The Cinchona Primary Amine-Catalyzed Asymmetric Epoxidation and Hydroperoxidation of α,β-Unsaturated Carbonyl Compounds with Hydrogen Peroxide

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General Information

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All solvents used in the reactions were distilled from appropriate drying agents prior to use. Reactions were monitored by thin layer chromatography on silica gel pre-coated plastic sheets (0.2 mm, Machery-Nagel). Visualization was accomplished by irradiation with UV light at 254 nm and/or p-anisaldehyde stain (0.7 mL p-anisaldehyde, 250 mL EtOH, 9.5 mL conc. H₂SO₄, 2.7 mL glacial AcOH) or potassium permanganate stain (1.5 g KMnO₄, 10 g K₂CO₃, 1.25 mL 10% NaOH, 200 mL H₂O). Column chromatography was performed on Merck silica gel (60, particle size 0.040-0.063 mm). Proton and carbon NMR spectra were recorded on Bruker AV-600, Bruker AV-500, Bruker AV-400 or Bruker AV-300 spectrometer in deuterated solvent. Proton chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard (CDCl₃ δ 7.26). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet, c. m = centered multiplet, br = broad), coupling constants (Hz) and integration. ¹³C chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard (CDCl₃, δ 77.0). High resolution mass spectra were determined on a Bruker APEX III FTMS (7 T magnet). Infrared spectra were taken on a Perkin Elmer Spectrum 100 FTIR and are reported in reciprocal centimeters (cm⁻¹). Optical rotations were determined with Autopol IV polarimeter (Rudolph Research Analytical) at 589 nm and 25 °C. Data are reported as follows: [α]_λ^{temp}, concentration (c in g/100 mL), and solvent. The enantiomeric excesses were determined by GC or HPLC analysis employing a chiral stationary phase column specified in the individual experiment, by comparing the samples with the appropriate racemic mixtures. Diastereomeric ratios were determined by GC or ¹H NMR analysis of the crude reaction mixture.
Optimization of the Epoxide/Hydroperoxide Ratio in Acyclic Enones 2

Table 1. The effect of the acid co-catalysts (HX) and temperature on the peroxyhemiketal 3a to epoxide 4a ratio in the reaction of 3-decen-2-one (2a).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Acid co-catalyst (HX)</th>
<th>pKₐ (H₂O)</th>
<th>[mol%]</th>
<th>T [°C]</th>
<th>Conv. [%]</th>
<th>3a:4a</th>
<th>er(4a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>pTsOH • H₂O</td>
<td>-2.80</td>
<td>20</td>
<td>28</td>
<td>82 (48 h)</td>
<td>35:65</td>
<td>98:2</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>20</td>
<td>30</td>
<td>28</td>
<td>98 (48 h)</td>
<td>31:69</td>
<td>92.8</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>30</td>
<td>10</td>
<td>65</td>
<td>(48 h)</td>
<td>35:65</td>
<td>94.5:5.5</td>
</tr>
<tr>
<td>4</td>
<td>F₃C-</td>
<td>0.52</td>
<td>20</td>
<td>50</td>
<td>full (20 h)</td>
<td>57:43</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>5</td>
<td>F₃C-</td>
<td>0.52</td>
<td>20</td>
<td>32</td>
<td>full (24 h)</td>
<td>68:32</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>6</td>
<td>F₃C·</td>
<td>0.52</td>
<td>30</td>
<td>28</td>
<td>95 (24 h)</td>
<td>70:30</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>7</td>
<td>(TFA)</td>
<td>0.52</td>
<td>30</td>
<td>28</td>
<td>97 (48 h)</td>
<td>72:28</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>8</td>
<td>(TFA)</td>
<td>0.52</td>
<td>30</td>
<td>10</td>
<td>76 (48 h)</td>
<td>73:27</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>9</td>
<td>n.a.</td>
<td>20</td>
<td>32</td>
<td>97 (48 h)</td>
<td>69:31</td>
<td>&gt;99.5:0.5</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>F₃C·</td>
<td>3.07</td>
<td>20</td>
<td>32</td>
<td>44 (28 h)</td>
<td>n.d.</td>
<td>99.5:0.5</td>
</tr>
<tr>
<td>11</td>
<td>F₃C·</td>
<td>3.07</td>
<td>20</td>
<td>32</td>
<td>full (24 h)</td>
<td>68:32</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>12</td>
<td>F₃C·</td>
<td>3.07</td>
<td>20</td>
<td>32</td>
<td>88 (48 h)</td>
<td>78:22</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>13</td>
<td>F₃C·</td>
<td>3.07</td>
<td>20</td>
<td>50</td>
<td>full (20 h)</td>
<td>60:40</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>14</td>
<td>Cl₃C·</td>
<td>0.65</td>
<td>20</td>
<td>32</td>
<td>full (24 h)</td>
<td>70:30</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>15</td>
<td>Cl₃C·</td>
<td>0.65</td>
<td>20</td>
<td>28</td>
<td>97 (48 h)</td>
<td>72:28</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>16</td>
<td>Cl₃C·</td>
<td>0.65</td>
<td>20</td>
<td>20</td>
<td>90 (48 h)</td>
<td>75:25</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>17</td>
<td>Cl₃C·</td>
<td>0.65</td>
<td>20</td>
<td>10</td>
<td>79 (48 h)</td>
<td>75:25</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>18</td>
<td>Cl₃C·</td>
<td>1.35</td>
<td>20</td>
<td>32</td>
<td>84 (48 h)</td>
<td>77:23</td>
<td>&gt;99.5:0.5</td>
</tr>
<tr>
<td>Entry</td>
<td>Acid</td>
<td>(\text{pK}_a (\text{H}_2\text{O}))^a</td>
<td>[mol%]</td>
<td>T [° C]</td>
<td>Conv. [%]^b</td>
<td>(3\text{a}:4\text{a})^c</td>
<td>(\text{er}(4\text{a}))^d</td>
</tr>
<tr>
<td>-------</td>
<td>-----------------</td>
<td>----------------------------------------</td>
<td>---------</td>
<td>---------</td>
<td>-------------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>23</td>
<td>PhCO_2H</td>
<td>4.20</td>
<td>20</td>
<td>28</td>
<td>15</td>
<td>n.d.</td>
<td>95.5:4.5</td>
</tr>
<tr>
<td>19</td>
<td>HOAc</td>
<td>4.76</td>
<td>20</td>
<td>28</td>
<td>&lt;10</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>20</td>
<td>EtCO_2H</td>
<td>4.87</td>
<td>20</td>
<td>28</td>
<td>&lt;10</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>21</td>
<td>i-PrCO_2H</td>
<td>n.a.</td>
<td>20</td>
<td>28</td>
<td>&lt;10</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>22</td>
<td>2,4-(NO_2)_2-C_6H_4CO_2H</td>
<td>2.17¹</td>
<td>20</td>
<td>32</td>
<td>98% (48 h)</td>
<td>75:25</td>
<td>99.5:0.5</td>
</tr>
<tr>
<td>24</td>
<td>4-NO_2-C_6H_4CO_2H</td>
<td>3.44</td>
<td>20</td>
<td>32</td>
<td>45 (28 h)</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>25</td>
<td>2,6-F_2-C_6H_4CO_2H</td>
<td>n.a.</td>
<td>20</td>
<td>32</td>
<td>52 (28 h)</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>26</td>
<td>3,5-(CF_3)_2-C_6H_4CO_2H</td>
<td>n.a.</td>
<td>20</td>
<td>32</td>
<td>43 (28 h)</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>29</td>
<td>(PhO)_2PO(OH)</td>
<td>1.29º</td>
<td>20</td>
<td>32</td>
<td>96 (24 h)</td>
<td>64:36</td>
<td>99.5:0.5</td>
</tr>
</tbody>
</table>

\(^a\)The \(\text{pK}_a\) values are adopted from the \(\text{pK}_a\) compilations of Williams and Bordwell (http://www.chem.wisc.edu/areas/reich/pkatable/). \(^b\)Determined by GC. \(^c\)Determined by \(^1\)H NMR of the crude mixture. \(^d\)Determined by chiral GC. \(^e\)Extensive side product formation observed. \(^f\)\(\text{pK}_a\) of 2-NO_2-C_6H_4CO_2H \(^g\)\(\text{pK}_a\) of (MeO)_2PO(OH).

**Table 2.** The effect of the water content (hydrogen peroxide concentration) on the peroxyhemiketal 3a to epoxide 4a ratio in the reaction of 3-decen-2-one (2a).

\[
\begin{array}{cccccc}
\hline
\text{Entry} & \text{H}_2\text{O}_2 \text{ equiv.} & \text{H}_2\text{O}_2 \text{ conc. [wt\%]} & \text{Conv. [%]}^a & \text{3a:4a ratio}^b & \text{er}(4a)^c \\
\hline
1 & 1.2 & 50 & \text{full (24 h)} & 65:35 & >99.5:0.5 \\
2 & 1.5 & 50 & \text{full (24 h)} & 70:30 & >99.5:0.5 \\
3 & 2 & 50 & \text{full (24 h)} & 71:29 & >99.5:0.5 \\
4 & 5 & 50 & \text{full (24 h)} & 76:24 & 99.5:0.5 \\
5 & 1.5 & 30 & \text{full (24 h)} & 76:24 & >99.5:0.5 \\
6¹ & 1.5 & 30 & \text{full (36 h)} & 77:23 & >99.5:0.5 \\
7 & 3 & 30 & \text{full (24 h)} & 80:20 & >99.5:0.5 \\
8 & 1.5 & 25 & \text{full (30 h)} & 78:22 & >99.5:0.5 \\
9 & 3 & 25 & \text{full (30 h)} & 81:19 & 99.5:0.5 \\
10 & 1.5 & 10 & 79 (6 d) & 78:22 & 99:1 \\
11 & 1.5 & 5 & 57 (6 d) & n.d. & 98:2 \\
\hline
\end{array}
\]

\(^a\)Determined by GC. \(^b\)Determined by \(^1\)H NMR of the crude mixture. \(^c\)Determined by chiral GC. \(^e\)At 28 °C.
Table 3. The effect of time on the peroxyhemiketal 3a to epoxide 4a ratio in the reaction of 3-decen-2-one (2a).

<table>
<thead>
<tr>
<th>Entry</th>
<th>t [h]</th>
<th>Conv. [%]</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.5</td>
<td>42</td>
<td>71:29</td>
</tr>
<tr>
<td>2</td>
<td>24</td>
<td>97</td>
<td>72:28</td>
</tr>
<tr>
<td>3</td>
<td>28</td>
<td>full</td>
<td>72:28</td>
</tr>
<tr>
<td>4</td>
<td>10 d</td>
<td>full</td>
<td>66:34</td>
</tr>
</tbody>
</table>

* Determined by 1H NMR of the crude mixture.

Synthetic Procedures and Spectral Data

Catalyst Synthesis

9-Amino(9-deoxy)epiquinine (1a)

Quinine (6.48 g, 20.0 mmol) and triphenylphosphine (6.30 g, 24.0 mmol, 1.2 equiv) were dissolved in THF (100 mL) and the solution was cooled to 0 °C. Then diisopropyl azodicarboxylate (4.64 mL, 24.0 mmol, 1.2 equiv) was added all at once followed by the dropwise addition of a solution of diphenyl phosphoryl azide (5.16 mL, 24.0 mmol, 1.2 equiv) in THF (40 mL). Then the reaction mixture was allowed to warm to room temperature, stirred overnight (12 h), and the resulting solution was further heated to 50 °C for additional 2 h. Next, triphenylphosphine (6.82 g, 26.0 mmol, 1.3 equiv) was added.

and the heating (50 °C) was maintained until the gas evolution has ceased (3 h). Then, the solution was cooled to room temperature, and water (2 mL) was added. After stirring for 12 h, the solvents were removed under reduced pressure, and the residue was extracted with CH₂Cl₂ and 10% aqueous HCl (1:1, 200 mL). The phases were separated, and the aqueous phase was repeatedly washed with CH₂Cl₂ (4 × 100 mL). Then, the aqueous phase was made alkaline with excess aqueous ammonia at 0 °C and subsequently extracted with CH₂Cl₂ (4 × 100 mL). The combined organic phases were dried (Na₂SO₄), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, methanol/EtOAc 50:50 with 1% aq. NH₄OH) affording the title compound as a white semi-solid (4.93 g, 15.3 mmol, 76%). The analytical data were identical in all respects to those previously reported.

¹H NMR (400 MHz, CDCl₃) δ 8.73 (d, J = 4.5 Hz, 1H, CH₂'), 8.01 (d, J = 9.2 Hz, 1H, CH²'), 7.64 (br s, 1H, CH³'), 7.43 (br d, J = 4.2 Hz, 1H, CH³'), 7.36 (dd, J = 9.1, 2.8 Hz, 1H, CH⁴'), 5.78 (ddd, J = 17.3, 10.1, 7.3 Hz, 1H, CH=CH₂), 5.00-4.93 (m, 2H, CH=C₃H₂), 4.57 (br d, J = 9.7 Hz, 1H, CH⁹NH₂), 3.94 (s, 3H, OCH₃), 3.26 (dd, J = 13.8, 10.0 Hz, 1H, CHH₁), 3.21-3.15 (m, 1H, CH₂H₆), 3.11-3.02 (m, 1H, CH₈), 2.82-2.75 (m, 2H, CHH₅ and CHH₆), 2.30-2.23 (m, 1H, CHH¹), 1.94 (br s, 2H, NH₂), 1.62-1.58 (m, 1H, CH¹), 1.57-1.50 (m, 2H, CH₂⁵), 1.45-1.36 (m, 1H, CHH⁷), 0.75 (ddt, J = 13.6, 7.5, 1.9 Hz, 1H, CHH⁷).

¹³C NMR (100 MHz, CDCl₃) δ 157.6 (Cq⁶OMe), 147.8 (C²H), 147.0 (Cq), 144.7 (Cq), 141.7 (CH=CH₂), 131.8 (C₄H), 128.7 (Cq⁴s), 121.2 (C³H), 119.9 (C⁵H), 114.3 (CH=CH₂), 102.0 (C⁵H), 61.9 (C⁶H), 56.3 (C₃H₂), 55.5 (OCH₃), 52.5 (C⁹HNH₂), 40.9 (C⁴H₂), 39.8 (C³H), 28.2 (C⁵H₂), 27.5 (C⁴H), 26.0 (C³H₂).

MS (El-DE) m/z (%) 323 [M⁺] (2), 199 (1), 187 (15), 160 (2), 136 (100), 108 (6), 95 (3), 82 (8), 70 (5), 56 (4), 42 (4).


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9-Amino(9-deoxy)epiquinidine (1b): Amine 1b was prepared starting from quinidine (1.95 g, 6.0 mmol) following the same procedure described for the synthesis of 9-amino(9-deoxy)epiquinine (1a). After hydrolyzing the reaction overnight (12 h), the solvents were removed under reduced pressure, and the residue was extracted with CH₂Cl₂ and 10% aqueous HCl (1:1, 200 mL). The phases were separated, the aqueous phase was concentrated in vacuo, and the residue was crystallized from methanol. The white precipitate was collected and dissolved in water. Then the aqueous phase was made alkaline by the addition of K₂CO₃, and repeatedly extracted with CH₂Cl₂ (3 × 50 mL). The combined organic phases were dried (Na₂SO₄) and evaporated under reduced pressure affording the pure title compound (820 mg, 2.54 mmol, 42%) as a pale yellow viscous oil.

**¹H NMR** (400 MHz, CDCl₃) δ 8.72 (d, J = 4.6 Hz, 1H, CH₂'), 8.00 (d, J = 9.1 Hz, 1H, CH₆'), 7.60 (br s, 1H, CH₅'), 7.50 (br s, 1H, CH₃'), 7.34 (dd, J = 9.2, 2.7 Hz, 1H, CH₅'), 5.86 (ddd, J = 17.0, 10.6, 6.4 Hz, 1H, CH=CH₂), 5.07-5.01 (m, 2H, CH=C₃H₂), 4.64 (br d, J = 9.1 Hz, 1H, CH₅NH₂), 3.94 (s, 3H, OCH₃), 3.04-2.88 (m, 5H, C₃H₈, C₅H₂, and C₆H₂), 2.24 (app. br q, J = 8.0 Hz, 1H, CH₃), 2.02 (br s, 2H, NH₂), 1.60-1.56 (m, 1H, CH₃), 1.54-1.48 (m, 2H, CH₅'), 1.11 (dd, J = 13.4, 8.8 Hz, 1H, CHH₃), 0.96-0.88 (m, 1H, CHH₃).

**¹³C NMR** (100 MHz, CDCl₃) δ 157.6 (Cq₆OMe), 147.8 (C₂H), 147.5 (Cq), 144.7 (Cq), 140.7 (CH=CH₂), 131.8 (C₅H), 128.7 (C₄H), 121.6 (C₃H), 119.9 (C₃H), 114.4 (CH=CH₂), 101.4 (C₅H), 62.4 (C₄H), 55.4 (OCH₃), 51.6 (CH₅NH₂), 49.5 (C₆H₂), 47.4 (C₃H₂), 39.4 (C₃H), 27.6 (C₄H), 26.7 (C₅H₂), 25.0 (C₇H₂).

**MS** (EI-DE) m/z (%) 323 [M⁺] (63), 306 (10), 282 (3), 265 (2), 240 (2), 200 (8), 187 (100), 160 (11), 137 (67), 122 (11), 108 (33), 95 (10), 82 (43), 70 (15), 56 (11), 42 (7).

**HRMS** (ESI+) calcd for C₂₀H₂₆N₃O [(M+H)+] 324.2067, found 324.2070.

(S)-(6-methoxy-2-phenylquinolin-4-yl)((2S, 4S, 8R)-8-vinylquinuclidin-2-yl)methanamine (1c): Amine 1a (220 mg, 0.680 mmol) was suspended in dry tBuOMe (8 mL) and cooled to -10 °C in an ice/EtOH bath. Phenyllithium (3.40 mmol, 5 equiv) was added to this solution and the reaction mixture was stirred for 1 h, then warmed to r.t. and stirred for 5 h. The reaction
was quenched with HOAc (440 µL) at 0 °C, followed by the addition of water (10 mL) and EtOAc (10 mL). Then iodine (340 mg) was added and mixture was stirred for 10 min, and a solution of sodium metabisulfite (130 mg in 5 mL water) was added. The mixture was basified with ammonia (20% solution in water, 4.8 mL) and then the organic layer was washed with water. The aqueous phase was extracted with CH2Cl2 (20 mL x 3). The collected organic phases were dried over anhydrous MgSO4, filtrated, evaporated under reduced pressure. Purification by column chromatography (EtOAc/MEOH/aq NH4OH = 9/1/0.1) afforded the title compound in 61% yield.

**1H NMR** (500 MHz, CDCl3) δ 8.11-8.16 (m, 3H), 7.99 (br s, 1H), 7.71 (br s, 1H), 7.51-7.54 (m, 2H), 7.39-7.46 (m, 2H), 5.76-5.83 (m, 1H), 4.95-5.02 (m, 2H), 4.68 (br s, 1H), 3.99 (s, 3H), 3.16-3.33 (m, 3H), 2.83-2.85 (m, 2H), 2.30 (br s, 1H), 2.05 (br s, 2H), 1.59-1.64 (m, 2H), 1.45 (m, 1H), 0.84-0.88 (m, 3H, CH2CH3).

**13C NMR** (125 MHz, CDCl3) δ 157.5, 154.9, 144.9, 141.7, 139.8, 132.2, 129.0, 128.8, 127.3, 121.3, 114.4, 60.4, 60.4, 56.3, 55.6, 53.4, 41.0, 39.8, 28.2, 27.6, 26.0, 21.1, 14.2.

**HRMS** (ESI+) m/z calcd for C26H30N3O1 [(M+H)+] 400.2383, found 400.2383.

**9-Amino(9-deoxy)epi-cinchonidine (1d):** Amine 1d was prepared starting from cinchonidine (1.77 g, 6.0 mmol) following the same procedure described for the synthesis of 9-amino(9-deoxy)epiquinine (1a). Purification by flash column chromatography (silica gel, methanol/EtOAc 50:50 with 1% aq. NH4OH) gave the title compound as colorless viscous oil (1.23 g, 4.19 mmol, 70%).

**1H NMR** (400 MHz, CDCl3) δ 8.87 (d, J = 4.6 Hz, 1H, CH=CH2), 8.33 (br s, 1H, CH=CH2), 8.11 (dd, J = 8.6, 0.8 Hz, 1H, CH2=CH), 7.68 (dd, J = 8.3, 6.9, 1.3 Hz, 1H, CH3), 7.56 (ddd, J = 8.5, 6.9, 1.3 Hz, 1H, CH=CH2), 7.49 (br d, J = 4.1 Hz, 1H, CH=CH2), 5.77 (ddd, J = 17.2, 10.1, 7.3 Hz, 1H, CH=CH2), 4.99-4.91 (m, 2H, CH=CH2), 4.67 (br d, J = 9.1, 1H, CH2=CH2), 3.24 (dd, J = 13.9, 10.1 Hz, 1H, CHH2), 3.20-3.13 (m, 1H, CHH), 3.04 (app. br q, J = 8.7 Hz, 1H, CH=CH2), 2.81-2.73 (m, 2H, CHH2 and CHH), 2.27-2.21 (m, 1H, CH3), 2.01 (br s, 2H, NH2), 1.59-1.50 (m, 3H, CH4 and CH5), 1.38 (app. br t, J = 11.6 Hz, 1H, CHH), 0.71 (ddt, J = 13.6, 7.5, 1.9 Hz, 1H, CHH).

**13C NMR** (100 MHz, CDCl3) δ 150.3 (C2H), 148.7 (Cq4), 148.6 (Cq8), 141.8 (CH=CH2), 130.4 (CH3H), 128.9 (C5H), 127.8 (Cq4), 126.4 (C6H), 123.3 (Cq5H), 119.6 (Cq3H), 114.2 (CH=CH2), 61.9
Catalytic Asymmetric Hydroperoxidation of Acyclic Enones 2

General Procedure

Catalyst salt [1a • 2 TCA] was prepared in situ by the addition of 9-amino(9-deoxy)epiquinine (1a; 32.3 mg, 0.1 mmol, 10 mol%) to a solution of trichloroacetic acid (32.6 mg, 0.2 mmol, 20 mol%) in dioxane (4 mL). Then, enone 2 (1.0 mmol, 1.0 equiv) was added, and 20 minutes later, aqueous hydrogen peroxide (30 wt%, 304 μL, 3.0 mmol, 3 equiv). After 20-48 h of stirring at 32°C, the reaction mixture was extracted with Et2O (3 × 25 mL) and the combined organic phases were washed with brine, dried (Na2SO4), filtered, and concentrated in vacuo. The crude product was subjected to flash column chromatography (silica gel, eluent: Et2O-pentane) to afford the corresponding pure peroxyhemiketal 3. The optical purity was determined after converting the peroxyhemiketal to the corresponding epoxide (with 1N NaOH (1 equiv) in Et2O) or to the corresponding aldol-type product (with triethylphosphite (2 equiv) in Et2O).

Scope of Optically Active 3-Hydroxy-1,2-dioxolanes 3

(5R)-5-Hexyl-3-methyl-1,2-dioxolan-3-ol ((5R)-3a): Peroxyhemiketal 3a was prepared according to the general procedure. The reaction mixture was stirred for 36 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 5-10% Et2O in pentane) provided the title compound 3a as a colorless oil (123 mg, 653 μmol, 65%; 98.5:1.5 er). The enantiomeric ratio was determined after converting
peroxyhemiketal 3a into the corresponding epoxide 4a. The enantiomers were analyzed by GC using a chiral BGB-176/SE-52 column 29.5 m (80 °C, 1.2 °C/min until 115 °C, 18 °C/min until 220 °C, 10 min at 220 °C, 0.6 bar H2); major enantiomer: $\tau_R = 24.41$ min, minor enantiomer: $\tau_R = 26.10$ min.

**Characterized as mixture of hemiketal epimers (1:1 dr).**

$^1$H NMR (500 MHz, CD$_2$Cl$_2$) $\delta$ 4.41-4.36 (m, 1H), 4.31-4.26 (m, 1H), 2.96 (br s, 2H), 2.77-2.72 (m, 1H), 2.69-2.65 (m, 1H), 2.26-2.18 (m, 2H), 1.72-1.55 (m, 4H), 1.52 (s, 3H), 1.51 (s, 3H), 1.47-1.35 (m, 2H), 1.34-1.24 (m, 14H), 0.89-0.87 (m, 6H).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) $\delta$ 105.9, 105.0, 82.7, 81.3, 53.1, 52.8, 35.2, 32.6, 32.3, 32.2, 29.8, 29.7, 26.7, 26.5, 23.4, 23.1, 22.9, 14.4, 14.4.

**MS** (EI-DE) m/z (%) 188 [M$^+$] (1), 155 (56), 137 (3), 113 (8), 95 (7), 81 (5), 71 (63), 55 (14), 43 (100), 29 (12).

**HRMS** (EI-FE) calcd for C$_{10}$H$_{20}$O$_3$ [M$^+$] 188.1413, found 188.1412.

**5R**-3-Methyl-5-phenethyl-1,2-dioxolan-3-ol (5R)-3b: Peroxyhemiketal 3b was prepared according to the general procedure. The reaction mixture was stirred for 36 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 5-40% Et$_2$O in pentane) provided the title compound 3b as a colorless oil (141 mg, 677 μmol, 68%; 97:3 er). The enantiomeric ratio was determined after converting peroxyhemiketal 3b into the corresponding epoxide 4b. The enantiomers were analyzed by GC using a chiral BGB-176/BGB-15 column 30 m (80 °C, 1.2 °C/min until 145 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.6 bar H$_2$); major enantiomer: $\tau_R = 46.17$ min, minor enantiomer: $\tau_R = 47.42$ min. The absolute configuration of 3b was assigned by converting it to the corresponding aldol product 16b and comparing its optical rotation to the literature value (cf. characterization of 16b). The absolute configuration of all other peroxyhemiketals was assigned by analogy. **Characterized as mixture of hemiketal epimers (1:1 dr).**

$^1$H NMR (500 MHz, CD$_2$Cl$_2$) $\delta$ 7.30-7.27 (m, 4H), 7.21-7.18 (m, 6H), 4.43-4.37 (m, 1H), 4.34-4.28 (m, 1H), 2.94-2.93 (m, 2H), 2.80-2.61 (m, 6H), 2.30-2.22 (m, 2H), 2.06-1.97 (m, 2H), 1.95-1.88 (m, 1H), 1.77-1.70 (m, 1H), 1.54 (s, 3H), 1.51 (s, 3H).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) $\delta$ 142.0, 141.8, 129.0, 129.0, 128.9, 128.9, 126.6, 126.5, 106.0, 105.0, 81.8, 80.5, 52.9, 52.8, 37.0, 34.5, 32.9, 32.7, 23.4, 22.8.
MS (EI-DE) m/z (%) 208 [M⁺] (trace), 190 (3), 174 (10), 159 (2), 148 (2), 131 (15), 117 (21), 104 (93), 91 (100), 87 (7), 77 (15), 65 (14), 58 (4), 51 (9), 43 (77), 39 (76).

HRMS (CI-FE, i-butane) calcd for C₁₂H₁₇O₃ [M+H]⁺ 209.1175, found 209.1178.

(5R)-5-Isobutyl-3-methyl-1,2-dioxolan-3-ol ((5R)-3c): Peroxyhemiketal 3c was prepared according to the general procedure. The reaction mixture was stirred for 36 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 5-30% Et₂O in pentane) provided the title compound 3c as a colorless oil (98 mg, 612 µmol, 61%; 97.5:2.5 er). The enantiomeric ratio was determined after converting peroxyhemiketal 3c into the corresponding epoxide 4c. The enantiomers were analyzed by GC using a chiral BGB-176/BGB-15 column 30 m (60 °C, 0.8 °C/min until 80 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.6 bar H₂); major enantiomer: τᵣ = 15.10 min, minor enantiomer: τᵣ = 17.20 min. Characterized as mixture of hemiketal epimers (1:1 dr).

¹H NMR (500 MHz, CD₂Cl₂) δ 4.53-4.47 (m, 1H), 4.39-4.33 (m, 1H), 3.03-2.98 (m, 2H), 2.79-2.75 (m, 1H), 2.71-2.67 (m, 1H), 2.25-2.21 (m, 1H), 2.20-2.17 (m, 1H), 1.73-1.56 (m, 4H), 1.53 (s, 3H), 1.51 (s, 3H), 1.50-1.44 (m, 1H), 1.30-1.25 (m, 1H), 0.93-0.90 (m, 12H).

¹³C NMR (125 MHz, CD₂Cl₂) δ 105.9, 104.9, 81.3, 79.7, 53.7, 53.2, 44.1, 41.7, 26.6, 26.1, 23.5, 23.3, 23.2, 22.9, 22.8, 22.5.

MS (EI-DE) m/z (%) 160 [M⁺]² (2), 135 (0.09), 127 (39), 109 (10), 95 (3), 85 (12), 77 (1), 71 (96), 69 (14), 57 (23), 43 (100), 41 (25), 29 (18).


(5S)-5-Cyclohexyl-3-methyl-1,2-dioxolan-3-ol ((5S)-3d): Peroxyhemiketal 3d was prepared according to the general procedure. The reaction mixture was stirred for 48 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 5-30% Et₂O in pentane) provided the title compound 3d as a colorless oil (101 mg, 542 µmol, 54%; 98:2 er). The enantiomeric ratio was determined after converting peroxyhemiketal 3d into the corresponding epoxide 4d. The enantiomers were analyzed by GC using a chiral BGB-176/SE-52 column 29.5 m (80 °C, 1.2 °C/min until 130 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H₂); major enantiomer: τᵣ = 32.73 min, minor enantiomer: τᵣ = 33.99 min. Characterized as mixture of
hemiketal epimers (1:1 dr).

$^1$H NMR (500 MHz, CD$_2$Cl$_2$) δ 4.11-4.06 (m, 1H), 4.05-4.00 (m, 1H), 3.00 (br s, 2H), 2.68-2.64 (m, 1H), 2.60-2.56 (m, 1H), 2.34-2.28 (m, 2H), 1.91-1.86 (m, 1H), 1.83-1.79 (m, 1H), 1.75-1.53 (m, 10H), 1.52 (s, 3H), 1.50 (s, 3H), 1.31-1.12 (m, 6H), 1.08-0.90 (m, 4H).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) δ 105.8, 105.0, 86.7, 85.2, 51.1, 50.3, 42.6, 41.2, 30.3, 29.9, 29.7, 29.3, 26.8, 26.7, 26.4, 26.3, 26.1, 26.0, 23.4, 22.6.

MS (EI-DE) m/z (%) 186 [M$^+$] (2), 153 (50), 135 (14), 125 (1), 111 (8), 95 (16), 83 (71), 71 (60), 67 (20), 55 (100), 43 (95), 29 (21).

HRMS (CI-FE, NH$_3$) calcd for C$_{10}$H$_{22}$NO$_3$ [M+NH$_4$]$^+$ 204.1598, found 204.1600.

(5R)-5-(3-Butenyl)-3-methyl-1,2-dioxolan-3-ol ((5R)-3e): Peroxyhemiketal 3e was prepared according to the general procedure. The reaction mixture was stirred for 36 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 5-30% Et$_2$O in pentane) provided the title compound 3e as a colorless oil (109 mg, 689 μmol, 69%; 97.5:2.5 er). The enantiomeric ratio was determined after converting peroxyhemiketal 3e into the corresponding aldol-type product 16e. The enantiomers were analyzed by HPLC using a chiral Chiralpak IA column (10% iPrOH/heptane, 0.5 mL/min); major enantiomer: $\tau_R = 13.19$ min, minor enantiomer: $\tau_R = 12.41$ min. Characterized as mixture of hemiketal epimers (1:1 dr).

$^1$H NMR (500 MHz, CD$_2$Cl$_2$) δ 5.86-5.77 (m, 2H), 5.07-5.02 (m, 2H), 5.00-4.96 (m, 2H), 4.44-4.39 (m, 1H), 4.34-4.28 (m, 1H), 3.10 (br s, 2H), 2.80-2.76 (m, 1H), 2.69-2.65 (m, 1H), 2.29-2.25 (m, 1H), 2.24-2.21 (m, 1H), 2.19-2.05 (m, 4H), 1.83-1.75 (m, 2H), 1.73-1.54 (m, 2H), 1.53 (s, 3H), 1.51 (s, 3H).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) δ 138.3, 138.1, 115.5, 115.4, 105.9, 105.0, 81.9, 80.6, 52.8, 52.7, 34.4, 31.9, 30.9, 30.7, 23.4, 22.8.

MS (EI-DE) m/z (%) 140 (trace), 125 (10), 107 (2), 97 (2), 83 (10), 71 (18), 55 (28), 43 (100), 41 (13), 29 (14).

HRMS (CI-FE, i-butane) calcd for C$_8$H$_{15}$O$_3$ [M+H]$^+$ 159.1020, found 159.1021.

(5R)-5-(3-Bromopropyl)-3-methyl-1,2-dioxolan-3-ol ((5R)-3f): Peroxyhemiketal 3f was prepared according to the general procedure. The reaction mixture was stirred for 24 h at
32 °C. Purification of the crude product by flash column chromatography (silica gel, 25-40% Et₂O in pentane) provided the title compound 3f as a colorless oil (81 mg, 360 μmol, 72%; 97:3 er). The enantiomeric ratio was determined after converting dioxolane 3f into the corresponding epoxide 4f. The enantiomers were analyzed by GC using a chiral BGB-176/BGB-15 column 30 m (100 °C, 1.2 °C/min until 135 °C, 18 °C/min until 220 °C, 5 min at 320 °C, 0.5 bar H₂); major enantiomer: τₚ = 19.07 min, minor enantiomer: τₚ = 20.64 min. Contains traces of (E)-7-chloro-3,4-epoxyheptan-2-one. Characterized as mixture of hemiketal epimers (1:1 dr).

¹H NMR (400 MHz, THF-d₈) δ 5.36 (s, 1H, OₐH), 5.33 (s, 1H, OₐH), 4.38-4.32 (m, 1H, CₗH), 4.25-4.18 (m, 1H, CₗH), 3.51-3.40 (m, 4H, CₗH₂Br), 2.68-2.64 (m, 1H, CₗH₂COH), 2.61-2.55 (m, 1H, CₗH₂COH), 2.22-2.17 (m, 1H, CₗH₂COH), 2.16-2.10 (m, 1H, CₗH₂COH), 2.00-1.80 (m, 4H, CₗH₂), 1.79-1.68 (m, 3H, CₗH₂), 1.63-1.54 (m, 1H, CₗH₂), 1.41 (s, 3H, CₗH₃), 1.39 (s, 3H, CₗH₃).

¹³C NMR (100 MHz, THF-d₈): δ 105.9 (Cₗq), 104.9 (Cₗq), 81.9 (CH), 80.7 (CH), 53.6 (COCH₂CO), 53.5 (COCH₂CO), 34.4 (CH₂), 34.4 (CH₂, 2C), 31.9 (CH₂), 31.0 (CH₂), 30.9 (CH₂), 24.6 (CH₃), 23.6 (CH₃).

(5R)-3-Methyl-5-(5-(tetrahydro-2H-pyran-2-yl oxy)pentyl)-1,2-dioxolan-3-ol ((5R)-3g):

Peroxyhemiketal 3g was prepared according to the general procedure. The reaction mixture was stirred for 36 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 30-40% Et₂O in pentane) provided the title compound 3g (87 mg, 318 μmol, 64%; 96.5:3.5 er) as a colorless oil. The enantiomeric ratio was determined after converting peroxyhemiketal 3g into the corresponding THP-deprotected epoxide 4k The enantiomers were analyzed by GC using a chiral Ivadex 1 column 25m (80 °C, 1.0 °C/min until 155 °C, 18 °C/min until 220 °C, 10 min at 320 °C, 0.6 bar H₂); major enantiomer: τₚ = 60.79 min, minor enantiomer: τₚ = 61.52 min. Characterized as mixture of diastereomers.

¹H NMR (400 MHz, THF-d₈) δ 5.30 (s, 2H, OₐH), 5.26 (s, 2H, OₐH), 4.53 (t, J = 3.2 Hz, 4H, CHO_H₃), 4.34-4.28 (m, 2H, CHH), 4.21-4.14 (m, 2H, CHH), 3.80-3.74 (m, 4H, OCH₃_H₃), 3.67 (dt, J = 9.5, 6.6 Hz, 4H, THPOCH₃H), 3.44-3.38 (m, 4H, OCH₃_H₃), 3.30 (dt, J = 9.5, 6.4 Hz, 4H, THPOCH₃H), 2.65-2.53 (m, 4H, CH₂C₉H₉OH), 2.18-2.07 (m, 4H, CH₂C₉H₉OH), 1.84-1.76 (m, 4H, CH₂), 1.65-1.42 (m, 40H, CH₂), 1.40 (s, 12H, CH₃), 1.38 (s, 12H, CH₃).
$^{13}$C NMR (100 MHz, THF-d8) $\delta$ 105.8 (2C, C$_{q}$OH), 104.9 (2C, C$_{q}$OH), 99.3 (4C, OCHO), 82.7 (2C, CH$_2$CHCH$_2$), 81.3 (2C, CH$_2$CHCH$_2$), 68.0 (4C, THPOCH$_2$), 62.3 (4C, OCH$_2$THP), 54.0 (2C, CH$_2$C$_{q}$OH), 53.6 (2C, CH$_2$C$_{q}$OH), 35.8 (2C, CH$_2$), 33.3 (2C, CH$_2$), 31.9 (4C, CH$_2$), 31.0 (2C, CH$_2$), 30.9 (2C, CH$_2$), 27.6 (2C, CH$_2$), 27.5 (2C, CH$_2$), 27.5 (2C, CH$_2$), 27.3 (2C, CH$_2$), 26.9 (4C, CH$_2$), 24.4 (2C, CH$_3$), 23.8 (2C, CH$_3$), 20.5 (4C, CH$_2$).

**MS** (El-DE) $m/z$ (%) 274 [M$^+$] (trace), 185 (2), 173 (1), 155 (1), 139 (1), 115 (1), 99 (6), 85 (100), 81 (9), 69 (9), 55 (13), 43 (38).

**HRMS** (ESI+) calcd for C$_{14}$H$_{26}$O$_5$Na [(M+Na)$^+$] 297.1670, found 297.1672.

(5R)-5-($\text{-}$tert-Butyldimethylsilyloxy)ethyl)-3-methyl-1,2-dioxolan-3-ol ((5R)-3h): Peroxyhemiketal 3h was prepared according to the general procedure. The reaction mixture was stirred for 36 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 15-20% Et$_2$O in pentane) provided the title compound as a colorless oil (89 mg, 340 μmol, 68%; 98:2 er). The enantiomeric ratio was determined after converting peroxyhemiketal 3h into the corresponding epoxide 4h. The enantiomers were analyzed by GC using a chiral BGB-176/BGB-15 column 30 m (80 °C, 1.2 °C/min until 150 °C, 18 °C/min until 220 °C, 5 min at 320 °C, 0.5 bar H$_2$); major enantiomer: $\tau_R$ = 34.84 min, minor enantiomer: $\tau_R$ = 35.96 min. *Characterized as mixture of hemiketal epimers (1:1 dr).*

$^1$H NMR (400 MHz, THF-d8) $\delta$ 5.34 (s, 1H, OH), 5.28 (s, 1H, OH), 4.52-4.46 (m, 1H, CH), 4.35-4.28 (m, 1H, CH), 3.85-3.64 (m, 4H, TBSOCH$_2$), 2.69-2.55 (m, 2H, CH$_2$C$_{q}$OH), 2.25-2.15 (m, 2H, CH$_2$C$_{q}$OH), 1.92-1.75 (m, 3H, TBSOCH$_2$CH$_2$), 1.64-1.55 (m, 1H, TBSOCH$_2$CH$_2$), 1.41 (s, 3H, C$_{q}$OHCH$_3$), 1.39 (s, 3H, C$_{q}$OHC$_3$), 0.90 (s, 18H, C$_q$(CH$_3$)$_3$), 0.04 (s, 12H, Si(CH$_3$)$_2$).

$^{13}$C NMR (100 MHz, THF-d8) $\delta$ 105.8 (C$_{q}$OH), 104.9 (C$_{q}$OH), 79.9 (CH), 78.3 (CH), 61.3 (TBSOCH$_2$), 61.0 (TBSOCH$_2$), 53.8 (CH$_2$C$_{q}$OH), 53.6 (CH$_2$C$_{q}$OH), 38.9 (TBSOCH$_2$CH$_2$), 36.7 (TBSOCH$_2$CH$_2$), 26.6 (6C, C$_q$(CH$_3$)$_3$), 24.3 (C$_q$OHCH$_3$), 23.7 (C$_q$OHCH$_3$), 19.2 (2C, C$_q$Me$_3$), 5.02 (2C, Si(CH$_3$)$_2$), 5.05 (2C, Si(CH$_3$)$_2$).

**MS** (El-DE) $m/z$ (%) 205 (1), 187 (1), 173 (1), 157 (2), 145 (8), 131 (32), 115 (22), 101 (26), 89 (9), 75 (100), 59 (12), 43 (24), 29 (4).

**HRMS** (ESI+) calcd for C$_{12}$H$_{20}$O$_4$SiNa [(M+Na)$^+$] 285.1491, found 285.1493.
(5R)-5-(3-Ethoxy-3-oxopropyl)-3-methyl-1,2-dioxolan-3-ol ((5R)-3i): Peroxyhemiketal 3i was prepared according to the general procedure. The reaction mixture was stirred for 24 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 25-50% Et₂O in pentane) provided the title compound 3i (71 mg, 348 µmol, 70%; 96.5:3.5 er) as a colorless oil. The enantiomeric ratio was determined after converting peroxyhemiketal 3i into the corresponding epoxide 4i. The enantiomers were analyzed by GC using a chiral BGB-176/SE-52 column 30 m (80 °C, 1.2 °C/min until 130 °C, 18 °C/min until 220 °C, 5 min at 320 °C, 0.5 bar H₂); major enantiomer: τ_R = 36.32 min, minor enantiomer: τ_R = 37.59 min. Characterized as mixture of hemiketal epimers (1:1 dr).

^1H NMR (400 MHz, CD₂Cl₂) δ 4.47-4.41 (m, 1H, CH), 4.38-4.31 (m, 1H, CH), 4.11 (q overlapped, J = 7.2 Hz, 2H, CH₂CH₃), 4.10 (q overlapped, J = 7.1 Hz, 2H, CH₂CH₃), 2.83-2.78 (m, 1H, CH₂CqOH), 2.71-2.51 (m, 3H, CH₂COH and OH), 2.45-2.22 (m, 6H, CH₂), 2.05-1.90 (m, 3H, CH₂), 1.81-1.73 (m, 1H, CH₂), 1.53 (s, 3H, CH₃), 1.51 (s, 3H, CH₃), 1.24 (t overlapped, J = 7.2 Hz, 3H, CH₂CH₃), 1.23 (t overlapped, J = 7.3 Hz, 3H, CH₂CH₃).

^13C NMR (100 MHz, CD₂Cl₂) δ 172.9 (C=O), 172.8 (C=O), 105.5 (CqOH), 104.5 (CqOH), 80.8 (CH), 79.8 (CH), 60.7 (CH₂CH₃), 60.5 (CH₂CH₃), 52.3 (CH₂, cycl.), 51.9 (CH₂, cycl.), 30.7 (CH₂), 30.6 (CH₂), 29.9 (CH₂), 27.2 (CH₂), 22.9 (CH₃), 22.3 (CH₃), 14.1 (CH₂CH₃), 14.0 (CH₂CH₃).

MS (El) m/z (%) 172 (3), 141 (2), 126 (11), 115 (5), 98 (28), 85 (13), 73 (12), 55 (13), 43 (100), 29 (37).

HRMS (ESI+) calcd for C₉H₁₆O₅Na [(M+Na)^+] 227.0890, found 227.0890.

(5R)-5-(3-Oxobutyl)-3-methyl-1,2-dioxolan-3-ol ((5R)-3j): Peroxyhemiketal 3j was prepared according to the general procedure. Catalyst [1a • 2 TFA] (10 mol%) was used together with 50 wt% aqueous hydrogen peroxide (1.5 equiv) as oxidant. The reaction mixture was stirred for 24 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 30-50% Et₂O in pentane) provided the title compound 3j (26 mg, 151 µmol, 30%; 96:4 er) as a colorless oil. The enantiomeric ratio was determined after converting peroxyhemiketal 3j into the corresponding epoxide 4j. The enantiomers were analyzed by GC using a chiral BGB-176/SE-52 column 30 m (80 °C, 1.2 °C/min until 120 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H₂); major enantiomer: τ_R = 28.87 min, minor enantiomer: τ_R = 30.28...
min. Characterized as a mixture of three hemiketal isomers (~1:1:0.8).

\[ \text{1H NMR (500 MHz, THF-d8) 3-hydroxy-1,2-dioxolane (mixture of hemiketal epimers (dr~1:1)):} \ δ 5.33 (br s, 1H, \text{O}\text{H}), 5.30 (br s, 1H, \text{OH}), 4.37-4.28 (m, 1H, \text{CH}), 4.21-1.25 (m, 1H, \text{CH}), 2.64 (dd, \text{J} = 12.0, 7.0 Hz, 1H, \text{CH}_2\text{cyl.}), 2.58-2.46 (m, 3H, \text{CH}_2\text{cyl.}), 2.20-2.05 (m, 10H, \text{CH}_2\text{cyl.}), 2.20-2.05 (m, 10H, \text{CH}_2\text{cyl.}), 1.88-1.62 (m, 4H, \text{CH}_2\text{cyl.}), 1.40 (s, 3H, \text{CH}_3\alpha\text{OH}), 1.38 (s, 3H, \text{CH}_3\alpha\text{OH}); 3-hydroxy-1,2-dioxane:} \ δ 5.34 (br s, 1H, \text{O}\text{H}), 4.37-4.28 (m, 1H, \text{CH}), 2.58-2.46 (m, 4H, \text{CH}_2\text{cyl.} and \text{CH}_2\text{cyl.}), 2.20-2.05 (m, 3H, \text{CH}_3\alpha\text{OH}), 1.88-1.62 (m, 2H, \text{CHCH}_2\text{cyl.}), 1.39 (s, 3H, \text{CH}_3\alpha\text{OH}). \]

\[ 3\text{-hydroxy-1,2-dioxolane (mixture of hemiketal epimers (dr~1:1)):} \ δ 206.8 (\text{C}\alpha\text{OH}), 206.5 (\text{C}\alpha\text{OH}), 105.9 (\text{C}\alpha\text{OH}), 105.0 (\text{C}\alpha\text{OH}), 81.8 (\text{CH}), 80.6 (\text{CH}), 53.5 (\text{CH}_2\text{cyl.}), 53.4 (\text{CH}_2\text{cyl.}), 40.3 (\text{CH}_2\text{cyl.}), 40.2 (\text{CH}_2\text{cyl.}), 29.8 (\text{CH}_2\text{cyl.}), 29.8 (\text{CH}_2\text{cyl.}), 29.7 (\text{CH}_2\text{cyl.}), 27.1 (\text{CH}_2\text{cyl.}), 24.3 (\text{CH}_2\text{cyl.}), 23.6 (\text{CH}_2\text{cyl.}); 3\text{-hydroxy-1,2-dioxane:} \ δ 204.4 (\text{C}\alpha\text{OH}), 99.2 (\text{C}\alpha\text{OH}), 77.5 (\text{CH}), 47.6 (\text{CH}_2\text{cyl.}), 34.2 (\text{CH}_2\text{cyl.}), 31.0 (\text{CH}_2\text{cyl.}), 26.9 (\text{CHCH}_2\text{cyl.}), 26.7 (\text{CH}_3\alpha\text{OH}). \]

\begin{center}
\begin{tikzpicture}
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (A) at (0,0) {\text{\textbf{S-18}}};
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (B) at (1,0) {\text{\textbf{O}}};
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (C) at (0,-1) {\text{\textbf{O}}};
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (D) at (1,-1) {\text{\textbf{O}}};
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (E) at (0,-2) {\text{\textbf{O}}};
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (F) at (1,-2) {\text{\textbf{O}}};
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (G) at (0,-3) {\text{\textbf{O}}};
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (H) at (1,-3) {\text{\textbf{O}}};
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (I) at (0,-4) {\text{\textbf{O}}};
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (J) at (1,-4) {\text{\textbf{O}}};
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (K) at (0,-5) {\text{\textbf{O}}};
\node[draw, shape=circle, fill=white, minimum size=0.5cm] (L) at (1,-5) {\text{\textbf{O}}};
\end{tikzpicture}
\end{center}

\text{(5R)-5-(5-Hydroxypentyl)-3-methyl-1,2-dioxolan-3-ol ((5R)-3k)}: Peroxyhemiketal 3k was prepared according to the general procedure. Catalyst [1a \cdot 2 TFA (10 mol%) was used together with 50 wt% aqueous hydrogen peroxide (1.5 equiv) as oxidant. The reaction mixture was stirred for 36 h at 50 °C. Purification of the crude reaction mixture by flash column chromatography (silica gel, 10-40% Et\_2O in CH\_2Cl\_2) provided the title compound 3k (12 mg, 63.1 μmol, 25%) as a colorless oil along with a mixture of the corresponding epoxide 4k (11 mg, 64.0 μmol, 26%; 98:2 er) and unreacted starting material 2k (10 mg, 65.0 μmol, 26%). Characterized as a mixture of hemiketal epimers (1:1 dr).

\[ \text{1H NMR (400 MHz, THF-d8) δ 5.31 (s, 1H, \text{C}q\text{OH}), 5.27 (s, 1H, \text{C}q\text{OH}), 4.34-4.28 (m, 1H, \text{CH}), 4.17 (\text{quint, J = 7.3 Hz, 1H, CH}), 3.46 (t, J = 5.5 Hz, 4H, \text{CH}_2\text{OH}), 3.35 (br s, 2H, \text{CH}_2\text{OH}), 2.64-2.55 (m, 2H, \text{CH}_2\text{cyl.}), 2.20-2.07 (m, 2H, \text{CH}_2\text{cyl.}), 1.67-1.31 (m, 16H, -(\text{CH}_2)_4\text{H}), 1.40 (s \text{overlapped, 3H, CH}_3), 1.38 (s \text{overlapped, 3H, CH}_3). \]

\[ \text{13C NMR (100 MHz, THF-d8) 105.8 (\text{C}q\text{OH}), 104.9 (\text{C}q\text{OH}), 82.7 (\text{CH}), 81.4 (\text{CH}), 62.7 (\text{CH}_2\text{OH}), 62.7 (\text{CH}_2\text{OH}), 54.0 (\text{CH}_2\text{cyl.}), 53.6 (\text{CH}_2\text{cyl.}), 35.9 (\text{CH}_2), 34.3 (\text{CH}_2), 34.2 (\text{CH}_2), 33.4 (\text{CH}_2), 27.6 (\text{CH}_2), 27.3 (\text{CH}_2), 27.3 (\text{CH}_2), 27.1 (\text{CH}_2), 24.4 (\text{CH}_3), 23.8 (\text{CH}_3). \]
**MS** (EI-DE) \( m/z \) (%) 157 (5), 139 (5), 125 (1), 121 (2), 111 (1), 97 (13), 81 (15), 79 (4), 71 (21), 55 (18), 43 (100), 41 (26), 31 (13).

