Supplementary Information (SI) for Chemical Communications.

SUPPLEMENTARY INFORMATION

Asymmetric cyclopropanation *via* electro-organocatalytic cascade

Anastasiya Krech, ‡ Marharyta Laktsevich-Iskryk, ‡ Nora Deil, Mihhail Fokin, Mariliis Kimm and Maksim Ošeka*

‡ These authors contributed equally.

Department of Chemistry and Biotechnology, Tallinn University of Technology, Akadeemia tee 15, Tallinn 12618, Estonia.

E-mail: maksim.oseka@taltech.ee

Table of contents

1. General information

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III instrument at 400 MHz for ^{1}H and 100.6 MHz for ^{13}C. ^{1}H NMR spectra are reported in parts per million (ppm) downfield relative to $CDCl_3$ (7.26 ppm) and ^{13}C NMR spectra are reported in ppm relative to $CDCl_3$ (77.16 ppm). HRMS measurements were performed on Agilent 6540 UHD Accurate-Mass Q-TOF LC/MS system (Agilent Technologies, Santa Clara, CA, US) equipped with AJS-ESI source. Precoated silica gel plates (Merck 60 F254 or F254, Supelco Sigma-Aldrich™) were used for TLC analysis. Flash column chromatography was performed on a Biotage® Isolera Prime with silica gel Kieselgel 63–200 µm. Purchased chemicals (Sigma Aldrich, TCI, Honeywell and Fluorochem) and solvents (Honeywell, Keemiakaubandus AS, Lach:ner) were used as received.

For all electrochemical reactions, a homemade cell was used, together with a six-channel power supply (Fig. S1). The cell consists of a working electrode and a counter electrode. The material used for the electrodes were Stainless Steel electrode (316L) and Graphite AC-K800 premium Grade (purchased by IKA).

HPLC determination of enantiomeric excess was performed with an Agilent Technologies 1200 series chromatograph by using appropriate chiral columns (see below). Specific rotations were measured using an Anton Paar MCP 500 polarimeter.

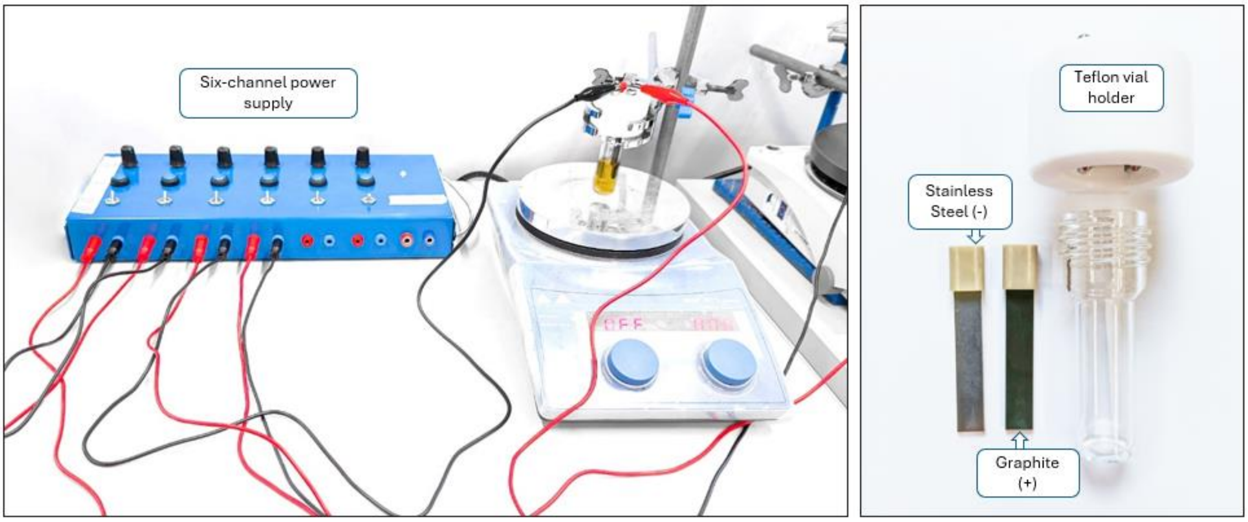
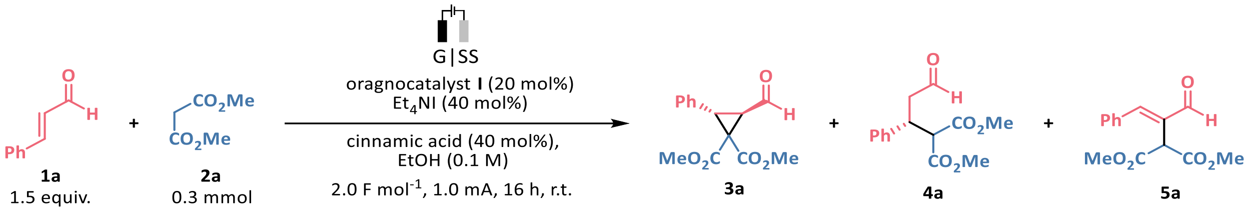


Figure S1. Electrochemical reaction setup.

2. Optimization of reaction conditions

2.1. Screening of EtOH conditions

Organocatalyst **I** (0.06 mmol, 20 mol%, 19.5 mg), TEAI (0.12 mmol, 40 mol%, 30.8 mg), and cinnamic acid (0.12 mmol, 17.8 mg) were dissolved in EtOH (0.1 M, 3 mL). To the resulting solution, cinnamic aldehyde (0.45 mmol, 1.5 equiv., 57 µL) and dimethyl malonate (0.3 mmol, 1 equiv., 34 µL) were sequentially added. The reaction vessel was sealed with a Teflon cap equipped with stainless steel and graphite electrodes (gap between electrodes of 0.5 cm) and flushed with Ar for 5 minutes. The vial was then connected to a power supply, and the reaction mixture was electrolyzed under a constant current of 1 mA for 16 hours while stirring at 800 rpm. After completion of the reaction, the cap was removed, and the electrodes were rinsed with CH_2Cl_2. The reaction mixture was combined with the rinses, and the resulting solution was analyzed by ^{1}H NMR using trimethoxybenzene as an external standard.



<table>
<tr><th rowspan="2">Entry</th><th rowspan="2">Deviation from reaction conditions</th><th colspan="3">NMR yield, %^{a}</th><th rowspan="2">d.r. of 3a^b</th></tr>
<tr><th>3a</th><th>4a</th><th>5a</th></tr>
<tr><td>1</td><td>None</td><td>57</td><td>6</td><td>11</td><td>>20:1</td></tr>
<tr><td>2</td><td>3 equiv. of 1a</td><td>37</td><td>27</td><td>-</td><td>>20:1</td></tr>
<tr><td>3</td><td><i>n</i>Bu$_4$NI instead of <i>n</i>Et$_4$NI</td><td>22</td><td>7</td><td>4</td><td>>20:1</td></tr>
<tr><td>4</td><td>Me$_4$NI instead of <i>n</i>Et$_4$NI</td><td>28</td><td>5</td><td>4</td><td>>20:1</td></tr>
<tr><td>5</td><td>Me$_4$NBr instead of <i>n</i>Et$_4$NI</td><td>-</td><td>26</td><td>-</td><td></td></tr>
<tr><td>6</td><td>Cat. II—IV as organocatalysts</td><td>31-52</td><td>3-16</td><td>3-11</td><td>>20:1</td></tr>
<tr><td>7</td><td>10 mol% of cat. I</td><td>42</td><td>12</td><td>4</td><td>>20:1</td></tr>
<tr><td>8</td><td>Pt as a cathode</td><td>36</td><td>25</td><td>6</td><td>>20:1</td></tr>
<tr><td>9</td><td>Graphite as a cathode</td><td>42</td><td>11</td><td>6</td><td>>20:1</td></tr>
<tr><td>10</td><td>TFA instead of cinnamic acid</td><td>47</td><td>19</td><td>-</td><td>>20:1</td></tr>
<tr><td>11</td><td>Without cinnamic acid</td><td>37</td><td>6</td><td>-</td><td>>20:1</td></tr>
<tr><td>10</td><td>At 0 °C</td><td>33</td><td>19</td><td>3</td><td>>20:1</td></tr>
<tr><td>11</td><td>Constant potential, 2 V, 16 h</td><td>27</td><td>-</td><td>7</td><td>>20:1</td></tr>
<tr><td>12</td><td>No electricity</td><td>-</td><td>52</td><td>-</td><td></td></tr>
<tr><td>13</td><td>No halogen source</td><td>-</td><td>41</td><td>-</td><td></td></tr>
</table>

Table S1. ^{a}Yields were determined by ^{1}H NMR analysis of the crude reaction mixture using trimethoxybenzene as an internal standard. ^{b}Diastereomeric ratio of **3a** was determined by ^{1}H NMR analysis of the crude reaction mixture.

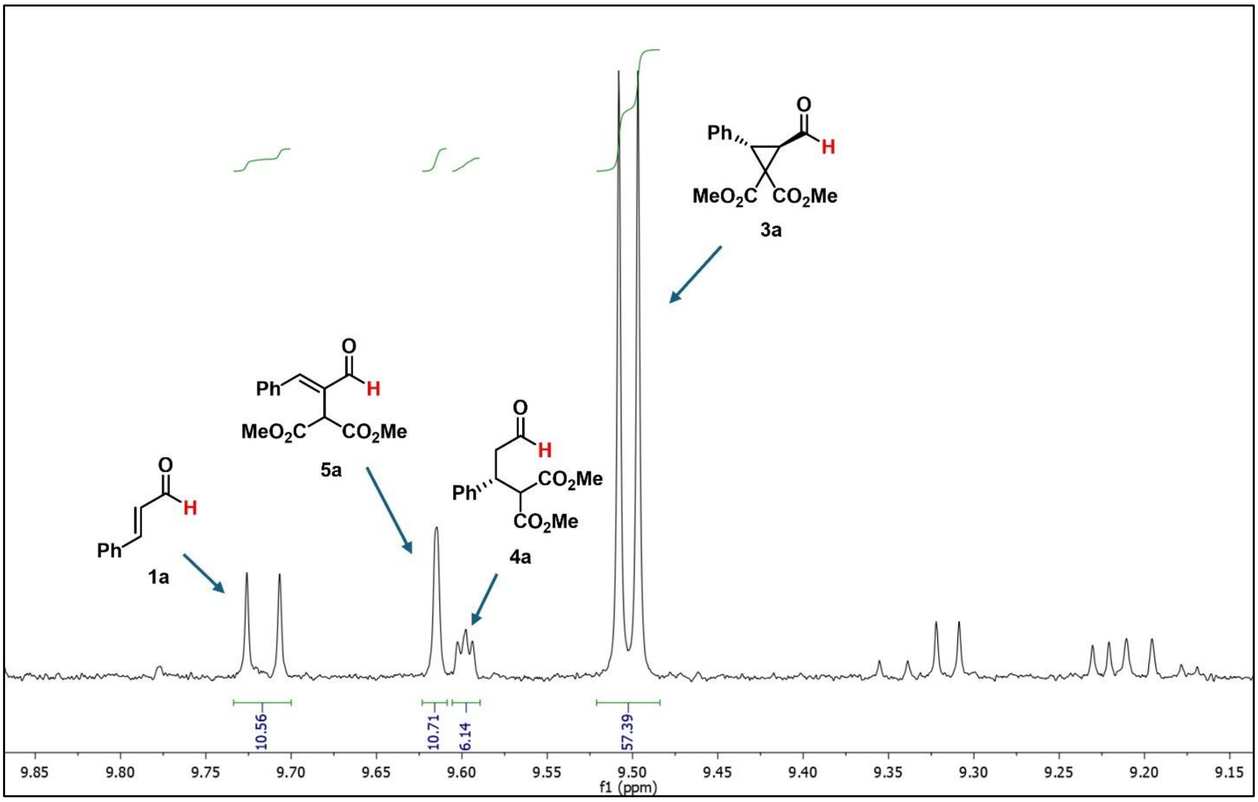
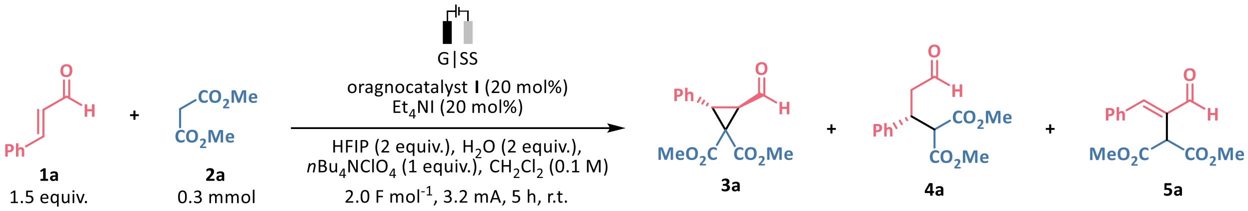


Figure S2. Characteristic signals of the main products and cinnamic aldehyde in ^{1}H NMR spectrum of the reaction mixture (**Table S1**, Entry 1).

2.2. *Screening of additional parameters for standard reaction conditions*

Organocatalyst **I** (0.06 mmol, 20 mol%, 19.5 mg), $TBAClO_4$ (0.3 mmol, 1 equiv., 102.6 mg), TEAI (0.06 mmol, 20 mol%, 15.4 mg) were dissolved in CH_2Cl_2 (0.1 M, 3 mL). To the resulting solution, HFIP (0.6 mmol, 2 equiv., 63.0 µL), H_2O (0.6 mmol, 2 equiv., 10.8 µL), cinnamic aldehyde (0.45 mmol, 1.5 equiv., 57 µL) and dimethyl malonate (0.3 mmol, 1 equiv., 34 µL) were sequentially added. The reaction vessel was sealed with a Teflon cap equipped with stainless steel and graphite electrodes (gap between electrodes of 0.5 cm) and flushed with Ar for 5 minutes. The vial was then connected to a power supply, and the reaction mixture was electrolyzed under a constant current of 3.2 mA for 5 hours while stirring at 800 rpm. After completion of the reaction, the cap was removed, and the electrodes were rinsed with CH_2Cl_2. The reaction mixture was combined with the rinses, and the resulting solution was analyzed by ^{1}H NMR using trimethoxybenzene as an external standard.

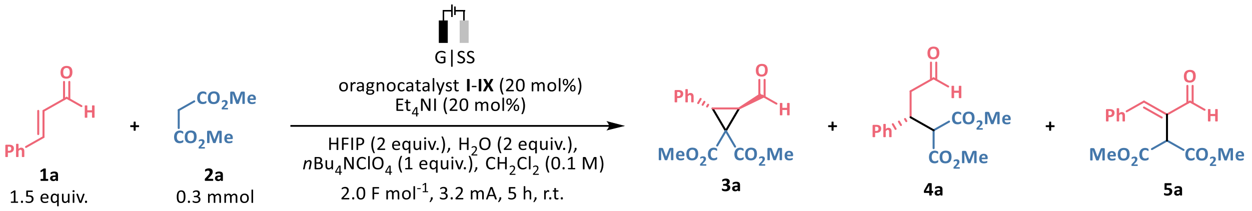


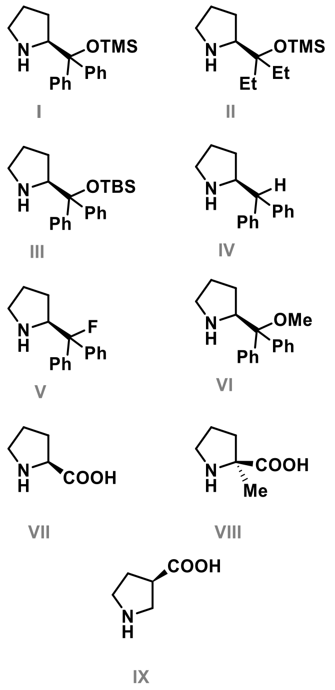
Entry	Deviation from reaction conditions	NMR yield, %[a]			d.r. of 3a[b]
		3a	4a	5a	
1	None	59	-	12	>20:1
2	10 mol% of **I**	37	-	-	>20:1
3	30 mol% of **I**	48	-	22	>20:1
4	nBu$_4$NBF$_4$ or nBu$_4$NPF$_6$ as electrolytes	55	-	14-18	>20:1
5	1 equiv. of **1a**, 1 equiv. of **2a**	49	-	8	>20:1
6	3 equiv. of **1a**, 1 equiv. of **2a**	53	6	-	>20:1
7	EtOH (2 equiv.) instead of HFIP	39	-	7	>20:1
8	EtOH (2 equiv.) instead of H_2O	47	5	10	>20:1
9	1 equiv. of H_2O	17	27	6	>20:1
10	4 equiv. of H_2O	50	-	6	>20:1
11	Constant potential, 2 V, 20 h	48	-	17	>20:1
13	At 10 °C or at 35 °C	33-49	-	0-17	>20:1
14	At 0 °C, 2 F mol^{-1}, 1 mA, 16 h,	53	-	6	>20:1
15	CH_2Cl_2 1:1 EtOH as solvent	29	-	-	>20:1
16	With dimethoxybiphenyl (50 mol %), RVC cathode, 2.5 F mol^{-1}, 3.3 mA, 6 h	63	-	13	>20:1

Table S2. [a]Yields were determined by ^{1}H NMR analysis of the crude reaction mixture using trimethoxybenzene as an internal standard. [b]Diastereomeric ratio of **3a** was determined by ^{1}H NMR analysis of the crude reaction mixture.

2.3. *Screening of organocatalysts*

Proline-based organocatalyst (**I-IX**) (0.06 mmol, 20 mol%), TBAClO4 (0.3 mmol, 1 equiv., 102.6 mg), TEAI (0.06 mmol, 20 mol%, 15.4 mg) were dissolved in CH_2Cl_2 (0.1 M, 3 mL). To the resulting solution, HFIP (0.6 mmol, 2 equiv., 63.0 µL), H_2O (0.6 mmol, 2 equiv., 10.8 µL), cinnamic aldehyde (0.45 mmol, 1.5 equiv., 57 µL) and dimethyl malonate (0.3 mmol, 1 equiv., 34 µL) were sequentially added. The reaction vessel was sealed with a Teflon cap equipped with stainless steel and graphite electrodes (gap between electrodes of 0.5 cm) and flushed with Ar for 5 minutes. The vial was then connected to a power supply, and the reaction mixture was electrolyzed under a constant current of 3.2 mA for 5 hours while stirring at 800 rpm. After completion of the reaction, the cap was removed, and the electrodes were rinsed with CH_2Cl_2. The reaction mixture was combined with the rinses, and the resulting solution was analyzed by ^{1}H NMR using trimethoxybenzene as an external standard.



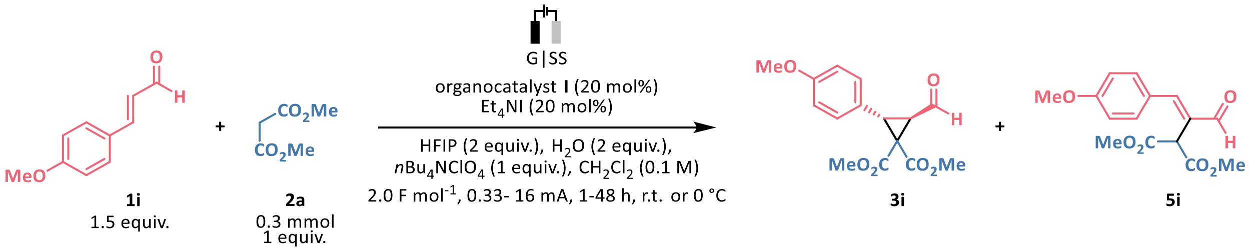


Entry	Organocatalyst	NMR yield, % ^{a}			d.r. of 3a ^{b}	*ee* of 3a, % ^{c}
		3a	4a	5a		
1	Cat. I	59	-	12	>20:1	96
2	Cat. II	46	-	2	>20:1	86
3	Cat. III	41	8	10	>20:1	n.d.
4	Cat. IV	38	-	8	>20:1	82
5	Cat. V	39	-	5	>20:1	92
6	Cat. VI	49	-	7	>20:1	70
7	Cat. VII	11	-	-	>20:1	n.d.
8	Cat. VIII	8	-	-	>20:1	n.d.
9	Cat. IX	21	-	-	>20:1	n.d.

Table S3. ^{a}Yields were determined by ^{1}H NMR analysis of the crude reaction mixture using trimethoxybenzene as an internal standard. ^{b}Diastereomeric ratio of **3a** was determined by ^{1}H NMR analysis of the crude reaction mixture. n.d.: not determined. ^{c}Enantiomeric ratio of **3a** was determined by chiral HPLC analysis.

3. Effect of temperature on reaction outcome

Organocatalyst **I** (0.06 mmol, 20 mol%, 19.5 mg), $TBAClO_4$ (0.3 mmol, 1 equiv., 102.6 mg), TEAI (0.06 mmol, 20 mol%, 15.4 mg) were dissolved in CH_2Cl_2 (0.1 M, 3 mL). To the resulting solution, HFIP (0.6 mmol, 2 equiv., 63.0 µL), H_2O (0.6 mmol, 2 equiv., 10.8 µL), (*E*)-3-(4-methoxyphenyl)acrylaldehyde (0.45 mmol, 1.5 equiv., 73 mg) and dimethyl malonate (0.3 mmol, 1 equiv., 34 µL) were sequentially added. The reaction vessel was sealed with a Teflon cap equipped with stainless steel and graphite electrodes (gap between electrodes of 0.5 cm) and flushed with Ar for 5 minutes. The vial was then connected to a power supply, and the reaction mixture was electrolyzed under a constant current for the defined period (1-8 h at r.t., 10-48 h at 0 °C) while stirring at 800 rpm. After completion of the reaction, the cap was removed, and the electrodes were rinsed with CH_2Cl_2. The reaction mixture was combined with the rinses, and the resulting solution was analyzed by ^{1}H NMR using trimethoxybenzene as an external standard. Each column on the graph (Figure S3) corresponds to the result of a distinct experiment.



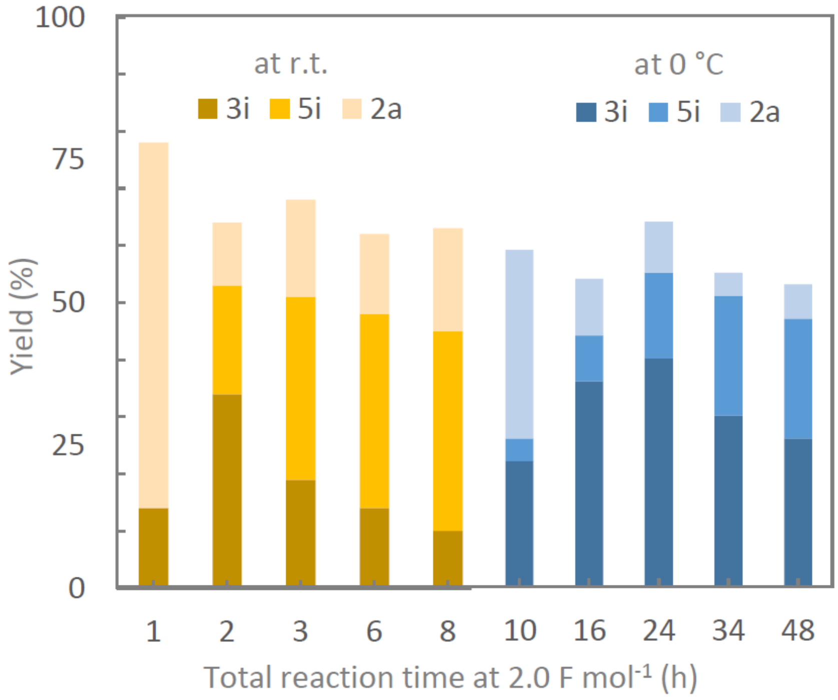
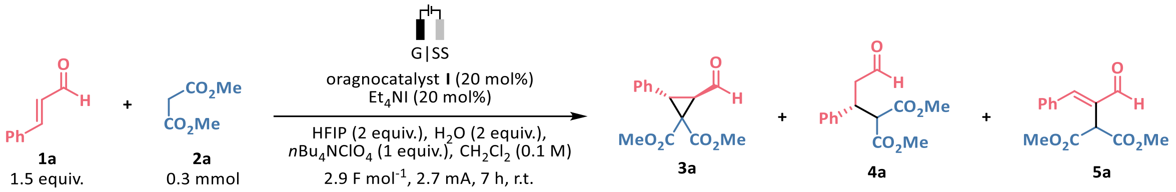


Figure S3. The outcome of the reaction between **1i** and **2a** at varying temperatures and reaction times.

3. Kinetic studies of the model reaction

Organocatalyst **I** (0.06 mmol, 20 mol%, 19.5 mg), TBAClO₄ (0.3 mmol, 1 equiv., 102.6 mg) and TEAI (0.06 mmol, 20 mol%, 15.4 mg) were dissolved in CH_2Cl_2 (0.1 M, 3 mL). To the resulting solution, HFIP (0.6 mmol, 2 equiv., 63.0 µL), H_2O (0.6 mmol, 2 equiv., 10.8 µL), cinnamic aldehyde (0.45 mmol, 1.5 equiv., 57 µL), dimethyl malonate (0.3 mmol, 1 equiv., 34 µL) and the internal standard dimethyacetamide (0.15 mmol, 14 µL) were sequentially added. The reaction vessel was sealed with a Teflon cap equipped with stainless steel and graphite electrodes (gap between electrodes of 0.5 cm) and flushed with Ar for 5 minutes. The vial was then connected to a power supply, and the reaction mixture was electrolyzed under a constant current of 2.7 mA for 7 hours while stirring at 800 rpm. The progress of the reaction was monitored by ^1H NMR by withdrawing 50 µL samples from the reaction mixture after defined periods and diluting them with $CDCl_3$.



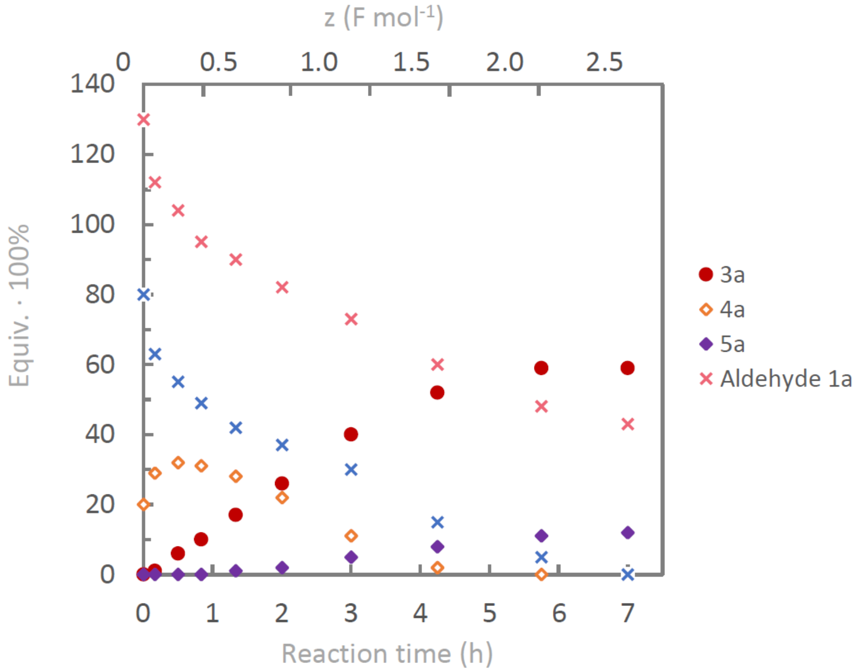
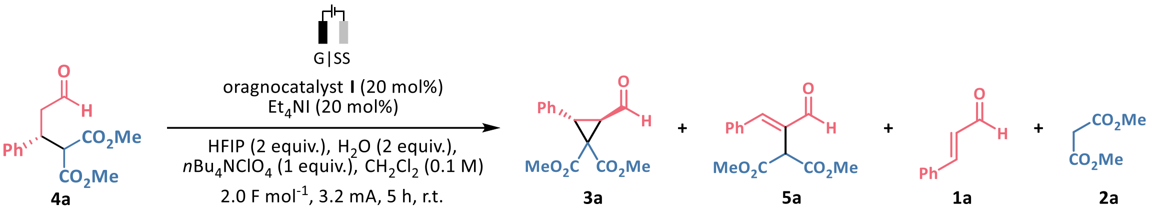


Figure S4. Kinetic studies of the model reaction.

Comment: Kinetics experiments for model reaction of cinnamic aldehyde **1a** and dimethyl malonate **2a** was performed, where we investigated the formation of intermediate **4a** (product of the first addition of malonate to iminium ion), cyclopropane **3a**, byproduct **5a** and the conversions of starting compounds over the addition of electrons and, thus, reaction time. Even before turning on the electricity, intermediate **4a** is formed in 20% yield and over the addition of 0.2 F mol^{-1} electrons the amount of **4a** continues to increase to 30%, together with the start of the formation of product 3. Then **4a** degrades over time and it is fully consumed at 1.7 F mol^{-1}, however the amount of **3a** still increases together with its byproduct **5a**. When performing the reaction with an excess of electrons over 2 F mol^{-1}, cyclopropane **3a** does not form anymore and even starts to degrade to **5a**.

