Electronic Supplementary Information for

Enantioselective crossed intramolecular [2+2] photocycloaddition reactions mediated by a chiral chelating Lewis acid

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1. General Information

All reactions sensitive to air or moisture were carried out in flame-dried glassware under argon pressure using standard Schlenk techniques. Dry tetrahydrofuran (THF), diethyl ether (Et_2O) and dichloromethane (CH_2Cl_2) were obtained from an MBraun MB-SPS 800 solvent purification system. Dry 1,2-dichloroethane (DCE) is commercially available (Merck or Acros Organics) and was employed without further purification. Technical solvents (pentane, diethyl ether, dichloromethane, methanol, hexanes, ethyl acetate, cyclohexane) were distilled prior employing them in column chromatography.

Flash column chromatography was performed on silica gel 60 (Merck, 230-400 mesh), on sfär silica D (Biotage®, 6o µm) or on basic alumina (Merck, aluminium oxide 90 active basic, 70-230 mesh) with the indicated eluent mixtures. Thin layer chromatography (TLC) was performed on silica coated glass plates (silica 60 F254) with detection by UV-light (λ = 254 nm) and employing potassium permanganate ($KMnO_4$) or cerium ammonium molybdate (CAM) stain developer solutions followed by heat treatment.

Nuclear Magnetic Resonance (NMR) spectra were recorded at room temperature either on a Bruker AVHD-300, AVHD-400, AVHD-500 or an AV-500 cryo. NMR spectra were calibrated to the respective residual solvent signals of $CDCl_3$ [δ (^{1}H) = 7.26 ppm, δ (^{13}C) = 77.16 ppm], CD_2Cl_2 [δ (^{1}H) = 5.32 ppm, δ (^{13}C) = 53.84 ppm] or DMSO-D_6 [δ (^{1}H) = 2.50 ppm]. Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet; br, broad signal. Apparent multiplets which occur as a result of coupling constant equality between magnetically non-equivalent protons are marked as virtual (*virt.*).

Mass Spectroscopy (MS) and High-Resolution Mass Spectroscopy (HRMS) was performed on a Thermo Scientific LTQ-FT Ultra (ESI) or a Thermo Scientific DFS-HRMS spectrometer (EI).

UV/Vis Spectroscopy was performed on a Perkin Elmer Lambda 35 UV/Vis spectrometer. Spectra were recorded using a Hellma precision cell made of quartz SUPRASIL® with a pathway of 1.0 mm.

Infrared spectra (IR) were recorded on a JASCO IR-4100 or a Perkin Elmer Frontier IR-FTR spectrometer by ATR technique.

Chiral Gas Chromatography (GC) was performed on an Agilent 7890 B gas chromatograph using an Agilent CycloSil-B column (30 m x 0.25 mm x 0.25 µm, SN:

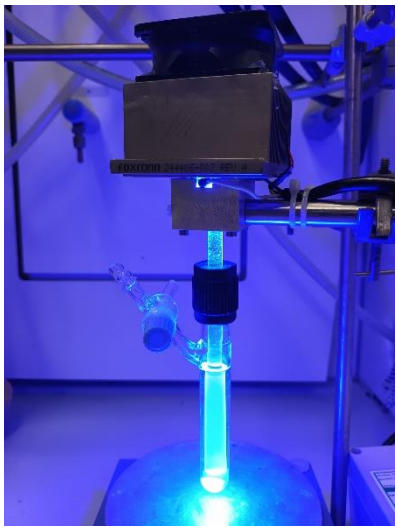
USF620714H) or a Macherey-Nagel Lipodex E column (25 m x 0.25 mm, SN: 23393-92) with a flame ionization detector. The temperature method is given for the corresponding compounds.

High Performance Liquid Chromatography (HPLC) analyses were performed using a chiral stationary phase [*Chiralcel* OJ-RH (150 x 4.6 mm), *Chiralpak* OD-RH (150 x 4.6 mm) or *Chiralpak* AS-H (250 x 4.6 mm), *Daicel Chemical Industries*] with UVD 340 Photodiode Array Detector, P580 Pump and an ASI-100 Automated Sample Injector at 20 ºC, while a mixture of *n*-heptane/isopropanol (normal phase) or water/acetonitrile (reverse phase) was used as mobile phase. The exact conditions for the analyses are specified in each case.

Specific Rotation was determined using a Bellingham+Stanley ADP440+ polarimeter and is reported as follows: $[\alpha]^{T}_{D}$ (c in g per 100 mL of solvent).

Melting points were determined using a Kofler ("Thermopan", Fs Reichert, Wien) apparatus.

2. Setup for the Photochemical Reactions



Photochemical experiments using a LED (λ = 437 nm) operated at a constant current (700 mA) were carried out in a Schlenk tube (diameter = 1.0 cm) with a polished quartz rod as an optical fibre, which was roughened by sandblasting at one end. The roughed end has to be completely submerged in the solvent during the reaction, in order to guarantee optimal and reproducible irradiation conditions.[1]

Figure S1: Photoreactor setup.

3. Emission and Characteristics of the 437, 424, 382 and 368 nm LEDs

The characteristics of the specific LED employed for the photochemical reactions can be found in the following datasheet:

Datasheet LED036 Av-440-10W

Basic Information

Type	High-Power-LED
Description	Avonec 440-450 nm / 10 W
Manufacturer / Supplier	n/a / Avonec
Order number / Date of purch.	n/a / 01/2016
Internal lot / serial number	2016-01 / LED036

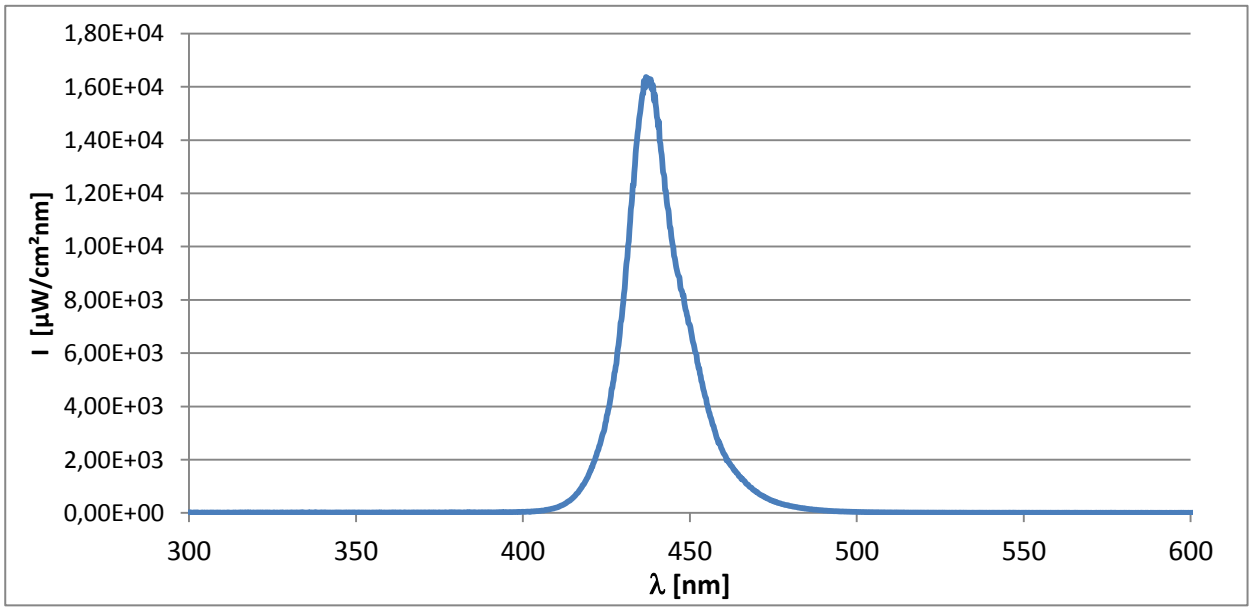
Specification Manufacturer

Type / size	10 emitter / ca. 1 x 1 mm
Mechanical specification	module, dye-area ca. 7.5 x 4 mm
Electrical specification	700 mA, UF 16 V
Wavelength (range, typ.)	440-450 nm, typ. n/a
Spectral width (FWHM)	n/a
Datasheet	n/a

Characterization

Description of measurement	Measured with Ocean-optics USB4000 spectrometer using a calibrated setup (cosine corrector/fibre). The distance between the emitting surface and the surface of the cosine corrector was 20 mm. The LED was operated at 700 mA on a passive heat-sink at approx. 20 °C
Measured wavelength	437 nm
Measured spectral width	18 nm
Integral Reference intensity	353000 µW/cm² (380-530 nm @ 20 mm distance, 4 mm cosine corr.)

Spectrum



Datasheet LED068 LUXEON Z 420nm

Basic Information

Type	High-Power-LED
Description	Luxeon Z 420 nm on a Saber Z5 Base-Plate
Manufacturer / Supplier	Philips Lumileds / Luxeonstar
Order number / Date of purch.	n/a / 03/2018
Internal lot / serial number	2018-03 / LED065

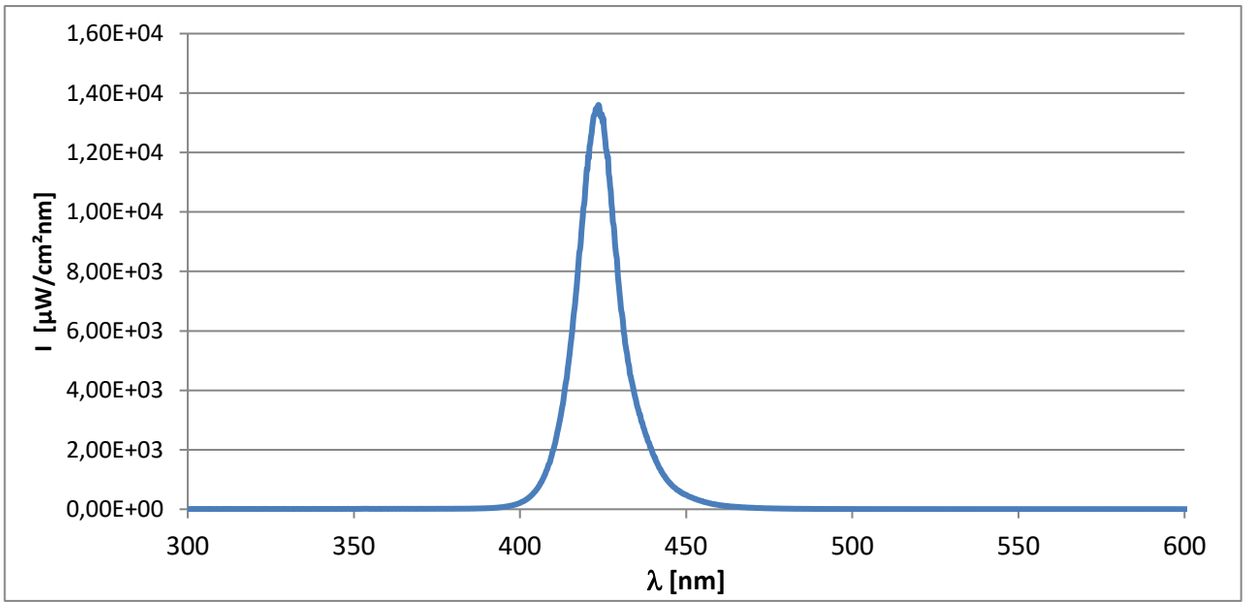
Specification Manufacturer

Type / size	4 emitters / ca. 1 x 1 mm
Mechanical specification	
Electrical specification	700 mA, UF 12.2 V
Wavelength (range, typ.)	420-425 nm, typ. n/a
Spectral width (FWHM)	n/a
Datasheet	LuxeonZUV.pdf

Characterization

Description of measurement	Measured with Ocean-optics USB4000 spectrometer using a calibrated setup (cosine corrector/fibre). The distance between the emitting surface and the surface of the cosine corrector was 20 mm. The LED was operated at 700 mA on a passive heat-sink at approx. 20 °C	
Measured dominant wavelength / Int.	424 nm	13558 µW/mm²nm
Measured spectral width (FWHM)	14 nm	
Integral Reference intensity / range	236390 µW/cm²	350-500 nm

Spectrum



Datasheet LED033 Av-380-3W

Basic Information

Type	High-Power-LED
Description	Avonec 370-380 nm / 3 W
Manufacturer / Supplier	n/a / Avonec
Order number / Date of purch.	n/a / 07/2016
Internal lot / serial number	2016-07 / LED033

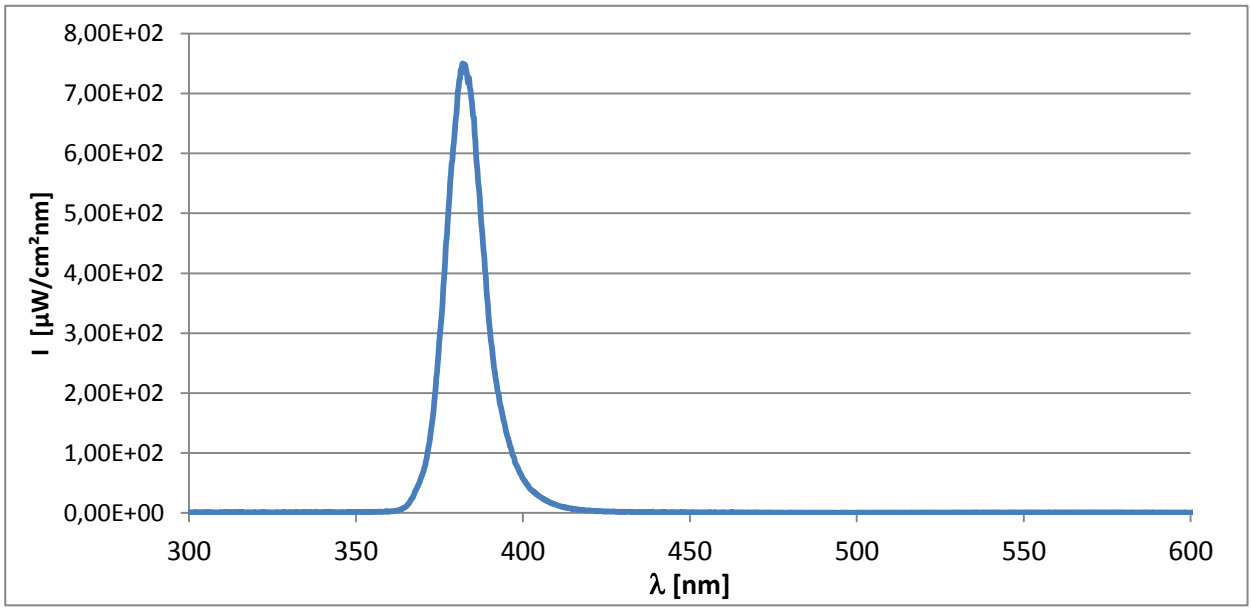
Specification Manufacturer

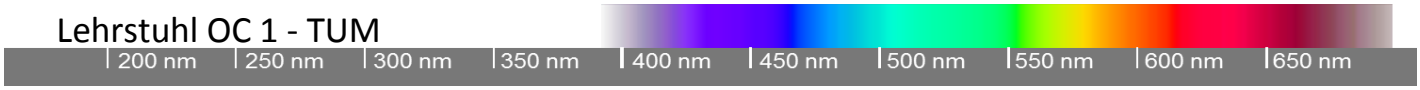
Type / size	single emitter / ca. 1 x 1 mm
Mechanical specification	
Electrical specification	700 mA, UF 3.8 V
Wavelength (range, typ.)	380-390 nm, typ. n/a
Spectral width (FWHM)	n/a
Datasheet	n/a

Characterization

Description of measurement	Measured with Ocean-optics USB4000 spectrometer using a calibrated setup (cosine corrector/fibre). The distance between the emitting surface and the surface of the cosine corrector was 20 mm. The LED was operated at 700 mA on a passive heat-sink at approx. 20 °C
Measured wavelength	382 nm
Measured spectral width	13 nm
Integral Reference intensity	11360 µW/cm² (350-425 nm @ 20 mm distance, 4 mmcosine corr.)

Spectrum





Datasheet LED040

366 / 10W

Basic Information

Ultra-High-Power UV-A-LED

Type	High-Power-LED
Description	
Manufacturer / Supplier	Mouser
Order number / Date of purch.	LZ4-44UV00-0000 / 06/2016
Internal lot / serial number	2016-01 / LED040

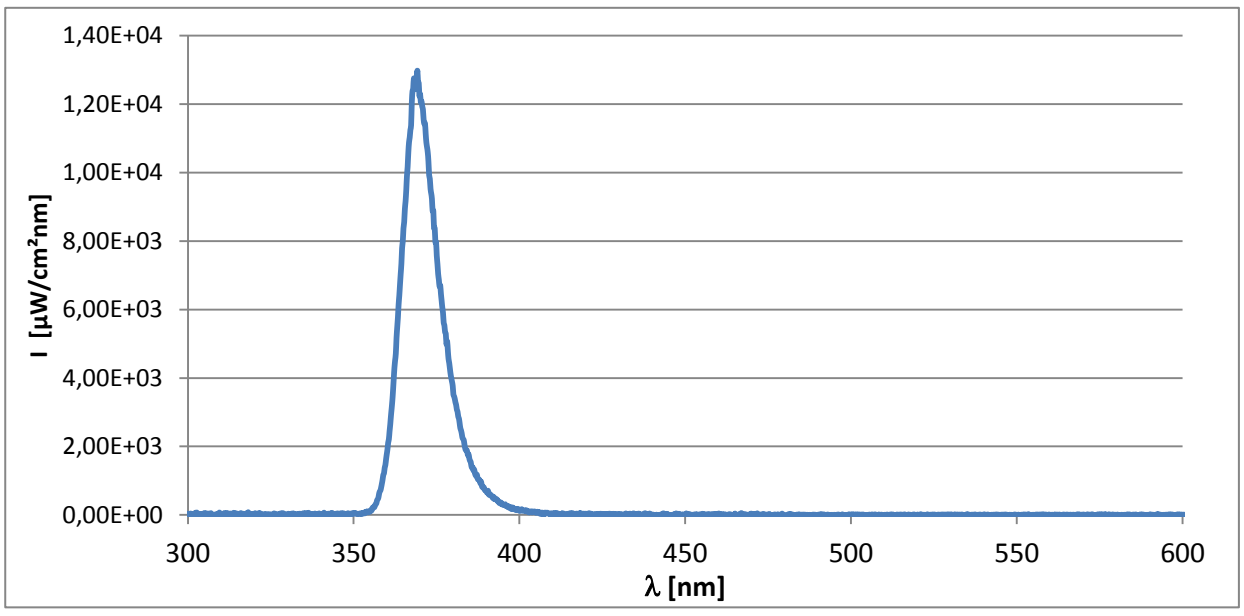
Specification Manufacturer

Type / size	quattro emitter / not spec.
Mechanical specification	
Electrical specification	700 mA @18V
Wavelength (range, typ.)	
Spectral width (FWHM)	
Datasheet	LZ4-04UV-series

Characterization

Description of measurement	Measured with Ocean-optics USB4000 spectrometer using a calibrated setup (cosine corrector/fibre). The distance between the emitting surface and the surface of the cosine corrector was 20 mm. The LED was operated at 500 mA on a passive heat-sink at approx. 20 °C
Measured wavelength	368 nm
Measured spectral width	12 nm
Integral Reference intensity	18605 µW/cm² (350-425 nm @ 20 mm distance, 4 mmcosine corr.)

Spectrum

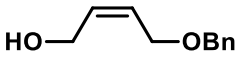


4. Experimental Procedures and Characterisation

Enones **4a**, **4b**, **4c**, **4g** and **4m** were obtained following our previously reported procedures.[2] The enantiopure Λ-catalyst **6** employed in the photoreactions was obtained following the procedure reported by Meggers and coworkers.[3] In all the cases the analytical data of the synthetized compounds and catalyst were in accordance with the data reported in the literature.[2,3]

5. Characterisation Data for the Enones (4d-f and 4h-l) and their Precursors

(*Z*)-4-(Benzyloxy)but-2-en-1-ol (S1)



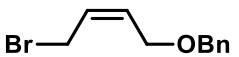
A stirred suspension of NaH (880 mg, 22.0 mmol, 60% mineral oil) in dry THF (60 mL) was cooled to 0 ºC. Then, *cis*-2-buten-1,4-diol (5.29 g, 60.0 mmol) was dropwise added and the resulting mixture stirred for 30 min at 0 ºC, followed by the addition of benzyl bromide (3.42 g, 20.0 mmol). The reaction mixture was let warm to rt and stirred for further 14 hours. Then, a saturated solution of NH_4Cl was added and extracted with EtOAc. The organic phase was washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (from 20 to 33% EtOAc in hexanes) to obtain 3.27 g of product **S1** as a yellowish oil (92% yield).

R_f = 0.29 (33% EtOAc in hexanes).

The NMR data were in accordance with the data reported in the literature.[4]

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.32 (m, 4H), 7.32 – 7.28 (m, 1H), 5.86 – 5.80 (m, 1H), 5.78 – 5.71 (m, 1H), 4.53 (s, 2H), 4.20 – 4.16 (m, 2H), 4.12 – 4.08 (m, 2H), 1.68 (br s, 1H).

(*Z*)-{[(4-Bromobut-2-en-1-yl)oxy]methyl}benzene (S2)



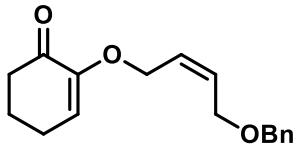
PBr_3 (0.63 mL, 6.6 mmol) was dropwise added to a stirred solution of **S1** (2.95 g, 16.5 mmol) in dry Et_2O (33 mL) at 0 ºC. The reaction mixture was let warm to rt and stirred for 12 hours, before being quenched by the addition of a saturated solution of $NaHCO_3$. After extraction with Et_2O, the organic phase was washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (2% EtOAc in hexanes) to obtain 3.78 g of product **S2** as a yellowish oil (95% yield).

$\mathbf{R_f}$ = 0.12 (2% EtOAc in hexanes).

The NMR data were in accordance with the data reported in the literature.[4]

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 – 7.27 (m, 5H), 5.96 – 5.85 (m, 1H), 5.81 – 5.71 (m, 1H), 4.54 (s, 2H), 4.16 (dd, *J* = 6.3, 1.5 Hz, 2H), 3.99 (d, *J* = 8.1 Hz, 2H).

(*Z*)-2-{[4-(Benzyloxy)but-2-en-1-yl]oxy}cyclohex-2-en-1-one (4d)



S2 (1.45 g, 6.00 mmol) was dropwise added to a stirred suspension of 1,2-cyclohexanedione (561 mg, 5.00 mmol) and anhydrous K_2CO_3 (830 mg, 6.00 mmol) in dry DMF (20 mL). The reaction mixture was stirred at rt until full conversion was achieved, as judged by TLC analysis (36 hours). Then the mixture was diluted with Et_2O and brine was added. After separation of the organic phase, the latter was washed three times with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (20% EtOAc in hexanes) to obtain 300 mg of product **4d** as a pale-yellow oil (22% yield).

$\mathbf{R_f}$ = 0.16 (20% EtOAc in hexanes).

IR: ṽ [cm^{-1}] = 2928, 1726, 1454, 1275, 1099, 1073, 749, 700.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.26 (m, 5H), 5.84 (t, *J* = 4.6 Hz, 1H), 5.83 – 5.77 (m, 2H), 4.52 (s, 2H), 4.40 – 4.34 (m, 2H), 4.13 – 4.07 (m, 2H), 2.53 – 2.48 (m, 2H), 2.40 (td, *J* = 6.0, 4.6 Hz, 2H), 1.99 – 1.93 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 194.5, 150.3, 138.1, 129.6, 128.6 (2C), 128.3, 128.0 (2C), 127.9, 118.5, 72.5, 66.0, 63.9, 39.0, 24.6, 23.0.

HRMS (ESI): calculated for $C_{17}H_{20}NaO_3^+$, $[M+Na]^+$ = 295.1305; found = 295.1304.

(*Z*)-4-methoxybut-2-en-1-ol (S3)

A stirred suspension of NaH (1.00 g, 25.0 mmol, 60% mineral oil) in dry THF (20 mL) was cooled to 0 ºC. Then, *cis*-2-buten-1,4-diol (6.61 g, 75.0 mmol) was dropwise added and the resulting mixture stirred for 30 min at 0 ºC, followed by the addition of 1.56 mL of methyl iodide (25.0 mmol). The reaction mixture was let warm to rt and stirred for further 16 hours. Then, a saturated solution of NH_4Cl was added and extracted with EtOAc. The organic phase was washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (from 50% to 66% of EtOAc in *n*-pentane) to obtain 1.12 g of product **S3** as a colourless oil (44% yield).

R_f = 0.29 (50% EtOAc in *n*-pentane).

The NMR data were in accordance with the data reported in the literature.[5]

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.87 – 5.75 (m, 1H), 5.74 – 5.62 (m, 1H), 4.20 (d, *J* = 6.0 Hz, 2H), 3.99 (d, *J* = 6.0 Hz, 2H), 3.34 (s, 3H).

(*Z*)-1-Bromo-4-methoxybut-2-ene (S4)

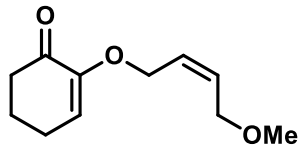
PBr_3 (0.42 mL, 4.4 mmol) was dropwise added to a stirred solution of **S3** (1.12 g, 11.0 mmol) in dry Et_2O (22 mL) at 0 ºC. The reaction mixture was let warm to rt and stirred for 16 hours, before being quenched by the addition of a saturated solution of $NaHCO_3$. After extraction with Et_2O, the organic phase was washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (3% Et_2O in *n*-pentane) to obtain 1.11 g of product **S4** as a colourless oil (61% yield).

R_f = 0.28 (3% EtOAc in hexanes).

The NMR data were in accordance with the data reported in the literature.[5]

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.96 – 5.83 (m, 1H), 5.76 – 5.65 (m, 1H), 4.06 (dd, *J* = 6.3, 1.6 Hz, 2H), 4.01 (dd, *J* = 8.3, 0.7 Hz, 2H), 3.36 (s, 3H).

(*Z*)-2-[(4-methoxybut-2-en-1-yl)oxy]cyclohex-2-en-1-one (4e)



S4 (990 mg, 6.00 mmol) was dropwise added to a stirred suspension of 1,2-cyclohexanedione (561 mg, 5.00 mmol) and anhydrous K_2CO_3 (830 mg, 6.00 mmol) in dry DMF (20 mL). The reaction mixture was stirred at rt until full conversion was achieved, as judged by TLC analysis (40 hours). Then the mixture was diluted with Et_2O and brine was added. After separation of the organic phase, the latter was washed three times with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (20% EtOAc in hexanes) to obtain 231 mg of product **4e** as a colourless oil (24% yield).

R_f = 0.24 (33% EtOAc in hexanes).

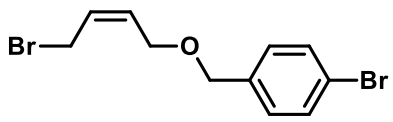
IR: $\tilde{\nu}$ [cm^{-1}] = 2929, 1733, 1267, 1101, 737, 702.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.90 (t, *J* = 4.6 Hz, 1H), 5.83 – 5.69 (m, 2H), 4.40 (dd, *J* = 5.5, 1.4 Hz, 2H), 4.01 (dd, *J* = 5.8, 1.1 Hz, 2H), 3.34 (s, 3H), 2.53 – 2.49 (m, 2H), 2.42 (td, *J* = 6.0, 4.6 Hz, 2H), 2.01 – 1.94 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 194.3, 150.3, 129.6, 127.9, 118.6, 68.4, 63.8, 58.2, 38.9, 24.5, 22.9.

HRMS (ESI): calculated for $C_{11}H_{16}NaO_3^+$, $[M+Na]^+$ = 219.0992; found = 219.0993.

(*Z*)-1-Bromo-4-{[(4-bromobut-2-en-1-yl)oxy]methyl}benzene (S5)



A stirred suspension of NaH (880 mg, 22.0 mmol, 60% mineral oil) in dry THF (60 mL) was cooled to 0 ºC. Then, *cis*-2-buten-1,4-diol (5.29 g, 60.0 mmol) was dropwise added and the resulting mixture stirred for 30 min at 0 ºC, followed by the addition of 4-bromobenzyl bromide (5.00 g, 20.0 mmol). The reaction mixture was let warm to rt and stirred for further 24 hours. Then, a saturated solution of NH_4Cl was added and extracted with EtOAc. The organic phase was washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was dissolved in 40 mL of dry Et_2O and cooled to 0 ºC, followed by dropwise addition of PBr_3 (8.00 mmol). The reaction mixture was let warm to rt and stirred for further 24 hours. Thus, a saturated solution of NH_4Cl was added and extracted with Et_2O. The organic phase was washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (2% EtOAc in hexanes) to obtain 4.90 g of product **S5** as a colourless oil (77% yield).

R_f = 0.24 (2% EtOAc in hexanes).

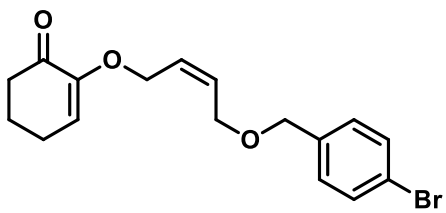
IR: ṽ [cm^{-1}] = 2877, 1496, 1455, 1099.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52 – 7.44 (m, 2H), 7.25 – 7.20 (m, 2H), 5.91 (dtt, *J* = 11.0, 8.2, 1.5 Hz, 1H), 5.74 (dtt, *J* = 11.0, 6.3, 0.8 Hz, 1H), 4.48 (s, 2H), 4.15 (dd, *J* = 6.3, 1.5 Hz, 2H), 3.98 (dd, *J* = 8.2, 0.8 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 136.9, 131.2 (2C), 130.7, 129.0 (2C), 128.2, 121.2, 71.2, 64.9, 26.5.

HRMS (ESI): calculated for $C_{11}H_{12}Br_2NaO^+$, $[M+Na]^+$ = 340.9147; found = 340.9151.

(*Z*)-2-{[4-(Benzyloxy)but-2-en-1-yl]oxy}cyclohex-2-en-1-one (4f)



S5 (1.92 g, 6.00 mmol) was dropwise added to a stirred suspension of 1,2-cyclohexanedione (561 mg, 5.00 mmol) and anhydrous K_2CO_3 (830 mg, 6.00 mmol) in dry DMF (20 mL). The reaction mixture was stirred at rt until full conversion was achieved, as judged by TLC

analysis (36 hours). Then the mixture was diluted with Et_2O and brine was added. After separation of the organic phase, the latter was washed three times with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (from 33% to 50% EtOAc in hexanes) to obtain 106 mg of product **4f** as a colourless oil (6% yield).

R_f = 0.10 (33% EtOAc in hexanes).

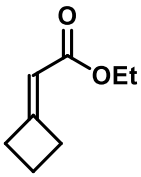
IR: $\tilde{\nu}$ [cm^{-1}] = 2930, 1734, 1488, 1262, 1070, 1011, 804.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 – 7.44 (m, 2H), 7.23 – 7.18 (m, 2H), 5.85 – 5.75 (m, 3H), 4.46 (s, 2H), 4.35 – 4.32 (m, 2H), 4.10 – 4.08 (m, 2H), 2.52 – 2.49 (m, 2H), 2.40 (td, *J* = 6.1, 4.6 Hz, 2H), 2.00 – 1.93 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 194.2, 150.2, 137.1, 131.5 (2C), 129.4 (2C), 129.3, 128.1, 121.5, 118.5, 71.5, 65.9, 63.7, 38.8, 24.5, 22.9.

HRMS (ESI): calculated for $C_{17}H_{19}BrNaO_3^+$, $[M+Na]^+$ = 373.0410; found = 373.0411.

Ethyl 2-cyclobutylideneacetate (S6)



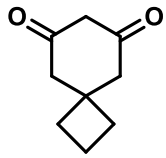
A stirred suspension of NaH (1.82 g, 45.4 mmol, 60% mineral oil) in dry THF (30 mL) was cooled to 0 ºC. Then 9.0 mL of triethyl phosphonoacetate (45 mmol) were dropwise added and the resulting mixture stirred for 30 min at 0 ºC. Subsequently a THF solution (5 mL) of cyclobutanone (2.65 g, 37.8 mmol) was added at 0 ºC. The reaction mixture was let warm to rt and stirred for further 18 hours. Water was added and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (from 0 to 6% EtOAc in hexanes) to obtain 2.61 g of product **S6** as a colourless oil (49% yield).

R_f = 0.31 (4% EtOAc in hexanes).

The NMR data were in accordance with the data reported in the literature.[6]

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.58 (*virt.* p, *J* = 2.3 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.19 – 3.07 (m, 2H), 2.89 – 2.78 (m, 2H), 2.09 (*virt.* p, *J* = 8.0 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H).

Spiro[3.5]nonane-6,8-dione (S7)

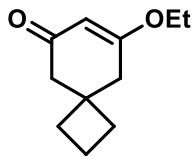


Diethyl 1,3-acetonedicarboxylate (4.51 g, 22.3 mmol) was dropwise added to a suspension of NaH (1.79 g, 44.7 mmol, 60% mineral oil) in dry THF (18 mL) at 0 ºC. After stirring at this temperature for 20 min the α,β-unsaturated ester **S6** (2.61 g, 18.6 mmol) was dropwise added. The reaction mixture was stirred for 30 min at rt, then stirred at reflux for 20 min. Subsequently, a suspension of sodium ethoxide (3.81 g, 56.0 mmol) in 24 mL of ethanol was added and the corresponding reaction mixture was stirred at reflux for 5 hours. Then a solution of KOH (20.9 g, 373 mmol) in 83 mL of water was added and stirred at reflux for further 4 hours. After cooling to rt the organic solvents were removed at reduced pressure and the aqueous phase was washed with diethyl ether before being acidified to acid pH with concentrated HCl. After 4 hours of stirring at 80 ºC the mixture was allowed to cool to rt and extracted twice with DCM. The combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was suspended in 10 mL of MTBE and allowed to stir for 20 min before being filtered over a Büchner funnel to obtain 1.01 g of product **S7** as a white solid (36% yield).

The NMR data (for the keto-enol tautomer) were in accordance with the literature.[6]

^{1}H NMR (400 MHz, DMSO): δ 11.01 (br s, 1H), 5.16 (s, 1H), 2.36 (s, 4H), 1.90 – 1.80 (m, 2H), 1.80 – 1.72 (m, 4H).

8-Ethoxyspiro[3.5]non-7-en-6-one (S8)



The 1,3-diketone **S7** (1.00 g, 6.58 mmol) was stirred for 2 hours at reflux conditions in a Dean-Stark apparatus in the presence of *p*-TsOH (31.3 mg, 0.165 mmol), 3 mL of ethanol and 20 mL of toluene. After cooling to rt the solvents were removed at reduced pressure and the residue was purified by flash chromatography on silica gel (20% EtOAc in hexanes) to obtain 1.16 g of **S8** as a colourless oil (98% yield).

R_f = 0.24 (20% EtOAc in hexanes).

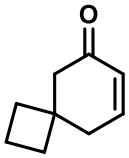
IR: ṽ [cm^{-1}] = 2934, 1651, 1601, 1377, 1357, 1214, 734.

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.31 (s, 1H), 3.89 (q, *J* = 7.0 Hz, 2H), 2.49 (s, 2H), 2.44 (s, 2H), 1.97 – 1.78 (m, 6H), 1.36 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 197.1, 174.6, 101.5, 63.3, 48.3, 40.8, 37.7, 30.9 (2C), 14.1, 13.2.

HRMS (ESI): calculated for $C_{11}H_{17}O_2^+$, $[M+H]^+$ = 181.1223; found = 181.1220.

Spiro[3.5]non-7-en-6-one (S9)



A solution of enone **S8** (1.16 g, 6.43 mmol) in 10 mL of dry Et_2O was dropwise added to a suspension of $LiAlH_4$ (122 mg, 3.21 mmol) in 20 mL of dry Et_2O at 0 ºC. After stirring for 13 hours at rt the reaction mixture was quenched with water and stirred for 1 hour at rt in the presence of 20 mL of a 10% aq. solution of sulfuric acid. After extraction with diethyl ether, the combined organic phases were washed with brine and dried over Na_2SO_4. Thus, after evaporation of the solvents at reduced pressure, the residue was purified by flash chromatography on silica gel (10% EtOAc in hexanes) to obtain 754 mg of **S9** as a colourless oil (86% yield).

R_f = 0.26 (10% EtOAc in hexanes).

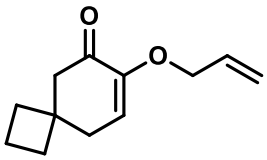
IR: $\tilde{\nu}$ [cm^{-1}] = 2920, 2859, 1672, 1441, 1359, 1227.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.87 (dt, *J* = 10.0, 4.1 Hz, 1H), 6.00 (dt, *J* = 10.0, 2.0 Hz, 1H), 2.52 (s, 2H), 2.46 (dd, *J* = 4.1, 2.0 Hz, 2H), 1.96 – 1.80 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 198.5, 147.6, 129.3, 49.6, 39.6, 38.1, 31.6 (2C), 14.5.

HRMS (ESI): calculated for $C_9H_{13}O^+$, $[M+H]^+$ = 137.0961; found = 137.0956.

7-(Allyloxy)spiro[3.5]non-7-en-6-one (4h)



To a methanol solution (12 mL) of enone **S9** (754 mg, 5.54 mmol) 2.0 mL of H_2O_2 (30%) were dropwise added at 0 ºC, followed by 0.2 mL of 1 M NaOH solution. After stirring for 5 hours at 0 ºC, the reaction mixture was extracted twice with CH_2Cl_2 and the combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was dropwise added (as an allylic alcohol solution – 10 equiv. of allyl alcohol) to a cooled suspension of NaH (266 mg, 6.64 mmol, 60% mineral oil) in allyl alcohol (20 equiv.) at 0 ºC. After 34 hours stirring at rt the reaction mixture was diluted with diethyl ether and water. After extraction of the aqueous phase with diethyl ether, the combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (10% EtOAc in hexanes) to obtain 382 mg of **4h** as a colourless oil which solidified as a white solid upon standing (36% yield).

R_f = 0.25 (10% EtOAc in hexanes).

mp = 50-55 ºC

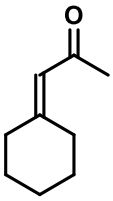
IR: $\tilde{\nu}$ [cm^{-1}] = 2929, 1690, 1624, 1164, 1083, 989, 924.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.97 (ddt, *J* = 17.3, 10.6, 5.5 Hz, 1H), 5.74 (t, *J* = 4.6 Hz, 1H), 5.32 (*virt*. dq, *J* = 17.3, 1.5 Hz, 1H), 5.24 (*virt.* dq, *J* = 10.6, 1.5 Hz, 1H), 4.30 (*virt.* dt, *J* = 5.5, 1.5 Hz, 2H), 2.60 (s, 2H), 2.51 (d, *J* = 4.6 Hz, 2H), 1.97 – 1.77 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 194.0, 150.5, 132.8, 117.9, 115.8, 68.7, 50.6, 40.1, 37.2, 31.9 (2C), 15.2.

HRMS (ESI): calculated for $C_{12}H_{17}O_2^+$, $[M+H]^+$ = 193.1223; found = 193.1217.

1-Cyclohexylidenepropan-2-one (S10)



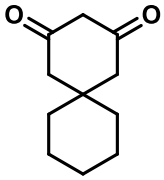
A stirred solution of KOH (2.02 g, 36.0 mmol) in a 4:1 mixture of ethanol:water (72 mL) was cooled to 0 ºC. Then 5.98 g (36.0 mmol) of dimethylacetylmethylphosphonate were dropwise added at the same temperature, followed by the addition of cyclohexanone (2.36 g, 24.0 mmol) at rt. The resulting reaction mixture was stirred for 36 hours. Then water and diethyl ether were added and the aqueous phase was extracted with diethyl ether. The combined organic phases were washed with brine and the solvents removed at reduced pressure. The residue was taken up in diethyl ether, washed with brine once again and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (from 0 to 4% EtOAc in hexanes) to obtain 2.28 g of product **S10** as a pale pink oil (69% yield).

R_f = 0.33 (4% EtOAc in hexanes).

The NMR data were in accordance with the data reported in the literature.[7]

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.98 (s, 1H), 2.80 – 2.75 (m, 2H), 2.20 – 2.11 (m, 5H), 1.71 – 1.55 (m, 6H).