**HRMS** (ESI+) calcd for C\(_9\)H\(_{18}\)AgO\(_4\) [(M+Ag\(^{+}\)] 297.0249, found 297.0249.

**(5R)-3,5-Dipentyl-1,2-dioxolan-3-ol (5R)-3l**: Peroxymetekatal 3l was prepared according to the general procedure. The reaction mixture was stirred for 48 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 10-20% Et\(_2\)O in pentane) provided the title compound 3l as a colorless oil (46 mg, 201 \( \mu \)mol, 40%; 97:3 er). The enantiomeric ratio was determined after converting dioxolane 3l into the corresponding epoxide 4l. The enantiomers were analyzed by GC using a chiral G-TA column 30 m (80 °C, 1 °C/min until 130 °C, 18 °C/min until 180 °C, 10 min at 320 °C, 0.9 bar H\(_2\)); major enantiomer: \( \tau_R = 43.80 \text{ min}, \) minor enantiomer: \( \tau_R = 43.02 \text{ min}. \) Characterized as a mixture of hemiketal epimers (1:1 dr).

\(^1\text{H NMR}\) (500 MHz, THF-d8) \( \delta \) 5.20 (s, 1H, O\_H), 5.16 (s, 1H, O\_H), 4.33-4.28 (m, 1H, C\_H), 4.15-4.09 (m, 1H, C\_H), 2.61-2.52 (m, 2H, C\_H\_2C\_qOH), 2.10-2.04 (m, 2H, C\_H\_2C\_qOH), 1.68-1.26 (m, 32H, C\_H), 0.92-0.88 (m, 12H, C\_H\_3).

\(^{13}\text{C NMR}\) (125 MHz, THF-d8) \( \delta \) 107.7 (\_C\_qOH), 106.9 (\_C\_qOH), 82.6 (C\_H), 81.0 (C\_H), 52.4 (C\_H\_2_cycl.), 52.1 (C\_H\_2_cycl.), 38.3 (C\_H), 37.9 (C\_H), 35.8 (C\_H), 33.4 (C\_H), 33.4 (C\_H), 33.3 (C\_H), 33.1 (C\_H), 33.0 (C\_H), 27.4 (C\_H), 27.2 (C\_H), 25.9 (C\_H), 25.7 (C\_H), 23.8 (C\_H), 23.7 (C\_H), 14.7 (C\_H), 14.7 (C\_H), 14.6 (C\_H).

**MS** (EI) \( m/z \) (%) 230 [M\(^+\)] (1), 197 (100), 159 (1), 141 (3), 127 (30), 117 (5), 99 (50), 81 (6), 71 (30), 55 (30), 43 (90), 29 (24).

**HRMS** (EI-DE) calcd for C\(_{13}\)H\(_{26}\)O\(_3\) [M\(^+\)] 230.1880, found 230.1882.

**(5R)-3-Isopropyl-5-methyl-1,2-dioxolan-3-ol (5R)-3n**: Peroxymetekatal 3n was obtained by the general procedure. Catalyst salt [1a • 2 TCA] (20 mol%) was used and the reaction mixture was stirred for 48 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 30-40% Et\(_2\)O in pentane) provided the title compound 3n (57 mg, 391 \( \mu \)mol, 39%; 96:4 er) as a colorless oil. The enantiomeric ratio was determined after converting peroxyhemikatal 3n into the corresponding epoxide 4n. The enantiomers
were analyzed by GC using a chiral Lipodex G column 25 m (50 °C, 1.2 °C/min until 80 °C, 18 °C/min until 220 °C, 10 min at 230 °C, 0.5 bar H2); major enantiomer: \( \tau_R = 8.36 \) min, minor enantiomer: \( \tau_R = 8.80 \) min. *Characterized as a mixture of hemiketal epimers (1:1 *dr*).*

**\(^1\)H NMR** (400 MHz, THF-d8) \( \delta \) 6.98 (s, 1H, O\( \text{H} \)), 6.97 (s, 1H, O\( \text{H} \)), 6.34 (app. sext, \( J = 6.3 \) Hz, 1H, \( \text{C}H\text{CH}_2 \)), 6.10-6.03 (m, 1H, \( \text{C}H\text{CH}_2 \)), 4.51 (dd, \( J = 12.6, 7.3 \) Hz, 1H, \( \text{CH}H \)), 4.33 (dd, \( J = 12.1, 6.8 \) Hz, 1H, \( \text{CH}H \)), 3.93 (dd, \( J = 12.0, 6.3 \) Hz, 1H, \( \text{CH}H \)), 3.81 (dd, \( J = 12.1, 6.8 \) Hz, 1H, \( \text{CH}H \)), 3.72 (hept, \( J = 7.0 \) Hz, 2H, \( \text{CHMe}_2 \)), 3.09 (d, \( J = 6.0 \) Hz, 3H, \( \text{CH}H\text{CH} \)), 3.04 (d, \( J = 6.3 \) Hz, 3H, \( \text{CH}H\text{CH} \)), 2.81 (t, \( J = 6.8 \) Hz, 12H, \( \text{CH}H\text{CH}_3 \)).

**\(^{13}\)C NMR** (125 MHz, THF-d8) \( \delta \) 110.2 (\( \text{C}q\text{OH} \)), 109.2 (\( \text{C}q\text{OH} \)), 78.6 (\( \text{C}H\text{CH}_2 \)), 76.9 (\( \text{C}H\text{CH}_2 \)), 52.0 (\( \text{C}H\text{H}_2 \)), 51.8 (\( \text{C}H\text{H}_2 \)), 36.1 (\( \text{CHMe}_2 \)), 35.9 (\( \text{CHMe}_2 \)), 20.3 (\( \text{CH}_3 \)), 19.1 (\( \text{CH}_3 \)), 18.8 (\( \text{CH}_3 \)), 18.3 (\( \text{CH}_3 \)), 18.1 (\( \text{CH}_3 \)), 17.4 (\( \text{CH}_3 \)).

**GC-MS** (GC-EI) \( m/z \) (%) 146 [M+] (trace), 128 (1), 113 (12), 103 (6), 85 (4), 71 (22), 61 (17), 43 (100), 27 (8).

**HRMS** (EI-FE) calcd for C\( _7 \)H\( _{14} \)O\( _3 \) [M+] 146.0941, found 146.0943.

\( (5\text{R})-3\)-Ethyl-5-methyl-1,2-dioxolan-3-ol ((5\text{R})-3\text{o}): The title compound was isolated after 24 h at 32 °C and purification by flash column chromatography (silica gel, 10-30\% Et\( _2 \)O in pentane) as a colorless oil (74 mg, 560 \( \mu \)mol, 56%; 97:3 *er*). The enantiomeric ratio was determined after converting dioxolane 3\text{o} to the corresponding epoxide 4\text{o}. The enantiomers were analyzed by GC using a chiral BGB-178/BGB-15 column 30 m (60 °C, 1.0 °C/min until 80 °C, 18 °C/min until 220 °C, 10 min at 220 °C, 0.4 bar H\( _2 \)); major enantiomer: \( \tau_R = 14.73 \) min, minor enantiomer: \( \tau_R = 15.98 \) min. *Characterized as a mixture of hemiketal epimers (1:1 *dr*).*

**\(^1\)H NMR** (400 MHz, CD\( _2 \)Cl\( _2 \)) \( \delta \) 4.60 (app. sext, \( J = 6.2 \) Hz, 1H, \( \text{CH} \)), 4.40-4.32 (m, 1H, \( \text{CH} \)), 3.12 (br s, 2H, \( \text{O}H \)), 2.71 (dd overlapped, \( J = 12.8, 7.5 \) Hz, 1H, \( \text{CHH}_{\text{cycl}} \)), 2.69 (dd overlapped, \( J = 12.6, 7.1 \) Hz, 1H, \( \text{CHH}_{\text{cycl}} \)), 2.17 (dd overlapped, \( J = 12.6, 5.8 \) Hz, 1H, \( \text{CHH}_{\text{cycl}} \)), 2.13 (dd overlapped, \( J = 12.8, 8.5 \) Hz, 1H, \( \text{CHH}_{\text{cycl}} \)), 1.84-1.71 (m, 4H, \( \text{CH}_2\text{CH}_3 \)), 1.30 (d, \( J = 6.3 \) Hz, 3H, \( \text{CH}_3\text{CH} \)), 1.26 (d, \( J = 6.1 \) Hz, 3H, \( \text{CH}_3\text{CH} \)), 1.02 (t overlapped, \( J = 7.5 \) Hz, 3H, \( \text{CH}_2\text{CH}_3 \)), 1.00 (t overlapped, \( J = 7.6 \) Hz, 3H, \( \text{CH}_2\text{CH}_3 \)).

**\(^{13}\)C NMR** (100 MHz, CD\( _2 \)Cl\( _2 \)) 108.5 (\( \text{C}q\text{OH} \)), 107.3 (\( \text{C}q\text{OH} \)), 78.4 (\( \text{CH} \)), 76.9 (\( \text{CH} \)), 52.3 (\( \text{CH}_2\text{cycl} \)), 52.0 (\( \text{CH}_2\text{cycl} \)), 29.9 (\( \text{CH}_3\text{CH} \)), 29.7 (\( \text{CH}_2\text{CH}_3 \)), 20.3 (\( \text{CH}_3\text{CH} \)), 17.0 (\( \text{CH}_3\text{CH} \)), 9.2 (\( \text{CH}_2\text{CH}_3 \)), 8.9
(CH₂CH₃).  

**MS** (EI-DE) m/z (%) 132 [M⁺] (3), 115 (1), 99 (100), 91 (1), 87 (3), 85 (27), 81 (4), 75 (3), 71 (24), 69 (3), 61 (25), 57 (59), 43 (60), 31 (9), 29 (40), 27 (14).  


3-Ethyl-5-nonyl-1,2-dioxolan-3-ol (3p): Peroxyhemiketal 3p was prepared according to the general procedure. The reaction mixture was stirred for 48 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 10-20% Et₂O in pentane) provided the title compound 3p as a colorless oil (59 mg, 240 μmol, 48%; 98:2 er). The enantiomeric ratio was determined after converting dioxolane 3p into the corresponding epoxide 4p. The enantiomers were analyzed by GC using a chiral Lipodex E column 25 m (100 °C, 1.2 °C/min until 180 °C, 18 °C/min until 220 °C, 10 min at 320 °C, 0.5 bar H₂); major enantiomer: τᵣ = 37.10 min, minor enantiomer: τᵣ = 35.28 min.

Characterized as a mixture of hemiketal epimers (1:1 dr).

**¹H NMR** (500 MHz, THF-d₈) δ 5.18 (s, 1H, O₃H), 5.15 (s, 1H, O₃H), 4.33-4.28 (m, 1H, CH), 4.12 (quint, J = 7.1 Hz, 1H, CH), 2.61-2.50 (m, 2H, CH₂CqOH), 2.10-2.02 (m, 2H, CH₂CqOH), 1.71-1.52 (m, 7H, CH₂), 1.42-1.36 (m, 3H, CH₂), 1.35-1.26 (m, 26H, CH₂), 0.97 (t, J = 7.6 Hz, 3H, CqOHCH₂CH₃), 0.96 (t, J = 7.6 Hz, 3H, CqOHCH₂CH₃), 0.89 (t, J = 6.8 Hz, 6H, CH₃).

**¹³C NMR** (125 MHz, THF-d₈) 108.1 (CqOH), 107.2 (CqOH), 82.7 (CH), 81.1 (CH), 51.9 (CH₂cyl.), 51.5 (CH₂cyl.), 35.7 (CH₂), 33.3 (CH₂), 33.2 (2C, CH₂), 31.2 (CH₂), 30.9 (CH₂), 30.9 (CH₂), 30.9 (CH₂), 30.8 (CH₂), 30.8 (CH₂), 30.8 (CH₂), 30.8 (CH₂), 30.6 (2C, CH₂), 27.5 (CH₂), 27.5 (CH₂), 23.9 (2C, CH₂), 14.7 (2C, CH₂), 9.9 (CqOHCH₂CH₃), 9.7 (CqOHCH₂CH₃).

**MS** (EI) m/z (%) 244 [M⁺] (1), 211 (77), 197 (1), 181 (1), 155 (9), 137 (2), 95 (8), 85 (50), 71 (17), 57 (100), 43 (46), 29 (34).

**HRMS** (EI-DE) calcd for C₁₄H₂₈O₃ [M⁺] 244.2038, found 244.2038.

Achiral peroxyhemiketal 11 has been described in the literature³

³ Dussault, P.; Liu, X. Org. Lett. 1999, 1, 1391
Catalytic Asymmetric Epoxidation of Acyclic Enones

General Procedure

Catalyst salt [1a • 2 TFA] was prepared in situ by the addition of amine 1a (32.3 mg, 0.1 mmol, 10 mol%) to a solution of trifluoroacetic acid (15.3 µL, 0.2 mmol, 20 mol%) in dioxane (4 mL). Then enone 2 (1.0 mmol, 1.0 equiv) was added, and 20 minutes later, aqueous hydrogen peroxide (50 wt%, 92 µL, 1.5 mmol, 1.5 equiv). After 12-48 h at 50°C, the reaction mixture was extracted with Et₂O (3×25 mL). The combined organic phases were washed with brine and concentrated under reduced pressure to a volume of 5 mL. Aqueous 1N NaOH solution (1.0 mL, 1.0 mmol, 1.0 equiv) was added and the reaction mixture stirred until TLC analysis indicated complete conversion to the epoxide (10 min to 1 h). The reaction mixture was extracted with Et₂O (3×25 mL), and the combined organic phases were washed with brine, dried (Na₂SO₄), and filtered. Evaporation of the solvent furnished the crude product, which was purified by flash column chromatography (silica gel, eluent: Et₂O-pentane) to afford pure α,β-epoxy ketones 4.

Scope of Optically Active α,β-Epoxyketones 4

(3S,4R)-3,4-Epoxy-2-decanone (3S,4R)-4a: Epoxide (3S,4R)-4a was prepared according to the general procedure. The reaction mixture was stirred for 12 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et₂O in pentane) provided the title compound 4a as a colorless oil (127 mg, 747 µmol, 75%; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (80 °C, 1.2 °C/min until 120 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.6 bar H₂); major enantiomer: τ_R = 19.73 min, minor enantiomer: τ_R = 21.60 min.
$^1$H NMR (500 MHz, CD$_2$Cl$_2$) δ 3.14 (d, $J = 2.0$ Hz, 1H, CH$_{epo}$C(=O)), 3.05 (td, $J = 5.5$, 1.9 Hz, 1H, CH$_2$CH$_{epo}$), 2.02 (s, 3H, CH$_3$(C(=O))), 1.64-1.55 (m, 2H, CH$_2$CH$_{epo}$), 1.49-1.41 (m, 2H, CH$_2$CH$_2$CH$_{epo}$), 1.37-1.25 (m, 6H, (CH$_2$)$_3$CH$_3$), 0.89 (t, $J = 7.0$ Hz, 3H, (CH$_2$)$_5$CH$_3$).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) δ 206.2 (C(=O)), 60.4 (CH$_{epo}$C(=O)), 58.6 (CH$_2$CH$_{epo}$), 32.4 (CH$_2$CH$_{epo}$), 32.2 (CH$_2$), 29.5 (CH$_2$), 26.3 (CH$_2$CH$_2$CH$_{epo}$), 24.8 (CH$_3$(C(=O))), 23.1 (CH$_2$), 14.4 ((CH$_2$)$_3$CH$_3$).

GC-MS (GC-EI) m/z (%) 170 [M$^+$] (trace), 139 (7), 125 (1), 109 (4), 97 (12), 85 (54), 81 (9), 69 (21), 55 (41), 43 (100), 39 (9), 29 (17).

HRMS (CI-FE, i-butane) calcd for C$_{10}$H$_{19}$O$_2$ [(M+H)$^+$] 171.1384, found 171.1385.

(3R,4S)-3,4-Epoxy-2-decanone ((3R,4S)-4a): 9-Amino(9-deoxy)epiquinidine (1b) was used instead of 1a under otherwise identical conditions. The reaction mixture was stirred for 12 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et$_2$O in pentane) provided the title compound ent-4a as a colorless oil (137 mg, 807 μmol, 81%; 96:4 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/SE-52 column 30 m (80 °C, 1.2 °C/min until 115°C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.6 bar H$_2$); major enantiomer: τ$_R$ = 25.06 min, minor enantiomer: τ$_R$ = 24.13 min.

(3S,4R)-3,4-Epoxy-6-phenyl-2-hexanone ((3S,4R)-4b): Epoxide (3S,4R)-4b was prepared according to the general procedure. The reaction mixture was stirred for 12 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et$_2$O in pentane) provided the title compound 4b as a colorless oil (162 mg, 854 μmol, 85%; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (80 °C, 1.2 °C/min until 140 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.6 bar H$_2$); major enantiomer: τ$_R$ = 45.23 min, minor enantiomer: τ$_R$ = 46.65 min.

$^1$H NMR (500 MHz, CD$_2$Cl$_2$) δ 7.32-7.28 (m, 2H, C$_6$H$_5$), 7.23-7.20 (m, 3H, C$_6$H$_5$), 3.15 (d, $J = 1.8$ Hz, 1H, CH$_{epo}$C(=O)), 3.09 (td, $J = 5.6$, 1.8 Hz, 1H, CH$_2$CH$_{epo}$), 2.85-2.72 (m, 2H, PhCH$_2$), 1.99 (s, 3H, CH$_3$), 1.96-1.91 (m, 2H, CH$_2$CH$_{epo}$).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) δ 205.7 (C(=O)), 141.3 (C$_{q}$-Ph), 129.1 (2C, CH$_{Ph}$), 128.9 (2C, CH$_{Ph}$), 126.7 (CH$_{Ph,p}$), 60.3 (CH$_{epo}$C(=O)), 58.1 (CH$_2$CH$_{epo}$), 34.1 (CH$_2$), 32.5 (CH$_2$), 25.0 (CH$_3$).
**MS (EI-DE) m/z (%)**

190 [M⁺] (4), 172 (4), 157 (2), 147 (14), 134 (5), 129 (37), 117 (38), 104 (34), 91 (100), 85 (22), 77 (8), 65 (17), 57 (8), 51 (6), 43 (64), 27 (5).

**HRMS (EI-FE) calcd for C₁₂H₁₄O₂ [M⁺] 190.0992, found 190.0994.**

**3R,4S-3,4-Epoxy-6-phenyl-2-hexanone (3R,4S-4b):** Epoxide (3R,4S)-4b was prepared according to the general procedure. 9-Amino(9-deoxy)epiquinidine (1b) was used instead of 1a under otherwise identical conditions. The reaction mixture was stirred for 12 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et₂O in pentane) provided the title compound ent-4b as a colorless oil (171 mg, 90% 95:5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (80 °C, 1.2 °C/min until 160 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.6 bar H₂); major enantiomer: τ_R = 47.30 min, minor enantiomer: τ_R = 46.86 min.

**3S,4R-3,4-Epoxy-5-phenyl-2-pentanone (3S,4R-4q):** Epoxide (3S,4R)-4q was prepared according to the general procedure. Catalyst [1a • 3 TFA] was used under otherwise identical conditions. After 12 h at 50 °C, the conversion was determined to be 94% by H NMR of the crude mixture (37% epoxide 4q, 33% 5-benzyl-3-methyl-1,2-dioxolan-3-ol (3q), 24% (E)-5-phenylpent-4-en-2-one (iso-2q, vide infra)). The enantiomeric ratio of epoxide 4q was determined to be 99:1 er by GC using a chiral Lipodex E column 25 m (80 °C, 1.2 °C/min until 145 °C, 18 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H₂); major enantiomer: τ_R = 42.87 min, minor enantiomer: τ_R = 41.72 min.

**H NMR (500 MHz, CDCl₃) δ 7.32-7.21 (m, 5H, C₆H₅), 3.28 (td, J = 5.2, 1.9 Hz, 1H, CH₂CH₃), 2.93 (app. qd, J = 14.4, 5.2 Hz, 2H, PhCH₂), 2.19 (3H, CH₃).**

**E-5-Phenylpent-4-en-2-one (iso-2q): **H NMR (500 MHz, CDCl₃) δ 7.35-7.21 (m, 5H, C₆H₅), 6.45 (d, J = 16.0 Hz, 1H, PhCH=), 6.28 (dt, J = 15.8, 7.5 Hz, 1H, =CHCH₂), 3.31 (d, J = 7.2 Hz, 2H, =CHCH₂), 2.19 (3H, CH₃).
(3S,4R)-3,4-Epoxy-6-methyl-2-heptanone ((3S,4R)-4c): Epoxide (3S,4R)-4c was prepared according to the general procedure. The reaction mixture was stirred for 18 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et2O in pentane) provided the title compound 4c as a colorless oil (109 mg, 768 μmol, 77%; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (60 °C, 0.8 °C/min until 80 °C, 18 °C/min until 220 °C, 10 min at 220 °C, 0.6 bar H2); major enantiomer: τR = 15.45 min, minor enantiomer: τR = 17.76 min.

1H NMR (500 MHz, CD2Cl2) δ 3.12 (d, J = 1.9 Hz, 1H, CHepoC(=O)), 3.06 (td, J = 5.8, 1.9 Hz, 1H, CH2Cepo), 2.03 (s, 3H, CH3C(=O)), 1.83 (hept, J = 6.7 Hz, 1H, CHMe2), 1.48 (dd, J = 6.5 Hz, 2H, CH2), 0.98 (d, J = 4.6 Hz, 3H, CH(CH3)2), 0.97 (d, J = 4.6 Hz, 3H, CH(CH3)2).

13C NMR (125 MHz, CD2Cl2) δ 206.2 (C=O), 60.5 (CHepoC(=O)), 57.6 (CH2CHepo), 41.1 (CH2), 27.0 (CHMe2), 24.9 (CH2C=O), 23.1 (CH(CH3)2), 22.6 (CH(CH3)2).

MS (EI-DE) m/z (%) 142 [M+] (2), 127 (6), 100 (10), 85 (100), 81 (6), 74 (2), 69 (3), 57 (26), 55 (12), 43 (79), 41 (14), 27 (11).

HRMS (CI-FE, i-butane) calcd for C8H15O2 [(M+H)+] 143.1071, found 143.1072.

(3S,4R)-3,4-Epoxy-6,6-dimethyl-2-heptanone ((3S,4R)-4r): Epoxide (3S,4R)-4r was prepared according to the general procedure. The reaction mixture was stirred for 18 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et2O in pentane) provided the title compound 4r as a colorless oil (127 mg, 812 μmol, 81%; >99.5:0.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (80 °C, 1.0 °C/min until 100 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H2); major enantiomer: τR = 15.39 min, minor enantiomer: τR = 16.03 min.

1H NMR (500 MHz, CD2Cl2) δ 3.10-3.07 (m, 2H, CHepo), 2.04 (s, 3H, CH3C(=O)), 1.53-1.44 (m, 2H, CH2), 1.00 (s, 9H, Cq(CH3)3).

13C NMR (125 MHz, CD2Cl2) δ 206.2 (C=O), 60.2 (CHepoC(=O)), 56.2 (CH2CHepo), 46.3 (CH2), 31.1 (CqMe3), 29.9 (3C, Cq(CH3)3), 25.0 (CH3C(=O)).

GC-MS (GC-EI) m/z (%) 156 [M+] (trace), 141 (1), 125 (1), 107 (1), 100 (11), 95 (4), 85 (53), 69 (16), 57 (97), 43 (100), 41 (41), 29 (24), 27 (7).

HRMS (CI-FE, i-butane) calcd for C9H17O2 [(M+H)+] 157.1227, found 157.1229.
(3S,4R)-3,4-Epoxy-5-methyl-2-hexanone ((3S,4R)-4s): Epoxide (3S,4R)-4s was prepared according to the general procedure. 20 mol% of catalyst [1a • 2 TFA] was used under otherwise identical conditions. The reaction mixture was stirred for 48 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et2O in pentane) provided the title compound 4s as a colorless oil (64 mg, 497 μmol, 50% (reduced yield due to the high volatility of 4s); 98:2 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (15 min at 60 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.6 bar H2); major enantiomer: τR = 8.34 min, minor enantiomer: τR = 10.30 min.

1H NMR (500 MHz, CD2Cl2) δ 3.19 (d, J = 1.9 Hz, 1H, CHepoC(=O)), 2.87 (dd, J = 6.6, 1.9 Hz, 1H, CHCΗepo), 2.03 (s, 3H, CH3C(=O)), 1.62 (hept, J = 6.7 Hz, 1H, CHMe2), 1.03 (d, J = 6.6 Hz, 3H, CH(CH3)2), 0.97 (d, J = 7.0, 3H, CH(CH3)2).

13C NMR (125 MHz, CD2Cl2) δ 206.1 (C=O), 63.4 (CHCΗepo), 59.2 (CHepoC(=O)), 30.8 (CHMe2), 24.6 (CH3C(=O)), 18.9 (CH(CH3)2), 18.2 (CH(CH3)2).

GC-MS (GC-EI) m/z (%) 128 [M+] (trace), 113 (14), 97 (2), 95 (13), 85 (94), 83 (1), 69 (5), 67 (33), 65 (3), 59 (13), 55 (9), 45 (4), 43 (100), 41 (21), 39 (7), 29 (10).

(3S,4R)-3,4-Epoxy-4-cyclohexyl-2-butanone ((3S,4R)-4d): Epoxide (3S,4R)-4d was prepared according to the general procedure. 20 mol% of catalyst [1a • 2 TFA] was used under otherwise identical conditions. The reaction mixture was stirred for 48 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et2O in pentane) provided the title compound 4d as a colorless oil (140 mg, 842 μmol, 84%; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/SE-52 column 29.5 m (80 °C, 1.2 °C/min until 135 °C, 18 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H2); major enantiomer: τR = 33.22 min, minor enantiomer: τR = 34.35 min.

1H NMR (500 MHz, CD2Cl2) δ 3.21 (d, J = 2.3 Hz, 1H, CHepoC(=O)), 2.86 (dd, J = 6.5, 2.3 Hz, 1H, CHCHepo), 2.02 (s, 3H, CH3), 1.85-1.80 (m, 1H, CH2), 1.78-1.72 (m, 2H, CH2), 1.72-1.64 (m, 2H, CH2), 1.35-1.07 (m, 6H, CHcycl. and CH2).

13C NMR (125 MHz, CD2Cl2) δ 206.3 (C=O), 62.7 (CHCHepo), 59.3 (CHepoC(=O)), 40.4 (CHcycl.), 30.0 (CH2), 29.3 (CH2), 26.7 (CH2), 26.1 (CH2), 26.0 (CH2), 24.8 (CH3).

MS (EI-DE) m/z (%) 168 [M+] (2), 153 (1), 125 (1), 113 (3), 108 (7), 100 (2), 95 (11), 85 (100), 81.
(22), 70 (5), 67 (17), 55 (24), 43 (45), 29 (10).

HRMS (ESI+) calcd for C_{10}H_{16}NaO_{2} [(M+Na)^+] 191.1042, found 191.1042.

(3S,4R)-3,4-Epoxy-7-octen-2-one ((3S,4R)-4e): Epoxide (3S,4R)-4e was prepared according to the general procedure. The reaction mixture was stirred for 12 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et_{2}O in pentane) provided the title compound 4e as a colorless oil (107 mg, 764 μmol, 76%; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (80 °C, 0.8 °C/min until 100 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H_{2}); major enantiomer: τ_{R} = 11.06 min, minor enantiomer: τ_{R} = 12.59 min.

\textbf{1H NMR} (500 MHz, CD_{2}Cl_{2}) \ δ 5.84 (ddt, J = 17.0, 10.3, 6.6 Hz, 1H, CH=CH_{2}), 5.07 (ddd, J = 17.1, 3.4, 1.7 Hz, 1H, CH=CH_{trans-H}), 3.95 (ddd, J = 14.2, 10.3, 1.7 Hz, 1H, CH=CH_{cis-H}), 3.08 (td, J = 5.5, 1.9 Hz, 1H, CH_{2}CH_{epo}), 2.28-2.17 (m, 2H, CH_{2}CHCH_{epo}), 2.03 (s, 3H, CH_{3}).

\textbf{13C NMR} (125 MHz, CD_{2}Cl_{2}) δ 205.9 (C=O), 137.7 (CH=CH_{2}), 115.9 (CH=CH_{2}), 60.4 (CH_{epo}C(=O)), 58.1 (CH_{2}CH_{epo}), 31.6 (CH_{2}), 30.5 (CH_{2}), 25.0 (CH_{3}).

\textbf{MS} (EI-DE) m/z (%) 140 [M^{+}] (trace), 107 (3), 97 (34), 85 (30), 79 (8), 73 (3), 67 (11), 57 (22), 55 (11), 43 (100), 41 (34), 39 (18), 27 (13).

HRMS (CI-FE, i-butane) calcd for C_{10}H_{16}O_{2} [(M+H)^+] 141.0916, found 141.0916.

(3S,4R)-7-Bromo-3,4-epoxy-2-heptanone ((3S,4R)-4f): Epoxide (3S,4R)-4f was prepared according to the general procedure. The reaction mixture was stirred for 18 h at 50 °C. Purification by flash column chromatography (silica gel, 10-25% Et_{2}O in pentane) provided the title compound 4f as a colorless oil (77 mg, 374 μmol, 75%; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (100 °C, 1.2 °C/min until 135 °C, 18 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H_{2}); major enantiomer: τ_{R} = 19.40 min, minor enantiomer: τ_{R} = 20.75 min. Contains 11% (determined by GC) of (E)-7-chloro-3,4-epoxyheptan-2-one.

\textbf{1H NMR} (400 MHz, CD_{2}Cl_{2}) δ 3.47 (td, J = 6.6, 1.5 Hz, 2H, BrCH_{2}), 3.20 (d, J = 2.1 Hz, 1H, C_{epo}HJC(=O)), 3.11-3.08 (m, 1H, C_{epo}HCH_{2}), 2.05-1.98 (m, 2H, BrCH_{2}CH_{2}), 2.03 (s, 3H, CH_{3}), 1.92-
1.83 (m, 1H, CH\textsubscript{H}C\textsubscript{epo}H), 1.73-1.65 (m, 1H, CH\textsubscript{H}C\textsubscript{epo}H).

\textsuperscript{13}C NMR (100 MHz, CD\textsubscript{2}Cl\textsubscript{2}): \(\delta\) 205.2 (C=O), 59.5 (C\textsubscript{epo}HC(=O)), 57.1 (C\textsubscript{epo}HCH\textsubscript{2}), 33.0 (BrCH\textsubscript{2}), 30.3 (CH\textsubscript{2}C\textsubscript{epo}H), 29.1 (BrCH\textsubscript{2}CH\textsubscript{2}), 24.4 (CH\textsubscript{3}).

MS (EI) \(m/z\) (%) 165 (35), 163 (36), 135 (2), 121 (1), 109 (2), 95 (1), 85 (67), 69 (1), 55 (32), 43 (100), 27 (15).

HRMS (CI-FE) calcd for C\textsubscript{7}H\textsubscript{12}BrO\textsubscript{2} [(M+H)+] 207.0020, found 207.0021.

(3\textit{S},4\textit{R})-3,4-Epoxy-9-(tetrahydro-2\textit{H}-pyran-2-yloxy)nonen-2-one ((3\textit{S},4\textit{R})-4g):

Epoxide (3\textit{S},4\textit{R})-4g was prepared according to the general procedure. The reaction mixture was stirred for 18 h at 50 °C. Purification by flash column chromatography (silica gel, 20-30% Et\textsubscript{2}O in pentane) provided the title compound 4g as a colorless oil (113 mg, 440 \(\mu\)mol, 88%). The enantiomeric ratio was determined after deprotection of the THP ether (cf. epoxide 4l; vide infra). Characterized as mixture of THP ether diastereomers.

\textsuperscript{1}H NMR (500 MHz, CD\textsubscript{2}Cl\textsubscript{2}) \(\delta\) 4.53 (t, \(J = 3.7\) Hz, 1H, O-CH-O), 3.84-3.79 (m, 1H, OCH\textsubscript{THP}), 3.69 (dt, \(J = 9.5, 6.6\) Hz, 1H, THPOCH\textsubscript{H}), 3.48-3.43 (m, 1H, OCH\textsubscript{THP}), 3.35 (dt, \(J = 9.5, 6.6\) Hz, 1H, THPOCH\textsubscript{H}), 3.15 (d, \(J = 1.9\) Hz, 1H, C\textsubscript{epo}H(=O)), 3.06 (td, \(J = 5.2, 1.9\) Hz, 1H, C\textsubscript{epo}HCH\textsubscript{2}), 2.03 (s, 3H, CH\textsubscript{3}), 1.83-1.75 (m, 1H, CH\textsubscript{2}), 1.69-1.39 (m, 13H, CH\textsubscript{2}).

\textsuperscript{13}C NMR (125 MHz, CD\textsubscript{2}Cl\textsubscript{2}) 205.7 (C=O), 98.9 (O-CH-O), 67.2 (THPOCH\textsubscript{2}), 62.2 (OCH\textsubscript{2,THP}), 59.9 (C\textsubscript{epo}H(=O)), 58.0 (C\textsubscript{epo}HCH\textsubscript{2}), 31.8 (CH\textsubscript{2}), 30.9 (OCHCH\textsubscript{2}), 29.7 (CH\textsubscript{2}), 26.0 (CH\textsubscript{2}), 25.7 (CH\textsubscript{2}), 25.6 (CH\textsubscript{2}), 24.3 (CH\textsubscript{3}), 19.8 (CH\textsubscript{2}).

MS (EI-DE) \(m/z\) (%) 256 [M\textsuperscript{+}] (trace), 239 (1), 225 (2), 185 (1), 156 (11), 140 (10), 126 (6), 111 (2), 97 (17), 85 (100), 81 (10), 67 (14), 55 (14), 43 (50), 29 (8).

HRMS (ESI+) calcd for C\textsubscript{14}H\textsubscript{24}NaO\textsubscript{4} [(M+Na\textsuperscript{+})] 279.1565, found 279.1567.
(3S,4R)-3,4-Epoxy-6-tert-butyldimethylsilyloxyhexan-2-one ((3S,4R)-4h): Epoxide 4h was prepared according to the general procedure. The reaction mixture was stirred for 18 h at 50 °C. Purification by flash column chromatography (silica gel, 1-10% Et₂O in pentane) provided the title compound 4h as a colorless oil (88 mg, 359 μmol, 72%; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (80 °C, 1.2 °C/min until 125 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H₂); major enantiomer: 𝜏_R = 34.31 min, minor enantiomer: 𝜏_R = 35.48 min.

^1H NMR (500 MHz, CD₂Cl₂) δ 3.76 (t, J = 6.3 Hz, 2H, TBSOCH₂), 3.22-3.19 (m, 2H, CepoH), 2.03 (s, 3H, C(CH₃)₃), 1.87-1.81 (m, 1H, CepoHC), 1.79-1.73 (m, 1H, CepoHCH₂), 0.90 (s, 9H, Cq(C(CH₃)₃)), 0.07 (s, 3H, Si(C(CH₃)₂)), 0.06 (s, 3H, Si(C(CH₃)₂)).

^13C NMR (125 MHz, CD₂Cl₂) δ 205.4 (C=O), 59.9 (CepoHC(O)), 59.6 (TBSOCH₂), 55.9 (CH₂CepoH), 35.1 (CH₂CepoH), 25.7 (3C, C(CH₃)₃), 24.3 (CqMe₃), 18.2 (CH₃C(=O)), −5.7 (2C, Si(CH₃)₂).

MS (EI) m/z (%) 220 (1), 205 (2), 199 (4), 187 (11), 169 (1), 157 (100), 143 (8), 131 (2), 115 (7), 99 (4), 85 (3), 75 (16), 59 (4), 43 (9), 29 (1).

HRMS (ESI+) calcd for C₁₂H₂₄O₃SiNa [(M+Na)+] 267.1386, found 267.1387.

(3S,4R)-Ethyl 4,5-epoxy-6-oxoheptanoate ((3S,4R)-4i): Epoxide (3S,4R)-4i was prepared according to the general procedure. The reaction mixture was stirred for 24 h at 50 °C. Base treatment of the crude product with sodium ethoxide in THF followed by purification by flash column chromatography (silica gel, 15-30% Et₂O in pentane) provided the title compound as a colorless oil (75 mg, 405 μmol, 81%; 98:2 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/SE-52 column 30 m (80 °C, 1.2 °C/min until 130 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H₂); major enantiomer: 𝜏_R = 35.76 min, minor enantiomer: 𝜏_R = 37.27 min.

^1H NMR (500 MHz, CD₂Cl₂) δ 4.12 (q, J = 7.2 Hz, 2H, CH₂CH₃), 3.20 (d, J = 2.1 Hz, 1H, CepoHC(=O)), 3.16-3.14 (m, 1H, CepoHCH₂), 2.45 (t, J = 7.3 Hz, 2H, CH₂CO₂Et), 2.03 (s, 3H, CH₃C(=O)), 2.03-1.97 (m, 1H, CHHCepoH), 1.90-1.82 (m, 1H, CHHCepoH), 1.24 (t, J = 7.3 Hz, 3H, CH₂CH₃).

^13C NMR (125 MHz, CD₂Cl₂): δ 205.1 (C=O), 172.3 (CO₂Et), 60.7 (CH₂CH₃), 59.8 (CepoHC(=O)), 56.9 (CepoHCH₂), 30.1 (CH₂CO₂Et), 27.0 (CH₂CepoH), 24.5 (CH₃C(=O)), 14.0 (CH₂CH₃).
**MS** (EI) m/z (\%) 186 [M⁺] (trace), 143 (13), 125 (1), 115 (29), 99 (15), 85 (30), 69 (7), 55 (13), 43 (100), 29 (29).

**HRMS** (CI-FE) calcd for C₉H₁₅O₄ [(M+H)⁺] 187.0972, found 187.0970.

(3S,4R)-7-Oxo-3,4-epoxy-2-octanone ((3S,4R)-4j): Epoxide (3S,4R)-4j was prepared according to the general procedure. The reaction mixture was stirred for 24 h at 50 °C. Base treatment of the crude product was omitted. Purification by flash column chromatography (silica gel, 10-30% Et₂O in pentane) provided the title compound as a colorless oil (31 mg, 202 μmol, 40%; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/SE-52 column 30 m (80 °C, 1.2 °C/min until 120 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H₂); major enantiomer: τ_R = 29.03 min, minor enantiomer: τ_R = 30.33 min.

**¹H NMR** (500 MHz, CD₂Cl₂) δ 3.17 (d, J = 1.8 Hz, 1H, CH epoC(=O)), 3.12–3.10 (m, 1H, C epoCH₂), 2.56 (t, J = 7.0 Hz, 2H, CH₂C(=O)), 2.13 (s, 3H, CH₂C(=O)C₂H₅), 2.01 (s, 3H, CHepoC(=O)C₂H₅), 2.00–1.93 (m, 1H, CHH epoH), 1.78–1.72 (m, 1H, CHH epoH).

**¹³C NMR** (125 MHz, CD₂Cl₂) δ 207.1 (CH 2C=O), 205.6 (C epoCH₂C=O), 60.2 (C epoHC(=O)), 57.3 (CH₂ epoH), 39.2 (CH₂C(=O)), 30.0 (CH₃C(=O)CH₂), 25.9 (CH₂CepoH), 24.7 (CH₃C(=O)CHepo).

(4S,5R)-4,5-Epoxy-3-hexanone ((4S,5R)-4o): Epoxide (4S,5R)-4o was prepared according to the general procedure. The reaction mixture was stirred for 12 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et₂O in pentane) provided the title compound 4o as a colorless oil (63 mg, 552 μmol, 55% (reduced yield due to the high volatility of 4o); 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-178/OV-1701 30 m column (60 °C, 1.0 °C/min until 70 °C 20 °C/min until 220 °C, 10 min at 220 °C, 0.4 bar H₂); major enantiomer: τ_R = 12.45 min, minor enantiomer: τ_R = 12.74 min.

**¹H NMR** (500 MHz, CD₂Cl₂) δ 3.15 (d, J = 2.0 Hz, 1H, CH epoC(=O)), 2.44 (dq, J = 18.3, 7.4 Hz, 1H, CHH), 2.31 (dq, J = 18.5, 7.2 Hz, 1H, CHH), 1.37 (d, J = 5.2 Hz, 3H, CH₃CH epo), 1.00 (t, J = 7.3 Hz, 3H, CH₂CH₃).

**¹³C NMR** (125 MHz, CD₂Cl₂) δ 208.3 (C=O), 60.9 (CH epoC(=O)), 55.0 (CH₃CH epo), 31.2 (CH₂), 17.9 (CH₃CH epo), 7.3 (CH₂CH₃).

**GC-MS** (GC-EI) m/z (%) 114 [M⁺] (1), 99 (17), 85 (14), 83 (2), 69 (70), 57 (75), 53 (6), 43 (14), 41
(4S,5R)-4,5-Epoxy-3-tetradecanone ((4S,5R)-4p): Epoxide (4S,5R)-4p was prepared according to the general procedure. The reaction mixture was stirred for 24 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et₂O in pentane) provided the title compound 4p as a colorless oil (185 mg, 817 μmol, 82%; 99:1 er). The enantiomeric ratio was determined by GC using a chiral Lipodex E column 25 m (100 °C, 1.2 °C/min until 180 °C, 18 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H₂); major enantiomer: τᵣ = 30.53 min, minor enantiomer: τᵣ = 29.18 min.

\[ \text{H NMR} \quad \delta 3.19 (d, J = 2.0 Hz, 1H, CH_{epo}C(=O)), 3.01 (td, J = 5.5, 1.9 Hz, 1H, CH₂CH_{epo}), 2.44 (dq, J = 18.3, 7.3 Hz, 1H, CHH{C(=O)}), 2.32 (dq, J = 18.4, 7.2 Hz, 1H, CHHC{C(=O)}), 1.62-1.55 (m, 2H, CH₂CH{epo}), 1.48-1.41 (m, 2H, CH₂CH₂CH{epo}), 1.35-1.26 (m, 12H, (CH₂)₆CH₃), 1.01 (t, J = 7.2 Hz, 3H, C(=O)CH₂C{H₃}), 0.88 (t, J = 7.0 Hz, 3H, (CH₂)₈CH₃). \]

\[ \text{C NMR} \quad \delta 208.4 (C=O), 60.0 (CH_{epo}C(=O)), 59.0 (CH₂CH_{epo}), 32.4 (2C, CH₂), 31.2 (CH₂), 30.0 (2C, CH₂), 29.8 (2C, CH₂), 26.3 (CH₂), 23.2 (CH₂), 14.4 ((CH₂)₈CH₃), 7.4 (C=O)CH₂CH₃). \]

\[ \text{MS} \quad m/z (\%) 226 [M⁺] (2), 197 (1), 179 (1), 169 (2), 151 (3), 127 (1), 109 (4), 99 (43), 95 (11), 81 (7), 69 (6), 57 (100), 41 (15), 29 (26). \]

HRMS (ESI+) calcd for C₁₄H₂₆NaO₂ [(M+Na)⁺] 249.1826, found 249.1825.

(7S,8R)-7,8-Epoxy-6-tridecanone ((7S,8R)-4l): Epoxide (7S,8R)-4l was prepared according to the general procedure. The reaction mixture was stirred for 24 h at 50 °C. Purification by flash column chromatography (silica gel, 1-20% Et₂O in pentane) provided the title compound 4l as a colorless oil (161 mg, 758 μmol, 76%; 99:1 er). The enantiomeric ratio was determined by GC using a chiral G-TA column 30 m (80 °C, 1.0 °C/min until 125 °C, 20 °C/min until 180 °C, 10 min at 180 °C, 0.9 bar H₂); major enantiomer: τᵣ = 44.18 min, minor enantiomer: τᵣ = 43.42 min.

\[ \text{H NMR} \quad \delta 3.18 (d, J = 2.0 Hz, 1H, CH_{epo}C(=O)), 3.01 (td, J = 5.5, 2.0 Hz, 1H, CH₂CH_{epo}), 2.41 (ddd, J = 17.3, 8.3, 6.5 Hz, 1H, CHHC{C(=O)}), 2.28 (ddd, J = 17.3, 8.2, 6.8 Hz, 1H, CH₃). \]
CHHCCCCCC(=O)), 1.62-1.52 (m, 4H, CH₂), 1.48-1.42 (m, 2H, CH₂), 1.34-1.23 (m, 8H, CH₂), 0.91-0.87 (m, 6H, CH₃).

¹³C NMR (125 MHz, CD₂Cl₂) δ 208.1 (C=O), 60.1 (CHepoC(=O)), 58.9 (CH₂CHepo), 37.8 (CH₂C(=O)), 32.4 (CH₂), 32.0 (CH₂), 31.9 (CH₂), 26.0 (CH₂), 23.4 (CH₂), 23.1 (CH₂), 23.0 (CH₂), 14.3 (CH₃), 14.2 (CH₃).

MS (EI-DE) m/z (%) 212 [M⁺] (6), 169 (1), 156 (3), 141 (58), 125 (4), 112 (7), 99 (98), 95 (12), 82 (8), 71 (76), 55 (18), 43 (100), 29 (30).


(5S,6R)-5,6-Epoxy-2-methyl-4-undecanone ((5S,6R)-4m): Epoxide (5S,6R)-4m was prepared according to the general procedure. 20 mol% of catalyst [1a • 2 TFA] was used under otherwise identical conditions. The reaction mixture was stirred for 48 h at 50 °C. Base treatment of the crude product was omitted. Purification by flash column chromatography (silica gel, 1-20% Et₂O in pentane) provided the title compound 4m as a colorless oil (161 mg, 812 μmol, 81%; >99.5:0.5 er). The enantiomeric ratio was determined by GC using a chiral G-TA column 30 m (80 °C, 1.0 °C/min until 115 °C, 20 °C/min until 180 °C, 10 min at 180 °C, 0.9 bar H₂); major enantiomer: τᵣ = 30.89 min, minor enantiomer: τᵣ = 30.09 min.

¹H NMR (500 MHz, CD₂Cl₂) δ 3.16 (d, J = 2.0 Hz, 1H, CHepoC(=O)), 2.99 (td, J = 5.5, 1.9 Hz, 1H, CH₂CHepo), 2.31 (dd, J = 16.0, 6.0 Hz, 1H, CHHHi-Pr), 2.15 (dd, J = 16.2, 7.1 Hz, 1H, CHHHi-Pr), 2.11 (hept, J = 6.5 Hz, 1H, CHMe₂), 1.64-1.55 (m, 2H, CH₂CHepo), 1.48-1.42 (m, 2H, CH₂CH₂CHepo), 1.34-1.30 (m, 4H, (CH₂)₂CH₃), 0.92-0.88 (m, 9H, CH₃).

¹³C NMR (125 MHz, CD₂Cl₂) δ 207.7 (C=O), 60.2 (CHepoC(=O)), 58.7 (CH₂CHepo), 46.7 (CHHHi-Pr), 32.4 (CH₂), 32.0 (CH₂), 26.0 (CH₂), 24.6 (CHMe₂), 23.1 (CH₂), 22.9 (CH(CH₃)₂), 22.8 (CH(CH₃)₂), 14.3 ((CH₂)₃CH₃).

MS (EI-DE) m/z (%) 198 [M⁺] (1), 183 (1), 155 (1), 141 (2), 127 (33), 113 (5), 95 (6), 85 (75), 69 (5), 57 (100), 41 (30), 29 (18).

HRMS (ESI+) calcd for C₁₂H₂₂NaO₂ [(M+Na)+] 221.1513, found 221.1512.
(4S,5R)-4,5-Epoxy-2-Methyl-3-hexanone ((4S,5R)-4n): Epoxide (4S,5R)-4n was prepared according to the general procedure. 20 mol% of catalyst [1a • 2 TFA] was used under otherwise identical conditions. The reaction mixture was stirred for 48 h at 50 °C. Purification by flash column chromatography (silica gel, 2-7% Et₂O in pentane) provided the title compound as a colorless liquid (77 mg, 604 μmol, 60% (reduced yield due to the high volatility of 4n); 96.5:3.5 er). THF (5 mL) was used as solvent for the base treatment with aqueous 1N NaOH. The enantiomeric ratio was determined by GC using a chiral Lipodex G column 25 m (50 °C, 1.2 °C/min until 110 °C, 18 °C/min until 230 °C, 5 min at 230 °C, 0.5 bar H₂); major enantiomer: τₚ = 8.24 min, minor enantiomer: τₚ = 8.76 min.

1H NMR (500 MHz, CD₂Cl₂) δ 3.25 (d, J = 1.9 Hz, 1H, CₑpoH(C=O)), 3.03 (dq, J = 5.1, 2.0 Hz, 1H, MeCₑpoH), 2.70 (hept, J = 6.9 Hz, 1H, CHMe₂), 1.38 (d, J = 5.0 Hz, 3H, CH₂CₑpoH), 1.09 (d, J = 7.3 Hz, 3H, CH(CH₃)₂), 1.06 (d, J = 6.9 Hz, 3H, CH(CH₃)₂).

13C NMR (125 MHz, CD₂Cl₂) δ 210.5 (C=O), 59.5 (CₑpoH(C=O)), 55.0 (MeCₑpoH), 36.7 (CHMe₂), 18.3 (CH₃CₑpoH), 17.7 (CH(CH₃)₂), 17.4 (CH(CH₃)₂).

GC-MS (GC-EI) m/z (%) 128 [M⁺] (1), 113 (10), 85 (16), 83 (2), 71 (41), 69 (4), 58 (21), 55 (6), 45 (5), 43 (100), 41 (31), 39 (10), 29 (26).


