Manganese Catalyzed cis-Dihydroxylation of Electron Deficient Alkenes with H$_2$O$_2$

Pattama Saisaha, Dirk Pijper, Ruben P. van Summeren, Rob Hoen, Christian Smit, Johannes W. de Boer, Ronald Hage, Paul L. Alsters, Ben L. Feringa, Wesley R. Browne*

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Caution. The drying or concentration of acetone solutions that potentially contain hydrogen peroxide should be avoided. Prior to drying or concentrating of H$_2$O$_2$ should be tested for using peroxide test strips followed by neutralising over solid NaHSO$_3$ or another suitable reducing agent. When working with H$_2$O$_2$, especially in acetone, suitable protective safeguards should be in place at all times.

Caution. Perchlorate salts are potentially explosive in combination with organic solids and solvents. In the present study manganese(II) acetate or manganese(II) sulphate was found to give essentially identical reactivity and should be used above 2 gram reaction scales.

1. Synthesis and characterization of alkene substrates

Diethyl-2-methylfumarate:

\[
\text{EtO} \quad \text{Me} \quad \text{O} \quad \text{Et}
\]

Concentrated H$_2$SO$_4$ (0.6 mL) was added to a stirred mixture of mesaconic acid (5.29 g, 40.3 mmol) in EtOH (40 mL) at room temperature. The reaction mixture was stirred and heated at reflux for 16 h. After cooling, the reaction mixture was concentrated in vacuo and the residue was diluted with H$_2$O (20 mL), 2 M NaOH (20 mL), then extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over MgSO$_4$, filtered and concentrated in vacuo. The crude material was purified by vacuum distillation to afford diethyl-2-methylfumarate as a colourless oil (6.02 g, 32.3 mmol, 80%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.74 (q, 1H), 4.24 – 4.14 (m, 4H), 2.25 (d, 3H), 1.31 – 1.24 (m, 6H); $^{13}$C NMR (100.6 MHz, CDCl$_3$) $\delta$ 167.0, 165.8, 143.6, 126.5, 61.4, 60.5, 14.12, 14.07, 14.01; HRMS (ESI+) calc. for C$_9$H$_{13}$O$_4$ (M+H)$^+$ 187.0970, found 187.0965; elemental analysis (calc. for C$_9$H$_{14}$O$_4$) C 57.87% (58.05%), H 7.62% (7.58%).
$^1$H NMR spectrum of diethyl-2-methylfumarate in CDCl$_3$

APT NMR spectrum of diethyl-2-methylfumarate in CDCl$_3$
**N,N-Dibutylmalediamide:**

1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (7.50 g, 39.3 mmol) was added to a solution of maleic acid (1.52 g, 13.1 mmol), n-butylamine (3.1 mL, 31.4 mmol) and 1-hydroxybenzotriazole (4.20 g, 31.4 mmol) in THF (100 mL) cooled in an ice/water bath. The reaction mixture was stirred for 18 h and allowed to reach room temperature gradually. The reaction mixture was concentrated *in vacuo* and the residue diluted with EtOAc (50 mL) followed by addition of saturated aqueous NaHCO₃ solution (50 mL). The aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated *in vacuo*. N,N-Dibutylmalediamide (2.86 g, 12.6 mmol, 96%) was obtained as a yellow oil and used directly without further purification. ¹H NMR (400 MHz, CDCl₃) δ 9.07 (s, 1H), 6.07 (s, 1H), 3.24 (td, J = 7.2, 5.7 Hz, 2H), 1.54 – 1.45 (m, 2H), 1.39 – 1.28 (m, 2H), 0.88 (t, J = 7.3 Hz, 3H); ¹³C NMR (100.6 MHz, CDCl₃) δ 164.9, 132.5, 39.5, 31.1, 20.1, 13.6.

¹H NMR spectrum of N,N-dibutylmalediamide in CDCl₃
$^{13}$C NMR spectrum of N,N-dibutylmaleimide in CDCl$_3$

4-(Benzylnino)-4-oxobut-2-enoic acid:

A solution of benzylamine (3.10 g, 28.9 mmol) in dry Et$_2$O (100 mL) was added dropwise to a stirred solution of maleic anhydride (2.94 g, 30.0 mmol) in dry Et$_2$O (300 mL). The solution was stirred for a further 2 h then filtered, and the filtered solid was washed with Et$_2$O and dried in vacuo to give the crude amic acid (5.44 g, 26.5 mmol, 92%) which was used without further purification. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.33 (m, 5H), 6.86 (s, 1H), 6.35 (d, $J = 12.8$, 1H), 6.17 (d, $J = 12.8$, 1H), 4.54 (s, 2H), 3.90 (s, 1H); HRMS (APCI+) calc. for C$_{11}$H$_{12}$NO$_3$ (M+H)$^+$ 206.0817, found 206.0812.
1H NMR spectrum of 4-(benzylamino)-4-oxobut-2-enoic acid in CDCl₃

1-Benzyl-1H-pyrrole-2,5-dione:

A solution of crude 4-(benzylamino)-4-oxobut-2-enoic acid (3.72 g, 18.13 mmol) in glacial acetic acid (35 mL) was heated under reflux for 16 h then cooled and concentrated under reduced pressure. The residue was diluted with EtOAc (20 mL) and washed with aqueous 10% HCl, aqueous NaHCO₃, dried and evaporated under reduced pressure. The crude reaction mixture was purified by column chromatography (SiO₂, EtOAc/pentane = 30/70) to provide the product as a white solid (1.13 g, 6.02 mmol, 33%). m.p. 69.9-70.7 °C; 1H NMR (400 MHz, CDCl₃) δ 7.37 – 7.27 (m, 5H), 6.71 (s, 2H), 4.68 (s, 2H); 13C NMR (50 MHz, CDCl₃) δ 170.3, 136.1, 134.1, 128.6, 128.3, 127.8, 41.3; HRMS (APCI+) calc. for C₁₁H₁₀NO₂ (M+H)+ 188.0712, found 188.0706; elemental analysis (calc. for C₁₁H₉NO₂) C 70.45% (70.58%), H 4.83% (4.85%), N 7.43% (7.48%).
$^1$H NMR spectrum of 1-benzyl-1H-pyrrole-2,5-dione in CDCl$_3$

