Supporting Information for

# Enantioselective Synthesis of 1,2-Disubstituted Thiocyclobutanes *via* Michael Addition

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**(125 pages)**

# Contents

# 1. Experimental part

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise.

All chemicals were purchased from Acros, Aldrich, TCI, Merck, Fluorochem or Combi-Blocks and used as such.

Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. For flash chromatography, distilled technical grade solvents were used. TLC was performed on Merck silica gel 60 F254 TLC aluminum or glass plates and visualized with UV light and para-anysaldehyde stain.

$^{1}$H-NMR spectra were recorded on a Brucker DPX-400 400 MHz spectrometer in chloroform-*d* or DMSO-$d_6$, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm or the internal DMSO signal at 2.50 ppm as standard. The data is being reported as (s = singlet, d = doublet, t= triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation).$^{13}$C-NMR spectra were recorded with $^{1}$H-decoupling on a Brucker DPX-400 100 MHz spectrometer in chloroform-*d* or DMSO-$d_6$ all signals are reported in ppm with the internal chloroform signal at 77.0 ppm or the internal DMSO signal at 39.52 ppm as standard.

Melting points were measured on a Büchi B-540 melting point apparatus using open glass capillaries and are uncorrected.

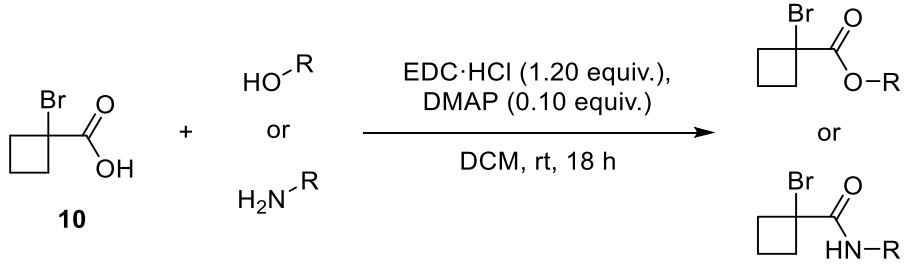
Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as $cm^{-1}$ (w = weak, m = medium, s = strong, br = broad).

High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. A standard data acquisition and instrument control system was utilized (Thermo Scientific) whereas the ion source was controlled by Chipsoft 8.3.1 software (Advion BioScience). Samples were loaded onto a 96-well plate (Eppendorf, Hamburg, Germany) within an injection volume of 5µl. The experimental condition for the ionization voltage was +1.4kV and the gas pressure was set at 0.30 psi. The temperature of ion transfer capillary was 275 °C, tube voltages. FTMS spectra were obtained in the 80-1000 m/z range in the reduce profile mode with a resolution set to 120,000. In all spectra one microscan was acquired with a maximum injection time value of 1000ms. Typical CID experiments were carried out using Normalized collision energy values of 26-28 and 5 Da of isolation width.

SFC analysis on the chiral stationary phase were performed on an Agilent 1260 Infinity II instrument using columns CHIRALPAK IA-3 and IC-3. HPLC analysis on chiral stationary phase was performed on an Agilent Acquity instrument using a Daicel CHIRALPAK IA chiral column. The exact conditions for the analyses are specified within the characterization section. SFC traces were compared to racemic samples.

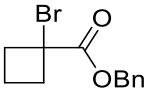
## 1.1. Synthesis of cyclobutenes

### *General procedure (A) for esterification or amidation of bromocyclobutane*




A solution of 1-bromocyclobutane-1-carboxylic acid **10** (1.00 equiv.), alcohol or amine (1.20 equiv.), EDC·HCl (1.20 equiv.) and DMAP (0.10 equiv.) in DCM was stirred at rt for 18 h. The mixture was then washed with water (1 x 100 mL), and the organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude bromocyclobutane was purified by flash chromatography.

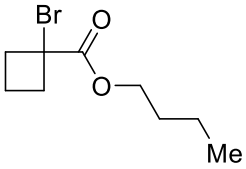
**1-Bromocyclobutanecarboxylic acid benzyl ester (11a)**




Prepared according to the general procedure A from 1-bromocyclobutane-1-carboxylic acid (150 mg, 838 µmol, 1.00 equiv.), benzylalcohol (109 mg, 1.01 mmol, 1.20 equiv.), EDC·HCl (193 mg, 1.01 mmol, 1.20 equiv.), DMAP (10.2 mg, 83.8 µmol, 0.100 equiv.), and DCM (4.0 mL). The crude product was purified by flash chromatography using PE/EtOAc 98:2 to afford **11a** as an oil (239 mg, 886 µmol, 79% yield).

Rf(PE/EtOAc 96:4): 0.71.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.50 – 7.30 (m, 5H, Ar*H*), 5.24 (s, 2H, OC$H_2$Ph), 3.05 – 2.84 (m, 2H, CC$H_2$), 2.72 – 2.52 (m, 2H, CC$H_2$), 2.33 – 2.10 (m, 1H, $CCH_2CH_2$), 2.00 – 1.78 (m, 1H, $CCH_2CH_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 171.5, 135.6, 128.7, 128.5, 128.1, 67.7, 54.3, 37.4, 16.9.
NMR spectra are in agreement with the reported data.[1]

**1-Bromocyclobutanecarboxylic acid butyl ester (11b)**



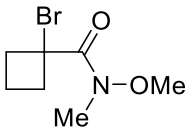

Prepared according to the general procedure A from 1-bromocyclobutane-1-carboxylic acid (895 mg, 5.00 mmol, 1.00 equiv.), 1-butanol (445 mg, 549 µL, 6.00 mmol, 1.20 equiv.), EDC·HCl (1.15 g, 6.00 mmol, 1.20 equiv.), DMAP (61.1 mg, 500 µmol, 0.100 equiv.), and DCM (12.1 mL). The crude product was purified by flash chromatography using PE/$Et_2O$ 90:10 to afford **11b** as an oil (942 mg, 4.01 mmol, 80% yield).

Rf(PE/$Et_2O$ 95:5): 0.50.

[1] E. G. L. Robert, V. Pirenne, M. D. Wodrich, J. Waser, *Angew. Chem. Int. Ed.* **2023**, *62*, e202302420.

$^{1}$H NMR (400 MHz, chloroform-*d*) δ 4.20 (t, *J* = 6.6 Hz, 2H, OC*H*$_2$), 2.99 – 2.79 (m, 2H, C(O)CC*H*$_2$), 2.62 (dddd, *J* = 13.9, 7.0, 5.0, 2.5 Hz, 2H, C(O)CC*H*$_2$), 2.22 (dtt, *J* = 11.5, 9.7, 5.9 Hz, 1H, C(O)CCH$_2$C*H*$_2$), 1.95 – 1.80 (m, 1H, C(O)CCH$_2$C*H*$_2$), 1.73 – 1.62 (m, 2H, OCH$_2$C*H*$_2$), 1.49 – 1.35 (m, 2H, OCH$_2$CH$_2$C*H*$_2$), 0.95 (t, *J* = 7.4 Hz, 3H, C*H*$_3$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 171.8, 66.0, 54.6, 37.4, 30.6, 19.2, 16.9, 13.8.
NMR spectra are in agreement with the reported data.[2]

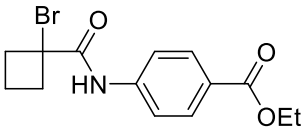
**1-Bromanyl-N-methoxy-N-methyl-cyclobutane-1-carboxamide (11c)**




Prepared according to the general procedure A from 1-bromocyclobutane-1-carboxylic acid (300 mg, 1.68 mmol, 1.00 equiv.), methoxy(methyl)amine hydrochloride (196 mg, 2.01 mmol, 1.20 equiv.), EDC·HCl (386 mg, 2.01 mmol, 1.20 equiv.), DMAP (20.5 mg, 168 µmol, 0.100 equiv.), and DCM (8.0 mL). The crude product was purified by flash chromatography using PE/EtOAc 80:20 to afford **11c** as an oil (267 mg, 1.20 mmol, 72% yield).

Rf(PE/EtOAc 9:1): 0.40.
$^{1}$H NMR (400 MHz, chloroform-d) δ 3.77 (s, 3H, OC*H*$_3$), 3.23 (s, 3H, NC*H*$_3$), 2.96 – 2.85 (m, 2H, CC*H*$_2$), 2.57 – 2.45 (m, 2H, CC*H*$_2$), 2.43 – 2.28 (m, 1H, CCH$_2$C*H*$_2$), 1.86 – 1.69 (m, 1H, CCH$_2$C*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-d) δ 174.7, 60.6, 57.0, 37.3, 33.3, 16.2.
NMR spectra are in agreement with the reported data.[1]

**Ethyl 4-(1-bromocyclobutane-1-carboxamido)benzoate (11d)**

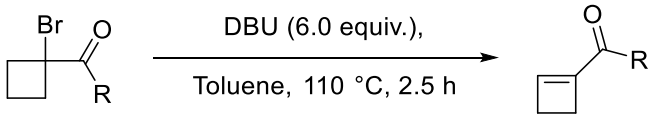



Prepared according to the general procedure A from 1-bromocyclobutane-1-carboxylic acid (716 mg, 4.00 mmol, 1.00 equiv.), ethyl 4-azanylbenzoate (793 mg, 4.80 mmol, 1.20 equiv.), EDC·HCl (920 mg, 4.80 mmol, 1.20 equiv.), DMAP (48.9 mg, 400 µmol, 0.100 equiv.), and DCM (9.71mL). The crude product was purified by flash chromatography using PE/EtOAc 90:10 to afford **11d** as a white solid (982 mg, 3.01 mmol, 75% yield).

Rf(PE/EtOAc 9:1): 0.29.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 8.17 (s, 1H, N*H*), 8.08 – 7.96 (m, 2H, Ar*H*), 7.70 – 7.59 (m, 2H, Ar*H*), 4.36 (q, *J* = 7.1 Hz, 2H, OC*H*$_2$), 3.10 (dtd, *J* = 8.8, 7.7, 5.0 Hz, 2H, CC*H*$_2$), 2.66 (dddd, *J* = 9.4, 7.3, 6.1, 3.3 Hz, 2H, CC*H*$_2$), 2.41 – 2.25 (m, 1H, CCH$_2$C*H*$_2$), 2.11 – 1.96 (m, 1H, CCH$_2$C*H*$_2$), 1.39 (t, *J* = 7.1 Hz, 3H, OCH$_2$C*H*$_3$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 169.2, 166.2, 141.6, 131.0, 126.7, 119.0, 61.1, 60.5, 38.0, 17.2, 14.5.
NMR spectra are in agreement with the reported data.[3]

## *General procedure (B) for dehydrobromination*

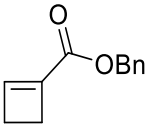
[2] A. A. Homon, O. V. Hryshchuk, S. Trofymchuk, O. Michurin, Y. Kuchkovska, D. S. Radchenko, O. O. Grygorenko, *Eur. J. Org. Chem.* **2018**, *2018*, 5596–5604.
[3] E. G. L. Robert, J. Waser, *Chem. Eur. J.* **2025**, *31*, e202403986.




**11a-d** **2a-d**

According to a reported procedure,[2] DBU (6.0 equiv.) in toluene was heated to 110 °C and the bromocyclobutane **11a-d** (1.00 equiv.) was added. The reaction was stirred at 110 °C for 2.5 h. White salts usually appear in suspension at the end of the reaction. The mixture was diluted in ether (100 mL) and then washed with water (1 x 100 mL), and the organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude cyclobutene was purified by flash chromatography.

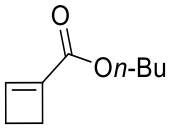
**Benzyl cyclobutene-1-carboxylate (2a)**




Prepared according to the general procedure B from **11a** (4.31 g, 3.20 mL, 16.0 mmol, 1.00 equiv.), DBU (14.6 g, 14.3 mL, 96.0 mmol, 6.00 equiv.) and toluene (50.3 mL). The crude product was purified by flash chromatography using PE/EtOAc 95:5 to afford **2a** as an oil (1.22 g, 6.47 mmol, 40% yield).

Rf(PE/EtOAc 95:5): 0.34.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.35 (dq, *J* = 16.7, 4.7 Hz, 5H, Ar*H*), 6.81 (s, 1H, C=C*H*), 5.18 (s, 2H, OC$H_2$Ph), 2.78 – 2.72 (m, 2H, C$H_2$CC(O)), 2.48 (t, *J* = 2.9 Hz, 2H, C$H_2$CH).
$^{13}$C NMR (101 MHz, chloroform-*d*, signals not fully resolved) δ 162.2, 147.2, 138.6, 136.2, 128.7, 128.3, 65.9, 29.3, 27.3.
NMR spectra are in agreement with the reported data.[4]

**Cyclobutene-1-carboxylic acid butyl ester (2b)**

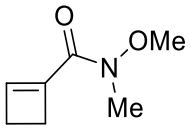



Prepared according to the general procedure B from **11b** (900 mg, 3.83 mmol, 1.00 equiv.), DBU (3.50 g, 3.43 mL, 23.0 mmol, 6.00 equiv.) and toluene (10.5 mL). The crude product was purified by flash chromatography using PE/EtOAc 95:5 to afford **2b** as an oil (331 mg, 2.14 mmol, 56% yield).

Rf(PE/$Et_2O$ 95:5): 0.37.
$^1$H NMR (400 MHz, chloroform-*d*) δ 6.76 (s, 1H, *H*C=C), 4.13 (t, *J* = 6.7 Hz, 2H, OC$H_2$), 2.78 – 2.66 (m, 2H, C$H_2$CC(O)), 2.46 (dd, *J* = 4.4, 2.0 Hz, 2H, C$H_2$CH), 1.73 – 1.62 (m, 2H, $OCH_2CH_2$), 1.40 (h, *J* = 7.4 Hz, 2H, $OCH_2CH_2CH_2$), 0.94 (t, *J* = 7.4 Hz, 3H, $CH_3$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 162.6, 146.3, 139.0, 64.1, 30.9, 29.3, 27.2, 19.3, 13.9.
NMR spectra are in agreement with the reported data.[2]

[4] H. Xu, W. Zhang, D. Shu, J. B. Werness, W. Tang, *Angew. Chem. Int. Ed.* **2008**, *47*, 8933–8936.

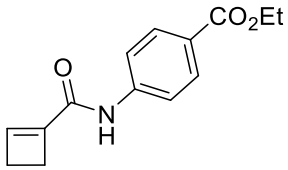
**N-Methoxy-N-methylcyclobutene-1-carboxamide (2c)**




Prepared according to the general procedure B from **11c** (1.33 g, 6.00 mmol, 1.00 equiv.), DBU (5.48 g, 5.37 mL, 36.0 mmol, 6.00 equiv.) and toluene (15.6 mL). The crude product was purified by flash chromatography using PE/EtOAc 80:20 to afford **2c** as an oil (393 mg, 2.78 mmol, 46% yield).

Rf(PE/EtOAc 80:20): 0.53.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 6.66 (s, 1H, *H*C=C), 3.70 (s, 3H, OC*H*$_3$), 3.23 (s, 3H, NC*H*$_3$), 2.90 – 2.71 (m, 2H, C*H*$_2$CC(O)), 2.48 (dd, *J* = 4.6, 1.9 Hz, 2H, C*H*$_2$CH).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 162.9, 144.8, 139.5, 61.5, 32.7, 30.6, 27.7.
NMR spectra are in agreement with the reported data.[5]

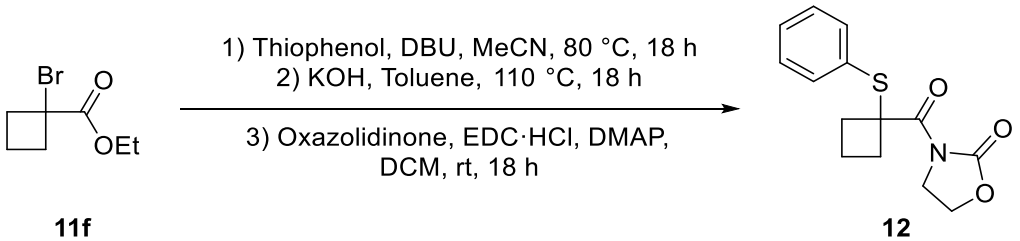
**Ethyl 4-(cyclobut-1-ene-1-carboxamido)benzoate (2d)**




Prepared according to the general procedure B from **11d** (571 mg, 1.75 mmol, 1.00 equiv.), DBU (1.60 g, 1.57 mL, 10.5 mmol, 6.00 equiv.) and toluene (4.54 mL). The crude product was purified by flash chromatography using PE/EtOAc 70:30 to afford **2d** as a white solid (128 mg, 522 µmol, 30% yield).

m.p.: 154-155 °C.
Rf(PE/EtOAc 7:3): 0.61.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 8.02 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.72 – 7.51 (m, 2H, Ar*H*), 7.36 (s, 1H, N*H*), 6.79 (t, *J* = 1.2 Hz, 1H, *H*C=C), 4.36 (q, *J* = 7.1 Hz, 2H, OC*H*$_2$), 2.88 – 2.68 (m, 2H, C(O)CC*H*$_2$), 2.59 – 2.46 (m, 2H, CHC*H*$_2$), 1.39 (t, *J* = 7.1 Hz, 3H, OCH$_2$C*H*$_3$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 166.2, 160.5, 142.6, 141.8, 141.6, 131.0, 126.2, 118.9, 61.0, 28.8, 26.4, 14.5.
IR ($\nu_{max}$, cm$^{-1}$) 3354 (w), 2982 (w), 2932 (m), 2853 (w), 1719 (s), 1602 (m), 1526 (m), 1328 (m), 1274 (s), 1249 (s), 1166 (s), 1105 (m), 1024 (m), 770 (w), 739 (m).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{15}NNaO_3^+$ 268.0944; Found 268.0951.

**3-(1-(Phenylthio)cyclobutane-1-carbonyl)oxazolidin-2-one (12)**




**11f** **12**

[5] J. M. Robinson, S. F. Tlais, J. Fong, R. L. Danheiser, *Tetrahedron* **2011**, *67*, 9890–9898.

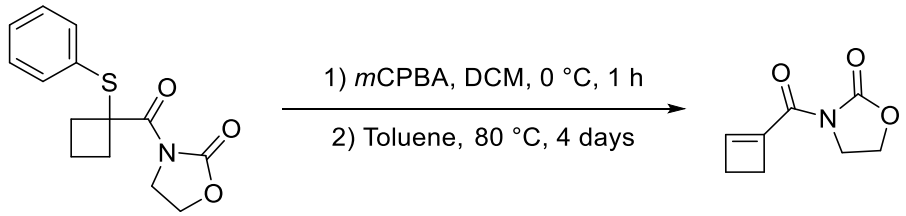
According to a reported procedure,[6] commercially available 1-bromocyclobutanecarboxylic acid ethyl ester **11f** (12.4 g, 9.71 mL, 60.0 mmol, 1.00 equiv.) was dissolved in MeCN (60.0 mL). Thiophenol (6.61 g, 6.12 mL, 60.0 mmol, 1.00 equiv.) and DBU (13.7 g, 13.4 mL, 90.0 mmol, 1.50 equiv.) were then added. The mixture was stirred at 80 °C for 18 h. The crude mixture was diluted in EtOAc (200 mL) and washed with brine (200 mL), and the organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting crude product was pure enough and taken to the next step without further purification.

KOH (13.5 g, 240 mmol, 4.00 equiv.) was heated in toluene (240 mL) at 110 °C and ethyl 1-(phenylthio)cyclobutane-1-carboxylate (14.2 g, 60.0 mmol, 1.00 equiv.) was added. The reaction was stirred at 110 °C for 18 h. The mixture was diluted in water (300 mL) and extracted with EtOAc (1 x 200 mL). The pH value of the aqueous layer was adjusted to 1 using HCl (1 M). The mixture was extracted with ethyl acetate (3 x 200 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude white solid was pure enough and taken to the next step without further purification.

A solution of 1-(phenylthio)cyclobutanecarboxylic acid (12.5 g, 60.0 mmol, 1.00 equiv.), 2-oxazolidinone (6.27 g, 72.0 mmol, 1.20 equiv.), EDC·HCl (13.8 g, 72.0 mmol, 1.20 equiv.) and DMAP (733 mg, 6.00 mmol, 0.100 equiv.) in DCM (150 mL) was stirred at rt for 18 h. The mixture was then washed with water (1 x 200 mL), and the organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography using PE/EtOAc 70:30 to afford **12** as a white solid (6.88 g, 24.8 mmol, 41% yield over 3 steps).

Rf(PE/EtOAc 7:3): 0.51.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.35 – 7.24 (m, 5H, Ar*H*), 4.47 (t, *J* = 8.1 Hz, 2H, OC$H_2$), 4.08 (t, *J* = 8.1 Hz, 2H, NC$H_2$), 2.79 – 2.63 (m, 2H, CC$H_2$), 2.45 – 2.30 (m, 2H, CC$H_2$), 2.30 – 2.13 (m, 1H, $CCH_2CH_2$), 1.81 (dtd, *J* = 15.9, 9.3, 4.7 Hz, 1H, $CCH_2CH_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.5, 152.2, 133.5, 133.3, 128.9, 128.1, 62.5, 53.6, 43.7, 31.7, 15.4.
NMR spectra are in agreement with the reported data.[6]

**3-(Cyclobut-1-ene-1-carbonyl)oxazolidin-2-one (2e)**




**12** **2e**

**12** (6.88 g, 24.8 mmol, 1.00 equiv.) was diluted in DCM (163 mL). *m*CPBA (5.28 g, 23.6 mmol, 0.950 equiv.) dissolved in DCM (85.0 mL) was then added dropwise for 15 min at 0 °C. The reaction was stirred at 0 °C for 45 min. The reaction mixture was then diluted in DCM (100 mL) and washed with a sat. $NaHCO_3$ solution (200 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was pure enough and taken to the next step without further purification.

The crude mixture was diluted in dry toluene (85.0 mL) under argon. The reaction was stirred at 80 °C for 4 days. The crude product was concentrated under reduced pressure and purified

[6] L. Ghisu, N. Melis, L. Serusi, A. Luridiana, F. Soddu, F. Secci, P. Caboni, R. Guillot, D. J. Aitken, A. Frongia, *Org. Biomol. Chem.* **2019**, *17*, 6143–6147.

by flash chromatography using PE/EtOAc 70:30 to afford **2e** as an oil (1.49 g, 8.92 mmol, 36% yield).

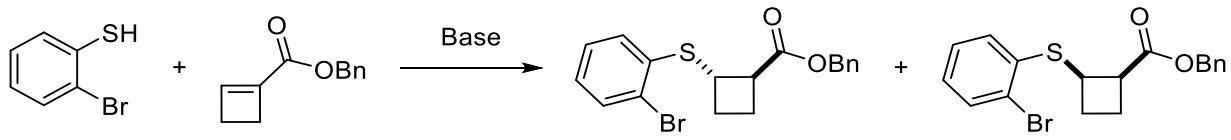
Rf(PE/EtOAc 8:2): 0.25.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.06 (d, *J* = 1.2 Hz, 1H, *H*C=C), 4.44 (t, *J* = 7.9 Hz, 2H, OC*H*$_2$), 4.05 (t, *J* = 8.0 Hz, 2H, NC*H*$_2$), 3.00 – 2.81 (m, 2H, C*H*$_2$C), 2.59 – 2.43 (m, 2H, CHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 161.8, 153.0, 150.4, 138.0, 62.7, 43.3, 30.7, 27.9.
NMR spectra are in agreement with the reported data.[6]

## 1.2. Optimization of the racemic sulfa-Michael addition

### *General procedure for the optimization of the reaction*

In a sealed vial under nitrogen, thiol **1a** and cyclobutene **2a** were diluted in 1 mL of solvent. DBU was then added. The reaction was stirred at the indicated temperature for the indicated time. The reaction mixture was concentrated under reduced pressure. The reaction mixture was analyzed by $^1$H NMR (400 MHz, chloroform-*d*) using dibromomethane as an internal standard and by integration of the SC*H* proton at 4.19 (q, *J* = 8.3 Hz, 1H) ppm.

### *Optimization table*




**1a** **2a** **3a** major **3'a** minor

| Entry | Base | Solvent | T °C | Time | NMR Yield (%)[b] | dr[c] |
|---|---|---|---|---|---|---|
| 1 | DBU | MeCN | 80 °C | 18 h | 82 | >95:5 |
| 2 | DBU | MeCN | rt | 18 h | quant. | >95:5 |
| 3 | $NEt_3$ | MeCN | rt | 18 h | 95 | 51:49 |
| 4 | TMG | MeCN | rt | 18 h | 90 | 64:36 |
| 5 | TBD | MeCN | rt | 18 h | 69 | 72:28 |
| 6 | $K_2CO_3$ | MeCN | rt | 18 h | 72 | 50:50 |
| 7 | DBU | EtOAc | rt | 18 h | quant. | 82:18 |
| 8 | DBU | MeCN | rt | 1 h | quant. | 64:36 |
| 9 | DBU | MeCN | rt | 2 h | 98 | 71:29 |
| 10 | DBU | MeCN + air | rt | 18 h | 81 | 86:14 |
| 11 | DBU | HPLC-MeCN | rt | 18 h | 97 | 89:11 |

[a]Reaction conditions: 1.0 equiv. thiol **1a** (0.1 mmol), 1.1 equiv. cyclobutene **2a**, 1.1 equiv. base. [b]1H NMR of the crude mixture with dibromomethane as an internal standard. [C]Measured on the crude $^1$H NMR.

## 1.3. Racemic sulfa-Michael addition onto cyclobutenes

### *General procedure (C) for the racemic sulfa-Michael addition*

In a sealed vial under nitrogen, thiol **1a-x** (0.3 mmol) and cyclobutene **2a-d** (1.1 equiv.) were diluted in 3 mL of MeCN. DBU (50.2 mg, 49.3 µL, 330 µmol, 1.10 equiv.) was then added. The reaction was stirred at rt for 18 h. The reaction mixture concentrated under reduced pressure and purified by flash chromatography. The mixture of diastereoisomers was isolated and the yield measured. For characterization purposes, a prep-TLC was then performed and only the major diastereoisomer was isolated and characterized, unless otherwise stated.

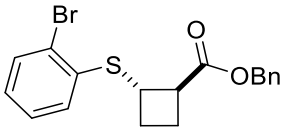
The dr was measured from the crude $^1$H NMR spectra by integration of the SC*H* proton.

### *General procedure (D) for the racemic sulfa-Michael addition*

In a sealed vial under nitrogen, thiol **1a-x** (0.3 mmol) and cyclobutene **2a-d** (1.1 equiv.) were diluted in 3 mL of MeCN. DBU (137 mg, 134 µL, 900 µmol, 3.00 equiv.) was then added. The reaction was stirred at 80 °C for 18 h. The reaction mixture concentrated under reduced pressure and purified by flash chromatography. The mixture of diastereoisomers was isolated and the yield measured. For characterization purposes, a prep-TLC was then performed and only the major diastereoisomer was isolated and characterized, unless otherwise stated.

The dr was measured from the crude $^1$H NMR spectra by integration of the SC*H* proton.

**Benzyl 2-((2-bromophenyl)thio)cyclobutane-1-carboxylate (3a)**




Prepared according to the general procedure C from 2-bromothiophenol (56.7 mg, 36.1 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3a** and **3'a** as an oil (111 mg, 294 µmol, 94% yield).

A scale up experiment with 2-bromothiophenol (189 mg, 120 µL, 1.00 mmol, 1.00 equiv.), cyclobutene **2a** (207 mg, 1.10 mmol, 1.10 equiv.) and DBU (167 mg, 164 µL, 1.10 mmol, 1.10 equiv.) was also accomplished using the same procedure and led to **3a** (306 mg, 811 µmol, 81% yield, dr >95:5).

The configuration of the two diastereoisomers obtained was determined by 2D-NOESY.

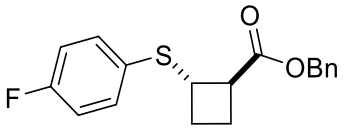
*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.58.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.52 (dd, *J* = 7.9, 1.3 Hz, 1H, Ar*H*), 7.38 – 7.28 (m, 5H, Ar*H*), 7.23 (dd, *J* = 7.9, 1.6 Hz, 1H, Ar*H*), 7.14 (td, *J* = 7.6, 1.3 Hz, 1H, Ar*H*), 7.00 (td, *J* = 7.6, 1.6 Hz, 1H, Ar*H*), 5.11 (s, 2H, OC$H_2$Ph), 4.19 (q, *J* = 8.3 Hz, 1H, SC*H*), 3.23 (q, *J* = 8.6 Hz, 1H, C*H*C(O)), 2.56 – 2.44 (m, 1H, SCHC$H_2$), 2.42 – 2.30 (m, 1H, C$H_2$CHC(O)), 2.23 (dq, *J* = 11.1, 8.9 Hz, 1H, C$H_2$CHC(O)), 2.08 (dq, *J* = 11.4, 9.2 Hz, 1H, SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.3, 137.2, 135.9, 133.1, 129.5, 128.7, 128.4, 128.3, 127.9, 127.2, 123.8, 66.7, 46.1, 41.7, 27.0, 22.6.
IR ($\nu_{max}$, cm$^{-1}$) 3036 (w), 2946 (m), 2863 (w), 1732 (s), 1705 (m), 1658 (m), 1577 (w), 1450 (m), 1386 (m), 1348 (m), 1253 (m), 1197 (s), 1160 (s), 1023 (m), 748 (s).
HRMS (Nanochip-based ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}{}^{79}BrO_2S^+$ 377.0205; Found 377.0211.

*Data for the cis- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.41.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.48 (dd, *J* = 7.9, 1.3 Hz, 1H, Ar*H*), 7.30 – 7.08 (m, 7H, Ar*H*), 7.02 – 6.93 (m, 1H, Ar*H*), 5.06 (q, *J* = 12.2 Hz, 2H, OC*H*$_2$Ph), 4.26 (q, *J* = 8.5 Hz, 1H, SC*H*), 3.66 (tt, *J* = 5.5, 3.2 Hz, 1H, C*H*C(O)), 2.62 – 2.30 (m, 3H, SCHC*H*$_2$ + C*H*$_2$CHC(O)), 2.29 – 2.14 (m, 1H, C*H*$_2$CHC(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 172.3, 138.6, 135.6, 132.8, 128.6, 128.5, 128.2, 127.9, 127.8, 126.5, 122.2, 66.9, 45.4, 42.0, 27.3, 21.2.
IR ($\nu_{max}$, cm$^{-1}$) 3065 (w), 3033 (w), 2951 (m), 1730 (s), 1660 (w), 1447 (m), 1433 (m), 1382 (m), 1346 (m), 1242 (m), 1163 (s), 1022 (m), 748 (s).
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{17}BrNaO_2S^+$ 399.0025; Found 399.0025.

**Benzyl 2-((4-fluorophenyl)thio)cyclobutane-1-carboxylate (3b)**

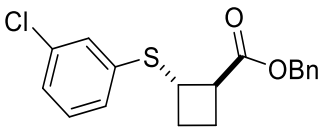



Prepared according to the general procedure C from 4-fluorobenzenethiol (38.5 mg, 32.3 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/Et$_2$O 98:2 to afford **3b** and **3'b** as an oil (83.4 mg, 264 µmol, 88% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.71.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.41 – 7.27 (m, 7H, Ar*H*), 7.02 – 6.86 (m, 2H, Ar*H*), 5.07 (s, 2H, OC*H*$_2$Ph), 3.97 (q, *J* = 8.6 Hz, 1H, SC*H*), 3.10 (q, *J* = 8.8 Hz, 1H, C*H*C(O)), 2.38 – 2.24 (m, 1H, SCHC*H*$_2$), 2.21 – 2.08 (m, 2H, C*H*$_2$CHC(O)), 2.04 – 1.86 (m, 1H, SCHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*, signals not fully resolved) δ 173.1, 162.5 (d, *J* = 247.5 Hz), 135.9, 134.7 (d, *J* = 8.2 Hz), 128.7, 128.4, 128.3, 116.1 (d, *J* = 21.8 Hz), 66.6, 46.4, 44.3, 26.8, 21.9.
$^{19}$F NMR (376 MHz, chloroform-*d*) δ -114.2 (tt, *J* = 8.7, 5.3 Hz).
IR ($\nu_{max}$, cm$^{-1}$) 3034 (w), 2989 (w), 2953 (w), 2114 (w), 1732 (s), 1589 (m), 1491 (s), 1455 (m), 1384 (m), 1350 (m), 1261 (s), 1224 (s), 1203 (s), 1159 (s), 1091 (m), 1033 (m), 917 (m), 824 (m), 744 (m).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}FO_2S^+$ 317.1006; Found 317.1003.

**Benzyl 2-((3-chlorophenyl)thio)cyclobutane-1-carboxylate (3c)**



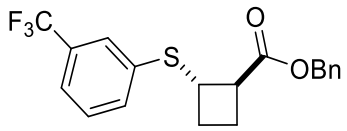

Prepared according to the general procedure C from 3-chlorobenzenethiol (43.4 mg, 34.4 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/Et$_2$O 95:5 to afford **3c** and **3'c** as an oil (81.9 mg, 246 µmol, 82% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.53.

$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.38 – 7.28 (m, 6H, Ar*H*), 7.20 – 7.13 (m, 3H, Ar*H*), 5.15 – 5.04 (m, 2H, OC*H*$_2$Ph), 4.10 (q, *J* = 8.5 Hz, 1H, SC*H*), 3.15 (q, *J* = 8.8 Hz, 1H, C*H*C(O)), 2.40 (qd, *J* = 8.5, 3.1 Hz, 1H, SCHC*H*$_2$), 2.30 – 2.12 (m, 2H, C*H*$_2$CHC(O)), 2.08 – 1.94 (m, 1H, SCHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.1, 137.3, 135.9, 134.7, 130.1, 130.0, 128.7, 128.5, 128.4, 128.3, 126.9, 66.7, 46.5, 42.8, 27.2, 22.2.
IR ($\nu_{max}$, cm$^{-1}$) 3035 (w), 2991 (w), 2944 (w), 1734 (s), 1579 (m), 1464 (m), 1385 (m), 1248 (m), 1198 (m), 1155 (s), 1083 (m), 1033 (m), 914 (m), 780 (s).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]$^+$ Calcd for $C_{18}H_{18}ClO_2S^+$ 333.0711; Found 333.0721.

**Benzyl 2-((3-(trifluoromethyl)phenyl)thio)cyclobutane-1-carboxylate (3d)**

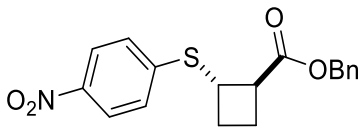



Prepared according to the general procedure C from 3-(trifluoromethyl)benzenethiol (53.5 mg, 40.8 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/Et$_2$O 95:5 to afford **3d** and **3'd** as an oil (97.9 mg, 267 µmol, 89% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.41.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.56 (s, 1H, Ar*H*), 7.44 (dd, *J* = 16.7, 7.8 Hz, 2H, Ar*H*), 7.39 – 7.27 (m, 6H, Ar*H*), 5.18 – 4.97 (m, 2H, OC*H*$_2$Ph), 4.15 (q, *J* = 8.6 Hz, 1H, SC*H*), 3.16 (qd, *J* = 9.2, 1.0 Hz, 1H, C*H*C(O)), 2.50 – 2.35 (m, 1H, SCHC*H*$_2$), 2.31 – 2.13 (m, 2H, C*H*$_2$CHC(O)), 2.03 (dq, *J* = 11.2, 9.4 Hz, 1H, SCHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.1, 136.9, 135.8, 133.3, 131.4 (q, *J* = 32.3 Hz), 129.4, 128.7, 128.4, 128.3, 123.9 (q, *J* = 272.7 Hz), 123.3 (q, *J* = 3.7 Hz), 66.7, 46.5, 42.6, 27.2, 22.3.
$^{19}$F NMR (376 MHz, chloroform-*d*) δ -62.8.
IR ($\nu_{max}$, cm$^{-1}$) 3044 (w), 2950 (w), 1728 (m), 1424 (w), 1321 (s), 1270 (m), 1166 (s), 1126 (s), 1073 (m), 908 (w), 798 (m), 738 (m).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]$^+$ Calcd for $C_{19}H_{18}F_3O_2S^+$ 367.0974; Found 367.0973.

**Benzyl 2-((4-nitrophenyl)thio)cyclobutane-1-carboxylate (3e)**



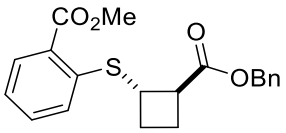

Prepared according to the general procedure C from 4-nitrobenzenethiol (46.6 mg, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/EtOAc 90:10 to afford **3e** and **3'e** as an oil (60.1 mg, 175 µmol, 58% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 95:5): 0.36.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.97 (d, *J* = 8.6 Hz, 2H, Ar*H*), 7.44 – 7.14 (m, 7H, Ar*H*), 5.22 – 4.94 (m, 2H, OC*H*$_2$Ph), 4.26 (q, *J* = 8.4 Hz, 1H, SC*H*), 3.20 (q, *J* = 8.8 Hz, 1H, C*H*C(O)),

2.56 – 2.45 (m, 1H, SCHC$H_2$), 2.44 – 2.31 (m, 1H, C$H_2$CHC(O)), 2.31 – 2.19 (m, 1H, C$H_2$CHC(O)), 2.13 – 1.97 (m, 1H SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.0, 146.4, 145.4, 135.6, 128.8, 128.7, 128.5, 127.2, 124.1, 66.9, 46.6, 40.9, 27.0, 22.6.
IR ($v_{max}$, cm$^{-1}$) 3101 (w), 2991 (w), 2946 (w), 2363 (w), 2330 (w), 1728 (s), 1577 (m), 1511 (s), 1478 (w), 1451 (w), 1383 (w), 1337 (s), 1242 (m), 1199 (m), 1159 (m), 1093 (m), 1029 (w), 852 (m), 738 (m).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}NO_4S^+$ 344.0951; Found 344.0947.

**Methyl 2-((2-((benzyloxy)carbonyl)cyclobutyl)thio)benzoate (3f)**



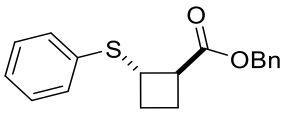

Prepared according to the general procedure C from 2-mercaptobenzoic acid methyl ester (50.5 mg, 41.4 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 86:14) was purified by flash chromatography using PE/EtOAc 85:15 to afford **3f** and **3'f** as an oil (106 mg, 299 µmol, quant.).

Prepared according to the general procedure D from 2-mercaptobenzoic acid methyl ester (50.5 mg, 41.4 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/EtOAc 85:15 to afford **3f** and **3'f** as an oil (74.9 mg, 210 µmol, 70% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 8:2): 0.72.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.94 (dd, *J* = 7.8, 1.5 Hz, 1H, Ar*H*), 7.40 – 7.26 (m, 6H, Ar*H*), 7.20 (d, *J* = 7.4 Hz, 1H, Ar*H*), 7.16 – 7.08 (m, 1H, Ar*H*), 5.14 (s, 2H, OC$H_2$Ph), 4.25 (q, *J* = 8.0 Hz, 1H, SC*H*), 3.90 (s, 3H, OC$H_3$), 3.23 (q, *J* = 8.6 Hz, 1H, C*H*C(O)), 2.64 – 2.51 (m, 1H, SCHC$H_2$), 2.48 – 2.35 (m, 1H, C$H_2$CHC(O)), 2.27 (dq, *J* = 11.3, 8.9 Hz, 1H, C$H_2$CHC(O)), 2.10 (dq, *J* = 11.5, 9.1 Hz, 1H, SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.6, 167.0, 141.2, 135.9, 132.5, 131.5, 128.7, 128.4, 128.3, 127.3, 126.6, 124.2, 66.7, 52.2, 45.6, 40.3, 27.1, 22.7.
IR ($v_{max}$, cm$^{-1}$) 2950 (w), 1717 (s), 1462 (m), 1436 (m), 1289 (m), 1246 (s), 1192 (m), 1146 (m), 1062 (s), 1044 (m), 743 (s).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{20}H_{21}O_4S^+$ 357.1155; Found 357.1156.

**Benzyl 2-(phenylthio)cyclobutane-1-carboxylate (3g)**




Prepared according to the general procedure C from benzenethiol (33.1 mg, 30.6 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 78:22) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3g** and **3'g** as an oil (86.1 mg, 289 µmol, 96% yield).

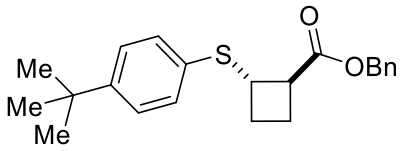
Prepared according to the general procedure D from benzenethiol (33.1 mg, 30.6 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product

(dr >95:5) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3g** and **3'g** as an oil (75.3 mg, 252 µmol, 84% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.46.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.33 (ddtt, *J* = 9.3, 7.2, 4.8, 2.1 Hz, 7H, Ar*H*), 7.25 – 7.17 (m, 3H, Ar*H*), 5.30 – 4.71 (m, 2H, OC$H_2$Ph), 4.08 (q, *J* = 8.5 Hz, 1H, SC*H*), 3.14 (q, *J* = 8.7 Hz, 1H, C*H*C(O)), 2.42 – 2.30 (m, 1H, SCHC$H_2$), 2.27 – 2.09 (m, 2H, C$H_2$CHC(O)), 2.00 (dq, *J* = 10.9, 9.4 Hz, 1H, SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.3, 136.0, 134.7, 131.4, 129.0, 128.7, 128.4, 128.2, 127.0, 66.6, 46.4, 43.3, 27.2, 22.0.
IR ($v_{max}$, $cm^{-1}$) 3062 (w), 2982 (w), 2949 (w), 1728 (s), 1585 (w), 1479 (m), 1441 (m), 1383 (m), 1348 (m), 1243 (s), 1195 (s), 1159 (s), 1091 (m), 1029 (m), 914 (m), 744 (s).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}O_2S^+$ 299.1100; Found 299.1110.

**Benzyl 2-((4-(tert-butyl)phenyl)thio)cyclobutane-1-carboxylate (3h)**



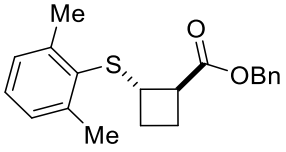

Prepared according to the general procedure C from 4-tert-butylbenzenethiol (49.9 mg, 50.4 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 84:16) was purified by flash chromatography using PE/$Et_2O$ 98:2 to afford **3h** and **3'h** as an oil (80.9 mg, 228 µmol, 76% yield).

Prepared according to the general procedure D from 4-tert-butylbenzenethiol (49.9 mg, 50.4 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/$Et_2O$ 98:2 to afford **3h** and **3'h** as an oil (95.9 mg, 271 µmol, 90% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.68.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.37 – 7.27 (m, 5H, Ar*H*), 7.25 (d, *J* = 8.5 Hz, 4H, Ar*H*), 5.15 – 5.00 (m, 2H, OC$H_2$Ph), 4.01 (q, *J* = 8.6 Hz, 1H, SC*H*), 3.18 – 3.05 (m, 1H, C*H*C(O)), 2.35 – 2.26 (m, 1H, SCHC$H_2$), 2.22 – 2.07 (m, 2H, C$H_2$CHC(O)), 1.97 (dq, *J* = 10.9, 9.4 Hz, 1H, SCHC$H_2$), 1.27 (s, 9H, C$(CH_3)_3$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.3, 150.3, 136.0, 131.6, 130.9, 128.7, 128.3, 128.2, 126.1, 66.5, 46.4, 43.6, 34.6, 31.4, 27.1, 21.9.
IR ($v_{max}$, $cm^{-1}$) 2961 (w), 2896 (w), 2872 (w), 1685 (m), 1614 (m), 1494 (m), 1407 (m), 1368 (m), 1182 (w), 1126 (w), 907 (s), 731 (s).
HRMS (Sicrit plasma/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{22}H_{27}O_2S^+$ 355.1726; Found 355.1725.

**Benzyl 2-((2,6-dimethylphenyl)thio)cyclobutane-1-carboxylate (3i)**



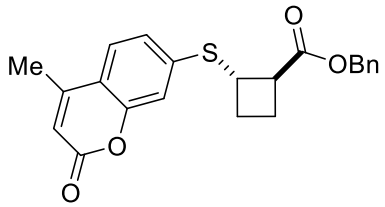
Prepared according to the general procedure C from 2,6-dimethylbenzenethiol (41.5 mg, 40.1 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 84:16) was purified by flash chromatography using PE/$Et_2O$ 98:2 to afford **3i** and **3'i** as an oil (97.5 mg, 299 µmol, quant.).

Prepared according to the general procedure D from 2,6-dimethylbenzenethiol (41.5 mg, 40.1 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/$Et_2O$ 98:2 to afford **3i** and **3'i** as an oil (91.0 mg, 279 µmol, 93% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.64.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.33 (td, *J* = 5.4, 2.7 Hz, 3H, Ar*H*), 7.29 – 7.22 (m, 2H, Ar*H*), 7.08 (q, *J* = 5.2 Hz, 3H, Ar*H*), 5.07 – 4.94 (m, 2H, OC*H*$_2$Ph), 3.81 – 3.67 (m, 1H, SC*H*), 3.16 – 3.03 (m, 1H, C*H*C(O)), 2.48 (s, 6H, ArC*H*$_3$), 2.27 – 2.17 (m, 1H, SCHC*H*$_2$), 2.14 – 1.92 (m, 3H, SCHC*H*$_2$ + C*H*$_2$CHC(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.1, 143.6, 136.0, 132.1, 128.6, 128.6, 128.3, 128.3, 128.2, 66.5, 47.0, 45.2, 27.7, 22.5, 22.0.
IR ($\nu_{max}$, cm$^{-1}$) 3058 (w), 2987 (w), 2948 (w), 1732 (s), 1454 (m), 1382 (m), 1349 (m), 1253 (m), 1193 (m), 1159 (s), 1033 (m), 917 (m), 773 (s), 740 (m).
HRMS (Sicrit plasma/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{20}H_{23}O_2S^+$ 327.1413; Found 327.1412.

**Benzyl 2-((4-methyl-2-oxo-2H-chromen-7-yl)thio)cyclobutane-1-carboxylate (3j)**




Prepared according to the general procedure C from 7-mercapto-4-methyl-coumarin (57.7 mg, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 88:12) was purified by flash chromatography using PE/EtOAc 60:40 to afford **3j** and **3'j** as an oil (106 mg, 279 µmol, 93% yield).

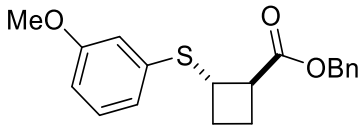
Prepared according to the general procedure D from 7-mercapto-4-methyl-coumarin (57.7 mg, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/EtOAc 60:40 to afford **3j** and **3'j** as an oil (37.7 mg, 99.1 µmol, 33% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 6:4): 0.43.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.46 – 7.30 (m, 6H, Ar*H*), 7.18 (d, *J* = 1.8 Hz, 1H, Ar*H*), 7.13 (dd, *J* = 8.3, 1.8 Hz, 1H, Ar*H*), 6.21 (s, 1H, C=C*H*), 5.14 (s, 2H, OC*H*$_2$Ph), 4.24 (q, *J* = 8.4 Hz, 1H, SC*H*), 3.29 – 3.13 (m, 1H, C*H*C(O)), 2.59 – 2.45 (m, 1H, SCHC*H*$_2$), 2.41 – 2.20 (m, 5H, $CH_3$ + C*H*$_2$CHC(O)), 2.07 (dq, *J* = 11.4, 9.4 Hz, 1H, SCHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.0, 160.7, 153.8, 152.1, 141.8, 135.8, 128.7, 128.4, 128.3, 124.8, 124.1, 117.8, 115.9, 114.4, 66.8, 46.3, 41.6, 27.3, 22.5, 18.7.
IR ($\nu_{max}$, cm$^{-1}$) 3066 (w), 2950 (w), 2110 (w), 1727 (s), 1685 (w), 1602 (s), 1455 (w), 1386 (m), 1242 (w), 1202 (m), 1164 (m), 1029 (w), 961 (m), 852 (w), 752 (w).

HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{22}H_{21}O_4S^+$ 381.1155; Found 381.1152.

**Benzyl 2-((3-methoxyphenyl)thio)cyclobutane-1-carboxylate (3k)**



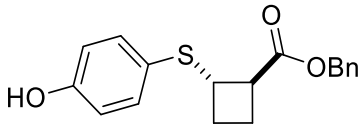

Prepared according to the general procedure C from 3-methoxybenzenethiol (42.1 mg, 37.2 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 86:14) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3k** and **3'k** as an oil (98.4 mg, 299 µmol, quant.).

Prepared according to the general procedure D from 3-methoxybenzenethiol (42.1 mg, 37.2 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 89:11) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3k** and **3'k** as an oil (98.1 mg, 299 µmol, quant. yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.31.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.41 – 7.28 (m, 5H, Ar*H*), 7.16 (t, *J* = 7.9 Hz, 1H, Ar*H*), 6.95 – 6.87 (m, 2H, Ar*H*), 6.75 (ddd, *J* = 8.3, 2.5, 0.8 Hz, 1H, Ar*H*), 5.17 – 4.97 (m, 2H, OC*H*$_2$Ph), 4.11 (q, *J* = 8.5 Hz, 1H, SC*H*), 3.76 (s, 3H, OC*H*$_3$), 3.21 – 3.08 (m, 1H, C*H*C(O)), 2.44 – 2.32 (m, 1H, SCHC*H*$_2$), 2.19 (dtd, *J* = 17.9, 9.3, 2.3 Hz, 2H, C*H*$_2$CHC(O)), 2.01 (dq, *J* = 11.0, 9.4 Hz, 1H, SCHC*H*$_2$).
$^{13}$C NMR 13C NMR (101 MHz, $CDCl_3$) δ 173.3, 159.9, 136.0, 135.9, 129.8, 128.7, 128.3, 128.2, 123.2, 116.1, 112.9, 66.6, 55.4, 46.4, 43.0, 27.2, 22.1.
IR ($\nu_{max}$, cm$^{-1}$) 3065 (w), 2943 (w), 2835 (w), 1728 (m), 1589 (s), 1520 (w), 1480 (s), 1418 (s), 1383 (m), 1285 (s), 1242 (s), 1192 (m), 1156 (s), 1040 (s), 863 (m), 781 (s).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}O_3S^+$ 329.1206; Found 329.1207.

**Benzyl 2-((4-hydroxyphenyl)thio)cyclobutane-1-carboxylate (3l)**




Prepared according to the general procedure C from 4-mercaptophenol (37.9 mg, 30.3 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 57:43) was purified by flash chromatography using PE/EtOAc 80:20 to afford **3l** and **3'l** as an oil (92.4 mg, 294 µmol, 98% yield).

Prepared according to the general procedure D from 4-mercaptophenol (37.9 mg, 30.3 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/EtOAc 80:20 to afford **3l** and **3'l** as an oil (64.3 mg, 205 µmol, 68% yield).

The configuration of the minor diastereoisomer obtained was determined by X-rays analysis.

*Data for the trans- diastereoisomer:*

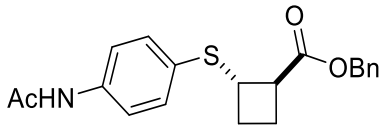
Rf(PE/EtOAc 8:2): 0.43.

$^1$H NMR (400 MHz, chloroform-*d*, O*H* signal not resolved) δ 7.41 – 7.26 (m, 7H, Ar*H*), 6.77 – 6.69 (m, 2H, Ar*H*), 5.07 (d, *J* = 2.1 Hz, 2H, OC$H_2$Ph), 3.88 (q, *J* = 8.5 Hz, 1H, SC*H*), 3.07 (q, *J* = 8.9 Hz, 1H, C*H*C(O)), 2.28 – 2.17 (m, 1H, SCHC$H_2$), 2.09 (td, *J* = 9.3, 6.2 Hz, 2H, C$H_2$CHC(O)), 2.01 – 1.84 (m, 1H, SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.4, 155.9, 136.0, 135.9, 128.7, 128.3, 128.2, 124.1, 116.1, 66.5, 46.1, 44.9, 26.6, 21.7.
IR ($\nu_{max}$, cm$^{-1}$) 3405 (m), 2950 (m), 1732 (s), 1632 (m), 1602 (m), 1581 (m), 1497 (s), 1456 (m), 1433 (m), 1383 (m), 1350 (m), 1267 (s), 1216 (s), 1166 (s), 1029 (w), 845 (w), 744 (m).
HRMS (ESI/QTOF) m/z: [M + Na]$^+$ Calcd for $C_{18}H_{18}NaO_3S^+$ 337.0869; Found 337.0871.

*Data for the cis- diastereoisomer:*

m.p.: 96-98 °C.
Rf(PE/EtOAc 8:2): 0.30.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.32 (s, 5H, Ar*H*), 7.25 – 7.17 (m, 2H, Ar*H*), 6.76 – 6.66 (m, 2H, Ar*H*), 5.20 (d, *J* = 12.3 Hz, 1H, OC$H_2$Ph), 5.09 (d, *J* = 12.3 Hz, 1H, OC$H_2$Ph), 4.76 (s, 1H, O*H*), 4.06 (q, *J* = 8.4 Hz, 1H, SC*H*), 3.58 – 3.44 (m, 1H, C*H*C(O)), 2.49 – 2.22 (m, 3H, SCHC$H_2$ + C$H_2$CH(O)), 2.09 (dt, *J* = 10.7, 8.5 Hz, 1H, C$H_2$CH(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 172.7, 155.0, 135.9, 133.1, 128.7, 128.6, 128.3, 127.0, 116.0, 66.7, 45.8, 45.3, 28.0, 20.8.
IR ($\nu_{max}$, cm$^{-1}$) 3040 (m), 2953 (m), 2928 (m), 1728 (s), 1710 (s), 1605 (m), 1584 (m), 1496 (s), 1353 (m), 1263 (s), 1215 (s), 1173 (s), 1069 (m), 987 (s), 910 (s), 831 (m), 738 (m).
HRMS (ESI/QTOF) m/z: [M + Na]$^+$ Calcd for $C_{18}H_{18}NaO_3S^+$ 337.0869; Found 337.0871.

**Benzyl 2-((4-acetamidophenyl)thio)cyclobutane-1-carboxylate (3m)**




Prepared according to the general procedure C from N-(4-sulfanylphenyl)acetamide (50.2 mg, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 75:25) was purified by flash chromatography using PE/EtOAc 70:30 to afford **3m** and **3'm** as an oil (101 mg, 285 µmol, 95% yield).

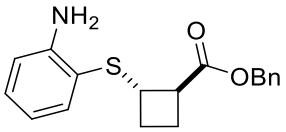
Prepared according to the general procedure D from N-(4-sulfanylphenyl)acetamide (50.2 mg, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/EtOAc 70:30 to afford **3m** and **3'm** as an oil (93.9 mg, 264 µmol, 88% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 7:3): 0.69.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.48 – 7.29 (m, 9H, Ar*H*), 7.19 (s, 1H, N*H*), 5.08 (q, *J* = 2.8 Hz, 2H, OC$H_2$Ph), 3.97 (q, *J* = 8.6 Hz, 1H, SC*H*), 3.09 (q, *J* = 8.9 Hz, 1H, C*H*C(O)), 2.29 (dtd, *J* = 11.3, 7.9, 3.4 Hz, 1H, SCHC$H_2$), 2.22 – 2.05 (m, 5H, C(O)C$H_3$ + C$H_2$CHC(O)), 2.02 – 1.88 (m, 1H, SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.2, 168.3, 137.5, 136.0, 133.6, 129.0, 128.7, 128.3, 128.2, 120.2, 66.5, 46.2, 44.1, 26.9, 24.8, 21.9.
IR ($\nu_{max}$, cm$^{-1}$) 3310 (m), 3101 (m), 2993 (m), 2946 (m), 2359 (w), 2104 (s), 1725 (s), 1671 (s), 1592 (s), 1527 (s), 1494 (s), 1455 (m), 1393 (s), 1372 (m), 1310 (s), 1252 (s), 1206 (s), 1158 (s), 1032 (m), 960 (m), 831 (m), 748 (s).

HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{20}H_{22}NO_3S^+$ 356.1315; Found 356.1312.

**Benzyl 2-((2-aminophenyl)thio)cyclobutane-1-carboxylate (3n)**



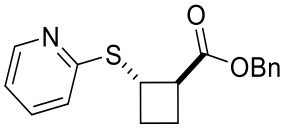

Prepared according to the general procedure C from 2-aminobenzenethiol (37.6 mg, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 82:18) was purified by flash chromatography using PE/EtOAc 80:20 to afford **3n** and **3'n** as an oil (92.0 mg, 294 µmol, 98% yield).

Prepared according to the general procedure D from 2-aminobenzenethiol (37.6 mg, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 94:6) was purified by flash chromatography using PE/EtOAc 80:20 to afford **3n** and **3'n** as an oil (82.5 mg, 263 µmol, 88% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 8:2): 0.70.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.44 – 7.29 (m, 6H, Ar*H*), 7.14 (td, *J* = 8.0, 1.6 Hz, 1H, Ar*H*), 6.76 – 6.54 (m, 2H, Ar*H*), 5.09 (s, 2H, OC*H*$_2$Ph), 4.31 (br s, 2H, N*H*$_2$), 3.85 – 3.72 (m, 1H, SC*H*), 3.07 (q, *J* = 8.6 Hz, 1H, C*H*C(O)), 2.26 – 2.11 (m, 1H, SCHC*H*$_2$), 2.11 – 1.88 (m, 3H, C*H*$_2$CHC(O) + SCHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.1, 149.5, 138.1, 136.1, 130.7, 128.7, 128.3, 128.2, 118.3, 115.1, 114.8, 66.5, 45.7, 44.5, 26.6, 21.6.
IR ($\nu_{max}$, cm$^{-1}$) 3468 (w), 3357 (m), 3062 (m), 3029 (w), 2993 (m), 2950 (m), 1726 (s), 1607 (s), 1480 (s), 1448 (m), 1379 (w), 1348 (m), 1307 (m), 1242 (s), 1197 (s), 1159 (s), 1027 (m), 961 (w), 910 (w), 748 (s).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{18}H_{20}NO_2S^+$ 314.1209; Found 314.1224.

**Benzyl 2-(pyridin-2-ylthio)cyclobutane-1-carboxylate (3o)**




Prepared according to the general procedure C from 2-pyridinethiol (33.3 mg, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 81:19) was purified by flash chromatography using PE/$Et_2O$ 98:2 to afford **3o** and **3'o** as an oil (71.1 mg, 237 µmol, 79% yield).

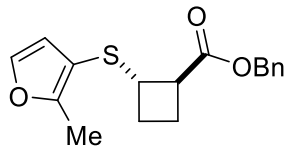
Prepared according to the general procedure D from 2-pyridinethiol (33.3 mg, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/$Et_2O$ 98:2 to afford **3o** and **3'o** as an oil (63.0 mg, 210 µmol, 70% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.53.

$^1$H NMR (400 MHz, chloroform-*d*) δ 8.30 – 8.21 (m, 1H, Ar*H*), 7.42 (td, *J* = 7.7, 1.9 Hz, 1H, Ar*H*), 7.36 – 7.27 (m, 5H, Ar*H*), 7.11 (d, *J* = 8.1 Hz, 1H, Ar*H*), 6.92 (ddd, *J* = 7.4, 4.9, 1.0 Hz, 1H, Ar*H*), 5.19 – 5.07 (m, 2H, OC*H*$_2$Ph), 4.62 (q, *J* = 8.6 Hz, 1H, SC*H*), 3.33 – 3.21 (m, 1H, C*H*C(O)), 2.54 – 2.39 (m, 1H, SCHC*H*$_2$), 2.32 (td, *J* = 9.3, 6.3 Hz, 2H, C*H*$_2$CHC(O)), 2.19 – 2.04 (m, 1H, SCHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.5, 159.1, 149.5, 136.1, 136.1, 128.6, 128.2, 128.2, 122.1, 119.6, 66.5, 47.2, 40.1, 26.7, 22.7.
IR ($\nu_{max}$, cm$^{-1}$) 3041 (w), 2979 (w), 2946 (w), 1728 (s), 1578 (s), 1559 (m), 1453 (s), 1415 (s), 1383 (m), 1348 (m), 1267 (m), 1242 (m), 1191 (s), 1155 (s), 1127 (s), 1029 (m), 759 (s).
HRMS (ESI/QTOF) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{17}NNaO_2S^+$ 322.0872; Found 322.0861.

**Benzyl 2-((2-methylfuran-3-yl)thio)cyclobutane-1-carboxylate (3p)**



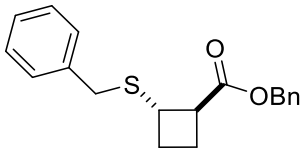

Prepared according to the general procedure C from 2-methyl-3-furanthiol (34.2 mg, 32.9 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 76:24) was purified by flash chromatography using PE/Et$_2$O 95:5 to afford **3p** and **3'p** as an oil (88.6 mg, 293 µmol, 98% yield).

Prepared according to the general procedure D from 2-methyl-3-furanthiol (34.2 mg, 32.9 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/Et$_2$O 95:5 to afford **3p** and **3'p** as an oil (69.2 mg, 229 µmol, 76% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.44.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.35 (dtt, *J* = 11.2, 7.4, 3.8 Hz, 5H, Ar*H*), 7.26 (d, *J* = 1.4 Hz, 1H, Ar*H*), 6.32 (d, *J* = 1.9 Hz, 1H, Ar*H*), 5.10 (s, 2H, OC*H*$_2$Ph), 3.69 (q, *J* = 8.8 Hz, 1H, SC*H*), 3.00 (q, *J* = 8.8 Hz, 1H, C*H*C(O)), 2.30 (s, 3H, C*H*$_3$), 2.21 – 2.10 (m, 1H, SCHC*H*$_2$), 2.10 – 1.99 (m, 2H, C*H*$_2$CHC(O)), 1.96 – 1.84 (m, 1H, SCHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.1, 156.8, 140.7, 136.1, 128.7, 128.3, 128.2, 116.4, 107.6, 66.5, 45.7, 44.8, 26.2, 21.5, 12.0.
IR ($\nu_{max}$, cm$^{-1}$) 2993 (w), 2946 (w), 2925 (w), 1732 (s), 1516 (w), 1451 (w), 1384 (w), 1348 (w), 1241 (m), 1191 (m), 1159 (s), 1091 (m), 1033 (w), 936 (w), 738 (m).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]$^+$ Calcd for $C_{17}H_{19}O_3S^+$ 303.1049; Found 303.1063.

**Benzyl 2-(benzylthio)cyclobutane-1-carboxylate (3q)**



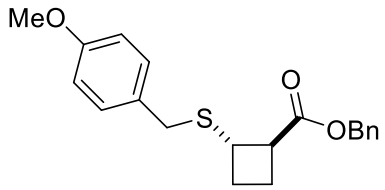

Prepared according to the general procedure C from phenylmethanethiol (37.3 mg, 35.2 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 50:50) was purified by flash chromatography using PE/Et$_2$O 98:2 to afford **3q** and **3'q** as an oil (93.4 mg, 299 µmol, quant.).

Prepared according to the general procedure D from phenylmethanethiol (37.3 mg, 35.2 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 93:7) was purified by flash chromatography using PE/$Et_2O$ 98:2 to afford **3q** and **3'q** as an oil (93.3 mg, 299 µmol, quant.).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.45.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.35 (q, *J* = 3.6 Hz, 5H, Ar*H*), 7.28 – 7.19 (m, 5H, Ar*H*), 5.11 (s, 2H, OC*H*$_2$Ph), 3.79 – 3.56 (m, 3H, SC*H*$_2$Ph + SC*H*), 3.13 (q, *J* = 8.7 Hz, 1H, C*H*C(O)), 2.30 – 2.01 (m, 3H, SCHC*H*$_2$ + C*H*$_2$CHC(O)), 1.97 – 1.78 (m, 1H, SCHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.5, 138.6, 136.0, 128.9, 128.7, 128.6, 128.4, 128.3, 127.1, 66.6, 47.6, 41.2, 36.0, 26.7, 22.0.
IR ($\nu_{max}$, cm$^{-1}$) 3062 (w), 3033 (w), 2950 (w), 1732 (s), 1497 (w), 1455 (m), 1382 (w), 1350 (m), 1242 (m), 1199 (m), 1159 (s), 1074 (w), 1033 (w), 957 (w), 911 (w).
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{20}NaO_2S^+$ 335.1076; Found 335.1085.

**Benzyl 2-((4-methoxybenzyl)thio)cyclobutane-1-carboxylate (3r)**

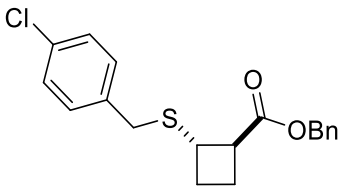



Prepared according to the general procedure D from (4-methoxyphenyl)methanethiol (46.3 mg, 41.3 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 92:8) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3r** and **3'r** as an oil (98.8 mg, 289 µmol, 96% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.29.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.34 (d, *J* = 4.3 Hz, 5H, Ar*H*), 7.16 (d, *J* = 8.6 Hz, 2H, Ar*H*), 6.87 – 6.75 (m, 2H, Ar*H*), 5.12 (s, 2H, OC*H*$_2$), 3.77 (s, 3H, OC*H*$_3$), 3.72 – 3.50 (m, 3H, SC*H*$_2$ + SC*H*), 3.13 (q, *J* = 8.7 Hz, 1H, C*H*C(O)), 2.26 – 2.04 (m, 3H, SCHC*H*$_2$ + C*H*$_2$CHC(O)), 1.96 – 1.80 (m, 1H, SCHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.6, 158.7, 136.0, 130.5, 130.0, 128.7, 128.4, 128.3, 114.0, 66.5, 55.4, 47.6, 41.1, 35.3, 26.6, 22.0.
IR ($\nu_{max}$, cm$^{-1}$) 2996 (w), 2950 (m), 2838 (w), 1730 (s), 1613 (w), 1512 (s), 1455 (w), 1248 (s), 1177 (m), 1156 (m), 1035 (m), 831 (w), 744 (m).
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{22}NaO_3S^+$ 365.1182; Found 365.1189.

**Benzyl 2-((4-chlorobenzyl)thio)cyclobutane-1-carboxylate (3s)**



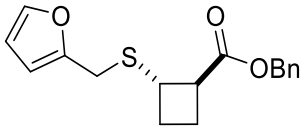

Prepared according to the general procedure D from (4-chlorophenyl)methanethiol (47.6 mg, 39.6 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The

crude product (dr >95:5) was purified by flash chromatography using PE/EtOAc 95:5 to afford **3s** and **3's** as an oil (92.7 mg, 267 µmol, 89% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 95:5): 0.68.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.40 – 7.29 (m, 5H, Ar*H*), 7.25 – 7.13 (m, 4H, Ar*H*), 5.17 – 5.02 (m, 2H, OC$H_2$), 3.77 – 3.43 (m, 3H, SC*H* + SC$H_2$), 3.18 – 3.04 (m, 1H, C*H*C(O)), 2.29 – 2.03 (m, 3H, SCHC$H_2$ + C$H_2$CHC(O)), 2.00 – 1.79 (m, 1H, SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.5, 137.2, 135.9, 132.8, 130.2, 128.8, 128.7, 128.5, 128.4, 66.6, 47.7, 41.1, 35.3, 26.5, 22.0.
IR ($v_{max}$, $cm^{-1}$) 3040 (w), 2984 (w), 2953 (w), 2872 (w), 1730 (s), 1492 (m), 1455 (w), 1382 (w), 1350 (w), 1242 (m), 1203 (m), 1159 (m), 1094 (m), 1015 (w), 910 (w), 830 (w), 748 (m).
HRMS (Nanochip-based ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{19}H_{20}ClO_2S^+$ 347.0867; Found 347.0868.

**Benzyl 2-((furan-2-ylmethyl)thio)cyclobutane-1-carboxylate (3t)**

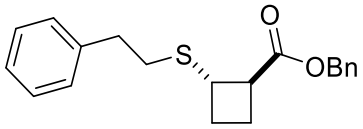



Prepared according to the general procedure D from 2-furylmethanethiol (34.2 mg, 30.3 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 94:6) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3t** and **3't** as an oil (72.7 mg, 240 µmol, 80% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.51.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.43 – 7.29 (m, 6H, Ar*H*), 6.26 (dd, *J* = 3.0, 2.0 Hz, 1H, Ar*H*), 6.09 (d, *J* = 3.2 Hz, 1H, Ar*H*), 5.14 (s, 2H, OC$H_2$), 3.83 – 3.63 (m, 3H, SC$H_2$ + SC*H*), 3.14 (q, *J* = 8.7 Hz, 1H, C*H*C(O)), 2.30 – 2.07 (m, 3H, SCHC$H_2$ + C$H_2$CHC(O)), 1.92 (qd, *J* = 10.0, 1.4 Hz, 1H, SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.4, 151.7, 142.1, 135.9, 128.7, 128.4, 128.3, 110.5, 107.4, 66.5, 47.6, 41.2, 28.0, 26.4, 21.9.
IR ($v_{max}$, $cm^{-1}$) 3115 (w), 3033 (w), 2989 (w), 2950 (w), 2871 (w), 1727 (s), 1501 (m), 1455 (w), 1389 (w), 1350 (m), 1245 (s), 1192 (m), 1154 (s), 1076 (w), 1030 (m), 1011 (m), 935 (m), 737 (s).
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{18}NaO_3S^+$ 325.0869; Found 325.0875.

**Benzyl 2-(phenethylthio)cyclobutane-1-carboxylate (3u)**




Prepared according to the general procedure C from 2-phenylethanethiol (41.5 mg, 40.3 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 50:50) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3u** and **3'u** as an oil (97.5 mg, 299 µmol, 100% yield, quant.).

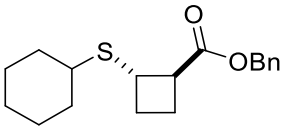
Prepared according to the general procedure D from 2-phenylethanethiol (41.5 mg, 40.3 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product

(dr >95:5) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3u** and **3'u** as an oil (97.8 mg, 299 µmol, quant.).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.44.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.38 – 7.25 (m, 7H, Ar*H*), 7.23 – 7.08 (m, 3H, Ar*H*), 5.13 (s, 2H, OC$H_2$Ph), 3.73 (q, *J* = 8.4 Hz, 1H, SC*H*), 3.12 (q, *J* = 9.0 Hz, 1H, C*H*C(O)), 2.89 – 2.70 (m, 4H, SC$H_2$C$H_2$Ph), 2.32 – 2.08 (m, 3H, SCHC$H_2$ + C$H_2$CHC(O)), 1.93 (p, *J* = 9.8 Hz, 1H, SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.6, 140.6, 136.0, 128.7, 128.6, 128.6, 128.4, 128.4, 126.5, 66.6, 47.7, 41.7, 36.6, 33.0, 26.8, 22.0.
IR ($v_{max}$, $cm^{-1}$) 3062 (w), 3028 (m), 2993 (w), 2870 (m), 2835 (w), 1725 (s), 1496 (m), 1382 (m), 1361 (m), 1329 (m), 1260 (s), 1243 (s), 1195 (s), 1087 (m), 1029 (m), 964 (m), 738 (m).
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{22}NaO_2S^+$ 349.1233; Found 349.1232.

**Benzyl 2-(cyclohexylthio)cyclobutane-1-carboxylate (3v)**

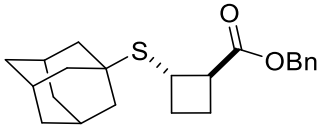



Prepared according to the general procedure D from cyclohexanethiol (34.9 mg, 36.7 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 93.7) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3v** and **3'v** as an oil (90.9 mg, 299 µmol, quant.).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.64.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.40 – 7.29 (m, 5H, Ar*H*), 5.13 (d, *J* = 1.8 Hz, 2H, OC$H_2$), 3.75 (q, *J* = 8.7 Hz, 1H, SC*H*CHC(O)), 3.09 (q, *J* = 8.5 Hz, 1H, C*H*C(O)), 2.66 (ddt, *J* = 10.5, 7.5, 3.7 Hz, 1H, SC$H^{cyclohex}$), 2.34 – 2.07 (m, 3H, SCHC$H_2$C$H_2$CHC(O)), 1.99 – 1.79 (m, 3H, SCHC$H_2$CH$_2$CHC(O) + C$H_2^{cyclohex}$), 1.74 – 1.64 (m, 2H, C$H_2^{cyclohex}$), 1.54 (d, *J* = 8.8 Hz, 1H, C$H_2^{cyclohex}$), 1.37 – 1.06 (m, 5H, C$H_2^{cyclohex}$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.7, 136.1, 128.7, 128.4, 128.3, 66.5, 48.2, 44.0, 40.2, 34.2, 34.0, 27.8, 26.2, 26.1, 25.8, 22.1.
IR ($v_{max}$, $cm^{-1}$) 3033 (w), 2932 (s), 2856 (m), 1732 (s), 1654 (w), 1584 (w), 1450 (m), 1343 (m), 1249 (m), 1190 (s), 1155 (s), 1083 (w), 1029 (m), 909 (w), 744 (m).
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{24}NaO_2S^+$ 327.1389; Found 327.1389.

