SUPPORTING INFORMATION

Intramolecular cyclopropylmethylation via non-classical carbenium ion

Marija Skvorcova, Aigars Jirgensons*
Latvian Institute of Organic Synthesis, Aizkraukles 21, Riga, LV-1006

1. General considerations ................................................................. 2
2. Substrate 1 synthesis..................................................................... 2
3. Optimization of conditions for the cyclopropylmethylation reaction .... 33
4. Cyclopropylmethylation reaction and characterization of the products.... 34
5. Structure determination of oxazoline 2b by X-ray of trichloroacetamide 22 ..40
5. NMR data ..................................................................................... 42
6. Chiral HPLC of compound 7j......................................................... 158
1. General considerations

All procedures were performed under argon atmosphere unless noted otherwise. Reagents and starting materials were obtained from commercial sources and used as received. The solvents were purified and dried by standard procedures prior to use. Flash column chromatography was carried out using silica gel (230–400 mesh). Thin layer chromatography (TLC) was performed on silica gel and was visualized by UV lamp or staining with KMnO₄. NMR spectra were recorded on 300, 400 and 600 MHz spectrometers with chemical shift values (δ) in parts per million using the residual chloroform, dimethylsulfoxide or methanol signal as an internal standard. Gas chromatographic (GC) analysis was performed on Agilent Technologies gas chromatographer with triple-axis detector, heating range 80-280 °C, column 30 m × 0.25 mm, 0.25 µm, 7 inch cage. HRMS analyses were performed on a hybrid quadrupole time-of-flight mass spectrometer equipped with an electrospray ion source.

2. Substrate 1 synthesis

Trichloroacetimidates cis/trans-1a were synthesized in five steps from commercially available 1,2-dihydroxybenzene (4) (Scheme 1). Acylation and subsequent allylation of hydroxy groups gave alkene 6. Separately racemic trans- and cis-isomers of 7a were obtained in cyclopropanation reaction from alkene 6 and ethyl diazoacetate in the presence of Rh catalyst. Reduction of ester gave alcohol cis/trans-8a, which was converted to corresponding imidate cis/trans-9a in the presence of DBU and CCl₃CN.

![Scheme 1](image-url)
2-Hydroxyphenyl acetate (5)

To a stirred solution of 1,2-dihydroxybenzene (4) (1.54 g, 13.97 mmol, 1.0 equiv) in MeCN (12 mL) was added acetic acid anhydride (1.3 mL, 13.97 mmol, 1.0 equiv). The mixture was refluxed until the starting material disappeared (TLC). Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 2:1) afforded 2.02 g (96%) of 2-hydroxyphenyl acetate (5) as a yellowish oil. This compound is known in the literature.¹

¹H NMR (300 MHz, CDCl₃, ppm) δ 7.18 – 7.06 (m, 1H), 7.00 (dd, J = 8.1 and 1.6 Hz, 1H), 6.93 (ddd, J = 8.8, 7.2 and 1.6 Hz, 1H), 6.89 – 6.78 (m, 1H), 5.30 (bs, 1H), 2.36 (s, 3H).

2-(Allyloxy)phenyl acetate (6)

Allyl bromide (1.0 mL, 11.90 mmol, 1.05 equiv) was added dropwise to a cooled (0 °C) solution of phenol 5 (1.72 g, 11.30 mmol, 1.0 equiv) and anhydrous K₂CO₃ (4.60 g, 34.00 mmol, 3.0 equiv) in DMF (10 mL). After the addition was complete, the mixture was allowed to warm to room temperature and stirred until the starting material disappeared (TLC), then the reaction mixture was diluted with water and extracted with ethyl acetate (2 × 10 mL). The organic layers were combined, washed with brine (2 × 15 mL) and dried over MgSO₄. Filtration and concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 6:1) afforded 1.74 g (80%) of 2-(allyloxy)phenyl acetate (6) as a colorless oil. This compound is known in the literature.²

²H NMR (300 MHz, CDCl₃, ppm) δ 7.17 (td, J = 8.4, 7.8 and 2.0 Hz, 1H), 7.04 (dd, J = 7.7 and 1.9 Hz, 1H), 6.95 (t, J = 7.5 Hz, 2H), 6.01 (ddt, J = 17.1, 10.0 and 5.0 Hz, 1H), 5.38 (dt, J = 17.4 and 1.8 Hz, 1H), 5.26 (dt, J = 10.7 and 1.7 Hz, 1H), 4.56 (dt, J = 5.0 and 1.7 Hz, 2H), 2.31 (s, 3H).

¹ Liu, J. et al. Tetrahedron 2016, 72, 4103.
Ethyl 2-((2-acetoxyphenoxy)methyl)cyclopropane-1-carboxylate (7a)

To a solution alkene 6 (466.9 mg, 2.43 mmol, 1.0 equiv) and rhodium (II) acetate dimer (10.7 mg, 2.40 μmol, 1 mol%) in DCM (20 mL) ethyl diazoacetate (831.5 mg, 7.29 mmol, 3.0 equiv) was added via syringe pump over 4 hours. The resulting mixture was stirred at room temperature for 12 hours. Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 6:1) afforded 277.9 mg (41%) of ethyl 2-((2-acetoxyphenoxy)methyl)cyclopropane-1-carboxylate (7a) as an inseparable mixture of diastereomers.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.18 – 7.10 (m, 2H), 7.05 – 6.96 (m, 2H), 6.98 – 6.86 (m, 4H), 4.31 (dd, $J = 10.2$, 5.9 Hz, 1H), 4.18 – 3.98 (m, 6H), 3.83 (dd, $J = 9.9$, 6.5 Hz, 1H), 2.29 (dd, $J = 1.4$, 0.4 Hz, 6H), 1.89 – 1.79 (m, 2H), 1.78 – 1.64 (m, 2H), 1.31 – 1.10 (m, 9H), 0.96 (ddd, $J = 8.4$, 6.3, 4.4 Hz, 1H).

HR-MS (ESI-TOF) m/z: calcd. for C$_{15}$H$_{18}$O$_5$Na 301.1052; found: 301.1066 [M+Na]$^+$. 

2-((2-(Hydroxymethyl)cyclopropyl)methoxy)phenol (cis- and trans-8a)

A solution of ester 7a (674.0 mg, 2.42 mmol, 1.0 equiv) in THF (24 mL) was cooled to 0 °C and LiAlH$_4$ (372.2 mg, 9.81 mmol, 4.05 equiv) was added in several portions. After the addition was complete, the mixture was allowed to warm to room temperature and then refluxed until the starting material disappeared (TLC). Reaction mixture was quenched with water (4.1 equiv) and filtered (to remove inorganic solids). A mixture of racemic trans- and cis-isomers trans-8a and cis-8a were obtained and their separation was done by column chromatography on silica gel (eluent hexanes/EtOAc 1:1.5). After purification 159 mg (34%) of cis-8a and 220 mg (47%) of trans-8a were obtained, both as colorless oils.

**Cis-isomer:** $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.00 – 6.85 (m, 4H), 6.82 (ddd, $J = 7.9$, 6.8, 2.4 Hz, 1H), 4.49 (dd, $J = 10.7$, 5.6 Hz, 1H), 4.09 (dd, $J = 11.5$, 4.5 Hz, 1H), 3.68 (t, $J = 10.5$ Hz, 1H), 3.44 – 3.32 (m, 1H), 2.24 (1H, bs), 1.58 – 1.44 (m, 1H), 1.41 (dddd, $J = 13.8$, 10.6, 8.5, 5.6 Hz, 1H), 0.91 (td, $J = 8.4$, 5.2 Hz, 1H), 0.30 (q, $J = 5.4$ Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 147.4, 145.8, 122.8, 119.9, 115.69, 115.1, 70.9, 62.7, 18.1, 14.9, 7.9.

HR-MS (ESI-TOF) m/z: calcd. for C$_{11}$H$_{14}$O$_3$Na 217.0841; found: 217.0832 [M+Na]$^+$. 


**Trans-isomer:** $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 6.96 – 6.74 (m, 4H), 6.17 (s, 1H), 4.02 (dd, $J = 10.2$, 6.3 Hz, 1H), 3.80 – 3.70 (m, 1H), 3.67 (dd, $J = 11.2$, 6.1 Hz, 1H), 3.36 (dd, $J = 11.2$, 7.6 Hz, 1H), 2.01 (s, 1H), 1.28 – 1.07 (m, 2H), 0.64 – 0.53 (m, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 225.8, 146.2, 145.9, 121.8, 120.1, 114.9, 112.7, 72.9, 65.9, 19.9, 16.4, 8.0.

HR-MS (ESI-TOF) m/z: calcd. for C$_{11}$H$_{14}$O$_3$Na 217.0841; found: 217.0842 [M+Na]$^+$. 


((1$S^*,2S^*$)-2-((2-Hydroxyphenoxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (trans-1a)

To a solution of alcohol trans-8a (16.9 mg, 0.087 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (3 mL) 4 Å molecular sieves were added. Reaction mixture was cooled to 0 oC and then DBU (13 µL, 0.087 mmol, 1.0 equiv) was added. Solution was stirred at 0 oC for 30 minutes. Then trichloroacetonitrile (18 µL, 0.174 mmol, 2.0 equiv) was added, and the reaction mixture was stirred until TLC showed complete conversion. Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 8:1) afforded 29.3 mg (99 %) of ((1$S^*,2S^*$)-2-((2-hydroxyphenoxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate as a colorless oil.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 8.21 (s, 1H), 6.86 (dt, $J = 7.8$, 1.2 Hz, 1H), 6.85 – 6.70 (m, 3H), 5.66 (s, 1H), 4.29 (dd, $J = 11.3$, 6.0 Hz, 1H), 4.10 – 3.91 (m, 2H), 3.75 (dd, $J = 10.1$, 7.2 Hz, 1H), 1.40 – 1.12 (m, 2H), 0.69 (ddt, $J = 17.7$, 8.3, 5.3 Hz, 2H).

Unstable under the conditions of HRMS.

((1$R^*,2S^*$)-2-((2-Hydroxyphenoxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (cis-1a)

Prepared by analogy to compound trans-1a from cis-8a (17.4 mg, 0.090 mmol, 1.0 equiv), DBU (13 µL, 0.090 mmol, 1.0 equiv), trichloroacetonitrile (18 µL, 0.179 mmol, 2.0 equiv), and DCM (3 mL). Yield: 32.0 mg (99 %).
\(^{1}\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 8.29 (bs, 1H), 6.97 – 6.76 (m, 4H), 5.86 (s, 1H), 4.61 (dd, \(J = 11.8, 6.4\) Hz, 1H), 4.26 – 4.05 (m, 3H), 1.67 – 1.47 (m, 2H), 1.04 (td, \(J = 8.5, 5.3\) Hz, 1H), 0.55 (q, \(J = 5.6\) Hz, 1H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\), ppm) \(\delta\) 162.9, 146.0, 145.7, 121.8, 120.0, 114.7, 112.2, 91.4, 69.5, 68.9, 15.4, 14.3, 8.5.

Unstable under the conditions of HRMS.

* Bis-trichloroacetimidate 1b was synthesized in two steps according to Scheme 2 from commercially available diethyl trans-1,2-cyclopropanedicarboxylate (7b). Reduction of diester gave diol 8b, which was converted to corresponding bis-trichloroacetimidate 1b in the presence of DBU and CCl\(_3\)CN.

\[
\begin{align*}
\text{EtO}_2\text{C} & \xrightarrow{\text{LiAlH}_4, \text{THF, } 0^\circ\text{C} - rt} \text{CO}_2\text{Et} \\
7b & \xrightarrow{\text{DBU, CCl}_3\text{CN}, \text{DCM, } 4\text{A MS, } \sigma^\circ\text{C}} \text{Cl}_3\text{C} & \xrightarrow{\text{OH}} \text{NH} \\
& \xrightarrow{\text{O}} \text{O} & \xrightarrow{\text{CCl}_3} \\
8b & \xrightarrow{\text{DBU, CCl}_3\text{CN}, \text{DCM, } 4\text{A MS, } \sigma^\circ\text{C}} \text{Cl}_3\text{C} & \xrightarrow{\text{NH}} \text{OH} \\
& \xrightarrow{\text{O}} \text{O} & \xrightarrow{\text{CCl}_3} \\
1b & \text{Cl}_3\text{C} & \xrightarrow{\text{NH}} \text{O} & \xrightarrow{\text{O}} \text{Cl}_3\text{C}
\end{align*}
\]

Scheme 2

((1S*,2S*)-Cyclopropane-1,2-diyl)dimethanol (8b)

Prepared by analogy to compound 8a from diester 7b (510.0 mg, 2.74 mmol, 1.0 equiv), LiAlH\(_4\) (416.0 mg, 10.96 mmol, 4.0 equiv), and THF (6 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded 178 mg (64 %) of ((1S*,2S*)-cyclopropane-1,2-diyl)dimethanol as a colorless oil. This compound is known in the literature.\(^3\)

\(^{1}\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 4.63 (bs, 2H), 3.77 (dd, \(J = 11.3, 4.6\) Hz, 2H), 2.99 (dd, \(J = 11.3, 8.7\) Hz, 2H), 1.02 – 0.87 (m, 2H), 0.42 – 0.30 (m, 2H).

((1S*,2S*)-Cyclopropane-1,2-diyl)bis(methylene) bis(2,2,2-trichloroacetimidate) (1b)

Prepared by analogy to compound 1a from diol 8b (170.0 mg, 1.66 mmol, 1.0 equiv), DBU (25 \(\mu\)L, 0.017 mmol, 0.1 equiv), trichloroacetonitrile (0.5 mL, 4.980 mmol, 3.0 equiv), and DCM (17 mL). Yield: 613.0 mg (94 %).

1H NMR (400 MHz, CDCl₃, ppm) δ 8.25 (bs, 2H), 4.27 – 4.18 (m, 2H), 4.18 – 4.07 (m, 2H), 1.38 (tt, J = 7.6, 5.0 Hz, 2H), 0.73 (dt, J = 11.5, 7.0 Hz, 2H).

13C NMR (101 MHz, CDCl₃, ppm) δ 162.8, 162.8, 91.5, 72.1, 72.1, 15.7, 8.6.  

Unstable under the conditions of HRMS.