APT NMR spectrum of 1-benzyl-1H-pyrrole-2,5-dione in CDCl$_3$
1-Benzyl-3,4-dimethyl-pyrrole-2,5-dione:

A solution of benzylamine (1.95 g, 18.2 mmol) in dry Et₂O (50 mL) was added dropwise to a stirred solution of dimethylmaleic anhydride (2.60 g, 20.0 mmol) in dry Et₂O (200 mL). The solution was stirred for a further 2 h then filtered, and the filtered solid was washed with Et₂O and dried in vacuo to give the crude amic acid (2.98 g) which was used without further purification. A solution of crude amic acid in glacial acetic acid (30 mL) was heated under reflux for 16 h then cooled and concentrated under reduced pressure. The residue was diluted with EtOAc (20 mL) and washed with aqueous 10% HCl, aqueous NaHCO₃, dried and evaporated under reduced pressure. The crude reaction mixture was purified by column chromatography (SiO₂, EtOAc/pentane = 30/70) to provide the product as a yellow oil (1.48 g, 6.89 mmol, 38% for 2 steps). 

\(^1\)H NMR (201 MHz, CDCl₃) δ 7.38 – 7.23 (m, 5H), 4.64 (s, 2H), 1.95 (s, 6H); 

\(^{13}\)C NMR (50 MHz, CDCl₃) δ 171.8, 137.2, 136.7, 128.5, 128.3, 127.6, 41.4, 8.7; 

HRMS (APCI+) calc. for C₁₃H₁₄NO₂ (M+H)\(^{+}\) 216.1025, found 216.1019; 

elemental analysis (calc. for C₁₃H₁₃NO₂) C 72.64% (72.54%), H 6.11% (6.09%), N 6.40% (6.51%).

\(^1\)H NMR spectrum of 1-benzyl-3,4-dimethyl-pyrrole-2,5-dione in CDCl₃
APT NMR spectrum of 1-benzyl-3,4-dimethyl-pyrrole-2,5-dione in CDCl$_3$
2. Procedures for catalyzed cis-dihydroxylation of alkenes reported in table 1

Entry 1. cis-dihydroxylation of diethyl fumarate using 2-butane as solvent

A stock solution containing both Mn(ClO$_4$)$_2$·6H$_2$O (7.3 mg, 20.0 µmol) and pyridine-2-carboxylic acid (7.5 mg, 60.0 µmol) in 2-butane (20 mL) was prepared. 1.0 mL of this stock solution (1.0 µmol Mn(ClO$_4$)$_2$·6H$_2$O, 0.1 mol%, and 3.0 µmol pyridine-2-carboxylic acid, 0.3 mol%) was added to the solution of diethyl fumarate (168 mg, 1.00 mmol) in 2-butane (0.5 mL), while stirring the mixture at room temperature. After addition of 17.0 µL of a 0.6 M stock (aqueous) of NaOAc (0.1 mmol, 1.0 mol%), the mixture was cooled in ice/water bath and, with stirring, H$_2$O$_2$ (50 wt% in water, 85 µL, 1.5 mmol, 1.5 equiv.) was added in one portion. The mixture was stirred for 16 h, allowing temperature to rise to room temperature. Excess solid NaHSO$_3$ was added to the reaction mixture, until no peroxides remained (shown by peroxide test-strips). The salts were filtered off, washed several times with acetone, after which the acetone was removed in vacuo, giving the product as a colourless oil (195 mg, 0.95 mmol, 95%).

$^{1}$H NMR spectrum of the cis-diol product of diethyl fumarate in CDCl$_3$
APT NMR spectrum of the cis-diol product of diethyl fumarate in CDCl₃
Entry 2. Diethyl 2-methylfumarate

Prior to the experiment, a stock solution containing both Mn(ClO$_4$)$_2$·6H$_2$O (22.0 mg, 0.06 mmol) and pyridine-2-carboxylic acid (45.0 mg, 0.36 mmol) in acetone (20 mL) was prepared. 1.0 mL of this stock solution (3.0 µmol Mn(ClO$_4$)$_2$·6H$_2$O, 0.3 mol%, and 18.0 µmol pyridine-2-carboxylic acid, 1.8 mol%) was added to the solution of diethyl 2-methylfumarate (191 mg, 1.03 mmol) in acetone (2 mL), while stirring the mixture at room temperature. After addition of 50.0 µL of a 0.6 M stock (aqueous) of NaOAc (30.0 µmol, 3.0 mol%), the mixture was cooled in an ice/water bath and H$_2$O$_2$ (50 wt% in water, 170 µL, 3.0 mmol, 3.0 equiv.) was added by using a syringe pump (rate 1 µL/min). The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, excess solid NaHSO$_3$ was added to the reaction mixture, until no peroxides were present in the mixture (shown by peroxide test-strips). The salts were filtered off, washed several times with excess acetone, after which the acetone was removed in vacuo, yielding the product as a colourless oil (207 mg, 0.94 mmol, 91%).