Studies on Hydroxy-Group Containing Substrates

Other substrates containing unprotected hydroxy groups were also examined. However, depending on the chain length separating the hydroxy group, various side reactions were encountered. Substrate 2t was found to undergo a competitive intramolecular oxa-Michael reaction, furnishing racemic tetrahydrofuran in quantitative yield (a). Substrate 2u containing a shorter linker was found to undergo elimination as the major side reaction, giving dienone in addition to the expected products. A reliable route to epoxide products containing a hydroxyl moiety was found to be the epoxidation of THP protected substrates (e.g. 2g, Table 2 entry 13), followed by a facile deprotection with ceric ammonium nitrate (CAN) without any loss of enantioselectivity (c).

(3S,4R)-3,4-Epoxy-9-hydroxy-2-nonanone (4k): To a vial containing THP ether 4g (40.0 mg, 156 μmol) dissolved in acetonitrile (1.6 mL) and borate buffer (pH = 8) (1.6 mL), was added with stirring CAN (2.7 mg, 4.68 μmol, 3 mol%). After 3 h at 60 °C, the mixture was cooled to room temperature, diluted with water (4 mL) and repeatedly extracted with Et2O (3×10 mL). The combined organic layers were washed with brine, dried over Na2SO4, filtered and concentrated under reduced pressure. After purification of the crude product by flash column chromatography (silica gel, 5-30% Et2O in CH2Cl2) the alcohol 4g (24 mg, 138 μmol, 88%; 98:2 er) was obtained as a colorless oil. The enantiomeric ratio was determined by GC using a chiral Iviadex 1 column 25 m (80 °C, 1.0 °C/min until 155 °C, 20 °C/min until 220 °C, 10 min at 320 °C, 0.6 bar H2); major enantiomer: τ_R = 60.50 min, minor enantiomer: τ_R = 61.21 min.

1H NMR (500 MHz, CD2Cl2) δ 3.60 (t, J = 6.5 Hz, 2H, CH2OH), 3.15 (d, J = 1.6 Hz, 1H, CepoHC=O), 3.06 (td, J = 5.6, 1.6 Hz, 1H, CH2CepoH), 1.69-1.37 (m, 9H, CH2 and OH).

13C NMR (125 MHz, CD2Cl2) 205.7 (C=O), 62.6 (CH2OH), 59.9 (CepoHC(=O)), 58.0 (CH2CepoH), 32.7 (CH2), 31.8 (CH2), 27.5 (CH2), 25.5 (CH2), 24.3 (CH3).

MS (EI) m/z (%) 129 (1), 111 (2), 99 (3), 93 (4), 85 (36), 81 (13), 67 (8), 55 (31), 43 (100), 39 (9), 31 (18).

HRMS (Cl-DE) calcd for C9H17O3 [(M+H)+] 173.1176, found 173.1178.

The tetrahydrofuran-derivative S-15 has been described in the literature.

Further Studies on the Hydroperoxidation and Epoxidation of Enones

This hypothesis is further supported by the formation of deconjugated enones iso-2b and iso-2q in the presence of catalytic salt [1a·2 TFA]. The observation that epoxide trans-4b was formed from (Z)-2b with a slightly lower optical purity than in the reaction of the corresponding (E)-enone (Scheme 3) may be rationalized by a minor contribution of conjugate addition of hydrogen peroxide to the (Z)-configured substrate which possibly delivers the opposite enantiomeric product.

We briefly tested β,β-disubstituted enones in the epoxidation, including the citral-derived enone S-3 and the symmetrically substituted mesityl oxide S-6. In both cases, incomplete conversion was observed due to considerably lower reactivity of these substrates. The conversion could be improved by higher reaction temperatures and longer times, although at the expense of enantioselectivity in the case of 10. Under the more forcing conditions, an E/Z mixture of enone S-3 affords peroxyhemiketal S-4 with a 56% yield and moderate enantioselectivity (78:22 er) along with epoxide S-5, which was formed with good diastereoselectivity and enantioselectivity for the major diastereomer, albeit a very low yield (Scheme 8a). Intriguingly, the symmetrically β,β-disubstituted mesityl oxide S-6 afforded an enantioenriched epoxide S-8 (81:19 er) along with the peroxyhemiketal S-7, suggesting that the

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6 Submitting pure (E) and (Z) isomers of enone 7 also revealed complete diastereoconvergence.
epoxide formation from the initially formed achiral hydroperoxidation product S-7 is under significant control by the chiral amine catalyst.

\[
\begin{align*}
\text{S-3} & \xrightarrow{\text{[1a·2 TFA] (20 mol\%) H}_2\text{O}_2 (50 wt\%; 3 equiv)} \text{1,4-dioxane (0.25 M) 70 °C, 48 h} \quad & \text{56% yield} \quad (-1:1 \text{ dr}) \quad 78:22 \text{ er} \\
\text{S-4} & \text{56% yield} \quad \tau_R = 7.71 \text{ min} \\
\text{S-5} & \text{78:22 er} \\
\text{S-6} & \xrightarrow{\text{[1a·2 TFA] (10 mol\%) H}_2\text{O}_2 (50 wt\%; 1.5 equiv)} \text{1,4-dioxane (0.25 M) 50 °C, 48 h} \quad & \text{38% yield} \quad \tau_R = 7.39 \text{ min} \\
\text{S-7} & \text{38% yield} \quad 81:19 \text{ er} \\
\text{S-8} & \text{81:19 er}
\end{align*}
\]

1-(3,3-dimethyloxiran-2-yl)ethanone (S-8): The epoxyketone S-8\(^7\) has been described in the literature. The enantiomeric ratio of epoxyketone S-8 was determined by GC using a chiral BGB-176/SE52 column 30 m (60 °C, 1 °C/min until 85 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.4 bar H\(_2\)); major enantiomer: \(\tau_R = 7.71 \text{ min}\), minor enantiomer: \(\tau_R = 7.39 \text{ min}\).

**Hydroperoxidation and Epoxidation of 4,8-Dimethylnona-3,7-dien-2-one (S-3)**

The general procedure for the catalytic asymmetric hydroperoxidation of \(\alpha,\beta\)-unsaturated ketones 2 was adapted to \(\beta,\beta\)-disubstituted enone 7 by using 20 mol% catalyst [1a·2 TFA] and 3 equiv. of hydrogen peroxide (50 wt%) and the reaction temperature was increased to 70 °C.

3,5-Dimethyl-5-(4-methylpent-3-enyl)-1,2-dioxolan-3-ol (S-4). The title compound was isolated after 48 h. Purification by flash column chromatography (silica gel; 5-10% Et\(_2\)O in pentane) as a colorless oil (56 mg, 280 \(\mu\)mol, 56%; 78:22 \(er\)). The enantiomeric ratio was determined after converting peroxyhemiketal S-4 into the corresponding epoxide S-5 (1:1 \(E/Z\)). The enantiomers were analyzed by GC using a

chiral BGB-176/SE-52 column 30 m (60 °C, 0.5 °C/min until 105 °C, 20 °C/min until 220 °C, 10 min at 320 °C, 0.4 bar H₂); (E)- S-5: major enantiomer: τ<sub>R</sub> = 81.04 min, minor enantiomer: τ<sub>R</sub> = 80.47 min; (Z)- S-5: major enantiomer: τ<sub>R</sub> = 71.83 min, minor enantiomer: τ<sub>R</sub> = 73.16 min. Characterized as a mixture of hemiketal epimers.

1H NMR (500 MHz, CDCl₃) δ 5.10-5.06 (m, 2H, =CCH₂), 2.93 (br s overlapped, 1H, OCH), 2.90 (br s overlapped, 1H, OCH), 2.53 (d, 1H, J = 12.8 Hz, CH₂,cycl.), 2.44 (s, 2H, CH₂,cycl.), 2.41 (d, 1H, J = 12.7 Hz, CHH,cycl.), 2.09-1.94 (m, 4H, =CHC₂), 1.73 (dd, 1H, J = 13.8, 11.4, 5.3 Hz, =CHCH₂CHH), 1.68-1.64 (m overlapped, 2H, =CHCH₂CHH), 1.54-1.48 (m overlapped, 1H, =CHCH₂CHH), 1.53 (s overlapped, 6H, CqoC₃H₃), 1.50 (s overlapped, 3H, CqOHC₃), 1.49 (s overlapped, 3H, CqOHC₃), 1.34 (s, 3H, CqalC₃H₃), 1.33 (s, 3H, CqalC₃H₃).

13C NMR (125 MHz, CDCl₃) δ 132.3 (Cqol), 131.9 (Cqol), 123.8 (CH₀), 123.5 (CH₀), 105.9 (CqOH), 105.7 (CqOH), 86.3 (Cqal), 85.9 (Cqal), 57.7 (CH₂,cycl.), 57.1 (CH₂,cycl.), 39.8 (CH₂CH₂CH₂), 37.9 (CH₂CH₂CH₂), 25.7 (2C, Cqal(CH₃)₂), 25.2 (CH₂Cqal), 23.5 (CH₄CH₂), 23.2 (CH₃CqOH), 23.1 (CH₃CqOH), 23.0 (CH₄CH₂), 22.3 (CH₂Cqal), 17.7 (Cqol(CH₃)₂), 17.6 (Cqol(CH₃)₂).

MS (EI-DE) m/z (%) 185 (1), 167 (1), 139 (1), 123 (2), 109 (5), 97 (3), 82 (16), 69 (32), 55 (22), 43 (100), 29 (9).

HRMS (ESI+) calcd for C₁₁H₂₀NaO₃ [(M+Na)<sup>+</sup>] 223.1307, found 223.1305.

3,4-Epoxy-4,8-dimethyl-7-nonen-2-one (S-5): Epoxy ketone S-5 was obtained as a colorless oil (9.1 mg, 50 μmol, 10% (88:12 dr((E)- S-5)/(Z)- S-5); 95.5:4.5 er((E)- S-5), 59.5:40.5 er((Z)- S-5)). Purification by flash column chromatography (silica gel; 1-10% Et₂O in pentane) provided pure samples of (E)- and (Z)-isomers of epoxy ketone S-5. The enantiomeric ratio was determined by GC using a chiral BGB-176/SE-52 column 30 m (60 °C, 0.5 °C/min until 105 °C, 20 °C/min until 220 °C, 10 min at 320 °C, 0.4 bar H₂); (E)- S-5: major enantiomer: τ<sub>R</sub> = 81.25 min, minor enantiomer: τ<sub>R</sub> = 80.71 min; (Z)- S-5: major enantiomer: τ<sub>R</sub> = 73.29 min, minor enantiomer: τ<sub>R</sub> = 72.18 min. The analytical data were identical in all respects to those previously reported.⁸

(E)-3,4-Epoxy-4,8-dimethyl-7-nonen-2-one ((E)-S-5)

\[ \begin{align*} 
\text{1H NMR (500 MHz, CD}_2\text{Cl}_2) \delta & \ 5.12 (t, J = 7.1 \text{ Hz}, 1H, =CHCH_2), 3.40 (s, 1H, C_{epo}H), \\
& \ 2.17 (s, 3H, CH_3C(=O)), 2.12 (\text{app. q}, 2H, =CHCH_2), 1.77 (\text{dd}, J = 14.2, \\
& \ 7.1 \text{ Hz}, 1H, CHHCH_{qepo}), 1.70 (s, 3H, CH_3C_{qol}), 1.62 (s, 3H, CH_3C_{qol}), 1.56-1.49 (m, 1H, CHHCH_{qepo}), \\
& \ 1.20 (s, 3H, CH_3C_{qepo}).
\end{align*} \]

\[ \begin{align*} 
\text{13C NMR (125 MHz, CD}_2\text{Cl}_2) \delta & \ 204.1 (C=O), 132.8 (C_{qol}), 123.4 (CH_{qol}), 65.2 (C_{epo}H), 63.4 (C_{qepo}), \\
& \ 38.5 (CH_3CH_2), 28.2 (CH_3C(=O)), 25.8 (CH_3), 24.1 (CH_2C_{qepo}), 17.7 (CH_3), 16.1 (CH_3).
\end{align*} \]

\[ \begin{align*} 
\text{MS (EI-DE) } m/z \ (\%) & \ 182 [M^+] (1), 164 (2), 149 (4), 139 (3), 121 (7), 109 (43), 99 (23), 82 (45), 69 \\
& \ (56), 67 (24), 55 (18), 43 (100), 27 (10).
\end{align*} \]

HRMS (EI-FE) calcd for C_{11}H_{18}O_2 [M^+] 182.1307, found 182.1307.

(Z)-3,4-Epoxy-4,8-dimethyl-7-nonen-2-one ((Z)-S-5)

\[ \begin{align*} 
\text{1H NMR (500 MHz, CD}_2\text{Cl}_2) \delta & \ 5.02 (t, J = 7.2 \text{ Hz}, 1H, =CHCH_2), 3.37 (s, 1H, \\
& \ C_{epo}H), 2.19 (s, 3H, CH_3), 2.14-1.98 (m, 2H, =CHCH_2), 1.66 (s, 3H, CH_3C_{qol}), \\
& \ 1.59 (s, 3H, CH_3C_{qol}), 1.57-1.42 (m, 2H, CH_2C_{qepo}), 1.40 (s, 3H, CH_3C_{qepo}).
\end{align*} \]

\[ \begin{align*} 
\text{13C NMR (125 MHz, CD}_2\text{Cl}_2) \delta & \ 204.0 (C=O), 132.8 (C_{qol}), 123.3 (CH_{qol}), 66.0 (C_{epo}H), 64.0 (C_{qepo}), \\
& \ 32.5 (CH_3CH_2), 28.5 (CH_3C(=O)), 25.8 (CH_3), 24.4 (CH_2C_{qepo}), 22.2 (CH_3), 17.6 (CH_3).
\end{align*} \]
One-Pot Synthesis of Aldol Products 6

**General Procedure**

\[
\begin{align*}
2 & \quad \text{[1a•2 TCA] (10 mol\%)} \\
& \quad \text{H}_2\text{O}_2 (30 \text{ wt\%}, 3 \text{ equiv)} \\
& \quad \text{dioxane (0.25 M), 32 °C, 12-48 h} \\
& \quad \text{then P(OEt)}_3 (5 \text{ equiv)} \\
& \quad 0^\circ \text{C to 32°C, 10 h} \\
& \quad \text{R}_1, \text{R}_2 = \text{Alk} \\
\end{align*}
\]

Catalyst salt [1a • 2 TCA] was prepared *in situ* by the addition of 9-amino(9-deoxy)epiquinine (1a; 32.3 mg, 0.1 mmol, 10 mol%) to a solution of trichloroacetic acid (32.6 mg, 0.2 mmol, 20 mol%) in dioxane (4 mL). Then, enone 2 (1.0 mmol, 1.0 equiv) was added, and 20 minutes later, aqueous hydrogen peroxide (30 wt%, 304 μL, 3.0 mmol, 3 equiv). After 36-48 h of stirring at 32°C, triethylphosphite (519 μL, 3.0 mmol, 3 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 10 h at room temperature. Additional triethylphosphite (346 μL, 2 mmol, 2 equiv) was added and the reaction was further stirred until TLC analysis indicated complete reduction of the peroxycetals (2 h). The reaction mixture was repeatedly extracted with Et₂O (3×25 mL) and the combined organic phases were washed with brine, dried (Na₂SO₄), and filtered. Removal of the volatiles under reduced pressure furnished the crude product, which was subjected to flash column chromatography (silica gel, eluent: Et₂O-pentane) to afford the corresponding pure aldol-type product 6.

**Catalytic hydrogenation procedure**: General hydroperoxidation procedure for enones 2 using 0.5 mmol substrate 2a was followed. Upon the standard aqueous workup, crude ¹H NMR analysis revealed 100% conversion and a 76:24 ratio of hydroperoxide 3a and epoxide 4a, respectively. The crude product mixture was dissolved in MeOH (25 mL), and Pd/C (15% wt, 11.6 mg) was added. The flask was equipped with a H₂ balloon, purged with H₂ 5 times and the reaction mixture was stirred under 1 atm. of H₂ for 4 h at room temperature, upon which all of the starting hydroperoxide was consumed. The crude reaction mixture was filtered through a pad of Celite and extracted with diethyl ether (3 x 10 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ and filtered.
Evaporation of the solvent under reduced pressure followed by flash column chromatography (20% Et₂O in pentane) afforded pure 6a as a colourless oil (52.2 mg, 0.30 mmol, 61%, 97:3 er) along with unchanged epoxide 4a (yield not determined).

Scope of Optically Active Aldol Products 6

(R)-4-Hydroxy-2-decanone ((R)-6a): Aldol product (R)-6a was prepared according to the general procedure. The reaction mixture was stirred for 36 h at 32 °C followed by in situ reduction with triethylphosphite. Purification of the crude product by flash column chromatography (silica gel, 10-50% Et₂O in pentane) provided the title compound as a colorless oil (102 mg, 592 μmol, 59%; 97:3 er). The enantiomeric ratio was determined by GC using a chiral G-TA column 30 m (80 °C, 1.0 °C/min until 115 °C, 20 °C/min, until 180 °C, 10 min at 320 °C, 0.9 bar H₂); major enantiomer: τR = 31.94 min, minor enantiomer: τR = 31.38 min.

1H NMR (500 MHz, CD₂Cl₂) δ 4.00-3.95 (m, 1H, CH(OH)), 2.81 (br s, 1H, OH), 2.61 (dd, J = 17.5, 2.7 Hz, 1H, C(=O)CH₂H), 2.48 (dd, J = 17.5, 9.3 Hz, 1H, C(=O)CHH₂H), 2.14 (s, 3H, C(=O)CH₃), 1.46-1.35 (m, 2H, CH₂CH₂CH(OH)), 1.34-1.26 (m, 8H, CH₃(CH₂)₄), 0.88 (t, J = 6.9 Hz, 3H, CH₃CH₂).

13C NMR (125 MHz, CD₂Cl₂) δ 210.3 (C(=O)), 67.9 (CH(OH)), 50.3 (C(=O)CH₂), 36.9 (CH₂CH₂CH(OH)), 32.2 (CH₂), 30.9 (C(=O)CH₃), 29.6 (CH₂), 25.8 (CH₂), 23.0 (CH₂), 14.2 ((CH₂)₅CH₃).

MS (EI-DE) m/z (%) 172 [M⁺] (trace), 154 (1), 139 (1), 125 (1), 111 (1), 96 (6), 87 (44), 84 (2), 69 (5), 55 (17), 43 (100), 29 (11).

HRMS (CI-FE, NH₃) calcd for C₁₀H₂₄NO₂ [(M+NH₄)⁺] 190.1805, found 190.1807.

(R)-4-Hydroxy-6-phenyl-2-hexanone ((R)-6b): Aldol product (R)-6b was prepared according to the general procedure. The reaction mixture was stirred for 36 h at 32 °C followed by in situ reduction with triethylphosphite. Purification of the crude product by flash column chromatography (silica gel, 10-60% Et₂O in pentane) provided the title compound as a colorless oil (102 mg, 531 μmol, 53%; 96.5:3.5 er). The enantiomeric ratio was determined by HPLC using a chiral Chiralpak IA column (10% i-PrOH in heptane, 0.5 mL/min); major
enantiomer: $\tau_R = 16.75$ min, minor enantiomer: $\tau_R = 15.41$ min.

**Optical rotation** $[\alpha]^D_{25} = 14.8$ (c = 1.1, CHCl$_3$, 96.5:3.5 er (R)) [Lit.$^9$: (R)-16b, $[\alpha]_{D}^{15} = 12.0$ (c = 1.1, CHCl$_3$, 94:6 er).

$^1$H NMR (500 MHz, CD$_2$Cl$_2$) $\delta$ 7.29-7.26 (m, 2H, CH$_{ar,m}$), 7.21-7.16 (m, 3H, CH$_{ar,o,p}$), 4.03-3.97 (m, 1H, CH$_{(OH)}$), 2.95 (d, $J = 3.5$ Hz, 1H, OH), 2.81-2.75 (m, 1H, PhCHH), 2.69-2.64 (m, 1H, PhCHH), 2.63 (dd, $J = 17.7$, 2.9 Hz, 1H, C(=O)CHH), 2.53 (dd, $J = 17.7$, 9.2 Hz, 1H, C(=O)CHH), 2.14 (s, 3H, CH$_3$), 1.80-1.73 (m, 1H, PhCH$_2$CHH), 1.70-1.64 (m, 1H, PhCH$_2$CHH).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) $\delta$ 210.2 (C(=O)), 142.5 (C$_{qar}$), 128.8 (2C, CH$_{ar,o}$), 128.7 (2C, CH$_{ar,m}$), 126.1 (CH$_{ar,p}$), 67.2 (CH$_{(OH)}$), 50.3 (C(=O)CH$_2$), 38.5 (PhCH$_2$CH$_2$), 32.0 (PhCH$_2$), 30.9 (CH$_3$).

**MS** (EI-DE) $m/z$ (%) 192 (2), 174 (34), 159 (4), 131 (29), 117 (17), 104 (17), 91 (73), 87 (9), 77 (10), 65 (11), 58 (4), 51 (6), 43 (100), 39 (6), 27 (4).

**HRMS** (CI-FE, NH$_3$) calcd for C$_{12}$H$_{20}$NO$_2$ [(M+NH$_4$)$^+$] 210.1493, found 210.1494.

(R)-4-Hydroxy-6-methyl-2-heptanone ((R)-6c): Aldol product (R)-6c was prepared according to the general procedure. The reaction mixture was stirred for 36 h at 32 °C followed by in situ reduction with triethylphosphite. Purification of the crude product by flash column chromatography (silica gel, 10-40% Et$_2$O in pentane) provided the title compound as a colorless oil (81 mg, 562 $\mu$mol, 56%; 96.5:3.5 er). The enantiomeric ratio was determined by HPLC using a chiral Chiralpak IA column (10% i-PrOH in heptane, 0.5 mL/min); major enantiomer: $\tau_R = 11.84$ min, minor enantiomer: $\tau_R = 11.39$ min.

$^1$H NMR (500 MHz, CD$_2$Cl$_2$) $\delta$ 4.10-4.04 (m, 1H, CH$_{(OH)}$), 2.84 (br s, 1H, OH), 2.58 (dd, $J = 17.7$, 2.9 Hz, 1H, CHHC(=O)), 2.47 (dd, $J = 17.7$, 9.2 Hz, 1H, CHHC(=O)), 2.14 (s, 3H, C(=O)CH$_3$), 1.80-1.72 (m, 1H, CH$_3$Me$_2$), 1.41 (ddd, $J = 13.6$, 9.1, 5.6 Hz, 1H, i-PrCH$_2$H), 1.12 (ddd, $J = 13.4$, 8.6, 4.5 Hz, 1H, i-PrCH$_2$H), 0.90 (d, $J = 6.6$ Hz, 6H, CH(CH$_3$)$_2$).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) $\delta$ 210.2 (C(=O)), 66.0 (CH(OH)), 50.8 (C(=O)CH$_2$), 46.0 (i-PrCH$_2$), 30.9 (C(=O)CH$_3$), 24.7 (CHMe$_2$), 23.4 (CH(CH$_3$)$_2$), 22.1 (CH(CH$_3$)$_2$).

**MS** (EI-DE) $m/z$ (%) 144 [M$^+$] (trace), 126 (9), 111 (10), 108 (25), 93 (5), 87 (100), 83 (7), 69 (17), 58 (20), 43 (90), 29 (5).

**HRMS** (CI-FE, NH$_3$) calcd for C$_8$H$_{20}$NO$_2$ [(M+NH$_4$)$^+$] 162.1494, found 162.1494.

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(S)-4-Cyclohexyl-4-hydroxy-2-butanone ((S)-6d): Aldol product (S)-6d was prepared according to the general procedure. The reaction mixture was stirred for 48 h at 32 °C followed by in situ reduction with triethylphosphite. Purification of the crude product by flash column chromatography (silica gel, 10-40% Et₂O in pentane) provided the title compound as a colorless oil (78 mg, 458 μmol, 46%; 96:4 er). The enantiomeric ratio was determined by HPLC using a chiral Chiralpak IA column (10% i-PrOH in heptane, 0.5 mL/min); major enantiomer: τ_R = 14.65 min, minor enantiomer: τ_R = 13.19 min.

^1H NMR (500 MHz, CD₂Cl₂) δ 3.78-3.73 (m, 1H, CH(OH)), 2.77 (br s, 1H, OH), 2.61 (dd, J = 17.3, 2.7 Hz, 1H, CHH(=O)), 2.49 (dd, J = 17.4, 9.9 Hz, 1H, CHH(=O)), 2.15 (s, 3H, CH₃), 1.84-1.79 (m, 1H, CH₂), 1.77-1.71 (m, 2H, CH₂), 1.68-1.61 (m, 2H, CH₂), 1.35-1.27 (m, 1H, CH₆cyc), 1.26-1.10 (m, 3H, CH₂), 1.07-0.94 (m, 2H, CH₂).

^13C NMR (125 MHz, CD₂Cl₂) δ 210.6 (C(=O)), 72.0 (C(=O)CH₂), 47.5 (C(=O)CH₂), 43.4 (CH₆cyc), 30.9 (CH₃), 29.2 (CH₂), 28.5 (CH₂), 26.9 (CH₂), 26.6 (CH₂), 26.5 (CH₂).

MS (El-DE) m/z (%) 170 [M⁺] (trace), 152 (3), 137 (2), 112 (5), 109 (3), 95 (12), 87 (80), 83 (6), 67 (14), 58 (9), 55 (26), 43 (100), 39 (9), 29 (10).

HRMS (Cl-FE, NH₃) calcd for C₁₀H₂₂NO₂ [(M+NH₄)+] 188.1650, found 188.1651.

4-Hydroxyoct-7-en-2-one (6e): Aldol product 6e was prepared according to the general procedure. The reaction mixture was stirred for 36 h at 32 °C followed by in situ reduction with triethylphosphite. Purification of the crude product by flash column chromatography (silica gel, 10-40% Et₂O in pentane) provided the title compound as a colorless oil (78 mg, 549 μmol, 55%; 96:4 er). The enantiomeric ratio was determined by HPLC using a chiral Chiralpak IA column (10% i-PrOH in heptane, 0.5 mL/min); major enantiomer: τ_R = 13.35 min, minor enantiomer: τ_R = 12.51 min.

^1H NMR (500 MHz, CD₂Cl₂) δ 5.84 (dddd, J = 17.0, 9.3, 7.7, 5.9 Hz, 1H, CH₂=CH), 5.04 (app. dq, 1H, J = 17.2, 1.8 Hz, CHHtransH=CH), 4.96 (app. dq, 1H, J = 9.4, 1.5 Hz, 1H, CHHcis=CH), 4.03-3.98 (m, 1H, CH(OH)), 2.86 (d, J = 3.8 Hz, 1H, OH), 2.61 (dd, J = 17.3, 3.0 Hz, 1H, CHH(=O)), 2.50 (dd, J = 17.7, 9.3 Hz, 1H, CHH(=O)), 2.24-2.07 (m, 2H, CH₂), 2.14 (s, 3H, CH₃), 1.57-1.42 (m, 2H, CH₂).

^13C NMR (125 MHz, CD₂Cl₂) δ 210.1 (C(=O)), 138.8 (CH₂=CH), 114.8 (CH₂=CH), 67.3 (CH(OH)), 142.20
50.3 (C(=O)CH₂), 35.9 (=CHCH₂CH₂), 30.9 (CH₃), 30.1 (=CHCH₂).

**MS (EI-DE) m/z (%)** 142 [M⁺] (trace), 127 (1), 124 (2), 109 (4), 100 (7), 94 (11), 87 (1), 81 (6), 67 (8), 58 (10), 43 (100), 41 (16), 29 (10).

**HRMS (Cl-FE, NH₃) calecd for C₈H₁₈NO₂ [(M+NH₄)⁺] 160.1337, found 160.1338.

**Organoselenium-Mediated Reductive Cleavage of Epoxide 4m**

To access the aldol-like products 6 from enone substrates that do not form peroxyhemiketals but only furnish epoxides, we found that reductive epoxide cleavage with *in situ* generated phenyl selenide represents an excellent alternative strategy.⁺ Thus, epoxide 4m could be reduced to the corresponding product 6f in a good yield and with essentially unchanged optical purity.


(R)-6-hydroxy-2-methylundecan-4-one (S-9). Under argon, acetic acid (15 μL, 0.075 mmol, 0.5 equiv) was added to an ethanolic solution of sodium phenylselenide, prepared by the reduction of diphenylselenide (52.5 mg, 0.225 mmol, 1.5 equiv) with sodium borohydride (17 mg, 0.45 mmol, 3.0 equiv) in ethanol (1 mL), and the mixture was stirred for five minutes at room temperature. The resulting solution was added at once to a solution of α,β-epoxy ketone 4m (30 mg, 0.15 mmol, 1.0 equiv) in ethanol (0.6 mL) at 0 °C. After five minutes at room temperature, the reaction mixture was diluted with EtOAc and washed with brine. The aqueous layer was extracted with EtOAc twice, and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (silica gel, 0-20% Et₂O in pentane) provided the corresponding β-hydroxy ketone S-9 as a colorless oil (27.0 mg, 0.135 mmol, 89%; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral Lipodex-G
column 25 m (isocratic at 85°C, 0.5 bar H₂); major enantiomer: \( \tau_R = 96.02 \) min, minor enantiomer: \( \tau_R = 97.99 \) min.

\(^1\)H NMR (500 MHz, CDCl₃) \( \delta \) 4.02 (c. m, 1H), 3.08 (br s, 1H), 2.57 (dd, \( J = 17.6 \) Hz, \( J = 2.6 \) Hz, 1H), 2.45 (dd, \( J = 17.6 \) Hz, \( J = 9.2 \) Hz, 1H), 2.30 (d, \( J = 7.0 \) Hz, 2H), 2.14 (sept, \( J = 6.8 \) Hz, 1H), 1.54-1.22 (m, 8H), 0.92 (s, 3H), 0.91 (s, 3H), 0.88 (t, \( J = 6.8 \) Hz, 3H)

\(^{13}\)C NMR (125 MHz, CDCl₃) \( \delta \) 212.4, 67.6, 52.6, 49.5, 36.4, 31.8, 25.2, 24.6, 22.62, 22.55, 14.05.

Synthesis of 1,2-Dioxolane 8

Direct reduction of peroxyhemiketal 3a: Peroxyhemiketal 3a (20.0 mg, 106 μmol, 1.0 equiv) and triethylsilane (25.3 μL, 158 μmol, 3.2 equiv) were dissolved in CH2Cl2 (1 mL). At −78 °C, TfOH (10.3 μL, 116.6 μmol, 1.1 equiv) was added dropwise. After stirring for 5 min, the reaction was quenched by the addition of saturated aqueous NaHCO3 solution and extracted with Et2O three times. The combined organic layers were dried (Na2SO4), filtered, and evaporated. Flash column chromatography (silica gel, 0-5% Et2O in pentane) afforded spectroscopically pure dioxolane 8 as a colourless oil (13.6 mg, 79.1 μmol, 80%; 3:1 dr (cis/trans)).

(5R)-5-hexyl-3-methoxy-3-methyl-1,2-dioxolane (7). p-Toluenesulfonic acid monohydrate (4.6 mg, 0.027 mmol) was added to a solution of peroxyhemiketal 3a (50 mg, 0.27 mmol; 98.5:1.5 er) in methanol (3 mL). After stirring for 22 h at room temperature, the solvent was removed in vacuo and the residue washed with water and diethyl ether three times to afford peroxyketal 7 (49.6 mg, 0.245 mmol, 92%) as a spectroscopically pure colourless oil. Characterized as a mixture of diastereoisomers d1 + d2 (6:4 dr).

1H NMR (500 MHz, CDCl3) δ 4.42 (pent, J = 6.0 Hz, 1H, d1), 4.32 (pent, J = 7.1 Hz, 1H, d2) 3.33 (s, 3H, d1), 3.32 (s, 3H, d2), 2.80 (dd, J = 12.4 Hz, J = 7.1 Hz, 1H, d1), 2.58 (dd, J = 12.5 Hz, J = 7.4 Hz, 1H, d2), 2.33 (dd, J = 12.5 Hz, J = 8.5 Hz, 1H, d2), 2.17 (dd, J = 12.4 Hz, J = 6.0 Hz, 1H, d1),
1.76-1.66 (m, 1H, d₁+d₂), 1.64-1.53 (m, 1H, d₁+d₂), 1.49 (s, 3H, d₁), 1.48 (s, 3H, d₂), 1.48-1.19 (m, 8H, d₁+d₂), 0.88 (c. m, 3H, d₁+ d₂)

13C NMR (125 MHz, CDCl₃) δ 107.9, 106.8, 82.1, 80.9, 52.5, 52.3, 49.5, 49.3, 34.8, 31.8, 31.7, 31.6, 29.2, 29.1, 26.3, 26.1, 22.57, 22.55, 19.2, 18.0, 14.1.


cis-(3R,5S)-3-Hexyl-5-methyl-1,2-dioxolane (cis-8): Peroxyketal 7 (20.0 mg, 98.9 µmol, 1.0 equiv) and triethylsilane (25.3 µL, 158 µmol, 1.6 equiv) were dissolved in CH₂Cl₂ (1 mL). At −78 °C, TiCl₄ (12 µL, 108.8 µmol, 1.1 equiv) was added dropwise. After stirring for 5 min, the reaction was quenched by the addition of saturated aqueous NaHCO₃ solution and extracted with Et₂O three times. The combined organic layers were dried (Na₂SO₄), filtered, and evaporated. Flash column chromatography (silica gel, 0-5% Et₂O in pentane) afforded spectroscopically pure dioxolane 8 as a colourless oil (13.6 mg, 79.1 µmol, 80%; 3:1 dr (cis/trans)).

1H NMR (400 MHz, CD₂Cl₂) cis-isomer: δ 4.37-4.28 (m, 1H, CHMe), 4.25-4.14 (m, 1H, n-HexCH), 2.79 (dd, J = 11.6, 7.2 Hz, 1H, CHCH₂CH₂), 1.76 (dd, J = 11.9, 6.8 Hz, 1H, CHCH₂CH₂), 1.70-1.59 (m, 1H, CH₂CH₂CH₂), 1.53-1.43 (m, 1H, CH₂CH₂CH₂), 1.37-1.22 (m, 8H, (CH₂)₄CH₃), 1.23 (d overlapped, 3H, J = 6.1 Hz, 1H, CHCH₂CH₂), 0.88 (t, J = 6.8 Hz, 3H, (CH₂)₅CH₃); trans-isomer: δ 4.37-4.28 (m, 1H, CHMe), 4.25-4.14 (m, 1H, n-HexCH), 2.31-2.18 (m, 2H, CHCH₂CH₂), 1.70-1.59 (m, 1H, CH₂CH₂CH₂), 1.53-1.43 (m, 1H, CH₂CH₂CH₂), 1.37-1.22 (m, 8H, (CH₂)₄CH₃), 1.23 (d overlapped, 3H, J = 6.1 Hz, 1H, CHCH₂CH₂), 0.88 (t, J = 6.8 Hz, 3H, (CH₂)₅CH₃).

13C NMR (100 MHz, CD₂Cl₂) cis-isomer: δ 81.7 (n-HexCH), 77.3 (CHMe), 48.1 (CHCH₂CH₂), 34.5 (CH₂CH₂CH₂), 32.1 (CH₂), 29.6 (CH₂), 26.7 (CH₂), 23.0 (CH₂), 19.1 (CHCH₃), 14.2 ((CH₂)₃CH₃); trans-isomer: δ 81.4 (n-HexCH), 77.1 (CHMe), 47.4 (CHCH₂CH₂), 33.6 (CH₂CH₂CH₂), 32.1 (CH₂), 29.6 (CH₂), 26.5 (CH₂), 23.0 (CH₂), 18.5 (CHCH₃), 14.2 ((CH₂)₃CH₃).

GC-MS (GC-EI) m/z (%) 172 [M⁺] (1), 131 (1), 113 (3), 95 (15), 87 (10), 81 (8), 69 (28), 55 (36), 43 (100), 29 (15).

HRMS (EI-FE) calcd for C₁₀H₂₀O₂ [M⁺]: 172.1461, found 172.1463.
Synthesis of Epoxyalcohol S-10

(S)-1-((2S,3S)-3-hexyloxiran-2-yl)ethanol (S-10): According to the procedure adapted from Yamaguchi and colleagues\textsuperscript{11}, a suspension of Zn(ClO\textsubscript{4})\textsubscript{2}·6H\textsubscript{2}O (244 mg, 0.66 mmol, 1.12 equiv) in dry diethyl ether (1 mL) was cooled to 0 °C, and epoxide 4a (100 mg, 0.59 mmol, 1 equiv) was added. After stirring for 10 min, NaBH\textsubscript{4} (47.4 mg, 1.25 mmol, 2 equiv) was added. The solution was stirred for 1 hour at 0 °C, warmed up to r.t. and 0.5 mL of MeOH were added. After 1 h, the reaction was quenched with Rochelle’s salt, extracted with diethyl ether three times, washed with brine, dried over MgSO\textsubscript{4} and filtered. Removal of the solvent under reduced pressure and flash chromatography (40% Et\textsubscript{2}O in pentane) afforded S-10 as a colourless oil (96.1 mg, 0.56 mmol, 95%, dr determined from the crude mixture = 94:6).

\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 3.97 (c. m, 1H), 2.98 (td, \(J = 5.7\) Hz, \(J = 2.0\) Hz, 1H), 2.75 (t, \(J = 2.9\) Hz, 1H), 2.06 (br s, 1H), 1.65-1.26 (m, 10H), 1.24 (d, \(J = 6.7\) Hz, 3H), 0.88 (t, \(J = 6.8\) Hz, 1H).

\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) \(\delta\) 64.7, 61.7, 55.0, 31.7, 31.6, 29.0, 26.0, 22.5, 18.8, 14.0.

HRMS (m/z) caleed for C\textsubscript{10}H\textsubscript{20}O\textsubscript{2}Na [M+Na]\textsuperscript{+}: 195.1356, found: 195.1356.

Catalytic Asymmetric Epoxidation of Cyclic Enones

**General Procedure**

Catalyst salt \([1a \cdot 2 \text{TFA}]\) was prepared *in situ* by the addition of 9-amino(9-deoxy)epi-quinine (1a; 32.3 mg, 0.1 mmol, 10 mol%) to a solution of trifluoroacetic acid (TFA; 15.3 µL, 0.2 mmol, 20 mol%) in dioxane (4 mL). Then, cyclic enone 9 (1.0 mmol, 1.0 equiv) was added, and 20 minutes later, aqueous hydrogen peroxide (50 wt%; 92 µL, 1.5 mmol, 1.5 equiv). After 12-72 h of stirring at 30°C (unless otherwise specified), the reaction mixture was extracted with Et₂O (3 × 25 mL). The combined organic phases were washed with brine, dried (Na₂SO₄), and filtered. For the highly volatile product 10a, the resulting solution was analyzed by GC for yield and er determination. Removal of the volatiles furnished the crude product, which was purified by flash column chromatography (silica gel, eluent: Et₂O-pentane) to afford pure cyclic α,β-epoxy ketone 10.

**Scope of Optically Active Cyclic α,β-Epoxyketones 10**

**2,3-Epoxycyclohexanone (10a):** After 24 h at 30 °C, the conversion was determined to be 91% by GC using an Optima-5-Accent column (5 min at 40°C, 5.0 °C/min until 100 °C, 25 °C/min until 250 °C, 1.0 min at 250°C, 0.35 bar He; starting material: \(\tau_R = 12.34\) min, product: \(\tau_R = 15.65\) min). After purification by flash column chromatography (silica gel, 5-10% Et₂O in pentane) (2S,3S)-10a was obtained as a clear liquid (65 mg, 580 µmol, 58% (reduced yield due to the high volatility of 10a); 97:3 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (80 °C, 1.2 °C/min until 105 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H₂); major enantiomer: \(\tau_R = 16.22\) min, minor enantiomer: \(\tau_R = 17.08\) min.
\(^1\)H NMR (500 MHz, CD\(_2\)Cl\(_2\)) \(\delta 3.57-3.55 (m, 1H, CH\_2C\_epoH), 3.15 (d, J = 4.2 Hz, 1H, C\_epoHC(=O)), 2.47 (dt, J = 17.5, 4.6 Hz, 1H, CH\_HC(=O)), 2.26-2.19 (m, 1H, CH\_HC\_epoH), 2.07-2.00 (m, 1H, CH\_HHC(=O)), 1.94-1.84 (m, 2H, CH\_HHC(=O) and CH\_CH2CH\_CH2), 1.69-1.60 (m, 1H, CH\_CH2CH2).

\(^13\)C NMR (100 MHz, CD\(_2\)Cl\(_2\)) \(\delta 206.0 (C=O), 56.2 (CH\_2\_C\_epo), 55.4 (C\_epoHC(=O)), 36.7 (CH\_2C(=O)), 23.2 (CH\_2CH\_epo), 17.3 (CH\_2CH2CH2).

The analytical data were identical in all respects to those of the commercially available 2,3-epoxycyclohexanone (10a; Sigma-Aldrich).

\((2R,3R)\)-4,4-Dimethyl-2,3-epoxycyclohexanone \((2R,3R)-10b\): The title compound was isolated after purification by flash column chromatography (silica gel, 2% Et\(_2\)O in pentane) as a clear liquid (118 mg, 840 \(\mu\)mol, 84%; 97:3 er). The enantiomeric ratio was determined by GC using a chiral Hydrodex-\(\beta\)-TBDAc column 25 m (80 °C, 1.5 \(^\circ\)C/min until 170 °C, 20 \(^\circ\)C/min until 220 °C, 10 min at 220 °C, 0.6 bar H\(_2\)); major enantiomer: \(\tau_R = 21.91\) min, minor enantiomer: \(\tau_R = 25.75\) min.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 3.20 (d, J = 3.9 Hz, 1H, C\_epoHC(=O)), 3.15 (dd, J = 4.0, 1.3 Hz, 1H, CMe2C\_epoH), 2.37 (ddd, J = 18.9, 6.3, 3.1 Hz, 1H, CH\_HC(=O)), 2.20-2.13 (m, 1H, CH\_HHC(=O)), 1.88 (ddd, J = 13.6, 11.8, 6.4 Hz, 1H, CH\_HHCMe2), 1.31 (ddddd, J = 13.6, 7.1, 3.0, 1.2 Hz, 1H, CH\_HHCMe2), 1.19 (s, 3H, CH\_3), 1.04 (s, 3H, CH\_3).

\(^13\)C NMR (75 MHz, CD\(_2\)Cl\(_2\)) \(\delta 205.9 (C=O), 64.1 (CMe2CH\_epo), 55.9 (CH\_epoC(=O)), 33.1 (CH\_2C(=O)), 30.7 (CqMe2), 29.7 (CH\_2CqMe2), 27.4 (CH\_3), 22.8 (CH\_3).

MS (El) \(m/z\) (%) 140 [M\(^+\)] (14), 124 (2), 111 (20), 97 (27), 85 (58), 69 (100), 55 (73), 43 (29), 41 (95), 39 (32), 29 (31).

HRMS calcd for C\(_8\)H\(_{12}\)O\(_2\) [M\(^+\)] 140.0839, found 140.0837.

\((2R,3R)-5,5\)-Dimethyl-2,3-epoxycyclohexanone \((2R,3R)-10c\): The title compound was isolated after purification by flash column chromatography (silica gel, 3% Et\(_2\)O in pentane) as a clear liquid (101 mg, 720 \(\mu\)mol, 72%; 96:4 er). The enantiomeric ratio was determined by GC using a chiral Hydrodex-\(\beta\)-TBDAc column 25 m (80 °C, 1.2 \(^\circ\)C/min until 120 °C, 20 \(^\circ\)C/min until 220 °C, 10 min at 220 °C, 0.5 bar H\(_2\)); major enantiomer: \(\tau_R = 27.55\) min, minor enantiomer: \(\tau_R = 29.57\) min.
**1H NMR** (300 MHz, CD$_2$Cl$_2$) δ 3.48 (t, $J = 4.1$ Hz, 1H, CH$_2$Cepo$H$), 3.14 (d, $J = 3.8$ Hz, 1H, CepoHC($\equiv$O)), 2.61 (d, $J = 13.2$ Hz, 1H, CHHC($\equiv$O)), 2.00 (d, $J = 15.4$ Hz, 1H, CHHCH$_3$), 1.86-1.74 (m, 2H, CHHCH$\equiv$O and CHHCH$_3$), 1.00 (s, 3H, CH$_3$), 0.90 (s, 3H, CH$_3$).

**13C NMR** (75 MHz, CD$_2$Cl$_2$) δ 207.5 (C$\equiv$O), 57.4 (C$\equiv$O), 55.0 (CH$_2$Cepo), 49.0 (CH$_2$C($\equiv$O)), 37.5 (CH$_2$CH$_3$), 37.4 (CqMe$_2$), 31.0 (CH$_3$), 28.1 (CH$_3$).

**GC-MS** (EI-DE) m/z (%) 140 [M$^+$] (20), 125 (1), 112 (4), 97 (20), 83 (100), 79 (8), 69 (28), 55 (28), 53 (13), 43 (19), 41 (73), 39 (34), 27 (20).

**HRMS** calcld for C$_8$H$_{12}$O$_2$ [M$^+$] 140.0839, found 140.0837.

(2$R$,3$R$)-3,5,5-Trimethyl-2,3-epoxycyclohexanone ((2$R$,3$R$)-10d): The title compound was isolated after purification by flash column chromatography (silica gel, 1.5% Et$_2$O in pentane) as a clear liquid (80 mg, 520 µmol, 52%; 95.5:4.5 er). The enantiomeric ratio was determined by GC using a chiral Hydrodex-$\beta$-TBDAce column 25 m (60 °C, 1.0 °C/min until 90 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H$_2$); major enantiomer: $\tau_R = 27.24$min, minor enantiomer: $\tau_R = 27.80$ min.

**1H NMR** (500 MHz, CDCl$_3$) δ 3.01 (s, 1H, Cepo$H$), 2.58 (d, $J = 13.5$ Hz, 1H, CHHC($\equiv$O)), 2.04 (d, $J = 14.7$ Hz, 1H, CqepoCH$H$), 1.77 (ddd, $J = 13.4$, 2.0, 1.0 Hz, 1H, CHHHC($\equiv$O)), 1.70 (dd, $J = 14.8$, 2.2 Hz, 1H, CqepoCH$H$), 1.38 (s, 3H, CqepoCH$_3$), 0.98 (s, 3H, CH$_3$), 0.87 (s, 3H, CH$_3$).

**13C NMR** (75 MHz, CDCl$_3$) δ 207.8 (C$\equiv$O), 64.2 (Cqepo), 61.4 (CH$_3$), 48.0 (CH$_2$C($\equiv$O)), 42.7 (CH$_2$Cqepo), 36.1 (CqMe$_2$), 30.8 (Cq(CH$_3$)$_2$), 27.8 (Cq(CH$_3$)$_2$), 24.0 (CqepoCH$_3$).

**MS** (EI-DE) m/z (%) 154 [M$^+$] (30), 139 (33), 126 (17), 111 (12), 97 (25), 83 (100), 69 (50), 55 (39), 53 (9), 43 (40), 41 (65), 29 (23).

**HRMS** calcld for C$_9$H$_{14}$O$_2$ [M$^+$] 154.0992, found 154.0994.

(2$R$,3$S$)-2,6,6-Trimethyl-2,3-epoxy-1,4-cyclohexanedione ((2$R$,3$S$)-10e): 20 mol% catalytic salt [1a • 2 TFA] was used. The title compound was isolated after 48 h at 50 °C and purification by flash column chromatography (silica gel, 2.5% Et$_2$O in pentane) as a clear oil (82 mg, 488 µmol, 49%; 96:4 er). The enantiomeric ratio was determined by GC using a chiral BGB-178/OV-1701 column 30 m (80 °C, 1.2 °C/min until 130°C, 20 °C/min until 220°C, 10 min at 220 °C, 0.5 bar H$_2$); major enantiomer: $\tau_R = \ldots$
19.27 min, minor enantiomer: \( \tau_R = 22.67 \) min.

\(^1\)H NMR (300 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 3.49 (d, \( J = 1.1 \) Hz, 1H, C\(_\text{epo} \)H), 3.15 (d, \( J = 13.6 \) Hz, 1H, CHH), 2.15 (dd, \( J = 13.5, 1.2 \) Hz, 1H, CHH), 1.55 (s, 3H, CH\(_3\)), 1.28 (s, 3H, CH\(_3\)), 1.08 (s, 3H, CH\(_3\)).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 205.6 (C=O), 204.1 (C=O), 64.8 (C\(_\text{epo} \)), 62.8 (CH\(_\text{epo} \)), 47.0 (CH\(_2\)), 45.5 (C\(_\text{qMe}_2\)), 26.9 (CH\(_3\)), 26.1 (CH\(_3\)), 15.9 (C\(_\text{qepo} \)CH\(_3\)).

MS (EI) \( m/z \) (%) 168 \([\text{M}^+\]) (59), 153 (27), 125 (65), 85 (77), 83 (21), 69 (34), 56 (100), 43 (91), 41 (95), 39 (41), 27 (34).

HRMS calecd for C\(_9\)H\(_{12}\)O\(_3\) \([\text{M}^+\]) 168.0785, found 168.0786.

(2\(S\),3\(S\))-2,3-Epoxy-3-methylcyclohexanone ((2\(S\),3\(S\))-10f): The title compound was isolated after 24 h at 30 °C and purification by flash column chromatography (silica gel, 2-10% Et\(_2\)O in pentane) as a clear oil (88 mg, 698 µmol, 70% (reduced yield due to the high volatility of 20g); 98:2 er). The enantiomeric ratio was determined by GC using a chiral BGB-178/OV-1701 column 30 m (80 °C, 1.2 °C/min until 105 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H\(_2\)); major enantiomer: \( \tau_R = 16.79 \) min, minor enantiomer: \( \tau_R = 19.18 \) min.

\(^1\)H NMR (400 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 3.01 (s, 1H, C\(_\text{epo} \)H), 2.42 (dt, \( J = 17.6, 4.1 \) Hz, 1H, CHHHC(=O)), 2.13-1.84 (m, 4H, CHH(=O), CH\(_2\)C\(_\text{epo} \), and CH\(_2\)CHHCH\(_2\)), 1.66-1.58 (m, 1H, CH\(_2\)CH\(_2\)CHH\(_2\)), 1.42 (s, 3H, CH\(_3\)).

\(^{13}\)C NMR (75 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 206.7 (C=O), 62.6 (C\(_\text{epo} \)), 62.3 (CH\(_\text{epo} \)), 36.1 (CH\(_2\)C(=O)), 28.7 (CH\(_2\)C\(_\text{epo} \)), 22.3 (CH\(_3\)), 17.5 (CH\(_2\)CH\(_2\)CH\(_2\)).