Trichloroacetimidates 1c,d were synthesized in four steps according to Scheme 3 from commercially available (R)-(−)-glycidol (9). Cyclopropanes 7c,d were obtained in Horner-Wadsworth-Emmons reaction from stabilized phosphonate 11 and epoxides 10c,d. Reduction of ester groups gave alcohols 8c,d, which were transformed to the corresponding trichloroacetimidates 1c,d in the reaction with CCl₃CN using DBU as a base.

Note: Oxirane 10c (Ar = Ph) was commercially available.
(S)-2-(((3-Methoxybenzyl)oxy)methyl)oxirane (10d)

(R)-Glycidol (9) (0.4 mL, 6.03 mmol, 1.0 equiv) was added slowly to a suspension of NaH (313.3 mg, 7.83 mmol, 1.3 equiv) in anhydrous DMF (10 mL) at 0 °C. After 20 min, 3-methoxybenzyl bromide (1.1 mL, 7.83 mmol, 1.3 equiv) was added dropwise at 0 °C. The reaction mixture was stirred at room temperature. After completion (monitored by TLC), the reaction mixture was quenched with ice-cooled water (10 mL) and diluted with ethyl acetate (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried with Na2SO4, concentrated under reduced pressure, and purified by silica gel column chromatography (eluant EtOAc/hexane 1:6). Compound 10d (505 mg, 43%) was obtained as a colorless liquid. This compound is known in the literature.4

1H NMR (300 MHz, CDCl3, ppm) δ 7.35 – 7.22 (m, 1H), 7.01 – 6.80 (m, 3H), 4.68 – 4.50 (m, 2H), 3.89 – 3.74 (m, 4H), 3.47 (dd, J = 11.4 and 5.8 Hz, 1H), 3.22 (ddt, J = 5.8, 4.2 and 2.9 Hz, 1H), 2.84 (dd, J = 5.1 and 4.1 Hz, 1H), 2.65 (dd, J = 5.0 and 2.7 Hz, 1H).

[α]D20 = -2.0 (c = 1.0, CHCl3).

Ethyl (1R,2R)-2-((benzylxy)methyl)cyclopropane-1-carboxylate (7c)

To a suspension of sodium hydride (385.6 mg, 9.64 mmol, 2.1 equiv, 60% in mineral oil) in toluene (24 mL) was added triethylphosphonoacetate (11) (1.82 mL, 9.18 mmol) dropwise over 30 min. After stirring at room temperature for 10 minutes ether 10c (0.7 mL, 4.59 mmol, 1.0 equiv) was added dropwise, followed by heating at reflux for 14 hours. The solution was cooled to room temperature, diluted with ethyl acetate (30 mL), then washed with saturated aqueous ammonium chloride (2 x 15 mL). After drying over magnesium sulfate and concentration in vacuo, the crude material was purified via flash column chromatography (6:1 petrol:ether eluant), to yield ethyl (1R,2R)-2-((benzylxy)methyl)cyclopropane-1-carboxylate (532 mg, 50 %) as a colourless oil. This compound is known in the literature.5

$^1$H NMR (300 MHz, CDCl$_3$, ppm) δ 7.38 – 7.27 (m, 5H), 4.52 (s, 2H), 4.12 (qd, $J$ = 7.2 and 1.1 Hz, 2H), 3.51 – 3.29 (m, 2H), 1.74 (dq, $J$ = 8.8, 6.2 and 4.0 Hz, 1H), 1.62 – 1.51 (m, 1H), 1.31 – 1.15 (m, 4H), 0.86 (ddd, $J$ = 8.4, 6.3 and 4.3 Hz, 1H).

$[\alpha]_D^{20} = -77$ (c = 1.0, CHCl$_3$).

**Ethyl (1$R$,2$R$)-2-(((3-methoxybenzyl)oxy)methyl)cyclopropane-1-carboxylate (7d)**

![Image](image)

Prepared by analogy to compound 7c from ether 10d (480.8 mg, 2.48 mmol, 1.0 equiv), triethylphosphonoacetate 11 (0.98 mL, 4.95 mmol, 2.0 equiv), sodium hydride (207.9 mg, 5.20 mmol, 2.1 equiv, 60 % in mineral oil), and toluene (24 mL), Yield: 385 mg (59 %).

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.22 (t, $J$ = 8.1 Hz, 1H), 6.91 – 6.84 (m, 2H), 6.84 – 6.76 (m, 1H), 4.47 (s, 2H), 4.16 – 4.04 (m, 2H), 3.78 (s, 3H), 3.42 (dd, $J$ = 10.4 and 6.0 Hz, 1H), 3.32 (dd, $J$ = 10.4 and 6.7 Hz, 1H), 1.71 (dddd, $J$ = 12.8, 8.9, 6.3 and 4.1 Hz, 1H), 1.54 (dddd, $J$ = 8.8, 4.9, 4.1 Hz, 1H), 1.27 – 1.13 (m, 4H), 0.83 (ddd, $J$ = 8.3, 6.3, 4.2 Hz, 1H).

$^1$C NMR (101 MHz, CDCl$_3$, ppm) δ 173.6, 159.6, 139.7, 129.3, 119.7, 113.2, 112.7, 72.4, 71.4, 60.4, 55.0, 21.5, 18.4, 14.1, 12.8.

HR-MS (ESI-TOF) m/z: calcd. for C$_{15}$H$_{20}$O$_4$Na 287.1259; found: 287.1251 [M+Na]$^+$. $[\alpha]_D^{20} = -74$ (c = 1.0, CHCl$_3$).

**((1$R$,2$R$)-2-((Benzyloxy)methyl)cyclopropyl)methanol (8c)**

Prepared by analogy to compound 8a from ester 7c (214.61 mg, 0.916 mmol, 1.0 equiv), LiAlH$_4$ (76.48 mg, 2.015 mmol, 2.2 equiv), and THF (22 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded ((1$R$,2$R$)-2-((benzyloxy)methyl)cyclopropyl)methanol (8c) (136 mg, 77 %) as a colorless oil. This compound is known in the literature.$^6$

$^1$H NMR (300 MHz, CDCl$_3$, ppm) δ 7.32 – 7.14 (m, 5H), 4.45 (s, 2H), 3.47 – 3.10 (m, 4H), 2.52 (bs, 1H), 1.01 – 0.82 (m, 2H), 0.46 – 0.31 (m, 2H).

$[\alpha]_D^{20} = -11.6$ (c = 1.0, CHCl$_3$).

---

((1R,2R)-2-(((3-Methoxybenzyl)oxy)methyl)cyclopropyl)methanol (8d)

Prepared by analogy to compound 8a from ester 7d (346.39 mg, 1.31 mmol, 1.0 equiv), LiAlH$_4$ (109.43 mg, 2.88 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded ((1R,2R)-2-(((3-methoxybenzyl)oxy)methyl)cyclopropyl)methanol (8d) (234 mg, 80%) as a colorless oil.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.22 (t, $J = 8.1$ Hz, 1H), 6.88 (dd, $J = 7.4$ and 1.3 Hz, 2H), 6.83 – 6.75 (m, 1H), 4.47 (s, 2H), 3.77 (s, 3H), 3.45 (dd, $J = 11.2$ and 6.1 Hz, 1H), 3.43 – 3.27 (m, 2H), 3.23 (dd, $J = 10.2$ and 6.9 Hz, 1H), 2.57 (bs, 1H), 1.04 – 0.85 (m, 2H), 0.49 – 0.36 (m, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 159.6, 139.8, 129.3, 119.8, 113.1, 112.9, 73.4, 72.4, 65.9, 55.1, 19.7, 16.7, 7.9.

HR-MS (ESI-TOF) m/z: calcd. for C$_{13}$H$_{17}$O$_2$ 205.1229; found: 205.1239 [M-H$_2$O+H]$^+$. 

$^{[\alpha]}$D$_{20}$ = -22.2 (c = 1.0, CHCl$_3$).

((1R,2R)-2-((Benzyloxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1c)

Prepared by analogy to compound 1a from alcohol 8c (122.2 mg, 0.636 mmol, 1.0 equiv), DBU (19 µL, 0.127 mmol, 0.2 equiv), trichloroacetonitrile (0.13 mL, 1.335 mmol, 2.1 equiv), and DCM (12 mL). Yield: 209 mg (98%).

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 8.24 (bs, 1H), 7.38 – 7.21 (m, 5H), 4.54 (dd, $J = 16.1$ and 11.9 Hz, 2H), 4.26 – 4.12 (m, 2H), 3.38 (d, $J = 6.5$ Hz, 2H), 1.30 – 1.12 (m, 2H), 0.66 (dt, $J = 8.5$ and 5.1 Hz, 1H), 0.59 (dt, $J = 8.4$ and 5.3 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 162.8, 138.4, 128.3, 127.6, 127.5, 91.5, 72.9, 72.6, 72.3, 16.9, 15.4, 8.5.

Unstable under the conditions of HRMS. 

$^{[\alpha]}$D$_{20}$ = -5.1 (c = 1.0, CHCl$_3$).
**(1R,2R)-2-(((3-Methoxybenzyl)oxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1d)**

Prepared by analogy to compound 1a from alcohol 8d (170.0 mg, 0.765 mmol, 1.0 equiv), DBU (23 µL, 0.153 mmol, 0.2 equiv), trichloroacetonitrile (0.16 mL, 1.606 mmol, 2.1 equiv), and DCM (12 mL). Yield: 256 mg (91%).

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 8.25 (s, 1H), 7.25 (t, $J = 7.8$ Hz, 1H), 6.95 – 6.87 (m, 2H), 6.86 – 6.78 (m, 1H), 4.59 – 4.47 (m, 2H), 4.27 – 4.13 (m, 2H), 3.81 (s, 3H), 3.39 (d, $J = 6.5$ Hz, 2H), 1.31 – 1.13 (m, 2H), 0.67 (dt, $J = 8.5$ and 5.1 Hz, 1H), 0.60 (dt, $J = 8.4$ and 5.2 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 162.8, 159.7, 140.0, 129.3, 119.8, 113.1, 112.8, 91.5, 72.9, 72.6, 72.1, 55.2, 16.9, 15.4, 8.5.

Unstable under the conditions of HRMS.

$[\alpha]_{D}^{20} = -22.8$ (c = 1.0, CHCl$_3$).

Trichloroacetimidate 1e was synthesized in four steps according to Scheme 4 from commercially available ethyl 2-formyl-1-cyclopropanecarboxylate (12). Reductive amination of aldehyde 12 with amine 13 gave ester 14. Mesylation of amine 14 and subsequent reduction of ester group gave alcohol 8e, which was converted to corresponding trichloroacetimidate 1e in the presence of DBU and CCl$_3$CN.

![Scheme 4](image-url)
Ethyl (1S*,2S*)-2-(((3-methoxybenzyl)amino)methyl)cyclopropane-1-carboxylate (14)

A solution of amine 13 (0.97 mL, 7.555 mmol, 1.0 equiv), and cyclopropanecarboxaldehyde 12 (1.0 mL, 7.555 mmol, 1.0 equiv) in methylene chloride (12 mL) was stirred at room temperature under an argon atmosphere for 1 h. Sodium triacetoxyborohydride (2.4 g, 11.333 mmol, 1.5 equiv) was added portionwise to the reaction mixture, and the mixture was stirred at room temperature under an argon atmosphere overnight. After 19 h of the reaction time, saturated aq. NaHCO₃ solution (10 mL) was added to the reaction mixture, and the resulting mixture was stirred vigorously for 1 h. The layers were separated, and the aqueous layer was washed with CH₂Cl₂ (3 × 10 mL). The combined CH₂Cl₂ extract was washed with water (20 mL), dried over MgSO₄, and concentrated in vacuo to give a crude product. The isolated crude was purified by flash column chromatography using an ethyl acetate/ methanol solvent gradient (from 1:0 to 0:1). The free base 14 (475 mg, 24% yield) was obtained as a yellow oil.

**¹H NMR (400 MHz, CDCl₃, ppm) δ 7.27 – 7.16 (m, 1H), 6.91 – 6.84 (m, 2H), 6.81 – 6.73 (m, 1H), 4.08 (qd, J = 7.1, 1.5 Hz, 2H), 3.81 – 3.73 (m, 5H), 2.73 (bs, 1H), 2.63 – 2.48 (m, 2H), 1.69 – 1.55 (m, 1H), 1.43 (dt, J = 8.7, 4.4 Hz, 1H), 1.27 – 1.12 (m, 4H), 0.75 (ddd, J = 8.3, 6.3, 4.2 Hz, 1H).**

**¹³C NMR (101 MHz, CDCl₃, ppm) δ 173.7, 159.8, 140.9, 129.4, 120.4, 113.6, 112.7, 60.5, 55.2, 53.2, 51.6, 22.1, 19.2, 14.2, 13.8.**

**HR-MS (ESI-TOF) m/z: calcd. for C_{15}H_{22}NO_{3} 264.1600; found: 264.1609 [M+H]^+.**

Ethyl (1S*,2S*)-2-((N-(3-methoxybenzyl)methylsulphonamido)methyl)cyclopropane-1-carboxylate (7e)

Mesyl chloride (61 µL, 0.78 1mmol, 1.05 equiv) was added dropwise to a cooled (0 °C) solution of ethyl (1S*,2S*)-2-(((3-methoxybenzyl)amino)methyl)cyclopropane-1-carboxylate (14) (196 mg, 0.744 mmol, 1.0 equiv) and Et₃N (0.22 mL, 1.563 mmol, 2.0 equiv) in DCM (12 mL) and reaction mixture was stirred at room temperature overnight. Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 1:1) afforded 212 mg (83 %) of N-((1S*,2S*)-2-(hydroxymethyl)cyclopropyl)methyl)-N-(3-methoxybenzyl)-methanesulphonamide as a colorless oil.
1H NMR (400 MHz, CDCl3, ppm) δ 7.28 – 7.19 (m, 1H), 6.94 – 6.85 (m, 2H), 6.81 (dd, J = 8.3, 2.6 Hz, 1H), 4.50 – 4.32 (m, 2H), 4.08 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 3.21 – 3.04 (m, 2H), 2.91 (s, 3H), 1.58 – 1.50 (m, 1H), 1.47 (td, J = 8.5, 3.6 Hz, 1H), 1.22 (t, J = 7.1 Hz, 3H), 1.16 (dt, J = 9.3, 4.7 Hz, 1H), 0.75 (ddd, J = 8.5, 6.2, 4.5 Hz, 1H).