$^1$H NMR (500 MHz, -10 °C, CDCl$_3$) $\delta$ 4.32 (d, $J = 8.0$ Hz, 1H), 4.28 – 4.18 (m, 4H), 4.00 (s, 1H), 3.79 (d, $J = 8.6$ Hz, 1H), 1.44 (s, 3H), 1.26 (m, 6H); $^{13}$C NMR (100.6 MHz, CDCl$_3$) $\delta$ 174.2, 171.2, 76.7, 75.0, 62.3, 62.0, 21.8, 14.0, 13.9; HRMS (ESI+) calc. for C$_9$H$_{16}$O$_6$ (M+Na)$^+$ 243.0845, found 243.0839; elemental analysis (calc. for C$_9$H$_{16}$O$_6$) C 49.19% (49.09%), H 7.48% (7.32%).
$^1$H NMR spectrum of the cis-diol product of diethyl 2-methylfumarate (-10 °C, 500 MHz) in CDCl$_3$

APT NMR spectrum of the cis-diol product of diethyl 2-methylfumarate in CDCl$_3$
Entry 3. Diethyl maleate

A stock solution containing Mn(ClO$_4$)$_2$.6H$_2$O (22.0 mg, 0.06 mmol) and pyridine-2-carboxylic acid (45.0 mg, 0.36 mmol) in acetone (20 mL) was prepared. 5.0 mL of this stock solution (15.0 µmol Mn(ClO$_4$)$_2$.6H$_2$O, 0.3 mol%, and 90.0 µmol pyridine-2-carboxylic acid, 1.8 mol%) was added to the solution of diethyl maleate (890 mg, 5.01 mmol) in acetone (25.0 mL), while stirring the mixture at room temperature. After addition of 0.25 mL of a 0.6 M (aqueous) NaOAc (150.0 µmol, 3.0 mol%), the mixture was stirred with cooling in an ice/water bath and H$_2$O$_2$ (50 wt% in water, 850 µL, 15.0 mmol, 3.0 equiv.) was added via syringe pump (rate 3 µL/min). The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, the mixture was added to saturated aqueous NaHCO$_3$ (20 mL) and CH$_2$Cl$_2$ (20 mL). After separation of the layers, the aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 20 mL). The combined organic layers were dried on MgSO$_4$ and after filtration the solvents were evaporated in vacuo. The crude material was purified by column chromatography (SiO$_2$, EtOAc/pentane = 40/60 to 100/0 ) to provide the recovered starting material (213 mg, 1.24 mmol, 25%) and the product as a white solid (489 mg, 2.37 mmol, 47%). m.p. 57.3-58.1 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 4.55 (s, 2H), 4.27 (m, 4H), 3.18 (s, 2H), 1.32 – 1.27 (t, 6H); $^{13}$C NMR (100.6 MHz, CDCl$_3$) δ 171.0, 72.9, 62.2, 14.0; HRMS (ESI+) calc. for C$_8$H$_{14}$O$_6$ (M+Na)$^+$ 229.0688, found 229.0682; elemental analysis (calc. for C$_8$H$_{14}$O$_6$) C 47.99% (46.60%), H 7.07% (6.84%).

N.B. Optimization of conditions for diethyl maleate (improved conversion with lowering substrate loading)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Diethyl maleate</th>
<th>Mn(ClO$_4$)$_2$.6H$_2$O</th>
<th>Pyridine-2-COOH</th>
<th>NaOAc</th>
<th>Temperature</th>
<th>H$_2$O$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>3.0 mmol</td>
<td>0.1 mol%</td>
<td>0.6 mol%</td>
<td>1.5 equiv.</td>
<td>0°C to r.t.</td>
<td>1.5 equiv.</td>
</tr>
<tr>
<td>b</td>
<td>1.0 mmol</td>
<td>0.3 mol%</td>
<td>1.8 mol%</td>
<td>1.5 equiv.</td>
<td>0°C to r.t.</td>
<td>1.5 equiv.</td>
</tr>
<tr>
<td>c</td>
<td>0.25 mmol</td>
<td>1.2 mol%</td>
<td>7.2 mol%</td>
<td>1.5 equiv.</td>
<td>0°C to r.t.</td>
<td>1.5 equiv.</td>
</tr>
</tbody>
</table>

**Condition a:** 33% conv. by Raman spectroscopy

**Condition b:** 63% conv., 55% diol product by $^1$H NMR spectroscopy

**Condition c:** 63% conv., 55% diol product by $^1$H NMR spectroscopy
$^1$H NMR spectrum of the cis-diol product of diethyl maleate in CDCl$_3$.

APT NMR spectrum of the cis-diol product of diethyl maleate in CDCl$_3$. 

Entry 4. Maleimide

A stock solution containing Mn(ClO$_4$)$_2$·6H$_2$O (9.1 mg, 25 µmol) and pyridine-2-carboxylic acid (18.5 mg, 150 µmol) in acetone (50 mL) was prepared. 30.0 mL of this stock solution (15.0 µmol Mn(ClO$_4$)$_2$·6H$_2$O, 0.3 mol%, and 90.0 µmol pyridine-2-carboxylic acid, 1.8 mol%) was added to maleimide (485 mg, 5.0 mmol), while stirring the mixture at room temperature. After addition of 150.0 µL of a 0.6 M (aqueous) NaOAc (90.0 µmol, 3.0 mol%), the mixture was stirred with cooling in an ice/water bath and H$_2$O$_2$ (50 % wt in water, 425 µL, 7.5 mmol, 1.5 equiv.) was added in one portion. The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, excess solid NaHSO$_3$ was added to the reaction mixture to remove residual peroxides (verified using peroxide test-strips). The salts were filtered off, washed several times with excess acetone, after which the acetone was removed in vacuo, giving the product as a white solid (640 mg, 4.88 mmol, 98 %). m.p. 124.7-125.2 °C; $^1$H NMR (400 MHz, CD$_3$OD) δ 4.41 (s, 2H); $^{13}$C NMR (100.6 MHz, CD$_3$OD) δ 179.0, 70.4; HRMS (ESI+) calc. for C$_4$H$_6$NO$_4$ (M+H)$^+$ 132.0297, found 132.0291; elemental analysis (calc. for C$_4$H$_5$NO$_4$) C 36.60% (36.65%), H 3.76% (3.84%), N 10.71% (10.69%).