4. Kinetic studies of 4a cyclopropanation

Organocatalyst **I** (0.06 mmol, 20 mol%, 19.5 mg), $TBAClO_4$ (0.3 mmol, 1 equiv., 102.6 mg) and TEAI (0.06 mmol, 20 mol%, 15.4 mg) were dissolved in CH_2Cl_2 (0.1 M, 3 mL). To the resulting solution, HFIP (0.6 mmol, 2 equiv., 63.0 µL), H_2O (0.6 mmol, 2 equiv., 10.8 µL), **4a** (0.3 mmol, 1 equiv., 79.3 mg) and the internal standard dimethyacetamide (0.15 mmol, 14 µL) were sequentially added. The reaction vessel was sealed with a Teflon cap equipped with stainless steel and graphite electrodes (gap between electrodes of 0.5 cm) and flushed with Ar for 5 minutes. The vial was then connected to a power supply, and the reaction mixture was electrolyzed under a constant current of 3.2 mA for 5 hours while stirring at 800 rpm. The progress of the reaction was monitored by ^1H NMR by withdrawing 50 µL samples from the reaction mixture after defined periods and diluting them with $CDCl_3$.



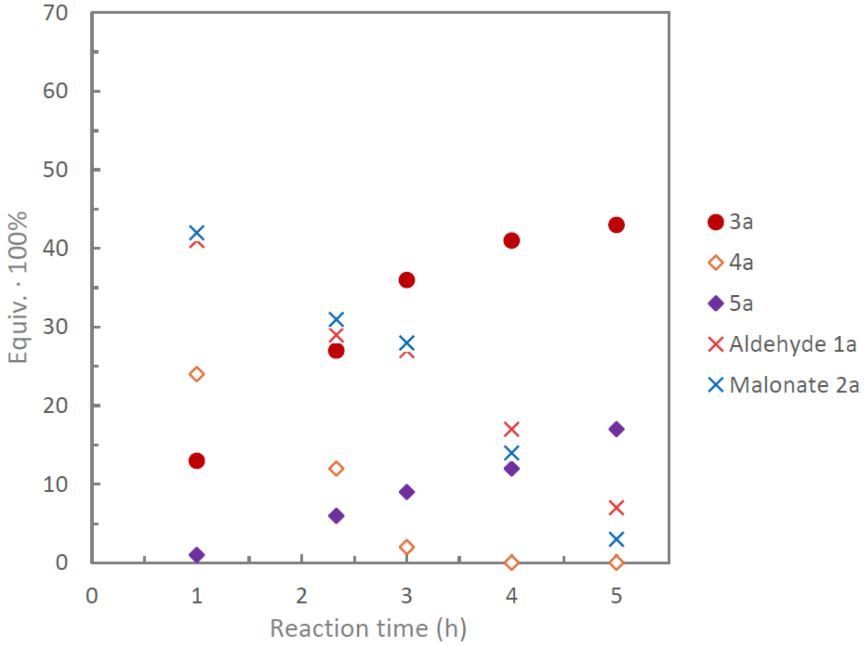
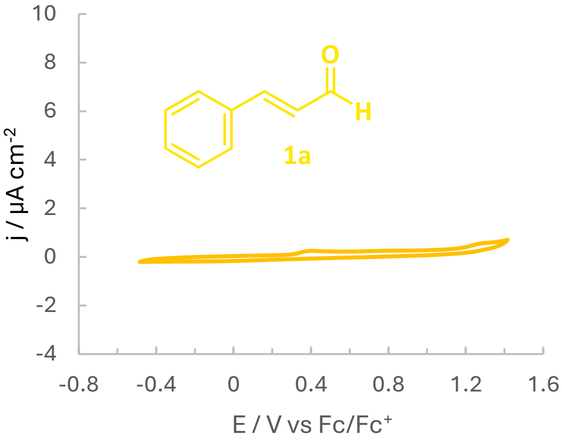


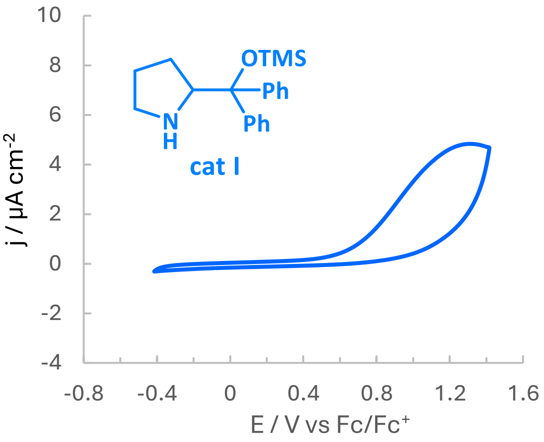
Figure S5. Kinetic studies of the control reaction from **4a**.

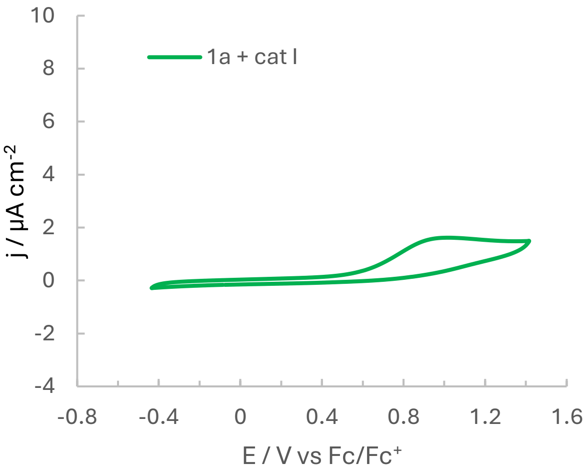
5. Cyclic voltammetry

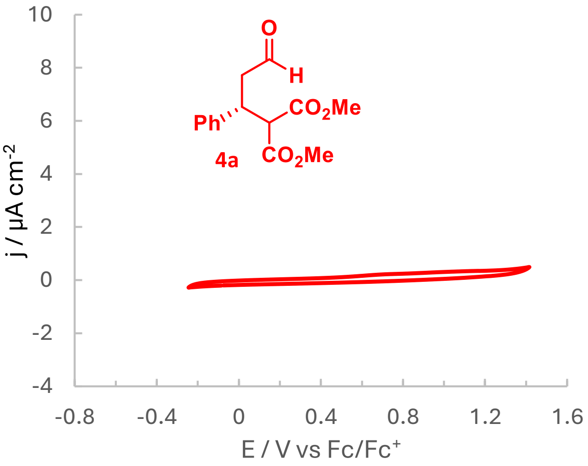
The cyclic voltammetry experiments were conducted using a three-electrode cell. For analysis, a PalmSens EmStat4LR potentiostat was utilized, with a glassy carbon disc (diameter: 3 mm) serving as the working electrode, and a platinum wire as the counter electrode. Prior to each experiment, the glassy carbon disc was polished with 0.05 µm alumina slurry in distilled water. Ag wire in 10 mM solution of $AgNO_3$ in *n*Bu_4NPF_6 (0.1 M) in acetonitrile was used as a reference electrode and this compartment was separated from the rest of the cell with a frit. Anhydrous acetonitrile was stored over molecular sieves and used as the solvent. Tetrabutylammonium hexafluorophosphate was recrystallized from ethanol prior to use.

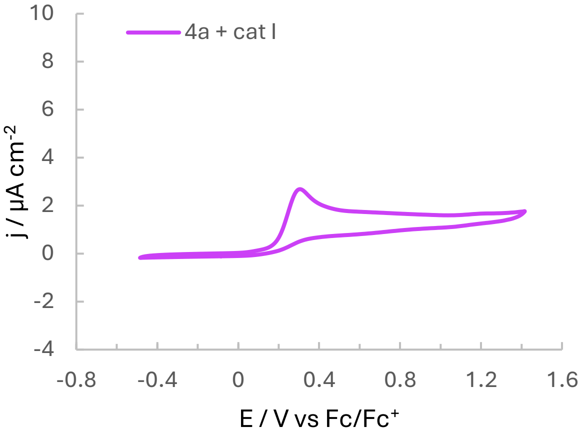
The analyte was dissolved in the electrolyte (10 mM solution in 0.1 M *n*Bu_4NPF_6 in acetonitrile, for Et_4NI, *n*Bu_4NBr and TEMPO 2 mM solution). Before measurements, the electrochemical cell was flushed with argon, charged with 3 mL of the analyte solution, and flushed with a stream of argon for 5 min. The measurements were conducted at a scan rate of 100 mV/s. The measurements were started at the open circuit potential (OCP). The range of the scanned potentials was −0.5 / +1.5 V. CV diagrams are presented in IUPAC plotting convention. The CV spectra were realigned with respect to Fc^+/Fc couple. Half-wave potentials and E_p (peak potentials) for all the compounds were determined with PSTrace5 software.

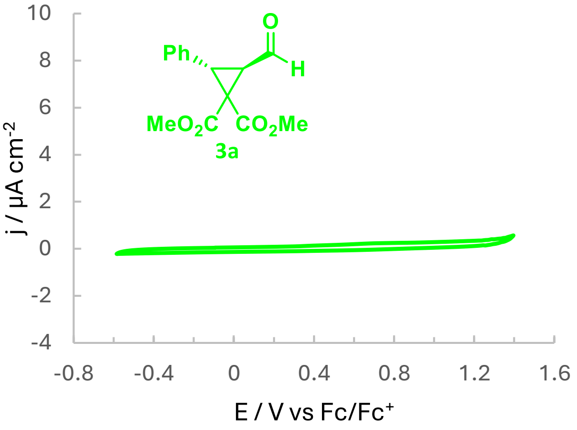


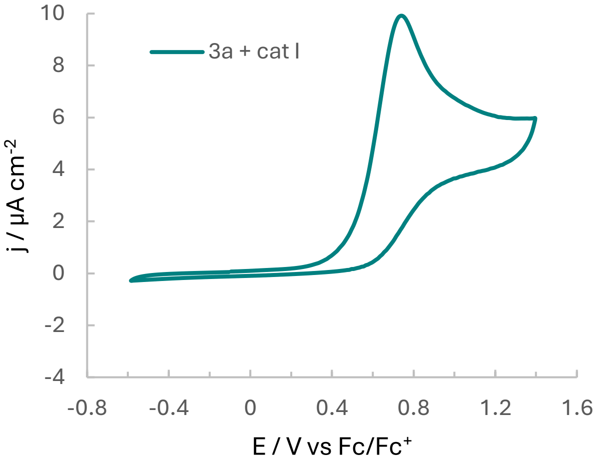


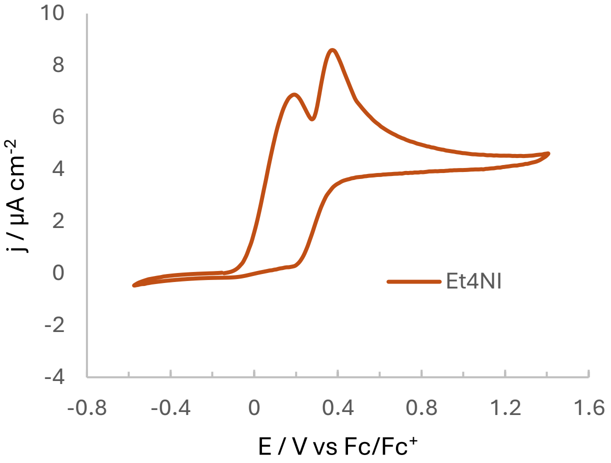


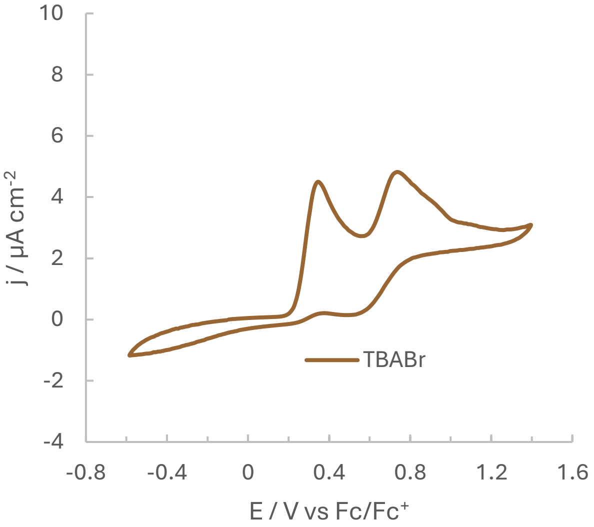


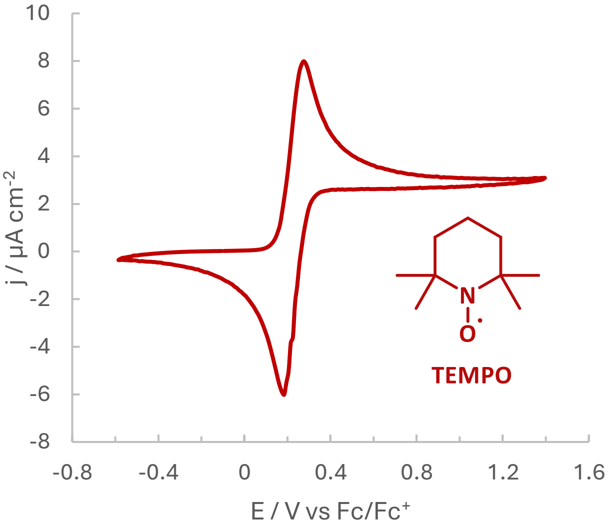

4a + cat I
j / μA cm-2
10
8
6
4
2
0
-2
-4
-0.8
-0.4
0
0.4
0.8
1.2
1.6
E / V vs Fc/Fc+


Ph
O
H
MeO2C
CO2Me
3a
j / μA cm-2
10
8
6
4
2
0
-2
-4
-0.8
-0.4
0
0.4
0.8
1.2
1.6
E / V vs Fc/Fc+

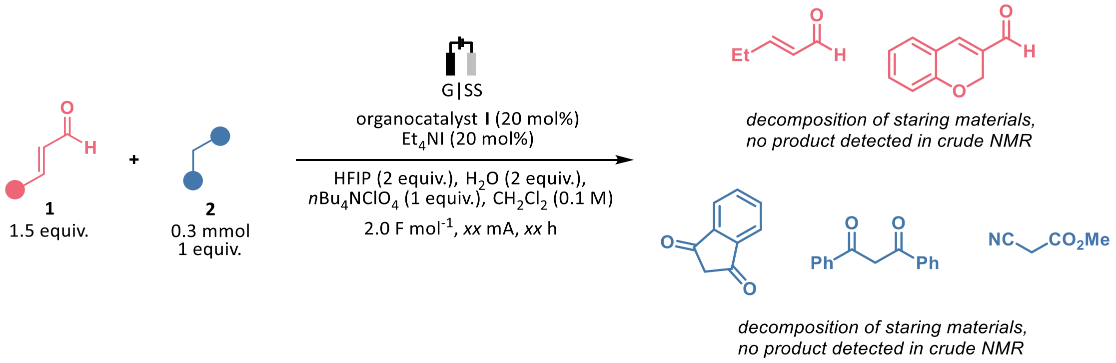

3a + cat I
j / μA cm-2
10
8
6
4
2
0
-2
-4
-0.8
-0.4
0
0.4
0.8
1.2
1.6
E / V vs Fc/Fc+


Et4NI
j / μA cm-2
10
8
6
4
2
0
-2
-4
-0.8
-0.4
0
0.4
0.8
1.2
1.6
E / V vs Fc/Fc+


TBABr
j / μA cm-2
10
8
6
4
2
0
-2
-4
-0.8
-0.4
0
0.4
0.8
1.2
1.6
E / V vs Fc/Fc+

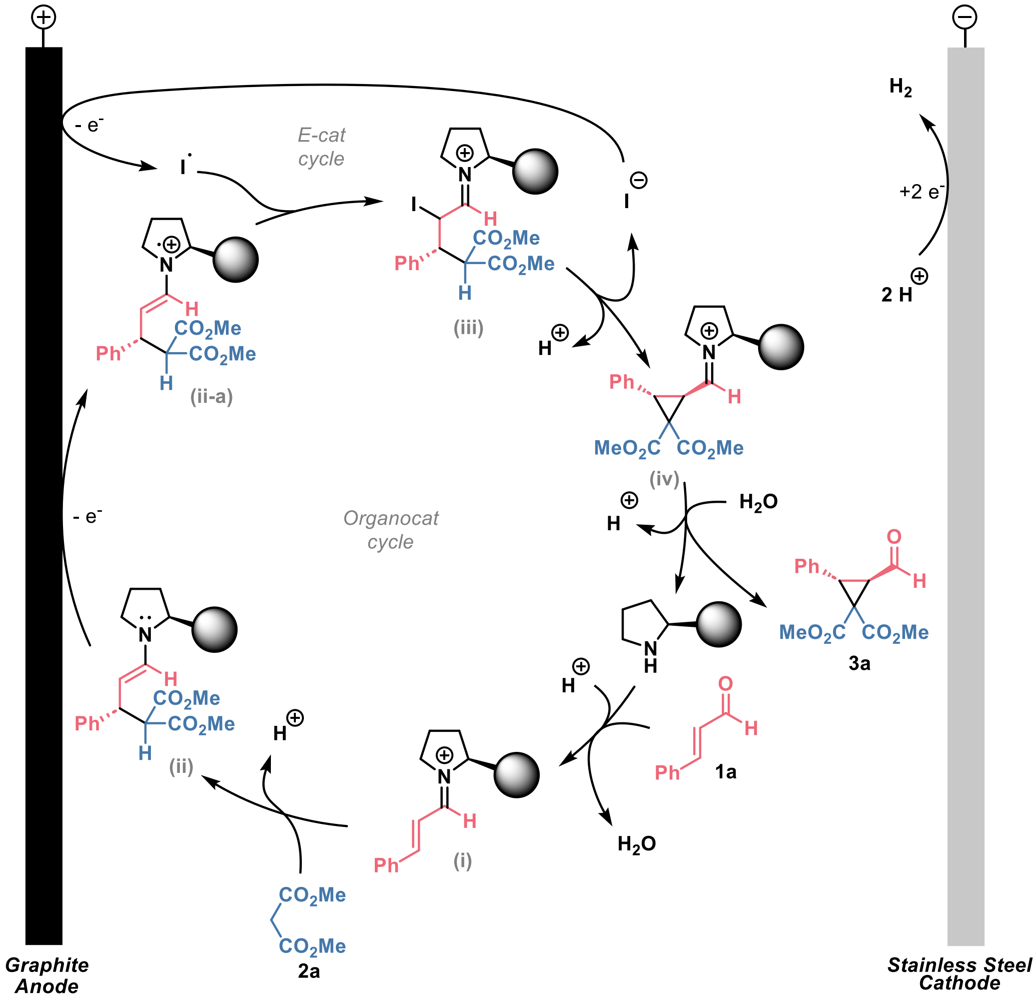

N
O
TEMPO
j / μA cm-2
10
8
6
4
2
0
-2
-4
-6
-8
-0.8
-0.4
0
0.4
0.8
1.2
1.6
E / V vs Fc/Fc+

6. Substrate scope limitations



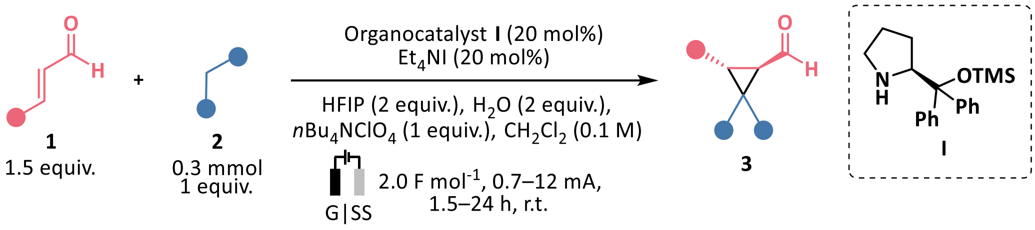
Scheme S1. Substrate scope limitations.

7. Alternative mechanism

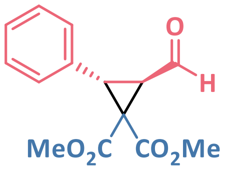


Scheme S2. Alternative mechanism of the reaction through anodic oxidation of enamine intermediate (ii) to radical cation which captures iodine radical formed in electrocatalytic cycle.

8. General procedure

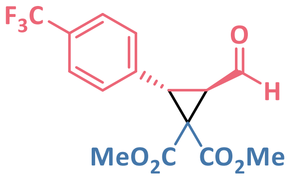


Organocatalyst **I** (0.06 mmol, 20 mol%, 19.5 mg), $TBAClO_4$ (0.3 mmol, 1 equiv., 102.6 mg), TEAI (0.06 mmol, 20 mol%, 15.4 mg) were dissolved in CH_2Cl_2 (0.1 M, 3 mL). To the resulted solution were sequentially added HFIP (0.6 mmol, 2 equiv., 63.0 µL), H_2O (0.6 mmol, 2 equiv., 10.8 µL), Michael donor (0.3 mmol, 1 equiv.) and α,β-unsaturated aldehyde (0.45 mmol, 1.5 equiv.). The reaction vessel was sealed with a Teflon cap equipped with stainless steel and graphite electrodes (gap between electrodes of 0.5 cm) and flushed with Ar for 5 min. Then the vial was connected to a power supply and the reaction mixture was electrolyzed under a constant current for a defined time while being stirred at 800 rpm. After the completion of the reaction, the cap was removed, and the electrodes were rinsed with CH_2Cl_2. The reaction mixture was combined with rinses and concentrated under the reduced pressure. The residue was then purified by flash chromatography to yield the corresponding cyclopropane product.



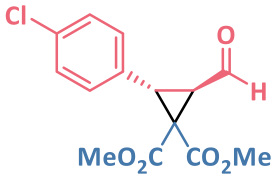
3a

Dimethyl (2*R*,3*S*)-2-formyl-3-phenylcyclopropane-1,1-dicarboxylate (3a): synthesized according to general procedure from (*E*)-cinnamaldehyde and dimethylmalonate at 3.2 mA for 5 hours. Purified by column chromatography on silica gel (eluent: 0 → 5% Et_2O in PE/CH_2Cl_2 = 1:1) to give **3a** (45 mg, 0.17 mmol) as a yellowish oil in 57% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.47 (d, *J* = 4.5 Hz, 1H), 7.30 – 7.16 (m, 5H), 3.83 – 3.78 (m, 4H), 3.44 (s, 3H), 3.37 (dd, *J* = 7.5, 4.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.2, 166.6, 165.2, 132.3, 128.6, 128.5, 128.2, 53.5, 53.0, 44.7, 38.4, 35.8. HPLC (Chiralpak AS-H, i-PrOH/hexane = 10/90, flow rate = 1 mL/min, λ = 210 nm): t_{major} = 10.8 min, t_{minor} = 12.4 min, *ee* = 96%. $[\alpha]_D^{22}$ = - 60.5 (c = 0.12 in $CHCl_3$). Spectral data are in agreement with previously reported.[1]



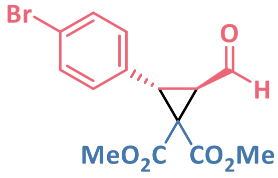
3b

Dimethyl (2*R*,3*S*)-2-formyl-3-(4-(trifluoromethyl)phenyl)cyclopropane-1,1-dicarboxylate (3b): synthesized according to general procedure from (*E*)-3-(4-(trifluoromethyl)phenyl)acrylaldehyde and dimethylmalonate at 4.4 mA for 4 hours. Purified by column chromatography on silica gel (eluent: 0 → 2% Et_2O in PE/CH_2Cl_2 = 1:1) to give **3b** (63 mg, 0.19 mmol) as a yellowish oil in 64% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (d, *J* = 4.1 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 2H), 7.39 – 7.34 (m, 2H), 3.85 – 3.81 (m, 4H), 3.50 (s, 3H), 3.43 (dd, *J* = 7.6, 4.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.5, 166.2, 165.0, 136.5, 130.49 (q, $^2J_{C,F}$ = 32.7 Hz), 129.1, 125.6 (q, $^3J_{C,F}$ = 3.8 Hz), 124.01 (q, $^1J_{C,F}$ = 272.1 Hz, CF_3), 53.6, 53.3, 44.8, 38.1, 35.2. HPLC (Chiralpak OJ-H, i-PrOH/hexane = 4/96, flow rate = 1 mL/min, λ = 210 nm): t_{major} = 28.6 min, t_{minor} = 41.2 min, *ee* = 96%. $[\alpha]_D^{22}$ = - 45.9 (c = 0.17 in $CHCl_3$). Spectral data are in agreement with previously reported.[1]



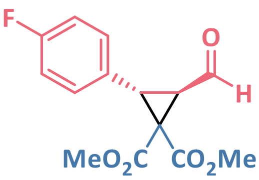
3c

Dimethyl (2*R*,3*S*)-2-(4-chlorophenyl)-3-formylcyclopropane-1,1-dicarboxylate (3c): synthesized according to general procedure from (*E*)-3-(4-(chlorophenyl)acrylaldehyde and dimethylmalonate at 4.4 mA for 4 hours. Purified by column chromatography on silica gel (eluent: 0 → 3% Et_2O in PE/CH_2Cl_2 = 1:1) to give **3c** (47 mg, 0.16 mmol) as a yellowish oil in 53% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (d, *J* = 4.2 Hz, 1H), 7.31 – 7.24 (m, 2H), 7.21 – 7.13 (m, 2H), 3.82 (s, 3H), 3.76 (d, *J* = 7.5 Hz, 1H), 3.51 (s, 3H), 3.36 (dd, *J* = 7.5, 4.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.8, 166.4, 165.1, 134.2, 130.8, 130.0, 128.9, 53.6, 53.2, 44.7, 38.3, 35.1. HPLC (Chiralpak OJ-H, i-PrOH/hexane = 10/90, flow rate = 1 mL/min, λ = 210 nm): t_{major} = 22.5 min, t_{minor} = 32.9 min, *ee* = 98%. $[\alpha]_D^{22}$ = - 32.9 (c = 0.26 in $CHCl_3$). Spectral data are in agreement with previously reported.[2]



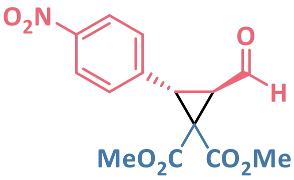
3d

Dimethyl (2*R*,3*S*)-2-(4-bromophenyl)-3-formylcyclopropane-1,1-dicarboxylate (3d): synthesized according to general procedure from (*E*)-3-(4-(bromophenyl)acrylaldehyde and dimethylmalonate at 5 mA for 3.5 hours. Purified by column chromatography on silica gel (eluent: 0 → 2% Et_2O in PE/CH_2Cl_2 = 1:1) to give **3d** (63 mg, 0.18 mmol) as a yellowish oil in 62% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (d, *J* = 4.2 Hz, 1H), 7.46 – 7.39 (m, 2H), 7.13 – 7.07 (m, 2H), 3.82 (s, 3H), 3.75 (d, *J* = 7.5 Hz, 1H), 3.51 (s, 3H), 3.36 (dd, *J* = 7.5, 4.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.7, 166.4, 165.0, 131.8, 131.4, 130.3, 122.4, 53.6, 53.2, 44.7, 38.2, 35.2. HPLC (Chiralpak OJ-H, i-PrOH/hexane = 10/90, flow rate = 1 mL/min, λ = 210 nm): t_{major} = 26.3 min, t_{minor} = 40.0 min, *ee* = 98%. $[\alpha]_D^{22}$ = - 52.9 (c = 0.16 in $CHCl_3$). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{14}H_{13}BrO_5Na^+$ 362.9839, found 362.9833.



