (8.77 mL, 62.44 mmol, 3.00 equiv.) in dry CH_2Cl_2 (25 mL) was slowly added at 0 °C. The reaction was allowed to warm to r.t. and stirred overnight (12 h). Water (30 mL) was added, the phases were separated and aqueous phase was extracted with CH_2Cl_2 (3x 30 mL). All organic phases were combined and washed with H_2O (30 mL) and brine (30 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 5:1) yielded amide **58** as a white crystalline solid (5.27 g, 19.1 mmol, 92%).

R_f = 0.35 (CH/EA 5:1).

Mp.: 95-96 °C.

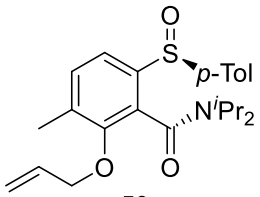
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 7.17 – 7.13 (m, 1H), 7.03 – 6.98 (m, 2H), 6.04 (ddt, *J* = 17.2, 10.8, 5.5 Hz, 1H), 5.37 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.19 (dq, *J* = 10.4, 1.4 Hz, 1H), 4.55 (ddt, *J* = 12.3, 5.5, 1.4 Hz, 1H), 4.34 (ddt, *J* = 12.3, 5.6, 1.5 Hz, 1H), 3.67 (hept, *J* = 6.7 Hz, 1H), 3.49 (hept, *J* = 6.8 Hz, 1H), 2.29 (s, 3H), 1.55 (dd, *J* = 6.8, 3.7 Hz, 6H), 1.17 (d, *J* = 6.7 Hz, 3H), 1.02 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 169.0, 153.0, 134.2, 133.4, 131.8, 131.22, 124.3, 117.1, 74.75, 51.2, 45.8, 20.9, 20.8 , 20.7, 20.4, 16.4 (2x).

HRMS (ESI (+), 6.0 eV): $[M+Na]^+$ calcd for $[C_{17}H_{25}NO_2+Na]^+$ = 298.1778; Found 298.1780.

The experimental data are in agreement with those previously published.[17]

5.1.4. (*S*)-2-(Allyloxy)-*N*,*N*-diisopropyl-3-methyl-6-(*p*-tolylsulfinyl)benzamide (59)



59

^{t}BuLi (1.7M in pentane, 17.4 mL, 29.5 mmol, 1.10 equiv.) was added over a period of 15 min to a stirring solution of amide **58** (7.38 g, 26.8 mmol, 1.00 equiv.) in dry THF (130 mL) at −78 °C. After 0.5 h the solution was transferred *via* cannula to a stirring solution of (1*R*,2*S*,5*R*)-(–)-Menthyl (*S*)-*p*-toluenesulfinate (Andersen reagent) in dry THF (130 mL) at r.t. and the reaction was allowed to stir for 90 min at ambient temperature. Aq. sat. NH_4Cl solution (100 mL) was added, the layers were separated and the aqueous layer was extracted with EtOAc (3x 100 mL). All organic phases were combined and washed with brine (150 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and

[17] (a) Essig, S.; Bretzke, S.; Müller, R.; Menche, D. *J. Am. Chem. Soc.* **2012**, *134*, 19362–19365. (b) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (c) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

purification of the residue by flash column chromatography over silica gel (CH/EA 3:1) yielded enantiomeric pure sulfoxide **59** as a white solid (7.96 g, 19.3 mmol, 72%).

R_f = 0.31 (CH/EA 5:1).

Mp.: 99-102 °C.

$[\alpha]_D^{20}$ = −107.9 ($CHCl_3$, c = 1.0).

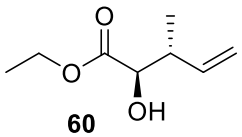
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 7.72 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.27 – 7.24 (m, 3H), 6.08 – 5.97 (m, 1H), 5.37 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.22 (dq, *J* = 10.4, 1.4 Hz, 1H), 4.57 (ddt, *J* = 12.1, 5.6, 1.4 Hz, 1H), 4.32 (ddt, *J* = 12.1, 5.6, 1.5 Hz, 1H), 3.76 (hept, *J* = 6.8 Hz, 1H), 3.60 (hept, *J* = 6.8 Hz, 1H), 2.35 (s, 3H), 2.29 (s, 3H), 1.63 (d, *J* = 6.8 Hz, 3H), 1.59 (d, *J* = 6.8 Hz, 3H), 1.25 (d, *J* = 6.7 Hz, 3H), 1.22 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 165.5, 152.4, 142.3, 142.2, 140.8, 135.5, 133.6, 132.5, 129.9, 124.7, 120.9, 117.5, 75.1, 52.0, 46.4, 21.5, 21.1, 20.8, 20.5, 20.4, 16.5.

HRMS (ESI-(+), 5.0 eV): $[M+Na]^+$ calcd for $[C_{24}H_{31}NO_3S+Na]^+$ = 436.1917; Found 436.1920.

The experimental data are in agreement with those previously published. [18]

5.1.5. Ethyl (2*R*,3*R*)-2-hydroxy-3-methylpent-4-enoate (60)



60

trans-2-Butene (19 mL, 195 mmol, 2.80 equiv.) was added via transfer cannula to a stirring suspension of KO^{t}Bu (8.03 g, 71.6 mmol, 1.03 equiv.) in dry THF (38 mL) at −78 °C. ^{n}BuLi (2.5M in hexane, 28.0 mL, 69.5 mmol, 1.00 equiv.) was added over a period of 30 min. After 30 min the solution was warmed up to −45 °C and stirred for 10 min. A solution of (+)-Ipc$_2$BOMe (26.0 g, 82 mmol, 1.18 equiv.) in dry Et_2O (83 mL) was added over a period of 30 min at −78 °C, followed by addition of $BF_3{\cdot}OEt_2$ (12.3 mL, 97.3 mmol, 1.40 equiv.) over a period of 20 min. Ethyl glyoxylate (4.9M in toluene, 35.5 mL, 174 mmol, 2.50 equiv.) was added over a period of 30 min and stirring was continued for 4 h at −78 °C. NaOH (1.0m in water, 157 mL, 2.25 equiv.) was added at r.t., followed by careful addition of aq. H_2O_2 solution (30 %*v/v*, 21.7 mL, 2.76 equiv.). The solution was allowed to warm to r.t. and stirred for 2 h. The layers were separated and the aqueous phase was extracted with Et_2O (3x 100 mL). All organic phases were combined and washed with water (30 mL) and brine

[18] (a) Essig, S.; Bretzke, S.; Müller, R.; Menche, D. *J. Am. Chem. Soc.* **2012**, *134*, 19362–19365. (b) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (c) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

(30 mL). Drying over $MgSO_4$, careful removal of the solvent *in vacuo* (40 °C, 50 mbar) and vacuum destillation (64-65 °C, 5.4 mbar) yielded crotyl alcohol **60** as a colourless liquid (6.10 g, 38.6 mmol, 56%).

R$_f$ = 0.14 (CH/EA 10:1).

[α]$_D^{20}$ = −2.3 ($CHCl_3$, c = 1.0).

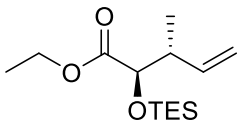
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 5.75 (ddd, *J* = 17.8, 9.8, 8.0 Hz, 1H), 5.08 (d, *J* = 1.5 Hz, 1H), 5.05 (dd, *J* = 4.2, 1.5 Hz, 1H), 4.32 – 4.16 (m, 2H), 4.10 (d, *J* = 3.4 Hz, 1H), 2.70 – 2.61 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.16 (d, *J* = 7.0 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 174.3, 137.8, 116.6, 74.5, 61.8, 42.1, 16.5, 14.4.

HRMS (ESI-(+), 6.0 eV: $[M+H]^+$ calcd for $[C_8H_{14}O_3+H]^+$ = 159.1016; Found 159.1018.

The experimental data are in agreement with those previously published. [19]

5.1.6. Ethyl-(2*R*,3*R*)-3-methyl-2-((triethylsilyl)oxy)pent-4-enoate (61)



61

TESOTf (9.10 mL, 47.5 mL, 1.25 equiv.) was slowly added to a stirring solution of crotyl alcohol **60** (6.02 g, 38.0 mmol, 1.00 equiv.) and 2,6-lutidine (11.1 mL, 95.1 mmol, 2.50 equiv.) in dry CH_2Cl_2 (130 mL) at 0 °C. The reaction was allowed to warm to r.t. and stirred for 1 h. Water (100 mL) was added, the phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 100 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 30:1) yielded TES ether **61** as a colourless liquid (9.43 g, 34.6 mmol, 91%).

R$_f$ = 0.30 (CH/EA 30:1).

[α]$_D^{20}$ = +18.9 ($CHCl_3$, c = 1.0).

^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 5.82 (ddd, *J* = 17.2, 10.3, 8.0 Hz, 1H), 5.05 – 4.98 (m, 2H), 4.22 – 4.11 (m, 2H), 4.07 (d, *J* = 4.7 Hz, 1H), 2.65 – 2.54 (m, 1H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.61 (qd, *J* = 7.9, 2.7 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 173.0, 139.2, 115.4, 76.3, 60.7, 42.9, 16.6, 14.4, 6.9, 4.8.

HRMS (ESI (+), 6.0 eV): $[M+Na]^+$ calcd for $[C_{14}H_{28}O_3Si+H]^+$ = 295.1700; Found 295.1719.

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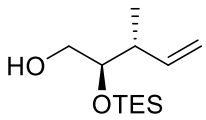
[19] (a) Essig, S.; Bretzke, S.; Müller, R.; Menche, D. *J. Am. Chem. Soc.* **2012**, *134*, 19362–19365. (b) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (c) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

The experimental data are in agreement with those previously published.[13]

5.1.7. (2*R*,3*R*)-3-Methyl-2-((triethylsilyl)oxy)pent-4-en-1-ol (62)



61

DIBALH (1.0M in CH_2Cl_2, 41.0 mL, 2.10 equiv.) was slowly added to a stirring solution of Ester **61** (2.67 g, 9.80 mmol, 1.00 equiv.) in dry CH_2Cl_2 at −78 °C. The reaction was allowed to warm to r.t. and stirred for 1 h. Et_2O (100 mL) was added, the solution was poured into aq. sat. Rochelle-salt solution (100 mL) and stirred vigorously until two phases appeared. The layers were separated and the aqueous phase was extracted with Et_2O (3x 50 mL). Drying over $MgSO_4$ and removal of the solvent *in vacuo* yielded alcohol **62** as a colourless liquid, which was used in the next step without further purification (2.26 g, 9.81 mmol, quant.).

$\boldsymbol{R_f}$ = 0.29 (CH/EA 9:1).

$\mathbf{[\alpha]_D^{20}}$ = +2.6 ($CHCl_3$, c = 1.0).

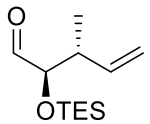
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 5.81 (ddd, *J* = 17.5, 10.4, 7.5 Hz, 1H), 5.09 – 4.95 (m, 2H), 3.65 (q, *J* = 5.1 Hz, 1H), 3.53 (d, *J* = 5.0 Hz, 2H), 2.45 – 2.35 (m, 1H), 1.83 (d, *J* = 11.2 Hz, 1H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.63 (q, *J* = 7.9 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 140.6, 114.9, 64.4, 41.4, 15.3, 7.0, 5.24.

HRMS (ESI-(+), 6.0 eV): $[M+Na]^+$ calcd for $[C_{12}H_{26}O_2Si+Na]^+$ = 253.1594; Found 253.1591.

The experimental data are in agreement with those previously published. [20]

5.1.8. (2*R*,3*R*)-3-Methyl-2-((triethylsilyl)oxy)pent-4-enal (63)



63

[20] (a) Essig, S.; Bretzke, S.; Müller, R.; Menche, D. *J. Am. Chem. Soc.* **2012**, *134*, 19362–19365. (b) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (c) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

DMSO (425 µL, 5.93 mmol, 2.60 equiv.) in dry CH_2Cl_2 (3.50 mL) was slowly added over a period of 5 min to a stirring solution of $(COCl)_2$ (270 µL, 3.08 mmol, 1.35 equiv.) in dry CH_2Cl_2 (10.5 mL) at −78 °C. After 25 min alcohol **62** (525 mg, 2.28 mmol, 1.00 equiv.) in dry CH_2Cl_2 (3.50 mL) was added and the solution stirred for 1 h. NEt_3 (1.25 mL, 9.12 mmol, 4.00 equiv.) was slowly added dropwise, stirring was continued for additional 30 min and the reaction was allowed to warm to r.t. over 1 h. Water (11 mL) was added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 15 mL). All organic phases were combined and washed with brine (15 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 50:1) yielded aldehyde **63** as a yellow liquid (432 mg, 1.89 mmol, 83%).

$\boldsymbol{R}_f$ = 0.30 (CH/EA 50:1).

$[\alpha]_D^{20}$ = +16.6 ($CHCl_3$, c = 1.0).

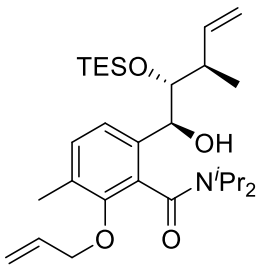
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 9.55 (d, *J* = 2.2 Hz, 1H), 5.87 – 5.76 (m, 1H), 5.07 – 5.04 (m, 1H), 5.03 (d, *J* = 1.0 Hz, 1H), 3.85 (dd, *J* = 4.5, 2.2 Hz, 1H), 2.62 – 2.53 (m, 1H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.61 (q, *J* = 7.7 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 204.6, 138.4, 116.0, 81.0, 41.8, 16.2, 6.8, 4.9.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{12}H_{24}O_2Si+H]^+$ = 251.1438; Found 251.1445.

The experimental data are in agreement with those previously published.[21]

5.1.9. 2-(Allyloxy)-6-((1*S*,2*R*,3*R*)-1-hydroxy-3-methyl-2-((triethylsilyl)oxy)pent-4-en-1-yl)-*N*,*N*-diisopropyl-3-methylbenzamide (64)



64

^{t}BuLi (1.7M in pentane, 4.06 mL, 6.91 mmol, 1.20 equiv.) was slowly added to a solution of amide **59** (2.38 g, 5.76 mmol, 1.00 equiv.) in dry THF (50 mL) at −90 °C and stirred for 15 min. Aldehyde **63** (1.84 g, 8.06 mmol, 1.40 equiv.) in dry THF (6.70 mL) was slowly added and the solution was allowed to stir for 1 h, before it was allowed to warm to −78 °C and stirred for additional 30 min. Aq. sat. NH_4Cl solution (40 mL) was added, the layers were separated and the aqueous phase was

[21] (a) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (b) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

extracted with EtOAc (3x 50 mL). All organic phases were combined and washed with brine (50 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 6:1) yielded benzylic alcohol **64** as a colourless, viscid oil (2.03 g, 4.03 mmol, 71%).

$\boldsymbol{R_f}$ = 0.28 (CH/EA 6:1).

$\mathbf{[\alpha]_D^{20}}$ = +39.5 ($CHCl_3$, c = 1.0).

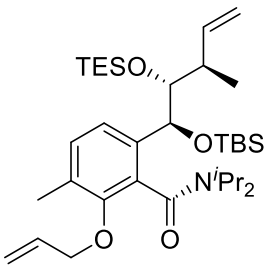
^{1}H-NMR (500 MHz, $CDCl_3$): δ [ppm] = 7.19 – 7.12 (m, 2H), 6.03 (ddt, *J* = 17.2, 10.5, 5.5 Hz, 1H), 5.92 (ddd, *J* = 17.4, 10.3, 8.5 Hz, 1H), 5.36 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.20 (dq, *J* = 10.4, 1.4 Hz, 1H), 5.12 (ddd, *J* = 17.3, 2.3, 1.0 Hz, 1H), 5.02 (ddd, *J* = 10.3, 2.2, 0.7 Hz, 1H), 4.46 (ddt, *J* = 12.3, 5.7, 1.4 Hz, 1H), 4.40 (d, *J* = 9.2 Hz, 1H), 4.25 (ddt, *J* = 12.3, 5.4, 1.5 Hz, 1H), 4.18 (dd, *J* = 9.2, 2.0 Hz, 1H), 3.76 (hept, *J* = 6.6 Hz, 1H), 3.50 (hept, *J* = 6.8 Hz, 1H), 2.83 – 2.75 (m, 1H), 2.27 (d, *J* = 0.6 Hz, 3H), 1.64 – 1.58 (m, 1H), 1.55 (d, *J* = 6.8 Hz, 3H), 1.54 (d, *J* = 6.9 Hz, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.15 (d, *J* = 7.1 Hz, 3H), 1.04 (d, *J* = 6.7 Hz, 3H), 0.77 (t, *J* = 8.0 Hz, 9H), 0.43 (qd, *J* = 7.9, 1.8 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 168.9, 152.5, 140.5, 138.7, 134.2, 134.1, 131.1, 130.6, 123.0, 117.1, 115.3, 76.7, 72.1, 51.7, 46.0, 41.5, 32.5, 24.4, 20.9, 20.6, 20.5, 20.4, 17.3, 16.1, 7.0, 5.6.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{29}H_{49}NO_4Si]^+$)= 504.3504; Found 504.3480.

The experimental data are in agreement with those previously published. [22]

5.1.10. 2-(Allyloxy)-6-((5*S*,6*R*)-6-((*R*)-but-3-en-2-yl)-8,8-diethyl-2,2,3,3-tetramethyl-4,7-dioxa-3,8-disiladecan-5-yl)-*N*,*N*-diisopropyl-3-methylbenzamide (65)



65

TBSOTf (600 µL, 2.61 mmol, 2.50 equiv.) was added to a stirring solution of benzylic alcohol **64** (526 mg, 1.04 mmol, 1.00 equiv.) and 2,6-lutidine (610 µL, 5.22 mmol, 5.00 equiv.) in dry CH_2Cl_2 (18 mL) at 0 °C. The reaction was allowed to warm to r.t. and stirred overnight (21 h). Water (5 mL) was added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 10 mL). All organic phases were combined and dried over $MgSO_4$. Removal of the solvent *in vacuo* and

[22] (a) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (b) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

purification of the residue by flash chromatography over silica gel (CH/EA 50:1) yielded TBS ether **65** as a colourless oil (580 mg, 980 µmol, 90%).

R_f = 0.36 (CH/EA 50:1).

$[\alpha]_D^{20}$ = −14.8 ($CHCl_3$, c = 0.8).

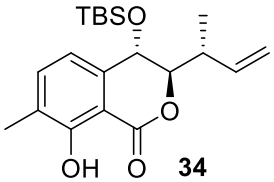
^{1}H-NMR (700 MHz, $CDCl_3$): δ [ppm] = 7.13 (d, J = 7.9 Hz, 1H), 7.09 (d, J = 8.0 Hz, 1H), 6.02 (ddt, J = 17.2, 10.7, 5.4 Hz, 1H), 5.86 (ddd, J = 17.3, 10.3, 9.0 Hz, 1H), 5.35 (dq, J = 17.2, 1.7 Hz, 1H), 5.16 (dq, J = 10.5, 1.4 Hz, 1H), 5.06 – 4.98 (m, 2H), 4.54 (ddt, J = 12.5, 5.5, 1.5 Hz, 1H), 4.39 (d, J = 8.8 Hz, 1H), 4.17 (ddt, J = 12.4, 5.5, 1.6 Hz, 1H), 3.83 – 3.74 (m, 2H), 3.48 (hept, J = 6.7 Hz, 1H), 2.79 (p, J = 7.5 Hz, 1H), 2.25 (s, 3H), 1.55 (t, J = 7.0 Hz, 6H), 1.15 – 1.10 (m, 9H), 0.82 (s, 9H), 0.74 (t, J = 8.0 Hz, 9H), 0.38 (dq, J = 15.0, 8.1 Hz, 3H), 0.28 (dq, J = 15.0, 8.1 Hz, 3H), 0.10 (s, 3H), -0.37 (s, 3H).

^{13}C-NMR (175 MHz, $CDCl_3$): δ [ppm] = 167.5, 152.9, 140.5, 139.0, 134.4, 134.2, 130.8, 130.4, 123.7, 116.7, 115.5, 81.7, 74.7, 71.5, 50.8, 45.8, 41.2, 26.1, 21.5, 21.1, 20.7, 20.5, 19.2, 18.1, 16.1, 7.2, 5.5, --5.9, -5.2.

HRMS (ESI (+), 6.0 eV): $[M+Na]^+$ calcd for $[C_{35}H_{62}NO_4Si_2+Na]^+$ = 640.4188; Found 640.4189.

The experimental data are in agreement with those previously published. [23]

5.1.11. (3*R*,4*S*)-3-((*R*)-But-3-en-2-yl)-4-((*tert*-butyldimethylsilyl)oxy)-8-hydroxy-7-methylisochroman-1-one (34)



34

$Pd(PPh_3)_4$ (3.30 mg, 2.85 µmol, 0.01 equiv.) was added to a stirring suspension of allyl ether **65** (176 mg, 285 µmol, 1.00 equiv.) in dry MeOH (2.40 mL) at r.t. and stirred for 10 min. Dry K_2CO_3 (118 mg, 855 µmol, 3.00 equiv.) was added and stirring was continued for 1 h. The mixture was concentrated *in vacuo*, diluted in CH_2Cl_2 (3 mL) and H_2O (5 mL) and was acidified with aq. HCl (1.0m) to pH = 6. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 3 mL). All organic phases were combined and washed with brine (5 mL). Drying over $MgSO_4$ and removal of the solvent gave a red oil, which was transferred into a septum sealed microwave vessel. Dry toluene (2.30 mL) and AcOH (490 µL, 8.55 mmol, 30.0 equiv.) were added and the solution was heated up to 220 °C in a microwave reactor for 3.5 h (Ramp Time: 30 min; Holding Time: 180 min; Power: 300 W;

[23] (a) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (b) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

Max Power: Off). Water (2 mL) was added, the layers were separated and the aqueous phase was extracted with EtOAc (3x 10 mL). All organic phases were combined and washed with brine (10 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 30:1) gave isochromanone **34** as a white paste (88.4 mg, 244 µmol, 86%).

$\boldsymbol{R_f}$ = 0.29 (CH/EA 30:1).

$[\alpha]_D^{20}$ = +70.2 ($CHCl_3$, c = 1.0).

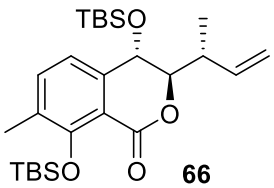
^{1}H-NMR (700 MHz, $CDCl_3$): δ [ppm] = 11.27 (d, *J* = 0.5 Hz, 1H), 7.34 (dt, *J* = 7.5, 0.8 Hz, 1H), 6.72 (d, *J* = 7.5 Hz, 1H), 5.82 (ddd, *J* = 17.2, 10.4, 7.5 Hz, 1H), 5.07 (dt, *J* = 10.4, 1.2 Hz, 1H), 5.02 (dt, *J* = 17.2, 1.3 Hz, 1H), 4.72 (d, *J* = 3.6 Hz, 1H), 4.39 (dd, *J* = 7.2, 3.6 Hz, 1H), 2.40 (p, *J* = 6.5 Hz, 1H), 2.27 (d, *J* = 1.0 Hz, 3H), 1.07 (d, *J* = 6.9 Hz, 3H), 0.87 (s, 9H), 0.13 (s, 3H), –0.01 (s, 3H).

^{13}C-NMR (175 MHz, $CDCl_3$): δ [ppm] = 168.7, 160.2, 138.1, 137.6, 136.9, 127.2, 117.4, 116.7, 107.0, 88.2, 66.9, 39.3, 25.9, 18.2, 17.2, 15.8, –4.01, –4.10.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{20}H_{30}O_4Si+H]^+$ = 363.1986; Found 363.1991.

The experimental data are in agreement with those previously published. [24]

5.1.12. (3*R*,4*S*)-3-((*R*)-But-3-en-2-yl)-4,8-bis((*tert*-butyldimethylsilyl)oxy)-7-methylisochroman-1-one (66)



66

TBSOTf (950 µL, 4.12 mmol, 2.00 equiv.) was added to a stirring solution of phenol **34** (746 mg, 2.06 mmol, 1.00 equiv.) and 2,6-lutidine (960 µL, 8.24 mmol, 4.00 equiv.) in dry CH_2Cl_2 (8.0 mL) at 0 °C. The reaction was allowed to warm to r.t. and stirred for 2.5 h. Water (10 mL) was added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 15 mL). All organic phases were combined and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 30:1) yielded bis-silyl ether **66** as a colourless paste (982 mg, 2.06 mmol, quant.).

$\boldsymbol{R_f}$ = 0.36 (CH/EA 30:1).

$[\alpha]_D^{20}$ = +86.0 (MeOH, c = 0.5).

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[24] (a) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (b) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

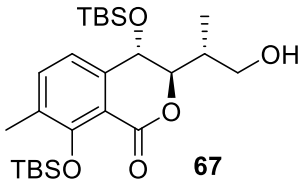
^{1}H-NMR (700 MHz, $CDCl_3$): δ [ppm] = 7.33 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 5.96 (ddd, *J* = 17.4, 10.5, 7.0 Hz, 1H), 5.09 (dt, *J* = 10.5, 1.3 Hz, 1H), 5.05 (dt, *J* = 17.2, 1.4 Hz, 1H), 4.70 (d, *J* = 4.6 Hz, 1H), 4.19 (dd, *J* = 7.1, 4.6 Hz, 1H), 2.39 (ht, *J* = 6.9, 1.2 Hz, 1H), 2.26 (d, *J* = 0.7 Hz, 3H), 1.07 (d, *J* = 6.9 Hz, 3H), 1.04 (s, 9H), 0.88 (s, 9H), 0.17 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.02 (s, 3H).

^{13}C-NMR (175 MHz, $CDCl_3$): δ [ppm] = 161.9, 154.9, 139.6, 138.7, 135.7, 131.8, 119.3, 116.3, 116.1, 86.4, 67.9, 38.4, 27.1, 26.2, 25.9, 18.8, 18.3, 17.7, 17.3, –3.21, –3.26, –3.91, –4.02.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{26}H_{44}O_4Si_2+H]^+$ = 477.2856; Found 477.2860.

The experimental data are in agreement with those previously published. [25]

5.1.13. (3*R*,4*S*)-4,8-bis((*tert*-Butyldimethylsilyl)oxy)-3-((*R*)-1-hydroxypropan-2-yl)-7-methylisochroman-1-one (67)



2,6-Lutidine (100 µL, 868 µmol, 2.00 equiv.), $NaIO_4$ (372 mg, 1.74 mmol, 4.00 equiv.) and OsO_4 (2.5 wt% in ^{t}BuOH, 110 µL, 0.02 equiv.) were added to a stirring solution of alkene **66** (207 mg, 434 µmol, 1.00 equiv.) in dioxane/H_2O (3:1, 4.3 mL) at r.t. and stirred for 3 h. Water (4 mL) and CH_2Cl_2 (4 mL) were added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 3 mL). All organic phases were combined and washed with brine (6 mL). Drying over $MgSO_4$ and removal of the solvent *in vacuo* gave a green-brownish oil, which was immediately dispensed in MeOH (8 mL) and cooled to 0 °C. $NaBH_4$ (82.1 mg, 2.17 mmol, 5.00 equiv.) was added to the stirring solution, the reaction was allowed to warm to r.t. and stirred for 20 min. CH_2Cl_2 (3 mL) and aq. sat. $NaHCO_3$ solution (3 mL) were added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 4 mL). All organic phases were combined and washed with brine (4 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography yielded alcohol **67** as a colourless oil (199 mg, 414 µmol, 95%).

R_f = 0.31 (CH/EA 4:1).

$[\alpha]_D^{20}$ = +70.0 (MeOH, c = 0.2).

^{1}H-NMR (500 MHz, d_6-acetone): δ [ppm] = 7.46 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.07 (d, *J* = 7.5 Hz, 1H), 4.95 (d, *J* = 2.5 Hz, 1H), 4.41 (dd, *J* = 9.8, 2.5 Hz, 1H), 3.72 – 3.66 (m, 1H), 3.65 – 3.59 (m, 1H), 2.27 (s, 3H),

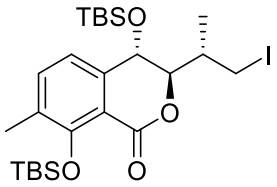
[25] (a) Essig, S.; Schmalzbauer, B.; Bretzke, S.; Scherer, O.; Koeberle, A.; Werz, O.; Müller, R.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1333–1357. (b) Essig, S.; Menche, D. *J. Org. Chem.* **2016**, *81*, 1943–1966.

1.60 – 1.49 (m, 1H), 1.04 (s, 9H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.85 (s, 9H), 0.20 (s, 3H), 0.16 (s, 3H), 0.14 (s, 3H), 0.01 (s, 3H).

^{13}C-NMR (175 MHz, d$_6$-acetone): δ [ppm] = 161.7, 155.2, 139.5, 136.4, 132.6, 121.3, 117.7, 84.8, 68.6, 63.4, 63.3, 38.43, 26.5, 26.1, 19.2, 18.6, 17.8, 13.9, –3.1, –3.2, –4.2, –4.4.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{25}H_{44}O_5Si_2]^+$ = 481.2800; Found 481.2807.

5.1.14. (3*R*,4*S*)-4,8-bis((*tert*-Butyldimethylsilyl)oxy)-3-((*S*)-1-iodopropan-2-yl)-7-methylisochroman-1-one (35)



35

I_2 (118 mg, 465 µmol, 1.30 equiv.) was added to a solution of PPh_3 (122 mg, 465 µmol, 1.30 equiv.) and imidazole (66.0 mg, 966 µmol, 2.70 equiv.) in dry CH_2Cl_2 (2.3 mL) at 0 °C and stirred for 15 min. A solution of alcohol **67** (172 mg, 358 µmol, 1.00 equiv.) in dry CH_2Cl_2 (2.3 mL) was added slowly and the reaction was allowed to warm to r.t. After 1.5 h. the solution was filtered over a plug of silica gel and rinsed with CH/EA (4:1). Aq. pH 7-buffer solution (5 mL) and aq. sat. Na_2SO_3 solution (5 mL) were added to the filtrate, the layers were separated and the aqueous phase was extracted with EtOAc (3x 10 mL). All organic phases were combined and washed with brine (15 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 30:1) yielded alkyl iodide **35** as a colourless oil (206 mg, 348 µmol, 97%).

R_f = 0.29 (CH/EA 30:1).

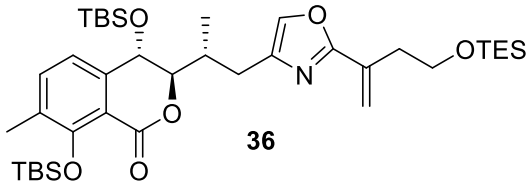
$[\alpha]_D^{20}$ = +72.5 (MeOH, c = 0.4).

^{1}H-NMR (500 MHz, d$_6$-acetone): δ [ppm] = 7.48 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.09 (d, *J* = 7.5 Hz, 1H), 5.01 (d, *J* = 2.7 Hz, 1H), 4.29 (dd, *J* = 9.5, 2.7 Hz, 1H), 3.52 (dd, *J* = 9.9, 2.8 Hz, 1H), 3.42 (dd, *J* = 9.9, 6.7 Hz, 1H), 2.27 (d, *J* = 0.7 Hz, 3H), 1.47 – 1.36 (m, 1H), 1.04 (d, *J* = 6.4 Hz, 12H), 0.86 (s, 9H), 0.22 (s, 3H), 0.18 (s, 3H), 0.15 (s, 3H), 0.03 (s, 3H).

^{13}C-NMR (125 MHz, d$_6$-acetone): δ [ppm] = 161.2, 155.3, 139.3, 136.6, 132.8, 121.2, 117.4, 86.5, 68.2, 37.3, 26.4, 26.0, 19.2, 18.6, 17.7, 17.6, 13.9, –3.0, –3.2, –4.2, –4.4.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{25}H_{43}IO_4Si_2]^+$ = 591.1817; Found 591.1831.

5.2. (3*R*,4*S*)-4,8-bis((*tert*-Butyldimethylsilyl)oxy)-7-methyl-3-((*R*)-1-(2-(4-((triethylsilyl)oxy)but-1-en-2-yl)oxazol-4-yl)propan-2-yl)isochroman-1-one (36)



36

Anhydrous LiCl (68.7 mg, 1.62 mmol, 4.20 equiv.) was heated under vacuum at 170 °C for 5 min. Zinc powder (325 mesh, 49.3 mg, 755 µmol, 1.96 equiv.) was added and dried again under vacuum at 150 – 170 °C for 5 min. The reaction flask was flushed with argon (3x) and dry THF (160 µL) was added. $C_2H_4Br_2$ (0.2 g/mL in dry THF, 27 µL, 26.9 µmol, 0.07 equiv.) and TMSCl (0.07m in dry THF, 81 µL, 5.39 µmol, 1.40 mol-%) were added to the stirring suspension and the reaction was heated to 50 °C for 10 min. A solution of alkyl iodide **35** (318 mg, 539 µmol, 1.40 equiv.) in dry THF (540 µL) was added and stirred for 2 h at this temperature. The solution was allowed to cool down to r.t. and a solution of Pd(dtpbf)Cl_2 (12.6 mg, 19.3 µmol, 0.05 equiv.) in dry NMP (690 µL), followed by a solution of $AsPh_3$ (35.4 mg, 116 µmol, 0.30 equiv.) and iodooxazole **27** (146 mg, 385 µmol, 1.00 equiv.) in dry THF (690 µL) were added. The reaction flask was covered in aluminium foil and the reaction was allowed to stir for 20 h. EtOAc (5 mL) and aq. sat. NH_4Cl solution (5 mL) were added, the layers were separated and the aqueous phase was extracted with EtOAc (3x 10 mL). All organic phases were combined, washed with water (2x 10 mL) and brine (10 mL) and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 19:1) yielded alkyl oxazole **36** as a yellow oil (181 mg, 253 µmol, 66%).R_f = 0.29 (CH/EA 30:1).

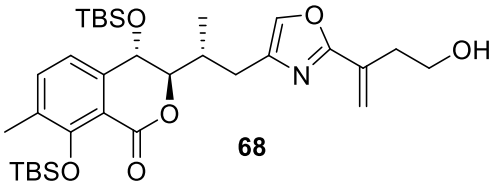
$[\alpha]_D^{20}$ = +70.0 (MeOH, c = 0.2).

^{1}H-NMR (700 MHz, d_6-acetone): δ [ppm] = 7.63 (q, *J* = 0.6 Hz, 1H), 7.47 (dq, *J* = 7.5, 0.7 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 5.91 (d, *J* = 1.3 Hz, 1H), 5.41 (q, *J* = 1.2 Hz, 1H), 5.01 (d, *J* = 3.1 Hz, 1H), 4.32 (dd, *J* = 9.1, 3.1 Hz, 1H), 3.81 (tt, *J* = 7.0, 3.5 Hz, 2H), 2.96 (ddd, *J* = 14.5, 3.3, 1.2 Hz, 1H), 2.79 – 2.76 (m, 4H), 2.68 (td, *J* = 6.6, 1.1 Hz, 2H), 2.51 – 2.45 (m, 1H), 2.28 (d, *J* = 0.7 Hz, 3H), 1.99 – 1.93 (m, 1H), 1.06 (s, 9H), 0.94 – 0.93 (m, 1H), 0.90 (t, *J* = 8.0 Hz, 9H), 0.87 (s, 10H), 0.53 (q, *J* = 8.0 Hz, 6H), 0.23 (d, *J* = 5.7 Hz, 6H), 0.17 (d, *J* = 2.9 Hz, 4H), 0.04 (s, 3H).

^{13}C-NMR (125 MHz, d_6-acetone): δ [ppm] = 162.3, 161.6, 155.2, 140.4, 139.8, 136.5, 134.2, 132.5, 121.0, 118.9, 117.7, 87.6, 68.5, 62.1, 37.2, 34.8, 29.2, 27.5, 26.5, 26.1, 19.2, 18.6, 17.7, 15.6, 7.06, 5.02, –2.98, –3.03, –4.01, –4.34.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{38}H_{65}NO_6Si_3+H]^+$ = 716.4192; Found 716.4181.

5.3. (*3R,4S*)-4,8-bis((*tert*-Butyldimethylsilyl)oxy)-3-((*R*)-1-(2-(4-hydroxybut-1-en-2-yl)oxazol-4-yl)propan-2-yl)-7-methylisochroman-1-one (68)



68

Formic acid (38 µL, 1.01 mmol, 4.00 equiv.) was added to a solution of TES ether **36** (181 mg, 253 µmol, 1.00 equiv.) in MeOH/CH_2Cl_2 (2:1, 3.9 mL) at 0 °C and stirred for 1.5 h. Aq. sat. $NaHCO_3$ solution (5 mL) and CH_2Cl_2 (5 mL) were added and the aqueous phase was extracted with CH_2Cl_2 (3x 4 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash chromatography over silica gel (CH/EA 4:1) yielded alcohol **68** as a colourless oil (93.1 mg, 155 µmol, 61%).

$\boldsymbol{R}_f$ = 0.22 (CH/EA, 4:1).

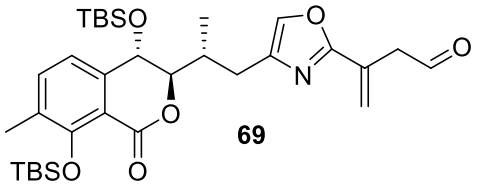
$[\alpha]_D^{20}$ = +66.7 (MeOH, c = 0.3).

^{1}H-NMR (700 MHz, d_6-acetone): δ [ppm] = 7.63 (s, 1H), 7.46 (dq, *J* = 7.5, 0.7 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 5.91 (d, *J* = 1.3 Hz, 1H), 5.42 (q, *J* = 1.3 Hz, 1H), 5.01 (d, *J* = 3.1 Hz, 1H), 4.33 (dd, *J* = 9.1, 3.1 Hz, 1H), 3.73 – 3.69 (m, 1H), 3.63 (t, *J* = 5.6 Hz, 2H), 2.94 (ddd, *J* = 14.5, 3.4, 1.2 Hz, 1H), 2.72 – 2.63 (m, 2H), 2.49 (dd, *J* = 14.5, 9.9 Hz, 1H), 2.28 (d, *J* = 0.7 Hz, 3H), 1.98 – 1.91 (m, 1H), 1.06 (s, 9H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.87 (s, 9H), 0.24 (s, 3H), 0.22 (s, 3H), 0.17 (s, 3H), 0.04 (s, 3H).

^{13}C-NMR (175 MHz, d_6-acetone): δ [ppm] = 162.6, 161.6, 155.2, 140.3, 136.4, 121.0, 118.7, 117.7, 87.5, 68.4, 34.9, 29.2, 26.5, 26.1, 17.7, 15.7, –3.0, –3.1, –4.0, –4.3.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{32}H_{51}NO_6Si_2+H]^+$ = 602.3328; Found 602.3328.

5.4. 3-(4-((R)-2-((3R,4S)-4,8-bis((*tert*-Butyldimethylsilyl)oxy)-7-methyl-1-oxoisochroman-3-yl)propyl)oxazol-2-yl)but-3-enal (69)



69

IBX (64.1 mg, 229 µmol, 3.00 equiv.) was added to a stirring solution of alcohol **68** (45.9 mg, 76.3 µmol, 1.00 equiv.) in EtOAc (820 µL) and heated to 85 °C under reflux for 3 h. The solution was allowed to cool down to r.t. and filtered through a plug of silica gel to yield aldehyde **69** as a yellow oil (38.9 mg, 64.8 µmol, 85%).

R_f = 0.24 (CH/EA 9:1).

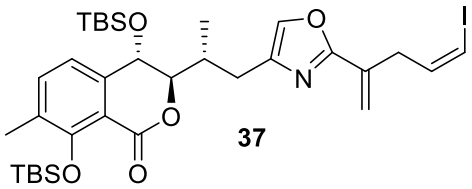
$[\alpha]_D^{20}$ = +70.0 (MeOH, c = 0.2).

^{1}H-NMR (500 MHz, d_6-acetone): δ [ppm] = 9.68 (dt, *J* = 6.9, 1.6 Hz, 1H), 7.68 (s, 1H), 7.46 (dd, *J* = 7.5, 0.9 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.09 (d, *J* = 0.8 Hz, 1H), 5.56 (t, *J* = 1.1 Hz, 1H), 5.00 (d, *J* = 3.2 Hz, 1H), 4.31 (dd, *J* = 9.0, 3.2 Hz, 1H), 3.57 (dt, *J* = 2.8, 1.3 Hz, 2H), 2.93 (ddd, *J* = 14.5, 3.4, 1.2 Hz, 1H), 2.56 – 2.43 (m, 1H), 2.28 (d, *J* = 0.7 Hz, 3H), 1.93 (dddd, *J* = 10.0, 9.1, 6.9, 3.5 Hz, 1H), 1.06 (s, 10H), 0.87 (s, 12H), 0.22 (s, 7H), 0.17 (s, 3H), 0.04 (s, 4H).

^{13}C-NMR (125 MHz, d_6-acetone): δ [ppm] = 199.0, 161.9, 161.6, 155.2, 140.6, 139.8, 137.1, 136.4, 132.5, 129.7, 121.1, 121.0, 117.6, 87.5, 68.4, 47.6, 34.8, 29.1, 26.5, 26.1, 17.7, 15.7, –3.1, –3.1, –4.0, –4.34.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{32}H_{49}NO_6Si_2+H]^+$ = 600.3171; Found 600.3175.

5.5. *(3R,4S)*-4,8-bis((*tert*-Butyldimethylsilyl)oxy)-3-((*R*)-1-(2-((*Z*)-5-iodopenta-1,4-dien-2-yl)oxazol-4-yl)propan-2-yl)-7-methylisochroman-1-one (37)



NaHMDS (1.0m in THF, 153 µL, 1.25 equiv.) was added to a stirring solution of (iodomethyl)-triphenylphosphonium iodide (84.3 mg, 159 µmol, 1.30 equiv.) in dry THF (570 µL) at r.t. and stirred for 5 min. DMI (260 µL) was added and the solution was cooled down to −78 °C. A precooled solution of aldehyde **69** (73.4 mg, 122 µmol, 1.00 equiv.) was added and the reaction stirred for 1 h. Aq. sat. NH_4Cl solution (6 mL) and EtOAc (6 mL) were added, the layers were separated and the aqueous phase was extracted with EtOAc (3x 6 mL). All organic extracts were washed with brine (10 mL) and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash chromatography (CH/EA 19:1) yielded (*Z*)-Vinyliodide **37** as a yellow oil (57.6 mg, 79.6 µmol, 65%).

R_f = 0.26 (CH/EA 19:1).

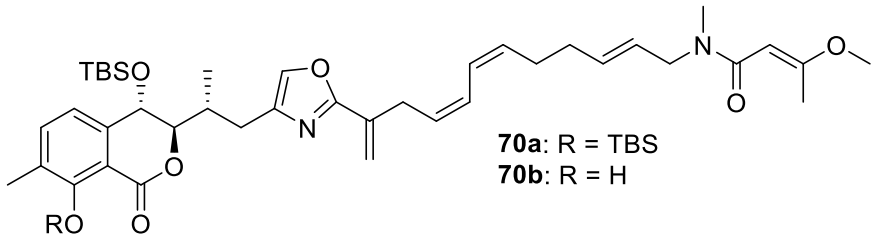
$[\alpha]_D^{20}$ = +70.0 (MeOH, c = 0.2).

^{1}H-NMR (700 MHz, d_6-acetone): δ [ppm] = 7.67 (s, 1H), 7.46 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 6.51 (dt, *J* = 6.9, 1.3 Hz, 1H), 6.41 (q, *J* = 7.0 Hz, 1H), 5.92 (q, *J* = 0.9 Hz, 1H), 5.44 – 5.40 (m, 1H), 5.01 (d, *J* = 3.1 Hz, 1H), 4.34 (dd, *J* = 9.2, 3.1 Hz, 1H), 3.32 (ddq, *J* = 6.5, 5.0, 1.2 Hz, 2H), 2.97 (ddd, *J* = 14.6, 3.4, 1.3 Hz, 1H), 2.52 – 2.46 (m, 1H), 2.28 (s, 3H), 2.02 – 1.94 (m, 1H), 1.06 (s, 9H), 0.89 (d, *J* = 6.7 Hz, 3H), 0.87 (s, 9H), 0.25 (s, 3H), 0.23 (s, 3H), 0.18 (s, 3H), 0.04 (s, 3H).

^{13}C-NMR (175 MHz, d_6-acetone): δ [ppm] = 162.0, 161.6, 155.2, 140.5, 139.7, 138.9, 136.9, 136.4, 133.9, 132.5, 121.1, 117.7, 87.5, 85.2, 68.5, 38.6, 34.8, 29.2, 26.5, 26.1, 17.7, 15.7, –2.9, –2.98, –4.01, –4.32.

HRMS (ESI (+), 6.0 eV): $[M+H]^+$ calcd for $[C_{33}H_{50}INO_5Si_2+H]^+$ = 724.2345; Found 724.2340.

5.6. 3,8-bis-*tert*-Butyldimethylsilyl-ajudazol A (70a)



To a solution of (*Z*)-vinylboronate **31** (41.7 mg, 119 µmol, 1.50 equiv.) and Cs_2CO_3 (130 mg, 398 µmol, 5.00 equiv.) in H_2O (57 µL, 50.0 equiv.) was added a solution of $Pd(dppf)Cl_2$ (8.70 mg, 11.9 µmol, 0.15 equiv.) in dry DMF (70 µL) and a solution of (*Z*)-vinyliodide **37** (20.3 mg, 28.0 µmol, 1.00 equiv.) in dry THF (210 µL) subsequently. The solution was degassed by freeze-pump-thaw-cycles (3x) and stirred in the dark for 19 h. Et_2O (3 mL) and aq. sat. $NaHCO_3$ solution (3 mL) were added, the layers were separated and the aqueous phase was extracted with Et_2O (3x 4 mL). All organic extracts were combined and washed with aq. sat. $NaHCO_3$ solution (4 mL), water (2x 4 mL) and brine (4 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography (CH:EA 3:1) yielded bis-silylated Ajudazol A (**70a**) and 8-*tert*-butyldimethylsilyl-Ajudazol A (**70b**) as an orange oil (39 mg, 50 µmol, 63%).

R_f = 0.21 (CH/EA 3:1).

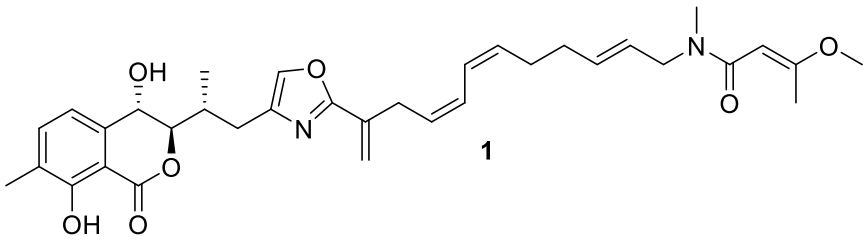
$[\alpha]_D^{20}$ = −20.0 (MeOH, c = 0.1).

^{1}H-NMR (500 MHz, d_6-acetone): δ [ppm] = 7.65 (s, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 7.5 Hz, 1H), 6.48 – 6.30 (m, 2H), 5.88 (d, *J* = 1.1 Hz, 1H), 5.70 – 5.52 (m, 3H), 5.54 – 5.38 (m, 1H), 5.37 (s, 1H), 5.34 (s, 1H), 5.01 (d, *J* = 3.0 Hz, 1H), 4.34 (dd, *J* = 9.2, 3.0 Hz, 1H), 3.92 (dd, *J* = 5.8, 1.6 Hz, 2H), 3.61 (s, 5H), 3.34 (td, *J* = 16.4, 14.6, 7.7 Hz, 2H), 3.00 – 2.93 (m, 4H), 2.85 (s, 3H), 2.78 – 2.75 (m, 1H), 2.53 – 2.44 (m, 1H), 2.28 (s, 3H), 2.26 – 2.15 (m, 2H), 2.14 (s, 5H), 2.02 – 1.89 (m, 1H), 1.06 (s, 9H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 9H), 0.25 (s, 3H), 0.23 (s, 3H), 0.17 (s, 3H), 0.04 (s, 3H).

^{13}C-NMR (125 MHz, d_6-acetone): δ [ppm] = 162.3, 161.6, 155.2, 140.4, 139.7, 136.8, 136.4, 135.9, 132.7, 132.5, 128.5, 126.7, 126.2, 124.6, 121.1, 117.7, 117.3, 92.20, 87.6, 68.5, 55.3, 52.5, 49.2, 34.9, 34.3, 33.3, 32.8, 30.9, 29.3, 28.0, 26.5, 26.1, 17.7, 15.7, –3.00, –3.02, –4.02, –4.33.

HRMS-ESI-(+): $[M+H]^+$ calcd for $[C_{46}H_{70}N_2O_7Si_2+H]^+$ = 819.4794 and $[C_{40}H_{56}N_2O_7Si+H]^+$ = 705.3930; Found 819.4786 and 705.3930.

5.7. Ajudazol A (1)



To an ice-cooled solution of compound **70a** and **70b** (37.9 mg, 46.3 µmol, 1.00 equiv.) in dry THF (1.9 mL) were added dry pyridine (860 µL) and HF·Pyridine (570 µL). The solution was allowed to warm to r.t. and stirred for 3 h. pH 7 buffer solution (4 mL) and EtOAc (4 mL) were added at 0 °C and the layers were separated and the aqueous phase was extracted with EtOAc (3x 5 mL), All organic extracts were combined washed with pH 7 buffer solution (3x 4 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by preparative HPLC ($MeOH/H_2O$ 80:20 → 100:0 → 80:20, RP C-18, flow: 14 mL/min, pressure 173 – 89 mbar, retention time 9.30 min) yielded Ajudazol A (**1**) as a white solid (14.6 mg, 24.7 µmol, 53%).

$\boldsymbol{R_f}$ = 0.31 (CH/EA 1:1).

$[\alpha]_D^{20}$ = +3.3 (MeOH, c = 0.8).

^{1}H-NMR (700 MHz, d_6-acetone): δ [ppm] = 11.29 (s, 1H), 7.71 (t, *J* = 1.1 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 6.43 – 6.36 (m, 1H), 5.92 (d, *J* = 1.3 Hz, 1H), 5.66 – 5.56 (m, 2H), 5.51 (q, *J* = 11.4, 8.4, 7.1 Hz, 1H), 5.45 (dt, *J* = 11.0, 8.0 Hz, 1H), 5.41 (p, *J* = 1.4 Hz, 1H), 5.33 (s, 2H), 5.00 (t, *J* = 6.7 Hz, 1H), 4.47 (dd, *J* = 8.2, 4.6 Hz, 1H), 3.92 (dt, *J* = 6.1, 1.3, 1.3 Hz, 2H), 3.62 (s, 1H), 3.61 – 3.58 (m, 2H), 3.43 – 3.34 (m, 2H), 3.00 – 2.90 (m, 1H), 2.84 (s, 1H), 2.82 (d, *J* = 8.7 Hz, 8H), 2.57 (dd, *J* = 14.7, 8.6 Hz, 1H), 2.48 (dqt, *J* = 8.9, 6.8, 4.5 Hz, 1H), 2.30 (q, *J* = 7.4 Hz, 2H), 2.22 (s, 3H), 2.19 – 2.15 (m, 1H), 2.13 (s, 3H), 1.09 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR (175 MHz, d_6-acetone): δ [ppm] = 170.2, 168.1, 162.4, 160.6, 140.9, 138.9, 136.5, 135.8, 132.8, 132.7, 128.5, 126.9, 126.3, 125.8, 124.7, 117.60, 116.7, 107.3, 92.2, 88.1, 65.4, 55.3, 52.5, 49.3, 35.1, 34.0, 33.3, 32.8, 31.0, 28.0, 27.9, 18.7, 16.7, 15.4.

HRMS-ESI-(+): $[M+H]^+$ calcd for $[C_{34}H_{42}N_2O_7+H]^+$ = 591.3065; Found 591.3067.

The experimental data are in agreement with those previously published.[26]

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[26] Jansen, R.; Kunze, B.; Reichenbach, H.; Höfle, G. *Eur. J. Org. Chem.* **2002**, 917-921.

Figure 1. Analytical UV/VIS-HPLC trace of synthetic ajudazol A (**1**)

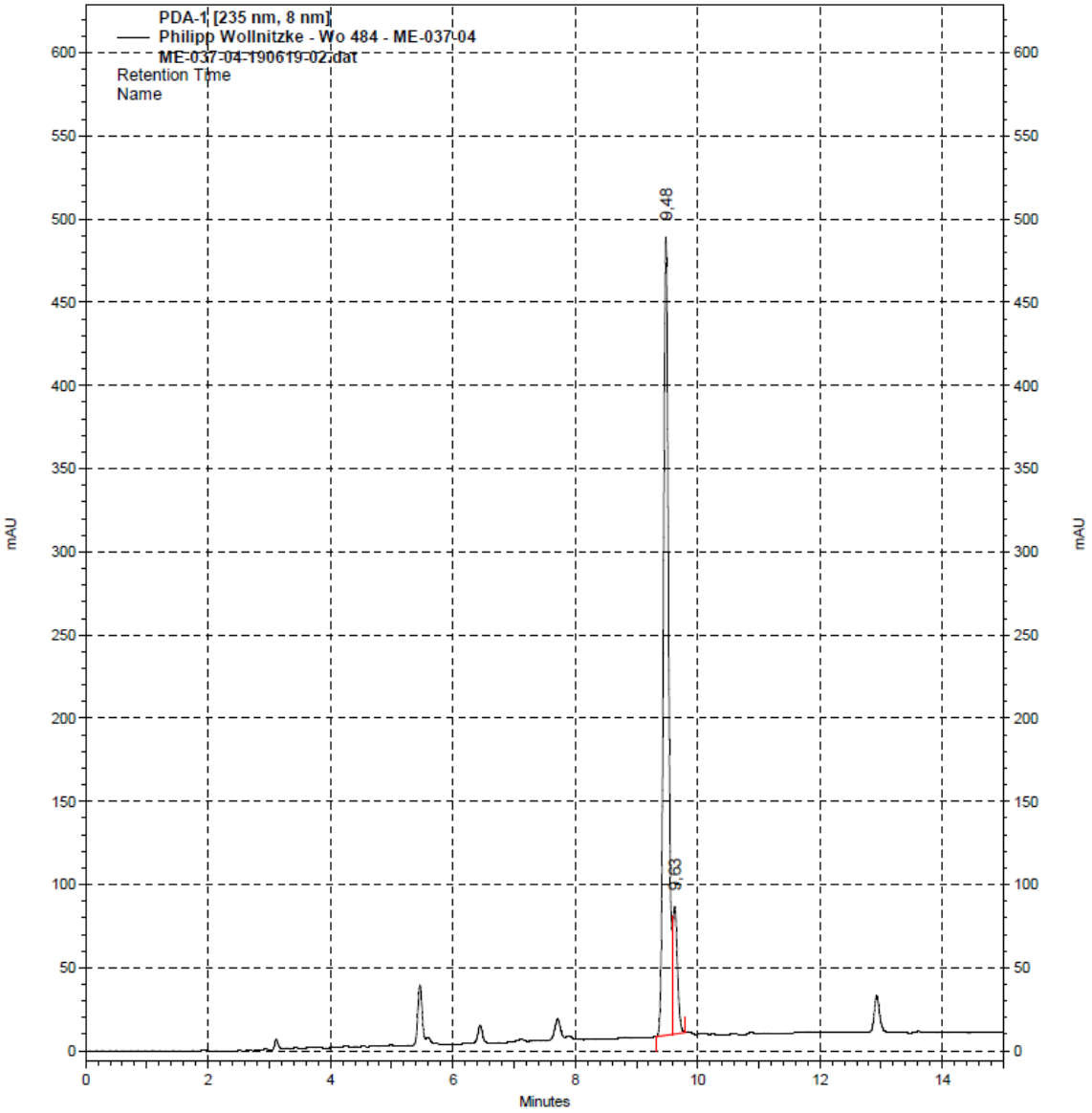
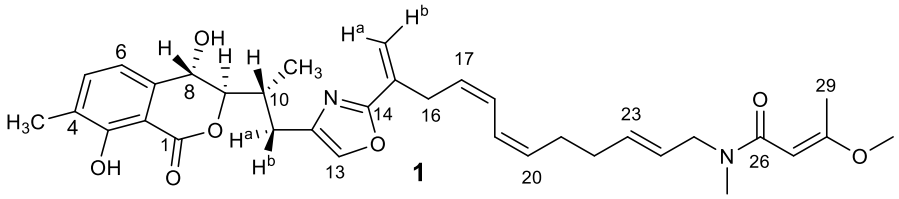


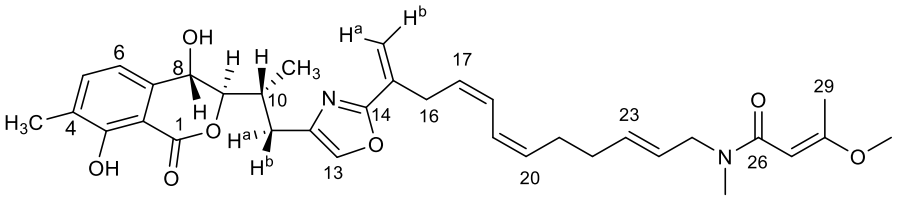
Table 2. NMR-Data of synthetic ajudazol A (**1**) (d_6-acetone, 700/175 MHz, r.t.) in comparison with natural ajudazol A (d_6-DMSO/D_2O, 600/150 MHz, 80 °C) Chemical shifts δ are given in [ppm].



Synthetic (700/175 MHz, d_6-acetone, r.t.)					Natural (600/150 MHz, d_6-DMSO, 80 °C)			
Atom	**δ_H**	**m**	***J* [Hz]**	**δ_C**	**δ_H**	**m**	***J* [Hz]**	**δ_c [ppm]**
1	–	–	–	170.19	–	–	–	168.62
2	–	–	–	107.25	–	–	–	106.26
3	–	–	–	160.64	–	–	–	158.63
3-OH	11.29	s	–	–	11.10	s	br	–
4	–	–	–	125.79	–	–	–	125.11
4-CH_3	2.22	s	–	15.45	2.17	s	br	14.82
5	7.47	d	7.6	137.99	7.44	dd	7.6, 0.8	137.24
6	7.05	d	7.6	116.71	6.95	d	7.6	116.63
7	–	–	–	140.91	–	–	–	140.21
8	5.00	t	6.71	65.37	4.79	d	6.7	63.87
9	4.47	dd	8.2, 4.6	88.09	4.39	dd	6.7, 5.6	87.26
10	2.48	dqt	8.9, 6.4, 4.5	34.04	2.20	m	–	33.29
10-CH_3	1.09	d	6.6	16.72	0.94	d	6.9	15.78
11_a	2.95	m	–	28.04	2.78	ddd	14.8, 4.7, 1.1	27.63
11_b	2.57	dd	14.7, 8.6		2.45	dd	14.9, 8.7	
12	–	–	–		–	–	–	139.39
13	7.71	s	–	136.51	7.68	s	–	135.75
14	–	–	–	162.43	–	–	–	161.02
15	–	–	–	135.83	–	–	–	134.36
15-CH_a	5.92	s	–	117.60	5.85	s	br	117.42
15-CH_b	5.41	s	–		5.35	s	br	
16	3.38	m	–	31.02	3.27	d	7.8 br	30.03
17	5.60	m	–	128.45	5.52	m	–	127.64
18	6.40	m	–	126.25	6.29	m	–	125.20
19	6.40	m	–	124.67	6.28	m	–	123.64
20	5.45	m	–	132.68	5.45	m	–	131.97
21	2.30	q	7.4	27.94	2.19	m	–	26.75
22	2.17	m	–	33.25	2.08	m	–	31.36
23	5.60	m	–	132.78	5.54	ddt	15.4, 6.7, 1.4	131.97
24	5.51	m	126.86	126.86	5.39	dt	15.3, 5.7, br	125.70
25	3.92	dt	6.1, 1.3	52.46/49.28	3.84	d	5.7 br	50.05/49.21
25-NCH_3	2.84/2.82	s	br	35.06/32.81	2.82	s	–	35.01/35.00
26	–	–	–	168.07	–	–	–	167.96
27	5.33	s	br	92.20	5.24	s	br	91.84
28	–	–	–	n.s.	–	–	–	166.96
28-OCH_3	3.62/3.60	s	br	55.29	3.53	s	–	54.76
29	2.13	s	br	18.73	2.04	s	br	18.10

Legend: br = broad signal, n.s. = not visible due to distinctive amide resonance.

Table 3. ^{1}H- and ^{13}C-NMR spectroscopic data of synthetic ajudazol A (**1**) at −40 °C (500/125 MHz)



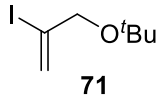
Atom	Measurement in d^{6}–acetone (500/125 MHz)					
	δ_H [ppm] (*E*)	δ_H [ppm] (*Z*)	m	δ_C [ppm] (*E*)	δ_C [ppm] (*Z*)	m
1	–		–	170.10		s
2	–		–	106.77		s
3	–		–	160.18		s
3-OH	11.30		s	–		–
4	–		–	125.71		d
4-CH_3	2.19		s	15.54		s
5	7.49		d	137.82		s
6	7.08		d	116.20		d
7	–		–	140.37		s
8	5.06		dd	64.39		d
9	4.45		dt	87.60		d
10	2.49[a]		m	34.73		m
10-CH_3	1.01		d	16.36		s
11_a	2.93[b]		m	26.97		d
11_b	2.52[a]		m			
12	–		–	140.37		s
13	7.85		s	136.63		s
14	–		–	162.06		s
15	–		–	135.14		s
15-CH_a	5.93		s	117.66		s
15-CH_b	5.43		s			
16	3.37		t	30.52		s
17	5.58[c]		dq	127.89		d
18	6.42[d]		m	126.21		d
19	6.42[d]		m	124.31		d
20	5.48[e]		dq	132.95		d
21	2.27		p	27.58		s
22	2.17[f]		m	33.11		s
23	5.58[c]		dq	132.42		d
24	5.48[e]		dq	126.53		d
25	3.91	3.88	d	52.07	48.90	s
25-NCH_3	2.81[g]	2.93[b]	s	32.63	32.91	d
26	–		–	168.69		d
27	5.31	5.36	s	91.72		s
28	–		–	167.50		d
28-OCH_3	3.57	3.61	d	55.19		d
29	2.12[f]		m	16.36		s

[a] overlapping Signals: H-10/H-11_b, [b]overlapping signals: H-11_a/(*Z*)-NCH_3, [c] overlapping signals: H-17/H-23, [d] overlapping signals: H-18/H-19, [e] overlapping signals: H-20/H-24, [f] overlapping signals: H-22/H-29, [g] overlap with solvent residual signal (d_6-acetone)

6. Additional studies

6.1. Sulfone displacement

6.1.1. 3-(*tert*-Butoxy)-2-iodoprop-1-ene (71)



71

A stirring solution of 2-iodoprop-2-en-1-ol (**39**) (10.4 g, 56.5 mmol, 1.00 equiv.) in heptane (28 mL) containing amberlyst-15 (2.83 g, 50 mg/mmol) was infused with an excess of isobutylene gas for 3 h. The mixture was filtrated and the solvent was removed *in vacuo* (100 mbar, 40 °C). Distillation of the residue (48 °C, 6 mbar) gave **70** as a colourless liquid (11.2 g, 46.5 mmol, 82%).

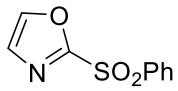
R$_f$ = 0.49 (CH/EA 29:1).

^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 6.42 (q, *J* = 1.7 Hz, 1H), 5.83 (q, *J* = 1.4 Hz, 1H), 3.97 (t, *J* = 1.6 Hz, 2H), 1.23 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ [ppm] = 124.6, 108.8, 74.4, 27.8.

MS (EI (+), 70.0 eV): $[M]^{\bullet+}$ calcd for $[C_7H_{13}IO]^{\bullet+}$ = 240.0006; Found 240.0008.

6.1.2. 2-Phenylsulfonyloxazole (72)



72

Ammonium molybdate tetrahydrate (2.50 g, 2.02 mmol, 2.20 equiv.) was dissolved in aq. hydrogen peroxide solution (35% *v/v*, 485 mL, 2.20 equiv.) at 0 °C and stirred for 15 min. The resulting yellow solution was added dropwise to a solution of thiooxazole **8** (7.66 g, 43.2 mmol, 1.00 equiv.) in EtOH (700 mL) and the reaction was allowed to warm to r.t. and stirred overnight (18 h). Et_2O (500 mL) was added, the layers were separated and the aqueous phase was extracted with Et_2O (3x 500 mL). All organic extracts were combined and washed with brine (250 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography (CH/EA 3:2) gave sulfonyloxazole **72** as white solid (8.67 g, 41.4 mmol, 96%).

R$_f$ = 0.28 (CH:EA 3:2).

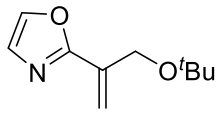
Mp.: 82-83 °C.

^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 8.08 – 8.16 (m, 2H), 7.78 (s, 1H), 7.66 – 7.75 (m, 1H), 7.60 (dd, *J* = 8.5, 7.1 Hz, 2H), 7.30 (s, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ [ppm] = 158.9, 142.3, 138.0, 135.1, 129.7, 129.4, 129.0.

HRMS (EI (+), 70.0 eV): $[M^{+\bullet}]$ calcd for $[C_9H_7NO_3S]^{+\bullet}$ = 334.9113, Found 334.9105.

6.1.3. 2-(3-*tert*-Butoxy)prop-1-en-2-yl)oxazole (73)



73

To a stirring solution of 3-(*tert*-butoxy)-2-iodoprop-1-ene (**71**) (1.09 g,4.53 mmol, 1.50 equiv.) in Et_2O (53 mL) was added dropwise *tert*-Butyllithium (1.7M in pentane, 5.30 mL, 9.01 mmol, 3.00 equiv.) at –78 °C and stirred for 2 h. The mixture was added to a stirring solution of 2-(Phenylsulfonyl)oxazole (**72**) (632 mg, 3.02 mmol, 1.00 equiv.) in THF (23 mL) at room temperature via cannula and stirred for 10 min. The reaction was quenched with water (100 mL) and the phases were separated. The aqueous layer was extracted with DCM (3x 100 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification via flash column chromatography (CH/EA 4:1) gave **73** as a colourless liquid.

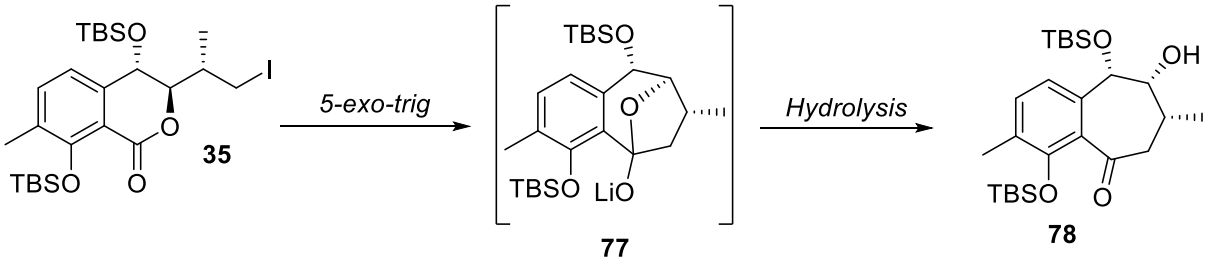
^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.60 (d, *J* = 0.8 Hz, 1H), 7.13 (d, *J* = 0.9 Hz, 1H), 6.11 (q, *J* = 1.6 Hz, 1H), 5.78 (q, *J* = 1.9 Hz, 1H), 4.37 (t, *J* = 1.8 Hz, 2H), 1.27 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ [ppm] = 158.9, 142.3, 138.0, 135.1, 129.7, 129.4, 129.0.

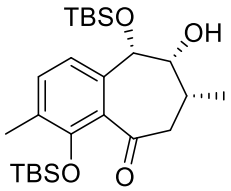
HRMS (EI (+), 70.0 eV): $[M]^+$ calcd for $[C_{10}H_{15}NO_2^{+\bullet}–CH_3^{\bullet}]^+$: 166.0863; Found 166.0871.

6.2. Lithiation studies of Western subunit 35

Suzuki coupling of Western subunit **35** with 4-iodoxazoles were not feasible. In consequence the polarity inversion of alkyl iodide **35** was investigated. Unsuccessful results followed from decomposition and an unexpected side product formed by a *5-exo-trig*-cyclization:



6.2.1. (7*R*,8*R*,9*S*)-4,9-*bis*((*tert*-butyldimethylsilyl)oxy)-8-hydroxy-3,7-dimethyl-6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-5-one (78)



78

^{t}BuLi (1.7M in ^{n}pentane, 40 µL, 67 µmol, 2.00 equiv.) was added to a stirring solution of alkyl iodide **35** at –96 °C and stirred for 1 h. D_2O (91 µL, 5.03 mmol, 150 equiv.) was added and the solution was allowed to warm to r.t. Water (600 µL) and CH_2Cl_2 (600 µL) were added, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3x 800 µL). All organic phases were combined and dried over $MgSO_4$. Removal of the solvent *in vacuo* and purification of the residue by flash column chromatography ocer silica gel (CH/EA 30:1) yielded ketone **78** as a colourless oil (0.6 mg, 1.29 µmol, 4%).

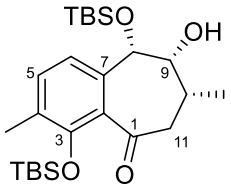
R_f = 0.13 (CH/EA 30:1).

^{1}H-NMR (500 MHz, CD_2Cl_2): δ [ppm] = 7.15 (dq, *J* = 7.6, 0.8 Hz, 1H), 6.76 (d, *J* = 7.5 Hz, 1H), 4.81 (d, *J* = 5.1 Hz, 1H), 3.84 – 3.73 (m, 1H), 2.79 (dd, *J* = 19.0, 13.2 Hz, 1H), 2.54 (d, *J* = 10.1 Hz, 1H), 2.22 (d, *J* = 0.7 Hz, 3H), 2.17 (dd, *J* = 18.1, 2.2 Hz, 2H), 1.26 (d, *J* = 6.9 Hz, 3H), 0.99 (s, 9H), 0.84 (s, 9H), 0.12 (s, 3H), 0.06 (s, 3H), 0.02 (s, 3H), -0.32 (s, 3H).

^{13}C-NMR (125 MHz, CD_2Cl_2): δ [ppm] = 204.0, 151.9, 138.3, 132.9, 131.9, 121.3, 77.4, 72.9, 45.0, 32.7, 26.3, 26.1, 18.5.

HRMS (ESI (+), 6.0 eV): $[M+Na]^+$ calcd for $[C_{25}H_{44}O_4Si_2+Na]^+$ = 487.2670; Found 487.2670.

Table 4. NMR-Data of compound **78** (CD_2Cl_2, 500/125 MHz, r.t.).



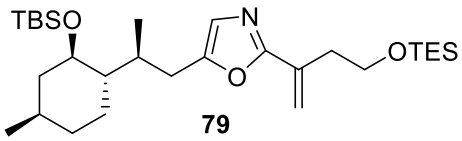
78

Atom	δ_H [ppm]	m	*J* [Hz]	δ_C [ppm]
1	–	–	–	203.97
2	–	–	–	130.50
3	–	–	–	151.86
4	–	–	–	131.89
4-Me	2.22	s	–	18.53
5	7.15	d	7.6	121.26
6	6.76	d	7.5	132.88
7	–	–	–	138.27
8	4.81	d	5.1	77.36
9	3.77	m	–	72.90
10	2.15	m[a]	–	32.74
10-Me	1.00	d	6.9	17.65
11	2.17	m[a]	–	44.96
	2.79	dd	19.0, 13.2	

[a] Overlapping signals $H^{10} \leftrightarrow H^{11}$.

