Supporting Information accompanying
DNA-Based Catalytic Enantioselective Intermolecular Oxa-Michael Addition Reactions
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Figure S 1. Yield of the oxa-Michael product as function of methanol content. [a] Determined by NMR. Conditions: 0.15 mM [Cu(NO₃)₂·3 H₂O], 20 mM MOPS pH 6.5, 1 mM 1a, RT, 1d.

Table S 1. Screening of reaction conditions
20 mM MES pH 5.5

<table>
<thead>
<tr>
<th>MeOH (v/v%)</th>
<th>Conv.</th>
<th>Ratio 2/3</th>
<th>ee 2a</th>
<th>ee 3a</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>Full</td>
<td>24/76</td>
<td>55%</td>
<td>57%</td>
</tr>
<tr>
<td>20%</td>
<td>Full</td>
<td>41/59</td>
<td>56%</td>
<td>58%</td>
</tr>
<tr>
<td>30%</td>
<td>Full</td>
<td>43/57</td>
<td>49%</td>
<td>54%</td>
</tr>
<tr>
<td>40%</td>
<td>Full</td>
<td>45/55</td>
<td>49%</td>
<td>53%</td>
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</tbody>
</table>

20 mM MOPS pH 6.5

<table>
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<th>MeOH (v/v%)</th>
<th>Conv.</th>
<th>Ratio 2/3</th>
<th>ee 2a</th>
<th>ee 3a</th>
</tr>
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<tbody>
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<td>49%</td>
<td>53%</td>
</tr>
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<td>20%</td>
<td>86%</td>
<td>41/59</td>
<td>50%</td>
<td>55%</td>
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<tr>
<td>30%</td>
<td>83%</td>
<td>1/1</td>
<td>53%</td>
<td>57%</td>
</tr>
<tr>
<td>40%</td>
<td>82%</td>
<td>59/41</td>
<td>64%</td>
<td>66%</td>
</tr>
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</table>

20 mM MOPS pH 7.5

<table>
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<tr>
<th>MeOH (v/v%)</th>
<th>Conv.</th>
<th>Ratio 2/3</th>
<th>ee 2a</th>
<th>ee 3a</th>
</tr>
</thead>
<tbody>
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<td>27%</td>
<td>43%</td>
</tr>
<tr>
<td>20%</td>
<td>52%</td>
<td>6/4</td>
<td>42%</td>
<td>52%</td>
</tr>
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<td>30%</td>
<td>55%</td>
<td>64/36</td>
<td>42%</td>
<td>52%</td>
</tr>
<tr>
<td>40%</td>
<td>61%</td>
<td>6/4</td>
<td>42%</td>
<td>52%</td>
</tr>
</tbody>
</table>

General conditions: 0.66 mg/ml st-DNA, 1 mM 1a, 0.15 mM Cu(NO₃)₂, 0.165 mM L1, 4°C, 1d
Figure S 2. Time profile for the reaction of 1a.

Figure S 3. Time profile for the reaction of 1b.
Experimental section:

General remarks.

Salmon testes DNA was obtained from Sigma. Ligands L1-4 and 2-acyl imidazole substrates were synthesized according to published procedures. Enantiomeric excess determination was performed by HPLC analysis on a Shimadzu 10AD-VP system. 1H-NMR and 13C-NMR were recorded on a Varian 400 (400 MHz). Chemical shifts (δ) are quoted in ppm using residual solvent as internal standard (δH 7.26 and δC 77.0 for CDCl3). Mass spectra were recorded on a LTQ ORBITRAP XL.
Catalytic Oxa-Michael addition, representative procedure.