MS (EI-DE) \( m/z \) (%) 126 \([\text{M}^+\]) (78), 111 (8), 97 (46), 83 (35), 81 (21), 79 (5), 71 (79), 69 (26), 67 (8), 58 (3), 55 (61), 53 (12), 43 (89), 41 (100), 39 (49), 31 (2), 27 (36).

HRMS (EI-FE) calecd for C\(_7\)H\(_{10}\)O\(_2\) \([\text{M}^+\]) 126.0680, found 126.0681.

(2\(S\),3\(S\))-3-Ethyl-2,3-epoxycyclohexanone ((2\(S\),3\(S\))-10g): The title compound was isolated after 30 h at 50 °C and purification by flash column chromatography (silica gel, 5-10% Et\(_2\)O in pentane) as a clear oil (102 mg, 728 µmol, 73% ; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-178/OV-1701 column 30 m (80 °C, 1.2 °C/min until 115 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H\(_2\)); major enantiomer: \( \tau_R = 23.73 \) min, minor enantiomer: \( \tau_R = 25.43 \) min.

\(^{13}\)C NMR (75 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 206.7 (C=O), 64.8 (C\(_\text{epo} \)), 62.8 (CH\(_\text{epo} \)), 47.0 (CH\(_2\)), 45.5 (C\(_\text{qMe}_2\)), 26.9 (CH\(_3\)), 26.1 (CH\(_3\)), 15.9 (C\(_\text{qepo} \)CH\(_3\)).

MS (EI) \( m/z \) (%) 126 \([\text{M}^+\]) (78), 111 (8), 97 (46), 83 (35), 81 (21), 79 (5), 71 (79), 69 (26), 67 (8), 58 (3), 55 (61), 53 (12), 43 (89), 41 (100), 39 (49), 31 (2), 27 (36).

HRMS (EI-FE) calecd for C\(_7\)H\(_{10}\)O\(_2\) \([\text{M}^+\]) 126.0680, found 126.0681.
$^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 3.03 (s, 1H, C$_{3p}$H), 2.45 (dt, $J = 17.4, 4.3$ Hz, 1H, CH$_{4c,2}$H), 2.12-1.95 (m, 2H, CH$_{4c,2}$H, and CH$_{1}$HCH$_{1}$H), 1.94-1.83 (m, 2H, CH$_{1}$HCH$_{1}$H, and CH$_{2}$HCH$_{2}$), 1.78-1.61 (m, 3H, C$_{3c,2}$HMe$_{2}$, and CH$_{2}$C$_{3c,2}$H), 0.96 (t, $J = 7.5$ Hz, 3H, CH$_{3}$H).

$^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) $\delta$ 206.9 (C$\equiv$O), 66.3 (C$_{3p}$C$_{3p}$), 61.1 (CH$_{3p}$), 36.4 (CH$_{2}$C(=O)), 29.2 (CH$_{2}$CH$_{3}$), 26.5 (CH$_{2}$C$_{3p}$), 17.8 (CH$_{2}$CH$_{2}$CH$_{2}$), 8.8 (CH$_{3}$).

MS (EI-DE) m/z (%) 140 [M$^+$] (90), 125 (5), 111 (49), 107 (1), 97 (55), 85 (79), 79 (12), 67 (24), 57 (30), 55 (84), 43 (38), 41 (100), 39 (58), 29 (92), 27 (77).

HRMS (EI-FE) calcd for C$_8$H$_{12}$O$_2$ [M$^+$] 140.0836, found 140.0837.

(2S,3R)-2,3-Epoxy-3-isobutylcyclohexanone ((2S,3R)-10h): The title compound was isolated after 48 h at 50 °C and purification by flash column chromatography (silica gel, 5-10% Et$_2$O in pentane) as a clear oil (123 mg, 731 µmol, 73%; 98:2 er). The enantiomeric ratio was determined by GC using a chiral BGB-178/OV-1701 column 30 m (80 °C, 0.8 °C/min until 120 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H$_2$); major enantiomer: $\tau_R = 43.77$ min, minor enantiomer: $\tau_R = 45.20$ min.

$^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 2.98 (s, 1H, C$_{3p}$H), 2.45 (dt, $J = 17.4, 4.3$ Hz, 1H, C(=O)CH$_{4c,2}$H), 2.11-1.81 (m, 5H, C(=O)CH$_{4c,2}$H, CH$_{2}$C$_{3p}$, CHMe$_2$, and CH$_{2}$CH$_{2}$HC$_{3p}$), 1.67-1.60 (m, 2H, CH$_{2}$CH$_{2}$HC$_{3p}$ and CHHI-Pr), 1.40 (dd, $J = 13.8, 8.1$ Hz, 1H, CHHI-Pr), 0.96 (d, $J = 6.6$ Hz, 3H, CH(CH$_{3}$)$_2$), 0.91 (d, $J = 6.6$ Hz, 3H, CH(CH$_{3}$)$_2$).

$^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) $\delta$ 206.9 (C$\equiv$O), 64.8 (C$_{3p}$C$_{3p}$), 61.8 (CH$_{3p}$), 45.4 (CH$_{2}$-Pr), 36.4 (C(=O)CH$_{2}$), 26.5 (CH$_{2}$C$_{3p}$), 25.4 (CHMe$_2$), 23.2 (CH(CH$_{3}$)$_2$), 22.7 (CH(CH$_{3}$)$_2$), 17.7 (CH$_{2}$CH$_{2}$CH$_{3}$).

MS (El-DE) m/z (%) 168 [M$^+$] (45), 153 (7), 139 (7), 126 (36), 112 (31), 79 (32), 67 (43), 55 (56), 41 (100), 39 (43), 27 (54).

HRMS (El-FE) calcd for C$_{10}$H$_{16}$O$_2$ [M$^+$] 168.1149, found 168.1150.

(2S,3R)-2,3-Epoxy-3-isopropylcyclohexanone ((2S,3R)-10i): The title compound was isolated after 48 h at 50 °C and purification by flash column chromatography (silica gel, 5-10% Et$_2$O in pentane) as a clear oil (121 mg, 785 µmol, 79%; 99:1 er). The enantiomeric ratio was determined by GC using a chiral BGB-178/OV-1701 column 30 m (80 °C, 1.2 °C/min until 120 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H$_2$); major enantiomer: $\tau_R =$
27.79 min, minor enantiomer: \( \tau_R = 29.24 \) min.

\(^1\text{H NMR} \) (400 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 3.03 (s, 1H, C\(_{\text{epo}}\)H), 2.46 (dt, \( J = 17.3, 4.7 \) Hz, 1H, CHHC(=O)), 2.11-1.99 (m, 2H, CHHC(=O) and CHHHC\(_{\text{epo}}\)), 1.95-1.83 (m, 2H, CHHHC\(_{\text{epo}}\) and CH\(_2\)CHCHCH\(_2\)), 1.70-1.60 (m, 2H, CH\(_2\)CHCH\(_2\) and CHHMe\(_2\)), 1.03 (d, \( J = 6.8 \) Hz, 3H, CH(CH\(_3\))\(_2\)), 0.97 (d, \( J = 7.0 \) Hz, 3H, CH(CH\(_3\))\(_2\)).

\(^{13}\text{C NMR} \) (100 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 207.0 (C=O), 69.3 (C\(_{\text{qepo}}\)), 61.1 (CH\(_{\text{epo}}\)), 36.6 (CH\(_2\)C(=O)), 34.5 (CHMe\(_2\)), 23.3 (CH\(_2\)C\(_{\text{qepo}}\)), 18.1 (CH\(_2\)CH\(_2\)CH\(_2\)), 18.0 (CH(CH\(_3\))\(_2\)), 17.9 (CH(CH\(_3\))\(_2\)).

\( \text{MS} \) (EI-DE) \( m/z \) (%) 154 [M\(^+\)] (61), 139 (4), 125 (24), 111 (78), 99 (34), 81 (41), 71 (6), 69 (30), 55 (93), 53 (18), 43 (84), 41 (100), 29 (32), 27 (56)

\( \text{HRMS} \) (EI-FE) calcd for C\(_9\)H\(_{14}\)O\(_2\) [M\(^+\)] 154.0993, found 154.0994.

**(2S,3R)-3-tert-Butyl-2,3-epoxycyclohexanone** ((2S,3R)-10j): The title compound was isolated after 48 h at 50 °C and purification by flash column chromatography (silica gel, 5-10% Et\(_2\)O in pentane) as a clear oil (57 mg, 339 \( \mu \)mol, 68%; 99.5:0.5 \( \text{er} \)). The enantiomeric ratio was determined by GC using a chiral Hydrodex-\( \beta \)-TBDAc column 25 m (100 °C, 1.2 \( ^\circ \)C/min until 125 \( ^\circ \)C, 18 \( ^\circ \)C/min until 220 \( ^\circ \)C, 10 min at 320 °C, 0.5 bar H\(_2\)); major enantiomer: \( \tau_R = 13.22 \) min, minor enantiomer: \( \tau_L = 14.25 \) min.

\(^1\text{H NMR} \) (500 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 3.21 (s, 1H, C\(_{\text{epo}}\)H), 2.46 (dt, \( J = 17.7, 4.7 \) Hz, 1H, CHHC(=O)), 2.19-2.13 (m, 1H, CH\(_2\)), 2.07-1.99 (m, 1H, CH\(_2\)), 1.95-1.86 (m, 2H, CH\(_2\)), 1.67-1.60 (m, 1H, CH\(_2\)), 0.97 (s, 9H, CH\(_3\)).

\(^{13}\text{C NMR} \) (125 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 207.3 (C=O), 70.5 (C\(_{\text{qepo}}\)), 59.2 (C\(_{\text{epo}}\)H), 36.1 (CH\(_2\)C(=O)), 34.0 (CqMe\(_3\)), 25.4 (3C, CH\(_3\)), 23.2 (C\(_{\text{qepo}}\)CH\(_2\)), 17.8 (CH\(_2\)CH\(_2\)CH\(_2\)).

\( \text{MS} \) (EI-DE) \( m/z \) (%) 168 [M\(^+\)] (22), 153 (5), 139 (14), 125 (39), 113 (15), 96 (87), 83 (24), 69 (61), 55 (100), 41 (57), 29 (26).

\( \text{HRMS} \) (EI-FE) calcd for C\(_{10}\)H\(_{16}\)O\(_2\) [M\(^+\)] 168.1150, found 168.1150.
(2S,3R)-2,3-Epoxy-3-allylcyclohexanone ((2S,3R)-10k): The title compound was isolated after 48 h at 50 °C and purification by flash column chromatography (silica gel, 2-15% Et₂O in pentane) as a clear oil (34.8 mg, 229 µmol, 23%; 97.5:2.5 er). The enantiomeric ratio was determined by GC using a chiral Hydrodex-β-TBDAc column 25 m (21 min at 125 °C, 14 °C/min until 230 °C, 10 min at 230°C, 0.6 bar H₂); major enantiomer: τ_R = 24.39 min, minor enantiomer: τ_R = 25.96 min.

^1^H NMR (500 MHz, CD₂Cl₂) δ 5.77 (ddt, J = 17.0, 10.1, 7.1 Hz, 1H, CH=CH₂), 5.17-5.13 (m, 2H, CH=CH₂), 3.06 (s, 1H, CepoH), 2.48-2.38 (m, 3H, CH₂CH=CH₂ and CHHC(=O)), 2.13-2.09 (m, 1H, CH₂ cyc.), 2.05-1.98 (m, 1H, CH₂ cyc.), 1.93-1.85 (m, 2H, CH₂ cyc.), 1.67-1.61 (m, 1H, CH₂ cyc.).

^1^C NMR (125 MHz, CD₂Cl₂) δ 206.5 (C=O), 132.3 (CH=CH₂), 119.1 (CH=CH₂), 64.7 (Cepo), 60.6 (CHepo), 40.6 (CH₂CH=CH₂), 36.3 (CH₂C(=O)), 26.7 (CH₂Cepo), 17.7 (CH₂CH₂CH₂).

MS (EI-DE) m/z (%) 152 [M⁺] (8), 137 (4), 123 (60), 109 (13), 97 (41), 91 (11), 79 (53), 69 (29), 67 (61), 55 (85), 53 (23), 41 (100), 39 (55), 29 (18), 27 (31).

HRMS (EI-FE) calcd for C₉H₁₂O₂ [M⁺] 152.0836, found 152.0837.

The facile isomerization of 9k is probably enhanced upon formation of the iminium ion with catalyst 1a, which should lead to increased acidity in the γ'-position. This effect was used by the group of Deng to develop an enantioselective isomerization of 3-cyclohexenones into 2-cyclohexenones using a newly developed type of diamine catalysts.¹²

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(E)-3-(1-propenyl)cyclohex-2-enone (S-11): The title compound (70.2 mg, 516 μmol, 52%) was obtained as a side product in the epoxidation reaction of 3-allylcyclohex-2-enone (9k).

$^1$H NMR (500 MHz, CD$_2$Cl$_2$) $\delta$ 6.30-6.22 (m, 2H, C$_q$=CH and CH=CH$_3$), 5.81-5.80 (m, 1H, CH=CHCH$_3$), 2.45 (t, $J = 5.9$ Hz, CH$_2$C(=O)), 2.34 (t, $J = 6.6$ Hz, CH$_2$Cq=CH), 2.00 (quint, $J = 6.4$ Hz, CH$_2$CH$_2$CH$_2$), 1.87 (d, $J = 5.6$ Hz, CH$_3$).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) $\delta$ 202.2 (C=O), 157.9 (Cq=CH), 134.2 (CH=CH), 133.0 (CH=CH), 126.4 (Cq=CH), 38.2 (CH$_3$(=O)), 25.4 (CH$_2$Cq=CH), 23.0 (CH$_2$CH$_2$CH$_2$), 19.2 (CH$_3$).

(2S,3R)-2,3-Epoxy-3-phenethylcyclohexanone ((2S,3R)-10l): The title compound was isolated after 48 h at 50 °C and purification by flash column chromatography (silica gel, 1-10% Et$_2$O in pentane) as a clear oil (182 mg, 843 μmol, 84%; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (100 °C, 1.2 °C/min until 180 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H$_2$); major enantiomer: $\tau_R = 56.99$ min, minor enantiomer: $\tau_R = 58.46$ min.

$^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 7.31-7.27 (m, 2H, C$_{ar}$), 7.23-7.18 (m, 3H, C$_{ar}$), 3.01 (s, 1H, C$_{epo}$H), 2.74 (t, $J = 8.3$ Hz, 2H, CH$_2$Ph), 2.46 (dt, $J = 17.0$, 4.7 Hz, 1H, C(=O)CH$_2$H), 2.20-2.12 (m, 1H, CH$_2$Cq$_{epo}$), 2.08-1.87 (m, 5H, C(=O)CH$H$, CH$H$C$_{epo}$, CH$_2$CH$_2$H$CH_2$, and CH$_2$CH$_2$Ph), 1.71-1.62 (m, 1H, CH$_2$CH$_2$H$CH_2$).

$^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) $\delta$ 206.5 (C=O), 141.5 (C$_{lar}$), 128.8 (2C, CH$_{ar}$), 128.6 (2C, CH$_{ar}$), 126.5 (CH$_{ar,p}$), 65.1 (C$_{epo}$), 61.4 (CH$_{epo}$), 38.2 (CH$_2$CH$_2$Ph), 36.3 (C(=O)CH$_2$), 31.2 (CH$_2$Ph), 26.9 (CH$_2$C$_{epo}$), 17.8 (CH$_2$CH$_2$CH$_2$).

MS (EI-DE) $m/z$ (%): 216 [M$^+$] (2), 198 (2), 187 (1), 169 (3), 154 (1), 143 (11), 128 (4), 104 (100), 97 (13), 91 (69), 79 (13), 69 (5), 65 (17), 55 (12), 41 (31).

HRMS (EI-DE) caleed for C$_{14}$H$_{16}$O$_2$ [M$^+$] 216.1149, found 216.1150.

3-Benzyl-2,3-epoxycyclohexanone (10m): The title compound (2S,3R)-10m was isolated after 48 h at 50 °C and purification by flash column chromatography (silica gel, 2-10% Et$_2$O in pentane) as a clear oil (158 mg, 781 μmol, 78%; 99:1 er). The enantiomeric ratio was determined by GC using a chiral Hydrodex-β-TBDAc column 25 m (100 °C, 1.2 °C/min until 175 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.4 bar H$_2$); major enantiomer: $\tau_R =$
45.74 min, minor enantiomer: \( \tau_R = 46.65 \) min.

9-amino(9-deoxy)epiquinidine (1b) was used (instead of 1a). The title compound \((2R,3S)-10m\) was isolated after 48 h at 50 °C and purification by flash column chromatography (silica gel, 2-10% Et2O in pentane) as a clear oil (156 mg, 771 \( \mu \)mol, 77%; 98.5:1.5 er). The enantiomeric ratio was determined by GC using a chiral Hydrodex-\( \beta\)-TBDAc column 25 m (100 °C, 1.2 °C/min until 175 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.4 bar H2); major enantiomer: \( \tau_R = 46.37 \) min, minor enantiomer: \( \tau_R = 45.88 \) min.

\( ^1H \) NMR (400 MHz, CD2Cl2) \( \delta \) 7.34-7.21 (m, 5H, C6H5), 3.04 (s, 1H, CepoH), 2.98 (s, 2H, CH2Ph), 2.44 (dt, \( J = 17.7, 4.4 \) Hz, 1H, C(=O)CH), 2.10-1.95 (m, 2H, C(=O)CH and CCH2Cqepo), 1.89-1.80 (m, 2H, CH2Cqepo and CH2Cqepo), 1.65-1.56 (m, 1H, CH2CH2CH2).

\( ^{13}C \) NMR (100 MHz, CD2Cl2) \( \delta \) 206.4 (C=O), 136.2 (Cqar), 130.0 (2C, CHar), 128.8 (2C, CHar), 127.3 (CHar,p), 65.4 (Cqepo), 60.8 (Cepo), 42.4 (CH2Ph), 36.4 (C(=O)CH2), 26.7 (CH2Cqepo), 17.6 (CH2CH2CH2).

MS (EI-DE) \( m/z \) (%): 202 [M+], 184 (5), 173 (53), 156 (4), 145 (12), 129 (46), 117 (21), 91 (100), 78 (11), 65 (28), 55 (28), 51 (15), 39 (36).


\((2S,3S)-2,3\text{-Epoxy-4-methylcyclohexanone}\) \((2S,3S)-10q\): After 24 h at 30 °C, the conversion was determined to be 94% (54:46 \( dr \) \( (\text{anti/syn}) \)) by GC/MS. The enantiomeric ratio was determined by GC using a chiral BGB-178/OV-1701 column 30 m (80 °C, 0.8 °C/min until 105 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H2). \( \text{anti-10q:} \) 93.5:6.5 \( \text{er} \) (major enantiomer: \( \tau_R = 27.25 \) min, minor enantiomer: \( \tau_R = 29.13 \) min); \( \text{syn-10q:} \) 99:1 \( \text{er} \) (minor enantiomer: \( \tau_R = 28.64 \) min, minor enantiomer: \( \tau_R = 29.65 \) min).

\( \text{anti-10q:} \) \( ^1H \) NMR (500 MHz, CD2Cl2) \( \delta \) 3.37 (dd, \( J = 3.7, 2.2 \) Hz, 1H, CHCHepo), 2.46-2.40 (m, 2H, CHMe and CHH(=O)), 2.18-2.04 (m, 2H, CHH(=O) and CHHCH), 1.48-1.41 (m, 1H, CHHCH), 1.08 (d, \( J = 7.2 \) Hz, 3H, CH3).

\( ^{13}C \) NMR (125 MHz, CD2Cl2) \( \delta \) 206.5 (C=O), 66.0 (CHCHepo), 61.7 (CHepoC(=O)), 33.3 (CH2C(=O)), 27.9 (CHMe), 25.6 (CH2CH), 15.9 (CH3).

GC-MS (GC-EI) \( m/z \) (%): 126 [M+].

HRMS (EI-FE) calcd for C7H10O2 [M+] 126.0680, found 126.0681.
syn-10q: $^1$H NMR (500 MHz, CD$_2$Cl$_2$) $\delta$ 3.38 (d, $J = 3.9$ Hz, 1H, CHCH$_{epo}$), 3.16 (d, $J = 3.8$ Hz, 1H, CH$_{epo}$C(=O)), 2.42 (ddd, $J = 18.6$, 5.0, 3.5 Hz, 1H, CHHC(=O)), 2.19-2.12 (m, 1H, CHMe), 2.07 (ddd, $J = 18.6$, 11.8, 6.9 Hz, 1H, CHHC(=O)), 1.67-1.57 (m, 2H, CH$_2$CH), 1.22 (d, $J = 6.9$ Hz, 3H, CH$_3$).

13C NMR (125 MHz, CD$_2$Cl$_2$) $\delta$ 205.6 (C(=O)), 60.1 (CHC$_{epo}$), 55.9 (CH$_{epo}$C(=O)), 36.5 (CH$_2$C(=O)), 29.3 (CHMe), 24.1 (CH$_2$CH), 18.8 (CH$_3$).

GC-MS (GC-EI) $m/z$ (%) 126 [M$^+$.]

HRMS (EI-FE) calcd for C$_7$H$_{10}$O$_2$ [M$^+$] 126.0680, found 126.0681.

Subjecting a more sterically biased substrate 4-tert-butyl-2-cyclohexenone rac-S-10 gave anti-epoxide S-18$^{13}$ in 48% yield, after 4 d at 50 °C, with a diastereomeric ratio of 92:8 (anti/syn). Although the remaining starting material (44%) was significantly enantioenriched with 86:14 er, the enantiomeric ratio of anti-epoxide S-18 remained relatively low (79.5:20.5 er).

(2S,3S)-2,3-Epoxy-4-tert-butyleyclohexanone ((2S,3S)-S-18): After 96 h at 50 °C, the conversion was determined to be 56% by GC/MS with a yield of epoxide S-10 of 48% (92:8 dr (anti/syn)). The enantiomeric ratio was determined by GC using a chiral Hydrodex-β-TBDAc column 25 m (100 °C, 1.2 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H$_2$). anti-S-10$^{14}$: 79.5:20.5 er (major enantiomer: $\tau_R = 26.00$ min, minor enantiomer: $\tau_R = 29.01$ min).$^{15}$

anti-20s: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.49-3.47 (m, 1H, CHCH$_{epo}$), 3.15 (d, $J = 3.8$ Hz, 1H, CH$_{epo}$C(=O)), 2.70-2.62 (m, 1H, CHHC(=O)) 2.15-2.09 (m, 1H,CHHC(=O)), 2.02-1.94 (m, 2H, CHt-Bu and CHMe), 1.74-1.64 (m, 1H, CHHCH), 0.99 (s, 9H, CH$_3$).

13C NMR (100 MHz, CDCl$_3$) $\delta$ 208.3 (C(=O)), 61.5 (CHCH$_{epo}$), 55.2 (CH$_{epo}$C(=O)), 43.5 (CHt-Bu), 34.7 (CH$_2$C(=O)), 32.6 (CqMe$_3$), 27.6 (3C, CH$_3$), 26.1 (CH$_2$CH).

MS (EI-DE) $m/z$ (%) 168 [M$^+$] (8), 153 (1), 139 (4), 125 (2), 112 (21), 107 (4), 97 (8), 83 (24), 70 (32), 67 (11), 57 (100), 41 (43), 39 (16), 29 (19).

HRMS (EI-FE) calcd for C$_{10}$H$_{16}$O$_2$ [M$^+$] 168.1152, found 168.1150.

$^{13}$ The relative configuration of S-11 was assigned by NOE analysis.

$^{14}$ The relative configuration was assigned on the basis of NOE correlations

**anti-(2S,3S,5S)-2,3-Epoxy-3-methyl-5-phenylcyclohexanone** (anti-(2S,3S,5S)-10r): After 48 h at 50 °C, the conversion was determined to be 83% by GC/MS with a yield of epoxide 10r of 75% (97:3 dr (anti/syn)). The enantiomeric ratio was determined to be 98.5:1.5 by chiral GC using a Hydrodex-β-TBDAc column 25 m (80 °C, 1.2 °C/min until 180 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H2); major enantiomer: \( \tau_R = 67.61 \) min, minor enantiomer: \( \tau_R = 69.91 \) min.

**\(^1\)H NMR** (500 MHz, CD2Cl2) \( \delta \) 7.33 (t, \( J = 7.7 \) Hz, 2H, \( CH_{Ph,m} \)), 7.24-7.20 (m, 3H, \( CH_{Ph,o,p} \)), 3.34 (tt, \( J = 12.3, 4.5 \) Hz, 1H, \( CH_{Ph} \)), 3.14 (s, 1H, \( CH_{epo} \)), 2.63 (dd, \( J = 18.7, 4.9 \) Hz, 1H, \( CHHC(=O) \)), 2.34 (dd, \( J = 14.3, 3.9 \) Hz, 1H, \( CHHCqMe \)), 2.23 (dd, \( J = 18.6, 12.7 \) Hz, 1H, \( CHHC(=O) \)), 2.11 (dd, \( J = 15.0, 12.4 \) Hz, 1H, \( CHHCqMe \)), 1.49 (s, 3H, \( CH_3 \)).

**\(^{13}\)C NMR** (125 MHz, CD2Cl2) \( \delta \) 205.3 (C=O), 143.8 (CqPh), 129.0 (2C, \( CH_{Ph,m} \)), 127.3 (2C, \( CH_{Ph,o} \)), 127.1 (CHPh), 61.5 (CHepo), 61.4 (Cqepo), 44.0 (CH2C(=O)), 36.8 (CH2Cqepo), 34.3 (CHPh), 21.9 (CH3).

**MS** (EI-DE) \( m/z \) (%) 202 \( [M^+] \) (23), 184 (17), 174 (68), 159 (84), 145 (47), 131 (100), 115 (49), 103 (84), 91 (74), 85 (33), 77 (62), 69 (50), 65 (22), 51 (31), 43 (54), 27 (16).

Scope of Optically Active Cyclic $\alpha,\beta$-Epoxyketones 12

2,3-Epoxycycloheptanone (12a): The title compound (2S,3S)-12a was isolated after 24 h at 50 °C and purification by flash column chromatography (silica gel, 3-15% Et$_2$O in pentane) as a clear liquid (78 mg, 621 $\mu$mol, 62%; >99.5:0.5 er). The enantiomeric ratio was determined by GC using a chiral Hrodex-$\beta$-TBDAc column 25 m (80 °C, 1.5 °C/min until 120 °C, 20 °C/min until 220 °C, 10 min at 220°C, 0.6 bar H$_2$); major enantiomer: $\tau_R = 20.66$ min, minor enantiomer: $\tau_R = 24.29$ min.

$^1$H NMR (300 MHz, CD$_2$Cl$_2$) $\delta$ 3.37-3.35 (m, 2H, $CH_{epo}$), 2.62 (ddd, $J = 13.6$, 11.3, 3.8 Hz, 1H, C($\equiv$O)CHH), 2.48-2.40 (m, 1H, CHH$CH_{epo}$), 2.30-2.23 (m, 1H, C($\equiv$O)CHH), 1.87-1.63 (m, 4H, C($\equiv$O)CH$_2$C$H$, CHH$CH_{epo}$, and CH$_2$CH$_2$CH$_{epo}$), 1.06-0.91 (m, 1H, C($\equiv$O)CH$_2$CHH).

$^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) $\delta$ 210.1 (C$\equiv$O), 59.5 (C($\equiv$O)CH$_{epo}$), 55.1 (CH$_2$CH$_{epo}$), 40.6 (C($\equiv$O)CH$_2$), 27.5 (CH$_2$CH$_{epo}$), 23.6 (C($\equiv$O)CH$_2$CH$_2$), 23.1 (CH$_2$CH$_2$CH$_{epo}$).

GC-MS (GC-EI) $m/z$ (%) 126 [M$^+$] (16), 110 (12), 97 (33), 83 (24), 81 (35), 79 (14), 70 (58), 68 (32), 55 (79), 41 (100), 39 (52), 27 (37).

HRMS (EI-FE) calcd for C$_7$H$_{10}$O$_2$ [M$^+$] 126.0679, found 126.0681.

(2S,3S)-2,3-Epoxy-3-ethylcycloheptanone ((2S,3S)-12b): The title compound was isolated after 20 h at 50 °C and purification by flash column chromatography (silica gel, 5% Et$_2$O in pentane) as a clear oil (127 mg, 824 $\mu$mol, 82%; >99.5:0.5 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/BGB-15 column 30 m (80 °C, 1.2 °C/min until 220 °C, 10 min at 220 °C, 0.5 bar H$_2$); major enantiomer: $\tau_R = 18.25$ min, minor enantiomer: $\tau_R = 19.50$ min.

$^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 3.20 (d, $J = 1.3$ Hz, 1H, $C_{epo}H$), 2.67 (ddd, $J = 13.5$, 11.0, 4.1 Hz, 1H, C($\equiv$O)CHH), 2.24-2.18 (m, 1H, C($\equiv$O)CHH), 2.18-2.12 (m, 1H, CHH$C_{epo}$), 1.87-1.66 (m, 5H, CHH$C_{epo}$, C($\equiv$O)CH$_2$CHH, CH$_2$CH$_2$C$_{epo}$, and CHH$C_{h}$), 1.59-1.49 (m, 1H, CHH$C_{h}$), 1.13-1.02 (m, 1H, C($\equiv$O)CH$_2$CHH), 0.93 (t, $J = 7.5$ Hz, 3H, $CH_3$).

$^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) $\delta$ 210.7 (C$\equiv$O), 65.0 (CH$_{epo}$), 64.9 (C$_{epo}$), 41.1 (C($\equiv$O)CH$_2$), 31.9
(CH₂CH₃), 31.4 (CH₂C₇epo), 25.3 (C(=O)CH₂CH₂), 23.9 (CH₂CH₂C₇epo), 9.1 (CH₃).

**GC-MS (GC-EI) m/z (%)** 154 [M⁺] (1), 138 (1), 125 (11), 109 (12), 98 (68), 93 (8), 83 (29), 67 (35), 55 (100), 53 (16), 41 (65), 29 (57), 27 (23).

**HRMS (EI-FE) calcd for C₉H₁₄O₂ [M⁺] 154.0995, found 154.0994.**

(2S,3R)-3-Benzyl-2,3-epoxycycloheptanone ((2S,3R)-12c): The title compound was isolated after 20 h at 50 °C and purification by flash column chromatography (silica gel, 5-10% Et₂O in pentane) as a clear oil (184 mg, 851 µmol, 85%; >99.5:0.5 er). The enantiomeric ratio was determined by HPLC using a chiral Chiralpak IA column (2% i-PrOH in heptane, 0.5 mL/min); major enantiomer: τᵣ = 13.74 min, minor enantiomer: τᵣ = 14.83 min.

**1H NMR** (400 MHz, CD₂Cl₂) δ 7.33-7.22 (m, 5H, C₆H₅), 3.20 (d, J = 1.2 Hz, 1H, C₇epoH), 2.94 (dd, J = 18.8, 14.3 Hz, 2H, C₇Ph), 2.67 (ddd, J = 13.4, 11.0, 4.0 Hz, 1H, C(=O)CH₂), 2.25-2.16 (m, 2H, C(=O)CH₂ and C₇H₂C₇epo), 1.86-1.63 (m, 4H, CH₂C₇epo, C₇H₂CH₂C₇epo, and C(=O)CH₂C₇H), 1.11-1.00 (m, 1H, C(=O)CH₂CH₂H).

**13C NMR** (75 MHz, CD₂Cl₂) δ 210.3 (C=O), 136.5 (C₇epo), 130.1 (2C, C₇H₅), 128.8 (2C, C₇H₅), 127.2 (C₇H₅), 64.6 (C₇epo), 64.1 (C₇epo), 44.6 (C₇Ph), 41.1 (C(=O)CH₂), 31.7 (CH₂C₇epo), 25.2 (C(=O)CH₂CH₂), 23.9 (CH₂CH₂C₇epo).

**MS (EI-DE) m/z (%)** 216 [M⁺] (22), 198 (3), 187 (9), 169 (6), 159 (3), 143 (7), 129 (12), 118 (30), 104 (4), 97 (20), 91 (100), 78 (8), 65 (18), 55 (11), 41 (23).

**HRMS (EI-DE) calcd for C₁₄H₁₆O₂ [M⁺] 216.1152, found 216.1150.**

(2S,3S)-2,3-Epoxycyclooctanone ((2S,3S)-12d): After 24 h at 50 °C and base treatment of the crude product in THF, purification by flash column chromatography (silica gel, 10-40% Et₂O in pentane) provided the title compound as a colorless solid (77 mg, 550 µmol, 55%; 98:2 er). The enantiomeric ratio was determined by GC using a chiral BGB-176/SE-52 30 m (80 °C, 2 °C/min until 135 °C, 18 °C/min until 220 °C, 10 min at 220°C, 0.6 bar H₂); major enantiomer: τᵣ = 23.43 min, minor enantiomer: τᵣ = 21.95 min.

**1H NMR** (500 MHz, CD₂Cl₂) δ 3.70 (d, J = 5.4 Hz, 1H, C₇epoC(=O)), 3.22 (ddd, J = 9.8, 5.3, 3.7 Hz, 1H, CH₂C₇epo), 2.66 (ddd, J = 13.2, 7.7, 4.2 Hz, 1H, CHHC(=O)), 2.30 (ddd, J = 13.6, 10.1, 3.6 Hz, 1H, CHH(=O)), 2.19-2.14 (m, 1H, CHHCH₃), 1.94-1.87 (m, 1H, CHHCH₂C(=O)), 1.77-1.70 (m,
1H, $\text{CH}_2(\text{CH}_2)_2\text{O}_{\text{epo}}$, 1.69-1.62 (m, 1H, CH$\text{H}$CH$_2$(=O)), 1.60-1.51 (m, 2H, CH$_2$CH$_2$CH$_{\text{epo}}$), 1.49-1.40 (m, 1H, CH$\text{H}$(CH$_2$)$_2$CH$_{\text{epo}}$), 0.99-0.91 (m, 1H, CH$\text{H}$CH$_{\text{epo}}$).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) δ 207.3 ($\text{C}=$O), 58.8 (CH$_{\text{epo}}$C(=O)), 55.7 (CH$_2$CH$_{\text{epo}}$), 43.0 (CH$_2$(=O)), 27.2 (2C, CH$_2$CH$_{\text{epo}}$ and CH$_2$(CH$_2$)$_2$CH$_{\text{epo}}$), 24.7 (CH$_2$CH$_2$(=O)), 24.6 (CH$_2$CH$_2$CH$_{\text{epo}}$).

MS (EI-DE) m/z (%) 140 [M+] (18), 111 (5), 97 (16), 83 (37), 79 (17), 70 (30), 57 (27), 55 (100), 53 (11), 41 (84), 39 (43), 27 (45).

HRMS (EI-DE) calcd for C$_8$H$_{12}$O$_2$ [M+] 140.0836, found 140.0837.

$^{1}$H NMR (500 MHz, CD$_2$Cl$_2$) δ 3.51 (d, $J=1.6$ Hz, 1H, C$_{\text{epo}}$HC(=O)), 2.93 (td, $J=9.5, 2.2$ Hz, 1H, CH$_2$C$_{\text{epo}}$H), 2.91-2.87 (m, 1H, CHHC(=O)), 2.32-2.67 (m, 1H, CH$\text{H}$(=O)), 2.23-2.17 (m, 1H, CH$\text{H}$(CH$_2$)$_n$H), 1.84-1.69 (m, 3H, -(CH$_2$)$_n$-), 1.54-1.35 (m, 9H, -(CH$_2$)$_n$-), 1.29-1.24 (m, 1H, -(CH$_2$)$_n$- and CH$\text{H}$CH$_{\text{epo}}$H).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) δ 206.9 (C=O), 61.2 (CH$_2$C$_{\text{epo}}$H), 59.2 (C$_{\text{epo}}$HC(=O)), 41.4 (CH$_2$(=O)), 32.2 (CH$_2$C$_{\text{epo}}$H), 26.9 (CH$_2$), 26.5 (CH$_2$), 25.7 (CH$_2$), 25.5 (CH$_2$), 24.4 (CH$_2$), 24.0 (CH$_2$), 23.2 (CH$_2$).

MS (EI) m/z (%) 196 [M+] (8), 178 (1), 168 (1), 149 (2), 139 (4), 135 (6), 121 (14), 111 (29), 107 (8), 98 (54), 84 (31), 67 (36), 55 (100), 41 (92), 29 (39).

HRMS (EI-DE) calcd for C$_{12}$H$_{20}$O$_2$ [M+] 196.1465, found 196.1463.

$(E)$-(2$^S$,3$^R$)-2,3-Epoxycyclododecanone (12e): The title compound was isolated after 20 h at 50 °C and purification by flash column chromatography (silica gel, 10-20% Et$_2$O in pentane) as a white solid (45 mg, 229 µmol, 92%; 99.5:0.5 er). The enantiomeric ratio was determined by GC using a chiral Hydrodex-β-TBDAc column 25 m (100 °C, 1.2 °C/min until 170 °C, 20 °C/min until 220 °C, 10 min at 320 °C, 0.6 bar H$_2$); major enantiomer: $\tau_R = 54.36$ min, minor enantiomer: $\tau_R = 53.35$ min.

$^{1}$H NMR (500 MHz, CD$_2$Cl$_2$) δ 3.51 (d, $J=1.6$ Hz, 1H, C$_{\text{epo}}$HC(=O)), 2.93 (td, $J=9.5, 2.2$ Hz, 1H, CH$_2$C$_{\text{epo}}$H), 2.91-2.87 (m, 1H, CHHC(=O)), 2.32-2.67 (m, 1H, CH$\text{H}$(=O)), 2.23-2.17 (m, 1H, CH$\text{H}$(CH$_2$)$_n$H), 1.84-1.69 (m, 3H, -(CH$_2$)$_n$-), 1.54-1.35 (m, 9H, -(CH$_2$)$_n$-), 1.29-1.24 (m, 1H, -(CH$_2$)$_n$- and CH$\text{H}$CH$_{\text{epo}}$H).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) δ 206.9 (C=O), 61.2 (CH$_2$C$_{\text{epo}}$H), 59.2 (C$_{\text{epo}}$HC(=O)), 41.4 (CH$_2$(=O)), 32.2 (CH$_2$C$_{\text{epo}}$H), 26.9 (CH$_2$), 26.5 (CH$_2$), 25.7 (CH$_2$), 25.5 (CH$_2$), 24.4 (CH$_2$), 24.0 (CH$_2$), 23.2 (CH$_2$).

MS (EI) m/z (%) 196 [M+] (8), 178 (1), 168 (1), 149 (2), 139 (4), 135 (6), 121 (14), 111 (29), 107 (8), 98 (54), 84 (31), 67 (36), 55 (100), 41 (92), 29 (39).

HRMS (EI-DE) calcd for C$_{12}$H$_{20}$O$_2$ [M+] 196.1465, found 196.1463.

$(E)$-2,3-Epoxycyclopentadecanone (23f): The title compound (2$^S$,3$^R$)-23f was isolated after 20 h at 50 °C and purification by flash column chromatography (silica gel, 5-15% Et$_2$O in pentane) as a white solid (52 mg, 218 µmol, 87%; 99.5:0.5 er). The enantiomeric ratio was determined by GC using a chiral Hydrodex-β-TBDAc column 25m (100 °C, 1.2 °C/min until 185 °C, 18 °C/min until 220 °C, 10 min at 320 °C, 0.6 bar H$_2$); major enantiomer: $\tau_R = 65.00$ min, minor enantiomer: $\tau_R = 63.68$ min.
9-amino(9-deoxy)epiquinidine (1b) was used (instead of 1a). The title compound (2R,3S)-12f was isolated after 20 h at 50 °C and purification by flash column chromatography (silica gel, 5-15% Et₂O in pentane) as a white solid (51 mg, 215 µmol, 86%; 99.5:0.5 er). The enantiomeric ratio was determined by GC using a chiral Hydrodex-β-TBDAc column 25 m (100 °C, 1.2 °C/min until 190 °C, 18 °C/min until 230 °C, 5 min at 320 °C, 0.6 bar H₂); major enantiomer: τ_R = 64.72 min, minor enantiomer: τ_R = 65.60 min.

**1H NMR** (500 MHz, CD₂Cl₂) δ 3.27 (d, J = 1.9 Hz, 1H, C_{epo}H{C(=O)}), 3.01 (td, J = 8.6, 2.7 Hz, 1H, CH₂C_{epo}H), 2.47-2.39 (m, 2H, CH₂C{C(=O)}), 2.06-2.00 (m, 1H, CHH_{epo}H), 1.73-1.63 (m, 2H, -(CH₂)ₙ-), 1.53-1.50 (m, 2H, -(CH₂)ₙ-), 1.39-1.21 (m, 17H, -(CH₂)ₙ- and C_{epo}HCHH).

**13C NMR** (125 MHz, CD₂Cl₂) δ 207.0 (C{C(=O)}), 60.2 (C_{epo}HC{C(=O)}), 59.2 (CH₂C_{epo}H), 37.6 (CH₂C{C(=O)}), 31.0 (CH₂C_{epo}H), 27.5 (CH₂), 27.1 (CH₂), 26.9 (CH₂), 26.6 (CH₂), 26.4 (CH₂), 26.4 (CH₂), 26.2 (CH₂), 25.7 (CH₂), 24.9 (CH₂), 22.6 (CH₂).

**MS** (EI) m/z (%) 238 [M⁺] (19), 220 (1), 209 (1), 195 (3), 177 (3), 163 (3), 149 (3), 121 (12), 111 (29), 98 (48), 81 (38), 67 (39), 55 (100), 41 (86), 29 (34).


### Hydroperoxidation of Cycloheptenone (11a) and Cyclooctenone (11d)

The reactions of 2-cycloheptenone (11a) and 2-cyclooctenone (11d) were performed according to the general procedure for the catalytic asymmetric hydroperoxidation of acyclic α,β-unsaturated ketones 2.

7,8-Dioxabicyclo[4.2.1]nonan-1-ol/3-hydroperoxycycloheptanone (13a):
The reaction mixture was stirred for 24 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 20-60% Et₂O in pentane) provided peroxide 13a as a clear oil (79 mg, 551 µmol, 55%; 95:5 er). The enantiomeric ratio was determined after converting peroxide 13a into 2,3-epoxycycloheptanone (12a). The enantiomers were analyzed by GC using a chiral Hydrodex-β-TBDAc column 25 m (80 °C, 1.5 °C/min until 135 °C, 20 °C/min until 220 °C, 10 min at 220 °C, 0.6 bar H₂); major enantiomer: τ_R = 24.31 min, minor enantiomer: τ_R = 28.24 min. 7,8-Dioxabicyclo[4.2.1]nonan-1-ol (13a) exists in equilibrium with 3-hydroperoxycycloheptanone (13a‘): 80:20 (in THF).

**1H NMR** (500 MHz, THF-d8) 7,8-dioxabicyclo[4.2.1]nonan-1-ol (13a): δ 5.43 (br s, 1H, OH), 4.42-
4.40 (m, 1H, CH), 2.61 (d, J = 12.6 Hz, 1H, CHCHHCq), 2.50 (dd, J = 12.0, 6.7 Hz, 1H, CHCHHCq), 1.93-1.83 (m, 2H, CH), 1.77-1.74 (m, 3H, CH), 1.61-1.53 (m, 2H, CH), 1.43-1.37 (m, 1H, CHHCH); 3-hydroperoxycycloheptanone (13a?): δ 9.39 (br s, 1H, OOH), 4.09-4.04 (m, 1H, CH), 2.77 (dd, J = 14.7, 3.0 Hz, 1H, CHCHHC(=O)), 2.68 (dd, J = 14.8, 8.8 Hz, 1H, CHCHHC(=O)), 2.42-2.31 (m, 2H, CH2CH2C(=O)), 1.93-1.83 (m, 2H, CH), 1.77-1.74 (m, 4H, CH).

13C NMR (125 MHz, THF-d8) 7,8-dioxabicyclo[4.2.1]nonan-1-ol (13a): δ 108.1 (Cq), 81.3 (CH), 48.9 (CHCHHCq), 37.3 (CH2), 35.9 (CH2), 24.7 (CH2), 24.3 (CH2); 3-hydroperoxycycloheptanone (13a?): δ 209.3 (C=O), 81.0 (CH), 48.4 (CHCHHC(=O)), 45.1 (CH2CH2C(=O)), 35.0 (CH2), 26.2 (CH2), 25.4 (CH2).

MS (EI-DE) m/z (%) 144 [M+] (10), 126 (1), 111 (100), 97 (16), 83 (18), 69 (12), 55 (52), 41 (37), 39 (15), 29 (23).

HRMS (EI-FE) calcd for C7H12O3 [M+] 144.0787, found 144.0786.

3-Hydroperoxycyclooctanone/8,9-dioxabicyclo[5.2.1]decan-1-ol (13b):
The reaction mixture was stirred for 24 h at 32 °C. Purification of the crude product by flash column chromatography (silica gel, 5-35% Et2O in pentane) provided peroxide 13b as a clear oil (93 mg, 571 μmol, 59%; 97:3 er). The enantiomeric ratio was determined after converting peroxide 13b into 2,3-epoxycyclooctanone (12d). The enantiomers were analyzed by GC using a chiral BGB-176/SE-52 30 m (80 °C, 2 °C/min until 140 °C, 20 °C/min until 220 °C, 10 min at 220°C, 0.6 bar H2); major enantiomer: τR = 27.52 min, minor enantiomer: τR = 25.41 min. 3-Hydroperoxycyclooctanone (13b) exists in equilibrium with 8,9-dioxabicyclo[5.2.1]decan-1-ol (13b?): 70:30 (in THF).

1H NMR (500 MHz, CD2Cl2) 3-Hydroperoxycyclooctanone (13b): δ 8.98 (br s, 1H, OOH), 4.32-2.47 (m, 1H, CH), 2.91 (dd, J = 12.1, 3.6 Hz, 1H, CHCHHC(=O)), 2.87 (d, J = 11.7 Hz, 1H, CHCHHC(=O)), 2.43-2.32 (m, 2H, CH2CH2C(=O)), 1.97-1.91 (m, 2H, CH2), 1.88-1.23 (m, 6H, -(CH2)n-); 8,9-Dioxabicyclo[5.2.1]decan-1-ol (13b?): δ 4.58-4.56 (m, 1H, CH), 3.02 (br s, 1H, OH), 2.88-2.84 (m, 2H, CHCH2Cq), 2.19-2.13 (m, 1H, CH2), 1.98-1.28 (m, 8H, -(CH2)n-), 0.88 (t, J = 7.6 Hz, 1H, CH2).

13C NMR (125 MHz, CD2Cl2) 3-Hydroperoxycyclooctanone (13b): δ 213.9 (C=O), 82.8 (CH), 44.0 (CHCH2C(=O)), 42.4 (CH2CH2C(=O)), 29.6 (CH2), 28.1 (CH2), 22.9 (CH2), 19.7 (CH2); 8,9-Dioxabi-
cyclo[5.2.1]decan-1-ol (13b\textsuperscript{b}): δ 105.5 (Cq), 80.1 (CH), 52.6 (CHCH\textsubscript{2}Cq), 37.3 (CH\textsubscript{2}), 35.5 (CH\textsubscript{2}), 28.0 (CH\textsubscript{2}), 26.2 (CH\textsubscript{2}), 25.3 (CH\textsubscript{2}).

**MS** (EI-DE) \( m/z \) (%) 158 [M\textsuperscript{+}] (18), 141 (2), 125 (64), 107 (18), 97 (17), 83 (21), 69 (12), 55 (100), 43 (56), 41 (44), 29 (21).

**HRMS** (CI-FE, i-butane) calcd for C\textsubscript{8}H\textsubscript{15}O\textsubscript{3} [(M+H\textsuperscript{+})] 159.1022, found 159.1021.

**Organoselenium-Mediated Reductive Cleavage of Epoxides 12**

**General Procedure\textsuperscript{16}**

Under argon, acetic acid (15 \( \mu \)L, 0.25 mmol, 0.5 equiv) was added to an ethanolic solution of sodium phenylselenide, prepared by the reduction of diphenylselenide (234 mg, 0.75 mmol, 1.5 equiv) with sodium borohydride (57 mg, 1.5 mmol, 3.0 equiv) in ethanol (3 mL), and the mixture was stirred for five minutes at room temperature. The resulting solution was added at once to a solution of \( \alpha,\beta \)-epoxy ketone 12 (0.5 mmol, 1.0 equiv) in ethanol (2 mL) at 0 °C. After five minutes at room temperature, the reaction mixture was diluted with Et\textsubscript{2}O or EtOAc (15 mL) and washed with brine (5 mL). The aqueous layer was repeatedly extracted with Et\textsubscript{2}O or EtOAc (2×10 mL). The combined organic layers were washed with brine, dried over Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated under reduced pressure. Purification of the crude product by flash column chromatography (silica gel, eluent: Et\textsubscript{2}O-CH\textsubscript{2}Cl\textsubscript{2}) provided the corresponding \( \beta \)-hydroxy ketone 15.

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Scope of Optically Active Cyclic Aldol Products 15

(S)-3-Hydroxy-cyclohexanone ((S)-15a): The title compound was prepared according to the general procedure and obtained as a colorless oil (54 mg, 470 μmol, 94%; 96:4 er) after purification by flash column chromatography (silica gel, 25-50% Et2O in CH2Cl2). The enantiomeric ratio was determined by GC using a chiral Hydrodex-β-TBDAc column 25 m (35 min at 150 °C, 5 °C/min until 220°C, 10 min at 220 °C, 0.5 bar H2); major enantiomer: τR = 17.65 min, minor enantiomer: τR = 21.68 min.

1H NMR (500 MHz, CD2Cl2) δ 4.18-4.13 (m, 1H, CH), 2.59 (dd, J = 14.2, 4.1 Hz, 1H, CHCHHC(=O)), 2.35 (dd, J = 14.0, 7.4 Hz, 1H, CHCHHC(=O)), 2.27 (t, J = 6.6 Hz, 2H, CH2C(=O)), 2.12 (br s, 1H, OH), 2.07-1.95 (m, 2H, CH2CHHCH and CH2CHHCH2), 1.77-1.65 (m, 2H, CH2CHHCH and CH2CHHCH2).

