Remote α- and β-C(sp^3)-H Alkenylation of Amines via Visible-Light Supported Paired Electrolysis

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Electronic supporting materials

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1. General information

All reactions involving air- or moisture-sensitive reagents or intermediates were carried out in pre-heated glassware using standard Schlenk techniques at ambient room temperature, unless otherwise specified. All commercially available reagents were purchased from Sigma-Aldrich, Alfa Aesar, TCI Chemicals, Across Organics, BLDpharm, or Ambeed in the highest purity grade and used without further purification.

The following solvents (Across ExtraDry solvents with Across Seal® cap) were purchased from Across Organics, stored under 3 or 4 Å activated molecular sieves, and collected under positive argon pressure: acetonitrile (MeCN), dimethylformamide (DMF), dimethylacetamide (DMA), chloroform ($CHCl_3$), and methanol (MeOH).

Anhydrous tetrahydrofuran (THF) was prepared by distillation over sodium in the presence of benzophenone and stored and handled in gas-tight glass ampoules.

Thin layer chromatography (TLC) was performed on Merck silica gel 60 F-254 plates and visualized by fluorescence quenching under UV light or by using standard stain solutions (Hannesian’s stain, KMnO4 stain, vaniline stain, iodine, and bromocresol green stain for free carboxylic acids).

Column chromatography was performed on Merck or Fluka silica gel 60 (40–63 μm) by standard gravity technique or by using automated Flash chromatography systems (Reveleris X2 Flash chromatograph, Buchi C-815 Flash chromatograph, or CombiFlash chromatograph equipped with ELSD and UV-VIS detectors). For small-scale purifications, commercially available silica-gel (230-400 mesh) pre-packed cartridges were used (4 g, 12 g, 24 g and 40 g) and for larger scale ones, the self-packed column cartridges (Biotage, 80 g, 120 g, 220 g, and 330 g) with Merck silica gel 60 (40-63 μm) were used.

NMR Spectra (^1H, ^{13}C) were performed at 25°C and 80°C. ^1H NMR spectra were referenced to residual non-deuterated chloroform (δ 7.26 ppm) in CDCl3 and residual DMSO-d_5 (δ 2.50 ppm) in DMSO-*d6*. ^{13}C NMR spectra were referenced to CDCl3 (δ 77.2 ppm) and DMSO-*d6* (δ 39.5 ppm). Data is presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant *J* (Hz) and integration.

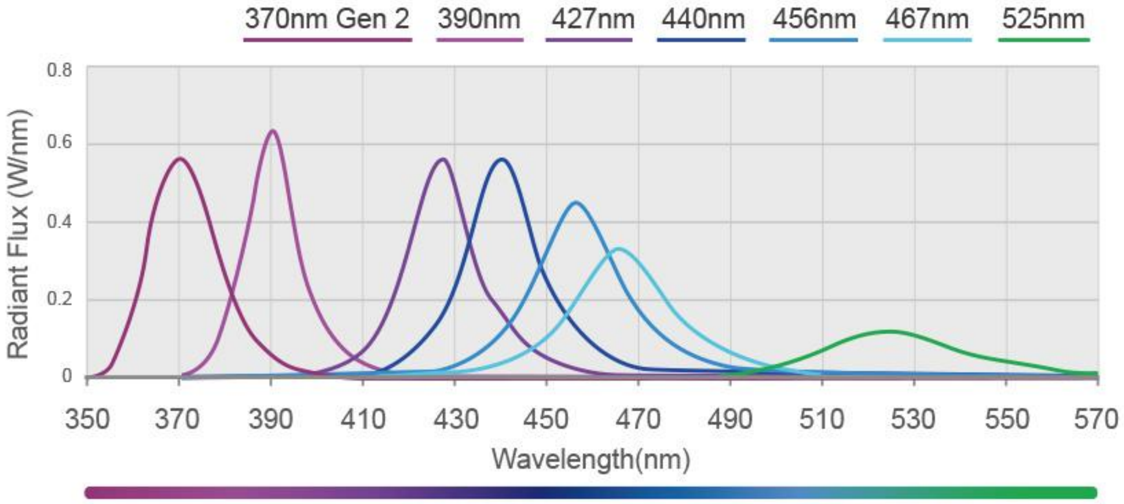
HRMS spectra were recorded on MaldiSYNAPT G2-S HDMS (Waters) spectrometer (for ESI & APCI) and AutoSpec Premier spectrometer (for EI). IR spectra were recorded on FTIR Jasco 6200 spectrometer. UV-Vis spectra were recorded on Hitachi U-1900 spectrophotometer. Fluorescent spectra were recorded on Hitachi F-7000 fluorescence spectrophotometer.Melting points were measured by MPH-H2 melting point meter and were not corrected. Optical rotation was recorded on JASCO P-2000 spectropolarimeter. HPLC analysis was performed on Hitachi HPLC chromatograph (Hitachi L-2130 pump, Hitachi Diode Array L-2450). GC analysis was performed on PerkinElmer Clarus 680 chromatograph equipped with FID detector.

2. Photoelectrochemical setup

For all photochemical transformations the reaction mixtures were irradiated by visible light generated by the Kessil® LED lamps (at 100%, 50% and 25% intensity of light) by COB LED chip modules. Every time the reaction vessel(s) were placed in 5 cm distance from the light source. To maintain constant temperature of the process the vials and lamps were cooled with 2-3 high-speed fans (3000-4500 rpm) connected to thermocontroller equipped with thermocouple element which was mounted directly the reaction vial wall. In case of COB LED lamps, active cooling was used (the LED chip was glued with thermoconductive paste to aluminum radiator equipped with fan module).

Specification of light sources:

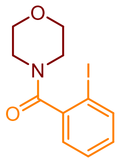
Lamp type		**λ_{max}**	**Electric power consumption**	**Beam angle**	**Average light intensity**
Kessil PR160L		427 nm	45 W	56°	399mW/cm^2
Kessil PR160L		440 nm	45 W	56°	399mW/cm^2
Kessil PR160L		456 nm	50 W	56°	350 mW/cm^2



3. Synthesis of substrates

3.1. Synthesis of *N*-protected amines

List of 2-iodobenzoylated heterocycles examined



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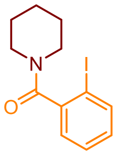

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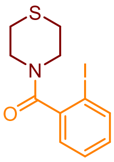

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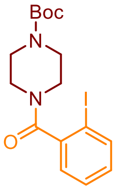

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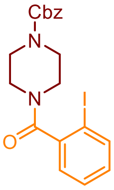

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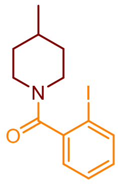

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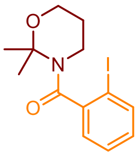

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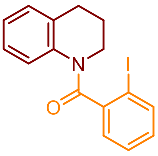

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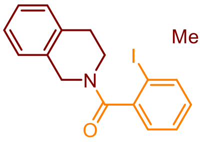

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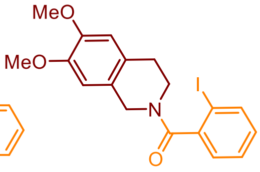

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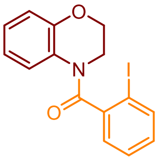

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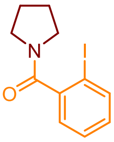

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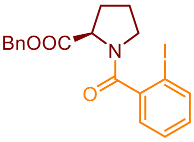

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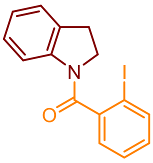

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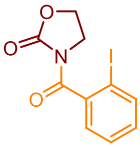

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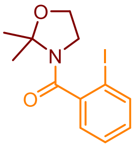

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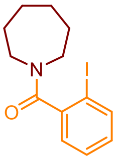

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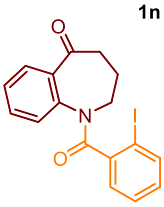

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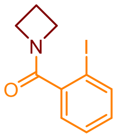

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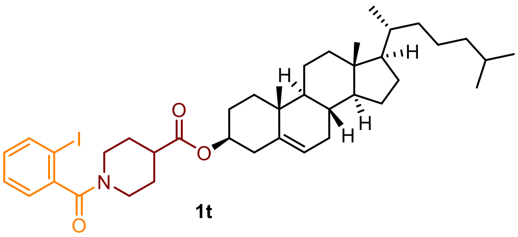

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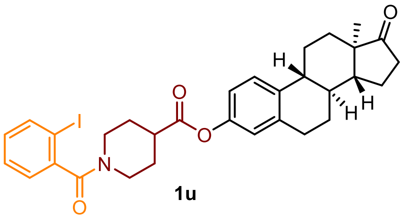

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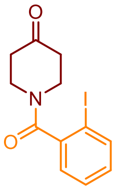

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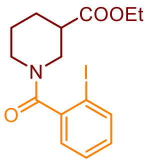

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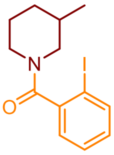

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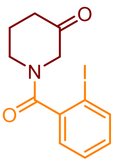

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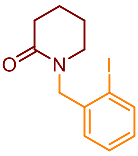

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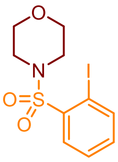

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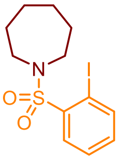

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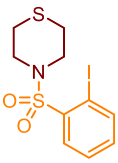

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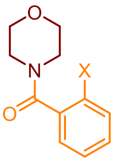
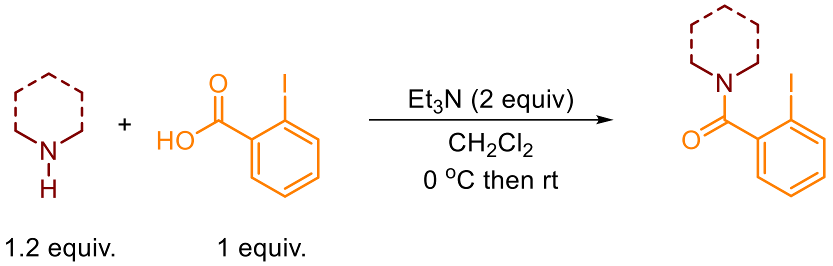
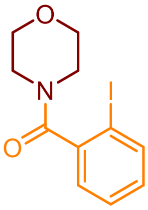


SI-1a, X: Br
SI-1b, X: Cl



General procedure: In an oven-dried round-bottom flask was charged with amine (6 mmol, 1.2 equiv.), Et_3N (10 mmol, 2 equiv.), CH_2Cl_2 (20 mL) and cooled the reaction mixture to 0 °C using the ice bath and then 2-iodobenzoyl chloride (5 mmol, 1 equiv.) was added dropwise to the reaction mixture and stirred overnight at room temperature. After the starting material was consumed (monitored by TLC), the reaction was quenched by adding 1M HCl (10 ml) and extracted with CH_2Cl_2 (2×20 mL). The combined organic phase was washed with brine and dried over Na_2SO_4. The solvent was concentrated and the product was purified by chromatography on silica gel.

***N*-(2-iodobenzoyl)morpholine (1a):**



Yield: 6.00 g (72%) starting from 2-iodobenzoyl chloride (7.03 g, 26.4 mmol) and morpholine (2.76 g, 31.7 mmol, 2.8 mL).

Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v);

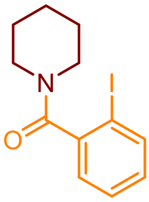
White solid, **m.p.** 91-92 °C [Lit.[1] 91°C];

Spectral data in agreement with previous reports.[2],[3]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.39 (td, *J* = 7.5, 1.1 Hz, 1H), 7.19 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.08 (td, *J* = 7.7, 1.6 Hz, 1H), 3.84 (m, *J* = 13.2, 9.5, 3.5 Hz, 2H), 3.76 (m, *J* = 11.8, 6.5, 3.2, 2.6 Hz, 3H), 3.57 (ddd, *J* = 11.6, 6.5, 3.2 Hz, 1H), 3.27 (ddd, *J* = 13.5, 6.5, 3.2 Hz, 1H), 3.17 (ddd, *J* = 13.4, 6.7, 3.2 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.5, 141.9, 139.4, 130.5, 128.6, 127.2, 92.6, 66.8, 66.7, 47.4, 42.1.

***N*-(2-iodobenzoyl)piperidine (1b):**



Yield: 2.80 g (88%) starting from 2-iodobenzoyl chloride (2.70 g, 10.12 mmol) and piperidine (1.03 g, 12.15 mmol, 1.2 mL).

Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

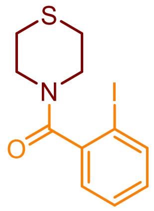
TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v); colorless oil;

Spectral data in agreement with previous reports.[2],[3]

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.81 (d, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.17 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.05 (td, *J* = 7.7, 1.6 Hz, 1H), 3.83 – 3.75 (m, 1H), 3.72 – 3.65 (m, 1H), 3.24 – 3.16 (m, 1H), 3.15 – 3.08 (m, 1H), 1.78 – 1.59 (m, 5H), 1.50 – 1.38 (m, 1H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 169.3, 142.9, 139.3, 130.0, 128.4, 127.0, 92.6, 48.1, 42.7, 26.4, 25.5, 24.6.

N-(2-iodobenzoyl)thiomorpholine (1c):



Yield: 2.80 g (87%) starting from 2-iodobenzoyl chloride (2.58 g, 9.69 mmol) and thiomorpholine (1.20 g, 11.63 mmol, 1.2 mL).

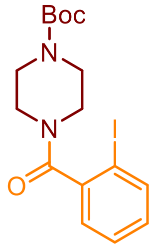
Purification: flash column chromatography on SiO$_2$, eluent: AcOEt/hexanes 50:50 v/v.

TLC: *R*$_F$ 0.5 (AcOEt/hexanes 50:50 v/v); colorless oil; Spectral data in agreement with previous reports.[2],[3]

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.83 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.38 (td, *J* = 7.5, 1.1 Hz, 1H), 7.16 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.07 (td, *J* = 7.7, 1.6 Hz, 1H), 4.13 – 4.05 (m, 1H), 4.05 – 3.98 (m, 1H), 3.54 (ddd, *J* = 13.8, 7.4, 2.9 Hz, 1H), 3.43 (ddd, *J* = 13.8, 7.6, 2.9 Hz, 1H), 2.86 – 2.67 (m, 3H), 2.48 (ddd, *J* = 14.0, 7.4, 2.8 Hz, 1H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 169.6, 142.1, 139.5, 130.4, 128.6, 127.0, 92.6, 49.6, 44.1, 28.0, 27.4.

N^1-Boc *N*^{4}-(2-iodobenzoyl)piperazine (1d):



Yield: 1.76 g (79%) starting from 2-iodobenzoyl chloride (1.43 g, 5.37 mmol) and *N*-Boc piperazine (1.2 g, 6.44 mmol). Purification: column chromatography on SiO$_2$, eluent: AcOEt/hexanes 50:50 v/v.

TLC: *R*$_F$ 0.5 (AcOEt/hexanes 50:50 v/v);

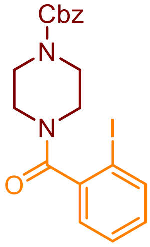
Yellow solid, m.p. 109-110 °C [Lit.[1] 111 °C];

Spectral data in agreement with previous reports.[1],[2],[3]

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.83 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.39 (td, *J* = 7.5, 1.1 Hz, 1H), 7.18 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.08 (td, *J* = 7.7, 1.7 Hz, 1H), 3.88 – 3.77 (m, 1H), 3.77 – 3.66 (m, 1H), 3.62 – 3.46 (m, 3H), 3.40 – 3.30 (m, 1H), 3.29 – 3.19 (m, 1H), 3.18 – 3.08 (m, 1H), 1.46 (s, 9H);

^{13}C NMR (101 MHz, CDCl$_3$) δ 169.6, 154.6, 142.1, 139.5, 130.5, 128.6, 127.2, 92.6, 80.5, 46.9, 43.5, 41.6 (v br), 28.5.

*N*¹-Cbz *N*⁴-(2-iodobenzoyl)piperazine (1e):



Yield: 1.87 g (80%) starting from 2-iodobenzoyl chloride (1.38 g, 5.18 mmol) and *N*-Cbz piperazine (1.37g, 6.22 mmol).

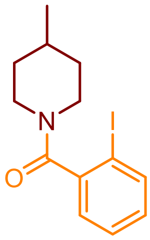
Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v); colorless oil. Spectral data in agreement with previous reports.[2],[3]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.43 – 7.28 (m, 6H), 7.18 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.09 (td, *J* = 7.7, 1.7 Hz, 1H), 5.14 (s, 2H), 3.86 (s, 1H), 3.72 (d, *J* = 14.9 Hz, 1H), 3.62 (dq, *J* = 13.7, 4.1, 3.6 Hz, 3H), 3.44 (ddd, *J* = 13.2, 6.8, 3.5 Hz, 1H), 3.32 – 3.22 (m, 1H), 3.32 – 3.22 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.6, 155.2, 141.9, 139.4, 136.4, 130.6, 128.7, 128.6, 128.3, 128.1, 127.1, 92.5, 67.6, 46.7, 41.5.

4-methyl *N*-(2-iodobenzoyl)piperidine (1f):



Yield: 2.44 g (86%) starting from 2-iodobenzoyl chloride (2.29 g, 8.61 mmol) and 4-methylpiperidine (1.03 g, 10.33 mmol).

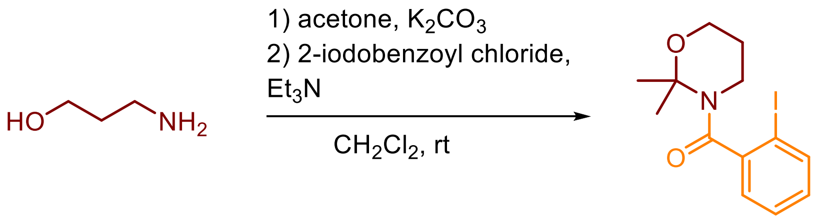
Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v); yellow oil;
Spectral data in agreement with previous reports.[2],[3]

^{1}H NMR (500 MHz, $CDCl_3$, mixture of rotamers) δ 7.81 (dd, *J* = 14.3, 7.9 Hz, 1H), 7.36 (q, *J* = 7.8 Hz, 1H), 7.24 – 7.10 (m, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 4.78 – 4.65 (m, 1H), 3.40 – 3.29 (m, 1H), 3.05 (td, *J* = 12.9, 2.8 Hz, 0.5×1H), 2.95 – 2.86 (m, 0.5×1H), 2.78 (tt, *J* = 12.8, 3.5 Hz, 1H), 1.82 – 1.71 (m, 1H), 1.70 – 1.50 (m, 2H), 1.50 – 1.28 (m, 1H), 1.26 – 1.00 (m, 1H), 0.97 (t, *J* = 6.6 Hz, 3H);

^{13}C NMR (126 MHz, $CDCl_3$, mixture of rotamers) δ 169.2, 169.1, 142.8, 142.8, 139.33, 139.0, 129.9, 129.9, 128.3, 128.2, 126.9, 126.8, 92.6, 92.4, 47.6, 46.9, 41.9, 41.8, 34.5, 34.3, 33.7, 33.4, 31.1, 31.0, 21.7, 21.6.

N-Bz 2,2-dimethyl-1,3-oxazinane (1g):



Anhydr. K_2CO_3 (1.5c g, 11.0 mmol, 1.36 eq) was placed with magnetic mixer in an oven-dried 10-mL round-bottom flask sealed with septa, followed by an addition of anhydr. CH_2Cl_2 (12 mL), 3-amino-1-propanol and 1.1 mL of acetone (0.87 g, 14.9 mmol). The resulting mixture was stirred at room temperature overnight. Next, Et_3N (1.64 g, 16.2 mmol, 2 equiv.) was added followed by dropwise addition of a solution of 2-iodobenzoyl chloride (2.38 g, 8.9 mmol) in 10 mL of anhydr. CH_2Cl_2. The resulting mixture was stirred at room temperature overnight. On the next day, the reaction mixture was diluted with water and extracted with CH_2Cl_2 (3× 50 mL). The combined organic extracts were washed with brine, dried over anhydr. Na_2SO_4, filtered and solvent and volatiles were removed. The residue was purified by flash column chromatography on neutralized to provide product **1g** (1.6g, 59%) as a white solid. M.p. 98-99°C.

Purification: automated flash column chromatography on SiO_2

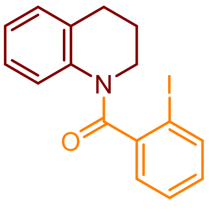
Cartridge size	1× 120 g (silica gel)
Flow	45 mL/min
Eluent	40% AcOEt in petroleum ether (+ 1-2% v/v Et_3N) for 15 min, then gradient from 40% to 45% AcOEt in PE for 5 min, and 45% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.6 (40% EtOAc in Hexanes)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.36 (td, *J* = 7.5, 1.2 Hz, 1H), 7.17 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.04 (td, *J* = 7.7, 1.7 Hz, 1H), 3.96 – 3.81 (m, 2H), 3.40 – 3.29 (m, 1H), 3.27 – 3.15 (m, 1H), 2.04 – 1.91 (m, 1H), 1.88 – 1.74 (m, 7H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 143.8, 139.3, 129.9, 128.5, 126.7, 92.2, 89.4, 57.6, 40.9, 24.7, 24.4, 23.7.

HRMS (ESI-TOF+) *m/z* calcd for $C_{13}H_{16}NO_2INa$ [(M+Na)+] 368.0123; Found 368.0124.

N-(2-iodobenzoyl)-1,2,3,4-tetrahydroquinoline (1h):



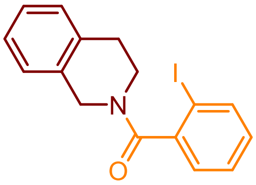
Yield: 2.21 g (76%) starting from 2-iodobenzoyl chloride (2.12 g, 7.97 mmol) and 1,2,3,4-tetrahydroquinoline (1.27 g, 9.56 mmol).
Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 20:80 v/v.

TLC: *R*F 0.5 (AcOEt/hexanes 20:80 v/v); White solid, **m.p.** 138-139 °C; [Lit. 133-135 °C[4]]; Spectral data in agreement with previous reports.[5],[6]

^{1}H NMR (600 MHz, dmso-d6, 80 oC, mixture of rotamers) δ 7.83 (d, *J* = 7.9 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.17 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.16 – 7.10 (m, 1H), 7.03 (t, *J* = 7.3 Hz, 1H), 7.00 – 6.91 (m, 1H), 3.79 – 3.52 (m, 2H), 2.84 (t, *J* = 6.7 Hz, 2H), 2.05 – 1.93 (m, 2H);

^{13}C NMR (151 MHz, DMSO-d_6, 80 °C, mixture of rotamers) δ 168.4, 142.5, 138.5, 137.5, 131.0, 129.9, 128.2, 127.8, 124.9, 124.2, 123.7, 92.8, 44.4 (v br), 26.0, 22.7.

N-(2-iodobenzoyl)-1,2,3,4-tetrahydroisoquinoline (1i):



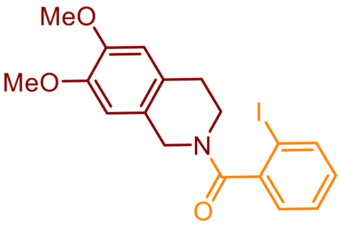
Yield: 2.30 g (79%) starting from 2-iodobenzoyl chloride (2.13 g, 7.98 mmol) and 1,2,3,4-tetrahydroisoquinoline (1.28 g, 9.59 mmol). Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 20:80 v/v.

TLC: *R*F 0.5 (AcOEt/hexanes 20:80 v/v); pale-yellow oil; Spectral data in agreement with previous reports.[2]

^{1}H NMR (500 MHz, $CDCl_3$, mixture of rotamers) δ 7.84 (d, *J* = 7.8 Hz, 1H), 7.46 – 7.35 (m, 1H), 7.33 – 6.88 (m, 6H), 5.20 – 4.74 (m, 1H), 4.50 – 4.24 (m, 1H), 4.09 – 3.95 (m, 1H), 3.56 – 3.39 (m, 1H), 3.10 – 2.74 (m, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.02, 169.69, 142.72, 142.63, 139.36, 134.76, 133.87, 132.71, 132.59, 130.41, 130.35, 129.01, 128.68, 128.61, 128.57, 127.23, 127.11, 127.02, 126.88, 126.80, 126.73, 126.46, 126.09, 92.68, 92.51, 48.78, 44.60, 44.35, 40.04, 29.61, 28.50.

N-(2-iodobenzoyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (1j):



Yield: 1.60 g (87%) starting from 2-iodobenzoyl chloride (1.16 g, 4.35 mmol) and 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (1.20 g, 5.22 mmol).

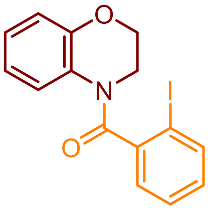
Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 20:80 v/v.

TLC: *R*F 0.5 (AcOEt/hexanes 20:80 v/v); pale-yellow solid, **m.p.:** 113-114 °C;

^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers) δ 7.89 (d, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 7.5 Hz, 0.6×1H), 7.22 (d, *J* = 8.0 Hz, 0.4×1H), 7.17 (td, *J* = 7.7, 1.7 Hz, 1H), 6.85 (s, 0.5×1H), 6.75 (s, 0.5×1H) 6.72 (s, 0.6×1H), 6.58 (s, 0.4×1H), 4.70 (s, 1H), 4.21 (s, 1H), 3.90 – 3.60 (m, 8H), 3.33 (t, *J* = 5.9 Hz, 1H), 2.84 – 2.79 (br m, 1H), 2.76 – 2.69 (m, 1H);

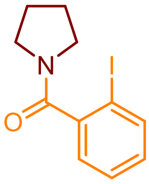
^{13}C NMR (126 MHz, DMSO-*d*$_6$, mixture of rotamers) δ 169.2, 168.9, 148.6, 148.5, 143.2, 139.3, 130.7, 128.9, 127.6, 126.6, 125.3, 113.4, 111.6, 110.9, 93.3, 93.1, 56.5, 56.4, 48.3, 44.6, 43.8, 28.8, 27.8;
HRMS (ESI-TOF+) *m/z* calcd for $C_{18}H_{17}NO_3I$ [(M+H)+] 422.0253; found 422.0248.

N-(2-iodobenzoyl)-benzo[*b*]morpholine (1k):



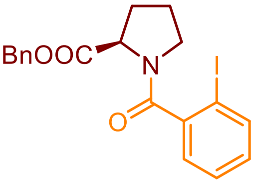
Yield: 1.36 g (92%) starting from 2-iodobenzoyl chloride (1.08 g, 4.05 mmol) and benzo[*b*]morpholine (0.66 g, 4.87 mmol). Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 20:80 v/v.
TLC: R_F 0.5 (AcOEt/hexanes 20:80 v/v); yellow oil;
Spectral data in agreement with previous reports.[3]
^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80 °C) δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.52 – 7.43 (m, 1H), 7.40 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H), 7.01 (t, *J* = 7.8 Hz, 1H), 6.89 (dd, *J* = 8.2, 1.5 Hz, 1H), 6.84 – 6.65 (m, 1H), 4.36 (br s, 2H), 3.72 (br s, 2H);
^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C) δ 167.5, 146.1, 141.5, 138.6, 130.3, 128.1, 127.8, 125.2, 125.1, 122.9, 119.3, 116.5, 92.5, 65.1.

N-(2-iodobenzoyl)pyrrolidine (1l):



Yield: 3.87 g (92%) starting from 2-iodobenzoyl chloride (3.75 g, 14.06 mmol) and pyrrolidine (1.20 g, 16.87 mmol, 1.4 mL). Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.
TLC: R_F 0.5 (AcOEt/hexanes 20:80 v/v); yellow solid, **m.p.** 77-78 °C [Lit.[1] 75 °C]
Spectral data in accordance with previous reports.[2],[3]
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.37 (td, *J* = 7.5, 1.1 Hz, 1H), 7.22 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.05 (td, *J* = 7.7, 1.6 Hz, 1H), 3.65 (t, *J* = 6.9 Hz, 2H), 3.14 (t, *J* = 6.7 Hz, 2H), 1.99 – 1.93 (m, 2H), 1.93 – 1.86 (m, 2H);
^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 143.9, 139.1, 130.0, 128.4, 126.8, 92.1, 48.4, 45.5, 25.9, 24.5.

(*R*)-*N*-(2-iodobenzoyl)proline benzyl ester (1m):



Yield: 800 mg (89%) starting from 2-iodobenzoyl chloride (551 mg, 2.07 mmol) and D-proline benzyl ester hydrochloride (1.20 g, 16.87 mmol, 1.4 mL). Purification:

column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

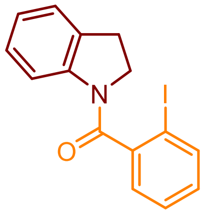
TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v); Colorless sticky oil; **$[\alpha]_D^{23}$** +59.3 (c 1.8, $CHCl_3$);

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, mixture of rotamers/conformers in a ratio 3:1) δ 7.88 (d, *J* = 8.3 Hz, 0.75×1H), 7.84 (d, *J* = 7.9 Hz, 0.25×1H), 7.50 – 7.30 (m, 5H), 7.24 – 7.02 (m, 3H), 5.21 (s, 0.75×2H), 5.03 – 4.96 (m, 0.25×2H), 4.58 (dd, *J* = 8.8, 4.5 Hz, 0.75×1H), 4.06 (dd, *J* = 8.6, 2.9 Hz, 0.25×1H), 3.71 – 3.57 (m, 0.25×2H), 3.26 – 3.15 (m, 0.75×2H), 2.37 – 2.23 (m, 1H), 2.09 – 1.83 (m, 3H).

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, mixture of rotamers/conformers) δ 170.78, 167.51, 142.50, 138.56, 138.41, 135.70, 130.09, 130.02, 128.01, 127.96, 127.72, 127.55, 127.52, 127.38, 127.07, 126.61, 91.42, 65.92, 65.57, 60.11, 58.01, 48.02, 45.56, 30.32, 28.68, 24.02, 22.05;

HRMS (ESI-TOF+) *m/z* calcd for $C_{19}H_{18}NO_3INa$ [(M+Na)+] 458.0229; found 458.0232.

N-(2-iodobenzoyl)indoline (1n):



Yield: 2.13 g (68%) starting from 2-iodobenzoyl chloride (2.38 g, 8.92 mmol) and indoline (1.28 g, 10.70 mmol, 1.2 mL). Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 30:70 v/v. TLC: R_F 0.4 (AcOEt/hexanes 20:80 v/v);

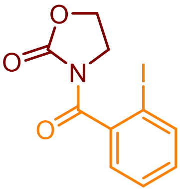
Off-white solid, **m.p.** 127-128 °C [Lit.[1] 127 °C]

Spectral data in accordance with previous reports.[2],[3]

^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers) δ 8.15 (d, *J* = 7.9 Hz, 1H), 7.91 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.52 (qd, *J* = 7.3, 1.1 Hz, 1H), 7.42 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.30 – 7.17 (m, 4H), 7.07 (td, *J* = 7.4, 1.1 Hz, 1H), 3.65 (t, *J* = 8.3 Hz, 2H), 3.10 (t, *J* = 8.3 Hz, 2H);

^{13}C NMR (126 MHz, DMSO-d_6, mixture of rotamers) δ 167.8, 167.1, 143.6, 143.1, 142.6, 141.2, 139.6, 139.3, 133.9, 132.9, 131.7, 131.1, 129.5, 129.1, 128.2, 127.6, 127.4, 127.3, 126.2, 125.5, 124.7, 123.8, 116.8, 113.3, 93.8, 93.1, 49.9, 48.0, 27.9, 26.6.

N-(2-iodobenzoyl)oxazolidine-2-one (1o):



Yield: 2.31 g (75%) starting from 2-iodobenzoyl chloride (2.85 g, 10.69 mmol) and oxazolidine-2-one (1.2 g, 12.83 mmol). Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

TLC: R_F = 0.4 (AcOEt/hexanes 50:50 v/v);

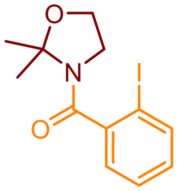
White solid, **m.p.:** 110-111 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.41 (td, *J* = 7.6, 1.1 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.15 (td, *J* = 7.7, 1.7 Hz, 1H), 4.48 (dd, *J* = 8.6, 7.4 Hz, 2H), 4.20 (dd, *J* = 8.6, 7.4 Hz, 2H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 152.1, 140.4, 138.8, 131.3, 128.0, 127.5, 91.7, 62.3, 42.5;

HRMS (ESI-TOF+) *m/z* calcd for $C_{10}H_8NO_3INa$ [(M+Na)+] 339.9447; found 339.9445.

N-(2-iodobenzoyl)-2,2-dimethyloxazolidine (1p):



Prepared following the procedure for **1g**. Yield: 3.8 g (77%) starting from 2-aminoethanol (0.91 g, 15 mmol mmol) Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 40:60 v/v. TLC: R_F 0.65 (AcOEt/hexanes 50:50 v/v); white solid.

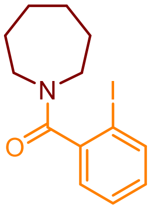
m.p. 86-87 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.39 (td, *J* = 7.5, 1.1 Hz, 1H), 7.23 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.11 – 7.02 (m, 1H), 3.97 (t, *J* = 6.3 Hz, 2H), 3.29 (t, *J* = 6.1 Hz, 2H), 1.75 (s, 6H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 143.9, 139.4, 130.3, 128.7, 126.5, 95.1, 91.7, 63.6, 48.0, 24.4;

HRMS (ESI-TOF) *m/z* calcd for $C_{12}H_{14}NO_2INa$ [(M+Na)+] 363.9967; found 353.9965.

N-(2-iodobenzoyl)azepane (1q):



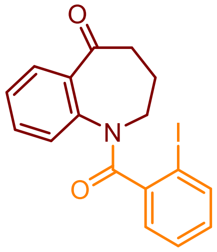
Yield: 1.5 g (90%) starting from 2-iodobenzoyl chloride (1.34 g, 5.04 mmol) and azepane (0.60 g, 6.05 mmol, 0.58 mL). Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v); yellow sticky solid. Spectral data in accordance with previous reports.[1]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.36 (td, *J* = 7.5, 1.1 Hz, 1H), 7.18 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.04 (td, *J* = 7.7, 1.6 Hz, 1H), 3.87 – 3.70 (m, 1H), 3.69 – 3.54 (m, 1H), 3.22 (t, *J* = 5.4 Hz, 2H), 1.94 – 1.77 (m, 2H), 1.77 – 1.45 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 143.4, 139.3, 129.9, 128.3, 127.1, 92.9, 49.4, 45.5, 29.0, 28.0, 27.5, 26.8.

N-(2-iodobenzoyl)-1,2,3,4-tetrahydro-5*H*-benzo[*b*]azepin-5-one (1r):

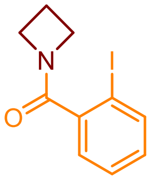


Yield: 2.10 g (86%) starting from 2-iodobenzoyl chloride (1.65 g, 6.02 mmol) and azepane (0.60 g, 6.05 mmol, 0.58 mL). Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 20:80 v/v.
TLC: R_F 0.5 (AcOEt/hexanes 20:80 v/v);
yellow solid; **m.p.** 141-142 °C;
^{1}H NMR (500 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 7.76 – 7.67 (m, 2H), 7.26 – 7.20 (m, 2H), 7.10 – 7.00 (m, 2H), 6.85 (td, *J* = 7.7, 1.6 Hz, 1H), 6.78 (s, 1H), 3.72 – 3.51 (m, 1H), 2.89 (t, *J* = 6.1 Hz, 2H), 2.28 – 2.05 (m, 2H), 1.97 – 1.77 (m, 1H);

^{13}C NMR (126 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 202.4, 170.2, 141.7, 139.5, 135.3, 133.0, 130.7, 130.1, 129.5, 129.4, 128.8, 128.6, 128.0, 127.5, 127.3, 95.0, 92.6 50.4, 46.1, 40.2, 39.9, 34.2, 24.4, 21.8;

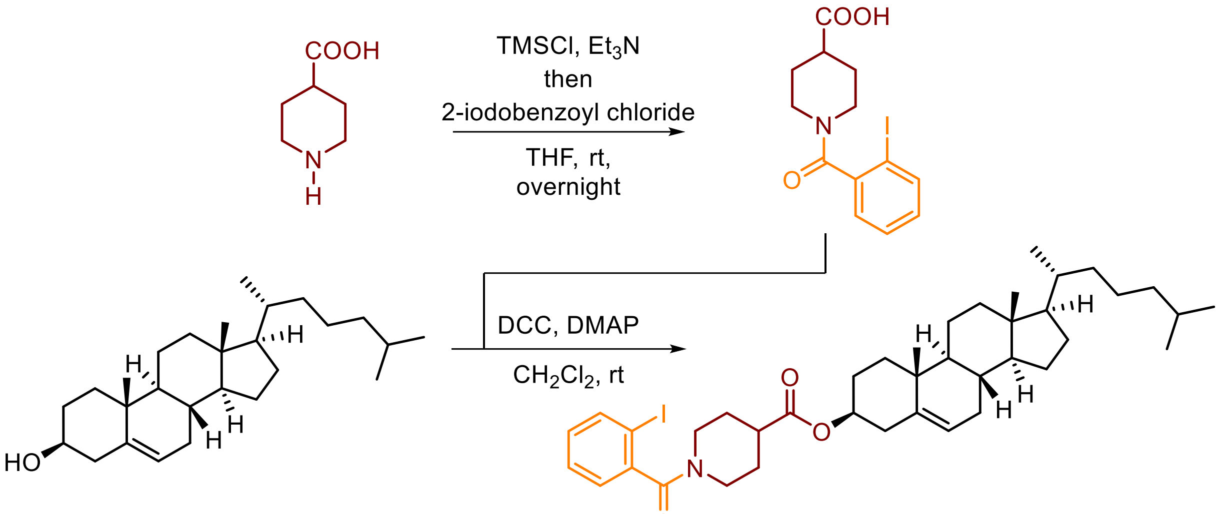
HRMS (ESI-TOF) *m/z* calcd for $C_{17}H_{14}NO_2INa$ [(M+Na)+] 413.9967; found 413.9959.

N-(2-iodobenzoyl)azetidine (1s):



Yield: 2.31 g (75%) starting from 2-iodobenzoyl chloride (2.85 g, 10.69 mmol) and azetidine hydrochloride (1.2 g, 12.83 mmol). Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.
TLC: R_F 0.48 (AcOEt/hexanes 50:50 v/v); White solid, **m.p.:** 117-118 °C; Spectral data in accordance with previous reports.[7]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (td, *J* = 7.5, 1.1 Hz, 1H), 7.23 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.06 (td, *J* = 7.7, 1.7 Hz, 1H), 4.26 – 4.19 (m, 2H), 3.96 – 3.87 (m, 2H), 2.39 – 2.26 (m, 2H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 140.8, 139.4, 130.7, 128.4, 127.7, 92.5, 51.3, 48.6, 15.7.

Cholesterol derivative 1t:



1t

An oven-dried 25 mL round-bottom flask containing a stirring bar was charged with piperidine-4-carboxylic acid (1.00 g, 7.74 mmol) and capped under N_2 atmosphere (glovebox) with a septum. Then, TMSCl (1.34 mL, 1.15 g, 10.6 mmol) and dry THF (30 mL) ware added followed by dropwise addition of Et_3N (1.5 mL, 1.07 g, 10.6 mmol). The resulting mixture was stirred for 2 h. Then, 2-iodobenzoyl chloride (1.88 g, 7.04 mmol) in 5 mL of THF was added and the resulting mixture was stirred overnight, before diluting with 50 mL water and extracting with 2M NaOH followed by neutralizing with 2M HCl and extracted with CH_2Cl_2. After drying over anhydr. Na_2SO_4 and removal of solvent, to the crude piperidine derivative, DCC (1.60 g, 7.74 mmol), cholesterol (2.72 g, 7.04 mmol), DMAP (86 mg, 0.7 mmol) and 30 mL of CH_2Cl_2 were added and stirred at room temperature until completion (monitored by TLC). After aqueous work-up and extraction with CH_2Cl_2, the crude product **1t** (mixture of rotamers) was isolated by automated flash column chromatography to give 2.5 g (44%, 2 steps) as a white solid.

Cartridge size	1× 120 g (silica gel)
Flow	35 mL/min
Eluent	10% AcOEt in petroleum ether for 15 min, then gradient from 10% to 15% AcOEt in PE for 5 min, and 15% AcOEt in PE for 10 min, then gradient from 15% to 25% AcOEt in PE for 5min, and 25% AcOEt in PE for 20 min.
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.35 (30% AcOEt in hexanes))

m.p. 151-152°C

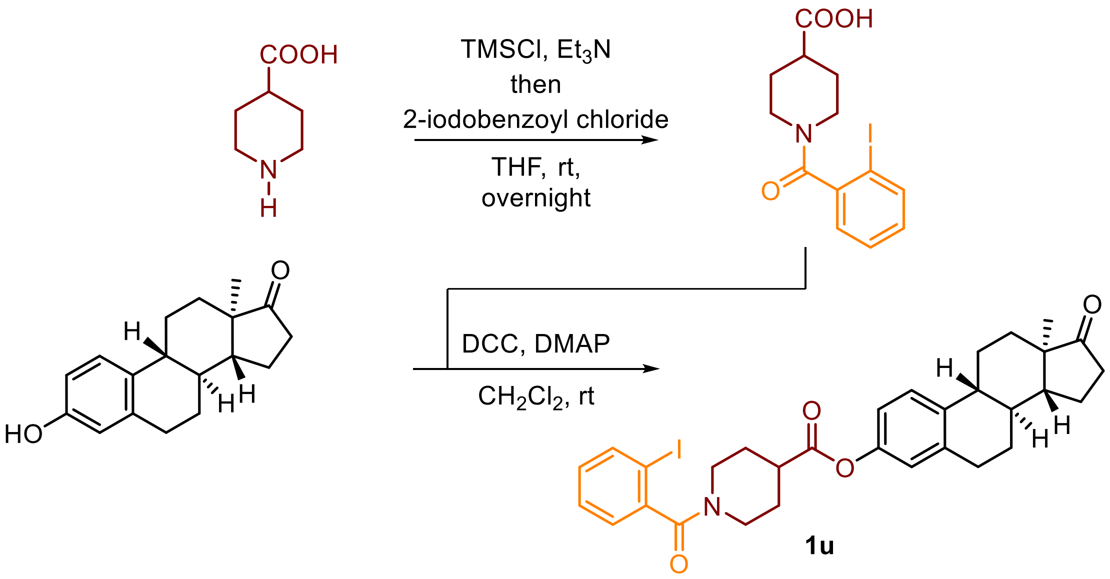
$[\alpha]_D^{28}$ −19.2 (*c* 0.83, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$ mixture of rotamers) δ 7.82 (t, *J* = 8.8 Hz, 1H), 7.18 (ddd, *J* = 28.7, 7.6, 1.7 Hz, 1H), 7.06 (t, *J* = 7.7 Hz, 1H), 5.37 (t, *J* = 4.9 Hz, 1H), 4.68 – 4.47 (m, 2H), 3.48 – 3.32 (m, 1H), 3.16 – 2.94 (m, 2H), 2.59 – 2.49 (m, 1H), 2.35 – 2.24 (m, 2H), 2.11 – 1.91 (m, 4H), 1.91 – 1.72 (m, 5H), 1.64 – 1.40 (m, 9H), 1.39 – 1.21 (m, 5H), 1.21 – 1.05 (m, 7H), 1.05 – 0.94 (m, 7H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.86 (dd, *J* = 6.6, 2.2 Hz, 6H), 0.67 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 173.75, 173.59, 169.44, 169.38, 142.64, 142.54, 139.62, 139.58, 139.51, 139.28, 130.29, 130.24, 128.57, 128.41, 127.11, 126.92, 122.95, 92.65, 92.50, 74.38, 74.37, 56.83, 56.29, 50.16, 46.56, 46.08, 42.46, 41.21, 41.17, 41.05, 40.94, 39.87, 39.66, 38.23, 38.21, 37.09, 36.73, 36.33, 35.92, 32.04, 32.00, 28.55, 28.35, 28.14, 27.99, 27.91, 27.68, 24.42, 23.97, 22.95, 22.69, 21.18, 19.45, 18.86, 12.00.

HRMS (ESI-TOF) *m/z* calcd for $C_{40}H_{58}NO_3INa$ [(M+Na)+] 750.3359; found 750.3349.

Estrone derivative 1u:



1u

An oven-dried 25 mL round-bottom flask containing a stirring bar was charged with piperidine-4-carboxylic acid (0.50 g, 3.87 mmol) and capped under N_2 atmosphere (glovebox) with a septum. Then, TMSCl (670 μL, 0.57 g, 5.3 mmol) and dry THF (15 mL) ware added followed by dropwise addition of Et_3N (740 μL, 0.53 g, 5.3 mmol). The resulting mixture was stirred for 2 h. Then, 2-iodobenzoyl chloride (0.94 g, 3.52 mmol) in 5 mL of THF was added and the resulting mixture was stirred overnight, before diluting with 30 mL water and extracting with 2M NaOH followed by neutralizing with 2M HCl and extracted with CH_2Cl_2. After drying over anhydr. Na_2SO_4 and removal of solvent, to the crude piperidine derivative, DCC (0.80 g, 3.87 mmol), estrone (0.95 g, 3.52 mmol), DMAP (43 mg, 0.35 mmol) and 30 mL of CH_2Cl_2 were added and stirred at room temperature until completion (monitored by TLC). After aqueous work-up and extraction with CH_2Cl_2, the crude product **1u** (mixture of rotamers) was isolated by automated flash column chromatography to give 1.57 g (41%, 2 steps) as a white solid.

Cartridge size	1× 120 g (silica gel)
Flow	35 mL/min
Eluent	40% AcOEt in petroleum ether for 15 min, then gradient from 40% to 45% AcOEt in PE for 5 min, and 45% AcOEt in PE for 10 min, then gradient from 45% to 50% AcOEt in PE for 5 min, and 50% AcOEt in PE for 20 min.
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.45 (50% AcOEt in hexanes))

m.p. 189-191°C

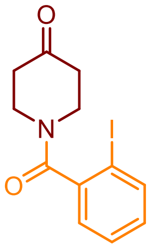
[α]$_D^{28}$ +65.1 (c 0.9, CHCl$_3$);

^{1}H NMR (500 MHz, CDCl$_3$ mixture of rotamers) δ 7.87 – 7.81 (m, 1H), 7.41 – 7.36 (m, 1H), 7.28 (d, *J* = 8.6 Hz, 1H), 7.20 (ddd, *J* = 26.3, 7.6, 1.7 Hz, 1H), 7.08 (td, *J* = 7.6, 1.4 Hz, 1H), 6.85 – 6.76 (m, 2H), 4.69 – 4.51 (m, 1H), 3.54 – 3.39 (m, 2H), 3.24 – 3.02 (m, 2H), 2.95 – 2.78 (m, 2H), 2.50 (dd, *J* = 19.0, 8.7 Hz, 1H), 2.43 – 2.35 (m, 1H), 2.32 – 1.84 (m, 11H), 1.82 – 1.38 (m,10H), 1.38 – 1.22 (m, 2H), 1.18 – 1.02 (m, 2H), 0.90 (s, 3H);

^{13}C NMR (126 MHz, CDCl$_3$) δ 220.77, 173.02, 172.94, 169.48, 169.42, 148.58, 148.55, 142.52, 142.42, 139.53, 139.31, 138.26, 138.24, 137.72, 137.69, 130.37, 130.33, 128.61, 128.46, 127.11, 126.92, 126.58, 126.56, 121.50, 121.48, 118.67, 118.65, 92.63, 92.47, 50.57, 49.20, 48.05, 46.46, 45.97, 44.27, 41.17, 41.05, 40.97, 40.85, 38.14, 35.96, 34.05, 31.68, 29.51, 28.51, 28.31, 27.95, 27.66, 26.44, 25.89, 25.77, 25.05, 21.71, 13.95;

HRMS (ESI-TOF) *m/z* calcd for C$_{31}$H$_{34}$NO$_4$INa [(M+Na)+] 634.1430; found 634.1431.

N-(2-iodobenzoyl)piperidin-4-one (1v):

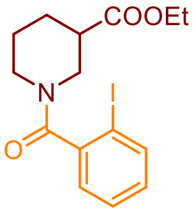


Yield: 1.40 g (62%) starting from 2-iodobenzoyl chloride (1.74 g, 6.51 mmol) and 4-piperidin-4-one hydrochloride (1.20 g, 7.82 mmol). Purification: column chromatography on SiO$_2$, eluent: AcOEt/hexanes 50:50 v/v.
TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v); yellow oil;
Spectral data in agreement with previous reports.[3]

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.85 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.41 (td, *J* = 7.5, 1.1 Hz, 1H), 7.29 – 7.21 (m, 1H), 7.11 (td, *J* = 7.7, 1.6 Hz, 1H), 4.26 – 4.19 (m, 1H), 3.99 – 3.83 (m, 1H), 3.65 – 3.38 (m, 2H), 2.70-2.52 (m, 3H), 2.48 – 3.37 (m, 1H);

^{13}C NMR (126 MHz, CDCl$_3$) δ 206.4, 169.80, 141.8, 139.5, 130.7, 128.7, 127.0, 100.1, 92.4, 45.8, 41.4, 41.0, 40.9.

Ethyl *N*-(2-iodobenzoyl)piperidine-3-carboxylate (1w):



Yield: 1.80 g (72%) starting from 2-iodobenzoyl chloride (1.72 g, 6.44 mmol) and ethyl piperidine-3-carboxylate (1.20 g, 7.82 mmol).

Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

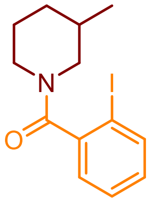
TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v); yellow sticky oil;

^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 7.81 (dt, *J* = 8.0, 4.0 Hz, 1H), 7.41 – 7.32 (m, 1H), 7.22 – 7.00 (m, 2H), 4.91 – 4.64 (m, 1H), 4.34 – 4.26 (m, 0.3×1H) 4.23 – 3.96 (m, 2H), 3.54 – 3.44 (m, 0.5×1H), 3.38 – 2.88 (m, 2H), 2.80 – 2.64 (m, 1H), 2.60 – 2.50 (m, 0.3×1H), 2.39 – 2.28 (m, 0.2×1H), 2.23 – 2.02 (m, 1H), 1.92 – 1.52 (m, 3H), 1.30 – 1.11 (m, 3H);

^{13}C NMR (101 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 173.23, 172.75, 139.47, 139.29, 139.25, 130.38, 130.26, 128.54, 128.43, 127.38, 127.10, 126.91, 92.53, 60.84, 60.80, 48.53, 48.40, 47.65, 47.03, 43.54, 43.47, 42.26, 42.04, 41.84, 41.51, 41.44, 41.01, 27.94, 27.64, 27.55, 27.40, 24.98, 24.47, 23.68, 14.32, 14.20.

HRMS (ESI-TOF+) *m/z* calcd for $C_{15}H_{18}NO_3INa$ [(M+Na)+] 410.0229; found 410.0226.

3-methyl *N*-(2-iodobenzoyl)piperidine (1x):



Yield: 2.10 g (84%) starting from 2-iodobenzoyl chloride (2.00 g, 7.51 mmol) and 3-methylpiperidine (0.89 g, 9.03 mmol, 1 mL).

Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

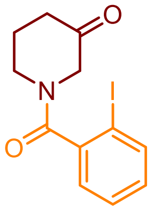
TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v); yellow oil;

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, mixture of rotamers/conformers) δ 7.87 (d, *J* = 7.9 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.14 (td, *J* = 7.7, 1.6 Hz, 1H), 4.51 – 4.17 (m, 1H), 3.22 – 3.10 (m, 1H), 2.99 – 2.85 (m, 1H), 2.70 – 2.53 (m, 1H), 1.85 – 1.41 (m, 4H), 1.30 – 1.11 (m, 1H), 1.02 – 0.66 (m, 3H).

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C) δ 167.6, 142.7, 138.4, 129.6, 127.9, 126.6, 92.4 (v br), 47.6, 41.0, 31.9, 30.5, 24.9, 18.2.

HRMS (ESI-TOF+) *m/z* calcd for $C_{13}H_{16}NONa$ [(M+Na)+] 352.0174; found 352.0172.

N-(2-iodobenzoyl)piperidin-3-one (1y):



Yield: 0.9 g (74%) starting from 2-iodobenzoyl chloride (980 mg, 3.69 mmol) and 3-methylpiperidin-3-one hydrochloride (500 mg, 3.69 mmol).

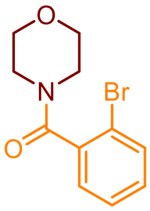
Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v); yellow oil;

^{1}H NMR (500 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 7.84-7.77 (m, 1H), 7.43 – 7.37 (m, 1H), 7.19 (ddd, *J* = 17.1, 7.6, 1.7 Hz, 1H), 7.10 (qd, *J* = 7.8, 1.7 Hz, 1H), 4.47 – 4.27 (m, 1H), 4.08 – 4.01 (m, 1H), 3.88 – 3.81 (m, 1H), 3.71 (d, *J* = 17.5 Hz, 1H), 3.46 – 3.34 (m, 1H), 2.66 – 2.48 (m, 2H), 2.24 – 2.01 (m, 2H), 1.92 (q, *J* = 7.6, 7.1 Hz, 1H);

^{13}C NMR (126 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 204.28, 204.24, 169.98, 169.96, 168.88, 142.05, 141.71, 141.39, 139.81, 139.41, 139.38, 134.25, 133.09, 131.69, 130.80, 130.64, 128.82, 128.66, 128.03, 127.29, 127.09, 94.56, 92.50, 92.38, 60.52, 56.73, 52.52, 45.27, 40.89, 38.54, 29.78, 22.90, 21.80, 14.30.

N-(2-bromobenzoyl)morpholine (SI-1a):



Yield: 1.16 g (75%) starting from 2-bromobenzoyl chloride (1.26 g, 5.74 mmol) and morpholine (1.2 g, 12.83 mmol). Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v);

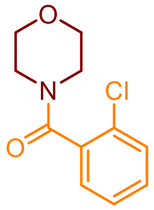
White solid, **m.p.** °C; [Lit.[8] 92-93 °C]

Spectral data in accordance with previous report.[8]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.9, 2.9 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.24 (dq, *J* = 7.0, 3.1, 2.5 Hz, 2H), 3.90 – 3.82 (m, 1H), 3.81 – 3.67 (m, 4H), 3.56 (ddd, *J* = 11.9, 6.4, 3.3 Hz, 1H), 3.26 (ddd, *J* = 13.8, 6.5, 3.3 Hz, 1H), 3.17 (ddd, *J* = 13.6, 6.8, 3.3 Hz, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.7, 137.6, 132.8, 130.5, 127.8, 127.7, 119.1, 66.7, 66.6, 47.1, 42.0.

N-(2-chlorobenzoyl)morpholine (SI-1b):



Yield: 1.05 g (81%) starting from 2-chlorobenzoyl chloride (1.26 g, 5.74 mmol) and morpholine (0.60 g, 6.89 mmol). Purification: column chromatography on SiO_2, eluent: AcOEt/hexanes 50:50 v/v.

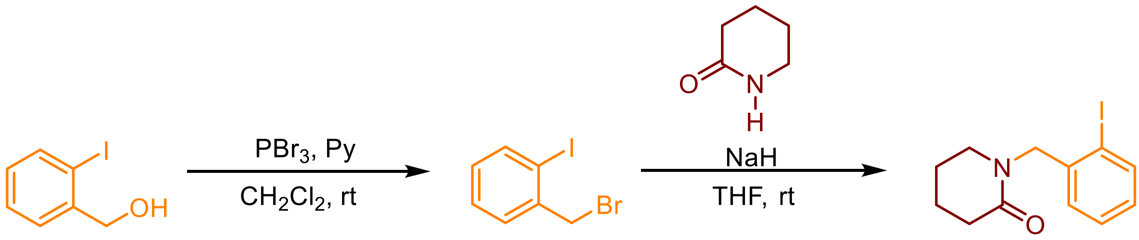
TLC: R_F 0.5 (AcOEt/hexanes 50:50 v/v);

White solid, **m.p.** 75-76 °C; [Lit.[8] 73 °C]; Spectral data in accordance with previous report.[9]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.25 (m, 4H), 3.92 – 3.82 (m, 1H), 3.81 – 3.71 (m, 3H), 3.67 (ddd, *J* = 11.6, 6.7, 3.2 Hz, 1H), 3.57 (ddd, *J* = 11.5, 6.3, 3.3 Hz, 1H), 3.27 (ddd, *J* = 13.5, 6.2, 3.2 Hz, 1H), 3.19 (ddd, *J* = 13.5, 6.7, 3.3 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 135.5, 130.5, 130.4, 129.8, 127.9, 127.4, 66.9, 66.8, 47.2, 42.1.

1-(2-iodobenzyl)piperidin-2-one (9):



Step 1: To a well-stirred and ice-cooled solution of 2-iodobenzyl alcohol derivative (3.00 g, 12.82 mmol, 1 equiv.) in dry CH_2Cl_2 (50 mL) was added dry pyridine (1.01 g, 1.0 mL, 12.82 mmol, 1 equiv.) and PBr_3 (1.8 mL, 5.21 g, 19.23 mmol, 1.5 equiv.) successively and the whole reaction mixture was allowed to stir at the same temperature for 30 minutes until complete conversion of the starting material (TLC). The reaction was quenched by the addition of water (50 mL) and extracted with CH_2Cl_2 (3×30 mL). The combined organic extracts were dried over anhydr. Na_2SO_4 and concentrated under reduced pressure to obtain the crude 2-iodobenzyl bromide which was used immediately (without purification) in the next step as it is somewhat unstable in nature.

Step 2: To a suspension of NaH (60% dispersion in mineral oil, 1.1 equiv., 266 mg) in anhydr. THF (20 mL) was dropwise added a solution of δ-valerolactam (1.00 g, 10.09 mmol, 1 equiv.) in THF (5 mL) at 0 °C. The mixture was warmed to rt and stirred for 2 h. 2-iodobenzyl bromide (1.2 equiv.) was then added dropwise, and the mixture was stirred for a further 2 h. The reaction was quenched with H_2O (50 mL) and the aqueous layer extracted with EtOAc (3 × 30 mL). The combined organic extracts were washed with brine, dried over anhydr. $MgSO_4$, and concentrated in vacuo. The crude residue was purified via flash chromatography

(EtOAc/hexanes, 4:1 v/v) to afford 1.90 g (60%) of the respective *N*-alkyl lactam **9** as an off-white solid.

TLC: R_F 0.5 (AcOEt/hexanes 1:1 v/v);

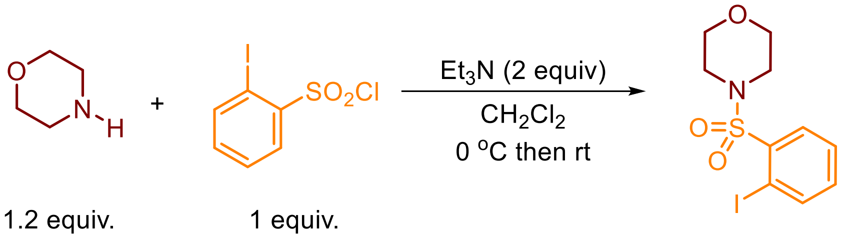
m.p. 93-94 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.31 (td, *J* = 7.5, 1.3 Hz, 1H), 7.14 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.95 (td, *J* = 7.6, 1.7 Hz, 1H), 4.65 (s, 2H), 3.22 (t, *J* = 5.7 Hz, 2H), 2.51 (t, *J* = 6.3 Hz, 2H), 1.90 – 1.75 (m, 4H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 139.5, 138.8, 128.9, 128.6, 128.0, 99.0, 54.8, 47.7, 32.3, 23.2, 21.3;

HRMS (ESI-TOF+) *m/z* calcd for $C_{12}H_{14}NOINa$ [(M+Na)+] 338.0018; found 338.0016.

4-((2-iodophenyl)sulfonyl)morpholine (10):



In an oven-dried round-bottom flask was charged with morpholine (350 mg, 3.97 mmol, 0.35 mL, 1.2 equiv.) and Et_3N (670 mg, 0.92 mL, 6.6 mmol, 2 equiv.). CH_2Cl_2 (13 mL) was added and the resulting mixture was cooled 0 °C using the ice bath. Next, 2-iodosulfonyl chloride (1.00 g, 3.30 mmol, 1 equiv.) in 5 mL of anhydr. CH_2Cl_2 was added dropwise over 10 min. A cooling bath was removed and the resulting mixture stirred overnight at room temperature. After the starting material was consumed (monitored by TLC), the reaction was quenched by adding 1M HCl (10 ml) and extracted with CH_2Cl_2 (2×20 mL). The combined organic phase was washed with brine and dried over Na_2SO_4. The solvent was concentrated and the product was purified by automated flash chromatography on silica gel to provide product **10** (1.10 g, 94%) as a white solid.

Cartridge size	1× 120 g (silica gel)
Flow	45 mL/min
Eluent	45% AcOEt in petroleum ether for 10 min, then gradient from 45% to 60% AcOEt in PE for 15 min, and 60% AcOEt in PE for 10 min.
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.7 (50% AcOEt in hexanes))

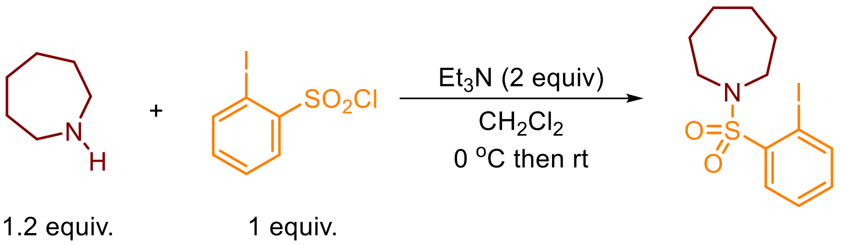
m.p. 141-142 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (td, *J* = 8.1, 1.5 Hz, 2H), 7.50 (td, *J* = 7.6, 1.2 Hz, 1H), 7.21 (td, *J* = 7.6, 1.7 Hz, 1H), 3.77 – 3.70 (m, 4H), 3.30 – 3.23 (m, 4H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 140.0, 133.8, 132.1, 128.4, 92.8, 66.3, 45.7;

HRMS (ESI-TOF) *m/z* calcd for $C_{10}H_{12}NO_3SINa$ [(M+Na)+] 375,9480; found 375.9479.

1-((2-iodophenyl)sulfonyl)azepane (13):



In an oven-dried round-bottom flask was charged with azepane (118 mg, 1.19 mmol, 135 μL, 1.2 equiv.) and Et_3N (200 mg, 280 μL, 2.0 mmol, 2 equiv.). CH_2Cl_2 (5 mL) was added and the resulting mixture was cooled 0 °C using the ice bath. Next, 2-iodosulfonyl chloride (340 mg, 1.1 mmol, 1 equiv.) in 5 mL of anhydr. CH_2Cl_2 was added dropwise over 10 min. A cooling bath was removed and the resulting mixture stirred overnight at room temperature. After the starting material was consumed (monitored by TLC), the reaction was quenched by adding 1M HCl (10 ml) and extracted with CH_2Cl_2 (2×20 mL). The combined organic phase was washed with brine and dried over Na_2SO_4. The solvent was concentrated and the product was purified by automated flash chromatography on silica gel to provide product **13** (386 mg, 94%) as a white solid.

Cartridge size	1× 120 g (silica gel)
Flow	45 mL/min
Eluent	10% AcOEt in petroleum ether for 10 min, then gradient from 10% to 20% AcOEt in PE for 15 min, and 20% AcOEt in PE for 10 min.
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.7 (20% AcOEt in hexanes)

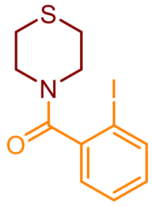
m.p. 152-153 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.03 (m, 2H), 7.50 – 7.42 (m, 1H), 7.16 (td, *J* = 7.6, 1.7 Hz, 1H), 3.44 – 3.35 (m, 4H), 1.80 – 1.62 (m, 8H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1, 142.4, 133.1, 131.5, 128.3, 92.2, 48.9, 29.5, 27.2;

HRMS (ESI-TOF) *m/z* calcd for $C_{12}H_{16}NO_2SINa$ [(M+Na)+] 387.9833; found 387.9843

1-((2-iodophenyl)sulfonyl)thiomorpholine (16):



Yield: 305 mg (83%) starting from 2-iodobenzosulfonyl chloride (300 mg, 0.99 mmol) and thiomorpholine (102 mg, 0.99 mmol).

Purification: automated flash column chromatography

Cartridge size	1× 120 g (silica gel)
Flow	45 mL/min
Eluent	10% AcOEt in petroleum ether for 10 min, then gradient from 10% to 20% AcOEt in PE for 15 min, and 20% AcOEt in PE for 10 min.
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.4 (20% AcOEt in hexanes)

m.p. 121-122 °C;

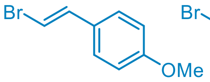
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.06 (m, 2H), 7.52 – 7.45 (m, 1H), 7.20 (td, *J* = 7.6, 1.7 Hz, 1H), 3.64 – 3.52 (m, 4H), 2.75 – 2.64 (m, 4H);

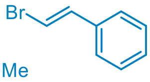
^{13}C NMR (101 MHz, $CDCl_3$) δ 143.28, 140.85, 133.67, 132.04, 128.43, 92.54, 47.71, 27.31;

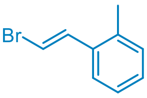
HRMS (ESI-TOF) *m/z* calcd for $C_{10}H_{12}NO_2S_2Na$ [(M+Na)+] 391.9252; found 391.9249.

3.2. Synthesis of vinyl halides

List of vinyl halides employed for the scope studies


2a


2b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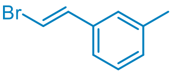
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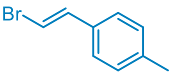
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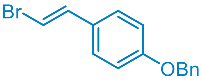
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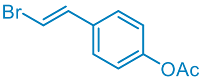
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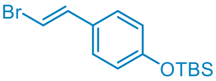
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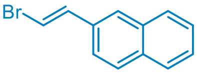
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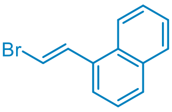
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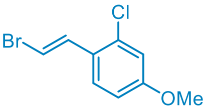
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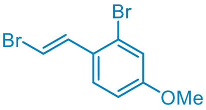
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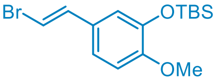
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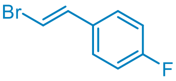
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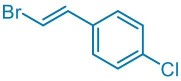
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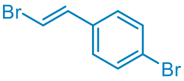
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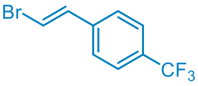
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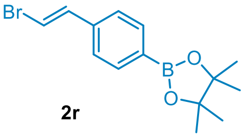
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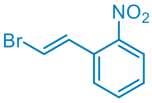
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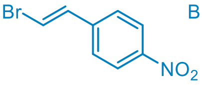
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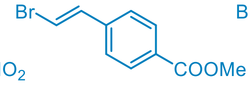
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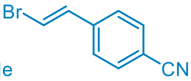
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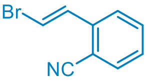
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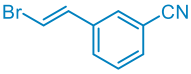
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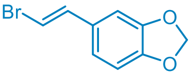
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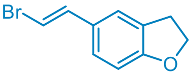
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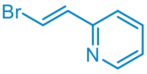
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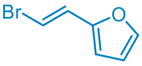
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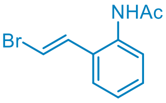
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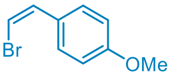
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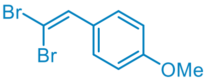
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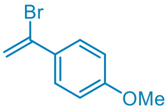
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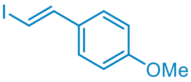
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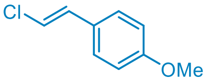
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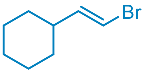
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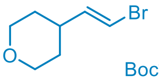
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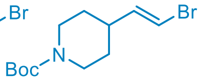
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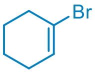
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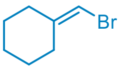
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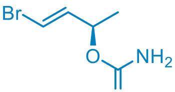
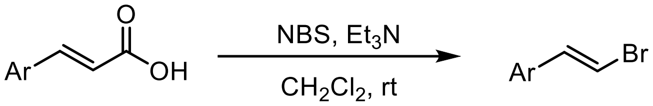
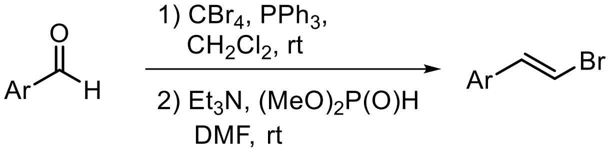

28

Synthesis of vinyl bromides – Method A



General procedure: Et_3N (5 mol%) was added to a solution of acrylic acid (1.0 equiv.) in CH_2Cl_2 (c 0.2-0.3 M). The mixture was stirred at 25 °C for 5 minutes, and *N*-bromosuccinimide (NBS) (1.2 equiv.) was slowly added to keep the internal temperature below 25 °C. After 20-30 minutes, CO_2 evolution stopped, indicating the completion of the reaction. The volatiles and solvent were evaporated under reduced pressure, and the remaining residue was purified by flash chromatography over silica gel to afford the corresponding vinyl bromide.

Synthesis of vinyl bromides – Method B:

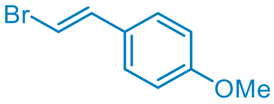


General procedure: To a flame-dried flask was charged with aldehyde (1 equiv.), CBr_4 (1.5 equiv.) and anhydr. CH_2Cl_2 (c 0.2-0.3 M). The flask was cooled to 0 °C, at which point a solution of PPh_3 (3 equiv.) in CH_2Cl_2 (c 0.2-0.3 M) was added dropwise via addition funnel over 30 min. The solution was stirred at 0 °C under argon for 1 h. Next, about half of the volume of CH_2Cl_2 was removed under reduced pressure. The residue was treated with pentane to precipitate triphenylphosphine oxide (TPPO). After filtration and evaporation of the solvent, the residue was again dissolved in pentane which led to further precipitation of TPPO. Filtration and evaporation of the solvent afforded the crude dibromide which was directly used for the next step.

To a solution of the crude dibromide (1 equiv.) and Et_3N (3 equiv.) in DMF (c 0.2-0.3 M) was added dimethyl phosphite (3 equiv.). The resulting solution was stirred overnight at room temperature. Then, water was added to the mixture, which was extracted with pentane. The combined organic phases were washed with an aqueous solution of HCl (1 M), dried over anhydr. Na_2SO_4, filtered, and concentrated. The crude material was purified by flash chromatography.

3.2.1. 2-Aryl substituted vinyl halides

(*E*)-1-(2-bromovinyl)-4-methoxybenzene (2a):



Yield: 5.00 g (76%, method A*) starting from (*E*)-3-(4-methoxyphenyl)acrylic acid (5.53 g, 31.04 mmol). *E/Z* ratio >98:2 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in Hexanes)

White solid, **m.p.** 54-55 °C [Lit. 53-54 °C,[10] 55-56 °C[11]];

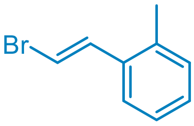
Spectral data in accordance with previous reports.[11]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 2H), 7.04 (d, *J* = 14.0 Hz, 1H), 6.88 – 6.83 (m, 2H), 6.61 (d, *J* = 13.9 Hz, 1H), 3.81 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 136.7, 128.9, 127.5, 114.4, 104.1, 55.4.

β-Bromostyrene (2b) [CAS 103-64-0] was purchased from Fluorochem (cat. No.: F049835).

(*E*)-1-(2-bromovinyl)-2-methylbenzene (2c):



2c

Yield: 1.00 g (55%, method B) starting from 2-methylbenzaldehyde (9.33 mmol). *E/Z* mixture in a ratio 11:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in Hexanes)

Colorless oil. Spectral data with accordance with previous report.[12]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 13.9 Hz, 2H), 7.23 – 7.13 (m, 3H), 6.65 (d, *J* = 13.8 Hz, 1H), 2.35 (s, 3H);

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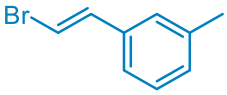
* Yield: 1.03 g (70%, 2 steps, method B) starting from 1.95 g (6.09 mmol) of 4-methoxybenzaldehyde.

^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 135.31, 135.25, 130.6, 128.3, 126.4, 126.0, 107.4, 20.0.

(*E*)-1-(2-bromovinyl)-3-methylbenzene (2d):



Yield: 1.20 g (66%, method B) starting from 3-methylbenzaldehyde (1.21 g, 9.33 mmol). *E/Z* mixture in a ratio 15.6:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

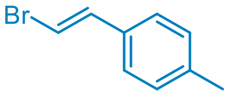
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.9 (1% EtOAc in Hexanes)

Colorless oil; Spectral data with accordance with previous report.[12]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.18 (m, 1H), 7.14 – 7.04 (m, 4H), 6.75 (d, *J* = 13.9 Hz, 1H), 2.36 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 137.3, 135.9, 129.1, 128.7, 126.8, 123.3, 106.3, 21.4.

(*E*)-1-(2-bromovinyl)-4-methylbenzene (2e):



Yield: 1.24 g (68%, 2 steps, method B) starting from 4-methylbenzaldehyde (1.10 g, 9.13 mmol). *E/Z* mixture in a ratio 15:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in Hexanes)

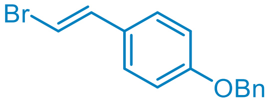
white solid, **m.p.:** 46-47 °C [Lit.[13] 45-46 °C]

Spectral data with accordance with previous report.[13]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 14.0 Hz, 1H), 6.71 (d, *J* = 14.0 Hz, 1H), 2.34 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 137.2, 133.3, 129.6, 129.1, 126.1, 105.6, 21.4.

(*E*)-1-(benzyloxy)-4-(2-bromovinyl)benzene (2f):



Yield: 864 mg (63%, 2 steps, method B) starting from 4-(benzyloxy)benzaldehyde (1.00 g, 4.71 mmol). *E/Z* mixture in a ratio 15:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in Hexanes)

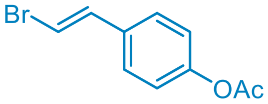
White solid, **m.p.:** 92-93 °C [Lit. 91-92 °C,[14] 77-78 °C[15]];

Spectral data in accordance with previous report.[14],[15]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.37 (m, 4H), 7.36 – 7.31 (m, 2H), 7.24 – 7.21 (m, 2H), 7.04 (d, *J* = 13.9 Hz, 1H), 6.95 – 6.88 (m, 2H), 6.61 (d, *J* = 14.0 Hz, 1H), 5.06 (s, 2H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 136.8, 136.7, 134.0, 128.9, 128.8, 128.2, 127.6, 127.5, 115.3, 104.3, 70.2.

(*E*)-4-(2-bromovinyl)phenyl acetate (2g):



Yield: 922 mg (56%, 2 steps, method B) starting from 4-(formyl)phenyl acetate (1.12 g, 6.82 mmol). *E/Z* mixture in a ratio 12:1 (^{1}H NMR).

Purification: flash column chromatography on SiO_2,

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in Hexanes)

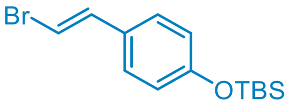
Brown solid, **m.p.:** 59-60 °C;

Spectral data in accordance with previous report.[16]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H), 7.08 – 7.00 (m, 3H), 6.73 (d, *J* = 13.9 Hz, 1H), 2.29 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 150.5, 136.2, 133.7, 127.1, 122.0, 106.7, 21.1.

O-TBS (*E*)-4-(2-bromovinyl)phenol (2h):



Yield: 2.60 mg (52%, 3 steps including *O*-silylation, and olefination/elimination sequence (method B) starting from 4-hydroxybenzaldehyde (2.00 g, 16.38 mmol). *E/Z* mixture in a ratio 18:1 (^{1}H NMR).

Purification: flash column chromatography on SiO_2,

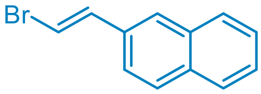
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in Hexanes)

yellow viscous oil; Spectral data in accordance with previous reports.[17]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.13 (m, 2H), 7.03 (d, *J* = 13.9 Hz, 1H), 6.82 – 6.76 (m, 2H), 6.61 (d, *J* = 13.9 Hz, 1H), 0.99 (s, 9H), 0.21 (s, 6H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 136.8, 129.5, 127.5, 120.5, 104.3, 25.8, 18.4, –4.3;

(*E*)-2-(2-bromovinyl)naphthalene (2i):



Yield: 963 mg (64%, 2 steps, method B) starting from 2-naphtylaldehyde (1.00 g, 6.40 mmol). *E/Z* mixture in a ratio 18:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.9 (1% EtOAc in Hexanes)

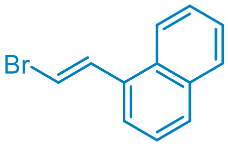
Brown solid, **m.p.** 90-91 °C [Lit.[18] 84-85 °C (EtOH)]

Spectral data in accordance with previous report.[18]

^{1}H NMR (400 MHz, CDCl3) δ 7.87 – 7.76 (m, 3H), 7.68 (d, *J* = 1.7 Hz, 1H), 7.53 – 7.44 (m, 3H), 7.27 (d, *J* = 14.0 Hz, 1H), 6.90 (d, *J* = 13.9 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 137.4, 133.6, 133.5, 133.2, 128.7, 128.2, 127.9, 126.7, 126.5, 126.4, 123.0, 107.0.

(*E*)-1-(2-bromovinyl)naphthalene (2j):



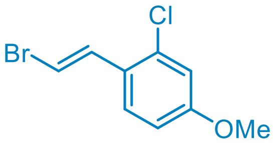
Yield: 1.07 g (62%, 2 steps, method B) starting from 1-naphtylaldehyde (1.15 g, 7.36 mmol). *E/Z* ratio >99:1 (^{1}H NMR).

Purification: flash column chromatography on SiO_2, with 5% AcOEt in hexanes as an eluent. Colorless oil; Spectral data in accordance with previous report.[18]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.6 Hz, 1H), 7.91 – 7.81 (m, 3H), 7.60 – 7.42 (m, 4H), 6.79 (d, *J* = 13.7 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 135.1, 133.72, 133.69, 130.7, 128.9, 128.7, 126.6, 126.2, 125.7, 124.4, 123.8, 108.6.

(*E*)-1-(2-bromovinyl)-2-chloro-4-methoxybenzene (2k):



Yield: 922 mg (68%, 2 steps, method B) starting from 2-chloro-4-methoxybenzaldehyde (580 mg, 3.40 mmol). *E* isomer only (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in Hexanes)

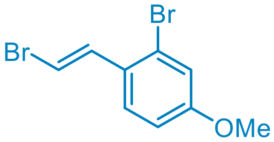
White solid, **m.p.:** 54-55 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 14.0 Hz, 1H), 7.31 (d, *J* = 8.7 Hz, 1H), 6.90 (d, *J* = 2.6 Hz, 1H), 6.78 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.66 (d, *J* = 14.0 Hz, 1H), 3.80 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 133.2, 127.6, 126.7, 114.7, 113.6, 106.8, 55.6;

HRMS (ESI-TOF+) *m/z* calcd for $C_9H_8BrClONa$ [(M+Na)+] 268.9345; found 268.9344.

(*E*)-2-bromo-1-(2-bromovinyl)-4-methoxybenzene (2l):



Yield: 845 mg (63%, 2 steps, method B) starting from 2-bromo-4-methoxybenzaldehyde (1.00 g, 4.65 mmol). *E/Z* ratio 14:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min

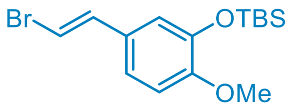
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.9 (1% EtOAc in Hexanes)

White solid, **m.p.:** 57-58 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 13.9 Hz, 1H), 7.31 (d, *J* = 8.7 Hz, 1H), 7.09 (d, *J* = 2.6 Hz, 1H), 6.83 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.63 (d, *J* = 13.9 Hz, 1H), 3.80 (s, 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.1, 135.7, 128.7, 127.7, 123.4, 118.1, 114.3, 107.1, 55.7.

HRMS (APCI-TOF+) *m/z* calcd for $C_9H_9OBr_2$ [(M+H)+] 290.9020; found 290.9017.

O-TBS (E)-4-(2-bromovinyl)-3-methoxyphenol (2m):



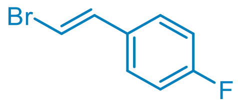
Yield: 1.98 g (47%, 3 steps including O-silylation and olefination/elimination sequence (method B)) starting from vanilin (2.00 g, 13.15 mmol). *E/Z* mixture in a ratio 17:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.9 (1% EtOAc in Hexanes)

yellow oil;
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, *J* = 13.9 Hz, 1H), 6.82 – 6.75 (m, 3H), 6.61 (d, *J* = 13.9 Hz, 1H), 3.83 – 3.80 (m, 3H), 1.00 (s, 9H), 0.16 (s, 6H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 151.3, 145.7, 137.1, 130.0, 121.2, 119.4, 109.7, 104.4, 55.6, 25.8, 18.6, –4.5.

(*E*)-1-(2-bromovinyl)-4-fluorobenzene (2n):



Yield: 1.18 g (63%, 2 steps, method B) starting from 4-fluorobenzaldehyde (1.16 g, 9.33 mmol). *E/Z* ratio 15:1 (^{1}H NMR) and 14:1 (by ^{19}F NMR).

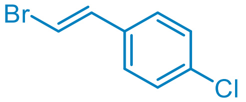
Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.9 (1% EtOAc in Hexanes)

Low melting solid [Lit.[11] 27 °C]
Spectral data in accordance with previous reports.[11]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.22 (m, 2H), 7.12 – 6.98 (m, 3H), 6.70 (d, *J* = 14.0 Hz, 1H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0 and 161.5 (d, $J_{C\text{-}F}$ = 248 Hz), 136.1, 132.29 and 132.26 (d, $J_{C\text{-}F}$ = 3.6 Hz), 127.88 and 127.80 (d, $J_{C\text{-}F}$ = 8.1 Hz), 116.0 and 115.8 (d, $J_{C\text{-}F}$ = 21.8 Hz), 106.25 and 106.22 (d, $J_{C\text{-}F}$ = 2.5 Hz);

^{19}F NMR (376 MHz, $CDCl_3$) δ –112.9.

(*E*)-1-(2-bromovinyl)-4-chlorobenzene (2o):



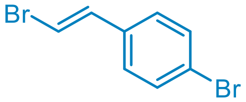
Yield: 1.03 g (65%, 2 steps, method B) starting from 4-chlorobenzaldehyde (1.00 g, 7.11 mmol). *E/Z* 19.5:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	1% AcOEt in petroleum ether for 15 min, then gradient from 1% to 3% AcOEt in PE for 2 min, and 3% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.6 (1% EtOAc in Hexanes)

White solid, **m.p.:** 48-49 °C [Lit.[10] 48-49 °C];
Spectral data in accordance with previous report.[19]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 14.1 Hz, 1H), 6.76 (d, *J* = 14.0 Hz, 1H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 134.5, 134.2, 129.1, 127.4, 107.3.

(*E*)-1-bromo-4-(2-bromovinyl)benzene (2p):



Yield: 987 mg (69%, 2 steps, method B) starting from 4-bromobenzaldehyde (1.00 g, 5.41 mmol). *E/Z* ratio 9:1 (^{1}H NMR).

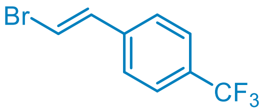
Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.9 (1% EtOAc in Hexanes)

pale yellow soild, **m.p.:** 69-70 °C [Lit.[20] 69-70 °C];
Spectral data in accordance with previous report.[20]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.43 (m, 2H), 7.19 – 7.13 (m, 2H), 7.04 (d, J = 14.0 Hz, 1H), 6.78 (d, J = 14.0 Hz, 1H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 136.2, 134.9, 132.1, 127.7, 122.3, 107.5.

(E)-1-(2-bromovinyl)-4-(trifluoromethyl)benzene (2q):



Yield: 1.02 g (56%, 2 steps, method B) starting from 4-(trifluoromethyl)benzaldehyde (1.27 g, 7.32 mmol). *E/Z* ratio 11:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

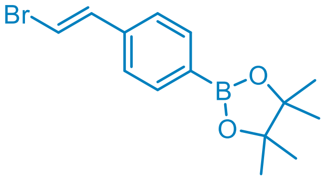
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in Hexanes)

Low melting solid. Spectral data in accordance with previous report.[20]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.3 Hz, 2H), 7.40 (d, J = 8.1 Hz, 2H), 7.14 (d, J = 14.1 Hz, 1H), 6.91 (d, J = 14.0 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.3, 136.1, 130.2 (q, JC-F = 32.5 Hz), 126.4, 126.0 (q, JC-F = 3.8 Hz), 124.2 (q, JC-F = 272.3 Hz), 109.5;

^{19}F NMR (376 MHz, $CDCl_3$) δ –62.7.

(*E*)-2-(4-(2-bromovinyl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2r):



Yield: 1.01 g (77%, 2 steps, method B) starting from 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (1.00 g, 4.31 mmol). *E/Z* ratio 9:1 (^{1}H NMR).

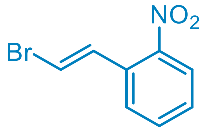
Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.7 (1% EtOAc in Hexanes)

White solid, **m.p.:** 37 °C [Lit.[20] 36-37 °C]; Spectral data in accordance with previous report.[20]
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 7.8 Hz, 2H), 7.26 (d, J = 7.8 Hz, 2H), 7.08 (d, J = 14.0 Hz, 1H), 6.81 (d, J = 14.0 Hz, 1H), 1.31 (s, 4× 3H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 138.6, 137.4, 135.4, 134.8, 125.5, 107.8, 84.0, 25.0.

(*E*)-1-(2-bromovinyl)-2-nitrobenzene (2s):



Yield: 1.00 g (64%, 2 steps, method B) starting from 2-nitrobenzaldehyde (1.00 g, 6.62 mmol). *E*-isomer only (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

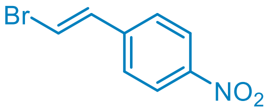
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	1% AcOEt in petroleum ether (PE) for 15 min, then gradient from 1% to 3% AcOEt in PE for 2 min, and 3% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (3% EtOAc in Hexanes)

Yellowish solid, **m.p.** 49 °C [Lit.[15] 48-50 °C]; Spectral data in accordance with previous report.[15]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.68 – 7.60 (m, 1H), 7.59 (dd, *J* = 7.6, 1.4 Hz, 1H)7.52 – 7.43 (m, 2H), 6.79 (d, *J* = 13.8 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 133.7, 133.2, 131.6, 129.1, 128.9, 125.1, 111.2.

(*E*)-1-(2-bromovinyl)-4-nitrobenzene (2t):



Yield: 1.00 g (66%, 2 steps, method B) starting from 4-nitrobenzaldehyde (1.00 g, 6.62 mmol). E isomer only (1H NMR).

Purification: automated flash column chromatography on SiO_2

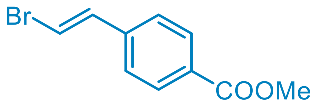
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	1% AcOEt in petroleum ether (PE) for 15 min, then gradient from 1% to 3% AcOEt in PE for 2 min, and 3% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.6 (3% EtOAc in Hexanes)

Yellow solid, **m.p.:** 162-163 °C [lit.[13b] 158-160 °C]; Spectral data in accordance with previous report.[15]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.18 (d, *J* = 14.1 Hz, 1H), 7.03 (d, *J* = 14.0 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 142.0, 135.5, 126.8, 124.4, 111.8.

Methyl (*E*)-4-(2-bromovinyl)benzoate (2u):



Yield: 1.03 g (70%, method B) starting from methyl 4-formylbenzoate (1.00 g, 6.09 mmol). *E/Z* ratio 13:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

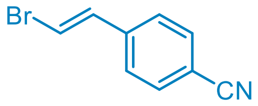
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in Hexanes)

white solid, **m.p.:** 81-82 °C [Lit.[18] 60-61 °C (hexane)]; Spectral data in accordance with previous report.[18]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.3 Hz, 2H), 7.14 (d, *J* = 14.0 Hz, 1H), 6.92 (d, *J* = 14.1 Hz, 1H), 3.91 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 140.2, 136.5, 130.3, 126.1, 109.5, 52.3.

(*E*)-4-(2-bromovinyl)benzonitrile (2v):



Yield: 912 mg (57%, method B) starting from 4-formylbenzonitrile (1.00 g, 7.63 mmol). *E/Z* ratio 26:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

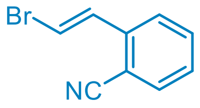
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in Hexanes)

White solid; **m.p.:** 105-106 °C [Lit.[15] 105-106 °C]; Spectral data in accordance with previous report.[15]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 14.1 Hz, 1H), 6.96 (d, *J* = 14.1 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.2, 135.8, 132.8, 126.7, 118.7, 111.8, 111.0.

(*E*)-2-(2-bromovinyl)benzonitrile (2w):



Yield: 1.09 g (68%, method B) starting from methyl 2-formylbenzonitrile (1.00 g, 7.63 mmol). *E* isomer only (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

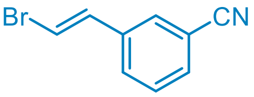
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in Hexanes)

White solid, **m.p.:** 87-88 °C [Lit.[21] 86 °C]; Spectral data in accordance with previous reports.[21]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.60 – 7.47 (m, 2H), 7.47 – 7.34 (m, 2H), 7.07 (d, *J* = 14.0 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 133.4, 133.3, 133.1, 128.5, 126.0, 117.6, 112.3, 110.6.

(*E*)-3-(2-bromovinyl)benzonitrile (2x):



Yield: 1.02 g (64%, method B) starting from methyl 3-formylbenzonitrile (1.00 g, 7.63 mmol). *E/Z* ratio 9.7:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

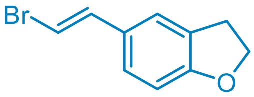
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.7 (1% EtOAc in Hexanes)

Colorless oil; Spectral data in accordance with previous report.[19]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 2H), 7.52 (dt, *J* = 7.9, 1.6 Hz, 1H), 7.44 (t, *J* = 7.9 Hz, 1H), 7.09 (d, *J* = 14.1 Hz, 1H), 6.89 (d, *J* = 14.1 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 137.2, 135.2, 131.6, 130.3, 129.8, 129.6, 118.5, 113.3, 109.8.

(*E*)-5-(2-bromovinyl)-2,3-dihydrobenzofuran (2y):



Yield: 1.10 g (62%, method B) starting from methyl 5-formyl-2,3-dihydrobenzofuran (1.18 g, 7.94 mmol). *E/Z* ratio 96:4 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)

TLC	R_F = 0.8 (1% EtOAc in Hexanes)

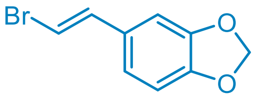
Brown solid, **m.p.:** 59-60 °C

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.16 (s, 1H), 7.07 – 6.99 (m, 2H), 6.73 (d, *J* = 8.3 Hz, 1H), 6.57 (d, *J* = 13.9 Hz, 1H), 4.58 (t, *J* = 8.7 Hz, 2H), 3.20 (t, *J* = 8.7 Hz, 2H);

^{13}C NMR (101 MHz, CDCl$_3$) δ 160.5, 137.0, 128.9, 127.9, 126.8, 122.6, 109.6, 103.4, 71.6, 29.6;

HRMS (ESI-TOF+) *m/z* calcd for C$_{10}$H$_{10}$OBr [(M+H)+] 224.9915; found 224.9917.

(*E*)-5-(2-bromovinyl)benzo[*d*][1,3]dioxole (2z):



Yield: 1.75 g (62%, 3 steps, oxidation with MnO$_2$ and olefination/elimination sequence by the method B) starting from piperonol (2.06 g, 13.16 mmol). *E*/*Z* mixture in a ratio 94:6 (^{1}H NMR).

Purification: automated flash column chromatography on SiO$_2$

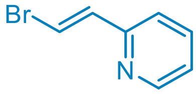
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.7 (1% EtOAc in Hexanes)

white solid, **m.p.:** 52-53 °C [Lit.[13a] 52-53 °C], Spectral data in accordance with previous reports.[13a]

^{1}H NMR (500 MHz, CDCl$_3$) δ 6.99 (d, *J* = 13.9 Hz, 1H), 6.81 (d, *J* = 1.5 Hz, 1H), 6.78 – 6.71 (m, 2H), 6.59 (d, *J* = 13.9 Hz, 1H), 5.96 (s, 2H);

^{13}C NMR (126 MHz, CDCl$_3$) δ 148.3, 147.9, 136.8, 130.4, 121.1, 108.6, 105.6, 104.7, 101.4.

(*E*)-2-(2-bromovinyl)pyridine (2aa):



Yield: 970 mg (51%, 2 steps, method B) starting from methyl 2-formyl-pyridine (1.13 g, 10.51 mmol). *E*-isomer only (^{1}H NMR).

Purification: automated flash column chromatography on SiO$_2$

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	3% AcOEt in petroleum ether (PE) for 15 min, then gradient from 3% to 5% AcOEt in PE for 2 min, and 3% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.6 (5% EtOAc in Hexanes)

Brown oil. Spectral data in accordance with precious reports.[22]

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.53 (d, *J* = 4.7 Hz, 1H), 7.62 (td, *J* = 7.7, 1.8 Hz, 1H), 7.37 (d, *J* = 13.7 Hz, 1H), 7.21 – 7.06 (m, 3H);
^{13}C NMR (101 MHz, CDCl$_3$) δ 154.2, 149.9, 136.9, 136.7, 122.9, 121.8, 112.8.
Warring! Vinyl bromide ***2aa*** *polymerizes within few days even if stored at –40 °C and therefor it is recommended to prepare it freshly before use.*

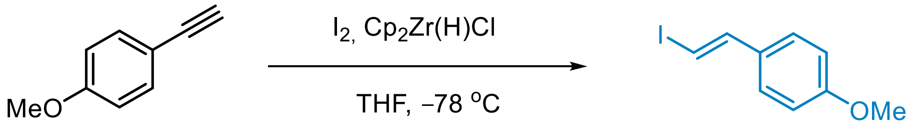
2-(2-bromovinyl)furan (2ab):

Yield: 895 mg (54%, 2 steps, method B) starting from methyl furfural (1.13 g, 10.51 mmol). *E/Z* mixture in a ratio 5:2 (^{1}H NMR). Purification: automated flash column chromatography on SiO$_2$

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.86 (1% EtOAc in Hexanes)

yellow oil. Spectral data in accordance with previous reports.[11]
^{1}H NMR for (*E*)-isomer (500 MHz, CDCl$_3$) δ 7.37 (d, *J* = 1.8 Hz, 1H), 6.88 (d, *J* = 13.8 Hz, 1H), 6.72 (d, *J* = 13.8 Hz, 1H), 6.37 (dd, *J* = 3.3, 1.9 Hz, 1H), 6.25 (d, *J* = 3.3 Hz, 1H);
^{1}H NMR for (*Z*)-isomer (500 MHz, CDCl$_3$) δ 7.45 (d, *J* = 1.8 Hz, 1H), 7.09 (d, *J* = 3.5 Hz, 1H), 7.05 (d, *J* = 8.3 Hz, 1H), 6.48 (dd, *J* = 3.5, 1.8 Hz, 1H), 6.31 (d, *J* = 8.3 Hz, 1H);
^{13}C NMR (126 MHz, CDCl$_3$)(*E/Z* mixture in a ratio 5:2) δ 151.2(*E*), 150.7(*Z*), 142.7(*E*), 142.2(*Z*), 125.5(*E*), 122.3(*Z*), 111.7(*Z*), 111.6(*Z*), 111.5(*E*), 108.8(*E*), 105.4(*E*), 104.4(*Z*).
Warring! Vinyl bromide ***2ab*** *polymerizes within days even at –40 °C and therefor it is recommended to prepare it freshly before use.*

(*E*)-1-(2-iodovinyl)-4-methoxybenzene (SI-2a):



SI-2a

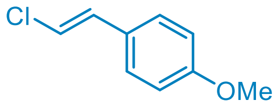
4-Methoxyphenyl acetylene (170 mg, 1.29 mmol, 1.0 equiv.) was added dropwise to a solution of the Schwarz reagent (332 mg, 1.29 mmol, 1.0 equiv.) in anhydr. THF (50 mL). The resulting mixture was stirred at room temperature for 20 minutes, then cooled to −78 °C and a solution of I$_2$ (330 mg, 1.29 mmol, 1.0 equiv.) in 5 mL of THF was added. The solution was allowed to warm to room temperature and was stirred for another 30 minutes. After that time the reaction mixture was poured into Et_2O (100 mL). The resulting precipitate was filtered off using a silica plug and the filtrate was washed with $Na_2S_2O_3$ solution (50 mL), H_2O (50 mL) and brine (50 mL), dried over anhydr. Na_2SO_4, filtrated and concentrated under reduced pressure. The crude product was purified by flash chromatography (100% pentane) to provide 150 mg (44%) of vinyl iodide **SI-2a** (E/Z ratio > 99:1) as a yellowish solid with spectral data in accordance with previous reports.[23] Due to its nature, it is recommended to store compound **SI-2a** at freezer (–15°C or below) and minimize its exposition on a sunlight.

M.p.: 96-97 °C [Lit.[23] 95-96°C];

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 14.9 Hz, 1H), 7.23 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.63 (d, *J* = 14.9 Hz, 1H), 3.81 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9, 144.4, 130.8, 127.4, 114.2, 73.7, 55.4.

(*E*)-1-(2-chlorovinyl)-4-methoxybenzene (SI-2b):



Yield: 789 mg (83%, method A) starting from (*E*)-3-(4-methoxyphenyl)acrylic acid (1.00 g, 5.61 mmol). E/Z ratio 21:1 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

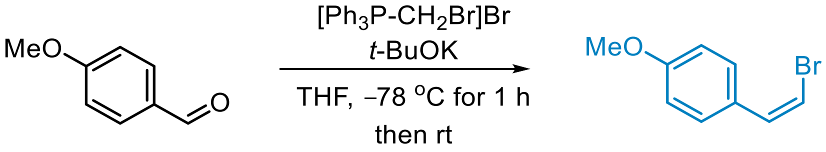
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.9 (1% EtOAc in Hexanes)

Colorless oil. Spectral data in accordance with previous report.[24]

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 13.7 Hz, 1H), 6.51 (d, *J* = 13.7 Hz, 1H), 3.81 (s, 3H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 159.7, 132.8, 127.8, 127.5, 116.5, 114.3, 55.4.

(*Z*)-1-(2-bromovinyl)-4-methoxybenzene (19):



A suspension of *p*-anisaldehyde (785 mg, 0.7 mL, 5.75 mmol, 1.0 equiv.) and phosphonium salt (3.01 g, 6.90 mmol, 1.2 equiv.) in 60 mL of anhydr. THF (0.1M) was cooled to –78 °C and stirred for 5 min. A base, *t*-BuOK (810 mg, 7.19 mmol, 1.25 equiv.) in 10 mL of THF, was added in one portion and the resulting mixture was stirred at –78 °C for 1 h. After 1h, the reaction mixture was allowed to warm to rt and stirred at rt for 8 h. Sat. aq. solution of NH_4Cl was added and the resulting layers were separated. The aqueous layer was extracted with Et_2O (3×50 mL) and the combined organic layers were washed with brine, dried over $MgSO_4$, and the solvents were evaporated under reduced pressure. The residue was purified by flash column chromatography to yield 700 mg (57%) of the olefin vinyl bromide **19** as a colorless oil. *E/Z* ratio 17.5:1 (1H NMR); Spectral data in accordance with previous reports.[26]

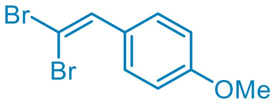
Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 40 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.9 (1% EtOAc in hexanes)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.1 Hz, 1H), 6.92 (d, *J* = 8.8 Hz, 2H), 6.31 (d, *J* = 8.1 Hz, 1H), 3.83 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 134.0, 131.7, 130.6, 113.7, 104.3, 55.4.

1-(2,2-dibromovinyl)-4-methoxybenzene (20):



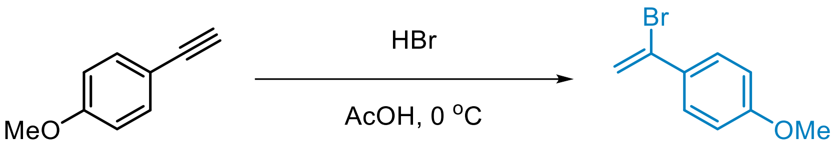
Yield: 2.00 g (83%, prepared by use olefination protocol from the method B) starting from *p*-anisaldehyde (1.12 g, 8.22 mmol).

Purification: flash column chromatography on SiO_2 using pentane/CH_2Cl_2 = 20:1 v/v as eluents; low melting pale yellow solid [Lit.[25] 37-38 °C]; TLC R_F = 0.9 (1% AcOEt in hexanes); Spectral data in accordance with previous reports.[25]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.48 (m, 2H), 7.41 (s, 1H), 6.93 – 6.86 (m, 2H), 3.82 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 136.4, 130.0, 127.9, 113.9, 87.4, 55.4.

1-(1-bromovinyl)-4-methoxybenzene (21):



21

A solution of HBr in acetic acid (33%, w/w, 610 µL, 10,58 mmol, 3.1 equiv.) was added dropwise via syringe to 4-ethynylanisol (450 mg, 3.41 mmol, 1 equiv.) at 0 °C. The reaction mixture was stirred for 30 min at 0 °C. The reaction mixture was transferred to a separatory funnel that had been charged with dichloromethane (100 mL). The diluted product mixture was washed with water (20 mL). The aqueous layer was isolated, and it was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over Na_2SO_4. The dried solution was filtered, and the filtrate was concentrated. The residue was purified by automated flash column chromatography (eluting with 1% Et_2O–hexanes initially, grading to 10% Et_2O–hexanes, linear gradient) to afford 640 mg (88%) of 1-(1-bromovinyl)-4-methoxybenzene (**21**) as a white solid (**m.p.:** 38 °C; Lit.[27] 36-37 °C) Spectral data in accordance with previous reports.[27]

It is recommended to store this compound in freezer (–10 °C) and avoid a long exposition to the light.

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.7 (1% EtOAc in hexanes)

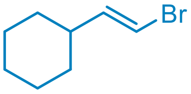
m.p.: 38 °C; Lit.[27] 36-37 °C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.9 Hz, 1H), 6.87 (d, *J* = 8.9 Hz, 1H), 6.01 (d, *J* = 2.0 Hz, 1H), 5.68 (d, *J* = 2.0 Hz, 1H), 3.83 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.4, 131.3, 130.9, 128.8, 116.0, 113.7, 55.5.

3.2.2. 2-Alkyl substituted vinyl halides

(*E*)-(2-bromovinyl)cyclohexane (SI-2c):



Yield: 870 mg (51%, 2 steps, method B) starting from cyclohexanecarbaldehyde (1.00 g, 8.92 mmol). *E/Z* ratio >98:<2 (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

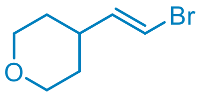
Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.8 (1% EtOAc in hexanes)

Colorless oil; Spectral data in accordance with previous report.[28],[29]

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.03–1.35 (m, 5 H), 1.60–1.80 (m, 5 H), 1.97–2.06 (m, 1 H), 5.99 (dd, J = 13.6, 1.3 Hz, 1 H), 6.14 (dd, J = 13.6, 7.2 Hz, 1 H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.7, 103.1, 41.8, 32.3, 25.9, 25.7.

(*E*)-4-(2-bromovinyl)tetrahydro-2*H*-pyran (SI-2d):



Yield: 950 mg (56%, 2 steps, method B) starting from tetrahydro-2*H*-pyran-4-carbaldehyde (1.01 g, 8.85 mmol). yellow oil;

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 15 min, then gradient from 0% to 1% AcOEt in PE for 2 min, and 1% AcOEt in PE for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.7 (1% EtOAc in hexanes)

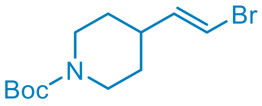
Colorless oil;

^{1}H NMR (500 MHz, DMSO-d_6) δ 6.32 (d, *J* = 13.6 Hz, 1H), 6.20 (dd, *J* = 13.6, 7.0 Hz, 1H), 3.82 (ddd, *J* = 11.5, 4.7, 2.0 Hz, 2H), 3.30 (td, *J* = 11.7, 2.1 Hz, 2H), 2.35 – 2.24 (m, 1H), 1.57 (ddd, *J* = 13.1, 4.1, 2.1 Hz, 2H), 1.42 – 1.30 (m, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 142.1, 104.8, 66.4, 38.2, 31.4.

HRMS (APCI-TOF+) *m/z* calcd for $C_7H_{12}BrO$ [(M+H)+]: 191.0072; found 191.0071.

N-Boc (*E*)-4-(2-bromovinyl)piperidine (SI-2e):



Yield: 700 mg (31%, 2 steps, method B) starting from *N*-Boc piperidine-4-carbaldehyde (2.00 g, 9.38 mmol). *E*-isomer only (^{1}H NMR).

Purification: automated flash column chromatography on SiO_2

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 10 min, then gradient from 0% to 1% AcOEt in PE for 15 min
Detection	ELSD & UV (254 nm)

TLC	R_F = 0.7 (1% EtOAc in Hexanes)

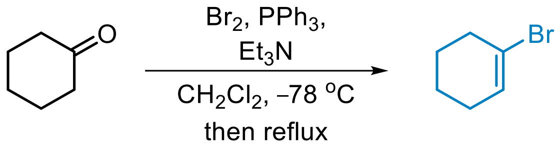
Colorless oil. TLC: R_f = 0.9 (1% AcOEt in hexanes);

^{1}H NMR (500 MHz, DMSO-d_6, mixture of rotamers/conformers in a ratio ca. 4.5:1) δ 6.34 (d, J = 13.6 Hz, 1H), 6.20 (dd, J = 13.6, 7.2 Hz, 1H), 4.00 – 3.79 (br m, 2H), 2.87 – 2.56 (br m, 2H), 2.31 – 2.15 (m, 1H), 1.68 – 1.57 (m, 2H), 1.39 (s, 9H), 1.25 – 1.13 (m, 2H);

^{13}C NMR (126 MHz, DMSO-d_6, mixture of rotamers/conformers) δ 153.7, 141.8, 105.0, 78.5, 43.2 (v br), 39.0, 30.6, 28.0.

MS: compund undergoes fragmentation (ESI, APCI): [(M+Na)+] 312 Da (int. 10%); [(((M-Boc)+H)+H)+] 190 Da (int. 100%); [((M-*t*-BuO)+H_2O+H)+] 236 Da (int. 75%).

1-bromocyclohex-1-ene (SI-2f):



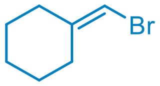
To a flame-dried round bottom flask was charged with PPh_3 (2.79 g, 10.62 mmol, 1.1 equiv.) The atmosphere was exchanged three times with argon and equipped with an argon balloon. Anhydr. CH_2Cl_2 was added (30 mL) and the resulting solution was cooled to –78 °C. Then, Br_2 (0.6 mL, 11.59 mmol, 1.2 equiv.) was added slowly and allowed to stir for 5 minutes before the slow addition of Et_3N (1.7 mL, 12.55 mmol, 1.3 equiv.). The reaction mixture was stirred for another 5 minutes before the addition of cyclohexanone (1 mL, 9.66 mmol, 1 equiv.). The reaction mixture was warmed to rt and stirred overnight. Then, the reaction mixture was refluxed for 2 hours. The crude reaction mixture was then concentrated and purified by automated flash column chromatography to afford the compound **SI-2f** as a colorless oil (760 mg, 49% yield) with spectral data in accordance with previous reports.

Cartridge size	1× 80 g (silica gel)
Flow	45 mL/min
Eluent	petroleum ether (PE) for 10 min, then gradient from 0% to 1% AcOEt in PE for 15 min
Detection	ELSD & UV (254 nm)
TLC	R_F = 0.9 (1% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6) δ 6.08 – 6.01 (m, 1H), 2.41 – 2.33 (m, 2H), 2.10 – 2.00 (m, 2H), 1.73 – 1.63 (m, 2H), 1.59 – 1.51 (m, 2H);

^{13}C NMR (126 MHz, DMSO-d_6) δ 129.0, 121.9, 34.7, 26.9, 24.0, 20.5.

(bromomethylene)cyclohexane (SI-2g):

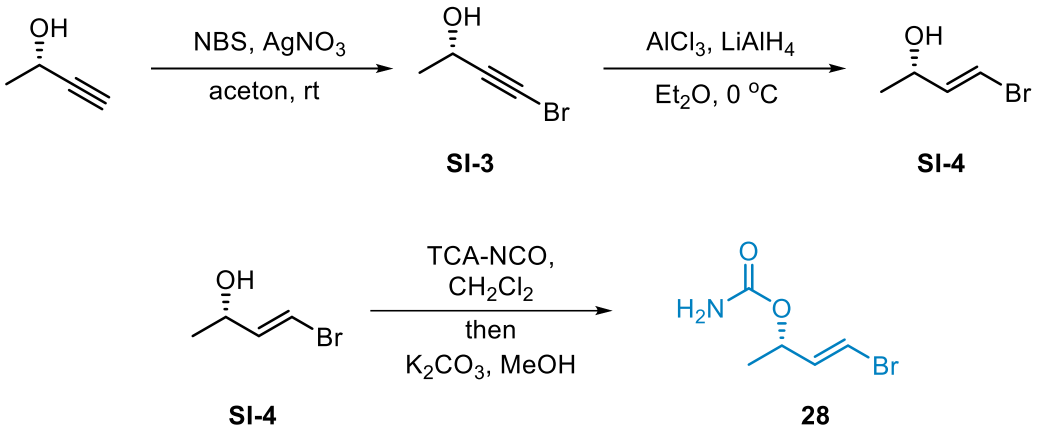


This compound was prepared following the general method B starting from cyclohenanone (3.0 g, 30.6 mmol). After standard work-up and extraction with pentane, the crude product was purified by a vacuum distillation (b.p. 100-105 °C at 100 mbar) to provide 2.35 g (44%) of **SI-2g** as a yellowish oil.
Note: This compound was stored in freezer (−20 °C) and vessel was covered with tin foil as a light protection.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (p, *J* = 1.1 Hz, 1H), 2.36 – 2.24 (m, 2H), 2.21 – 2.11 (m, 2H), 1.61 – 1.49 (m, 6H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.3, 97.7, 35.7, 31.2, 28.0, 26.8, 26.3.

(*S*,*E*)-4-bromobut-3-en-2-yl carbamate (28):



<u>*Step 1:*</u> A flask was charged with $AgNO_3$ (2.42 g, 14.27 mmol, 20 mol%) and NBS (14.00 g, 78.47 mmol, 1.1 eq.), covered with a tinfoil and flushed with argon. Next, acetone (142 mL, c 0.5 M) was added and mixture was cooled to –10 °C followed by dropwise addition of (*S*)-but-3-yn-2-ol (5.00g, 71.34 mmol). The mixture was allowed to warm to rt. When reaction was completed (TLC analysis, ca. 2 h, $KMnO_4$ stain) the mixture was filtrated through Celite®, washed with acetone and carefully evaporated. The residue was dissolved in Et_2O and washed with sat. $NaHCO_3$. Aqueous layer was washed twice with Et_2O and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated carefully to obtain bromoalkyne **SI-3** which was used directly in the next step. Caution: several bromoalkynes were found to be lachrymators!

Step 2: $LiAlH_4$ (7.39 g, 194.65 mmol, 2 eq.) was suspended in anhydr. Et_2O (325 mL) and cooled to 0 °C. In other flask, $AlCl_3$ (19.46 g, 145.99 mmol, 1.5 eq.) was carefully dissolved (dissolving is highly exothermic) at 0 °C in diethyl ether (150 mL) and the resulting solution added dropwise to $LiAlH_4$ suspension. Next, a solution of the crude bromoalkyne in Et_2O (50 mL) was added dropwise and the resulting mixture was allowed to warm to rt. When reaction was completed (TLC analysis, $KMnO_4$ stain, ca. 3 h) K-Na tartate was added carefully and solids were removed by filtration through Celite®, washed with Et_2O. After drying over anhydr. Na_2SO_4, filtrate was carefully concentrated on a rotatory evaporator and purified by a column chromatography (15-25% Et_2O in pentane) on to obtain 7.60 g of vinyl bromide **SI-4**.

Step 3: To a cooled (0 °C) solution of **SI-4** (7.60 g, 50.33 mmol) in anhydr. CH_2Cl_2 (250 mL, 0.2 M) trichloroacetyl isocyanate (TCA-NCO) (11.38 g, 60.40 mmol, 1.2 eq.) was added dropwise and mixture was allowed to warm to rt. When reaction was completed (TLC analysis, $KMnO_4$ stain, ca. 30-45 min) solvent and volatiles were removed and the residue was dissolved in MeOH-water (600 mL, 4:1 v/v, 0.1 M). The resulting solution was cooled to 0 °C and K_2CO_3 (27.82 g, 201.32 mmol, 4 eq.) was added in one portion. After adjustment to rt and the reaction mixture stirred overnight. Next, methanol was evaporated and the residue treated with CH_2Cl_2 (200 mL) and water (200 mL). Aqueous layer was washed twice with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and filtered, and solvent was removed by rotatory evaporator. The resulting white solid was recrystalized in water to provide 4.80 g of compound **28** (49%, overall yield of 3 steps). Spectral data in accordance with previous report.[30]

m.p. 96–98 °C;

$[\alpha]_D^{25}$ –58.6 (c 1.18, $CHCl_3$);

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.39 (dd, *J* = 13.7, 1.1 Hz, 1H), 6.20 (dd, *J* = 13.7, 6.6 Hz, 1H), 5.21 (pd, *J* = 6.6, 1.1 Hz, 1H), 4.81 (s, 2H), 1.32 (d, *J* = 6.6 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 137.2, 108.8, 70.8, 20.0.;

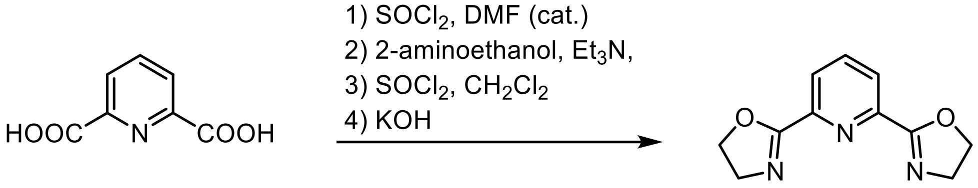
HRMS (ESI-TOF) *m/z* calcd for $C_5H_8NO_2BrNa$ [(M+Na)+] 215.9636; found: 215.9632;

FTIR (film) ν: 3421, 3332, 3271, 3199, 2977, 1683, 1623, 1452, 1393, 1044 cm^{-1}.

3.2.3. Synthesis of other reagents

3.2.3.1. Synthesis of PyBOX ligands

2,6-bis(4,5-dihydrooxazol-2-yl)pyridine (L8a):



Step 1: To a mixture of pyridine-2,6-dicarboxylic acid (2.50 g, 15 mmol) in DMF (200 mL) was added $SOCl_2$ (30 mL, 48.80 g, 410.2 mmol). The mixture was refluxed for 2 h, during which time the insoluble powder gradually dissolved. The excess amount of $SOCl_2$ was removed by atmospheric distillation, and the residual amount of $SOCl_2$ was removed under reduced pressure by co-distillation with a small amount of toluene. Product, pyridine-2,6-dicarbonyl dichloride **SI-05** (3.05 g, >99 %) was obtained as a pale white solid which was used directly in the next step.

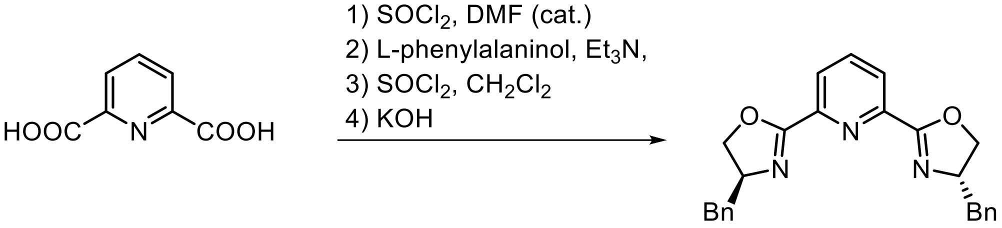
Step 2 &3: To a solution of 2-aminoethanol (3.05 g, 49.93 mmol) and Et_3N (6.5 mL, 47.06 mmol) in CH_2Cl_2 (100 mL) was cooled in an ice bath, and a solution of **SI-05** (3.05 g) in CH_2Cl_2 (30 mL) was added over 10 min. A white precipitate was generated immediately. After stirring at room temperature for 1 day, the reaction mixture was cooled to 0 °C and $SOCl_2$ (51.17g, 430.11 mmol, 31.5 mL) was added. After 30 min, it was adjusted to rt, and then the resulting mixture was refluxed for 2 h. The white precipitate dissolved, and the colour of the solution turned violent. Next, the solution was concentrated under reduced pressure, and the residual amount of $SOCl_2$ was removed under reduced pressure by co-distillation with a small amount of toluene. The residue was triturated with dichloromethane (30 mL) and the resulting solution was washed with sat. aq. $NaHCO_3$ (15 mL), water (15 mL), and brine (15 mL) and then dried with Na_2SO_4. After filtration, the solvent and volatiles were removed, and the crude product was subjected to flash chromatography on SiO2 [petroleum ether (PE)/EtOAc, 2:1 to 1:1 v/v] to give the product, N^2,N^6-Bis(2-chloroethyl)pyridine-2,6-dicarboxamide (**SI-06**) (2.98 g, 65.5% in two steps) as a white solid.

Step 4: To a solution of **SI-06** (5.04 g, 17.37 mmol) in MeOH (150 mL) was added KOH (2.13 g, 37.93 mmol). The resulting mixture was refluxed for 4 h, and white precipitate was generated during the course of the reaction. Next. the mixture was concentrated under reduced pressure and the residue was triturated with dichloromethane (30 mL). This solution was washed with water (50 mL) and brine (50 mL) and then dried over anhydr. Na_2SO_4. Filtration and removal of solvent provided ligand **L8a** (2.23 g, 60%, overall yield 39% in 4 steps) as a white solid which was additionally dried under high vacuum. Spectral data in accordance with previous reports.[31]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.8 Hz, 2H), 7.88 – 7.80 (m, 1H), 4.54 – 4.44 (m, 4H), 4.08 (t, *J* = 9.6 Hz, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 146.8, 137.4, 125.6, 68.4, 55.1.

2,6-bis((S)-4-benzyl-4,5-dihydrooxazol-2-yl)pyridine (L8b):



Ligand **L8b** was prepared following the protocol for preparation ligand **L8a** starting from pyridine-2,6-dicarboxylic acid (24.5 mmol) and L-phenylalaninol (9.26 g, 61.27 mmol). Yield: 5.36 g (overall 60% in 4 steps); white solid.

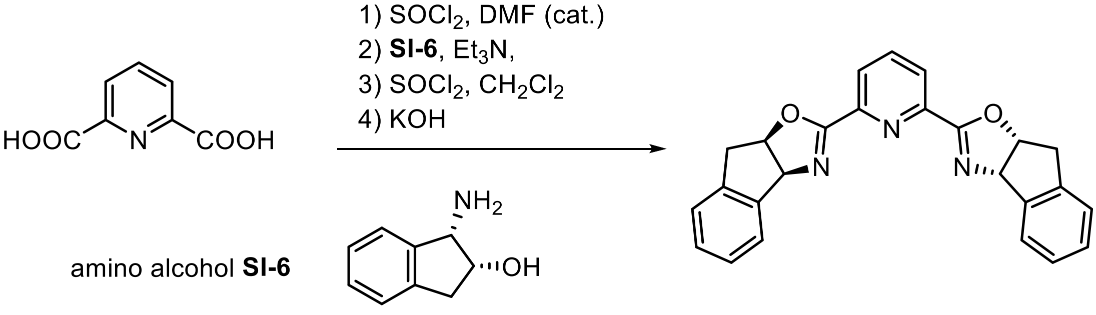
m.p. 148-149 °C; [Lit.[32] 155-156 °C];

$[\alpha]_D^{28}$ −35.8 (c 0.9, $CHCl_3$) [Lit.[33] −38 (c 0.67, $CHCl_3$)];

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.8 Hz, 2H), 7.88 (t, *J* = 7.8 Hz, 1H), 7.33 – 7.27 (m, 4H), 7.25 – 7.20 (m, 6H), 4.69 – 4.59 (m, 2H), 4.45 (t, *J* = 9.0 Hz, 2H), 4.25 (t, *J* = 8.6, 7.6 Hz, 2H), 3.26 (dd, *J* = 13.8, 5.3 Hz, 2H), 2.74 (dd, *J* = 13.8, 9.0 Hz, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 162.8, 146.9, 137.8, 137.4, 129.3, 128.7, 126.7, 125.9, 72.7, 68.2, 41.8.

(3a*S*,8a*R*)-2,6-bis(3a,8a-dihydro-8*H*-indeno[1,2-*d*]oxazol-2-yl)pyridine (L8c):



Ligand **L8c** was prepared following the protocol for the preparation of the ligand **L8a** starting from pyridine-2,6-dicarboxylic acid (24.5 mmol) and (1*S*,2*R*)-1-amino-2-indanol (**SI-6**)(9.26 g, 61.27 mmol). Yield: 5.36 g (overall 60% in 4 steps); Spectral data in accordance with precious reports.[33-34]

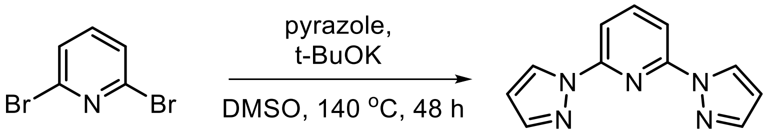
m.p. 268-269 °C; [Lit.[34] 265-268 °C], white solid;

$[\alpha]_D^{27}$ −431 (*c* 0.67, $CHCl_3$) [Lit.[33] −493 (*c* 1.0, $CHCl_3$)][Lit.[34] −364 (*c* 1.04, CH_2Cl_2)];

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.8 Hz, 2H), 7.76 (t, *J* = 7.9 Hz, 1H), 7.58 – 7.50 (m, 2H), 7.24 (d, *J* = 2.5 Hz, 6H), 5.76 (d, *J* = 8.0 Hz, 2H), 5.58 (dt, *J* = 8.2, 4.3 Hz, 2H), 3.47 (d, *J* = 4.3 Hz, 4H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9, 147.0, 141.5, 139.9, 137.2, 128.6, 127.5, 126.0, 125.7, 125.4, 84.3, 77.0, 39.7.

(2,6-Bis(pyrazol-1-yl)pyridine (L10):



In a round-bottomed flask charged with a stir bar, the pyrazole (1.15 g, 16.89 mmol, 2.0 equiv.) was dissolved in DMSO (21 mL, 0.4 M). Next, *t*-BuOK (2.00 g, 17.73 mmol, 2.1 equiv.) was added portionwise, and the resulting mixture was stirred at room temperature for 10 min. After 10 min, the 2,6-dibromopyridine (2.00 g, 8.44 mmol, 1.0 equiv.) was added and the resulting mixture was kept at 140 °C for 48 h. After cooling down to room temperature, the product was precipitated by adding water. The solid was collected via filtration and washed with water (If the product did not precipitate with the addition of water, the product was extracted using CH_2Cl_2. The organic layer was then washed with brine, dried with MgSO4, filtered, and concentrated). The crude product was then purified by silica gel chromatography (Rf 0.5 in 45% EtOAC in Hex) to give 2,6-bis(pyrazol-1-yl)pyridine (**L10**) as a white solid (1.30 g, 73%).

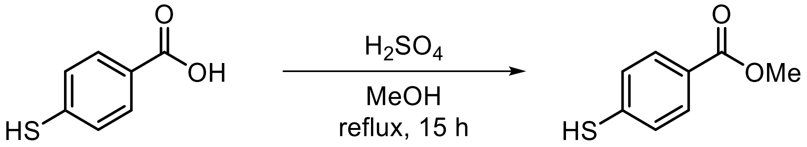
m.p. 140-141 °C [Lit. 139 °C[35], 141-143 °C[36], 136-138 °C[37]]

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 2.7 Hz, 2H), 7.92 (dd, *J* = 8.8, 7.1 Hz, 1H), 7.87 – 7.82 (m, 2H), 7.75 (d, *J* = 1.6 Hz, 2H), 6.51 – 6.43 (m, 2H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.1, 142.5, 141.5, 127.1, 109.5, 108.1.

3.2.3.2. Synthesis of thiols and disulfides

Synthesis of methyl 4-mercaptobenzoate (5ab)



4-Mercaptobenzoic acid (1.50 g, 9.73 mmol, 1.0 equiv) was dissolved in MeOH (20 mL) and to this mixture sulfuric acid (96%, 500 µL, 920 mg, 9.77 mmol, 1.0 equiv) was added. The reaction mixture was refluxed for 15 h. The reaction was quenched by addition of EtOAc (50 mL) and an aqueous solution of $NaHCO_3$ (50 mL). The aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to obtain the crude product. It was recrystalized from EtOAc:Hex to give 1.47 g (8.74 mmol, 90%) of product **5ab** as a white solid.

Note: The purity of thiol ***5ab*** *is essential for successful outcome of the alkenylation process as well it can influence the yields of products and side products. It should look like following figure after recrystallization.*

M.p. 54-55°C [Lit. 53-55 °C,[38] 55-56 °C[39]]

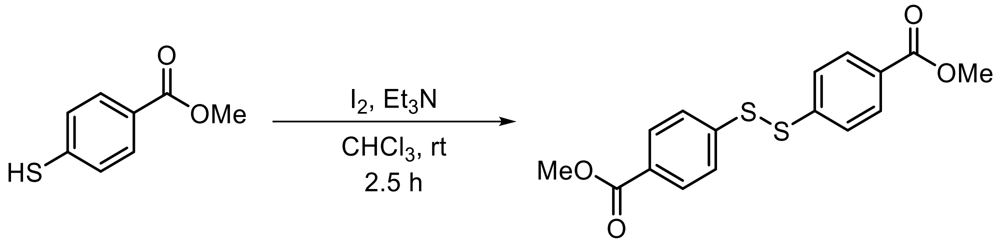
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.1 Hz, 1H), 7.29 (s, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 3.89 (s, 3H), 3.59 (s, 1H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 138.3, 130.2, 128.1, 127.2, 52.0;

FTIR (film) ν: 3398, 2580, 2554, 1933, 1716, 1598, 1402, 1280, 1114, 760 cm^{-1};

HRMS (ESI-TOF) *m/z* calcd for $C_8H_8O_2SNa$ [(M+Na)+] 191.0137. Found: 191.0139.

Synthesis of bis(4-methoxycarbonylphenyl) disulfide (5ba):



Solutions of methyl 4-sulfanylbenzoate (221 mg, 1.32 mmol) in $CHCl_3$ (10 mL) and I_2 (250 mg, 0.98 mmol) in $CHCl_3$ (10 mL) were added separately and simultaneously over 1 h to a vigorously stirred solution of Et_3N (275 µL, 1.98 mmol) in $CHCl_3$ (10 mL). After stirring at room temperature for 1.5 h, the resulting mixture was washed with aqueous saturated $Na_2S_2O_3$, dried over $MgSO_4$, and the solvent evaporated. The residue was purified by silica gel flash column chromatography (cartridge: 24 g, eluent: chloroform, flow: 20 mL/min) to provide 240 mg (73%) of desired disulfide as a white solid.

M.p. 131-132 °C [Lit. 130-131 °C,[40] 126-127 °C[41]];

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.95 (d, J = 8.6 Hz, 1H), 7.66 (d, J = 8.6 Hz, 4H), 3.83 (s, 6H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 165.5, 141.2, 130.1, 128.5, 126.2, 52.2;

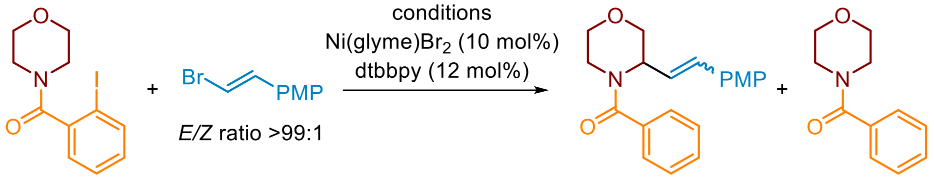
FTIR (film) *v*: 1935, 1715, 1590, 1435, 1278, 1110, 752 cm^{-1};

HRMS (ESI-TOF) *m/z* calcd for $C_{16}H_{15}O_4S_2$ [(M+H)+] 335.0412; found 335.0410.

4. Photoelectrochemical alkenylation of saturated heterocycles

4.1. Initial experiments

Table SI-1. Screening of initial conditions



1a 2a 3aa 4a

Ent.	Conditions	Conv. of **1a**	Yield of **3aa**	Yield of **4a**	Ref.
1a.	[Ir(ppy)$_2$(dtbbpy)]PF$_6$ (1 mol%), K$_3$PO$_4$ (3 eq), MeCN, 26 °C, TBABr (5 eq), blue light irradiation (450-460 nm)	>99%	traces (GC)	87% (isol.)	[42]
1b.	[Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ (1 mol%), Hantzch's ester (3 eq), MeCN, 26 °C, blue light irradiation (450-460 nm)	>99%	traces (GC)	90% (isol.)	[43]
2a.	4-CzIPN (2 mol%), *i*-Pr$_2$NEt (3 eq), solvent, 26 °C, blue light irradiation (450-460 nm)	45%	traces (GC)	27% (isol.)	[44]
2b.	4-CzIPN (2 mol%), Et$_3$N (3 eq), solvent, 26 °C, blue light irradiation (450-460 nm)	57%	traces (GC)	33% (isol.)	-
2c.	4-CzIPN (2 mol%), *n*-Bu$_3$N (3 eq), solvent, 26 °C, blue light irradiation (425 nm)	61%	traces (GC)	41% (isol.)	-
3a.	TTMS (2 eq), DCE, 26 °C, blue light irradiation (450-460 nm)	>99%	traces (GC)	90% (isol.)	[45]
3b.	4-CzIPN (2 mol%), TTMS (2 eq), DCE, 26 °C, blue light irradiation (450-460 nm)	>99%	traces (GC)	89% (isol.)	-
4a.	Cs$_2$CO$_3$ (3 eq), DMSO, 26 °C, blue light irradiation (440 nm)	0%	0% (GC)	0% (GC)	[3]
4b.	Cs$_2$CO$_3$ (3 eq), DMSO, 26 °C, blue light irradiation (395 nm)	>99%	<10% (GC)	70% (isol.)	-
4c.	Cs$_2$CO$_3$ (3 eq), DMSO, 26 °C, blue light irradiation (365 nm)	>99%	traces (GC)	83% (isol.)	-
	4-DPAIPN (2 mol%), mesna **5aa** (20 mol%), HCOOCs (3 eq), DMSO, blue light irradiation (440 nm)	>99%	~15% (NMR)	68% (isol.)	[46]
5a.	(+)Ni|Graphite(-), TBACl (1 eq), DMF, rt, 15 mA, 6 h	>99%	traces (GC)[b]	35% (isol.)	[47]
5b.	(+)Zn|Graphite(-), TBABF$_4$ (1 eq), DMSO/MeCN 9:1 v/v, 40 °C, 9 mA, 4 h	90%	traces (GC)[b]	62% (isol.)	[48]
5c.	(+)Graphite|SS(-), TBABF4 (1 eq), phenantrene (1 eq). MeCN 12 mA, 4 h	92%	traces (GC)[b]	55% (isol.)	[49]
5d.	(+) RVC|Ni$_{\text{foam}}$(-), TBABF$_4$ (2 eq), HCOOCs (3 eq.), thiol **5ab** (30 mol%), DMSO, 28 °C, 3 mA, irradiation (395 nm), 12 h	91%	35% (GC)	43% (isol.)	-

[a] determined by GC, [b] formation of homo- and cross-coupling products;
DCE = dichloroethane; TTMS = (TMS)$_3$SiH; ppy = phenylpyridine; dtbbpy = 4,4'-di-t-butyl-2,2'-bipyridine; SS = stainless steel.

4.2. Optimization studies

Standardized Procedure:

Vial A: In a glovebox, an oven dried ElectraSyn vial (10 mL) was charged with model PMP vinyl bromide (0.6 mmol, 1.0 equiv), *N*-Bz^I morpholine (0.66 mmol, 1.1 equiv),† formic acid salt (1.8 mmol, 3.0 equiv), thiol (0.12 mmol, 0.2 equiv) and

---

† Bz^I = 2-iodo benzoyl

electrolyte (0.6 mmol, 1.0 equiv). A magnetic stir bar was added, and PTFE cap equipped with electrodes was mounted (Note 4).

Vial B: In a glovebox, an oven dried 5-mL vial was charged with Ni salt (0.06 mmol, 0.1 equiv) and ligand (0.066 mmol, 0.11 equiv.). A magnetic stir bar was added and the vial was closed with septum cap (Note 4).

Both vials were taken out from a glovebox ad their content was kept under argon. To the vial A 4 mL of anhydrous DMSO was added. A 2 mL of anhydrous DMSO was added to the vial B, and the resulting mixture was stirred magnetically for 10 min at 60 ºC to prepare the Ni(ligand)Br_2 complex. After cooling down, a solution from the vial B was transferred to the vial A connected to ElectraSyn 2.0 galvanostat.

ElectraSyn 2.0 setup:

Electrolysis mode	Constant current
Electrolysis mode	Undivided cell
Reference electrode	No
Current	3 mA
Charge	2.2 F/mol
Time	12 h
Alternating polarity	Depending on electrode set (*vide infra*)

The electrolysis process was started and the reaction mixture was irradiated with visible light (for specific wavelengths *vide infra*) for 12 hours. After that time, the conversion of the starting materials (**1a** and **2a**), and yield of the product(s) **3aa** as well as of type-**4** deiodinated product were determined by GC.

FID-GC chromatograph setup:

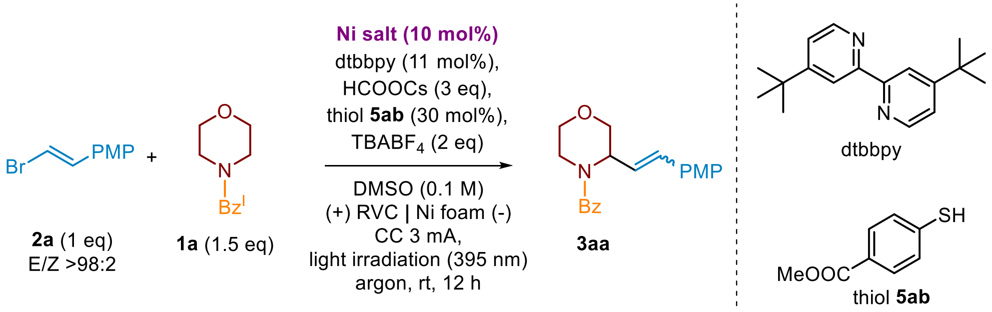
Column type	GL Sciences InertCap FFAP
Column length × ø,	30 m × 0.25 mm
Band film thickness	0.25 µm
Injector temperature	200 ºC
Gas flow	1mL/min
Temperature program	Initial temp.: 250 ºC for 0.85 min; Gradient from 250 ºC to 320 ºC for 10 min; End temp. 320 ºC for 5 min

Compound:	**1a**	**4a**	**5ab**	**5bb**	**(Z)-3aa**	**(E)-3aa**	**1a/2a cross-coupling products**	**2a homocoupling products**
Rt [min]	4.87	3.0	2.3	8.35	8.37	9.54	8	2.4-2.6

4.2.1. Optimization of qualitative parameters

Note: The order of the following sections corresponds to an order of the parameters which were examined during the optimization studies.

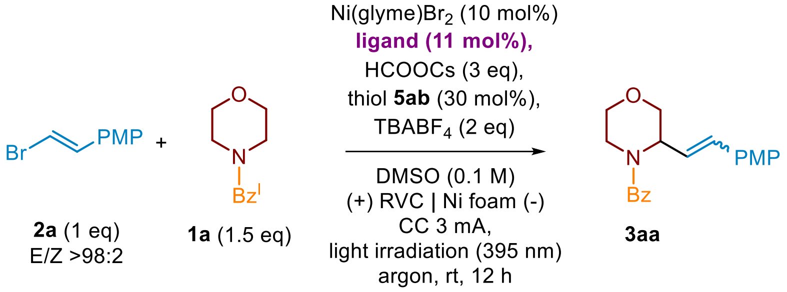
4.2.1.1. Nickel salt selection

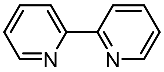
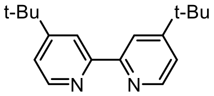
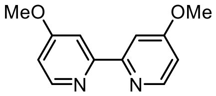
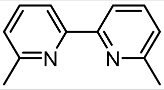
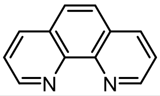
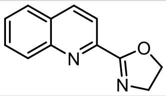


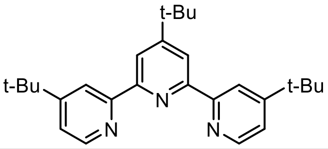
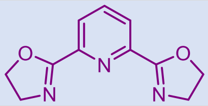
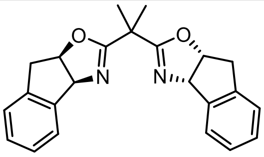
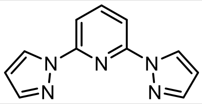
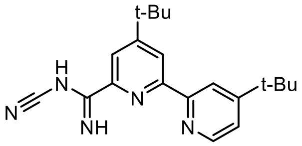
Entry	Ni salt	SMC [%]^a	PDY [%]^a	E/Z ratio
1	Ni(glyme)Cl_2	>91	35	82:18
2	**Ni(glyme)Br_2**	**89**	**51**	90:10
3	NiI_2	>99	51	99:01
4	$Ni(OTf)_2$	93	7	94:06
5	$Ni(cod)_2$	88	33	97:03
6	Ni(dtbbpy)Br_2	>99	53	69:31

^{a} determined by GC; SMC = staring material's conversion; PDY = product's yield; Bz^I = 2-iodobenzoyl

4.2.1.2. Ligand selection

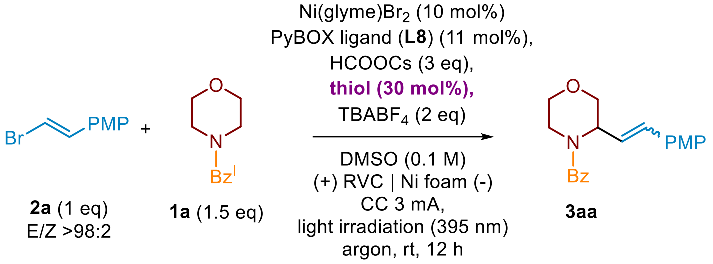


Entry	Ligand		SMC [%]^{a,b}	PDY [%]^a	E/Z ratio
1	L1		>99	22	66:34
2	L2 (4,4'-dtbbpy)		89	51	90:10
3	L3		96	45	65:35
4	L4		99	56	22:78
5	L5		>99	33	86:14
6	L6		98	25	98:2

7	L7		>99	49	59:41
8	**L8**		**>99**	**67**	60:40
9	L9 (*rac*)		90	26	96:4
10	L10		>99	50	76:24
11	L11		91	34	87:13

[a] determined by GC, SMC = staring material's conversion; PDY = product's yield; Bz^I = 2-iodobenzoyl.