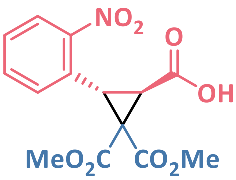
3e

Dimethyl (2*R*,3*S*)-2-(4-fluorophenyl)-3-formylcyclopropane-1,1-dicarboxylate (3e): synthesized according to general procedure from (*E*)-3-(4-(fluorophenyl)acrylaldehyde and dimethylmalonate at 4.4 mA for 4 hours. Purified by column chromatography on silica gel (eluent: 0 → 2% Et_2O in PE/CH_2Cl_2 = 1:1) to give **3e** (47 mg, 0.17 mmol) as a yellowish oil in 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (d, *J* = 4.3 Hz, 1H), 7.24 – 7.17 (m, 2H), 7.03 – 6.95 (m, 2H), 3.82 (s, 3H), 3.80 – 3.76 (m, 1H), 3.50 (s, 3H), 3.36 (dd, *J* = 7.5, 4.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.9, 166.5, 165.1, 162.6 (d, *J* = 247.5 Hz), 130.3 (d, *J* = 8.4 Hz), 128.1 (d, *J* = 3.1 Hz), 115.7 (d, *J* = 21.8 Hz), 53.5, 53.1, 44.7, 38.5, 35.0. HPLC (Chiralpak OJ-H, i-PrOH/hexane = 3/97, flow rate = 1 mL/min, λ = 210 nm): t_{major} = 38.8 min, t_{minor} = 54.3 min, *ee* = 97%. $[\alpha]_D^{22}$ = - 57.4 (c = 0.16 in $CHCl_3$). Spectral data are in agreement with previously reported.[2]



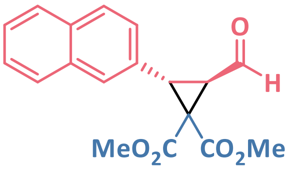
3f

Dimethyl (2*R*,3*S*)-2-formyl-3-(4-nitrophenyl)cyclopropane-1,1-dicarboxylate (3f): synthesized according to general procedure from (*E*)-3-(4-nitrophenyl)acrylaldehyde and dimethylmalonate at 3.2 mA for 5 hours. Purified by column chromatography on silica gel (eluent: 0 → 7% Et_2O in PE/CH_2Cl_2 = 1:1) to give **3f** (55 mg, 0.18 mmol) as a yellowish oil in 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (d, *J* = 3.8 Hz, 1H), 8.22 – 8.10 (m, 2H), 7.47 – 7.39 (m, 2H), 3.85 (s, 4H), 3.53 (s, 3H), 3.47 (dd, *J* = 7.6, 3.8 Hz, 1H); ^{13}C NMR (125 MHz, CDCl3): δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.1, 165.9, 164.9, 147.8, 139.8, 129.7, 123.8, 53.8, 53.5, 45.0, 38.2, 35.1; HPLC (*ee* was determined after converted to the corresponding enone with $Ph_3P=CHCO_2Et$,[2] Chiralpak AS-H, *i*PrOH/hexane = 10/90, flow rate = 1 mL/min, λ = 254 nm): t_{major} = 37.2 min, t_{minor} = 27.9 min, *ee* = 94%. $[\alpha]_D^{22}$ = - 46.7 (c = 0.20 in $CHCl_3$). Spectral data are in agreement with previously reported.[2]



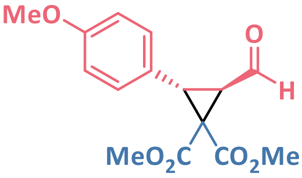
3g

Dimethyl (2*R*,3*S*)-2-formyl-3-(2-nitrophenyl)cyclopropane-1,1-dicarboxylate (3g): synthesized according to general procedure from (*E*)-3-(2-nitrophenyl)acrylaldehyde and dimethylmalonate at 3.2 mA for 5 hours. Purified by column chromatography on silica gel (eluent: 0 → 7% Et_2O in PE/CH_2Cl_2 = 1:1) to give **3g** (62 mg, 0.2 mmol) as a yellowish oil in 67% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (d, *J* = 4.5 Hz, 1H), 8.05 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.62 – 7.56 (m, 1H), 7.53 – 7.47 (m, 1H), 7.38 – 7.33 (m, 1H), 4.28 (d, *J* = 7.8 Hz, 1H), 3.85 (s, 3H), 3.49 (s, 3H), 3.22 (dd, *J* = 7.8, 4.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.6, 166.1, 165.4, 149.9, 133.6, 131.4, 129.6, 128.5, 125.2, 53.7, 53.4, 43.4, 39.2, 34.3. HPLC (Chiralpak AS-H, i-PrOH/hexane = 25/75, flow rate = 0.5 mL/min, λ = 210 nm): t_{major} = 14.0 min, t_{minor} = 31.6 min, *ee* = 97%. $[\alpha]_D^{22}$ = + 38.1 (c = 0.14 in $CHCl_3$). Spectral data are in agreement with previously reported.[2]

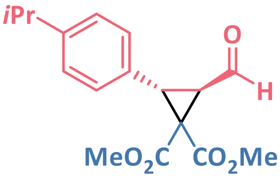


3h

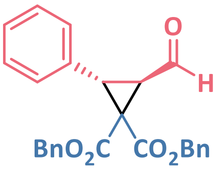
Dimethyl (2*R*,3*S*)-2-formyl-3-(naphthalen-2-yl)cyclopropane-1,1-dicarboxylate (3h): synthesized according to general procedure from (*E*)-3-(naphthalen-2-yl)acrylaldehyde and dimethylmalonate at 3.2 mA for 5 hours. Purified by column chromatography on silica gel (eluent: 0 → 5% Et_2O in PE/CH_2Cl_2 = 1:1) to give **3h** (39 mg, 0.12 mmol) as a yellowish oil in 42% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (d, *J* = 4.4 Hz, 1H), 7.77 – 7.68 (m, 3H), 7.62 (s, 1H), 7.44 – 7.38 (m, 2H), 7.28 (dd, *J* = 8.5, 1.9 Hz, 1H), 3.91 (dd, *J* = 7.5, 1.0 Hz, 1H), 3.79 (s, 3H), 3.46 (dd, *J* = 7.5, 4.5 Hz, 1H), 3.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.2, 166.7, 165.2, 133.2, 133.0, 129.7, 128.4, 128.0, 127.8, 127.7, 126.6, 126.5, 126.2, 53.6, 53.1, 44.9, 38.6, 36.0. HPLC (Chiralpak OJ-H, i-PrOH/hexane = 5/95, flow rate = 1 mL/min, λ = 230 nm): t_{major} = 28.5 min, t_{minor} = 61.0 min, *ee* = 97%. $[\alpha]_D^{22}$ = - 66.1 (c = 0.16 in $CHCl_3$). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{18}H_{16}O_5Na^+$ 335.0890, found 335.0889.


3i

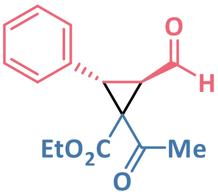
Dimethyl (2*R*,3*S*)-2-formyl-3-(4-methoxyphenyl)cyclopropane-1,1-dicarboxylate (3i): synthesized according to general procedure from (*E*)-3-(4-methoxyphenyl)acrylaldehyde and dimethylmalonate at 3.2 mA for 5 hours. Purified by column chromatography on silica gel (eluent: 2 → 5% Et_2O in PE/CH_2Cl_2 = 1:1) to give **3i** (35 mg, 0.12 mmol) as a yellowish oil in 40% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.47 (d, *J* = 4.6 Hz, 1H), 7.17 – 7.12 (m, 2H), 6.85 – 6.80 (m, 2H), 3.82 (s, 3H), 3.79 – 3.76 (m, 4H), 3.49 (s, 3H), 3.34 (dd, *J* = 7.5, 4.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3, 166.8, 165.3, 159.5, 129.7, 124.1, 114.0, 55.4, 53.5, 53.1, 44.7, 38.7, 35.4. HPLC (Chiralpak OJ-H, i-PrOH/hexane = 10/90, flow rate = 1 mL/min, λ = 210 nm): t_{major} = 49.3 min, t_{minor} = 52.9 min, *ee* = 98%. $[\alpha]_D^{22}$ = -49.7 (c = 0.4 in $CHCl_3$). Spectral data are in agreement with previously reported.[1]


3j

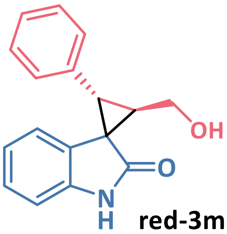
Dimethyl (2*R*,3*S*)-2-formyl-3-(4-isopropylphenyl)cyclopropane-1,1-dicarboxylate (3j): synthesized according to general procedure from (*E*)-3-(4-isopropylphenyl)acrylaldehyde and dimethylmalonate at 1 mA for 16 hours. Purified by column chromatography on silica gel (eluent: 0 → 2% Et_2O in PE/CH_2Cl_2 = 1:1) to give **3j** (44 mg, 0.14 mmol) as a yellowish oil in 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.48 (d, *J* = 4.6 Hz, 1H), 7.19 – 7.06 (m, 4H), 3.85 – 3.75 (m, 4H), 3.47 (s, 3H), 3.36 (dd, *J* = 7.5, 4.6 Hz, 1H), 2.87 (hept, *J* = 7.0 Hz, 1H), 1.21 (d, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.3, 166.8, 165.3, 149.0, 129.5, 128.5, 126.7, 53.5, 53.0, 44.7, 38.6, 35.7, 33.9, 24.0. HPLC (Chiralpak OD-H, i-PrOH/hexane = 10/90, flow rate = 1 mL/min, λ = 210 nm): t_{major} = 7.3 min, t_{minor} = 13.5 min, *ee* = 98%; $[\alpha]_D^{20}$ = - 47.6 (c = 0.18 in $CHCl_3$). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{17}H_{20}O_5Na^+$ 327.1203, found 327.1202.


3k

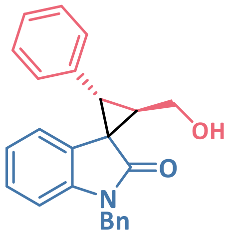
Dibenzyl (2*R*,3*S*)-2-formyl-3-phenylcyclopropane-1,1-dicarboxylate (3k): synthesized according to general procedure from (*E*)-cinnamaldehyde and dibenzymalonate at 3.2 mA for 5 hours. Purified by column chromatography on silica gel (eluent: 0 → 30% Et_2O in PE) to give **3k** (66 mg, 0.16 mmol) as a yellowish oil in 53% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (d, *J* = 4.6 Hz, 1H), 7.37 – 7.17 (m, 15H), 6.99 – 6.92 (m, 2H), 5.27 (d, *J* = 12.2 Hz, 1H), 5.18 (d, *J* = 12.2 Hz, 1H), 4.87 (d, *J* = 12.2 Hz, 1H), 4.80 (d, *J* = 12.2 Hz, 1H), 3.86 (d, *J* = 7.6 Hz, 1H), 3.40 (dd, *J* = 7.6, 4.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.0, 166.0, 164.6, 135.0, 134.8, 132.1, 128.8, 128.7, 128.7, 128.7, 128.6, 128.5, 128.4, 128.2, 68.4, 68.0, 44.9, 38.5, 35.9. HPLC (Chiralpak AD-H, i-PrOH/hexane = 10/90, flow rate = 1 mL/min, λ = 210 nm): t_{major} = 27.2 min, t_{minor} = 22.3 min, *ee* = 96%; $[\alpha]_D^{22}$ = - 56.1 (c = 0.34 in $CHCl_3$). Spectral data are in agreement with previously reported.[3]


3l

Ethyl (2*R*,3*S*)-1-acetyl-2-formyl-3-phenylcyclopropane-1-carboxylate (3l): synthesized as a mixture of diastereomers (2:1) according to general procedure from (*E*)-cinnamaldehyde and ethyl 3-oxobutanoate at 12 mA for 1.5 hours. Purified by column chromatography on silica gel (eluent: 0 → 20% Et_2O in PE) to give **3l** (31 mg, 0.12 mmol) as white amorphous solid in 30% yield (major diastereomer). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (d, *J* = 4.7 Hz, 1H), 7.32 – 7.23 (m, 3H), 7.19 – 7.13 (m, 2H), 4.41 – 4.23 (m, 2H), 3.89 (d, *J* = 7.6 Hz, 1H), 3.49 (dd, *J* = 7.6, 4.7 Hz, 1H), 1.98 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.5, 196.1, 167.3, 131.5, 128.8, 128.4, 128.3, 62.8, 51.8, 37.4, 36.9, 29.4, 14.2. HPLC (Chiralpak OD-H, i-PrOH/hexane = 10/90, flow rate = 1 mL/min, λ = 210 nm): t_{major} = 8.1 min, t_{minor} = 10.5 min, *ee* = 94%; $[\alpha]_D^{22}$ = - 91.3 (c = 0.11 in $CHCl_3$). Spectral data are in agreement with previously reported.[4]


red-3m

(2*R*,3*S*)-2'-Oxo-3-phenylspiro[cyclopropane-1,3'-indoline]-2-carbaldehyde (red-3m): synthesized according to general procedure from (*E*)-cinnamaldehyde and indolin-2-one at 4.4 mA for 4 hours at -10°C. The resulting mixture was diluted with MeOH (5 mL) and quenched with $NaBH_4$ (1.5 mmol, 5 equiv., 56.8 mg). After stirring for 5 min, H_2O (5 mL) was added. The mixture was extracted with CH_2Cl_2 (4 x 15 mL), combined organic fractions were washed with brine (15 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by reversed phase flash column chromatography (eluent: 10 → 60% MeCN in H_2O) to give **red-3m** (33 mg, 0.12 mmol) as a yellowish oil in 41% yield as an inseparable mixture of diastereomers (3.4:1). ^{1}H NMR *major diastereomer* (400 MHz, CD_3OD) δ 7.31 – 7.15 (m, 7H), 7.08 – 7.00 (m, 1H), 7.00 – 6.93 (m, 1H), 4.14 (dd, *J* = 12.0, 6.4 Hz, 1H), 3.99 (dd, *J* = 12.0, 7.9 Hz, 1H), 3.27 (d, *J* = 8.5 Hz, 1H), 2.79 (td, *J* = 8.1, 6.2 Hz, 1H). ^{1}H NMR *minor diastereomer characteristic signals* (400 MHz, MeOD) δ 6.61 (td, *J* = 7.6, 1.0 Hz, 1H), 5.99 (dd, *J* = 7.6, 1.2 Hz, 1H), 4.22 (dd, *J* = 11.7, 6.2 Hz, 1H), 2.68 (td, *J* = 7.8, 6.2 Hz, 1H). ^{13}C NMR *major diastereomer* (101 MHz, MeOD) δ 177.5, 143.1, 136.2, 130.9, 130.3, 129.9, 129.4, 128.9, 122.7, 122.1, 110.9, 60.3, 42.8, 39.5, 39.4. ^{13}C NMR *minor diastereomer* (101 MHz, MeOD) δ 179.1, 142.6, 136.2, 128.5, 128.0, 127.8, 127.6, 122.2, 121.8, 110.9, 110.5, 59.1, 41.7, 40.1, 38.2. HPLC (Chiralpak OJ-H, *i*-PrOH/hexane = 10/90, flow rate = 1 mL/min, λ = 230 nm): *major diastereomer* t = 36.3 min, *ee* >99%; minor diastereomer t = 10.1 min, *ee* >99%. Spectral data are in agreement with previously reported.[5]



red-3n

(2*R*,3*S*)-1'-Benzyl-2'-oxo-3-phenylspiro[cyclopropane-1,3'-indoline]-2-carbaldehyde (red-3n): synthesized according to general procedure from (*E*)-cinnamaldehyde and 1-benzylindolin-2-one at 8.8 mA for 2 hours. The resulting mixture was diluted with MeOH (5 mL) and quenched with $NaBH_4$ (1.5 mmol, 5 equiv., 56.8 mg). After stirring for 5 min, H_2O (5 mL) was added. The mixture was extracted with CH_2Cl_2 (4 x 15 mL), combined organic fractions were washed with brine (15 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: 0 → 30% Et_2O in PE/CH_2Cl_2 = 1:1) to give **red-3n** (59 mg, 0.17 mmol) as a yellowish oil in 56% yield as an inseparable mixture of diastereomers (4.8:1). ^{1}H NMR *major diastereomer* (400 MHz, $CDCl_3$) δ 7.38 – 7.13 (m, 12H), 7.08 – 7.01 (m, 1H), 6.85 – 6.79 (m, 1H), 4.91 (d, *J* = 15.7 Hz, 1H), 4.83 (d, *J* = 15.6 Hz, 1H), 4.31 – 4.21 (m, 1H), 4.14 – 4.04 (m, 1H), 3.26 (d, *J* = 8.4 Hz, 1H), 3.05 (td, *J* = 8.4, 6.1 Hz, 1H). ^{1}H NMR *minor diastereomer characteristic signals* (400 MHz, $CDCl_3$) δ 6.67 (td, *J* = 7.6, 1.0 Hz, 1H), 5.99 – 5.94 (m, 1H), 5.13 – 4.97 (m, 2H), 3.83 (d, *J* = 8.2 Hz, 1H), 2.73 – 2.66 (m, 1H). ^{13}C NMR *major diastereomer* (101 MHz, $CDCl_3$) δ 173.3, 143.2, 136.3, 134.2, 129.4, 128.8, 128.1, 127.8, 127.6, 127.5, 127.5, 127.1, 122.1, 120.5, 109.3, 60.7, 44.1, 42.2, 38.5, 37.6. ^{13}C NMR *minor diastereomer* (101 MHz, $CDCl_3$) δ 176.8, 142.2, 136.1, 134.7, 130.0, 129.0, 128.5, 127.8, 127.7, 127.3, 126.7, 122.0, 120.8, 109.0, 59.2, 44.3, 39.6, 39.6, 37.5. HPLC *major diastereomer* (Chiralpak OJ-H, *i*-PrOH/hexane = 20/80, flow rate = 1 mL/min, λ = 210 nm): t_{major} = 15.5 min, t_{minor} = 29.4 min, *ee* >99%. HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{24}H_{21}NO_2Na^+$ 378.1465, found 378.1462.

9. References

1 H. Xie, L. Zu, H. Li, J. Wang and W. Wang, *J. Am. Chem. Soc.*, 2007, **129**, 10886–10894.

2 P. Llanes, C. Rodríguez-Escrich, S. Sayalero and M. A. Pericàs, *Org. Lett.*, 2016, **18**, 6292–6295.

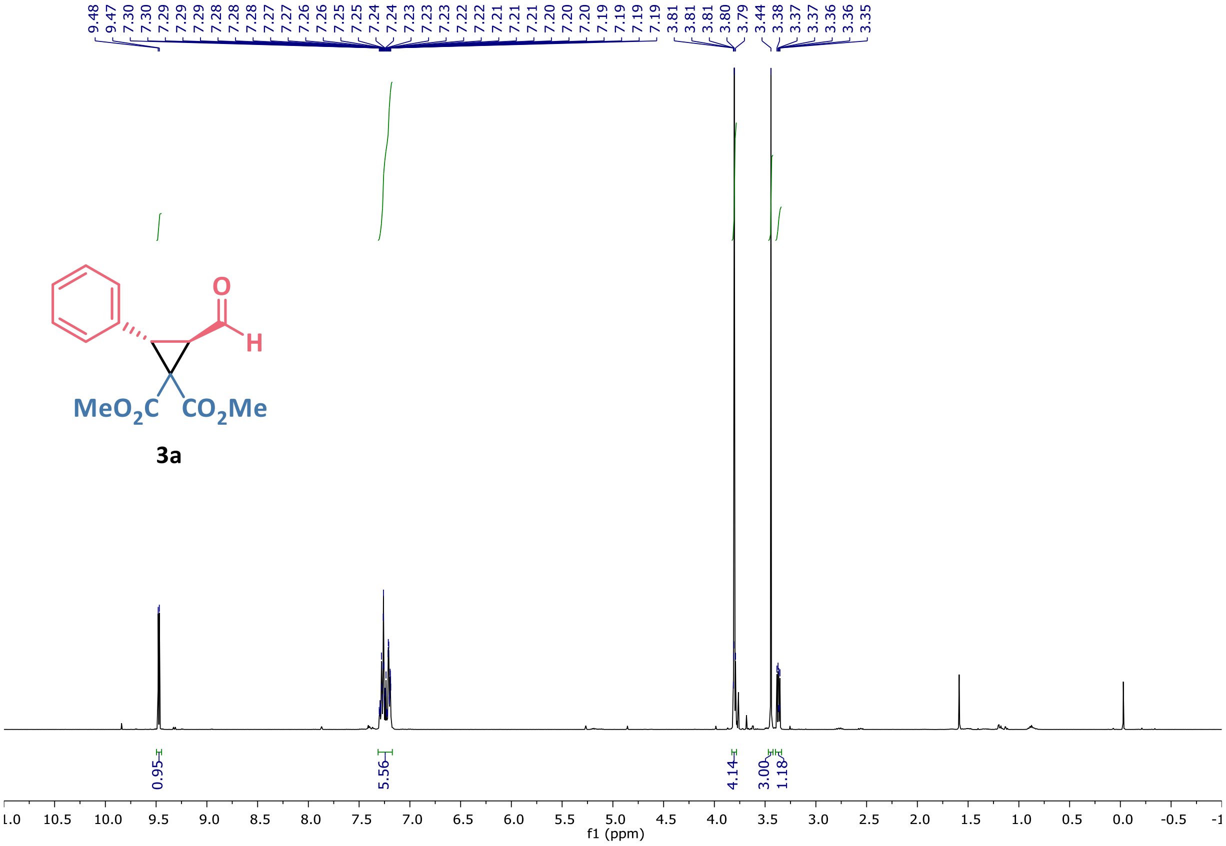
3 I. Ibrahem, G. Zhao, R. Rios, J. Vesely, H. Sundén, P. Dziedzic and A. Córdova, *Chemistry A European J*, 2008, **14**, 7867–7879.

4 X. Companyó, A. Alba, F. Cárdenas, A. Moyano and R. Rios, *Eur J Org Chem*, 2009, **2009**, 3075–3080.

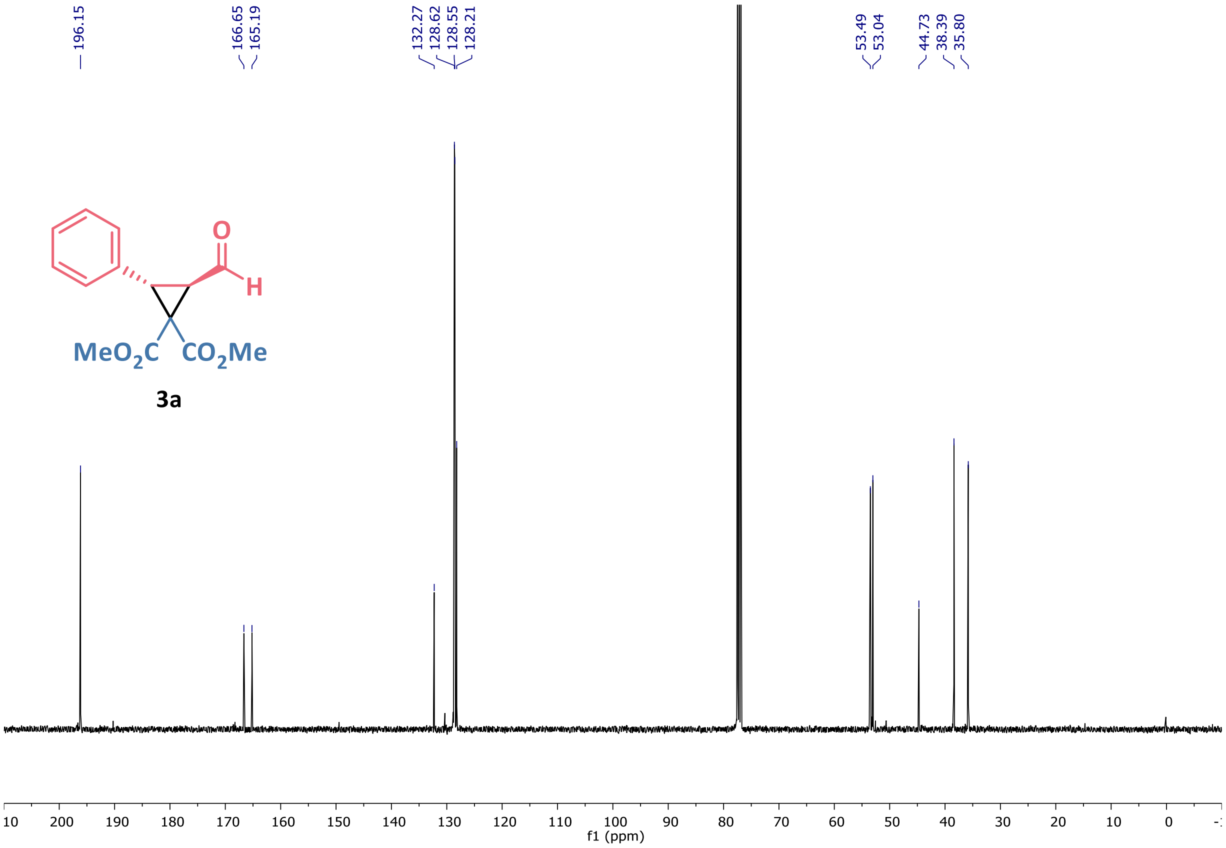
5 Z. Li, H. Zhang, L. Zhao, Y. Ma, Q. Wu, H. Ren, Z. Lin, J. Zheng and X. Yu, *Chem. Commun.*, 2024, **60**, 3579–3582.

10. NMR spectra

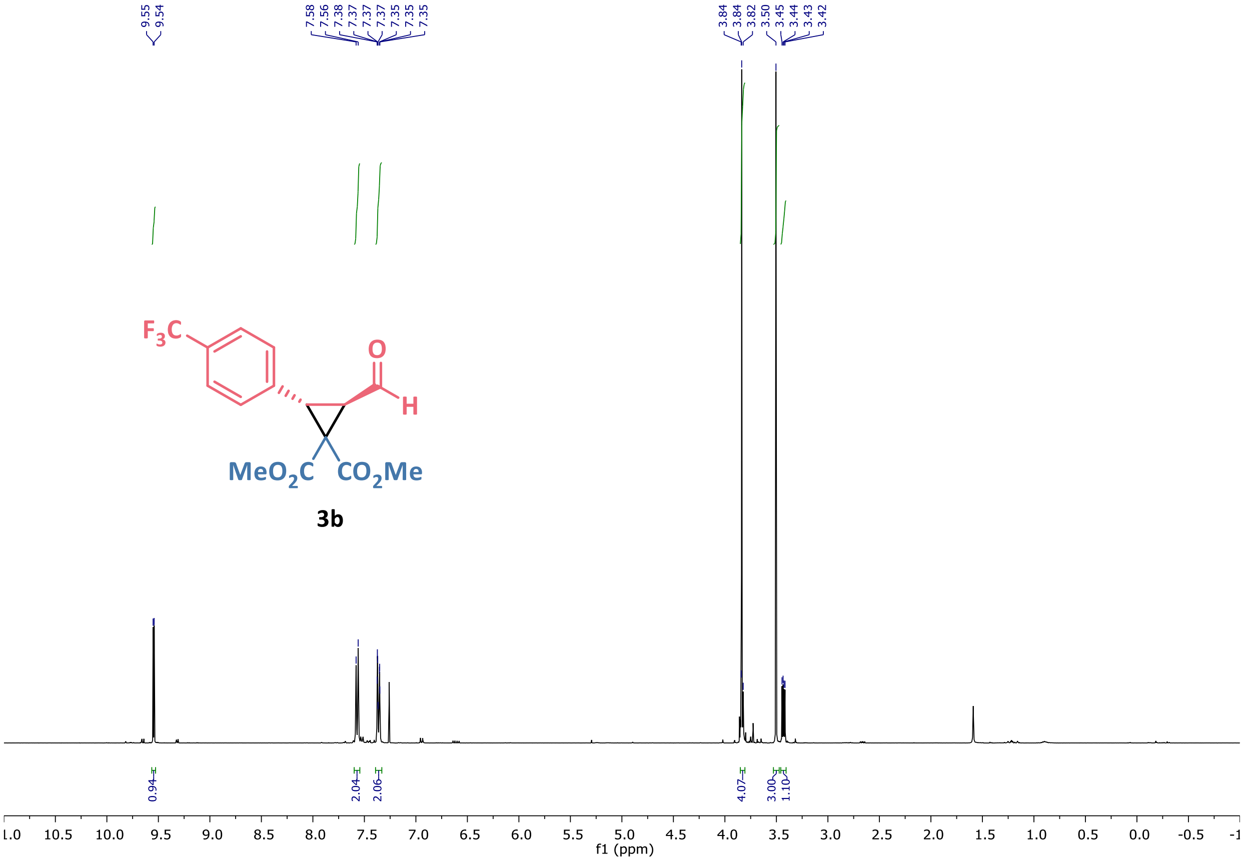
^{1}H NMR of **3a** (400 MHz, CDCl$_3$)