Spiro[5.5]undecane-2,4-dione (S11)



Sodium metal (547 mg, 23.8 mmol) was added to 30 mL of dry ethanol. The suspension was stirred until the sodium completely dissolved and, once back to rt, diethyl malonate (1.90 g, 11.9 mmol) was added to the resulting colourless solution, followed by the addition of enone **S10** (1.64 g, 11.9 mmol) in 6.0 mL of dry ethanol. The reaction mixture was stirred at reflux for 24 hours and then cooled to rt. Subsequently, a solution of KOH (6.67 g, 119 mmol) in 24 mL of water was added and stirred at reflux for further 36 hours. After cooling to rt the organic solvents were removed at reduced pressure and the aqueous phase was washed with diethyl ether before being acidified to acid pH with concentrated HCl. Thus, EtOAc

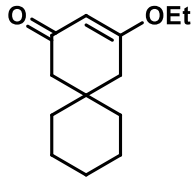
was added and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine and dried over Na_2SO_4. In the end, after evaporation of the solvents at reduced pressure, the resulting residue was purified by flash chromatography on silica gel (50% EtOAc in hexanes) to obtain 1.59 g of product **S11** as a pale yellow solid (74% yield).

R_f = 0.17 (50% EtOAc in hexanes).

The NMR data were in accordance with the data reported in the literature.[8]

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.34 (s, 2H), 2.59 (s, 4H), 1.54 – 1.30 (m, 10H).

4-Ethoxyspiro[5.5]undec-3-en-2-one (S12)



The 1,3-diketone **S11** (1.94 g, 10.75 mmol) was stirred for 14 hours at reflux conditions in a Dean-Stark apparatus in the presence of *p*-TsOH (51.0 mg, 0.268 mmol), 4.0 mL of ethanol and 20 mL of toluene. After cooling to rt the solvents were removed at reduced pressure and the residue was purified by flash chromatography on silica gel (20% EtOAc in hexanes) to obtain 2.00 g of **S12** as a yellowish oil (89% yield).

R_f = 0.37 (20% EtOAc in hexanes).

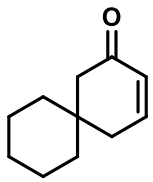
IR: ṽ [cm^{-1}] = 2927, 1655, 1607, 1377, 1210.

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.32 (s, 1H), 3.89 (q, *J* = 7.0 Hz, 2H), 2.33 (s, 2H), 2.28 (s, 2H), 1.52 – 1.40 (m, 10H), 1.36 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 198.4, 175.2, 100.9, 63.7, 48.1, 40.1, 36.0 (2C), 34.7, 25.7, 21.2 (2C), 13.7.

HRMS (ESI): calculated for $C_{13}H_{21}O_2^+$, $[M+H]^+$ = 209.1536; found = 209.1532.

Spiro[5.5]undec-3-en-2-one (S13)



A solution of enone **S12** (2.00 g, 9.62 mmol) in 8.0 mL of dry Et_2O was dropwise added to a suspension of $LiAlH_4$ (183 mg, 4.82 mmol) in 30 mL of dry Et_2O at 0 ºC. After stirring for 14 hours at rt the reaction mixture was quenched with water and stirred for 1 hour at rt in the presence of 50 mL of a 10% aq. solution of sulfuric acid. After extraction with diethyl ether, the combined organic phases were washed with brine and dried over Na_2SO_4. Thus, after evaporation of the solvents at reduced pressure, the residue was purified by flash chromatography on silica gel (10% EtOAc in hexanes) to obtain 678 mg of **S13** as a colourless oil (43% yield).

R_f = 0.21 (10% EtOAc in hexanes).

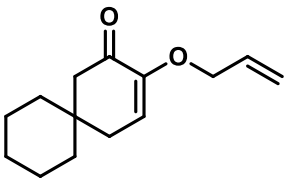
IR: ṽ [cm^{-1}] = 2925, 2857, 1678, 1452, 1388, 1247.

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.84 (dt, *J* = 10.1, 4.2 Hz, 1H), 6.00 (dt, *J* = 10.1, 2.1 Hz, 1H), 2.35 (s, 2H), 2.30 (dd, *J* = 4.2, 2.1 Hz, 2H), 1.62 – 1.35 (m, 10H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 199.5, 147.8, 128.8, 49.4, 37.3, 36.4, 36.3 (2C), 26.0, 21.3 (2C).

HRMS (ESI): calculated for $C_{11}H_{17}O^+$, $[M+H]^+$ = 165.1274; found = 165.1270.

3-(Allyloxy)spiro[5.5]undec-3-en-2-one (4i)



To a methanol solution (8 mL) of enone **S13** (678 mg, 4.13 mmol) 1.5 mL of H_2O_2 (30%) were dropwise added at 0 ºC, followed by 0.15 mL of 1 M NaOH solution. After stirring for 5 hours at 0 ºC, the reaction mixture was extracted twice with DCM and the combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was dropwise added (as an allylic alcohol solution – 10 equiv. of allyl alcohol) to a cooled suspension of NaH (242 mg, 6.05 mmol, 60% mineral oil) in allyl alcohol (20 equiv.) at 0 ºC. After 36 hours stirring at rt the reaction mixture was diluted with diethyl ether and water. After extraction of the aqueous phase with diethyl ether, the combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (8% EtOAc in hexanes) to obtain 352 mg of **4i** as a colourless oil (39% yield).

R_f = 0.26 (10% EtOAc in hexanes).

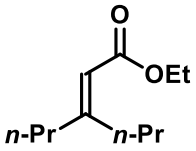
IR: ṽ [cm^{-1}] = 2926, 2856, 1731, 1453, 1173, 1121, 735.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.98 (ddt, *J* = 17.3, 10.6, 5.5 Hz, 1H), 5.71 (t, *J* = 4.7 Hz, 1H), 5.32 (*virt.* dq, *J* = 17.3, 1.5 Hz, 1H), 5.24 (*virt.* dq, *J* = 10.6, 1.5 Hz, 1H), 4.31 (*virt.* dt, *J* = 5.5, 1.5 Hz, 2H), 2.44 (s, 2H), 2.34 (d, *J* = 4.7 Hz, 2H), 1.48 – 1.39 (m, 10H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 194.4, 149.9, 133.1, 118.1, 115.6, 68.8, 50.1, 36.8, 36.4 (2C), 36.1, 26.4, 21.7 (2C).

HRMS (ESI): calculated for $C_{14}H_{21}O_2^+$, $[M+H]^+$ = 221.1536; found = 221.1533.

Ethyl 3-propylhex-2-enoate (S14)



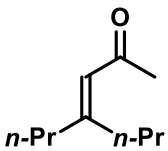
A stirred suspension of NaH (1.60 g, 40.0 mmol, 60% mineral oil) in dry THF (40 mL) was cooled to 0 ºC. Then 7.94 mL of triethyl phosphonoacetate (40.0 mmol) were dropwise added and the resulting mixture stirred for 30 min at 0 ºC. Subsequently a THF solution (20 mL) of 4-heptanone (2.28 g, 20.0 mmol) was added at 0 ºC. The reaction mixture was let warm to rt and stirred at reflux for 14 hours. After cooling to rt, water was added and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (from 1 to 4% EtOAc in hexanes) to obtain 3.69 g of product **S14** as a colourless oil (100% yield).

$\mathbf{R_f}$ = 0.36 (2% EtOAc in hexanes).

The NMR data were in accordance with the data reported in the literature.[9]

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.62 (s, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.65 – 2.51 (m, 2H), 2.15 – 2.06 (m, 2H), 1.56 – 1.39 (m, 4H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.99 – 0.88 (m, 6H).

4-Propylhept-3-en-2-one (S15)



40.0 mL of a 2 M solution of *i*-PrMgCl (4 equiv.) in THF were dropwise added to a stirred solution of ester **S14** (3.69 g, 20.0 mmol) and *N*,*O*-dimethylhydroxylamine hydrochloride (3.90 g, 40.0 mmol) in 40 mL of dry THF at -10 ºC. The resulting reaction mixture was let warm to rt and stirred for 4 hours before being quenched with a saturated solution of NH_4Cl and extracted with EtOAc. The combined organic phases were washed with brine and dried over Na_2SO_4. The obtained residue was dissolved in 40 mL of dry THF and 7.95 mL of a 3 M solution of MeMgBr (1.2 equiv.) in diethyl ether were dropwise added at 0 ºC. The resulting mixture was let warm until rt and stirred overnight before being quenched with a saturated solution of NH_4Cl and extracted with EtOAc. The combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (5% EtOAc in hexanes) to obtain 2.21 g of product **S15** as a colourless oil (72% yield).

$\mathbf{R_f}$ = 0.56 (10% EtOAc in hexanes).

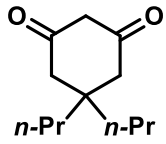
IR: $\tilde{\nu}$ [cm^{-1}] = 2936, 1710, 1481, 1355, 1099.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.02 (s, 1H), 2.54 – 2.49 (m, 2H), 2.16 (s, 3H), 2.12 – 2.06 (m, 2H), 1.54 – 1.39 (m, 4H), 0.96 – 0.90 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 196.8, 161.8, 122.7, 40.2, 33.6, 31.0, 21.4, 20.4, 13.7, 13.2.

HRMS (ESI): calculated for $C_{10}H_{19}O^+$, $[M+H]^+$ = 155.1430; found = 155.1426.

5,5-Dipropylcyclohexane-1,3-dione (S16)



Sodium metal (659 mg, 28.7 mmol) was added to 38 mL of dry ethanol. The suspension was stirred until the sodium completely dissolved and, once back to rt, diethyl malonate (4.59 g, 28.7 mmol) was added to the resulting colourless solution, followed by the addition of enone **S15** (2.21 g, 14.3 mmol) in 5.0 mL of dry ethanol. The reaction mixture was stirred at reflux for 24 hours and then cooled to rt. Subsequently, a solution of KOH (8.04 g, 143 mmol) in 29 mL of water was added and stirred at reflux for further 36 hours. After cooling to rt the organic solvents were removed at reduced pressure and the aqueous phase was washed with diethyl ether before being acidified to acid pH with concentrated HCl. Thus, EtOAc was added and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine and dried over Na_2SO_4. In the end, after evaporation of the solvents at reduced pressure, the resulting residue was purified by flash chromatography on silica gel (50% EtOAc in hexanes) to obtain 2.05 g of product **S16** as a pale yellow solid (73% yield).

R_f = 0.30 (50% EtOAc in hexanes).

IR: $\tilde{\nu}$ [cm^{-1}] = 2958, 1570, 1406, 1223, 1143, 751.

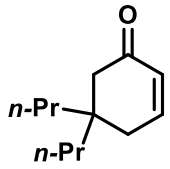
^{1}H NMR (500 MHz, $CDCl_3$): δ 3.32 (s, 2H), 2.51 (s, 4H), 1.26 – 1.13 (m, 8H), 0.86 (t, J = 6.6 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 204.2 (2C), 57.8, 51.1 (2C), 40.2 (2C), 36.5, 16.6 (2C), 14.6 (2C).

A 2:1 mixture of tautomers was observed in $CDCl_3$ (the reported NMR signals are the data of the major 1,3-diketone tautomer).

HRMS (ESI): calculated for $C_{12}H_{21}O_2^+$, $[M+H]^+$ = 197.1536; found = 197.1533.

5,5-Dipropylcyclohex-2-en-1-one (S17)



The 1,3-diketone **S16** (2.04 g, 10.4 mmol) was stirred for 14 hours at reflux conditions in a Dean-Stark apparatus in the presence of *p*-TsOH (50.0 mg, 0.263 mmol), 4.0 mL of ethanol and 30 mL of toluene. After cooling to rt the solvents were removed at reduced pressure and a solution of the residue in 12 mL of dry Et_2O was dropwise added to a suspension of $LiAlH_4$ (197 mg, 5.19 mmol) in 30 mL of dry Et_2O at 0 ºC. After stirring for 16 hours at rt the reaction mixture was quenched with a saturated solution of NH_4Cl and stirred for 2 hours at rt in the presence of 50 mL of a 10% aq. solution of sulfuric acid. After extraction with diethyl ether, the combined organic phases were washed with brine and dried over Na_2SO_4. Thus, after evaporation of the solvents at reduced pressure, the residue was purified by flash chromatography on silica gel (3% EtOAc in hexanes) to obtain 1.55 g of **S17** as a colourless oil (83% yield).

R_f = 0.34 (4% EtOAc in *n*-pentane).

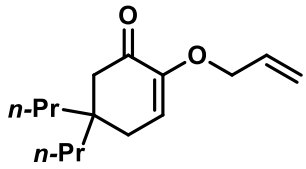
IR: ṽ [cm^{-1}] = 2923, 2844, 1676, 1471, 1390, 1239.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.87 – 6.79 (m, 1H), 6.03 – 5.96 (m, 1H), 2.29 (s, 2H), 2.26 – 2.20 (m, 2H), 1.36 – 1.13 (m, 8H), 0.91 – 0.83 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 200.4, 148.4, 129.3, 48.9, 40.0 (2C), 39.4, 36.7, 16.8 (2C), 14.9 (2C).

HRMS (ESI): calculated for $C_{12}H_{21}O^+$, $[M+H]^+$ = 181.1587; found = 181.1585.

2-(Allyloxy)-5,5-dipropylcyclohex-2-en-1-one (4j)



To a methanol solution (9 mL) of enone **S17** (1.55 g, 8.57 mmol) 3.0 mL of H_2O_2 (30%) were dropwise added at 0 ºC, followed by 0.30 mL of 1 M NaOH solution. After stirring for 7 hours at 0 ºC, the reaction mixture was extracted twice with EtOAc and the combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was dropwise added (as an allylic alcohol solution – 10 equiv. of allyl alcohol) to a cooled suspension of NaH (514 mg, 22.4 mmol, 60% mineral oil) in allyl alcohol (20 equiv.) at 0 ºC. After 36 hours stirring at rt the reaction mixture was diluted with diethyl ether and water. After extraction of the aqueous phase with diethyl ether, the combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the

residue was purified by flash chromatography on silica gel (5% EtOAc in *n*-pentane) to obtain 406 mg of **4j** as a pale-yellow oil (20% yield).

R_f = 0.24 (5% EtOAc in cyclohexane).

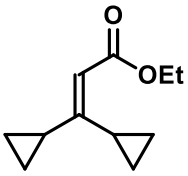
IR: ṽ [cm^{-1}] = 2958, 2930, 1688, 1630, 1167, 734.

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.97 (ddt, *J* = 17.3, 10.6, 5.5 Hz, 1H), 5.69 (t, *J* = 4.7 Hz, 1H), 5.31 (*virt.* dq, *J* = 17.3, 1.5 Hz, 1H), 5.23 (*virt.* dq, *J* = 10.6, 1.5 Hz, 1H), 4.30 (*virt.* dt, *J* = 5.5, 1.5 Hz, 2H), 2.37 (s, 2H), 2.27 (d, *J* = 4.7 Hz, 2H), 1.38 – 1.11 (m, 8H), 0.85 (t, *J* = 6.9 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 194.6, 149.9, 133.0, 118.0, 115.8, 68.8, 49.4, 39.6 (2C), 39.4, 35.1, 16.8 (2C), 14.8 (2C).

HRMS (ESI): calculated for $C_{15}H_{24}NaO_2^+$, $[M+Na]^+$ = 259.1669; found = 259.1668.

Ethyl 3,3-dicyclopropylacrylate (S18)



A stirred suspension of NaH (1.60 g, 40.0 mmol, 60% mineral oil) in dry THF (40 mL) was cooled to 0 ºC. Then 7.94 mL of triethyl phosphonoacetate (40.0 mmol) were dropwise added and the resulting mixture stirred for 30 min at 0 ºC. Subsequently a THF solution (20 mL) of dicyclopropylketone (2.20 g, 20.0 mmol) was added at 0 ºC. The reaction mixture was let warm to rt and stirred at reflux for 36 hours. After cooling to rt, water was added and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (from 1 to 4% EtOAc in hexanes) to obtain 1.99 g of product **S18** as a pale-yellow oil (55% yield).

R_f = 0.33 (2% EtOAc in hexanes).

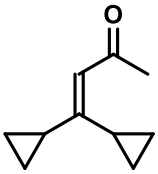
IR: ṽ [cm^{-1}] = 2981, 1709, 1620, 1248, 1193, 1151, 1039, 926.

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.40 (s, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.29 (tt, *J* = 8.4, 5.3 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.00 – 0.83 (m, 5H), 0.76 – 0.68 (m, 2H), 0.58 – 0.49 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 167.8, 166.1, 111.2, 59.5, 14.5, 14.3, 11.8, 7.8 (2C), 7.4 (2C).

HRMS (ESI): calculated for $C_{11}H_{17}O_2^+$, $[M+H]^+$ = 181.1223; found = 181.1222.

4,4-Dicyclopropylbut-3-en-2-one (S19)



22.0 mL of a 2 M solution of *i*-PrMgCl (4 equiv.) in THF were dropwise added to a stirred solution of ester **S18** (1.98 g, 11.0 mmol) and *N,O*-dimethylhydroxylamine hydrochloride (2.15 g, 22.0 mmol) in 33 mL of dry THF at -10 ºC. The resulting reaction mixture was stirred for 1 hour until 5 ºC, then 3 hours at rt, before being quenched with a saturated solution of NH_4Cl and extracted with EtOAc. The combined organic phases were washed with brine and dried over Na_2SO_4. The obtained residue was dissolved in 22 mL of dry THF and 4.4 mL of a 3 M solution of MeMgBr (1.2 equiv.) in diethyl ether were dropwise added at 0 ºC. The resulting mixture was let warm to rt and stirred overnight before being quenched with a saturated solution of NH_4Cl and extracted with EtOAc. The combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (10% EtOAc in hexanes) to obtain 1.40 g of product **S19** as a colourless oil (85% yield).

R_f = 0.37 (10% EtOAc in hexanes).

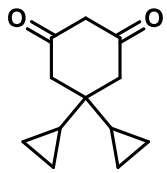
IR: $\tilde{\nu}$ [cm^{-1}] = 2925, 2855, 1726, 1461, 1378, 1108.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.77 (s, 1H), 3.42 – 3.30 (m, 1H), 2.17 (s, 3H), 1.00 – 0.84 (m, 5H), 0.78 – 0.71 (m, 2H), 0.58 – 0.50 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 199.1, 165.7, 118.8, 32.3, 14.6, 11.7, 8.2 (2C), 7.9 (2C).

HRMS (ESI): calculated for $C_{10}H_{15}O^+$, $[M+H]^+$ = 151.1117; found = 151.1111.

5,5-Dicyclopropylcyclohexane-1,3-dione (S20)



Sodium metal (429 mg, 18.7 mmol) was added to 24 mL of dry ethanol. The suspension was stirred until the sodium completely dissolved and, once back to rt, diethyl malonate (2.99 g, 18.7 mmol) was added to the resulting colourless solution, followed by the addition of enone **S19** (1.40 g, 9.34 mmol) in 4.0 mL of dry ethanol. The reaction mixture was stirred at reflux for 24 hours and then cooled to rt. Subsequently, a solution of KOH (5.24 g, 93.4 mmol) in 19 mL of water was added and stirred at reflux for further 36 hours. After cooling to rt the organic solvents were removed at reduced pressure and the aqueous phase was washed with diethyl ether before being acidified to acid pH with concentrated HCl. Thus, EtOAc was added and the aqueous phase was extracted with EtOAc. The combined organic phases were washed with brine and dried over Na_2SO_4. In the end, after evaporation of the solvents at reduced pressure, the resulting residue was purified by flash

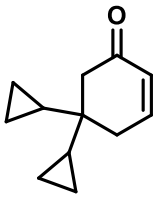
chromatography on silica gel (50% EtOAc in hexanes) to obtain 1.52 g of product **S20** as a pale yellow solid (85% yield).

R_f = 0.26 (50% EtOAc in hexanes).

The NMR data were in accordance with the data reported in the literature.[10]

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.35 (s, 2H), 2.41 (s, 4H), 0.70 – 0.56 (m, 2H), 0.45 – 0.27 (m, 8H).

5,5-Dicyclopropylcyclohex-2-en-1-one (S21)



The 1,3-diketone **S20** (1.52 g, 7.92 mmol) was stirred for 14 hours at reflux conditions in a Dean-Stark apparatus in the presence of *p*-TsOH (38.0 mg, 0.200 mmol), 3.0 mL of ethanol and 20 mL of toluene. After cooling to rt the solvents were removed at reduced pressure and a solution of the residue in 12 mL of dry Et_2O was dropwise added to a suspension of $LiAlH_4$ (152 mg, 4.00 mmol) in 20 mL of dry Et_2O at 0 ºC. After stirring for 16 hours at rt the reaction mixture was quenched with a saturated solution of NH_4Cl and stirred for 2 hours at rt in the presence of 50 mL of a 10% aq. solution of sulfuric acid. After extraction with diethyl ether, the combined organic phases were washed with brine and dried over Na_2SO_4. Thus, after evaporation of the solvents at reduced pressure, the residue was purified by flash chromatography on silica gel (4% EtOAc in *n*-pentane) to obtain 977 mg of **S21** as a colourless oil (70% yield).

R_f = 0.19 (4% EtOAc in *n*-pentane).

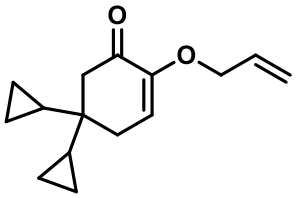
IR: $\tilde{\nu}$ [cm^{-1}] = 3007, 1677, 1389, 1251, 1019, 733.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.84 (dt, *J* = 10.1, 4.2 Hz, 1H), 6.00 (dt, *J* = 10.1, 2.1 Hz, 1H), 2.15 (s, 2H), 2.12 (dd, *J* = 4.2, 2.1 Hz, 2H), 0.81 – 0.68 (m, 2H), 0.37 – 0.25 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 199.9, 148.4, 129.3, 46.4, 37.2, 34.6, 18.1 (2C), 0.8 (2C), 0.5 (2C).

HRMS (ESI): calculated for $C_{12}H_{17}O^+$, $[M+H]^+$ = 177.1274; found = 177.1272.

2-(Allyloxy)-5,5-dicyclopropylcyclohex-2-en-1-one (4k)



To a methanol solution (12 mL) of enone **S21** (972 mg, 5.52 mmol) 2.25 mL of H_2O_2 (30%) were dropwise added at 0 ºC, followed by 0.23 mL of 1 M NaOH solution. After stirring for 7 hours at 0 ºC, the reaction mixture was extracted twice with

EtOAc and the combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was dropwise added (as an allylic alcohol solution – 10 equiv. of allyl alcohol) to a cooled suspension of NaH (331 mg, 8.28 mmol, 60% mineral oil) in allyl alcohol (20 equiv.) at 0 ºC. After 36 hours stirring at rt the reaction mixture was diluted with diethyl ether and water. After extraction of the aqueous phase with diethyl ether, the combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (5% EtOAc in *n*-pentane) to obtain 207 mg of **4k** as a pale yellow solid (16% yield).

R_f = 0.19 (5% EtOAc in cyclohexane).

mp = 30-35 ºC

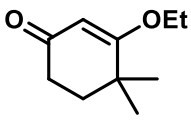
IR: ṽ [cm^{-1}] = 2924, 2855, 1717, 1466, 1119, 973, 922.

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.97 (ddt, *J* = 17.4, 10.7, 5.5 Hz, 1H), 5.70 (t, *J* = 4.6 Hz, 1H), 5.31 (*virt.* dq, *J* = 17.4, 1.6 Hz, 1H), 5.26 – 5.20 (m, 1H), 4.31 (*virt.* dt, *J* = 5.5, 1.6 Hz, 2H), 2.25 (s, 2H), 2.19 (d, *J* = 4.6 Hz, 2H), 0.82 – 0.70 (m, 2H), 0.39 – 0.23 (m, 8H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 194.2, 149.9, 133.0, 118.0, 115.9, 68.8, 47.0, 37.1, 33.0, 18.1 (2C), 0.9 (2C), 0.6 (2C).

HRMS (ESI): calculated for $C_{15}H_{20}NaO_2^+$, $[M+Na]^+$ = 255.1356; found = 255.1355.

3-Ethoxy-4,4-dimethylcyclohex-2-en-1-one (S22)



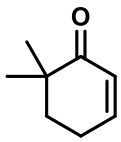
4,4-Dimethyl-1,3-cyclohexandione (5.03 g, 35.9 mmol) was stirred for 18 hours at reflux conditions in a Dean-Stark apparatus in the presence of *p*-TsOH (171 mg, 0.899 mmol), 6.8 mL of ethanol and 54 mL of toluene. After cooling to rt the solvents were removed at reduced pressure and the residue was purified by flash chromatography on silica gel (from 5% to 20% EtOAc in hexanes) to obtain 1.32 g of **S22** as a colourless oil (22% yield).

R_f = 0.18 (20% EtOAc in hexanes).

The NMR data were in accordance with the data reported in the literature.[11]

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.24 (s, 1H), 3.87 (q, *J* = 7.0 Hz, 2H), 2.40 (t, *J* = 6.7 Hz, 2H), 1.82 (t, *J* = 6.7 Hz, 2H), 1.36 (t, *J* = 7.0 Hz, 3H), 1.20 (s, 6H).

6,6-Dimethylcyclohex-2-en-1-one (S23)



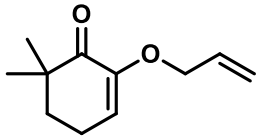
A solution of enone **S22** (1.32 g, 7.85 mmol) in 8.0 mL of dry Et_2O was dropwise added to a suspension of $LiAlH_4$ (99.3 mg, 2.62 mmol) in 26 mL of dry Et_2O at 0 ºC. After stirring for 12 hours at rt the reaction mixture was quenched with water and stirred for 1 hour at rt in the presence of 50 mL of a 10% aq. solution of sulfuric acid. After extraction with diethyl ether, the combined organic phases were washed with a saturated solution of $NaHCO_3$, brine and dried over Na_2SO_4. Thus, after evaporation of the solvents at reduced pressure, the residue was purified by flash chromatography on silica gel (10% EtOAc in hexanes) to obtain 550 mg of **S23** as a colourless oil (56% yield).

$\mathbf{R_f}$ = 0.44 (10% EtOAc in hexanes).

The NMR data were in accordance with the data reported in the literature.[11]

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.86 (dt, *J* = 10.0, 4.0 Hz, 1H), 5.91 (dt, *J* = 10.0, 2.0 Hz, 1H), 2.37 (tdd, *J* = 6.1, 4.0, 2.0 Hz, 2H), 1.83 (t, *J* = 6.1 Hz, 2H), 1.11 (s, 6H).

2-(Allyloxy)-6,6-dimethylcyclohex-2-en-1-one (4l)



To a methanol solution (8.8 mL) of enone **S23** (550 mg, 4.43 mmol) 1.3 mL of H_2O_2 (30%) were dropwise added at 0 ºC, followed by 0.14 mL of 1 M NaOH solution. After stirring for 22 hours at rt the reaction mixture was extracted twice with DCM and the combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was dropwise added (as an allylic alcohol solution – 10 equiv. of allyl alcohol) to a cooled suspension of NaH (354 mg, 8.86 mmol, 60% mineral oil) in allyl alcohol (20 equiv.) at 0 ºC. After 34 hours stirring at rt the reaction mixture was diluted with diethyl ether and water. After extraction of the aqueous phase with diethyl ether, the combined organic phases were washed with brine and dried over Na_2SO_4. After evaporation of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (6% EtOAc in hexanes) to obtain 480 mg of **4l** as a pale-yellow oil (60% yield).

$\mathbf{R_f}$ = 0.12 (5% EtOAc in hexanes).

IR: $\tilde{\nu}$ [cm^{-1}] = 2922, 2851, 1686, 1628, 1232, 1210, 1091, 1062, 923, 826.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.98 (ddt, *J* = 17.3, 10.6, 5.4 Hz, 1H), 5.79 (t, *J* = 4.5 Hz, 1H), 5.33 (*virt.* dq, *J* = 17.3, 1.5 Hz, 1H), 5.24 (*virt.* dq, *J* = 10.6, 1.5 Hz, 1H), 4.29 (*virt.*

dt, *J* = 5.4, 1.5 Hz, 2H), 2.40 (td, *J* = 6.1, 4.5 Hz, 2H), 1.80 (t, *J* = 6.1 Hz, 2H), 1.14 (s, 6H).

^{13}C NMR (101 MHz, CD_2Cl_2): δ 199.3, 149.0, 133.7, 117.9, 117.2, 69.0, 42.6, 36.5, 24.3 (2C), 21.4.

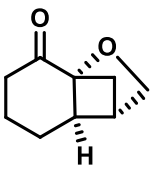
HRMS (ESI): calculated for $C_{11}H_{16}NaO_2^+$, $[M+Na]^+$ = 203.1043; found = 203.1039.

6. General Procedure for the Enantioselective [2+2] Photocycloaddition

An oven-dried Schlenk tube, equipped with a magnetic stir bar, was charged with catalyst **6** (1.73 mg, 2.00 μmol), the corresponding enone **4** (0.100 mmol) and 10 mL of dry DCE. The reaction mixture was deoxygenated by three cycles of "freeze-pump-thaw" and stirred at room temperature under blue LED irradiation (λ = 437 nm), as illustrated in the reaction setup, for the indicated time. The solvent was removed under reduced pressure and the crude mixture was purified by flash chromatography to afford the corresponding cyclobutane **5** in stated yield and enantiomeric purity.

7. Characterisation Data for the Enantioenriched Cyclobutanes (5)

(3*S*,3a*R*,7a*R*)-Hexahydro-7*H*-3,7a-methanobenzofuran-7-one. (5a)



5a was prepared according to the general procedure after 14 hours of irradiation and purified by flash chromatography on silica gel (from 20 to 50% EtOAc in hexanes) to obtain 13.0 mg of product as a white solid (86% yield). The enantiomeric excess (92% *ee*) was determined by GC on a *Macherey-Nagel Lipodex E* column [τ_{major} = 14.8 min, τ_{minor} = 13.4 min; 60 ºC (1 min), 170 ºC (15 ºC/min), 200 ºC (4 ºC/min), 200 ºC (5 min)].

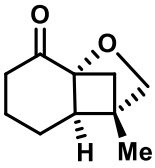
R_f = 0.28 (50% EtOAc in hexanes).

$[\alpha]^{24}_D$ = + 60 (*c* = 0.94, $CHCl_3$).

The NMR data were in accordance with the data reported in the literature.[2]

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.93 (d, *J* = 6.0 Hz, 1H), 3.84 (d, *J* = 6.0 Hz, 1H), 2.87 (d, *J* = 3.0 Hz, 1H), 2.83 (dd, *J* = 8.1, 3.0 Hz, 1H), 2.43 – 2.34 (m, 2H), 2.29 (*virt.* dt, *J* = 11.0, 7.1 Hz, 1H), 2.22 – 2.04 (m, 2H), 1.92 – 1.80 (m, 2H), 1.75 – 1.62 (m, 1H).

(3*S*,3a*R*,7a*R*)-3-Methylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (5b)



5b was prepared according to the general procedure after 14 hours of irradiation and purified by flash chromatography on silica gel (from 20 to 50% EtOAc in hexanes) to obtain 6.8 mg of product as a white solid (41% yield). The enantiomeric excess (84% *ee*) was determined by GC on a *Macherey-Nagel Lipodex E* column [τ_{major} = 14.3 min, τ_{minor} = 13.0 min; 60 ºC (1 min), 170 ºC (15 ºC/min), 200 ºC (4 ºC/min), 200 ºC (5 min)].

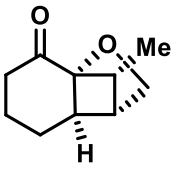
R_f = 0.37 (50% EtOAc in hexanes).

$[\alpha]^{24}_D$ = + 53 (*c* = 0.86, $CHCl_3$).

The NMR data were in accordance with the data reported in the literature.[2]

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.74 (d, *J* = 5.9 Hz, 1H), 3.64 (dd, *J* = 5.9, 1.2 Hz, 1H), 2.59 (d, *J* = 8.0 Hz, 1H), 2.41 – 2.29 (m, 2H), 2.26 – 2.20 (m, 1H), 2.14 (*virt.* ddt, *J* = 11.1, 6.2, 2.9 Hz, 1H), 2.02 – 1.95 (m, 1H), 1.87 (*virt.* t, *J* = 8.0 Hz, 1H), 1.82 – 1.64 (m, 2H), 1.24 (s, 3H).

(3*S*,3a*R*,7a*R*,8*R*)-8-Methylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (5c)



5c was prepared according to the general procedure after 24 hours of irradiation and purified by flash chromatography on silica gel (from 10 to 40% EtOAc in hexanes) to obtain 11.4 mg of product as a white solid (69% yield). The enantiomeric excess (81% *ee*) was determined by GC on a *Macherey-Nagel Lipodex E* column [τ_{major} = 25.3 min, τ_{minor} = 22.0 min; 100 ºC (1 min), 150 ºC (15 ºC/min), 150 ºC (30 min), 200 ºC (15 ºC/min)].

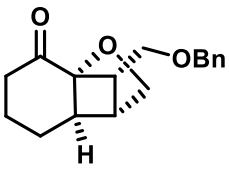
R_f = 0.23 (33% EtOAc in hexanes).

$[\alpha]^{24}_D$ = + 54 (*c* = 0.82, $CHCl_3$).

The NMR data were in accordance with the data reported in the literature.[2]

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.88 (d, *J* = 6.5 Hz, 1H), 3.75 (d, *J* = 6.5 Hz, 1H), 3.05 (qd, *J* = 6.4, 2.9 Hz, 1H), 2.65 (d, *J* = 2.9 Hz, 1H), 2.41 – 2.28 (m, 2H), 2.21 (dd, *J* = 11.0, 6.7 Hz, 1H), 2.14 – 2.07 (m, 1H), 2.07 – 2.00 (m, 1H), 1.91 (*virt.* tdd, *J* = 14.1, 11.0, 3.7 Hz, 1H), 1.75 – 1.63 (m, 1H), 0.90 (d, *J* = 6.4 Hz, 3H).

(3*R*,3a*R*,7a*S*,8*S*)-8-[(Benzyloxy)methyl]hexahydro-7*H*-3,7a-methanobenzofuran-7-one (5d)



5d was prepared according to the general procedure after 14 hours of irradiation and purified by flash chromatography on silica gel (25% EtOAc in cyclohexane) to obtain 12.6 mg of product as a yellow oil (46% yield). The enantiomeric excess (90% *ee*) was determined by reverse phase HPLC on a *Daicel Chiralcel* OJ-RH column [τ_{major} = 11.9 min, τ_{minor} = 12.7 min; flow rate 1.0 mL/min; acetonitrile:water = gradient from 20:80 to 100:0 in 30 min; T = 5 ºC, λ = 215 nm].

R_f = 0.17 (25% EtOAc in cyclohexane).

IR: ṽ [cm^{-1}] = 2925, 1717, 1452, 1274, 1114, 714.

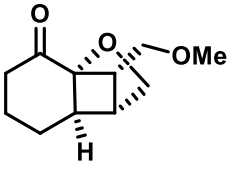
$[\alpha]^{24}_D$ = + 31 (*c* = 1.26, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 – 7.30 (m, 2H), 7.29 – 7.24 (m, 3H), 4.48 (d, *J* = 11.9 Hz, 1H), 4.38 (d, *J* = 11.9 Hz, 1H), 3.76 (s, 2H), 3.47 (dd, *J* = 10.0, 7.2 Hz, 1H), 3.38 (dd, *J* = 10.0, 5.5 Hz, 1H), 3.21 (ddd, *J* = 7.2, 5.5, 2.9 Hz, 1H), 2.84 (d, *J* = 2.9 Hz, 1H), 2.48 – 2.33 (m, 2H), 2.24 (dd, *J* = 10.9, 6.6 Hz, 1H), 2.12 (*virt.* ddq, *J* = 14.0, 5.2, 2.8 Hz, 1H), 2.08 – 2.01 (m, 1H), 1.93 (*virt.* tdd, *J* = 14.2, 10.9, 3.7 Hz, 1H), 1.70 (*virt.* qt, *J* = 13.5, 4.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 203.2, 138.2, 128.5 (2C), 127.8 (3C), 88.4, 73.6, 67.9, 65.4, 53.4, 49.7, 43.3, 40.0, 27.2, 24.3.

HRMS (ESI): calculated for $C_{17}H_{20}NaO_3^+$, $[M+Na]^+$ = 295.1305; found = 295.1305.

(3*R*,3a*R*,7a*S*,8*S*)-8-(Methoxymethyl)hexahydro-7*H*-3,7a-methanobenzofuran-7-one (5e)



5e was prepared according to the general procedure after 14 hours of irradiation and purified by flash chromatography on silica gel (from 20 to 50% EtOAc in hexanes) to obtain 8.5 mg of product as a colorless oil (43% yield). The enantiomeric excess (94% *ee*) was determined by GC on a *Macherey-Nagel Lipodex E* column [τ_{major} = 28.7 min, τ_{minor} = 32.3 min; 100 ºC (1 min), 150 ºC (15 ºC/min), 150 ºC (30 min), 200 ºC (15 ºC/min)].

R_f = 0.18 (50% EtOAc in hexanes).

IR: ṽ [cm^{-1}] = 2925, 17161460, 1109, 848, 750.

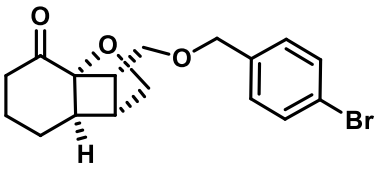
$[\alpha]^{24}_D$ = + 37 (*c* = 0.92, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.81 (d, *J* = 6.8 Hz, 1H), 3.78 (d, *J* = 6.8 Hz, 1H), 3.37 (dd, *J* = 10.1, 7.2 Hz, 1H), 3.29 (dd, *J* = 10.1, 5.3 Hz, 1H), 3.26 (s, 3H), 3.16 (ddd, *J* = 7.2, 5.3, 2.9 Hz, 1H), 2.84 (d, *J* = 2.9 Hz, 1H), 2.48 – 2.33 (m, 2H), 2.23 (dd, *J* = 11.0, 6.7 Hz, 1H), 2.16 – 2.09 (m, 1H), 2.09 – 2.02 (m, 1H), 1.93 (*virt.* tdd, *J* = 14.2, 11.0, 3.8 Hz, 1H), 1.70 (*virt.* qt, *J* = 13.5, 4.4 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 203.3, 88.4, 68.0, 67.8, 59.3, 53.4, 49.6, 43.2, 40.0, 27.2, 24.3.

HRMS (ESI): calculated for $C_{11}H_{16}NaO_3^+$, $[M+Na]^+$ = 219.0992; found = 219.0993.

(3*R*,3a*R*,7a*S*,8*S*)-8-{[(4-Bromobenzyl)oxy]methyl}hexahydro-7*H*-3,7a-methanobenzofuran-7-one (5f)



5f was prepared according to the general procedure after 14 hours of irradiation and purified by flash chromatography on silica gel (30% EtOAc in hexanes) to obtain 12.9 mg of product as a pale yellow solid (37% yield). The enantiomeric excess (92% *ee*) was determined by normal phase HPLC on a *Daicel Chiralpak* AS-H column [τ_{major} = 24.0 min, τ_{minor} = 28.8 min; flow rate 1.0 mL/min; *i*-PrOH:*n*-heptane = 10:90; λ = 210 nm].

R_f = 0.15 (30% EtOAc in hexanes).

mp = 130 ºC

IR: ṽ [cm^{-1}] = 2941, 1715, 1488, 1091, 1011, 845, 804.

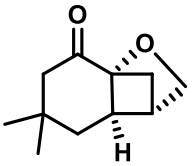
$[\alpha]^{24}_D$ = + 35 (*c* = 1.17, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47 – 7.42 (m, 2H), 7.15 – 7.11 (m, 2H), 4.41 (d, *J* = 12.0 Hz, 1H), 4.33 (d, *J* = 12.0 Hz, 1H), 3.77 (d, *J* = 6.8 Hz, 1H), 3.75 (d, *J* = 6.8 Hz, 1H), 3.46 (dd, *J* = 9.9, 7.7 Hz, 1H), 3.36 (dd, *J* = 9.9, 5.2 Hz, 1H), 3.20 (ddd, *J* = 7.7, 5.2, 2.9 Hz, 1H), 2.84 (d, *J* = 2.9 Hz, 1H), 2.46 – 2.35 (m, 2H), 2.24 (dd, *J* = 10.9, 6.6 Hz, 1H), 2.16 – 2.09 (m, 1H), 2.09 – 2.02 (m, 1H), 1.93 (*virt.* tdd, *J* = 14.3, 10.9, 3.7 Hz, 1H), 1.76 – 1.65 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 203.1, 137.3, 131.7 (2C), 129.4 (2C), 121.7, 88.4, 72.8, 67.9, 65.5, 53.3, 49.7, 43.3, 40.0, 27.2, 24.3.