13C NMR (101 MHz, CDCl3, ppm) δ 173.1, 159.9, 137.3, 129.8, 120.3, 113.5, 113.5, 60.7, 55.2, 50.7, 49.4, 39.7, 20.0, 19.5, 14.2, 13.9.

HR-MS (ESI-TOF) m/z: calcd. for C16H24NO5S 342.1375; found: 342.1369 [M+H]+.

N-(((1S*,2S*)-2-(Hydroxymethyl)cyclopropyl)methyl)-N-(3-methoxybenzyl)methanesulfonamide (8e)

Prepared by analogy to compound 8a from ester 7e (207.79 mg, 0.609 mmol, 1.0 equiv), LiAlH4 (50.82 mg, 1.339 mmol, 2.2 equiv), and THF (12 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded N-(((1S*,2S*)-2-(hydroxymethyl)cyclopropyl)methyl)-N-(3-methoxybenzyl)methanesulfonamide (8e) (167 mg, 92 %) as a colorless oil.

1H NMR (400 MHz, CDCl3, ppm) δ 7.30 – 7.18 (m, 1H), 6.94 – 6.86 (m, 2H), 6.80 (ddd, J = 8.3, 2.6, 1.0 Hz, 1H), 4.44 (s, 2H), 3.77 (s, 3H), 3.50 (dd, J = 11.2, 6.0 Hz, 1H), 3.26 – 3.13 (m, 2H), 2.98 (dd, J = 15.0, 7.4 Hz, 1H), 2.90 (s, 3H), 2.03 (bs, 1H), 0.98 – 0.80 (m, 2H), 0.41 (dt, J = 8.4, 5.1 Hz, 1H), 0.35 (dt, J = 8.5, 5.1 Hz, 1H).

13C NMR (101 MHz, CDCl3, ppm) δ 159.9, 137.8, 129.7, 120.3, 113.7, 113.2, 65.8, 55.2, 50.8, 50.7, 39.4, 20.5, 15.4, 8.8.

Unstable under the conditions of HRMS.

((1S*,2S*)-2-((N-(3-Methoxybenzyl)methylsulfonamido)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1e)

Prepared by analogy to compound 1a from alcohol 8e (226.47 mg, 0.756 mmol, 1.0 equiv), DBU (23 µL, 0.151 mmol, 0.2 equiv), trichloroacetonitrile (0.17 mL, 1.664 mmol, 2.2 equiv), and DCM (10 mL). Yield: 303 mg (90 %).

1H NMR (400 MHz, CDCl3, ppm) δ 8.27 (bs, 1H), 7.27 – 7.20 (m, 1H), 6.96 – 6.86 (m, 2H), 6.85 – 6.77 (m, 1H), 4.50 (s, 2H), 4.30 (dd, J = 11.4, 5.9 Hz, 1H), 3.88 (dd, J = 11.4, 8.2 Hz, 1H), 3.78 (s, 3H), 3.34 (dd, J = 15.1, 5.8 Hz, 1H), 2.95 – 2.83 (m, 4H),
1.24 – 1.10 (m, 1H), 1.09 – 0.96 (m, 1H), 0.57 (dt, J = 8.5, 5.1 Hz, 1H), 0.48 (dt, J = 8.6, 5.3 Hz, 1H).

^{13}\text{C NMR} (101 \text{ MHz, CDCl}_3, \text{ppm}) \delta 162.7, 159.9, 137.6, 129.7, 120.4, 113.8, 113.2, 91.4, 72.6, 55.2, 50.1, 49.7, 39.9, 16.7, 15.7, 8.8.

HR-MS (ESI-TOF) m/z: calcd. for C_{16}H_{21}N_2O_4Cl_3Na 465.0185; found: 465.0189 [M+Na]^+.

Trichloroacetimidate 1f was synthesized in four steps according to Scheme 5 from commercially available ethyl 2-formyl-1-cyclopropanecarboxylate (12). Alkene 24 was obtained in Wittig reaction from aldehyde 12 and triphenyl phosphonium salt 23 as mixture of inseparable E/Z-isomers. Ester 7f was obtained by reduction of double bond with CoCl_2 and NaBH_4. Finally, reduction of ester group gave alcohol 8f, which was transformed to corresponding trichloroacetimidate 1f in the presence of DBU and CCl_3CN.

\begin{center}
\begin{tikzpicture}
\node at (0,0) (A) {12};
\node at (2,0) (B) {23};
\node at (4,0) (C) {24};
\node at (6,0) (D) {7f};
\node at (8,0) (E) {1f};
\node at (10,0) (F) {8f};
\draw[->] (A) -- node[midway,above] {nBuLi} (B);
\draw[->] (B) -- node[midway,above] {THF, -10\degreeC - rt} (C);
\draw[->] (C) -- node[midway,above] {CoCl_2, NaBH_4} (D);
\draw[->] (D) -- node[midway,above] {LiAlH_4} (E);
\draw[->] (E) -- node[midway,above] {DBU, CCl_3CN} (F);
\end{tikzpicture}
\end{center}

**Scheme 5**

(3-Methoxyphenethyl)triphenylphosphonium bromide (23)

Triphenylphosphine (599.95 mg, 2.287 mmol) and 3-methoxyphenethyl bromide (491.99 mg, 2.287 mmol) was dissolved in 4 mL of dry toluene and refluxed under nitrogen for 12 h. After cooling to room temperature, the white precipitate was filtered off, washed with diethyl ether, and dried under vacuum. Yield: 897 mg (82%).

14
\(^1\)H NMR (400 MHz, Methanol-\(d_4\)) \(\delta\) 7.93 – 7.69 (m, 15H), 7.19 (dd, \(J = 9.2, 7.1\) Hz, 1H), 6.82 – 6.74 (m, 3H), 3.79 – 3.65 (m, 5H), 3.02 – 2.89 (m, 2H).

\(^{13}\)C NMR (101 MHz, Methanol-\(d_4\)) \(\delta\) 160.1, 140.1 (d, \(J = 15.2\) Hz), 134.92 (d, \(J = 3.0\) Hz), 133.5 (d, \(J = 10.0\) Hz), 130.1 (d, \(J = 12.5\) Hz), 129.6, 120.1, 118.7, 117.9, 113.7, 112.2, 54.3, 27.9 (d, \(J = 3.6\) Hz), 23.1 (d, \(J = 49.8\) Hz).

EA: Calcd for C\(_{27}\)H\(_{26}\)BrOP: C, 67.93%; H, 5.49%; found: C, 67.91%; H, 5.47%.

Mp (Hexane): 215.1 – 216.4 °C.

Ethyl \((1R^\star,2S^\star\)-2-(3-(3-methoxyphenyl)prop-1-en-1-yl)cyclopropane-1-carboxylate (24)

\(nBuLi\) (4.94 mL, 4.445 mmol, 1.1 equiv, 1 M in THF) was added dropwise to a suspension of triphenyl phosphonium salt 23 (1.929 g, 4.040 mmol, 1.0 equiv) in THF (100 mL) at 0 °C, and the mixture was stirred for 15 min at 0 °C. Then aldehyde 12 (0.59 mL, 4.445 mmol, 1.1 equiv) was added dropwise to resulting mixture and after the addition was complete, the mixture was allowed to warm to room temperature and stirred at room temperature overnight. The mixture was then quenched with sat. aq. \(\text{NH}_4\)Cl (10 mL) and diethyl ether (10 mL) was added. The phases were separated, aqueous layer was extracted with diethyl ether (2 \(\times\) 10 mL), and the combined organic extracts were dried (MgSO\(_4\)), filtered, and concentrated in vacuo. Purification by flash column chromatography (eluent hexanes/EtOAc 6:1) afforded ethyl \((1R^\star,2S^\star\)-2-(3-(3-methoxyphenyl)prop-1-en-1-yl)cyclopropane-1-carboxylate (24) (624.0 mg; 91%) as a mixture of inseparable Z/E-isomers (ratio of Z/E-24 was 2.6/1).

**Z-isomer:** \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 7.30 – 7.11 (m, 2H), 6.85 – 6.68 (m, 2H), 5.62 (dtt, \(J = 10.0, 7.5, 1.2\) Hz, 1H), 4.94 (ddq, \(J = 11.0, 9.5, 1.5\) Hz, 1H), 4.18 – 4.09 (m, 2H), 3.79 (s, 3H), 3.56 – 3.46 (m, 2H), 2.32 – 2.23 (m, 1H), 1.68 – 1.61 (m, 1H), 1.47 – 1.41 (m, 1H), 1.30 – 1.21 (m, 3H), 0.98 – 0.90 (m, 1H).

**E-isomer:** \(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 7.32 – 7.10 (m, 2H), 6.82 – 6.68 (m, 2H), 5.82 – 5.68 (m, 1H), 5.10 (ddt, \(J = 15.3, 8.4, 1.5\) Hz, 1H), 4.20 – 4.06 (m, 2H), 3.79 (d, \(J = 1.4\) Hz, 3H), 3.30 (dd, \(J = 6.8, 1.6\) Hz, 2H), 2.05 – 1.91 (m, 1H), 1.63 – 1.55 (m, 1H), 1.37 – 1.31 (m, 1H), 1.30 – 1.21 (m, 3H), 0.99 – 0.86 (m, 1H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\), ppm) \(\delta\) 173.5 and 171.9, 159.8 and 159.7, 142.2 and 141.9, 131.2 and 130.7, 129.4 and 129.4, 129.0 and 128.2, 120.9 and 120.7, 114.3 and
114.0, 111.4 and 111.3, 60.6 and 60.5, 55.1 and 55.1, 39.1 and 38.8, 33.9 and 33.8, 24.7 and 22.1, 20.9 and 19.2, 16.1 and 15.5, 14.5 and 14.3.

HR-MS (ESI-TOF) m/z: calcd. for C_{16}H_{21}O_{3} 261.1491; found: 261.1489 [M+H]^+

**Ethyl (1R*,2R*)-2-(3-(3-methoxyphenyl)propyl)cyclopropane-1-carboxylate (7f)**

Prepared by analogy to the literature procedure.\(^7\) A solution of alkene 24 (274.9 mg, 1.056 mmol, 1.0 equiv) in MeOH (5 mL) and anhydrous CoCl\(_2\) (27.42 mg, 0.211 mmol, 0.2 equiv) was stirred for 30 min under argon atmosphere. Then, NaBH\(_4\) (159.8 mg, 4.224 mmol, 4.0 equiv) in DMF (3 mL) was added at room temperature and stirred for additional 0.5 h. Then the reaction was quenched by water (10 mL) and the mixture was extracted with CH\(_2\)Cl\(_2\) (2 \times 10 mL). The organic phase was washed with water (3 \times 15 mL) to remove DMF, dried over MgSO\(_4\) and concentrated. The residues were chromatographed on silica gel (elution with hexanes/ethyl acetate 20:1) to afford the ester 7f (222.0 mg, 80 %) as a colorless oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 7.25 – 7.14 (m, 1H), 6.81 – 6.70 (m, 3H), 4.17 – 4.06 (m, 2H), 3.80 (s, 3H), 2.69 – 2.52 (m, 2H), 2.39 – 2.24 (m, 1H), 1.74 (p, J = 7.5 Hz, 1H), 1.70 – 1.55 (m, 1H), 1.44 – 1.28 (m, 3H), 1.30 – 1.21 (m, 3H), 1.16 (dt, J = 8.8, 4.7 Hz, 1H), 0.68 (ddd, J = 7.6, 5.9, 4.0 Hz, 1H).

\(^13\)C NMR (101 MHz, CDCl\(_3\), ppm) δ 174.4, 159.6, 143.9, 129.2, 120.8, 114.1, 110.9, 60.3, 55.1, 35.5, 32.5, 30.7, 22.6, 20.2, 15.4, 14.3.

HR-MS (ESI-TOF) m/z: calcd. for C_{16}H_{23}O_{3} 263.1647; found: 263.1649 [M+H]^+

\((1R*,2R*)-2-(3-(3-Methoxyphenyl)propyl)cyclopropyl)methanol (8f)**

Prepared by analogy to compound 8a from ester 7f (215.5 mg, 0.821 mmol, 1.0 equiv), LiAlH\(_4\) (68.59 mg, 1.807 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded 129 mg (71 %) of \((1R*,2R*)-2-(3-(3-methoxyphenyl)propyl)cyclopropyl)methanol as a colorless oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 7.20 (ddd, J = 8.6, 7.3, 1.5 Hz, 1H), 6.81 – 6.70 (m, 3H), 3.80 (d, J = 1.0 Hz, 3H), 3.50 – 3.38 (m, 2H), 2.61 (h, J = 7.9 Hz, 2H), 1.85

1.66 (m, 3H), 1.30 (q, $J = 7.0$ Hz, 2H), 0.84 (qt, $J = 7.0$, 4.5 Hz, 1H), 0.69 – 0.55 (m, 1H), 0.38 (dt, $J = 8.3$, 4.7 Hz, 1H), 0.31 (dt, $J = 8.1$, 4.9 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 159.6, 144.3, 129.2, 120.8, 114.2, 110.8, 67.0, 55.1, 35.7, 33.2, 31.2, 21.1, 16.9, 9.9.

HR-MS (ESI-TOF) m/z: calcd. for C$_{14}$H$_{19}$O 203.1436; found: 203.1433 [M-H$_2$O+H]$^+$

((1$R^*$,2$R^*$)-2-(3-(3-Methoxyphenyl)propyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1f)

Prepared by analogy to compound 1a from alcohol 8f (122 mg, 0.554 mmol, 1.0 equiv), DBU (17 µL, 0.111 mmol, 0.2 equiv), trichloroacetonitrile (0.12 mL, 1.218 mmol, 2.2 equiv), and DCM (8 mL). Yield: 191 mg (90 %).