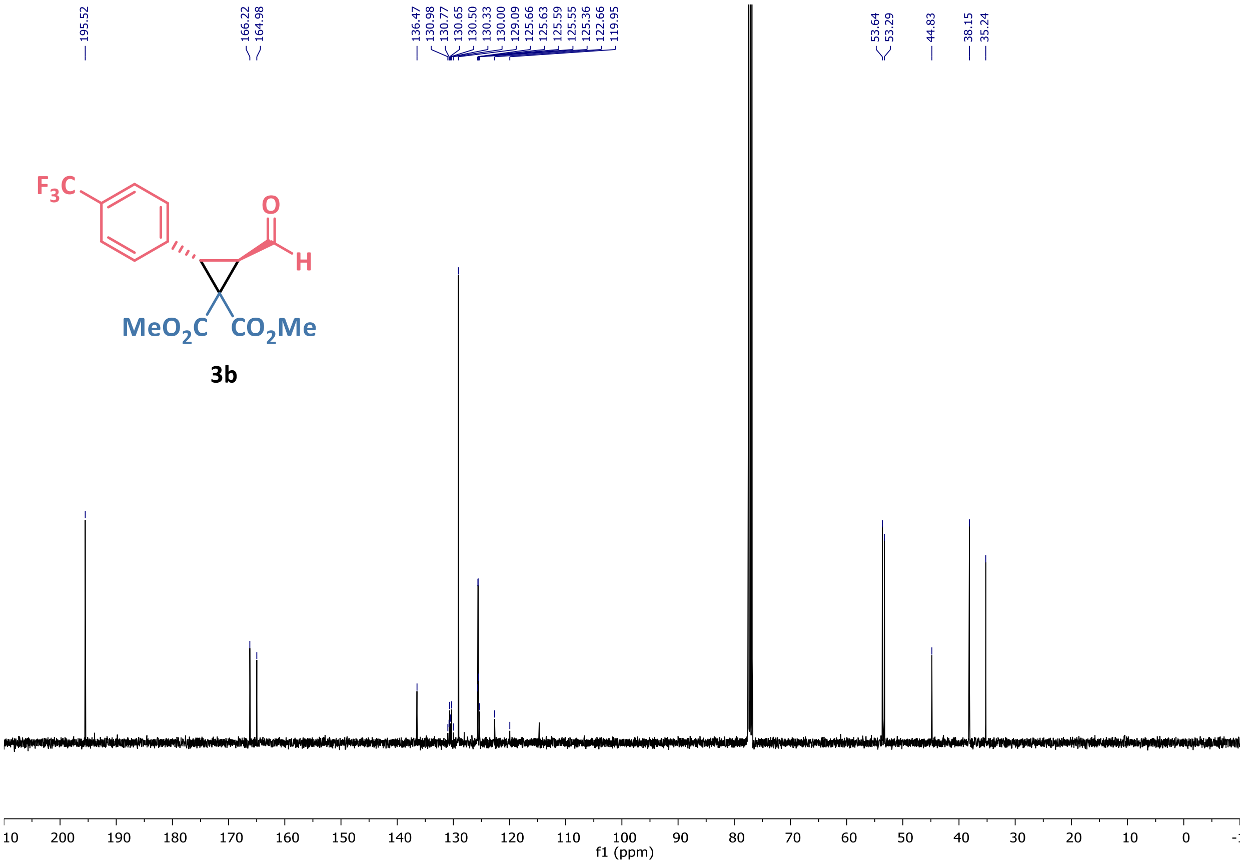
^{13}C NMR of **3a** (101 MHz, CDCl$_3$)



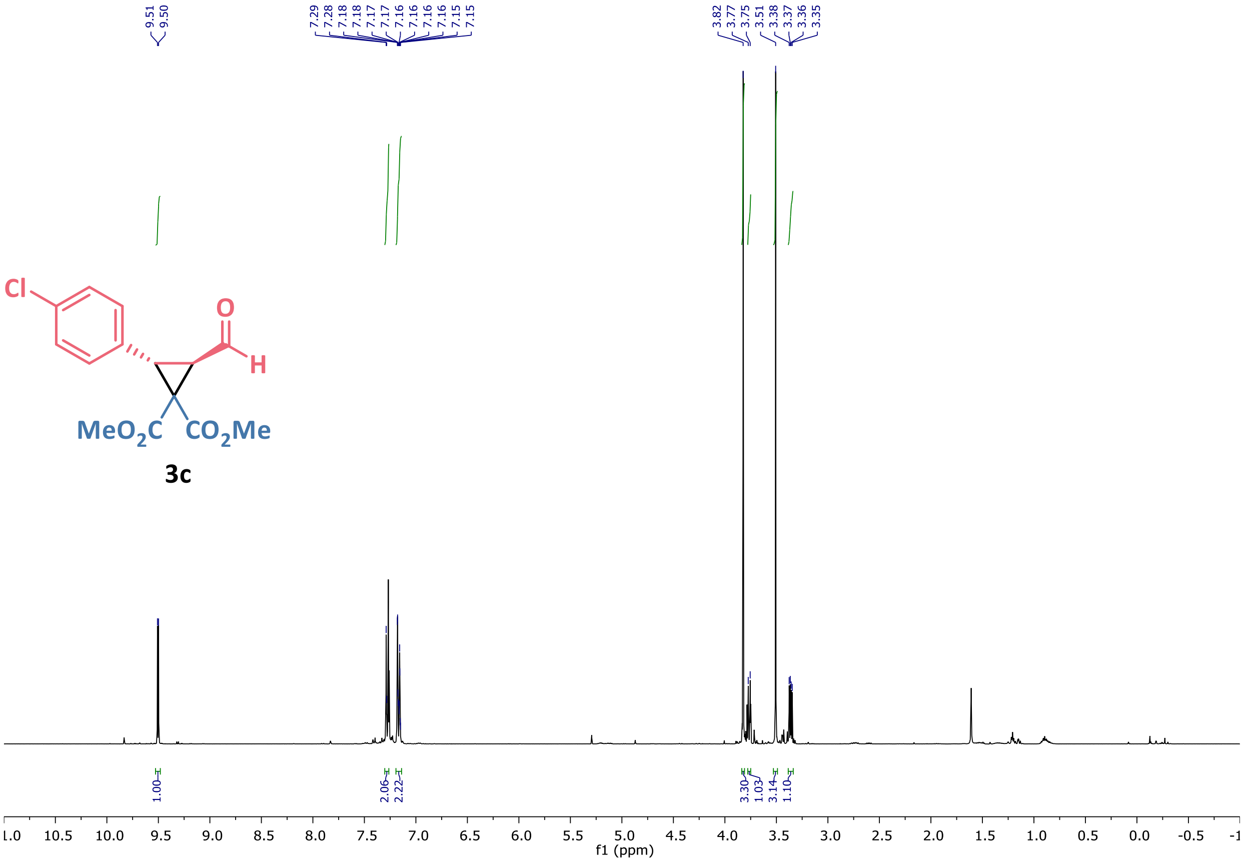
^{1}H NMR of **3b** (400 MHz, $CDCl_3$)



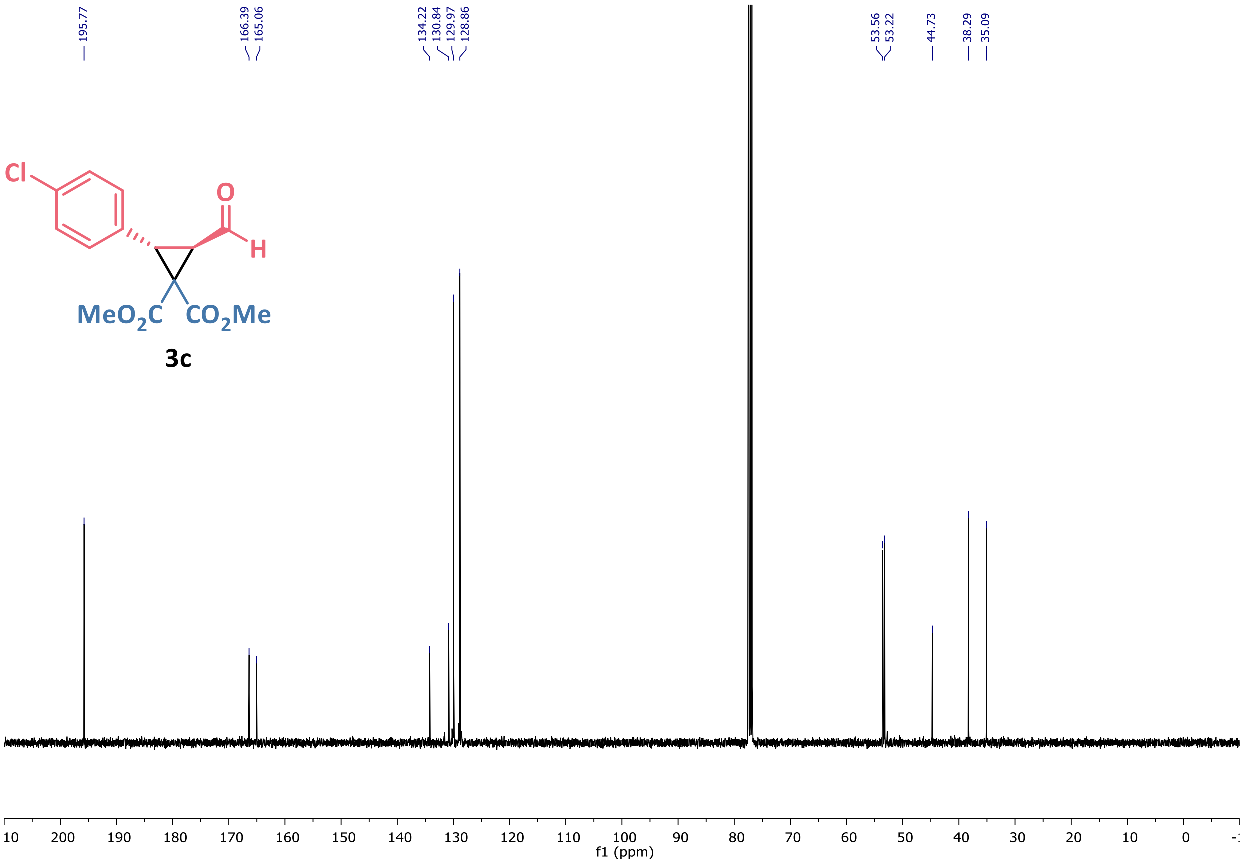
^{13}C NMR of **3b** (101 MHz, $CDCl_3$)



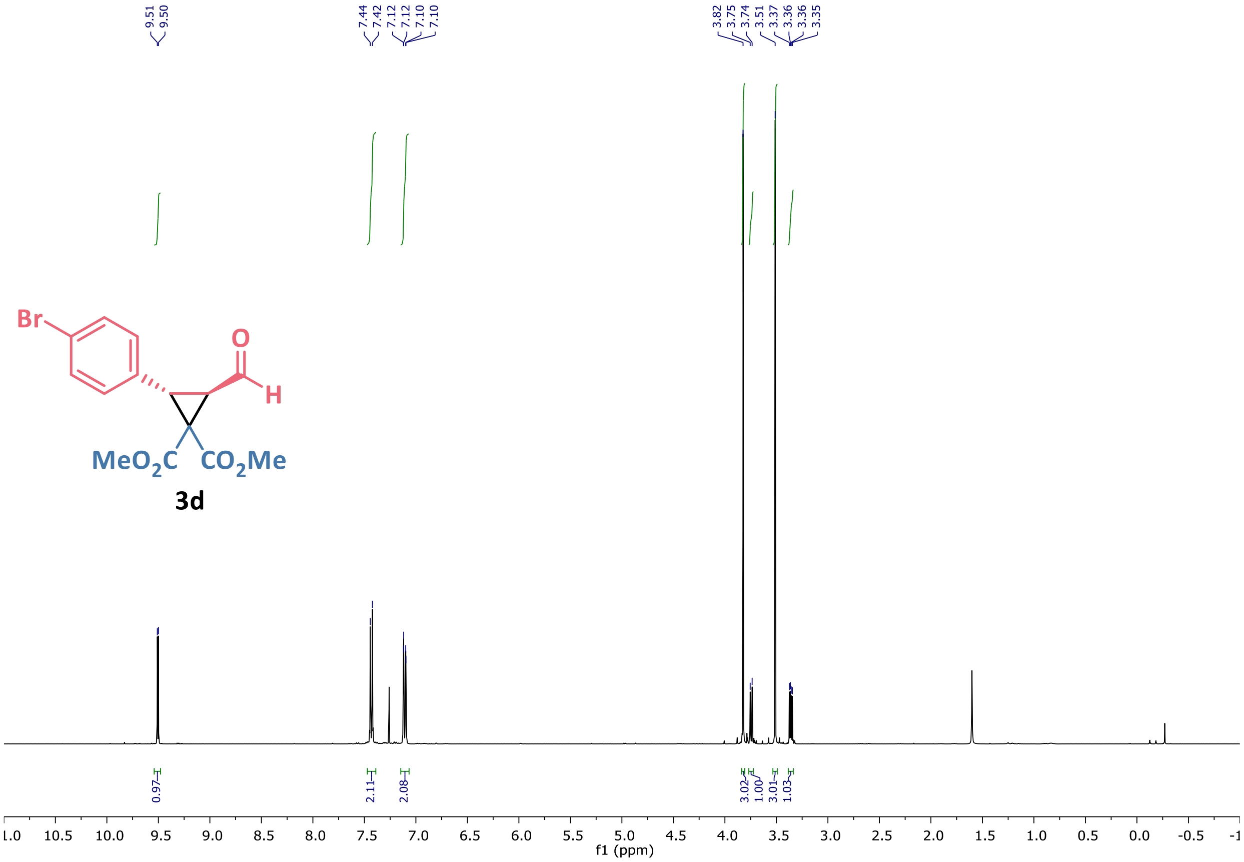
^{1}H NMR of **3c** (400 MHz, CDCl$_3$)



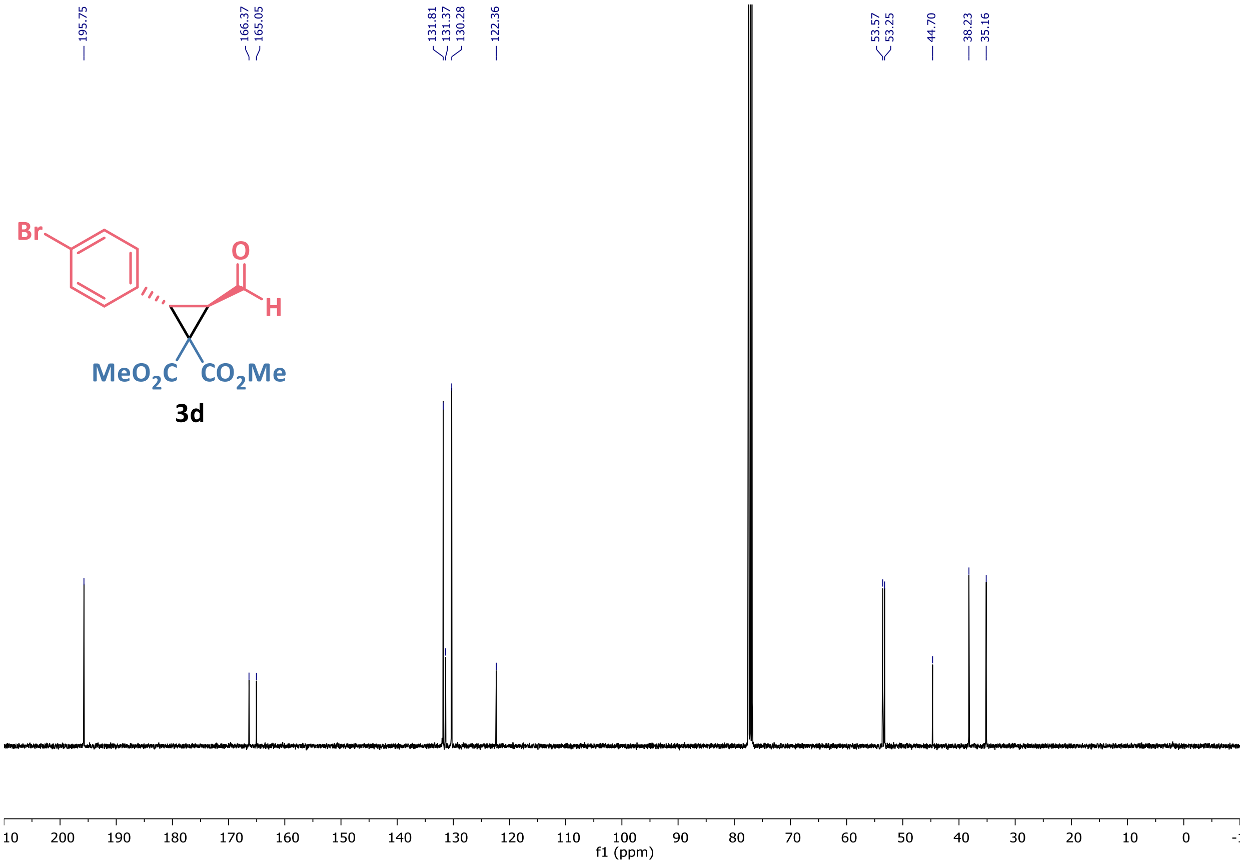
^{13}C NMR of **3c** (101 MHz, CDCl$_3$)



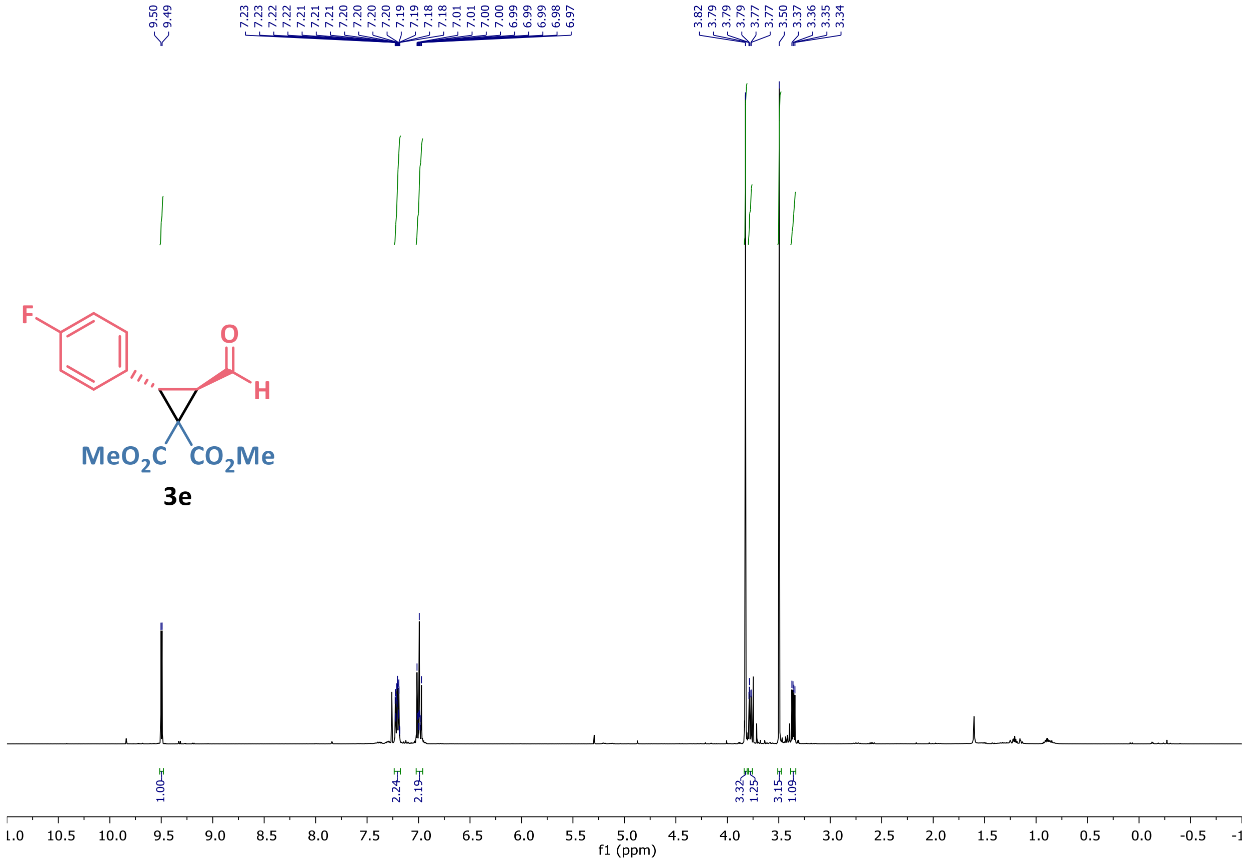
^{1}H NMR of **3d** (400 MHz, CDCl$_3$)



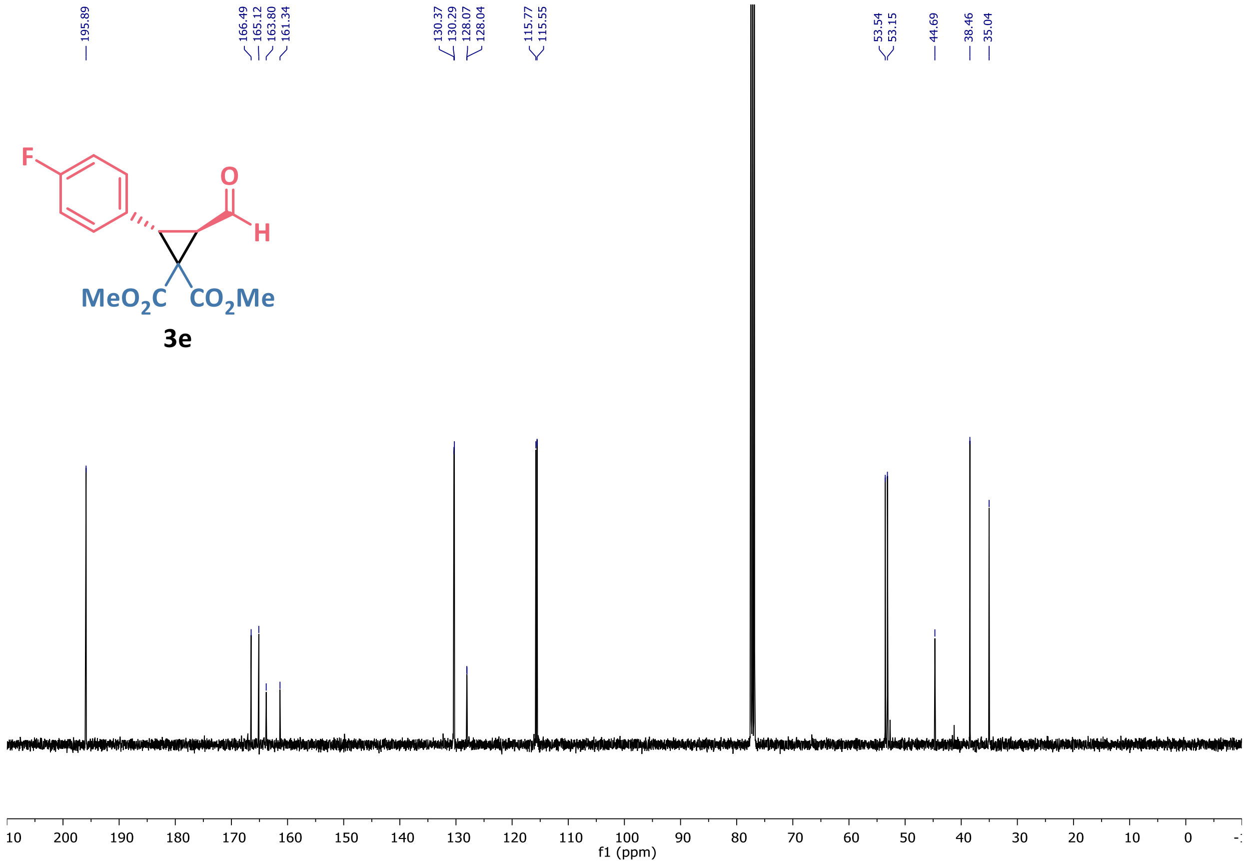
^{13}C NMR of **3d** (101 MHz, CDCl$_3$)



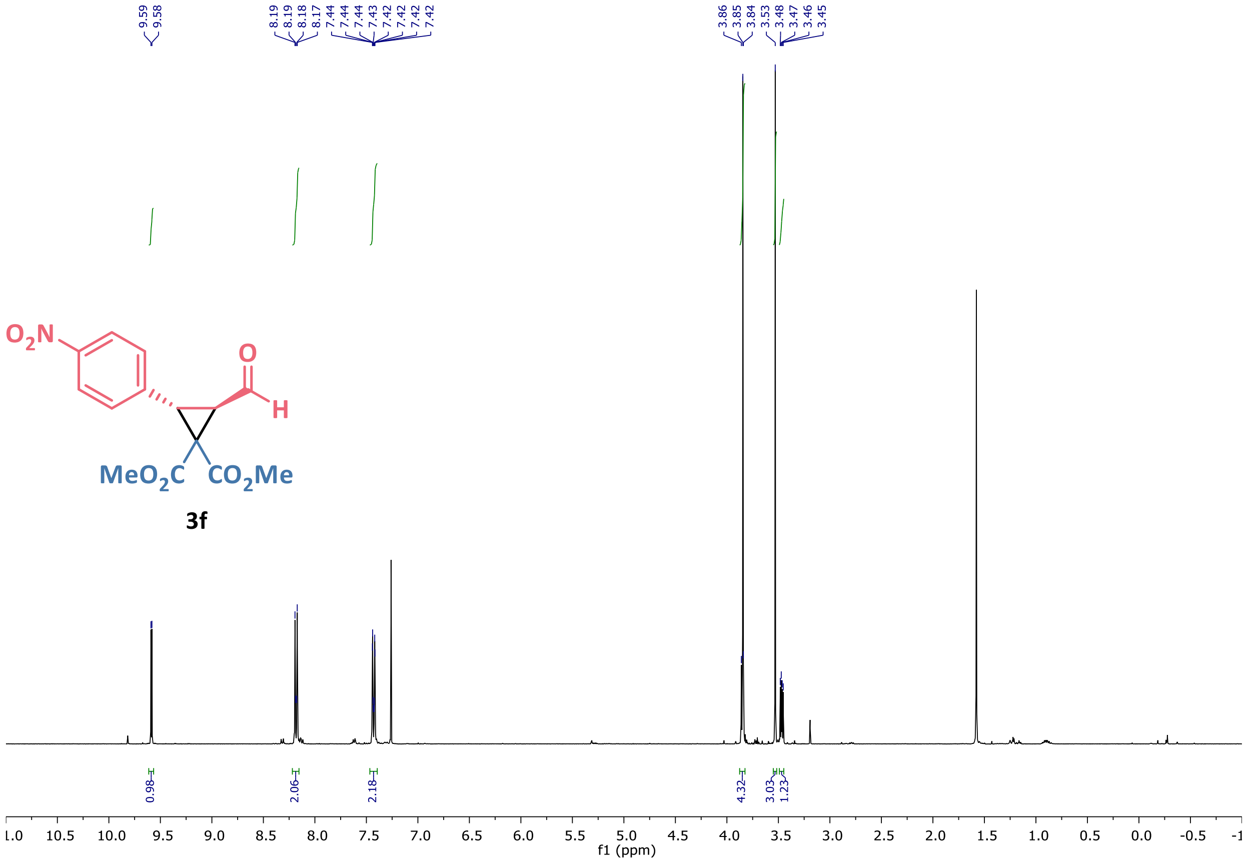
^{1}H NMR of **3e** (400 MHz, $CDCl_3$)



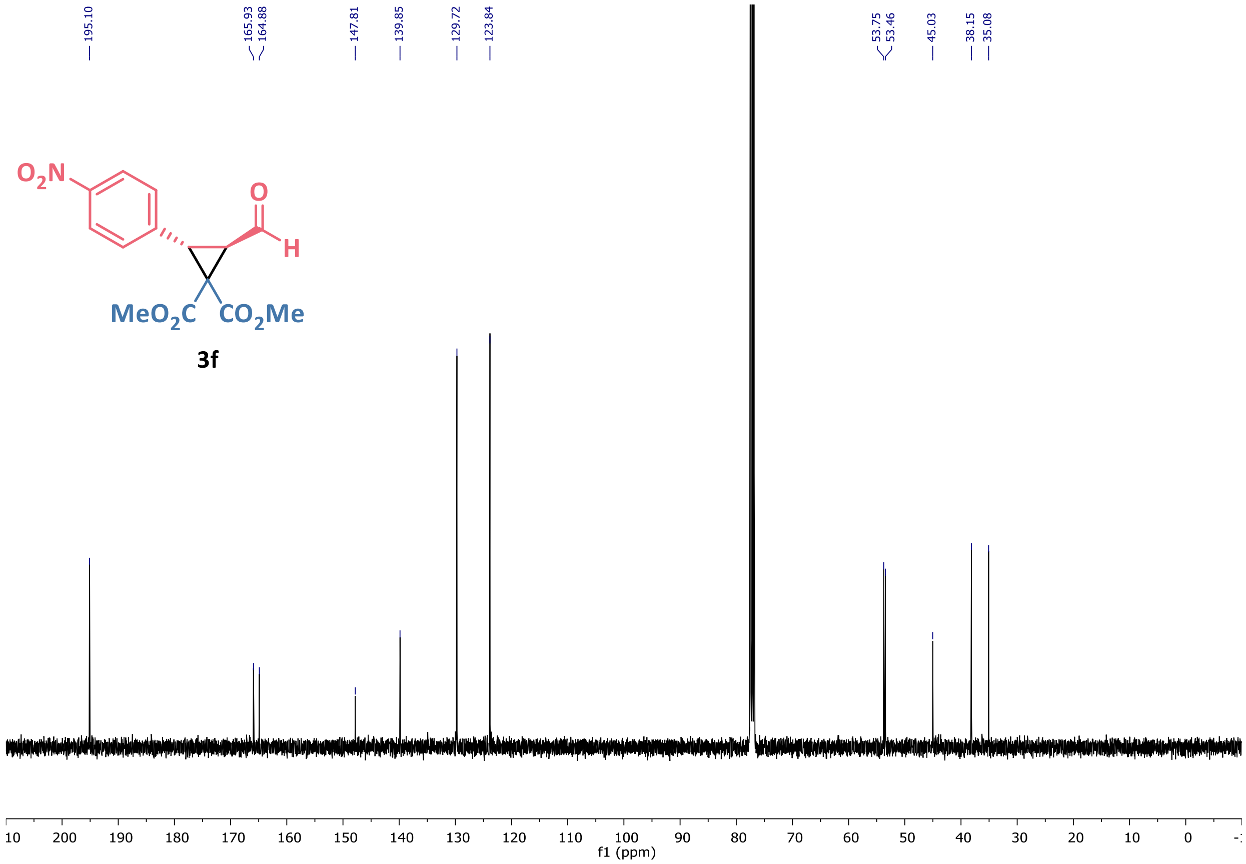
^{13}C NMR of **3e** (101 MHz, $CDCl_3$)