$^1$H NMR spectrum of the cis-diol product of maleimide in CD$_3$OD
$^{13}$C NMR spectrum of the $cis$-diol product of maleimide in CD$_3$OD
**Entry S5. N-Ethylmaleimide**

A stock solution containing Mn(ClO₄)₂·6H₂O (22.0 mg, 0.06 mmol) and pyridine-2-carboxylic acid (45.0 mg, 0.36 mmol) in acetone (20 mL) was prepared. 1.0 mL of this stock solution (3.0 µmol Mn(ClO₄)₂·6H₂O, 0.3 mol%, and 18.0 µmol pyridine-2-carboxylic acid, 1.8 mol%) was added to the solution of N-ethylmaleimide (122 mg, 0.96 mmol) in acetone (2 mL), while stirring the mixture at room temperature. After addition of 50.0 µL of a 0.6 M (aqueous) NaOAc (30.0 µmol, 3.0 mol%), the mixture was cooled in an ice/water bath and H₂O₂ (50 wt% in water, 170 µL, 3.0 mmol, 3.0 equiv.) was added via syringe pump (rate 1 µL/min). The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, excess solid NaHSO₃ was added to the reaction mixture, to remove residual peroxides (verified by peroxide test-strips). The salts were filtered off, washed several times with excess acetone, after which the acetone was removed in vacuo, giving product as a white solid (150 mg, 0.94 mmol, 98%). m.p. 122.6-123.9 °C; ¹H NMR (400 MHz, CD₃OD) δ 4.42 (s, 2H), 3.53 (q, J = 7.2 Hz, 2H), 1.15 (t, J = 7.2 Hz, 3H); ¹³C NMR (100.6 MHz, CD₃OD) δ 177.7, 69.3, 34.3, 13.0; elemental analysis (calc. for C₆H₉O₄N) C 44.24% (45.28%), H 5.64% (5.70%), N 8.99% (8.80%).

![1H NMR spectrum of the cis-diol product of N-ethylmaleimide in CD₃OD](image)

S17
$^{13}$C NMR spectrum of the cis-diol product of N-ethylmaleimide in CD$_3$OD
Entry 6. 1-Benzyl-pyrrole-2,5-dione

A stock solution containing Mn(ClO$_4$)$_2$·6H$_2$O (22.0 mg, 0.06 mmol) and pyridine-2-carboxylic acid (45.0 mg, 0.36 mmol) in acetone (20 mL) was prepared. 2.0 mL of this stock solution (6.0 µmol Mn(ClO$_4$)$_2$·6H$_2$O, 0.3 mol%, and 36.0 µmol pyridine-2-carboxylic acid, 1.8 mol%) was added to the solution of 1-benzyl-pyrrole-2,5-dione (377 mg, 2.01 mmol) in acetone (4 mL), while stirring the mixture at room temperature. After addition of 100.0 µL of a 0.6 M (aqueous) NaOAc (60.0 µmol, 3.0 mol%), the mixture was cooled in an ice/water bath and H$_2$O$_2$ (50 wt% in water, 227 µL, 4.0 mmol, 2.0 equiv.) was added via syringe pump (rate 2 µL/min). The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, excess solid NaHSO$_3$ was added to the reaction mixture, to remove residual peroxides (verified by peroxide test-strips). The salts were filtered off, washed several times with excess acetone, after which the acetone was removed in vacuo, giving product as a white solid (403 mg, 1.82 mmol, 91%), m.p. 131.7-132.9 °C; $^1$H NMR (400 MHz, DMSO-d$_6$) δ 7.35 – 7.22 (m, 5H), 4.55 (s, 2H), 4.42 (s, 2H); $^{13}$C NMR (100.6 MHz, DMSO-d$_6$) δ 176.3, 135.9, 128.4, 127.4, 127.4, 68.0, 40.9; HRMS (APCI+) calc. for C$_{11}$H$_{12}$NO$_4$ (M+H)$^+$ 222.0766, found 222.0761.

$^1$H NMR spectrum of the cis-diol product of 1-benzyl-pyrrole-2,5-dione in DMSO-d$_6$
$^{13}$C NMR spectrum of the cis-diol product of 1-benzyl-pyrrole-2,5-dione in DMSO-d$_6$
Entry 7. 1-Benzyl-3,4-dimethyl-pyrrole-2,5-dione