HRMS (ESI): calculated for $C_{17}H_{19}BrNaO_3^+$, $[M+Na]^+$ = 373.0410; found = 373.0412.

(3*S*,3a*R*,7a*R*)-5,5-Dimethylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (5g)



5g was prepared according to the general procedure after 14 hours of irradiation and purified by flash chromatography on silica gel (from 20 to 50% EtOAc in hexanes) to obtain 11.7 mg of product as a white solid (65% yield). The enantiomeric excess (84% *ee*) was determined by GC on a *Macherey-Nagel Lipodex E* column [τ_{major} = 12.9 min, τ_{minor} = 12.5 min; 60 ºC (1 min), 170 ºC (15 ºC/min), 200 ºC (4 ºC/min), 200 ºC (5 min)].

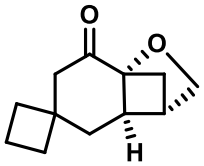
R_f = 0.36 (50% EtOAc in hexanes).

$[\alpha]^{24}_D$ = +17 (*c* = 0.96, $CHCl_3$).

The NMR data were in accordance with the data reported in the literature.[2]

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.96 (d, *J* = 6.1 Hz, 1H), 3.89 (d, *J* = 6.1 Hz, 1H), 2.84 (d, *J* = 3.1 Hz, 1H), 2.80 (ddd, *J* = 8.0, 3.1, 1.1 Hz, 1H), 2.42 – 2.35 (m, 2H), 2.05 (dd, *J* = 14.2, 2.3 Hz, 1H), 1.90 – 1.83 (m, 2H), 1.79 (ddd, *J* = 14.2, 6.9, 2.3 Hz, 1H), 1.10 (s, 3H), 0.88 (s, 3H).

(3'*S*,3a'*R*,7a'*R*)-Tetrahydrospiro{cyclobutane-1,5'-[3,7a]methanobenzofuran}-7'(6'*H*)-one (5h)



5h was prepared according to the general procedure after 14 hours of irradiation and purified by flash chromatography on silica gel (from 20 to 50% EtOAc in hexanes) to obtain 11.4 mg of product as a white solid (59% yield). The enantiomeric excess (80% *ee*) was determined by GC on a *Macherey-Nagel Lipodex E* column [τ_{major} = 16.0 min, τ_{minor} = 14.9 min; 60 ºC (1 min), 170 ºC (15 ºC/min), 200 ºC (4 ºC/min), 200 ºC (5 min)].

R_f = 0.43 (50% EtOAc in hexanes).

mp = 58-62 ºC

IR: ṽ [cm^{-1}] = 2929, 1715, 1469, 1422, 1127, 983, 899, 750.

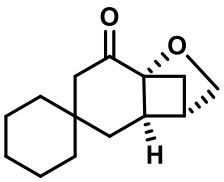
$[\alpha]^{24}_D$ = + 22 (*c* = 1.2, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.94 (d, *J* = 6.0 Hz, 1H), 3.86 (d, *J* = 6.0 Hz, 1H), 2.84 (d, *J* = 3.1 Hz, 1H), 2.81 (ddd, *J* = 7.9, 3.1, 1.1 Hz, 1H), 2.52 (dd, *J* = 14.1, 2.2 Hz, 1H), 2.45 (d, *J* = 14.1 Hz, 1H), 2.32 (ddd, *J* = 11.2, 7.9, 6.4 Hz, 1H), 2.18 (ddd, *J* = 13.9, 6.4, 2.2 Hz, 1H), 1.99 – 1.81 (m, 6H), 1.77 – 1.71 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 202.9, 88.6, 71.3, 52.4, 51.5, 45.8, 41.3, 41.2, 36.9, 33.2, 30.7, 15.5.

HRMS (ESI): calculated for $C_{12}H_{17}O_2^+$, $[M+H]^+$ = 193.1223; found = 193.1223.

(3'*S*,3a'*R*,7a'*R*)-Tetrahydrospiro{cyclohexane-1,5'-[3,7a]methanobenzofuran}-7'(6'*H*)-one (5i)



5i was prepared according to the general procedure after 14 hours of irradiation and purified by flash chromatography on silica gel (from 20 to 50% EtOAc in hexanes) to obtain 10.3 mg of product as a white solid (47% yield). The enantiomeric excess (80% *ee*) was determined by GC on a *Macherey-Nagel Lipodex E* column [τ_{major} = 21.3 min, τ_{minor} = 20.6 min; 60 ºC (1 min), 170 ºC (15 ºC/min), 200 ºC (4 ºC/min), 200 ºC (25 min)].

R_f = 0.52 (50% EtOAc in hexanes).

mp = 55-60 ºC

IR: ṽ [cm^{-1}] = 2925, 2854, 1715, 1453, 1120, 966, 927.

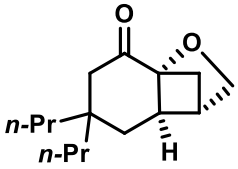
$[\alpha]^{24}_D$ = + 7 (*c* = 0.75, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.95 (d, *J* = 6.1 Hz, 1H), 3.87 (d, *J* = 6.1 Hz, 1H), 2.83 (d, *J* = 3.1 Hz, 1H), 2.81 (ddd, *J* = 7.9, 3.1, 1.0 Hz, 1H), 2.37 – 2.29 (m, 2H), 2.22 (d, *J* = 14.2 Hz, 1H), 2.10 (ddd, *J* = 14.2, 6.6, 2.4 Hz, 1H), 1.85 (*virt*. t, *J* = 7.8 Hz, 1H), 1.66 (dd, *J* = 14.2, 11.6 Hz, 1H), 1.51 – 1.34 (m, 8H), 1.28 – 1.21 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 203.4, 88.8, 71.6, 52.0, 50.8, 42.7, 41.2, 41.1, 39.7, 35.2, 33.1, 26.0, 22.0, 21.1.

HRMS (ESI): calculated for $C_{14}H_{20}NaO_2^+$, $[M+Na]^+$ = 243.1356; found = 243.1353.

(3*S*,3a*R*,7a*R*)-5,5-Dipropylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (5j)



5j was prepared according to the general procedure after 14 hours of irradiation and purified by flash chromatography on silica gel (from 10 to 40% EtOAc in hexanes) to obtain 17.2 mg of product as a pale yellow solid (73% yield). The enantiomeric excess (83% *ee*) was determined by GC on an *Agilent CycloSil-B* column [τ_{major} = 43.7 min, τ_{minor} = 43.2 min; 60 ºC (1 min), 220 ºC (3 ºC/min), 220 ºC (5 min)] after diastereoselective reduction to the corresponding alcohol (**10a**).

R_f = 0.24 (25% EtOAc in cyclohexane).

mp = 75-80 ºC

IR: ṽ [cm^{-1}] = 2957, 2927, 1717, 1466, 974, 923.

$[\alpha]^{24}_D$ = + 9.82 (*c* = 1.72, $CHCl_3$).

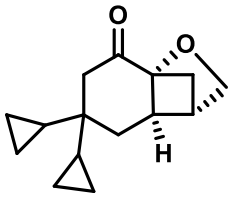
^{1}H NMR (500 MHz, $CDCl_3$): δ 3.96 (d, *J* = 6.0 Hz, 1H), 3.88 (d, *J* = 6.0 Hz, 1H), 2.82 (d, *J* = 3.1 Hz, 1H), 279 (ddd, *J* = 8.1, 3.1, 1.1 Hz, 1H), 2.35 – 2.26 (m, 2H), 2.15 (dd, *J*

= 14.2, 2.4 Hz, 1H), 1.90 (ddd, *J* = 14.2, 6.6, 2.4 Hz, 1H), 1.85 (*virt.* t, *J* = 7.8 Hz, 1H), 1.74 (dd, *J* = 14.2, 11.4 Hz, 1H), 1.34 – 1.07 (m, 8H), 0.90 (t, *J* = 7.0 Hz, 3H), 0.83 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 203.7, 88.7, 71.6, 52.2, 50.1, 45.3, 42.3, 41.3, 41.1, 36.9, 33.9, 16.7, 16.1, 14.9, 14.7.

HRMS (ESI): calculated for $C_{15}H_{24}NaO_2^+$, $[M+Na]^+$ = 259.1669; found = 259.1643.

(3*S*,3a*R*,7a*R*)-5,5-Dicyclopropylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (5k)



5k was prepared according to the general procedure after 14 hours of irradiation and purified by flash chromatography on silica gel (from 10 to 40% EtOAc in hexanes) to obtain 19.0 mg of product as a pale yellow solid (82% yield). The enantiomeric excess (81% *ee*) was determined by GC on an *Agilent CycloSil-B* column [τ_{major} = 201.6 min, τ_{minor} = 200.3 min; 60 ºC (1 min), 170 ºC (0.5 ºC/min), 170 ºC (5 min)] after diastereoselective reduction to the corresponding alcohol (**10b**).

R_f = 0.27 (25% EtOAc in cyclohexane).

mp = 40 ºC

IR: ṽ [cm^{-1}] = 2925, 2855, 1717, 1466, 1275, 1119, 973, 922.

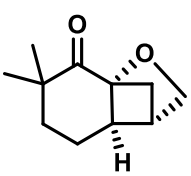
$[\alpha]^{24}_D$ = + 23 (*c* = 1.57, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.97 (d, *J* = 6.1 Hz, 1H), 3.89 (d, *J* = 6.1 Hz, 1H), 2.84 (d, *J* = 3.0 Hz, 1H), 2.74 (ddd, *J* = 8.1, 3.0, 1.0 Hz, 1H), 2.54 (*virt.* dt, *J* = 11.3, 7.3 Hz, 1H), 2.15 (d, *J* = 14.6 Hz, 1H), 2.02 (dd, *J* = 14.6, 2.3 Hz, 1H), 1.89 – 1.80 (m, 2H), 1.75 (dd, *J* = 13.9, 11.3 Hz, 1H), 0.66 (tt, *J* = 8.3, 5.9 Hz, 1H), 0.53 – 0.42 (m, 2H), 0.42 – 0.23 (m, 7H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 203.8, 88.5, 71.5, 51.6, 47.3, 42.8, 41.5, 41.3, 33.9, 18.3, 17.5, 1.4, 0.2, 0.1 (2C).

HRMS (ESI): calculated for $C_{15}H_{20}NaO_2^+$, $[M+Na]^+$ = 255.1356; found = 255.1355.

(3*S*,3a*R*,7a*R*)-6,6-Dimethylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (5l)



5l was prepared according to the general procedure after 24 hours of irradiation and purified by flash chromatography on silica gel (20% EtOAc in *n*-pentane) to obtain 6.8 mg of product as a yellow oil (38% yield). The enantiomeric excess (90% *ee*) was determined by GC on a

Macherey-Nagel Lipodex E column [τ_{major} = 24.3 min, τ_{minor} = 26.3 min; 100 ºC (1 min), 135 ºC (15 ºC/min), 135 ºC (30 min), 200 ºC (15 ºC/min)].

R_f = 0.15 (20% EtOAc in *n*-pentane).

IR: $\tilde{\nu}$ [cm^{-1}] = 2926, 1706, 1466, 1019, 968, 945, 935, 865.

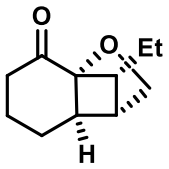
$[\alpha]^{24}_D$ = - 39 (*c* = 1.2, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.92 (d, *J* = 5.9 Hz, 1H), 3.79 (d, *J* = 5.9 Hz, 1H), 2.92 (ddd, *J* = 8.2, 3.2, 1.0 Hz, 1H), 2.86 (d, *J* = 3.2 Hz, 1H), 2.26 (*virt.* dt, *J* = 9.9, 7.8 Hz, 1H), 2.05 – 1.93 (m, 3H), 1.78 (*virt.* dt, *J* = 14.1, 3.5 Hz, 1H), 1.67 (ddd, *J* = 14.2, 11.5, 5.8 Hz, 1H), 1.23 (s, 3H), 1.12 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 208.2, 87.3, 70.4, 54.5, 45.0, 44.0, 41.9, 40.1, 26.1, 25.7, 21.4.

HRMS (ESI): calculated for $C_{11}H_{16}NaO_2^+$, $[M+Na]^+$ = 203.1043; found = 203.1041.

(3*S*,3a*R*,7a*R*,8*R*)-8-Ethylhexahydro-7*H*-3,7a-methanobenzofuran-7-one (5m)



5m was prepared according to the general procedure starting from (*Z*)-**4m** after 14 hours of irradiation and purified by flash chromatography on silica gel (from 0 to 40% EtOAc in hexanes) to obtain 9.2 mg of a mixture of the desired cyclobutane and an olefinic impurity. This by-product was removed by oxidation as reported in our precedent work.[2] The product mixture (51.0 μmol) was dissolved in 400 μL of DCE. Subsequently, 300 μL of water, $RuCl_3 \cdot xH_2O$ (1 small crystal) and 6.3 mg of $NaIO_4$ (29.6 μmol) were added and the reaction mixture was stirred at room temperature for 17 h. The reaction was quenched by addition of water and diluted with diethyl ether. The aqueous layer was extracted with diethyl ether and the combined organic phases were washed with brine and dried over Na_2SO_4. Thus, after evaporation of the solvents at reduced pressure, the residue was purified by flash chromatography on silica gel (from 0 to 40% EtOAc in hexanes) to obtain 8.2 mg of product as a white solid (47% yield). The enantiomeric excess (94% *ee*) was determined by GC on a *Macherey-Nagel Lipodex E* column [τ_{major} = 25.1 min, τ_{minor} = 23.8 min; 100 ºC (1 min), 150 ºC (15 ºC/min), 150 ºC (30 min), 200 ºC (15 ºC/min)]. When (*E*)-**4m** was employed as substrate, the same product was obtained in 47% yield and 86% ee.

R_f = 0.22 (25% EtOAc in hexanes).

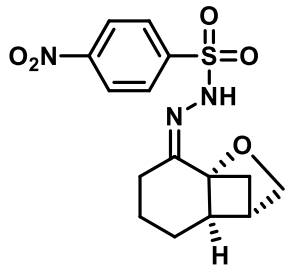
$[\alpha]^{24}_D$ = + 39 (*c* = 0.70, $CHCl_3$).

The NMR data were in accordance with the data reported in the literature.[2]

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.85 (d, *J* = 6.5 Hz, 1H), 3.74 (d, *J* = 6.5 Hz, 1H), 2.83 (ddd, *J* = 8.6, 6.1, 2.9 Hz, 1H), 2.71 (d, *J* = 2.9 Hz, 1H), 2.41 – 2.34 (m, 2H), 2.20 (dd, *J* = 11.0, 6.7 Hz, 1H), 2.15 – 2.09 (m, 1H), 2.07 – 1.99 (m, 1H), 1.92 (*virt.* tdd, *J* = 14.2, 11.0, 3.8 Hz, 1H), 1.76 – 1.64 (m, 1H), 1.49 – 1.36 (m, 1H), 1.30 – 1.20 (m, 1H), 0.78 (t, *J* = 7.5 Hz, 3H).

8. Characterisation Data for the Hydrazone (7)

***N*'-[(3*S*,3a*R*,7a*R*,*Z*)-Hexahydro-7*H*-3,7a-methanobenzofuran-7-ylidene]-4-nitrobenzenesulfonohydrazide (7)**



11.2 mg (73.6 µmol) of **5a** (*ee* of the sample = 92%) were dissolved in anhydrous CH_2Cl_2 (1.0 mL) and 4-nitrobenzenesulfonohydrazide (16.0 mg, 1.0 equiv.) were added. The reaction mixture was stirred overnight at room temperature and, after solvent removal, purified by flash chromatography on silica gel (20% EtOAc in hexanes) to obtain 19.0 mg of the desired product **7** as a pale yellow solid (73% yield).

R_f = 0.30 (33% EtOAc in hexanes).

mp = 145-150 ºC

IR: ṽ [cm^{-1}] = 3189, 2957, 2893, 1534, 1349, 1308, 1172, 1054, 922, 898, 851, 736, 681.

$[\alpha]^{24}_D$ = + 80 (*c* = 1.00, $CHCl_3$).

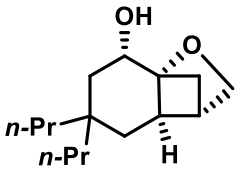
^{1}H NMR (500 MHz, $CDCl_3$): δ 10.44 (s, 1H), 8.37 – 8.32 (m, 2H), 8.14 – 8.09 (m, 2H), 3.97 (d, *J* = 5.9 Hz, 1H), 3.86 (d, *J* = 5.9 Hz, 1H), 2.75 (d, *J* = 3.2 Hz, 1H), 2.59 (dd, *J* = 8.4, 3.2 Hz, 1H), 2.43 (*virt.* dt, *J* = 15.8, 3.4 Hz, 1H), 2.09 – 1.85 (m, 4H), 1.79 (*virt.* t, J = 8.0 Hz, 1H), 1.62 – 1.51 (m, 1H), 1.33 – 1.22 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 151.5, 150.3, 145.0, 129.2 (2C), 124.2 (2C), 87.7, 71.6, 53.7, 40.2, 40.0, 32.8, 25.3, 25.0.

HRMS (ESI): calculated for $C_{15}H_{18}N_3O_5S^+$, $[M+H]^+$ = 352.0962; found = 352.0964.

9. Characterisation Data for the Derivatized Cyclobutanes (10-15)

(3*S*,3a*R*,7*S*,7a*R*)-5,5-Dipropylhexahydro-2*H*-3,7a-methanobenzofuran-7-ol (10a)



The diastereoselective reduction was achieved upon dropwise addition of DIBAL-H (0.364 mmol, 364 µL of a 1 M solution in hexanes, 5.0 equiv.) to a solution of ketone **5j** (17.2 mg, 72.8 µmol) in dry CH_2Cl_2 (1.5 mL) at -78 ºC. After 90 min the reaction was quenched with a saturated solution of NH_4Cl and extracted with EtOAc. After removal of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (8% EtOAc in *n*-pentane) to obtain 17.1 mg of product as a colourless oil (99% yield).

R_f = 0.25 (10% EtOAc in *n*-pentane).

IR: ṽ [cm^{-1}] = 2924, 2855, 1731, 1464, 1288, 965.

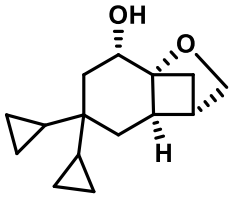
$[\alpha]^{24}_D$ = - 54 (*c* = 0.33, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.04 (dd, *J* = 3.7, 2.5 Hz, 1H), 3.87 – 3.82 (m, 2H), 2.67 (d, *J* = 3.1 Hz, 1H), 2.27 (dd, *J* = 8.1, 3.1 Hz, 1H), 2.06 – 1.92 (m, 2H), 1.84 (*virt.* dt, *J* = 15.1, 2.5 Hz, 1H), 1.79 (ddd, *J* = 13.8, 6.5, 2.5 Hz, 1H), 1.55 (ddd, *J* = 13.8, 12.3, 4.2 Hz, 1H), 1.47 – 1.36 (m, 2H), 1.32 – 1.10 (m, 8H), 0.90 – 0.83 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 88.8, 71.2, 66.4, 44.1, 43.3, 40.0, 39.0, 37.3, 37.2, 35.6, 35.3, 16.7, 16.3, 15.2, 15.1.

HRMS (ESI): calculated for $C_{15}H_{26}NaO_2^+$, $[M+Na]^+$ = 261.1825; found = 261.1828.

(3*S*,3a*R*,7*S*,7a*R*)-5,5-Dicyclopropylhexahydro-2*H*-3,7a-methanobenzofuran-7-ol (10b)



The diastereoselective reduction was achieved upon dropwise addition of DIBAL-H (0.323 mmol, 323 µL of a 1.0 M solution in hexanes, 5.0 equiv.) to a solution of ketone **5k** (15.0 mg, 64.6 µmol) in dry CH_2Cl_2 (1.3 mL) at -78 ºC. After 90 min the reaction was quenched with a saturated solution of NH_4Cl and extracted with EtOAc. After removal of the solvents at reduced pressure the residue was purified by flash chromatography on silica gel (15% EtOAc in *n*-pentane) to obtain 10.6 mg of product as a colourless oil (70% yield).

R_f = 0.12 (10% EtOAc in *n*-pentane).

IR: ṽ [cm^{-1}] = 2923, 2856, 1733, 1465, 1289, 765.

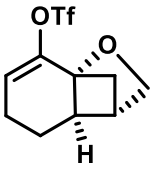
[α]$^{24}_{D}$ = - 32 (*c* = 1.2, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.11 (dd, *J* = 3.9, 2.4 Hz, 1H), 3.86 (s, 2H), 2.69 (d, *J* = 3.1 Hz, 1H), 2.22 – 2.14 (m, 2H), 2.12 (br s, 1H), 1.73 (*virt.* dt, *J* = 14.9, 2.4 Hz, 1H), 1.64 – 1.54 (m, 2H), 1.46 (*virt.* t, *J* = 7.9 Hz, 1H), 1.32 (dd, *J* = 14.9, 3.9 Hz, 1H), 1.17 (dd, *J* = 13.7, 11.1 Hz, 1H), 0.56 – 0.44 (m, 2H), 0.41 – 0.29 (m, 2H), 0.29 – 0.10 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 88.7, 71.1, 66.3, 42.8, 40.3, 38.6, 37.1, 33.0, 32.0, 19.2, 16.3, 1.4, 1.3, 0.2, -0.5.

HRMS (ESI): calculated for $C_{15}H_{22}NaO_2^+$, $[M+Na]^+$ = 257.1512; found = 257.1511.

(3*S*,3a*R*,7a*R*)-3,3a,4,5-tetrahydro-2*H*-3,7a-methanobenzofuran-7-yl trifluoromethanesulfonate (11)



152 mg (1.00 mmol) of **5a** (*ee* of the sample = 92%) were dissolved in 3.5 mL of anhydrous THF and cooled to -78 ºC. Then, 1.50 mL (1.50 mmol) of a 1 M solution in THF of LHMDS was dropwise added and stirred at the same temperature for 2 hours. 1.43 g (4.00 equiv.) of $PhNTf_2$ in 3.0 mL of anhydrous THF were dropwise added and stirred at -78 ºC for 30 min before removing the cooling bath and allowing the reaction mixture to stir for 12 hours at room temperature. The excess of LHMDS was quenched with a saturated aqueous solution of NH_4Cl, extracted with Et_2O, washed with brine and dried over Na_2SO_4. After removal of the solvents at reduced pressure the residue was purified by flash chromatography on basic alumina (10% Et_2O in *n*-pentane) to obtain 225 mg of product **11** as a colourless oil (79% yield).

R_f = 0.23 (10% Et_2O in *n*-pentane).

IR: ṽ [cm^{-1}] = 2894, 1416, 1204, 1142, 1039, 993, 898, 860, 811.

[α]$^{24}_{D}$ = - 61 (*c* = 1.00, $CHCl_3$).

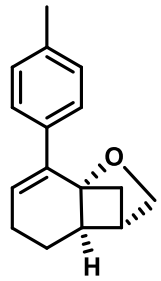
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.84 (t, *J* = 4.1 Hz, 1H), 3.96 (d, *J* = 5.9 Hz, 1H), 3.90 (d, *J* = 5.9 Hz, 1H), 2.81 (d, *J* = 3.1 Hz, 1H), 2.40 – 2.35 (m, 2H), 2.32 (ddd, *J* = 8.2, 3.1, 1.2 Hz, 1H), 2.18 (ddd, *J* = 12.7, 7.2, 5.1 Hz, 1H), 2.09 – 2.03 (m, 1H), 1.93 – 1.81 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 144.9, 123.5, 118.7 (q, *J* = 320.3 Hz), 82.4, 72.1, 53.1, 42.6, 39.9, 25.7, 22.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -73.8.

HRMS (ESI): calculated for $C_{10}H_{12}F_3O_4S^+$, $[M+H]^+$ = 285.0403; found = 285.0403.

(3*S*,3a*R*,7a*R*)-7-(*p*-tolyl)-3,3a,4,5-tetrahydro-2*H*-3,7a-methanobenzofuran (12)



In an oven dried vial were placed 28.4 mg (0.100 mmol) of **11**, 16.3 mg (1.20 equiv.) of *p*-tolylboronic acid, 2.2 mg (0.10 equiv.) of $Pd(OAc)_2$, 7.9 mg (0.30 equiv.) of PPh_3 and dissolved in 2.0 mL of 1,4-dioxane before adding 200 µL (2.00 equiv.) of a 1 M aqueous solution of Na_2CO_3. After purging the system with argon by bubbling for 5 min, the reaction mixture was stirred at rt until consumption of the starting material as judged by TLC (7 hours). Water was added to the reaction mixture, extracted with Et_2O, washed with brine and dried over Na_2SO_4. After removal of the solvents at reduced pressure the residue was purified by preparative thin layer chromatography (10% Et_2O in *n*-pentane) to obtain 16.5 mg of product **12** as a colourless oil (73% yield).

R_f = 0.20 (5% Et_2O in *n*-pentane).

IR: $\tilde{\nu}$ [cm^{-1}] = 2927, 2850, 1514, 1436, 1342, 1137, 920, 797.

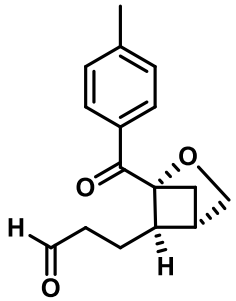
$[\alpha]^{24}_D$ = + 9 (*c* = 1.00, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.31 (m, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.11 (dd, *J* = 5.6, 2.6 Hz, 1H), 3.96 (d, *J* = 5.7 Hz, 1H), 3.87 (d, *J* = 5.7 Hz, 1H), 2.80 (d, *J* = 3.1 Hz, 1H), 2.41 (ddd, *J* = 7.9, 3.1, 1.1 Hz, 1H), 2.39 – 2.20 (m, 5H), 2.16 – 2.00 (m, 3H), 1.95 – 1.83 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 136.7, 135.9, 135.2, 129.0 (2C), 128.7, 126.1 (2C), 86.7, 71.5, 50.9, 44.0, 39.7, 25.5, 23.5, 21.2.

HRMS (ESI): calculated for $C_{16}H_{19}O^+$, $[M+H]^+$ = 227.1430; found = 227.1432.

3-{(1*R*,4*S*,5*R*)-1-(4-methylbenzoyl)-2-oxabicyclo[2.1.1]hexan-5-yl}propanal (13)



16.5 mg (72.9 µmol) of **12** were dissolved in 6.0 mL of anhydrous CH_2Cl_2 and cooled to -78 ºC. The solution was purged with argon and oxygen before switching on the ozone generator. Ozone was bubbled into the solution until the latter turned to blue. Thus, any excess of ozone was removed by subsequent purging by oxygen and argon and 38.2 mg (2.00 equiv.) of PPh_3 in anhydrous CH_2Cl_2were added. The reaction mixture was allowed to slowly warm to rt overnight and, after removal of the solvents under reduced pressure, the residue was purified by preparative thin layer chromatography (50% Et_2O in *n*-pentane) to obtain 14.8 mg of product **13** as a colourless oil (79% yield). The enantiomeric excess (92% *ee*) was determined by reverse phase HPLC on a *Daicel Chiralcel* OD-RH column [τ_{major} = 15.3 min, τ_{minor} = 14.8 min;

flow rate 1.0 mL/min; acetonitrile:water = gradient from 20:80 to 100:0 in 30 min; λ = 215 nm].

R_f = 0.17 (50% Et_2O in *n*-pentane).

IR: ν̃ [cm^{-1}] = 2956, 2922, 2890, 1723, 1668, 1605, 1345, 1167, 927, 740.

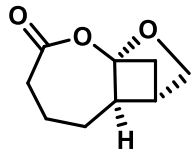
$[\alpha]^{24}_D$ = - 15 (*c* = 1.0, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.67 (*virt.* t, *J* = 1.4 Hz, 1H), 8.04 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 4.04 (d, *J* = 5.7 Hz, 1H), 3.96 (d, *J* = 5.7 Hz, 1H), 2.79 (ddd, *J* = 8.4, 3.4, 1.1 Hz, 1H), 2.74 (d, *J* = 3.4 Hz, 1H), 2.49 – 2.31 (m, 6H), 2.02 – 1.89 (m, 2H), 1.85 (*virt.* t, *J* = 8.0 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 201.6, 195.3, 144.6, 133.1, 129.7 (2C), 129.3 (2C), 93.1, 71.2, 58.6, 42.8, 40.2, 38.6, 21.9, 19.3.

HRMS (ESI): calculated for $C_{16}H_{19}O_3^+$, $[M+H]^+$ = 259.1329; found = 259.1331.

(3*S*,3a*R*,8a*S*)-hexahydro-7*H*-3,8a-methanofuro[2,3-b]oxepin-7-one (14)



To a stirring solution of 45.7 mg (0.300 mmol) of **5a** (*ee* of the sample = 92%) in anhydrous CH_2Cl_2 (3.0 mL) 202 mg of *m*-CPBA (77%, 3.00 equiv.) were added. The reaction mixture was stirred overnight at room temperature until full conversion as judged by TLC (10% EtOAc in CH_2Cl_2). The reaction mixture was subsequently washed with a 10% solution of Na_2SO_3, a saturated solution of $NaHCO_3$ and brine, before being dried over Na_2SO_4. After removal of the solvent at reduced pressure the residue was purified by flash chromatography on silica gel (50% EtOAc in hexanes) to obtain 13.1 mg of the desired product **14** as a white solid (26% yield).

R_f = 0.45 (10% EtOAc in CH_2Cl_2).

IR: ν̃ [cm^{-1}] = 2920, 1775, 1736, 1238, 1170, 1044, 911.

mp = 70-80 ºC

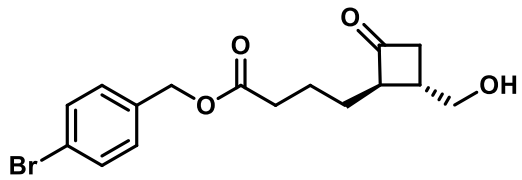
$[\alpha]^{24}_D$ = + 26 (*c* = 0.50, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.84 (s, 2H), 2.85 (dddd, *J* = 14.8, 9.2, 2.3, 0.9 Hz, 1H), 2.65 (dd, *J* = 7.9, 3.7 Hz, 1H), 2.61 – 2.49 (m, 3H), 2.17 – 2.08 (m, 1H), 2.05 (*virt.* t, *J* = 7.7 Hz, 1H), 2.00 – 1.90 (m, 1H), 1.86 – 1.73 (m, 1H), 1.69 – 1.57 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.4, 105.7, 69.8, 55.3, 40.5, 36.4, 36.1, 25.6, 21.9.

HRMS (ESI): calculated for $C_9H_{12}NaO_3^+$, $[M+Na]^+$ = 191.0679; found = 191.0678.

4-Bromobenzyl 4-[(1*R*,2*S*)-2-(hydroxymethyl)-4-oxocyclobutyl]butanoate (15)



12.2 mg (72.6 µmol) of **14** were dissolved in CH_2Cl_2 (0.73 mL), then 1.8 mg (0.20 equiv.) of DMAP, 67.8 mg (5.00 equiv.) of 4-bromobenzyl alcohol and 30.0 µL (3.00 equiv.) of triethylamine were added. After overnight stirring the solvent was removed and the residue was purified by flash chromatography on silica gel (from 10 to 50% EtOAc in hexanes) to obtain 15.6 mg of the desired product **15** as a colourless oil (60% yield). The enantiomeric excess (92% *ee*) was determined by normal phase HPLC on a *Daicel Chiralpak* AS-H column [τ_{major} = 34.8 min, τ_{minor} = 39.2 min; flow rate 1.0 mL/min; *i*-PrOH:*n*-heptane = 10:90; λ = 210 nm].

R_f = 0.22 (50% EtOAc in hexanes).

IR: ṽ [cm^{-1}] = 3456, 2925, 2856, 1773, 1734, 1490, 1352, 1071, 1013, 802.

$[\alpha]^{24}_D$ = + 18 (*c* = 0.50, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 – 7.45 (m, 2H), 7.24 – 7.19 (m, 2H), 5.05 (s, 2H), 3.87 – 3.75 (m, 2H), 3.07 – 3.00 (m, 1H), 2.96 (ddd, *J* = 17.3, 8.6, 2.4 Hz, 1H), 2.83 (ddd, *J* = 17.3, 7.4, 2.9 Hz, 1H), 2.41 – 2.33 (m, 2H), 2.29 – 2.19 (m, 1H), 1.85 (br s, 1H), 1.81 – 1.64 (m, 3H), 1.63 – 1.47 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 209.2, 173.3, 135.1, 131.9 (2C), 130.1 (2C), 122.4, 65.6, 65.5, 62.0, 46.8, 34.0, 33.2, 28.4, 22.6.

HRMS (ESI): calculated for $C_{16}H_{20}BrO_4^+$, $[M+H]^+$ = 355.0539; found = 355.0540.

10. NMR Spectra

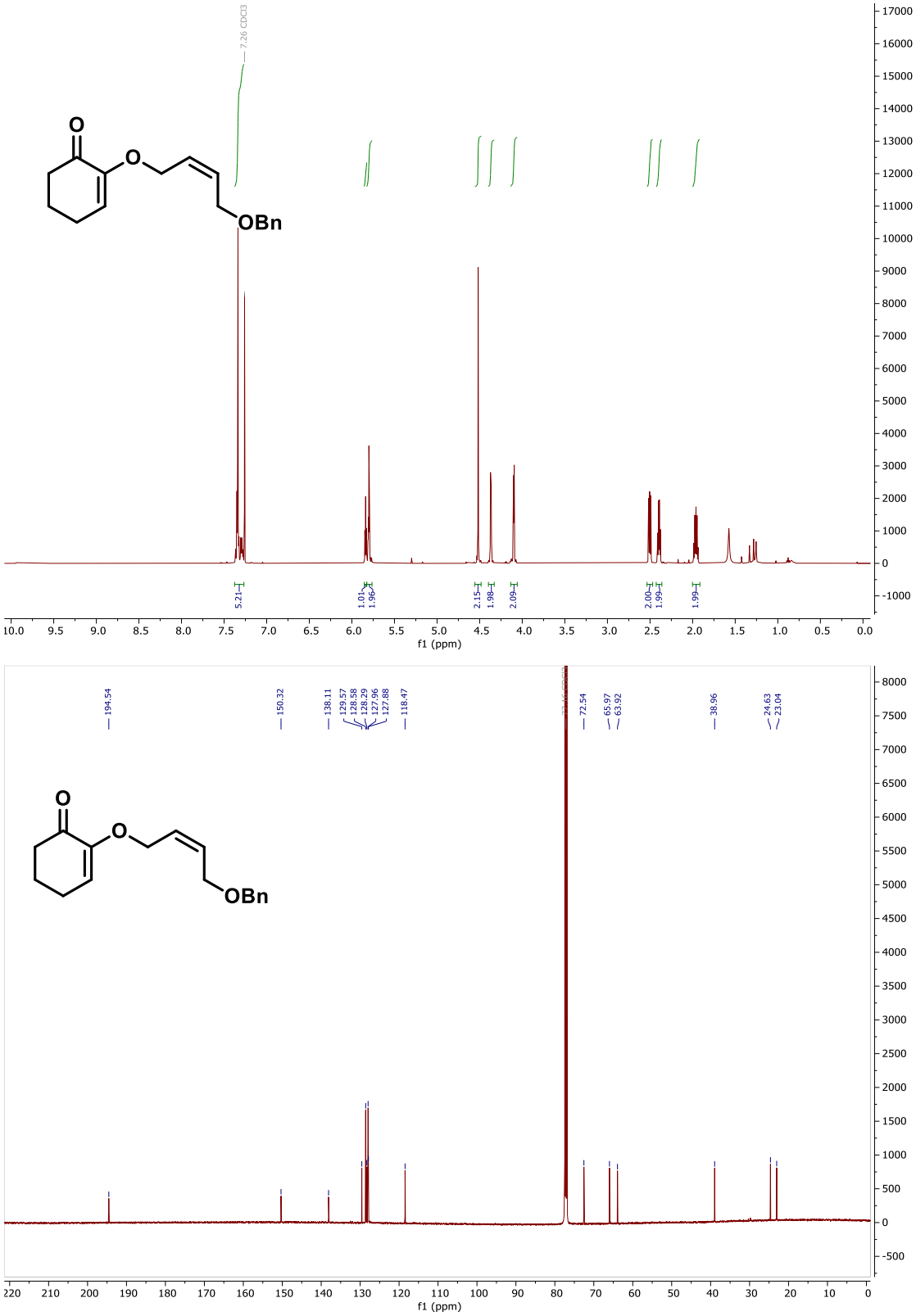


Figure S2: ^{1}H and ^{13}C NMR spectra for compound **4d** (500 and 126 MHz, $CDCl_3$, 300K).

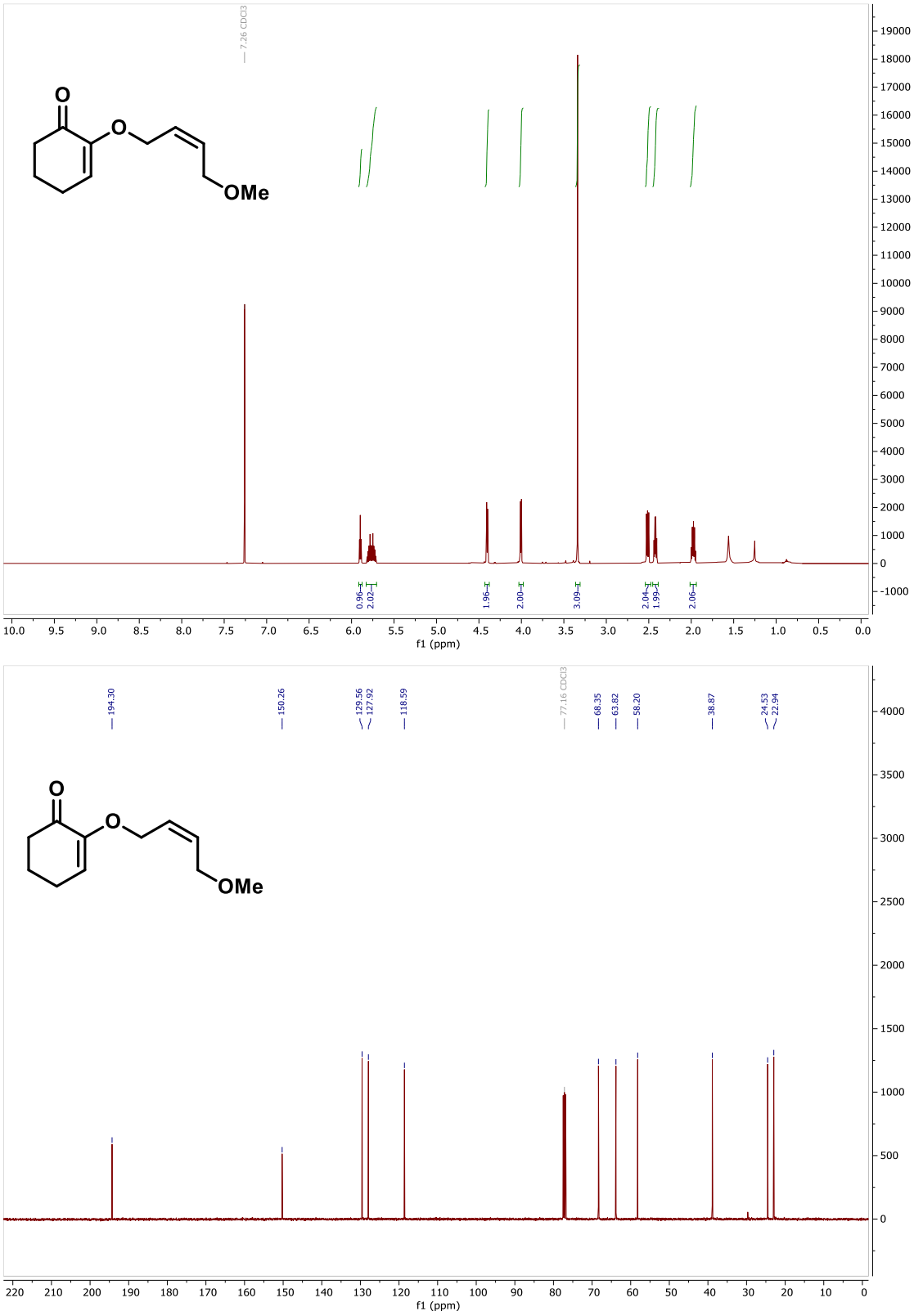


Figure S3: ^{1}H and ^{13}C NMR spectra for compound **4e** (500 and 101 MHz, $CDCl_3$, 300K).