6.3. C^5-alkylation of oxazoles by cross coupling

6.3.1. 5-((*S*)-2-((1*S*,2*R*,4*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-4-methylcyclohexyl)propyl)-2-(4-((triethylsilyl)oxy)but-1-en-2-yl)oxazole (79)



79

Anhydrous LiCl (155 mg, 3.66 mmol, 4.20 equiv.) was heated under vacuum at 150–170 °C for 5 min. Zinc powder (325 mesh, 112 mg, 1.71 mmol, 1.96 equiv.) was added and dried also under vacuum at 150–170 °C for 5 min. The reaction flask was flushed with argon (3x) and dry THF (360 µL) was added. $C_2H_4Br_2$ (5.5 µL, 61.0 µmol, 0.07 equiv.) and TMSCl (90 µL, 15 mg/mL in dry THF, 90 µL, 13.8 µmol, 1.40 mol%) were added to the stirring suspension and the reaction was heated to 50 °C for 10 min. A solution of alkyl iodide **21** (483 mg, 1.22 mmol, 1.40 equiv.) in dry THF (530 µL) was added and stirred for 2 h. The solution was allowed to cool down to r.t. and a solution of $Pd(dtpbf)Cl_2$ (28.4 mg, 43.6 µmol, 0.05 equiv.) in dry NMP (1.0 mL), followed by a solution of $AsPh_3$ (80.0 mg, 261 µmol,

0.30 equiv) and iodooxazole **27** (330 mg, 871 µmol, 1.00 equiv.) in dry THF (1.0 mL) were added. The flask was covered in aluminium foil and was allowed to stir for 2 h. EtOAc (4 mL) and aq. sat. NH_4Cl solution (4 mL) were added, the layers were separated and the aqueous phase was extracted with EtOAc (3x 9 mL). All organic phases were combined and washed with brine (10 mL). Drying over $MgSO_4$, removal of the solvent *in vacuo* and purification of the residue by flash column chromatography over silica gel (CH/EA 50:1) yielded alkyl oxazole **79** as a yellow oil (321 mg, 88.1 µmol, 10%).$\boldsymbol{R_f}$ = 0.11 (CH/EA 50:1).

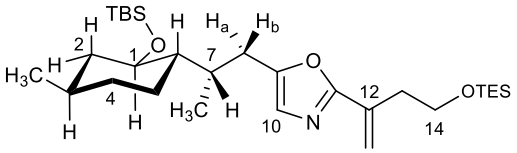
$\mathbf{[\alpha]_D^{20}}$ = −27.0 (MeOH, c = 1.0).

^{1}H-NMR (700 MHz, d$_6$-acetone): δ [ppm] = 6.81 (dd, *J* = 1.3, 0.6 Hz, 1H), 5.90 (d, *J* = 1.4 Hz, 1H), 5.40 (q, *J* = 1.3 Hz, 1H), 3.86 (td, *J* = 6.7, 2.1 Hz, 2H), 3.66 (td, *J* = 10.2, 4.3 Hz, 1H), 2.74 – 2.78 (m, 1H), 2.72 (tt, *J* = 6.7, 1.2 Hz, 2H), 2.49 (ddtd, *J* = 14.0, 6.9, 3.6, 2.3 Hz, 1H), 2.37 (dd, *J* = 14.8, 11.7 Hz, 1H), 2.00 (dddd, *J* = 12.3, 4.2, 3.4, 1.9 Hz, 1H),), 1.66 – 1.74 (m, 2H), , 1.43 – 1.52 (m, 1H), 1.26 – 1.33 (m, 1H), 1.07 – 1.15 (m, 1H),), 0.99 – 1.04 (m, 2H), 0.96 – 0.98 (m, 1H), 0.93 (d, *J* = 2.2 Hz, 12H),), 0.87 – 0.95 (m, 12H), 0.85 – 0.88 (m, 1H), 0.57 (q, J = 8.0 Hz, 6H), 0.16 (s, 3H), 0.13 (s, 3H).

^{13}C-NMR (175 MHz, d$_6$-acetone): δ [ppm] = 161.7, 153.3, 134.3, 125.3, 118.0, 72.6, 62.2, 51.3, 46.5, 37.2, 35.4, 32.2, 31.0, 27.8, 26.4, 24.7, 22.6, 18.6, 18.2, 7.1, 5.1, –3.29, –4.28.

HRMS (ESI (+), 5.0 eV $[M+H]^+$ calcd for $[C_{29}H_{55}NO_3Si_2+H]^+$ = 522.3793; Found 522.3791.

Table 5. NMR-Data of compound **79** (d_6-acetone, 700/175 MHz, r.t.).



79

Atom	δ_H [ppm]	m	*J* [Hz]	δ_C [ppm]
–Si-(**CH$_3$)$_2$**C(CH$_3$)$_3$	0.13/0.16	td	4.3, 10.2	–4.28/–3.29
–Si-(CH$_3$)$_2$**C**(CH$_3$)$_3$	–	–	–	18.63
–Si-(CH$_3$)$_2$C**(CH$_3$)$_3$**	0.91	–	–	26.43
1	3.66	td	4.3, 10.2	72.56
2_{ax}	1.01	m	–	46.49
2_{eq}	2.00	dddd	12.3, 4.2, 3.4, 1.9	
3	1.47	m	–	32.34
3-CH$_3$	0.93	m	–	30.97
4_{ax}	0.87	m	–	35.38
4_{eq}	1.69	m	–	
5_{ax}	1.12	m	–	24.74
5_{eq}	1.69	m	–	
6	1.29	m	–	51.30
7	0.91	m	–	22.59
7-CH$_3$	0.91	m	–	18.23
8_a	2.37	dd	14.8, 11.4	27.83
8_b	2.77	m	–	
9	6.81	s	–	153.53
10	–	–	–	125.33
11	–	–	–	161.68
12	–	–	–	134.27
12-CH$_a$	5.90	d	1.4	117.99
12-CH$_b$	5.40	q	1.2	
13	2.72	tt	1.2, 6.7	37.22
14	3.86	td	2.1, 6.7	62.24
–Si-**CH$_2$**CH$_3$	0.57	q	8.0	5.05
–Si-CH$_2$**CH$_3$**	0.91	m	–	7.07

7. Biological Studies

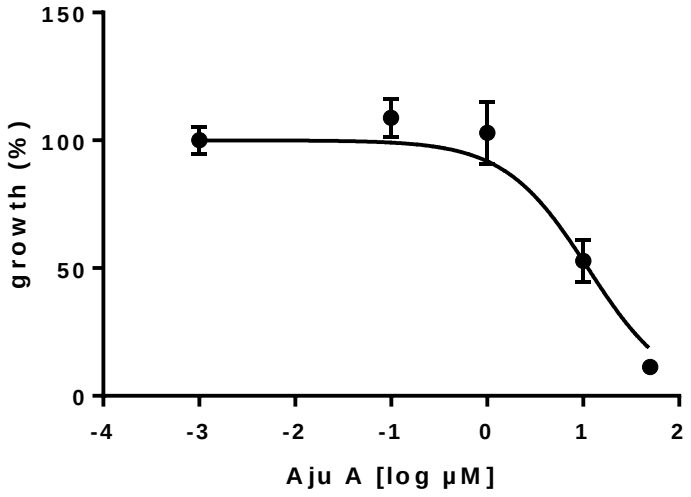


Figure 1. Half maximal inhibitory concentration of ajudazol A (**1**) measured by construction of a dose-response curve (Jurkat cell line). IC_{50} = 11.21 µM.

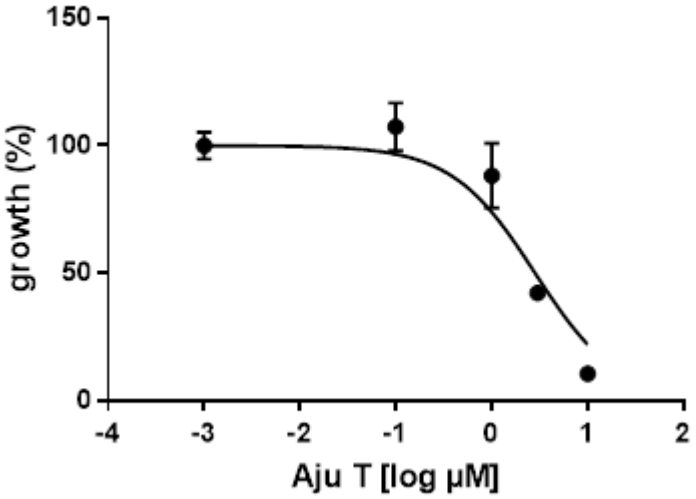


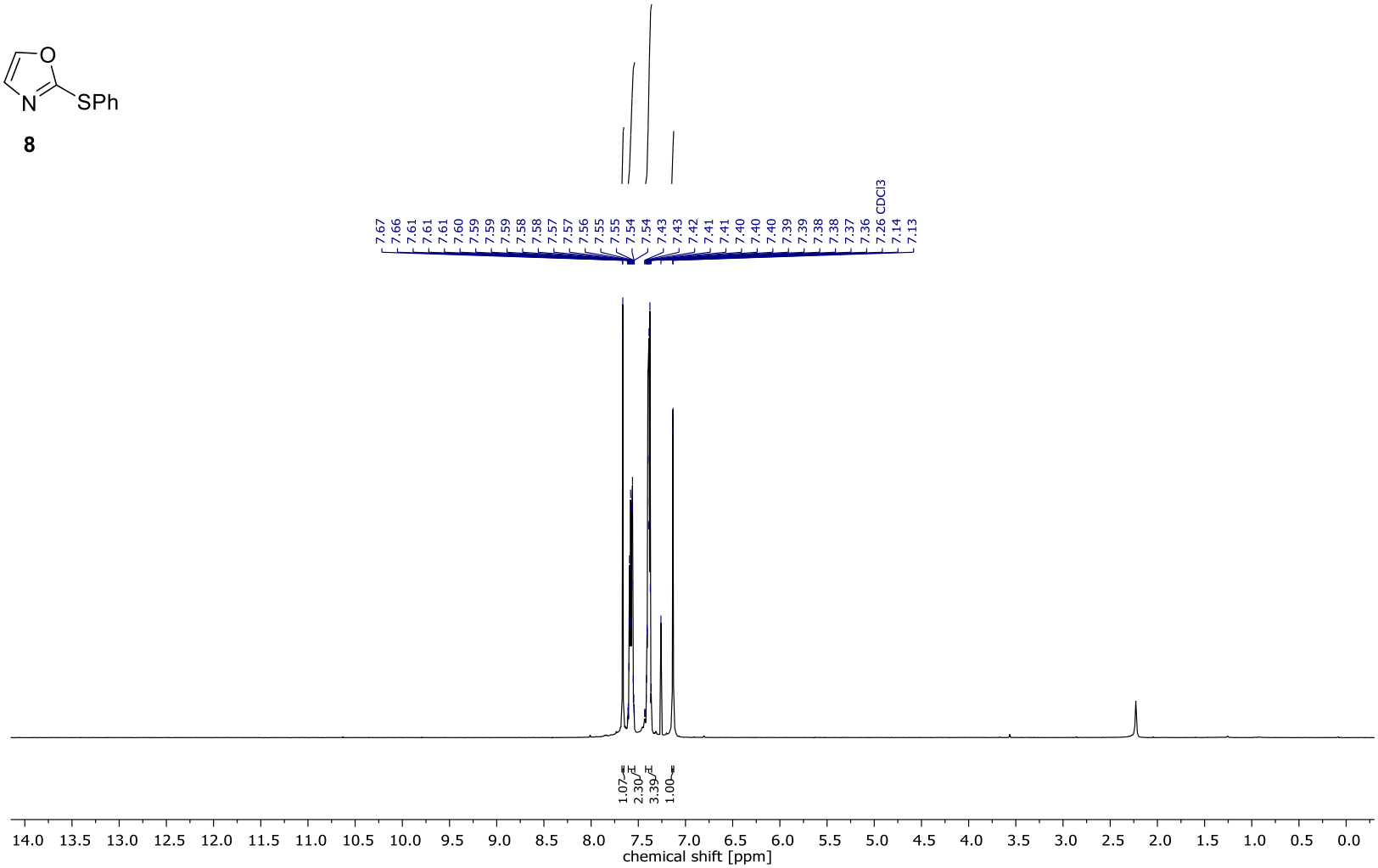
Figure 2. Half maximal inhibitory concentration of compound **33** measured by construction of a dose-response curve (Jurkat cell line). IC_{50} = 2.83 µM.

8. NMR-spectra

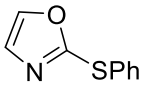
– Illustrations of the NMR spectra start on the next page –

1H-NMR, 300.13 MHz,
CDCl3

8



13C-NMR, 75.48 MHz,
CDCl3



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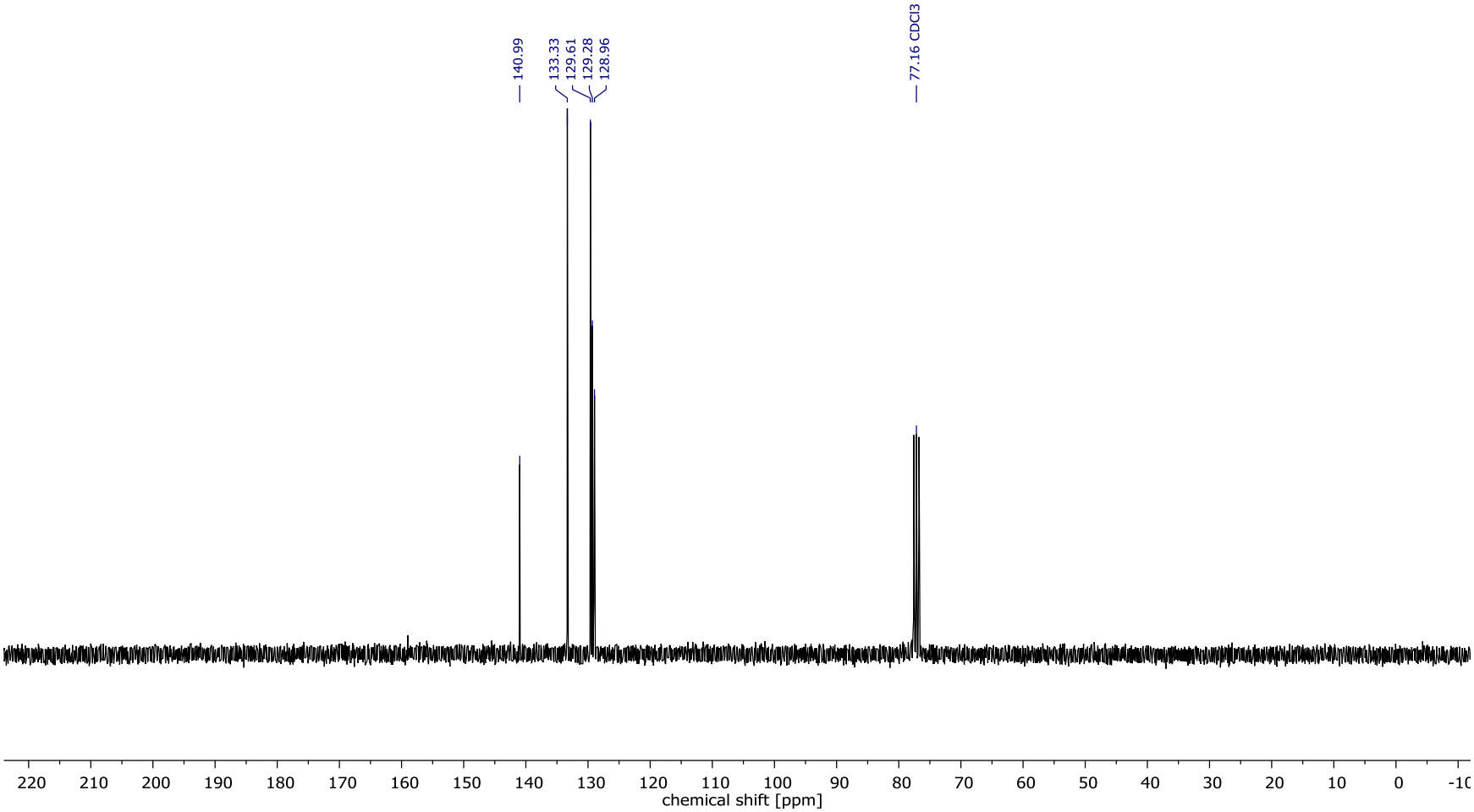
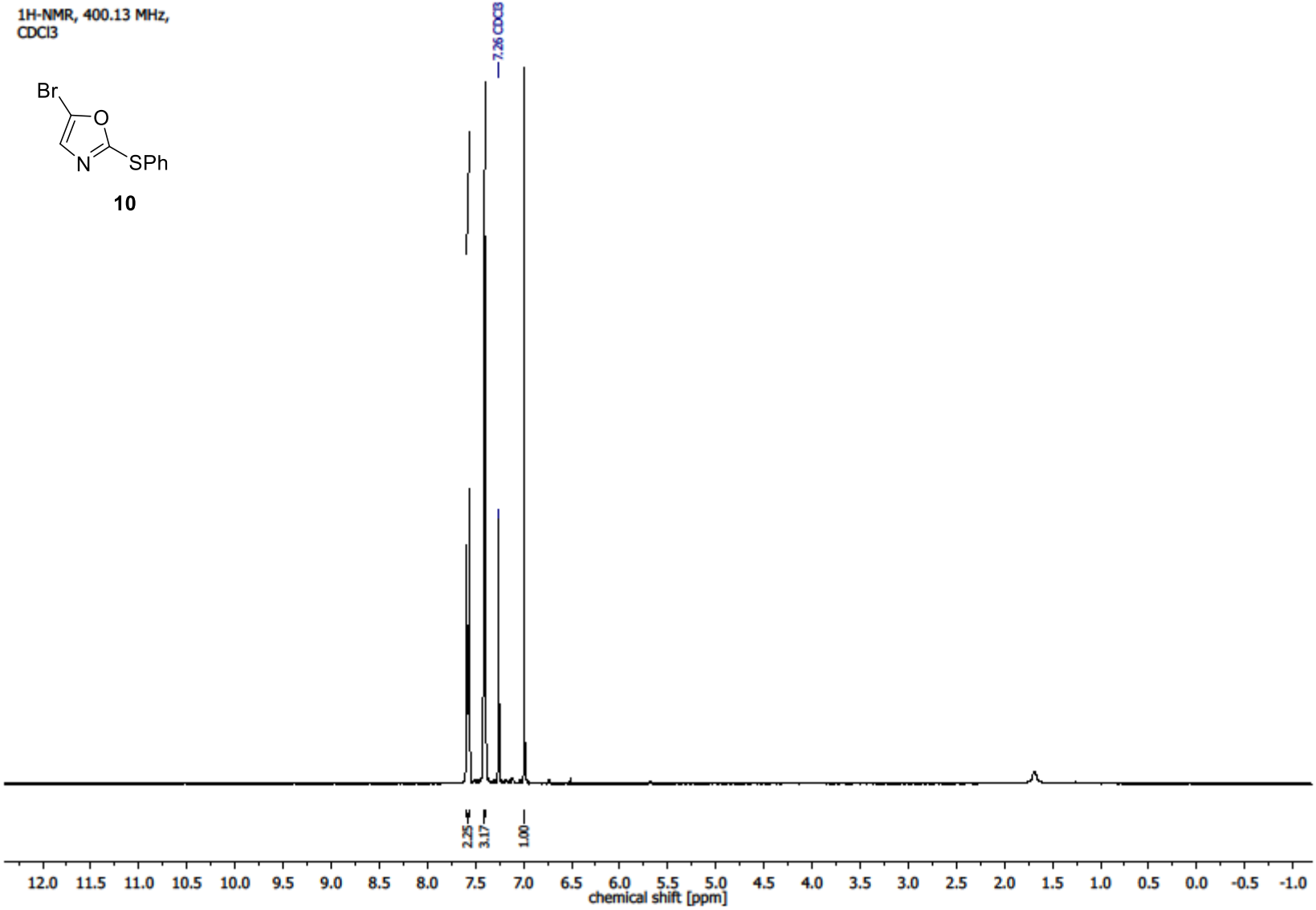
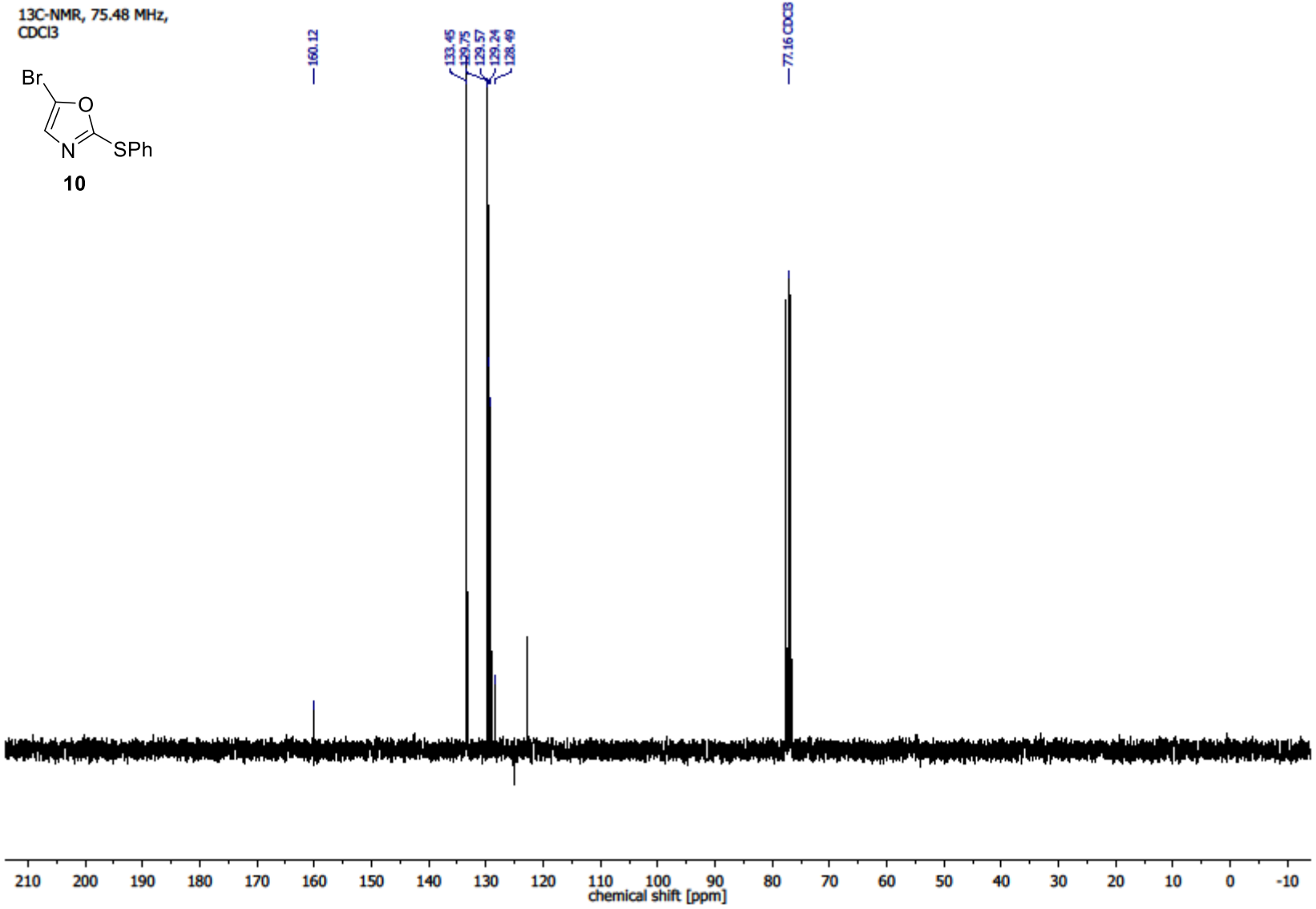


1H-NMR, 400.13 MHz,
CDCl3

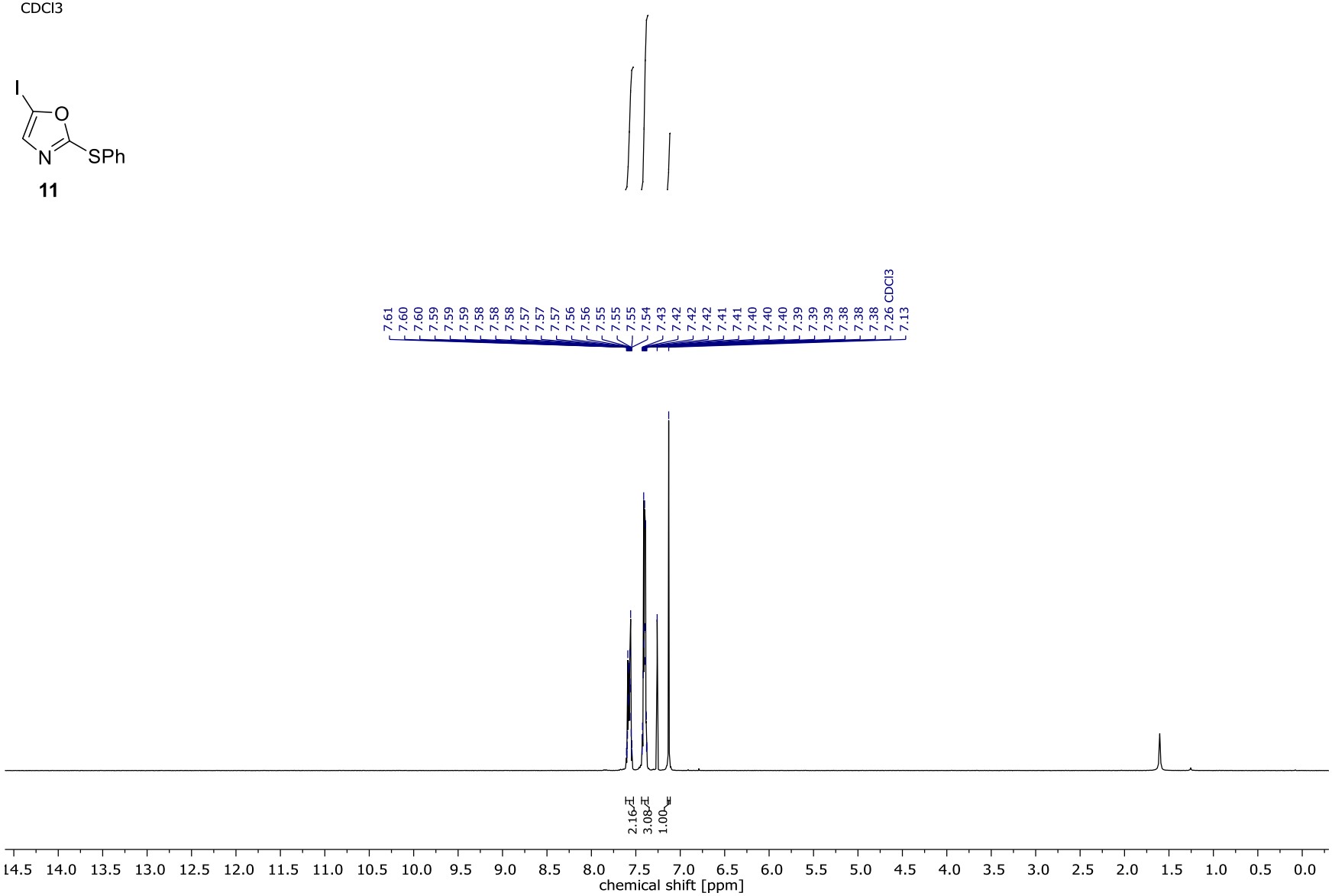
10



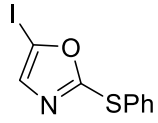

13C-NMR, 75.48 MHz,
CDCl3
Br
O
N
SPh
10
160.12
133.45
129.75
129.57
129.24
128.49
77.16 CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
chemical shift [ppm]

1H-NMR, 300.13 MHz,
CDCl3

11



13C-NMR, 75.48 MHz,
CDCl3



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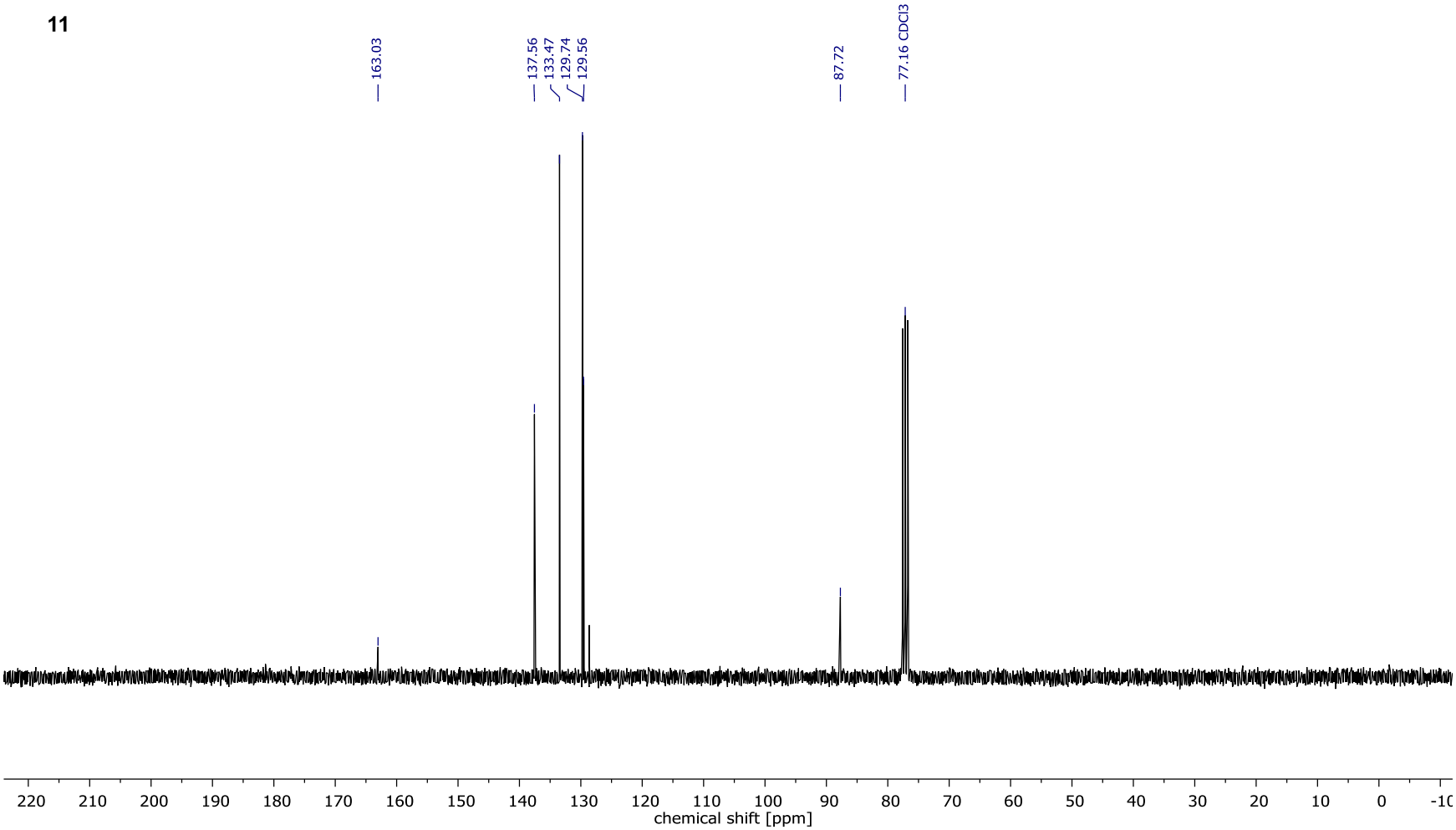
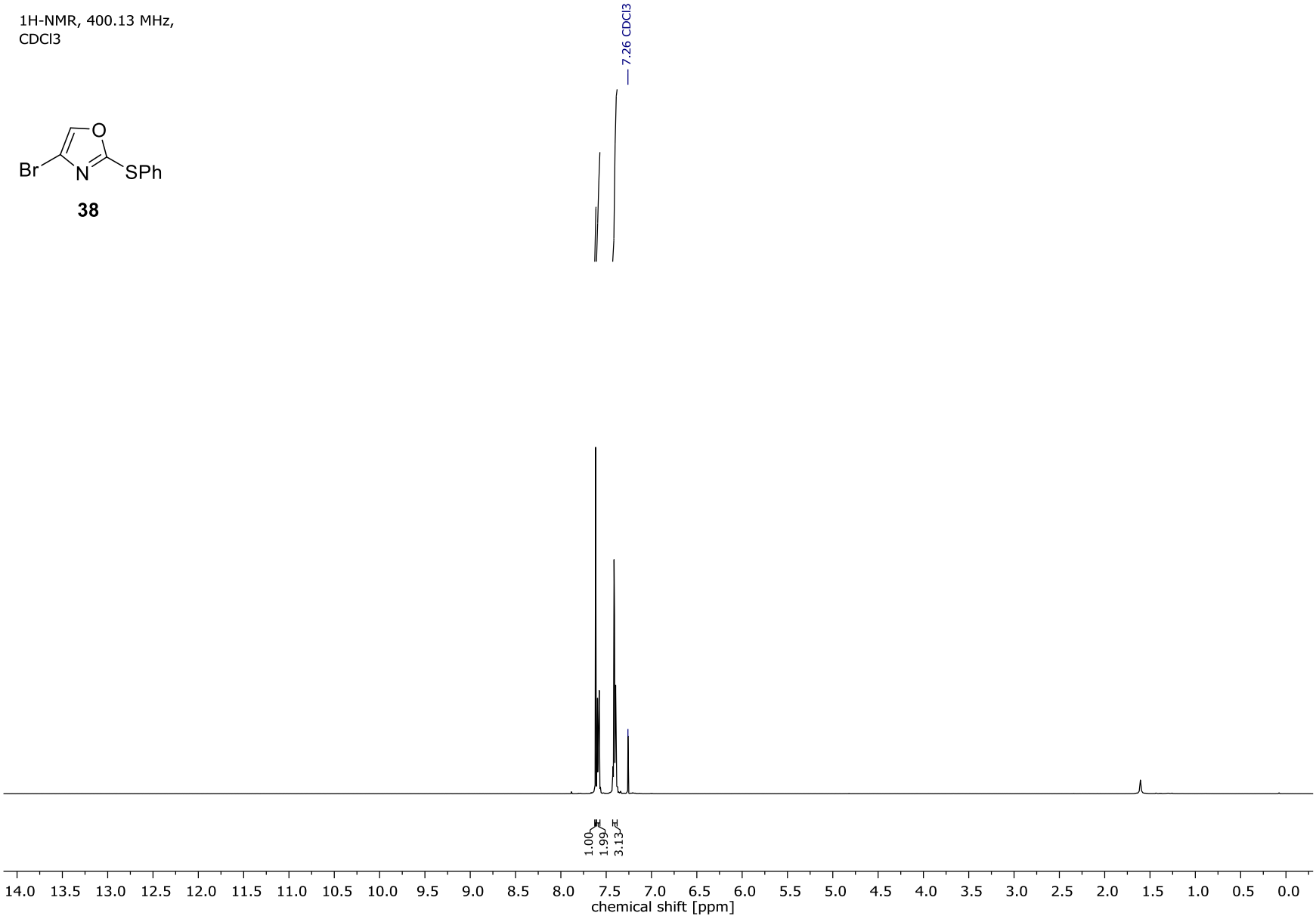