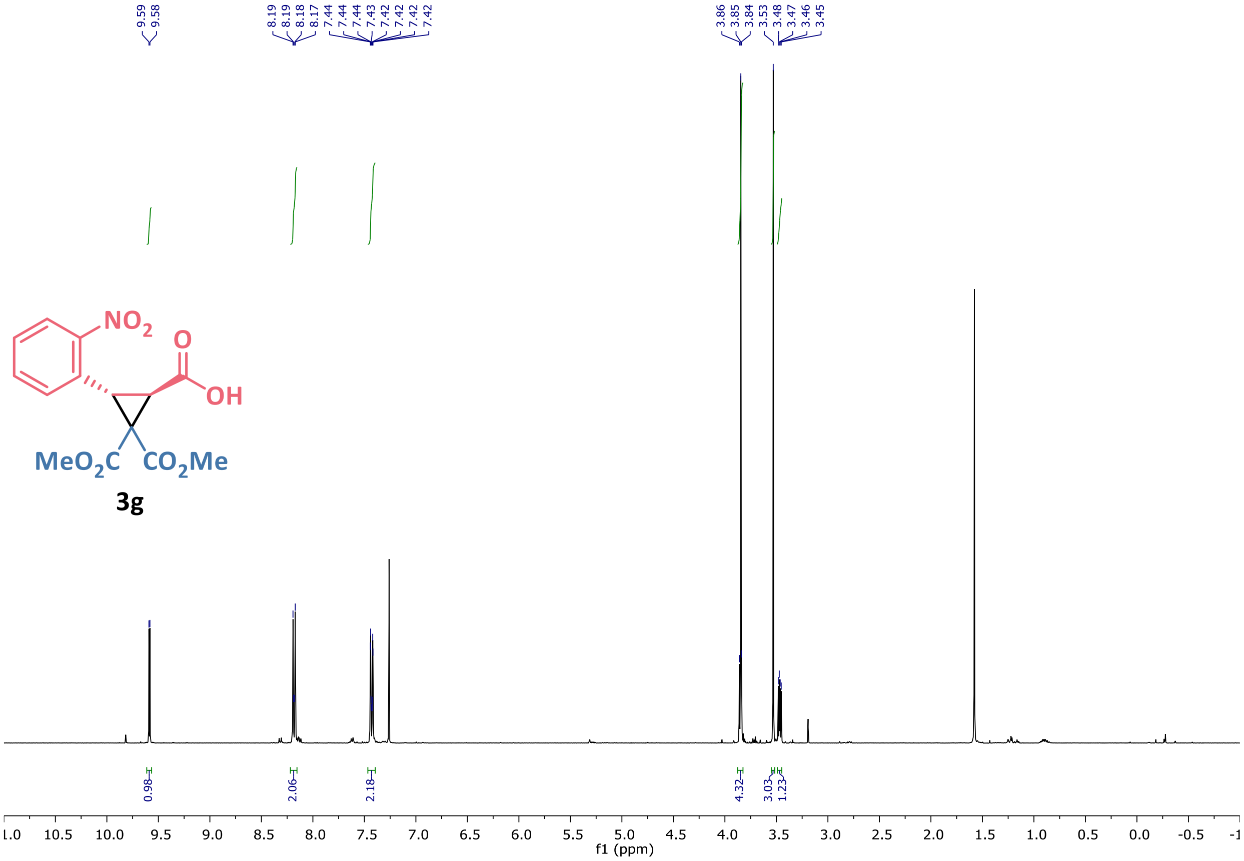
^{1}H NMR of **3f** (400 MHz, CDCl$_3$)



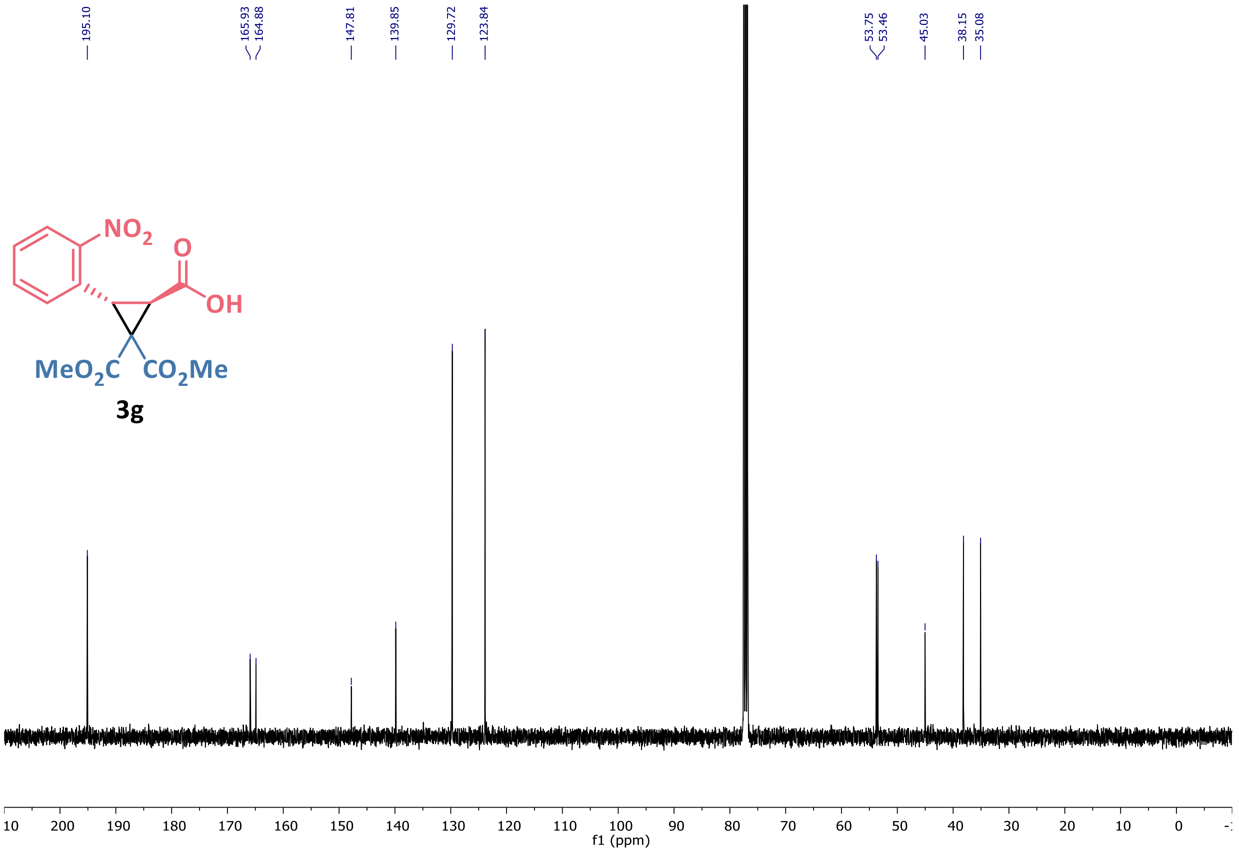
^{13}C NMR of **3f** (101 MHz, CDCl$_3$)



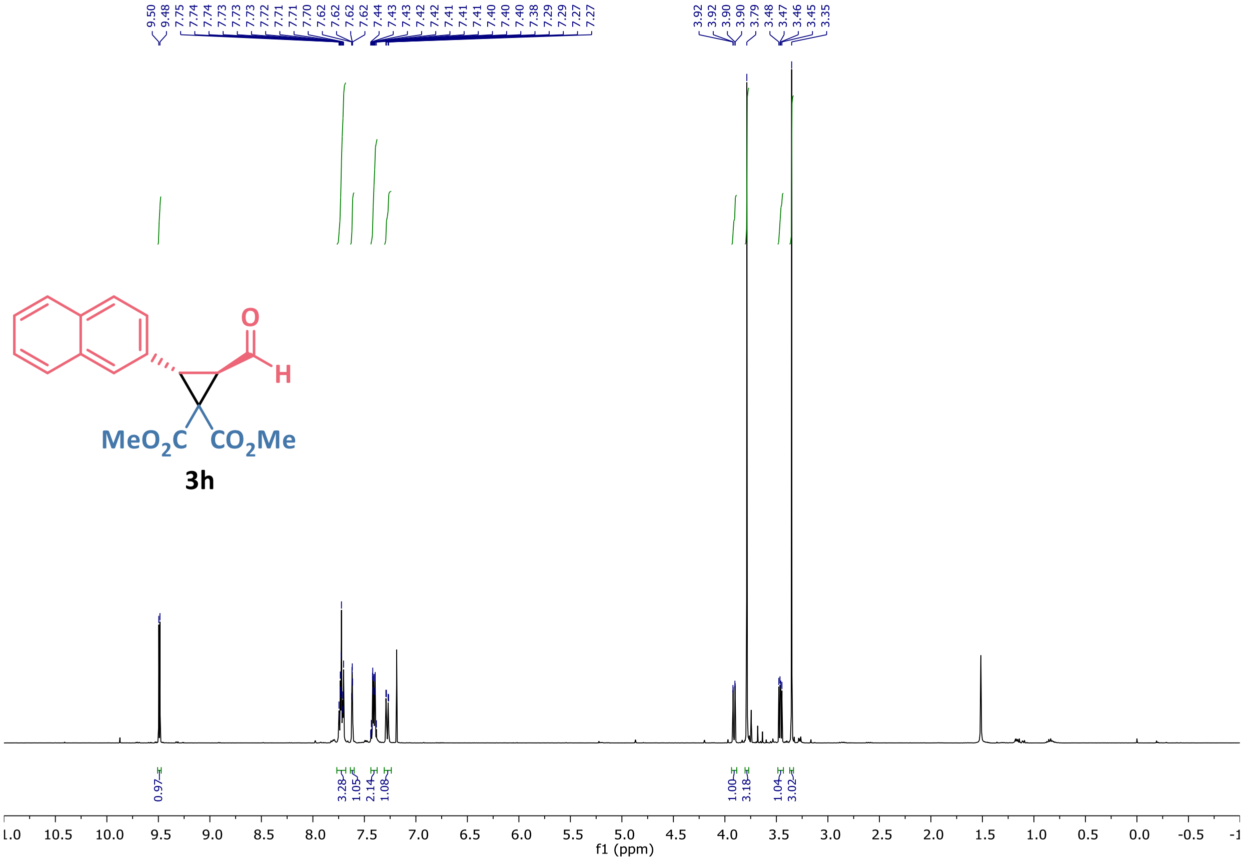
^{1}H NMR of **3g** (400 MHz, $CDCl_3$)



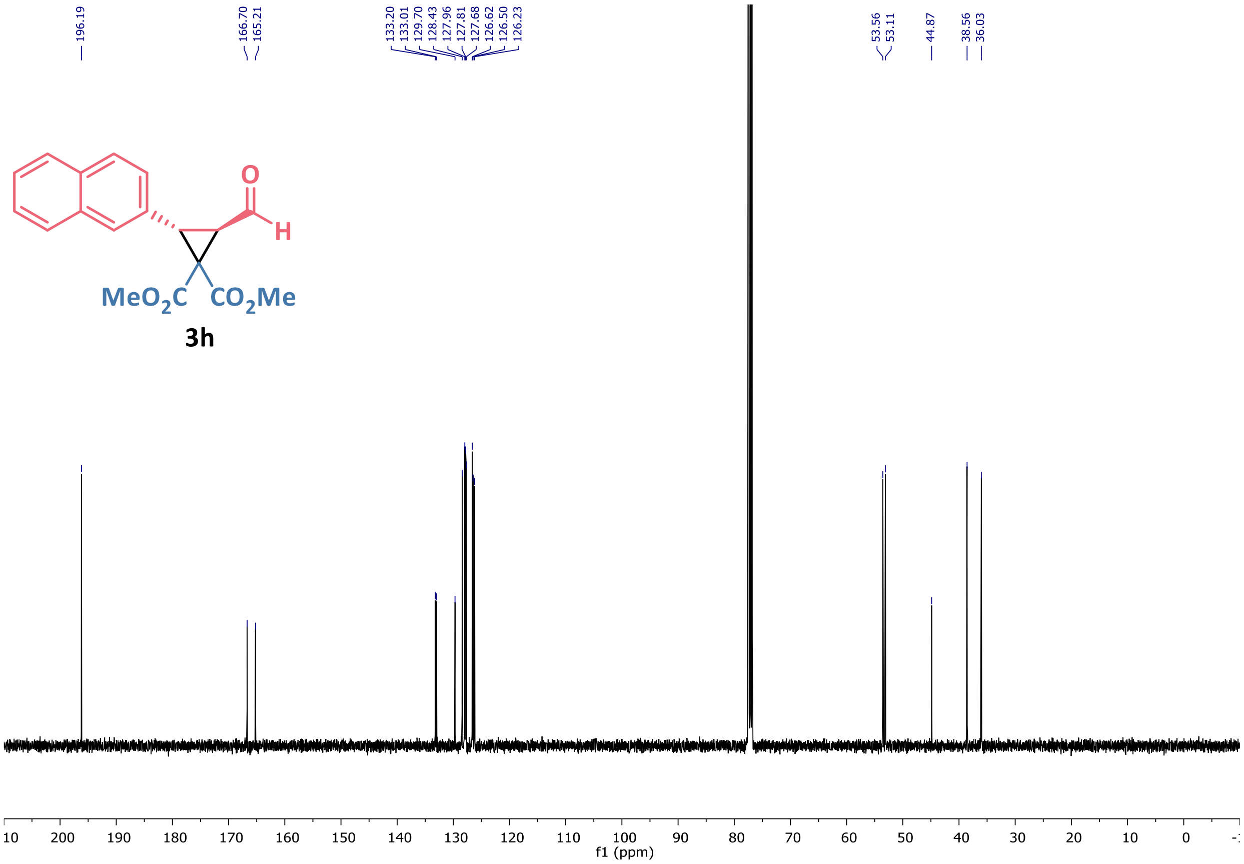
^{13}C NMR of **3g** (101 MHz, $CDCl_3$)



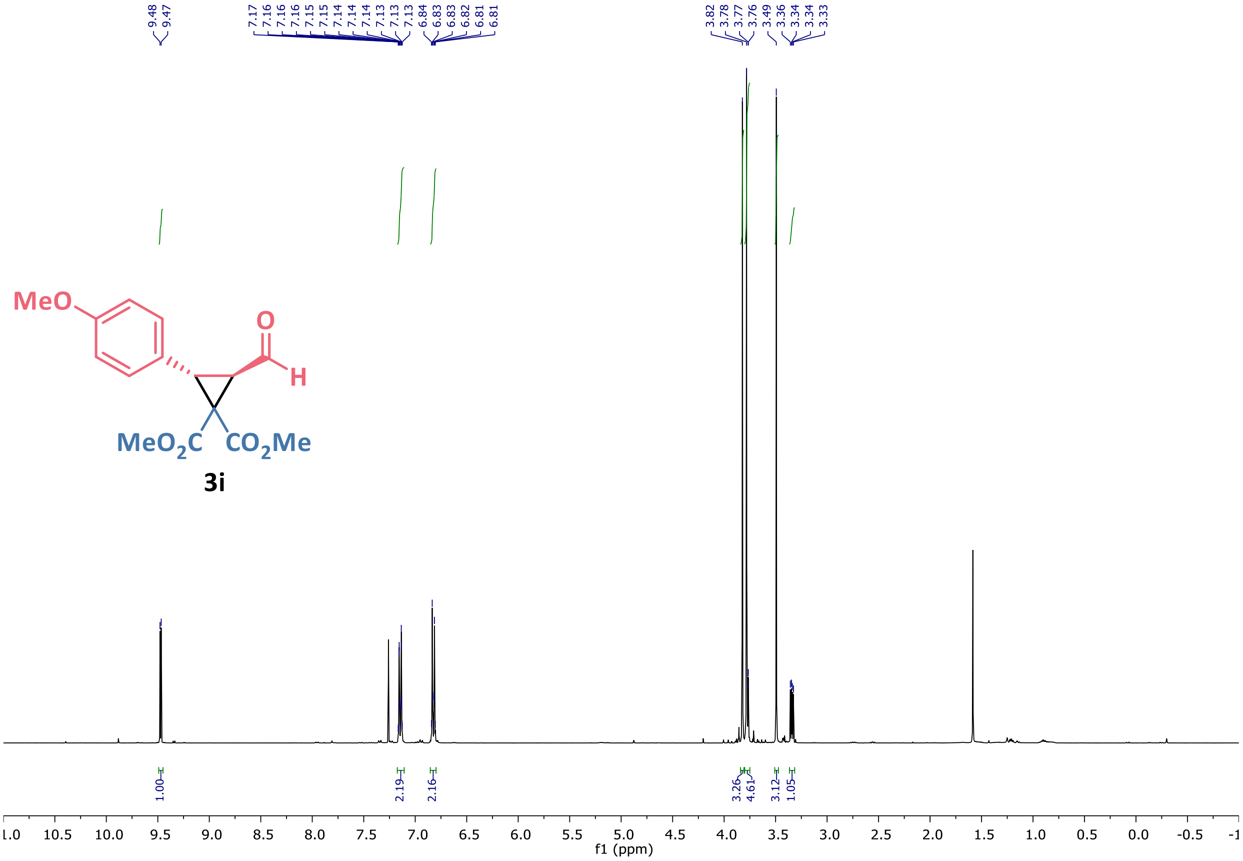
^{1}H NMR of **3h** (400 MHz, $CDCl_3$)



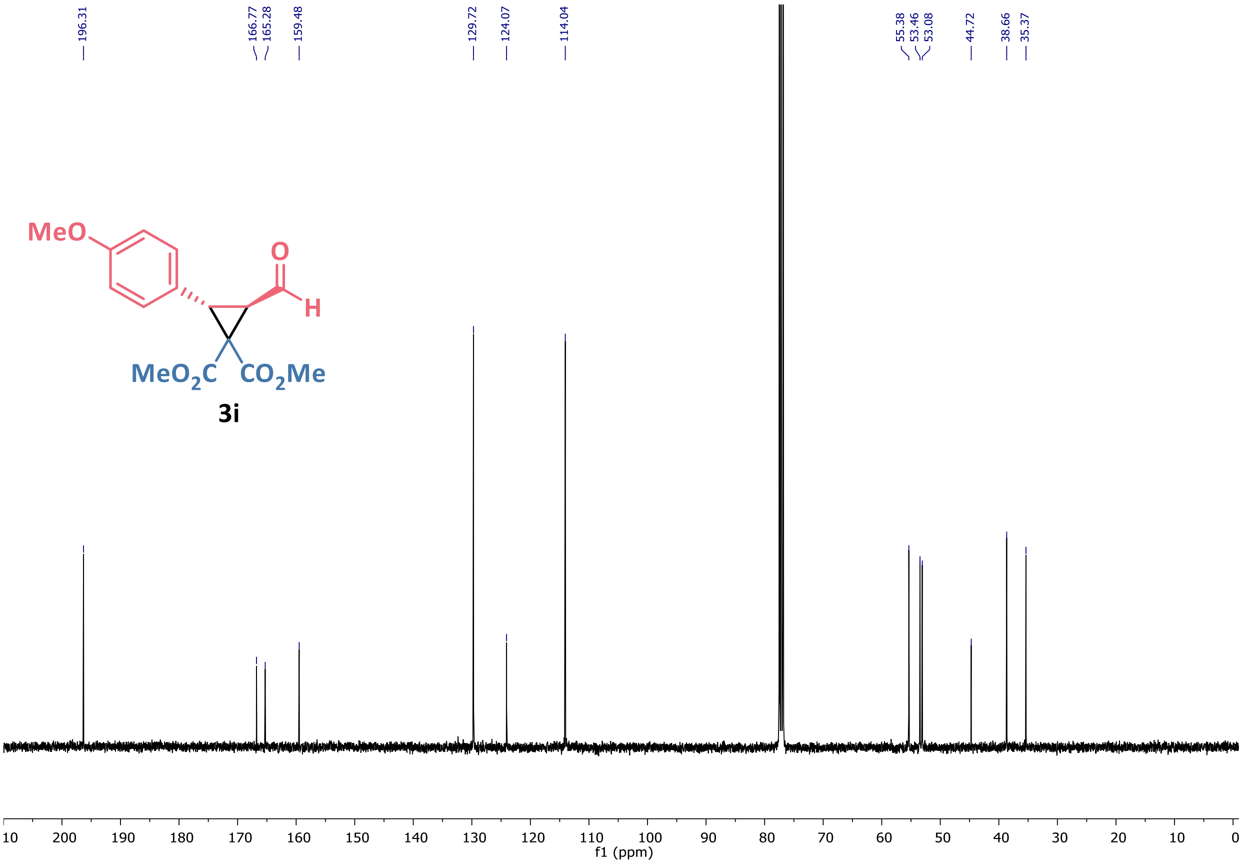
^{13}C NMR of **3h** (101 MHz, $CDCl_3$)



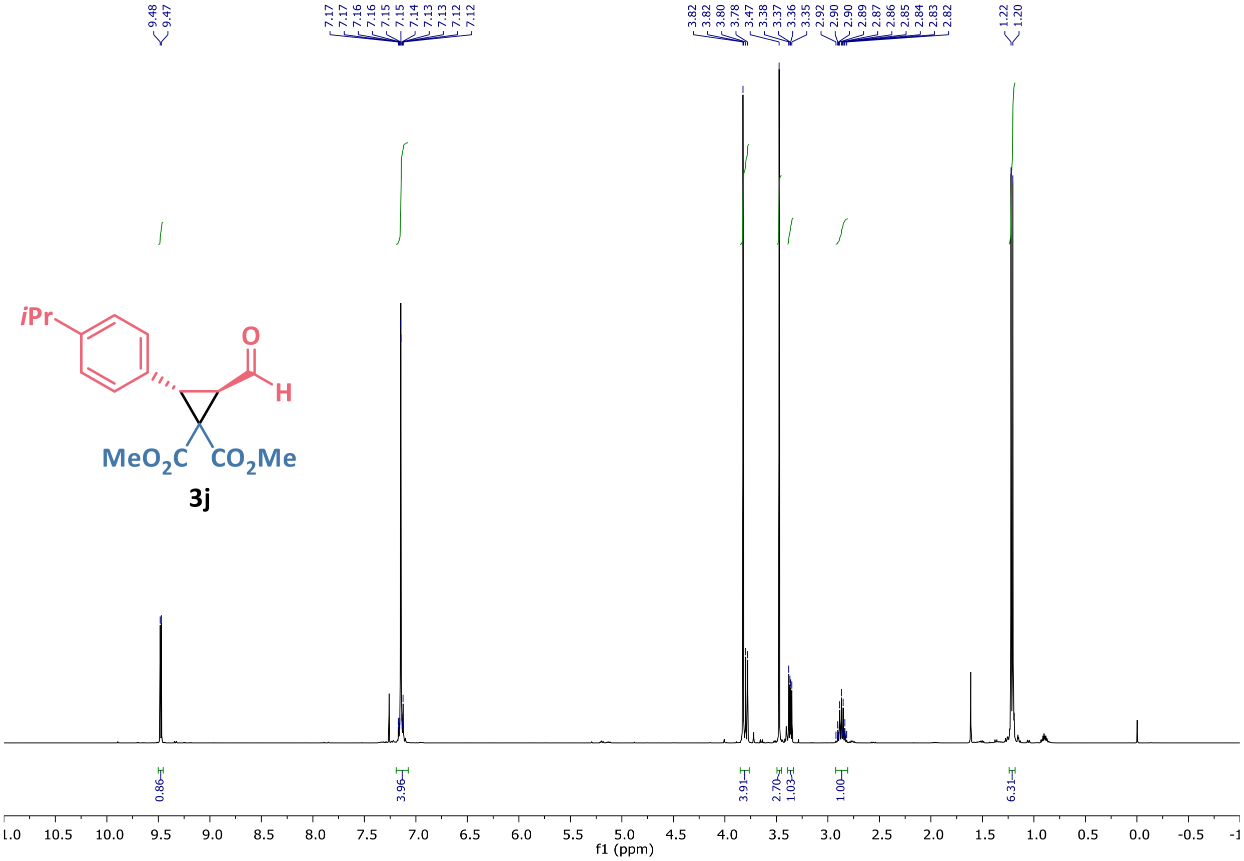
^{1}H NMR of **3i** (400 MHz, CDCl$_3$)



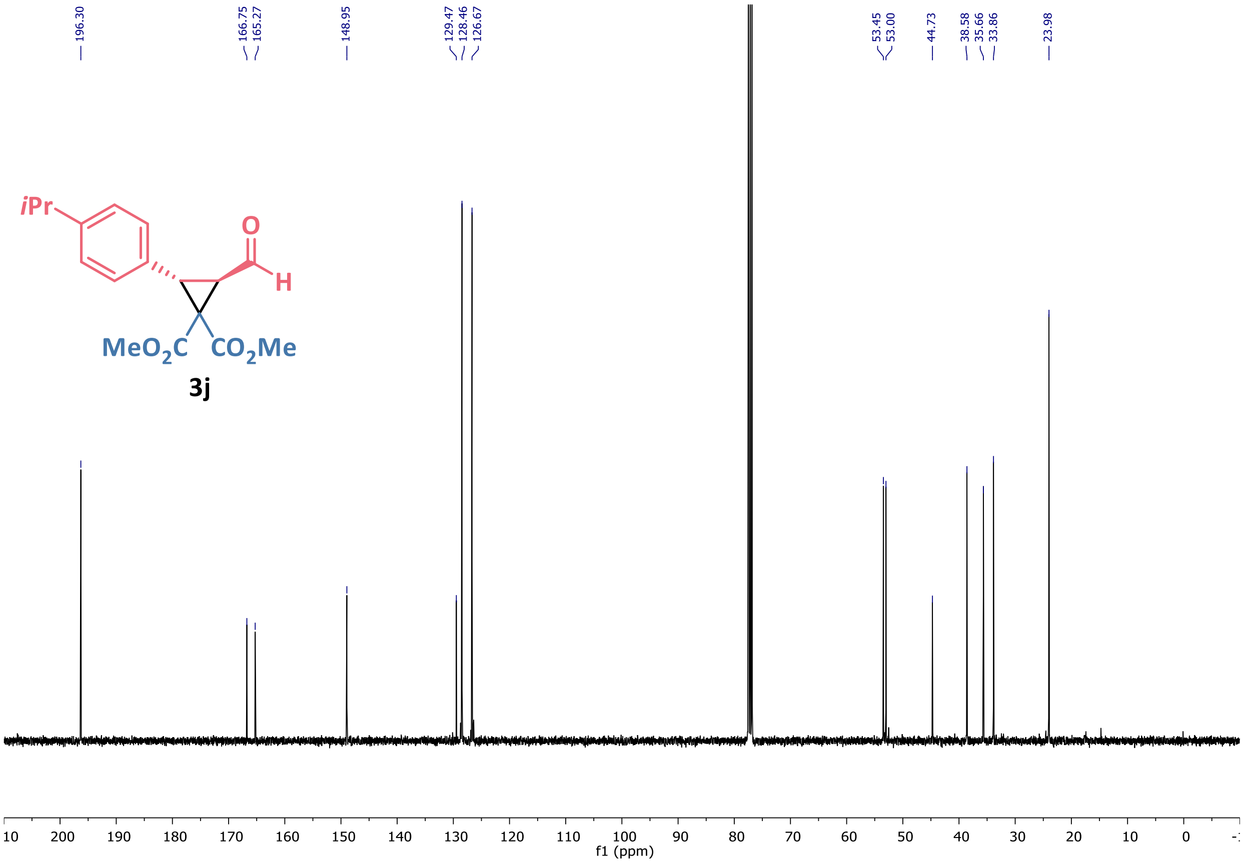
^{13}C NMR of **3i** (101 MHz, CDCl$_3$)