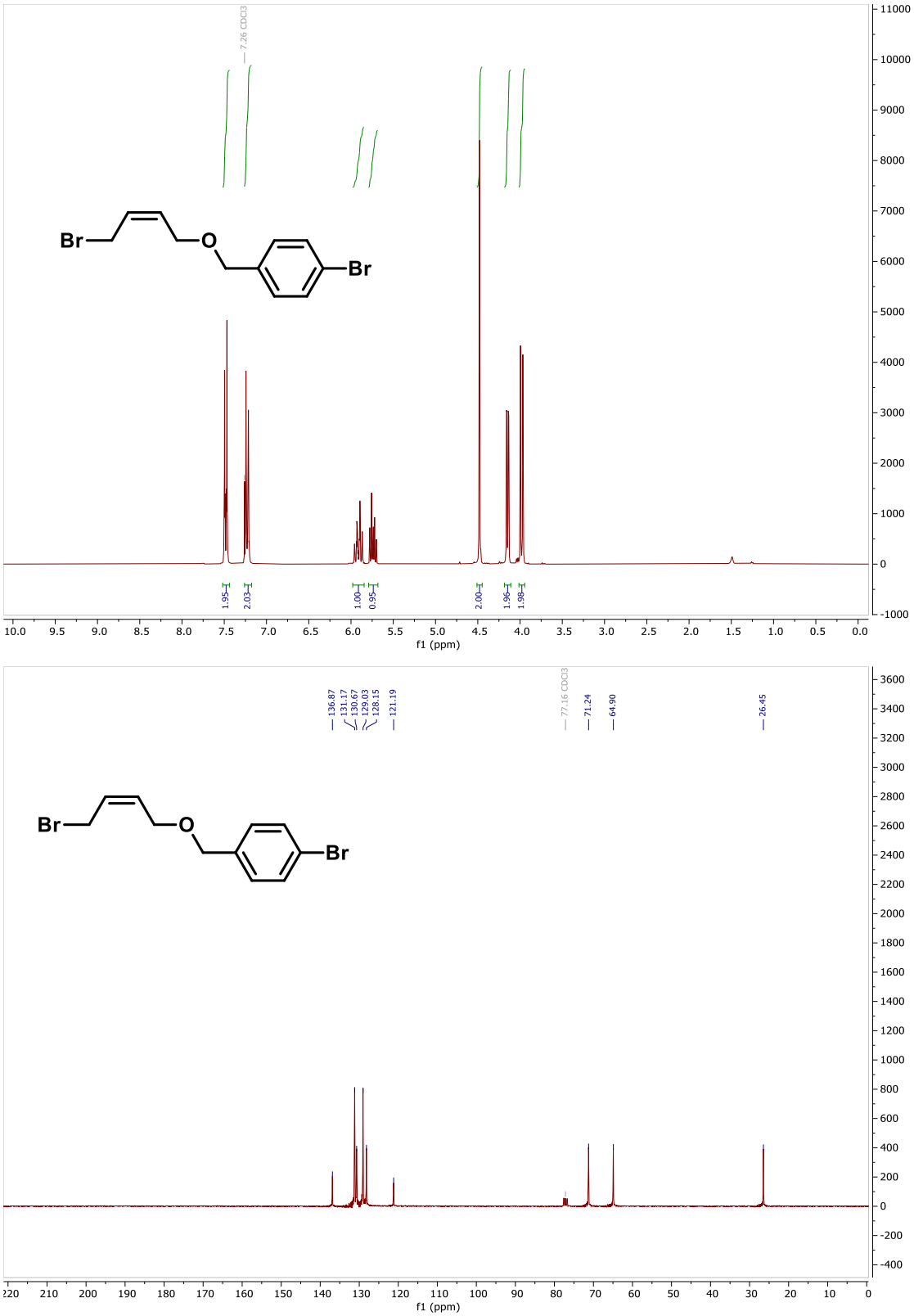


Figure S4: ^{1}H and ^{13}C NMR spectra for compound **S5** (300 and 75 MHz, $CDCl_3$, 300K).

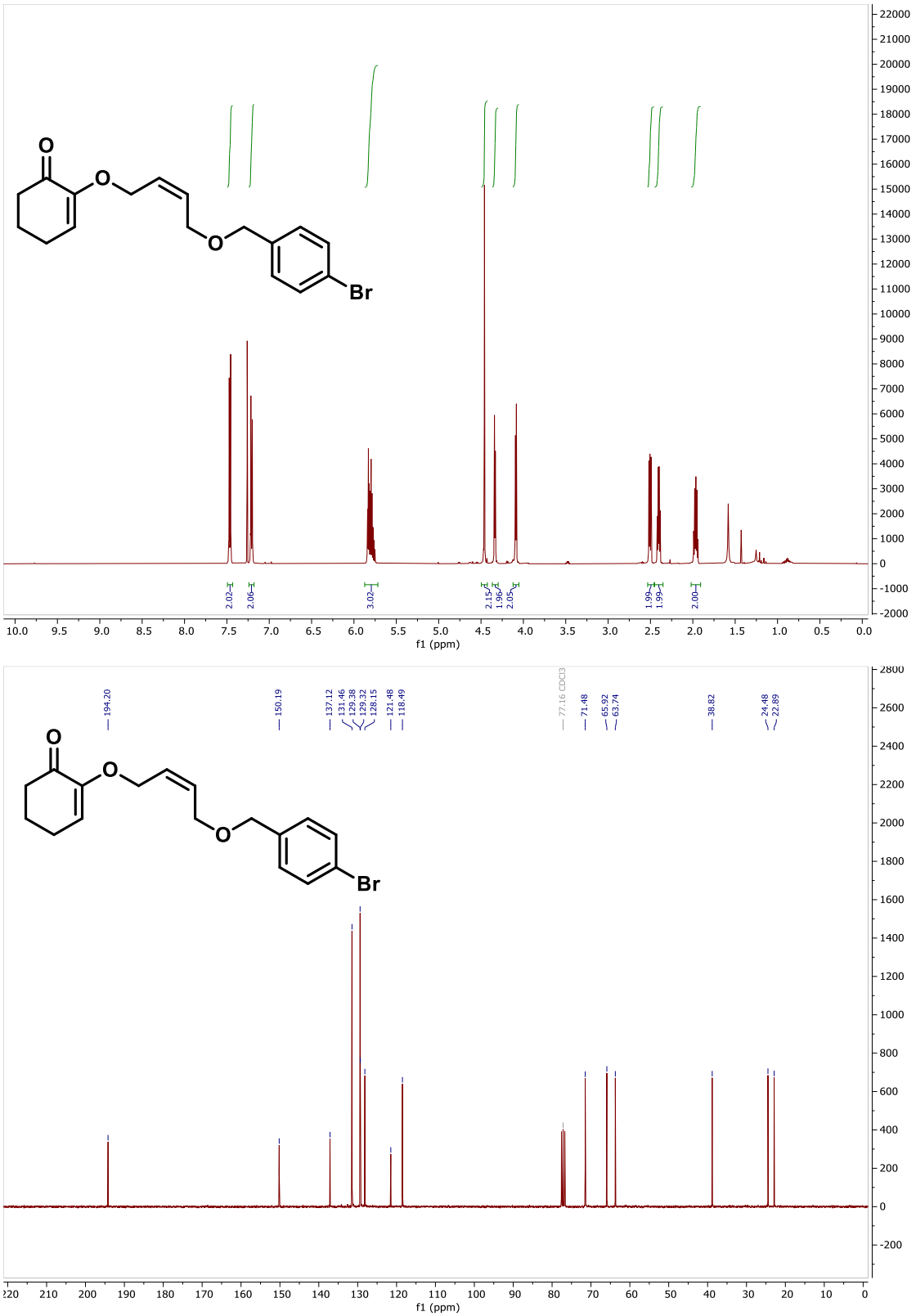


Figure S5: ^{1}H and ^{13}C NMR spectra for compound **4f** (500 and 75 MHz, $CDCl_3$, 300K).

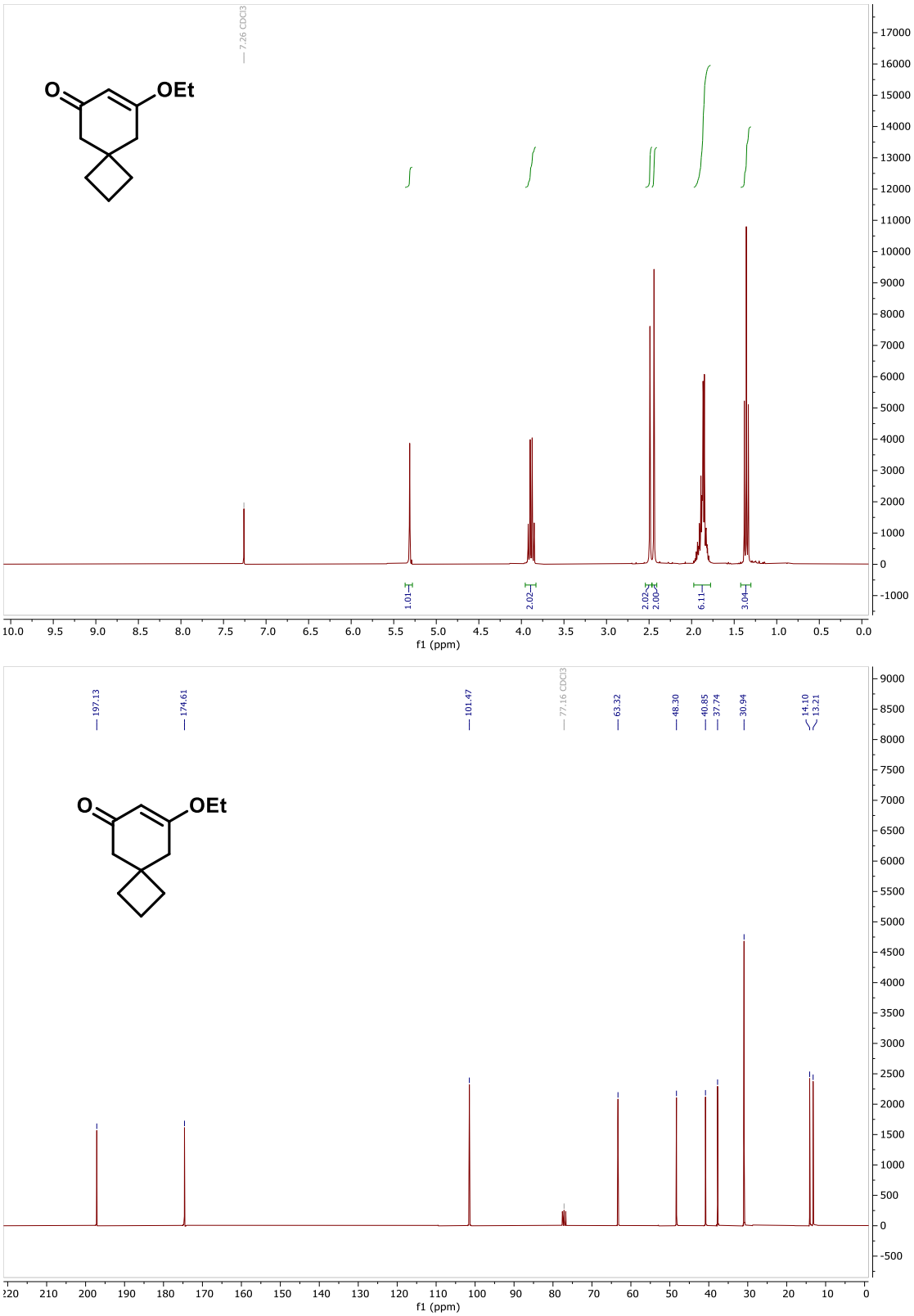


Figure S6: ^{1}H and ^{13}C NMR spectra for compound **S8** (300 and 75 MHz, $CDCl_3$, 300K).

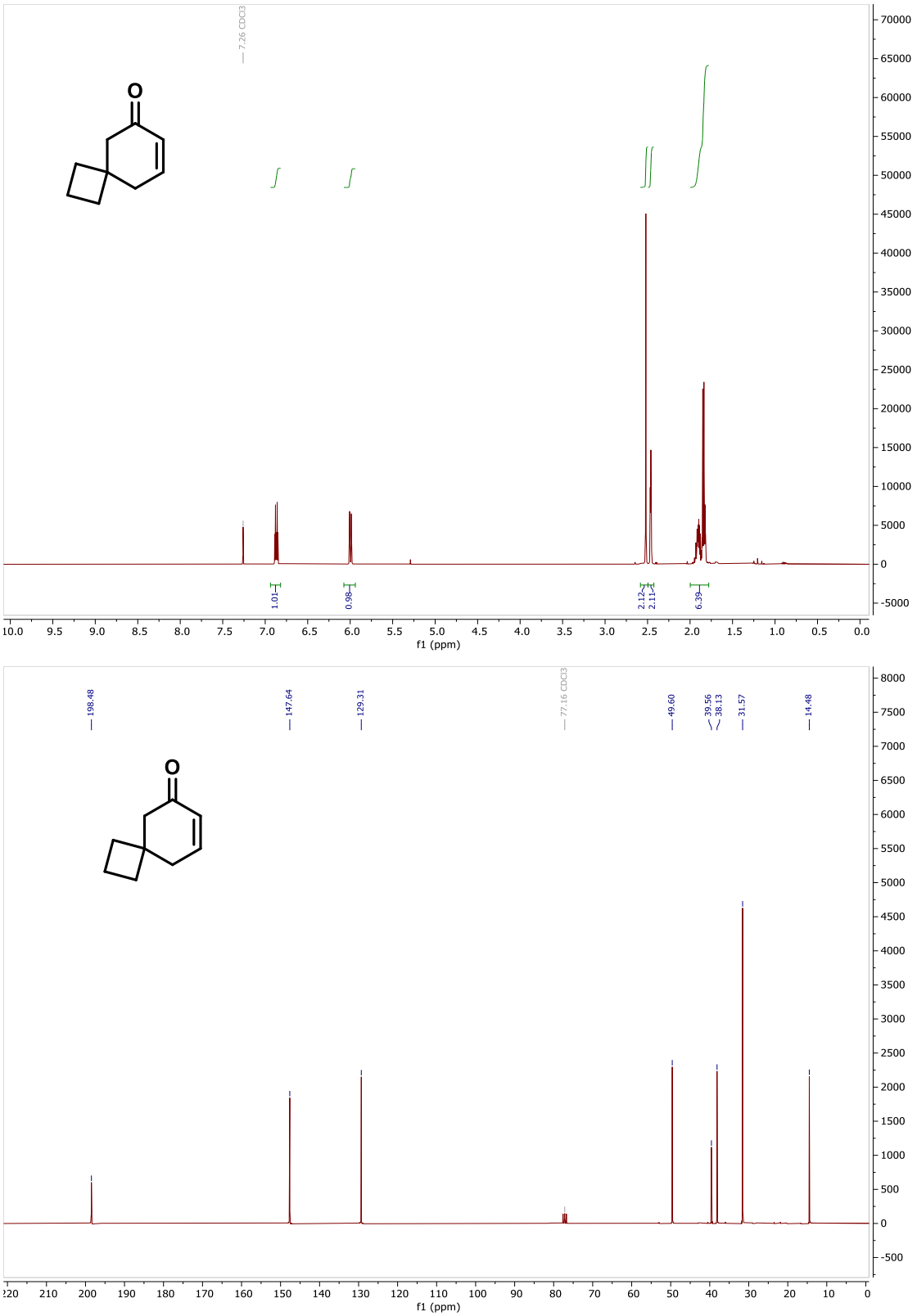


Figure S7: ^{1}H and ^{13}C NMR spectra for compound **S9** (500 and 75 MHz, $CDCl_3$, 300K).

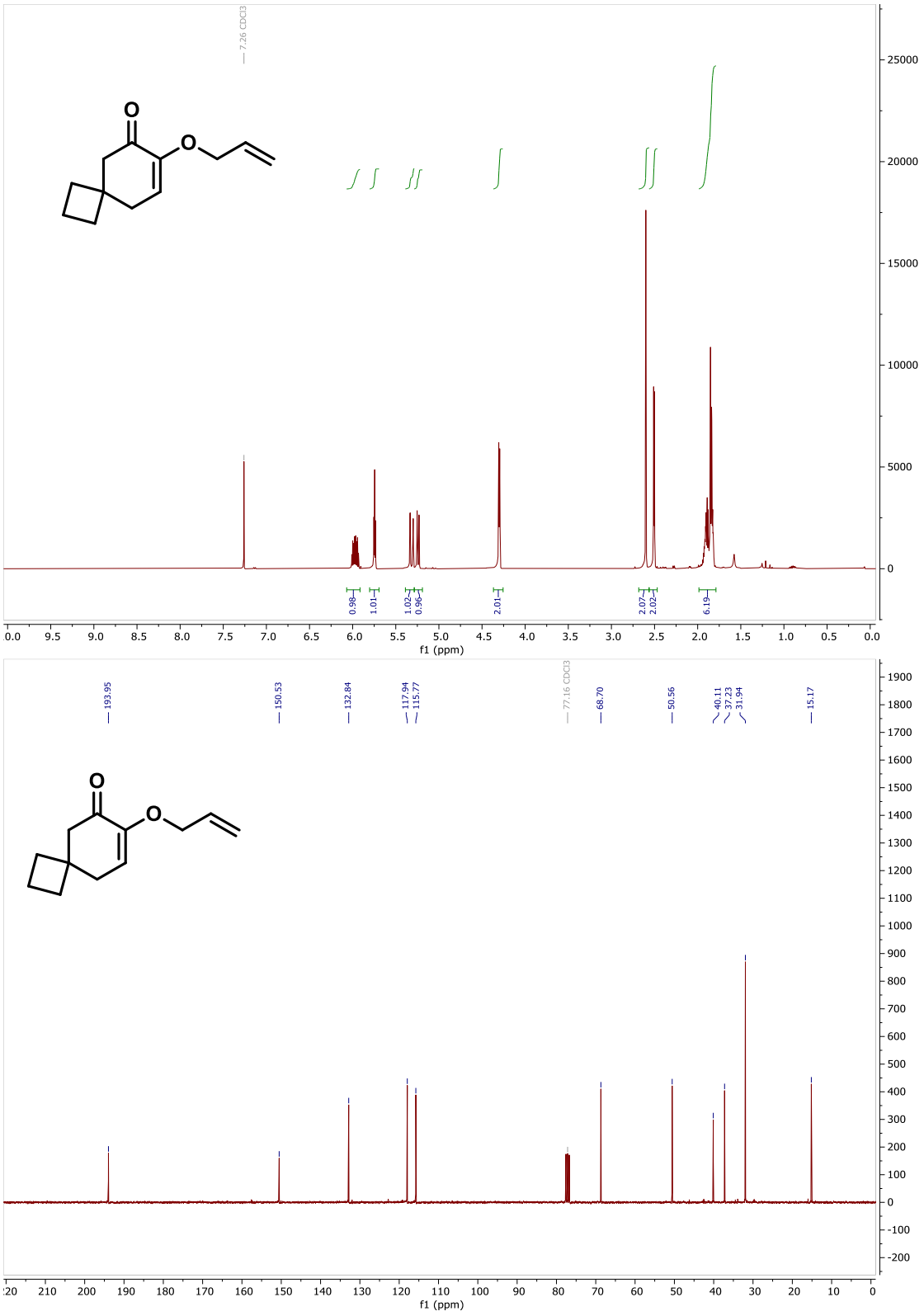


Figure S8: ^{1}H and ^{13}C NMR spectra for compound **4h** (500 and 75 MHz, $CDCl_3$, 300K).

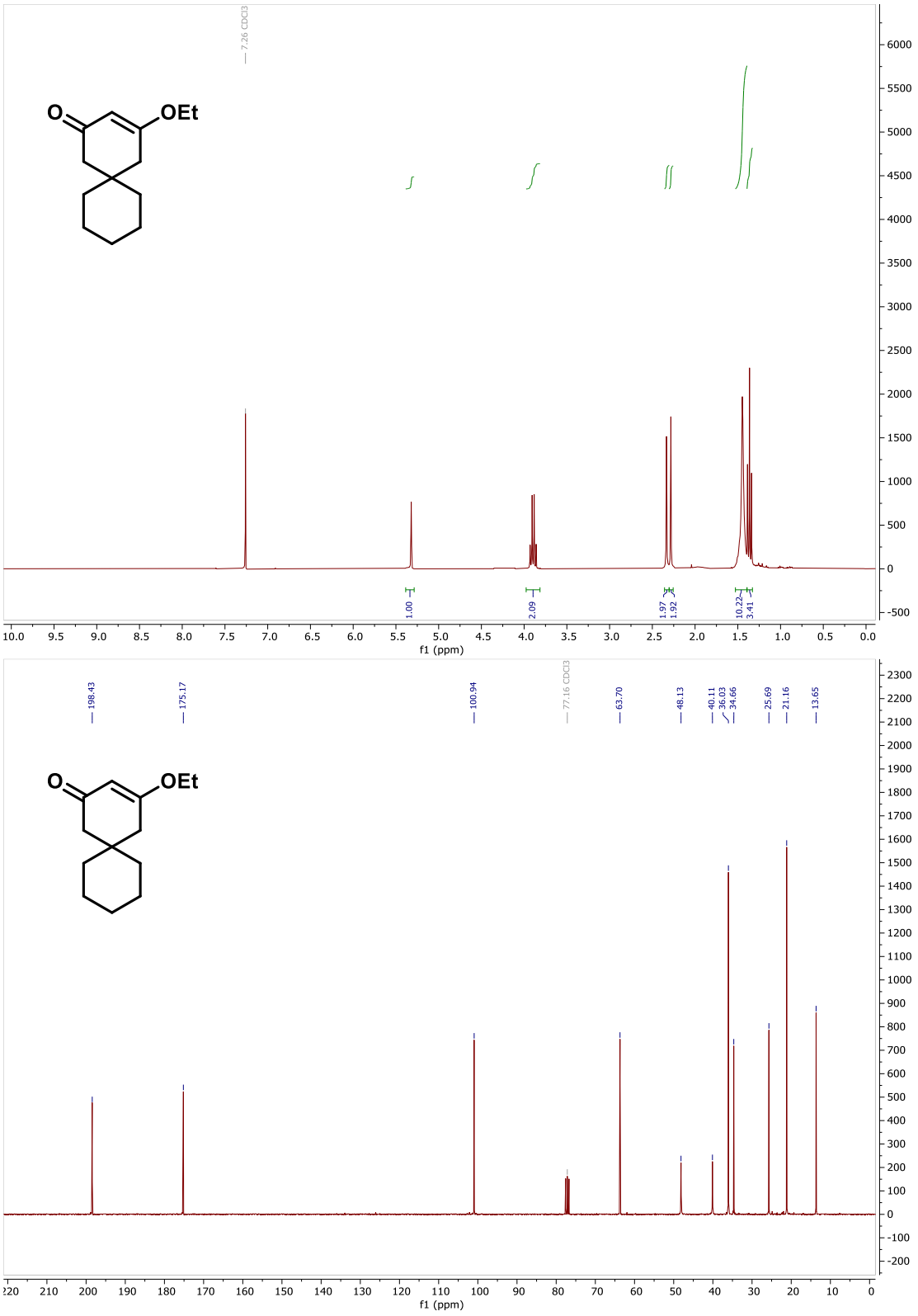


Figure S9: ^{1}H and ^{13}C NMR spectra for compound **S12** (300 and 75 MHz, $CDCl_3$, 300K).

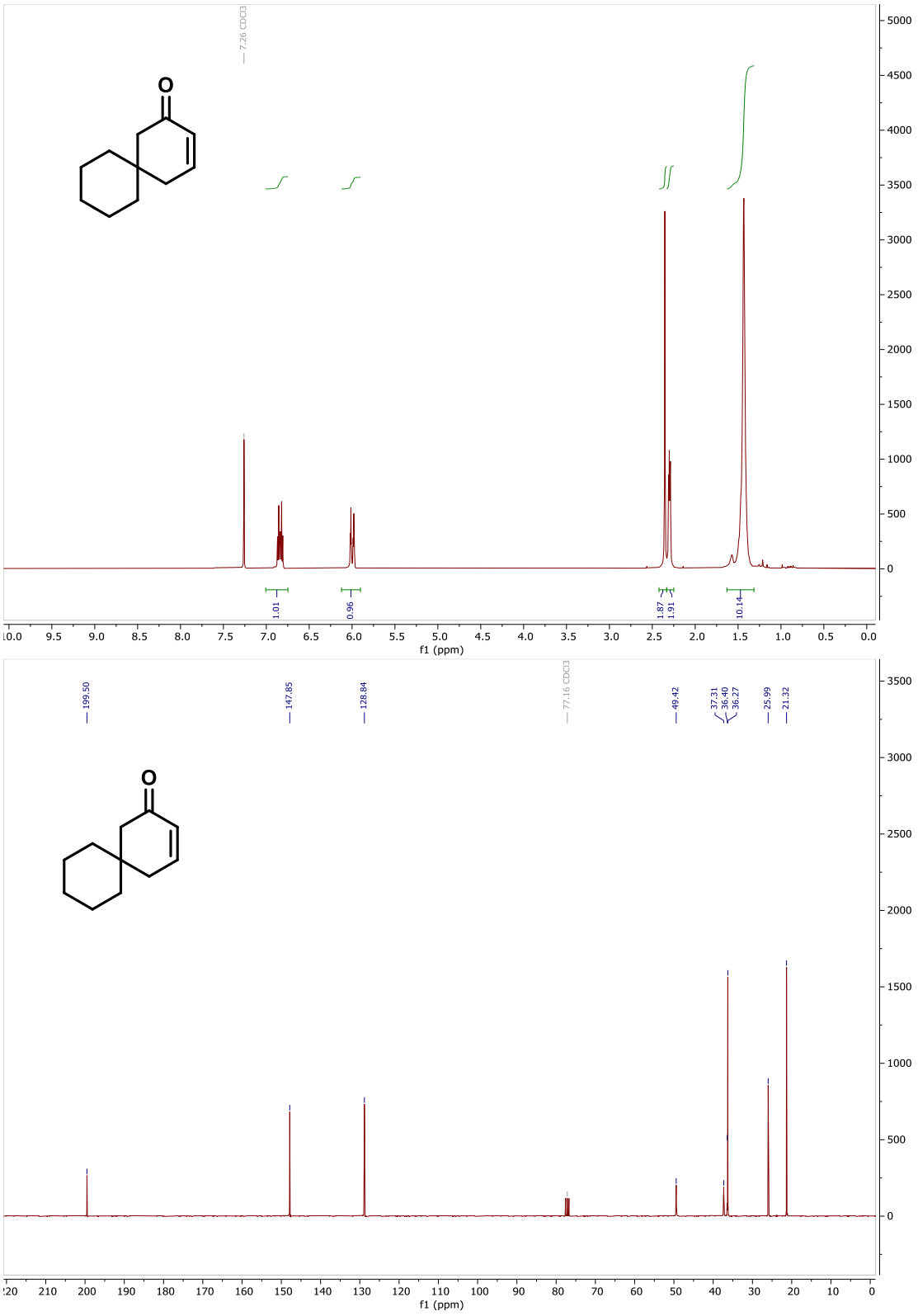


Figure S10: ^{1}H and ^{13}C NMR spectra for compound **S13** (300 and 75 MHz, $CDCl_3$, 300K).

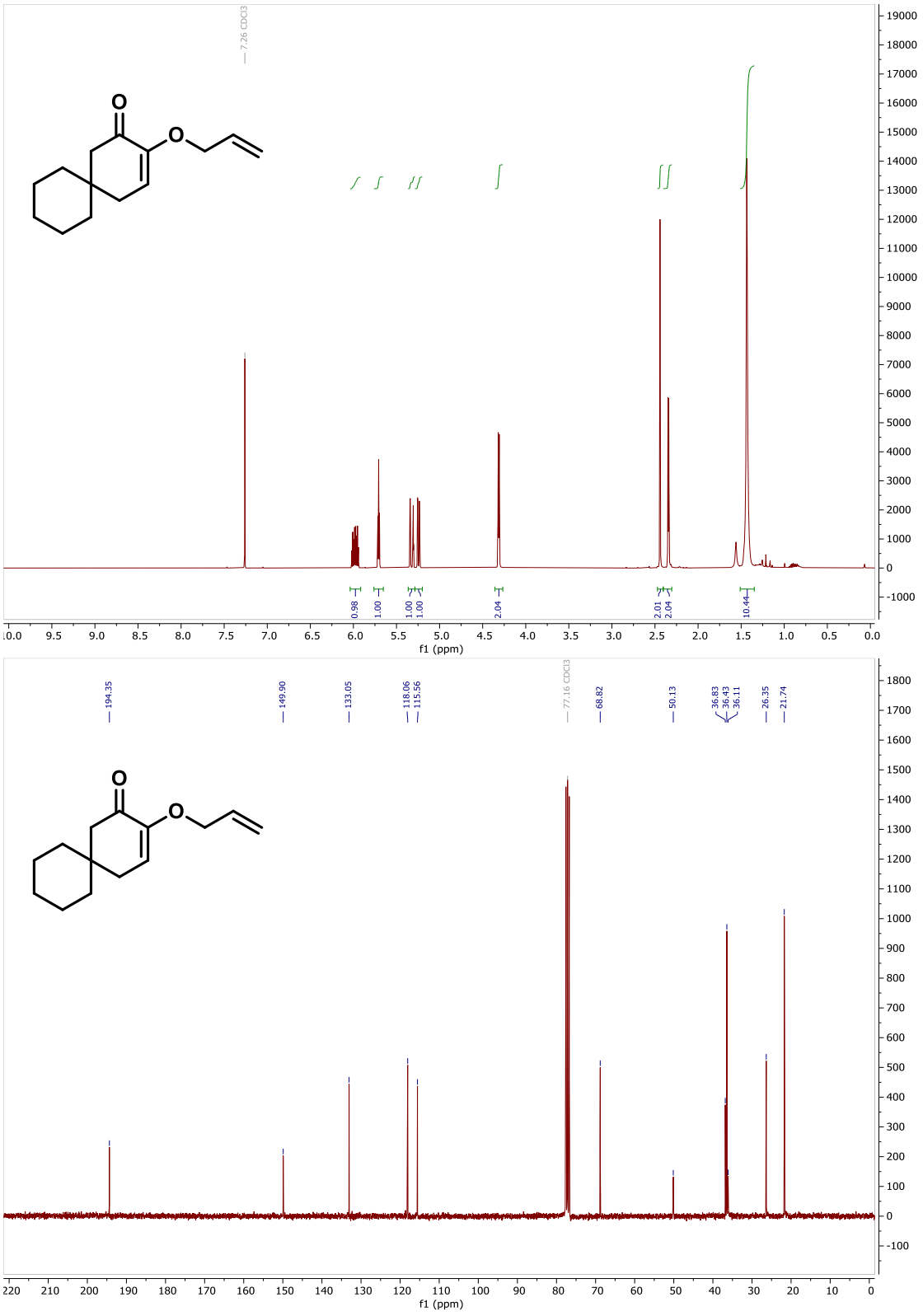


Figure S11: ^{1}H and ^{13}C NMR spectra for compound **4i** (500 and 75 MHz, $CDCl_3$, 300K).

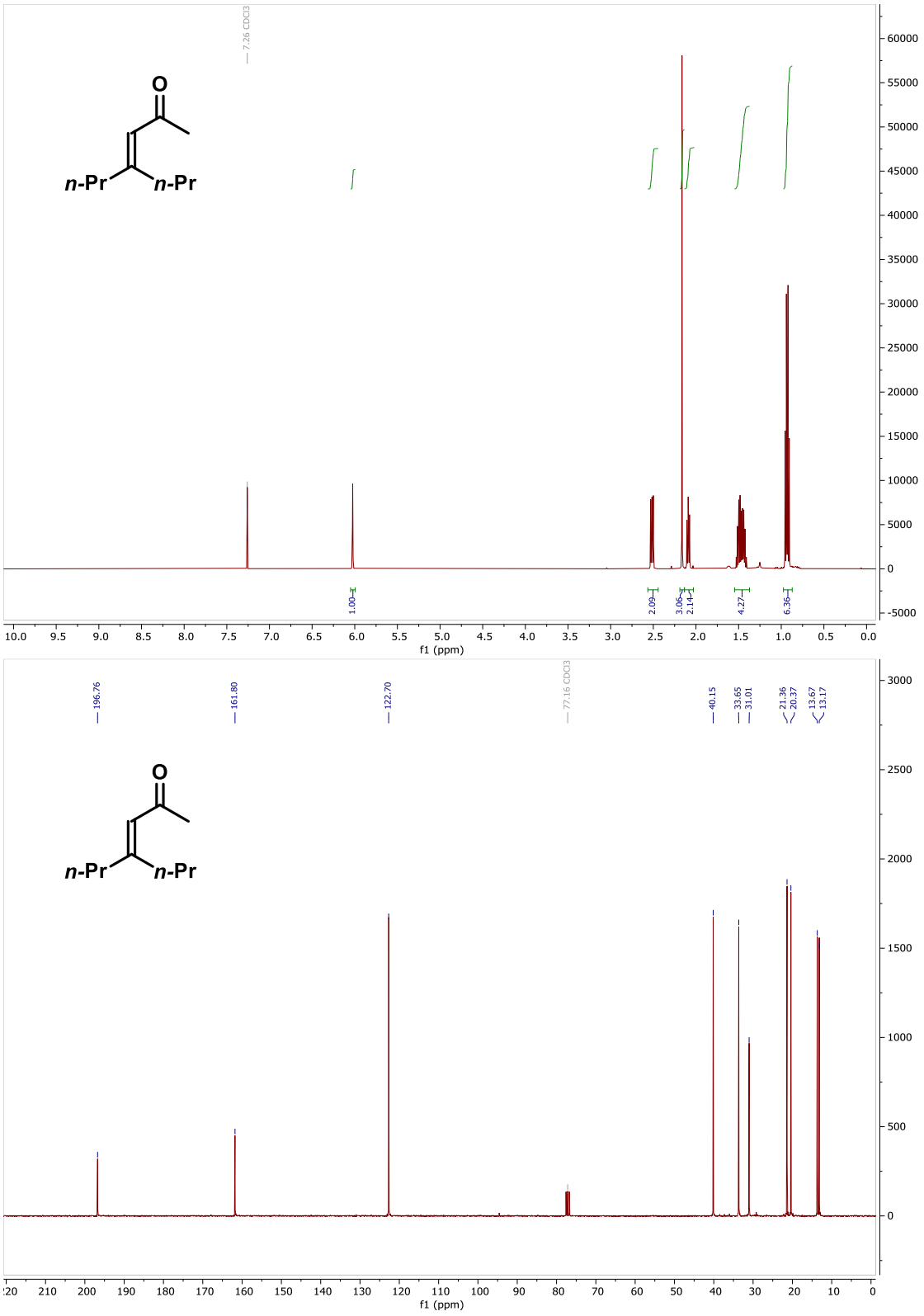


Figure S12: ^{1}H and ^{13}C NMR spectra for compound **S15** (500 and 75 MHz, $CDCl_3$, 300K).

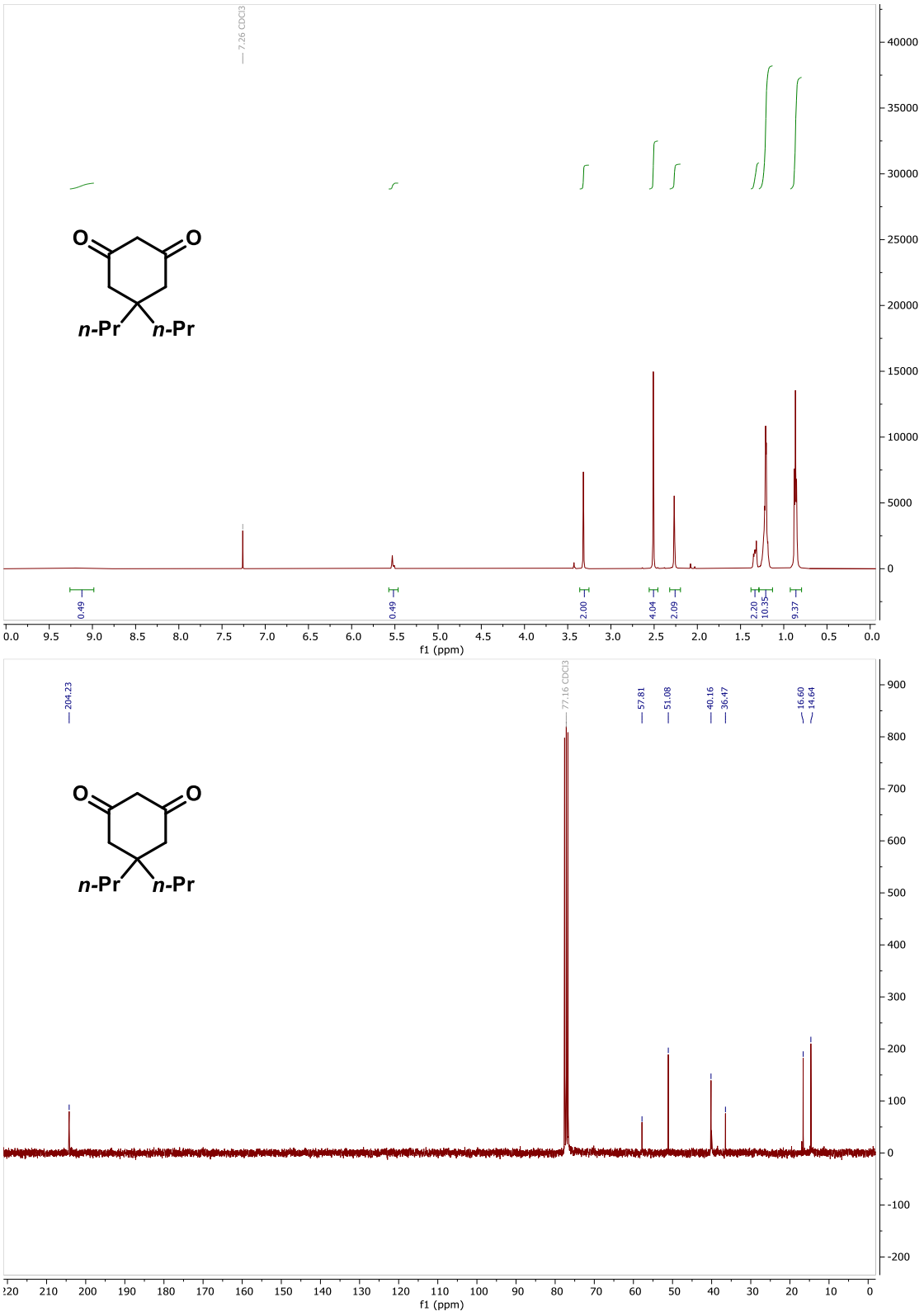


Figure S13: ^{1}H and ^{13}C NMR spectra for compound **S16** (500 and 75 MHz, $CDCl_3$, 300K).