4.2.1.3. Thiol selection

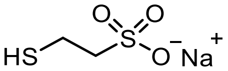
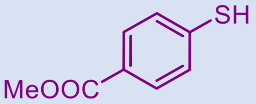
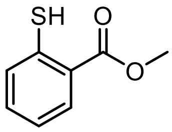
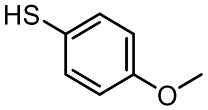
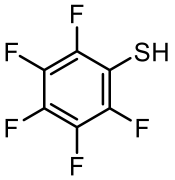


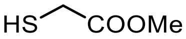
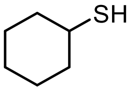
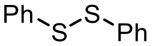
Ni(glyme)Br$_2$ (10 mol%)
PyBOX ligand (**L8**) (11 mol%),
HCOOCs (3 eq),
thiol (30 mol%),
TBABF$_4$ (2 eq)
DMSO (0.1 M)
(+) RVC | Ni foam (-)
CC 3 mA,
light irradiation (395 nm)
argon, rt, 12 h

2a (1 eq)
E/Z >98:2

1a (1.5 eq)

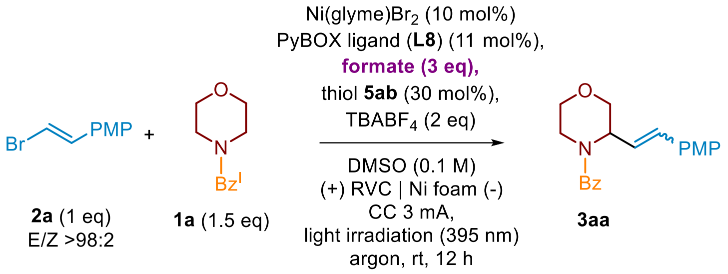
3aa

Entry		Thiol	SMC [%]^{a,b}	PDY [%]^{a}	E/Z ratio
1	**5aa**		78	6	86:14
2	**5ab**		**>99**	**67**	**60:40**
3	**5ac**		97	37	82:18
4	**5ad**		91	13	75:25
5	**5ae**		82	16	91:09

6	**5af**		63	3	4:96
7	**5ag**		>99	15	2:98
8	**5ba**		>99	51	79:21

[a] determined by GC, SMC = staring material's conversion; PDY = product's yield; Bz^I = 2-iodobenzoyl.

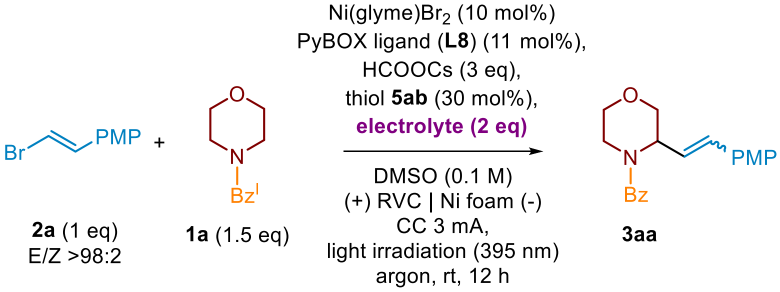
4.2.1.4. Formic acid salt selection



Entry	Salt of formic acid	SMC [%][a,b]	PDY [%][a]	E/Z ratio
1	**HCOOCs**	**>99**	**67**	**60:40**
2	HCOOCs (*dtbbpy instead of PyBox ligand*)	89	51	90:10
3	HCOOK	97	37	89:11
4	HCOONa	63	3	>99:1
5	HCOOLi	>99	15	88:12
6	HCOOTBA	78	6	78:22

[a] determined by GC, SMC = staring material's conversion; PDY = product's yield; TBA = tetra-*n*-butylammonium; TEA = tetraethylammonium; Bz^I = 2-iodobenzoyl.

4.2.1.5. Electrolyte selection

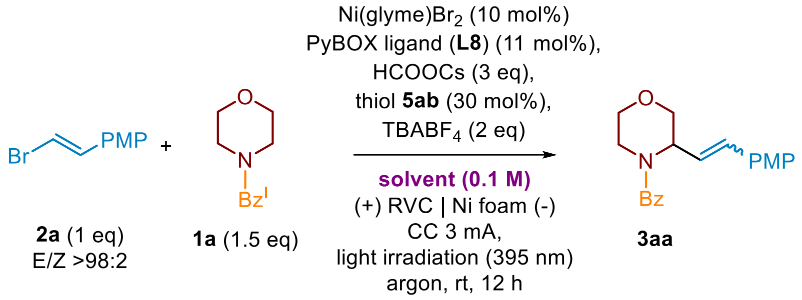


Entry	Electrolyte	SMC [%][a,b]	PDY [%][a]	E/Z ratio
1	**$TBABF_4$**	**>99**	**67**	60:40
2	$TBAPF_6$	97	42	84:16
3	TBACl	>99	47	21:79
4	TBABr	>99	60	39:61
5	$TBAClO_4$	>99	58	62:38
6	$TEABF_4$	95	36	83:17

7	TsOTEA	>99	0	85:15

[a] determined by GC, SMC = staring material's conversion; PDY = product's yield; TBA = tetra-*n*-butylammonium TEA = tetraethylammonium; Bz^I = 2-iodobenzoyl.

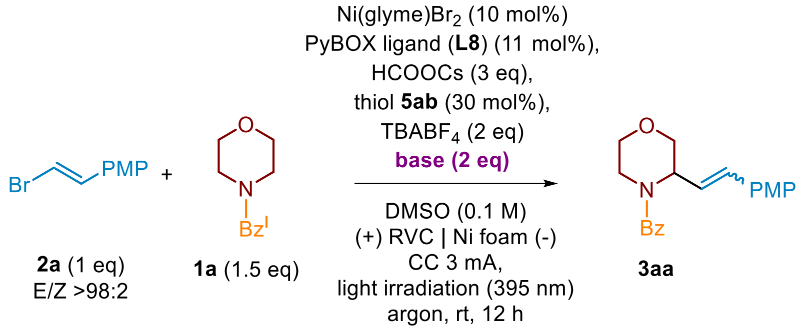
4.2.1.6. Solvent selection



Entry	Solvent	SMC [%]^{a,b}	PDY [%]^{a}	E/Z ratio
1	**DMSO**	**>99**	**67**	60:40
2	DMSO (*ligand **L2** instead of ligand **L8***)	89	51	90:10
3	MeCN	68	9	92:08
4	DMF	63	16	93:07
5	DMSO/H_2O (4:1v/v)	44	5	>99:1
6	DMSO/MeCN (1:1v/v)	46	11	>99:1

[a] determined by GC, SMC = staring material's conversion; PDY = product's yield.

4.2.1.7. Additional base selection

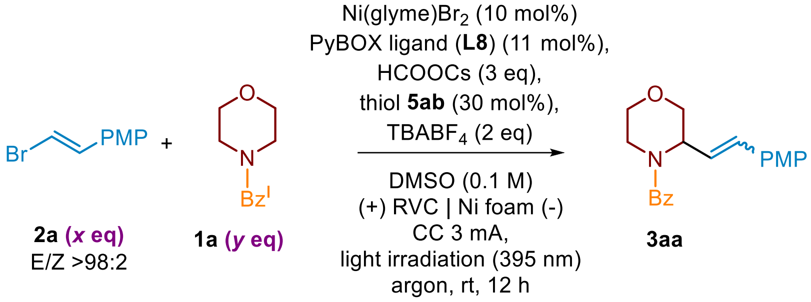


Entry	base	SMC [%]^{a,b}	PDY [%]^{a}
1	**none**	**>99**	**67**
2	K_2CO_3	>99	46
3	*i*-Pr_2NEt	>99	49

[a] determined by GC, SMC = staring material's conversion; PDY = product's yield; Bz^I = 2-iodobenzoyl.

4.2.2. Optimization of quantitative parameters

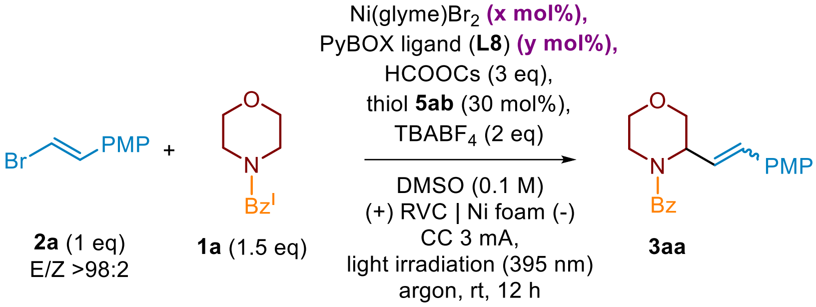
4.2.2.1. Starting materials loading



Entry	**2a** (*x* eq)	**1a** (*y* eq)	SMC [%][a]	PDY [%][a]	E/Z ratio
1	**1**	**1.5**	**>99**	**67**	**60:40**
2	1	1	>99	64	87:13
3	1.5	1	90	38	81:19
4	1	2	75	42	73:27

[a] determined by GC; SMC = staring material's conversion; PDY = product's yield; TBA = tetra-*n*-butylammonium; Bz^I = 2-iodobenzoyl.

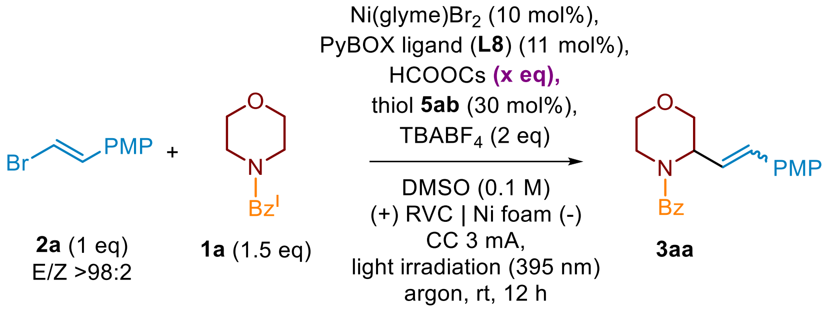
4.2.2.2. Ni salt and ligand loading



Entry	**Ni salt** (*x* mol%)	**ligand** (*y* mol%)	SMC [%][a]	PDY [%][a]	E/Z ratio
1	20	25	>99	49	72:28
2	**10**	**11**	**>99**	**67**	**60:40**
3	**5**	**5.5**	**>99**	**65**	**88:12**
4	3	3.5	67	53	91:09
5	1	1.2	60	50	83:17

[a] determined by GC; SMC = staring material's conversion; PDY = product's yield; TBA = tetra-*n*-butylammonium; Bz^I = 2-iodobenzoyl.

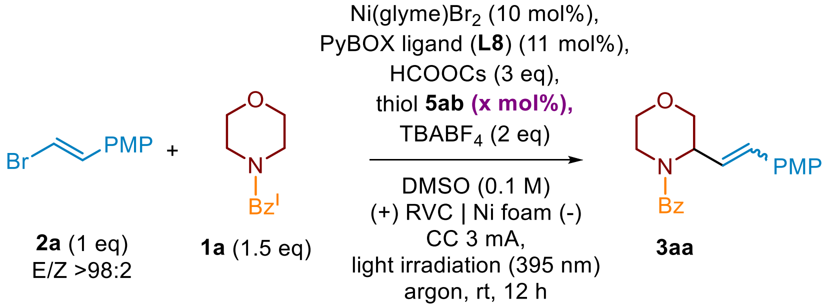
4.2.2.3. HCOOCs loading



Entry	HCOOCs loading (x equiv)	SMC [%][a,b]	PDY [%][a]	E/Z ratio
1	1	67	12	59:41
2	2	92	21	91:08
3	**3**	**>99**	**67**	**60:40**
4	4	>99	49	59:41

[a] determined by GC, SMC = staring material's conversion; PDY = product's yield; $\mathrm{Bz^I}$ = 2-iodobenzoyl.

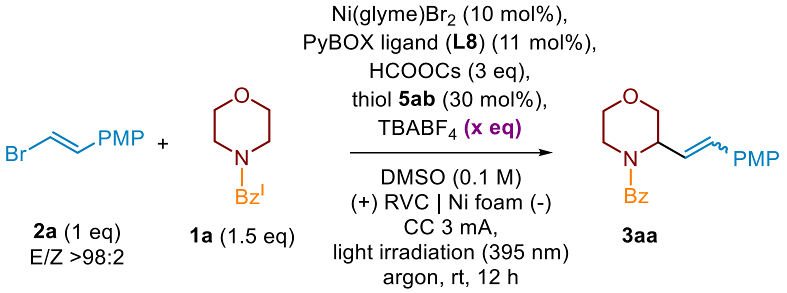
4.2.2.4. Thiol loading



Entry	Thiol loading (x mol%)	SMC [%][a,b]	PDY [%][a]	E/Z ratio
1	10	>99	29	73:27
2	20	>99	61	67:33
3	**30**	**>99**	**67**	**60:40**
4	40	>99	51	69 : 31

[a] determined by GC, SMC = staring material's conversion; PDY = product's yield; $\mathrm{Bz^I}$ = 2-iodobenzoyl.

4.2.2.5. Electrolyte loading



2a (1 eq)
E/Z >98:2

1a (1.5 eq)

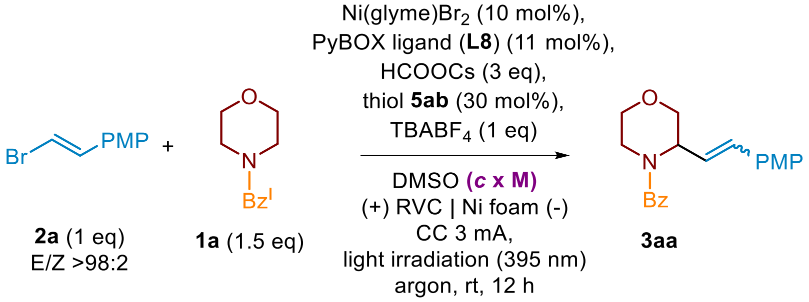
Ni(glyme)Br_2 (10 mol%),
PyBOX ligand (**L8**) (11 mol%),
HCOOCs (3 eq),
thiol **5ab** (30 mol%),
$TBABF_4$ **(x eq)**
DMSO (0.1 M)
(+) RVC | Ni foam (-)
CC 3 mA,
light irradiation (395 nm)
argon, rt, 12 h

3aa

Entry	Electrolyte loading (x equiv)	SMC [%]^{a,b}	PDY [%]^{a}	E/Z ratio
1	**1**	**>99**	**73**	**75:35**
2	2	>99	67	60:40
3	3	>99	51	87:13

[a] determined by GC, SMC = staring material's conversion; PDY = product's yield; Bz^I = 2-iodobenzoyl.

4.2.2.6. Concentration effect with respect to the limiting substrate 2a



2a (1 eq)
E/Z >98:2

1a (1.5 eq)

Ni(glyme)Br_2 (10 mol%),
PyBOX ligand (**L8**) (11 mol%),
HCOOCs (3 eq),
thiol **5ab** (30 mol%),
$TBABF_4$ (1 eq)
DMSO **(*c* x M)**
(+) RVC | Ni foam (-)
CC 3 mA,
light irradiation (395 nm)
argon, rt, 12 h

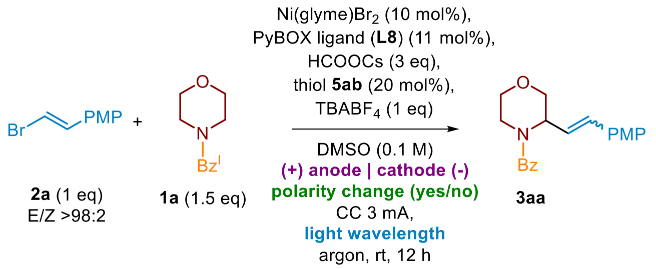
3aa

Entry	Concentration of **2a** (M)	SMC [%]^{a,b}	PDY [%]^{a}	E/Z ratio
1	0.05	>99	51	89:11
2	**0.1**	**>99**	**73**	**75:25**
3	0.2	>99	73	82:18

[a] determined by GC, SMC = staring material's conversion; PDY = product's yield; Bz^I = 2-iodobenzoyl.

4.2.3. Optimization of photoelectrochemical conditions

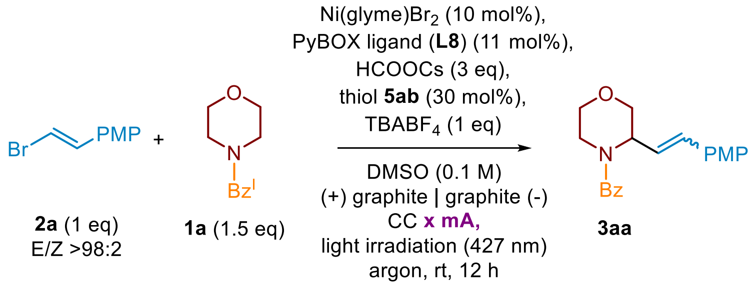
4.2.3.1. Electrode material and light wavelength selection



Entry	Anode (+)	Cathode (-)	PCE [time][b]	Light [nm]	SMC [%][a]	PDY [%][a]	E/Z ratio
1	RVC	Ni foam	no	395	>99	73	65:35
2	RVC	Ni foam	no	365	96	31	52:48
3	RVC	Ni foam	no	400	>99	38	62:38
4	RVC	Ni foam	no	427	>99	72	65:35
5	RVC	Ni foam	no	440	>99	56	62:38
6	RVC	Ni foam	no	450	84	39	69:31
7	RVC	RVC	no	395	>99	57	59:41
8	Graphite	Ni foam	no	395	>99	42	83: 17
9	Graphite	Graphite	yes (10 min)	395	>99	65	68:32
10	Graphite	Graphite	yes (5 min)	427	>99	50	85:15
11	**Graphite**	**Graphite**	**yes (10 min)**	**427**	**>99**	**87**	**72: 28**
12	Graphite	Graphite	yes (15 min)	427	88	44	90:10
13	Graphite	Graphite	yes (5 sec)	427	95	65	54:46

[a] determined by GC; [b] PCE = polarity change of electrodes (cycle duration in minutes, 3 mA for x min then −3 mA for x min); SMC = staring material's conversion; PDY = product's yield; Bz^I = 2-iodobenzoyl.

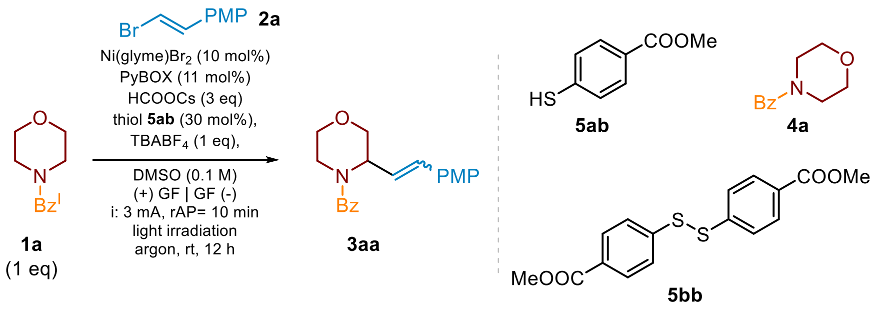
4.2.3.2. Current setup



Entry	Current (mA)	SMC [%][a]	PDY [%][a]	E/Z ratio
1	1	**>99**	48	70:30
2	2	**>99**	55	68:32
3	**3**	**>99**	**87[b]**	**72:28**
4	4	**>99**	59	78:12

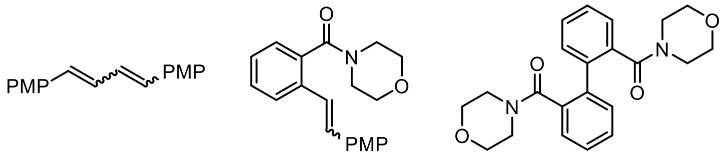
[a] determined by GC; SMC = staring material's conversion; PDY = product's yield; Bz^I = 2-iodobenzoyl.

4.2.4. Exclusion test & control experiments



Ent.	Deviation from optimal conditions	Conv. of **1a**^{a}	Yield of **3aa**^{a}	E/Z ratio
1.	none	>99%	87%	72:28
2.	without light irradiation	>90%^{b}	5%	-
3.	without electrolysis (@ 427 nm)	>99%^{b}	0%	-
4.	without electrolysis (@ 395 nm)	>90%^{b}	>10%	-
5.	without HCOOCs (@ 395 nm)	54%^{b}	0%	-
6.	without thiol (@ 427 nm)	38%^{b}	6%	80:20
7.	without thiol (@ 395 nm)	75%^{b}	6%	79:21
8.	without thiol and formate (@395)	25%^{b}	0%	-
9.	disulfide **5bb** instead of **5ab** (@ 395 nm)	>99%	51%	80:20
10.	without argon	>99%	70%	87:13
11.	non-anhydrous DMSO & HCOOCs·H$_2$O	87%	22-28%	-
12.	benzamide **4a** instead of **1a**	no reaction	-	-

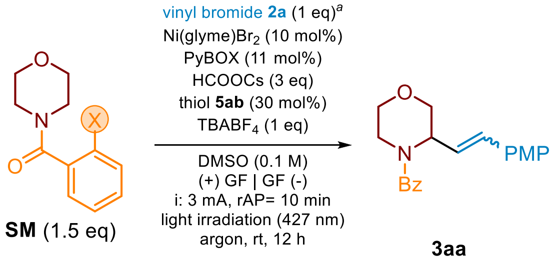
^{a} determined by GC analysis; ^{b} homocoupling and cross-coupling products assigned by MS:



Bz^I = 2-iodobenzoyl; PMP = 4-methoxyphenyl

4.3. Selection of cross-coupling partners

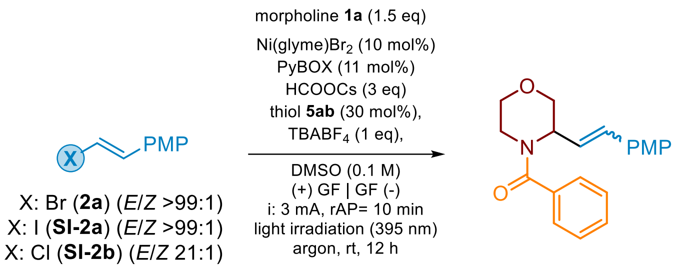
4.3.1. Selection of 2-halobenzamide-based HAT directing group



Ⓧ	Conv. of **SM***	Yield of **3aa**^{b}	*E/Z* ratio^b
I (**1a**)	>99%	86%	90:10
Br (**SI-1a**)	86%	57%	86:14
Cl (**SI-1b**)	45%	0%	-

^{a} *E/Z* ratio >99:1; ^{b} determined by GC; SM = starting material

4.3.2. Selection of vinyl halide cross-coupling partner

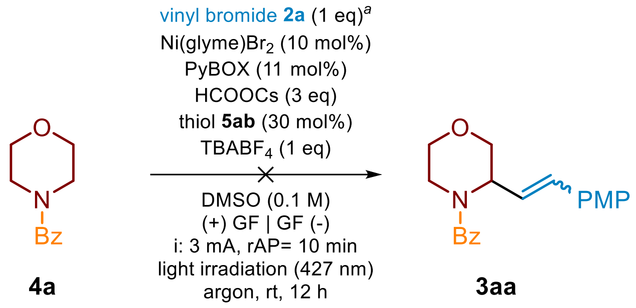


X	Conv. of **1a**[a]	Conv. of VB[a]	Yield of **3aa**[a]	(*E*/*Z*) ratio
I	>99%	>99%[b]	14%	72 : 28
Br	>99%	>99%	87%	72 : 28[b]
Br	>99%	>99%	65%	32 : 68
Cl	99%	58%	32%	96 : 4

[a] determinded by GC; [b] irradiation with blue light (427 nm); VB = vinyl halide

4.3.3. Control experiment with benzamide 4a

To exclude an alternative intermolecular HAT activation, the control reaction of benzamide **4a** with vinyl bromide **2a** under standard conditions was performed. No product **3aa** was formed after standard 12 hours, indicating that neither aryl thiyl radical nor CO_2 radical anion do not act as a HAT reagent to deliver the corresponding α-aminoalkyl radical intermediate for subsequent cross-coupling reaction.



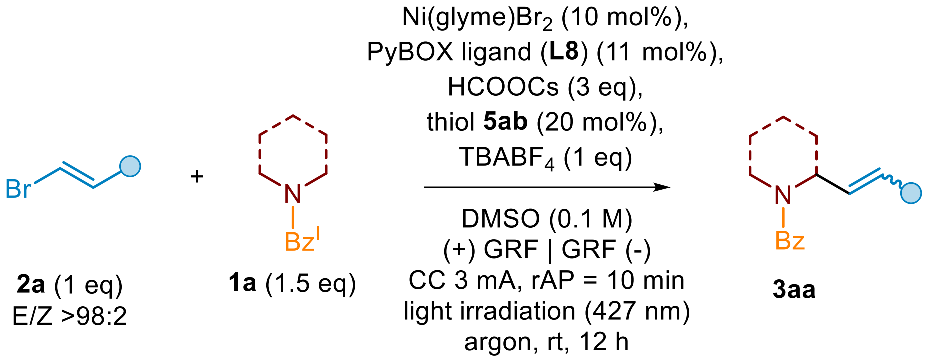
4a

3aa

not dectected by GC & MS

[a] *E*/*Z* ratio >99:1

5. Scope of photoelectrochemical alkenylation of heterocycles



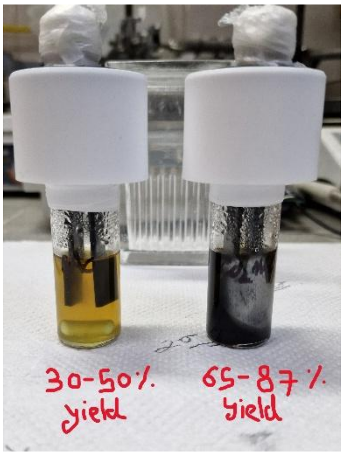
2a (1 eq)
E/Z >98:2

1a (1.5 eq)

3aa

General procedure: In a glove box, oven dry an ElectraSyn vial (vial A) (10 mL) equipped with a magnetic stir bar was charged with vinyl bromide (0.6 mmol, 1.0 equiv), 2-halobenzamide (0.66 mmol, 1.1 equiv), HCOOCs (1.8 mmol, 3.0 equiv), methyl 4-mercaptobenzoate **5ab** (0.12 mmol, 0.2 equiv) and n-Bu$_4$NBF$_6$ (0.6 mmol, 1.0 equiv). The vial was closed with a PTFE cap equipped with anode (graphite) and cathode (graphite). In another oven dry 5 ml vial (vial B) was charged with Ni(glyme)Br$_2$ (0.06 mmol, 0.1 equiv) and PyBOX ligand **L8** (0.066 mmol, 0.11 equiv). Magnetic stir bar was added and vial B was closed with septa cap. Both vials were taken out from a glove box and kept under argon. In as Vial A 4ml Under argon dry DMSO was added to both vials; 4 mL to the vial A and 2 mL to the vial B. The mixture in the vial B was kept stirred at 60°C for 10 min to prepare pre-nickel complex. After that time, solution of Ni-complex was transferred from the vial B to the vial A. which was added to vial A. Now, the vial A was installed on an ElectraSyn stand and electrolysis was started (Constant current 3 mA, time 12 h, alternating electrodes polarity change every 10 min) along with blue light irradiation by Kessil^{TM} LED lamp (427 nm, 5 cm away, with cooling fan to keep the reaction temperature at 25 °C) for 12 h. After completion of the reaction, the reaction mixture was transferred to a separatory funnel, the electrodes were rinsed with ethyl acetate (5 mL) and water. The aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organics were washed successively with brine (1 × 30 mL), then dried over MgSO$_4$ or Na$_2$SO$_4$. After removal of drying agent, solvents and volatiles were removed on a rotary evaporator. The crude product was purified via by automated flash chromatography. The obtained product was kept for under high vacuum (10^{-3} bar) at 70°C in the Kugelrohr apparatus for 10h to remove the traces of solvents.

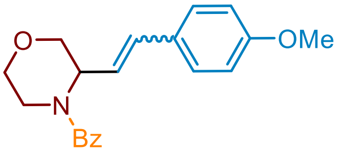
The progress of the reaction was followed by TLC by using UV (254 nm) detection and vanillin stain. E/Z-isomers ratio was assigned by ^{1}H NMR or GC analysis.



Note: During the reaction course, the reaction solution changes its color. It was noticed that the color of the solution at the end point allows for estimation of yield range: dark yellow/orange 30-50% (left vial), brown/black 65-90% (right vial).

5.1. Scope of 2-iodobenzamides

N-Bz 3-(4-methoxystyryl)morpholine (3aa):



Yield: 152 mg (78%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); E/Z ratio: 72:28. Brown oil.

Purification: automated flash column chromatography on SiO_2

Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min

Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)

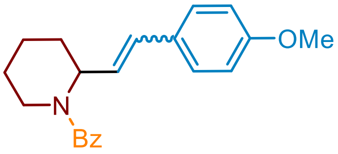
TLC: R_F = 0.45 (50% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 72:28 with conformers and rotamers) δ 7.48 – 7.41 (m, 5H, major), 7.39 (d, *J* = 8.7 Hz, 2H, major), 7.35 – 7.20 (m, 2H, minor), 7.05 (d, *J* = 8.2 Hz, 1H, *minor*), 6.91 (d, *J* = 8.6 Hz, 2H, major), 6.80 (d, *J* = 8.6 Hz, 1H, *minor*), 6.53 (d, *J* = 11.8 Hz, 1H, *minor*), 6.47 (d, *J* = 16.2 Hz, 1H, major), 6.31 (dd, *J* = 16.2, 5.4 Hz, 1H, major), 6.09 (dd, *J* = 11.8, 9.1 Hz, 1H, *minor*), 5.12 (d, *J* = 9.0 Hz, 1H, *minor*), 4.72 (s, 1H, major), 3.97 (d, *J* = 11.6 Hz, 1H, major), 3.93 – 3.79 (m, 2H, E/Z), 3.78 (s, 3H, major), 3.75 (s, 1H, *minor*), 3.74 – 3.68 (m, 2H, E/Z), 3.55 – 3.43 (m, 2H, E/Z), 3.38 (dd, *J* = 13.1, 3.6 Hz, 1H, E/Z);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 5:2 with conformers and rotamers) δ 169.30, 169.1, 158.8, 158.2, 135.6, 135.35, 130.8, 129.7, 129.1, 129.0, 128.8, 128.2, 127.9, 127.8, 127.2, 126.3, 126.1, 125.8, 124.2, 113.8, 113.5, 70.2, 69.3, 66.1, 65.9, 54.8, 54.8, 52.9, 49.5.

HRMS (ESI-TOF+) *m/z* calcd for $C_{20}H_{21}NO_3Na$ [(M+Na)+] 346.1419; found 346.1420.

N-Bz 2-(4-methoxystyryl)piperidine (3ab):



Yield: 140 mg (72%) starting from pyrrolidine benzamide **1b** (208 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 91.5:8.5. Brown oil.

Purification: automated flash column chromatography on SiO_2

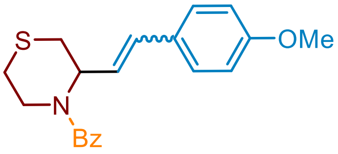
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 20 % EtOAc in petroleum ether for 10 min, then gradient from 20% to 30% AcOEt in petroleum ether for 15 min, and 50% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.51 (50% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, (*E/Z*)-isomer mixture in a ratio 91.5:8.5) δ 7.87 (d, *J* = 7.9 Hz, 1H, minor), 7.56 – 7.51 (m, 1H, minor), 7.47 – 7.36 (m, 7H, major), 7.34 – 7.04 (m, 1H,minor), 6.90 (d, *J* = 8.7 Hz, 2H, major), 6.81 (d, *J* = 8.7 Hz, 1H, minor), 6.45 (d, *J* = 11.8 Hz, 1H, minor), 6.40 (dd, *J* = 16.2, 1.9 Hz, 1H, major), 6.23 (dd, *J* = 16.2, 4.8 Hz, 1H, major), 6.03 (dd, *J* = 11.9, 8.8 Hz, 1H, minor), 5.35 (br s, 1H, minor), 4.96 (br s, 1H, major), 4.00 – 3.83 (m, 1H, mixture), 3.77 (s, 3H, major), 3.75 (s, 3H, minor), 3.08 (td, *J* = 13.1, 2.8 Hz, 1H, major), 1.94 – 1.82 (m, 1H, mixture), 1.81 – 1.57 (m, 5H, mixture), 1.52 – 1.39 (m, 1H, mixture).

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, (*E/Z*)-isomer mixture in a ratio 91.5:8.5) δ 169.3, 158.7, 136.5, 130.0, 129.0, 128.7, 128.4, 127.9, 127.7, 127.5, 127.3, 127.1, 125.89, 125.86, 125.7, 113.8, 113.5, 54.8, 29.1, 25.0, 19.1;

HRMS (ESI-TOF+) *m/z* calcd for $C_{21}H_{23}NO_2Na$ [(M+Na)+] 344.1626; found 344.1625.

N-Bz 3-(4-methoxystyryl)thiomorpholine (3ac):



Yield: 113 mg (55%) starting from thiomorpholine benzamide **1c** (220 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 79:21. Brown sticky oil.

Purification: automated flash column chromatography on SiO_2:

Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 40 % EtOAc in petroleum ether for 10 min, then gradient from 40% to 50% AcOEt in petroleum ether for 15 min, and 50% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.5 (50% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

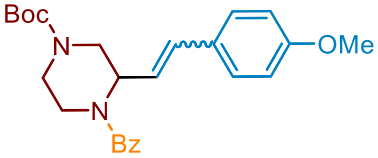
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, (*E/Z*)-isomer mixture in a ratio 79:21) δ 7.54 – 7.25 (m, E/Z-mixture), 7.19 – 7.07 (m, 4H, minor), 6.92 (d, *J* = 8.7 Hz, 2H, major), 6.81

(d, *J* = 8.7 Hz, 1H, minor), 6.58 (d, *J* = 11.9 Hz, 1H, minor), 6.48 (d, *J* = 16.2 Hz, 1H, major), 6.36 (dd, *J* = 16.2, 4.9 Hz, 1H, major), 6.23 (dd, *J* = 11.9, 8.2 Hz, 1H, minor), 5.56 (br s, 1H, minor), 5.18 (br s, 1H, major), 4.14 (br s, 1H, major), 4.07 – 3.94 (m, 1H, minor), 3.78 (s, 3H, major), 3.76 (s, 3H, minor), 3.76 – 3.68 (m, 3H, major), 3.48 – 3.28 (m, E/Z mixture), 3.12 (dt, *J* = 13.5, 4.2 Hz, 1H, major), 2.84 – 2.69 (m, E/Z mixture), 2.67 – 2.61 (m, E/Z mixture), 2.61 – 2.52 (m, E/Z mixture);

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C, (*E/Z*)-isomer mixture in a ratio 79:21) δ 169.8, 169.1, 158.8, 136.0, 135.9, 135.7, 131.0, 130.2, 129.3, 129.1, 129.1, 128.9, 128.9, 128.7, 128.02, 127.95, 127.8, 127.2, 126.5, 126.2, 126.1, 126.0, 125.8, 124.7, 113.8, 113.6, 113.5, 54.85, 54.79, 51.6, 46.6, 41.0, 31.5, 30.9, 26.6, 26.4;

HRMS (ESI-TOF+) *m/z* calcd for $C_{20}H_{21}NO_2SNa$ [(M+Na)+] 362.1191; found 362.1190.

N^4-Boc,*N*^{1}-Bz 2-(4-methoxystyryl)piperazine (3ad):



Yield: 208 mg (82%) starting from *N*-Boc piperazine benzamide **1d** (275 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 81:19. Brown sticky oil.

Purification: automated flash column chromatography on SiO_2:

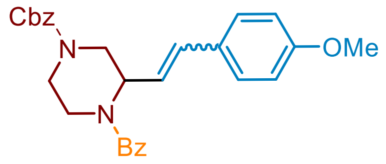
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 45% to 60% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.5 (50% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80 °C, (*E/Z*)-isomer mixture in a ratio 81:19) δ 7.49 – 7.43 (m, E/Z mixture), 7.35 (d, *J* = 8.7 Hz, 2H, major), 7.30 (t, *J* = 7.4 Hz, 1H, minor), 7.26 – 7.20 (m, 1H, minor), 7.09 (br d, *J* = 8.3 Hz, 1H, minor), 6.91 (d, *J* = 8.7 Hz, 2H, major), 6.83 (d, *J* = 8.7 Hz, 1H, minor), 6.51 (d, *J* = 11.9 Hz, 1H, minor), 6.46 (d, *J* = 16.2 Hz, 1H, major), 6.11 (dd, *J* = 16.2, 4.9 Hz, 1H, major), 5.82 (dd, *J* = 11.9, 8.6 Hz, 1H, minor), 5.26 (br s, 1H, minor), 4.89 (br s, 1H, major), 4.11 (d, *J* = 13.6 Hz, 1H), 3.94 – 3.82 (m, E/Z mixture), 3.77 (s, 3H, major), 3.76 (s, 3H, minor) 3.49 – 3.29 (m, E/Z mixture), 3.27 – 3.18 (m, E/Z mixture), 3.00 – 2.91 (m, E/Z mixture), 1.43 (s, 9H, minor), 1.39 (s, 9H, major);

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C, (*E/Z*)-isomer mixture in a ratio 81:19) δ 169.4, 169.2, 158.8, 158.2, 153.6, 135.7, 135.4, 130.7, 130.2, 129.0, 128.8, 128.7, 128.2, 128.0, 127.9, 127.8, 127.1, 126.5, 126.2, 126.1, 125.5, 124.0, 113.8, 113.6, 78.8, 54.8, 52.7, 49.2, 47.0, 46.3, 42.9, 42.8, 28.4, 27.6;

HRMS (ESITOF+) *m/z* calcd for $C_{25}H_{30}N_2O_4Na$ [(M+Na)+] 445.2103; found 445.2105.

N^4-Cbz,*N*^{1}-Bz 2-(4-methoxystyryl)piperazine (3ae):



Yield: 192 mg (70%) starting from *N*-Cbz piperazine benzamide **1e** (300 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 94:6. Pale-yellow sticky solid.

Purification: automated flash column chromatography on SiO_2:

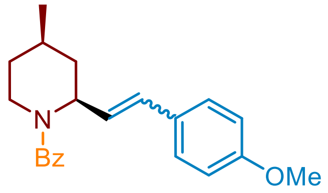
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 40 % EtOAc in petroleum ether for 10 min, then gradient from 40% to 50% AcOEt in petroleum ether for 15 min, and 50% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.57 (50% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80 °C, (*E/Z*)-isomers mixture in a ratio 94:6) δ 7.89 (d, *J* = 8.0 Hz, 1H, minor), 7.57 – 7.04 (m, E/Z mixture), 6.90 (d, *J* = 8.7 Hz, 2H, major), 6.81 (d, *J* = 8.5 Hz, 2H, minor), 6.47 (d, *J* = 16.2 Hz, 1H, major), 6.13 (dd, *J* = 16.2, 5.0 Hz, 1H, major), 5.83 (dd, *J* = 11.9, 8.6 Hz, 1H, minor), 5.19 – 5.06 (m, 2H, E/Z mixture), 4.94 (br s, 1H, major), 4.19 (d, *J* = 13.5 Hz, 1H, major), 4.02 – 3.96 (m, E/Z mixture), 3.95 – 3.87 (m, E/Z mixture), 3.78 (s, 3H, major), 3.76 (s, 3H, minor), 3.37 – 3.22 (m, 2H mixture), 3.61 – 2.97 (m, E/Z mixture);

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C, (*E/Z*)-isomers mixture in a ratio 94:6 including rotamers/conformers) δ 169.5, 168.1, 158.8, 158.3, 154.3, 154.1, 141.6, 138.5, 136.5, 136.4, 135.6, 135.3, 131.0, 129.9, 129.1, 128.9, 128.7, 128.0, 127.91, 127.87, 127.8, 127.35, 127.27, 127.2, 127.1, 127.0, 126.9, 126.8, 126.3, 126.1, 123.7, 92.3, 66.1, 66.0, 54.8, 54.7, 52.7, 46.4, 43.2, 43.0;

HRMS (ESI-TOF+) *m/z* calcd for $C_{28}H_{28}N_2O_4Na$ [(M+Na)+] 479.1947; found 479.1950.

N-Bz (2*R**,4*S**)-2-(4-methoxystyryl)-4-methylpiperidine (3af):



Yield: 208 mg (82%) starting from *N*-Boc piperazine benzamide **1f** (275 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); *dr*$_{(C2/C4)}$ >20:1; (*E/Z*)-isomers in a ratio: 93:7. Brown sticky oil.

Purification: automated flash column chromatography on SiO_2:

Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 35 % EtOAc in petroleum ether for 10 min, then gradient from 35% to 40% AcOEt in petroleum ether for 5 min, and 40% AcOEt in petroleum ether for 15 min

Detection: ELSD & UV (254 nm)

TLC: R_F = 0.54 (40% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

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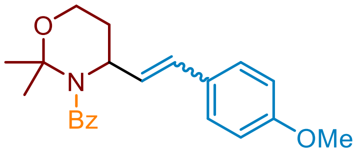
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *dr* >20:1, (*E/Z*)-isomers mixture in a ratio 93:7) spectral data for (*E*)-isomer: δ 7.45 – 7.35 (m, 7H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.37 (d, *J* = 16.2 Hz, 1H), 6.20 (dd, *J* = 16.2, 4.8 Hz, 1H), 5.54 – 4.67 (very broad m, 1H), 3.75 (s, 3H), 3.07 (s, 2H), 1.94 – 1.73 (m, 1H), 1.61 (br d, *J* = 13.2 Hz, 1H), 1.38 (td, *J* = 13.1, 5.8 Hz, 1H), 1.10 (td, *J* = 12.5, 4.5 Hz, 1H), 0.91 (d, *J* = 6.3 Hz, 3H);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *dr* >20:1, (*E/Z*)-isomers mixture in a ratio 93:7) spectral data for (*E*)-isomer: δ 169.2, 158.6, 136.5, 129.8, 129.0, 128.6, 127.8, 127.1, 126.1, 125.9, 113.7, 54.8, 37.7, 33.5, 25.4, 21.3;

HRMS (ESI-TOF+) *m/z* calcd for $C_{22}H_{25}NO_2Na$ [(M+Na)+] 358.1783; found 358.1785.

N-Bz 4-(4-methoxystyryl)-2,2-dimethyl-1,3-oxazinane (3ag):



Yield: 140 mg (66%) starting from 1,3-oxazinane benzamide **1g** (228 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 84.5:15.5. Brown sticky oil.

Purification: automated flash column chromatography on SiO_2:

Cartridge size: 1× 80 g (silica gel)

Flow: 45 mL/min

Eluent: 20% EtOAc in petroleum ether for 10 min, then gradient from 20% to 30% AcOEt in petroleum ether for 10 min, and 30% AcOEt in petroleum ether for 30 min

Detection: ELSD & UV (254 nm)

TLC: R_F = 0.8 (30% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

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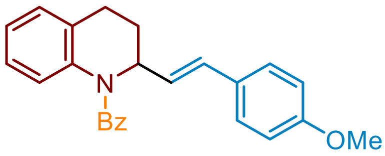
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, E/Z isomers mixture in a ratio 84.5:15.5) δ 7.91 – 7.85 (m, 2H, major), 7.83 (d, *J* = 7.0 Hz, 2H, minor), 7.54 – 7.48 (m, 1H, major), 7.48 – 7.43 (m, 2H, major), 7.41 – 7.37 (m, 2H, minor), 7.36 – 7.30 (m, 2H, major), 6.92 (d, *J* = 8.7 Hz, 2H, minor), 6.89 (d, *J* = 8.7 Hz, 2H, major), 6.49 (d, *J* = 15.8 Hz, 1H, major), 6.38 (d, *J* = 11.8 Hz, 1H, minor), 6.18 (dd, *J* = 16.0, 6.6 Hz, 1H, major), 5.66 (dd, *J* = 11.7, 9.6 Hz, 1H, minor), 5.19 (p, *J* = 7.9 Hz, 1H, minor), 4.79 (p, *J* = 7.3 Hz, 1H, major), 3.76 (s, 3H, major), 3.61 – 3.53 (m, 2H, major), 3.52 – 3.44 (m, 2H, minor), 2.09 (s, 3H, E/Z mixture), 1.93 – 1.83 (m, 2H, E/Z mixture), 1.29-1.24 (m, 3H, E/Z mixture);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, E/Z isomers mixture in a ratio 84.5:15.5) δ 165.4, 158.5, 134.7, 131.0, 130.4, 129.6, 129.3, 128.8, 128.6, 128.3, 127.7, 126.8, 126.7, 113.8, 113.5, 84.5, 57.7, 57.5, 54.8, 48.4, 44.7, 38.0, 37.4, 30.7, 29.6, 29.2, 28.5.

HRMS (ESI-TOF) *m/z* calcd for $C_{22}H_{25}NO_3Na$ [(M+Na)+] 374.1732; found 374.1730.

N-Bz (*E*)-2-(4-methoxystyryl)-1,2,3,4-tetrahydroquinoline (3ah):



Yield: 125 mg (57%) starting from benzamide **1h** (275 mg, 0.66 mmol) and vinyl bromide **1a** (128 mg, 0.60 mmol); 20% of starting material **1h** underwent dehalogenation process. Only (*E*)-isomer. Brown sticky oil.

Purification: automated flash column chromatography on SiO_2:

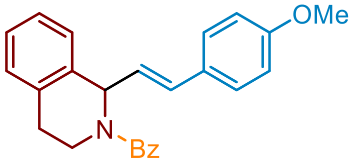
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	15 % EtOAc in petroleum ether for 10 min, then gradient from 15% to 30% AcOEt in petroleum ether for 15 min, and 30% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.7 (20% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.41 – 7.17 (m, 8H), 7.00 (td, *J* = 7.3, 1.4 Hz, 1H), 6.91 (td, *J* = 7.7, 1.6 Hz, 1H), 6.88 – 6.82 (m, 3H), 6.46 (dd, *J* = 16.0, 1.6 Hz, 1H), 6.03 (dd, *J* = 16.0, 5.4 Hz, 1H), 5.28 – 5.21 (m, 1H), 3.74 (s, 3H), 2.83 (t, *J* = 6.7 Hz, 2H,), 2.46 – 2.36 (m, 1H), 1.94 – 1.85 (m, 1H);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C) δ 168.9, 158.6, 137.5, 136.4, 132.0, 131.5, 129.5, 129.3, 129.1, 128.9, 127.6, 127.6, 127.4, 127.0, 126.3, 125.6, 125.1, 124.0, 113.7, 54.8, 54.2, 29.1, 24.0;

HRMS (ESI-TOF+) *m/z* calcd for $C_{25}H_{23}NO_2Na$ [(M+Na)+] 392.1626; found 392.1629.

N-Bz (*E*)-1-(4-methoxystyryl)-1,2,3,4-tetrahydroisoquinoline (3ai):



Yield: 78 mg (35%) starting from benzamide **1i** (275 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); 48% of the staring material **1i** underwent dehalogenation process. Only (*E*)-isomer. Brown waxy solid.

Purification: automated flash column chromatography on SiO_2:

Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	15 % EtOAc in petroleum ether for 10 min, then gradient from 15% to 30% AcOEt in petroleum ether for 15 min, and 30% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.7 (20% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

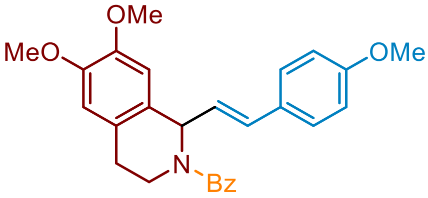
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.33 – 7.10 (m, 11H), 6.83 (d, *J* = 8.7 Hz, 1H), 6.37 (d, *J* = 16.1 Hz, 1H), 6.05 (dd, *J* = 16.1, 5.1 Hz, 1H), 5.17 – 5.03 (v br m, 1H), 5.00

– 4.87 (v br m, 1H), 4.48 (d, *J* = 17.2 Hz, 1H), 3.73 (s, 3H), 3.24 (dd, *J* = 16.2, 5.9 Hz, 1H), 2.97 (dd, *J* = 16.2, 2.6 Hz, 1H);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C) δ 170.5, 159.6, 143.1, 139.3, 137.2, 133.2, 133.1, 131.1, 129.9, 129.2, 128.9, 128.9, 128.0, 127.0, 127.0, 126.7, 126.4, 114.6, 55.7, 44.5, 44.1, 33.6;

HRMS (ESI-TOF+) *m/z* calcd for $C_{25}H_{23}NO_2Na$ [(M+Na)+] 392.1626; found 392.1627.

N-Bz (*E*)-6,7-dimethoxy-1-(4-methoxystyryl)-1,2,3,4-tetrahydroisoquinoline (3aj):



Yield: 72 mg (28%) starting from benzamide **1j** (280 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); Only (*E*)-isomer. Brown waxy solid. Low conversion of starting benzamide after standard 12 h (ca. 50%).

Purification: automated flash column chromatography on SiO_2:

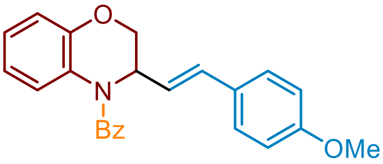
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	40 % EtOAc in petroleum ether for 10 min, then gradient from 15% to 30% AcOEt in petroleum ether for 15 min, and 30% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.4 (50% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.52 – 7.41 (m, 5H), 7.26 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.80 – 6.71 (m, 2H), 6.39 (d, *J* = 16.1 Hz, 1H), 6.06 (dd, *J* = 16.1, 5.2 Hz, 1H major E isomer), 5.26 – 4.66 (m, 2H), 4.38 (d, *J* = 16.9 Hz, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 3.74 (s, 3H), 3.15 (dd, *J* = 16.0, 5.9 Hz, 1H), 2.87 (dd, *J* = 16.0, 2.4 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C) δ 169.5, 158.7, 147.7, 147.6, 136.4, 130.2, 129.0, 128.7, 128.0, 127.2, 126.1, 125.5, 124.2, 124.0, 113.7, 112.7, 110.1, 55.55, 55.51, 54.8, 39.9, 39.8, 32.2;

HRMS (ESI-TOF+) *m/z* calcd for $C_{27}H_{27}NO_4Na$ [(M+Na)+] 452.1838; found 452.1837.

N-Bz (*E*)-3-(4-methoxystyryl)-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazine (3ak):



Yield: 115 mg (28%) starting from benzamide **1k** (280 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); Only (*E*)-isomer. Brown oil.

Purification: automated flash column chromatography on SiO_2:

Cartridge size:	1× 80 g (silica gel)

Flow: 45 mL/min

Eluent: 20 % EtOAc in petroleum ether for 10 min, then gradient from 20% to 50% AcOEt in petroleum ether for 5 min, and 25% AcOEt in petroleum ether for 10 min

Detection: ELSD & UV (254 nm)

TLC: R_F = 0.44 (50% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

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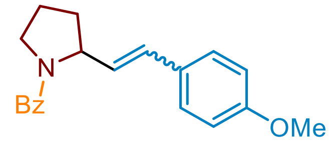
^{1}H NMR (600 MHz, DMSO-d_6, 80 °C) δ 7.57 – 7.53 (m, 2H), 7.52 – 7.47 (m, 1H), 7.46 – 7.41 (m, 2H), 7.27 – 7.19 (m, 3H), 7.00 – 6.93 (m, 1H), 6.93 – 6.80 (m, 3H), 6.74 – 6.69 (m, 1H), 6.51 (dd, *J* = 16.1, 1.8 Hz, 1H), 6.08 (dd, *J* = 16.1, 4.8 Hz, 1H), 5.12 (br d, *J* = 1.9 Hz, 1H), 4.55 (dd, *J* = 11.1, 1.7 Hz, 1H), 4.38 (dd, *J* = 11.2, 3.0 Hz, 1H), 3.74 (s, 3H);

^{13}C NMR (151 MHz, DMSO-d_6, 80 °C) δ 168.2, 158.8, 145.4, 135.4, 131.4, 130.0, 128.4, 128.0, 127.3, 127.2, 124.6, 124.5, 124.2, 122.2, 119.4, 116.2, 113.8, 68.2, 54.8, 52.3;

HRMS (APCI-TOF+) *m/z* calcd for $C_{24}H_{22}NO_3$ [(M+H)+] 372.1600; found 372.1602.

N-Bz 2-(4-methoxystyryl)pyrrolidine (3al):



Yield: 140 mg (75%) starting from pyrrolidine benzamide **1l** (200 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 90:10. Brown oil.

Purification: automated flash column chromatography on SiO$_2$

Cartridge size: 1× 80 g (silica gel)

Flow: 45 mL/min

Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 45% to 50% of AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min

Detection: ELSD & UV (254 nm)

TLC: R_F = 0.5 (50% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

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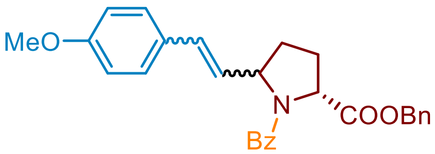
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, (*E/Z*)-isomers mixture in ratio 90:10, including rotamers/conformers) δ 7.56 – 7.19 (m, 7H, major), 6.87 (d, *J* = 8.5 Hz, 2H, major), 6.39 – 5.81 (m, 2H, major), 5.56 (dd, *J* = 11.7, 8.9 Hz, 1H, minor), 4.98 (br s, 1H, minor), 4.67 (br s, 1H, major), 3.77 (s, 3H, minor), 3.76 (s, 3H, major), 3.62 – 3.41 (m, 2H, major), 2.19 – 2.06 (m, 1H, major), 2.01 – 1.69 (m, 3H, major);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, (*E/Z*)-isomers mixture in a ratio 90:10) δ 168.4, 158.5, 158.0, 137.3, 137.0, 129.4, 129.0, 128.9, 128.4, 128.0, 127.6, 127.5, 127.2, 127.0, 126.34, 126.28, 113.7, 113.4, 59.0 (v br), 54.79, 54.76, 47.0 (v br), 31.4 (br), 23.0 (v br);

HRMS (ESI-TOF+) *m/z* calcd for $C_{20}H_{21}NO_2Na$ [(M+Na)+] 330.1470; found 330.1473.

***N*-Bz (2*R*)-5-((*E*)-4-methoxystyryl)proline benzyl ester (3am):**



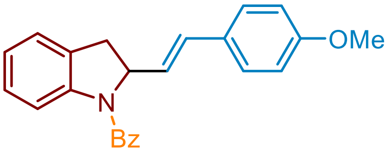
Yield: 115 mg (43%) starting from proline-derived benzamide **1m** (287 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol);

Purification: automated flash column chromatography on SiO_2

Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	35 % EtOAc in petroleum ether for 15 min, then gradient from 35% to 45% of AcOEt in petroleum ether for 5 min, and 45% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.72 (50% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

The alkenylation of **1m** delivered the set of inseparable 2,5-diastereoisomers in a ratio 70:30 (yield 43%) along product of the halogenation of **1m** (ca. 20%). The (*E/Z*)-ratio for the major diastereoisomer was assigned as 83:17 (by 1H NMR), and for the minor one 77:23. **HRMS** (APCI-TOF+) *m/z* calcd for $C_{24}H_{20}NO_2$ [(M+H)+] 354.1494; found 354.1496.

***N*-Bz (*E*)-2-(4-methoxystyryl)indoline (3an):**



Yield: 115 mg (53%) starting from indolidine-derived benzamide **1n** (200 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); Only (*E*)-isomer. Low melting waxy solid.

Purification: automated flash column chromatography on SiO_2

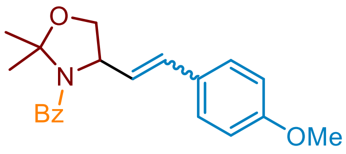
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	20 % EtOAc in petroleum ether for 10 min, then gradient from 20% to 30% of AcOEt in petroleum ether for 10 min, and 30% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.45 (30% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, mixture of rotamers) δ 7.97 – 7.10 (m, 12H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.07 – 5.92 (m, 2H), 5.20 – 5.09 (m, 1H), 3.74 (s, 3H), 3.58 (dd, *J* = 16.1, 9.4 Hz, 1H), 2.91 (dd, *J* = 16.1, 2.5 Hz, 1H);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, mixture of rotamers) δ 168.4, 158.7, 141.9, 136.9, 130.7, 129.4, 129.2, 128.4, 127.8, 127.1, 126.5, 126.45, 126.42, 124.7, 123.3, 115.9, 113.7, 62.0, 54.8, 34.7;

HRMS (ESI-TOF+) *m/z* calcd for $C_{28}H_{27}NO_4Na$ [(M+Na)+] 464.1838; found 464.1839.

***N*-Bz 4-(4-methoxystyryl)-2,2-dimethyloxazolidine (3ap):**



Yield: 102 mg (50%) starting from oxazoline-derived benzamide **1p** (219 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers mixture in ration 98:2. Brown oil.

Purification: automated flash column chromatography on SiO_2

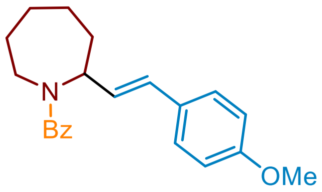
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 20 % EtOAc in petroleum ether for 10 min, then gradient from 20% to 30% of AcOEt in petroleum ether for 10 min, and 30% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.65 (30% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, (*E/Z*)-isomers mixture in a ratio 98:2) δ 7.53 – 7.27 (m, 5H), 7.11 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 5.82 (dd, *J* = 15.9, 7.3 Hz, 1H), 5.75 (d, *J* = 15.9 Hz, 1H), 4.57 (td, *J* = 6.2, 3.8 Hz, 1H), 4.20 (dd, *J* = 8.9, 6.2 Hz, 1H), 3.80 (dd, *J* = 8.9, 3.8 Hz, 1H), 3.74 (s, 3H), 1.74 (s, 3H), 1.66 (s, 3H);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, (*E/Z*)-isomers mixture in a ratio 98:2) δ 167.4, 158.7, 137.9, 130.7, 129.0, 128.6, 127.7, 127.5, 127.0, 125.9, 125.6, 113.6, 94.4, 68.1, 60.2, 54.8, 25.3, 23.8.

HRMS (ESI-TOF) *m/z* calcd for $C_{21}H_{23}NO_3Na$ [(M+Na)+] 360.1576; found 360.1579.

***N*-Bz (*E*)-2-(4-methoxystyryl)azepane (3aq):**



Yield: 148 mg (73%) starting from azepane benzamide **1q** (200 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 98:2. Brown oil.

Purification: automated flash column chromatography on SiO_2

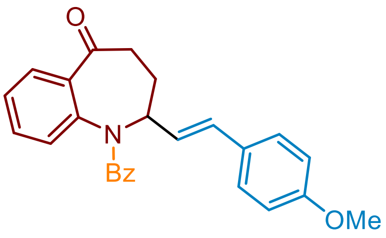
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 35 % EtOAc in petroleum ether for 10 min, then gradient from 35% to 40% AcOEt in petroleum ether for 8 min, and 40% AcOEt in petroleum ether for 20 min.
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.55 (40% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, rotamers/conformers of (*E*)-isomer) δ 7.53 – 7.29 (m, 7H), 6.89 (d, *J* = 8.7 Hz, 2H), 6.49 – 5.96 (v br m, 2H), 5.64 (dd, *J* = 11.8, 8.9 Hz, 1H), 5.15 (br m, 1H), 4.50 – 4.02 (m, 1H), 3.77 (s, 3H), 3.06 – 2.84 (m, 1H), 2.10 (s, 1H), 1.90 – 1.49 (m, 5H), 1.43 – 1.29 (m, 2H);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, rotamers/conformers of (*E*)-isomer) δ 170.2, 158.6, 138.4, 137.4, 129.0, 128.2, 128.0, 127.8, 127.5, 127.1, 126.7, 125.6, 113.8, 113.4, 58.8, 54.8, 33.5, 28.5, 26.5, 24.0;

HRMS (ESI-TOF+) *m/z* calcd for $C_{22}H_{25}NO_2Na$ [(M+Na)+] 358.1783; found 358.1788.

N-Bz 2-(4-methoxystyryl)-1,2,3,4-tetrahydro-5*H*-benzo[*b*]azepin-5-one (3ar):



Yield: 148 mg (73%) starting from azepane benzamide **1r** (200 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); For benzamide **1r**, the initial steps, a generation of an aryl radical and subsequent 1,5-HAT process, were slow, resulting in recovering of the small amounts of **1r**, along with its dehalogenation product (ca. 20%) and vinyl bromide homo-coupling products. Only (*E*)-isomer was observed. This product was contaminated with deiodinated benzamide.

Purification: automated flash column chromatography on SiO_2

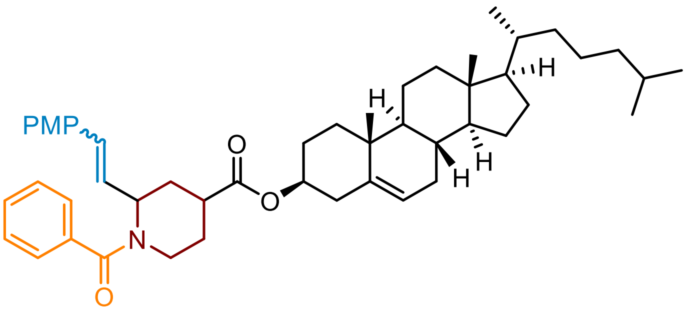
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	20 % EtOAc in petroleum ether for 10 min, then gradient from 20% to 30% AcOEt in petroleum ether for 15 min, and 30% AcOEt in petroleum ether for 20 min.
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.5 (30% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-d_6, inseparable mixture with *N*-Bz 1,2,3,4-tetrahydro-5*H*-benzo[*b*]azepin-5-one, **4r**) selected signals for **3ar**: δ 6.60 (d, *J* = 16.1 Hz, 1H), 6.10 (dd, *J* = 16.1, 6.2 Hz, 1H), 5.44 (s, 1H), 3.76 (s, 3H), 2.43 – 2.32 (m, 1H), 2.07 – 1.97 (m, 1H), 1.85 – 1.68 (m, 1H).

HRMS for **3ar** (ESI-TOF+) *m/z* calcd for $C_{26}H_{23}NO_3Na$ [(M+Na)+] 420.1576; found 420.1573.

LRMS for **4r** (ESI-TOF+) *m/z* 288 Da [(M+Na)+].

Product 3at



Yield: 285 mg (65%) starting from cholesterol derivative **1t** (480 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 91.5:8.5. White solid.

Purification: automated flash column chromatography on SiO_2

Cartridge size:	1× 80 g (silica gel)

Flow: 45 mL/min
Eluent: 20 % EtOAc in petroleum ether for 10 min, then gradient from 20% to 30% AcOEt in petroleum ether for 15 min, and 30% AcOEt in petroleum ether for 20 min.
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.45 (30% EtOAc in hexanes) (Visualization: UV-254, vanillin or KMnO$_4$ stain).

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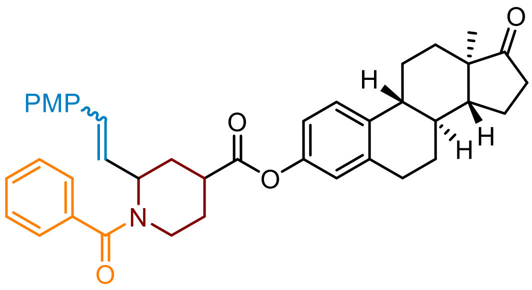
^{1}H NMR (500 MHz, DMSO-d_6 at 80°C, (*E/Z*)-mixture in a ratio 91.5:8:5 including rotamers) δ 7.48 – 7.37 (m, 7H, major), 7.33 – 7.16 (m, 1H, minor), 6.92 – 6.88 (m, 2H, major), 6.81 (d, *J* = 8.2 Hz, 1H, minor), 6.48 (d, *J* = 11.8 Hz, 1H, minor), 6.40 (d, *J* = 16.1 Hz, 1H, major), 6.26 (dd, *J* = 16.1, 5.0 Hz, 1H, major), 5.99 (dd, *J* = 11.8, 8.9 Hz, 1H, minor), 5.35 (d, *J* = 3.7 Hz, 1H, major), 5.08 (s, 1H, major), 4.56 – 4.46 (m, 1H, major), 3.78 (s, 3H, major), 3.75 (s, 1H, minor), 3.30 – 3.09 (m, 2H, major), 2.82 – 2.67 (m, 1H, major), 2.29 (d, *J* = 8.1 Hz, 2H, mixture), 2.08 (d, *J* = 13.5 Hz, 1H, mixture), 2.01 – 1.76 (m, 8H, mixture), 1.62 – 1.47 (m, 7H, mixture) , 1.45 – 1.29 (m, 6H, mixture), 1.30 – 1.22 (m, 2H, mixture), 1.21 – 1.05 (m, 8H, mixture), 1.00 (s, 6H, mixture), 0.92 (d, *J* = 6.5 Hz, 3H, mixture), 0.86 (dd, *J* = 6.7, 1.7 Hz, 6H, mixture), 0.68 (s, 3H, major);

^{13}C NMR (126 MHz, DMSO-d_6 at 80°C, (*E/Z*)-mixture in a ratio 91.5:8:5 including rotamers) δ 172.94, 169.33, 158.77, 139.22, 136.14, 130.47, 128.87, 127.95, 127.29, 125.99, 125.07, 121.60, 113.75, 73.09, 55.84, 55.44, 54.86, 49.27, 41.59, 38.95, 38.59, 37.27, 36.36, 36.15, 35.80, 35.36, 34.68, 31.83, 31.14, 30.98, 27.62, 27.22, 26.95, 26.90, 23.42, 22.87, 22.09, 21.89, 20.22, 18.52, 18.21, 11.27.

HRMS (APCI-TOF) *m/z* calcd for C$_{49}$H$_{68}$NO$_4$ [(M+H)+] 734.5148; found 734.5162.

Product 3au



Yield: 255 mg (69%) starting from estrone derivative **1u** (404 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 90.5:9.5. Off-white solid.

Purification: automated flash column chromatography on SiO$_2$

Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 45% to 60% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min.
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.65 (50% EtOAc in hexanes) (Visualization: UV-254, vanillin or KMnO$_4$ stain).

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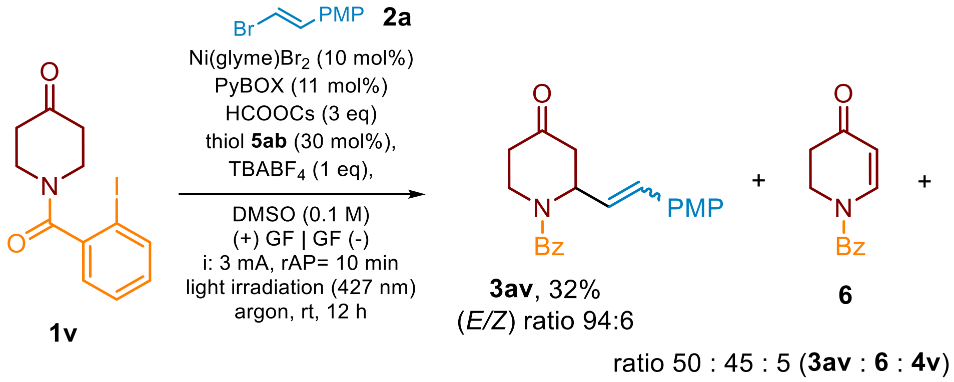
^{1}H NMR (500 MHz, DMSO-d_6 at 80 °C, mixture of (*E/Z*)-isomers in a ratio 90.5:9.5 including the rotamers) δ 7.49 – 7.40 (m, 7H, major), 7.35 – 7.18 (m, 2H, mixture), 6.92 (d, *J* = 8.8 Hz, 2H, major), 6.87 (dd, *J* = 8.5, 2.6 Hz, 1H, mixture), 6.85 – 6.79 (m, 1H, mixture), 6.52 (d, *J* = 11.8 Hz, 1H, minor), 6.46 (d, *J* = 16.2 Hz, 1H, major), 6.31 (dd, *J* = 16.1, 4.9 Hz, 1H, major), 6.06 (dd, *J* = 11.8, 8.8 Hz, 1H, minor), 5.12 (s, 1H, mixture), 3.78 (s, 3H, major), 3.76 (s, 1H, minor), 3.26 – 3.15 (m, 1H, mixture), 3.03 (dt, *J* = 12.3, 3.6 Hz, 1H, mixture), 2.89 – 2.80 (m, 2H, mixture), 2.46-2.42 (m, 1H, mixture), 2.40 – 2.35 (m, 1H, mixture), 2.29 – 2.22 (m, 2H, mixture), 2.12 – 2.03 (m, 2H, mixture), 2.02 – 1.93 (m, 3H, mixture), 1.83 – 1.78 (m, 1H, mixture), 1.73 – 1.36 (m, 8H, mixture), 1.30 – 1.23 (m, 1H, mixture), 0.86 (s, 3H, mixture);

^{13}C NMR (126 MHz, DMSO-d_6 at 80 °C, mixture of (*E/Z*)-isomers in a ratio 90.5:9.5 including the rotamers) δ 218.49, 172.42, 169.37, 158.79, 148.07, 137.41, 136.89, 136.12, 130.59, 129.13, 128.90, 128.86, 127.96, 127.76, 127.31, 126.02, 125.84, 125.61, 125.02, 120.76, 118.16, 113.75, 113.56, 54.86, 49.47, 46.83, 43.17, 37.27, 36.37, 34.91, 32.89, 31.69, 31.03, 28.33, 27.53, 25.35, 24.99, 23.96, 20.69, 13.15;

HRMS (APCI-TOF) *m/z* calcd for $C_{40}H_{44}NO_5$ [(M+H)+] 618.3219; found 618.3224.

C-H alkenylation of piperidin-4-one-derived benzamide 3av:



Yield: 65 mg (32%) of **3av**, 30 mg of **6** and 5 mg of **4v** starting from starting from piperidin-4-one benzamide **1v** (275 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 94:6. Brown sticky oil.

Purification: automated flash column chromatography on SiO_2:

Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	35 % EtOAc in petroleum ether for 10 min, then gradient from 35% to 40% AcOEt in petroleum ether for 5 min, and 40% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.34 (40% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, (*E/Z*)-isomers mixture of **3av** in a ratio 94:6, inseparable mixture with**6**) selected signals for **(*E*)-3av**: δ 7.37 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.42 (br d, *J* = 16.2 Hz, 1H), 6.17 (dd, *J* = 16.1, 5.1 Hz, 1H), 5.38 – 5.24 (br m, 1H), 4.05 (t, *J* = 7.2 Hz, 2H), 3.77 (s, 3H), 2.94 (dd, *J* = 15.1, 6.9 Hz, 1H), 2.66 – 2.54 (m, 3H);

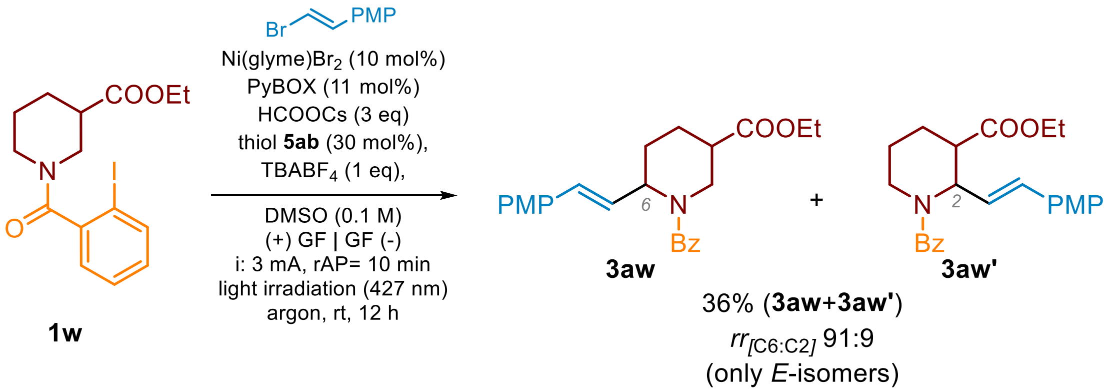
elected signals for **9**: δ 7.66 (d, *J* = 8.2 Hz, 1H), 5.26 (d, *J* = 8.2 Hz, 1H), 4.22 – 4.07 (br m, 1H), 3.50 (ddd, *J* = 13.7, 11.2, 4.1 Hz, 1H), 2.36 – 2.24 (m, 1H)

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C, (*E/Z*)-isomers mixture of **3av** in a ratio 94:6, inseparable mixture with **6**) δ 206.1(**3av**), 192.5 (**6**), 169.5, 169.1, 158.9, 144.1, 135.8, 133.0, 130.8 (**3av**), 129.3, 129.1, 128.6, 128.5, 128.2, 128.0, 127.8, 127.3, 126.2, 125.4(**3av**), 113.8(**3av**), 107.1 (**6**), 54.8(**3av**), 52.7 (**3av**), 43.9 (**3av**), 42.5 (**3av**), 39.5 (**6**), 39.3 (**6**);

HRMS for product **3av** (APCI-TOF+) *m/z* calcd for $C_{21}H_{22}NO_3$ [(M+H)+] 336.1600; found 336.1602.

LR MS for product **6** (APCI-TOF+) *m/z* 202.09 Da [(M+H)+]

N-Bz ethyl 6-((*E*)-4-methoxystyryl)piperidine-3-carboxylate (3aw):



Yield: 85 mg of product **3aw** (36%) along with dehalogenated starting material **4w** (53 mg, 0.20 mmol) pipecolic acid derived benzamide **1w** (255 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); Regioselectivity C2/C6: 9:91 (only *E* isomers) Brown sticky oil. Purification: automated flash column chromatography on SiO_2:

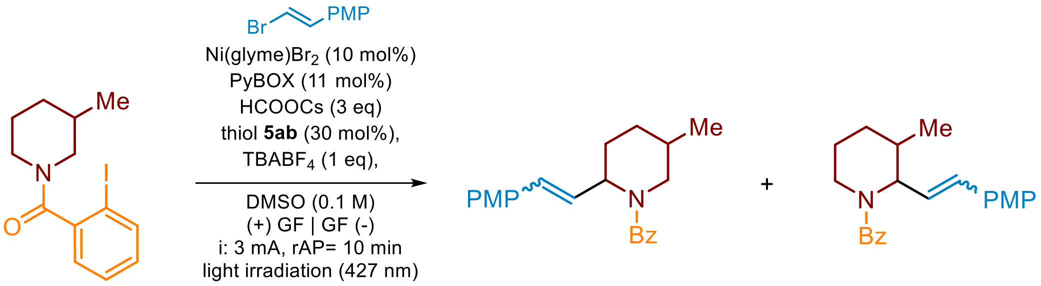
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 40 % EtOAc in petroleum ether for 10 min, then gradient from 40% to 45% AcOEt in petroleum ether for 5 min, and 45% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.44 (40% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80 °C) δ 7.48 – 7.41 (m, 5H), 7.41 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.42 (dd, *J* = 16.2, 2.0 Hz, 1H), 6.20 (dd, *J* = 16.2, 4.6 Hz, 1H), 5.03 – 4.79 (m, 1H), 4.34 – 4.12 (m, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.77 (s, 3H), 3.08 (t, *J* = 12.7 Hz, 1H), 2.62 – 2.53 (m, 1H), 1.99 – 1.69 (m, 4H), 1.17 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C) δ 171.9, 169.5, 158.7, 136.0, 130.4, 128.94, 128.86, 127.9, 127.2, 126.0, 125.2, 113.8, 59.6, 54.8, 40.9, 40.0, 39.9, 39.7, 39.5, 39.4, 39.2, 39.0, 27.9, 22.4, 13.5.

HRMS (ESI-TOF+) *m/z* calcd for $C_{24}H_{27}NO_4Na$ [(M+Na)+] 416.1838; found 416.1836.

C-H alkenylation of 3-methyl piperidine-derived benzamide 1x:



1x

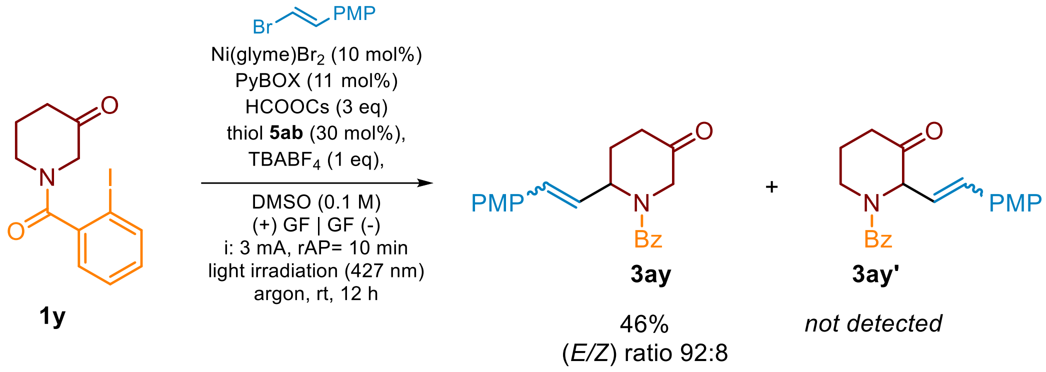
47% (**3ax+3ax'**)
rr$_{[C6:C2]}$ 5:1 (both *E*-isomers)

Yield: 95 mg (47%) starting from 3-methyl piperidine benzamide **1x** (217 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); Pale-yellow sticky solid. The alkenylation of **1x** proceeded at both C2 and C6 positions providing two (*E*)-isomers in ratio ca. 5:1 (**3ax/3ax'**). The ratio of minor (*Z*)-isomers was not assigned due to overlapping of the diagnostic signals. **HRMS** for **3ax/3ax'** (ESI-TOF+) *m/z* calcd for $C_{22}H_{25}NO_2Na$ [(M+Na)+] 358.1783; found 358.1786.

Purification: automated flash column chromatography on SiO_2:

Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	30 % EtOAc in petroleum ether for 10 min, then gradient from 35% to 40% AcOEt in petroleum ether for 8 min, and 40% AcOEt in petroleum ether for 10 min.
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.74 (40% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

C-H alkenylation of piperidin-3-onee-derived benzamide 1y:



Yield: 93 mg (46%) starting from piperidin-3-one benzamide **1y** (198 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); Pale-yellow sticky solid. The alkenylation of **1y** proceeded at C6 position (**3ay**) and provided (*E/Z*)-isomers mixture in a ratio 92:8.

Purification: automated flash column chromatography on SiO_2:

Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	30 % EtOAc in petroleum ether for 10 min, then gradient from 35% to 40% AcOEt in petroleum ether for 8 min, and 40% AcOEt in petroleum ether for 10 min.
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.75 (40% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

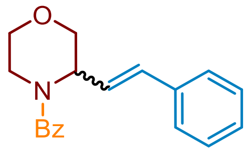
^{1}H NMR (500 MHz, DMSO-d_6 at 80 °C) δ 7.48 – 7.38 (m, 5H), 7.37 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 6.41 (d, J = 16.1 Hz, 1H), 6.25 (dd, J = 16.1, 5.2 Hz, 1H), 4.89 (br m, 1H), 4.28 (br m, 1H), 3.95 (d, J = 17.8 Hz, 1H), 3.76 (s, 3H), 2.56 – 2.43 (m, 2H), 2.33 – 2.23 (m, 1H), 2.09 – 1.97 (m, 2H);

^{13}C NMR (126 MHz, DMSO-d_6 at 80 °C) δ 206.0, 170.7, 159.7, 136.6, 130.9, 130.0, 129.6, 128.8, 128.2, 127.1, 126.1, 114.6, 55.7, 53.6 (v br), 51.8 (v br), 35.7, 26.8;

HRMS (ESI-TOF) *m/z* calcd for $C_{21}H_{21}NO_3Na$ [(M+Na)+] 358.1419; found 358.1424.

5.2. Scope of 2-aryl vinyl halides

N-Bz 3-(styryl)morpholine (3ba):



Yield: 126 mg (72%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2b** (110 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 90:10. Brown oil.

Purification: automated flash column chromatography on SiO_2

Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)

TLC: R_F = 0.4 (50% EtOAc in Hexanes)

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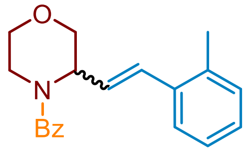
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 90:10) δ 7.82 (d, *J* = 8.2 Hz, 1H, minor), 7.52 – 7.39 (m, 7H, major), 7.34 (dd, *J* = 8.4, 6.9 Hz, 2H, major), 7.29 – 7.05 (m, 1H, minor), 6.61 (d, *J* = 11.9 Hz, 1H, minor), 6.54 (dd, *J* = 16.22, 5.1 Hz, 1H, major), 6.46 (dd, *J* = 16.2, 5.1 Hz, 1H, major), 6.19 (dd, *J* = 11.9, 9.1 Hz, 1H, minor), 5.10 (d, *J* = 9.0 Hz, 1H, minor), 4.76 (s, 1H, major), 4.06 – 3.92 (m, 1H, mixture), 3.92 – 3.80 (m, 1H, mixture), 3.81 – 3.68 (m, 2H, mixture), 3.54 – 3.44 (m, 1H, mixture), 3.43 – 3.32 (m, 1H, mixture);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, E/Z mixture in ratio 9:1) δ 169.4, 136.1, 135.5, 131.2, 129.5, 129.11, 129.06, 128.8, 128.1, 128.0, 127.9, 127.78, 127.75, 127.4, 127.2, 126.7, 126.4, 126.3, 126.1, 125.9, 70.2, 69.2, 66.0, 65.9, 52.8, 51.6;

HRMS (ESI-TOF+) *m/z* calcd for $C_{19}H_{19}NO_2Na$ [(M+Na)+] 316.1313; found 316.1315.

N-Bz 3-(2-methylstyryl)morpholine (3bb):



Yield: 118 mg (64%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2c** (118 mg, 0.60 mmol); *E/Z* ratio: 74:26. Brown oil.

Purification: automated flash column chromatography on SiO_2

Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)

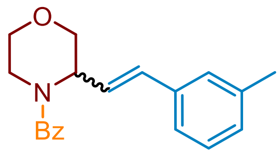
TLC: R_F = 0.65 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 74:26) δ 7.50 – 7.42 (m, mixture), 7.35 – 7.30 (m, 1H, minor), 7.29 – 7.24 (m, 1H, major), 7.22 – 7.13 (m, mixture), 7.10 (td, *J* = 7.4, 1.4 Hz, 1H, minor), 6.96 (t, *J* = 7.4 Hz, 1H, minor), 6.83 (br d, *J* = 7.6 Hz, 1H, minor), 6.72 (d, *J* = 16.0 Hz, 1H, major), 6.63 (d, *J* = 11.7 Hz, 1H, minor), 6.30 (dd, *J* = 16.1, 5.4 Hz, 1H, major), 6.25 (dd, *J* = 11.7, 8.8 Hz, 1H, minor), 4.87 (br d, *J* = 8.8 Hz, 1H minor), 4.76 (br s, 1H, major), 4.00 (d, *J* = 11.6 Hz, 1H, major), 3.91 – 3.70 (m, mixture), 3.64 (dd, *J* = 11.3, 3.3 Hz, 1H, minor), 3.51 (td, *J* = 11.7, 2.8 Hz, 1H, major), 3.45 (d, *J* = 9.2 Hz, 2H, minor), 3.42 – 3.35 (m, 1H, minor), 2.31 (s, 3H, major), 2.19 (s, 3H, minor).

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 74:26) δ 169.4, 169.0, 135.5, 135.2, 135.1, 134.9, 134.5, 129.7, 129.2, 129.12, 129.08, 128.8, 128.0, 127.8, 127.7, 127.53, 127.49, 127.0, 126.8, 126.3, 126.0, 125.6, 125.2, 125.0, 70.3, 69.2, 66.0, 65.9, 53.2, 49.7, 40.6, 18.9, 18.7;

HRMS (ESI-TOF+) *m/z* calcd $C_{20}H_{21}NO_2Na$ [(M+Na)+] 330.1470; found 330.1474.

N-Bz 3-(3-methylstyryl)morpholine (3bc):



Yield: 141 mg (76%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2d** (118 mg, 0.60 mmol); *E/Z* ratio: 88:12. Brown oil.

Purification: automated flash column chromatography on SiO_2

Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.65 (50% EtOAc in Hexanes)

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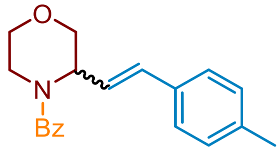
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 88:12) δ 7.49 – 7.20 (m, Ar, mixture), 7.15 – 7.05 (m, 1H major), 6.62 – 6.54 (d, J = 11.9 Hz, 1H, minor), 6.50 (d, *J* = 16.8 Hz, 1H, major), 6.44 (dd, *J* = 16.2, 4.9 Hz, 1H, major), 6.16 (dd, *J* = 11.9, 9.1 Hz, 1H, minor), 5.10 (br d, *J* = 8.7 Hz, 1H, minor), 4.75 (br s, 1H, major), 3.99 (d, *J* = 11.7 Hz, 1H, major), 3.89 – 3.69 (m, mixture), 3.54 – 3.34 (m, mixture), 2.32 (s, 3H, major), 2.23 (s, 3H, minor);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 88:12) δ 169.3, 137.3, 136.0, 135.5, 131.3, 130.3, 129.1, 128.8, 128.4, 128.0, 127.96, 127.86, 127.7, 127.3, 126.5, 126.4, 126.3, 126.1, 124.8, 123.2, 70.2, 69.2, 66.1, 65.9, 52.9, 40.7, 20.4.

HRMS (ESI-TOF+) *m/z* calcd $C_{20}H_{21}NO_2Na$ [(M+Na)+] 330.1470; found 330.1473.

N-Bz 3-(4-methylstyryl)morpholine (3bd):



Yield: 136 mg (74%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2e** (118 mg, 0.60 mmol); E/Z ratio: 85:15. Yellowish semi-solid.

Purification: automated flash column chromatography on SiO_2

Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.65 (50% EtOAc in Hexanes)

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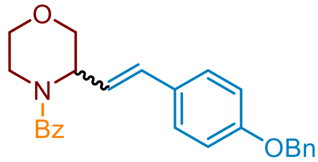
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, (*E/Z* mixture in ratio 85:15) δ 77.49 – 7.41 (m, mixture), 7.35 (d, *J* = 8.1 Hz, 2H, major), 7.33 – 7.20 (m, mixture), 7.16 (d, *J* = 7.9 Hz, 2H, major), 7.04 (d, *J* = 7.8 Hz, 2H, minor), 7.04 (d, *J* = 7.8 Hz, 2H, minor), 6.56 (d, *J* = 11.9 Hz, 1H, minor), 6.49 (d, *J* = 16.2 Hz, 1H, major), 6.39 (dd, *J* = 16.2, 5.2 Hz, 1H, major), 6.13 (dd, *J* = 11.9, 9.1 Hz, 1H, minor), 5.11 (br d, *J* = 9.1 Hz, 1H, minor), 4.74 (br s, 1H, major), 3.98 (d, *J* = 11.6 Hz, 1H, major), 3.90 – 3.68 (m, mixture), 3.53 – 3.32 (m, mixture), 2.31 (s, 3H major), 2.28 (s, 1H, major);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 85:15) δ 169.3, 136.6, 136.0, 135.5, 135.2, 133.3, 132.8, 131.1, 130.1, 128.7, 128.4, 128.0, 127.8, 127.7, 126.8, 126.3, 126.1, 125.9, 125.5, 70.2, 69.2, 66.0, 65.9, 52.8, 49.7, 40.7, 20.19, 20.16;

HRMS (ESI-TOF+) *m/z* calcd $C_{20}H_{21}NO_2Na$ [(M+Na)+] 330.1470; found 330.1476.

(*E*)-*N*-Bz 3-(4-(benzyloxy)styryl)morpholine (3be):



Yield: 177 mg (74%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2f** (175 mg, 0.60 mmol); (*E*)-isomer only. Brown oil.

Purification: automated flash column chromatography on SiO_2

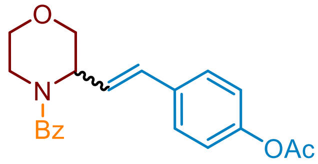
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.5 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, (*E*)-isomer only) δ 7.49 – 7.40 (m, 7H), 7.43 – 7.35 (m, 4H), 7.35 – 7.27 (m, 1H), 6.99 (d, *J* = 8.7 Hz, 2H), 6.47 (dd, *J* = 16.1, 1.7 Hz, 1H), 6.31 (dd, *J* = 16.2, 5.4 Hz, 1H), 5.13 (s, 2H), 4.72 (s, 1H), 3.97 (d, *J* = 11.6 Hz, 1H), 3.84 (dd, *J* = 11.8, 2.9 Hz, 1H), 3.77 (d, *J* = 13.9 Hz, 1H), 3.71 (dd, *J* = 11.6, 3.5 Hz, 1H), 3.49 (td, *J* = 11.6, 2.8 Hz, 1H), 3.36 (td, *J* = 12.8, 12.2, 3.6 Hz, 1H);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, (*E*)-isomer only) δ 169.3, 157.8, 136.8, 135.6, 130.7, 129.1, 129.0, 128.0, 127.9, 127.3, 127.2, 127.0, 126.3, 124.4, 114.8, 69.3, 69.2, 65.9, 52.9.

HRMS (APCI-TOF+) *m/z* calcd for $C_{26}H_{26}NO_3$ [(M+H)+] 400.1913; found 400.1909.

4-(2-(4-benzoylmorpholin-3-yl)vinyl)phenyl acetate (3bf):



Yield: 156 mg (74%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2g** (145 mg, 0.60 mmol); *E/Z* ratio: 60:40. Brown oil.

Purification: automated flash column chromatography on SiO_2

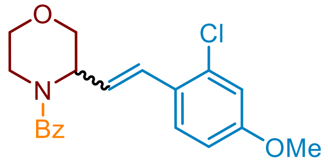
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.55 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E*/*Z* mixture in ratio 60:40) δ 7.50 (d, *J* = 8.6 Hz, 2H, major), 7.51 – 7.41 (m, 5H, major), 7.37 – 7.30 (m, 1H, minor), 7.28 (t, *J* = 7.4 Hz, 1H, minor), 7.24 – 7.20 (m, 1H, minor), 7.14 (d, *J* = 8.2 Hz, 1H, minor), 7.10 (d, *J* = 8.6 Hz, 2H, major), 7.00 (d, *J* = 8.5 Hz, 1H, minor), 6.59 (d, *J* = 11.9 Hz, 1H, minor), 6.54 (d, *J* = 16.2 Hz, 1H, major), 6.44 (dd, *J* = 16.2, 5.2 Hz, 1H, major), 6.19 (dd, *J* = 11.9, 9.2 Hz, 1H, minor), 5.09 (br d, *J* = 9.1 Hz, 1H, minor), 4.75 (br s, 1H, major), 3.99 (d, *J* = 11.6 Hz, 1H, major), 3.91 – 3.75 (m, 4H, mixture), 3.72 (dd, *J* = 11.6, 3.4 Hz, 2H, major), 3.53 – 3.42 (m, 2H, mixture), 3.38 (td, *J* = 12.9, 3.6 Hz, 1H, mixture), 2.26 (s, 1H, mixture).

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, E/Z mixture in ratio 60:40) δ 169.4, 169.2, 168.4, 168.3, 149.7, 149.3, 135.5, 135.2, 133.7, 133.1, 130.3, 129.3, 129.1, 128.9, 128.8, 128.0, 127.8, 127.5, 126.9, 126.3, 126.1, 121.4, 121.0, 70.2, 69.2, 66.0, 65.9, 52.8, 49.4, 20.3.

HRMS (APCI-TOF+) *m/z* calcd for $C_{21}H_{22}NO_4$ [(M+H)+] 352.1549; found 352.1548.

***N*-Bz 3-(2-chloro-4-methoxystyryl)morpholine (3bg):**



Yield: 154 mg (72%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2k** (148 mg, 0.60 mmol); *E*/*Z* ratio: 74:26. Brown oil.

Purification: automated flash column chromatography on SiO_2

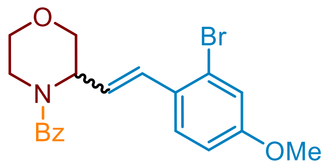
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 40 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.6 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E*/*Z* mixture in ratio 74:26 including conformers/rotamers) δ 7.63 (d, *J* = 8.7 Hz, 1H, major), 7.49 – 7.41 (m, 5H, major), 7.34 – 7.24 (m, 1H, minor), 7.18 (dt, *J* = 6.9, 1.5 Hz, 1H, minor), 7.02 (d, *J* = 2.6 Hz, 1H, major), 6.98 (d, *J* = 2.6 Hz, 1H, minor), 6.93 (dd, *J* = 8.7, 2.7 Hz, 1H, major), 6.75 (d, *J* = 16.2 Hz, 1H, major), 6.68 (dd, *J* = 8.5, 2.6 Hz, 1H, minor), 6.55 (d, *J* = 11.6 Hz, 1H, minor), 6.37 (dd, *J* = 16.1, 5.3 Hz, 1H, major), 6.28 (dd, *J* = 11.6, 9.1 Hz, 1H, minor), 4.85 (br d, *J* = 9.2 Hz, 1H, minor), 4.76 (br s, 1H, major), 3.99 (d, *J* = 11.7 Hz, 1H, major), 3.92 – 3.83 (m, 1H, mixture), 3.80 (s, 3H, mixture), 3.77 (s, 1H mixture), 3.75 – 3.65 (m, 1H, mixture), 3.54 – 3.30 (m, 3H, mixture);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in a ratio 74:26) δ 169.4, 169.1, 159.2, 159.0, 135.5, 135.1, 132.8, 132.2, 130.1, 129.1, 128.8, 128.1, 128.0, 127.72, 127.71, 127.5, 127.0, 126.5, 126.4, 126.2, 126.1, 126.0, 114.4, 114.2, 113.7, 112.6, 70.1, 69.2, 66.0, 65.9, 55.3, 55.2;

HRMS (APCI-TOF+) *m/z* calcd for $C_{20}H_{21}NO_3Cl$ [(M+H)+] 358.1210; found 358.1205.

N-Bz 3-(2-bromo-4-methoxystyryl)morpholine (3bh):



Yield: 55 mg (75%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2l** (175 mg, 0.60 mmol); *E/Z* ratio: 2:1. Pale-yellow solid.

Purification: automated flash column chromatography on SiO_2

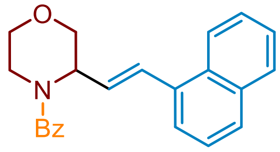
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.55 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 2:1 including conformers/rotamers) δ 7.61 (d, *J* = 8.7 Hz, 1H, major), 7.50 – 7.14 (m, E/Z mixture), 6.97 (dd, *J* = 8.7, 2.6 Hz, 1H, major), 6.96 – 6.88 (m, 1H, minor), 6.77 – 6.69 (m, 1H of E & 1H of Z), 6.50 (d, *J* = 11.6 Hz, 1H, minor), 6.33 (dd, *J* = 16.1, 5.2 Hz, 1H, major), 6.26 (dd, *J* = 11.6, 9.1 Hz, 1H, minor), 4.85 (br d, *J* = 9.1 Hz, 1H, minor), 4.76 (br s, 1H, mojor), 3.99 (d, *J* = 11.7 Hz, 1H, major), 3.92 – 3.65 (m, 3H of E & 4H of Z), 3.54 – 3.33 (m, 2H of E & 2H of Z);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 2:1 including conformers/rotamers) δ 169.4, 169.0, 159.2, 158.9, 135.5, 135.1, 130.0, 129.2, 129.1, 128.7, 128.1, 128.0, 127.95, 127.85, 127.74, 127.70, 127.5, 126.2, 126.0, 123.1, 122.8, 117.4, 117.3, 114.2, 113.1, 70.2, 69.2, 66.0, 65.9, 55.3, 55.2, 52.9, 49.6, 40.6.

HRMS (ESI-TOF+) *m/z* calcd for $C_{20}H_{20}NO_3BrNa$ [(M+Na)+] 424.0524; 424.0522.

(*E*)-*N*-Bz 3-(2-(naphthalen-1-yl)vinyl)morpholine (3bi):



Yield: 178 mg (86%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2j** (140 mg, 0.60 mmol); *E/Z* ratio: >98:2. Brown sticky solid.

Purification: automated flash column chromatography on SiO$_2$

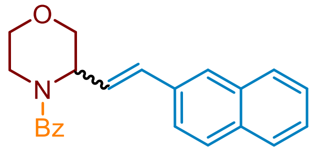
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 40 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.55 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E*-isomer) δ 7.93 – 7.84 (m, 4H), 7.71 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.55 – 7.42 (m, 7H), 6.72 (d, *J* = 16.3 Hz, 1H), 6.62 (dd, *J* = 16.2, 5.2 Hz, 1H), 4.83 (s, 1H), 4.05 (d, *J* = 11.8 Hz, 1H), 3.87 (dd, *J* = 11.2, 3.3 Hz, 1H), 3.80 (d, *J* = 10.8 Hz, 1H), 3.76 (dd, *J* = 11.7, 3.5 Hz, 1H), 3.52 (td, *J* = 11.5, 2.6 Hz, 1H), 3.43 (td, *J* = 12.7, 3.5 Hz, 1H);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E*-isomer) δ 169.4, 135.5, 133.6, 132.9, 132.3, 131.3, 129.1, 128.0, 127.6, 127.4, 127.3, 127.1, 126.3, 125.9, 125.5, 125.5, 123.4, 69.2, 65.9, 59.2, 52.9, 40.8;

HRMS (APCI-TOF+) *m/z* calcd for C$_{23}$H$_{22}$NO$_2$ [(M+H)+] 344.1651; found 344.1653.

N-Bz 3-(2-(naphthalen-2-yl)vinyl)morpholine (4bj):



Yield: 127 mg (62%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2i** (140 mg, 0.60 mmol); *E/Z* ratio: >87:13. Brown oil.

Purification: automated flash column chromatography on SiO$_2$

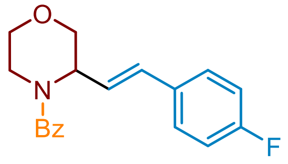
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 40 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.6 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in a ratio 87:13 including rotamers/conformers): major isomer: δ 8.09 (d, *J* = 8.9 Hz, 1H), 7.93 (d, *J* = 7.3 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.68 (d, *J* = 7.2 Hz, 1H), 7.60 – 7.46 (m, 5H), 7.29 (br d, *J* = 15.9 Hz, 1H), 6.48 (dd, *J* = 15.9, 5.5 Hz, 1H), 4.89 (s, 1H), 4.11 (d, *J* = 11.7 Hz, 1H), 3.93 – 3.88 (m, 1H), 3.88 – 3.81 (m, 1H), 3.80 (dd, *J* = 11.7, 3.5 Hz, 1H), 3.55 (td, *J* = 11.4, 11.0, 2.5 Hz, 2H), 3.52 – 3.43 (m, 2H);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in a ratio 87:13 including rotamers/conformers) δ 169.5, 135.6, 133.5, 133.0, 130.3, 129.8, 129.1, 128.7, 128.6, 128.4, 128.0, 127.8, 127.4, 127.4, 127.1, 126.4, 125.92, 125.85, 125.7, 125.43, 125.40, 125.2, 124.7, 124.0, 123.3, 123.0, 70.3, 69.2, 66.0, 65.9, 53.2, 40.8.

HRMS (APCI-TOF+) *m/z* calcd for $C_{23}H_{22}NO_2$ [(M+H)+] 344.1651; found 344.1647.

N-Bz (*E*)-3-(4-fluorostyryl)morpholine (3bk):



Yield: 108 mg (58%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2n** (121 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: >97:3. White solid.

Purification: automated flash column chromatography on SiO_2

Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.65 (50% EtOAc in Hexanes)

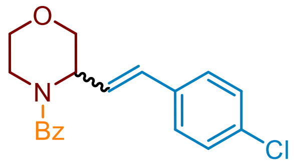
^{1}H NMR (500 MHz, DMSO-d_6, 80°C, *E/Z*-isomers in a ratio 97:3) δ 7.54 – 7.49 (m, 2H), 7.46 (s, 5H), 7.17 – 7.10 (m, 2H), 6.54 (d, *J* = 16.3 Hz, 1H), 6.42 (dd, *J* = 16.2, 5.2 Hz, 1H), 4.76 (br s, 1H), 3.99 (d, *J* = 11.6 Hz, 1H), 3.84 (dd, *J* = 11.3, 3.5 Hz, 1H), 3.80 – 3.75 (m, 1H), 3.72 (dd, *J* = 11.6, 3.4 Hz, 1H), 3.50 (td, *J* = 11.6, 2.7 Hz, 1H), 3.38 (td, *J* = 12.8, 3.7 Hz, 1H);

^{13}C NMR (126 MHz, DMSO-d_6, 80°C) δ 169.3, 162.4 and 160.4 (d, $J_{C\text{-}F}$ = 245 Hz), 135.5, 132.66 and 132.64 (d, $J_{C\text{-}F}$ = 3.2 Hz), 130.0, 129.1, 128.0, 127.9, 127.96 and 127.80 (d, $J_{C\text{-}F}$ = 8.1 Hz), 126.65, 126.63, 126.3, 114.95 and 114.78 (d, $J_{C\text{-}F}$ = 21.6 Hz), 69.2, 65.9, 52.8 (br), 40.7 (br);

^{19}F NMR (470 MHz, DMSO-d_6) δ −114.6 (ddd, $J_{H\text{-}F}$ = 14.4, 9.1, 5.5 Hz).

HRMS (ESI-TOF+) *m/z* calcd for $C_{19}H_{18}NO_2FNa$ [(M+Na)+] 334.1219; found 334.1222.

N-Bz 3-(4-chlorostyryl)morpholine (3bl):



Yield: 126 mg (64%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2o** (130 mg, 0.60 mmol); *E/Z* ratio: 74:26. White solid.

Purification: automated flash column chromatography on SiO_2

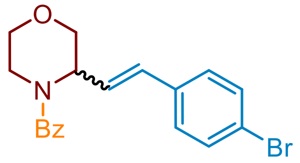
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.65 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in a ratio 74:26 including rotamers/conformers) δ 7.49 (d, *J* = 8.5 Hz, 2H, major), 7.48 – 7.40 (m, E/Z mixture), 7.37 (d, *J* = 8.5 Hz, 2H, major), 7.34 – 7.24 (m, E/Z mixture), 7.21 (d, *J* = 7.8 Hz, 2H, minor), 7.11 (d, *J* = 8.0 Hz, 2H, minor), 6.61 – 6.43 (m, 2H of E & 1H of Z), 6.23 (dd, *J* = 11.9, 9.3 Hz, 1H, minor), 5.05 (br d, *J* = 9.2 Hz, 1H, minor), 4.78 (br s, 1H, major), 4.00 (d, *J* = 11.6 Hz, 1H, major), 3.91 – 3.68 (m, 3H of E, 4H of Z), 3.55 – 3.31 (m, 2H of E & 2H of Z);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in a ratio 74:26 including rotamers/conformers) δ 169.3, 169.2, 135.5, 135.2, 135.0, 134.5, 131.8, 131.5, 130.0, 129.5, 129.1, 129.0, 128.8, 128.13, 128.08, 128.0, 127.78, 127.76, 127.74, 127.6, 126.3, 126.1, 70.1, 69.1, 66.0, 65.9, 52.7, 49.3, 40.8, 40.3;

HRMS (APCI-TOF+) *m/z* calcd for $C_{19}H_{19}NO_2Cl$ [(M+H)+] 328.1104; found 328.1105.

***N*-Bz 3-(4-bromostyryl)morpholine (3bm):**



Yield: 185 mg (83%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2p** (157 mg, 0.60 mmol); *E/Z* ratio: 77:23. Yellow oil.

Purification: automated flash column chromatography on SiO_2

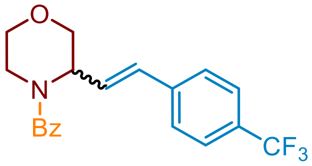
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.4 (50% EtOAc in hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in a ratio 77:23 including rotamers/conformers) δ 7.51 (d, *J* = 8.2 Hz, 2H, major), 7.48 – 7.18 (m, 10H mixture), 7.04 (d, *J* = 8.0 Hz, 2H, minor), 6.59 – 6.47 (m, 2H of E & 1H of Z), 6.24 (dd, *J* = 11.8, 9.3 Hz, 1H, minor), 5.05 (br d, *J* = 9.3 Hz, 1H, minor), 4.77 (br s, 1H, major), 4.00 (d, *J* = 11.6 Hz, 1H, major), 3.92 – 3.68 (m, 3H of E/Z), 3.55 – 3.34 (m, 2H of E/Z);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in a ratio 87:13 including rotamers/conformers) δ 169.3, 169.2, 135.45, 135.39, 135.1, 134.8, 131.3, 131.0, 130.7, 130.0, 129.8, 129.10, 129.05, 129.04, 129.0, 128.7, 128.2, 128.1, 127.94, 127.93, 127.87, 127.75, 127.73, 127.68, 127.1, 126.6, 126.3, 126.1, 125.9, 120.2, 1120.0, 70.1, 69.1, 66.0, 65.9, 52.7, 49.3, 40.8.

HRMS (APCI-TOF+) *m/z* calcd for $C_{19}H_{19}NO_2Br$ [(M+H)+] 372.0599; found 372.0600.

N-Bz 3-(4-(trifluoromethyl)styryl)morpholine (3bn):



Yield: 143 mg (66%) starting from morpholine benzamide **2a** (209 mg, 0.66 mmol) and vinyl bromide **2q** (151 mg, 0.60 mmol); *E/Z* ratio: 91:9. Pink-white solid.

Purification: automated flash column chromatography on SiO_2

Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.4 (50% EtOAc in hexanes)

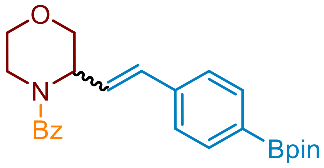
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in a ratio 91:9 including rotamers/conformers) δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.51 – 7.42 (m, mixture), 6.70 – 6.60 (m, 2H of *E* & 1H of *Z*), 6.33 (dd, *J* = 11.9, 9.4 Hz, 1H, minor), 5.03 (d, *J* = 9.7 Hz, 1H, minor), 4.91 – 4.70 (br s, 1H, major), 4.03 (d, *J* = 11.7 Hz, 1H, major), 3.92 – 3.70 (m, mixture), 3.56 – 3.35 (m, mixture);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in a ratio 91:9 including rotamers/conformers) δ 169.40, 140.17 (q, *J* = 1.6 Hz), 135.4, 130.2, 129.9, 129.4, 129.1, 128.9, 128.8, 128.4, 128.0, 127.9, 127.74, 127.69, 127.5, 127.1, 126.6, 126.3, 126.0, 124.92 (q, *J* = 3.8 Hz), 124.52 (q, *J* = 3.8 Hz), 122.8, 120.6, 70.1, 69.0, 66.0, 65.9, 52.1 (br), 49.4 (br), 40.9;

^{19}F NMR (470 MHz, DMSO-d_6) δ −61.1 (*E*), −61.3 (*Z*);

HRMS (ESI-TOF+) *m/z* calcd for $C_{20}H_{19}NO_2F_3$ [(M+H)+] 362.1368; found 362.1367.

N-Bz 3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)styryl)morpholine (3bo):



Yield: 160 mg (63%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2r** (185 mg, 0.60 mmol); *E/Z* ratio: 40:60. White solid.

Purification: automated flash column chromatography on SiO_2

Cartridge size:	1× 80 g (silica gel)

Flow: 45 mL/min
Eluent: 40 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.55 (50% EtOAc in Hexanes)

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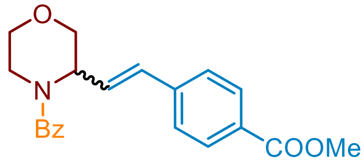
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in a ratio 40:60 including rotamers/conformers) δ 7.67 (d, *J* = 8.0 Hz, 2H, minor), 7.55 (d, *J* = 7.9 Hz, 2H, major isomer), 7.50 – 7.42 (m, 7H, minor), 7.34 – 7.23 (m, 3H, major), 7.22 – 7.16 (m, 2H, major), 7.09 (d, *J* = 7.5 Hz, 2H, major), 6.63 (d, *J* = 11.9 Hz, 1H, major), 6.59 – 6.50 (m, 2H, minor), 6.22 (dd, *J* = 11.9, 9.0 Hz, 1H, major), 5.10 (br d, *J* = 8.9 Hz, 1H, major), 4.78 (br s, 1H, minor), 4.01 (d, *J* = 11.6 Hz, 1H, minor), 3.93 – 3.81 (m, mixture), 3.82 – 3.76 (m, *E/Z* mixture), 3.75 – 3.67 (m, 2H, *E/Z* mixture), 3.53 – 3.32 (m, 2H, *E/Z* mixture), 1.32 (s, 12H, *E/Z* mixture);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in a ratio 40:60 including rotamers/conformers) δ 169.3, 169.1, 138.8, 138.5, 135.5, 135.2, 134.2, 133.8, 131.1, 130.1, 129.1, 128.8, 128.4, 128.1, 128.0, 127.7, 127.1, 126.3, 126.1, 125.3, 83.2, 73.2, 70.1, 69.1, 66.0, 65.9, 52.9, 49.4, 40.0, 28.4, 24.5, 24.25, 24.22, 24.21;

HRMS (ESI-TOF+) *m/z* calcd for $C_{25}H_{30}NO_4BNa$ [(M+Na)+] 442.2166; found 442.2169.

N-Bz methyl 4-(2-(morpholin-3-yl)vinyl)benzoate (3bp):



Yield: 140 mg (66.5%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2u** (145 mg, 0.60 mmol); *E/Z* ratio: 72:28. Brown oil.

Purification: automated flash column chromatography on SiO$_2$

Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.4 (50% EtOAc in Hexanes)

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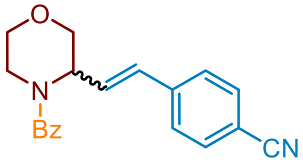
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 72:28 including conformers/rotamers) δ 7.48 – 7.41 (m, 5H, *E*-isomer), 7.39 (d, *J* = 8.7 Hz, 2H, *E*-isomer), 7.35 – 7.20 (m, 2H, *Z*-isomer), 7.05 (d, *J* = 8.2 Hz, 1H, *Z*-isomer), 6.91 (d, *J* = 8.6 Hz, 2H, *E*- isomer), 6.80 (d, *J* = 8.6 Hz, 1H, *Z*-isomer), 6.53 (d, *J* = 11.8 Hz, 1H, *Z*-isomer), 6.47 (d, *J* = 16.2 Hz, 1H, *E*-isomer), 6.31 (dd, *J* = 16.2, 5.4 Hz, 1H, *E*-isomer), 6.09 (dd, *J* = 11.8, 9.1 Hz, 1H, *Z*-isomer), 5.12 (d, *J* = 9.0 Hz, 1H, *Z*-isomer), 4.72 (s, 1H, *E*-isomer), 3.97 (d, *J* = 11.6 Hz, 1H, *E-i*somer), 3.93 – 3.79 (m, 2H, *E/Z*), 3.78 (s, 3H, *E*-

isomer), 3.75 (s, 1H, *Z*-isomer), 3.74 – 3.68 (m, 2H, *E*/*Z*), 3.55 – 3.43 (m, 2H, *E*/*Z*), 3.38 (dd, *J* = 13.1, 3.6 Hz, 1H, *E*/*Z*);

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C, *E/Z* mixture in ratio 72:28 including conformers/rotamers) δ 169.30, 169.1, 158.8, 158.2, 135.6, 135.35, 130.8, 129.7, 129.1, 129.0, 128.8, 128.2, 127.9, 127.8, 127.2, 126.3, 126.1, 125.8, 124.2, 113.8, 113.5, 70.2, 69.3, 66.1, 65.9, 54.8, 54.8, 52.9, 49.5.

HRMS (ESI-TOF+) *m/z* calcd for $C_{20}H_{21}NO_3Na$ [(M+Na)+] 346.1419; found 346.1420.

4-(2-(4-benzoylmorpholin-3-yl)vinyl)benzonitrile (3bq):



Yield: 61 mg (32%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2v** (125 mg, 0.60 mmol); *E/Z* ratio: 70:30. Brown oil.

Purification: automated flash column chromatography on SiO_2

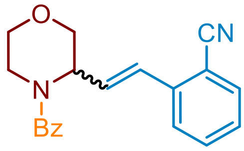
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.45 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80°C, *E/Z* mixture in ratio 70:30) δ 7.76 (d, *J* = 8.4 Hz, 2H, major), 7.68 (d, *J* = 8.4 Hz, 2H, major), 7.64 (d, *J* = 8.2 Hz, 1H, minor), 7.50 – 7.16 (m, mixture), 6.71 – 6.59 (m, 2H major & 1 H minor), 6.34 (dd, *J* = 11.9, 9.5 Hz, 1H, minor), 5.02 (br d, *J* = 9.3 Hz, 1H, minor), 4.81 (br s, 1H, major), 4.03 (d, *J* = 11.7 Hz, 1H, major), 3.92 – 3.87 (m, 1H mixture), 3.86 – 3.80 (m, 2H, mixture), 3.74 (ddd, *J* = 11.7, 6.8, 3.4 Hz, 3H, mixture), 3.54 – 3.44 (m, 2H, mixture), 3.39 (td, *J* = 12.8, 12.2, 3.6 Hz, 1H, major).

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C, *E/Z* mixture in ratio 70:30) δ 169.4, 169.3, 140.8, 140.5, 135.4, 135.1, 132.0, 131.6, 131.2, 130.0, 129.8, 129.1, 128.84, 128.80, 128.7, 128.0, 127.8, 126.8, 126.3, 126.1, 118.3, 118.1, 109.6, 109.5, 70.0, 69.0, 66.0, 65.9, 52.7, 49.3, 40.9;

HRMS (APCI-TOF+) *m/z* calcd for $C_{20}H_{19}N_2O_2$ [(M+H)+] 319.1447; 319.1446.

2-(2-(4-benzoylmorpholin-3-yl)vinyl)benzonitrile (3br):



Yield: 33 mg (17%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2w** (125 mg, 0.60 mmol); *E/Z* ratio: 86:14. Brown oil.

Purification: automated flash column chromatography on SiO_2

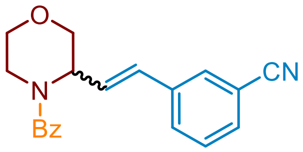
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.5 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80 °C, *E/Z* mixture in ratio 86:14) data for (*E*)-isomer: δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 7.7 Hz, 1H), 7.68 (t, *J* = 7.8 Hz, 1H), 7.47 (s, 6H), 6.82 (d, *J* = 16.0 Hz, 1H), 6.74 (dd, *J* = 16.1, 4.8 Hz, 1H), 4.88 (s, 1H), 4.04 (d, *J* = 11.8 Hz, 1H), 3.88 – 3.82 (m, 1H), 3.76 (dd, *J* = 11.8, 3.6 Hz, 1H), 3.63 – 3.60 (m, 1H), 3.52 – 3.47 (m, 1H), 3.44 – 3.37 (m, 1H);

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C, *E/Z* mixture in ratio 86:14) δ 169.5, 168.8, 138.9, 135.7, 135.4, 135.3, 134.8, 132.81, 132.76, 132.6, 132.5, 132.3, 132.2, 131.1, 129.7, 129.3, 129.13, 129.11, 128.99, 128.5, 128.01, 127.95, 127.90, 127.86, 127.8, 126.9, 126.5, 126.3, 126.25, 126.22, 125.8, 117.1, 117.0, 109.7, 69.0, 66.0, 65.9, 65.7, 51.6, 41.2;

HRMS (ESI-TOF+) *m/z* calcd for $C_{20}H_{18}N_2O_2Na$ [(M+Na)+] 341.1266; found 341.1265.

3-(2-(4-benzoylmorpholin-3-yl)vinyl)benzonitrile (3bs):



Yield: 80 mg (42%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2x** (125 mg, 0.60 mmol); *E/Z* ratio: 50:50. Pale-yellow oil.

Purification: automated flash column chromatography on SiO_2

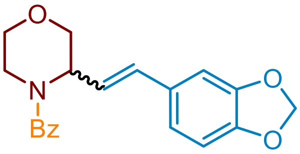
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.45 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80 °C, *E/Z* mixture in ratio 50:50) δ 8.03 – 7.14 (m, 18H, *E/Z*), 6.69 – 6.56 (m, 2H(*E*) &1H(*Z*)), 6.32 (dd, *J* = 11.9, 9.5 Hz, 1H, Z-isomer), 5.00 (br d, *J* = 9.1 Hz, 1H, *Z*-isomer), 4.80 (br s, 1H, *E*-isomer), 4.01 (d, *J* = 11.7 Hz, 1H, *E/Z*), 3.93 – 3.70 (m, 3H, *E/Z*), 3.54 – 3.36 (m, 2H, *E/Z*);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 50:50) δ 169.34 169.28, 137.5, 136.9, 135.4, 135.1, 132.4, 131.1, 130.5, 130.4, 130.2, 129.8, 129.4, 129.30, 129.29, 129.2, 129.1, 128.94, 128.89, 128.3, 128.0, 127.8, 127.7, 126.7, 126.3, 126.0, 118.1, 118.0, 111.6, 111.3, 70.0, 69.0, 66.0, 65.9, 52.7, 49.2, 40.3;

HRMS (ESI-TOF+) *m/z* calcd for $C_{20}H_{18}N_2O_2Na$ [(M+Na)+] 341.1266; found 341.1268.

N-Bz 3-(2-(benzo[*d*][1,3]dioxol-5-yl)vinyl)morpholine (3bt):



Yield: 156 mg (77%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2y** (136 mg, 0.60 mmol); *E/Z* ratio: 62:38. Brown oil.

Purification: automated flash column chromatography on SiO_2

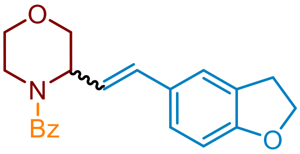
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 40 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.5 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 62:38) δ 7.48 – 7.43 (m, mixture), 7.37 – 7.22 (m, mixture), 7.10 (d, *J* = 1.7 Hz, 1H, major), 6.91 (dd, *J* = 8.1, 1.7 Hz, 1H, major), 6.84 (d, *J* = 8.0 Hz, 1H, major), 6.74 (d, *J* = 7.9 Hz, 1H, minor), 6.67 (br s, 1H, minor), 6.58 (br d, *J* = 7.9 Hz, 1H, minor), 6.50 (d, *J* = 11.8 Hz, 1H, minor), 6.46 (dd, *J* = 16.2, 1.6 Hz, 1H, major), 6.33 (dd, *J* = 16.1, 5.4 Hz, 1H, major), 6.10 (dd, *J* = 11.8, 9.3 Hz, 1H, minor), 6.01 – 5.94 (m, 2H of E & 2H of Z), 5.10 (br d, *J* = 8.6 Hz, 1H, minor), 4.73 (br s, 1H, major), 3.97 (d, *J* = 11.6 Hz, 1H, major), 3.92 – 3.67 (m, mixture), 3.54 – 3.43 (m, mixture), 3.43 – 3.32 (m, mixture);

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 62:38) δ 169.3, 169.2, 147.5, 146.9, 146.6, 146.1, 135.6, 135.2, 130.9, 130.6, 129.9, 129.7, 129.0, 128.8, 127.9, 127.7, 126.3, 126.2, 126.1, 124.8, 121.7, 120.6, 107.9, 107.7, 107.6, 105.3, 100.6, 100.5, 70.2, 69.2, 66.1, 65.9, 52.9, 49.5, 40.6, 40.2;

HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{19}NO_4Na$ [(M+Na)+] 360.1212; found 360.1214.

N-Bz 3-(2-(2,3-dihydrobenzofuran-5-yl)vinyl)morpholine (3bu):



Yield: 115 mg (57%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2z** (135 mg, 0.60 mmol); *E/Z* ratio: 68:32. Brown oil.

Purification: automated flash column chromatography on SiO_2

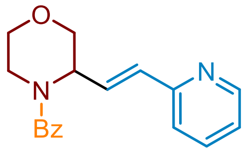
Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 40 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.65 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 68:32, including conformers/rotamers) δ 7.50 – 7.40 (m, 5H, major), 7.37 (s, 1H, minor), 7.30 – 7.25 (m, 1H, minor), 7.23 – 7.20 (m, 1H, major), 7.16 (d, *J* = 8.1 Hz, 1H, major), 6.93 (s, 1H minor), 6.82 (d, *J* = 8.1 Hz, 1H, major), 6.60 (d, *J* = 8.2 Hz, 1H, minor), 6.50 (d, *J* = 11.8 Hz, 1H, minor), 6.44 (dd, *J* = 16.2, 1.7 Hz, 1H, major), 6.27 (dd, *J* = 16.1, 5.5 Hz, 1H, major), 6.04 (dd, *J* = 11.8, 9.2 Hz, 1H, minor), 5.10 (br d, *J* = 9.1 Hz, 1H, minor), 4.70 (br s, 1H, major), 4.53 (t, *J* = 8.7 Hz, 2H, major), 4.50 – 4.47 (m, 1H, minor), 3.96 (d, *J* = 11.6 Hz, 1H, major), 3.89 – 3.81 (m, 2H, mixture), 3.81 – 3.74 (m, 2H, mixture), 3.74 – 3.68 (m, 1H, mixture), 3.53 – 3.42 (m, 2H, mixture), 3.36 (td, *J* = 12.8, 12.3, 3.7 Hz, 1H, mixture), 3.18 (t, *J* = 8.6 Hz, 1H, major), 3.14 – 3.08 (m, 1H, mixture).

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, *E/Z* mixture in ratio 68:32 including conformers/rotamers) δ 169.3, 169.2, 159.2, 158.6, 138.5, 135.6, 135.3, 131.2, 130.2, 129.0, 128.79, 128.76, 128.04, 127.96, 127.8, 127.7, 127.4, 126.9, 126.8, 126.28, 126.26, 126.1, 125.3, 124.5, 123.4, 122.4, 108.3, 108.1, 70.7, 70.6, 70.3, 69.3, 66.1, 65.9, 53.0, 49.6, 40.6, 28.61, 28.56.

HRMS (APCI-TOF+) *m/z* calcd for $C_{21}H_{22}NO_3$ [(M+H)+] 336.1600; found 336.1601.

***N*-Bz (*E*)-3-(2-(pyridin-2-yl)vinyl)morpholine (3bv):**



Yield: 115 mg (57%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2aa** (135 mg, 0.60 mmol); Only *E*-isomer. Brown oil.

Purification: automated flash column chromatography on SiO$_2$

Cartridge size: 1× 80 g (silica gel)
Flow: 45 mL/min
Eluent: 45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, then 60% AcOEt in petroleum ether for 10 min and 70% AcOEt in petroleum ether for 15 min.
Detection: ELSD & UV (254 nm)
TLC: R_F = 0.2 (50% EtOAc in Hexanes)

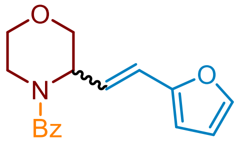
^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, only *E*-isomer) δ 8.54 (d, *J* = 4.6 Hz, 1H), 7.74 (td, *J* = 7.7, 1.9 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 6H), 7.26 – 7.20 (m, 1H), 6.91 (dd, *J* = 16.0, 5.2 Hz, 1H), 6.63 (d, *J* = 16.0 Hz, 1H), 4.83 (br s, 1H), 4.04 (d, *J* = 11.7 Hz, 1H), 3.85

(dd, *J* = 11.4, 3.6 Hz, 1H), 3.82 – 3.77 (m, 1H), 3.75 (dd, *J* = 11.7, 3.5 Hz, 1H), 3.51 (td, *J* = 11.6, 2.8 Hz, 1H), 3.37 (td, *J* = 12.8, 3.7 Hz, 1H);

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C, only *E*-isomer) δ 169.4, 154.1, 148.9, 136.2, 135.4, 131.4, 130.9, 129.1, 128.0, 126.3, 122.0, 121.3, 69.1, 65.9, 52.6, 40.8;

HRMS (ESI-TOF+) *m/z* calcd for $C_{18}H_{18}N_2O_2Na$ [(M+Na)+] 317.1266; found 317.1268.

***N*-Bz 3-(2-(furan-2-yl)vinyl)morpholine (3bw):**



Yield: 103 mg (61%) starting from morpholine benzamide **1a** (209 mg, 0.66 mmol) and vinyl bromide **2ab** (104 mg, 0.60 mmol); (*E/Z*)-isomer ratio: 95:5. Brown oil.

Purification: automated flash column chromatography on SiO_2

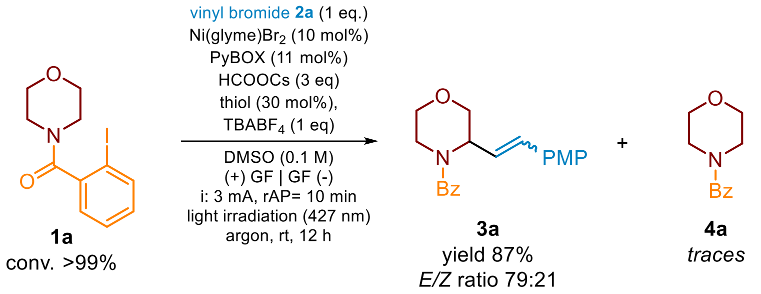
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, then 60% AcOEt in petroleum ether for 10 min and 70% AcOEt in petroleum ether for 15 min.
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.4 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80 °C, *E/Z* mixture in ratio 95:5) δ 7.60 – 7.56 (m, 1H), 7.52 – 7.42 (m, 5H), 6.50 – 6.45 (m, 2H), 6.42 (dd, *J* = 16.2, 1.8 Hz, 1H, major), 6.26 (dd, *J* = 16.2, 5.3 Hz, 1H, major), 6.02 (dd, *J* = 11.9, 8.8 Hz, 1H, minor), 5.34 (br d, J = 8.6 Hz, 1H, minor), 4.75 (br s, 1H), 3.97 (d, *J* = 11.7 Hz, 1H), 3.86 – 3.81 (m, 1H), 3.79 – 3.73 (m, 1H), 3.71 (dd, *J* = 11.7, 3.5 Hz, 1H), 3.49 (td, *J* = 11.7, 2.9 Hz, 1H), 3.36 – 3.26 (m, 1H);

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C, *E/Z* mixture in ratio 95:5) δ 169.4, 151.4, 142.1, 135.4, 129.1, 128.0, 126.3, 125.0, 120.1, 111.1, 107.9, 69.0, 65.9, 52.4, 40.7;

HRMS (ESI-TOF+) *m/z* calcd for $C_{17}H_{17}NO_3Na$ [(M+Na)+] 306.1106; found 306.1106.

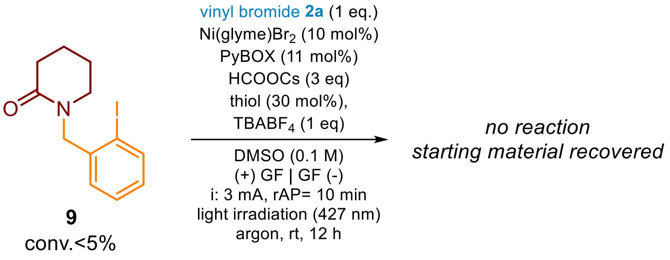
5.3. The scope of HAT directing group



1a
conv. >99%

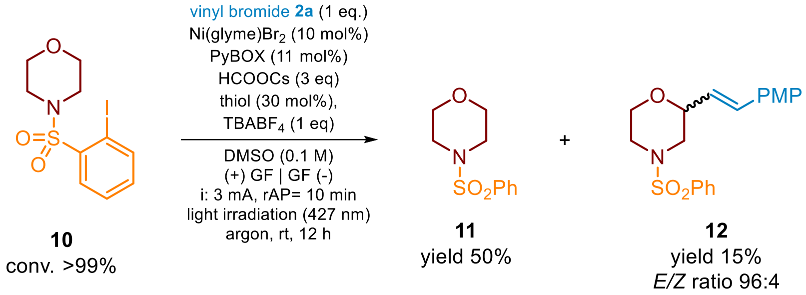
3a
yield 87%
E/Z ratio 79:21

4a
traces



no reaction
starting material recovered

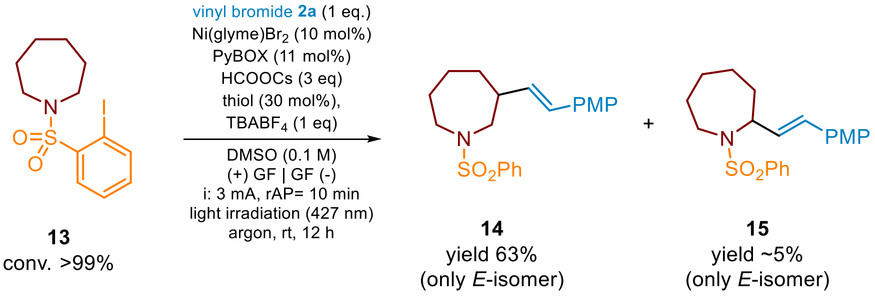
9
conv.<5%



10
conv. >99%

11
yield 50%

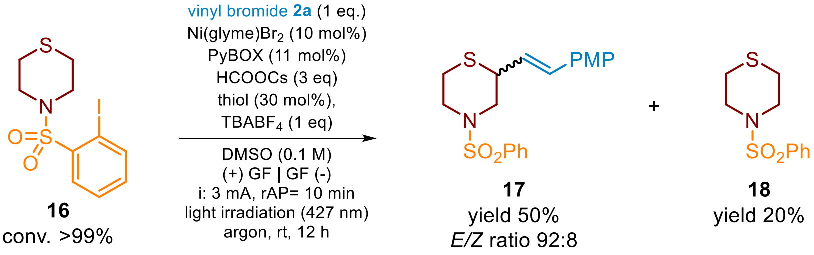
12
yield 15%
E/Z ratio 96:4



13
conv. >99%

14
yield 63%
(only *E*-isomer)

15
yield ~5%
(only *E*-isomer)

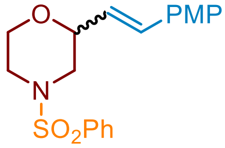


16
conv. >99%

17
yield 50%
E/Z ratio 92:8

18
yield 20%

2-(4-methoxystyryl)-4-(phenylsulfonyl)morpholine (12):



Yield: 45 mg (15%) starting from benzenesulfamide **10** (176 mg, 0.5 mmol) and vinyl bromide **2a** (213 mg, 1.00 mmol); (*E/Z*)-isomers in a ratio: 96:4. Off-white solid.

Purification: automated flash column chromatography on SiO_2

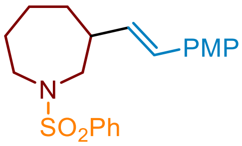
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 45% to 60% AcOEt in petroleum ether for 15 min, and 60% AcOEt in petroleum ether for 10 min.
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.65 (50% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-d_6 at 80 °C, *E/Z*-isomers mixture in a ratio 96:4) δ 7.71 – 7.60 (m, 5H), 7.34 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 6.60 (d, *J* = 16.1 Hz, 1H), 6.04 (dd, *J* = 16.1, 5.8 Hz, 1H), 4.15-4.10 (m, 1H), 3.94 (ddd, *J* = 11.7, 3.5, 1.9 Hz, 1H), 3.81 (s, 3H), 3.66 – 3.56 (m, 2H), 3.48 (dq, *J* = 11.6, 2.2 Hz, 1H), 2.51 – 2.41 (m, 3H), 2.25 (dd, *J* = 11.7, 10.0 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6 at 80 °C, *E/Z*-isomers mixture in a ratio 96:4) δ 158.9, 141.5, 135.2, 132.8, 130.3, 129.0, 127.3, 127.1, 126.5, 114.2, 74.5, 64.6, 55.1, 49.7, 44.9.

HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{21}NO_4SNa$ [(M+Na)+] 382.1089; found 382.1088.

(*E*)-3-(4-methoxystyryl)-1-(phenylsulfonyl)azepane (14):



Yield: 141 mg (63%) starting from azepane benzsulfamide **13** (241 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); only (*E*)-isomer. Brown oil.

Purification: automated flash column chromatography on SiO_2

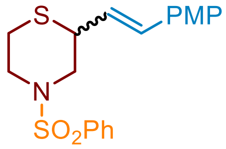
Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, then 60% AcOEt in petroleum ether for 10 min and 70% AcOEt in petroleum ether for 15 min.
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.45 (50% EtOAc in Hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 7.81 – 7.55 (m, 5H), 7.29 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.35 (d, *J* = 16.1 Hz, 1H), 6.03 (dd, *J* = 16.1, 7.6 Hz, 1H), 3.74 (s, 3H), 3.51 (dd, *J* = 13.9, 4.6 Hz, 1H), 3.37 (ddd, *J* = 13.2, 7.8, 4.9 Hz, 1H), 3.20 – 3.12 (m, 1H), 3.00 (dd, *J* = 14.0, 9.5 Hz, 1H), 2.55 – 2.49 (m, 1H), 1.84 – 1.71 (m, 2H), 1.66 – 1.54 (m, 1H), 1.53 – 1.44 (m, 2H);

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C) δ 159.2, 140.1, 132.9, 130.6, 130.4, 129.73, 129.71, 129.1, 127.6, 127.0, 114.6, 55.7, 53.2, 49.0, 43.5, 33.8, 28.9, 24.5;

HRMS (ESI-TOF) *m/z* calcd for $C_{21}H_{25}NO_3SNa$ [(M+Na)+] 394.1453; found 394.1455.

2-(4-methoxystyryl)-4-(phenylsulfonyl)thiomorpholine (17):



Yield: 110 mg (50%) starting from benzenesulfamide **16** (244 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol); (*E/Z*)-isomers in a ratio: 94:6. Off-white solid.

Purification: automated flash column chromatography on SiO_2

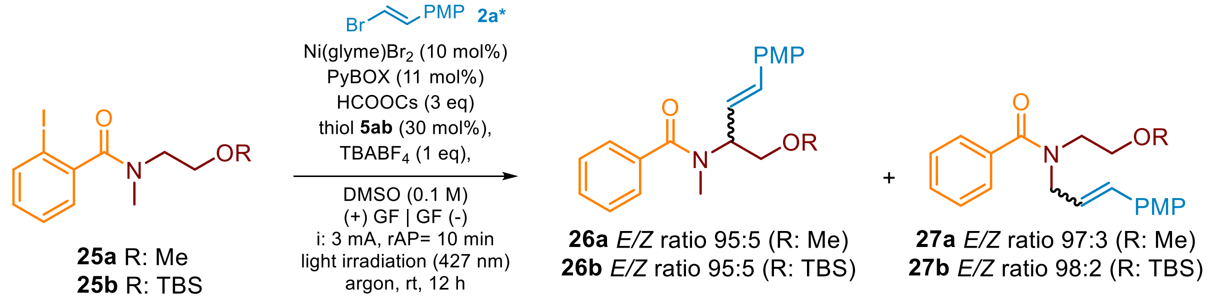
Cartridge size:	1× 80 g (silica gel)
Flow:	25 mL/min
Eluent:	10% EtOAc in petroleum ether for 10 min, then gradient from 10% to 20% AcOEt in petroleum ether for 15 min, and 20% AcOEt in petroleum ether for 10 min.
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.5 (20% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80°C, *E/Z*-isomers mixture in a ratio 94:6) for (*E*)-isomer δ 7.82 – 7.76 (m, 2H), 7.75 – 7.68 (m, 1H), 7.65 (ddd, *J* = 8.2, 6.6, 1.2 Hz, 2H), 7.34 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.62 (d, *J* = 15.9 Hz, 1H), 6.06 (dd, *J* = 15.9, 7.6 Hz, 1H), 3.84 – 3.77 (m, 1H), 3.77 (s, 3H), 3.77 – 3.69 (m, 1H), 3.71 – 3.63 (m, 1H), 2.93 – 2.75 (m, 4H);

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80°C, *E/Z*-isomers mixture in a ratio 94:6) δ 158.9, 136.9, 132.6, 131.5, 129.0, 128.6, 127.2, 126.6, 123.8, 113.8, 54.8, 51.9, 46.6, 40.8, 26.0;

HRMS (ESI-TOF) *m/z* calcd for $C_{19}H_{21}NO_3S_2Na$ [(M+Na)+] 398.0861; found 398.0858.

6. The *α*-C-H alkenylation of acyclic amines



25a R: Me
25b R: TBS

26a *E/Z* ratio 95:5 (R: Me)
26b *E/Z* ratio 95:5 (R: TBS)

27a *E/Z* ratio 97:3 (R: Me)
27b *E/Z* ratio 98:2 (R: TBS)

*E/Z ratio >99:1

for **25a**, yield 56%, **26a** : **27a** ratio 78.5 : 21.5
for **25b**, yield 36%, **26b** : **27b** ratio 72 : 28

Compound **26a**:

^{1}H NMR (500 MHz, DMSO-d_6, 80°C, *E/Z*-isomers mixture in a ratio of 95:5) for (*E*)-isomer δ 7.47 – 7.36 (m, 7H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.47 (d, *J* = 16.1 Hz, 1H major E isomer), 6.11 (dd, *J* = 16.0, 5.8 Hz, 1H), 4.83 (br m, 1H), 3.77 (s, 3H), 3.71 – 3.64 (m, 1H), 3.57 – 3.49 (m, 1H), 3.30 (s, 3H), 2.88 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6, 80°C, *E/Z*-isomers mixture in a ratio of 95:5) δ 170.7, 158.8, 136.7, 131.2, 130.3, 128.7, 127.8, 127.7, 127.3, 127.1, 126.6, 126.2, 122.3, 113.8, 71.0, 57.8, 57.7, 54.8, 39.8;

HRMS (APCI-TOF) *m/z* calcd for $C_{20}H_{24}NO_3$ [(M+H)+] 326.1756; found 326.1758.

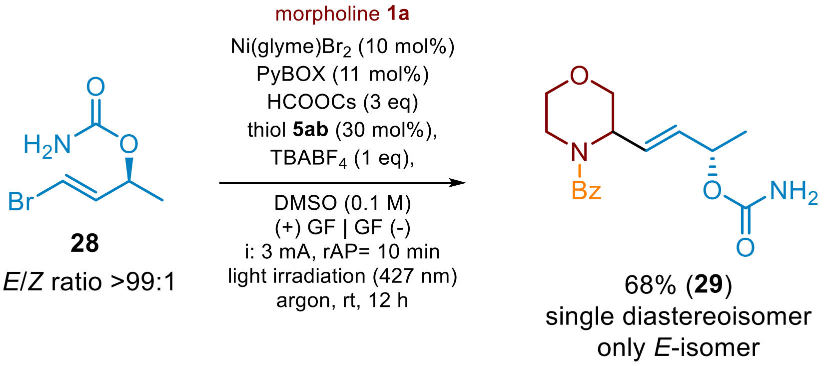
Compound **27a**:

^{1}H NMR (500 MHz, DMSO-d_6 at 80°C, *E/Z*-isomers mixture in a ratio of 97:3) for (*E*)-isomer δ 7.46 – 7.39 (m, 5H), 7.36 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.09 (dt, *J* = 15.9, 6.2 Hz, 1H), 4.12 (br s, 2H), 3.77 (s, 3H), 3.56-.52 (m, 4H), 3.25 (s, 3H);

^{13}C NMR (126 MHz, DMSO-d_6 at 80°C, *E/Z*-isomers mixture in a ratio of 97:3) δ 170.4, 158.7, 136.6, 131.1, 128.9, 128.6, 127.8, 127.1, 126.1, 122.7, 113.8, 69.3, 57.7, 54.8, 45.4;

HRMS (APCI-TOF) *m/z* calcd for $C_{20}H_{24}NO_3$ [(M+H)+] 326.1756; found 326.1757.

7. The *α*-C-H alkenylation with 2-alkyl substituted vinyl bromides



28
E/*Z* ratio >99:1

68% (**29**)
single diastereoisomer
only *E*-isomer

Yield: 125 mg (68.5%) starting from morpholine derivative **1a** (210 mg, 0.66 mmol) and vinyl bromide **28** (116 mg, 0.60 mmol, *E/Z* ratio >99:1). Off-white semi-solid.