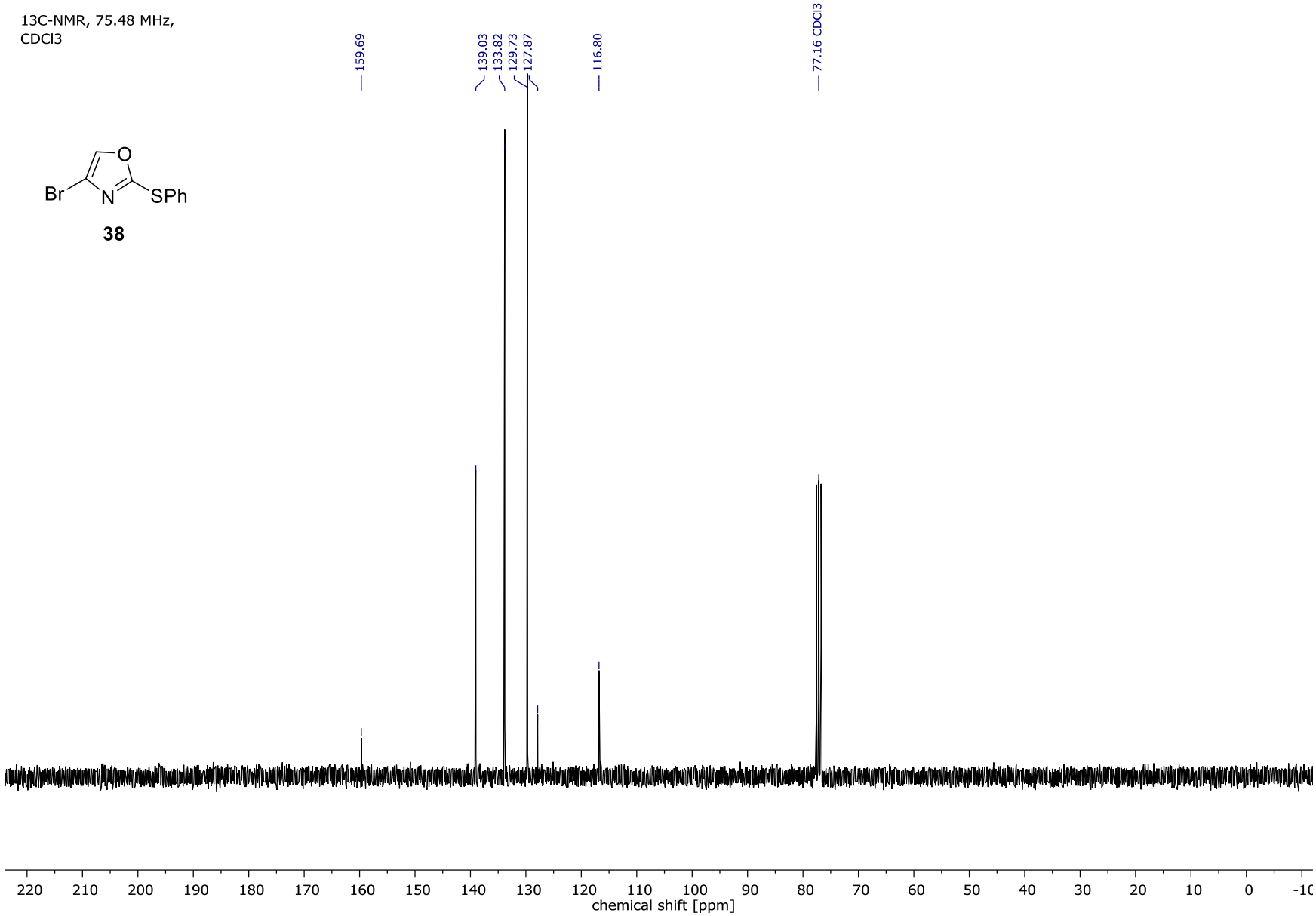
1H-NMR, 400.13 MHz,
CDCl3

38



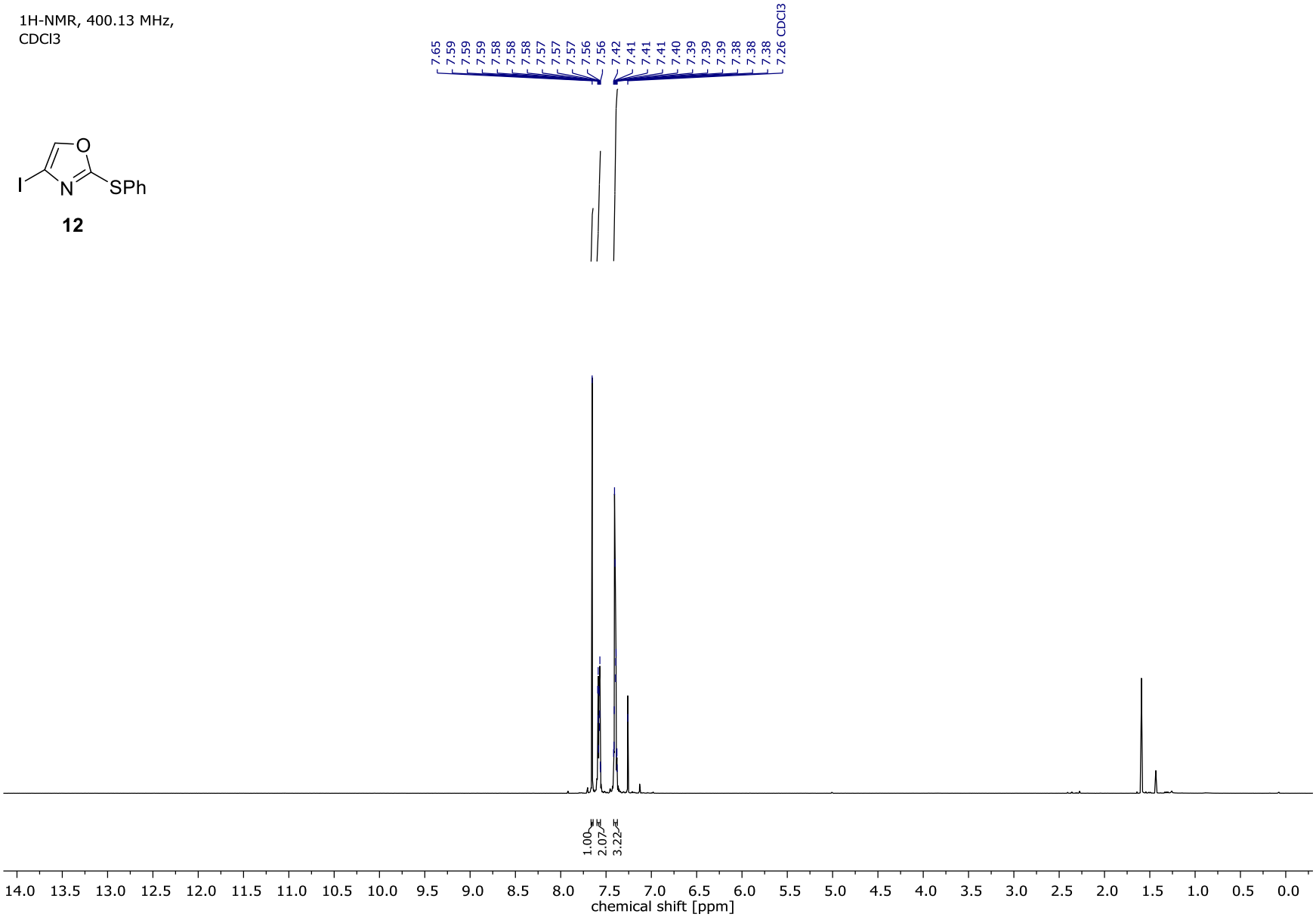
13C-NMR, 75.48 MHz,
CDCl3

38



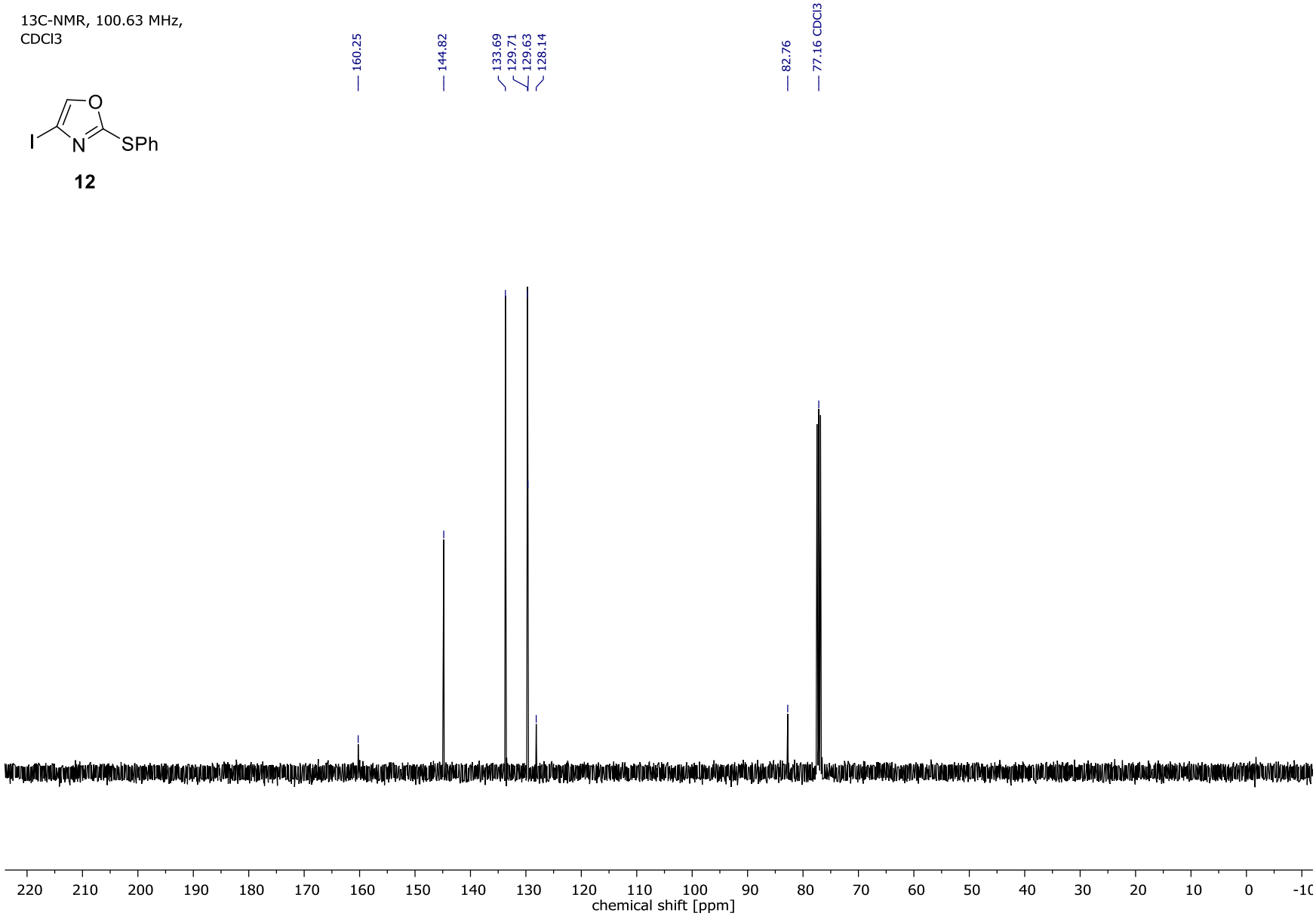
1H-NMR, 400.13 MHz,
CDCl3

12



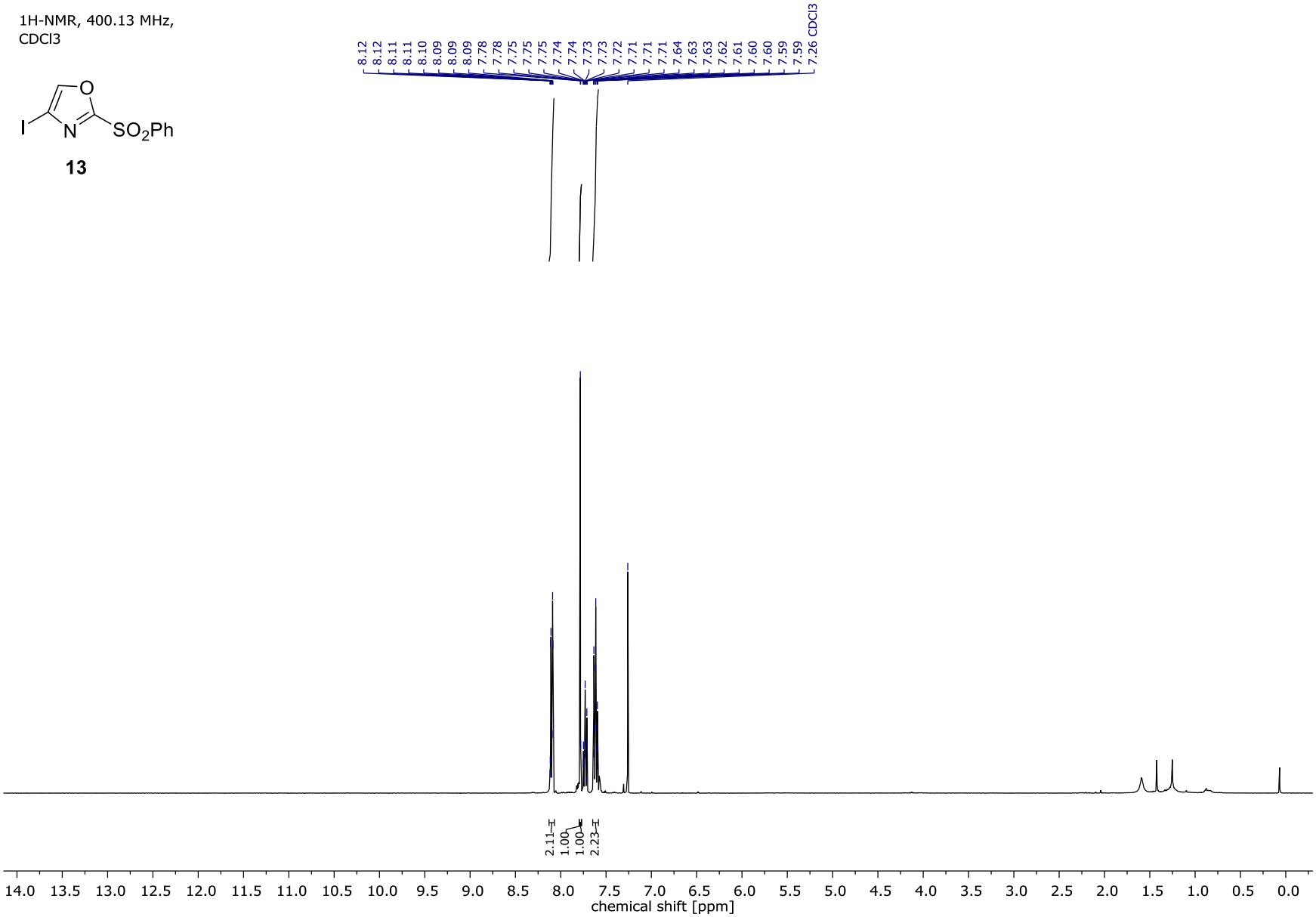
13C-NMR, 100.63 MHz,
CDCl3

12



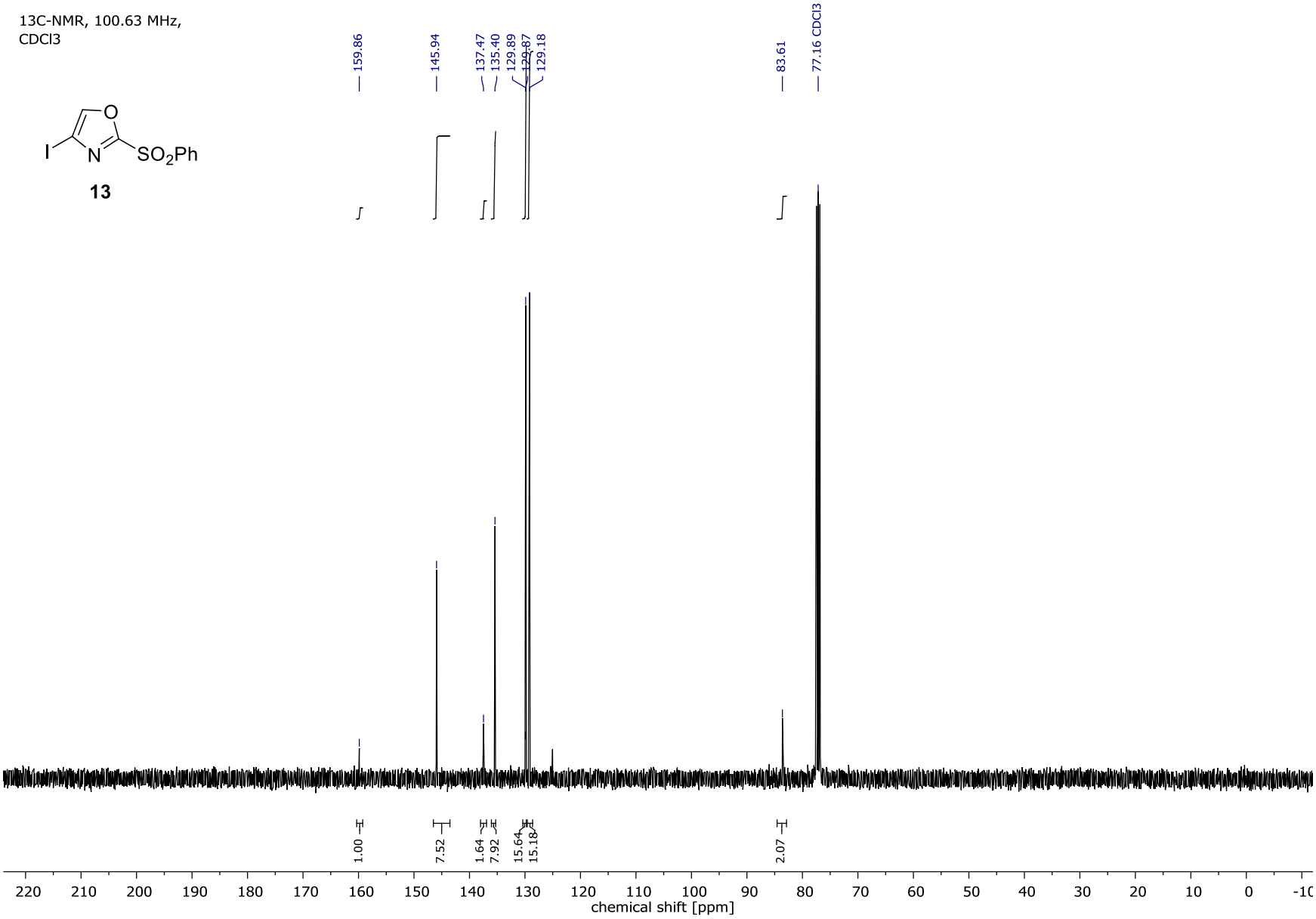
1H-NMR, 400.13 MHz,
CDCl3

13



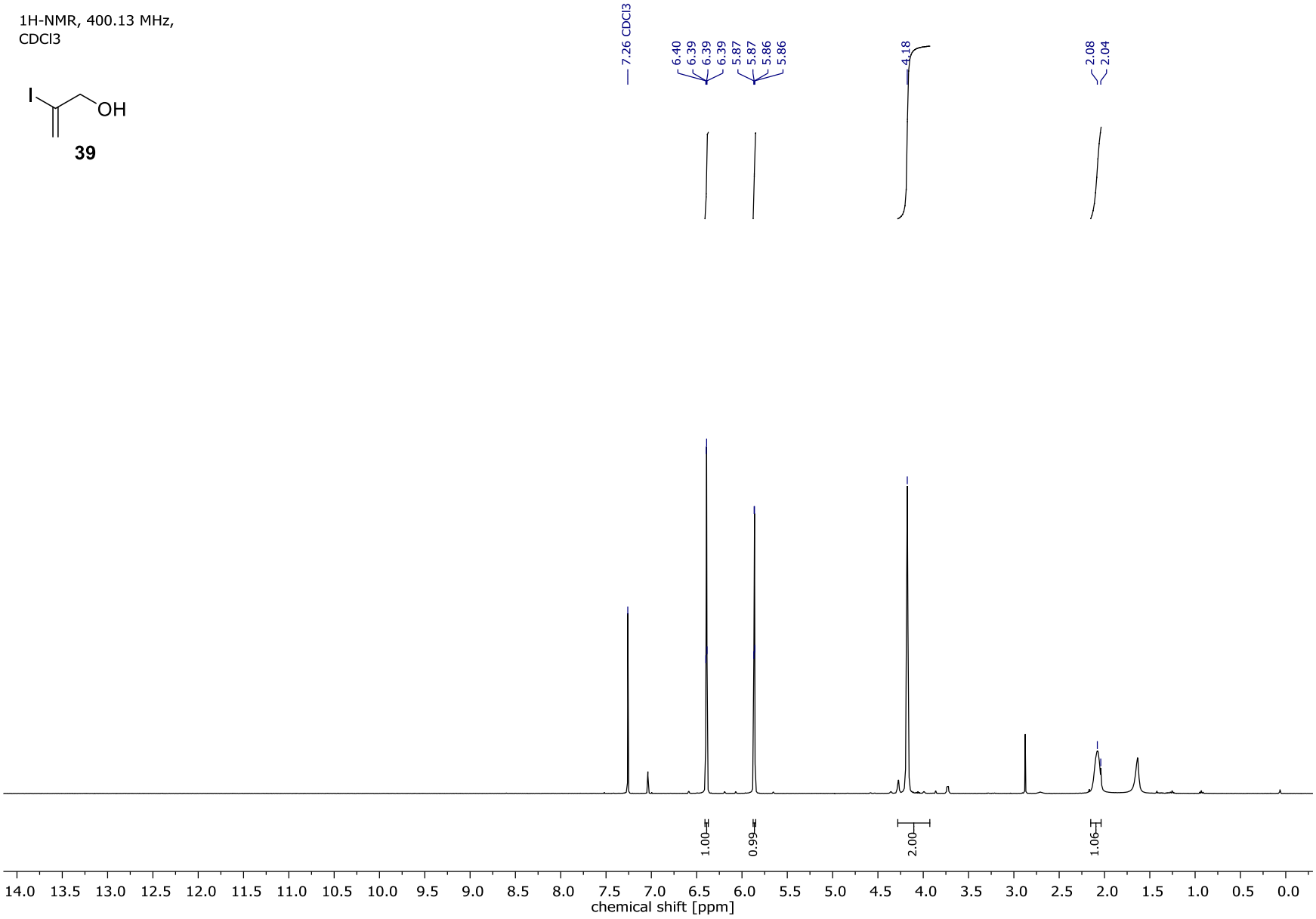
13C-NMR, 100.63 MHz,
CDCl3

13



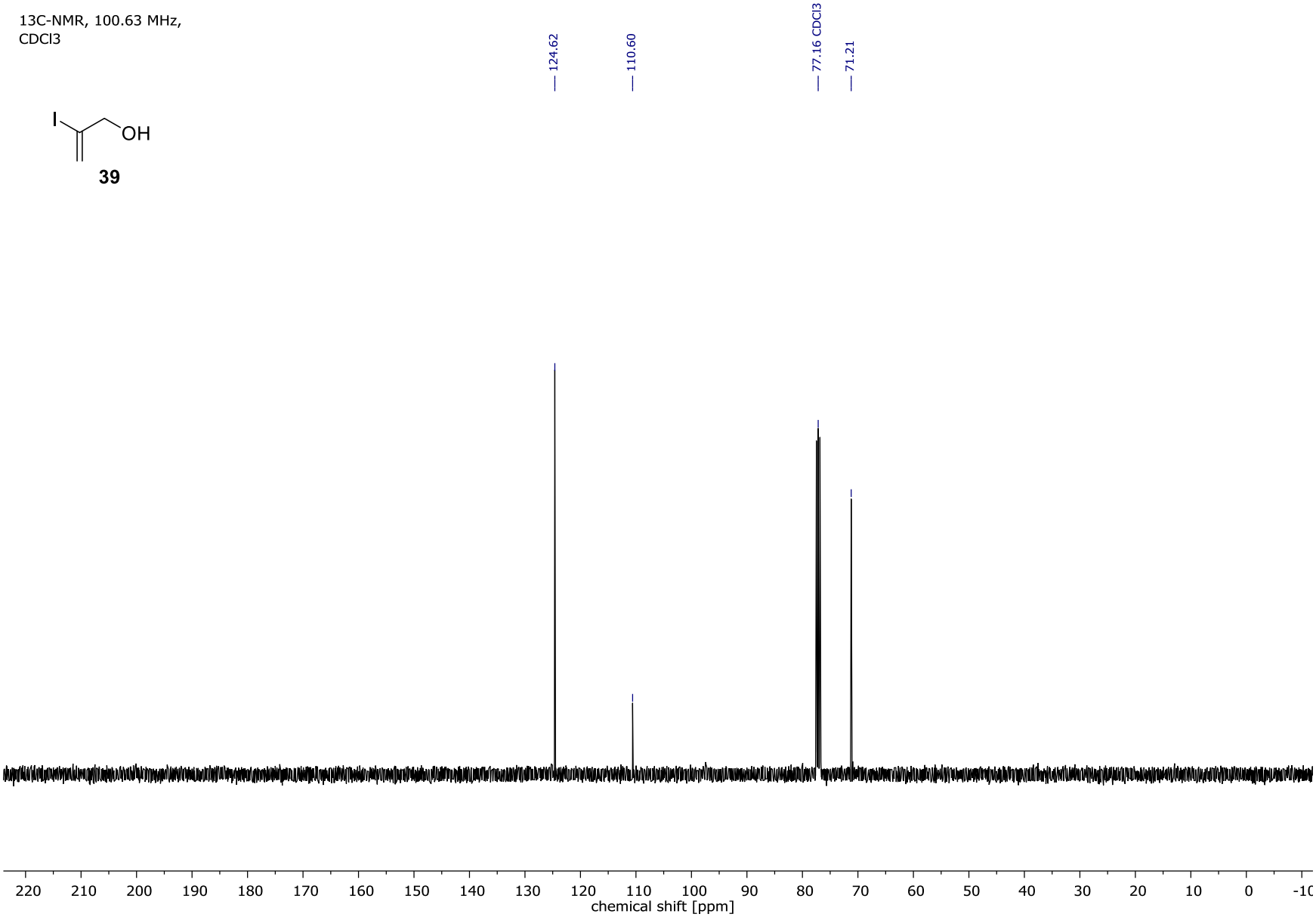
1H-NMR, 400.13 MHz,
CDCl3

39



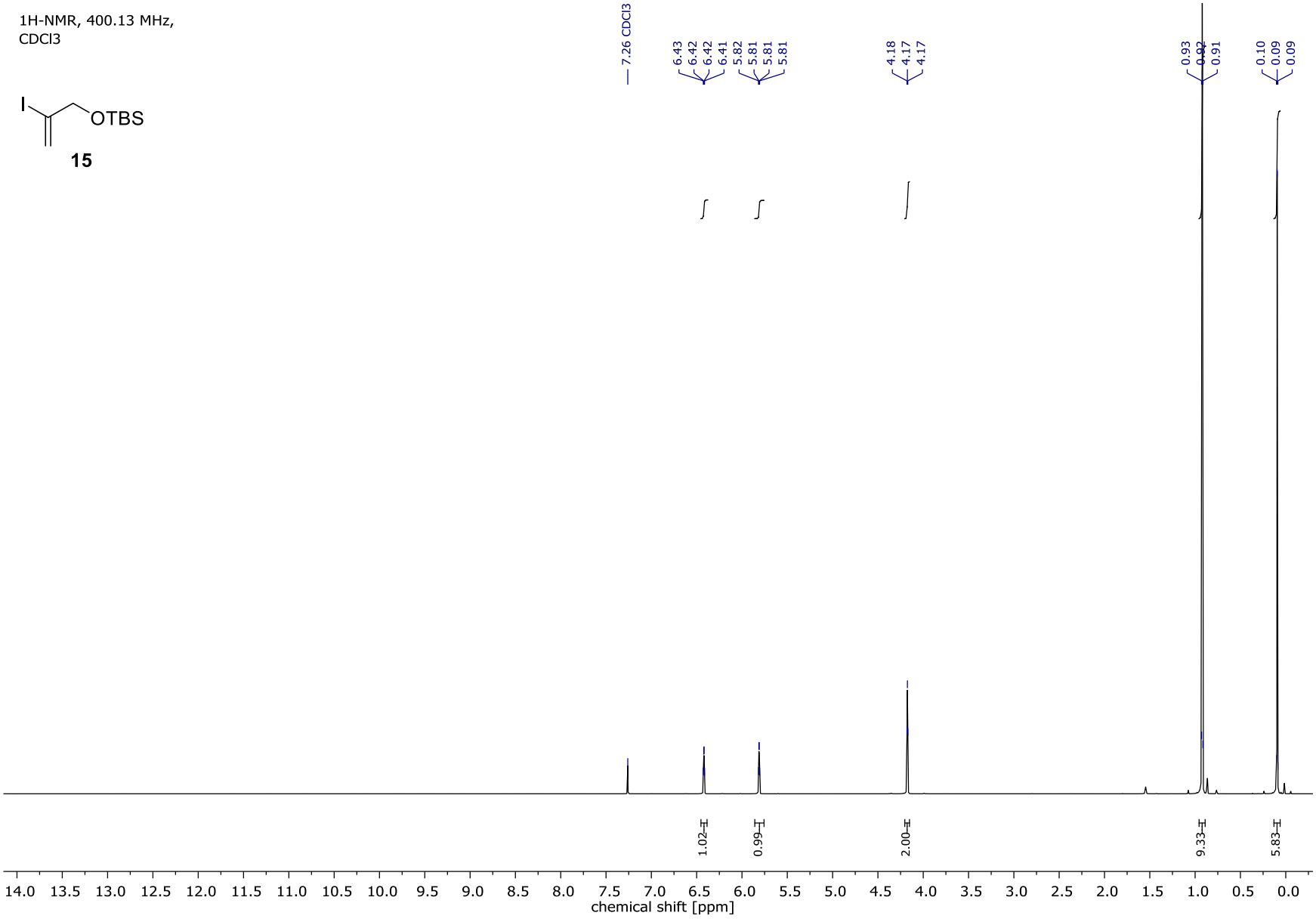
13C-NMR, 100.63 MHz,
CDCl3

39



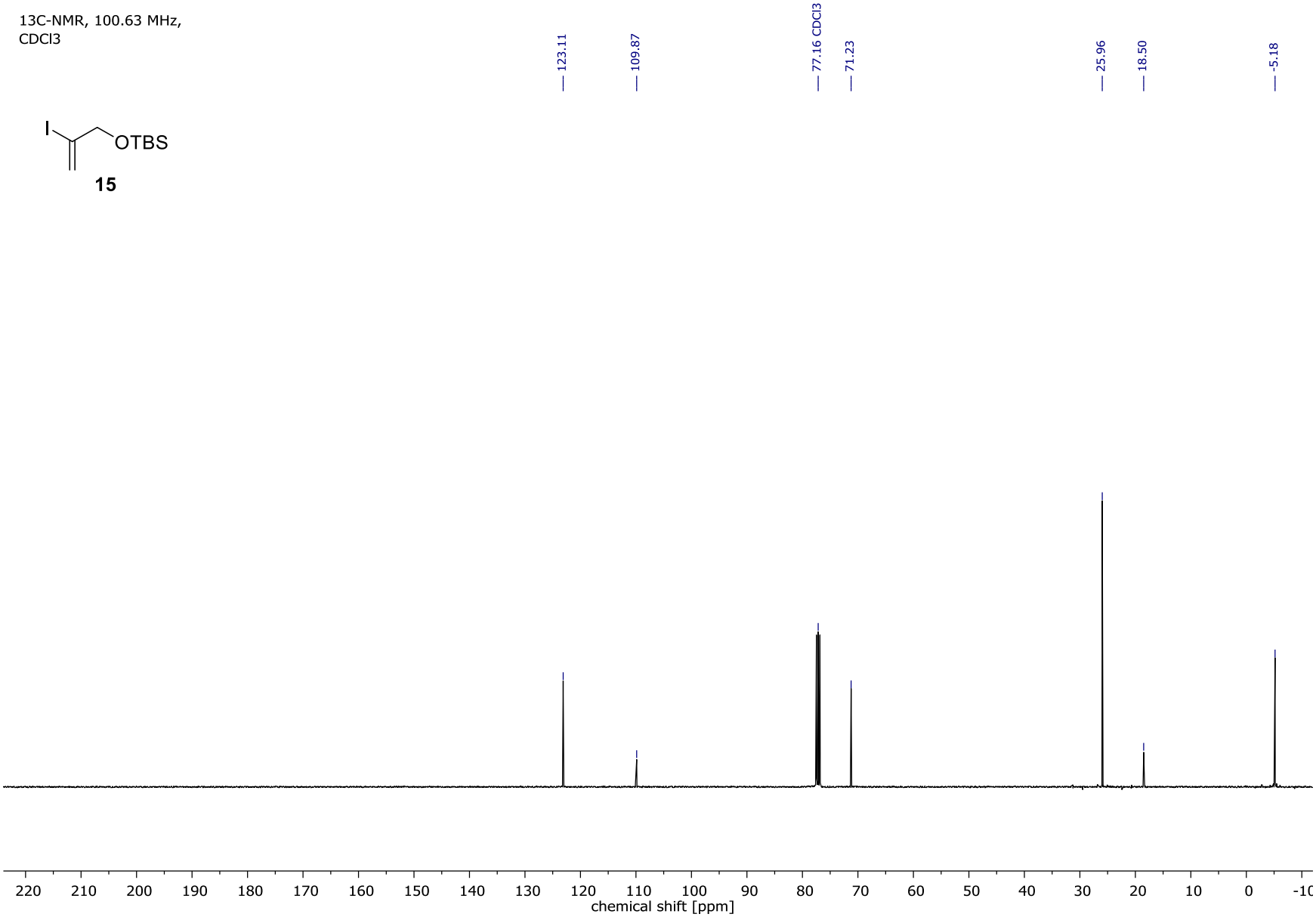
1H-NMR, 400.13 MHz,
CDCl3

15



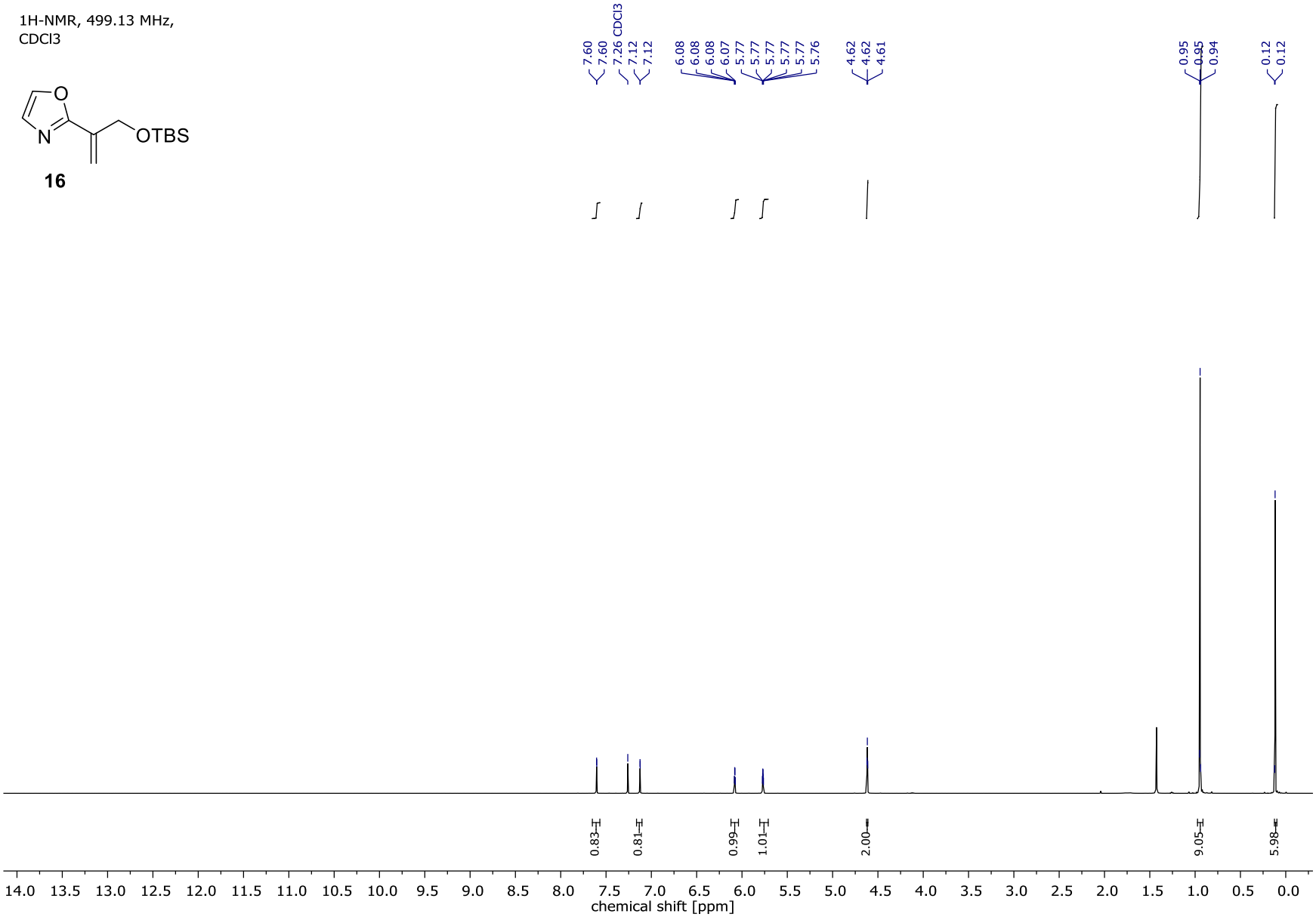
13C-NMR, 100.63 MHz,
CDCl3

15



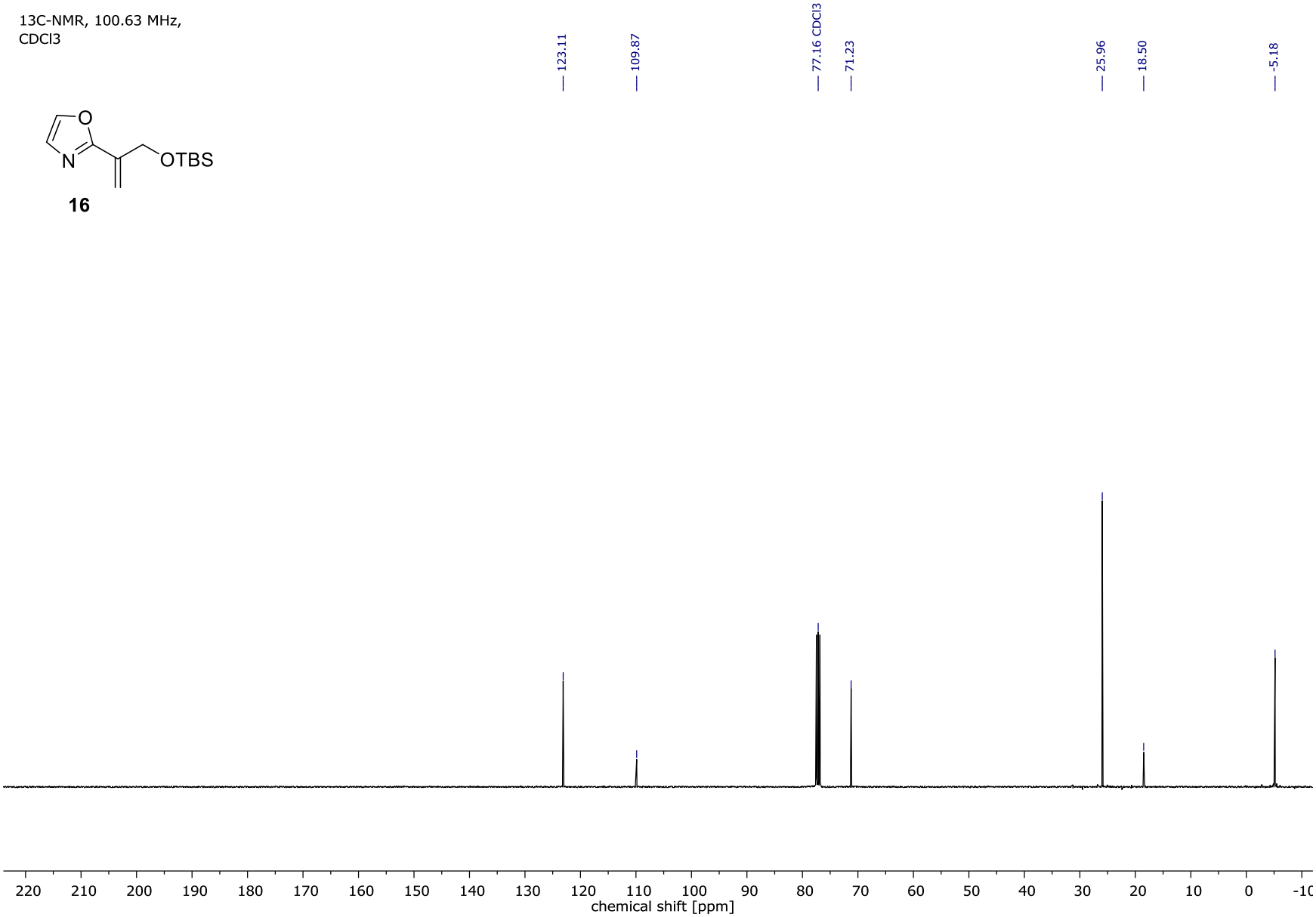
1H-NMR, 499.13 MHz,
CDCl3

16



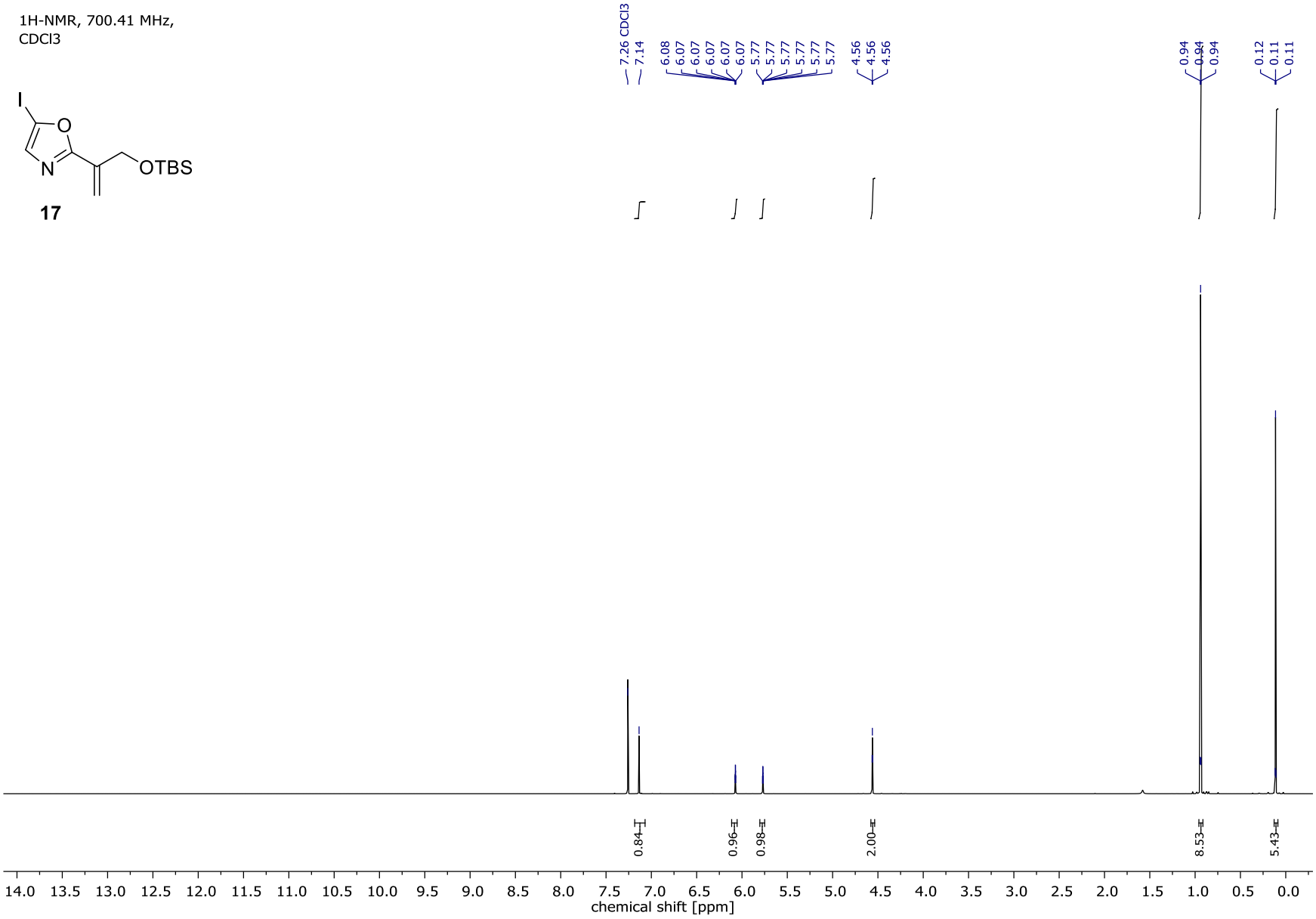
13C-NMR, 100.63 MHz,
CDCl3

16



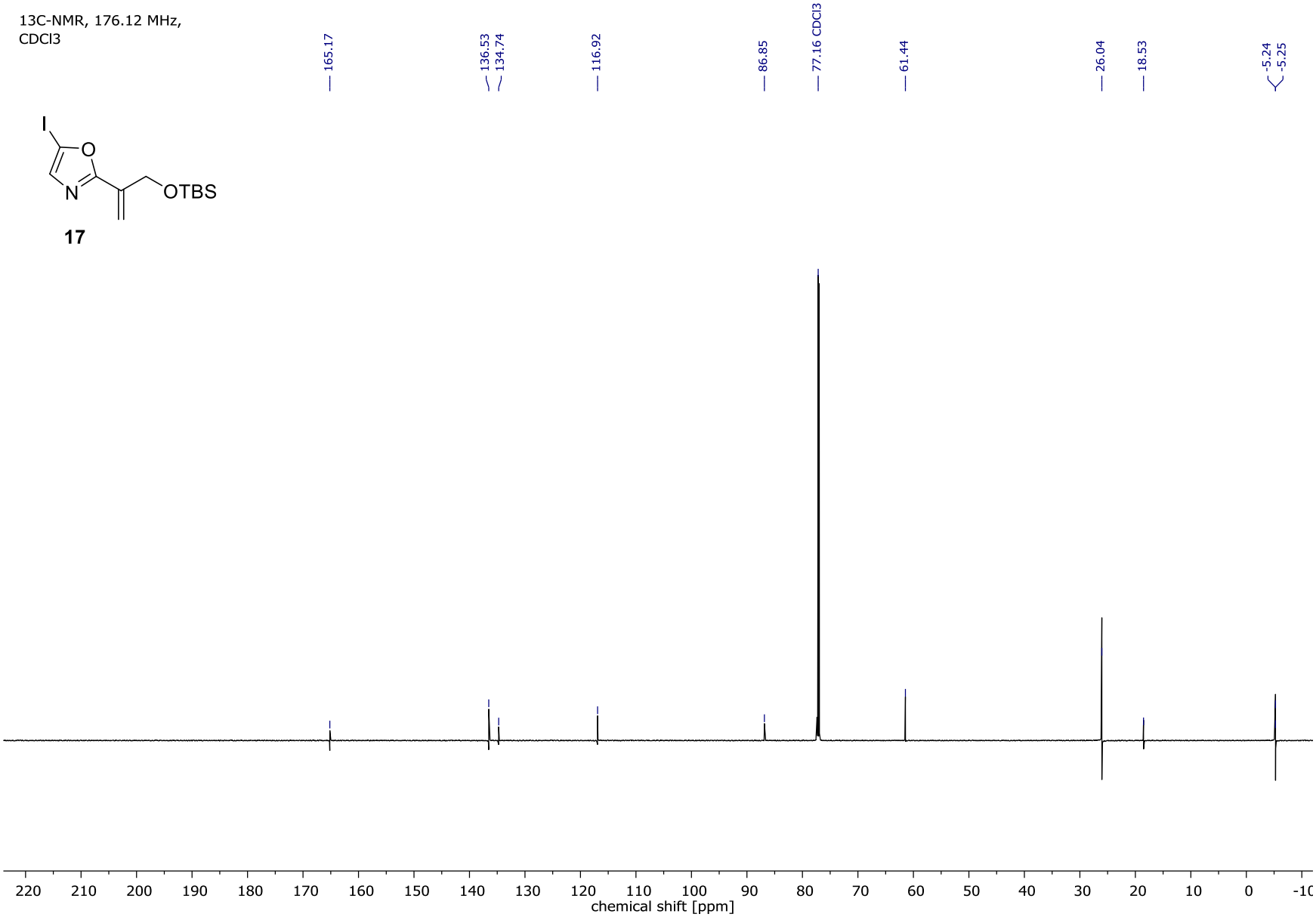
1H-NMR, 700.41 MHz,
CDCl3

17



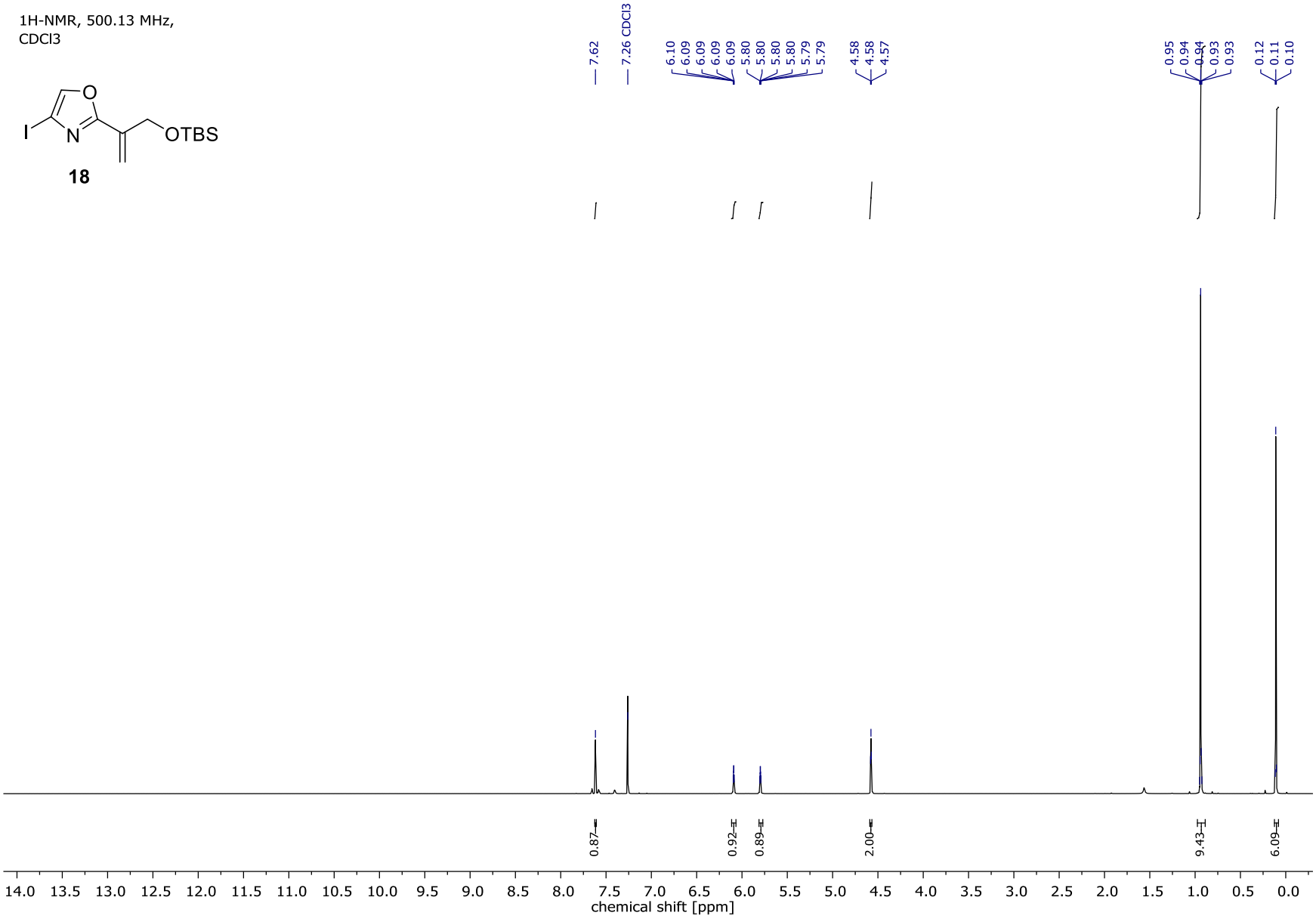
13C-NMR, 176.12 MHz,
CDCl3

17



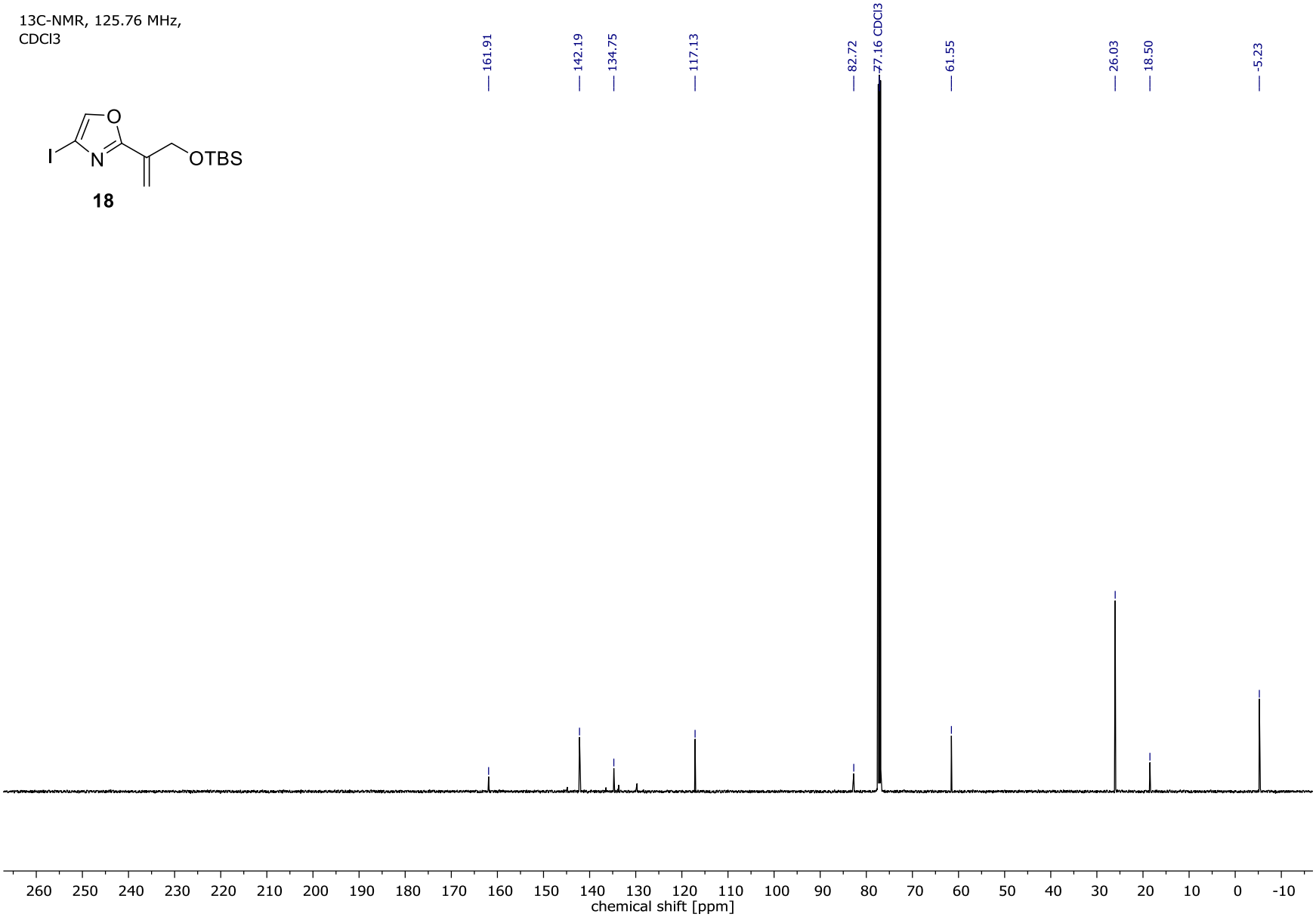
1H-NMR, 500.13 MHz,
CDCl3

18



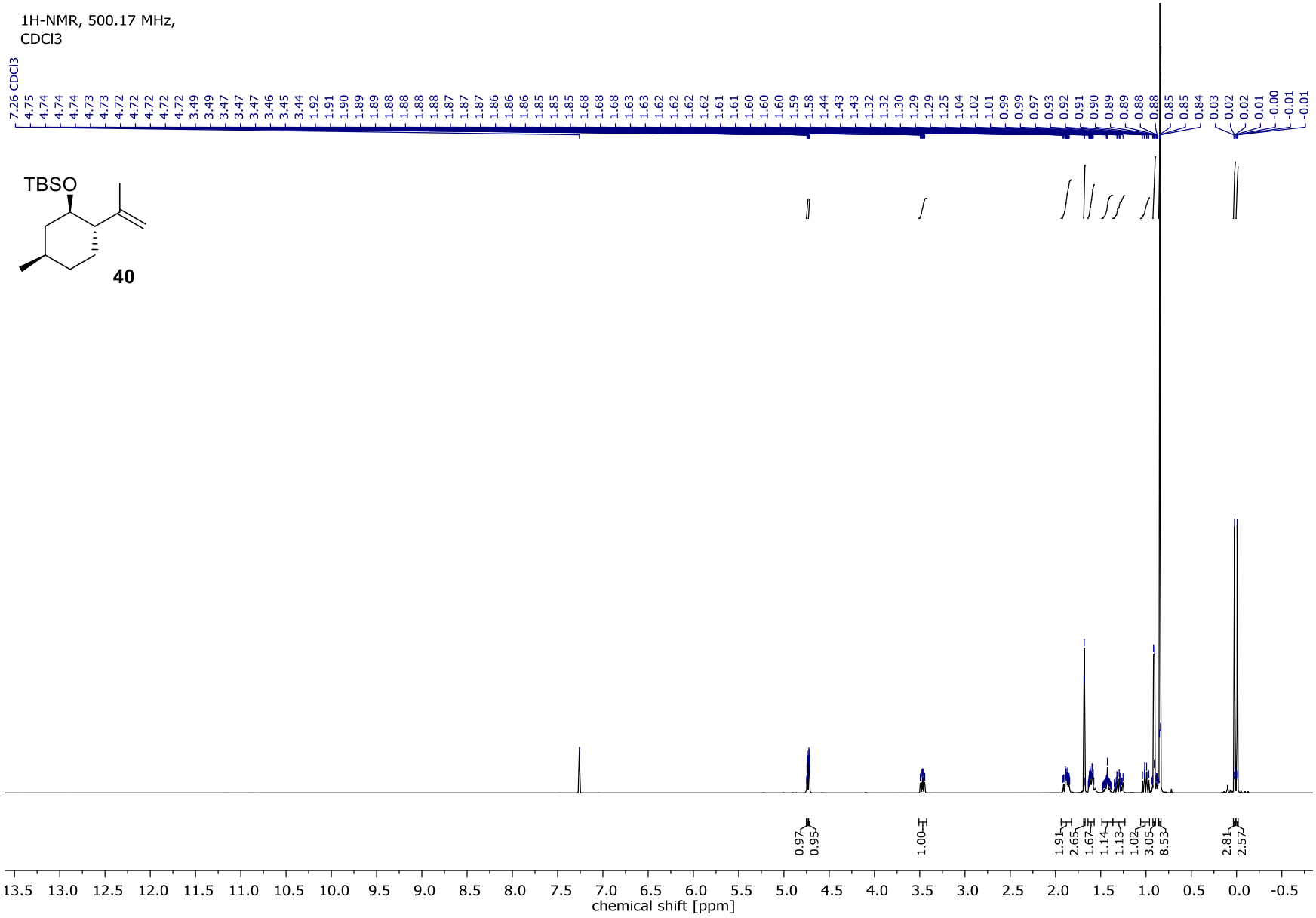
13C-NMR, 125.76 MHz,
CDCl3

18



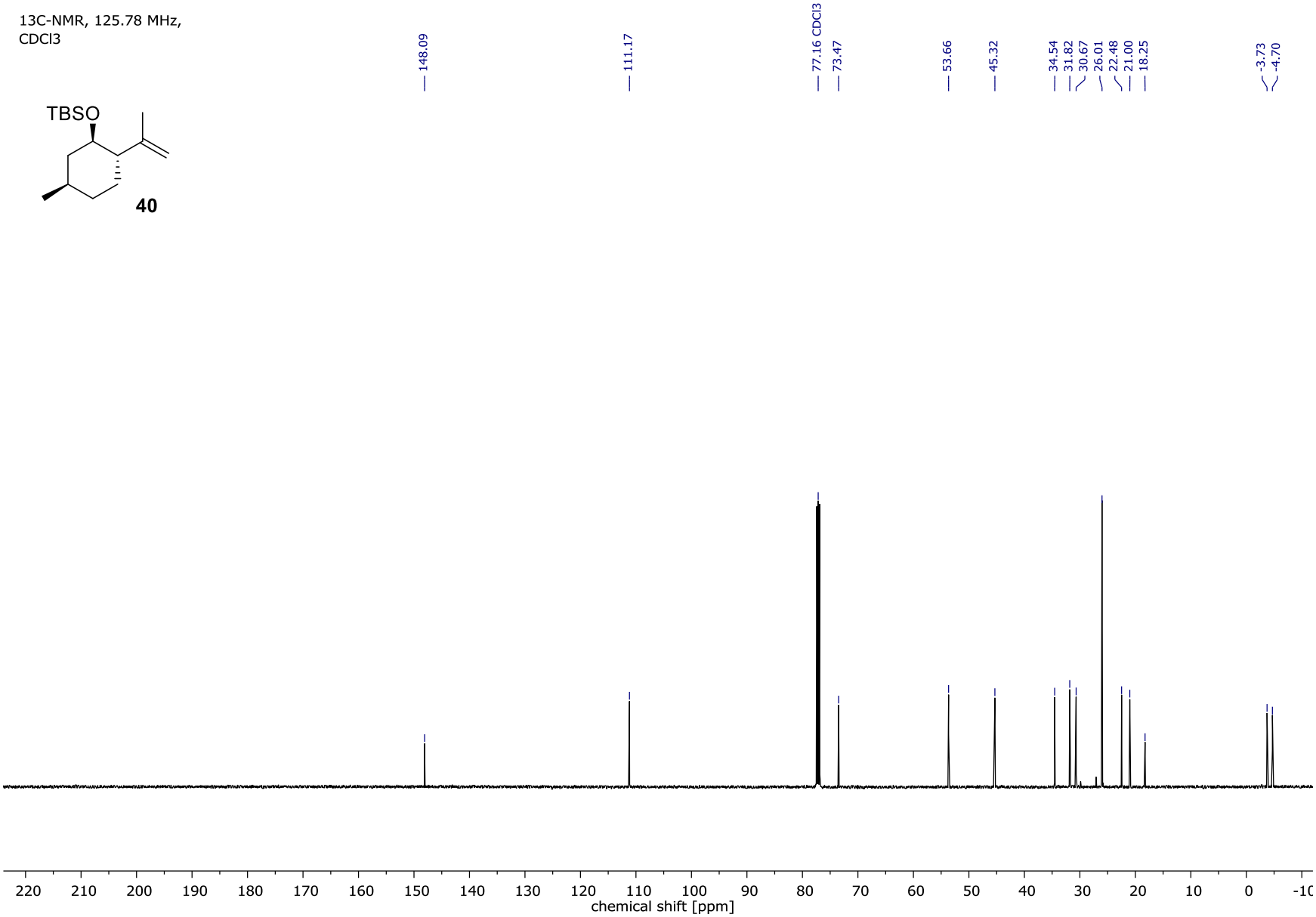
1H-NMR, 500.17 MHz,
CDCl3

40



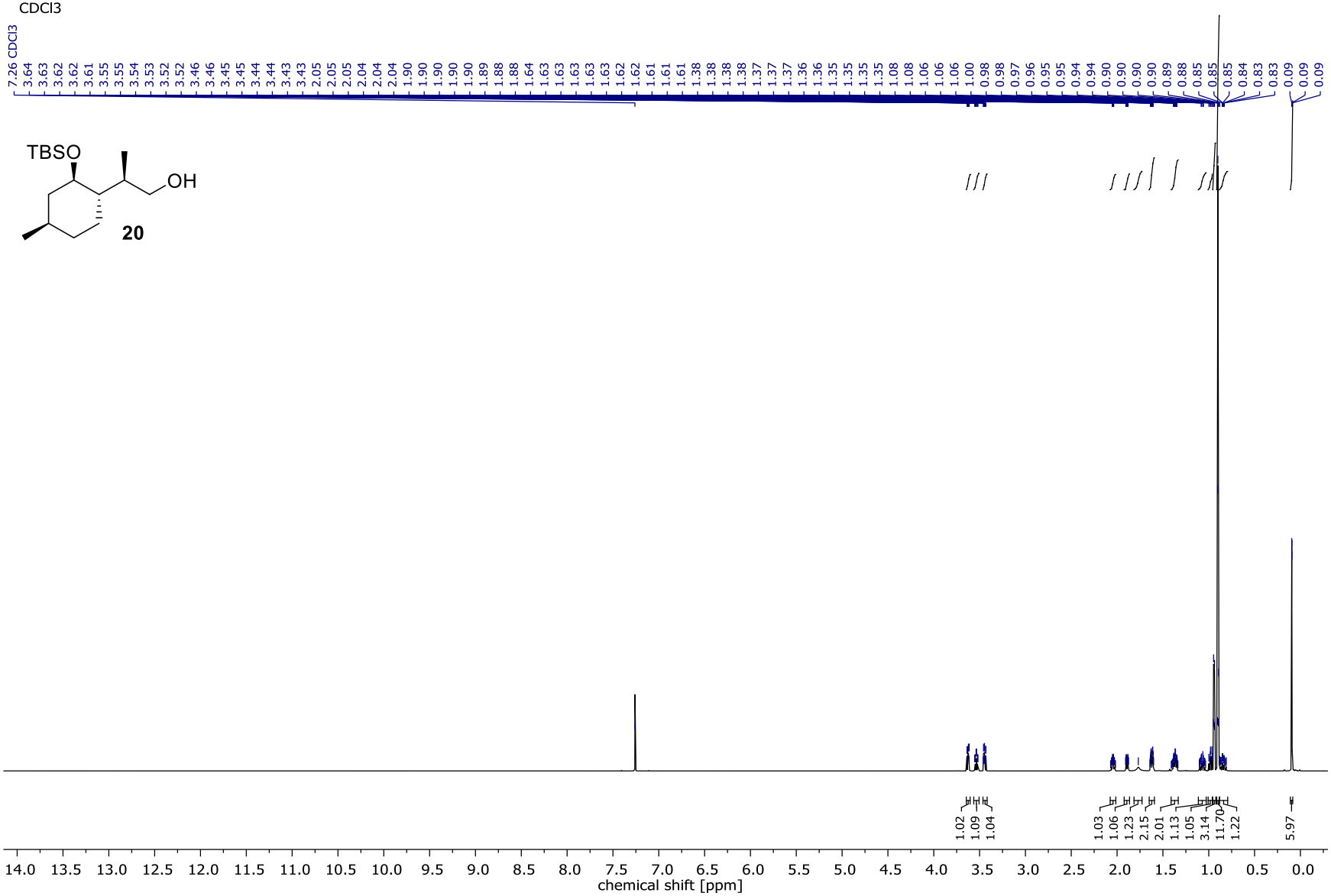
13C-NMR, 125.78 MHz,
CDCl3

40



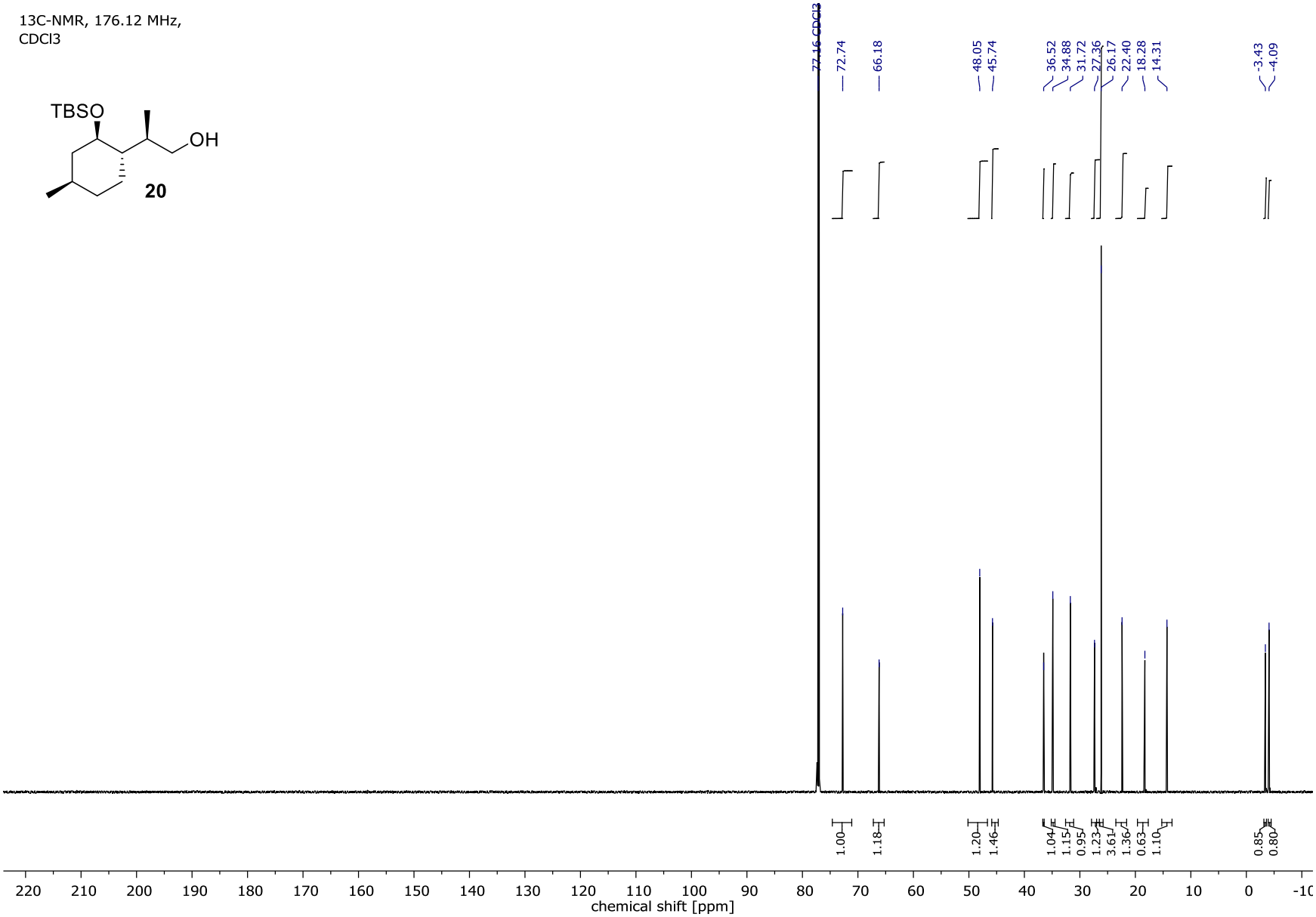
1H-NMR, 700.41 MHz,
CDCl3

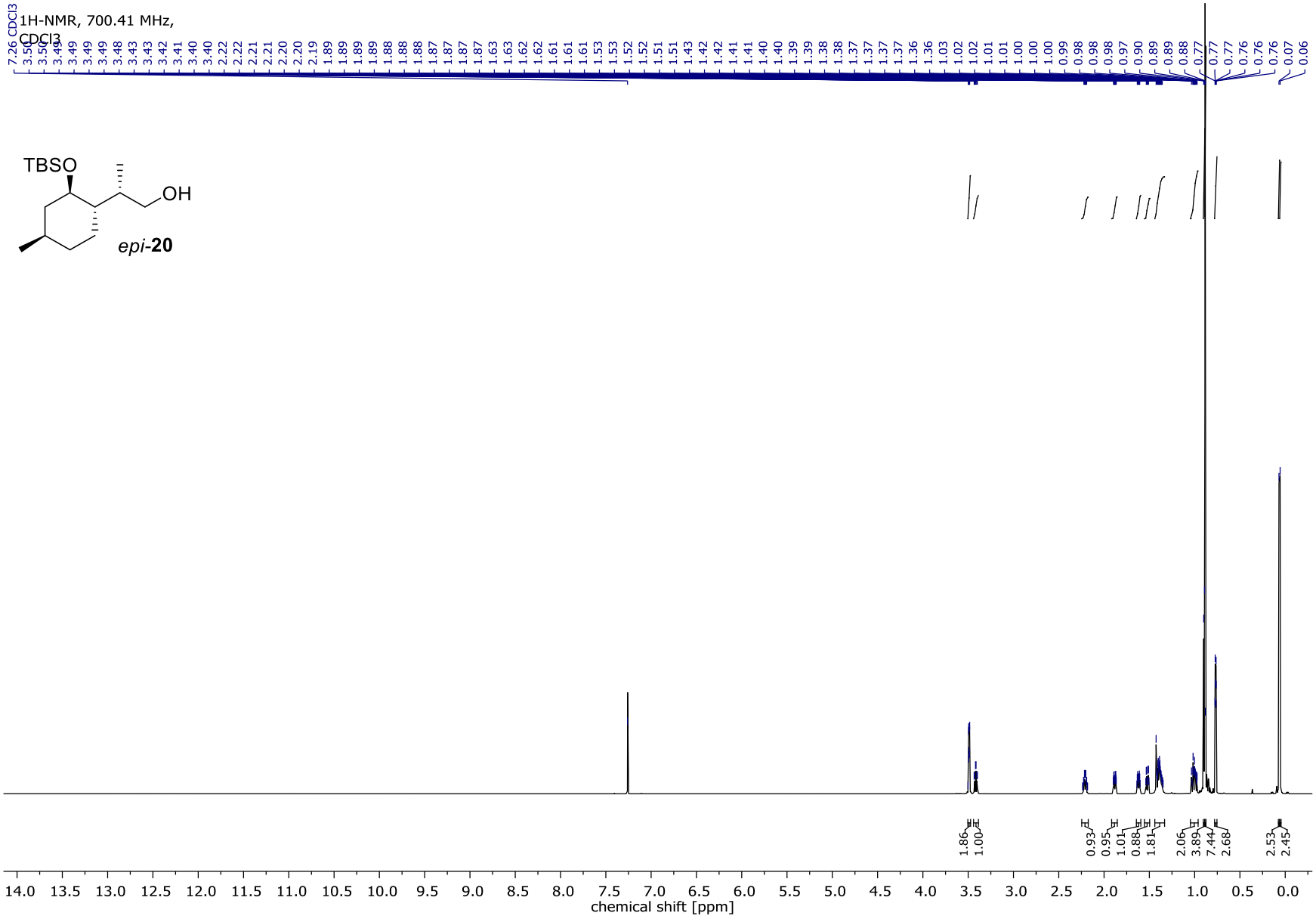
20



13C-NMR, 176.12 MHz,
CDCl3

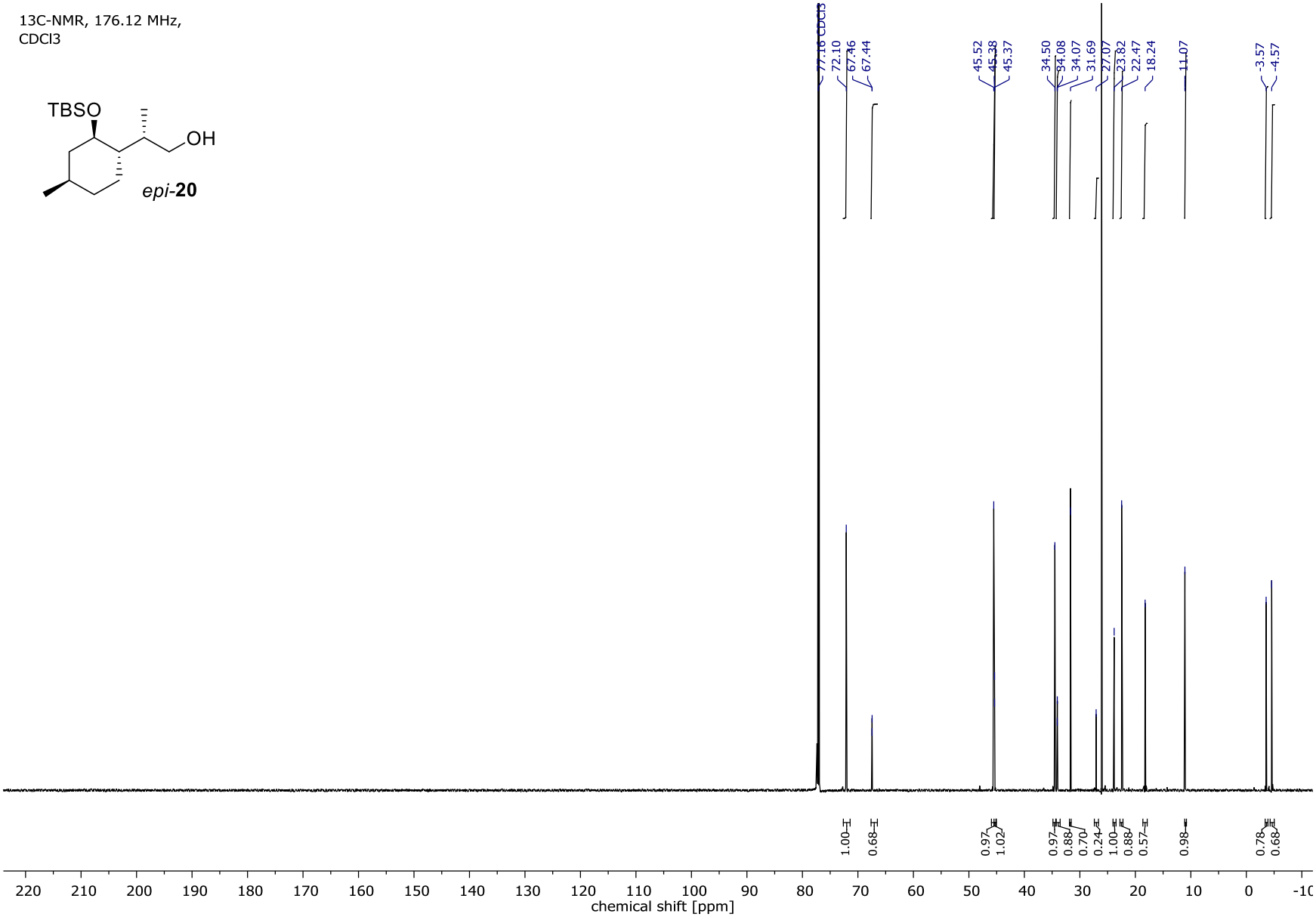
20

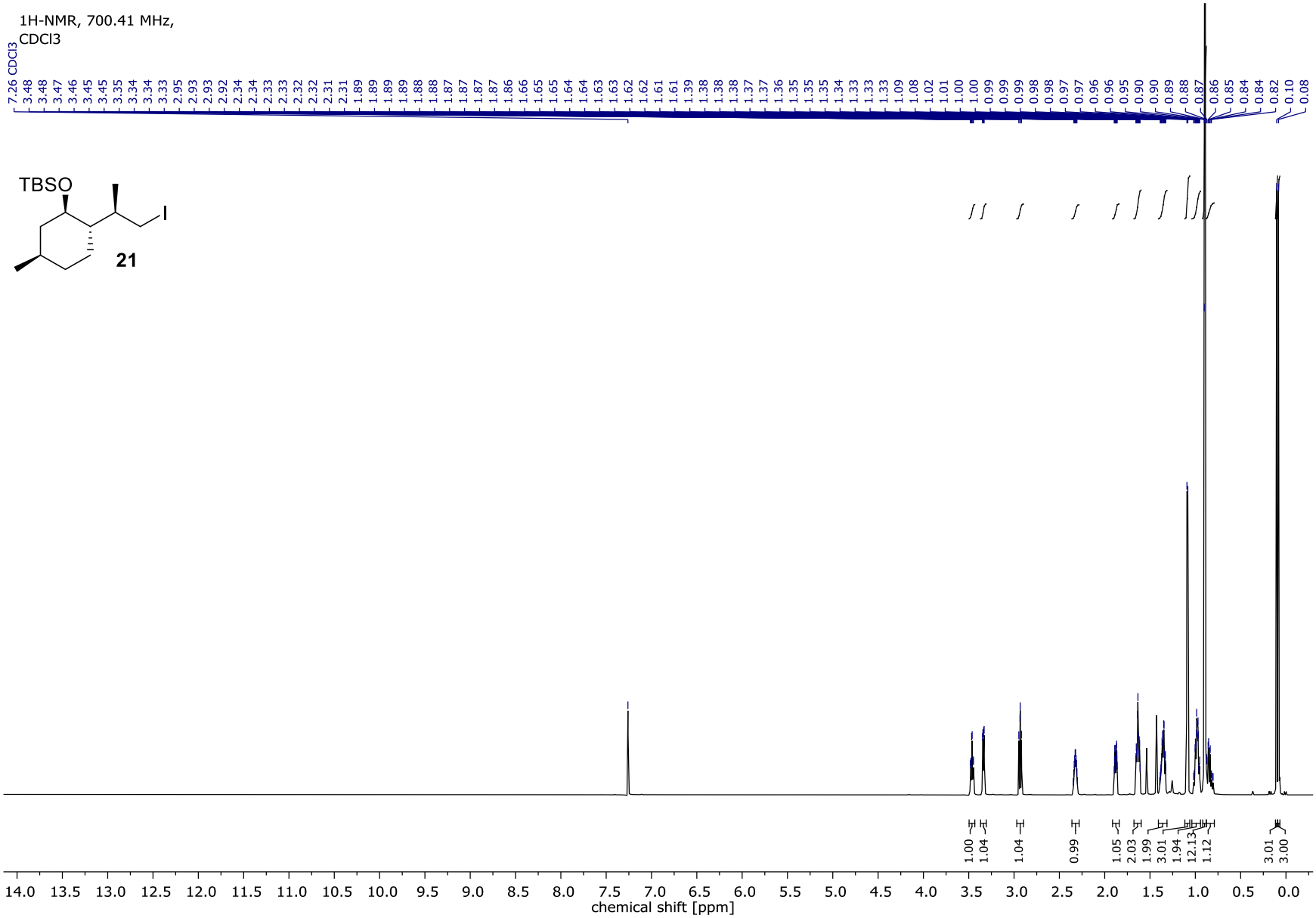



1H-NMR, 700.41 MHz,
CDCl3
7.26 CDCl3
TBSO
OH
epi-20
1.86
1.00
0.93
0.95
1.01
0.88
1.81
2.06
3.89
7.44
2.68
2.53
2.45
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
chemical shift [ppm]

13C-NMR, 176.12 MHz,
CDCl3

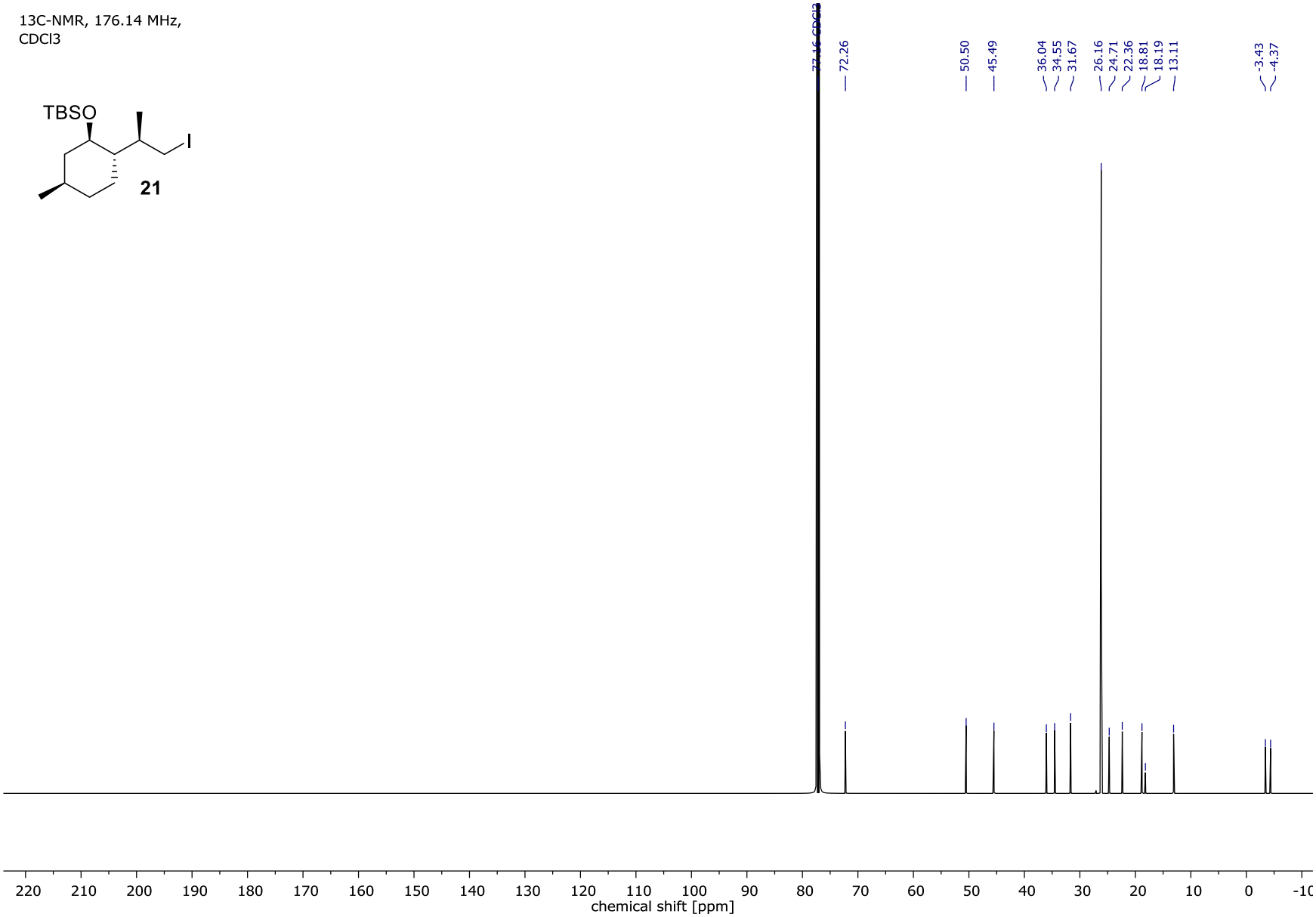
epi-**20**

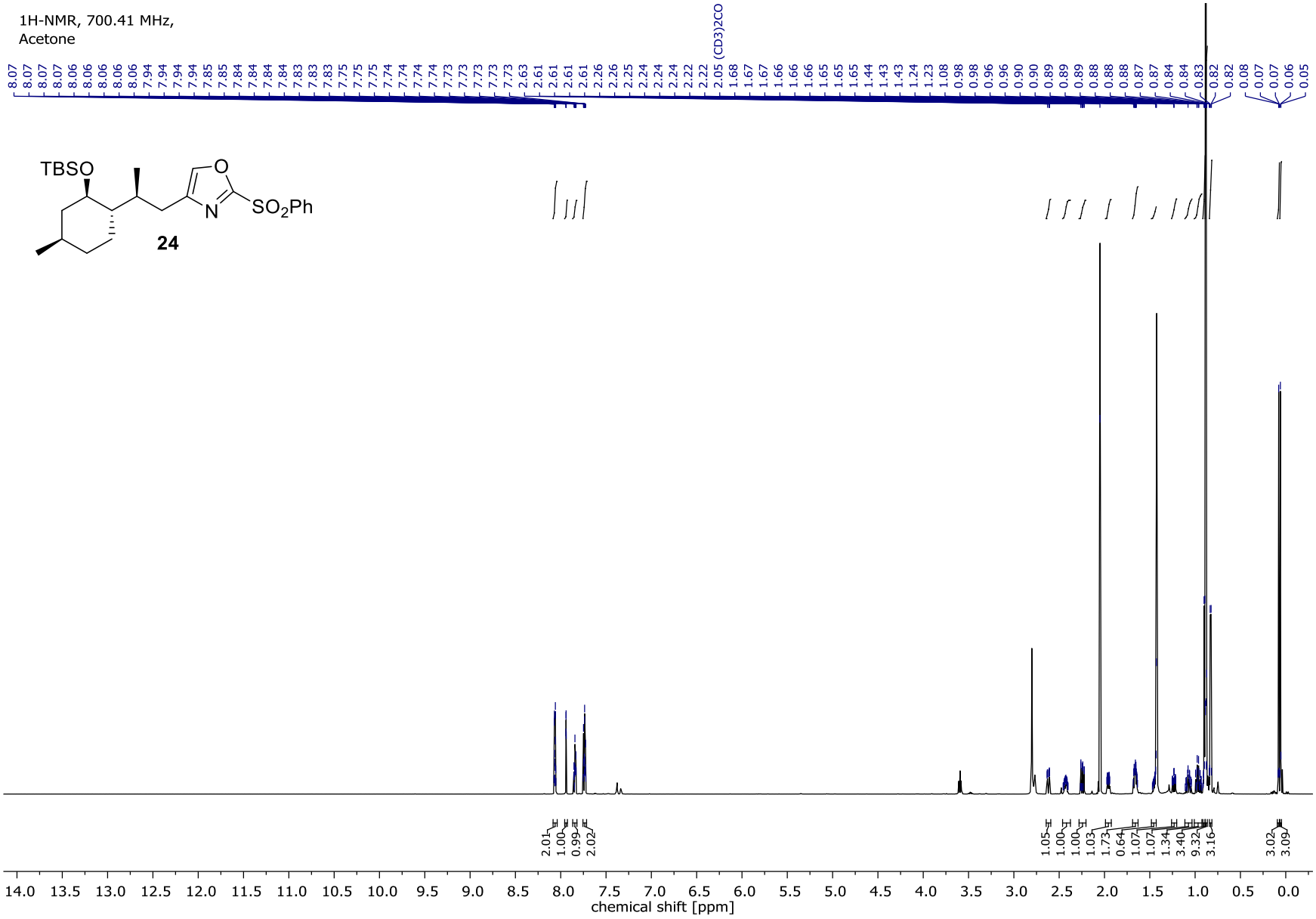


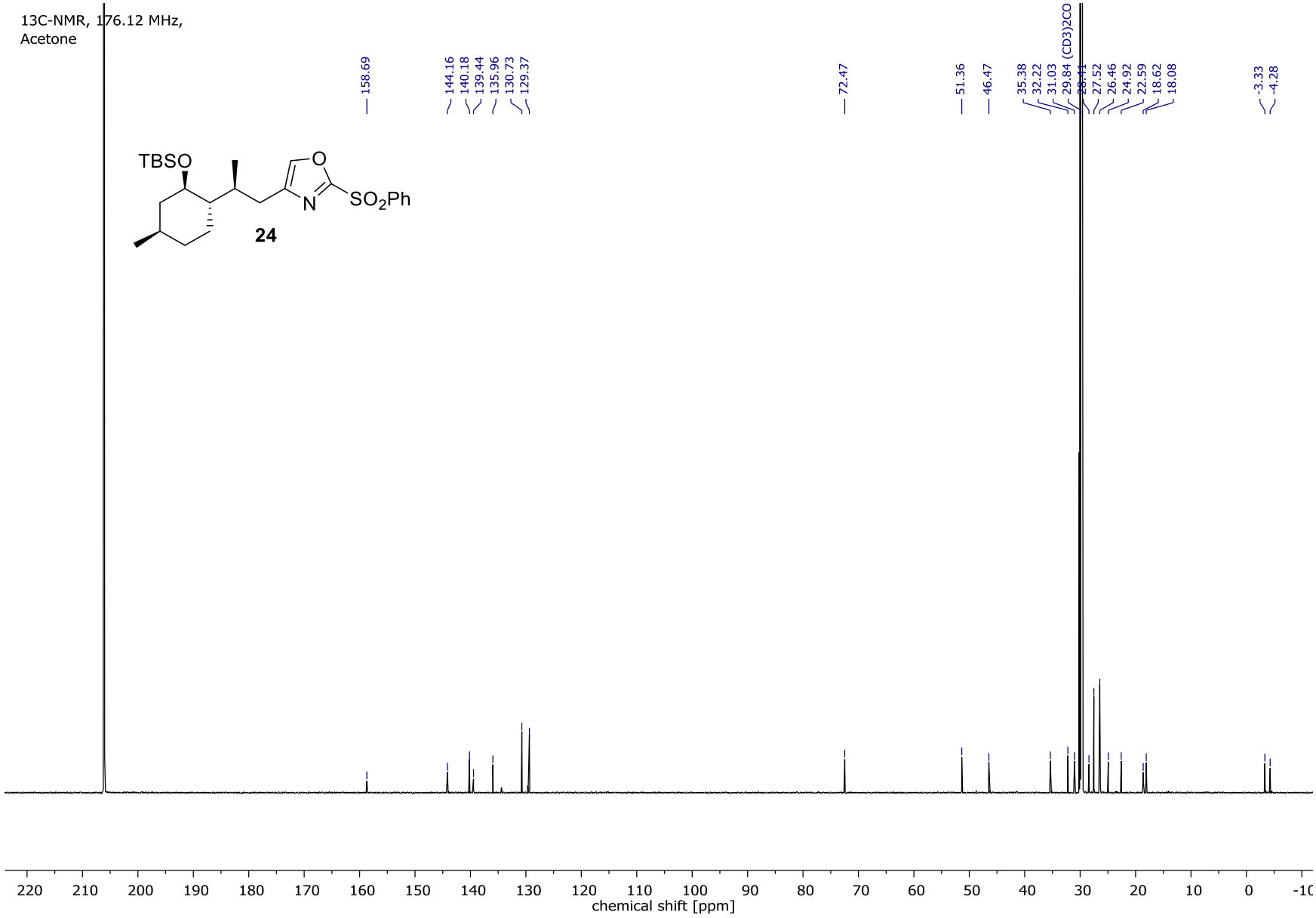

1H-NMR, 700.41 MHz,
CDCl3
TBSO
I
21
chemical shift [ppm]

13C-NMR, 176.14 MHz,
CDCl3

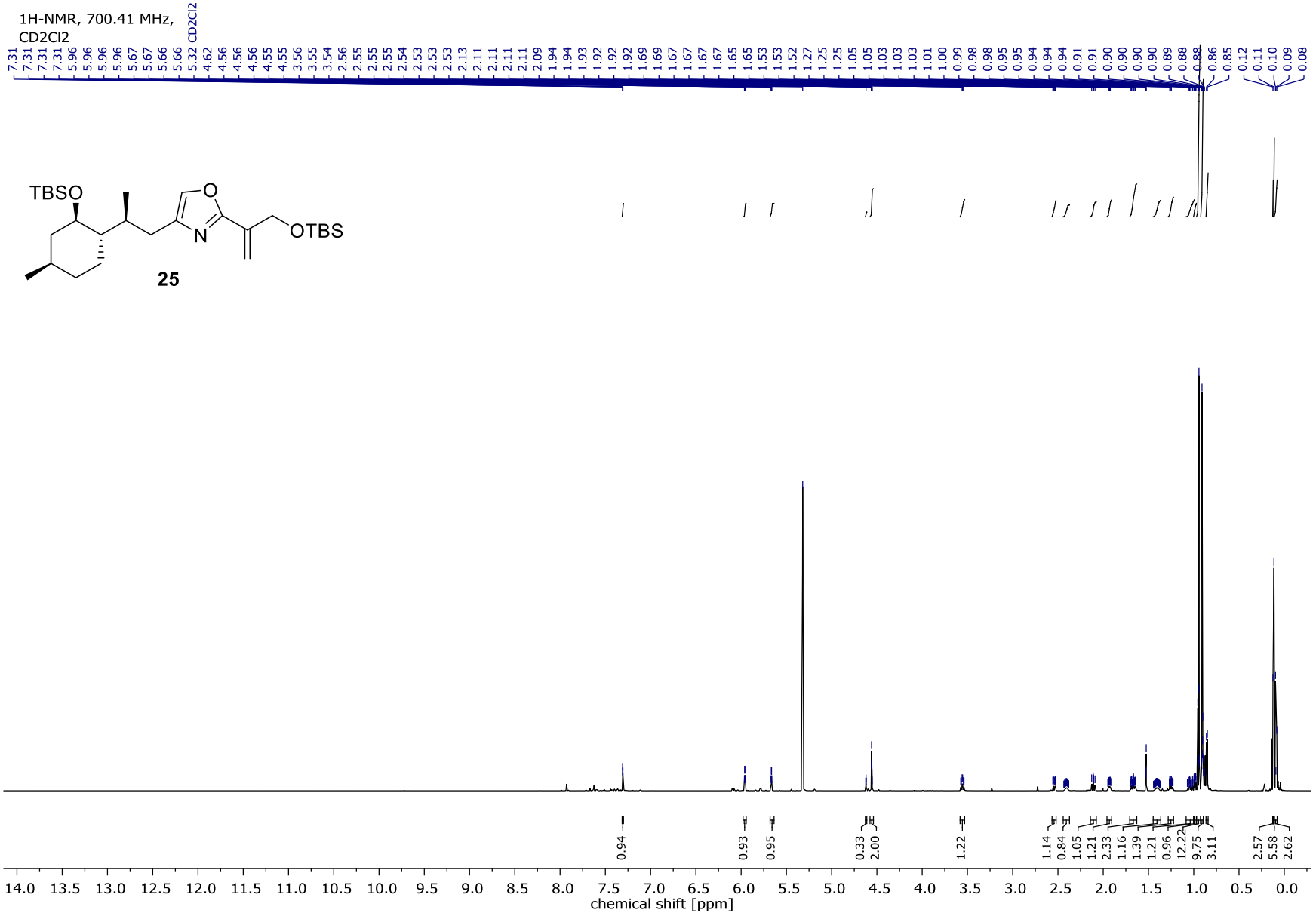
21




1H-NMR, 700.41 MHz,
Acetone
(CD3)2CO
TBSO
O
N
SO2Ph
24
chemical shift [ppm]

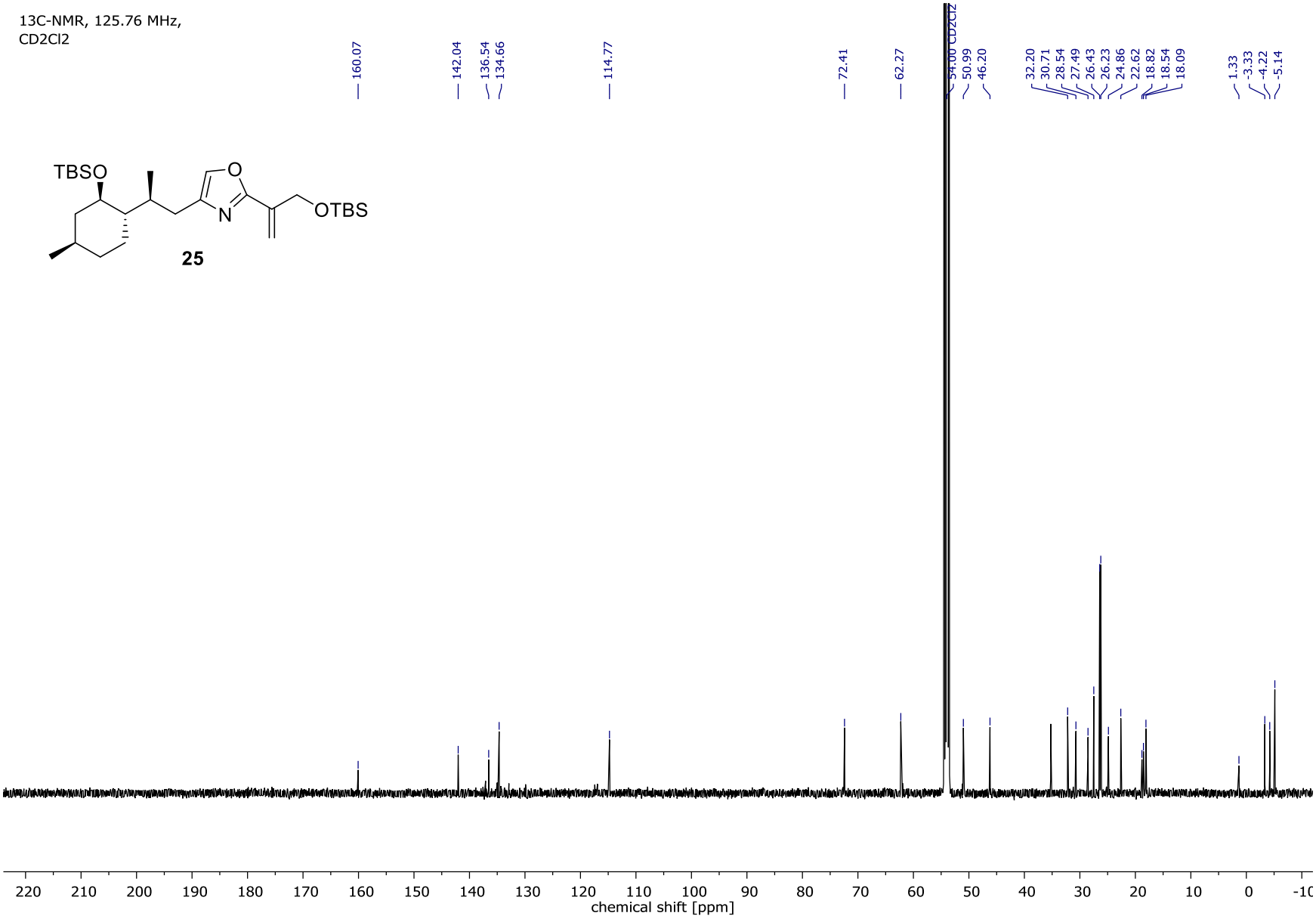

13C-NMR, 176.12 MHz,
Acetone
158.69
144.16
140.18
139.44
135.96
130.73
129.37
72.47
51.36
46.47
35.38
32.22
31.03
29.84 (CD3)2CO
28.41
27.52
26.46
24.92
22.59
18.62
18.08
-3.33
-4.28
TBSO
O
N
SO2Ph
24
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