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 8.20 (bs, 1H), 7.22 – 7.14 (m, 1H), 6.80 – 6.67 (m, 3H), 4.23 (dd, $J = 11.2$, 6.7 Hz, 1H), 4.04 (dd, $J = 11.2$, 7.8 Hz, 1H), 3.78 (s, 3H), 2.66 – 2.57 (m, 2H), 1.78 – 1.67 (m, 2H), 1.46 – 1.31 (m, 1H), 1.19 (dd, $J = 13.7$, 7.5 Hz, 1H), 1.02 (dt, $J = 12.5$, 8.1, 4.5 Hz, 1H), 0.85 – 0.72 (m, 1H), 0.56 – 0.47 (m, 1H), 0.40 (dt, $J = 8.3$, 5.1 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 163.0, 159.6, 144.2, 129.1, 120.8, 114.1, 110.9, 91.7, 73.7, 55.1, 35.5, 32.9, 30.9, 17.6, 16.8, 10.3.

HR-MS (ESI-TOF) m/z: calcd. for C$_{16}$H$_{21}$NO$_2$Cl$_3$ 364.0638; found: 364.0630 [M+H]$^+$

Trichloroacetimidate 1g was synthesized in five steps according to Scheme 6 from commercially available ethyl 2-formyl-1-cyclopropanecarboxylate (12). Reduction of aldehyde 12 gave alcohol 15, which under Appel reaction conditions was transformed to bromide 16. Alkylation of 3-methoxythiophenol with bromide 16 and subsequent reduction of ester group gave alcohol 8g, which was converted to corresponding trichloroacetimidate 1g in the presence of DBU and CCl$_3$CN.
Ethyl (1S*,2S*)-2-(hydroxymethyl)cyclopropane-1-carboxylate (15)

NaBH₄ (1.57 g, 41.55 mmol, 1.1 equiv) was added portionwise to a cooled (0 °C) solution of aldehyde 12 (5.0 mL, 37.77 mmol, 1.0 equiv) in MeOH (25 mL) and reaction mixture was stirred at 0 °C for 1 hour. Then solvent was evaporated and dry crude mixture quenched with water (10 mL) and extracted with EtOAc (2 × 15 mL). The combined organic layers were washed with water and brine, dried over MgSO₄, filtered and concentrated under reduced pressure. Alcohol 15 (5.1 g, 94 %) was used for the next step without further purification. This compound is known in the literature.⁸

¹H NMR (300 MHz, CDCl₃, ppm) δ 4.20 – 4.05 (m, 2H), 3.63 (dd, J = 11.5 and 6.1 Hz, 1H), 3.49 (dd, J = 11.5 and 6.8 Hz, 1H), 1.80 – 1.64 (m, 1H), 1.57 (dt, J = 8.8 and 4.5 Hz, 1H), 1.41 (bs, 1H), 1.34 – 1.16 (m, 4H), 0.86 (ddd, J = 8.5, 6.3 and 4.3 Hz, 1H).

Ethyl (1S*,2S*)-2-(bromomethyl)cyclopropane-1-carboxylate (16)

To a solution of alcohol 15 (4.0 g, 27.7 mmol, 1.0 equiv) and carbon tetrabromide (18.4 g, 55.5 mmol, 2.0 equiv) in DCM (50 mL) triphenylphosphine (14.6 g, 55.5 mmol, 2.0 equiv) was added. The reaction mixture was stirred at room temperature for 16 h. Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 10:1) afforded ethyl (1S*,2S*)-2-(bromomethyl)cyclopropane-1-carboxylate (16).

(5.2 g, 90 %) as a yellowish oil. This compound is known in the literature.\(^9\)

\(^{1}H\) NMR (300 MHz, CDCl\(_3\), ppm) \(\delta\) 4.14 (q, \(J = 7.0\) Hz, 2H), 3.34 (qd, \(J = 10.4, 7.4\) Hz, 2H), 1.91 (dddd, \(J = 8.8, 7.4, 6.1, 4.0\) Hz, 1H), 1.65 (dddd, \(J = 8.9, 5.1, 4.0\) Hz, 1H), 1.39 (dt, \(J = 8.3, 4.7\) Hz, 1H), 1.27 (t, \(J = 7.2\) Hz, 3H), 0.95 (dddd, \(J = 8.7, 6.1, 4.7\) Hz, 1H).

**Ethyl (1S*,2S*)-2-(((3-methoxybenzyl)thio)methyl)cyclopropane-1-carboxylate (7g)**

Prepared by analogy to compound 7i from 3-methoxythiophenol (472.6 mg, 3.064 mmol, 1.0 equiv), NaH (122.56 mg, 3.064 mmol, 1.0 equiv, 60 % dispersion in mineral oil), bromide 16 (634.5 mg, 3.064 mmol, 1.0 equiv), and DMF (2 mL). Yield: 675 mg (79 %).

\(^{1}H\) NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 7.24 – 7.18 (m, 1H), 6.93 – 6.87 (m, 2H), 6.78 (ddd, \(J = 8.3, 3.1, 1.3\) Hz, 1H), 4.12 (qd, \(J = 7.1, 1.3\) Hz, 2H), 3.80 (d, \(J = 1.3\) Hz, 3H), 3.73 (s, 2H), 2.46 (dddd, \(J = 13.5, 6.7, 1.4\) Hz, 1H), 2.36 (dddd, \(J = 13.5, 7.1, 1.4\) Hz, 1H), 1.68 – 1.54 (m, 1H), 1.52 – 1.43 (m, 1H), 1.25 (td, \(J = 7.2, 1.2\) Hz, 4H), 0.78 (ddddd, \(J = 8.4, 6.2, 4.4, 1.3\) Hz, 1H).

\(^{13}C\) NMR (101 MHz, CDCl\(_3\), ppm) \(\delta\) 173.5, 159.7, 139.7, 129.4, 121.1, 114.2, 112.6, 60.5, 55.2, 36.2, 34.3, 21.9, 20.7, 15.5, 14.2.

HR-MS (ESI-TOF) m/z: calcd. for C\(_{15}\)H\(_{20}\)O\(_3\)SNa 303.1031; found: 303.1035 [M+Na]\(^+\).

**((1S*,2S*)-2-(((3-Methoxybenzyl)thio)methyl)cyclopropyl)methanol (8g)**

Prepared by analogy to compound 8a from ester 7g (491.2 mg, 1.752 mmol, 1.0 equiv), LiAlH\(_4\) (146.28 mg, 3.854 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded ((1S*,2S*)-2-(((3-methoxybenzyl)thio)methyl)cyclopropyl)methanol (8g) (373 mg; 89%) as a colorless oil.

\(^{1}H\) NMR (400 MHz, CDCl\(_3\), ppm) \(\delta\) 7.22 – 7.16 (m, 1H), 6.90 – 6.85 (m, 2H), 6.78 – 6.72 (m, 1H), 3.78 (s, 3H), 3.72 (s, 2H), 3.47 (dddd, \(J = 11.2, 6.7, 2.0\) Hz, 1H), 3.34

(dd, J = 11.2, 7.2 Hz, 1H), 2.45 (ddd, J = 13.1, 6.6, 1.7 Hz, 1H), 2.30 (dd, J = 13.1, 7.4 Hz, 1H), 1.76 (bs, 1H), 0.99 – 0.86 (m, 1H), 0.90 – 0.77 (m, 1H), 0.49 (dt, J = 8.3, 5.1 Hz, 1H), 0.43 (dd, J = 8.4, 5.0, 1.6 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) $\delta$ 159.7, 140.1, 129.4, 121.2, 114.3, 112.5, 66.3, 55.2, 36.3, 35.6, 21.9, 17.0, 10.8.

HR-MS (ESI-TOF) m/z: calcd. for C$_{13}$H$_{17}$OS 221.1000; found: 221.1003 [M-H$_2$O+H]$^+$.  

((1S*,2S*)-2-(((3-Methoxybenzyl)thio)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1g)  

![Chemical structure](image)

Prepared by analogy to compound 1a from alcohol 8g (329.99 mg, 1.385 mmol, 1.0 equiv), DBU (41 $\mu$L, 0.277 mmol, 0.2 equiv), trichloroacetonitrile (0.31 mL, 3.046 mmol, 2.2 equiv), and DCM (22 mL). Yield: 479 mg (90%).  

$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.25 (bs, 1H), 7.21 (t, J = 7.8 Hz, 1H), 6.95 – 6.87 (m, 2H), 6.82 – 6.74 (m, 1H), 4.21 (dd, J = 11.2, 6.7 Hz, 1H), 4.09 (dd, J = 11.3, 7.4 Hz, 1H), 3.80 (s, 3H), 3.76 (d, J = 3.7 Hz, 2H), 2.40 (qd, J = 13.4, 6.9 Hz, 2H), 1.25 – 1.12 (m, 1H), 1.12 – 0.98 (m, 1H), 0.65 (dt, J = 8.4, 5.1 Hz, 1H), 0.53 (dt, J = 8.5, 5.2 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) $\delta$ 162.9, 159.7, 140.0, 129.4, 121.2, 114.3, 112.4, 91.5, 72.7, 55.2, 36.0, 35.1, 17.6, 17.3, 10.9.

HR-MS (ESI-TOF) m/z: calcd. for C$_{15}$H$_{18}$NO$_2$Cl$_3$SNa 404.0022; found: 404.0016 [M+Na]$^+$.  

Trichloroacetimidate 1i was synthesized in three steps according to Scheme 7 from building block 16. Alkylation of 3-methoxyphenol with bromide 16 and subsequent reduction of ester 7i gave alcohol 8i, which was converted to corresponding trichloroacetimidate 1i in the presence of DBU and CCl$_3$CN.

![Chemical structure](image)

Scheme 7
**Ethyl (1R*,2R*)-2-((3-methoxyphenoxy)methyl)cyclopropane-1-carboxylate (7i)**

A solution of 3-methoxyphenol (177.86 mg, 1.433 mmol, 1.0 equiv) in DMF (3 mL) was cooled to 0 °C and NaH (60.17 mg, 1.504, 1.05 equiv, 60% dispersion in mineral oil) was added in several portions. Reaction mixture was stirred at 0 °C for 10 min, then solution of bromide 16 (296.67 mg, 1.433 mmol, 1.0 equiv) in DMF (2 mL) was added. After addition was complete, the mixture was allowed to warm to room temperature and stirred at room temperature overnight. The reaction was quenched with sat. NH₄Cl aq. (10 mL), extracted with diethyl ether (3 x 10 mL), washed with brine (3 x 10 mL), dried over MgSO₄, filtered. Concentration under reduced pressure gave crude product. After purification by column chromatography on silica gel (eluting with hexanes/EtOAc 6:1) 292 mg (81%) of the desired compound was obtained as a colorless liquid.

1H NMR (400 MHz, CDCl₃, ppm) δ 7.16 (td, J = 8.1 and 0.5 Hz, 1H), 6.55 – 6.41 (m, 3H), 4.15 (qd, J = 7.1 and 1.0 Hz, 2H), 3.95 – 3.81 (m, 2H), 3.78 (s, 3H), 1.89 (dtd, J = 15.0, 6.3, 4.1 Hz, 1H), 1.74 – 1.65 (m, 1H), 1.34 – 1.22 (m, 4H), 0.99 (ddd, J = 8.4, 6.3 and 4.4 Hz, 1H).

13C NMR (101 MHz, CDCl₃, ppm) δ 173.5, 160.8, 159.8, 129.8, 106.6, 106.3, 101.1, 69.3, 60.6, 55.2, 20.9, 18.5, 14.2, 12.8.

Unstable under the conditions of HRMS.

**((1R*,2R*)-2-((3-Methoxyphenoxy)methyl)cyclopropyl)methanol (8i)**

Prepared by analogy to compound 8a from ester 7i (282.8 mg, 1.13 mmol, 1.0 equiv), LiAlH₄ (94.34 mg, 2.49 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded 226 mg (96%) of ((1R*,2R*)-2-((3-methoxyphenoxy)methyl)cyclopropyl) as a colorless oil.

1H NMR (400 MHz, CDCl₃, ppm) δ 7.16 (t, J = 8.2 Hz, 1H), 6.54 – 6.42 (m, 3H), 3.86 (dd, J = 9.9 and 6.4 Hz, 1H), 3.77 (s, 4H), 3.56 (dd, J = 11.2 and 6.5 Hz, 1H), 3.48 (dd, J = 11.2 and 6.9 Hz, 1H), 2.02 (bs, 1H), 1.25 – 1.08 (m, 2H), 0.61 (tt, J = 8.7 and 5.1 Hz, 2H).

13C NMR (101 MHz, CDCl₃, ppm) δ 160.7, 159.9, 129.8, 106.7, 106.3, 101.1, 71.2, 65.9, 55.2, 19.8, 16.1, 8.2.
HR-MS (ESI-TOF) m/z: calcd. for C$_{12}$H$_{15}$O$_2$ 191.1072; found: 191.1069 [M-H$_2$O+H]$^+$. 

((1S*,2S*)-2-((3-Methoxyphenoxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1i)

Prepared by analogy to compound 1a from alcohol 8i (116.2 mg, 0.56 mmol, 1.0 equiv), DBU (17 µL, 0.11 mmol, 0.2 equiv), trichloroacetonitrile (0.1 mL, 1.17 mmol, 2.1 equiv), and DCM (17 mL). Yield: 169.0 mg (86%).

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 8.26 (bs, 1H), 7.16 (t, $J = 8.2$ Hz, 1H), 6.54 – 6.42 (m, 3H), 4.31 – 4.18 (m, 2H), 3.85 (ddd, $J = 26.3$, 16.1 and 6.2 Hz, 2H), 3.78 (s, 3H), 1.44 – 1.30 (m, 2H), 0.82 – 0.69 (m, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 162.9, 160.8, 160.0, 129.8, 106.8, 106.6, 106.4, 101.0, 91.6, 72.3, 70.8, 55.2, 16.5, 15.4, 8.8.

Unstable under the conditions of HRMS.

Trichloroacetimidates 1k,h,l were synthesized in four steps according to Scheme 8 from alcohol 15. Silylation of alcohol and subsequental reductive etherification of aldehydes 18h,k,l gave ethers 7k,h,l. Reduction of ester groups gave alcohols 8h,k,l, which were transformed to corresponding trichloroacetimidates 1k,h,l in the presence of DBU and CCl$_3$CN.