Purification: automated flash column chromatography on SiO_2

Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	45 % EtOAc in petroleum ether for 10 min, then gradient from 50% AcOEt in petroleum ether for 15 min, then 60% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.4 (50% EtOAc in Hexanes)

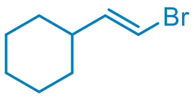
Product **29**:

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, single diastereoisomer, only *E*-isomer, mixture of rotamers) δ 7.46 – 7.41 (m, 3H), 7.40 – 7.34 (m, 2H), 6.18 (s, 2H), 5.83 (br dd, *J* = 15.9, 5.2, 1H), 5.71 – 5.56 (m, 1H), 5.20 – 5.11 (m, 1H), 4.55 (br s, 1H),3.89 – 3.78 (m, 2H), 3.77 – 3.69 (m, 1H), 3.64 (dd, *J* = 11.7, 3.5 Hz, 1H), 3.44 (td, *J* = 11.7, 2.9 Hz, 1H), 3.23 (td, *J* = 13.4, 4.0 Hz, 1H), 1.28 – 1.25 (m, 3H);

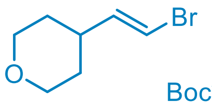
^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, single diastereoisomer, only *E*-isomer, mixture of rotamers) δ 169.3, 155.6, 135.5, 133.1, 133.0, 129.1, 128.0, 126.9, 126.8, 126.2, 68.9, 68.8, 68.5, 65.8, 52.1, 20.0.

HRMS (ESI-TOF) *m/z* cald for $C_{16}H_{20}N_2O_4Na$ [(M+Na)+] 327.1321; found 327.1319.

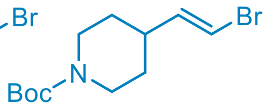
The C-H alkenylation with the aliphatic vinyl bromides **SI-2c**-**SI-2g** were unsuccessful. For these substrates the rate of debromination and homocoupling side reactions were significantly higher than the investigated XAT/HAT/cross-coupling sequence.



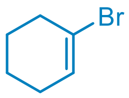
SI-2c



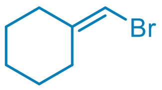
SI-2d



SI-2e



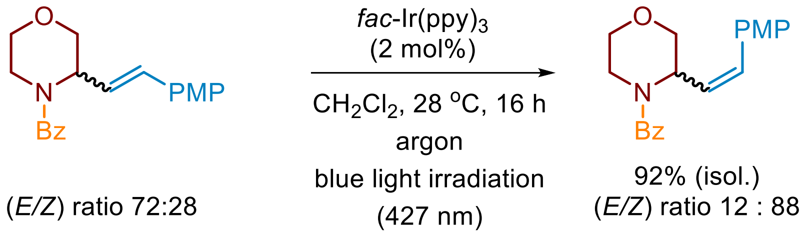
SI-2f



SI-2g

8. *E/Z* isomerization

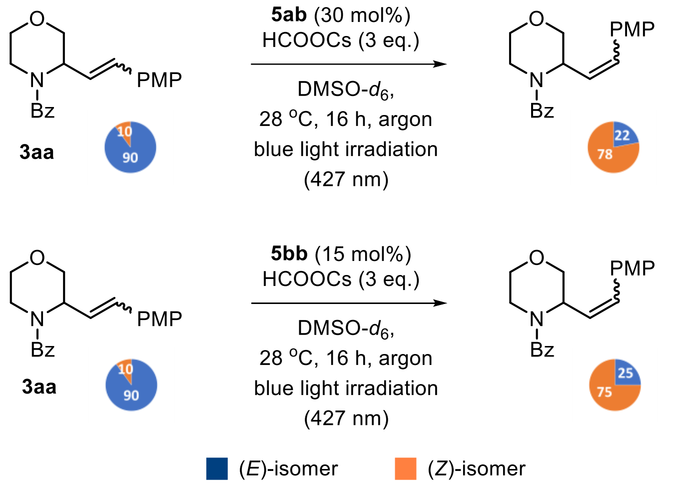
8.1. Photoisomerization of products in the presence of Ir complex



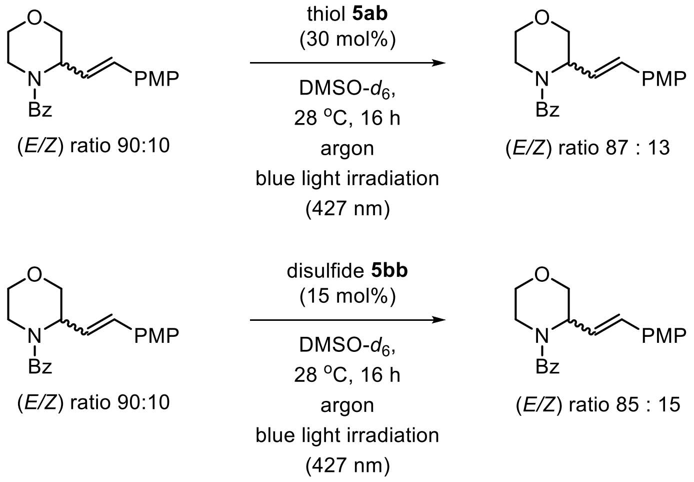
An oven-dried dried sealed tube was charged with compound ***(E/Z)*-3aa** (100 mg, 0.31 mmol, *E/Z* mixture in a ratio of 72:28) and *fac*-Ir(ppy)$_3$ (4 mg, 6.0 μmol, 2.0 mol%). Next, the vial was transferred to a glovebox and reagents were dissolved in dry CH_2Cl_2 (3.1 mL). After sealing tightly, the vial was removed from glovebox and the solution inside was irradiated with blue light (427 nm, 40 W, cooling with 4 fans, a light source-vial distance 3 cm) for 16 hours. After completion of the process, the reaction mixture was diluted with CH_2Cl_2 and filtered through the plug of silica gel with CH_2Cl_2 as an eluent. The collected fractions were combined and solvent was removed. The residue was purified by flash chromatography on silica gel to afford the desired product **3aa** in 92% yield and with *E/Z*-isomers ratio of 12:88.

8.2. Aryl thiyl radical mediated photoisomerization of products

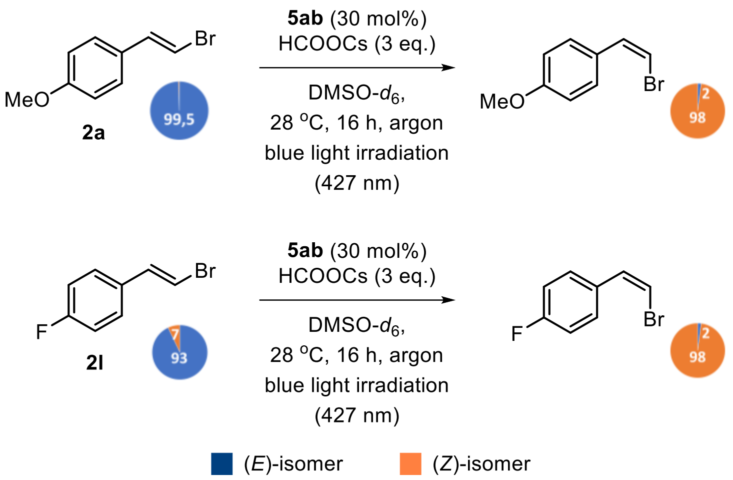
A 2-mL vial was charged with compound **3aa** (20 mg, 62 μmol, *E/Z* ratio 72:28), thiol **5ab** (3.1 mg, 19 μmol, 30 mol%) or disulfide **5bb** (3.1 mg, 9.3 μmol, 15 mol%) and HCOOCs (33 mg, 185 μmol, 3 eq.). The vial was sealed with a septum cap and the air was removed by argon. Under argon, DMSO-d_6 was added (0.8 mL) and the resulting mixture was irradiated with blue light (427 nm) for 16 h. The *E/Z*-isomers ratio of the product was assigned by ^{1}H NMR and GC analysis.



Experiments WITHOUT HCOOCs:

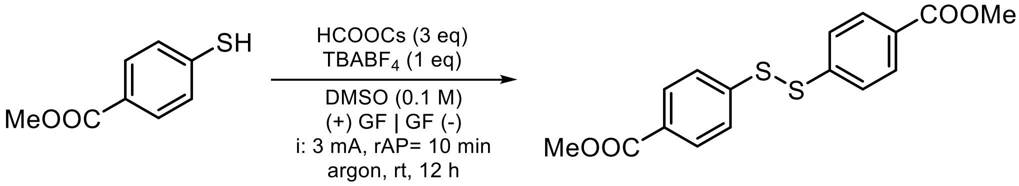


8.3. Aryl thiyl radical mediated photoisomerization of vinyl bromides



A 2-mL vial was charged with vinyl bromide **2a** (30 mg, 141 μmol, *E/Z* ratio 99.5:0.5) or **2l** (30 mg, 149 μmol, *E/Z* ratio 93:7), thiol **5ab** (7.1 mg, 42 μmol, 30 mol%) and HCOOCs (80 mg, 450 μmol, 3 eq.). The vial was sealed with a septum cap and the air was removed by argon. Under argon, DMSO-d_6 was added (2 mL) and the resulting mixture was irradiated with blue light (427 nm) for 16 h. The *E/Z*-isomers ratio of the product was assigned by ^{1}H NMR and GC analysis.

8.4. Electrochemical generation of disulfide 5bb from thiol 5ab



A 10-mL vial was charged with thiol **5ab** (30mg, 0.178 mmol), TBABF$_4$ (58.7mg, 0.535mmol) and the vial was sealed with PTFE cap equipped with two graphite electrodes. After purging with argon, DMSO (6mL) was added. The constant current (3 mA, rapid altering the polarization ever 10 min) was passed through resulting mixture for 12 h. Then, reaction mixture was diluted with water (30mL) and extracted with EtOAc. The combined organic layers were dried over anhydr. Na_2SO_4, solvent was evaporated and the resulting residue was purified by column chromatography to provide 37.4mg (63%) of disulfide **5bb**.

9. Mechanism studies

9.1. Radical trapping

The thiyl radical trapping experiments were carried out following general procedure with addition of 2 equiv. of TEMPO. Under these conditions, the conversion of **1a** was low and the product **3aa** was not observed. MS spectra analysis revealed the presence of the products resulting from trapping of the radical intermediates by TEMPO (Figure SI-1a). The product of an interception of thiyl radical by TEMPO was not detected probable due to low loading (only 30 mol%) of the initial thiol **5ab**. Therefore, the second experiment was performed with 1 eq. of thiol **5ab** and 2 eq. of TEMPO but without substrates **1a** and **2a**; other parameters was not changed. The analysis of MS spectra of crude reaction mixture revealed the presence of the expected thiyl radical trapping product along with disulfide **5bb** (Fig. SI-1b).

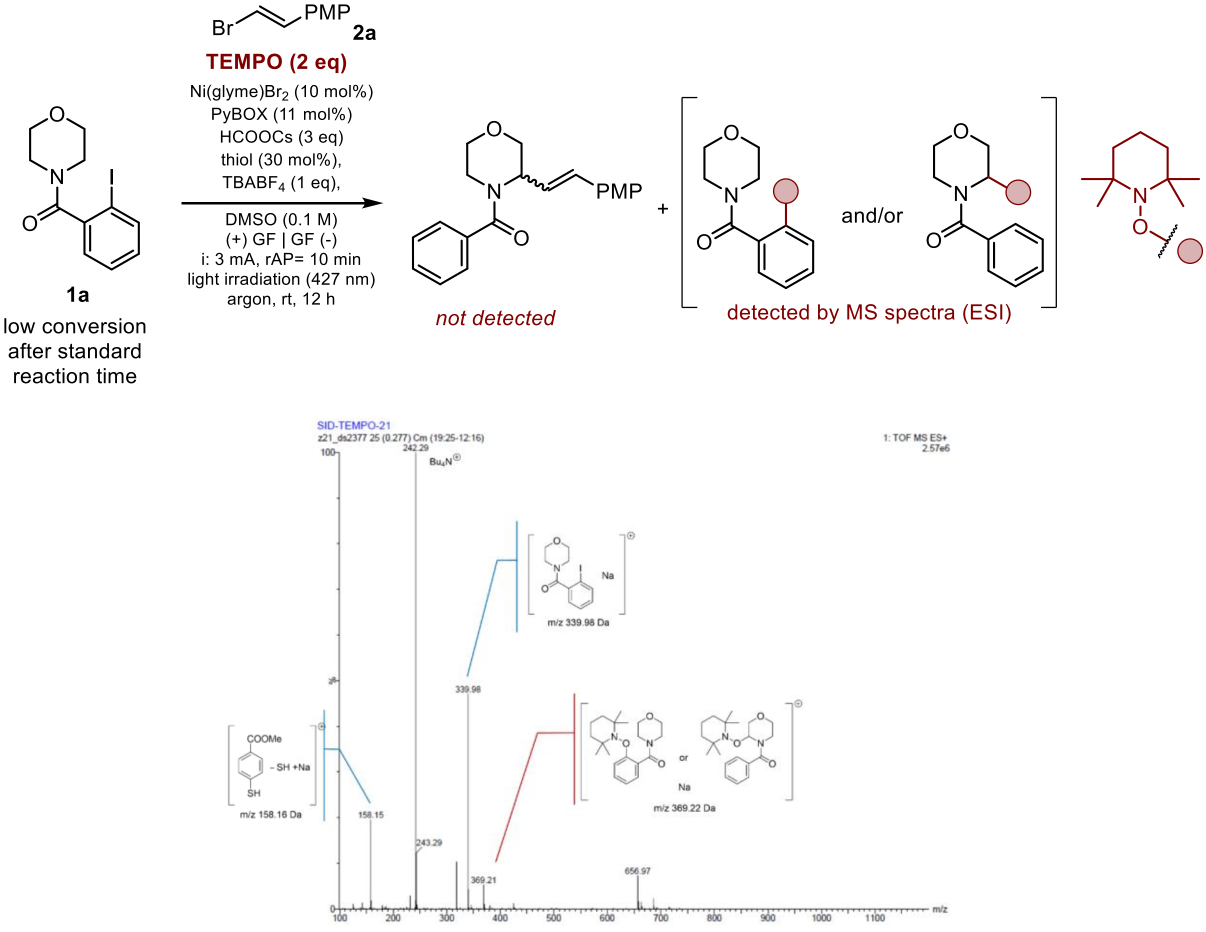
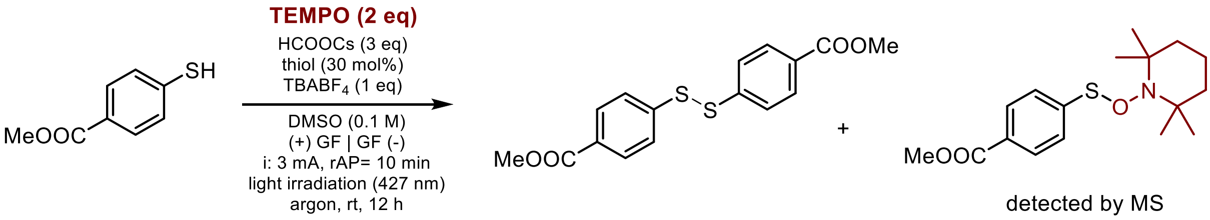


Figure SI-1a. Radical trapping experiments with TEMPO: trapping aryl/α-aminoalkyl radical intermediate.



detected by MS
[$(M+Cs)^+$] = 465 Da

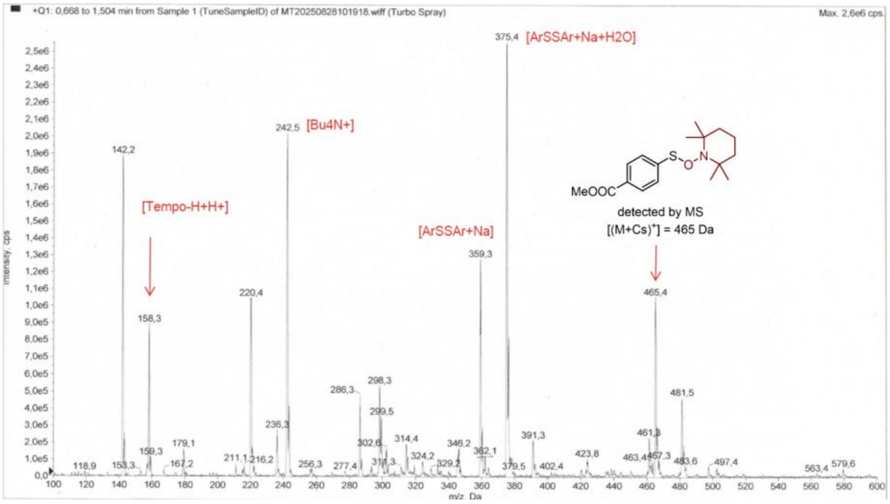
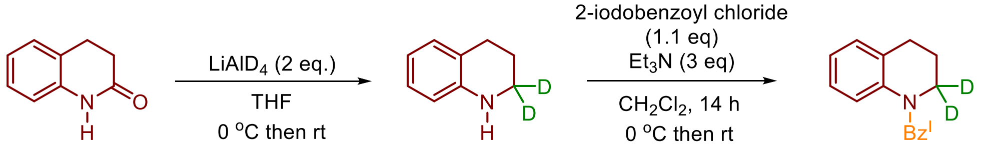


Figure SI-2b. Radical trapping experiments with TEMPO; trapping thiyl radical intermediate

9.2. Deuterium-labelling experiments

9.2.1. Synthesis of d-substrate 1h-d_2



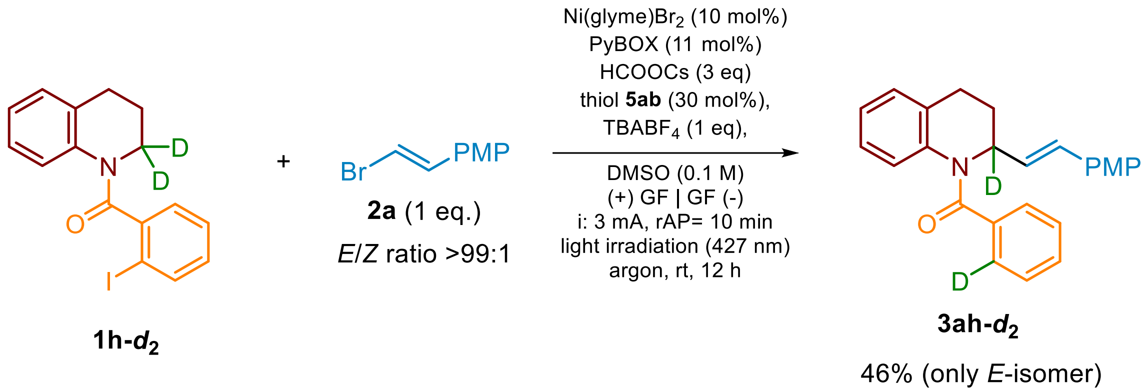
1h-d_2

To a solution of 3,4-dihydro-2(1*H*)-quinolinone (1.00 g, 6.8 mmol, 1.0 equiv.) in dry THF (60 mL) was added $LiAlD_4$ (575 mg, 13.6 mmol, 2.0 equiv., >95% D) at 0 °C and the reaction mixture was stirred overnight at room temperature. After completion of reaction (monitored by TLC), the reaction was quenched by sat. aq. Na_2SO_4, and extracted with EtOAc (3 × 50 mL). The combined organic layer was washed by brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford the corresponding deuterated tetrahydroquinoline, which was directly used in the next step without further purification. To a solution of crude deuterated tetrahydroquinoline and Et_3N (2.9 mL, 20.4 mmol, 3 equiv) in dry CH_2Cl_2 (50 mL) a solution of 2-iodobenzoyl chloride (2.00 g, 7.5 mmol, 1.1 equiv.) was added at 0 °C and the reaction mixture was stirred at rt for 14 h. After completion of reaction (monitored by TLC), the reaction was quenched by water, and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phase was washed by brine, dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by column chromatography on silica gel to afford the desired products **1h-*d*$_2$** as pale-yellow solid.

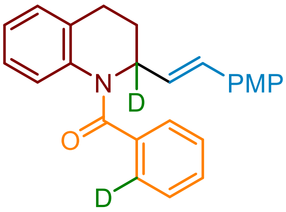
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 – 7.41 (m, 2H), 7.44 – 6.75 (m, 5H), 6.63 (d, *J* = 111.4 Hz, 1H), 2.92 – 2.86 (m, 2H), 2.16 – 1.92 (m, 2H).

HRMS (ESI-TOF+) *m/z* calcd for $C_{16}H_{12}D_2NOINa$ [(M+Na)+] 388.0143; found 388.0141.

9.2.2. Alkenylation of deuterated-substrate 1h-*d*$_2$



Compound 3ah-*d*$_2$:



Yield: 102 mg (46%) starting from benzamide **1h-*d*$_2$** (241 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol). Only (*E*)-isomer. Brown sticky oil.

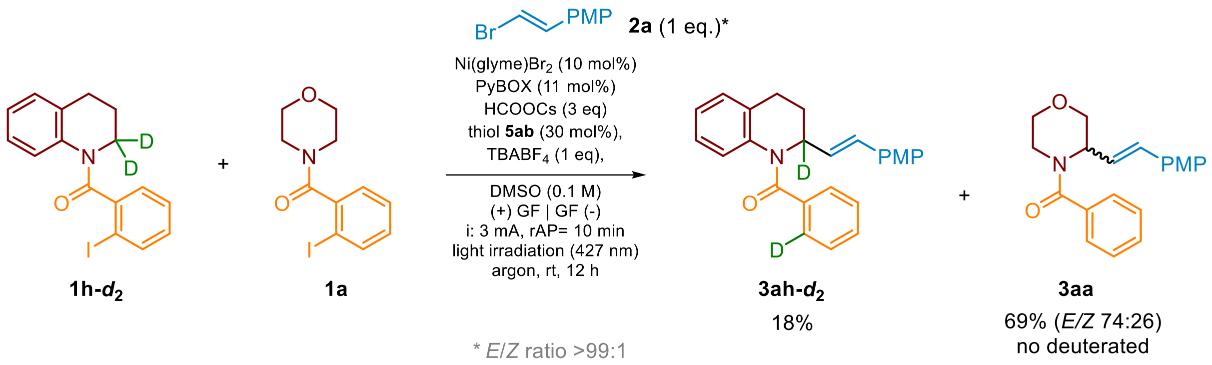
Purification: automated flash column chromatography on SiO_2:

Cartridge size:	1× 80 g (silica gel)
Flow:	45 mL/min
Eluent:	15 % EtOAc in petroleum ether for 10 min, then gradient from 15% to 30% AcOEt in petroleum ether for 15 min, and 30% AcOEt in petroleum ether for 10 min
Detection:	ELSD & UV (254 nm)
TLC:	R_F = 0.7 (20% EtOAc in hexanes) (Visualization: UV-254, vanillin or $KMnO_4$ stain).

^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80 °C) δ 7.41 – 7.17 (m, 8H), 7.00 (td, *J* = 7.3, 1.4 Hz, 1H), 6.91 (td, *J* = 7.7, 1.6 Hz, 1H), 6.88 – 6.82 (m, 3H), 6.46 (dd, *J* = 16.0, 1.6 Hz, 1H), 6.03 (dd, *J* = 16.0, 5.4 Hz, 1H), 5.28 – 5.21 (m, 1H), 3.74 (s, 3H), 2.90 – 2.82 (m, 2H) 2.36-2.08 (m, 2H);

HRMS (ESI-TOF+) *m/z* calcd for $C_{25}H_{21}D_2NO_2Na$ [(M+Na)+] 394.1752; found 394.1749.

9.2.3. Crossover experiment



Yield: 134 mg of product **3aa** (69%, E/Z ratio 74:26) and 40 mg of product **3ah-*d*₂** (18%, only *E*-isomer) starting from benzamide **1h-*d*₂** (241 mg, 0.66 mmol), benzamide **1a** (210 mg, 0.66 mmol) and vinyl bromide **2a** (128 mg, 0.60 mmol).

9.3. Photophysical studies

9.3.1. UV-Vis spectra for model substrates and reagents

Sample preparation

Methyl 4-mercaptobenzoate: A 20 mL glass vial containing 5.1 mg (0.0303 mmol) of thiol was sealed with septum, vacuumed and backfilled with argon for 3 times, then degassed DMSO (15 mL) was added via syringe to provide a 2×10^{-3} mM stock solution of thiol. 100 μL of the stock solution were taken and diluted further with DMSO in 5 mL volumetric flask. The resulting solution was purged with argon for 5 min. 2 mL of this solution was transferred into an argon filled quartz cuvette equipped with septum.

Deprotonated Methyl 4-mercaptobenzoate: a 20 mL vial containing magnetic dipole, Cs_2CO_3 (50 mg, 150 μmol) and methyl 4-mercaptobenzoate (8.6 mg, 51 μmol) was sealed with septum, vacuumed and backfilled with argon for 3 times, then degassed DMSO (15 mL) was added via syringe and the resulting mixture was stirred for 2.5 hours at room temperature under argon. Next, 2 mL of the solution was transferred into an argon filled quartz cuvette with septum.

Saturated solution of HCOOCs: A 20-mL vial was charged with 200 mg of HCOOCs and 15 mL of DMSO was added.

Thiol stock solution: A 20-mL vial was charged with thiol (5.1 mg) and 15 mL of DMSO was added (*c* 1.96×10^{-3} mM).

Cesium thiolate stock solution: A 20-mL vial was charged with thiol (8.6 mg) and Cs_2CO_3 (50 mg) and 15 mL of DMSO was added (*c* 3.4×10^{-3} mM).

<u>Quencher A (**1a**) solution:</u> A 20-mL vial was charged with morpholine 2-iodobenzamide (**1a**) (6.0 mg) and 15 mL of DMSO. 100 μL of this solution was transferred into 5-mL volumetric flask, and the flask was filled with DMSO to volume of 5 mL (c 4.5×10^{-5} mM).

<u>Quencher B (**2a**) solution:</u> A 20-mL vial was charged with 2-(4-methoxyphenyl)vinyl bromide (**2a**) (6.0 mg) and 15 mL of DMSO. 100 μL of this solution was transferred into 5-mL volumetric flask, and the flask was filled with DMSO to volume of 5 mL (c 3.75×10^{-5} mM).

<u>Quencher C (**3aa**, *E*/*Z* mixture 90:10) solution</u>: A 20-mL vial was charged with compound **3aa** (10.0 mg) and 10 mL of DMSO. 50 μL of this solution was transferred into 5-mL volumetric flask, and the flask was filled with DMSO to volume of 5 mL (c 3.09×10^{-5} mM).

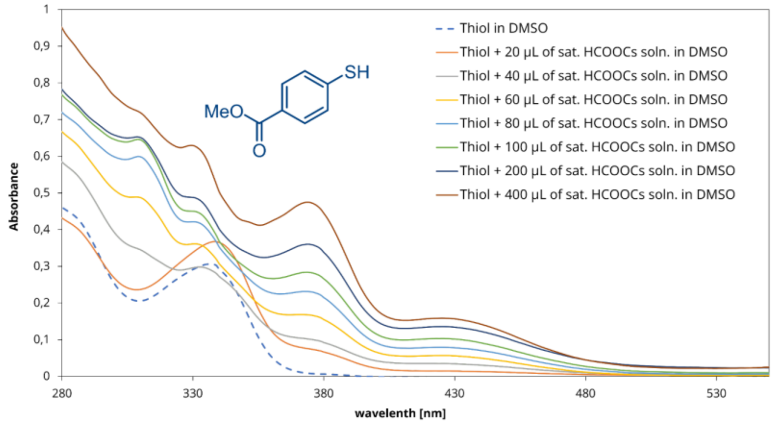


Figure SI-3. UV-Vis spectra of thiol **5ab** in DMSO (100 μL of stock solution in 5 mL volumetric flask) and UV-Vis spectra of thiol **5ab** (100 μL of stock solution) and sat. HCOOCs mixture in DMSO.

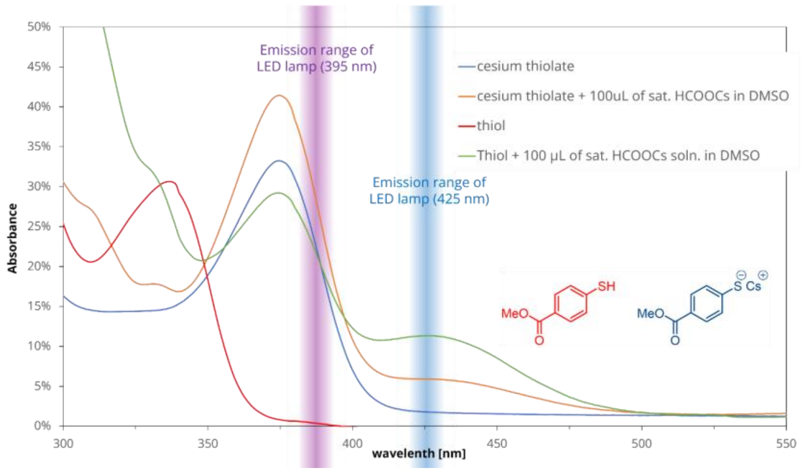


Figure SI-4. UV-Vis spectra of thiol **5ab**, and its cesium salt in DMSO with and without an addition of sat. HCOOCs in DMSO (100 μL).

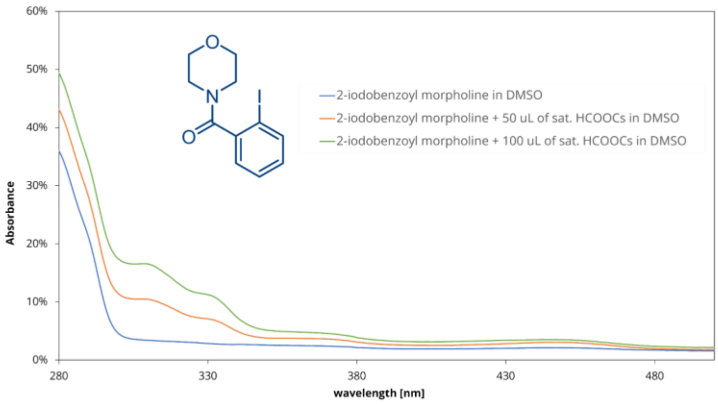


Figure SI-5. UV-Vis spectra of morpholine 2-iodobenzamide **1a** DMSO with and without an addition of sat. HCOOCs in DMSO.

The absorption of **1a** (

Figure **SI-3**) is out of operational range (395-425 nm) that indicates that compound **1a** is not the source of the reactive species. An addition of HCOOCs results in increase of absorbance but still the observed bands are out of operational range. The observed additional weak bands ca. 375 nm and 440 nm has minor influence on the reactivity of the molecule.

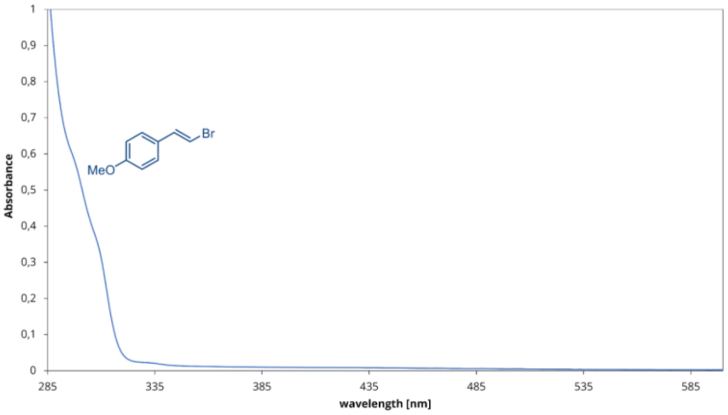


Figure SI-6. UV-Vis spectra of 2-(*p*-methoxyphenyl)vinyl bromide **2a** in sat. HCOOCs in DMSO.

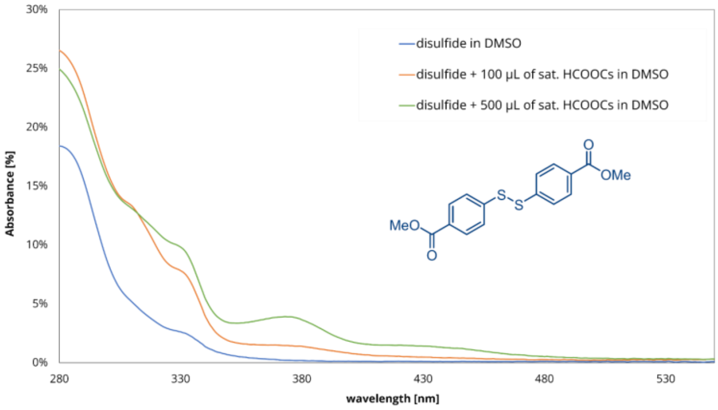


Figure SI-7. UV-Vis spectra of disulfide **5bb** DMSO with and without an addition of sat. HCOOCs in DMSO.

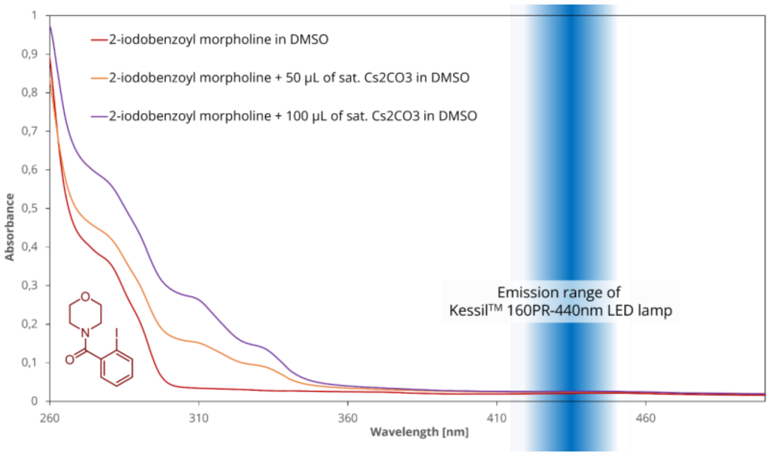


Figure SI-8. UV-VIS spectra of **1a** and **1a**+Cs_2CO_3 donor-acceptor complex.

9.3.2. Fluoresence quenching studies

A 100 µL of thiols' stock solution was transferred to six 5-mL volumetric flasks equipped with septum. To each flask an appropriate amount of **1a** solution was added (0-100 µL) and each flask was filled with DMSO to volume of 5 mL. Each solution was purged with argon for 5 min. Under argon, 2 mL of each the prepared solutions were transferred to quartz cuvette (10 mm) and UV spectra and fluorescence spectra were recorded.

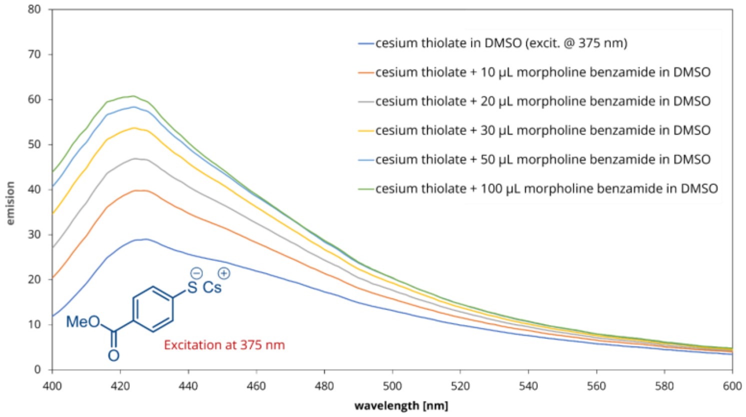


Figure SI-9. Fluoresence quenching of cesium thiolate (**5ab-Cs**) with morpholine 2-iodobenzamide **1a** in DMSO. Excitation at 375 nm.

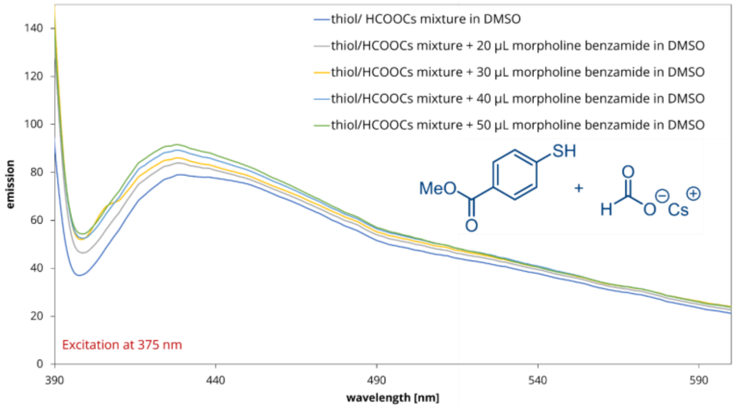


Figure SI-10. Fluoresence quenching of thiol **5ab**/HCOOCs mixture in DMSO with morpholine 2-iodobenzamide **1a** in DMSO. Excitation at 375 nm.

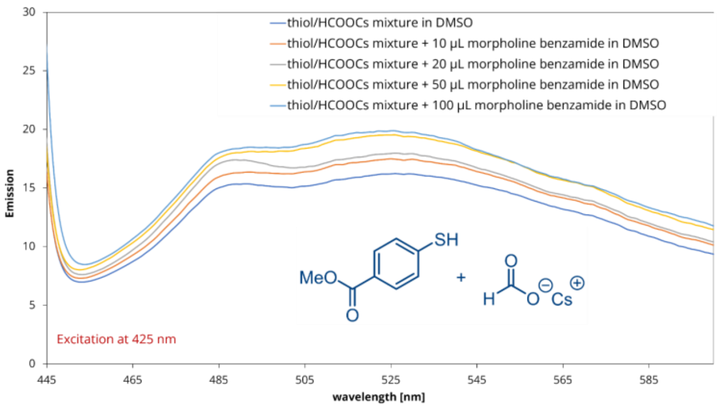


Figure SI-11. Fluoresence quenching of thiol **5ab**/HCOOCs mixture in DMSO with morpholine 2-iodobenzamide **1a** in DMSO. Excitation at 425 nm.

As showed in Figures SI-8-SI-10, an addition of benzamide **1a** to cesium thiolate and to thiol/HCOOCs mixture in DMSO did not quench the fluorescence neither after excitation with 375 nm nor 425 nm. The observed an increase in an emission band after adding each portion of **1a** indicates that the **1a** may act as a fluorescence sensitizer or energy donor. Presented results indicate that a direct interaction between excited thiolate and aryl halide did not proceed, therefore other reactive species is responsible for an activation of substrate **1a** to produced aryl radical for subsequent 1,5-HAT process.

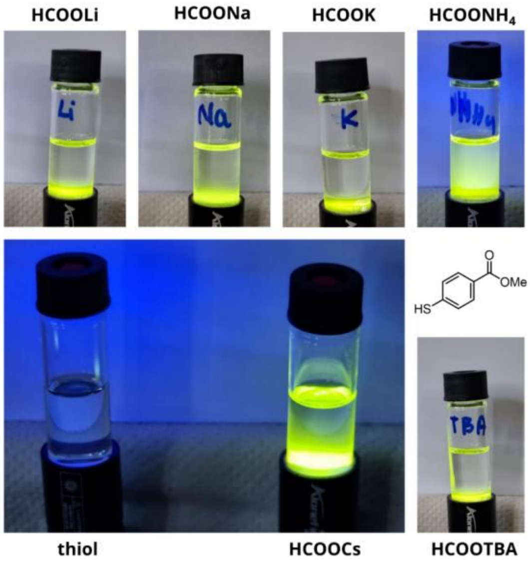


Figure SI-12. Emission experiments for the mixtures of thiol **5ab** with different formate salts in DMSO (excitation by 1W LED at 395 nm).

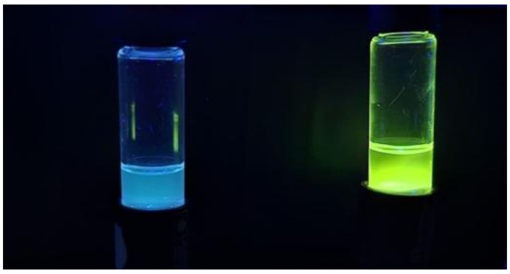


Figure SI-13. Emission experiment for thiol **5ab** in DMSO (left) and thiol **5ab** after addition of HCOOCs. Both solutions are irradiated with UV light (1W LED 365 nm).

A 100 μL of thiol **5ab** stock solution and 250 μL of sat. soln of HCOOCs stock solution was transferred to four 5-mL volumetric flasks equipped with septum. To each flask an appropriate amount of quencher **3aa** solution was added (0-50 μL) and each flask was filled with DMSO to volume of 5 mL. Each solution was purged with argon for 5 min. Under argon, 2 mL of each the prepared solutions were transferred to quartz cuvette (10 mm) and UV spectra and fluorescence spectra were recorded.

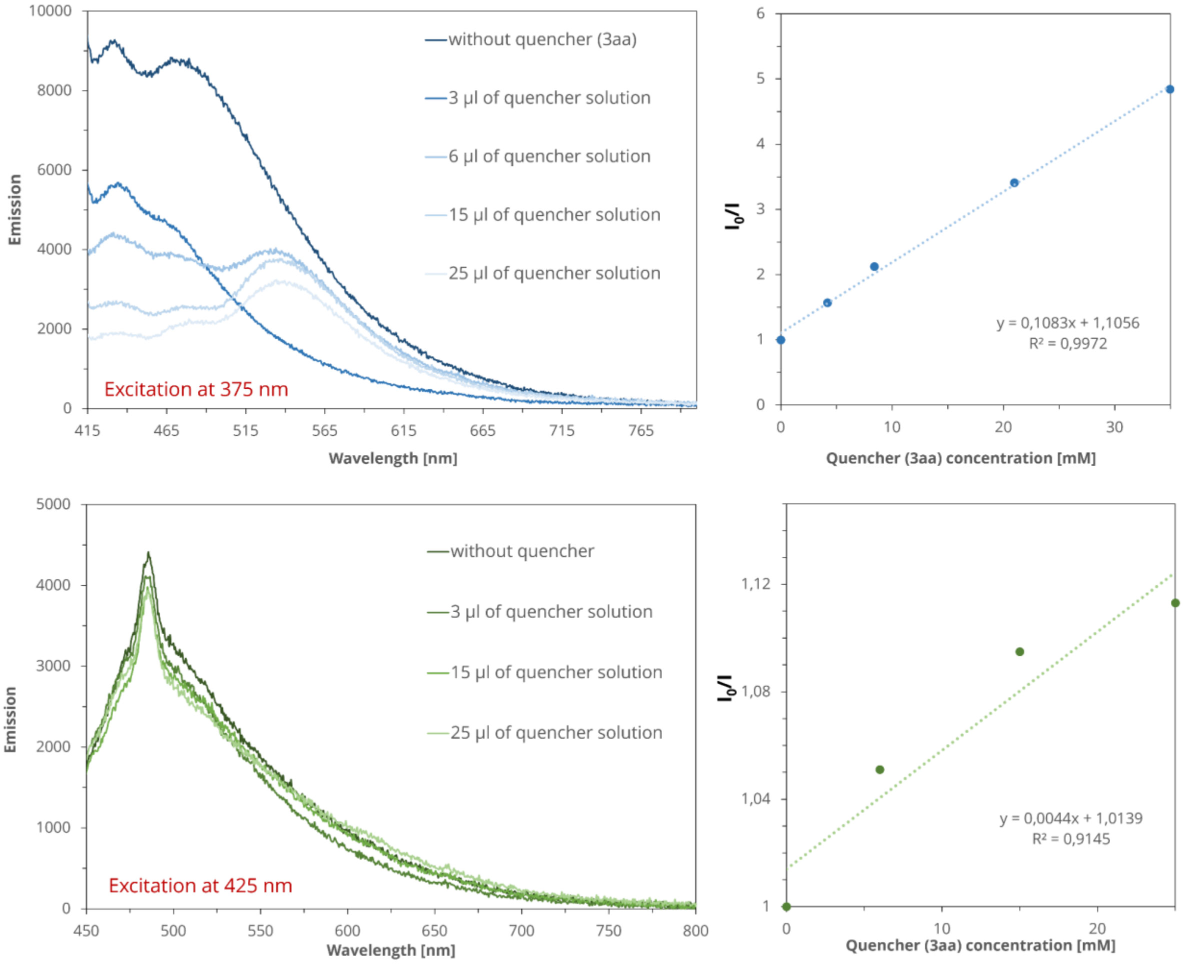


Figure SI-14. Fluoresence quenching of thiol **5ab**/HCOOCs mixture in DMSO with product **3aa** in DMSO. Excitation at 375 and 425 nm.

9.4. Electrochemical studies

Cyclic voltammetry (CV) was carried out on Ossila Potentiostat instrument equipped with a glassy carbon disk working electrode (Φ 3 mm). A silver wire coated with AgCl immersed in 1 M solution of $AgNO_3$ in MeCN and separated form analyte by a fritted glass disk was employed as the reference electrode. The Pt wire counter electrode completed the electrochemical setup.

The substrates were measured at the concentration of 0.01-0.02 M in electrolyte solution ($TBABF_4$ in MeCN). Measurements started from −3.0 V to +3.0 V and back to −3.0 V (scan rate 100 mV/s).

Electrolyte stock solution: 2.179 g of $TBABF_4$ was dissolve in anhydr. degassed MeCN and filled to volume of 100 mL (c = 0.1295 M).

Cyclic Voltametric measurements of model substrates. Potentials are quoted with the following notation: E_{red} refers to the cathodic peak potential and E_{ox} refers to the anodic peak potential.

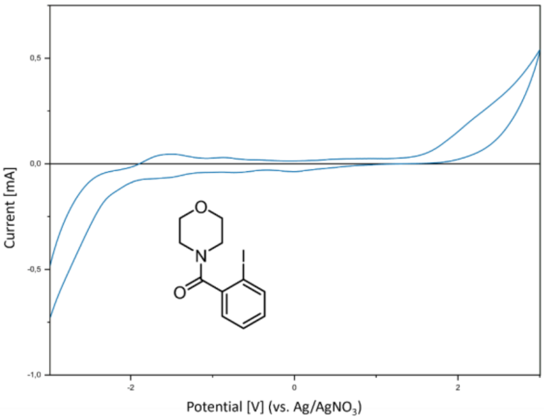


Figure SI-15. CV of *N*-(2-iodobenzoyl)morpholine **1a** 0.017 M in electrolyte solution (0.1295 M $TBABF_4$ in MeCN). Irreversible reduction E_{red} = −1.56 V.

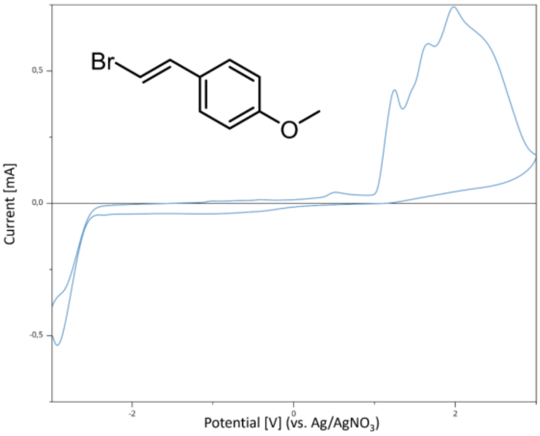


Figure SI-16. CV of (*E*)-1-(2-bromovinyl)-4-methoxybenzene 0.016 M in electrolyte solution (0.1295 M $TBABF_4$ in MeCN). Irreversible reduction E_{red} = −2.69 V.

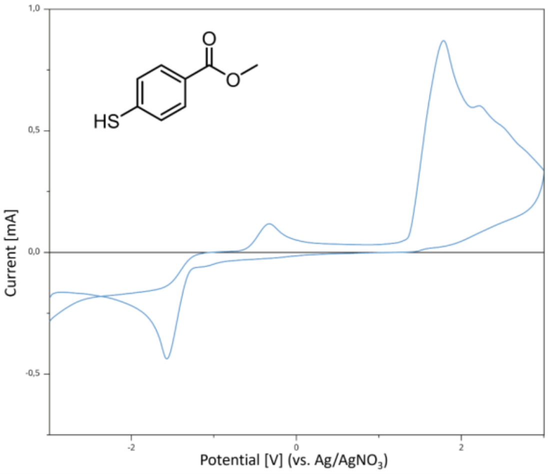


Figure SI-17. CV of methyl 4-mercaptobenzoate 0.016 M in electrolyte solution (0.1295 M $TBABF_4$ in MeCN). Irreversible reduction: E_{red1} = −1.39 V, oxidation: E_{ox12} = +1.88 V and E_{ox2} = +2.48 V.

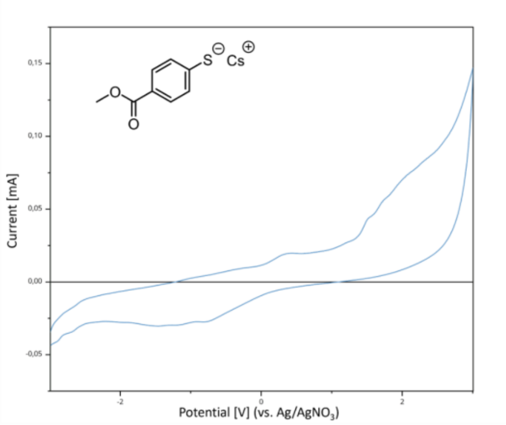


Figure SI-18. CV of methyl 4-mercaptobenzoate Cs salt 0.016 M in electrolyte solution (0.1295 M $TBABF_4$ in MeCN).

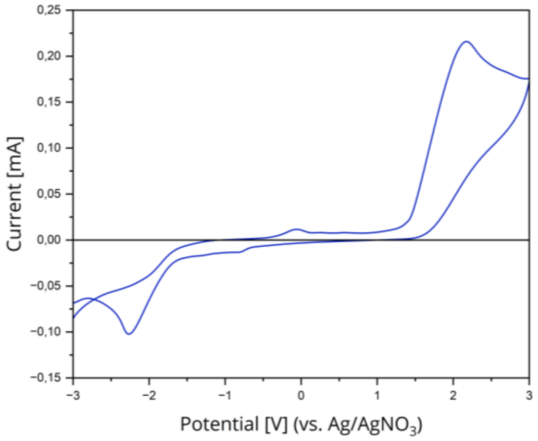


Figure SI-19. CV of disulfide **5bb** 0.014 M in electrolyte solution (0.1295 M $TBABF_4$ in MeCN). Irreversible reduction: E_{red1} = −1.88 V, oxidation: E_{red2} = -0.86 V and E_{ox} = +2.03 V.

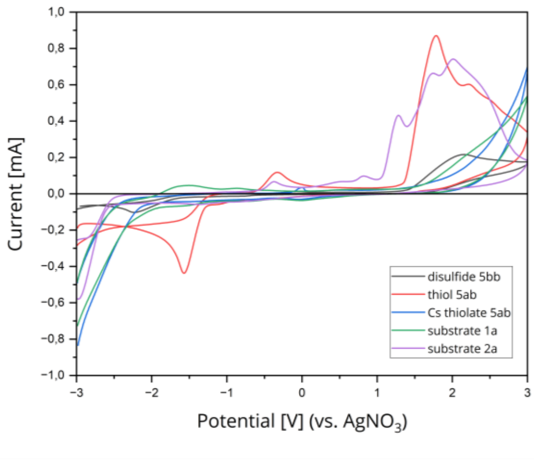


Figure SI-20. Overlay of CV traces of thiol **5ab**, its cesium salt, disulfide **5bb**, substrate **1a** and vinyl bromide **2a**.

9.5. Kinetic studies

Experiment 1: Model reaction between compound **1a** and vinyl bromide **2a** was performed under standard reaction condition without light irradiation. The concentration of substrate **1a**, thiol **5ab**, disulfide **5bb**, and side product **4a** were followed by GC monitoring as shown in

Figure **SI-21**.

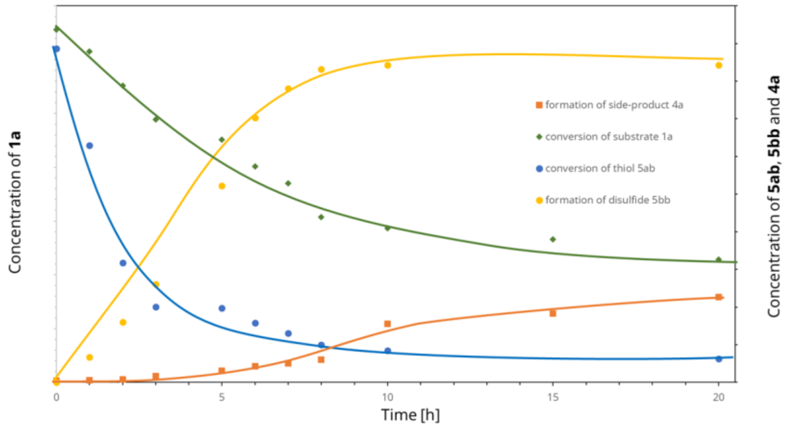


Figure SI-21. Concentration change for model reaction between substrate **1a** and vinyl bromide **4a** without blue light irradiation.

The reaction performed in the absence of light yielded only trace amounts of the desired product **3aa** (only 3% after 20 hours), suggesting that the generation of thiyl radical from disulfide via cathodic reduction (path C in Scheme 16 in the manuscript) either does not occur or proceeds at a rate where dimerization of the thiyl radical outpaces H-atom abstraction. Kinetic experiments appear to support the latter scenario. As shown in

Figure **SI-21**, under dark conditions, substrate **1a** undergoes slow conversion, forming primarily coupling byproducts. Simultaneously, the concentration of thiol **5ab** decreases and stabilizes within approximately 6 hours, while the concentration of disulfide increases to a constant level during the same period. This suggests the establishment of an equilibrium between RSH and RSSR, resulting in insufficient levels of thiyl radical species to promote the designed reaction sequence.

Experiment 2: Next, the same model reaction between compound **1a** and vinyl bromide **2a** was performed under standard reaction condition but without addition of HCOOCs. As previously, the concentration of substrate **1a**, thiol **5ab**, disulfide **5bb**, and side product **4a** were followed by GC monitoring as shown in

Figure **SI-22**.

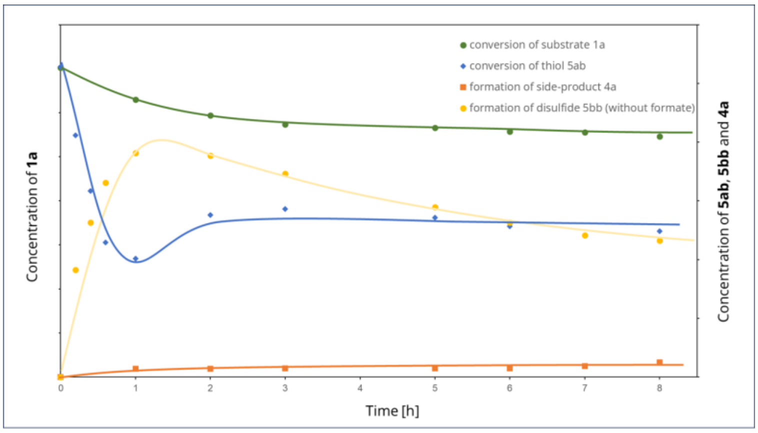
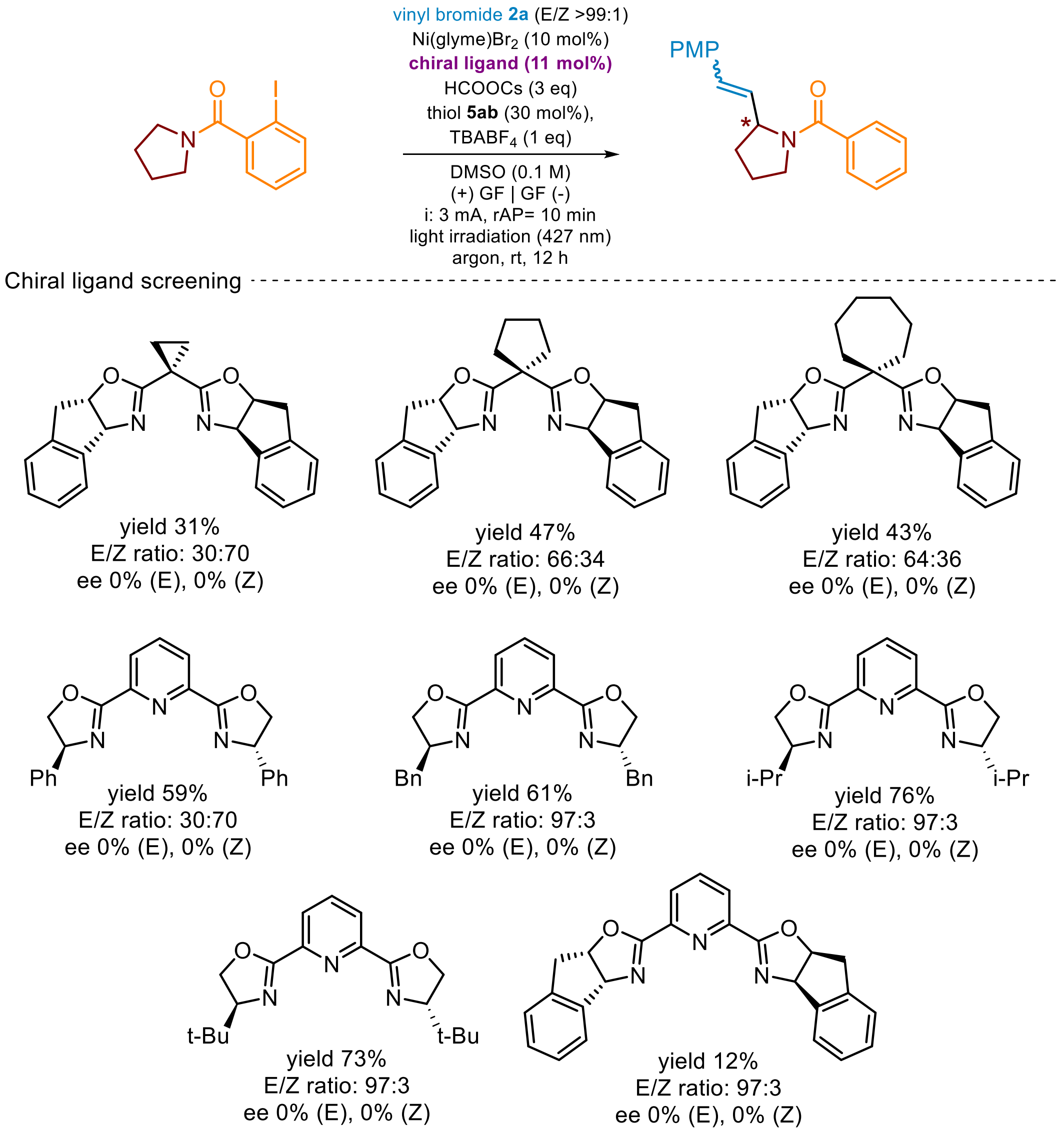


Figure SI-22. Concentration change for model reaction between substrate **1a** and vinyl bromide **4a** under a blue light irradiation without HCOOCs.

Upon irradiation of the reaction mixture, the kinetic profile changed significantly. The concentration of thiol **5ab** rapidly decreased during the first 60 minutes, then gradually increased to a stable level after approximately three hours. Concurrently, the concentration of disulfide **5bb** initially increased rapidly, then slightly decreased and stabilized after about three hours.

These observations support two possible hypotheses. The first posits that light irradiation shifts the thiol/disulfide equilibrium by promoting homolytic cleavage of the disulfide S-S bond, thereby generating thiyl radicals. While thiol dimerization continues, photolysis ensures a continuous supply of aryl thiyl radicals, facilitating the generation of $CO_2^{\cdot-}$ and initiating the sequence of XAT, 1,5-HAT, and cross-coupling processes. Alternatively, the second hypothesis suggests that light activates an alternate pathway (such as path B, Scheme 16 in the manuscript), enabling rapid consumption of thiol, possibly through a rapid anodic oxidation of species **47** to radical **42**. Simultaneously, both paths A and C may operate too, converting excess of the reactive thiyl radicals into disulfide, which serves as a reservoir and maintains their effective concentration to initiate all intended transformations, thereby enabling the formation of C(sp^3)-H alkenylation products. Unfortunately, due to of complexity of the entire system, it is not possible to judge undoubtedly which pathway, A or B, dominates, therefore, it seems to be more appropriate to assume that both paths operate simultaneously along with cathodic transformations of disulfide (path C, Scheme 16 in the manuscript).

10. Enantioselective C-H alkenylation of saturated heterocycles



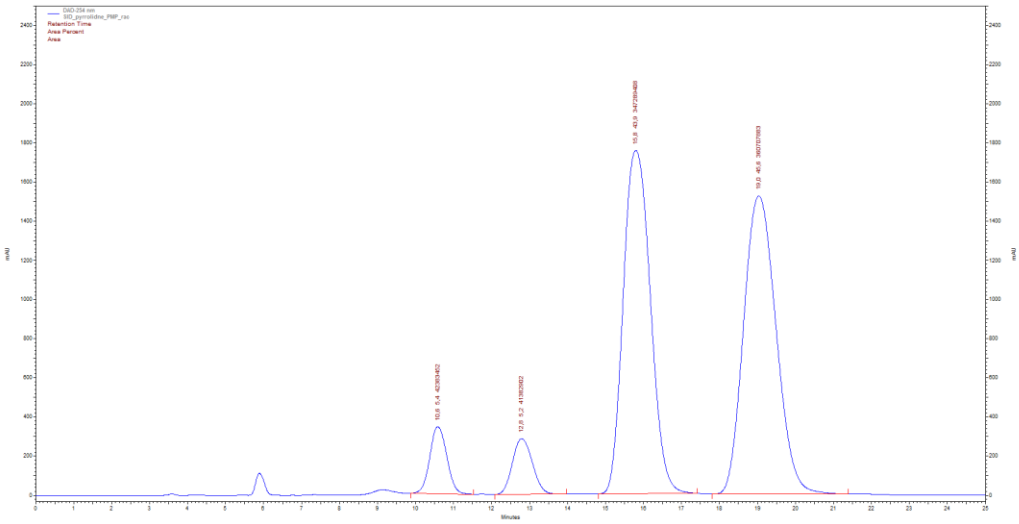
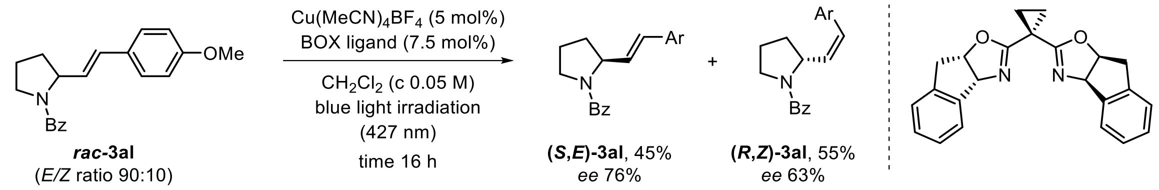


Figure SI-23. HPLC chromatography for racemate ***E/Z*-3aa** (*E/Z* ratio 90:10). HPLC: Chiralpak IA, hexanes/*i*-PrOH 85:15 v/v, 1 mL/min, UV det. 254 nm.

11. Kinetic resolution of product 3al



Following the protocol reported by Yu *et al.*:[50] To an oven-dried 8-mL screw-cap test tube (the diameter of the tube is 1.0 cm) equipped with a magnetic stir bar was added compound **3al** (65 mg, 211 mmol, 1.0 equiv., *E/Z* ratio 90:10), $Cu(CH_3CN)_4BF_4$ (2.7 mg, 11 µmol, 5.0 mol%) and BOX ligand (5.7 mg, 16 µmol, 7.5 mol%). After the tube was evacuated and refilled with argon for three times, freshly distilled dichloromethane (4.2 mL) was added via syringe and the resulting mixture was then positioned approximately 5 cm away from LED lamp and irradiated with a blue light of wavelength 427 nm. Two fans attached to the apparatus was used to maintain the temperature no more than 25 °C. The progress of *E/Z* isomerization and kinetic resolution was followed by HPLC analysis. The residual catalyst was removed by filtration over a SiO_2-plug, subsequent elution of the products with EtOAc and concentration in vacuo. The residue was purified by flash chromatography on silica gel (dopped with 2% w/w $AgNO_3$) to afford the desired products (*R*,*Z*)-**3al** (yield 55%) and (*S*,*E*)-**3al** (yield 45%). E/Z isomer ratio and enantiomeric enrichment were followd by HPLC analysis of the crude mixture (Fig. SI-24).

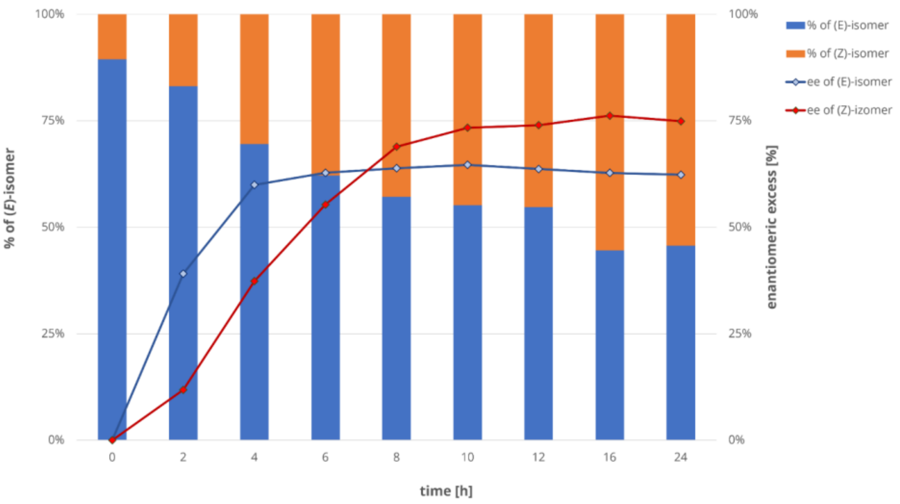


Figure SI-24. The change of E/Z isomer ratio and enantiomeric enrichment during kinetic resolution of compound **3al** in the presence of chiral Cu/BOX ligand.

(*R*,*Z*)-3al: **^{1}H NMR** (500 MHz, DMSO-d_6, 80 °C) δ 7.56 – 7.19 (m, 7H, major), 6.87 (d, *J* = 8.5 Hz, 2H, major), 6.39 – 5.81 (m, 2H, major), 5.56 (dd, *J* = 11.7, 8.9 Hz, 1H, minor), 4.98 (br s, 1H, minor), 4.67 (br s, 1H, major), 3.77 (s, 3H, minor), 3.76 (s, 3H, major), 3.62 – 3.41 (m, 2H, major), 2.19 – 2.06 (m, 1H, major), 2.01 – 1.69 (m, 3H, major); **^{13}C NMR** (126 MHz, DMSO-d_6, 80 °C) δ 168.4, 158.5, 158.0, 137.3, 137.0, 129.4, 129.0, 128.9, 128.4, 128.0, 127.6, 127.5, 127.2, 127.0, 126.34, 126.28, 113.7, 113.4, 59.0 (v br), 54.79, 54.76, 47.0 (v br), 31.4 (br), 23.0 (v br); **HRMS** (ESI-TOF+) *m/z* calcd for $C_{20}H_{21}NO_2Na$ [(M+Na)+] 330.1470; found 330.1472; HPLC (Chiralpak IA, Hexanes: *i*-PrOH 85:15 v/v, 1 mL/min) t_{minor} 11.0 min, t_{major} 13.3 min; *ee* 63%.

(*S*,*E*)-3al: **^{1}H NMR** (500 MHz, DMSO-d_6, 80 °C) δ 7.56 – 7.19 (m, 7H, major), 6.87 (d, *J* = 8.5 Hz, 2H, major), 6.39 – 5.81 (m, 2H, major), 5.56 (dd, *J* = 11.7, 8.9 Hz, 1H, minor), 4.98 (br s, 1H, minor), 4.67 (br s, 1H, major), 3.77 (s, 3H, minor), 3.76 (s, 3H, major), 3.62 – 3.41 (m, 2H, major), 2.19 – 2.06 (m, 1H, major), 2.01 – 1.69 (m, 3H, major); **^{13}C NMR** (126 MHz, DMSO-d_6, 80 °C) δ 168.4, 158.5, 158.0, 137.3, 137.0, 129.4, 129.0, 128.9, 128.4, 128.0, 127.6, 127.5, 127.2, 127.0, 126.34, 126.28, 113.7, 113.4, 59.0 (v br), 54.79, 54.76, 47.0 (v br), 31.4 (br), 23.0 (v br); **HRMS** (ESI-TOF+) *m/z* calcd for $C_{20}H_{21}NO_2Na$ [(M+Na)+] 330.1470; found 330.1471; HPLC (Chiralpak IA, Hexanes: *i*-PrOH 85:15 v/v, 1 mL/min) t_{minor} 16.8 min, t_{major} 20.5 min; *ee* 76%.

12. A large-scale synthesis of compound 3aa

To explore the practicality of this reaction, a scale-up experiment was carried out under the standard reaction conditions. Initially a reaction of **1a** and **2a** was performed in a 50-mL 3-neck round-bottom flask with angled side arms equipped with electrodes (Figure SI-25a & b), however, the desired product **3aa** was obtained in a significantly lower yield (57%, 0.86 g starting from 1.0 g (4.7 mmol) of substrate **2a**) in the compare to the same process at the 0.6 mmol scale. The change of reactor into 3-neck round-bottom flask with parallel side arms (Figure SI-25c) enhanced the yield to 61%. Finally, a placing additional to electrodes (Figure SI-25d) allowed to obtained 1.34 g (84%) of the desired product **3aa** (*E/Z* isomers ratio 90:10), starting from 1.06 g (5.00 mmol) of vinyl bromide **2a** and 1.74 g (5.53 mmol) of morpholine derivative **1a**. The reaction vessel was exposed to a blue light irradiation by two Kessil^{TM} LED lamps (427 nm, 7 cm away, with cooling fans (not presented in figure below) to keep the reaction temperature at 25 °C, Figure SI-25e). To ensure proper immersion of the electrodes in the reaction mixture, the amount of solvent used was increased (concentration from 0.1 M to 0.08 M).

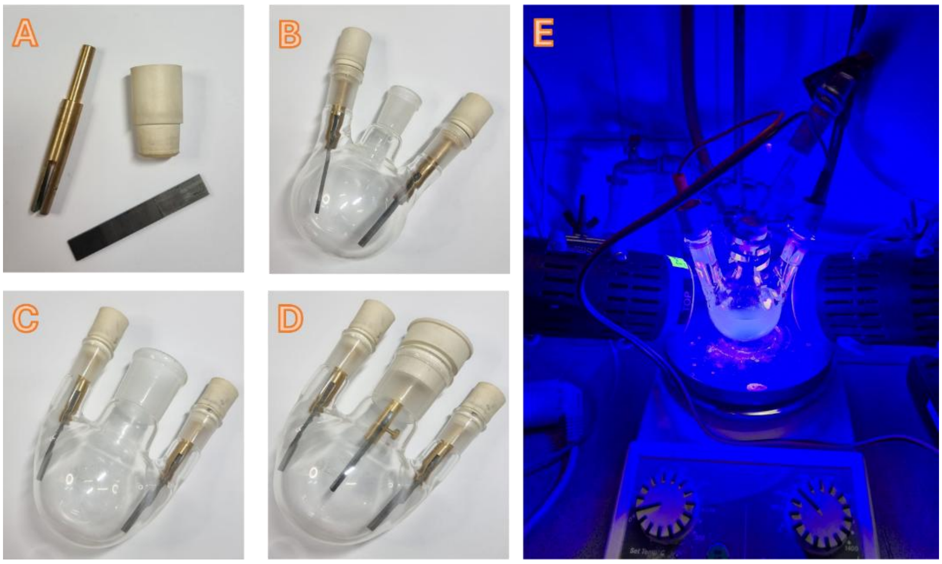
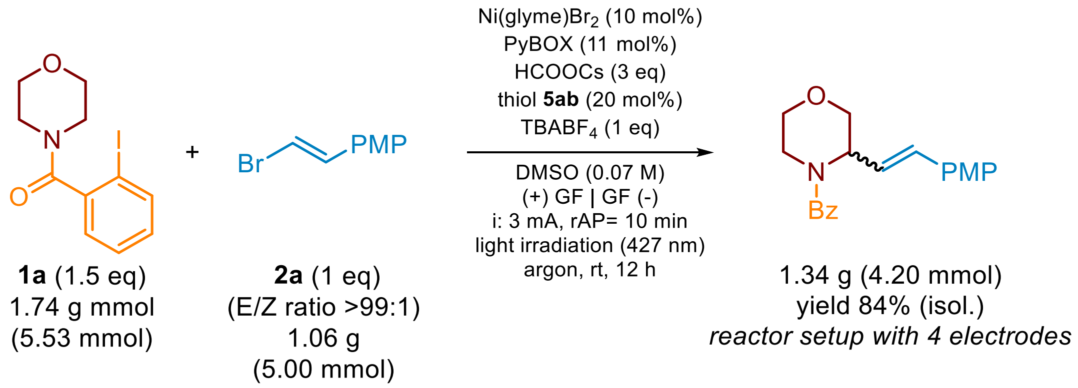


Figure SI-25. The reactor setup for a large-scale synthesis of compound **3aa**: (a) graphite electrode (54 × 8 × 2 mm) and electrode holder; (b) 3-neck round-bottom flask electrolyzer with angled side arms (2 electrodes setup); (c) 3-neck round-bottom flask electrolyzer with parallel side arms (2 electrodes setup); (d) 3-neck round-bottom flask electrolyzer with parallel side arms, 4 electrodes setup)[‡]; (e) a sample complete reaction set with LED lamp assembly (the cooling section has been omitted for better system presentation).

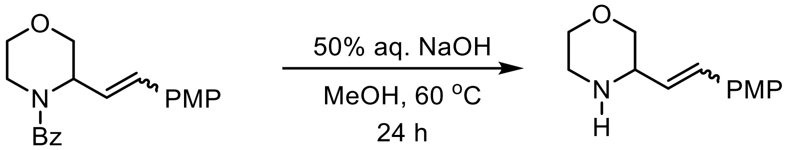
[‡] The middle electrode consists of two connected graphite electrodes with total dimensions of 54 × 16 × 2 mm



In a glove box, oven dry 100-mL 3-neck round-bottom flask (with angled side arms) (vessel A) was equipped with a magnetic stir bar and was charged with vinyl bromide (1.06 g, 5.0 mmol, 1.0 equiv), 2-iodobenzoyl morpholine **1a** (1.74 g, 5.5 mmol, 1.1 equiv), HCOOCs (2.67 g, 15 mmol, 3.0 equiv), methyl 4-mercaptobenzoate **5ab** (1.0 mmol, 168 mg, 0.2 equiv) and n-Bu$_4$NBF$_6$ (1.65 g, 5 mmol, 1.0 equiv). The flask was closed with three septa caps equipped with graphite electrodes (one electrode for side arms and two electrodes for a middle neck arm). Another oven dry 5 ml round-bottom flask (vessel B) was charged with Ni(glyme)Br$_2$ (1.54 mg, 0.5 mmol, 0.1 equiv) and PyBOX ligand **L8** (145 mg, 0.66 mmol, 0.11 equiv). Magnetic stir bar was added and flask B was closed with septa cap. Both flasks were taken out from a glove box and kept under argon. Under argon, 60 mL of dry DMSO was added to flask A and 10 mL to the flask B. The mixture in the flask B was kept stirred at 60 °C for 10 min to prepare nickel complex. After that time, solution of Ni-complex was transferred from the flask B to the flask A. Now, the electric cables were connected with an ElectraSyn stand and electrolysis was started (constant current 3 mA, time 12 h, alternating electrodes polarity change every 10 min) along with blue light irradiation by Kessil^{TM} LED lamp (427 nm, 5 cm away, with cooling fan to keep the reaction temperature at 25 °C) for 12 h. After completion of the reaction, the reaction mixture was transferred to a separatory funnel, the electrodes were rinsed with ethyl acetate (25 mL) and water. The aqueous layer was extracted with ethyl acetate (3 × 50 mL). The combined organics were washed successively with brine (1 × 50 mL), then dried over Na$_2$SO$_4$. After removal of drying agent, solvents and volatiles were removed on a rotary evaporator. The crude product was purified via by automated flash chromatography. The obtained product was kept for under high vacuum (10^{-3} bar) at 70 °C in the Kugelrohr apparatus for 10 h to remove the traces of solvents to deliver 1.36 g (84%) of product **3aa** (*E/Z* ratio 90:10).

13. Applications

13.1. Hydrolysis of compound 3aa



67% (**30**)
(*E*/*Z* ratio 69:31)

A 50% aqueous NaOH solution (5.2 mL) was added to a solution of **3aa** (323 mg, 1 mmol, *E/Z* ratio 70:30) in MeOH (5.2 mL) and the resulting mixture was refluxed for 24 hours. Upon completion of hydrolysis (TLC), reaction mixture was cooled down to room temperature, treated with sat. NH_4Cl solution (20 mL). and extracted with EtOAc (3×15 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), and the volatiles were removed under reduced pressure. The resulting residue was purified by automated flash column chromatography to provide 146 mg (67%) of amine **30** as a waxy solid.

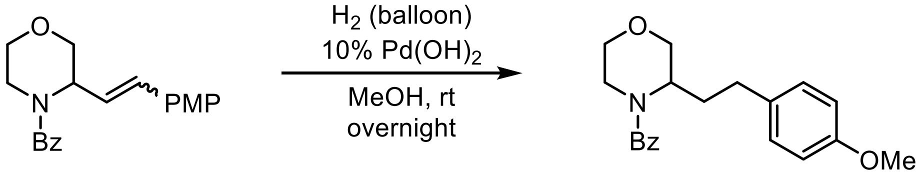
Cartridge size	1 × 80 g (silica gel)
Flow	45 mL/min
Eluent	50 % EtOAc in petroleum ether for 10 min, then gradient from 50% to 80% AcOEt in petroleum ether for 10 min, and 80% AcOEt in petroleum ether for 10 min.
Detection	ELSD & UV (254 nm)
TLC	R_F 0.25 (20% hexanes in AcOEt)

^{1}H NMR (500 MHz, $CDCl_3$, mixture of *E/Z* isomers in a ratio 69:31) δ 7.27 (d, *J* = 8.7 Hz, 2H, major), 7.20 (d, *J* = 8.6 Hz, 2H, minor), 6.86 (d, *J* = 8.7 Hz, 2H, minor), 6.82 (d, *J* = 8.7 Hz, 2H, major), 6.53 (d, *J* = 16.0 Hz, 1H, major), 6.48 (d, *J* = 11.8 Hz, 1H, minor), 5.92 (dd, *J* = 16.0, 7.1 Hz, 1H, major), 5.36 (dd, *J* = 11.8, 9.2 Hz, 1H, minor), 5.10 – 5.01 (m, 1H), 3.94 – 3.88 (m, 1H), 3.86 – 3.72 (m, 7H), 3.60 – 3.46 (m, mixture), 3.44 – 3.26 (m, mixture), 3.05 – 2.82 (m, mixture);

^{13}C NMR (126 MHz, $CDCl_3$, mixture of *E/Z* isomers in a ratio 69:31) δ 159.4, 158.9, 132.2, 131.5, 129.9, 129.5, 129.3, 128.5, 127.6, 125.7, 114.1, 113.9, 75.1, 72.0, 71.2, 69.3, 67.2, 67.1, 59.2, 57.9, 55.3, 53.4, 45.9, 45.6, 29.8, 28.4, 21.4, 16.6;

HRMS (ESI-TOF) *m/z* calcd for $C_{13}H_{18}NO_2$ [(M+H)+] 220.1338; found 220.1339.

13.2. Hydrogenation of compound 3aa



89% (**31**)

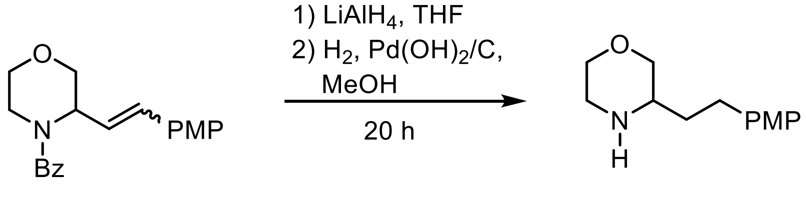
A pressure ampule was charged with $Pd(OH)_2/C$ (20 mg) and a solution of substrate **3aa** (323 mg, 1.0 mmol, E/Z ratio 70:30) in 25 mL of MeOH was added. Air was removed and a balloon with hydrogen was attached. The resulting mixture was saturated with hydrogen gas overnight. The end of the reaction was confirmed by MS analysis. Next, the reaction mixture was diluted with MeOH and filtered through a Celite pad. The removal of solvent provided product **31** as yellows oil (290 mg, 89%).

^{1}H NMR (500 MHz, DMSO-*d*$_6$, 80 °C, mixture of rotamers) δ 7.51 – 7.32 (m, 5H), 7.08 (d, *J* = 8.1 Hz, 1H), 6.81 (v br d, *J* = 8.1 Hz, 1H), 4.10 (s, 1H), 3.83 – 3.68 (m, 2H), 3.73 (s, 3H), 3.59 – 3.52 (m, 1H), 3.40 (dt, *J* = 11.2, 5.7 Hz, 1H), 3.31 (d, *J* = 12.7 Hz, 1H), 3.25 – 3.18 (m, 1H), 3.08 (d, *J* = 9.5 Hz, 1H), 2.60 – 2.43 (m, 2H), 2.08 – 1.99 (m, 2H);

^{13}C NMR (126 MHz, DMSO-*d*$_6$, 80 °C, mixture of rotamers) δ 170.0, 158.1, 136.7, 133.8, 129.7, 129.5, 128.8, 127.1, 114.4, 68.9, 68.8, 66.82, 66.80, 55.6 (v br), 51.4, 47.4, 47.2, 31.3, 31.0;

HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{23}NO_3Na$ [(M+Na)+] 348.1576; found 348.1575.

13.3. Synthesis of morpholine 3aa



3aa 89% (**32**)

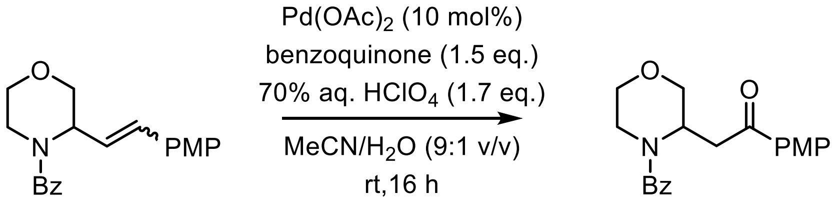
A solution of **3a** (325 mg, 1.0 mmol) in dry THF (25 mL) was treated with 1M soln. of $LiAlH_4$ (1.2 mL, 1.20 mmol) at room temperature. When reaction was completed, 4 mL of sat. aq. Na_2SO_4 was added, and the resulting mixture was stirred for 1 h. Next, it was diluted with Et_2O and filtered through a Celite pad. After removal of solvents, the residue was dissolved in 25 mL of MeOH and the resulting solution was transferred to a pressure ampoule containing $Pd(OH)_2/C$ (50 mg). Air was removed and balloon with hydrogen was attached. The resulting mixture was saturated with hydrogen overnight. Next, the mixture was diluted with MeOH and filtered through a Celite pad. The removal of solvent provided product **32** as brown oil (175 mg, 79%)

^{1}H NMR (500 MHz, DMSO-*d*$_6$, rotamers) δ 7.12 – 7.06 (m, 2H), 6.85 – 6.79 (m, 2H), 3.71 (s, 3H), 3.69 – 3.60 (m, 2H), 3.47 (td, *J* = 10.8, 2.6 Hz, 1H), 3.36 (t, *J* = 10.6 Hz, 1H), 3.07 (t, *J* = 10.3 Hz, 1H), 2.83 – 2.49 (m, 4H), 1.59 – 1.45 (m, 2H);

^{13}C NMR (126 MHz, DMSO-d_6, rotamers) δ 157.2, 133.5, 128.6, 113.5, 71.0, 66.2, 54.7 (br), 53.5 (br), 44.9 (br), 33.1, 29.8;

HRMS (ESI-TOF) *m/z* calcd for $C_{13}H_{20}NO_2$ [(M+H)+] 222.1494; found 222.1496.

13.4. Wacker oxidation of compound 3aa



79% (**33**)

To a solution of Pd(OAc)$_2$ (22.5 mg, 0.1 mmol, 0.10 equiv.), *p*-benzoquinone (162 mg, 1.5 mmol, 1.5 equiv.), 70% aqueous $HClO_4$ (72 µL) in MeCN (2.6 mL) was added a solution of amide **3aa** (317 mg, 1.0 mmol, *E/Z* ratio 70:30) in MeCN (2.6 mL) followed by addition of another portion of 70% aqueous $HClO_4$ (72 µL, total 1.74 mmol) and H_2O (660 µL) at room temperature. After stirring at room temperature for 16 h, the resulting solution was diluted with CH_2Cl_2 (20 mL) and H_2O (15 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by automated flash silica gel column chromatography to provide 268 mg (79%) of ketone **33** as brown oil.

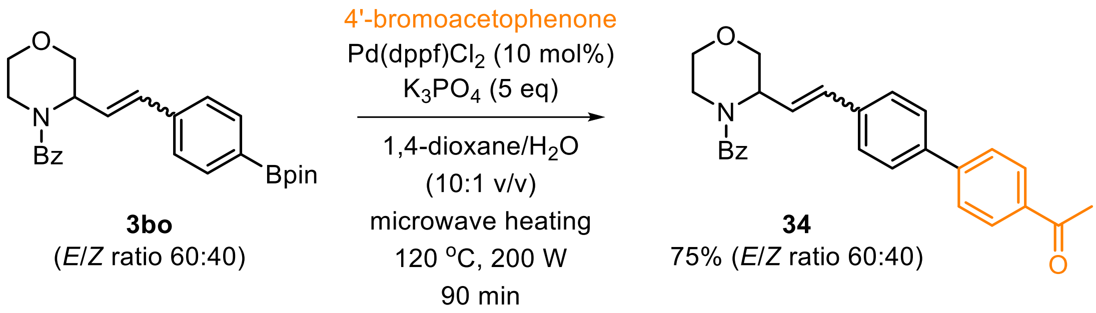
Cartridge size	1 × 80 g (silica gel)
Flow	45 mL/min
Eluent	45 % EtOAc in petroleum ether for 10 min, then gradient from 45% to 50% AcOEt in petroleum ether for 5 min, and 50% AcOEt in petroleum ether for 10 min.
Detection	ELSD & UV (254 nm)
TLC	R_F 0.4 (50% AcOEt in hexanes)

^{1}H NMR (500 MHz, DMSO-d_6 at 80°C) δ 7.96 (d, *J* = 6.9 Hz, 2H), 7.45 – 7.38 (m, 3H), 7.37 – 7.32 (m, 2H), 7.02 (d, *J* = 8.9 Hz, 2H), 4.63 (s, 1H), 3.86 (s, 4H), 3.81 – 3.72 (m, 2H), 3.71 – 3.58 (m, 2H), 3.48 – 3.37 (m, 2H), 3.22 (dd, *J* = 16.0, 5.4 Hz, 1H);

^{13}C NMR (126 MHz, DMSO-d_6 at 80°C) δ 195.9, 169.1, 163.0, 135.6, 132.2, 130.0, 129.4, 128.9, 128.8, 128.0, 127.9, 126.3, 113.6, 68.2, 66.0, 55.2, 36.8;

HRMS (ESI-TOF) *m/z* calcd for $C_{20}H_{21}NO_4Na$ [(M+Na)+] 362.1368; found 362.1369.

13.5. Suzuki cross-coupling with compound 3bo



A 5-mL vial was charged with boronic acid ester **3bo** (195 mg, 0.465 mmol, 2 equiv., *E/Z* ratio 60:40), K_3PO_4 (247 mg, 1.163 mmol, 5 equiv.), Pd(dppf)Cl_2 (1.7 mg, 2.3 μmol, 10 mol%) and 4'-bromoacetophenone (46 mg, 0.233 mmol, 1 equiv.). The vial was sealed with cap and air was removed and vial was filled with argon. Degassed solvents were added (1,4-dioxane 1.7 mL, water 0.7 mL) and the vessel was placed and kept in 120 °C for 90 min in the CEM Discover microwave reactor (120 °C, 200 W, high-speed stirring, pre-stirring for 60 s). Next, reaction mixture was diluted with water (50 mL) and the resulting mixture was extracted with EtOAc. The combined organic extracts were dried over anhydr. Na_2SO_4. After removal of a drying agent and solvents, the residue was purified by flash column chromatography (conditions below) to provide 72 mg (75%, *E/Z* ratio 60:40) of product **34**.

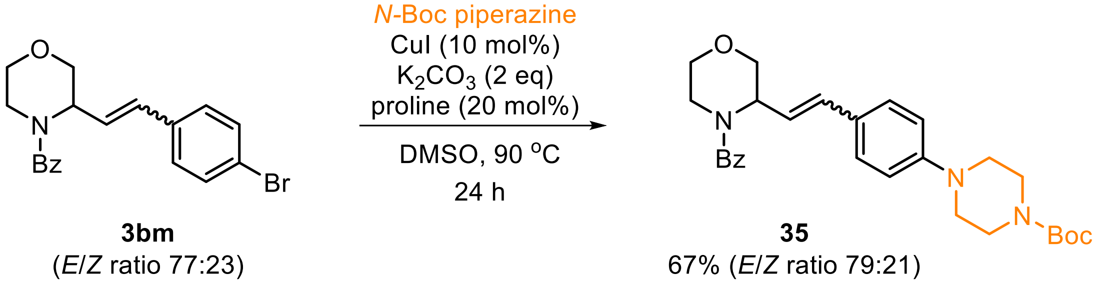
Cartridge size	1 × 80 g (silica gel)
Flow	45 mL/min
Eluent	45 % EtOAc in petroleum ether for 10 min, then gradient from 45% to 50% AcOEt in petroleum ether for 2 min, and 50% AcOEt in petroleum ether for 15 min
Detection	ELSD & UV (254 nm)
TLC	R_F 0.65 (50% EtOAc in hexanes)

^{1}H NMR (500 MHz, DMSO-d_6 at 80°C, *E/Z* mixture in a ratio 60:40 including rotamers) δ 8.06 – 8.01 (m, 4H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.60 (dd, *J* = 8.4, 2.2 Hz, 3H), 7.47 (s, 5H), 7.29 – 7.19 (m, 5H), 6.66 (d, *J* = 11.9 Hz, 1H, minor), 6.61 (br d, *J* = 16.4 Hz, 1H, major), 6.55 (dd, *J* = 16.2, 4.7 Hz, 1H, major), 6.25 (dd, *J* = 11.9, 9.2 Hz, 1H, minor), 5.16 (d, *J* = 9.2 Hz, 1H), 4.80 (s, 1H), 4.03 (d, *J* = 11.6 Hz, 1H), 3.93 – 3.71 (m, 6H), 3.55 – 3.46 (m, 2H), 3.45 – 3.37 (m, 1H), 2.60 (2×s, 3H);

^{13}C NMR (126 MHz, DMSO-d_6 at 80°C, *E/Z* mixture in a ratio 60:40 including rotamers) δ 196.77, 196.75, 169.4, 169.2, 143.7, 143.6, 137.7, 137.3, 136.1, 135.7, 135.6, 135.5, 135.5, 135.2, 130.6, 129.6, 129.0, 128.7, 128.5, 128.3, 127.99, 127.97, 127.7, 127.6, 126.7, 126.6, 126.35, 126.30, 126.22, 126.15, 126.1, 70.2, 69.2, 66.0, 65.9, 52.8, 49.5, 30.7, 28.5, 28.1, 26.1, 24.5, 21.5, 13.3;

HRMS (APCI-TOF) *m/z* calcd for $C_{27}H_{26}NO_3$ [(M+H)+] 412.1913; found 412.1917.

13.6. Ullmann cross-coupling of compound 3bm



According to protocol reported by Ma *et al.*:[51] A mixture of aryl bromide **3bm** (308 mg, 0.83 mmol, 1 eq, (*E/Z*)-isomers mixture in a ratio 77:23), *N*-Boc piperazine (308 mg, 1.66 mmol, 2 eq), K_2CO_3 (230 mg, 1.66 mmol, 2 eq), CuI (16 mg, 83 µmol, 10 mol%) and L-proline (20 mg, 165 µmol, 20 mol%) in 2 mL of DMSO was kept at 90 °C for 24 h. The cooled mixture was partitioned between water (30 mL) and ethyl acetate (30 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3×20 mL). The combined organic layers were dried over anhydr. Na_2SO_4, and concentrated in vacuo. The residue was purified by automated flash column chromatography to provide 265 mg (67%, *E/Z* ratio 79:21) of product **35** as brown oil.

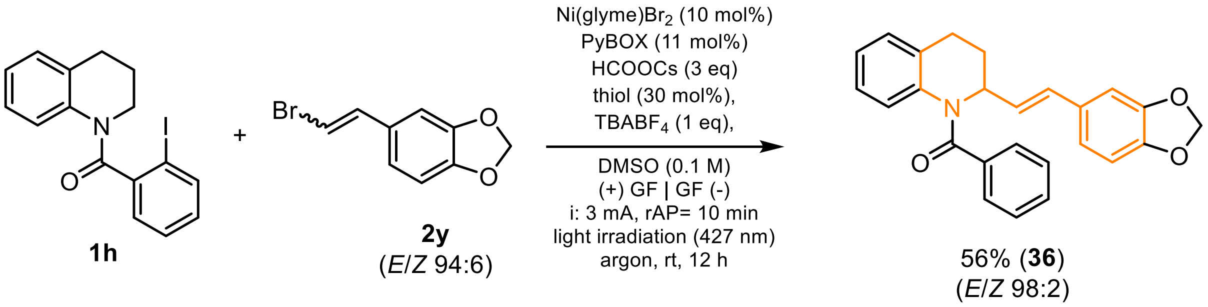
Cartridge size	1 × 80 g (silica gel)
Flow	45 mL/min
Eluent	35 % EtOAc in petroleum ether for 10 min, then gradient from 35% to 40% AcOEt in petroleum ether for 5 min, and 40% AcOEt in petroleum ether for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F 0.35 (40% EtOAc in hexanes)

^{1}H NMR (500 MHz, DMSO-d_6 at 80°C, (*E/Z*)-isomers mixture in a ratio 79:21) δ 7.50 – 7.40 (m, *E/Z* mixture), 7.32 (d, *J* = 8.7 Hz, 2H, major), 7.27 (t, *J* = 7.4 Hz, 1H, minor), 7.24 – 7.20 (m, 1H, minor), 7.00 (d, *J* = 8.3 Hz, 2H, minor), 6.91 (d, *J* = 8.8 Hz, 2H, major), 6.79 (d, *J* = 8.7 Hz, 2H, minor), 6.48 (d, *J* = 11.9 Hz, 1H, minor), 6.42 (d, *J* = 16.1 Hz, 1H, major), 6.26 (dd, *J* = 16.2, 5.5 Hz, 1H, major), 6.02 (dd, *J* = 11.9, 9.0 Hz, 1H, minor), 5.15 (br d, *J* = 9.1 Hz, 1H, minor), 4.71 (br s, 1H, major), 3.96 (d, *J* = 11.6 Hz, 1H, major), 3.89 – 3.80 (m, *E/Z* mixture), 3.79 – 3.66 (m, *E/Z* mixture), 3.53 – 3.42 (m, *E/Z* mixture), 3.40 – 3.30 (m, *E/Z* mixture), 3.20 – 3.10 (m, *E/Z* mixture), 1.44 (s, 9H, major) 1.42 (s, 9H, minor);

^{13}C NMR (126 MHz, DMSO-d_6 at 80°C, (*E/Z*)-isomers mixture in a ratio 79:21) δ 169.3, 169.1, 153.6, 150.0, 149.4, 135.6, 135.3, 131.0, 129.9, 129.0, 128.81, 128.77, 127.9, 127.7, 127.1, 126.8, 126.3, 126.1, 125.0, 123.1, 115.1, 114.8, 78.6, 70.2, 69.3, 66.1, 65.9, 53.0, 47.7, 47.6, 43.0, 42.8, 42.6, 28.5, 28.1, 27.7, 27.7, 21.5, 13.3.

HRMS (ESI-TOF) *m/z* calcd for $C_{28}H_{35}N_3O_4Na$ [(M+Na)+] 500.2525; found 500.2533.

13.7. Synthesis of galipinine precursor 36



Yield: 129 mg (56%) starting from compound **1h** (240 mg, 0.66 mmol) and vinyl bromide **2y** (136 mg, 0.60 mmol, *E*/*Z* ratio 94:6); (*E/Z*)-isomers in a ratio: 98:2. Off-white solid. Purification: automated flash column chromatography on SiO_2

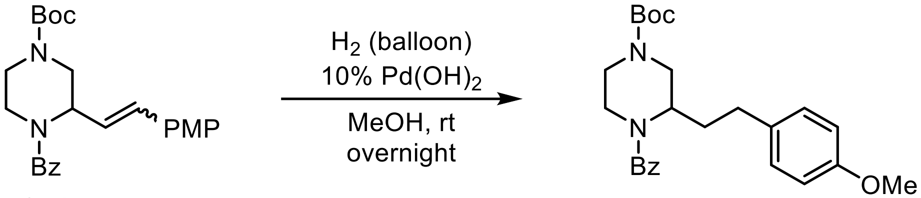
Cartridge size	1 × 80 g (silica gel)
Flow	45 mL/min
Eluent	40 % EtOAc in petroleum ether for 10 min, then gradient from 40% to 50% AcOEt in petroleum ether for 5 min, and 50% AcOEt in petroleum ether for 10 min
Detection	ELSD & UV (254 nm)
TLC	R_F 0.60 (50% EtOAc in hexanes)

^{1}H NMR (500 MHz, DMSO-d_6, 80 °C, mixture of rotamers) δ 7.56 – 7.49 (m, 1H), 7.16 – 6.96 (m, 8H), 6.84-6.52 (m, 3H), 6.74 – 6.54 (m, 5H), 6.48 – 6.44 (m, 2H), 6.13 (dd, *J* = 16.0, 1.6 Hz, 1H), 5.74 (dd, *J* = 16.0, 5.4 Hz, 1H), 5.64 (s, 2H), 4.96 – 4.90 (m, 1H), 3.34 (s, 1H), 2.52 (q, *J* = 7.0 Hz, 4H), 2.14 – 2.04 (m, 1H), 1.73 – 1.62 (m, 2H), 1.62 – 1.53 (m, 1H).

^{13}C NMR (126 MHz, DMSO-d_6, 80 °C, mixture of rotamers) δ 168.9, 168.3, 147.3, 146.4, 142.5, 138.5, 137.4, 136.4, 131.5, 130.6, 129.8, 129.6, 129.3, 128.2, 128.0, 127.7, 127.60, 127.57, 127.53, 127.4, 127.3, 126.9, 125.6, 125.1, 124.8, 124.3, 124.1, 124.0, 123.7, 123.6, 120.3, 107.6, 105.2, 100.5, 92.7, 54.2, 44.1, 29.1, 28.4, 25.9, 25.8, 24.0, 23.2, 22.7;

HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{21}NO_3Na$ [(M+Na)+] 406.1419; found 406.1413.

13.8. Hydrogenation of compound 3ad



3ad

89% (**40b**)

A pressure ampule was charged with 10% $Pd(OH)_2/C$ (16 mg) and a solution of substrate **3ad** (40 mg, 95 µmol) in 5 mL of MeOH was added. Air was removed and a balloon with hydrogen was attached. The resulting mixture was saturated with hydrogen gas overnight. The end of the reaction was confirmed by MS analysis. Next, the reaction mixture was diluted with MeOH and filtered through a Celite pad. The removal of solvent provided product **40b** as white semi solids (33 mg, 82%).

^{1}H NMR (500 MHz, DMSO-*d*$_6$, mixture of rotamers) δ 7.48 – 7.31 (m, 5H), 7.06 (d, *J* = 8.2 Hz, 2H), 6.81 (d, *J* = 8.2 Hz, 2H), 4.21 (br s, 1H), 3.96 (d, *J* = 13.8 Hz, 1H), 3.93 – 3.87 (m, 1H), 3.73 (s, 3H), 3.51 – 3.37 (m, 1H), 3.17 – 3.10 (m, 1H), 3.06 – 3.00 (m, 1H), 2.86 (td, *J* = 12.6, 3.6 Hz, 1H), 2.60 – 2.51 (m, 1H), 2.46 (d, *J* = 7.1 Hz, 1H), 1.92 – 1.78 (m, 2H), 1.43 (s, 9H), 1.42 (s, 9H);

^{13}C NMR (126 MHz, DMSO-*d*$_6$, mixture of rotamers) δ 170.1, 158.2, 154.7, 136.8, 133.6, 129.7, 129.4, 128.8, 127.0, 114.4, 79.6, 55.6, 46.0 (br), 43.8 (br), 31.3, 31.1, 28.5 (br);

HRMS (ESI-TOF) *m/z* calcd for $C_{25}H_{32}N_2O_4Na$ [(M+Na)+] 447.2260; 447.2256.

14. References

[1] M. G. Pizzio, E. G. Mata, P. Dauban, T. Saget, *Eur. J. Org. Chem.* **2023**, *26*, e202300616.
[2] S. Sarkar, S. Wagulde, X. Jia, V. Gevorgyan, *Chem* **2022**, *8*, 3096-3108.
[3] V. Srinivasu, K. Pal, S. Giri, D. Sureshkumar, *Org. Lett.* **2024**, *26*, 10328-10333.
[4] O. Miyata, A. Shirai, S. Yoshino, T. Nakabayashi, Y. Takeda, T. Kiguchi, D. Fukumoto, M. Ueda, T. Naito, *Tetrahedron* **2007**, *63*, 10092-10117.
[5] J. Lu, K. Yuan, J. Zheng, H. Zhang, S. Chen, J. Ma, X. Liu, B. Tu, G. Zhang, R. Guo, *Angew. Chem. Int. Ed.* **2024**, *63*, e202409310.
[6] V. K. Simhadri, R. Sur, V. R. Yatham, *Eur. J. Org. Chem.* **2024**, *27*, e202400490.
[7] R. Guo, H. Xiao, S. Li, Y. Luo, J. Bai, M. Zhang, Y. Guo, X. Qi, G. Zhang, *Angew. Chem. Int. Ed.* **2022**, *61*, e202208232.
[8] A. T. Nguyen, T. G. Luu, H.-K. Kim, *New J. Chem.* **2024**, *48*, 17485-17491.
[9] E. Bisz, M. Szostak, *Adv. Synth. Catal.* **2019**, *361*, 85-95.
[10] R. Robiette, J. Pospíšil, *Eur. J. Org. Chem.* **2013**, *2013*, 836-840.
[11] D. Müller, A. Alexakis, *Chem. Eur. J.* **2013**, *19*, 15226-15239.

[12] V. Pappula, R. R. Donthiri, C. M. Darapaneni, A. Subbarayappa, *Tetrahedron Lett.* **2014**, *55*, 1793-1795.

[13] (a) D. Hazarika, P. Phukan, *Tetrahedron Lett.* **2018**, *59*, 4593-4596; (b) L.-Y. He, M. Schulz-Senft, B. Thiedemann, J. Linshoeft, P. J. Gates, A. Staubitz, *Eur. J. Org. Chem.* **2015**, *2015*, 2498-2502.

[14] F. Ishibashi, S. Zha, T. Kondo, M. Sakamoto, M. Ueno, T. Fukuda, *Biosci. Biotech. Biochem.* **2022**, *87*, 148-157.

[15] W. Kumaki, H. Kinoshita, K. Miura, *Tetrahedron* **2022**, *110*, 132687.

[16] M. K. Zaman, R. Li, W. Deng, *J. Org. Chem.* **2023**, *88*, 15761-15766.

[17] S. N. Georgiades, J. Clardy, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3117-3121.

[18] C. Kuang, H. Senboku, M. Tokuda, *Tetrahedron* **2005**, *61*, 637-642.

[19] L. Mao, X. Tan, J. Wu, W. Wu, H. Jiang, *Org. Lett.* **2025**, *27*, 5063-5067.

[20] Y. Ye, H. Chen, K. Yao, H. Gong, *Org. Lett.* **2020**, *22*, 2070-2075.

[21] W. Davies, B. M. Holmes, J. F. Kefford, *J. Chem. Soc. (Res.)* **1939**, 357-360.

[22] (a) W. Sun, Q. Teng, D. Cheng, X. Li, X. Xu, *Tetrahedron Lett.* **2020**, *61*, 151410; (b) T.-T. Hao, H.-R. Liang, Y.-H. Ou-Yang, C.-Z. Yin, X.-L. Zheng, M.-L. Yuan, R.-X. Li, H.-Y. Fu, H. Chen, *J. Org. Chem.* **2018**, *83*, 4441-4454.

[23] B. Picard, T. Fukuyama, T. Bando, M. Hyodo, I. Ryu, *Org. Lett.* **2021**, *23*, 9505-9509.

[24] L. Xiao, Z. Xu, H. Li, *J. Org. Chem.* **2024**, *89*, 14489-14495.

[25] (a) T. Zhao, B. Xu, *Org. Lett.* **2010**, *12*, 212-215; (b) X. Y. Chen, L. Wang, M. Frings, C. Bolm, *Org. Lett.* **2014**, *16*, 3796-3799.

[26] K. Li, B. Zu, C. Mazet, *Org. Lett.* **2024**, *26*, 6047-6052.

[27] F. Romanov-Michailidis, K. F. Sedillo, J. M. Neely, T. Rovis, *J. Am. Chem. Soc.* **2015**, *137*, 8892-8895.

[28] Y. R. Bhorge, S.-H. Chang, C.-T. Chang, T.-H. Yan, *Tetrahedron* **2012**, *68*, 4846-4851.

[29] S. Wiesler, M. A. Bau, T. Niepel, S. L. Younas, H.-T. Luu, J. Streuff, *Eur. J. Org. Chem.* **2019**, *2019*, 6246-6260.

[30] M. Garbacz, S. Stecko, *Adv. Synth. Catal.* **2020**, *362*, 3213-3222.

[31] J. M. Graham, S. A. L. Rousseaux, *Chem. Commun.* **2025**, *61*, 893-896.

[32] S. Zhao, X. Zhang, Y. Zhang, H. Yang, Y. Huang, K. Zhang, T. Du, *New J. Chem.* **2015**, *39*, 7734-7737.

[33] S. E. Schaus, E. N. Jacobsen, *Org. Lett.* **2000**, *2*, 1001-1004.

[34] I. W. Davies, L. Gerena, N. Lu, R. D. Larsen, P. J. Reider, *J. Org. Chem.* **1996**, *61*, 9629-9630.

[35] Mai M. Khalaf, Amro A. Taha, Hany M. Abd El-Lateef, A. Abdou, *App. Organomet. Chem.* **2025**, *39*, e70108.

[36] S. Tao, E. Ji, L. Shi, N. Liu, L. Xu, B. Dai, *Synthesis* **2017**, *49*, 5120-5130.

[37] D. L. Jameson, K. A. Goldsby, *J. Org. Chem.* **1990**, *55*, 4992-4994.

[38] R. A. Croft, J. J. Mousseau, C. Choi, J. A. Bull, *Chem. Eur. J.* **2018**, *24*, 818-821.

[39] L. Katz, L. S. Karger, W. Schroeder, M. S. Cohen, *J. Org. Chem.* **1953**, *18*, 1380-1402.

[40] E. Carbonnel, T. Besset, T. Poisson, D. Labar, X. Pannecoucke, P. Jubault, *Chem. Commun.* **2017**, *53*, 5706-5709.

[41] F. Barba, F. Ranz, B. Batanero, *Tetrahedron Lett.* **2009**, *50*, 6798-6799.

[42] (a) S. K. Kariofillis, B. J. Shields, M. A. Tekle-Smith, M. J. Zacuto, A. G. Doyle, *J. Am. Chem. Soc.* **2020**, *142*, 7683-7689; (b) A. Q. Cusumano, B. C. Chaffin, A. G. Doyle, *J. Am. Chem. Soc.* **2024**, *146*, 15331-15344.

[43] X.-C. He, K.-R. Li, J. Gao, J.-P. Guan, H.-B. Chen, H.-Y. Xiang, K. Chen, H. Yang, *Org. Lett.* **2023**, *25*, 4056-4060.

[44] T. Constantin, F. Juliá, N. S. Sheikh, D. Leonori, *Chem. Sci.* **2020**, *11*, 12822-12828.

[45] Z. Li, W. Yan, X. Zhou, C. Yang, L. Guo, W. Xia, *Org. Chem. Front.* **2025**, *12*, 4946-4955.

[46] D. Kobus-Bartoszewicz, M. Zalewski, K. Melcer, M. Warda, S. Stecko, *Adv. Synth. Catal.* **2025**, *367*, e202401326.

[47] S. Wang, C. Yang, S. Sun, J. Wang, *Chem. Commun.* **2019**, *55*, 14035-14038.

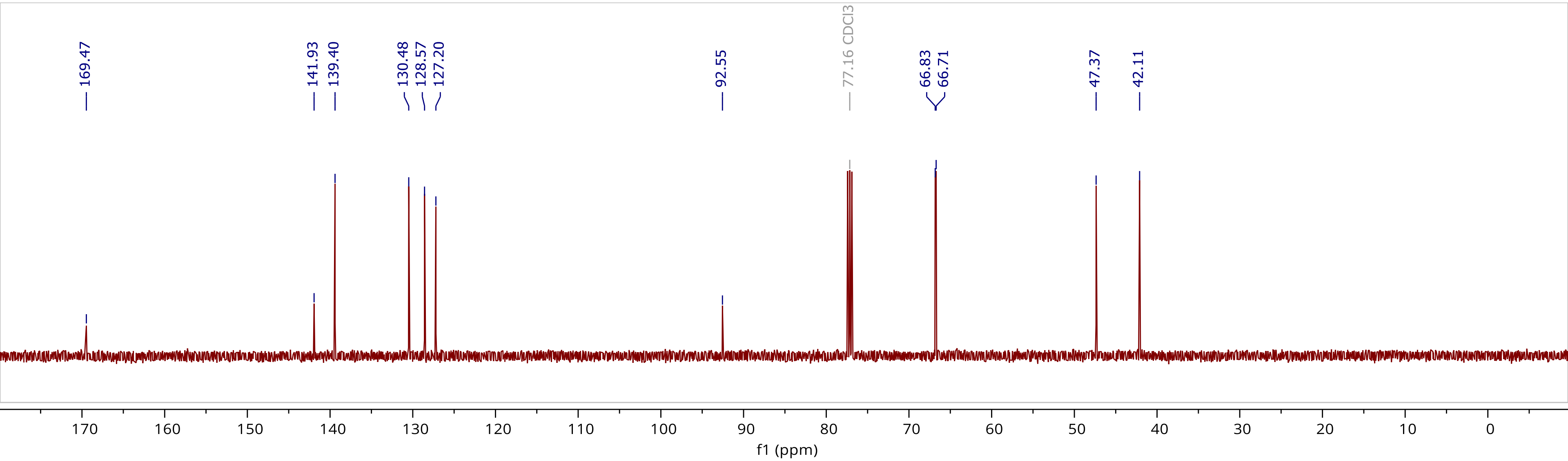
[48] Y. Lai, A. Halder, J. Kim, T. J. Hicks, P. J. Milner, *Angew. Chem. Int. Ed.* **2023**, *62*, e202310246.

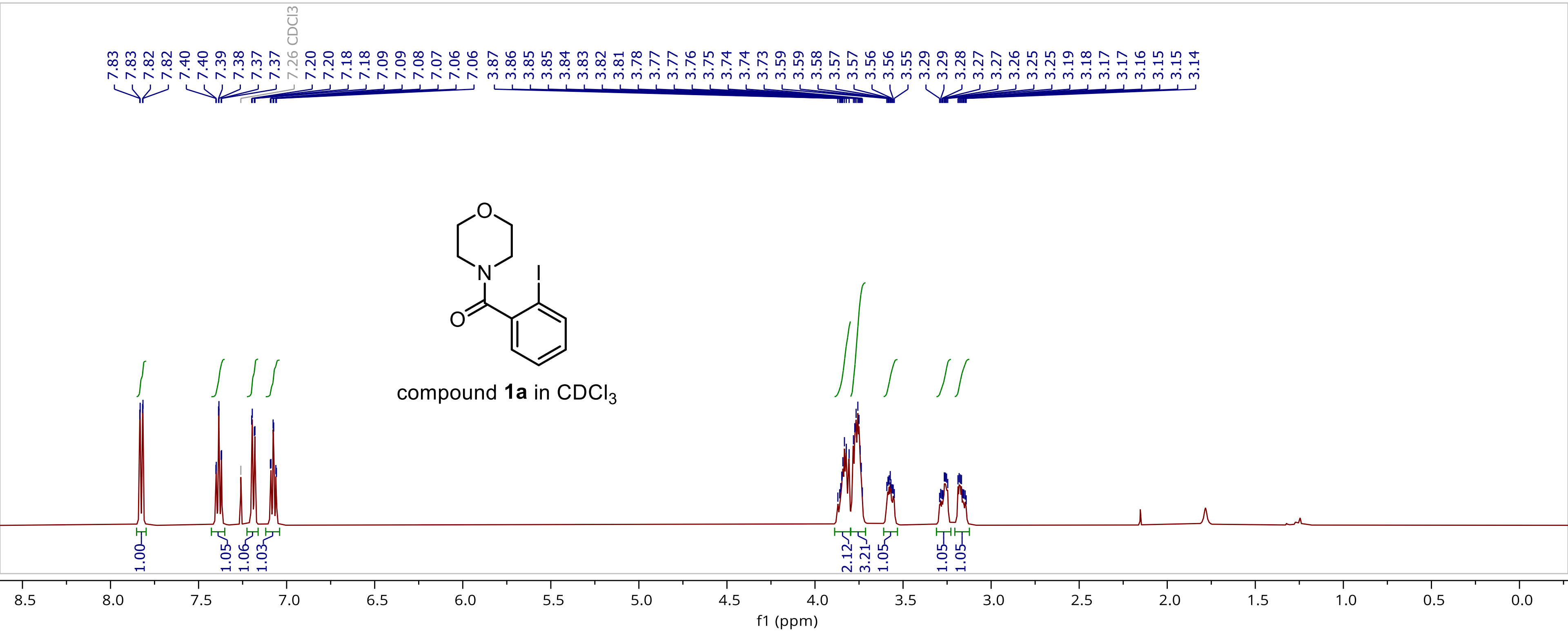
[49] A. A. Folgueiras-Amador, A. E. Teuten, M. Salam-Perez, J. E. Pearce, G. Denuault, D. Pletcher, P. J. Parsons, D. C. Harrowven, R. C. D. Brown, *Angew. Chem. Int. Ed.* **2022**, *61*, e202203694.

[50] H. Zhang, C. Huang, X.-A. Yuan, S. Yu, *J. Am. Chem. Soc.* **2022**, *144*, 10958-10967.

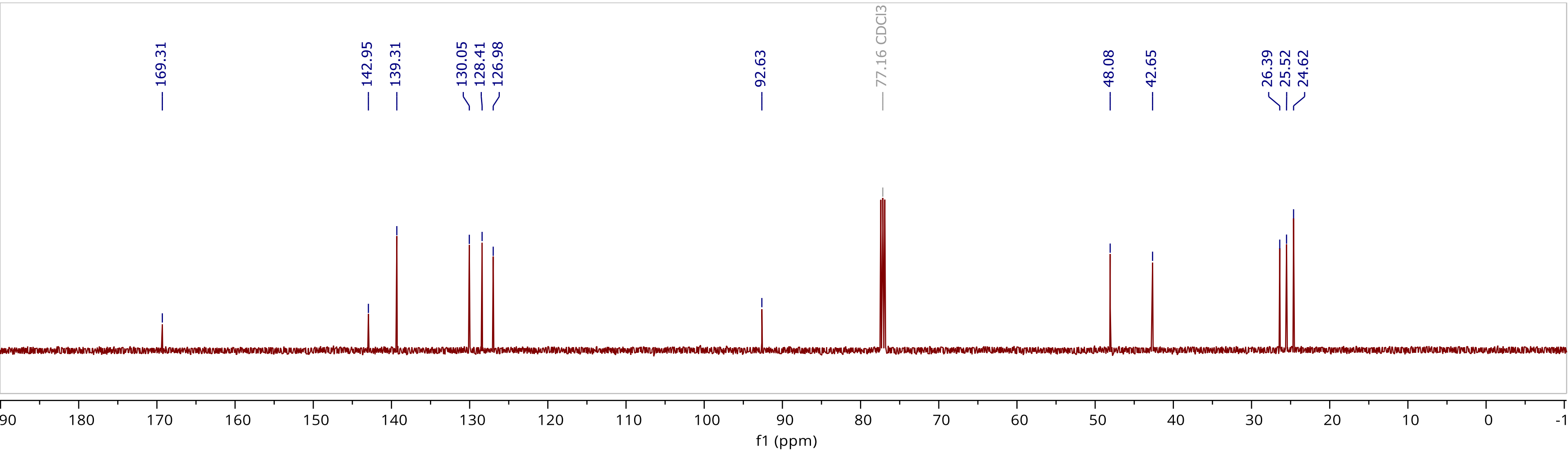
[51] D. Ma, Q. Cai, H. Zhang, *Org. Lett.* **2003**, *5*, 2453-2455.

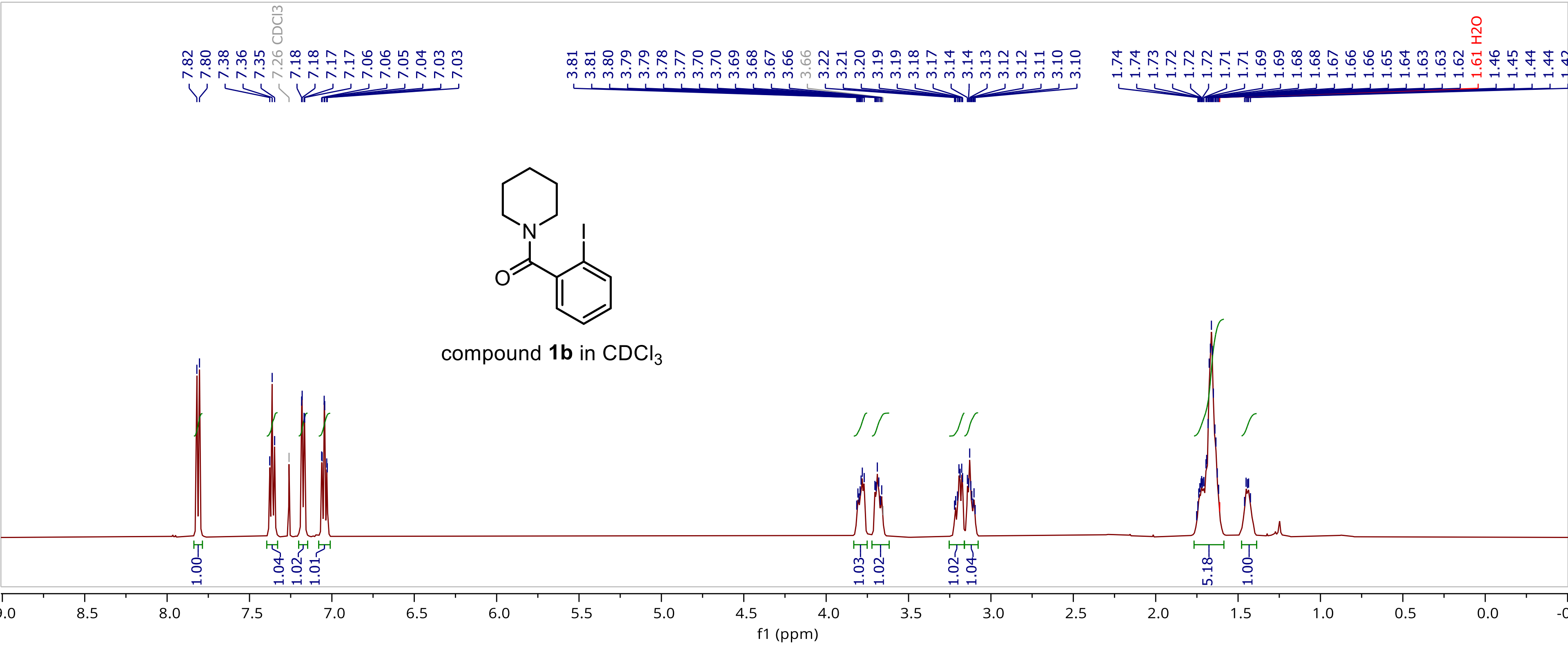
15. ^{1}H, ^{19}F and ^{13}C NMR spectra