1H-NMR, 700.41 MHz,
CD2Cl2



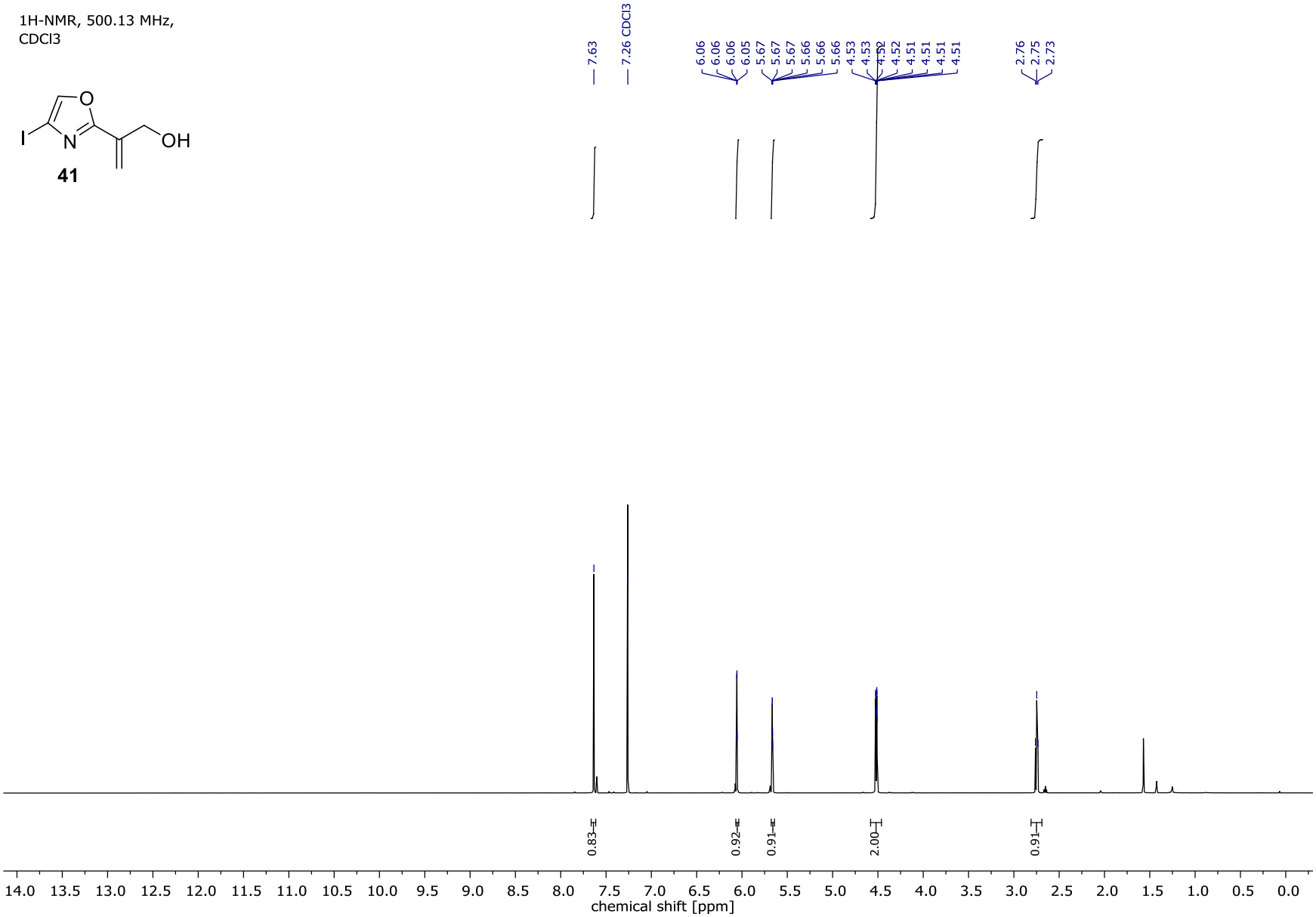
13C-NMR, 125.76 MHz,
CD2Cl2

25



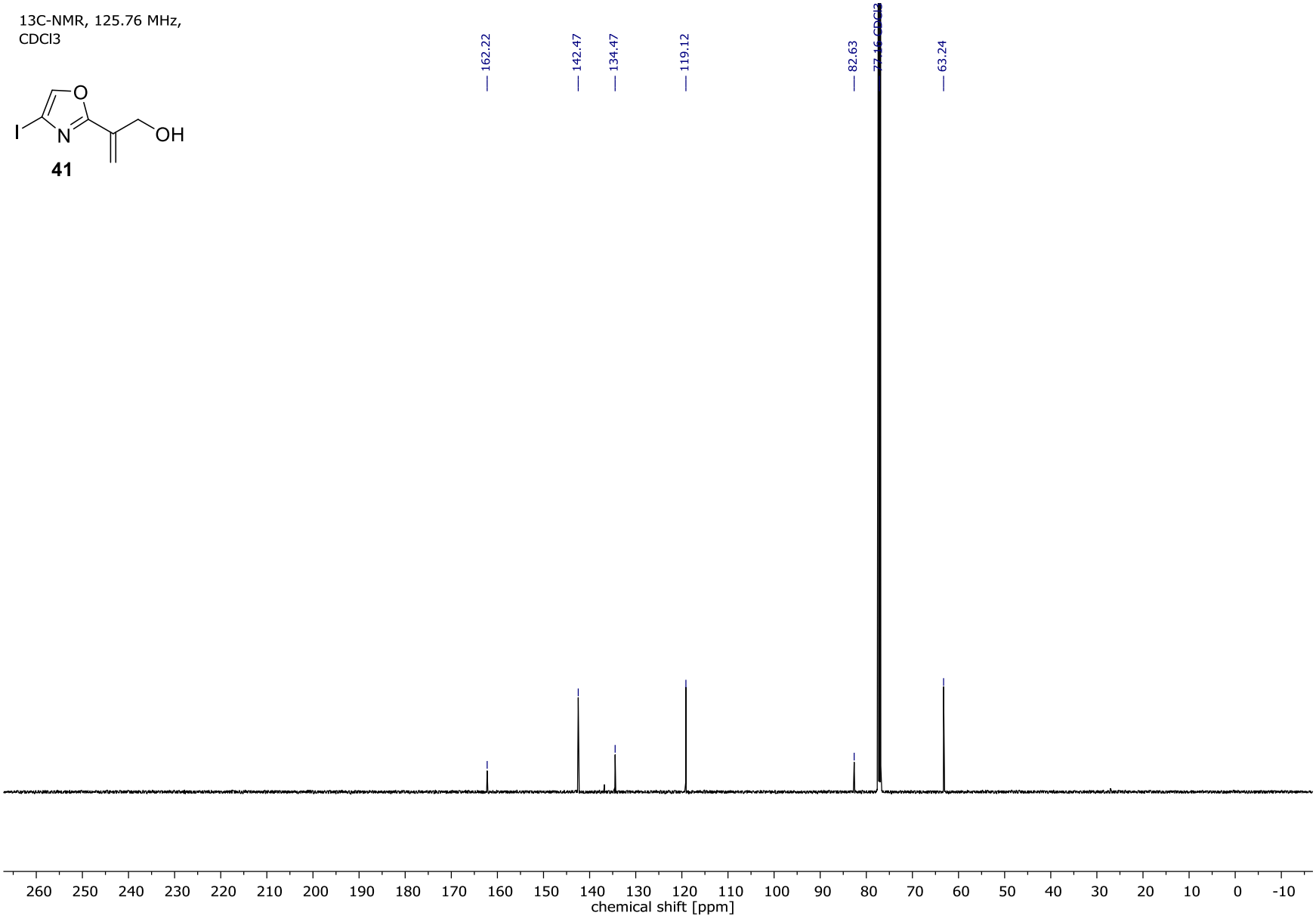
1H-NMR, 500.13 MHz,
CDCl3

41



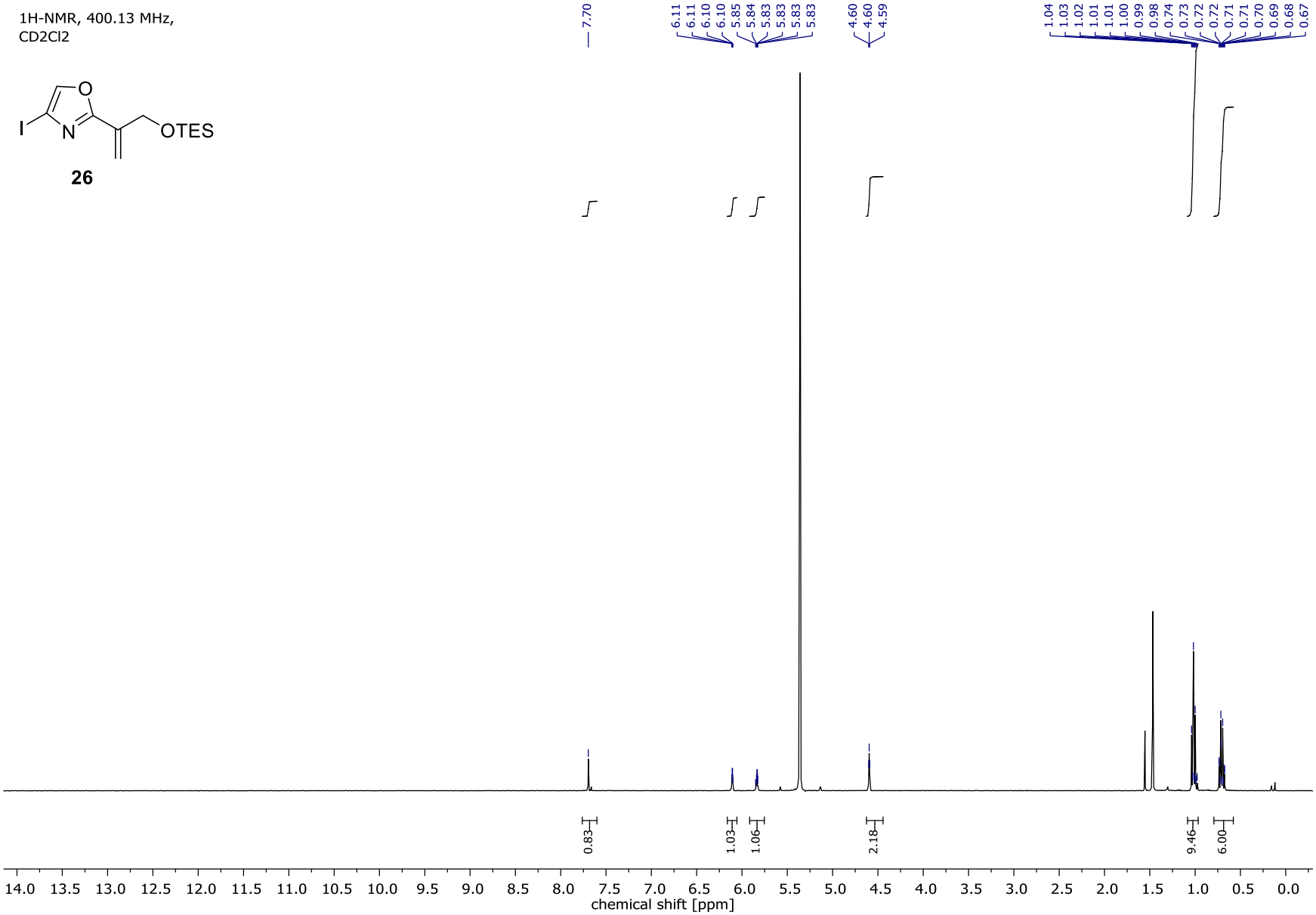
13C-NMR, 125.76 MHz,
CDCl3

41



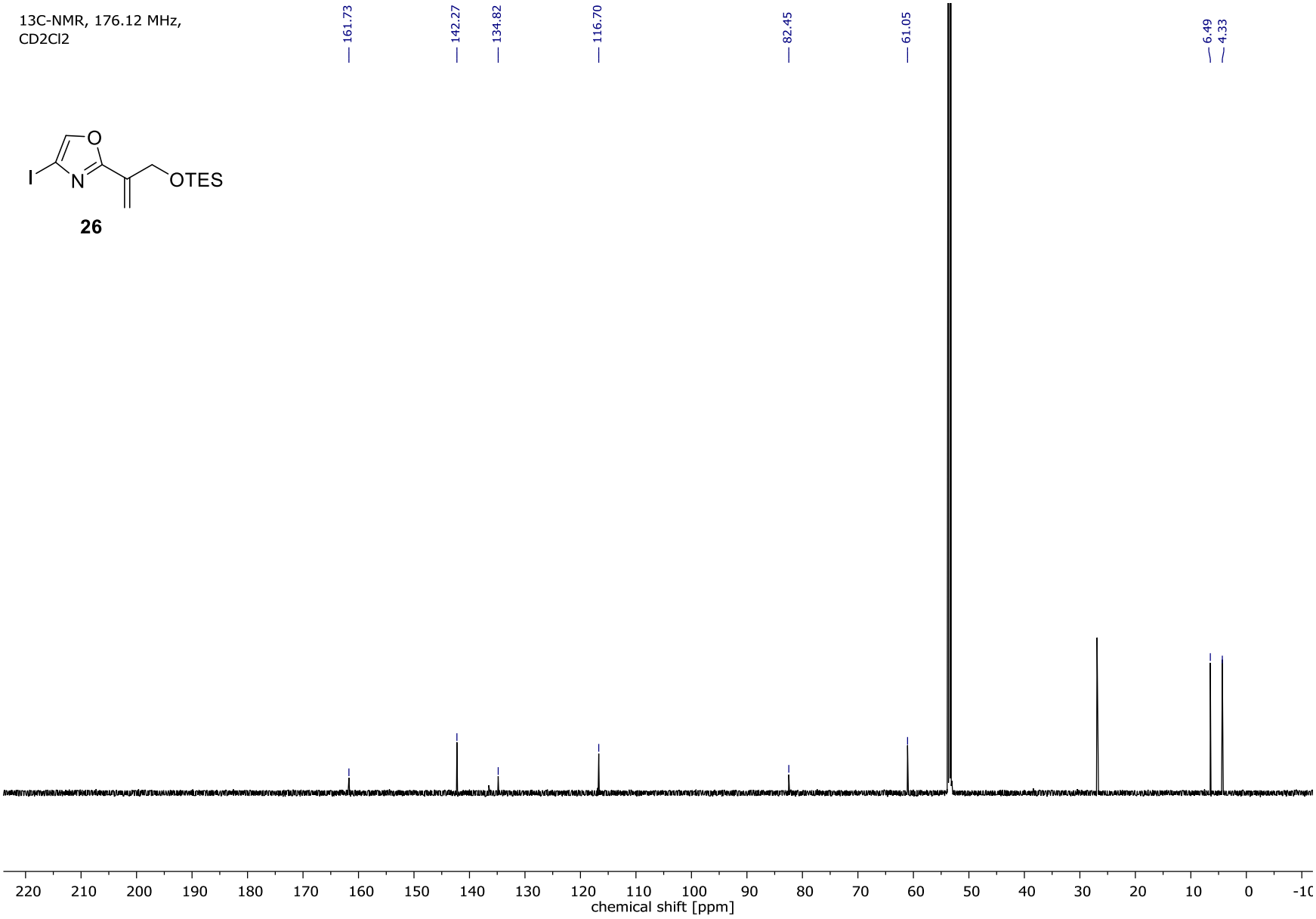
1H-NMR, 400.13 MHz,
CD2Cl2

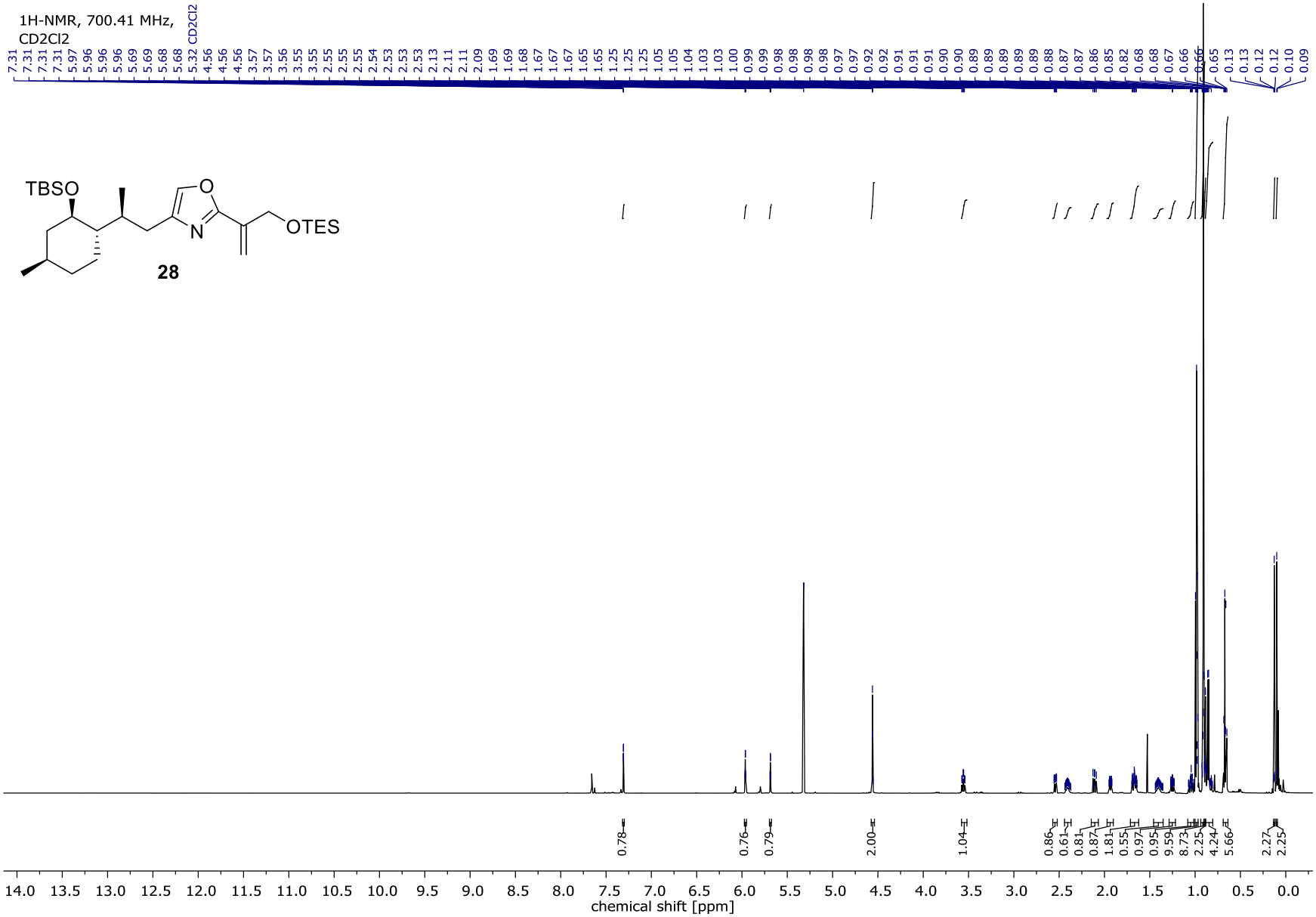
26



13C-NMR, 176.12 MHz,
CD2Cl2

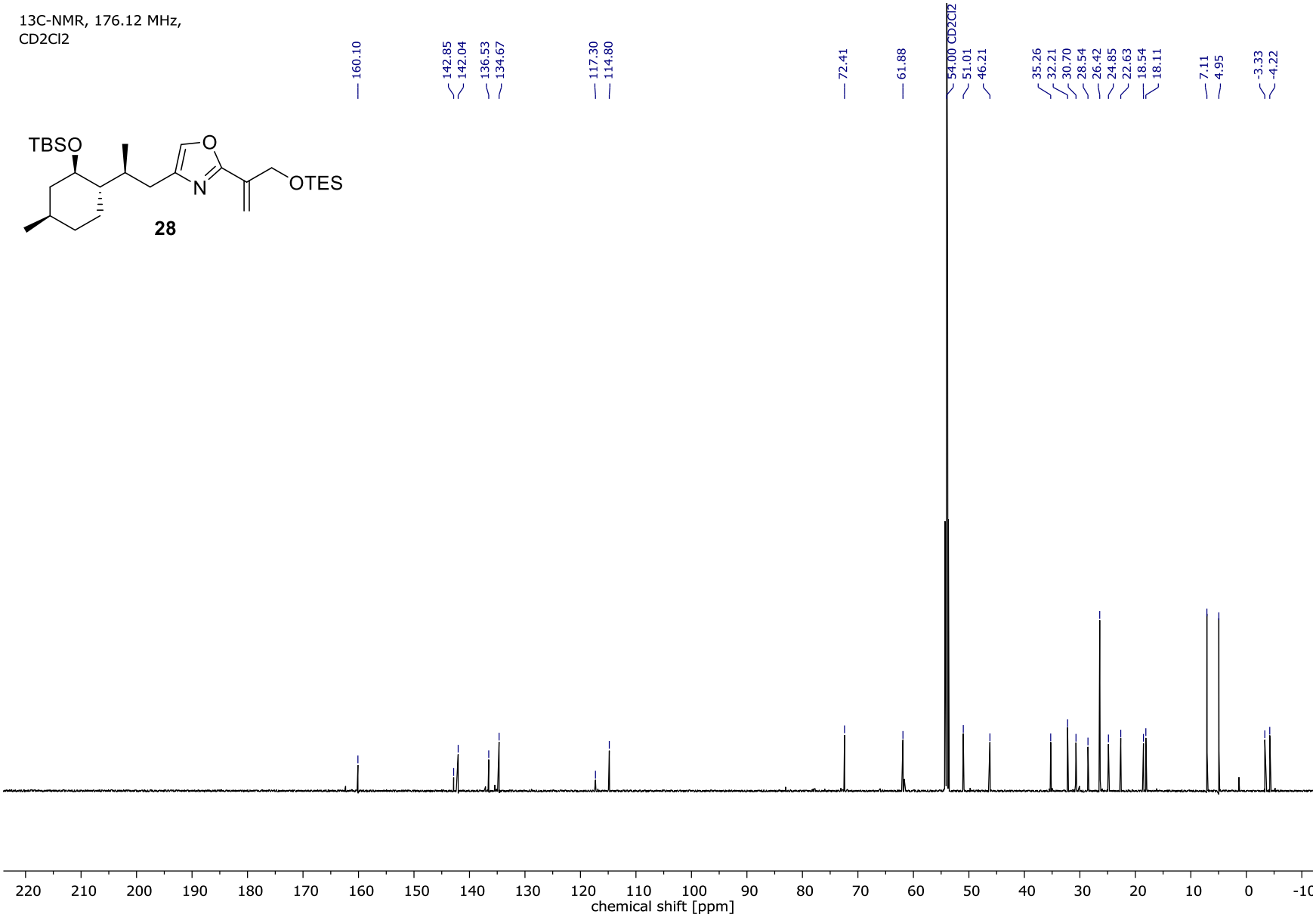
26




1H-NMR, 700.41 MHz,
CD2Cl2
CD2Cl2
TBSO
O
N
OTES
28
chemical shift [ppm]

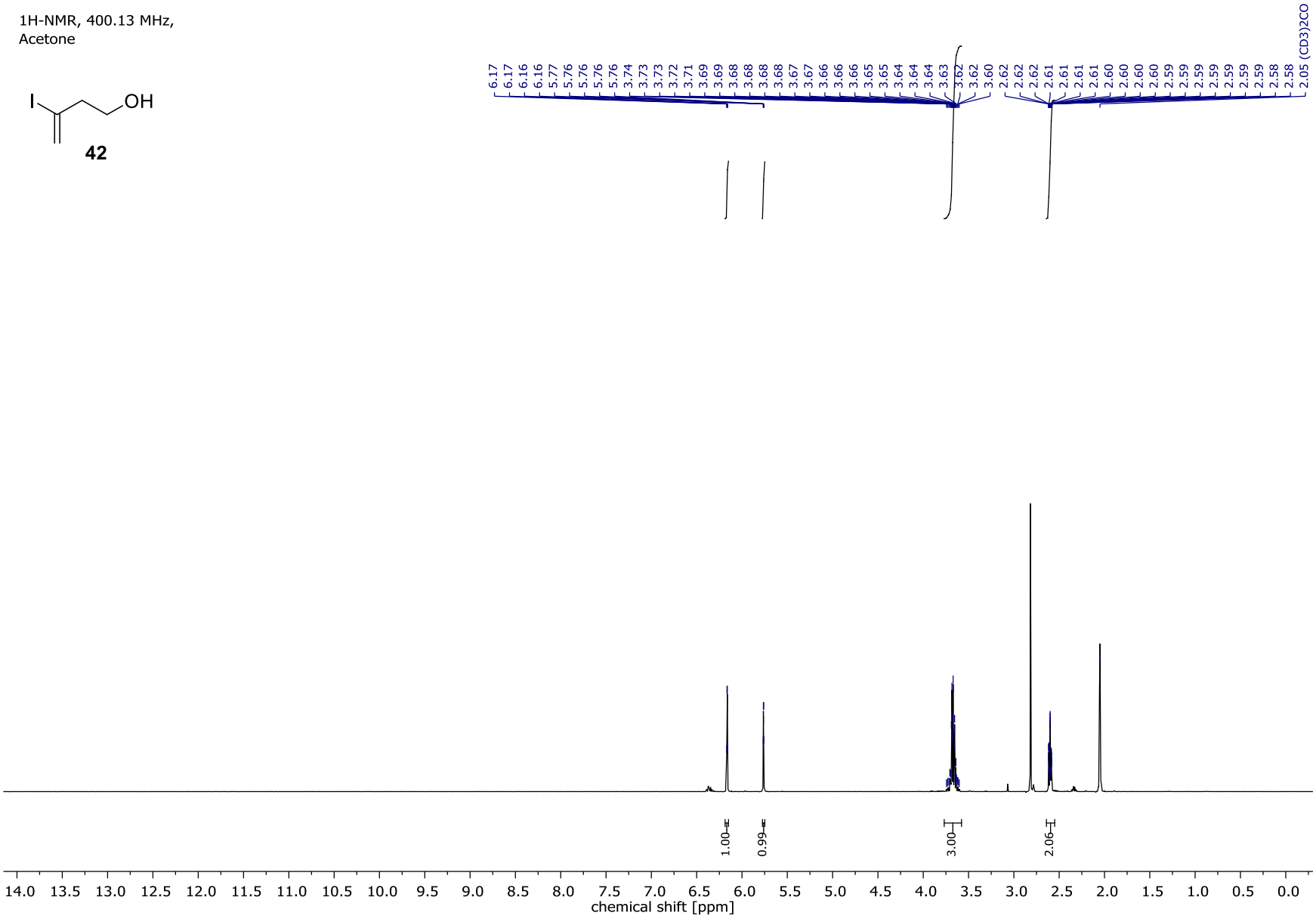
13C-NMR, 176.12 MHz,
CD2Cl2

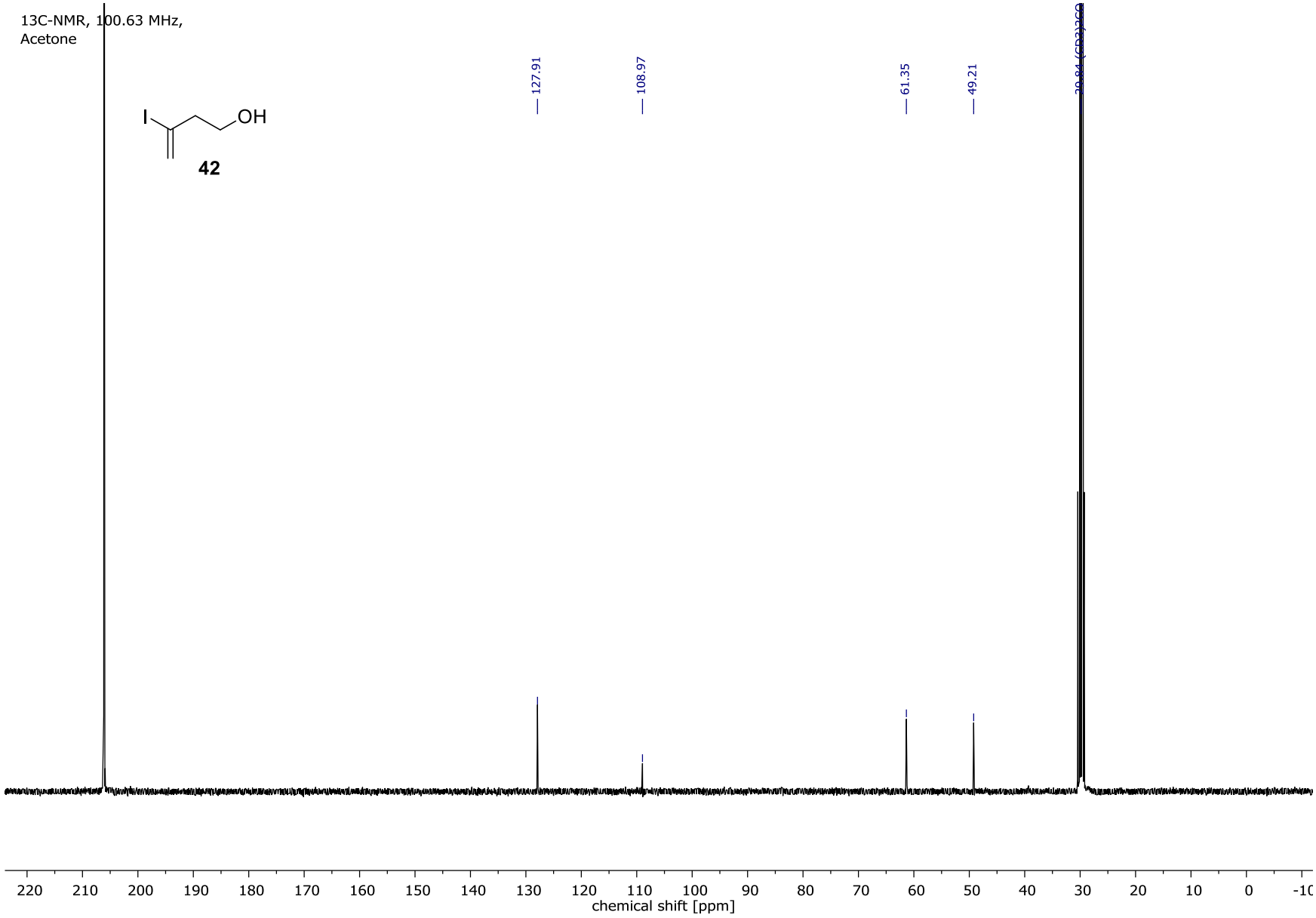
28



1H-NMR, 400.13 MHz,
Acetone

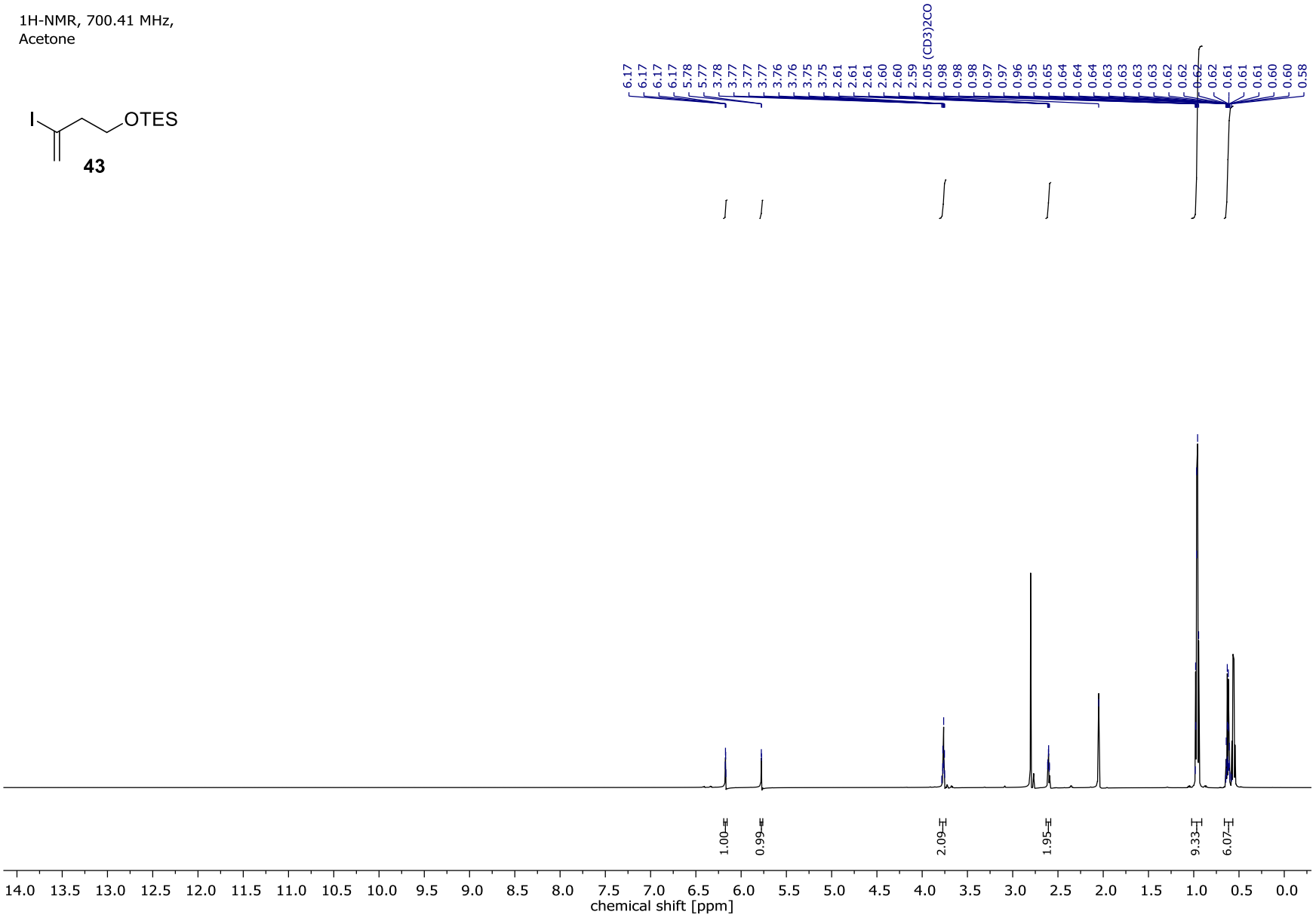
42

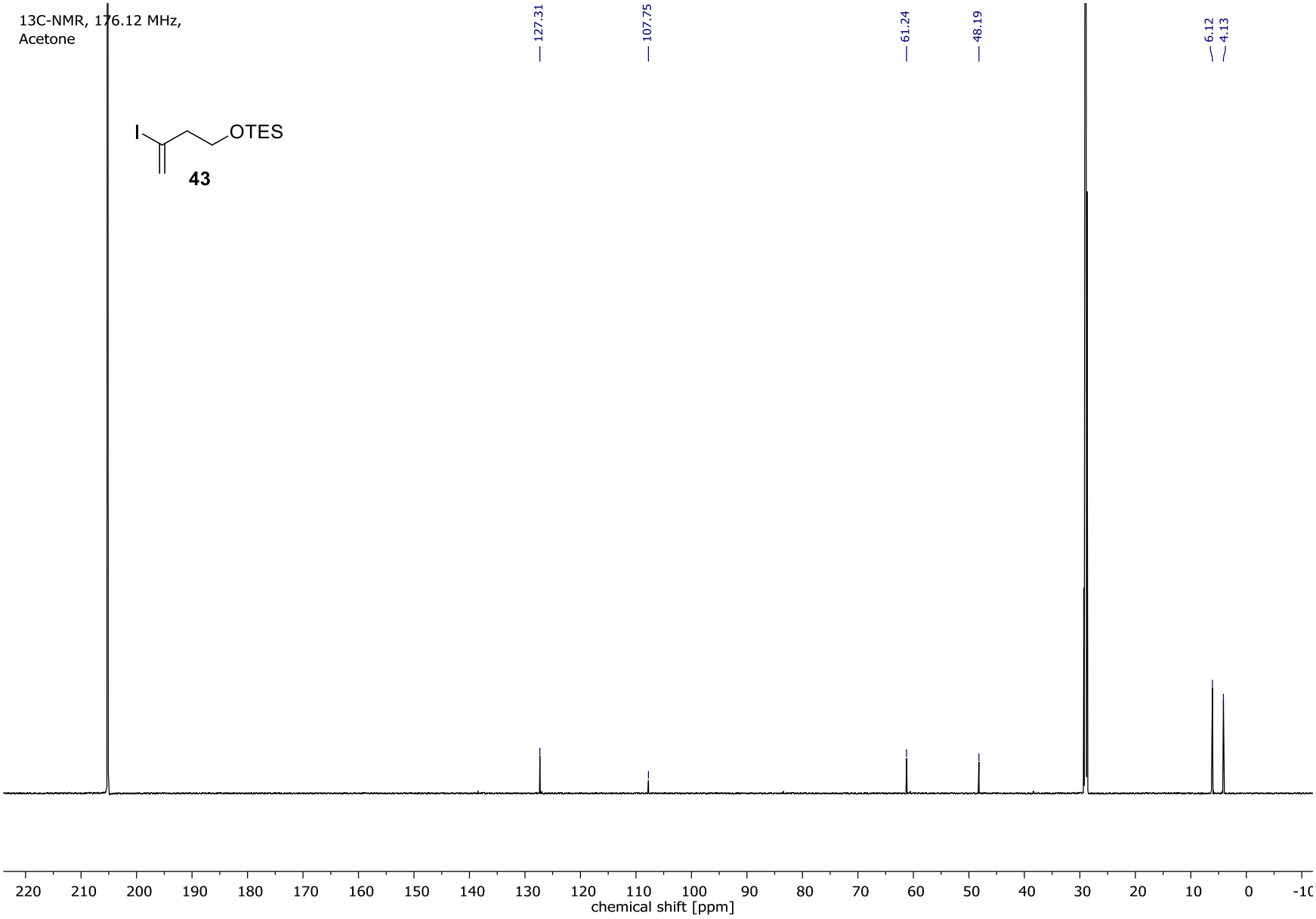



13C-NMR, 100.63 MHz,
Acetone
I
OH
42
127.91
108.97
61.35
49.21
30.84 (CD3)2CO
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
chemical shift [ppm]

1H-NMR, 700.41 MHz,
Acetone

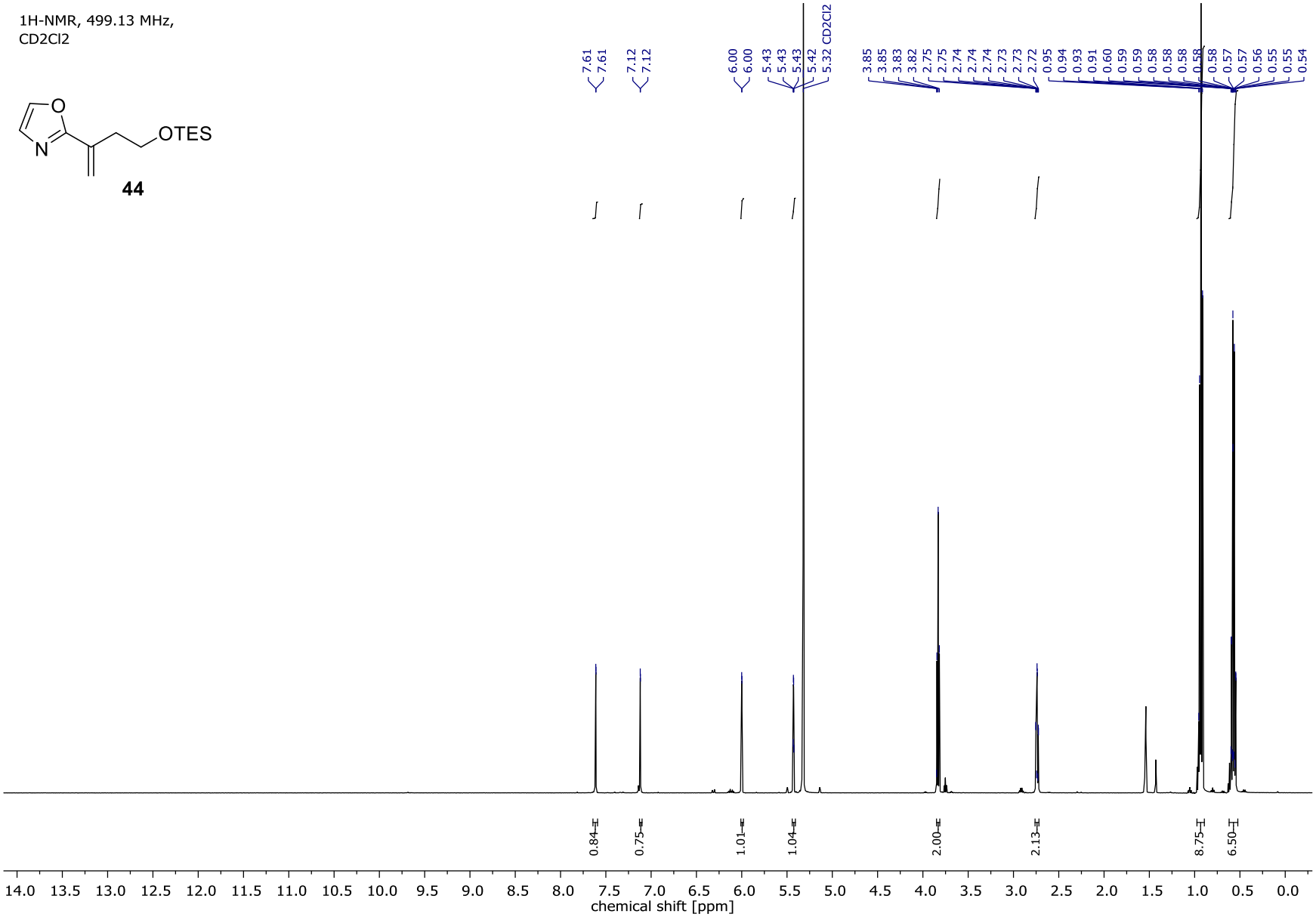
43




13C-NMR, 176.12 MHz,
Acetone
I
OTES
43
127.31
107.75
61.24
48.19
6.12
4.13
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

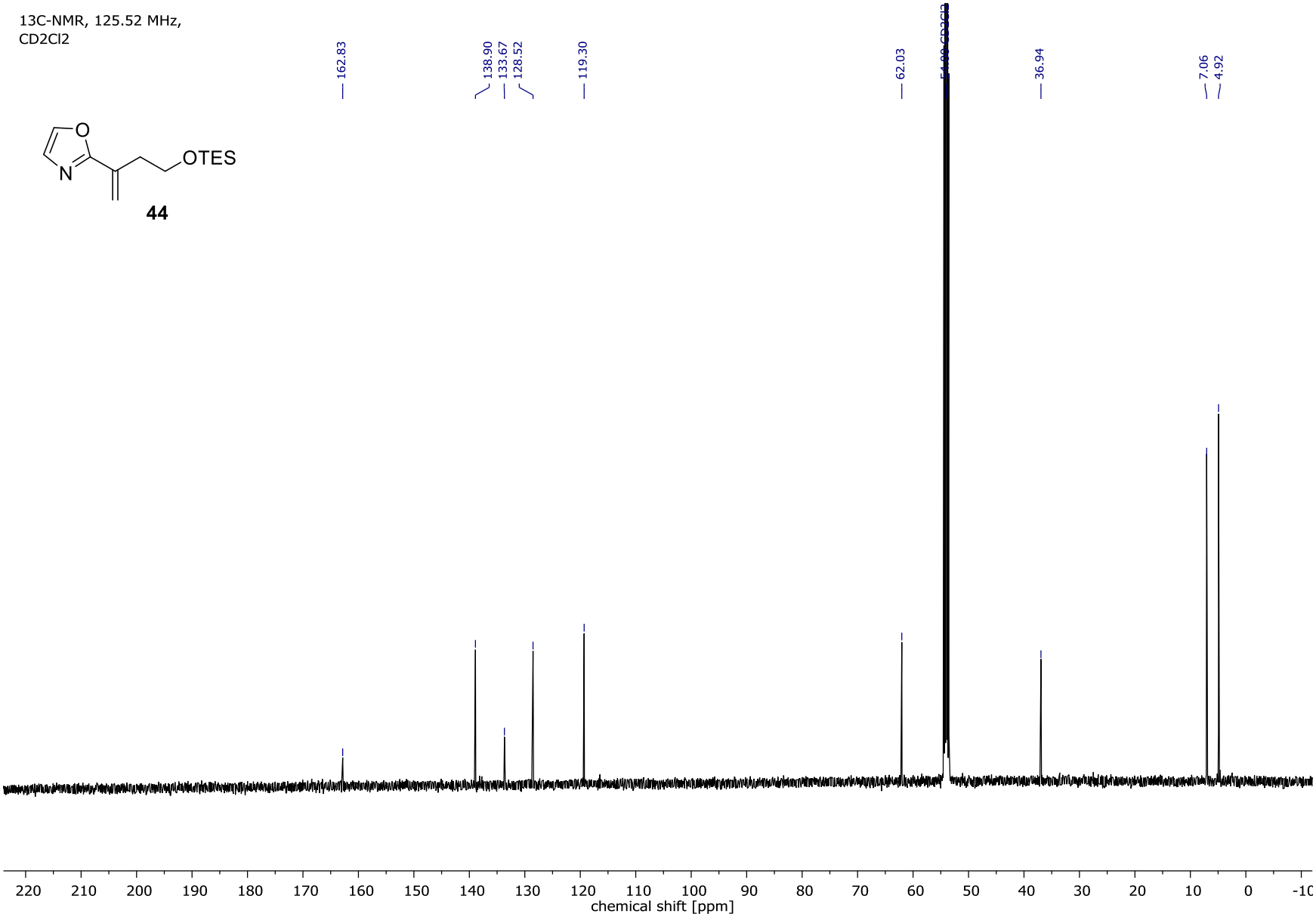
1H-NMR, 499.13 MHz,
CD2Cl2

44



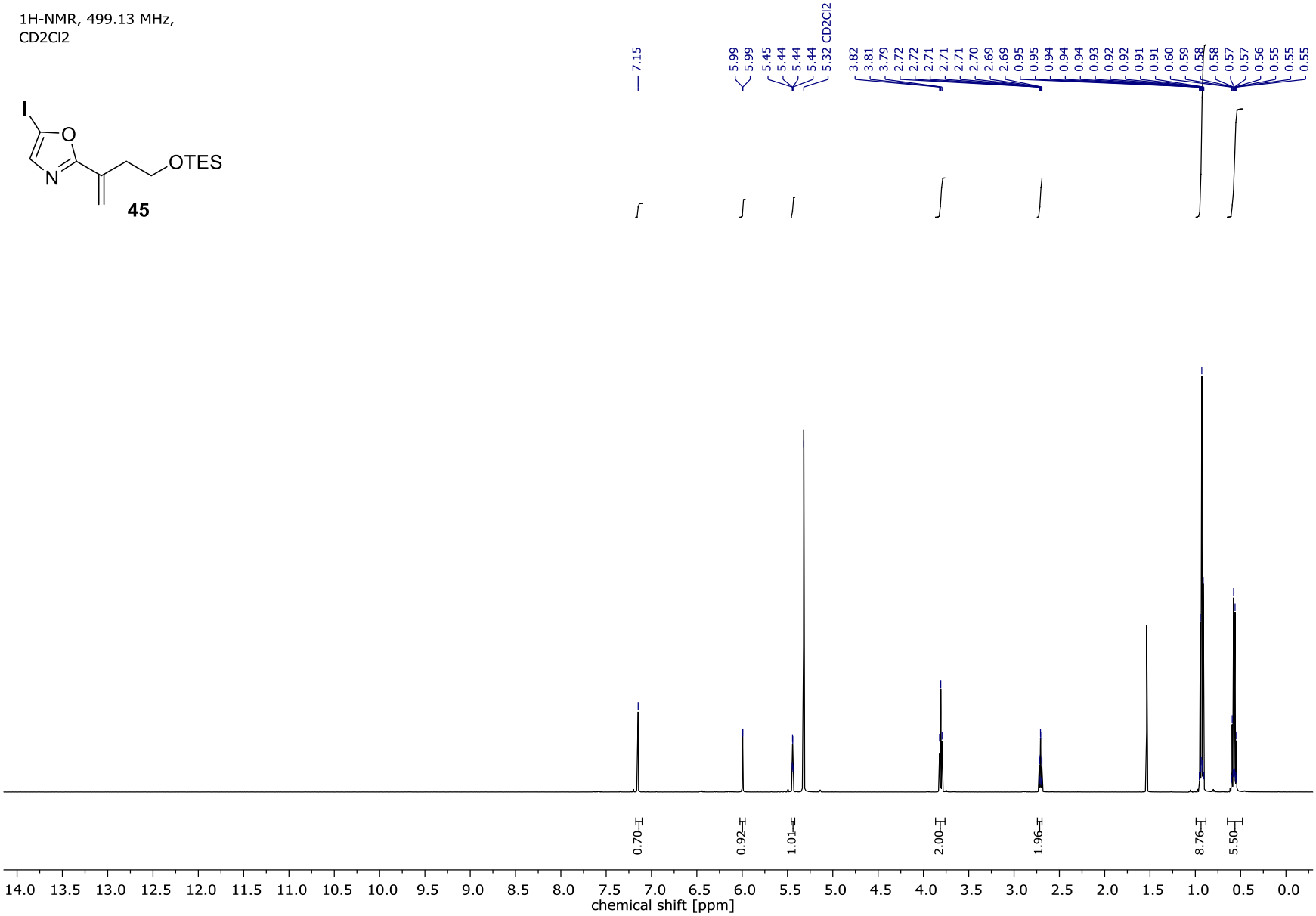
13C-NMR, 125.52 MHz,
CD2Cl2

44



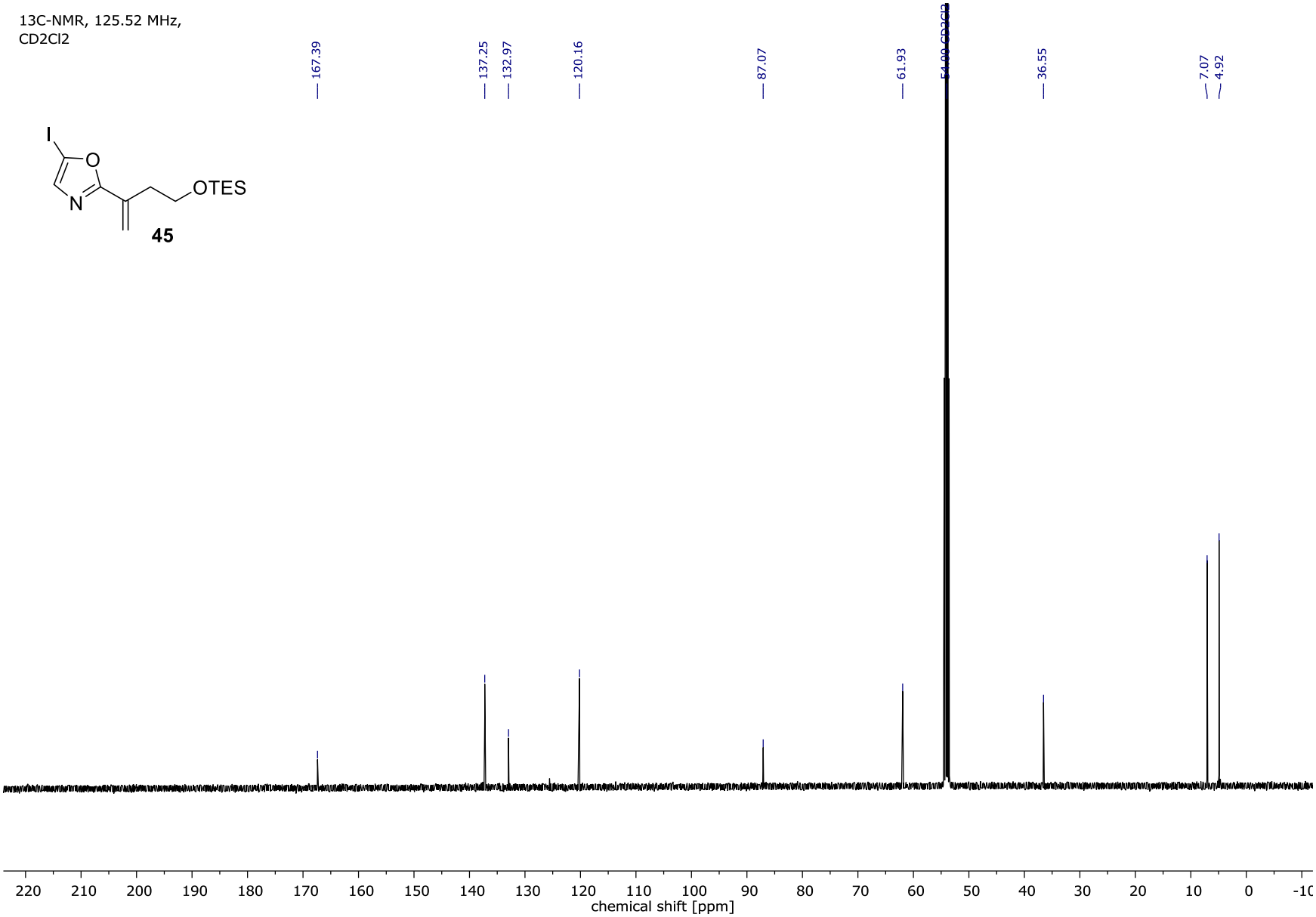
1H-NMR, 499.13 MHz,
CD2Cl2

45



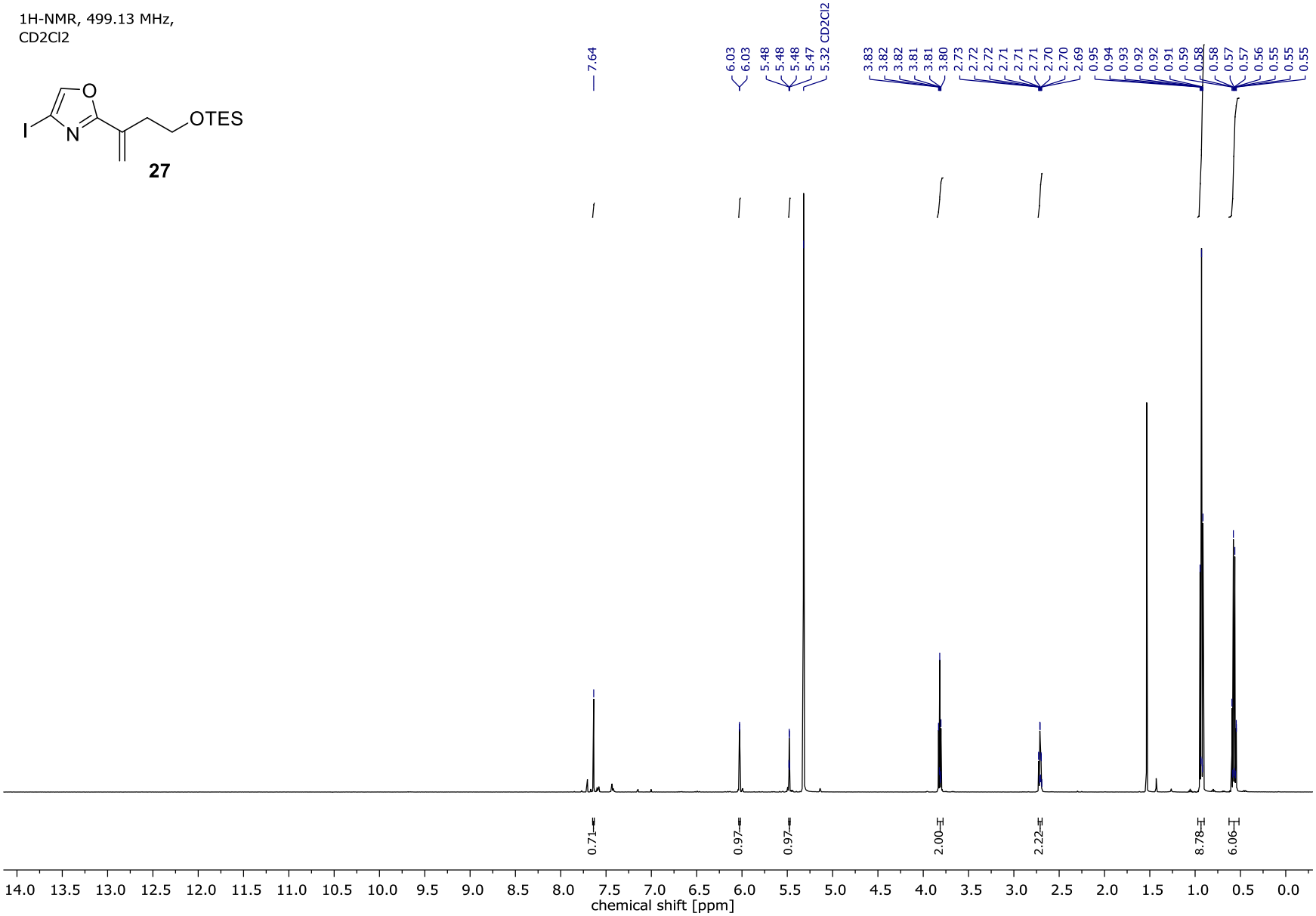
13C-NMR, 125.52 MHz,
CD2Cl2

45



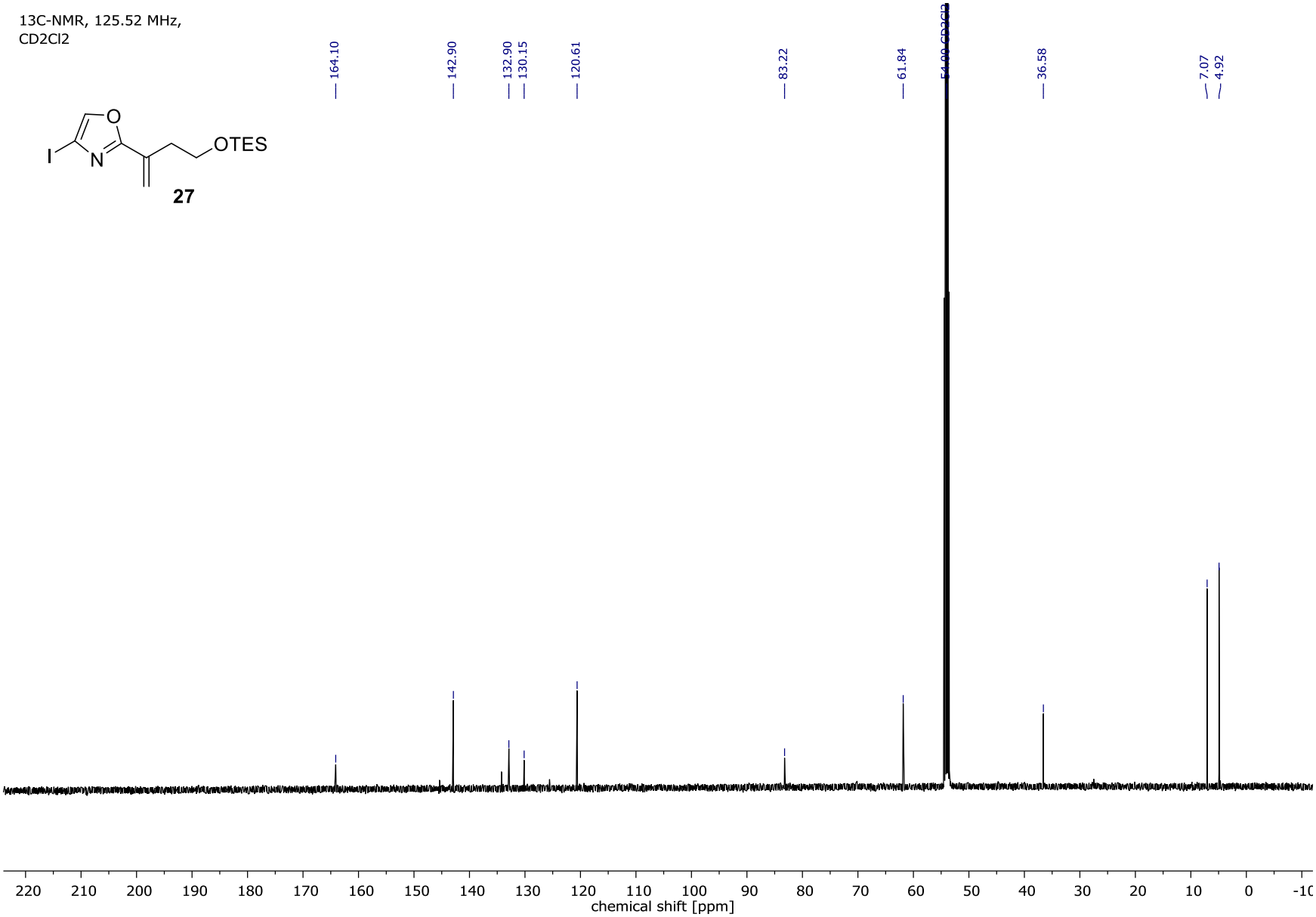
1H-NMR, 499.13 MHz,
CD2Cl2

27

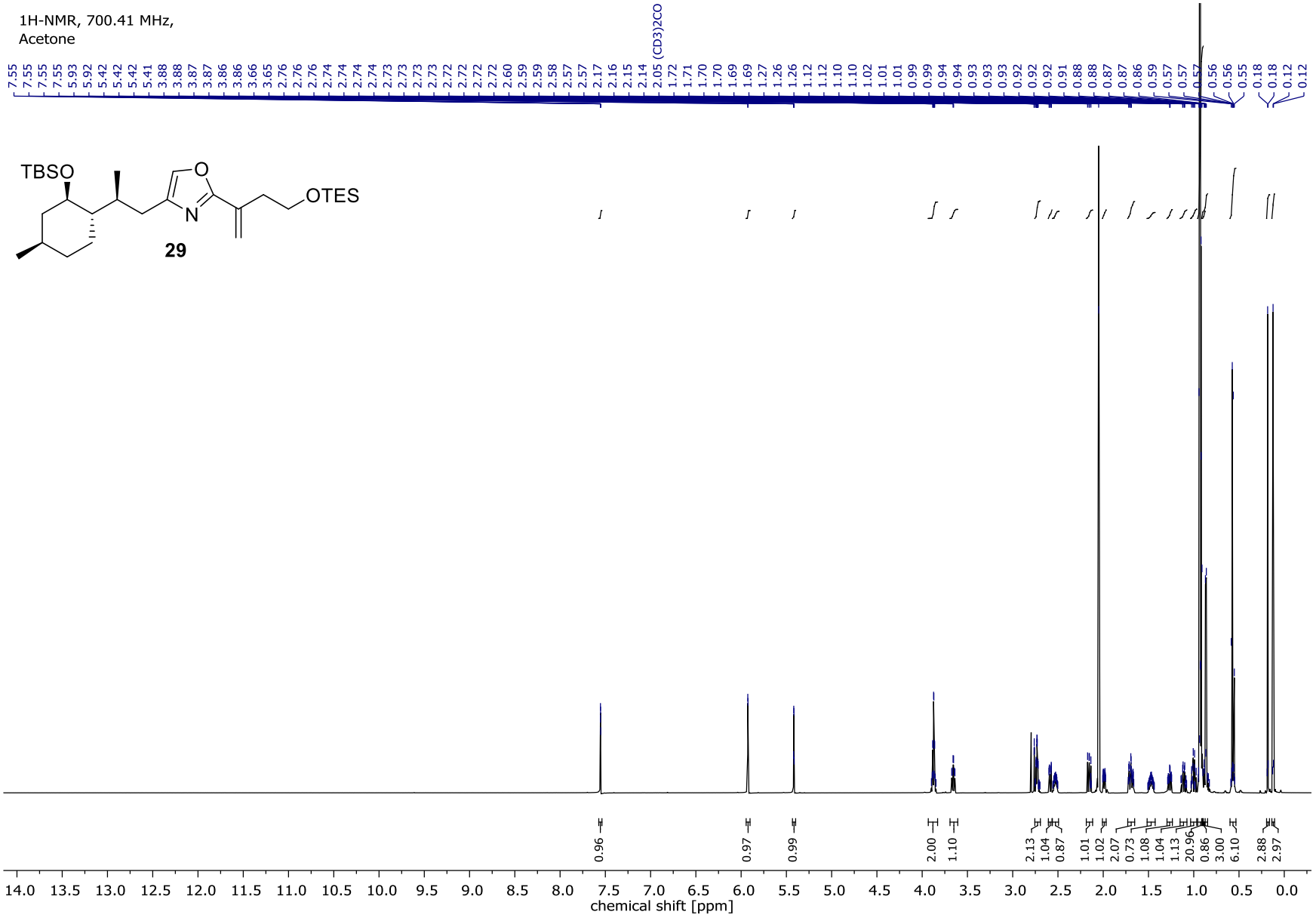


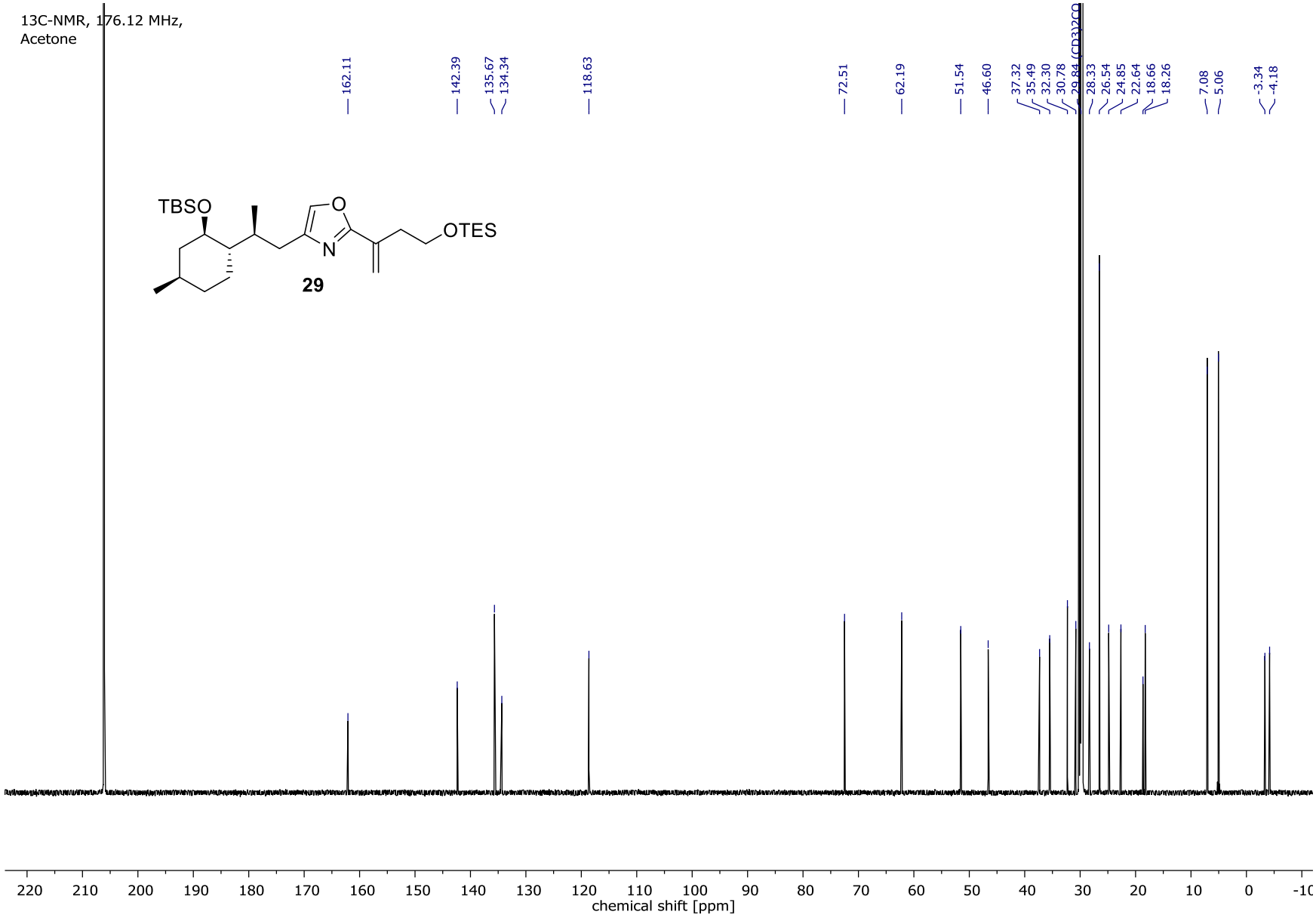
13C-NMR, 125.52 MHz,
CD2Cl2

27

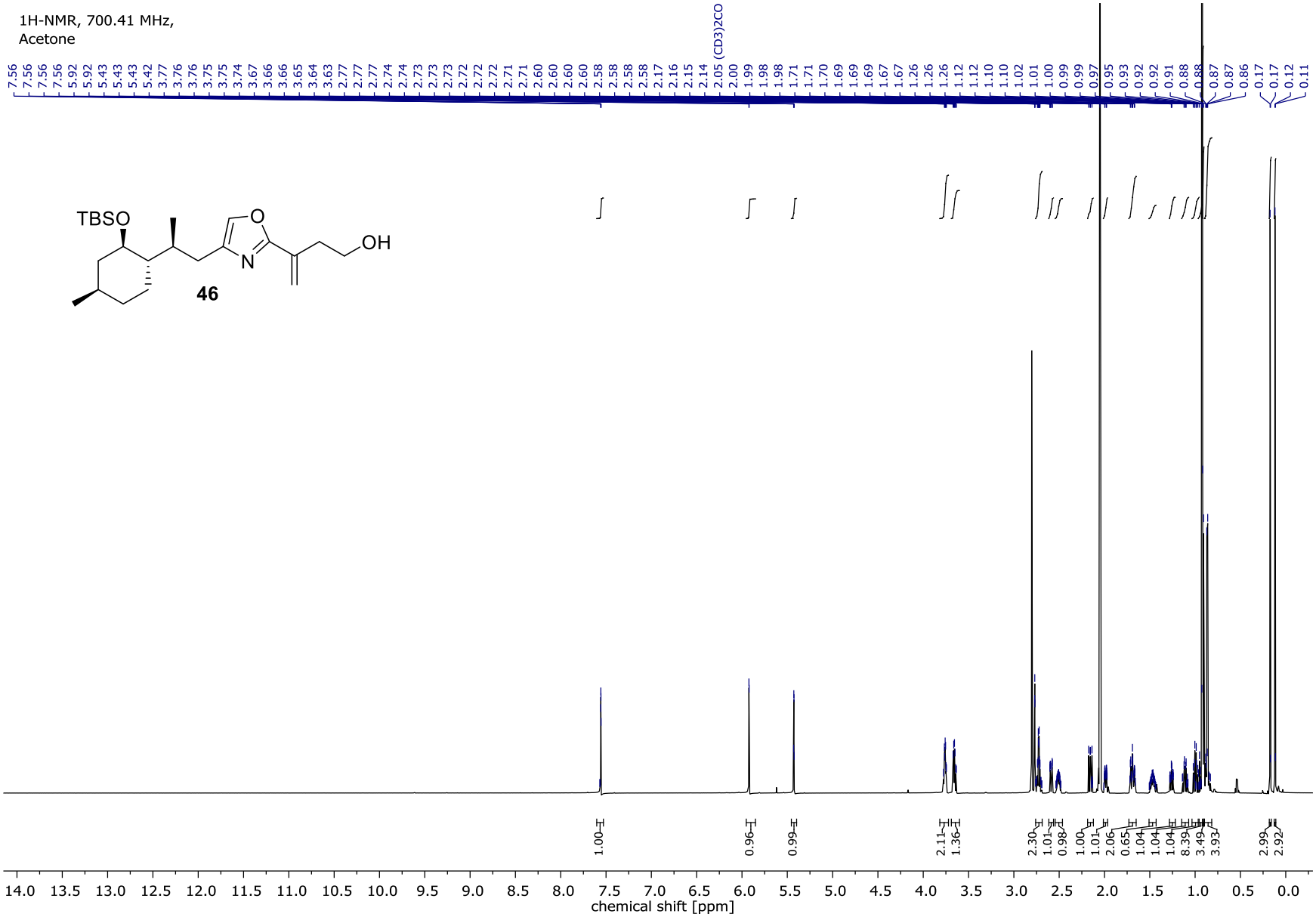


1H-NMR, 700.41 MHz,
Acetone

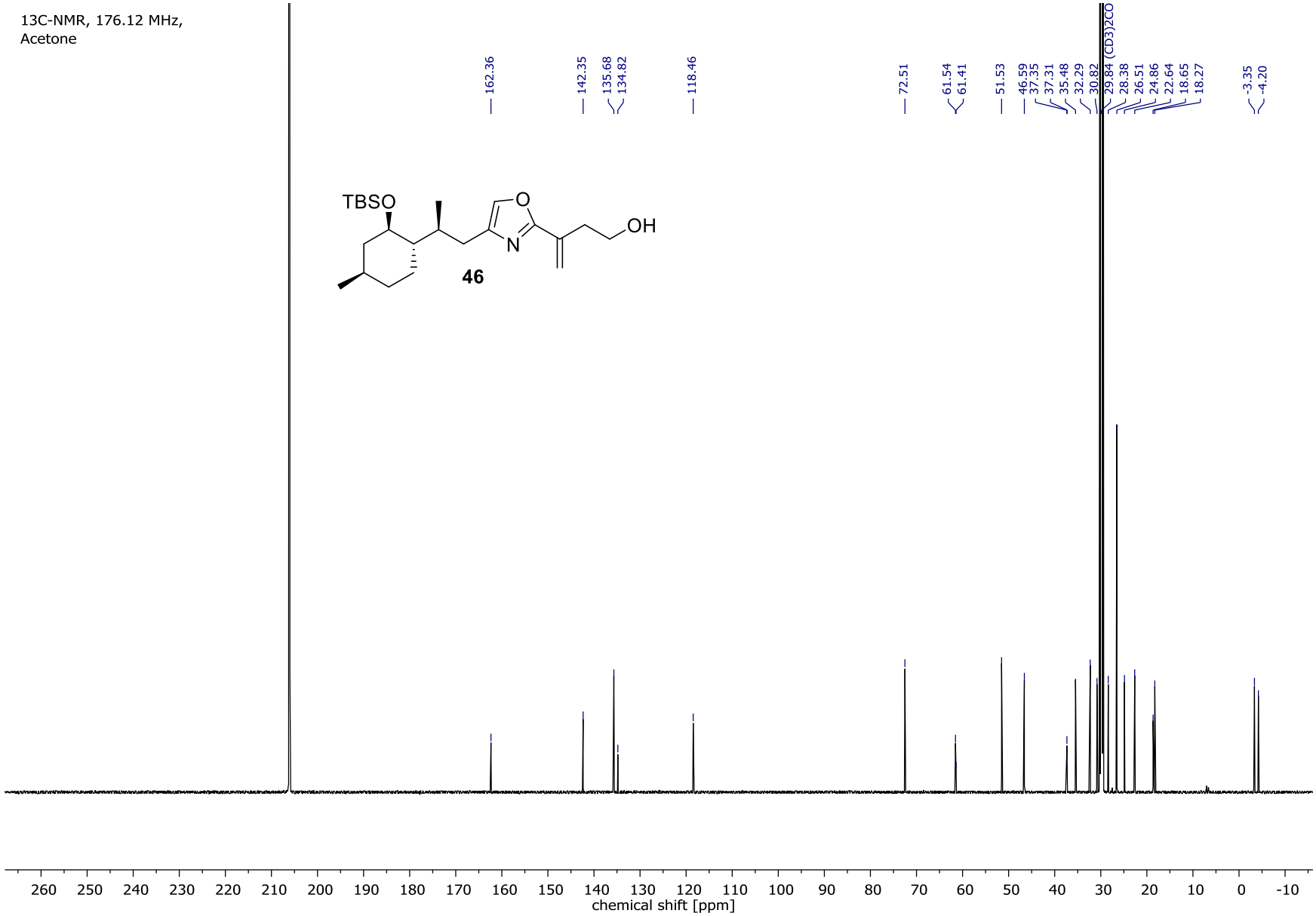


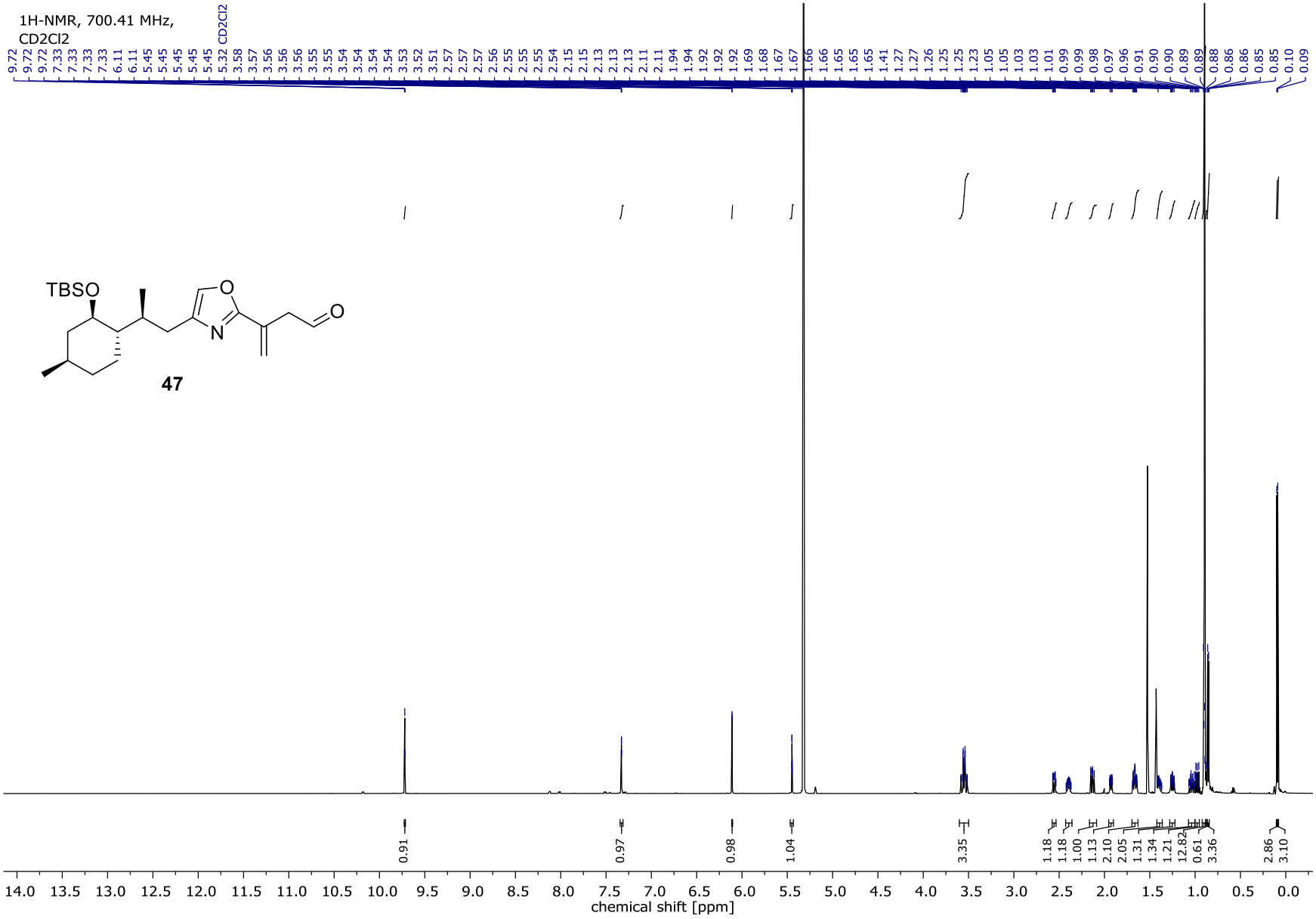

13C-NMR, 176.12 MHz,
Acetone
162.11
142.39
135.67
134.34
118.63
72.51
62.19
51.54
46.60
37.32
35.49
32.30
30.78
29.84 (CD3)2CO
28.33
26.54
24.85
22.64
18.66
18.26
7.08
5.06
-3.34
-4.18
TBSO
O
N
OTES
29
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