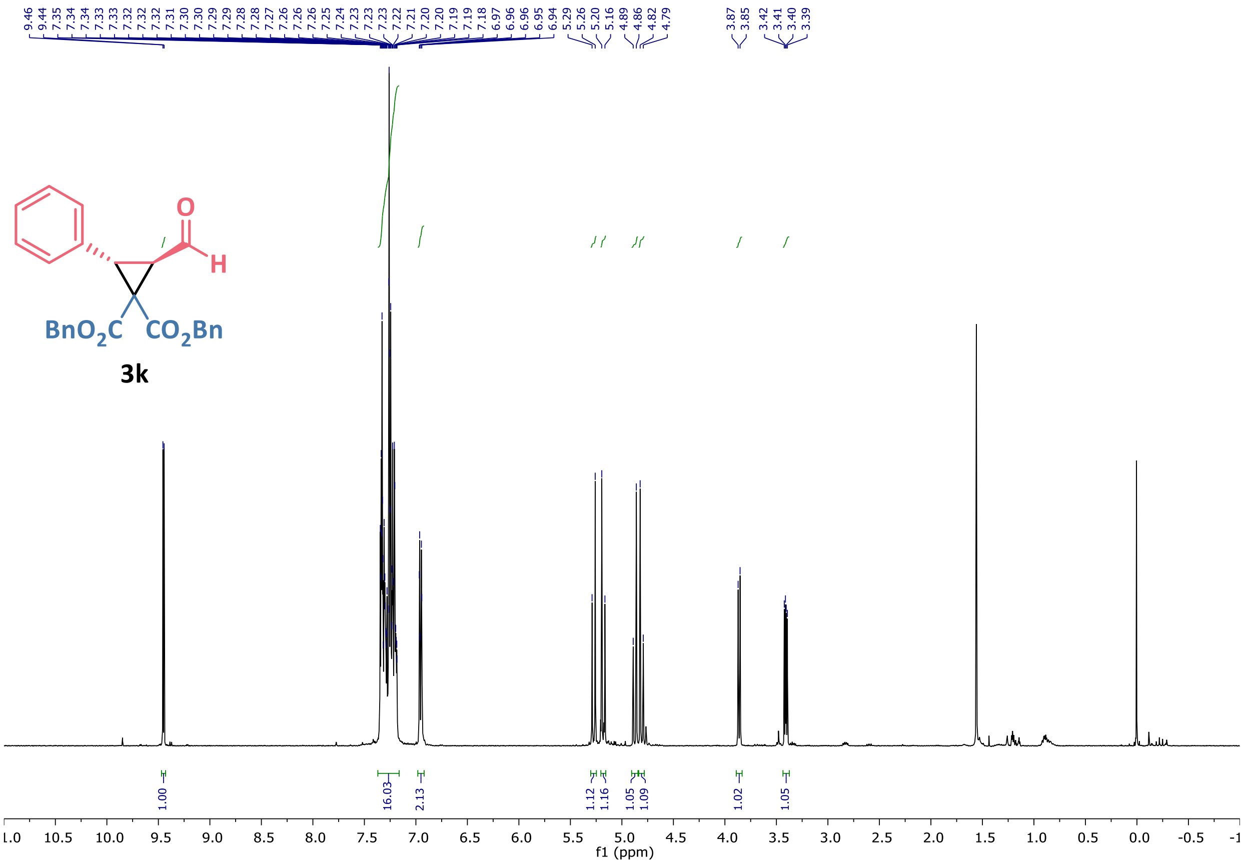
^{1}H NMR of **3j** (400 MHz, CDCl$_3$)



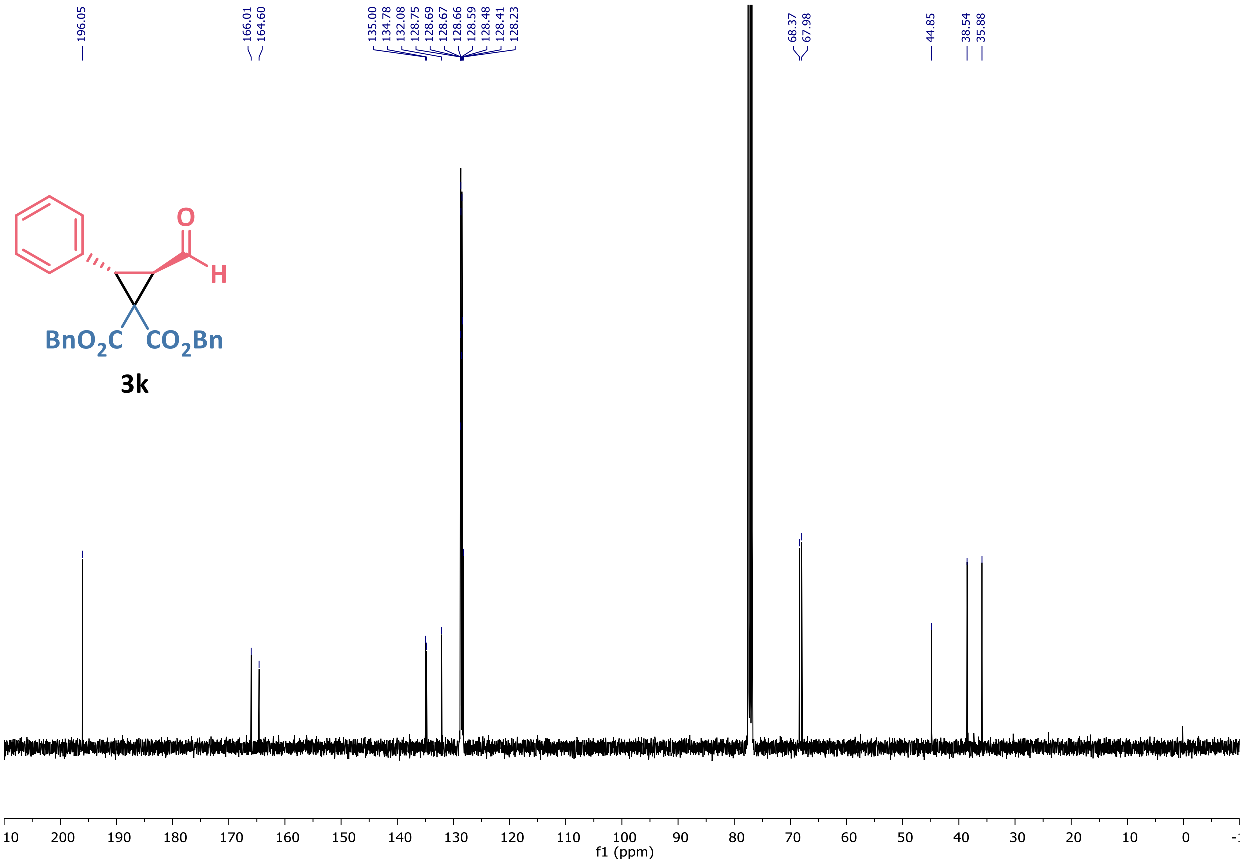
^{13}C NMR of **3j** (101 MHz, CDCl$_3$)



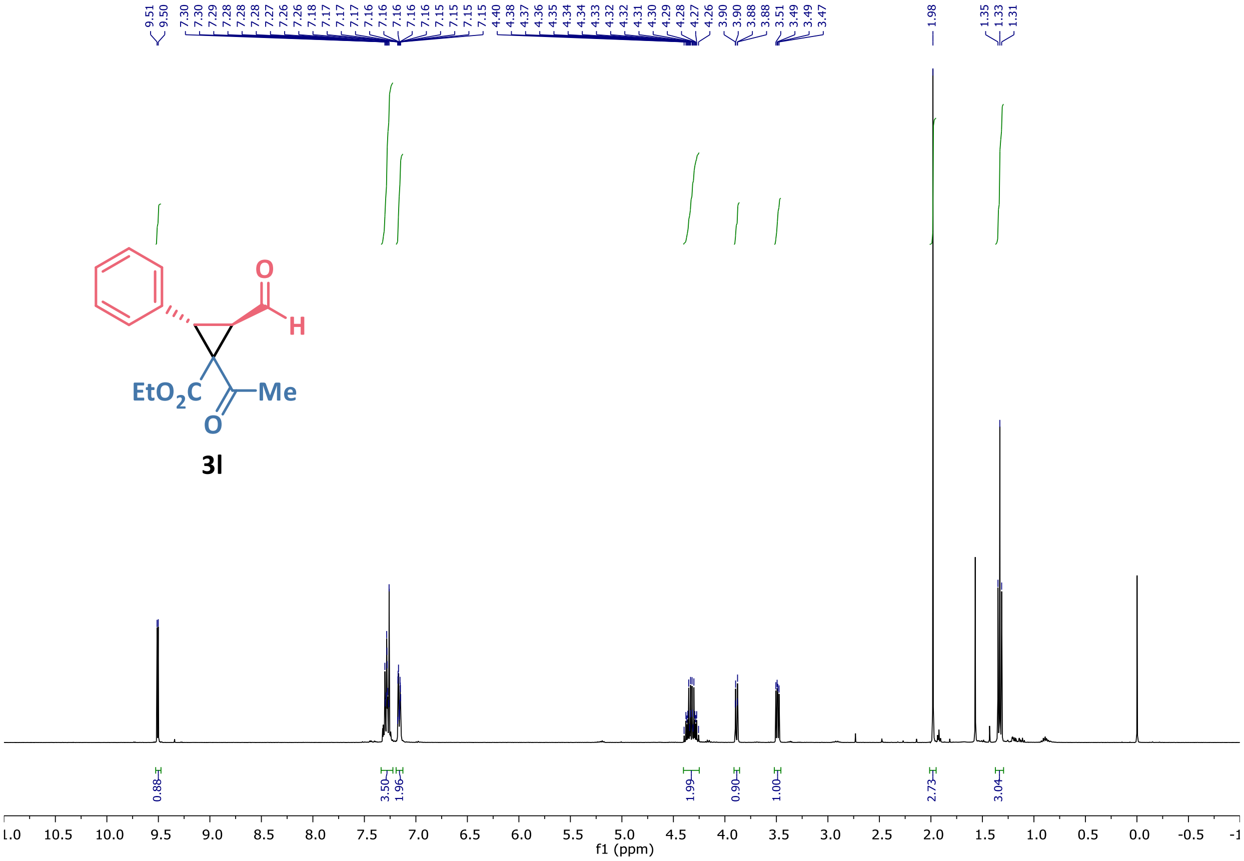
^{1}H NMR of **3k** (400 MHz, CDCl$_3$)



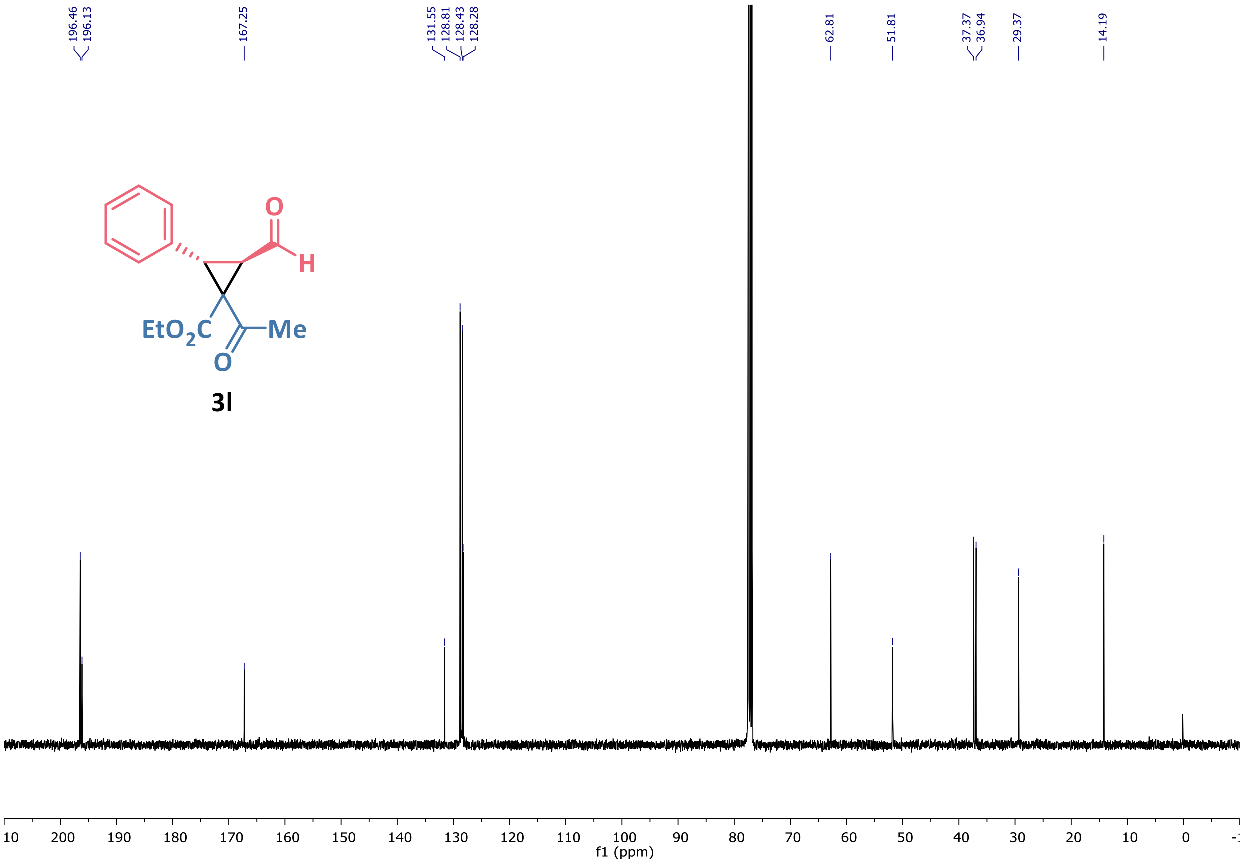
^{13}C NMR of **3k** (101 MHz, CDCl$_3$)



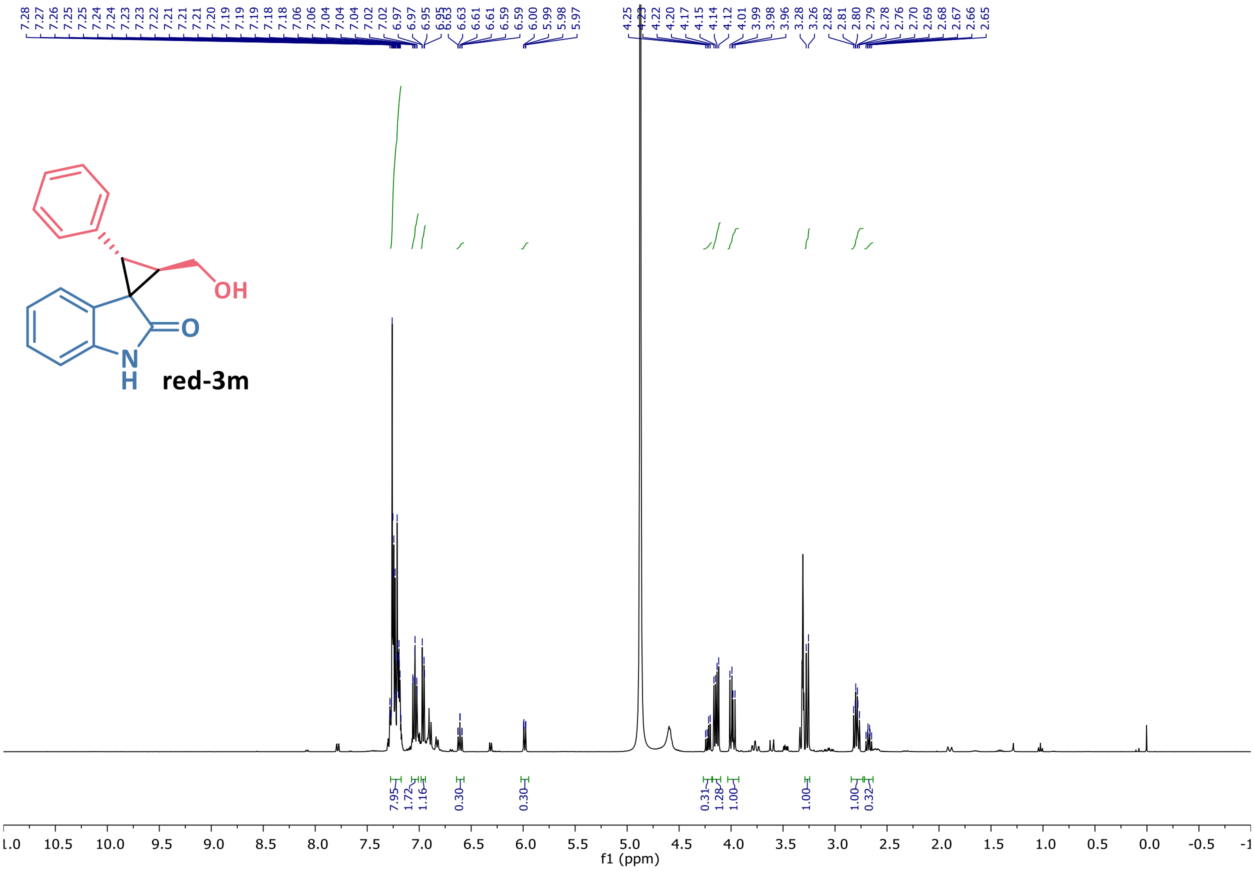
^{1}H NMR of **3l** (400 MHz, CDCl$_3$)



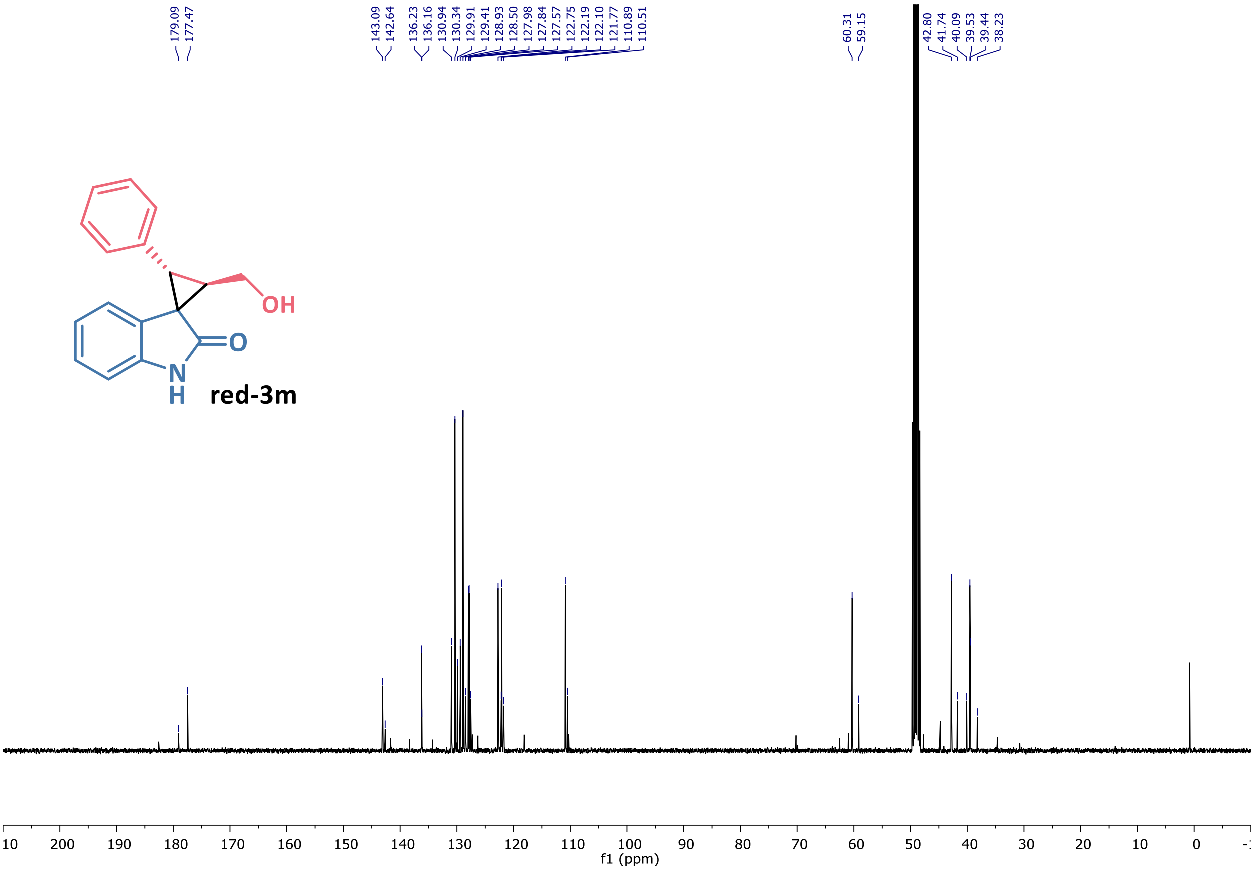
^{13}C NMR of **3l** (101 MHz, CDCl$_3$)



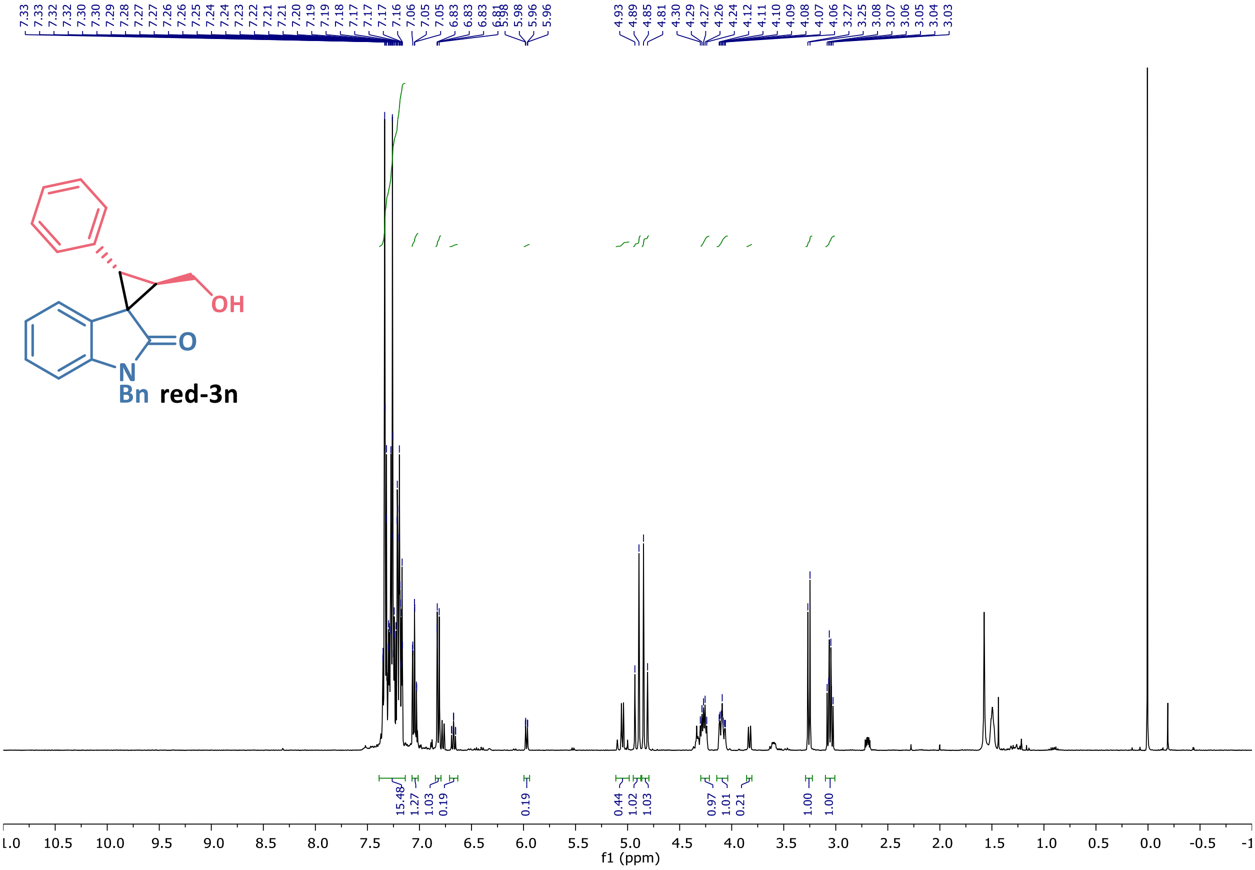
^{1}H NMR of **red-3m** (400 MHz, CD$_3$OD)



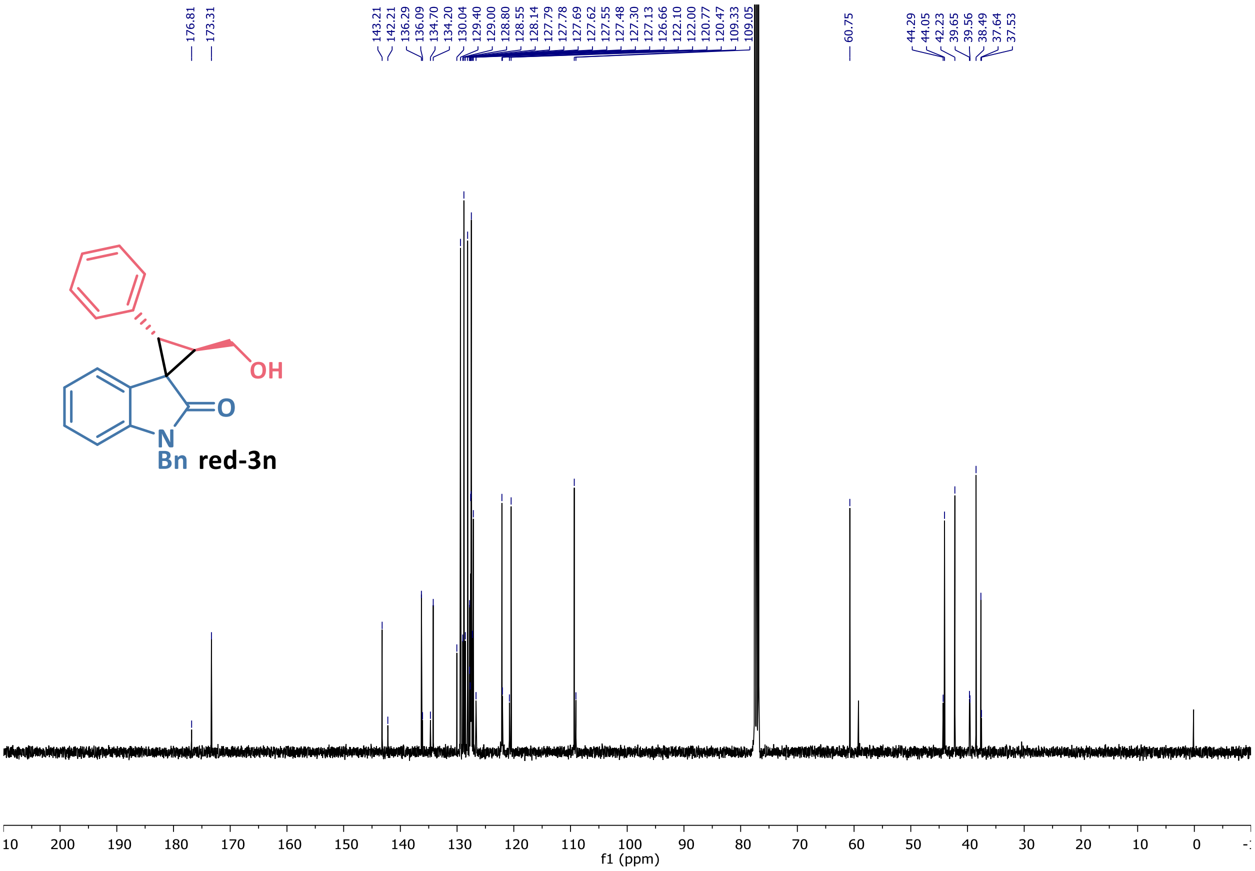
^{13}C NMR of **red-3m** (101 MHz, CD$_3$OD)



^{1}H NMR of **red-3n** (400 MHz, CDCl$_3$)

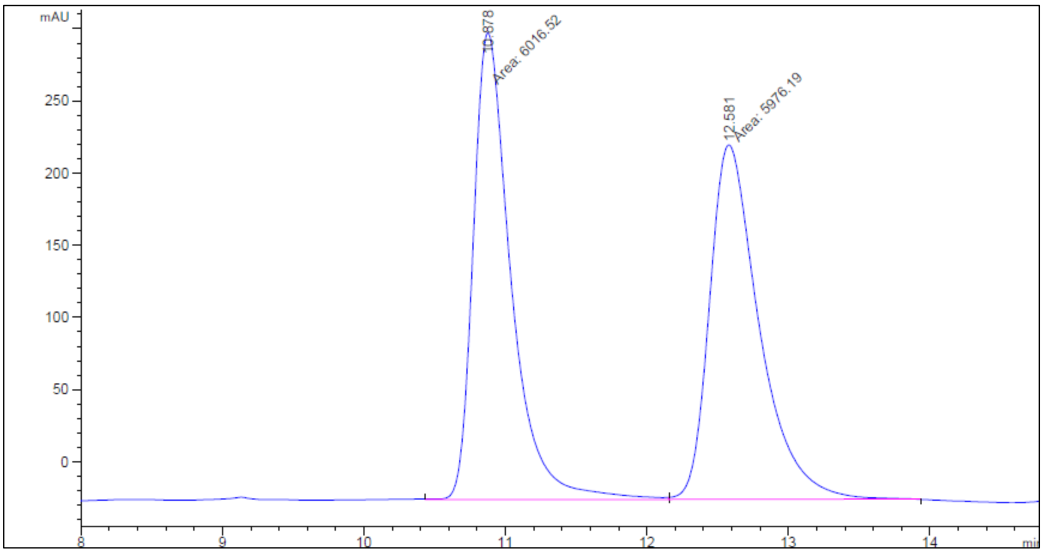


^{13}C NMR of **red-3n** (101 MHz, CDCl$_3$)