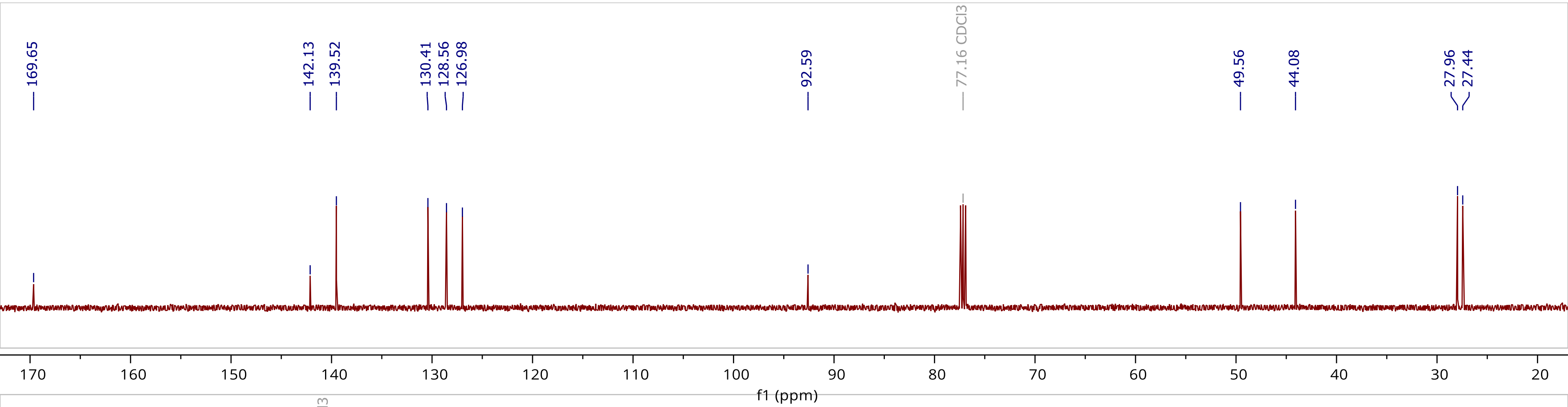


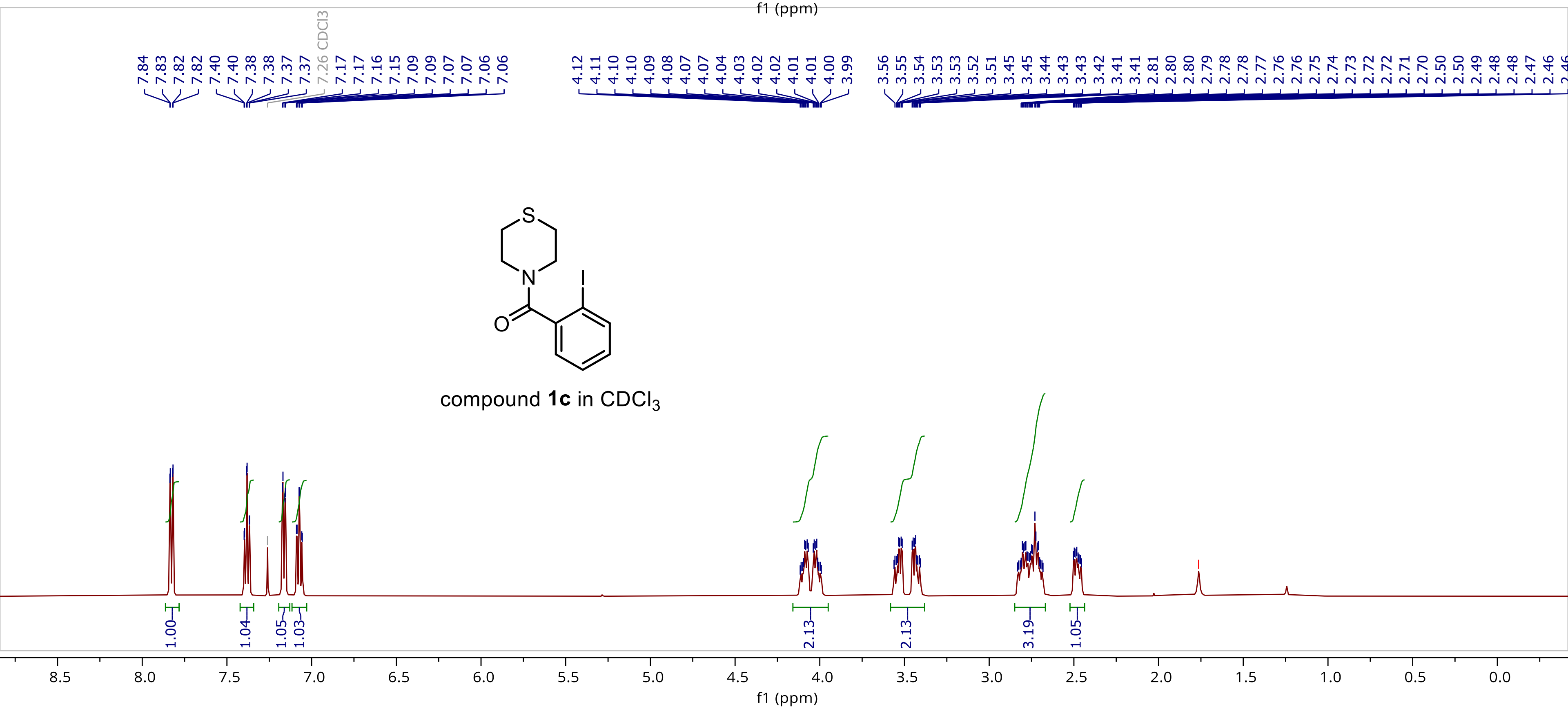
compound **1a** in $CDCl_3$

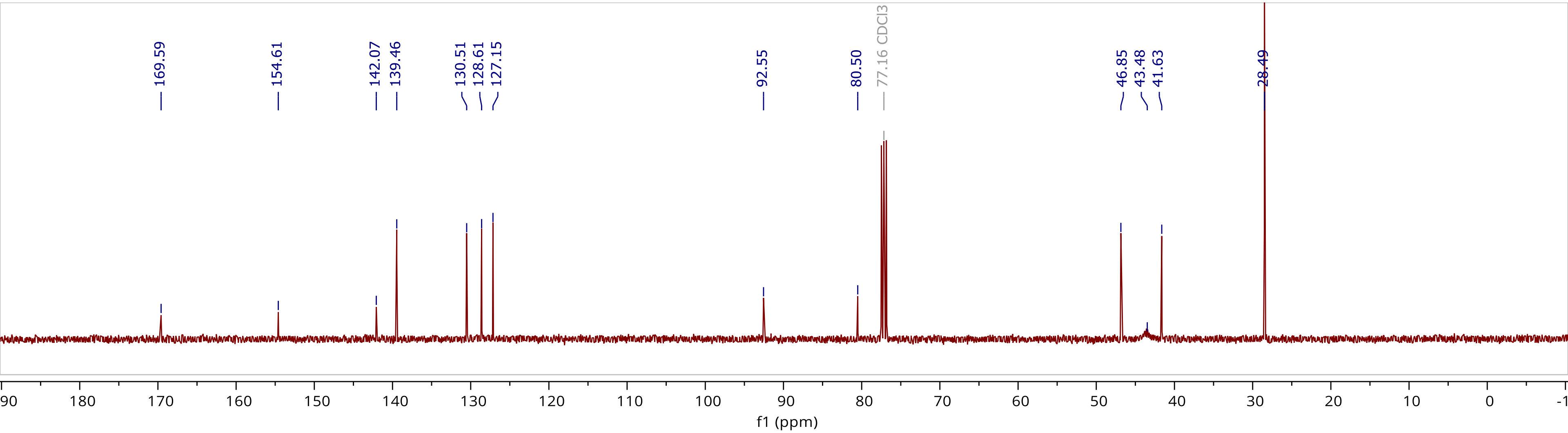


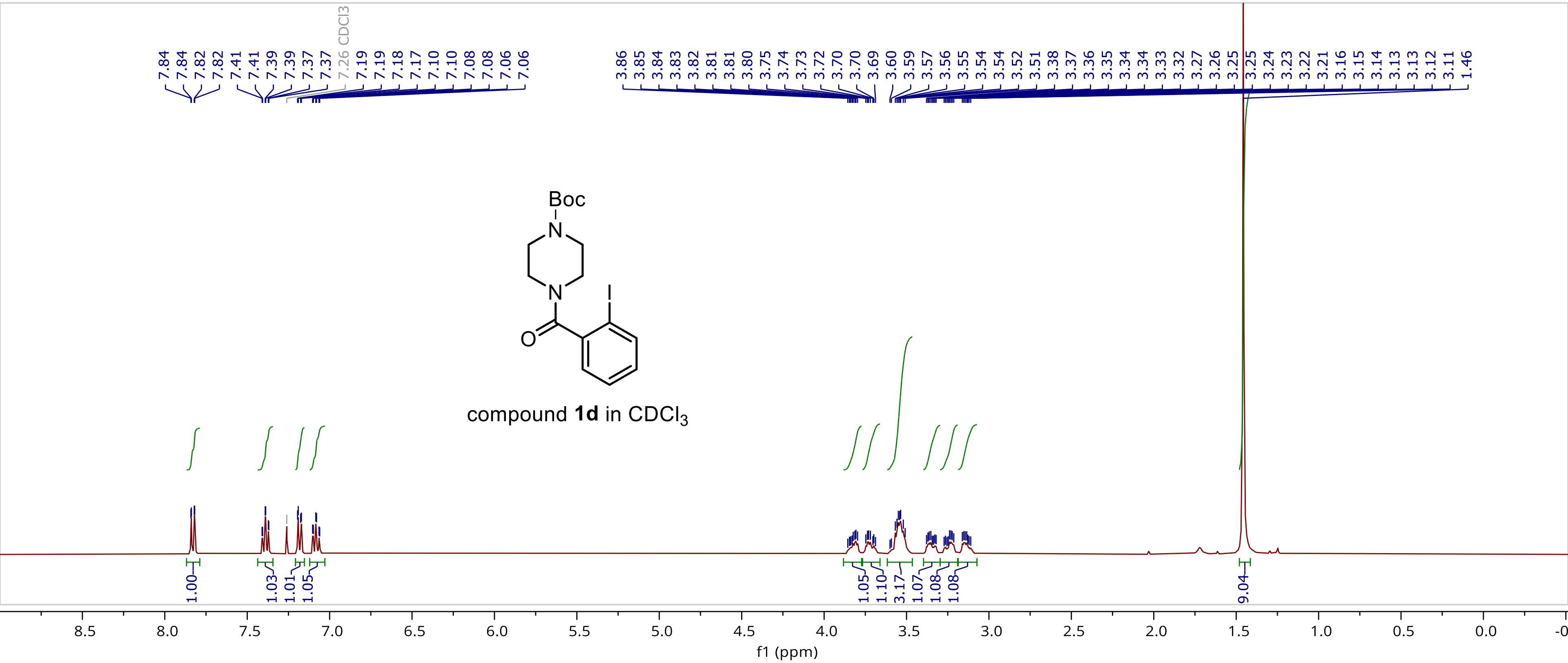


compound **1b** in $CDCl_3$

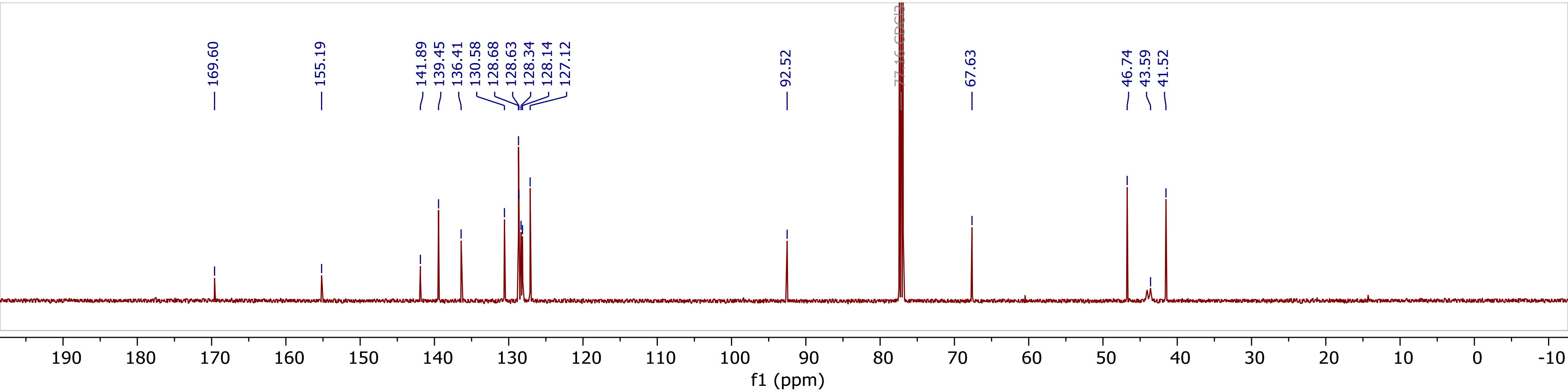


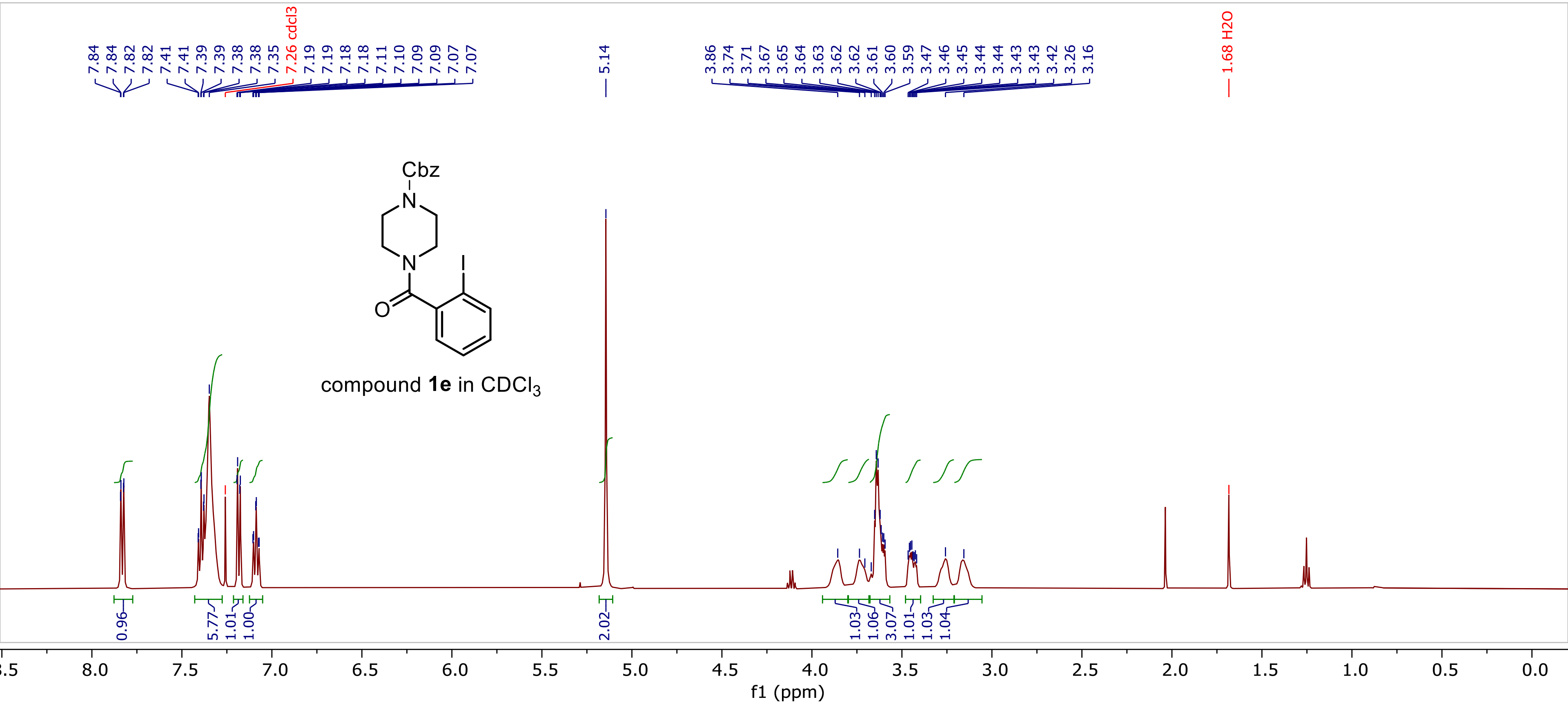

compound **1c** in $CDCl_3$



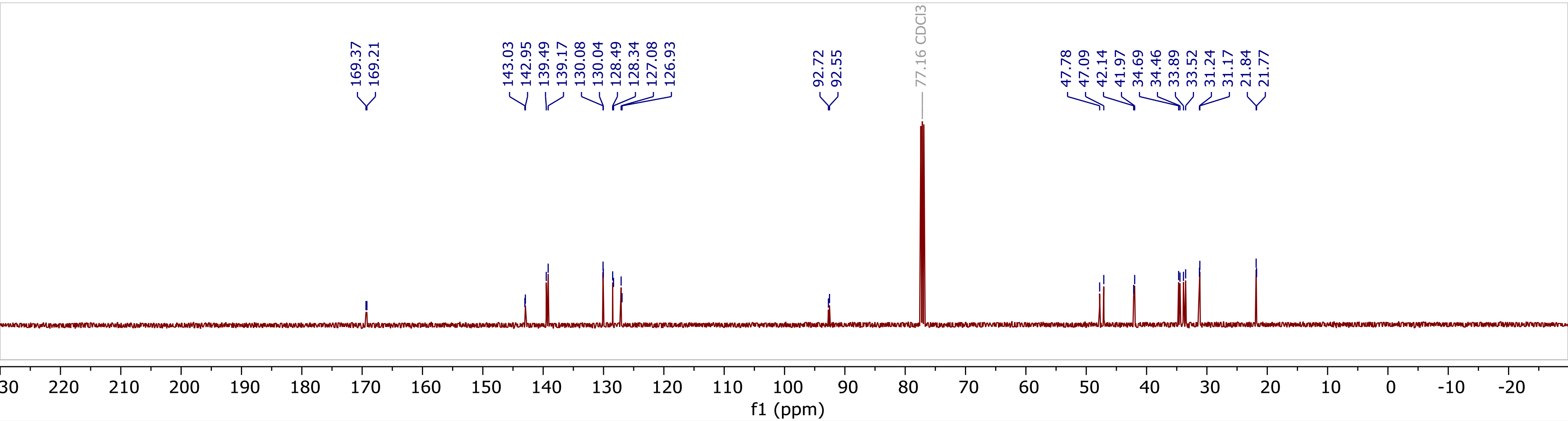


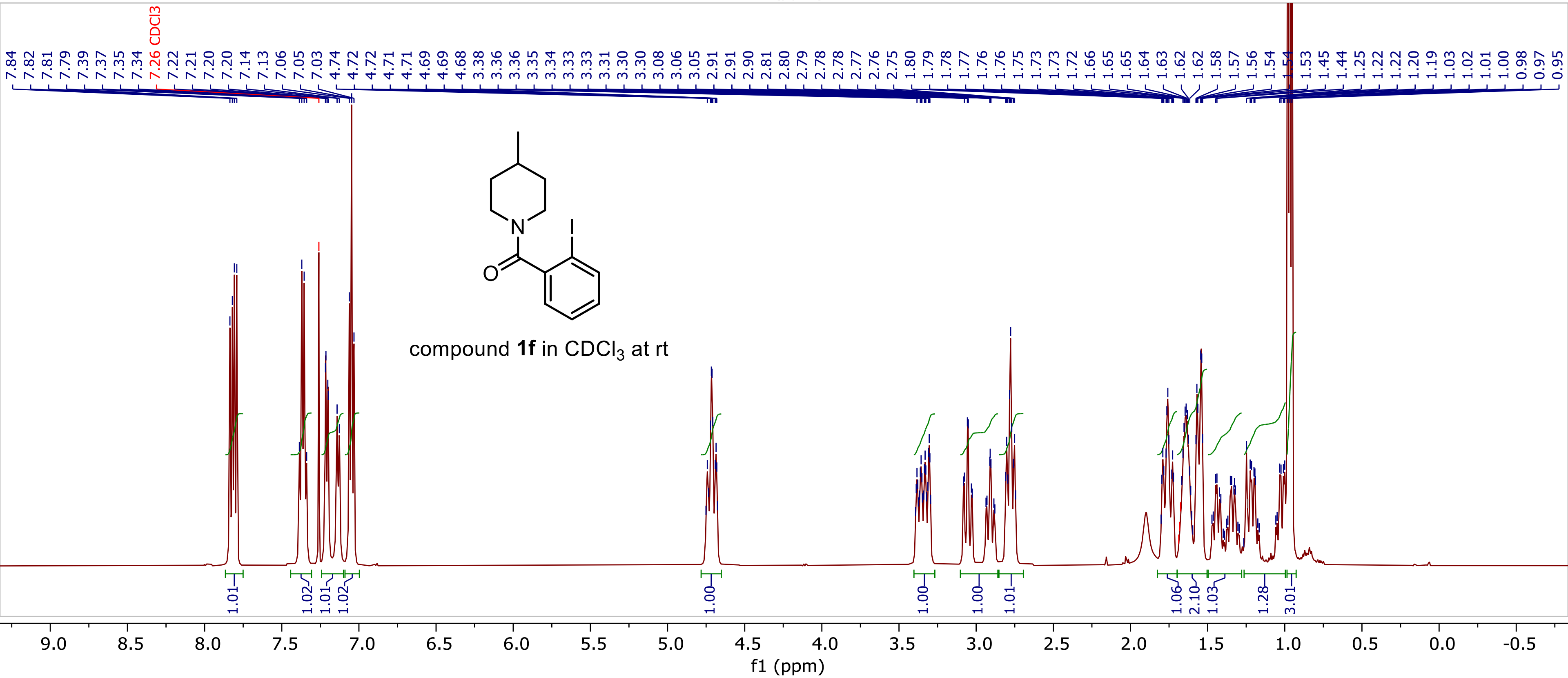
compound **1d** in $CDCl_3$



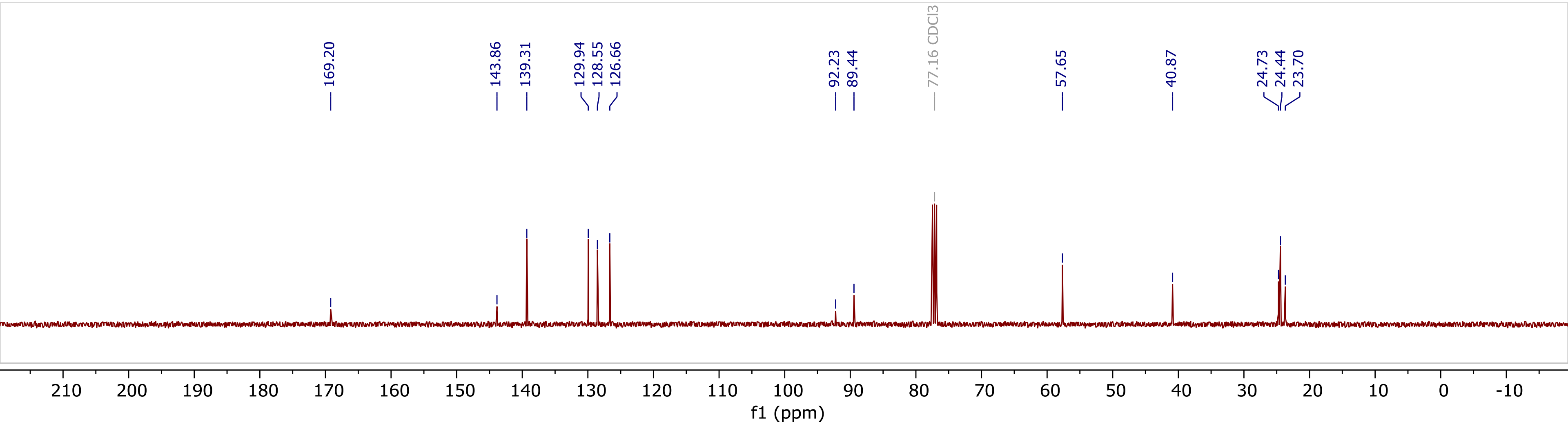


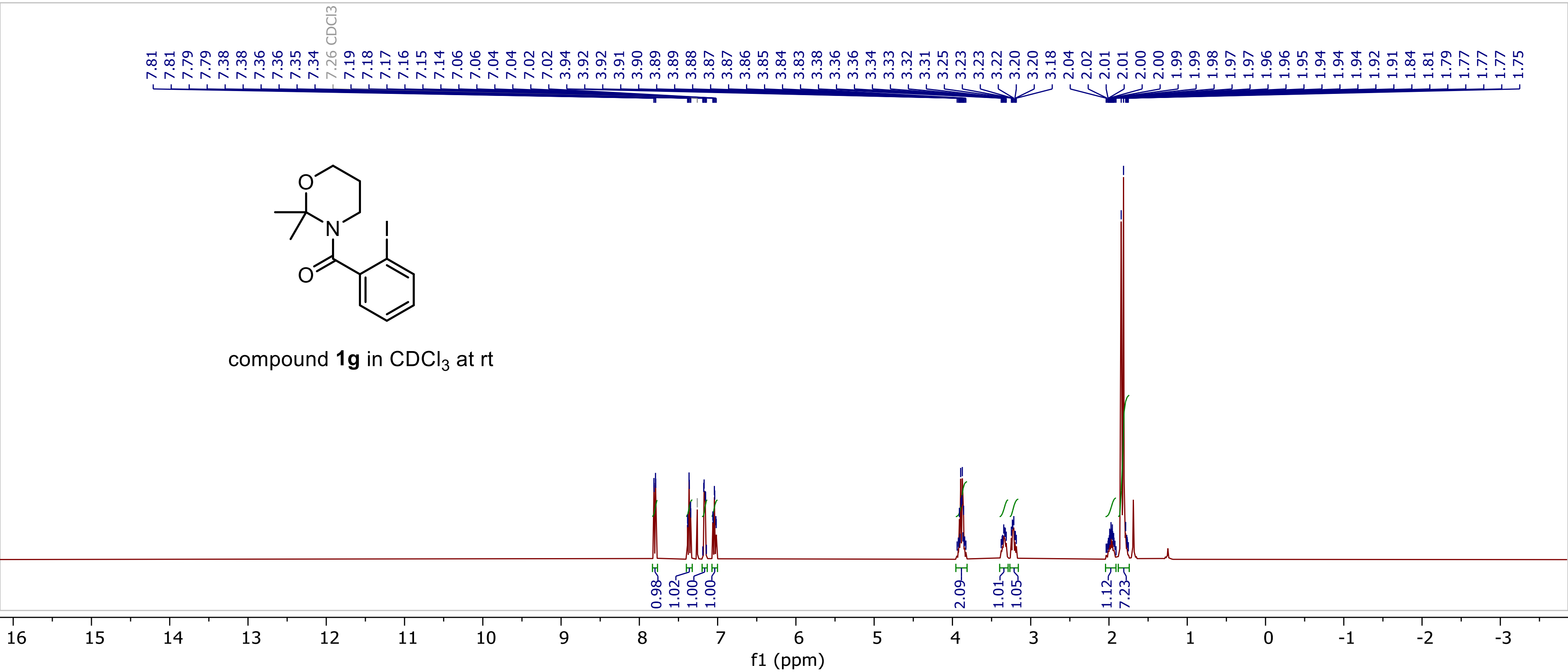
compound **1e** in $CDCl_3$



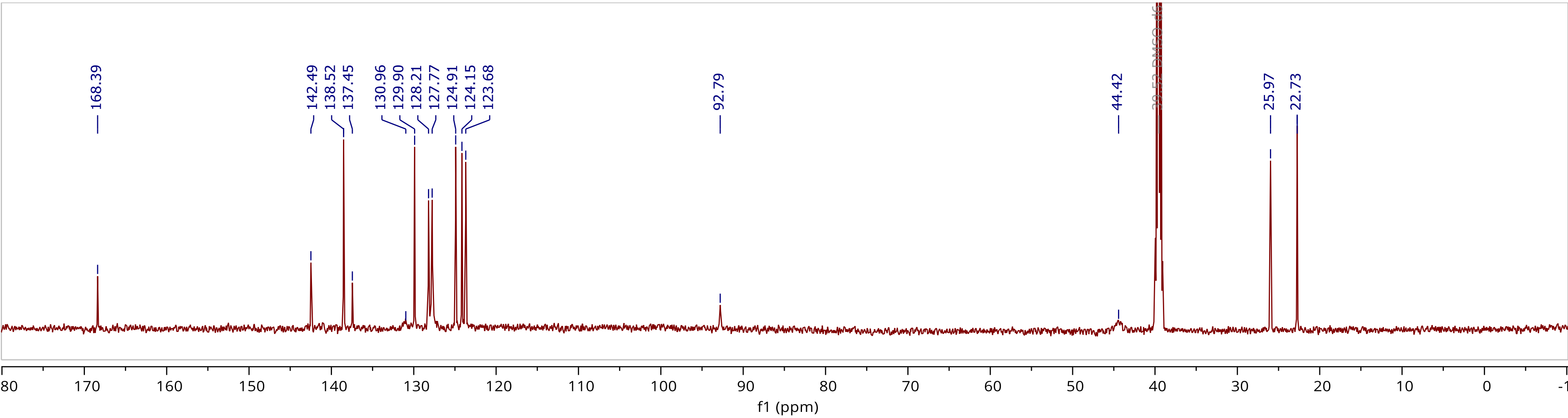


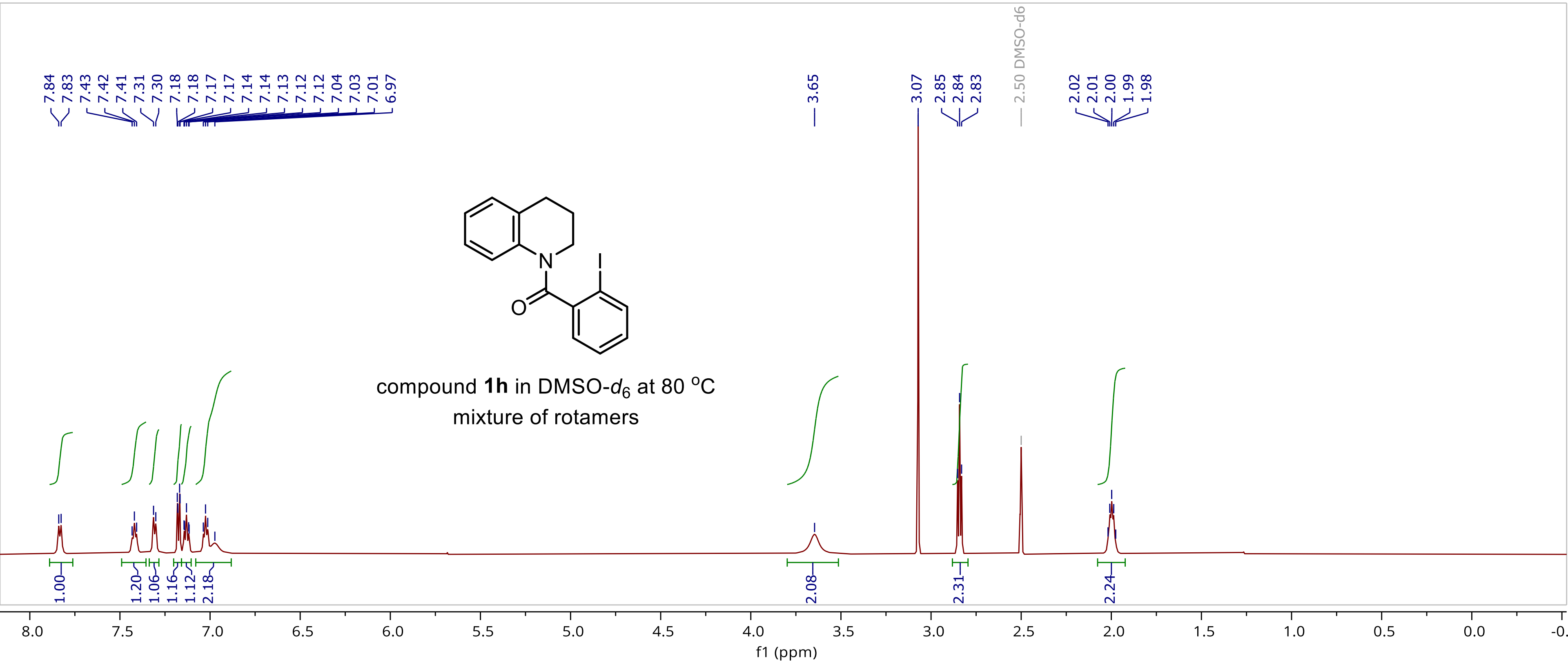
compound **1f** in $CDCl_3$ at rt



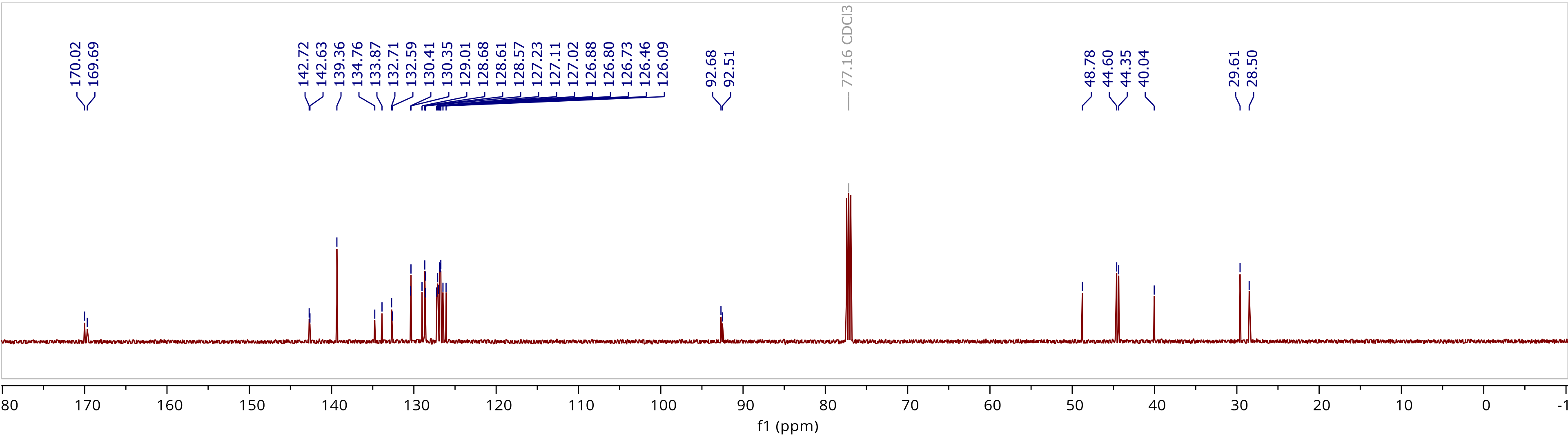


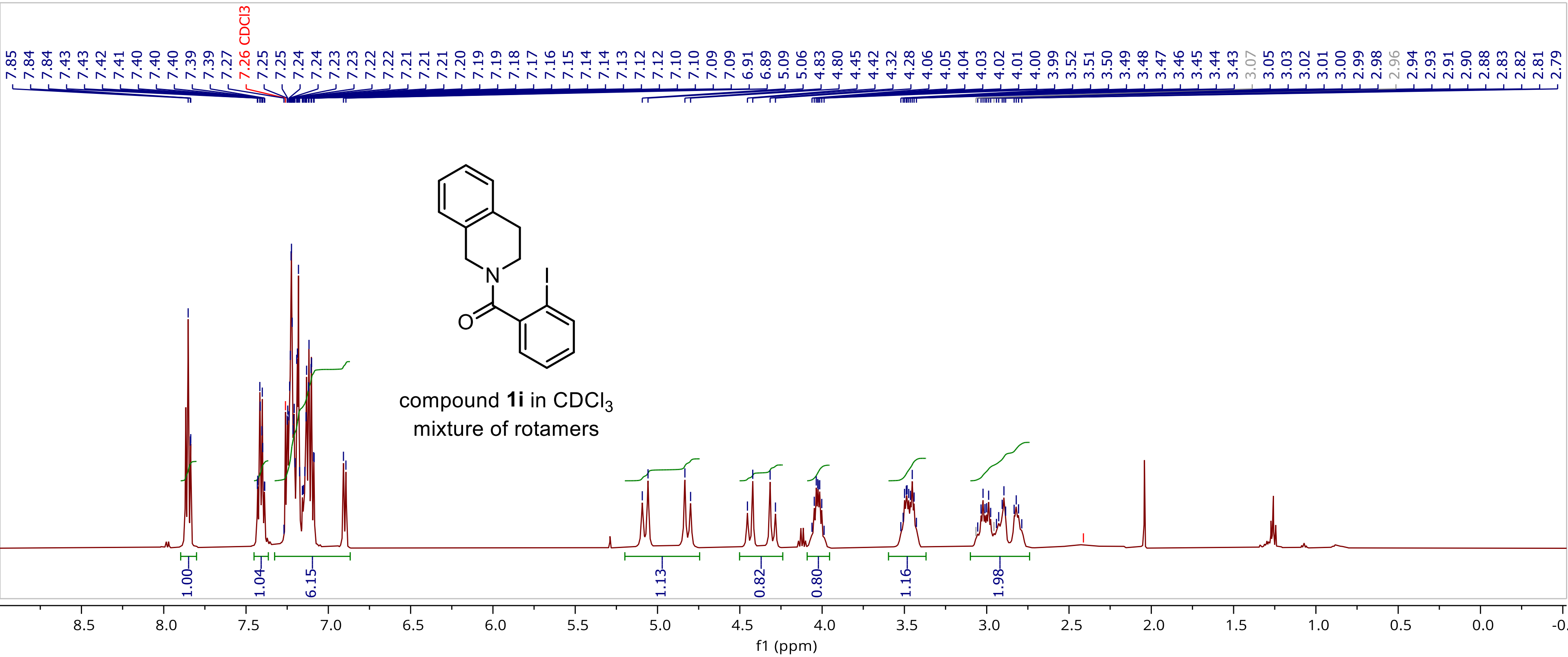
compound **1g** in CDCl$_3$ at rt



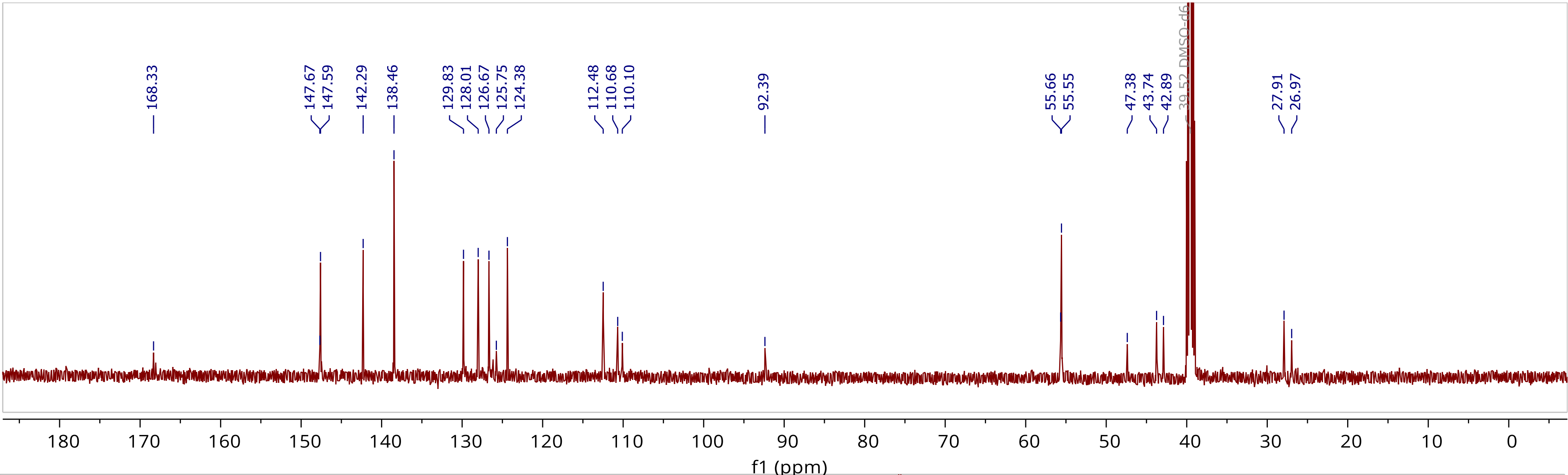


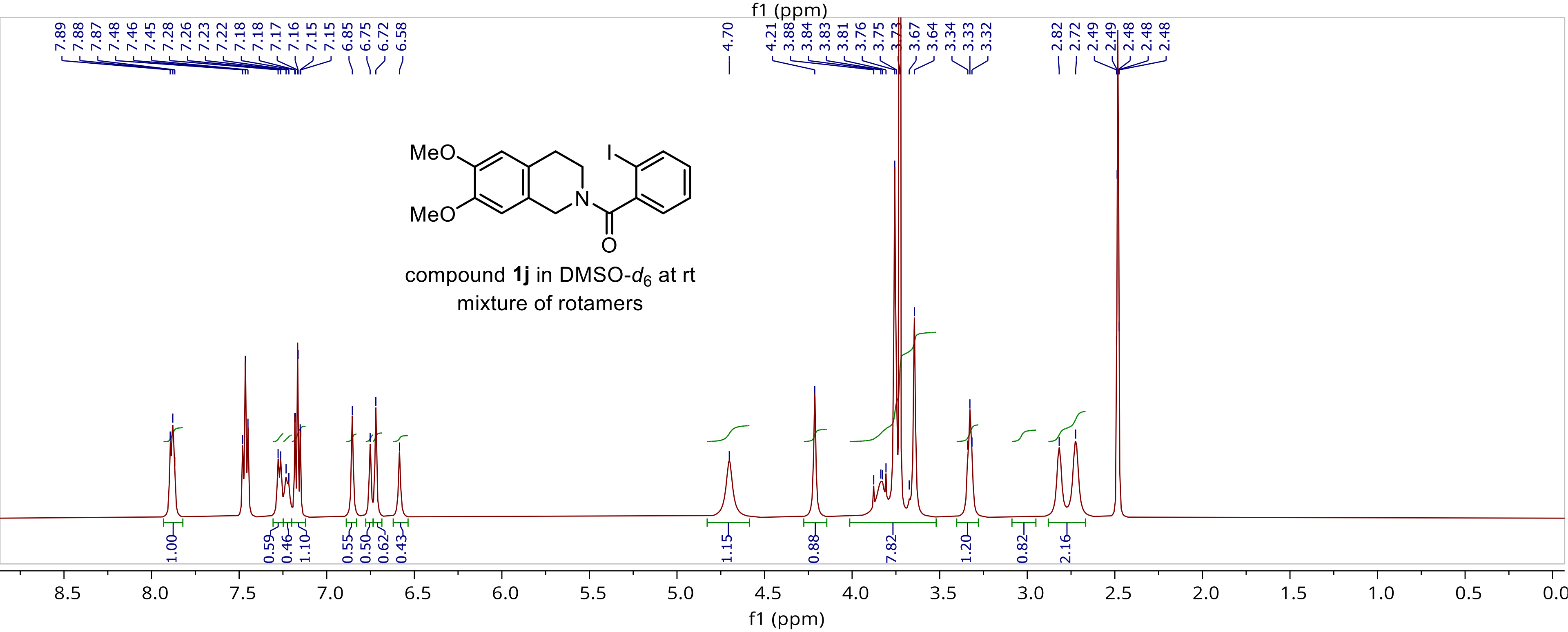
compound **1h** in DMSO-d_6 at 80 ^{o}C
mixture of rotamers

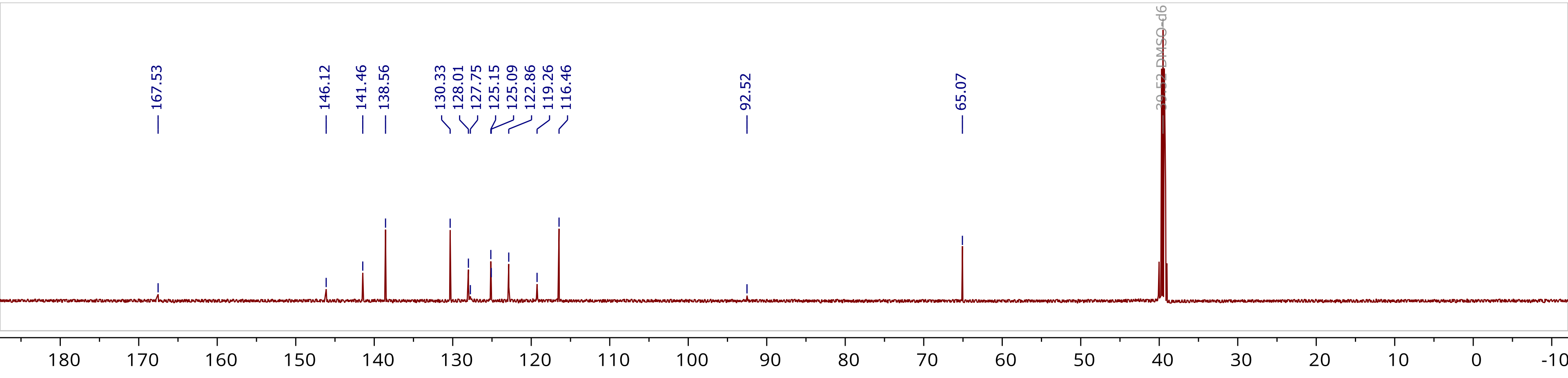


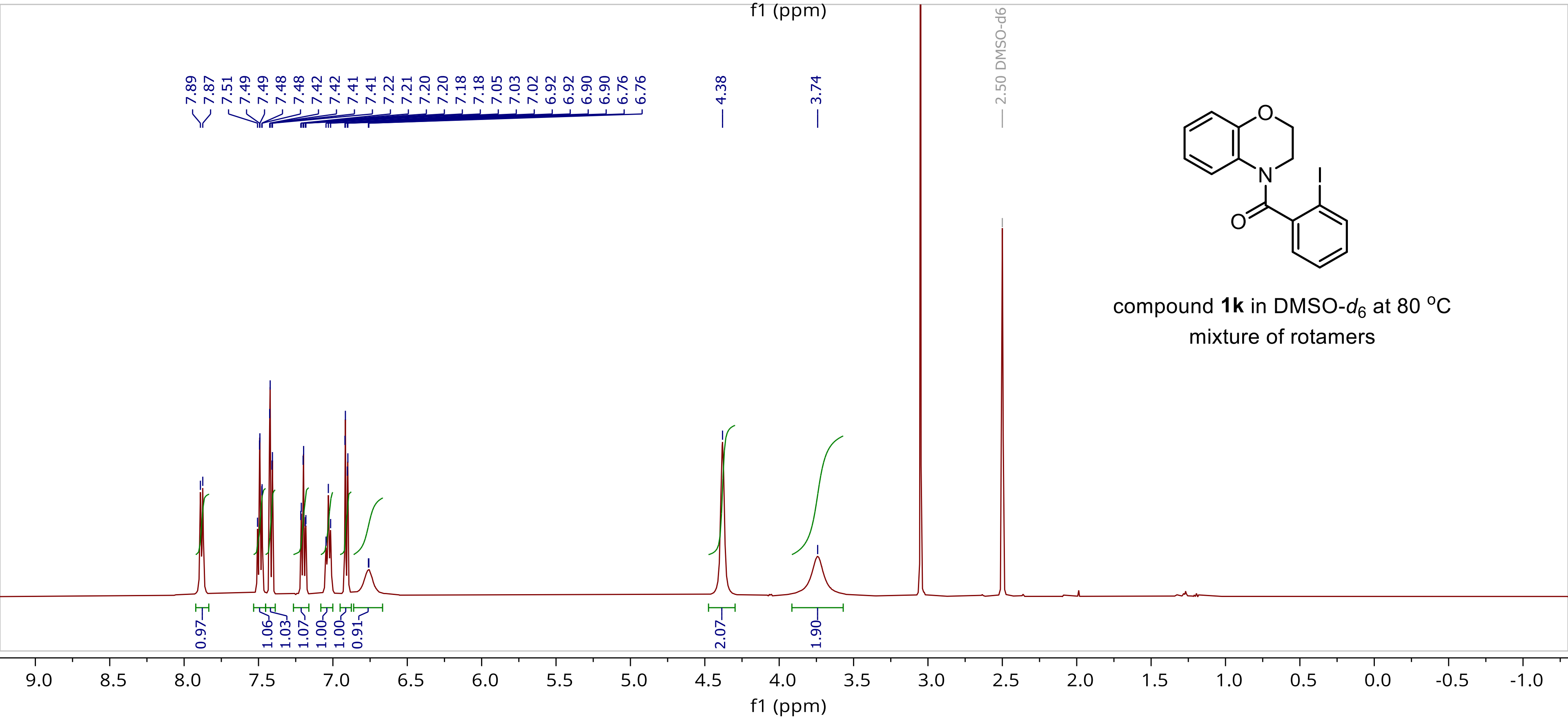


compound **1i** in $CDCl_3$
mixture of rotamers

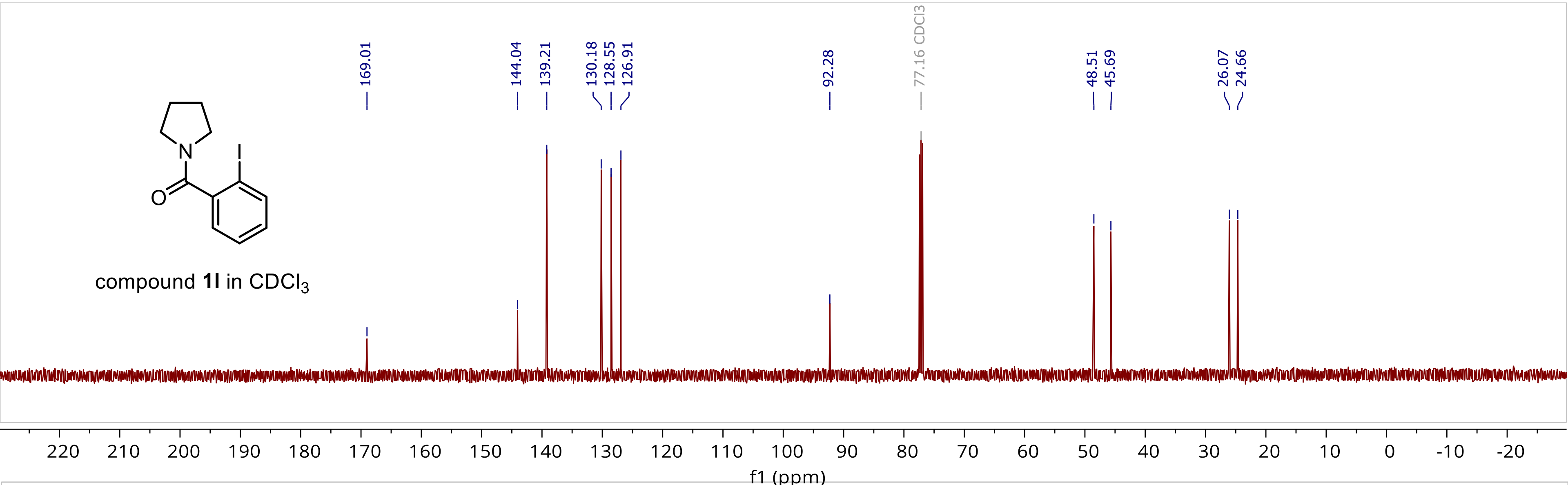

168.33
147.67
147.59
142.29
138.46
129.83
128.01
126.67
125.75
124.38
112.48
110.68
110.10
92.39
55.66
55.55
47.38
43.74
42.89
39.52 DMSO-d6
27.91
26.97
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

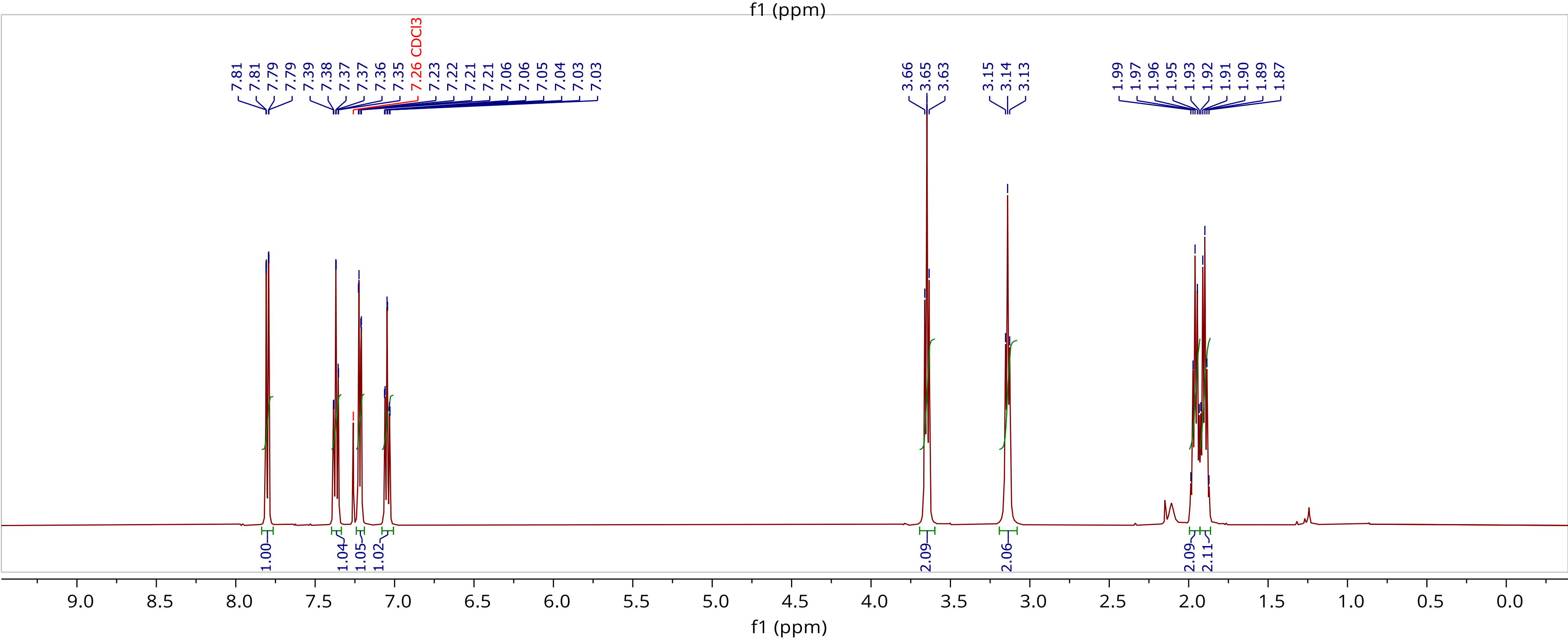

7.89
7.88
7.87
7.48
7.46
7.45
7.28
7.26
7.23
7.22
7.18
7.18
7.17
7.16
7.15
7.15
6.85
6.75
6.72
6.58
4.70
4.21
3.88
3.84
3.83
3.81
3.76
3.75
3.73
3.67
3.64
3.34
3.33
3.32
2.82
2.72
2.49
2.49
2.48
2.48
2.48
MeO
MeO
N
O
I
compound **1j** in DMSO-d_6 at rt
mixture of rotamers
1.00
0.59
0.46
1.10
0.55
0.50
0.62
0.43
1.15
0.88
7.82
1.20
0.82
2.16
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
f1 (ppm)

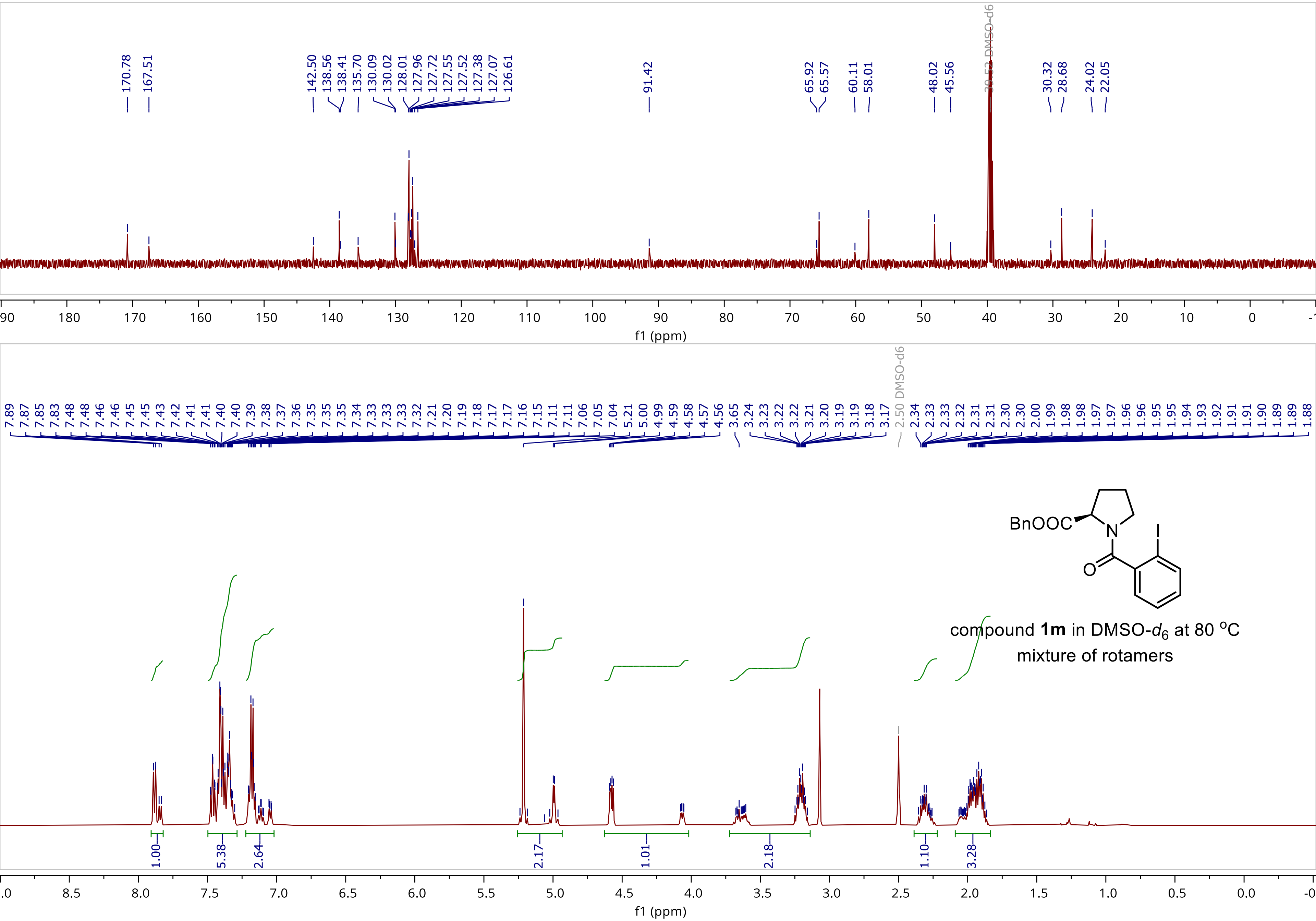




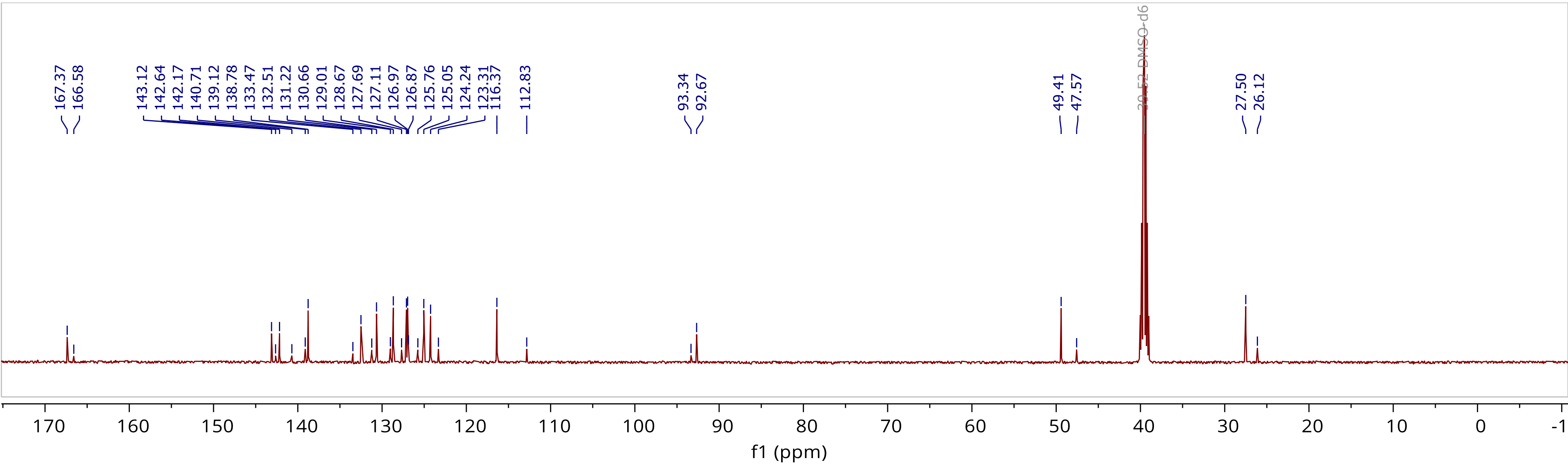
compound **1k** in DMSO-d_6 at 80 ^{o}C
mixture of rotamers

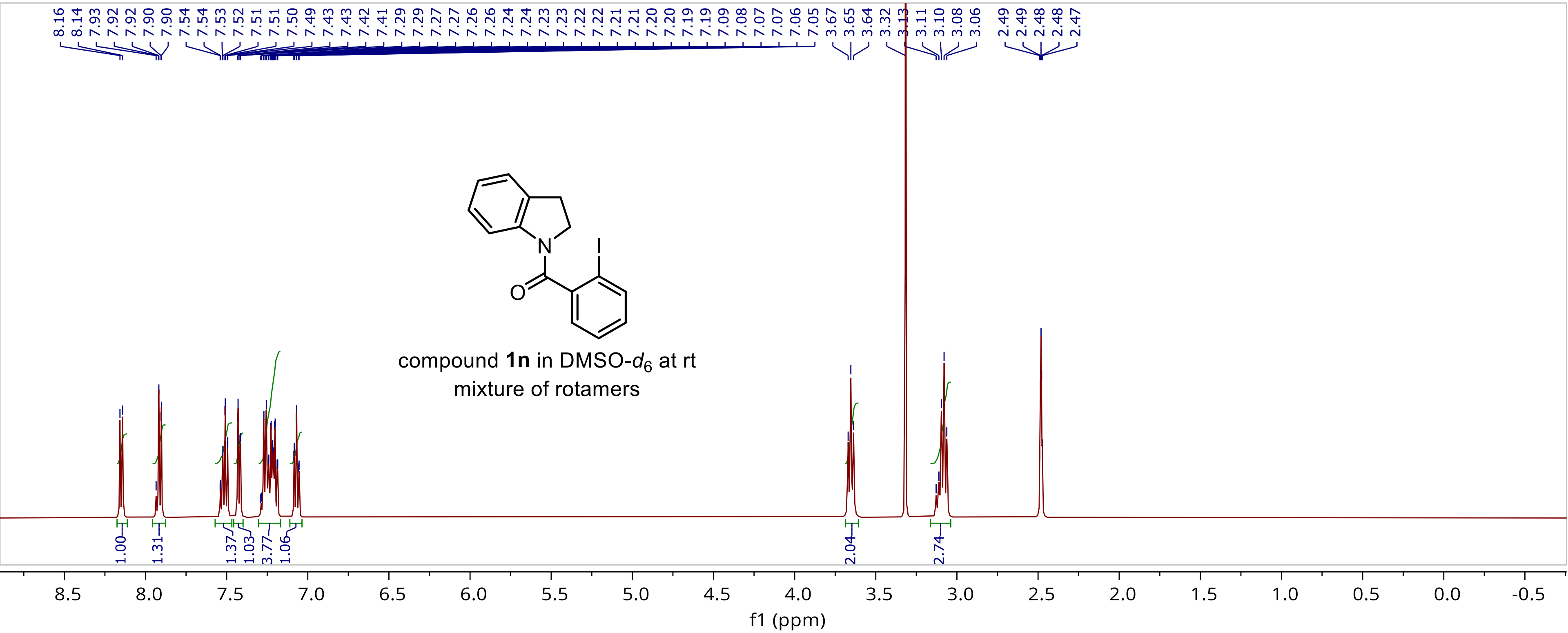

compound **1l** in CDCl$_3$
I
N
O
169.01
144.04
139.21
130.18
128.55
126.91
92.28
77.16 CDCl3
48.51
45.69
26.07
24.66
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


7.81
7.81
7.79
7.79
7.39
7.38
7.37
7.37
7.36
7.35
7.26 CDCl3
7.23
7.22
7.21
7.21
7.06
7.06
7.05
7.04
7.03
7.03
3.66
3.65
3.63
3.15
3.14
3.13
1.99
1.97
1.96
1.95
1.93
1.92
1.91
1.90
1.89
1.87
1.00
1.04
1.05
1.02
2.09
2.06
2.09
2.11
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
f1 (ppm)

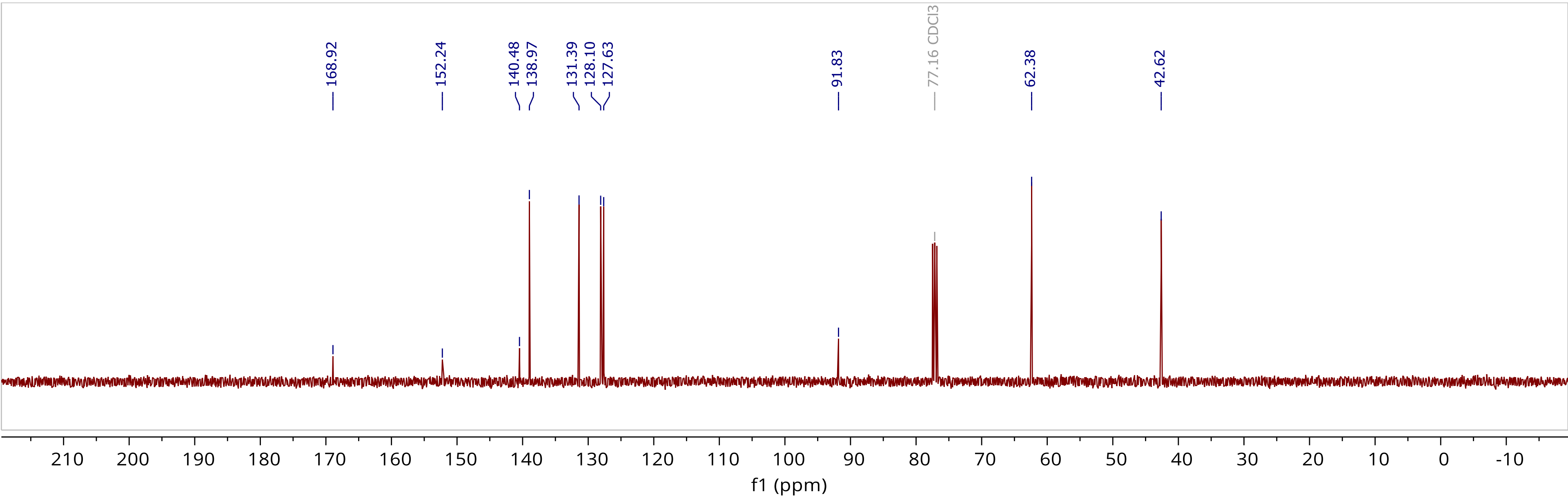


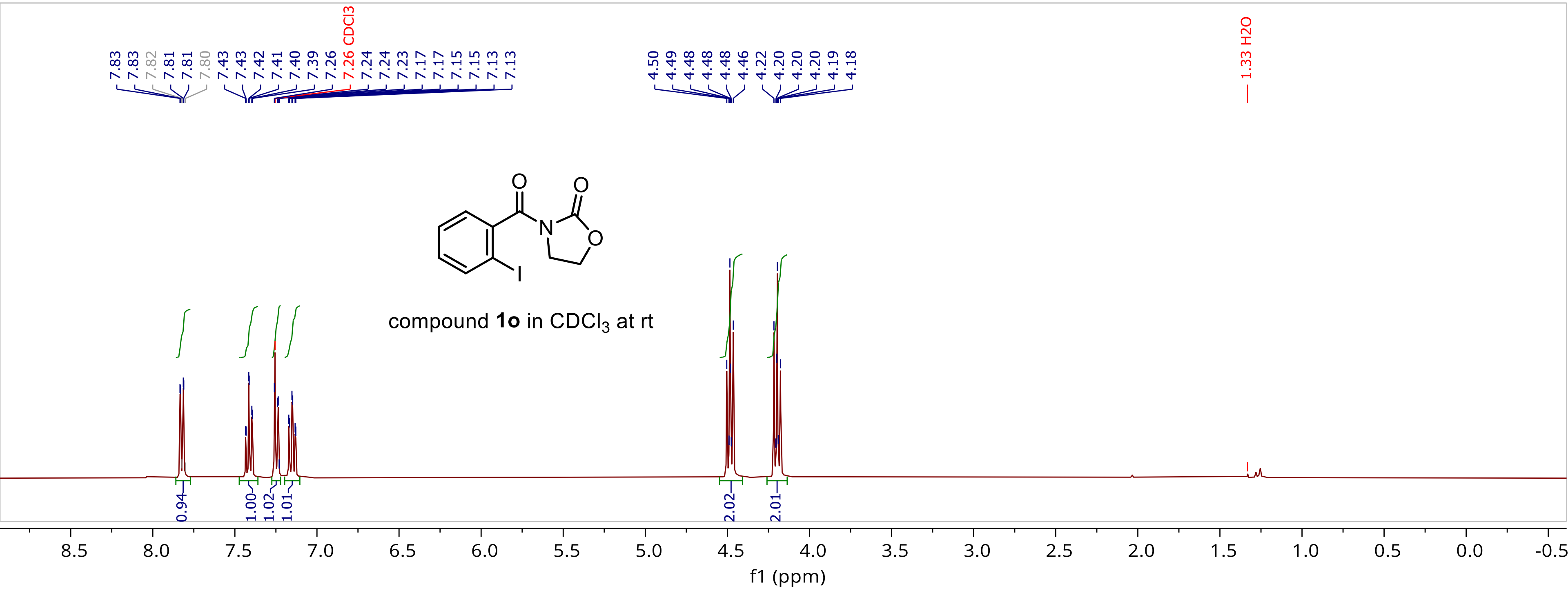
compound **1m** in DMSO-d_6 at 80 °C
mixture of rotamers



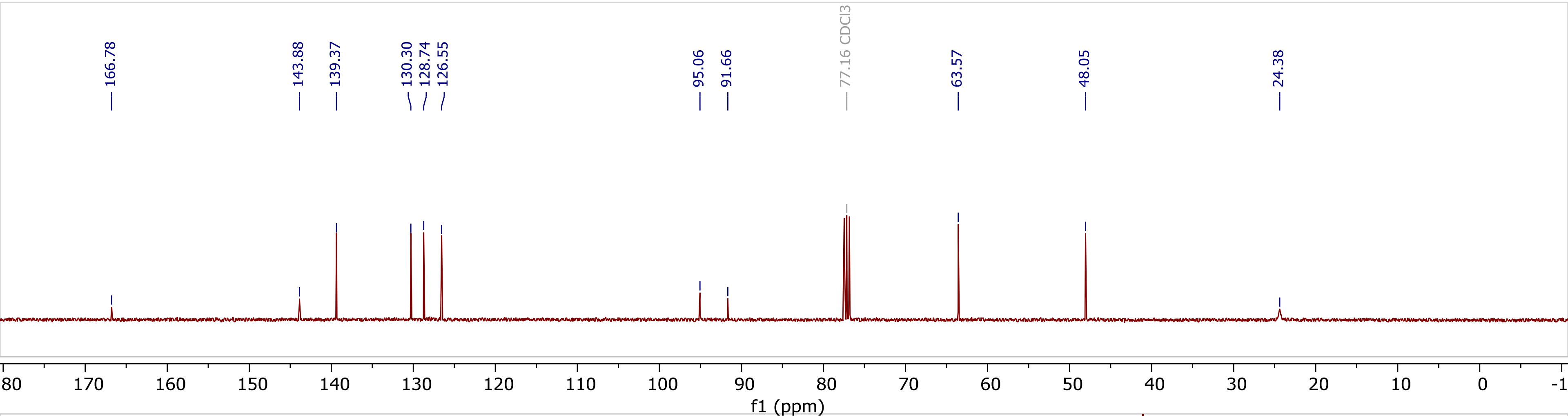


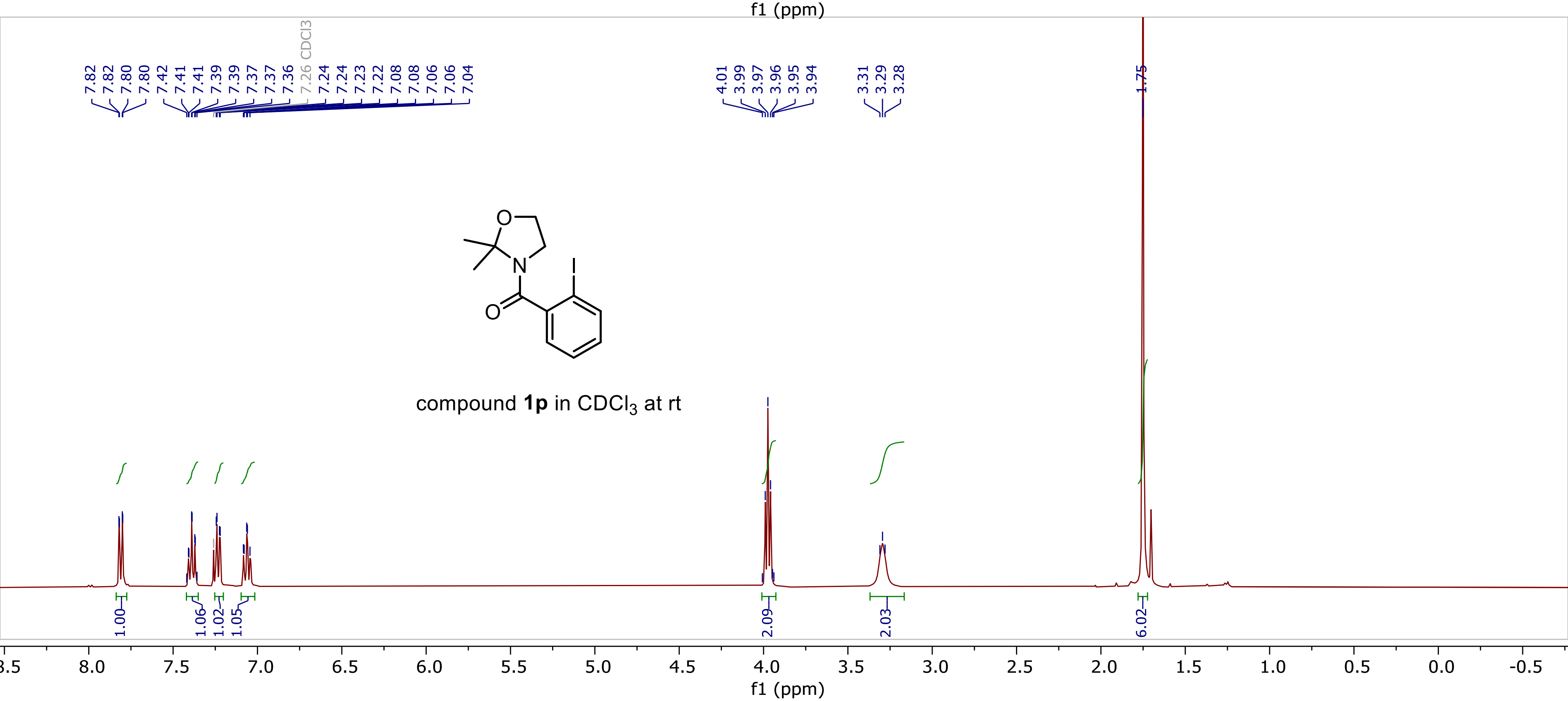
compound **1n** in DMSO-d_6 at rt
mixture of rotamers



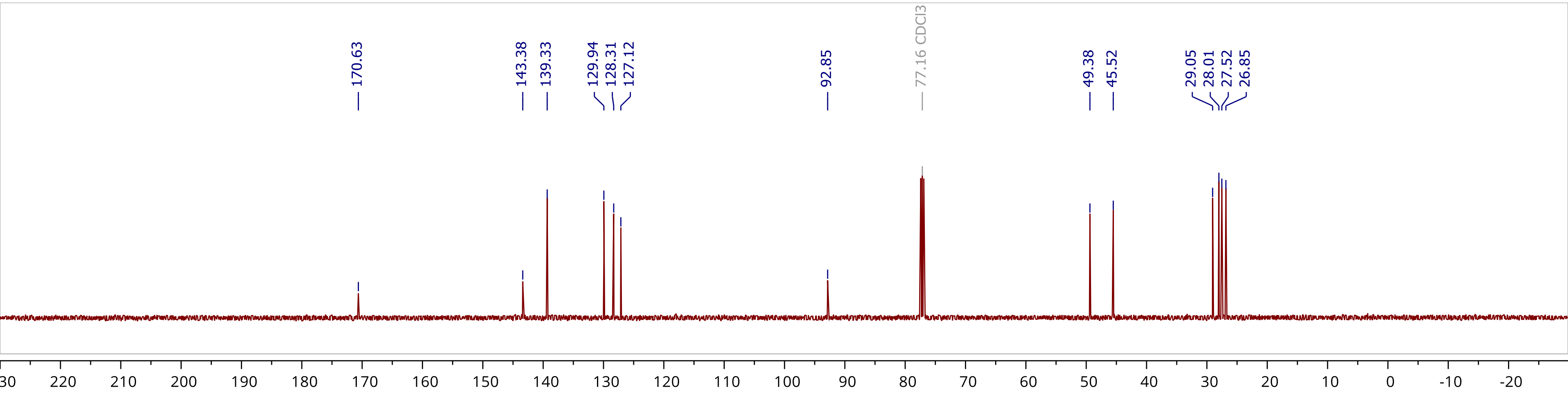


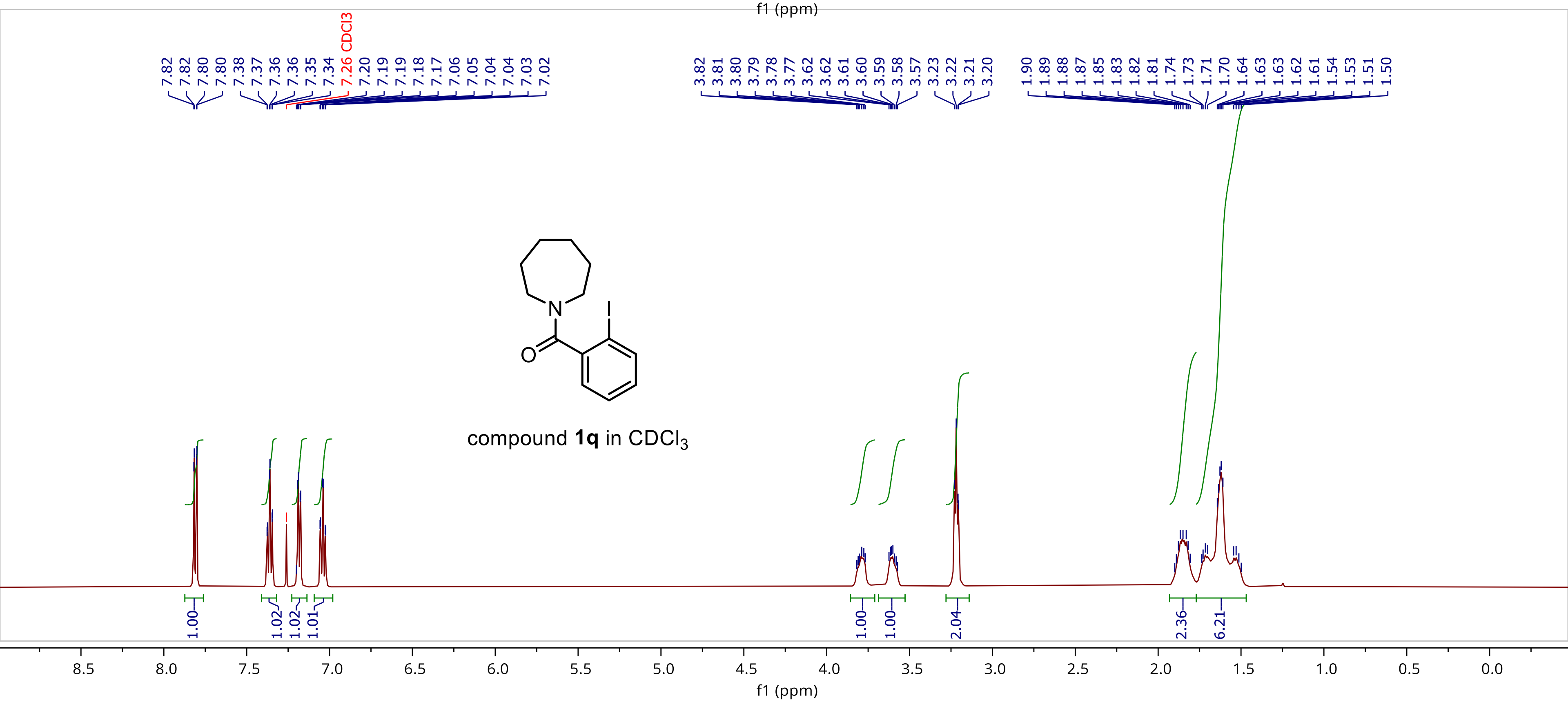
compound **1o** in $CDCl_3$ at rt



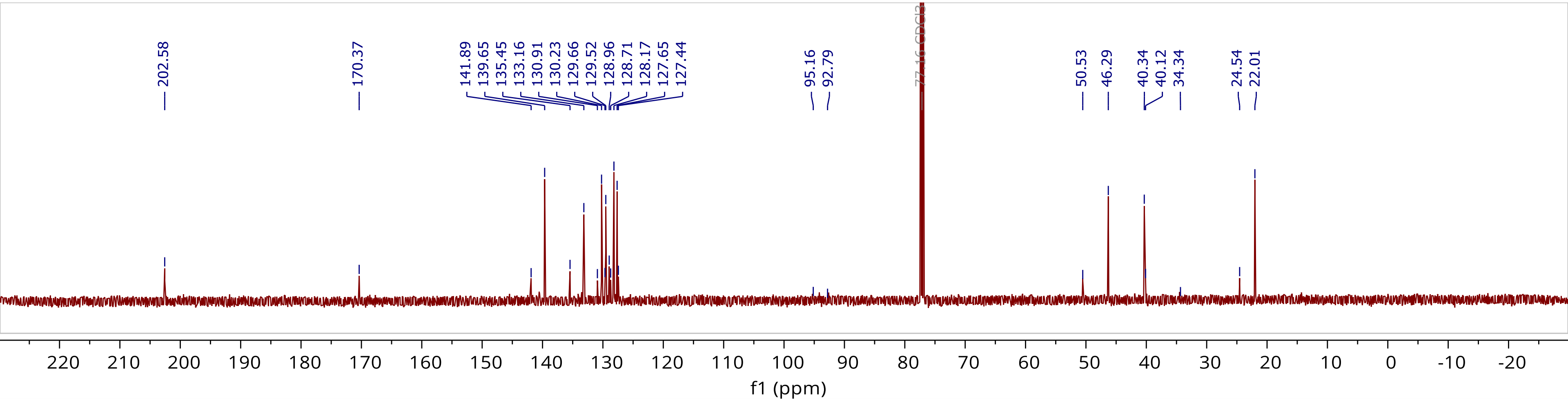


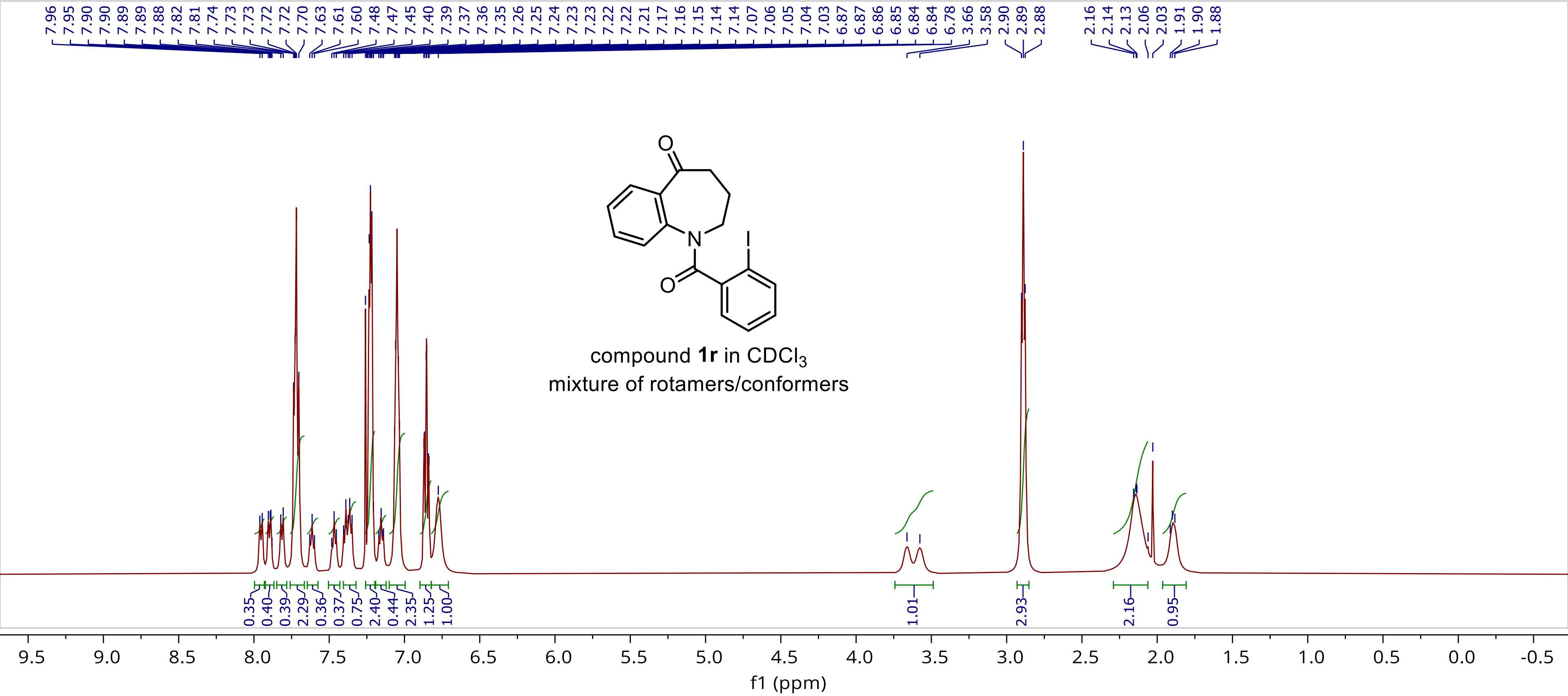
compound **1p** in CDCl$_3$ at rt





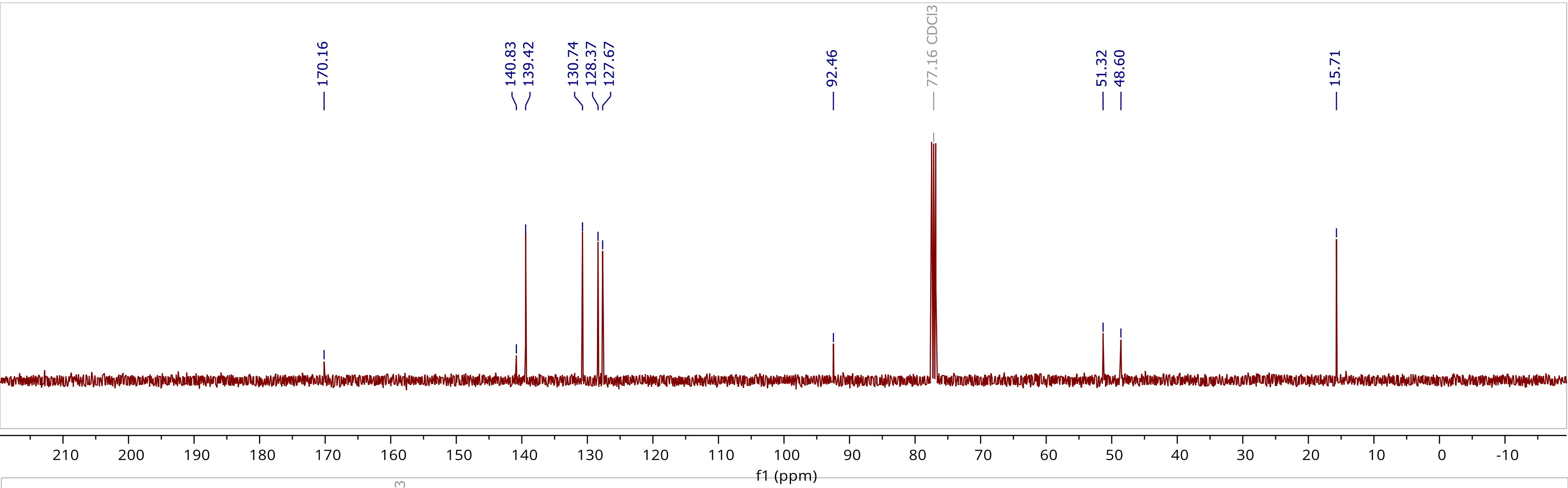
compound **1q** in CDCl$_3$

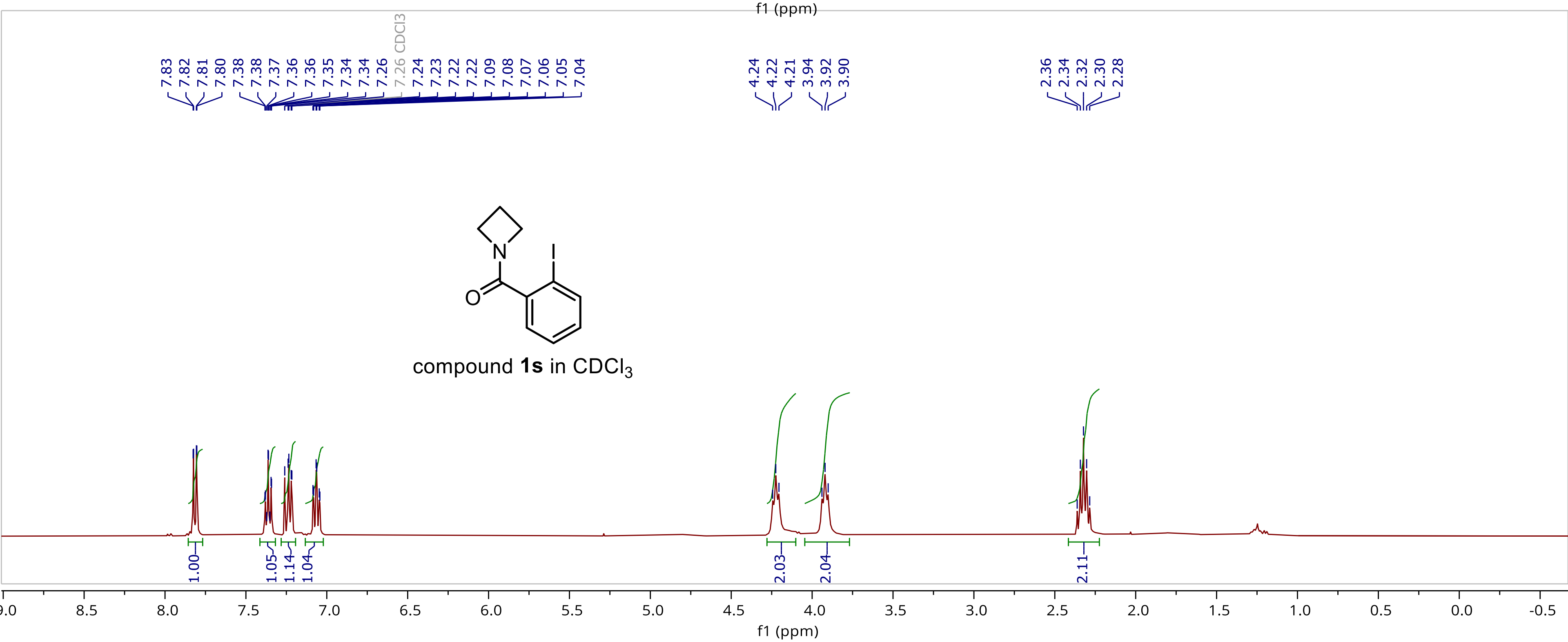




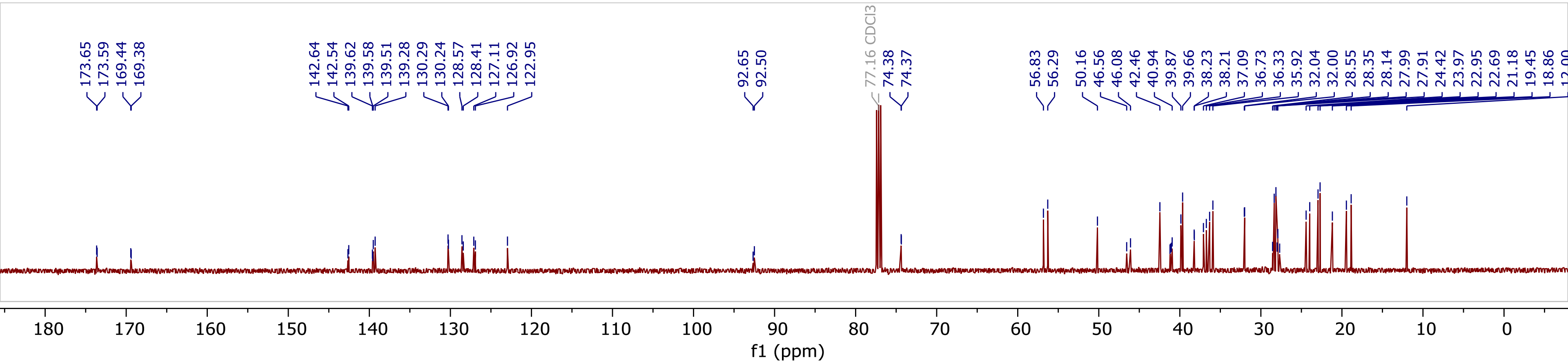
compound **1r** in $CDCl_3$

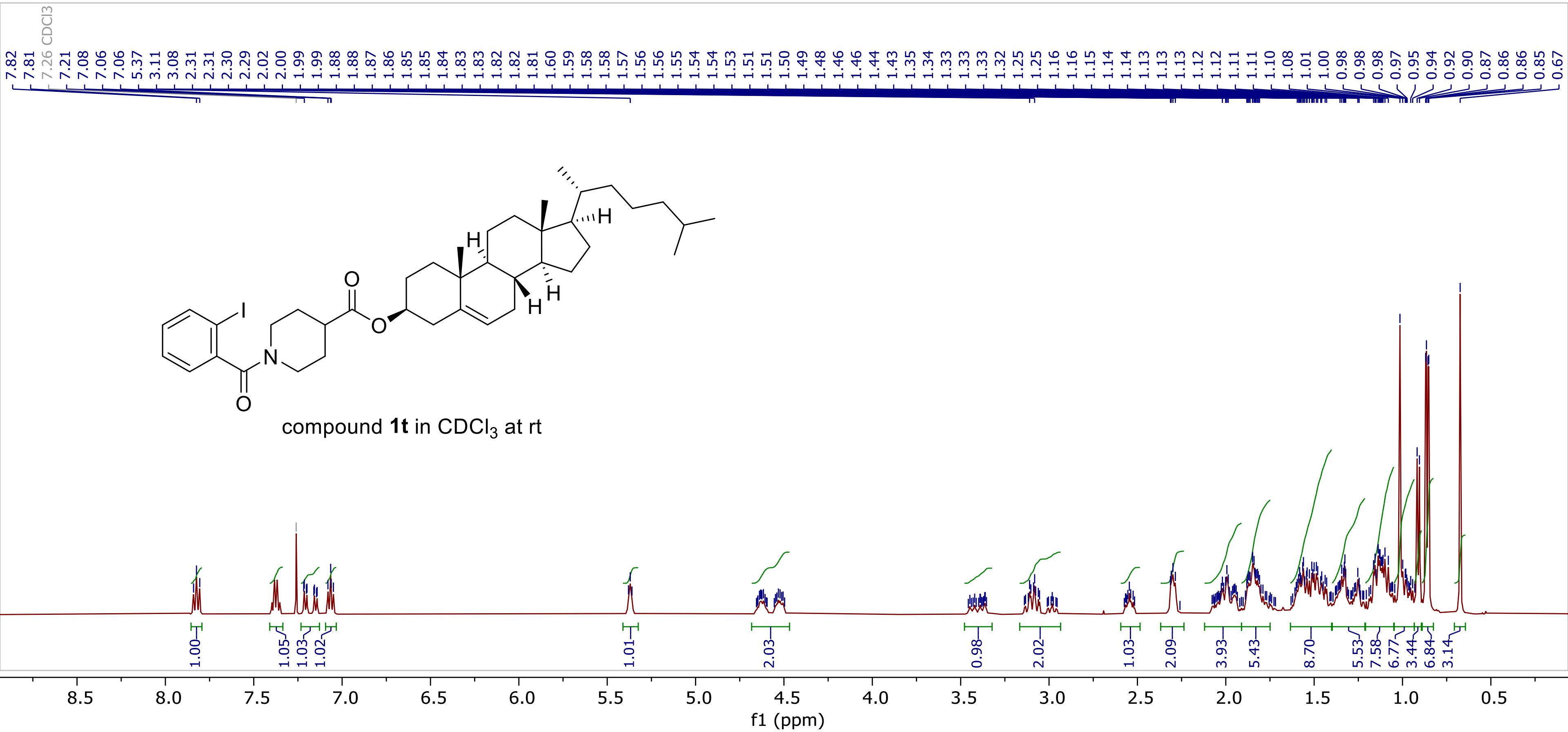
mixture of rotamers/conformers



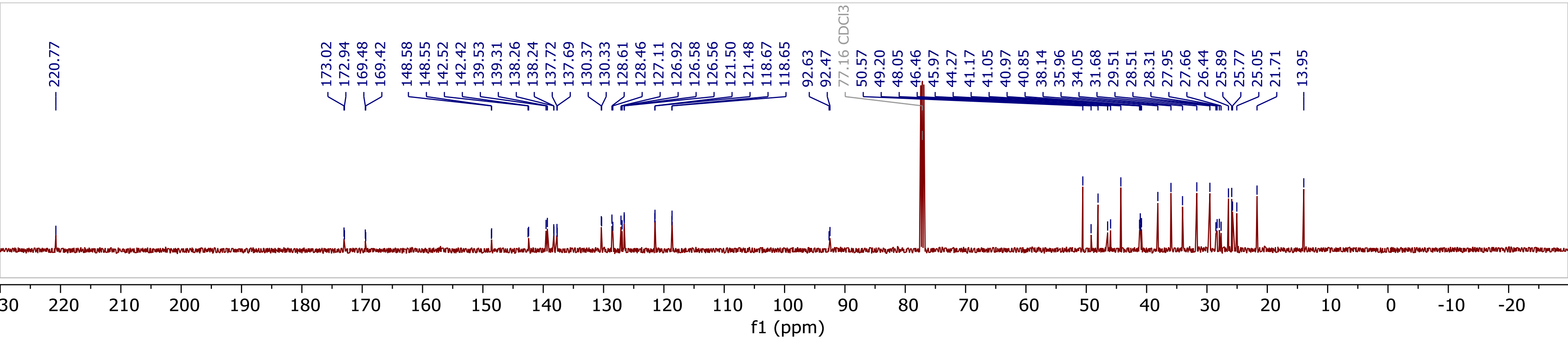


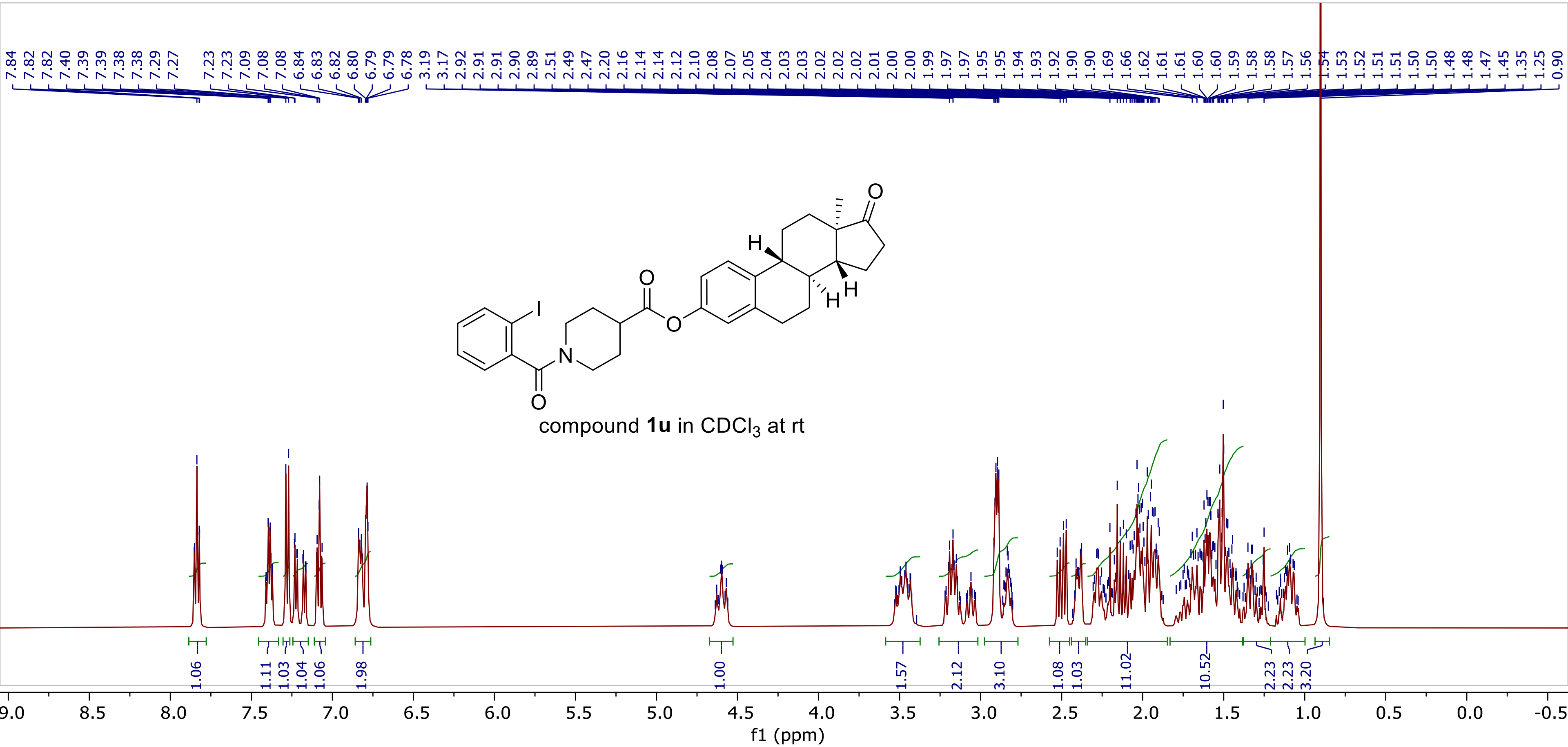
compound **1s** in $CDCl_3$



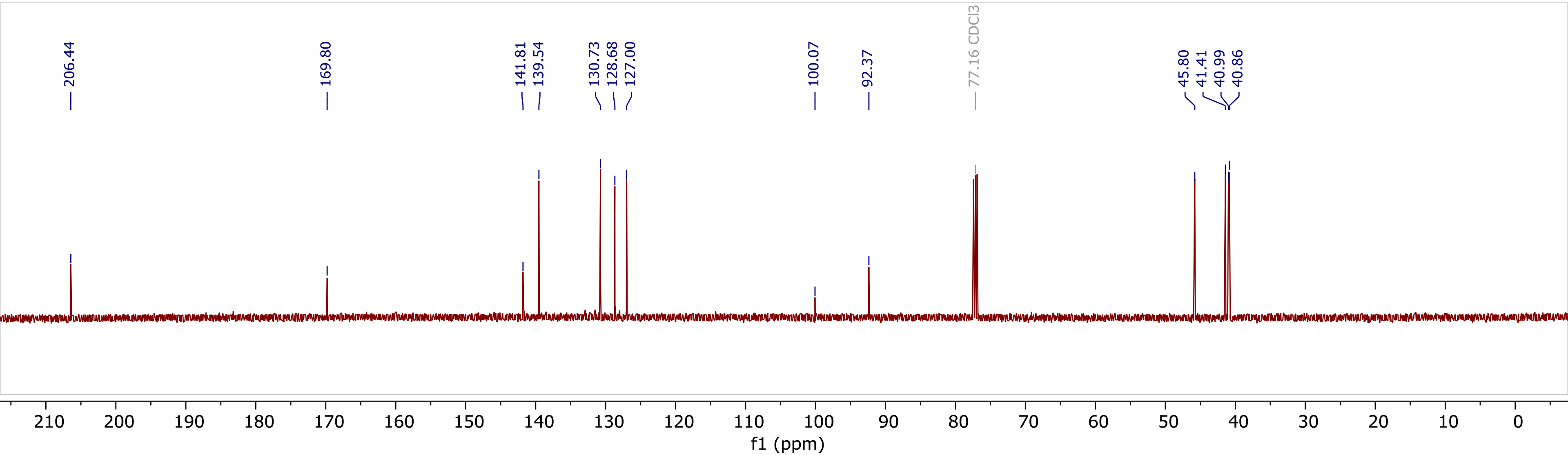


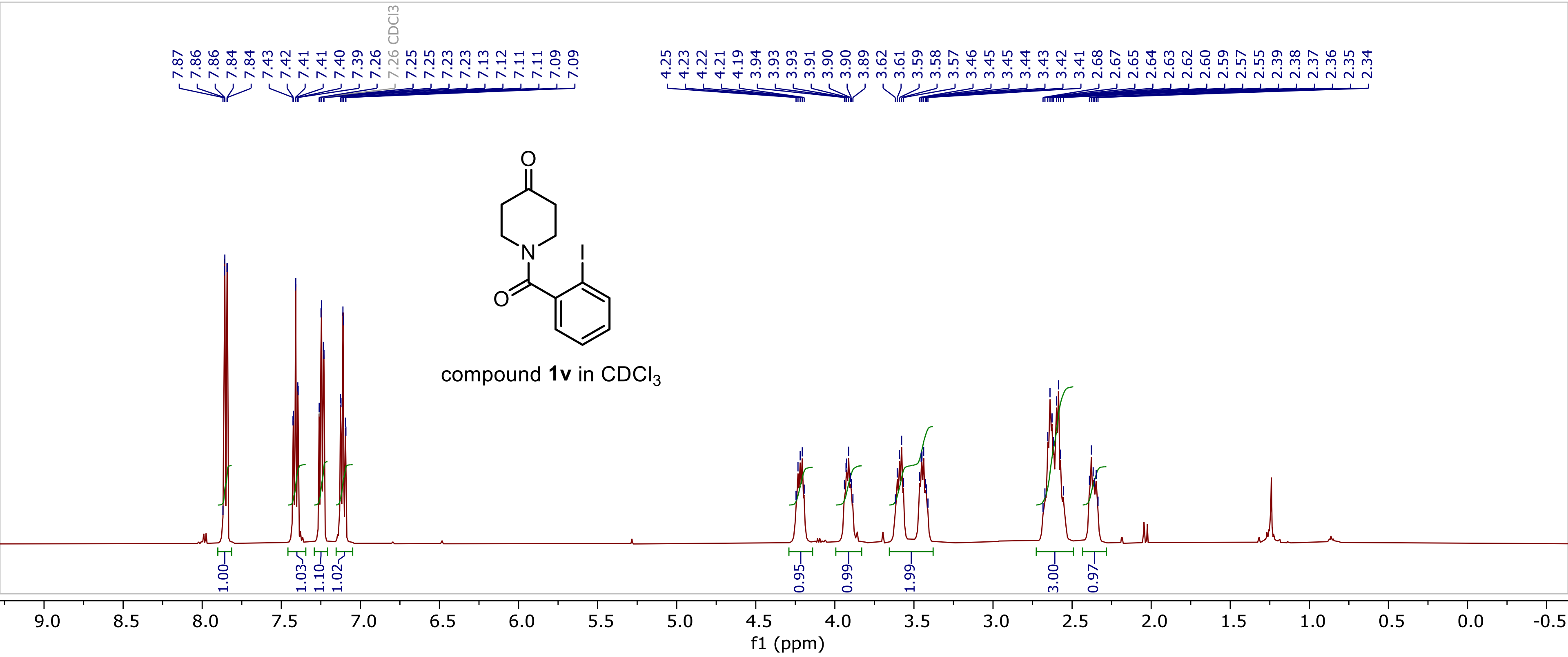
compound **1t** in $CDCl_3$ at rt



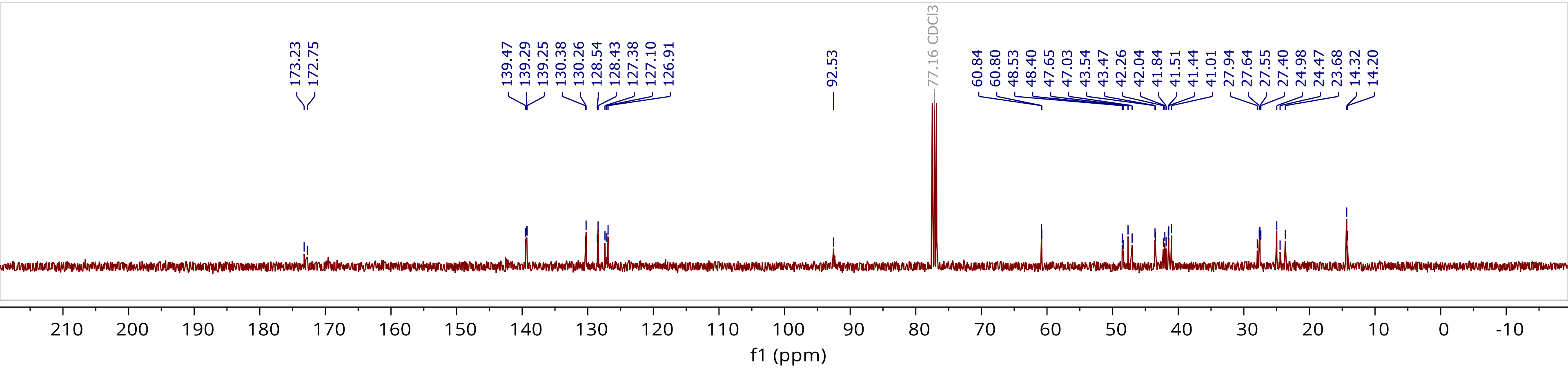


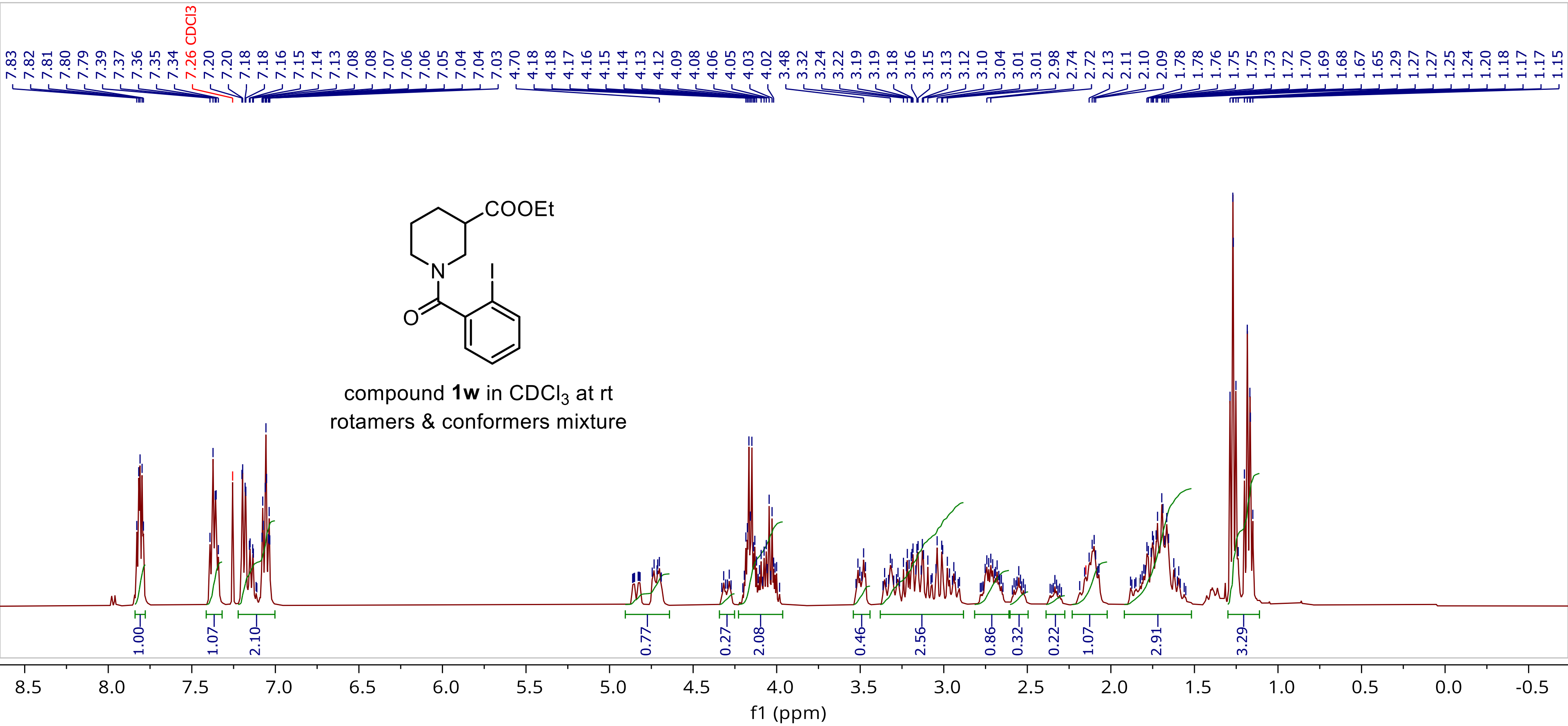
compound **1u** in CDCl$_3$ at rt



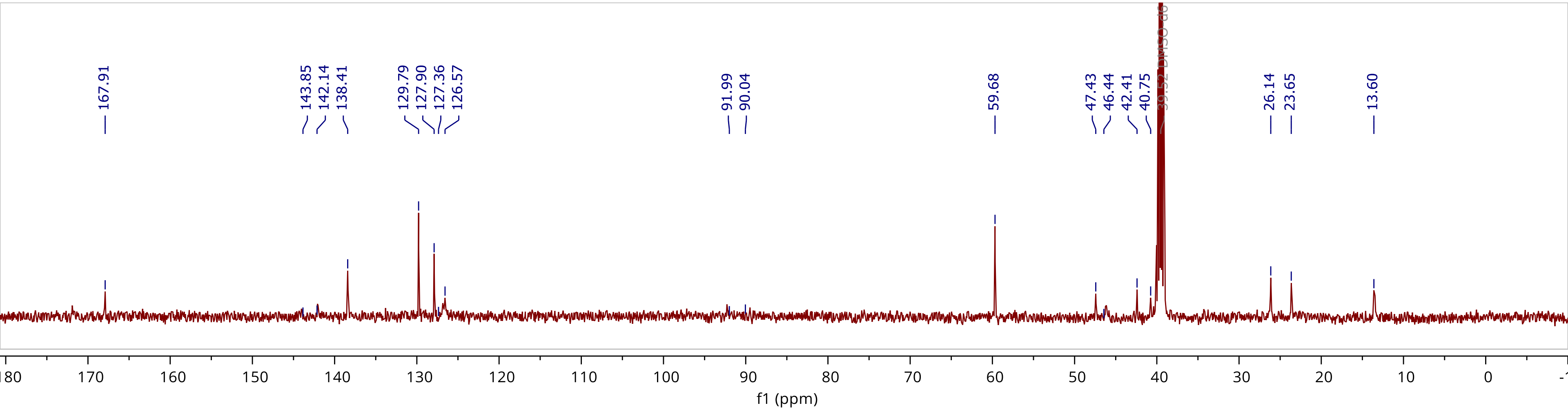


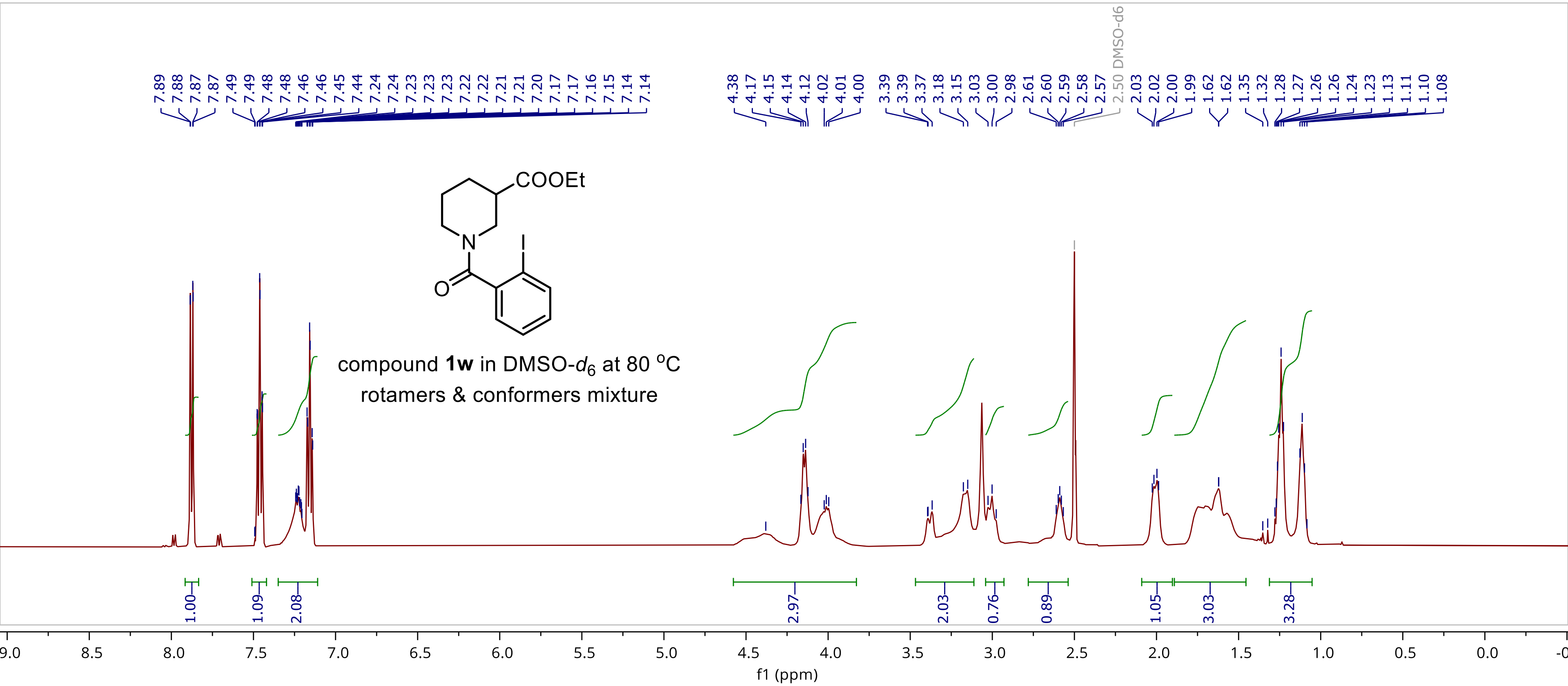
compound **1v** in $CDCl_3$

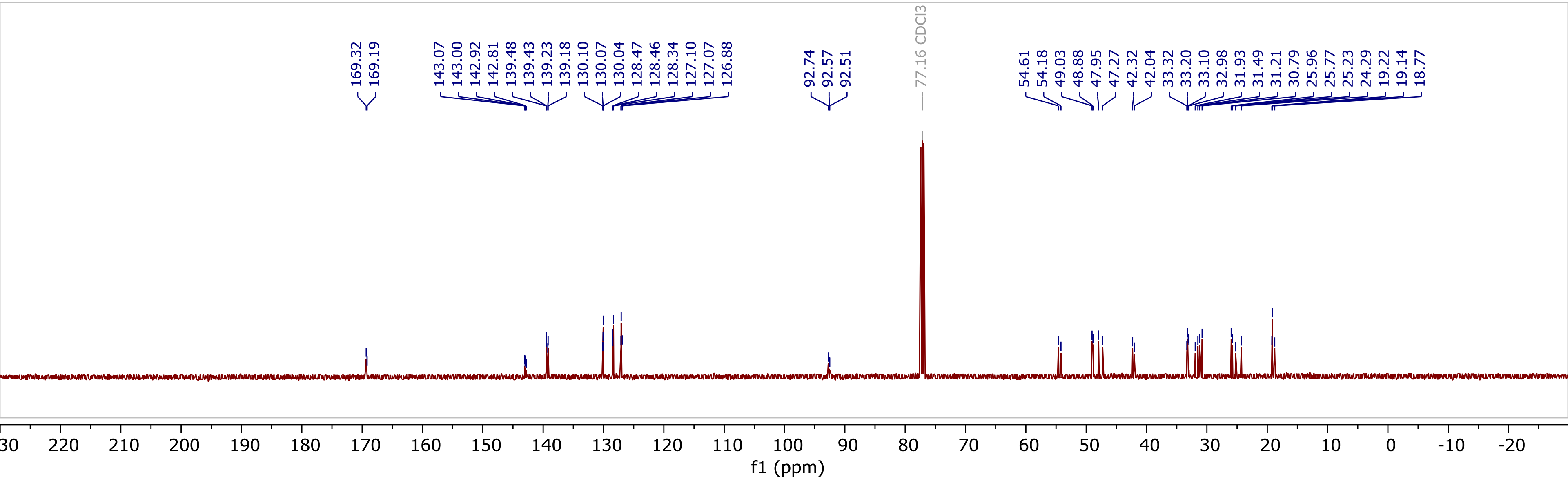


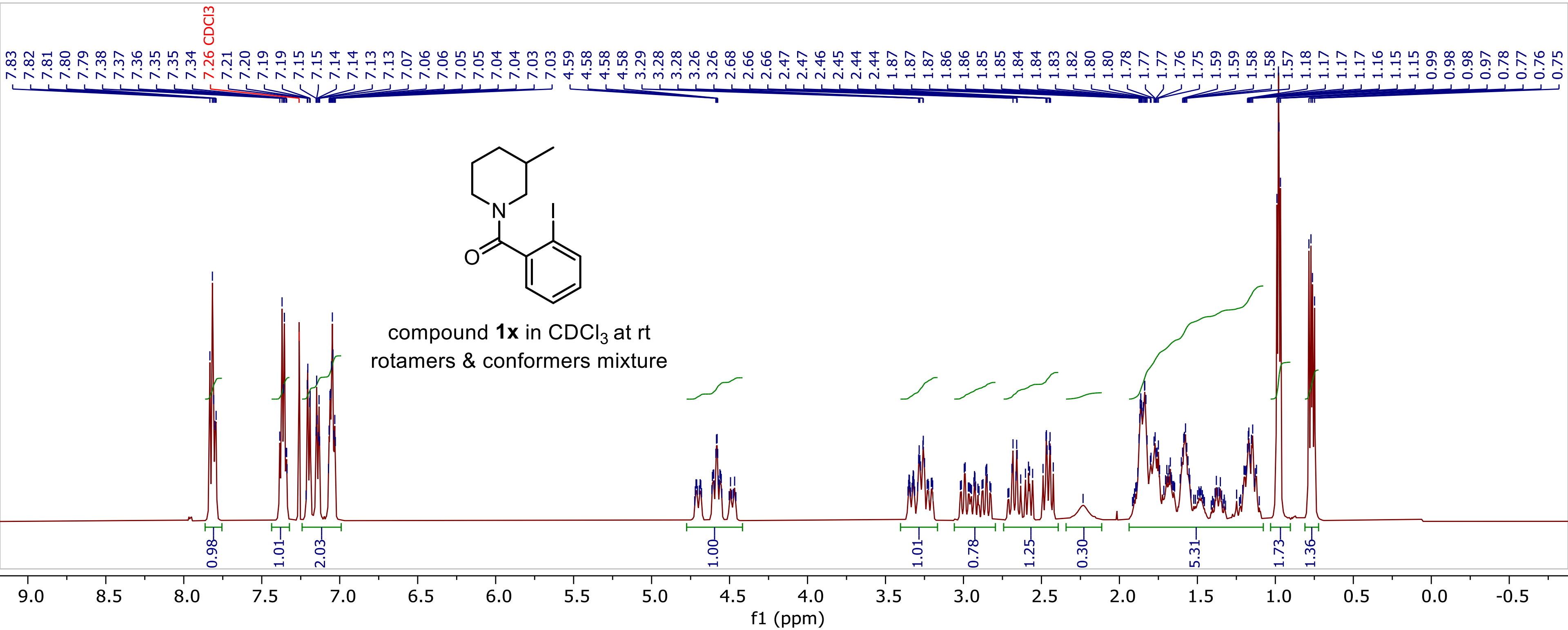


compound **1w** in CDCl$_3$ at rt
rotamers & conformers mixture

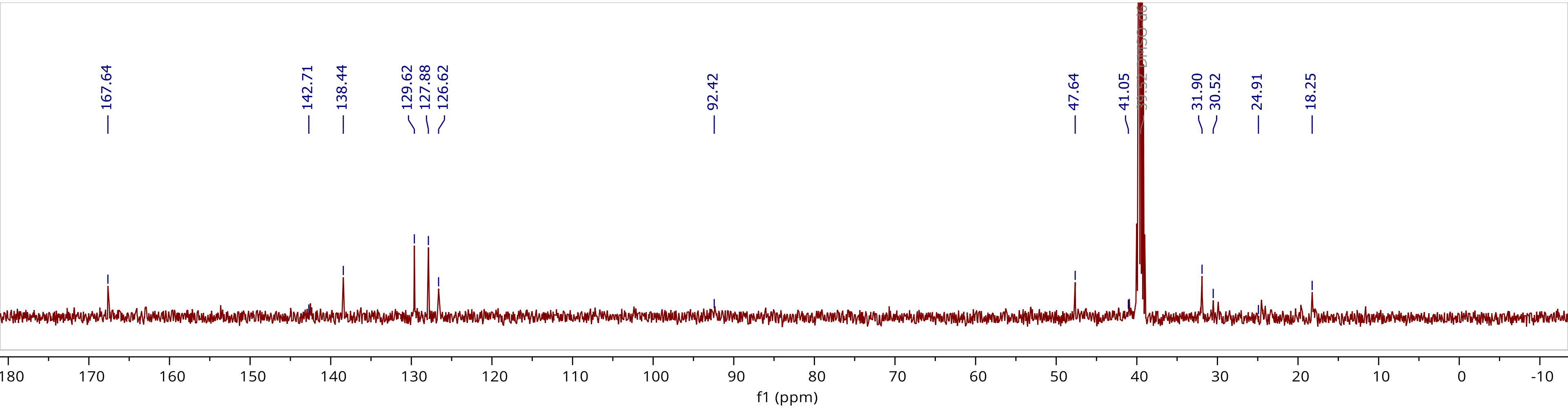


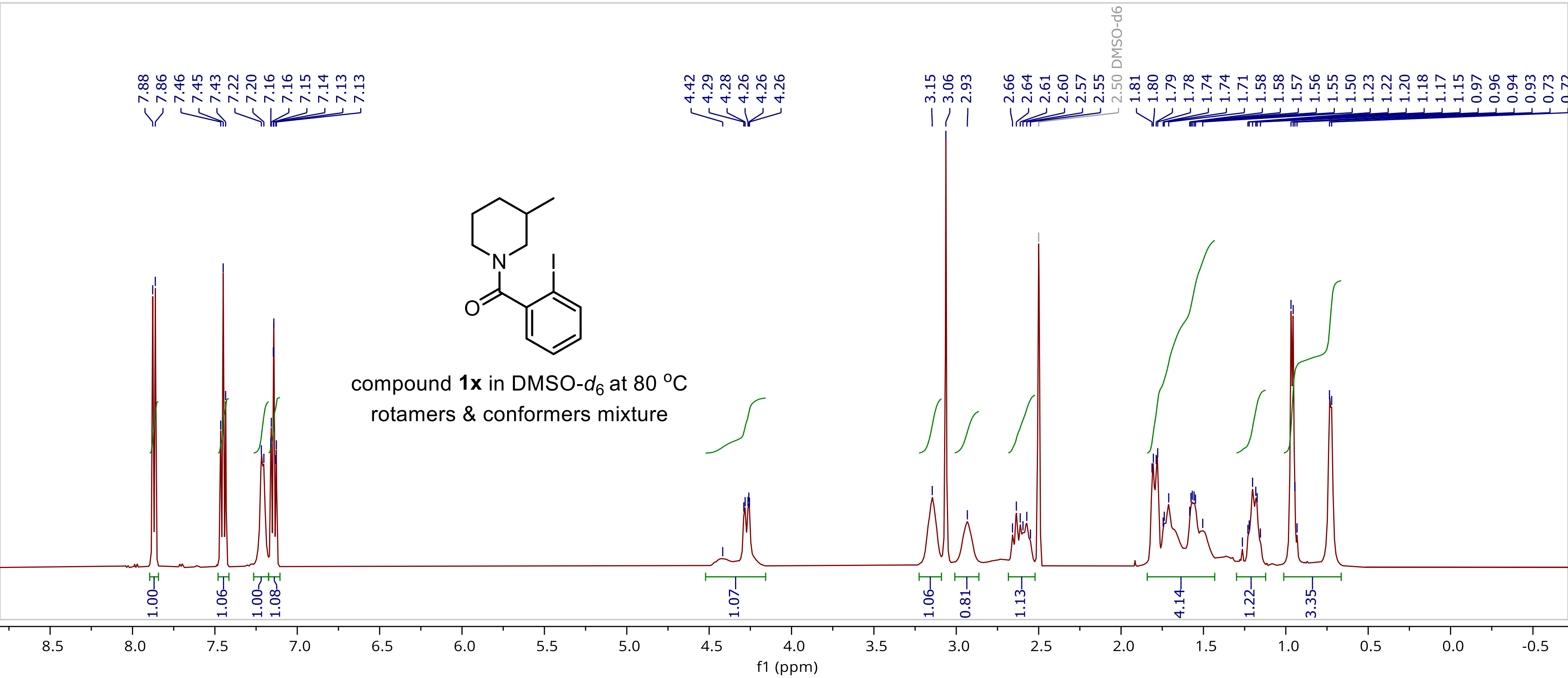

compound **1w** in DMSO-d_6 at 80 °C
rotamers & conformers mixture



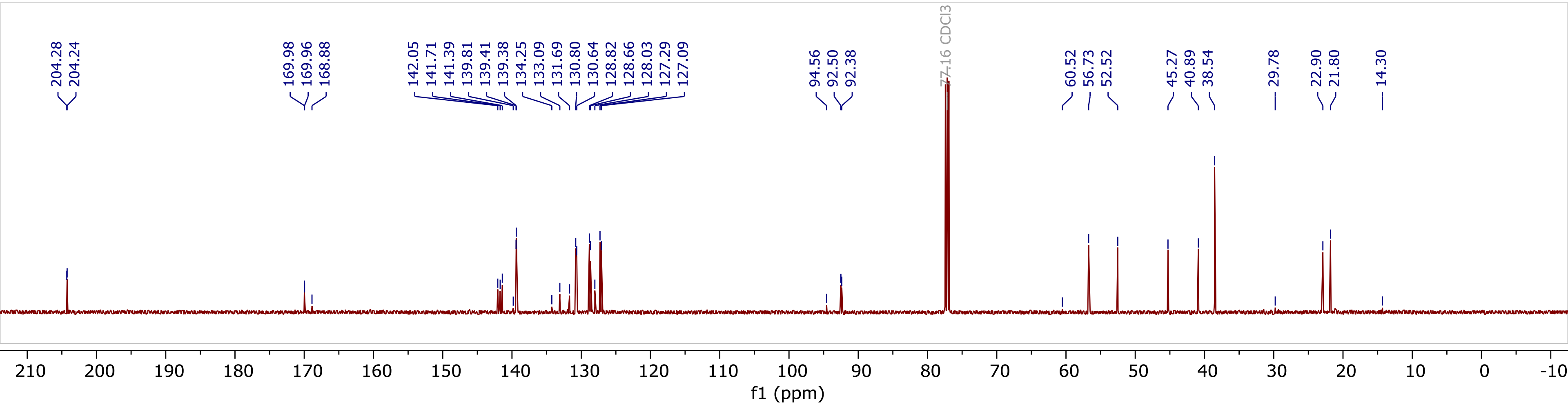


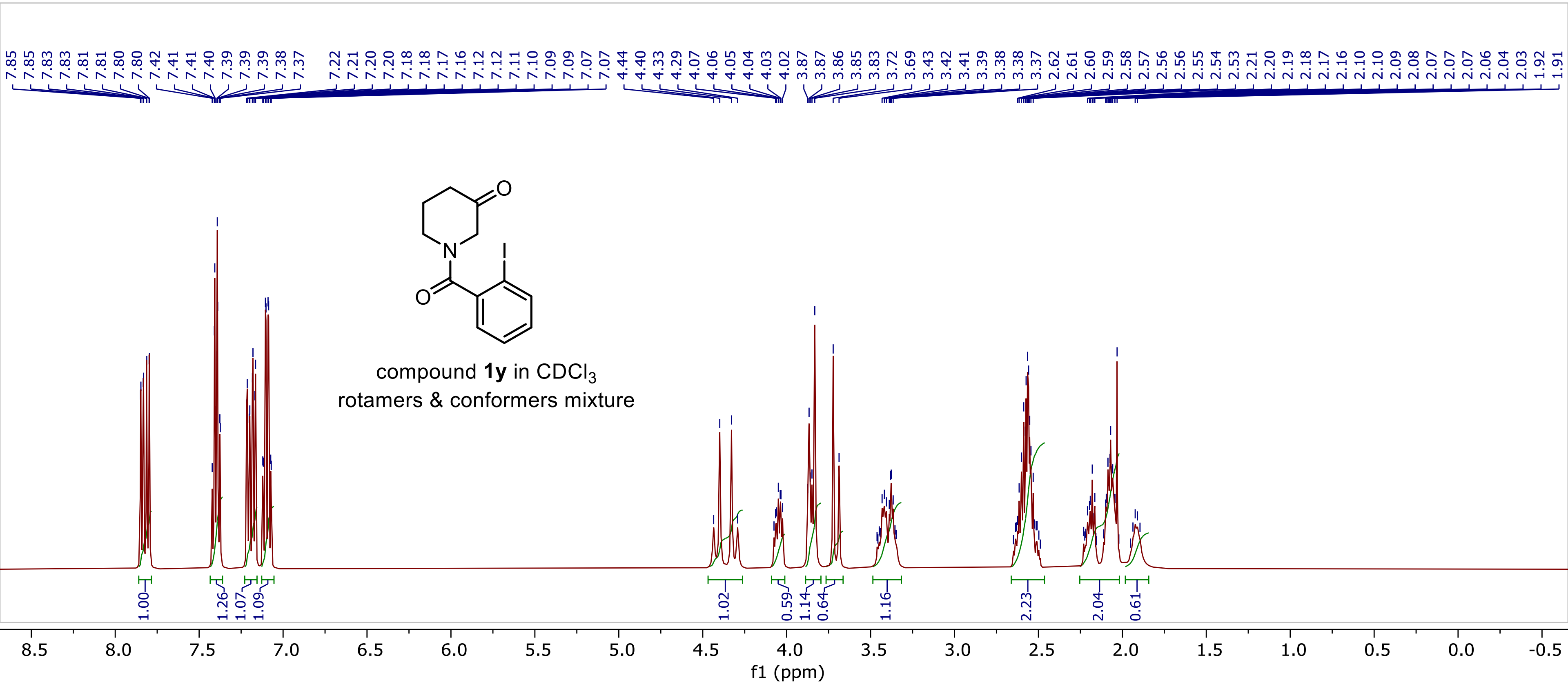
compound **1x** in $CDCl_3$ at rt
rotamers & conformers mixture



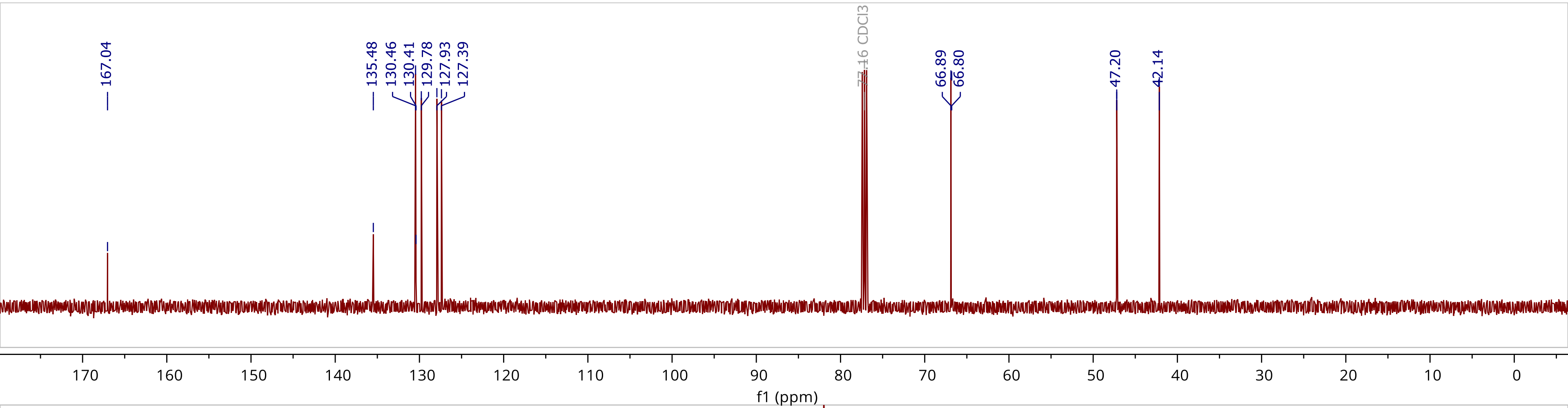


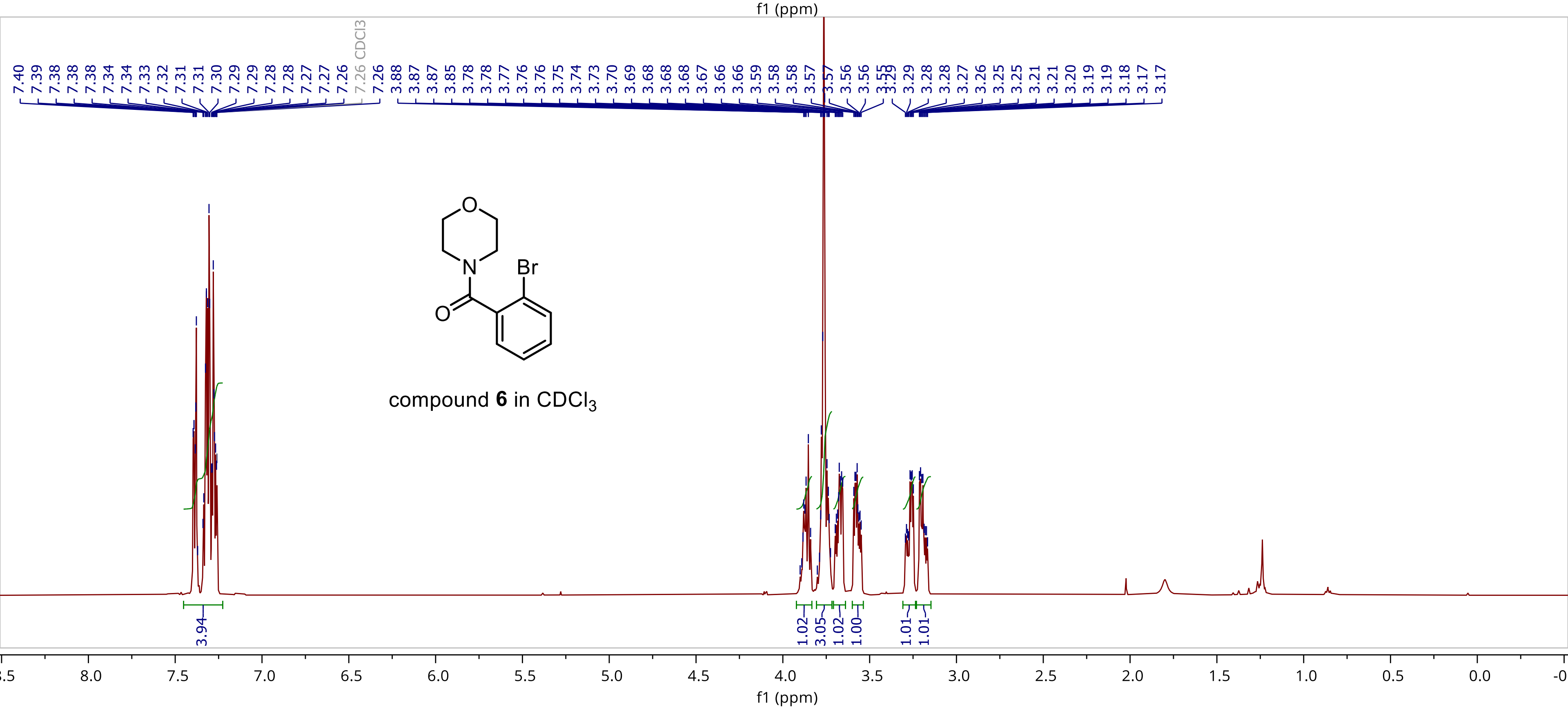
compound **1x** in DMSO-d_6 at 80 ^{o}C
rotamers & conformers mixture



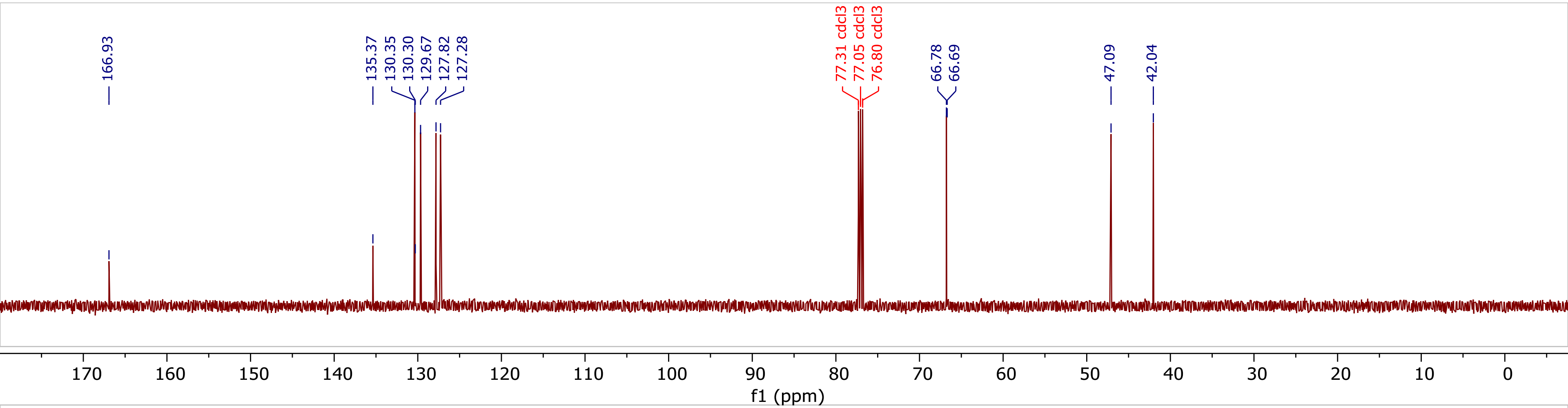


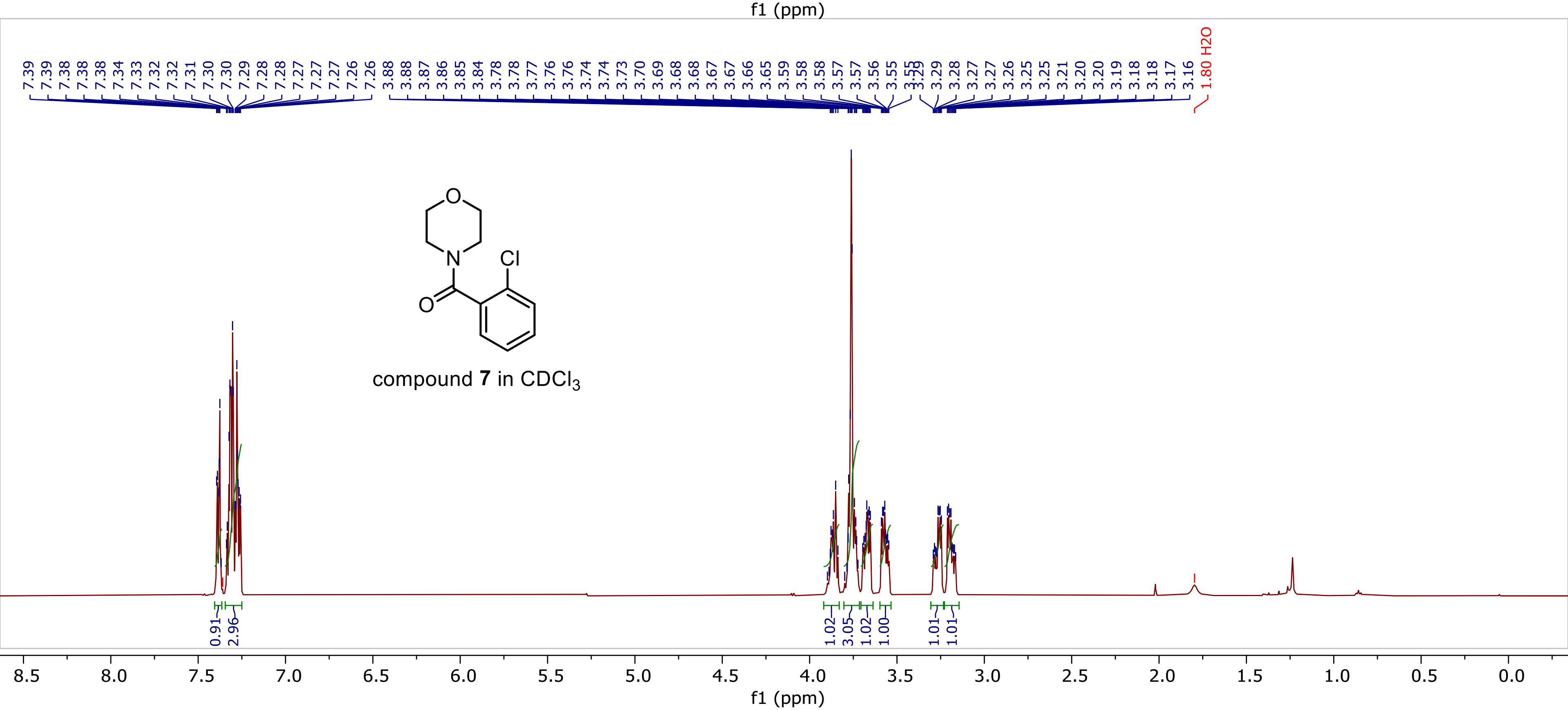
compound **1y** in $CDCl_3$
rotamers & conformers mixture



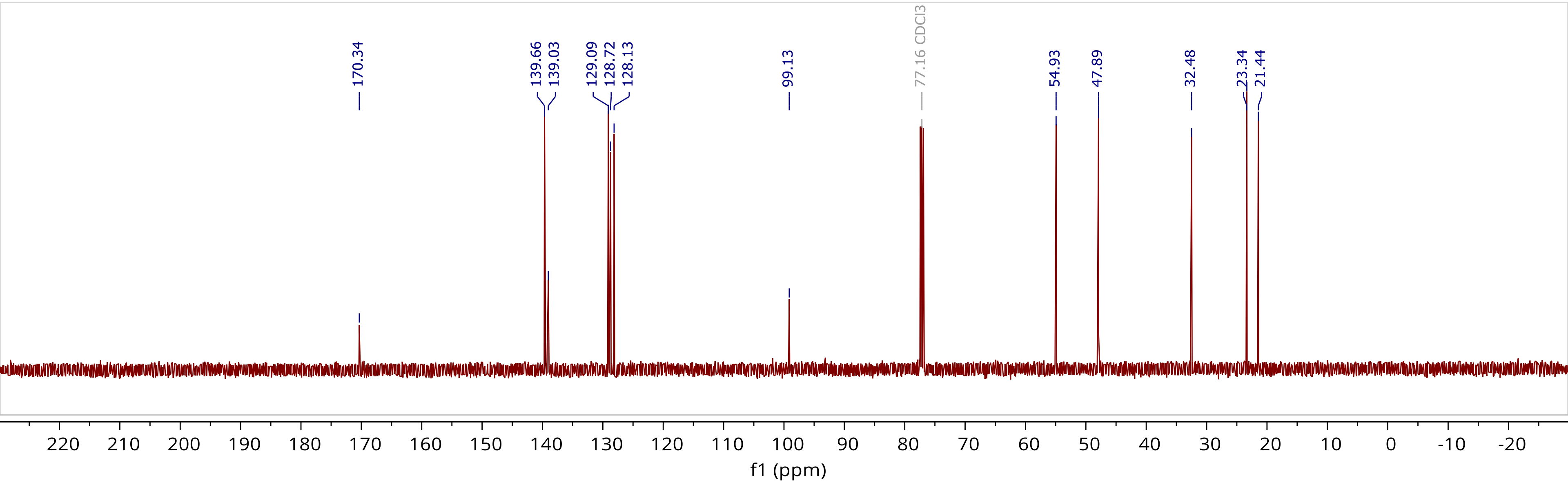


compound **6** in CDCl$_3$





compound **7** in CDCl$_3$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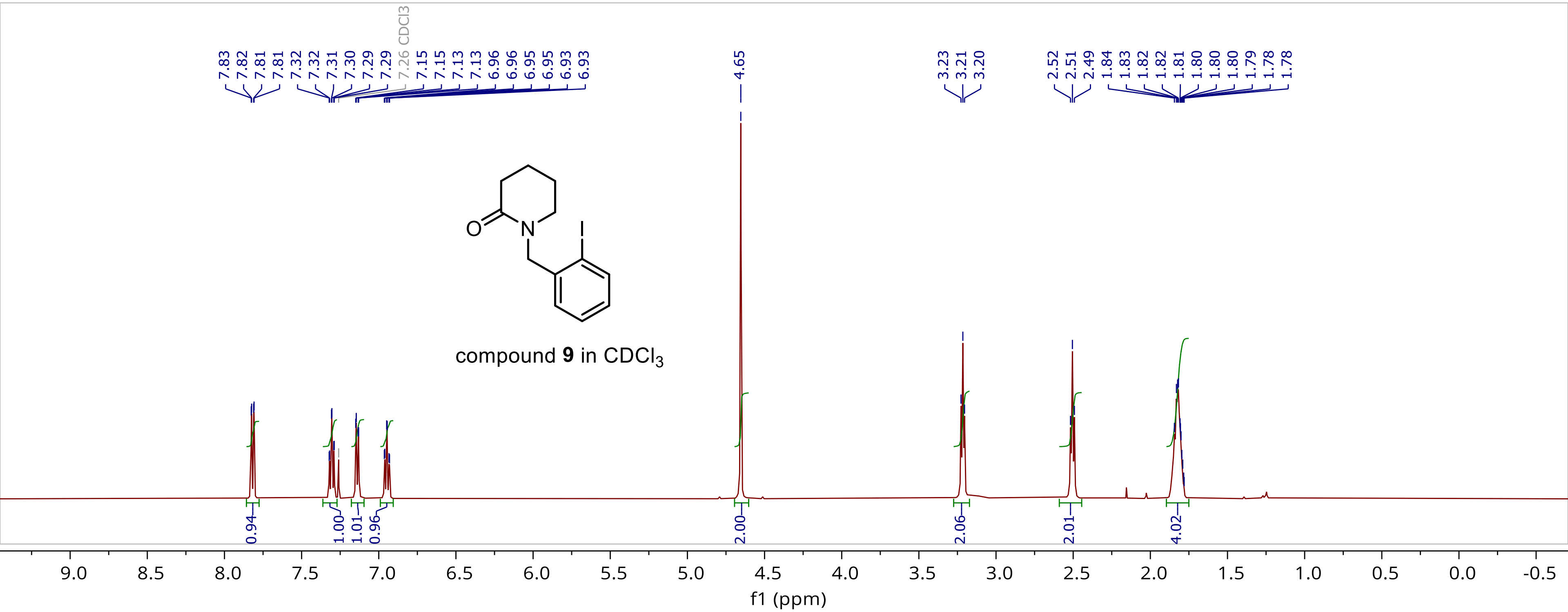
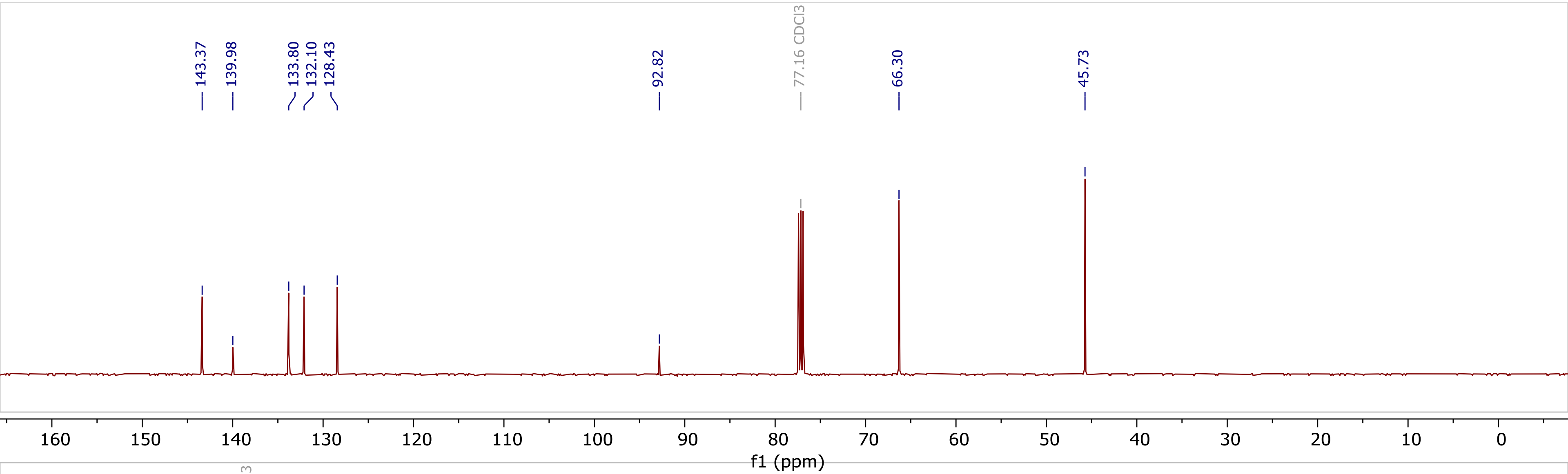
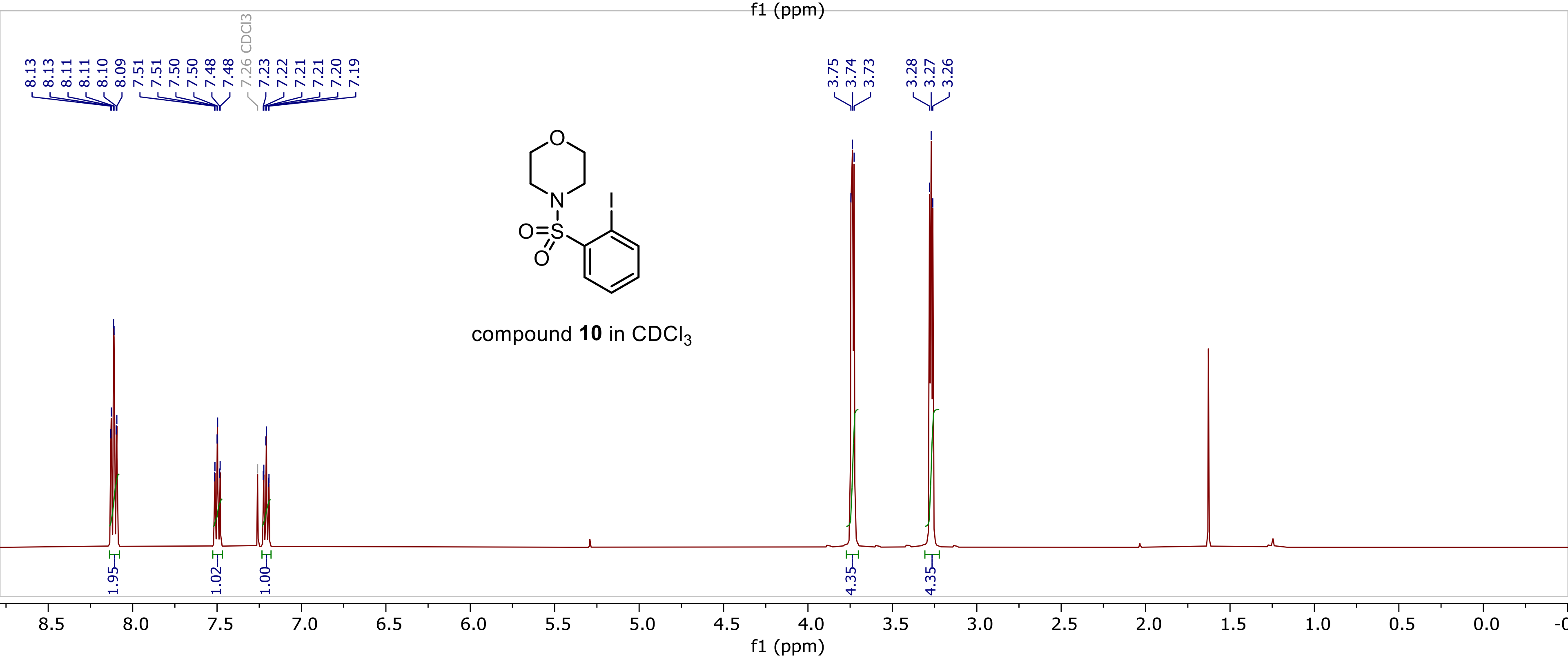
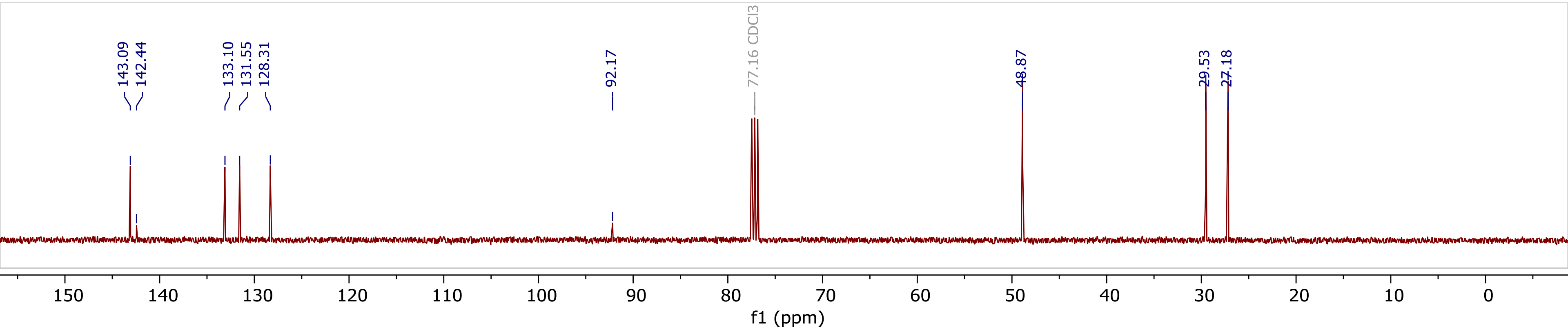
139.66
139.03
129.09
128.72
128.13
99.13
77.16 CDCl3
54.93
47.89
32.48
23.34
21.44
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