13C NMR (125 MHz, CD2Cl2): δ 209.5 (C=O), 69.8 (C), 50.3 (CHCHHC(=O)), 40.9 (CH2C(=O)), 32.8 (CH2CHCH), 20.7 (CH2CH2CH2).

MS (EI-DE) m/z (%) 114 [M+] (64), 96 (14), 86 (7), 81 (5), 73 (18), 68 (47), 60 (60), 58 (34), 55 (81), 44 (100), 42 (85), 31 (9), 27 (28).

HRMS (EI-FE) calcd for C6H10O2 [M+] 114.0680, found 114.0681.

(S)-3-Hydroxy-3-methyl-cyclohexanone ((S)-15b): The title compound was prepared according to the general procedure and obtained as a white solid (46 mg, 357 μmol, 89%; 95.5:4.5 er) after purification by flash column chromatography (silica gel, 10-20% Et2O in CH2Cl2). The enantiomeric ratio was determined by GC using a chiral Hydrodex-β-TBDAc column 25 m (60 min at 145 °C, 6 °C/min until 220°C, 10 min at 220 °C, 0.6 bar H2); major enantiomer: τR = 11.84 min, minor enantiomer: τR = 14.81 min.

1H NMR (500 MHz, CD2Cl2) δ 2.40 (d, J = 14.0 Hz, 1H, CqOHC≡C≡C(=O)), 2.36 (td, J = 13.9, 1.8 Hz, 1H, CqOHC≡C≡C(=O)), 2.33-2.22 (m, 2H, CH2C(=O)), 2.08-1.99 (m, 1H, CH2CHHCH2), 1.89-1.76 (m, 3H, CH2CHHCH2 and CH2CHHCH2), 1.55 (br s, 1H, OH), 1.33 (s, 3H, CH3).

13C NMR (125 MHz, CD2Cl2): δ 209.8 (C=O), 74.0 (CqOHC≡C≡C(=O)), 54.9 (CqOHC≡C≡C(=O)), 40.5 (CH2C(=O)), 37.7 (CH2C≡C≡C(=O)), 30.1 (CH3), 21.4 (CH2CH2CH2).

MS (EI-DE) m/z (%) 128 [M+] (29), 110 (16), 99 (7), 86 (34), 71 (57), 68 (74), 60 (17), 57 (86), 55
(100), 43 (97), 41 (71), 31 (13), 29 (43).


**((S)-3-Hydroxycycloheptanone ((S)-15c):** The title compound was prepared according to the general procedure and obtained as a colorless oil (31 mg, 242 μmol, 84%; 99:1 er) after purification by flash column chromatography (silica gel, 40-60% Et₂O in CH₂Cl₂). The enantiomeric ratio was determined by GC using a chiral Ivadex 7/PS086 column (25 m (40 min at 105 °C, 10 °C/min until 220°C, 10 min at 320 °C, 0.5 bar H₂); major enantiomer: τᵣ = 27.66 min, minor enantiomer: τᵣ = 29.55 min.

**1H NMR** (500 MHz, CD₂Cl₂) δ 4.06-4.02 (m, 1H, CH) 2.77-2.69 (m, 2H, CHCH₂C(=O)), 2.47-2.36 (m, 2H, CH₁₂C(=O)), 2.03 (br s, 1H, OH), 1.90-1.78 (m, 3H, CH₂CHHCH and CH₂CH₂H₂), 1.77-1.72 (m, 2H, CH₁₂CH₂C(=O)), 1.61-1.55 (m, 1H, CH₂CHHCH).

**13C NMR** (125 MHz, CD₂Cl₂) δ 211.5 (C=O), 67.6 (CH), 51.7 (CHCH₂C(=O)), 44.3 (CH₂C(=O)), 38.9 (CH₂CH₂), 24.4 (CH₂CH₂CH), 23.8 (CH₂CH₂C(=O)).

**MS** (EI) m/z (%) 128 [M⁺] (26), 113 (6), 100 (16), 95 (8), 85 (15), 71 (44), 69 (17), 58 (60), 55 (25), 43 (100), 27 (13).


**((R)-3-Hydroxycyclooctanone ((R)-15d):** The title compound was prepared according to the general procedure. The reaction was stirred for 19 h at room temperature (90% conversion). Aldol product 15d was obtained as a colorless oil (54 mg, 38 μmol, 53%; 86:14 er) after purification by flash column chromatography (silica gel, 40-60% Et₂O in CH₂Cl₂). The enantiomeric ratio was determined by GC using a chiral Ivadex 7 column (25 m (80 °C, 1 °C/min until 160°C, 20 °C/min until 220°C, 10 min at 220 °C, 0.5 bar H₂); major enantiomer: τᵣ = 41.2 min, minor enantiomer: τᵣ = 42.3 min.

**1H NMR** (500 MHz, CDCl₃) δ 4.07-4.02 (m, 1H, CH) 2.77 (dd, J = 11.7, 3.8 Hz, 1H, CHCH₂HC(=O)), 2.66 (dd, J = 11.4, 8.6 Hz, 1H, CHCH₂HC(=O)), 2.37-2.34 (m, 3H, CH₂ and OH), 1.99-1.86 (m, 2H, CH₂), 1.83-1.77 (m, 1H, CH₂), 1.66-1.44 (m, 4H, CH₂), 1.28-1.20 (m, 1H, CH₂).

**13C NMR** (125 MHz, CDCl₃) δ 214.2 (C=O), 70.5 (CH), 47.4 (CHCH₂C(=O)), 44.4 (CH₂C(=O)), 34.6 (CH₂CH₂CH), 28.1 (CH₂), 22.8 (CH₂), 19.7 (CH₂).
**Catalytic Asymmetric Epoxidation of Cyclopentenones 16**

**General Procedure**

Catalyst 1c (0.01 mmol) and (R)-Mosher’s acid 18 (0.02 mmol) were dissolved in dry 1,4-dioxane (0.4 mL). After stirring for 5 min, 16 (0.1 mmol) was added, followed by 50% aqueous hydrogen peroxide solution (0.15 mmol). After vigorous stirring for 168 h, the reaction mixture was poured into water (3 mL) and extracted with diethyl ether (3 x 5 mL). The organic fractions were dried over anhydrous MgSO₄ and concentrated under reduced pressure. Purification by flash column chromatography afforded epoxyketones 17.

**Preparation of Racemates**

Cyclopentenone 16 (0.5 mmol) and tert-butyl amine (0.015 mmol) were dissolved in methanol (3 mL) and 50% aqueous hydrogen peroxide solution (2.0 mmol) was added. After stirring for 24-48 h, the reaction mixture was poured into water and organic layer was extracted with diethyl ether. The organic fractions were dried over anhydrous MgSO₄ and concentrated under reduced pressure. Purification by flash column chromatography afforded *rac*-17.
Scope of Optically Active Cyclic \( \alpha,\beta \)-Epoxyketones 17

\((2S,3R)-2,3\)-Epoxycyclopentanone (17a): Purification: 50% diethyl ether/pentane. Colourless oil, 87%. The enantiomeric ratio was determined to be 95:5 er by chiral GC using a Lipodex E column 25 m (80 °C iso, 0.5 bar H\(_2\)); major enantiomer: \( \tau_R = 8.22 \) min, minor enantiomer: \( \tau_R = 9.60 \) min.

\(^1\)H NMR (300 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 3.89-3.88 (m, 1H, CH\(_2\)C\(_\text{Hepo}\)), 3.26 (d, \( J = 2.6 \) Hz, 1H, CH\(_\text{epoC(O)}\)), 2.37-2.17 (m, 2H, CH\(_\text{H}\)), 2.09-1.97 (m, 2H, CH\(_\text{H}\)).

\(^{13}\)C NMR (75 MHz, CD\(_2\)Cl\(_2\)) \( \delta \) 210.3 (C=O), 58.3 (CH\(_\text{epoC(O)}\)), 55.2 (CH\(_2\)CH\(_\text{epo}\)), 30.9 (CH\(_2\)C(=O)), 23.5 (CH\(_2\)CH\(_\text{epo}\)).

GC-MS (GC-EI) \( m/z \) (%): 98 [M\(^+\)] (41), 82 (13), 69 (25), 55 (22), 53 (6), 42 (100), 39 (37), 31 (1), 27 (18).

HRMS (EI-FE) calcd for C\(_5\)H\(_6\)O\(_2\) [M\(^+\)] 98.0367, found 98.0368.

The physical data are identical in all respects to those previously reported.\(^{17}\)

\((2S,3S)-\)Epoxy-3-(methyl)-cyclopentanone (17b): This compound been described in the literature.\(^{18}\)

The enantiomeric ratio was determined to be 95.5:4.5 er by chiral GC using a BGB-176/BGB-15 column (80 °C iso, 0.5 bar H\(_2\)); major enantiomer: \( \tau_R = 10.75 \) min, minor enantiomer: \( \tau_R = 12.49 \) min.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 3.23 (s, 1H), 2.33-2.45 (m, 1H), 2.22-2.29 (m, 1H), 2.06-2.17 (m, 2H), 1.03 (s, 9H).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 211.4, 125.5, 65.9, 59.1, 32.7, 32.1, 30.3, 26.2, 22.3.

HRMS (ESI+) \( m/z \) calcd for C\(_9\)H\(_{15}\)O\(_2\) 155.1072, found 155.1073.

\((2S,3R)-\)Epoxy-3-(\(\text{tert}\)-butyl)-cyclopentanone (17c): Purification: 50% ethylacetate/hexane. Colourless oil, 65%. The enantiomeric ratio was determined to be 96:4 er by chiral GC (Lipodex E, 95 °C, 0.5 bar H\(_2\)), major enantiomer: \( \tau_R = 8.46 \) min, minor enantiomer: \( \tau_R = 11.14 \) min.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 3.23 (s, 1H), 2.33-2.45 (m, 1H), 2.22-2.29 (m, 1H), 2.06-2.17 (m, 2H), 1.03 (s, 9H).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \) 211.4, 125.5, 65.9, 59.1, 32.7, 32.1, 30.3, 26.2, 22.3.

HRMS (ESI+) \( m/z \) calcd for C\(_9\)H\(_{15}\)O\(_2\) 155.1072, found 155.1073.


(2S,3R)-Epoxy-3-(benzyl)-cyclopentanone (17d): This compound been described in the literature.\textsuperscript{19} The enantiomeric ratio was determined to be 97.5:2.5 er by chiral GC using a Lipodex E column (130 °C iso, 0.5 bar H\textsubscript{2}); major enantiomer: $\tau_R = 26.62$ min, minor enantiomer: $\tau_R = 27.50$ min.

(2S,3S)-2,3-Epoxy-4,4-dimethylcyclopentanone (17e): This compound been described in the literature.\textsuperscript{20} The enantiomeric ratio was determined to be 96.5:3.5 er by chiral GC using a Lipodex G column (50 °C iso, 0.5 bar H\textsubscript{2}); major enantiomer: $\tau_R = 15.95$ min, minor enantiomer: $\tau_R = 16.76$ min.

\textsuperscript{20} Tang, Z.; Mathieu, B.; Tinant, B.; Dive, G.; Ghosez, L. \textit{Tetrahedron} 2007, 63, 8449.
Catalytic Asymmetric Epoxidation of $\alpha,\beta$-Disubstituted Enals 19

**General Procedure**

Phosphoric acid $(R)$-$21b$ (25.0 mg, 0.05 mmol, 0.2 equiv) and amine catalyst 1a (8.08 mg, 0.025 mmol, 0.1 equiv) were dissolved in dry THF (2 mL, 0.125 M) and stirred for 5 min under ambient atmosphere at room temperature. The $\alpha$-branched enal 19 (0.25 mmol, 1 equiv) was added and the mixture was stirred for an additional 5 min at room temperature. Aqueous hydrogen peroxide (77 $\mu$L, 50% w/w, 1.25 mmol, 5 equiv) was added, the reaction vessel was sealed and the reaction mixture was stirred for 24 h at 50 °C under an atmosphere of air. The reaction can be monitored by the disappearance of the starting material; the formed product is masked as a very polar species that appears as a poorly stainable spot on the TLC ($R_f$ ~ 0.1) and is presumably a hydroperoxide adduct of the aldehyde 20.

**Workup A:** The product 20 is liberated as the free aldehyde when the excess peroxide is quenched. This was performed by stirring the crude reaction mixture with 10% aqueous Na$_2$S$_2$O$_3$ (1 mL) for 10 min. The mixture was then diluted with water (5 mL) and diethyl ether (5 mL) and partitioned. The aqueous layer was washed with diethyl ether (5 mL x 3), and the combined organic layers were washed with brine and dried over Na$_2$SO$_4$. For yield determination, most compounds were directly reduced with NaBH$_4$ (14.1 mg, 0.375 mmol, 1.5 equiv) in EtOH (2 mL) at room temperature, stirring for 10 min. Saturated aqueous Na,K-tartrate (Rochelle’s salt) was then added and the reaction mixture stirred for 1 h. The resulting biphasic solution was diluted with diethyl ether (5 mL) and water (10 mL) and partitioned. The aqueous layer was washed extracted with EtOAc...
Evaporation of the solvent and flash column chromatography with the specified solvent system afforded the corresponding alcohols 20°.

**Workup B**: In cases when the epoxyaldehyde products 20 were very volatile, a modified workup procedure was used before reduction to the corresponding alcohol. The crude reaction mixture was quenched by adding solid Na₂S₂O₃ (250 mg) and the suspension was stirred for 1 h. It was then filtered through a pad of Celite, washing with 2-5 mL diethyl ether and 2 mL EtOH. To this filtrate was added solid NaBH₄ (14.1 mg, 0.375 mmol, 1.5 equiv) and the reaction mixture was stirred for 10 min. Saturated aqueous Na,K-tartrate (Rochelle’s salt) was added and the reaction mixture was stirred for 1 h. The resulting biphasic solution was diluted with diethyl ether (5 mL) and water (10 mL) and partitioned. The aqueous layer was washed extracted with EtOAc (5 mL x 2), and the combined organic layers were washed with brine and dried over Na₂SO₄. Evaporation of the solvent and flash column chromatography with the specified solvent system afforded the desired product.

**Preparation of Racemates**

All racemates of the aldehydes 20 and 23, as well as their corresponding alcohol derivatives were prepared according to the procedure described by Pihko *et al.*²¹

**Scope of Optically Active α,β-Epoxyaldehydes 20**

\(((2S,3S)-3-ethyl-2-methyloxiran-2-yl)methanol (20a’): Prepared according to the general procedure and workup B using commercial (E)-2-methylpent-2-enal (E/Z >20:1, 0.4 mmol) followed by reduction with NaBH₄. Purification by flash chromatography (50% Et₂O in pentane) afforded 20a’ as a colourless oil (19.9 mg, 0.17 mmol, 43%, 92:8 dr, 98.5:1.5 er)

\[ ^{1}H \text{ NMR (400 MHz, CDCl}_3) \delta 3.69 \text{ (dd, } J = 12.2 \text{ Hz, } J = 4.3 \text{ Hz, 1H, CH}_2\text{OH}), 3.58 \text{ (dd, } J = 12.2 \text{ Hz, } J = 8.2 \text{ Hz, 1H, CH}_2\text{OH}), 3.00 \text{ (t, } J = 6.4 \text{ Hz, 1H, CHO}_\text{epox}), 2.82 \text{ (minor diastereomer, t, } J = 6.4 \text{ Hz,}

1H, CHO_{epox}), 1.72 (br dd, 1H, OH), 1.68-1.50 (m, 2H, CH_{3}CH_{2}), 1.29 (s, 3H, CH_{3}), 1.04 (t, J = 7.5 Hz, 3H, CH_{3}CH_{2}).

^{13}\text{C NMR} (100 MHz, CDCl_{3}) only major diastereomer peaks detected: δ 65.4, 61.3, 60.9, 21.5, 14.1, 10.5.

FTIR (thin film) 3427, 2972, 2937, 2878, 1460, 1348, 1040, 909, 732 cm\(^{-1}\)

HRMS (m/z) calcd for C_{6}H_{13}O_{2} [M+H]\(^{+}\): 117.0916, found 117.0915.

[\alpha]_{D}^{25} = –14.1 (c 0.170, CHCl_{3}); Lit\(^{22}\): [\alpha]_{D}^{22} = –13.5 (c = 0.84, CHCl_{3}).

Chiral GC (Hydrodex-β TBDAc, 20 min at 100 °C, 8 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H_{2}) \(\tau_{R} = 9.1\) min (major enantiomer, major diastereomer), \(\tau_{R} = 11.0\) min (major enantiomer, minor diastereomer), \(\tau_{R} = 12.0\) min (minor enantiomer, major diastereomer), \(\tau_{R} = 13.2\) min (minor enantiomer, minor diastereomer).

(2R,3S)-3-ethyl-2-methyloxirane-2-carbaldehyde (20a): Chiral GC (BGB-176SE/ SE-52, 45 min at 40 °C, 8 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H_{2}): \(\tau_{R} = 29.9\) min (minor enantiomer, minor diastereomer), \(\tau_{R} = 32.2\) min (major enantiomer, minor diastereomer), \(\tau_{R} = 35.6\) min (minor enantiomer, major diastereomer), \(\tau_{R} = 35.9\) min (major enantiomer, major diastereomer).

Conditions for efficient separation of (2S,3R)-enriched mixture: Lipodex G (40 °C, 1 °C/min until 60 °C, 12 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H_{2}) \(\tau_{R} = 8.0\) min (major enantiomer, minor diastereomer), \(\tau_{R} = 8.9\) min (minor enantiomer, minor diastereomer), \(\tau_{R} = 9.1\) min (major enantiomer, major diastereomer), \(\tau_{R} = 10.9\) min (minor enantiomer, major diastereomer).

(2S,3S)-2-ethyl-3-propyloxiran-2-yl)methanol (20b’): Prepared according to the general procedure and workup B using commercial (E)-2-ethylhex-2-enal (E/Z = 94:6, 0.36 mmol) followed by reduction with NaBH\(_{4}\). Purification by flash chromatography (50% Et\(_{2}\)O in pentane) afforded 20b’ as a colourless oil (33.1 mg, 0.23 mmol, 64%, 83:17 dr, 99:1 er).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.76 (dd, $J = 12.1$ Hz, $J = 4.5$ Hz, 1H, CH$_2$OH), 3.61 (dd, $J = 12.1$ Hz, $J = 8.2$ Hz, 1H, CH$_2$OH), 3.67 (minor diastereomer, dd, $J = 11.8$ Hz, $J = 5.2$ Hz, 1H, CH$_2$OH), 3.05 (apparent t, $J = 5.6$ Hz, 1H, CHO$_{epox}$), 2.87 (minor diastereomer, dd, $J = 6.6$ Hz, $J = 5.7$ Hz, 1H, CHO$_{epox}$), 1.95-1.84 (minor diastereomer, 2H, CH$_2$CH$_3$), 1.81-1.71 (m, 2H, CH$_2$CH$_3$), 1.62-1.44 (m, 4H, CH$_3$CH$_2$CH$_2$), 1.02-0.95 (m, 6H, CH$_3$, CH$_3$).

$^{13}$C NMR (100 MHz, CDCl$_3$) major diastereomer: $\delta$ 63.96, 62.9, 60.4, 29.9, 21.8, 20.1 14.0, 9.3; minor diastereomer: $\delta$ 63.94, 63.3, 61.6, 30.0, 26.5, 20.0, 13.9, 8.9.

FTIR (thin film) 3431, 2963, 2937, 2876, 1465, 1381, 1048, 908, 733 cm$^{-1}$

HRMS (m/z) calcd for C$_8$H$_{17}$O$_2$ [M+H]$^+$: 145.1229. Found 145.1227.

[$\alpha$]$_D^{25}$: $-39.4$ (c 0.508, CHCl$_3$).

Chiral GC (Lipodex G, 70 °C isocratic, 0.5 bar H$_2$) $\tau_R = 29.3$ min (minor enantiomer, major diastereomer), $\tau_R = 32.0$ min (major enantiomer, major diastereomer), $\tau_R = 36.1$ min (major enantiomer, minor diastereomer), $\tau_R = 37.4$ min (minor enantiomer, minor diastereomer).

The absolute stereochemistry was assigned by analogy and the relative stereochemistry was confirmed by NOESY and $^{13}$C NMR experiments:

**Gamma effect**

(2R,3S)-2-ethyl-3-propyloxirane-2-carbaldehyde (20b): Chiral GC (BGB-177/BGB-15, 35 min at 70 °C, 8 °C/min until 220 °C, 5 min at 220 °C, 0.6 bar H$_2$): $\tau_R = 19.6$ min (minor enantiomer, minor diastereomer), $\tau_R = 21.4$ min (major enantiomer, minor diastereomer), $\tau_R = 22.6$ min (major enantiomer, major diastereomer), $\tau_R = 25.1$ min (minor enantiomer, major diastereomer).
((2S,3S)-2-benzyl-3-phenethyloxiran-2-yl)methanol (20c’): Prepared according to the general procedure and workup A using (E)-2-benzyl-5-phenylpent-2-enal (E/Z > 20:1, 0.25 mmol) followed by reduction with NaBH₄. Purification by flash chromatography (20% Et₂O in pentane) afforded 20c’ as a colourless oil (51.6 mg, 0.19 mmol, 77%, 90:10 dr, 99:1 er).

¹H NMR (500 MHz, CDCl₃) δ 7.33-7.15 (m, 10H, CH₆Ar), 3.59 (dd, J = 12.3 Hz, J = 4.2 Hz, 1H, CH₂OH), 3.48 (dd, J = 12.3 Hz, J = 8.5 Hz, 1H, CH₂OH), 3.19 (dd, J = 7.5 Hz, J = 5.2 Hz, 1H, CHOepox), 3.05 (minor diastereomer, d, J = 14.1 Hz, 1H, CHOepox), 2.98 (d, J = 14.8 Hz, 1H, PhCH₂), 2.96-2.89 (m, 1H, PhCH₂), 2.86-2.77 (m, 1H, PhCH₂), 2.70 (d, J = 14.8 Hz, 1H, PhCH₂), 2.68-2.64 (minor diastereomer, m, 1H), 2.13-1.99 (m, 2H, PhCH₂CH₂), 1.92-1.80 (minor diastereomer, m, 1H), 1.52 (dd, J = 8.5 Hz, J = 4.2 Hz, 1H, OH).

¹³C NMR (125 MHz, CDCl₃) major diastereomer: δ 141.1, 136.5, 129.3, 128.6, 128.48, 126.7, 126.2, 63.7, 63.1, 60.0, 35.0, 33.0; minor diastereomer (not all peaks detected): 136.3, 129.8, 128.44, 128.41, 126.3, 62.5, 61.6, 34.9, 32.7, 29.9.

FTIR (thin film) 3437, 3063, 3028, 2928, 1603, 1496, 1454, 1068, 1031, 908, 732, 700 cm⁻¹


[a] Dio²⁵ : – 38.0 (c 0.548, CHCl₃).

Chiral HPLC: Diastereomer separation: Zorbax XDB/C18, methanol/water = 70:30, flow rate 1.0 mL/min, 29.2 MPa, 210 nm. Upon separation, the major diastereomer was switched to a chiral column at 3.32 min till 3.42 min: Kromasil - AmyCoat, methanol/water = 98:2, flow rate 1.0 mL/min, 12.6 MPa, 220 nm). Major diastereomer: τᵣ = 6.8 min (major enantiomer), τᵣ = 8.4 min (minor enantiomer).

(1S,6S)-7-oxabicyclo[4.1.0]heptan-1-ylmethanol (20d’): Prepared according to the general procedure and workup B using commercial cyclohex-1-ene-carbaldehyde (0.36 mmol) followed by reduction with NaBH₄. Purification by flash chromatography (50% Et₂O in pentane) afforded 20d’ as a colourless oil (32.2 mg, 0.25 mmol, 70%, 98.5:1.5 er).

¹H NMR (400 MHz, CDCl₃) δ 3.68 (dd, J = 12.2 Hz, J = 3.0 Hz, 1H, CH₂OH), 3.59 (dd, J = 12.1
Hz, $J = 8.4$ Hz, 1H, CH$_2$OH), 3.26 (d, $J = 3.4$ Hz, 1H, CHO$_{epox}$), 2.01-1.95 (m, 1H, OH), 1.90-1.64 (m, 4H, CH$_2$), 1.54-1.41 (m, 2H, CH$_2$), 1.34-1.23 (m, 2H, CH$_2$).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 64.5, 60.1, 55.8, 25.3, 24.4, 19.9 19.7.

FTIR (thin film) 3417, 2938, 2872, 1435, 1032, 916, 731 cm$^{-1}$

HRMS (m/z) calcd for C$_7$H$_{13}$O$_2$ [M+H]$^+$: 129.0916. Found 129.0916.

$[\alpha]_b^{25}$: $-22.6$ (c 0.504, CHCl$_3$); Lit$^{[185]}$: $[\alpha]_b^{25}$ : $-22.8$ (c 2.6, CHCl$_3$, 93% ee).

Chiral GC (BGB-177/BGB-15, 90 °C isocratic, 0.6 bar H$_2$) $\tau_R = 32.2$ min (minor enantiomer), $\tau_R = 32.6$ min (major enantiomer).

The physical data are identical in all respects to those previously reported.$^{23}$

(1R,6S)-7-oxabicyclo[4.1.0]heptane-1-carbaldehyde (20d): Chiral GC (BGB-177/BGB-15, 65 °C isocratic, 0.7 bar H$_2$) $\tau_R = 31.7$ min (minor enantiomer), $\tau_R = 34.2$ min (major enantiomer).

(2S,3S)-2-methyl-3-phenyloxiran-2-yl)methanol (20e'): Prepared according to the general procedure and workup A using commercial (E)-2-methyl-3-phenylacrylaldehyde followed by reduction with NaBH$_4$. Purification by flash chromatography (30% Et$_2$O in pentane) afforded 20e' as a colourless oil (20.1 mg, 0.12 mmol, 49%, 97:3 dr, 97.5:3.5 er).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.41-7.34 (m, 2H, CH$_2$Ar), 7.34-7.28 (m, 3H, CH$_2$Ar), 4.23 (s, 1H, PhCH), 3.87 (d, $J = 12.4$ Hz, 1H, CH$_2$OH), 3.77 (d, $J = 12.4$ Hz, 1H, CH$_2$OH), 1.99 (br s, 1H, OH), 1.10 (s, 3H, CH$_3$).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 135.6, 128.1, 127.6, 126.4, 64.9, 63.6, 60.1, 13.5.

FTIR (thin film) 3412, 3064, 2932, 2870, 1605, 1495, 1451, 1385, 1249, 1070, 1040, 956, 601, 852 cm$^{-1}$

HRMS (m/z) calcd for C$_{10}$H$_{12}$O$_2$Na [M]: 164.0837. Found 164.0836.

m.p.: 52.2 – 53.2 °C.

$[\alpha]_b^{25}$: $-14.5$ (c 0.815, CHCl$_3$), Lit$^{[185]}$: $[\alpha]_b^{25}$ : $-16.9$ (c 2, CHCl$_3$, >98% ee)

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S-75
Chiral GC (Hydrodex – β-TBDAc, 60 min at 110 °C, 15 °C/min until 220 °C, 5 min at 220 °C, 0.6 bar H2): 
\( t_{R} = 42.6 \text{ min (major enantiomer, major diastereomer)}, \quad t_{R} = 46.3 \text{ min (major enantiomer, minor diastereomer)}, \quad t_{R} = 40.1 \text{ min (minor enantiomer, major diastereomer)}, \quad t_{R} = 51.6 \text{ min (minor enantiomer, minor diastereomer)}. \)

(2R,3S)-2-methyl-3-phenyloxirane-2-carbaldehyde (20e): Chiral GC (BGB-177, 60 min at 120 °C, 15 °C/min until 220 °C, 5 min at 220 °C, 0.6 bar N2): 
\( \tau_{R} = 30.6 \text{ min (minor enantiomer)}, \quad \tau_{R} = 31.0 \text{ min (major enantiomer)}. \)

4-((2S,3S)-3-(hydroxymethyl)-3-methyloxiran-2-yl)butyl acetate (20f'): Prepared according to the general procedure and workup A using (E)-6-methyl-7-oxohept-5-enyl acetate 19f (E/Z >20:1, 0.25 mmol) followed by reduction with NaBH4. Purification by flash chromatography (50% Et2O in pentane) afforded 20f' as a colourless oil (33.5 mg, 0.160 mmol, 66%, 97:3 er).

\[ \mathrm{1H NMR} \] (500 MHz, CDCl3) \( \delta \) 4.09 (apparent t, \( J = 6.6 \text{ Hz}, \ 2\mathrm{H}, \ \text{AcOCH}_2 \)), 3.68 (apparent d, \( J = 12.0 \text{ Hz}, \ 1\mathrm{H}, \ \text{CH}_2\text{OH} \)), 3.58 (dd, \( J = 12.0 \text{ Hz}, \ J = 6.9 \text{ Hz}, \ 1\mathrm{H}, \ \text{CH}_2\text{OH} \)), 3.04 (apparent t, \( J = 5.6 \text{ Hz}, \ 1\mathrm{H}, \ \text{CHO}_{\text{epox}} \)), 2.85 (minor diastereomer, apparent t, \( J = 6.1 \text{ Hz}, \ 1\mathrm{H}, \ \text{CHO}_{\text{epox}} \)), 2.06 (s, 3H, \( \text{CH}_3\text{CO}_2 \)), 2.01 (br s, 1H, \( \text{OH} \)), 1.74-1.48 (m, 6H, \( \text{CH}_2 \)), 1.29 (s, 3H, \( \text{CH}_3 \)).

\[ \mathrm{13C NMR} \] (125 MHz, CDCl3) major diastereomer: \( \delta \) 171.3, 65.3, 64.2, 60.9, 59.9, 28.4, 27.8, 23.0, 21.0, 14.2; minor diastereomer (not all peaks detected): 64.6, 64.2, 63.9, 27.7, 23.2, 20.2;

\[ \mathrm{FTIR} \] (thin film) 3447, 2955, 2868, 2250, 1736, 1458, 1433, 1387, 1367, 1240, 1035, 911, 868, 729 cm\(^{-1}\)

\[ \mathrm{HRMS} \] (m/z) caled for C\(_{10}\)H\(_{18}\)O\(_4\)Na [M+Na]\(^{+}\): 225.1097. Found 225.1099.

\[ [\alpha]_D^{25} = -17.7 \text{ (c 0.362, CHCl}_3) \].

Chiral GC (Lipodex G, 60 min at 120 °C, 15 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H\(_2\)): \( \tau_{R} = 37.9 \text{ min (minor enantiomer, major diastereomer)}, \quad \tau_{R} = 39.1 \text{ min (major enantiomer, major diastereomer)}, \quad \tau_{R} = 41.0 \text{ min (major enantiomer, minor diastereomer)}, \quad \tau_{R} = 42.2 \text{ min (minor enantiomer, minor diastereomer)}. \)
4-((2S,3R)-3-formyl-3-methyloxiran-2-yl)butyl acetate (20f): Chiral GC (BGB-174/BGB-1701, 40 min at 155 °C, 10 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H₂): τ<sub>r</sub> 22.1 min (major enantiomer, minor diastereomer), τ<sub>R</sub> = 23.8 min (minor enantiomer, minor diastereomer), τ<sub>r</sub> = 31.6 min (minor enantiomer, major diastereomer), τ<sub>R</sub> = 32.5 min (major enantiomer, major diastereomer).

((2S,3S)-2-methyl-3-phenethyloxiran-2-yl)methanol (20g'): Prepared according to the general procedure and workup A using (E)-2-methyl-5-phenylpent-2-enal (E/Z = 20:1, 0.25 mmol) followed by reduction with NaBH₄. Purification by flash chromatography (50% Et₂O in pentane) afforded 20g' as a colourless oil (36.2 mg, 0.19 mmol, 75%, 95:5 dr, 98.5:1.5 er).

<sup>1</sup>H NMR (500 MHz, CDCl₃) δ 7.31-7.28 (m, 2H, C₆H₄Ar), 7.22-7.19 (m, 3H, C₆H₄Ar), 3.63 (dd, J = 12.3 Hz, J = 3.9 Hz, 1H, CH₂OH), 3.52 (dd, J = 12.3 Hz, J = 8.8 Hz, 1H, CH₂OH), 3.48 (minor diastereomer, dd, J = 11.7 Hz, J = 5.8 Hz, 1H, CH₂OH), 3.38 (minor diastereomer, dd, J = 11.7 Hz, J = 6.2 Hz, 1H, CH₂OH), 3.09 (t, J = 6.2 Hz, 1H, CHO<sub>epox</sub>), 2.89-2.83 (m, 1H, PhCH₂), 2.76-2.70 (m, 1H, PhCH₂), 2.06-1.94 (m, 1H, PhCH₂CH₂), 1.88-1.81 (m, 1H, PhCH₂CH₂), 1.65 (br s, 1H, OH), 1.12 (s, 3H, CH₃).

<sup>13</sup>C NMR (125 MHz, CDCl₃) major diastereomer: δ 141.2, 128.49, 128.47, 126.2, 65.3, 61.2, 59.6, 32.7, 30.1, 14.1; minor diastereomer (not all signals detected): 142.4, 128.75, 128.6, 126.3, 64.3, 63.7, 20.1.

FTIR (thin film) 3427, 3027, 2928, 2861, 1604, 1496, 1454, 1073, 1039, 908, 749, 700 cm⁻¹


[α]<sub>D</sub><sup>25</sup> = −27.6 (c 0.521, CHCl₃).

Chiral HPLC: Diastereomer separation: Zorbax XDB/C18, acetonitrile/water = 25:75, flow rate 1.0 mL/min, 22.2 MPa, 210 nm. Upon separation, each diastereomer was switched to a chiral column at 5.57 min till 5.62 min for the minor diastereomer and 6.06 min till 6.11 min for the major diastereomer: Chiralpak AS-RH, acetonitrile/water = 30:70, flow rate 1.0 mL/min, 10.1 MPa, 210 nm). Minor diastereomer (cis-20g()): τ<sub>R</sub> = 10.9 min (major enantiomer), τ<sub>R</sub> = 11.6 min (minor
enantiomer). Major diastereomer (trans-20g\'): $\tau_R = 11.5$ min (minor enantiomer), $\tau_R = 12.21$ min (major enantiomer).

The absolute stereochemistry was assigned by analogy. The minor (2S, 3R) diastereomer cis-20g\' has been described.\textsuperscript{24}

(2R,3S)-2-methyl-3-phenethyloxirane-2-carbaldehyde (20g): Chiral GC (BGB-177/BGB-15, 60 min at 120 °C, 10 °C/min until 230 °C, 5 min at 230 °C, 0.7 bar H\textsubscript{2}) $\tau_R = 40.0$ min (major enantiomer, minor diastereomer), $\tau_R = 40.6$ min (minor enantiomer, minor diastereomer), $\tau_R = 45.1$ min (major enantiomer, major diastereomer), $\tau_R = 45.6$ min (minor enantiomer, major diastereomer).

**Stereoconvergence in the Epoxidation of 19g**

Based on our previous studies with enones \textbf{2}, we expected facile isomerization of the double bond under the reaction conditions. Although this assumption was validated when we tested the isomerization of (Z)-19 in the absence of hydrogen peroxide (entry 1), the diastereoconvergence of the reaction was only partial when hydrogen peroxide was present (entry 2). Presumably, the isomerization of the double bond and enal epoxidation occur at similar rates leading to the formation of 20g from both (E) and (Z)-configured starting materials. The overall result is a lower diastereo- and enantioselectivity of the major product compared to that obtained from pure (E)-19g (entry 3 vs. 2).

Preparation of an authentic sample for the determination of the absolute stereochemistry of epi-20g:

\[(\text{2S,3R})-2\text{-methyl-3-phenethyloxiran-2-yl)methanol (epi-20g\textsuperscript{+})}\]: Following the procedure of Prévost and Woerpel,\textsuperscript{25} a solution of (+)-diisopropyl tartrate (13.2 μL, 0.0625 mmol, 0.22 equiv) in dichloromethane (1 mL) with 4Å molecular sieves (16 mg) was cooled to -20 °C. Ti(O\textsubscript{i}Pr\textsubscript{4}) (4.6 μL, 0.0129 mmol, 0.16 equiv) was added, followed by tert-butylhydroperoxide (77.5 μL, 5.5 M in decanes, 0.426 mmol, 1.5 equiv). A solution of (Z)-2-methyl-5-phenylpent-2-en-1-ol (50 mg, 0.28 mmol, 1 equiv) in dichloromethane (0.2 mL) was added. The reaction mixture was stirred at – 20 °C for 16 h, warmed up to room temperature at treated with H\textsubscript{2}O (0.3 mL) and 30% NaOH (0.1 mL). After stirring the biphasic solution for 1h at room temperature, the mixture was extracted with dichloromethane three times, dried over Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated. Flash column chromatography eluting with 35% diethyl ether in pentane afforded epi-20g\textsuperscript{+} as a colourless oil (43.6 mg, 0.23 mmol, 80%).


<table>
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<th>entry</th>
<th>E/Z of \textsuperscript{19}g</th>
<th>H\textsubscript{2}O\textsubscript{2}</th>
<th>Conv. %\textsuperscript{a}</th>
<th>dr\textsuperscript{a}</th>
<th>er \textsuperscript{20}g\textsuperscript{b}</th>
<th>er epi-\textsuperscript{20}g\textsuperscript{b}</th>
<th>E/Z of recovered \textsuperscript{19}g</th>
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<tr>
<td>1</td>
<td>5:95</td>
<td>None</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>&gt;95:5</td>
</tr>
<tr>
<td>2</td>
<td>5:95</td>
<td>5 equiv</td>
<td>85</td>
<td>76:24</td>
<td>85:15</td>
<td>14:86</td>
<td>76:24</td>
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<tr>
<td>3</td>
<td>&gt;95:5</td>
<td>5 equiv</td>
<td>93.5</td>
<td>95:5</td>
<td>98.5:1.5</td>
<td>65:35</td>
<td>&gt;95:5</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Determined by NMR. \textsuperscript{b} Determined by GC with a chiral stationary phase. See SI for details on the determination of absolute configuration.
$^1$H NMR (500 MHz, CDCl$_3$) δ 7.31-7.28 (m, 2H, CH$_{Ar}$), 7.23-7.19 (m, 3H, CH$_{Ar}$), 3.47 (d, $J = 12.0$ Hz, 1H, CH$_2$OH), 3.38 (d, $J = 12.0$ Hz, 1H, CH$_2$OH), 2.89-2.84 (m, 2H, PhCH$_2$), 2.75-2.67 (m, 1H, CHO$_{epox}$), 2.05-1.98 (m, 1H, PhCH$_2$CH$_2$), 1.87-1.81 (m, 1H, PhCH$_2$CH$_2$), 1.60 (br s, 1H, OH), 1.32 (s, 3H, CH$_3$).

**Chiral HPLC:** Chiralpak AS-RH, acetonitrile/water = 30:70, flow rate 1.0 mL/min, 10.1 MPa, 210 nm. $\tau_R = 5.55$ min (major enantiomer), $\tau_R = 6.26$ min (minor enantiomer). *Since no diastereomer separation was required in this case, the sample was not pre-eluted on an achiral HPLC column.*

\[\textbf{((2S,3S)-2-methyl-3-phenethyloxiran-2-yl)methanol (20h')}: \text{Prepared according to the general procedure and workup A using (E)-2,4-diphenylbut-2-enal (E/Z > 20:1, 0.25 mmol) followed by reduction with NaBH}_4. \text{Purification by flash chromatography (50\% Et}_2\text{O in pentane) afforded 20h' as a colourless oil (29.4 mg, 0.12 mmol, 49\%, 56:44 dr, 95:5 er).}\]

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.46-7.05 (m, 10H, major + minor diast, CH$_{Ar}$), 4.32 (dd, $J = 12.3$ Hz, $J = 4.8$ Hz, 1H, major diast, CH$_2$OH), 4.14 (dd, $J = 12.3$ Hz, $J = 5.8$ Hz, 1H, major diast, CH$_2$OH), 4.06-3.91 (m, 2H, minor diast, CH$_2$OH), 3.61 (t, $J = 6.2$ Hz, 1H, minor diast, CHO$_{epox}$), 3.22 (t, $J = 6.4$ Hz, 1H, major diast, CHO$_{epox}$), 3.16 (dd, $J = 14.7$ Hz, $J = 6.4$ Hz, 1H, major diast, PhCH$_2$), 3.10 (dd, $J = 14.7$ Hz, $J = 6.3$ Hz, 1H, major diast, PhCH$_2$), 2.58 (dd, $J = 14.7$ Hz, $J = 6.8$ Hz, 1H, minor diast, PhCH$_2$), 2.52 (dd, $J = 14.7$ Hz, $J = 5.8$ Hz, 1H, minor diast, PhCH$_2$) 1.82 (br s, 1H, minor diast, OH), 1.73 (br s, 1H, major diast, OH).

$^{13}$C NMR (125 MHz, CDCl$_3$, mixture of 2 diastereomers) δ 138.9, 137.44, 137.40, 135.6, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.1, 127.9, 127.4, 127.0, 126.8, 128.6, 125.9, 68.7, 66.2, 64.4, 64.1, 63.2, 61.4, 34.9, 34.8.

FTIR (thin film) 3432, 3062, 3029, 2923, 1603, 1496, 1453, 1085, 1031, 939, 861, 762 cm$^{-1}$

HRMS (m/z) calcd for C$_{16}$H$_{16}$O$_2$Na [M+Na]$^+$: 263.1042. Found 263.1040.

**Chiral HPLC:** *Diastereomer separation:* Zorbax XDB/C18, elution gradient 0-9.5 min: methanol/water = 55:45, 9.5-12.5 min: methanol/water = 80:20, 12.5-20 min: methanol/water = 55:45, flow rate 1.0 mL/min, 32.8 MPa, 210 nm. *Upon separation, each diastereomer was switched to a chiral column at 7.38 min till 7.42 min for the minor diastereomer and 8.28 min till 8.33 min for the major diastereomer:* CelluCoat RP, acetonitrile/water = 40:60, flow rate 1.0 mL/min, 18.2 MPa, 210
Minor diastereomer: $\tau_R = 18.2$ min (minor enantiomer), $\tau_R = 19.4$ min (major enantiomer).
Major diastereomer: $\tau_R = 18.1$ min (major enantiomer), $\tau_R = 18.6$ min (minor enantiomer).

(2S,3R)-3-heptyloxirane-2-carbaldehyde (20i): Prepared according to the general procedure and workup A using commercial (E)-dec-2-enal. The yield (30%) was determined by GC analysis (95:5 dr, 70:30 er).

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ = 9.01 (d, $J = 6.2$ Hz, 1H), 3.18 - 3.15 (m, 1H), 3.09 (dd, $J = 6.2$ Hz, 1H), 1.23 - 1.63 (m, 10H), 0.86 (t, $J = 5.3$ Hz, 3H)

Chiral GC: (BGB-176, 90 °C iso, 0.5 bar H$_2$): $\tau_R = 12.1$ min (major enantiomer, major diastereomer), $\tau_R = 12.9$ min (minor enantiomer, major diastereomer), $\tau_R = 5.4$ min (major enantiomer, minor diastereomer), $\tau_R = 1.12$ min (minor enantiomer, minor diastereomer).

The physical data are identical in all respects to those previously reported.$^{26}$ The absolute stereochemistry was assigned by comparison of the chiral GC spectra with an authentic sample of (2R,3S)-31i which was prepared using the procedure of Wang and List.$^{26}$

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Catalytic Asymmetric Epoxidation of $\alpha$-Monosubstituted Enals 22

**General Procedure**

Phosphoric acid ($R$)-21a (37.6 mg, 0.05 mmol, 0.2 equiv) and amine catalyst 1a (8.08 mg, 0.025 mmol, 0.1 equiv) were dissolved in dry THF (2 mL, 0.125 M) and stirred for 5 min under ambient atmosphere at room temperature. The $\alpha$-branched enal 22 (0.25 mmol, 1 equiv) was added and the mixture was stirred for an additional 5 min at room temperature. Aqueous hydrogen peroxide (77 μL, 50% w/w, 1.25 mmol, 5 equiv) was added, the reaction vessel was sealed and the reaction mixture was stirred for 24 h at 50 °C under an atmosphere of air. The reaction can be monitored by the disappearance of the starting material; the formed product is masked as a very polar species that appears as a poorly stainable spot on the TLC ($R_f \sim 0.1$) and is presumably a hydroperoxide adduct of the aldehyde 22. **Workup A:** The product 23 is liberated as the free aldehyde when the excess peroxide is quenched. This was performed by stirring the crude reaction mixture with 10% aqueous Na$_2$S$_2$O$_3$ (1 mL) for 10 min. The mixture was then diluted with water (5 mL) and diethyl ether (5 mL) and partitioned. The aqueous layer was washed with diethyl ether (5 mL x 3), and the combined organic layers were washed with brine and dried over Na$_2$SO$_4$. For yield or er determination, some compounds were directly reducted with NaBH$_4$ (14.1 mg, 0.375 mmol, 1.5 equiv) in EtOH (2 mL) at room temperature, stirring for 10 min. Saturated aqueous Na,K-tartrate (Rochelle’s salt) was then added and the reaction mixture stirred for 1 h. The resulting biphasic solution was diluted with diethyl ether (5 mL) and water (10 mL) and partitioned. The aqueous layer was washed extracted with EtOAc
(5 mL x 2), and the combined organic layers were washed with brine and dried over Na₂SO₄. Evaporation of the solvent and flash column chromatography with the specified solvent system afforded the corresponding alcohols 23³.

**Workup B**: In cases when the epoxyaldehyde products 23 were very volatile, a modified workup procedure was used before reduction to the corresponding alcohol. The crude reaction mixture was quenched by adding solid Na₂S₂O₃ (250 mg) and the suspension was stirred for 1 h. It was then filtered through a pad of Celite, washing with 2-5 mL diethyl ether and 2 mL EtOH. To this filtrate was added solid NaBH₄ (14.1 mg, 0.375 mmol, 1.5 equiv) and the reaction mixture was stirred for 10 min. Saturated aqueous Na,K-tartrate (Rochelle’s salt) was added and the reaction mixture was stirred for 1 h. The resulting biphasic solution was diluted with diethyl ether (5 mL) and water (10 mL) and partitioned. The aqueous layer was washed extracted with EtOAc (5 mL x 2), and the combined organic layers were washed with brine and dried over Na₂SO₄. Evaporation of the solvent and flash column chromatography with the specified solvent system afforded the desired product.

**Scope of Optically Active α,β-Epoxyaldehydes 23**

(R)-2-benzyloxirane-2-carbaldehyde (23a): Prepared according to the general procedure and workup A using 2-benzylacrylaldehyde (0.25 mmol). Purification by flash chromatography (20% Et₂O in pentane) afforded 23a as a colourless oil (31.7 mg, 0.195 mmol, 78%, 99:1 er).

**1H NMR** (400 MHz, CDCl₃) δ 8.94 (s, 1H, CHO), 7.31-7.20 (m, 5H, CHAr), 3.21 (d, J = 1.4 Hz, 2H, PhCH₂), 3.00 (d, J = 4.6 Hz, 1H, CH₃CH₂Oepox), 2.85 (d, J = 4.6 Hz, 1H, CH₂CH₂Oepox).

**13C NMR** (100 MHz, CDCl₃): δ 198.6, 134.8, 129.9, 128.4, 127.0, 61.4, 48.9, 33.1.

**FTIR** (thin film) 3064, 3032, 2826, 1726, 1497, 1454, 1077, 1010, 907, 730 cm⁻¹

**HRMS** (m/z) calcd for C₁₀H₁₀O₂ [M⁺]: 162.0681. Found 162.0682.

**[α]D²⁵**: +47.0 (c 0.502, CHCl₃).

**Chiral GC** (BGB-178/BGB-15, 35 min at 115 °C, 8 °C/min until 220 °C, 0.6 bar H₂) τ₀ = 26.0 min (major enantiomer), τ₀ = 27.0 min (minor enantiomer).
The physical data are identical in all respects to those previously reported. The absolute stereochemistry was assigned by analogy.

(S)-(2-(oct-7-enyl)oxiran-2-yl)methanol (23b'): Prepared according to the general procedure and workup A using 2-methylenedec-9-enal (0.25 mmol) followed by reduction with NaBH₄. Purification by flash chromatography (30% Et₂O in pentane) afforded 23b' as a colourless oil (33.9 mg, 0.184 mmol, 74%, 98.5:1.5 er).

\[
\text{1H NMR (300 MHz, CDCl₃)} \delta 5.80 \text{ (ddt, } J = 17.4 \text{ Hz, } J = 10.2 \text{ Hz, } J = 6.7 \text{ Hz, CH}=\text{CH}_2), 5.03-4.99 \text{ (m, 2H, CH}=\text{CH}_2), 3.77 \text{ (dd, } J = 12.2 \text{ Hz, } J = 4.2 \text{ Hz, 1H, CH}_2\text{OH}), 3.64 \text{ (dd, } J = 12.2 \text{ Hz, } J = 8.6 \text{ Hz, 1H, CH}_2\text{OH}), 2.88 \text{ (d, } J = 4.7 \text{ Hz, 1H, CH}_2\text{Oepox}), 2.66 \text{ (d, } J = 4.7 \text{ Hz, 1H, CH}_2\text{Oepox}), 2.07-2.00 \text{ (m, 2H, CH}=\text{CHCH}_3), 1.82-1.26 \text{ (m, 11H, CH}_2).\]

\[
\text{13C NMR (75 MHz, CDCl₃): } \delta 139.0, 114.3, 62.8, 59.7, 49.8, 33.7, 32.0, 29.6, 28.9, 28.8, 24.6;\]

\[
\text{FTIR (thin film)} 3429, 3077, 2929, 2857, 2249, 1641, 1464, 1415, 1046, 908, 730 \text{ cm}^{-1}\]

\[
\text{HRMS (m/z) calcd for C}_{11}\text{H}_{21}\text{O}_2 [\text{M+H}^+] : 185.1542. \text{ Found } 185.1540.\]

\[
\alpha_D^{25} : -10.8 \text{ (c 0.574, CHCl}_3).\]

Chiral GC (Hydrodex-β TBDAc, 25 min at 150 °C, 10 °C/min until 220 °C, 0.5 bar H₂) \(\tau_R = 14.5\) min (major enantiomer), \(\tau_R = 15.4\) min (minor enantiomer).