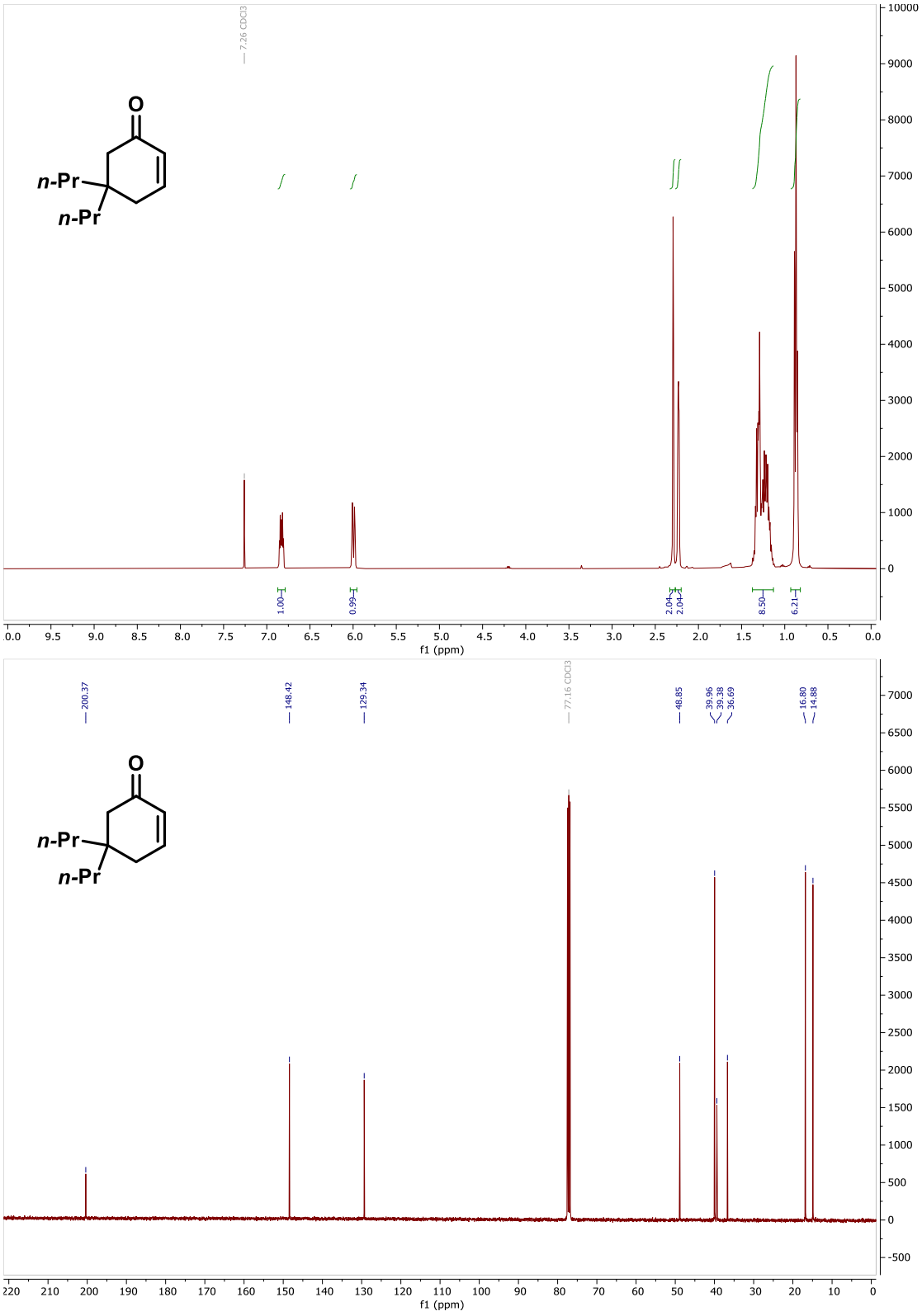


Figure S14: ^{1}H and ^{13}C NMR spectra for compound **S17** (400 and 101 MHz, $CDCl_3$, 300K).

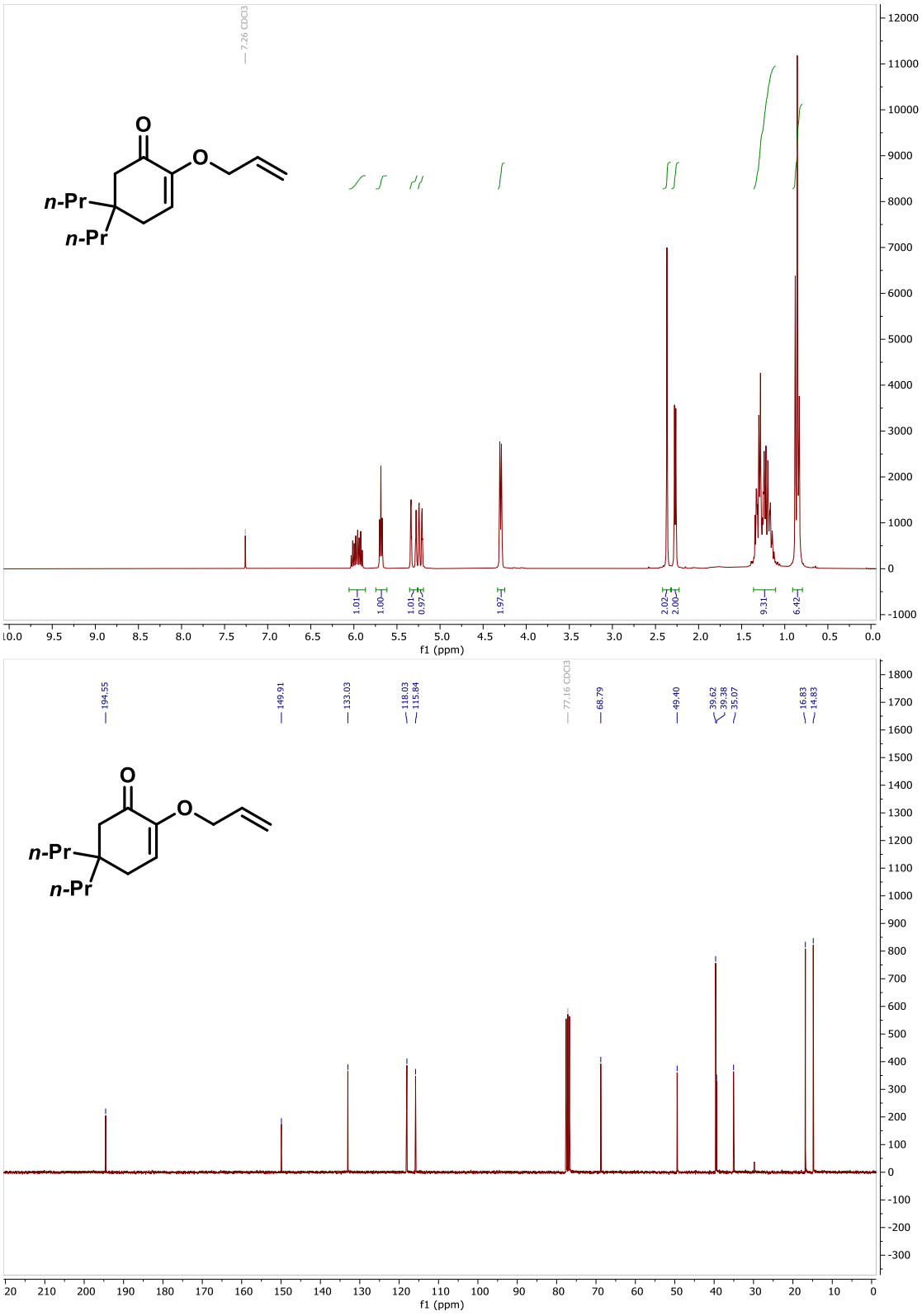


Figure S15: ^{1}H and ^{13}C NMR spectra for compound **4j** (300 and 75 MHz, $CDCl_3$, 300K).

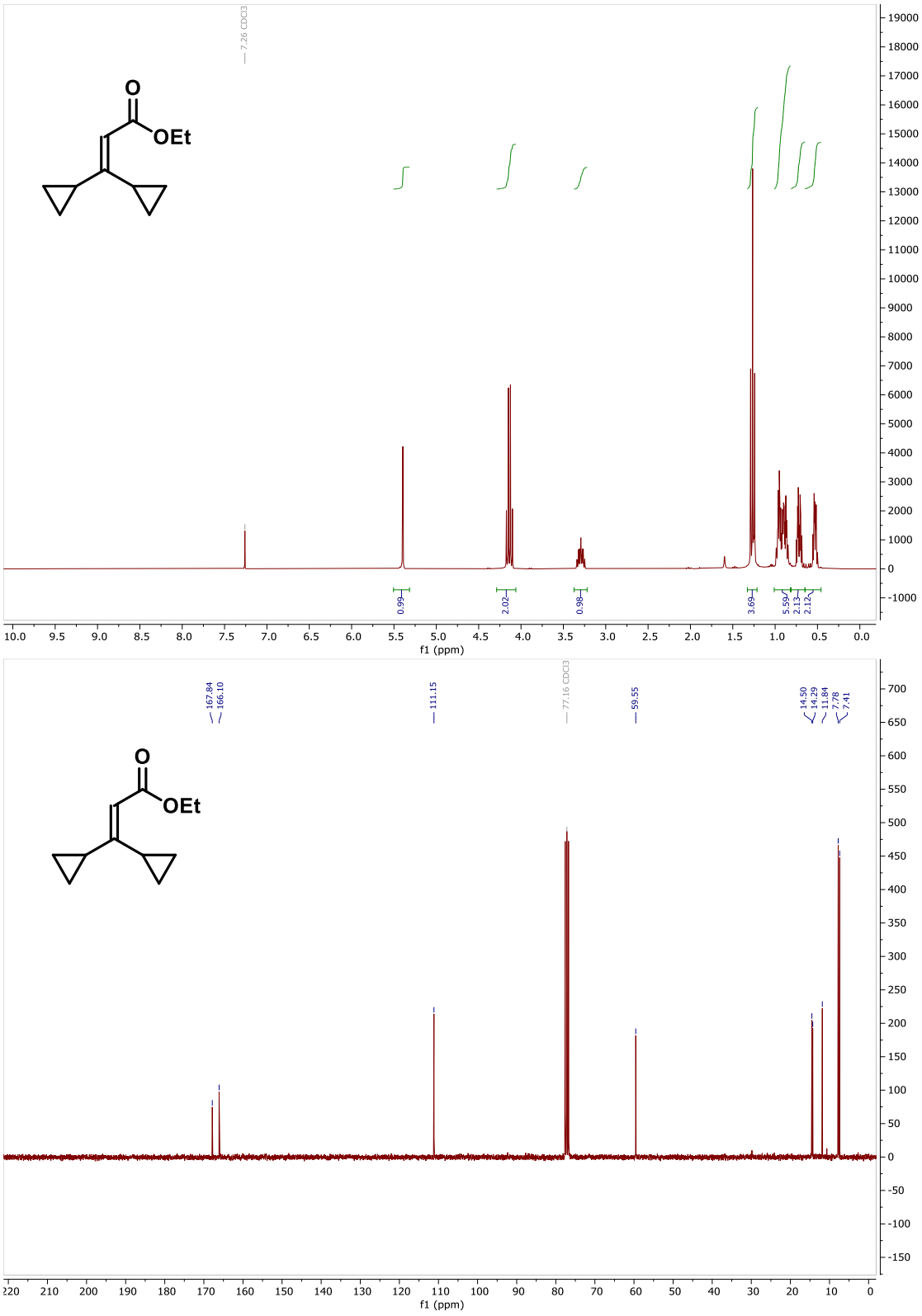


Figure S16: ^{1}H and ^{13}C NMR spectra for compound **S18** (300 and 75 MHz, $CDCl_3$, 300K).

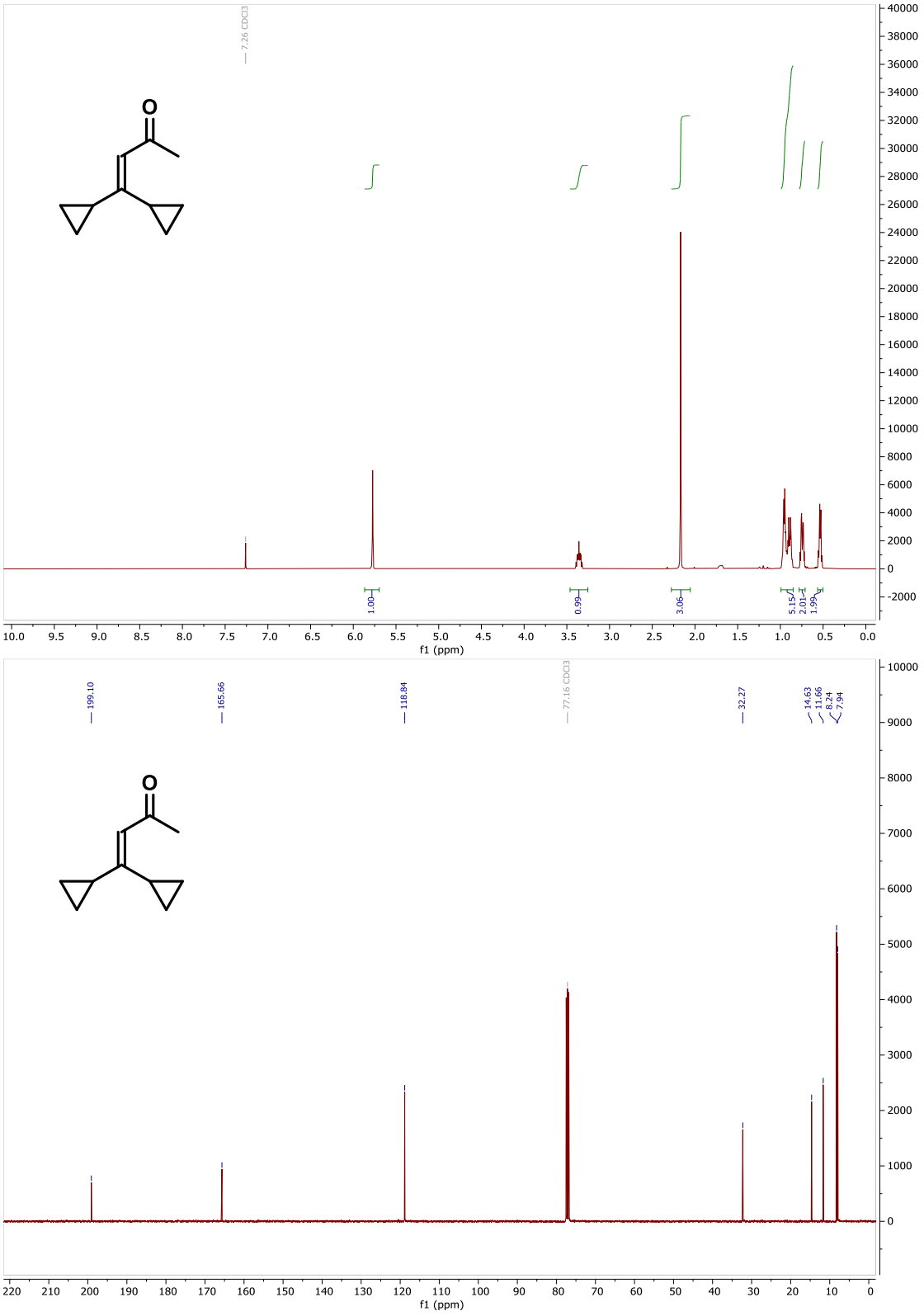


Figure S17: ^{1}H and ^{13}C NMR spectra for compound **S19** (400 and 101 MHz, $CDCl_3$, 300K).

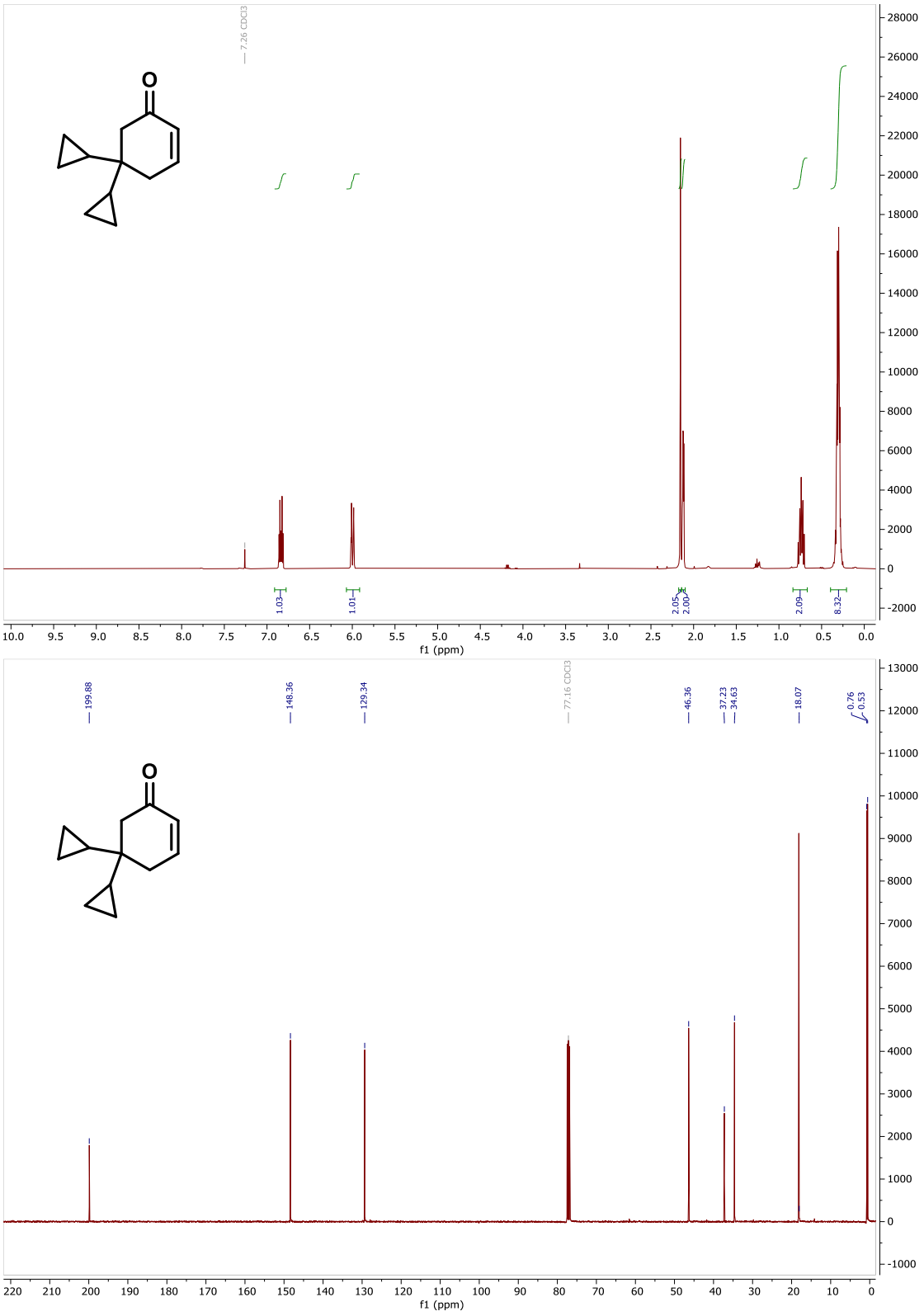


Figure S18: ^{1}H and ^{13}C NMR spectra for compound **S21** (400 and 101 MHz, $CDCl_3$, 300K).

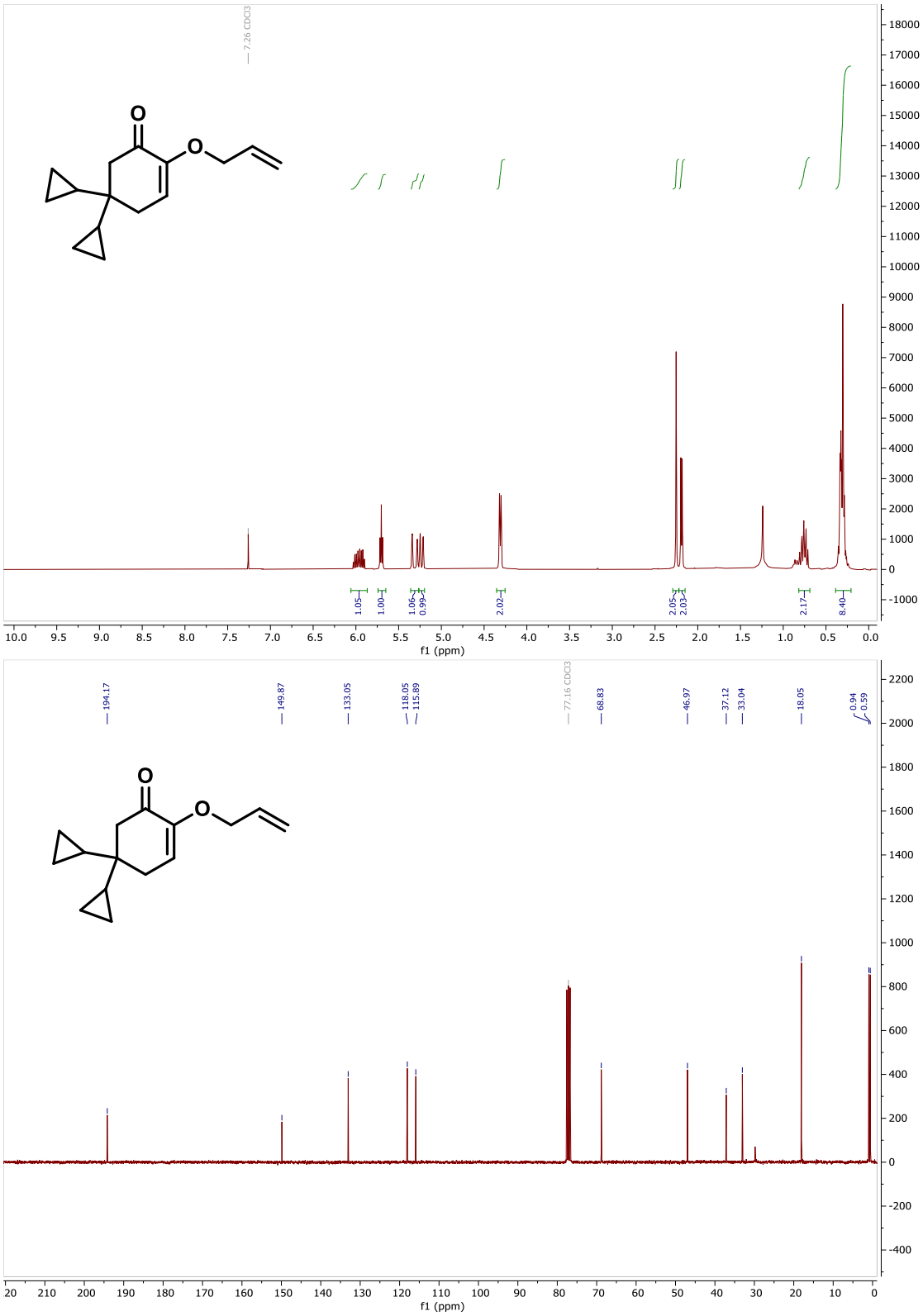


Figure S19: ^{1}H and ^{13}C NMR spectra for compound **4k** (300 and 75 MHz, $CDCl_3$, 300K).

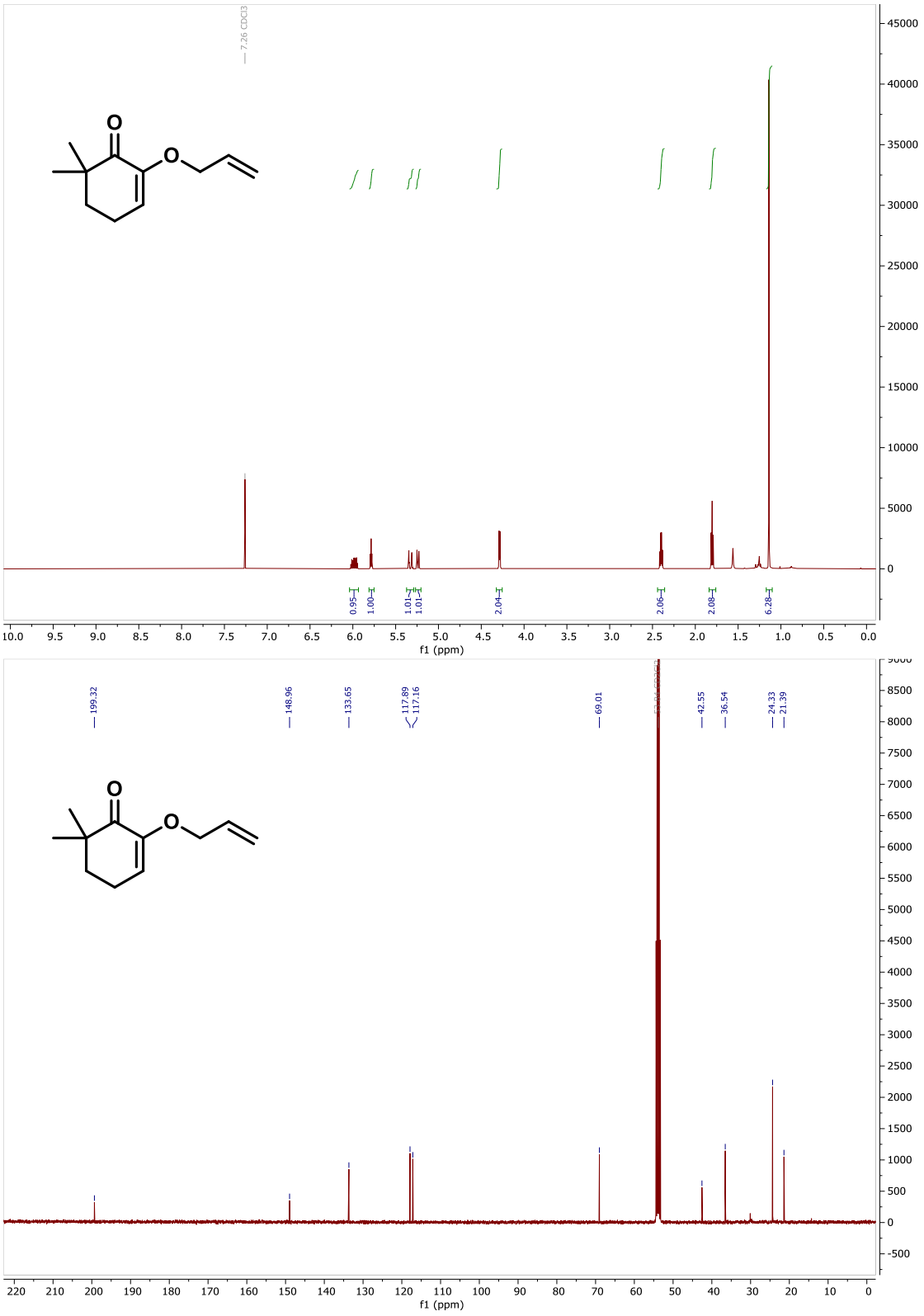


Figure S20: ^{1}H and ^{13}C NMR spectra for compound **4l** (500 and 101 MHz, $CDCl_3$ and CD_2Cl_2, 300K).

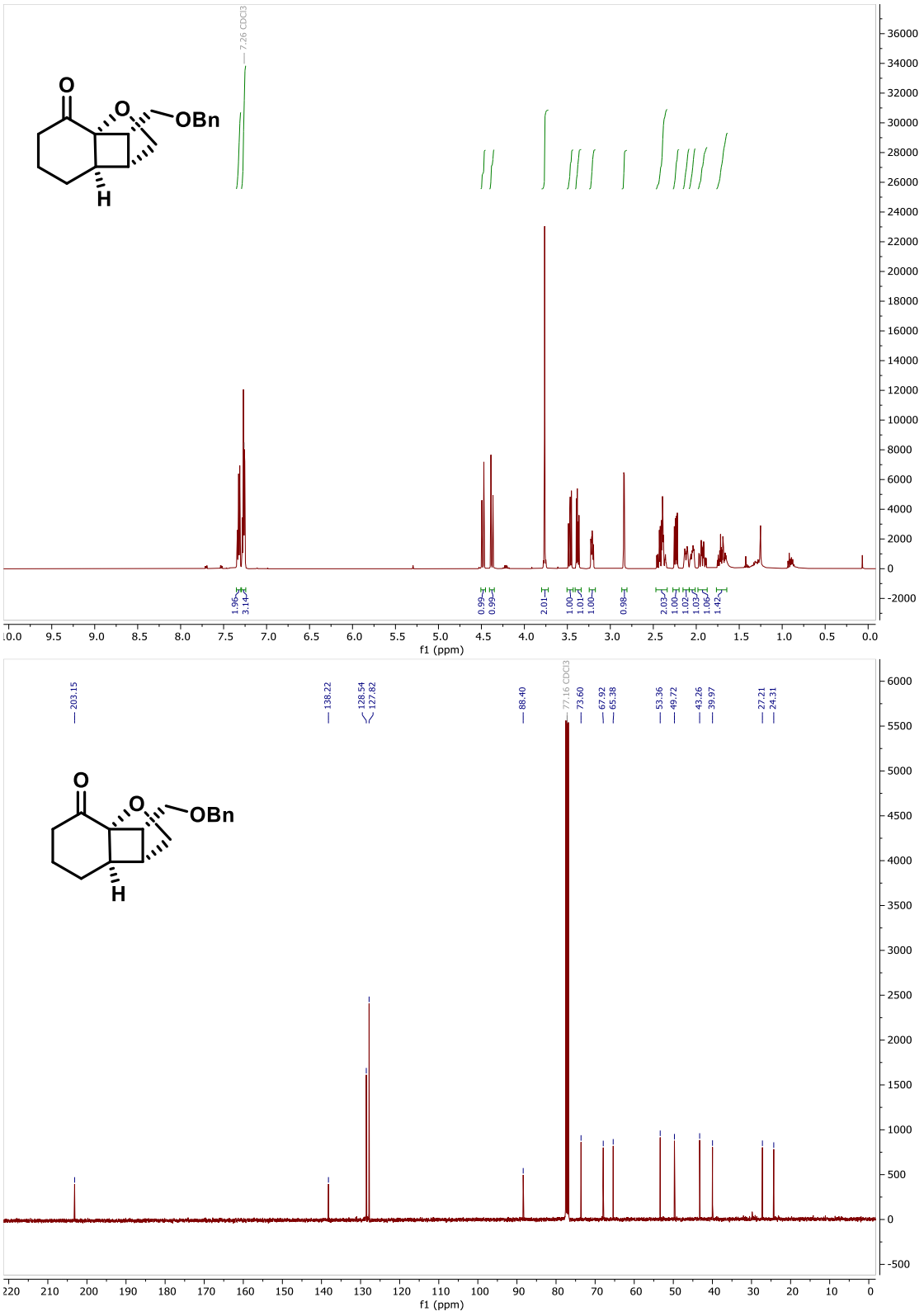


Figure S21: ^{1}H and ^{13}C NMR spectra for compound **5d** (500 and 101 MHz, $CDCl_3$, 300K).

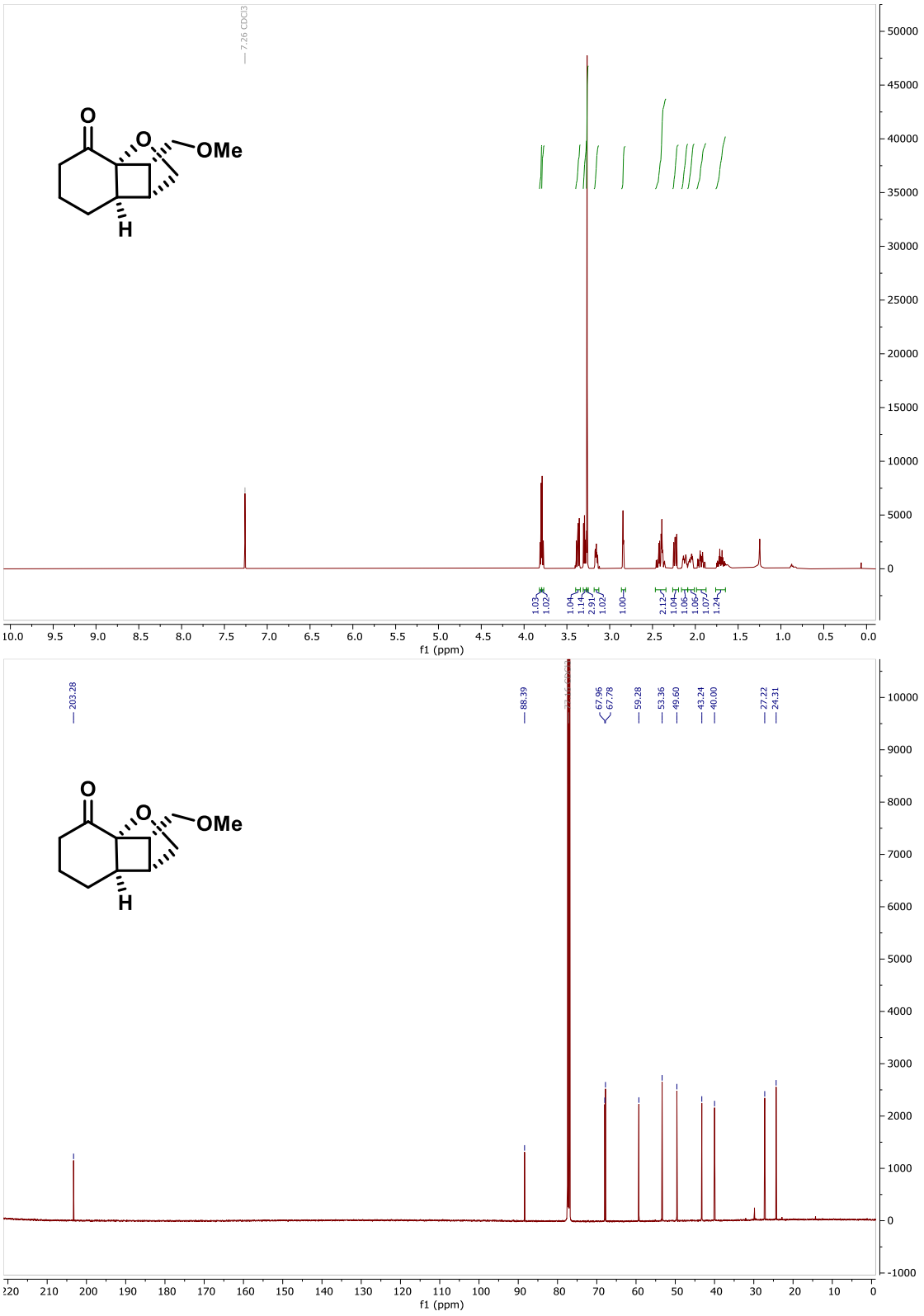


Figure S22: ^{1}H and ^{13}C NMR spectra for compound **5e** (500 and 126 MHz, $CDCl_3$, 300K).

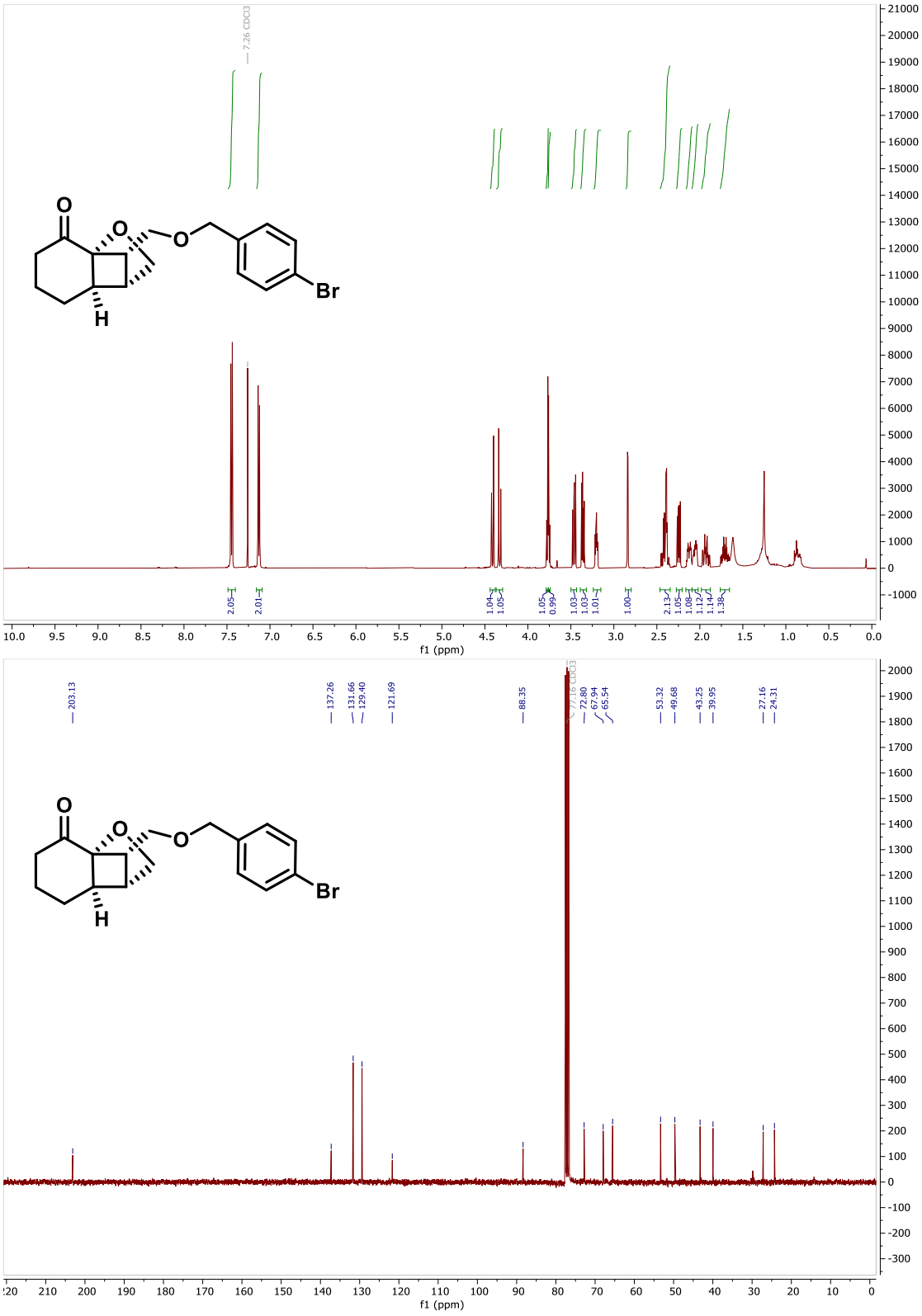


Figure S23: ^{1}H and ^{13}C NMR spectra for compound **5f** (500 and 75 MHz, $CDCl_3$, 300K).

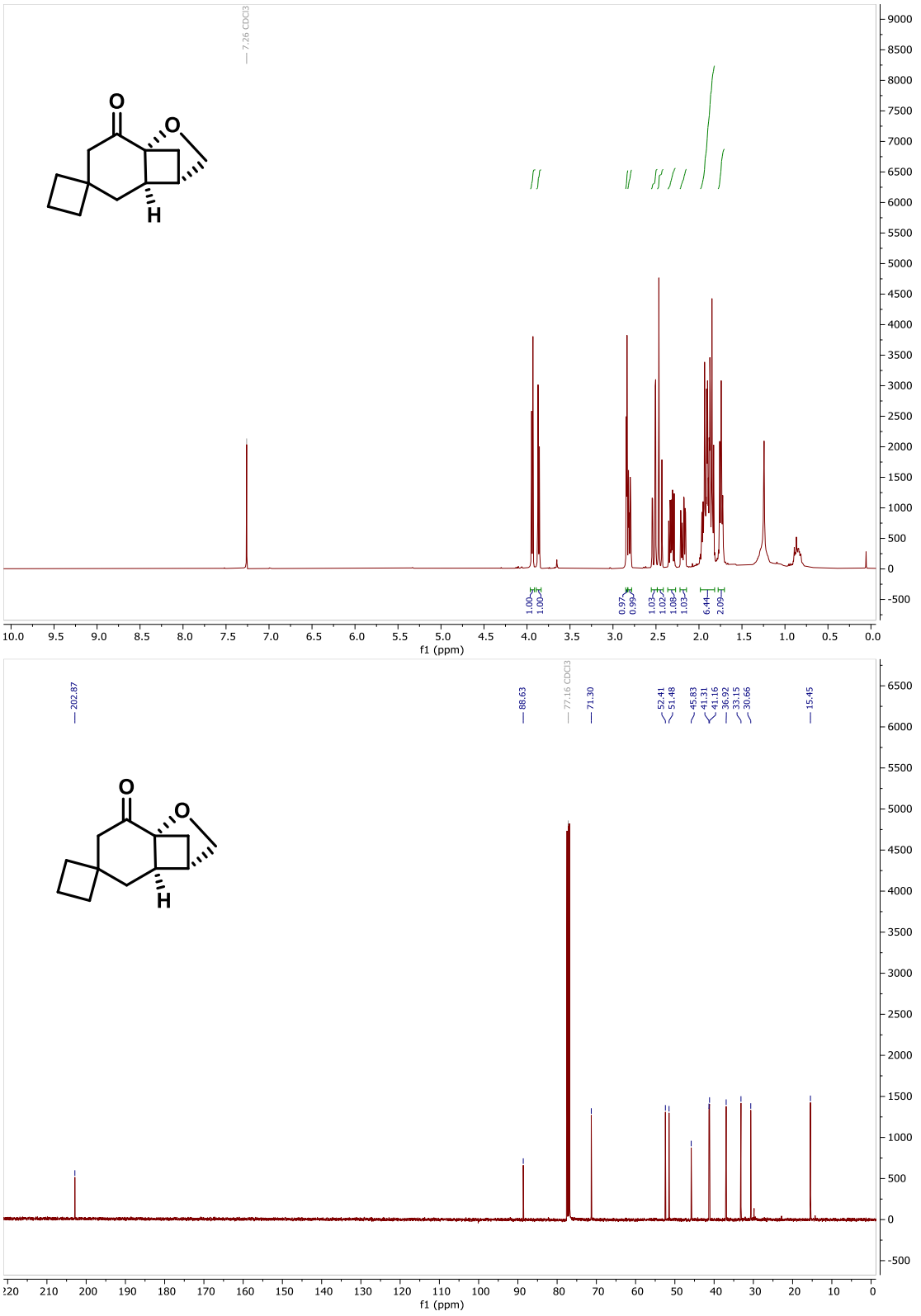


Figure S24: ^{1}H and ^{13}C NMR spectra for compound **5h** (400 and 101 MHz, $CDCl_3$, 300K).