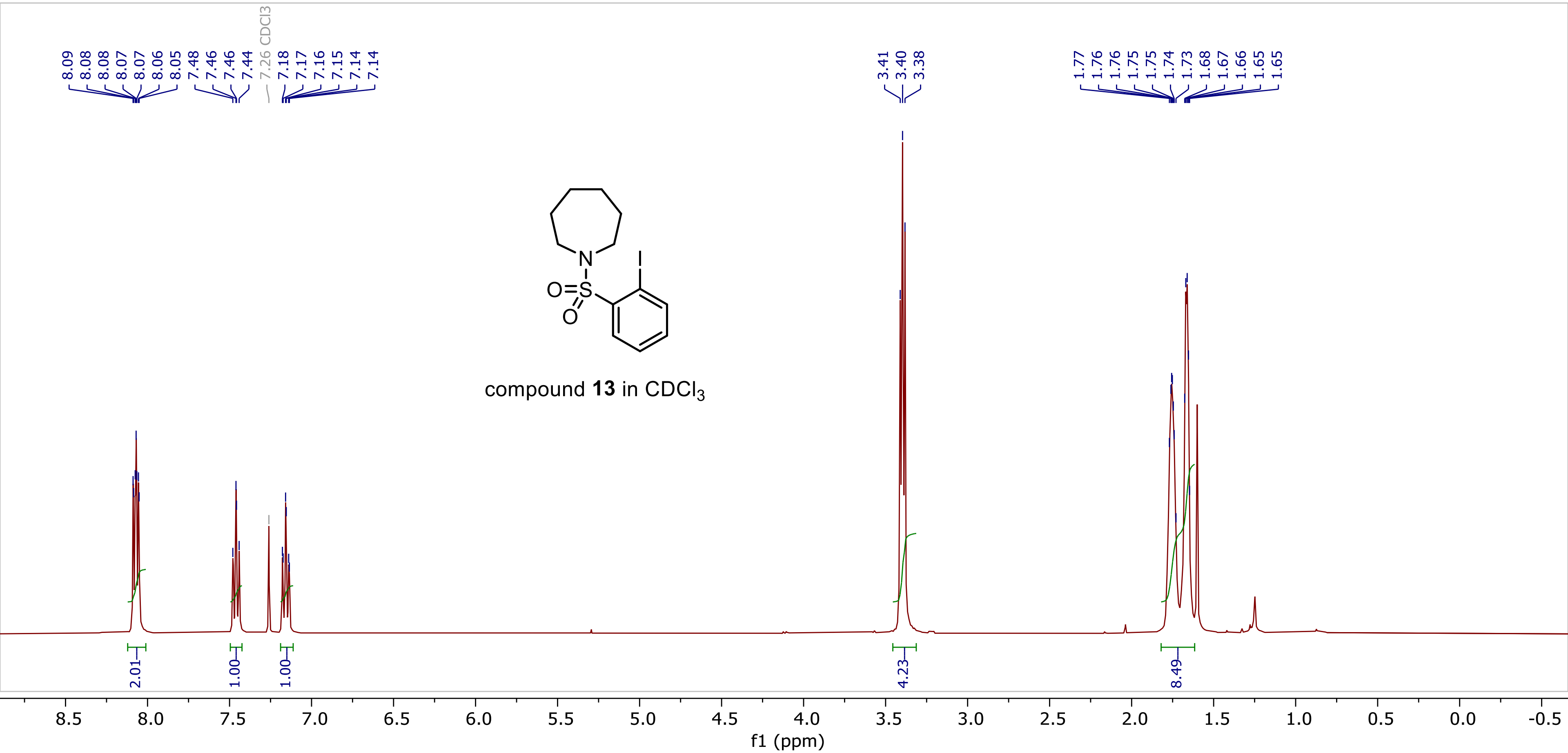

7.83
7.82
7.81
7.81
7.32
7.32
7.31
7.30
7.29
7.29
7.26 CDCl3
7.15
7.15
7.13
7.13
6.96
6.96
6.95
6.95
6.93
6.93
4.65
3.23
3.21
3.20
2.52
2.51
2.49
1.84
1.83
1.82
1.82
1.81
1.80
1.80
1.80
1.79
1.78
1.78
O
N
I
compound 9 in CDCl3
0.94
1.00
1.01
0.96
2.00
2.06
2.01
4.02
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)



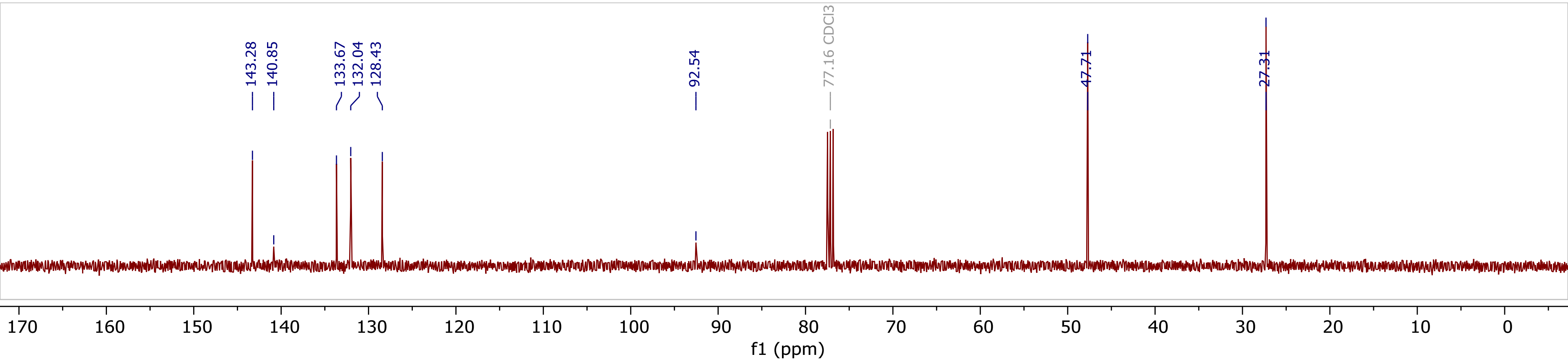


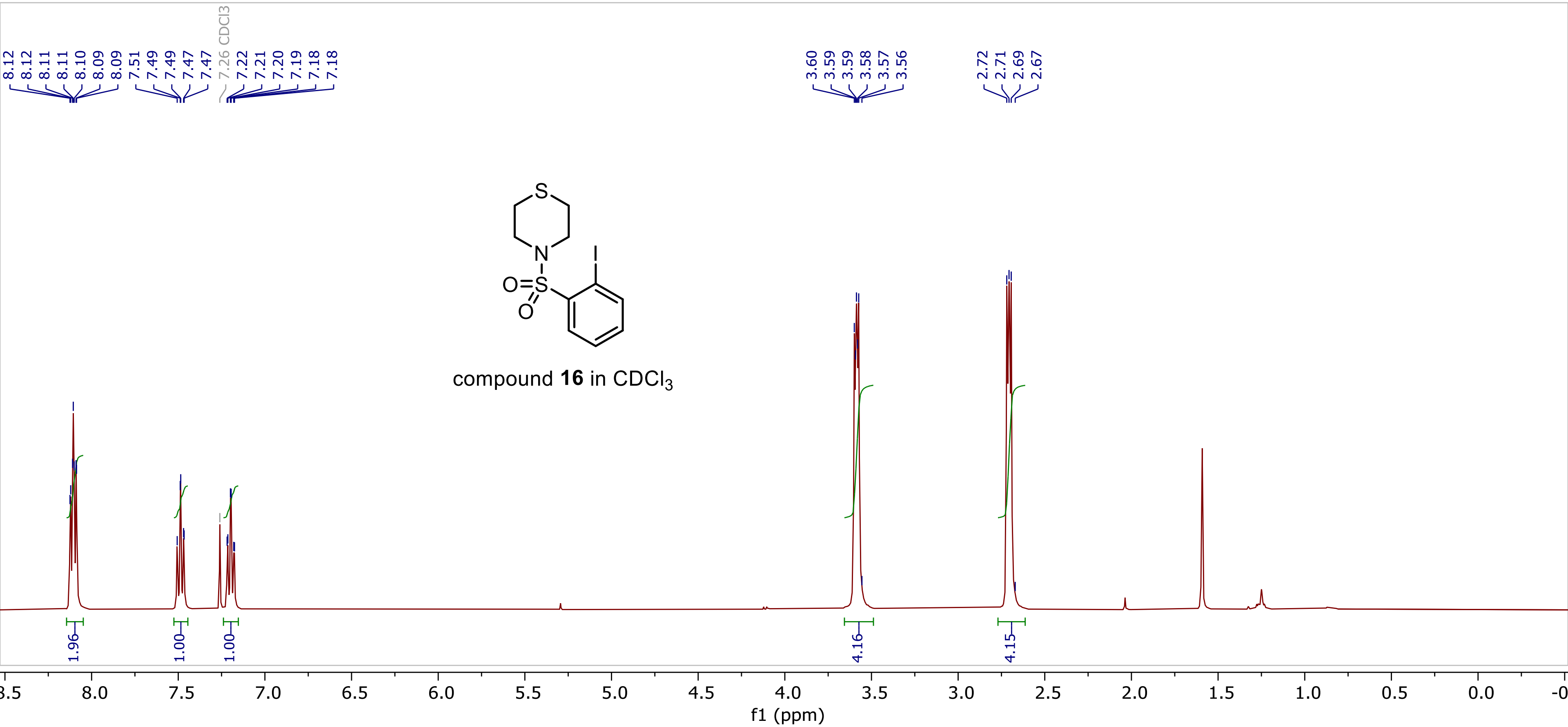
compound **10** in CDCl$_3$



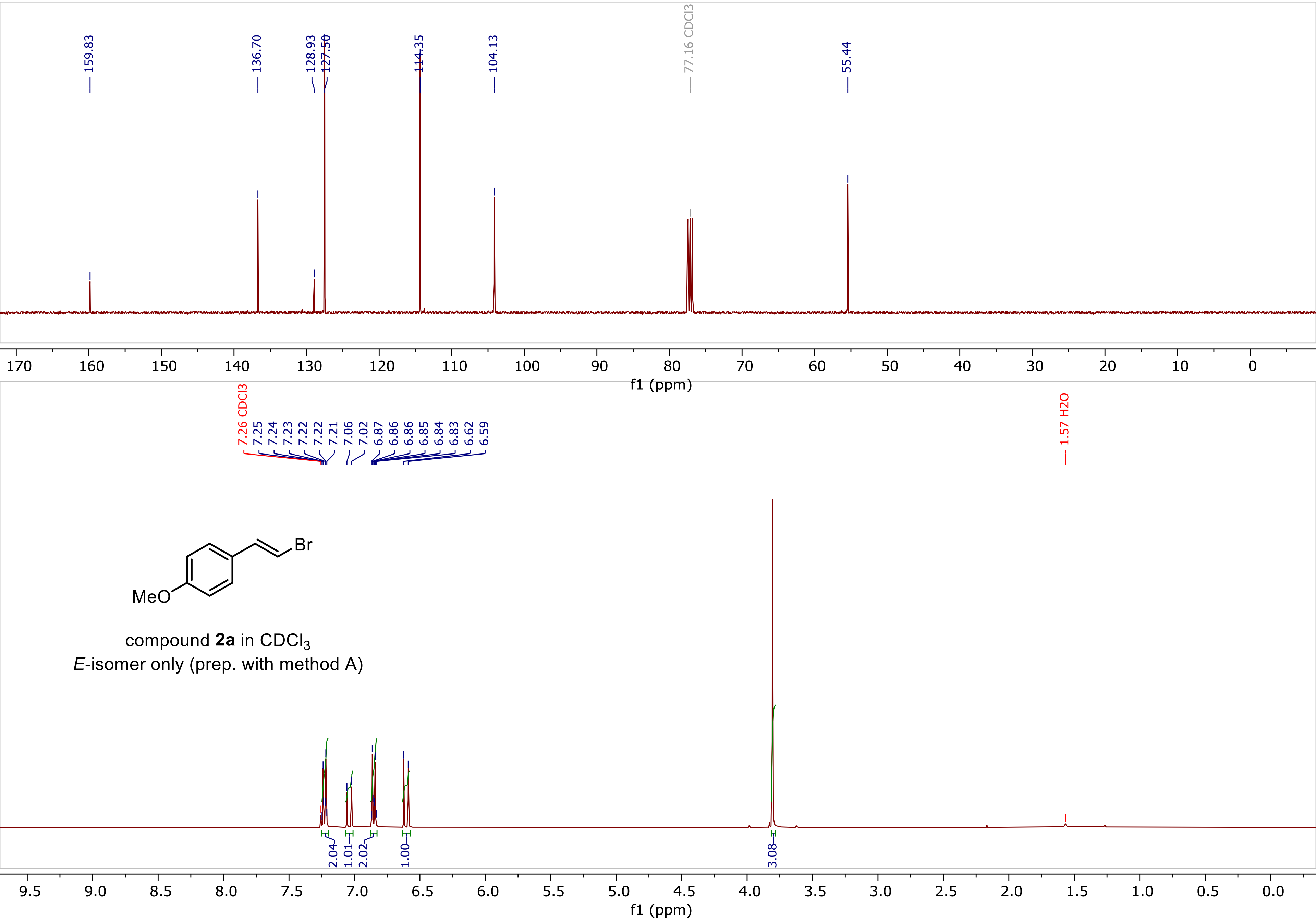


compound **13** in $CDCl_3$



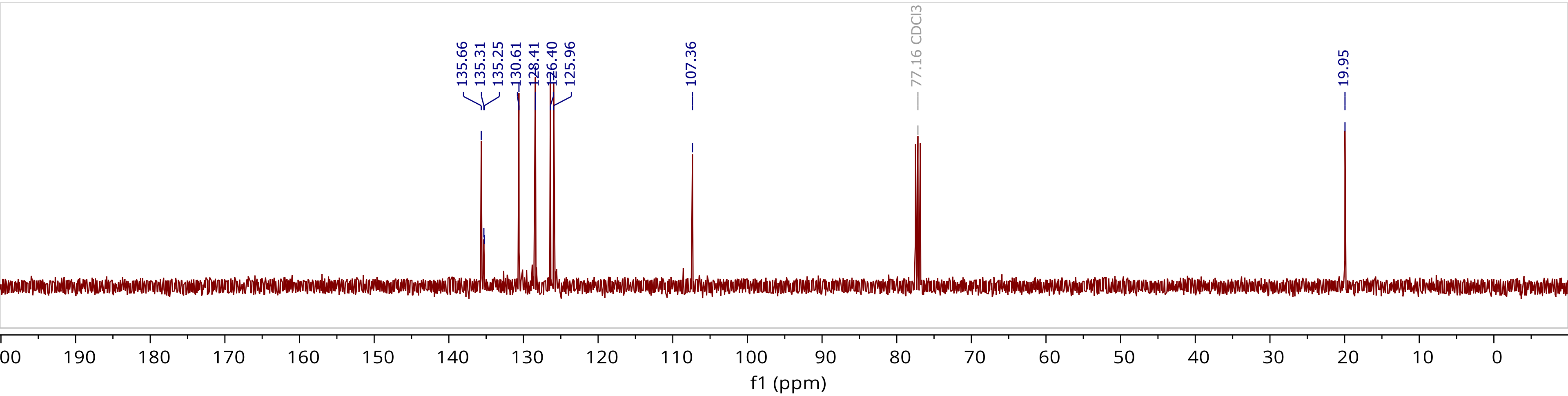


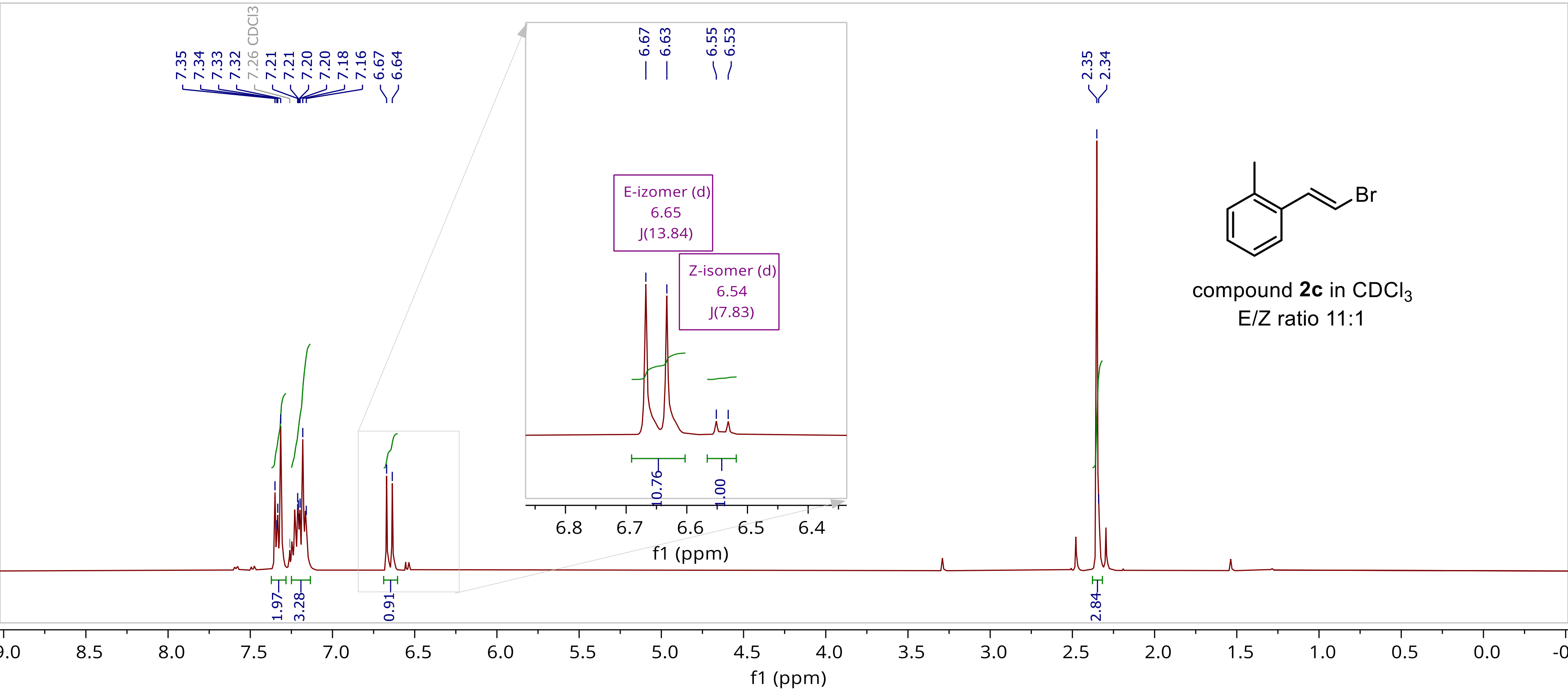
compound **16** in $CDCl_3$



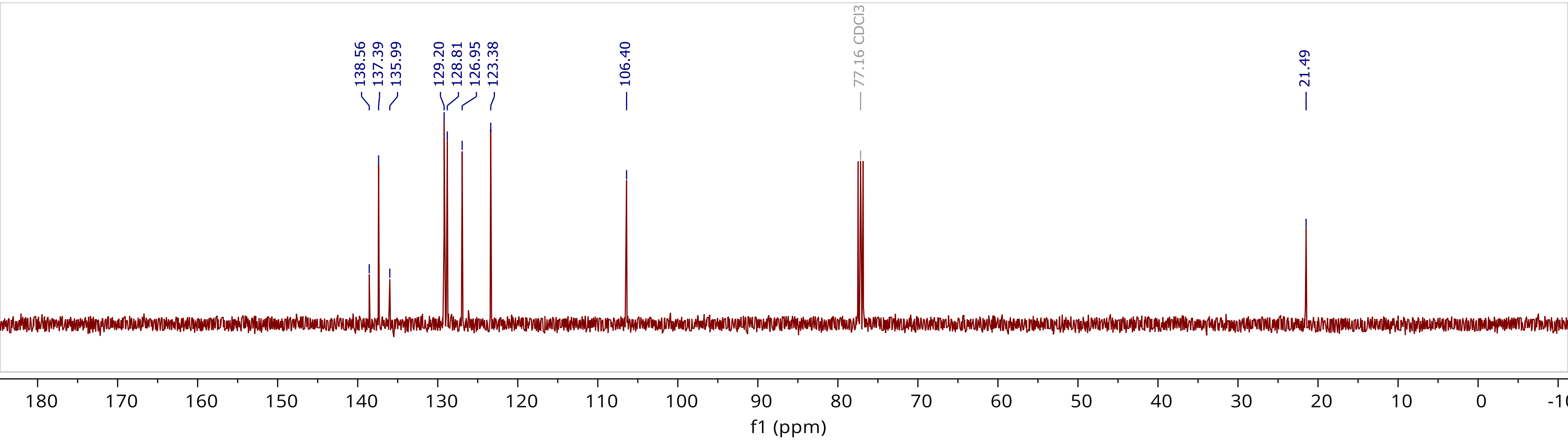
compound **2a** in $CDCl_3$

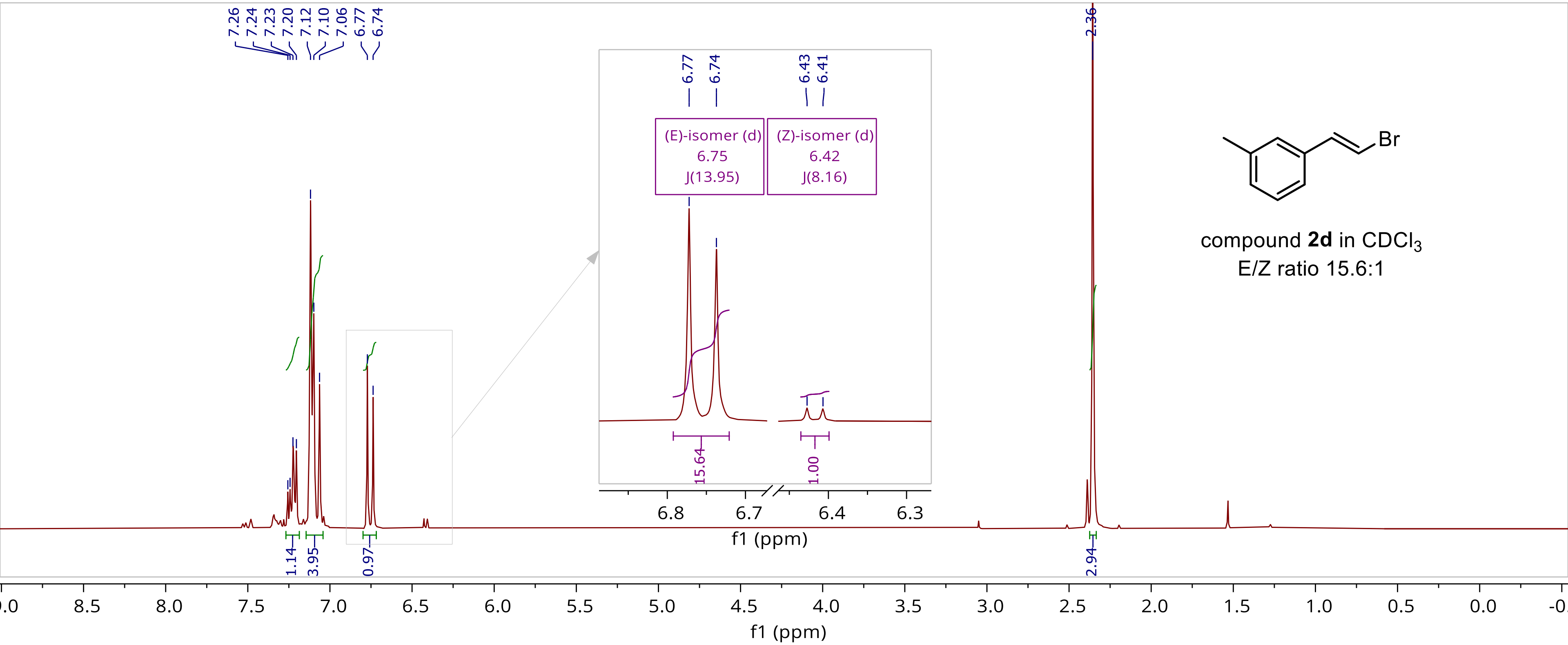
E-isomer only (prep. with method A)



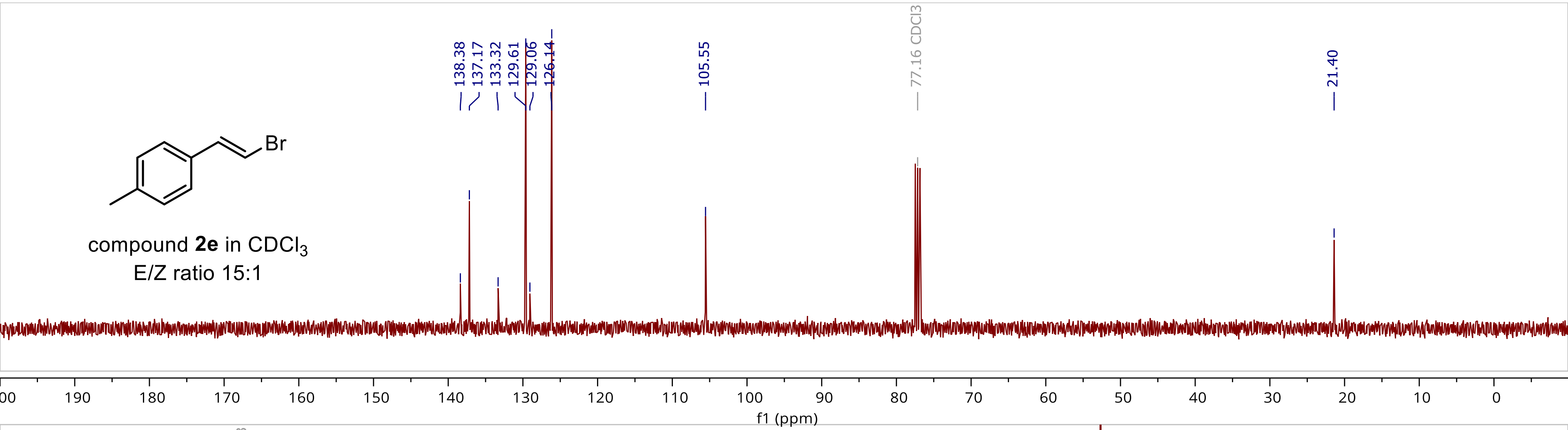


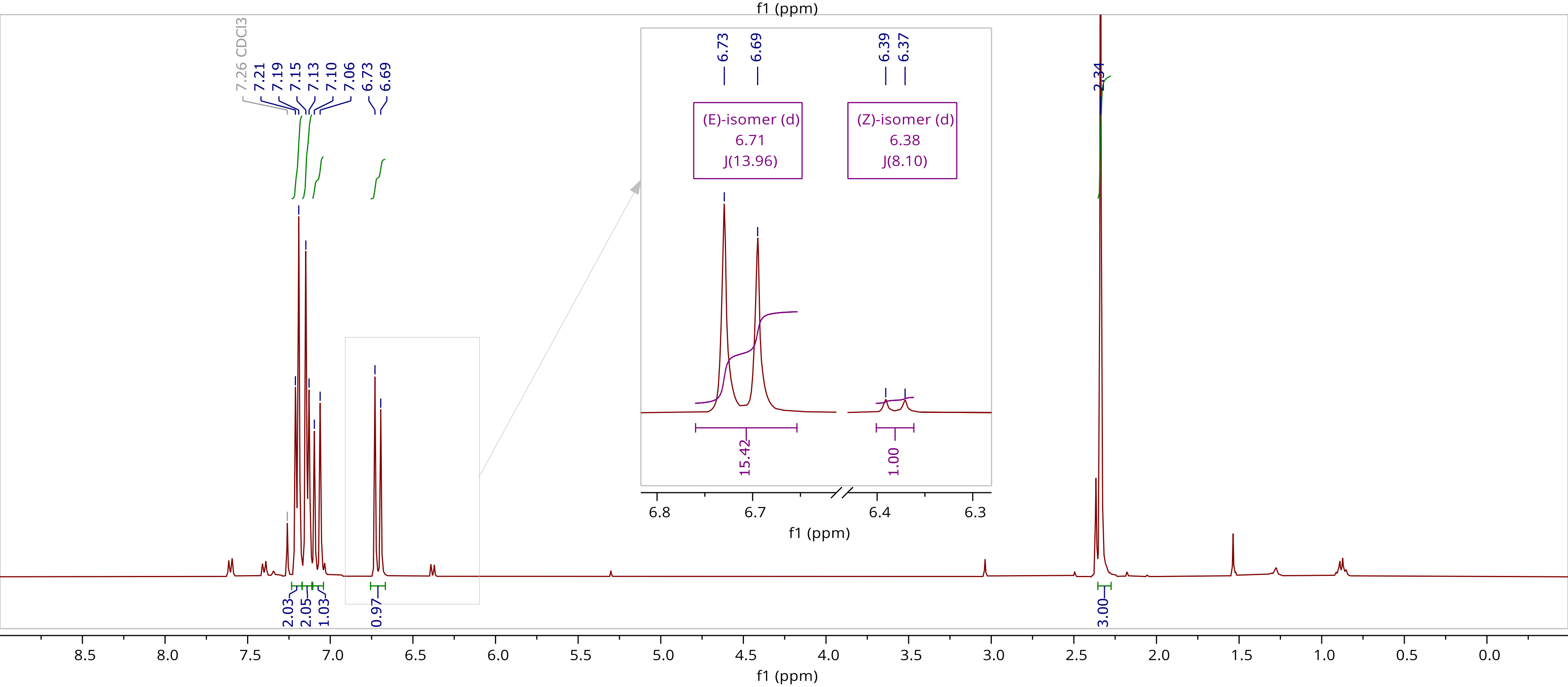
compound **2c** in CDCl$_3$
E/Z ratio 11:1

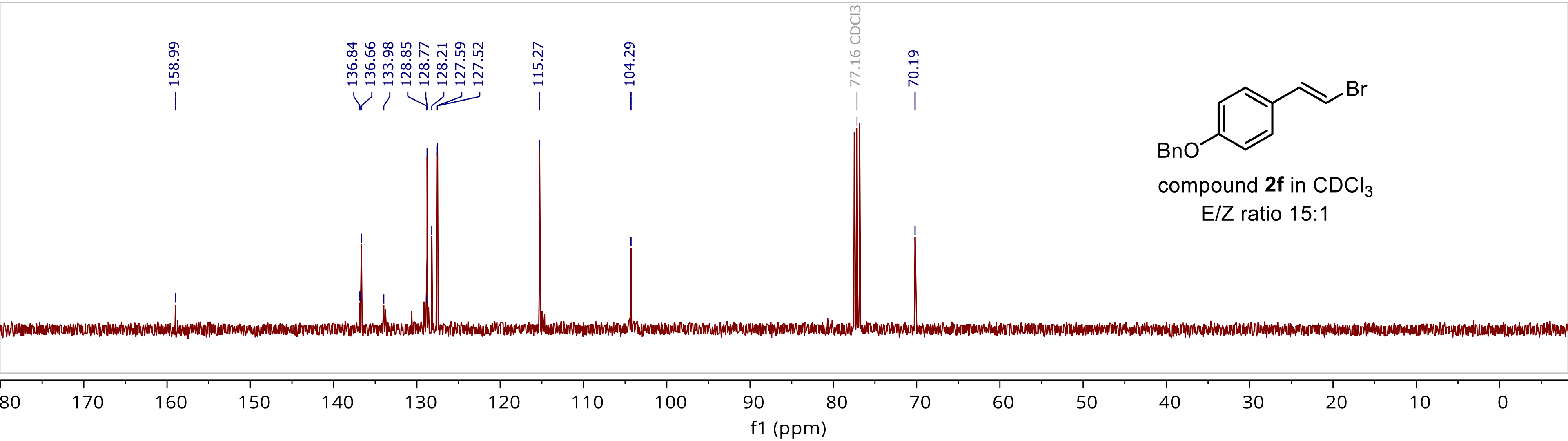




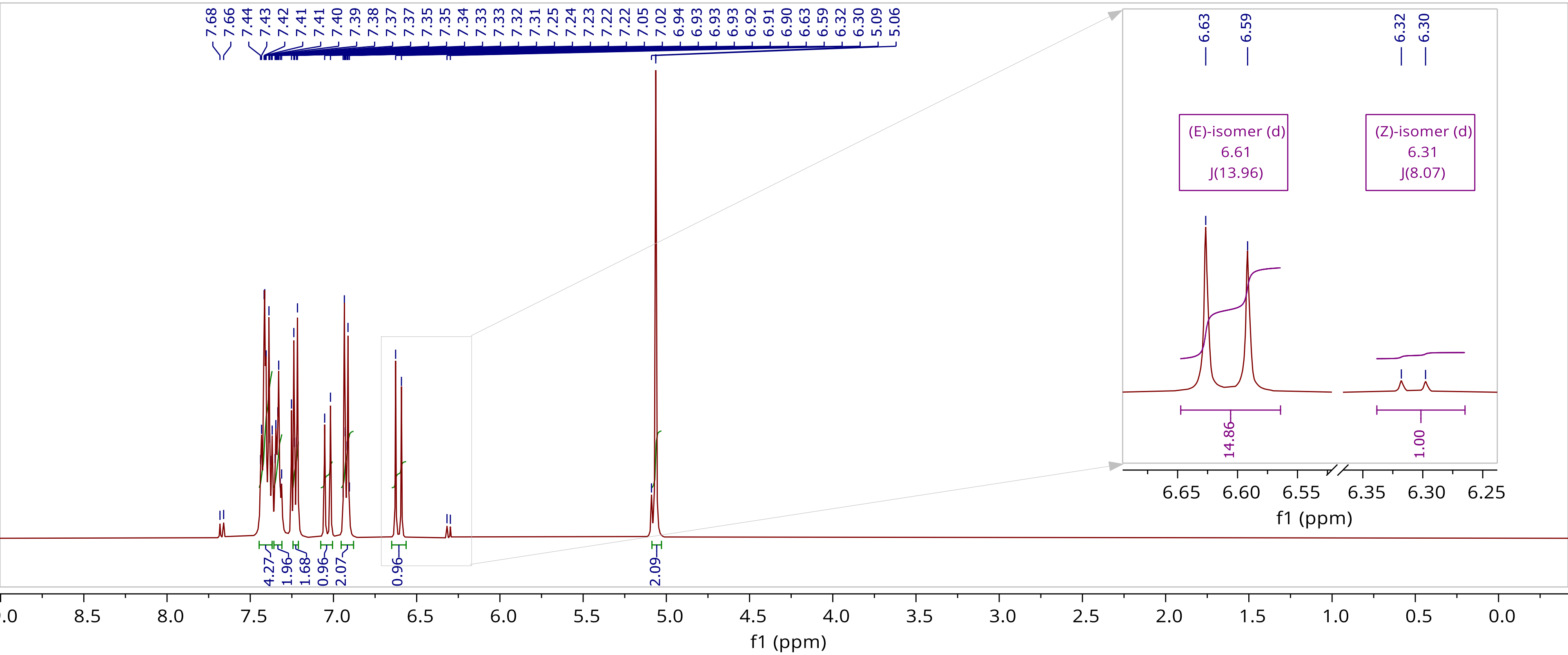
compound **2d** in CDCl$_3$
E/Z ratio 15.6:1

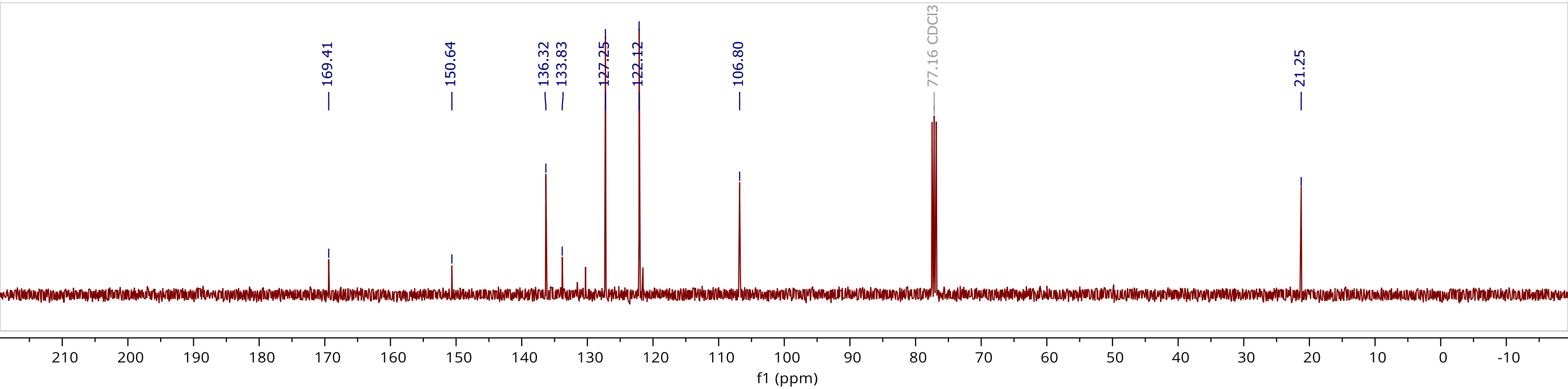

compound **2e** in $CDCl_3$
E/Z ratio 15:1

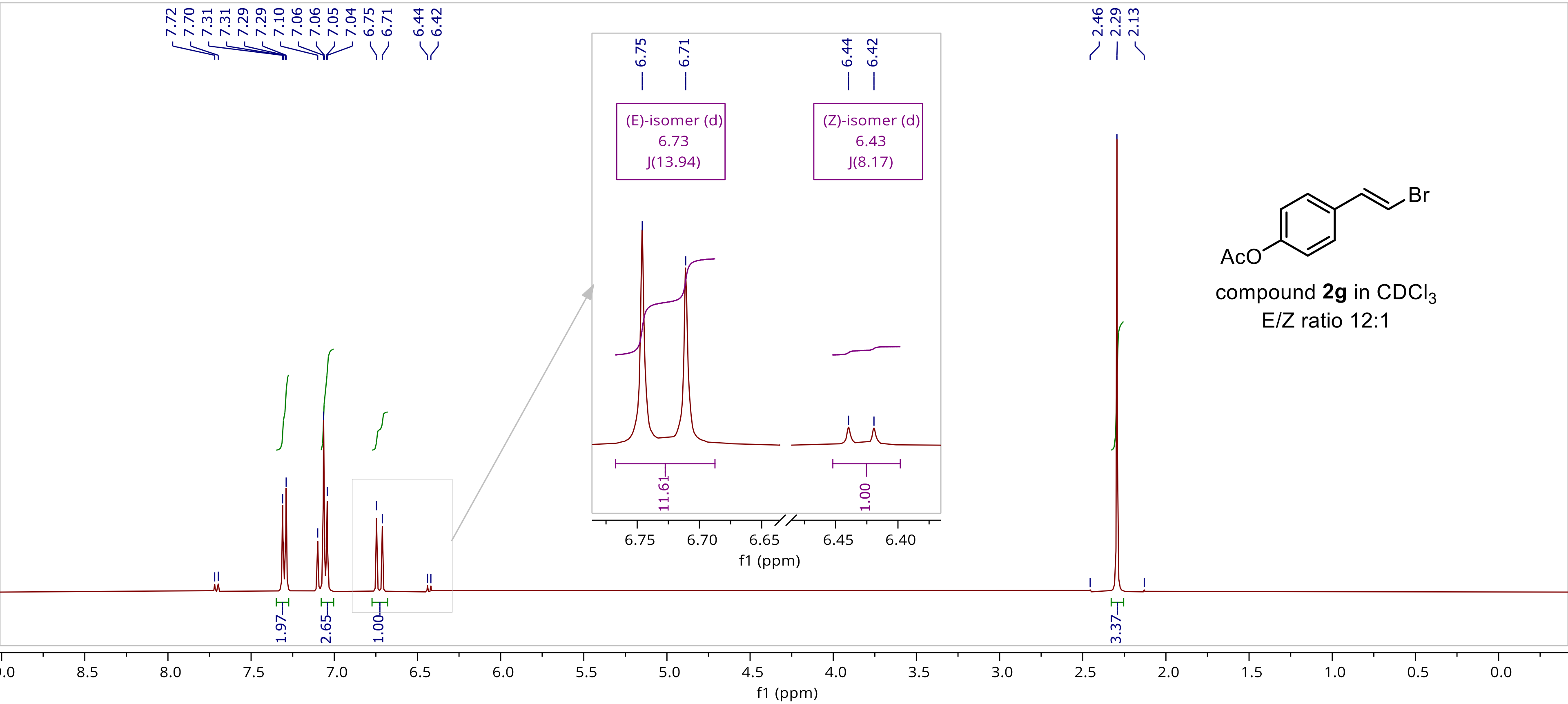




compound **2f** in $CDCl_3$
E/Z ratio 15:1

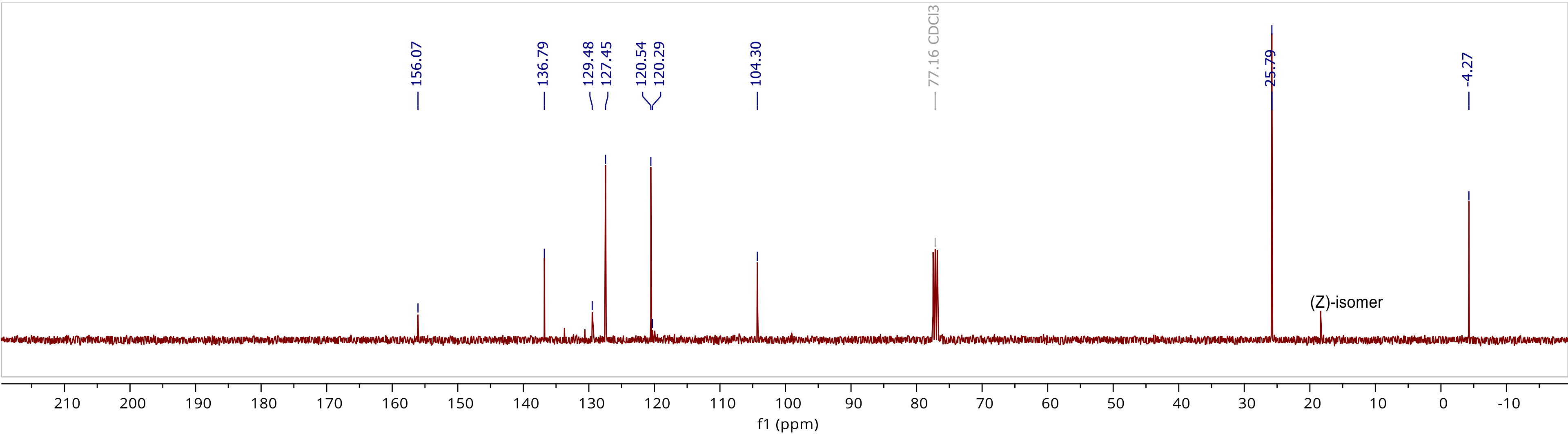


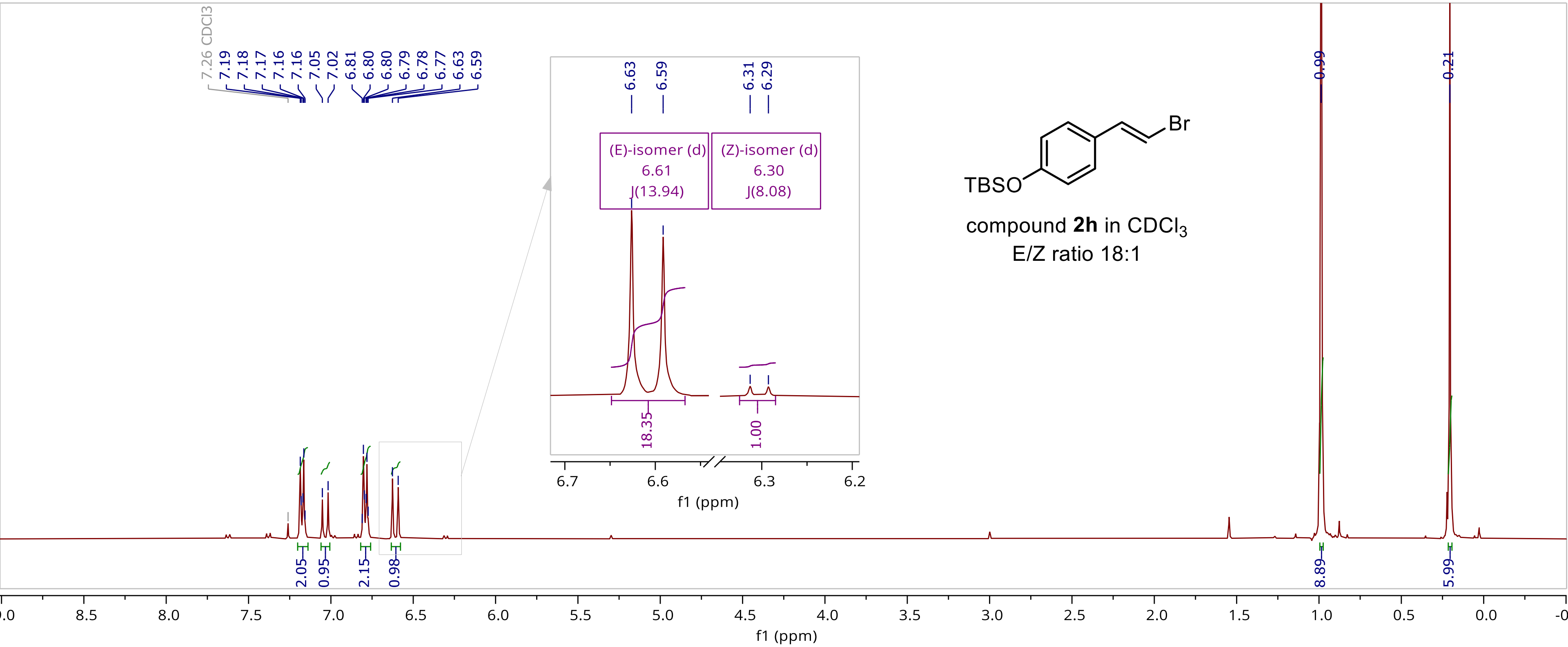




compound **2g** in $CDCl_3$

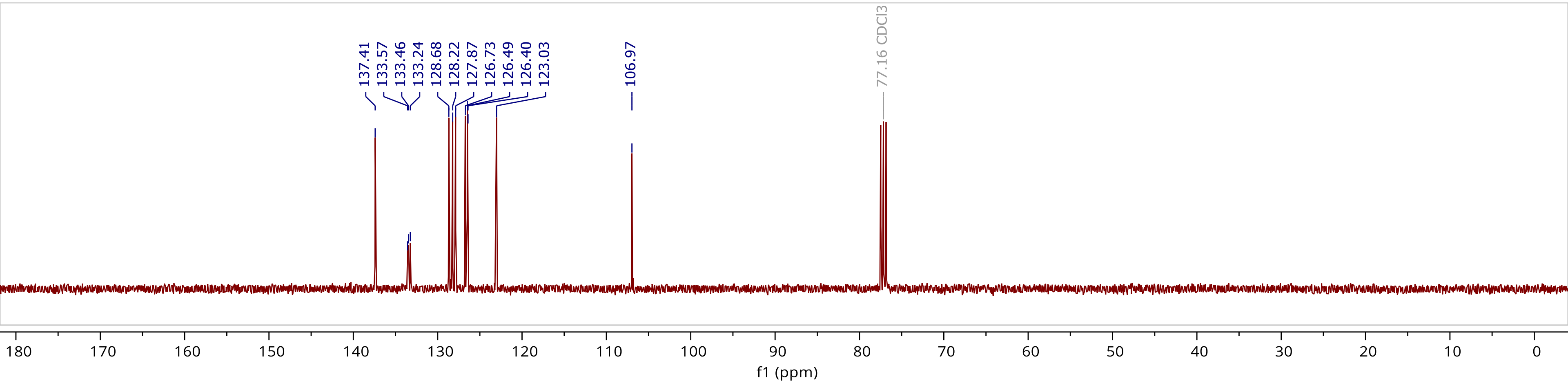
E/Z ratio 12:1

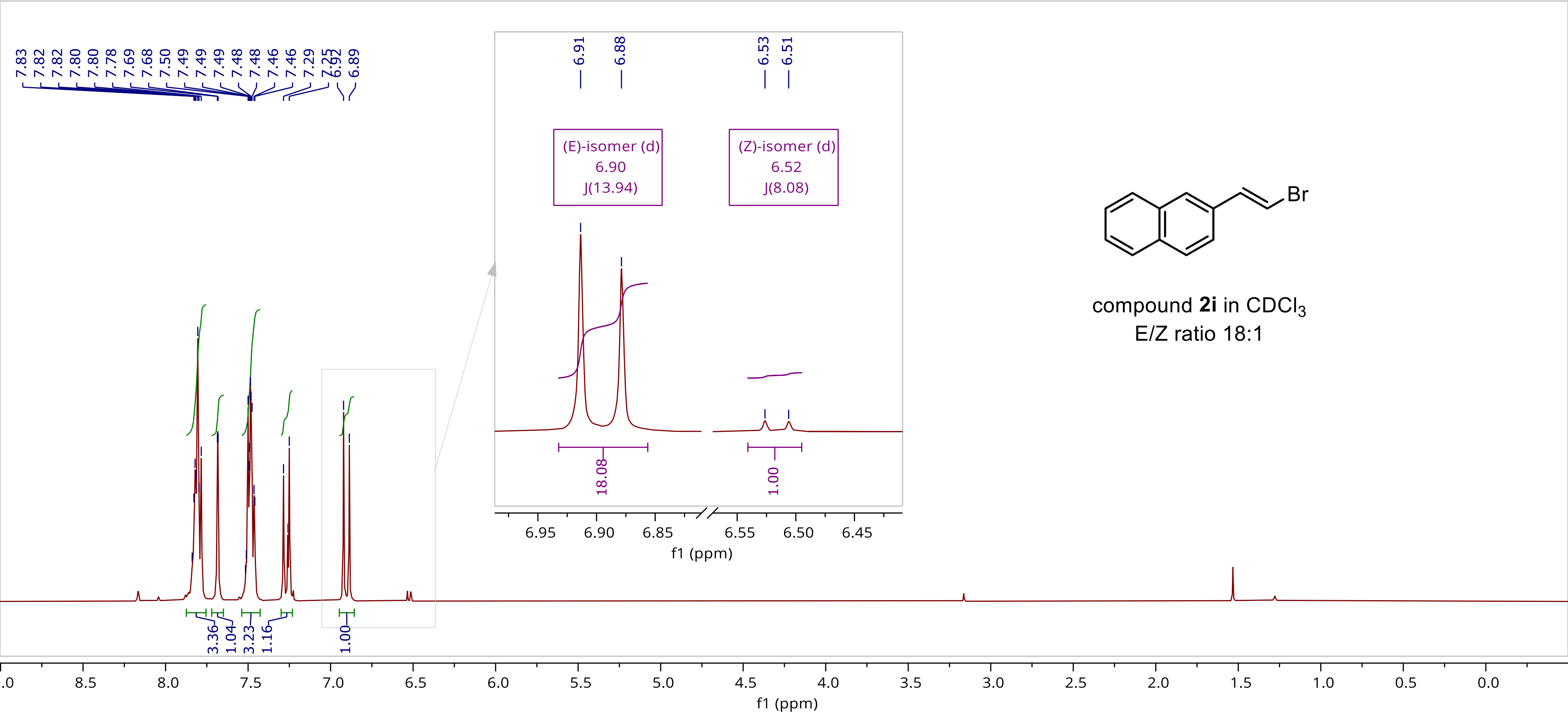




compound **2h** in $CDCl_3$

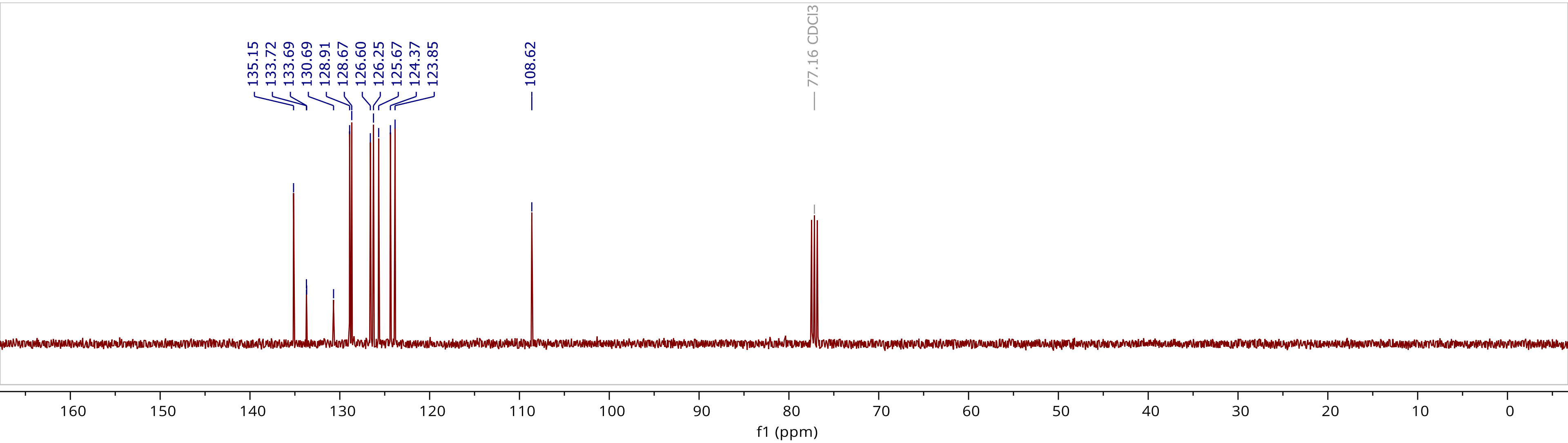
E/Z ratio 18:1

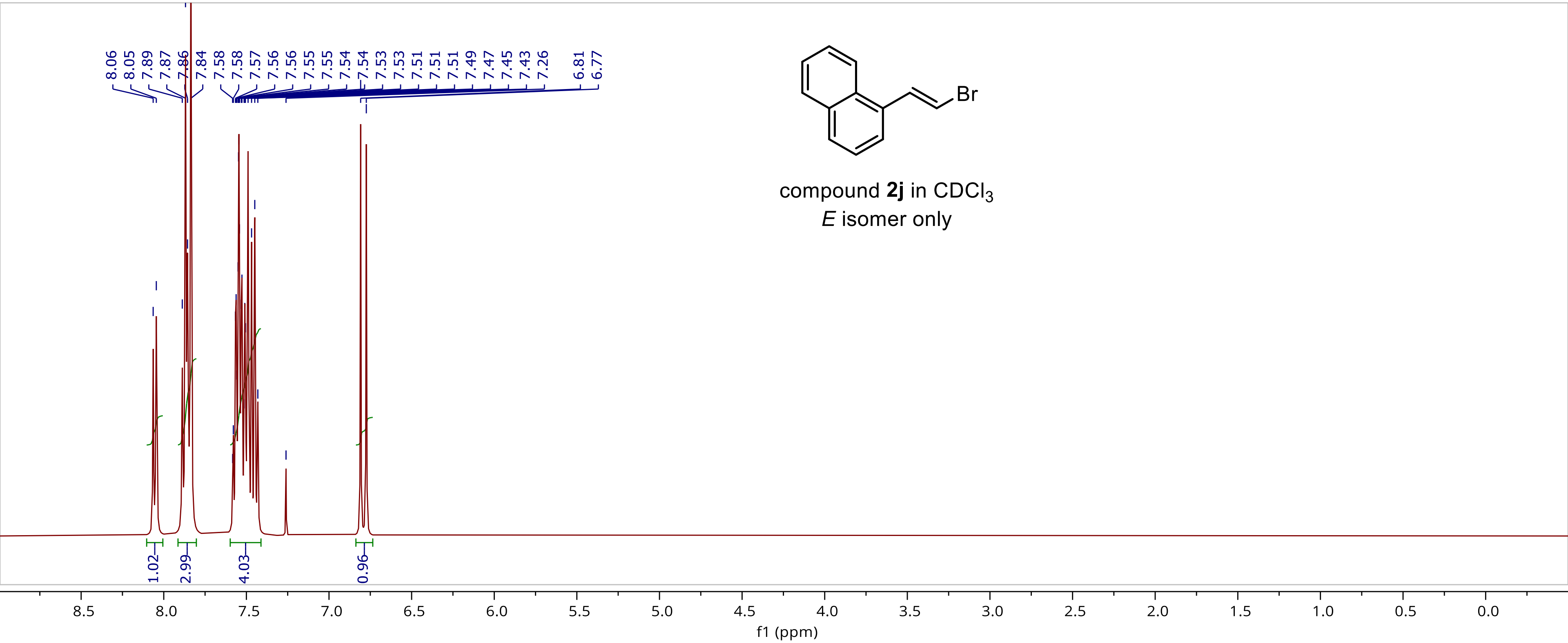




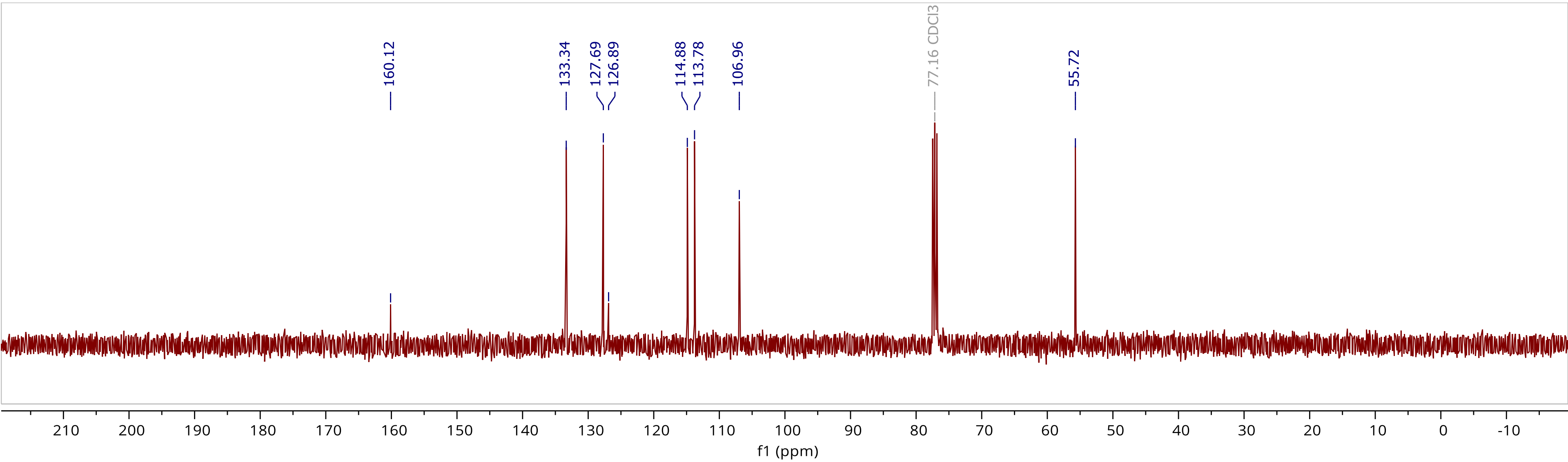
compound **2i** in CDCl$_3$

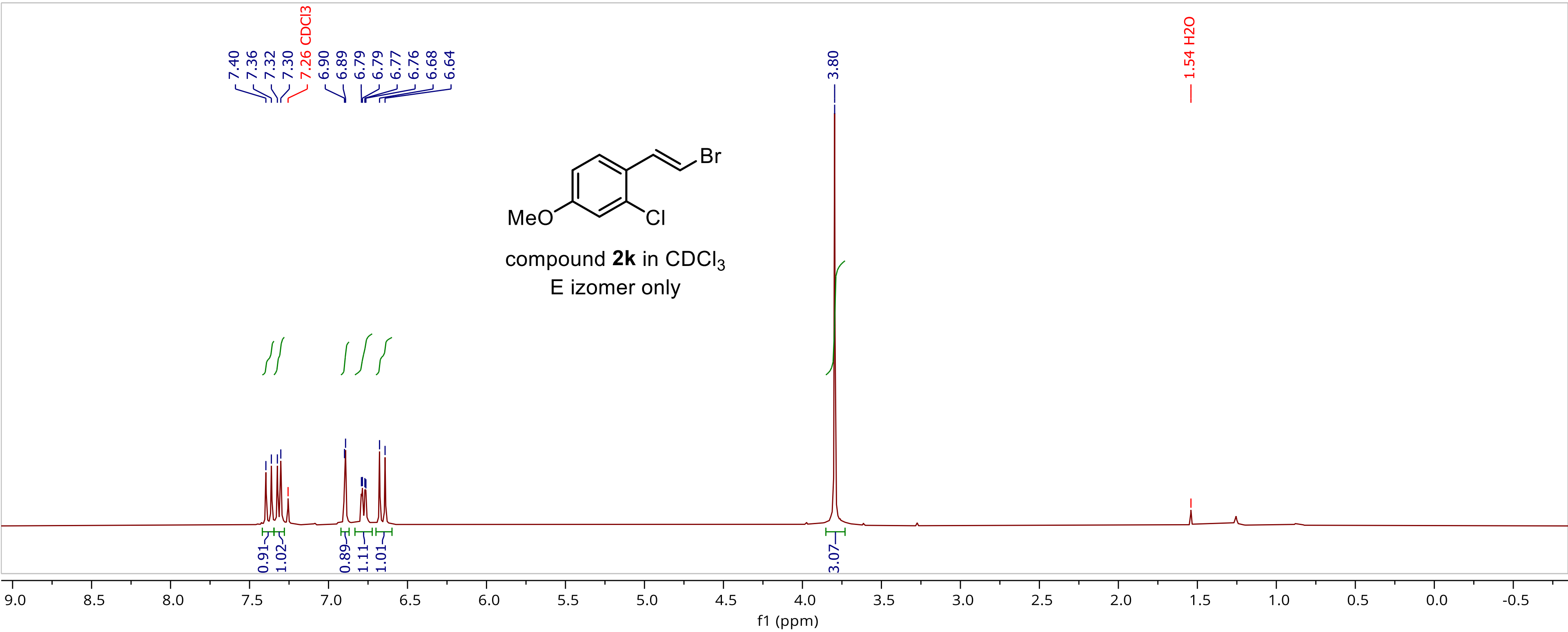
E/Z ratio 18:1



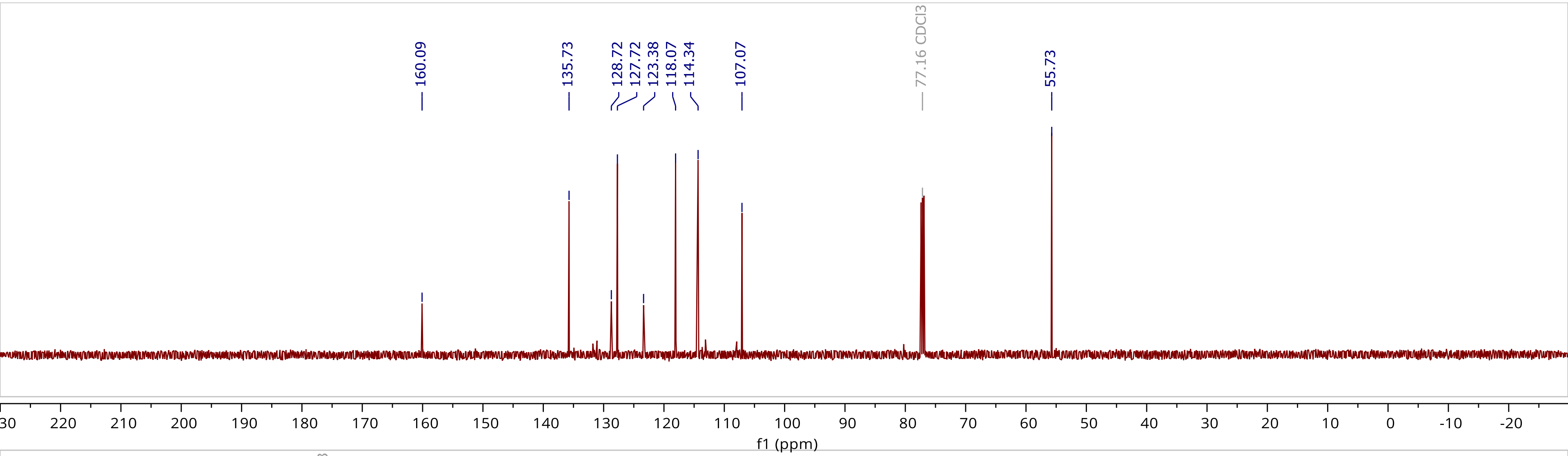


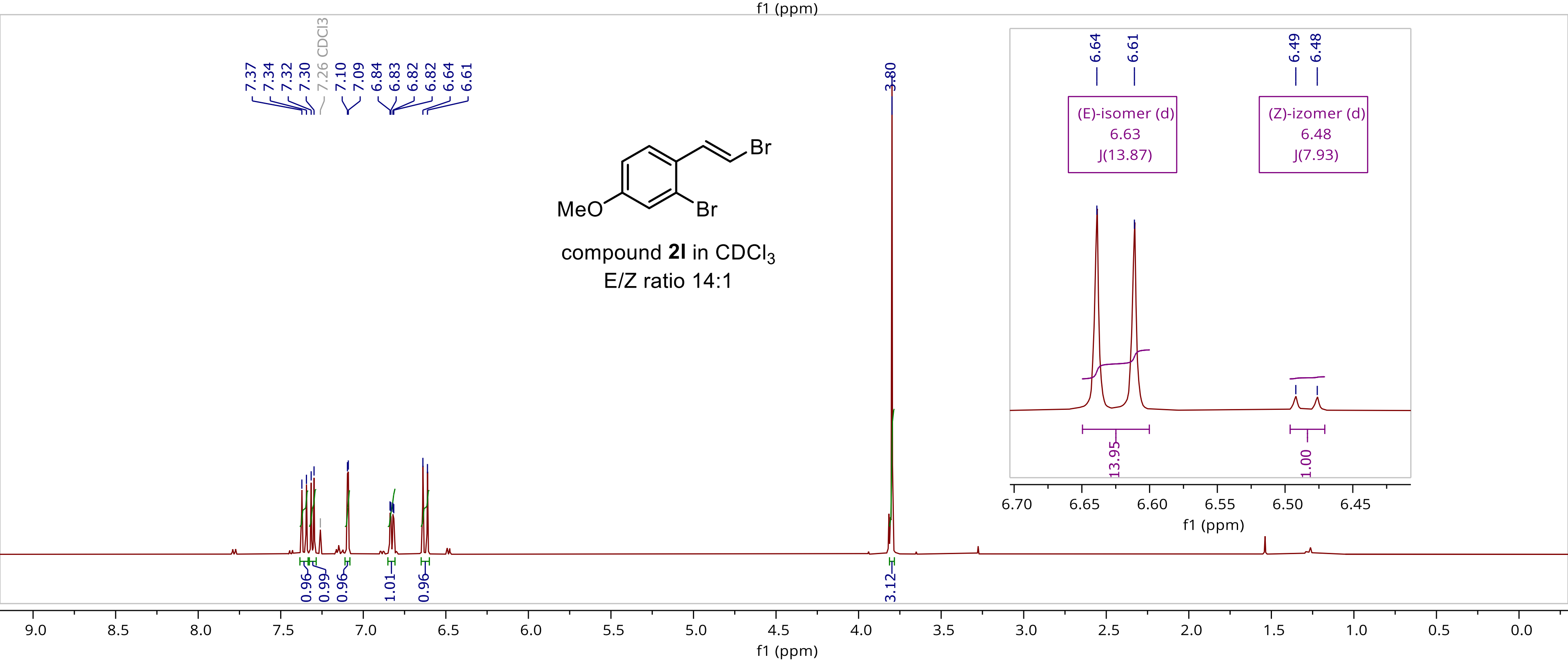
compound **2j** in $CDCl_3$
E isomer only





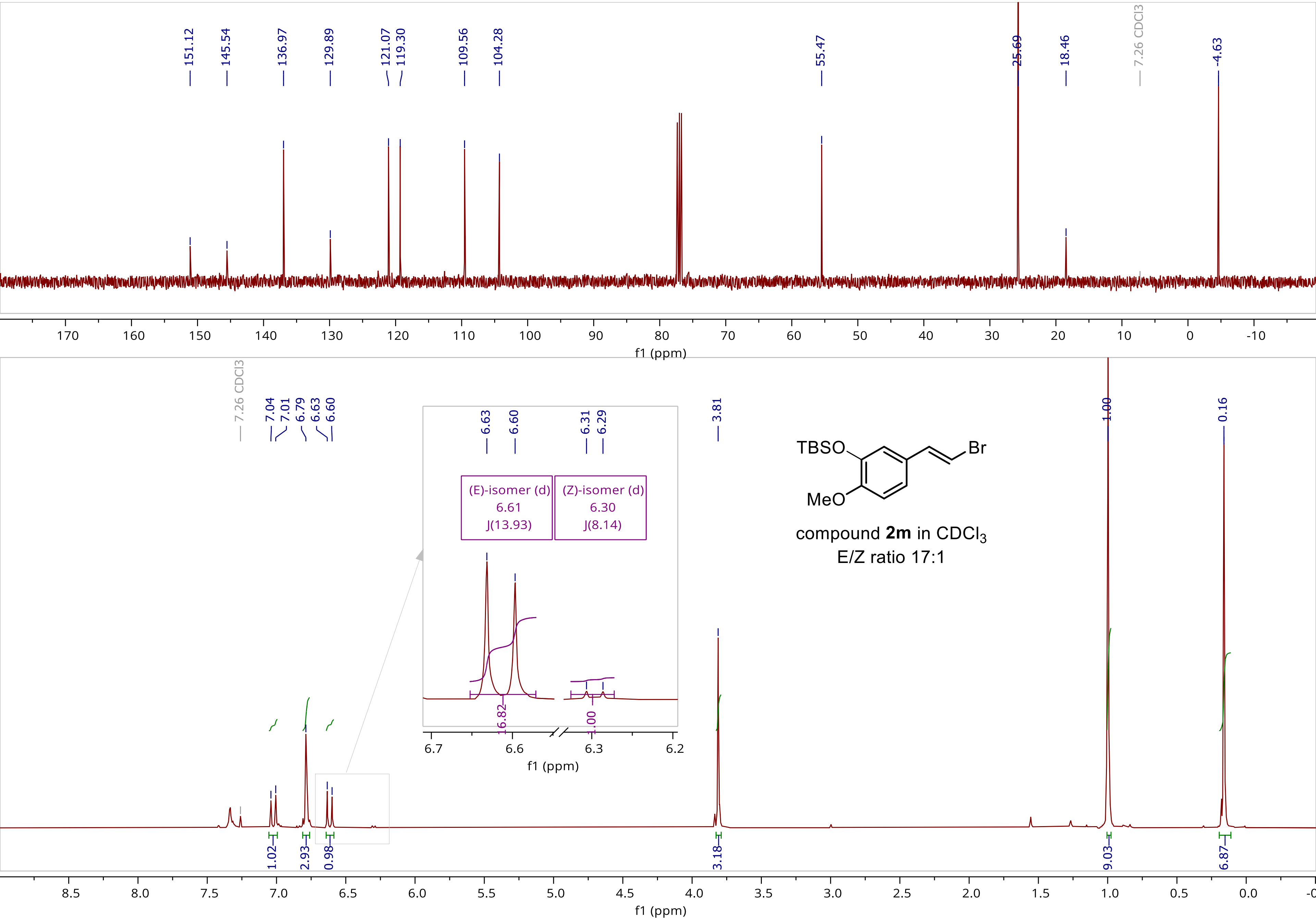
compound **2k** in $CDCl_3$
E izomer only

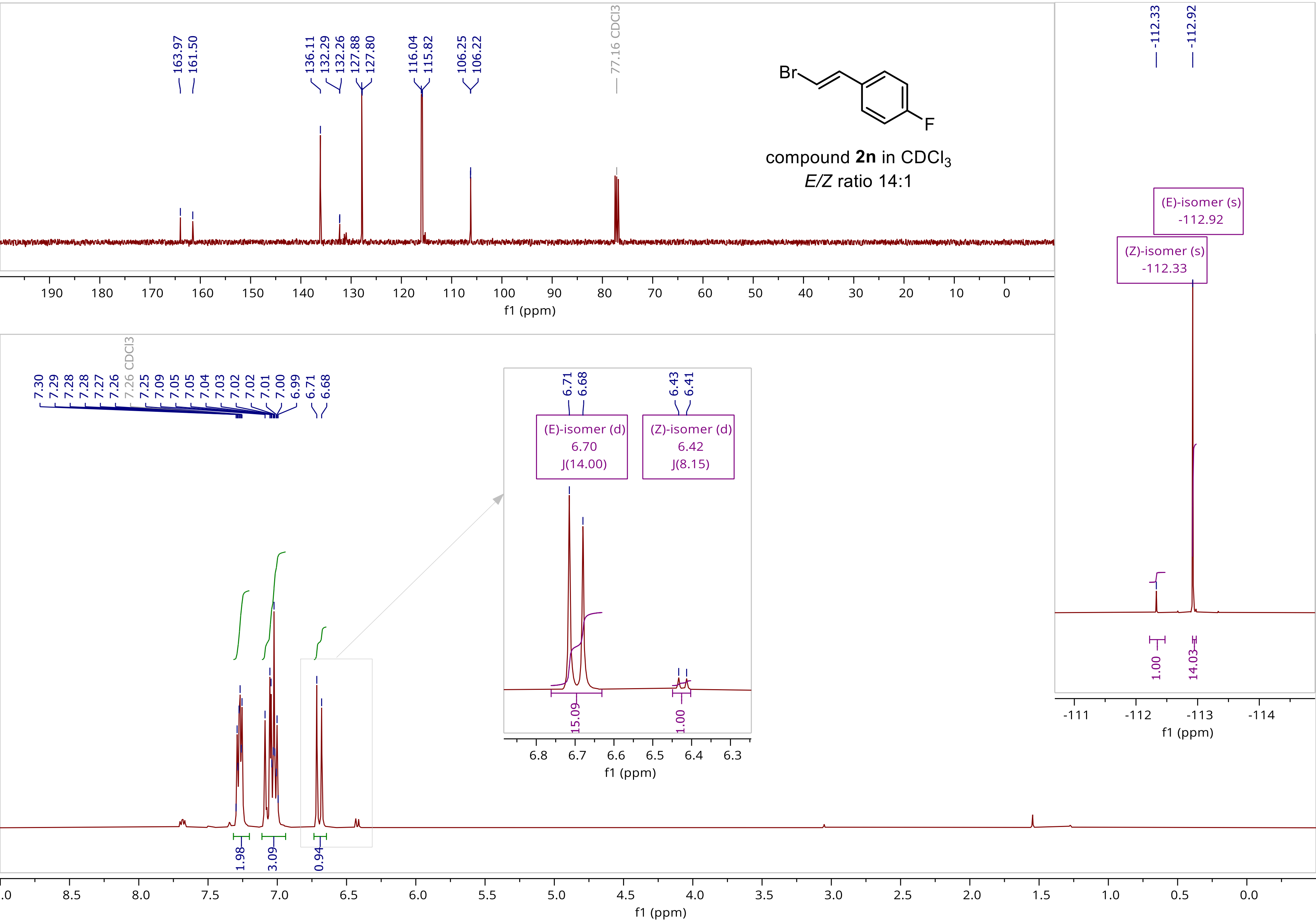




compound **2l** in $CDCl_3$

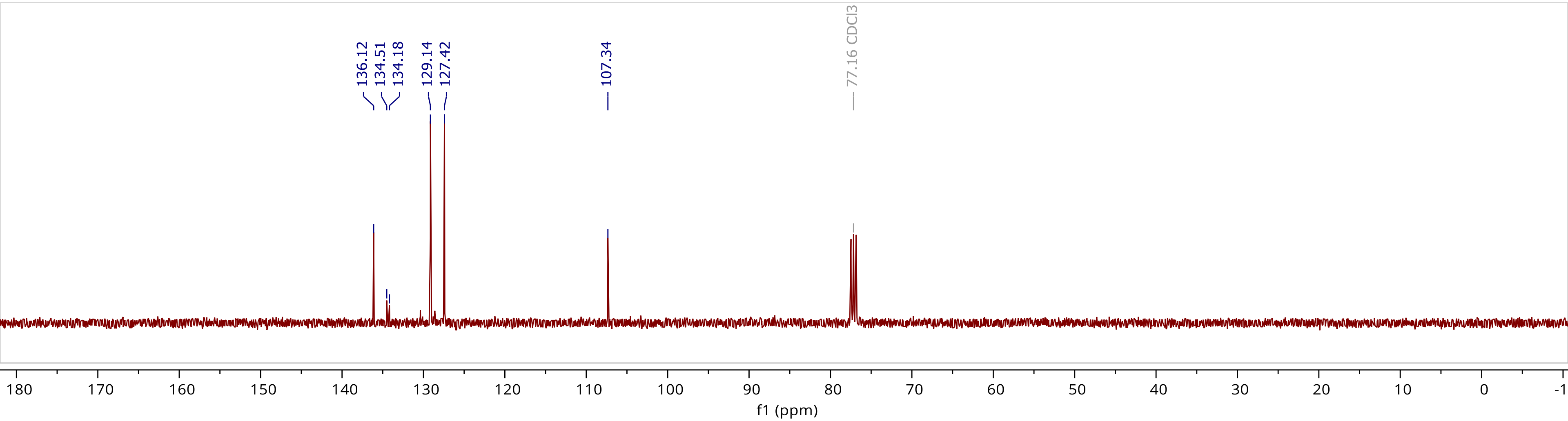
E/Z ratio 14:1

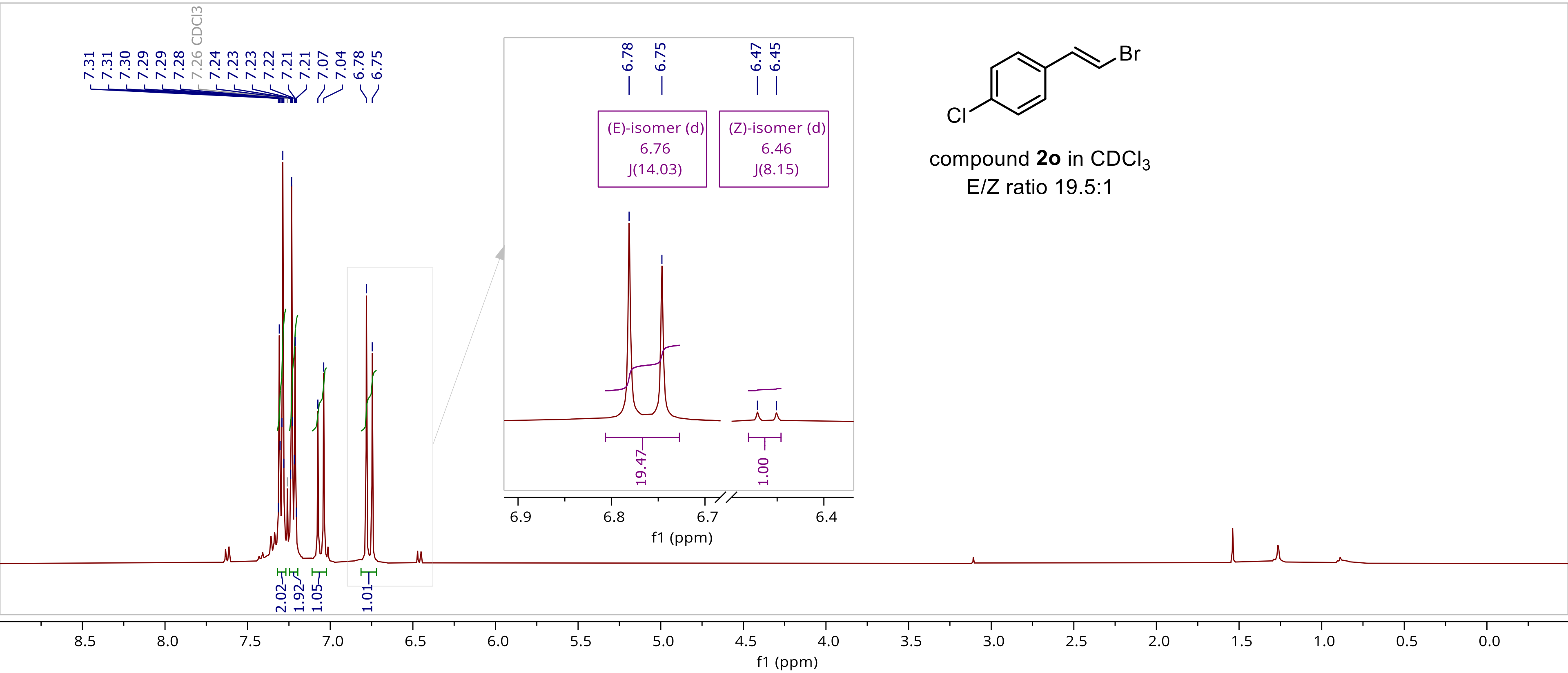

compound **2m** in $CDCl_3$
E/Z ratio 17:1



compound **2n** in CDCl$_3$

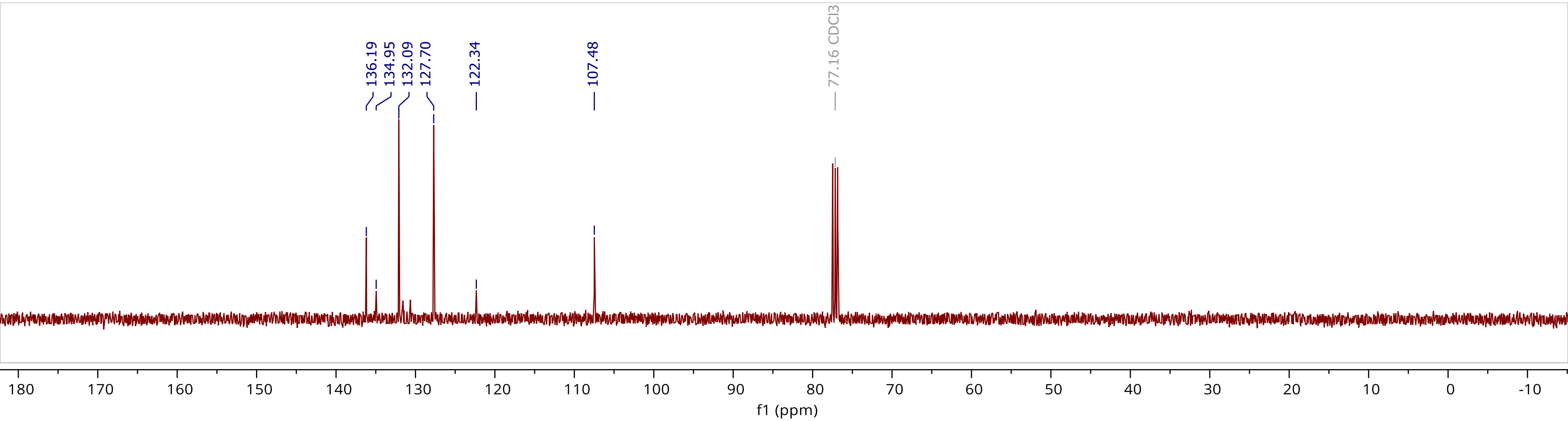
E/Z ratio 14:1

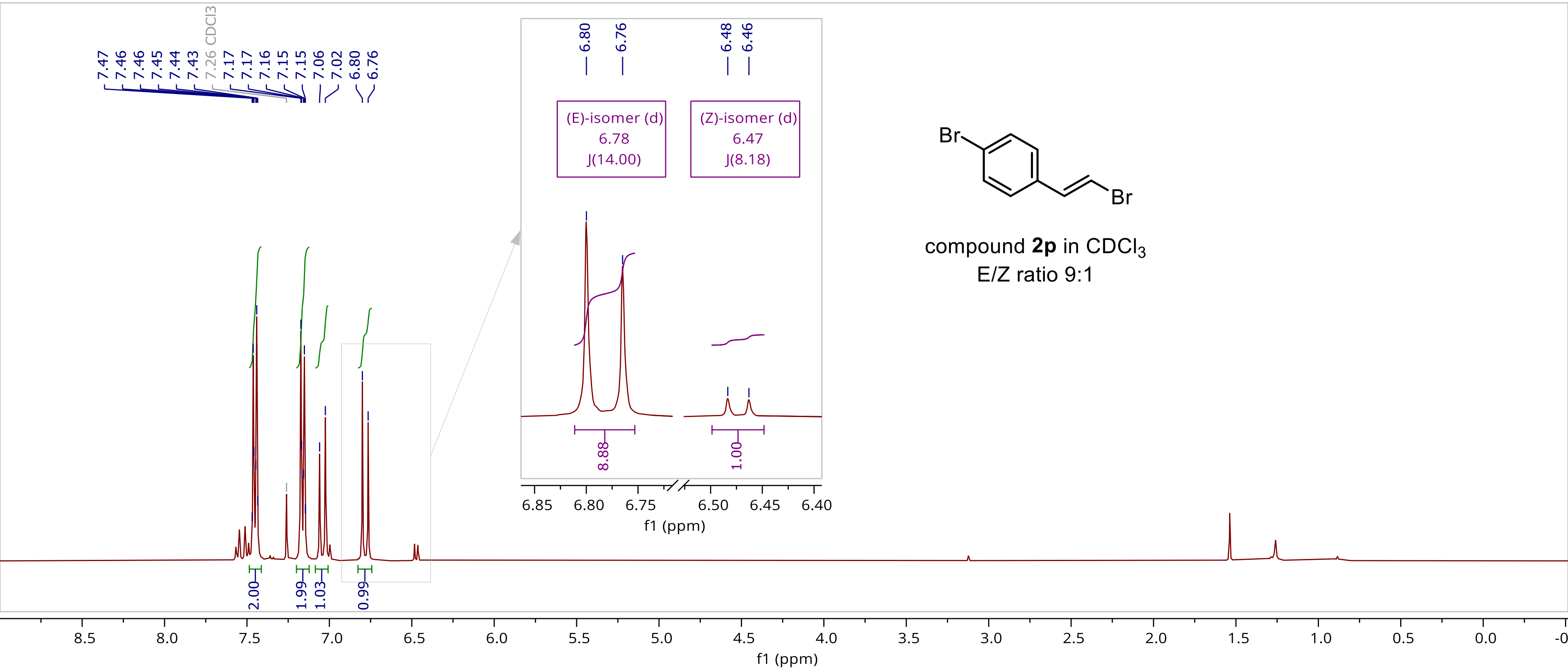




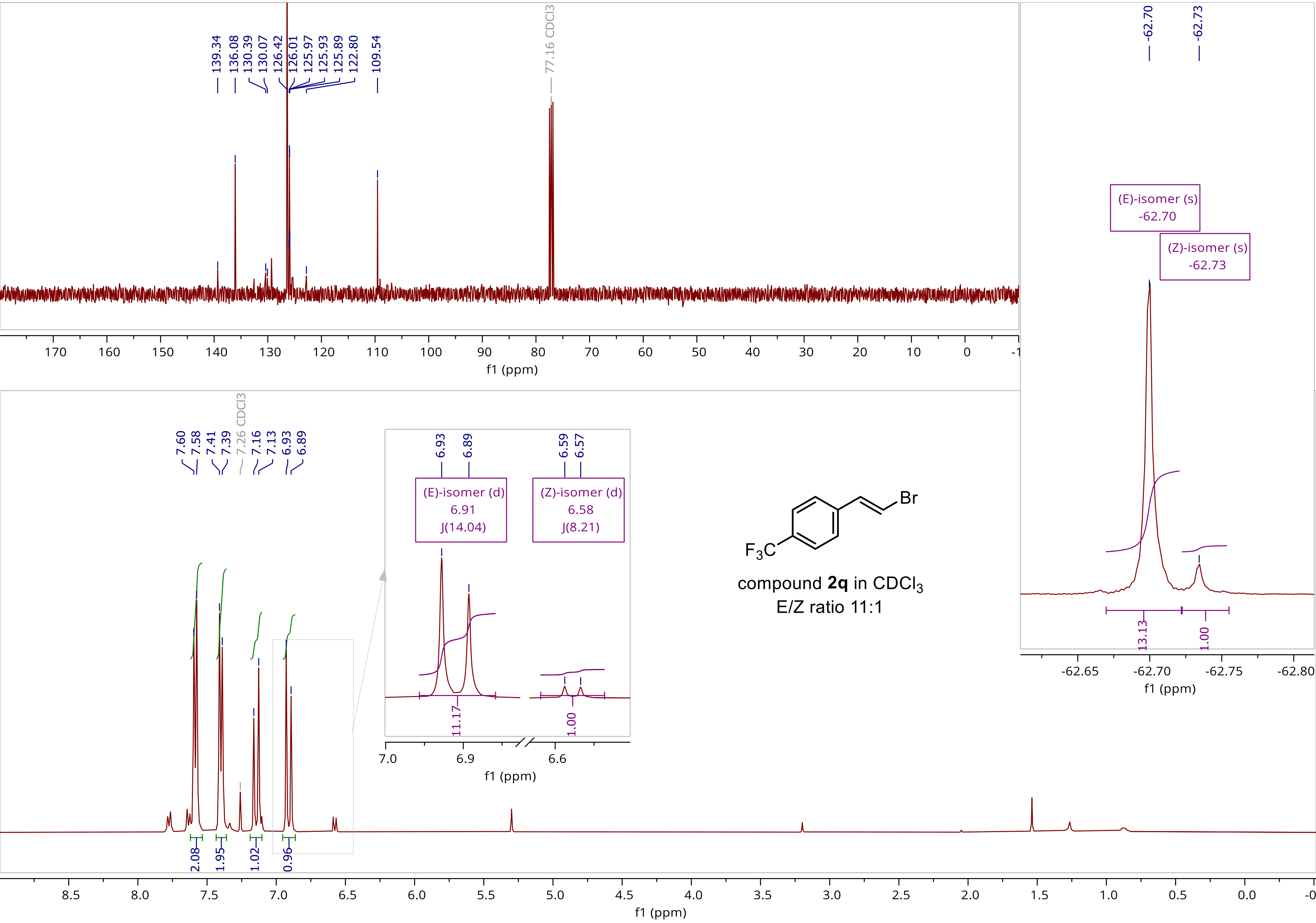
compound **2o** in $CDCl_3$

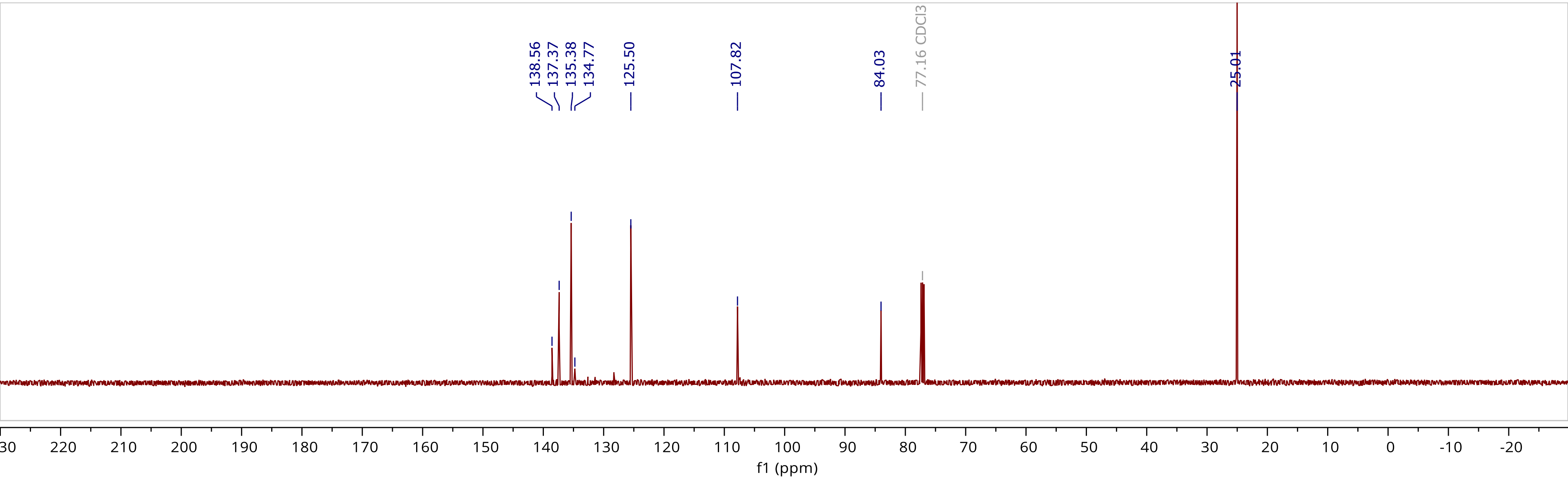
E/Z ratio 19.5:1

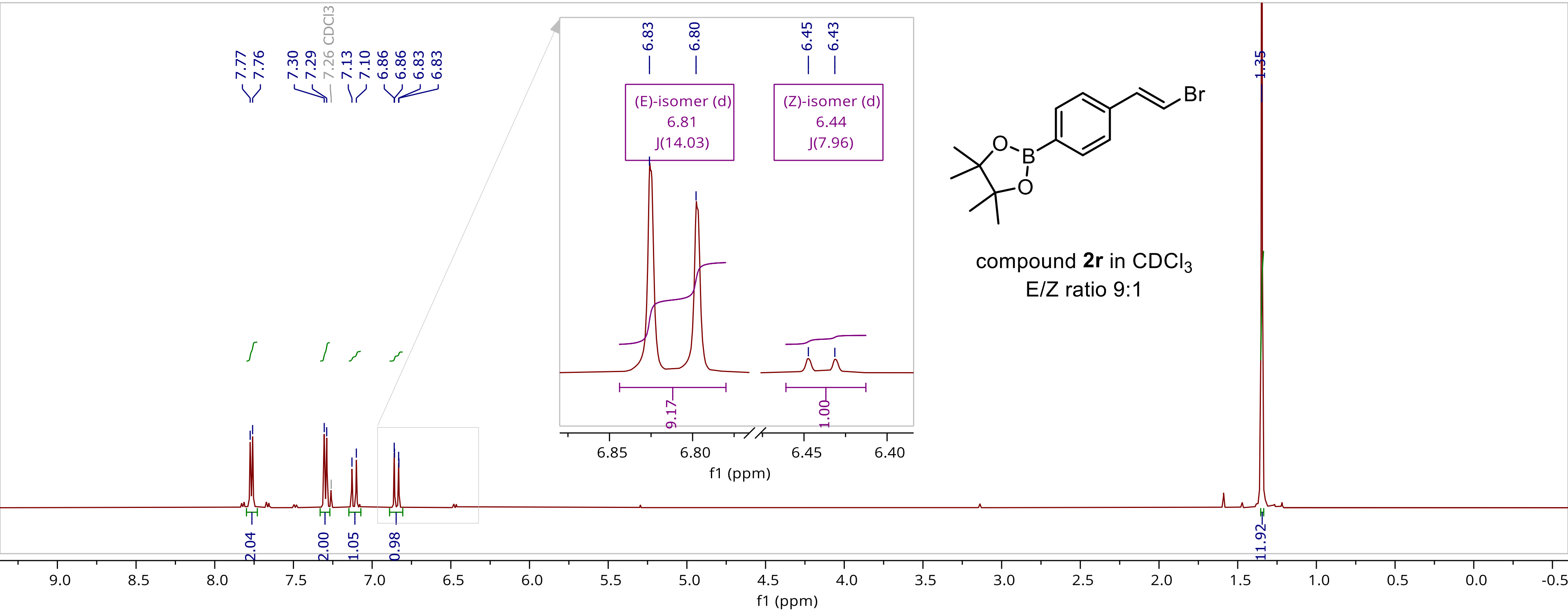




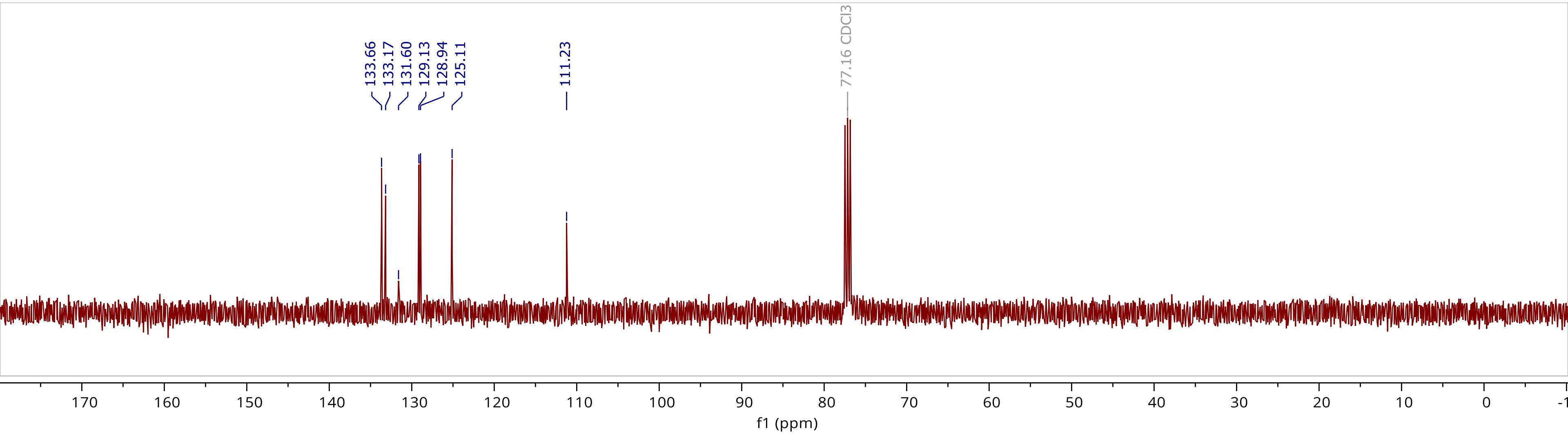
compound **2p** in $CDCl_3$
E/Z ratio 9:1

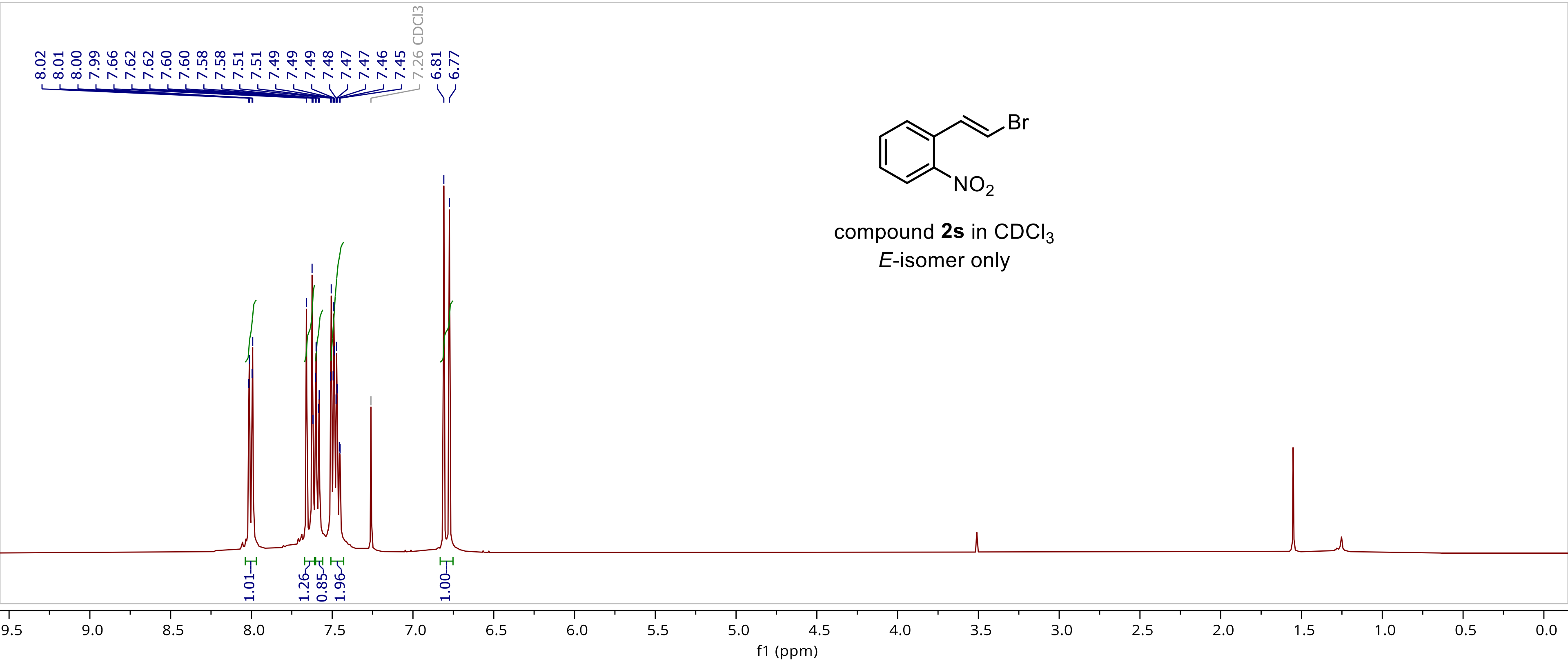

139.34
136.08
130.39
130.07
126.42
126.01
125.97
125.93
125.89
122.80
109.54
77.16 CDCl3
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
7.60
7.58
7.41
7.39
7.26 CDCl3
7.16
7.13
6.93
6.89
6.93
6.89
(E)-isomer (d)
6.91
J(14.04)
6.59
6.57
(Z)-isomer (d)
6.58
J(8.21)
11.17
1.00
7.0 6.9 6.6
f1 (ppm)
Br
F_3C
compound **2q** in $CDCl_3$
E/Z ratio 11:1
2.08
1.95
1.02
0.96
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
f1 (ppm)
-62.70
-62.73
(E)-isomer (s)
-62.70
(Z)-isomer (s)
-62.73
13.13
1.00
-62.65 -62.70 -62.75 -62.80
f1 (ppm)





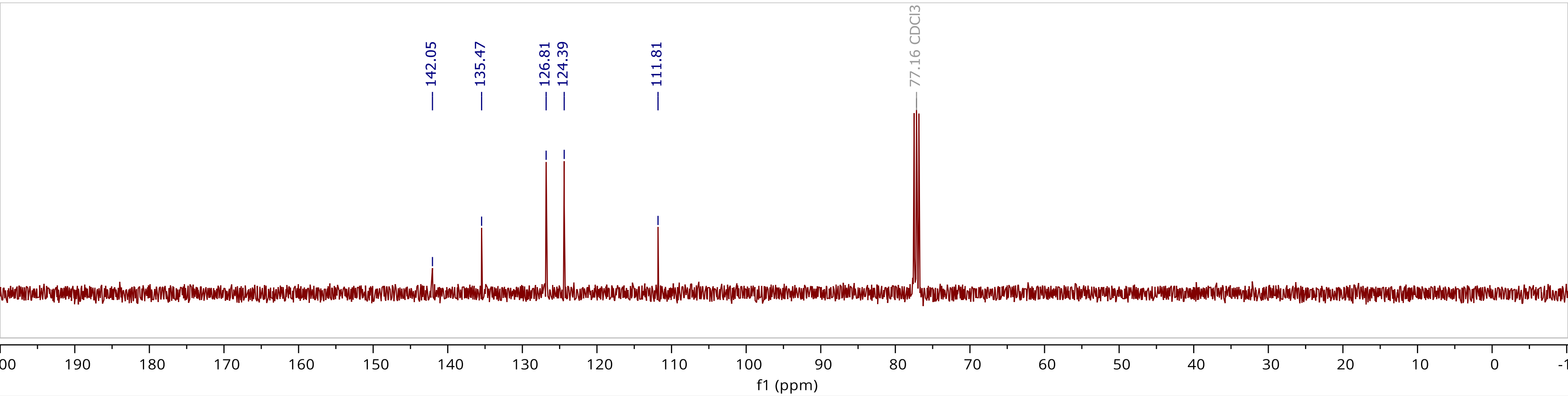
compound **2r** in $CDCl_3$
E/Z ratio 9:1

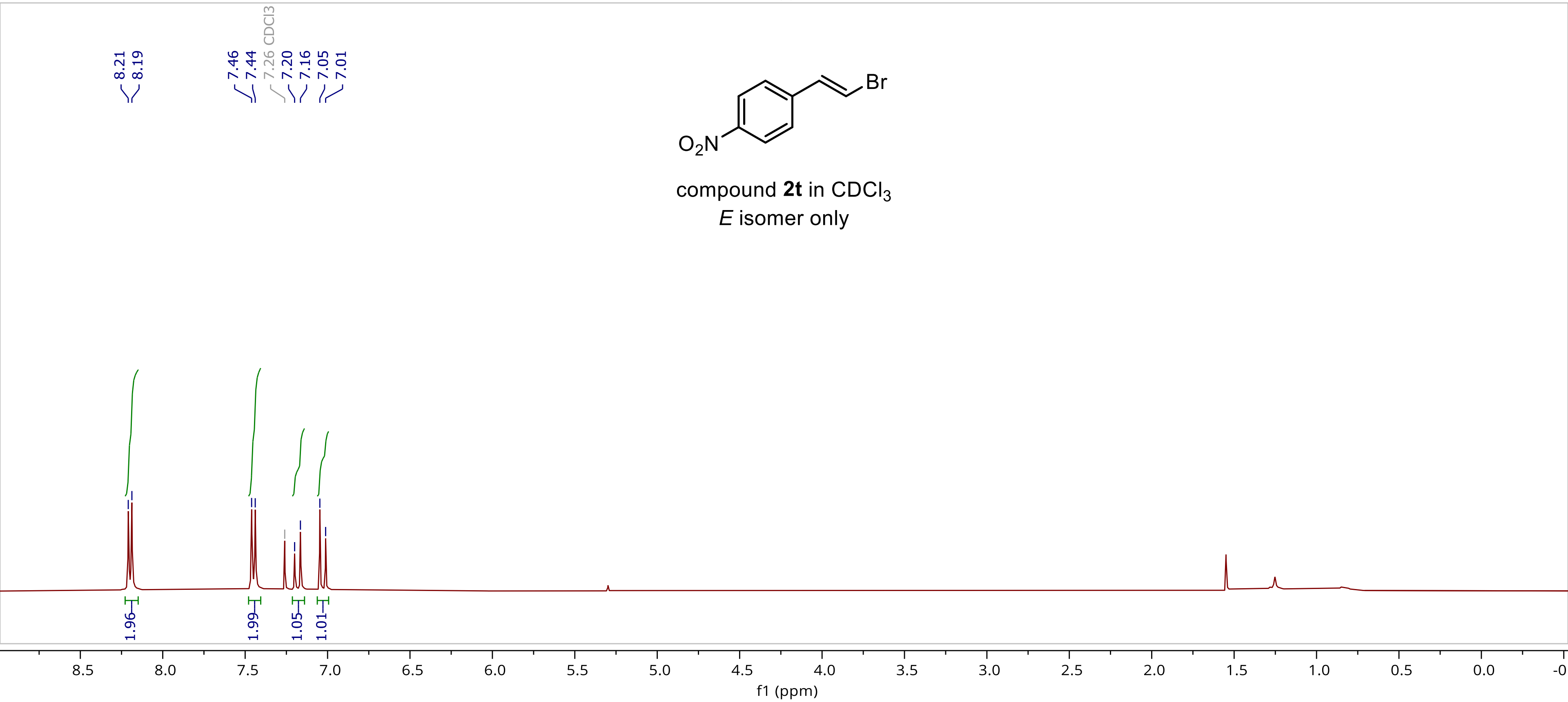




compound **2s** in $CDCl_3$

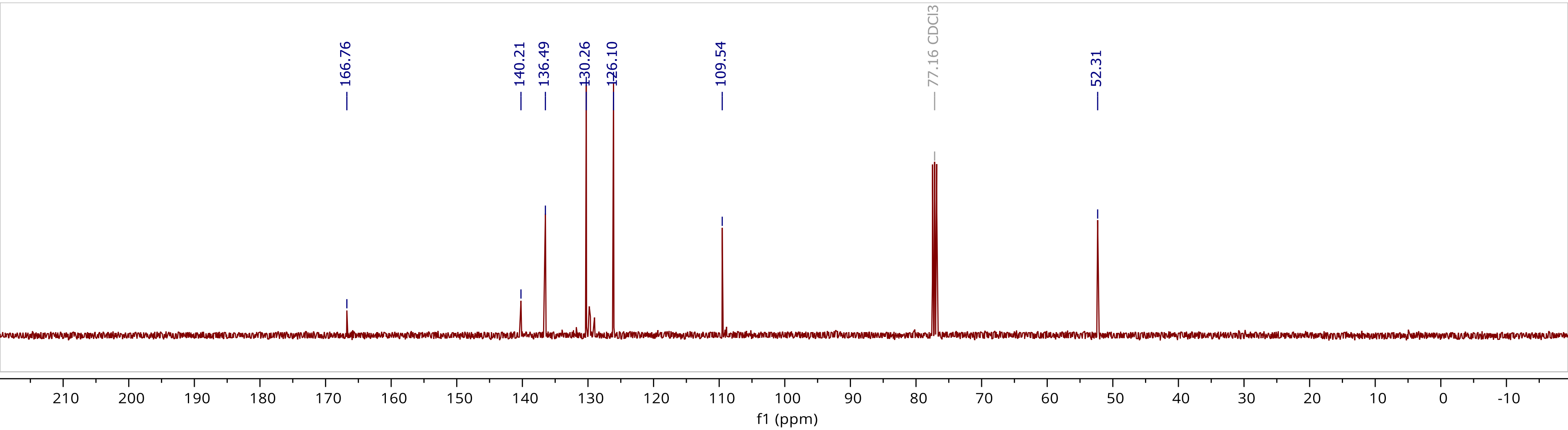
E-isomer only

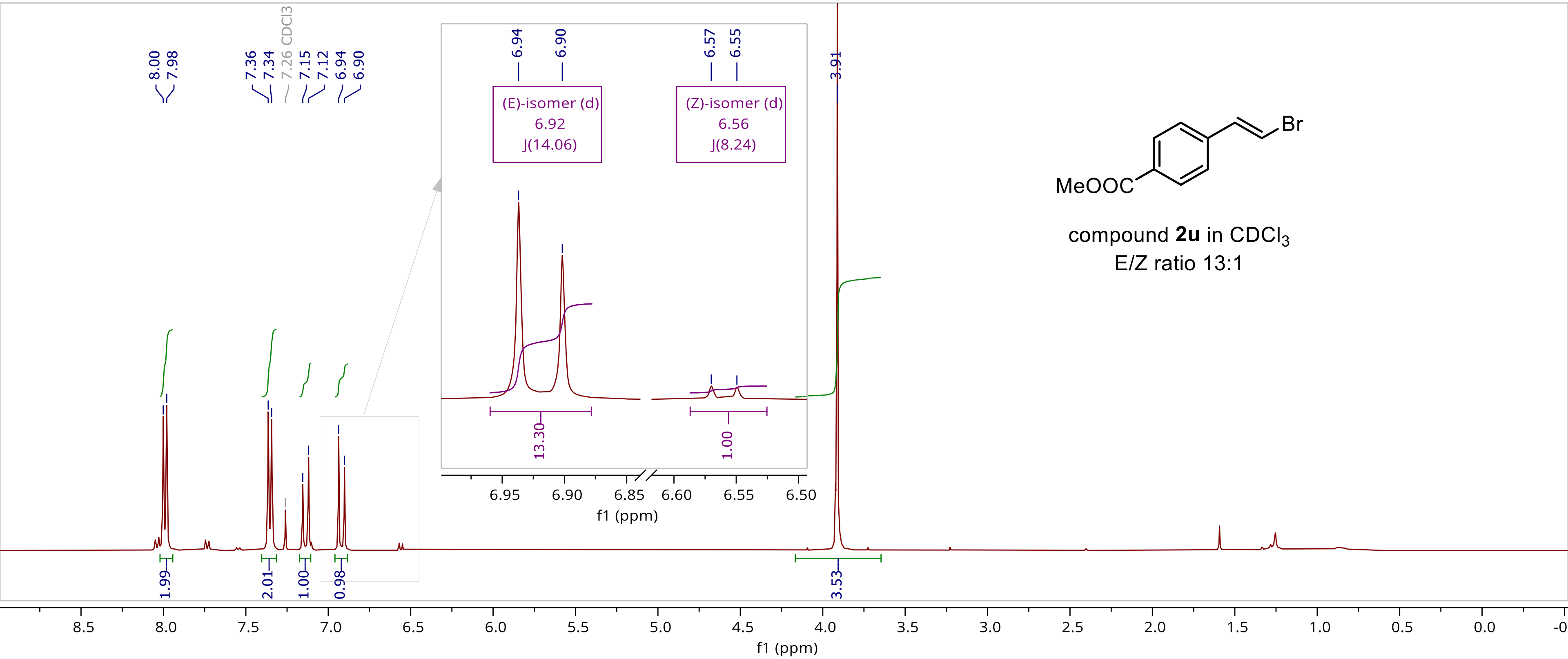




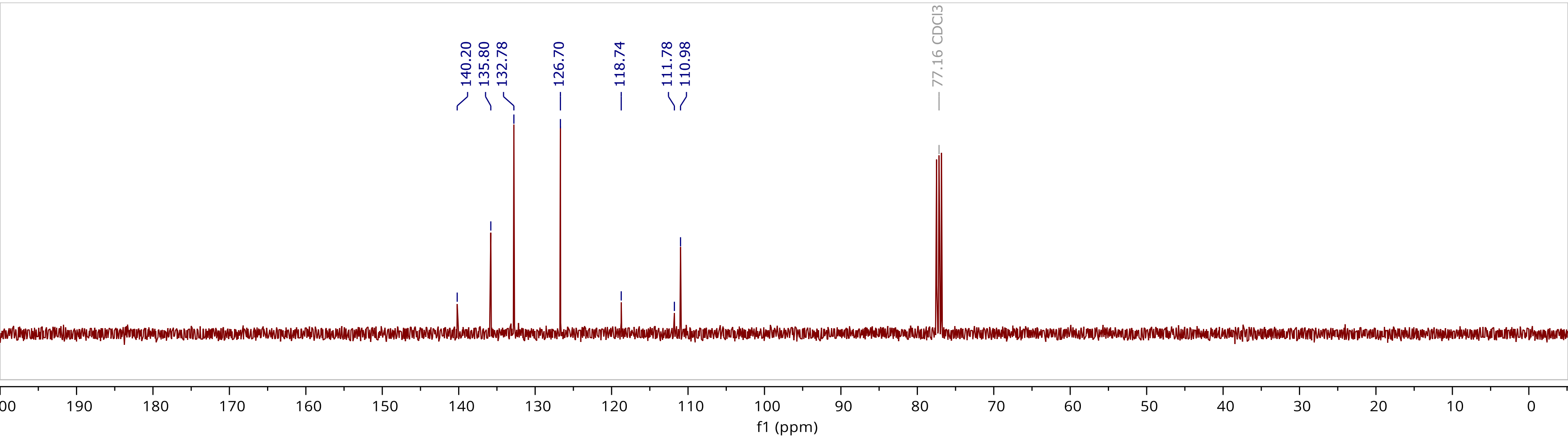
compound **2t** in $CDCl_3$

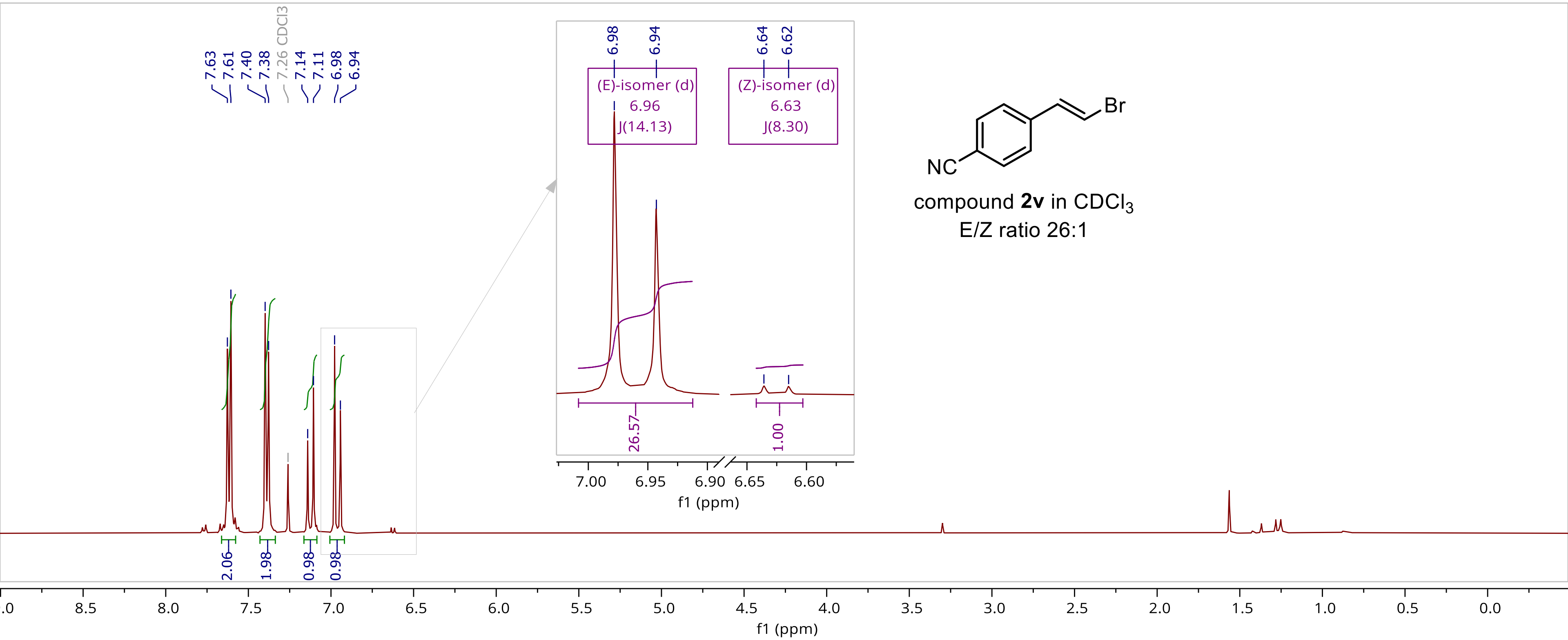
E isomer only





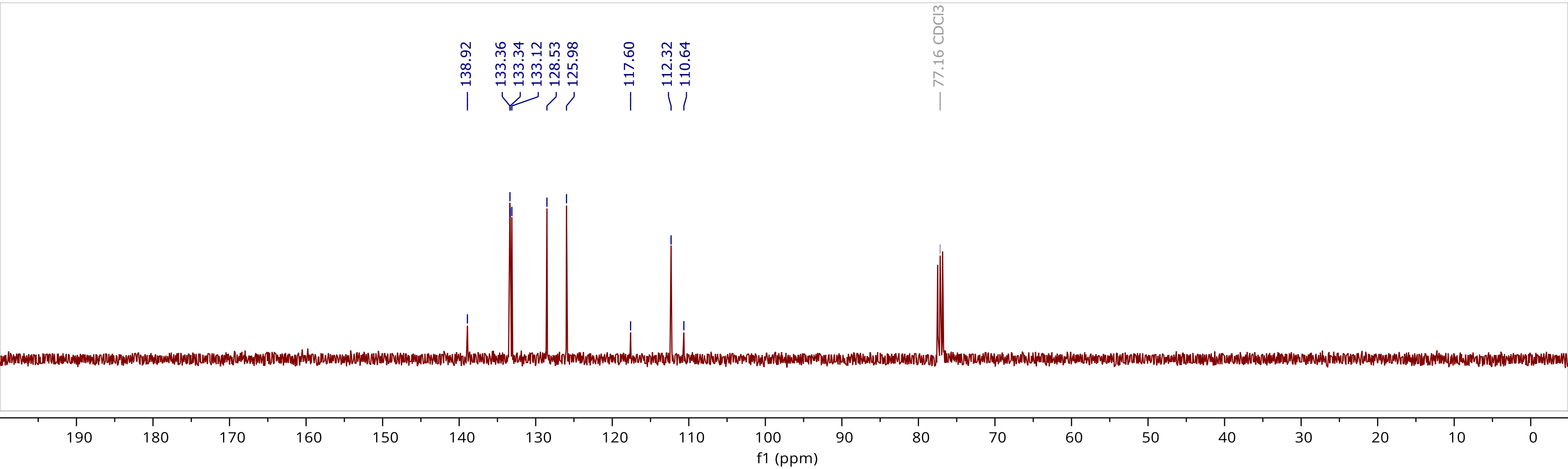
compound **2u** in $CDCl_3$
E/Z ratio 13:1