11. HPLC chromatograms

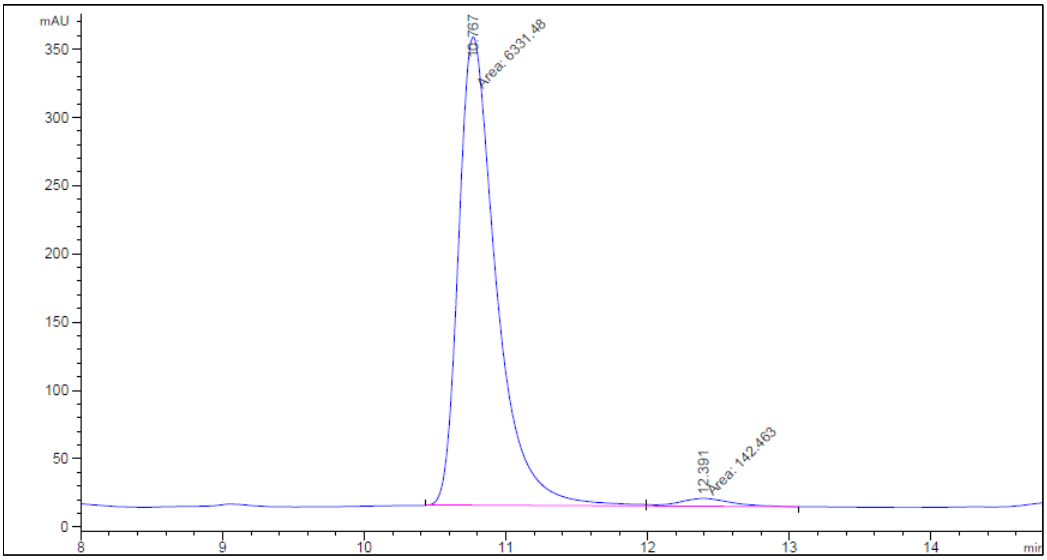
HPLC trace of *rac*-3a.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.878 MF     0.3100 6016.52441  323.45093  50.1682
   2  12.581 FM     0.4057 5976.18506  245.53014  49.8318
```

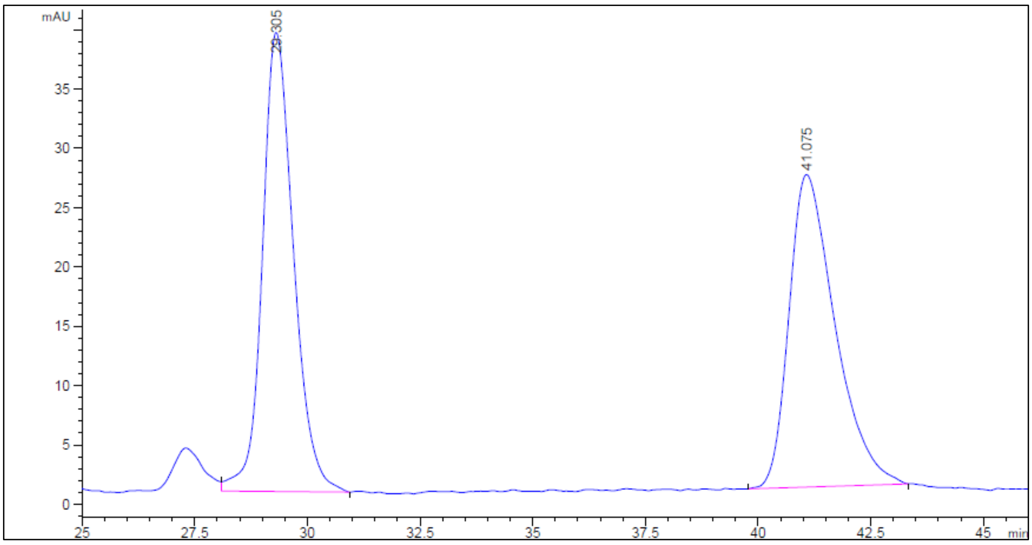
HPLC trace of 3a.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.767 MF     0.3080 6331.47705  342.65207  97.7994
   2  12.391 FM     0.4209  142.46320    5.64066   2.2006
```

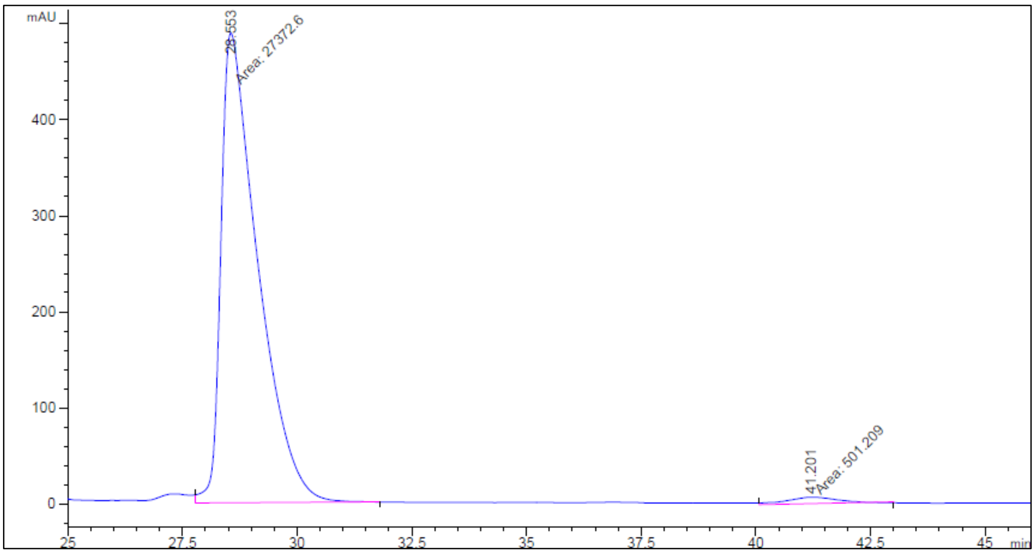
HPLC trace of *rac*-3b.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  29.305 VB    0.7321 1863.86963   38.68213  49.8734
   2  41.075 BB    1.0060 1873.33191   26.33040  50.1266
```

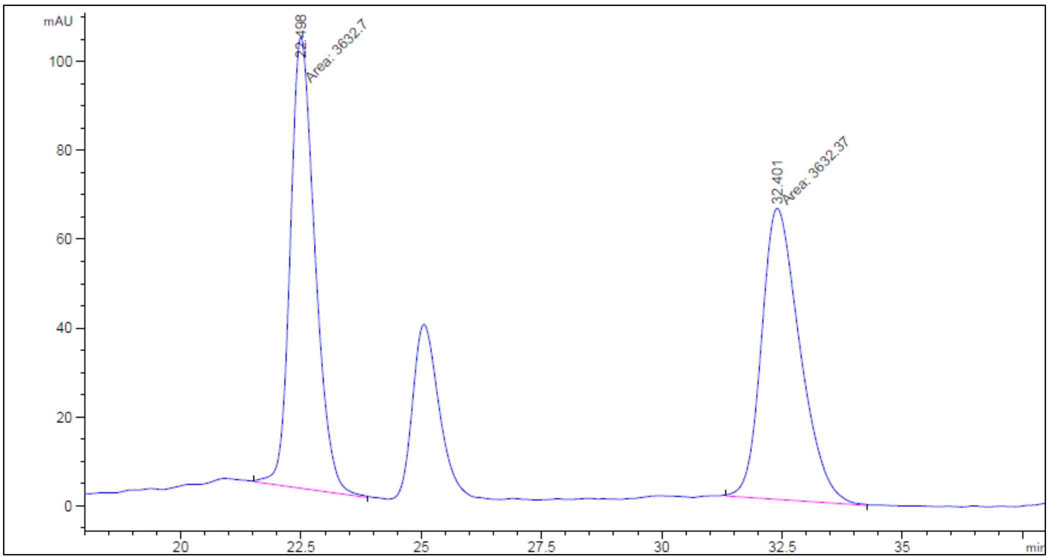
HPLC trace of 3b.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  28.553 FM    0.9324 2.73726e4  489.29459  98.2019
   2  41.201 MM    1.2817  501.20917    6.51752   1.7981
```

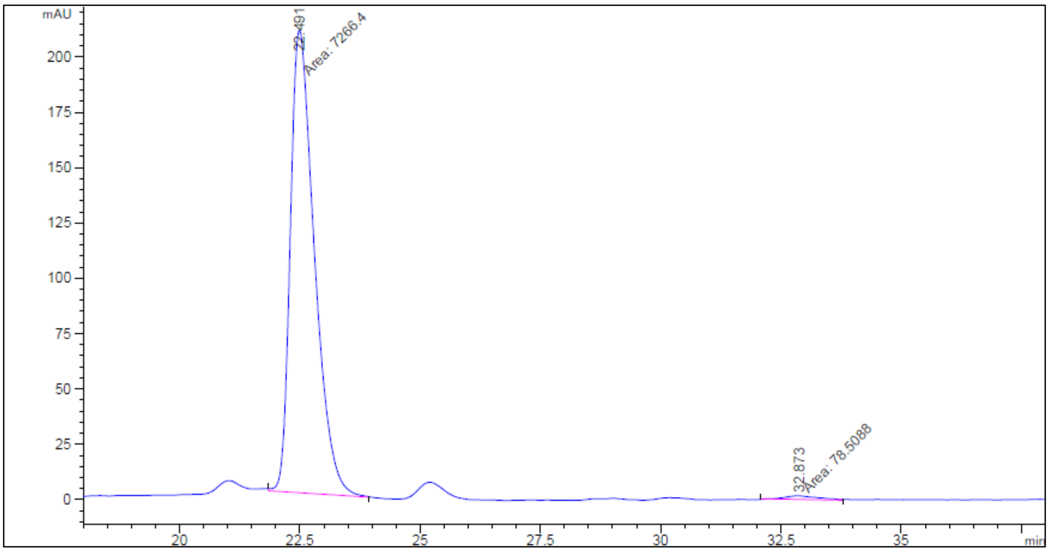
HPLC trace of *rac*-3c.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  22.498 MM    0.5961 3632.69629  101.57577  50.0023
   2  32.401 MM    0.9240 3632.36694   65.52168  49.9977
```

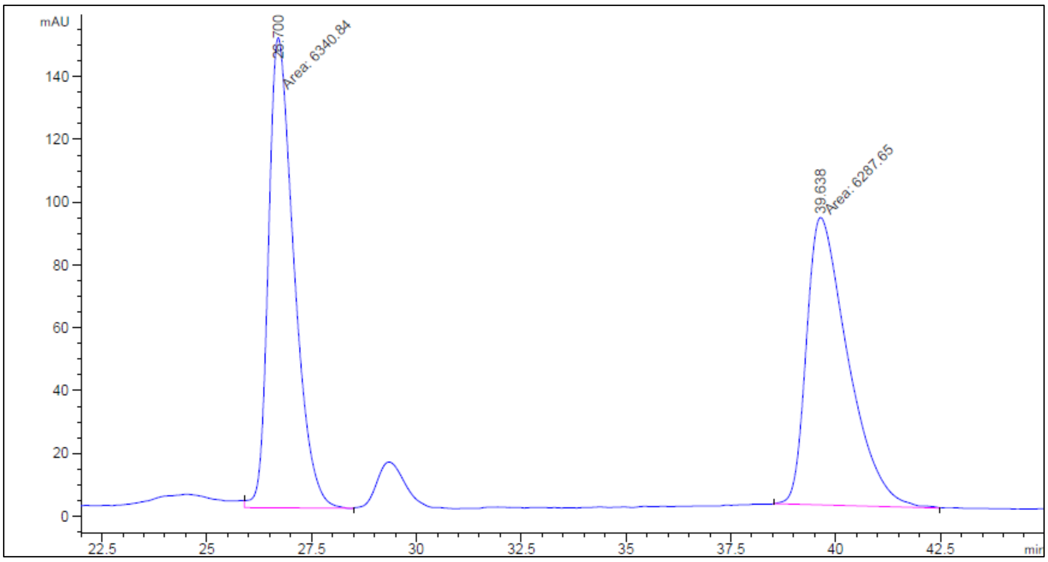
HPLC trace of 3c.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  22.491 MM    0.5794 7266.39893  209.00609  98.9311
   2  32.873 MM    0.8052   78.50882    1.62495   1.0689
```

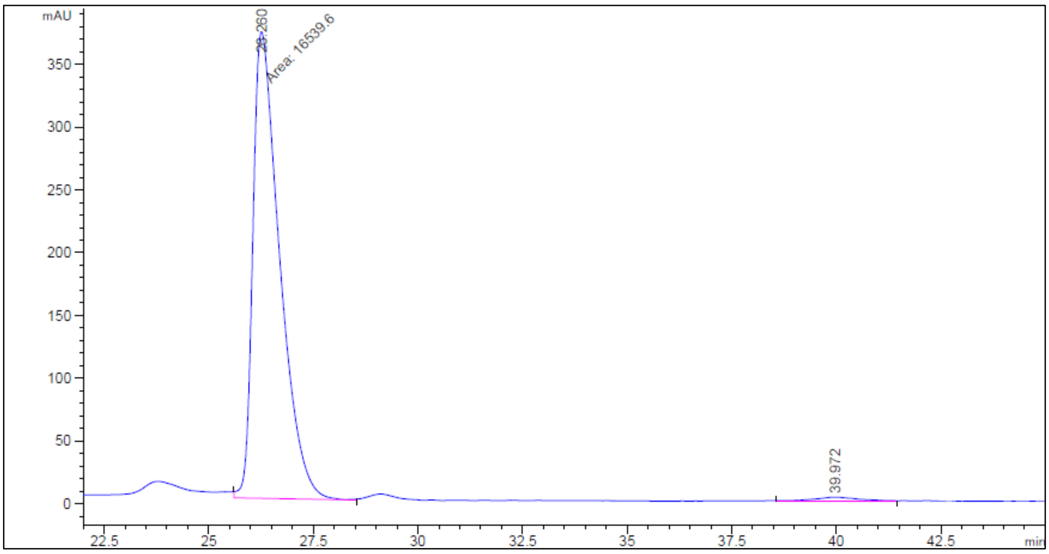
HPLC trace of *rac*-3d.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  26.700 MF    0.7059 6340.84082  149.70972  50.2106
   2  39.638 MM    1.1446 6287.64844   91.55206  49.7894
```

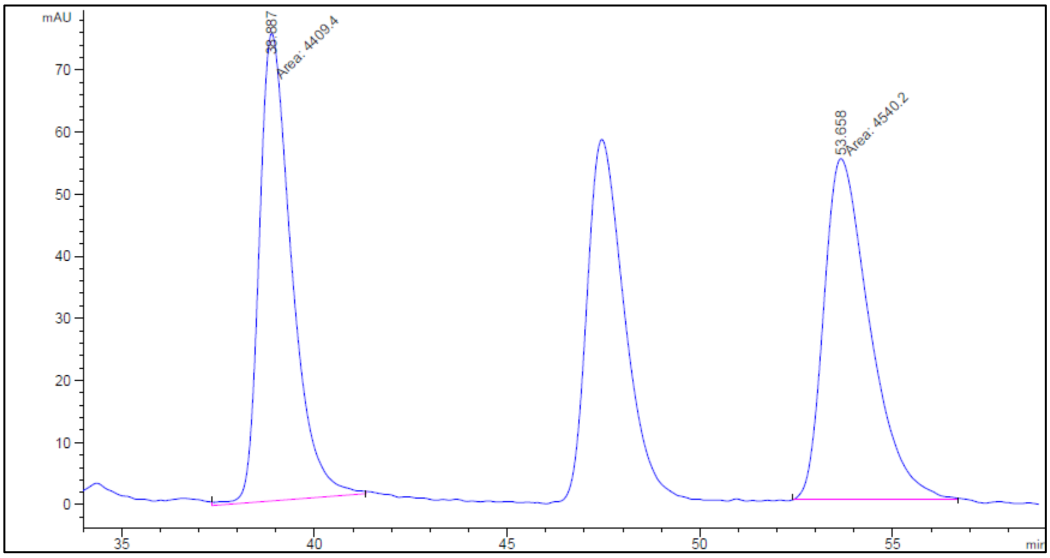
HPLC trace of 3d.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  26.260 FM    0.7419 1.65396e4  371.55261  98.7887
   2  39.972 BV    0.8499  202.80893    2.83064   1.2113
```

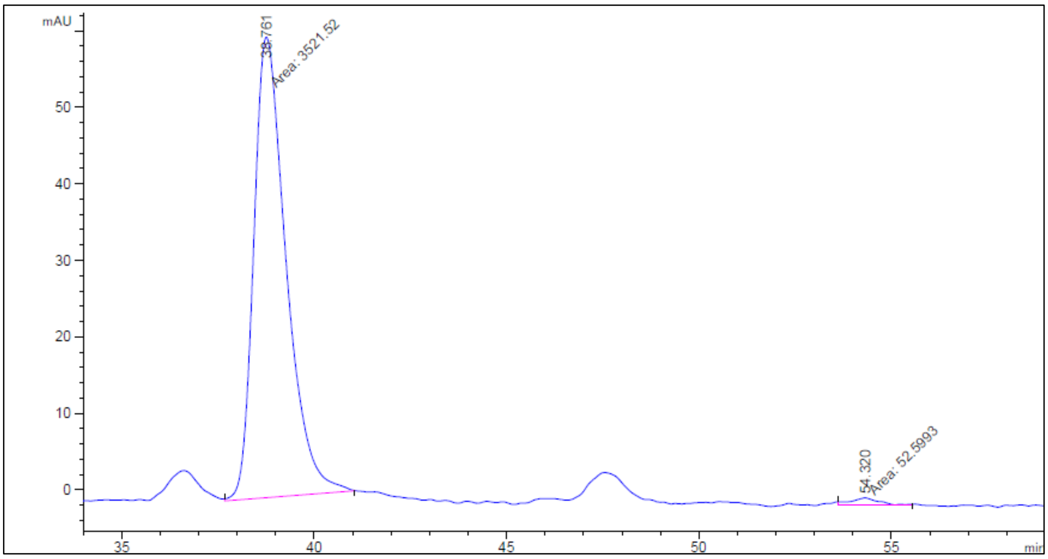
HPLC trace of *rac*-3e.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  38.887 MM    0.9767 4409.40430   75.24049  49.2693
   2  53.658 MM    1.3804 4540.20117   54.81925  50.7307
```

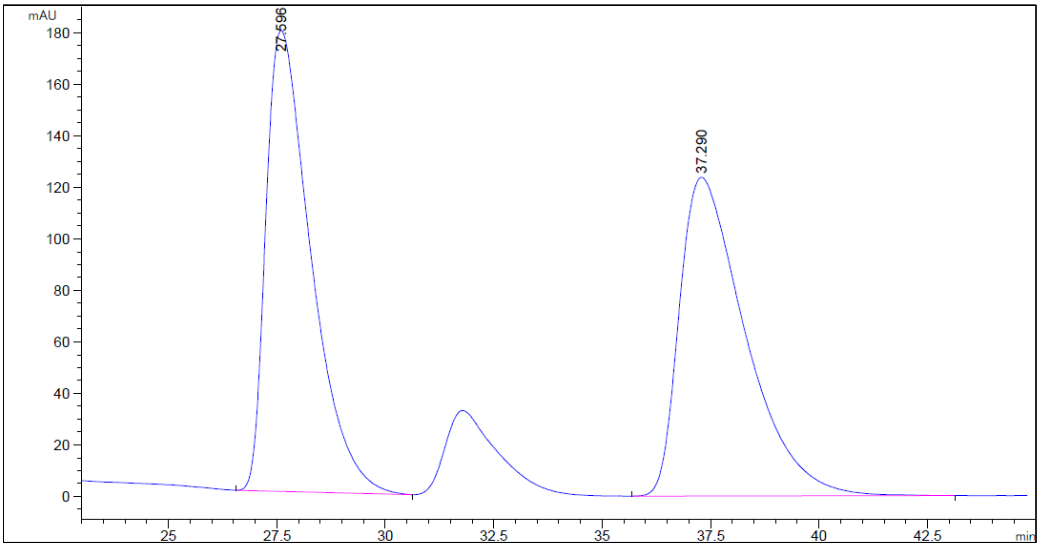
HPLC trace of 3e.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]   [mAU*s]      [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  38.761 MM    0.9747 3521.52100   60.21402  98.5283
   2  54.320 MM    0.8952   52.59932 9.79273e-1   1.4717
```

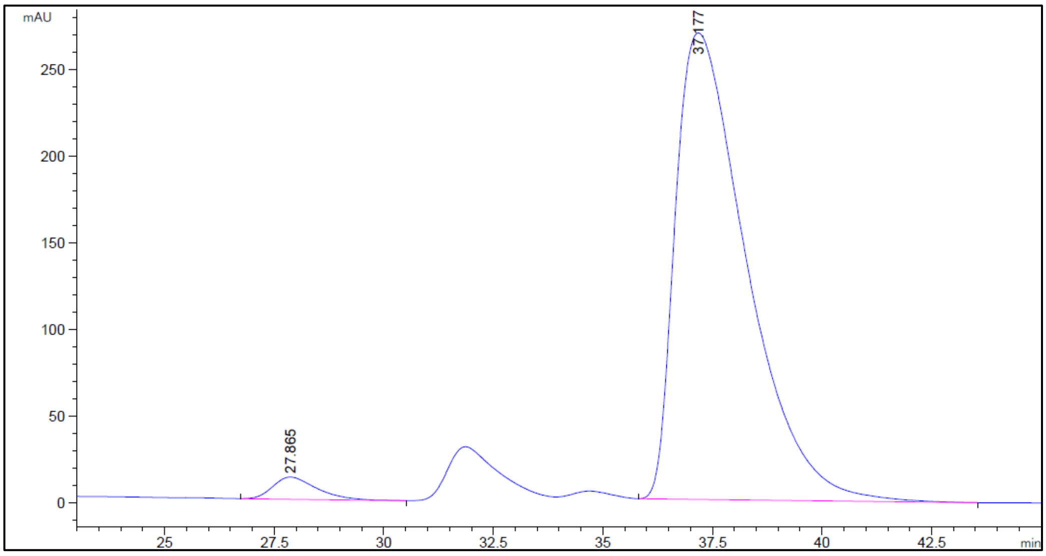
HPLC trace of *rac*-3f.



```
Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #    [min]        [min]  mAU    *s   [mAU    ]     %
----|-------|----|-------|----------|----------|--------|
   1  27.596 BB    1.0854 1.29427e4  178.96861 49.7454
   2  37.290 BB    1.5836 1.30752e4  123.74281 50.2546
```

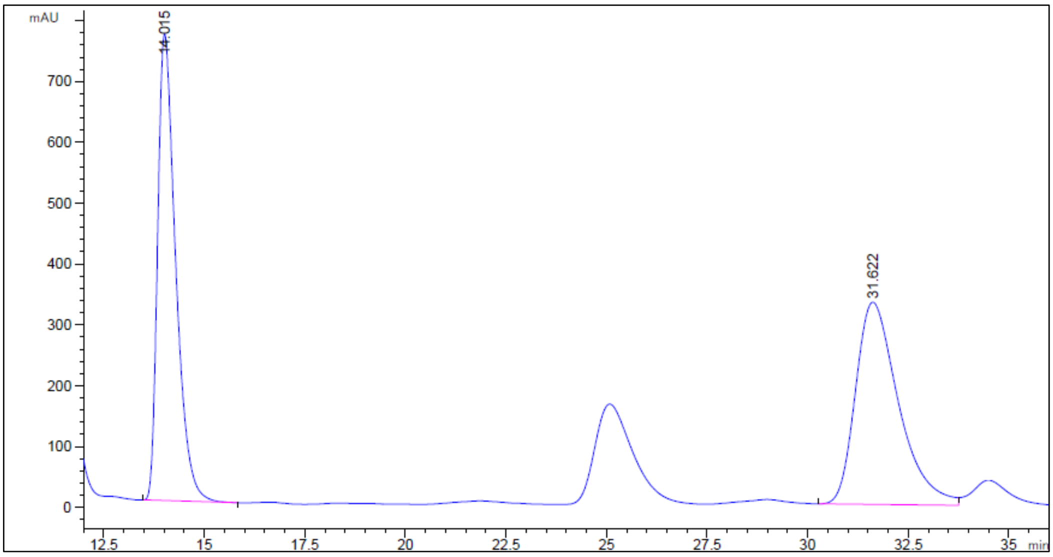
HPLC trace of 3f.



```
Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #    [min]        [min]  mAU    *s   [mAU    ]     %
----|-------|----|-------|----------|----------|--------|
   1  27.865 BB    0.9993  887.72388   12.85521  2.8422
   2  37.177 BB    1.6990 3.03462e4  269.00430 97.1578
```

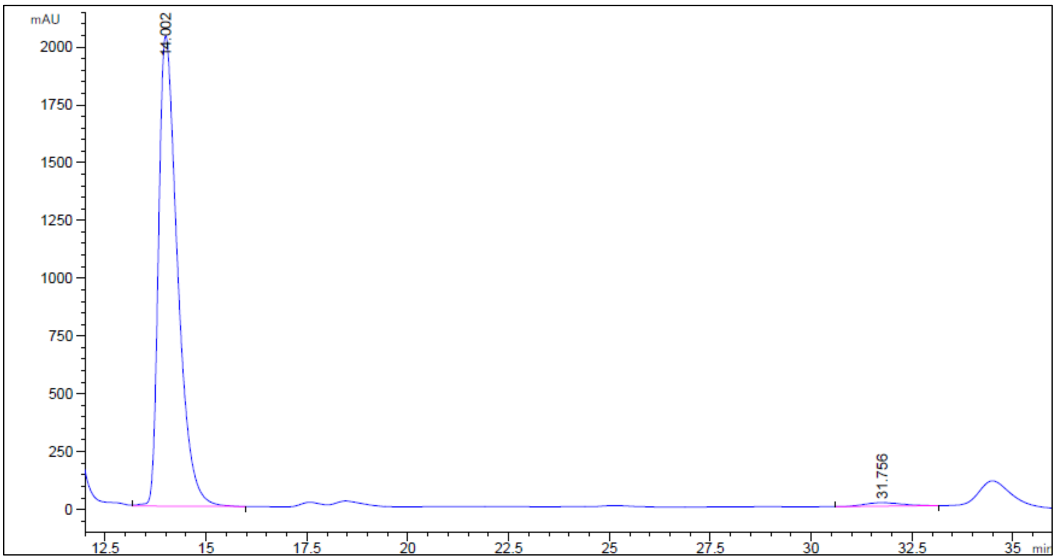
HPLC trace of *rac*-3g.



```
Signal 1: VWD1 A, Wavelength=210 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU    *s   [mAU    ]     %
----|-------|----|-------|----------|----------|--------|
   1  14.015 BB    0.4673 2.38360e4  767.21368  49.1651
   2  31.622 BV    1.1227 2.46455e4  332.40646  50.8349
```

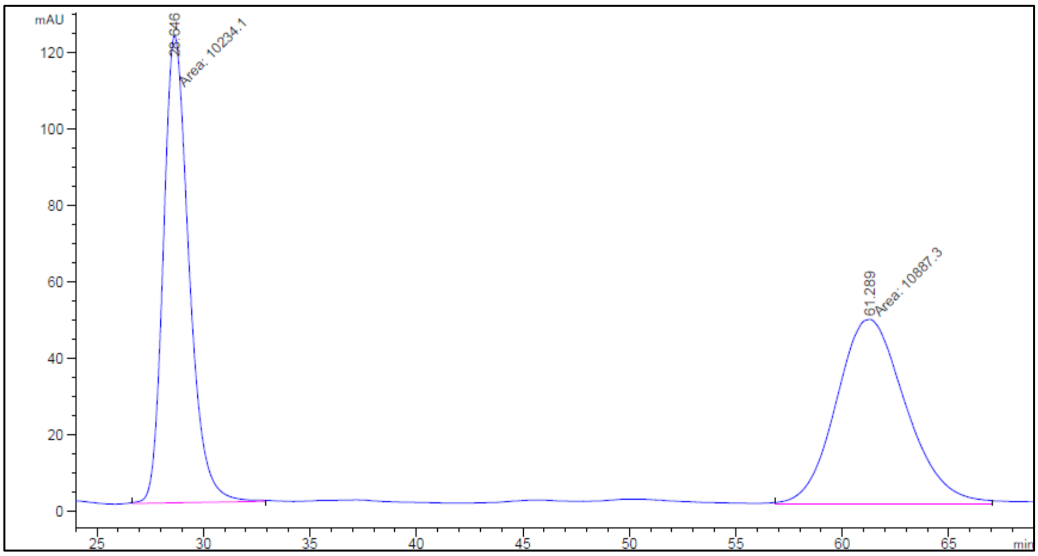
HPLC trace of 3g.



```
Signal 1: VWD1 A, Wavelength=210 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU    *s   [mAU    ]     %
----|-------|----|-------|----------|----------|--------
   1  14.002 VB    0.4987 6.64608e4 2036.22937  98.5454
   2  31.756 BB    0.9934  981.01923   15.22486   1.4546
```