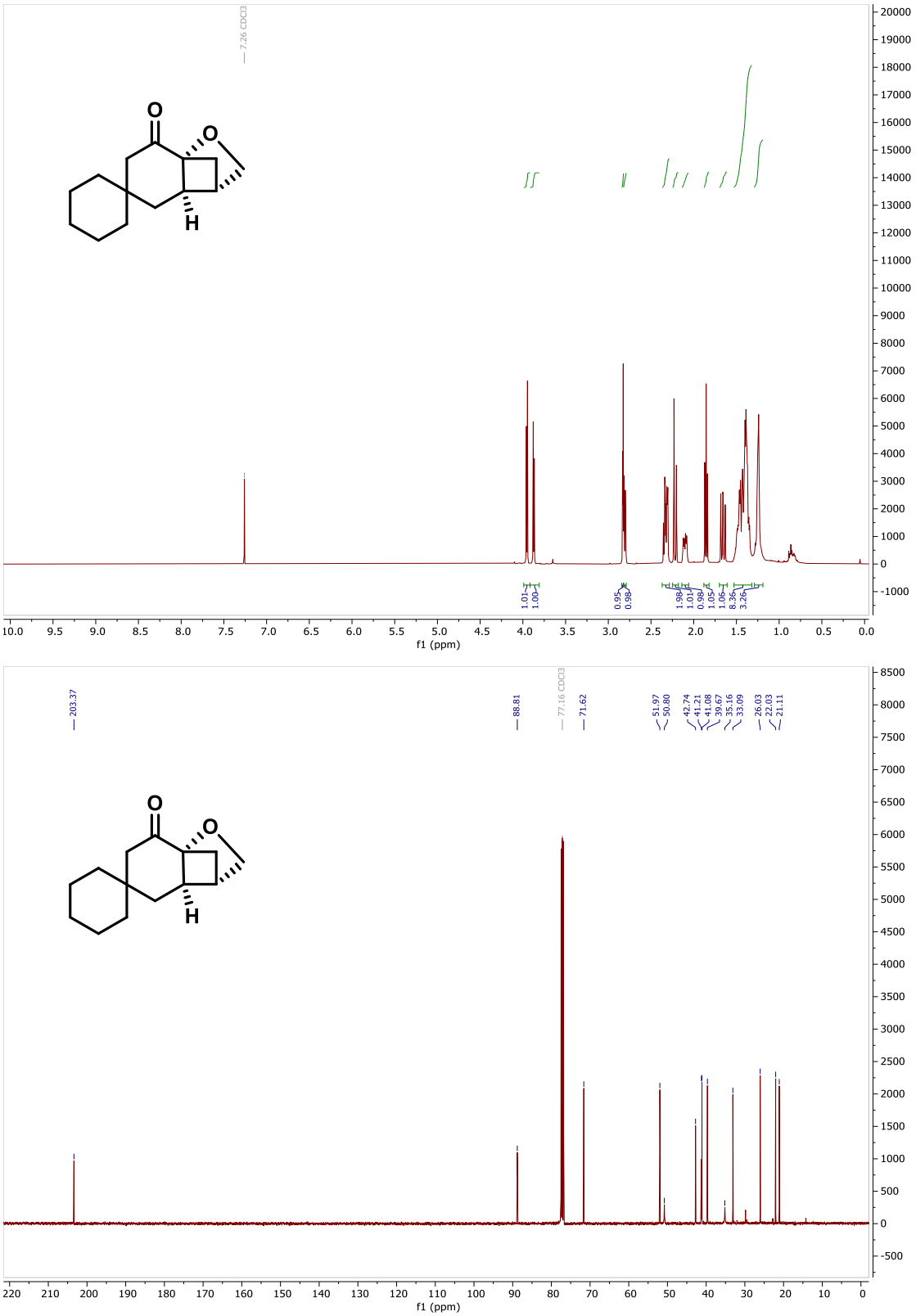


Figure S25: ^{1}H and ^{13}C NMR spectra for compound **5i** (500 and 101 MHz, $CDCl_3$, 300K).

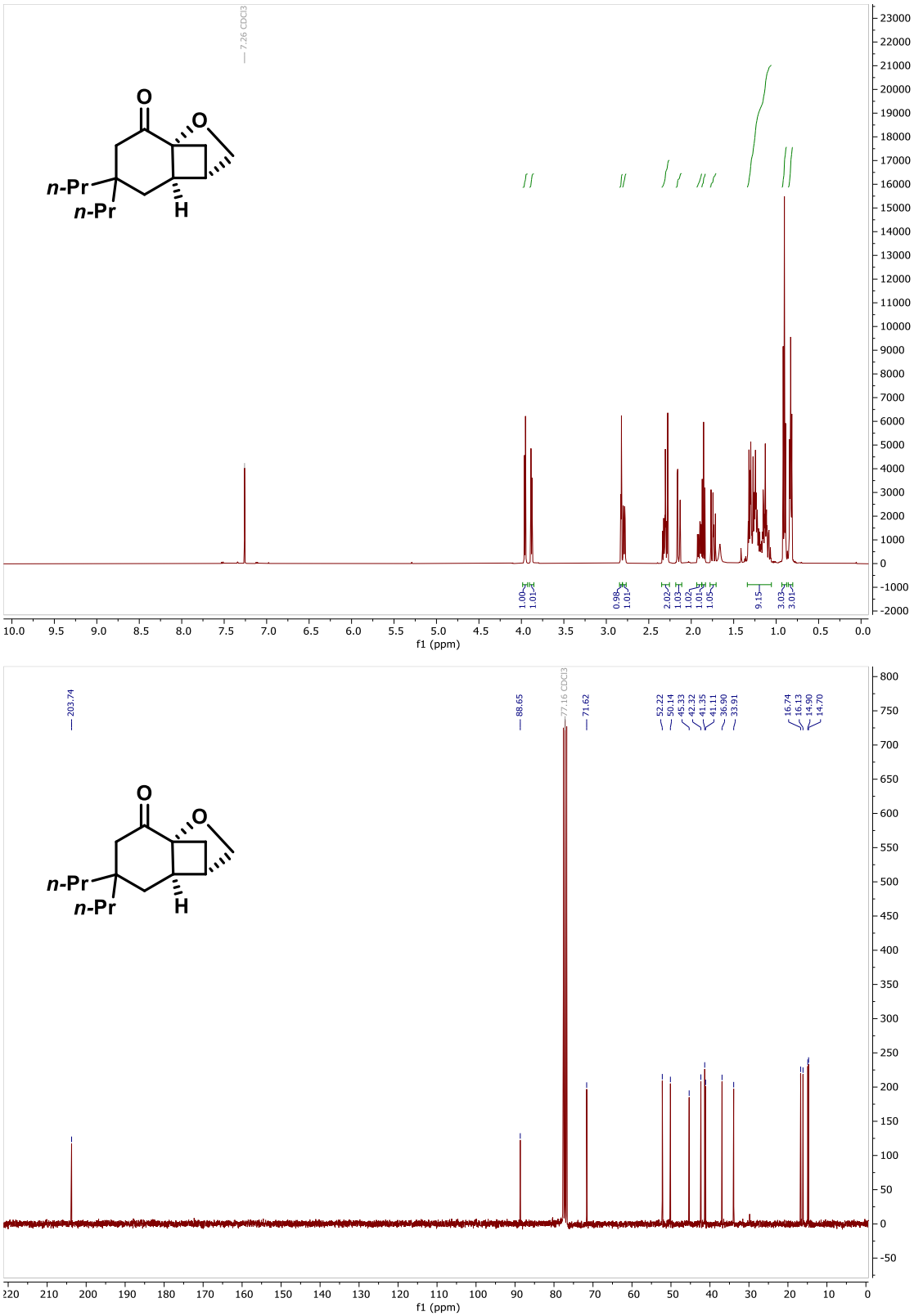


Figure S26: ^{1}H and ^{13}C NMR spectra for compound **5j** (500 and 75 MHz, $CDCl_3$, 300K).

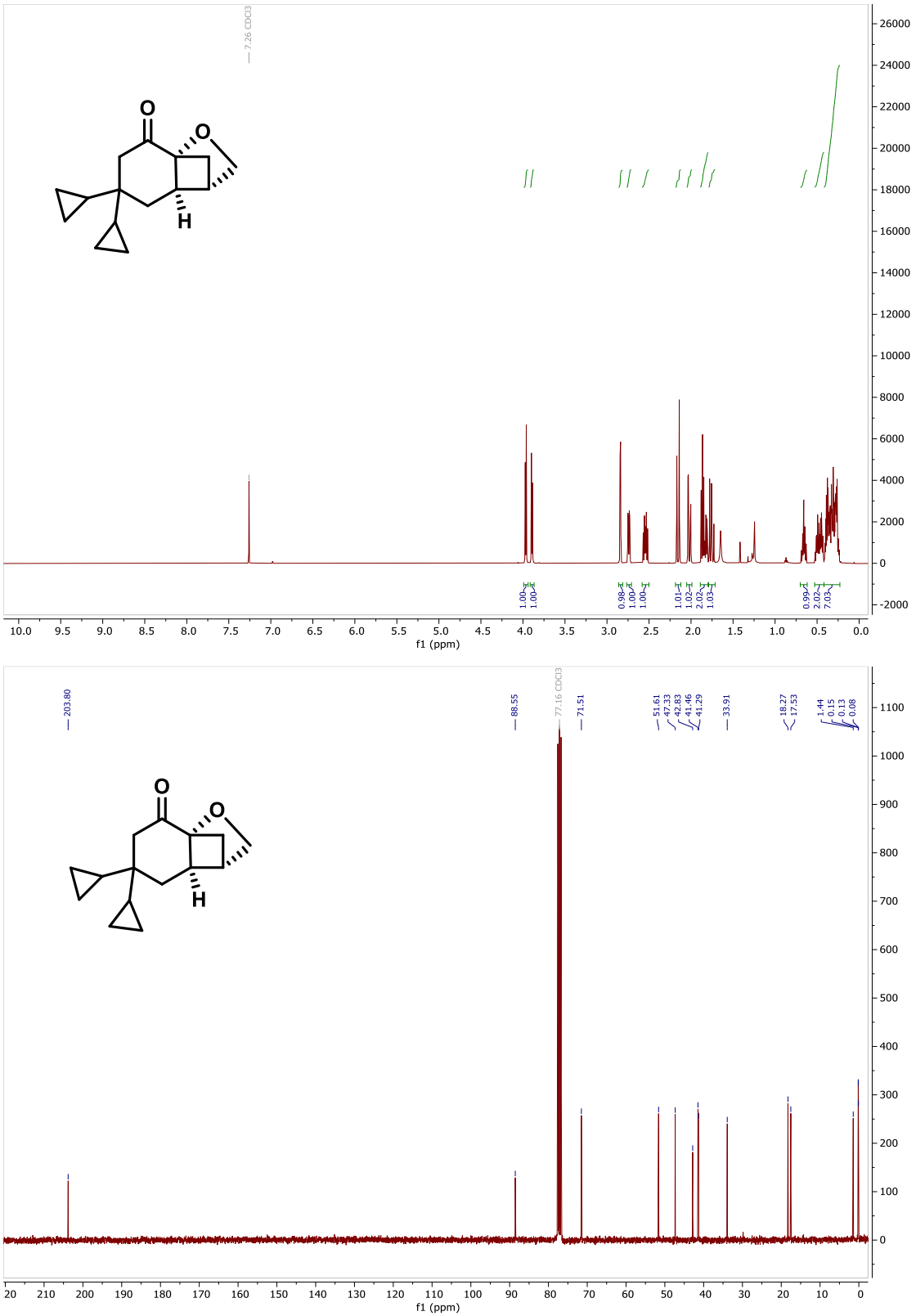


Figure S27: ^{1}H and ^{13}C NMR spectra for compound **5k** (500 and 75 MHz, $CDCl_3$, 300K).

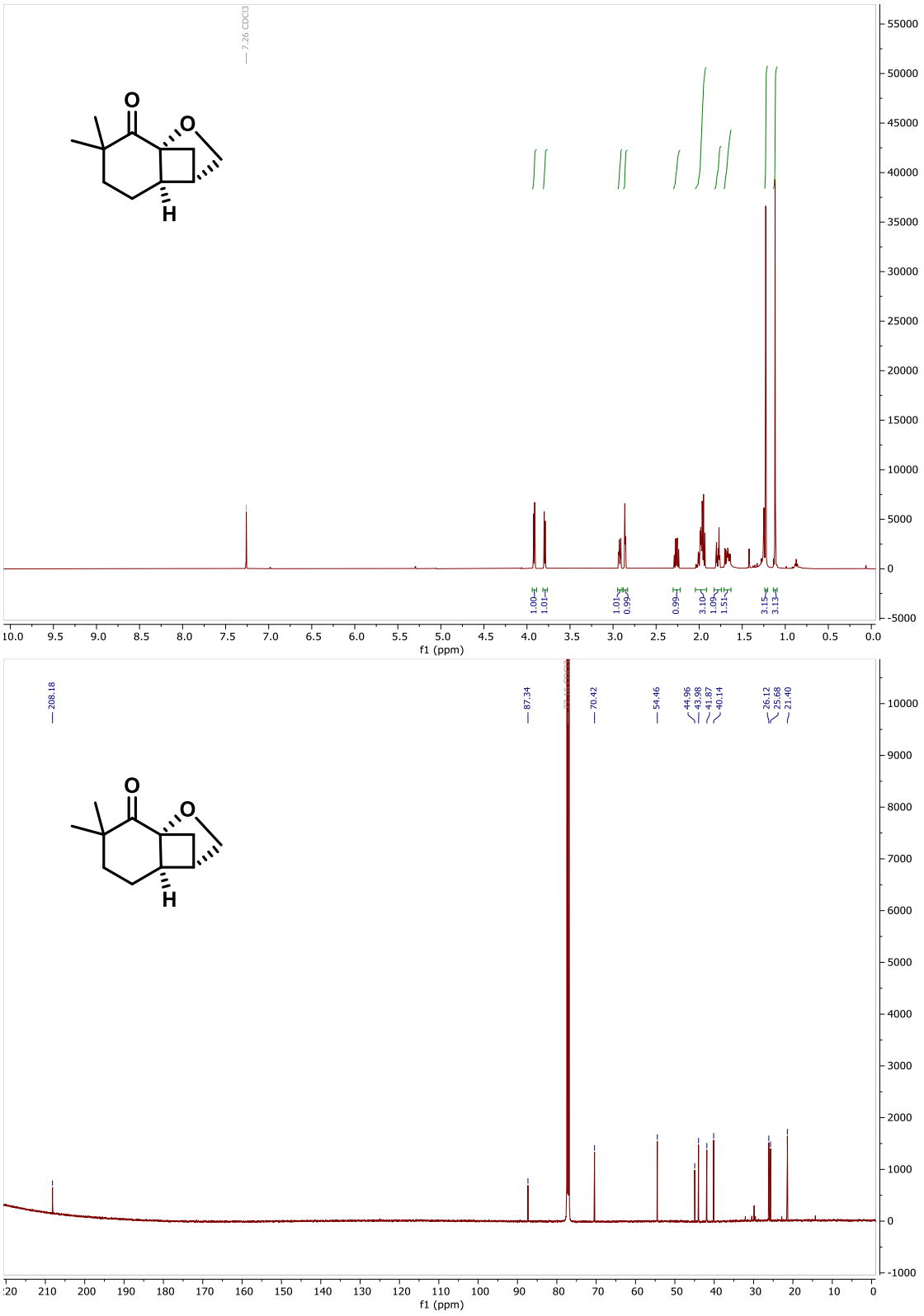


Figure S28: ^{1}H and ^{13}C NMR spectra for compound **5l** (500 and 126 MHz, $CDCl_3$, 300K).

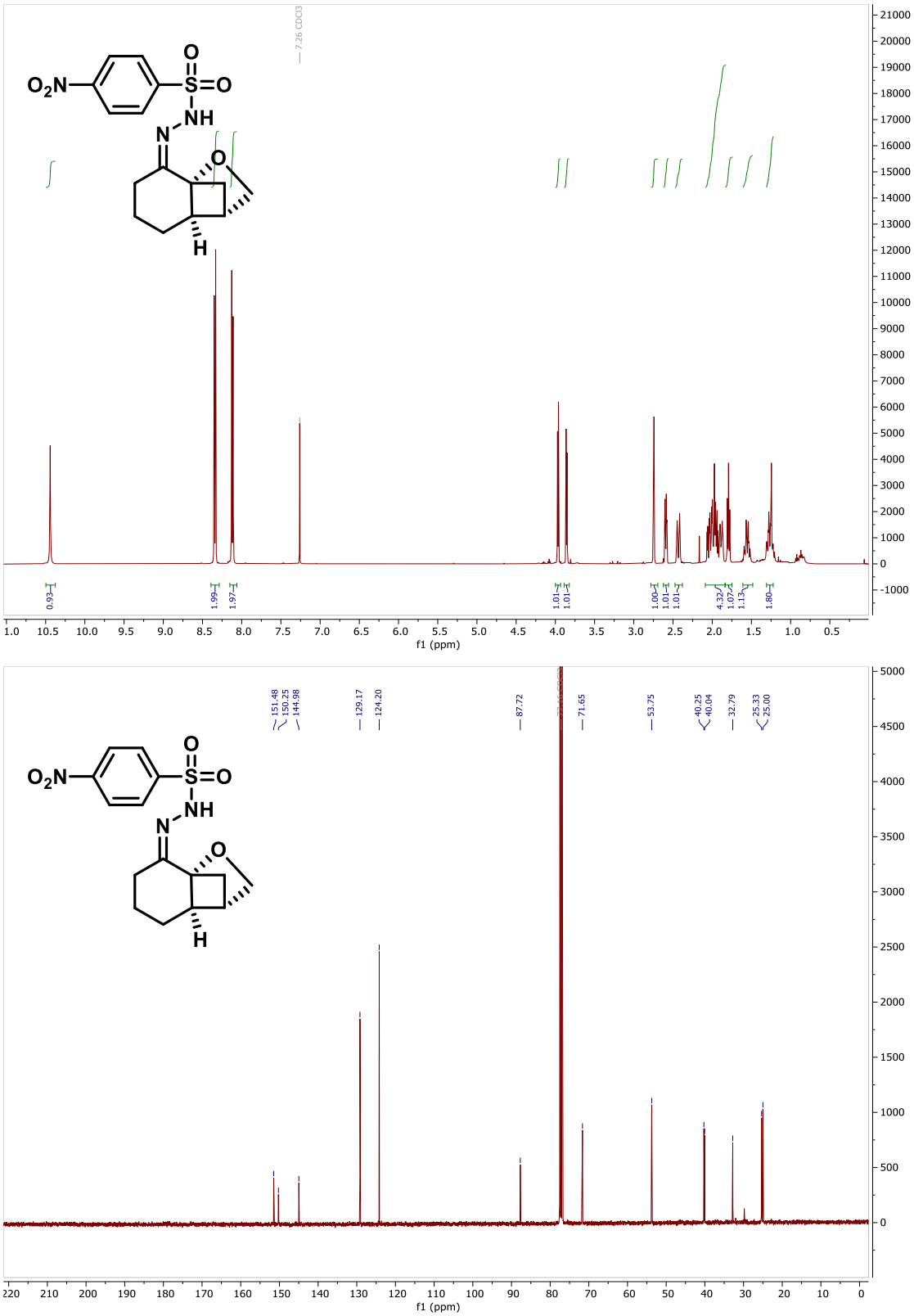


Figure S29: ^{1}H and ^{13}C NMR spectra for compound **7** (500 and 101 MHz, $CDCl_3$, 300K).

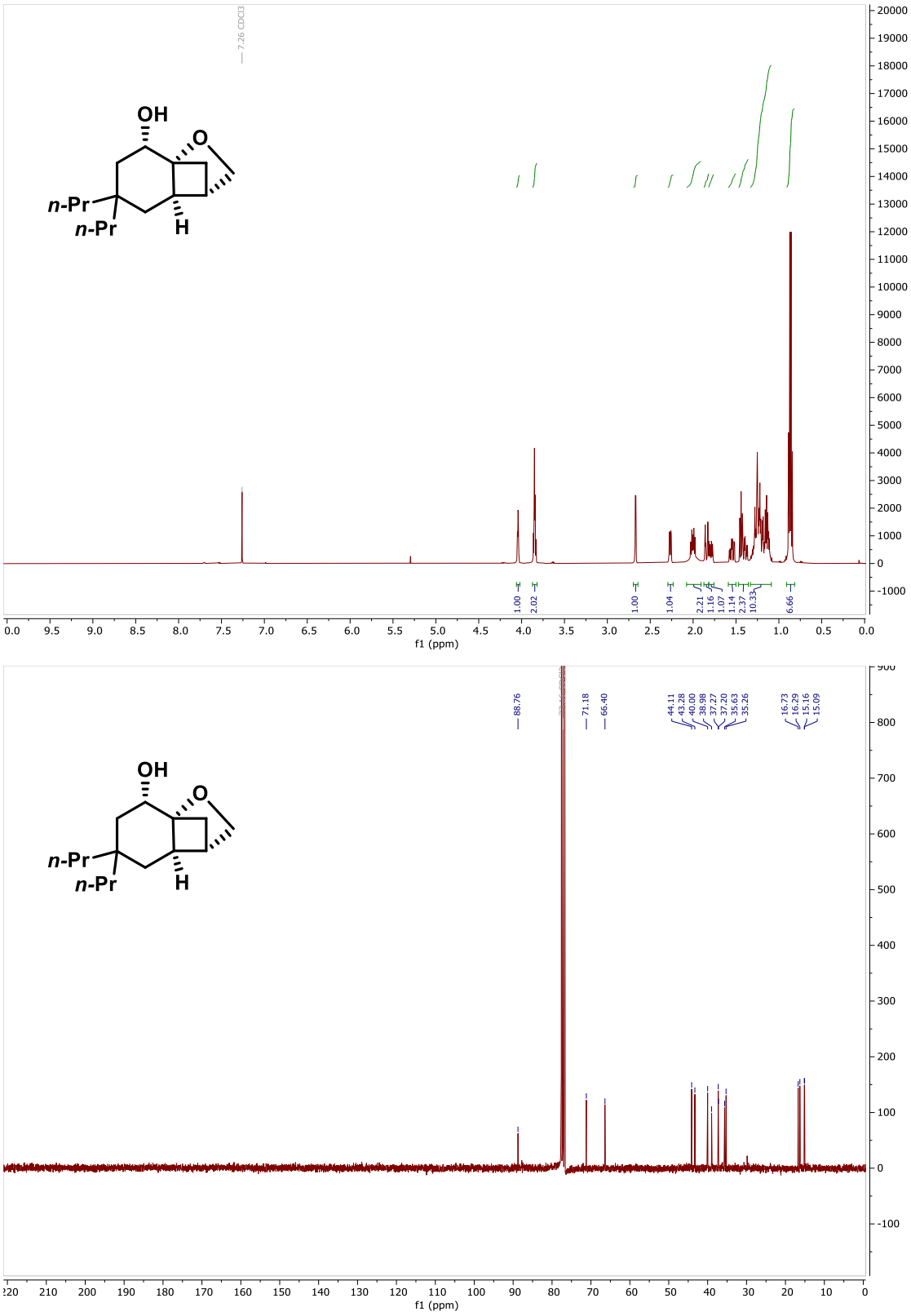


Figure S30: ^{1}H and ^{13}C NMR spectra for compound **10a** (500 and 75 MHz, $CDCl_3$, 300K).

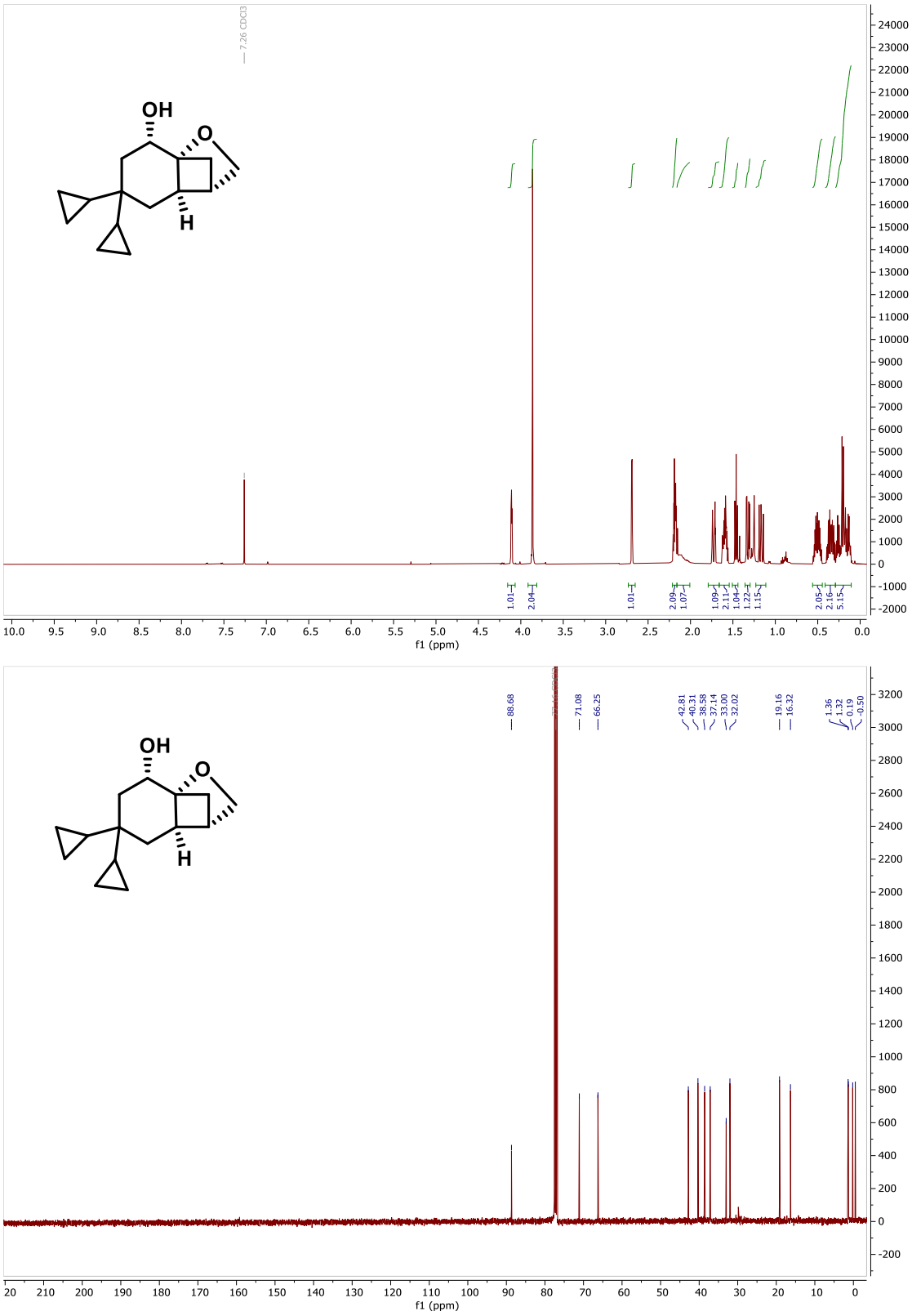
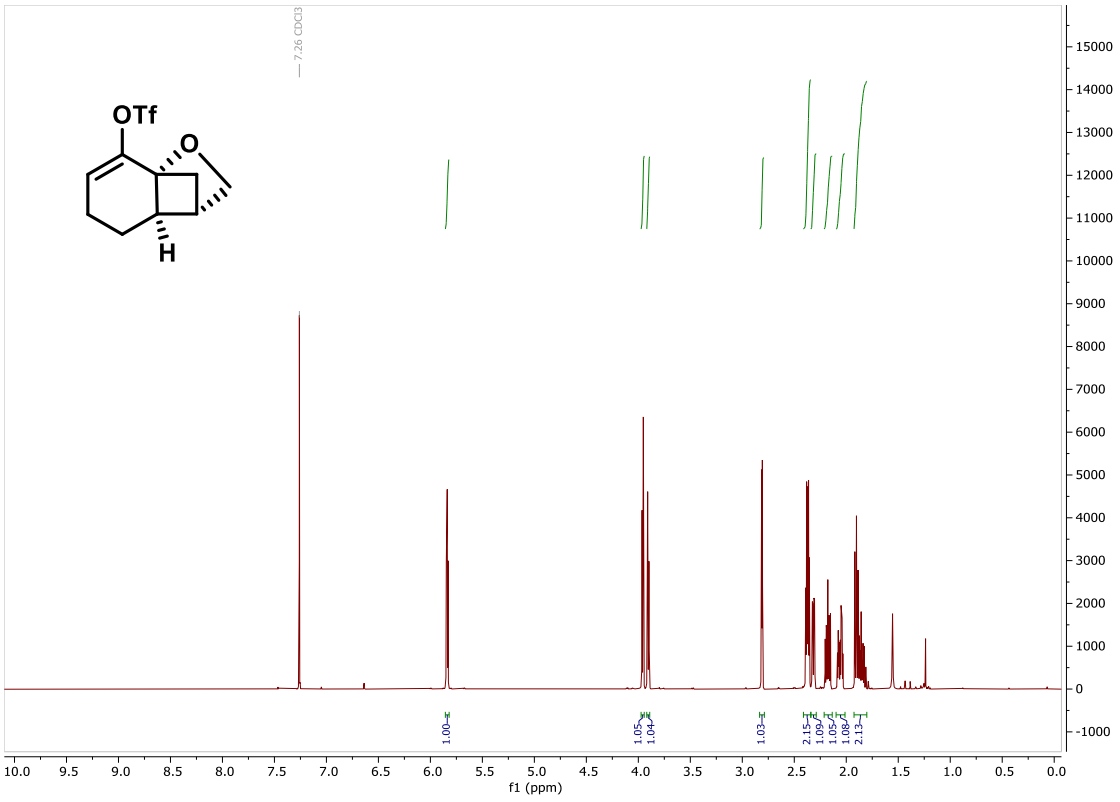
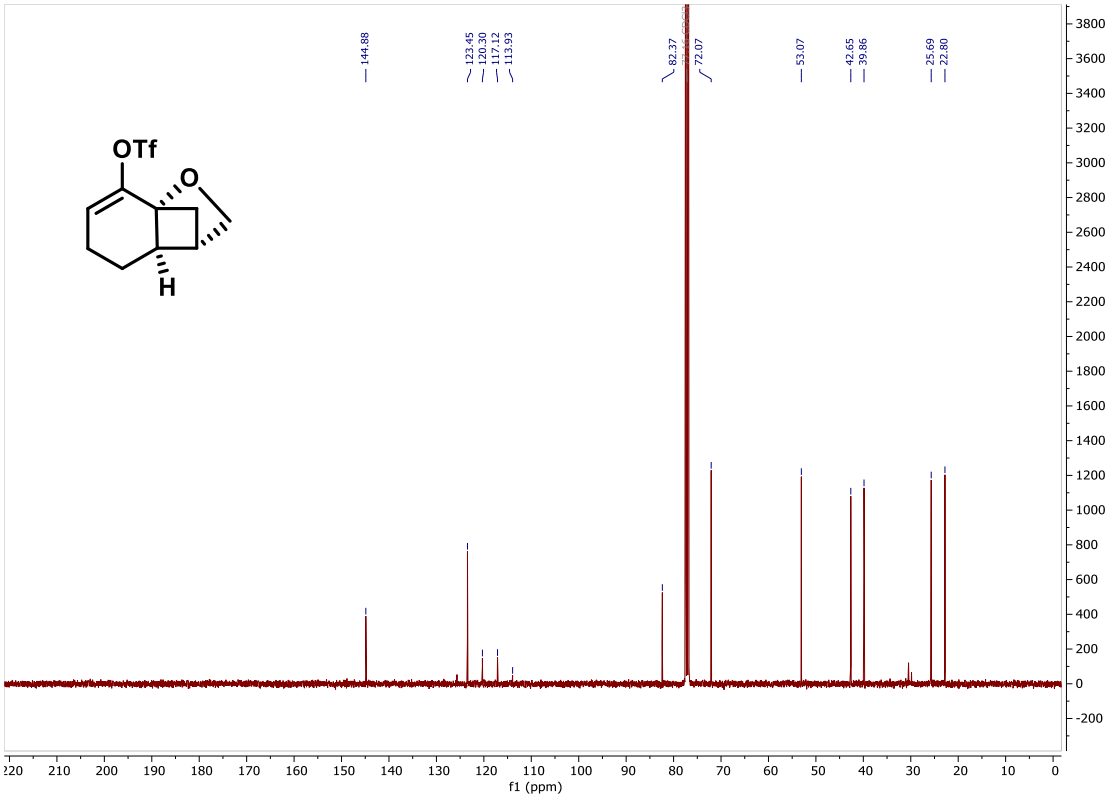


Figure S31: ^{1}H and ^{13}C NMR spectra for compound **10b** (500 and 101 MHz, $CDCl_3$, 300K).


OTf
O
H
7.26 CDCl3
1.00
1.05
1.04
1.03
2.15
1.09
1.05
1.08
2.13
f1 (ppm)


OTf
O
H
144.88
123.45
120.30
117.12
113.93
82.37
72.07
53.07
42.65
39.86
25.69
22.80
f1 (ppm)

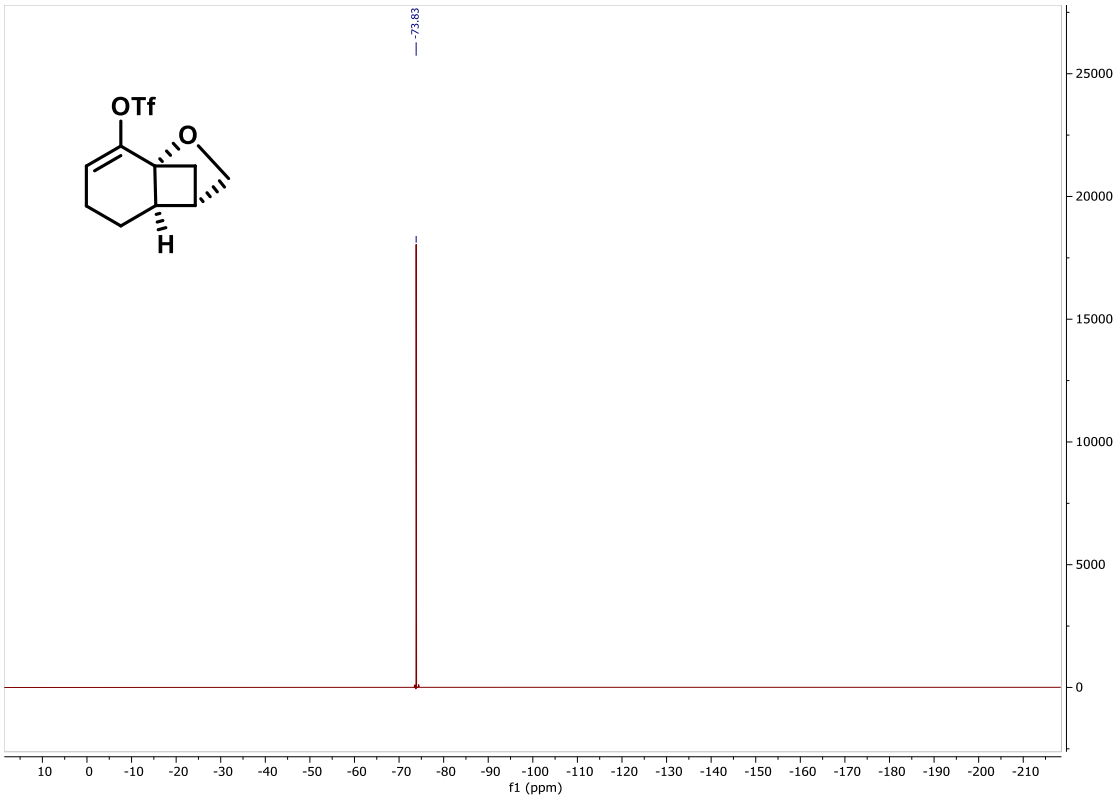


Figure S32: ^{1}H, ^{13}C and ^{19}F NMR spectra for compound **11** (500, 101 and 376 MHz, $CDCl_3$, 300K).

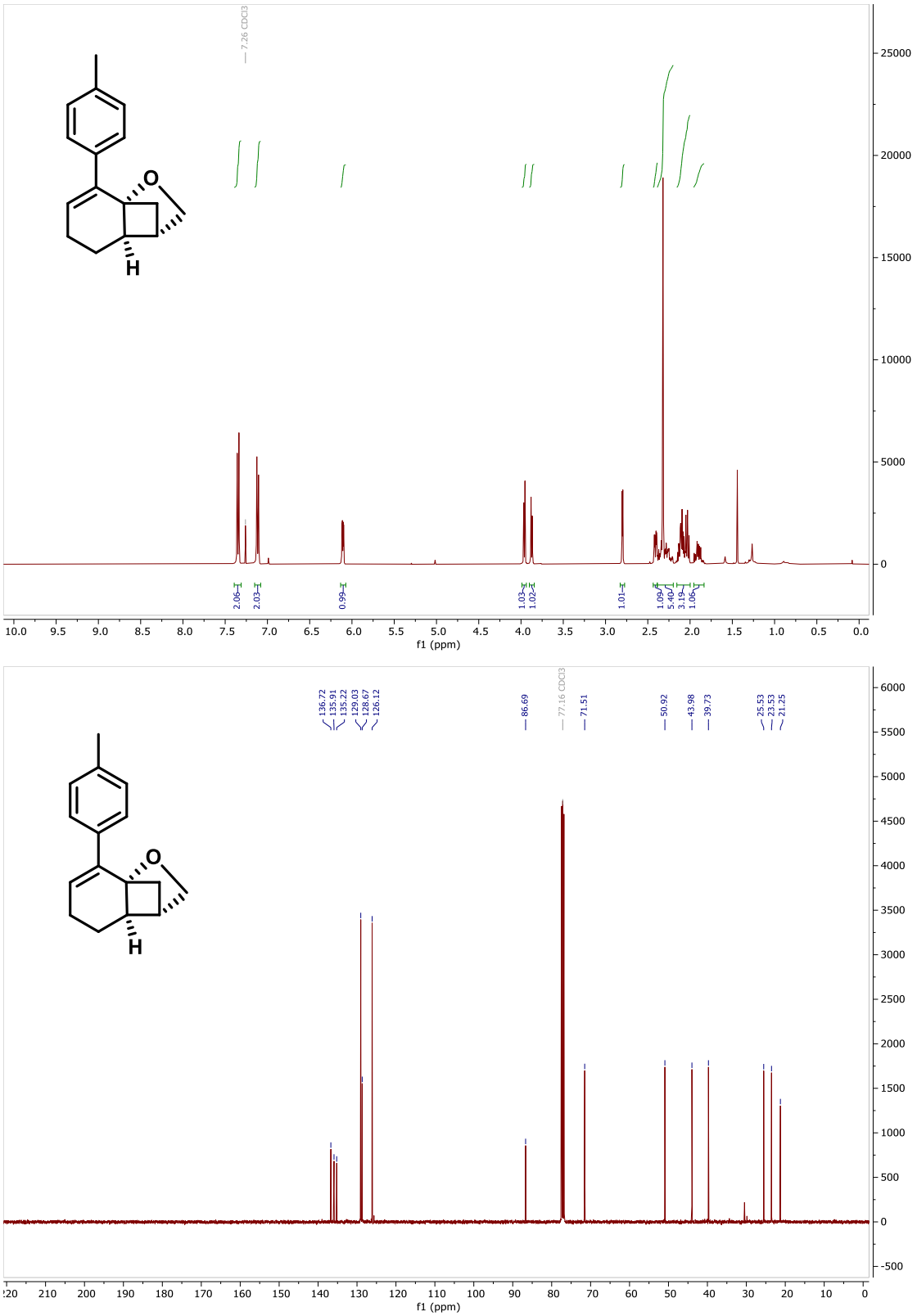


Figure S33: ^{1}H and ^{13}C NMR spectra for compound **12** (400 and 101 MHz, $CDCl_3$, 300K).