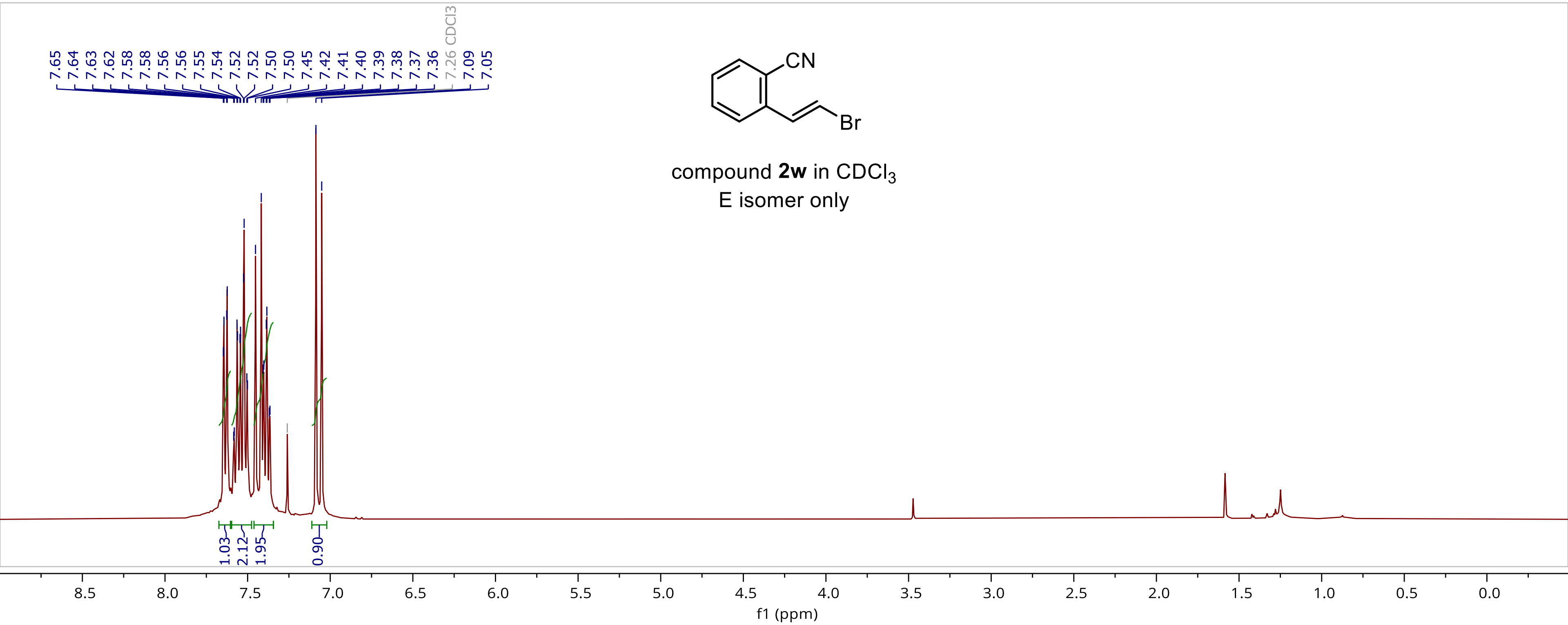




compound **2v** in CDCl$_3$

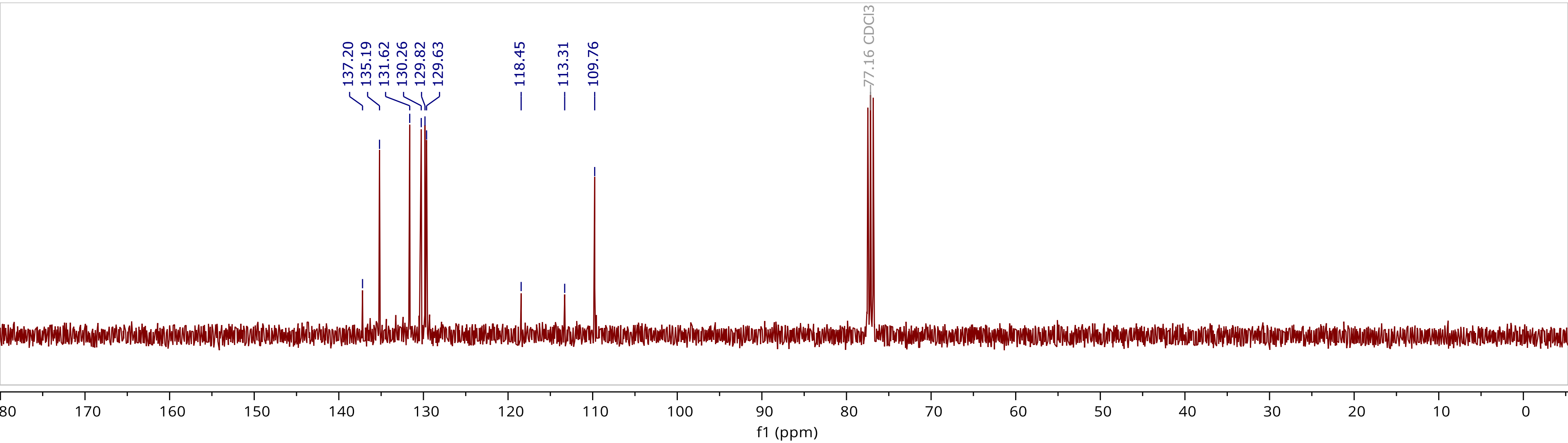
E/Z ratio 26:1

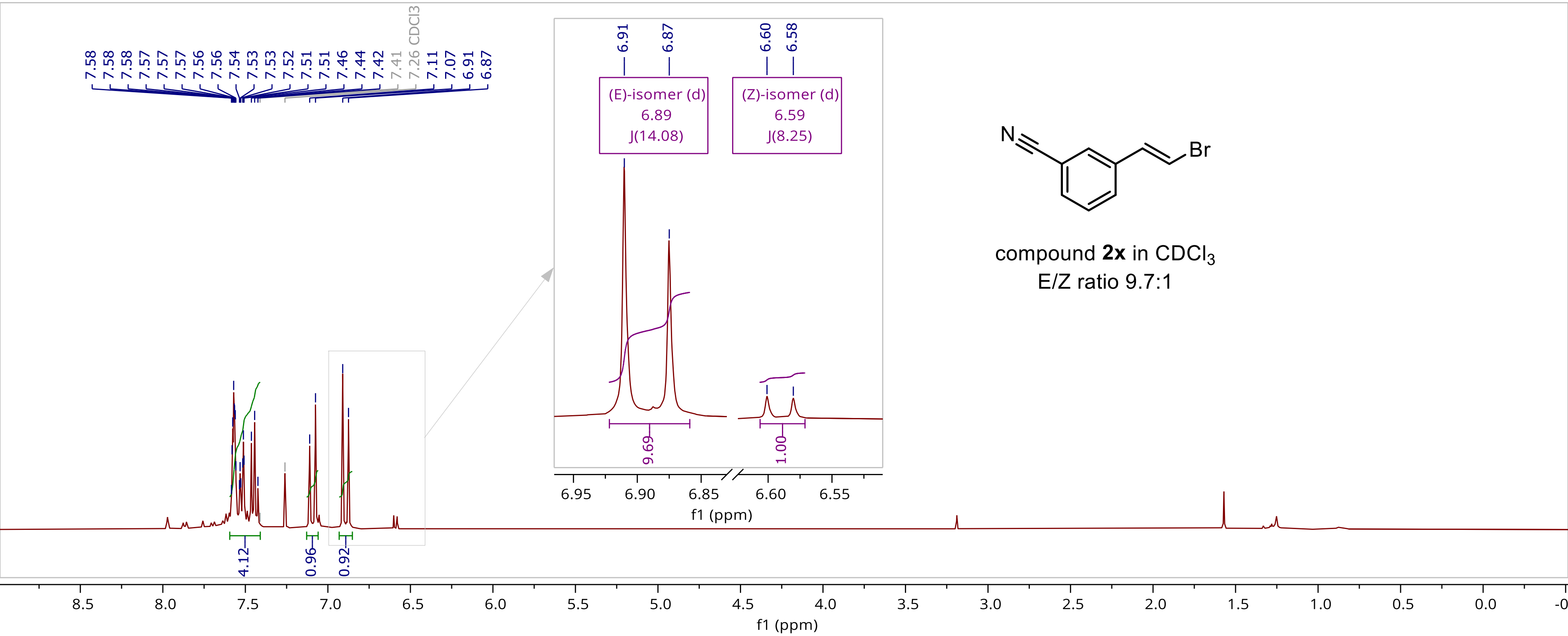




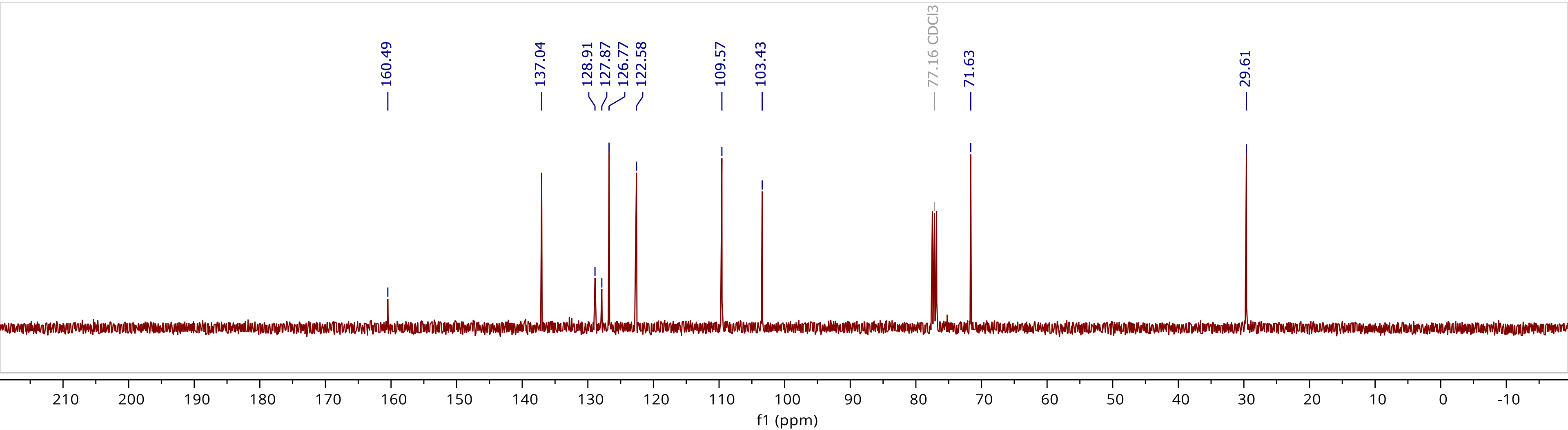
compound **2w** in CDCl$_3$

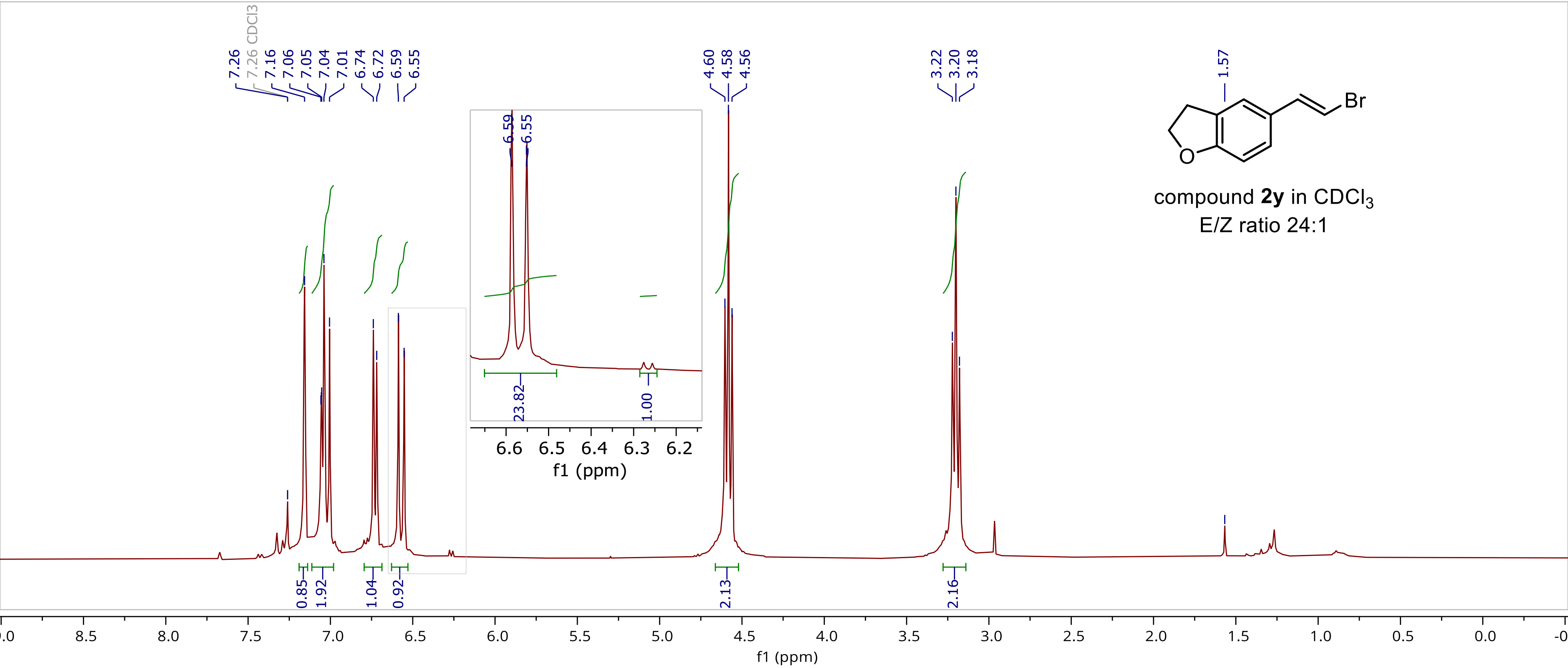
E isomer only



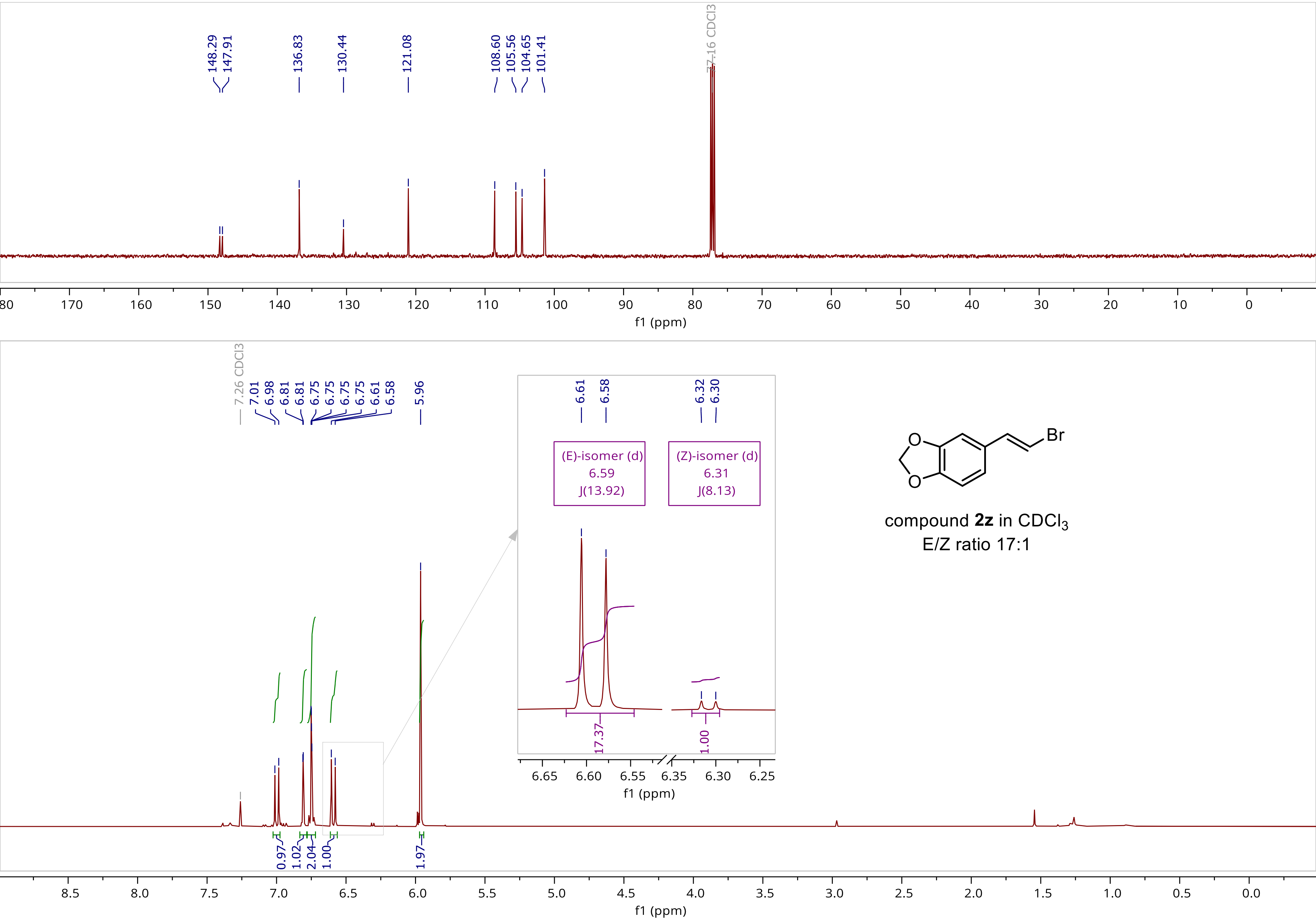


compound **2x** in $CDCl_3$
E/Z ratio 9.7:1



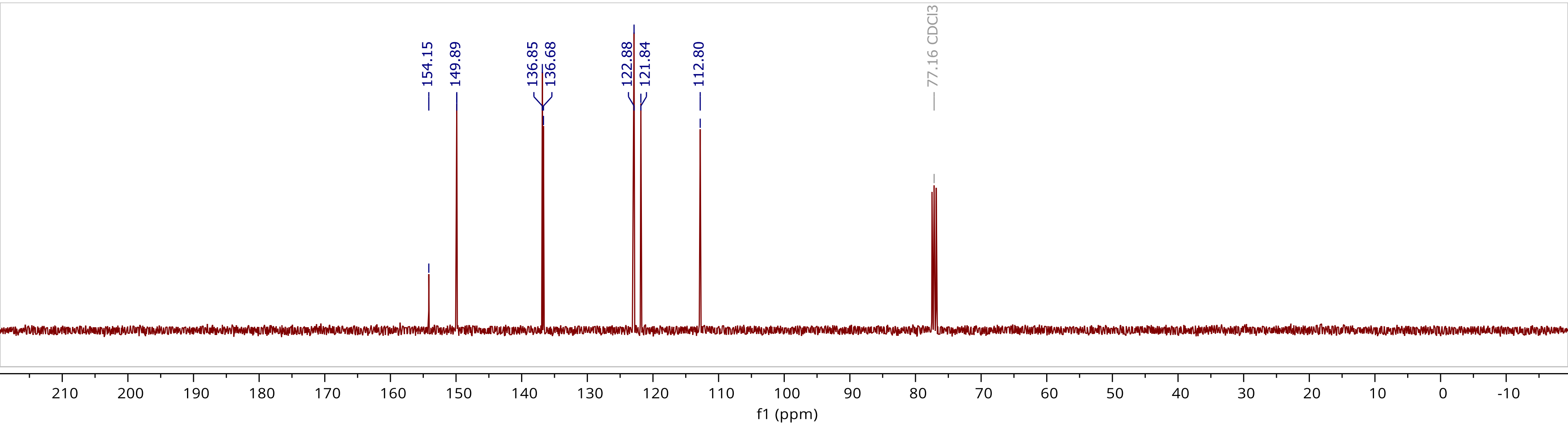


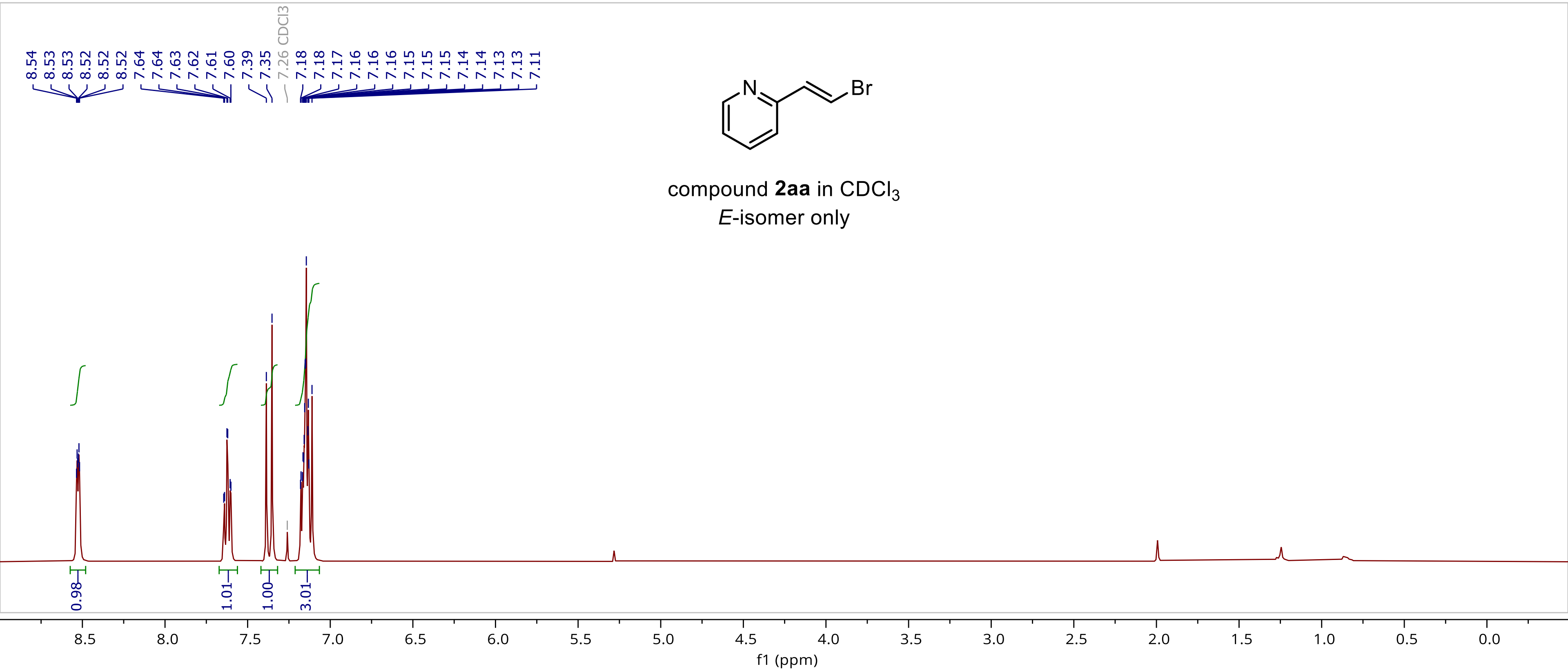
compound **2y** in $CDCl_3$
E/Z ratio 24:1



compound **2z** in CDCl$_3$

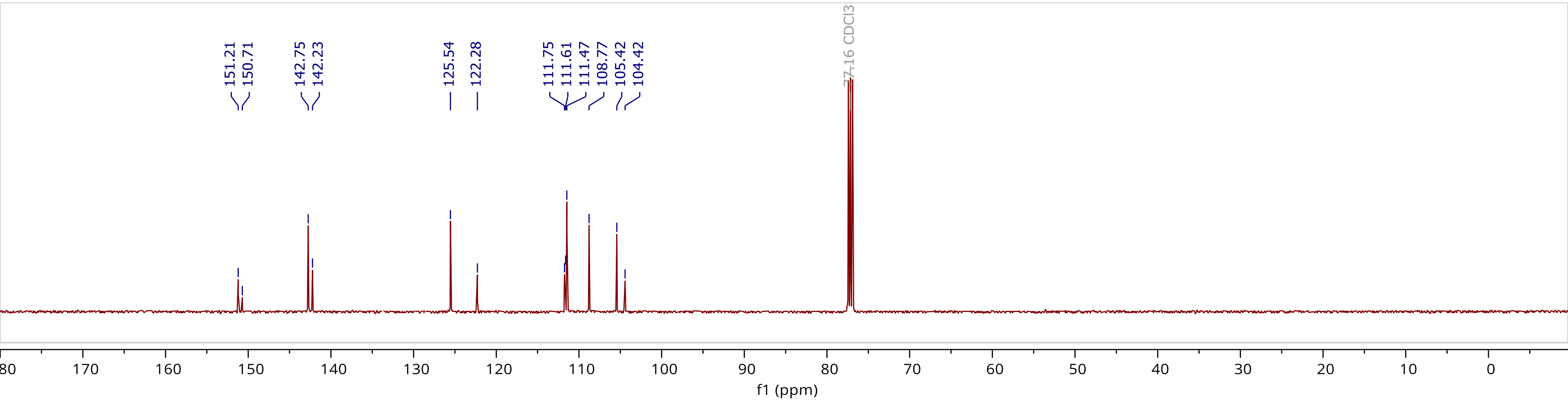
E/Z ratio 17:1

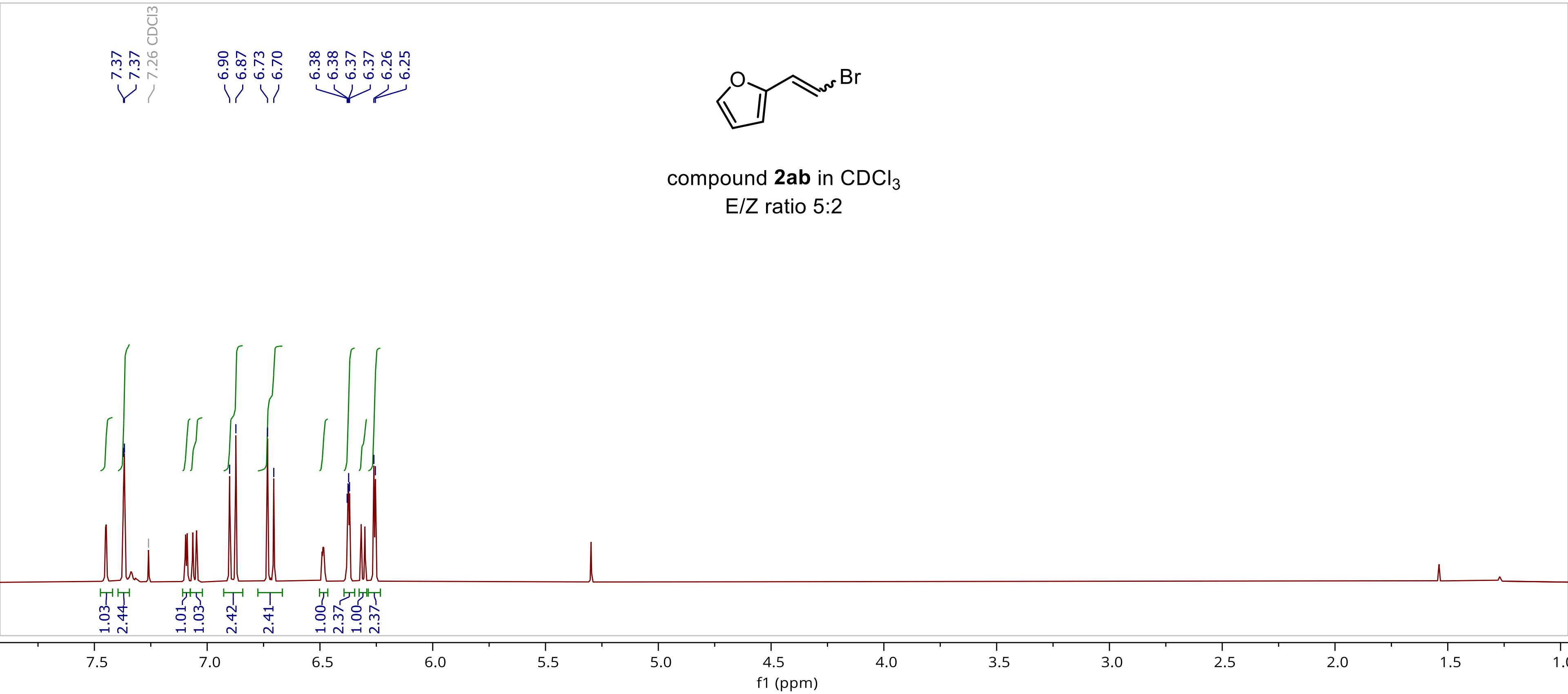




compound **2aa** in $CDCl_3$

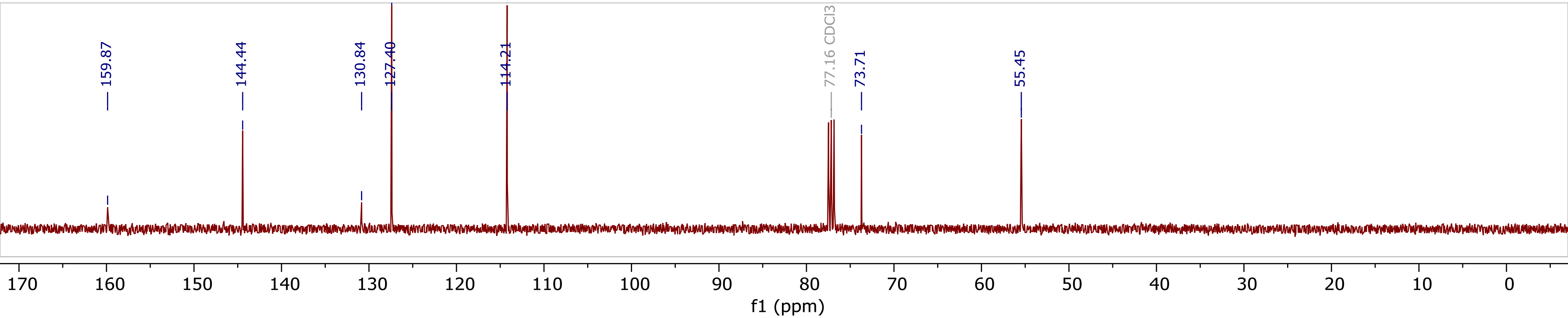
E-isomer only

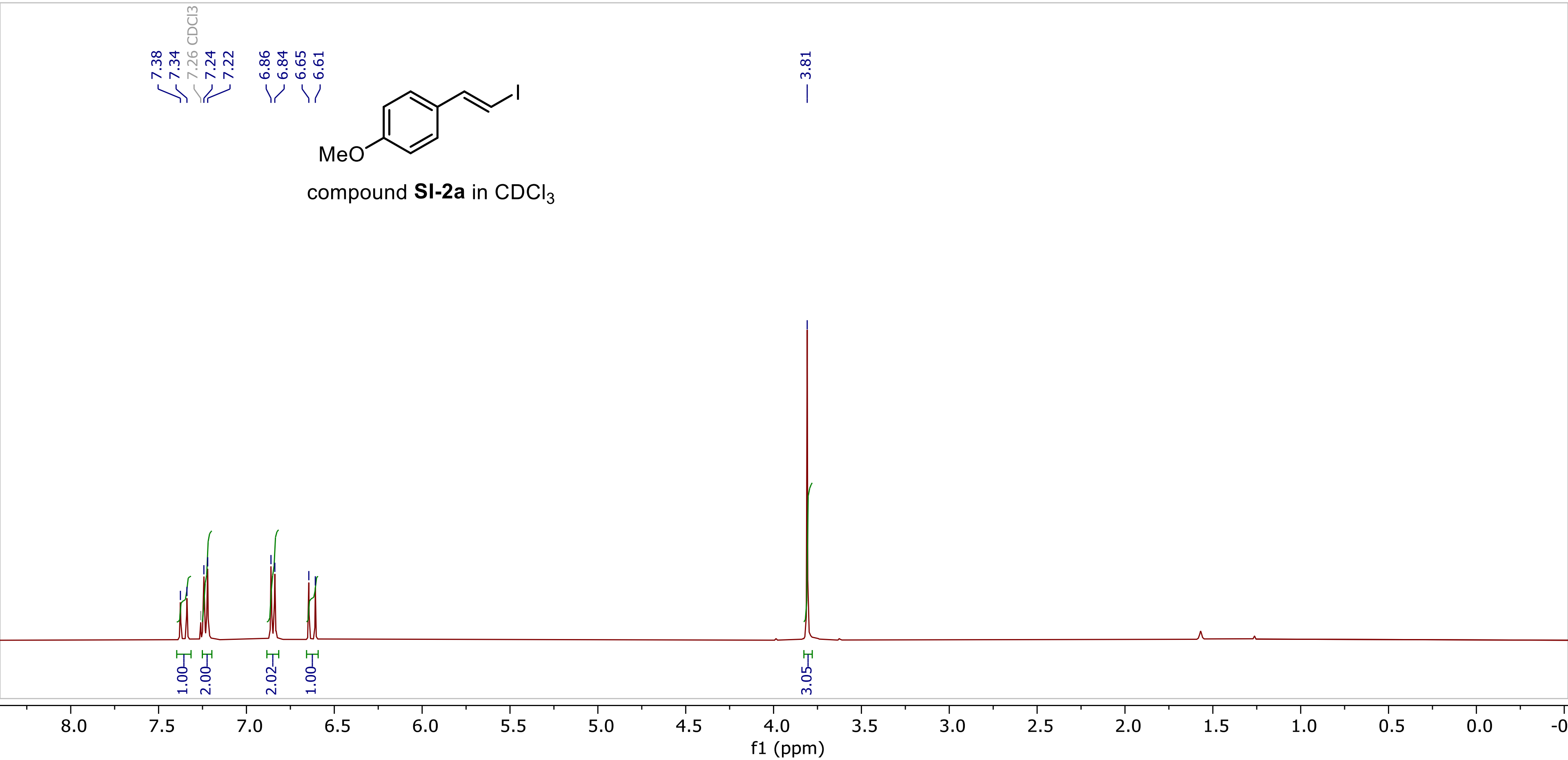




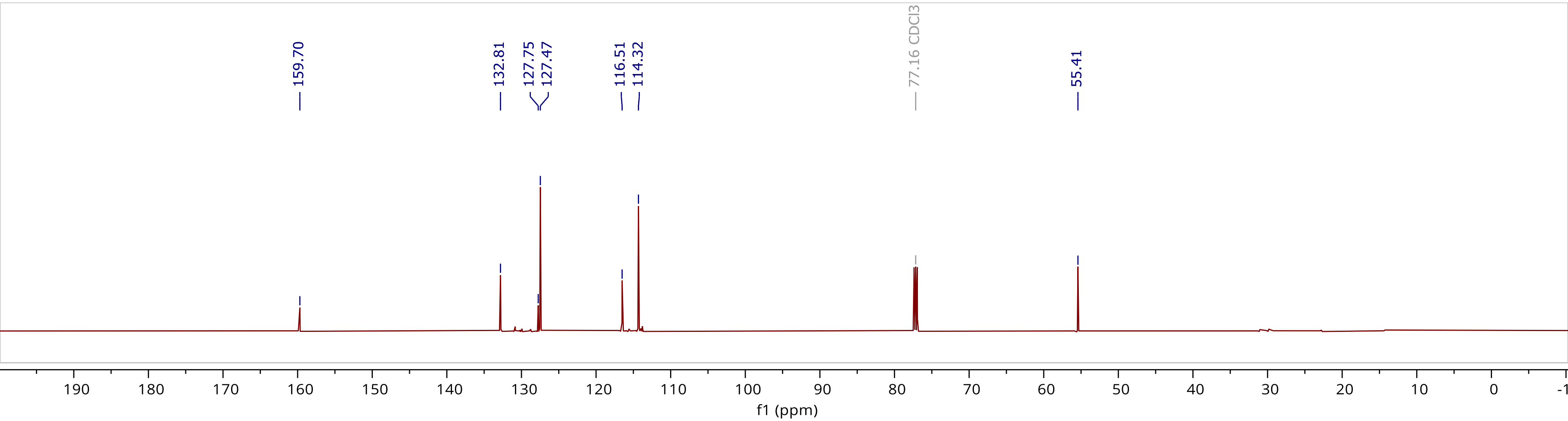
compound **2ab** in CDCl$_3$

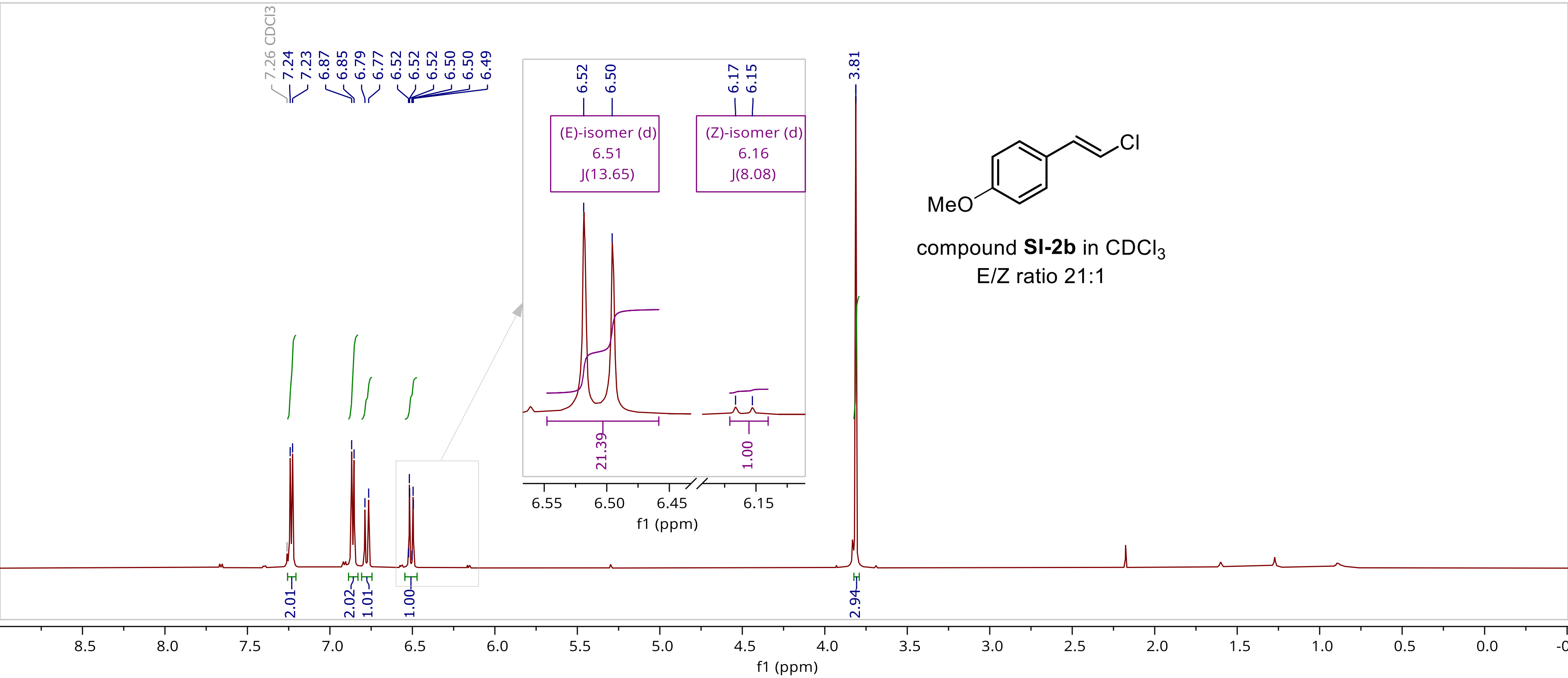
E/Z ratio 5:2



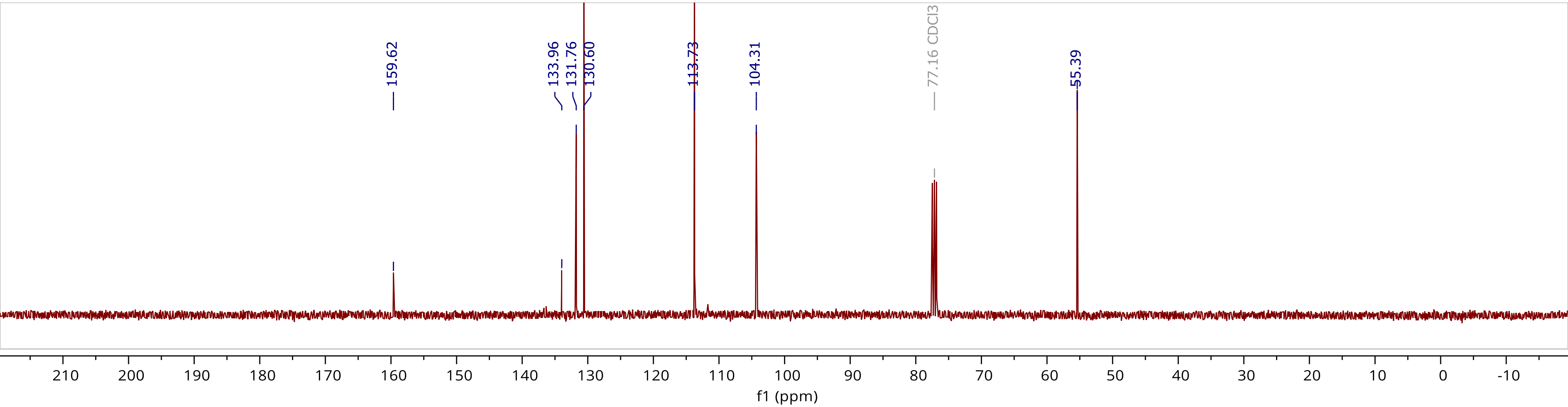


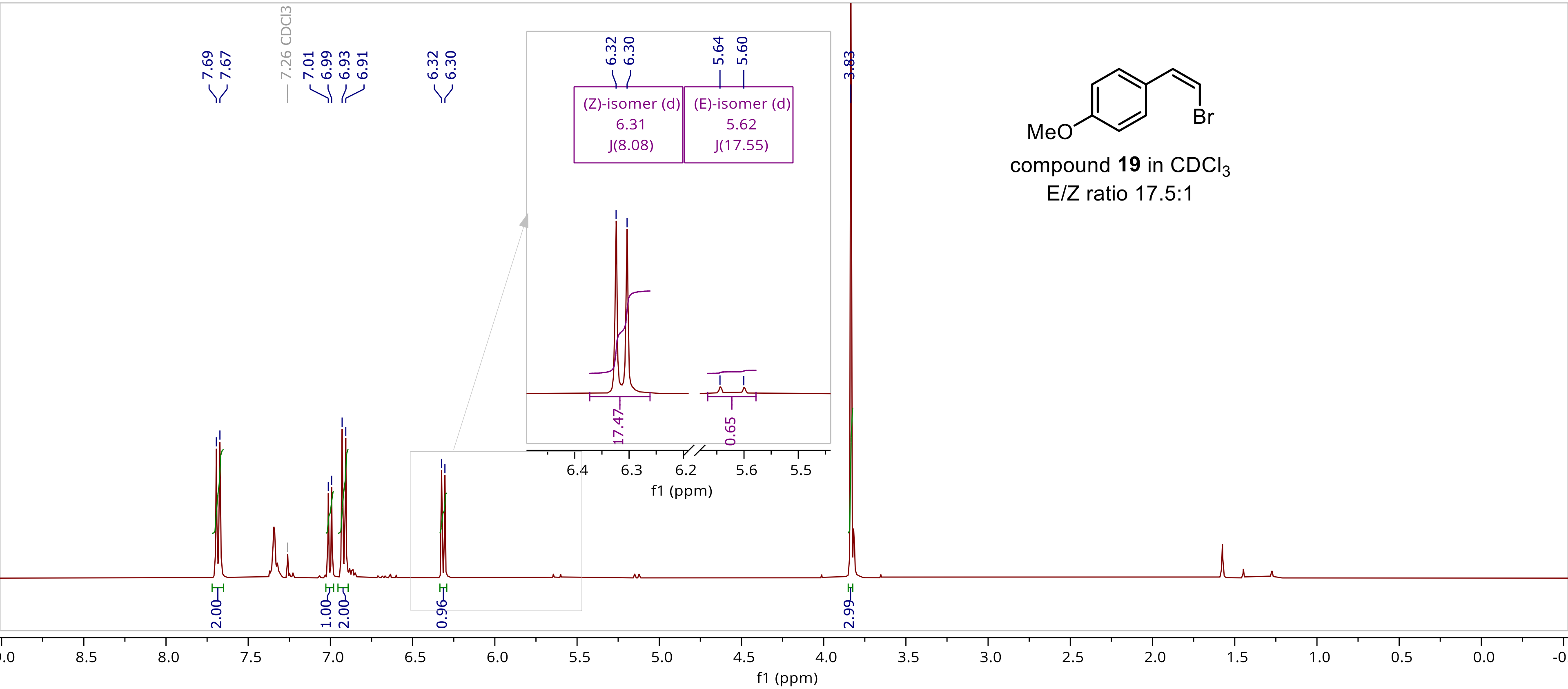
compound **SI-2a** in $CDCl_3$



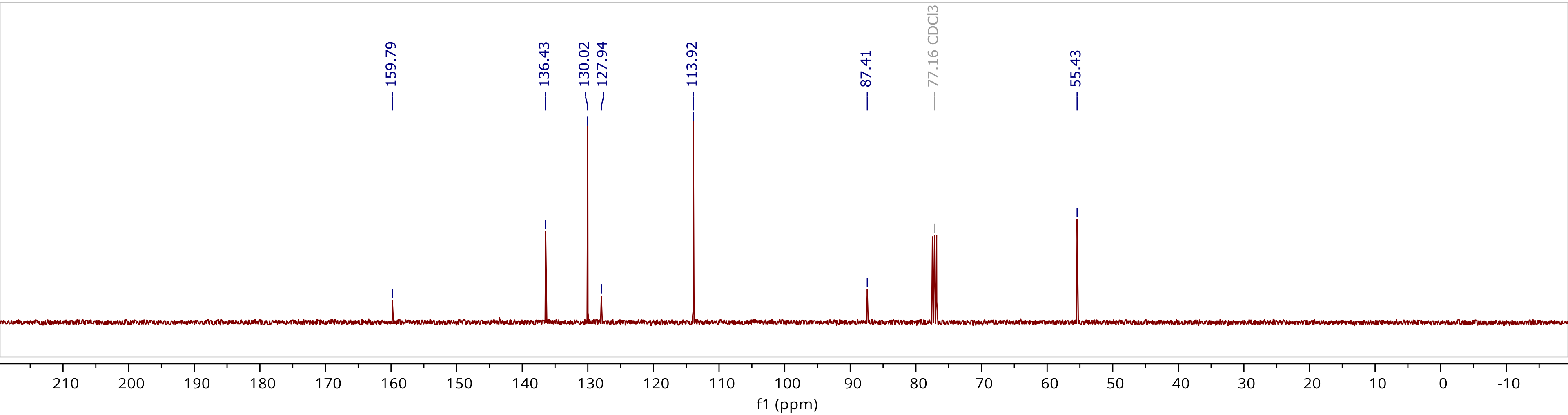


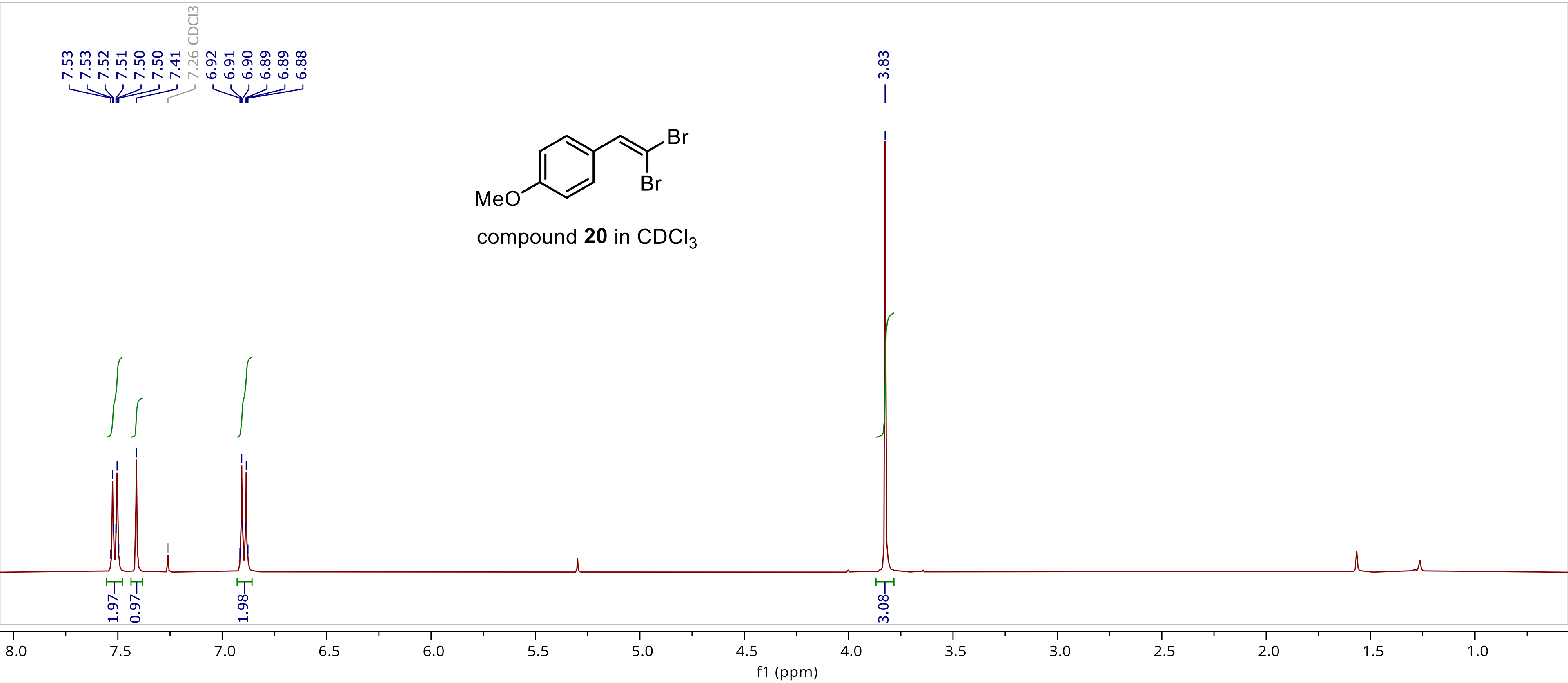
compound **SI-2b** in $CDCl_3$
E/Z ratio 21:1



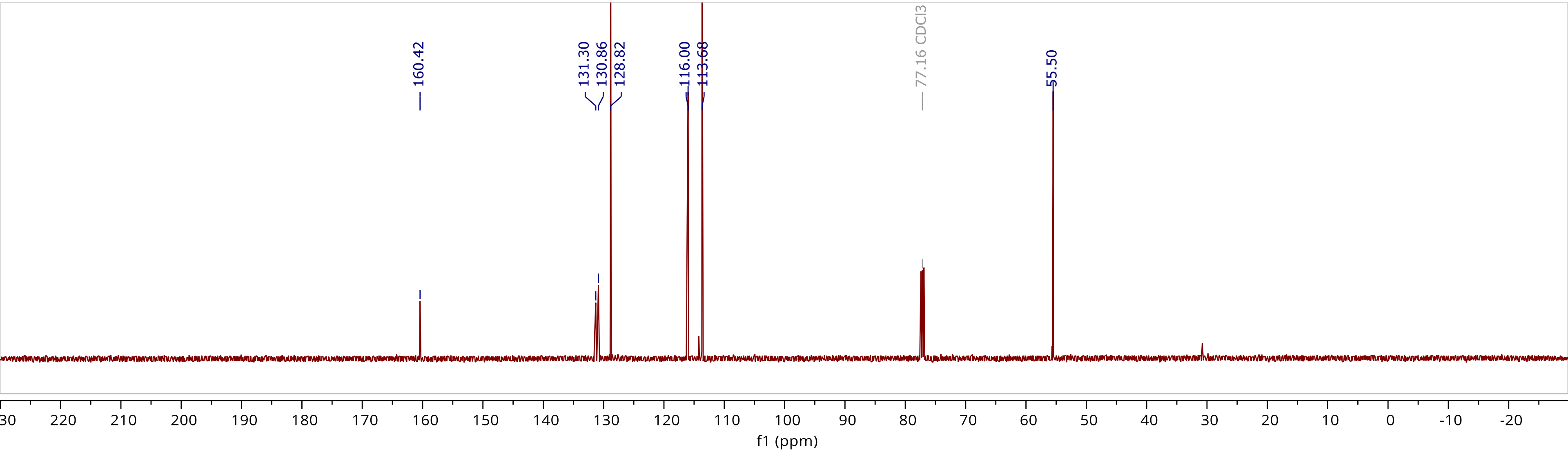


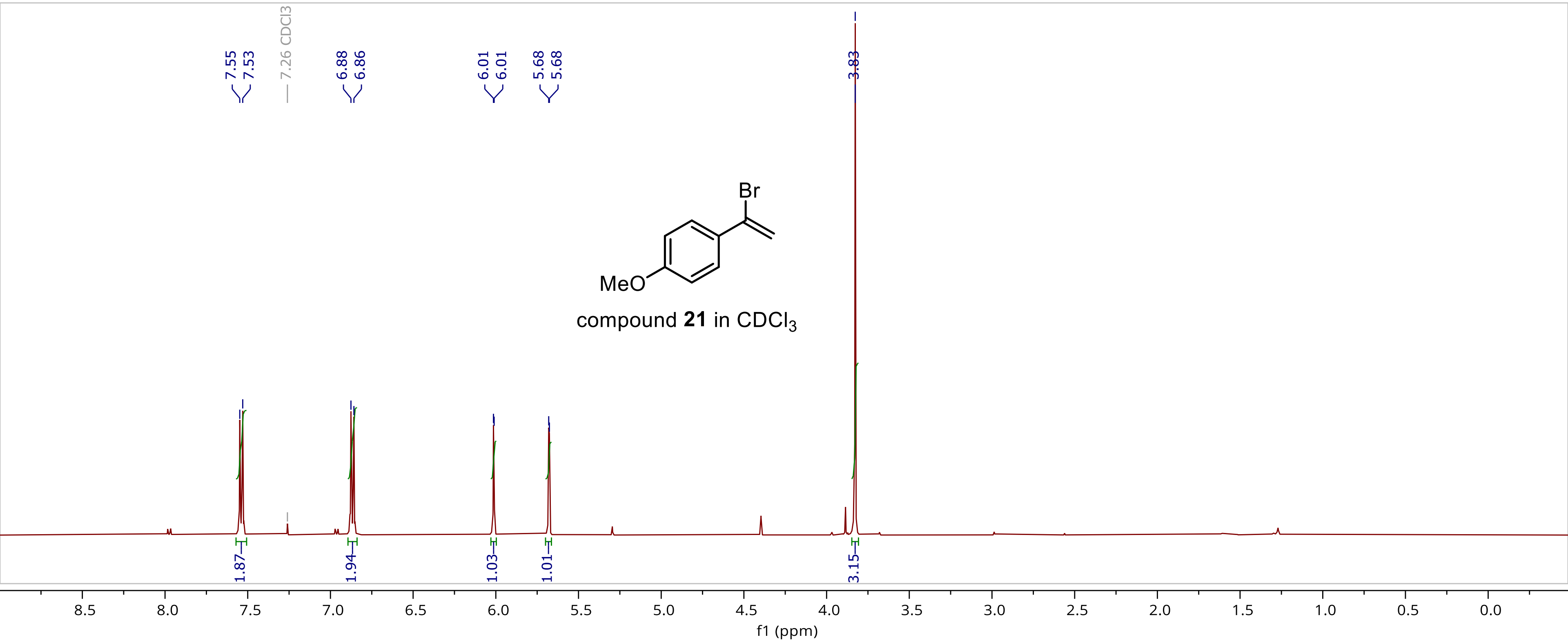
compound **19** in $CDCl_3$
E/Z ratio 17.5:1



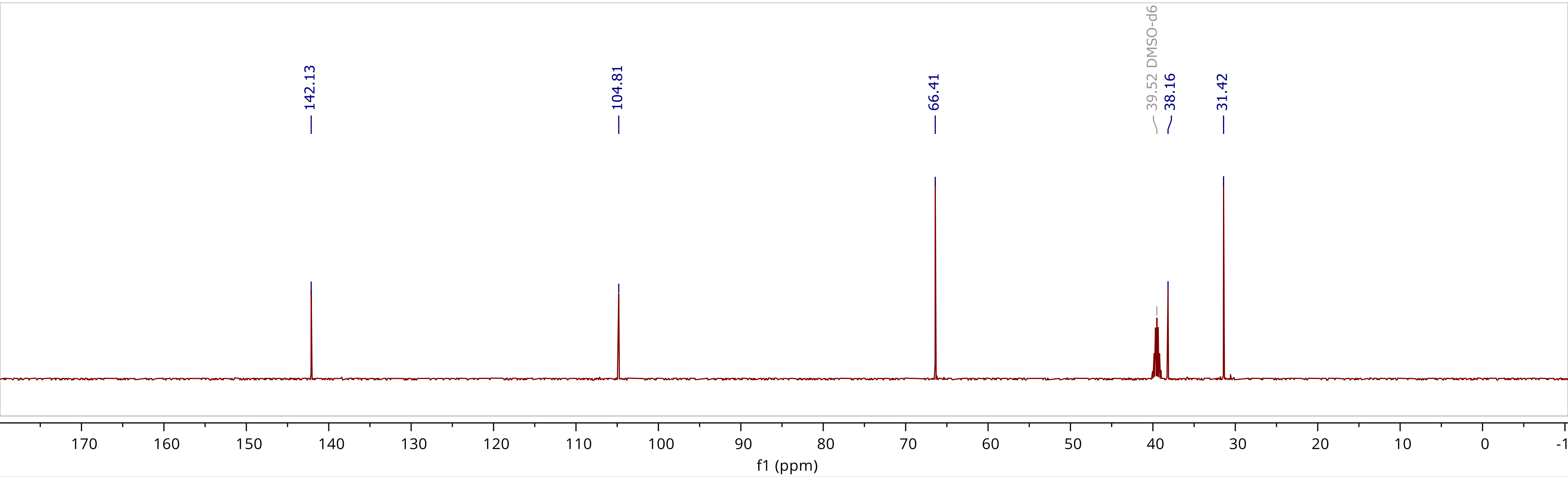


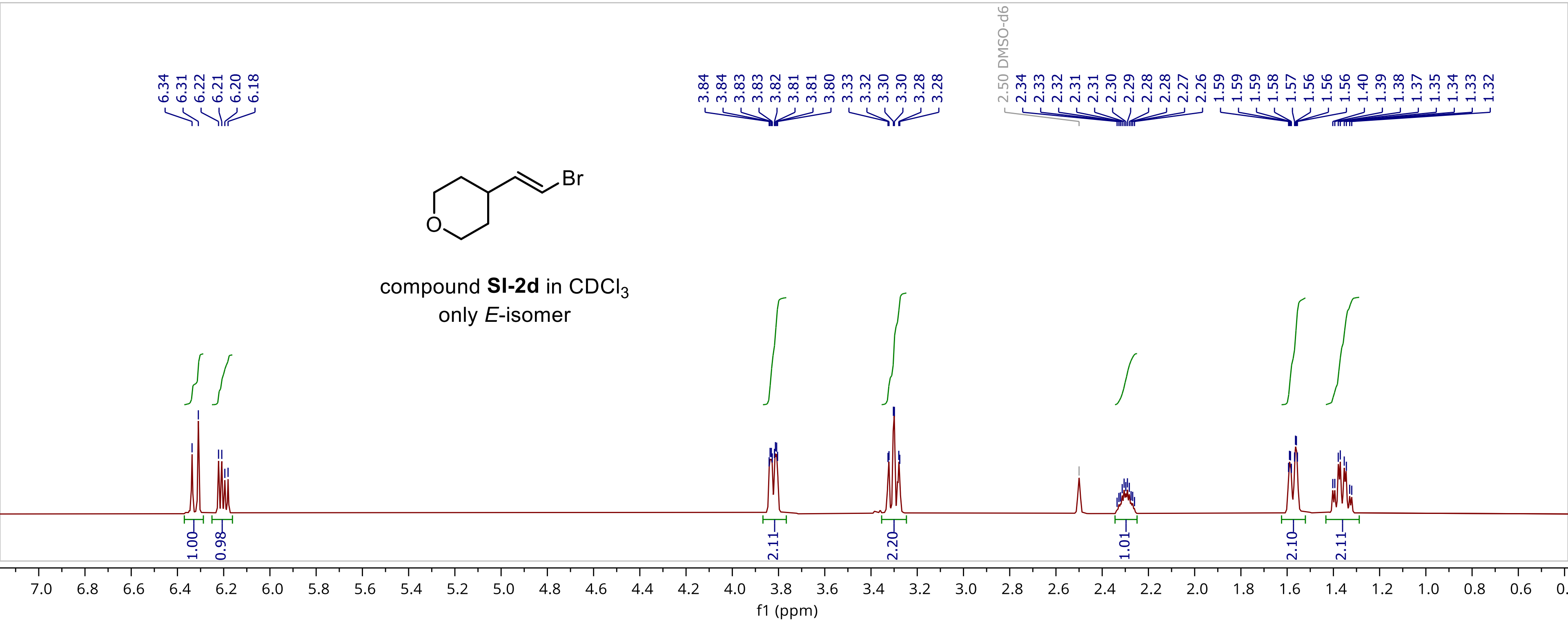
compound **20** in $CDCl_3$

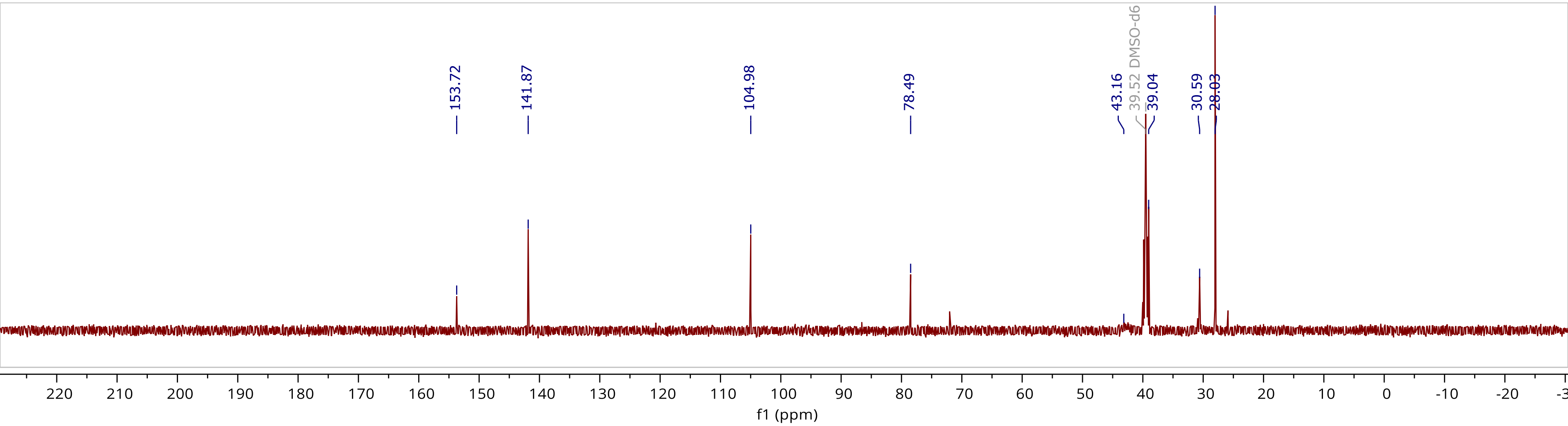


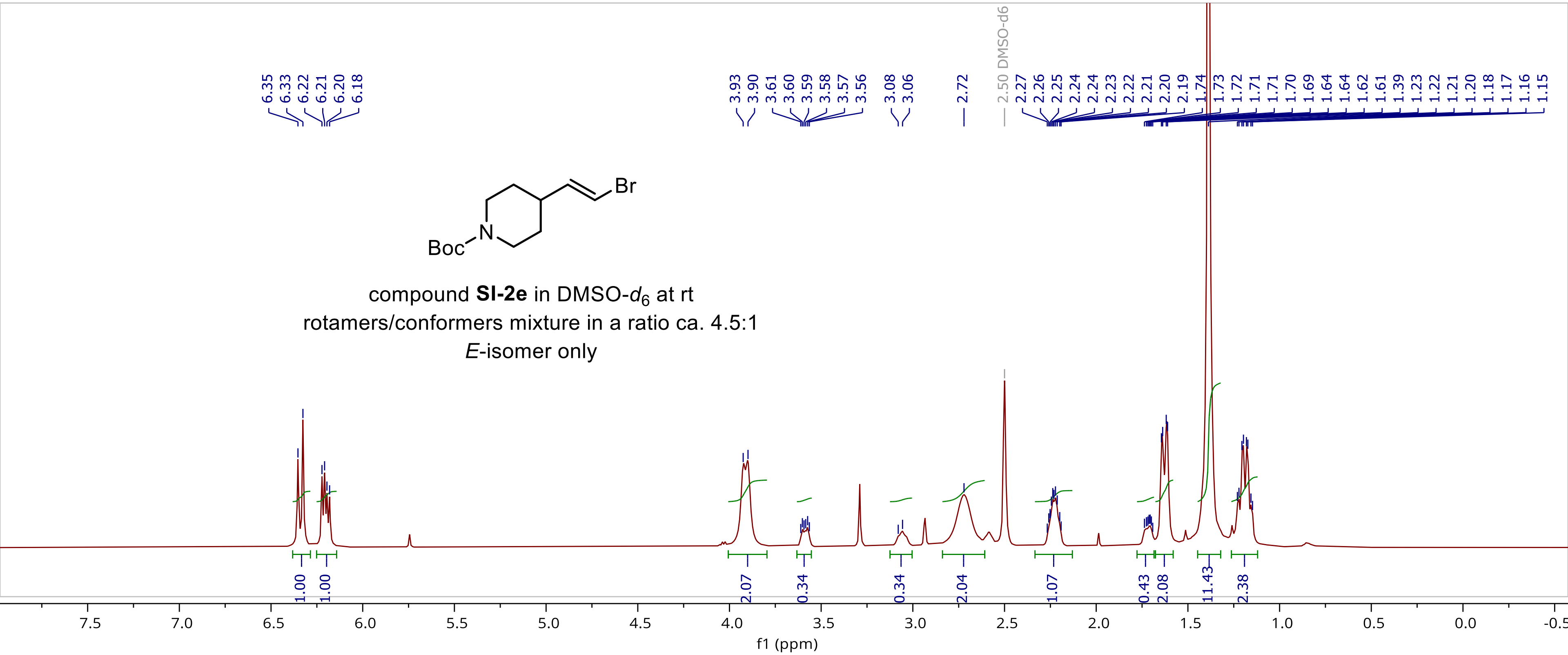


compound **21** in CDCl$_3$




compound **SI-2d** in $CDCl_3$
only *E*-isomer

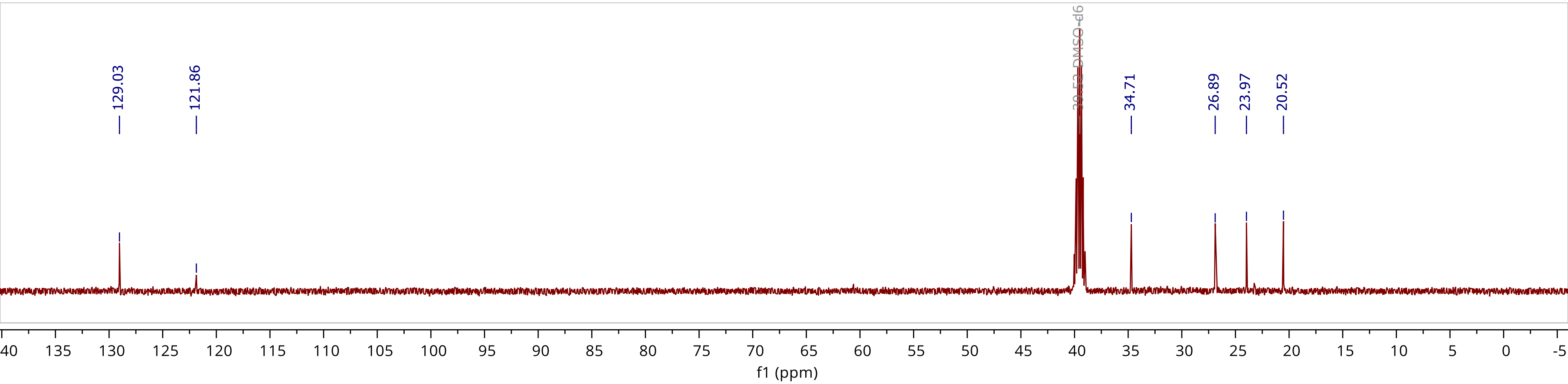


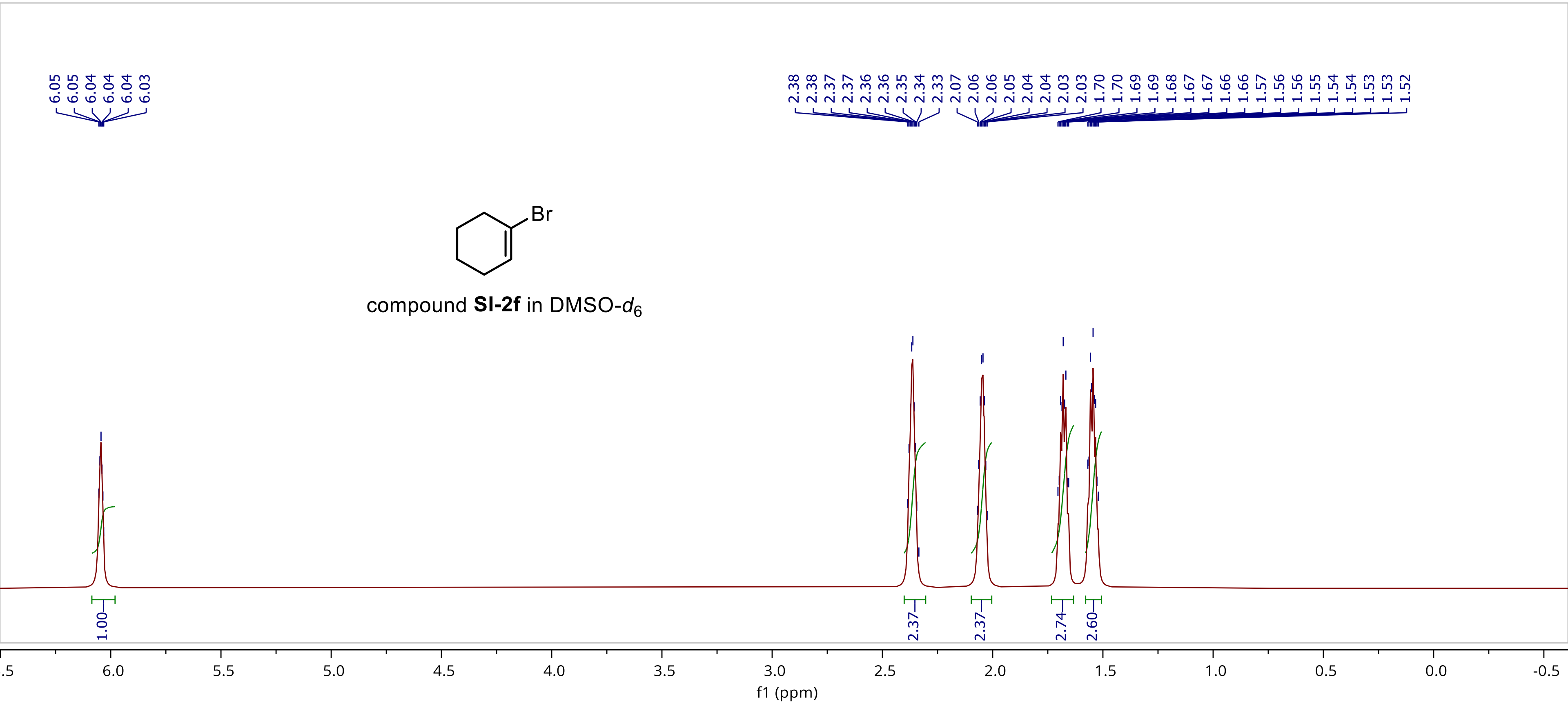


compound **SI-2e** in DMSO-d_6 at rt

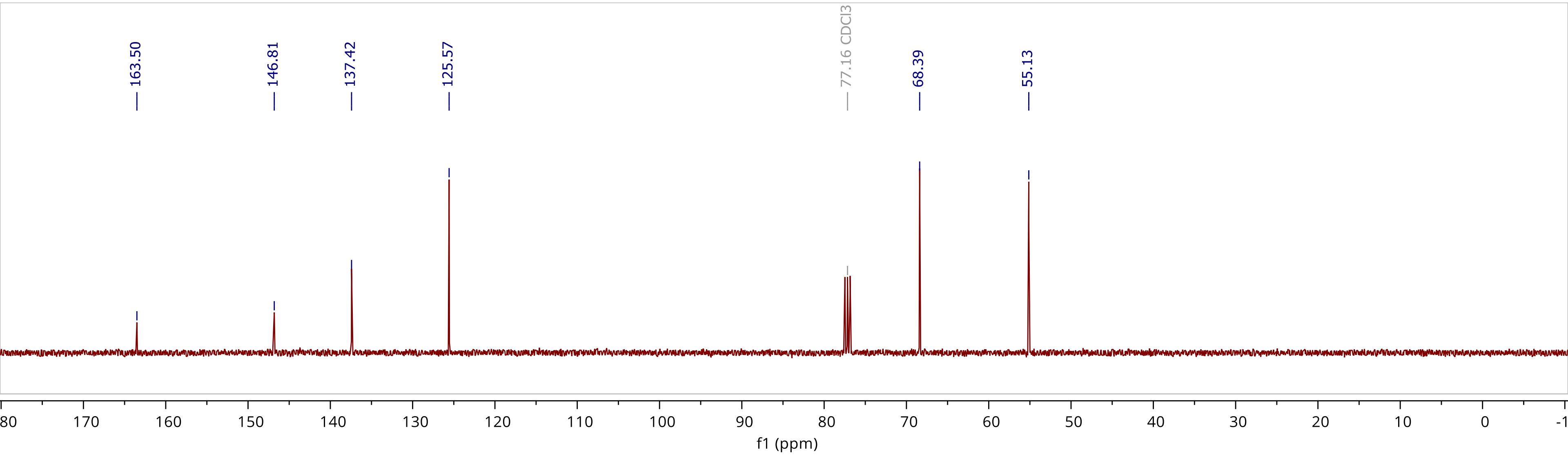
rotamers/conformers mixture in a ratio ca. 4.5:1

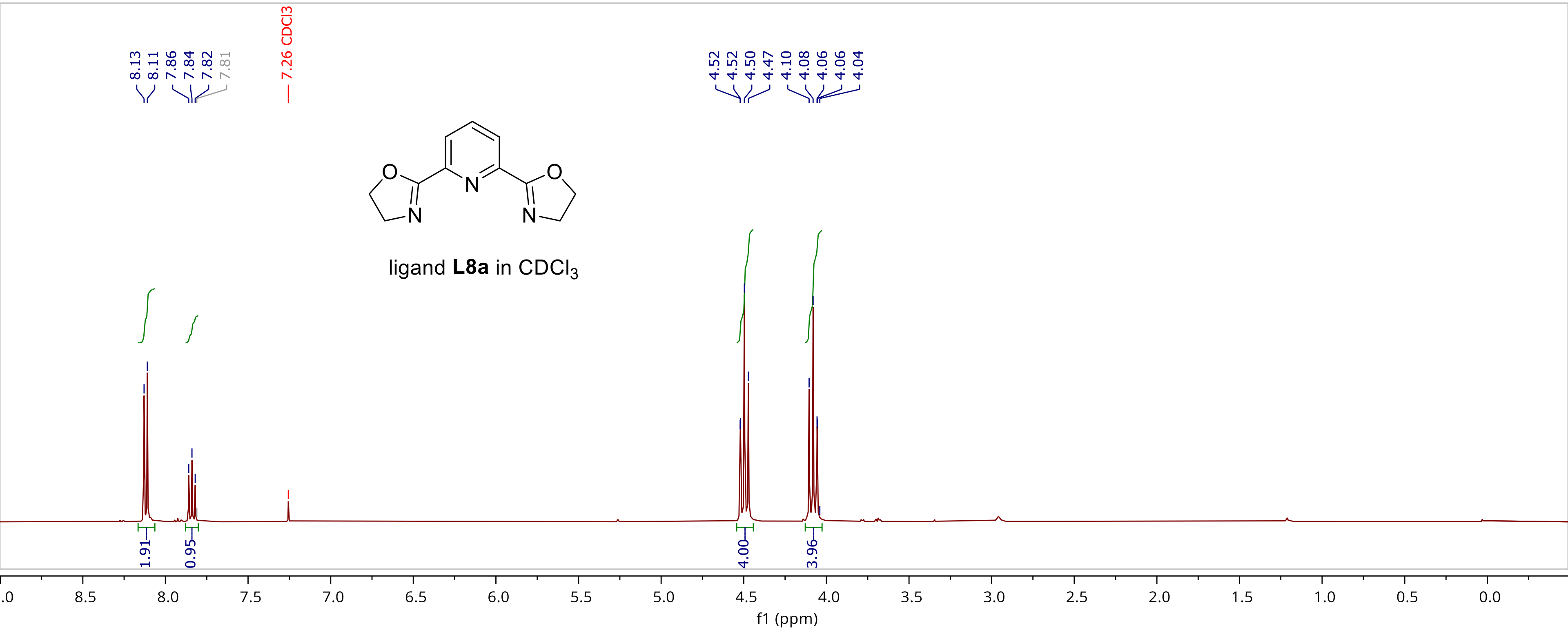
E-isomer only

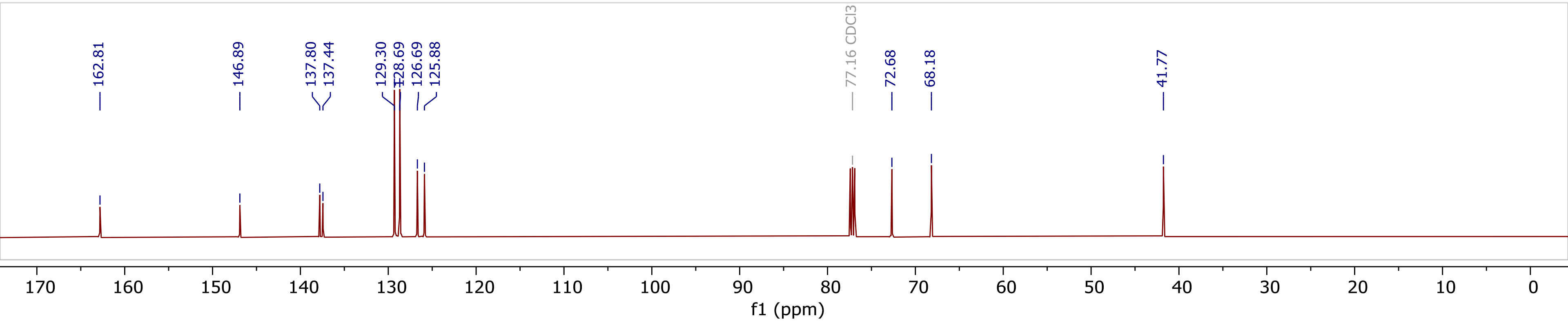


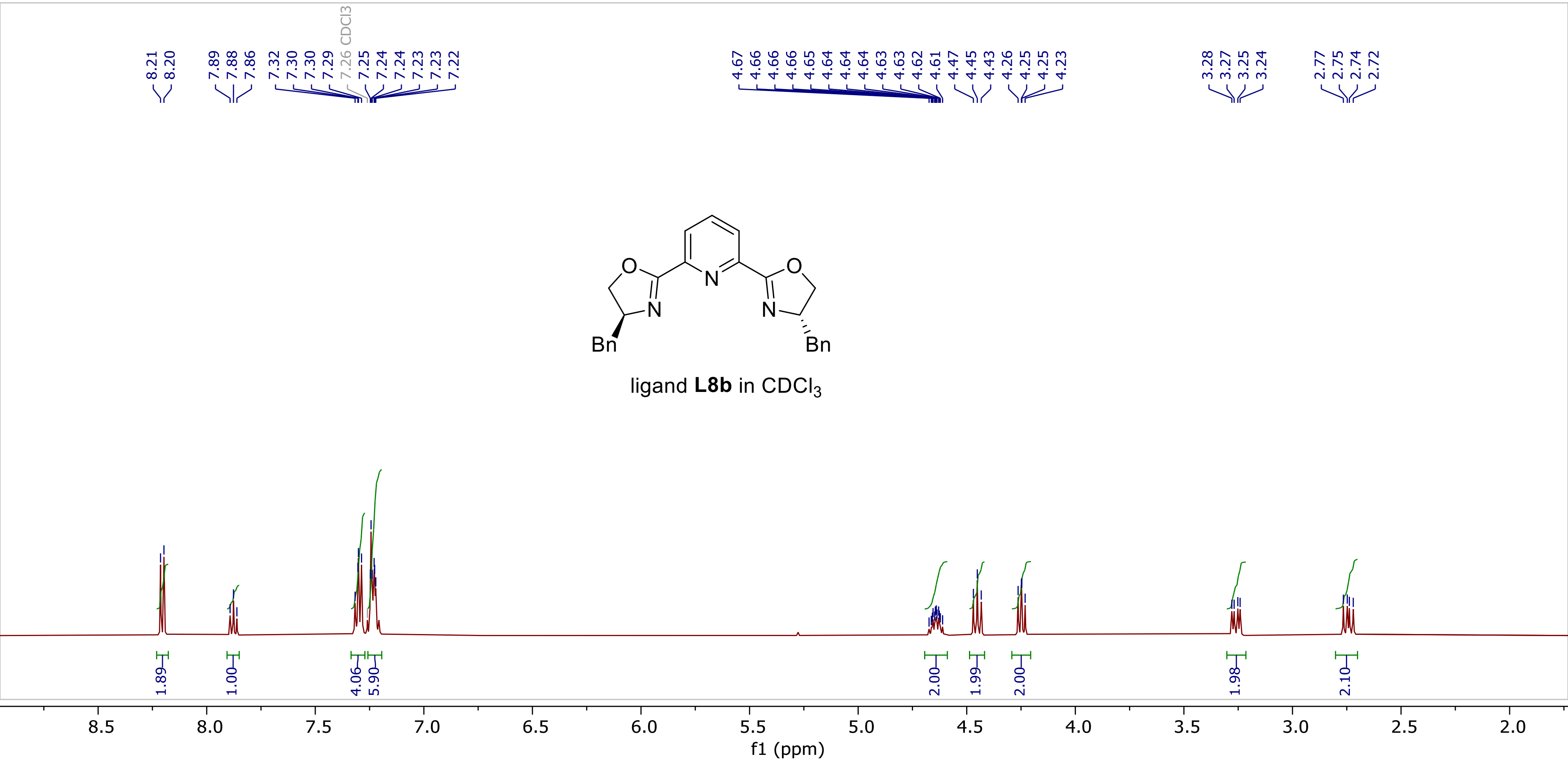


compound **SI-2f** in DMSO-d_6

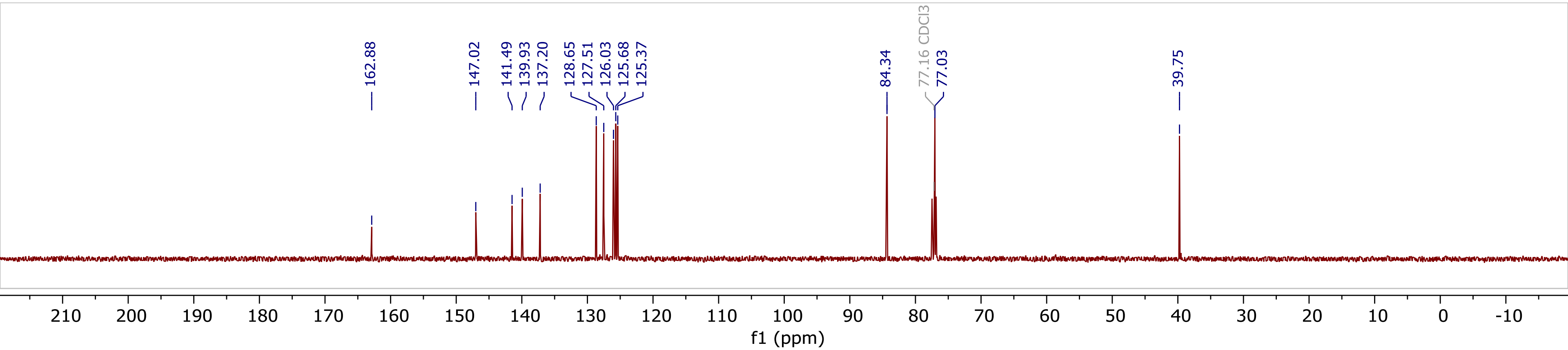

163.50
146.81
137.42
125.57
77.16 CDCl3
68.39
55.13
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

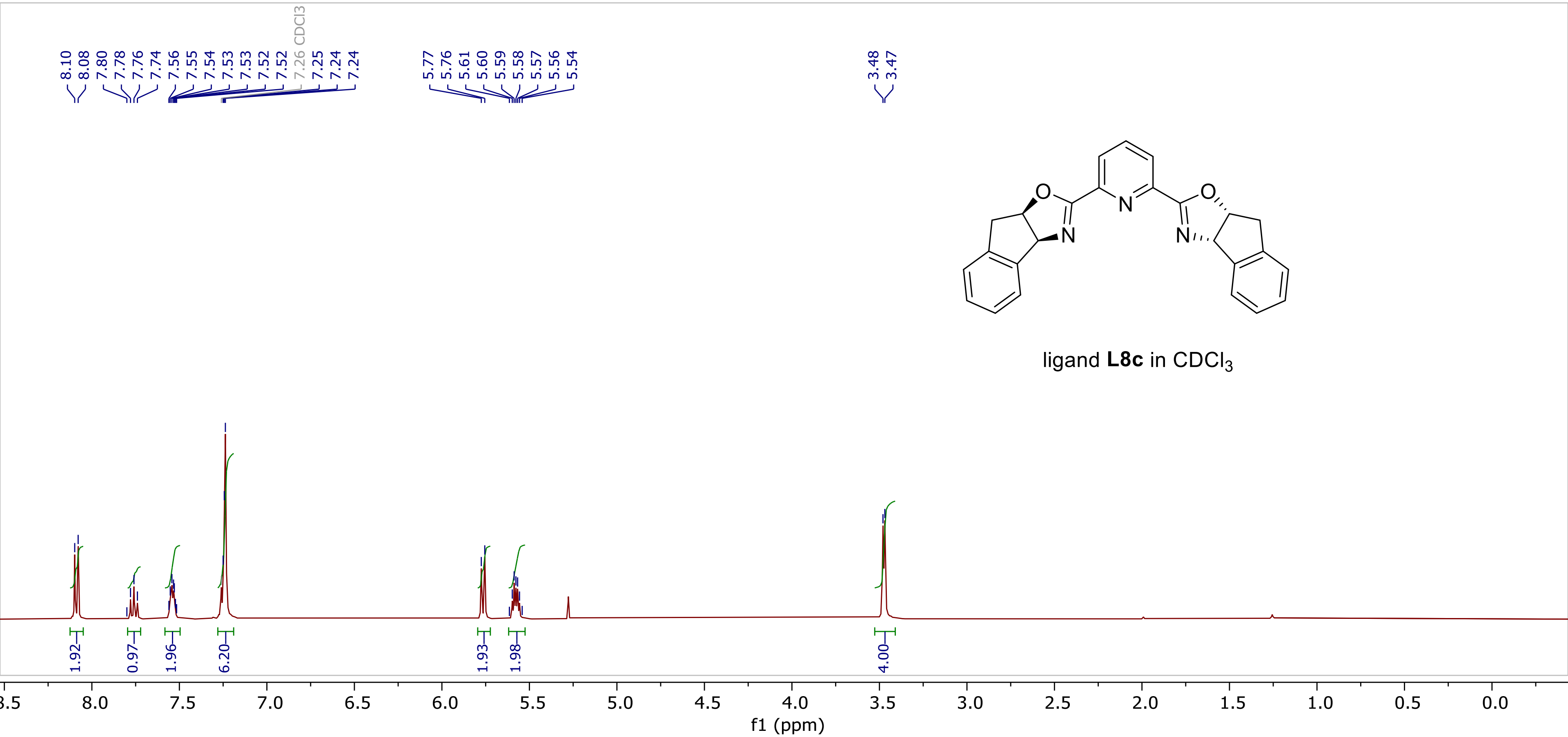

8.13
8.11
7.86
7.84
7.82
7.81
7.26 CDCl3
4.52
4.52
4.50
4.47
4.10
4.08
4.06
4.06
4.04
O
N
N
O
N
ligand **L8a** in $CDCl_3$
1.91
0.95
4.00
3.96
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



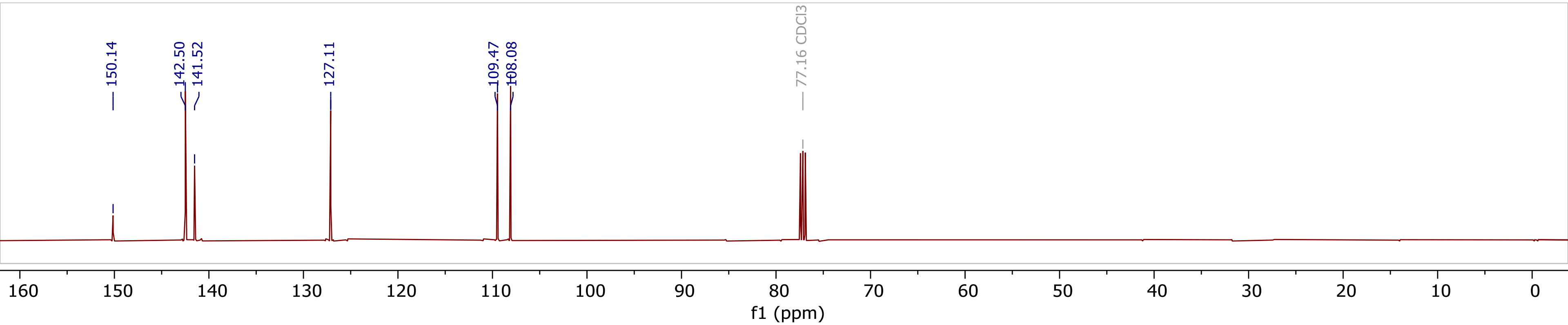


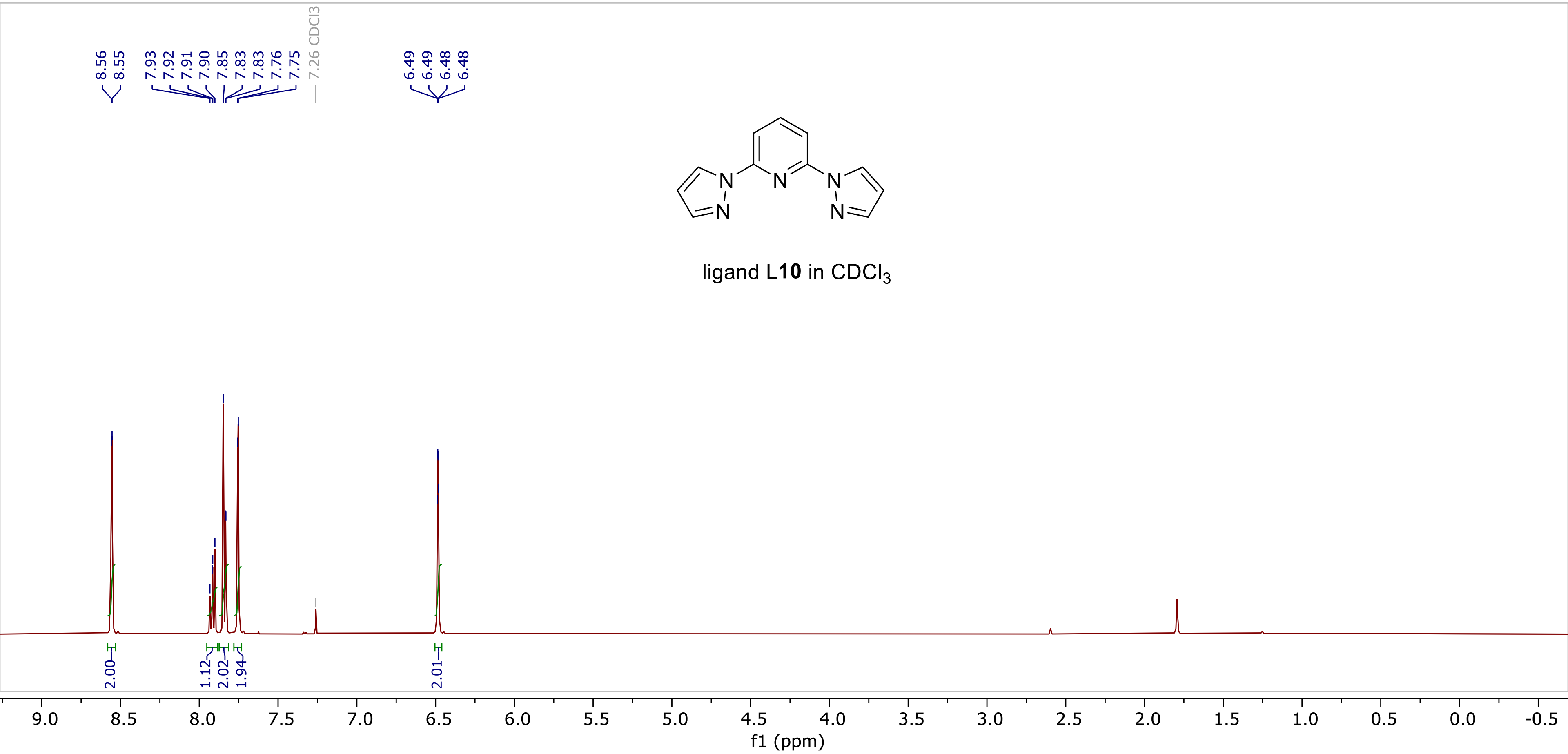
ligand **L8b** in CDCl$_3$



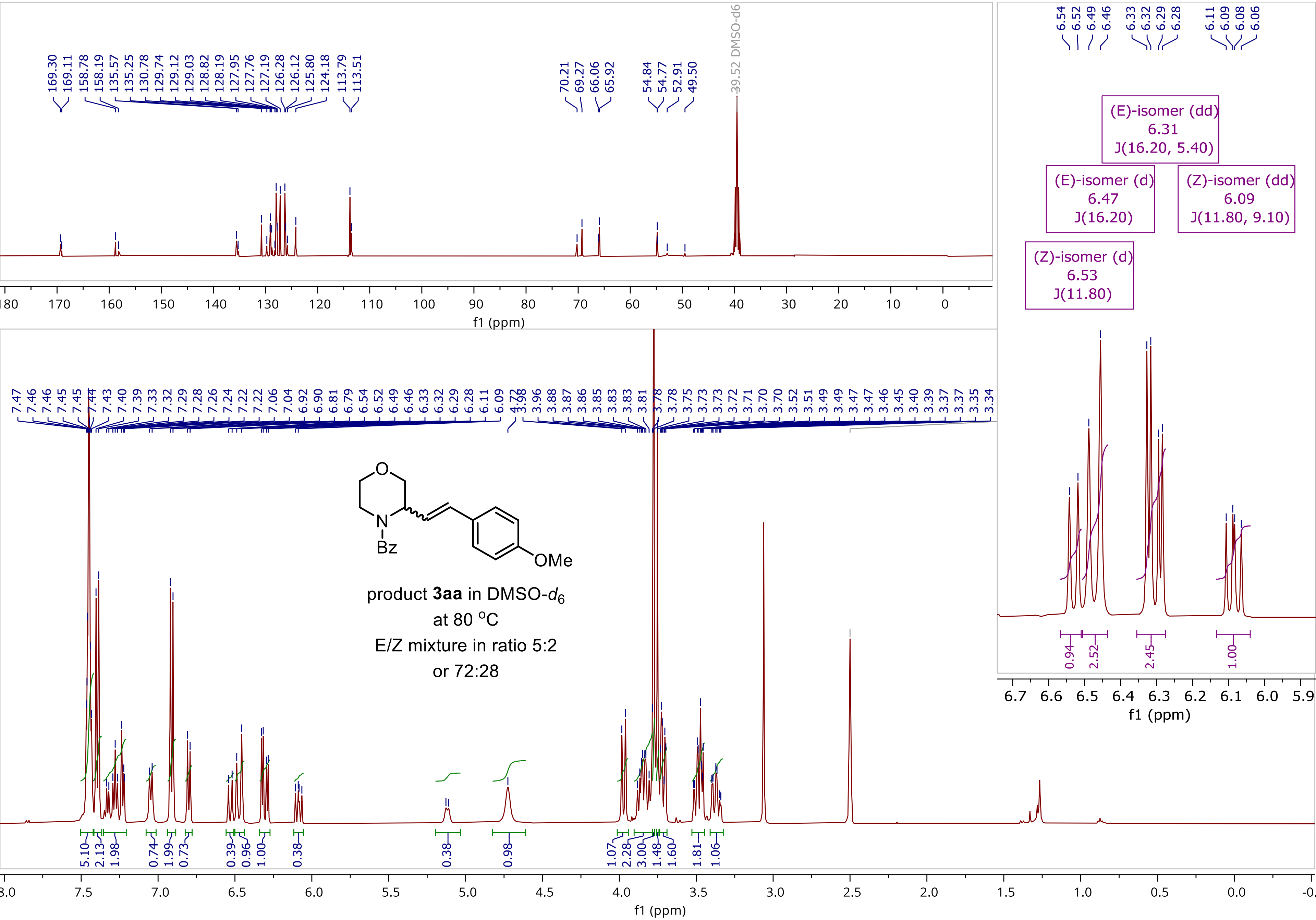


ligand **L8c** in $CDCl_3$





ligand L**10** in $CDCl_3$

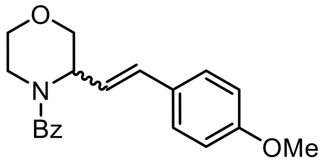


product **3aa** in DMSO-d_6

at 80 ^{o}C

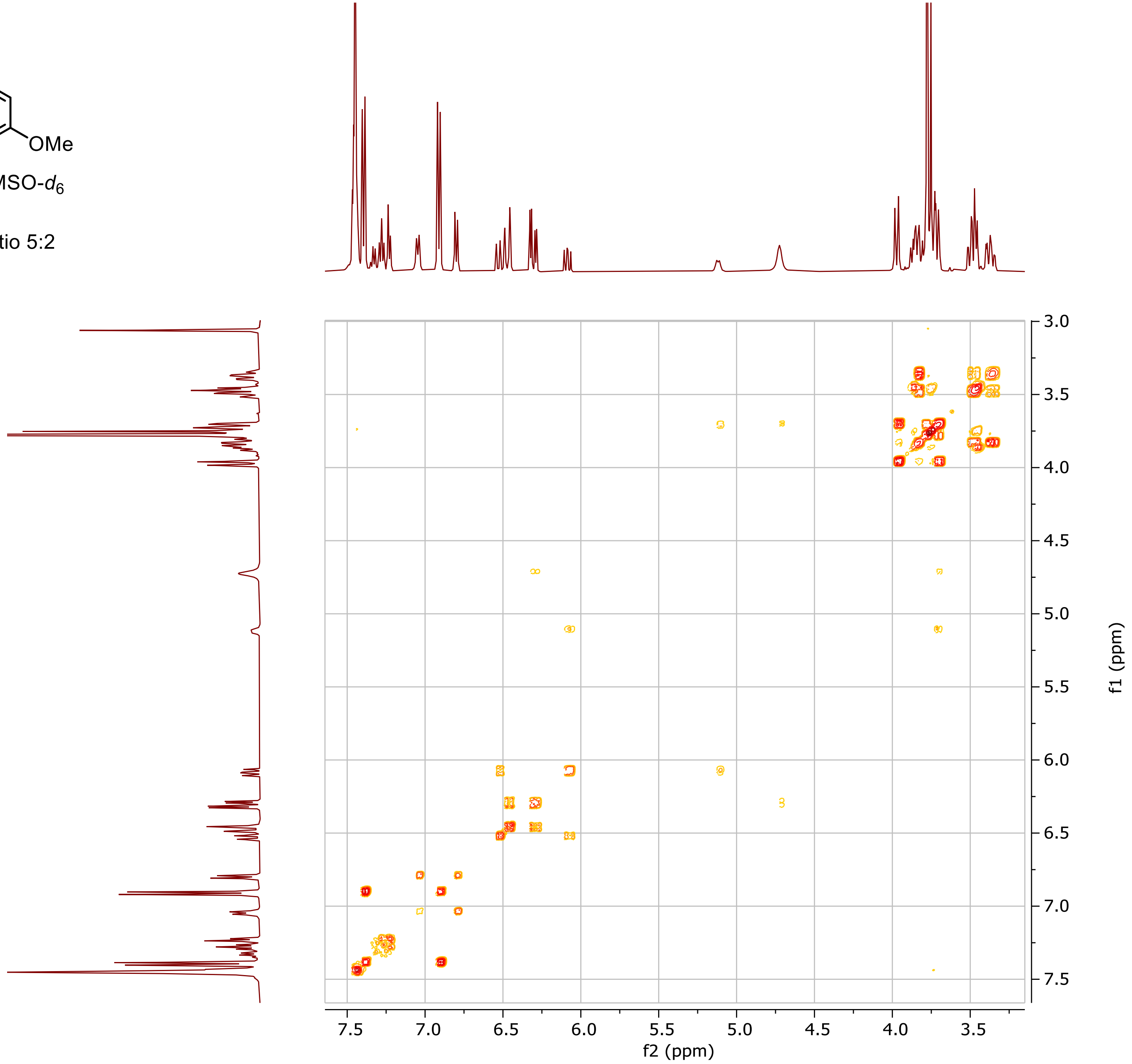
E/Z mixture in ratio 5:2

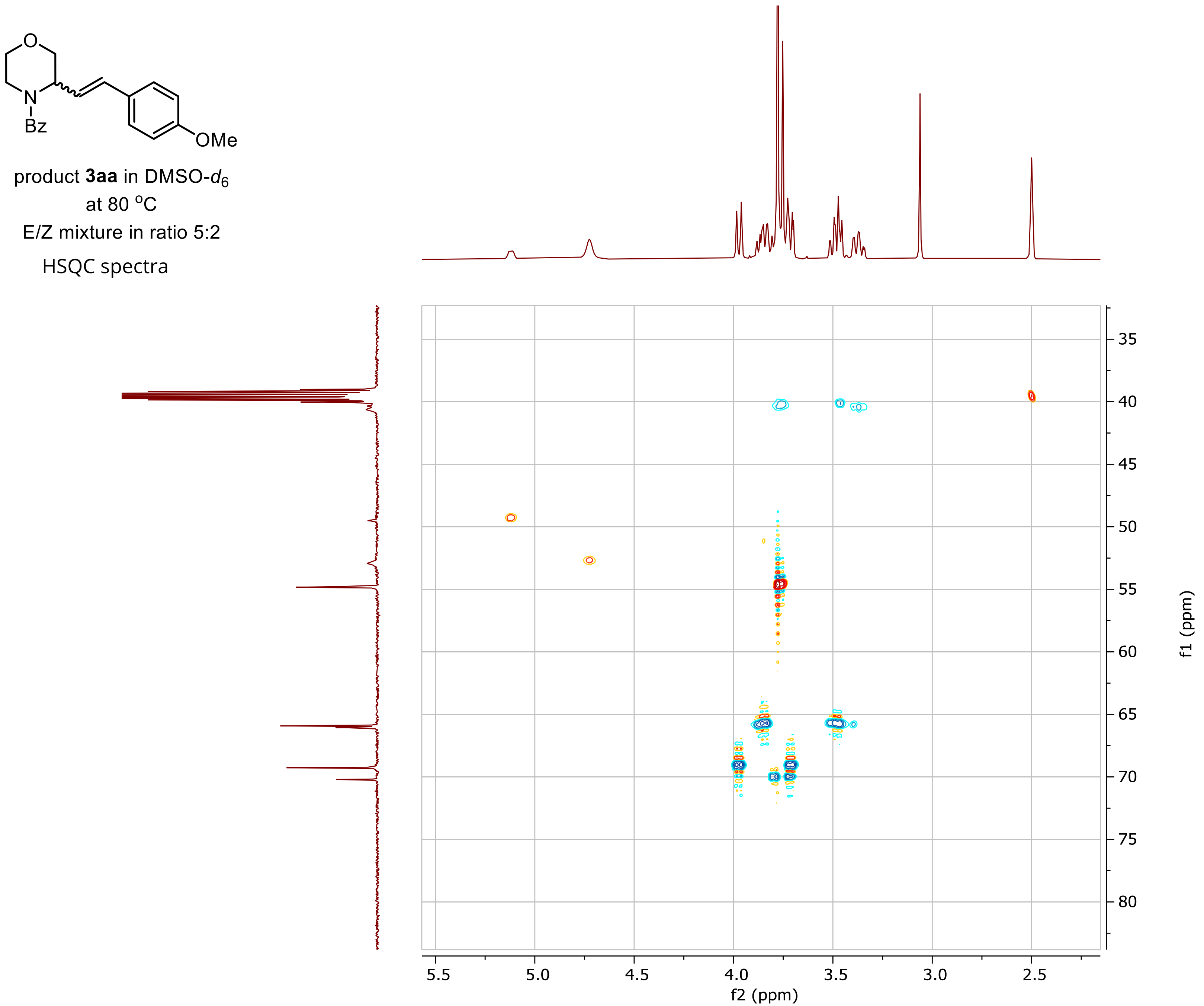
or 72:28



product **3aa** in DMSO-d_6
at 80 ^{o}C
E/Z mixture in ratio 5:2

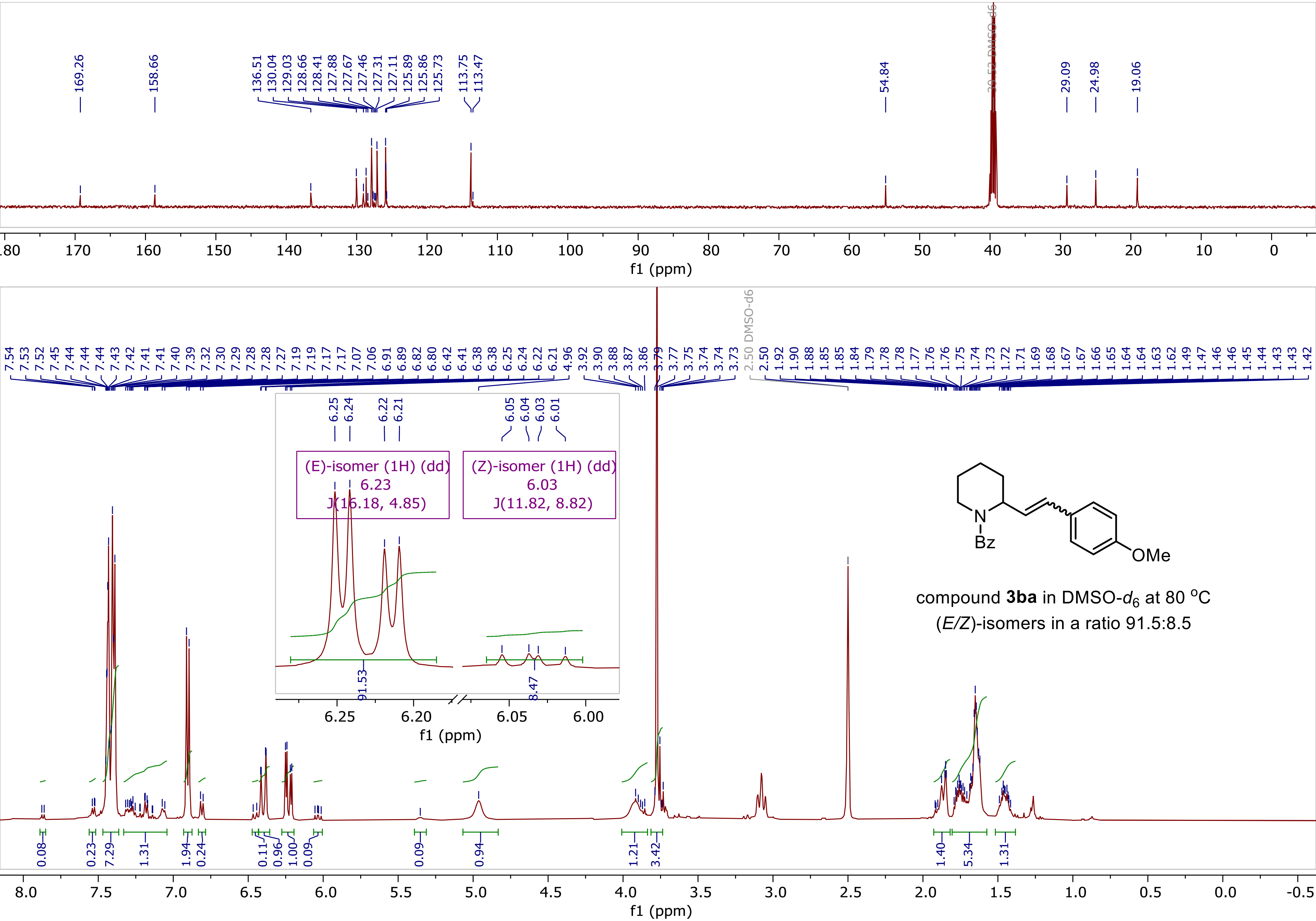
COSY spectra





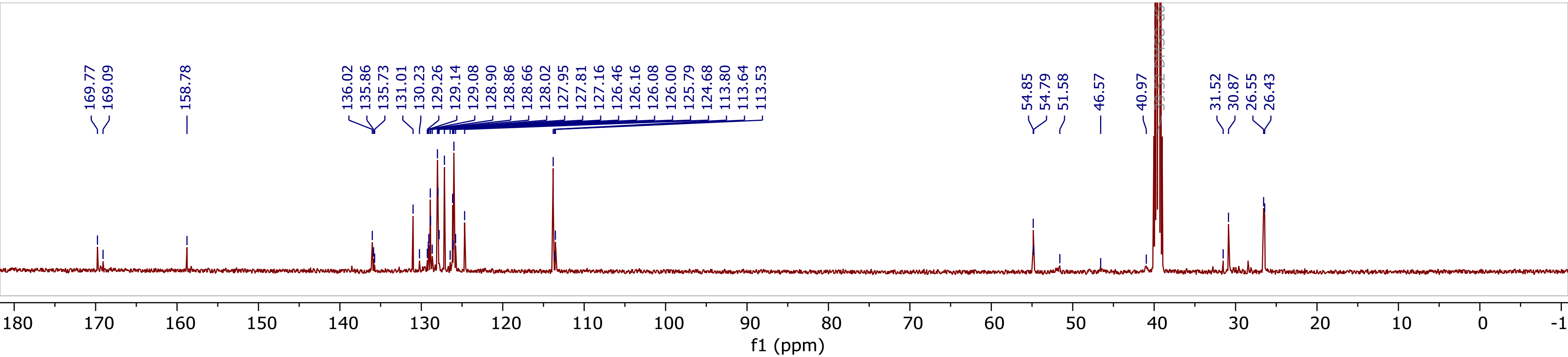
product **3aa** in DMSO-d_6
at 80 ^oC
E/Z mixture in ratio 5:2

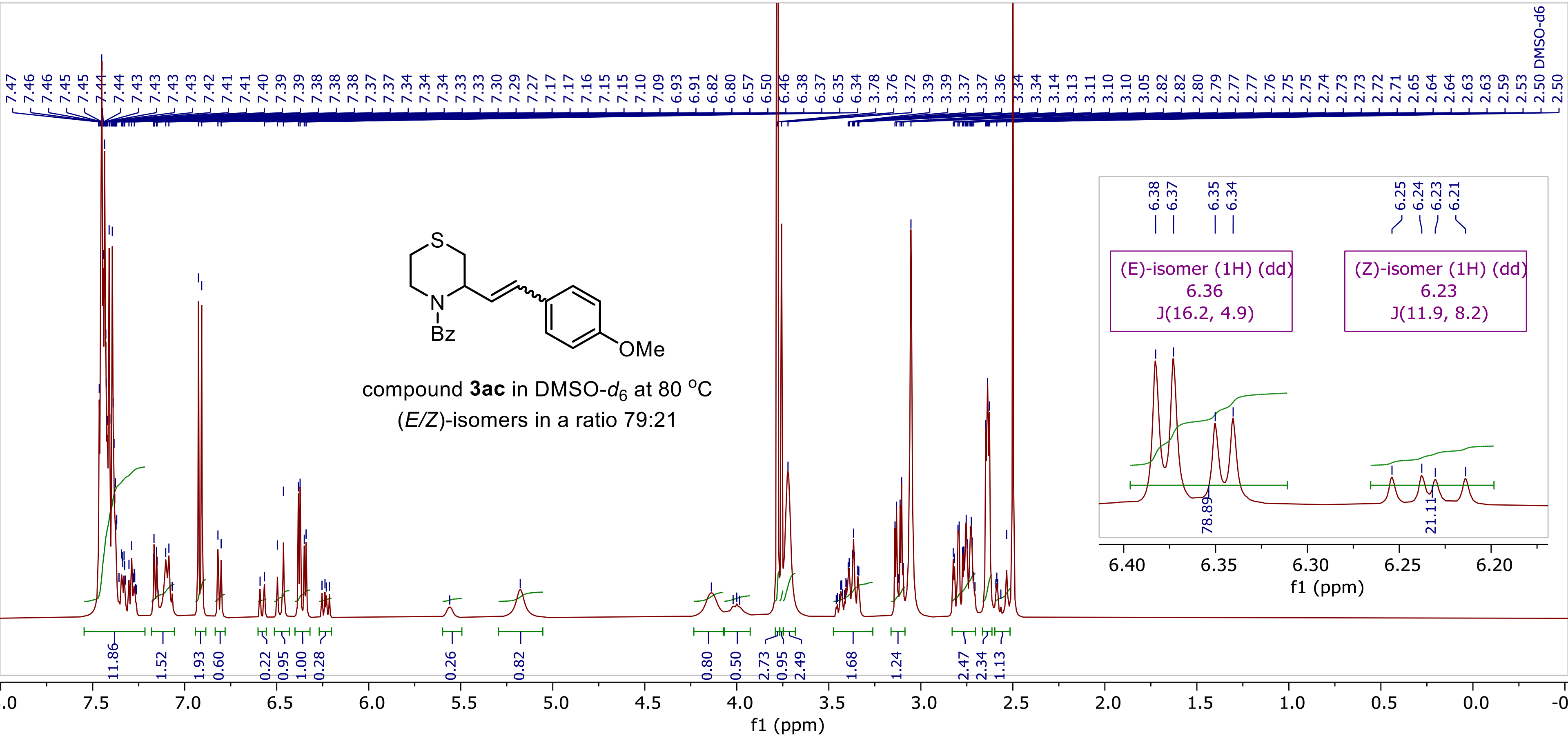
HSQC spectra



compound **3ba** in DMSO-d_6 at 80 °C

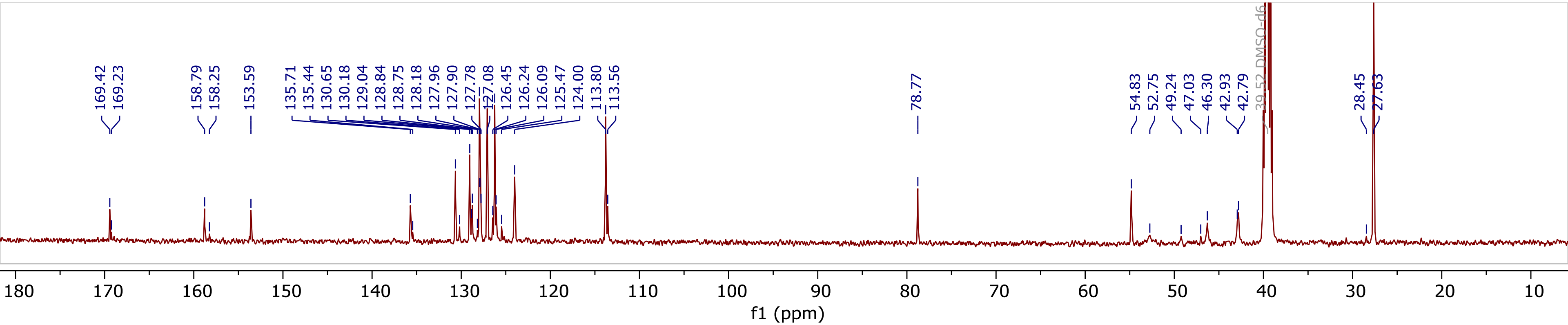
(*E*/*Z*)-isomers in a ratio 91.5:8.5

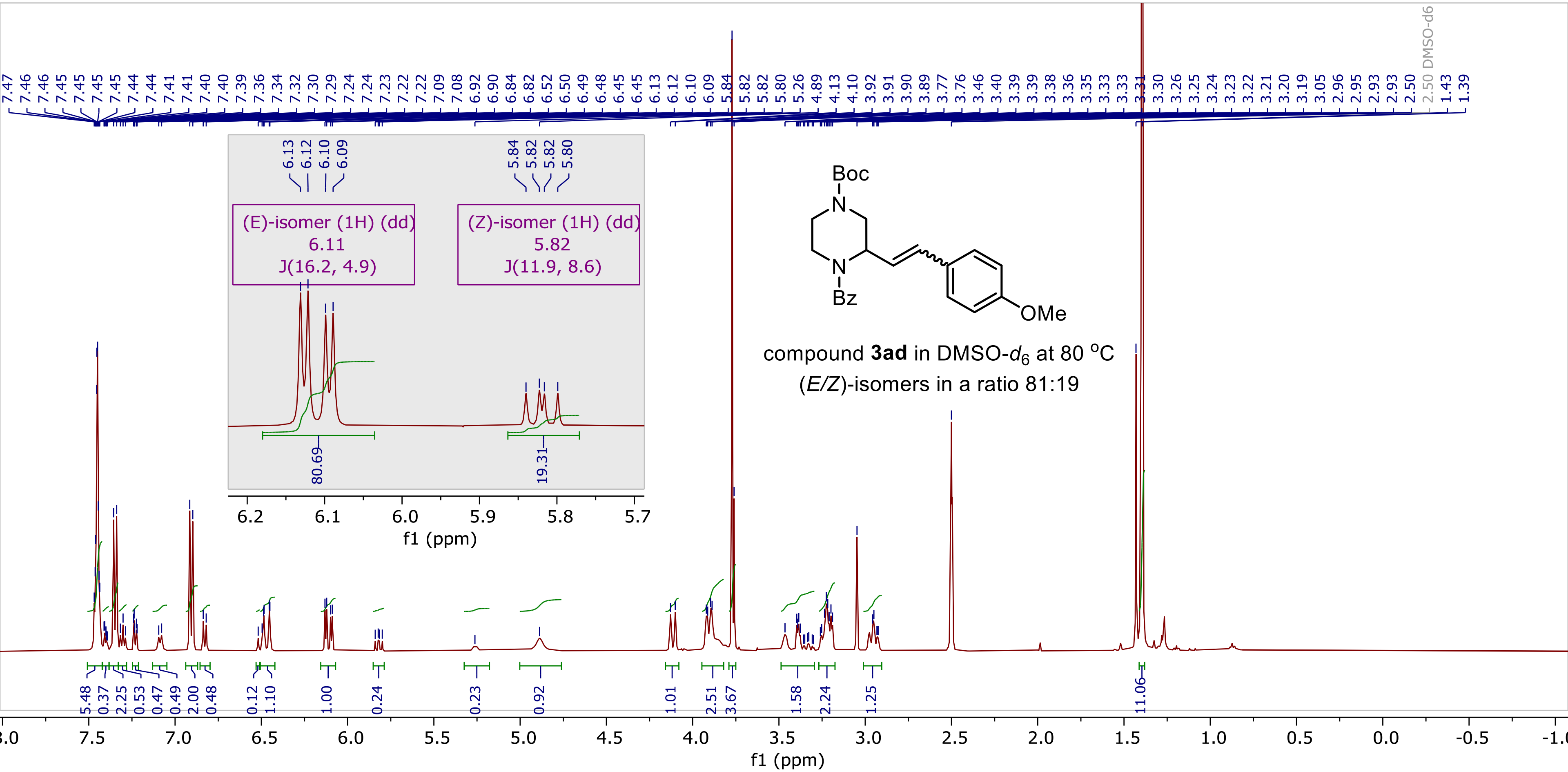




compound **3ac** in DMSO-d_6 at 80 °C

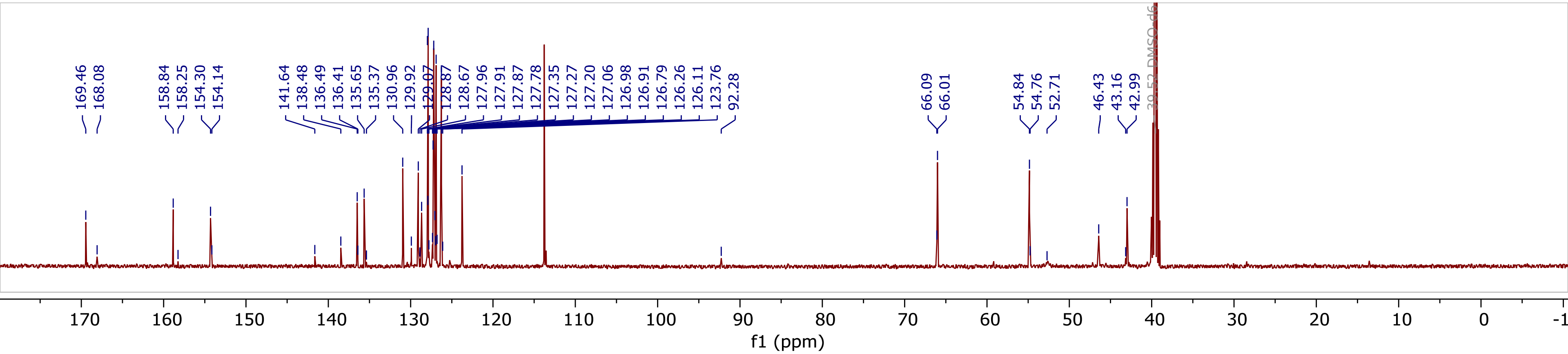
(*E*/*Z*)-isomers in a ratio 79:21

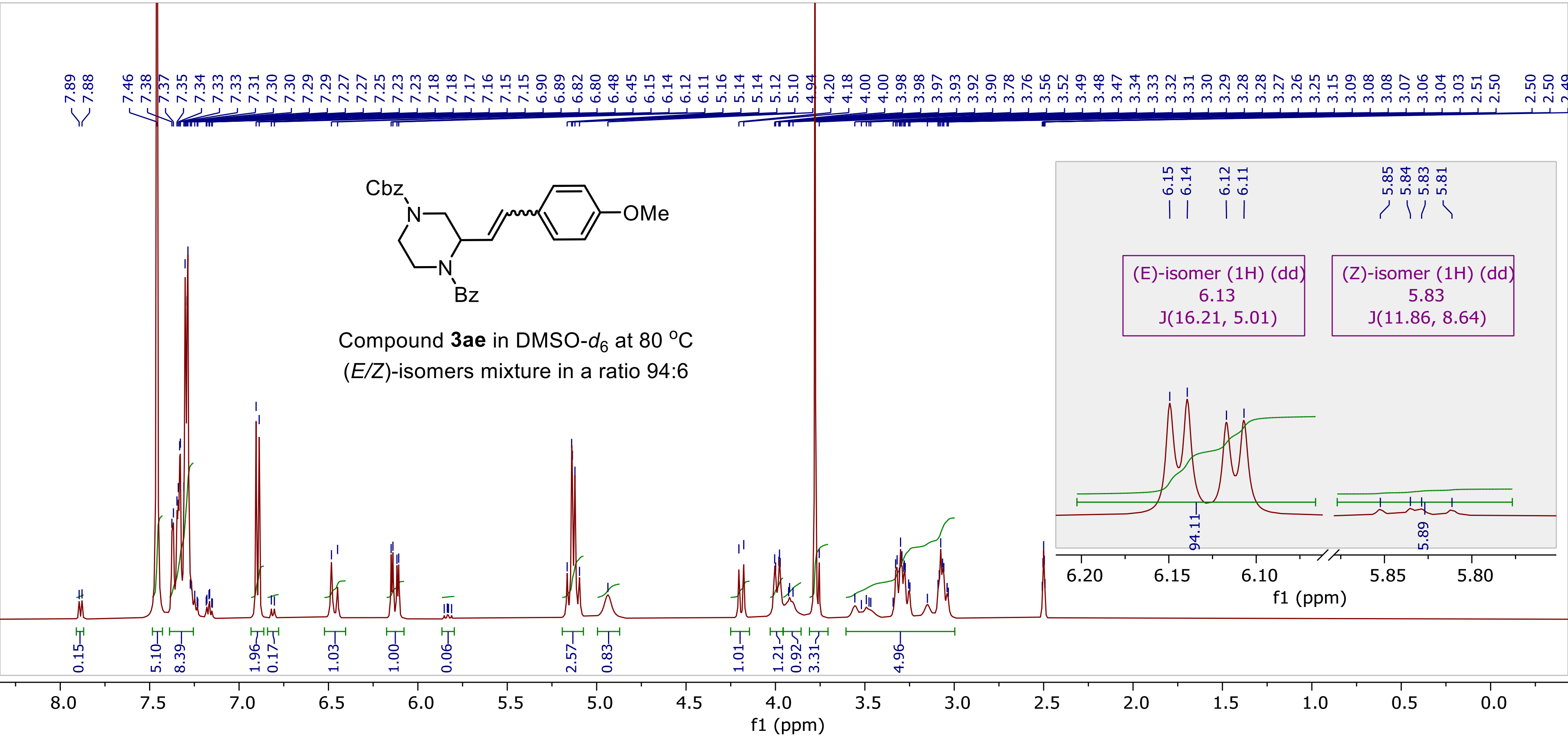




compound **3ad** in DMSO-d_6 at 80 °C

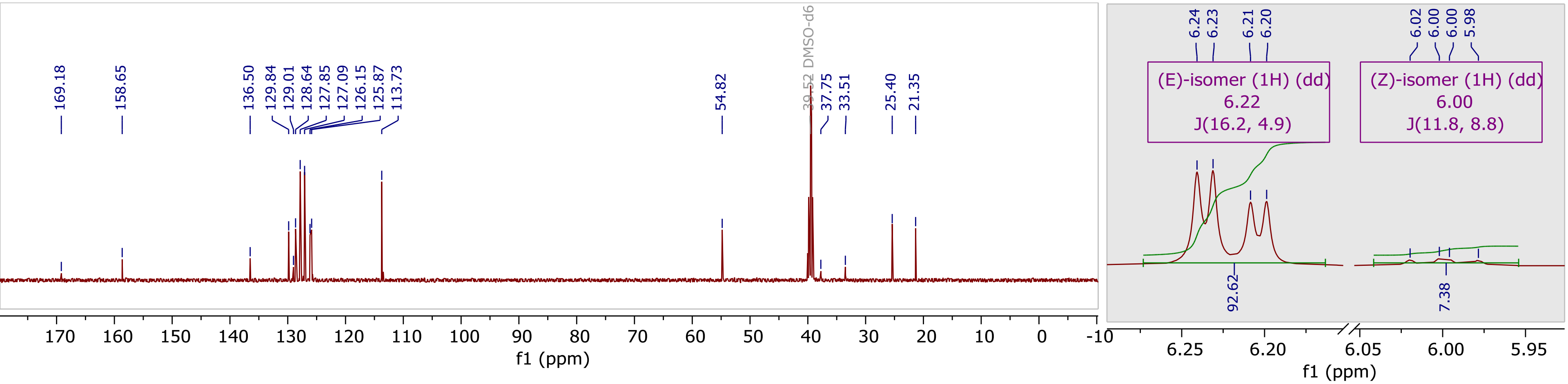
(*E/Z*)-isomers in a ratio 81:19

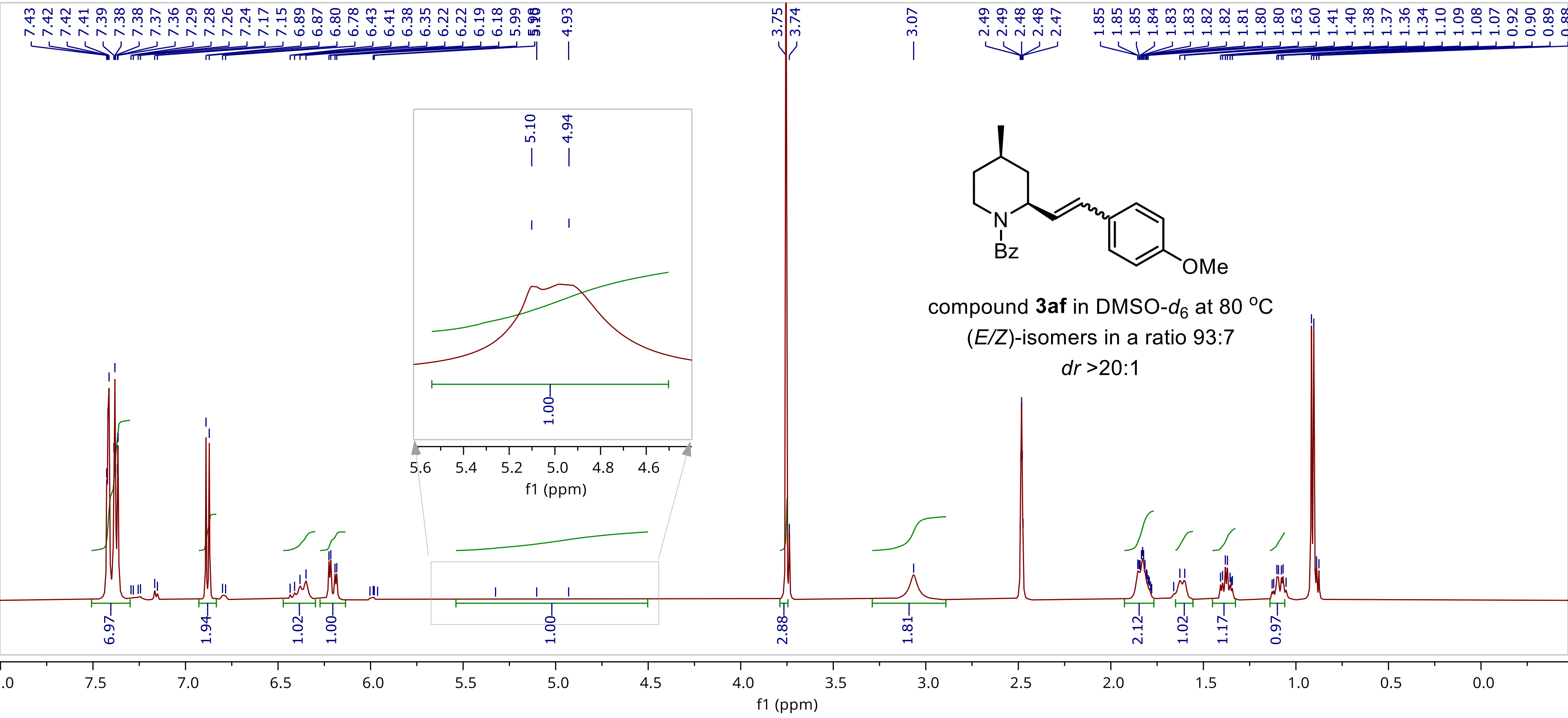




Compound **3ae** in DMSO-d_6 at 80 °C

(*E*/*Z*)-isomers mixture in a ratio 94:6

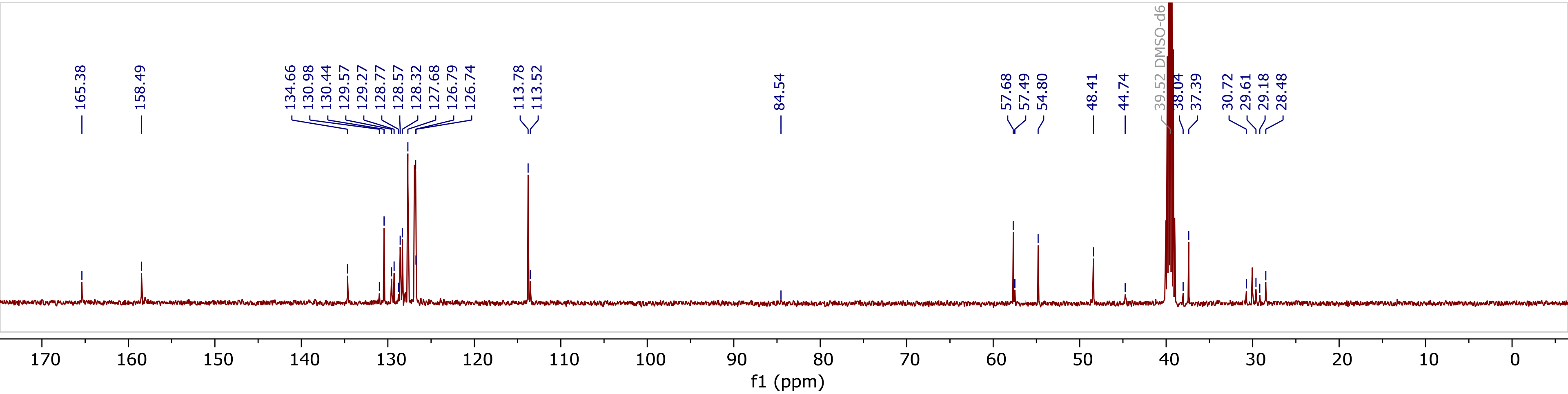


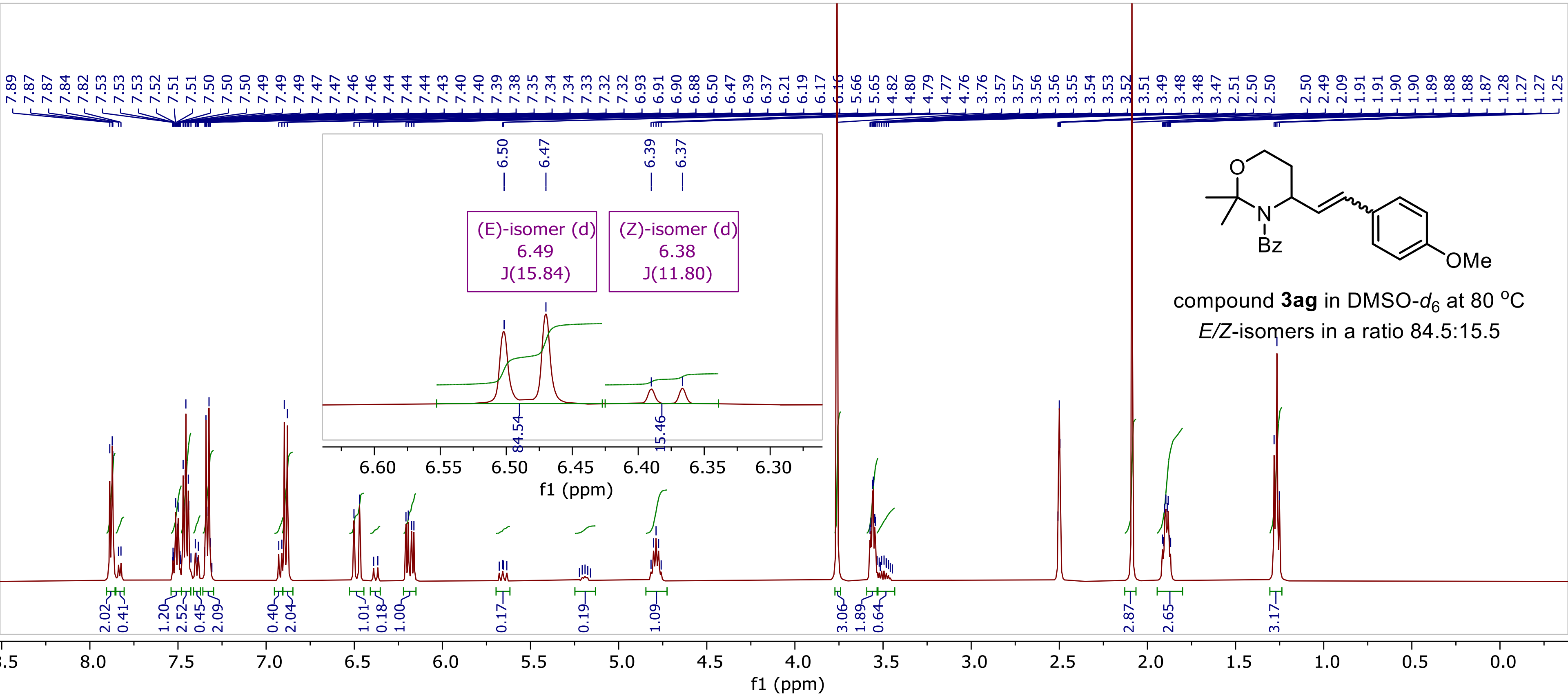


compound **3af** in DMSO-d_6 at 80 °C

(*E*/*Z*)-isomers in a ratio 93:7

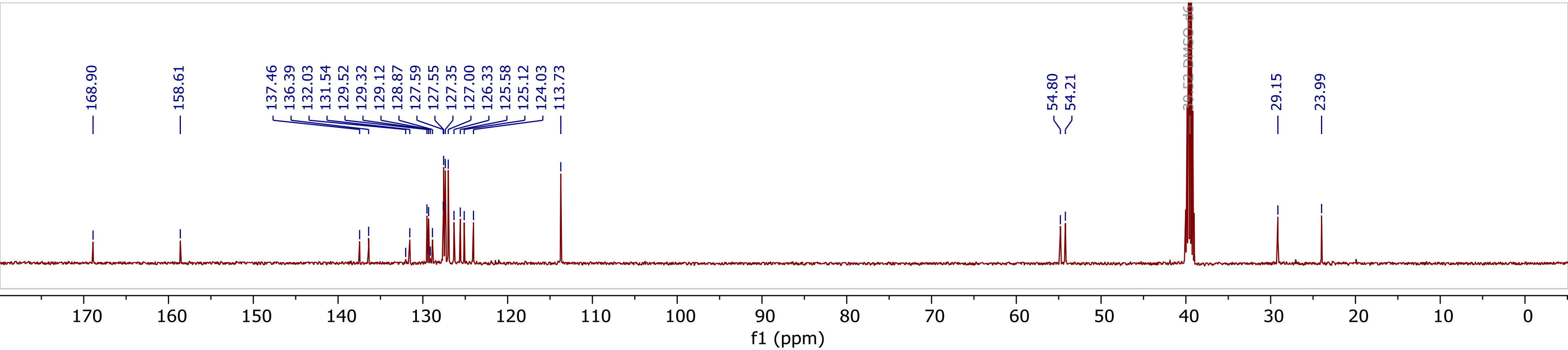
dr >20:1

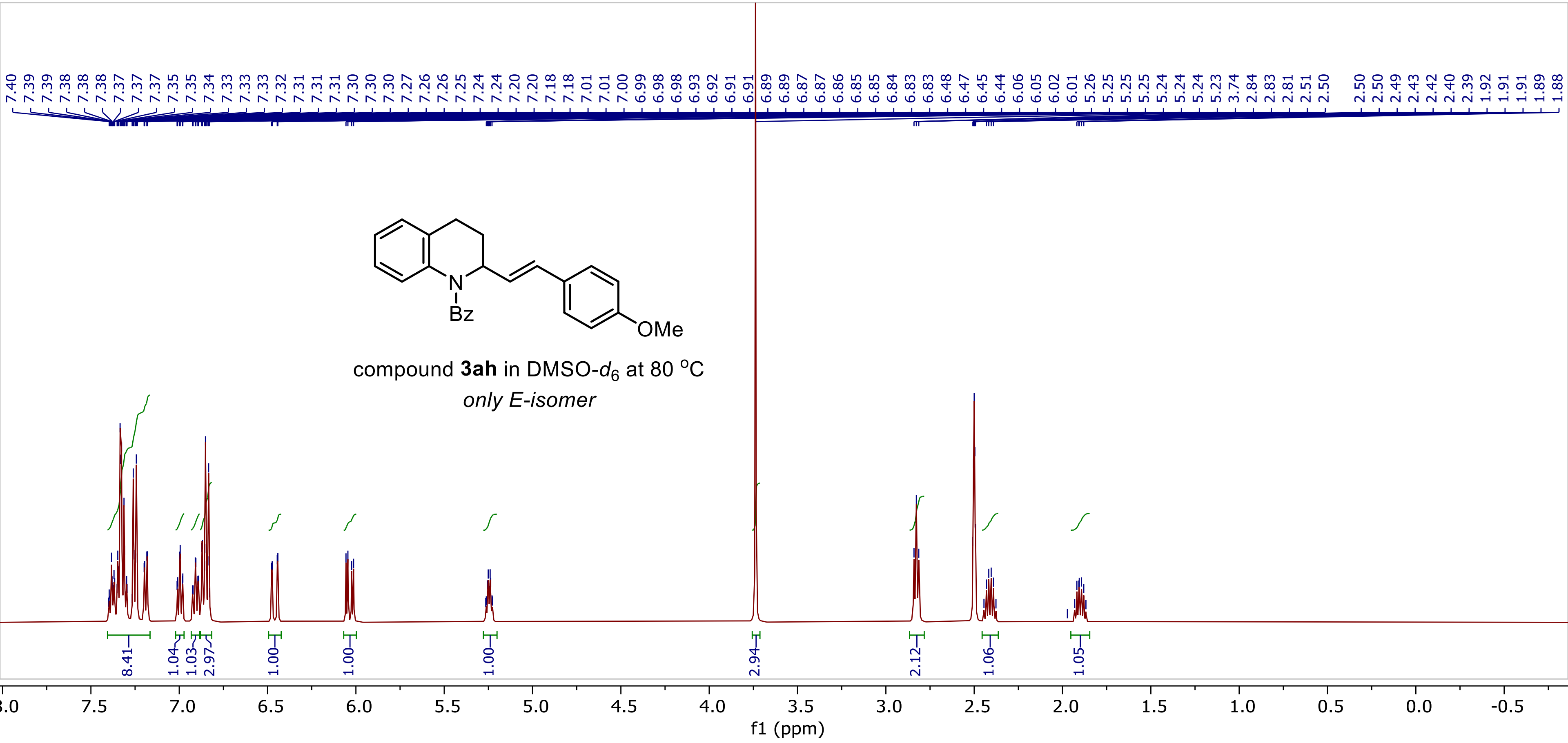




compound **3ag** in DMSO-d_6 at 80 ^oC

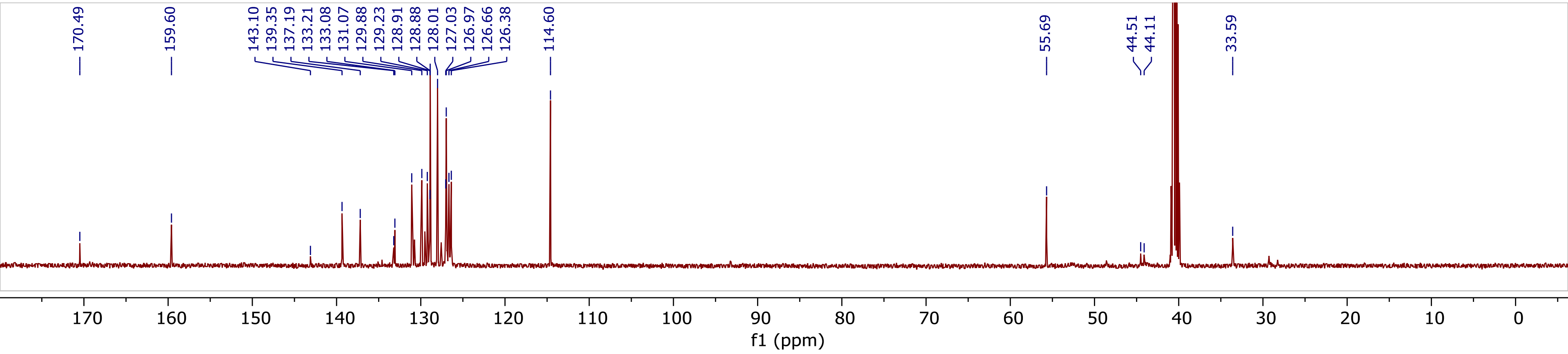
E/*Z*-isomers in a ratio 84.5:15.5

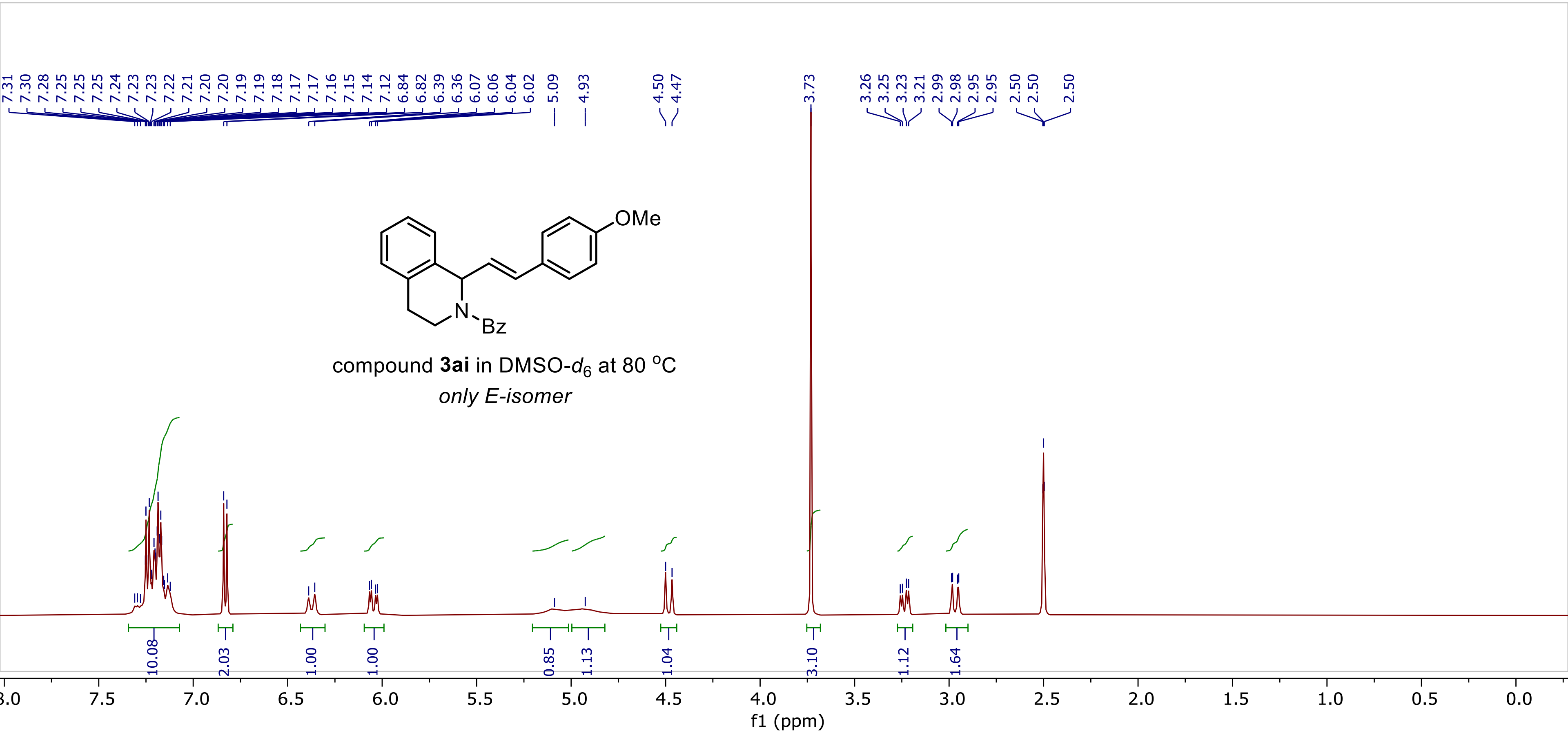




compound **3ah** in DMSO-d_6 at 80 °C

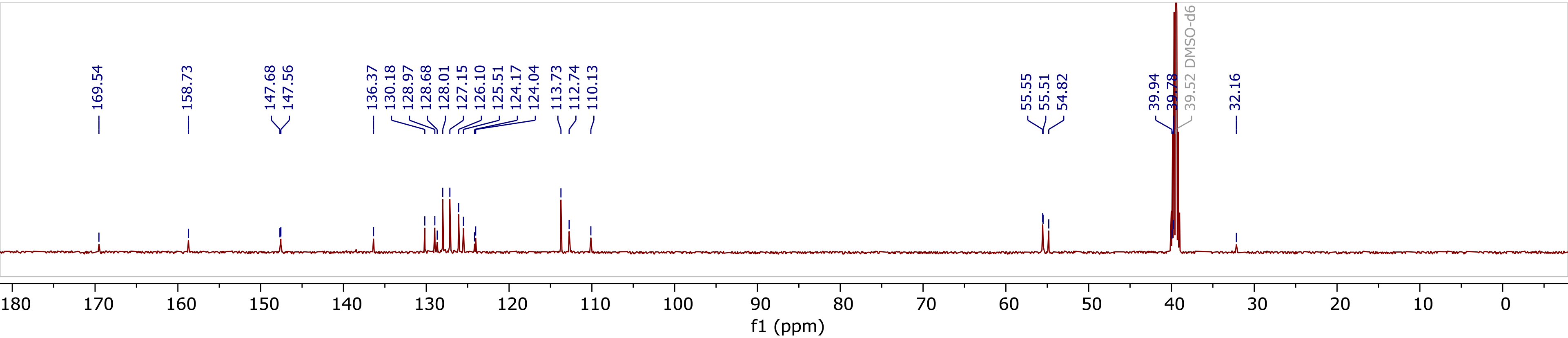
only E-isomer

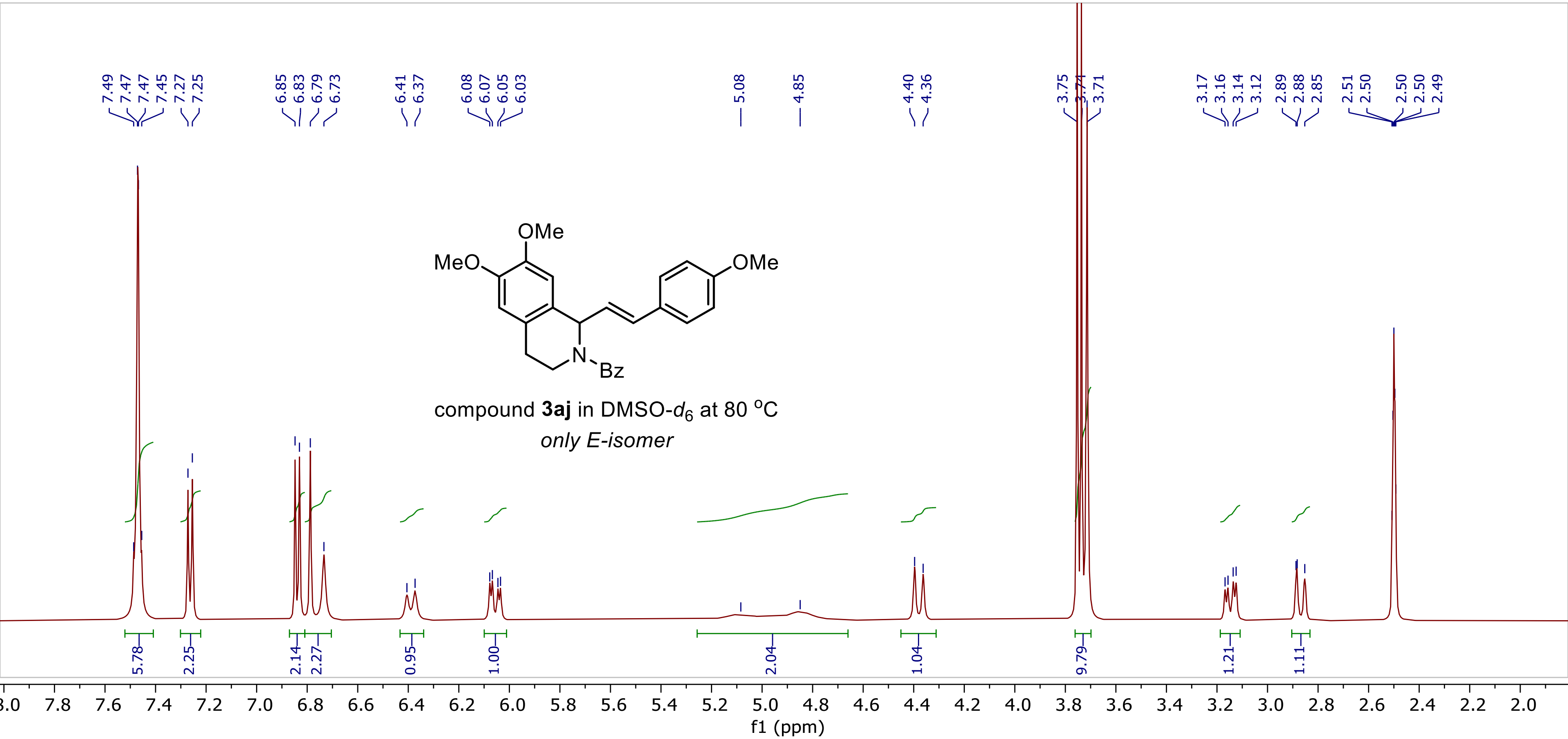




compound **3ai** in DMSO-d_6 at 80 ^{o}C

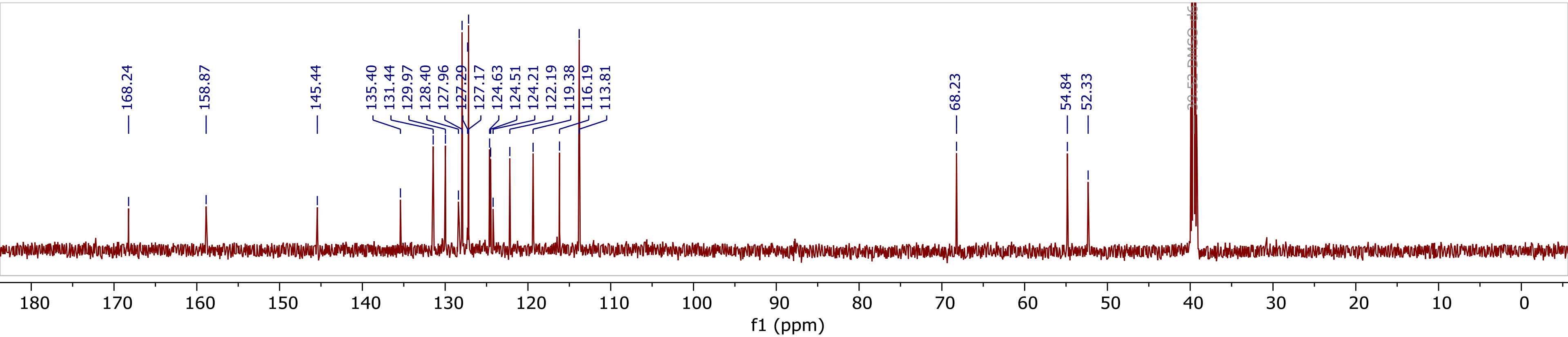
only E-isomer

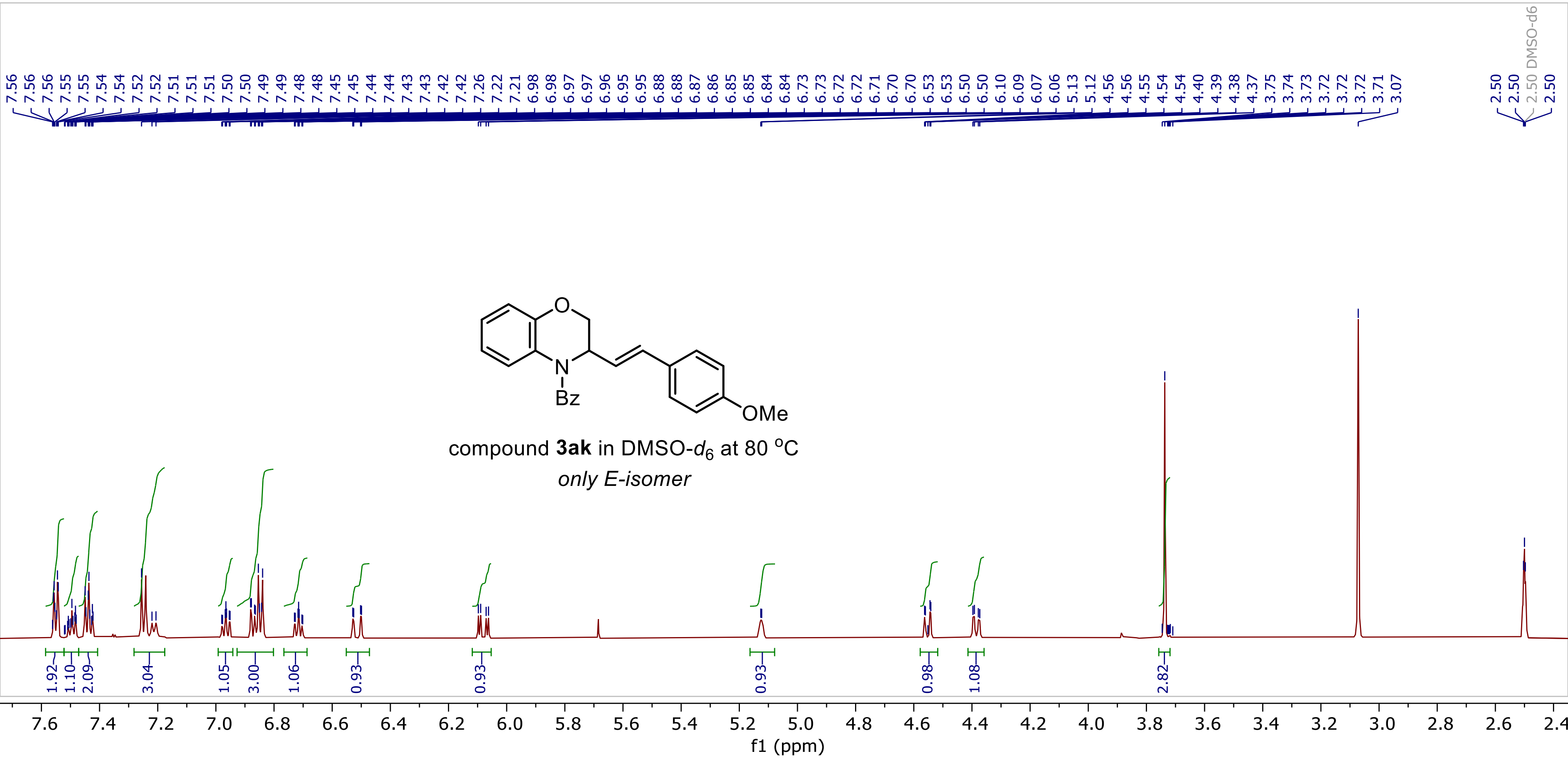




compound **3aj** in DMSO-d_6 at 80 ^oC

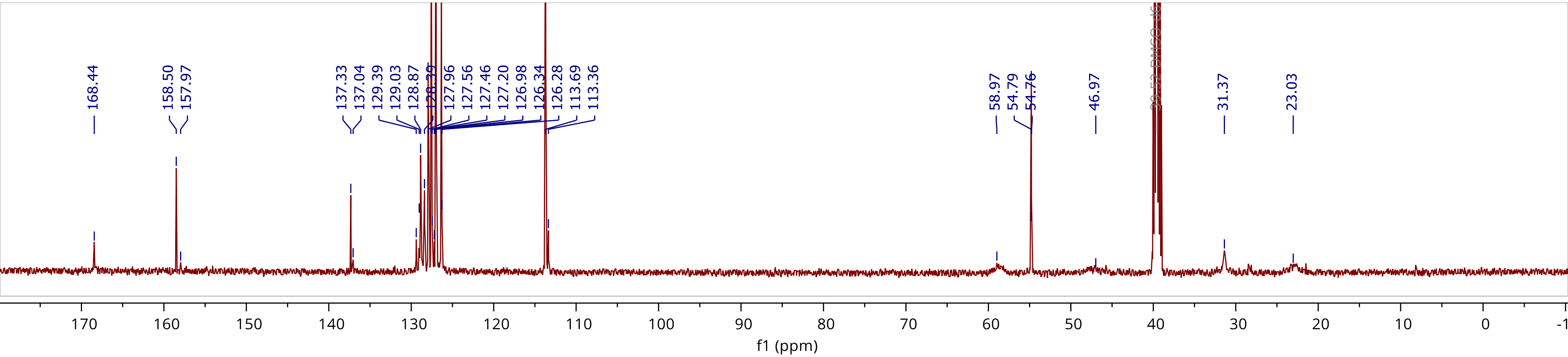
only E-isomer

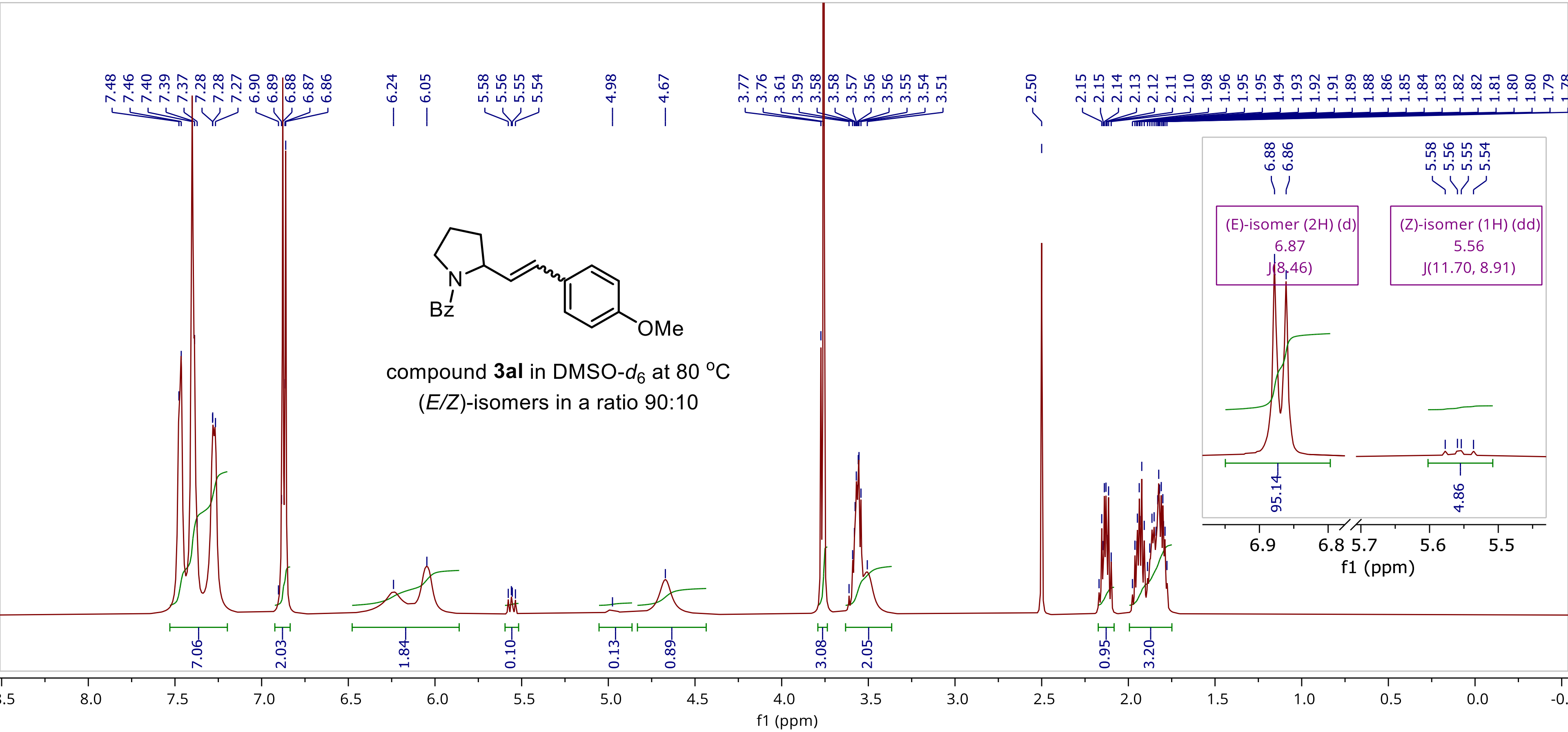




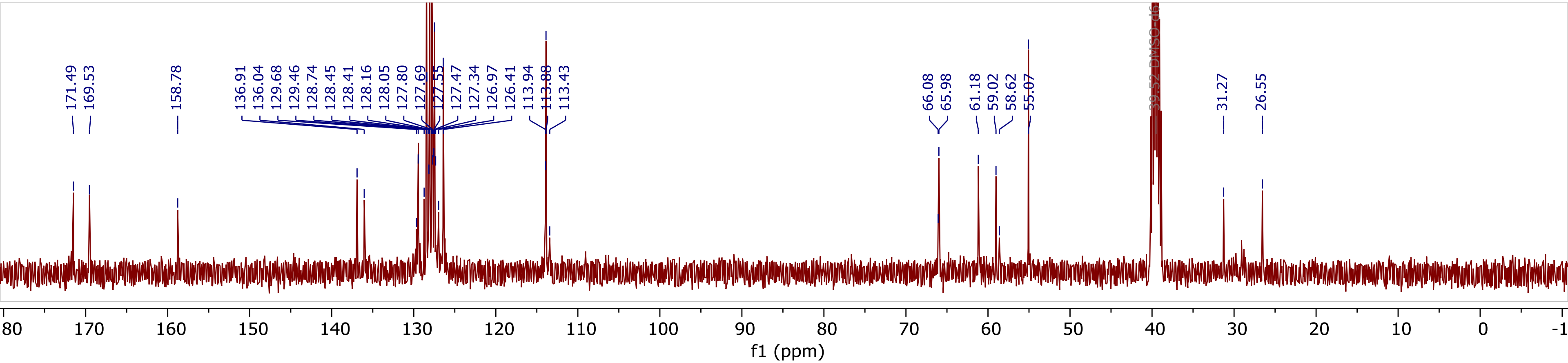
compound **3ak** in DMSO-d_6 at 80 ^{o}C