A stock solution containing Mn(ClO$_4$)$_2$.6H$_2$O (22.0 mg, 0.06 mmol) and pyridine-2-carboxylic acid (45.0 mg, 0.36 mmol) in acetone (20 mL) was prepared. 2.0 mL of this stock solution (6.0 µmol Mn(ClO$_4$)$_2$.6H$_2$O, 0.3 mol%, and 36.0 µmol pyridine-2-carboxylic acid, 1.8 mol%) was added to the solution of 1-benzyl-3,4-dimethyl-pyrrole-2,5-dione (431 mg, 2.00 mmol) in acetone (4 mL), while stirring the mixture at room temperature. After addition of 100.0 µL of a 0.6 M (aqueous) NaOAc (60.0 µmol, 3.0 mol%), the mixture was cooled in an ice/water bath and H$_2$O$_2$ (50 wt% in water, 227 µL, 4.0 mmol, 2.0 equiv.) was added via syringe pump (rate 2 µL/min). The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, excess solid NaHSO$_3$ was added to the reaction mixture, to remove residual peroxides (verified by peroxide test-strips). The salts were filtered off, washed several times with excess acetone, after which the acetone was removed *in vacuo*, giving the crude reaction mixture. The crude material was purified by column chromatography (SiO$_2$, EtOAc/pentane = 30/70 to 50/50 ) to provide the product as an off-white solid (374 mg, 1.50 mmol, 75%), m.p. 96.7-97.1 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.32 – 7.26 (m, 5H), 4.66 (s, 2H), 3.44 (s, 2H), 1.38 (m, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 177.0, 135.0, 128.8, 128.2, 128.1, 75.4, 42.3, 18.9; HRMS (APCI+) calc. for C$_{13}$H$_{16}$NO$_4$ (M+H)$^+$ 250.1079, found 250.1067.
$^1$H NMR spectrum of the cis-diol product of 1-benzyl-3,4-dimethyl-pyrrole-2,5-dione in CDCl$_3$
APT NMR spectrum of the *cis*-diol product of 1-benzyl-3,4-dimethyl-pyrrole-2,5-dione in CDCl$_3$
Entry 8. \(N,N\)-Dibutylmalediamide

A stock solution containing \(\text{Mn(ClO}_4\text{)}_2 \cdot 6\text{H}_2\text{O}\) (22.0 mg, 0.06 mmol) and pyridine-2-carboxylic acid (45.0 mg, 0.36 mmol) in acetone (20 mL) was prepared. 2.0 mL of this stock solution (6.0 \(\mu\text{mol Mn(ClO}_4\text{)}_2 \cdot 6\text{H}_2\text{O}, 0.3 \text{ mol\%, and 36.0 \(\mu\text{mol pyridine-2-carboxylic acid, 1.8 mol\%}\) was added to the solution of \(N,N\)-dibutylmalediamide (466 mg, 2.06 mmol) in acetone (10 mL), while stirring the mixture at room temperature. After addition of 100.0 \(\mu\text{L of a 0.6 M (aqueous) NaOAc (60.0 \(\mu\text{mol, 3.0 mol\%}, the mixture was cooled in an ice/water bath and \(\text{H}_2\text{O}_2\) (50 wt\% in water, 340 \(\mu\text{L, 6.0 mmol, 3.0 equiv.}) was added by using a syringe pump (rate 3 \(\mu\text{L/min). The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, the mixture was poured in saturated aqueous NaHCO\(_3\) (20 mL) and CH\(_2\)Cl\(_2\) (20 mL). After separation of the layers, the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3 x 20 mL). The combined organic layers were dried on MgSO\(_4\) and after filtration the solvents were evaporated in vacuo. The crude material was purified by recrystallization from hot Et\(_2\)O to provide the product as a white solid (175 mg, 0.67 mmol, 32\%). m.p. 160.1-160.9 °C; \(^1\text{H NMR (400 MHz, CDCl}_3\)) \(\delta 7.07\) (s, 2H), 5.69 (s, 2H), 4.00 (s, 2H), 3.34 – 3.26 (m, 4H), 1.58 – 1.48 (m, 4H), 1.41 – 1.31 (m, 4H), 0.94 (t, \(J = 7.3\) Hz, 6H); \(^{13}\text{C NMR (100.6 MHz, CDCl}_3\)) \(\delta 172.9, 70.1, 38.8, 31.4, 20.0, 13.7\); elemental analysis (calc. for \(\text{C}_{12}\text{H}_{24}\text{N}_2\text{O}_4\) C 55.17\% (55.36\%), H 9.29\% (9.29\%), N 10.68\% (10.76\%).
$^1$H NMR spectrum of the cis-diol product of $N,N$-dibutylmaleimide in CDCl$_3$

APT NMR spectrum of the cis-diol product of $N,N$-dibutylmaleimide in CDCl$_3$
Entry 9. n-Butyl acrylate

A stock solution containing both Mn(ClO$_4$)$_2$·6H$_2$O (5.4 mg, 15.0 µmol) and pyridine-2-carboxylic acid (11.0 mg, 90.0 µmol) in acetone (5 mL) was prepared. 1.0 mL of this stock solution (3.0 µmol Mn(ClO$_4$)$_2$·6H$_2$O, 0.3 mol%, and 18.0 µmol pyridine-2-carboxylic acid, 1.8 mol%) was added to the solution of n-butyl acrylate (121 mg, 0.94 mmol) in acetone (5 mL), while stirring the mixture at room temperature. After addition of 50.0 µL of a 0.6 M (aqueous) NaOAc (30.0 µmol, 3.0 mol%), the mixture was cooled in an ice/water bath and H$_2$O$_2$ (50 wt% in water, 113 µL, 2.0 mmol, 2.0 equiv.) was added by using a syringe pump (rate 3 µL/min). The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, the mixture was poured in saturated aqueous NaHCO$_3$ (20 mL) and CH$_2$Cl$_2$ (20 mL). After separation of the layers, the aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 20 mL). The combined organic layers were dried on MgSO$_4$ and after filtration the solvents were evaporated under reduced pressure. 1,2-Dichloroethane (44.0 mg, 0.44 mmol) was added to the crude reaction mixture as an external standard, and a sample was diluted with CDCl$_3$ to facilitate the measurement by $^1$H NMR spectroscopy. $^1$H NMR analysis of the solution provided a product yield relative to the external standard integration. This reaction showed 19% starting material remaining and 55% of the cis-diol product. $^1$H NMR of n-butyl acrylate (400 MHz, CDCl$_3$) δ 6.37 (dd, J = 17.3, 1.5 Hz, 1H), 6.09 (dd, J = 17.3, 10.4 Hz, 1H), 5.79 (dd, J = 10.4, 1.5 Hz, 1H), 4.13 (t, J = 6.7 Hz, 2H), 1.63 (dt, J = 14.9, 6.8 Hz, 2H), 1.43 – 1.31 (m, 2H), 0.91 (td, J = 7.4, 2.2 Hz, 3H) and $^1$H NMR of n-butyl 2,3-dihydroxypropanoate (400 MHz, CDCl$_3$) δ 4.26 – 4.22 (m, 1H), 4.20 (td, J = 6.7, 1.5 Hz, 2H), 3.91 – 3.76 (m, 2H), 3.51 (d, J = 4.9 Hz, 1H), 2.71 (s, 1H), 1.63 (dt, J = 14.9, 6.8 Hz, 2H), 1.43 – 1.31 (m, 2H), 0.91 (td, J = 7.4, 2.2 Hz, 3H).
$^1$H NMR spectrum in CDCl$_3$ of the product mixture from oxidation of $n$-butyl acrylate
### 3. Procedures for catalyzed oxidation of alkenes Table 2 entries 1-7