(R)-2-(oct-7-enyl)oxirane-2-carbaldehyde (23b):

\[
\text{1H NMR (500 MHz, CDCl₃)} \delta 8.88 \text{ (s, 1H, CHO), 5.80 (ddt, } J = 17.09 \text{ Hz, } J = 10.2 \text{ Hz, } J = 6.6 \text{ Hz, CH}=\text{CH}_2), 5.03-4.90 \text{ (m, 2H, CH}=\text{CH}_2), 3.02 \text{ (br s, 2H, CH}_2\text{Oepox), 2.09-1.88 \text{ (m, 3H, CH}_2), 1.76-1.66 \text{ (m, 1H, CH}_2), 1.46-1.21 \text{ (m, 8H, CH}_2).\]

\[
\text{13C NMR (100 MHz, CDCl₃): } \delta 199.1, 139.0, 114.3, 61.4, 49.6, 33.7, 29.5, 28.8, 28.7, 27.6, 24.3;\]

\[
\text{FTIR (thin film)} 3077, 2929, 2857, 1730, 1641, 1464, 1438, 1144, 910, 731 \text{ cm}^{-1}\]

\[
\text{HRMS (m/z) calcd for C}_{11}\text{H}_{19}\text{O}_2 [\text{M+H}^+] : 183.1385. \text{ Found } 183.1383.\]

Chiral GC (BGB-174/BGB-1701, 130 °C isocratic, then baked out at 8 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H2): $\tau_R = 27.8$ min (major enantiomer), $\tau_R = 29.3$ min (minor enantiomer).

(S)-(2-octyloxiran-2-yl)methanol (23d’): Prepared according to the general procedure B using 2-methylenedecanal 22d (0.25 mmol) followed by reduction with NaBH₄. Purification by flash chromatography (50% Et₂O in pentane) afforded 23d’ as a colourless oil (36.4 mg, 0.196 mmol, 78%, 99:1 er).

$^1$H NMR (500 MHz, CDCl₃) δ 3.78 (dd, $J = 12.1$, $J = 3.8$ Hz, 1H, CH$_2$OH), 3.64 (dd, $J = 12.1$ Hz, $J = 8.4$ Hz, 1H, CH$_2$OH), 2.89 (d, $J = 4.7$ Hz, 1H, CH$_2$Oepox), 2.67 (d, $J = 4.7$ Hz, 1H, CH$_2$Oepox), 1.80-1.75 (m, 1H, CH$_2$), 1.68 (br s, 1H, OH), 1.53-1.47 (m, 1H, CH$_2$), 1.39-1.23 (m, 12H, CH$_2$), 0.88 (t, $J = 6.7$ Hz, 3H, CH$_3$).

$^{13}$C NMR (125 MHz, CDCl₃): δ 62.7, 59.8, 49.8, 32.0, 31.8, 29.7, 29.2, 24.6, 22.6, 14.1.

FTIR (thin film) 3421, 2927, 2857, 2251, 1466, 1364, 1197, 1053, 908, 808, 731 cm$^{-1}$

[$\alpha$]$_b^{25}$: $-14.8$ (c 0.595, CHCl₃); Lit$^{[130]}$ [$\alpha$]$_b^{20}$: $-11.7$ (c 1.0, CHCl₃, 72% ee).

HRMS (m/z) calcd for C$_{11}$H$_{23}$O$_2$ [M+H$^+$]: 187.1698. Found 187.1699.

Chiral GC (BGB-177/BGB-15, 140 °C isocratic, then baked out at 220 °C, 0.6 bar H2) $\tau_R = 19.75$ min (major enantiomer), $\tau_R = 20.8$ min (minor enantiomer).

The physical data are identical in all respects to those previously reported.$^{28}$

(S)-2-((R)-1-phenylethyl)oxirane-2-carbaldehyde (anti-23e): Prepared according to the general procedure and workup A using racemic 2-methylene-3-phenylbutanal rac-23e (0.25 mmol). Analysis of the crude reaction mixture after 24 h showed 53% conversion of the starting material and two diastereomers 23e and epi-23e with dr = 83:17. Purification by flash chromatography

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(5% EtOAc in pentane) afforded 23e as a colourless oil (13.0 mg, 0.074 mmol, 30%, lowered yield due to incomplete separation from (S)-22e, 96:4 er).

$^1$H NMR (500 MHz, CDCl$_3$) δ 8.95 (s, 1H, CHO), 7.31-7.28 (m, 2H, CH$_{Ar}$), 7.26-7.21 (m, 3H, CH$_{Ar}$), 3.68 (q, J = 7.2 Hz, 1H, PhCH), 2.87 (d, J = 4.6 Hz, 1H, CH$_2$Oepox), 2.58 (d, J = 4.6 Hz, 1H, CH$_2$Oepox), 1.38 (d, J = 6.9 Hz, 3H, CH$_3$).

$^{13}$C NMR (125 MHz, CDCl$_3$): δ 199.0, 140.4, 128.5, 128.2, 127.1, 64.6, 48.9, 35.8, 16.2.

FTIR (thin film) 30314, 2979, 2940, 2821, 2255, 1733, 1496, 1454, 907, 865, 729 cm$^{-1}$

HRMS (m/z) calcd for C$_{11}$H$_{12}$O$_2$ [M$^+$]: 176.0837. Found 176.0839.

$[\alpha]_D^{25}$: + 41.5 (c 0.65, CHCl$_3$).

Chiral GC (G-BP, 40 min at 110 °C, 14 °C/min until 220 °C, 5 min at 220 °C, 0.6 bar H$_2$): $\tau_R$ = 25.3 min (minor enantiomer, major diastereomer 23e), $\tau_R$ = 27.0 min (major enantiomer, major diastereomer 23e), $\tau_R$ = 34.0 min (minor enantiomer, minor diastereomer epi-23e), $\tau_R$ = 36.3 min (major enantiomer, minor diastereomer epi-23e).

The physical data are identical in all respects to those previously reported.[88]

(S)-2-methylene-3-phenylbutanal (S)-22e: The physical data of this compound are identical in all respects to rac-22e. This compound was isolated by flash chromatography (5% EtOAc in pentane) as a colourless oil (8.79 mg, 0.055 mmol, 22%, lowered yield due to incomplete separation from 23e, 97:3 er).

$[\alpha]_D^{25}$: + 48.6 (c 0.44, CHCl$_3$), Lit (R enantiomer)$^{[135]}$: $[\alpha]_D^{25}$: − 38.7 (c 1.01, CHCl$_3$).

Chiral GC (G-BP, 40 min at 110 °C, 14 °C/min until 220 °C, 5 min at 220 °C, 0.6 bar H$_2$) $\tau_R$ = 13.9 min (major enantiomer), $\tau_R$ = 14.4 min (minor enantiomer).
Assignment of the absolute configuration:

(S)-22e: The absolute configuration was established by comparison of the optical rotation with the literature value.\(^{29}\)

23e: The relative *anti*-configuration was assigned by comparison of the chemical shifts in \(^1\text{H}\) and \(^{13}\text{C}\) NMR spectra with the literature values.\(^{30}\) The absolute configuration was assigned based on the configuration of the recovered enantioenriched starting material (S)-22e.


epi-23e: The relative syn-configuration was assigned by comparison of the chemical shifts in $^1$H and $^{13}$C NMR spectra with the literature values.\cite{88} The absolute configuration was tentatively assigned based on the observed dr and er values of all components of the reaction, such that the stoichiometry of the (R) and (S) enantiomers at C-3 is balanced. GC and NMR analyses of the crude reaction mixture indicated that (S)-22e, 23e and epi-23e were the only components of the reaction.

Preparation of Starting Materials

Preparation of Acyclic $\alpha,\beta$-Unsaturated Ketones

General Procedure A: Cross Metathesis (Enones 2f, 2i, 2j, 2k)

Methyl vinyl ketone (MVK; 12.5 mmol, 2.5 equiv) and Grubbs’ second generation catalyst (106 mg, 0.125 mmol, 2.5 mol%) were successively added to the solution of a terminal alkene (5 mmol, 1 equiv) in CH$_2$Cl$_2$ (50 mL). The reaction mixture was heated to reflux overnight (12-16 h) and then allowed to cool to room temperature. The volatiles were removed under reduced pressure and the crude product was purified by flash column chromatography (silica gel, eluent: Et$_2$O-pentane or Et$_2$O-CH$_2$Cl$_2$) to obtain the corresponding pure (E)-enone 2.
**(E)-7-Bromo-3-hepten-2-one (2f)**: The title compound was prepared according to the general procedure A from MVK and 5-bromo-1-pentene. The crude product was purified by flash column chromatography (silica gel, 5-15% Et₂O in pentane) to give enone **2f** (748 mg, 3.94 mmol, 78%) as a pale yellow oil. Contains 4% of **(E)-7-chloro-3-hepten-2-one** as determined by GC.

**¹H NMR** (500 MHz, CD₂Cl₂) δ 6.74 (dt, J = 15.9, 6.9 Hz, 1H, =CHCH₂), 6.09 (dt, J = 16.1, 1.4 Hz, 1H, CH=CHCH₂), 3.44 (t, J = 6.6 Hz, 2H, BrCH₂), 2.41-2.36 (m, 2H, =CHCH₂), 2.21 (s, 3H, CH₃), 2.06-2.00 (m, 2H, CH₂CH₂CH₂).

**¹³C NMR** (125 MHz, CD₂Cl₂): δ 198.0 (C=O), 145.7 (=CHCH₂), 132.1 (CH=CHCH₂), 32.9 (BrCH₂), 31.0 (CH₂CH₂CH₂), 30.8 (=CHCH₂), 26.8 (CH₃).

**GC-MS** (GC-EI) m/z 190 [M⁺].

**HRMS** (EI-FE) calcd for C₇H₁₁BrO [M⁺] 189.9992, found 189.9993.

**(E)-Ethyl 6-oxohept-4-enoate (2i)**: The title compound was prepared according to the general procedure A from MVK and ethyl 4-pentenoate. The crude product was purified by flash column chromatography (silica gel, 40-55% Et₂O in pentane) to give enone **2i** (679 mg, 3.99 mmol, 80%) as a pale yellow oil.

**¹H NMR** (300 MHz, CD₂Cl₂) δ 6.77 (dt, J = 15.9, 6.3 Hz, 1H, =CHCH₂), 6.08 (dt, J = 15.9, 1.5 Hz, 1H, CH=CHCH₂), 4.11 (q, J = 7.2 Hz, 2H, CH₂CH₃), 2.57-2.43 (m, 4H, CH₂), 2.20 (s, 3H, CH₃C(=O)), 1.23 (t, J = 7.1 Hz, 3H, CH₂CH₃).

**¹³C NMR** (100 MHz, CD₂Cl₂) δ 198.0 (C=O), 172.2 (CO₂Et), 145.7 (=CHCH₂), 131.7 (CH=CHCH₂), 60.5 (CH₂CH₃), 32.5 (CH₂CO₂Et), 27.5 (=CHCH₂), 26.7 (CH₃C(=O)), 14.0 (CH₂CH₃).

**MS** (EI-DE) m/z 170 [M⁺] (26), 155 (3), 141 (5), 124 (76), 109 (18), 97 (41), 83 (40), 68 (3), 55 (20), 43 (100), 29 (27).


**(E)-3-Octene-2,7-dione (2j)**: The title compound was prepared according to the general procedure A from MVK and 5-hexen-2-one. The crude product was purified by flash column chromatography (silica gel, 30-55% Et₂O in pentane) to give enone **2j** (698 mg, 4.98 mmol, 99%) as a pale yellow oil.

S-89
$^1$H NMR (300 MHz, CD$_2$Cl$_2$) $\delta$ 6.76 (dt, $J = 15.9, 6.7$ Hz, 1H, =CHCH$_2$), 6.03 (dt, $J = 16.1, 1.6$ Hz, 1H, CH=CHCH$_2$), 2.63-2.58 (m, 2H, CH$_2$), 2.49-2.41 (m, 2H, =CHH$_2$), 2.19 (s, 3H, CH$_3$C(=O)CH$_3$), 2.13 (s, 3H, CH$_3$C(=O)CH$_2$).

$^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) $\delta$ 206.6 (CH$_2$C(=O)), 198.1 (CH$_3$C(=O)), 146.3 (=CHCH$_2$), 131.6 (CH=CHCH$_2$), 41.5 (CH$_2$C(=O)CH$_2$), 26.7 (CH$_3$C(=O)CH$_3$), 26.2 (=CHCH$_2$).

MS (EI-DE) $m/z$ (%) 140 [M$^+$] (15), 122 (2), 97 (82), 83 (7), 79 (6), 69 (3), 55 (5), 43 (100), 41 (6), 27 (4).

HRMS (EI-FE) calcd for C$_8$H$_{12}$O$_2$ [M$^+$] 140.0836, found 140.0837.

(E)-9-hydroxy-3-non-en-2-one (2k): The title compound was prepared according to the general procedure A from MVK and 7-hydroxy-1-heptene. Flash column chromatography (silica gel, 10-30% Et$_2$O in CH$_2$Cl$_2$) afforded enone 2k (503 mg, 3.22 mmol, 64%) as a greenish oil (contains ruthenium trace impurities).

$^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 6.79 (dt, $J = 15.9, 7.0$ Hz, 1H, CH$_2$CH=), 6.03 (dt, $J = 16.2, 1.4$ Hz, 1H, CH$_2$CH=CH$_2$), 3.59 (t, $J = 6.6$ Hz, 2H, CH$_2$OH), 2.21 (app. qd overlapped, $J = 7.1, 1.4$ Hz, 2H, CH$_2$), 2.20 (s, 3H, CH$_3$), 1.75 (br s, 1H, OH), 1.56-1.46 (m, 4H, CH$_2$), 1.39 (s, 1H, CH$_2$).

$^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) $\delta$ 198.8 (C=O), 148.6 (CH$_2$C=H), 131.6 (CH$_2$CH=CH$_2$), 62.9 (CH$_2$OH), 32.9(CH$_2$), 32.7 (CH$_2$), 28.3 (CH$_2$), 26.9 (CH$_3$), 25.7 (CH$_2$).

MS (EI-DE) $m/z$ (%) 156 [M$^+$] (1), 138 (11), 123 (9), 113 (7), 95 (55), 84 (8), 81 (32), 71 (42), 67 (32), 58 (9), 55 (49), 53 (15), 43 (100), 41 (27), 31 (19).

HRMS (EI-FE, i-butane) calcd for C$_9$H$_{17}$O$_2$ [(M+H)$^+$] 157.1230, found 157.1229.

**General Procedure B: Wittig Olefination (Enones 2b, 2c, 2d, 2e, 2g, 2h, 2q, 2r, 5f)**

An aldehyde (20 mmol, 1 equiv) was dissolved in CH$_2$Cl$_2$ (30 mL) and 1-(triphenylphosphoranyli-
dene)-2-propanone (6.37 g, 20 mmol, 1 equiv) was added at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred until TLC or GC/MS analysis indicated complete consumption of the starting aldehyde (12-24 h). Then silica gel was added and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (silica gel, 10% Et2O in pentane) to afford the corresponding (E)-α,β-enone 2.

**(E)-6-Phenyl-3-hexen-2-one (2b):** The title compound was prepared according to the general procedure B from hydrocinnamaldehyde and 1-(triphenylphosphoranylidene)-2-propanone. The crude product was purified by flash column chromatography (silica gel, 10% Et2O in pentane) to give enone 2b (2.62 g, 15.0 mmol, 75%) as a pale yellow oil.

1H NMR (500 MHz, CDCl3) δ 7.30-7.27 (m, 2H, C₆H₄), 7.21-7.16 (m, 3H, C₆H₄), 6.80 (dt, J = 15.9, 6.9 Hz, 1H, =CHCH₂), 6.08 (dt, J = 16.1, 1.4 Hz, 1H, CH=CHCH₂), 2.78 (t, J = 7.7 Hz, 2H, PhCH₂), 2.54 (app. qd, J = 7.3, 1.4 Hz, 2H, =CHCH₂), 2.21 (s, 3H, CH₃).

13C NMR (125 MHz, CDCl₃) δ 198.6 (C=O), 147.1 (=CHCH₂), 140.7 (CqPh), 131.7 (CH=CHCH₂), 128.5 (2C, CH₃), 128.3 (2C, CH₃), 126.2 (CH₃), 34.4 (CH₂), 34.1 (CH₂), 26.9 (CH₃).

MS (EI-DE) m/z (%): 174 [M⁺] (5), 159 (4), 131 (5), 116 (16), 104 (2), 91 (100), 77 (2), 65 (10), 51 (3), 43 (9), 27 (2).


**(E)-6-Methylhept-3-en-2-one (2c):** The title compound was prepared according to the general procedure B from isovaleraldehyde with 1-(triphenylphosphoranylidene)-2-propanone. The crude product was purified by flash column chromatography (silica gel, 5% Et₂O in pentane) to give enone 2c (1.51 g, 12.0 mmol, 60% (reduced yield due to the high volatility of 2c)) as a pale yellow oil.

1H NMR (500 MHz, CDCl₃) δ 6.74 (dt, J = 16.0, 7.4 Hz, 1H, =CHCH₂), 6.03 (dt, J = 16.0, 1.4 Hz, 1H, CH=CHCH₂), 2.21 (s, 3H, CH₃), 2.08 (app. td, J = 7.1, 1.3 Hz, 2H, CH₂), 1.74 (hept, J = 6.7 Hz, 1H, CHMe₂), 0.90 (d, J = 6.7 Hz, 6H, CH(CH₃)₂).

13C NMR (125 MHz, CDCl₃) δ 198.6 (C=O), 147.3 (=CHCH₂), 132.3 (CH=CHCH₂), 41.7 (CH₂), 27.8 (CHMe₂), 26.8 (CH₃), 22.3 (2C, CH(CH₃)₂).

GC-MS (GC-EI) m/z: 126 [M⁺].

(E)-4-Cyclohexylbut-3-en-2-one (2d): The title compound was prepared according to the general procedure B from cyclohexanecarbaldehyde with 1-(triphenylphosphoranylidene)-2-propanone. The crude product was purified by flash column chromatography (silica gel, 10% Et₂O in pentane) to give enone 2d (2.80 g, 18.4 mmol, 92%) as a pale yellow oil.

¹H NMR (500 MHz, CD₂Cl₂) δ 6.71 (dd, J = 16.1, 6.8 Hz, 1H, =CHCH), 5.98 (dd, J = 16.3, 1.2 Hz, 1H, CH=CHCH), 2.20 (s, 3H, CH₃), 2.18-2.11 (m, 1H, =CHCH₂), 1.79-1.74 (m, 4H, CH₂), 1.70-1.66 (m, 1H, CH₂), 1.35-1.27 (m, 2H, CH₂), 1.24-1.11 (m, 3H, CH₂).

¹³C NMR (125 MHz, CD₂Cl₂) δ 199.0 (C=O), 153.5 (CH=CHCH), 129.1 (CH=CHCH), 41.0 (CHCH₂), 32.2 (2C, CHCH₂), 26.9 (CH₃), 26.3 (CH₂), 26.1 (2C, CH₂).

GC-MS (GC-EI) m/z 152 [M⁺].

HRMS (EI-FE) calcd for C₁₀H₁₆O [M⁺] 152.1200, found 152.1201.

(E)-Octa-3,7-dien-2-one (2e): The title compound was prepared according to the general procedure B from 4-pentenal and 1-(triphenylphosphoranylidene)-2-propanone. The crude product was purified by flash column chromatography (silica gel, 5-10% Et₂O in pentane) to give enone 2e (2.19 g, 17.6 mmol, 88%) as a pale yellow oil.

¹H NMR (500 MHz, CD₂Cl₂) δ 6.77 (dt, J = 16.1, 6.8 Hz, 1H, CH₂CH=CH), 6.05 (dt, J = 15.9, 1.5 Hz, 1H, CH₂CH=CH), 5.82 (ddt, J = 16.9, 11.7, 6.0 Hz, 1H, CH₂=CH), 5.06 (app. dq, J = 17.0, 1.7 Hz, 1H, CH₂=CH), 5.01 (app. dq, J = 10.5, 1.5 Hz, 1H, CH₂=CH), 2.35-2.30 (m, 2H, CH₂=CHCH), 2.25-2.21 (m, 2H, CH₂=CHCH₂), 2.20 (s, 3H, CH₃).

¹³C NMR (125 MHz, CD₂Cl₂) δ 198.5 (C=O), 147.6 (CH₂CH=CH), 137.7 (CH₂=CH), 131.9 (CH₂CH=CH), 115.5 (CH₂=CH), 32.5 (CH₂=CHCH₂), 32.0 (CH₂CH=CH), 26.9 (CH₃).

GC-MS (GC-EI) m/z 124 [M⁺] (trace), 122 (4), 109 (14), 95 (12), 91 (3), 81 (58), 79 (35), 11 (12), 66 (12), 55 (34), 53 (18), 51 (6), 43 (100), 41 (34), 27 (10).

HRMS (Cl-FE, i-butane) calcd for C₈H₁₃O [(M+H)+] 125.0966, found 125.0966.
(E)-9-(Tetrahydro-2H-pyran-2-yloxy)-3-non-2-one (2g):

6-(Tetrahydro-2H-pyran-2-yloxy)-1-hexanol: A solution of 1,6-hexanediol (2.36 g, 20.0 mmol, 1.7 equiv) and dihydropyrane (1.10 mL, 12.0 mmol) in THF (100 mL) in the presence of p-toluenesulfonic acid monohydrate (190 mg, 1.0 mmol) was stirred at 0 °C for 12 h. Then the solution was poured on saturated aqueous NaHCO₃ solution and extracted with Et₂O. The combined organic layers were dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, 40% EtOAc in hexanes) to provide the title compound (1.44 g, 7.13 mmol, 59%) as a colorless oil.

**¹H NMR** (500 MHz, CD₂Cl₂) δ 4.55 (t, J = 3.4 Hz, 1H, OCH₂), 3.88-3.81 (m, 1H, OCH₂HTHP), 3.72 (dt, J = 9.8, 6.8 Hz, 1H, THPOCH₂HH), 3.62 (t, J = 6.6 Hz, 2H, CH₂OH), 3.51-3.44 (m, 1H, OCH₂THP), 3.37 (dt, J = 9.6, 6.5 Hz, 1H, THPOCH₂HH), 1.86-1.35 (m, 15H, CH₂ and OCH₂).

**¹³C NMR** (125 MHz, CD₂Cl₂) δ 98.9 (OCH₂), 67.5 (THPOCH₂), 62.9 (OCH₂), 62.4 (OCH₂), 32.7 (CH₂), 30.8 (CH₂), 29.7 (CH₂), 26.0 (CH₂), 25.6 (CH₂), 25.5 (CH₂), 19.7 (CH₂).

**MS (EI-DE) m/z (%)** 202 [M⁺] (trace), 129 (2), 117 (4), 101 (27), 85 (100), 67 (10), 55 (43), 41 (22), 29 (9).

**HRMS** (CI-FE, i-butane) calcd for C₁₁H₂₃O₃ [(M+H)⁺] 203.1644, found 203.1647.

6-(Tetrahydro-2H-pyran-2-yloxy)hexanal: 6-(Tetrahydro-2H-pyran-2-yloxy)-1-hexanol (1.20 g, 5.93 mmol) was dissolved in CH₂Cl₂ (15 mL) and anhydrous DMSO (2.36 mL, 33.2 mmol, 5.6 equiv) and Et₃N (4.36 mL, 31.4 mmol, 5.3 equiv)
were added sequentially at room temperature. The resulting solution was cooled to 0 °C and \( \text{SO}_3 \cdot \text{py} \) complex (1.42 g, 8.90 mmol, 1.5 equiv) was added in several portions. The reaction mixture was kept at 0 °C for 1 h, and was then stirred at room temperature overnight (12 h). The reaction was quenched by the addition of water (10 mL) and extracted with \( \text{Et}_2\text{O} \) (2×25 mL). The combined organic layers were washed with water and brine, dried (\( \text{Na}_2\text{SO}_4 \)), filtered, and concentrated \textit{in vacuo}. The crude product was purified by flash column chromatography (silica gel, 20-30\% \( \text{Et}_2\text{O} \) in pentane) to afford the title compound (754 mg, 3.77 mmol, 64\%) as a colorless liquid.

\[ ^1\text{H NMR} \ (500 \text{ MHz}, \text{CD}_2\text{Cl}_2) \ \delta \ 9.73 \ (t, \ J = 1.7 \text{ Hz}, 1\text{H}, \text{CHO}), 4.53 \ (t, \ J = 3.8 \text{ Hz}, 1\text{H}, \text{CH}_{\text{THP}}), 3.83-3.79 \ (m, 1\text{H}, \text{OCH}_{\text{THP}}), 3.69 \ (dt, \ J = 9.6, 6.7 \text{ Hz}, 1\text{H}, \text{THPOCHH}), 3.47-3.43 \ (m, 1\text{H}, \text{OCH}_{\text{THP}}), 3.35 \ (dt, \ J = 9.6, 6.4 \text{ Hz}, 1\text{H}, \text{THPOCHH}), 2.42 \ (td, \ J = 7.3, 1.7 \text{ Hz}, 2\text{H}, \text{CH}_2\text{CHO}), 1.83-1.74 \ (m, 1\text{H}, \text{CH}_2), 1.69-1.47 \ (m, 9\text{H}, \text{CH}_2), 1.42-1.36 \ (m, 2\text{H}, \text{CH}_2). \]

\[ ^{13}\text{C NMR} \ (125 \text{ MHz}, \text{CD}_2\text{Cl}_2) \ \delta \ 202.9 \ (\text{C}=\text{O}), 99.2 \ (\text{O-C=O}), 67.5 \ (\text{THPOCHH}), 62.5 \ (\text{OCH}_2\text{THP}), 44.2 \ (\text{CH}_2\text{CHO}), 31.2 \ (\text{CH}_2), 29.9 \ (\text{CH}_2), 26.3 \ (\text{CH}_2), 26.0 \ (\text{CH}_2), 22.3 \ (\text{CH}_2), 20.1 \ (\text{CH}_2). \]

\( (E)-9-\text{(Tetrahydro-2H-pyran-2-yloxy)}-3\text{-nonen-2-one} \ (2\text{g}) \): The title compound was prepared according to the general procedure \( \text{B} \) from 6-(tetrahydro-2H-pyran-2-yloxy)hexanal with 1-(triphenylphosphoranylidene)-2-propanone. The crude product was purified by flash column chromatography (silica gel, 10-30\% \( \text{Et}_2\text{O} \) in pentane) to afford enone \( 2\text{g} \) (613 mg, 2.55 mmol, 85\%) as a colorless oil.

\[ ^1\text{H NMR} \ (500 \text{ MHz}, \text{CD}_2\text{Cl}_2) \ \delta \ 6.79 \ (dt, \ J = 15.9, 7.0 \text{ Hz}, 1\text{H}, =\text{CHCH}_2), 6.04 \ (dt, \ J = 15.9, 1.5 \text{ Hz}, 1\text{H}, \text{CH}=\text{CHCH}_2), 4.54-4.52 \ (br t, 1\text{H}, \text{OCHO}), 3.84-3.79 \ (m, 1\text{H}, \text{OCHH}_{\text{THP}}), 3.71-3.67 \ (m, 1\text{H}, \text{THPOCHH}), 3.47-3.43 \ (m, 1\text{H}, \text{OCHH}_{\text{THP}}), 3.37-3.33 \ (m, 1\text{H}, \text{THPOCHH}), 2.26-2.21 \ (m, 2\text{H}, \text{=CHCH}_2), 2.20 \ (s, 3\text{H}, \text{CH}_3), 1.82-1.75 \ (m, 1\text{H}, \text{CH}_2), 1.69-1.64 \ (m, 1\text{H}, \text{CH}_2), 1.60-1.47 \ (m, 8\text{H}, -\text{(CH}_2)_n-), 1.43-1.36 \ (m, 2\text{H}, \text{CH}_2). \]

\[ ^{13}\text{C NMR} \ (125 \text{ MHz}, \text{CD}_2\text{Cl}_2) \ \delta \ 198.3 \ (\text{C}=\text{O}), 148.2 \ (=\text{CHCH}_2), 131.4 \ (\text{CH}=\text{CHCH}_2), 98.9 \ (\text{OCHO}), 67.3 \ (\text{THPOCHH}), 62.2 \ (\text{OCH}_2\text{THP}), 32.4 \ (=\text{CHCH}_2), 30.1 \ (\text{CH}_2), 29.6 \ (\text{CH}_2), 28.1 \ (\text{CH}_2), 26.6 \ (\text{CH}_3), 25.9 \ (\text{CH}_2), 25.7 \ (\text{CH}_2), 19.8 \ (\text{CH}_2). \]

\text{MS} \ (\text{EI-DE}) \ m/z \ (%) \ 225 \ (2), 185 \ (1), 156 \ (11), 140 \ (10), 126 \ (6), 111 \ (2), 97 \ (17), 85 \ (100), 81 \ (10), 67 \ (14), 55 \ (14), 43 \ (50), 29 \ (8).

\text{HRMS} \ (\text{ESI}^+) \ \text{calcd for} \ C_{14}H_{24}NaO_3 [(\text{M+Na})^+] \ 263.1615, \text{found} \ 263.1618.
(E)-6-(tert-Butyldimethylsilyloxy)-3-hexen-2-one (2h):

\[
\text{TBSO} \overset{\text{OH}}{\longrightarrow} \overset{\text{CHO}}{\longrightarrow} \text{CH}_2\text{C}_2\text{H}_5, \text{r.t., 16 h}
\]

3-(tert-Butyldimethylsilyloxy)-1-propanol: 1,3-Propanediol (3.62 mL, 50.0 mmol, 1.0 equiv) was dissolved in CH$_2$Cl$_2$ (150 mL) and triethylamine (6.93 mL, 50.0 mmol, 1.0 equiv) and a solution of tert-butyldimethylsilyl chloride (7.54 g, 50.0 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (20 mL) were added. After stirring for 16 h at room temperature, the reaction mixture was successively extracted with 10% aqueous NaHCO$_3$ (50 mL), water (50 mL), and brine (50 mL). The organic layer was dried (Na$_2$SO$_4$), filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, 10-30% EtOAc in hexane) to afford the title compound (9.00 g, 47.3 mmol, 95%) as a colorless liquid.

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 3.81 (t, $J = 5.5$ Hz, 2H, TBSOC$_2$H$_2$), 3.78 (app. br q, $J = 5.1$ Hz, 2H, C$_2$H$_2$OH), 2.59 (br s, 1H, OH), 1.75 (quint, $J = 5.6$ Hz, 2H, CH$_2$CH$_2$CH$_2$), 0.88 (s, 9H, Cq(C$_3$H$_3$)$_3$), 0.05 (s, 6H, Si(C$_3$H$_3$)$_2$).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 63.0 (OCH$_3$), 62.5 (OCH$_2$), 34.2 (CH$_2$CH$_2$CH$_2$), 25.9 (3C, Cq(CH$_3$)$_3$), 18.1 (CqMe$_2$), -5.5 (2C, Si(CH$_3$)$_2$).

GC-MS (GC-EI) m/z (%) 133 (14), 115 (3), 105 (41), 91 (3), 75 (100), 59 (5), 45 (6), 29 (2).

HRMS (ESI+) calcd for C$_9$H$_{22}$NaO$_2$Si [(M+Na)$^+$] 213.1282, found 213.1281.

3-(tert-Butyldimethylsilyloxy)propanal: PCC (13.1 g, 60.6 mmol, 1.5 equiv) was added in one portion to a solution of 3-(tert-butyldimethylsilyloxy)-1-propanol (7.69 g, 40.4 mmol, 1.0 equiv) in CH$_2$Cl$_2$ (130 mL). The mixture was stirred for 3 h at room temperature. Then the solution was separated from the black insoluble material, which was repeatedly extracted with Et$_2$O (3 × 70 mL). The combined organic layers were filtered
through a plug of silica gel and evaporated to afford the title compound (5.20 g, 27.6 mmol) as a colorless liquid. The aldehyde was used in the next step without further purification.

\[ \text{H NMR} \ (500 \text{ MHz, CDCl}_3) \delta 9.78 \ (t, \ J = 2.0 \text{ Hz, } 1\text{H, } CHO), 3.97 \ (t, \ J = 6.0 \text{ Hz, } 2\text{H, } CH_2OTBS), 2.58 \ (td, \ J = 6.0, 2.3 \text{ Hz, } 2\text{H, } CH_2CHO), 0.86 \ (s, \ 9\text{H, Cq(CH}_3)_3), 0.04 \ (s, \ 6\text{H, Si(CH}_3)_2). \]

\[ \text{GC-MS (GC-EI)} \ m/z \ (%) 131 \ (72), 117 \ (7), 101 \ (100), 89 \ (3), 75 \ (33), 73 \ (9), 59 \ (27), 45 \ (9), 29 \ (4). \]

(E)-6-(tert-Butyldimethylsilyloxy)-3-hexen-2-one (2h): The title compound was prepared according to the general procedure B from 3-(tert-butyldimethylsilyloxy)propanal with 1-(triphenylphosphoranylidene)-2-propanone. The crude product was purified by flash column chromatography (silica gel, 5% Et₂O in pentane) to afford enone 2h (819 mg, 3.59 mmol, 72%) as a pale yellow oil.

\[ \text{H NMR} \ (500 \text{ MHz, CD}_2Cl_2) \delta 6.78 \ (dt, \ J = 16.1, \ 7.1 \text{ Hz, } 1\text{H, =CHCH}_2), 6.08 \ (dt, \ J = 16.1, \ 1.6 \text{ Hz, } 1\text{H, CH=CHCH}_2), 3.74 \ (t, \ J = 6.3 \text{ Hz, } 2\text{H, TBSOC}_2\text{H}_2), 2.42 \ (app. qd, \ J = 6.6, \ 1.3 \text{ Hz, } 2\text{H, =CHC}_2\text{H}_2), 2.21 \ (s, \ 3\text{H, C}_3\text{H}_3\text{C}(=O)), 0.89 \ (s, \ 9\text{H, Cq(CH}_3)_3), 0.05 \ (s, \ 6\text{H, Si(CH}_3)_2). \]

\[ \text{GC-MS (GC-EI)} \ m/z \ (%) 228 \ [\text{M}^+] \ (\text{trace}), 213 \ (3), 198 \ (5), 183 \ (2), 171 \ (93), 141 \ (100), 127 \ (33), 115 \ (4), 103 \ (6), 89 \ (11), 75 \ (27), 59 \ (4), 43 \ (6), 29 \ (2). \]

\[ \text{HRMS (ESI+)} \) calcd for C_{16}H_{30}NaO_2Si [(M+Na)^+] 251.1437, found 251.1438. \]

(E)-5-Phenyl-3-penten-2-one (2q): The title compound was prepared according to the general procedure B from phenylacetaldehyde with 1-(triphenylphosphoranylidene)-2-propanone. The reaction was constantly maintained at 0 °C. The crude product was purified by flash column chromatography (silica gel, 5-10% Et₂O in pentane) to afford enone 2q (414 mg, 2.58 mmol, 26%) as a pale yellow oil.

\[ \text{H NMR} \ (500 \text{ MHz, CDCl}_3) \delta 7.32-7.28 \ (m, \ 2\text{H, CH}_{\text{Ph}}), 7.24-7.21 \ (m, \ 1\text{H, CH}_{\text{Ph, p}}), 7.16-7.15 \ (m, \ 2\text{H, CH}_{\text{Ph}}), 6.89 \ (dt, \ J = 15.9, \ 6.9 \text{ Hz, } 1\text{H, =CHCH}_2), 6.05 \ (dt, \ J = 16.1, \ 1.6 \text{ Hz, } 1\text{H, CH=CHCH}_2), 3.52 \ (dd, \ J = 6.6, \ 1.3 \text{ Hz, } 2\text{H, PhCH}_2), 2.02 \ (s, \ 3\text{H, CH}_3). \]

\[ \text{C NMR} \ (125 \text{ MHz, CDCl}_3) \delta 198.5 \ (C=O), 146.3 \ (=CHCH_2), 137.6 \ (=CqPh), 132.0 \ (CH=CHCH_2), 128.8 \ (2\text{C, CH}_{\text{Ph}}), 128.7 \ (2\text{C, CH}_{\text{Ph}}), 126.8 \ (CH_{\text{Ph, p}}), 38.8 \ (CH_2), 26.9 \ (CH_3). \]
MS (EI-DE) m/z (%) 160 [M+] (59), 145 (27), 127 (31), 117 (100), 102 (3), 91 (38), 89 (8), 77 (5), 65 (17), 58 (9), 51 (11), 43 (57), 39 (15), 27 (3).

HRMS (EI-FE) calcd for C_{11}H_{12}O [M+] 160.0886, found 160.0888.

(E)-6,6-Dimethylhept-3-en-2-one (2r): The title compound was prepared according to the general procedure B from 3,3-dimethylbutanal with 1-(triphenylphosphoranylidene)-2-propanone. The crude product was purified by flash column chromatography (silica gel, 5% Et_{2}O in pentane) to give enone 2r (1.58 g, 11.3 mmol, 56% (reduced yield due to the high volatility of 2r)) as a pale yellow oil.

{\textbf{1H NMR}} (500 MHz, CDCl_{3}) \delta 6.79 (dt, J = 15.6, 7.9 Hz, 1H, =CHCH_{2}), 6.04 (dt, J = 15.9, 1.4 Hz, 1H, CH=CHCH_{2}), 2.22 (s, 3H, C(CH_{3})=O), 2.08 (dd, J = 7.8, 1.2 Hz, 2H, CH_{2}), 0.92 (s, 9H, Cq(C(H_{3}))_{3}).

{\textbf{13C NMR}} (125 MHz, CDCl_{3}) \delta 198.4 (C=O), 145.8 (=CHCH_{2}), 133.2 (CH=CHCH_{2}), 46.9 (CH_{2}), 31.4 (Cq), 29.4 (3C, Cq(CH_{3}))_{3}, 26.9 (CH_{3}C(=O)).

GC-MS (GC-EI) m/z 140 [M^+].

HRMS (CI-FE, i-butane) calcd for C_{9}H_{17}O [(M+H)+] 141.1280, found 141.1279.

(E)-5-Benzylxy-3-penten-2-one (13f): The title compound was prepared according to the general procedure B from benzyloxyacetaldehyde with 1-(triphenylphosphoranylidene)-2-propanone. The crude product was purified by flash column chromatography (silica gel, 5-15% Et_{2}O in pentane) to afford enone 13f (950 mg, 4.99 mmol, 88%) as a pale yellow oil.

{\textbf{1H NMR}} (500 MHz, CDCl_{3}) \delta 7.39-7.35 (m, 4H, CHPh), 7.33-7.29 (m, 1H, CH=CHCH_{2}), 6.31 (d, J = 16.1, 4.5 Hz, 1H, =CHCH_{2}), 6.80 (dt, J = 16.1, 1H, CH=CHCH_{2}), 4.46 (s, 2H, PhCH_{2}), 4.21 (dd, J = 4.5, 1.7 Hz, 2H, CH_{2}CH=), 2.24 (s, 3H, CH_{3}).

{\textbf{13C NMR}} (125 MHz, CDCl_{3}) \delta 198.4 (C=O), 143.6 (=CHCH_{2}), 138.6 (CqPh), 130.7 (CH=CHCH_{2}), 128.9 (2C, CHPh), 128.3 (CH_{2}Ph), 128.2 (2C, CHPh), 73.4 (CH_{2}), 69.4 (CH_{2}), 27.6 (CH_{3}).

MS (EI-DE) m/z (%) 190 [M^+] (trace), 160 (6), 145 (5), 132 (9), 117 (1), 107 (2), 99 (2), 91 (100), 84 (10), 65 (9), 51 (3), 43 (13), 29 (2).

HRMS (ESI+) calcd for C_{12}H_{14}O_{2}Na [(M+Na)^+] 213.0885, found 213.0886.
Synthesis of (E)-2-methyl-4-hexen-3-one (2n)

(E)-2-Methyl-4-hexen-3-one (2n) was prepared according to a procedure of Heathcock et al.\textsuperscript{31}

\[
\begin{align*}
\text{2n} & \xrightarrow{\text{LDA (1.05 equiv)}} \text{THF, } -78 \degree C, 30 \text{ min} \xrightarrow{\text{(2.5 equiv) acetaldehyde}} -78 \degree C, 1 \text{ h} \xrightarrow{\text{MsCl (1.18 equiv) pyridine, 0 } \degree C, 16 \text{ h}} \text{EtO, r.t.}
\end{align*}
\]

5-Hydroxy-2-methylhexan-3-one: To a solution of LDA, freshly prepared by addition of \textit{n}-BuLi (26.8 ml, 67.0 mmol, 1.05 equiv, 2.5M in hexanes) to diisopropylamine (9.40 mL, 67.0 mmol, 1.05 equiv) in THF (100 mL) at 0 °C, was added isopropylmethylketone (6.87 mL, 63.8 mmol) at −78 °C. After 30 min, acetaldehyde (9.01 mL, 159.5 mmol, 2.5 equiv) was added, and after stirring for 1h, the reaction was quenched by addition of saturated aqueous NaHCO\textsubscript{3}-solution (40 mL) at −78 °C. Then, the reaction mixture was allowed to warm to room temperature, and the layers were separated. The aqueous layer was extracted with Et\textsubscript{2}O (2×75 mL) and the combined organic phases were successively washed with cold 1% aqueous HCl (80 mL), saturated aqueous NaHCO\textsubscript{3}-solution (80 mL), and brine (80 mL), dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated under reduced pressure to give the title compound (7.91 g, 60.8 mmol, 95%) as a colorless oil.

\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 4.21-4.14 (m, 1H, CH(OH)), 3.23 (d, \(J = 3.3\) Hz, 1H, OH), 2.62 (dd, \(J = 18.1, 3.3\) Hz, 1H, CHH), 2.58-2.49 (m, 2H, CHH and CH(CH\textsubscript{3})\textsubscript{2}), 1.16 (d, \(J = 6.1\) Hz, 3H, CH(OH)CH\textsubscript{3}), 1.08 (d, \(J = 7.0\) Hz, 3H, CH(CH\textsubscript{3})\textsubscript{2}), 1.07 (d, \(J = 6.9\) Hz, 3H, CH(CH\textsubscript{3})\textsubscript{2}).

\textsuperscript{13}C NMR (125 MHz, CDCl\textsubscript{3}) \(\delta\) 216.1 (C=O), 63.9 (CH(OH)), 47.9 (CH\textsubscript{2}), 41.4 (CH(CH\textsubscript{3})\textsubscript{2}), 22.3 (CH(OH)CH\textsubscript{3}), 18.0 (CH(CH\textsubscript{3})\textsubscript{2}), 17.9 (CH(CH\textsubscript{3})\textsubscript{2}).

5-Methyl-4-oxohexan-2-yl methanesulfonate: The crude aldol product described above (7.91 g, 60.8 mmol) was dissolved in pyridine (60 mL) and methanesulfonyl chloride (5.59 mL, 71.7 mmol, 1.18 equiv) was added at 0 °C. The solution was kept at room temperature for 16 h. To work-up the reaction, water (120 mL) was added, and the mixture repeatedly extracted with Et₂O (3×100 mL). The combined organic layers were washed with saturated aqueous CuSO₄-solution (4×75 mL), and brine (100 mL), dried over Na₂SO₄, filtered, and concentrated in vacuo to give the title compound (7.95 g, 38.2 mmol, 63%) as a yellow oil.

¹H NMR (500 MHz, CDCl₃) δ 5.18-5.12 (m, 1H, CH(OMs)), 3.04-2.98 (m, 1H, CH₁), 2.99 (s, 3H, OSO₂C₃H₃), 2.62-2.54 (m, 2H, CH₂ and CH(CH₃)₂), 1.46 (d, J = 6.4 Hz, 3H, CH(OMs)C₃H₃), 1.09 (d, J = 6.9 Hz, 3H, CH(CH₃)₂), 1.08 (d, J = 7.0 Hz, 3H, CH(CH₃)₂).

¹³C NMR (125 MHz, CDCl₃) δ 210.7 (C=O), 75.8 (CH(OMs)), 46.3 (CH₂), 41.2 (CH(CH₃)₂), 38.0 (OSO₂C₃H₃), 21.6 (CH(OH)CH₃), 17.8 (CH(CH₃)₂), 17.8 (CH(CH₃)₂).

(E)-2-Methylhex-4-en-3-one (2n): The crude mesylate described above (7.85 g, 37.7 mmol) was dissolved in Et₂O (40 mL), and triethylamine (7.84 mL, 56.6 mmol, 1.5 equiv) was added. After stirring for 18 h at room temperature, water (80 mL) was added, and the mixture was extracted with Et₂O (3 × 80 mL). The combined organic layers were successively washed with cold aqueous 1% HCl (80 mL), saturated aqueous NaHCO₃ solution (80 mL), water (80 mL), and brine (80 mL). The organic phase was dried (Na₂SO₄), filtered, and evaporated. The crude product was purified by flash column chromatography (silica gel, 3-5% Et₂O in pentane) to afford enone 2n (2.64 g, 23.6 mmol, 62% (reduced yield due to the high volatility of 2n)) as a pale yellow oil.

¹H NMR (500 MHz, CD₂Cl₂) δ 6.85 (dq, J = 15.4, 6.8 Hz, 1H, =CH₂), 6.17 (dq, J = 15.4, 1.6 Hz, 1H, CH=CHCH₃), 2.80 (hept, J = 6.8 Hz, 1H, CH₆), 1.88 (dd, J = 7.0, 1.9 Hz, 3H, =CHCH₃), 1.06 (d, J = 6.6 Hz, 6H, CH(CH₃)₂).

¹³C NMR (125 MHz, CDCl₃) δ 203.7 (C=O), 142.4 (=CHCH₃), 130.3 (CH=CHCH₃), 38.6 (CHMe₂), 18.6 (2C, CH(CH₃)₂), 18.3 (=CHCH₃).

GC-MS (GC-EI) m/z 112 [M⁺].

HRMS (EI-FE) calcd for C₇H₁₂O [M⁺] 112.0888, found 112.0888.
Synthesis of (Z)-6-phenyl-3-hexen-2-one ((Z)-2b)

(Z)-6-Phenyl-3-hexen-2-one ((Z)-2b) was prepared according to a reaction sequence described by Heathcock et al. 32

![Reaction Scheme]

6-Phenylhex-3-yn-2-ol: n-BuLi (8.0 mL, 20.0 mmol, 2.5M in hexanes, 1.0 equiv) was added to a stirred solution of 4-phenylbut-1-yn-l-yn (2.81 mL, 20.0 mmol, 1.0 equiv) in THF (11 mL) at −78 °C. After 15 min, acetaldehyde (1.70 mL, 30.0 mmol, 1.5 equiv) was added over 1 min. Then the reaction mixture was allowed to warm to room temperature and after 1 h, the reaction was quenched by the addition of aqueous saturated NH₄Cl-solution (20 mL) and repeatedly extracted with Et₂O (3×50 mL). The combined organic phases were successively washed with water and brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, 20% Et₂O in pentane) and 6-phenylhex-3-yn-2-ol (3.13 g, 18.0 mmol, 90%) was obtained as a colorless oil.

1H NMR (500 MHz, CD₂Cl₂) δ 7.32-7.29 (m, 2H, CH₅Ph, m), 7.24-7.20 (m, 3H, CH₅Ph, o,p), 4.48-4.43 (m, 1H, CHO), 2.81 (t, J = 7.5 Hz, 2H, PhCH₂), 2.49 (td, J = 7.5, 1.9 Hz, 2H, PhCH₂CH₃), 1.92-1.88 (m, 1H, OH), 1.37 (d, J = 6.6 Hz, 3H, CH₃).

13C NMR (125 MHz, CD₂Cl₂) δ 141.4 (CqPh), 129.1 (2C, CH₅Ph), 128.8 (2C, CH₅Ph), 126.8 (CH₅Ph, p), 84.0 (C≡C), 83.8 (C≡C), 58.9 (COH), 35.5 (PhCH₂), 25.1 (CH₃), 21.4 (PhCH₂CH₃).

GC-MS (GC-EI) m/z (%) 173 (1), 156 (6), 141 (4), 129 (21), 115 (9), 102 (2), 91 (100), 77 (4), 65 (16), 51 (7), 43 (9), 29 (7).

HRMS (EI-FE) calcd for C₁₂H₁₅O [(M+H)+] 175.1124, found 175.1123.

6-Phenylhex-3-yn-2-one: A solution of 6-phenylhex-3-yn-2-ol (2.75 g, 15.8 mmol) and PCC (7.50 g, 34.7 mmol, 2.2 equiv) in CH₂Cl₂ (80 mL) was stirred at room temperature for 12 h. Florisil (5 g) was added to the reaction mixture, and stirring was continued for another 15 min. After filtration through a plug of silica gel (eluent: Et₂O), the solvents were removed in vacuo giving 6-phenylhex-3-yn-2-one (2.42 g, 14.1 mmol, 89%) as a clear oil, which was used in the next step without further purification.

**1H NMR** (500 MHz, CD₂Cl₂) δ 7.34-7.31 (m, 2H, C₆H₆Ph, m), 7.26-7.23 (m, 3H, C₆H₆Ph, o, p), 2.89 (t, J = 7.4 Hz, 2H, PhC₂H₂), 2.67 (t, J = 7.4 Hz, 2H, PhCH₂CH₂), 2.26 (s, 3H, CH₃).

**13C NMR** (125 MHz, CD₂Cl₂) δ 184.8 (C=O), 140.2 (C₆H₆Ph, q), 128.8 (2C, C₆H₆Ph, H₆Ph, o), 128.7 (2C, C₆H₆Ph, H₆Ph, m), 126.9 (C₆H₆Ph, p), 92.9 (CH₂C≡C), 82.0 (CH₂C≡C), 34.2 (PhCH₂), 32.9 (CH₃), 21.3 (PhCH₂CH₂).

**MS** (EI-DE) m/z (%) 172 [M⁺] (2), 157 (13), 144 (1), 129 (31), 115 (1), 102 (1), 91 (100), 77 (2), 65 (13), 51 (4), 43 (14), 27 (1).

**HRMS** (CI-FE, i-butane) calcd for C₁₂H₁₃O [(M+H)+] 173.0965, found 173.0966.

(Z)-6-phenyl-3-hexen-2-one ((Z)-2b): A mixture of ketone 6-phenylhex-3-yn-2-one (2.0 g, 11.6 mmol), quinoline (20 mg, 1 wt%), 5% Pd/BaSO₄ (200 mg, 10 wt%), and Et₂O (12 mL) as the solvent were placed under a hydrogen atmosphere (1 atm) and stirred at room temperature for 22 h. The catalyst was removed by filtration and the volatiles under reduced pressure. **1H NMR** of the crude product showed the desired (Z)-enone 2b contaminated with 25% of the (E)-isomer, which was separated by flash column chromatography (silica gel, 10-15% Et₂O in pentane). Pure (Z)-enone ((Z)-2b; 1.40 g, 8.04 mmol, 69%) was obtained as a pale yellow oil.