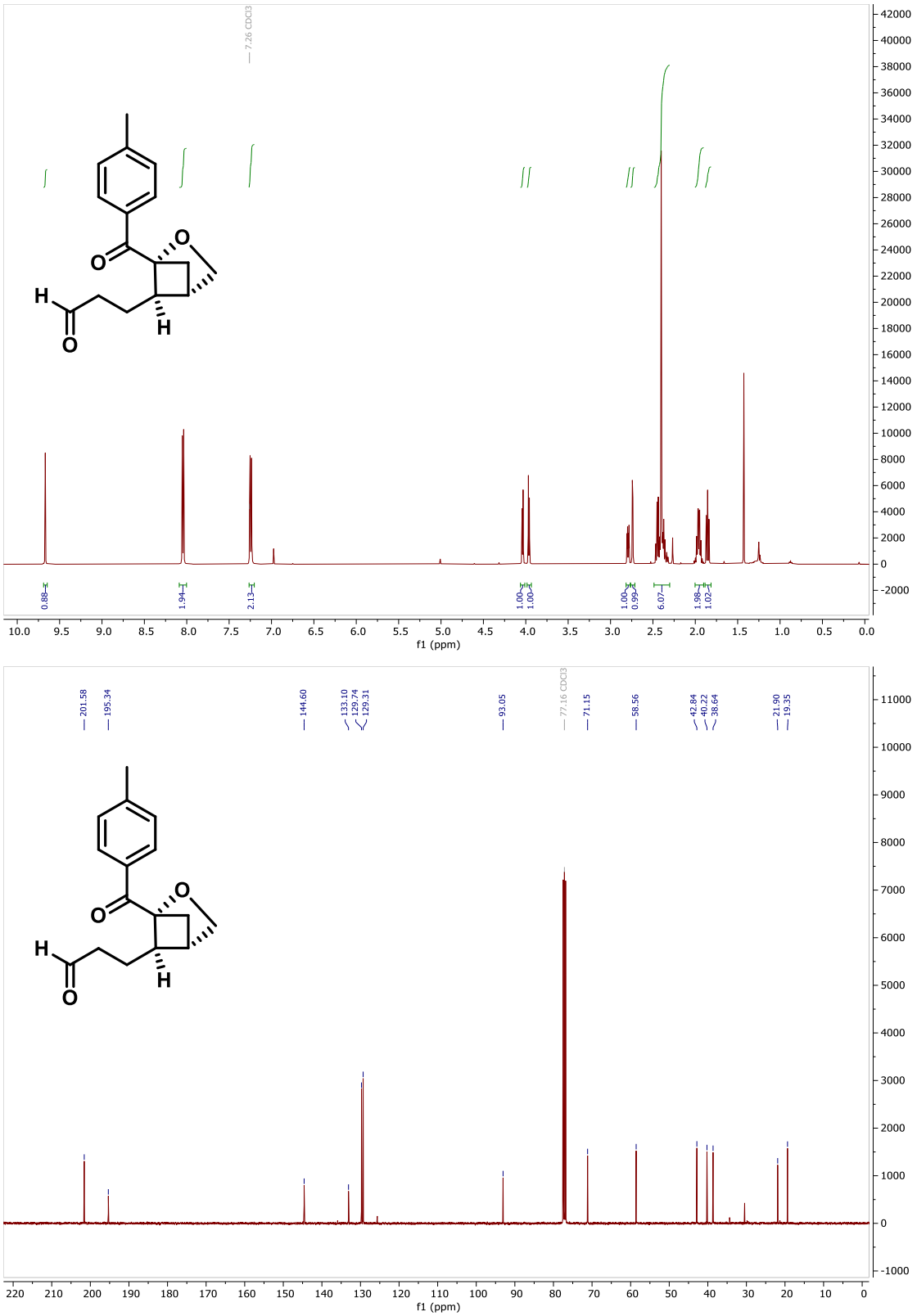


Figure S34: ^{1}H and ^{13}C NMR spectra for compound **13** (500 and 101 MHz, $CDCl_3$, 300K).

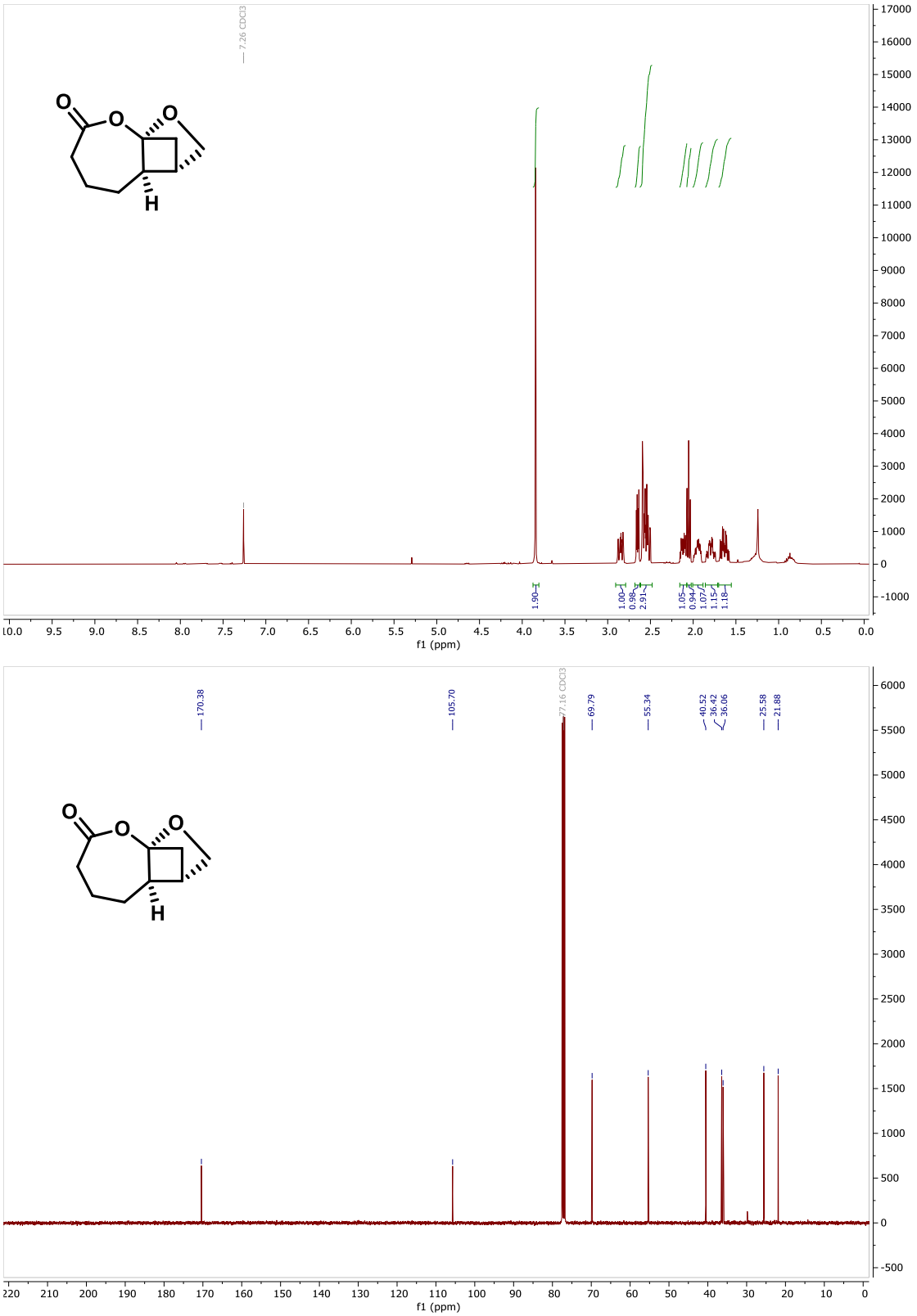


Figure S35: ^{1}H and ^{13}C NMR spectra for compound **14** (400 and 101 MHz, $CDCl_3$, 300K).

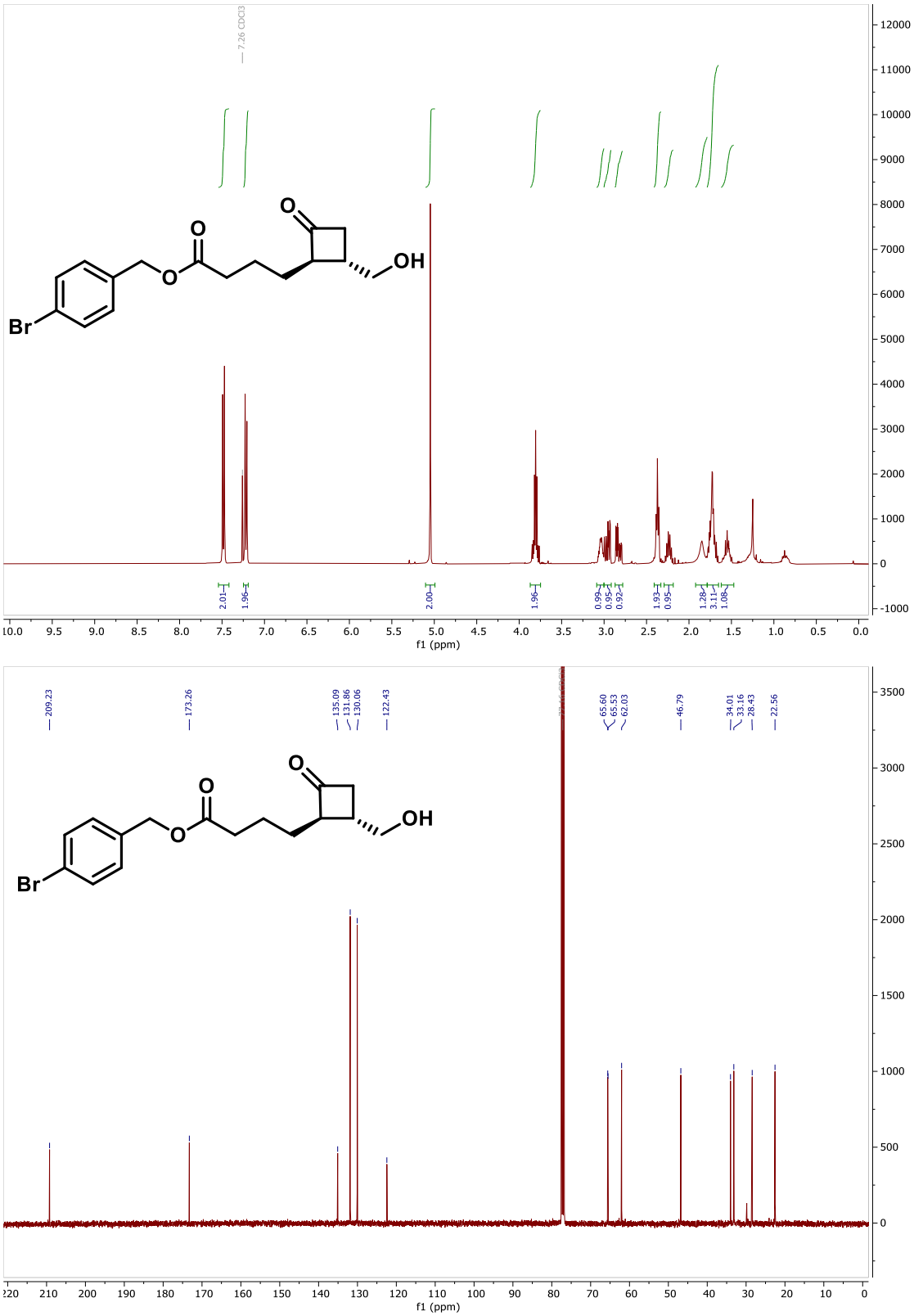


Figure S36: ^{1}H and ^{13}C NMR spectra for compound **15** (400 and 101 MHz, $CDCl_3$, 300K).

11. GC and HPLC Traces

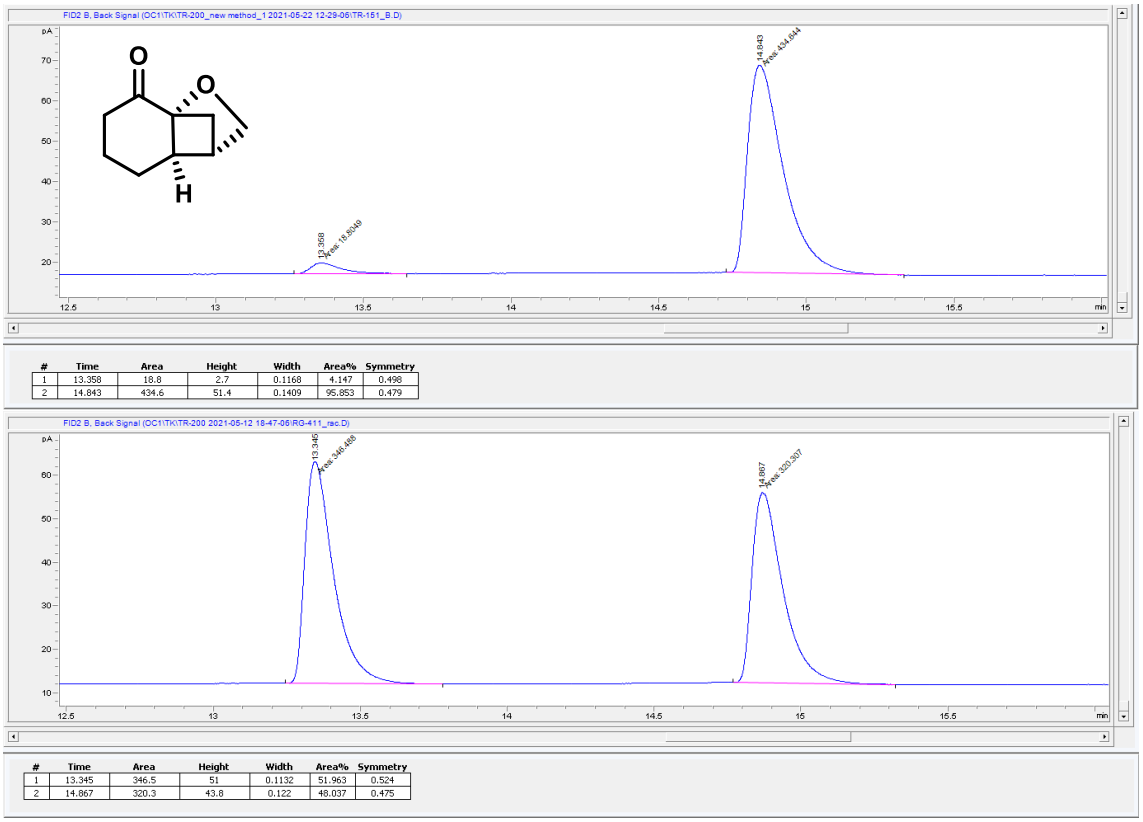


Figure S37: GC chromatograms for compound **5a** (enantioenriched and racemic samples).

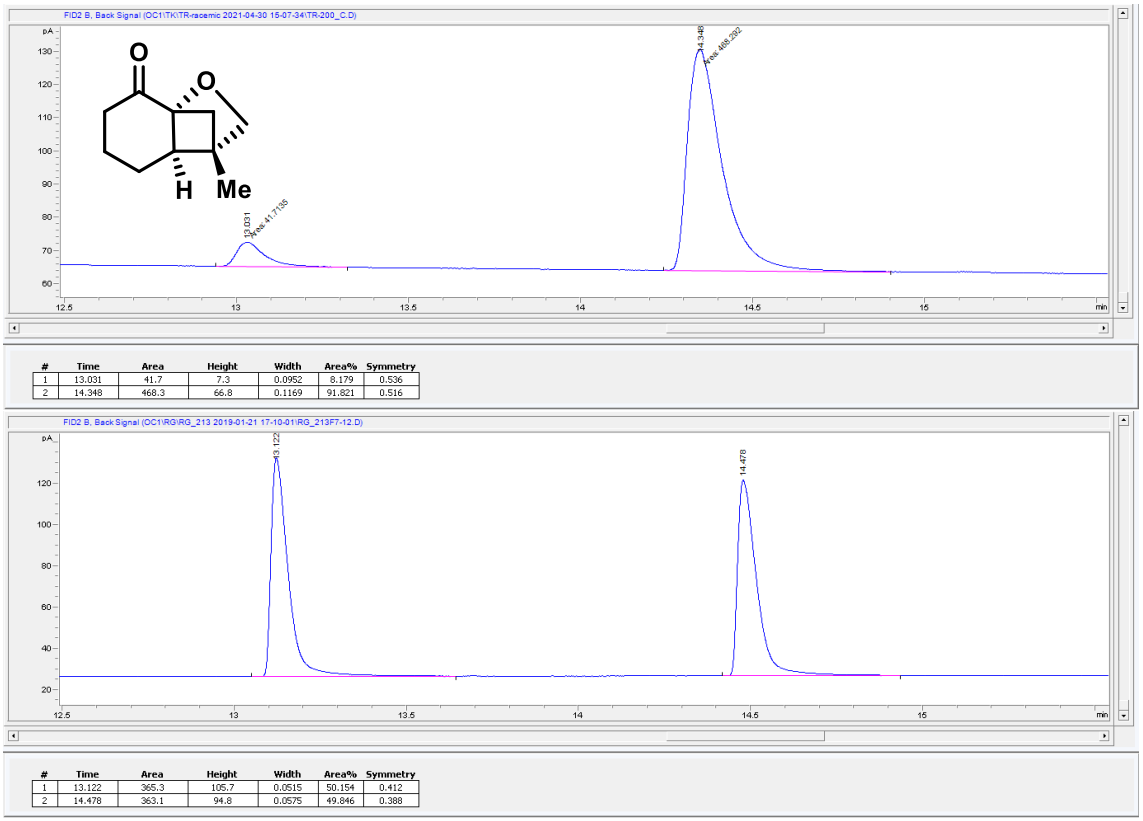


Figure S38: GC chromatograms for compound **5b** (enantioenriched and racemic samples).

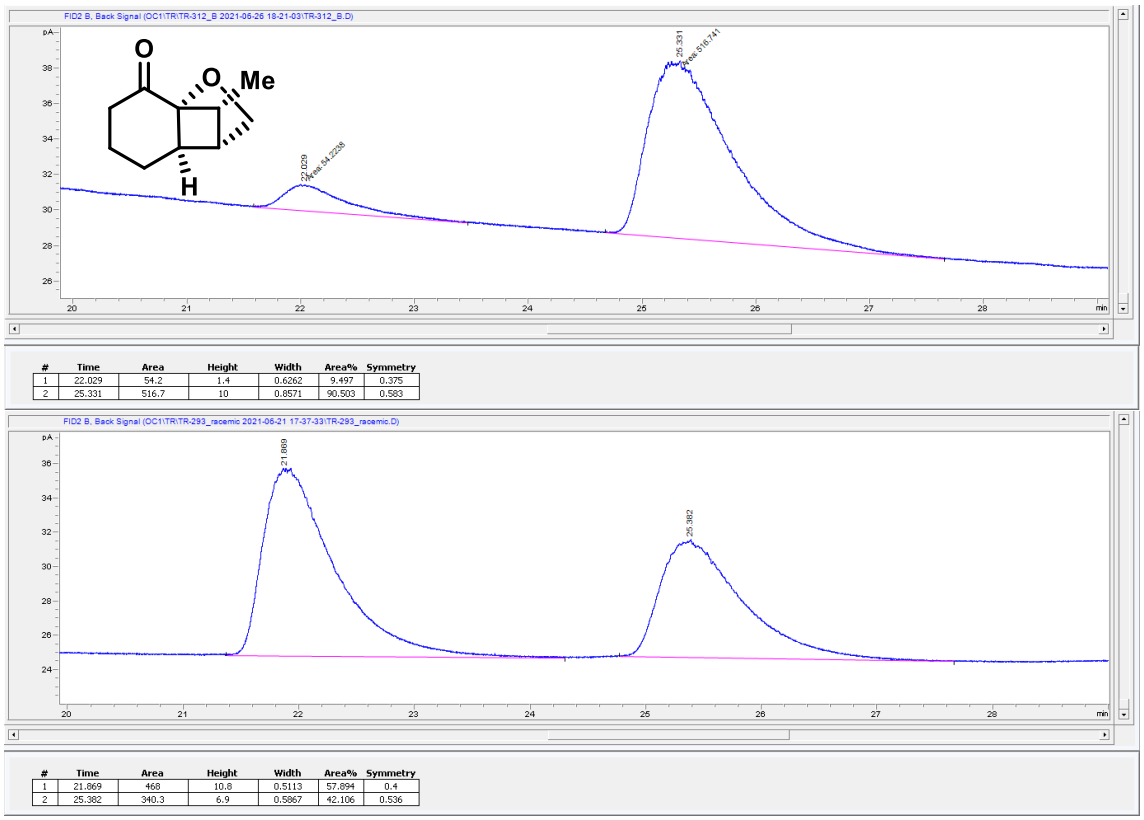
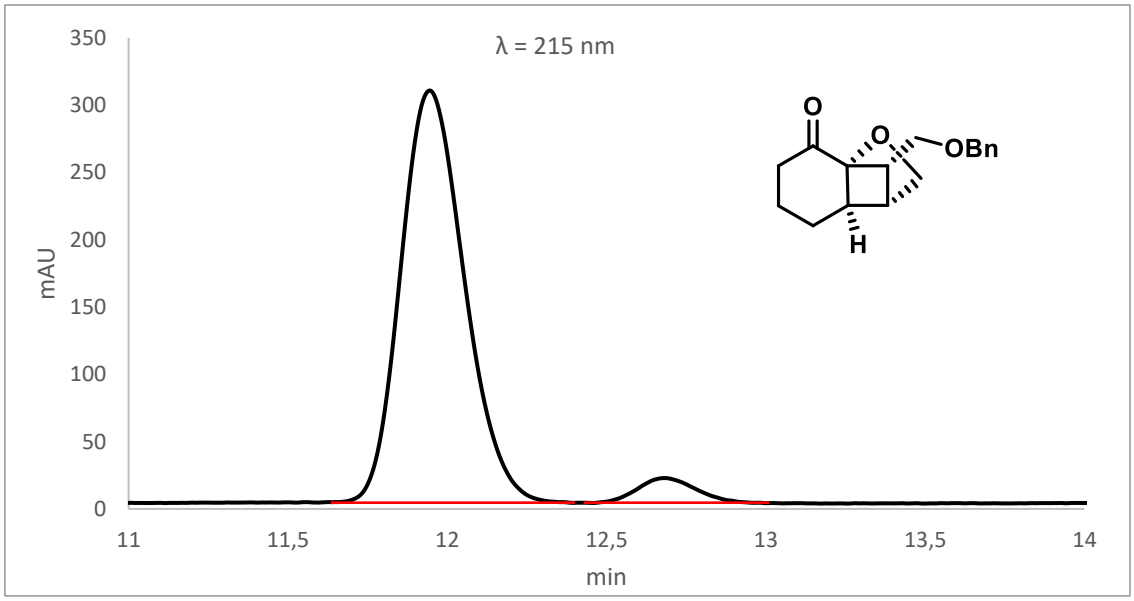
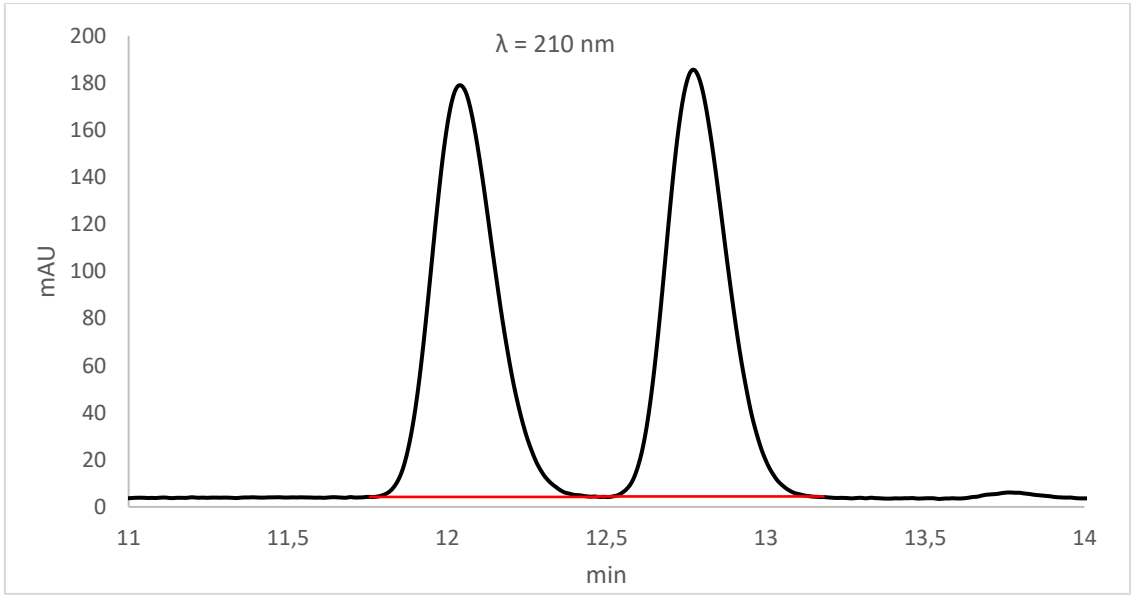


Figure S39: GC chromatograms for compound **5c** (enantioenriched and racemic samples).



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11,94	n.a.	305,963	70,690	94,81	n.a.	BMB
2	12,68	n.a.	18,339	3,867	5,19	n.a.	BMB*
Total:			324,302	74,557	100,00	0,000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	12,04	n.a.	174,902	40,644	49,93	n.a.	BM
2	12,77	n.a.	181,689	40,763	50,07	n.a.	MB
Total:			356,590	81,407	100,00	0,000	

Figure S40: HPLC chromatograms for compound **5d** (enantioenriched and racemic samples).

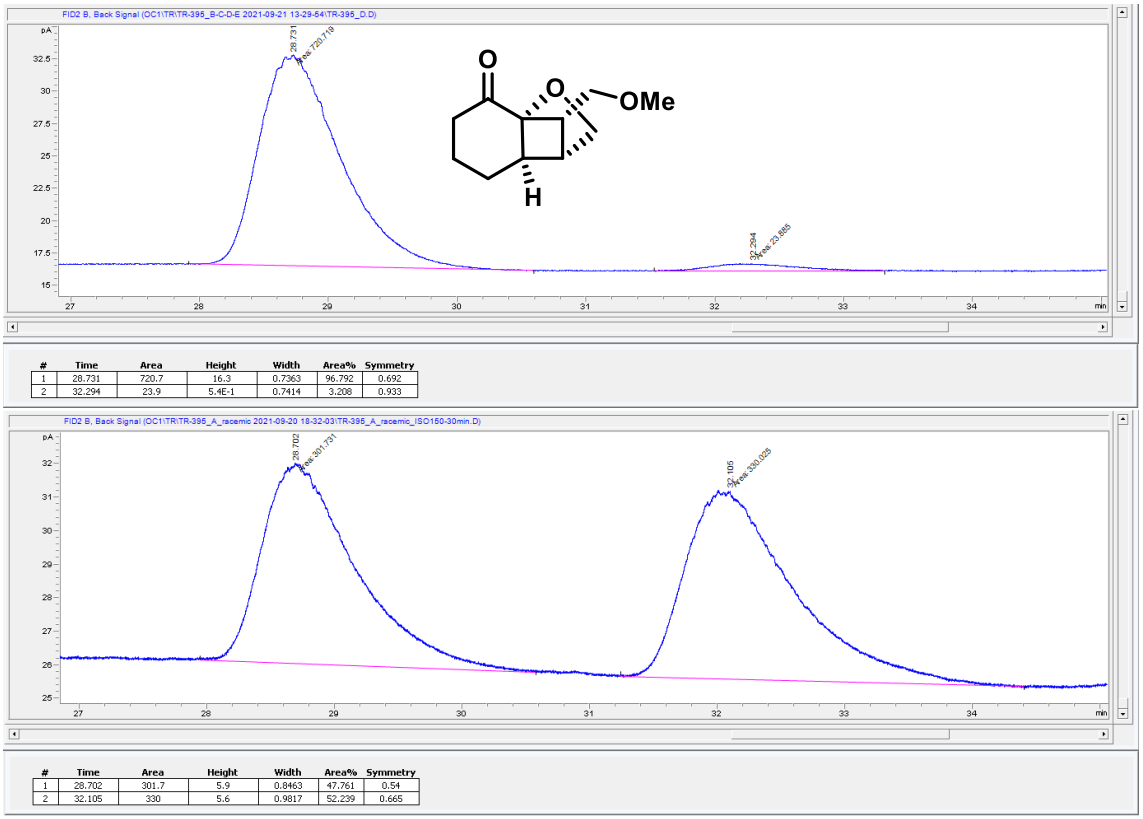
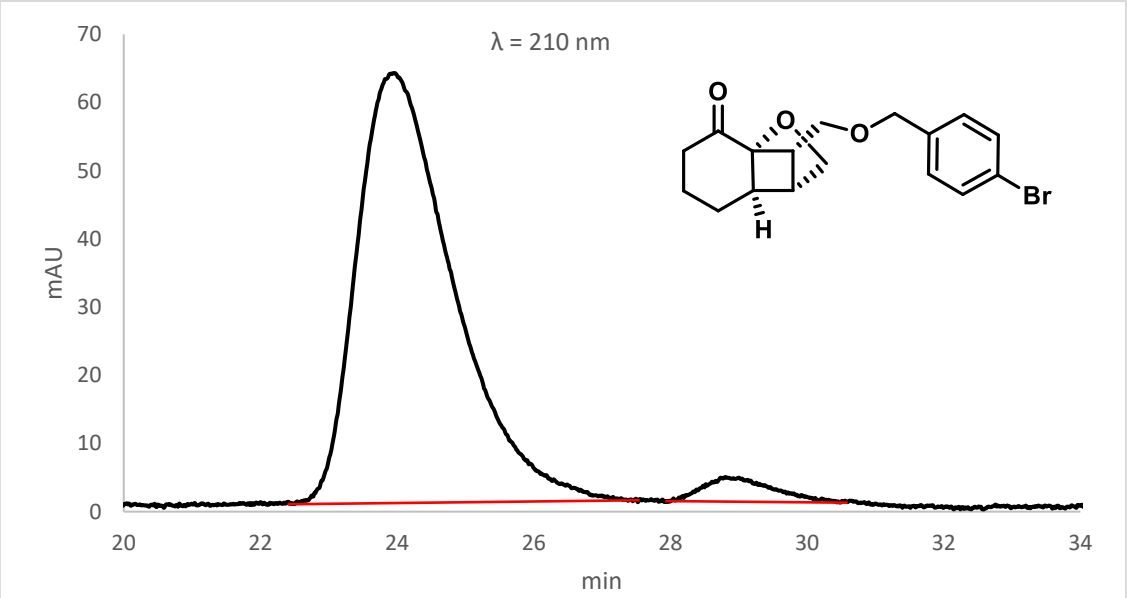
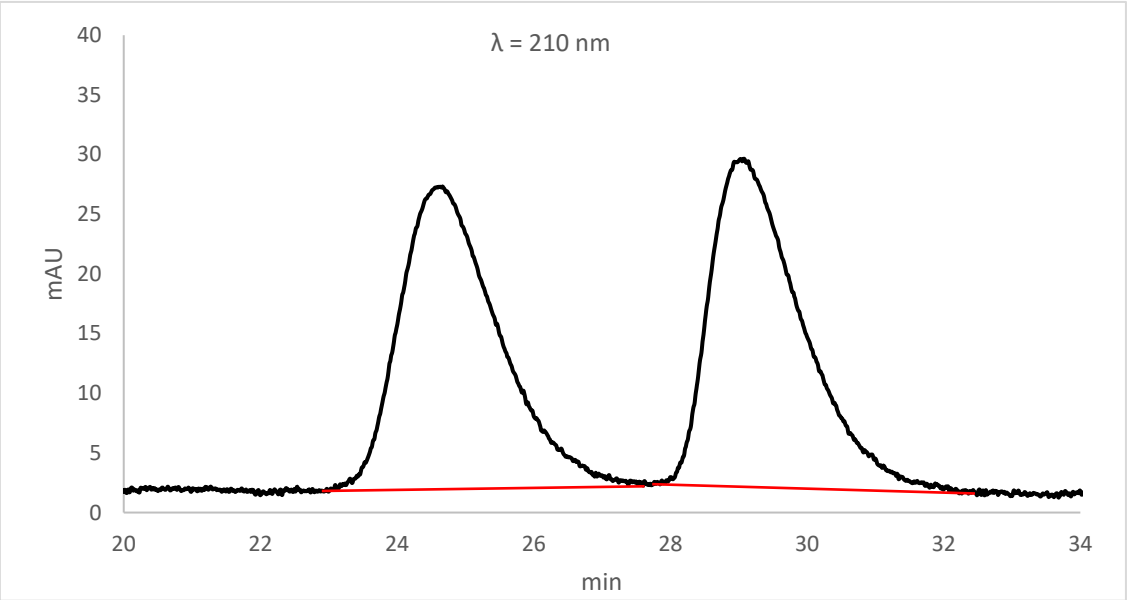


Figure S41: GC chromatograms for compound **5e** (enantioenriched and racemic samples).



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	23,96	n.a.	62,880	102,154	95,88	n.a.	BMB*
2	28,81	n.a.	3,618	4,391	4,12	n.a.	BMB*
Total:			66,498	106,545	100,00	0,000	



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	24,66	n.a.	25,380	42,510	49,55	n.a.	BMB*
2	29,07	n.a.	27,570	43,287	50,45	n.a.	BMB*
Total:			52,950	85,797	100,00	0,000	

Figure S42: HPLC chromatograms for compound **5f** (enantioenriched and racemic samples).

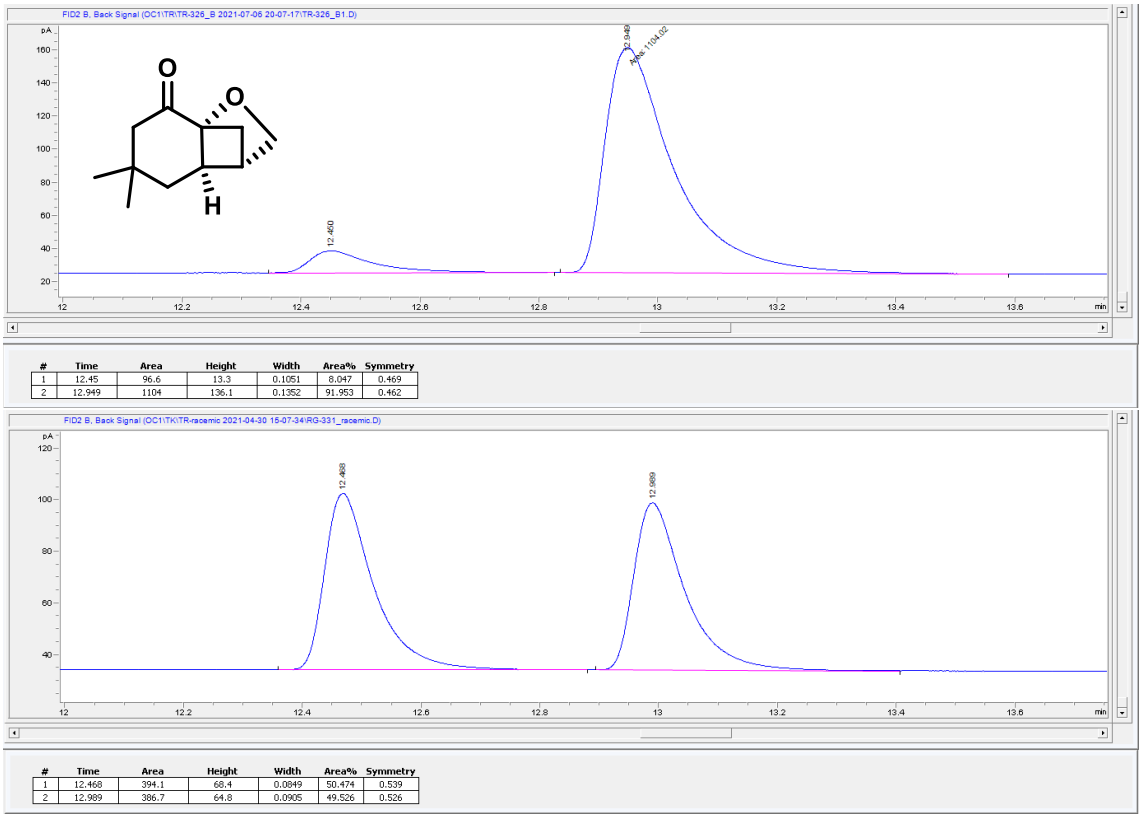


Figure S43: GC chromatograms for compound **5g** (enantioenriched and racemic samples).

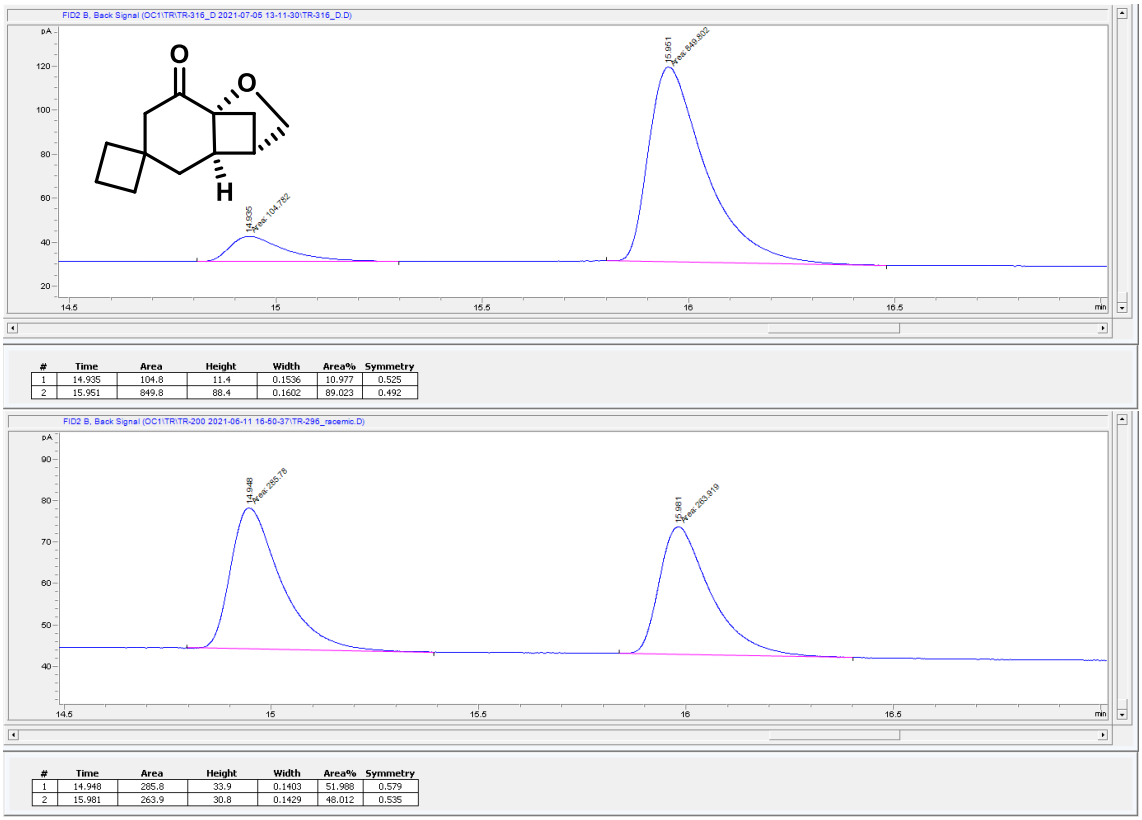


Figure S44: GC chromatograms for compound **5h** (enantioenriched and racemic samples).