**Benzyl 2-((adamantan-1-yl)thio)cyclobutane-1-carboxylate (3w)**




Prepared according to the general procedure C from adamantane-1-thiol (50.5 mg, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 29:71) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3w** and **3'w** as an oil (107 mg, 299 µmol, quant.).

Prepared according to the general procedure D from adamantane-1-thiol (50.5 mg, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product (dr 92:8)

was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3w** and **3'w** as an oil (100 mg, 281 µmol, 94% yield).

The configuration of the two diastereoisomers obtained was determined by 2D-NOESY.

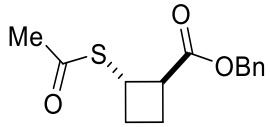
*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.44.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.46 – 7.29 (m, 5H, Ar*H*), 5.24 – 5.02 (m, 2H, OC*H*$_2$Ph), 3.84 (q, *J* = 8.8 Hz, 1H, SC*H*), 3.06 (q, *J* = 9.0 Hz, 1H, C*H*C(O)), 2.30 (qd, *J* = 8.8, 2.7 Hz, 1H, SCHC*H*$_2$), 2.22 – 2.04 (m, 2H, C*H*$_2$CHC(O)), 2.02 – 1.85 (m, 4H, SCHC*H*$_2$ + SCCH$_2$C*H*), 1.79 (d, *J* = 2.4 Hz, 6H, SCC*H*$_2$), 1.63 (q, *J* = 12.3 Hz, 6H, SCCH$_2$CHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.7, 136.1, 128.7, 128.36, 128.35, 66.5, 48.2, 45.9, 43.9, 36.6, 36.3, 29.8, 29.6, 22.6.
IR ($\nu_{max}$, cm$^{-1}$) 2907 (s), 2849 (m), 1732 (s), 1452 (m), 1347 (m), 1254 (m), 1192 (m), 1152 (s), 1040 (m), 741 (m).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{22}H_{29}O_2S^+$ 357.1883; Found 357.1876

*Data for the cis- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.36.
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.43 (dd, *J* = 8.1, 1.3 Hz, 2H, Ar*H*), 7.40 – 7.29 (m, 3H, Ar*H*), 5.24 (d, *J* = 12.2 Hz, 1H, OC*H*$_2$Ph), 5.16 (d, *J* = 12.2 Hz, 1H, OC*H*$_2$Ph), 3.92 (q, *J* = 9.0 Hz, 1H, SC*H*), 3.34 (tt, *J* = 8.5, 2.8 Hz, 1H, C*H*C(O)), 2.45 – 2.18 (m, 3H, SCHC*H*$_2$ + C*H*$_2$CHC(O)), 2.17 – 2.02 (m, 1H, C*H*$_2$CHC(O)), 1.97 (s, 3H, SCCH$_2$C*H*), 1.76 (q, *J* = 12.5 Hz, 6H, SCC*H*$_2$), 1.70 – 1.52 (m, 6H, SCCH$_2$CHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.4, 136.2, 128.9, 128.6, 128.3, 66.4, 47.9, 45.4, 43.8, 36.5, 36.4, 30.4, 29.8, 21.4.
IR ($\nu_{max}$, cm$^{-1}$) 3032 (w), 2903 (s), 2849 (m), 1729 (s), 1455 (m), 1382 (w), 1344 (m), 1278 (m), 1152 (s), 1043 (m), 910 (w), 752 (m), 734 (m).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{22}H_{29}O_2S^+$ 357.1883; Found 357.1880.

**Benzyl 2-(acetylthio)cyclobutane-1-carboxylate (3x)**



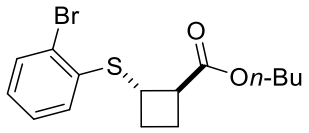

Prepared according to the general procedure C from thioacetic acid (22.8 mg, 21.1 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2a** (62.1 mg, 330 µmol, 1.10 equiv.). The crude product dr (dr 67:33) was purified by flash chromatography using PE/$Et_2O$ 95:5 to afford **3x** and **3'x** as an oil (56.3 mg, 213 µmol, 71% yield).

*Data for the mixture of diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.21.
1H NMR (400 MHz, chloroform-*d,* 65:35 mixture of diastereoisomers (major:minor)) δ 7.34 (td, *J* = 7.9, 5.0 Hz, 5H, Ar*H* (major+minor)), 5.25 – 5.01 (m, 2H, OC*H*$_2$Ph (major+minor)), 4.49 (q, *J* = 8.4 Hz, 0.35H, SC*H* (minor)), 4.32 (q, *J* = 9.0 Hz, 0.65H, SC*H* (major)), 3.62 – 3.46 (m, 0.35H, C*H*C(O) (minor), 3.19 (q, *J* = 8.9 Hz, 0.65H, C*H*C(O) (major)), 2.44 – 2.14 (m, 6.35H, C*H*$_2$CHC(O) (major+minor) + C(O)C*H*$_3$ (major+minor) + SCHC*H*$_2$ (major+minor)), 2.12 – 1.98 (m, 0.65H, SCHC*H*$_2$ (major)).

$^{13}$C NMR (101 MHz, chloroform-*d*, 65:35 mixture of diastereoisomers (major:minor)) δ 195.2, 195.2, 173.0, 172.8, 136.0, 136.0, 128.7, 128.6, 128.4, 128.3, 66.7, 66.6, 45.9, 44.9, 39.1, 38.3, 30.6, 30.4, 27.7, 26.6, 22.7, 21.9.
IR ($v_{max}$, $cm^{-1}$) 2982 (w), 2950 (w), 1736 (s), 1692 (s), 1455 (w), 1389 (w), 1353 (m), 1245 (m), 1186 (m), 1159 (s), 1132 (m), 1032 (w), 950 (m), 752 (m).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + Na]+ Calcd for C14H16NaO3S+ 287.0712; Found 287.0708.

**Butyl 2-((2-bromophenyl)thio)cyclobutane-1-carboxylate (3y)**



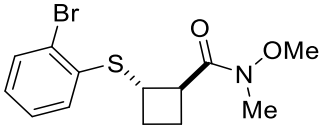

Prepared according to the general procedure C from 2-bromothiophenol (56.7 mg, 36.1 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2b** (50.9 mg, 330 µmol, 1.10 equiv.). The crude product (dr 73:27) was purified by flash chromatography using PE/EtOAc 98:2 to afford **3y** and **3'y** as an oil (101 mg, 294 µmol, 98% yield).

Prepared according to the general procedure D from 2-bromothiophenol (56.7 mg, 36.1 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2b** (50.9 mg, 330 µmol, 1.10 equiv.). The crude product (dr 94:6) was purified by flash chromatography using PE/EtOAc 98:2 to afford **3y** and **3'y** as an oil (98.8 mg, 288 µmol, 96% yield).

*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 98:2): 0.61.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.53 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.33 – 7.17 (m, 2H, Ar*H*), 7.05 – 6.96 (m, 1H, Ar*H*), 4.18 (q, *J* = 8.2 Hz, 1H, SC*H*), 4.07 (t, *J* = 6.7 Hz, 2H, OC$H_2$), 3.17 (q, *J* = 8.7 Hz, 1H, C*H*C(O)), 2.50 (qd, *J* = 8.6, 3.5 Hz, 1H, SCHC$H_2$), 2.41 – 2.28 (m, 1H, C$H_2$CHC(O)), 2.28 – 2.14 (m, 1H, C$H_2$CHC(O)), 2.14 – 2.00 (m, 1H, SCHC$H_2$), 1.70 – 1.49 (m, 2H, $OCH_2CH_2$), 1.34 (dq, *J* = 14.6, 7.4 Hz, 2H, $CH_2CH_3$), 0.92 (t, *J* = 7.4 Hz, 3H, C$H_3$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.6, 137.4, 133.1, 129.3, 127.9, 127.1, 123.7, 64.9, 46.2, 41.6, 30.8, 27.0, 22.6, 19.2, 13.9.
IR ($v_{max}$, $cm^{-1}$) 2960 (s), 2933 (m), 2872 (m), 1730 (s), 1447 (s), 1359 (m), 1231 (s), 1202 (s), 1163 (s), 1123 (m), 1089 (m), 1015 (m), 936 (m), 750 (s).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}{}^{79}BrO_2S^+$ 343.0362; Found 343.0373.

**2-((2-Bromophenyl)thio)-N-methoxy-N-methylcyclobutane-1-carboxamide (3z)**




Prepared according to the general procedure C from 2-bromothiophenol (56.7 mg, 36.1 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2c** (46.6 mg, 330 µmol, 1.10 equiv.). The crude product (dr 60:40) was purified by flash chromatography using PE/EtOAc 80:20 to afford **3z** and **3'z** as an oil (53.5 mg, 162 µmol, 54% yield).

Prepared according to the general procedure D from 2-bromothiophenol (56.7 mg, 36.1 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2c** (46.6 mg, 330 µmol, 1.10 equiv.). The crude product

(dr >95:5) was purified by flash chromatography using PE/EtOAc 80:20 to afford **3z** and **3'z** as an oil (92.1 mg, 279 µmol, 93% yield).

The configuration of the two diastereoisomers obtained was determined by 2D-NOESY.

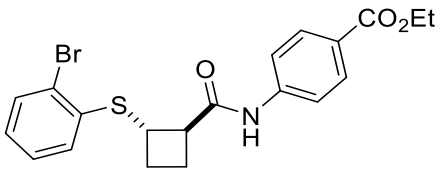
*Data for the trans- diastereoisomer:*

Rf(PE/EtOAc 8:2): 0.48.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.50 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.32 – 7.16 (m, 2H, Ar*H*), 6.98 (ddd, *J* = 8.7, 6.6, 2.4 Hz, 1H, Ar*H*), 4.33 (q, *J* = 8.3 Hz, 1H, SC*H*), 3.72 – 3.48 (m, 4H, C*H*C(O) + OC*H*$_3$), 3.17 (s, 3H, NC*H*$_3$), 2.52 (qd, *J* = 8.2, 3.1 Hz, 1H, SCHC*H*$_2$), 2.40 – 2.26 (m, 1H, C*H*$_2$CHC(O)), 2.26 – 2.16 (m, 1H, C*H*$_2$CHC(O)), 2.16 – 2.03 (m, 1H, SCHC*H*$_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.8, 138.0, 133.0, 128.3, 127.9, 126.5, 122.4, 61.8, 43.5, 40.2, 32.4, 27.2, 22.8.
IR ($\nu_{max}$, cm$^{-1}$) 2941 (m), 1656 (s), 1449 (s), 1426 (s), 1383 (m), 1256 (m), 1173 (m), 1109 (m), 1021 (m), 991 (m), 748 (s).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{13}H_{17}BrNO_2S^+$ 330.0158; Found 330.0167.

*Data for the cis- diastereoisomer:*

Rf(PE/EtOAc 8:2): 0.33.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.51 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.25 – 7.15 (m, 2H, Ar*H*), 7.03 – 6.92 (m, 1H, Ar*H*), 4.25 (q, *J* = 7.4 Hz, 1H, SC*H*), 3.95 (d, *J* = 7.4 Hz, 1H, C*H*C(O)), 3.61 (s, 3H, OC*H*$_3$), 3.17 (s, 3H, NC*H*$_3$), 2.76 – 2.59 (m, 1H, C*H*$_2$CH(O)), 2.60 – 2.45 (m, 1H, SCHC*H*$_2$), 2.22 (tt, *J* = 11.8, 6.3 Hz, 1H, SCHC*H*$_2$), 2.16 – 2.01 (m, 1H, C*H*$_2$CH(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 172.8, 138.3, 133.0, 129.1, 127.6, 126.7, 123.9, 61.3, 43.3, 41.0, 32.4, 28.2, 21.1.
IR ($\nu_{max}$, cm$^{-1}$) 2941 (m), 1660 (s), 1447 (s), 1426 (m), 1384 (m), 1246 (m), 1173 (m), 1116 (m), 1022 (m), 993 (m), 748 (s).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{13}H_{17}BrNO_2S^+$ 330.0158; Found 330.0167.

**Ethyl 4-(2-((2-bromophenyl)thio)cyclobutane-1-carboxamido)benzoate (3aa)**




Prepared according to the general procedure D from 2-bromothiophenol (56.7 mg, 36.1 µL, 300 µmol, 1.00 equiv.) and cyclobutene **2d** (80.9 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/$Et_2O$ 30:70 to afford **3aa** and **3'aa** as an oil (88.9 mg, 205 µmol, 68% yield).

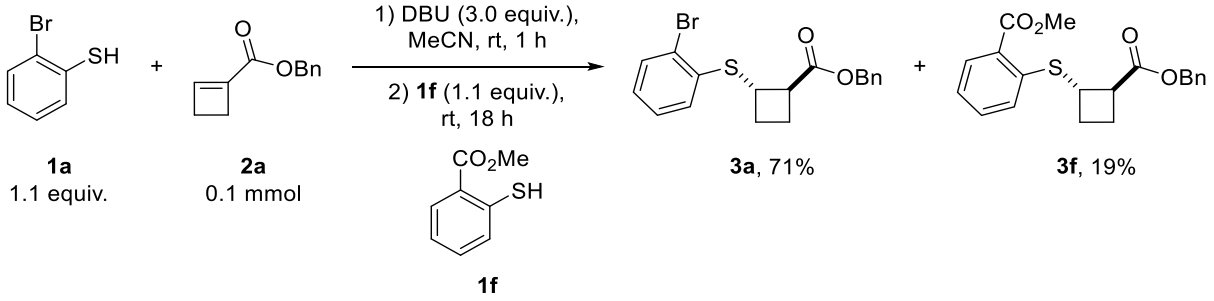
*Data for the trans- diastereoisomer:*

Rf(PE/$Et_2O$ 2:8): 0.71.
$^{1}$H NMR (400 MHz, chloroform-*d*) δ 8.05 – 7.89 (m, 2H, Ar*H*), 7.60 – 7.51 (m, 3H, Ar*H*), 7.47 (s, 1H, N*H*), 7.33 (dd, *J* = 7.9, 1.6 Hz, 1H, Ar*H*), 7.26 – 7.18 (m, 1H, Ar*H*), 7.05 (td, *J* = 7.7, 1.6 Hz, 1H, Ar*H*), 4.36 (q, *J* = 7.1 Hz, 2H, OC*H*$_2$), 4.14 (q, *J* = 8.4 Hz, 1H, SC*H*), 3.13 (q, *J* = 8.6 Hz, 1H, C*H*C(O)), 2.53 – 2.32 (m, 2H, SCHC*H*$_2$ + C*H*$_2$CHC(O)), 2.30 – 2.19 (m, 1H, C*H*$_2$CHC(O)), 2.18 – 2.05 (m, 1H, SCHC*H*$_2$), 1.38 (t, *J* = 7.1 Hz, 3H, $OCH_2CH_3$).

$^{13}$C NMR (101 MHz, chloroform-*d*) δ 171.0, 166.2, 141.8, 136.1, 133.4, 131.0, 130.9, 128.2, 128.1, 126.2, 124.9, 118.9, 61.0, 48.7, 43.2, 27.1, 21.4, 14.5.
IR ($\nu_{max}$, cm$^{-1}$) 3332 (w), 3060 (w), 2989 (w), 2939 (m), 2857 (w), 1712 (s), 1689 (s), 1597 (s), 1531 (s), 1447 (m), 1408 (m), 1278 (s), 1253 (s), 1173 (s), 1108 (s), 1020 (m), 860 (m), 767 (m), 745 (m).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{20}BrNNaO_3S^+$ 456.0239; Found 456.0252.

## 1.4. Crossover experiment

In a sealed vial under nitrogen, bromothiophenol **1a** (21.4 mg, 13.6 µL, 110 µmol, 1.10 equiv.) and cyclobutene **2a** (18.8 mg, 100 µmol, 1.00 equiv.) were diluted in 3 mL of MeCN. DBU (137 mg, 134 µL, 900 µmol, 3.00 equiv.) was then added. The reaction was stirred at rt for 1 h, at which time full conversion of **2a** was observed. Methyl thiosalicylate (18.5 mg, 15.2 µL, 110 µmol, 1.10 equiv) was then added and the reaction was stirred at rt for 18 h. The reaction mixture concentrated under reduced pressure and analyzed by $^1$H NMR using dibromomethane as internal standard; **3a** was observed in 71% NMR yield, **3f** in 19% NMR yield.



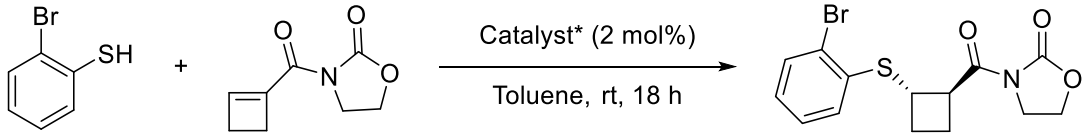
## 1.5. Optimization of the enantioselective sulfa-Michael addition

All catalysts were commercially available, purchased from Fluorochem or Combi-Blocks, and used as such.

### *General procedure for the optimization of the reaction*

In a sealed vial under nitrogen, the chiral catalyst and cyclobutene **2e** were diluted in 1 mL of solvent. Thiol **1a** was then added. The reaction was stirred at the indicated temperature for the indicated time. The reaction mixture was concentrated under reduced pressure. The reaction mixture was analyzed by $^{1}$H NMR (400 MHz, chloroform-*d*) using dibromomethane as an internal standard and by integration of the SC*H* proton at 4.28 (q, *J* = 8.5 Hz, 1H) ppm (yield and dr were measured). The crude was then purified by prep-TLC using PE/$Et_2O$ 30:70 and submitted to SFC analysis (IC column, 9% MeCN in supercritical $CO_2$, flow rate 0.75 mL/min, λ = 250.4 nm. tR(major) = 23.2 min, tR(minor) = 20.4 min).

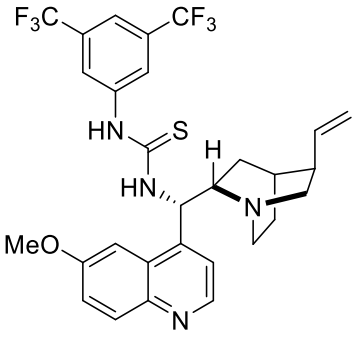
## *Screen of catalysts*



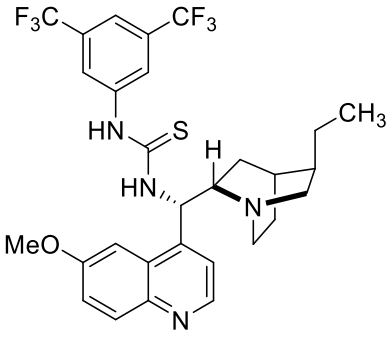

**1a**
0.1 mmol

**2e**
1.2 equiv.

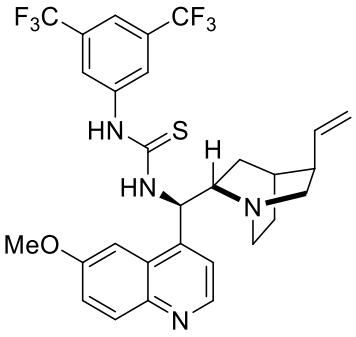
**4a**



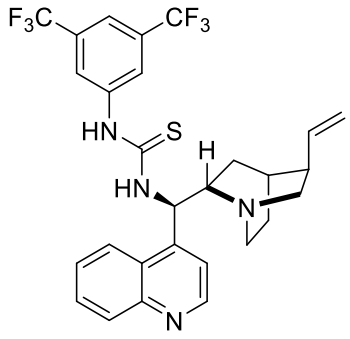

**Cat*1**
92% yield
dr 79:21
er 96:4



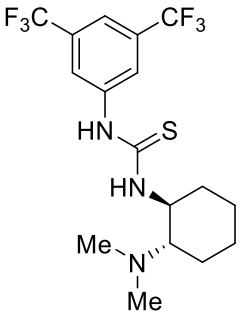

**Cat*2**
quant. yield
dr 85:15
er 96:4



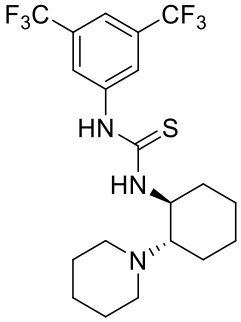

**Cat*3**
quant. yield
dr 71:29
er 6:94



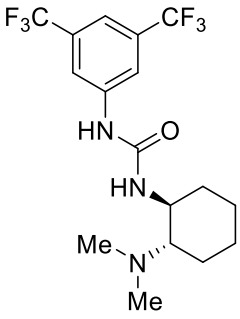

**Cat*4**
86% yield
dr 48:52
er 5:95



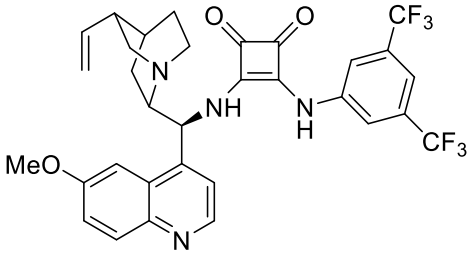

**Cat*5**
98% yield
dr 82:18
er 92:8



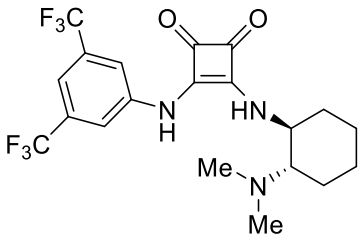

**Cat*6**
quant. yield
dr 55:45
er 38:62




**Cat*7**
84% yield
dr 66:34
er 86:13

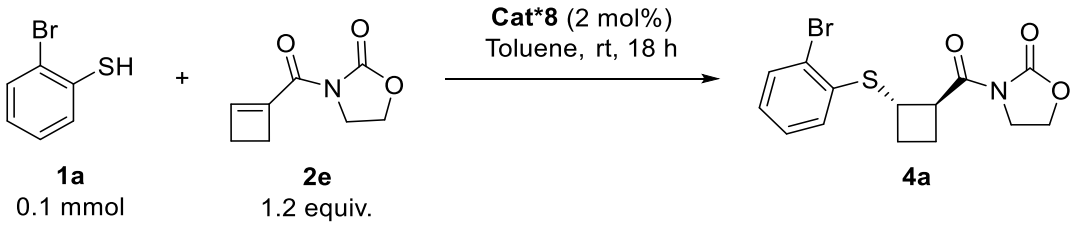



**Cat*8**
99% yield
dr 89:11
er 98:2




**Cat*9**
98% yield
dr 91:9
er 90:10

*Optimization table*




**1a**
0.1 mmol

**2e**
1.2 equiv.

**4a**

| Entry | Deviation from standard conditions | NMR Yield (%)[b] | dr[c] | er[d] |
|---|---|---|---|---|
| 1 | None | 99% | 89:11 | 98:2 |
| 2 | 5 mol% instead of 2 mol% of **Cat*8** | quant. | 90:10 | 98:2 |
| 3 | $CHCl_3$ instead of toluene | quant. | 90:10 | 97:3 |
| 4 | DCM instead of toluene | 97% | 78:22 | 96:4 |
| 5 | 0 °C instead of rt | quant. | 86:14 | 99:1 |
| 6 | 1.2 equiv. **1a** and 1.0 equiv. **2e** | 91% | 89:11 | 98:2 |
| 7 | 2 h instead of 18 h | 69% | 90:10 | 98:2 |

[a]Reaction conditions: 1.0 equiv. thiol **1a** (0.1 mmol), 1.2 equiv. cyclobutene **2e**, 2 mol% **Cat*8**. [b]1H NMR of the crude mixture with dibromomethane as an internal standard. [C]Measured on the crude $^1$H NMR. [d]Measured on the SFC chromatogram.

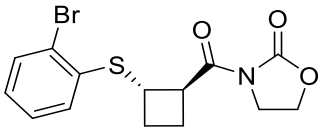
## 1.6. Enantioselective sulfa-Michael addition onto cyclobutenes

### *General procedure (E) for the enantioselective sulfa-Michael addition*

In a sealed vial under nitrogen, **Cat*8** (1.26 mg, 2.00 µmol, 0.0200 equiv.) and cyclobutene **2e** (18.4 mg, 110 µmol, 1.10 equiv.) were diluted in 1 mL of dry toluene. Thiol **1a-u** was then added. The reaction was stirred at room temperature for 18 h. The reaction mixture was concentrated under reduced pressure and purified by prep-TLC. The mixture of diastereoisomers was isolated and the yield measured. For characterization purposes, a prep-TLC was then performed and only the major diastereoisomer was isolated and characterized.

The dr was measured from the crude $^1$H NMR spectra by integration of the SC*H* proton. The er was measured from the SFC analysis of the purified major diastereoisomer.

**3-(2-((2-Bromophenyl)thio)cyclobutane-1-carbonyl)oxazolidin-2-one (4a)**




*Racemic:* Prepared according to the general procedure C from 2-bromothiophenol (18.9 mg, 12.0 µL, 100 µmol, 1.00 equiv.) and cyclobutene **2e** (55.2 mg, 330 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/$Et_2O$ 30:70 to afford **4a** and **4'a** as an oil (88.4 mg, 248 µmol, 83% yield).

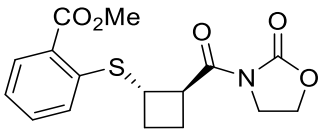
*Enantioenriched:* Prepared according to the general procedure E from 2-bromothiophenol (18.9 mg, 12.0 µL, 100 µmol, 1.00 equiv.). The crude product (dr 89:11) was purified by prep-TLC using PE/$Et_2O$ 30:70 to afford **4a** and **4'a** as an oil (35.2 mg, 98.8 µmol, 99% yield).

A scale up experiment with 2-bromothiophenol (151 mg, 96.2 µL, 800 µmol, 1.00 equiv.), cyclobutene **2e** (160 mg, 960 µmol, 1.20 equiv.) and **Cat*8** (10.1 mg, 16.0 µmol, 0.0200 equiv.) was also accomplished using the same procedure and led to **4a** (271 mg, 761 µmol, 95% yield, 91:9 dr, 98:2 er).

Rf(PE/EtOAc 8:2): 0.39.
$[\alpha]_D^{23}$ = 100.3 (c = 0.0467, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.53 (dd, *J* = 8.0, 1.3 Hz, 1H, Ar*H*), 7.33 (dd, *J* = 7.9, 1.5 Hz, 1H, Ar*H*), 7.29 – 7.20 (m, 1H, Ar*H*), 7.02 (td, *J* = 7.7, 1.6 Hz, 1H, Ar*H*), 4.49 – 4.33 (m, 3H, OC$H_2$ + SC*H*), 4.28 (q, *J* = 8.5 Hz, 1H, C*H*C(O)), 4.06 – 3.91 (m, 2H, NC$H_2$), 2.63 – 2.43 (m, 2H, SCHC$H_2$ + C$H_2$CH(O)), 2.22 – 1.98 (m, 2H, SCHC$H_2$ + C$H_2$CH(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 172.9, 153.1, 137.4, 133.1, 129.5, 127.9, 127.1, 123.8, 62.3, 45.5, 42.6, 39.4, 27.0, 23.9.
IR ($\nu_{max}$, $cm^{-1}$) 2921 (w), 1782 (s), 1692 (m), 1479 (w), 1386 (s), 1278 (w), 1227 (m), 1118 (w), 1042 (w), 911 (m), 740 (m).
HRMS (APCI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{14}BrNNaO_3S^+$ 377.9770; Found 377.9758.

The enantiomeric ratio was determined to be 98:2 by SFC analysis: IC column, 9% MeCN in supercritical $CO_2$, flow rate 0.75 mL/min, λ = 250.4 nm. tR(major) = 23.2 min, tR(minor) = 20.4 min.).

**Methyl 2-((2-(2-oxooxazolidine-3-carbonyl)cyclobutyl)thio)benzoate (4b)**



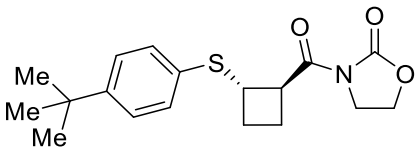
*Racemic:* Prepared according to the general procedure C from methyl 2-mercaptobenzoate (16.8 mg, 13.8 µL, 100 µmol, 1.00 equiv.) and cyclobutene **2e** (18.4 mg, 110 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/$Et_2O$ 30:70 to afford **4b** and **4'b** as a white solid (31.4 mg, 93.6 µmol, 94% yield).

*Enantioenriched:* Prepared according to the general procedure E from methyl 2-mercaptobenzoate (16.8 mg, 13.8 µL, 100 µmol, 1.00 equiv.). The crude product (dr >95:5) was purified by prep-TLC using PE/$Et_2O$ 25:75 to afford **4b** and **4'b** as a white solid (31.2 mg, 93.0 µmol, 93% yield).

m.p.:102-104 °C.
Rf(PE/$Et_2O$ 3:7): 0.31.
$[\alpha]_D^{23}$ = 80.4 (c = 0.0367, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.94 (dd, *J* = 7.8, 1.4 Hz, 1H, Ar*H*), 7.44 – 7.37 (m, 1H, Ar*H*), 7.33 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.15 (t, *J* = 7.5 Hz, 1H, Ar*H*), 4.49 (q, *J* = 7.9 Hz, 1H, SC*H*), 4.40 (td, *J* = 8.3, 3.3 Hz, 2H, OC$H_2$), 4.25 (q, *J* = 8.2 Hz, 1H, C*H*C(O)), 4.05 – 3.96 (m, 2H, NC$H_2$), 3.90 (s, 3H, OC$H_3$), 2.70 – 2.49 (m, 2H, SCHC$H_2$ + C$H_2$CHC(O)), 2.24 – 2.00 (m, 2H, SCHC$H_2$ + C$H_2$CHC(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.1, 167.0, 153.0, 141.3, 132.5, 131.4, 127.6, 126.9, 124.3, 62.3, 52.3, 45.1, 42.6, 38.1, 27.2, 24.2.
IR ($\nu_{max}$, $cm^{-1}$) 3011 (w), 2957 (w), 1782 (m), 1714 (s), 1465 (m), 1437 (m), 1390 (m), 1280 (s), 1252 (s), 1145 (w), 1116 (w), 1062 (m), 746 (s).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{17}NNaO_5S^+$ 358.0720; Found 358.0722.

The enantiomeric ratio was determined to be 97:3 by SFC analysis: IA column, 9% MeCN in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 260.4 nm. tR(major) = 5.8 min, tR(minor) = 12.2 min.

**3-(2-((4-(tert-Butyl)phenyl)thio)cyclobutane-1-carbonyl)oxazolidin-2-one (4c)**



*Racemic:* Prepared according to the general procedure C from 4-tert-butylbenzenethiol (16.6 mg, 17.3 µL, 100 µmol, 1.00 equiv.) and cyclobutene **2e** (18.4 mg, 110 µmol, 1.10 equiv.). The crude product (dr 93:7) was purified by flash chromatography using PE/$Et_2O$ 20:80 to afford **4c** and **4'c** as an oil (30.9 mg, 92.7 µmol, 93% yield).

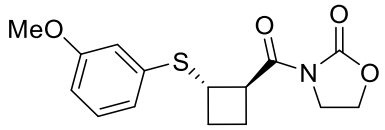
*Enantioenriched:* Prepared according to the general procedure E from 4-tert-butylbenzenethiol (16.6 mg, 17.3 µL, 100 µmol, 1.00 equiv.). The crude product (dr 91:9) was purified by prep-TLC using PE/$Et_2O$ 25:75 to afford **4c** and **4'c** as an oil (27.4 mg, 82.2 µmol, 82% yield).

Rf(PE/$Et_2O$ 2:8): 0.56.
$[\alpha]_D^{23}$ = 182.4 (c = 0.0167, $CHCl_3$).

$^1$H NMR (400 MHz, chloroform-*d*) δ 7.33 (s, 4H, Ar*H*), 4.51 – 4.33 (m, 2H, OC$H_2$), 4.32 – 4.19 (m, 2H, SC*H* + C*H*C(O)), 3.97 (qdd, *J* = 11.0, 9.1, 7.1 Hz, 2H, NC$H_2$), 2.51 – 2.28 (m, 2H, SCHC$H_2$ + C$H_2$CHC(O)), 2.18 – 1.90 (m, 2H, SCHC$H_2$ + C$H_2$CHC(O)), 1.32 (s, 9H, C(C$H_3$)$_3$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.1, 153.2, 150.1, 131.3, 131.3, 126.0, 62.2, 45.5, 42.6, 41.5, 34.7, 31.4, 27.0, 23.3.
IR ($\nu_{max}$, cm$^{-1}$) 2960 (m), 2909 (w), 2871 (w), 1779 (s), 1692 (s), 1491 (w), 1385 (s), 1270 (m), 1222 (m), 1119 (m), 1083 (w), 1044 (m), 824 (m), 759 (m).
HRMS (APCI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{23}NNaO_3S^+$ 356.1291; Found 356.1281.

The enantiomeric ratio was determined to be 99.7:0.3 by SFC analysis: IA column, 9% MeCN in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 214.4 nm. tR(major) = 3.3 min, tR(minor) = 2.2 min.

**3-(2-((3-Methoxyphenyl)thio)cyclobutane-1-carbonyl)oxazolidin-2-one (4d)**



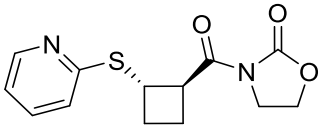

<u>*Racemic:*</u> Prepared according to the general procedure C from 3-methoxybenzenethiol (14.0 mg, 12.4 µL, 100 µmol, 1.00 equiv.) and cyclobutene **2e** (18.4 mg, 110 µmol, 1.10 equiv.). The crude product (dr 93:7) was purified by flash chromatography using PE/$Et_2O$ 20:80 to afford **4d** and **4'd** as an oil (27.3 mg, 88.8 µmol, 89% yield).

<u>*Enantioenriched:*</u> Prepared according to the general procedure E from 3-methoxybenzenethiol (14.0 mg, 12.4 µL, 100 µmol, 1.00 equiv.). The crude product (dr 88:12) was purified by prep-TLC using PE/$Et_2O$ 25:75 to afford **4d** and **4'd** as an oil (30.6 mg, 99.6 µmol, quant.).

Rf(PE/$Et_2O$ 2:8): 0.45.
$[\alpha]_D^{23}$ = 88.3 (c = 0.0433, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.18 (t, *J* = 7.9 Hz, 1H, Ar*H*), 6.98 – 6.87 (m, 2H, Ar*H*), 6.74 (ddd, *J* = 8.3, 2.5, 0.9 Hz, 1H, Ar*H*), 4.45 – 4.16 (m, 4H, SC*H* + C*H*C(O) + OC$H_2$), 4.07 – 3.83 (m, 2H, NC$H_2$), 3.80 (s, 3H, OC$H_3$), 2.50 – 2.28 (m, 2H, SCHC$H_2$ + C$H_2$CHC(O)), 2.16 – 1.93 (m, 2H, SCHC$H_2$ + C$H_2$CHC(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.1, 159.9, 153.1, 136.5, 129.8, 122.9, 115.6, 112.8, 62.2, 55.5, 45.7, 42.6, 41.2, 27.0, 23.3.
IR ($\nu_{max}$, cm$^{-1}$) 2991 (w), 2946 (w), 1778 (s), 1692 (s), 1588 (m), 1478 (m), 1385 (s), 1281 (m), 1228 (s), 1117 (m), 1079 (m), 1037 (s), 860 (m), 760 (m).
HRMS (APCI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{17}NNaO_4S^+$ 330.0770; Found 330.0763.

The enantiomeric ratio was determined to be 99:1 by SFC analysis: IA column, 18% MeOH in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 214.4 nm. tR(major) = 1.2 min, tR(minor) = 2.4 min.

**3-(2-(Pyridin-2-ylthio)cyclobutane-1-carbonyl)oxazolidin-2-one (4e)**



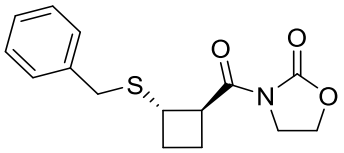

<u>*Racemic:*</u> Prepared according to the general procedure C from 2-pyridinethiol (11.1 mg, 100 µmol, 1.00 equiv.) and cyclobutene **2e** (18.4 mg, 110 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/$Et_2O$ 20:80 to afford **4e** and **4'e** as an oil (20.3 mg, 72.9 µmol, 73% yield).

*Enantioenriched:* Prepared according to the general procedure E from pyridine-2-thiol (11.1 mg, 100 µmol, 1.00 equiv.). The crude product (dr 61:39) was purified by prep-TLC using PE/$Et_2O$ 25:75 to afford **4e** and **4'e** as an oil (26.4 mg, 94.9 µmol, 95% yield).

Rf(PE/$Et_2O$ 2:8): 0.34.
$[\alpha]_D^{23}$ = 92.6 (c = 0.0300, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 8.39 – 8.29 (m, 1H, Ar*H*), 7.46 (td, *J* = 7.7, 1.9 Hz, 1H, Ar*H*), 7.16 (d, *J* = 8.1 Hz, 1H, Ar*H*), 6.95 (ddd, *J* = 7.3, 4.9, 0.9 Hz, 1H, Ar*H*), 4.71 (q, *J* = 8.3 Hz, 1H, SC*H*), 4.48 (q, *J* = 8.7 Hz, 1H, C*H*C(O)), 4.42 – 4.26 (m, 2H, OC$H_2$), 4.07 – 3.95 (m, 2H, NC$H_2$), 2.47 (ddt, *J* = 14.8, 12.7, 4.4 Hz, 2H, SCHC$H_2$ + C$H_2$CHC(O)), 2.30 – 2.06 (m, 2H, SCHC$H_2$ + C$H_2$CHC(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.2, 159.5, 153.2, 149.2, 136.1, 122.3, 119.6, 62.1, 45.3, 42.8, 39.2, 26.7, 23.4.
IR ($\nu_{max}$, $cm^{-1}$) 2993 (w), 2953 (w), 1779 (s), 1695 (s), 1578 (m), 1455 (m), 1415 (m), 1386 (s), 1275 (m), 1227 (m), 1127 (m), 1044 (m), 986 (w), 917 (w), 759 (m).
HRMS (APCI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{14}N_2NaO_3S^+$ 301.0617; Found 301.0604.

The enantiomeric ratio was determined to be 96:4 by SFC analysis: IA column, 9% MeCN in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 250.4 nm. tR(major) = 3.7 min, tR(minor) = 7.0 min.

**3-(2-(Benzylthio)cyclobutane-1-carbonyl)oxazolidin-2-one (4f)**



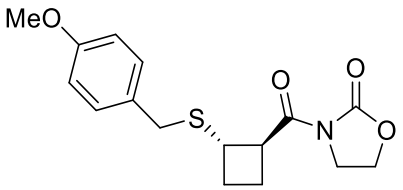

*Racemic:* Prepared according to the general procedure C from phenylmethanethiol (12.4 mg, 11.7 µL, 100 µmol, 1.00 equiv.) and cyclobutene **2e** (18.4 mg, 110 µmol, 1.10 equiv.). The crude product (dr 90:10) was purified by flash chromatography using PE/EtOAc 80:20 to afford **4f** and **4'f** as an oil (29.0 mg, 99.5 µmol, quant.).

*Enantioenriched:* Prepared according to the general procedure E from phenylmethanethiol (12.4 mg, 11.7 µL, 100 µmol, 1.00 equiv.). The crude product (dr 68:32) was purified by prep-TLC using PE/$Et_2O$ 30:70 to afford **4f** and **4'f** as an oil (29.0 mg, 99.5 µmol, quant. yield).

Rf(PE/EtOAc 8:2): 0.41.
$[\alpha]_D^{23}$ = 145.4 (c = 0.0200, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.35 (d, *J* = 7.2 Hz, 2H, Ar*H*), 7.29 (dd, *J* = 8.2, 6.7 Hz, 2H, Ar*H*), 7.24 – 7.18 (m, 1H, Ar*H*), 4.47 – 4.27 (m, 2H, OC$H_2$), 4.12 (q, *J* = 9.1 Hz, 1H, SC*H*), 4.01 – 3.82 (m, 3H, CHC(O) + NC$H_2$), 3.79 – 3.61 (m, 2H, SC$H_2$Ph), 2.47 – 2.32 (m, 1H, SCHC$H_2$), 2.21 – 2.10 (m, 1H, C$H_2$CHC(O)), 2.03 – 1.79 (m, 2H, SCHC$H_2$ + C$H_2$CHC(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.2, 153.1, 138.9, 129.0, 128.5, 126.9, 62.2, 46.7, 42.5, 39.4, 36.3, 26.5, 23.8.
IR ($\nu_{max}$, $cm^{-1}$) 2987 (w), 2943 (w), 1779 (s), 1692 (s), 1483 (w), 1453 (w), 1386 (s), 1267 (m), 1224 (s), 1116 (m), 1077 (m), 1044 (m), 759 (m).
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{17}NNaO_3S^+$ 314.0821; Found 314.0824.

The enantiomeric ratio was determined to be 98:2 by SFC analysis: IA column, 9% MeCN in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 220.4 nm. tR(major) = 2.9 min, tR(minor) = 8.7 min.

**3-(2-((4-Methoxybenzyl)thio)cyclobutane-1-carbonyl)oxazolidin-2-one (4g)**



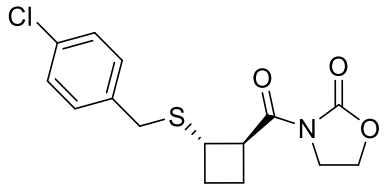

*Racemic:* Prepared according to the general procedure C from (4-methoxyphenyl)methanethiol (15.4 mg, 13.8 µL, 100 µmol, 1.00 equiv.) and cyclobutene **2e** (18.4 mg, 110 µmol, 1.10 equiv.). The crude product (dr 91:9) was purified by flash chromatography using PE/$Et_2O$ 20:80 to afford **4g** and **4'g** as an oil (26.7 mg, 83.1 µmol, 83% yield).

*Enantioenriched:* Prepared according to the general procedure E from (4-methoxyphenyl)methanethiol (15.4 mg, 13.8 µL, 100 µmol, 1.00 equiv.). The crude product (dr 91:9) was purified by prep-TLC using PE/$Et_2O$ 30:70 to afford **4g** and **4'g** as an oil (19.9 mg, 61.9 µmol, 62% yield).

Rf(PE/$Et_2O$ 2:8): 0.44.
$[\alpha]_D^{23}$ = 119.6 (c = 0.0167, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.30 – 7.22 (m, 2H, Ar*H*), 6.86 – 6.78 (m, 2H, Ar*H*), 4.36 (t, *J* = 8.1 Hz, 2H, OC$H_2$), 4.11 (q, *J* = 9.1 Hz, 1H, SC*H*), 3.97 – 3.83 (m, 3H, C*H*C(O) + NC$H_2$), 3.79 (s, 3H, OC$H_3$), 3.75 – 3.58 (m, 2H, SC$H_2$), 2.47 – 2.31 (m, 1H, SCHC$H_2$), 2.18 (dt, *J* = 9.9, 8.6 Hz, 1H, C$H_2$CHC(O)), 2.01 – 1.82 (m, 2H, SCHC$H_2$ + C$H_2$CHC(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.2, 158.6, 153.1, 130.8, 130.1, 113.9, 62.2, 55.4, 46.7, 42.6, 39.4, 35.7, 26.4, 23.9.
IR ($\nu_{max}$, $cm^{-1}$) 2992 (w), 2927 (w), 2842 (w), 1779 (s), 1689 (s), 1613 (w), 1512 (s), 1386 (s), 1246 (s), 1181 (m), 1119 (w), 1076 (w), 1044 (m), 837 (w), 759 (m).
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{19}NNaO_4S^+$ 344.0927; Found 344.0931.

The enantiomeric ratio was determined to be 97:3 by SFC analysis: IA column, 16% MeCN in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 214.4 nm. tR(major) = 1.8 min, tR(minor) = 5.5 min.

**3-(2-((4-Chlorobenzyl)thio)cyclobutane-1-carbonyl)oxazolidin-2-one (4h)**




*Racemic:* Prepared according to the general procedure C from (4-chlorophenyl)methanethiol (15.9 mg, 13.2 µL, 100 µmol, 1.00 equiv.) and cyclobutene **2e** (18.4 mg, 110 µmol, 1.10 equiv.). The crude product (dr 93:7) was purified by flash chromatography using PE/$Et_2O$ 20:80 to afford **4h** and **4'h** as an oil (30.2 mg, 92.7 µmol, 93% yield).

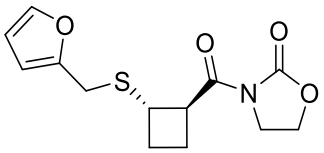
*Enantioenriched:* Prepared according to the general procedure E from (4-chlorophenyl)methanethiol (15.9 mg, 13.2 µL, 100 µmol, 1.00 equiv.). The crude product (dr >95:5) was purified by prep-TLC using PE/$Et_2O$ 30:70 to afford **4h** and **4'h** as an oil (32.5 mg, 99.8 µmol, quant.).

Rf(PE/$Et_2O$ 2:8): 0.67.
$[\alpha]_D^{23}$ = 76.7 (c = 0.0867, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.34 – 7.20 (m, 4H, Ar*H*), 4.46 – 4.28 (m, 2H, OC$H_2$), 4.19 – 4.04 (m, 1H, SC*H*), 4.00 – 3.77 (m, 3H, NC$H_2$ + C*H*C(O)), 3.74 – 3.60 (m, 2H, SC$H_2$), 2.48

– 2.31 (m, 1H, SCHC*H*$_2$), 2.25 – 2.08 (m, 1H, C*H*$_2$CHC(O)), 1.99 – 1.77 (m, 2H, SCHC*H*$_2$ + C*H*$_2$CHC(O) ).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.1, 153.1, 137.5, 132.6, 130.4, 128.6, 62.2, 46.9, 42.5, 39.3, 35.7, 26.4, 23.9.
IR ($\nu_{max}$, cm$^{-1}$) 2986 (w), 2948 (w), 2923 (w), 2866 (w), 1777 (s), 1689 (s), 1490 (m), 1384 (s), 1274 (m), 1220 (s), 1116 (m), 1091 (m), 1045 (m), 835 (w), 755 (m).
HRMS (ESI/QTOF) m/z: [M + Na]$^+$ Calcd for $C_{15}H_{16}ClNNaO_3S^+$ 348.0432; Found 348.0439.

The enantiomeric ratio was determined to be 98:2 by SFC analysis: IA column, 16% MeCN in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 214.4 nm. tR(major) = 2.0 min, tR(minor) = 5.4 min.

**3-(2-((Furan-2-ylmethyl)thio)cyclobutane-1-carbonyl)oxazolidin-2-one (4i)**



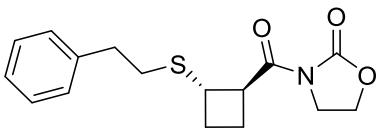
*Racemic:* Prepared according to the general procedure C from 2-furylmethanethiol (11.4 mg, 10.1 µL, 100 µmol, 1.00 equiv.) and cyclobutene **2e** (18.4 mg, 110 µmol, 1.10 equiv.). The crude product (dr >95:5) was purified by flash chromatography using PE/$Et_2O$ 30:70 to afford **4i** and **4'i** as an oil (28.0 mg, 99.5 µmol, quant.).

*Enantioenriched:* Prepared according to the general procedure E from 2-furylmethanethiol (11.4 mg, 10.1 µL, 100 µmol, 1.00 equiv.). The crude product (dr 90:10) was purified by prep-TLC using PE/$Et_2O$ 25:75 to afford **4i** and **4'i** as an oil (22.2 mg, 78.9 µmol, 79% yield).

Rf(PE/$Et_2O$ 3:7): 0.39.
$[\alpha]_D^{23}$ = 94.3 (c = 0.0267, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.34 (dd, *J* = 1.8, 0.8 Hz, 1H, Ar*H*), 6.29 (dd, *J* = 3.2, 1.9 Hz, 1H, Ar*H*), 6.23 – 6.16 (m, 1H, Ar*H*), 4.40 (t, *J* = 8.1 Hz, 2H, OC*H*$_2$), 4.19 – 4.06 (m, 1H, SC*H*), 4.03 – 3.90 (m, 3H, NC*H*$_2$ + C*H*C(O)), 3.81 – 3.67 (m, 2H, SC*H*$_2$), 2.53 – 2.38 (m, 1H, SCHC*H*$_2$), 2.28 – 2.12 (m, 1H, C*H*$_2$CHC(O)), 2.04 – 1.86 (m, 2H, SCHC*H*$_2$ + C*H*$_2$CHC(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.2, 153.1, 152.1, 142.1, 110.5, 107.4, 62.3, 46.8, 42.6, 39.4, 28.3, 26.5, 23.7.
IR ($\nu_{max}$, cm$^{-1}$) 2990 (w), 2946 (w), 1780 (s), 1689 (s), 1472 (w), 1386 (s), 1270 (m), 1220 (m), 1123 (w), 1077 (w), 1045 (m), 743 (m).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + Na]$^+$ Calcd for $C_{13}H_{15}NNaO_4S^+$ 304.0614; Found 304.0625.

The enantiomeric ratio was determined to be 99:1 by SFC analysis: IA column, 18% MeOH in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 214.4 nm. tR(major) = 1.1 min, tR(minor) = 2.8 min.

**3-(2-(Phenethylthio)cyclobutane-1-carbonyl)oxazolidin-2-one (4j)**



*Racemic:* Prepared according to the general procedure C from 2-phenylethanethiol (13.8 mg, 13.6 µL, 100 µmol, 1.00 equiv.) and cyclobutene **2e** (18.4 mg, 110 µmol, 1.10 equiv.). The crude product (dr 95:5) was purified by flash chromatography using PE/$Et_2O$ 20:80 to afford **4j** and **4'j** as an oil (23.8 mg, 77.9 µmol, 78% yield).

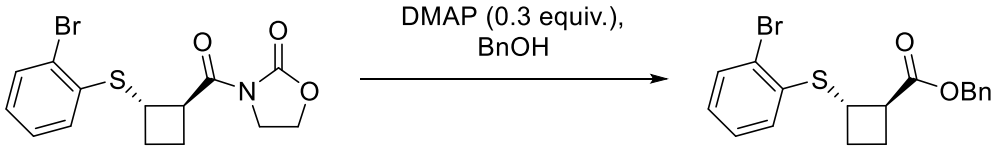
*Enantioenriched:* Prepared according to the general procedure E from 2-phenylethanethiol (13.8 mg, 13.6 µL, 100 µmol, 1.00 equiv.). The crude product (dr 85:15) was purified by prep-TLC using PE/$Et_2O$ 25:75 to afford **4j** and **4'j** as an oil (28.0 mg, 91.7 µmol, 92% yield).

Rf(PE/$Et_2O$ 2:8): 0.51.
$[\alpha]_D^{23}$ = 163.4 (c = 0.0133, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.34 – 7.23 (m, 2H, Ar*H*), 7.21 (dd, *J* = 7.1, 3.6 Hz, 3H, Ar*H*), 4.48 – 4.29 (m, 2H, OC$H_2$), 4.19 – 4.05 (m, 1H, SC*H*), 4.04 – 3.83 (m, 3H, NC$H_2$ + C*H*C(O)), 2.98 – 2.67 (m, 4H, SC$H_2$C$H_2$Ph), 2.54 – 2.40 (m, 1H, SCHC$H_2$), 2.32 – 2.16 (m, 1H, C$H_2$CHC(O)), 2.09 – 1.85 (m, 2H, SCHC$H_2$ + C$H_2$CHC(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.3, 153.2, 140.8, 128.7, 128.6, 126.4, 62.3, 46.9, 42.6, 39.4, 36.7, 33.0, 26.7, 23.6.
IR ($\nu_{max}$, $cm^{-1}$) 3027 (w), 2947 (w), 2925 (w), 2859 (w), 1782 (s), 1691 (s), 1496 (w), 1476 (w), 1389 (s), 1265 (m), 1225 (m), 1119 (m), 1083 (w), 1051 (w).
HRMS (APCI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{19}NNaO_3S^+$ 328.0978; Found 328.0975.

The enantiomeric ratio was determined to be 95:5 by SFC analysis: IA column, 9% MeCN in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 214.4 nm. tR(major) = 2.7 min, tR(minor) = 6.3 min.

## 1.7. Product modifications

**Benzyl 2-((2-bromophenyl)thio)cyclobutane-1-carboxylate (3a)**




**4a**
97:3 er

**3a**, 46%
97:3 er

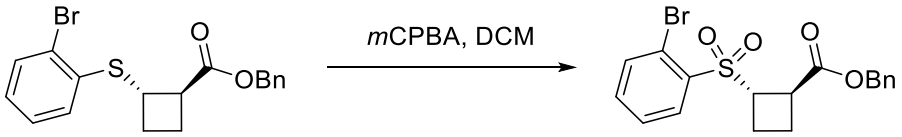
*Racemic:* The racemic compound was described above as **3a** (page 11).

*Enantioenriched:* Cyclobutane **4a** (28.0 mg, 78.6 µmol, 1.00 equiv.) was diluted in BnOH (786 µL) and DMAP (2.88 mg, 23.6 µmol, 0.300 equiv.) was added. The reaction mixture was stirred at rt for 18 h. The mixture was then concentrated under reduced pressure. The crude mixture was purified by prep-TLC using PE/$Et_2O$ 95:5 to afford **3a** as an oil (13.5 mg, 35.8 µmol, 46% yield).

$[\alpha]_D^{23}$ = 56.4 (c = 0.0333, $CHCl_3$).

The enantiomeric ratio was determined to be 97:3 by SFC analysis: IA column, 15% MeOH in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 214.4 nm. tR(major) = 22.9 min, tR(minor) = 26.9 min.

**Benzyl 2-((2-bromophenyl)sulfonyl)cyclobutane-1-carboxylate (5)**




**3a**
97:3 er

**5**, 95%
97:3 er

*Racemic:* Cyclobutane **3a** (37.7 mg, 100 µmol, 1.00 equiv.) was diluted in DCM (1.00 mL) and *m*CPBA (56.0 mg, 250 µmol, 2.50 equiv.) was then added at 0 °C. The reaction was stirred at rt for 3 h. The reaction was then diluted in DCM (10 mL) and washed with sat. $NaHCO_3$ solution (10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product **5** (40.0 mg, 97.7 µmol, 98% yield) was pure enough without further purification.

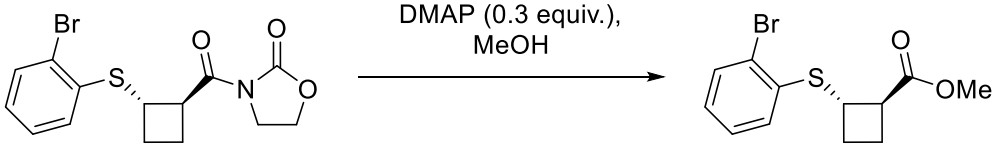
*Enantioenriched:* the same procedure as described above was implemented on enantioenriched **3a** (15.1 mg, 40.0 µmol, 1.00 equiv.) to afford **5** as an oil (10.3 mg, 25.2 µmol, 95% yield).

$[\alpha]_D^{23}$ = 7.3 (c = 0.0400, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 8.10 (dd, *J* = 7.7, 1.9 Hz, 1H, Ar*H*), 7.63 (dd, *J* = 7.8, 1.3 Hz, 1H, Ar*H*), 7.46 – 7.32 (m, 5H, Ar*H*), 7.19 (dd, *J* = 6.6, 3.0 Hz, 2H, Ar*H*), 4.99 – 4.87 (m, 2H, OC$H_2$Ph), 4.83 – 4.70 (m, 1H, SC*H*), 3.67 – 3.53 (m, 1H, C*H*C(O)), 2.71 – 2.54 (m, 1H, SCHC$H_2$), 2.43 – 2.12 (m, 3H, C$H_2$CHC(O) + SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 171.5, 137.0, 135.6, 135.4, 134.8, 132.6, 128.7, 128.5, 128.4, 127.9, 121.4, 67.0, 56.0, 39.1, 21.1, 18.9.

IR ($v_{max}$, $cm^{-1}$) 3069 (w), 2957 (w), 1733 (s), 1573 (w), 1447 (m), 1314 (s), 1249 (m), 1199 (m), 1150 (s), 1026 (m), 737 (s).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}BrO_4S^+$ 409.0104; Found 409.0120.

The enantiomeric ratio was determined to be 97:3 by SFC analysis: IC column, 7% MeCN in supercritical $CO_2$, flow rate 0.75 mL/min, λ = 270.4 nm. tR(major) = 65.4 min, tR(minor) = 70.3 min.

**Methyl 2-((2-bromophenyl)thio)cyclobutane-1-carboxylate (6)**




**4a**
97:3 er

**8**, 95%
97:3 er

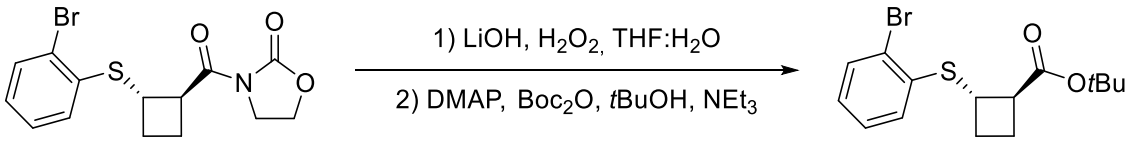
*Racemic:* Cyclobutane **4a** (35.6 mg, 100 µmol, 1.00 equiv.) was diluted in dry MeOH (1.0 mL) and DMAP (3.67 mg, 30.0 µmol, 0.300 equiv.) was added. The reaction mixture was stirred at rt for 2 h. The mixture was then concentrated under reduced pressure. The crude mixture was purified by prep-TLC using PE/$Et_2O$ 90:10 to afford **8** as an oil (10.5 mg, 34.9 µmol, 87% yield).

*Enantioenriched:* the same procedure as described above was implemented on enantioenriched **4a** (35.6 mg, 100 µmol, 1.00 equiv.) to afford **8** as an oil (11.4 mg, 37.8 µmol, 95% yield).

Rf(PE/$Et_2O$ 9:1): 0.37.
$[\alpha]_D^{23}$ = 91.3 (c = 0.0100, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.54 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.36 – 7.17 (m, 2H, Ar*H*), 7.03 (dt, *J* = 8.4, 4.5 Hz, 1H, Ar*H*), 4.18 (q, *J* = 8.3 Hz, 1H, SC*H*), 3.66 (s, 3H, OC$H_3$), 3.19 (q, *J* = 8.8 Hz, 1H, C*H*C(O)), 2.56 – 2.43 (m, 1H, SCHC$H_2$), 2.40 – 2.28 (m, 1H, C$H_2$CHC(O)), 2.22 (p, *J* = 9.2 Hz, 1H, C$H_2$CHC(O)), 2.16 – 1.91 (m, 1H, SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 173.9, 137.2, 133.2, 129.3, 127.9, 127.1, 123.7, 52.1, 45.9, 41.7, 27.2, 22.6.
IR ($v_{max}$, $cm^{-1}$) 3059 (w), 2993 (w), 2951 (m), 2922 (m), 2852 (w), 1732 (s), 1574 (w), 1448 (m), 1361 (m), 1247 (m), 1210 (m), 1165 (m), 1039 (m), 1022 (m).
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{12}H_{13}BrNaO_2S^+$ 322.9712; Found 322.9716.

The enantiomeric ratio was determined to be 97:3 by SFC analysis: IC column, 6% MeOH in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 214.4 nm. tR(major) = 1.3 min, tR(minor) = 1.5 min.

***tert*-Butyl 2-((2-bromophenyl)thio)cyclobutane-1-carboxylate (7)**




**4a**
97:3 er

**9**, 42%
97:3 er

*Racemic:* Cyclobutane **4a** (71.2 mg, 200 µmol, 1.00 equiv.) was diluted in THF (1.3 mL) and $H_2O$ (0.7 mL). LiOH monohydrate (16.8 mg, 400 µmol, 2.00 equiv.) and hydrogen peroxide 30w% (136 mg, 123 µL, 1.20 mmol, 6.00 equiv) were added at 0 °C. The reaction mixture was stirred at rt for 18 h. The reaction mixture was quenched with sat. $Na_2SO_3$ (1 mL), diluted with sat. $NaHCO_3$ (10 mL), washed with EtOAc (10 mL). The pH value of the aqueous layer was adjusted to 1 using HCl (1 M). The mixture was extracted with EtOAc (3 x 20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure.

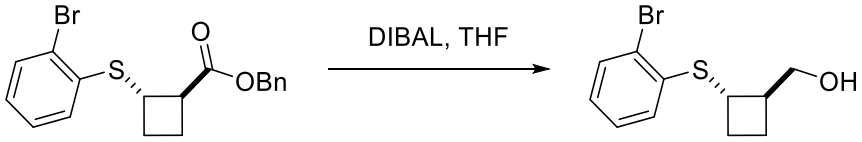
To the crude mixture was added DMAP (2.44 mg, 20.0 µmol, 0.100 equiv.), $Boc_2O$ (65.5 mg, 300 µmol, 1.50 equiv.), $NEt_3$ (40.5 mg, 55.8 µL, 400 µmol, 2.00 equiv.) and *t*BuOH (29.6 mg, 38.0 µL, 400 µmol, 2.00 equiv.) in this order. The reaction was stirred neat at rt for 18 h. The reaction mixture was diluted with DCM (10 mL), washed with brine (2 x 10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was purified by prep-TLC using PE/$Et_2O$ 90:10 to afford **9** as an oil (31.6 mg, 92.1 µmol, 46% yield).

*Enantioenriched:* the same procedure as described above was implemented on enantioenriched **4a** (71.2 mg, 200 µmol, 1.00 equiv.) to afford **11** as an oil (28.9 mg, 84.2 µmol, 42% yield).

Rf(PE/EtOAc 9:1): 0.85.
$[\alpha]_D^{23}$ = 37.8 (c = 0.0270, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.53 (dd, *J* = 7.9, 1.3 Hz, 1H, Ar*H*), 7.37 – 7.14 (m, 2H, Ar*H*), 7.02 (ddd, *J* = 7.9, 7.3, 1.8 Hz, 1H, Ar*H*), 4.14 (q, *J* = 8.2 Hz, 1H, SC*H*), 3.14 – 3.01 (m, 1H, C*H*C(O)), 2.54 – 2.41 (m, 1H, SCHC$H_2$), 2.41 – 2.24 (m, 1H, C$H_2$CHC(O)), 2.22 – 1.95 (m, 2H, SCHC$H_2$ + C$H_2$CHC(O)), 1.42 (s, 9H, C(C$H_3$)$_3$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 172.9, 137.6, 133.1, 129.2, 127.9, 126.9, 123.5, 81.0, 47.5, 41.4, 28.1, 26.7, 22.5.
IR ($\nu_{max}$, $cm^{-1}$) 3062 (w), 2978 (m), 2938 (w), 2873 (w), 1721 (s), 1451 (m), 1367 (m), 1249 (m), 1151 (s), 1021 (w), 844 (w).
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{19}BrNaO_2S^+$ 365.0181; Found 365.0190.

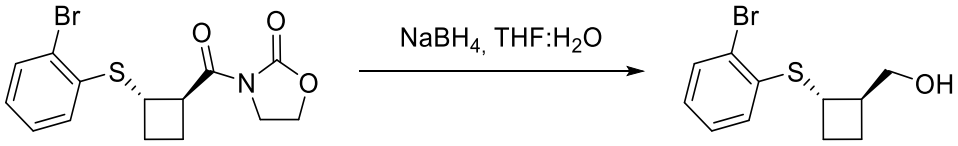
The enantiomeric ratio was determined to be 97:3 by SFC analysis: IA column, 1% MeCN in supercritical $CO_2$, flow rate 0.75 mL/min, λ = 214.4 nm. tR(major) = 7.1 min, tR(minor) = 8.3 min.

**(2-((2-Bromophenyl)thio)cyclobutyl)methanol (8)**




**3a** **7**, quant.

*Racemic:* Cyclobutane **3a** (37.7 mg, 100 µmol, 1.00 equiv.) was diluted in dry THF (2.50 mL) and the mixture was cooled to 0 °C. Diisobutylaluminium hydride (56.9 mg, 400 µL, 400 µmol, 1 M in toluene, 4.00 equiv.) was added dropwise and the reaction mixture was stirred at room temperature for 10 minutes. The reaction was diluted with ether and cooled to 0°C, 400 µL of water were added, followed by 400 µL of 15 % sodium hydroxide and 900 µL of water. The mixture was warmed to room temperature and stirred for 15 min. $MgSO_4$ was added and the mixture stirred for an additional 15 min. The mixture was filtered and concentrated under reduced pressure. The crude product was purified by prep-TLC using PE/EtOAc 60:40 to afford **7** as an oil (27.2 mg, 99.6 µmol, quant.).




**3a**
97:3 er

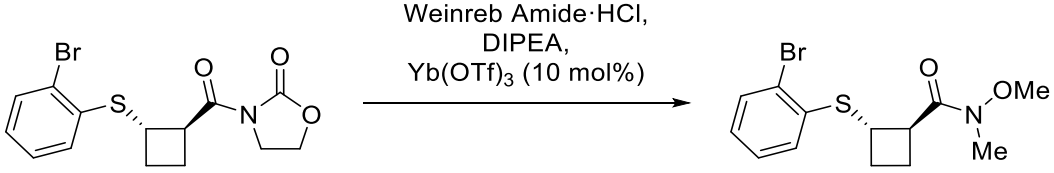
**7**, 92%
97:3 er

*Enantioenriched:* To a solution of cyclobutane **4a** (35.6 mg, 100 µmol, 1.00 equiv.) in THF (0.8 mL) and $H_2O$ (0.2 mL) was added $NaBH_4$ (15.1 mg, 400 µmol, 4.00 equiv.). The reaction was stirred at rt for 2 h. The reaction mixture was quenched with sat. $NH_4Cl$ (10 mL), extracted with EtOAc (3 x 10 mL) dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by prep-TLC using PE/EtOAc 60:40 to afford **7** as an oil (25.1 mg, 91.9 µmol, 92% yield).

Rf(PE/EtOAc 6:4): 0.63.
$[\alpha]_D^{23}$ = 129.3 (c = 0.0700, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.53 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.26 – 7.23 (m, 2H, Ar*H*), 7.01 (dp, *J* = 8.4, 4.1 Hz, 1H, Ar*H*), 3.76 (q, *J* = 8.0 Hz, 1H, SC*H*), 3.69 (t, *J* = 4.5 Hz, 2H, C*H*$_2$OH), 2.60 (ddt, *J* = 13.7, 8.4, 4.2 Hz, 1H, SCHC*H*), 2.55 – 2.43 (m, 1H, SCHC*H*$_2$), 2.14 (qd, *J* = 9.0, 3.1 Hz, 1H, SCHCH$_2$C*H*$_2$), 2.02 (dq, *J* = 11.2, 8.9 Hz, 1H, SCHC*H*$_2$), 1.92 – 1.79 (m, 1H, SCHCH$_2$C*H*$_2$), 1.41 (t, *J* = 5.0 Hz, 1H, O*H*).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 138.3, 133.1, 128.6, 127.9, 126.7, 123.3, 64.7, 45.0, 41.0, 28.1, 21.1.
IR ($\nu_{max}$, $cm^{-1}$) 3372 (m), 2979 (m), 2938 (m), 2863 (m), 1574 (w), 1448 (s), 1429 (m), 1253 (m), 1112 (m), 1067 (m), 1022 (s).
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{13}BrNaOS^+$ 294.9763; Found 294.9763.

The enantiomeric ratio was determined to be 97:3 by SFC analysis: IA column, 6% MeOH in supercritical $CO_2$, flow rate 0.50 mL/min, λ = 270.4 nm. tR(major) = 35.6 min, tR(minor) = 41.3 min.

**Enantioenriched 2-((2-Bromophenyl)thio)-N-methoxy-N-methylcyclobutane-1-carboxamide (3z)**




**4a**,
er 97:3

**3z**, 62%
er 97:3

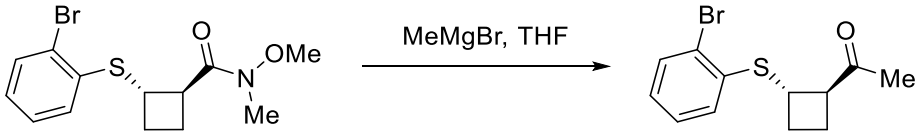
*Racemic:* The racemic compound was described above as **3z** (page 25).

*Enantioenriched:* Cyclobutane **4a** (17.8 mg, 50.0 µmol, 1.00 equiv.), methoxy(methyl)amine;hydrochloride (14.6 mg, 150 µmol, 3.00 equiv.), and $Yb(OTf)_3$ (3.10 mg, 5.00 µmol, 0.100 equiv.) were diluted in dry MeCN (0.5 mL) and DIPEA (19.4 mg, 26.1 µL, 150 µmol, 3.00 equiv.) was added. The reaction mixture was stirred at 90 °C for 48 h. The mixture was then concentrated under reduced pressure. The crude mixture was purified by prep-TLC using PE/EtOAc 80:20 to afford **3z** as an oil (10.2 mg, 30.9 µmol, 62% yield).

$[\alpha]_D^{23}$ = 62.7 (c = 0.0110, $CHCl_3$).

The enantiomeric ratio was determined to be 97:3 by SFC analysis: IC column, 10% MeOH in supercritical $CO_2$, flow rate 2.0 mL/min, λ = 214.4 nm. tR(major) = 2.3 min, tR(minor) = 2.1 min.

**1-(2-((2-Bromophenyl)thio)cyclobutyl)ethan-1-one (9)**




**3z**
97:3 er

**10**, 91%
97:3 er

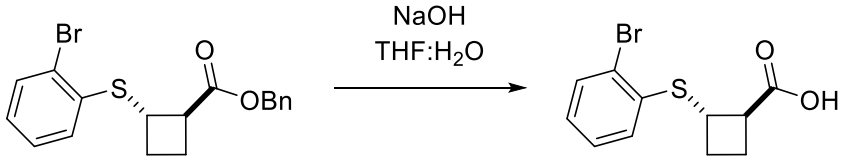
*Racemic:* Cyclobutane **3z** (66.0 mg, 200 µmol, 1.00 equiv.) was diluted in dry THF (2.0 mL) and MeMgBr (28.6 mg, 80.0 µL, 240 µmol, 3.00M in $Et_2O$, 1.20 equiv.) was added at -78 °C. The reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was quenched with sat. $NH_4Cl$ (10 mL), extracted with EtOAc (3 x 10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford **10** as an oil (52.4 mg, 184 µmol, 92% yield) which was pure enough without further purification.

*Enantioenriched:* the same procedure as described above was implemented on enantioenriched **3z** (7.90 mg, 23.9 µmol, 1.00 equiv.) to afford **10** as an oil (6.20 mg, 21.7 µmol, 91% yield).