1H-NMR, 700.41 MHz,
Acetone



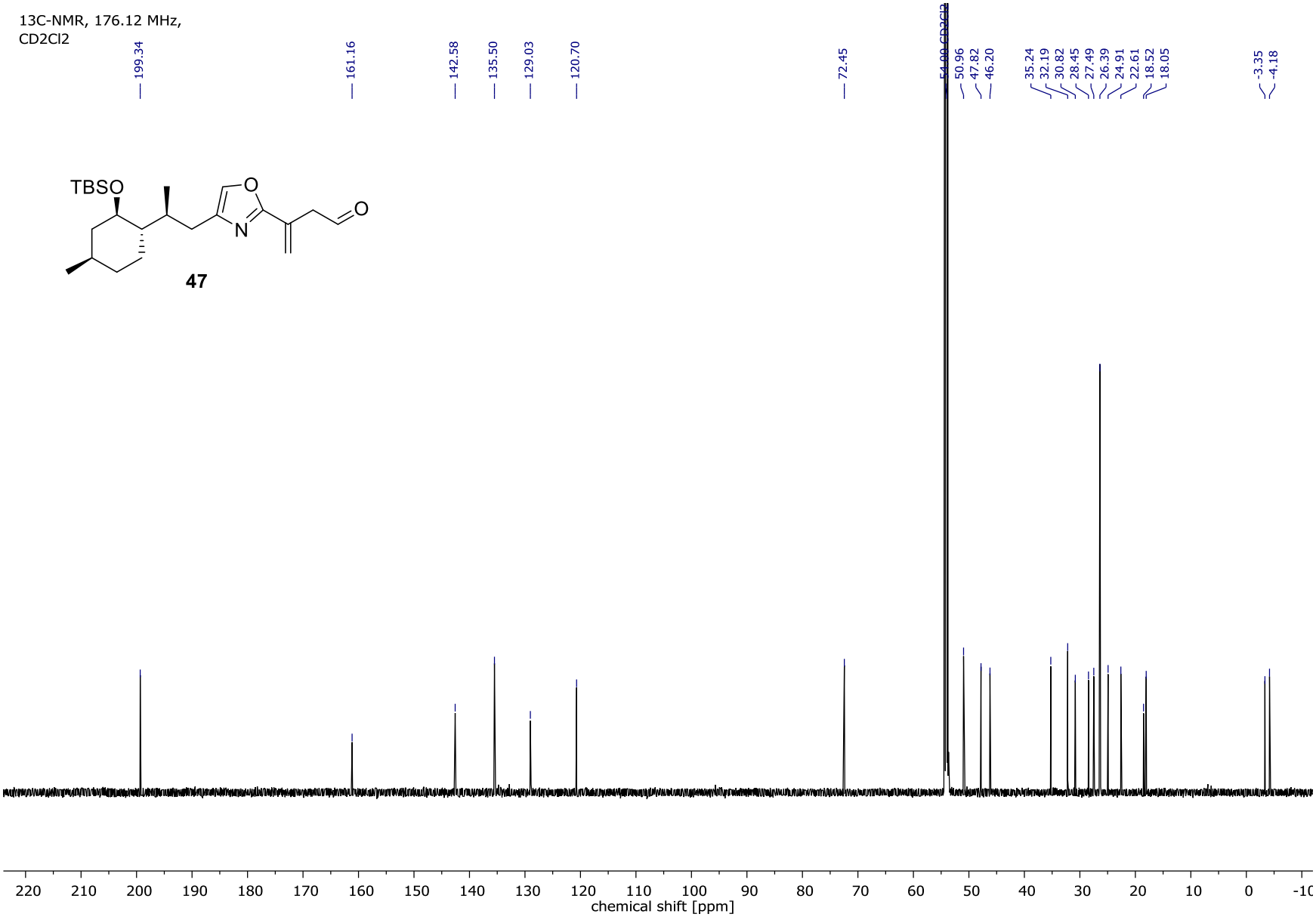
13C-NMR, 176.12 MHz,
Acetone

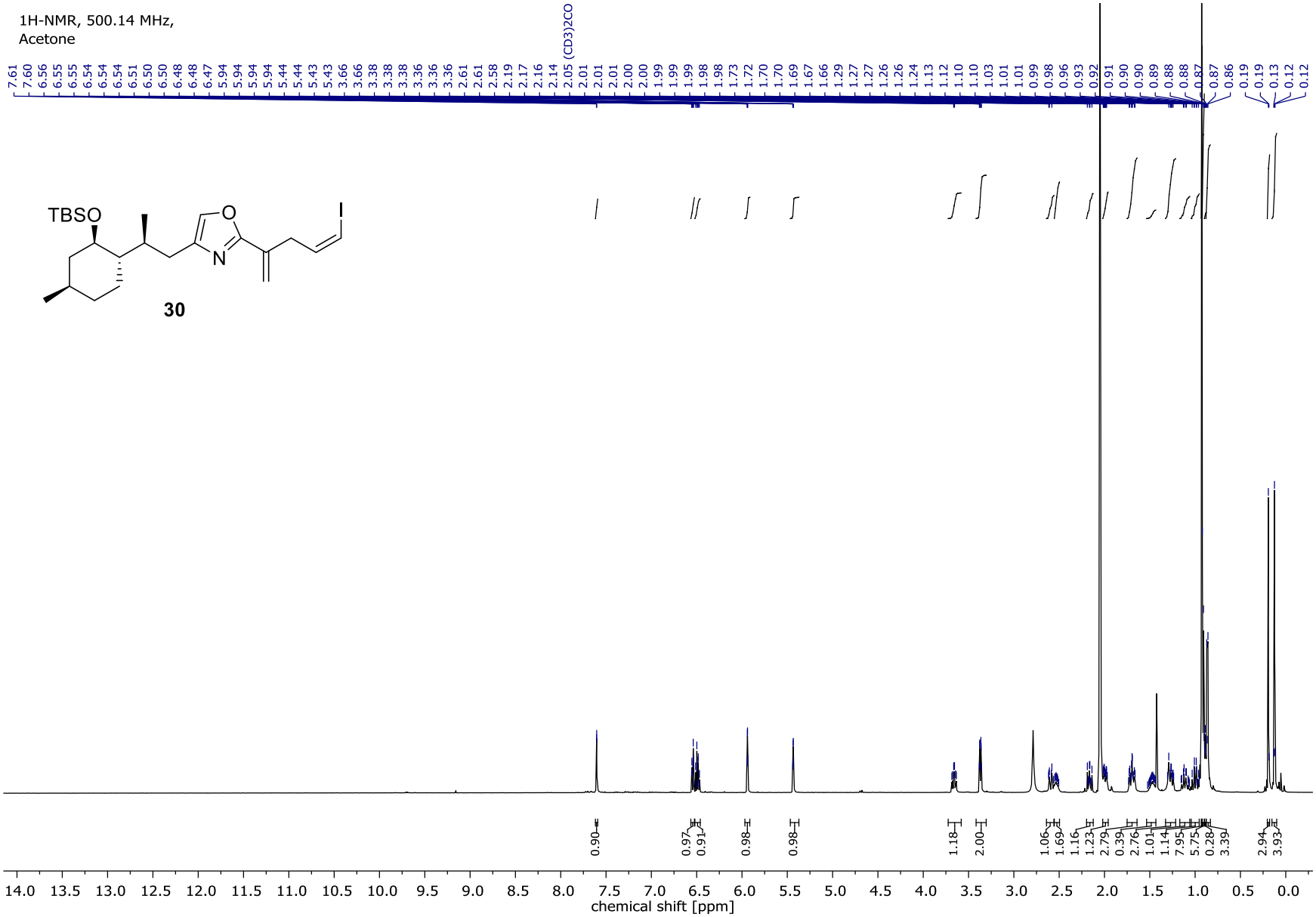


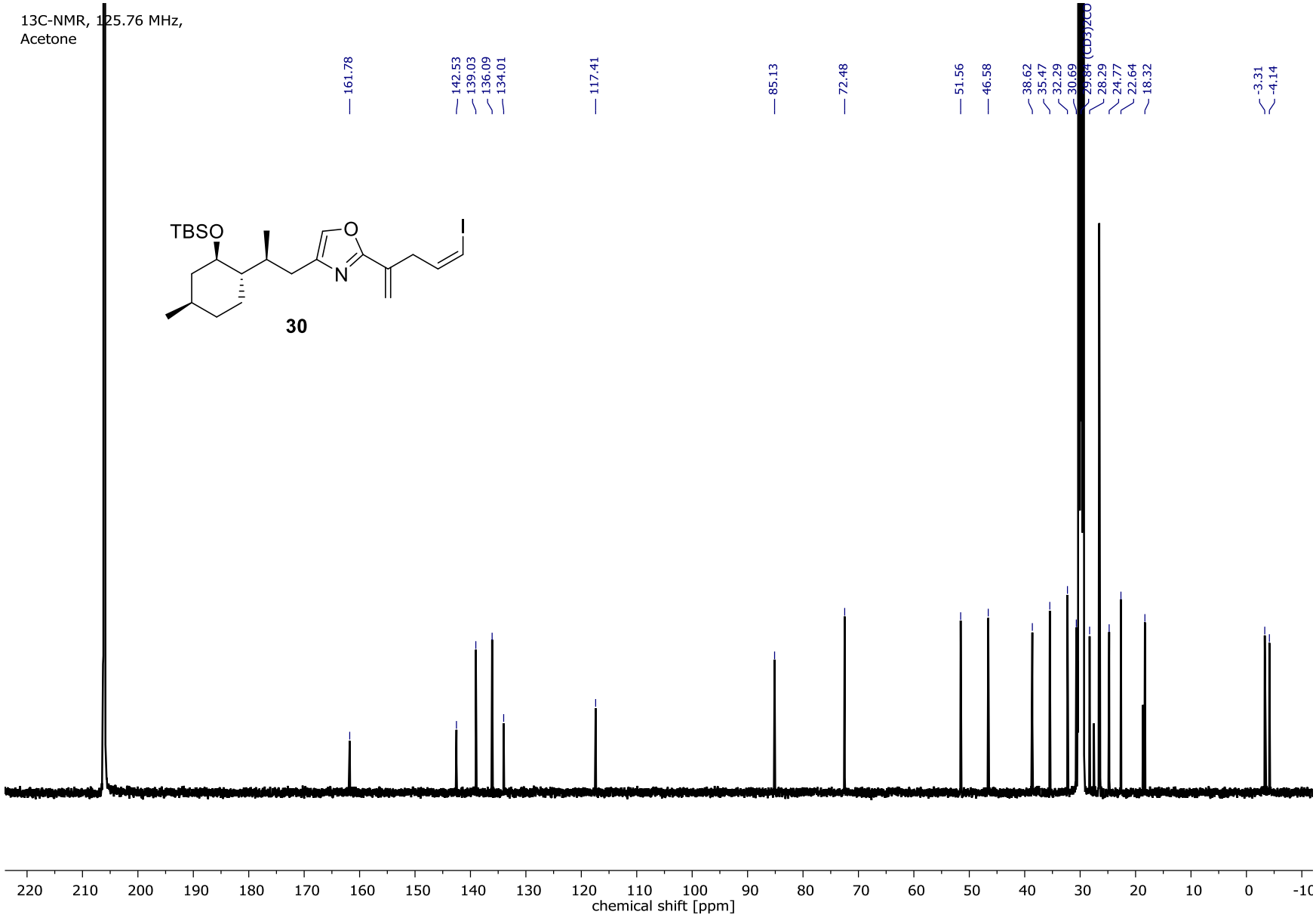

1H-NMR, 700.41 MHz,
CD2Cl2
CD2Cl2
TBSO
O
N
O
47
chemical shift [ppm]

13C-NMR, 176.12 MHz,
CD2Cl2

47

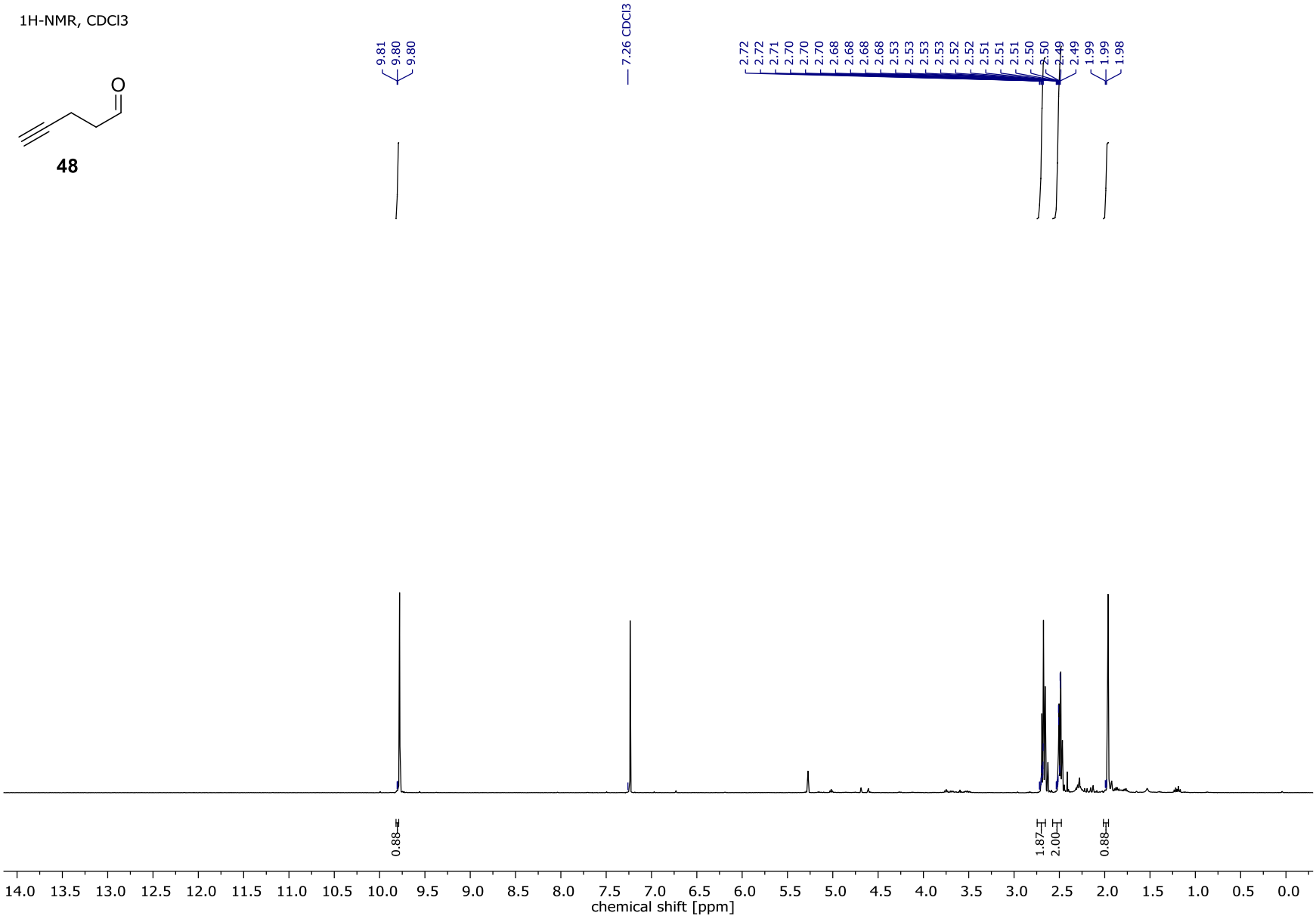



1H-NMR, 500.14 MHz,
Acetone
(CD3)2CO
TBSO
O
N
I
30
chemical shift [ppm]


13C-NMR, 125.76 MHz,
Acetone
161.78
142.53
139.03
136.09
134.01
117.41
85.13
72.48
51.56
46.58
38.62
35.47
32.29
30.69
29.84
28.29
24.77
22.64
18.32
-3.31
-4.14
TBSO
O
N
I
30
chemical shift [ppm]

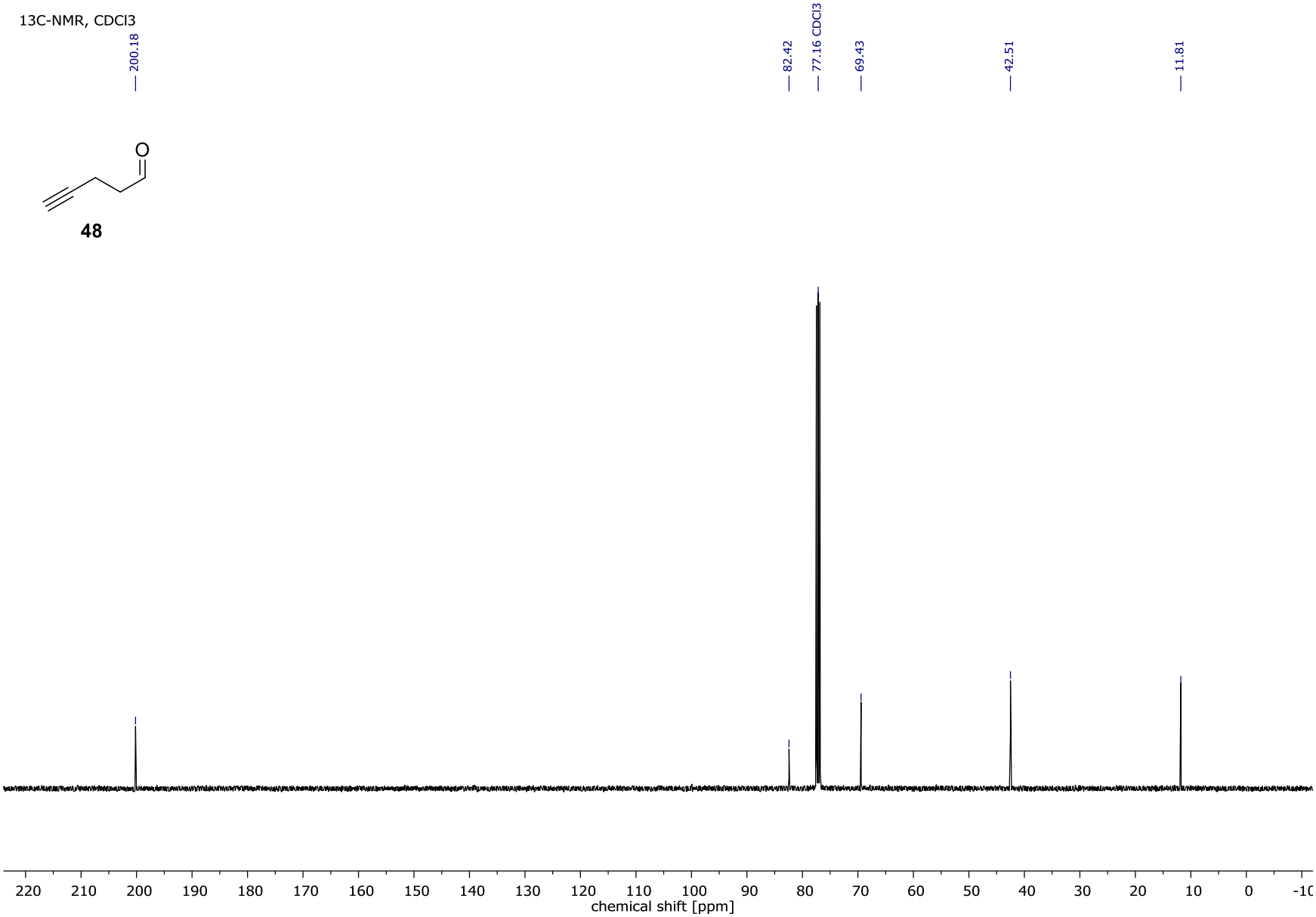
1H-NMR, CDCl3

48



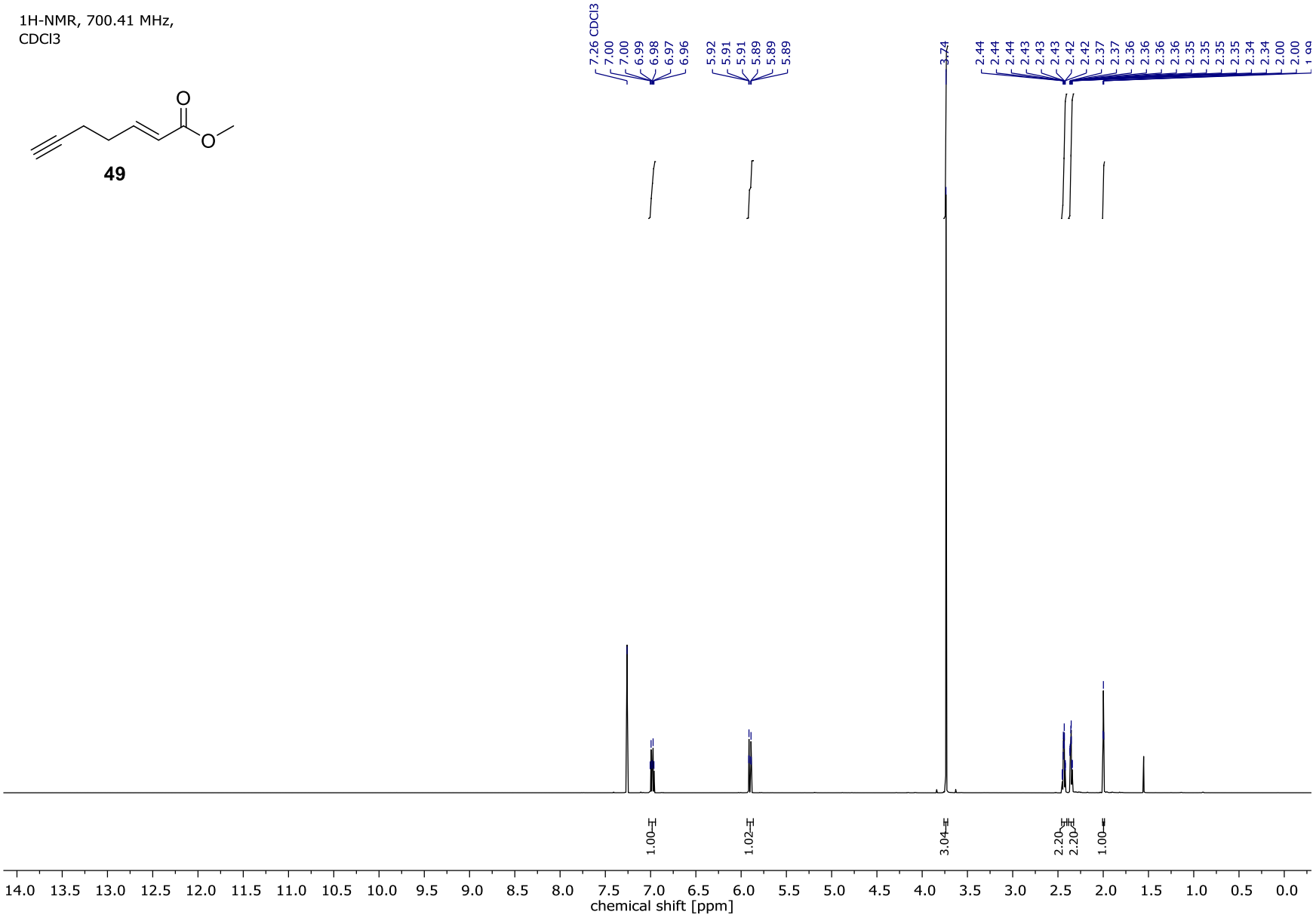
13C-NMR, CDCl3

48



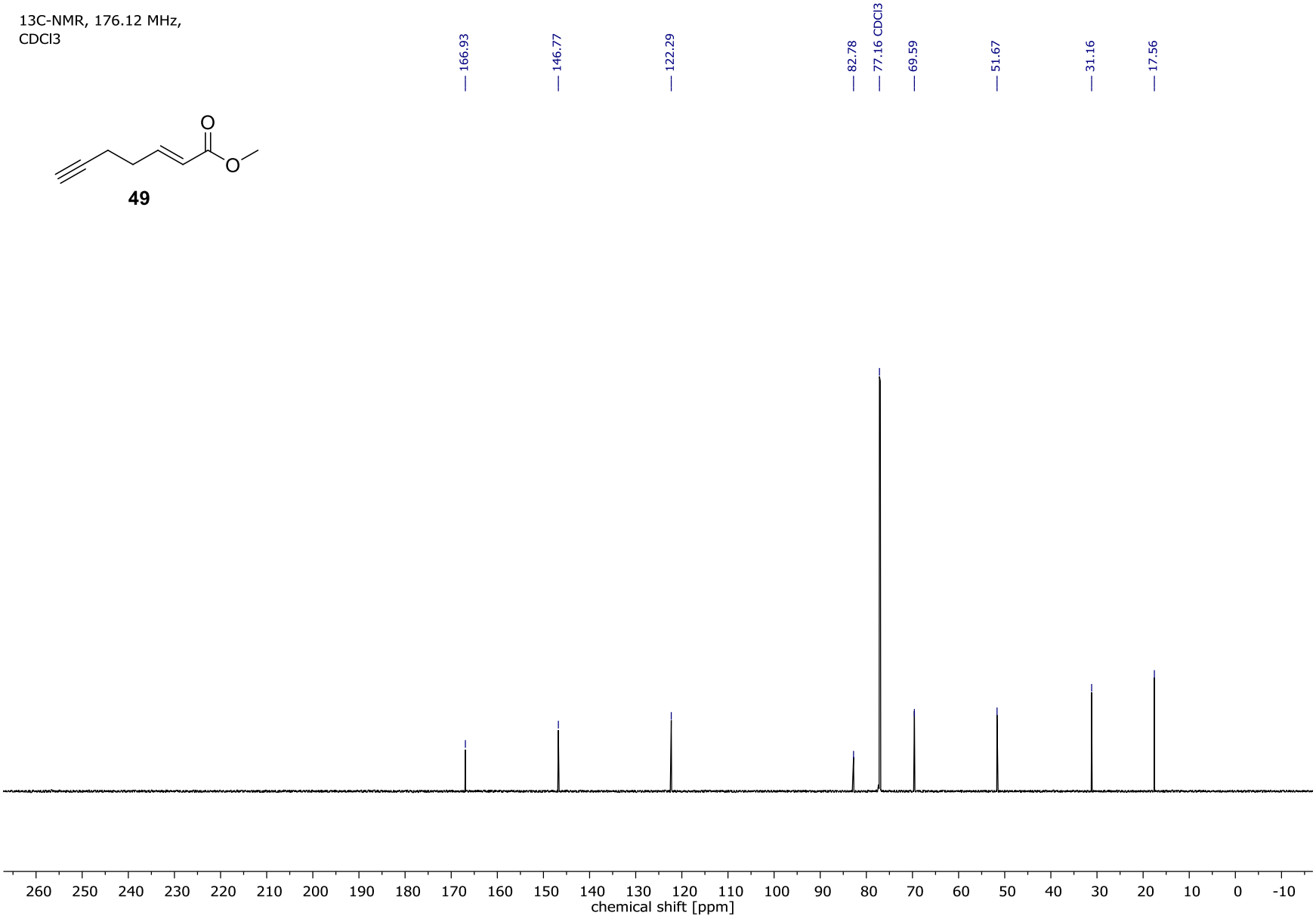
1H-NMR, 700.41 MHz,
CDCl3

49



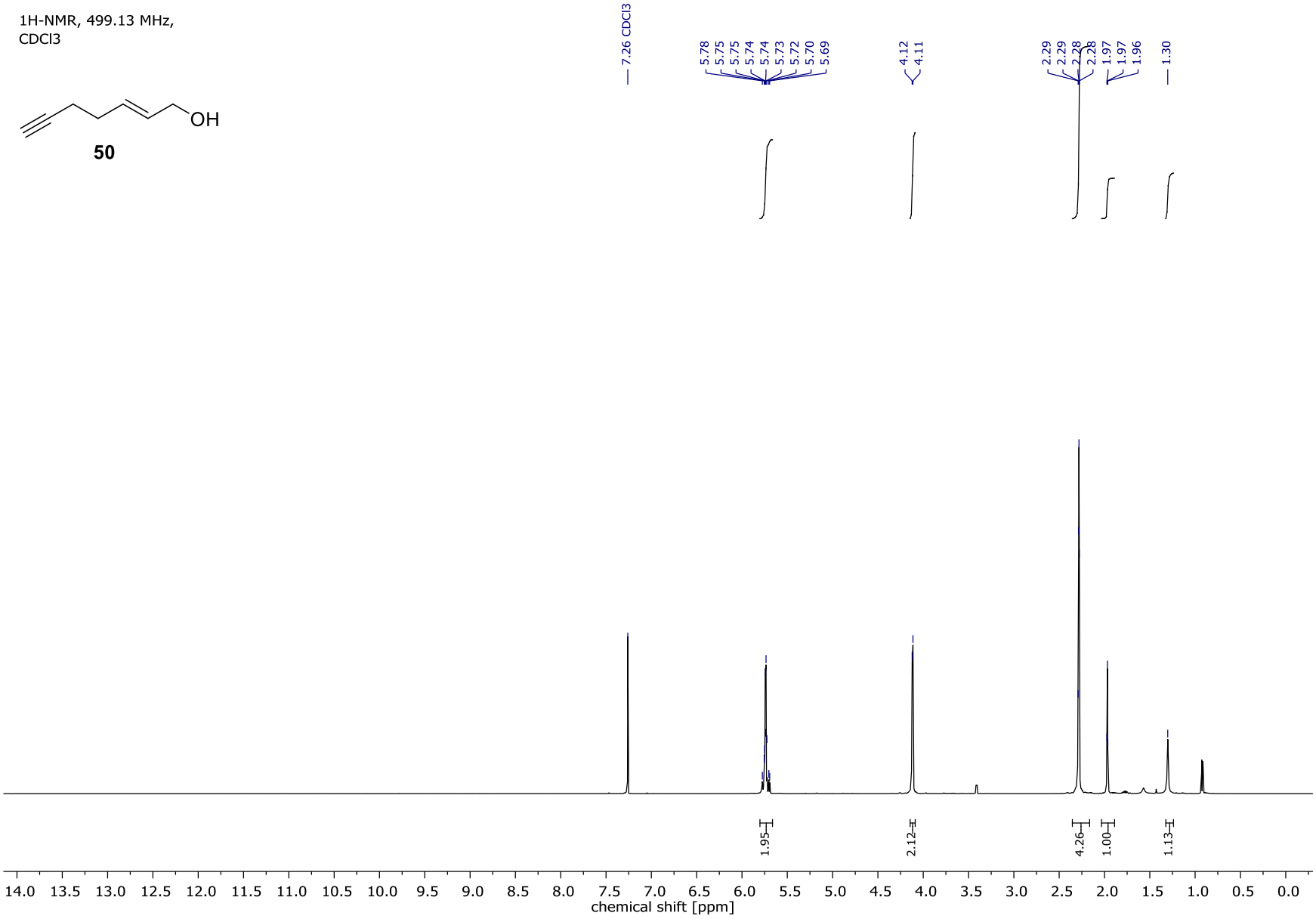
13C-NMR, 176.12 MHz,
CDCl3

49



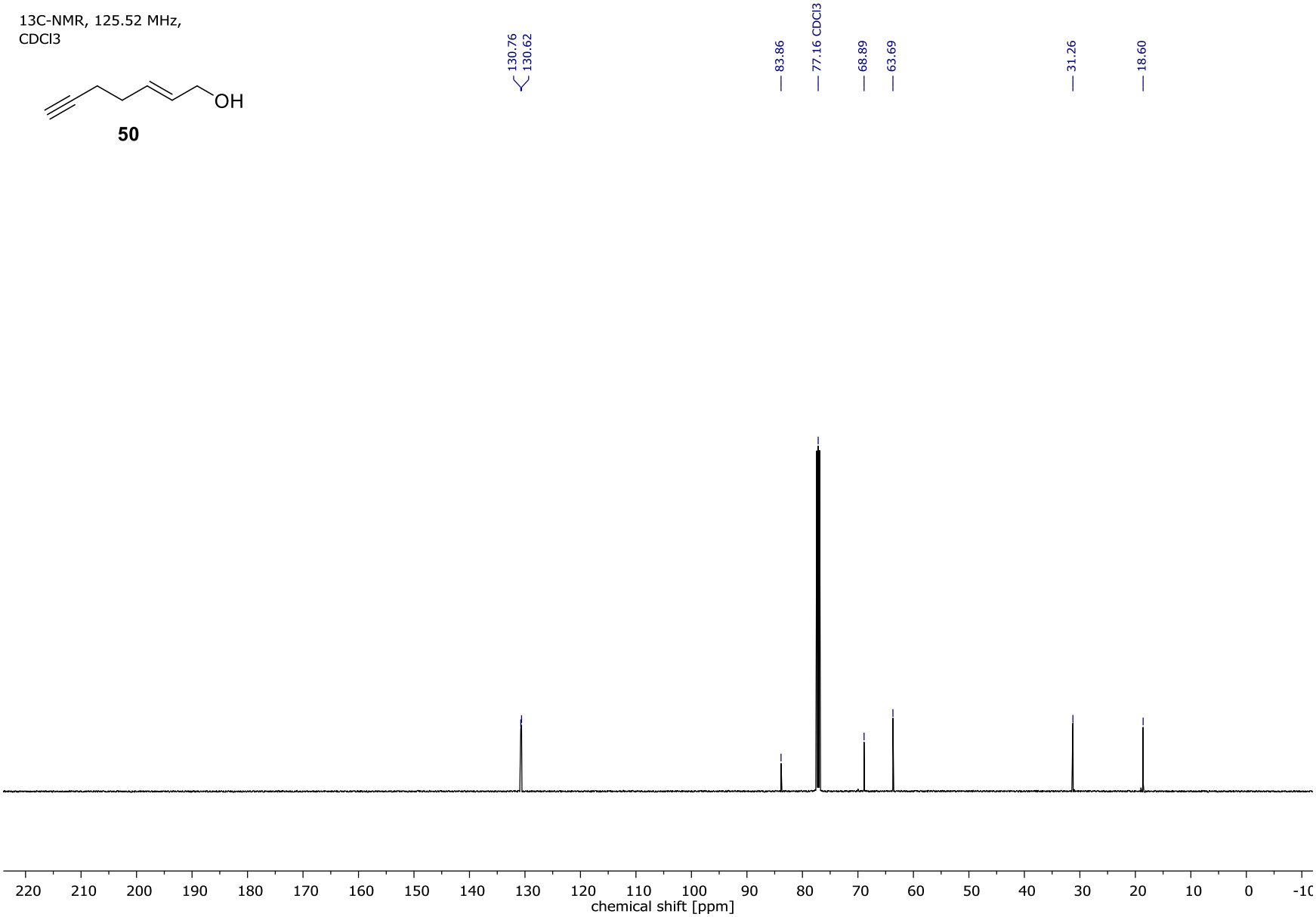
1H-NMR, 499.13 MHz,
CDCl3

50



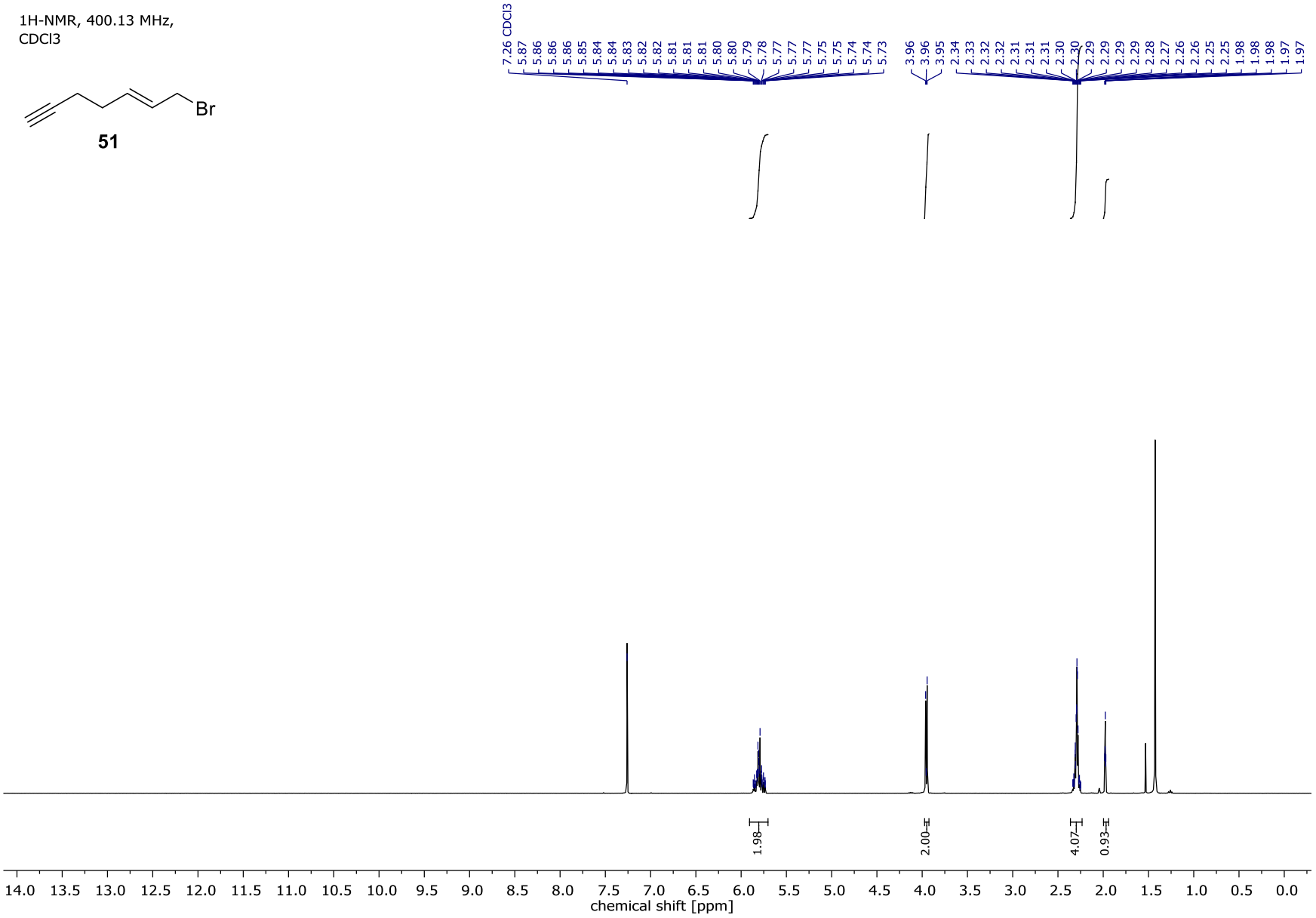
13C-NMR, 125.52 MHz,
CDCl3

50



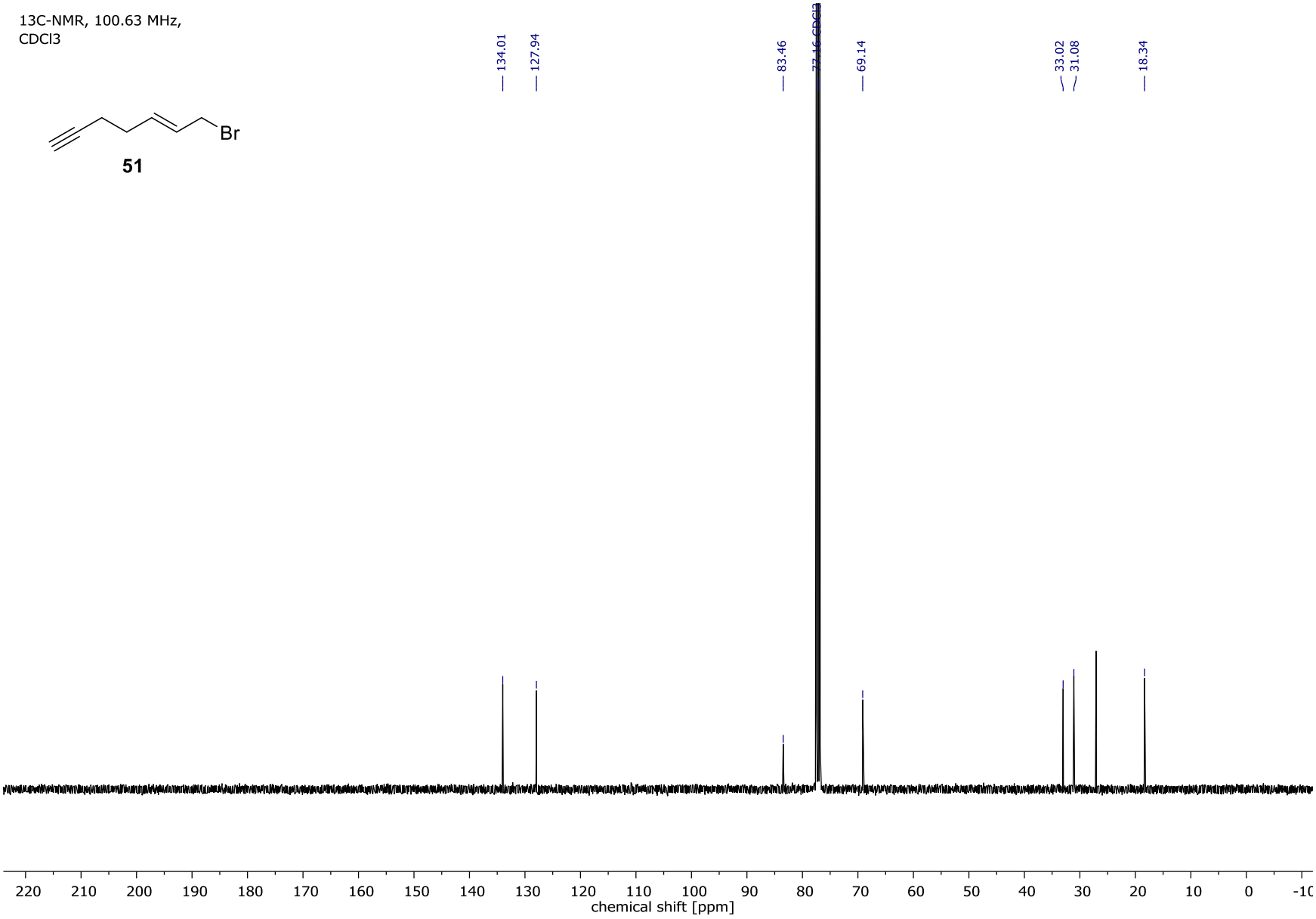
1H-NMR, 400.13 MHz,
CDCl3

51



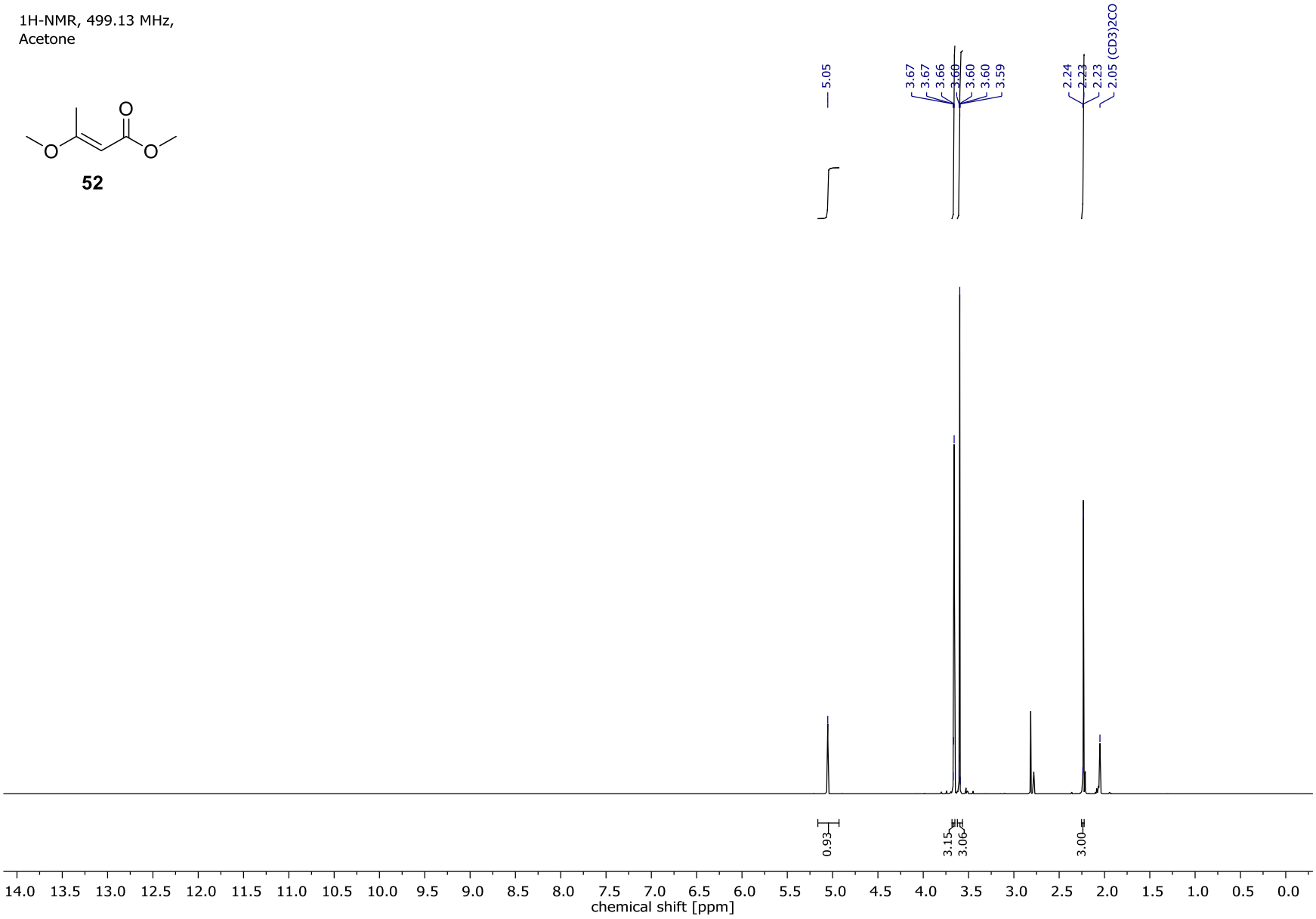
13C-NMR, 100.63 MHz,
CDCl3

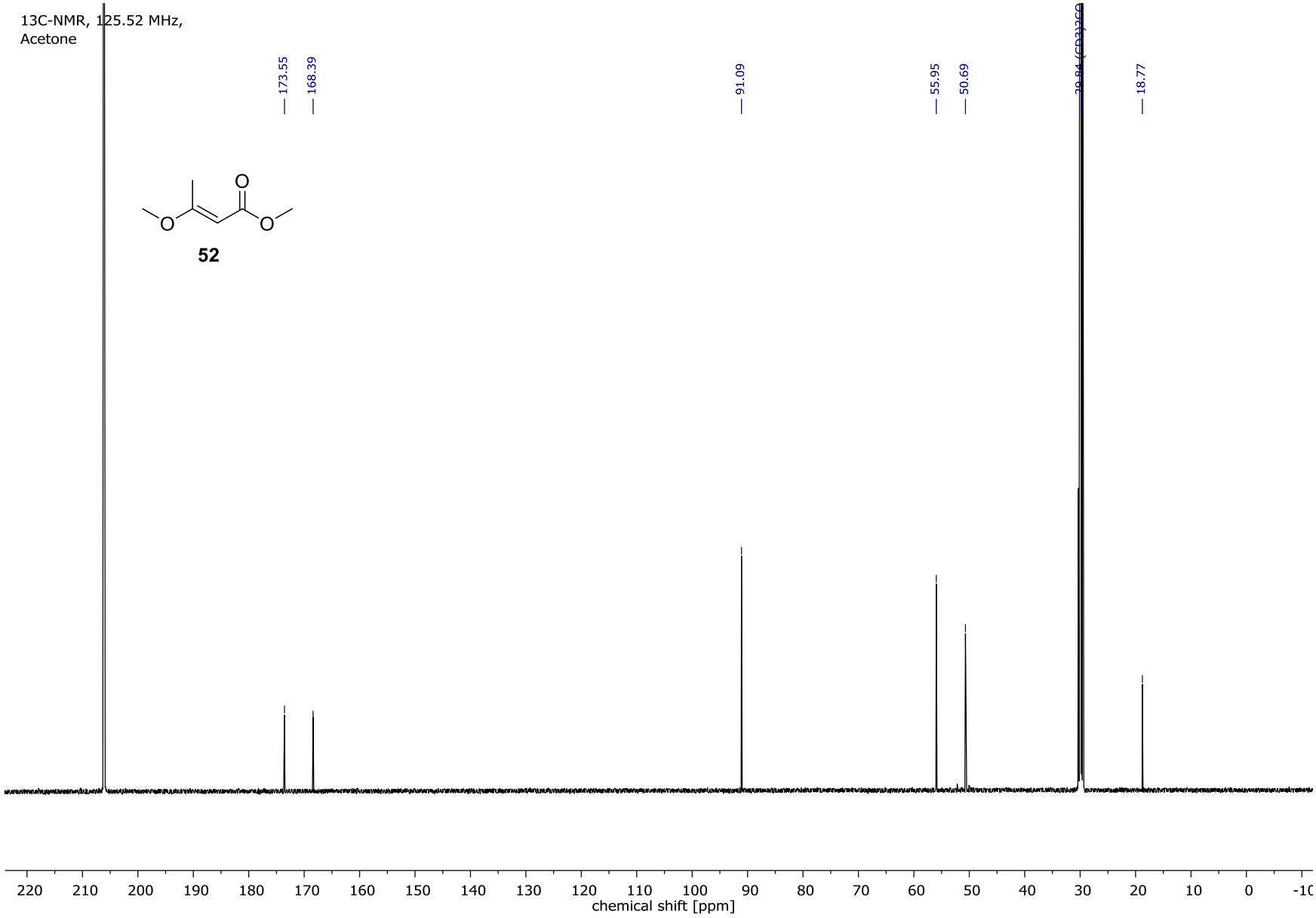
51



1H-NMR, 499.13 MHz,
Acetone

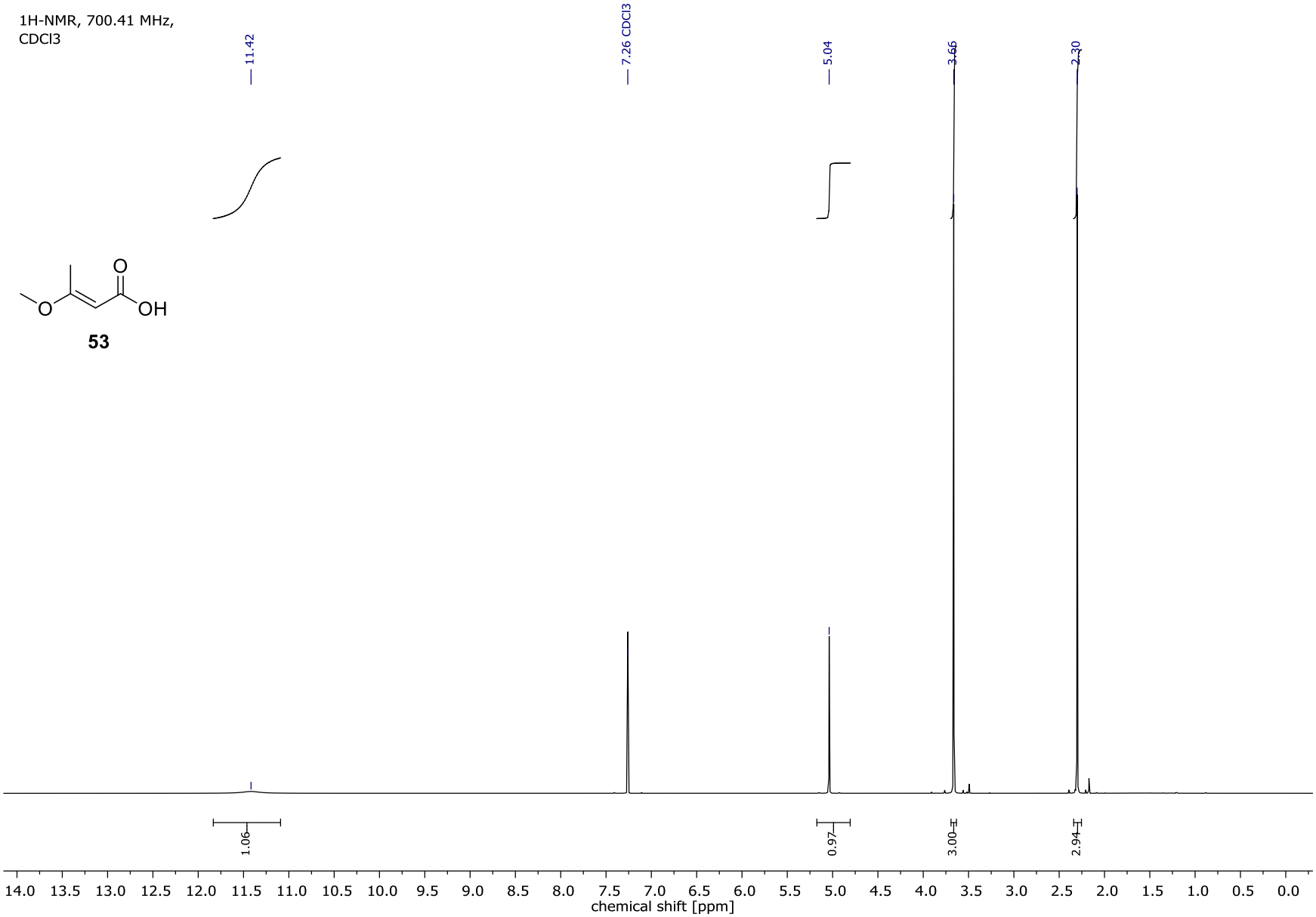
52




13C-NMR, 125.52 MHz,
Acetone
173.55
168.39
91.09
55.95
50.69
30.84 (CD3)2CO
18.77
O
O
O
52
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