A buffered solution (20 mM MOPS, pH 6.5) of DNA bound catalyst (0.67 mg/ml salmon testes DNA, 0.165 mM L1 and 0.15 mM [Cu(NO3)2]·3 H2O was prepared by mixing a solution of salmon testes DNA (5 ml of a 2 mg/ml solution in 60 mM MOPS, prepared 24 h in advance) with an aqueous solution of catalyst (2.5 ml of a 0.90 mM solution of [Cu(NO3)2]·3 H2O and 0.99 mM L1 in water) and adding water and alcohol to a total volume of 15 ml. The mixture was cooled to 4 °C and 15 μmol of the appropriate α,β unsaturated 2-acyl imidazole dissolved in 10 μL MeCN was added. The reaction was mixed by continuous inversion at 4 °C, followed by extraction of the product with Et2O. After drying (Na2SO4) and removal of the solvent the crude product was analyzed by NMR and HPLC using a chiral stationary phase.

Oxa-michael addition general synthesis of racemates:

A buffered solution (20 mM MOPS, pH 6.5) containing 40% alcohol and 0.15 mM [Cu(NO3)2]·3 H2O was prepared. To this mixture 15 μmol of enone dissolved in 10 μL MeCN was added. The reaction was mixed by continuous inversion at RT, followed by extraction of the product with Et2O. After drying (Na2SO4) and removal of the solvent the crude product was purified by column chromatography (EtOAc/heptanes 1:4).

References:
3-methoxy-4-methyl-1-(1-methyl-1H-imidazol-2-yl)pentan-1-one (2a)

After column chromatography the product was obtained as a slightly yellow oil.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.14 (s, 1H), 7.02 (s, 1H), 3.99 (s, 3H), 3.70 (dt, $J = 8.4, 4.2$ Hz, 1H), 3.41 (dd, $J = 16.4, 8.4$ Hz, 1H), 3.32 (s, 3H), 3.07 (dd, $J = 16.3, 3.7$ Hz, 1H), 1.95 (dq, $J = 6.7, 1.9$ Hz, 1H), 0.93 (dd, $J = 6.8, 1.7$ Hz, 6H).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 191.5, 143.1, 128.7, 126.9, 81.8, 57.6, 40.5, 36.3, 30.7, 18.1, 17.5. HRMS: m/z :211.14377 (M+1) , (Calcd. 211.14410; M+1)
3-methoxy-1-(1-methyl-1H-imidazol-2-y1)butan-1-one (2b)

After column chromatography the product was obtained as a slightly yellow oil.

$^{1}$H-NMR (400 MHz, CDCl$_3$) $\delta$ 7.12 (d, $J = 0.8$ Hz, 1H), 7.01 (s, 1H), 3.99 (s, 3H), 3.99 (dd, $J = 18.0$, 5.3 Hz, 1H), 3.48 (dd, $J = 15.7$, 7.5 Hz, 1H), 3.32 (s, 3H), 3.05 (dd, $J = 15.7$, 5.3 Hz, 1H), 1.24 (d, $J = 6.2$ Hz, 3H).

$^{13}$C-NMR (75 MHz, CDCl$_3$) 191.2, 143.9, 129.3, 127.2, 73.6, 56.4, 46.1, 36.4, 19.6.

HRMS: m/z :183.11288 (M+1) , (Calcd. 183.11280; M+1)
After column chromatography the product was obtained as a slightly yellow oil.

$^{1}H$ NMR (400 MHz, CDCl$_3$) $\delta$ 7.13 (s, 1H), 7.01 (s, 1H), 4.00 (s, 3H), 3.85 (m, 1H), 3.46 (dd, $J$ = 16.0, 7.5 Hz, 1H), 3.33 (s, 3H), 3.10 (dd, $J$ = 16.0, 4.9 Hz, 1H), 1.68 – 1.47 (m, 2H), 1.46 – 1.32 (m, 2H), 1.47 – 1.20 (m, 6H), 0.87 (t, $J$ = 6.9 Hz, 1H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 191.27, 143.24, 129.03, 126.92, 77.29, 56.61, 43.60, 36.15, 33.94, 31.90, 24.82, 22.58, 14.00.