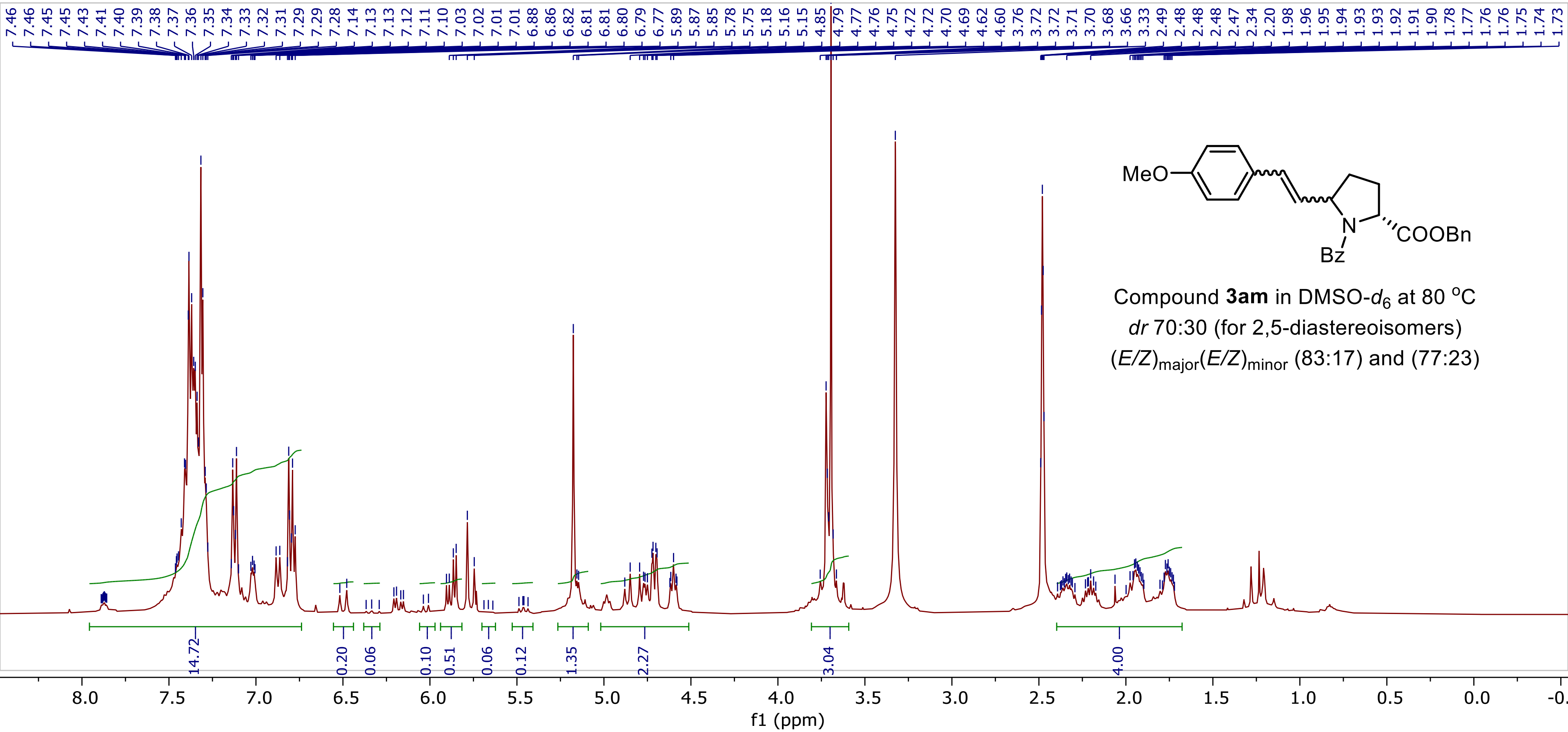
only E-isomer




compound **3al** in DMSO-d_6 at 80 ^{o}C

(*E/Z*)-isomers in a ratio 90:10

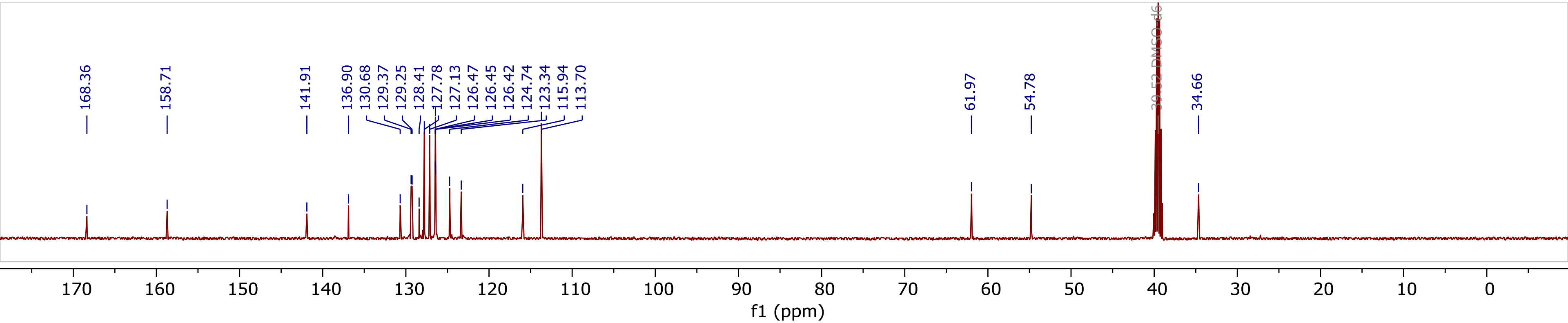


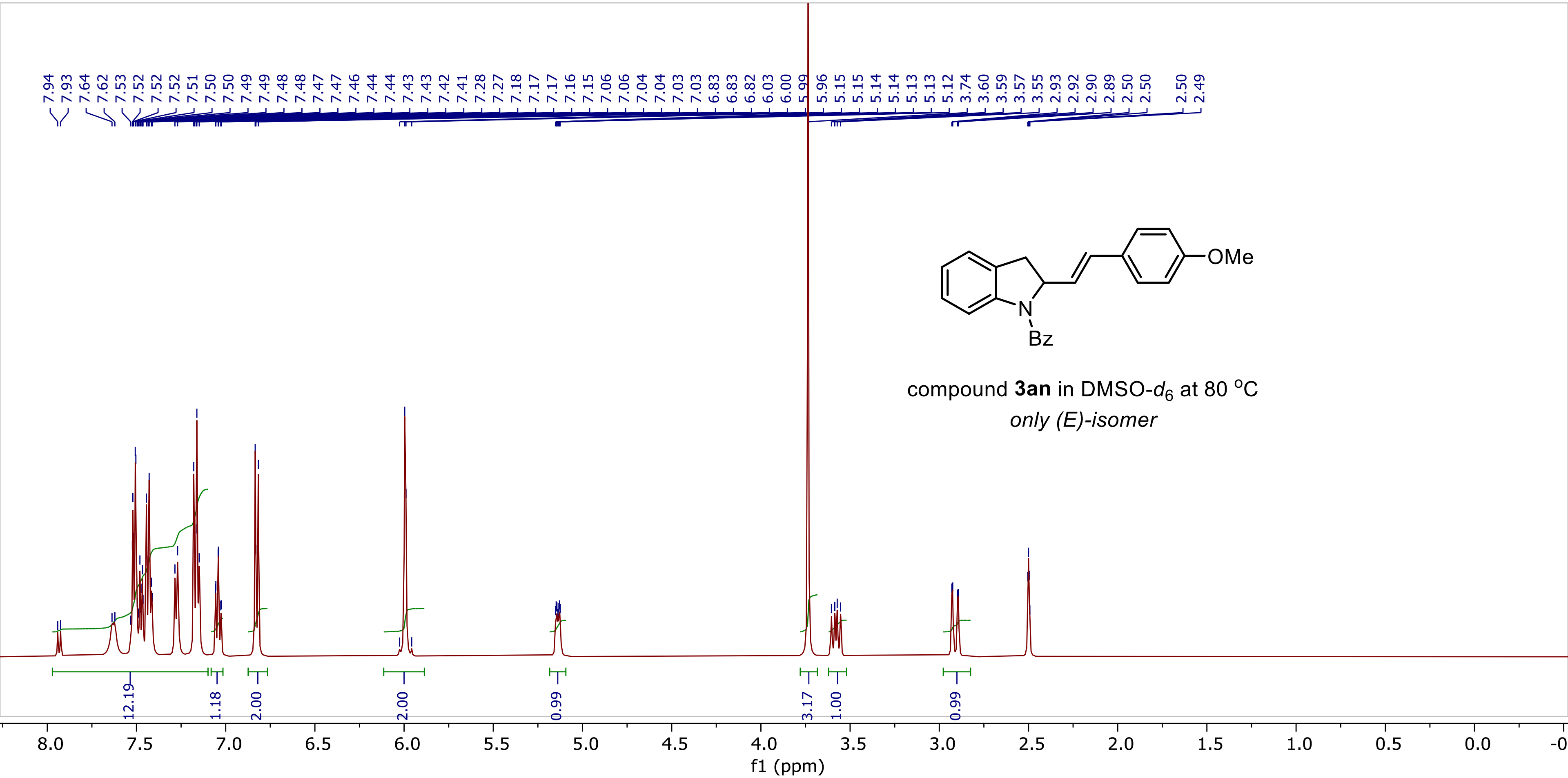


Compound **3am** in DMSO-d_6 at 80 °C

dr 70:30 (for 2,5-diastereoisomers)

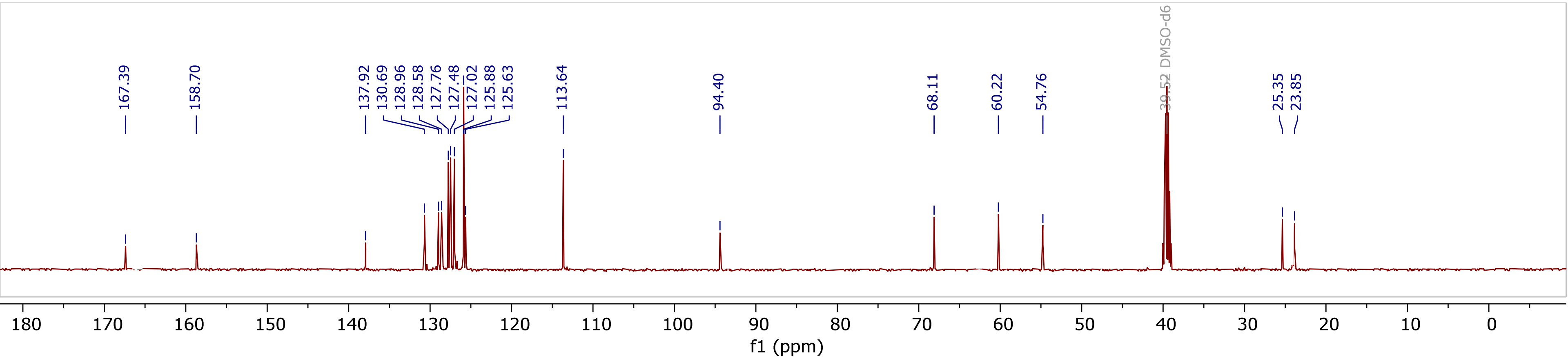
$(E/Z)_{major}(E/Z)_{minor}$ (83:17) and (77:23)

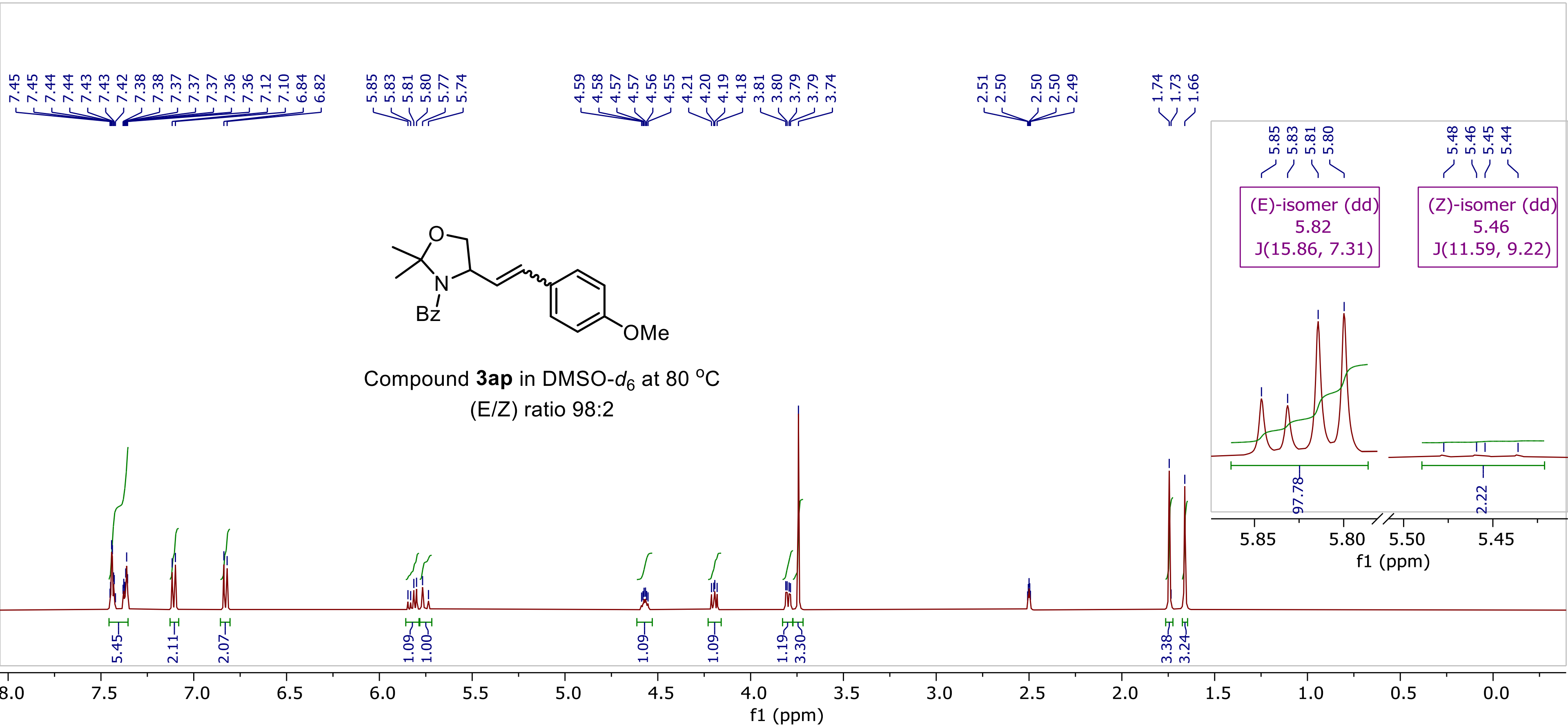




compound **3an** in DMSO-d_6 at 80 ^{o}C

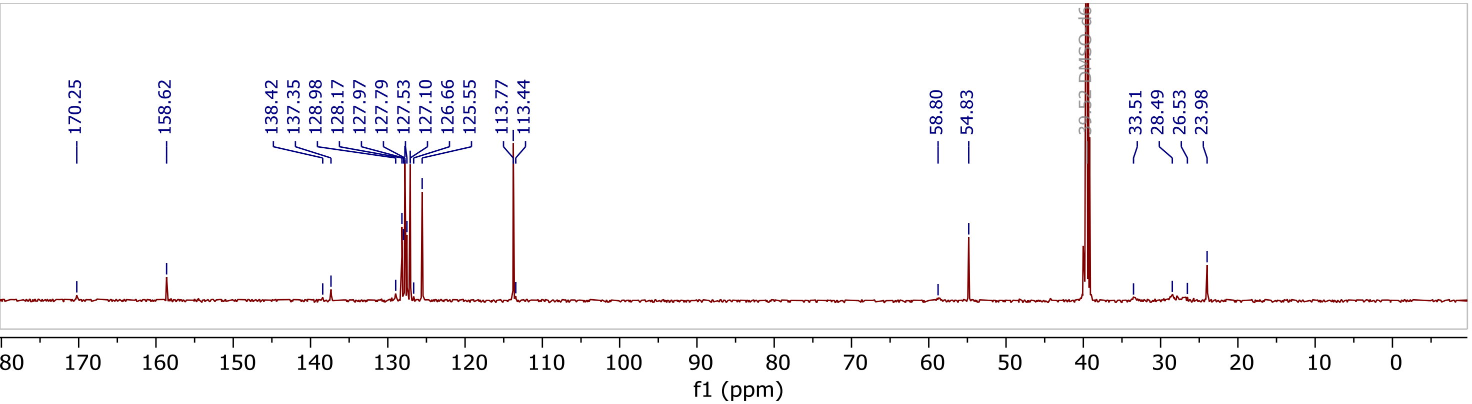
only (E)-isomer

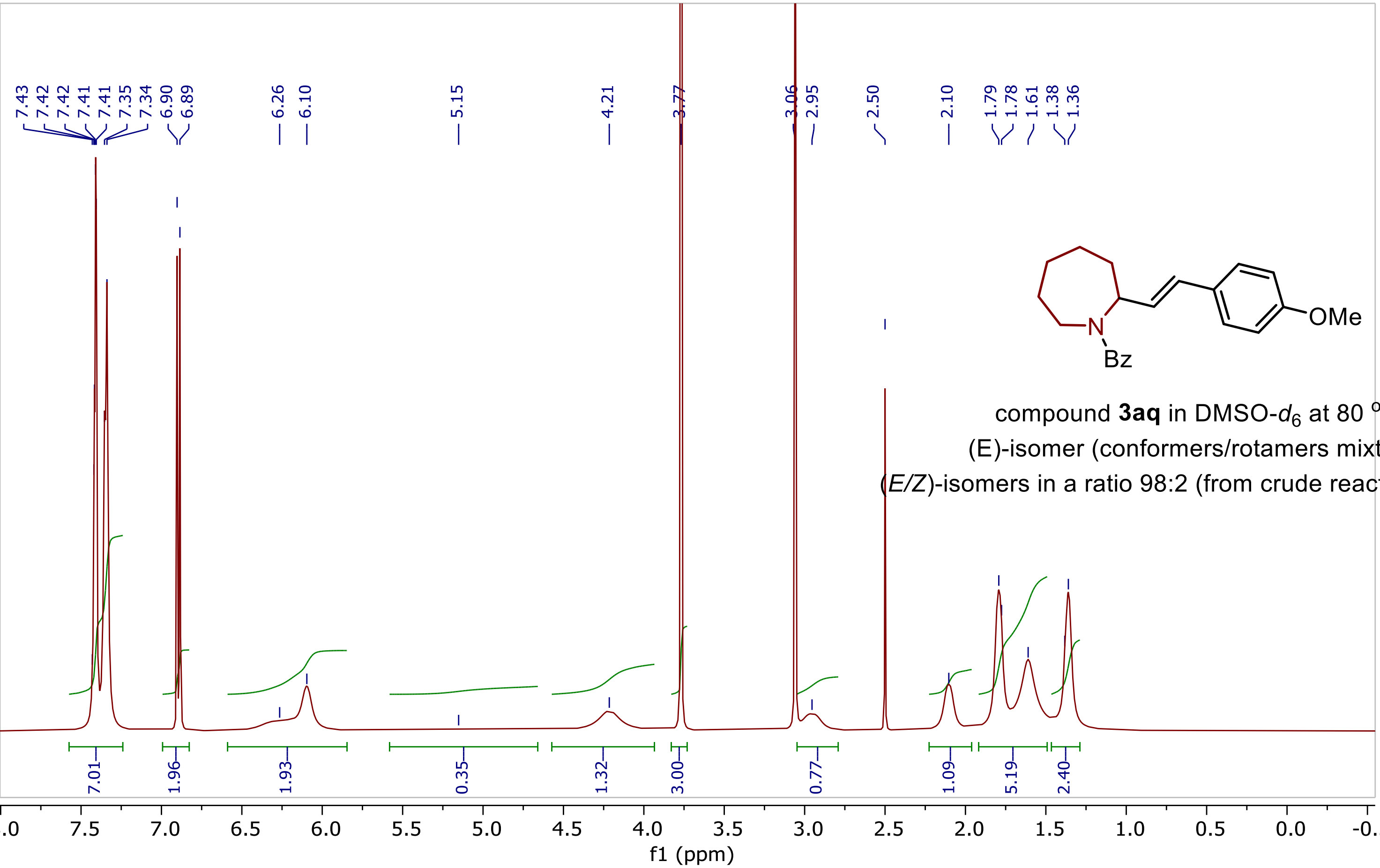




Compound **3ap** in DMSO-d_6 at 80 °C

(E/Z) ratio 98:2



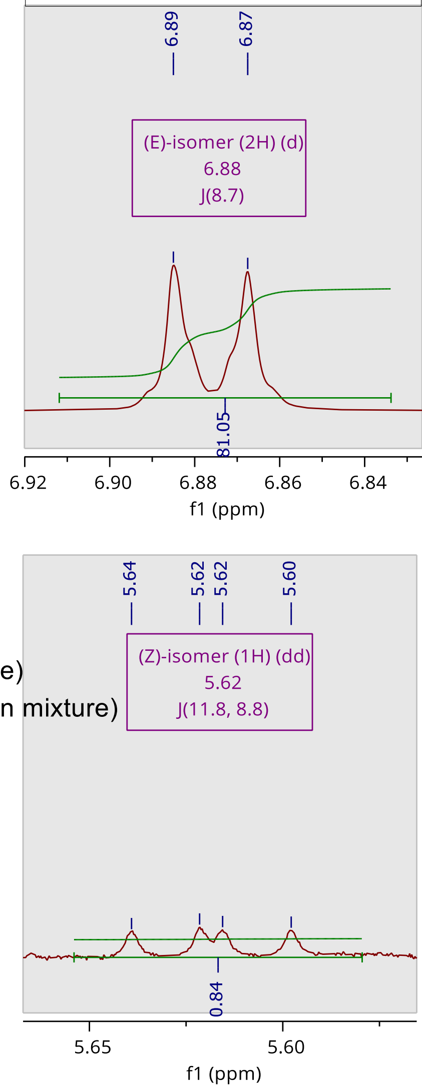


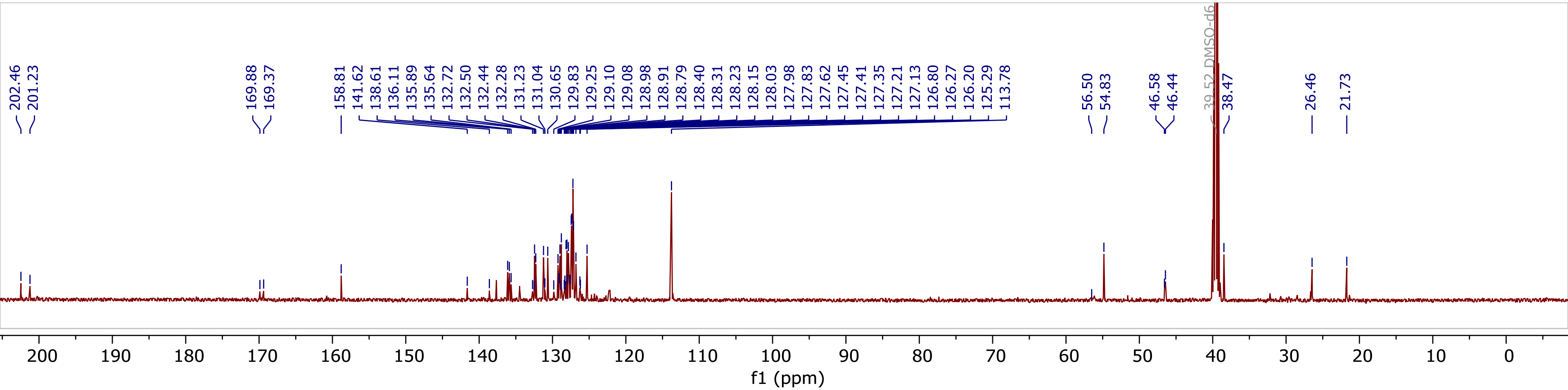
compound **3aq** in DMSO-d_6 at 80 °C

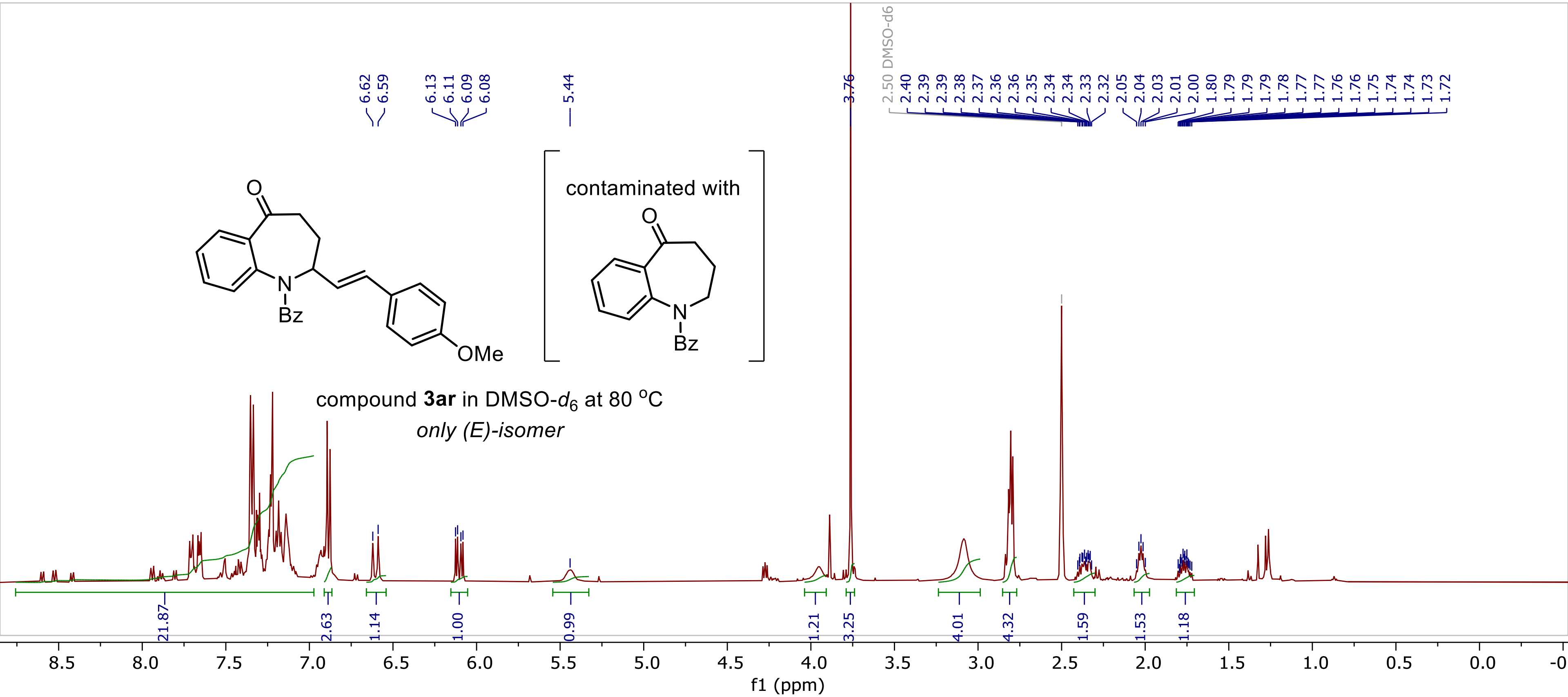
(E)-isomer (conformers/rotamers mixture)

(*E/Z*)-isomers in a ratio 98:2 (from crude reaction mixture)

(*E/Z*)-isomer ratio assignment from the crude reaction mixture



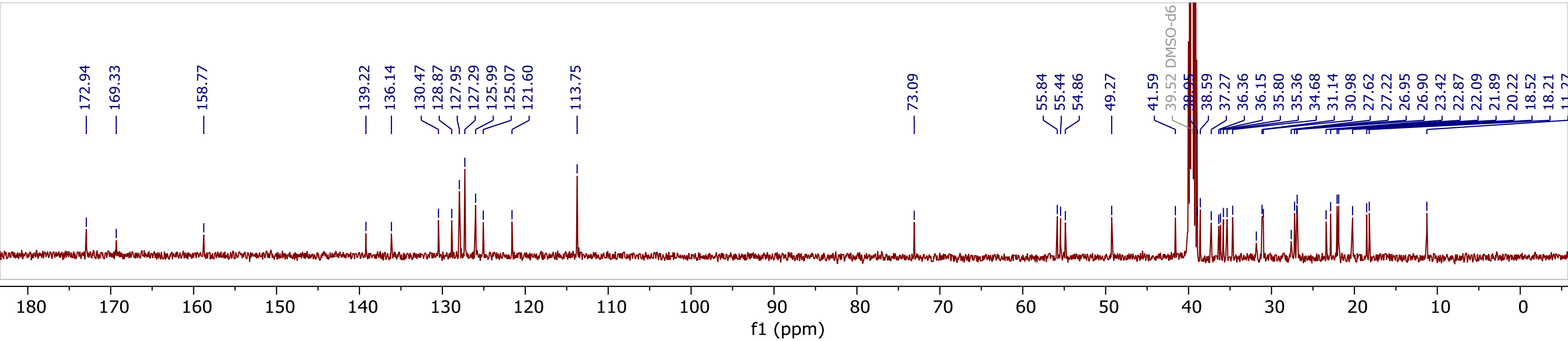


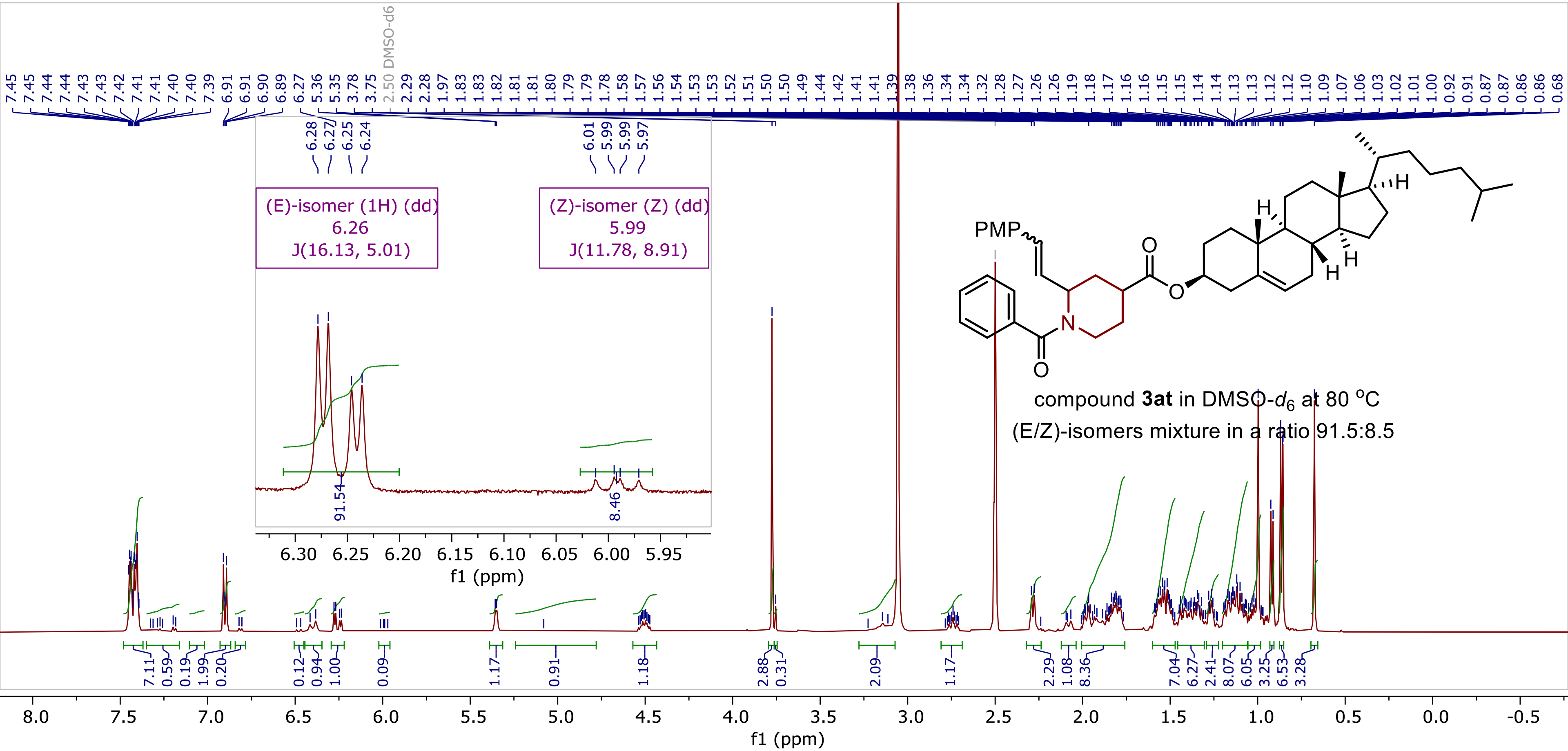


contaminated with

compound **3ar** in DMSO-d_6 at 80 ^{o}C

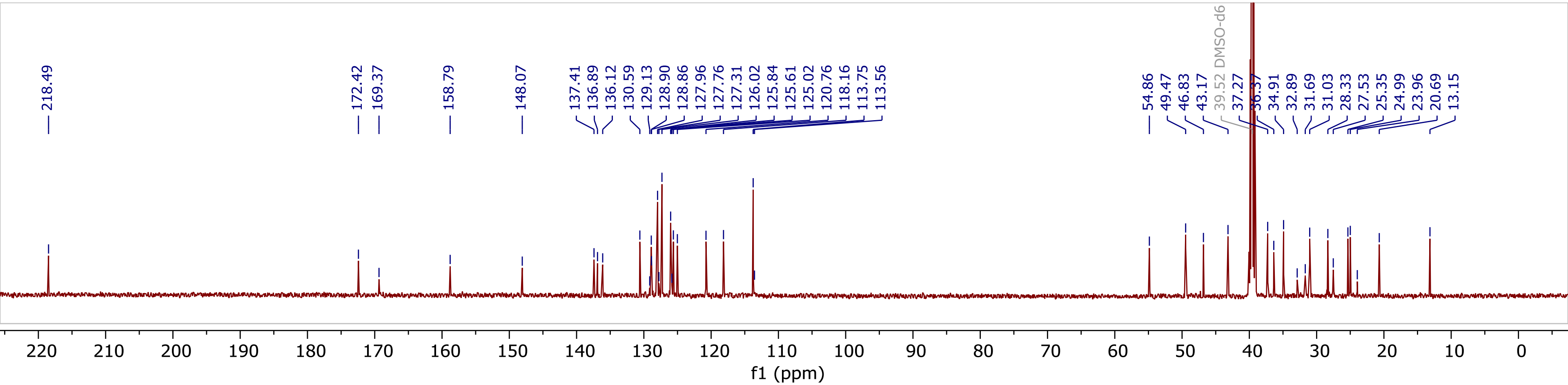
only (E)-isomer

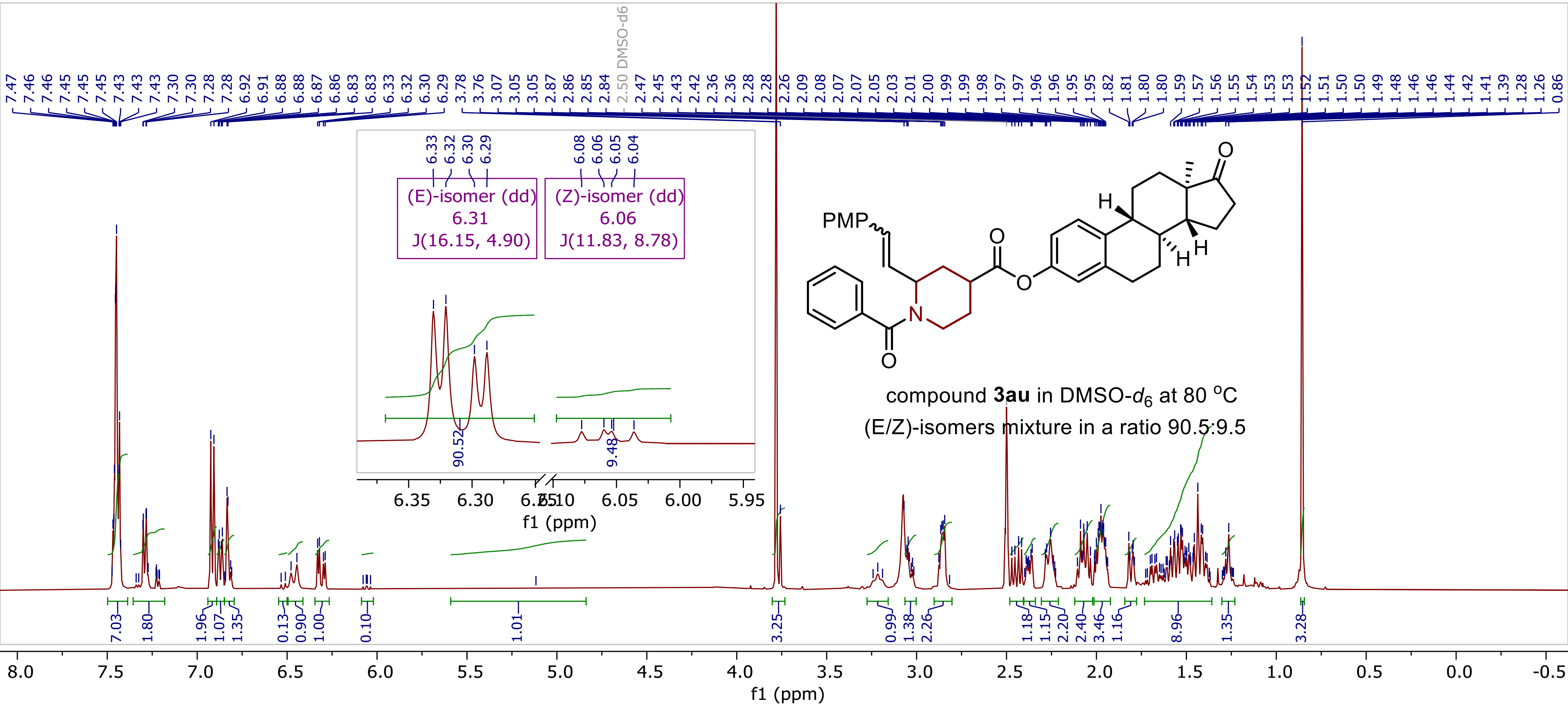




compound **3at** in DMSO-d_6 at 80 °C

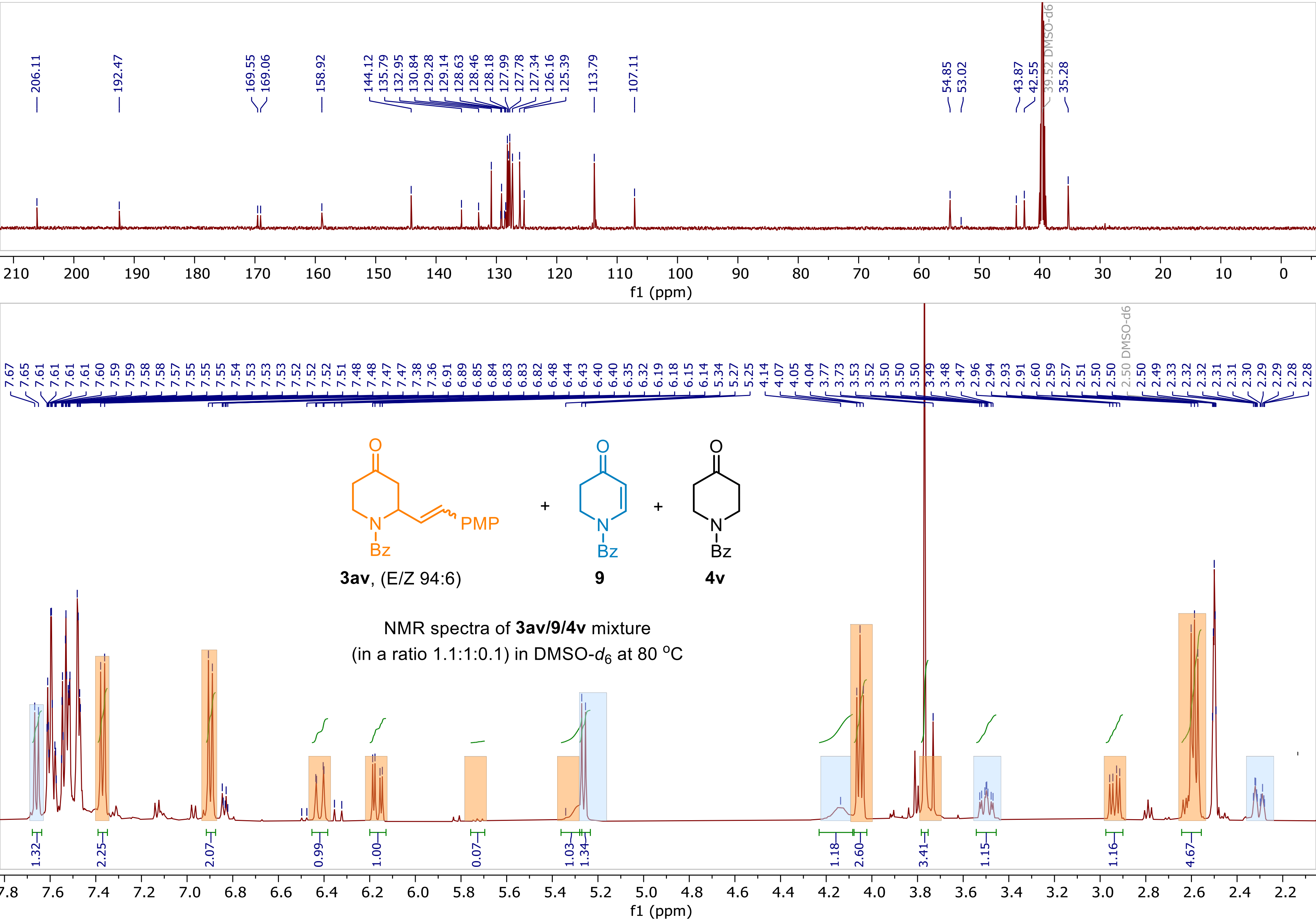
(E/Z)-isomers mixture in a ratio 91.5:8.5



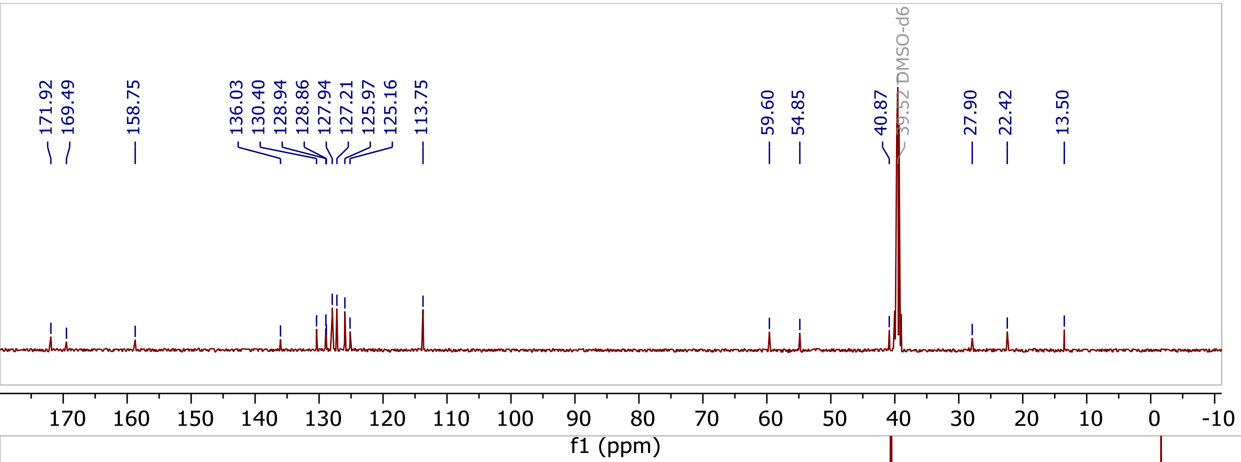


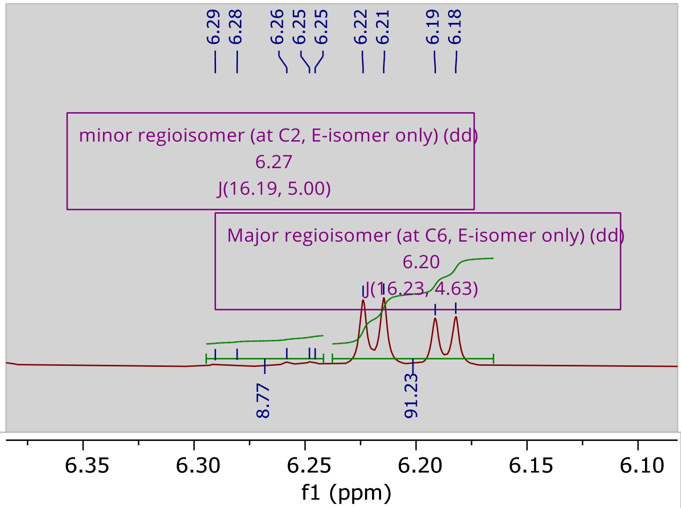
compound **3au** in DMSO-d_6 at 80 ^{o}C

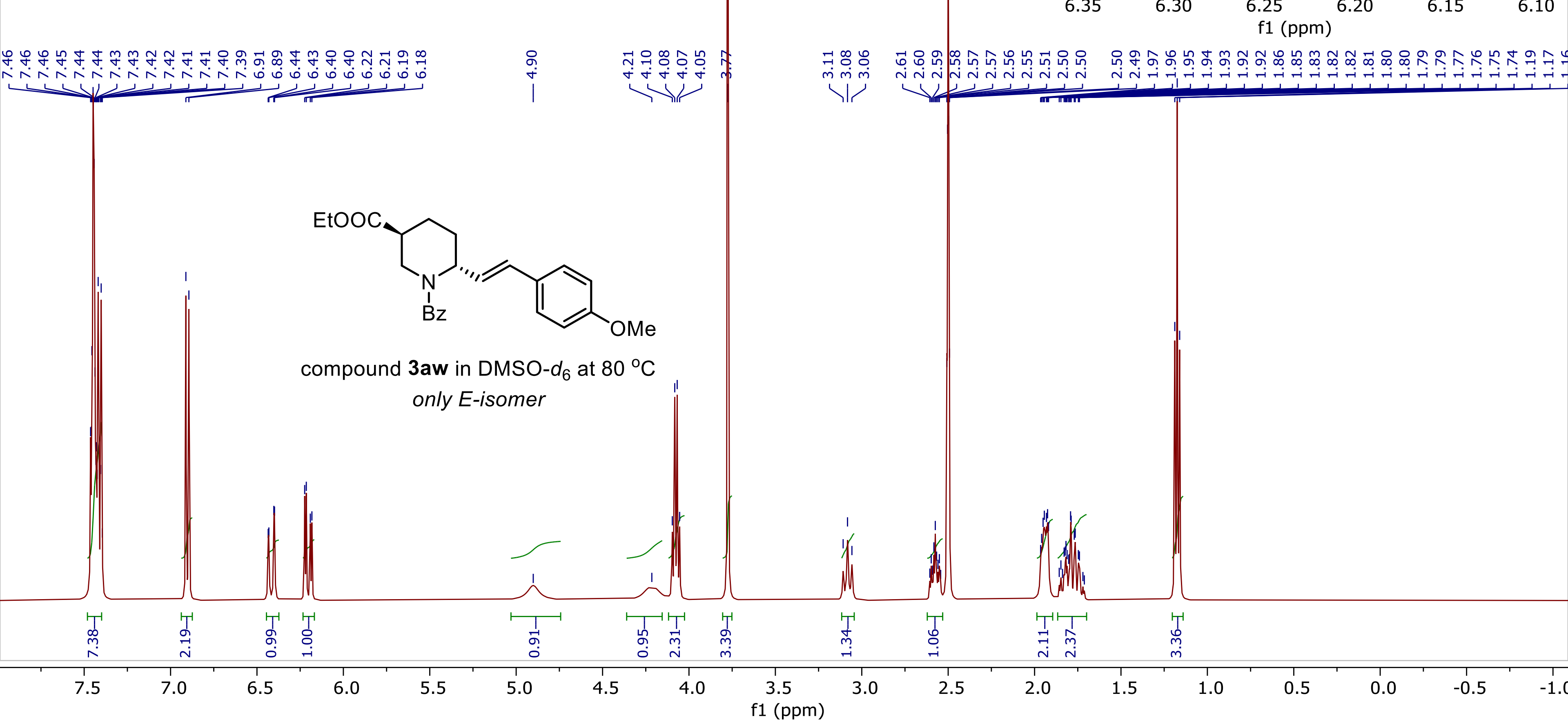
(E/Z)-isomers mixture in a ratio 90.5:9.5



NMR spectra of **3av/9/4v** mixture (in a ratio 1.1:1:0.1) in DMSO-d_6 at 80 ^{o}C

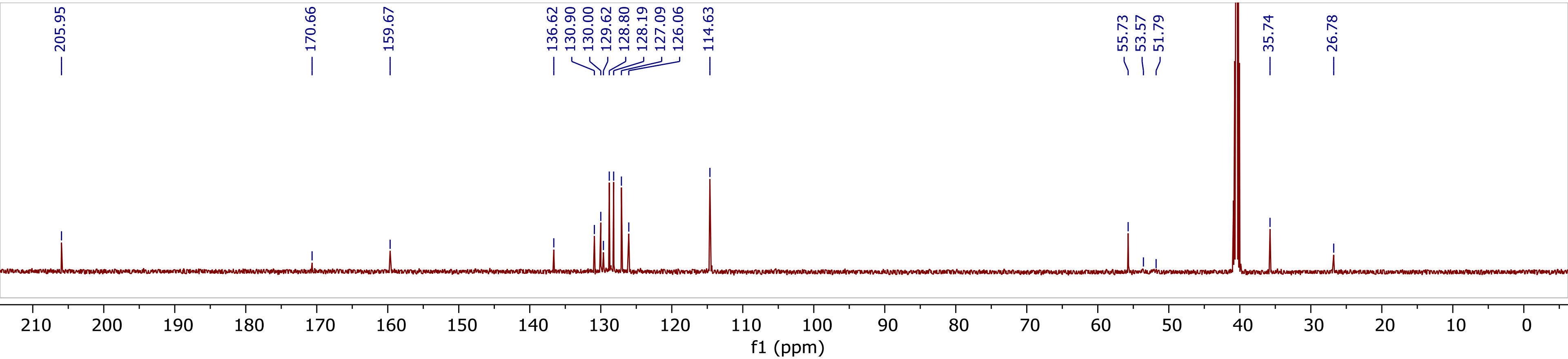


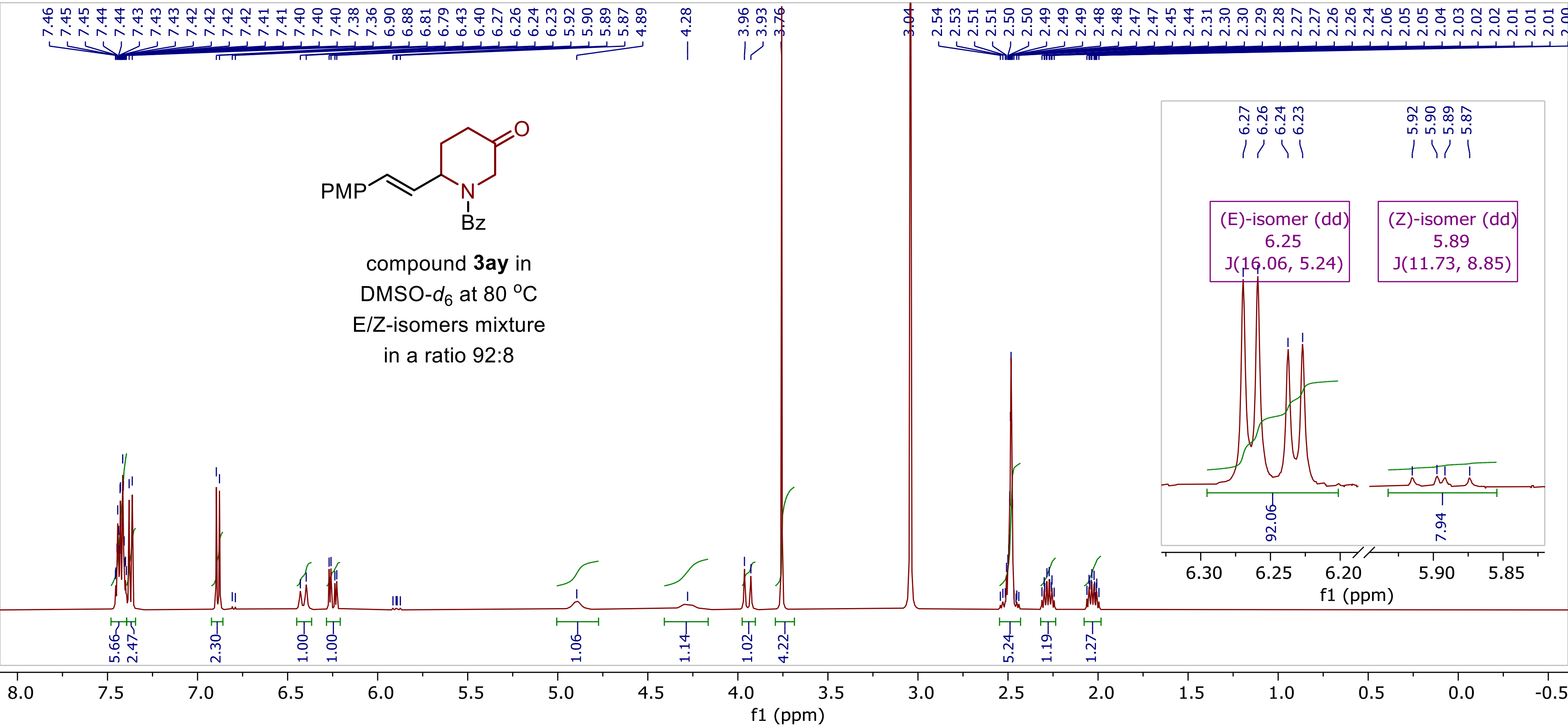




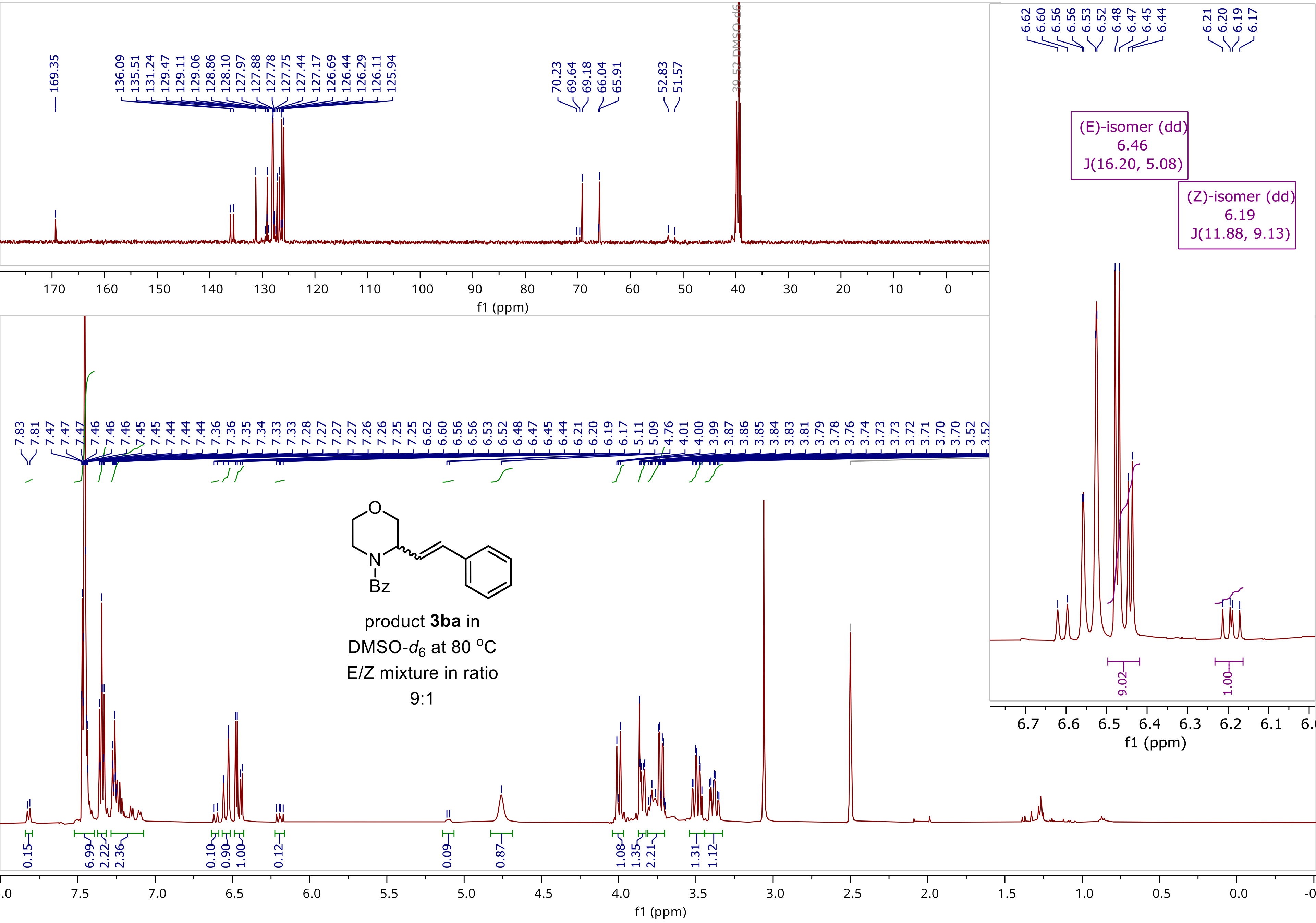
compound **3aw** in DMSO-d_6 at 80 °C

only E-isomer

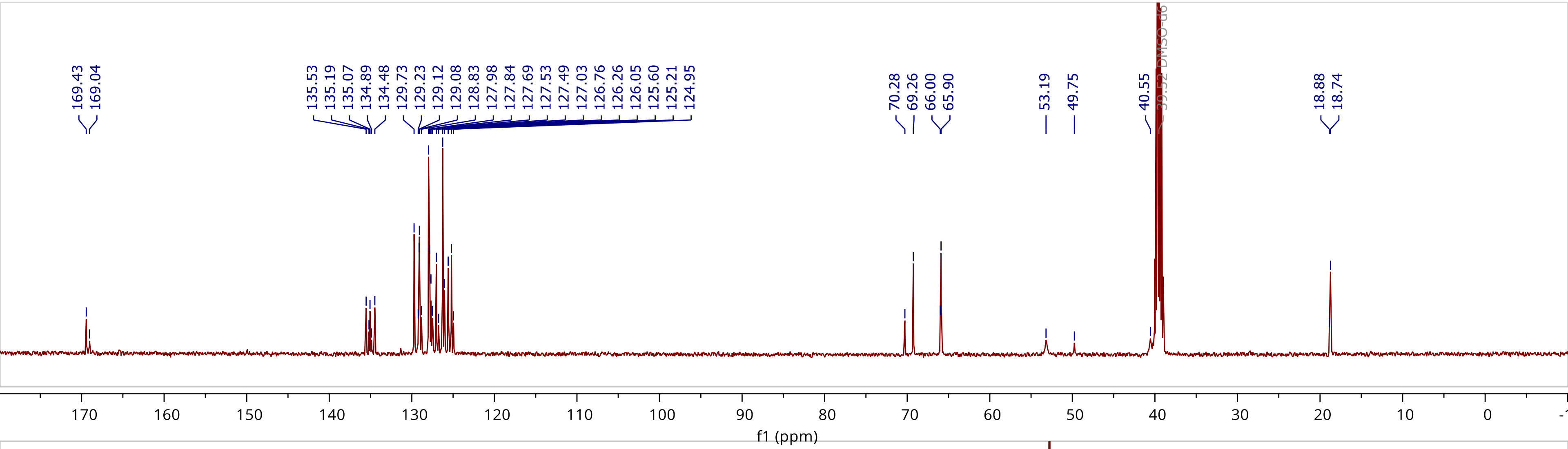


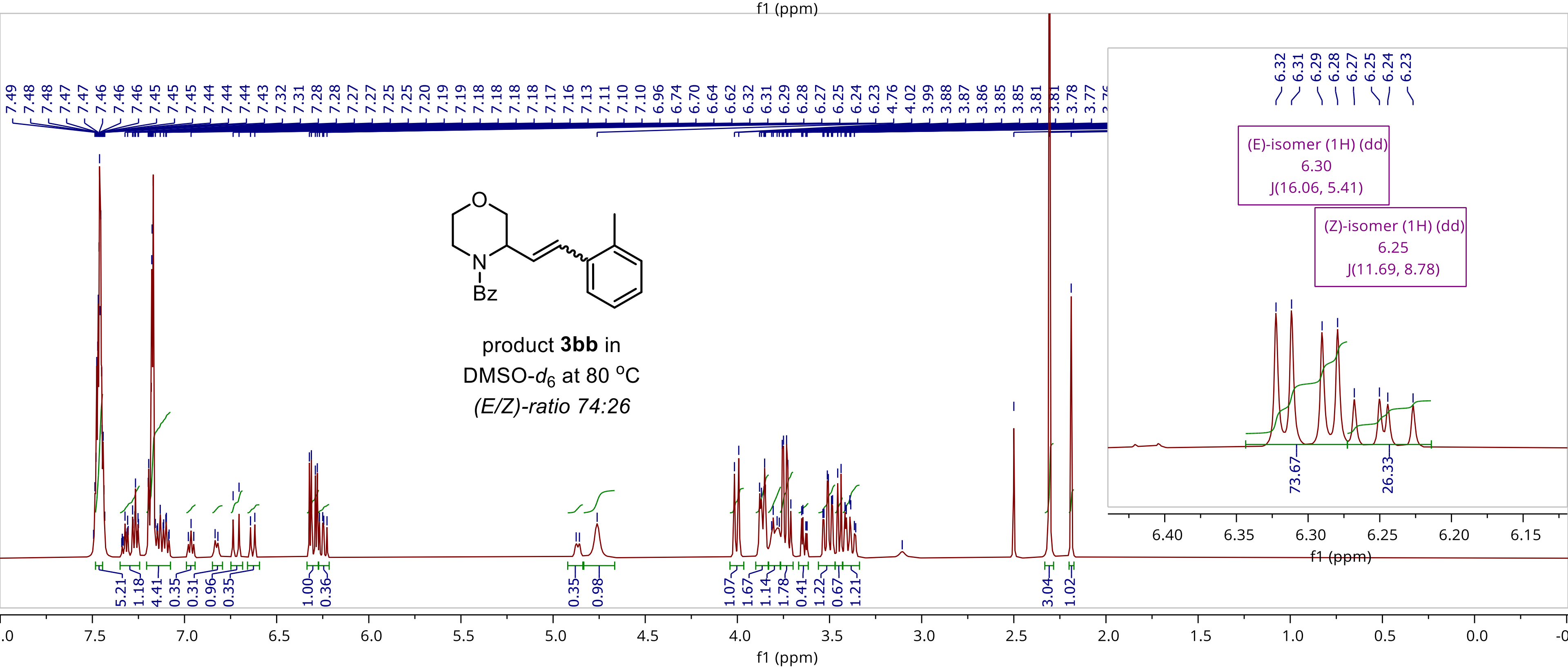


compound **3ay** in
DMSO-d_6 at 80 °C
E/Z-isomers mixture
in a ratio 92:8

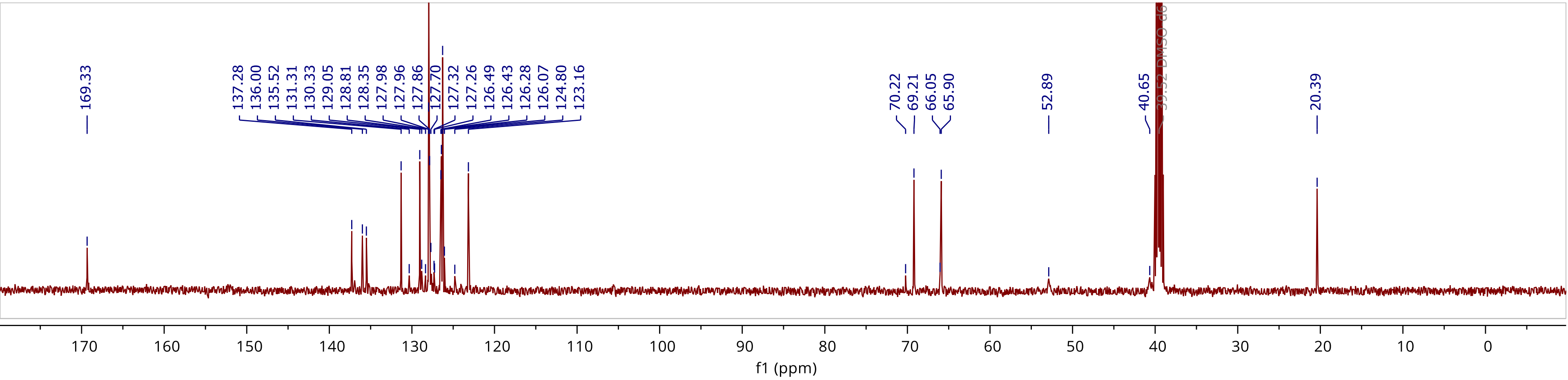


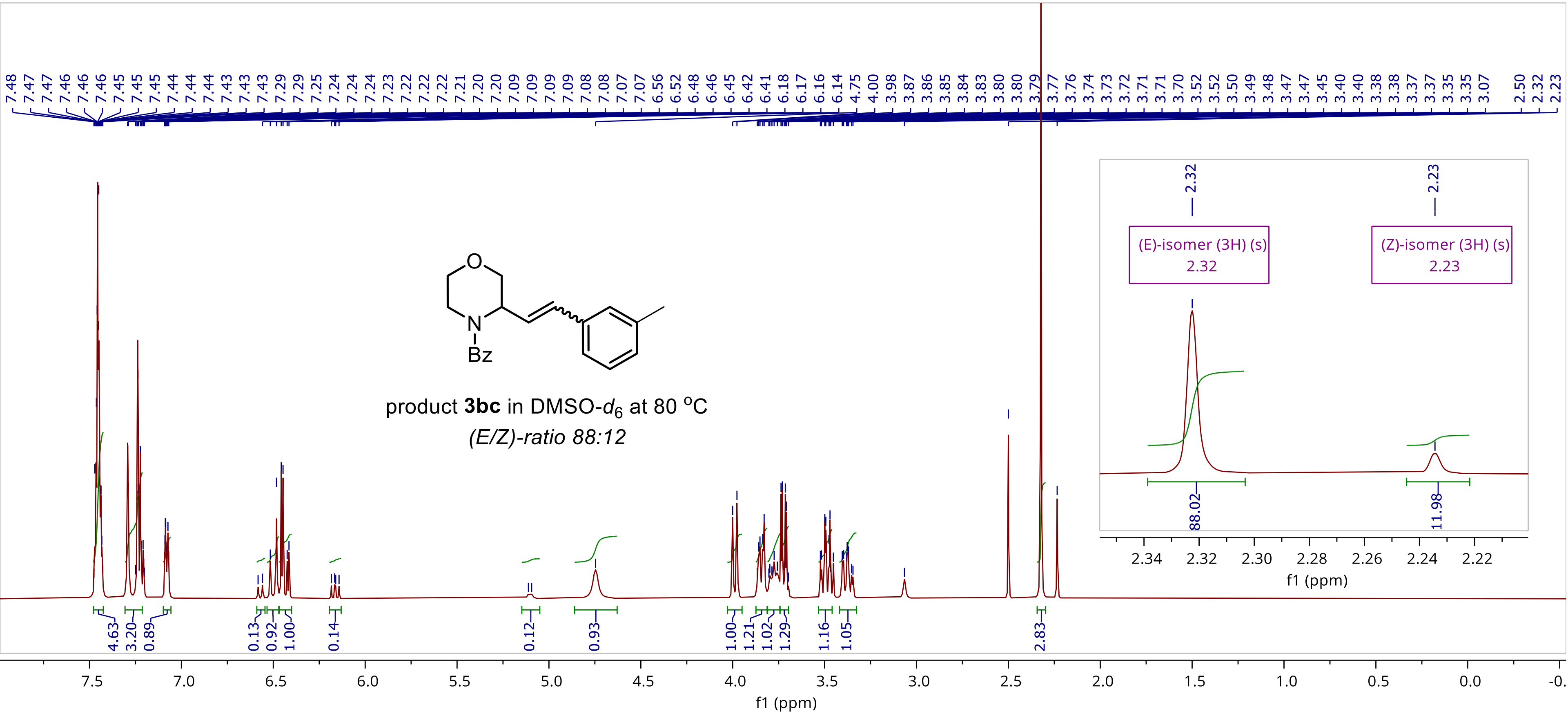
product **3ba** in
DMSO-d_6 at 80 ^{o}C
E/Z mixture in ratio
9:1





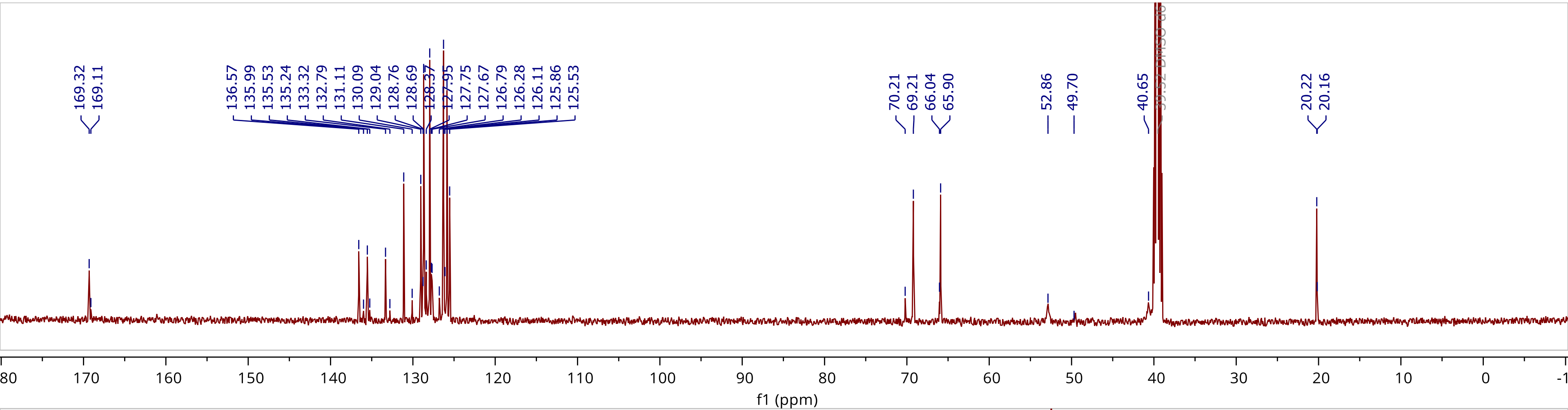
product **3bb** in
DMSO-d_6 at 80 ^{o}C
(E/Z)-ratio 74:26

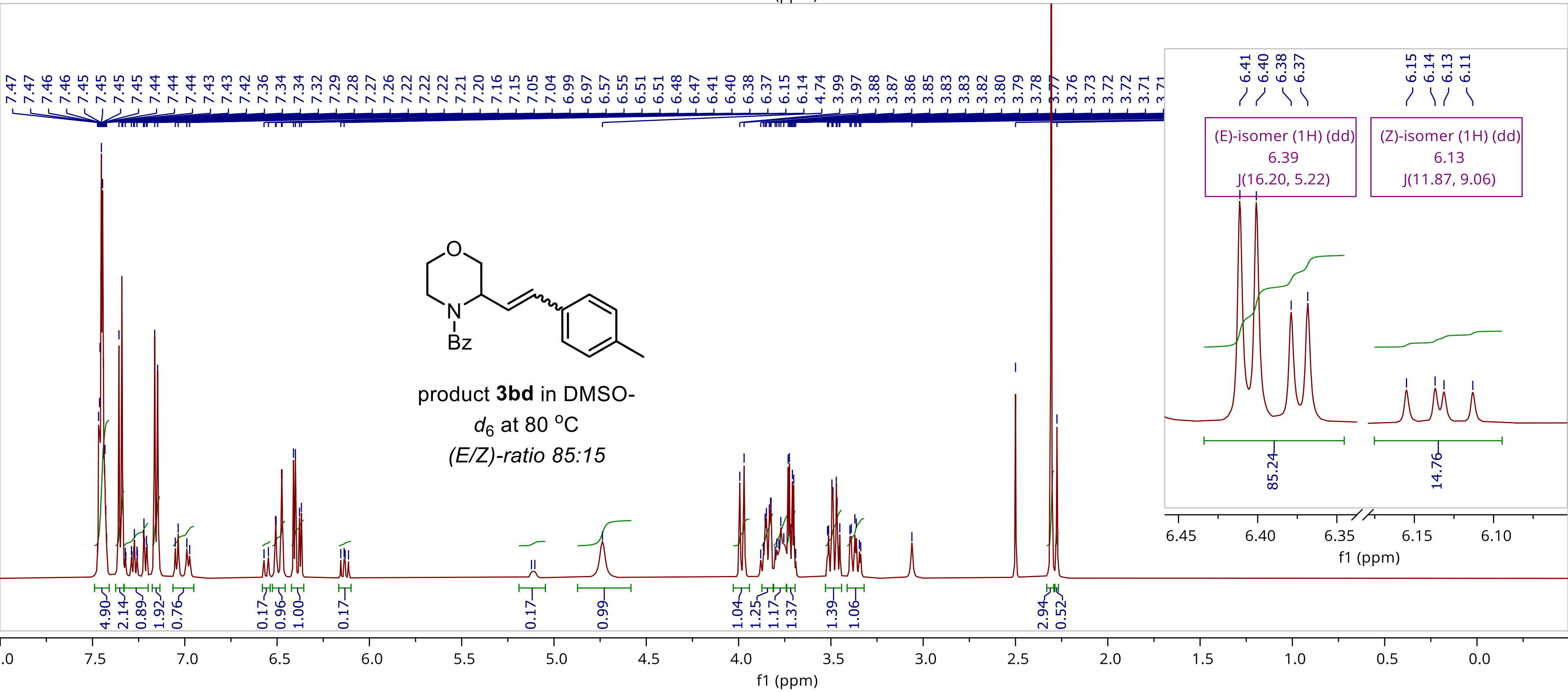


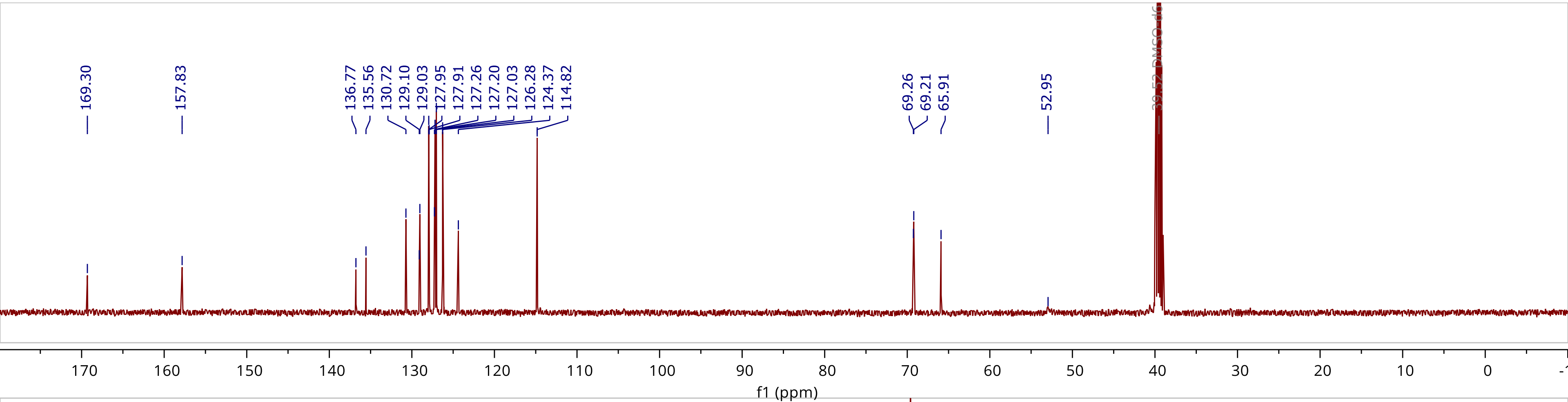


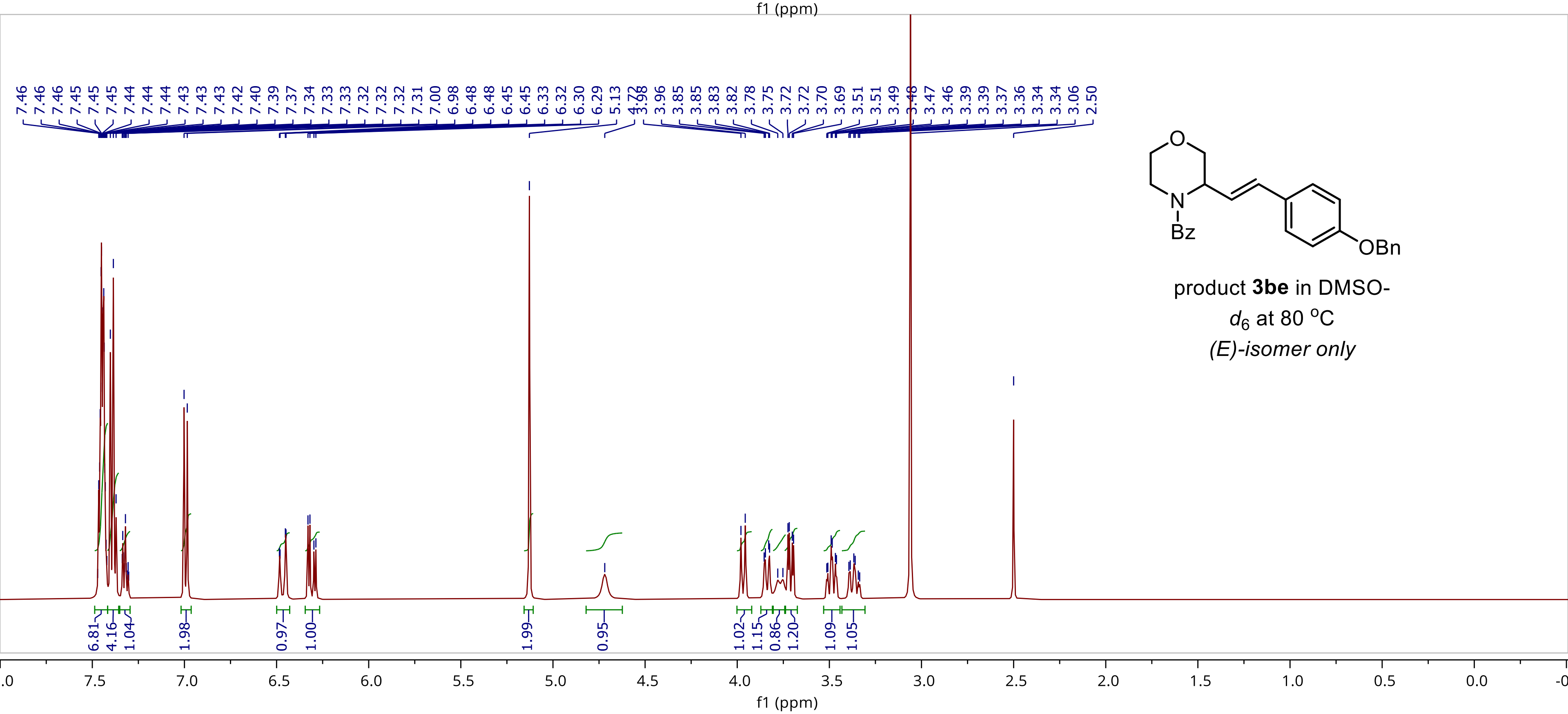
product **3bc** in DMSO-d_6 at 80 °C

(E/Z)-ratio 88:12


169.32
169.11
136.57
135.99
135.53
135.24
133.32
132.79
131.11
130.09
129.04
128.76
128.69
128.37
127.95
127.75
127.67
126.79
126.28
126.11
125.86
125.53
70.21
69.21
66.04
65.90
52.86
49.70
40.65
39.52 DMSO-d6
20.22
20.16
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

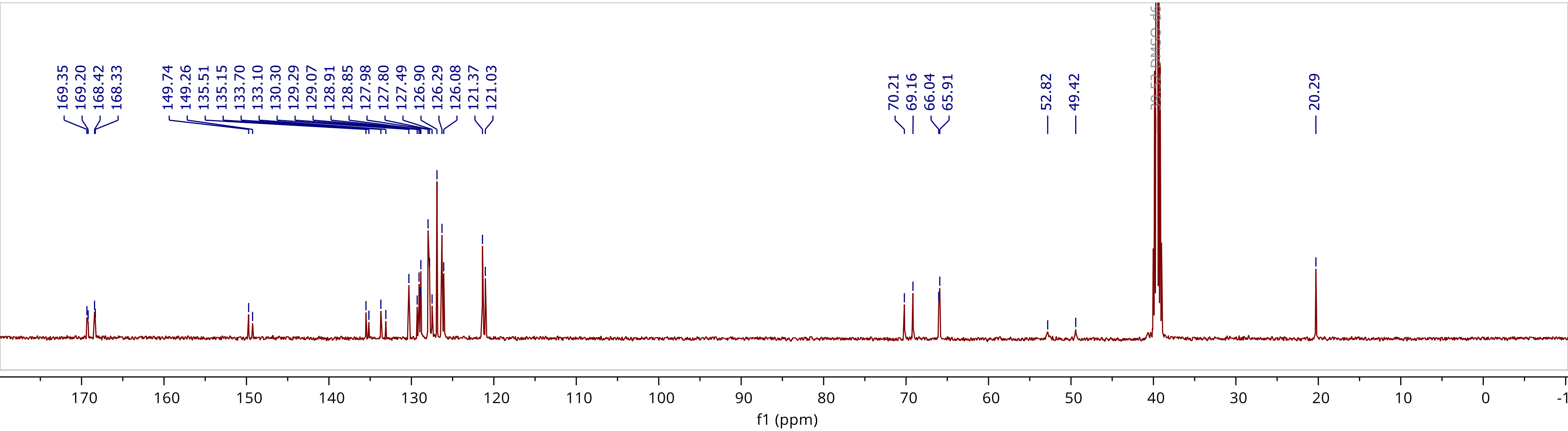

7.47
7.47
7.46
7.46
7.45
7.45
7.45
7.45
7.44
7.44
7.43
7.43
7.42
7.36
7.34
7.34
7.32
7.29
7.28
7.27
7.26
7.22
7.22
7.22
7.21
7.20
7.16
7.15
7.05
7.04
6.99
6.97
6.57
6.55
6.51
6.51
6.48
6.47
6.41
6.40
6.38
6.37
6.15
6.14
4.74
3.99
3.97
3.88
3.87
3.86
3.85
3.83
3.83
3.82
3.80
3.79
3.78
3.77
3.76
3.73
3.72
3.72
3.71
3.71
O
N
Bz
product **3bd** in DMSO-d_6 at 80 ^{o}C
(E/Z)-ratio 85:15
6.41
6.40
6.38
6.37
6.15
6.14
6.13
6.11
(E)-isomer (1H) (dd)
6.39
J(16.20, 5.22)
(Z)-isomer (1H) (dd)
6.13
J(11.87, 9.06)
85.24
14.76
6.45
6.40
6.35
6.15
6.10
f1 (ppm)
4.90
2.14
0.89
1.92
0.76
0.17
0.96
1.00
0.17
0.17
0.99
1.04
1.25
1.17
1.37
1.39
1.06
2.94
0.52
.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
f1 (ppm)

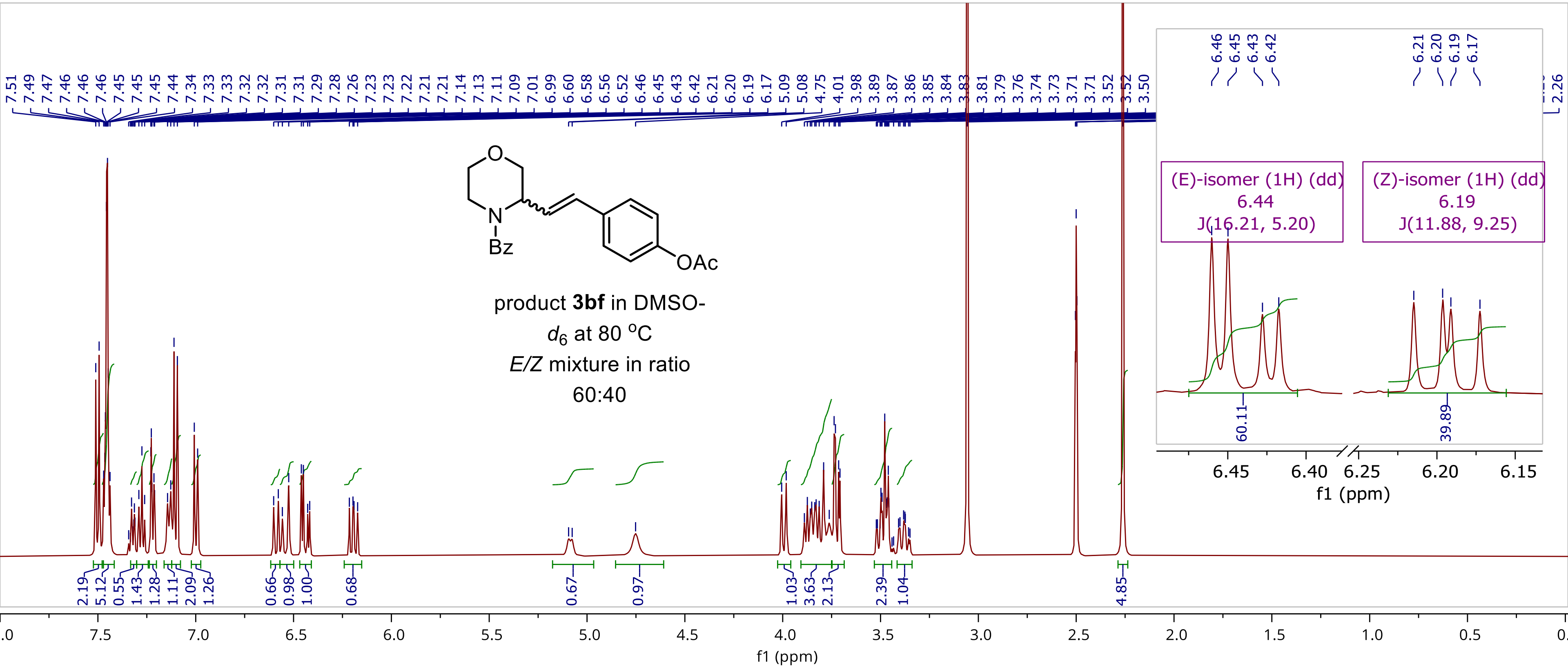




product **3be** in DMSO-d_6 at 80 °C

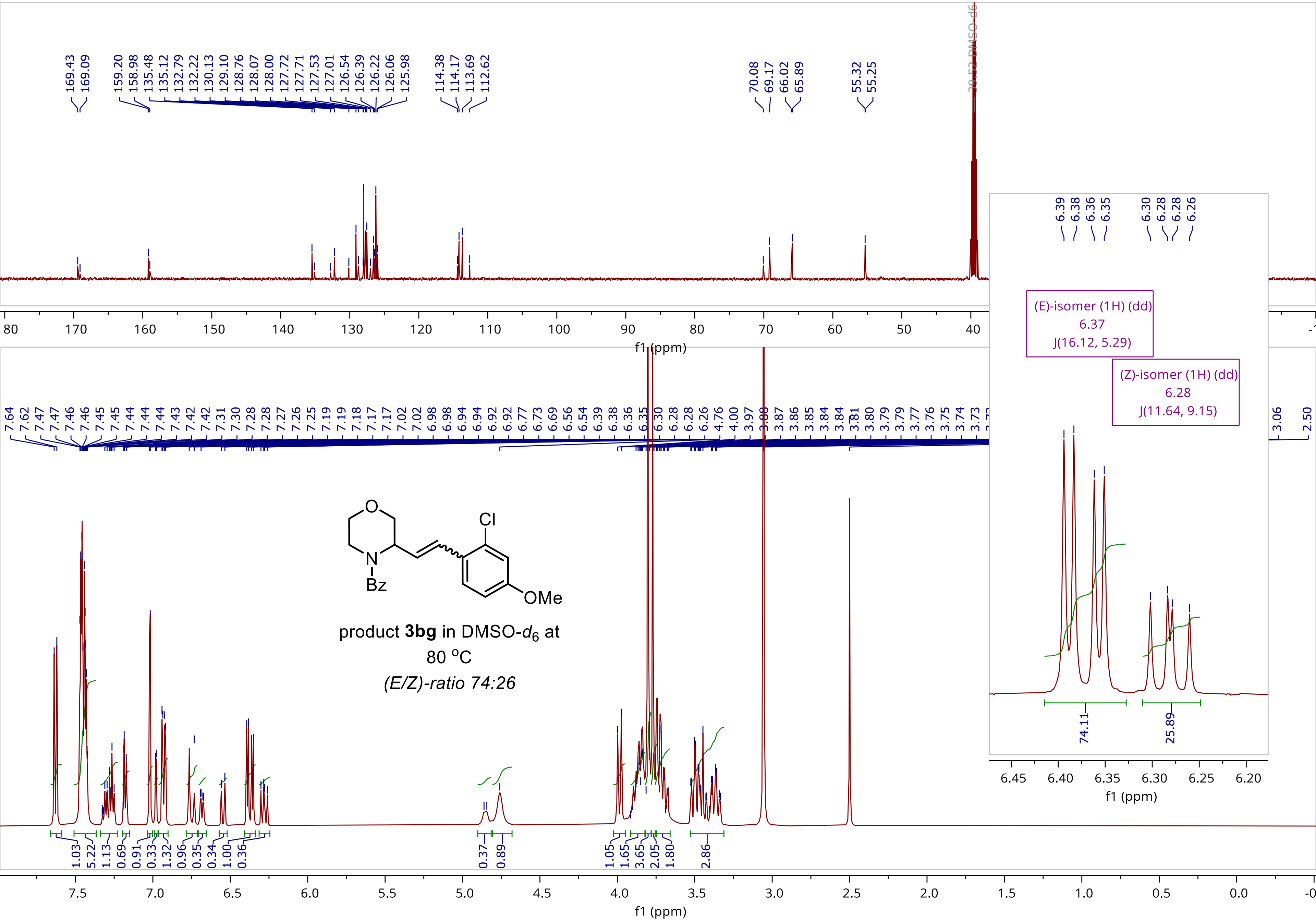
(E)-isomer only

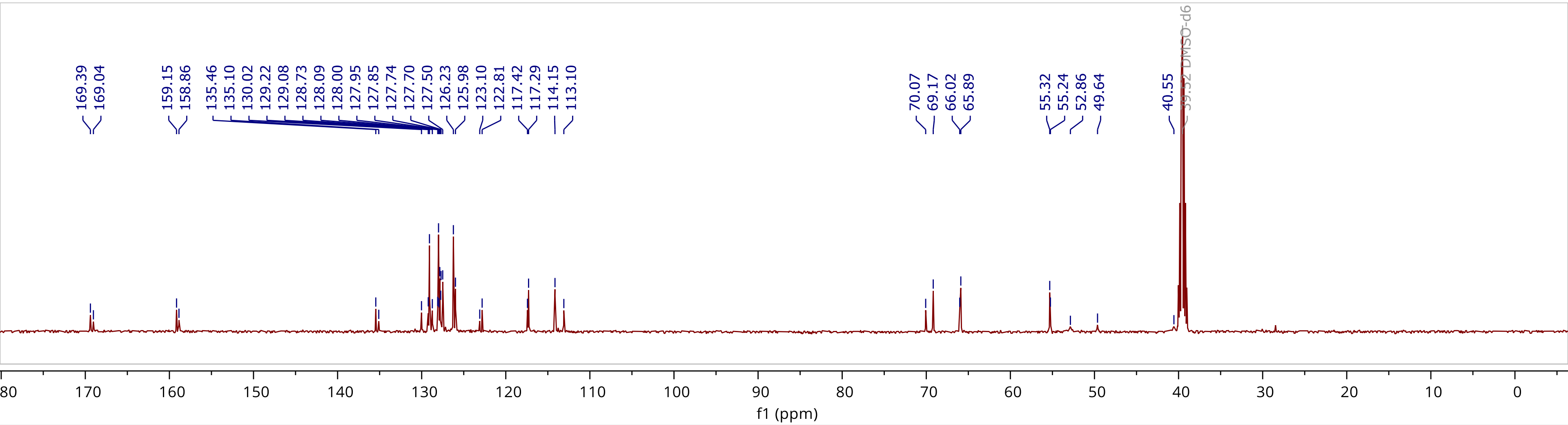


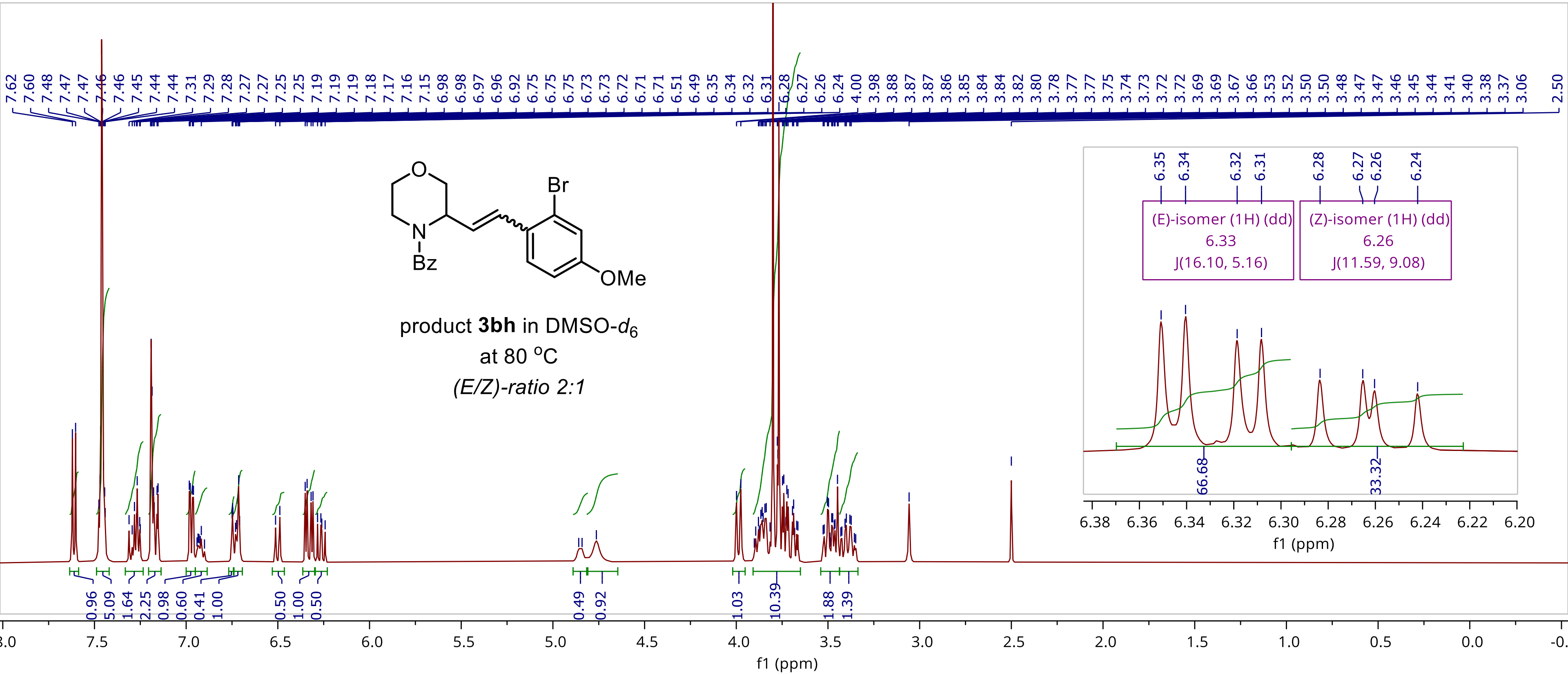


product **3bf** in DMSO-*d*$_6$ at 80 ^{o}C

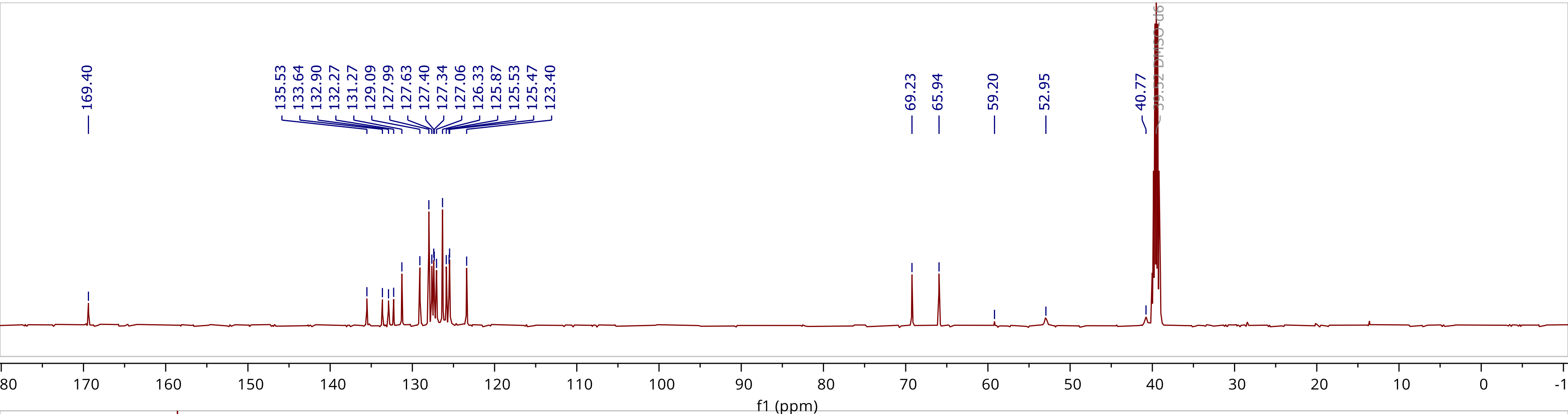
E/Z mixture in ratio 60:40

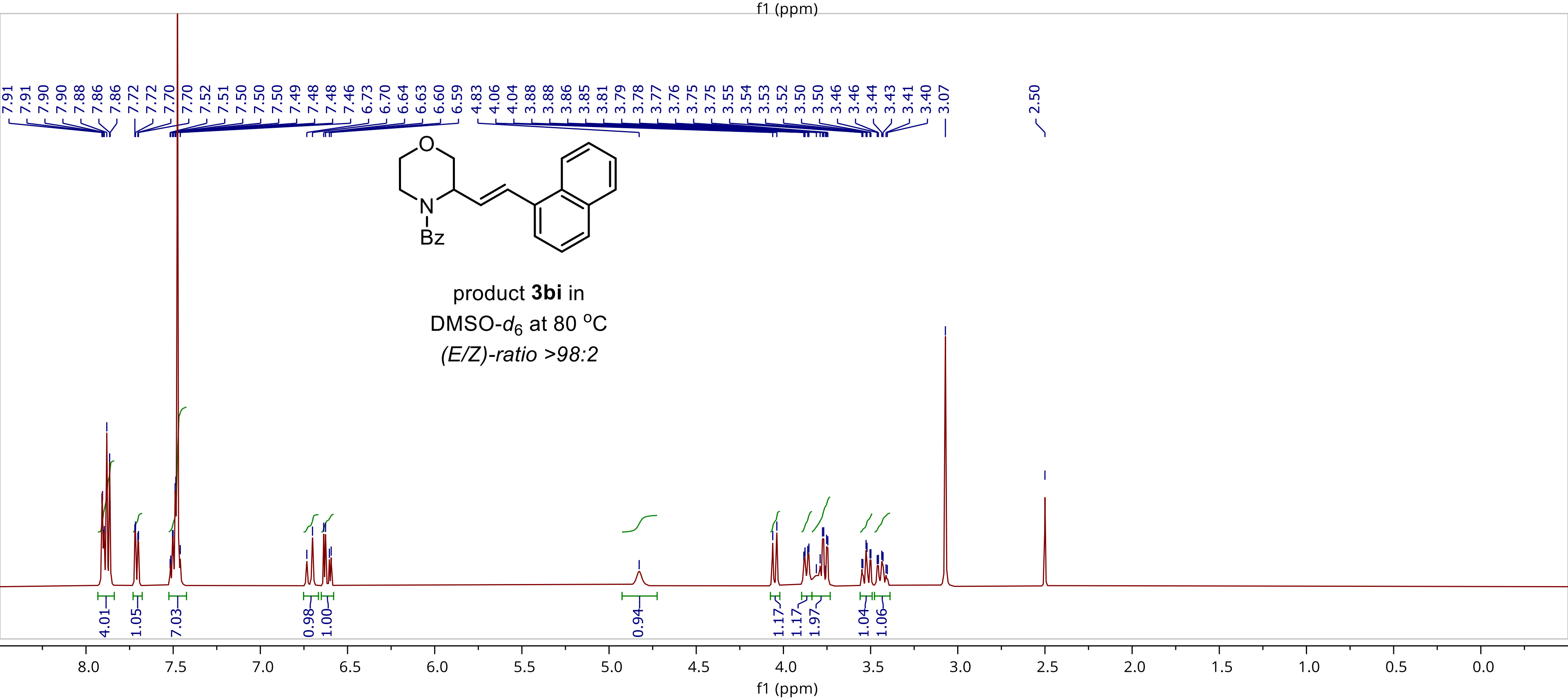

169.43
169.09
159.20
158.98
135.48
135.12
132.79
132.22
130.13
129.10
128.76
128.07
128.00
127.72
127.71
127.53
127.01
126.54
126.39
126.22
126.06
125.98
114.38
114.17
113.69
112.62
70.08
69.17
66.02
65.89
55.32
55.25
39.52 DMSO-d6
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
f1 (ppm)
6.39
6.38
6.36
6.35
6.30
6.28
6.28
6.26
(E)-isomer (1H) (dd)
6.37
J(16.12, 5.29)
(Z)-isomer (1H) (dd)
6.28
J(11.64, 9.15)
74.11
25.89
6.45
6.40
6.35
6.30
6.25
6.20
f1 (ppm)
7.64
7.62
7.47
7.47
7.46
7.46
7.45
7.45
7.44
7.44
7.44
7.43
7.42
7.42
7.31
7.30
7.28
7.28
7.27
7.26
7.25
7.19
7.19
7.18
7.17
7.17
7.02
7.02
6.98
6.98
6.94
6.94
6.92
6.92
6.77
6.73
6.69
6.56
6.54
6.39
6.38
6.36
6.35
6.30
6.28
6.28
6.26
4.76
4.00
3.97
3.88
3.87
3.86
3.85
3.84
3.84
3.81
3.80
3.79
3.79
3.77
3.76
3.75
3.74
3.73
3.06
2.50
O
N
Bz
Cl
OMe
product **3bg** in DMSO-d_6 at 80 °C
(E/Z)-ratio 74:26
1.03
5.22
1.13
0.69
0.91
0.33
1.32
0.96
0.35
0.34
1.00
0.36
0.37
0.89
1.05
1.65
3.65
2.05
1.80
2.86
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
f1 (ppm)



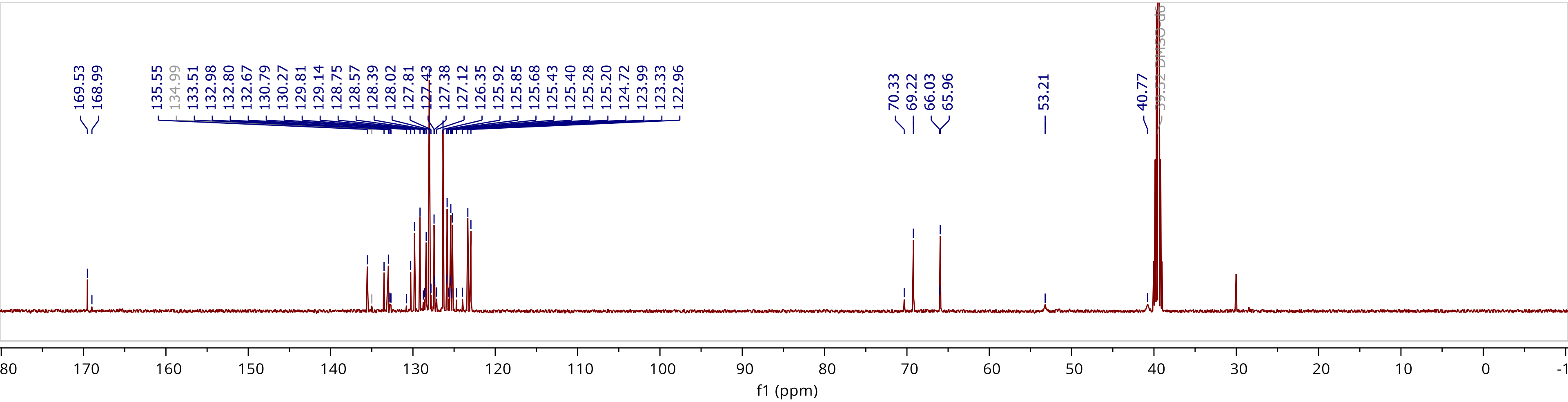


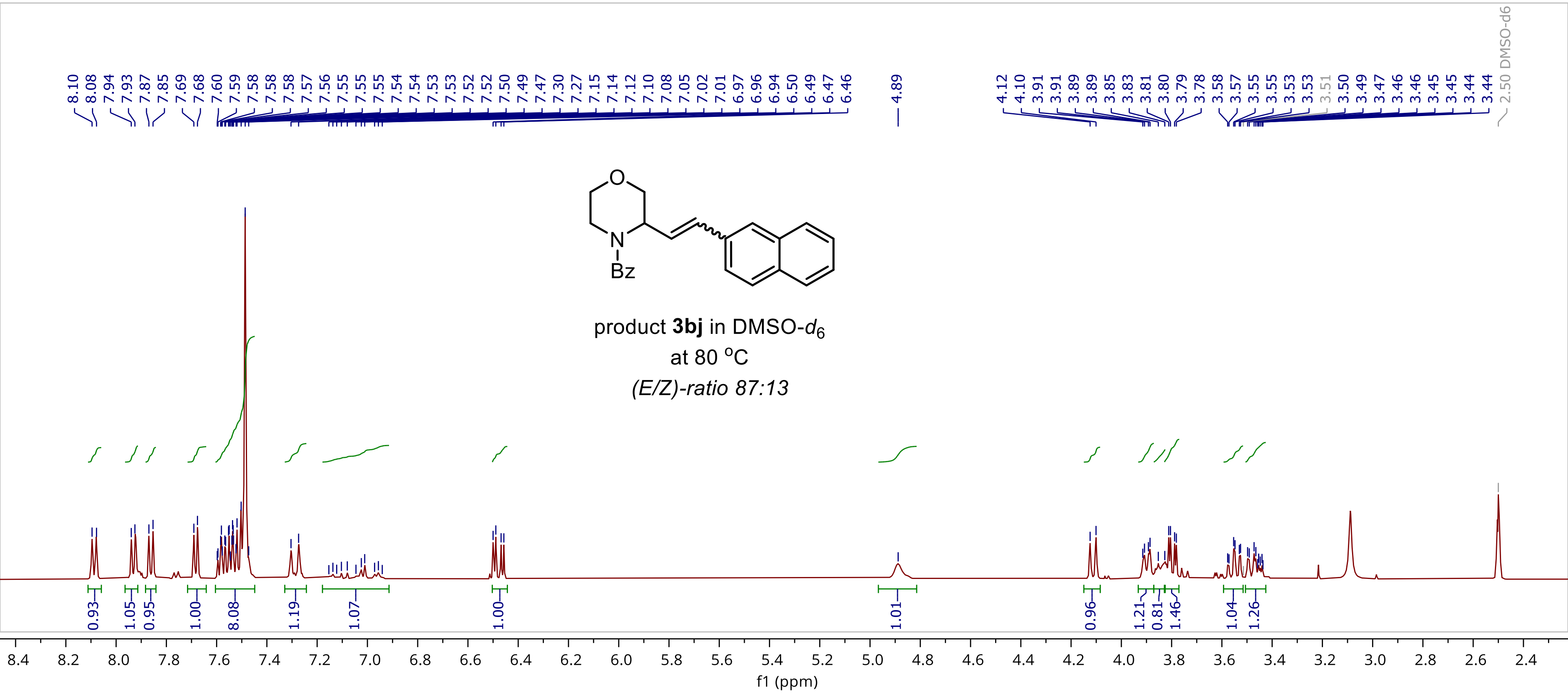
product **3bh** in DMSO-d_6
at 80 °C
(E/Z)-ratio 2:1





product **3bi** in
DMSO-d_6 at 80 ^{o}C
(E/Z)-ratio >98:2

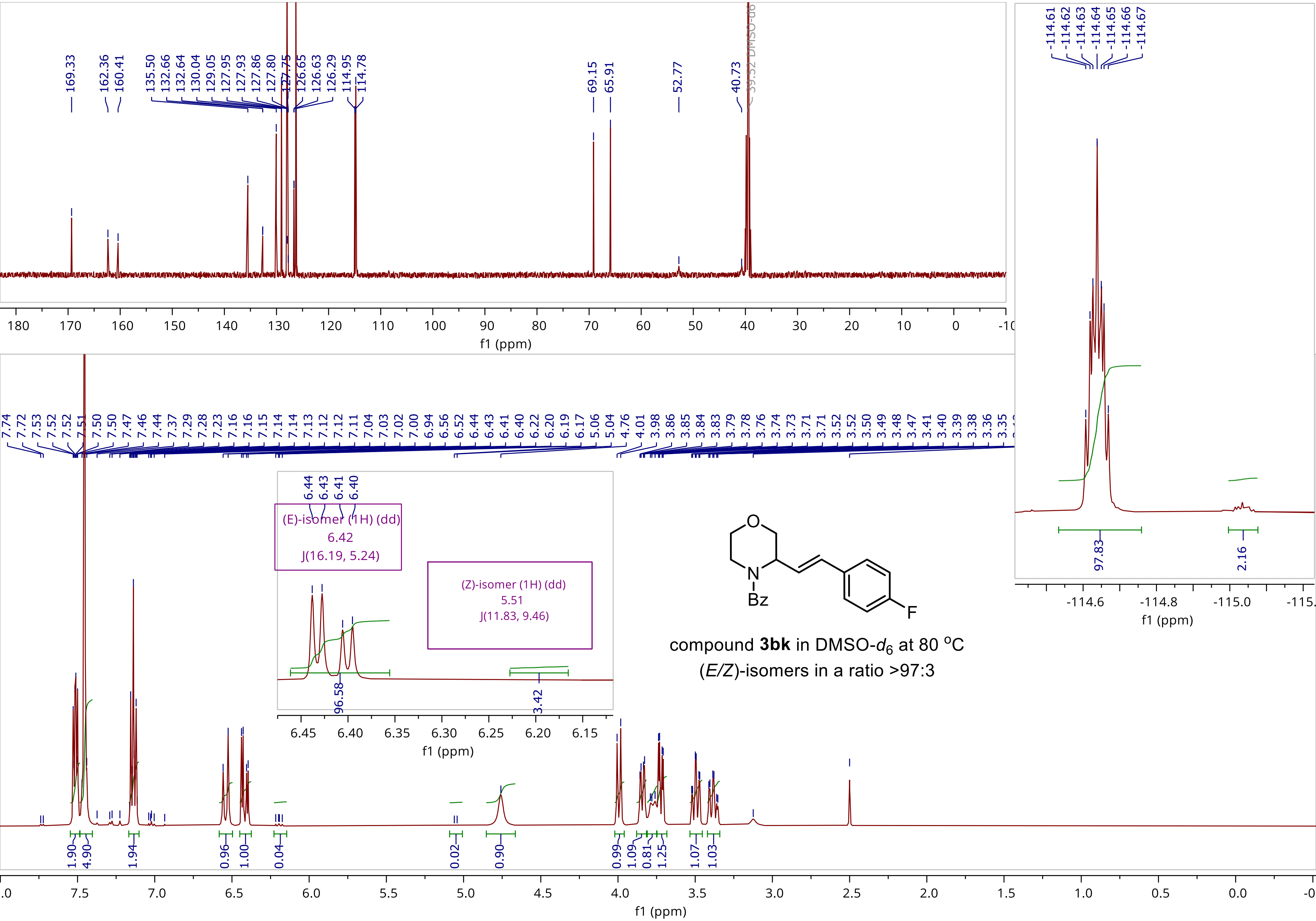




product **3bj** in DMSO-d_6

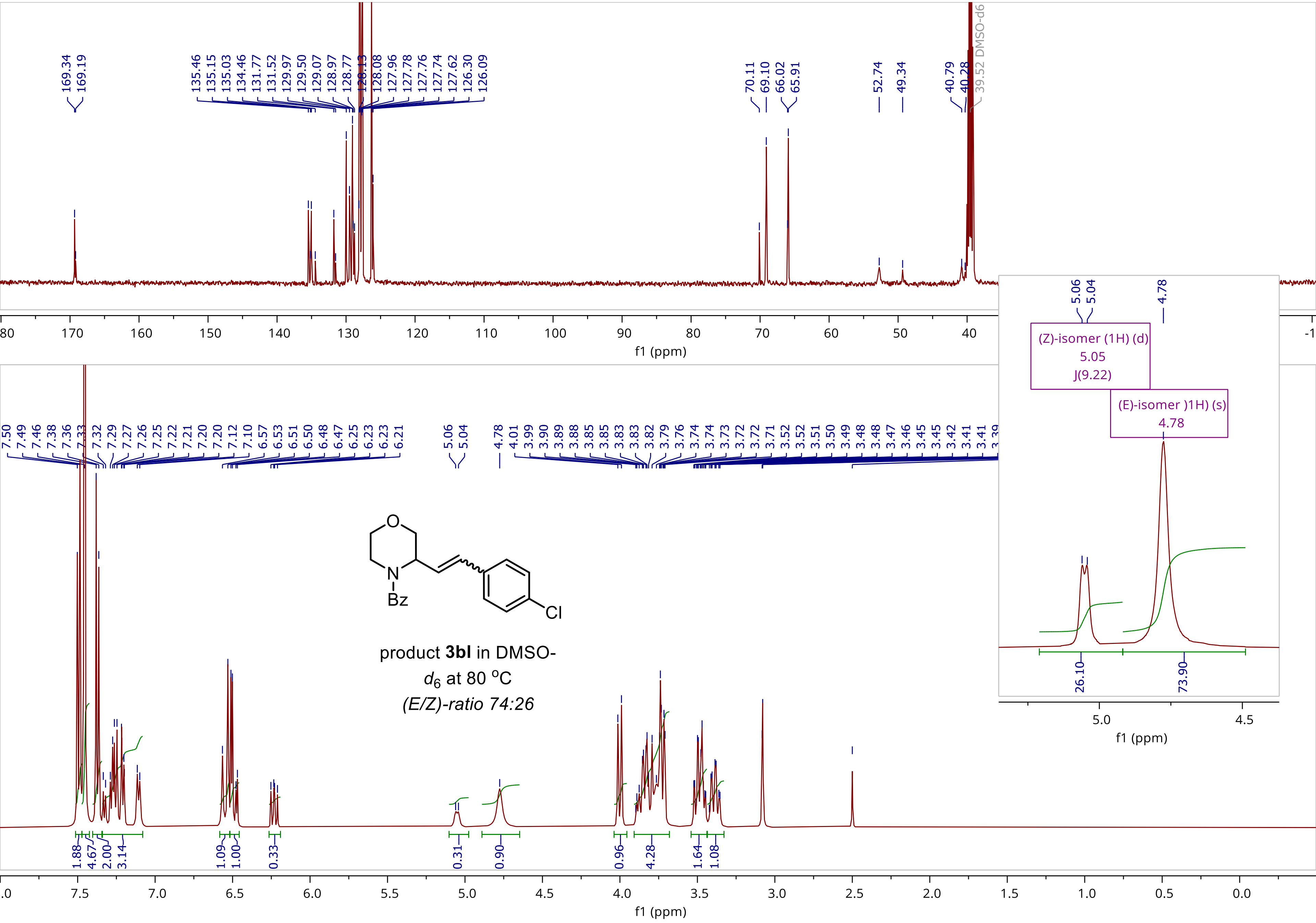
at 80 °C

(E/Z)-ratio 87:13

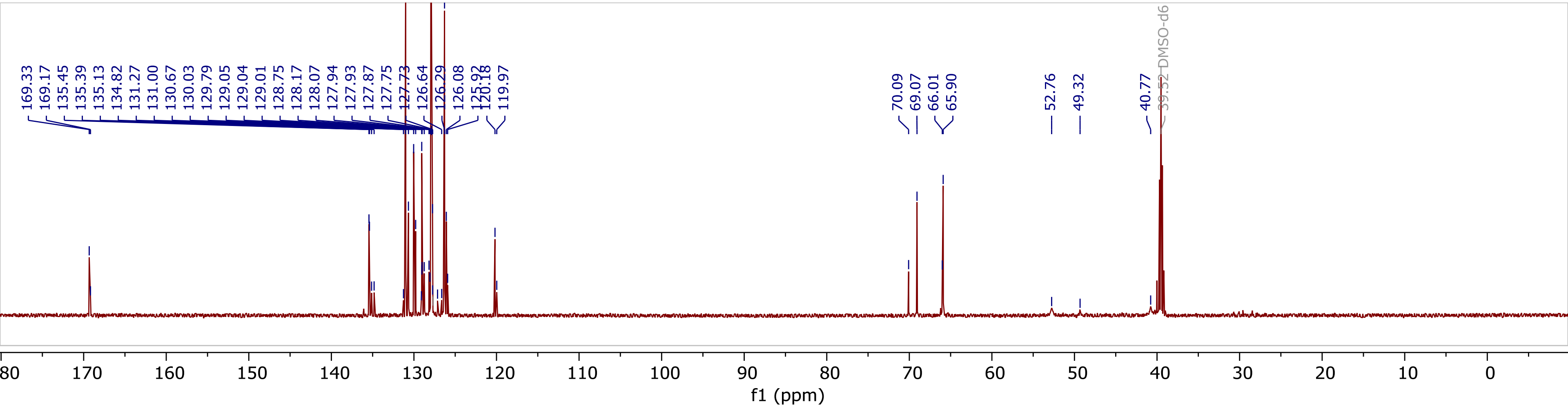


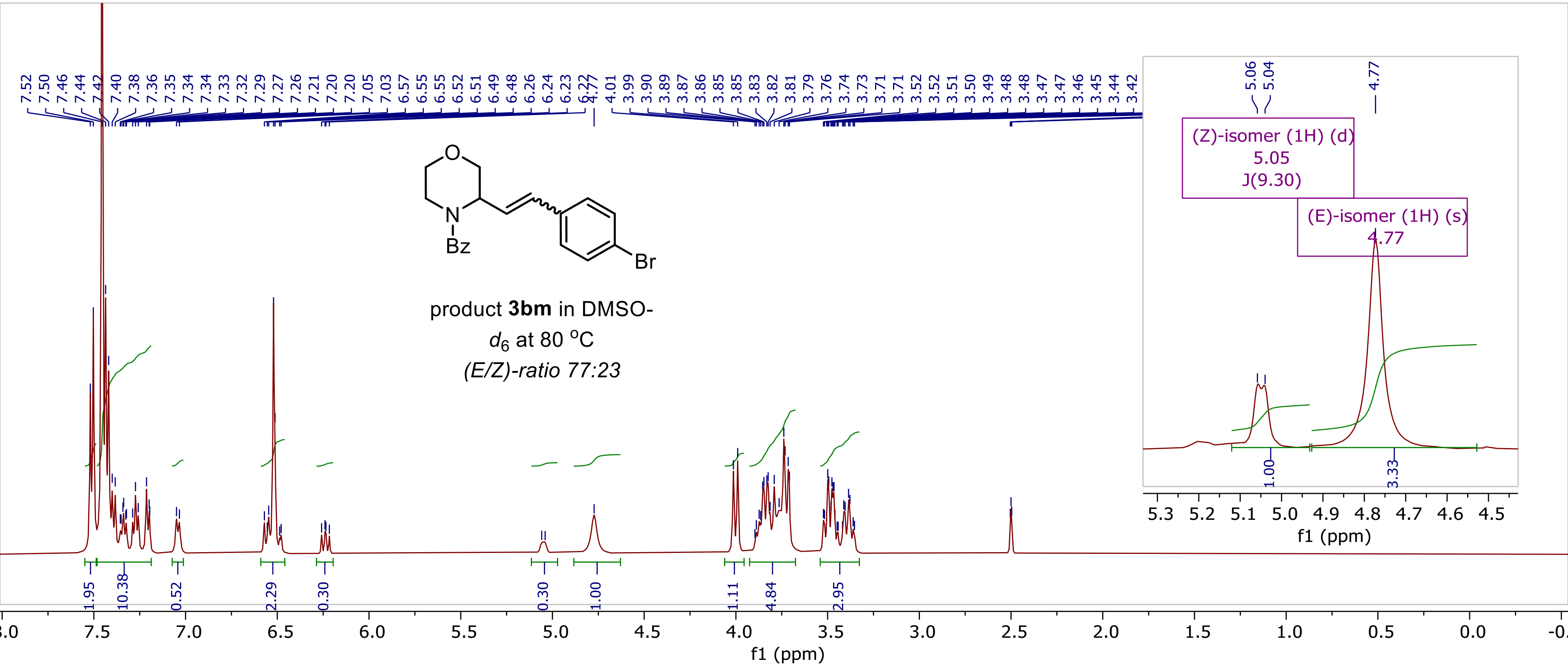
compound **3bk** in DMSO-d_6 at 80 °C

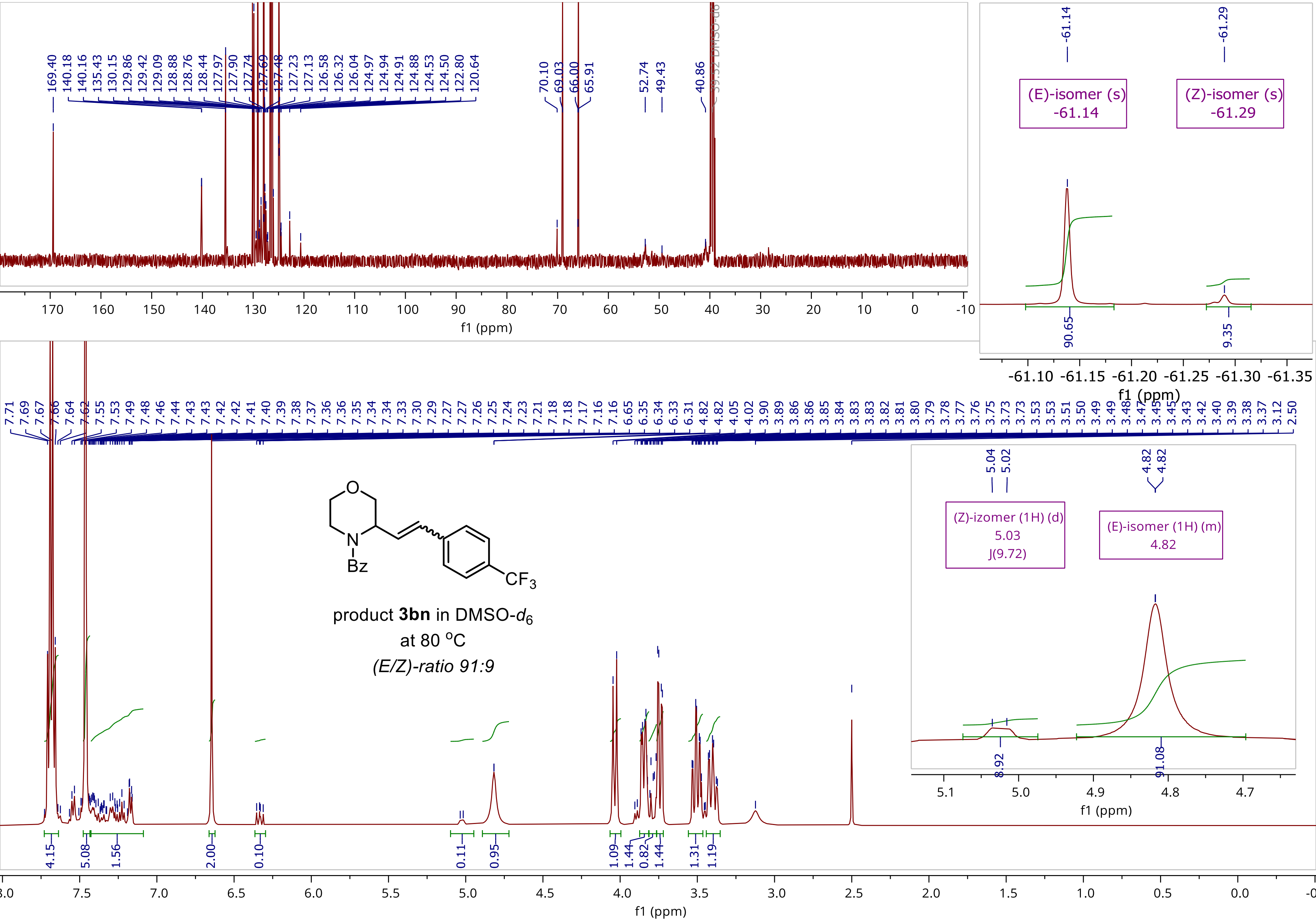
(*E*/*Z*)-isomers in a ratio >97:3



product **3bl** in DMSO-d_6 at 80 °C
(E/Z)-ratio 74:26


169.33
169.17
135.45
135.39
135.13
134.82
131.27
131.00
130.67
130.03
129.79
129.05
129.04
129.01
128.75
128.17
128.07
127.94
127.93
127.87
127.75
127.73
126.64
126.29
126.08
125.92
120.18
119.97
70.09
69.07
66.01
65.90
52.76
49.32
40.77
39.52 DMSO-d6
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

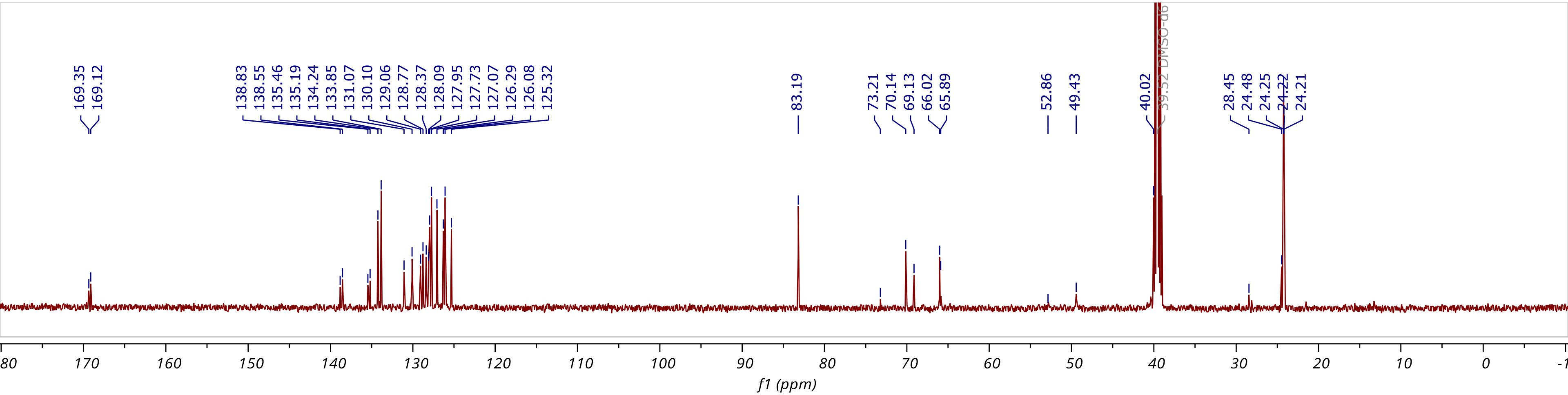

7.52
7.50
7.46
7.44
7.42
7.40
7.38
7.36
7.35
7.34
7.34
7.33
7.32
7.29
7.27
7.26
7.21
7.20
7.20
7.05
7.03
6.57
6.55
6.55
6.52
6.51
6.49
6.48
6.26
6.24
6.23
6.22
4.77
4.01
3.99
3.90
3.89
3.87
3.86
3.85
3.85
3.83
3.82
3.81
3.79
3.76
3.74
3.73
3.71
3.71
3.52
3.52
3.51
3.50
3.49
3.48
3.48
3.47
3.47
3.46
3.45
3.44
3.42
O
N
Bz
Br
product **3bm** in DMSO-d_6 at 80 ^{o}C
(E/Z)-ratio 77:23
1.95
10.38
0.52
2.29
0.30
0.30
1.00
1.11
4.84
2.95
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
-0.5
f1 (ppm)
5.06
5.04
4.77
(Z)-isomer (1H) (d)
5.05
J(9.30)
(E)-isomer (1H) (s)
4.77
1.00
3.33
5.3
5.2
5.1
5.0
4.9
4.8
4.7
4.6
4.5
f1 (ppm)