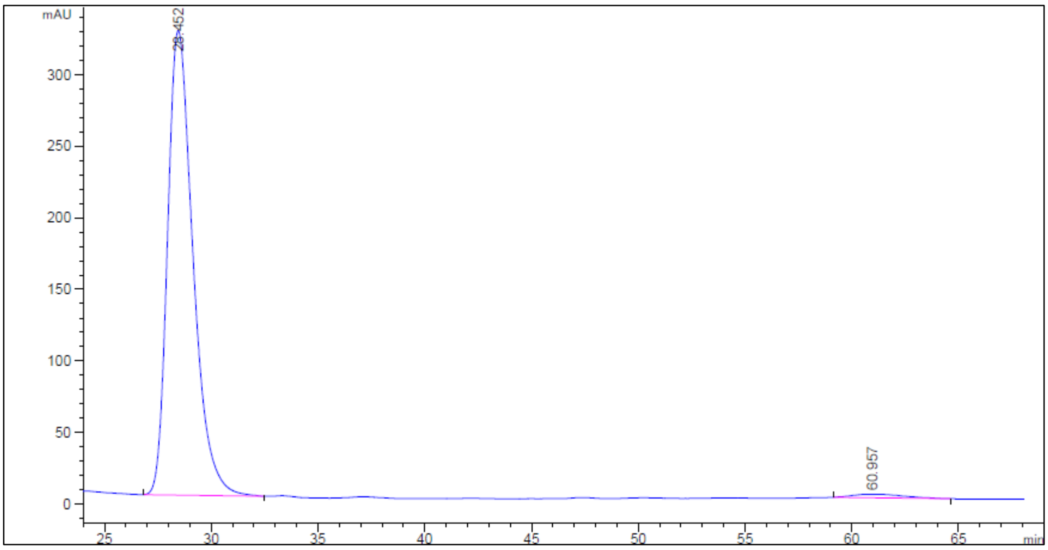
HPLC trace of *rac*-3h.



```
Signal 1: MWD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  28.646 MM    1.3974 1.02341e4  122.05883  48.4536
   2  61.289 MM    3.7718 1.08873e4   48.10785  51.5464
```

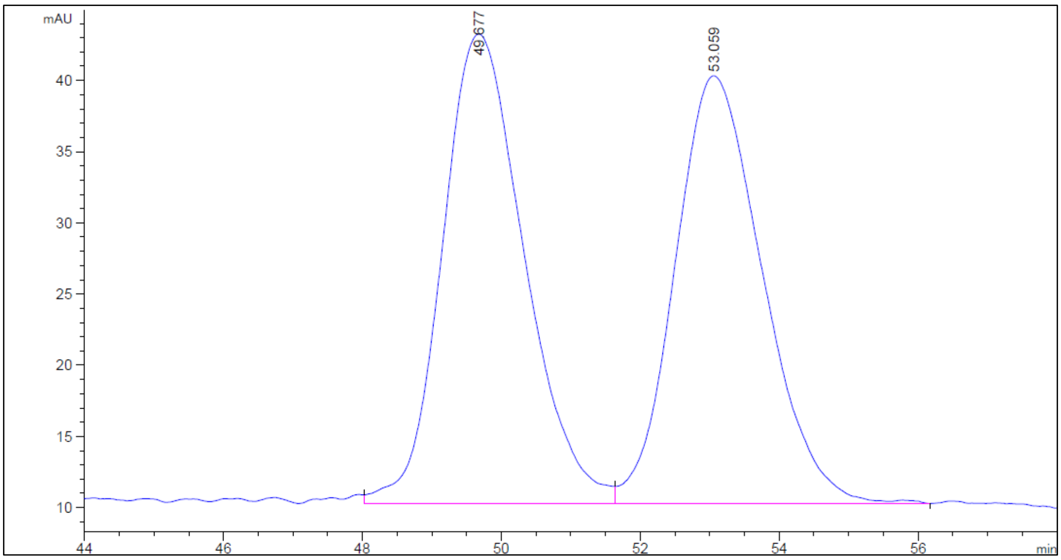
HPLC trace of 3h.



```
Signal 1: MWD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  28.452 BB    1.2452 2.68562e4  324.62097  98.4979
   2  60.957 BB    1.9636  409.56146    2.44081   1.5021
```

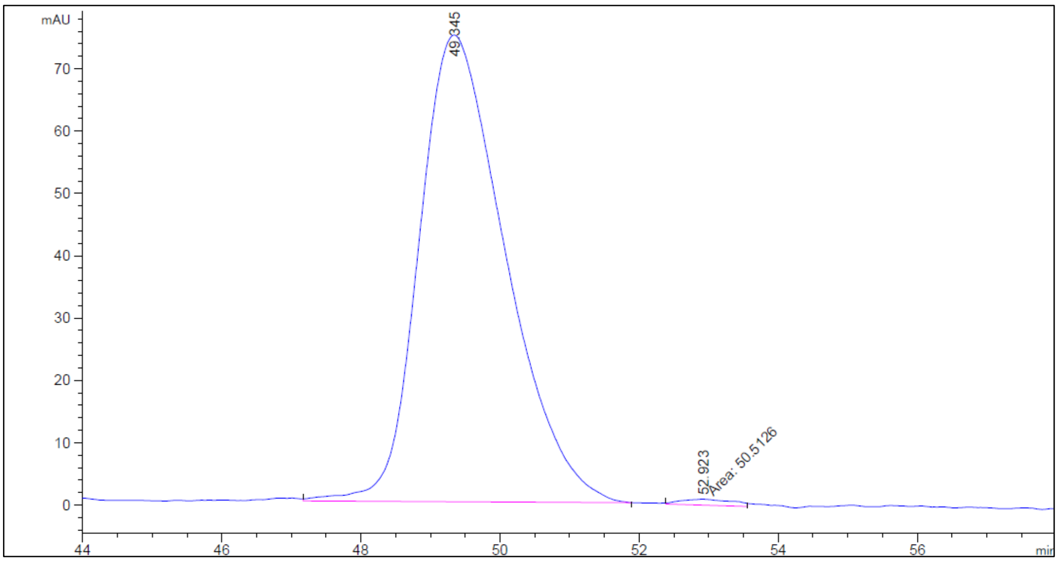
HPLC trace of *rac*-3i.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width      Area       Height      Area
  #    [min]        [min]   [mAU*s]      [mAU]        %
----|--------|----|-------|----------|----------|--------|
   1  49.677 VV    1.1946 2697.23291   32.96581  50.6633
   2  53.059 VV    1.1943 2626.60962   30.03388  49.3367
```

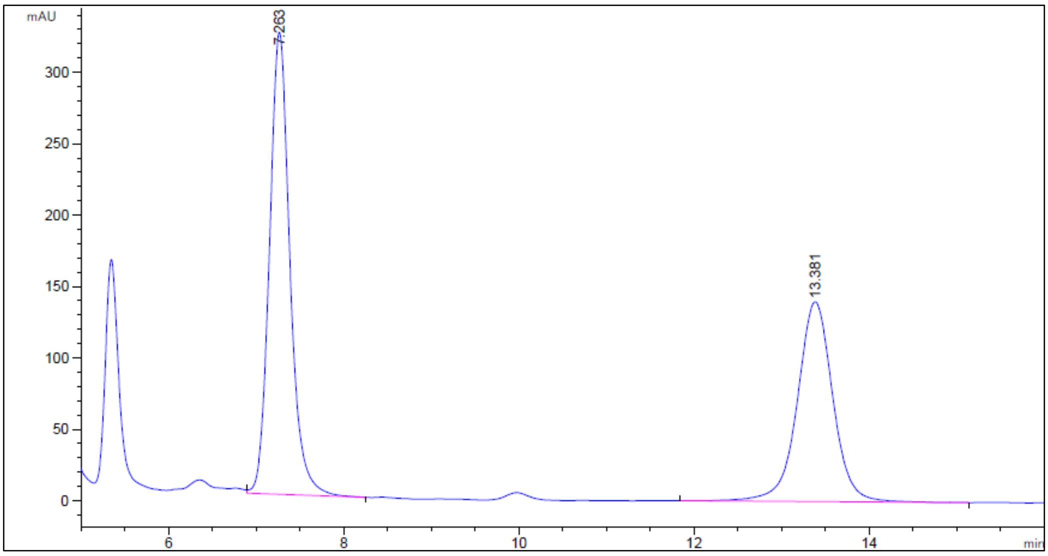
HPLC trace of 3i.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width      Area       Height      Area
  #    [min]        [min]   [mAU*s]      [mAU]        %
----|--------|----|-------|----------|----------|--------|
   1  49.345 VB    1.2353 6453.86865   74.89473  99.2234
   2  52.923 MM    0.8715   50.51263 9.65973e-1   0.7766
```

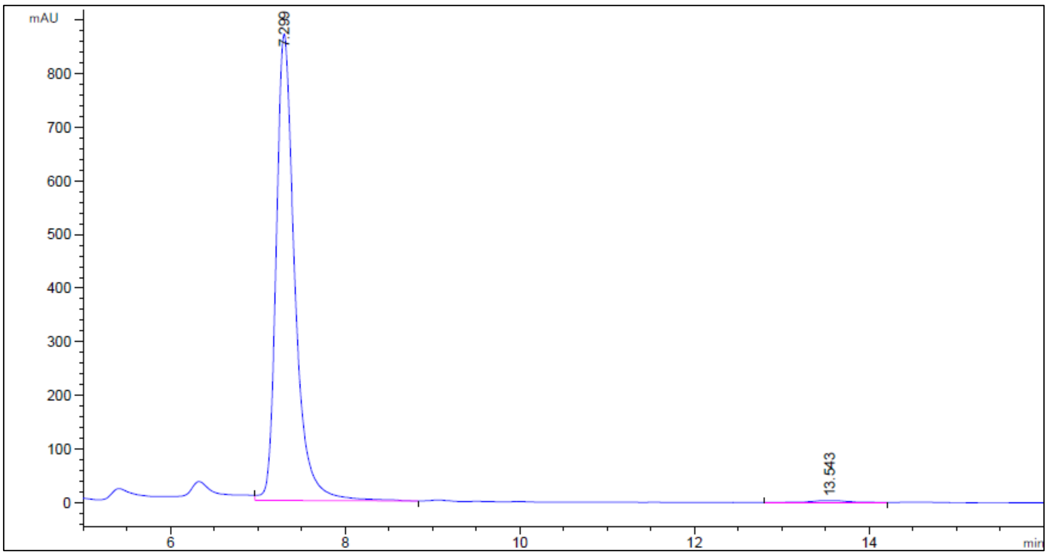
HPLC trace of *rac*-3j.



```
Signal 1: VWD1 A, Wavelength=210 nm

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]  mAU    *s   [mAU    ]     %
----|-------|----|-------|----------|----------|--------|
   1   7.263 VB    0.2460 5246.13672  323.38766 56.9965
   2  13.381 BB    0.4307 3958.18384  139.83783 43.0035
```

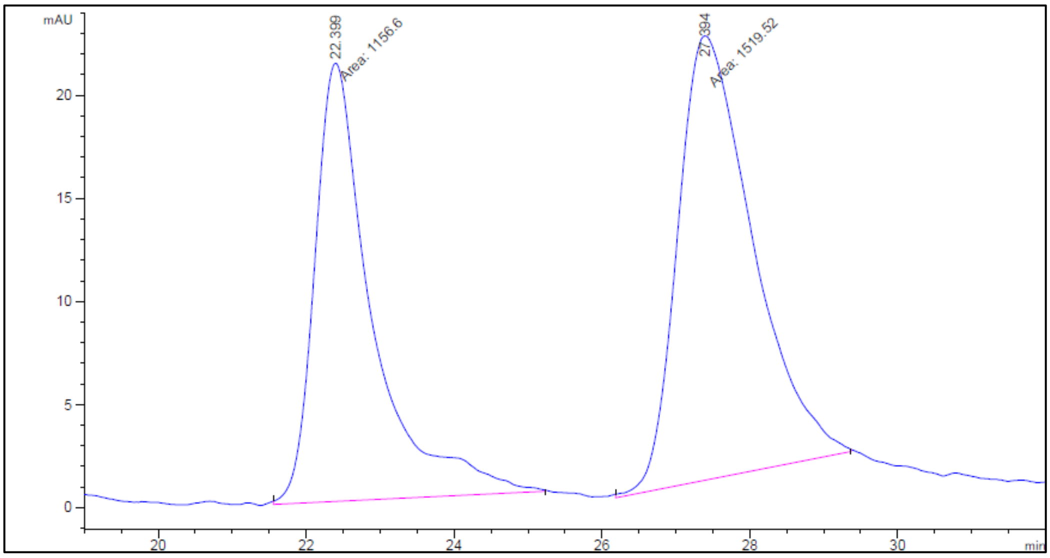
HPLC trace of *rac*-3j.



```
Signal 1: VWD1 A, Wavelength=210 nm

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]  mAU    *s   [mAU    ]     %
----|-------|----|-------|----------|----------|--------|
   1   7.299 VB    0.2226 1.29193e4  870.70148 99.1623
   2  13.543 BB    0.4419  109.14244    3.87762  0.8377
```

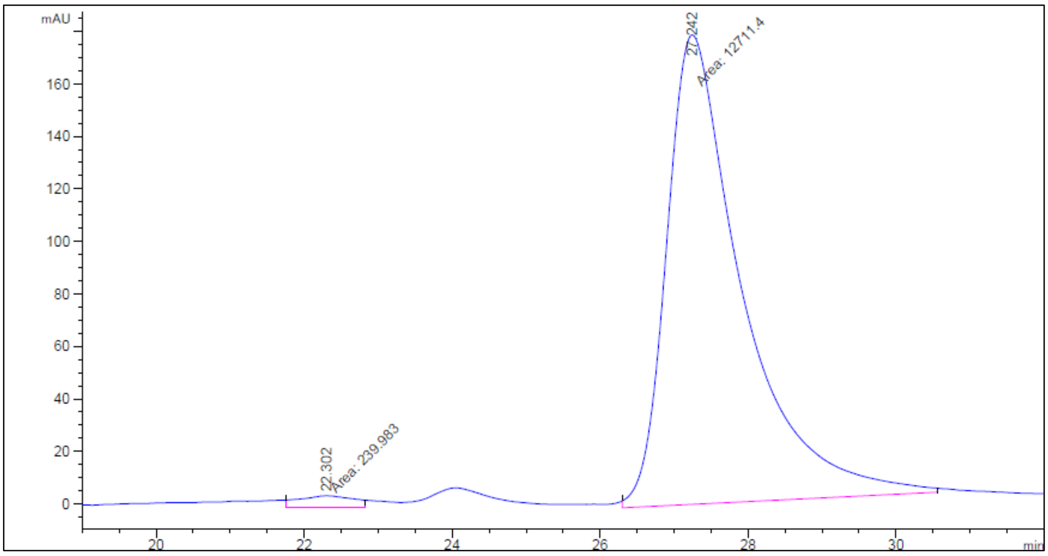
HPLC trace of *rac*-3k.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area       Height      Area
  #    [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  22.399 MM     0.9070 1156.59644   21.25306  43.2192
   2  27.394 MM     1.1748 1519.51794   21.55719  56.7808
```

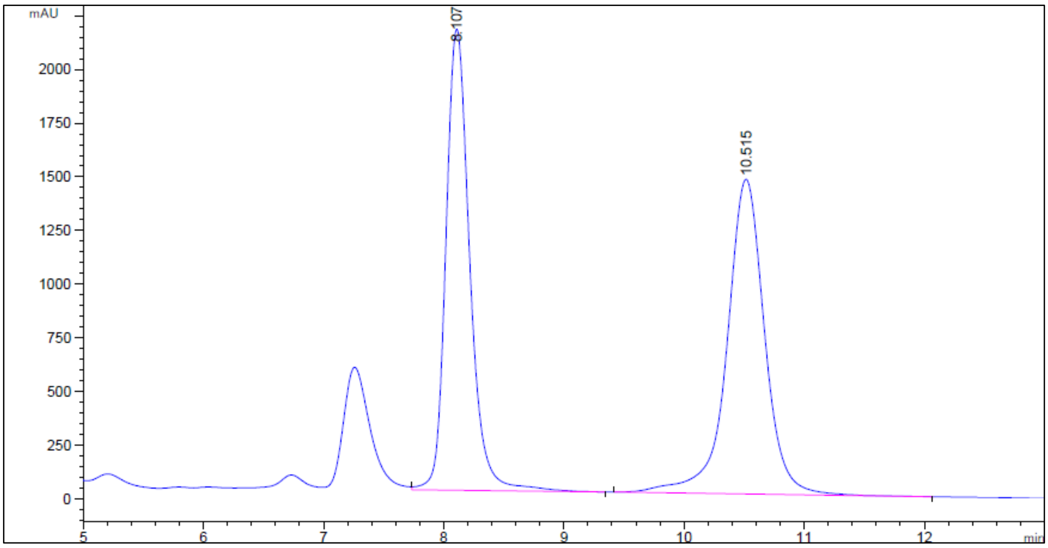
HPLC trace of 3k.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area       Height      Area
  #    [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  22.302 MM     0.8682  239.98329    4.60683   1.8530
   2  27.242 MM     1.1844 1.27114e4   178.87932  98.1470
```

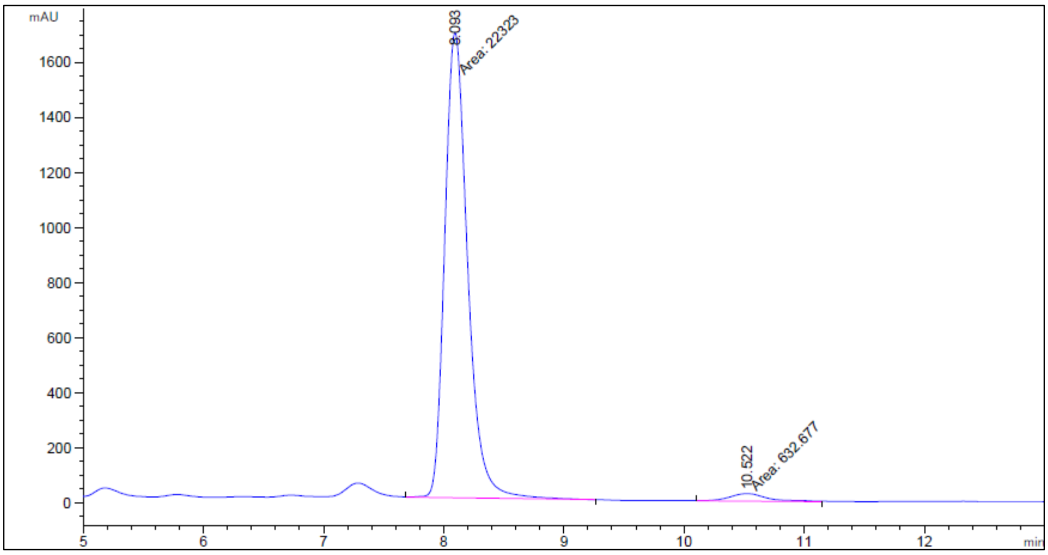
HPLC trace of *rac*-3l.



```
Signal 1: VWD1 A, Wavelength=210 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU    *s   [mAU    ]     %
----|-------|----|-------|----------|----------|--------|
   1   8.107 VB    0.2120 2.96724e4 2150.11060  48.1133
   2  10.515 BB    0.3302 3.19996e4 1467.02209  51.8867
```

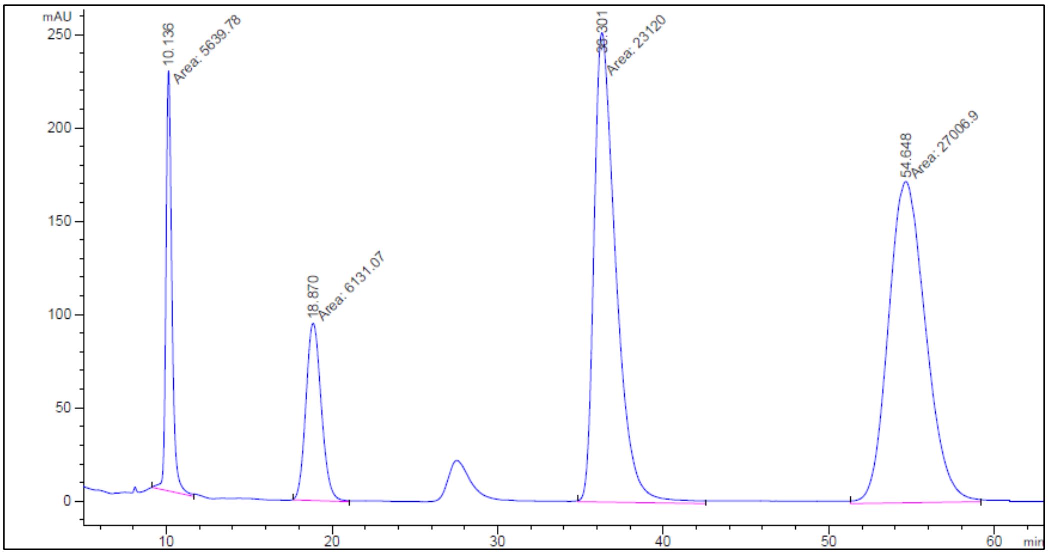
HPLC trace of 3l.



```
Signal 1: VWD1 A, Wavelength=210 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU    *s   [mAU    ]     %
----|-------|----|-------|----------|----------|--------|
   1   8.093 MM    0.2201 2.23230e4 1690.71277  97.2439
   2  10.522 MM    0.3757  632.67700   28.06989   2.7561
```

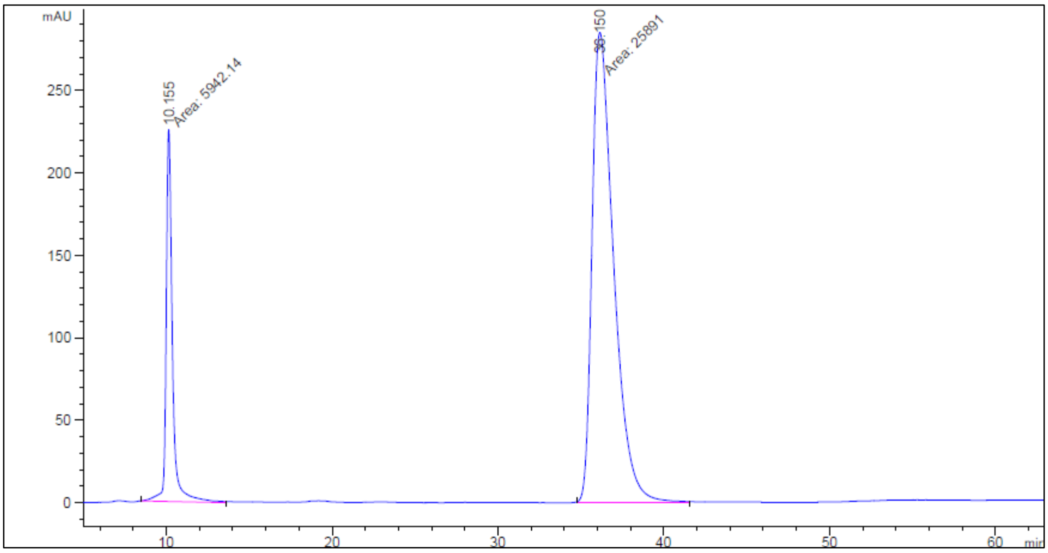
HPLC trace of *rac*-red-3m.



```
Signal 1: MWD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.136 MM    0.4178 5639.77881  224.97307   9.1114
   2  18.870 MM    1.0762 6131.07275   94.94581   9.9052
   3  36.301 MM    1.5329 2.31200e4   251.37956  37.3519
   4  54.648 MM    2.6160 2.70069e4   172.06026  43.6315
```

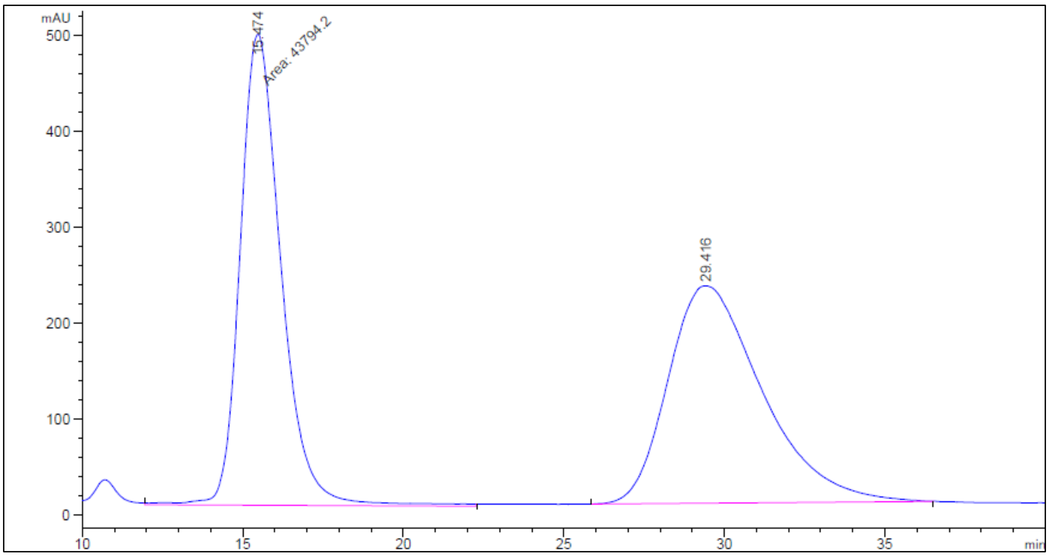
HPLC trace of red-3m.



```
Signal 1: MWD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.155 MM    0.4389 5942.14307  225.65591  18.6665
   2  36.150 MM    1.5129 2.58910e4   285.22424  81.3335
```

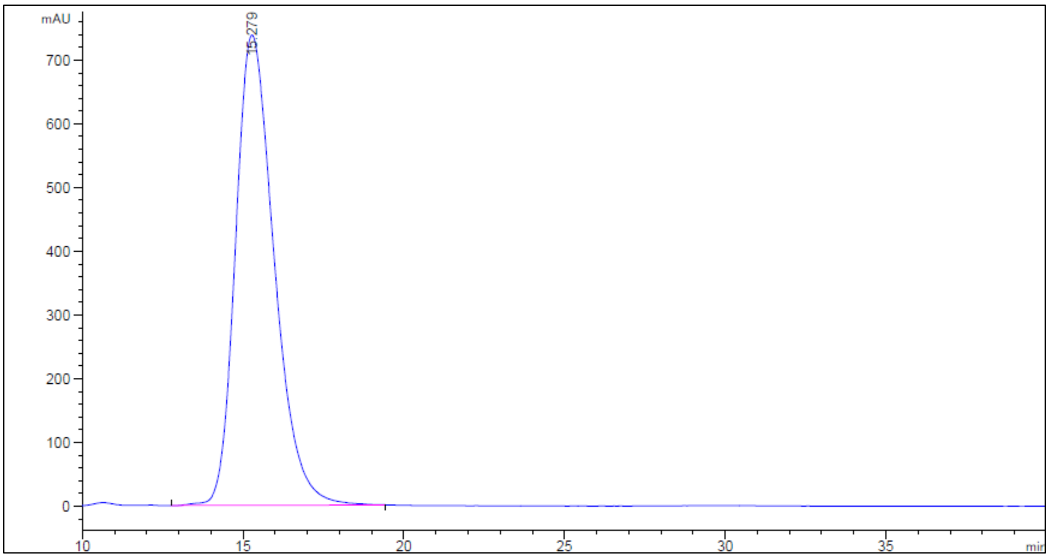
HPLC trace of *rac*-red-3n.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  15.474 MM    1.4852 4.37942e4  491.45636  48.6330
   2  29.416 BB    2.6569 4.62562e4  226.85381  51.3670
```

HPLC trace of red-3n.



```
Signal 1: MWD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  15.279 VB    1.2879 6.18549e4  737.92737 100.0000
```