**Entry 1. cis-Cyclooctene**

A stock solution containing both Mn(ClO$_4$)$_2$·6H$_2$O (22.0 mg, 0.06 mmol) and pyridine-2-carboxylic acid (373.0 mg, 3.0 mmol) in acetone (20 mL) was prepared prior to the experiment. 3.33 mL of this stock solution (10.0 µmol Mn(ClO$_4$)$_2$·6H$_2$O, 0.1 mol%, and 500.0 µmol pyridine-2-carboxylic acid, 5.0 mol%) was added to the solution of cis-cyclooctene (1.18 g, 10.1 mmol) in acetone (16.67 mL) and H$_2$O (2.67 mL), while stirring the mixture at room temperature. After addition of 150.0 µL of a 0.6 M stock (aqueous) of NaOAc (90.0 µmol, 0.9 mol%), the mixture was cooled in an ice/water bath and H$_2$O (50 wt% in water, 850 µL, 15.0 mmol, 1.5 equiv.) was added by using a syringe pump (rate 6 µL/min). The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, the mixture was poured in saturated aqueous NaHCO$_3$ (30 mL) and CH$_2$Cl$_2$ (30 mL). After separation of the layers, the aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 30 mL). The combined organic layers were dried on MgSO$_4$ and after filtration the solvents were evaporated in vacuo. The crude mixture was determined by $^1$H NMR spectroscopy and showed 97% conversion, ratio of epoxide:diol:α-hydroxy ketone compounds = 6:1:1. The crude material was purified by column chromatography (SiO$_2$, EtOAc/pentane = 20/80 to 100/0) to provide cis-cyclooctane oxide as a colourless solid (770 mg, 6.10 mmol, 60%), cis-1,2-cyclooctane diol as a colourless solid (174 mg, 1.21 mmol, 12%) and 2-hydroxycyclooctanone as a pale yellow solid (137 mg, 0.96 mmol, 10%). $^1$H NMR of cis-cyclooctane oxide (200 MHz, CDCl$_3$) δ 2.97 – 2.83 (m, 2H), 2.22 – 2.06 (m, 2H), 1.74 – 1.38 (m, 8H), 1.31 (m, 2H) and $^{13}$C NMR (100.6 MHz, CDCl$_3$) δ 55.6, 26.6, 26.3, 25.6; $^1$H NMR of cis-1,2-cyclooctane diol (400 MHz, CDCl$_3$) δ 3.91 (d, $J$ = 10.1, 2H), 1.97 – 1.82 (m, 2H), 1.67 (m, 4H), 1.59 – 1.41 (m, 6H) and $^{13}$C NMR (100.6 MHz, CDCl$_3$) δ 73.1, 30.1, 26.2, 23.7; $^1$H NMR of 2-hydroxycyclooctanone (400 MHz, CDCl$_3$) δ 4.18 (dd, $J$ = 6.5, 2.8, 1H), 3.72 (s, 1H), 2.72 (dd, $J$ = 12.2, 3.8, 1H), 2.39 – 2.29 (m, 2H), 2.08 – 1.91 (m, 2H), 1.76 (m, 4H), 1.45 – 1.30 (m, 2H), 0.91 (m, 1H).
NMR spectrum in CDCl$_3$ of the product mixture from oxidation of cis-cyclooctene
Entry 2. Cyclohexene

A stock solution containing both Mn(ClO$_4$)$_2$·6H$_2$O (3.6 mg, 0.01 mmol) and pyridine-2-carboxylic acid (62.0 mg, 0.5 mmol) in acetone-d$_6$ (20 mL) was prepared prior to the experiment. 1.5 mL of this stock solution (0.75 µmol Mn(ClO$_4$)$_2$·6H$_2$O, 0.1 mol%, and 37.5 µmol pyridine-2-carboxylic acid, 5.0 mol%) was added to the solution of cyclohexene (54 mg, 0.65 mmol) and 1,2-dichlorobenzene (46 mg, 0.31 mmol) in H$_2$O (200 µL), while stirring the mixture at room temperature. After addition of 11.3 µL of a 0.6 M stock (aqueous) of NaOAc (6.8 µmol, 0.9 mol%), the mixture was cooled in an ice/water bath and H$_2$O$_2$ (50 wt% in water, 64 µL, 1.13 mmol, 1.5 equiv.) was added in one portion. The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, the mixture was measured by $^1$H NMR spectroscopy. $^1$H NMR analysis of the solution provided product yield relative to the internal standard (1,2-dichlorobenzene) integration and the products were identified by comparison to the $^1$H NMR spectra of authentic samples. This reaction showed 100% conversion, 54% epoxide formation, 2% diol formation, 14% $\alpha$-hydroxy ketone formation and 3% enone formation.