HRMS: m/z :239.17589 (M+1), (Calcd. 239.17540; M+1)
3-methoxy-4,4-dimethyl-1-(1-methyl-1H-imidazol-2-yl)pentan-1-one (2d)

After column chromatography the product was obtained as a slightly yellow oil.

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.14 (s, 1H), 7.02 (s, 1H), 4.00 (s, 3H), 3.56 (dd, $J = 8.1, 3.3$ Hz, 1H), 3.37 (dd, $J = 16.8, 8.1$ Hz, 1H), 3.35 (s, 3H), 3.18 (dd, $J = 16.8, 3.3$ Hz, 1H), 0.94 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 192.1, 143.3, 129.1, 126.9, 85.2, 59.9, 40.8, 36.2, 35.7, 26.0. HRMS: m/z: 225.15983 (M+1), (Calcd. 225.15975; M+1)
3-ethoxy-4-methyl-1-(1-methyl-1H-imidazol-2-yl)pentan-1-one (2f)

After column chromatography the product was obtained as a slightly yellow oil.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.13 (s, 1H), 7.01 (s, 1H), 3.99 (s, 3H), 3.78 (dt, $J = 8.0$, 4.6 Hz, 1H), 3.50 (q, $J = 7.0$ Hz, 2H), 3.37 (dd, $J = 16.1$, 7.8 Hz, 1H), 3.12 (dd, $J = 16.1$, 4.1 Hz, 1H), 1.91 (h, $J = 6.5$ Hz, 1H), 1.09 (t, $J = 7.0$ Hz, 3H), 0.95 (d, $J = 6.8$ Hz, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta = 191.8$, 143.1, 129.0, 126.8, 80.3, 65.2, 41.2, 36.1, 31.6, 18.1, 18.0, 15.5. HRMS: m/z :183.11288 (M+1) , (Calcd. 183.11280; M+1)
3-isopropoxy-4-methyl-1-(1-methyl-1H-imidazol-2-yl)pentan-1-one (2g)

After column chromatography the product was obtained as a slightly yellow oil.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.13 (d, $J = 4.9$ Hz, 1H), 7.00 (d, $J = 6.7$ Hz, 1H), 3.99 (s, 3H), 3.93 (t, $J = 5.9$ Hz, 1H), 3.80 (m, 1H), 3.67 (m, 1H), 3.55 (dd, $J = 15.5, 5.9$ Hz, 1H), 3.06 (dd, $J = 15.4, 6.0$ Hz, 1H), 1.12 (d, $J = 6.1$ Hz, 3H), 1.03 (d, $J = 6.1$ Hz, 3H), 0.99 (d, $J = 6.1$ Hz, 3H), 0.81 (d, $J = 6.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 192.1, 128.8, 126.4, 80.0, 71.0, 63.4, 40.8, 36.1, 24.1, 23.1, 22.2, 20.1. C2-imidazole is missing.

HRMS: m/z :239.17602 (M+1) , (Calcd. 239.17531; M+1)
4-methyl-1-(1-methyl-1H-imidazol-2-yl)-3-propoxypentan-1-one (2h)

After column chromatography the product was obtained as a slightly yellow oil.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.13 (d, $J$ = 0.8 Hz, 1H), 7.00 (s, 1H), 3.99 (s, 3H), 3.85 – 3.69 (m, 1H), 3.42 – 3.33 (m, 3H), 3.09 (dd, $J$ = 16.0, 4.2 Hz, 1H), 1.92 (dt, $J$ = 13.6, 6.8 Hz, 2H), 0.94 (d, $J$ = 6.9 Hz, 6H), 0.82 (t, $J$ = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 191.8, 143.4, 129.0, 126.8, 80.3, 65.2, 41.2, 36.2, 31.60, 18.1, 18.0, 15.5. HRMS: m/z :239.17602 (M+1), (Calcd. 239.17595; M+1)