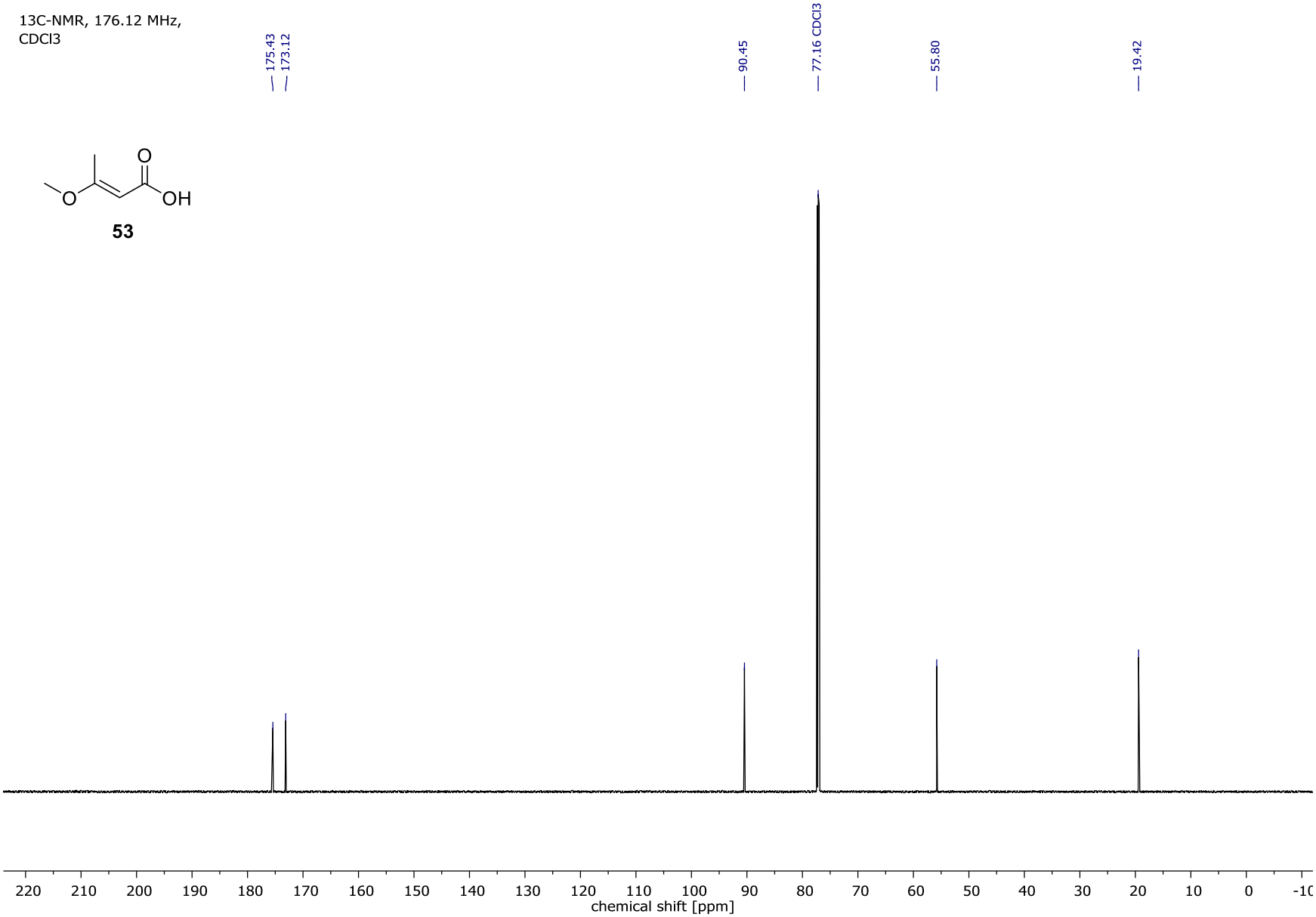
1H-NMR, 700.41 MHz,
CDCl3

53



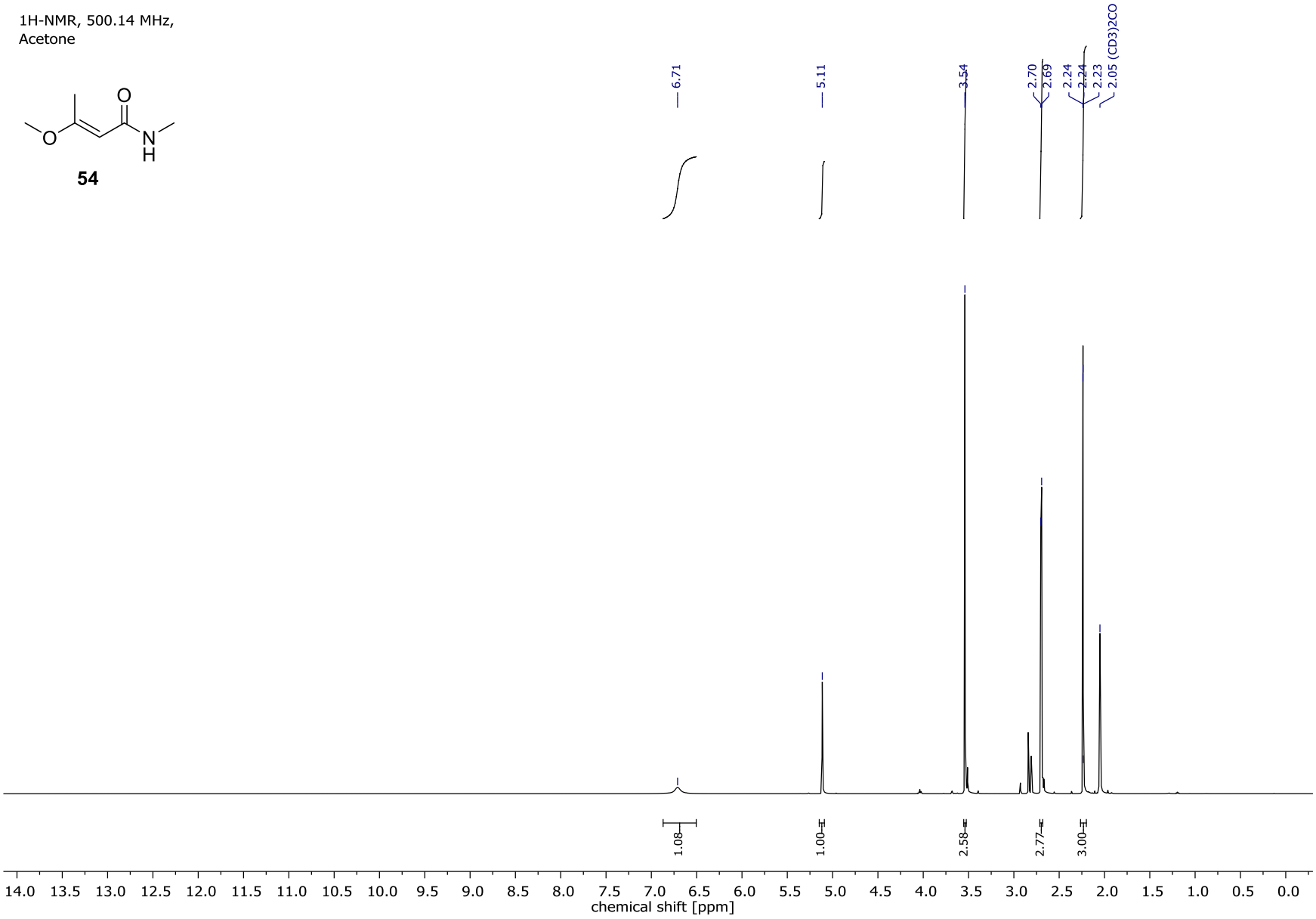
13C-NMR, 176.12 MHz,
CDCl3

53

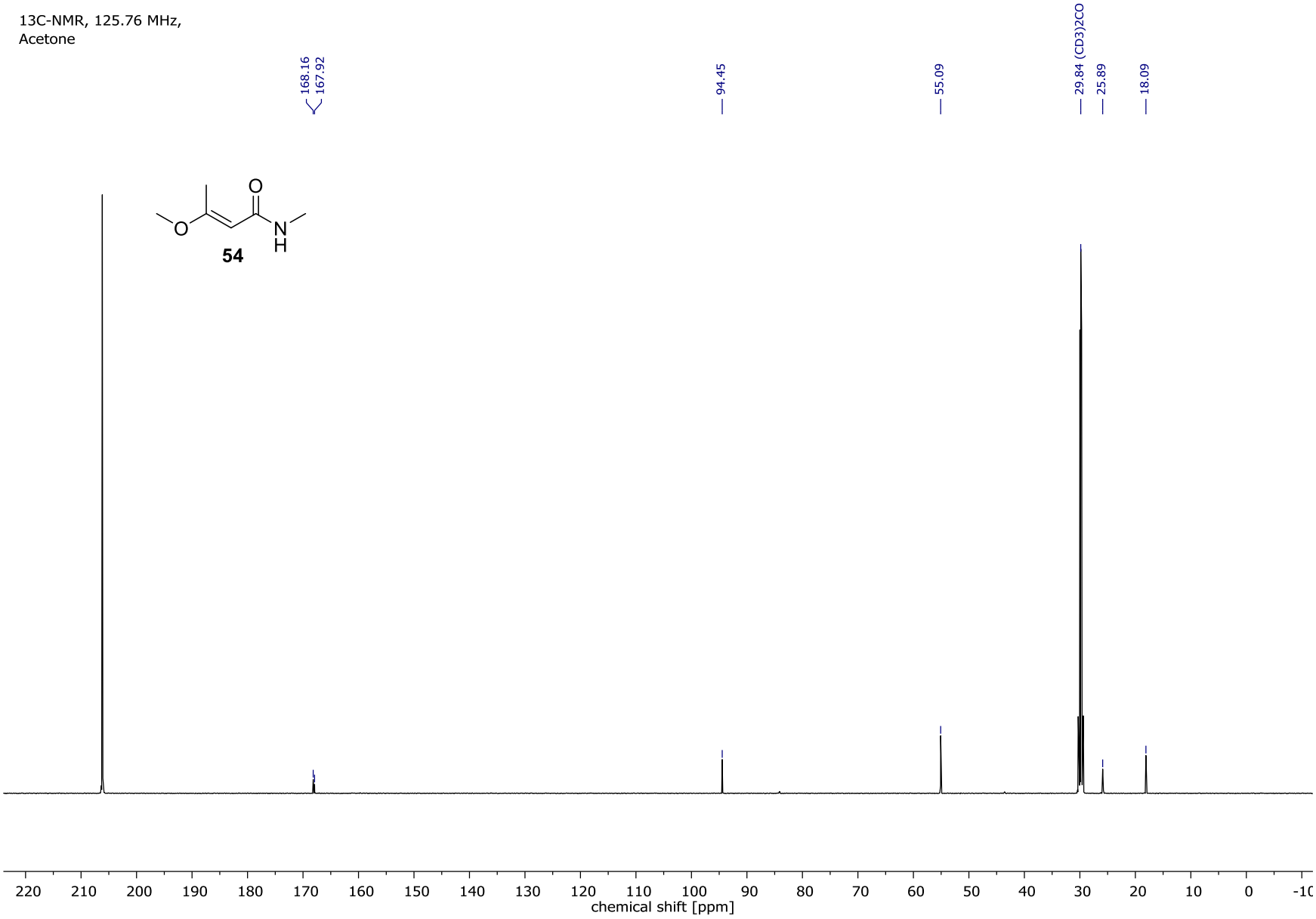


1H-NMR, 500.14 MHz,
Acetone

54

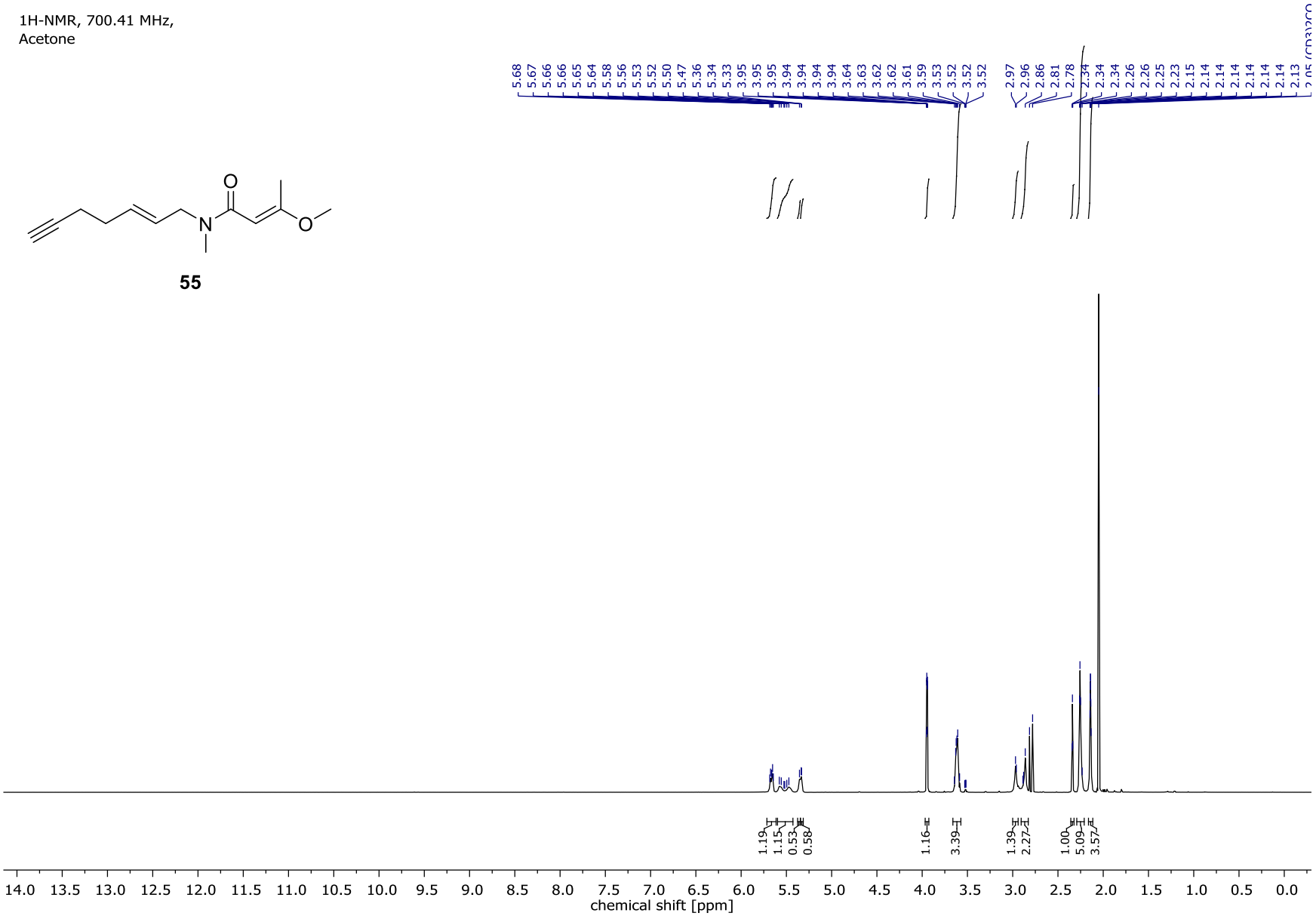


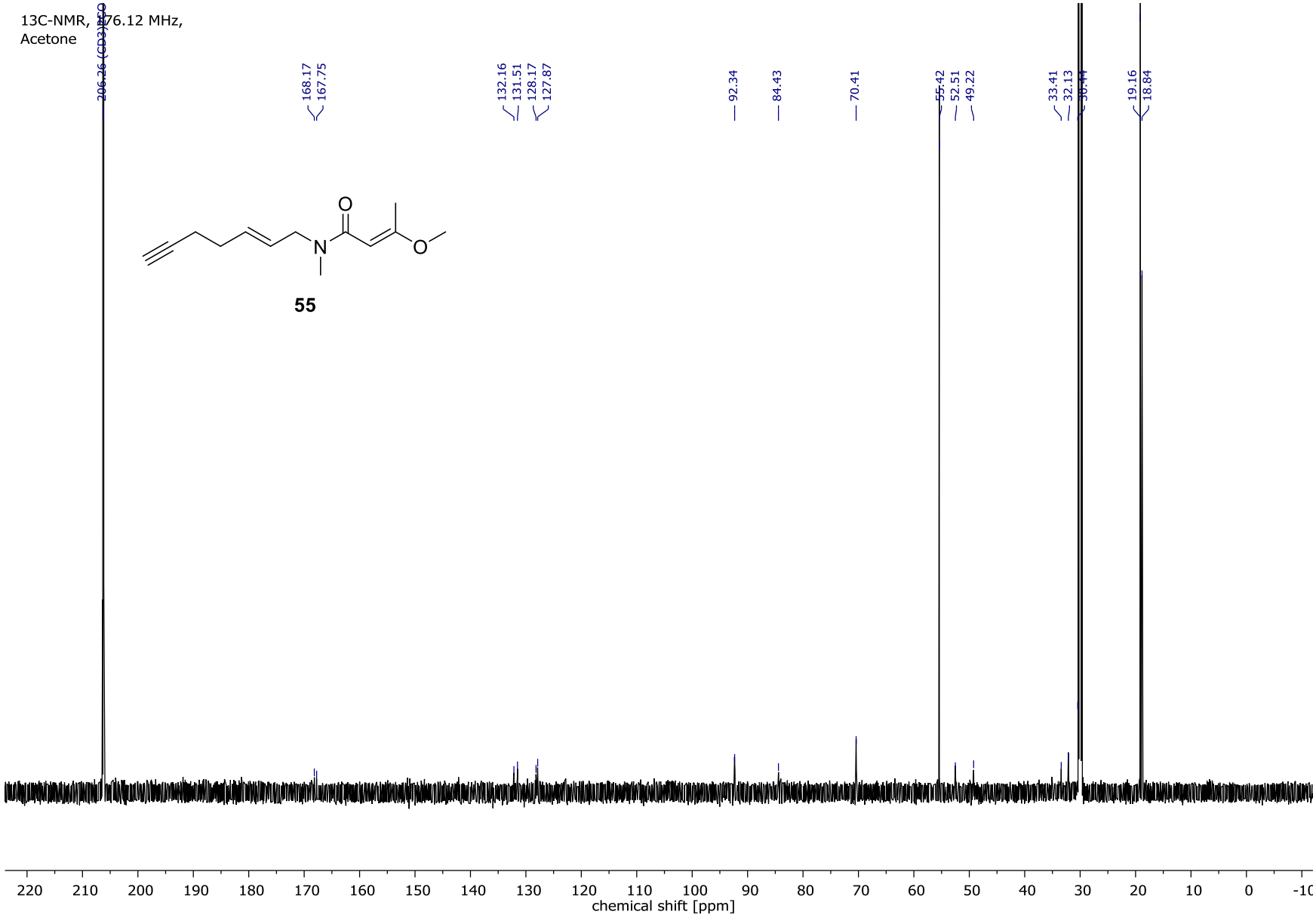
13C-NMR, 125.76 MHz,
Acetone



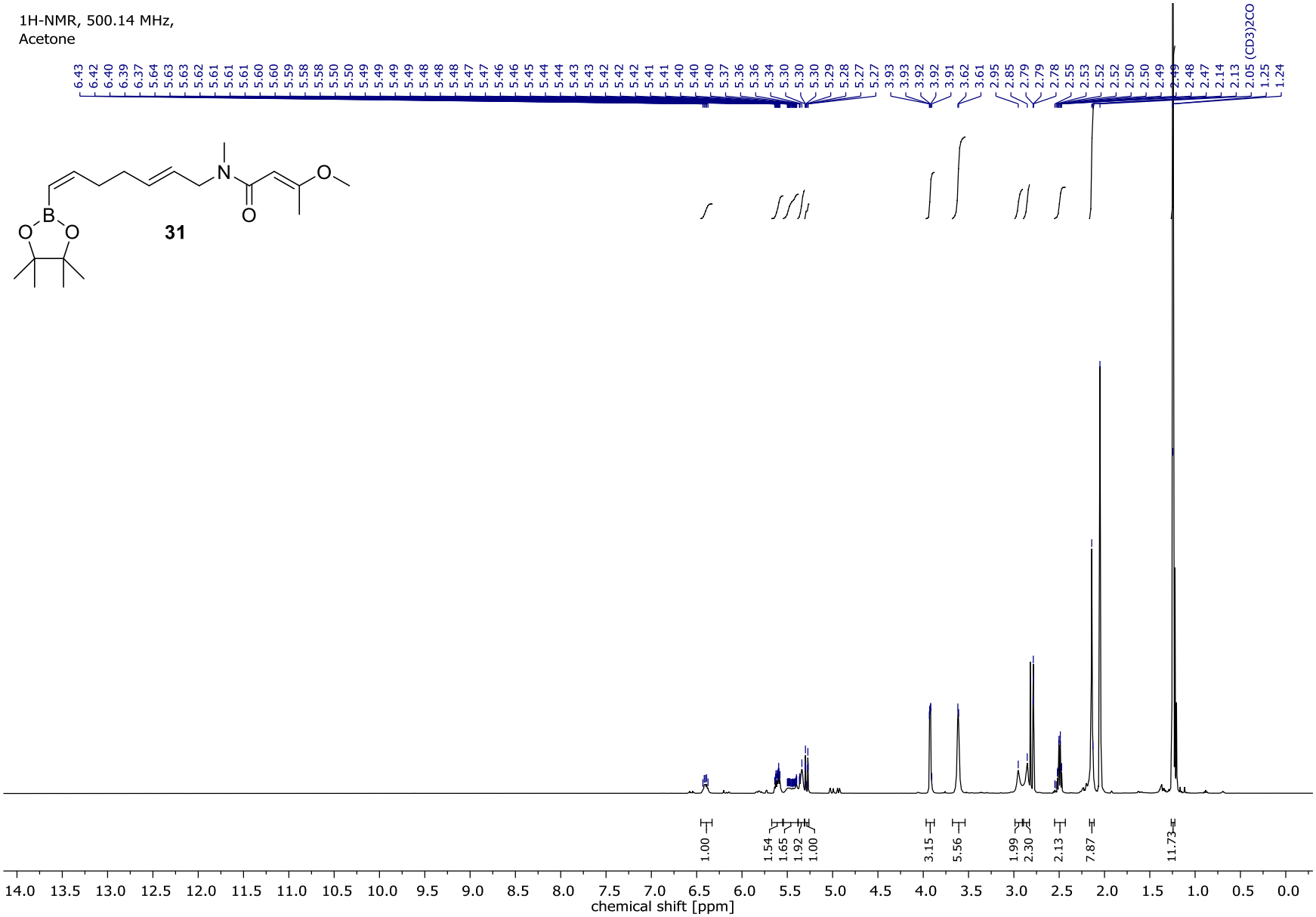
1H-NMR, 700.41 MHz,
Acetone

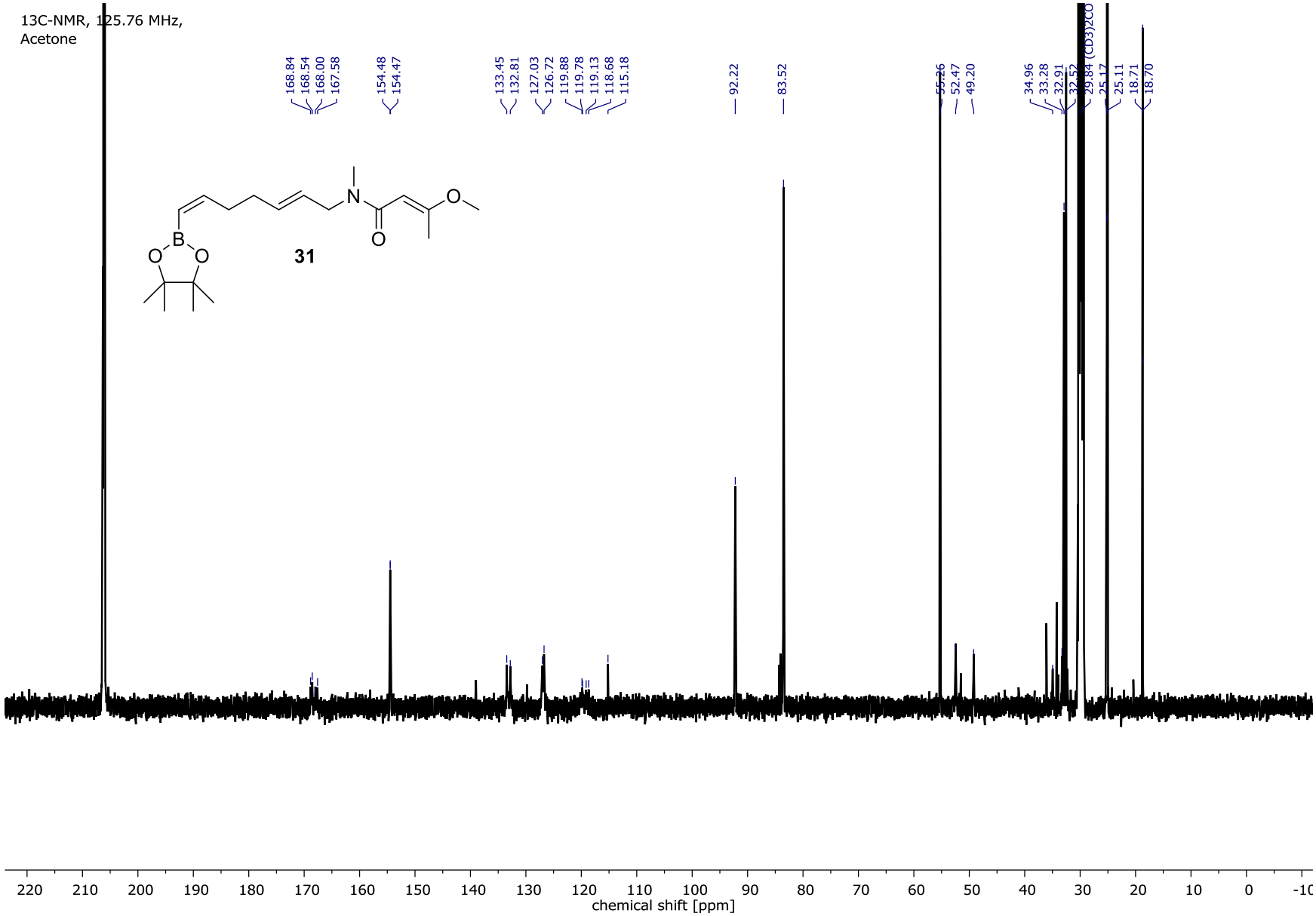
55

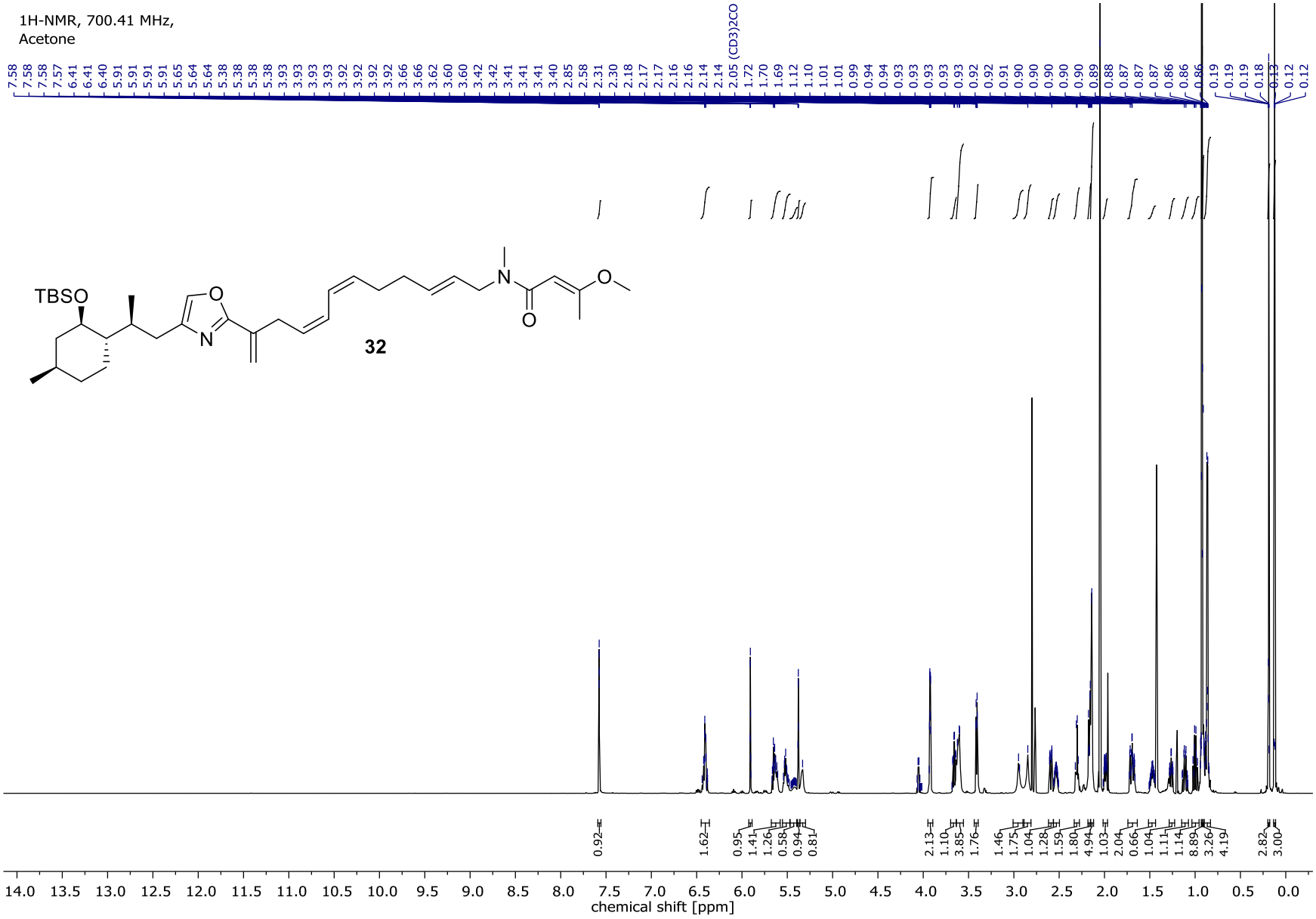



13C-NMR, 176.12 MHz,
Acetone
206.26 (CD3)2CO
168.17
167.75
132.16
131.51
128.17
127.87
92.34
84.43
70.41
55.42
52.51
49.22
33.41
32.13
30.44
19.16
18.84
O
N
O
55
chemical shift [ppm]

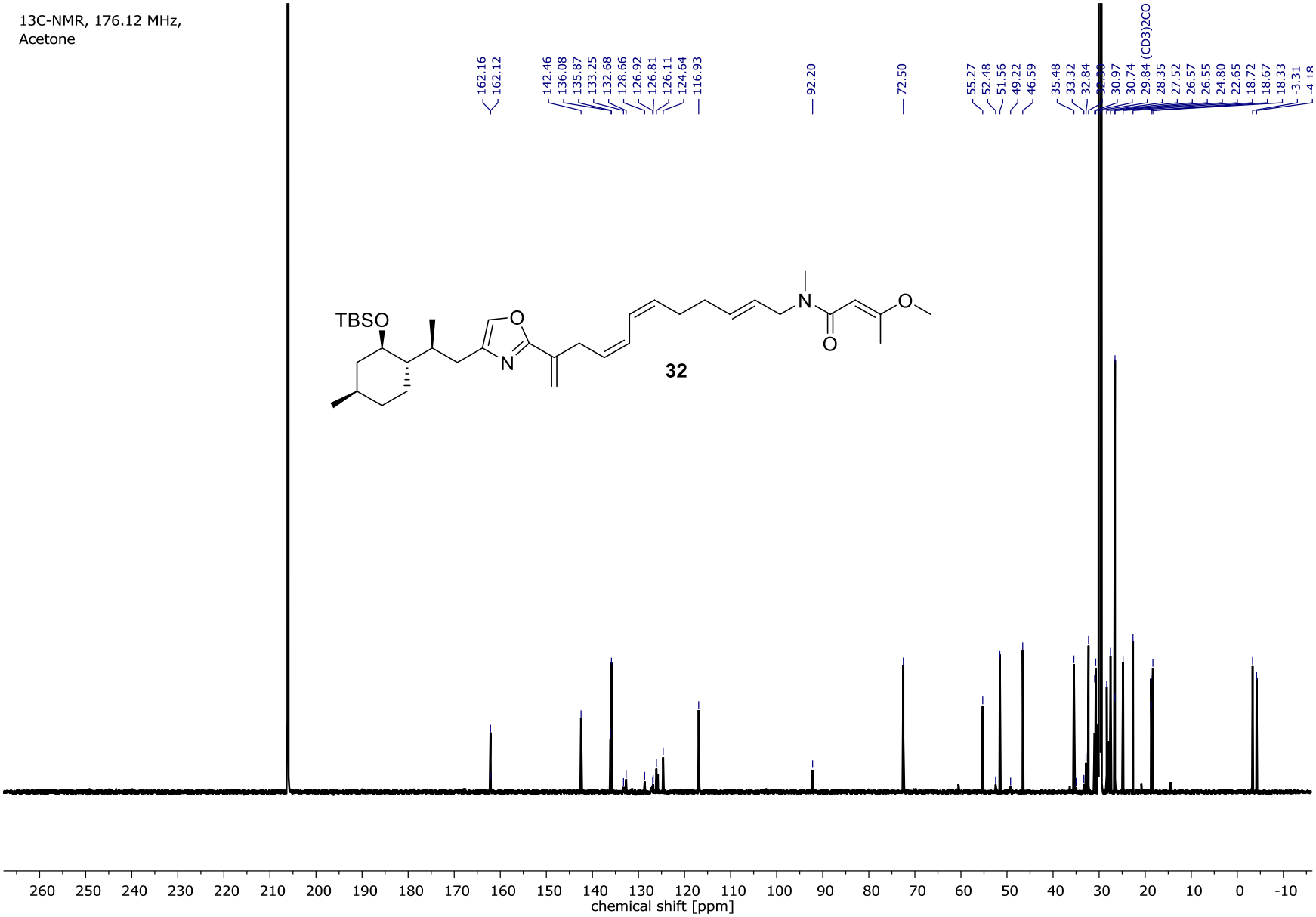
1H-NMR, 500.14 MHz,
Acetone



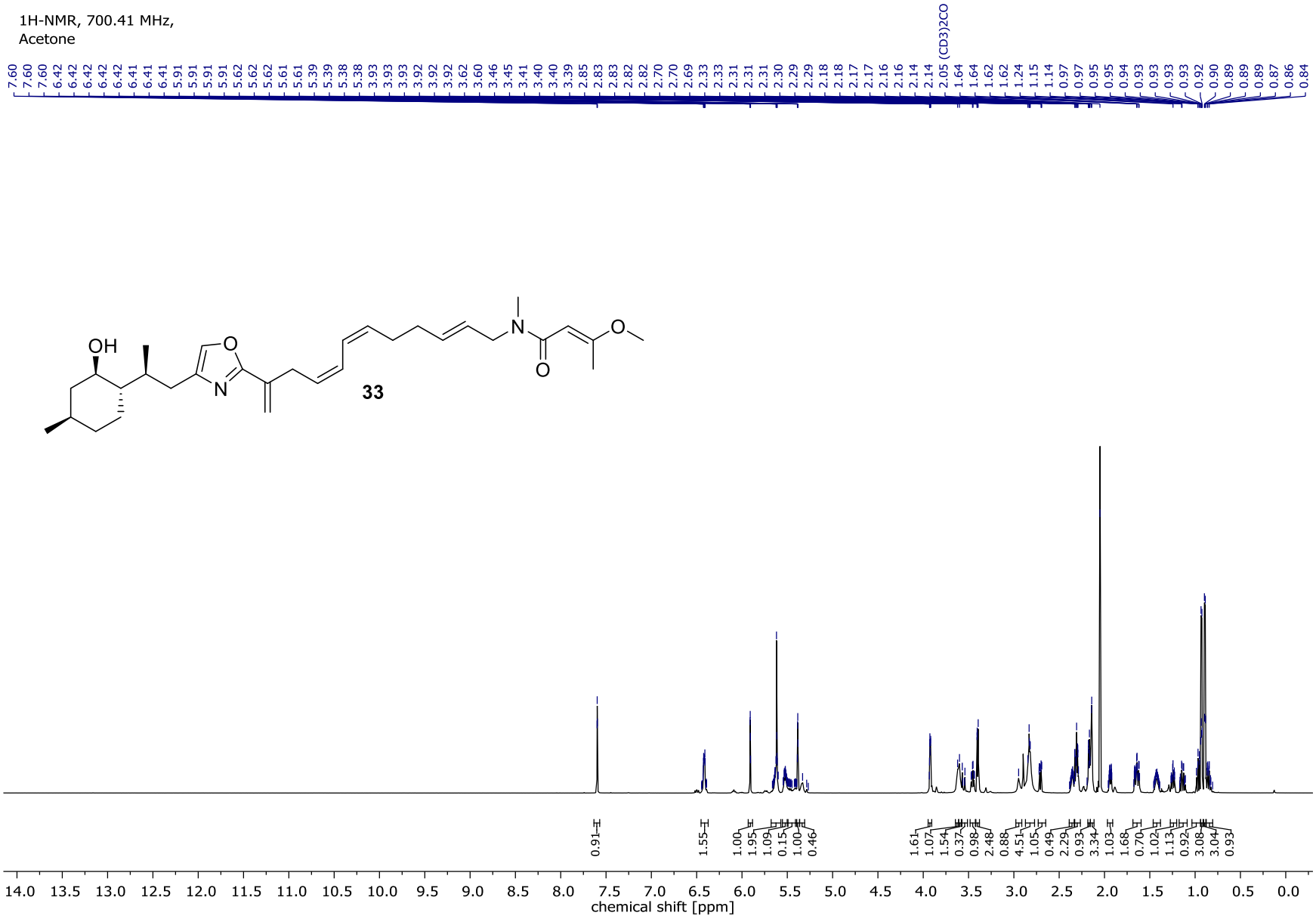

13C-NMR, 125.76 MHz,
Acetone
168.84
168.54
168.00
167.58
154.48
154.47
133.45
132.81
127.03
126.72
119.88
119.78
119.13
118.68
115.18
92.22
83.52
55.26
52.47
49.20
34.96
33.28
32.91
32.52
29.84 (CD3)2CO
25.17
25.11
18.71
18.70
31
chemical shift [ppm]


1H-NMR, 700.41 MHz,
Acetone
(CD3)2CO
TBSO
O
N
N
O
O
32
chemical shift [ppm]

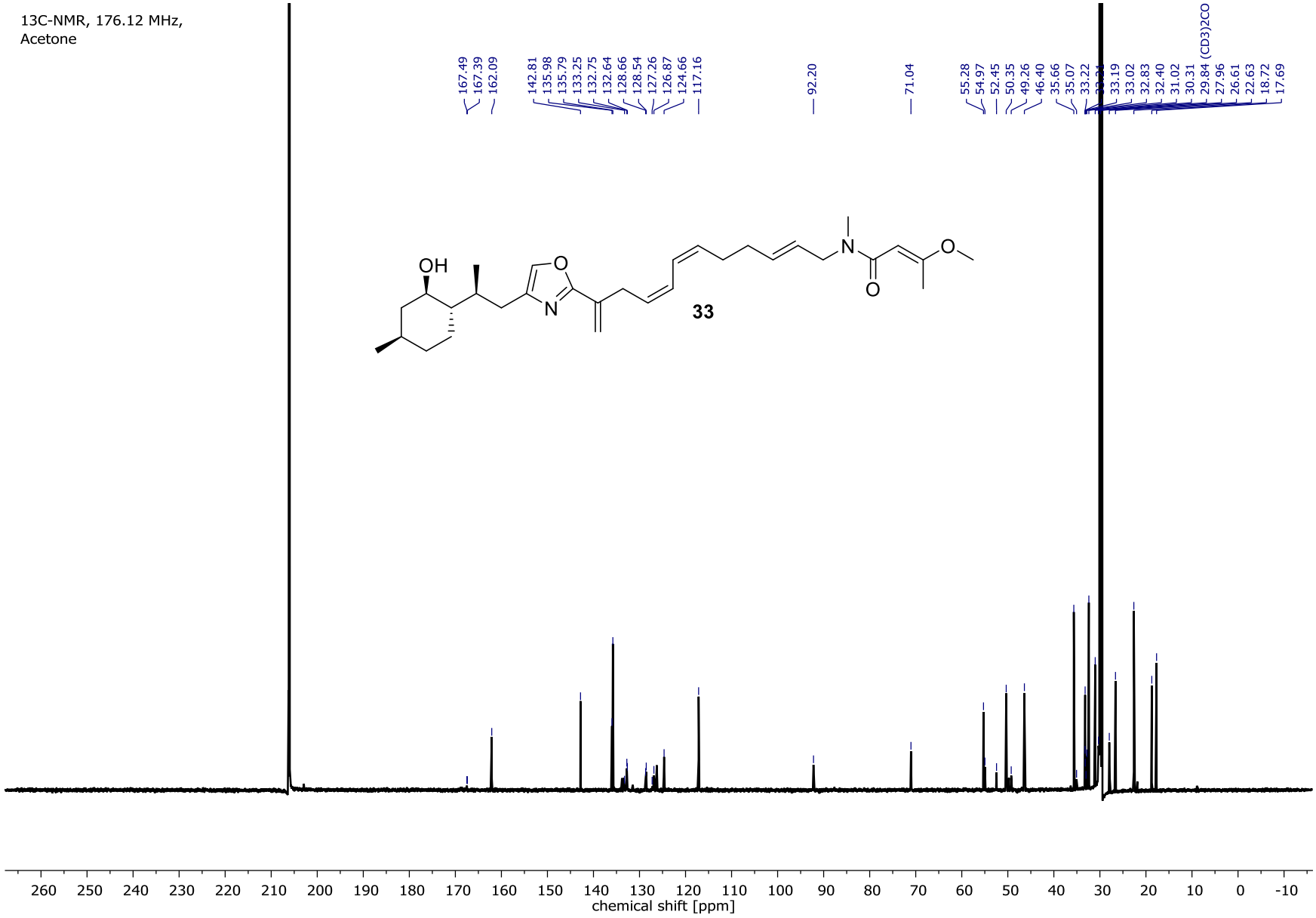
13C-NMR, 176.12 MHz,
Acetone



1H-NMR, 700.41 MHz,
Acetone

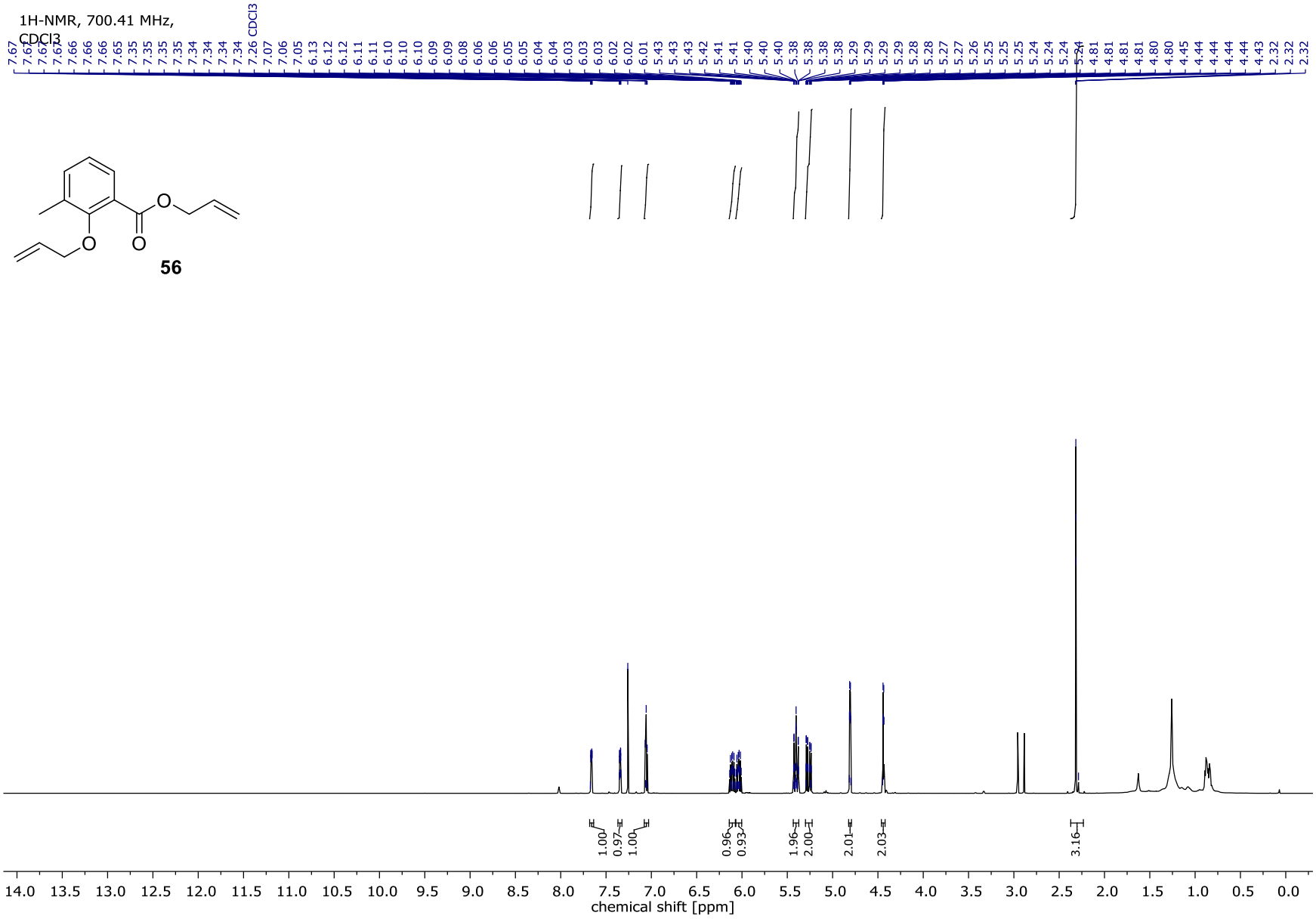


13C-NMR, 176.12 MHz,
Acetone



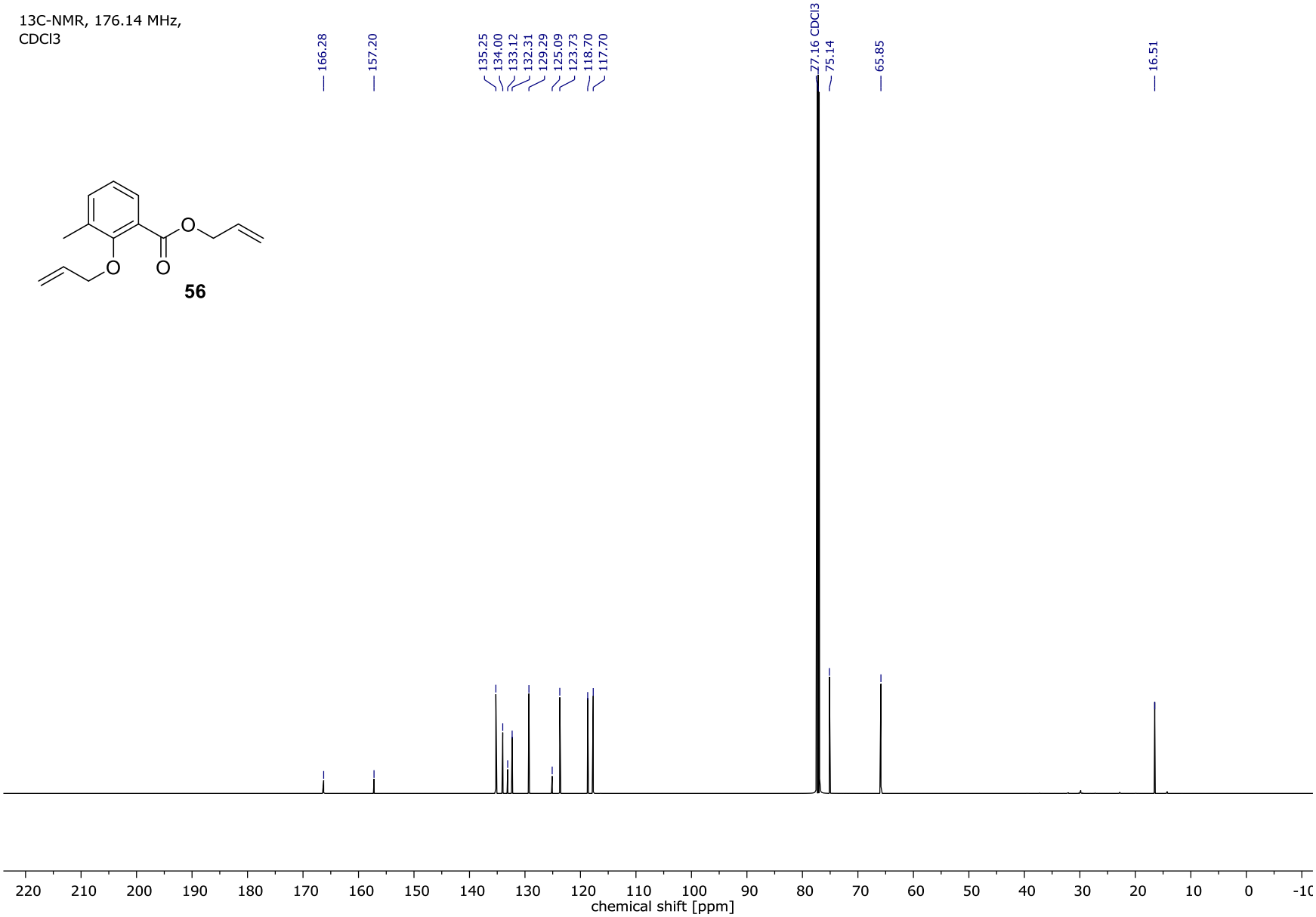
1H-NMR, 700.41 MHz,
CDCl3

56



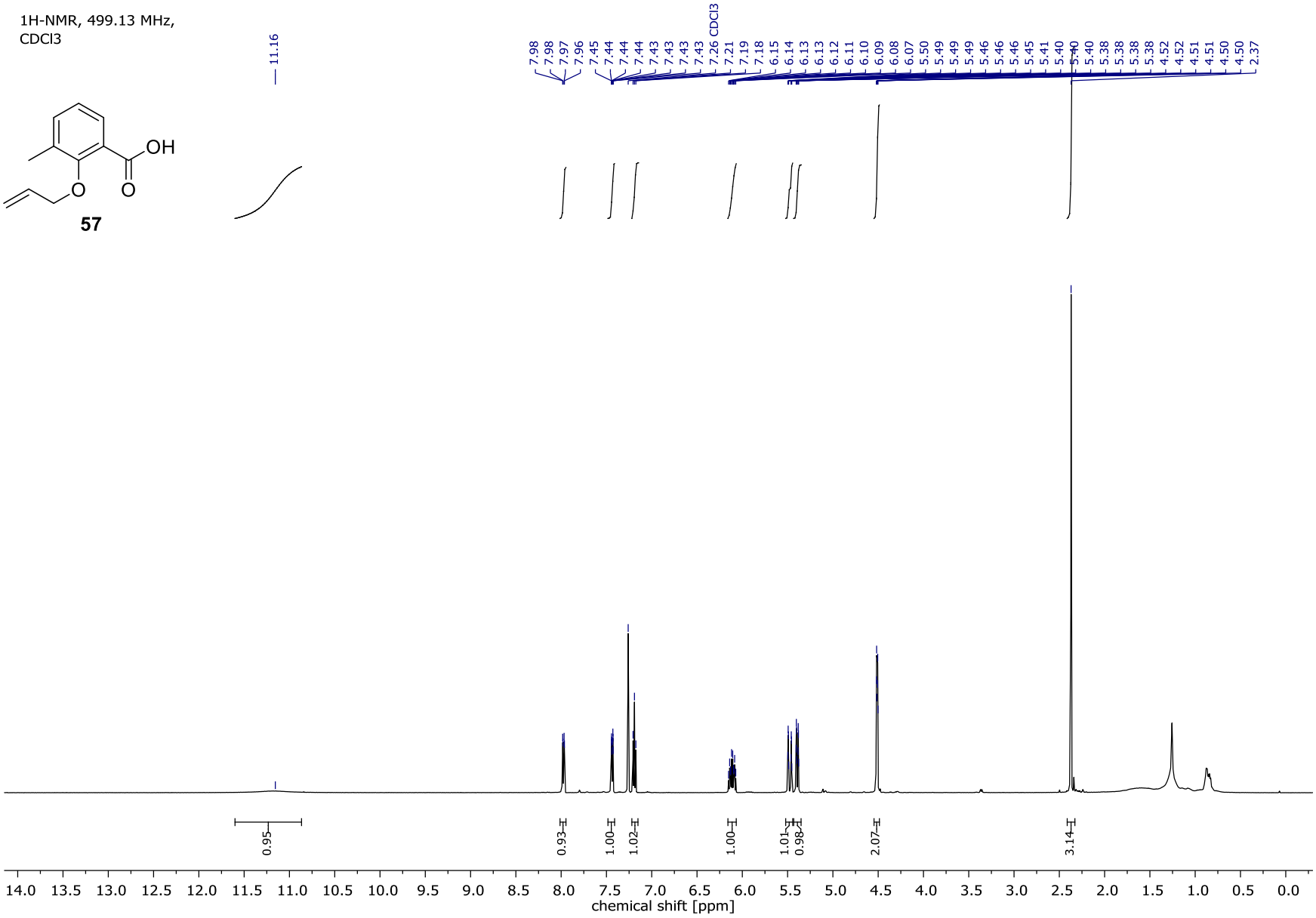
13C-NMR, 176.14 MHz,
CDCl3

56



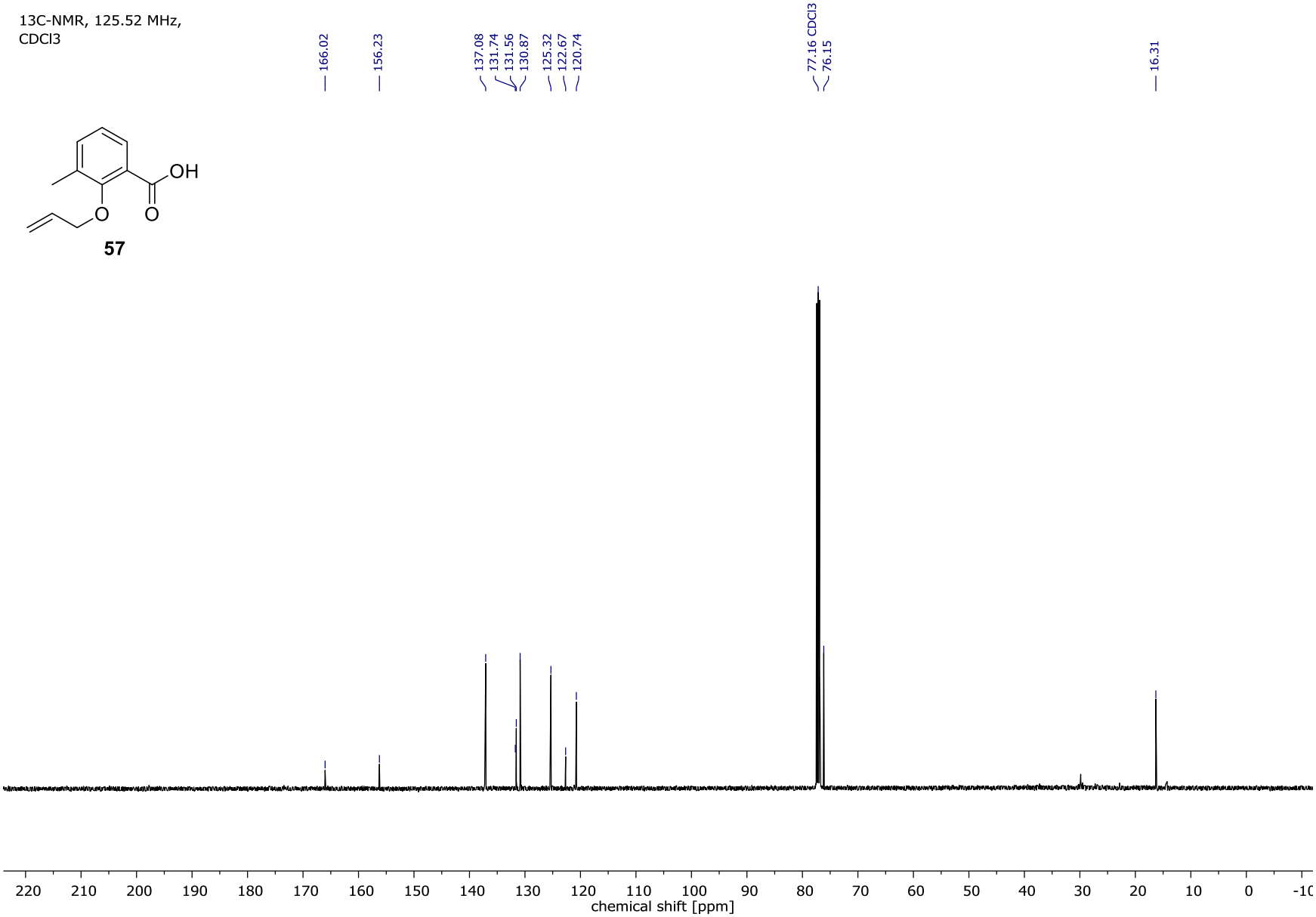
1H-NMR, 499.13 MHz,
CDCl3

57



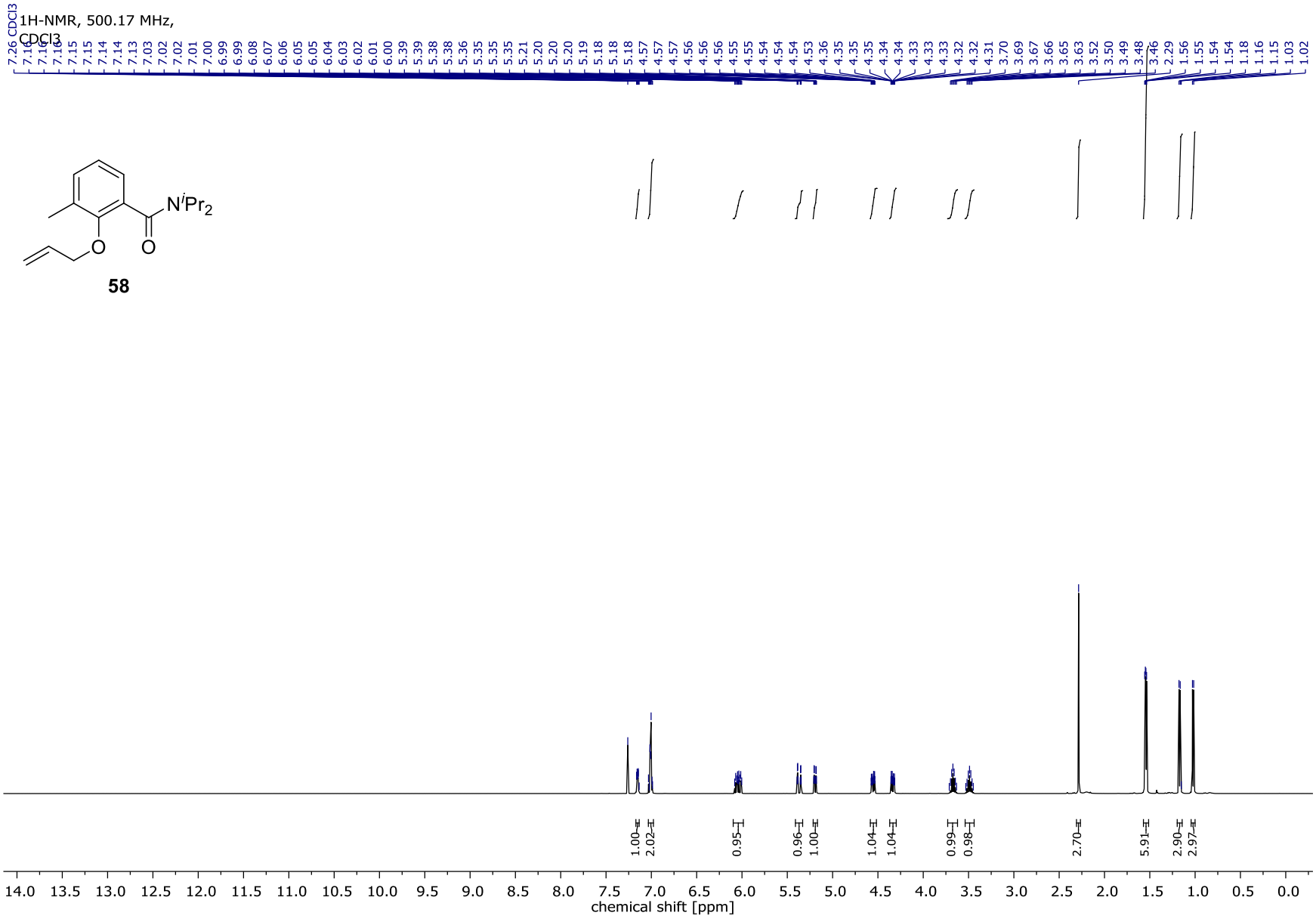
13C-NMR, 125.52 MHz,
CDCl3

57



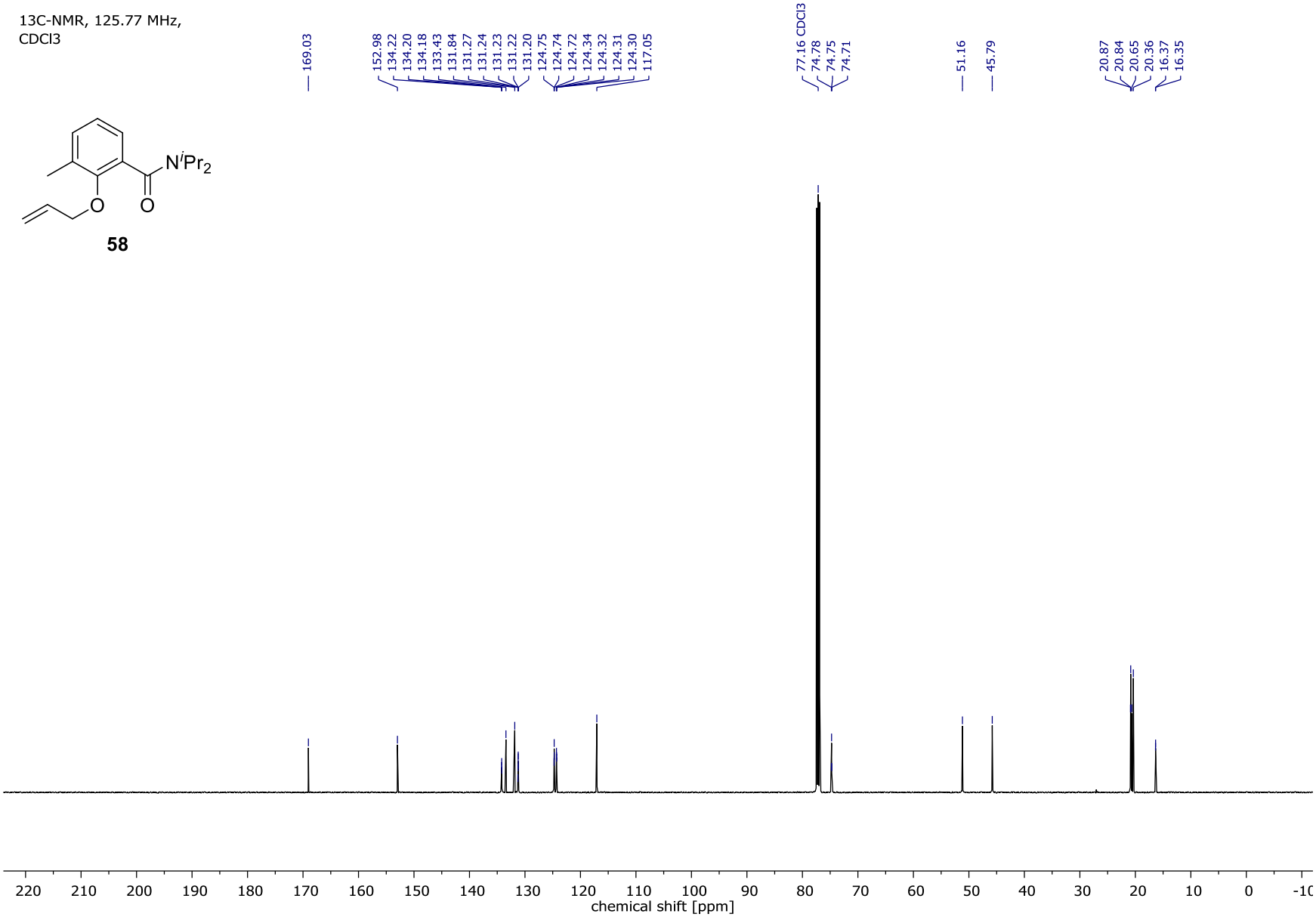
1H-NMR, 500.17 MHz,
CDCl3

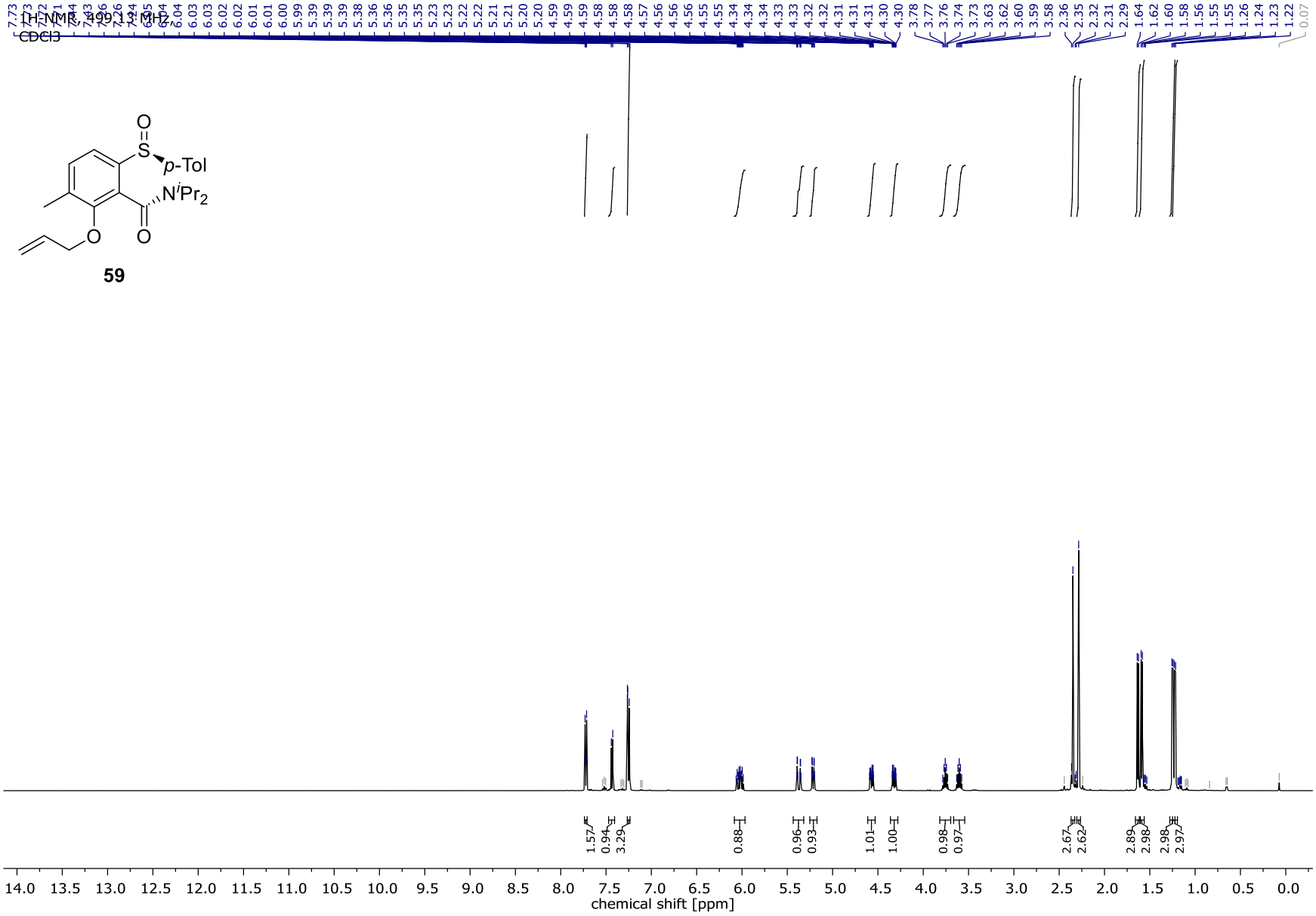
58



13C-NMR, 125.77 MHz,
CDCl3

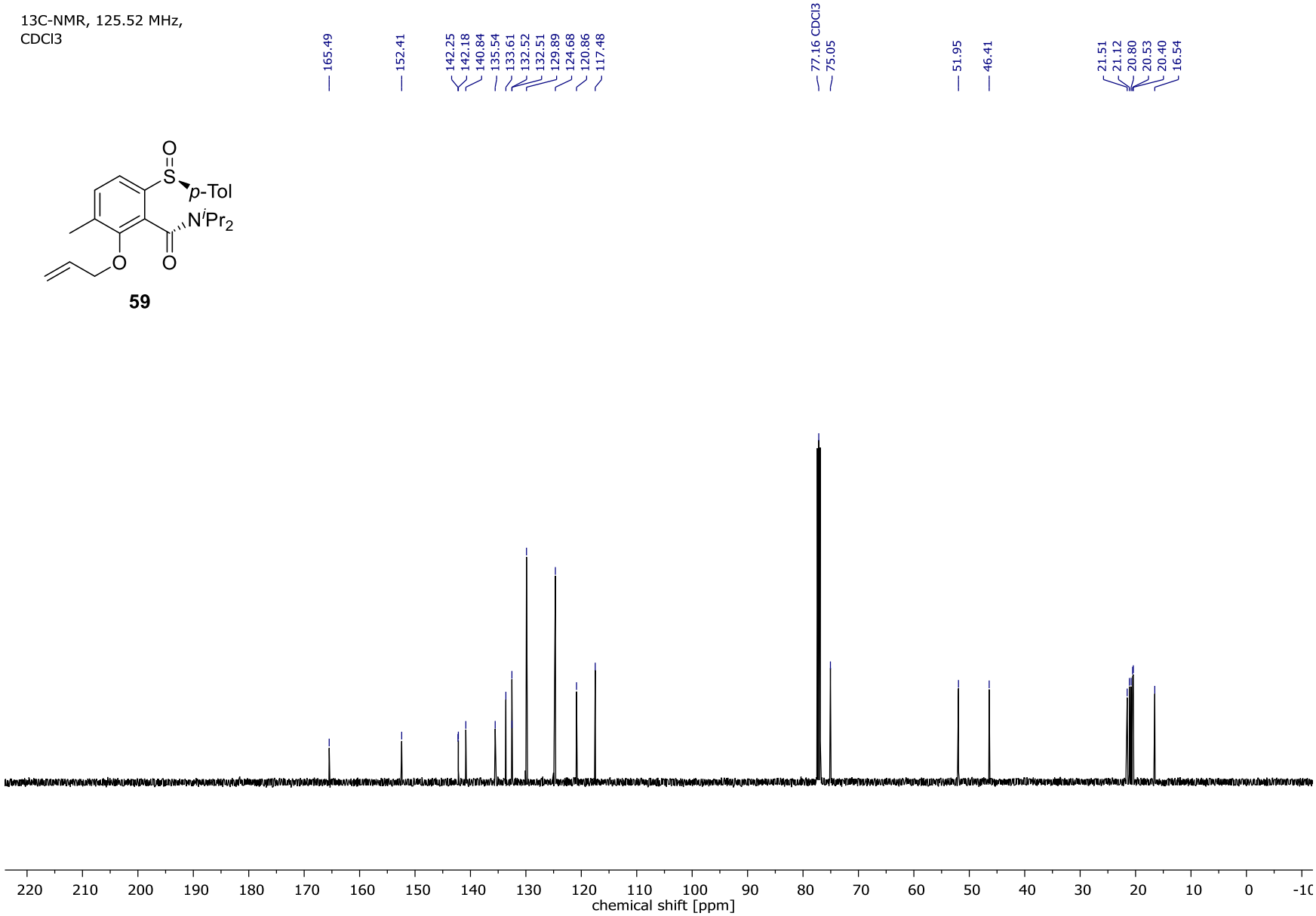
58




1H-NMR, 499.13 MHz
CDCl3
p-Tol
N^{i}Pr$_2$
59
chemical shift [ppm]