$[\alpha]_D^{23}$ = 60.7 (c = 0.0567, $CHCl_3$).
$^1$H NMR (400 MHz, chloroform-*d*) δ 7.62 – 7.46 (m, 1H, Ar*H*), 7.32 – 7.16 (m, 2H, Ar*H*), 7.03 (ddd, *J* = 8.0, 6.6, 2.3 Hz, 1H, Ar*H*), 4.12 (q, *J* = 8.0 Hz, 1H, SC*H*), 3.32 (q, *J* = 8.3 Hz, 1H, C*H*C(O)), 2.50 – 2.39 (m, 1H, SCHC$H_2$), 2.39 – 2.23 (m, 1H, C$H_2$CHC(O)), 2.21 – 1.96 (m, 5H, C$H_3$ + SCHC$H_2$ + C$H_2$CHC(O)).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 207.5, 137.4, 133.2, 129.1, 128.0, 127.1, 123.4, 53.0, 40.3, 28.3, 26.6, 21.8.
IR ($\nu_{max}$, $cm^{-1}$) 3059 (w), 2947 (m), 2862 (w), 2098 (w), 1744 (m), 1710 (s), 1476 (m), 1448 (s), 1430 (m), 1361 (m), 1252 (m), 1188 (m), 1022 (m), 850 (m).
HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}BrOS^+$ 284.9943; Found 284.9948.

The enantiomeric ratio was determined to be 97:3 by chiral HPLC analysis: IA column, 99:1 hexane/isopropanol, flow rate 1.0 mL/min, λ = 214.4 nm. tR(major) = 9.6 min, tR(minor) = 10.7 min.

**2-[(2-Bromophenyl)thio]cyclobutanecarboxylic acid (10)**




**3a**

**6**, quant.

To a solution of cyclobutane **3a** (113 mg, 300 µmol, 1.00 equiv.) in THF (1.20 mL) and water (1.20 mL) was added sodium hydroxide (48.0 mg, 1.20 mmol, 4.00 equiv.). The reaction was stirred at rt for 4 h. The mixture was washed with EtOAc (3 x 20 mL). The pH value of the

aqueous layer was adjusted to 1 using HCl (1 M). The mixture was extracted with EtOAc (3 x 20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford **6** (86.0 mg, 299 µmol, quant.) as an amorphous solid that was pure enough without further purification.

$^{1}$H NMR (400 MHz, chloroform-*d*) δ 7.55 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.30 – 7.20 (m, 2H, Ar*H*), 7.09 – 6.95 (m, 1H, Ar*H*), 4.18 (q, *J* = 8.2 Hz, 1H, SC*H*), 3.22 (q, *J* = 8.7 Hz, 1H, C*H*C(O)), 2.52 (ddt, *J* = 11.8, 8.7, 4.4 Hz, 1H, SCHC$H_2$), 2.40 (qd, *J* = 9.4, 3.5 Hz, 1H, C$H_2$CHC(O)), 2.32 – 2.18 (m, 1H, C$H_2$CHC(O)), 2.09 (dq, *J* = 11.3, 9.1 Hz, 1H, SCHC$H_2$).
$^{13}$C NMR (101 MHz, chloroform-*d*) δ 178.6, 136.9, 133.2, 129.6, 128.0, 127.4, 124.0, 45.4, 41.5, 27.2, 22.6.
IR ($v_{max}$, $cm^{-1}$) 3059 (m), 2953 (m), 1704 (s), 1559 (w), 1451 (s), 1422 (m), 1260 (m), 1224 (m), 1019 (m), 937 (w), 910 (w), 744 (s).
HRMS (ESI/QTOF) m/z: $[M + H_{-1}]^-$ Calcd for $C_{11}H_{10}BrO_2S^-$ 284.9590; Found 284.9586.

## 1.8. Proposed model for stereoinduction

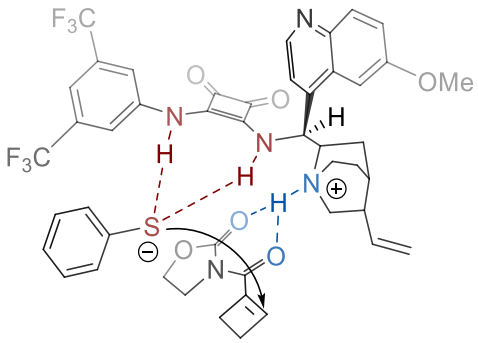



**Figure S1:** Proposed stereoinduction model applying Houk's Brønsted acid-hydrogen bonding model.[7]

[7] a) M. N. Grayson, K. N. Houk, *J. Am. Chem. Soc.* **2016**, *138*, 1170–1173; b) J. Guo, M. W. Wong, *J. Org. Chem.* **2017**, *82*, 4362–4368.

# 2. References


[1] E. G. L. Robert, V. Pirenne, M. D. Wodrich, J. Waser, *Angew. Chem. Int. Ed.* **2023**, *62*, e202302420.

[2] A. A. Homon, O. V. Hryshchuk, S. Trofymchuk, O. Michurin, Y. Kuchkovska, D. S. Radchenko, O. O. Grygorenko, *Eur. J. Org. Chem.* **2018**, *2018*, 5596–5604.

[3] E. G. L. Robert, J. Waser, *Chem. Eur. J.* **2025**, *31*, e202403986.

[4] H. Xu, W. Zhang, D. Shu, J. B. Werness, W. Tang, *Angew. Chem. Int. Ed.* **2008**, *47*, 8933–8936.

[5] J. M. Robinson, S. F. Tlais, J. Fong, R. L. Danheiser, *Tetrahedron* **2011**, *67*, 9890–9898.

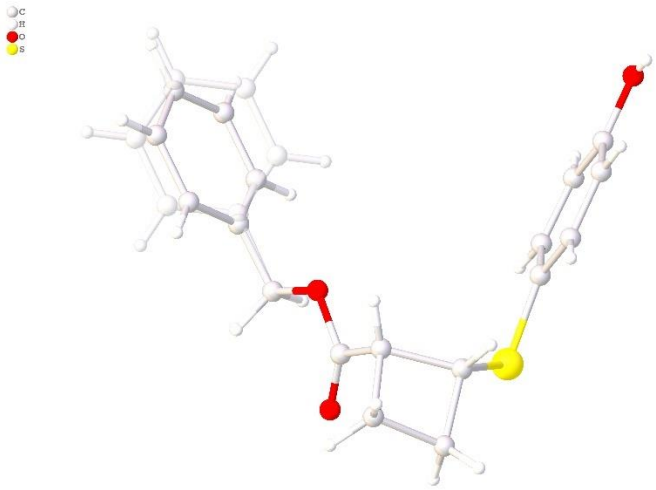
[6] L. Ghisu, N. Melis, L. Serusi, A. Luridiana, F. Soddu, F. Secci, P. Caboni, R. Guillot, D. J. Aitken, A. Frongia, *Org. Biomol. Chem.* **2019**, *17*, 6143–6147.

[7] a) M. N. Grayson, K. N. Houk, *J. Am. Chem. Soc.* **2016**, *138*, 1170–1173; b) J. Guo, M. W. Wong, *J. Org. Chem.* **2017**, *82*, 4362–4368.

# 3. X-rays crystallographic data

## 3.1 Compound **3'l** (CCDC number 2383043)

The crystal suitable for X-ray measurement for compound **3'l** was obtained by evaporation of dichloromethane.



**Experimental.** Single clear pale colourless prism-shaped crystals of **6x** were used as supplied. A suitable crystal with dimensions 0.22 × 0.04 × 0.04 $mm^3$ was selected and mounted on a XtaLAB Synergy R, DW system, HyPix-Arc 150 diffractometer. The crystal was kept at a steady *T* = 139.98(10) K during data collection. The structure was solved with the ShelXT (Sheldrick, 2015) solution program using dual methods and by using Olex2 1.5 (Dolomanov et al., 2009) as the graphical interface. The model was refined with ShelXL 2019/3 (Sheldrick, 2015) using full matrix least squares minimisation on $F^2$.

| **Compound** | **3'l** |
|---|---|
| Formula | $C_{18}H_{18}O_3S$ |
| $D_{calc.}$/ g cm$^{-3}$ | 1.317 |
| $\mu$/mm$^{-1}$ | 1.896 |
| Formula Weight | 314.38 |
| Colour | clear pale colourless |
| Shape | prism |
| Size/mm$^3$ | 0.22×0.04×0.04 |
| $T$/K | 139.98(10) |
| Crystal System | monoclinic |
| Space Group | $C2/c$ |
| $a$/Å | 19.0857(3) |
| $b$/Å | 5.32972(8) |
| $c$/Å | 31.1946(4) |
| $\alpha$/° | 90 |
| $\beta$/° | 92.5193(14) |
| $\gamma$/° | 90 |
| V/Å$^3$ | 3170.09(8) |
| $Z$ | 8 |
| $Z'$ | 1 |
| Wavelength/Å | 1.54184 |
| Radiation type | Cu K$_\alpha$ |
| $\Theta_{min}$/° | 2.836 |
| $\Theta_{max}$/° | 75.774 |
| Measured Refl's. | 31855 |
| Indep't Refl's | 3263 |
| Refl's I≥2 $\sigma$(I) | 2815 |
| $R_{int}$ | 0.0363 |
| Parameters | 274 |
| Restraints | 0 |
| Largest Peak | 0.303 |
| Deepest Hole | -0.291 |
| GooF | 1.040 |
| $wR_2$ (all data) | 0.0997 |
| $wR_2$ | 0.0948 |
| $R_1$ (all data) | 0.0438 |
| $R_1$ | 0.0365 |

**Table 1**: Fractional Atomic Coordinates (×10$^4$) and Equivalent Isotropic Displacement Parameters (Å$^2$×10$^3$) for **3'l**. $U_{eq}$ is defined as 1/3 of the trace of the orthogonalised $U_{ij}$.

| **Atom** | **x** | **y** | **z** | $U_{eq}$ |
|---|---|---|---|---|
| S1 | 2099.9(2) | 6857.5(7) | 3004.5(2) | 32.07(12) |
| O1 | 4937.3(6) | 5359(2) | 3807.5(4) | 38.7(3) |
| O2 | 527.5(6) | 6121(2) | 3479.3(4) | 39.2(3) |
| O3 | 1215.1(6) | 4102(2) | 3969.5(3) | 35.5(3) |
| C1 | 1674.4(8) | 3880(3) | 2914.1(5) | 29.3(3) |
| C2 | 1020.1(8) | 3983(3) | 2604.3(5) | 32.2(3) |
| C3 | 678.4(8) | 2013(3) | 2890.1(5) | 32.7(3) |
| C4 | 1218.5(8) | 2622(3) | 3260.7(5) | 30.0(3) |
| C5 | 2926.4(7) | 6150(3) | 3257.6(5) | 28.4(3) |
| C6 | 3345.5(8) | 4157(3) | 3139.4(5) | 32.7(3) |
| C7 | 4012.9(8) | 3850(3) | 3321.2(5) | 31.9(3) |
| C8 | 4279.0(8) | 5561(3) | 3620.0(5) | 31.3(3) |
| C9 | 3869.2(9) | 7567(3) | 3737.8(6) | 42.9(4) |
| C10 | 3194.6(9) | 7830(3) | 3562.1(6) | 39.5(4) |
| C11 | 945.2(7) | 4470(3) | 3574.0(5) | 30.7(3) |
| C12 | 937.0(10) | 5709(4) | 4302.5(5) | 45.3(4) |

| Atom | x | y | z | $U_{eq}$ |
|---|---|---|---|---|
| C13 | 1139.4(15) | 4712(6) | 4709.1(7) | 33.7(15) |
| C14 | 1604.2(18) | 6034(6) | 4980.1(7) | 43.1(10) |
| C15 | 1815.5(18) | 5037(7) | 5376.7(7) | 47.7(11) |
| C16 | 1562.1(18) | 2718(6) | 5502.3(8) | 51.6(18) |
| C17 | 1097(2) | 1396(5) | 5231.3(11) | 47.2(12) |
| C18 | 885.9(18) | 2393(6) | 4834.7(11) | 44.4(10) |
| C19 | 1197.3(14) | 4485(6) | 4743.3(7) | 41.6(19) |
| C24 | 728.9(11) | 3065(8) | 4970.9(11) | 41.2(10) |
| C23 | 946.3(14) | 1962(7) | 5358.0(11) | 42.7(11) |
| C22 | 1632.2(16) | 2278(6) | 5517.5(8) | 39.0(13) |
| C21 | 2100.6(14) | 3698(7) | 5289.9(9) | 43.4(10) |
| C20 | 1883.1(14) | 4802(7) | 4902.8(8) | 42.1(10) |

**Table 2**: Anisotropic Displacement Parameters ($\times 10^4$) for **3'l**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + ... + 2hka^* \times b^* \times U_{12}]$

| Atom | $U_{11}$ | $U_{22}$ | $U_{33}$ | $U_{23}$ | $U_{13}$ | $U_{12}$ |
|---|---|---|---|---|---|---|
| S1 | 28.1(2) | 25.4(2) | 42.6(2) | 1.40(15) | -0.05(14) | 3.13(13) |
| O1 | 29.4(6) | 35.2(6) | 50.9(7) | -4.0(5) | -3.2(5) | 4.0(5) |
| O2 | 40.0(6) | 37.6(6) | 40.2(6) | 2.0(5) | 5.0(5) | 13.8(5) |
| O3 | 36.1(6) | 38.6(6) | 31.8(5) | -4.7(5) | -0.2(4) | 7.5(5) |
| C1 | 26.9(7) | 27.0(7) | 34.1(8) | -1.1(6) | 3.5(6) | 2.3(6) |
| C2 | 32.4(8) | 32.9(8) | 31.4(8) | 0.0(6) | 1.3(6) | 0.5(6) |
| C3 | 30.7(8) | 31.6(8) | 35.8(8) | -0.1(6) | 1.2(6) | -1.2(6) |
| C4 | 30.0(7) | 28.1(7) | 32.0(7) | 2.2(6) | 1.5(6) | 3.4(6) |
| C5 | 26.5(7) | 24.6(7) | 34.2(7) | 2.1(6) | 4.2(6) | 1.1(5) |
| C6 | 34.8(8) | 30.2(8) | 33.1(8) | -4.5(6) | 1.0(6) | 4.5(6) |
| C7 | 32.6(8) | 28.8(7) | 34.4(8) | -1.8(6) | 2.4(6) | 7.4(6) |
| C8 | 27.1(7) | 27.9(7) | 39.0(8) | 2.1(6) | 1.6(6) | 0.5(6) |
| C9 | 34.6(9) | 30.8(8) | 62.7(11) | -15.8(8) | -5.2(8) | 2.4(7) |
| C10 | 33.1(8) | 28.2(8) | 56.8(10) | -10.5(7) | -0.7(7) | 5.0(6) |
| C11 | 27.2(7) | 30.5(7) | 34.6(8) | 2.1(6) | 2.2(6) | 1.7(6) |
| C12 | 51.8(10) | 45.1(10) | 39.3(9) | -9.2(8) | 5.0(7) | 12.3(8) |
| C13 | 32(3) | 35(3) | 34(3) | -7(2) | 5(2) | 4(2) |
| C14 | 51(2) | 46(2) | 33.3(17) | -6.9(15) | 7.1(15) | -3.8(19) |
| C15 | 54(2) | 57(3) | 32.2(18) | -8.9(17) | 1.0(15) | -7(2) |
| C16 | 72(4) | 55(3) | 28(3) | -1(2) | 7(3) | 9(3) |
| C17 | 54(3) | 46(2) | 43(3) | 0.8(19) | 12(2) | -2(2) |
| C18 | 45(2) | 44(2) | 45(3) | -7.9(18) | 3.4(18) | 0.2(18) |
| C19 | 52(4) | 46(4) | 27(3) | -4(3) | -1(3) | 16(3) |
| C24 | 37(2) | 48(2) | 39(2) | -5.4(18) | 1.8(16) | -0.1(17) |
| C23 | 49(2) | 44(2) | 36(2) | 0.6(18) | 6.8(18) | 0.9(19) |
| C22 | 45(3) | 38(2) | 34(3) | -1.3(19) | 2(2) | 3(2) |
| C21 | 46(2) | 43(2) | 40.5(19) | 0.0(16) | -6.7(16) | 3.6(18) |
| C20 | 45(2) | 42(2) | 39.9(19) | 2.6(16) | 3.7(15) | 1.7(17) |

**Table 3**: Bond Lengths in Å for **3'l**.

| Atom | Atom | Length/Å |
|---|---|---|
| S1 | C1 | 1.7992(15) |
| S1 | C5 | 1.7730(15) |
| O1 | C8 | 1.3667(18) |
| O2 | C11 | 1.2149(18) |
| O3 | C11 | 1.3304(18) |
| O3 | C12 | 1.4640(19) |
| C1 | C2 | 1.546(2) |
| C1 | C4 | 1.568(2) |
| C2 | C3 | 1.541(2) |
| C3 | C4 | 1.549(2) |
| C4 | C11 | 1.497(2) |
| C5 | C6 | 1.389(2) |
| C5 | C10 | 1.387(2) |
| C6 | C7 | 1.381(2) |

| Atom | Atom | Length/Å |
|---|---|---|
| C7 | C8 | 1.384(2) |
| C8 | C9 | 1.384(2) |
| C9 | C10 | 1.384(2) |
| C12 | C13 | 1.413(3) |
| C12 | C19 | 1.582(3) |
| C13 | C14 | 1.3900 |
| C13 | C18 | 1.3900 |
| C14 | C15 | 1.3900 |
| C15 | C16 | 1.3900 |
| C16 | C17 | 1.3900 |
| C17 | C18 | 1.3900 |
| C19 | C24 | 1.3900 |
| C19 | C20 | 1.3900 |
| C24 | C23 | 1.3900 |
| C23 | C22 | 1.3900 |
| C22 | C21 | 1.3900 |
| C21 | C20 | 1.3900 |

**Table 4**: Bond Angles in ° for **3'l**.

| Atom | Atom | Atom | Angle/° |
|---|---|---|---|
| C5 | S1 | C1 | 105.59(7) |
| C11 | O3 | C12 | 115.72(12) |
| C2 | C1 | S1 | 114.41(11) |
| C2 | C1 | C4 | 89.35(11) |
| C4 | C1 | S1 | 121.97(10) |
| C3 | C2 | C1 | 87.99(11) |
| C2 | C3 | C4 | 90.24(11) |
| C3 | C4 | C1 | 86.93(11) |
| C11 | C4 | C1 | 112.88(12) |
| C11 | C4 | C3 | 112.68(12) |
| C6 | C5 | S1 | 123.76(12) |
| C10 | C5 | S1 | 117.51(11) |
| C10 | C5 | C6 | 118.43(14) |
| C7 | C6 | C5 | 120.86(14) |
| C6 | C7 | C8 | 120.19(14) |
| O1 | C8 | C7 | 122.64(14) |
| O1 | C8 | C9 | 117.84(14) |
| C9 | C8 | C7 | 119.52(14) |
| C8 | C9 | C10 | 120.01(15) |
| C9 | C10 | C5 | 120.97(15) |
| O2 | C11 | O3 | 123.76(14) |
| O2 | C11 | C4 | 124.13(13) |
| O3 | C11 | C4 | 112.11(12) |
| O3 | C12 | C19 | 105.41(16) |
| C13 | C12 | O3 | 108.88(17) |
| C14 | C13 | C12 | 119.8(2) |
| C14 | C13 | C18 | 120.0 |
| C18 | C13 | C12 | 120.2(2) |
| C13 | C14 | C15 | 120.0 |
| C14 | C15 | C16 | 120.0 |
| C15 | C16 | C17 | 120.0 |
| C18 | C17 | C16 | 120.0 |
| C17 | C18 | C13 | 120.0 |
| C24 | C19 | C12 | 118.95(19) |
| C24 | C19 | C20 | 120.0 |
| C20 | C19 | C12 | 121.05(19) |
| C19 | C24 | C23 | 120.0 |
| C22 | C23 | C24 | 120.0 |
| C21 | C22 | C23 | 120.0 |
| C22 | C21 | C20 | 120.0 |
| C21 | C20 | C19 | 120.0 |

**Table 5**: Torsion Angles in ° for **3'l**.

| Atom | Atom | Atom | Atom | Angle/° |
|---|---|---|---|---|
| S1 | C1 | C2 | C3 | -142.77(11) |
| S1 | C1 | C4 | C3 | 136.19(12) |
| S1 | C1 | C4 | C11 | 22.83(17) |
| S1 | C5 | C6 | C7 | 173.69(12) |
| S1 | C5 | C10 | C9 | -172.51(14) |
| O1 | C8 | C9 | C10 | -178.94(16) |
| O3 | C12 | C13 | C14 | 113.4(2) |
| O3 | C12 | C13 | C18 | -65.3(3) |
| O3 | C12 | C19 | C24 | -102.1(2) |
| O3 | C12 | C19 | C20 | 77.6(3) |
| C1 | S1 | C5 | C6 | 41.02(15) |
| C1 | S1 | C5 | C10 | -145.38(13) |
| C1 | C2 | C3 | C4 | 17.80(11) |
| C1 | C4 | C11 | O2 | 65.42(19) |
| C1 | C4 | C11 | O3 | -114.37(14) |
| C2 | C1 | C4 | C3 | 17.50(11) |
| C2 | C1 | C4 | C11 | -95.86(13) |
| C2 | C3 | C4 | C1 | -17.56(11) |
| C2 | C3 | C4 | C11 | 95.99(14) |
| C3 | C4 | C11 | O2 | -31.1(2) |

| Atom | Atom | Atom | Atom | Angle/° |
|---|---|---|---|---|
| C3 | C4 | C11 | O3 | 149.13(13) |
| C4 | C1 | C2 | C3 | -17.58(11) |
| C5 | S1 | C1 | C2 | -166.56(10) |
| C5 | S1 | C1 | C4 | 87.87(12) |
| C5 | C6 | C7 | C8 | -1.2(2) |
| C6 | C5 | C10 | C9 | 1.4(3) |
| C6 | C7 | C8 | O1 | -179.48(14) |
| C6 | C7 | C8 | C9 | 0.6(2) |
| C7 | C8 | C9 | C10 | 1.0(3) |
| C8 | C9 | C10 | C5 | -2.0(3) |
| C10 | C5 | C6 | C7 | 0.1(2) |
| C11 | O3 | C12 | C13 | 165.89(18) |
| C11 | O3 | C12 | C19 | 166.77(16) |
| C12 | O3 | C11 | O2 | 4.6(2) |
| C12 | O3 | C11 | C4 | -175.65(13) |
| C12 | C13 | C14 | C15 | -178.7(3) |
| C12 | C13 | C18 | C17 | 178.7(3) |
| C12 | C19 | C24 | C23 | 179.7(3) |
| C12 | C19 | C20 | C21 | -179.7(3) |
| C13 | C14 | C15 | C16 | 0.0 |
| C14 | C13 | C18 | C17 | 0.0 |
| C14 | C15 | C16 | C17 | 0.0 |
| C15 | C16 | C17 | C18 | 0.0 |
| C16 | C17 | C18 | C13 | 0.0 |
| C18 | C13 | C14 | C15 | 0.0 |
| C19 | C24 | C23 | C22 | 0.0 |
| C24 | C19 | C20 | C21 | 0.0 |
| C24 | C23 | C22 | C21 | 0.0 |
| C23 | C22 | C21 | C20 | 0.0 |
| C22 | C21 | C20 | C19 | 0.0 |
| C20 | C19 | C24 | C23 | 0.0 |

**Table 6**: Hydrogen Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **3'l**. $U_{eq}$ is defined as 1/3 of the trace of the orthogonalised $U_{ij}$.

| Atom | x | y | z | $U_{eq}$ |
|---|---|---|---|---|
| H1 | 5101(13) | 4080(50) | 3720(8) | 74(8) |
| H1A | 2012(9) | 2720(30) | 2807(5) | 34(4) |
| H2A | 755(10) | 5630(40) | 2625(6) | 49(5) |
| H2B | 1099(9) | 3590(30) | 2302(6) | 36(5) |
| H3A | 185(10) | 2290(30) | 2956(5) | 36(5) |
| H3B | 741(9) | 300(40) | 2788(5) | 38(5) |
| H4 | 1464(9) | 1240(30) | 3414(5) | 33(4) |
| H6 | 3178(10) | 2980(40) | 2929(6) | 43(5) |
| H7 | 4289(10) | 2540(40) | 3249(6) | 45(5) |
| H9 | 4055(11) | 8730(40) | 3944(7) | 58(6) |
| H10 | 2911(11) | 9190(40) | 3656(6) | 54(6) |
| H12A | 1122.74 | 7433.43 | 4275.54 | 54 |
| H12B | 419.12 | 5782.09 | 4269.47 | 54 |
| H12C | 418.24 | 5757.4 | 4277.95 | 54 |
| H12D | 1118.48 | 7441.05 | 4278.45 | 54 |
| H14 | 1777.46 | 7619.17 | 4894.22 | 52 |
| H15 | 2133.23 | 5940.34 | 5561.91 | 57 |
| H16 | 1706.49 | 2036.19 | 5773.4 | 62 |
| H17 | 923.97 | -189.14 | 5317.21 | 57 |
| H18 | 568.19 | 1489.65 | 4649.51 | 53 |
| H24 | 260.15 | 2848.7 | 4861.96 | 49 |
| H23 | 626.19 | 990.96 | 5513.59 | 51 |
| H22 | 1780.77 | 1524.01 | 5782.04 | 47 |

| Atom | x | y | z | $U_{eq}$ |
|---|---|---|---|---|
| H21 | 2569.32 | 3914.78 | 5398.86 | 52 |
| H20 | 2203.29 | 5772.53 | 4747.23 | 51 |

**Table 7**: Hydrogen Bond information for **3'l**.

| D | H | A | d(D-H)/Å | d(H-A)/Å | d(D-A)/Å | D-H-A/deg |
|---|---|---|---|---|---|---|
| O1 | H1 | O2[1] | 0.80(3) | 1.94(3) | 2.7424(17) | 176(3) |

––––

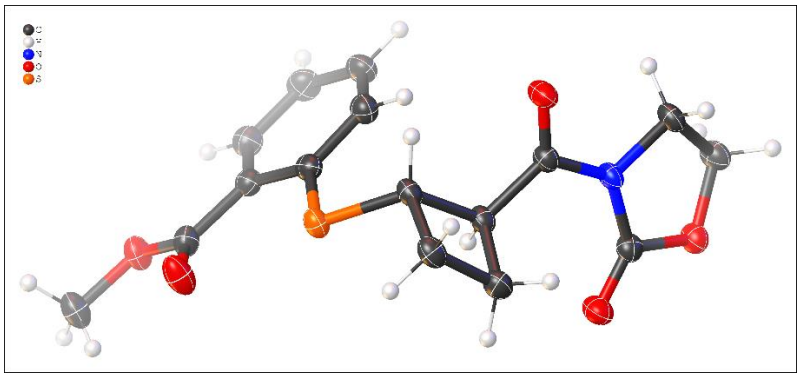
[1]1/2+x,-1/2+y,+z

**Table 8**: Atomic Occupancies for all atoms that are not fully occupied in **3'l**.

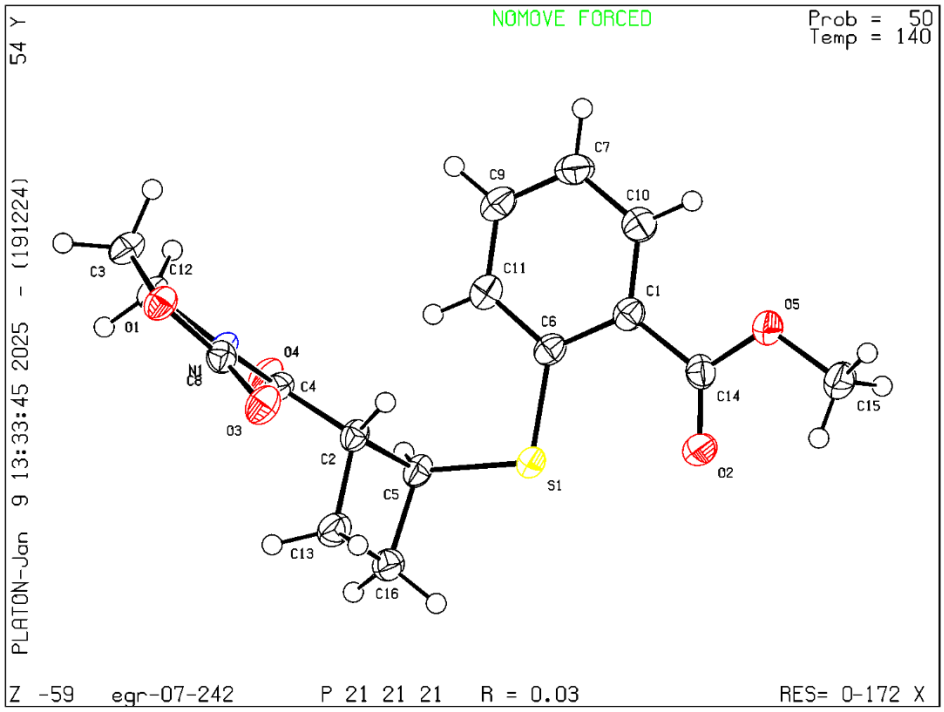
| Atom | Occupancy | Atom | Occupancy | Atom | Occupancy |
|---|---|---|---|---|---|
| H12A | 0.503(5) | C16 | 0.503(5) | C23 | 0.497(5) |
| H12B | 0.503(5) | H16 | 0.503(5) | H23 | 0.497(5) |
| H12C | 0.497(5) | C17 | 0.503(5) | C22 | 0.497(5) |
| H12D | 0.497(5) | H17 | 0.503(5) | H22 | 0.497(5) |
| C13 | 0.503(5) | C18 | 0.503(5) | C21 | 0.497(5) |
| C14 | 0.503(5) | H18 | 0.503(5) | H21 | 0.497(5) |
| H14 | 0.503(5) | C19 | 0.497(5) | C20 | 0.497(5) |
| C15 | 0.503(5) | C24 | 0.497(5) | H20 | 0.497(5) |
| H15 | 0.503(5) | H24 | 0.497(5) | | |

## 3.2 Compound **4b** (CCDC number 2415842)

The crystal suitable for X-ray measurement for compound **4b** was obtained by evaporation of dichloromethane.



**Experimental.** Single colourless plate-shaped crystals of **4b** were used as supplied. A suitable crystal with dimensions 0.09 × 0.04 × 0.02 mm$^3$ was selected and mounted on an XtaLAB Synergy R, DW system, HyPix-Arc 150 diffractometer. The crystal was kept at a steady $T$ = 140.00(10) K during data collection. The structure was solved with the ShelXT 2018/2 (Sheldrick, 2015) solution program using dual methods and by using Olex2 1.5 (Dolomanov et al., 2009) as the graphical interface. The model was refined with ShelXL 2019/3 (Sheldrick, 2015) using full matrix least squares minimisation on $F^2$.




*Model has Chirality at **C2** (Sohncke SpGr)* ***R** Verify*
*Model has Chirality at **C5** (Sohncke SpGr)* ***S** Verify*

**Table 9**: Fractional Atomic Coordinates (×10$^4$) and Equivalent Isotropic Displacement Parameters (Å$^2$×10$^3$) for **4b**. $U_{eq}$ is defined as 1/3 of the trace of the orthogonalised $U_{ij}$.

| Atom | x | y | z | $U_{eq}$ |
|---|---|---|---|---|
| S1 | 1509.4(15) | 8641.2(8) | 6260.3(2) | 25.50(18) |

| Atom | x | y | z | $U_{eq}$ |
|---|---|---|---|---|
| O1 | -1391(5) | 4158(2) | 6045.1(6) | 29.7(5) |
| O2 | 4880(4) | 4750(2) | 5216.4(7) | 30.8(5) |
| O3 | 5220(4) | 2351(2) | 5293.2(6) | 26.6(5) |
| O4 | 4509(5) | 10824(2) | 6582.0(7) | 37.5(6) |
| O5 | 8013(5) | 10560(2) | 6999.7(7) | 30.3(5) |
| N1 | 2058(5) | 3469(3) | 5653.9(7) | 21.8(5) |
| C1 | -340(6) | 7185(3) | 6027.9(9) | 23.8(6) |
| C2 | 1357(6) | 6078(3) | 5784.2(9) | 22.7(6) |
| C3 | 406(7) | 6788(3) | 5379.0(9) | 29.9(7) |
| C4 | -1524(6) | 7762(3) | 5617.8(9) | 27.6(6) |
| C5 | 511(6) | 4529(3) | 5839.0(9) | 22.0(6) |
| C6 | 4126(6) | 3656(3) | 5376.7(8) | 23.6(6) |
| C7 | 4055(6) | 1256(3) | 5558.8(9) | 28.2(6) |
| C8 | 1512(6) | 1936(3) | 5722.3(10) | 25.0(6) |
| C9 | 3366(6) | 7757(3) | 6647.0(8) | 24.1(6) |
| C10 | 5401(6) | 8494(3) | 6864.3(8) | 25.0(6) |
| C11 | 6946(7) | 7736(4) | 7146.6(9) | 29.2(7) |
| C12 | 6512(7) | 6283(4) | 7223.8(9) | 33.3(7) |
| C13 | 4485(7) | 5573(3) | 7019.9(10) | 31.4(7) |
| C14 | 2938(6) | 6290(4) | 6737.1(9) | 28.4(7) |
| C15 | 5877(6) | 10064(3) | 6795.3(9) | 27.2(7) |
| C16 | 8589(8) | 12087(3) | 6944.5(11) | 34.9(7) |

**Table 10**: Anisotropic Displacement Parameters ($\times 10^4$) for **4b**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + \ldots + 2hka^* \times b^* \times U_{12}]$

| Atom | $U_{11}$ | $U_{22}$ | $U_{33}$ | $U_{23}$ | $U_{13}$ | $U_{12}$ |
|---|---|---|---|---|---|---|
| S1 | 28.2(4) | 18.3(3) | 29.9(4) | -0.6(3) | -2.9(3) | -0.5(3) |
| O1 | 29.0(11) | 20.8(10) | 39.2(11) | 1.2(9) | 10.1(11) | -1.1(10) |
| O2 | 28.9(12) | 24.5(12) | 39.1(12) | 0.8(9) | 7.7(10) | -2.8(9) |
| O3 | 23.4(11) | 22.6(11) | 34.0(11) | -1.7(9) | 3.6(9) | 4.1(9) |
| O4 | 38.4(13) | 23.9(11) | 50.1(14) | 3.1(10) | -16.3(11) | -1.0(10) |
| O5 | 31.7(12) | 23.8(11) | 35.5(11) | -2.2(9) | -6.4(10) | -2.1(10) |
| N1 | 18.9(12) | 15.2(12) | 31.1(12) | 0.6(10) | 3.0(9) | 1.6(10) |
| C1 | 21.3(14) | 17.5(14) | 32.4(15) | -0.9(12) | 1.8(12) | -1.2(12) |
| C2 | 19.1(13) | 18.7(14) | 30.3(14) | -1.5(11) | 1.5(12) | -1.2(12) |
| C3 | 35.8(17) | 23.6(15) | 30.1(16) | 2.8(12) | 1.0(14) | -0.9(14) |
| C4 | 23.8(15) | 23.0(15) | 36.0(16) | 1.0(12) | -4.6(13) | -1.9(14) |
| C5 | 21.0(14) | 18.6(14) | 26.4(14) | 1.1(11) | -0.6(12) | 2.2(12) |
| C6 | 19.7(14) | 23.8(14) | 27.4(14) | -2.3(13) | 0.0(11) | -0.9(13) |
| C7 | 25.3(15) | 21.4(14) | 38.0(16) | 3.6(13) | 3.2(12) | 3.4(13) |
| C8 | 22.4(14) | 16.1(13) | 36.5(15) | 1.4(11) | 1.4(13) | -0.3(13) |
| C9 | 25.5(15) | 21.5(14) | 25.4(14) | -0.1(11) | 4.6(12) | 3.3(13) |
| C10 | 26.6(15) | 24.0(15) | 24.4(14) | -1.6(12) | 3.9(12) | 1.7(13) |
| C11 | 26.8(17) | 30.5(16) | 30.2(16) | -1.2(13) | 1.0(13) | 2.0(14) |
| C12 | 38.5(18) | 31.1(16) | 30.5(15) | 6.3(14) | -2.6(15) | 6.6(18) |
| C13 | 38.2(18) | 22.5(16) | 33.4(17) | 4.2(13) | 4.2(14) | 1.7(14) |
| C14 | 30.6(17) | 23.7(14) | 30.8(15) | -1.0(13) | 2.3(12) | 0.4(14) |
| C15 | 28.6(17) | 26.1(16) | 26.7(15) | -5.3(12) | -1.2(12) | -0.7(13) |
| C16 | 36.2(18) | 23.2(15) | 45.4(18) | -1.5(14) | -6.0(17) | -3.7(16) |

**Table 11**: Bond Lengths in Å for **4b**.

| Atom | Atom | Length/Å |
|---|---|---|
| S1 | C1 | 1.801(3) |
| S1 | C9 | 1.769(3) |
| O1 | C5 | 1.217(4) |
| O2 | C6 | 1.199(4) |

| Atom | Atom | Length/Å |
|---|---|---|
| O3 | C6 | 1.351(4) |
| O3 | C7 | 1.455(4) |
| O4 | C15 | 1.204(4) |
| O5 | C15 | 1.343(4) |
| O5 | C16 | 1.450(4) |
| N1 | C5 | 1.387(4) |
| N1 | C6 | 1.388(4) |
| N1 | C8 | 1.459(4) |
| C1 | C2 | 1.550(4) |
| C1 | C4 | 1.559(4) |
| C2 | C3 | 1.552(4) |
| C2 | C5 | 1.503(4) |
| C3 | C4 | 1.534(4) |
| C7 | C8 | 1.518(4) |
| C9 | C10 | 1.417(4) |
| C9 | C14 | 1.403(4) |
| C10 | C11 | 1.393(4) |
| C10 | C15 | 1.486(4) |
| C11 | C12 | 1.382(5) |
| C12 | C13 | 1.381(5) |
| C13 | C14 | 1.375(4) |

**Table 12**: Bond Angles in ° for **4b**.

| Atom | Atom | Atom | Angle/° |
|---|---|---|---|
| C9 | S1 | C1 | 103.13(14) |
| C6 | O3 | C7 | 109.7(2) |
| C15 | O5 | C16 | 115.4(3) |
| C5 | N1 | C6 | 127.9(2) |
| C5 | N1 | C8 | 120.8(2) |
| C6 | N1 | C8 | 111.1(2) |
| C2 | C1 | S1 | 115.2(2) |
| C2 | C1 | C4 | 89.6(2) |
| C4 | C1 | S1 | 107.6(2) |
| C1 | C2 | C3 | 89.5(2) |
| C5 | C2 | C1 | 114.3(2) |
| C5 | C2 | C3 | 114.6(2) |
| C4 | C3 | C2 | 90.5(2) |
| C3 | C4 | C1 | 89.7(2) |
| O1 | C5 | N1 | 118.8(3) |
| O1 | C5 | C2 | 123.7(3) |
| N1 | C5 | C2 | 117.5(2) |
| O2 | C6 | O3 | 122.3(3) |
| O2 | C6 | N1 | 128.7(3) |
| O3 | C6 | N1 | 108.9(2) |
| O3 | C7 | C8 | 105.0(2) |
| N1 | C8 | C7 | 100.9(2) |
| C10 | C9 | S1 | 121.0(2) |
| C14 | C9 | S1 | 121.0(2) |
| C14 | C9 | C10 | 118.0(3) |
| C9 | C10 | C15 | 120.5(3) |
| C11 | C10 | C9 | 119.4(3) |
| C11 | C10 | C15 | 120.1(3) |
| C12 | C11 | C10 | 121.4(3) |
| C13 | C12 | C11 | 119.2(3) |
| C14 | C13 | C12 | 120.7(3) |
| C13 | C14 | C9 | 121.3(3) |
| O4 | C15 | O5 | 122.9(3) |
| O4 | C15 | C10 | 124.4(3) |
| O5 | C15 | C10 | 112.7(3) |

**Table 13**: Torsion Angles in ° for **4b**.

| Atom | Atom | Atom | Atom | Angle/° |
|---|---|---|---|---|
| S1 | C1 | C2 | C3 | -103.2(2) |
| S1 | C1 | C2 | C5 | 139.9(2) |
| S1 | C1 | C4 | C3 | 110.1(2) |
| S1 | C9 | C10 | C11 | -175.6(2) |
| S1 | C9 | C10 | C15 | 4.9(4) |
| S1 | C9 | C14 | C13 | 176.0(3) |
| O3 | C7 | C8 | N1 | -20.1(3) |
| C1 | S1 | C9 | C10 | 170.5(2) |
| C1 | S1 | C9 | C14 | -7.1(3) |
| C1 | C2 | C3 | C4 | -6.3(2) |
| C1 | C2 | C5 | O1 | 2.3(4) |
| C1 | C2 | C5 | N1 | -175.4(2) |
| C2 | C1 | C4 | C3 | -6.3(2) |
| C2 | C3 | C4 | C1 | 6.2(2) |
| C3 | C2 | C5 | O1 | -99.0(3) |
| C3 | C2 | C5 | N1 | 83.3(3) |
| C4 | C1 | C2 | C3 | 6.2(2) |
| C4 | C1 | C2 | C5 | -110.8(3) |
| C5 | N1 | C6 | O2 | -6.1(5) |
| C5 | N1 | C6 | O3 | 175.9(3) |
| C5 | N1 | C8 | C7 | -165.8(2) |

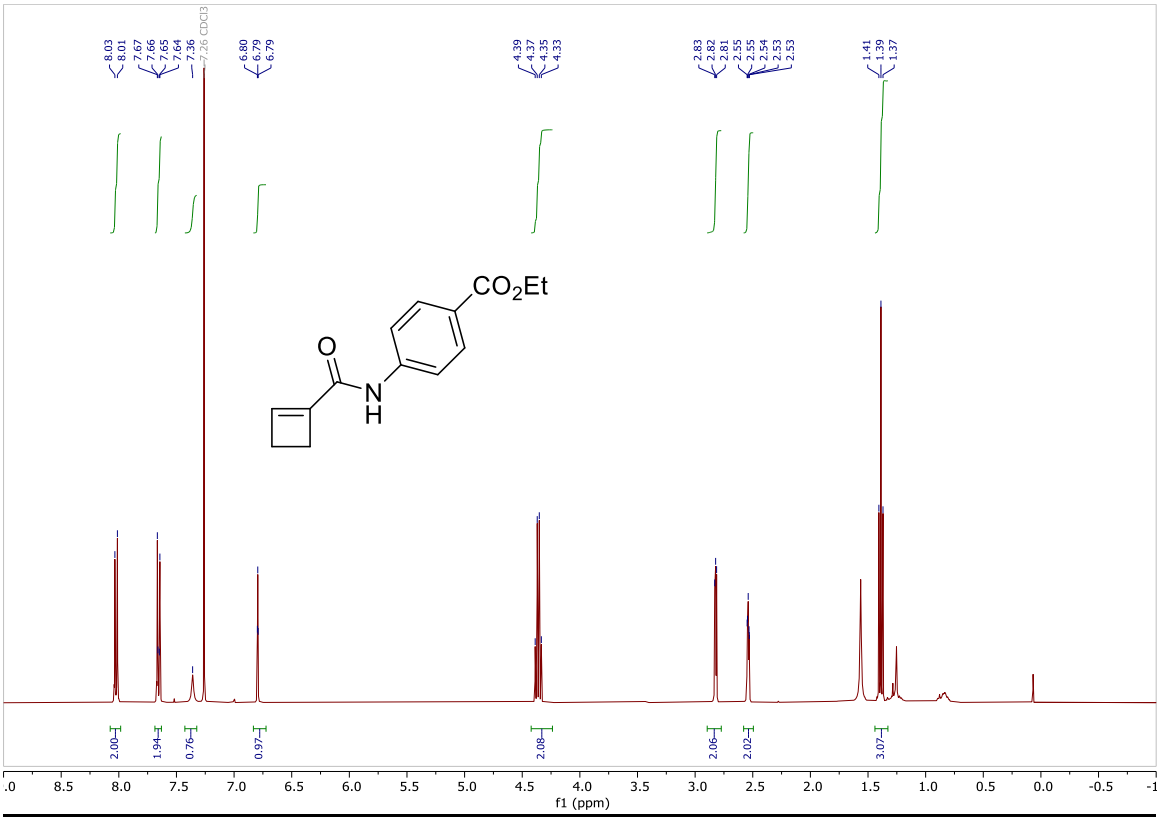
| Atom | Atom | Atom | Atom | Angle/° |
|---|---|---|---|---|
| C5 | C2 | C3 | C4 | 110.3(3) |
| C6 | O3 | C7 | C8 | 17.4(3) |
| C6 | N1 | C5 | O1 | 173.0(3) |
| C6 | N1 | C5 | C2 | -9.2(4) |
| C6 | N1 | C8 | C7 | 17.3(3) |
| C7 | O3 | C6 | O2 | 175.1(3) |
| C7 | O3 | C6 | N1 | -6.7(3) |
| C8 | N1 | C5 | O1 | -3.3(4) |
| C8 | N1 | C5 | C2 | 174.5(3) |
| C8 | N1 | C6 | O2 | 170.5(3) |
| C8 | N1 | C6 | O3 | -7.5(3) |
| C9 | S1 | C1 | C2 | -68.5(2) |
| C9 | S1 | C1 | C4 | -166.6(2) |
| C9 | C10 | C11 | C12 | -0.9(5) |
| C9 | C10 | C15 | O4 | 5.6(5) |
| C9 | C10 | C15 | O5 | -174.8(3) |
| C10 | C9 | C14 | C13 | -1.6(4) |
| C10 | C11 | C12 | C13 | -0.8(5) |
| C11 | C10 | C15 | O4 | -173.9(3) |
| C11 | C10 | C15 | O5 | 5.7(4) |
| C11 | C12 | C13 | C14 | 1.2(5) |
| C12 | C13 | C14 | C9 | 0.0(5) |
| C14 | C9 | C10 | C11 | 2.0(4) |
| C14 | C9 | C10 | C15 | -177.4(3) |
| C15 | C10 | C11 | C12 | 178.6(3) |
| C16 | O5 | C15 | O4 | -0.4(5) |
| C16 | O5 | C15 | C10 | 179.9(3) |

**Table 14**: Hydrogen Fractional Atomic Coordinates (×10$^4$) and Equivalent Isotropic Displacement Parameters (Å$^2$×10$^3$) for **4b**. $U_{eq}$ is defined as 1/3 of the trace of the orthogonalised $U_{ij}$.

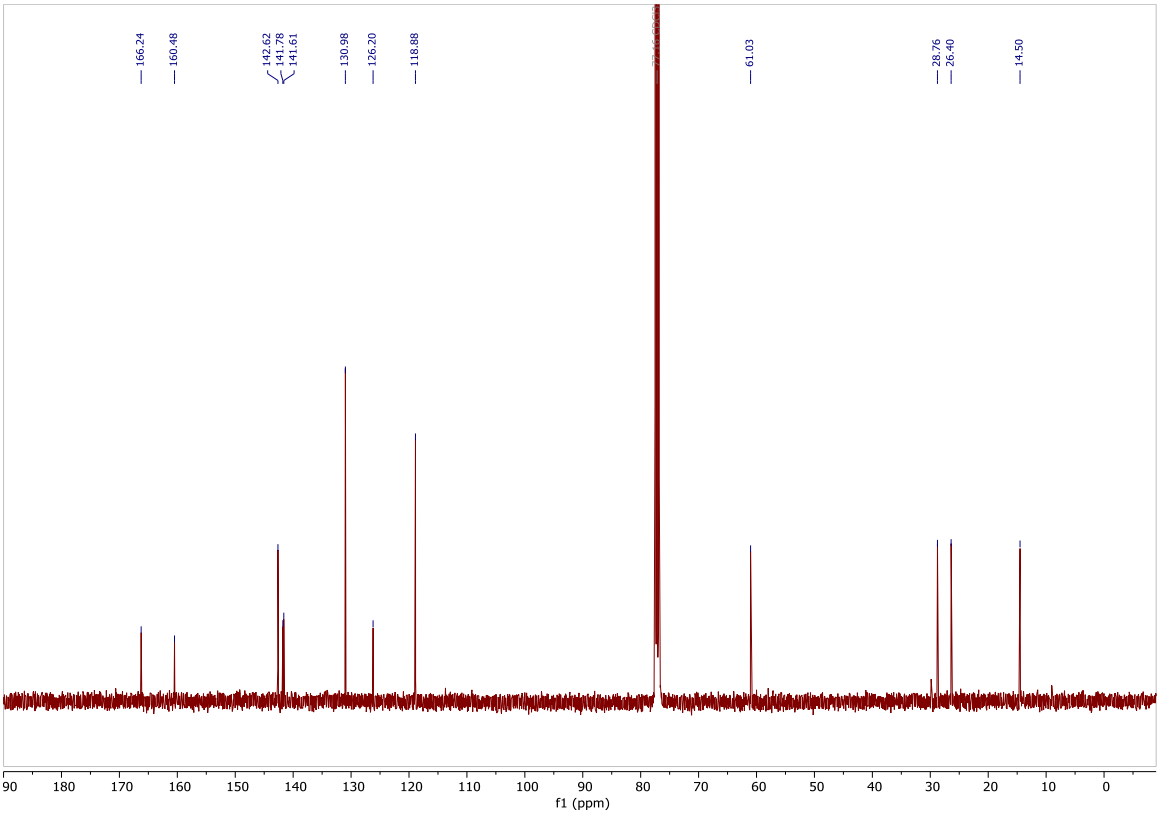
| Atom | x | y | z | $U_{eq}$ |
|---|---|---|---|---|
| H1 | -1687.76 | 6730.55 | 6213.47 | 29 |
| H2 | 3312.07 | 6214.06 | 5830.68 | 27 |
| H3A | 1824.4 | 7330.28 | 5234.26 | 36 |
| H3B | -497.91 | 6104.52 | 5191.2 | 36 |
| H4A | -3424.65 | 7510.75 | 5577.11 | 33 |
| H4B | -1221.64 | 8810.25 | 5573.35 | 33 |
| H7A | 5284.51 | 1012.11 | 5785.77 | 34 |
| H7B | 3652.95 | 362.86 | 5402.78 | 34 |
| H8A | -72.34 | 1608.87 | 5566.81 | 30 |
| H8B | 1254.19 | 1720.23 | 6016.68 | 30 |
| H11 | 8326.24 | 8227.91 | 7289.18 | 35 |
| H12 | 7596.85 | 5778.3 | 7414.92 | 40 |
| H13 | 4154.47 | 4579.38 | 7075.52 | 38 |
| H14 | 1554.02 | 5781.07 | 6600.15 | 34 |
| H1 xx | 7913.86 | 12405.79 | 6677.68 | 52 |
| H16B | 10520.28 | 12241.59 | 6956.55 | 52 |
| H16C | 7721.22 | 12645.93 | 7162.18 | 52 |

# 4. NMR Spectra

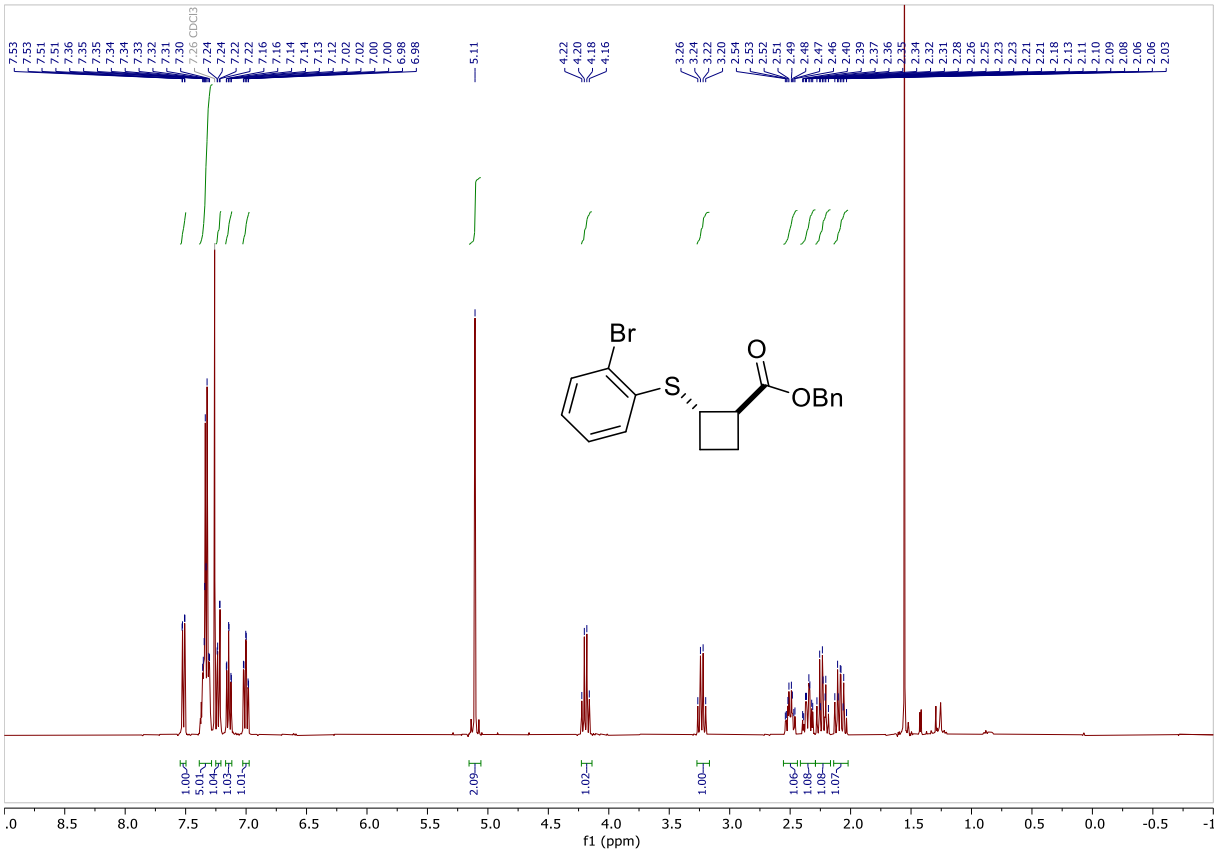
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (2d)



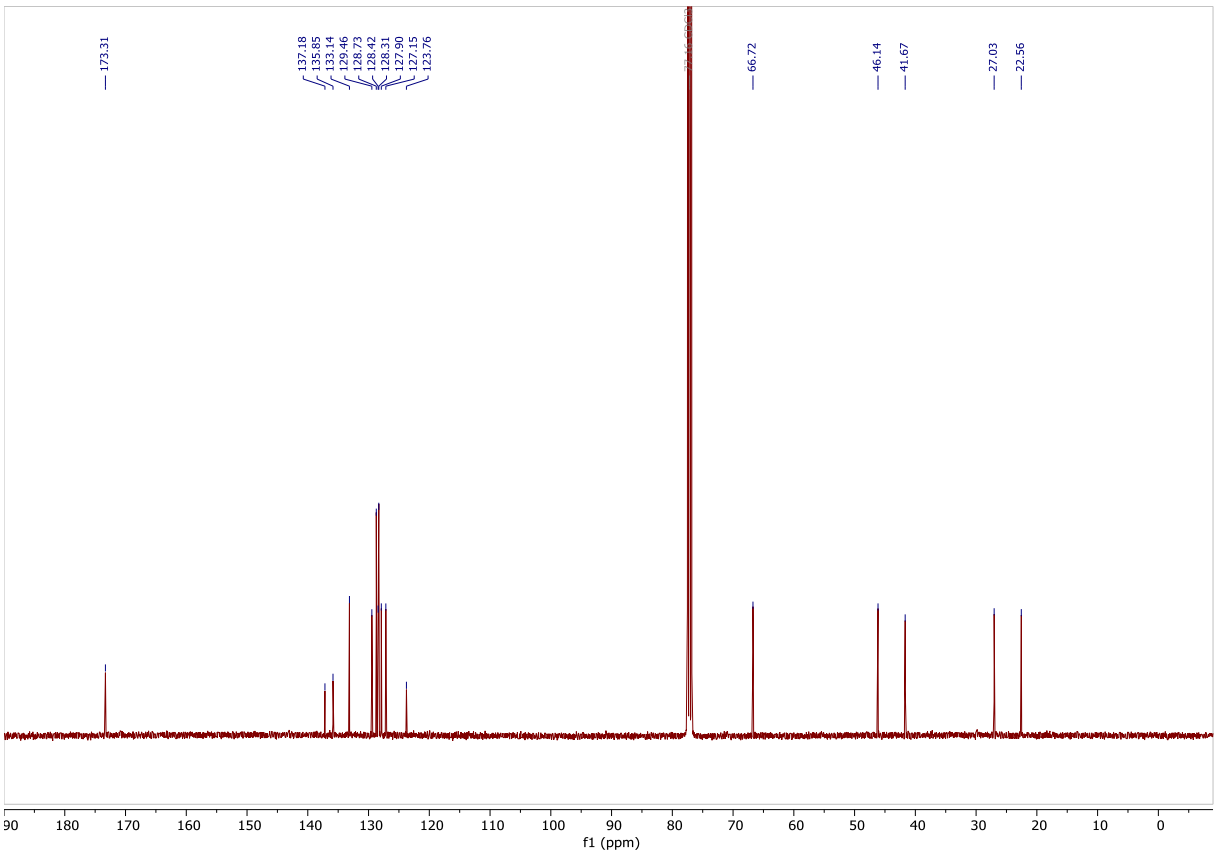

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (2d)



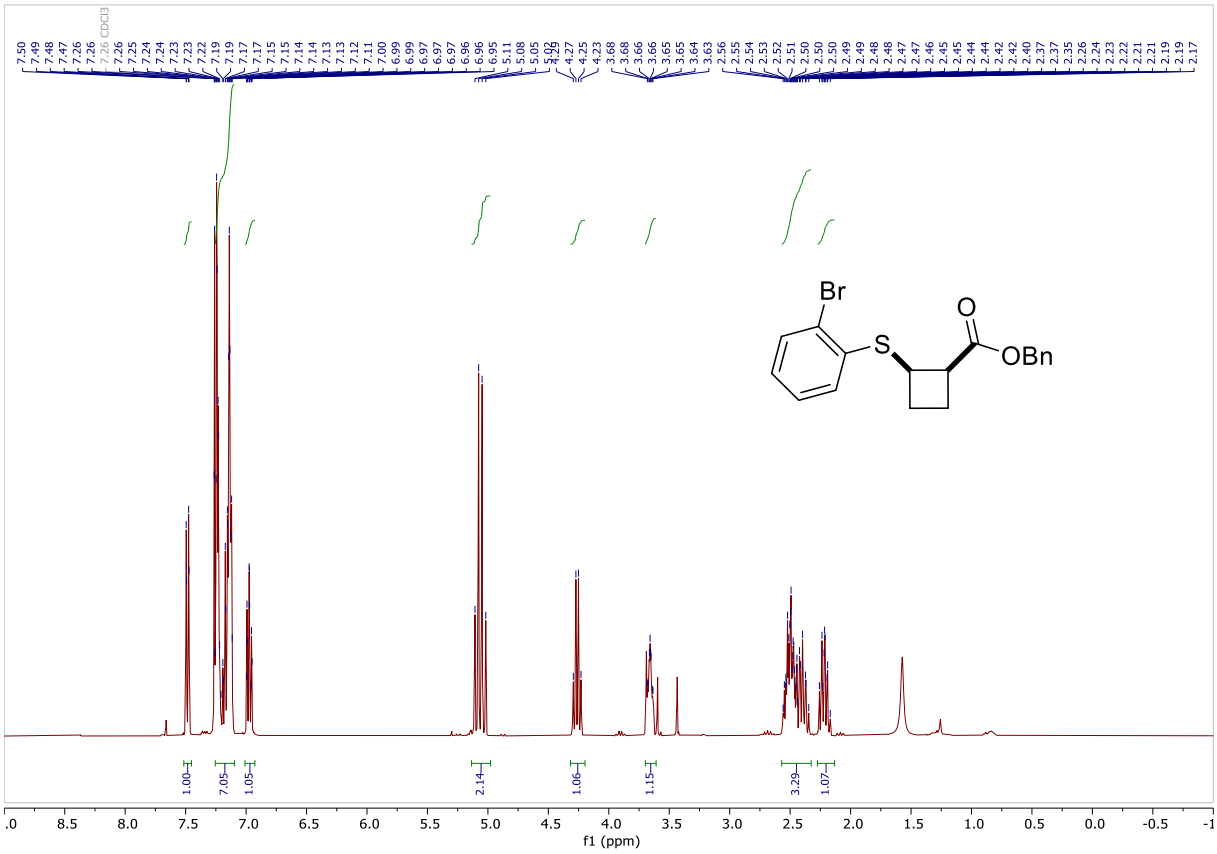
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3a)



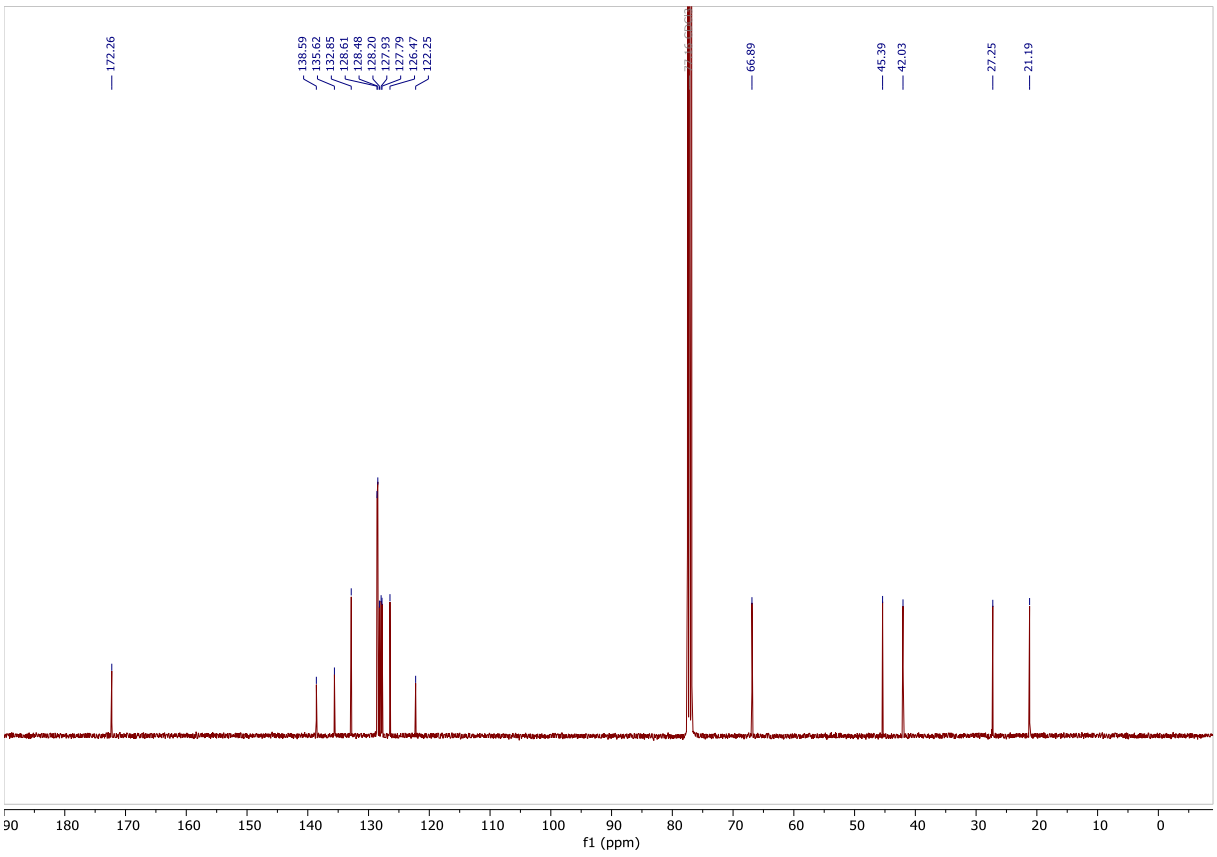

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3a)



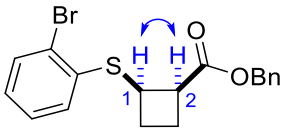
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3'a)

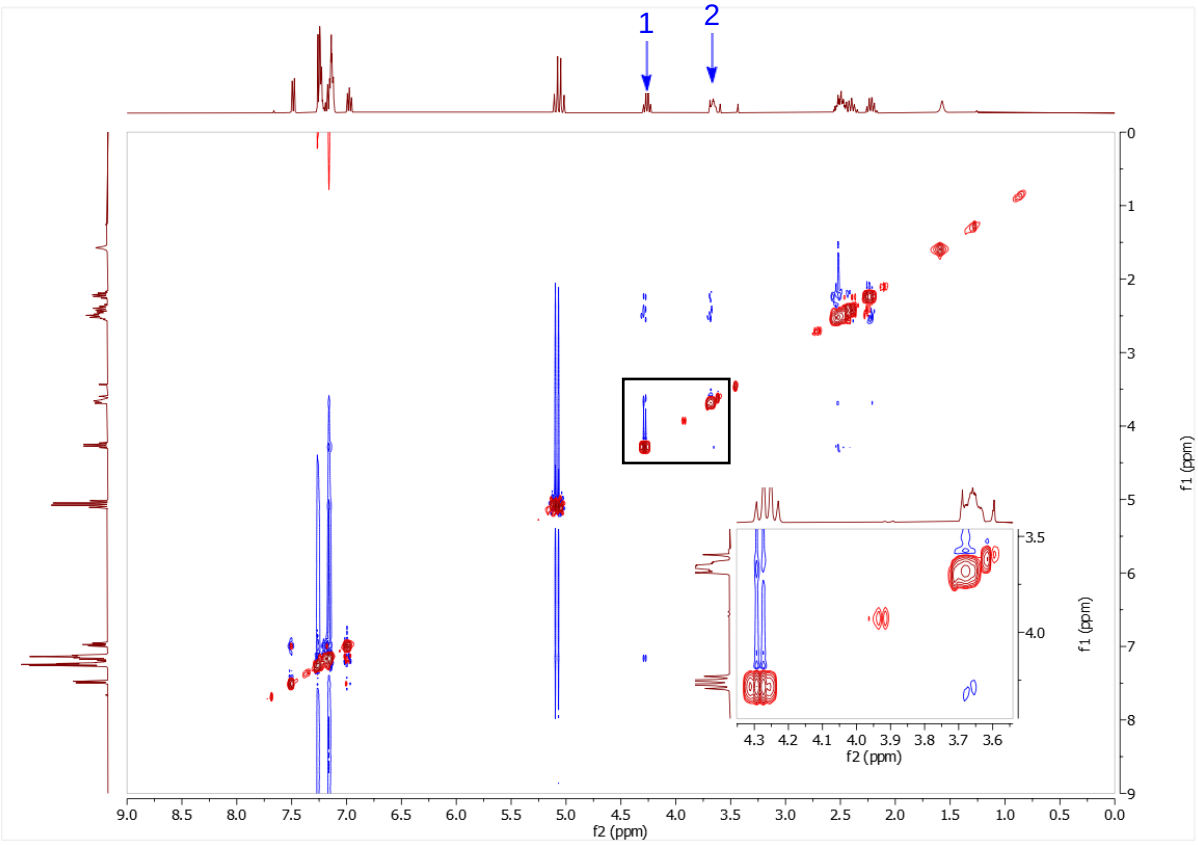



## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3'a)

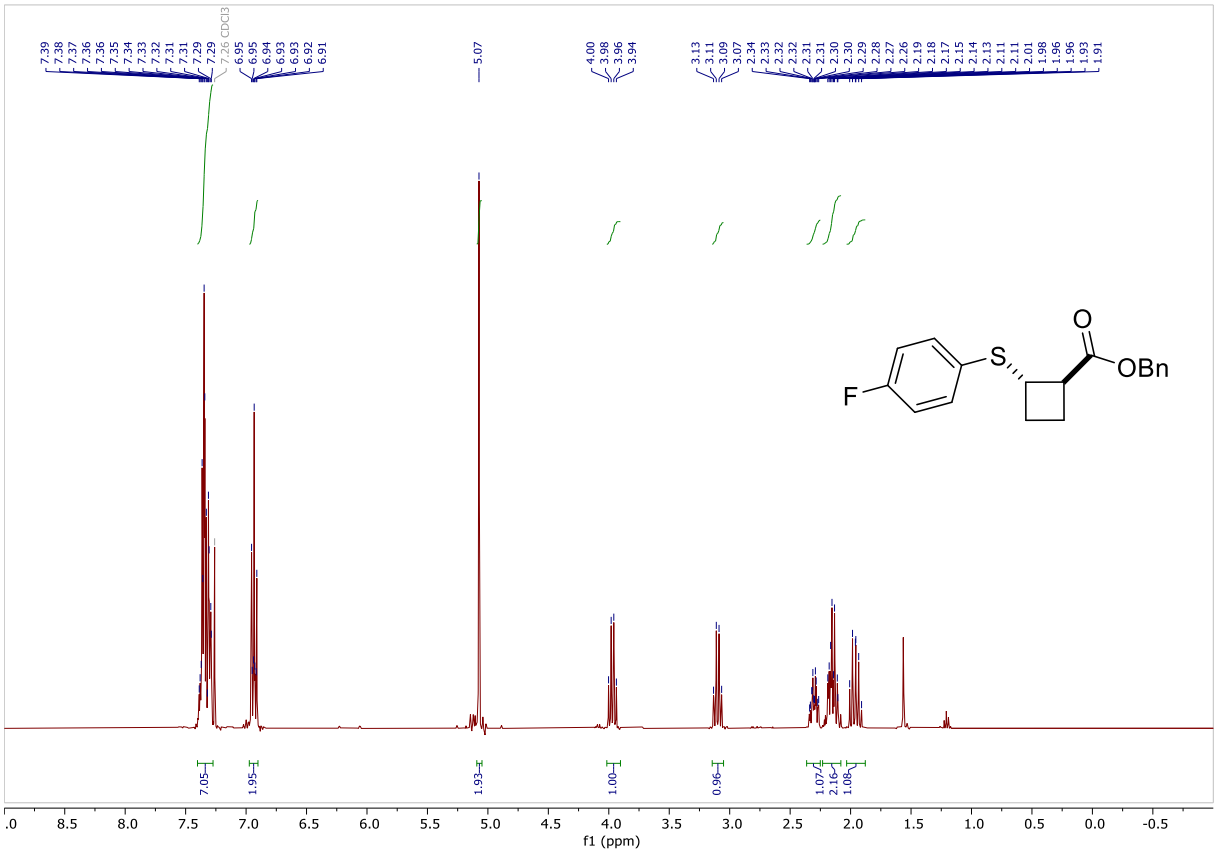


**2D-NOESY (400 MHz, chloroform-*d*) (3'a)**

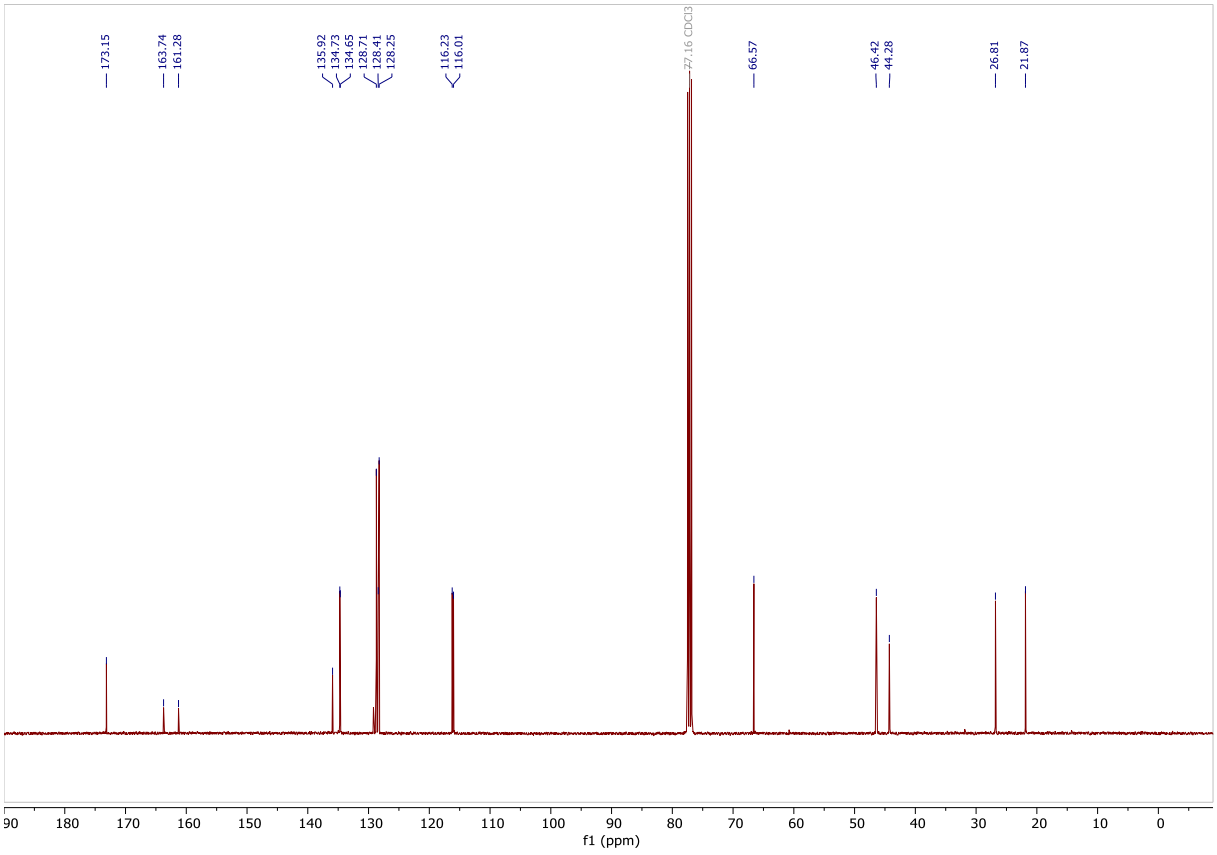


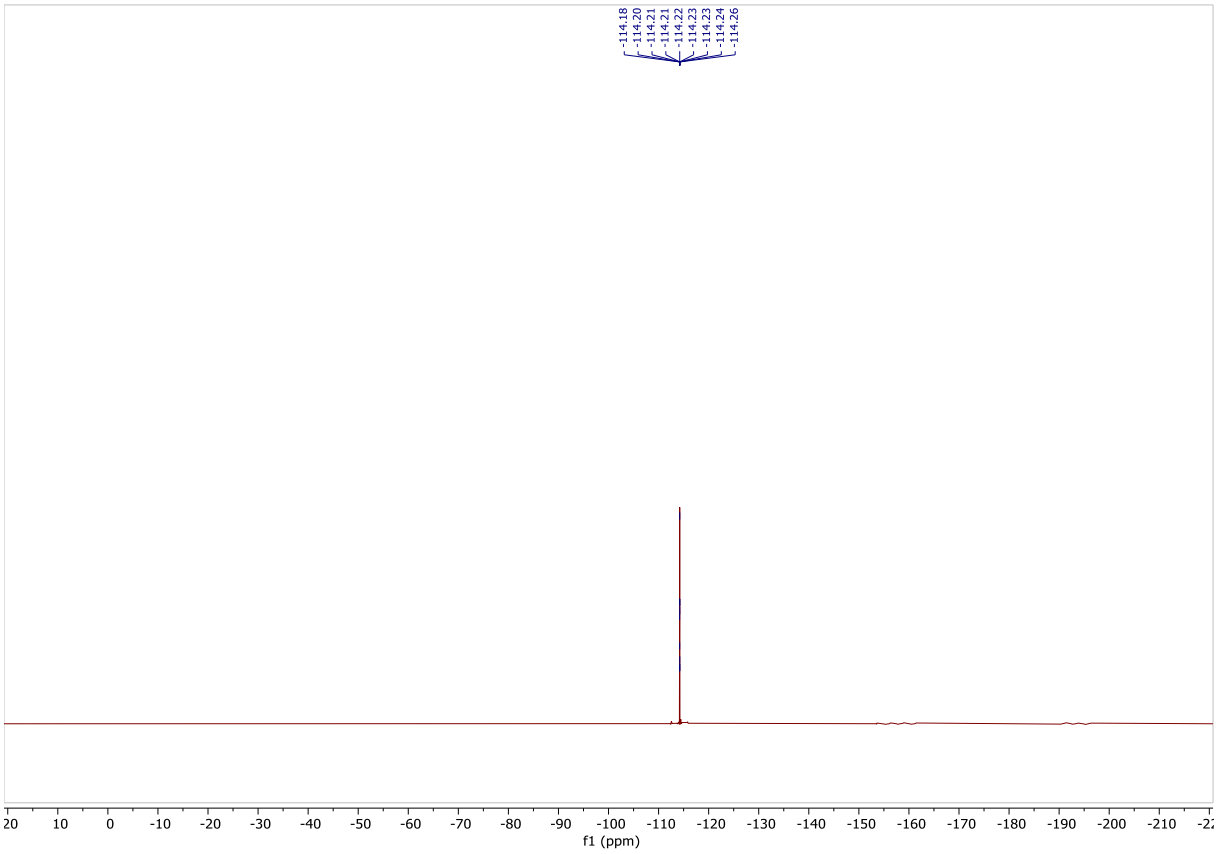
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3b)