Scheme 8
Ethyl \((1S^*,2S^*)-2-(((\text{trimethylsilyl})\text{oxy})\text{methyl})\text{cyclopropane-1-carboxylate (rac-17)}\)

\[
\text{TMSCI} (0.85 \text{ mL}, 6.722 \text{ mmol}, 1.2 \text{ equiv}) \text{ was added dropwise to a cooled (0 °C) solution of alcohol 15 (807.6 mg, 5.602 mmol, 1.0 equiv) and Et}_3\text{N (0.94 mL, 6.722 mmol, 1.2 equiv) in THF (10 mL) and reaction mixture was stirred at room temperature overnight. The reaction solvent was evaporated to dryness. The crude mixture was diluted with dist. water (15 mL) and extracted with diethyl ether (2 \times 15 \text{ mL}). Combined organic phase was dried over MgSO}_4 \text{ and filtered. Alcohol 17 (1.1 g, 89\%) was used for the next step without further purification.}
\]

\[^1\text{H NMR} (400 \text{ MHz, CDCl}_3, \text{ppm}) \delta 4.09 (\text{q, } J = 7.0 \text{ Hz, 2H}), 3.52 (\text{qd, } J = 11.0 \text{ and 5.7 Hz, 2H}), 1.69 – 1.54 (\text{m, 1H}), 1.54 – 1.47 (\text{m, 1H}), 1.28 – 1.17 (\text{m, 3H}), 1.13 (\text{dtd, } J = 8.9, 4.5 \text{ and 1.9 Hz, 1H}), 0.87 – 0.76 (\text{m, 1H}), 0.08 (\text{s, 9H}).
\]

\[^{13}\text{C NMR} (101 \text{ MHz, CDCl}_3, \text{ppm}) \delta 173.9, 63.6, 60.3, 23.9, 18.0, 14.2, 12.6, -0.5.\]

Unstable under the conditions of HRMS.

Ethyl \((1S^*,2S^*)-2-(((3,5-\text{dimethoxybenzyl})\text{oxy})\text{methyl})\text{cyclopropane-1-carboxylate (7h)}\)

Prepared according to literature procedure.\(^{10,11}\) To a suspension of anhydrous FeCl\(_3\) (19.47 mg, 0.12 mmol, 5 mol%) and aldehyde 18h (399.02 mg, 2.401 mmol, 1.0 equiv) in nitromethane (4 mL) was added silyl ether rac-17 (519.5 mg, 2.401 mmol, 1.0 equiv) and triethylsilane (0.46 mL, 2.905 mmol, 1.2 equiv) successively at 0 °C under atmosphere of argon. After 20 h of stirring, the reaction mixture was poured into sat. NaHCO\(_3\) aq. solution and extracted with EtOAc. The combined extracts were washed with brine. After being dried over Na\(_2\)SO\(_4\) the extracts were concentrated in vacuo.\(^{12}\) After purification by column chromatography on silica gel (eluting with hexanes/EtOAc 4:1) of the desired compound 7h (401 mg, 57 %) was obtained as a colorless liquid.

---


\(^{12}\) In some of the cases, to remove unreacted aldehyde 18, the crude reaction mixture were dissolved in MeOH and NaBH\(_4\) (2.0 equiv) were added. After 5 min acetone (5 mL) was added and the reaction mixture were concentrated in vacuo and purified by column chromatography on silica gel.
$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 6.47 – 6.46 (m, 2H), 6.38 – 6.36 (m, 1H), 4.44 (s, 2H), 4.10 (qdd, $J = 7.1$, 2.1, 0.8 Hz, 2H), 3.77 (s, 6H), 3.42 (dd, $J = 10.4$, 6.0 Hz, 1H), 3.32 (dd, $J = 10.4$, 6.7 Hz, 1H), 1.79 – 1.65 (m, 1H), 1.62 – 1.49 (m, 1H), 1.29 – 1.14 (m, 4H), 0.88 – 0.78 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 173.7, 160.9, 140.6, 105.3, 99.7, 72.5, 71.5, 60.5, 55.3, 21.6, 18.6, 14.2, 12.9.

HR-MS (ESI-TOF) m/z: calcd. for C$_{16}$H$_{22}$O$_5$Na 317.1365; found: 317.1374 [M+Na]$^+$.  

Ethyl (1$S^*$.2$S^*$)-2-((benzofuran-3-ylmethoxy)methyl)cyclopropane-1-carboxylate (7k)

Prepared by analogy to compound 7h from aldehyde 18k (211.63 mg, 1.448 mmol, 1.0 equiv), silyl ether rac-17 (313.3 mg, 1.448 mmol, 1.0 equiv), anhydrous FeCl$_3$ (11.7 mg, 0.072 mmol, 5 mol%), triethylsilane (0.28 mL, 1.752 mmol, 1.2 equiv), and MeNO$_2$ (6 mL).

Yield: 236 mg (59%).

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.65 (ddd, $J = 7.5$, 1.7, 0.8 Hz, 1H), 7.57 (s, 1H), 7.47 (dq, $J = 8.1$, 1.0 Hz, 1H), 7.34 – 7.20 (m, 2H), 4.65 (s, 2H), 4.10 (qd, $J = 7.1$, 1.6 Hz, 2H), 3.46 (dd, $J = 10.3$, 6.1 Hz, 1H), 3.37 (dd, $J = 10.4$, 6.7 Hz, 1H), 1.73 (dq, $J = 8.9$, 6.3, 4.1 Hz, 1H), 1.54 (dt, $J = 8.4$, 4.5 Hz, 1H), 1.28 – 1.15 (m, 4H), 0.83 (dd, $J = 8.4$, 6.3, 4.3 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 173.6, 1555, 142.8, 126.9, 124.5, 122.7, 120.1, 117.6, 111.4, 71.4, 63.0, 60.5, 21.4, 18.5, 14.2, 12.8.

Unstable under the conditions of HRMS.

Ethyl (1$S^*$.2$S^*$)-2-((thiophen-3-ylmethoxy)methyl)cyclopropane-1-carboxylate (7l)

Prepared by analogy to compound 7h from aldehyde 18l (0.4 mL, 4.565 mmol, 1.0 equiv), silyl ether rac-17 (987.71 mg, 4.565 mmol, 1.0 equiv), anhydrous FeCl$_3$ (37.0 mg, 0.228 mmol, 5 mol%), triethylsilane (0.88 mL, 5.52 mmol, 1.2 equiv), and MeNO$_2$ (10 mL). Yield: 803.0 mg (73%).

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.30 (ddd, $J = 5.0$, 2.9 and 0.5 Hz, 1H), 7.20 (ddq, $J = 2.8$, 1.4 and 0.8 Hz, 1H), 7.06 (ddd, $J = 5.0$, 1.3 and 0.5 Hz, 1H), 4.53 (s, 2H), 4.12 (qdd, $J = 7.0$, 2.0 and 0.6 Hz, 2H), 3.43 (dd, $J = 10.4$ and 6.1 Hz, 1H), 3.35
(dd, J = 10.4 and 6.6 Hz, 1H), 1.79 – 1.66 (m, 1H), 1.55 (dt, J = 8.4 and 4.3 Hz, 1H), 1.30 – 1.21 (m, 3H), 1.20 (dt, J = 9.1, 4.5 Hz, 1H), 0.84 (ddd, J = 8.4, 6.3, 4.3 Hz, 1H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\), ppm) δ 173.7, 139.3, 127.2, 126.0, 122.7, 71.5, 67.9, 60.5, 21.5, 18.6, 14.2, 12.9.

Unstable under the conditions of HRMS.

\([(1S^* ,2S^*)-2-((3,5-Dimethoxybenzyl)oxy)methyl)cyclopropyl)methanol (8h)\]

Prepared by analogy to compound 8a from ester 7h (346.9 mg, 1.179 mmol, 1.0 equiv), LiAlH\(_4\) (98.41 mg, 2.593 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded \((1S^* ,2S^*)-2-((3,5\text{-dimethoxybenzyl)oxy)methyl)cyclopropyl)methanol (8h)\) (283 mg, 95 %) as a colorless oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 6.51 – 6.48 (m, 2H), 6.37 (td, J = 2.4, 1.1 Hz, 1H), 4.46 (s, 2H), 3.78 (d, J = 1.4 Hz, 6H), 3.54 – 3.44 (m, 1H), 3.45 – 3.33 (m, 2H), 3.26 (ddd, J = 10.2, 6.9, 1.7 Hz, 1H), 2.14 (bs, 1H), 1.08 – 0.94 (m, 2H), 0.53 – 0.41 (m, 2H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\), ppm) δ 160.8, 140.8, 105.3, 99.6, 73.4, 72.5, 66.2, 55.3, 19.8, 16.7, 8.0.

HR-MS (ESI-TOF) m/z: calcd. for C\(_{14}\)H\(_{20}\)O\(_4\)Na 275.1259; found: 275.1259 [M-H\(_2\)O+H]\(^+\).

\([(1S^* ,2S^*)-2-((Benzofuran-3-ylmethoxy)methyl)cyclopropyl)methanol (8k)\]

Prepared by analogy to compound 8a from ester 7k (228.7 mg, 0.834 mmol, 1.0 equiv), LiAlH\(_4\) (69.61 mg, 1.834 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded \((1S^* ,2S^*)-2-((benzofuran-3-ylmethoxy)methyl)cyclopropyl)methanol (8k)\) (175 mg, 90 %), as a colorless oil.

\(^1\)H NMR (400 MHz, CDCl\(_3\), ppm) δ 7.65 (ddd, J = 7.5, 1.6, 0.8 Hz, 1H), 7.57 (s, 1H), 7.49 – 7.43 (m, 1H), 7.33 – 7.19 (m, 2H), 4.65 (s, 2H), 3.43 (ddd, J = 18.0, 10.7, 6.2 Hz, 2H), 3.36 – 3.22 (m, 2H), 2.37 (bs, 1H), 1.06 – 0.86 (m, 1H), 0.49 – 0.38 (m, 2H).

\(^{13}\)C NMR (101 MHz, CDCl\(_3\), ppm) δ 155.5, 142.9, 127.0, 124.5, 122.7, 120.1, 117.7, 111.4, 73.3, 66.0, 62.9, 19.7, 16.6, 7.9.
Unstable under the conditions of HRMS.

\((1S^*,2S^*)-2-((\text{Thiophen}-3-\text{ylmethoxy})\text{methyl})\text{cyclopropyl})\text{methanol (8l)}\\
\text{Prepared by analogy to compound 8a from ester 7l (256.9 mg, 1.069 mmol, 1.0 equiv), LiAlH}_4 (89.26 mg, 2.352 mmol, 2.2 equiv), and THF (24 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded } \((1S^*,2S^*)-2-((\text{thiophen}-3-\text{ylmethoxy})\text{methyl})\text{-cyclopropyl})\text{methanol (8l)} (186 mg, 88%) as a colorless oil.

\(^1\text{H NMR (400 MHz, CDCl}_3, \text{ppm) } \delta 7.28 (\text{dd, } J = 4.9 \text{ and } 2.9 \text{ Hz, 1H}), 7.19 (\text{ddq, } J = 3.0, 1.5 \text{ and } 0.8 \text{ Hz, 1H}), 7.06 (\text{dd, } J = 5.0 \text{ and } 1.3 \text{ Hz, 1H}), 4.52 (\text{s, 1H}), 3.48 (\text{dd, } J = 11.2 \text{ and } 6.1 \text{ Hz, 1H}), 3.45 – 3.29 (\text{m, 2H}), 3.24 (\text{dd, } J = 10.2 \text{ and } 7.0 \text{ Hz, 1H}), 2.37 (\text{s, 1H}), 1.05 – 0.92 (\text{m, 1H}), 0.51 – 0.40 (\text{m, 2H}).

\(^{13}\text{C NMR (101 MHz, CDCl}_3, \text{ppm) } \delta 139.4, 127.8, 125.9, 122.7, 73.4, 67.7, 66.1, 19.8, 16.7, 7.9.

HR-MS (ESI-TOF) m/z: calcd. for C\text{10}H\text{13}O\text{S} 181.0687; found: 181.0685 \([M-H_2O+H]^+].

\((1S^*,2S^*)-2-((3,5-\text{Dimethoxybenzyl})\text{oxy})\text{methyl})\text{cyclopropyl)methyl 2,2,2-\text{trichloroacetimidate (1h)}\\
\text{Prepared by analogy to compound 1a from alcohol 8h (197.4 mg, 0.782 mmol, 1.0 equiv), DBU (23 } \mu\text{L, 0.157 mmol, 0.2 equiv), trichloroacetoniitrile (0.17 mL, 1.722 mmol, 2.2 equiv), and DCM (12 mL). Yield: 287 mg (93%).

\(^1\text{H NMR (400 MHz, CDCl}_3, \text{ppm) } \delta 8.24 (\text{bs, 1H}), 6.50 (\text{dt, } J = 2.3, 0.8 \text{ Hz, 2H}), 6.37 (\text{t, } J = 2.4 \text{ Hz, 1H}), 4.55 – 4.43 (\text{m,2}), 4.20 (\text{dd, } J = 6.9, 1.8 \text{ Hz, 2H}), 3.78 (\text{s, 6H}), 3.38 (\text{d, } J = 6.6 \text{ Hz, 2H}), 1.32 – 1.12 (\text{m, 2H}), 0.67 (\text{dt, } J = 8.4, 5.1 \text{ Hz, 1H}), 0.59 (\text{dt, } J = 8.4, 5.2 \text{ Hz, 1H}).

\(^{13}\text{C NMR (101 MHz, CDCl}_3, \text{ppm) } \delta 162.8, 160.8, 140.8, 105.2, 99.6, 91.5, 72.9, 72.6, 72.2, 55.3, 16.9, 15.4, 8.5.

HR-MS (ESI-TOF) m/z: calcd. for C\text{16}H\text{20}N\text{O}\text{4}Cl\text{3}Na 418.0356; found: 418.0351 \([M+Na]^+].\)
(1S*,2S*)-2-((Benzofuran-3-ylmethoxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1k)

Prepared by analogy to compound 1a from alcohol 8k (161.3 mg, 0.694 mmol, 1.0 equiv), DBU (21 µL, 0.139 mmol, 0.2 equiv), trichloroacetonitrile (0.15 mL, 1.528 mmol, 2.2 equiv), and DCM (15 mL). Yield: 249 mg (95%).