**1H NMR** (500 MHz, CD₂Cl₂) δ 7.30-7.27 (m, 2H, CH₆H₆Ph, m), 7.22-7.17 (m, 3H, CH₆H₆Ph, o and p), 6.15 (dt, J = 11.3, 1.3 Hz, 1H, CH≡CHCH₂), 6.08 (dt, J = 11.4, 7.1 Hz, 1H, =CHCH₂), 2.90 (app. qd, J = 7.6, 1.2 Hz, 2H, =CHCH₂), 2.74 (t, J = 7.7 Hz, 2H, PhCH₂), 2.15 (s, 3H, CH₃).

**13C NMR** (125 MHz, CD₂Cl₂) δ 198.9 (C=O), 146.5 (=CHCH₂), 141.5 (C₆H₆Ph), 128.5 (2C, CH₆H₆Ph, o), 128.4 (2C, CH₆H₆Ph, m), 127.6 (CH=CHCH₂), 126.0 (CH₆H₆Ph, p), 35.1 (PhCH₂), 31.4 (CH₃), 30.9 (=CHCH₂).

**MS** (EI-DE) m/z (%) 174 [M⁺] (19), 159 (3), 141 (2), 131 (33), 117 (7), 104 (19), 91 (100), 83 (2), 77 (3), 65 (12), 51 (3), 43 (21), 39 (4), 27 (2).

Synthesis of 4,8-dimethylnona-3,7-dien-2-one (S-3)

4,8-Dimethylnona-3,7-dien-2-one (S-3) was prepared according to a procedure of Shibasaki et al.\textsuperscript{33}

\[\text{MeLi (2.4 mL, 39.0 mmol, 1.3 equiv; 1.6M in Et}_2\text{O)} \text{ was added at } -78 \, ^\circ\text{C to a solution of citral (5.14 mL, 30.0 mmol, 1.0 equiv; geranial/neral 64:36) in Et}_2\text{O (150 mL). After stirring at the same temperature for 1.5 h, 1 N aqueous HCl was added slowly. The phases were separated and the aqueous phase was extracted twice with Et}_2\text{O. The combined organic layers were washed with water and brine, dried (Na}_2\text{SO}_4\text{), and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel; 20-30% Et}_2\text{O in pentane) to the title compound (4.55 g, 27.1 mmol, 90%; E/Z 64:36) as a colorless liquid. Characterized as a mixture of 3E/3Z-isomers.}\]

\[\begin{align*}
\text{1H NMR (500 MHz, CD}_2\text{Cl}_2) \delta & \text{5.21-5.17 (m, 2H, C_Hol), 5.14-5.08 (m, 2H, C_Hol), 4.56-4.47 (m, 2H, C_HOH), 2.11-1.97 (m, 8H, C_H}_2\text{), 1.71-1.66 (m, 12H, C}_3\text{C}_3\text{), 1.61 (s, 6H, C}_3\text{C}_3\text{), 1.42-1.40 (m, 2H, O_H), 1.19-1.16 (m, 6H, CH}_3\text{).} \\
\text{13C NMR (125 MHz, CD}_2\text{Cl}_2) \delta & \text{137.4 (CH}_2\text{C}_3\text{), 131.9 (Me}_2\text{C}_3\text{), 129.8 (CH}_3\text{C}_3\text{), 124.3 (CH}_3\text{C}_3\text{), 64.9 (CHOH), 39.8 (CH}_2\text{C}_3\text{), 26.8 (CH}_3\text{C}_3\text{), 25.7 (CH}_3\text{), 23.8 (CH}_3\text{), 17.7 (CH}_3\text{), 16.4 (CH}_3\text{); 3Z-4,8-dimethylnona-3,7-dien-2-ol: } \delta \text{ 137.7 (CH}_2\text{C}_3\text{), 132.6 (Me}_2\text{C}_3\text{), 130.7 (CH}_3\text{C}_3\text{), 124.3 (CH}_3\text{C}_3\text{), 64.4 (CHOH), 32.5 (CH}_2\text{C}_3\text{), 26.9 (CH}_3\text{C}_3\text{), 25.7 (CH}_3\text{), 23.8 (CH}_3\text{), 23.3 (CH}_3\text{), 17.7 (CH}_3\text{).}
\end{align*}\]

GC-MS (GC-EI) 3E-4,8-dimethylnona-3,7-dien-2-ol: m/z (%) 168 [M^+] (trace), 150 (4), 135 (9), 123 (4), 107 (53), 91 (13), 79 (20), 69 (100), 53 (11), 43 (34), 41 (72), 29 (8); 3Z-4,8-dimethylnona-3,7-dien-2-ol: m/z (%) 168 [M^+] (trace), 150 (6), 121 (5), 107 (72), 93 (18), 82 (28), 69 (100), 65 (6), 59 (2), 53 (13), 41 (85), 39 (19), 29 (9).

HRMS (EI-DE) caled for C\textsubscript{11}H\textsubscript{20}O [M^+] 168.1513, found 168.1514.

\textsuperscript{33} H. Usuda, A. Kuramochi, M. Kanai, M. Shibasaki, Org. Lett. 2004, 6, 4387
4,8-Dimethylnona-3,7-dien-2-one (S-3): To a suspension of alcohol 4,8-dimethylnona-3,7-dien-2-ol (2.20 g, 13.1 mmol) and powdered 4Å MS (6.54 g) in CH₂Cl₂ (40 mL) were added successively at 0 °C NMO (2.67 g, 19.7 mmol, 1.5 equiv) and TPAP (233 mg, 0.66 mmol, 0.05 mol%). After stirring for 45 min at ambient temperature, the mixture was filtered through a short pad of silica gel (eluent: EtOAc). The filtrate was concentrated under reduced pressure and flash column chromatography (silica gel, 8% Et₂O in pentane) afforded pure fractions of 3E- and 3Z-isomers in addition to mixed fractions as colorless oils [3E-4,8-dimethylnona-3,7-dien-2-one ((E)-7; 450 mg, 2.71 mmol, 21%); 3Z-4,8-dimethylnona-3,7-dien-2-one ((Z)-7; 303 mg, 1.82 mmol, 14%); 3Z/E-4,8-dimethylnona-3,7-dien-2-one (1.17 g, 7.04 mmol, 54%; E/Z 73:27)].

(3E)-4,8-Dimethylnona-3,7-dien-2-one (E-S-3):

1H NMR (500 MHz, CD₂Cl₂) δ 6.06 (s, 1H, =CHC(=O)), 5.11-5.07 (m, 1H, =CH₂), 2.17-2.11 (m overlapped, 4H, CH₃), 2.13 (s overlapped, 3H, CH₃), 1.68 (s, 3H, CH₃), 1.61 (s, 3H, CH₃).

13C NMR (125 MHz, CD₂Cl₂) δ 198.8 (C=O), 158.1 (CH₂C₉H₈), 132.8 (Me₂C₉H₈), 124.0 (CH₉), 123.5 (CH₉), 41.4 (CH₃C₉H₈), 31.9 (CH₃C(=O)), 26.5 (CH₉CH₂), 25.7 (CH₃), 19.2 (CH₃), 17.7 (CH₃).

GC-MS (GC-EI) m/z (%) 166 [M⁺] (5), 151 (8), 133 (2), 123 (24), 108 (21), 98 (19), 93 (7), 83 (56), 69 (100), 53 (10), 41 (80), 39 (16), 27 (6).

HRMS (EI-FE) calcd for C₁₁H₁₈O [M⁺] 166.1356, found 166.1358.

(3Z)-4,8-Dimethylnona-3,7-dien-2-one (Z-S-3):

1H NMR (500 MHz, CD₂Cl₂) δ 6.06 (s, 1H, =CHC(=O)), 5.15-5.12 (m, 1H, =CH₂), 2.55 (dd, J = 7.9 Hz, 2H, CH₂C₉H₈), 2.14-2.09 (m overlapped, 2H, =CHCH₃), 2.11 (s overlapped, 3H, CH₃C(=O)), 1.86 (d, J = 1.3 Hz, 3H, CH₃), 1.68 (s, 3H, CH₃), 1.62 (s, 3H, CH₃).

13C NMR (125 MHz, CD₂Cl₂) δ 198.2 (C=O), 158.7 (CH₂C₉H₈), 132.4 (Me₂C₉H₈), 124.5 (CH₉), 124.1 (CH₉), 33.9 (CH₃C₉H₈), 31.8 (CH₃C(=O)), 27.1 (CH₉CH₂), 25.7 (CH₃), 25.5 (CH₃), 17.7 (CH₃).

GC-MS (GC-EI) m/z (%) 166 [M⁺] (6), 151 (10), 133 (4), 123 (34), 108 (34), 98 (23), 83 (75), 69 (100), 65 (5), 59 (5), 55 (16), 41 (90), 39 (21), 27 (8).

HRMS (EI-FE) calcd for C₁₁H₁₈O [M⁺] 166.1356, found 166.1358.
Preparation of Cyclic α,β-Unsaturated Ketones

General Procedure A: Protocol of Woods \(^3^4\) (Enones 9j, 9l, 9n, 9o, 9q, 11b, 11c)

3-Ethoxy-2-cyclohexenone or –heptenone (21.4 mmol, 1.0 equiv) in THF (15 mL) was added dropwise to a solution of a Grignard reagent (1 M in Et₂O or THF, 1.5-2.0 equiv) at 0 °C under argon. Once the addition was complete, the resulting solution was allowed to warm to room temperature and stirred until TLC indicated complete disappearance of the starting material (2-18 h). The reaction was slowly quenched with diluted aqueous acid (1 N HCl or 5% H₂SO₄) at 0 °C. The layers were separated, and the aqueous layer extracted with Et₂O (3×50 mL). The combined organic layers were washed successively with saturated aqueous NaHCO₃-solution, water, and brine, dried (Na₂SO₄), filtered, and evaporated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, eluent: Et₂O-pentane) to yield 3-substituted 2-cyclohexenone and –heptenone derivatives 9 and 11.

3-Isopropyl-2-cyclohexenone (9j): The title compound was prepared according to the general procedure A from 3-ethoxy-2-cyclohexenone and isopropyl magnesium chloride (2 M in Et₂O). Purification by flash column chromatography (silica gel, 20% Et₂O in pentane) gave enone 9j (2.10 g, 15.2 mmol, 71%) as a pale yellow liquid.

\(^1\)H NMR (300 MHz, CD₂Cl₂) δ 5.81 (q, \(J = 1.4\) Hz, 1H, \(-\text{CH}\)), 2.41 (hept, \(J = 6.9\) Hz, 1H, \(\text{CHMe}_2\)), 2.33-2.28 (m, 4H, \(\text{CH}_2\text{C}(=\text{O})\) and \(\text{CH}_2\text{Cqol}\)), 1.96 (quint, \(J = 6.2\) Hz, 2H, \(\text{CH}_2\text{CH}_2\text{CH}_2\)), 1.09 (d, \(J = 7.2\) Hz, 6H, \(\text{CH}(\text{CH}_3)_2\)).

\(^13\)C NMR (75 MHz, CDCl₃) δ 200.3 (C=O), 171.8 (Cq=CH), 123.6 (Cq=CH), 37.6 (CH₂C(=O)), 35.7 (CHMe₂), 27.7 (CH₂Cqol), 22.9 (CH₂CH₂CH₂), 20.6 (2C, CH(CH₃)₂).

GC-MS (GC-EI) m/z 138 [M⁺].

3-ALLYL-2-CYCLOHEXENONE (9l): The title compound was prepared according to the general procedure A from 3-ethoxy-2-cyclohexenone and allyl magnesium chloride (2 M in THF). Purification by flash column chromatography (silica gel, 20% Et₂O in pentane) gave enone 9l (893 mg, 6.55 mmol, 47%) as a colorless liquid.³⁵

³¹H NMR (500 MHz, CDCl₃) δ 5.87 (s, 1H, Cq=CH₂), 5.76 (ddt, J = 16.7, 10.3, 6.8 Hz, 1H, CH–CH₂), 5.14-5.09 (m, 2H, CH=CH₂), 2.92 (d, J = 7.1 Hz, 2H, CH₂CH=CH₂), 2.34 (t, J = 6.8 Hz, 2H, CH₂C(=O)), 2.27 (br t, J = 6.1 Hz, 2H, CH₂CH₂Cqol), 1.97 (quint, J = 6.4 Hz, 2H, CH₂CH₂CH₂).

¹³C NMR (125 MHz, CDCl₃) δ 199.8 (C=O), 164.1 (Cq=CH), 133.2 (CH=CH₂), 126.3 (Cq=CH), 118.3 (CH=CH₂), 42.2 (CH₂CH=CH₂), 37.3 (C=OCH₂), 29.5 (CH₂CH₂Cqol), 22.6 (CH₂CH₂CH₂).

MS (EI-DE) m/z (%) 136 [M⁺] (74), 121 (8), 108 (42), 93 (8), 79 (100), 77 (18), 74 (1), 67 (19), 53 (9), 41 (19), 39 (43), 29 (2), 27 (13).


3-BENZYL-2-CYCLOHEXENONE (9n): The title compound was prepared according to the general procedure A from 3-ethoxy-2-cyclohexenone and benzyl magnesium chloride (1 M in Et₂O). Purification by flash column chromatography (silica gel, 20% Et₂O in pentane) gave enone 9n (3.02 g, 16.2 mmol, 76%) as a colorless liquid.

³¹H NMR (500 MHz, CD₂Cl₂) δ 7.33-7.30 (m, 2H, CHPh, m), 7.28-7.24 (m, 1H, CHPh, p), 7.21-7.18 (m, 2H, CHPh, o), 5.80 (s, 1H, =CHH), 3.52 (s, 2H, PhCH₂), 2.31 (t, J = 6.8 Hz, 2H, CH₂C(=O)), 2.25 (br t, J = 6.0 Hz, 2H, CH₂Cqol), 1.94 (quint, J = 6.4 Hz, 2H, CH₂CH₂CH₂).

¹³C NMR (125 MHz, CD₂Cl₂) δ 199.6 (C=O), 164.9 (Cqol), 137.8 (CqPh), 129.5 (2C, CHPh, o), 129.0 (2C, CHPh, m), 127.1 (CHPh, p), 127.0 (=CH), 44.7 (PhCH₂), 37.7 (CH₂C(=O)), 29.6 (CH₂Cqol), 23.1 (CH₂CH₂CH₂).

MS (EI-DE) m/z (%) 186 [M⁺] (100), 168 (8), 158 (91), 142 (9), 129 (58), 115 (34), 102 (3), 91 (30), 77 (9), 67 (26), 51 (15), 39 (46), 27 (11).


3-Phenyl-2-cyclohexenone (9o): The title compound was prepared according to the general procedure A from 3-ethoxy-2-cyclohexenone and phenyl magnesium chloride (2 M in THF). Purification by flash column chromatography (silica gel, 30% Et₂O in pentane) gave enone 9o (3.60 g, 20.9 mmol, 98%) as a white solid.1\[^{36}\]

\(^1\)H NMR (500 MHz, CD₂Cl₂) δ 7.57-7.55 (m, 2H, CH₂Ph), 7.43-7.40 (m, 3H, CH₂Ph), 6.37 (t, J = 1.5 Hz, 1H, =CH), 2.77 (td, J = 6.0, 1.4 Hz, 2H, CH₂C(qol)), 2.44 (app. t, J = 6.8 Hz, 2H, CH₂C(=O)), 2.14 (quint, J = 6.3 Hz, 2H, CH₂CH₂CH₂).

\(^13\)C NMR (125 MHz, CD₂Cl₂) δ 199.6 (C=O), 159.9 (Cq=CH), 139.3 (CqPh), 130.1 (CH₂Ph), 129.0 (2C, CH₂Ph), 126.4 (2C, CH₂Ph), 125.6 (Cq=CH), 37.6 (CH₂C(=O)), 28.4 (CH₂C(qol)), 23.2 (CH₂CH₂CH₂).

3-Vinyl-2-cyclohexenone (9p): The title compound was prepared according to the general procedure A from 3-ethoxy-2-cyclohexenone and vinyl magnesium bromide (1 M in THF). Purification by flash column chromatography (silica gel, 15-25% Et₂O in pentane) gave enone 9p (1.97 g, 16.1 mmol, 75%) as a colorless oil.

\(^1\)H NMR (500 MHz, CD₂Cl₂) δ 6.50 (dd, J = 17.6, 10.7 Hz, 1H, CH=CH₂), 5.89 (s, 1H, Cq=CH), 5.70 (d, J = 17.7 Hz, 1H, CH=CH₃), 5.45 (d, J = 10.7 Hz, 1H, CH=CH₃), 2.47 (br t, J = 6.1 Hz, 2H, CH₂C(qol)), 2.37 (t, J = 6.8 Hz, 2H, CH₂C(=O)), 2.02 (quint, J = 6.4 Hz, 2H, CH₂CH₂CH₂).

\(^13\)C NMR (126 MHz, CD₂Cl₂) δ 200.1 (C=O), 157.1 (Cq=CH), 138.3 (CH=CH₂), 128.4 (Cq=CH), 120.7 (CH=CH₂), 37.8 (CH₂C(=O)), 24.6 (CH₂), 22.6 (CH₂).

GC-MS (GC-EI) m/z 122 [M⁺].

HRMS (EI-FE) calcd for C₈H₁₀O [M⁺] 122.0730, found 122.0732.

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3-Ethynyl-2-cyclohexenone (9q): The title compound was prepared according to the general procedure A from 3-ethoxy-2-cyclohexenone and ethynyl magnesium bromide (0.5 M in THF). Purification by flash column chromatography (silica gel, 10-25% Et$_2$O in pentane) gave enone 9q (1.33 g, 11.1 mmol, 77%) as a colorless liquid.

$^1$H NMR (500 MHz, CD$_2$Cl$_2$) $\delta$ 6.21 (t, $J$ = 1.6 Hz, 1H, =$\text{CCH}$), 3.59 (s, 1H, =$\text{CCH}$), 2.45 (td, $J$ = 6.1, 1.7 Hz, 2H, CH$_2$C$_{q\text{ol}}$), 2.34 (t, $J$ = 6.7 Hz, 2H, CH$_2$C(=O)), 2.02 (quint, $J$ = 6.3 Hz, 2H, CH$_2$CH$_2$CH$_2$).

$^{13}$C NMR (125 MHz, CD$_2$Cl$_2$) $\delta$ 198.4 ($\text{C=O}$), 142.3 ($\text{Cq=CH}$), 134.2 ($\text{Cq=CH}$), 87.0 ($\text{Cq=CH}$), 82.8 ($\text{Cq=CH}$), 37.6 (CH$_2$C(=O)), 30.5 (CH$_2$C$_{q\text{ol}}$), 22.9 (CH$_2$CH$_2$CH$_2$).

GC-MS (GC-EI) m/z (%) 120 [M$^+$] (44), 92 (100), 89 (2), 77 (4), 64 (54), 50 (12), 42 (5), 39 (15), 27 (3).

HRMS (EI-FE) calcd for C$_8$H$_8$O [M$^+$] 120.0576, found 120.0575.

3-Ethyl-2-cycloheptenone (11b): The title compound was prepared according to the general procedure A from 3-ethoxy-2-cycloheptenone and ethyl magnesium bromide (3 M in THF). Purification by flash column chromatography (silica gel, 20% Et$_2$O in pentane) gave enone 11b (570 mg, 4.12 mmol, 61%) as a pale yellow liquid. 3-Ethoxy-2-cycloheptenone was obtained by heating a mixture of 1,3-cycloheptanedione (0.85 g, 6.74 mmol), dry ethanol (1.7 mL), and a catalytic amount of p-toluene sulfonic acid monohydrate (17 mg) in benzene (40 mL) under reflux with a Dean-Stark trap. After 12 h, the mixture was allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The resulting crude 3-ethoxy-2-cycloheptenone (~90% purity) was used without further purification for the synthesis of 3-ethyl-2-cycloheptenone (11b).

$^1$H NMR (400 MHz, CD$_2$Cl$_2$) $\delta$ 5.83 (s, 1H, =$\text{CCH}$), 2.52 (t, $J$ = 6.1 Hz, 2H, CH$_2$C(=O)), 2.41 (t, $J$ = 5.8 Hz, 2H, CH$_2$C$_{q\text{ol}}$), 2.22 (qd, $J$ = 7.4, 1.2 Hz, 2H, CH$_2$CH$_3$), 1.81-1.72 (m, 4H, CH$_2$(CH$_2$)$_2$CH$_2$), 1.08 (t, $J$ = 7.4 Hz, 3H, CH$_2$CH$_3$).

$^{13}$C NMR (75 MHz, CD$_2$Cl$_2$) $\delta$ 203.9 ($\text{C=O}$), 163.8 ($\text{Cq=CH}$), 128.2 ($\text{Cq=CH}$), 42.5 ($\text{CH}_2\text{C(=O)}$), 34.1 (C$_{q\text{ol}}$CH$_2$, cycl.), 32.9 (CH$_2$CH$_3$), 25.5 (CH$_2$, cycl.), 21.7 (CH$_2$, cycl.), 12.3 (CH$_3$).

MS (EI-DE) m/z (%) 138 [M$^+$] (29), 109 (100), 96 (18), 81 (32), 79 (10), 67 (17), 53 (17), 39 (20), 27 (17).


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**3-Benzyl-2-cycloheptenone (11c):** The title compound was prepared according to the general procedure A from 3-ethoxy-2-cycloheptenone (*vide supra*) and benzyl magnesium chloride (1 M in Et₂O). Purification by flash column chromatography (silica gel, 20% Et₂O in pentane) gave enone 23c (551 mg, 2.75 mmol, 41%) as a pale yellow liquid.

**1H NMR** (400 MHz, CD₂Cl₂) δ 7.34-7.19 (m, 5H, C₆H₅), 5.89 (s, 1H, =CH), 3.49 (s, 2H, CH₂Ph), 2.53 (t, J = 6.4 Hz, 2H, CH₂C(=O)), 2.37 (t, J = 5.9 Hz, 2H, CH₂Cqol), 1.78-1.64 (m, 4H, CH₂(CH₂)₂CH₂).

**13C NMR** (75 MHz, CD₂Cl₂) δ 203.8 (C=O), 160.2 (Cqol), 138.4 (CqPh), 130.9 (=CH), 129.5 (2C, CH₉Ph), 128.9 (2C, CH₉Ph), 127.0 (CH₉Ph, p), 47.3 (CH₂Ph), 42.6 (CH₂C(=O)), 32.7 (CH₂Cqol), 25.6 (CH₂CH₂Cqol), 21.7 (CH₂CH₂C(=O)).

**MS** (EI-DE) m/z (%) 200 [M⁺] (14), 182 (1), 171 (4), 158 (4), 143 (3), 129 (13), 115 (12), 109 (100), 91 (15), 81 (24), 65 (12), 53 (11), 39 (14), 27 (6).


**General Procedure B: Saegusa Oxidation**³⁷ (Enones 9q, 9s, 11d, 11e, 11f)

To a solution of LDA, freshly prepared from n-BuLi (13.2 ml, 33.0 mmol, 1.1 equiv, 2.5M in hexanes) and diisopropylamine (5.06 mL, 36.0 mmol, 1.2 equiv) in THF (46 mL) at 0 °C, was added a cyclic ketone (30.0 mmol, 1.0 equiv) dissolved in THF (18 ml) at −78 °C. After stirring for 30 min, the solution was warmed to room temperature and stirred for additional 30 min at room temperature. After re-cooling to −78 °C, TMSCl (6.47 ml, 51.0 mmol, 1.7 equiv) was added, and stirring was continued for 1 h. The reaction was quenched with saturated aqueous NH₄Cl solution and extracted with Et₂O (3 × 150 mL). The combined organic layers were dried (Na₂SO₄), filtered, and concentrated in vacuo. The crude silyl enol ether was dissolved in DMSO (600 mL), and Pd(OAc)₂ (673 mg, 3.00 mmol, 10 mol%)...
was added. The flask was carefully evacuated, purged with O₂, and equipped with an O₂ ballon. After stirring for 12 h at room temperature, the reaction mixture was poured into ice water (300 mL), and repeatedly extracted with Et₂O (2 × 300 mL). The combined organic phases were washed with brine, dried (Na₂SO₄), filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (silica gel, eluent: Et₂O-pentane) to afford the corresponding pure cyclic α,β-unsaturated ketones 9 and 11.

4-Methyl-2-cyclohexenone (9q): The title compound was prepared according to the general procedure B from 4-methylcyclohexanone (1.84 mL, 15.0 mmol). Purification by flash column chromatography (silica gel, 10-20% Et₂O in pentane) gave cyclohexenone 9r (1.36 g, 12.3 mmol, 82%) as a clear oil.

¹H NMR (500 MHz, CD₂Cl₂) δ 6.80 (ddd, J = 10.2, 2.6, 1.3 Hz, 1H, =CHCH), 5.88 (dd, J = 10.1, 2.5 Hz, 1H, CH=CHCH), 2.58-2.50 (m, 1H, CHMe), 2.42 (dt, J = 16.7, 4.7 Hz, 1H, CHHC(=O)), 2.33 (ddd, J = 16.8, 12.2, 4.7 Hz, 1H, CHHC(=O)), 2.09 (ddq, J = 13.6, 5.0, 1.3 Hz, 1H, CHHCH), 1.68-1.61 (m, 1H, CHHCH), 1.14 (d, J = 7.3 Hz, 3H, CH₃).

¹³C NMR (125 MHz, CD₂Cl₂) δ 199.6 (C=O), 156.5 (CH=CHCH), 128.8 (CH=CHCH), 37.2 (CH₂C(=O)), 31.5 (CHMe), 31.3 (CH₂CH), 20.3 (CH₃).

GC-MS (GC-EI) m/z 110 [M⁺] (51), 95 (4), 82 (100), 79 (4), 68 (67), 65 (6), 54 (56), 41 (18), 39 (40), 27 (20).

HRMS (EI-GE) calc'd for C₇H₁₀O [M⁺] 110.0731, found 110.0732.

4-tert-Butyl-2-cyclohexenone (S-12): The title compound was prepared according to the general procedure B from 4-tert-butylcyclohexanone (2.31 g, 15.0 mmol). Purification by flash column chromatography (silica gel, 5% EtOAc in hexanes) gave cyclohexenone S-9 (1.52 g, 9.97 mmol, 66%) as a clear oil.

¹H NMR (500 MHz, CDCl₃) δ 6.99 (dt, J = 10.6, 2.1 Hz, 1H, =CHCH), 6.01 (dd, J = 10.4, 2.8 Hz, 1H, CH=CHCH), 2.50 (dt, J = 16.9, 3.9 Hz, 1H, CHHC(=O)), 2.32 (ddd, J = 16.4, 14.4, 4.9 Hz, 1H, CHHC(=O)), 2.20-2.16 (m, 1H, CHHCH), 2.11-2.05 (m, 1H, CHHCH), 1.76-1.67 (m, 1H, CHt-Bu), 0.96 (s, 9H, CH₃).

¹³C NMR (125 MHz, CDCl₃) δ 200.90 (C=O), 152.9 (CH=CHCH), 130.0 (CH=CHCH), 46.8 (CHt-Bu),
37.8 (CH₂C(=O)), 32.9 (C₆Me₃), 27.3 (3C, CH₃), 24.4 (CH₂CH).

**MS (EI-DE) m/z** 152 [M⁺] (5), 137 (5), 119 (1), 109 (6), 96 (100), 91 (2), 81 (5), 67 (11), 57 (83), 53 (6), 41 (53), 39 (23), 29 (36), 27 (19).

**HRMS (EI-FE) calcd for C₁₀H₁₆O [M⁺] 152.1202, found 152.1201.

2-Cyclooctenone (11d): The title compound was prepared according to the general procedure B from cyclooctanone (3.79 g, 30.0 mmol). Purification by flash column chromatography (silica gel, 5-10% Et₂O in pentane) gave 2-cyclooctenone (11d; 2.38 g, 19.2 mmol, 64%) as a clear oil.

**¹H NMR** (500 MHz, CD₂Cl₂) δ 6.33 (dt, J = 12.5, 7.1 Hz, 1H, CH₂C=), 5.94 (d, J = 12.5 Hz, 1H, CH₂CH=C=), 2.60 (t, J = 6.9 Hz, 2H, CH₂C(=O)), 2.52-2.47 (m, 2H, CH₂CH=), 1.82-1.77 (m, 2H, CH₂CH₂C(=O)), 1.63-1.53 (m, 4H, CH₂CH₂CH₂ and CH₂(CH₂)₂C(=O)).

**¹³C NMR** (125 MHz, CD₂Cl₂) δ 205.4 (C=O), 141.5 (CH₂C=), 132.2 (CH₂CH=C=), 42.7 (CH₂C=O), 28.6 (CH₂CH=), 25.3 (CH₂(CH₂)₃C(=O)), 23.2 (CH₂CH₂CH=), 22.7 (CH₂CH₂C=O).

**GC-MS (GC-EI) m/z** 124 [M⁺] (8), 109 (1), 95 (11), 91 (2), 81 (100), 68 (40), 65 (4), 53 (39), 51 (5), 41 (23), 39 (34), 27 (17).


(E)-2-Cyclododecenone (11e): The title compound was prepared according to the general procedure B from cyclododecanone (2.73 g, 15.0 mmol). Stoichiometric Pd(OAc)₂ (3.37 g, 15.0 mmol) in acetonitrile (20 mL) was used in the oxidation step. Purification by flash column chromatography (silica gel, 2% Et₂O in pentane) gave pure (E)-enone 11e (1.40 g, 7.80 mmol, 52%) as a clear oil.

**¹H NMR** (500 MHz, CD₂Cl₂) δ 6.74 (td, J = 15.3, 7.7 Hz, 1H, CH=CHCH₂), 6.29 (d, J = 16.1 Hz, 1H, CH=CHCH₂), 2.46-2.44 (m, 2H, CH₂C(=O)), 2.28-2.24 (m, 2H, CH=CHH₂), 1.71-1.67 (m, 2H, CH₂), 1.62-1.57 (m, 2H, CH₂), 1.42-1.37 (m, 2H, CH₂), 1.33-1.29 (m, 4H, CH₂), 1.28-1.21 (m, 4H, CH₂).

**¹³C NMR** (125 MHz, CD₂Cl₂) δ 203.1 (C=O), 146.7 (=CHCH₂), 131.4 (CH=CHCH₂), 40.2 (CH₂C(=O)), 32.8 (=CHCH₂), 26.8 (CH₂), 25.6 (CH₂), 25.4 (CH₂), 25.4 (CH₂), 25.0 (CH₂), 24.8 (CH₂), 24.0 (CH₂).
MS (EI) m/z (%) 180 [M⁺] (49), 162 (2), 151 (6), 137 (11), 123 (11), 109 (45), 98 (51), 95 (29), 84 (39), 81 (100), 68 (65), 55 (78), 41 (76), 27 (23).


(E)-2-Cyclopentadecenone (11f): The title compound was prepared according to the general procedure B from cyclopentadecanone (3.37 g, 15.0 mmol). Stoichiometric Pd(OAc)₂ (3.37 g, 15.0 mmol) in acetonitrile (20 mL) was used in the oxidation step. Purification by flash column chromatography (silica gel, 2% Et₂O in pentane) gave pure (E)-enone 11f (2.16 g, 9.71 mmol, 65%) as a clear oil.

¹H NMR (500 MHz, CD₂Cl₂) δ 6.78 (td, J = 15.3, 7.7 Hz, 1H, =C=CH₂CH₂), 6.16 (d, J = 16.1 Hz, 1H, CH=CHCH₂), 2.47-2.45 (m, 2H, CH₂C(=O)), 2.29-2.25 (m, 2H, =CHCH₂), 1.68-1.62 (m, 2H, CH₂), 1.56-1.51 (m, 2H, CH₂).

¹³C NMR (125 MHz, CD₂Cl₂) δ 201.5 (C=O), 148.0 (CH=CHCH₂), 130.8 (CH=CHCH₂), 40.1 (CH₂C(=O)), 31.7 (CHCH₂), 27.1 (CH₂), 27.0 (CH₂), 26.8 (3C, -(CH₂)₃), 26.6 (CH₂), 26.3 (CH₂), 26.1 (CH₂), 25.5 (CH₂), 25.3 (CH₂).

MS (EI) m/z (%) 222 [M⁺] (92), 207 (2), 193 (2), 179 (4), 164 (20), 151 (7), 135 (12), 121 (14), 109 (53), 96 (63), 81 (52), 68 (57), 55 (100), 41 (78), 29 (24).


Synthesis of 3-tert-butylcyclohex-2-enone (9k)³⁸

A flask was charged with 10% Pd/C (96 mg, 0.09 mmol, 2.5 mol%), CH₂Cl₂ (70 mL), TBHP (3.29 mL, 18.1 mmol, 5.5 M in decane, 5 equiv), K₂CO₃ (124 mg, 0.91 mmol, 25 mol%), and 1-tert-butylcyclohexene (500 mg, 3.62 mmol, 54 uL, 0.32 mmol, 1 equiv) under argon. The mixture was stirred at 0 °C for 12 h. After removal of the solvent at 0 °C under reduced, the crude product was purified by flash column chromatography (silica gel, 30-60% Et₂O in pentane) to provide the title compound (320 mg, 2.10 mmol, 58%) as a clear liquid.

¹H NMR (500 MHz, CD₂Cl₂) δ 5.88 (t, J = 1.3 Hz, 1H, =CH), 2.34 (td, J = 6.0, 1.3 Hz, 2H, CH₂Cqol), 2.30 (app. t, J = 6.6 Hz, 2H, CH₂C(=O)), 1.94 (quint, J = 6.3 Hz, 2H, CH₂CH₂CH₂), 1.12 (s, 9H, CH₃). ¹³C NMR (125 MHz, CD₂Cl₂) δ 200.4 (C=O), 173.9 (CH=CH), 123.1 (CH=CH), 37.8 (CH₂C(=O)), 36.9 (CqMe₃), 28.4 (3C, C(CH₃)₃), 26.3 (CH₂), 23.7 (CH₂).

GC-MS (GC-EI) m/z (%) 152 [M⁺] (31), 137 (11), 124 (35), 109 (100), 96 (67), 81 (39), 79 (13), 67 (32), 65 (7), 57 (20), 41 (32), 29 (7).

HRMS (EI-FE) calcd for C₁₀H₁₆O [M⁺] 152.1202, found 152.1201.

Synthesis of ((S)-3-Methyl-5-phenyl-2-cyclohexenone (S)-(9r))

Acetic acid (36.0 mg, 0.6 mmol, 60 mol%) was added to a solution of 9-amino(9-deoxy)epiquinine (1a; 64.7 mg, 0.2 mmol, 20 mol%) in toluene. After cooling to −15°C, 4-phenyl-2,6-heptandione (204 mg, 1.0 mmol) was added. The resulting mixture was stirred at −15°C for 48 h. The reaction mixture was then directly subjected to flash column chromatography (silica gel, 20% Et₂O in pentane) to afford the cyclohexenone derivative 9r (159 mg, 842 µmol, 84%; 95.5:4.5 er) as a colorless solid. The enantiomeric ratio was determined by HPLC using a chiral Chiralcel OJ-H column (10% i-PrOH in heptane, 0.5 mL/min); major enantiomer: \( \tau_R = 21.71 \text{ min} \), minor enantiomer: \( \tau_S = 3.86 \text{ min} \).

\(^1\)H NMR (500 MHz, CDCl₃) \( \delta \) 7.36-7.33 (m, 2H, CHPh), 7.27-7.23 (m, 3H, CHPh), 5.92 (s, 1H, =CH), (hept., \( J = 5.5 \text{ Hz} \), 1H, CH₆), 2.60-2.47 (m, 4H, CH₂), 2.00 (s, 3H, CH₃).

\(^13\)C NMR (125 MHz, CD₂Cl₂) \( \delta \) 198.8 (C=O), 162.0 (Cq=), 144.1 (CqPh), 129.0 (2C, CHPh), 127.2 (2C, CHPh), 127.1 (CH), 126.6 (CH), 44.3 (CH₂C(=O)), 41.2 (CH₆), 39.2 (CH₂C₆H₃), 24.4 (CH₃).

MS (EI-DE) m/z (%) 186 [M⁺] (41), 171 (2), 158 (1), 142 (6), 128 (4), 115 (4), 104 (14), 91 (4), 82 (100), 77 (7), 65 (3), 54 (10), 39 (10), 27 (2).


Synthesis of Cyclopentenones 16

Starting materials 16b, 16c, 16d, 16e have been reported in the literature.

Preparation of α-Branched α,β-Unsaturated Aldehydes

Compounds 19a, 19b, 19d and 19e were obtained from commercial sources (Sigma-Aldrich, TCI Europe) and used without purification if freshly purchased or distilled prior to use.

(E)-2-benzyl-5-phenylpent-2-enal (19c) Following the procedure of List et al.,43 to a solution of 3-phenylpropanal (1 g, 7.45 mmol, 1 equiv) in dichloromethane (7.45 mL) was added morpholinium trifluoroacetate (300 mg, 1.49 mmol, 0.2 equiv) and the mixture was stirred at reflux for 19 h. Removal of the solvent under reduced pressure and flash chromatography (10% Et₂O in pentane) afforded 19c as a colourless oil (800 mg, 3.2 mmol, 86%, E/Z = 97:3).

**1H NMR** (500 MHz, CDCl₃) δ 9.43 (s, 1H, CHO), 7.30-7.27 (m, 2H, CH₆), 7.24-7.20 (m, 3H, CH₆), 7.17-7.09 (m, 5H, CH₆), 6.61 (apparent t, J = 6.9 Hz, 1H, C=CH), 3.57 (s, 2H, PhCH₂), 2.77-2.70 (m, 4H, PhCH₂CH₂).

**13C NMR** (125 MHz, CDCl₃): δ 194.6, 154.8, 142.8, 140.5, 139.1, 128.6, 128.5, 128.4, 128.3, 126.4, 126.1, 34.5, 31.1, 29.7.

**FTIR** (thin film) 3085, 3062, 3027, 2924, 2821, 2716, 1680, 1639, 1601, 1495, 1453, 1137, 1076, 1030, 1002, 883, 733, 697 cm⁻¹

**HRMS (m/z)** calcd for C₁₈H₁₈O [M⁺]: 250.1358, found: 250.1357.

The spectroscopic data are identical in all respects to those previously reported.44

(E)-6-methyl-7-oxohept-5-en-1-y acetate (19f): Prepared by Grubbs metathesis from hex-5-en-1-y acetate and methacrylaldehyde according to the reported procedure.45

**1H NMR** (500 MHz, CDCl₃) δ 9.41 (s, 1H, CHO), 6.47 (tq, J = 7.3 Hz, J = 1.3 Hz, 1H, C=CH), 4.10 (t, J = 6.4 Hz, 2H, AcOCH₂), 2.40 (q, J = 7.5 Hz, 2H, CH₂C=CH), 2.06 (s, 3H, CO₂CH₃), 1.76-1.56 (m, 7H, CH₃, CH₂).

**13C NMR** (125 MHz, CDCl₃): δ 195.2, 171.1, 153.7, 139.8, 64.0, 28.5, 28.3, 24.9, 21.0, 9.3.

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**FTIR** (thin film) 2949, 2867, 2715, 2256, 1736, 1684, 1645, 1457, 1388, 1366, 1236, 1047, 908, 729 cm⁻¹


The physical data are identical in all respects to those previously reported.⁴⁵

**(E)-2-methyl-5-phenylpent-2-enal (19g)** Following the procedure of Chatterjee et al.,⁴⁵ to a stirring solution of Grubbs second generation catalyst (53 mg, 0.063 mmol, 6.3 mol%) and 4-phenyl-1-butene (150.2 μL, 1.0 mmol, 1 equiv) in dry dichloromethane (2.5 mL) under argon was added methacrylaldehyde (82.6 μL, 1.0 mmol, 1 equiv) dropwise via a syringe. The mixture was stirred at reflux for 12 h and the solvent was removed under reduced pressure. Purification by flash chromatography (4% Et₂O in pentane) afforded 19g as a yellow oil (226 mg, 1.3 mmol, 65%, E/Z > 20:1).

**¹H NMR** (500 MHz, CDCl₃) δ 9.38 (s, 1H, CHO), 7.33-7.19 (m, 5H, CH₅), 6.50 (tq, J = 7.3 Hz, J = 1.3 Hz, 1H, C=CH₂), 2.82 (apparent t, J = 7.5 Hz, 2H, PhCH₂), 2.68 (apparent q, J = 7.5 Hz, 2H, PhCH₂CH₂), 1.69 (br. s, 3H, CH₃).

**¹³C NMR** (125 MHz, CDCl₃): δ 195.3, 153.3, 140.6, 139.9, 128.6, 128.4, 126.3, 34.4, 30.7, 9.2.

**FTIR** (thin film) 3062, 3028, 2926, 2821, 2713, 1684, 1644, 1454, 1360, 1240, 1015, 700 cm⁻¹


The physical data are identical in all respects to those previously reported.⁴⁶

**2-methylcyclohex-1-enecarbaldehyde (19j)**: Following the procedure of Piers et al.,⁴⁷ to a solution of 1-methylcyclohept-1-ene (200 mg, 1.81 mmol, 1 equiv) in MeCN (9 mL), CCl₄ (9 mL) and water (13 mL) was added NaIO₄ (1.6 g, 7.60 mmol, 4.2 equiv) followed by RuO₂•xH₂O (4.8 mg, 0.036 mmol, 0.02 equiv), and the mixture was stirred vigorously for 1h at room temperature. The mixture was diluted with water and extracted with CH₂Cl₂ three times. The combined organic layers were washed with brine, dried over Na₂SO₄ and the

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solvent was carefully evaporated. The crude reaction mixture was diluted with CH₂Cl₂ (18 mL) and L-proline (20.7 mg, 0.18 mmol, 0.1 equiv) was added. After 14h, AcOH (104 uL, 1.81 mmol, 1 equiv) was added, and the reaction mixture was stirred at room temperature for 34h after which all of the starting material was consumed. The crude reaction mixture was diluted with ether, washed with sat. aq. NaHCO₃ and extracted with ether three times. The combined organic layers were washed with brine, dried over Na₂SO₄ and evaporated under reduced pressure. Flash chromatography (30% Et₂O in pentane) afforded 19j as a colourless oil (76.3 mg, 0.61 mmol, 34%).

¹H NMR (500 MHz, CDCl₃) δ 10.15 (s, 1H, CHO), 2.23–2.16 (m, 4H, CH₂C=CH₂), 2.14 (br s, 3H, CH₃), 1.66–1.57 (m, 4H, CH₂).

The spectroscopic data are identical in all respects to those previously reported.⁴⁷

Synthesis of (Z)-19g

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\[\begin{align*}
\text{F₃CH₂CO}_2PO & \rightarrow \text{BuOK} \rightarrow \text{F₃CH₂CO}_2PO \\
& \text{Me} \rightarrow \text{F₃CH₂CO}_2PO \\
& \text{Ph} \rightarrow \text{KHMDS} \rightarrow \text{Ph} \rightarrow \text{CHO} \\
& \text{DIBAL} \rightarrow \text{OH} \rightarrow \text{Swern} \rightarrow \text{(Z)-31g}
\end{align*}\]
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Methyl 2-(bis(2,2,2-trifluoroethoxy)phosphoryl)propanoate: Following the procedure of Sano et al.,⁴⁸ to a solution of tBuOK (1.27g, 11.3 mmol, 1.2 equiv) in THF (13 mL) was slowly added methyl bis(2,2,2-trifluoroethyl)phosphonoacetate (2 mL, 9.46 mmol, 1 equiv) at 0 °C under argon. The mixture was stirred at 0 °C for 30 min under argon, and methyl iodide (2.96 mL, 47.3 mmol, 5 equiv) was slowly added at 0 °C. The solution was warmed up to room temperature, stirred for 23 h and treated with a saturated aqueous solution of NH₄Cl. The reaction mixture was extracted with EtOAc three times, dried over Na₂SO₄, filtered and concentrated. Flash column chromatography eluting with 30% EtOAc in hexanes afforded the title compound as a colourless oil (2.30 g, 6.93 mmol, 73%).

1H NMR (500 MHz, CDCl₃) δ: 4.49-4.38 (m, 4H, F₃CC₂H₂), 3.78 (s, 3H, CO₂CH₃), 3.20 (dq, \(J_{H,P} = 22.8\) Hz, \(J = 7.4\) Hz, 1H, P(O)CH₂CH₃), 1.52 (dd, \(J_{H,P} = 19.3\) Hz, \(J = 7.4\) Hz, 3H, CH₃).

(Z)-methyl 2-methyl-5-phenylpent-2-enoate: Following the procedure of Still and Gennari, a solution of methyl 2-(bis(2,2,2-trifluoroethoxy)phosphoryl)propanoate (332 mg, 1 mmol, 1 equiv) and 18-crown-6 (1.32 g, 5 mmol, 5 equiv) in THF (20 mL) was cooled to -78 °C under argon and treated with KHMD (199.5 mg, 1 mmol, 1 equiv). 3-Phenylpropanal (133 μL, 1 mmol, 1 equiv) was added and the resulting mixture was stirred at – 78 °C for 1h. Saturated aqueous solution of NH₄Cl was added and the product was extracted with diethyl ether three times, dried over Na₂SO₄, filtered and concentrated. The title compound (Z/E > 20:1 by 1H NMR) was used without purification.

1H NMR (500 MHz, CDCl₃) δ: 7.30-7.17 (m, 5H, C₆H₅), 5.98 (td, \(J = 6.9\) Hz, \(J = 1.2\) Hz, 1H, C=CH), 3.72 (s, 3H, CO₂CH₃), 2.81-2.70 (m, 4H, PhCH₂CH₂), 1.89 (d, \(J = 1.2\) Hz, 3H, CH₃).

The physical data are identical in all respects to those previously reported.

(Z)-2-methyl-5-phenylpent-2-en-1-ol: Crude (Z)-methyl 2-methyl-5-phenylpent-2-enoate described above (1 mmol) was dissolved in dichloromethane (3 mL) under argon and cooled to -78 °C. DIBAL (4.8 mL, 1M in hexanes, 4.8 mmol, 4.8 equiv) was added dropwise and the solution was stirred for 1 h at – 78 °C. The reaction was quenched with aqueous Rochelle’s salt and stirred vigorously for 2 h. The crude reaction mixture was extracted with dichloromethane three times, dried over Na₂SO₄, filtered and concentrated. Flash column chromatography eluting with 15% diethyl ether in pentane afforded the title compound as a colourless oil (93.2 mg, 0.53 mmol, 53% over two steps).

1H NMR (500 MHz, CDCl₃) δ: 7.30-7.16 (m, 5H, C₆H₅), 5.33 (t, \(J = 7.6\) Hz, 1H, C=CH), 3.92 (s, 2H, C₆H₄OH), 2.66 (apparent t, \(J = 7.2\) Hz, 2H, PhCH₂CH₂), 2.37 (c. m, 2H, PhCH₂CH₂), 1.76 (d, \(J = 1.1\) Hz, 3H, CH₃).

The physical data are identical in all respects to those previously reported.\textsuperscript{50}

\((Z)\)-2-methyl-5-phenylpent-2-enal (\((Z)\)-19g): Oxalyl chloride (50.3 μL, 0.59 mmol, 2 equiv) was dissolved in dichloromethane (9 mL) and the solution was cooled to −78 °C. DMSO (83.2 μL, 1.17 mmol, 4 equiv) was added dropwise at −78 °C and the solution was stirred for 30 min. A solution of \((Z)\)-2-methyl-5-phenylpent-2-en-1-ol in dichloromethane (2 mL) was added dropwise and the reaction was stirred for 30 min. Et\textsubscript{3}N (244 μL, 1.76 mmol 6 equiv) was added dropwise and the solution was stirred for 1 h at −78 °C. The reaction was warmed up to room temperature, treated with a saturated aqueous solution of NH\textsubscript{4}Cl and extracted with dichloromethane three times, dried over Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated. \(^1\)H NMR analysis of the crude reaction mixture indicated \(Z/E\) ratio of 97:3. Flash column chromatography eluting with 15% diethyl ether in pentane afforded \((Z)\)-31g as a colourless oil (38.2 mg, 0.22 mmol, 75%, \(Z:E = 95:5\)).

\(^1\)HNMR (500 MHz, CDCl\textsubscript{3}) \(\delta\): 10.0 (s, 1H, CHO), 9.38 (s, 0.05 H, E-isomer, CHO), 7.31-7.17 (m, 5H, CH\textsubscript{Ar}), 6.53 (td, \(J = 8.0\) Hz, 1H, C=CH), 2.91-2.78 (m, 4H, PhCH\textsubscript{2}CH\textsubscript{2}), 1.76 (d, \(J = 1.1\) Hz, 3H, CH\textsubscript{3}).

\(^{13}\)C NMR (125 MHz, CDCl\textsubscript{3}): \(\delta\) 191.0, 147.9, 140.3, 136.6, 128.6, 128.5, 126.4, 35.7, 28.5, 16.4.

\textbf{FTIR} (thin film) 3063, 3028, 2925, 2859, 1678, 1645, 1496, 1435, 1242, 1016, 907, 730, 700 cm\textsuperscript{-1}.

The physical data are identical in all respects to those previously reported.\textsuperscript{51}

\(2\)-benzylacrylaldehyde (22a): Prepared from 3-phenylpropanal and formaldehyde according to the reported procedure.\textsuperscript{52}

\(^1\)H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\): 9.60 (s, 1H, CHO), 7.31-7.17 (m, 5H, CH\textsubscript{Ar}), 6.10 (s, 1H, C=CH\textsubscript{2}), 6.07 (s, 1H, C=CH\textsubscript{2}), 3.57 (s, 2H, PhCH\textsubscript{2}).

\(^{13}\)C NMR (125 MHz, CDCl\textsubscript{3}): \(\delta\) 194.0, 149.8, 138.1, 135.3, 129.2, 128.6, 126.5, 34.2.

\textbf{FTIR} (thin film) 3087, 3063, 3029, 2919, 2824, 2701, 1686, 1602, 1496, 1453, 1434, 1245, 1075, 950, 737, 699 cm\textsuperscript{-1}.


HRMS ($m/z$) calcd for C$_{10}$H$_{10}$O [M]$^+$: 146.0732, found: 146.0733.