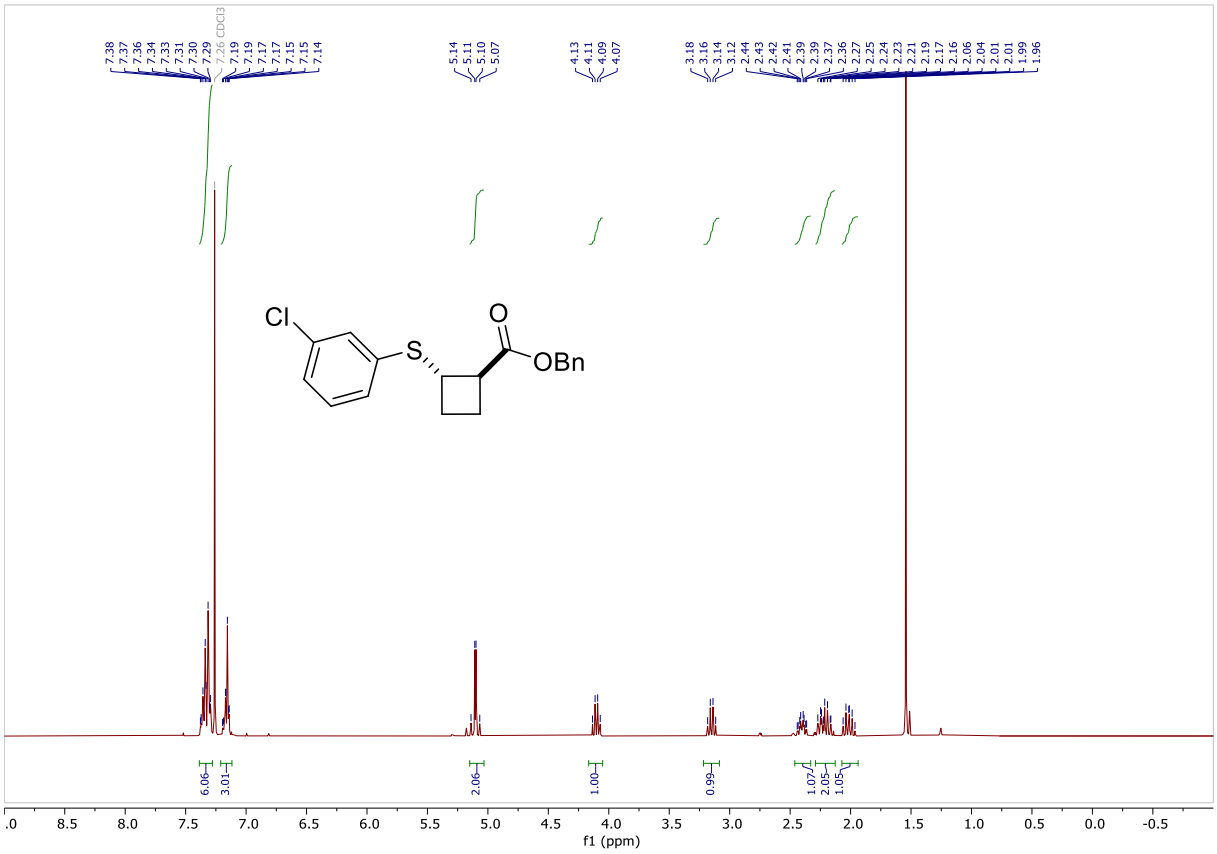

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3b)



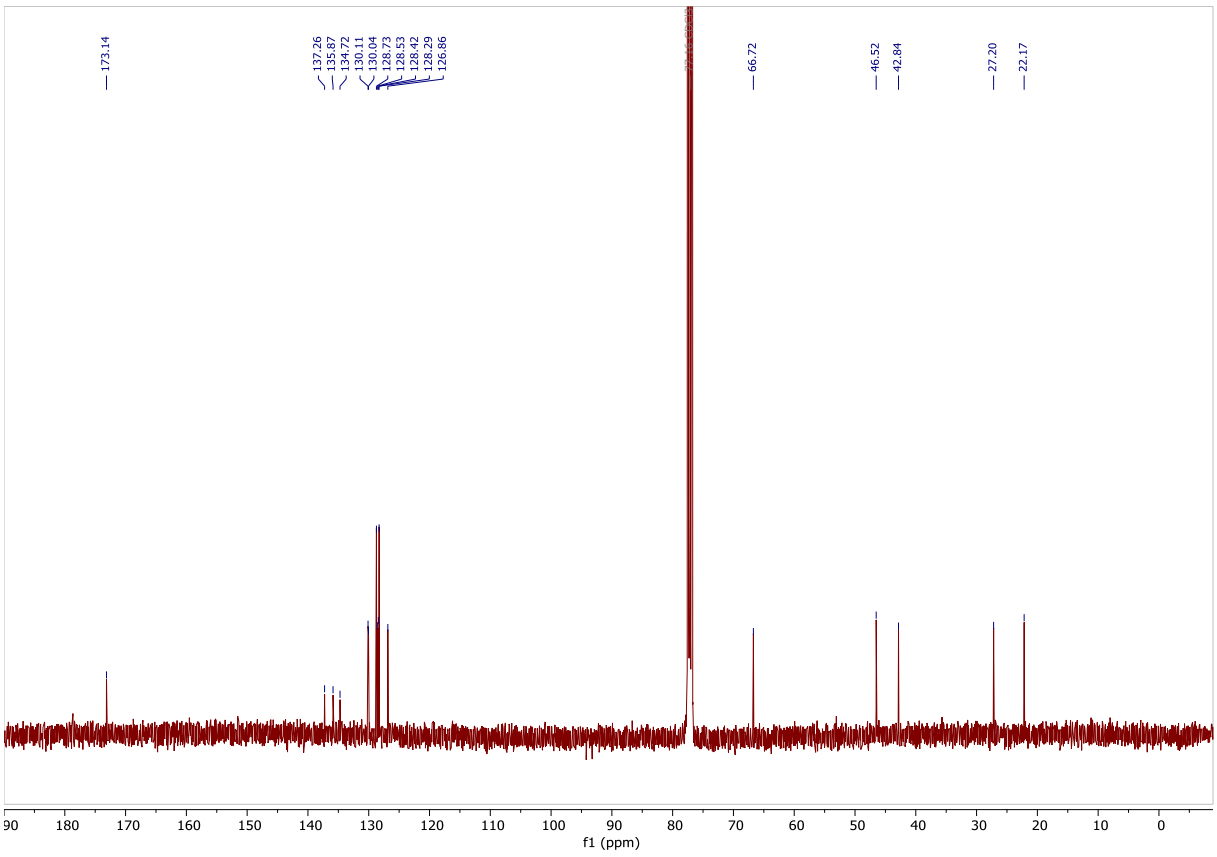
**$^{19}$F-NMR (376 MHz, chloroform-*d*) (3b)**



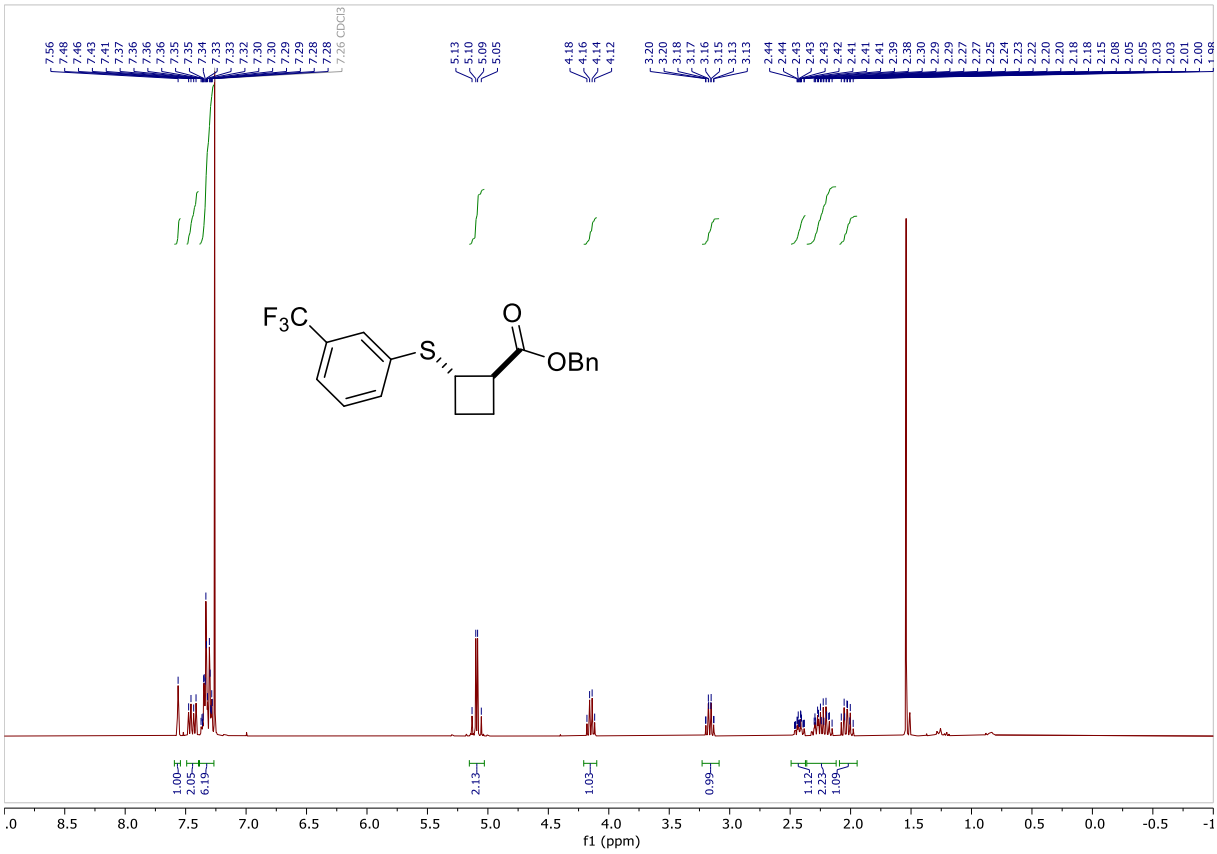
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3c)



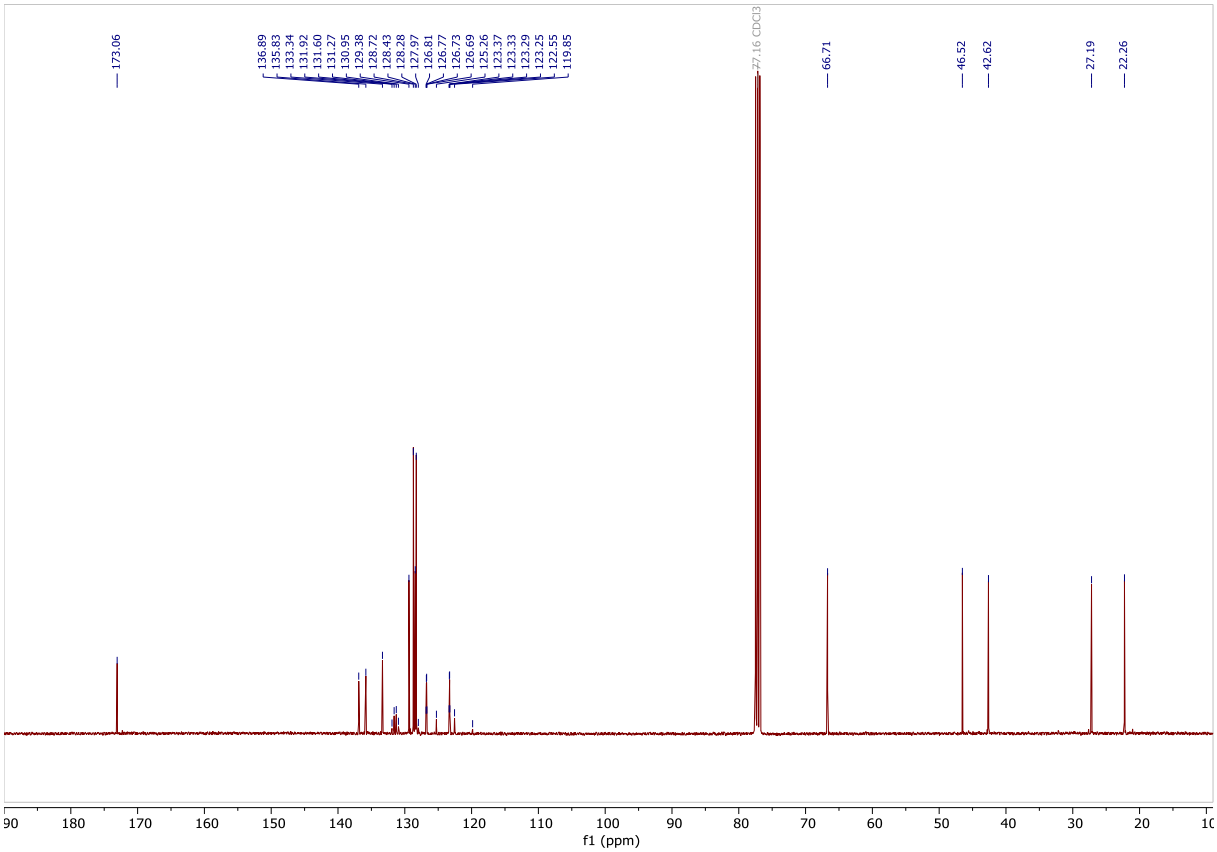

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3c)



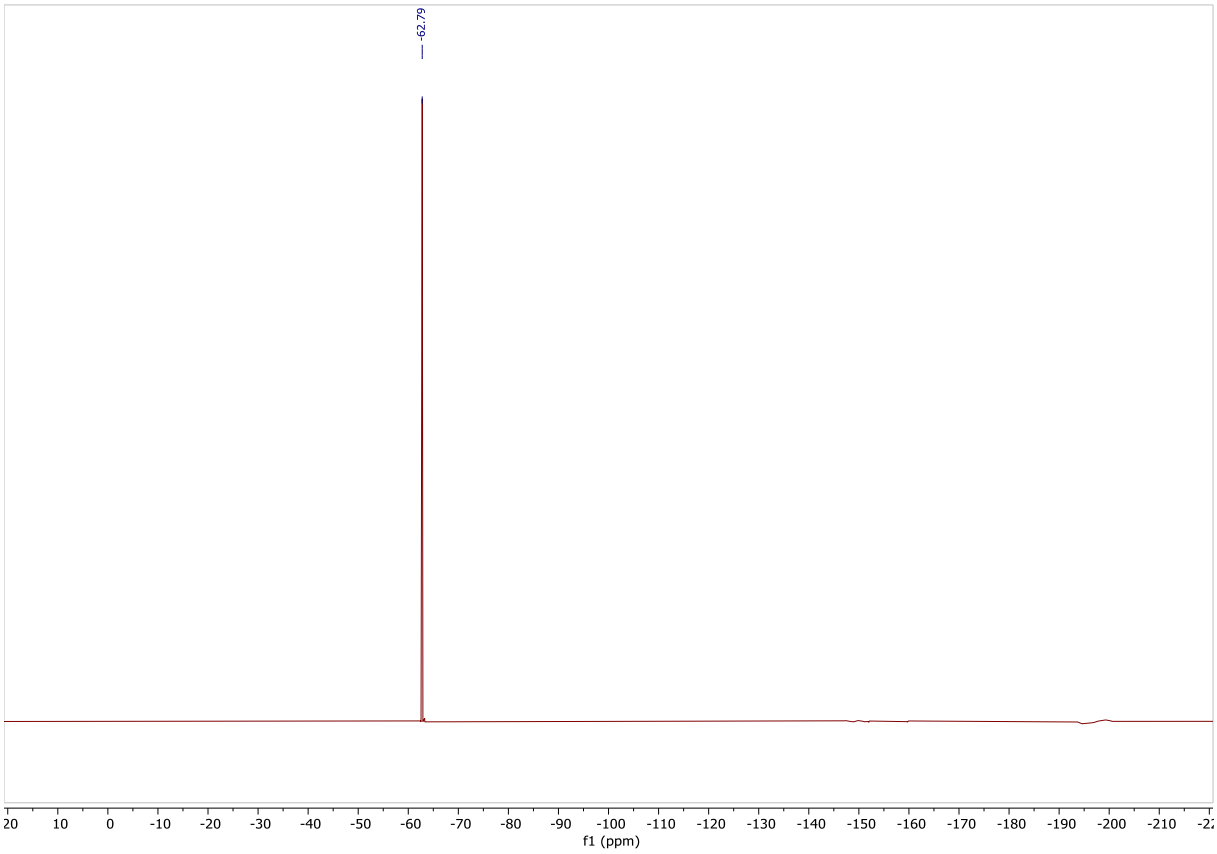
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3d)



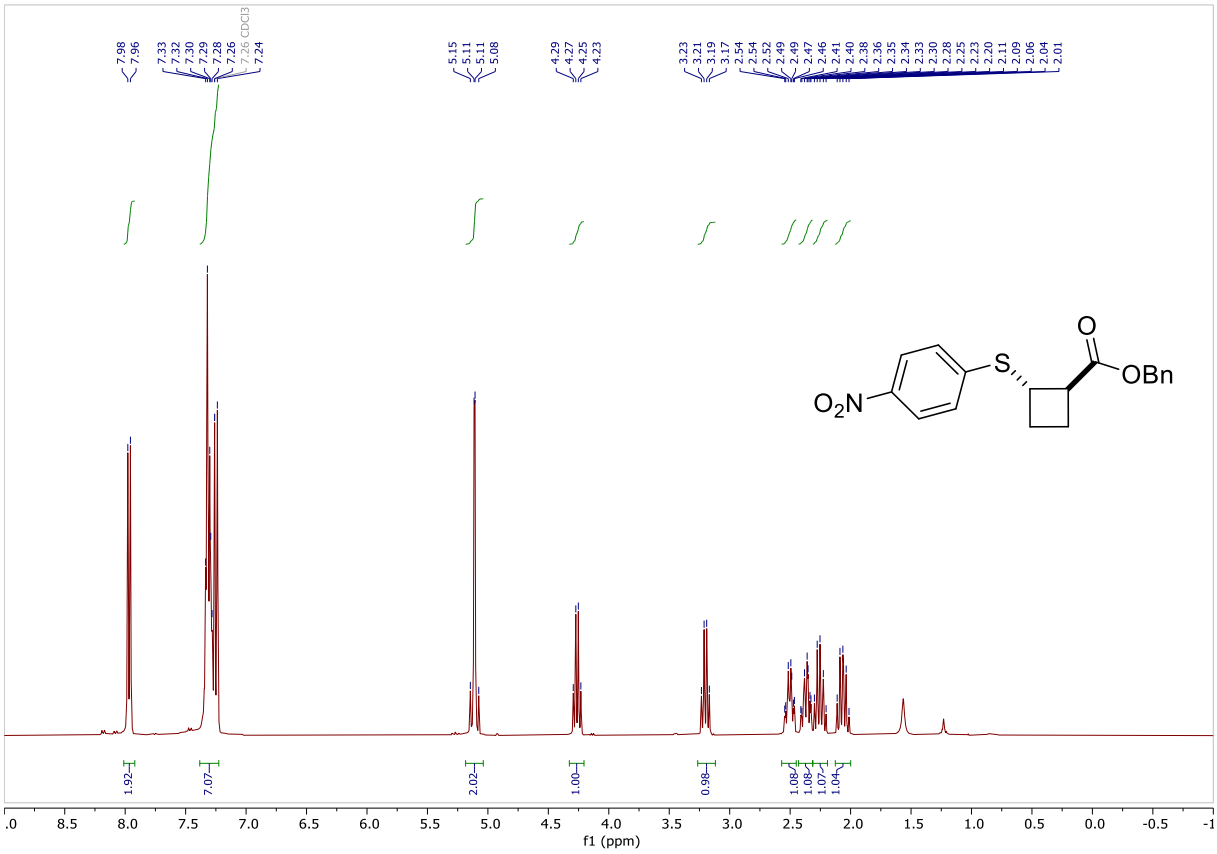

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3d)



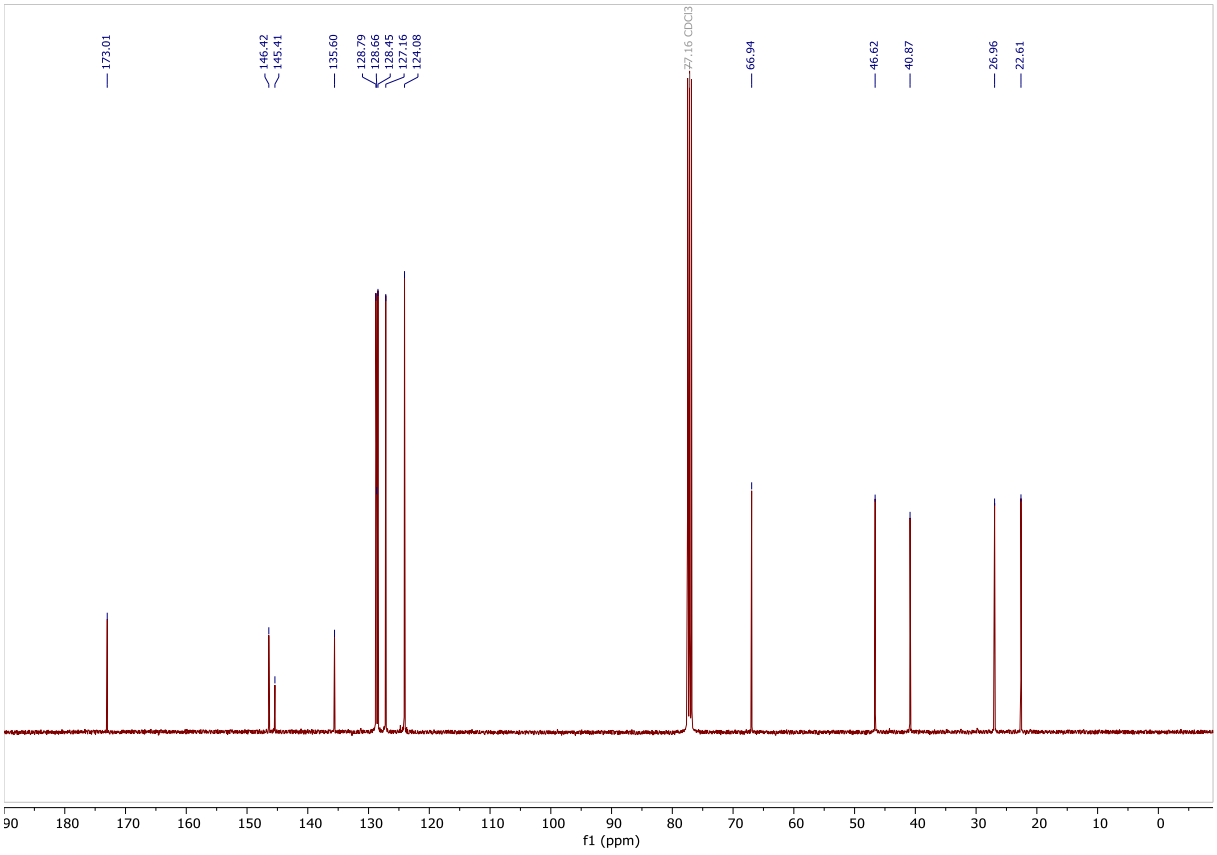
**$^{19}$F-NMR (376 MHz, chloroform-*d*) (3d)**



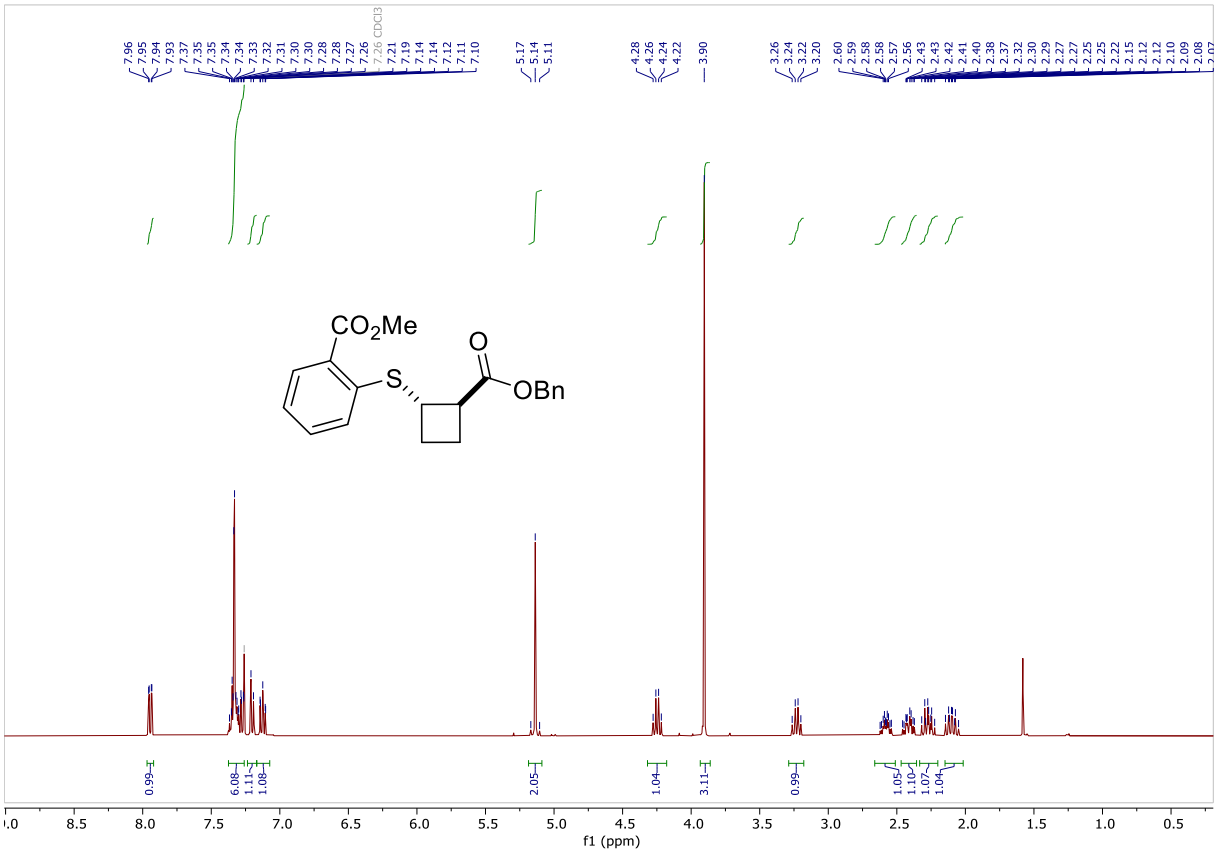
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3e)



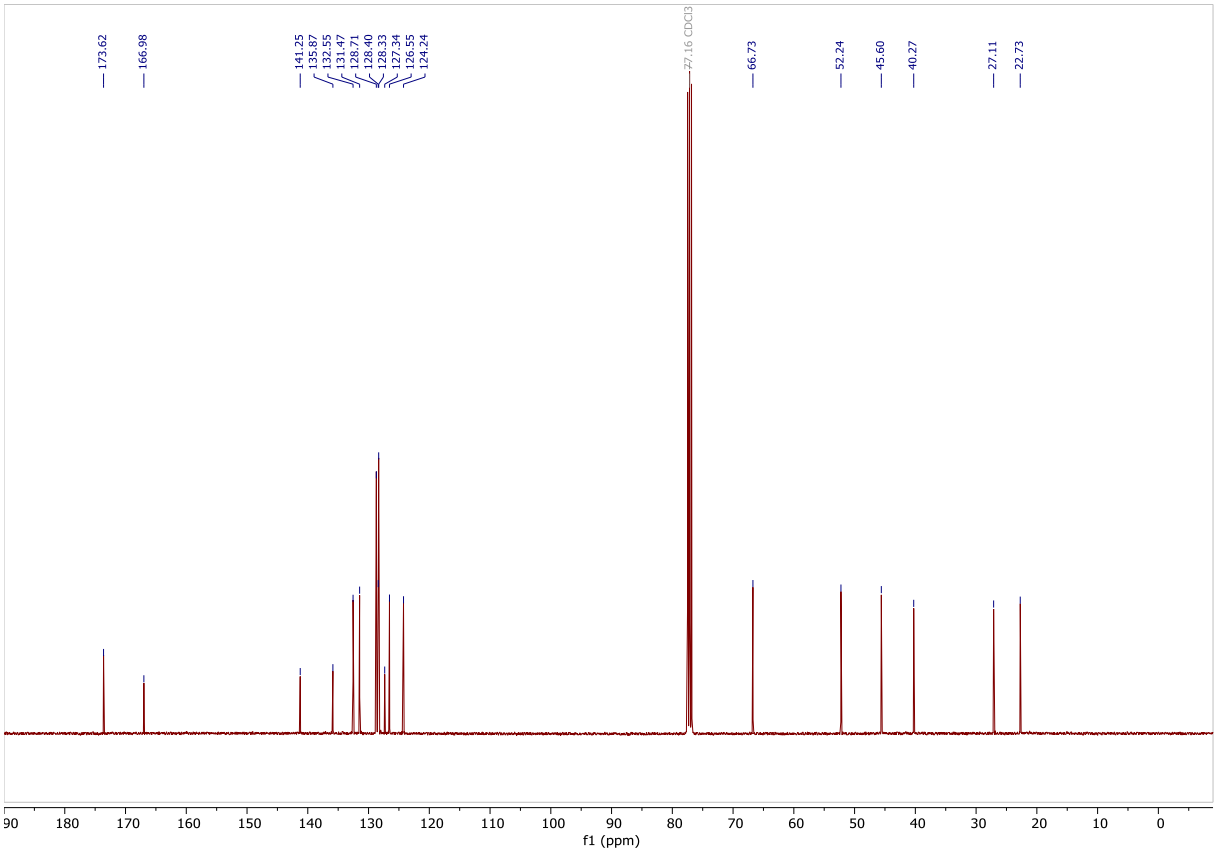

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3e)



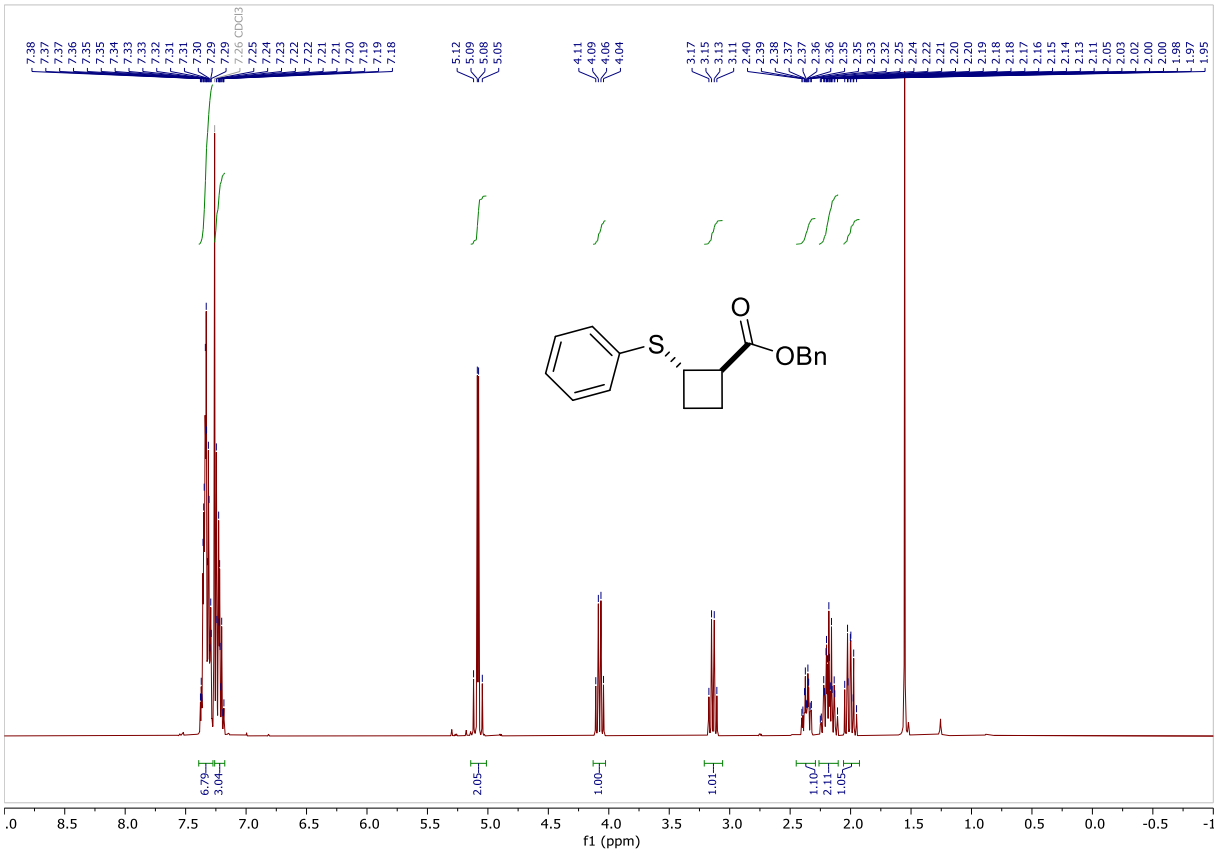
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3f)



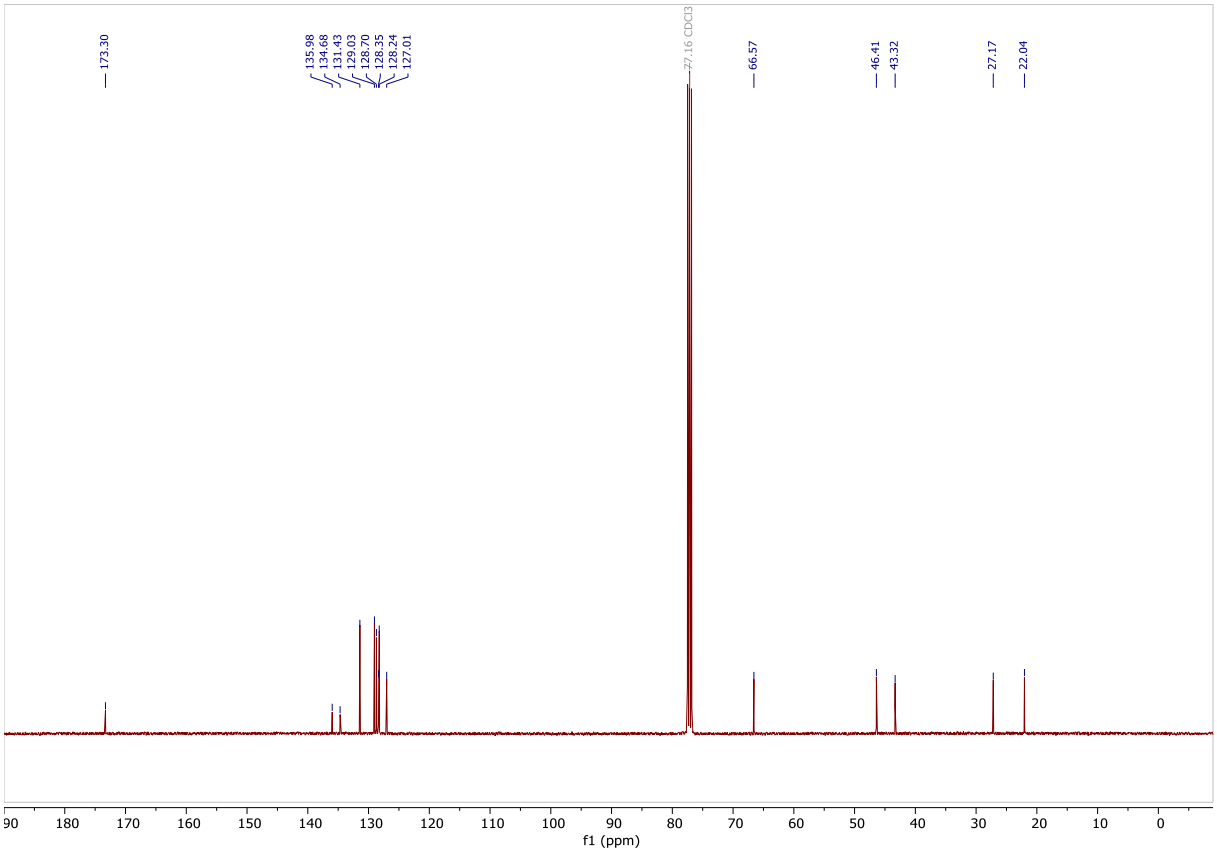

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3f)



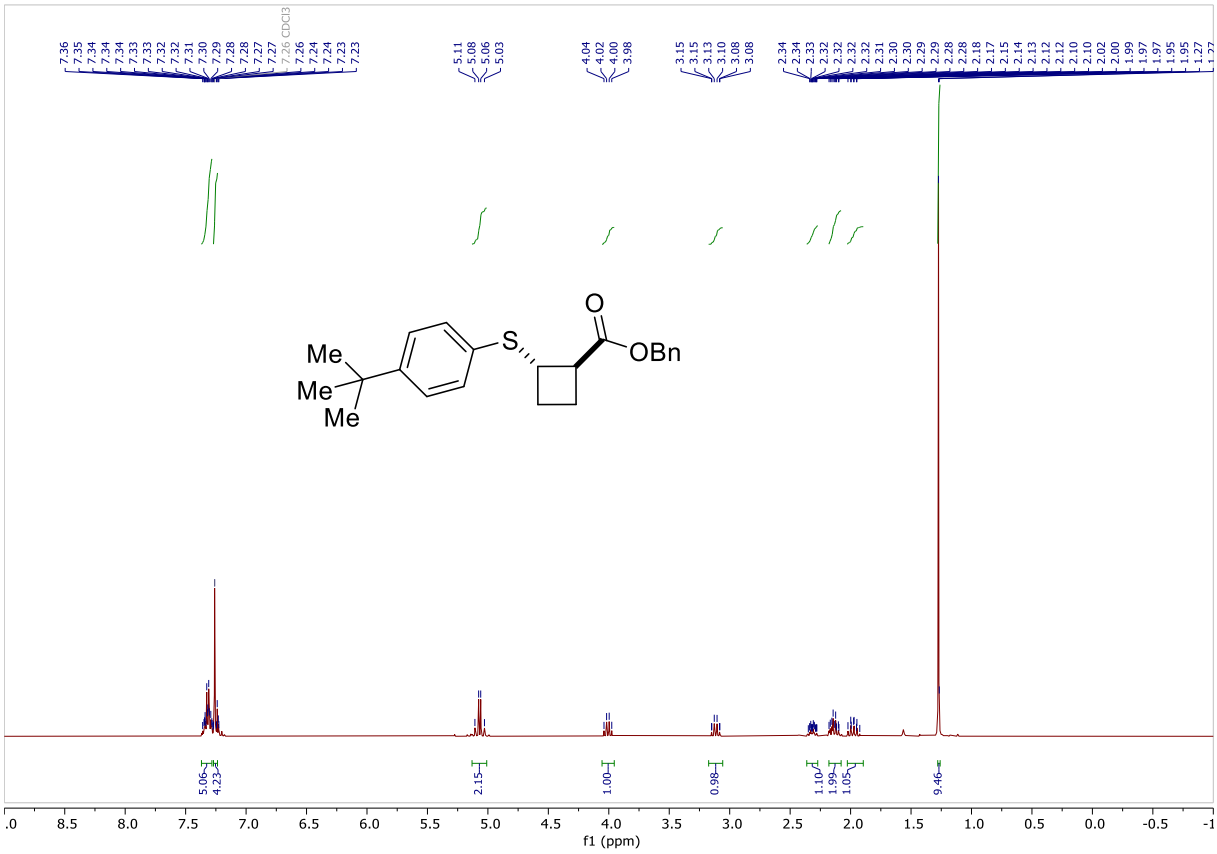
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3g)



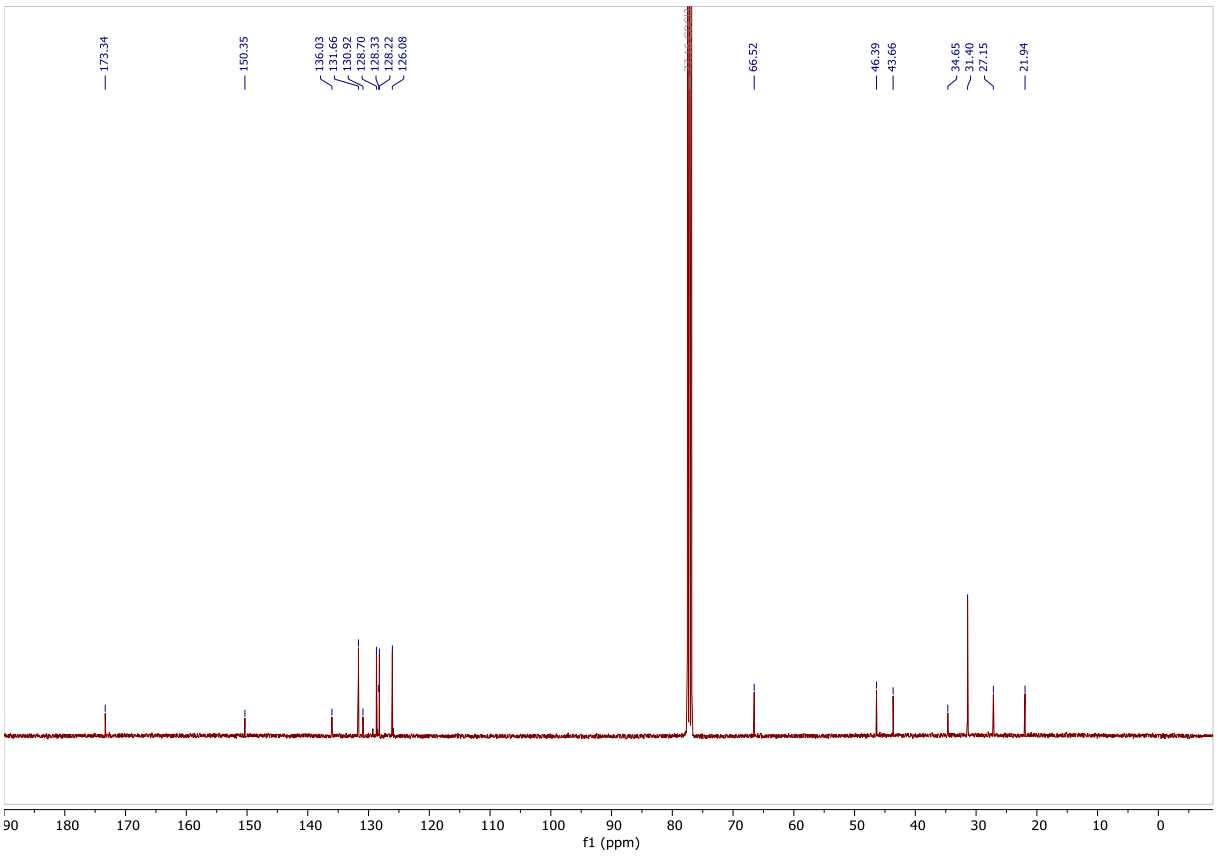

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3g)



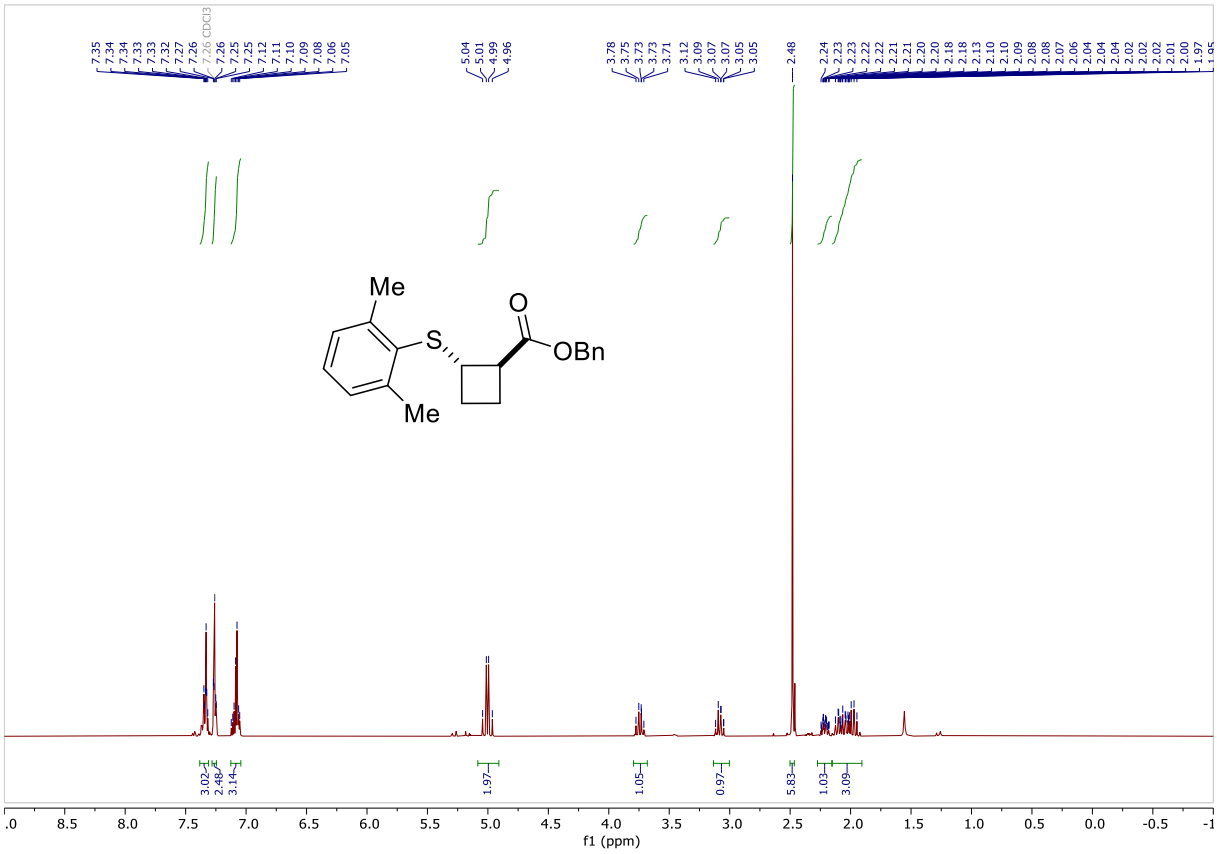
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3h)



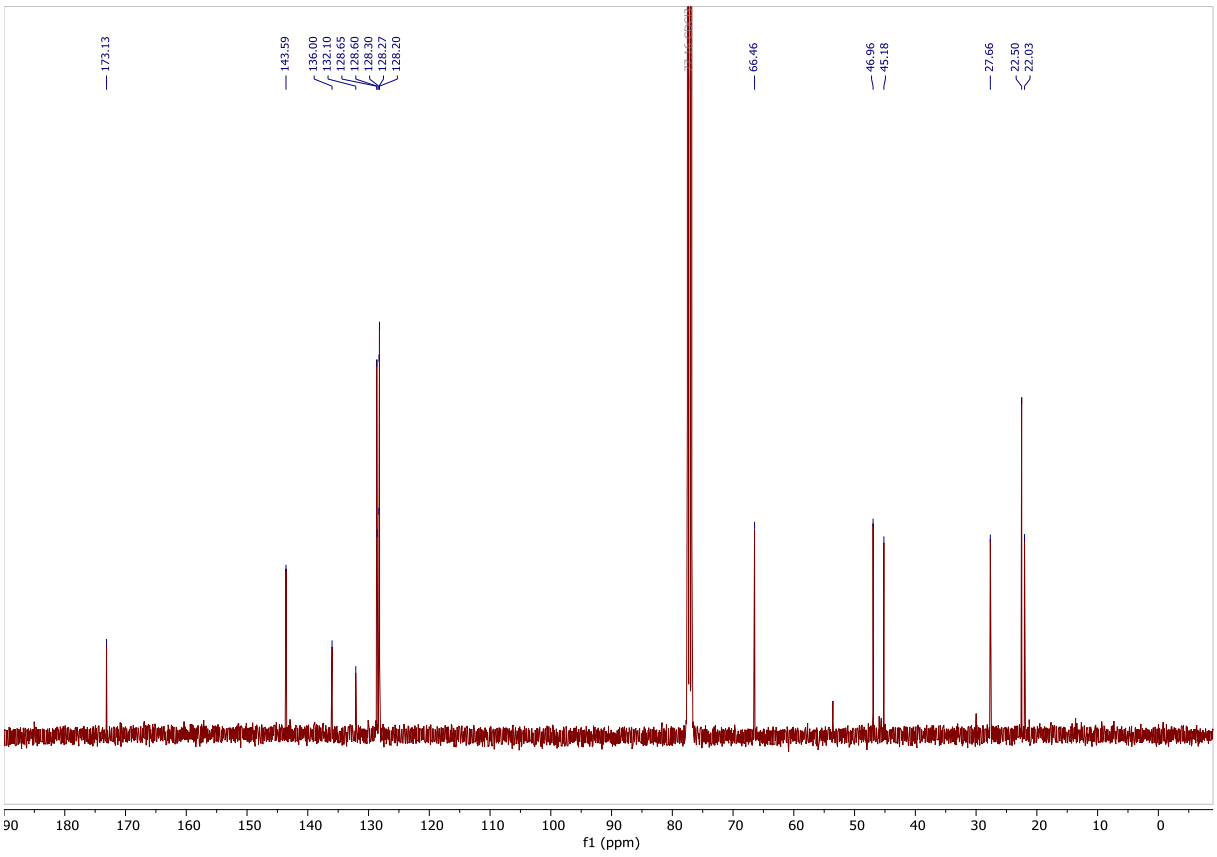

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3h)



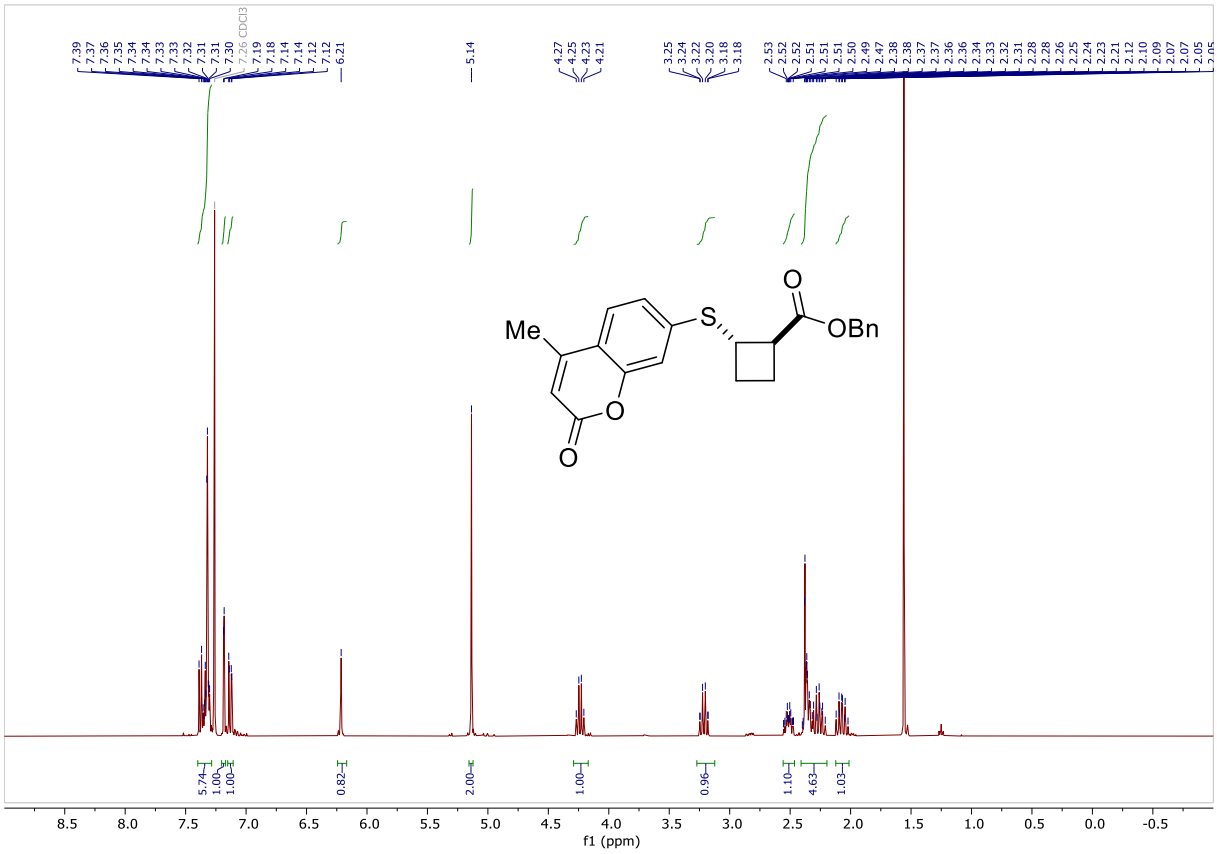
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3i)



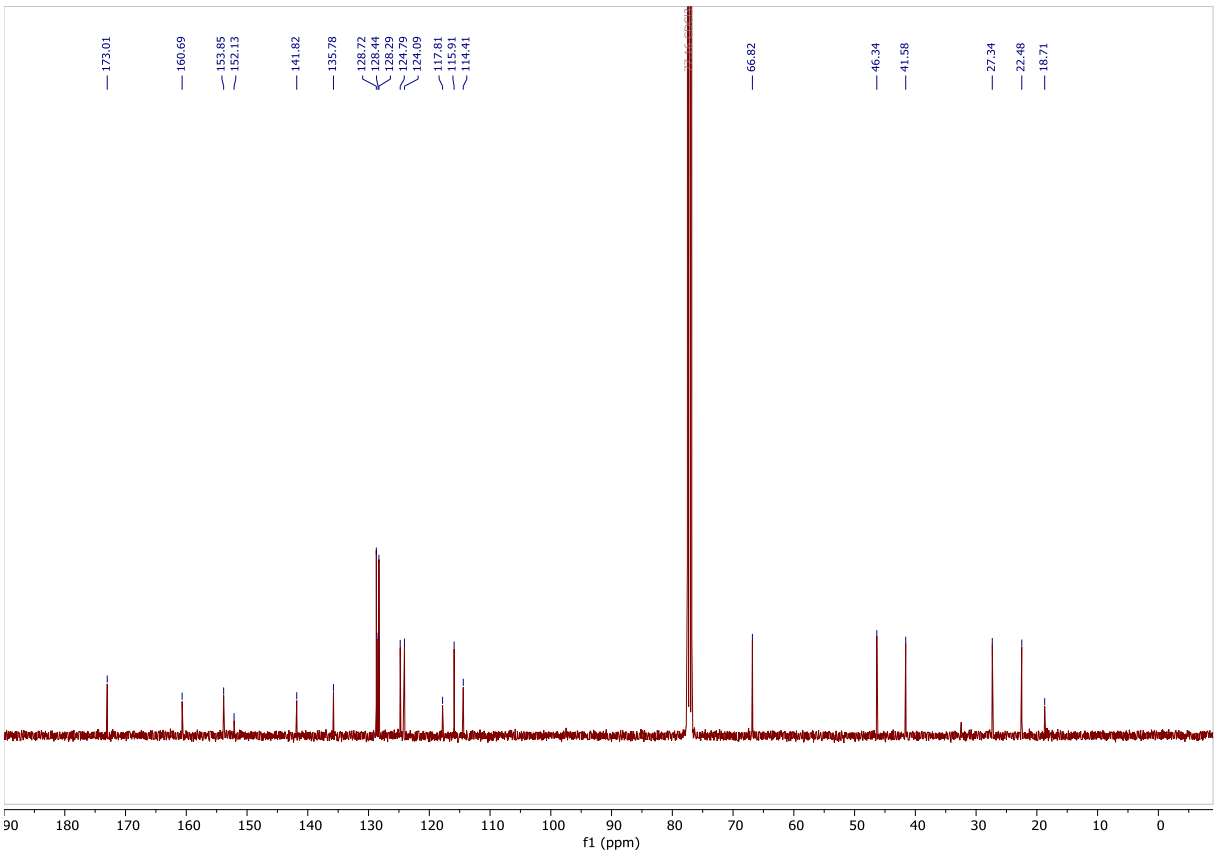

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3i)



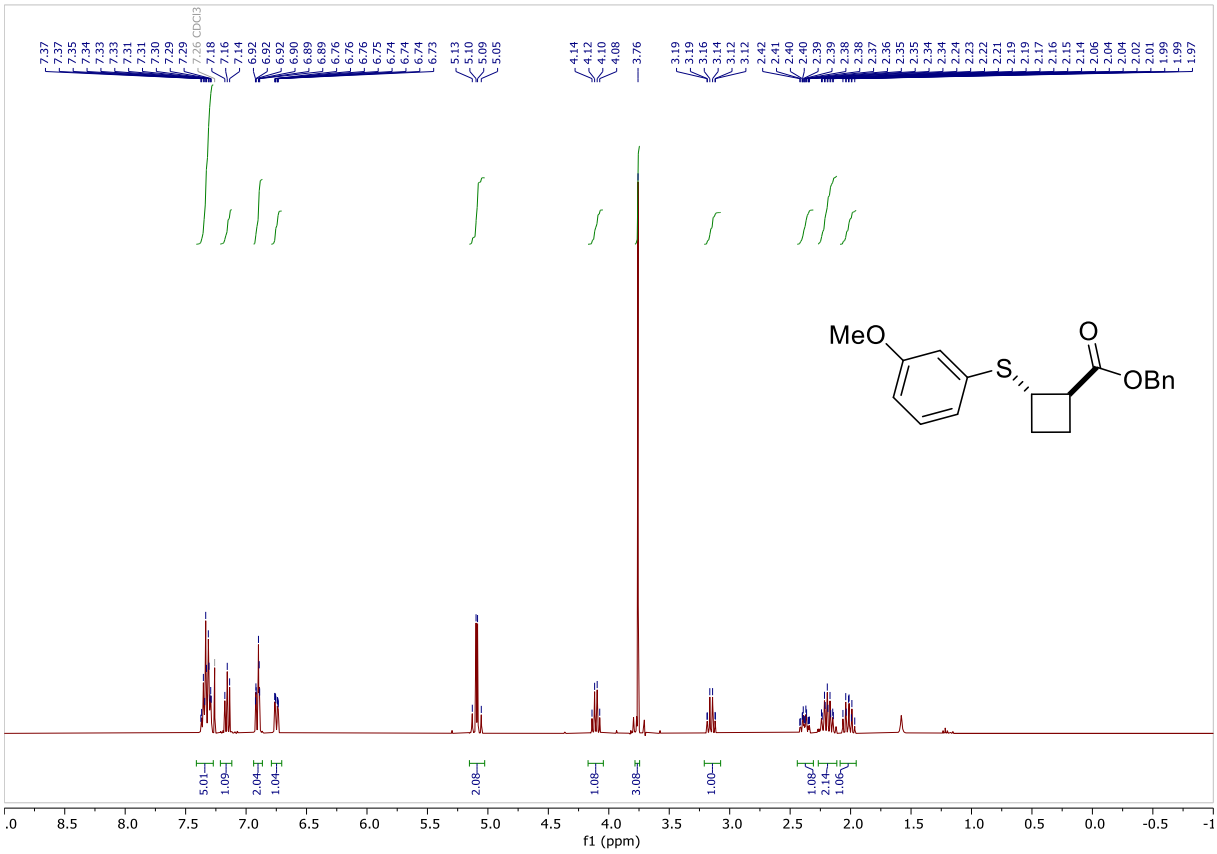
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3j)



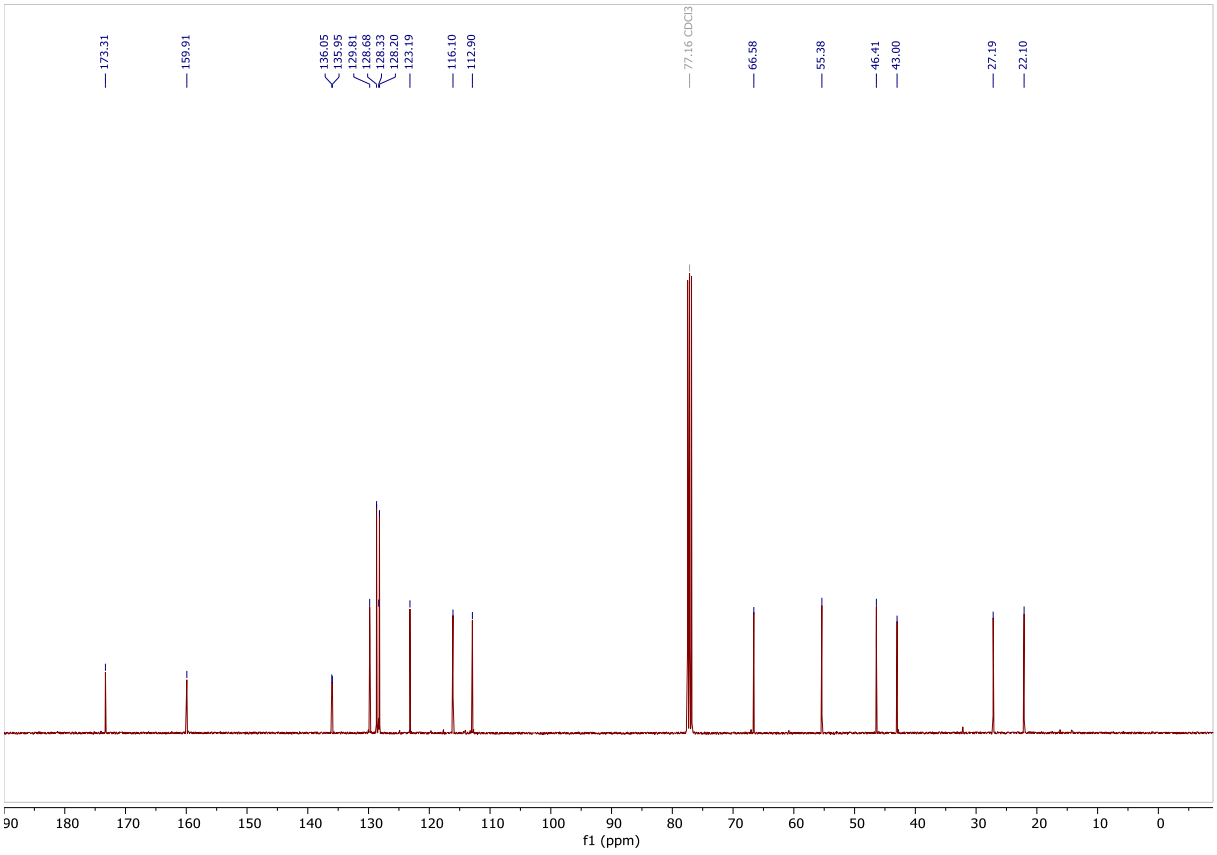

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3j)



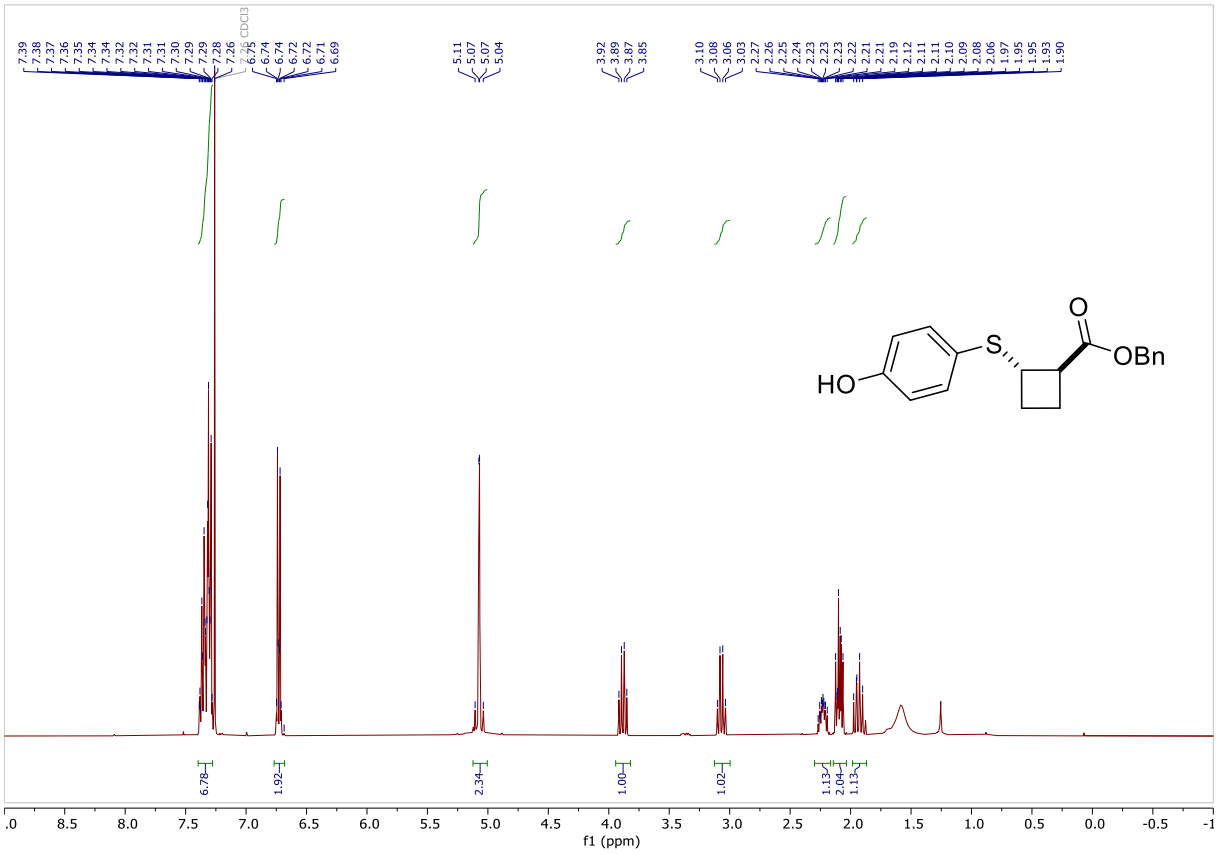
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3k)