1H NMR (400 MHz, CDCl3, ppm) δ 8.23 (bs, 1H), 7.65 (ddt, J = 7.5, 1.6, 0.8 Hz, 1H), 7.58 (s, 1H), 7.49 – 7.43 (m, 1H), 7.34 – 7.18 (m, 2H), 4.75 – 4.63 (m, 2H), 4.18 (qd, J = 11.3, 6.9 Hz, 2H), 3.41 (d, J = 6.5 Hz, 2H), 1.29 – 1.11 (m, 2H), 0.65 (dt, J = 8.5, 5.1 Hz, 1H), 0.57 (dt, J = 8.4, 5.2 Hz, 1H).

13C NMR (101 MHz, CDCl3, ppm) δ 162.9, 155.5, 142.8, 127.1, 124.5, 122.7, 120.2, 117.8, 111.4, 91.5, 72.8, 72.6, 62.8, 16.9, 15.5, 8.5.

HR-MS (ESI-TOF) m/z: calcd. for C16H16NO3Cl3Na 398.0093; found: 398.0098 [M+Na]+.

((1S*,2S*)-2-((Thiophen-3-ylmethoxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1l)

Prepared by analogy to compound 1a from alcohol 8l (173.99 mg, 0.877 mmol, 1.0 equiv), DBU (26 µL, 0.175 mmol, 0.2 equiv), trichloroacetonitrile (0.19 mL, 1.843 mmol, 2.2 equiv), and DCM (10 mL). Yield: 276 mg (92%).

1H NMR (400 MHz, CDCl3, ppm) δ 8.24 (bs, 1H), 7.29 (dd, J = 5.0, 2.9 Hz, 1H), 7.20 (ddd, J = 3.0, 1.3, 0.8 Hz, 1H), 7.08 – 7.06 (m, 1H), 4.62 – 4.50 (m, 2H), 4.27 – 4.12 (m, 2H), 3.38 (d, J = 6.7 Hz, 2H), 1.30 – 1.11 (m, 2H), 0.66 (dt, J = 8.6, 5.1 Hz, 1H), 0.59 (dt, J = 8.4, 5.2 Hz, 1H).

13C NMR (101 MHz, CDCl3, ppm) δ 162.9, 139.6, 127.3, 125.9, 122.6, 91.5, 72.9, 72.6, 67.56, 16.9, 15.5, 8.5.

HR-MS (ESI-TOF) m/z: calcd. for C12H14NO3Cl3SNa 363.9709; found: 363.9711 [M+Na]+.

Enantioenriched trichloroacetimidate 1j (ee 97.8 %) was synthesized in five steps according to Scheme 9 from previously obtained benzyl ether 7c. Removal of protecting group and subsequent silylation of alcohol gave silyl ether 17. Reductive
etherification of 3-furaldehyde gave ether 7j, which further was reduced and transformed to corresponding trichloroacetimidate 1j.

Enantiomeric excess of ester 7j (97.8 %) was determined by SFC analysis on chiral phase (Chiralpak IC-2; 4.6x250 mm; 10 % IPA + 90 % Hex; F=1 mL/min; T=25 °C; t_r (major) 8.7 min, t_r (minor) 9.3 min).

Scheme 9

**Ethyl (1R,2R)-2-(hydroxymethyl)cyclopropane-1-carboxylate (15)**

To suspension of benzylether 7c (408.3 mg, 1.743 mmol, 1.0 equiv) and Pd/C (40.8 mg, 10 wt%) in MeOH (5 mL) triethylsilane (2.8 mL, 17.426 mmol, 10 equiv) was added. The mixture was stirred at room temperature for 6 h, then filtered through a short pad of celite and concentrated under reduced pressure. Purification by column chromatography on silica gel (eluent: EtOAc) afforded ethyl (1R,2R)-2-(hydroxymethyl)cyclopropane-1-carboxylate (15) (210 mg, 84 %) as a colorless oil. This compound is known in the literature.\(^\text{13}\)

\(^1\)H NMR (300 MHz, CDCl\(_3\), ppm) δ 4.20 – 4.05 (m, 2H), 3.63 (dd, \(J = 11.5 \text{ and } 6.1 \text{ Hz, 1H}\)), 3.49 (dd, \(J = 11.5 \text{ and } 6.8 \text{ Hz, 1H}\)), 1.80 – 1.64 (m, 1H), 1.57 (dt, \(J = 8.8 \text{ and } 4.5 \text{ Hz, 1H}\)), 1.41 (bs, 1H), 1.34 – 1.16 (m, 4H), 0.86 (ddd, \(J = 8.5, 6.3 \text{ and } 4.3 \text{ Hz, 1H}\)).

\([\alpha]_D^{20} = -69.5 \text{ (c = 1.0, CHCl}_{3}\)).

**Ethyl (1R,2R)-2-(((trimethylsilyl)oxy)methyl)cyclopropane-1-carboxylate (17)**

Prepared by analogy to rac-17 from enantioenriched alcohol 15 (168 mg, 1.165 mmol, 1.0 equiv), TMSCl (0.18 mL, 1.398 mmol,

1.2 equiv), Et₃N (0.2 mL, 1.398 mmol, 1.2 equiv) and THF (6 mL). Yield: 215 mg (72 %)

¹H NMR (400 MHz, CDCl₃, ppm) δ 4.09 (q, J = 7.0 Hz, 2H), 3.52 (qd, J = 11.0 and 5.7 Hz, 2H), 1.69 – 1.54 (m, 1H), 1.54 – 1.47 (m, 1H), 1.28 – 1.17 (m, 3H), 1.13 (ddt, J = 8.9, 4.5 and 1.9 Hz, 1H), 0.87 – 0.76 (m, 1H), 0.08 (s, 9H).

¹³C NMR (101 MHz, CDCl₃, ppm) δ 173.9, 63.6, 60.3, 23.9, 18.0, 14.2, 12.6, -0.5.

Unstable under the conditions of HRMS. 

[α]₀D²₀ = -59.5 (c = 1.0, CHCl₃).

**Ethyl (1R,2R)-2-((furan-3-ylmethoxy)methyl)cyclopropene-1-carboxylate (7j)**

Prepared by analogy to compound 7h from aldehyde 3-furaldehyde (97 µL, 1.159 mmol, 1.2 equiv), enantioenriched silyl ether 17 (209.0 mg, 0.966 mmol, 1.0 equiv), anhydrous FeCl₃ (7.8 mg, 0.048 mmol, 5 mol%), triethylsilane (0.19 mL, 1.169 mmol, 1.21 equiv), and MeNO₂ (10 mL). Yield: 110 mg (51 %).

¹H NMR (400 MHz, CDCl₃, ppm) δ 7.40 – 7.39 (m, 2H), 6.45 – 6.36 (m, 1H), 4.38 (s, 2H), 4.20 – 4.03 (m, 2H), 3.41 (dd, J = 10.4 and 6.1 Hz, 1H), 3.33 (dd, J = 10.4 and 6.6 Hz, 1H), 1.78 – 1.64 (m, 1H), 1.59 – 1.49 (m, 1H), 1.25 (td, J = 7.1 and 0.4 Hz, 3H), 1.25 – 1.15 (m, 1H), 0.83 (ddd, J = 8.3, 6.3 and 4.2 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃, ppm) δ 173.7, 143.4, 140.6, 122.1, 110.3, 71.3, 63.8, 60.5, 21.5, 18.6, 14.2, 12.9.

HR-MS (ESI-TOF) m/z: calcd. for C₁₂H₁₆O₄Na 247.0946; found: 247.0945 [M+Na]⁺. 

[α]₀D²₀ = -40.3 (c = 1.0, CHCl₃).

**((1R,2R)-2-((Furan-3-ylmethoxy)methyl)cyclopropyl)methanol (8j)**

Prepared by analogy to compound 8a from enantioenriched ester 7j (107.7 mg, 0.480 mmol, 1.0 equiv), LiAlH₄ (40.1 mg, 1.057 mmol, 2.2 equiv), and THF (20 mL). Purification by column chromatography on silica gel (elucent EtOAc) afforded 85.1 mg (97 %) of ((1R,2R)-2-((furan-3-ylmethoxy)methyl)cyclopropyl) as a colorless oil.

¹H NMR (400 MHz, CDCl₃, ppm) δ 7.42 – 7.34 (m, 2H), 6.43 – 6.36 (m, 1H), 4.38 (s, 2H), 3.48 (dd, J = 11.2 and 6.3 Hz, 1H), 3.37 (ddd, J = 8.6, 6.2 and 3.0 Hz, 2H), 3.23 (ddt, J = 10.2, 6.9 and 2.0 Hz, 1H), 2.39 (bs, 1H), 1.05 – 0.90 (m, 2H), 0.52 – 0.39 (m, 2H).
$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) $\delta$ 143.3, 140.6, 122.2, 110.3, 73.2, 66.1, 63.7, 19.7, 16.6, 7.9.

HR-MS (ESI-TOF) m/z: calcd. for C$_{10}$H$_{14}$O$_3$Na 205.0841; found: 205.0842 [M+Na]$^+$. $[\alpha]_{D}^{20} = -38.7$ (c = 1.0, CHCl$_3$).

$((1R,2R)-2-((Furan-3-ylmethoxy)methyl)cyclopropyl)methyl$ 2,2,2-trichloroacetimidate (1j)

Prepared by analogy to compound 1a from enantioenriched alcohol 8j (80.8 mg, 0.575 mmol, 1.0 equiv), DBU (17 $\mu$L, 0.115 mmol, 0.2 equiv), trichloroacetonitrile (0.12 mL, 1.207 mmol, 2.1 equiv), and DCM (12 mL). Yield: 133 mg (71%).

$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.24 (bs, 1H), 7.43 – 7.35 (m, 2H), 6.41 (dq, $J =$ 1.3 and 0.5 Hz, 1H), 4.48 – 4.35 (m, 2H), 4.26 – 4.12 (m, 2H), 3.36 (d, $J =$ 6.7 Hz, 2H), 1.29 – 1.10 (m, 2H), 0.66 (dt, $J =$ 8.5, 5.1 Hz and 1H), 0.58 (dt, $J =$ 8.4, 5.2 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) $\delta$ 162.9, 143.3, 140.5, 122.3, 110.3, 91.5, 72.7, 72.6, 63.5, 16.9, 15.5, 8.5.

Unstable under the conditions of HRMS.

Trichloroacetimidate 1m was synthesized in three steps according to Scheme 10 from building block 16. Alkylation of furan-2-ylmethanol (19) with bromide 16 and subsequent reduction of ester group gave alcohol 8m, which was converted to corresponding trichloroacetimidate 1m in the presence of DBU and CCl$_3$CN.
Ethyl (1S*,2S*)-2-((furan-2-ylmethoxy)methyl)cyclopropane-1-carboxylate (7m)

Prepared by analogy to compound 7i from furfuryl alcohol (19) (158.0 mg, 1.610 mmol, 1.0 equiv), NaH (67.6 mg, 1.691 mmol, 1.05 equiv, 60% dispersion in mineral oil), bromide 16 (504.5.5 mg, 1.691 mmol, 1.05 equiv), and DMF (5 mL). Yield: 85 mg (23%).

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.40 (dt, $J = 1.5$, 0.8 Hz, 1H), 6.34 (dd, $J = 3.2$, 1.9 Hz, 1H), 6.31 (dt, $J = 3.2$, 0.7 Hz, 1H), 4.46 (s, 2H), 4.17 – 4.06 (m, 2H), 3.46 – 3.32 (m, 2H), 1.76 – 1.65 (m, 1H), 1.58 – 1.51 (m, 1H), 1.25 (td, $J = 7.2$, 0.7 Hz, 3H), 1.23 – 1.17 (m, 1H), 0.84 (ddd, $J = 8.4$, 6.3, 4.3 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 173.7, 151.6, 142.8, 110.2, 109.3, 71.5, 64.5, 60.5, 21.4, 18.6, 14.2, 12.9.

HR-MS (ESI-TOF) m/z: calcd. for C$_{12}$H$_{16}$O$_4$Na 247.0946; found: 247.0947 [M+Na]$^+$. 

((1S*,2S*)-2-((Furan-2-ylmethoxy)methyl)cyclopropyl)methanol (8m)

Prepared by analogy to compound 8a from ester 7m (78.0 mg, 0.348 mmol, 1.0 equiv), LiAlH$_4$ (27.06 mg, 0.713 mmol, 2.05 equiv), and THF (10 mL). Purification by column chromatography on silica gel (eluent EtOAc) afforded of ((1S*,2S*)-2-((furan-2-ylmethoxy)methyl)cyclopropyl)methanol (8m) (62.5 mg, 99%) as a colorless oil.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.40 (dd, $J = 1.9$, 0.9 Hz, 1H), 6.37 – 6.27 (m, 2H), 4.47 (s, 2H), 3.55 – 3.35 (m, 3H), 3.29 (dd, $J = 10.2$, 7.0 Hz, 1H), 1.68 (bs, 1H), 1.09 – 0.93 (m, 1), 0.55 – 0.43 (m, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 149.3, 140.1, 107.6, 106.5, 74.1, 63.7, 61.8, 17.2, 14.0, 5.5.

HR-MS (ESI-TOF) m/z: calcd. for C$_{10}$H$_{13}$O$_2$ 165.0916; found: 165.0913 [M-H$_2$O+H]$^+$. 

((1S*,2S*)-2-((Furan-2-ylmethoxy)methyl)cyclopropyl)methyl 2,2,2-trichloroacetimidate (1m)

Prepared by analogy to compound 1a from alcohol 8m (62.1 mg, 0.341 mmol, 1.0 equiv), DBU (10 µL, 0.068 mmol, 0.2 equiv),
trichloroacetonitrile (72 µL, 0.716 mmol, 2.1 equiv), and DCM (5 mL). Yield: 103.1 mg (93%).

$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 8.24 (bs, 1H), 7.40 (dd, $J$ = 1.8, 0.9 Hz, 1H), 6.33 (dd, $J$ = 3.6, 1.6 Hz, 1H), 6.32 – 6.29 (m, 1H), 4.54 – 4.44 (m, 2H), 4.19 (dd, $J$ = 6.9, 0.9 Hz, 2H), 3.39 (dd, $J$ = 6.7, 2.2 Hz, 2H), 1.29 – 1.12 (m, 2H), 0.67 (dt, $J$ = 8.5, 5.1 Hz, 2H), 0.59 (dt, $J$ = 8.5, 5.2 Hz, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) $\delta$ 162.9, 151.8, 142.7, 110.2, 109.1, 91.5, 72.9, 72.5, 64.1, 16.7, 15.5, 8.6.