$^1$H NMR spectrum in acetone-d$_6$ of the product mixture from oxidation of cyclohexene
Entry 3. 1-Methyl-1-cyclohexene

A stock solution containing both Mn(ClO$_4$)$_2$·6H$_2$O (3.6 mg, 0.01 mmol) and pyridine-2-carboxylic acid (62.0 mg, 0.5 mmol) in acetone-d$_6$ (20 mL) was prepared prior to the experiment. 1.5 mL of this stock solution (0.75 µmol Mn(ClO$_4$)$_2$·6H$_2$O, 0.1 mol%, and 37.5 µmol pyridine-2-carboxylic acid, 5.0 mol%) was added to the solution of 1-methyl-1-cyclohexene (69 mg, 0.70 mmol) and 1,2-dichlorobenzene (54 mg, 0.37 mmol) in H$_2$O (200 µL), while stirring the mixture at room temperature. After addition of 11.3 µL of a 0.6 M stock (aqueous) of NaOAc (6.8 µmol, 0.9 mol%), the mixture was cooled in an ice/water bath and H$_2$O$_2$ (50 wt% in water, 64 µL, 1.13 mmol, 1.5 equiv.) was added in one portion. The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, the mixture was measured by $^1$H NMR spectroscopy. $^1$H NMR spectroscopic analysis of the solution provided product yield relative to the internal standard (1,2-dichlorobenzene) integration and the products were identified by comparison to the $^1$H NMR spectra of authentic samples. This reaction showed 100% conversion, 64% epoxide formation and 8% diol formation.

$^1$H NMR spectrum in acetone-d$_6$ of the product mixture from oxidation of 1-methyl-1-cyclohexene
Entry 4. 1-Octene

A stock solution containing both Mn(ClO$_4$)$_2$·6H$_2$O (3.6 mg, 0.01 mmol) and pyridine-2-carboxylic acid (62.0 mg, 0.5 mmol) in acetone-d$_6$ (20 mL) was prepared prior to the experiment. 1.5 mL of this stock solution (0.75 µmol Mn(ClO$_4$)$_2$·6H$_2$O, 0.1 mol%, and 37.5 µmol pyridine-2-carboxylic acid, 5.0 mol%) was added to the solution of 1-octene (83 mg, 0.74 mmol) and 1,2-dichlorobenzene (50 mg, 0.34 mmol) in H$_2$O (200 µL), while stirring the mixture at room temperature. After addition of 11.3 µL of a 0.6 M stock (aqueous) of NaOAc (6.8 µmol, 0.9 mol%), the mixture was cooled in an ice/water bath and H$_2$O$_2$ (50 wt% in water, 64 µL, 1.13 mmol, 1.5 equiv.) was added in one portion. The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, the mixture was measured by $^1$H NMR. $^1$H NMR spectroscopic analysis of the solution provided the product yield relative to the internal standard (1,2-dichlorobenzene) integration and the products were identified by comparison to the $^1$H NMR spectra of authentic samples. This reaction showed 82% conversion, 35% epoxide formation, 9% diol formation and 18% $\alpha$-hydroxy ketone formation.

$^1$H NMR spectrum in acetone-d$_6$ of the product mixture from oxidation of 1-octene
Entry 5. Styrene

A stock solution containing both Mn(ClO$_4$)$_2$·6H$_2$O (3.6 mg, 0.01 mmol) and pyridine-2-carboxylic acid (62.0 mg, 0.5 mmol) in acetone-d$_6$ (20 mL) was prepared prior to the experiment. 1.5 mL of this stock solution (0.75 µmol Mn(ClO$_4$)$_2$·6H$_2$O, 0.1 mol%, and 37.5 µmol pyridine-2-carboxylic acid, 5.0 mol%) was added to the solution of styrene (70 mg, 0.67 mmol) and 1,2-dichlorobenzene (55 mg, 0.37 mmol) in H$_2$O (200 µL), while stirring the mixture at room temperature. After addition of 11.3 µL of a 0.6 M stock (aqueous) of NaOAc (6.8 µmol, 0.9 mol%), the mixture was cooled in an ice/water bath and H$_2$O$_2$ (50 wt% in water, 64 µL, 1.13 mmol, 1.5 equiv.) was added in one portion. The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, 1,1,2,2-tetrachloroethane (49 mg, 0.29 mmol) was added to the mixture and measured by $^1$H NMR spectroscopy. $^1$H NMR spectroscopic analysis of the solution provided product yield relative to the internal standard (1,1,2,2-tetrachloroethane) integration and the products were identified by comparison to the $^1$H NMR spectra of authentic samples. This reaction showed 100% conversion, 75% epoxide formation, 4% diol formation, 9% α-hydroxy ketone formation and trace amount of overoxidation products (benzaldehyde, benzoic acid).