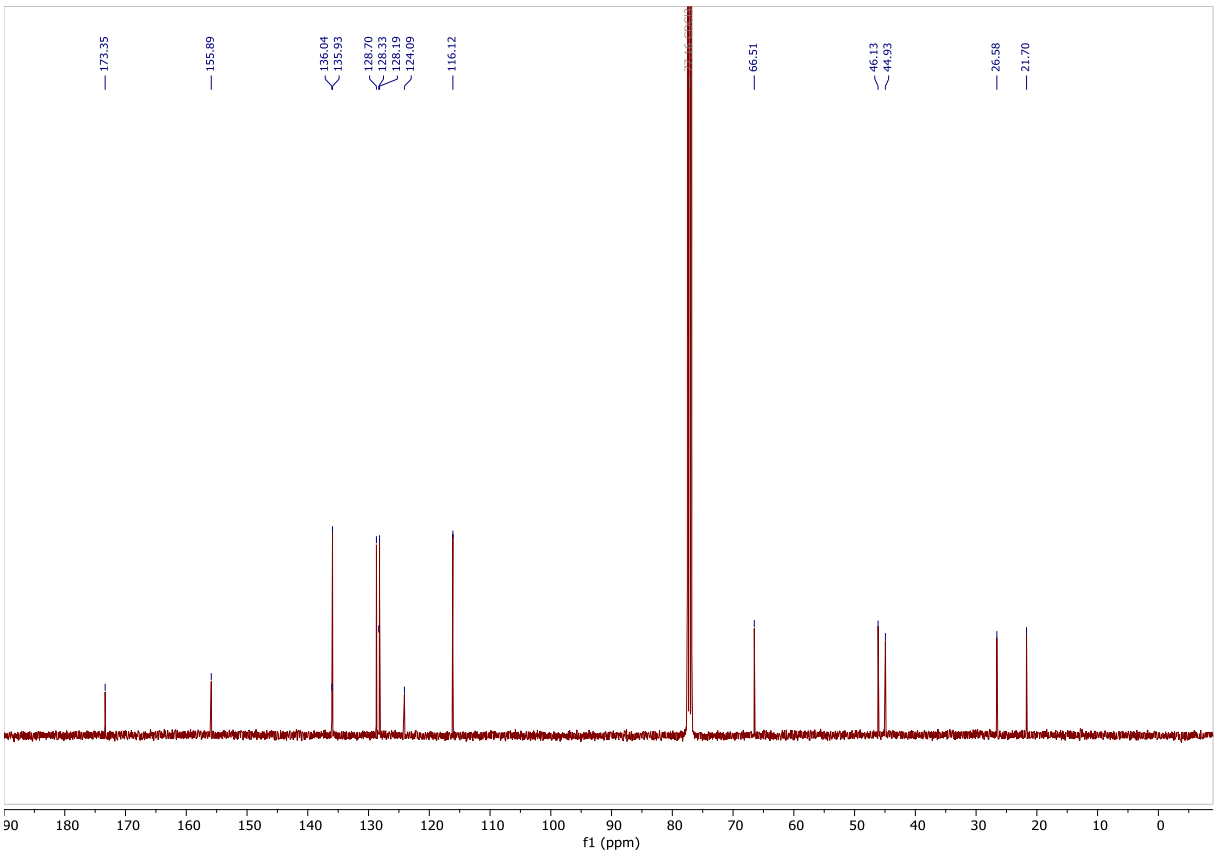

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3k)



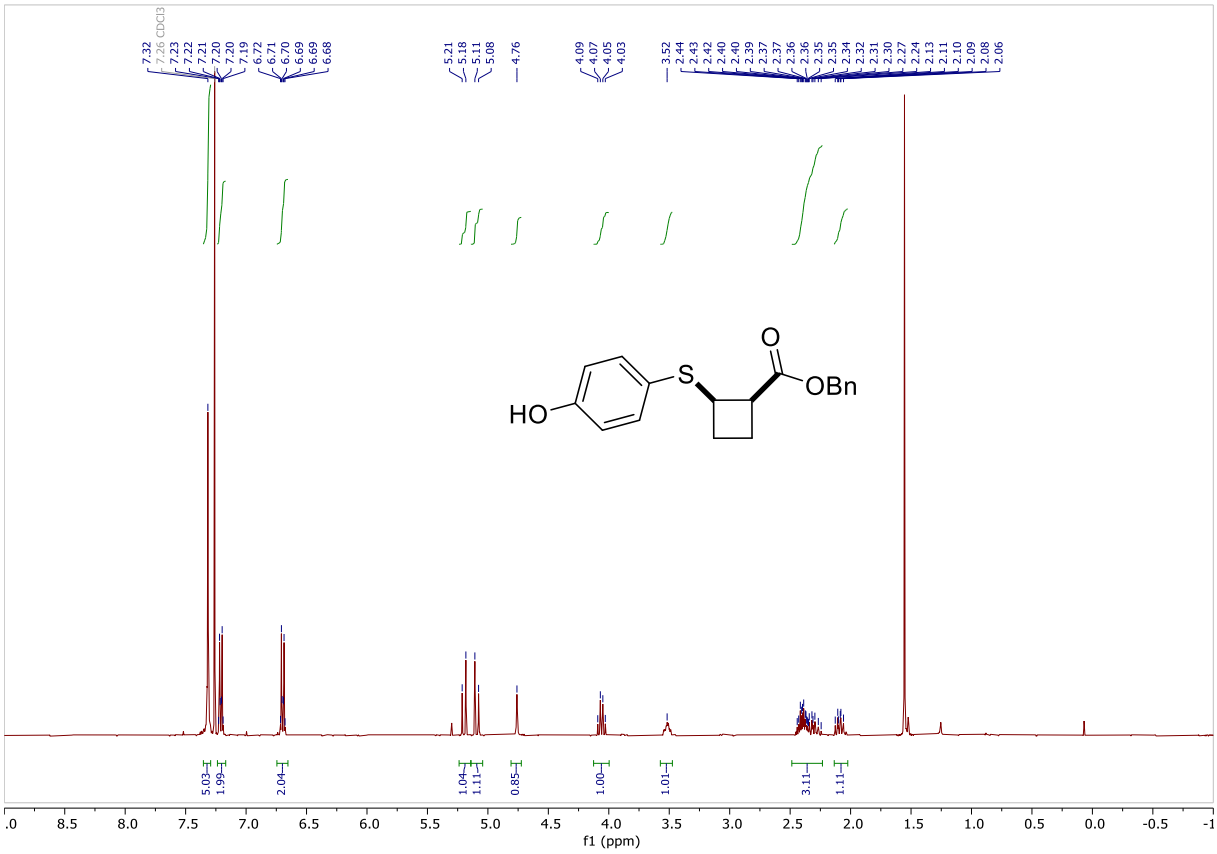
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3l)



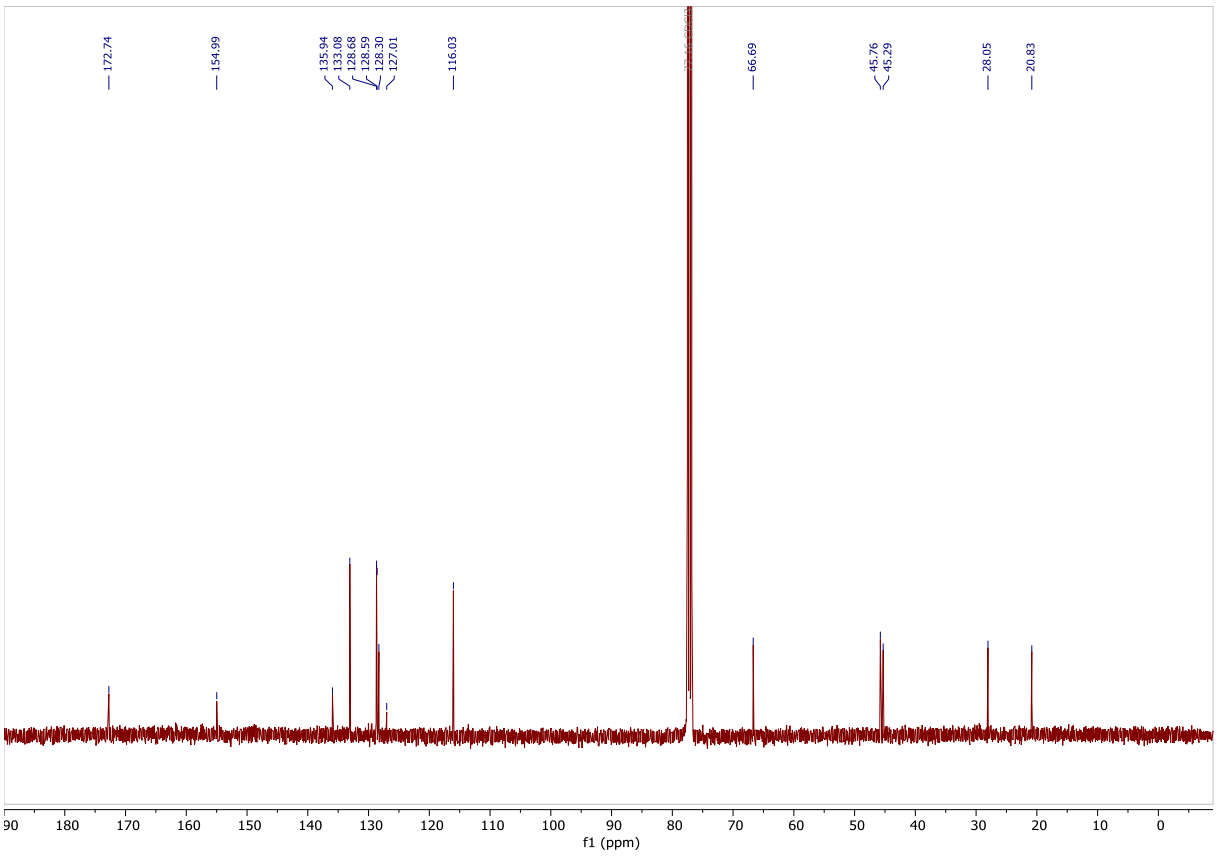

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3l)



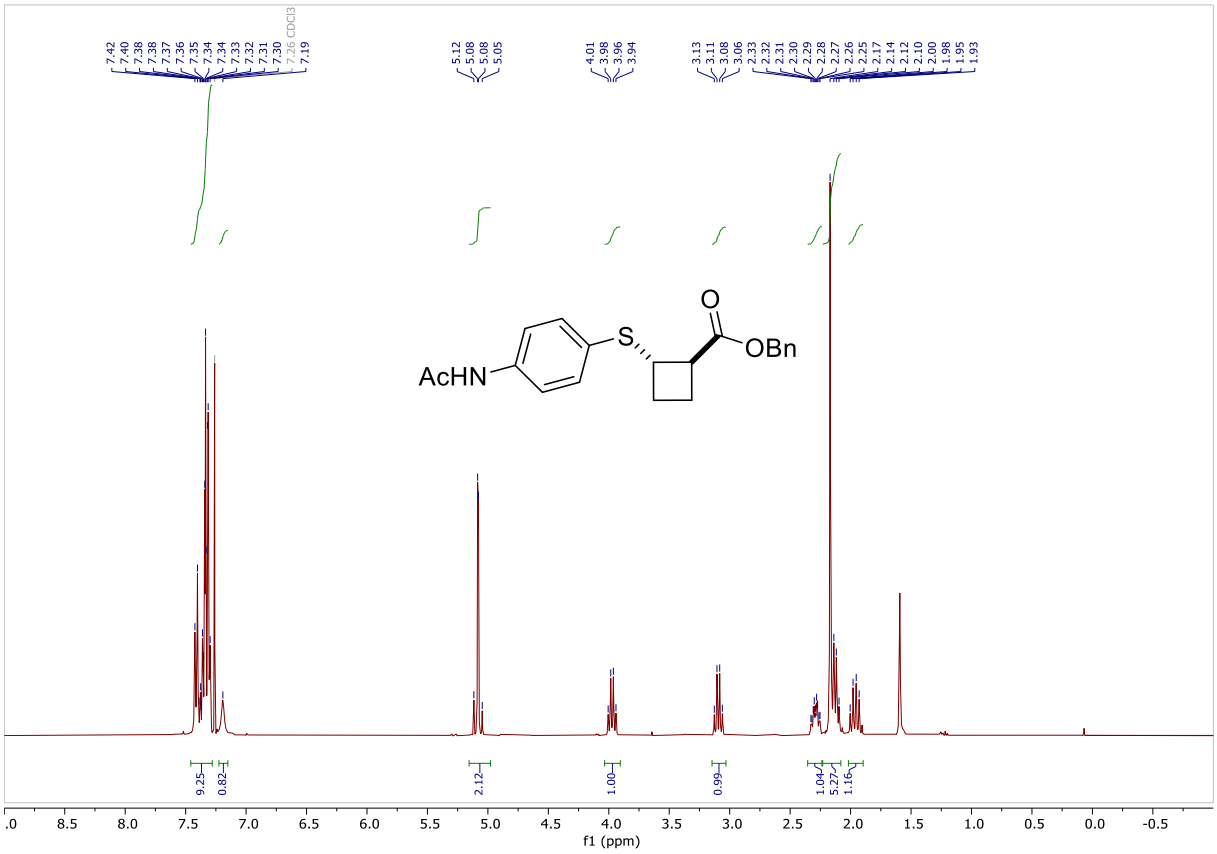
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3'l)



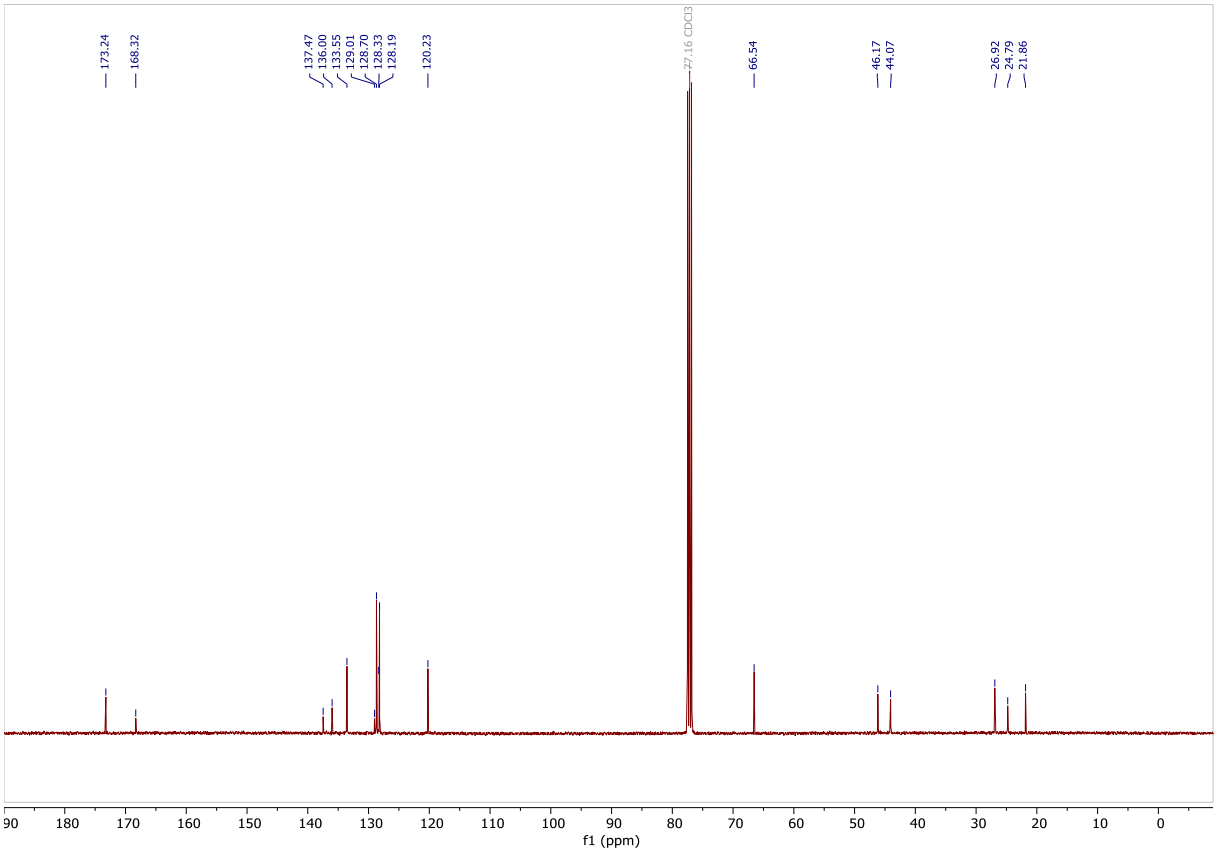

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3'l)



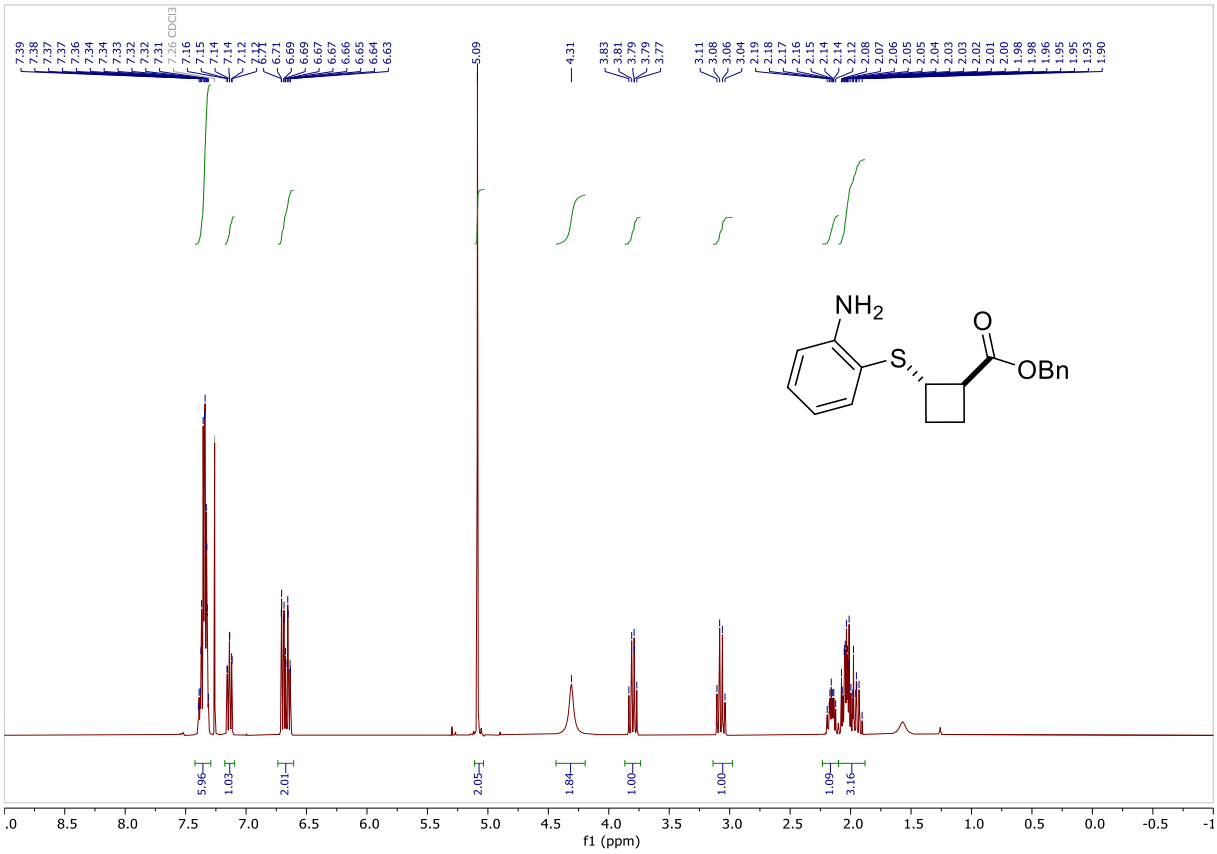
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3m)



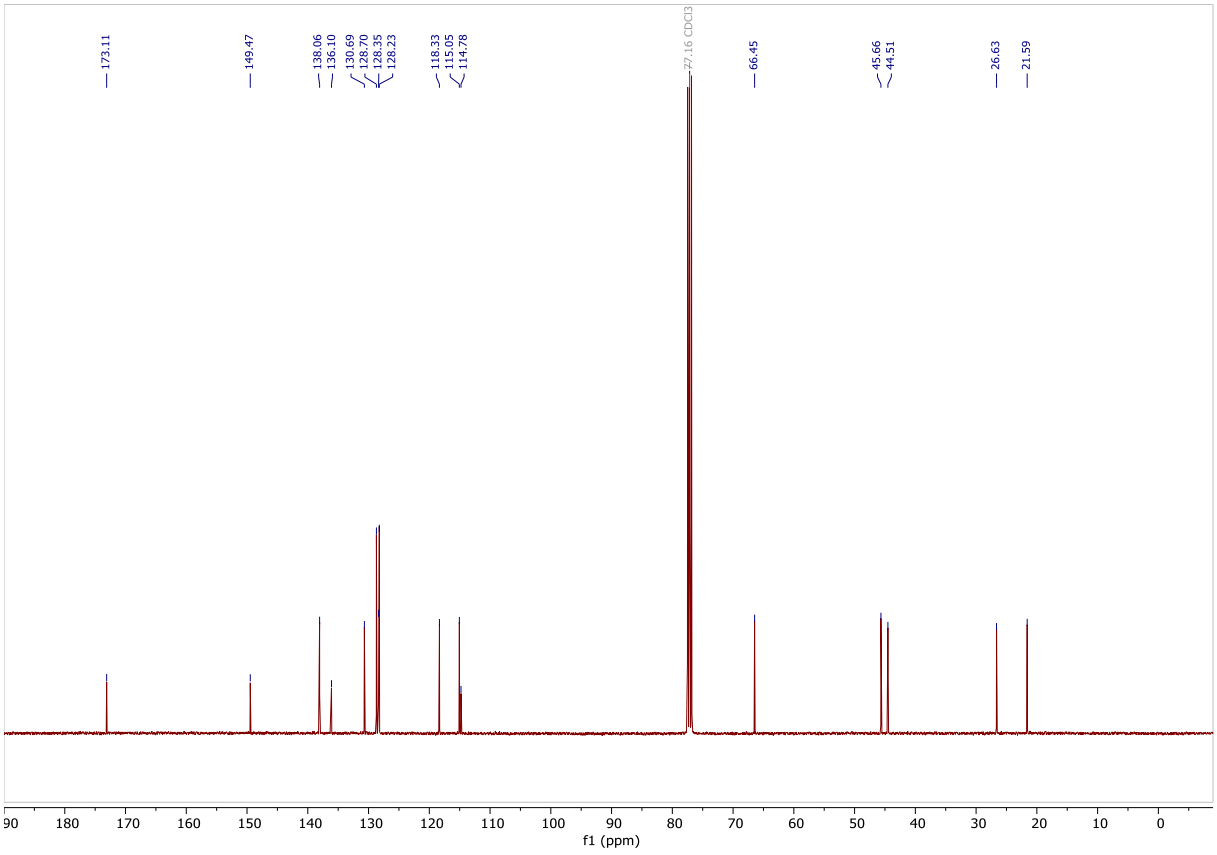

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3m)



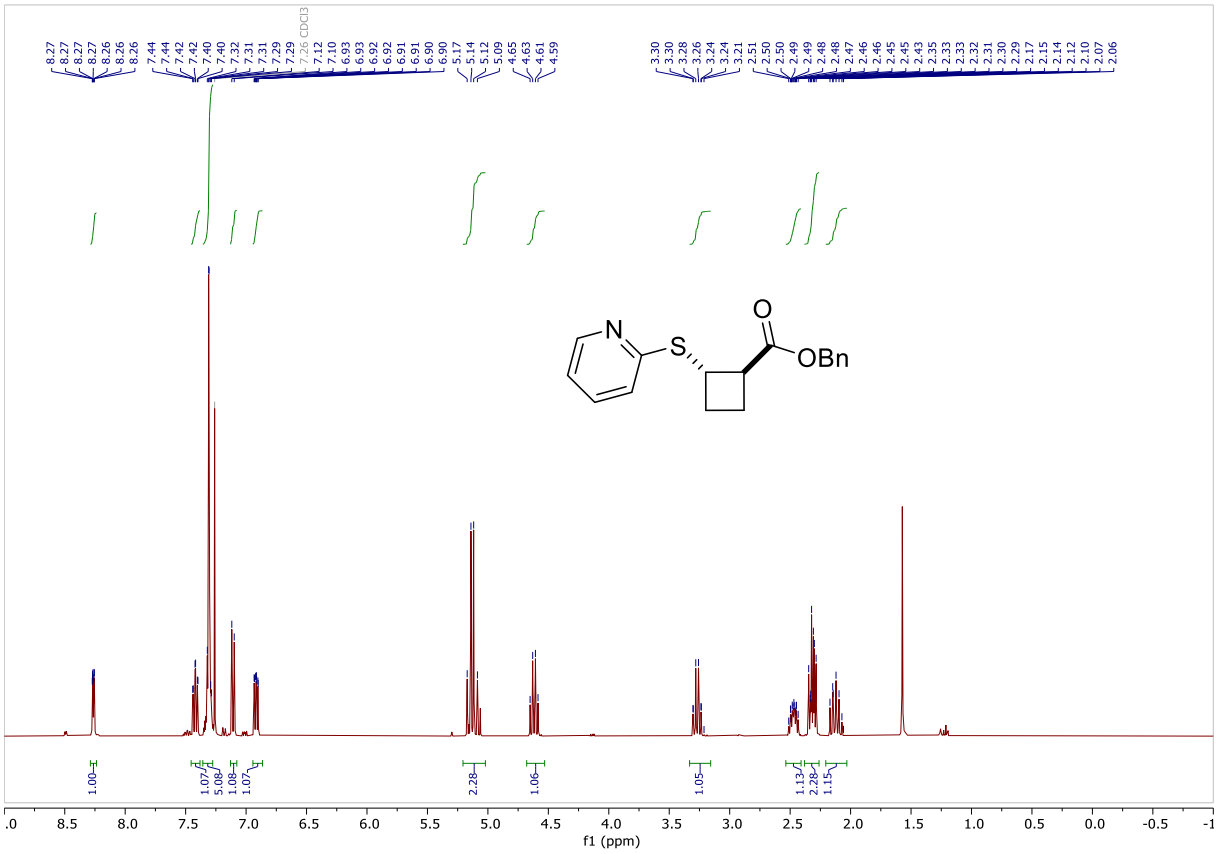
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3n)



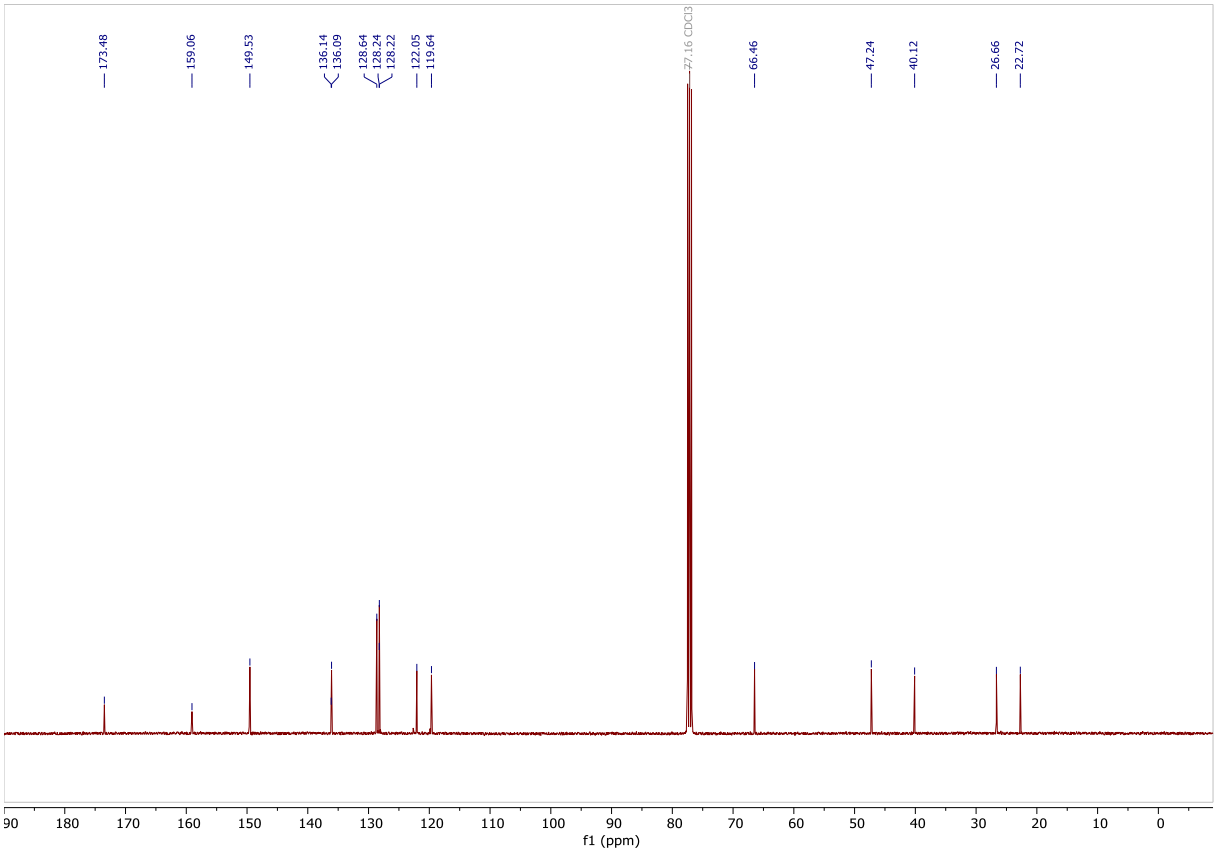

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3n)



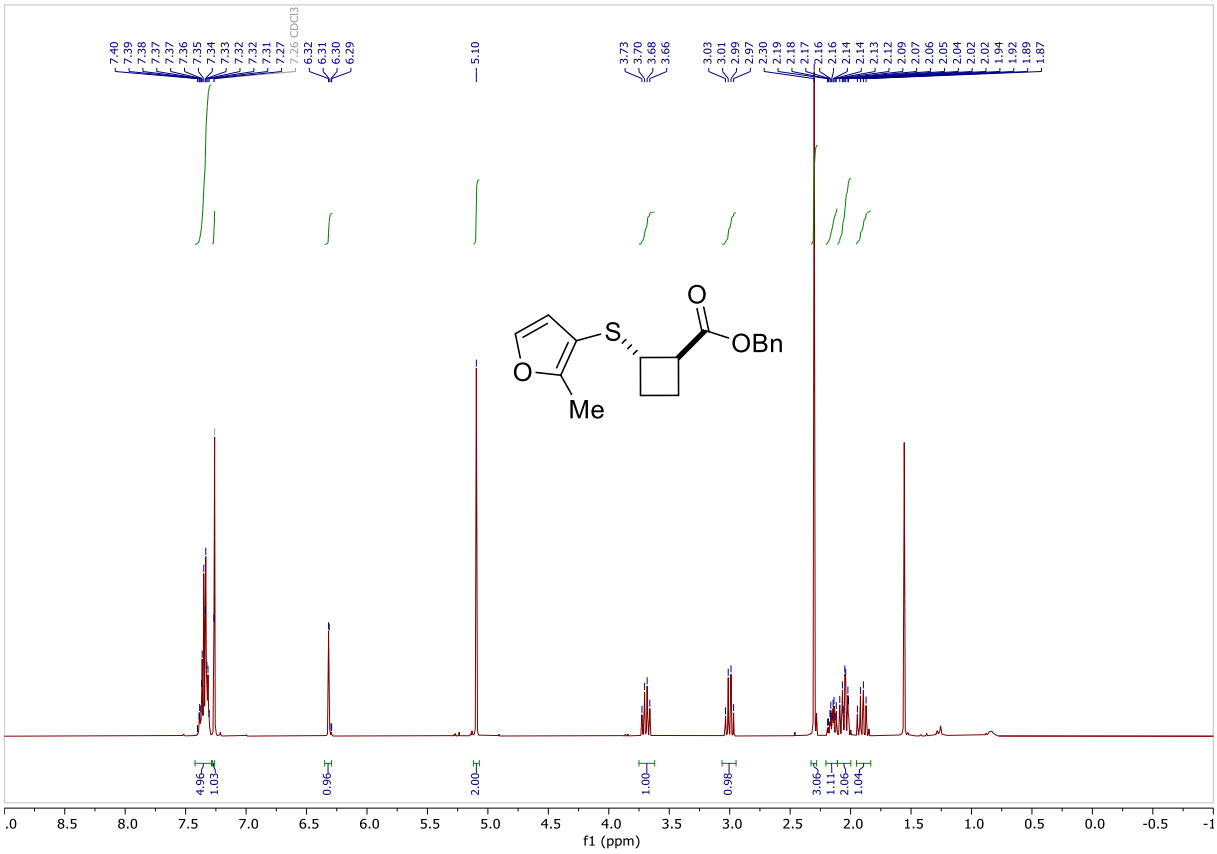
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3o)



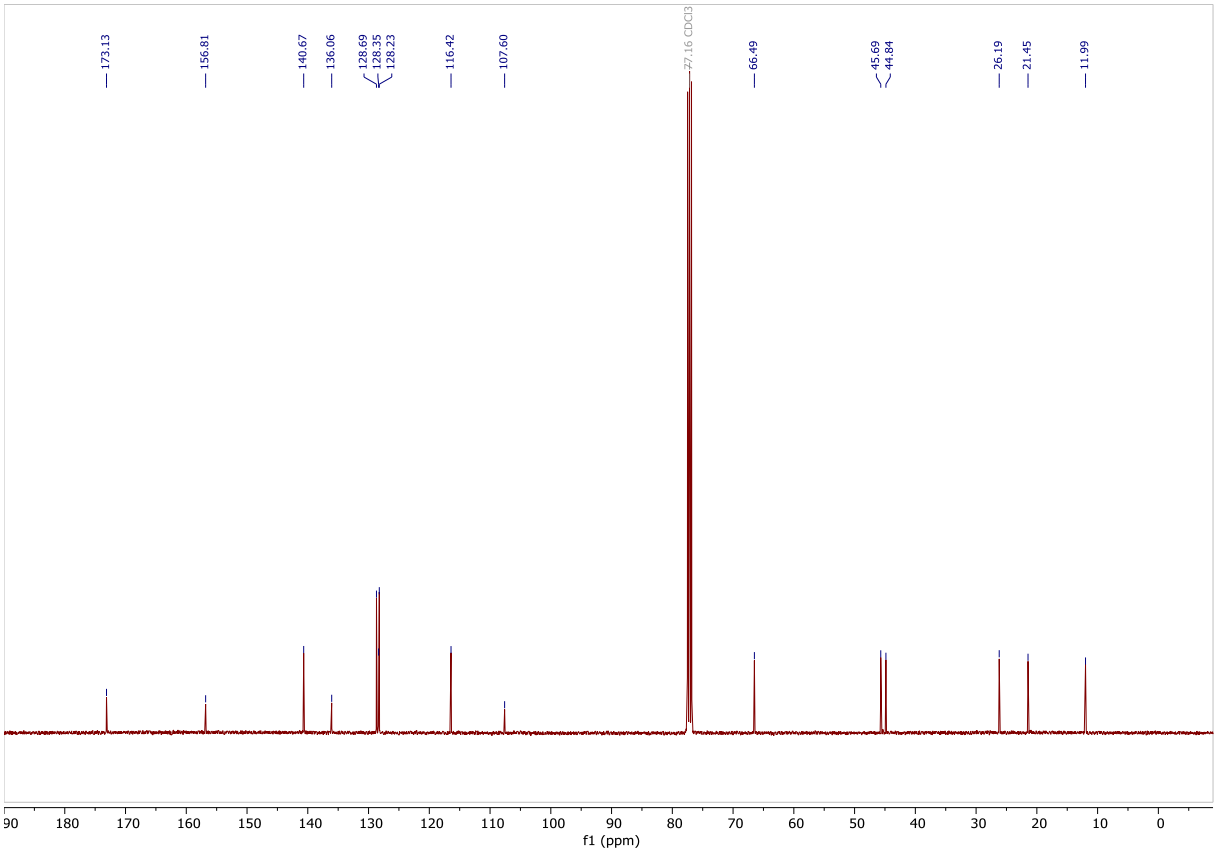

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3o)



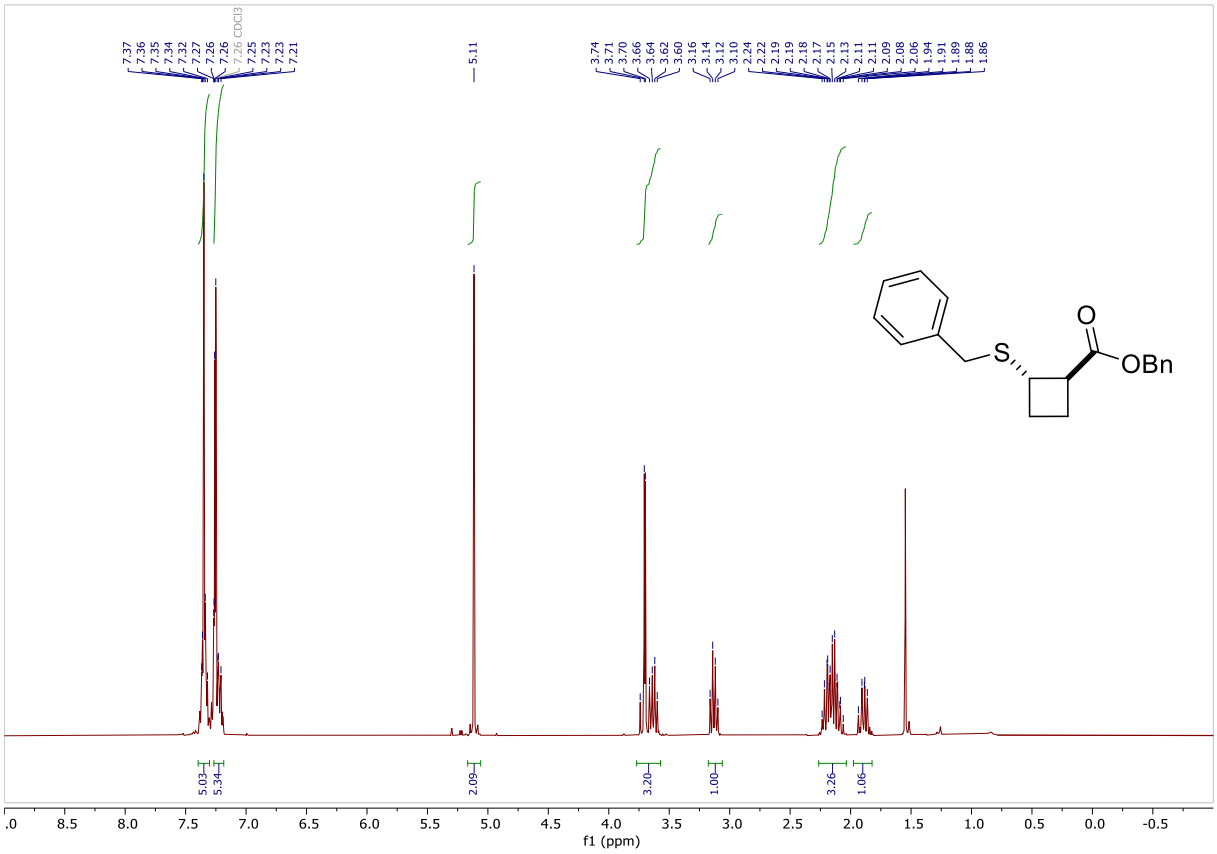
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3p)



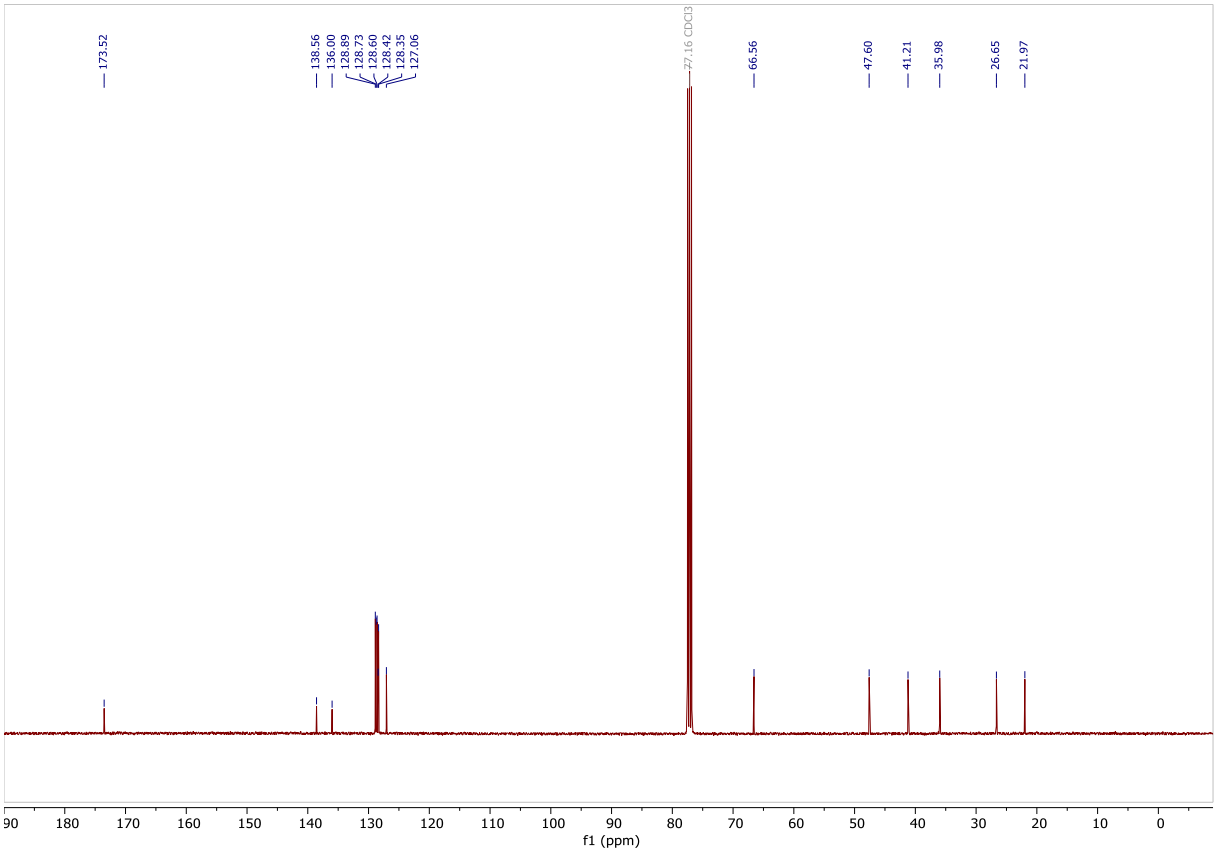

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3p)



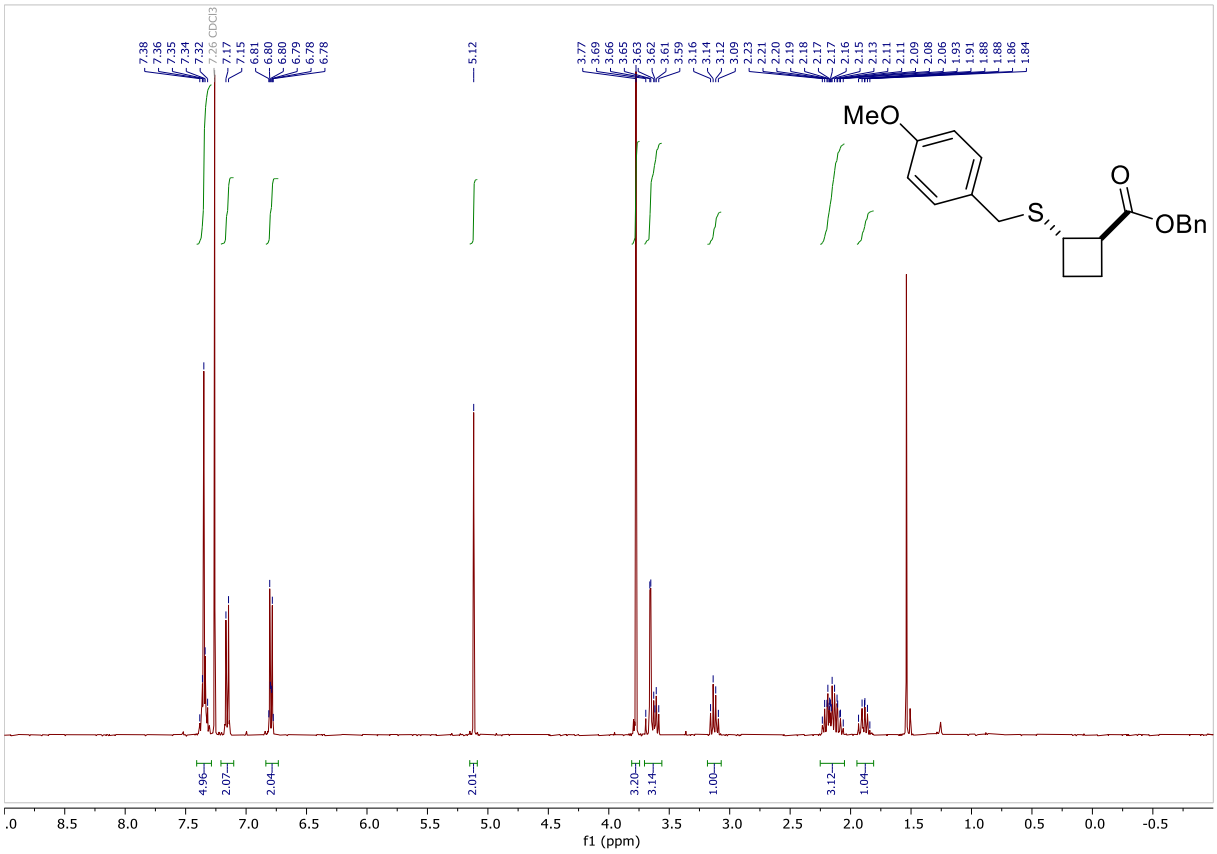
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3q)



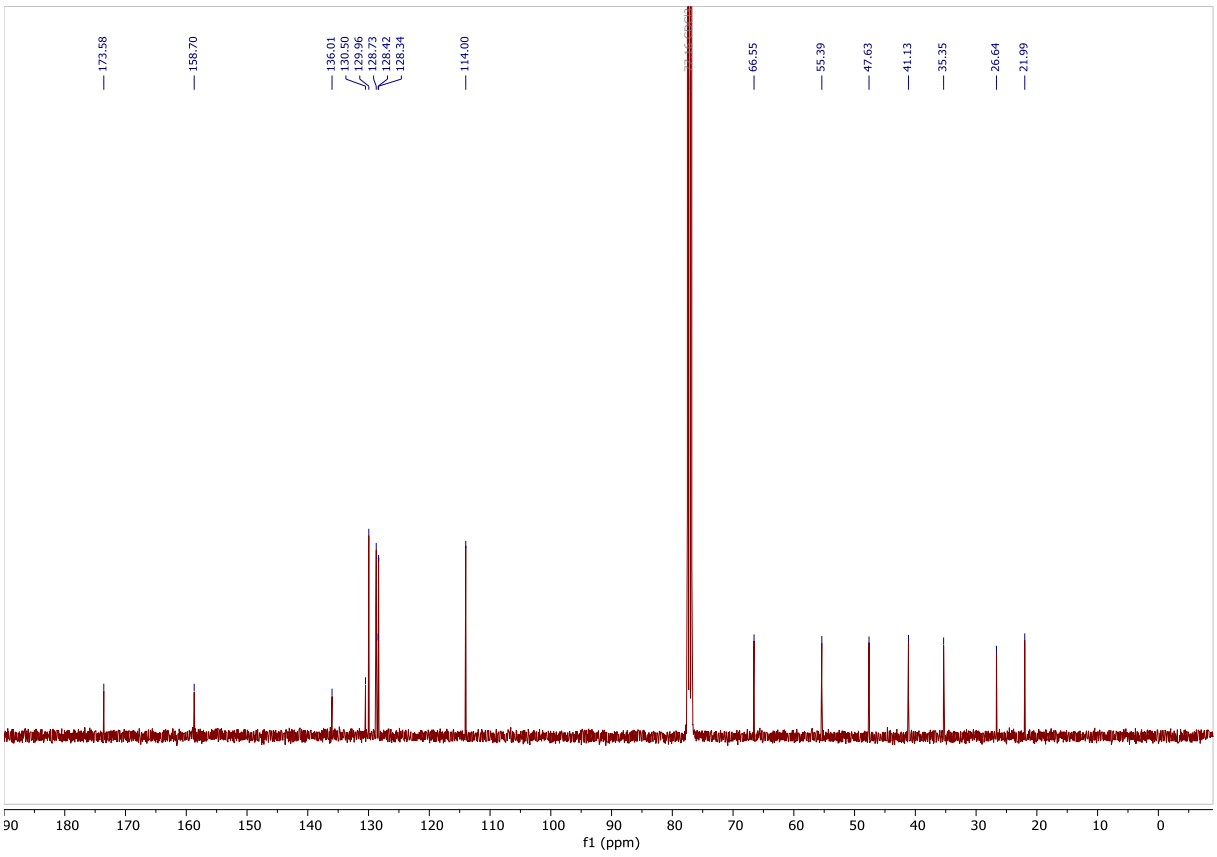

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3q)



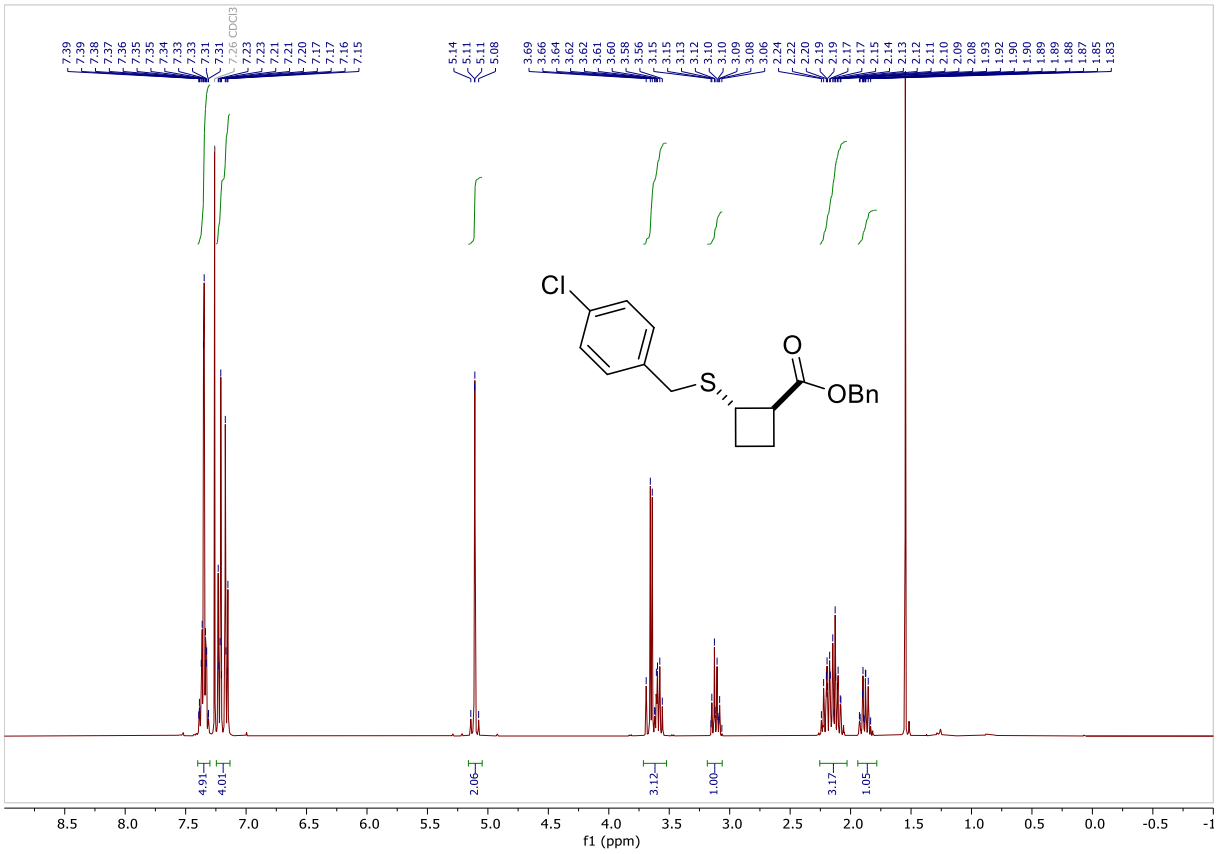
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3r)



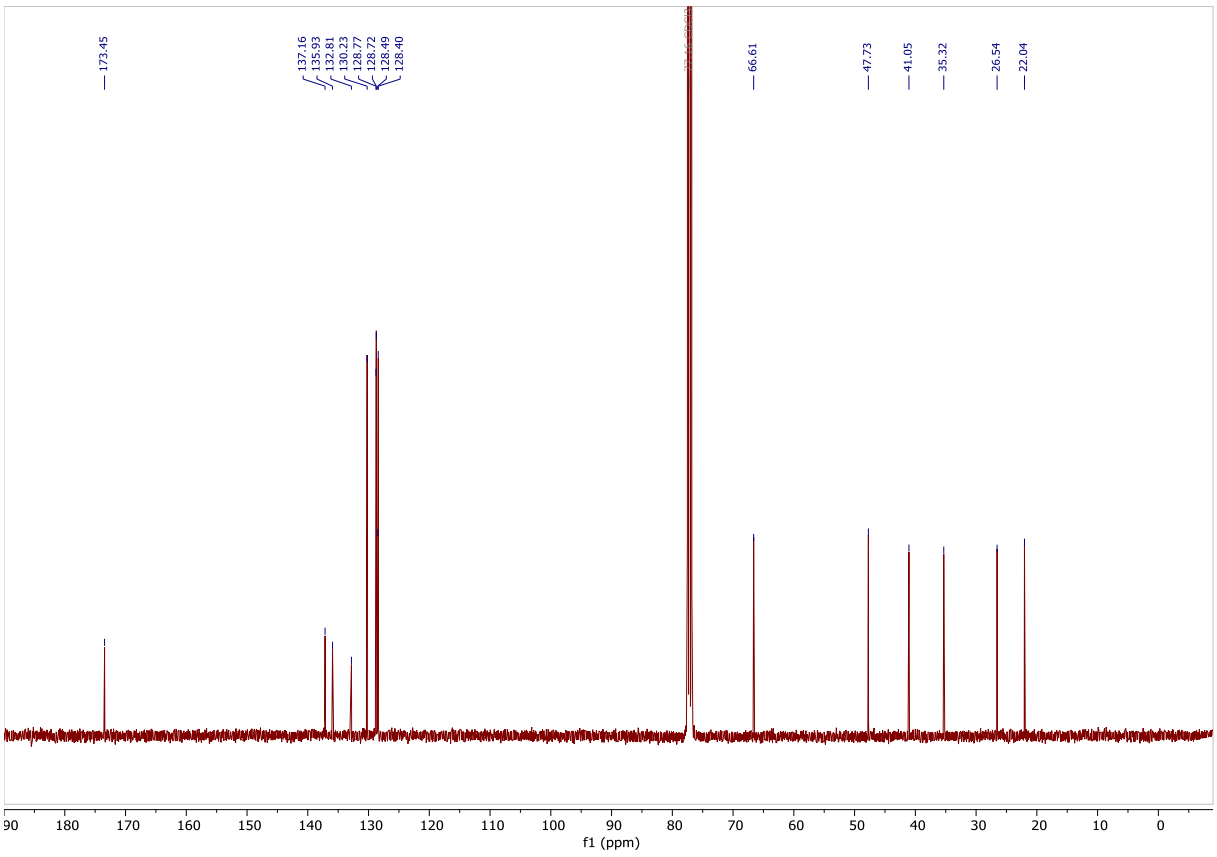

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3r)



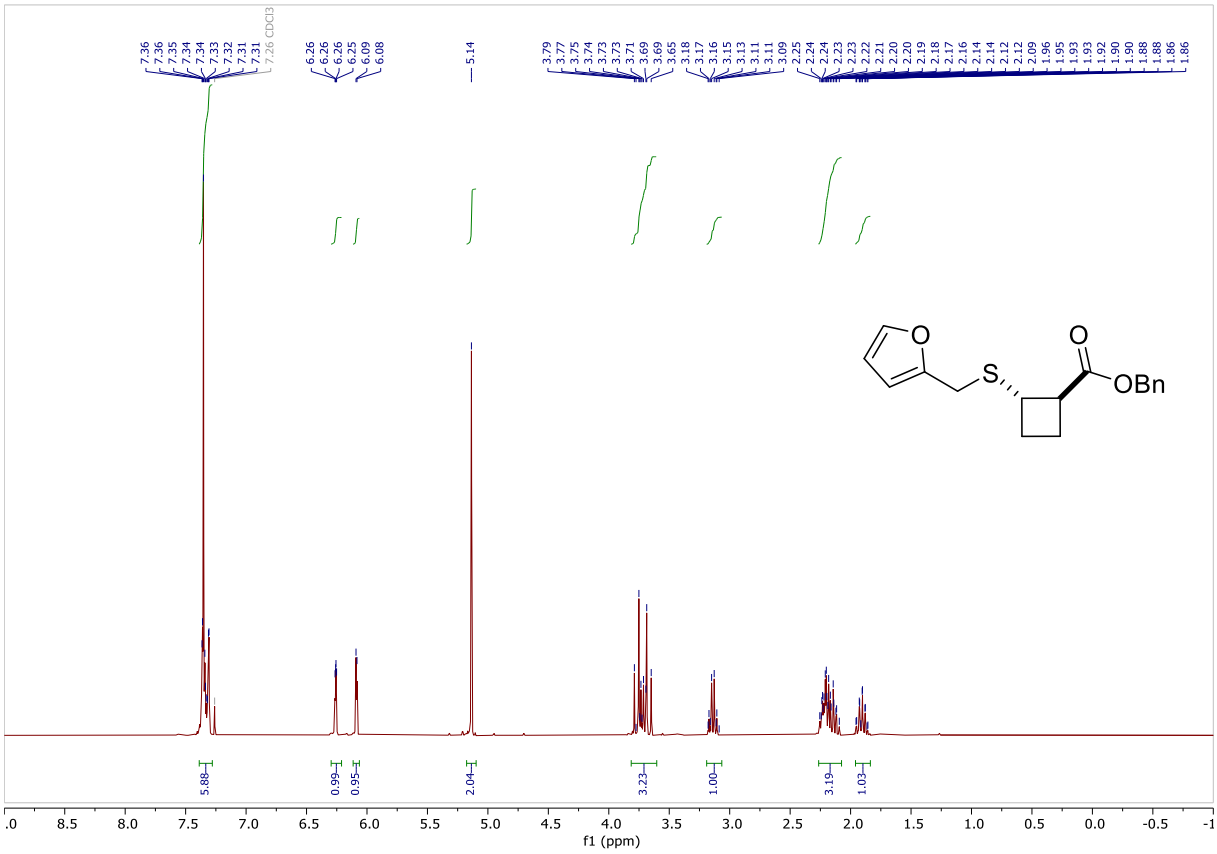
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3s)



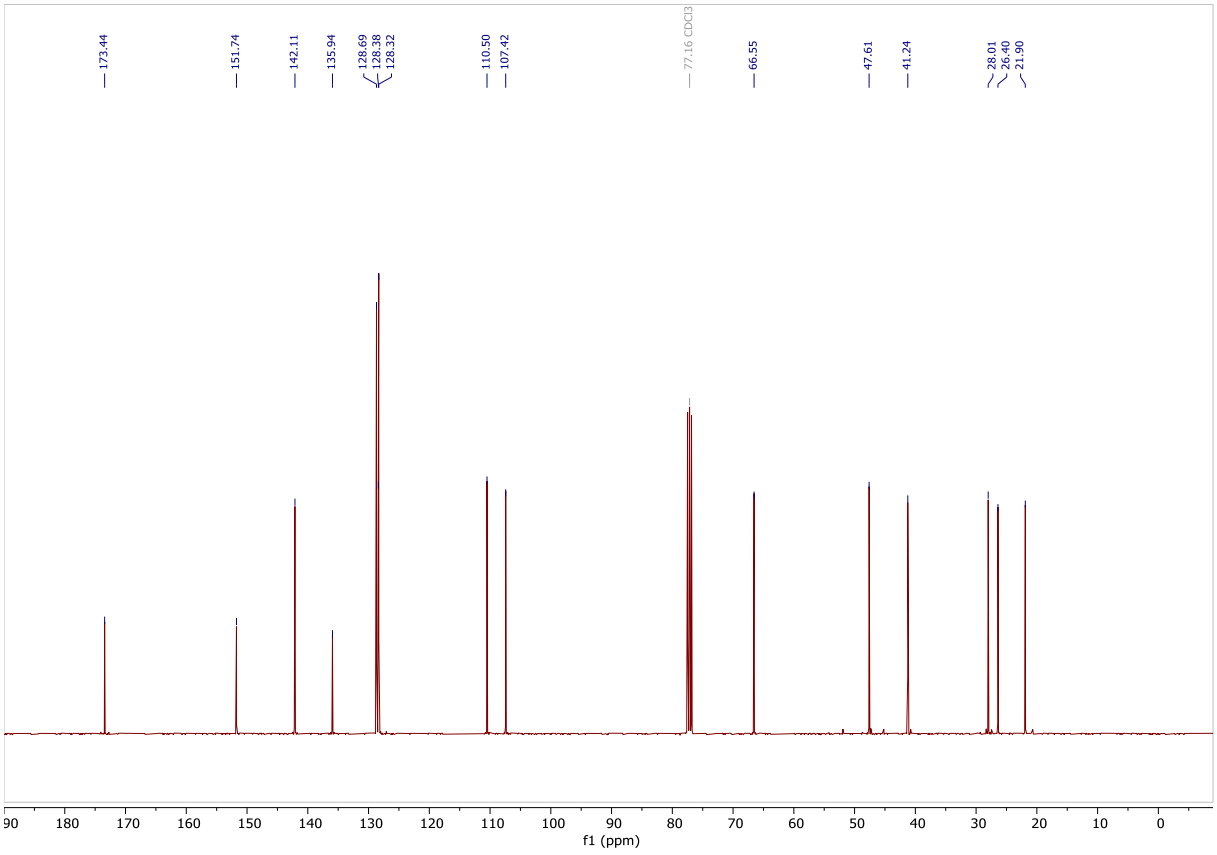

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3s)



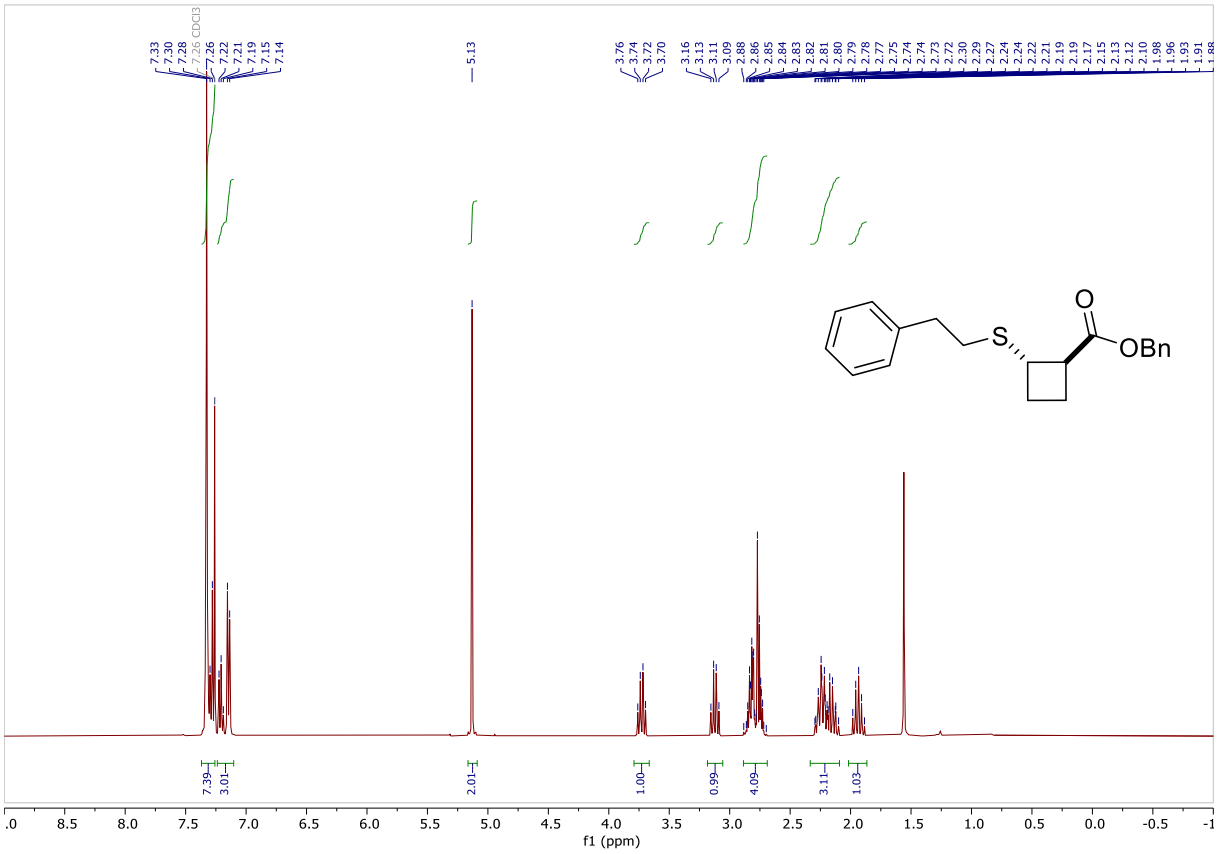
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3t)



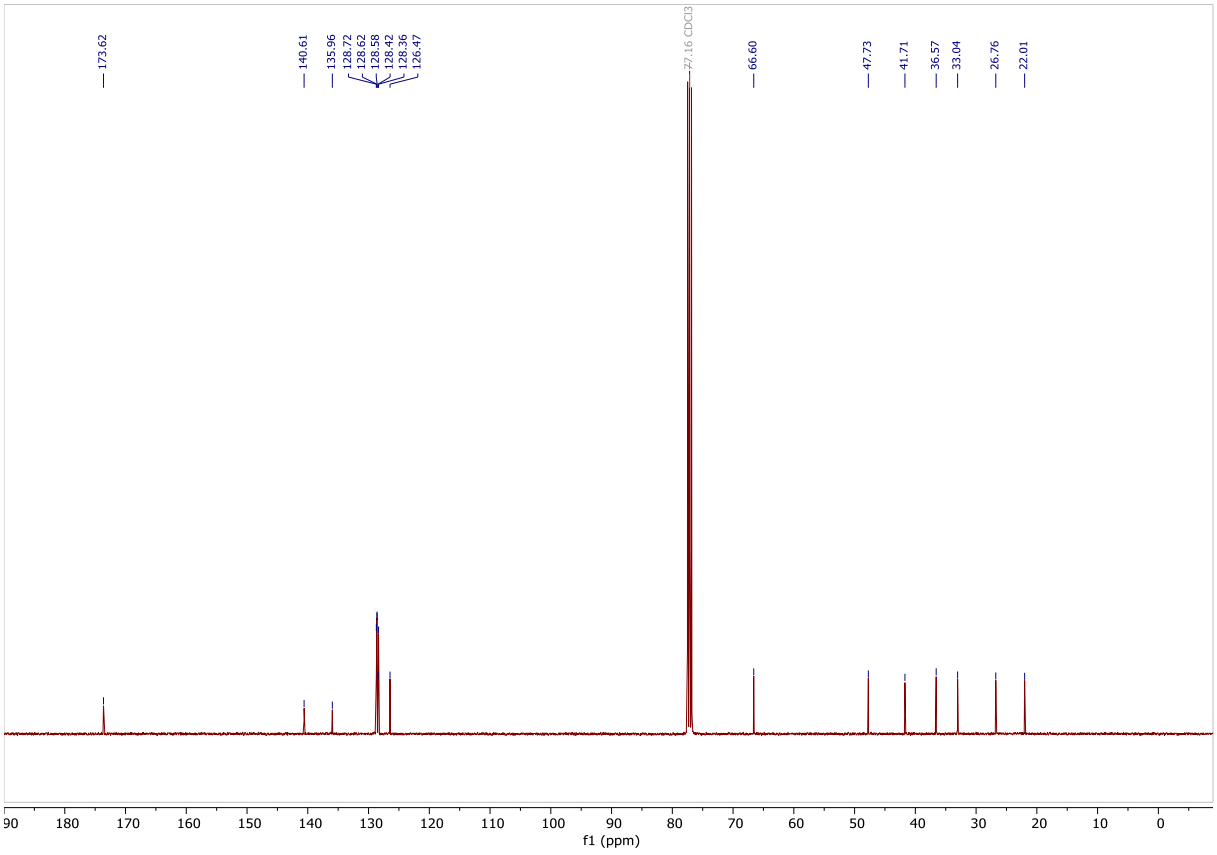

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3t)



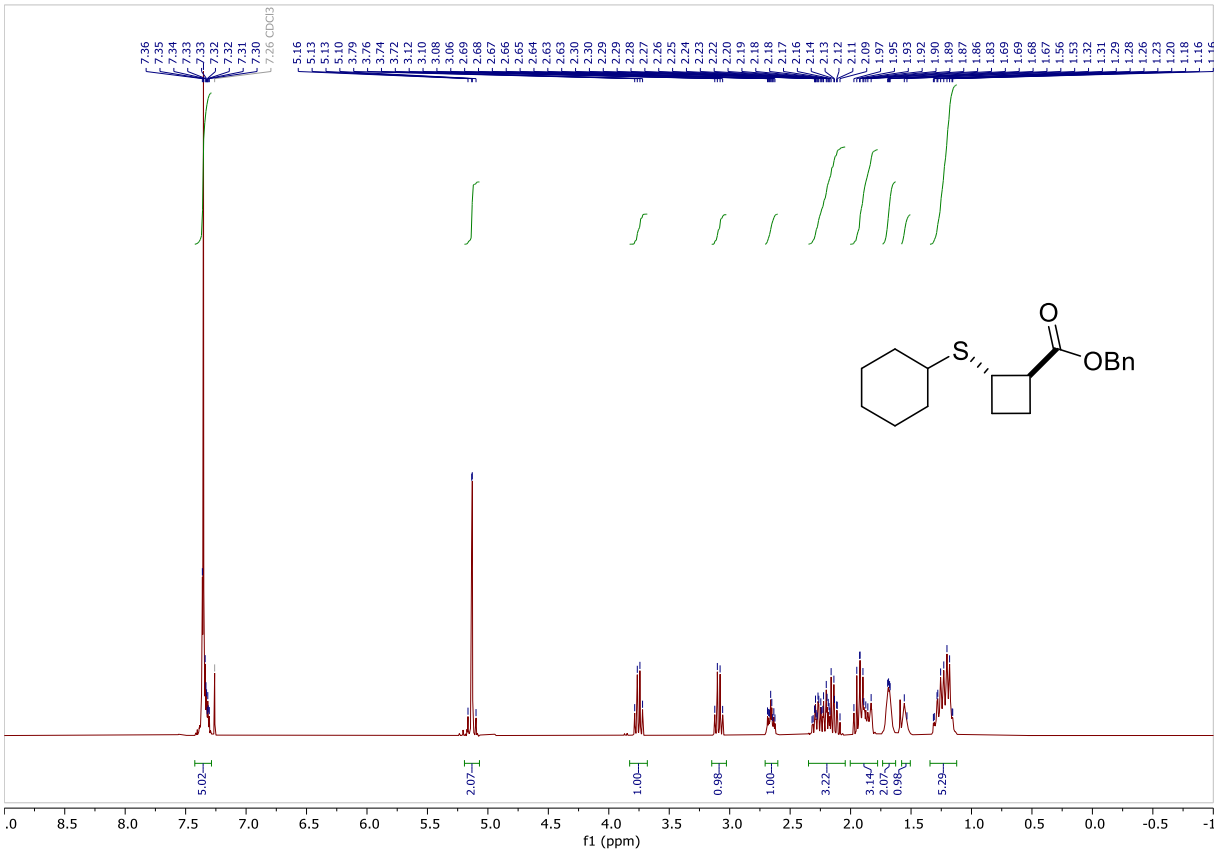
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3u)