Unstable under the conditions of HRMS.
3. Optimization of conditions for the cyclopropylmethylation reaction

Several Lewis acids and solvents have been screened using imidate 1a as starting material (see Table S1). These studies revealed B(C₆F₅)₃ as optimal catalyst and CH₃NO₂ as reaction media in room temperature to achieve the best yield of product 2a. The configuration of the substrate E-1a or Z-1a had practically no impact on the product 2a yield (table S1, entry 1-3). Since E-configuration disubstituted cyclopropanes were easier to access, the substrate scope investigation was performed with E-configured substrates 1.

Table S1. LA promoted rearrangement of 1a

<table>
<thead>
<tr>
<th>entry</th>
<th>starting material</th>
<th>LA (10 mol%)</th>
<th>solvent</th>
<th>time</th>
<th>NMR yield of 2a*, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Z-1a</td>
<td>Cu(OTf)₂</td>
<td>DCM</td>
<td>1d</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>Z-1a</td>
<td>BF₃OEt₂</td>
<td></td>
<td>10 min</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>E-1a</td>
<td>Cu(OTf)₂</td>
<td></td>
<td>4h</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>E-1a</td>
<td>(CuOTf)₂C₆H₆</td>
<td>DCM</td>
<td>7d</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>E-1a</td>
<td>(C₆F₅)₃B</td>
<td></td>
<td>2h</td>
<td>50</td>
</tr>
<tr>
<td>6</td>
<td>E-1a</td>
<td>(C₆F₅)₃B</td>
<td></td>
<td>2h</td>
<td>65 (58)b</td>
</tr>
<tr>
<td>7</td>
<td>E-1a</td>
<td>Fe(OTf)₃</td>
<td></td>
<td>4h</td>
<td>55</td>
</tr>
<tr>
<td>8</td>
<td>E-1a</td>
<td>(C₆F₅)₃B</td>
<td>CH₃NO₂</td>
<td>2h</td>
<td>80 (80)b</td>
</tr>
<tr>
<td>9</td>
<td>E-1a</td>
<td></td>
<td>EtOAc</td>
<td>2h</td>
<td>60</td>
</tr>
<tr>
<td>10</td>
<td>E-1a</td>
<td></td>
<td>MeCN</td>
<td>2h</td>
<td>30</td>
</tr>
<tr>
<td>11</td>
<td>E-1a</td>
<td></td>
<td>THF</td>
<td>7d</td>
<td>no reaction</td>
</tr>
<tr>
<td>12</td>
<td>E-1a</td>
<td></td>
<td>Toluene</td>
<td>2h</td>
<td>60</td>
</tr>
<tr>
<td>13</td>
<td>E-1a</td>
<td></td>
<td>AcOH</td>
<td>7d</td>
<td>slow decomposition of starting material</td>
</tr>
</tbody>
</table>

*a using 1,4-bis(trichloromethyl)benzene as internal standard; b isolated yield.
4. Cyclopropylmethylation reaction and characterization of the products

**General procedure for rearrangement/cyclization**

Molecular sieves (4 Å) and Lewis acid catalyst (0.05 mmol, 10 mol%) were added to a stirred solution of trichloroacetimidate 1 (0.50 mmol) in nitromethane (5 mL) at rt. After reaction was complete (TLC control in the first minute of the reaction), TEA (50 mol%) was added to the reaction mixture, then reaction solvent was removed under reduced pressure. The residue was purified by chromatography on a short silica gel column eluting with a mixture of light petroleum ether and ethyl acetate to afford desired products 2.

![Diagram of reaction](image)

**Scheme 11**

2-Cyclopropyl-2,3-dihydrobenzo[b][1,4]dioxine (2a)

Prepared according to general procedure: from trichloroacetimidate 1a (72.0 mg, 0.213 mmol), (C₆F₅)₃B (10.9 mg, 0.021 mmol, 10 mol%) and MeNO₂ (4 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 10:1) afforded 2-cyclopropyl-2,3-dihydrobenzo[b][1,4]dioxine (2a) (30 mg, 80%) as a colorless oil.

$^1$H NMR (400 MHz, CDCl₃, ppm) δ 6.94 – 6.77 (m, 4H), 4.33 (ddd, $J = 11.3, 2.3, 0.7$ Hz, 1H), 4.01 (ddd, $J = 11.2, 8.2, 0.7$ Hz, 1H), 3.47 – 3.37 (m, 1H), 1.08 – 0.94 (m, 1H), 0.78 – 0.66 (m, 1H), 0.69 – 0.52 (m, 2H), 0.45 – 0.34 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl₃, ppm) δ 143.5, 143.2, 121.4, 121.1, 117.3, 116.9, 77.5, 67.9, 11.3, 2.9, 1.7.

Unstable under the conditions of HRMS.

4-Cyclopropyl-2-(trichloromethyl)-4,5-dihydrooxazole (2b)

Prepared according to general procedure: from trichloroacetimidate 1b (330.0 mg, 0.844 mmol), BF₃OEt₂ (11 µL, 0.084 mmol, 10 mol%) and DCM (10 mL). Purification by column chromatography on silica gel...
(eluent hexanes/EtOAc 8:1) afforded 4-cyclopropyl-2-(trichloromethyl)-4,5-dihydrooxazole (2b) (165 mg, 85%) as a colorless oil.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 4.68 (dd, $J = 9.6$, 8.4 Hz, 1H), 4.36 (t, $J = 8.3$ Hz, 1H), 3.87 (dt, $J = 9.6$, 8.0 Hz, 1H), 0.98 (qt, $J = 8.1$, 4.9 Hz, 1H), 0.63 (ddddd, $J = 9.0$, 8.1, 5.7, 4.5 Hz, 1H), 0.59 – 0.51 (m, 1H), 0.50 – 0.39 (m, 1H), 0.38 – 0.27 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) $\delta$ 162.7, 86.7, 76.0, 70.8, 15.1, 2.9, 2.1.

Unstable under the conditions of HRMS.

### 4-Cyclopropylisochromane (2c)

Prepared according to general procedure: From trichloroacetimidate 1c (34.1 mg, 0.101 mmol), (C$_6$F$_5$)$_3$B (5.19 mg, 0.010 mmol, 10 mol%) and MeNO$_2$ (1 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 10:1) afforded 4-cyclopropylisochromane (2c) (5.6 mg, 32%) as a colorless oil.

$^1$H NMR (300 MHz, CDCl$_3$, ppm) $\delta$ 7.32 – 7.12 (m, 5H), 4.47 (d, $J = 9.0$ Hz, 2H), 3.53 (d, $J = 5.8$ Hz, 2H), 3.11 (ddt, $J = 10.3$, 8.2, 5.1 Hz, 1H), 0.85 (qt, $J = 8.2$, 5.2 Hz, 1H), 0.55 – 0.23 (m, 3H), 0.22 – 0.08 (m, 1H).

HR-MS (ESI-TOF) m/z: calcd. for C$_{12}$H$_{15}$O 175.1123; found: 175.1122 [M+H]$^+$.

### 4-Cyclopropyl-7-methoxyisochromane (2d)

Prepared according to general procedure: From trichloroacetimidate 1d (155.3 mg, 0.424 mmol), (C$_6$F$_5$)$_3$B (21.68 mg, 0.042 mmol, 10 mol%) and MeNO$_2$ (4.3 mL). Two regioisomers 2d and 2d’ were obtained and their separation was done by column chromatography on silica gel (eluent hexanes/EtOAc 4:1). After purification isomer 2d (61.2 mg, 71%) and isomer 2d’ (14.5 mg, 17%) were both obtained as colorless oils.

Major isomer: $^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.41 (d, $J = 8.5$ Hz, 1H), 6.78 (ddt, $J = 8.5$, 2.7 and 0.8 Hz, 1H), 6.52 (d, $J = 2.7$ Hz, 1H), 4.75 (dd, $J = 24.5$ and 15.1 Hz, 1H), 3.98 (dd, $J = 11.1$ and 4.4 Hz, 1H), 3.84 (dd, $J = 11.2$ and 6.0 Hz, 1H), 3.79 (s, 3H), 1.94 (dt, $J = 10.4$ and 5.2 Hz, 1H), 0.98 – 0.82 (m, 1H), 0.75 – 0.66 (m, 1H), 0.56 – 0.43 (m, 2H), 0.30 – 0.18 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) $\delta$ 157.9, 135.4, 129.6, 128.9, 112.7, 108.6, 70.5, 68.4, 55.2, 41.7, 15.1, 5.2, 2.5.

HR-MS (ESI-TOF) m/z: calcd. for C$_{13}$H$_{17}$O$_2$ 205.1229; found: 205.1226 [M+H]$^+$.
4-Cyclopropyl-5-methoxyisochromane (2d’)

Isolated as a minor isomer: $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.15 (t, $J = 7.9$ Hz, 1H), 6.73 (d, $J = 8.2$ Hz, 1H), 6.64 – 6.56 (m, 1H), 4.87 (d, $J = 15.4$ Hz, 1H), 4.74 (dq, $J = 15.2$ and 0.9 Hz, 1H), 4.15 (dd, $J = 10.9$ and 1.5 Hz, 1H), 3.82 (s, 3H), 3.72 (dd, $J = 10.8$ and 2.8 Hz, 1H), 2.34 – 2.25 (m, 1H), 1.14 (dtt, $J = 8.8$, 8.1 and 5.0 Hz, 1H), 0.74 – 0.67 (m, 1H), 0.57 – 0.39 (m, 2H), 0.25 – 0.14 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 157.3, 135.6, 126.9, 126.0, 116.4, 108.0, 70.0, 67.6, 55.1, 36.4, 15.8, 5.2, 3.1. Unstable under the conditions of HRMS.

4-Cyclopropyl-7-methoxy-2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinoline (2e)

Prepared according to general procedure: From trichloroacetimidate 1e (215.58 mg, 0.486 mmol), (C$_6$F$_5$)$_3$B (24.87 mg, 0.049 mmol, 10 mol%) and MeNO$_2$ (5 mL). Two regioisomers 2e and 2e’ were obtained and their separation was done by column chromatography on silica gel (eluent hexanes/EtOAc 2:1). After purification isomer 2d (84 mg, 61 %) and isomer 2d’ (29 mg, 21 %) were both obtained as colorless oils.

Major isomer: $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.48 – 7.38 (m, 1H), 6.78 (ddt, $J = 8.6$, 2.8, 0.7 Hz, 1H), 6.59 (d, $J = 2.7$ Hz, 1H), 4.47 – 4.30 (m, 2H), 3.76 (s, 3H), 3.60 – 3.50 (m, 1H), 3.36 (dd, $J = 11.9$, 6.8, 2.2 Hz, 1H), 2.82 (s, 3H), 2.12 – 2.02 (m, 1H), 0.96 – 0.81 (m, 1H), 0.77 – 0.64 (m, 1H), 0.60 – 0.42 (m, 2H), 0.33 – 0.21 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 158.3, 132.4, 129.5, 129.0, 113.3, 110.7, 55.3, 48.9, 47.6, 42.7, 35.3, 15.6, 5.7, 2.8.

HR-MS (ESI-TOF) m/z: calcd. for C$_{14}$H$_{20}$NO$_3$S 282.1164; found: 282.1164 [M+H]$^+$. 

4-Cyclopropyl-5-methoxy-2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinoline (2e’)

Isolated as a minor isomer: $^1$H NMR (300 MHz, CDCl$_3$, ppm) δ 7.18 (t, $J = 8.0$ Hz, 1H), 6.74 (dd, $J = 13.3$, 7.9 Hz, 2H), 4.71 (d, $J = 15.4$ Hz, 1H), 4.21 (d, $J = 15.4$ Hz, 1H), 3.99 (ddd, $J = 11.5$, 2.1, 1.1 Hz, 1H), 3.81 (s, 3H), 3.02 (dd, $J = 11.5$, 3.1 Hz, 1H), 2.88 (s, 3H), 2.63 (dt, $J = 8.9$, 2.3 Hz, 1H), 1.05 (qt, $J = 8.8$, 5.0 Hz, 1H), 0.69 (ddddd, $J = 9.3$, 5.1, 3.1, 1.1 Hz, 1H)
1.6 Hz, 1H), 0.49 (ddd, J = 8.0, 3.0, 1.6 Hz, 2H), 0.21 (ddddd, J = 9.6, 4.9, 3.1, 1.6 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 157.2, 132.4, 127.4, 126.1, 118.5, 108.5, 55.2, 48.6, 46.8, 37.2, 35.2, 15.9, 5.2, 3.4.

HR-MS (ESI-TOF) m/z: calcd. for C$_{14}$H$_{20}$NO$_3$S 282.1164; found: 282.1166 [M+H]$^+$. 

1-Cyclopropyl-6-methoxy-1,2,3,4-tetrahydronaphthalene (2f)

Prepared according to general procedure: from trichloroacetimidate 1f (187.0 mg, 0.513 mmol), (C$_6$F$_5$)$_3$B (26.25 mg, 0.051 mmol, 10 mol%) and MeNO$_2$ (5 mL). Two regioisomers 2f and 2f$'$ were obtained which were separated by column chromatography on silica gel (eluent hexanes/EtOAc 2:1). After purification isomer 2f (35 mg, 34%) and isomer 2f$'$ (23 mg, 22%) were both obtained as colorless oils.

$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.47 (d, J = 8.6 Hz, 1H), 6.72 (ddd, J = 8.5, 2.8, 0.7 Hz, 1H), 6.65 – 6.58 (m, 1H), 3.79 (d, J = 0.8 Hz, 3H), 2.85 – 2.67 (m, 2H), 2.00 – 1.89 (m, 2H), 1.91 – 1.81 (m, 1H), 1.77 – 1.63 (m, 2H), 0.92 – 0.78 (m, 1H), 0.76 – 0.63 (m, 1H), 0.53 – 0.40 (m, 2H), 0.26 – 0.13 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 157.5, 138.1, 133.2, 128.9, 113.4, 111.6, 55.2, 42.7, 30.1, 30.0, 21.2, 18.0, 6.4, 2.6.