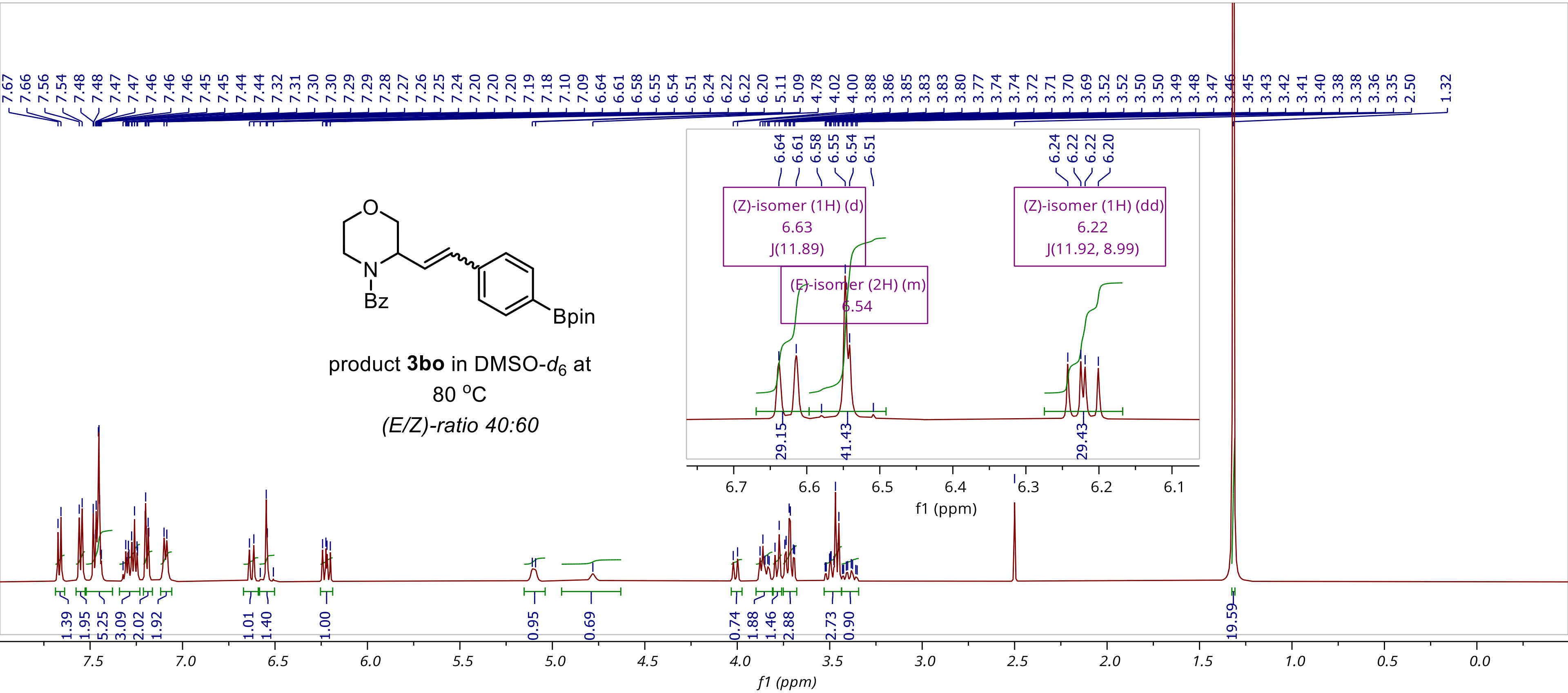


product **3bn** in DMSO-d_6

at 80 °C

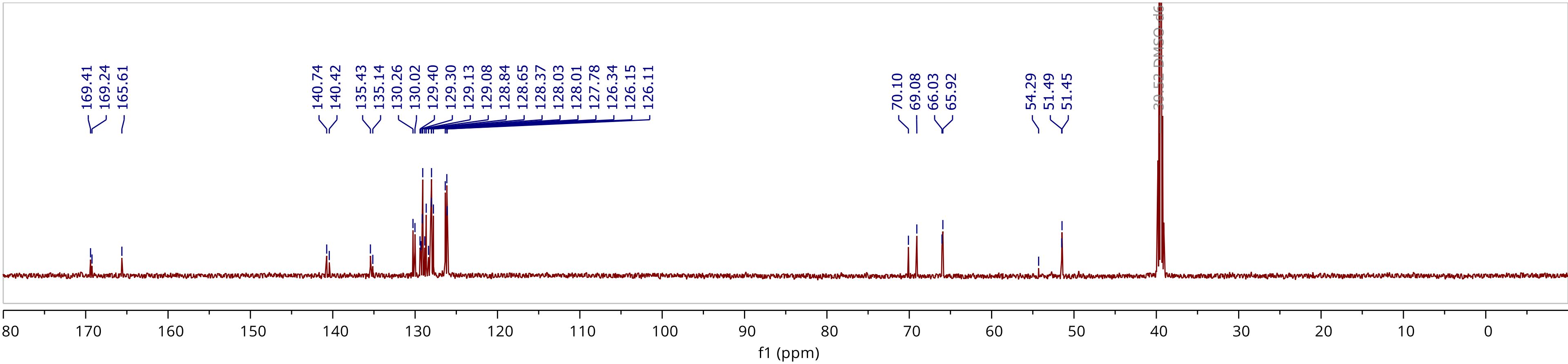
(E/Z)-ratio 91:9

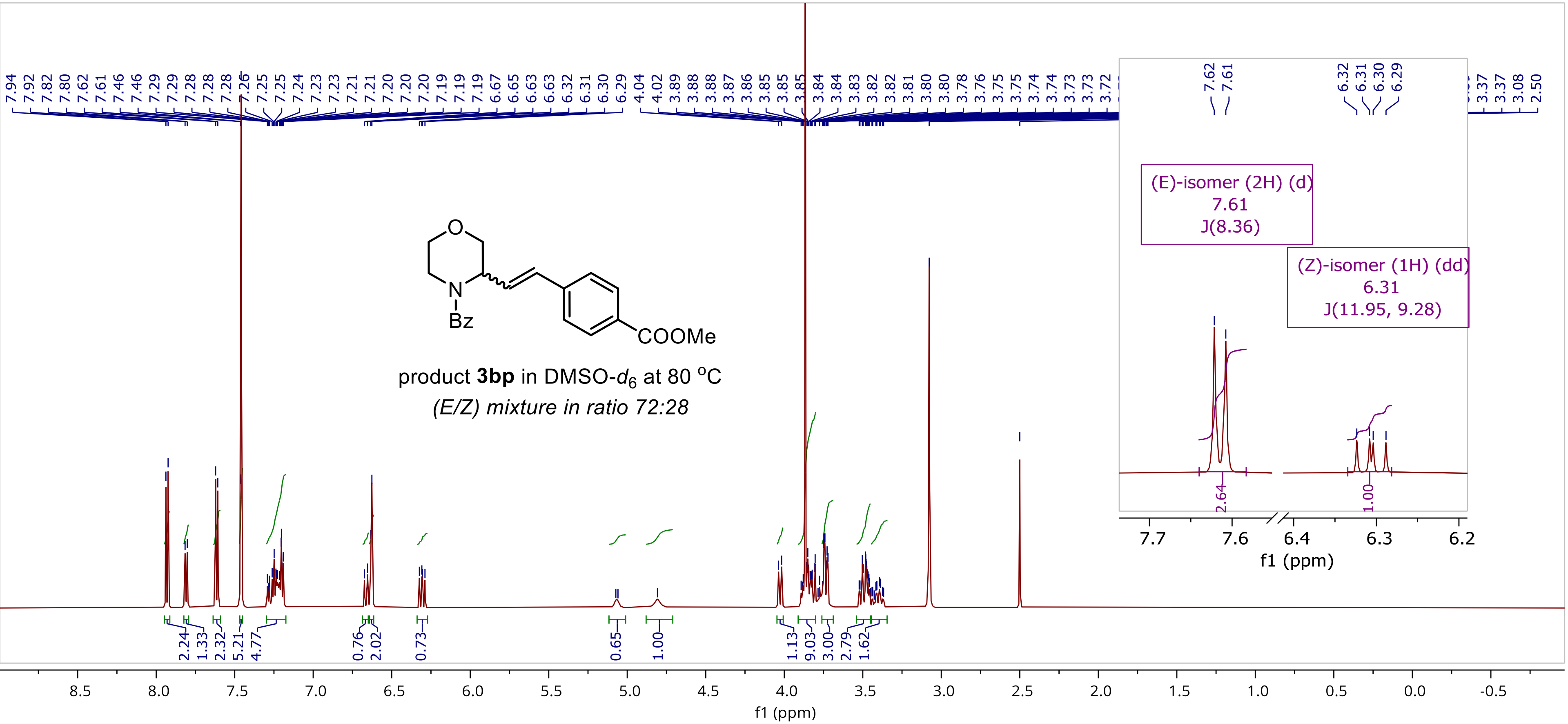




product **3bo** in DMSO-d_6 at 80 °C

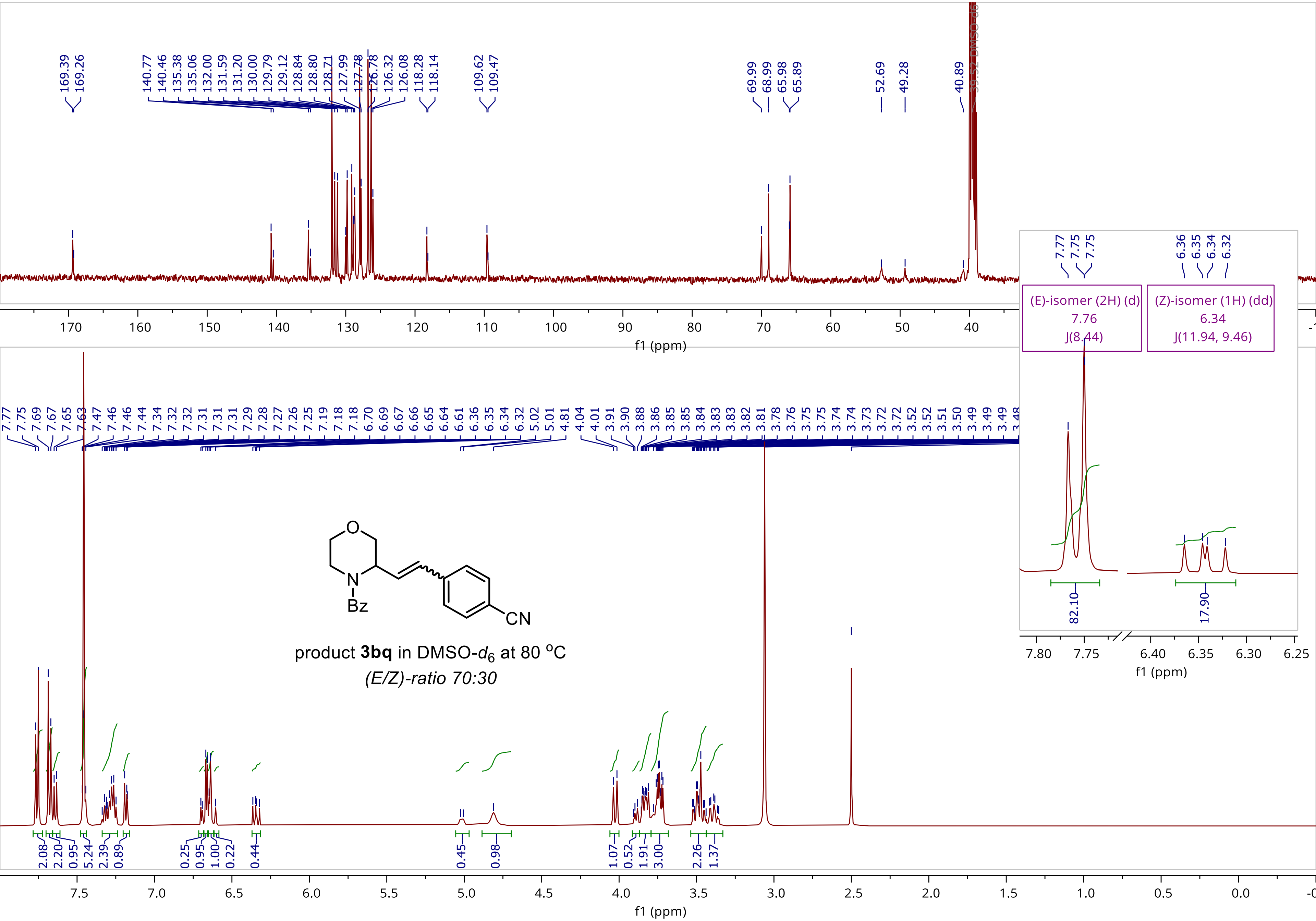
(E/Z)-ratio 40:60





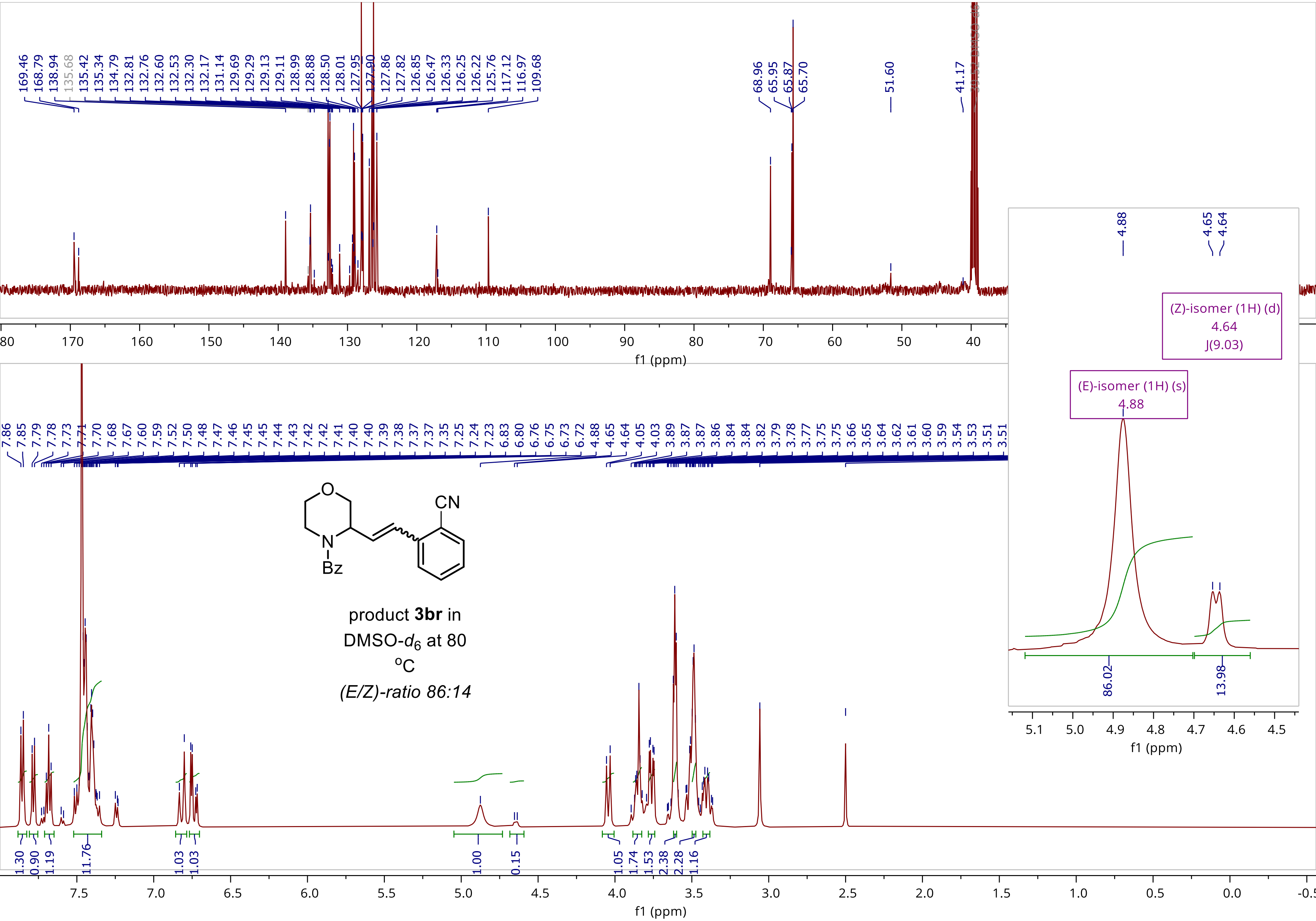
product **3bp** in DMSO-d_6 at 80 °C

(E/Z) mixture in ratio 72:28



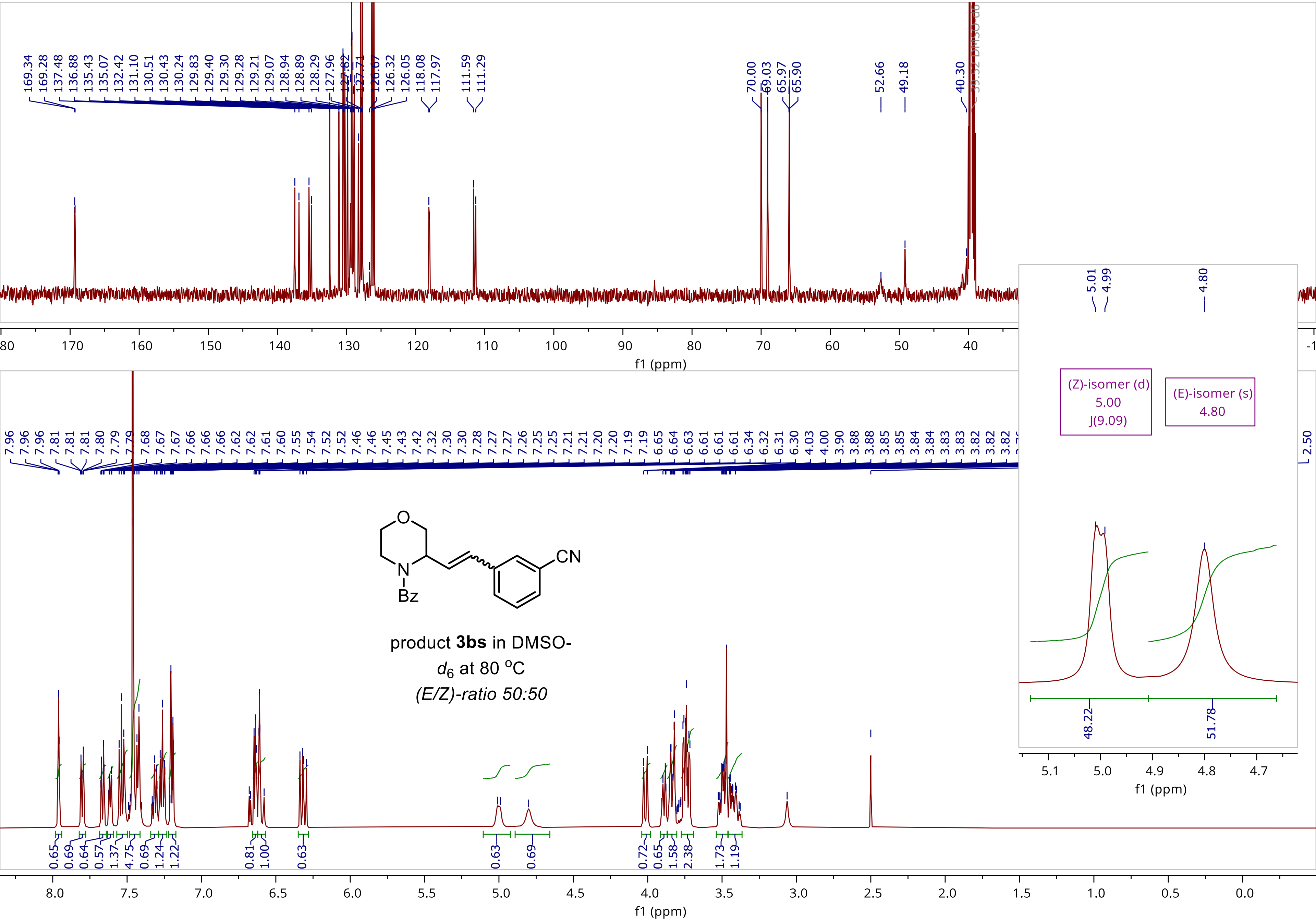
product **3bq** in DMSO-d_6 at 80 °C

(E/Z)-ratio 70:30



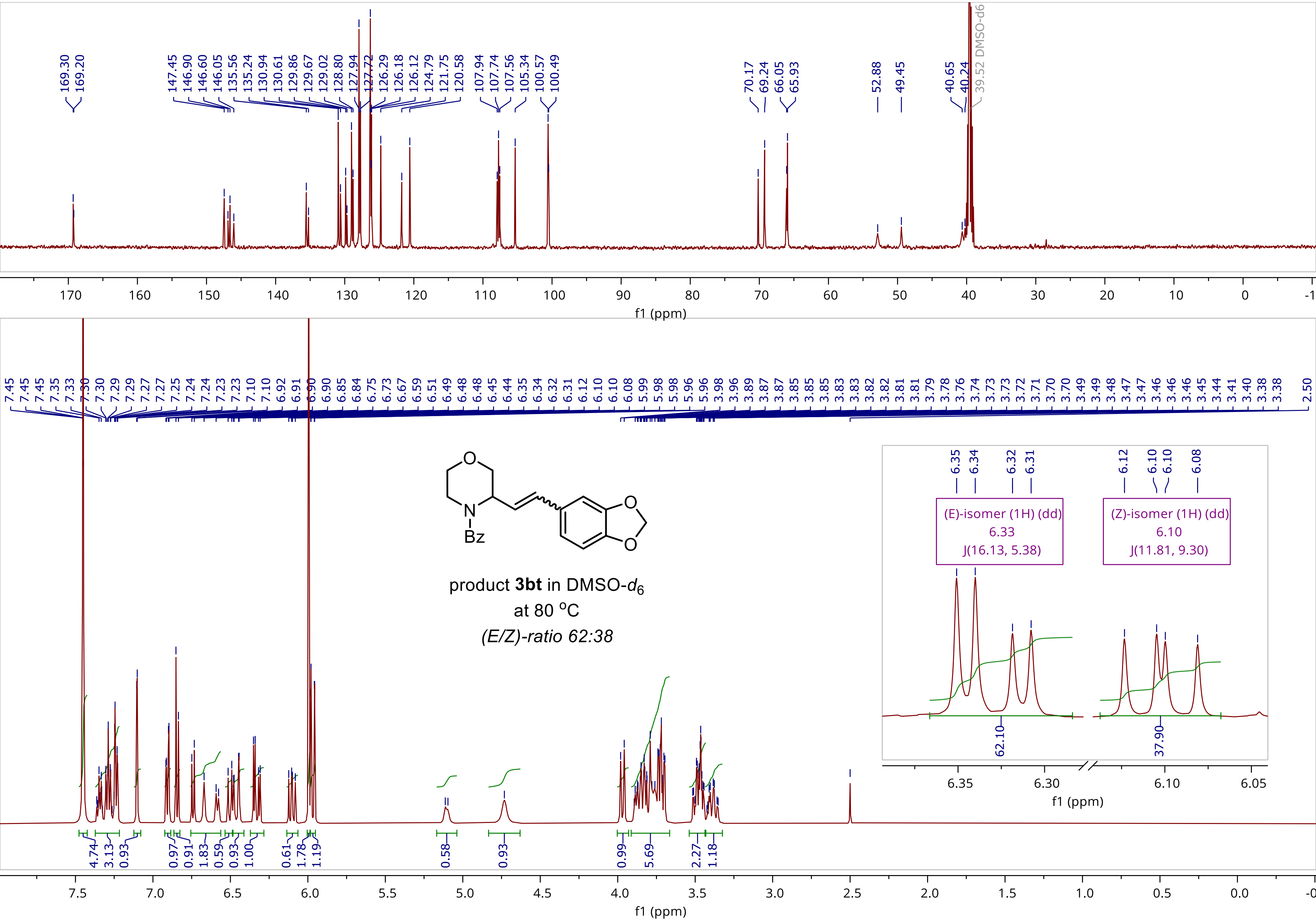
product **3br** in DMSO-d_6 at 80 °C

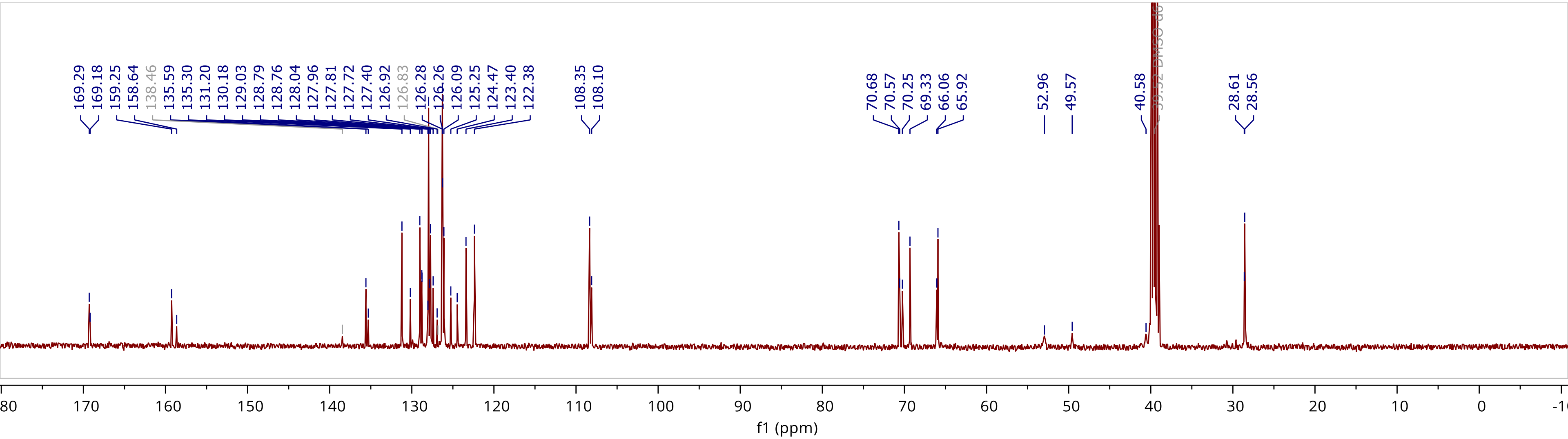
(E/Z)-ratio 86:14

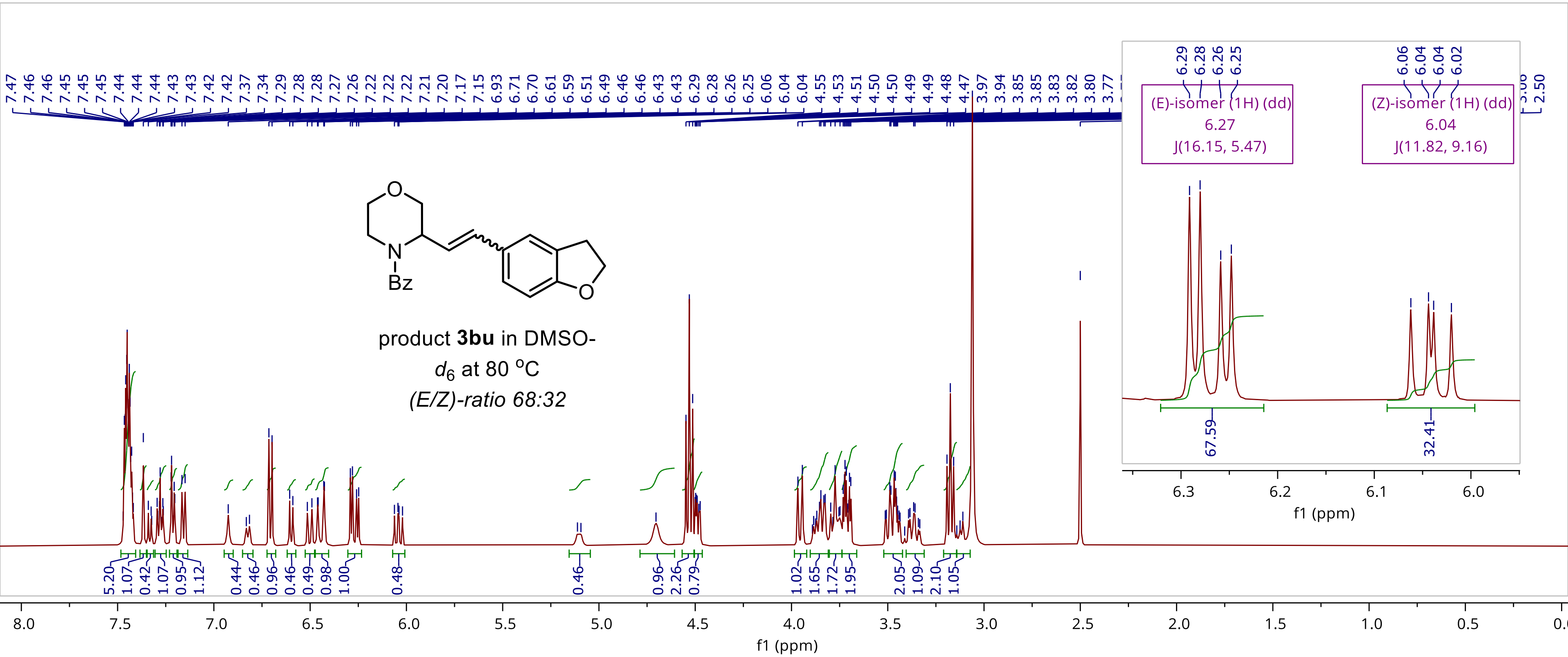


product **3bs** in DMSO-*d*$_6$ at 80 °C

(E/Z)-ratio 50:50

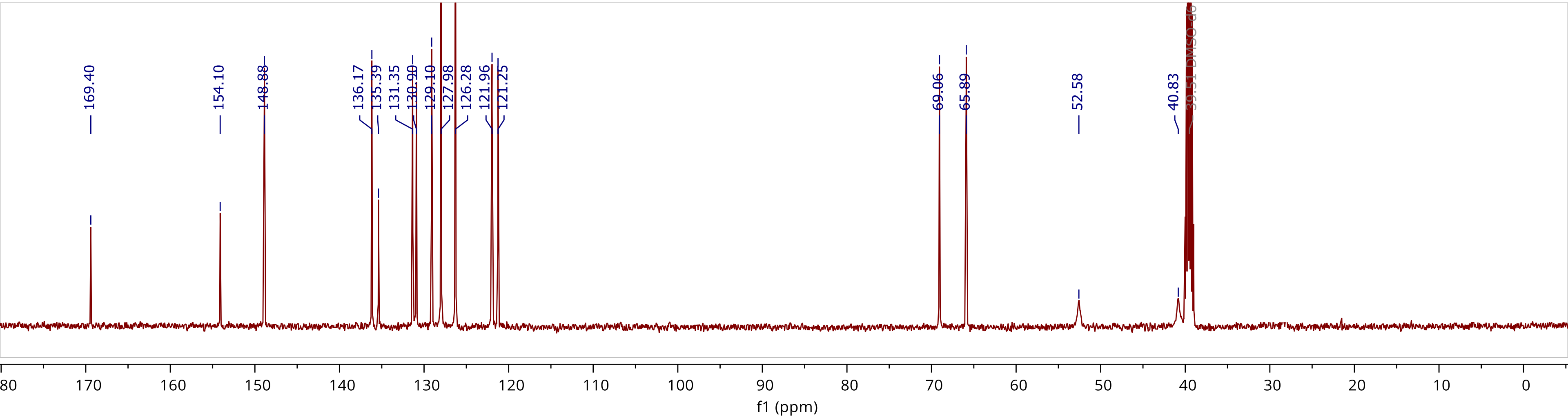

product **3bt** in DMSO-d_6
at 80 °C
(E/Z)-ratio 62:38

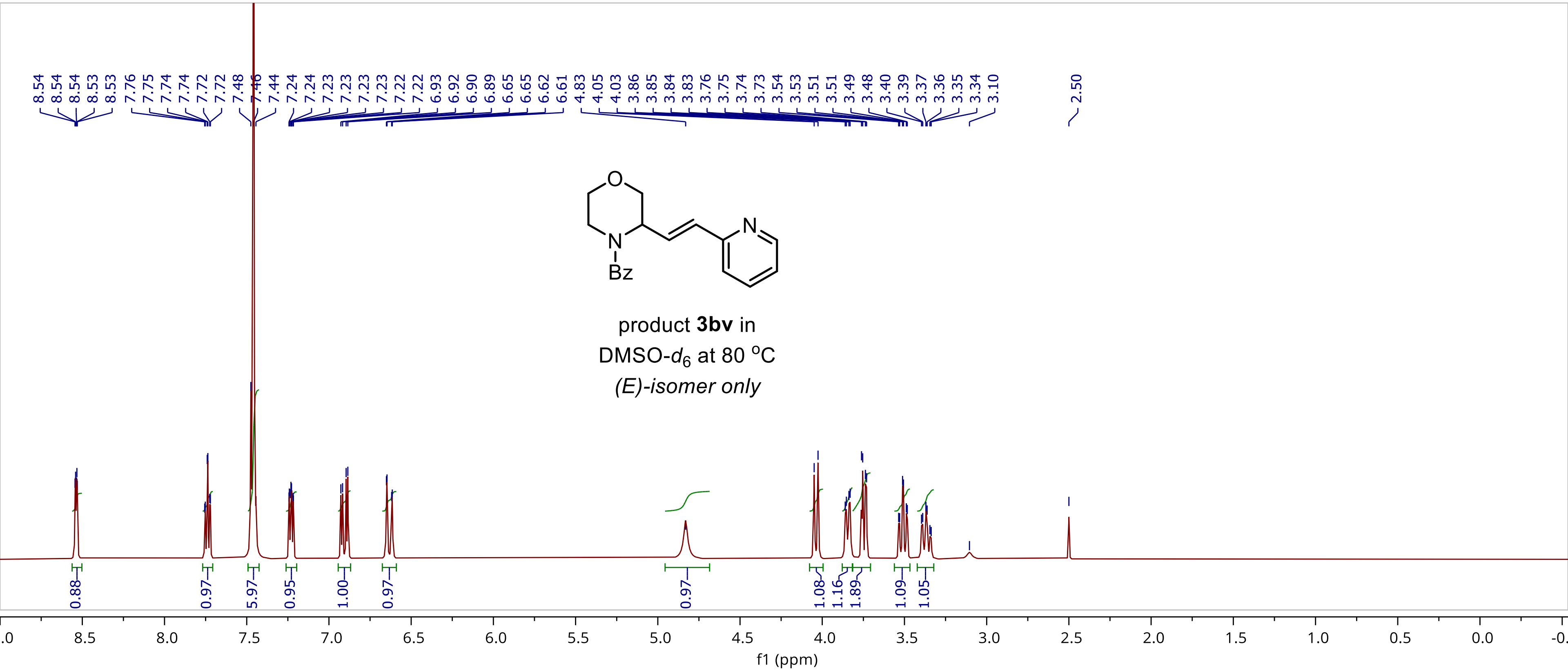




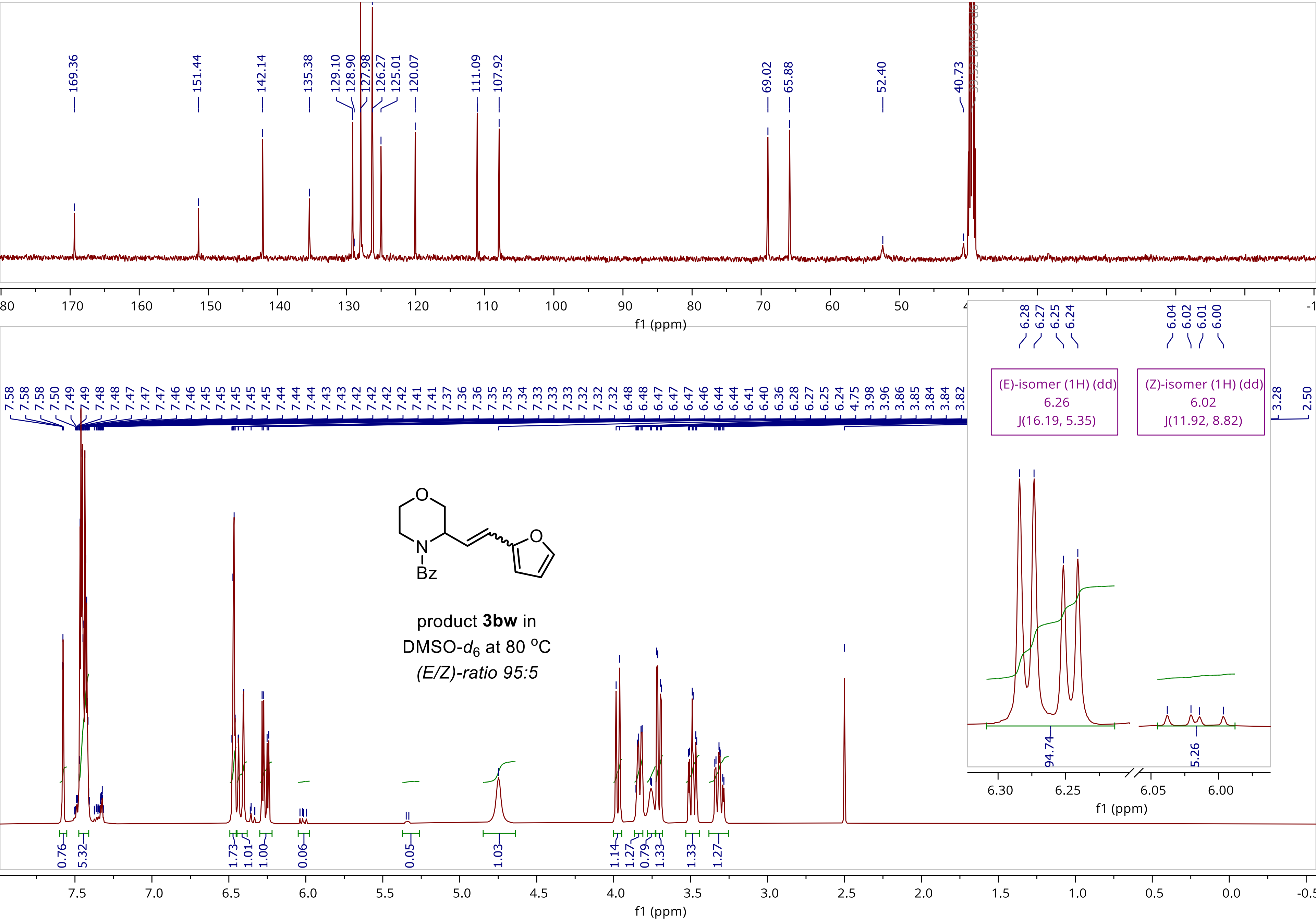
product **3bu** in DMSO-d_6 at 80 °C

(E/Z)-ratio 68:32

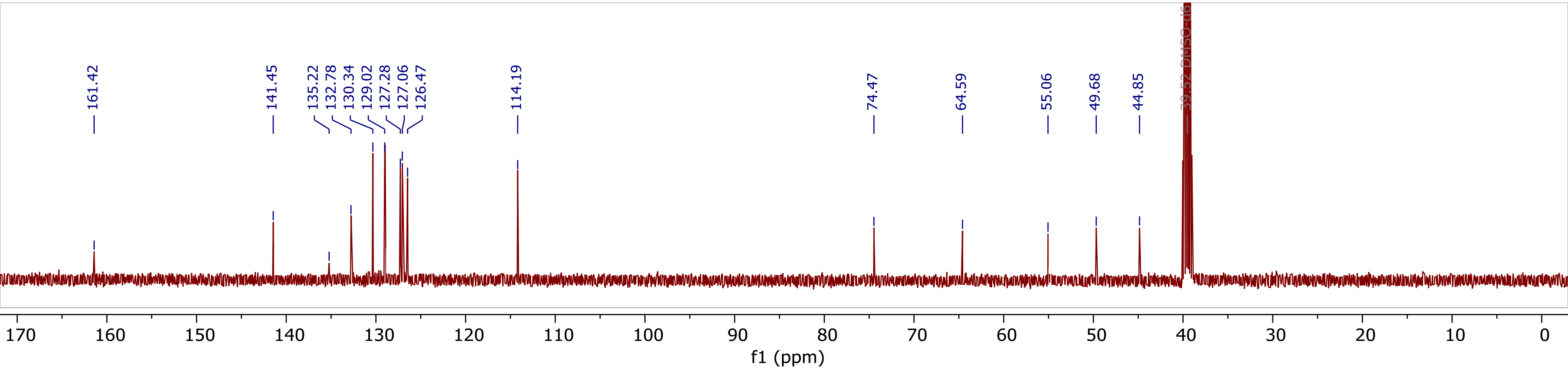


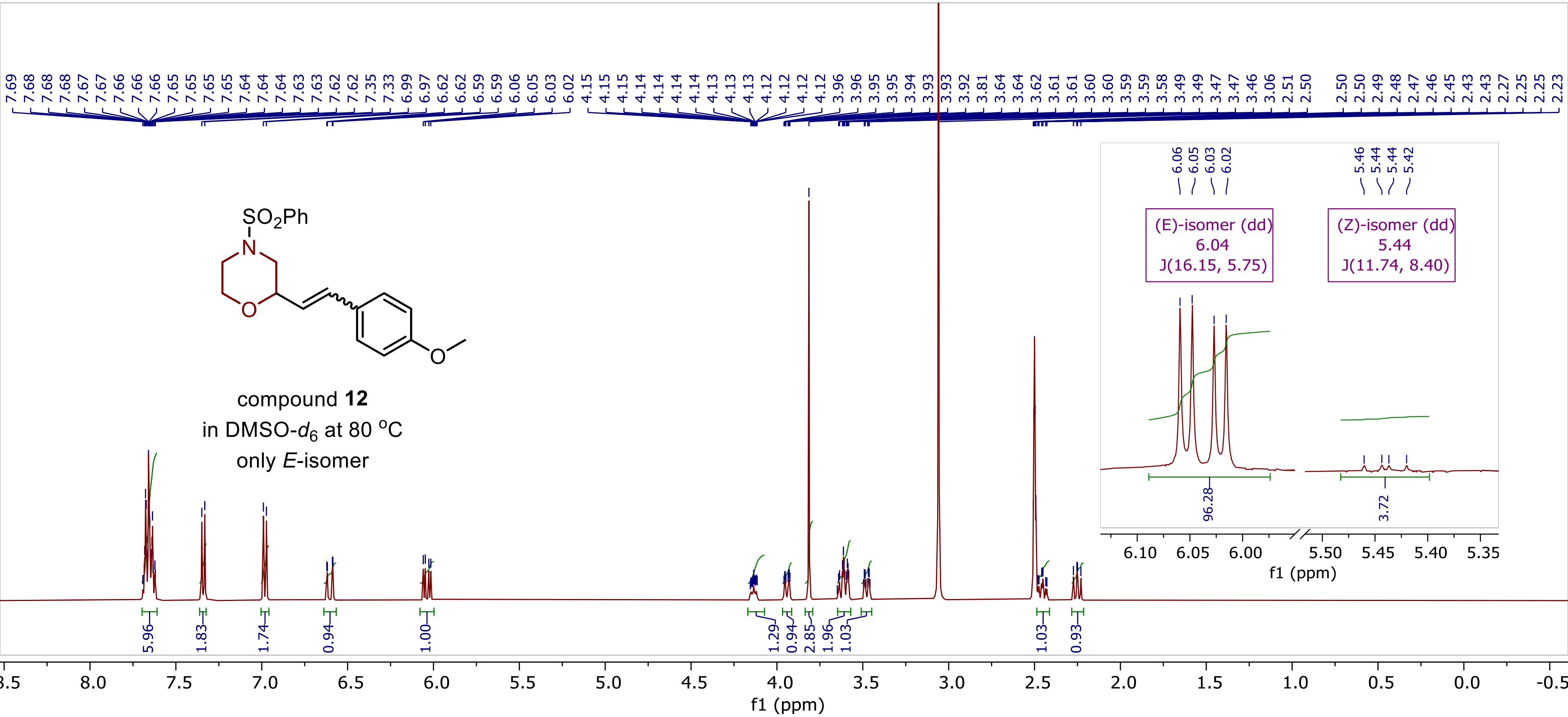


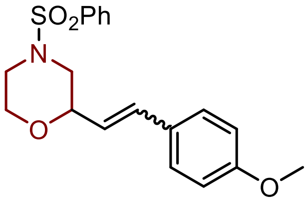
product **3bv** in
DMSO-d_6 at 80 ^{o}C
(E)-isomer only



product **3bw** in
DMSO-d_6 at 80 °C
(E/Z)-ratio 95:5




compound **12**
in DMSO-d_6 at 80 °C
only *E*-isomer

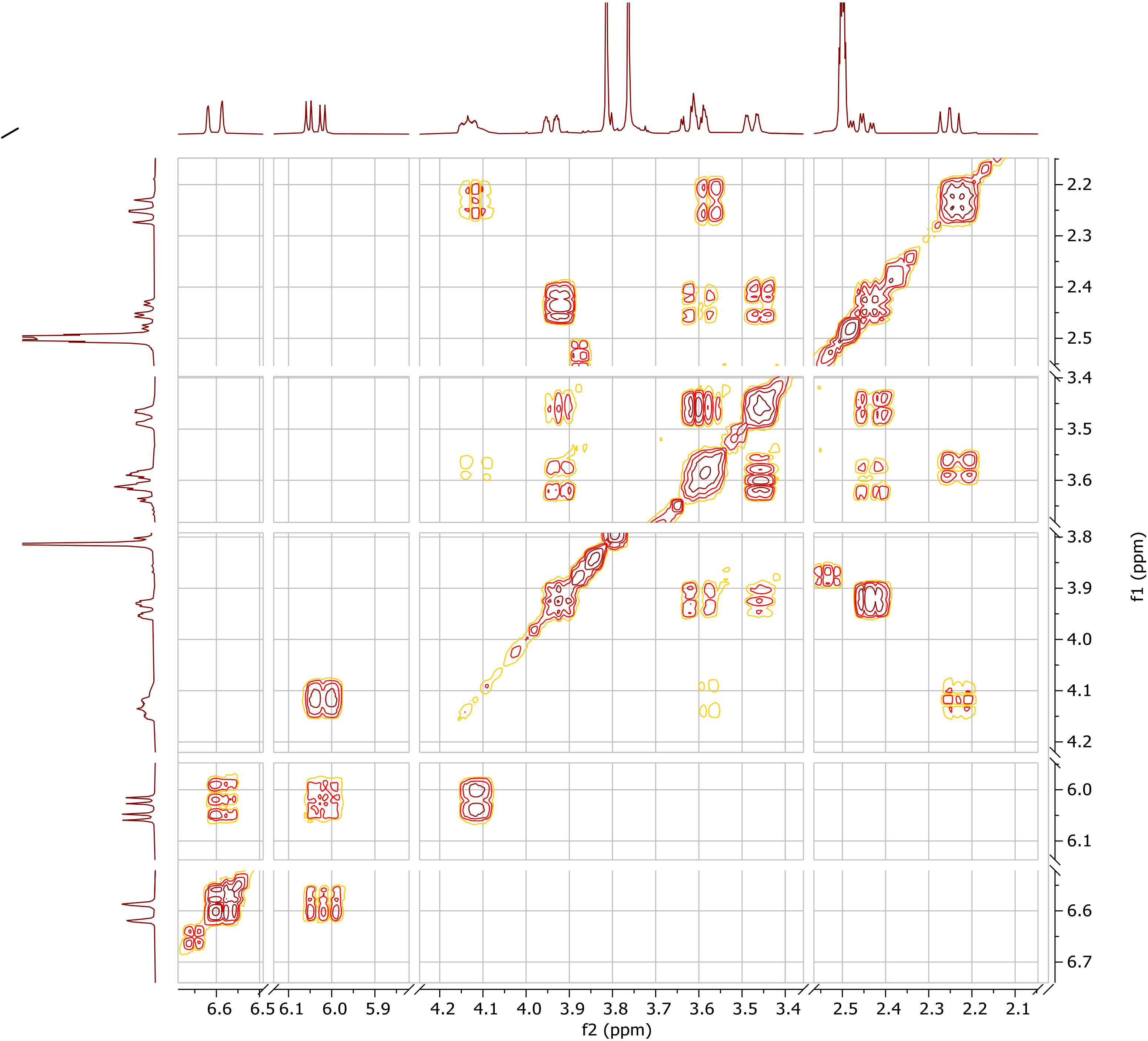


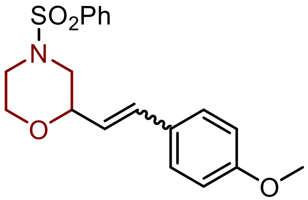
compound **12**

in DMSO-d_6 at 80 ^{o}C

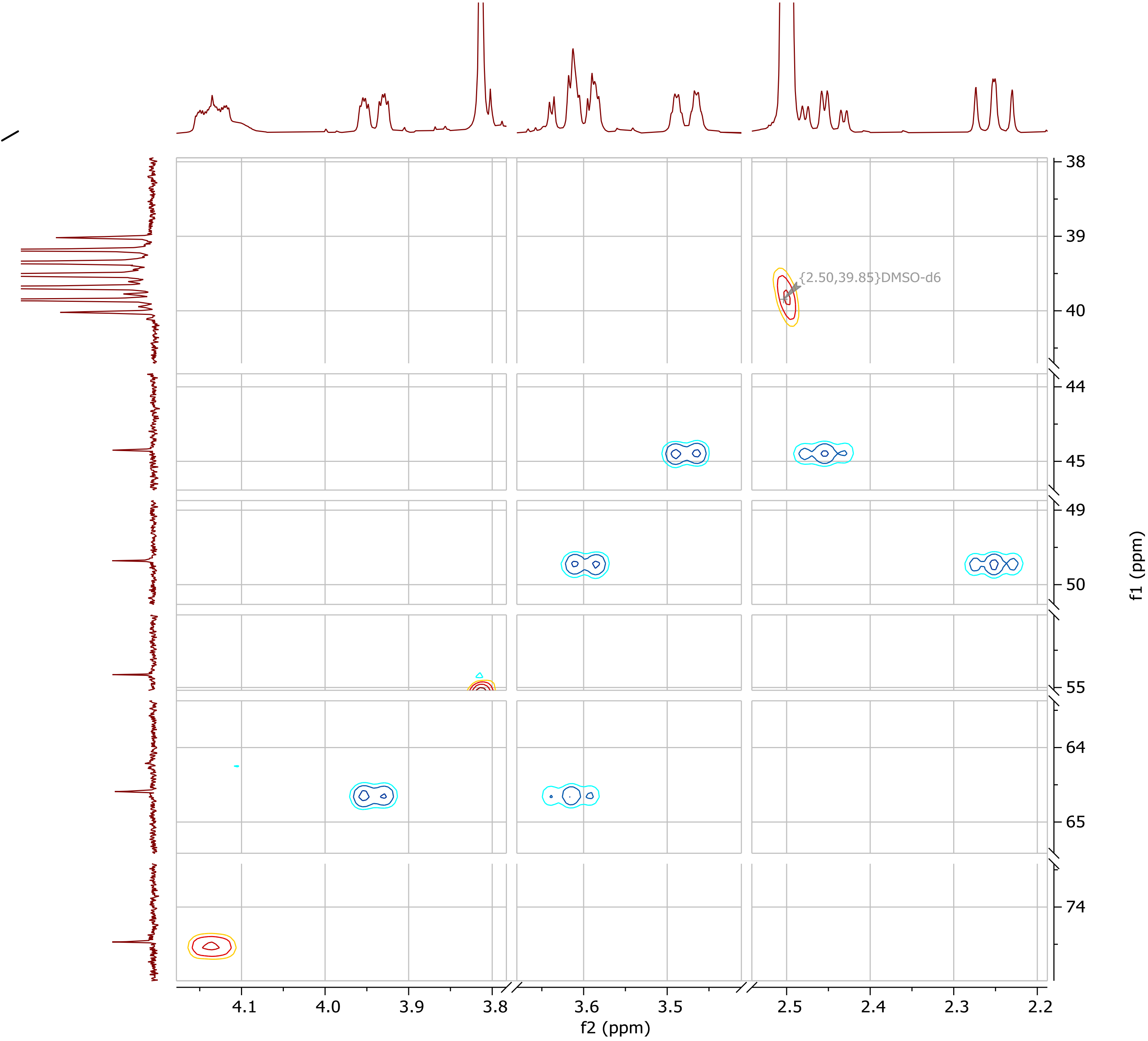
only *E*-isomer

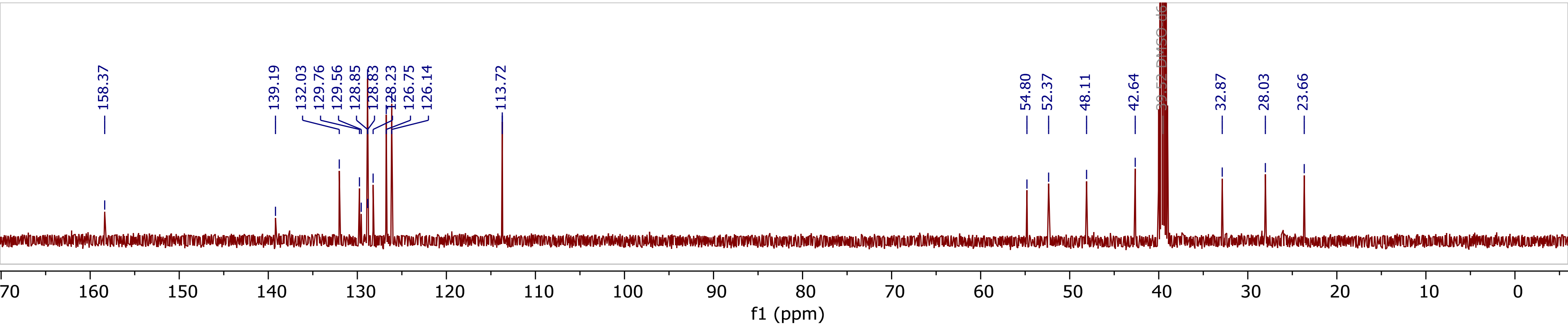
2D (COSY)

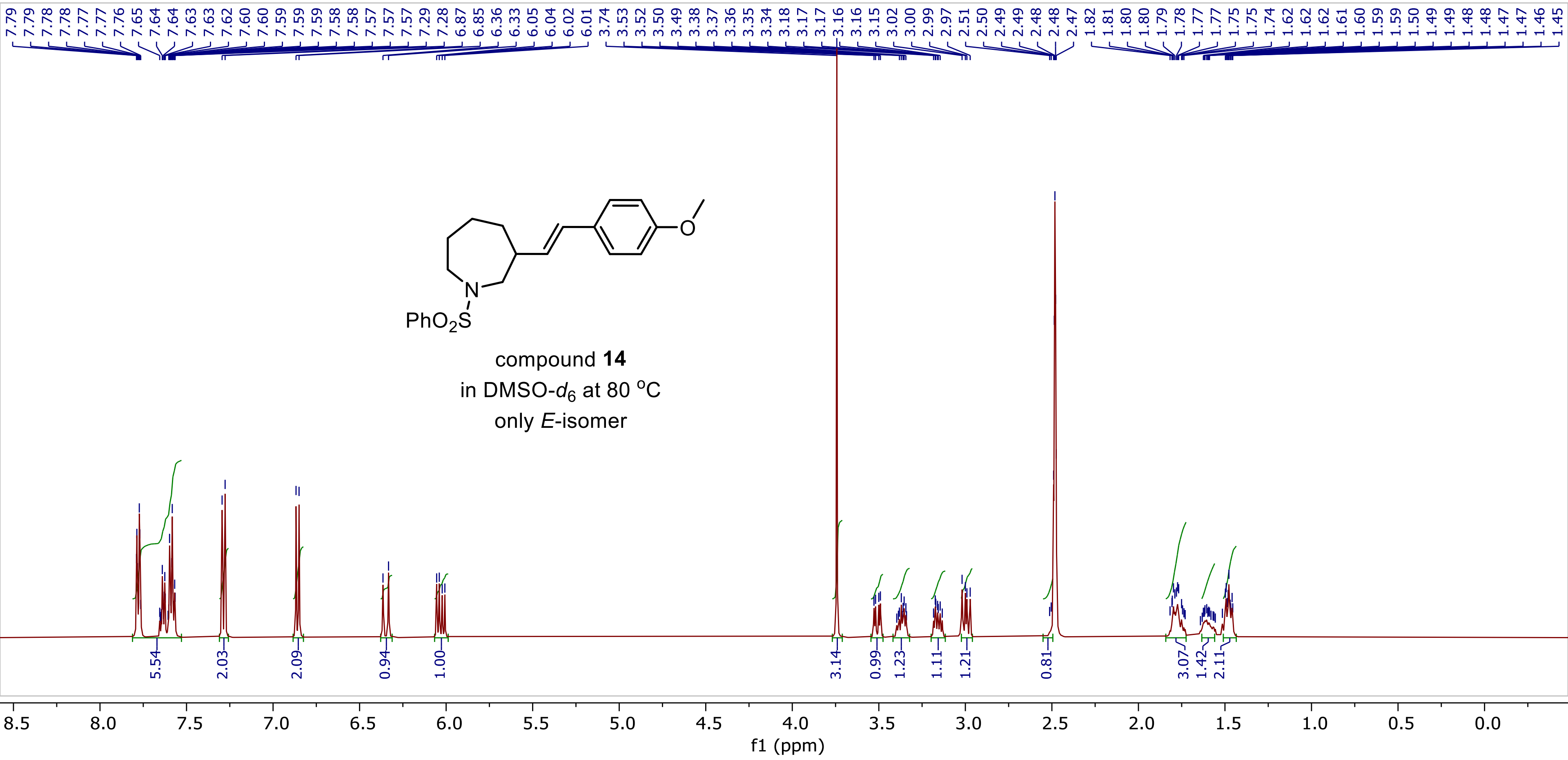




compound **12**
in DMSO-d_6 at 80 ^{o}C
only *E*-isomer
2D (HSQC)



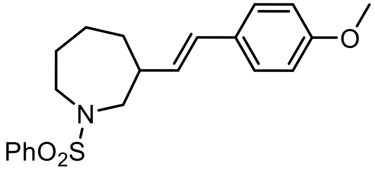




compound **14**

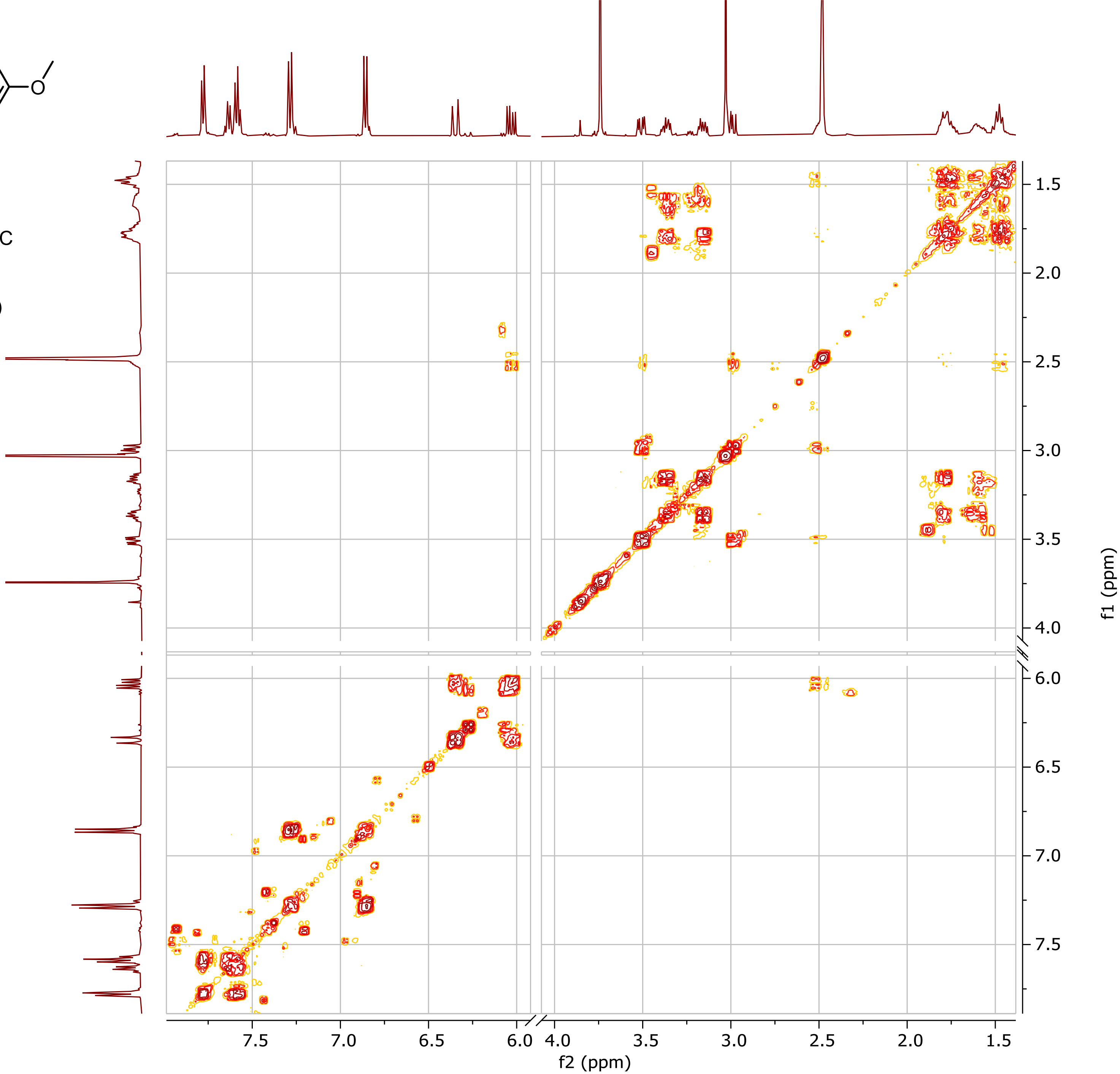
in DMSO-d_6 at 80 °C

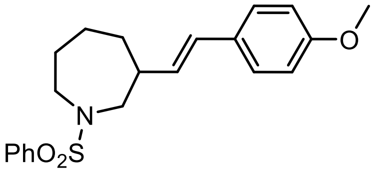
only *E*-isomer



compound **14**
in DMSO-d_6 at 80 ^{o}C
only *E*-isomer

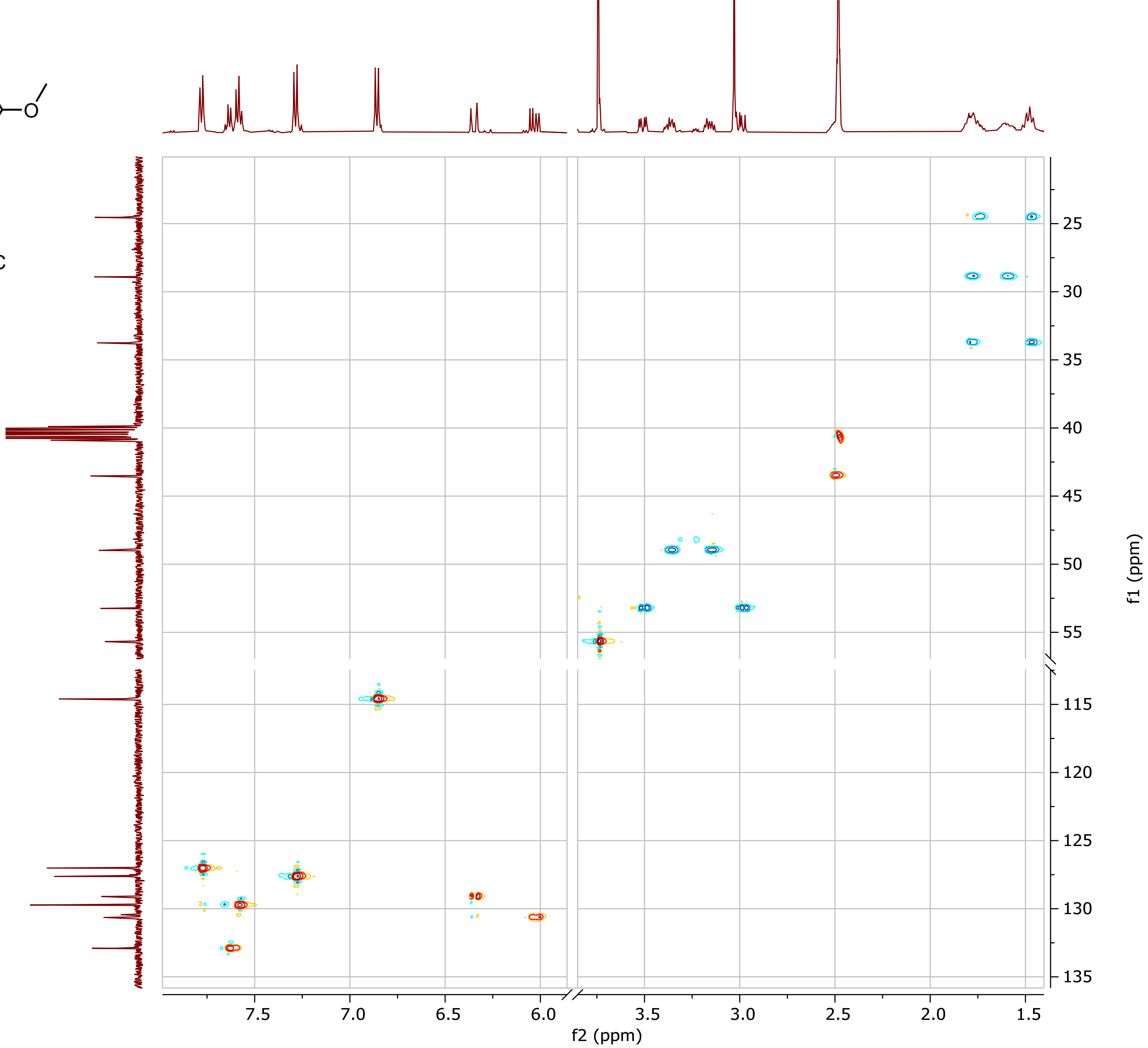
2D NMR (COSY)

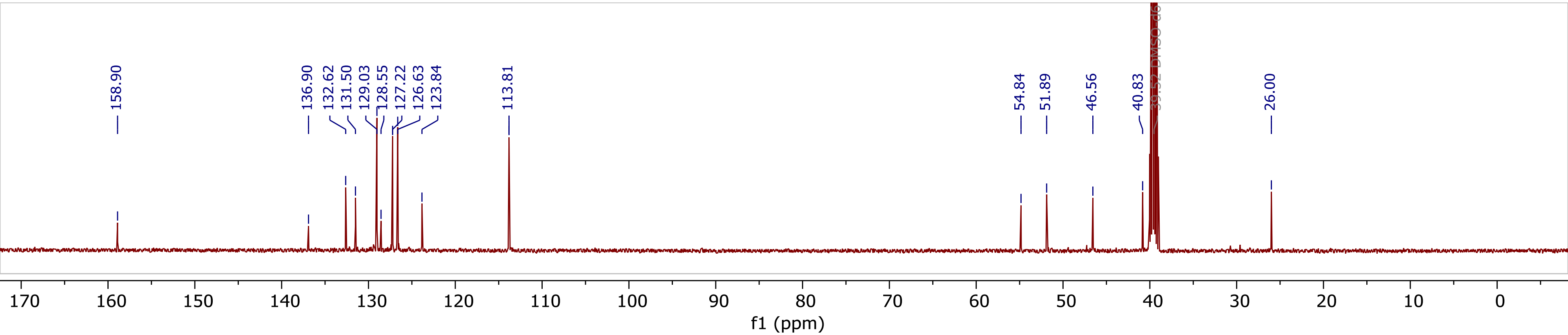


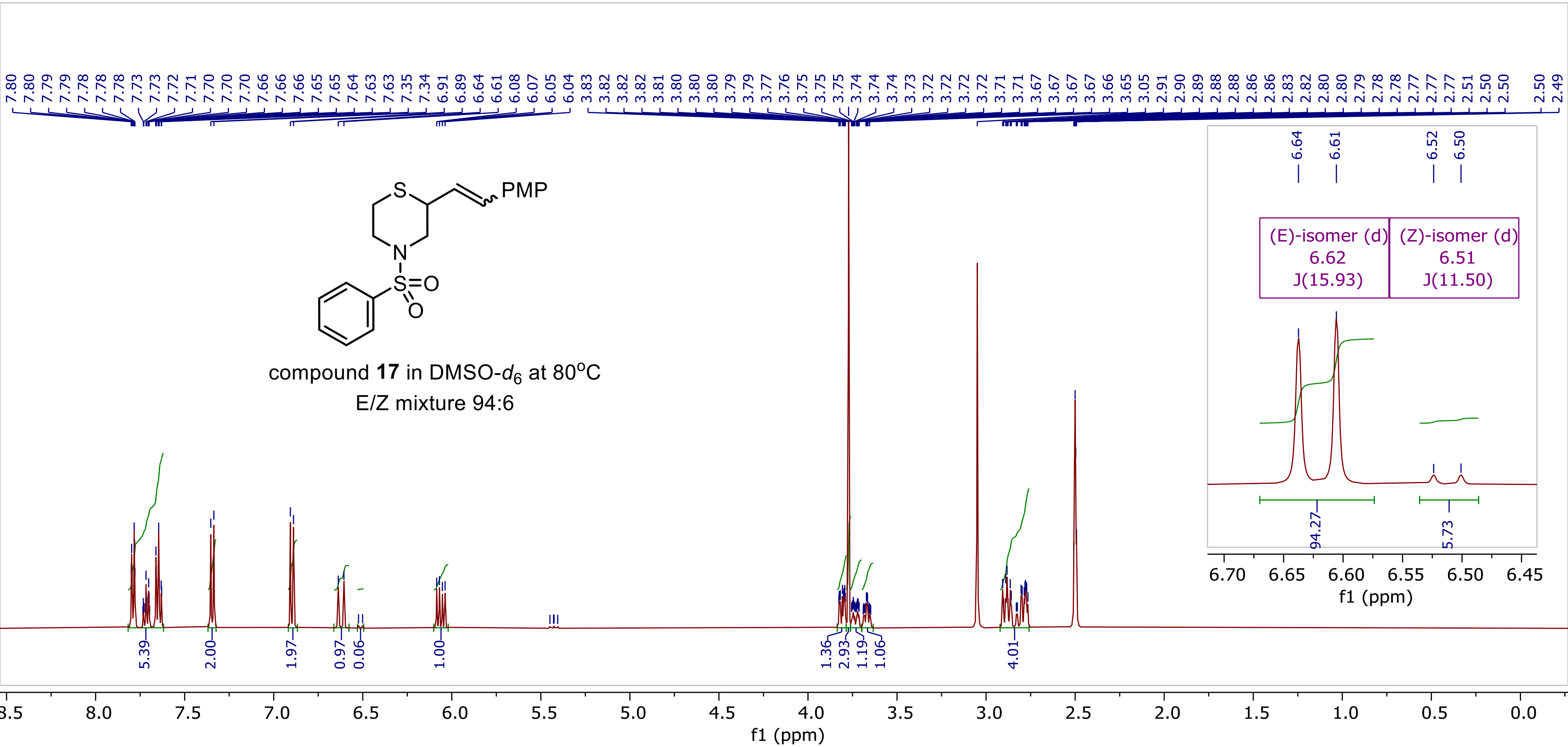


compound **14**
in DMSO-d_6 at 80 ^{o}C
only *E*-isomer

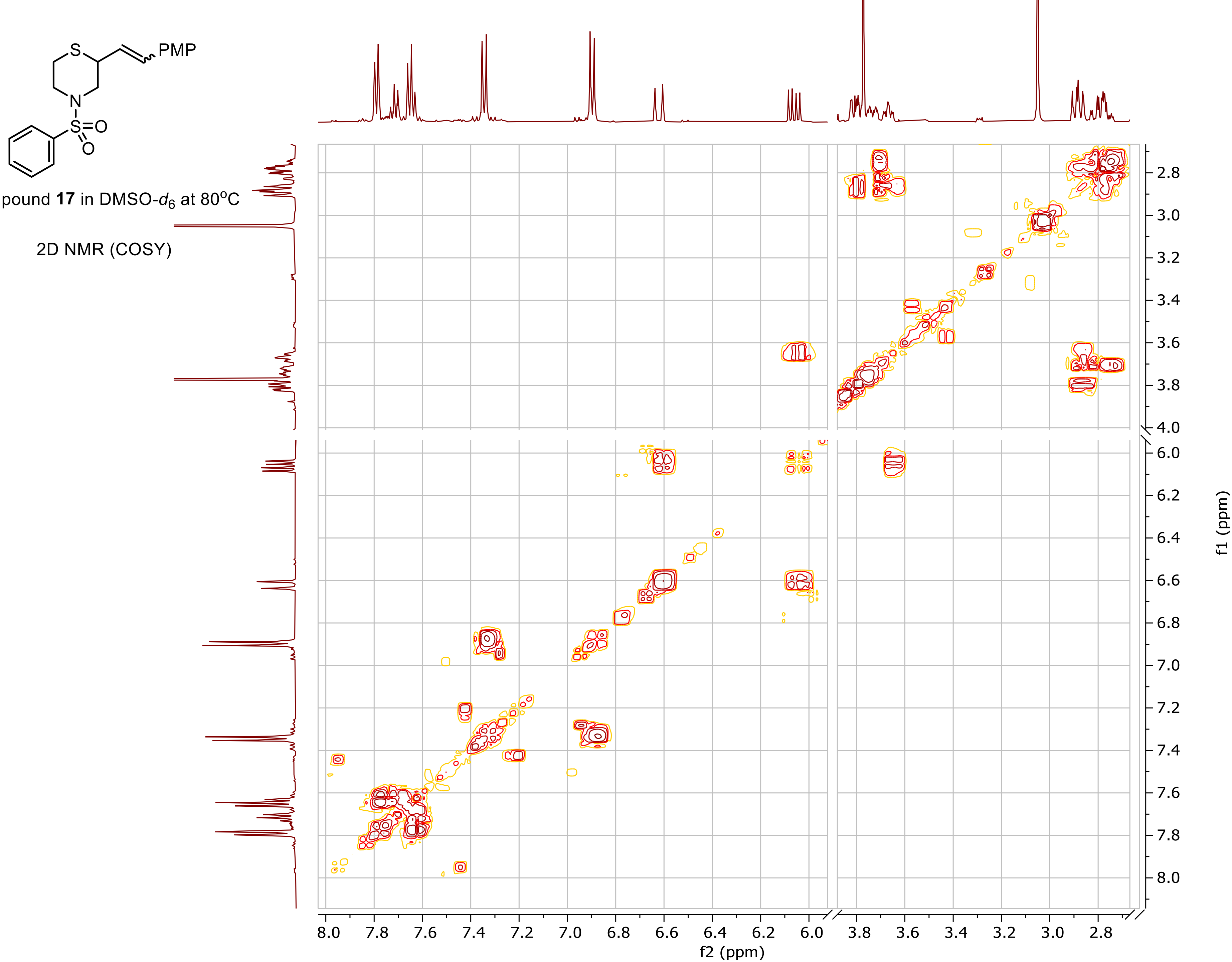
2D NMR (HSQC)





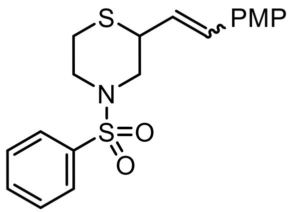


compound **17** in DMSO-d_6 at 80°C
E/Z mixture 94:6



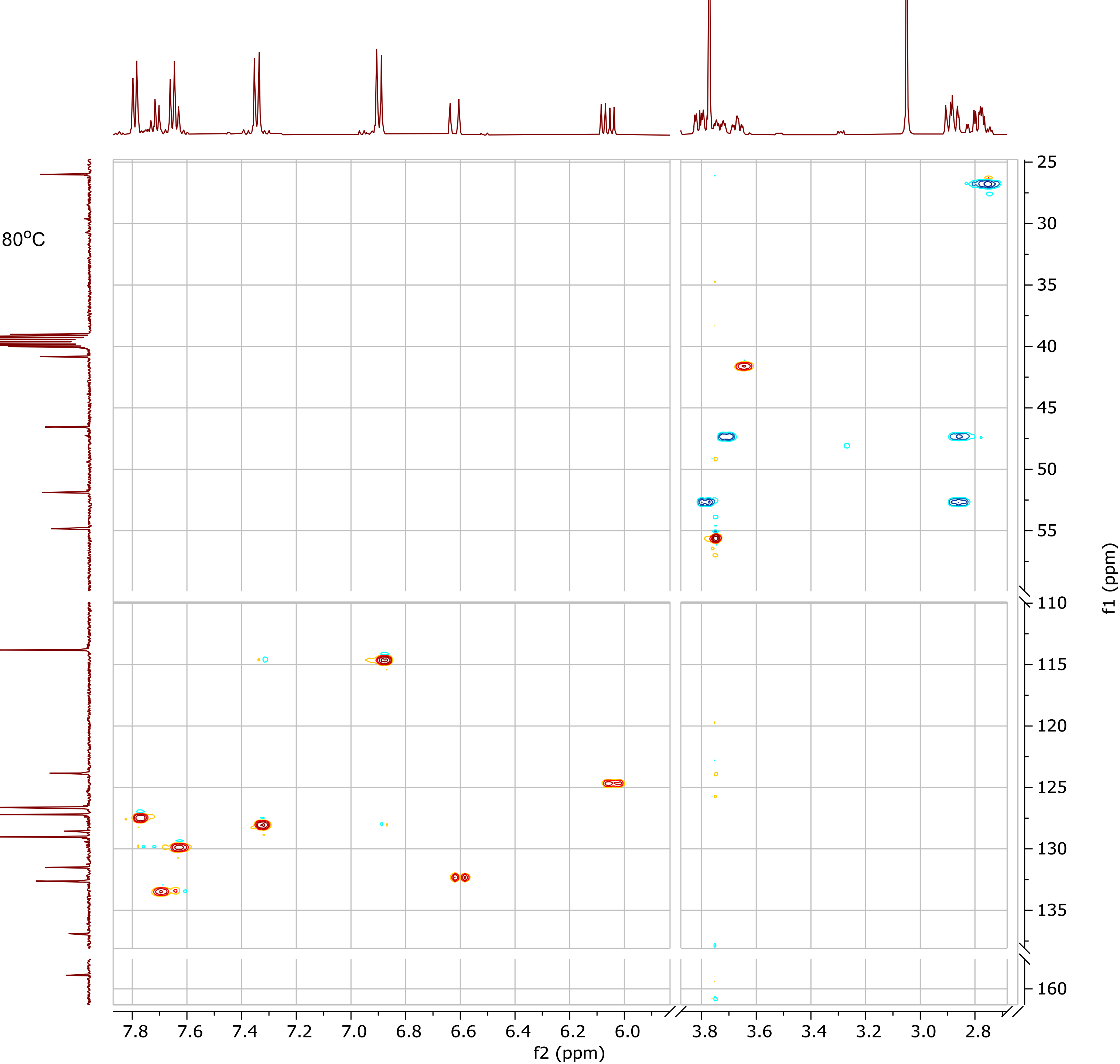
compound **17** in DMSO-d_6 at 80°C

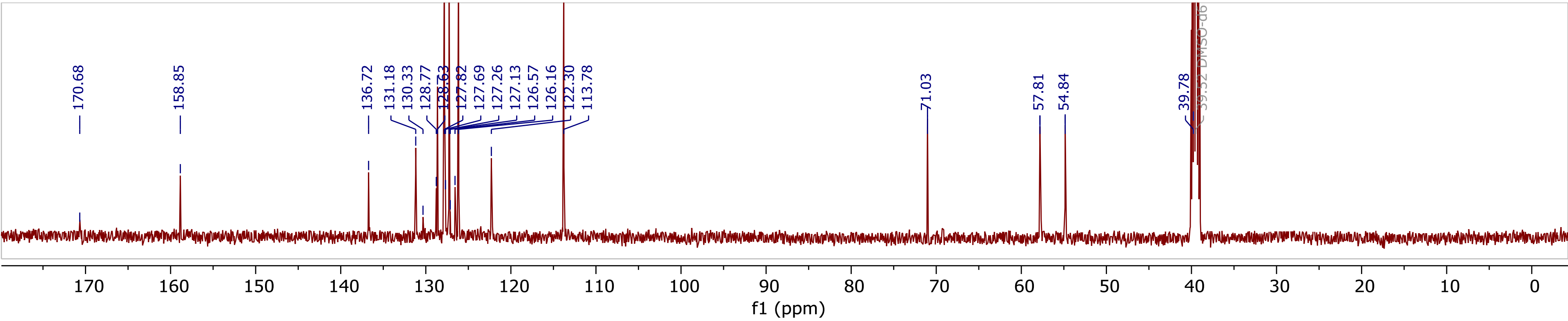
2D NMR (COSY)

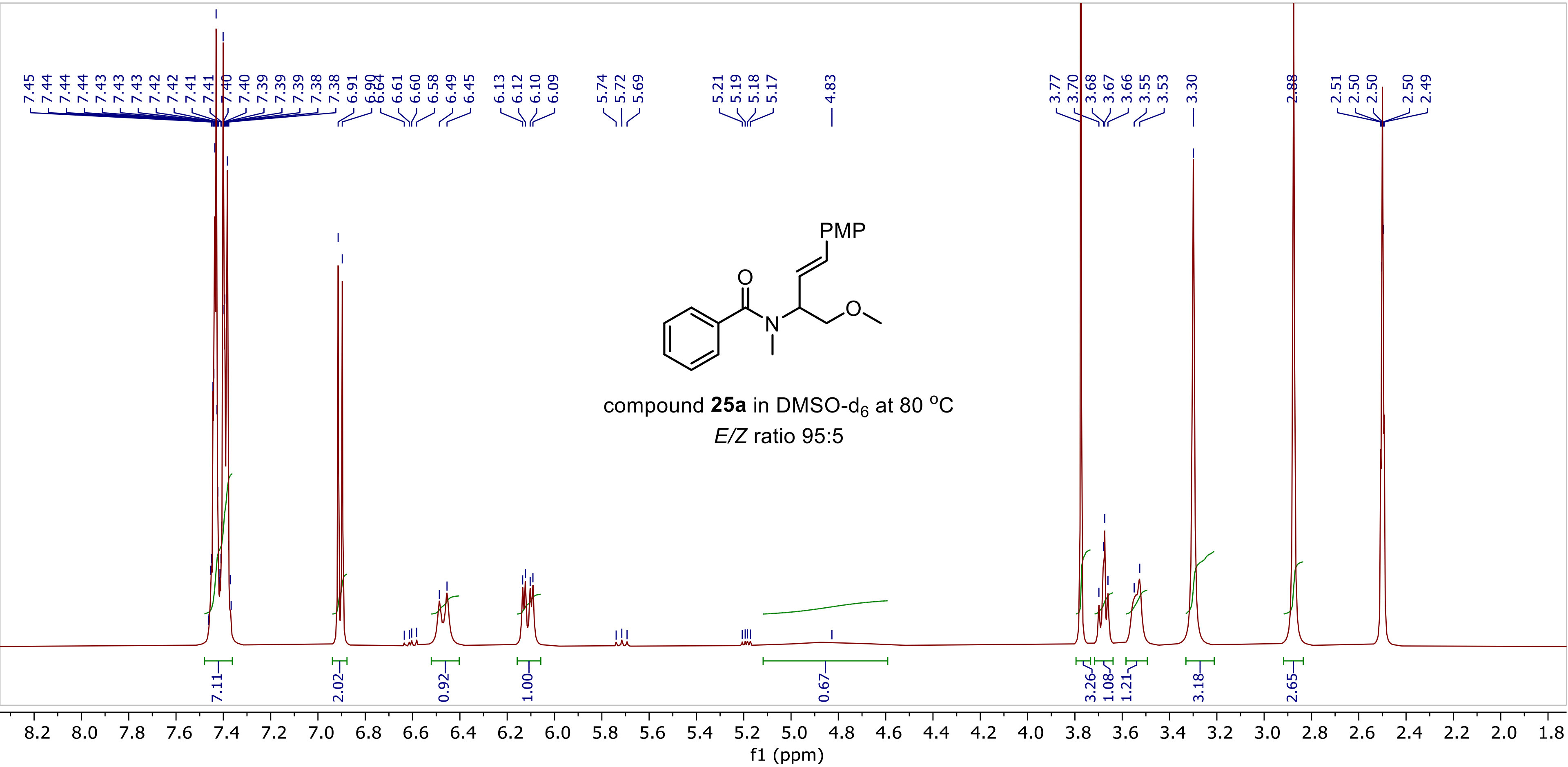


compound **17** in DMSO-d_6 at 80°C

2D NMR (HSQC)

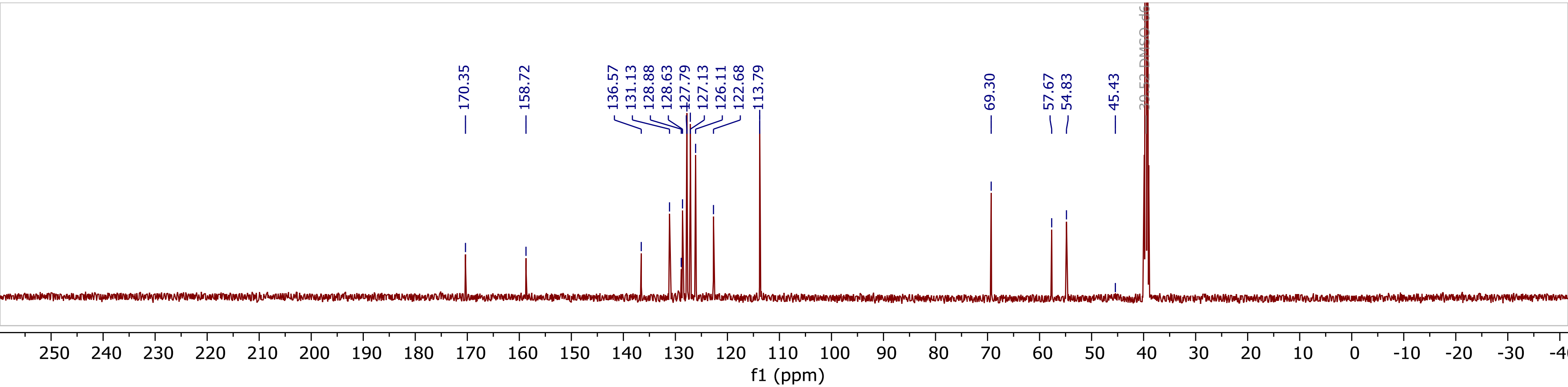


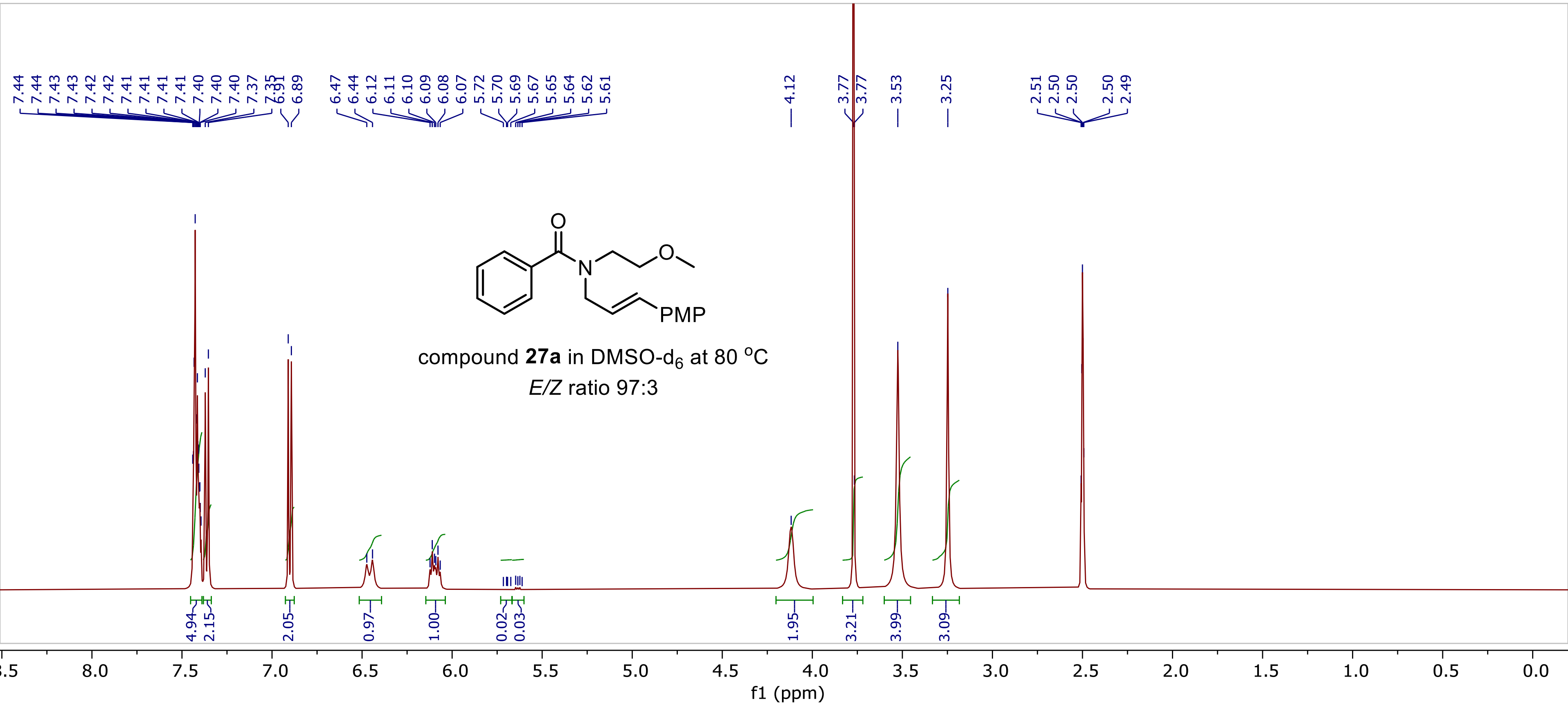




compound **25a** in DMSO-d_6 at 80 ^{o}C

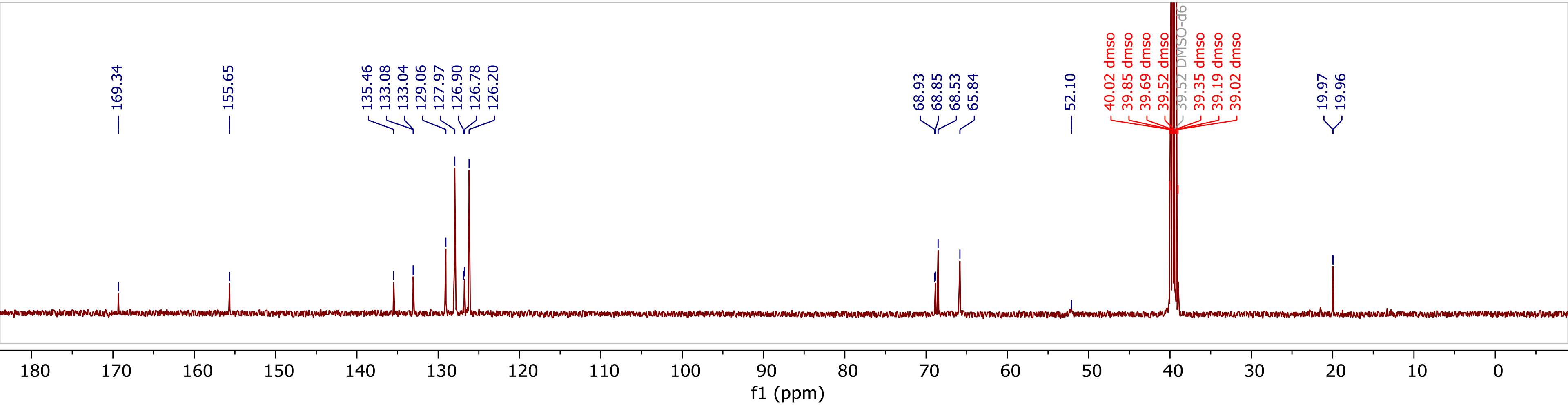
E/Z ratio 95:5

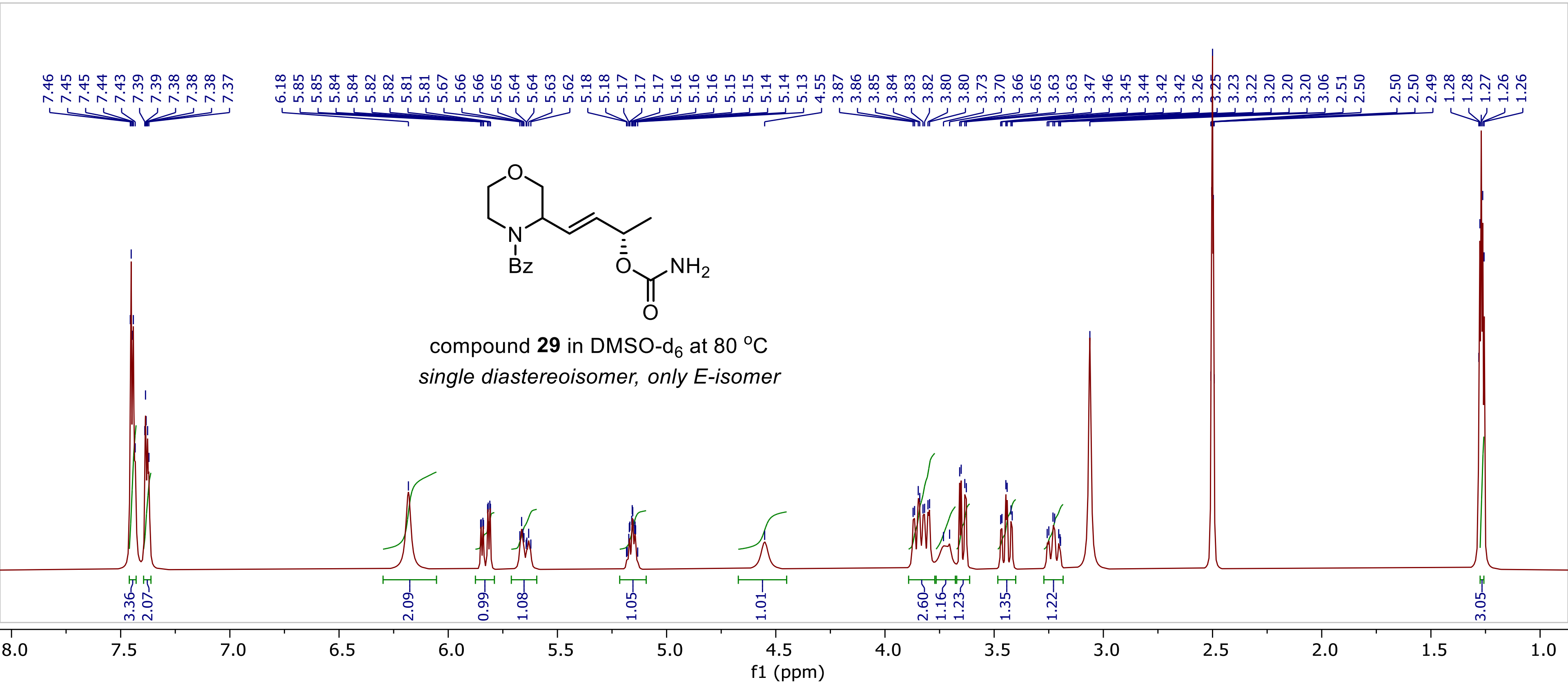




compound **27a** in DMSO-d_6 at 80 °C

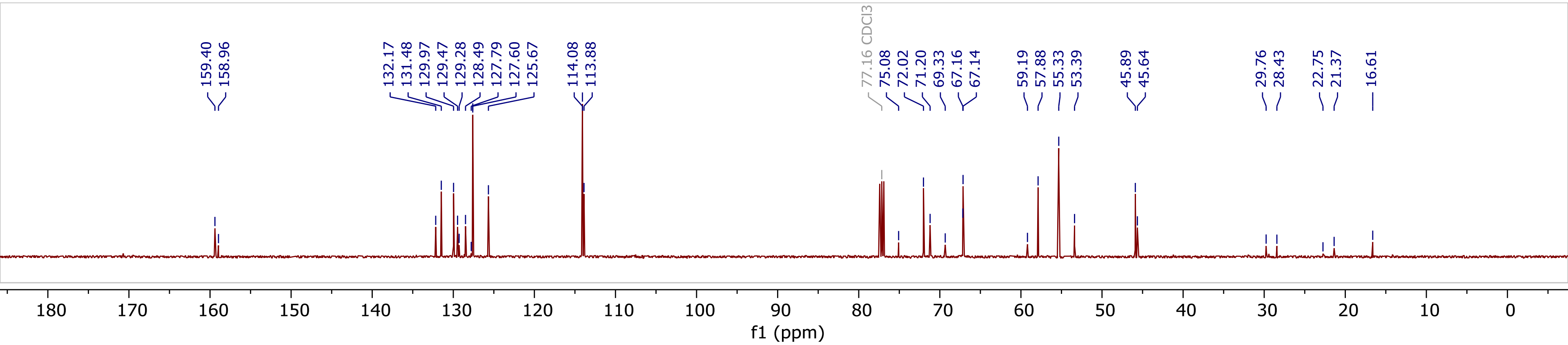
E/Z ratio 97:3

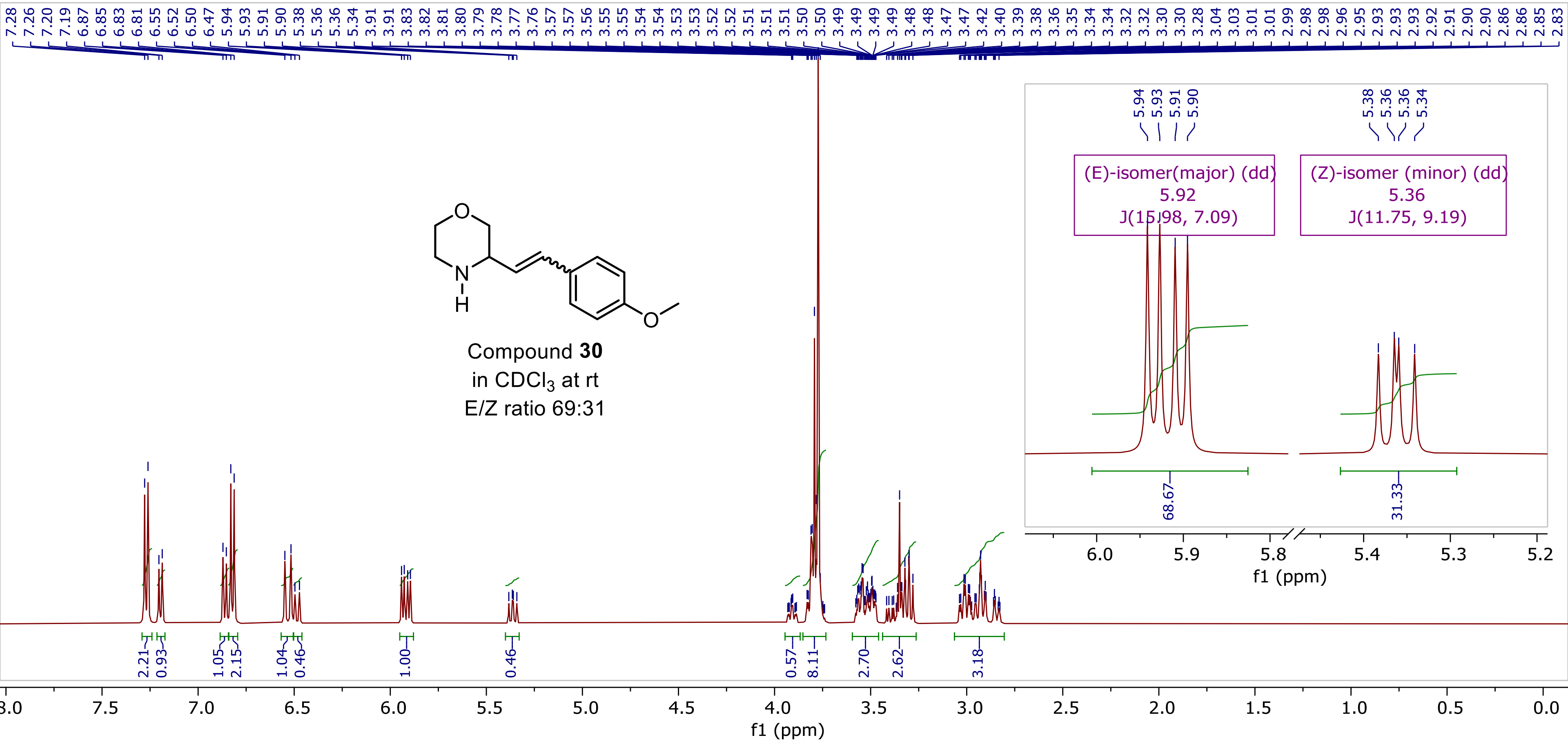




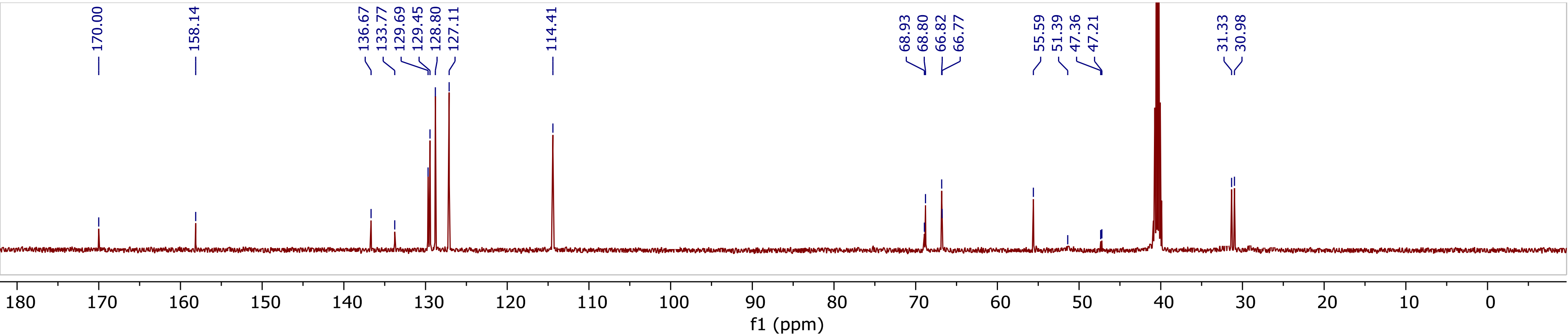
compound **29** in DMSO-d_6 at 80 °C

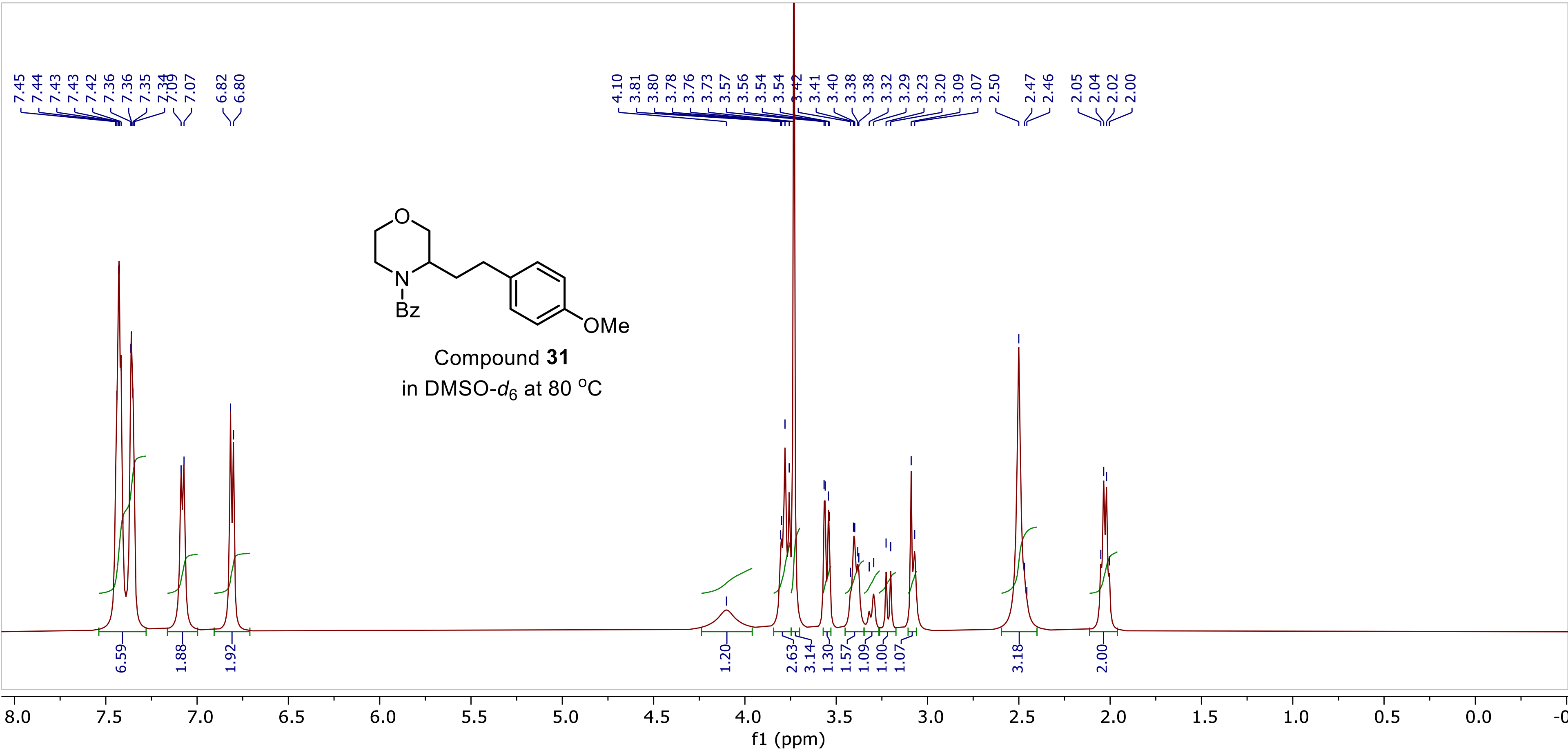
single diastereoisomer, only E-isomer



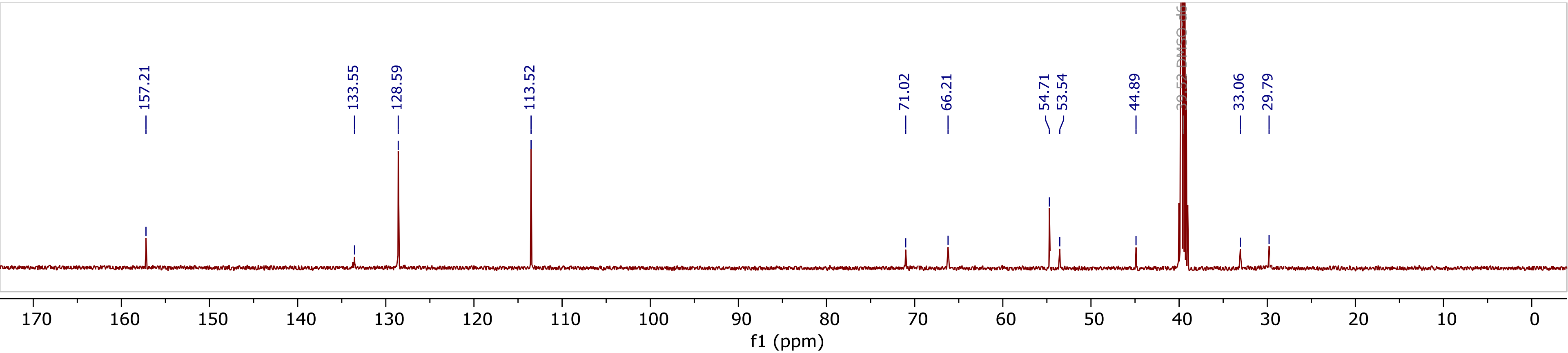


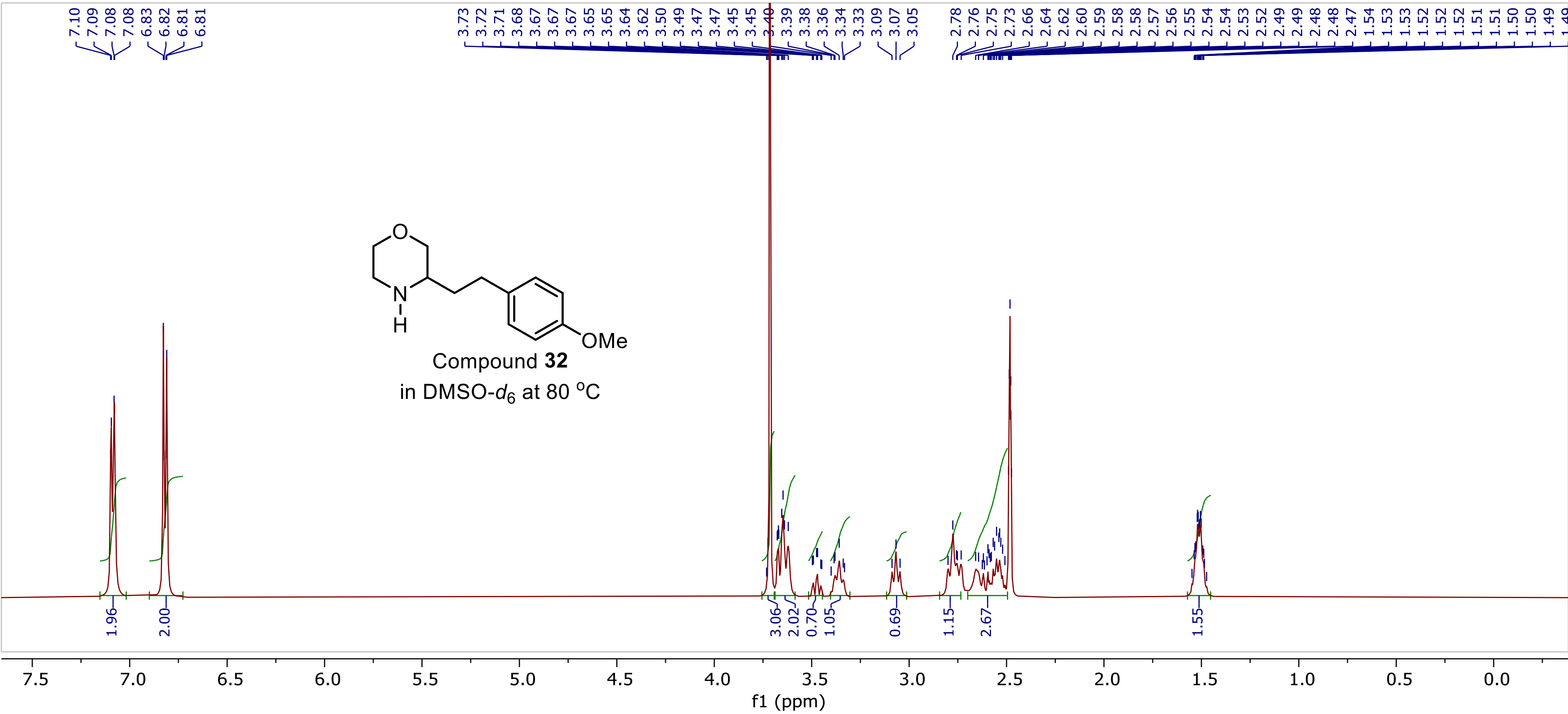
Compound **30**
in $CDCl_3$ at rt
E/Z ratio 69:31



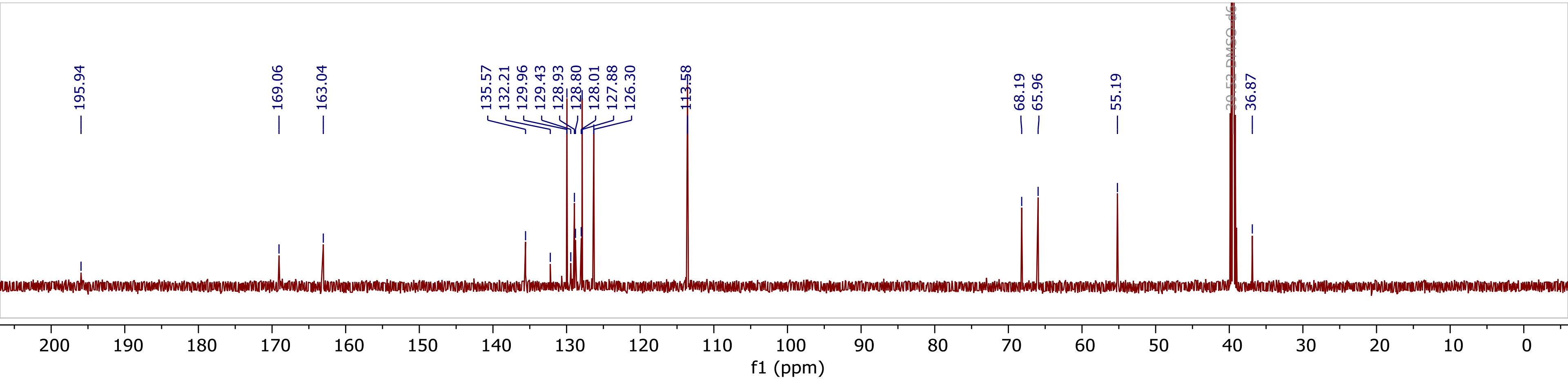


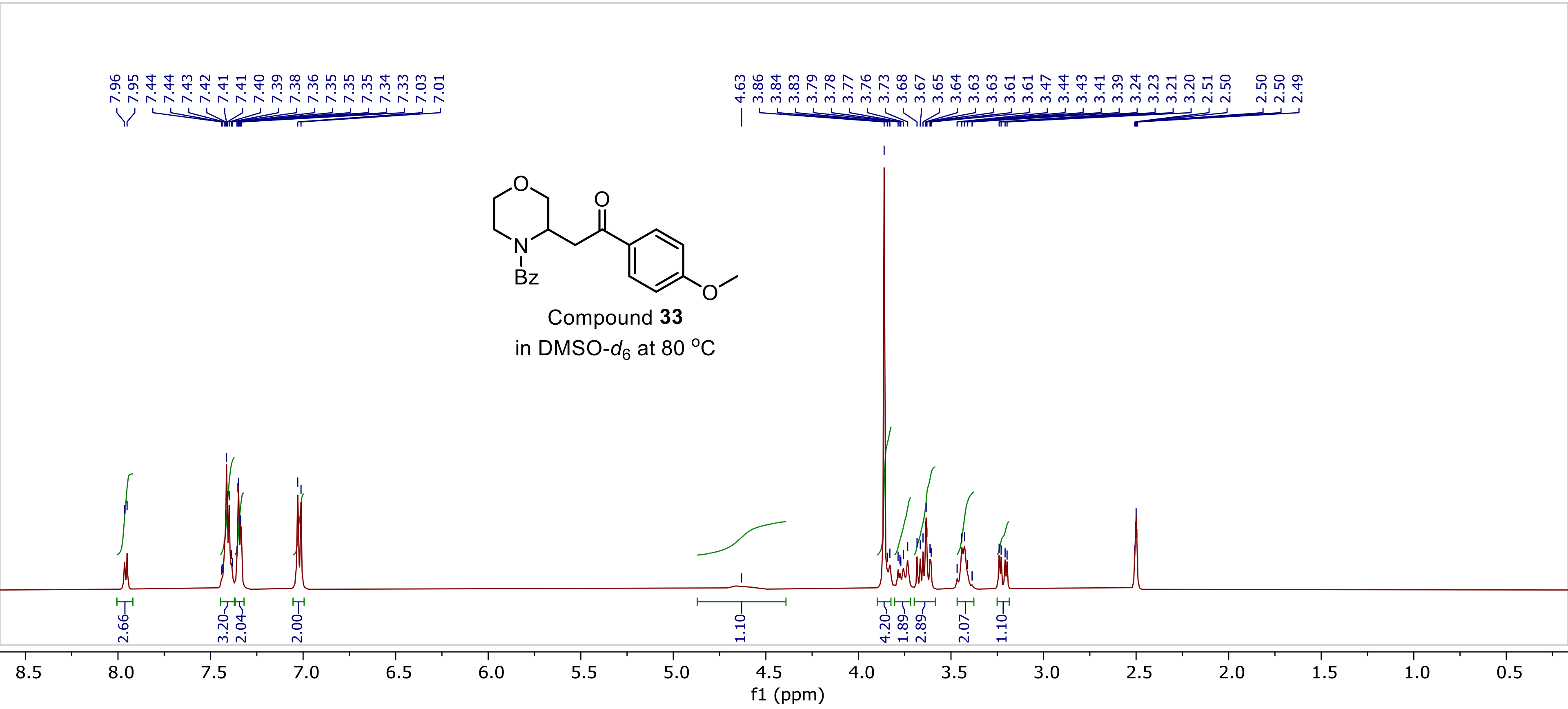
Compound **31**
in DMSO-d_6 at 80 ^{o}C



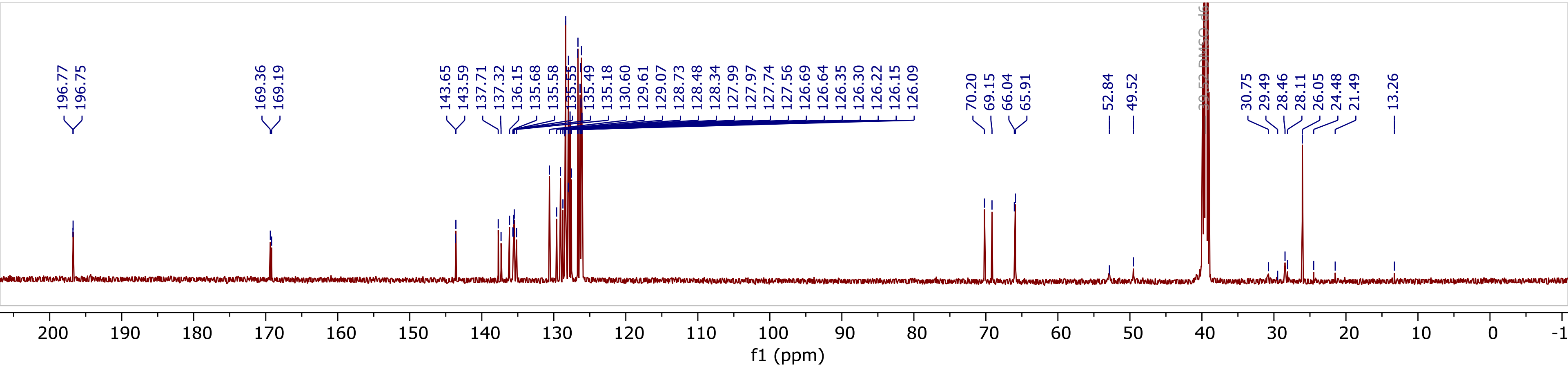


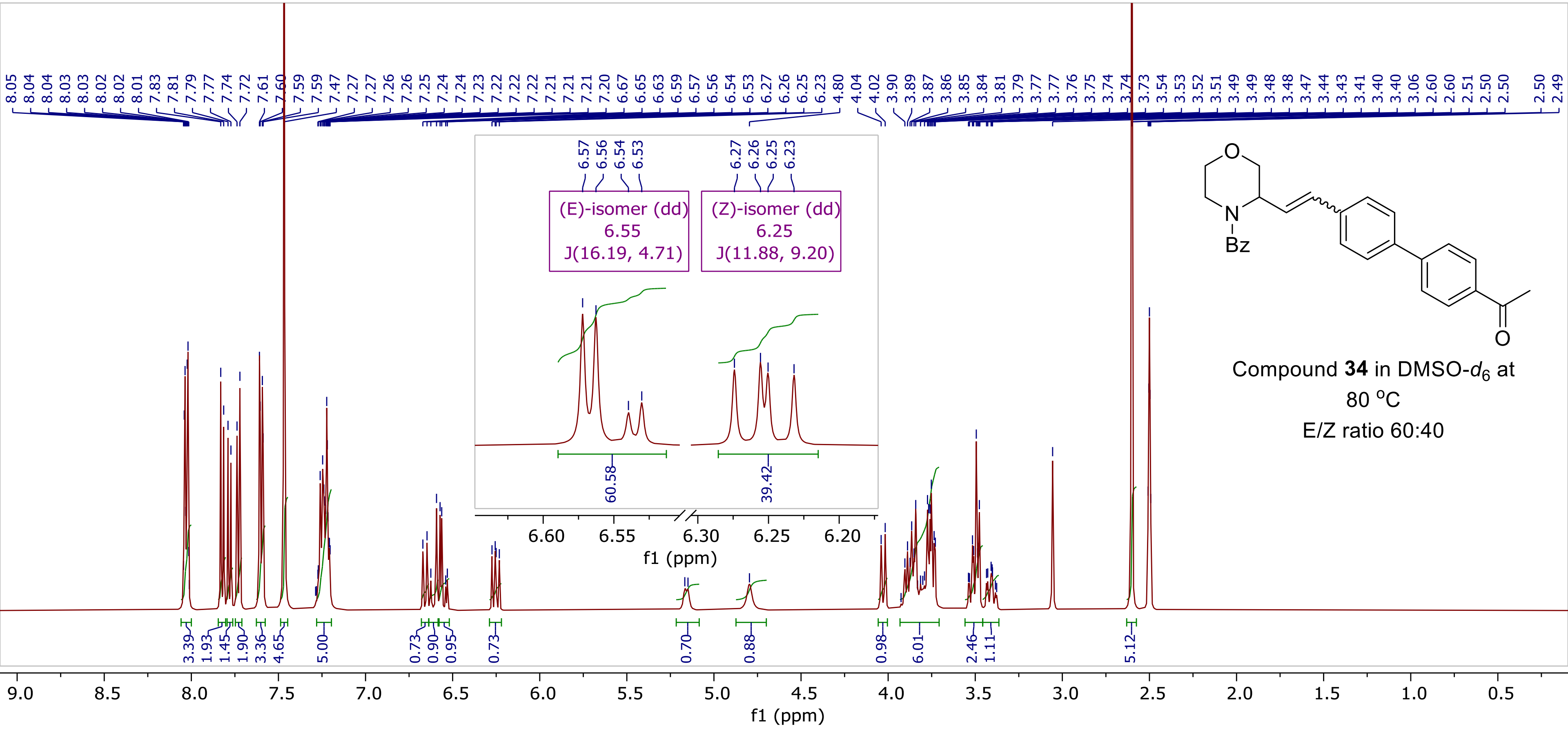
Compound **32**
in DMSO-d_6 at 80 ^{o}C





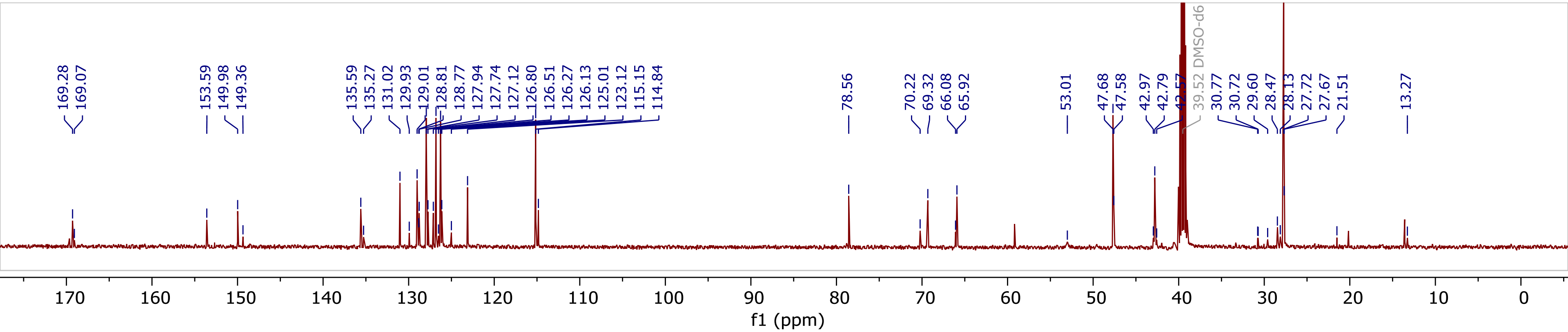
Compound **33**
in DMSO-d_6 at 80 °C

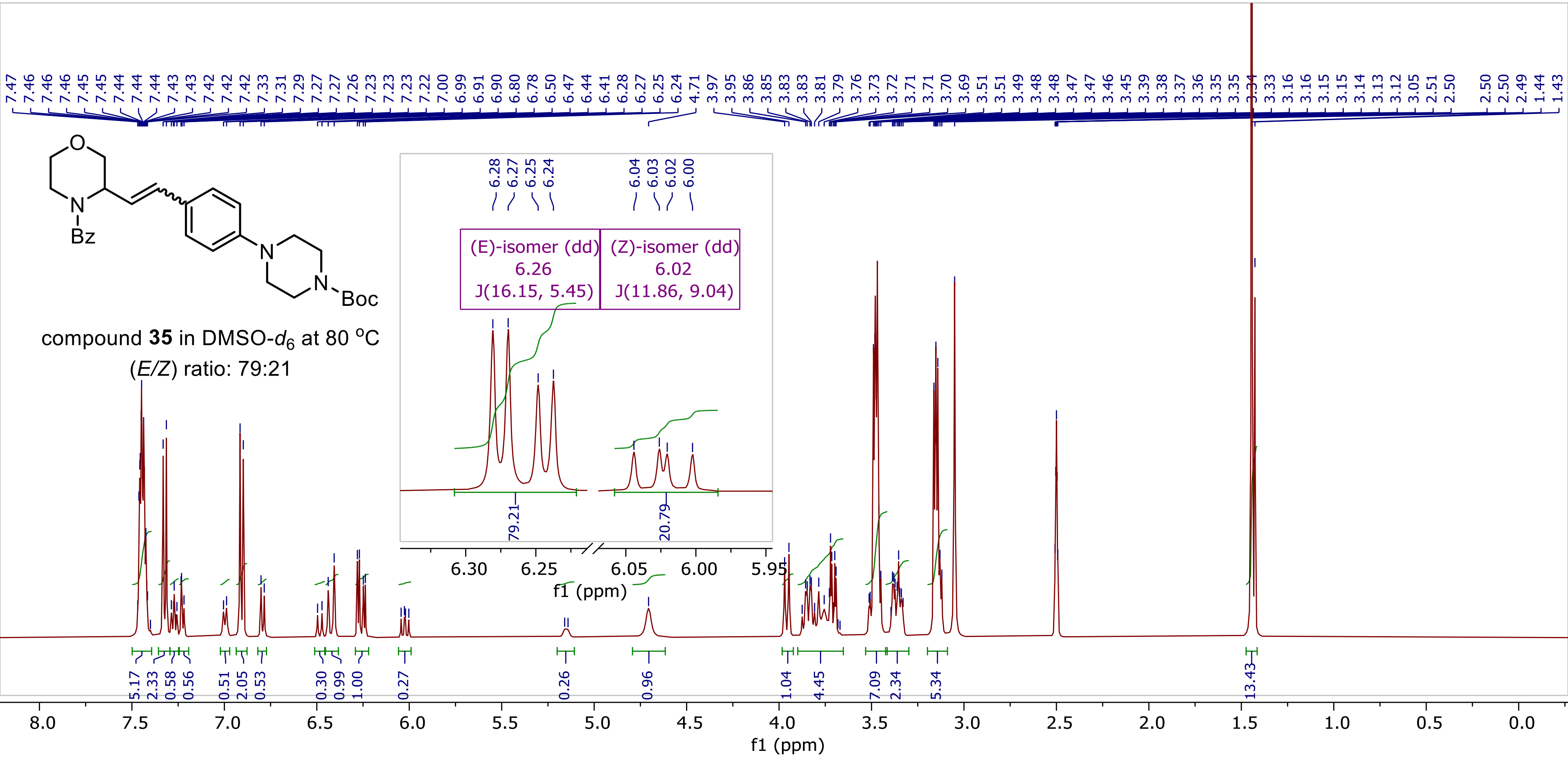




Compound **34** in DMSO-d_6 at 80 ^{o}C

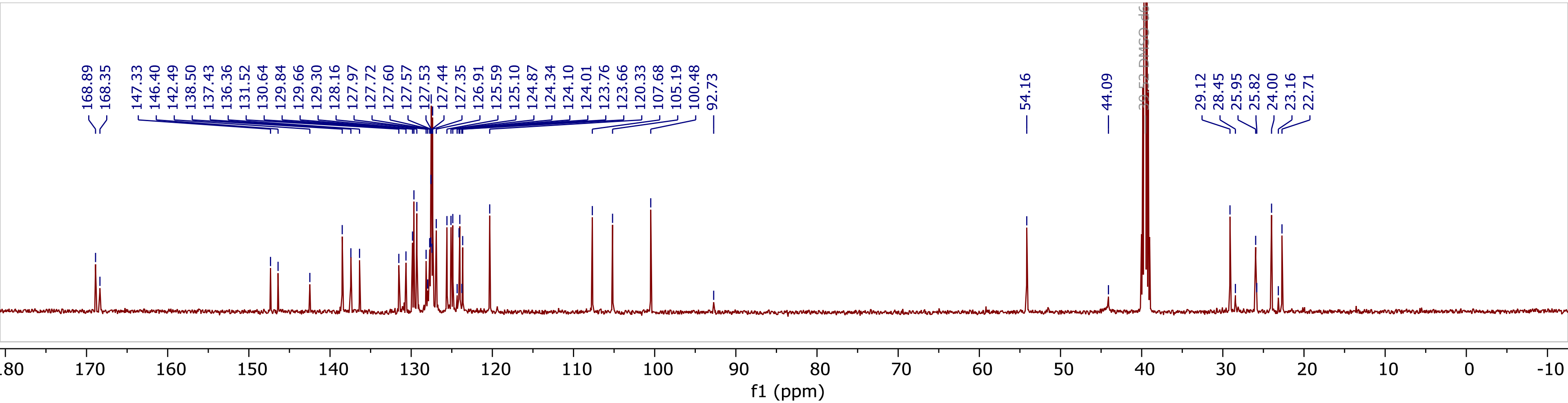
E/Z ratio 60:40

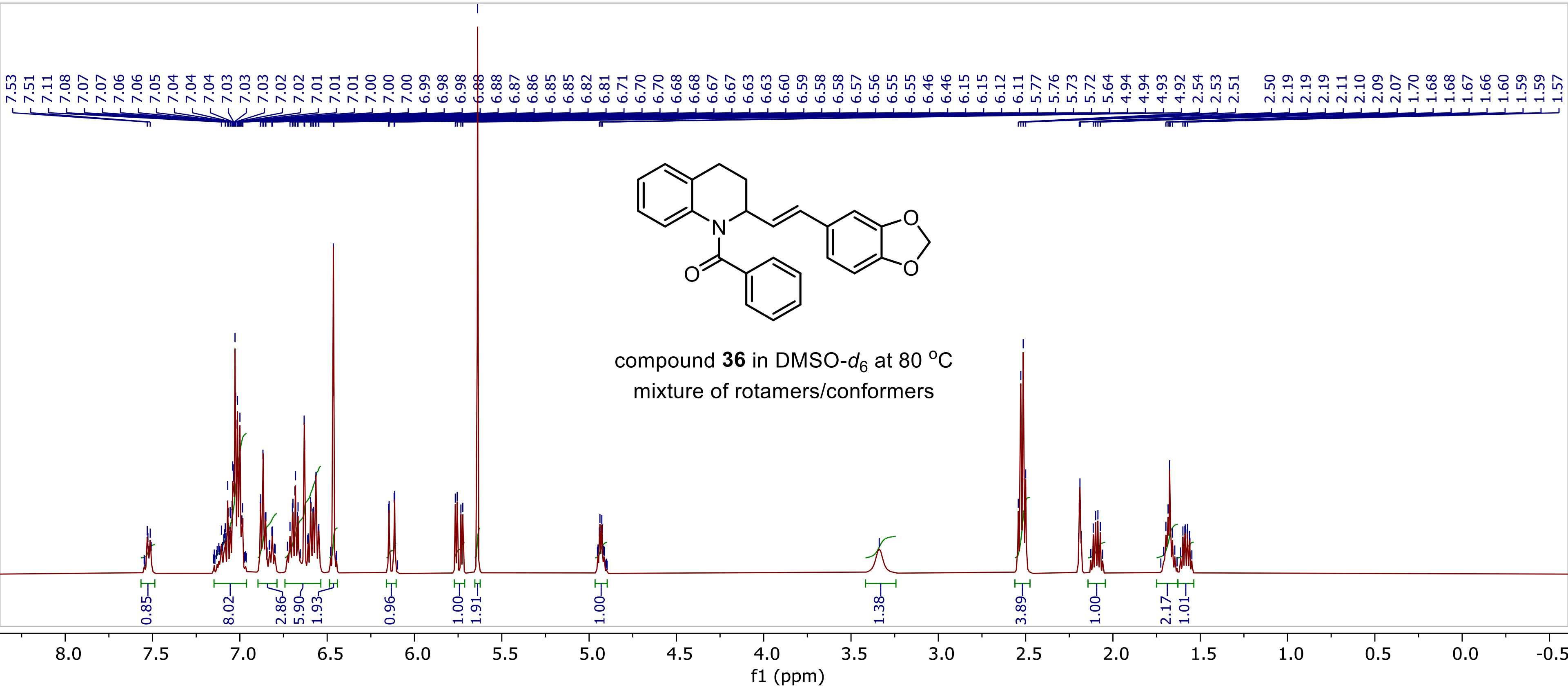




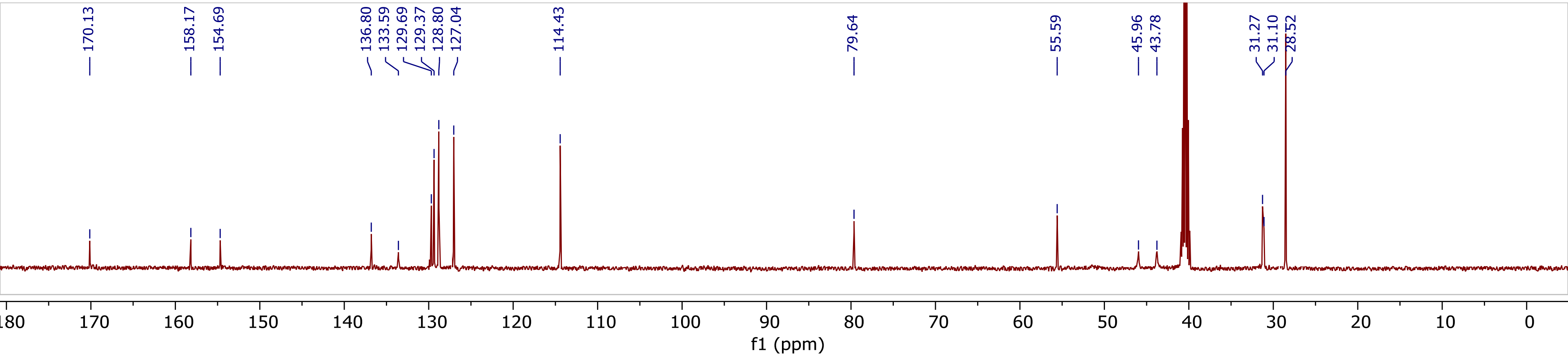
compound **35** in DMSO-d_6 at 80 ^{o}C

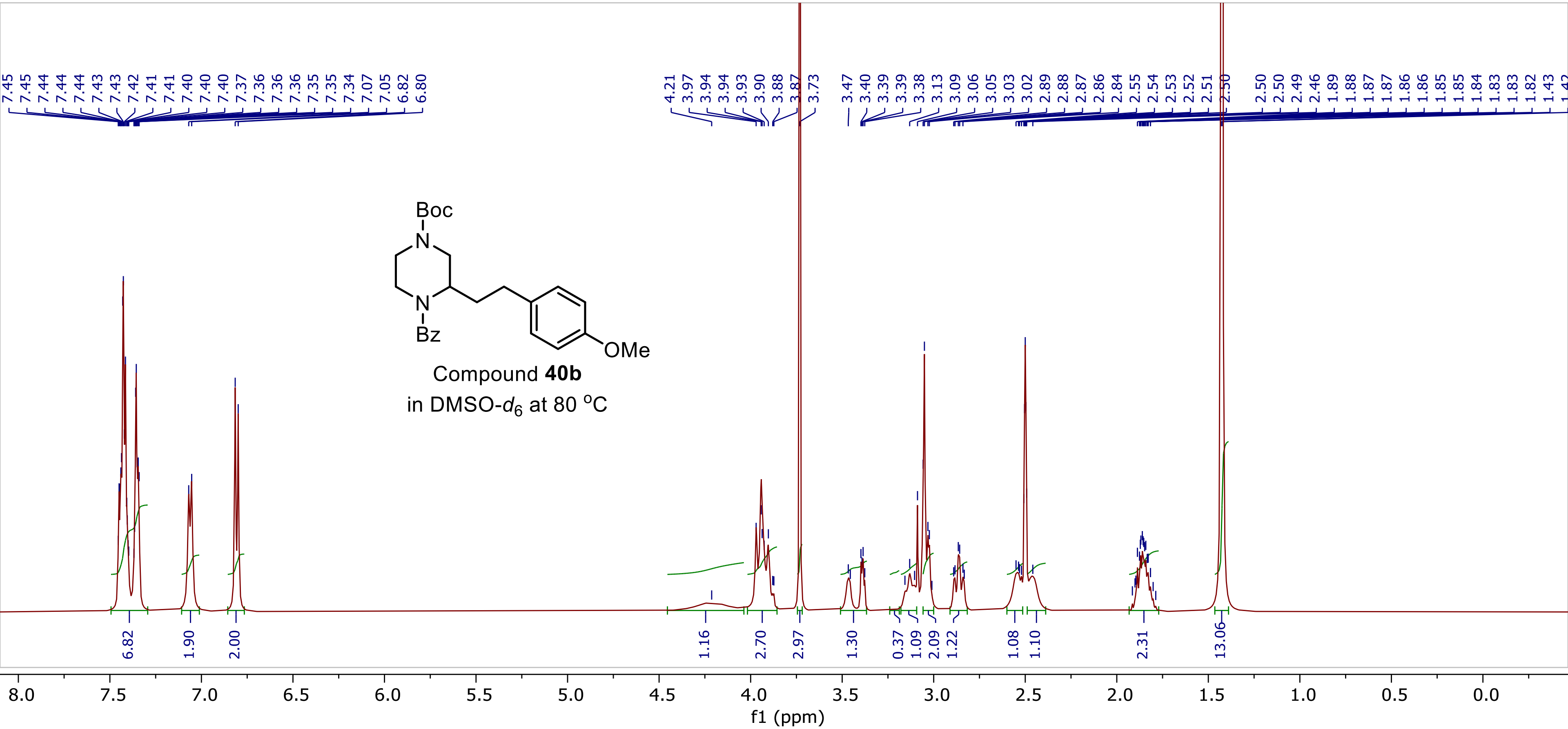
(*E/Z*) ratio: 79:21





compound **36** in DMSO-d_6 at 80 °C
mixture of rotamers/conformers





Compound **40b**
in DMSO-d_6 at 80 ^{o}C