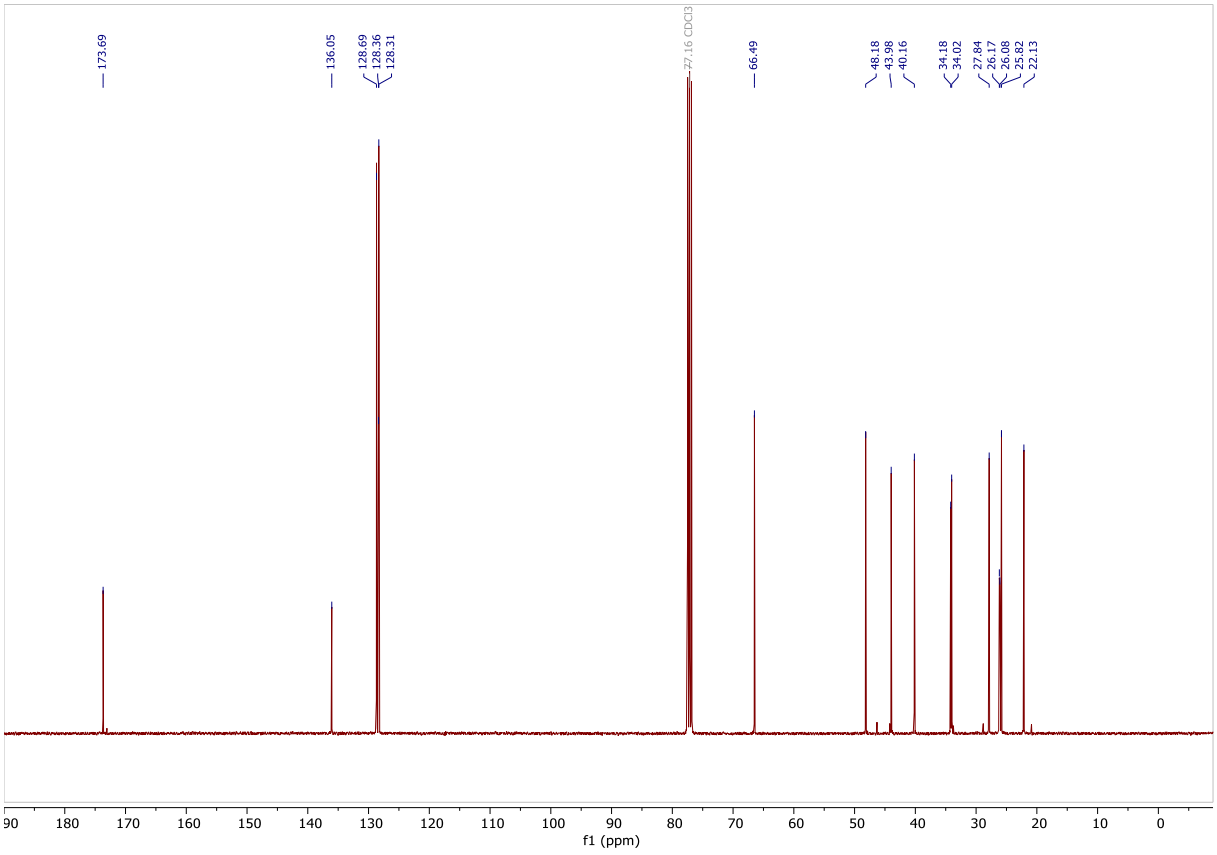

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3u)



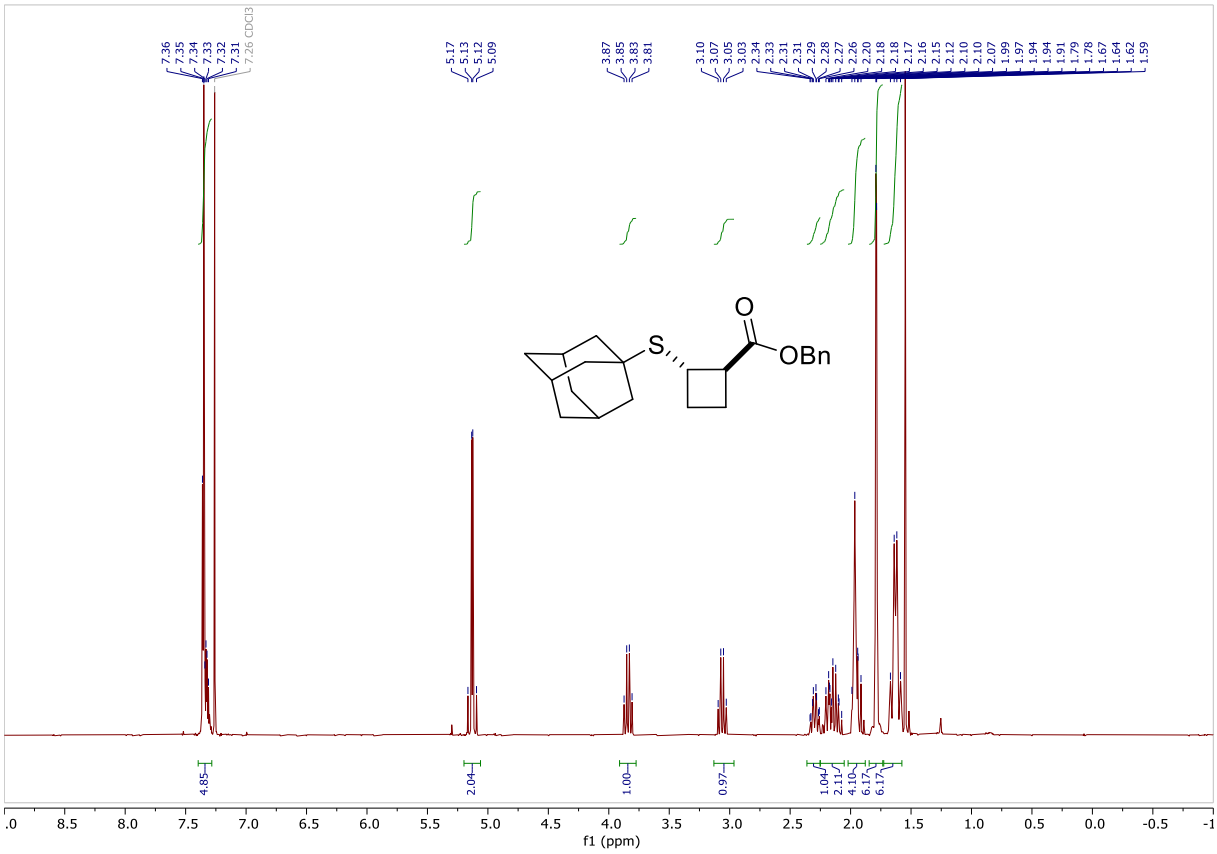
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3v)



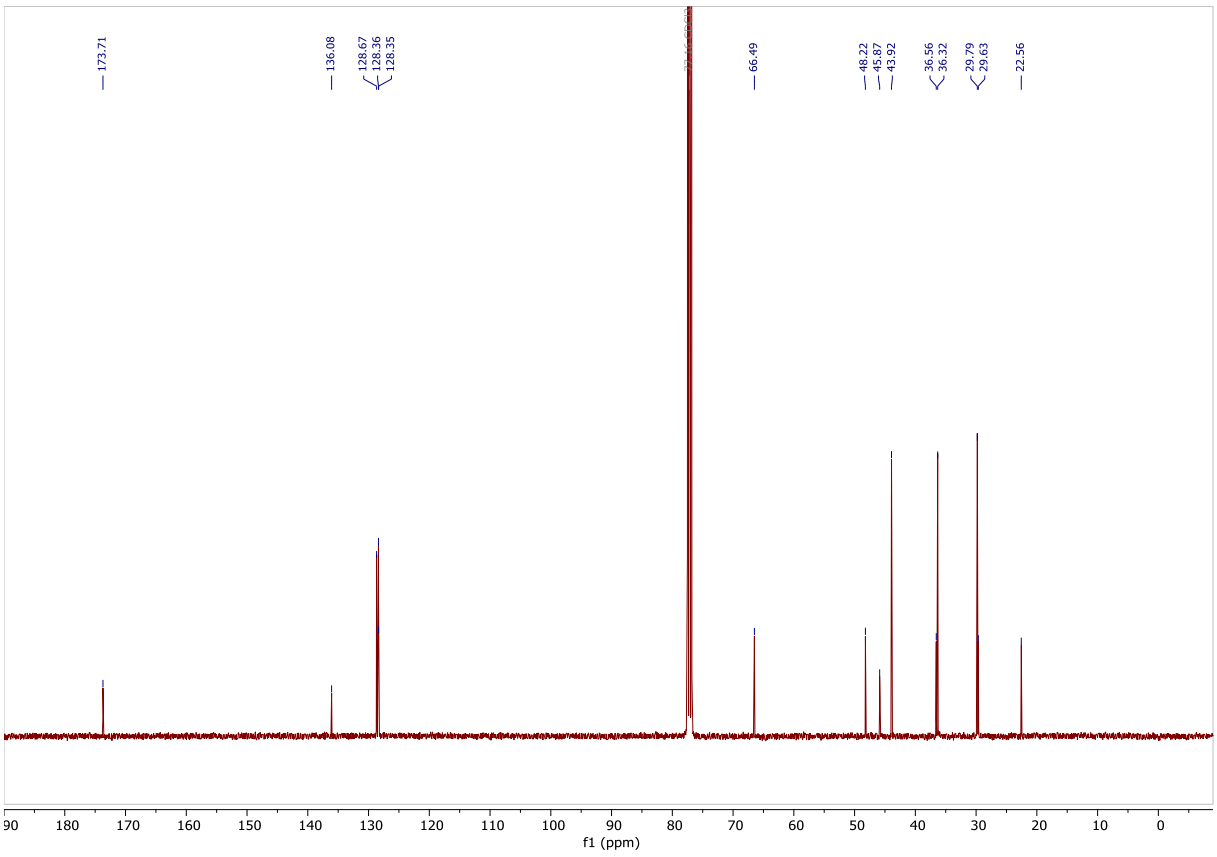

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3v)



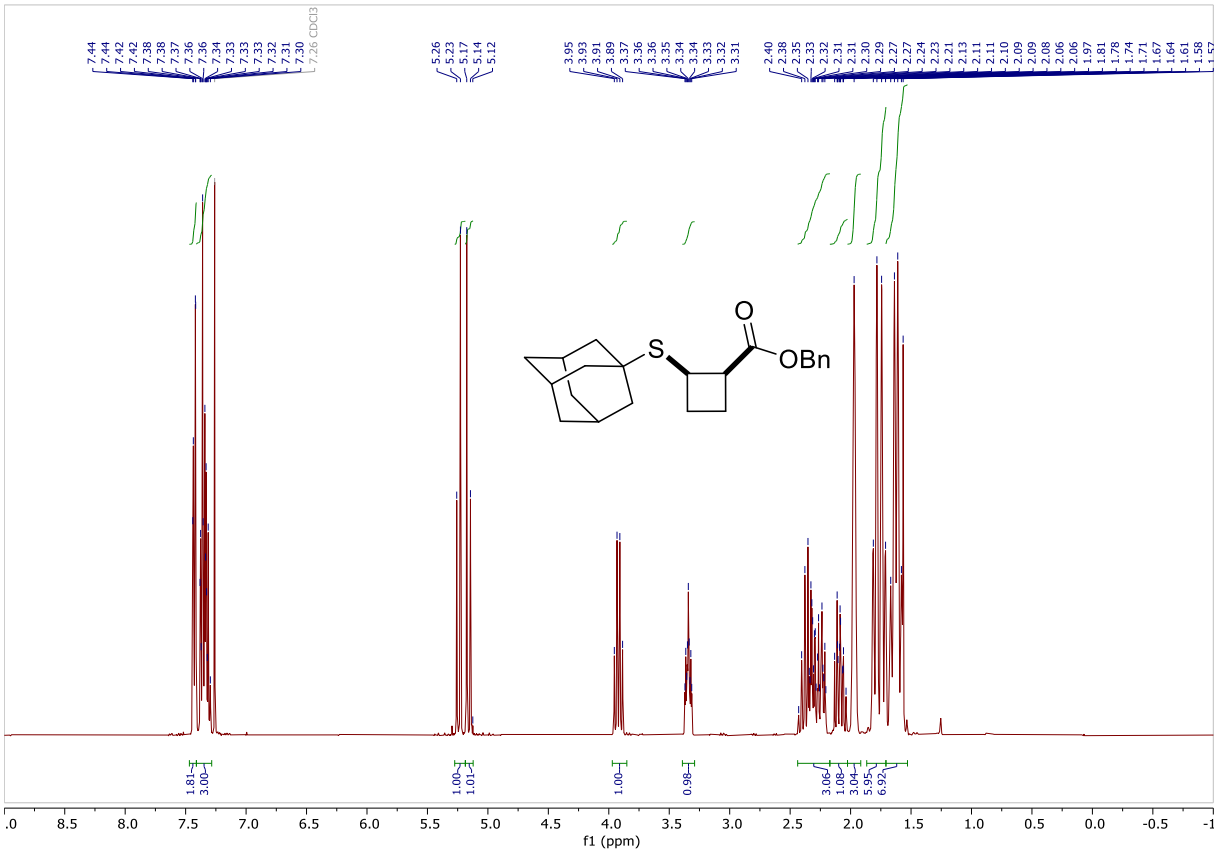
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3w)



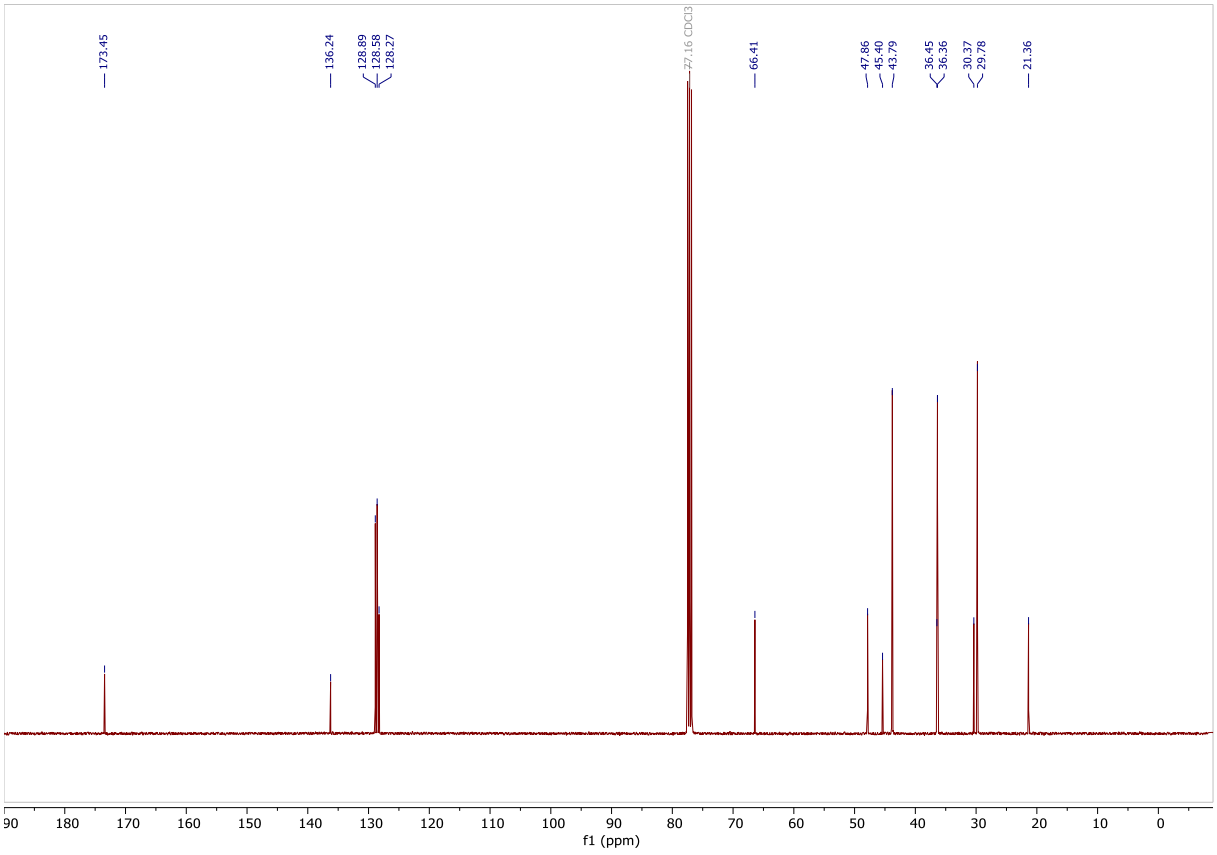

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3w)



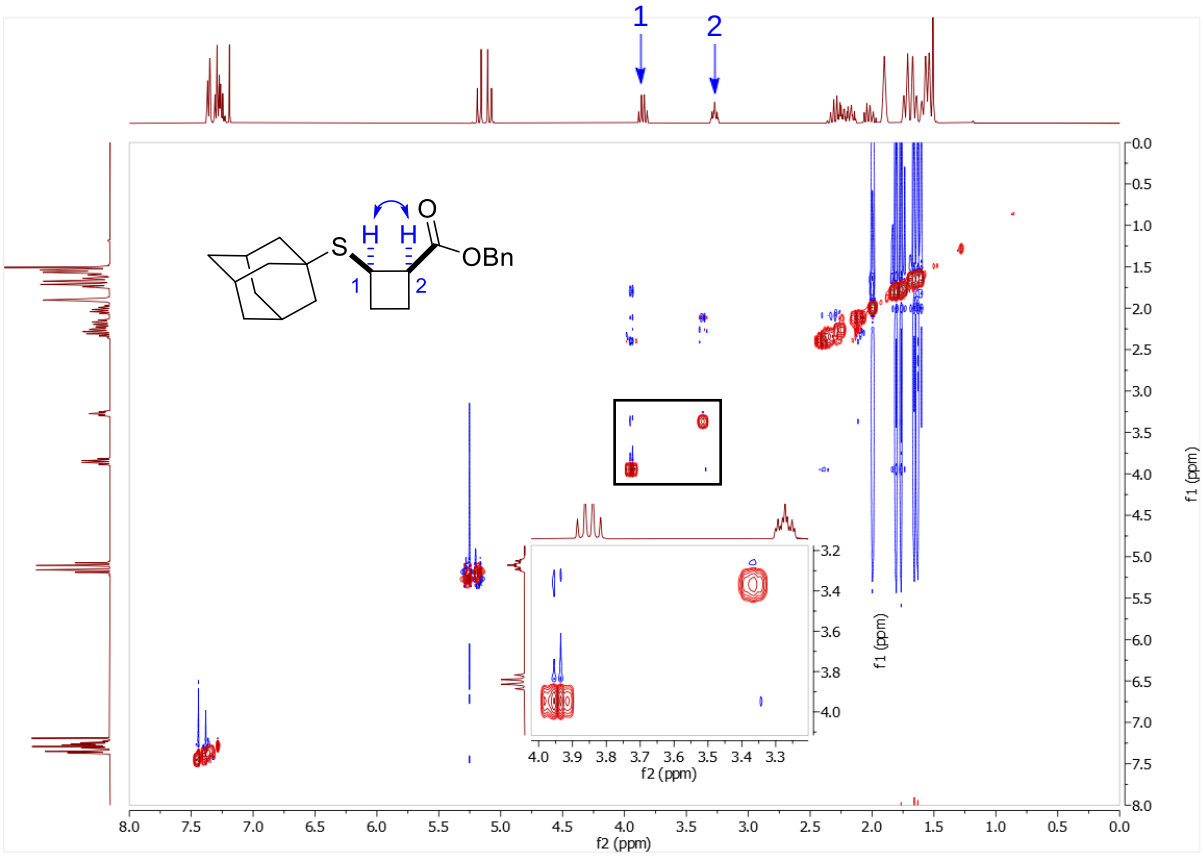
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3'w)



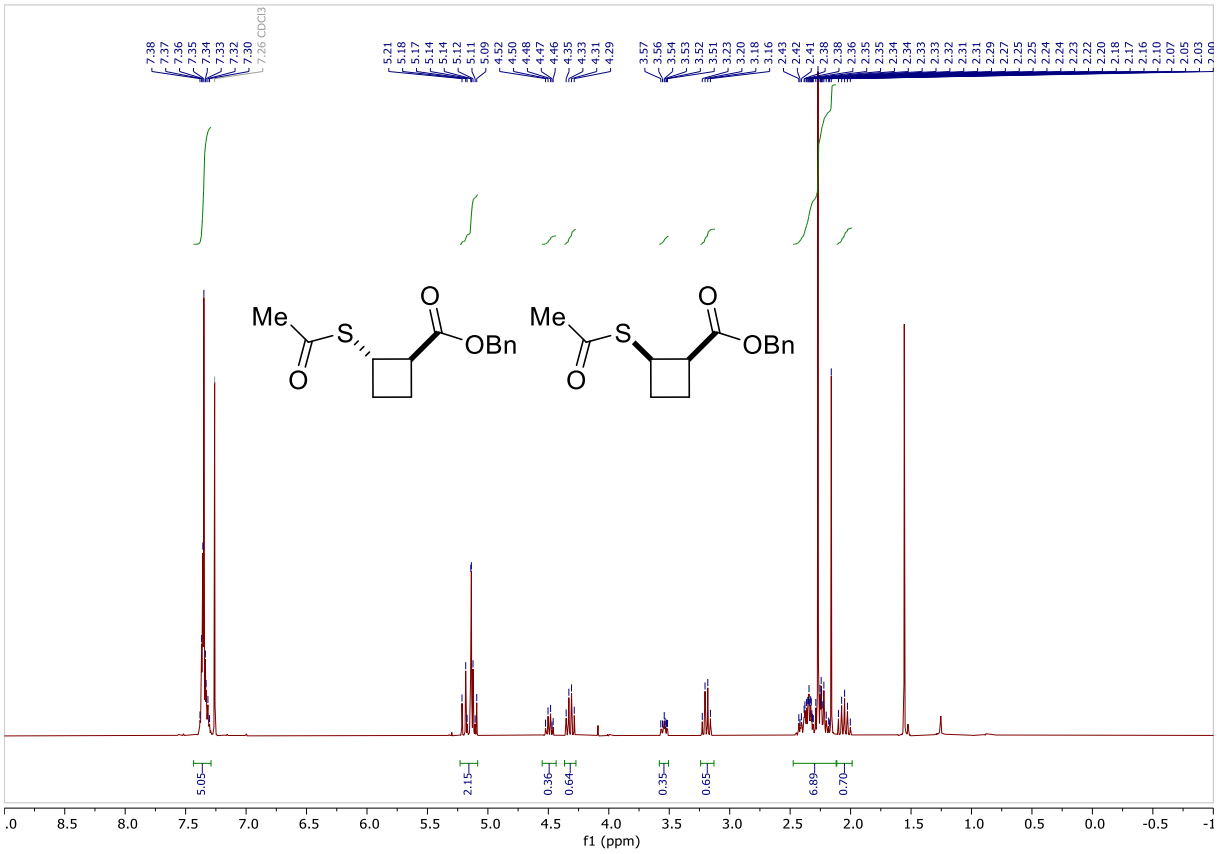

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3'w)



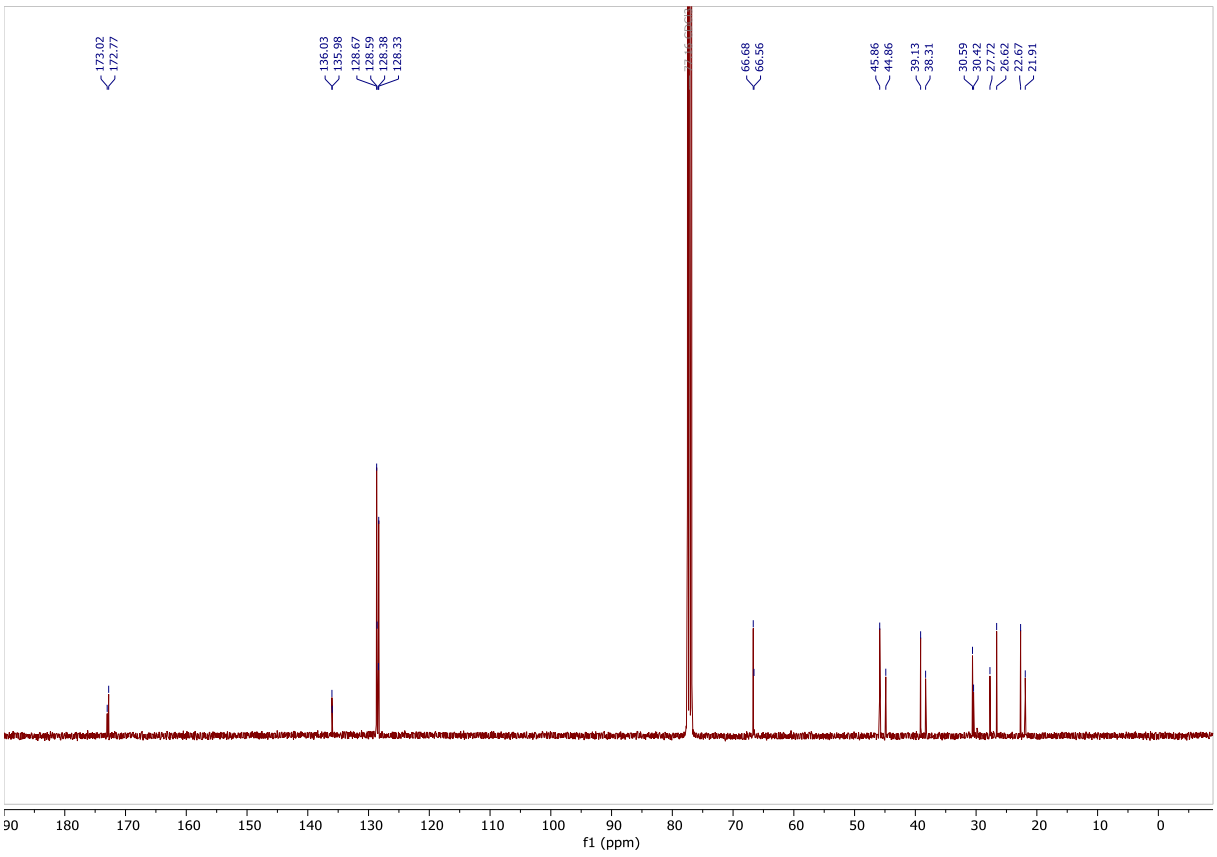
**2D-NOESY (400 MHz, chloroform-*d*) (3'w)**



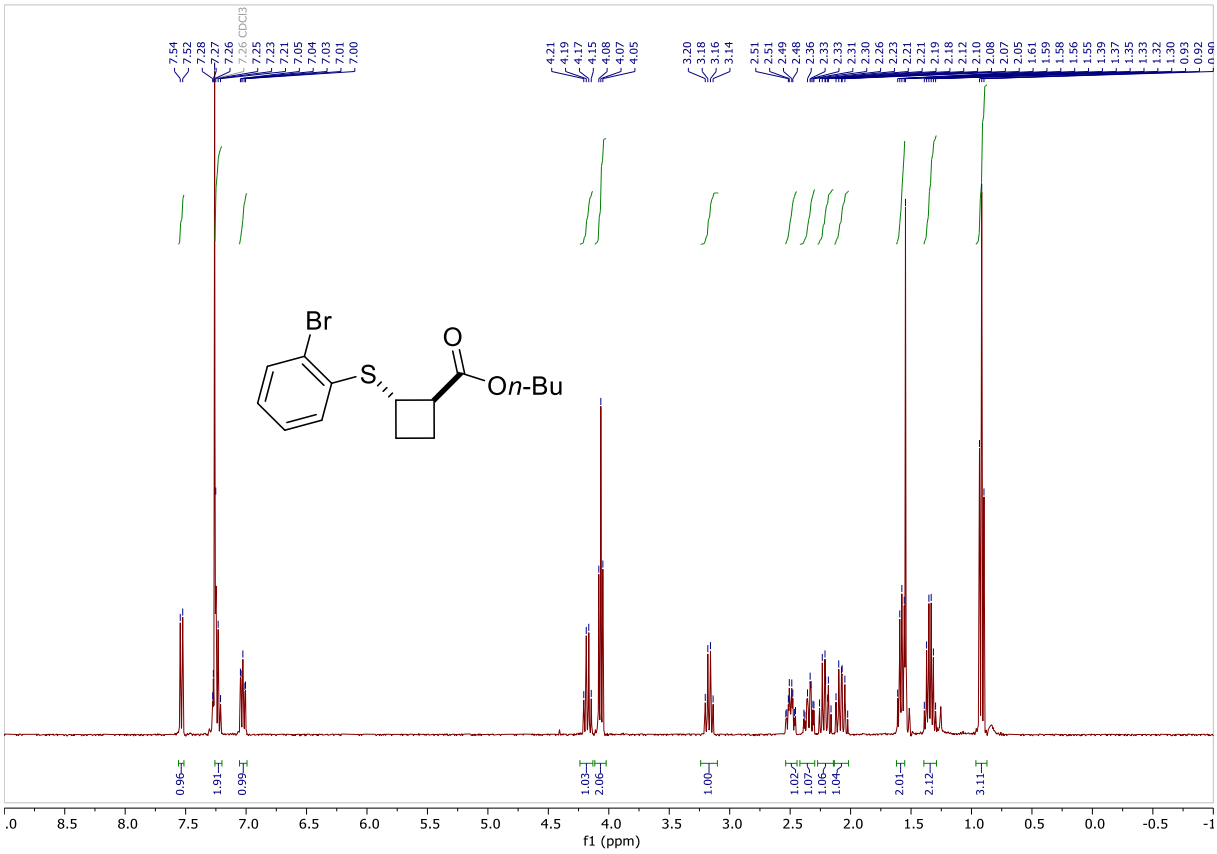
**$^{1}$H-NMR (400 MHz, chloroform-*d*) (3x:3'x 65:35 mixture of diastereoisomers)**



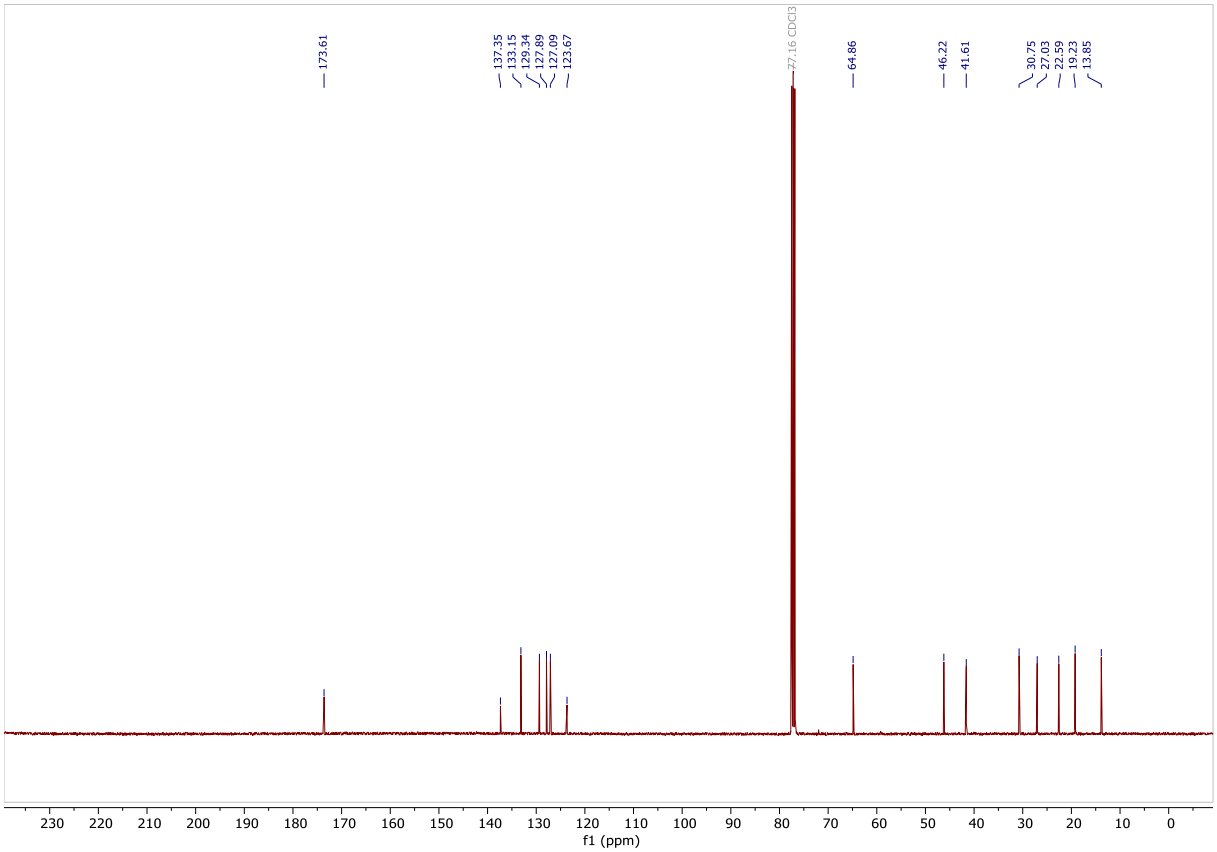

**$^{13}$C-NMR (101 MHz, chloroform-*d*) (3x:3'x 65:35 mixture of diastereoisomers)**



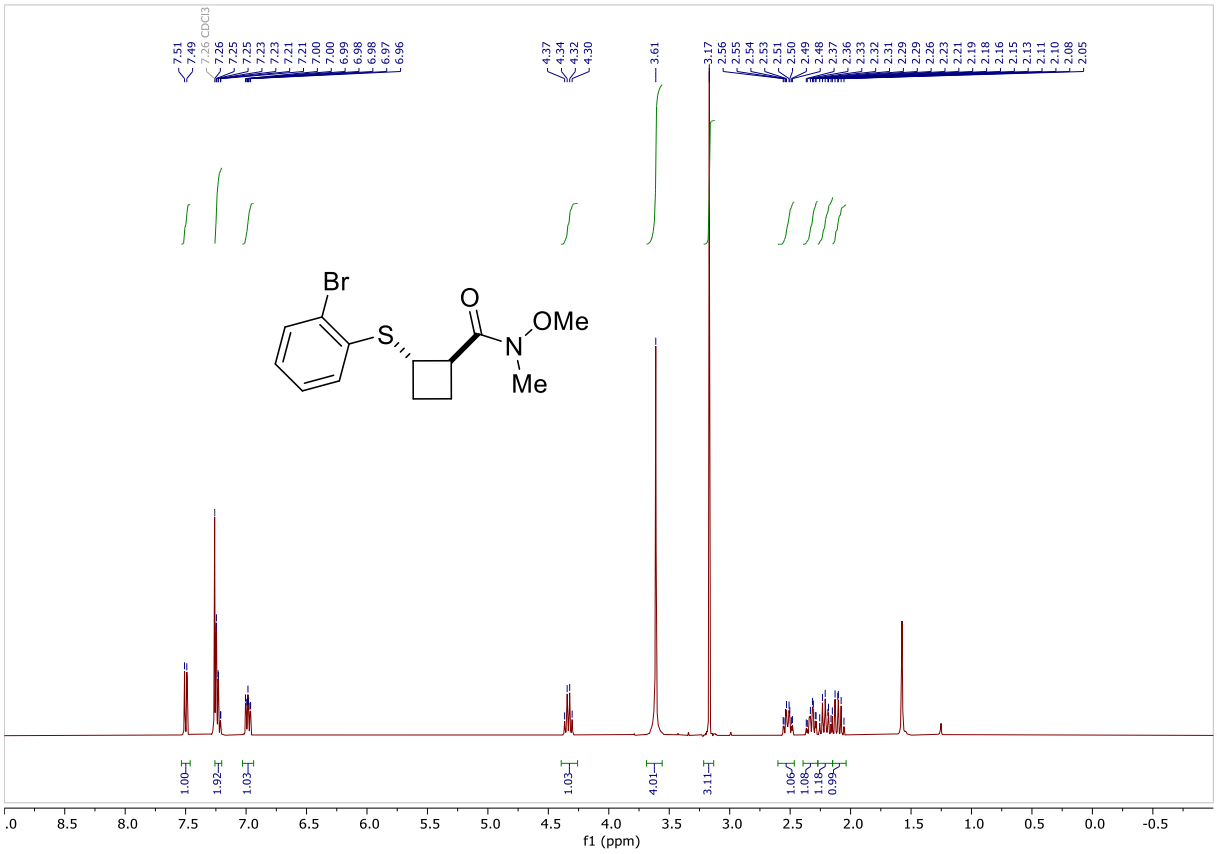
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3y)



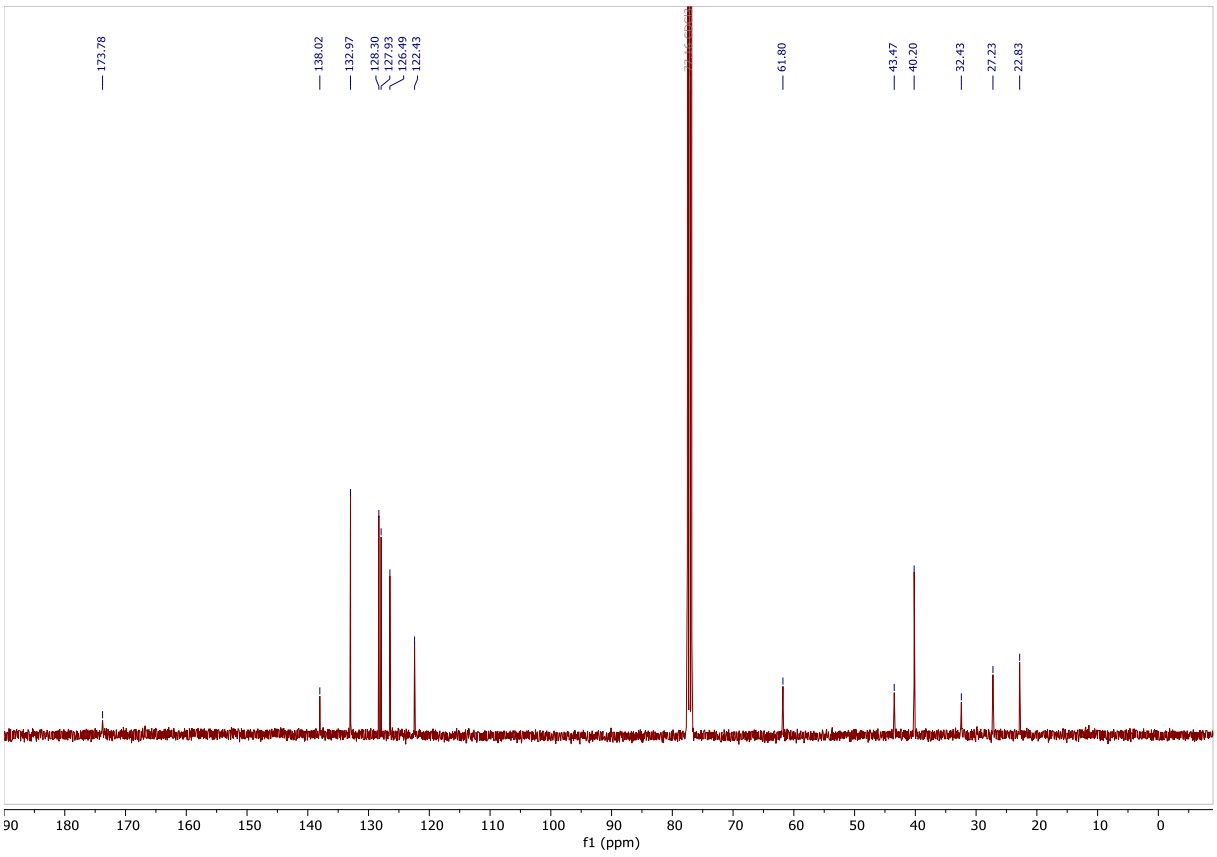

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3y)



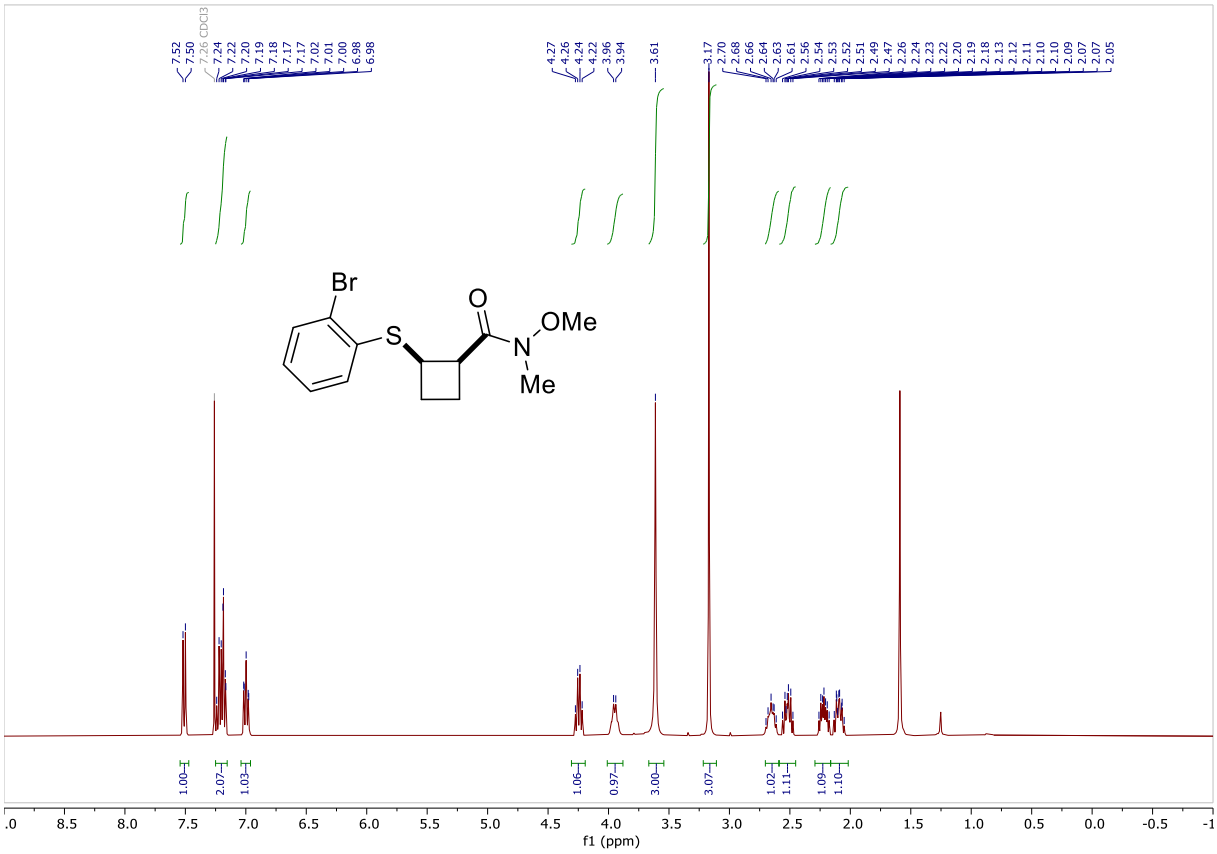
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3z)



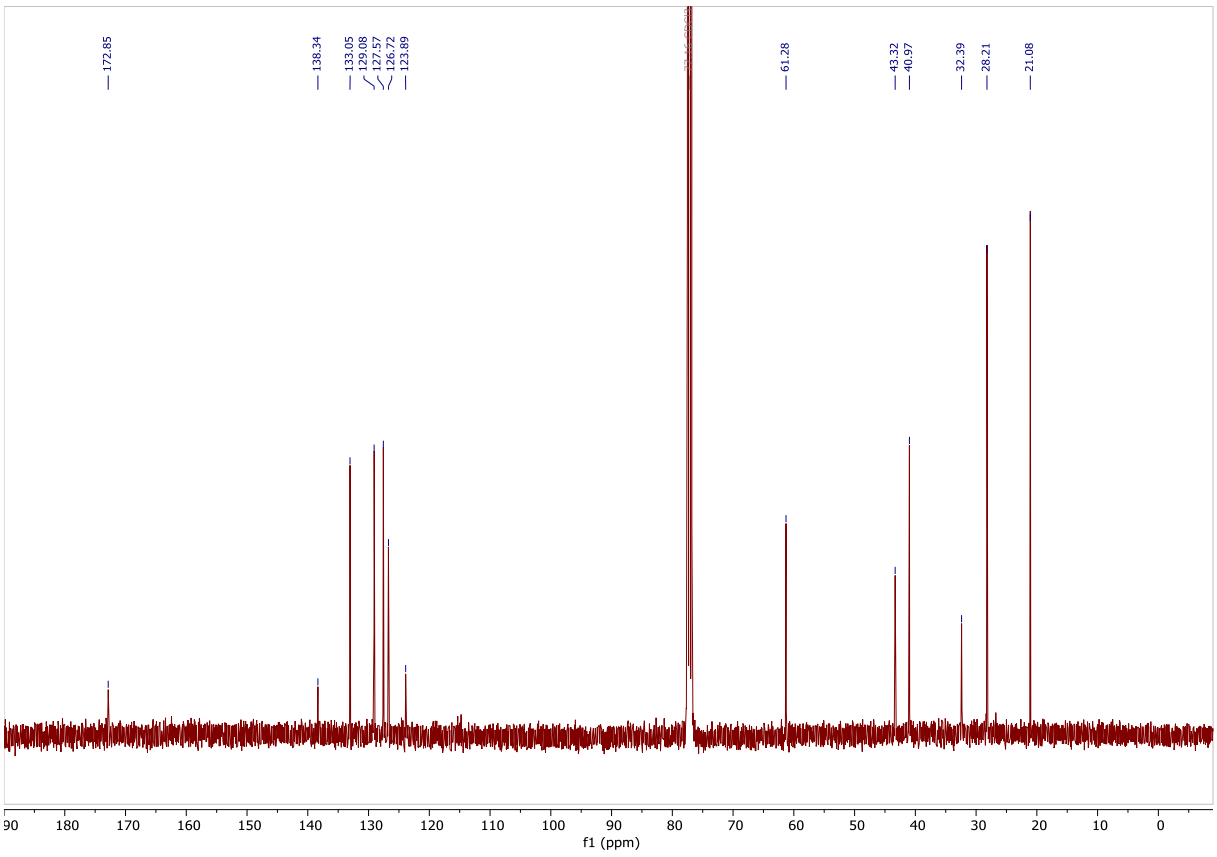

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3z)



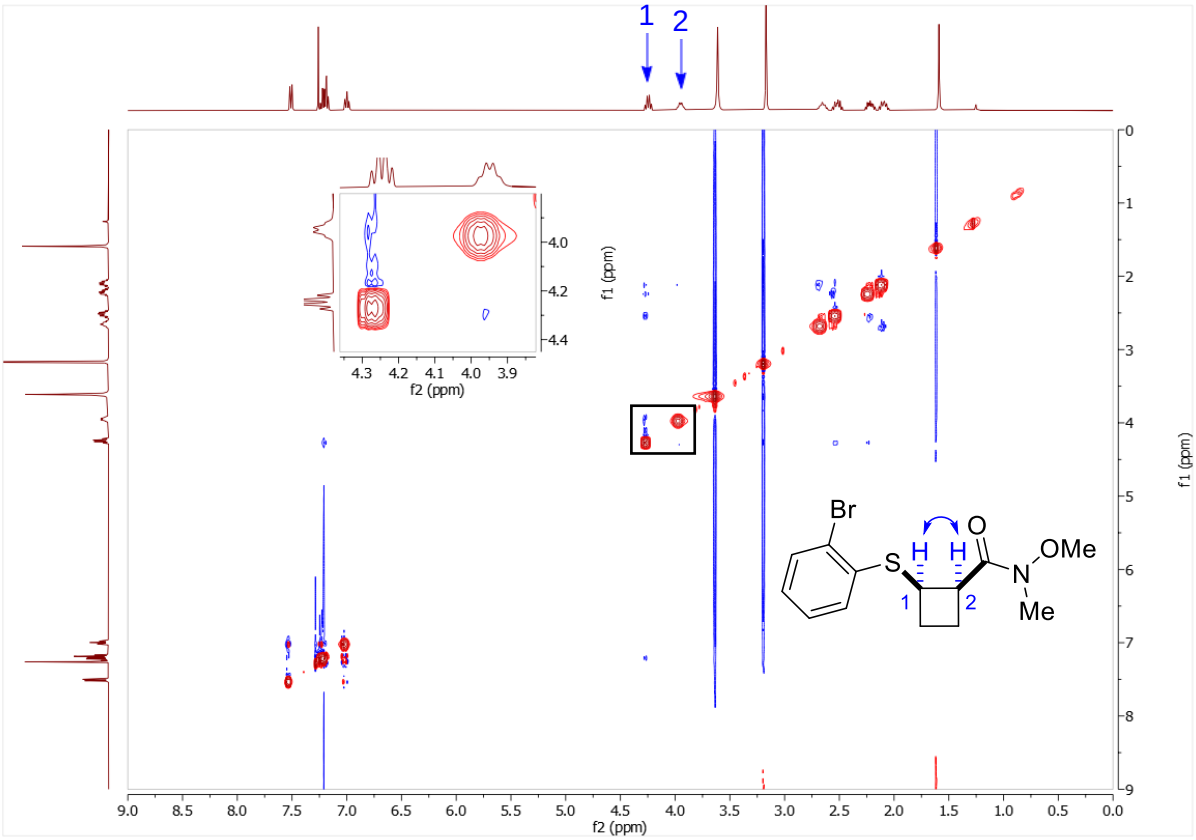
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3'z)



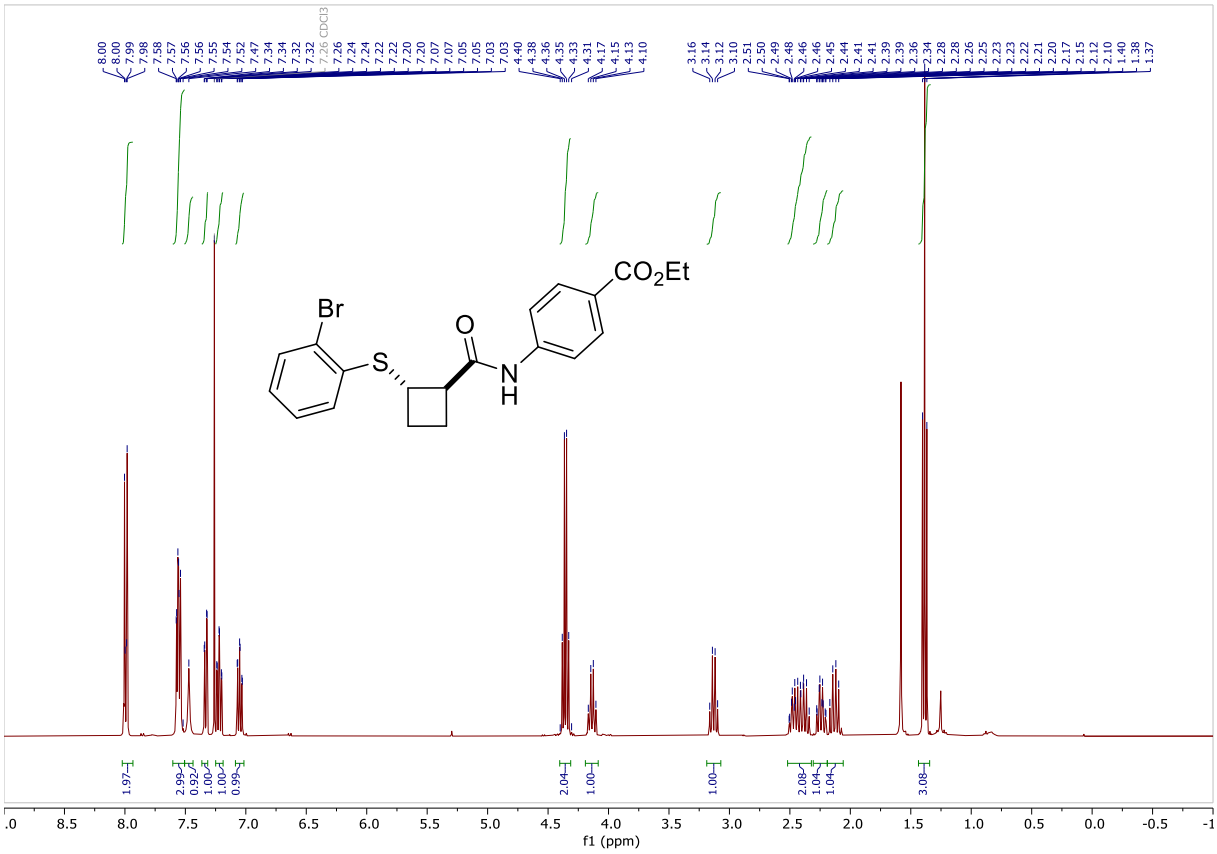

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3'z)



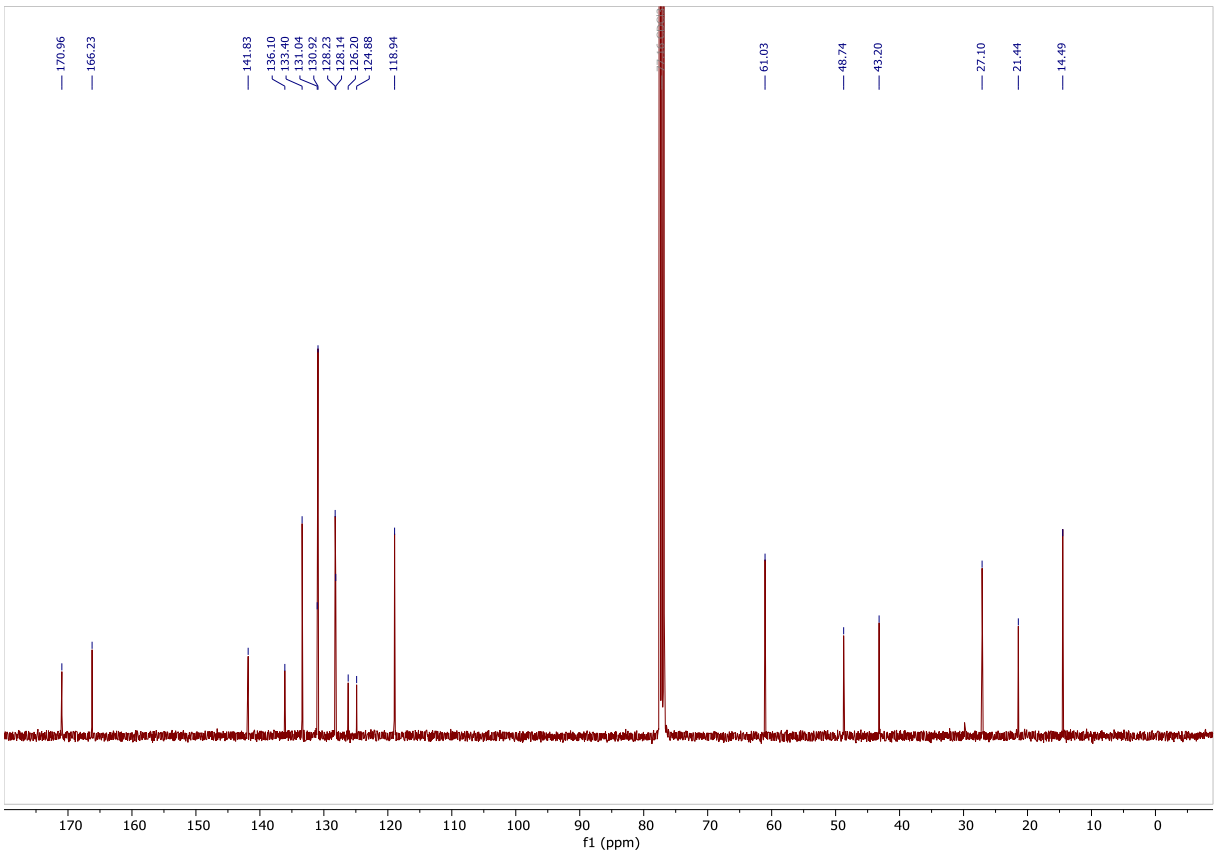
**2D-NOESY (400 MHz, chloroform-*d*) (3'z)**



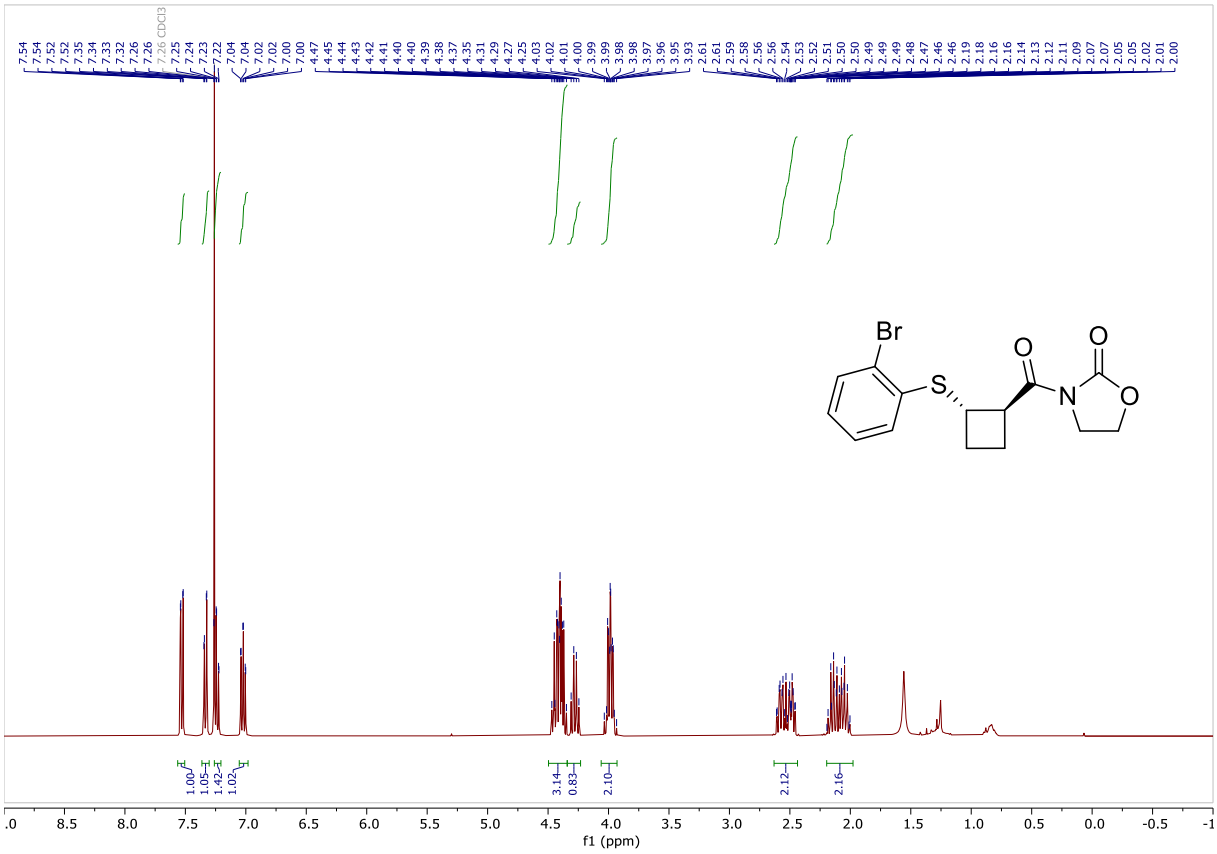
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (3aa)



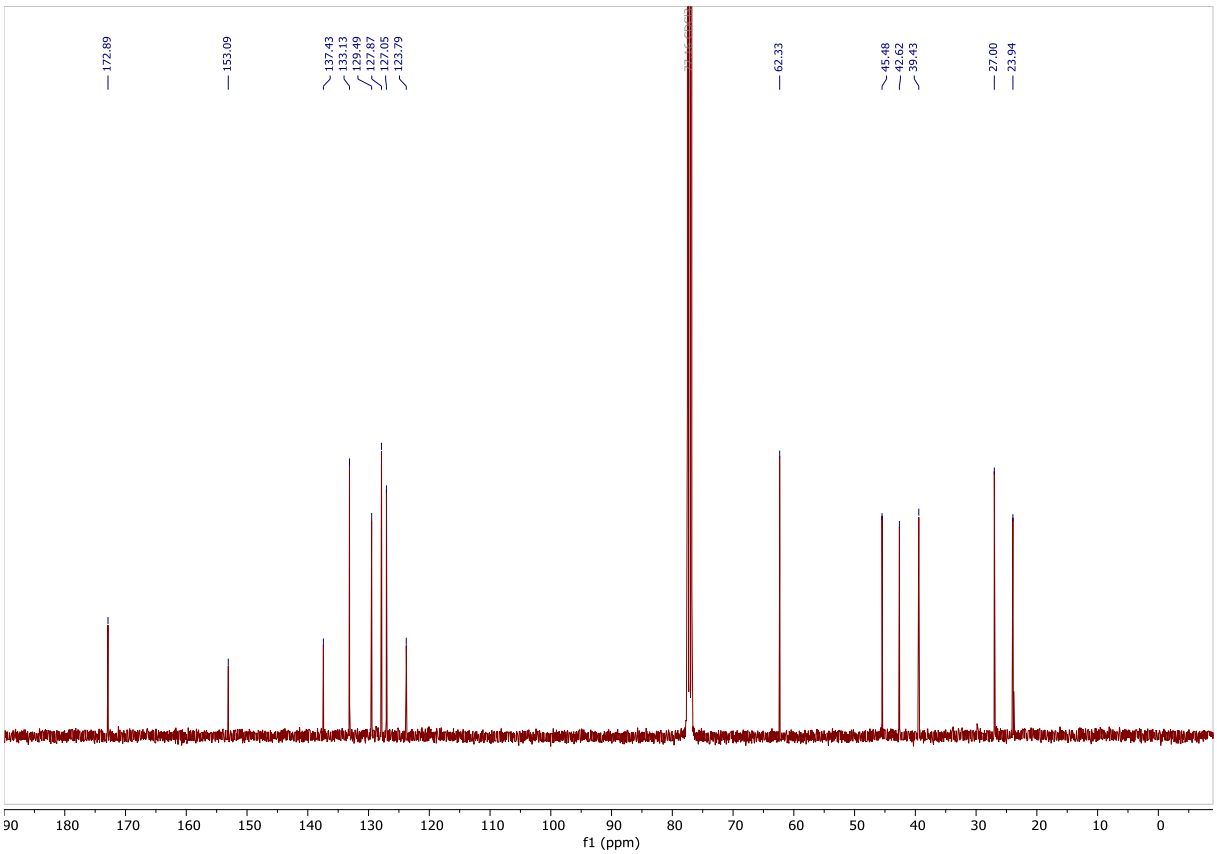

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (3aa)



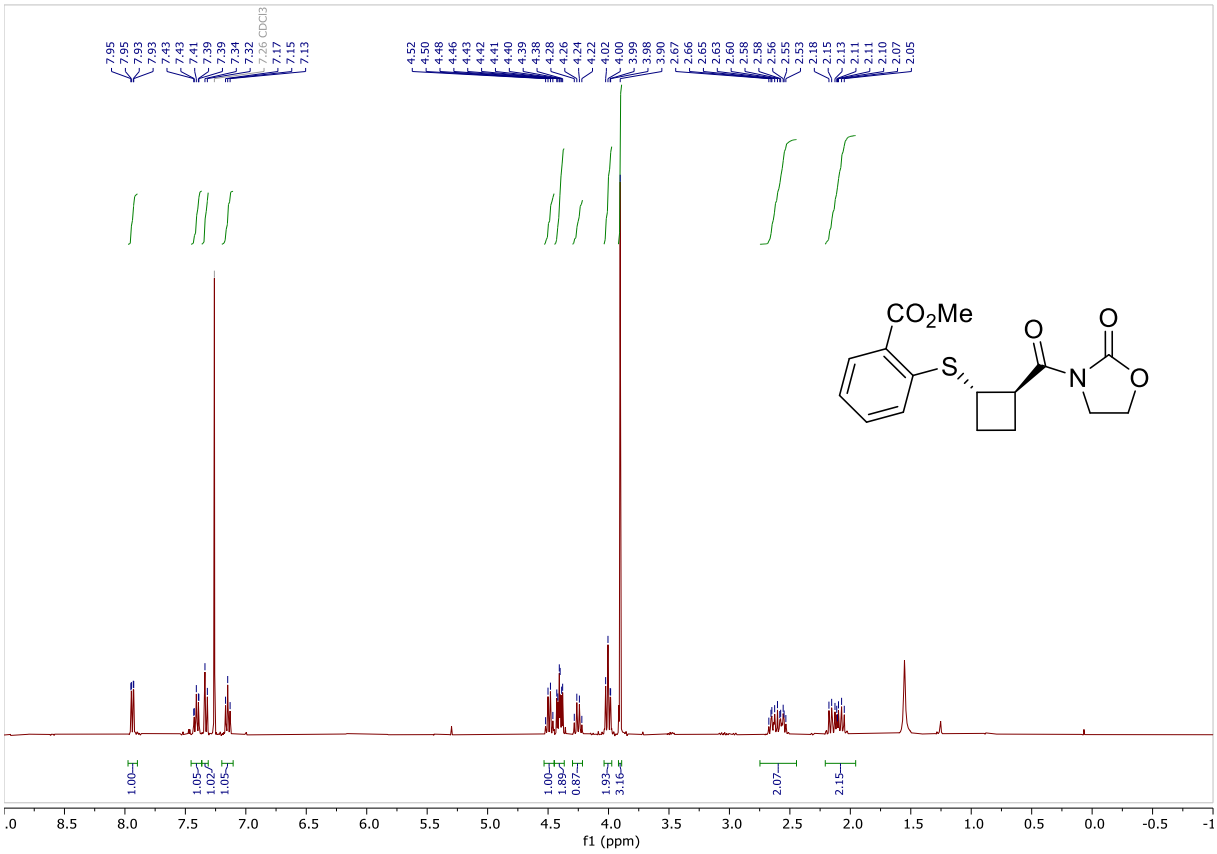
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (4a)



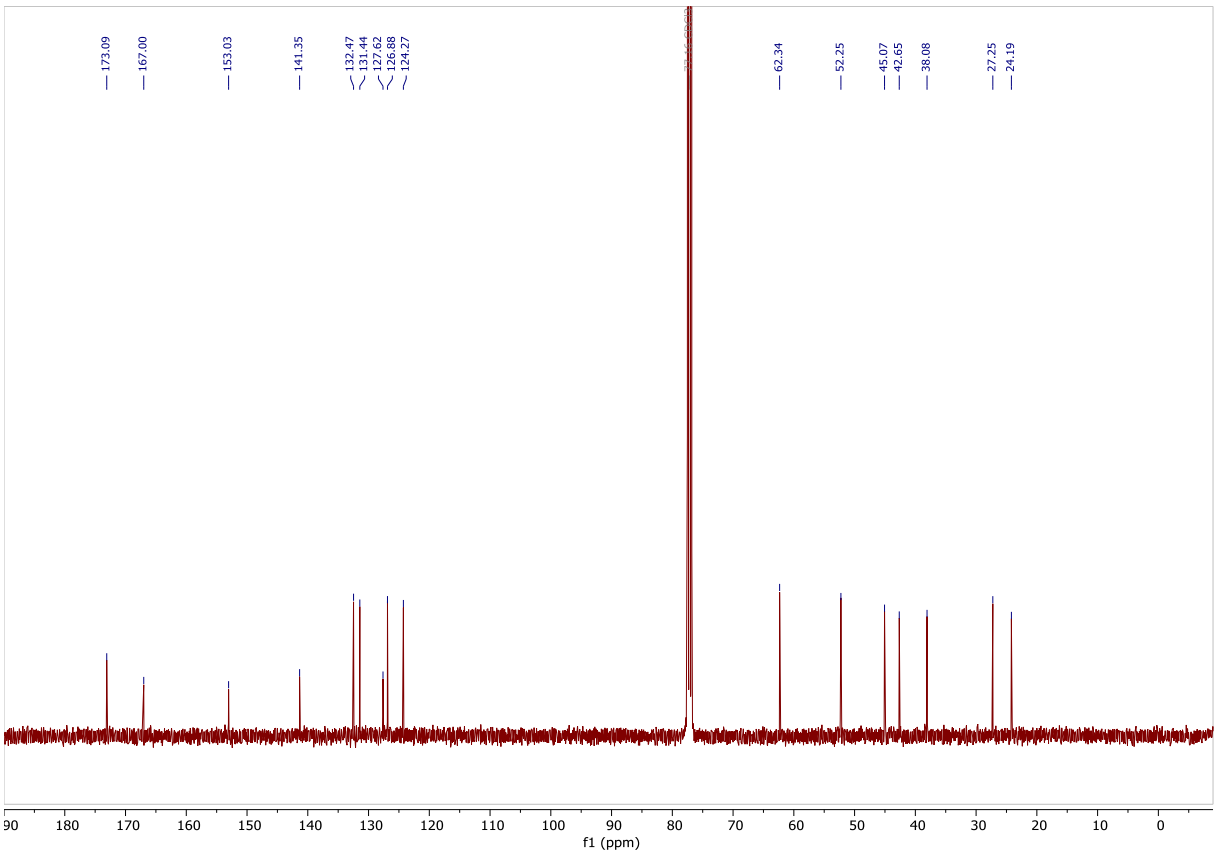

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (4a)



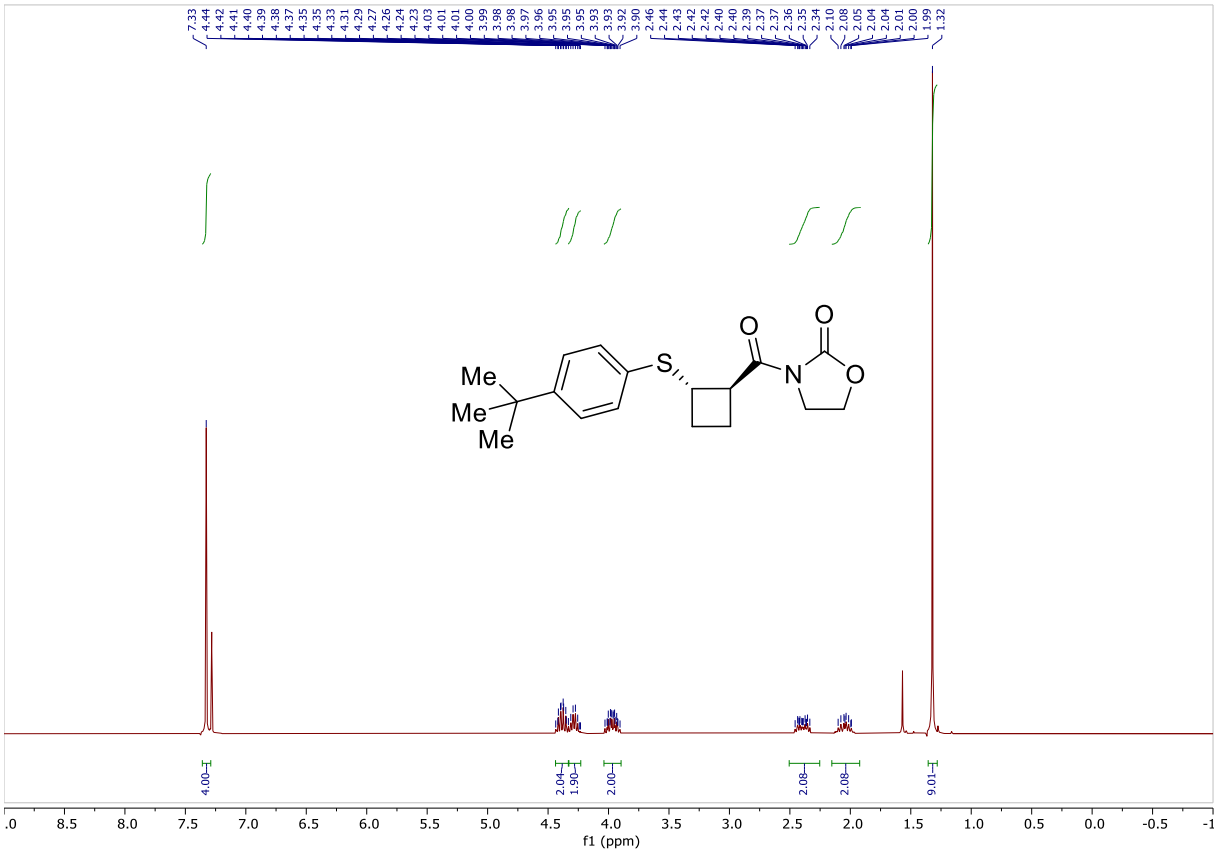
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (4b)