No ionization in HRMS.

1-Cyclopropyl-8-methoxy-1,2,3,4-tetrahydronaphthalene (2f$'$)

Isolated as a minor isomer: $^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 7.08 (t, J = 7.9 Hz, 1H), 6.70 (dd, J = 12.2, 7.9 Hz, 2H), 3.79 (s, 3H), 2.92 – 2.68 (m, 2H), 2.57 (ddd, J = 8.1, 5.1, 2.3 Hz, 1H), 2.15 – 1.91 (m, 2H), 1.77 (ddt, J = 13.0, 7.3, 3.7 Hz, 1H), 1.67 (tq, J = 13.2, 5.0, 4.2 Hz, 1H), 0.91 – 0.81 (m, 1H), 0.67 – 0.56 (m, 1H), 0.52 – 0.40 (m, 1H), 0.43 – 0.30 (m, 1H), 0.18 – 0.07 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 157.5, 138.1, 129.4, 126.0, 121.5, 107.2, 54.9, 35.1, 29.0, 28.7, 18.3, 16.9, 5.9, 2.8.

No ionization in HRMS.
4-Cyclopropyl-6,8-dimethoxyisochromane (2h)

Prepared according to general procedure: From trichloroacetimidate 1h (99.0 mg, 0.250 mmol), (C₆F₅)₃B (9.03 mg, 0.025 mmol, 10 mol%) and MeNO₂ (2.5 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 8:1) afforded 4-cyclopropyl-6,8-dimethoxyisochromane (2h) (54 mg, 92%) as a colorless oil.

¹H NMR (400 MHz, CDCl₃, ppm) δ 6.34 (d, J = 2.5 Hz, 1H), 6.12 (d, J = 2.4 Hz, 1H), 4.82 (d, J = 15.3 Hz, 1H), 4.70 (d, J = 15.2 Hz, 1H), 4.14 (dd, J = 10.8, 1.5 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.70 (dd, J = 10.8, 2.9 Hz, 1H), 2.27 – 2.16 (m, 1H), 1.11 (qt, J = 8.2, 5.0 Hz, 1H), 0.67 (td, J = 9.4, 5.4 Hz, 1H), 0.56 – 0.37 (m, 2H), 0.22 – 0.11 (m, 1H).

¹³C NMR (101 MHz, CDCl₃, ppm) δ 158.9, 158.4, 136.1, 118.5, 99.3, 96.7, 70.3, 67.9, 55.3, 55.1, 36.1, 15.9, 4.9, 3.0.

HR-MS (ESI-TOF) m/z: calcd. for C₁₄H₁₉O₃ 235.1334; found: 235.1335 [M+H]^+.

7-Cyclopropyl-6,7-dihydro-4H-furo[3,2-c]pyran (2j)

Prepared according to general procedure: from racemic and enantioenriched trichloroacetimidate 1j (200.0 mg, 0.612 mmol), (C₆F₅)₃B (31.4 mg, 0.061 mmol, 10 mol%) and MeNO₂ (6 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 15:1) afforded 7-cyclopropyl-6,7-dihydro-4H-furo[3,2-c]pyran (2j) (76 mg, 76%) as a colorless oil.

¹H NMR (400 MHz, CDCl₃, ppm) δ 7.31 (dd, J = 2.0, 0.8 Hz, 1H), 6.20 (d, J = 2.0 Hz, 1H), 4.66 – 4.52 (m, 2H), 3.97 (dd, J = 11.2, 4.7 Hz, 1H), 3.80 (dd, J = 11.2, 5.5 Hz, 1H), 2.20 – 2.11 (m, 1H), 0.92 – 0.81 (m, 1H), 0.67 – 0.55 (m, 1H), 0.53 – 0.39 (m, 2H), 0.28 – 0.17 (m, 1H).

¹³C NMR (101 MHz, CDCl₃, ppm) δ 150.7, 141.3, 115.6, 106.9, 70.2, 64.5, 40.4, 12.2, 3.4, 2.4.

Unstable under the conditions of HRMS.

4-Cyclopropyl-3,4-dihydro-1H-pyrano[4,3-b]benzofuran (2k)

Prepared according to general procedure: from trichloroacetimidate 1k (64.3 mg, 0.171 mmol), (C₆F₅)₃B (8.74 mg, 0.017 mmol, 10
mol%) and MeNO$_2$ (1.7 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 10:1) afforded 4-cyclopropyl-3,4-dihydro-1H-pyrano[4,3-b]benzofuran (2k) (33.4 mg, 91%) as a colorless oil.

${}^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.48 (dq, $J = 8.0$, 0.8 Hz, 1H), 7.35 (dd, $J = 7.4$, 1.7, 0.8 Hz, 1H), 7.29 – 7.15 (m, 2H), 4.89 – 4.73 (m, 2H), 4.06 (dd, $J = 11.2$, 4.6 Hz, 1H), 3.92 (dd, $J = 11.2$, 5.2 Hz, 1H), 2.28 (ddd, $J = 7.1$, 6.0, 4.0 Hz, 1H), 1.02 – 0.89 (m, 1H), 0.74 – 0.62 (m, 1H), 0.63 – 0.46 (m, 2H), 0.34 – 0.23 (m, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) $\delta$ 154.4, 153.8, 125.8, 123.6, 122.5, 118.5, 111.7, 111.3, 70.1, 63.6, 40.5, 12.2, 3.8, 2.7.

Unstable under the conditions of HRMS.

7-Cyclopropyl-6,7-dihydro-4H-thieno[3,2-c]pyran (2l)

Prepared according to general procedure: from trichloroacetimidate 1l (49.31 mg, 0.144 mmol), (C$_6$F$_5$)$_3$B (5.2 mg, 0.014 mmol, 10 mol%) and MeNO$_2$ (1.4 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 10:1) afforded 7-cyclopropyl-6,7-dihydro-4H-thieno[3,2-c]pyran benzofuran (2l) (25.5 mg, 98%) as a colorless oil.

${}^1$H NMR (400 MHz, CDCl$_3$, ppm) $\delta$ 7.13 (d, $J = 5.2$ Hz, 1H), 6.72 (d, $J = 5.2$ Hz, 1H), 4.71 (d, $J = 2.2$ Hz, 2H), 4.08 (dd, $J = 11.2$, 4.8 Hz, 1H), 3.68 (dd, $J = 10.8$, 7.4 Hz, 1H), 2.13 (tdd, $J = 9.3$, 3.9, 2.3 Hz, 1H), 0.87 (dt, $J = 10.0$, 8.0, 5.0 Hz, 1H), 0.71 – 0.59 (m, 1H), 0.60 – 0.48 (m, 1H), 0.42 (dq, $J = 9.2$, 4.9 Hz, 1H), 0.30 (td, $J = 9.3$, 4.8 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) $\delta$ 137.9, 133.5, 123.2, 123.2, 70.0, 66.7, 41.9, 14.8, 3.9, 3.7.

Unstable under the conditions of HRMS.

2,2,2-Trichloro-N-(9-cyclopropyl-1,7-dioxaspiro[4.4]non-3-en-2-yl)acetamide (2m)

Prepared according to general procedure: from trichloroacetimidate 1m (64.2 mg, 0.197 mmol), (C$_6$F$_5$)$_3$B (10.1 mg, 0.020 mmol, 10 mol%) and MeNO$_2$ (3 mL). Purification by column chromatography on silica gel (eluent hexanes/EtOAc 4:1) afforded of 2,2,2-trichloro-N-(9-cyclopropyl-1,7-dioxaspiro[4.4]non-3-en-2-yl)acetamide (2m) (51 mg, 85%) as a mixture of inseperable diastereomers (dr 2:1).
$^1$H NMR (400 MHz, CDCl$_3$, ppm) δ 6.96 (d, $J = 9.5$ Hz, 0.3H, minor diastereomer) and 6.82 (d, $J = 7.7$ Hz, 0.7H, major diastereomer), 6.59 (dt, $J = 9.3$, 1.5 Hz, 0.3H, minor diastereomer) and 6.51 (dt, $J = 8.7$, 1.6 Hz, 0.7H, major diastereomer), 6.02 (dd, $J = 5.8$, 1.7 Hz, 0.7H, major diastereomer) and 5.99 (dd, $J = 5.8$, 1.6 Hz, 0.3H, minor diastereomer)), 5.94 (dd, $J = 5.8$, 1.3 Hz, 0.7H, major diastereomer) and 5.91 (dd, $J = 5.8$, 1.4 Hz, 0.3H, minor diastereomer), 4.11 – 3.74 (m, total 4H, both diastereomers), 1.44 (dddd, $J = 11.2$, 9.7, 7.9, 1.7 Hz, total 1H, both diastereomers), 0.90 – 0.76 (m, total 1H, both diastereomers), 0.59 – 0.39 (m, total 2H, both diastereomers), 0.21 – 0.10 (m, 0.6H, minor diastereomer), 0.10 – 0.02 (m, 1.4H, major diastereomer).

$^{13}$C NMR (101 MHz, CDCl$_3$, ppm) δ 160.9, 160.7, 134.7, 134.6, 127.2, 126.6, 98.1, 97.7, 92.2, 92.2, 87.9, 87.4, 77.9, 77.5, 72.9, 72.8, 54.2, 53.4, 6.3, 5.4, 3.2, 3.1, 2.7, 1.7.

Unstable under the conditions of HRMS.

5. Structure determination of oxazoline 2b by X-ray of trichloroacetamide 22

To approve structure of oxazoline 2b it was hydrolyzed to trichloroacetamide 22 in the presence of $p$-TsOH·H$_2$O (Scheme 12). Product 22 was obtained as a white crystalline compound. Product configuration was determined by X-ray diffraction. Crystal of 22 was grown in system hexane/methylene chloride 1/1.

Derivatization procedure of 2b and characterization of product 22

2,2,2-Trichloro-N-(1-cyclopropyl-2-hydroxyethyl)acetamide (22)

Oxazoline 2b (92.9 mg, 0.407 mmol) was dissolved in mixture of pyridine and water (4:1, 4 mL), then $p$-TsOH·H$_2$O (77.3 mg, 0.407, 1.0 equiv) was added. The mixture was heated at 80 °C for 4 h, then EtOAc (4 mL) was added. The layers were separated and the organic layer was washed with 5 % KHSO$_4$ aq. (4 × 5 mL) and sat. CuSO$_4$ aq. (1 × 5 mL). Organic
phase was dried over MgSO₄ and filtered. Concentration in vacuum followed by purification by flash column chromatography (eluent hexanes/EtOAc 2:1) afforded 2,2,2-trichloro-\(N\)-(1-cyclopropyl-2-hydroxyethyl)acetamide (22) (81.0 mg, 81%) as a white crystalline compound.

\(^1\)H NMR (400 MHz, CDCl₃, ppm) \(\delta\) 7.04 (bs, 1H), 3.86 (qd, \(J = 11.1, 4.0\) Hz, 2H), 3.28 (ddt, \(J = 9.5, 7.9, 4.0\) Hz, 1H), 2.03 (bs, 1H), 1.09 (ddt, \(J = 9.6, 8.0, 4.9\) Hz, 1H), 0.66 – 0.58 (m, 2H), 0.53 – 0.45 (m, 1H), 0.39 – 0.32 (m, 1H).

\(^{13}\)C NMR (101 MHz, CDCl₃, ppm) \(\delta\) 162.1, 92.7, 64.6, 58.3, 12.4, 3.3, 3.1.

EA: Calcd for C\(_7\)H\(_{10}\)Cl\(_3\)NO\(_2\): C, 34.11%; H, 4.09%; N, 5.68%; found: C, 34.13%; H, 4.11%; N, 5.70%.

Mp (Hexane): 78.1 – 79.7 °C.

**X-ray structure of trichloroacetamide 22**

![X-ray structure of trichloroacetamide 22](image)

**Figure S1** ORTEP diagram of derivatization product 22 (Displacement ellipsoid are drawn at 50% probability level)
5. NMR data

![NMR spectra image]
trans-8a
as a mixture of inseparable Z/E-isomers
$7f$
1m

- 162.87
- 151.83
- 142.68
- 139.48
- 129.09
- 91.52
- 72.86
- 72.54
- 64.13
- 16.73
- 15.45
- 8.58
2b
as mixture of diastereomers

2m
6. Chiral HPLC of compound 7j

Racemic 7j

IC2_Ch 151

Sample Information

Sample Name: #585_C151_MS-1506-80C
Sample Type: Unknown
Vibit: 33
Injection #: 1
Injection Volume: 10.00 uL
Run Time: 30.0 Minutes

Acq. Method: Iz_210_284_F1_100A
Processing Method: Ch151 IC2_10%IPA

Channel Name: W2489 ChA
Proc. Chnl. Descr.: W2489 ChA 210nm

Data Acquired: 11/5/2015 11:56:34 AM EET
Data Processed: 11/5/2015 12:26:33 PM EET

Chiralpak IC2-2 (4.6x250 mm)
Iz 10% IPA/90% Hex, F=1 mL/min, T=25°C

<table>
<thead>
<tr>
<th>Peak Name</th>
<th>RT</th>
<th>Area</th>
<th>% Area</th>
<th>Height</th>
<th>EP Plate Count</th>
<th>Resolution</th>
<th>Selectivity</th>
<th>Width @ 50%</th>
<th>Width @ 1%</th>
<th>K’ Prine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 A</td>
<td>8.549</td>
<td>9537601</td>
<td>49.60</td>
<td>921120</td>
<td>15816</td>
<td>0.166</td>
<td>1.514</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 B</td>
<td>9.153</td>
<td>9590707</td>
<td>50.40</td>
<td>803153</td>
<td>13181</td>
<td>2.056</td>
<td>1.118</td>
<td>0.188</td>
<td>1.692</td>
<td></td>
</tr>
<tr>
<td>Sum</td>
<td>19228308.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 c=1.35 mg/mL (KF)

Reported by User: System
Project Name: Alliance-4_2015
Report Method: IC2_Ch 151
Report Method ID: 0500
Page: 1 of 1

12:27:30 PM Europe/Riga

158
Enantioenriched 7j