2-methylenedec-9-enal (22b): Following the reported procedure,$^{52}$ pyrrolidine (17 μL, 0.2 mmol, 0.1 equiv) and 4-(dimethylamino)benzoic acid (66 mg, 0.4 mmol, 0.2 equiv) were dissolved in dichloromethane (2 mL) and 36.5% aq. formaldehyde (160 μL, 2 mmol, 1 equiv) was added followed by dec-9-enal (365 μL, 2 mmol, 1 equiv). The reaction was stirred at 45 °C for 45 min and cooled to r.t. The crude mixture was washed with 10% aq. NaHCO$_3$, extracted with dichloromethane three times, and the combined organic layers were washed with brine, dried over Na$_2$SO$_4$ and evaporated under reduced pressure. Flash column chromatography eluting with 5% Et$_2$O in pentane afforded 22b as a colourless oil (128.6 mg, 0.77 mmol, 39%).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.54 (s, 1H, CHO), 6.24 (c. m, 1H, HC(O)C=CH$_2$), 5.98 (br d, $J = 0.7$ Hz, 1H, HC(O)C=CH$_2$), 5.80 (ddt, $J = 17.1$ Hz, $J = 10.1$ Hz, $J = 6.7$ Hz, CH=CH$_2$), 5.02-4.91 (m, 2H, CH=CH$_2$), 2.23 (t, $J = 7.5$ Hz, 2H, H$_2$C=CCH$_2$), 2.06-2.00 (m, 2H, H$_2$C=CHCH$_2$), 1.49-1.29 (m, 8H).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 194.8, 150.5, 139.1, 133.9, 114.2, 33.7, 29.1, 28.9, 28.8, 27.8, 27.7.

FTIR (thin film) 3078, 2978, 2928, 2857, 1695, 1641, 1464, 1440, 1329, 995, 942, 910, 850 cm$^{-1}$

HRMS ($m/z$) calcd for C$_{11}$H$_{18}$O [M]$^+$: 166.1358, found: 166.1359.

The physical data are identical in all respects to those previously reported.$^{53}$

2-methylenepentanal (22c): Prepared from pentanal and formaldehyde according to the reported procedure.$^{52}$

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.55 (s, 1H, CHO), 6.26 (s, 1H, C=CH$_2$), 6.00 (s, 1H, C=CH$_2$), 2.21 (t, $J = 7.6$ Hz, 2H, H$_2$C=CCH$_2$), 1.49 (apparent sext, 2H, CH$_2$CH$_2$), 0.93 (t, $J = 7.4$ Hz, 3H, CH$_3$).

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 194.8, 150.2, 134.1, 29.8, 20.95, 14.1.

FTIR (thin film) 2961, 2932, 2874, 2704, 1686, 1640, 1464, 1379, 1087, 944, 876, 744 cm$^{-1}$

HRMS ($m/z$) calcd for C$_6$H$_{10}$O [M]$^+$: 98.0732, found: 98.0731.

2-methylenedecanal (22d): Prepared from decanal and formaldehyde according to the reported procedure.$^{52}$

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\textbf{1H NMR} (500 MHz, CDCl$_3$) $\delta$ 9.71 (s, 1H, CHO), 6.25 (br s, 1H, C=CH$_2$), 5.99 (br s, 1H, C=CH$_2$), 2.23 (t, $J$ = 7.6 Hz, 2H, H$_2$C=C=CH$_2$), 1.44 (c. m, 2H, CH$_2$), 1.33-1.23 (m, 10H, C$_7$H$_{15}$), 0.88 (t, $J$ = 6.7 Hz, 3H, CH$_3$).

\textbf{13C NMR} (125 MHz, CDCl$_3$): $\delta$ 194.9, 150.5, 134.0, 31.9, 29.4, 29.3, 29.2, 27.77, 27.75, 22.7, 14.1.

\textbf{FTIR} (thin film) 2926, 2856, 2256, 1694, 1628, 1466, 1330, 1106, 942, 907, 729 cm$^{-1}$

\textbf{HRMS} ($m/z$) calcd for C$_{11}$H$_{20}$O [M$^+$]: 168.1514, found: 168.1514.

\textbf{2-methylene-3-phenylbutanal (rac-22e)}: Prepared from 3-phenylbutanal and formaldehyde according to the reported procedure.\textsuperscript{52}

\textbf{1H NMR} (500 MHz, CDCl$_3$) $\delta$ 9.54 (s, 1H, CHO), 7.30-7.18 (m, 5H, CH$_\text{Ar}$), 6.24 (br d, $J$ = 1.1 Hz, 1H, , C=CH$_2$), 6.08 (br s, 1H, , C=CH$_2$), 4.03 (q, $J$ = 7.2 Hz, 1H, CH$_3$CH), 1.43 (d, 7.1 Hz, 3H, CH$_3$).

\textbf{13C NMR} (125 MHz, CDCl$_3$): $\delta$ 193.9, 154.3, 143.6, 133.7, 128.4, 127.5, 126.4, 37.2, 20.0.

\textbf{FTIR} (thin film) 3062, 3029, 2972, 2937, 2878, 2817, 2670, 2256, 1693, 1493, 1453, 1245, 948, 907, 730, 699 cm$^{-1}$

\textbf{HRMS} ($m/z$) calcd for C$_{11}$H$_{12}$O [M$^+$]: 160.0888, found: 160.0886.

The spectroscopic data are identical in all respects to those previously reported.\textsuperscript{52}
Mechanistic Studies

Structure Activity Correlations

In order to evaluate the role of the primary amine moiety in 1a in covalent aminocatalysis, we carried out the epoxidation of 2-cyclohexen-1-one 9a in the presence of derivatives S-13-S-16 and their salts as catalysts. The results employing the standard catalyst salt [1a·2 TFA] are provided for comparison in entry 1. As expected, the N-methylated amine S-13, which represents a more congested secondary amine equivalent of catalyst 1a, mediated the reaction with a significantly diminished yield and lower enantioselectivity (entry 2). Catalyst S-14, which is capable of hydrogen bonding catalysis but lacks a primary amine moiety was found to give racemic product in a very low yield (entry 3). Interestingly, pairing this catalyst with the Brønsted acid co-catalyst TFA dramatically improved the enantioselectivity, although the yield remained low (entry 4). Sulfonamide catalyst S-15 was found to give only traces of the product in the presence or absence of the Brønsted acid co-catalyst (entries 5-6), though a similar effect of the Brønsted acid co-catalyst was observed on the enantioselectivity of the reaction as with the thiourea derivative S-14. Quinine S-16 and its ammonium salt [S-16·TFA] showed no activity (entries 8-10). Taken together, these results suggest that although noncovalent catalysis is feasible in the reaction, it achieves only very low yields and modest enantioselectivity (entries 4 and 6). Indeed, the presence of the primary amine moiety in 1a is crucial for the observed reaction rate and enantioselectivity, supporting a mechanism proceeding through iminium activation and not via other activation modes such as general base catalysis or phase-transfer catalysis.

ESI-MS Studies

We monitored the hydroperoxidation and epoxidation of acyclic enones by using Electrospray-Ionization Mass Spectroscopy (ESI-MS). For this purpose we carried out the reaction of 3-decen-2-one (2a) with aqueous hydrogen peroxide in the presence of catalytic amounts of the 9-amino(9-deoxy)epiquinine catalyst salt [1a • 2 TXA] (X = F, Cl). In one experiment, the standard conditions of the epoxidation reaction were used (Scheme 1a), and in the other, the optimized hydroperoxidation protocol was employed (Scheme 1b).

**Scheme 1.** Test reactions for ESI-MS analysis: reaction of 3-decen-2-one (2a) with hydrogen peroxide under (a) epoxidation and (b) hydroperoxidation conditions.
Samples were taken from the reaction mixtures at different time intervals over 24 hours and submitted to ESI-MS analysis. Spectra recorded prior to hydrogen peroxide addition (Figure 1) and after 1 and 12 hours of reaction time, respectively, are depicted in the following figures (Figure 2 and Figure 3).

It should be noted that 3-decen-2-one (2a), its corresponding epoxide 4a and peroxide 3a could not be detected by ESI-MS, as the spectrometer utilized could only detect molecules with molecular weights higher than 200 g mol$^{-1}$. Therefore, neither signals corresponding to the starting material nor to the products appear in Figures 1-3.

The ESI-MS spectra of the samples taken prior to hydrogen peroxide addition (Figure 1) showed a signal at $m/z$ 460 which corresponds to the iminium ion A formed by condensation of 9-amino(9-deoxy)epiquinine (1a) with 3-decen-2-one (2a). Moreover, the signal of 9-amino(9-deoxy)epiquinine at $m/z$ 324 [(1a+H)$^+$] could be identified. The signal at $m/z$ 596 could not be assigned at this stage.

The fact that the signal at $m/z$ 460 could not be detected any longer after addition of hydrogen peroxide (Figure 2), indicates that iminium ion A is consumed by hydrogen peroxide, and thus validates our assumption that iminium ions such as A are indeed intermediates in our epoxidation/hydroperoxidation reaction. The signal corresponding to 9-amino(9-deoxy)epiquinine at $m/z$ 324 [(1a+H)$^+$] is still present. After 1 h of reaction time, two new signals have appeared at $m/z$ 476 and 494, which match the masses of the iminium ion B derived from 2,3-epoxy-2-decanone (4a) and iminium ion C derived from the corresponding $\beta$-hydroperoxyketone which upon hydrolysis affords peroxyhemiketal 3a.

![Figure 1. ESI-MS spectrum of reaction (a) recorded prior to H$_2$O$_2$-addition.](image-url)
Figure 2. ESI-MS spectra after 1 hour from the reaction (a) with [1a • 2 TFA] at 50 °C and (b) [1a • 2 TCA] at 32 °C.

The fact that the signal of the unsaturated iminium ion A at m/z 460 cannot be detected in the presence of hydrogen peroxide suggests that its concentration remains low under reaction conditions. Thus, based on these results, we may propose that neither the conjugate H$_2$O$_2$-addition nor the intramolecular epoxide closure, but indeed the formation of the iminium ion intermediate A represents the rate-limiting step of these transformations.

More specifically, as we have shown that the iminium ion is generally detectable if present in the reaction mixture and at the same time we don’t detect A any more when hydrogen peroxide is present,
we can conclude that its concentration under these conditions is low. Therefore the iminium ion formation has to be slower than the peroxide addition. At the same time, as we can detect the iminium ion resulting from peroxide addition \( \text{C} \), the iminium ion resulting from ring closure \( \text{B} \) and the free catalyst \( 1\text{a} \) alongside each other the rates of their formation and consumption have to be of comparable magnitude. Thus our proposed catalytic cycle consists of 3 comparably fast reactions and one clearly slower one, which leads us to propose that the iminium ion formation is the rate limiting step of our reaction.

Additionally in reaction (a) run at 50 °C, additional signals at \( m/z \) 340, 492, and 510 can be detected which presumably arise from the oxidation of the catalyst under reaction conditions (Figure 2a). Since an excess of oxidant was used and the amine was employed in catalytic amount, we expect that the signal at \( m/z \) 340 may correspond to monooxygenated 9-amino(9-deoxy)epiquinine \( 1\text{a}_{\text{o}} \). Moreover, signals at \( m/z \) 492 and 510 were assigned to iminium ions \( \text{B}_{\text{o}} \) and \( \text{C}_{\text{o}} \), analogous to \( \text{B} \) and \( \text{C} \), but incorporating oxygenated 9-amino(9-deoxy)epiquinine \( 1\text{a}_{\text{o}} \) instead of \( 1\text{a} \). On the contrary, in reaction (b) run at 32 °C only one signal of low intensity at \( m/z \) 510 was detected to witness beginning catalyst oxidation (Figure 2b).

After 12 hours at 50 °C, the ESI-MS spectrum of the sample from reaction (a) indicates extensive catalyst oxidation (Figure 3a). Strong signals at \( m/z \) 340 and 492 match (as mentioned above) monooxygenated 9-amino(9-deoxy)epiquinine \( 1\text{a}_{\text{o}} \) and its corresponding iminium ion formed with \( \alpha,\beta \)-epoxy decanone \( \text{B}_{\text{o}} \), respectively. On the contrary, signals at \( m/z \) 324, 476, and 494 have suffered a considerable loss of intensity. The epoxidation of decenone at 50 °C with \([1\text{a} \cdot 2 \text{TFA}] \) (10 mol%) generally requires 10 hours to go to completion. Partially oxidized amine \( 1\text{a}_{\text{o}} \) could already be detected after 1 h of reaction time (at ~20% conversion). Double oxidation of amine \( 1\text{a} \), in other words a signal at \( m/z \) 356, could not be perceived throughout the ESI-MS experiments.
Figure 3. ESI-MS spectra after 12 hours from the reaction (a) with [1a • 2 TFA] at 50 °C and (b) [1a • 2 TCA] at 32 °C.
**N-oxidation of catalyst 1a**

**Synthesis of 9-amino(9-deoxy)epiquinine N-oxide (24)**

9-amino(9-deoxy)epiquinine N-oxide (24): 9-Amino-(9-deoxy)epiquinine (1a) (100 mg, 0.31 mmol) was dissolved in dichloromethane (3 mL) and cooled to −78 °C. Under ambient atmosphere, m-CPBA (60 mg, 0.27 mmol, 0.87 equiv, 77% purity) was added, and the reaction mixture was stirred for 1 h at −78 °C. The crude reaction mixture was then directly loaded onto a silica gel column packed with a 900:100:6.5 solvent mixture of CH$_2$Cl$_2$:MeOH:NH$_3$ conc. and eluted with the same solvent mixture. The first eluted product corresponds to the excess starting material (1a). Further elution yielded the title compound 24 as an oil which becomes a highly hygroscopic amorphous white foam after washing with ether and evaporating the solvent under reduced pressure (92.8 mg, 0.27 mmol, quant. based on m-CPBA.).

$^1$H NMR (500 MHz, MeOD) δ 8.71 (d, $J = 4.6$ Hz, 1H, H-2’), 7.98 (d, $J = 9.2$ Hz, 1H, H-8’), 7.73 (br s, 1 H, H-5’), 7.64 (d, $J = 4.6$ Hz, 1H, H-3’), 7.48 (dd, $J = 9.2$ Hz, $J = 2.5$ Hz, 1H, H-7’), 5.92 (ddd, $J = 17.2$ Hz, $J = 10.5$ Hz, $J = 6.8$ Hz, 1H, H-10), 5.38-5.08 (m, 3H, H-9 + H-11), 4.08 (c. m, 1H, H-6b), 4.03 (s, 3H, C-12), 3.89 (br s, 1H, H-8), 3.70 (dd, $J = 12.9$ Hz, $J = 10.6$ Hz, 1H, H-2a), 3.53-3.37 (m, 2H, H-2b + H-6a), 2.99-2.88 (m, 1H, H-3), 2.15-1.79 (m, 3H, H-5 + H-7b), 1.76 (c. m, 1H, H-4), 1.09-0.99 (m, 1H, H-7a).

$^{13}$C NMR (150 MHz, MeOD) δ 160.3 (C-6’), 148.4 (C-2’), 147.6 (C-8a’), 144.9 (C-4’), 139.3 (C-10), 131.5 (C-8’), 129.7 (C-4a’), 124.15 (C-7’), 121.8 (C-3’), 117.2 (C-11), 102.0 (C-5’), 74.7 (C-8), 71.7 (C-2), 58.5 (C-6), 56.3 (C-12), 52.0 (C-9), 41.6 (C-3), 28.8 (C-7), 28.0 (C-4), 27.8 (C-5).

$^{15}$N-NMR (60 MHz, MeOD, $\delta_{\text{N}\text{H}} = 0$ ppm) δ 296.5 (quinoline N), 117.5 (N-oxide), primary amine could not be detected.

FTIR (thin film) 3264, 2943, 2216, 1620, 1590, 1507, 1474, 1432, 1359, 1309, 1263, 1236, 1175, 1135, 1083, 1028, 987, 909, 856, 830, 725.


S-126
Kinetic study

A kinetic study on the oxidation of the amine salt [1a·2TFA] to [24·2TFA] was performed by taking aliquots of the reaction over 18 h (Table 1). Two methods were employed to determine the reaction conversion: aliquots diluted in THF-d8 (approx. 0.1 mL sample + 0.3 mL THF-d8) were analyzed by 1H NMR spectrometry, and aliquots diluted in MeOH (0.2 -1 μL in 1 mL MeOH) were analyzed by ion pair chromatography (IPC, 50 mm Zorbax Eclipse Plus C18, 1.8 μm, 4.6 mm i.D.; mobile phase: methanol/5 mm DiKGA pH 4.6 = 50:50, 1.0 mL/min, 220 nm, 308K). The conversion vs. time graph (Figure 4) was plotted using the average conversion obtained from both methods. This graph shows no apparent autocatalytic effect.

Table 4. Conversion of the amine salt [1a·2TFA] to [24·2TFA] in the presence of excess aq. H2O2, monitored over 18 h.

<table>
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<tr>
<th>Reaction time, h</th>
<th>Conv. % (NMR)</th>
<th>Conv. % (IPC)</th>
<th>Reaction time, h</th>
<th>Conv. % (NMR)</th>
<th>Conv. % (IPC)</th>
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</table>
Figure 4. Oxidation of the amine salt [1a·2TFA] to [24·2TFA] in the presence of excess aq. H₂O₂.

Reduction of 9-amino(9-deoxy)epiquinine N-oxide 40 to 9-amino(9-deoxy)epiquinine 1a

9-Amino(9-deoxy)epiquinine N-oxide (24) (20.6 mg, 0.061 mmol) was dissolved in acetone (0.8 mL) and H₂SO₃ (6% wt, 0.1 mL, 0.073 mmol, 1.2 equiv) was added dropwise at 0 °C. The reaction mixture was stirred for 17 h, dissolved in dichloromethane, washed with sat. aq. NaHCO₃, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. The resulting white amorphous foam (11.1 mg, 0.034 mmol, 56%) was obtained as a spectroscopically pure compound, whose physical data were identical in all respects to 9-amino-(9-deoxy)epiquinine (1a).
The Effect of the Counteranion Coordination Strength in Catalyst Salts [1a·2HX] on the Enantioselectivity of Enal Epoxidation

\[
\begin{align*}
\text{Et} &\quad \text{Me} \\
\text{19a} &\quad \text{O} \\
\text{H} \quad \text{H} \\
\end{align*}
\]

\[
\begin{align*}
\text{Et} &\quad \text{Me} \\
\text{20a} &\quad \text{O} \\
\text{H} \quad \text{H} \\
\end{align*}
\]

1a (10 mol%) acid (20 mol%)

Conditions A: H₂O₂ (50 wt. %, 5 equiv), THF (0.125 M), 50 °C, 24 h

Conditions B: H₂O₂ (50 wt. %, 1.5 equiv), 1,4-Dioxane (0.125 M), 50 °C, 24 h

<table>
<thead>
<tr>
<th>Entry</th>
<th>Acid co-catalyst</th>
<th>Conditions</th>
<th>Conversion, %</th>
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<th>er (trans)</th>
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</table>

\(^a\) Determined by GC, \(^b\) Determined by chiral-phase GC.
NMR Investigations of Imine Salts 26

(S,E)-1-(6-methoxyquinolin-4-yl)-N-((E)-2-methyl-3-phenylallylidene)-1-(((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methanamine (25): 9-Amino-(9-deoxy)epiquinine (1a) (400 mg, 1.24 mmol) and (E)-2-methyl-3-phenylacrylaldehyde (183 µL, 1.30 mmol, 1.05 equiv) were dissolved in methanol (4 mL) and activated 4 Å molecular sieves (0.5 g) were added. After stirring the reaction mixture overnight, TLC control (CH$_2$Cl$_2$: MeOH:conc.9:1:0.065) showed the disappearance of the starting material. The mixture was filtered through a pad of Celite washing with dichloromethane, and the solvent was evaporated under reduced pressure to afford the title compound in quantitative yield, containing 5% of the excess (E)-2-methyl-3-phenylacrylaldehyde. This compound was found to be fairly stable to hydrolysis and could be handled in the air and with non-dried solvents. For long-term storage, it was kept under argon at 4 °C as a solid and in a vacuum-sealed NMR tube as a solution.

$^1$H NMR (600 MHz, CDCl$_3$) δ 8.64 (d, $J = 4.5$ Hz, 1H, H-2’), 7.96 (s, 1H, H-13), 7.92 (d, $J = 9.2$ Hz, 1H, H-8’), 7.87 (d, $J = 2.8$ Hz, 1H, H-5’), 7.39 (d, $J = 4.5$ Hz, 1H, H-3’), 7.28 (dd, $J = 9.2$ Hz, $J = 2.8$ Hz, 1H, H-7’), 7.25-7.16 (m, 5H, H-18 + H-19 + H-20), 6.67 (br s, 1H, H-16), 5.69 (ddd, $J = 17.3$ Hz, $J = 10.3$ Hz, $J = 7.4$ Hz, 1H, H-10), 4.88 (ddd, $J = 17.3$ Hz, $J < 2$ Hz, $J < 2$ Hz 1H, H-11a), 4.84 (ddd, $J = 10.3$ Hz, $J < 2$ Hz, $J < 2$ Hz 1H, H-11b), 4.69 (d, $J = 9.5$ Hz, 1H, H-9), 3.89 (s, 3H, H-12), 3.53 (ddd, $J = 10$ Hz, $J = 9.5$ Hz, $J = 8$ Hz 1H, H-8), 3.15 (dd, $J = 13.8$ Hz, $J = 10.3$ Hz, 1H, H-2a), 3.13 (ddd, $J = 14$ Hz, $J = 9$ Hz, $J = 2.5$ Hz, 1H, H-6b), 2.69 (ddd, $J = 14$ Hz, $J = 10.5$ Hz, $J = 5.9$ Hz, 1H, H-6a), 2.67 (dd, $J = 13.8$ Hz, $J = 6.0$ Hz, 1H, H-2b), 2.15 (c. m, 1H, H-3), 2.07 (d, $J < 2$ Hz, 3H, H-15), 1.56 (c. m, 1H, H-4), 1.47 (c. m, 2H, H-5a + H-5b), 1.26 (ddd, $J = 13.7$ Hz, $J = 10$ Hz, $J = 3.7$ Hz, 1H, H-7b), 0.81 (ddd, $J = 13.7$ Hz, $J = 8$ Hz, $J < 2$ Hz, 1H, H-7a).

$^{13}$C NMR (150 MHz, CDCl$_3$) δ 165.7 (C-13), 157.3 (C-6’), 147.7 (C-2’), 146.1 (C-4’), 145.1 (C-8’), 142.0 (C-10), 139.44 (C-16), 137.15 (C-14), 136.7 (C-17), 131.7 (C-8’), 129.3 (C-19), 128.3 (C-18), 128.0 (C-19), 127.1 (C-21), 126.7 (C-18), 126.3 (C-17), 126.0 (C-16), 125.6 (C-15), 123.9 (C-14), 121.0 (C-2), 118.8 (C-3), 106.7 (C-13), 104.2 (C-14), 103.1 (C-15), 101.7 (C-16), 99.1 (C-17), 98.5 (C-18), 96.6 (C-19), 95.2 (C-20), 93.0 (C-21), 90.0 (C-22), 88.7 (C-23), 87.4 (C-24), 86.1 (C-25), 84.8 (C-26), 83.5 (C-27), 82.2 (C-28), 81.0 (C-29), 79.8 (C-30), 78.6 (C-31), 77.4 (C-32), 76.2 (C-33), 75.0 (C-34), 73.8 (C-35), 72.6 (C-36), 71.4 (C-37), 70.2 (C-38), 69.0 (C-39), 67.8 (C-40), 66.6 (C-41), 65.4 (C-42), 64.2 (C-43), 63.0 (C-44), 61.8 (C-45), 60.6 (C-46), 59.4 (C-47), 58.2 (C-48), 57.0 (C-49), 55.8 (C-50), 54.6 (C-51), 53.4 (C-52), 52.2 (C-53), 51.0 (C-54), 49.8 (C-55), 48.6 (C-56), 47.4 (C-57), 46.2 (C-58), 45.0 (C-59), 43.8 (C-60), 42.6 (C-61), 41.4 (C-62), 40.2 (C-63), 39.0 (C-64), 37.8 (C-65), 36.6 (C-66), 35.4 (C-67), 34.2 (C-68), 33.0 (C-69), 31.8 (C-70), 30.6 (C-71), 29.4 (C-72), 28.2 (C-73), 27.0 (C-74), 25.8 (C-75), 24.6 (C-76), 23.4 (C-77), 22.2 (C-78), 21.0 (C-79), 19.8 (C-80), 18.6 (C-81), 17.4 (C-82), 16.2 (C-83), 15.0 (C-84), 13.8 (C-85), 12.6 (C-86), 11.4 (C-87), 10.2 (C-88), 9.0 (C-89), 7.8 (C-90), 6.6 (C-91), 5.4 (C-92), 4.2 (C-93), 3.0 (C-94), 1.8 (C-95), 0.8 (C-96).
128.0 (C-4a’), 127.6 (C-20), 121.5 (C-3’), 121.3 (C-7’), 114.2 (C-11), 103.3 (C-5’), 74.8 (C-9), 60.4 (C-8), 56.6 (C-2), 55.5 (C-12), 41.0 (C-6), 40.0 (C-3), 28.35 (C-5), 28.0 (C-4), 26.0 (C-7), 13.5 (C-15).

$^{15}$N-NMR (60 MHz, CDCl$_3$, $\delta$$_{NNH}$ = 0 ppm) $\delta$ 333.8 (imine N), 305.2 (quinoline N), 24.3 (quinuclidine N).

MS (EI): $m/z$ = 451 [M], 308, 293, 266, 225, 199, 173, 160, 136, 81, 42.

HRMS ($m/z$) calcd for C$_{30}$H$_{33}$N$_3$ONa [M+H]$^+$: 474.2516. Found: 474.2519.
(S,E)-1-(6-methoxyquinolin-4-yl)-N-((E)-2-methyl-3-phenylallylidene)-1-((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methanamine trifluoroacetic acid salt (26a): Imine 25 (20 mg, 0.044 mmol) was dissolved in dry CDCl₃ in a flame-dried two-necked flask containing 20 mg activated 4 Å molecular sieves. To this suspension, trifluoroacetic acid (3.3 μL, 0.044 mmol, 1 equiv) was added. After stirring for 5 min, the solution was transferred into a flame-dried NMR tube using an HPLC syringe filter to remove molecular sieves and sealed under vacuum.

1H NMR (600 MHz, CDCl₃) δ 12.5 (br s, 1H, NH), 8.73 (d, J = 4.4 Hz, 1H, H-2’), 8.02 (d, J = 9.4 Hz, 1H, H-8’), 7.99 (s, 1H, H-13), 7.75 (br s, 1H, H-5’), 7.38 (dd, J = 9.4 Hz, J = 2.8 Hz, 1H, H-7’), 7.35 (br s, 1H, H-3’), 7.31-7.22 (m, 5H, H-18 + H-19 + H-20), 6.68 (br s, 1H, H-16), 5.68 (ddd, J = 17.2 Hz, J = 6.6 Hz, 1H, H-10), 5.16-5.07 (m, 2H, H-11a + H-11b), 4.90 (br s, 1H, H-9), 4.28 (br s, 1H, H-8), 3.98 (s, 3H, H-12), 3.72 (dd, J = 14 Hz, J = 10 Hz, 1H, H-2a), 3.52 (c. m, 1H, H-6b), 3.35 (c. m, 1H, H-6a), 3.27 (c. m, 1H, H-2b), 2.65 (dt, J = 10 Hz, J = 5.2 Hz, 1H, H-3), 2.18 (d, J = 1.2 Hz, 3H, H-15), 2.00 (c. m, 1H, H-4), 1.96 (c. m, 2H, H-5a + H-5b), 1.71 (dd, J = 13.2 Hz, J = 10.8 Hz, 1H, H-7b), 1.35 (d, J = 13.2, 1H, H-7a).

13C NMR (150 MHz, CDCl₃) δ 169.6 (C-13), 162.3 (q, J = 34.3 Hz, COCF₃), 158.3 (C-6’), 147.2 (C-2’), 145.4 (C-4’), 142.1 (2C, C-8a’ + 16), 137.1 (2C, C-14 + C-10), 136.1 (C-17), 132.3 (C-8’), 129.5 (C-18), 128.3 (C-19), 128.1 (C-20), 127.1 (C-4a’), 122.5 (C-7’), 122.1 (C-3’), 117.3 (C-11), 116.9 (q, J = 293.7 Hz, COCF₃), 103.7 (C-5’), 74.4 (C-9), 60.0 (C-8), 56.1 (C-12), 53.8 (C-2), 40.5 (C-6), 36.9 (C-3), 27.0 (C-4), 24.9 (C-5), 24.3 (C-7), 12.7 (C-15)

15N-NMR (60 MHz, CDCl₃, δNH = 0 ppm,) δ 318.3 (imine N), 310.4 (quinoline N), 40.5 (quinuclidine N).

19F-NMR (376 MHz, CDCl₃) δ -79.5.

MS or HRMS were not performed due to extreme sensitivity of the title compound to hydrolysis.
Selected NOESY correlation

![Diagram 1]

Selected NOESY correlation

![Diagram 2]

\[ J_{8H-9H} \approx 10 \text{ Hz} \]

\[ \phi_{8C8C9H9} \approx 180^\circ \]
(S,E)-1-(6-methoxyquinolin-4-yl)-N-((E)-2-methyl-3-phenylallylidene)-1-((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methanamine bis-trifluoroacetic acid salt (26b): Imine 25 (19.9 mg, 0.044 mmol) was dissolved in dry CDCl\textsubscript{3} in a flame-dried two-necked flask containing 20 mg activated 4 Å molecular sieves. To this suspension trifluoroacetic acid (6.5 μL, 0.088 mmol, 2 equiv) was added. After stirring for 5 min, this solution was transferred to a flame-dried NMR tube using an HPLC syringe filter to remove molecular sieves and sealed under vacuum.

\textbf{1H NMR} (600 MHz, CDCl\textsubscript{3}) \(\delta\) 12.0 (br s, 1H, N\textsubscript{H}), 8.88 (d, \(J = 5.0\) Hz, 1H, H-2\textsuperscript{'}), 8.23 (d, \(J = 9.3\) Hz, 1H, H-8\textsuperscript{'}), 8.13 (s, 1H, H-13), 7.98 (br s, 1H, H-13), 7.77 (d, \(J = 9.3\) Hz, 1H, H-3\textsuperscript{'}), 7.50 (dd, \(J = 9.2\) Hz, \(J = 2.4\) Hz, 1H, H-7\textsuperscript{'}), 7.30-7.18 (m, 5H, H-18 + H-19 + H-20), 6.74 (s, 1H, H-16), 5.66 (ddd, \(J = 17.2\) Hz, \(J = 10.4\) Hz, \(J = 6.4\) Hz, 1H, H-10), 5.15 (c. m, 1H, H-9). 5.13 (dd, \(J = 10.2\) Hz, \(J = 1.2\) Hz, 1H, H-11a), 5.10 (dd, \(J = 17.2\) Hz, \(J = 1.2\) Hz, 1H, H-11b), 4.34 (dt, \(J = 9.6\) Hz, \(J = 6.0\) Hz, 1H, H-8), 4.03 (s, 3H, H-12), 3.67 (c. m, 1H, H-6b), 3.65 (dd, 1H, \(J = 13.8\) Hz, \(J = 10.6\) Hz, H-8a), 3.34 (c. m, 1H, H-6a), 3.31 (ddd, \(J = 13.8\) Hz, \(J = 6.0\) Hz, \(J = 1.6\) Hz, 1H, H-2b), 2.65 (dt, \(J = 10.8\) Hz, \(J = 6.0\) Hz, 1H, H-3), 2.15 (d, \(J = 1.2\) Hz, 3H, H-15), 2.12-1.90 (m, 3H, H-4 + H-5a + H-5b), 1.74 (ddd, \(J = 13.6\) Hz, \(J = 9.6\) Hz, \(J = 2.0\) Hz, 1H, H-7b), 1.40 (d, \(J = 13.6\) Hz, 1H, H-7a).

\textbf{13C NMR} (150 MHz, CDCl\textsubscript{3}) \(\delta\) 171.2 (C-13), 162.1 (q, \(J = 35.7\) Hz, COCF\textsubscript{3}), 159.7 (C-6\textsuperscript{'}), 147.7 (C-4\textsuperscript{'}), 143.4 (C-16), 143.0 (C-2\textsuperscript{'}), 139.5 (C-8a\textsuperscript{'}), 136.6 (C-10), 136.5 (C-14), 135.7 (C-17), 129.5 (C-19), 128.4 (C-20), 128.36 (C-18), 128.0 (C-4a\textsuperscript{'}), 127.3 (C-8\textsuperscript{'}), 125.6 (C-7\textsuperscript{'}), 122.5 (C-3\textsuperscript{'}), 117.6 (C-11), 116.6 (q, \(J = 291.4\) Hz, COCF\textsubscript{3}), 103.6 (C-5\textsuperscript{'}), 73.2 (br, C-9), 59.8 (C-8), 56.4 (C-12), 53.8 (C-2), 40.9 (C-6), 36.6 (C-3), 26.8 (C-4), 24.4 (C-5), 23.9 (C-7), 12.6 (C-15).

\textbf{15N-NMR} (60 MHz, CDCl\textsubscript{3}, \(\delta_{NH3} = 0\) ppm) \(\delta\) 313.9 (imine-N), quinoline N could not be detected, quinuclidine N could not be detected.

\textbf{15N-NMR} (60 MHz, CDCl\textsubscript{3}, \(T = 296\) K, \(\delta_{NH3} = 0\) ppm) \(\delta\) 294 (quinoline N), 103 (N-oxide), amide N not detected under these conditions.

\textbf{19F-NMR} (376 MHz, CDCl\textsubscript{3}) \(\delta\) -79.5.
MS or HRMS was not performed due to extreme sensitivity of the title compound to hydrolysis.

Selected NOESY correlation

(S,E)-1-(6-methoxyquinolin-4-yl)-N-((E)-2-methyl-3-phenylallylidene)-1-((1S,2S,4S,5R)-5 vinylquinuclidin-2-yl)methanamine (R)-TRIP salt (26c) :
Imine 25 (20 mg, 0.044 mmol) was dissolved in dry CDCl$_3$ in a flame-dried two-necked flask containing 20 mg activated 4 Å molecular sieves. To this suspension, (R)-TRIP (21a) (31 mg, 0.044 mmol, 1 equiv) was added. After stirring for 5 min, this solution was transferred to a flame-dried NMR tube using an HPLC syringe filter to remove molecular sieves and sealed under vacuum.

$^1$H NMR (600 MHz, CDCl$_3$, 223K, 2 conformers in 3:1 ratio, only major conformer described) δ 12.72 (br s, 1H, NH), 8.83 (d, $J = 4.7$ Hz, 1H, H-2’), 8.08 (d, $J = 9.3$ Hz, 1H, H-8’), 7.88 (d, $J = 8.4$ Hz, 2H, H-5a), 7.85 (s, 2H, H-3a), 7.49 (dd, $J = 8.2$ Hz, $J = 5.4$ Hz, 2H, H-6a), 7.45 (dd, $J = 9.4$ Hz, $J = 2.2$ Hz, 1H, H-7’), 7.35 (d, $J = 8.5$ Hz, 2H, H-8a), 7.30 (dd, $J = 8$ Hz, $J = n.d.$, 2H, H-7a), 7.22-7.16 (m, 3H, H-19 + H-20), 7.08 (c. m, 1H, H-13), 7.075 (s, 2H, H-15a), 7.073 (d, $J = 4.3$ Hz, 1H, H-3’), 6.99 (br s, 3H, H-5’ + H-13a), 6.63 (br s, 2H, C-18), 6.05 (s, 1H, H-16), 5.61 (dd, $J = 16.7$ Hz, $J = 10.4$ Hz, $J = 6.2$ Hz, 1H, H-10), 5.12 (d, $J = 10.8$ Hz, 1H, H-9), 5.06 (d, $J = 10.5$ Hz, 1H, H-11E), 4.99 (d, $J = 17.1$ Hz, 1H, H-11Z), 4.18 (c. m, 1H, H-2ex), 3.91 (s, 3H, H-12), 3.41 (t, $J = 10.3$ Hz, 1H, H-8), 3.08 (br s, 2H, H-40a), 2.91 (sept, $J = 6.8$ Hz, 2H, H-30a), 2.75 (t, $J = 11.5$ Hz, 1H, H-6ex), 2.60 (c. m, 1H, H-6en), 2.62 (sept, $J = 6.6$ Hz, 2H, H-20a), 2.43 (c. m, 2H, H-3 + H-2en), 1.80 (c. m, 1H, H-4), 1.77 (t, $J = 12.0$ Hz, 1H, H-7en), 1.54 (c. m, 2H, H-5), 1.29 (c. m, 6H, H-31a), 1.28 (c. m, 6H, H-32a), 1.20 (s, 3H, H-15), 1.18 (c. m, 6H, H-42a), 1.05 (s, 6H, H-22a), 1.04 (s, 6H, H-41a), 0.96 (c. m, 1H, H-7ex), 0.88 (d, $J = 6.7$ Hz, 6H, H-21a).

$^{13}$C NMR (150 MHz, CDCl$_3$) δ 169.4 (C-13), 158.7 (C-6’), 148.75 (d, $J_{P-C} = 9.1$ Hz, C-1a), 148.5 (C-16a), 147.6 (C-12a), 147.7 (C-2’), 147.3 (C-14a), 145.1 (C-4’), 133.7 (C-11a), 141.8 (C-8a’), 141.3 (C-16), 137.6 (C-10 + C-14), 136.1 (C-17), 133.7 (C-11a), 133.45 (d, $J_{P-C} = 2.4$ Hz, C-2a), 132.9 (C-9a), 132.5 (C-8’), 131.2 (C-3a), 130.3 (C-4a), 129.3 (C-18), 128.2 (C-19 + C-4a’), 128.0 (C-5a), 127.6 (C-20), 126.9 (C-8a), 125.5 (C-7a), 124.3 (C-6a), 122.82 (d, $J_{P-C} = 2$ Hz, C-10a), 121.8 (C-7’), 121.6 (br, C-3’), 120.6 (C-15a), 119.6 (C-13a), 116.7 (C-11), 102.0 (C-5”), 64.0 (br, C-9), 61.2 (C-8), 55.7 (C-12), 54.0 (C-2), 39.3 (C-6), 36.6 (C-3), 34.2 (C-30a), 31.1 (C-40a), 30.7 (C-20a), 26.8 (C-4), 26.4 (C-41a), 25.1 (C-5), 24.3 (C-7), 24.7 (C-21a), 24.3 (C-31a), 24.1 (C-32a), 23.8 (C-22a), 23.6 (C-42a), 11.9 (C-15).

$^{15}$N-NMR (60 MHz, CDCl$_3$, T = 223 K, $\delta_{\text{NH}} = 0$ ppms) δ 320.5 (imine N), 307.5 ($J_{\text{NH21}} = 10.3$ Hz, quinoline N), 40.5 ($J_{\text{NH+}} = 70$ Hz, quinuclidine N).

$^{31}$P-NMR (202 MHz, CDCl$_3$, T = 223K, 2 species in a 3:1 ratio) δ 6.2 (3:1), 5.6 (3:1)

MS or HRMS was not performed due to extreme sensitivity of the title compound to hydrolysis.
Summary of $^{15}$N NMR data for salts 26

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<th>Acid partner HX (salt)</th>
<th>Equiv HX</th>
<th>Imine-N$_{21}$, ppm</th>
<th>Quinoline-N$_{22}$, ppm</th>
<th>Quinuclidine-N$_{1}$, ppm</th>
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<tr>
<td>TFA (26a)</td>
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<td>(R)-TRIP (26c)</td>
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<td>TFA (26b)</td>
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<td>not detected</td>
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<tr>
<td>(R)-TRIP (26d)</td>
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<td>not detected</td>
<td>40.6</td>
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$^a$ in MeOD as solvent
Summary of $^1$H NMR data for salts 26

<table>
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<tr>
<th>Proton assignment</th>
<th>25 Shift, ppm</th>
<th>26a (1 TFA) Shift, ppm</th>
<th>26b (2 TFA) Shift, ppm</th>
<th>26c (1 TRIP) Shift, ppm</th>
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<td>N-H</td>
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<tr>
<td>2a (ex)</td>
<td>3.15</td>
<td>3.72</td>
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<td>2b (en)</td>
<td>2.67</td>
<td>3.27</td>
<td>3.31</td>
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<td>1.47</td>
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<td>6a (en)</td>
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<td>3.35</td>
<td>3.34</td>
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<td>6b (ex)</td>
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<td>7a (ex)</td>
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<td>7b (en)</td>
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<td>11a (Z)</td>
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<td>11b (E)</td>
<td>4.84</td>
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<td>5.10</td>
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</table>
NMR-studies on the effect of solvents on the ion pairing

Nevertheless, when we prepared a mixture of 25 with 0.5 equiv of (R)-TRIP (salt 26e), $^1$H NMR analysis clearly indicated the presence of two distinct species and not an average of partly protonated structures. DOSY spectroscopy further confirmed two sets of peaks with different diffusion coefficients, corresponding to unprotonated imine 25 ($7.3 \times 10^{-10}$ m$^2$/s) and the monoprotonated TRIP salt 26c ($5.7 \times 10^{-10}$ m$^2$/s) in which $[25+\text{H}]^+$ and the negatively charged counteranion of TRIP diffused together (Figure 4.15 (a)). This implied that despite the lack of geometrically specific binding between 25 and (R)-TRIP, the ion pair association is relatively strong in neat CDCl$_3$. 

<table>
<thead>
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</table>
We next examined how the ion pairing was affected by the presence of a protic solvent or a protic additive, since an excess of aqueous hydrogen peroxide is employed in the epoxidation of enals 19. In neat methanol, complete ion separation was observed for the salt 26c as indicated by a DOSY experiment. Under these conditions, the [25+H]+ cation and the TRIP− anion clearly diffused at different rates (Figure 4.15 (b)). However, since the environment of a standard epoxidation reaction is only slightly protic, we also examined the effect of a protic additive in chloroform. Under the optimized conditions of epoxidation, a combined 144 equiv of H2O2 and H2O with respect to the catalyst are present in ca. 987 equiv of solvent (THF), which corresponds to a 1:7 ratio of protic to aprotic media. Based on these calculations, we prepared a sample of 26a in CDCl3 containing 7 equiv of MeOH55 with respect to 26a, which corresponded to a similar 1:10 ratio of protic to aprotic solvent.

55 Since the presence of water or aqueous hydrogen peroxide would cause immediate and complete hydrolysis of salts 41 and 42a-d, methanol was chosen to simulate the slightly protic environment of the epoxidation.
A 1-D $^1$H, $^{19}$F HOESY of this sample revealed weak non-specific cross-peaks, suggesting that the ion association remained largely undisrupted. Although direct observation of the diffusion coefficient of the counteranion by DOSY was not possible as a trifluoroacetate anion lacks protons, the diffusion coefficient of the iminium species was found to be between that of 25 alone and the heavier TRIP salt 26c, further supporting the existence of ion pairing. Hence, we concluded that under the slightly protic reaction conditions, the counteranion remains in close association with the iminium cation [25+H]$^+$, albeit this association lacks any obvious organization.

**Studies on the Effect of the Quinoline Moiety**

A significantly weaker and reversed facial selectivity in the epoxidation of enal 19a with an achiral Bronsted acid co-catalyst TFA compared to catalyst 1a highlights the role of the quinoline moiety in the chiral induction. Pairing catalyst S-17 with the chiral acids (R)-21a and (S)-21a conversely resulted in considerably weaker mismatched and matched scenarios, respectively.

![Chemical structures](image)

<table>
<thead>
<tr>
<th>entry</th>
<th>amine</th>
<th>acid</th>
<th>conversion [%]</th>
<th>$\delta r$</th>
<th>$\delta_{(trans)}$</th>
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<td>TFA</td>
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<td>49</td>
<td>79:21</td>
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</table>

* Determined by GC. $^b$ Determined by GC with a chiral stationary phase. $^c$ The catalyst salt was poorly soluble
NMR-derived model: computational details

The NMR-derived model for the iminium structures 25 and [25+H]^+ structures were calculated using XPLOR-NIH Ver. 2.9.7.\textsuperscript{[149]} The low-level force-field defined in the parameter for 25 was simply generated by PRODRG. Distance restraints derived from NOE cross peaks integrals over 5 different mixing times of 0, 100, 200, 300, 500 and 750 ms were applied using the “RELAXATION”\textsuperscript{[187]} function of XPLOR to account for spin-diffusion effect while $J$-coupling-derived restraints were imposed by using the “DIHEDRAL”\textsuperscript{[149]} function of the XPLOR-program. The simulated annealing computation operated in the following way: an initial molecular model was first minimized with a gradient criterion of less than 0.5 kcal/mol. The molecule is then set to a temperature of 2000K over a period of 8.1 ps, in steps of 1.25 fs. The molecule evolves at this temperature for 8.1 ps (6500 steps), thus sampling conformational space extensively. This is followed by a first cooling period lasting 6.25 ps down to 1000 K then by a second cooling period of 2.5ps down to 100K, both followed by Powell energy minimisation. This protocol was repeated 500 times and the 20 resulting conformers with lowest energy were preserved. During the first cooling period (5000 steps), NOE and $J$-coupling-derived dihedral angle terms are gradually raised from their initial weighting (0.02 kcal mol$^{-1}$Å$^{-2}$ and 1.0 kcal mol$^{-1}$deg$^{-2}$) to their final weighting of (20.0 kcal mol$^{-1}$Å$^{-2}$ and 1000 kcal mol$^{-1}$deg$^{-2}$) respectively.

List of NOE integrals (no units) used in XPLOR simulated annealing:

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List of dihedral angles used in XPLOR simulated annealing

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<th>Atom3</th>
<th>Atom4</th>
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<td>C9</td>
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List of additional distance restraint used in XPLOR simulated annealing

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XPLOR-based structure calculations: experimental summary

<table>
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<th>Results for structural models of 25 and [25+H]^+ (20 best of 500)</th>
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<th>[25+H]^+</th>
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<td>Full Relaxation Matrix violations</td>
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<tr>
<td>% of peak volumes with deviations within range 0.5-1.5</td>
<td>94%</td>
<td>94%</td>
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<tr>
<td>Other violations</td>
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<tr>
<td>dihedral angles &gt;5º (&gt;7º)</td>
<td>1 (0)</td>
<td>0 (0)</td>
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<td>bond angles &gt;5º (&gt;7º)</td>
<td>6 (0)</td>
<td>3 (0)</td>
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<tr>
<td>bond lengths &gt;0.05 Å (&gt;0.07 Å)</td>
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<td>5 (0)</td>
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Overlay of the resulting five lowest energy structures derived from the NMR data (NOE and J couplings are depicted in green for the free imine 25 and in black for the protonated species [25+H]^+). These structures are in overall agreement with the applied restraints with very low levels of violations and with relatively low residual energy. The flexibility of certain moieties such as in the phenyl group...
or in the ethylene group is present due to the lack of restraints measured by NMR.

NMR-Spectra of Previously Unpublished Compounds

The spectra of compounds previously published by our group are omitted here and can be found in the corresponding original publication.56

2c

2c
\[ \text{THPO} \quad \text{C}_{11}\text{H}_{22}\text{O}_{3} \quad 202.29 \]

\[ \text{THPO} \quad \text{C}_{11}\text{H}_{22}\text{O}_{3} \quad 202.29 \]

\[ \text{OH} \quad \text{THPO} \quad \text{C}_{11}\text{H}_{22}\text{O}_{3} \quad 202.29 \]
\begin{align*}
\text{THPO} & \quad \text{C}_{11}\text{H}_{20}\text{O}_{3} \\
& \quad \text{200.27}
\end{align*}
$\text{C}_9\text{H}_{16}\text{O}$

140.22

$2r$

$\text{C}_9\text{H}_{16}\text{O}$

140.22

$2r$
\[ \text{THPO} \quad \text{C}_{14}\text{H}_{36}\text{O}_{5} \quad 274.35 \]

\[ \text{THPO} \quad \text{C}_{14}\text{H}_{36}\text{O}_{5} \quad 274.35 \]

3g

3g

S-162
3k
4i

EtO

C₉H₁₄O₄

186.21

4i

EtO

C₉H₁₄O₄

186.21

S-174
$E$-S-3

$E$-S-3
Z-S-5
6f

6f
S-6

S-6

S-6
anti-10q
$\text{O}_2\text{C}_7\text{H}_{10}\text{O}_2$

$\text{Me}$

$\text{C}_{126.15}$

$\text{syn-10q}$
anti-S-18

\[
\text{C}_{10}\text{H}_{16}\text{O}_2 \\
168.23
\]

anti-S-18
anti-10r
13a

C₇H₁₂O₃
144,17
The image contains a chemical structure with a spectrum analysis. The molecule is labeled as 25. The spectrum is divided into different sections, each with labels indicating chemical shifts. There are also annotations for particular peaks and chemical shifts in parts per million (ppm). The spectrum is accompanied by a detailed chart showing the distribution of chemical shifts across various peaks.
NOESY:
COSY:
NOESY:
COSY:
NOESY:
COSY:
Determination of Enantiomeric Ratios: GC-Traces

4f:

```
\begin{align*}
{\text{C}_7\text{H}_{11}\text{BrO}_2} & \\
207.07
\end{align*}
```

![GC Trace Images]

---

Instrument parameters:

- Temperature: 
- Flow rate: 
- Column: 
- Detector: 
- Injection volume: 
- Carrier gas: 
- Column dimensions: 
- Oven program: 
- Column type: 
- Detector: 
- Detector type: 
- Sampler: 
- Split ratio: 
- Split type: 
- Make-up gas: 
- Flow rate: 
- Temperature: 
- Pressure: 
- Size: 
- Weight: 
- Length: 
- Width: 
- Height: 

---

Box 63 9/10
6f:
15d:

C₆H₁₂O₂

142.20

---

Sample: L3/J-461-01-09-8752/1
Prepared: 15-Dec-99 15:57:43

Instrument parameters:

Instrument: HP-4890
Injection: 2.5 µl (10 µl)
Temperature: 250°C
Column: DB-1 (30 m x 0.25 mm)
Flow rate: 1.0 ml/min
Detector: FID

Retention time:

13.20 min.

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Sample: L3/J-461-01-09-8752/2
Prepared: 15-Dec-99 15:57:43

Instrument parameters:

Instrument: HP-4890
Injection: 2.5 µl (10 µl)
Temperature: 250°C
Column: DB-1 (30 m x 0.25 mm)
Flow rate: 1.0 ml/min
Detector: FID

Retention time:

13.20 min.