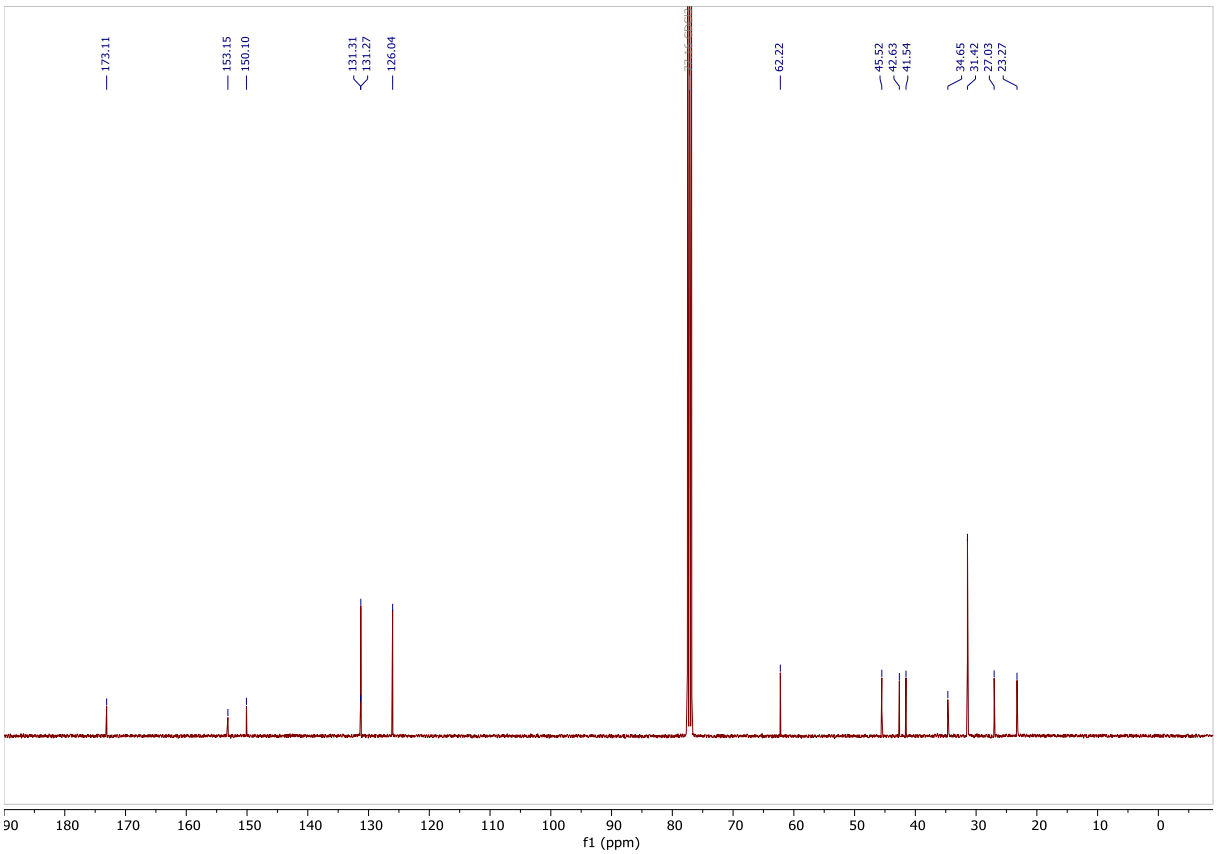

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (4b)



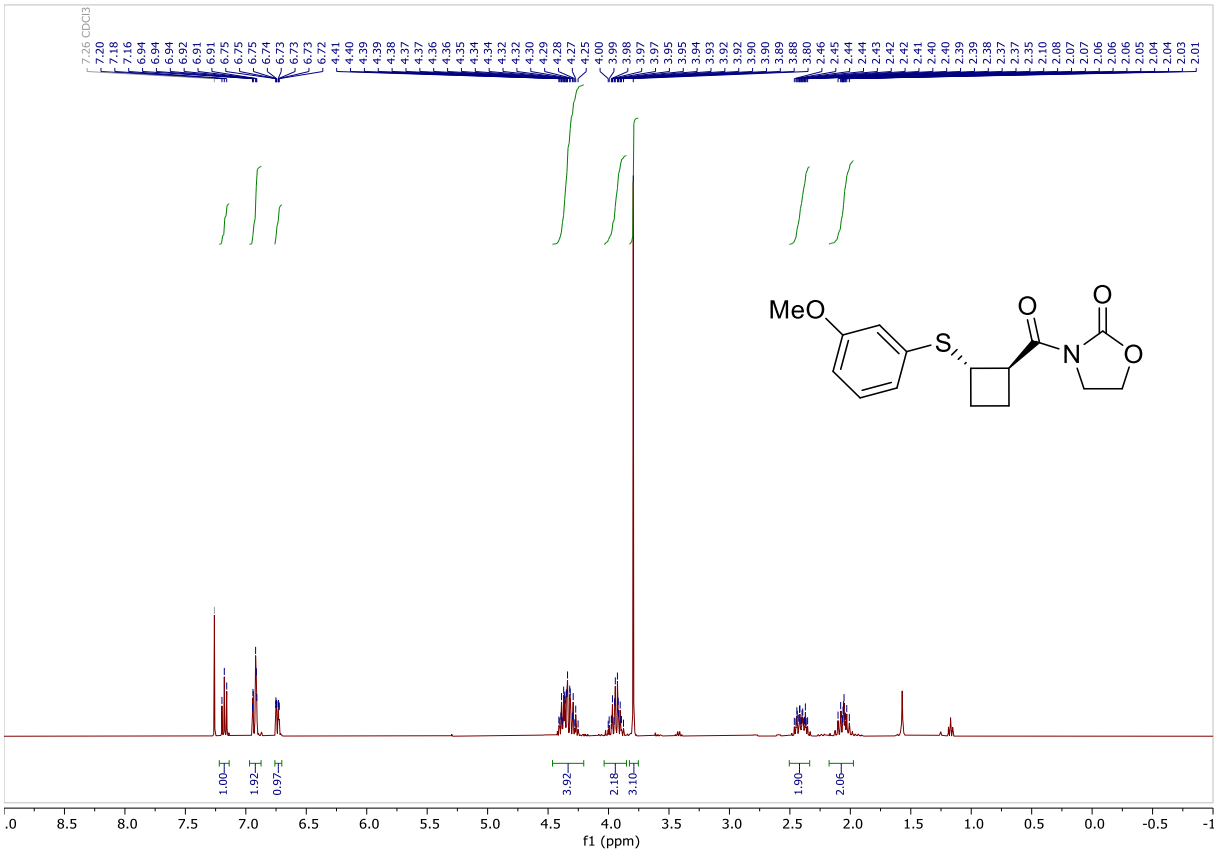
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (4c)



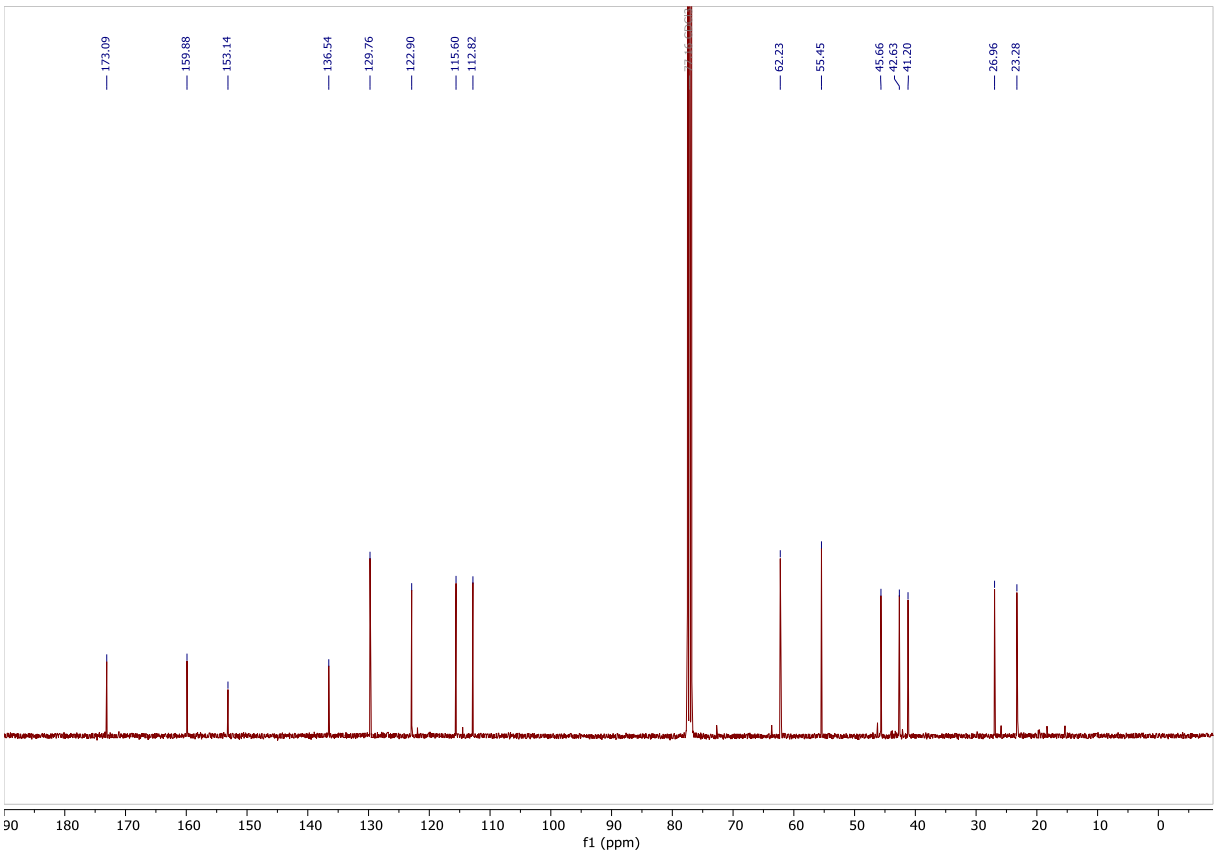

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (4c)



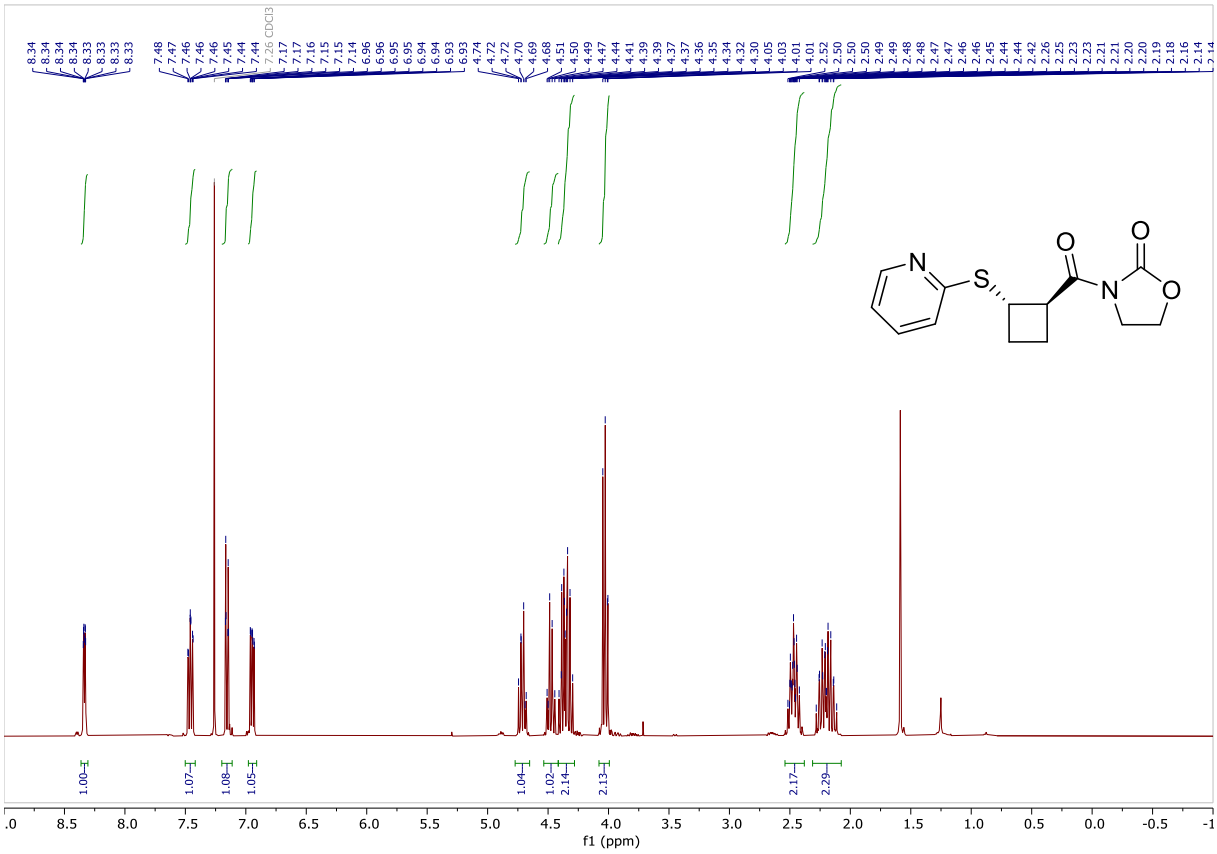
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (4d)



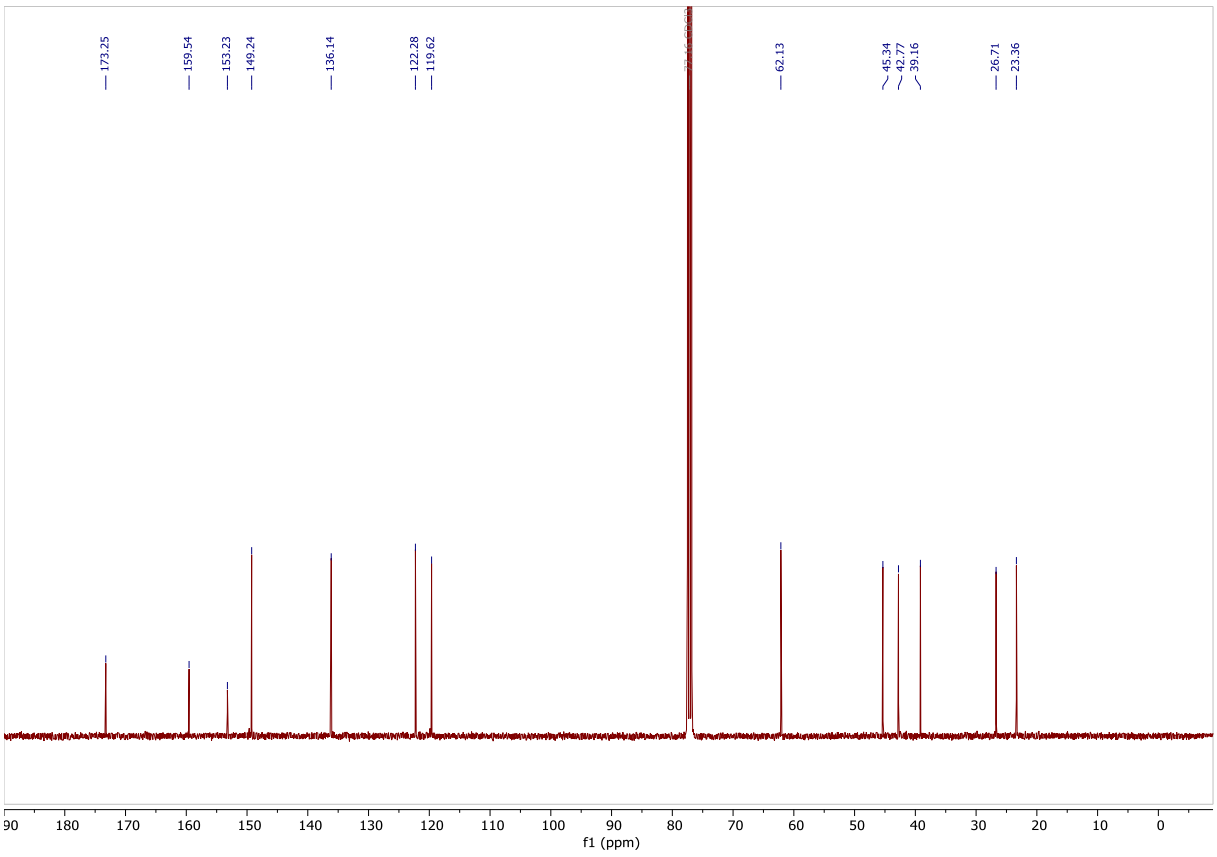

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (4d)



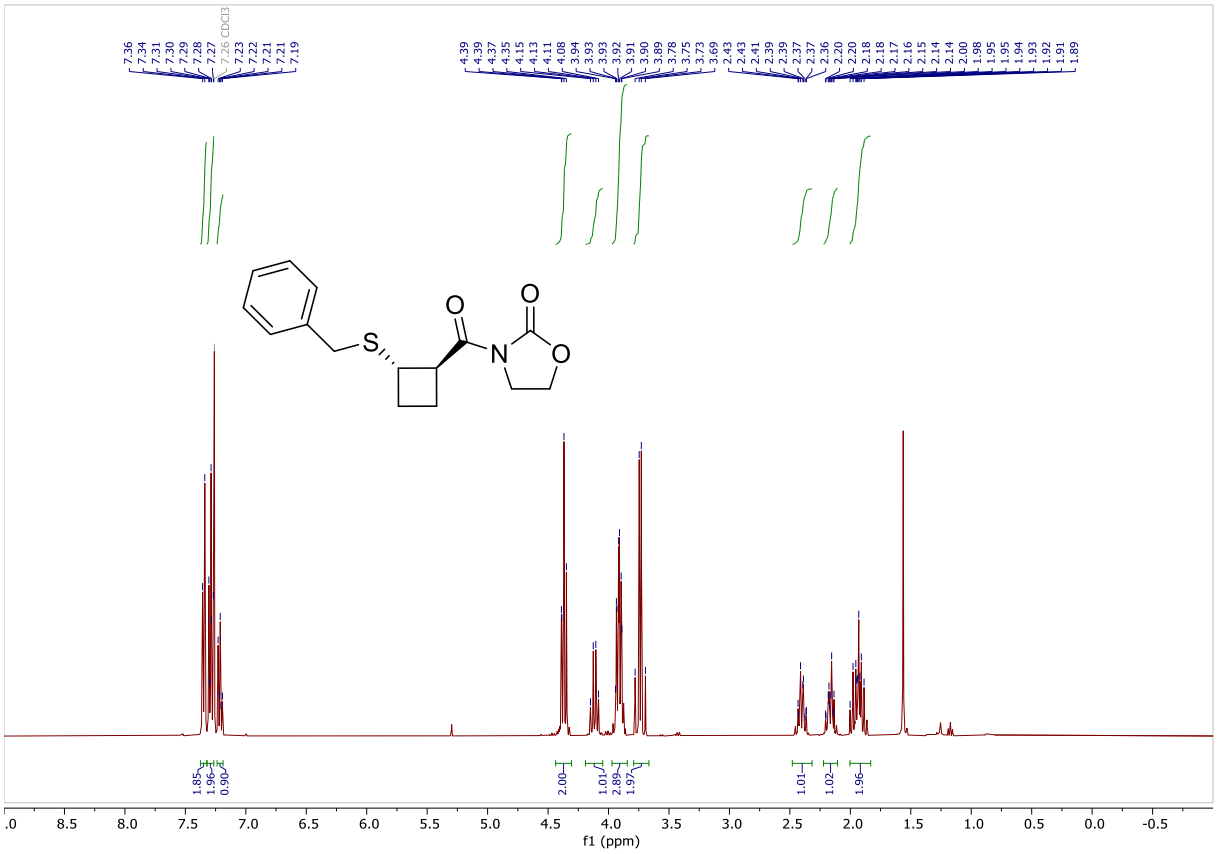
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (4e)



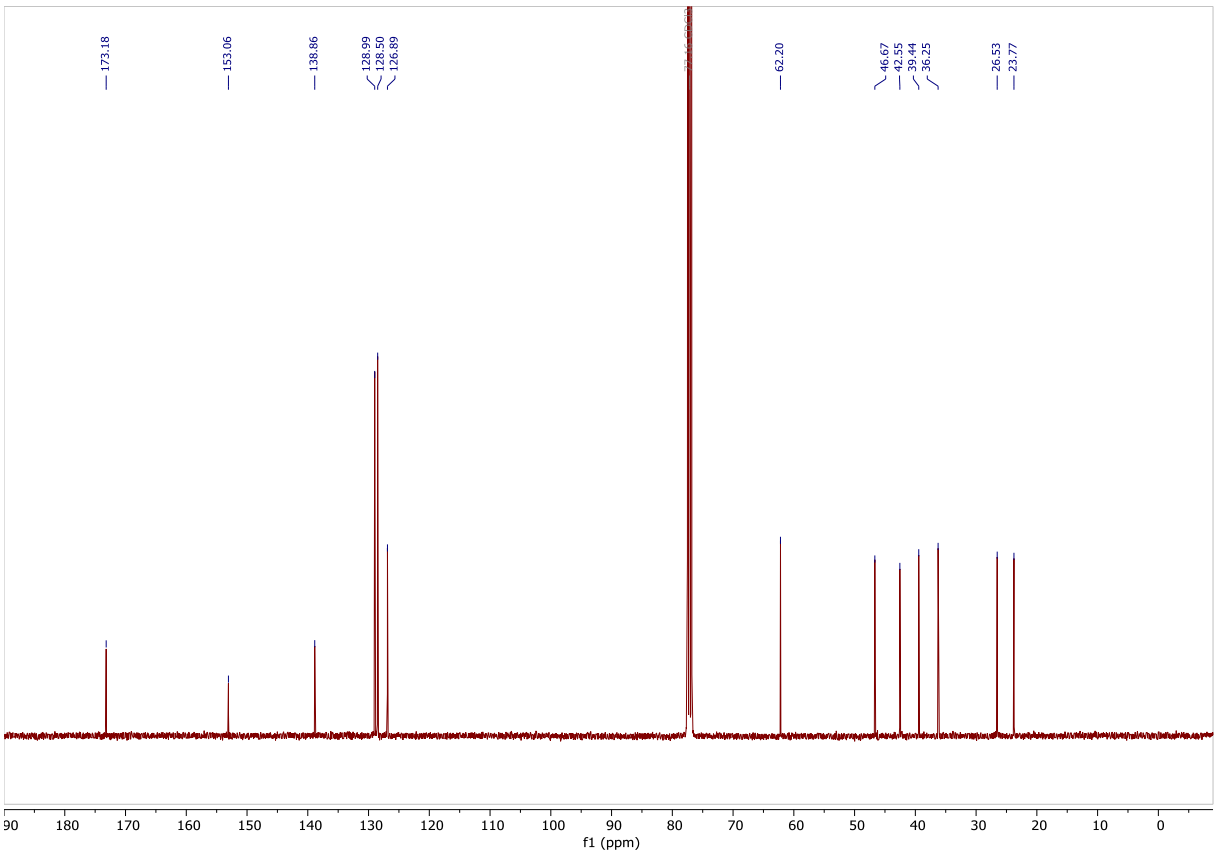

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (4e)



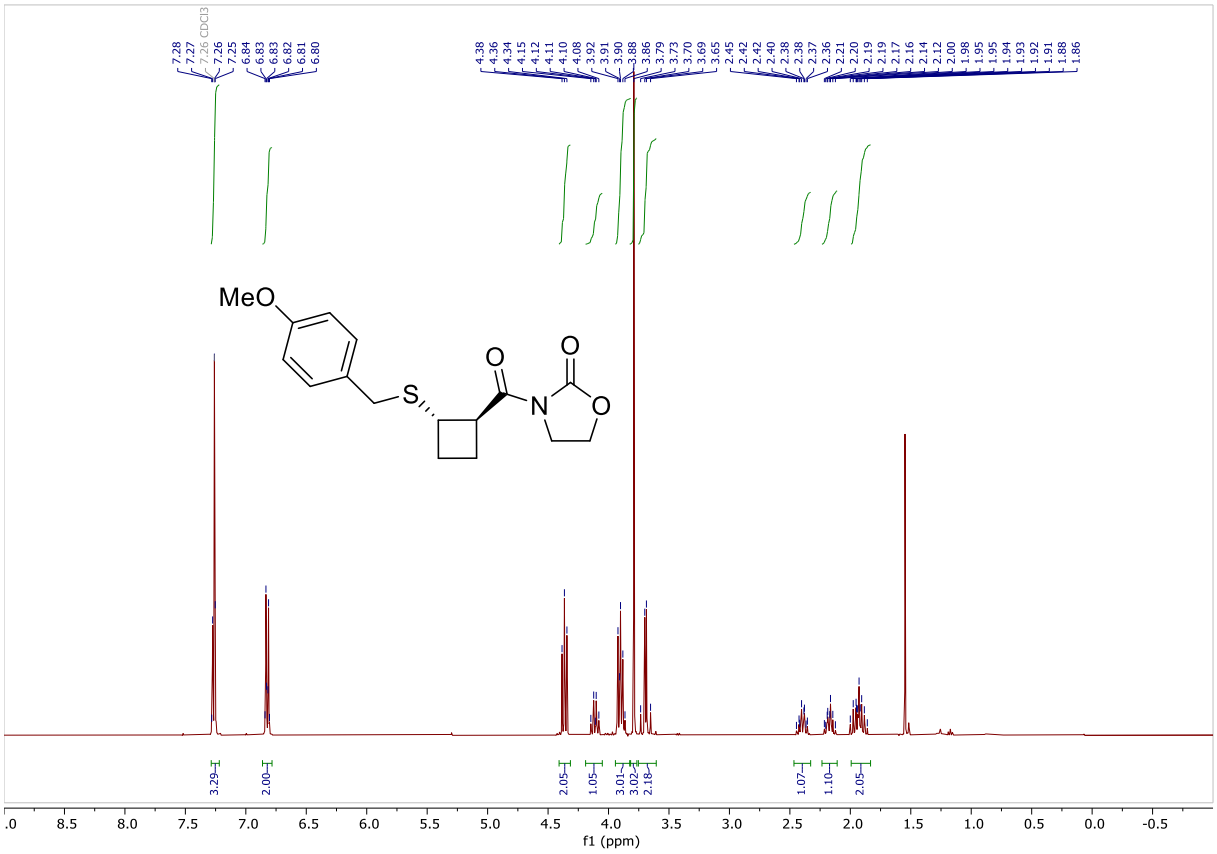
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (4f)



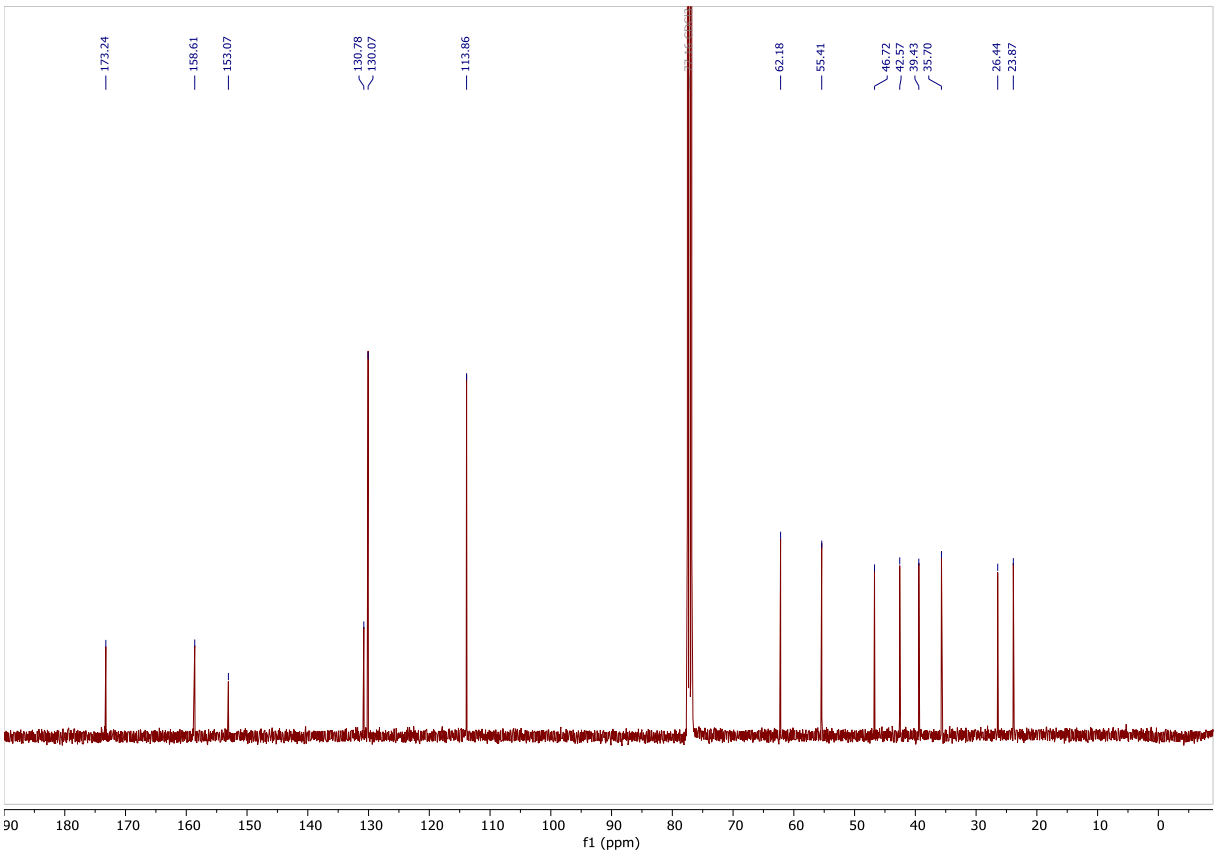

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (4f)



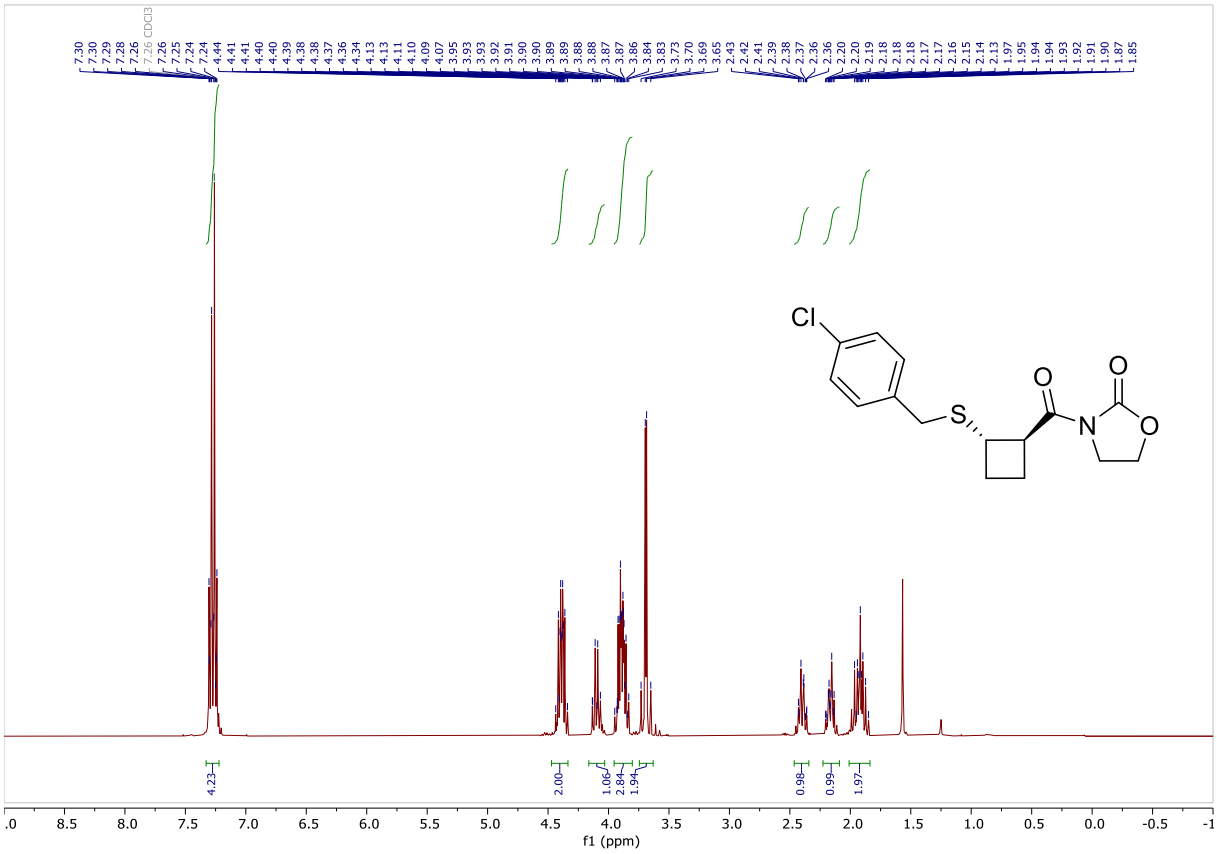
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (4g)



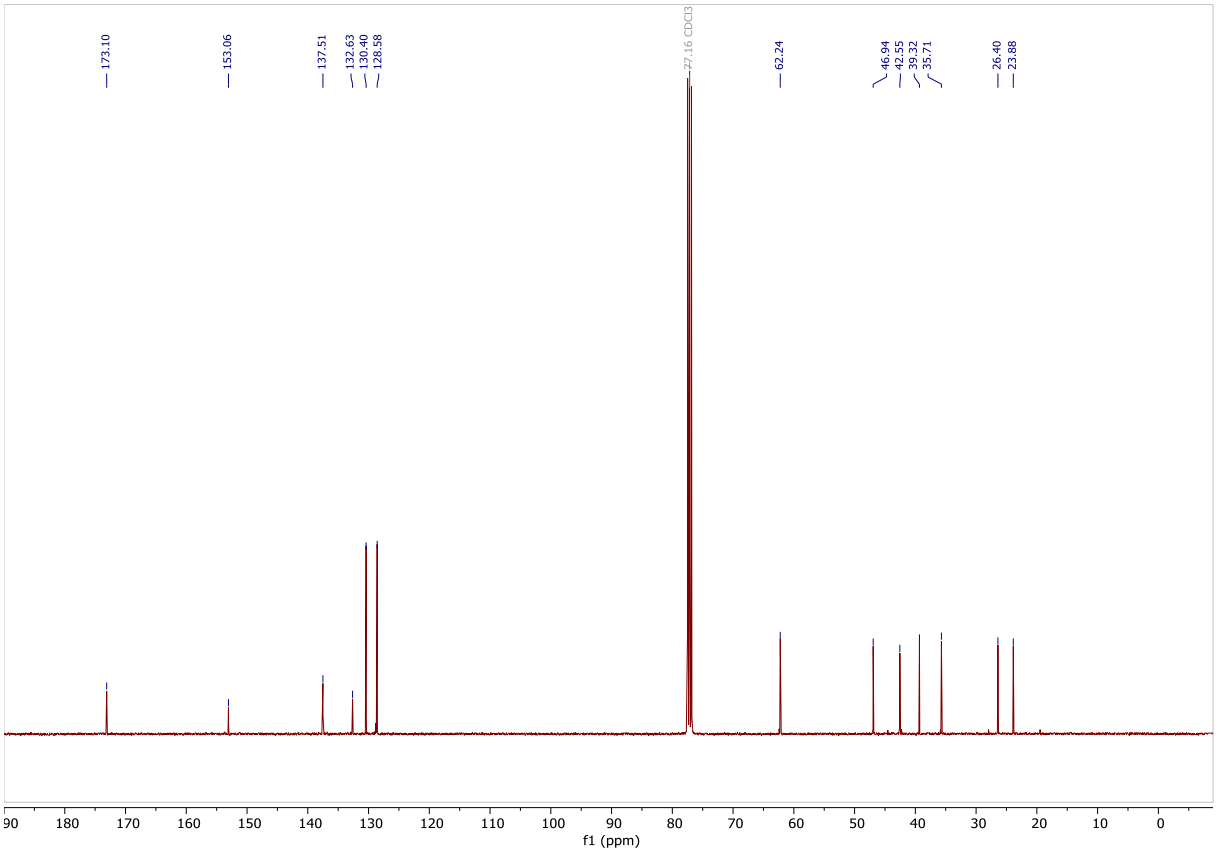

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (4g)



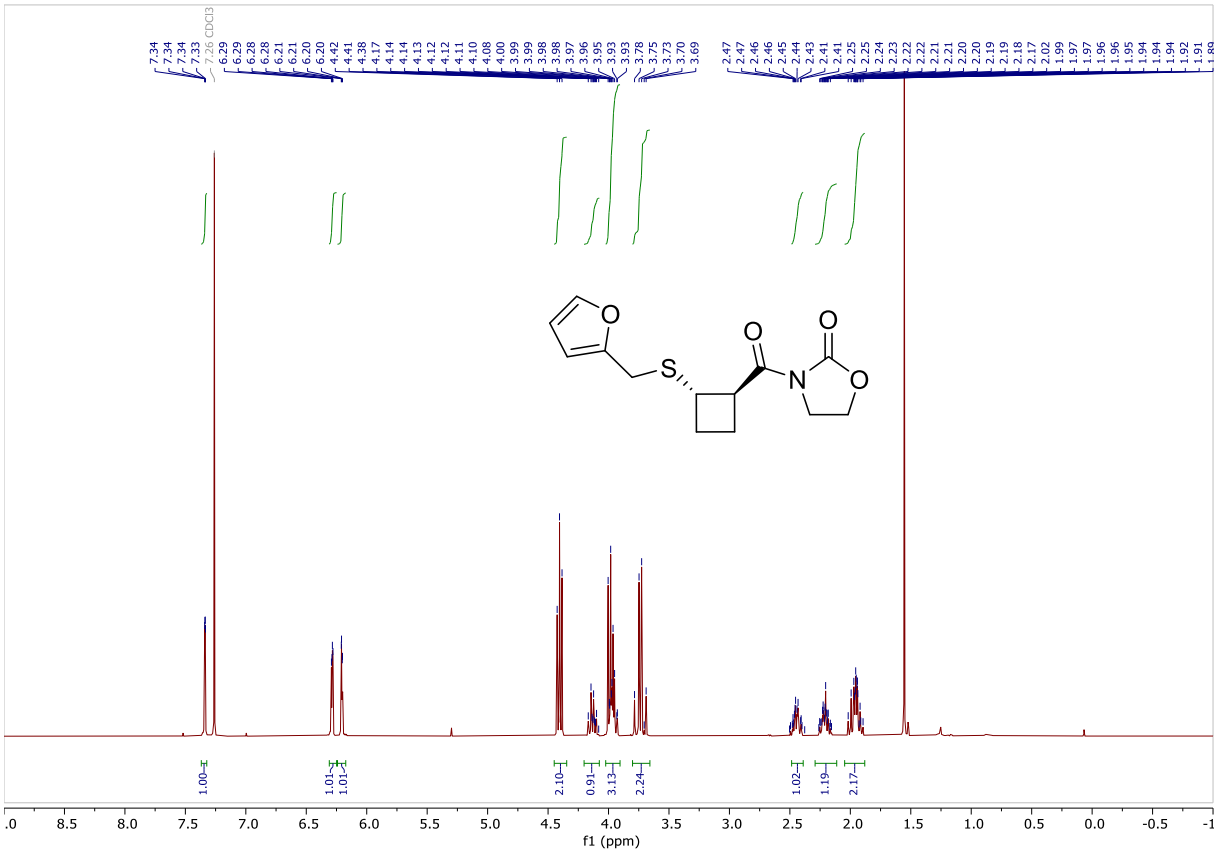
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (4h)



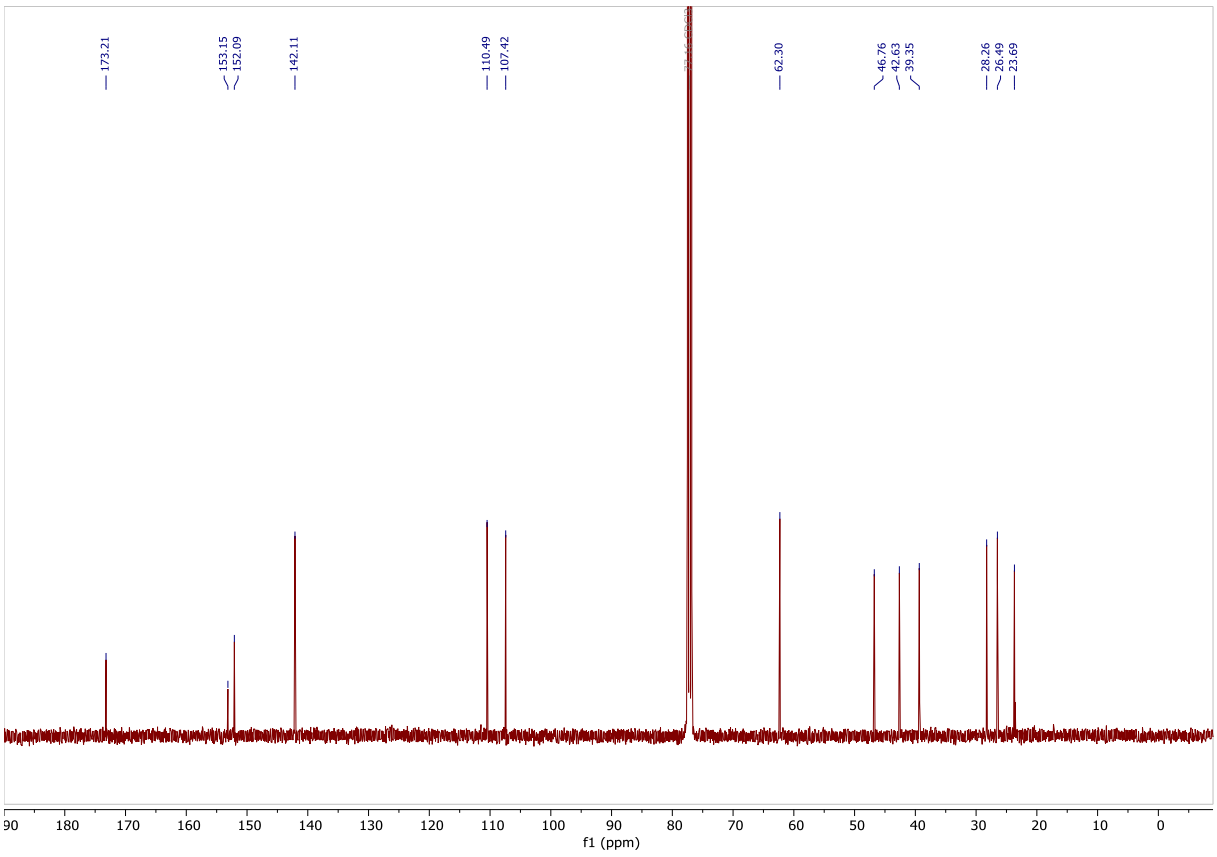

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (4h)



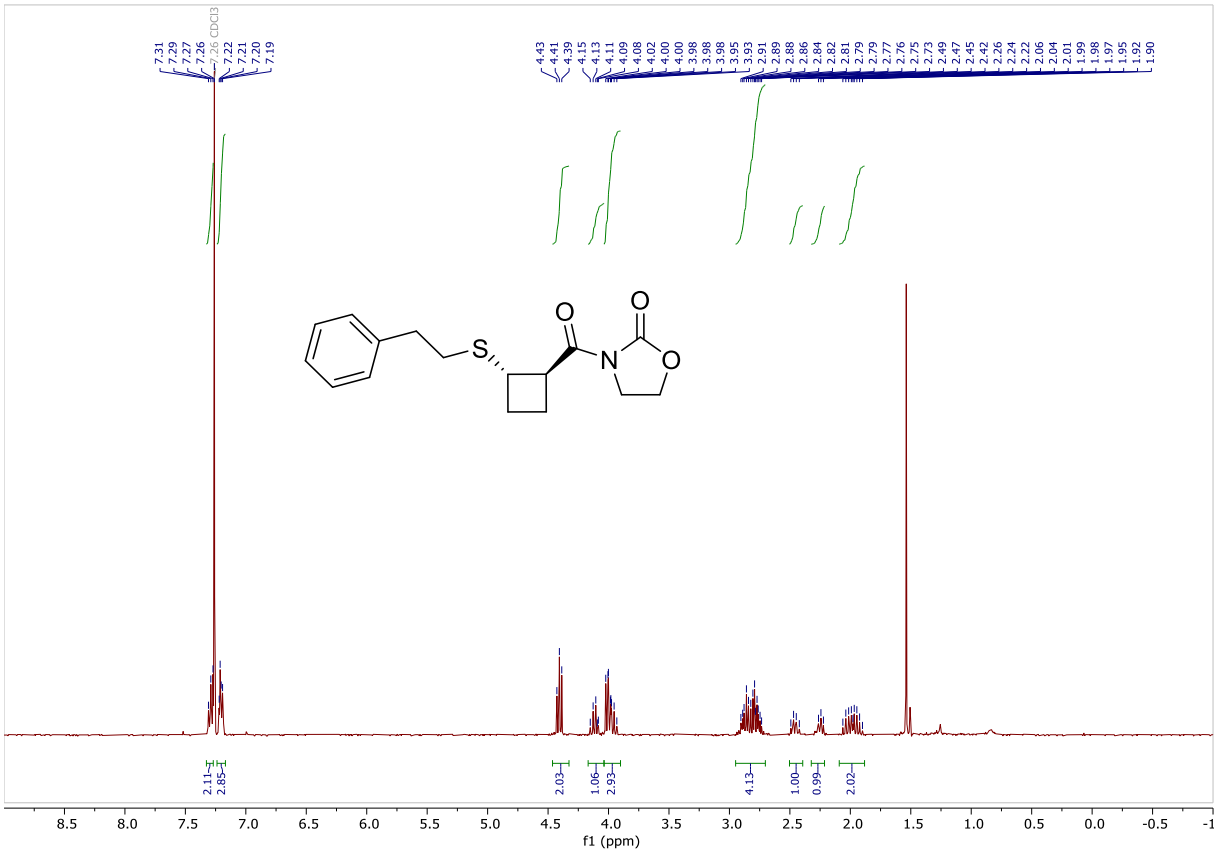
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (4i)



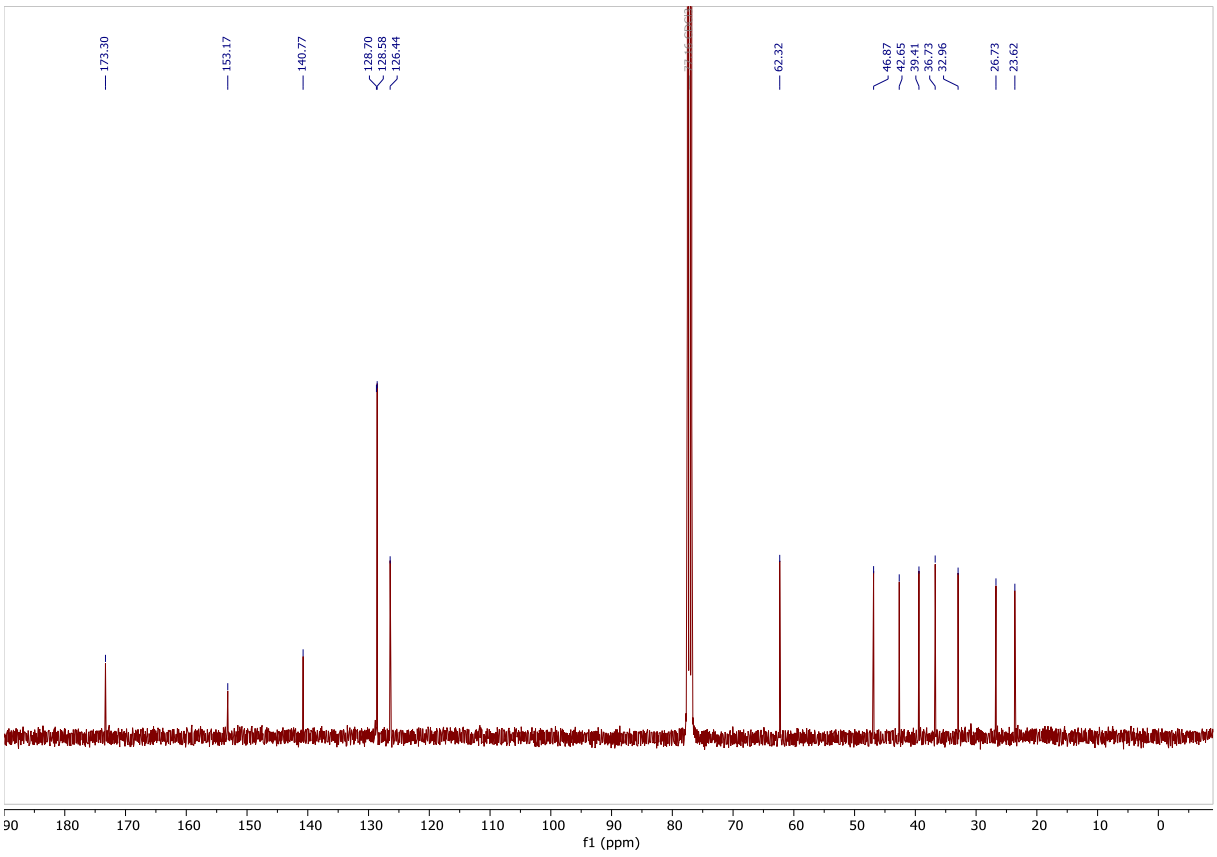

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (4i)



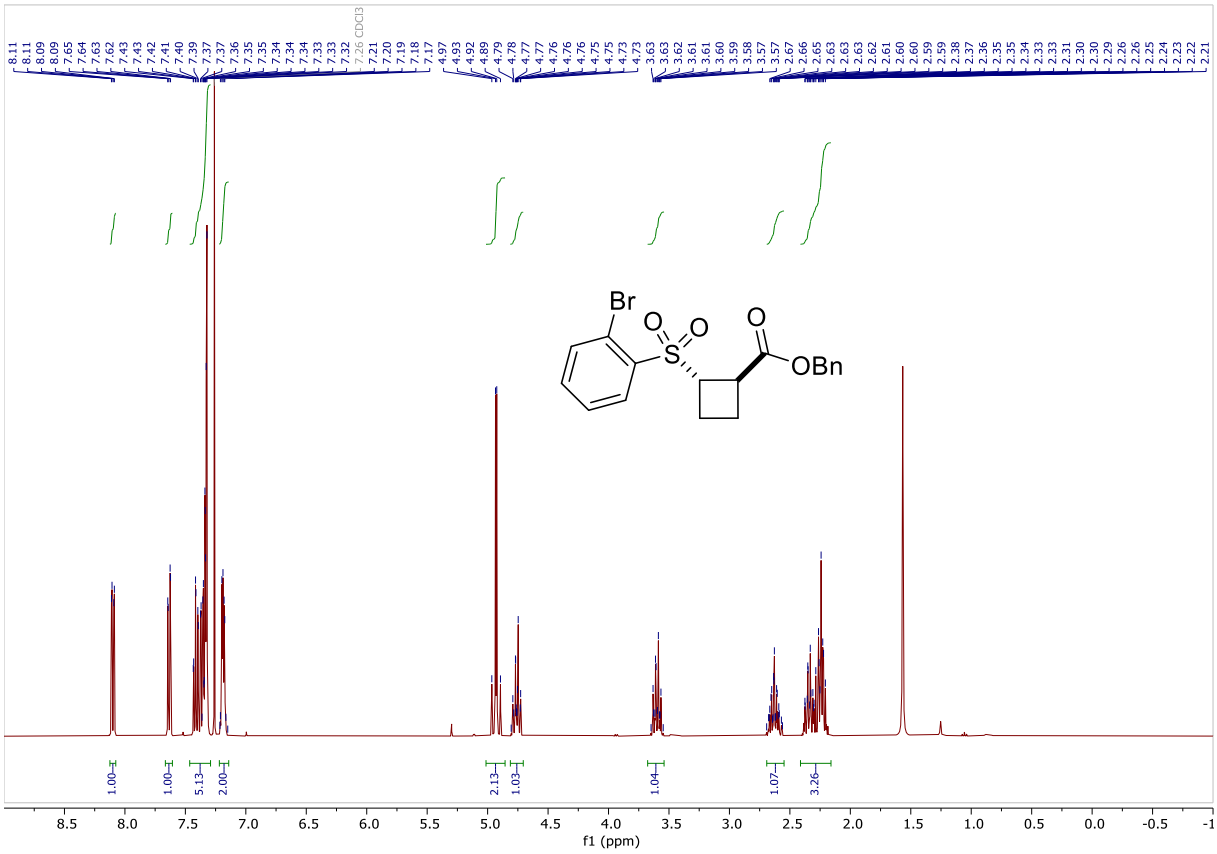
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (4j)



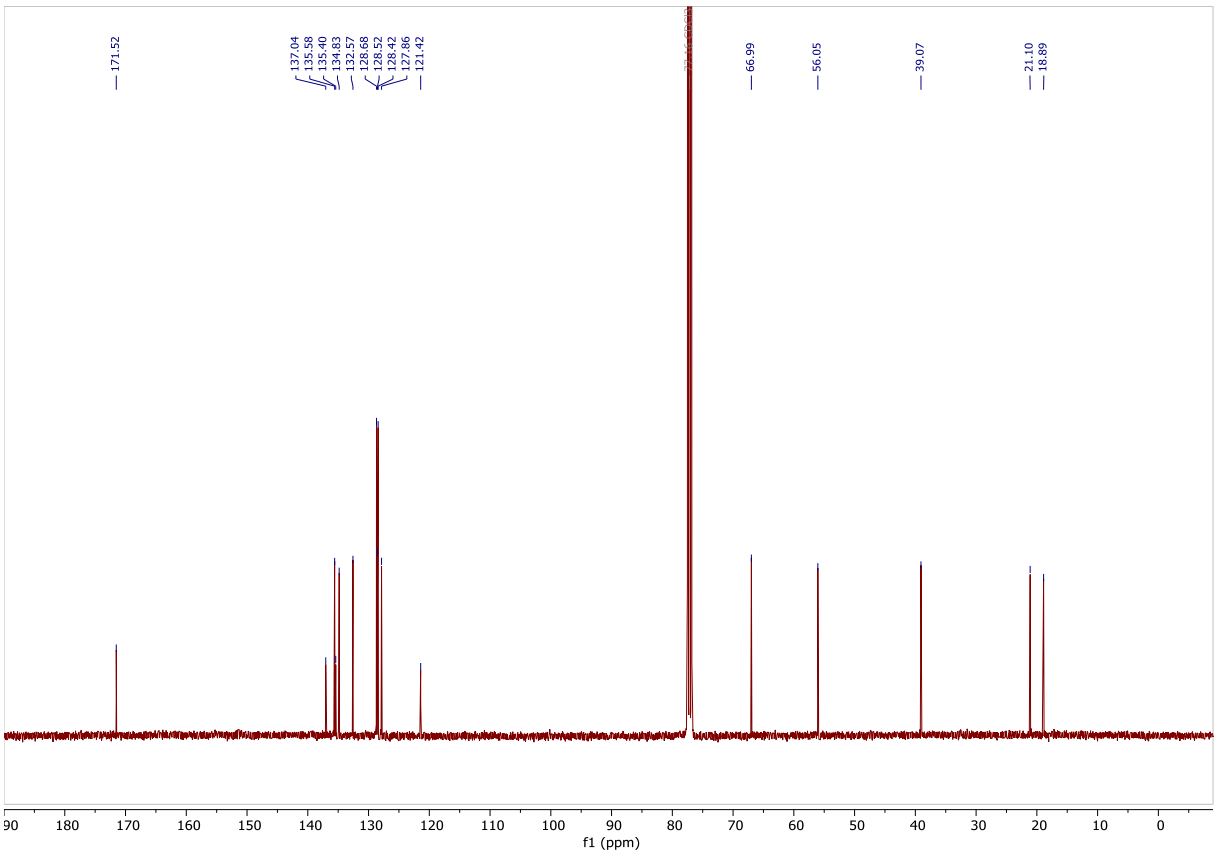

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (4j)



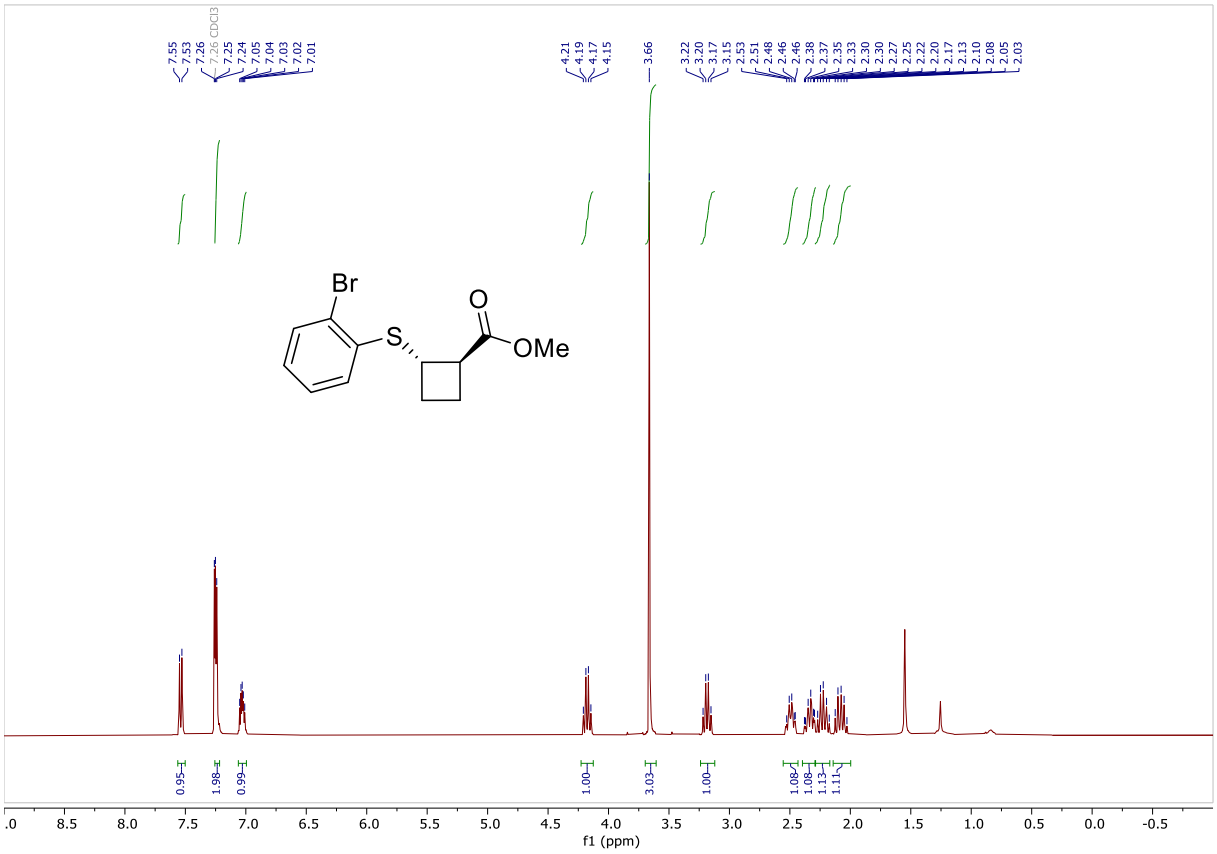
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (5)



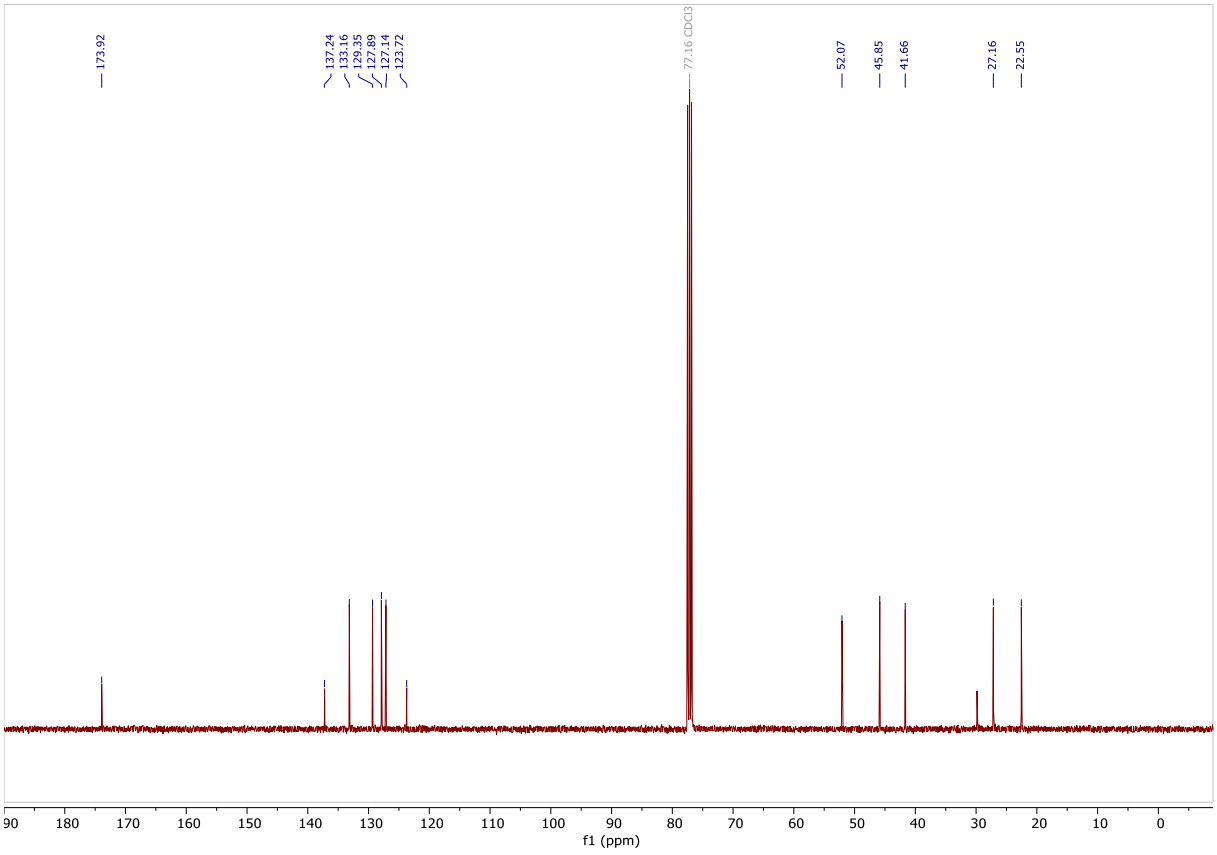

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (5)



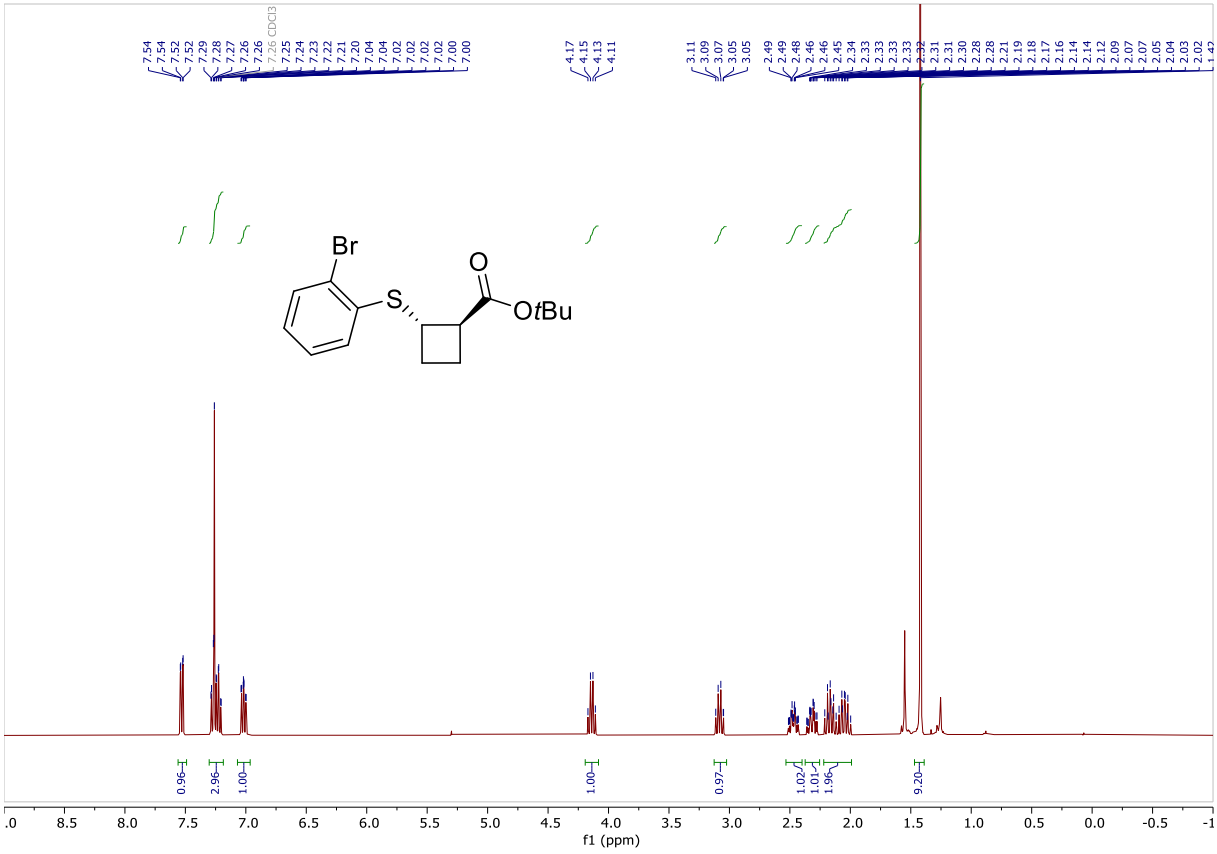
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (6)



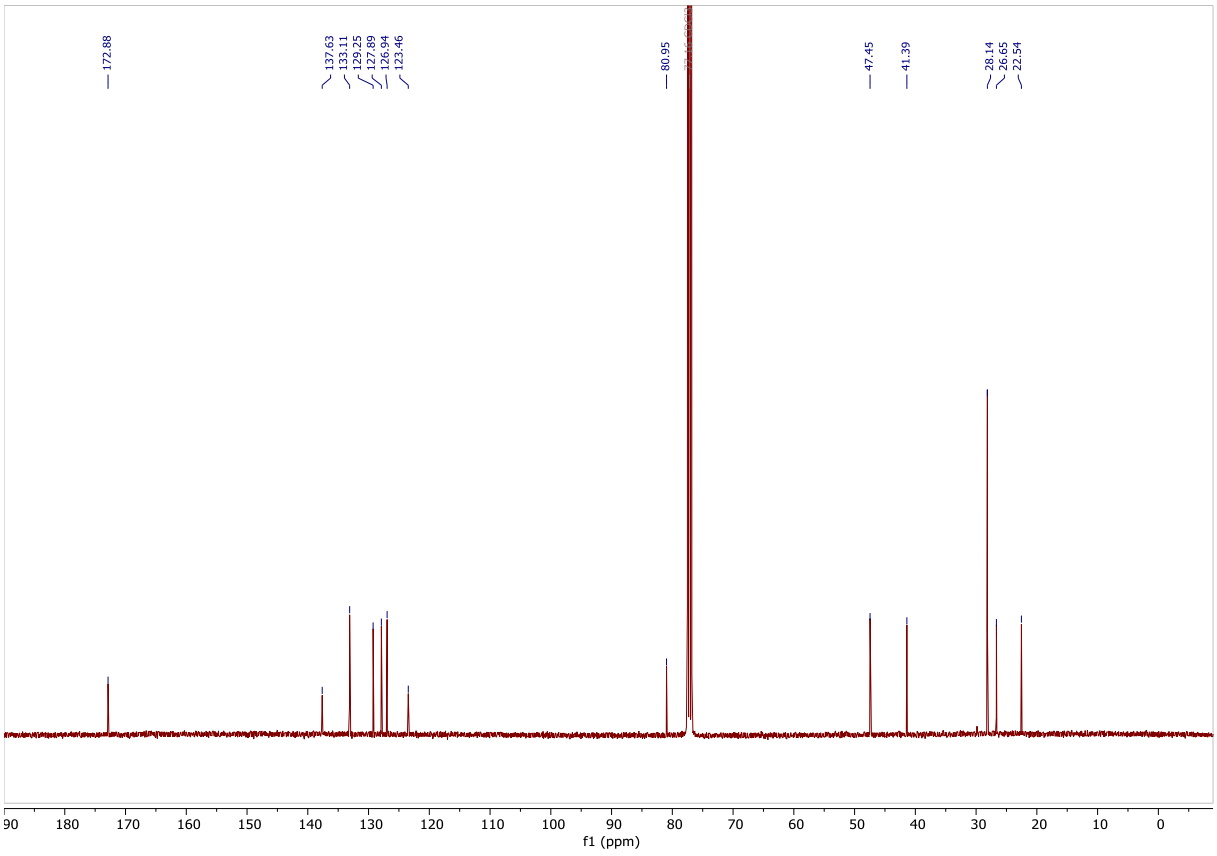

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (6)



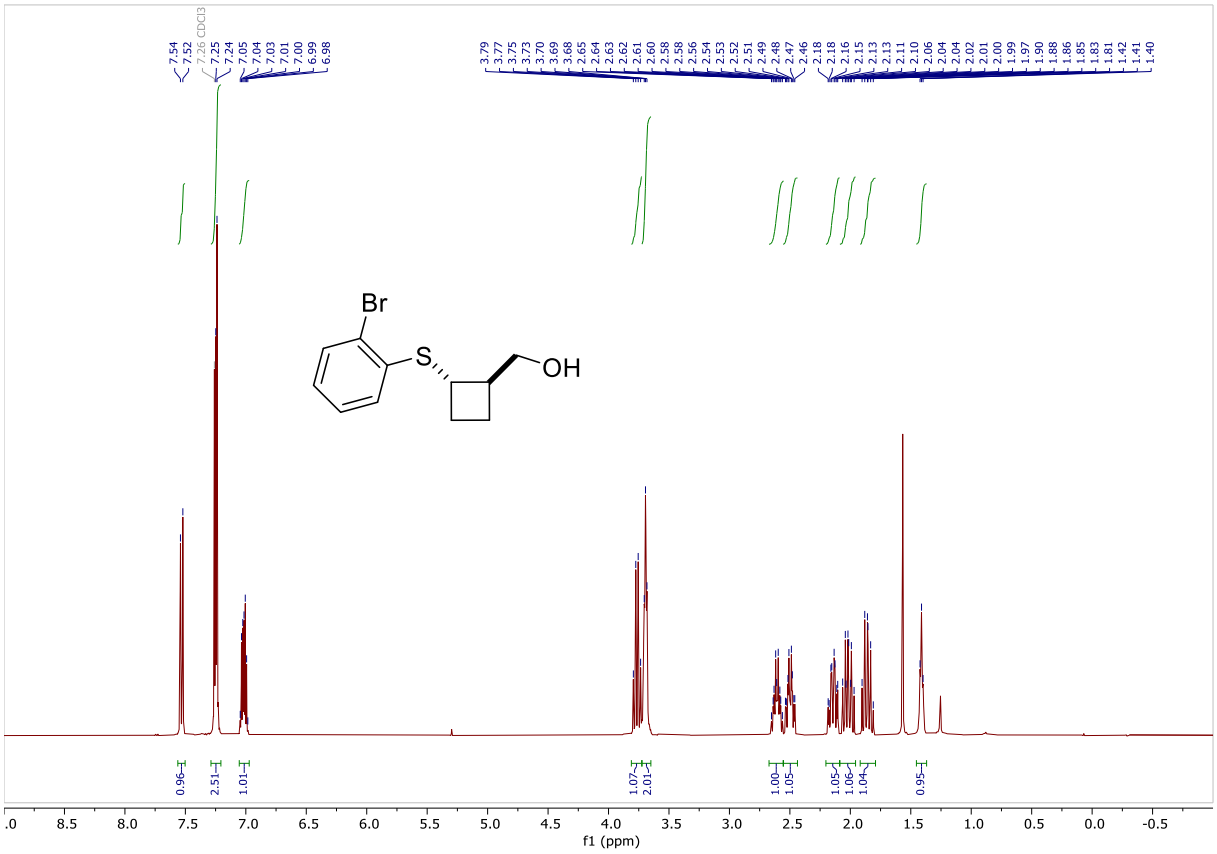
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (7)