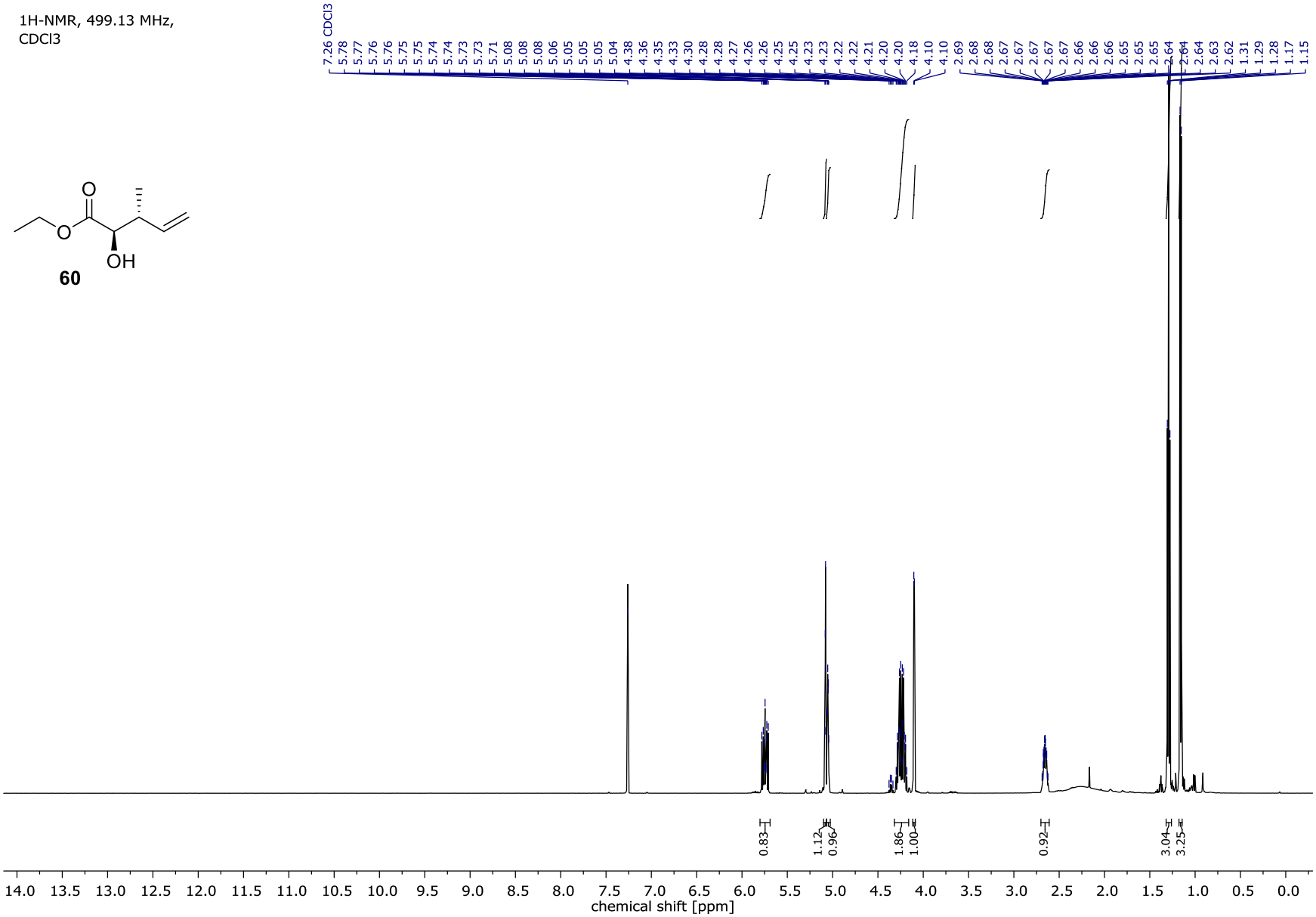
13C-NMR, 125.52 MHz,
CDCl3

59



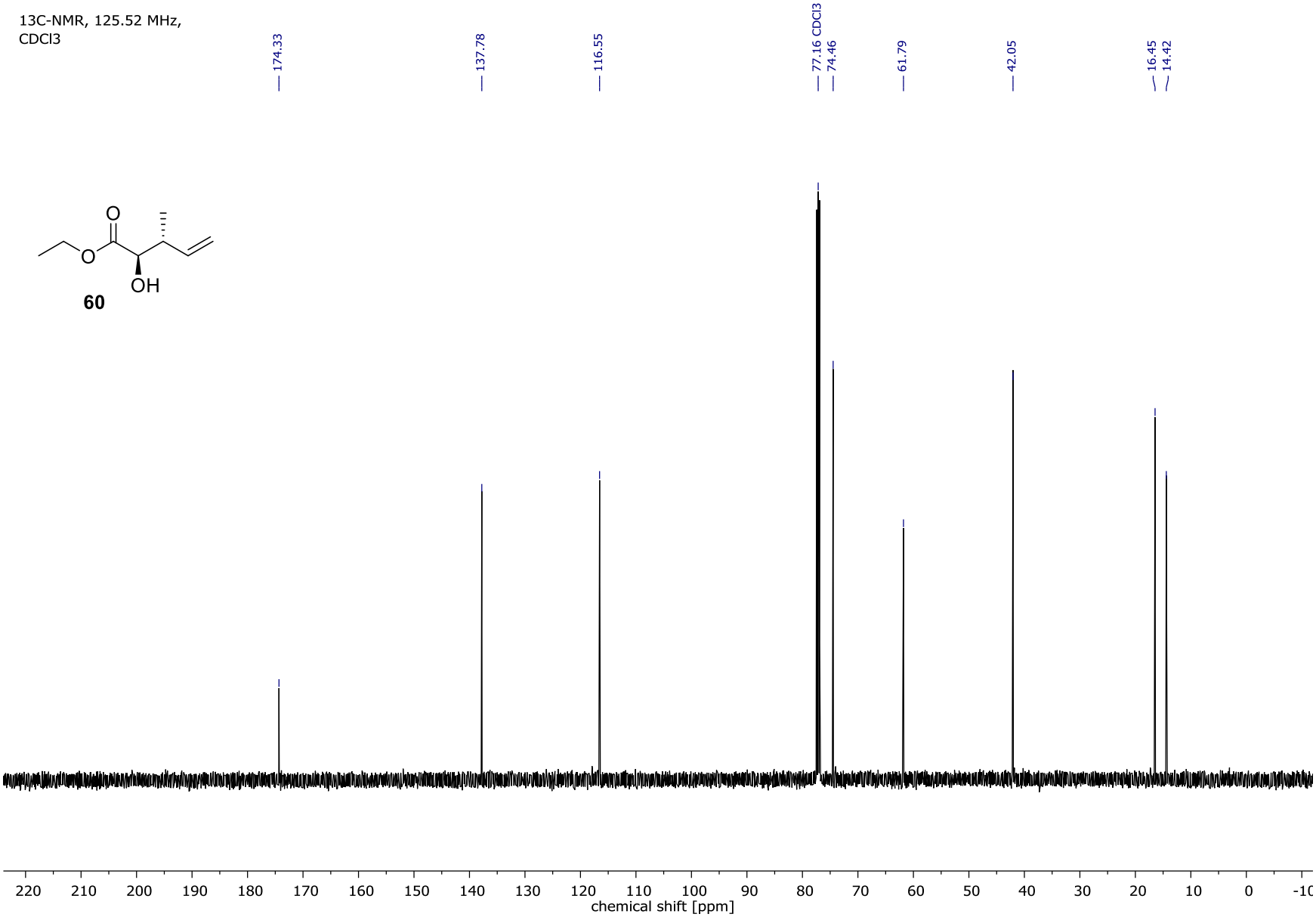
1H-NMR, 499.13 MHz,
CDCl3

60



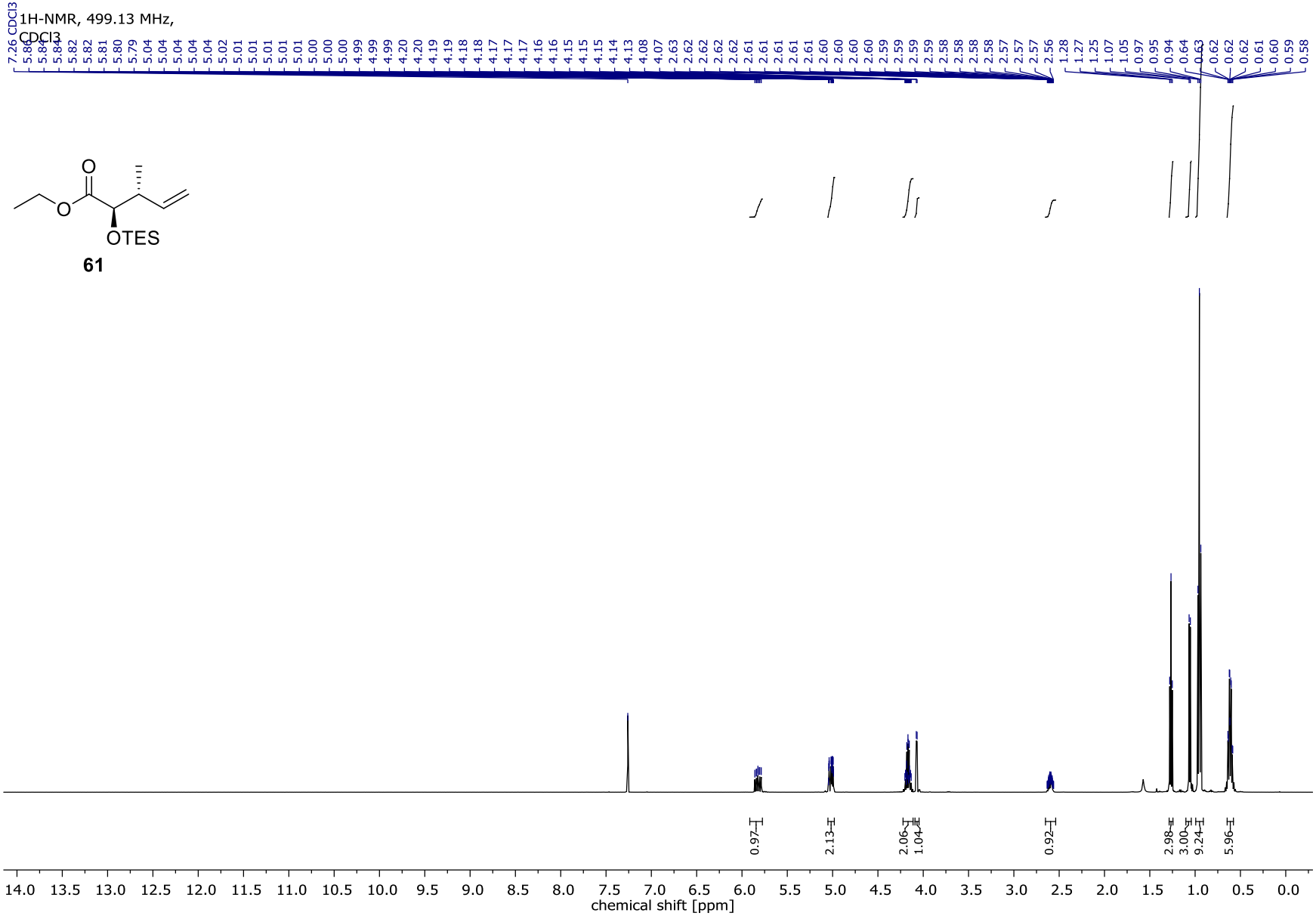
13C-NMR, 125.52 MHz,
CDCl3

60



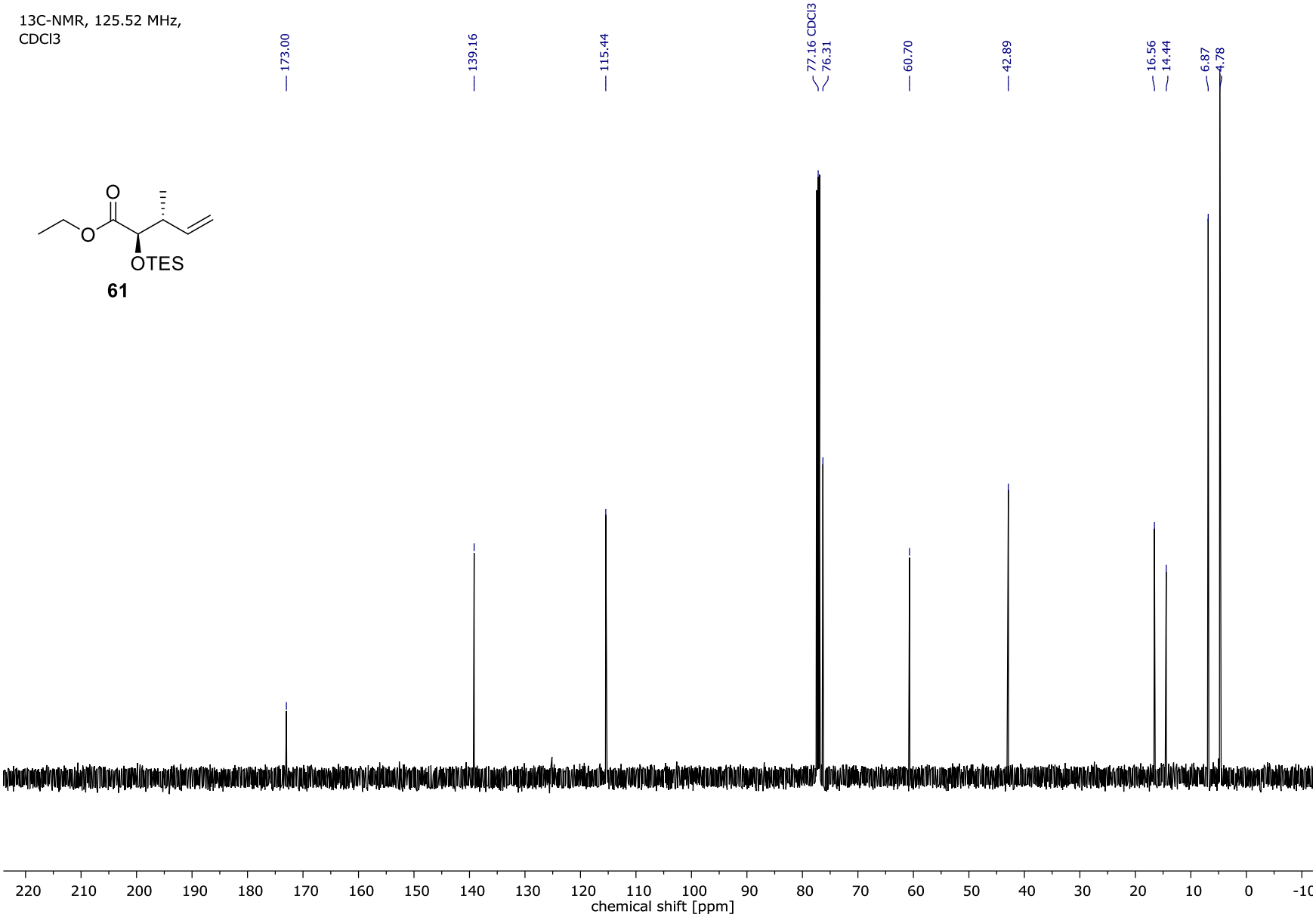
1H-NMR, 499.13 MHz,
CDCl3

61



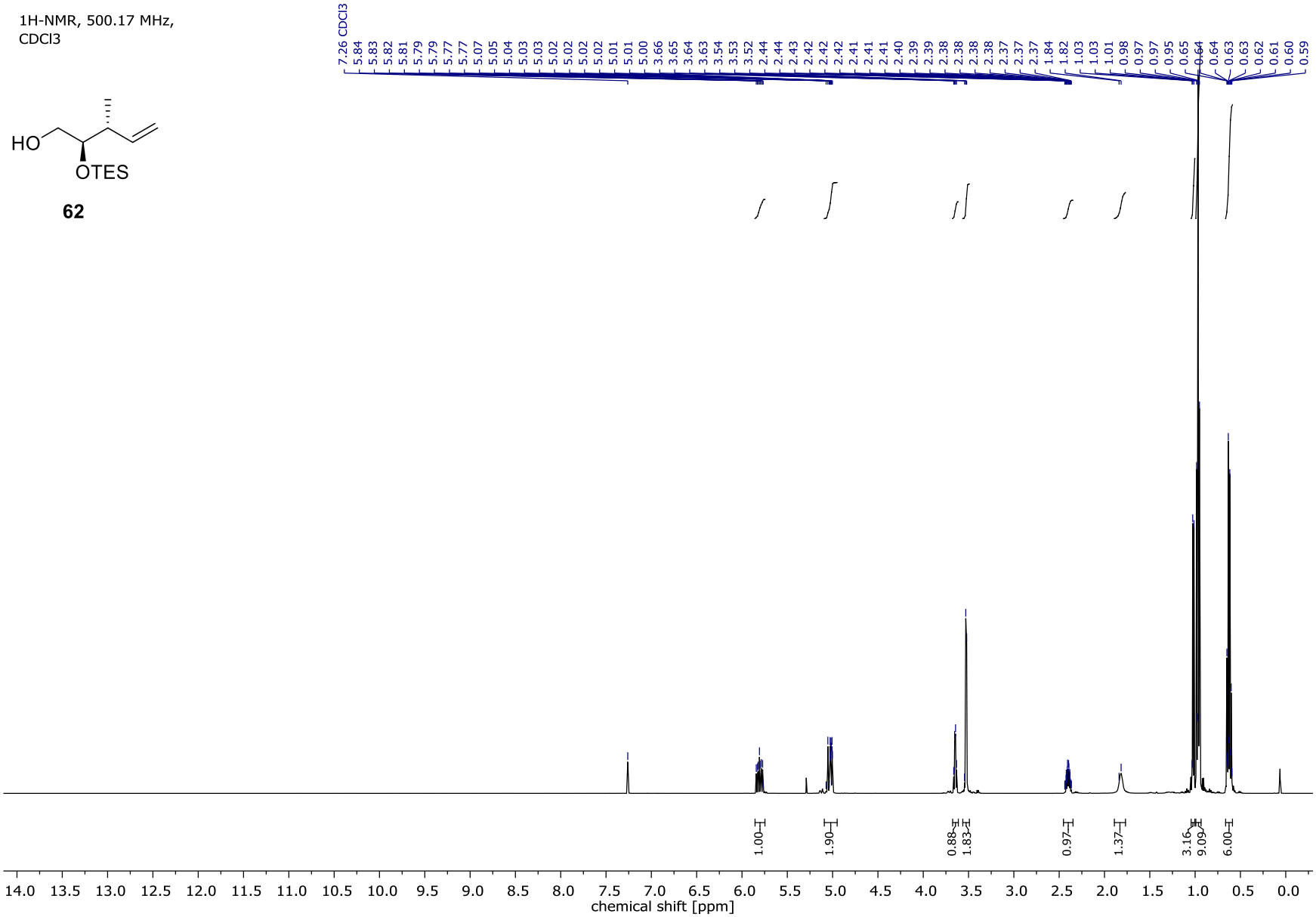
13C-NMR, 125.52 MHz,
CDCl3

61



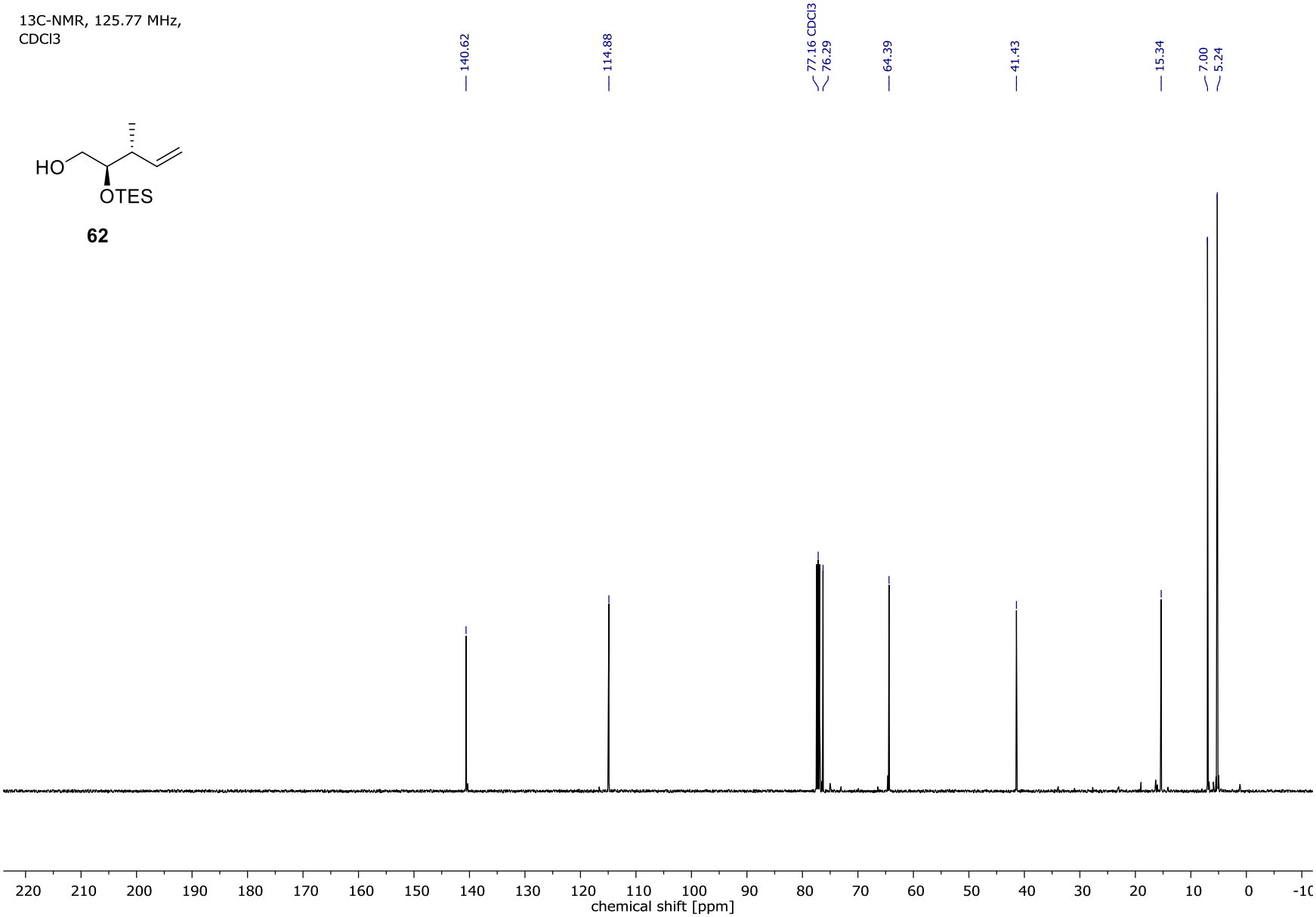
1H-NMR, 500.17 MHz,
CDCl3

62

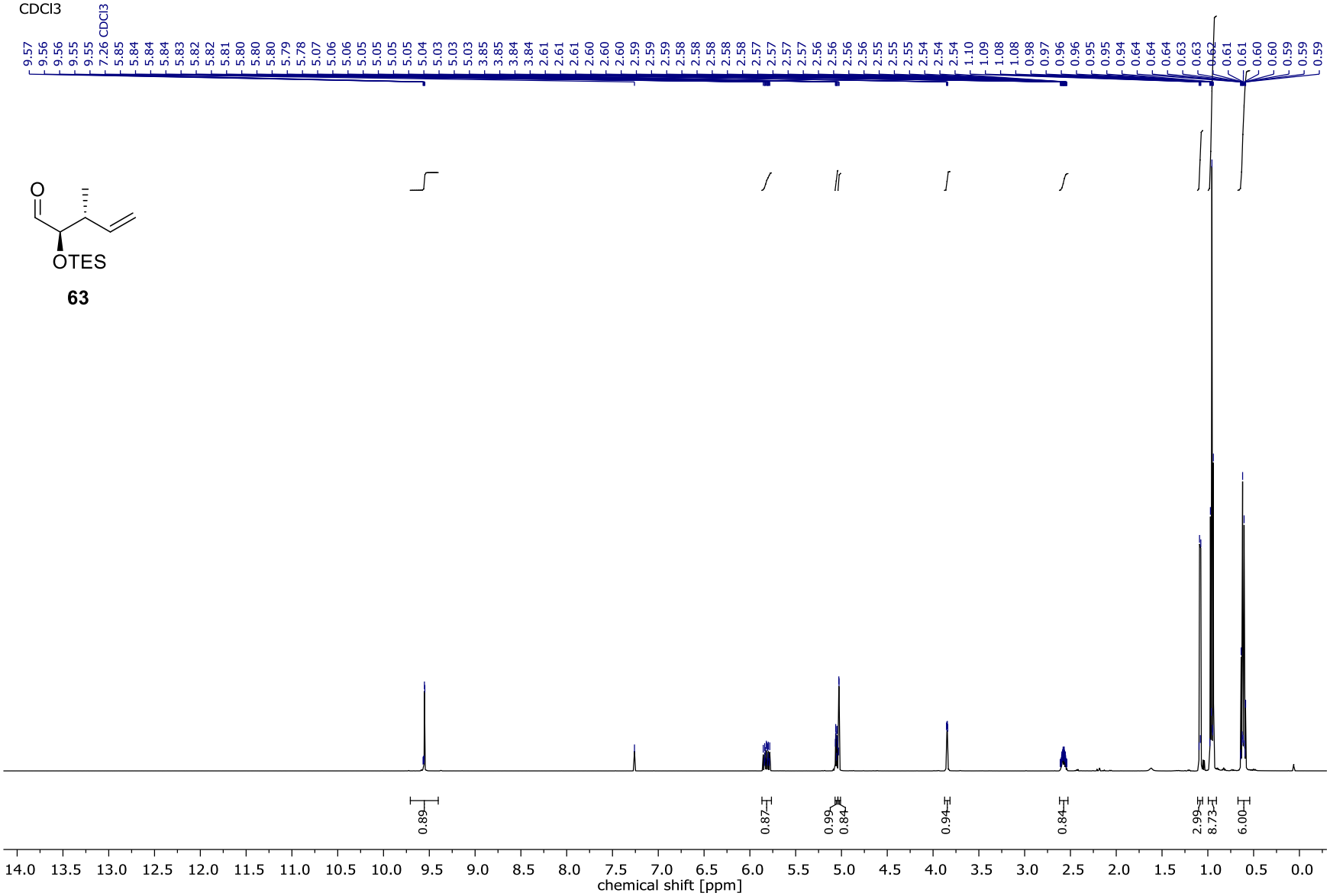


13C-NMR, 125.77 MHz,
CDCl3

62



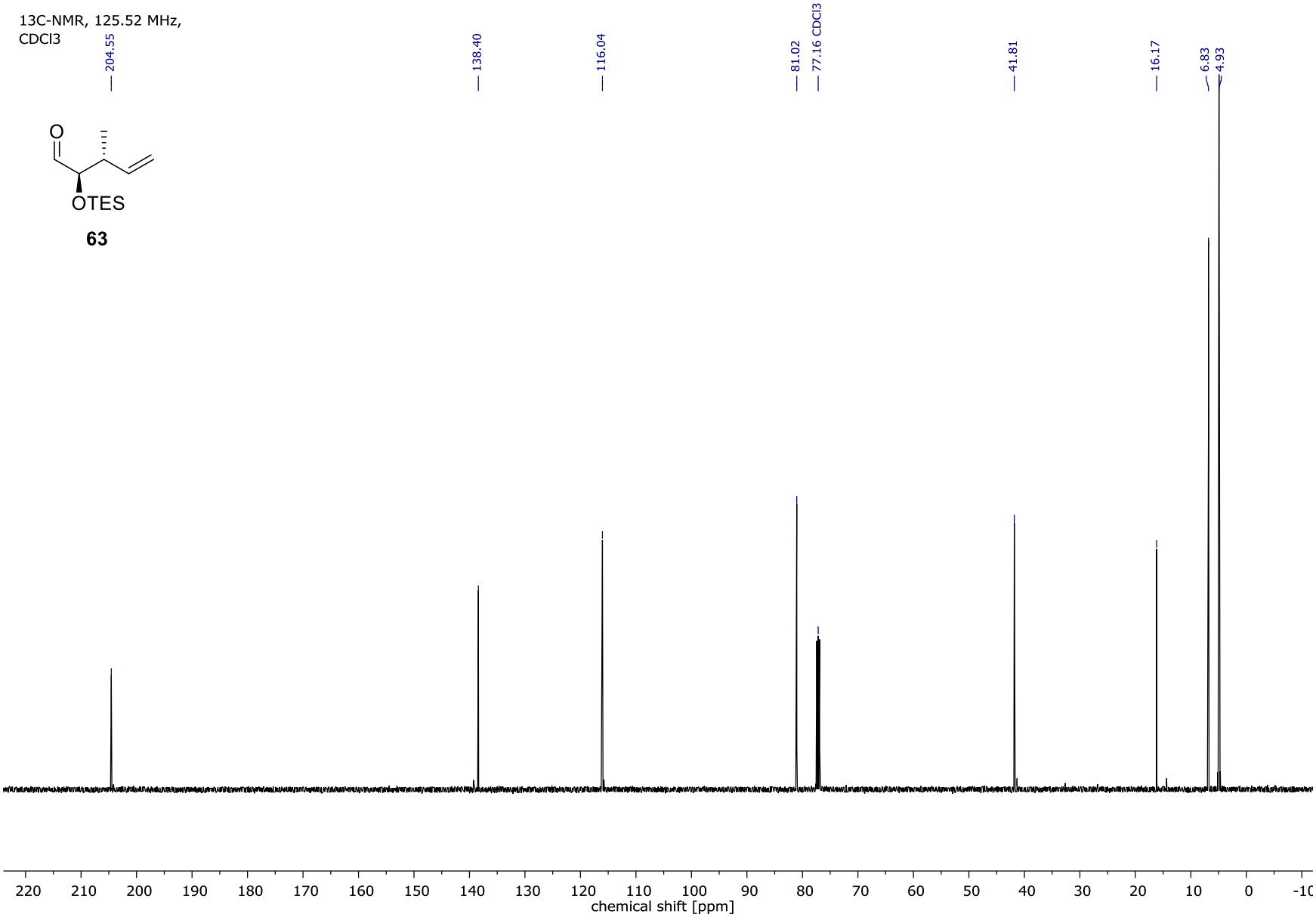
1H-NMR, 499.13 MHz,
CDCl3



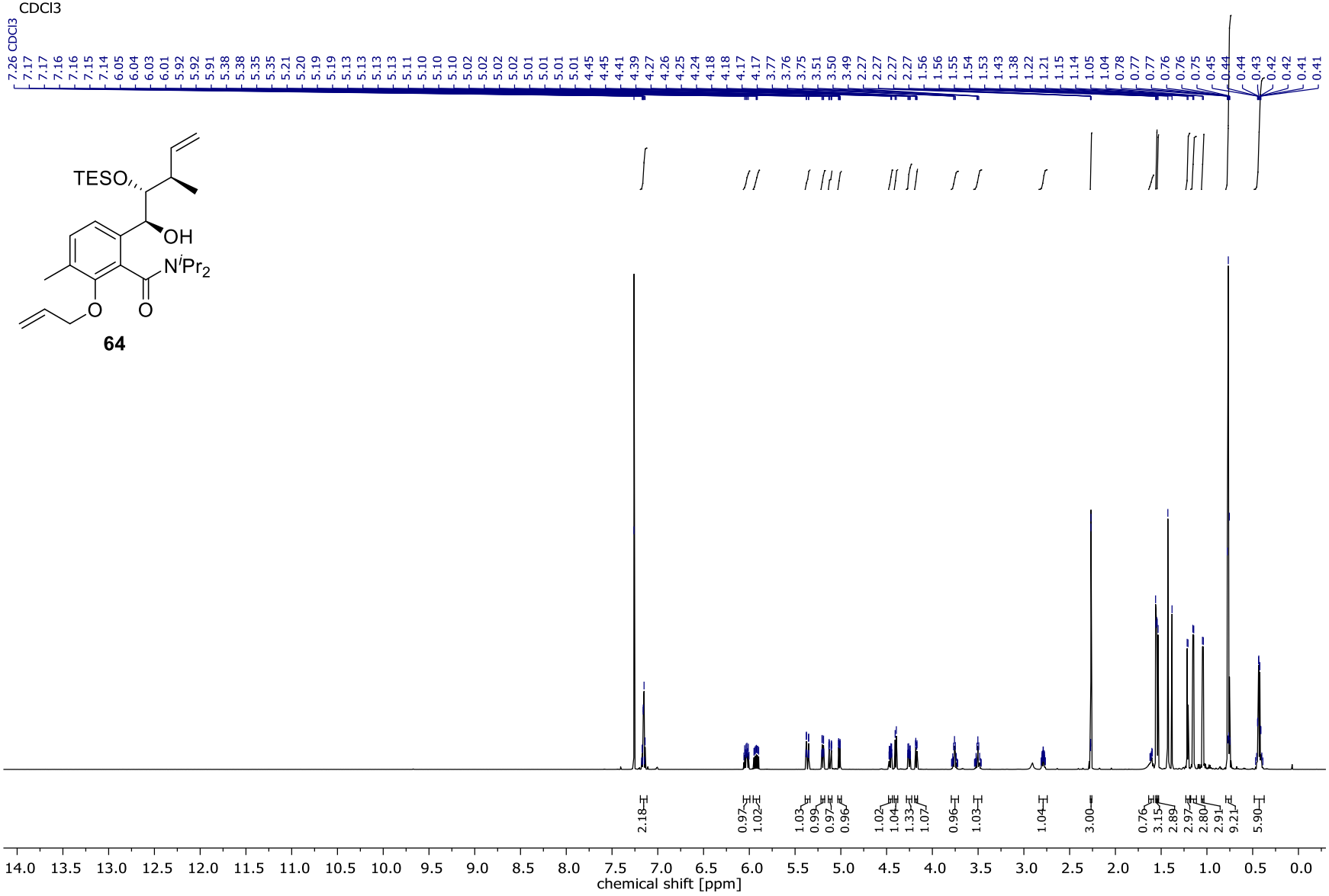
63

13C-NMR, 125.52 MHz,
CDCl3

63

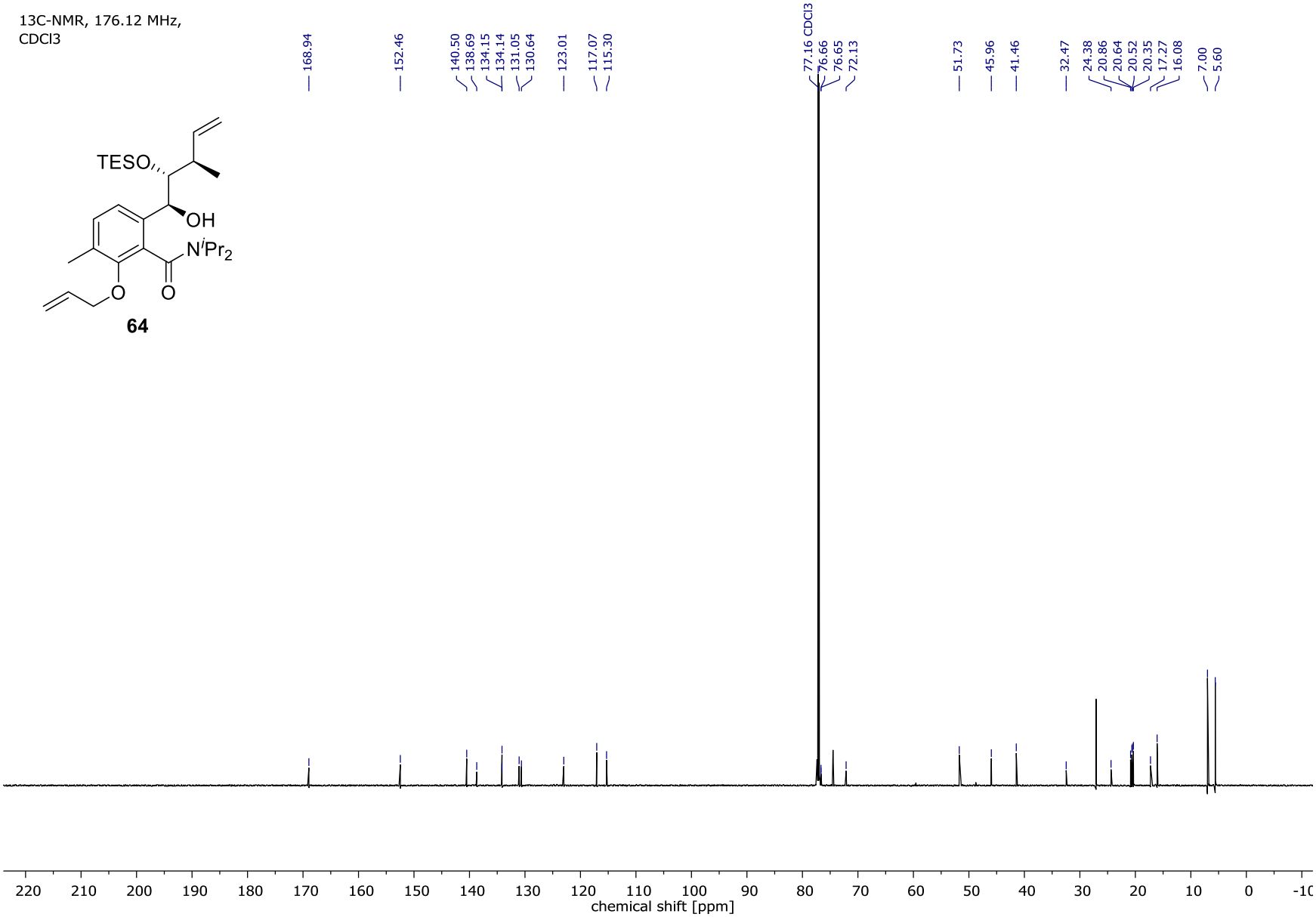


1H-NMR, 700.41 MHz,
CDCl3

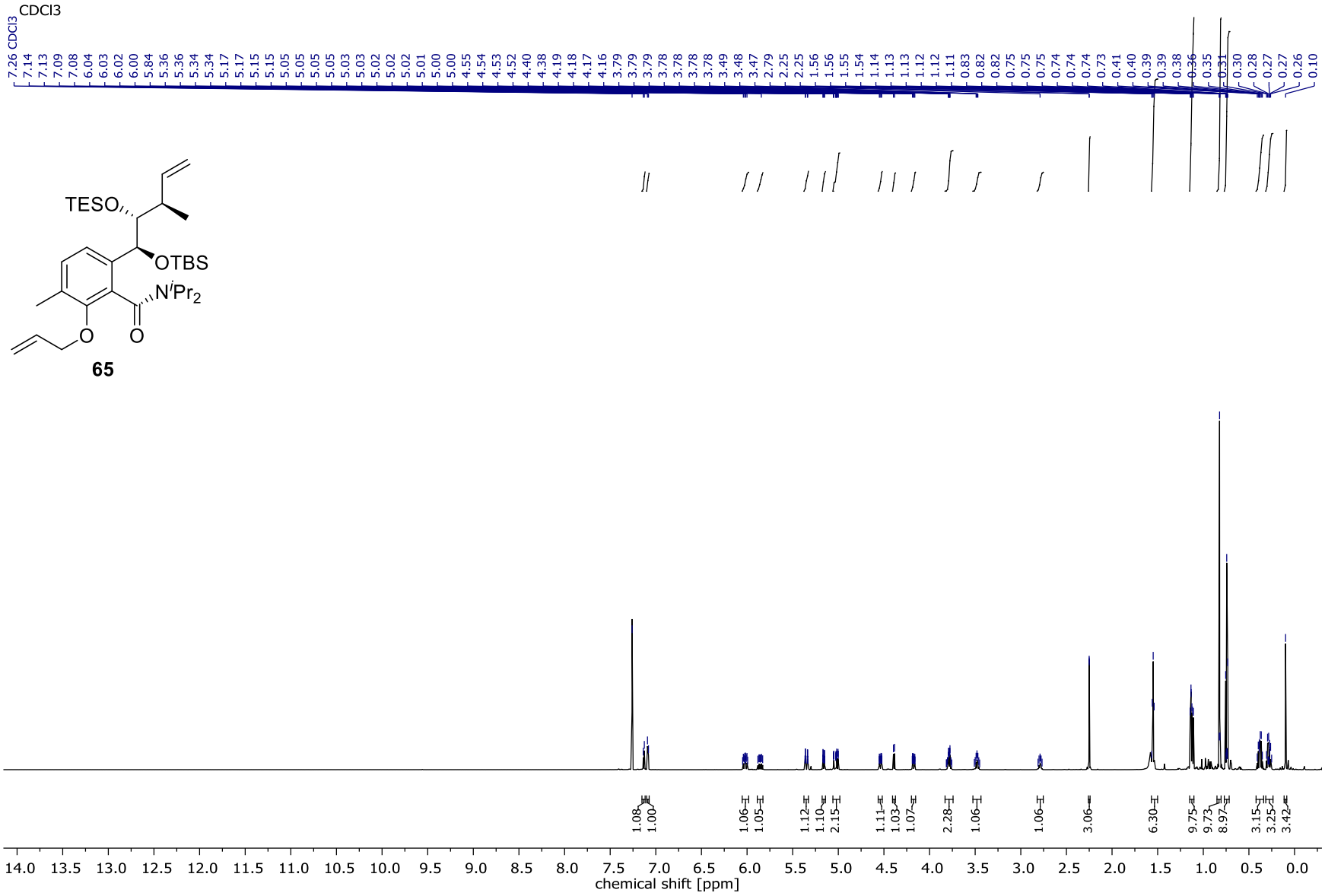


13C-NMR, 176.12 MHz,
CDCl3

64

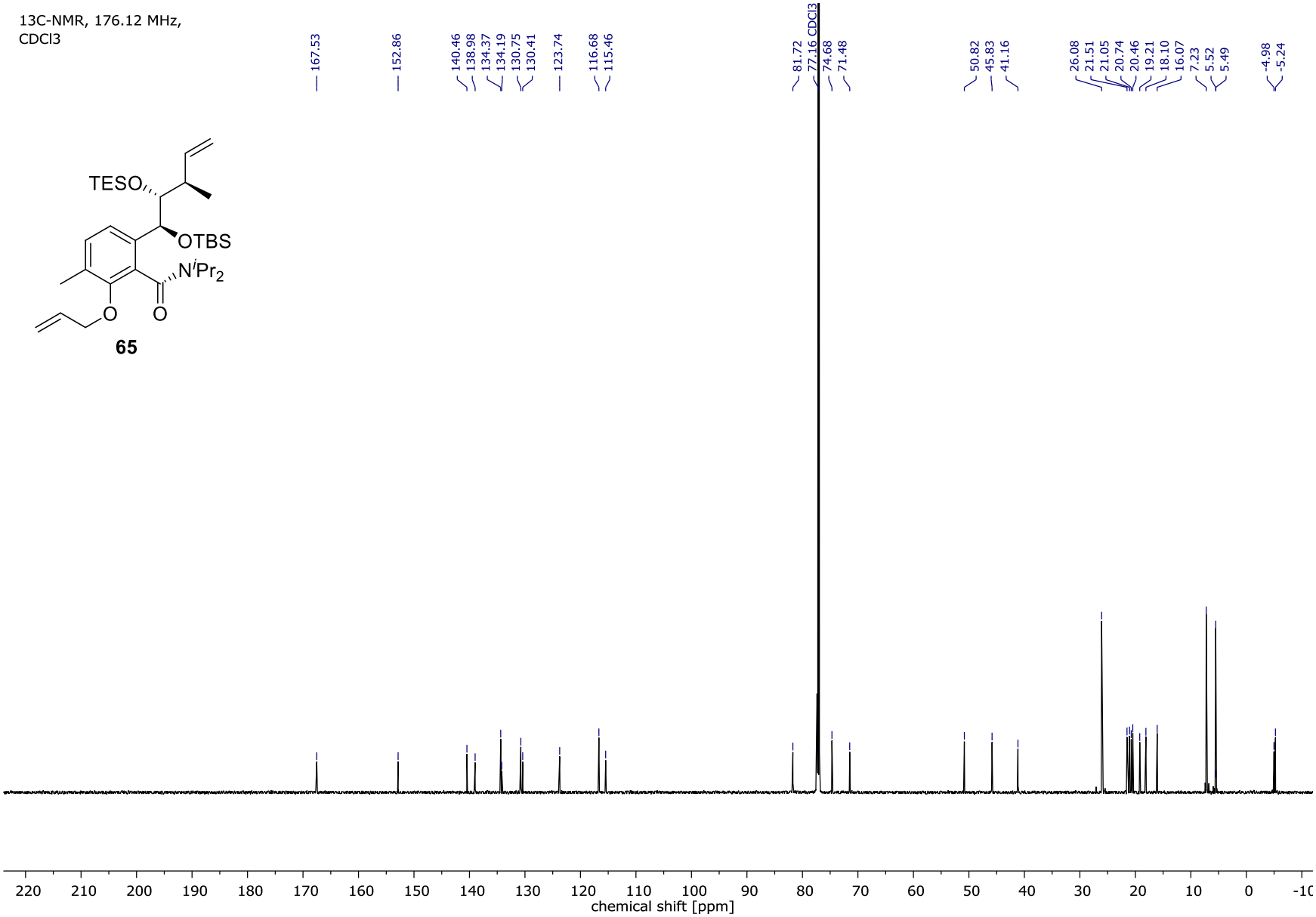


1H-NMR, 700.41 MHz,
CDCl3



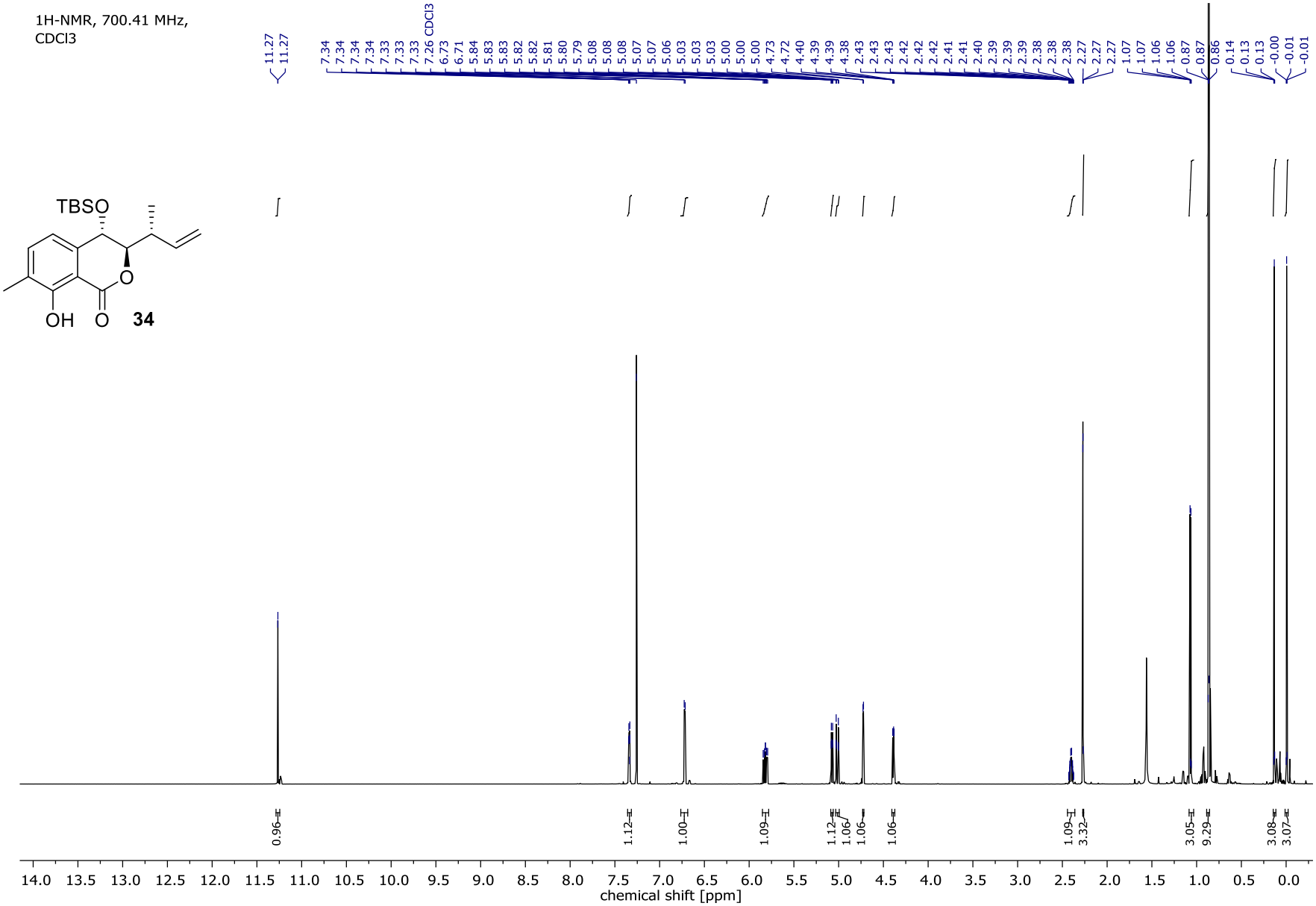
13C-NMR, 176.12 MHz,
CDCl3

65

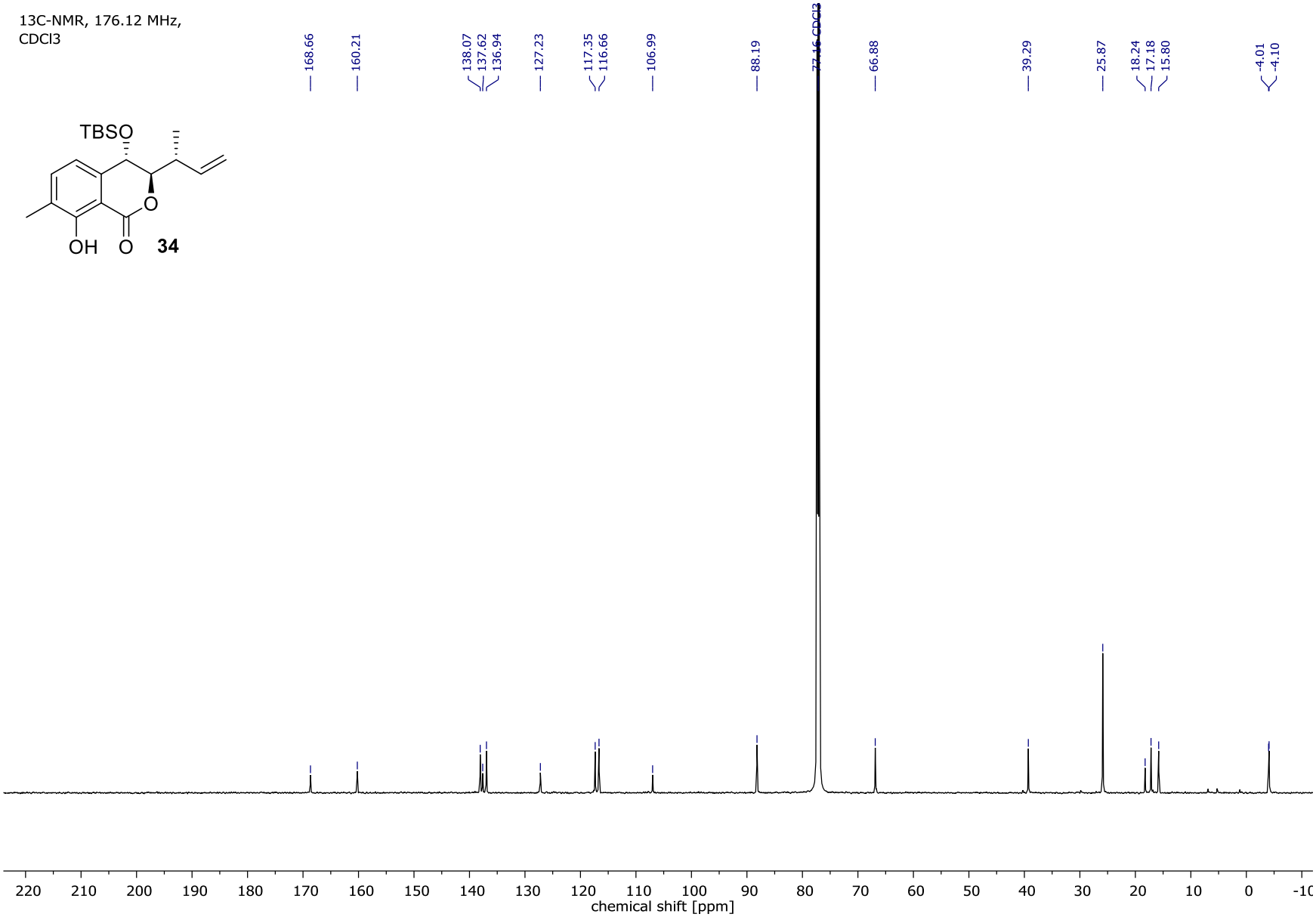


1H-NMR, 700.41 MHz,
CDCl3

34

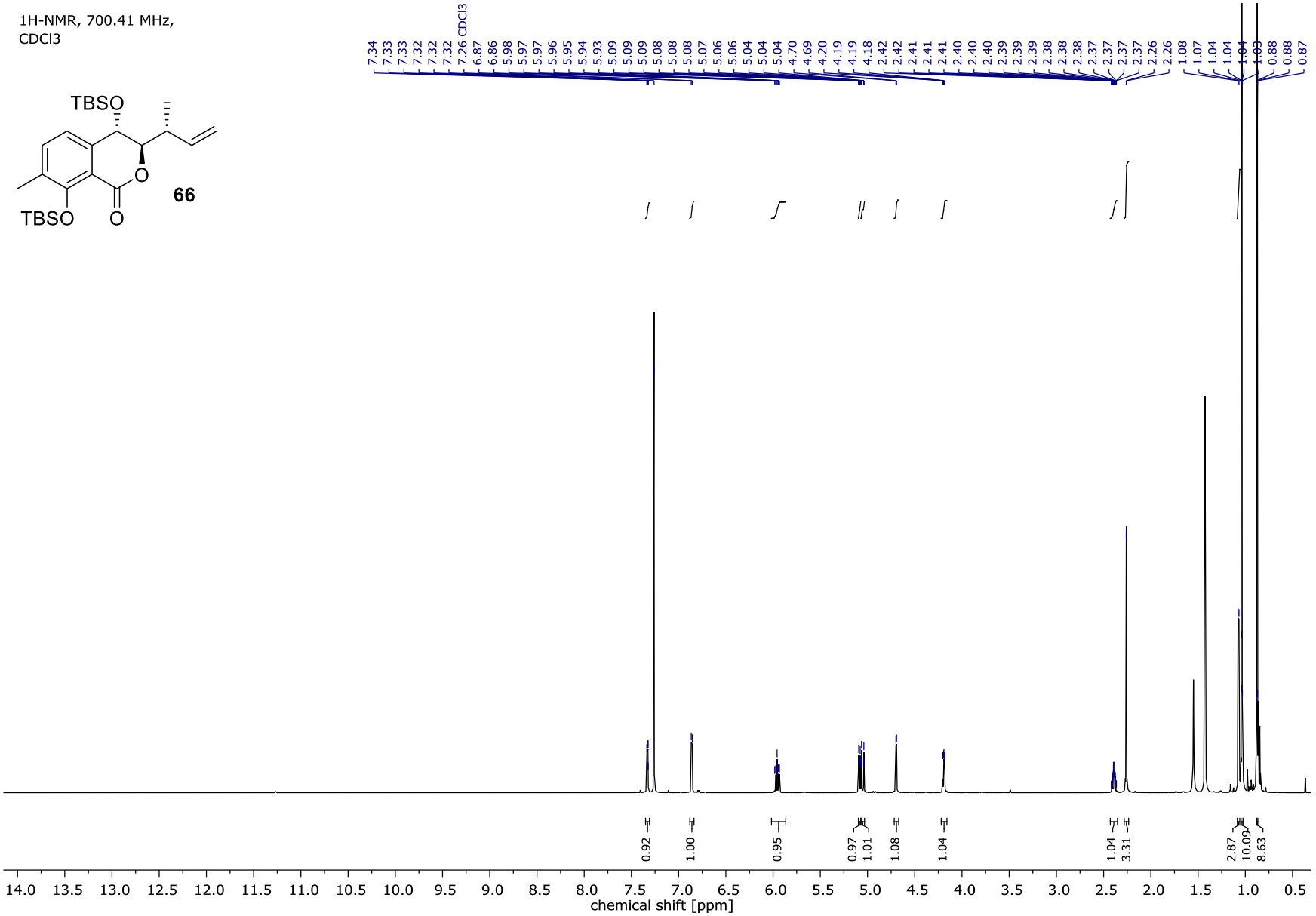


13C-NMR, 176.12 MHz,
CDCl3



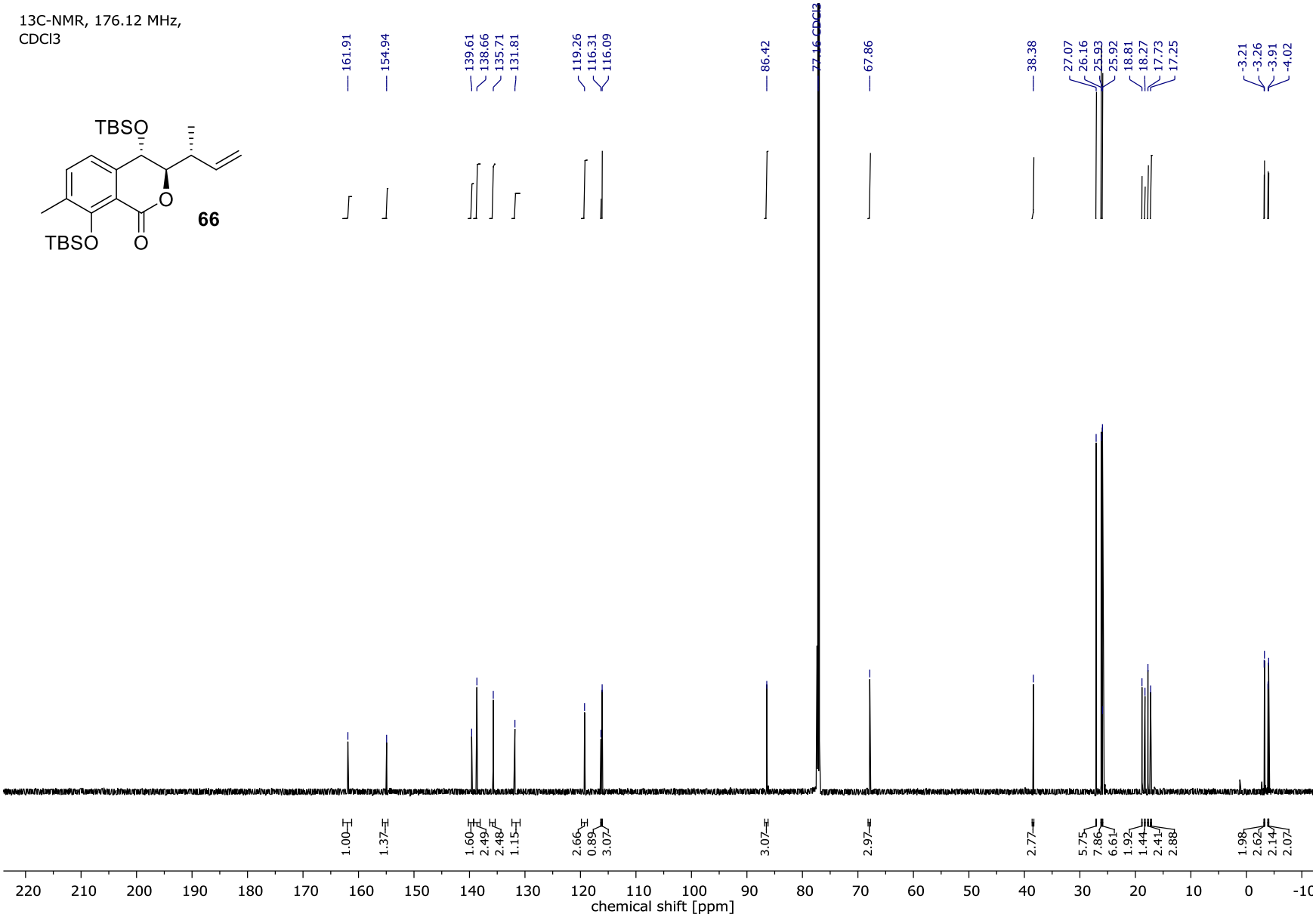
1H-NMR, 700.41 MHz,
CDCl3

66



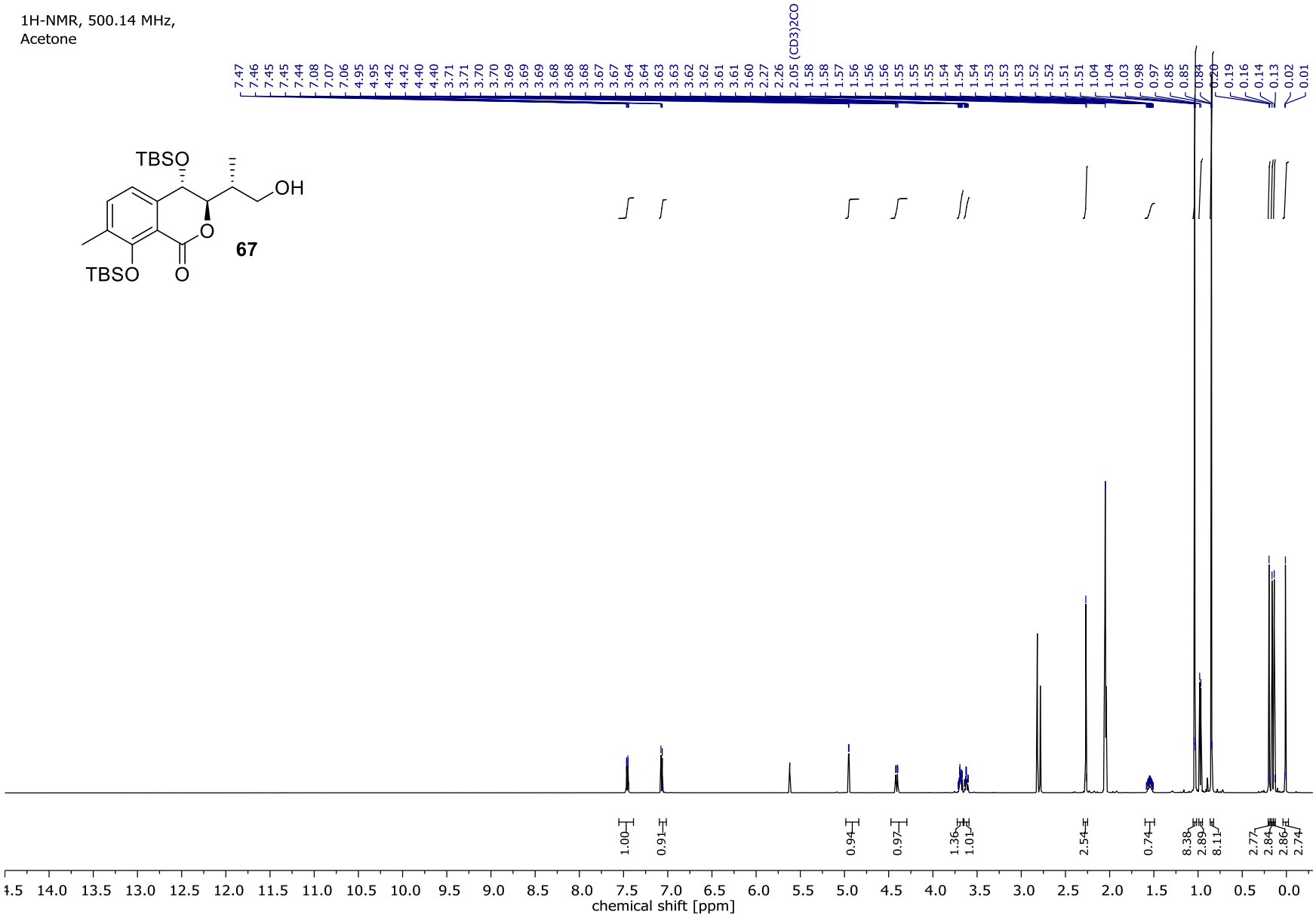
13C-NMR, 176.12 MHz,
CDCl3

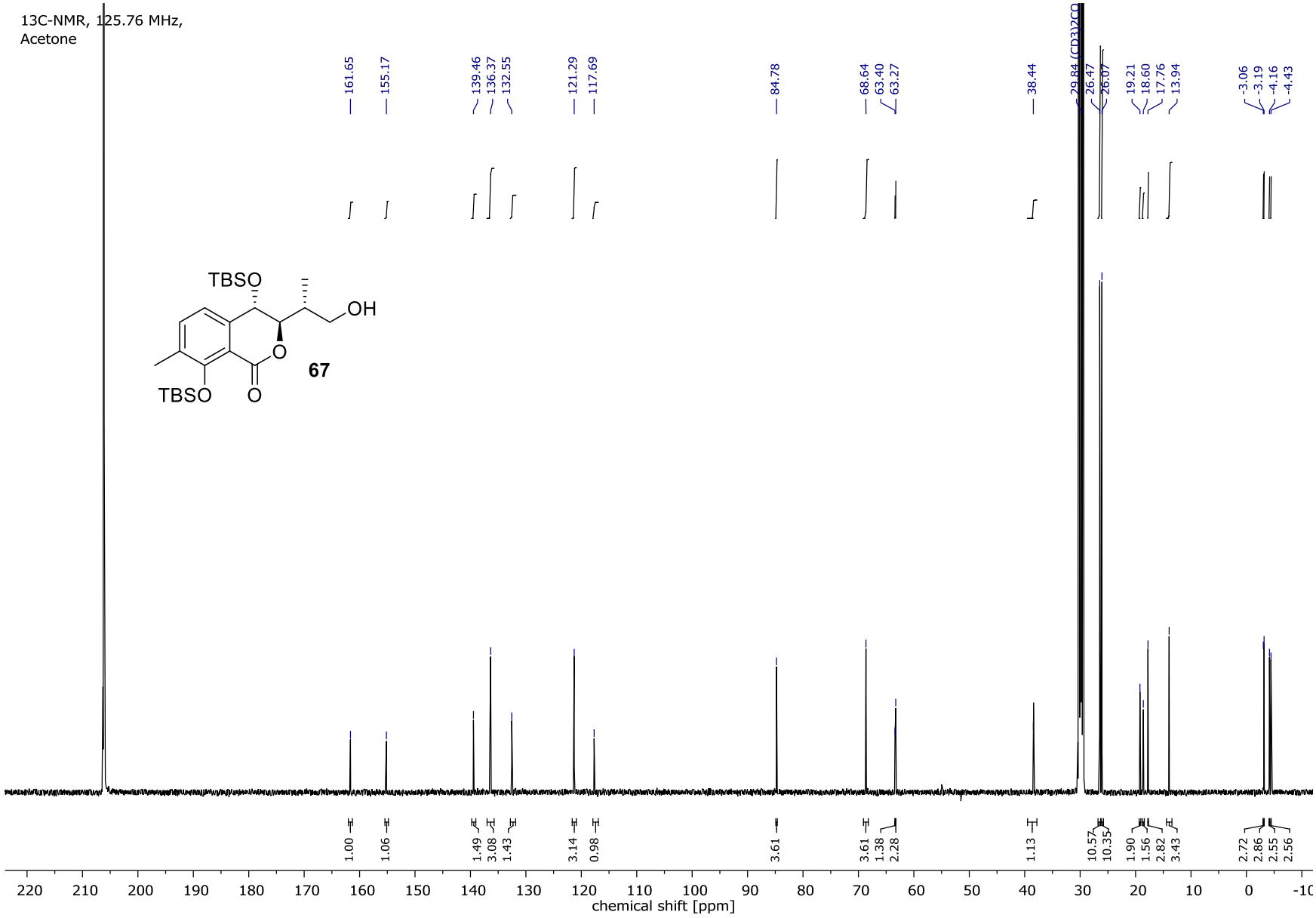
66



1H-NMR, 500.14 MHz,
Acetone

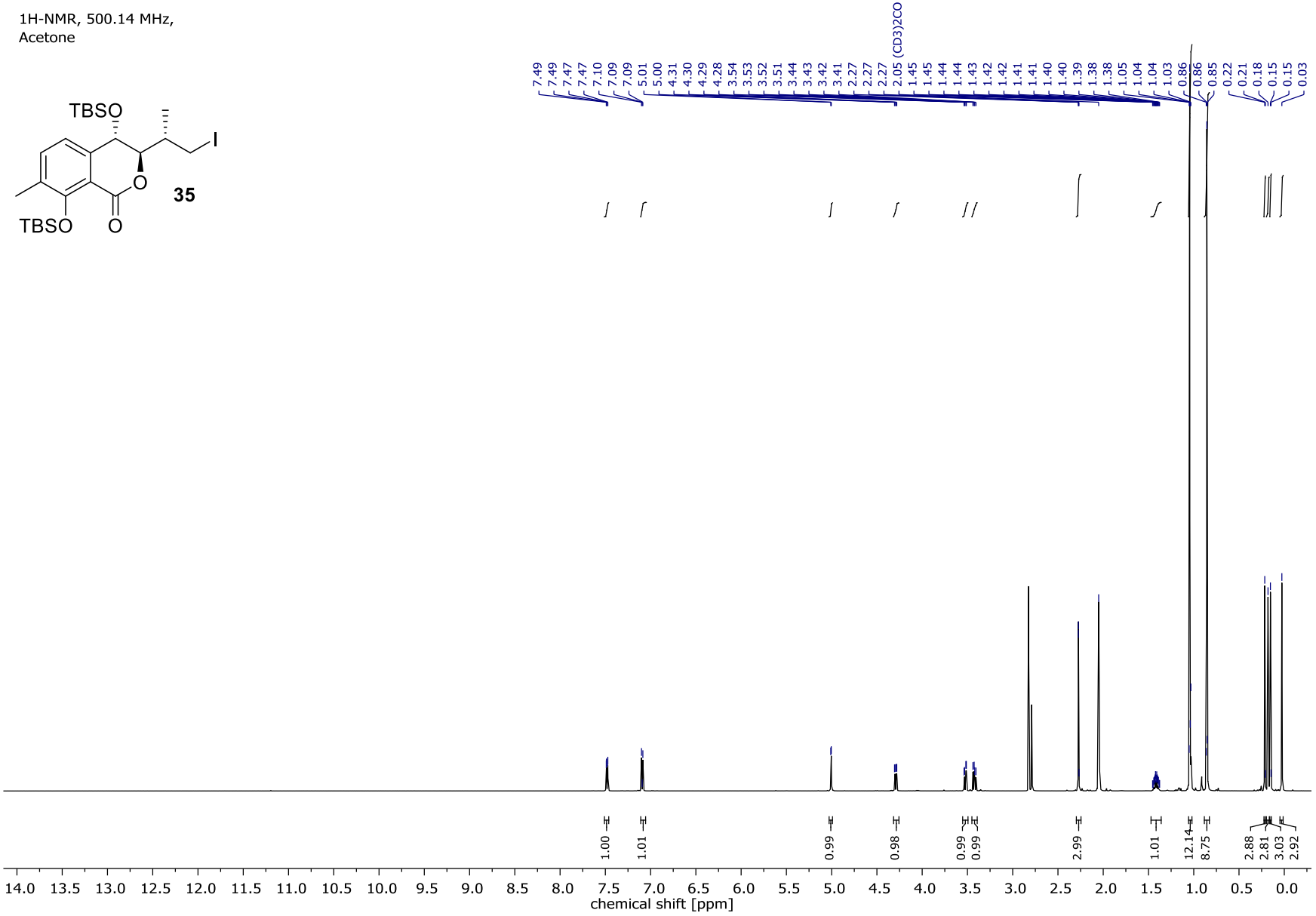
67

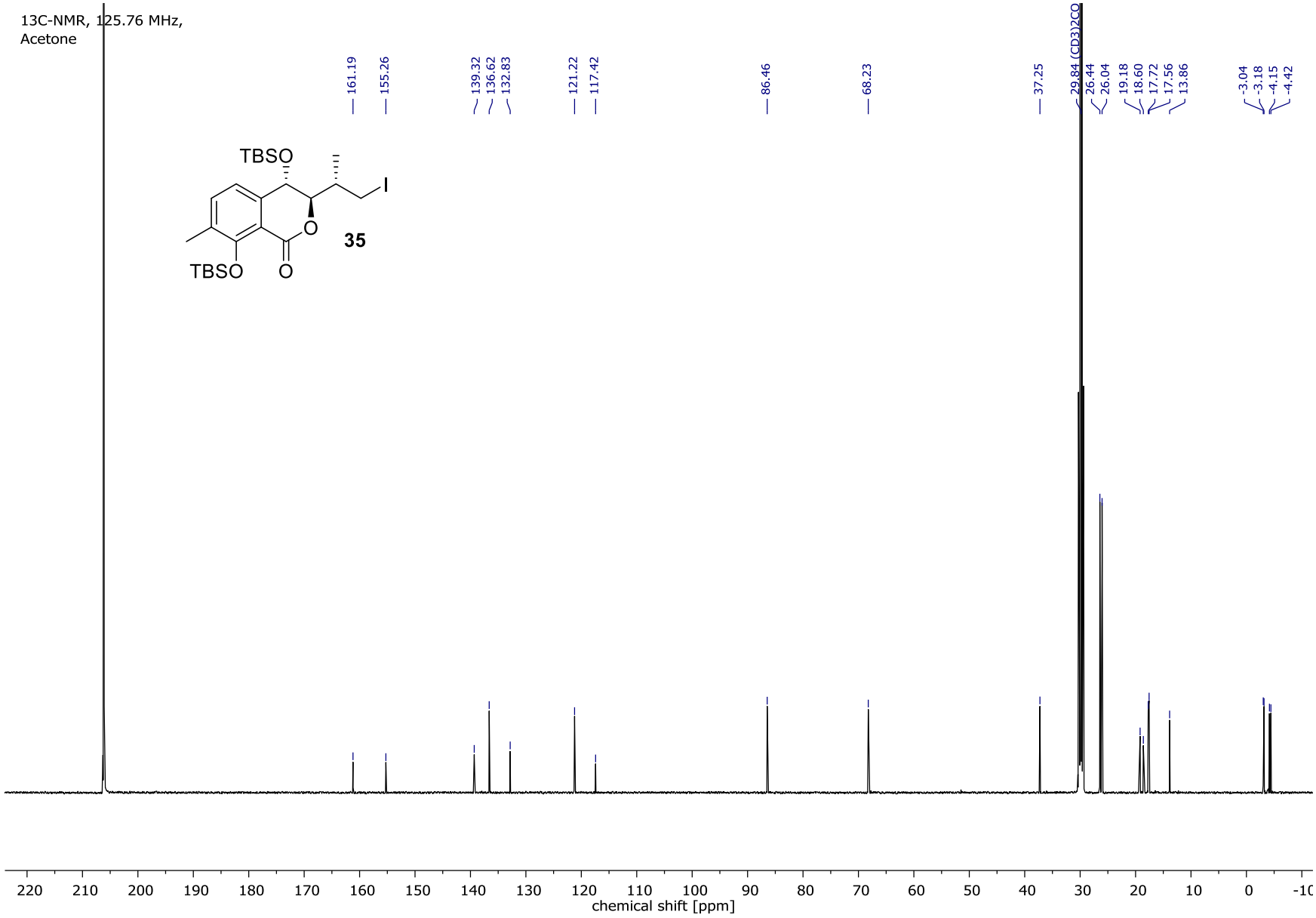



13C-NMR, 125.76 MHz,
Acetone
161.65
155.17
139.46
136.37
132.55
121.29
117.69
84.78
68.64
63.40
63.27
38.44
29.84 (CD3)2CO
26.47
26.07
19.21
18.60
17.76
13.94
-3.06
-3.19
-4.16
-4.43
TBSO
OH
O
TBSO
O
67
1.00
1.06
1.49
3.08
1.43
3.14
0.98
3.61
3.61
1.38
2.28
1.13
10.57
10.35
1.90
1.56
2.82
3.43
2.72
2.86
2.55
2.56
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

1H-NMR, 500.14 MHz,
Acetone

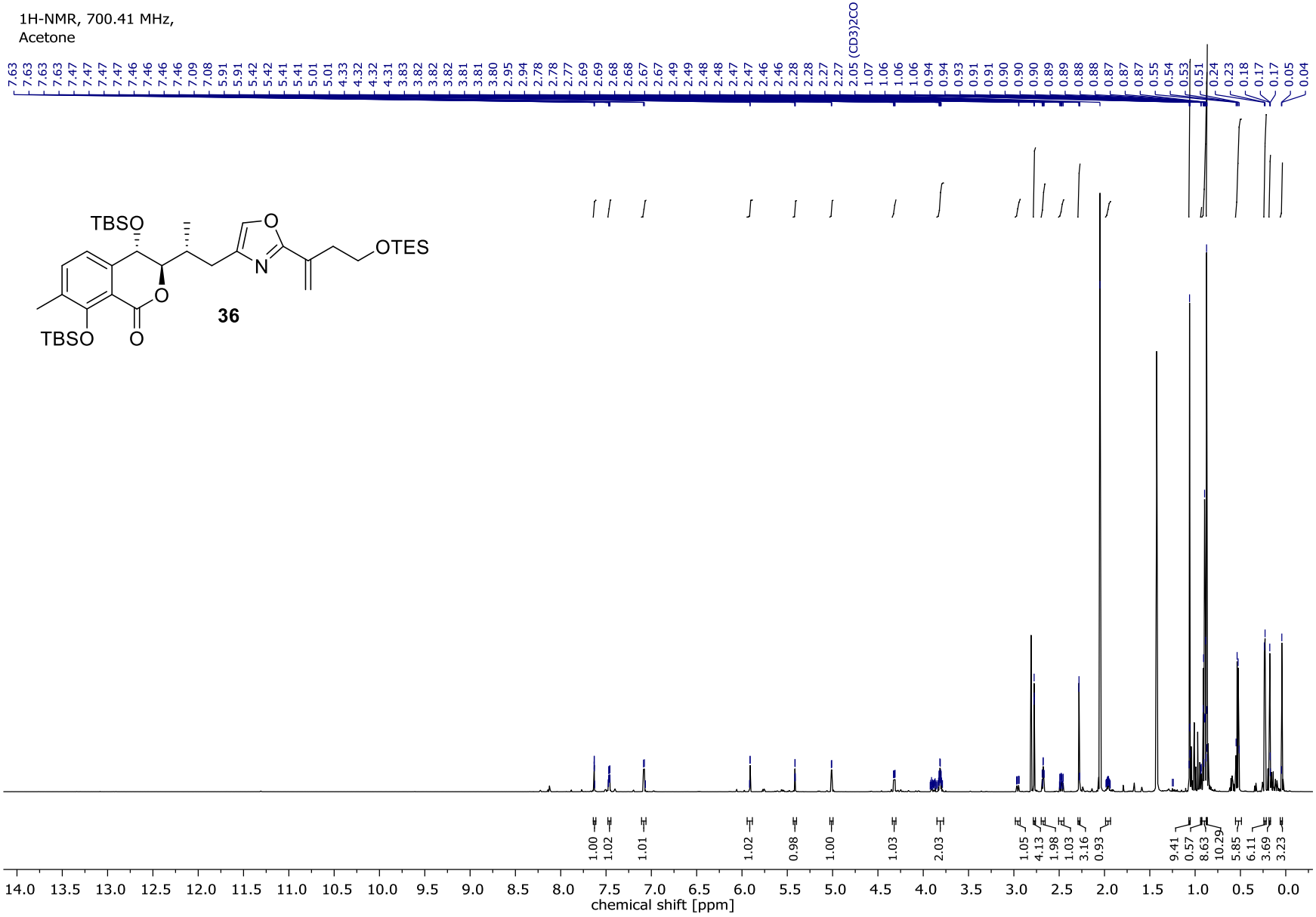
35

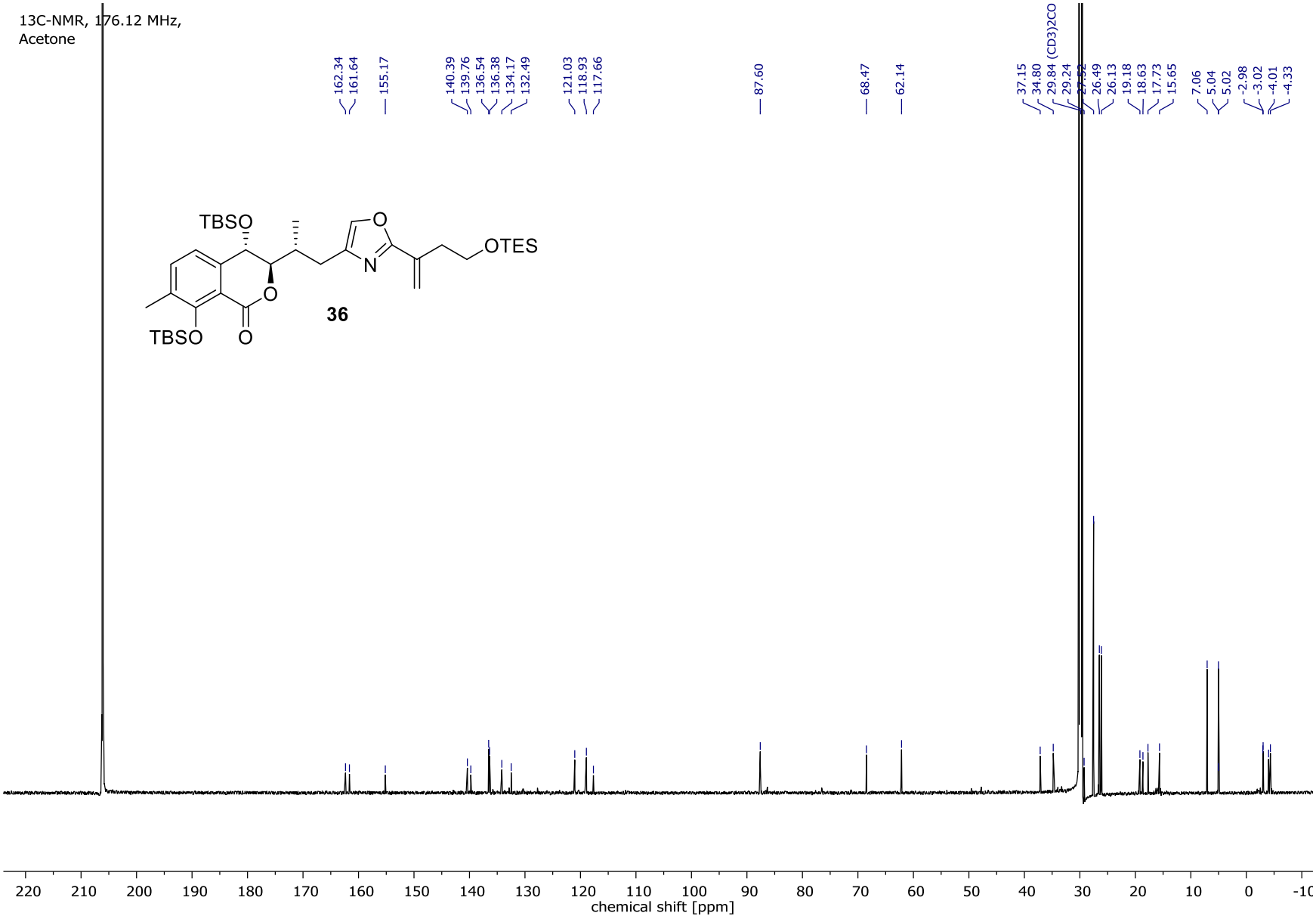



13C-NMR, 125.76 MHz,
Acetone
161.19
155.26
139.32
136.62
132.83
121.22
117.42
86.46
68.23
37.25
29.84 (CD3)2CO
26.44
26.04
19.18
18.60
17.72
17.56
13.86
-3.04
-3.18
-4.15
-4.42
TBSO
TBSO
O
O
I
35
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
chemical shift [ppm]

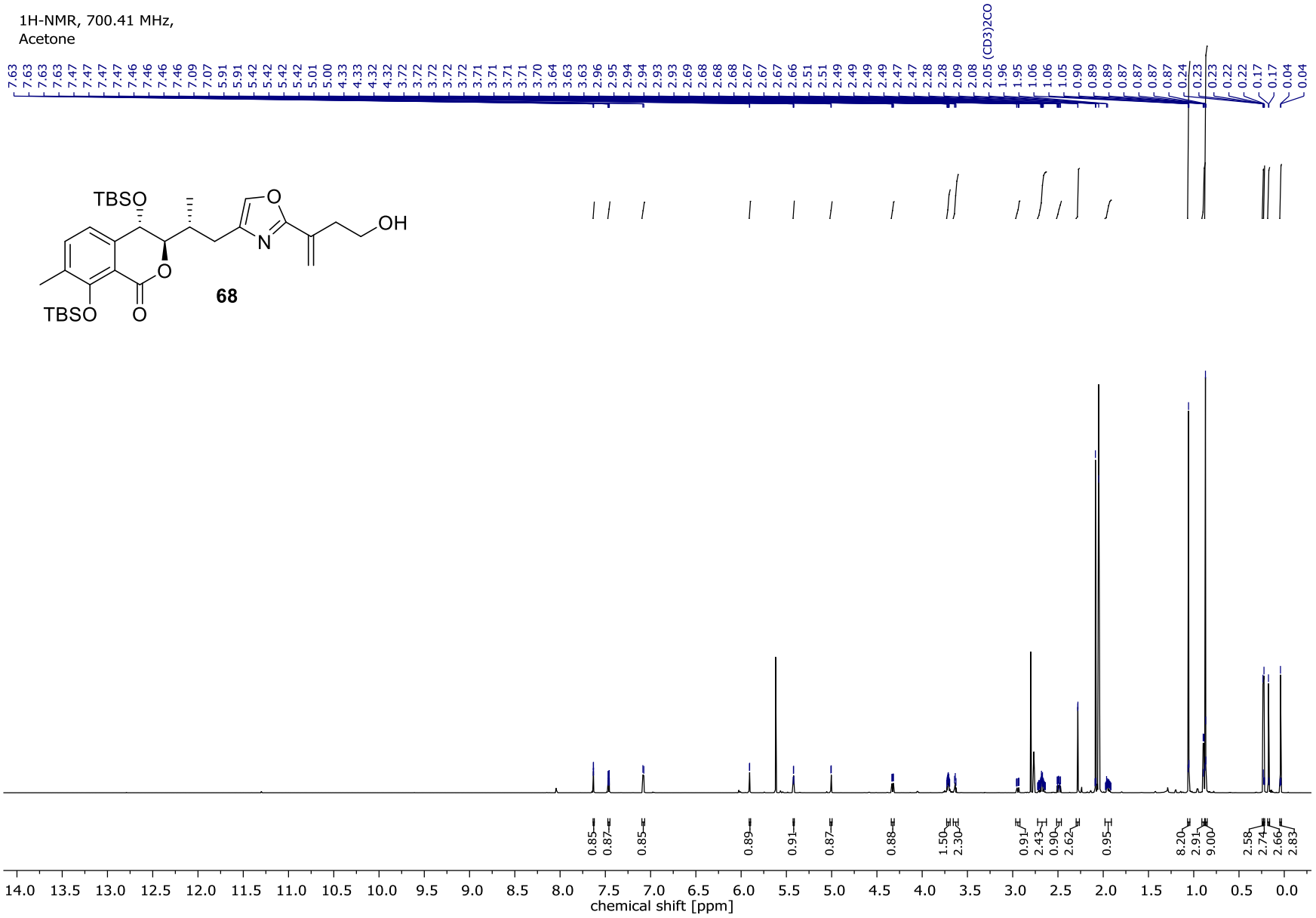
1H-NMR, 700.41 MHz,
Acetone

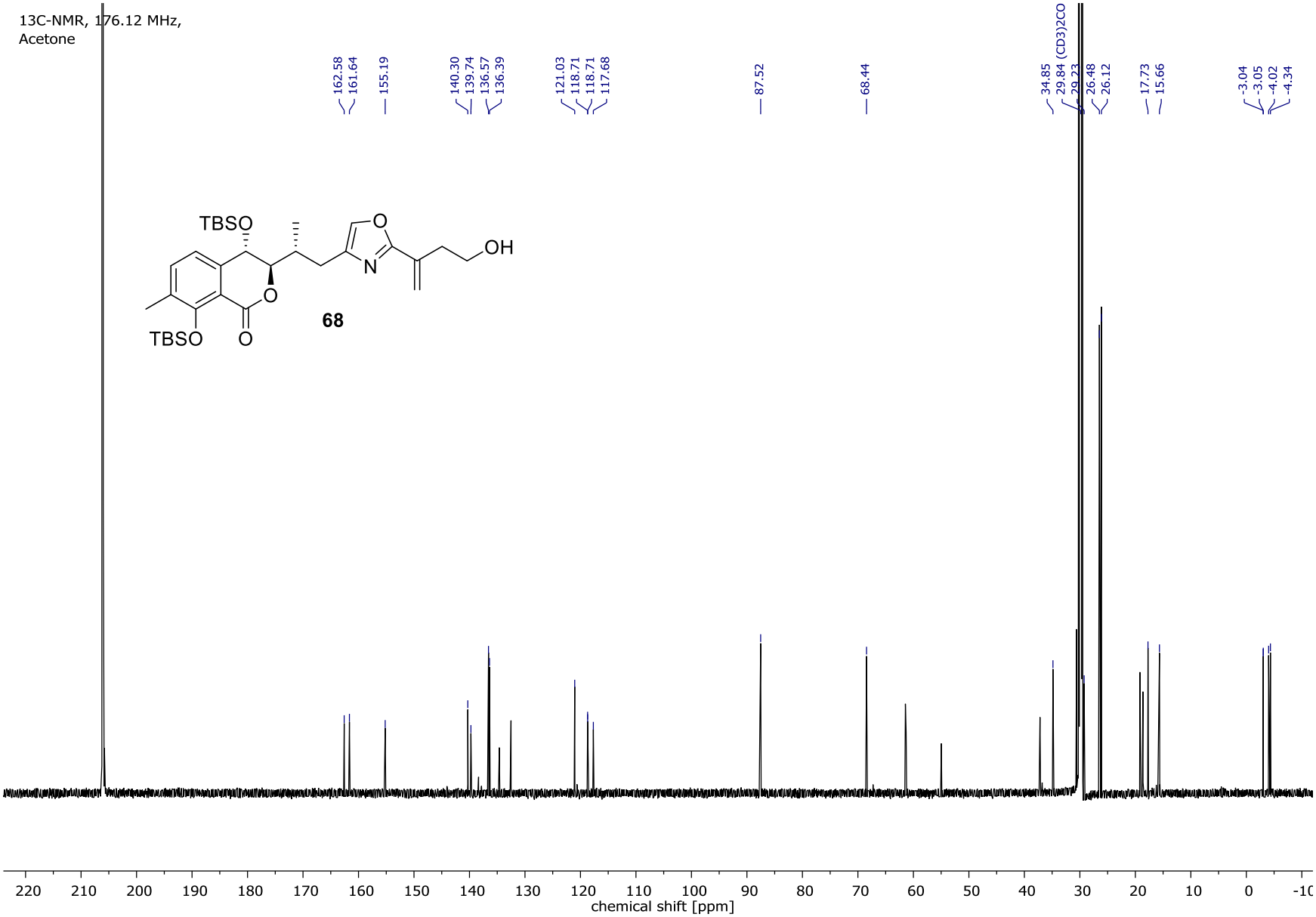
36



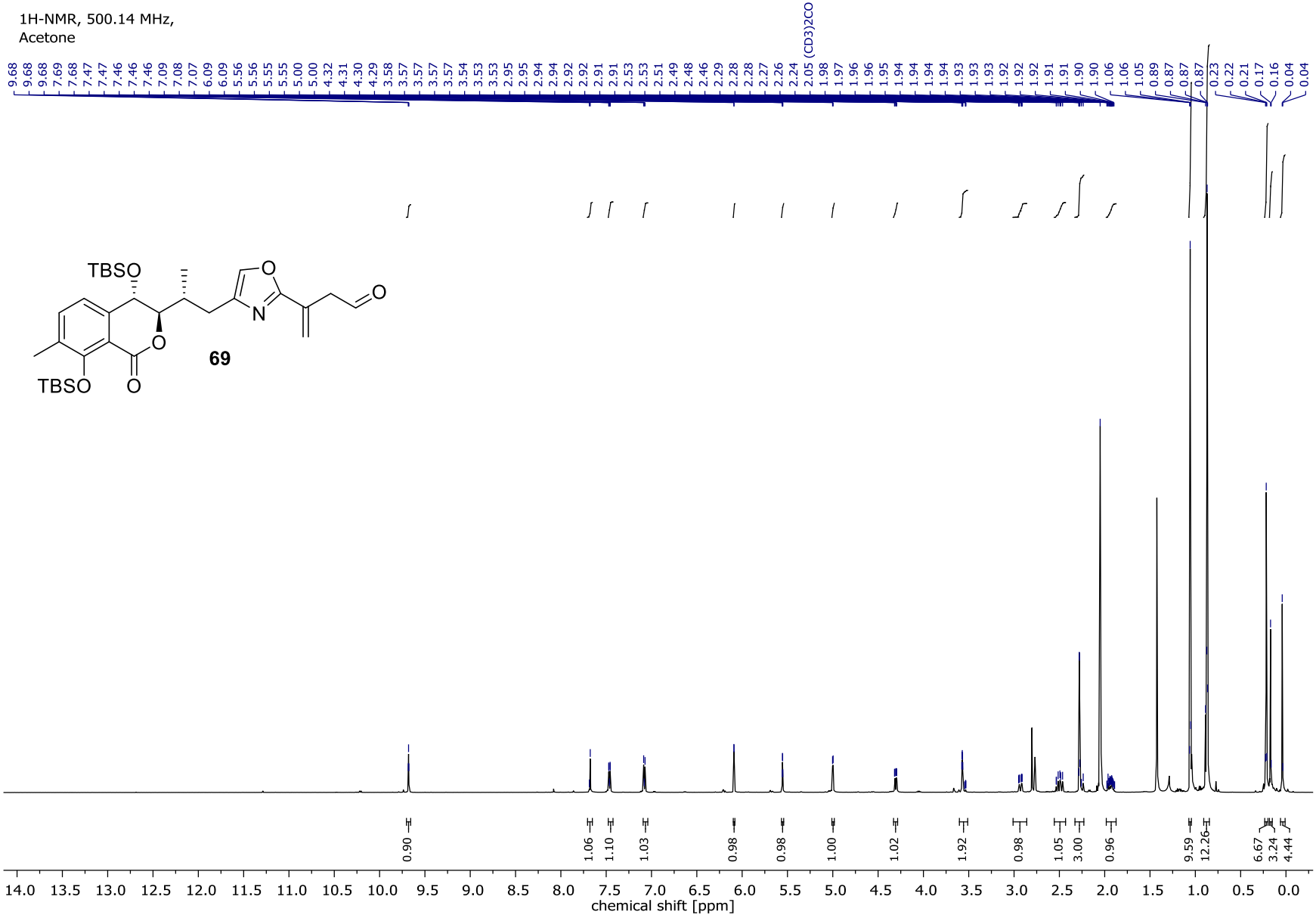

13C-NMR, 176.12 MHz,
Acetone
162.34
161.64
155.17
140.39
139.76
136.54
136.38
134.17
132.49
121.03
118.93
117.66
87.60
68.47
62.14
37.15
34.80
29.84 (CD3)2CO
29.24
27.52
26.49
26.13
19.18
18.63
17.73
15.65
7.06
5.04
5.02
-2.98
-3.02
-4.01
-4.33
TBSO
TBSO
O
O
N
O
OTES
36
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
chemical shift [ppm]