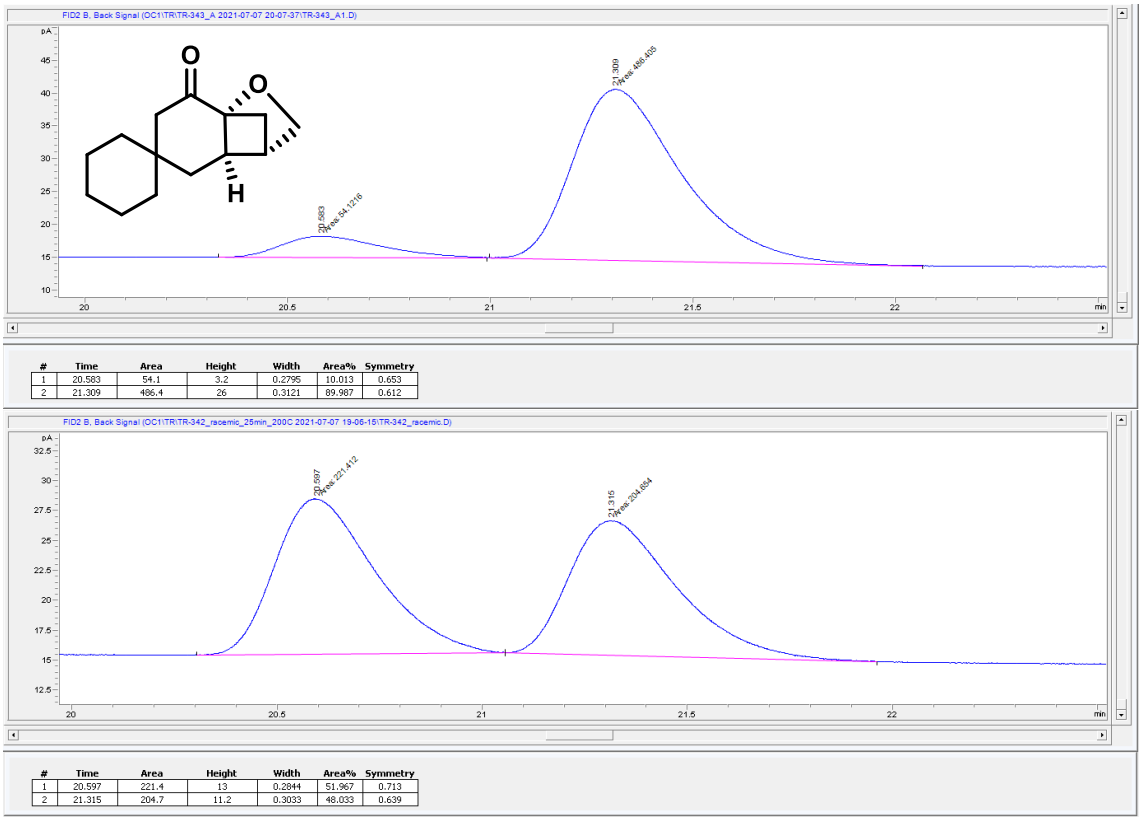


Figure S45: GC chromatograms for compound **5i** (enantioenriched and racemic samples).

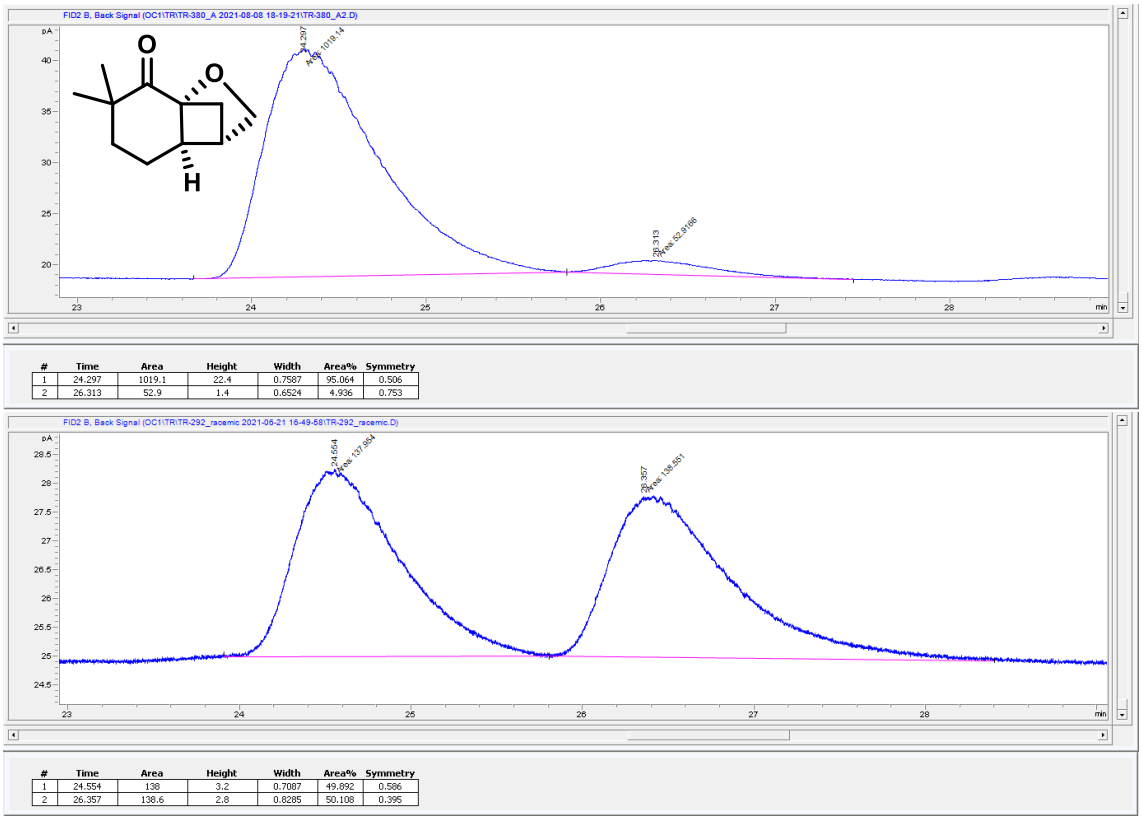
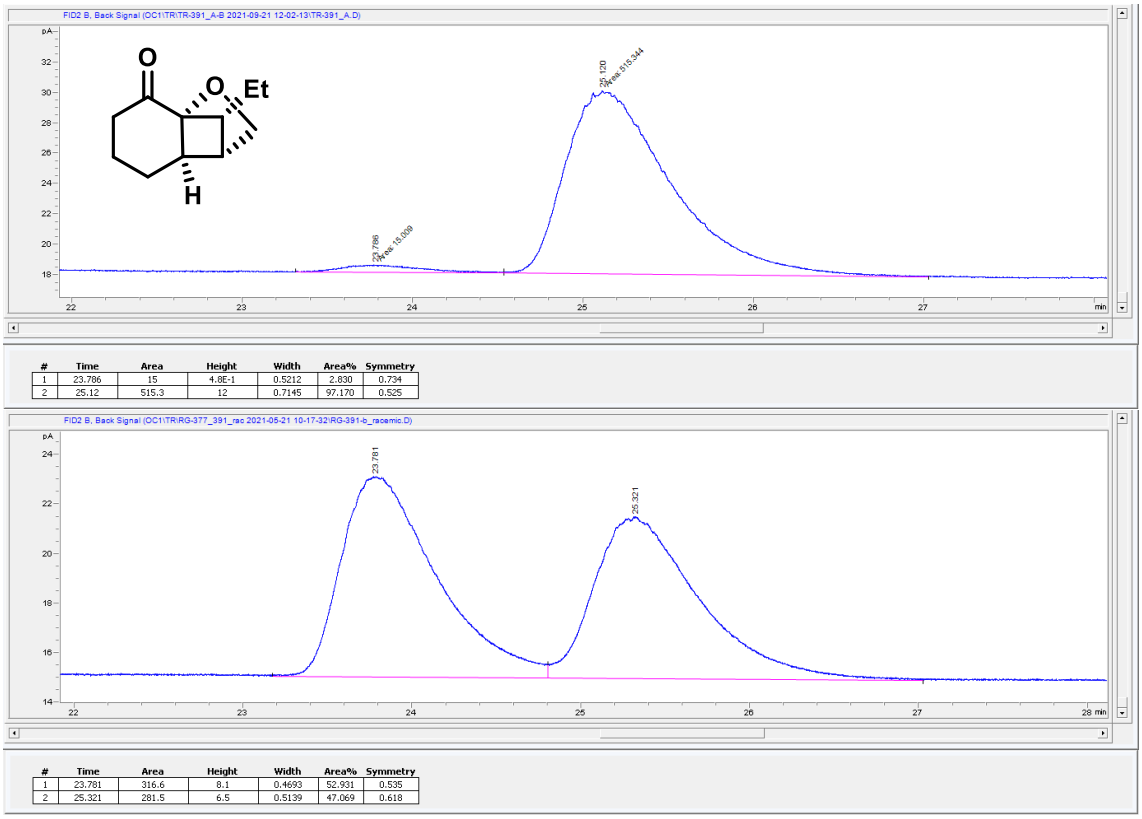


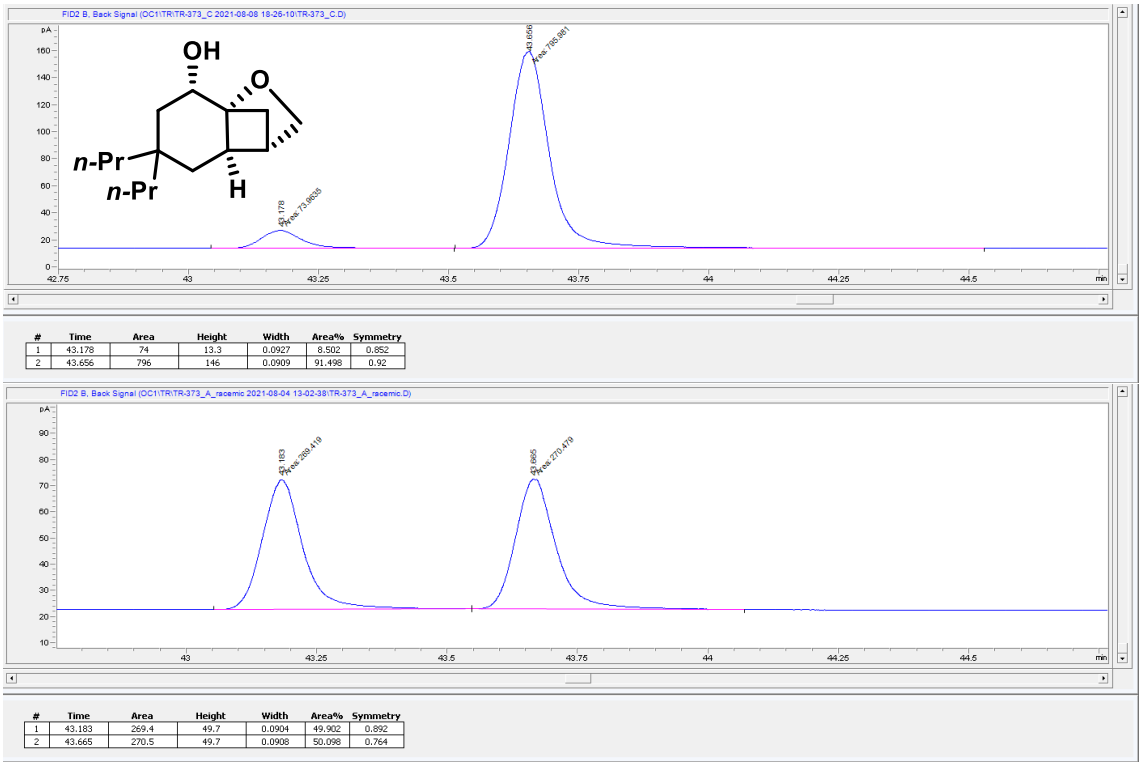
Figure S46: GC chromatograms for compound **5l** (enantioenriched and racemic samples).



#	Time	Area	Height	Width	Area%	Symmetry
1	23.786	15	4.8E-1	0.5212	2.830	0.734
2	25.12	515.3	12	0.7145	97.170	0.525

#	Time	Area	Height	Width	Area%	Symmetry
1	23.781	316.6	8.1	0.4693	52.931	0.535
2	25.321	281.5	6.5	0.5139	47.069	0.618

Figure S47: GC chromatograms for compound **5m** (enantioenriched and racemic samples).



#	Time	Area	Height	Width	Area%	Symmetry
1	43.178	74	13.3	0.0927	8.502	0.852
2	43.656	796	146	0.0909	91.498	0.92

#	Time	Area	Height	Width	Area%	Symmetry
1	43.183	269.4	49.7	0.0904	49.902	0.892
2	43.665	270.5	49.7	0.0908	50.098	0.764

Figure S48: GC chromatograms for compound **10a** (enantioenriched and racemic samples).

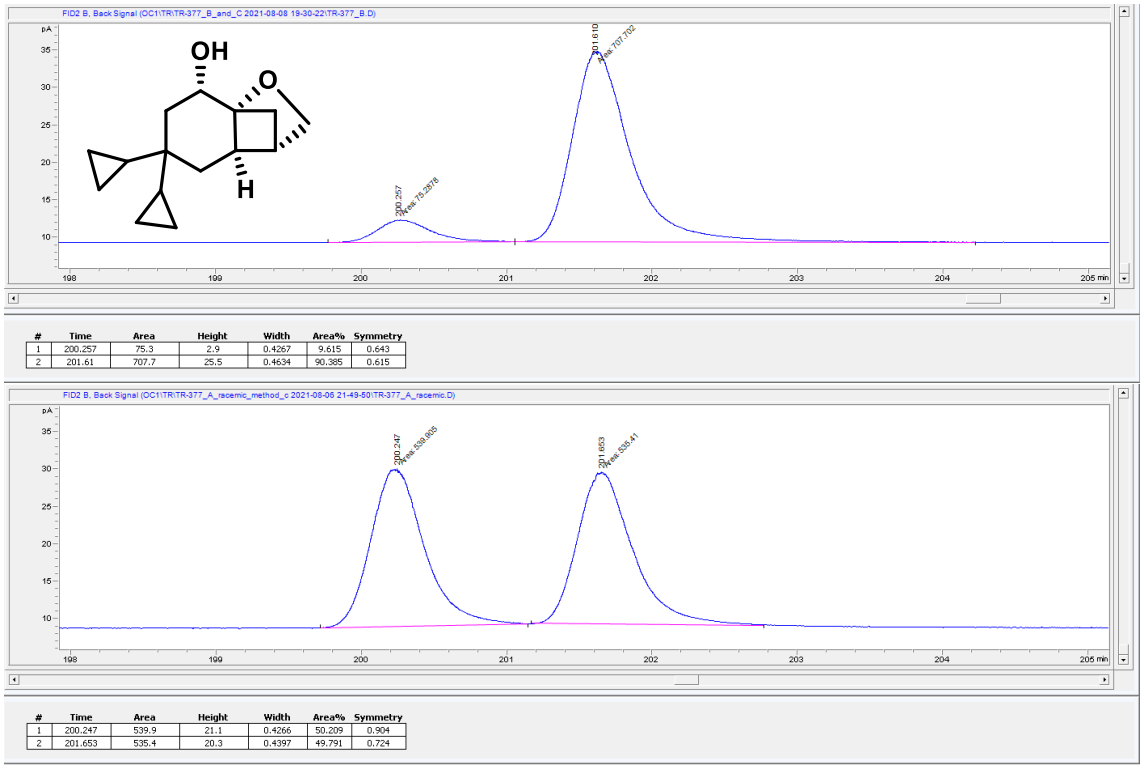
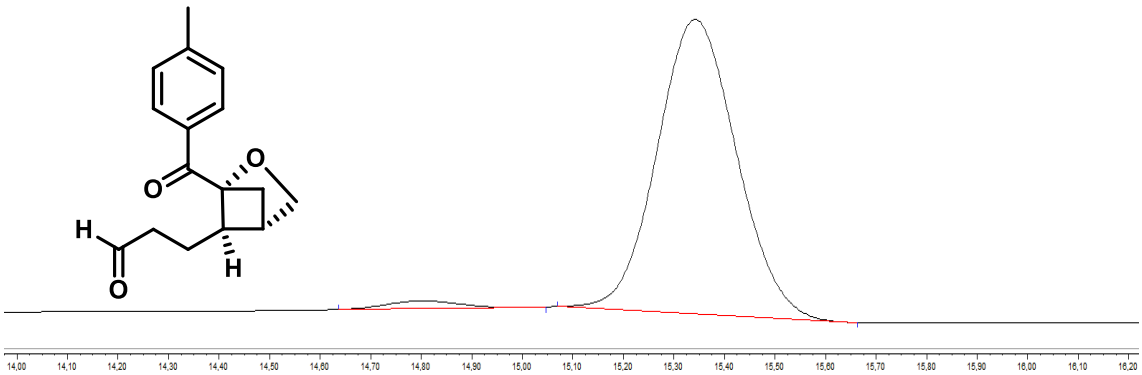
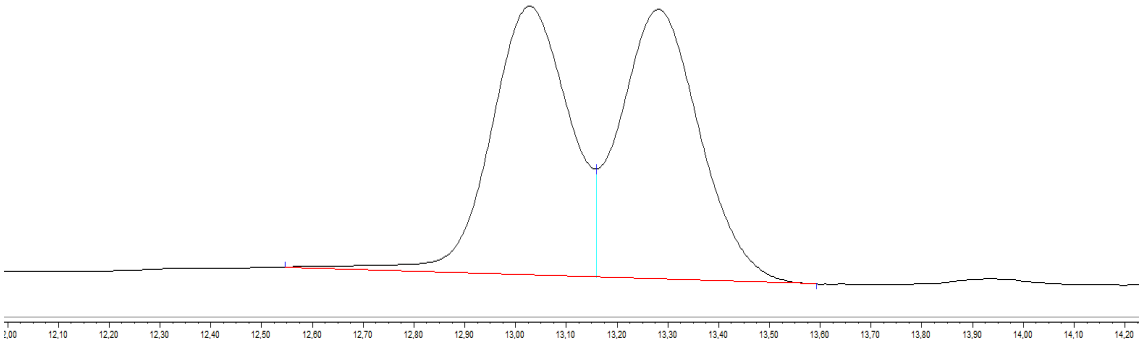


Figure S49: GC chromatograms for compound **10b** (enantioenriched and racemic samples).

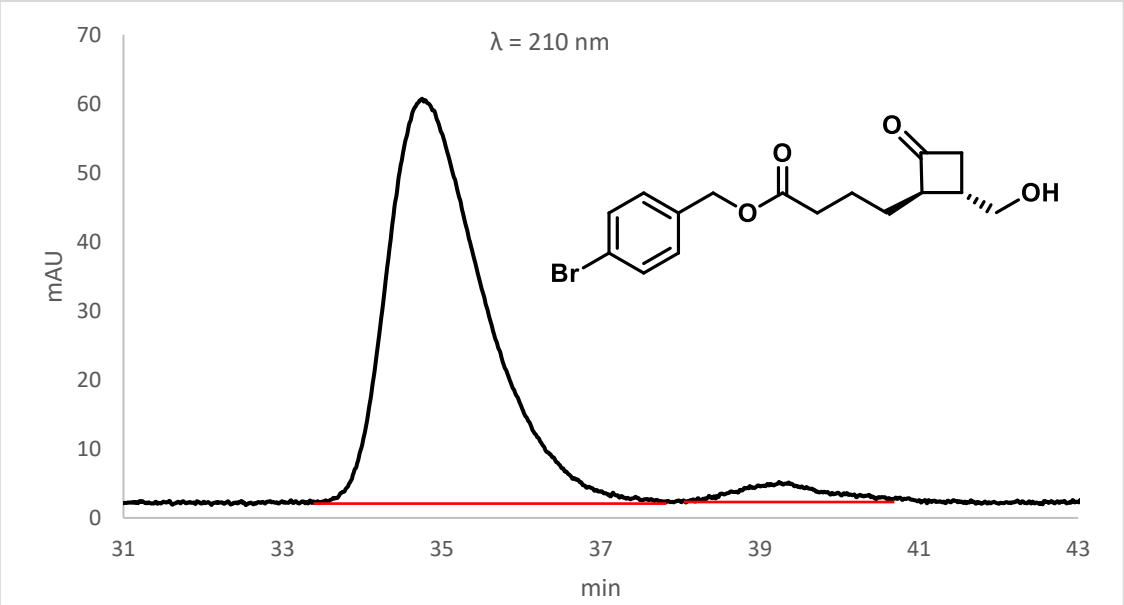


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	14,80	n.a.	9,310	1,499	2,26	n.a.	BMB*
2	15,34	n.a.	356,240	64,875	97,74	n.a.	BMB*
Total:			365,550	66,374	100,00	0,000	

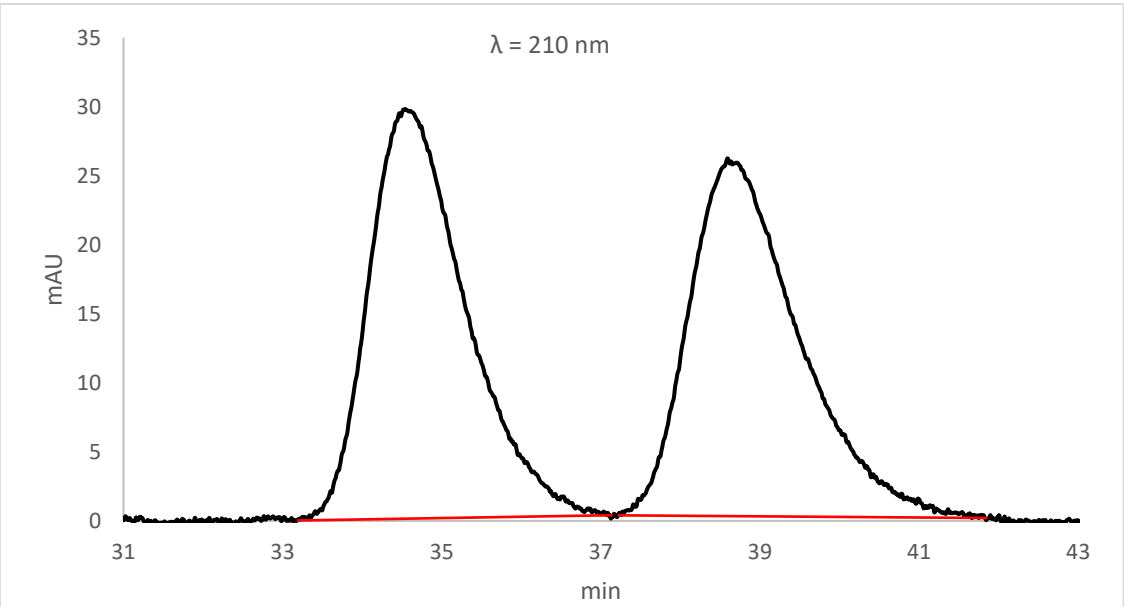


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	13,03	n.a.	125,305	22,512	49,65	n.a.	BM
2	13,28	n.a.	125,725	22,827	50,35	n.a.	MB
Total:			251,031	45,339	100,00	0,000	

Figure S50: HPLC chromatograms for compound **13** (enantioenriched and racemic samples).



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	34,76	n.a.	58,482	81,774	96,21	n.a.	BMB*
2	39,24	n.a.	2,731	3,218	3,79	n.a.	BMB*
Total:			61,213	84,992	100,00	0,000	



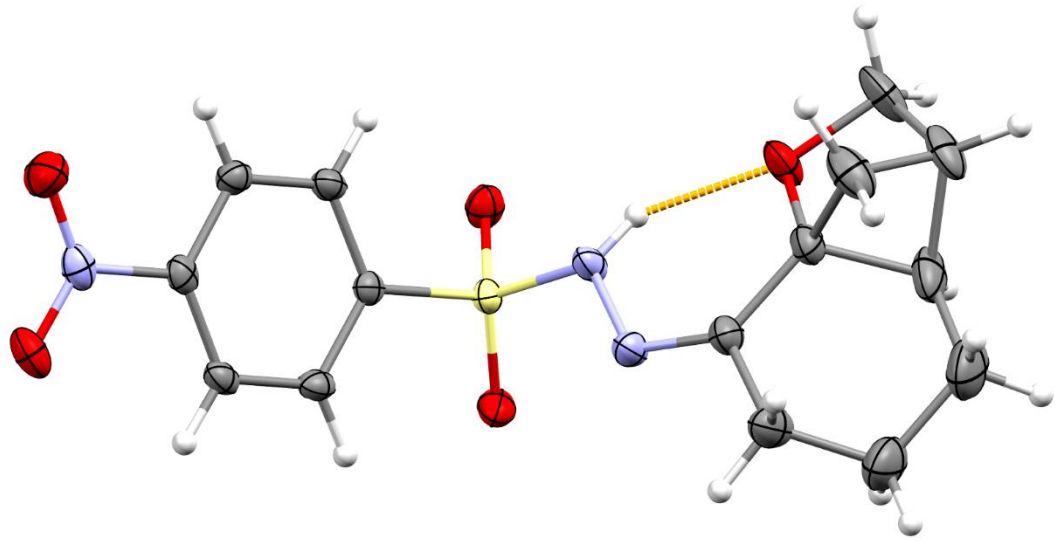
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	34,54	n.a.	29,672	42,041	50,43	n.a.	BMB*
2	38,59	n.a.	25,938	41,324	49,57	n.a.	BMB*
Total:			55,610	83,365	100,00	0,000	

Figure S51: HPLC chromatograms for compound **15** (enantioenriched and racemic samples).

12. Absolute Configuration Determination by X-ray Analysis

Data were collected on a Bruker D8 Venture single crystal X-ray diffractometer equipped with a CMOS detector (Bruker Photon-100), a TXS rotating anode with MoK_α radiation (λ = 0.71073 Å), and a Helios optic using the APEX3 software package.[12] Measurements were performed on single crystals coated with perfluorinated ether. The crystals were fixed on top of a kapton micro sampler and frozen under a stream of cold nitrogen. A matrix scan was used to determine the initial lattice parameters. Reflections were corrected for Lorentz and polarisation effects, scan speed, and background using SAINT.[13] Absorption correction, including odd and even ordered spherical harmonics was performed using SADABS.[13] Space group assignments were based upon systematic absences, E statistics, and successful refinement of the structures. The structures were solved using SHELXT with the aid of successive difference Fourier maps, and were refined against all data using SHELXL in conjunction with SHELXLE.[14-16] Hydrogen atoms were calculated in ideal positions as follows: Methyl hydrogen atoms were refined as part of rigid rotating groups, with a C–H distance of 0.98 Å and $U_{iso(H)} = 1.5 \cdot U_{eq(C)}$. Non-methyl hydrogen atoms were placed in calculated positions and refined using a riding model, with methylene and aromatic C–H distances of 0.99 Å and 0.95 Å, respectively, and other C–H distances of 1.00 Å, all with $U_{iso(H)} = 1.2 \cdot U_{eq(C)}$. Non-hydrogen atoms were refined with anisotropic displacement parameters. Full-matrix least-squares refinements were carried out by minimizing $\Sigma w(F_o^2 - F_c^2)^2$ with the SHELXL weighting scheme.[14] Neutral atom scattering factors for all atoms and anomalous dispersion corrections for the non-hydrogen atoms were taken from *International Tables for Crystallography*.[17] Images of the crystal structures were generated with Mercury.[18] CCDC 2130504 contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

Compound 7 (CCDC 2130504)



Diffractometer operator C. Jandl
scanspeed 2-20 s per frame
dx 50 mm
4392 frames measured in 14 data sets
phi-scans with delta_phi = 0.5
omega-scans with delta_omega = 0.5
shutterless mode

Crystal data

2($C_{15}H_{17}N_3O_5S$)

M_r = 351.38	D_x = 1.488 Mg m^{-3}
Monoclinic, $P2_1$	Melting point: ? K
Hall symbol: P 2yb	Mo $K\alpha$ radiation, λ = 0.71073 Å
a = 6.5937 (6) Å	Cell parameters from 9924 reflections
b = 22.424 (2) Å	θ = 2.6–27.2°
c = 10.7128 (11) Å	μ = 0.24 mm^{-1}
β = 97.951 (3)°	T = 100 K
V = 1568.7 (3) Å^3	Fragment, colourless
Z = 4	0.21 × 0.07 × 0.07 mm
F(000) = 736	

Data collection

Bruker D8 Venture diffractometer

Radiation source: TXS rotating anode

Helios optic monochromator

Detector resolution: 16 pixels mm^{-1}

phi– and ω–rotation scans

Absorption correction: multi-scan *SADABS* 2016/2, Bruker

T_{min} = 0.718, T_{max} = 0.746

54792 measured reflections

6656 independent reflections

6512 reflections with $I > 2\sigma(I)$

R_{int} = 0.022

θ_{max} = 26.7°, θ_{min} = 2.6°

h = −8 8

k = −28 28

l = −13 13

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)]$ = 0.030

$wR(F^2)$ = 0.080

S = 1.06

6656 reflections

441 parameters

1 restraint

0 constraints

Primary atom site location: iterative

Secondary atom site location: difference Fourier map

Hydrogen site location: mixed

H atoms treated by a mixture of independent and constrained refinement

$W = 1/[\Sigma^2(FO^2) + (0.0417P)^2 + 0.6965P]$ WHERE $P = (FO^2 + 2FC^2)/3$

$(\Delta/\sigma)_{max}$ = 0.001

$\Delta\rho_{max}$ = 0.61 e $Å^{-3}$

$\Delta\rho_{min}$ = −0.28 e $Å^{-3}$

Extinction correction: none

Extinction coefficient: -

Absolute structure: Flack, Parsons[19,20]

Absolute structure parameter: 0.017 (7)

13. Determination of Quantum Yield

In a heat-gun dried vial, substrate **4a**, catalyst (9-thioxanthenone or **6**) if necessary, and *n*-undecane as internal standard (50 mol%) were dissolved in degassed CH_2Cl_2 or DCE (10 mM) under positive argon pressure. 2.5 mL of this solution were transferred to a sealable cuvette with a septum screw cap under argon pressure.

This solution was stirred and irradiated with a LED (for emission data, see data sheets) operated at a constant current (700 mA) at room temperature in a previously described setup.[21] The light intensity that was passing the cuvette was continuously measured by a calibrated setup consisting of a cosine-corrector, a 600 µm fiber and an Ocean Optics USB4000 spectrometer. At specific time points, aliquots of 50 µL were taken and diluted with 50 µL CH_2Cl_2. The samples were analyzed by calibrated achiral GLC (performed on an Agilent 6890 Series gas chromatograph using a HP-5 column; poly-dimethyl/diphenyl-siloxane, 95/5 with a flame ionization detector) to obtain the concentration of the individual compounds.

The amount of formed product during an interval of irradiation was calculated by its concentration and the sample volume at that time point. From the measured light intensity, the absorbed energy was calculated by subtraction from the reference intensity of the LED, measured with only solvent in the cuvette and without substrate **4a** or catalyst, and integration over time. Based on the maximum emission wavelength of the LED, the amount of absorbed photons during that interval was calculated.

With the quantum yield as the variable, a best fit of obtained and expected amount of product (amount of absorbed photons × quantum yield) was performed by non-linear regression (least square fit, GRG nonlinear as solving method). Errors are estimated by a Monte Carlo approach at 90% confidence level (assumed standard deviation of concentration error = 5%, 1000 runs).[22] Figure S52 shows the calculated amount of

formed product of the measured aliquots over time for the four conducted experiments as noted in Table S1. The determined quantum yields are also listed. While the best fit of the uncatalyzed photoreaction is of first order, the catalyzed reactions are of zero order in the considered time frames, as expected.

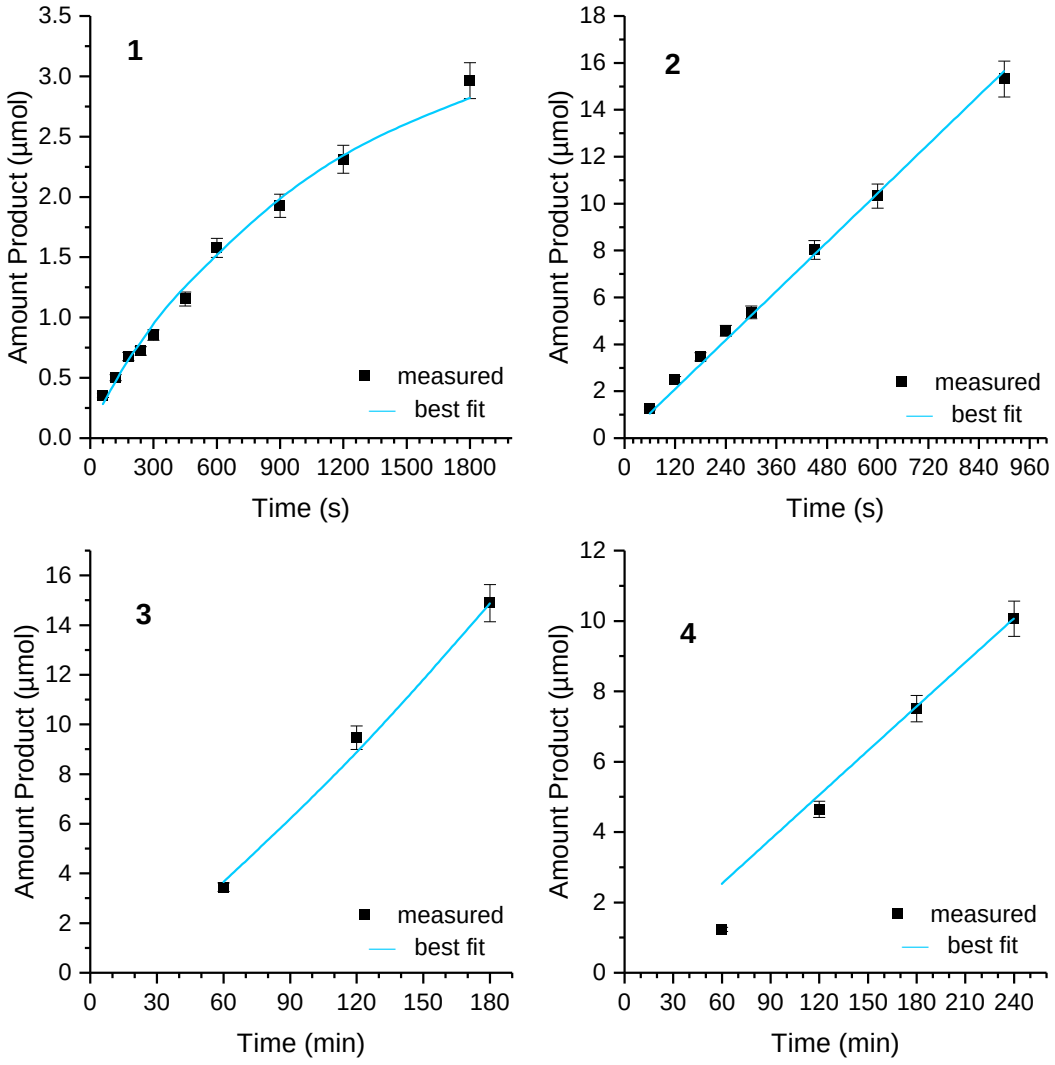


Figure S52: Calculated amount of product over time in the four experiments (see Table S1) and best fit for quantum yield determination.

Table S1. Conducted quantum yield experiments.

#	λ_{max}(LED)	Solvent	Catalyst	Quantum Yield
1	368 nm	CH_2Cl_2	none	0.321 ± 0.034
2	382 nm	CH_2Cl_2	TXT (10 mol%)	0.316 ± 0.011
3	424 nm	DCE	TXT (2 mol%)	0.299 ± 0.055
4	424 nm	DCE	**6** (2 mol%)	0.003 ± 0.001

14. References

1) (a) D. Rackl, V. Kais, P. Kreitmeier and O. Reiser, *Beilstein J. Org. Chem.*, 2014, **10**, 2157-2165; (b) D. Lenhart, A. Bauer, A. Pöthig and T. Bach, *Chem. Eur. J.*, 2016, **22**, 6519-6523.

2) R. Graßl, C. Jandl and T. Bach, *J. Org. Chem.*, 2020, **85**, 11426-11439.

3) J. Ma, X. Zhang, X. Huang, S. Luo and E. Meggers, *Nat. Protoc.*, 2018, **13**, 605-632.

4) K. Hirano, A. T. Biju, I. Piel and Frank Glorius, *J. Am. Chem. Soc.*, 2009, **131**, 14190-14191.

5) K. J. Emery, T. Tuttle and J. A. Murphy, *Org. Biomol. Chem*., 2017, **15**, 8810–8819.

6) X. Jin, W. Xu, J. Yang, J. Lu, Y. Fu, L. Xie, Q. Zhu and W. Dong, *Tetrahedron Lett.*, 2015, **56**, 6287-6289.

7) L. Lempenauer, E. Duñach and G. Lemière, *Org. Lett*., 2016, **18**, 1326-1329.

8) A. A. Frimer, V. Marks, P. Gilinsky-Sharon, L. Aljadeff and H. E. Gottlieb, *J. Org. Chem*., 1995, **60**, 4510-4520.

9) M. Rodríguez, G. Font, J. Nadal-Moradell, A. Hernán-Gómez, M. Costas, *Adv. Synth. & Catal*., 2020, **362**, 5116-5123.

10) C. Zhao, D. Guo, K. Munkerup, K.-W. Huang, F. Li and J. Wang, *Nat. Commun.*, 2018, **9**, 611.

11) K. Winska, A. Grudniewska, A. Chojnacka, A. Białonska and C. Wawrzenczyk, *Tetrahedron Asymmetry*, 2010, **21**, 670-678.

12) *APEX suite of crystallographic software*, APEX 3, Version 2019-1.0, Bruker AXS Inc., Madison, Wisconsin, USA, 2019.

13) *SAINT*, Version 8.40A and *SADABS*, Version 2016/2, Bruker AXS Inc., Madison, Wisconsin, USA, 2016/2019.

14) G. M. Sheldrick, *Acta Crystallogr. Sect. A*, 2015, **71**, 3-8.

15) G. M. Sheldrick, *Acta Crystallogr. Sect. C*, 2015, **71**, 3-8.

16) C. B. Hübschle, G. M. Sheldrick and B. Dittrich, *J. Appl. Cryst.*, 2011, **44**, 1281-1284.

17) *International Tables for Crystallography, Vol. C* (Ed.: A. J. Wilson), Kluwer Academic Publishers, Dordrecht, The Netherlands, 1992, Tables 6.1.1.4 (pp. 500–502), 4.2.6.8 (pp. 219–222), and 4.2.4.2 (pp. 193–199).

18) C. F. Macrae, I. J. Bruno, J. A. Chisholm, P. R. Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J. van de Streek and P. A. Wood, *J. Appl. Cryst.*, 2008, **41**, 466-470.

19) H. D. Flack, *Acta Crystallogr. Sect A*, 1983, **39**, 876-881.

20) S. Parsons, H. D. Flack and T. Wagner, *Acta Crystallogr. Sect B*, 2013, **69**, 249-259.

21) F. M. Hörmann, C. Kerzig, T. S. Chung, A. Bauer, O. S. Wenger and T. Bach, *Angew. Chem. Int. Ed.*, 2020, **59**, 9659-9668.

22) This method was also applied in: A. Hölzl-Hobmeier, A. Bauer, A. Vieira Silva, S. M. Huber, C. Bannwarth and T. Bach, *Nature*, 2018, **564**, 240-243.