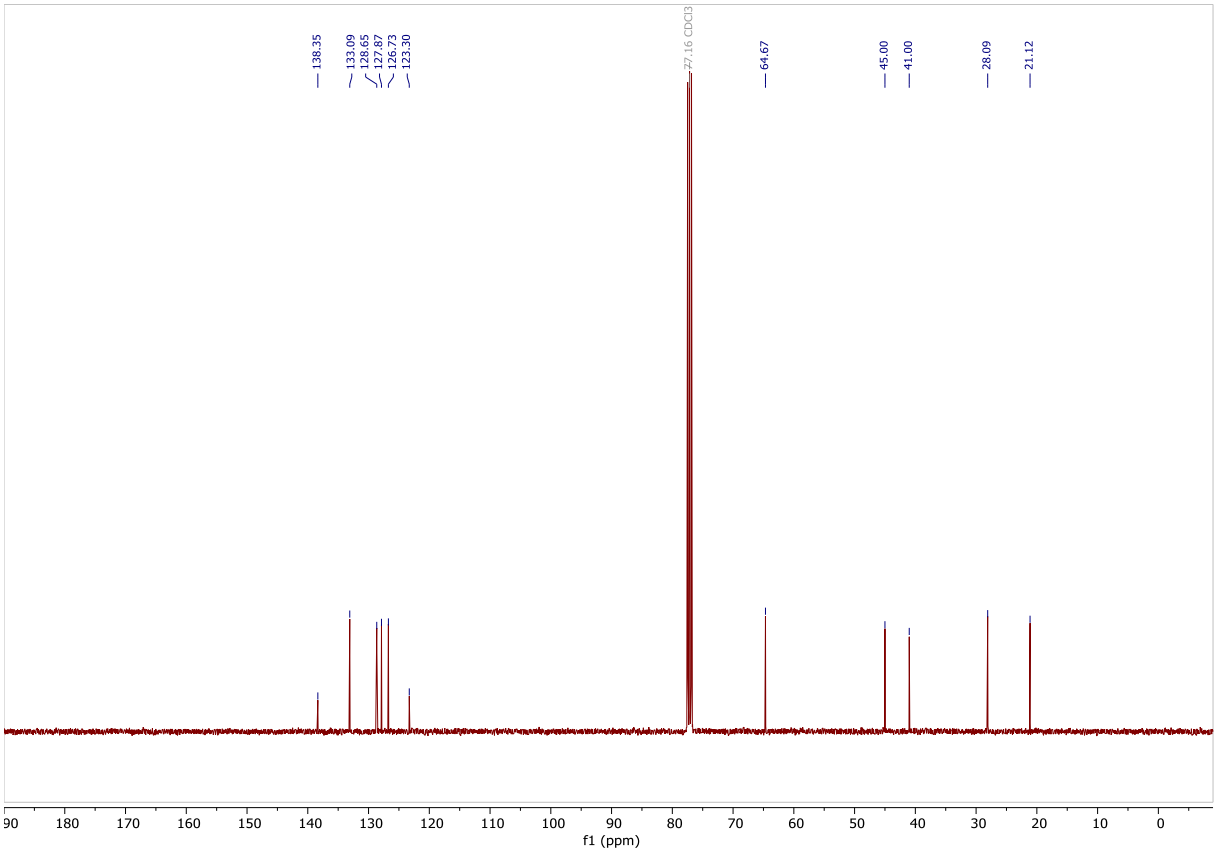

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (7)



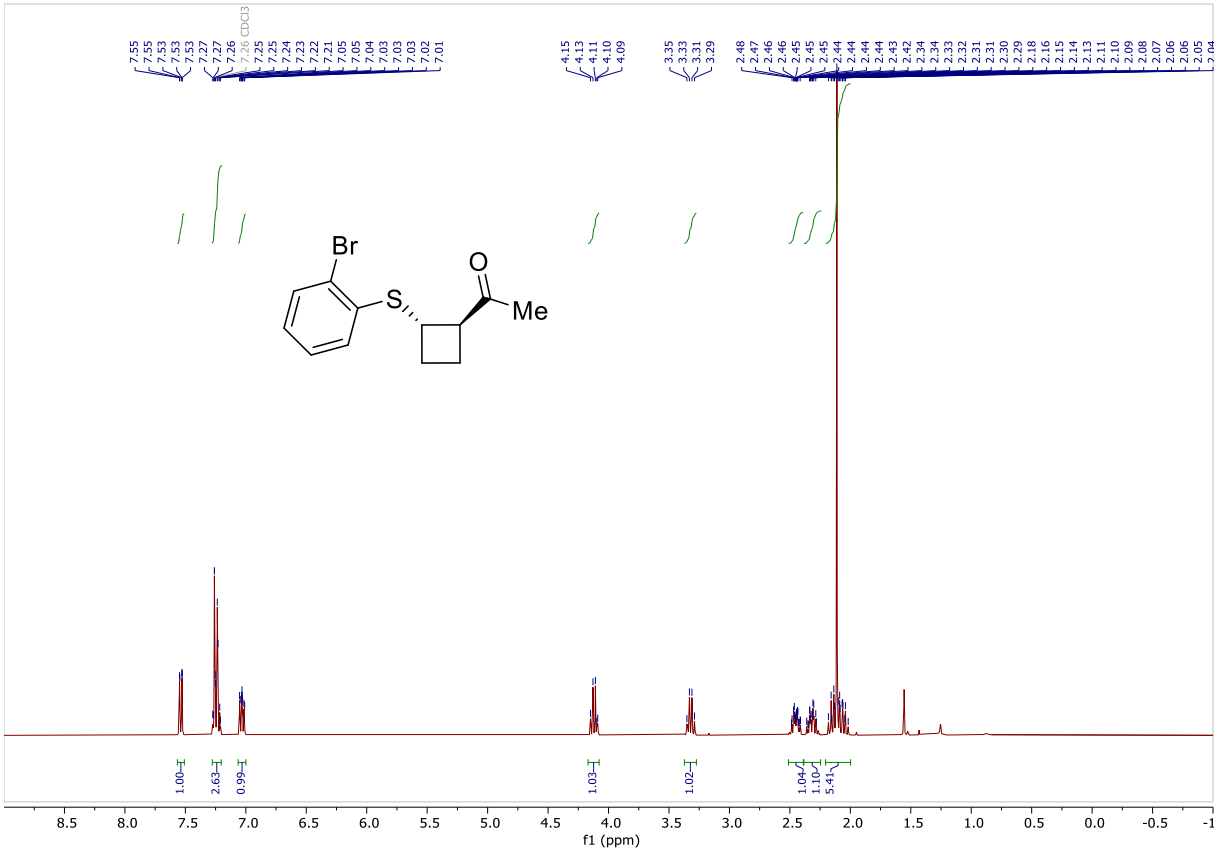
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (8)



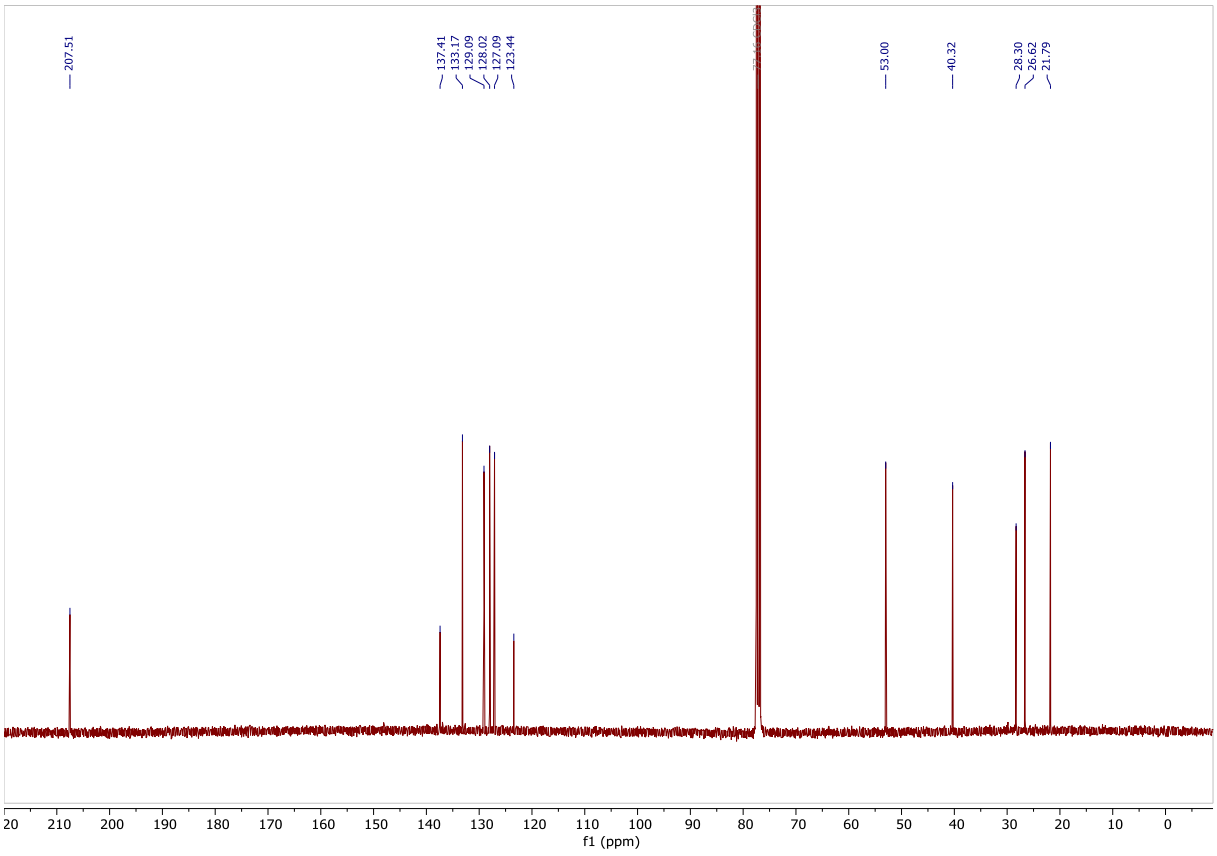

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (8)



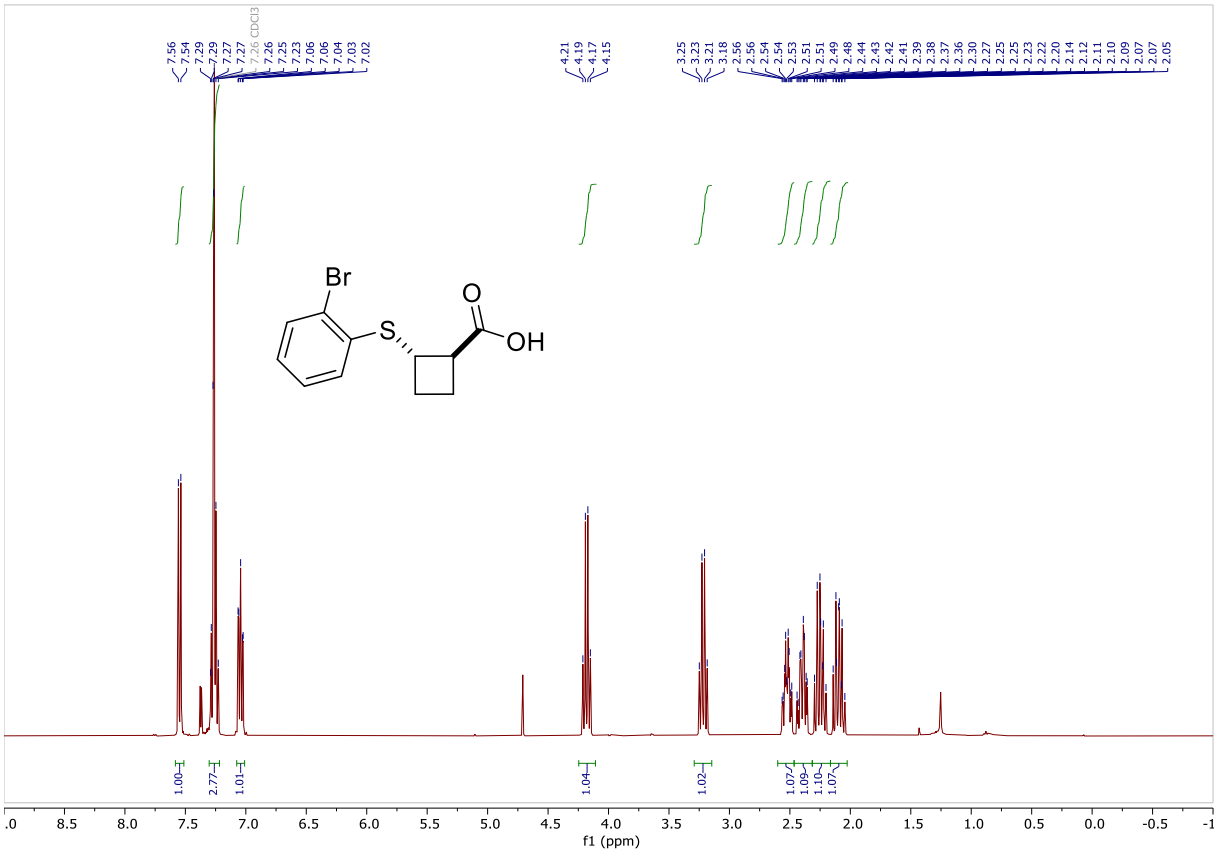
## $^{1}$H-NMR (400 MHz, chloroform-*d*) (9)



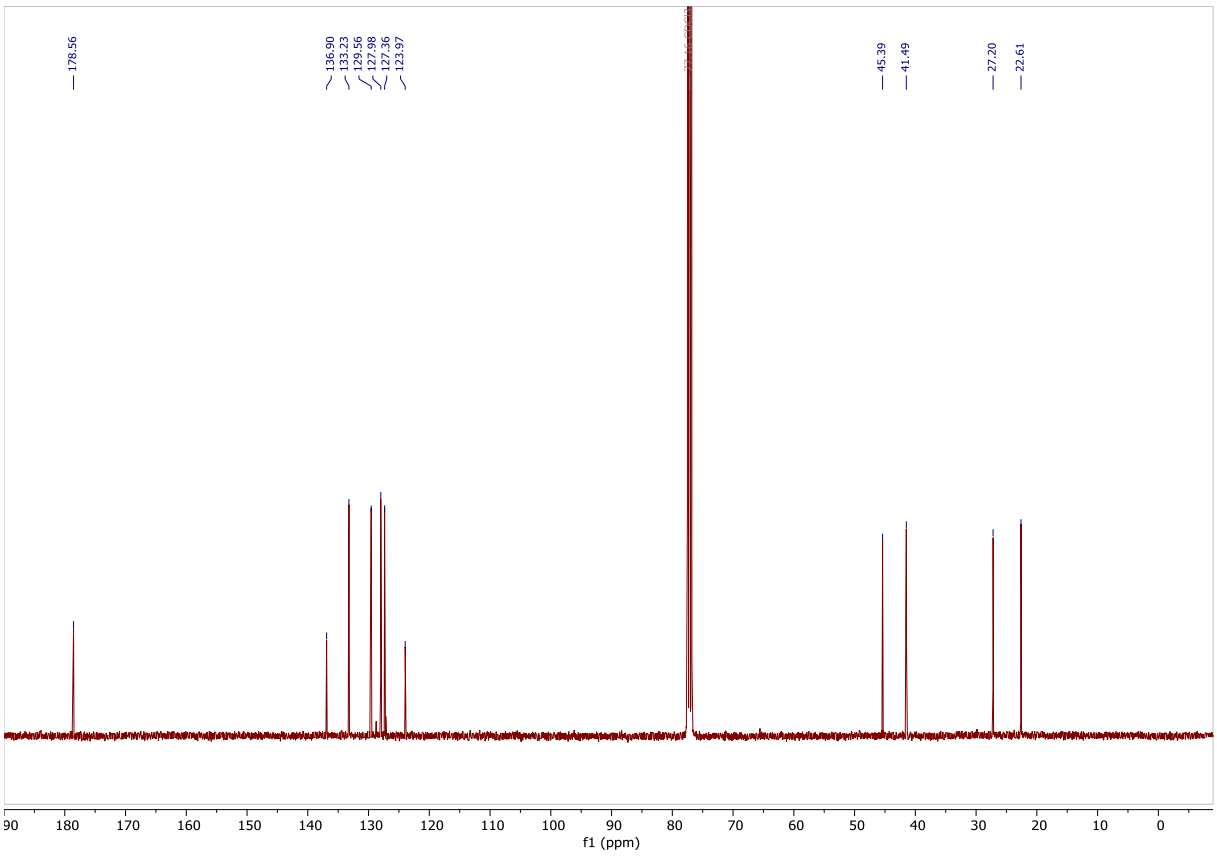

## $^{13}$C-NMR (101 MHz, chloroform-*d*) (9)



## $^{1}$H-NMR (400 MHz, chloroform-*d*) (10)

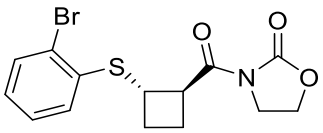



## $^{13}$C-NMR (101 MHz, chloroform-*d*) (10)

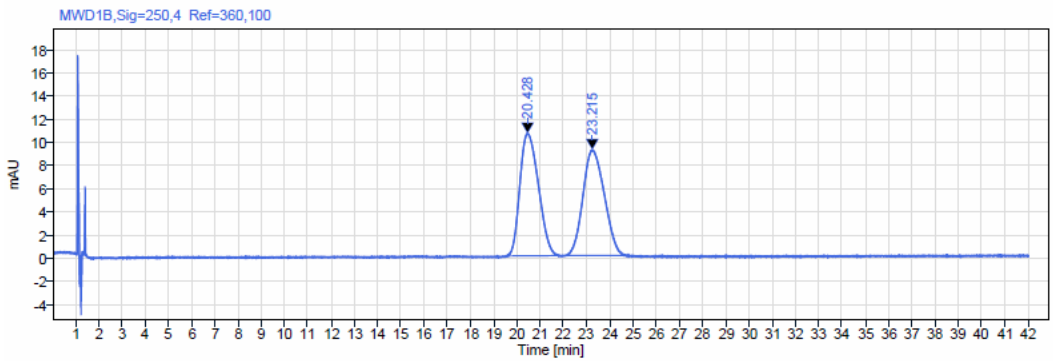


# 5. SFC traces

**4a**

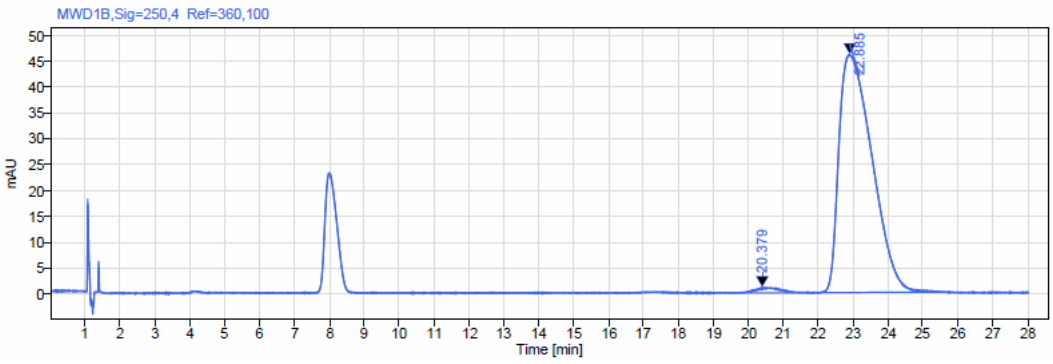



*Racemic:*



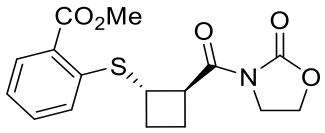

| Signal: | MWD1B,Sig=250,4 Ref=360,100 | | | | | |
|---|---|---|---|---|---|---|
| **RT [min]** | **Type** | **Width [min]** | **Area** | **Height** | **Area%** | **Name** |
| 20.428 | MM m | 2.18 | 586.09 | 10.58 | 50.07 | |
| 23.215 | MM m | 2.81 | 584.40 | 9.15 | 49.93 | |
| | | **Sum** | **1170.50** | | | |

*Enantioenriched:*

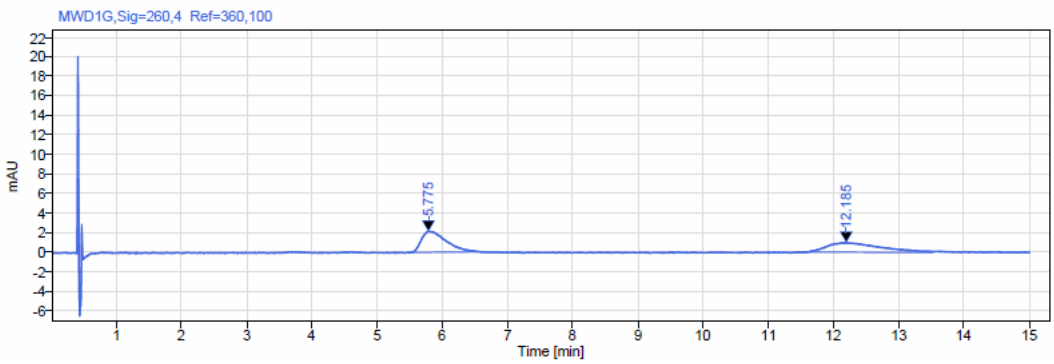



| Signal: | MWD1B,Sig=250,4 Ref=360,100 | | | | | |
|---|---|---|---|---|---|---|
| **RT [min]** | **Type** | **Width [min]** | **Area** | **Height** | **Area%** | **Name** |
| 20.379 | MM m | 1.94 | 48.91 | 1.13 | 1.58 | |
| 22.885 | MM m | 3.59 | 3042.04 | 46.37 | 98.42 | |
| | | **Sum** | **3090.94** | | | |

**4b**



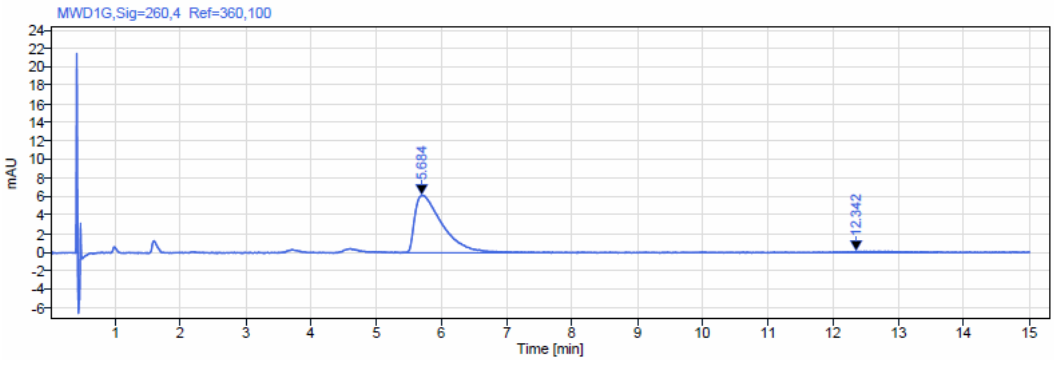

*Racemic:*




**Signal:** MWD1G,Sig=260,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 5.775 | MM m | 1.12 | 56.78 | 2.14 | 50.30 | |
| 12.185 | MM m | 2.01 | 56.10 | 1.00 | 49.70 | |
| | | **Sum** | **112.88** | | | |

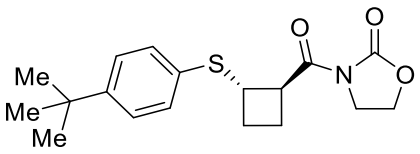
*Enantioenriched:*



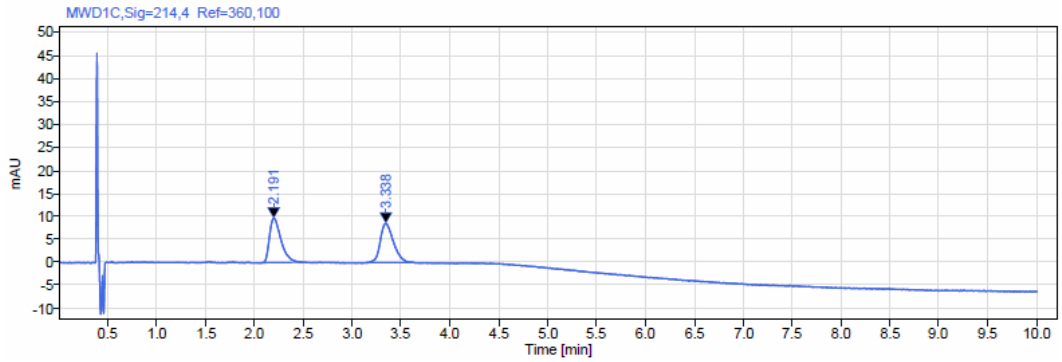

**Signal:** MWD1G,Sig=260,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 5.684 | MM m | 2.25 | 183.16 | 6.21 | 96.72 | |
| 12.342 | MM m | 1.59 | 6.20 | 0.14 | 3.28 | |
| | | **Sum** | **189.37** | | | |

**4c**



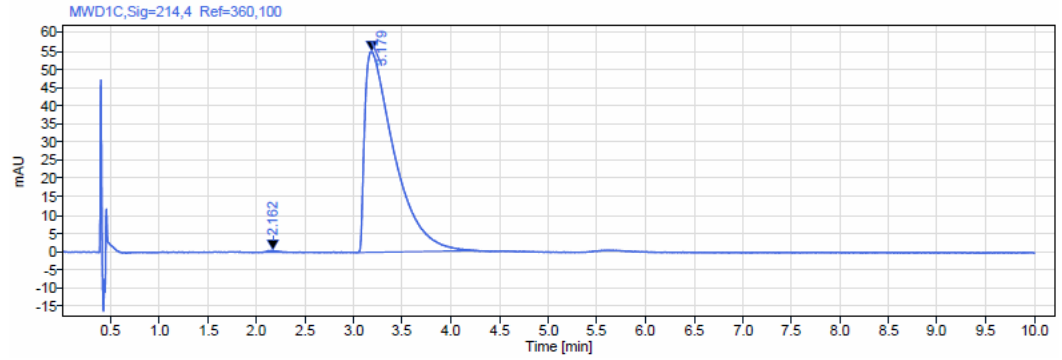

*Racemic:*




**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 2.191 | MM m | 0.46 | 78.84 | 9.61 | 49.65 | |
| 3.338 | MM m | 0.48 | 79.95 | 8.53 | 50.35 | |
| | | **Sum** | **158.80** | | | |

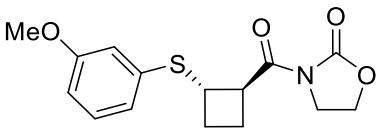
*Enantioenriched:*



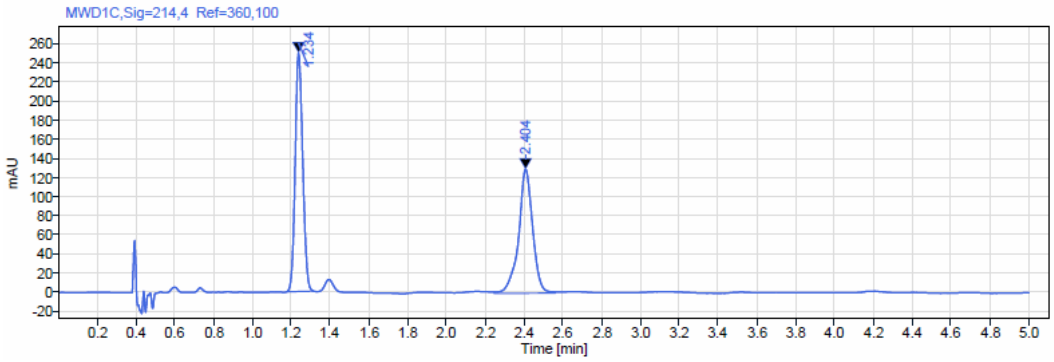

**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 2.162 | MM m | 0.27 | 3.28 | 0.49 | 0.28 | |
| 3.179 | MM m | 1.21 | 1158.09 | 55.01 | 99.72 | |
| | | **Sum** | **1161.37** | | | |

**4d**



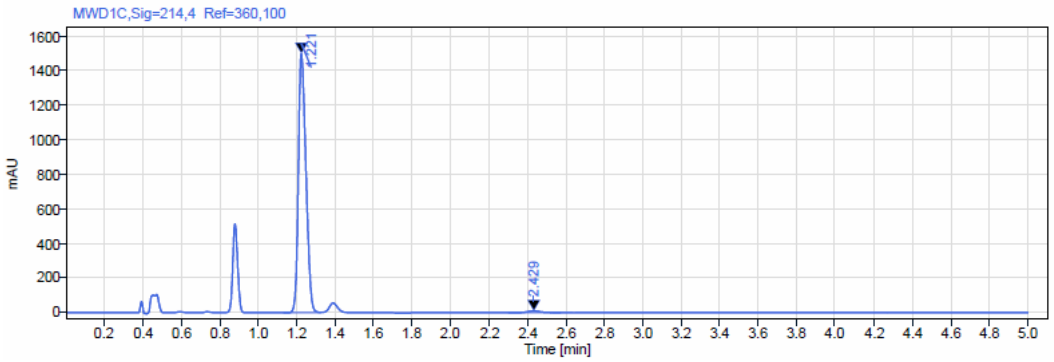

*Racemic:*




**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 1.234 | MM m | 0.14 | 675.15 | 250.22 | 50.73 | |
| 2.404 | MM m | 0.31 | 655.65 | 130.07 | 49.27 | |
| | | **Sum** | **1330.80** | | | |

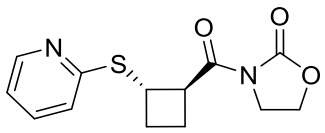
*Enantioenriched:*



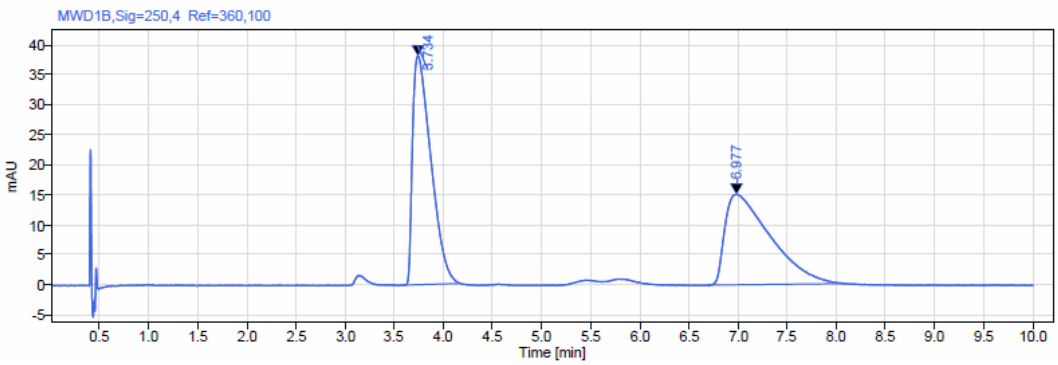

**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 1.221 | MM m | 0.19 | 4115.04 | 1502.97 | 98.86 | |
| 2.429 | MM m | 0.27 | 47.62 | 9.91 | 1.14 | |
| | | **Sum** | **4162.66** | | | |

**4e**



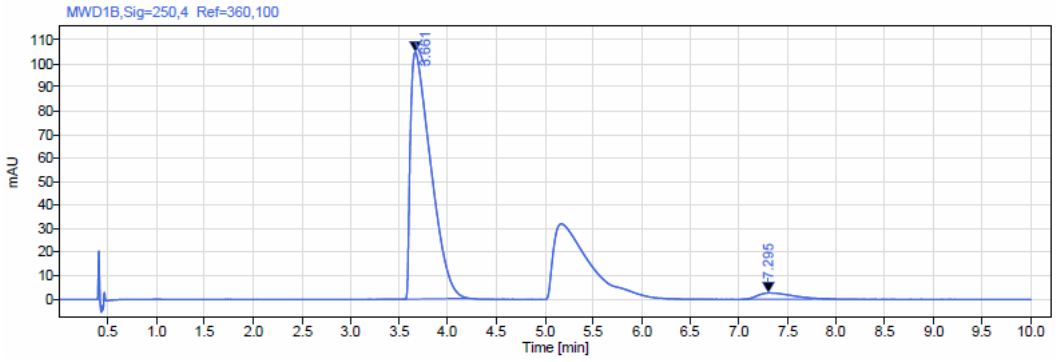
*Racemic:*




**Signal:** MWD1B,Sig=250,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 3.734 | MM m | 0.58 | 494.08 | 38.02 | 50.52 | |
| 6.977 | MM m | 1.40 | 483.91 | 15.03 | 49.48 | |
| | | **Sum** | **977.99** | | | |

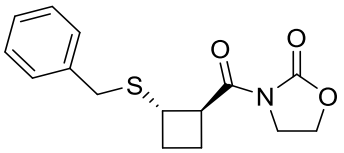
*Enantioenriched:*



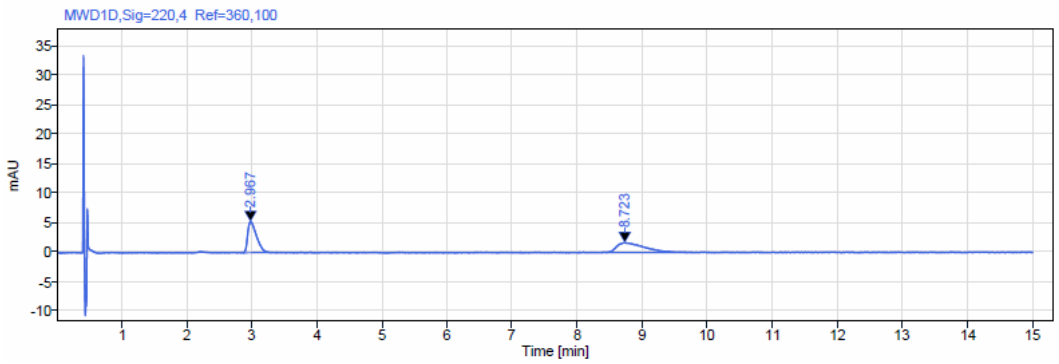

**Signal:** MWD1B,Sig=250,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 3.661 | MM m | 0.69 | 1527.96 | 105.02 | 95.94 | |
| 7.295 | MM m | 0.89 | 64.66 | 2.65 | 4.06 | |
| | | **Sum** | **1592.62** | | | |

**4f**

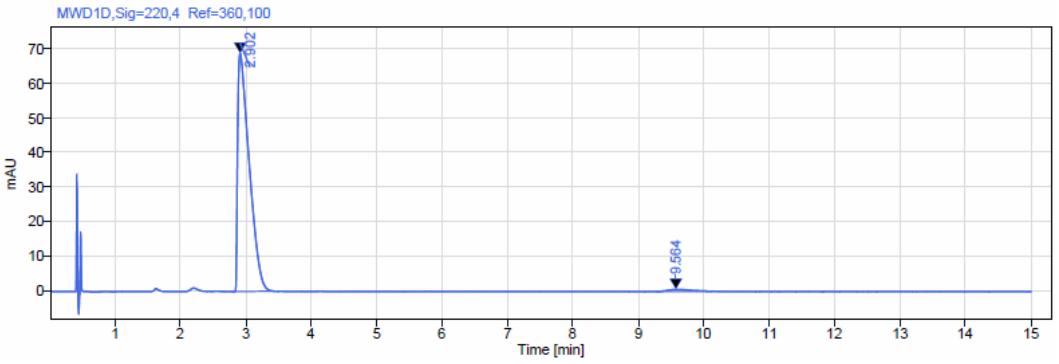



*Racemic:*



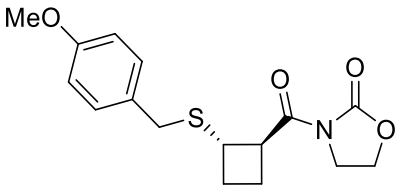

| Signal: | MWD1D,Sig=220,4 Ref=360,100 | | | | | |
|---|---|---|---|---|---|---|
| **RT [min]** | **Type** | **Width [min]** | **Area** | **Height** | **Area%** | **Name** |
| 2.967 | MM m | 0.44 | 49.36 | 5.26 | 50.29 | |
| 8.723 | MM m | 1.19 | 48.78 | 1.65 | 49.71 | |
| | | **Sum** | **98.14** | | | |

*Enantioenriched:*

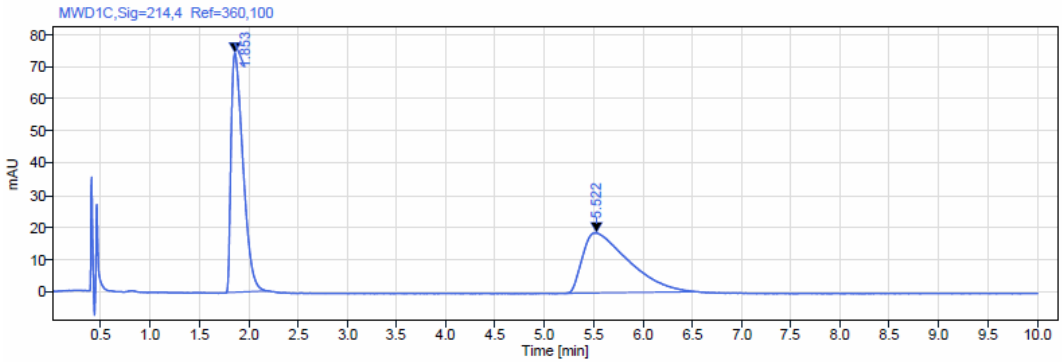



| Signal: | MWD1D,Sig=220,4 Ref=360,100 | | | | | |
|---|---|---|---|---|---|---|
| **RT [min]** | **Type** | **Width [min]** | **Area** | **Height** | **Area%** | **Name** |
| 2.902 | MM m | 0.67 | 842.60 | 68.81 | 98.13 | |
| 9.564 | MM m | 0.85 | 16.04 | 0.64 | 1.87 | |
| | | **Sum** | **858.64** | | | |

**4g**



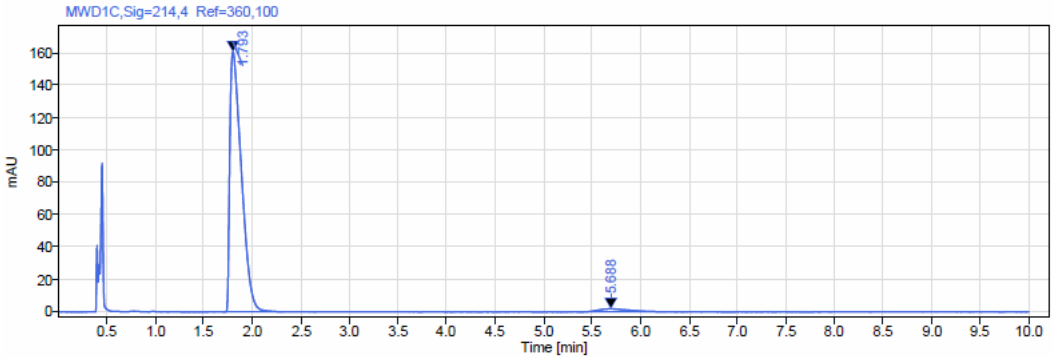

*Racemic:*




**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 1.853 | MM m | 0.42 | 623.46 | 74.21 | 50.87 | |
| 5.522 | MM m | 1.33 | 602.09 | 18.63 | 49.13 | |
| | | **Sum** | **1225.54** | | | |

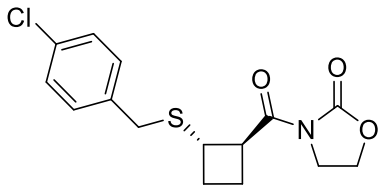
*Enantioenriched:*



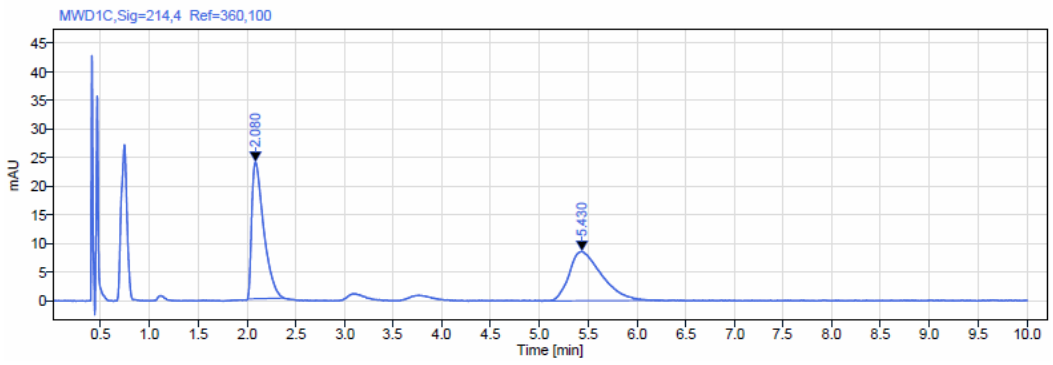

**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 1.793 | MM m | 0.61 | 1333.80 | 161.03 | 96.94 | |
| 5.688 | MM m | 0.93 | 42.12 | 1.92 | 3.06 | |
| | | **Sum** | **1375.92** | | | |

**4h**



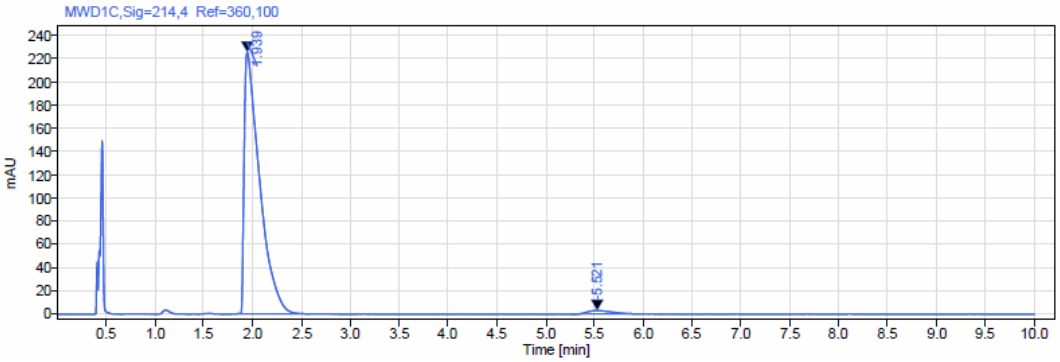

*Racemic:*




**Signal:** MWD1C,Sig=214,4 Ref=360,100

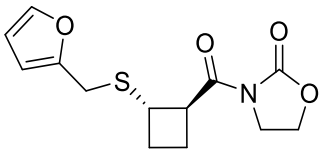
| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 2.080 | MM m | 0.37 | 204.16 | 23.91 | 50.63 | |
| 5.430 | MM m | 1.22 | 199.10 | 8.63 | 49.37 | |
| | | **Sum** | **403.26** | | | |

*Enantioenriched:*



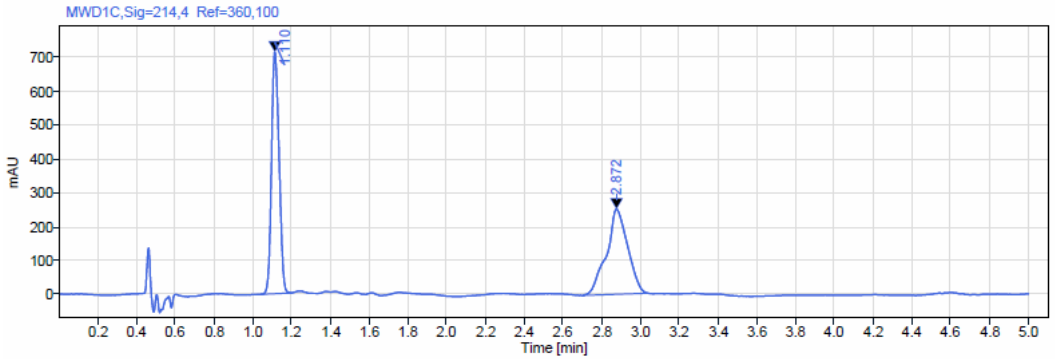

**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 1.939 | MM m | 0.78 | 2478.73 | 225.92 | 97.91 | |
| 5.521 | MM m | 0.73 | 52.95 | 3.01 | 2.09 | |
| | | **Sum** | **2531.69** | | | |



**4i**

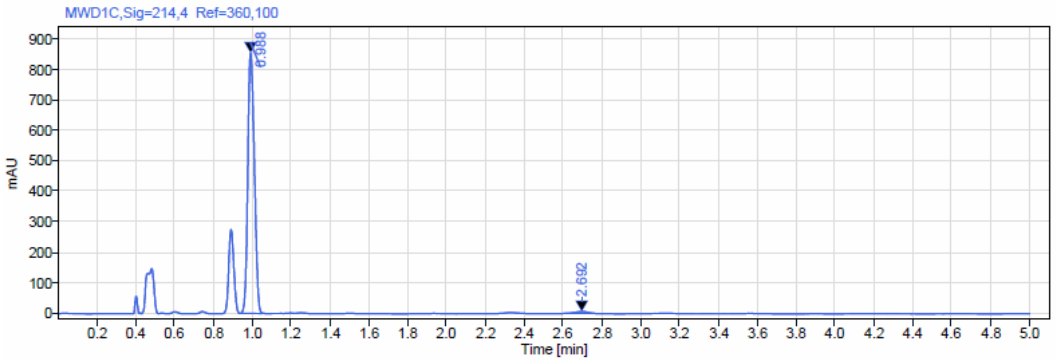
*Racemic:*




**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 1.110 | MM m | 0.18 | 1930.71 | 713.17 | 50.31 | |
| 2.872 | MM m | 0.34 | 1906.66 | 251.18 | 49.69 | |
| | | **Sum** | **3837.37** | | | |

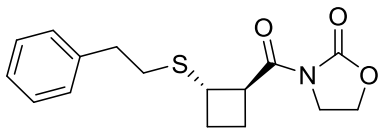
*Enantioenriched:*



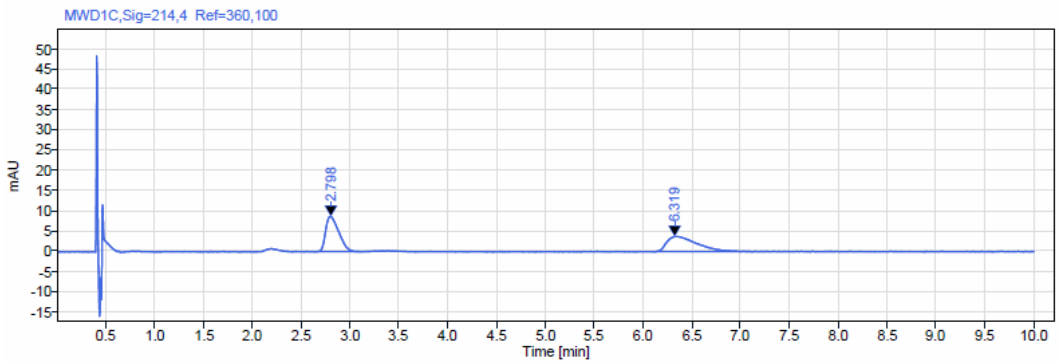

**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 0.988 | MM m | 0.11 | 2004.09 | 855.40 | 98.70 | |
| 2.692 | MM m | 0.15 | 26.35 | 6.15 | 1.30 | |
| | | **Sum** | **2030.44** | | | |

**4j**



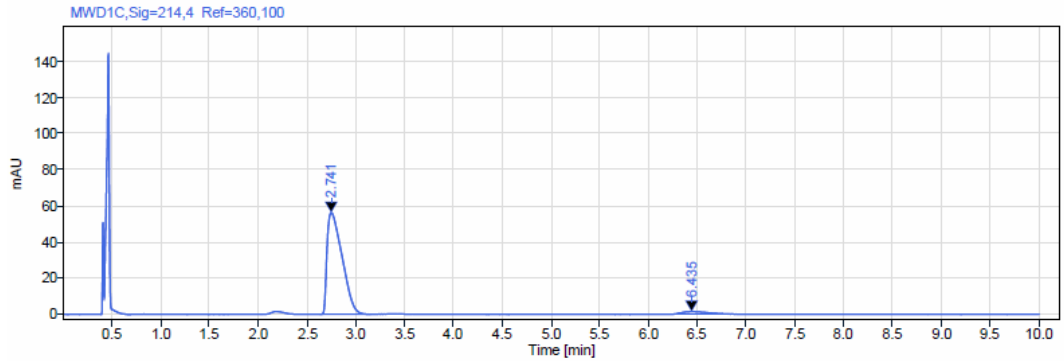

*Racemic:*




**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 2.798 | MM m | 0.49 | 80.74 | 8.69 | 49.86 | |
| 6.319 | MM m | 1.05 | 81.21 | 3.73 | 50.14 | |
| | | **Sum** | **161.95** | | | |

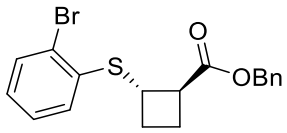
*Enantioenriched:*



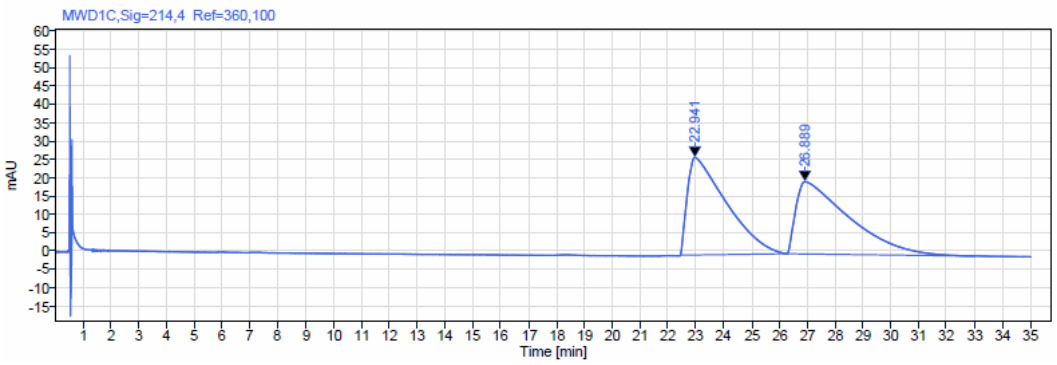

**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 2.741 | MM m | 0.52 | 602.55 | 56.51 | 95.35 | |
| 6.435 | MM m | 0.86 | 29.37 | 1.50 | 4.65 | |
| | | **Sum** | **631.93** | | | |

**3a**

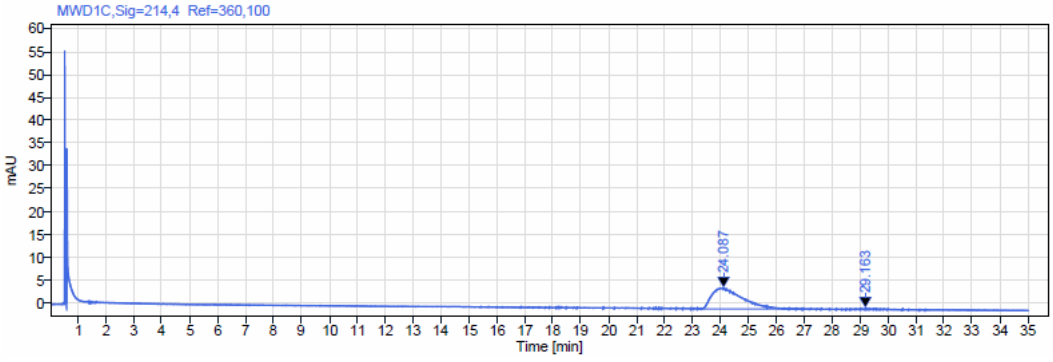



*Racemic:*



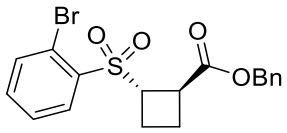

| Signal: | MWD1C,Sig=214,4 Ref=360,100 | | | | | |
|---|---|---|---|---|---|---|
| **RT [min]** | **Type** | **Width [min]** | **Area** | **Height** | **Area%** | **Name** |
| 22.941 | MM m | 3.79 | 2575.75 | 26.64 | 49.75 | |
| 26.889 | MM m | 6.79 | 2601.47 | 19.75 | 50.25 | |
| | | **Sum** | **5177.22** | | | |

*Enantioenriched:*

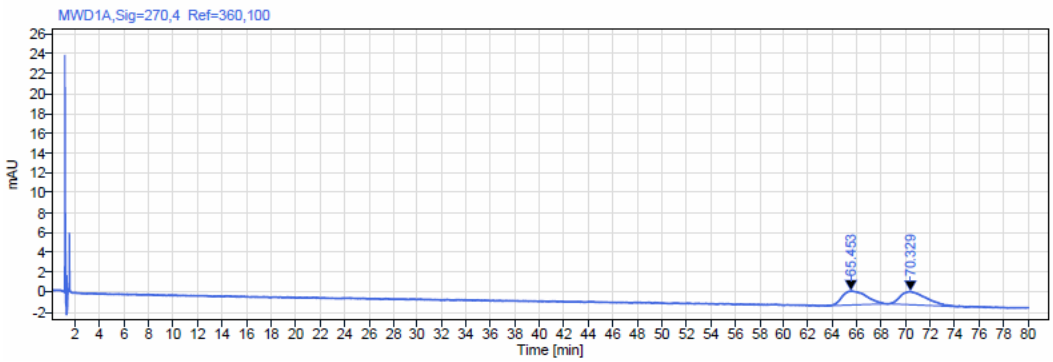



| Signal: | MWD1C,Sig=214,4 Ref=360,100 | | | | | |
|---|---|---|---|---|---|---|
| **RT [min]** | **Type** | **Width [min]** | **Area** | **Height** | **Area%** | **Name** |
| 24.087 | MM m | 3.87 | 346.47 | 4.61 | 97.11 | |
| 29.163 | MM m | 2.10 | 10.31 | 0.38 | 2.89 | |
| | | **Sum** | **356.78** | | | |

**5**



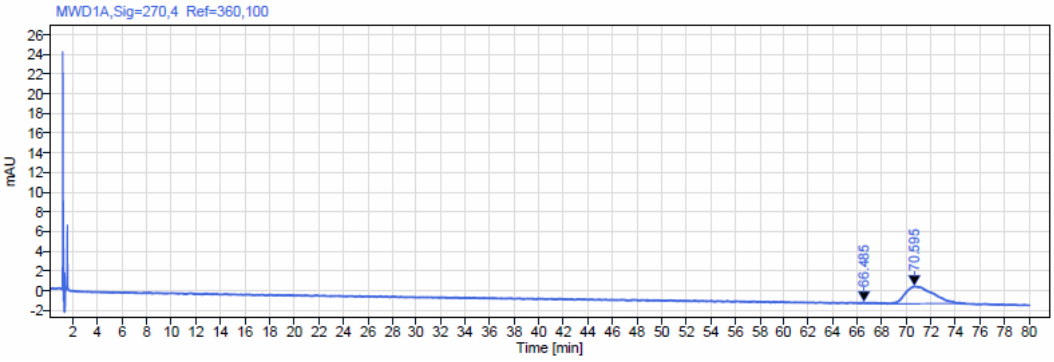

*Racemic:*




**Signal:** MWD1A,Sig=270,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 65.453 | MM m | 4.96 | 192.54 | 1.43 | 49.66 | |
| 70.329 | MM m | 5.85 | 195.19 | 1.35 | 50.34 | |
| | | **Sum** | **387.73** | | | |

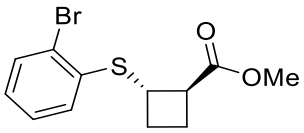
*Enantioenriched:*



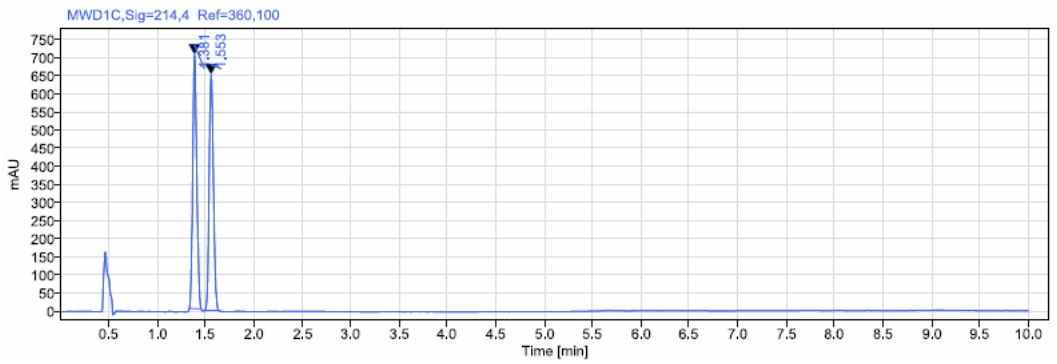

**Signal:** MWD1A,Sig=270,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 66.485 | MM m | 2.35 | 8.21 | 0.15 | 2.89 | |
| 70.595 | MM m | 5.87 | 276.20 | 1.79 | 97.11 | |
| | | **Sum** | **284.41** | | | |

**6**



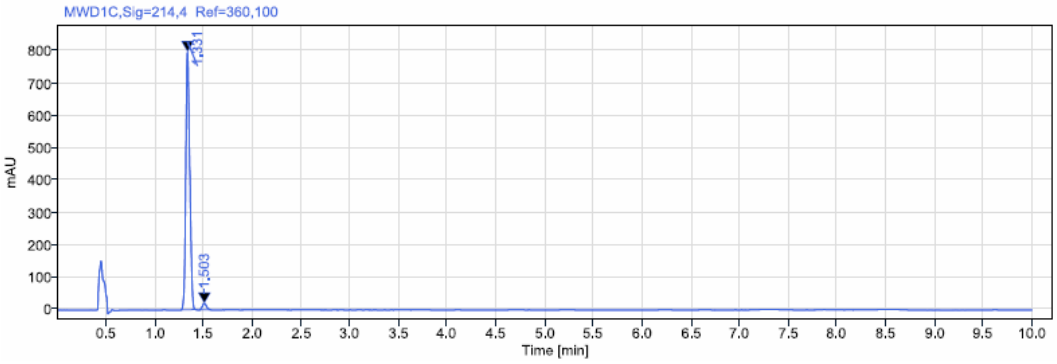

*Racemic:*




**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 1,381 | MM m | 0,12 | 2048,17 | 701,02 | 50,80 | |
| 1,553 | MM m | 0,15 | 1983,75 | 652,35 | 49,20 | |
| | | **Sum** | **4031,92** | | | |

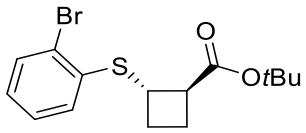
*Enantioenriched:*



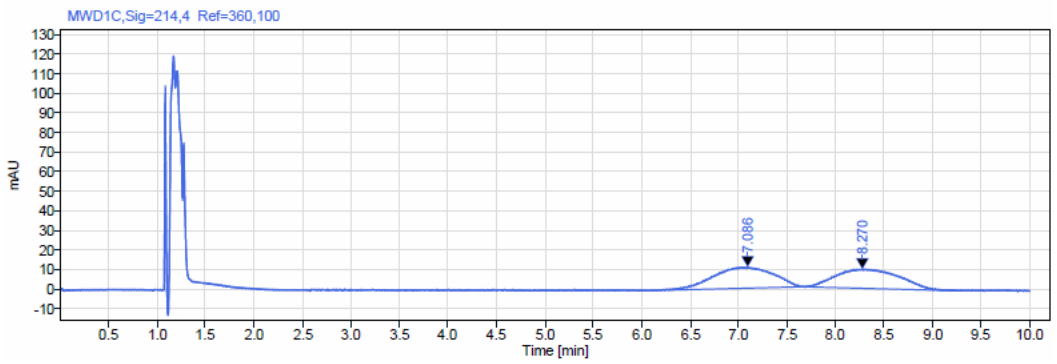

**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 1,331 | MM m | 0,14 | 2253,58 | 796,81 | 97,41 | |
| 1,503 | MM m | 0,12 | 59,87 | 19,92 | 2,59 | |
| | | **Sum** | **2313,45** | | | |

**7**



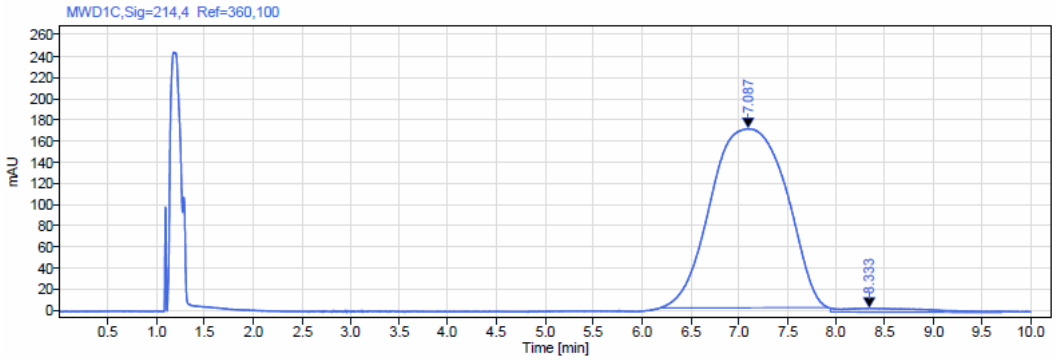

*Racemic:*




**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 7.086 | MM m | 1.39 | 459.75 | 10.77 | 50.76 | |
| 8.270 | MM m | 1.55 | 446.04 | 9.77 | 49.24 | |
| | | **Sum** | **905.79** | | | |

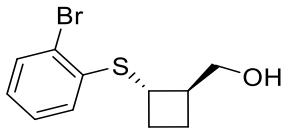
*Enantioenriched:*



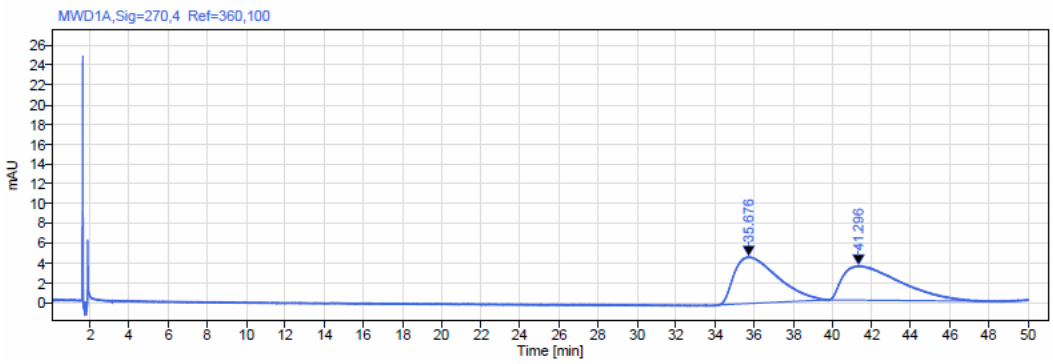

**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 7.087 | MM m | 1.72 | 9077.36 | 168.66 | 97.37 | |
| 8.333 | MM m | 1.76 | 245.18 | 3.66 | 2.63 | |
| | | **Sum** | **9322.54** | | | |

**8**



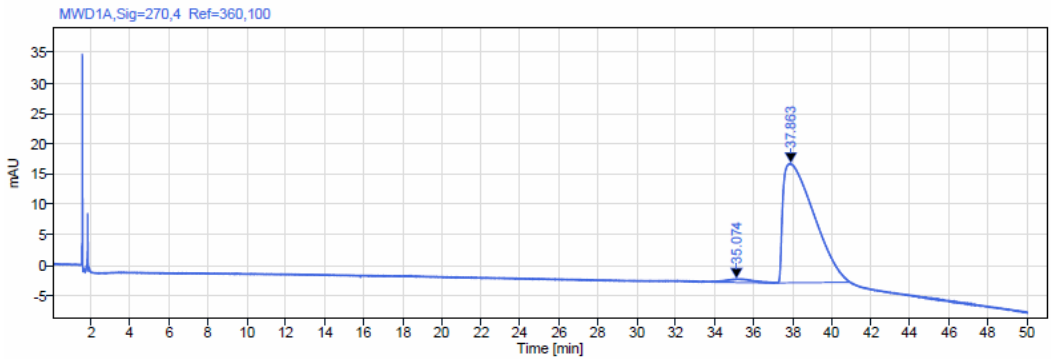

*Racemic:*




**Signal:** MWD1A,Sig=270,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 35.676 | MM m | 5.55 | 719.05 | 4.76 | 50.44 | |
| 41.296 | MM m | 8.55 | 706.47 | 3.52 | 49.56 | |
| | | **Sum** | **1425.52** | | | |

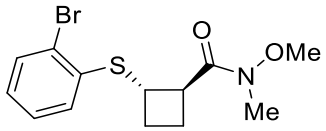
*Enantioenriched:*



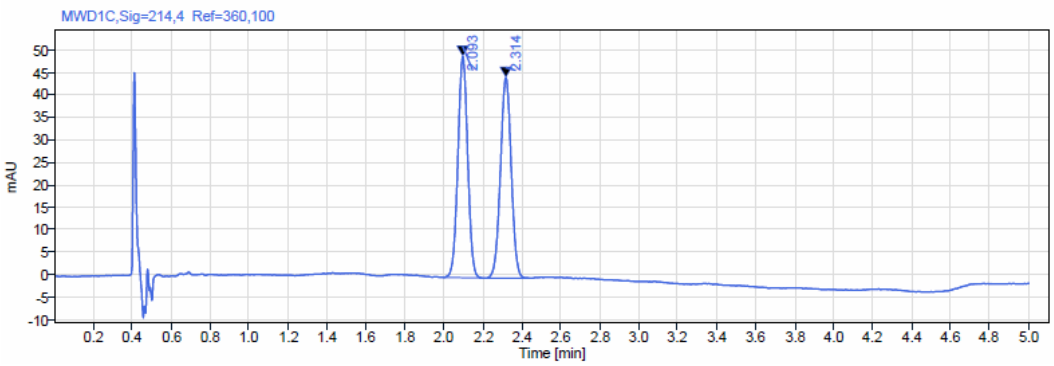

**Signal:** MWD1A,Sig=270,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 35.074 | MM m | 3.50 | 55.69 | 0.63 | 2.51 | |
| 37.863 | MM m | 3.69 | 2159.88 | 19.69 | 97.49 | |
| | | **Sum** | **2215.57** | | | |

**3z**



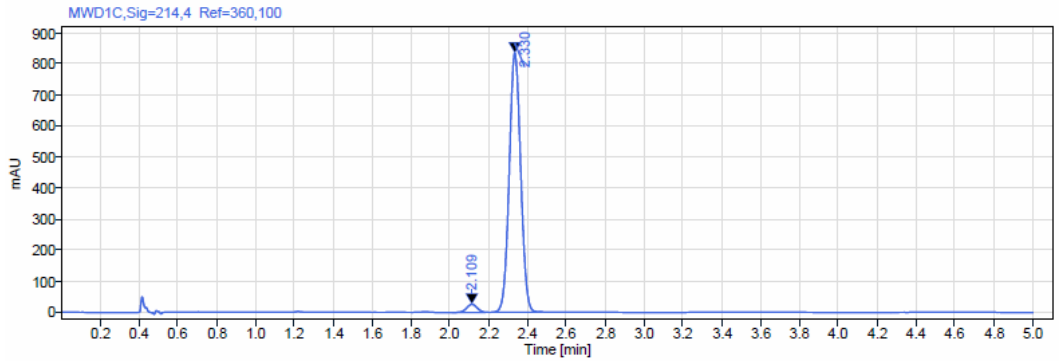

*Racemic:*




**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 2.093 | MM m | 0.23 | 171.67 | 49.15 | 50.08 | |
| 2.314 | MM m | 0.23 | 171.11 | 44.56 | 49.92 | |
| | | **Sum** | **342.78** | | | |

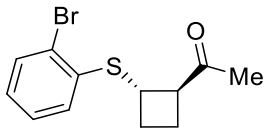
*Enantioenriched:*



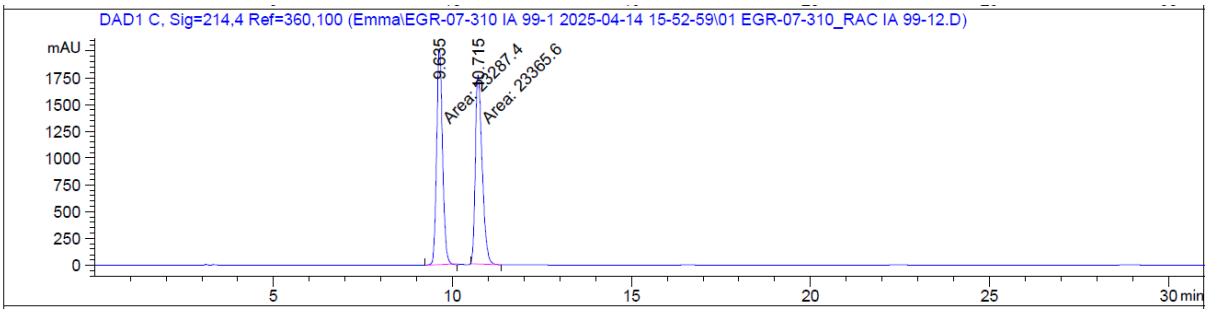

**Signal:** MWD1C,Sig=214,4 Ref=360,100

| RT [min] | Type | Width [min] | Area | Height | Area% | Name |
|---|---|---|---|---|---|---|
| 2.109 | MM m | 0.20 | 97.87 | 26.17 | 2.78 | |
| 2.330 | MM m | 0.26 | 3424.70 | 836.26 | 97.22 | |
| | | **Sum** | **3522.57** | | | |

**9**



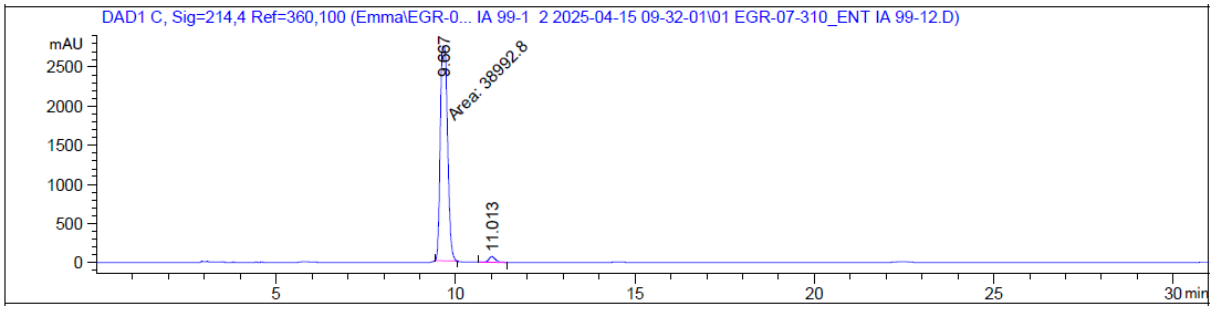

*Racemic:*




Signal 3: DAD1 C, Sig=214,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.635 | MM | 0.1926 | 2.32874e4 | 2015.40210 | 49.9162 |
| 2 | 10.715 | MM | 0.2206 | 2.33656e4 | 1764.92322 | 50.0838 |
| Totals : | | | | 4.66530e4 | 3780.32532 | |

*Enantioenriched:*




Signal 3: DAD1 C, Sig=214,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.667 | MM | 0.2365 | 3.89928e4 | 2748.00073 | 97.6764 |
| 2 | 11.013 | BB | 0.1973 | 927.59180 | 72.47859 | 2.3236 |
| Totals : | | | | 3.99204e4 | 2820.47932 | |