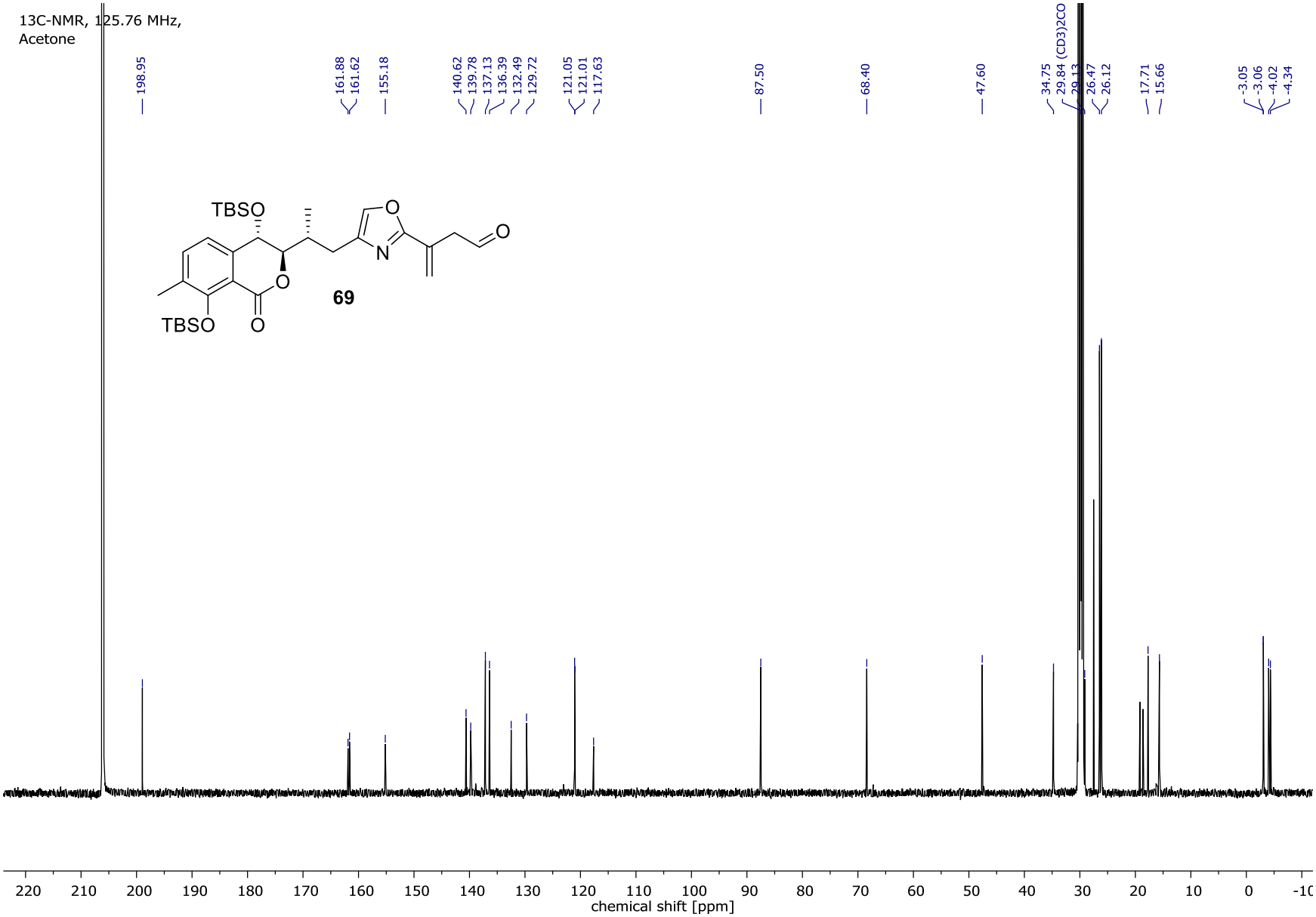
1H-NMR, 700.41 MHz,
Acetone




13C-NMR, 176.12 MHz,
Acetone
162.58
161.64
155.19
140.30
139.74
136.57
136.39
121.03
118.71
118.71
117.68
87.52
68.44
34.85
29.84 (CD3)2CO
29.23
26.48
26.12
17.73
15.66
-3.04
-3.05
-4.02
-4.34
TBSO
TBSO
O
O
O
N
OH
68
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
chemical shift [ppm]

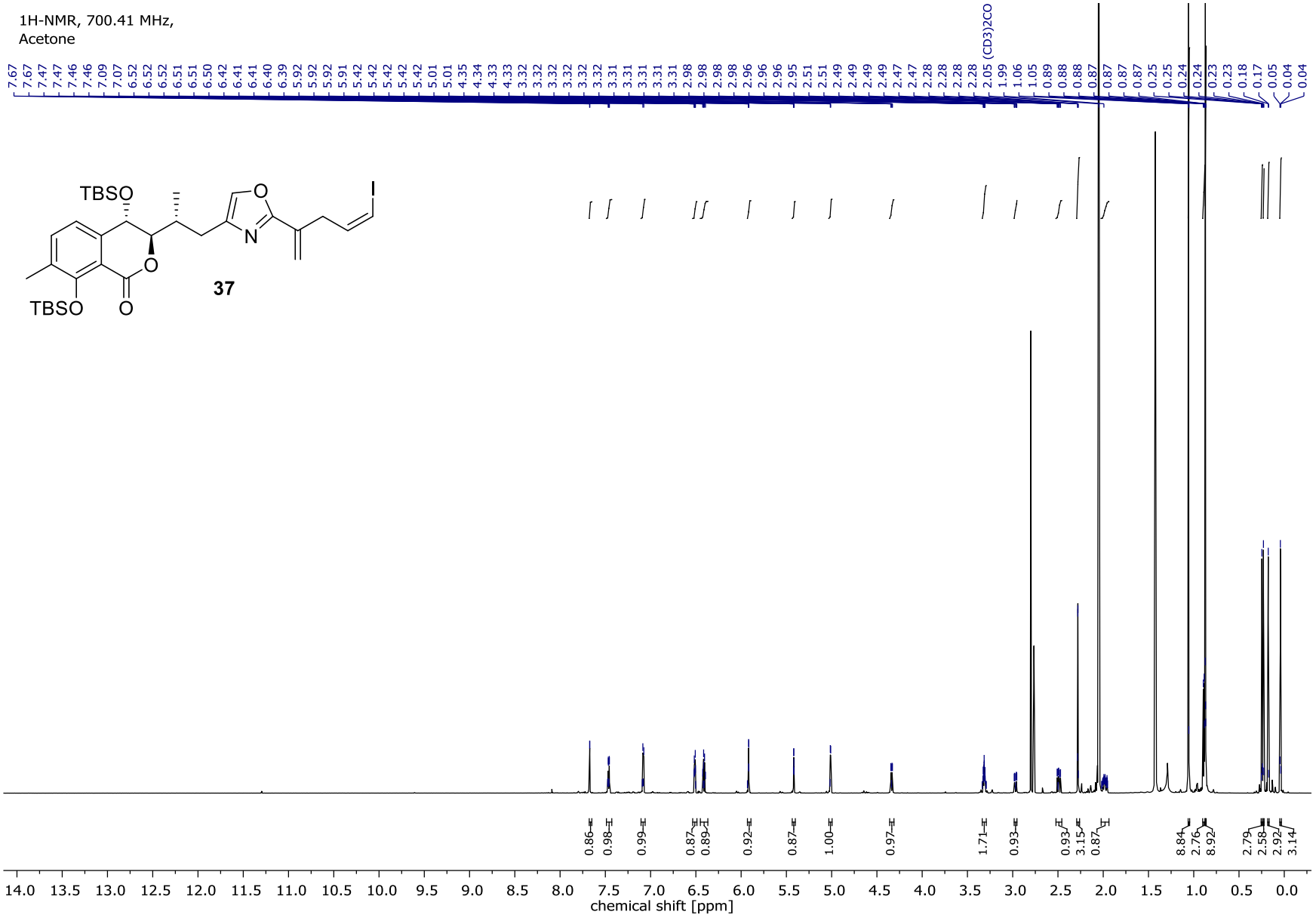
1H-NMR, 500.14 MHz,
Acetone

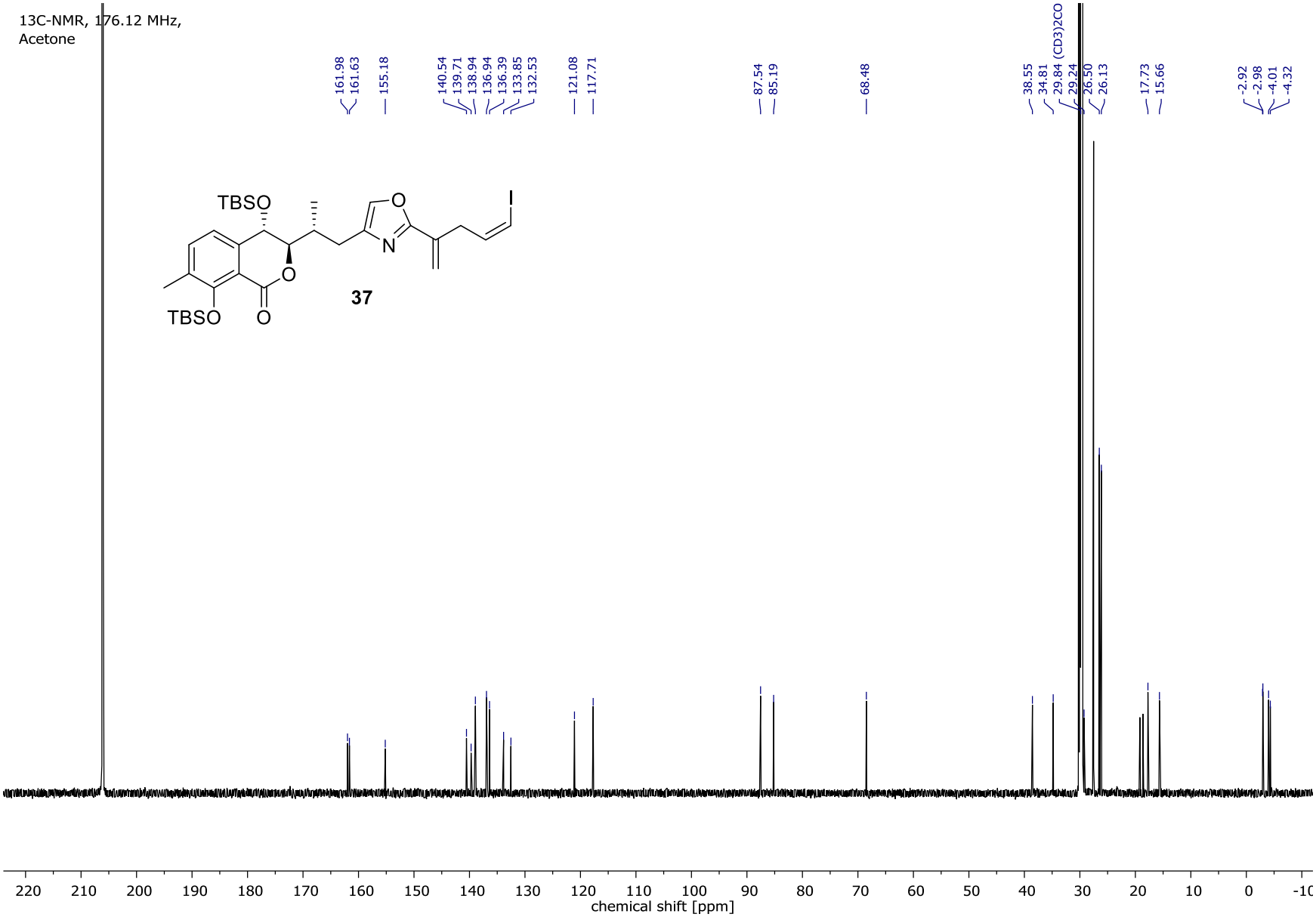



13C-NMR, 125.76 MHz,
Acetone
198.95
161.88
161.62
155.18
140.62
139.78
137.13
136.39
132.49
129.72
121.05
121.01
117.63
87.50
68.40
47.60
34.75
29.84 (CD3)2CO
29.13
26.47
26.12
17.71
15.66
-3.05
-3.06
-4.02
-4.34
TBSO
TBSO
O
O
O
O
N
69
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
chemical shift [ppm]

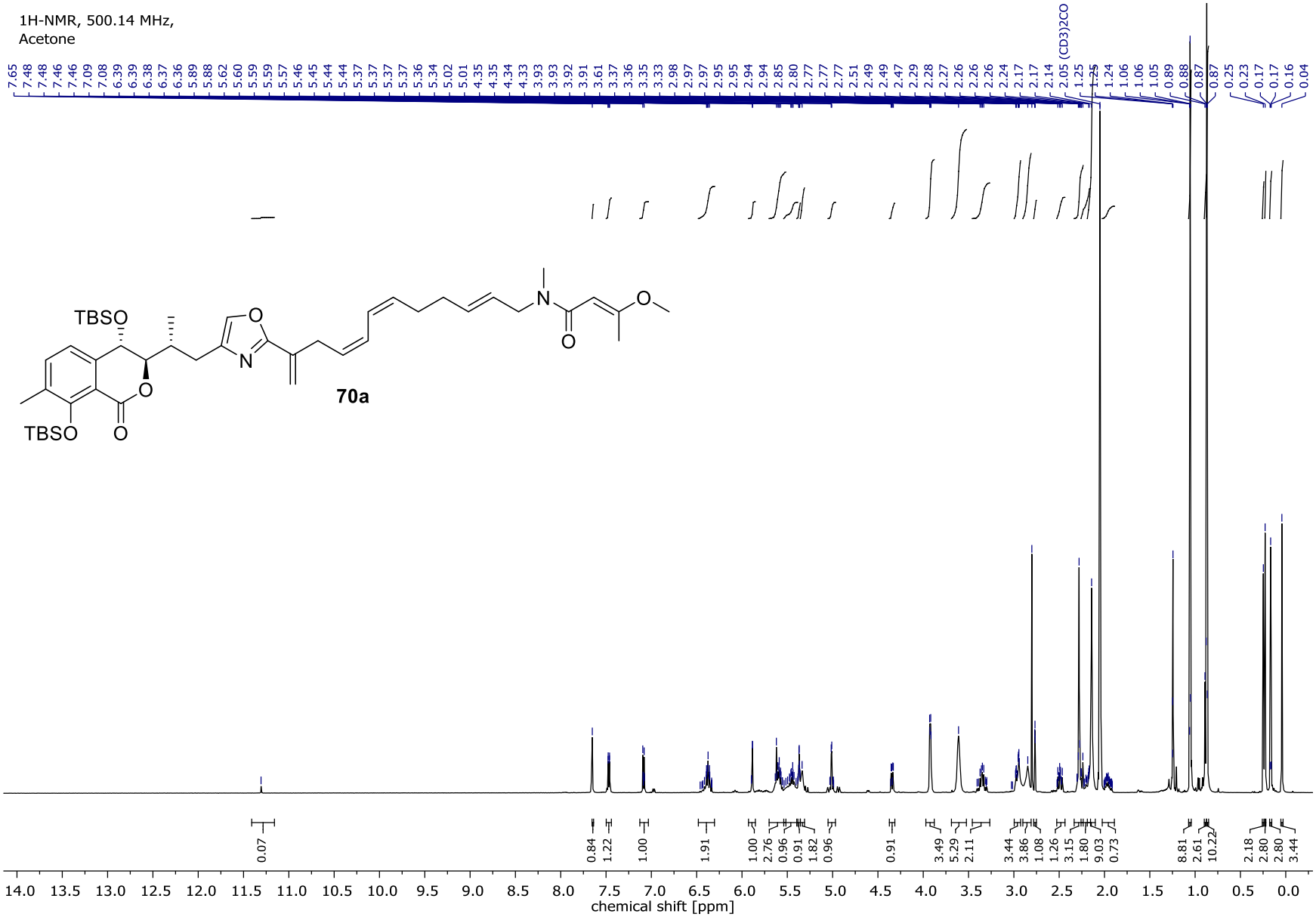
1H-NMR, 700.41 MHz,
Acetone

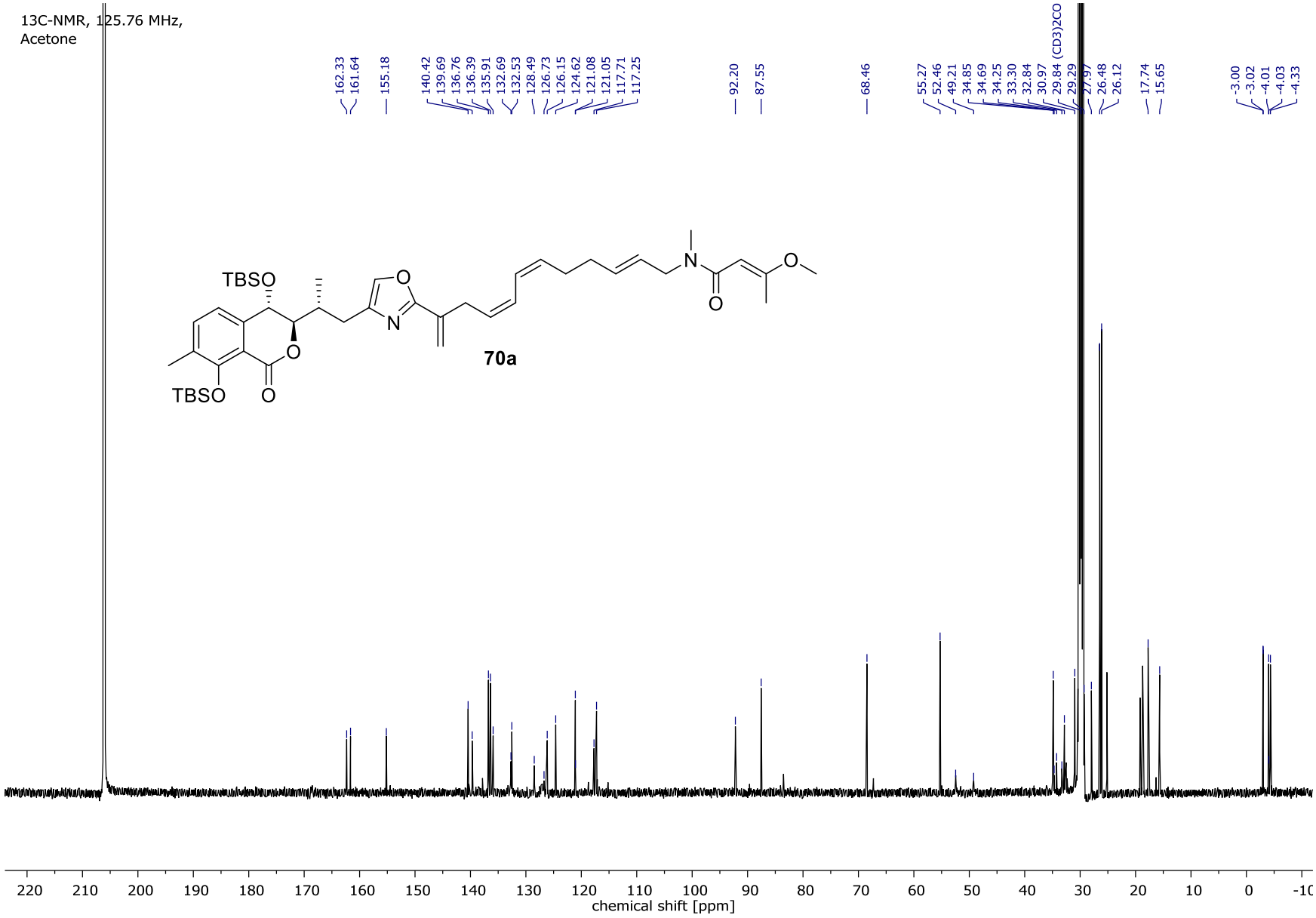
37



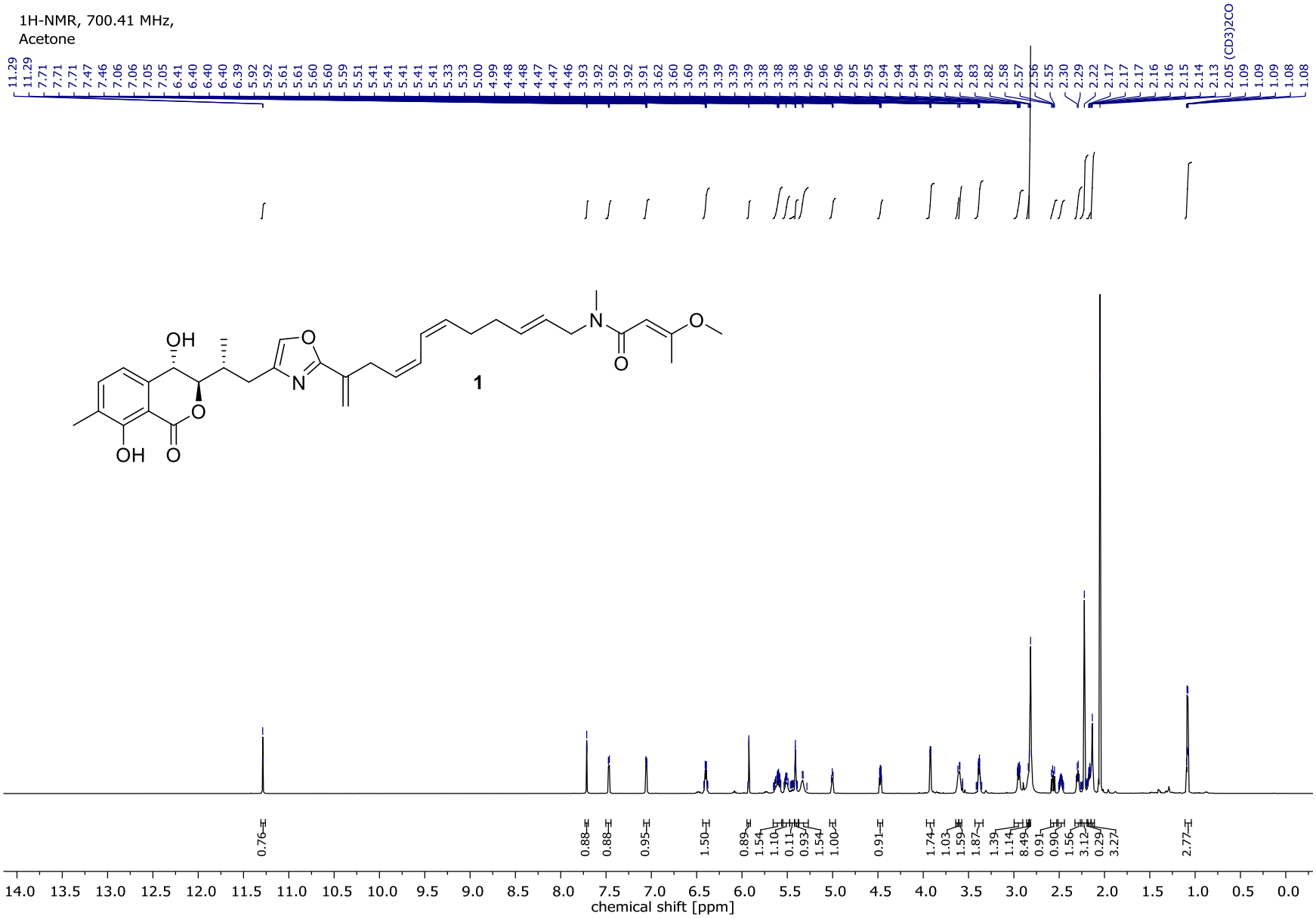

13C-NMR, 176.12 MHz,
Acetone
161.98
161.63
155.18
140.54
139.71
138.94
136.94
136.39
133.85
132.53
121.08
117.71
87.54
85.19
68.48
38.55
34.81
29.84 (CD3)2CO
29.24
26.50
26.13
17.73
15.66
-2.92
-2.98
-4.01
-4.32
TBSO
TBSO
O
O
O
N
I
37
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
chemical shift [ppm]

1H-NMR, 500.14 MHz,
Acetone

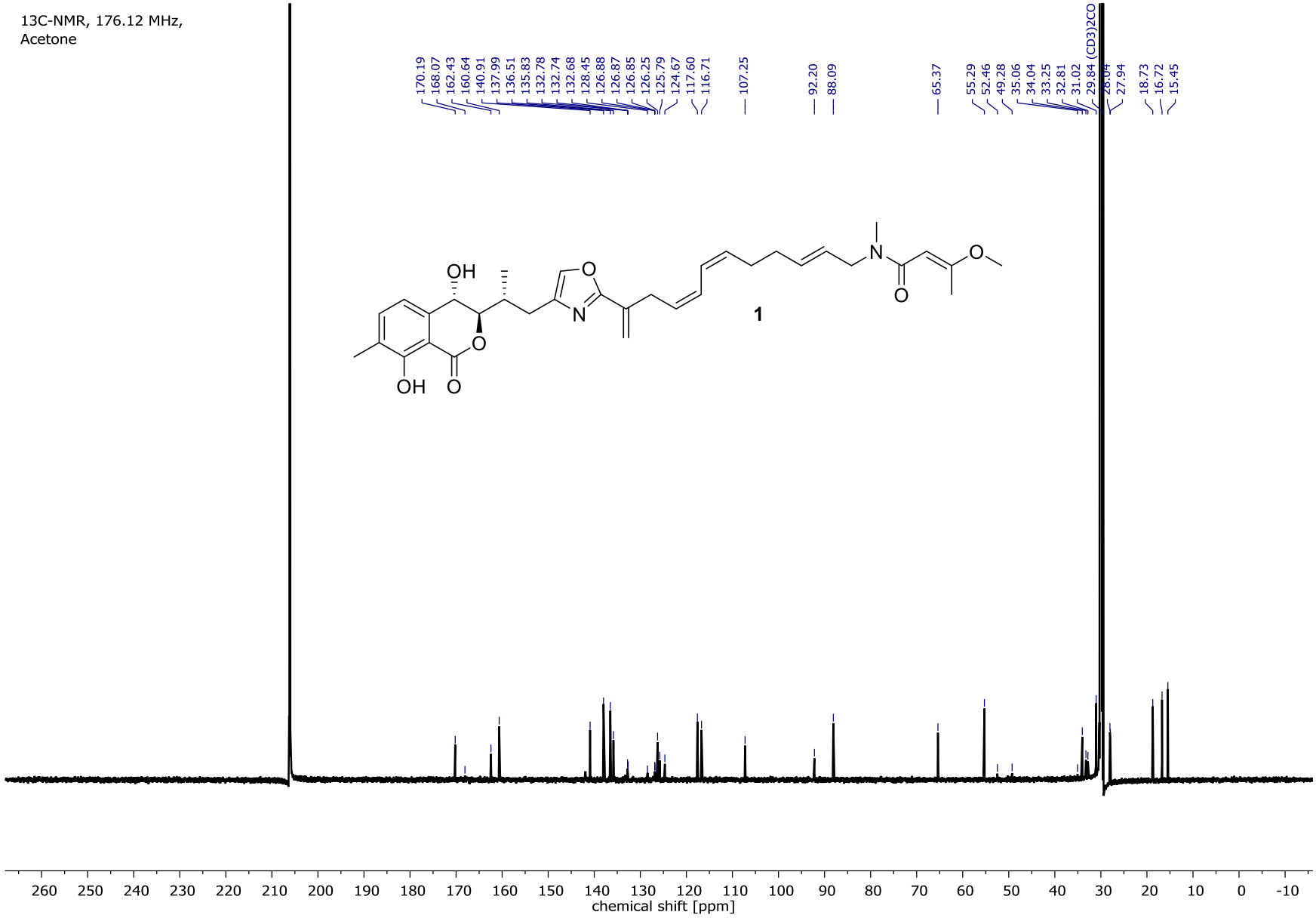



13C-NMR, 125.76 MHz,
Acetone
162.33
161.64
155.18
140.42
139.69
136.76
136.39
135.91
132.69
132.53
128.49
126.73
126.15
124.62
121.08
121.05
117.71
117.25
92.20
87.55
68.46
55.27
52.46
49.21
34.85
34.69
34.25
33.30
32.84
30.97
29.84 (CD3)2CO
29.29
27.97
26.48
26.12
17.74
15.65
-3.00
-3.02
-4.01
-4.03
-4.33
TBSO
TBSO
O
O
O
N
N
O
O
70a
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
chemical shift [ppm]

1H-NMR, 700.41 MHz,
Acetone

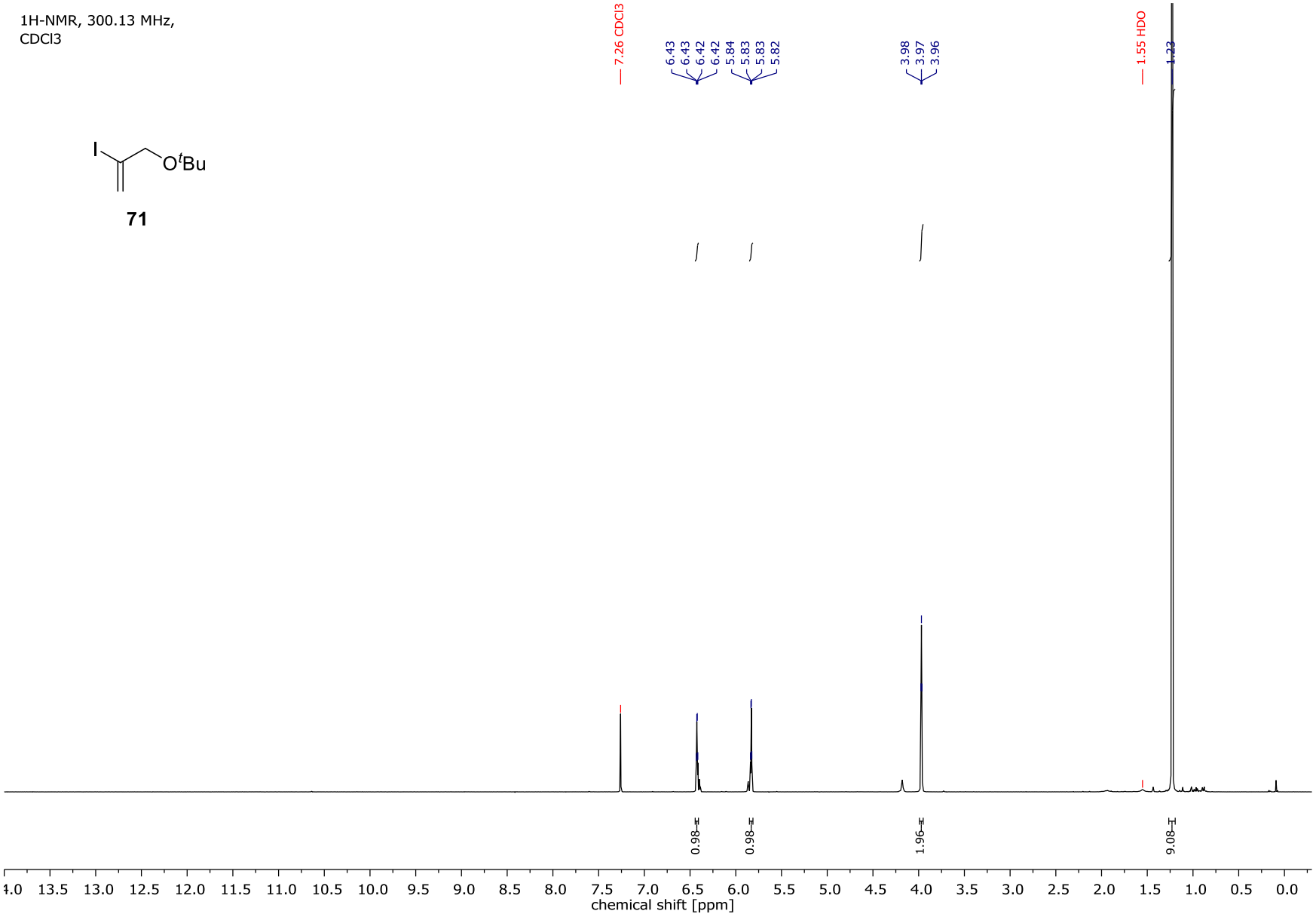


13C-NMR, 176.12 MHz,
Acetone



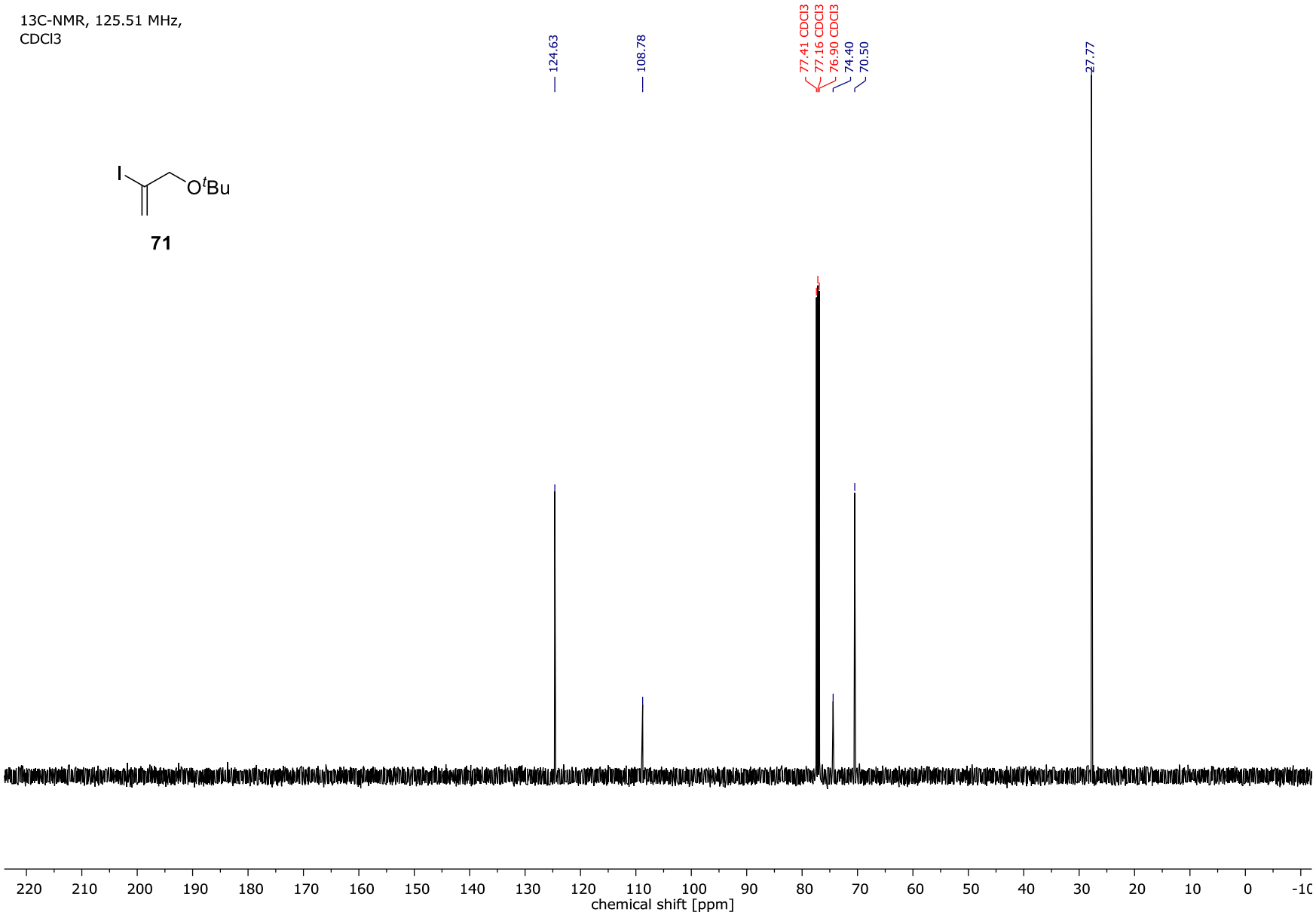
1H-NMR, 300.13 MHz,
CDCl3

71



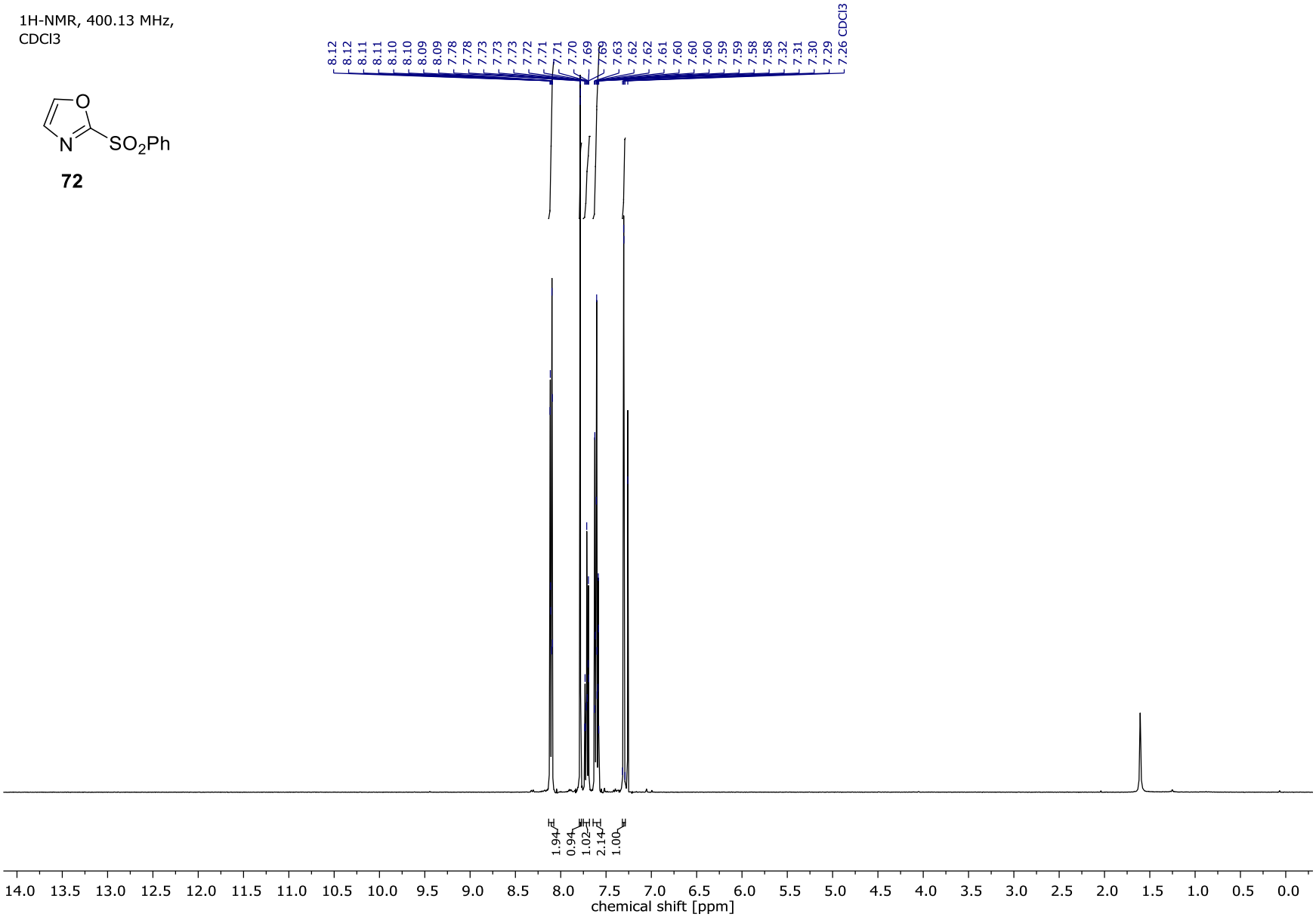
13C-NMR, 125.51 MHz,
CDCl3

71



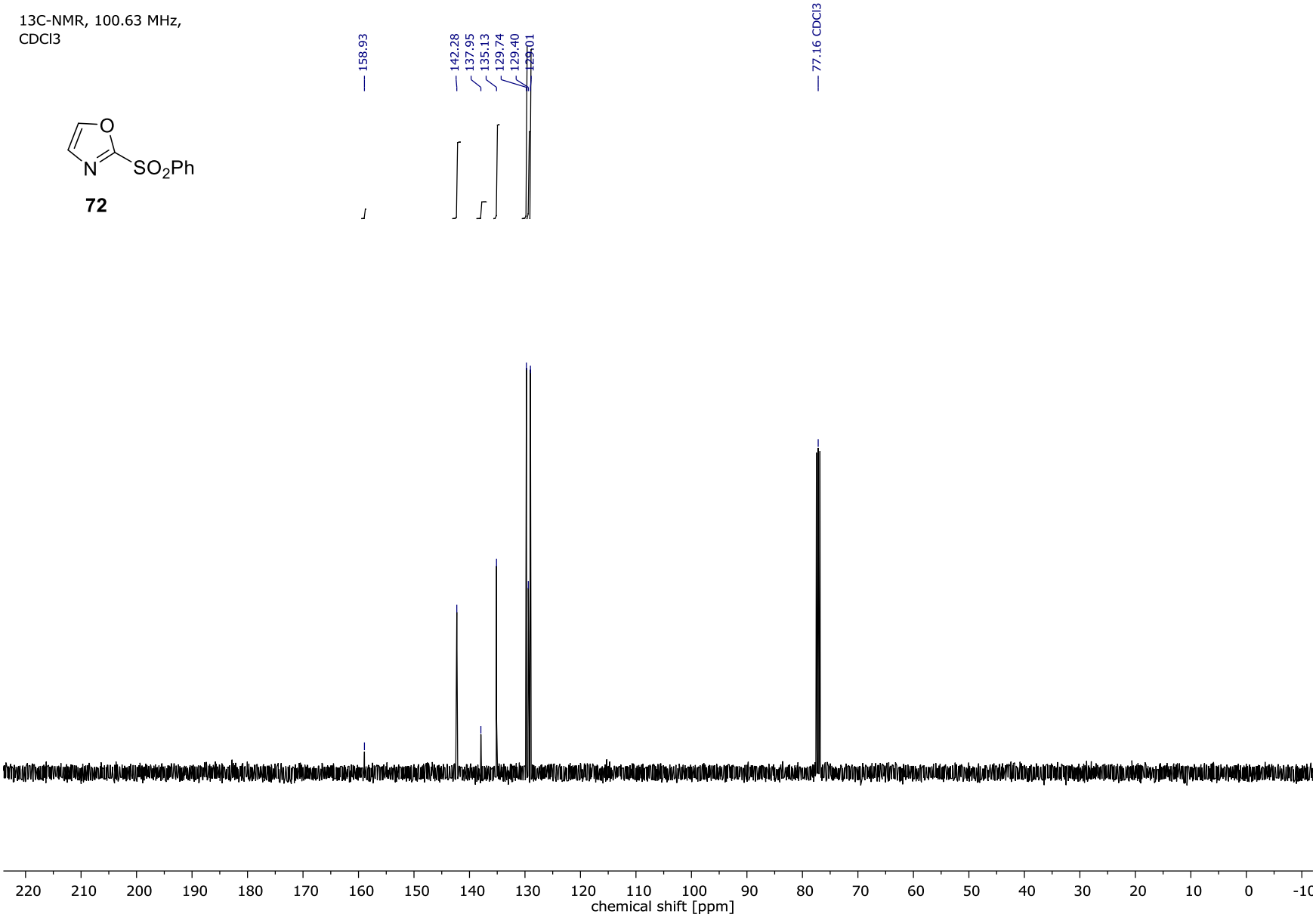
1H-NMR, 400.13 MHz,
CDCl3

72



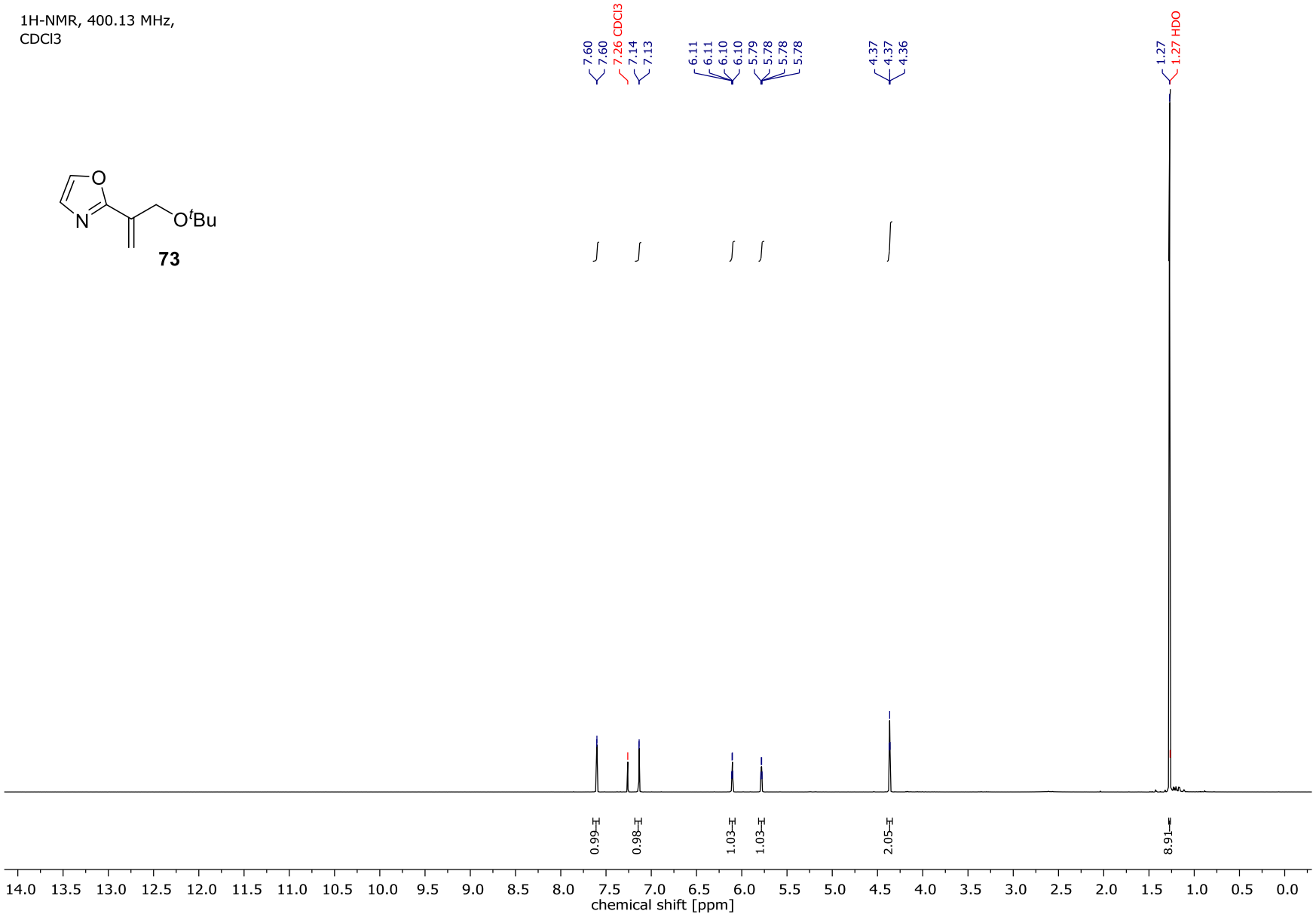
13C-NMR, 100.63 MHz,
CDCl3

72



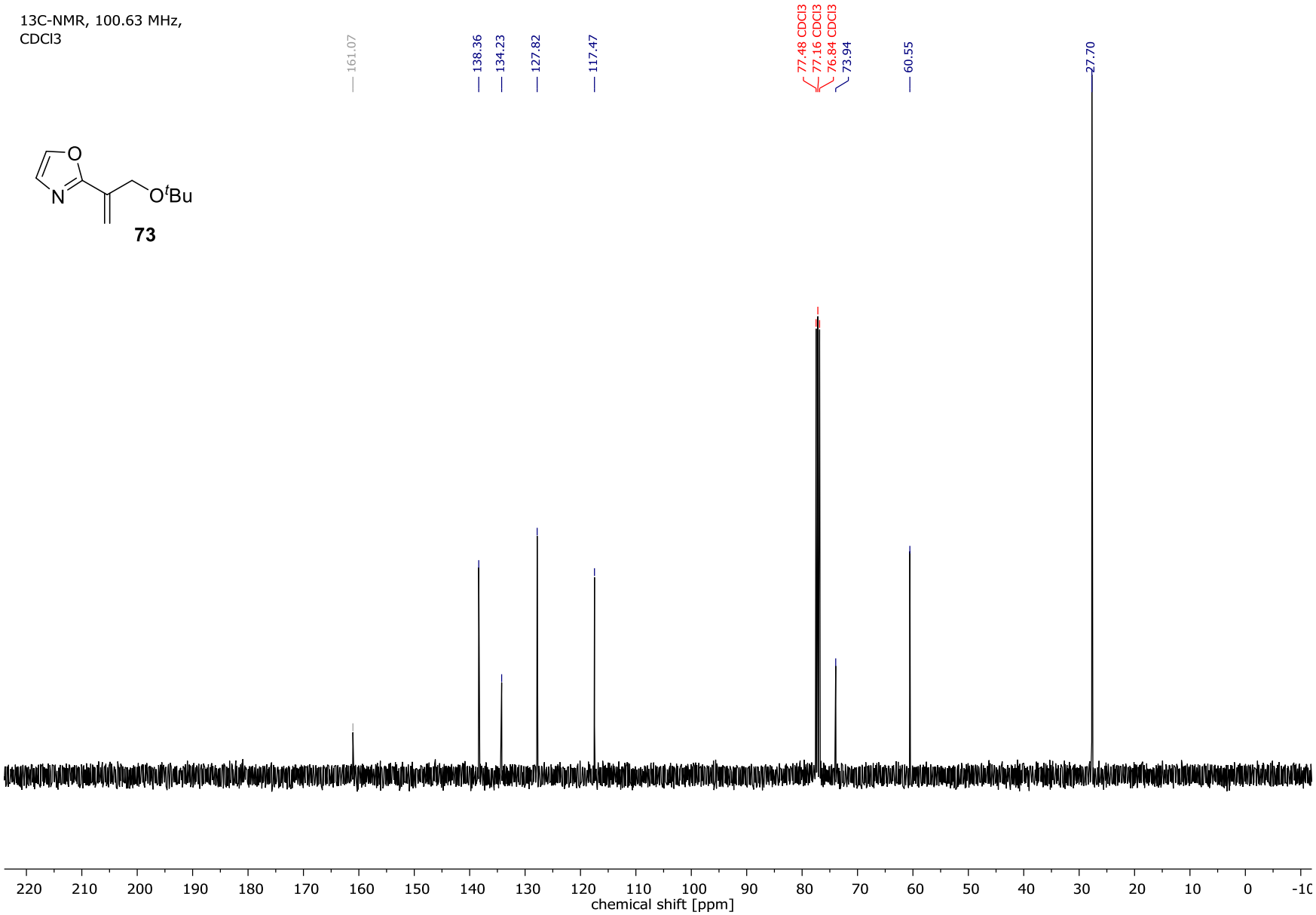
1H-NMR, 400.13 MHz,
CDCl3

73



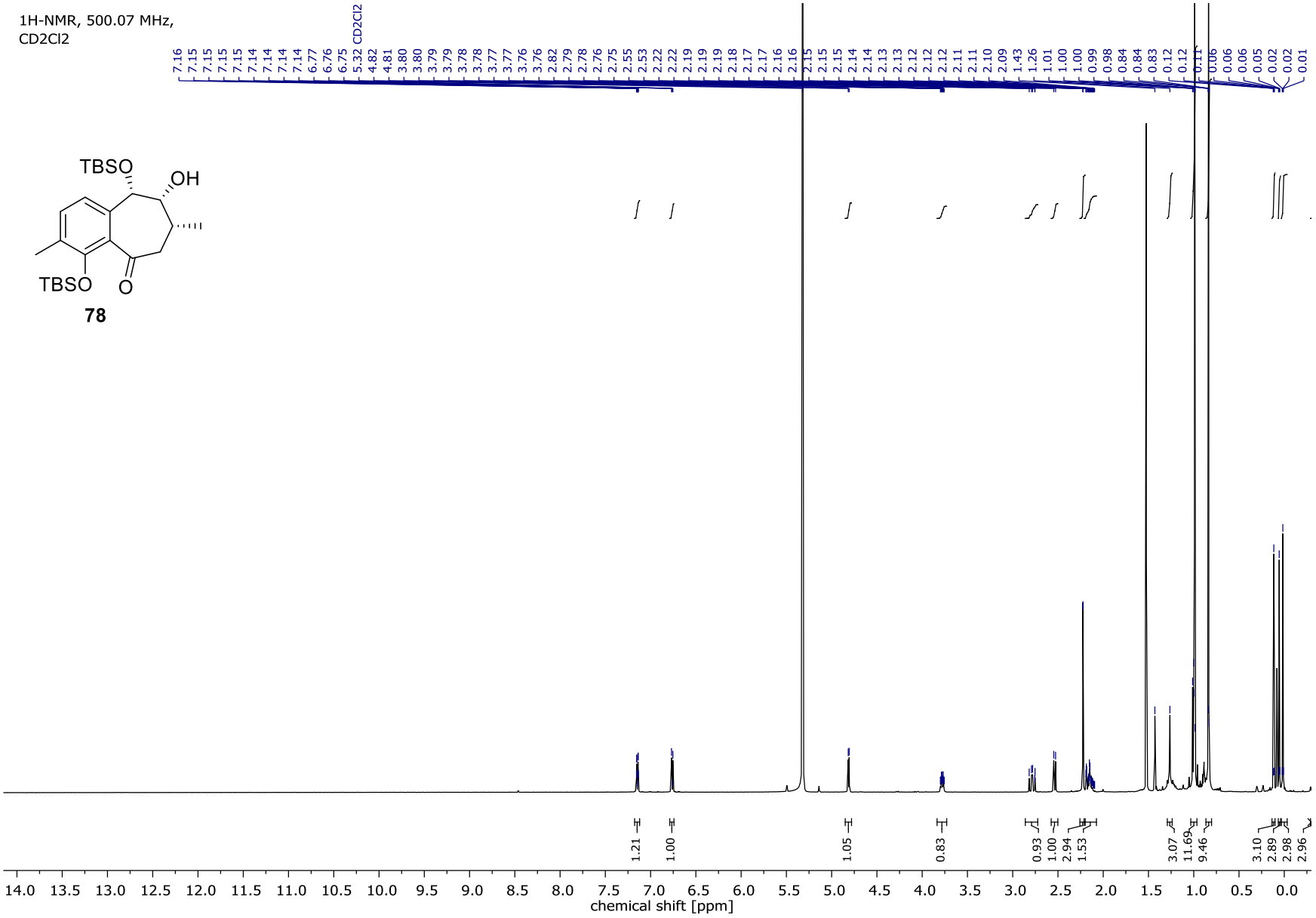
13C-NMR, 100.63 MHz,
CDCl3

73



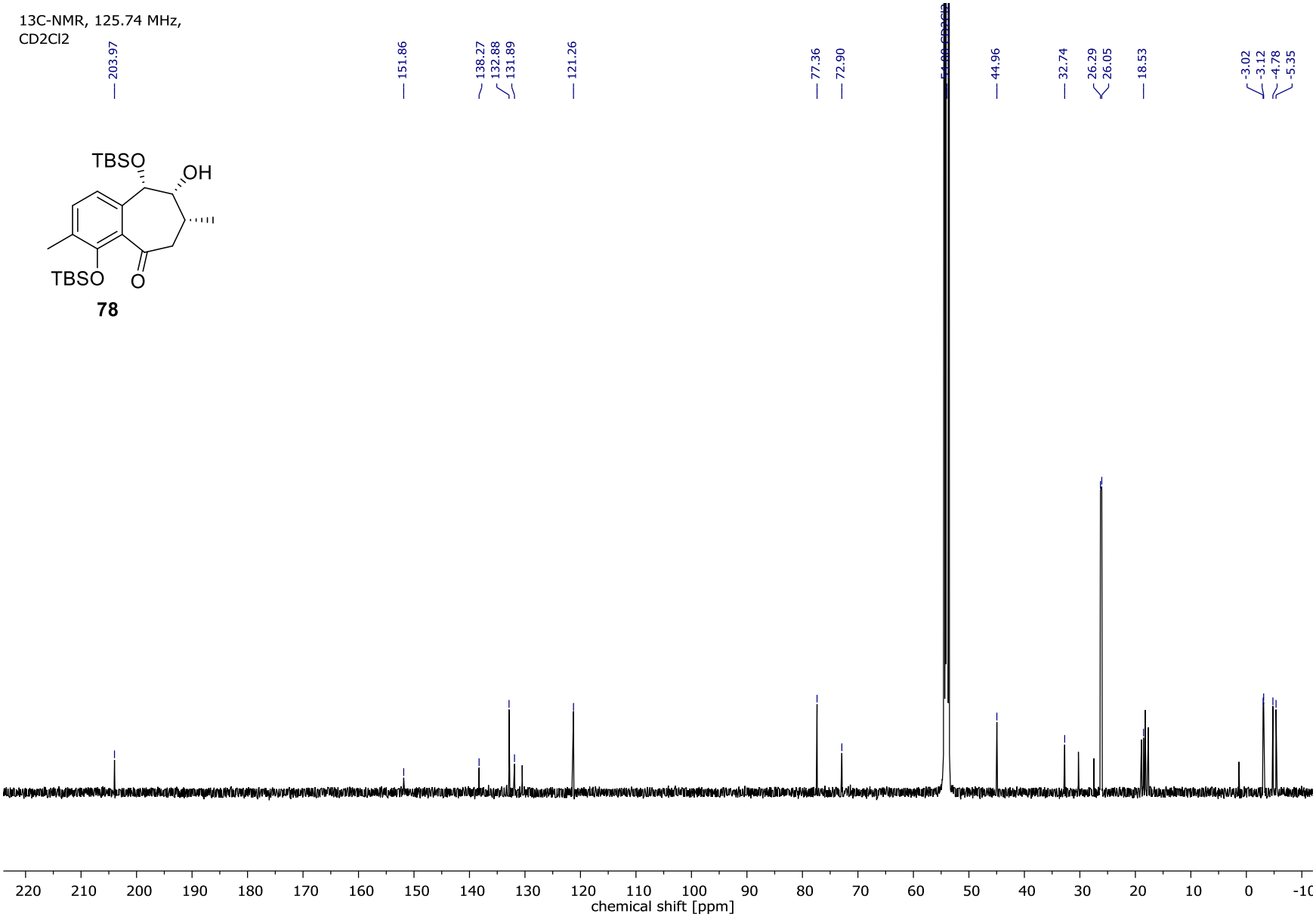
1H-NMR, 500.07 MHz,
CD2Cl2

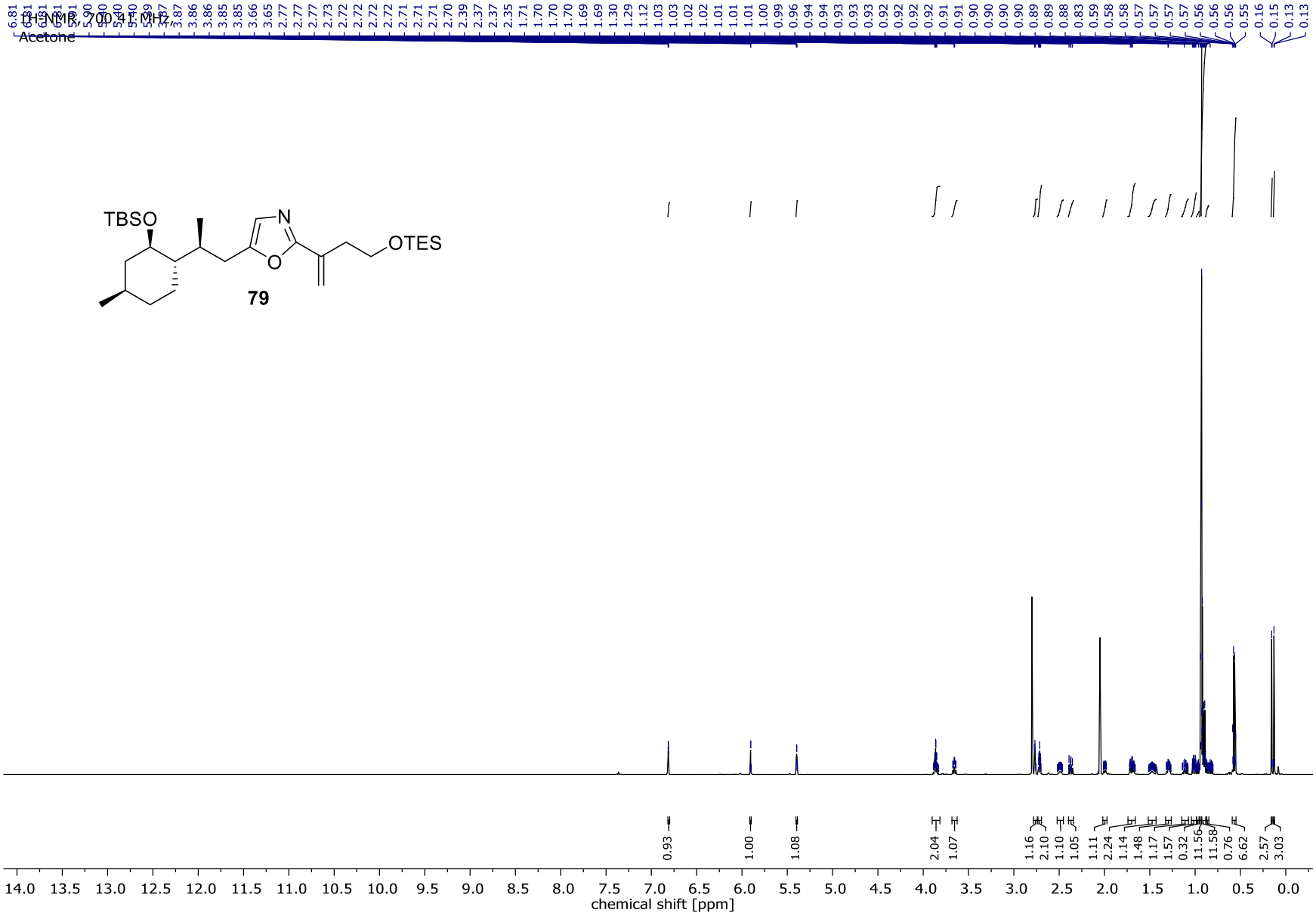
78

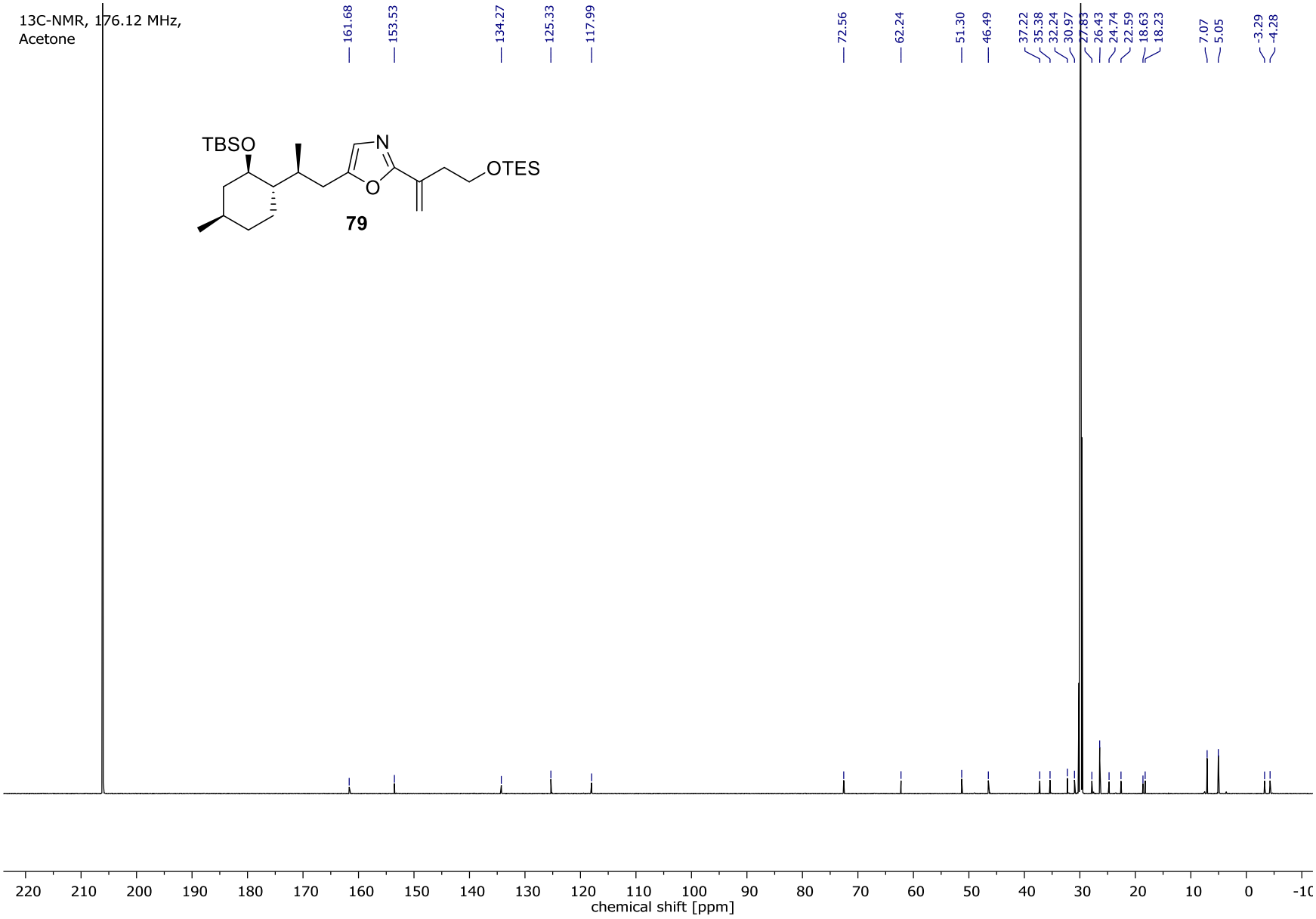


13C-NMR, 125.74 MHz,
CD2Cl2

78




1H-NMR, 700.41 MHz
Acetone
TBSO
N
O
OTES
79
chemical shift [ppm]


13C-NMR, 176.12 MHz,
Acetone
161.68
153.53
134.27
125.33
117.99
72.56
62.24
51.30
46.49
37.22
35.38
32.24
30.97
27.83
26.43
24.74
22.59
18.63
18.23
7.07
5.05
-3.29
-4.28
TBSO
N
O
OTES
79
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
chemical shift [ppm]