$^1$H NMR spectrum in acetone-d$_6$ of the product mixture from oxidation of styrene
Entry 6. *trans*-β-Methylstyrene

A stock solution containing both Mn(ClO₄)₂·6H₂O (3.6 mg, 0.01 mmol) and pyridine-2-carboxylic acid (62.0 mg, 0.5 mmol) in acetone-d₆ (20 mL) was prepared prior to the experiment. 1.5 mL of this stock solution (0.75 µmol Mn(ClO₄)₂·6H₂O, 0.1 mol%, and 37.5 µmol pyridine-2-carboxylic acid, 5.0 mol%) was added to the solution of *trans*-β-methylstyrene (78 mg, 0.65 mmol) and 1,2-dichlorobenzene (58 mg, 0.39 mmol in H₂O (200 µL), while stirring the mixture at room temperature. After addition of 11.3 µL of a 0.6 M stock (aqueous) of NaOAc (6.8 µmol, 0.9 mol%), the mixture was cooled in an ice/water bath and H₂O₂ (50 wt% in water, 64 µL, 1.13 mmol, 1.5 equiv.) was added in one portion. The mixture was stirred for 16 h, allowing the temperature to rise to room temperature. After 16 h, 1,1,2,2-tetrachloroethane (67 mg, 0.40 mmol) was added to the mixture and measured by ¹H NMR spectroscopy. ¹H NMR analysis of the solution provided product yield relative to the internal standard (1,1,2,2-tetrachloroethane) integration and the products were identified by comparison to the ¹H NMR spectra of authentic samples. This reaction showed 100% conversion, 65% epoxide formation, 7% diol formation, 12% α-hydroxy ketone formation.

¹H NMR spectrum in acetone-d₆ of the product mixture obtained upon oxidation of *trans*-β-methylstyrene
Entry 7. 2-Methyl-2-pentene

A stock solution containing both Mn(ClO$_4$)$_2$·6H$_2$O (3.6 mg, 0.01 mmol) and pyridine-2-carboxylic acid (62.0 mg, 0.5 mmol) in acetone-d$_6$ (20 mL) was prepared prior to the experiment. 1.5 mL of this stock solution (0.75 µmol Mn(ClO$_4$)$_2$·6H$_2$O, 0.1 mol%, and 37.5 µmol pyridine-2-carboxylic acid, 5.0 mol%) was added to the solution of 2-methyl-2-pentene (67 mg, 0.78 mmol) and 1,2-dichlorobenzene (53 mg, 0.36 mmol) in H$_2$O (200 µL), while stirring the mixture at room temperature. After addition of 11.3 µL of a 0.6 M stock (aqueous) of NaOAc (6.8 µmol, 0.9 mol%), the mixture was cooled in an ice/water bath and H$_2$O$_2$ (50 wt% in water, 64 µL, 1.13 mmol, 1.5 equiv.) was added in one portion. The mixture was stirred for 16 h, allowing temperature to rise to room temperature. After 16 h, the mixture was measured by $^1$H NMR spectroscopy. $^1$H NMR spectroscopic analysis of the solution provided product yield relative to the internal standard (1,2-dichlorobenzene) integration and the products were identified by comparison to the $^1$H NMR spectra of authentic samples. This reaction showed 100% conversion, 62% epoxide formation, 13% diol formation.

$^1$H NMR spectrum in acetone-d$_6$ of the product mixture from oxidation of 2-methyl-2-pentene.
**4. Oxidation of pyridine-2-carboxaldehyde to pyridine-2-carboxylic acid**

Pyridine-2-carboxaldehyde (3 mmol, 0.32 g) and Mn(ClO$_4$)$_2$.6H$_2$O (3 µmol added as 2 mL of a stock solution in acetone, 10.8 mg in 20 mL) were added to 4 mL of acetone and cooled in an ice/water bath. After addition of 340 µL of H$_2$O$_2$ (50 wt% in water, 0.34 mL, 6 mmol, 2 equiv.), the mixture was stirred for 16 h, allowing the temperature to rise slowly to room temperature. The reaction mixture was diluted with H$_2$O (10 mL) and extracted with CH$_2$Cl$_2$. The organic extract was dried over MgSO$_4$ and solvent was removed in vacuo.

$^1$H NMR spectrum in CDCl$_3$ of crude product of oxidation of pyridine-2-carboxaldehyde after work up showing pyridine-2-carboxylic acid and pyridine-2-carboxylic acid-N-oxide.
5. Stability of rac-diethyl oxirane-2,3-dicarboxylate

The epoxide product of diethyl fumarate was subjected to typical reaction conditions to determine the involvement of epoxide ring-opening in the reaction. Under optimised reaction conditions for diethyl fumarate over 24 hours no change was noted by Raman spectroscopy. The reaction was subsequently quenched on saturated aqueous NaHCO$_3$, extracted with CH$_2$Cl$_2$, dried and solvent removed in vacuo. The $^1$H NMR spectrum obtained for the recovered material showed only the initial epoxide. The stability of the epoxide under reaction conditions confirms that cis-diol products are from direct cis-dihydroxylation and not from initial epoxidation followed by ring-opening.
6. Competition experiments and affect of added acetic acid on reaction rate

6.1 Competition experiment in the oxidation of diethyl fumarate and diethyl maleate

\[ \text{EtO} \quad \begin{array}{c} \text{EtO} \\ \text{CO} \\ \text{CO} \end{array} \quad \begin{array}{c} + \\ \text{1.5 equiv. } \text{H}_2\text{O}_2 \\ 0.1 \text{ mol\% } \text{Mn(ClO}_4)_2 \cdot 6\text{H}_2\text{O} \\ 0.3 \text{ mol\% } \text{pyridine-2-CO}_2\text{H} \\ 1.0 \text{ mol\% } \text{NaOAc} \end{array} \quad \begin{array}{c} \text{EtO} \\ \text{HO} \\ \text{HO} \end{array} \quad \begin{array}{c} \text{EtO} \\ \text{CO} \\ \text{CO} \end{array} \quad \begin{array}{c} 5 \\ \text{1,2-dichlorobenzene} \\ \text{acetone} \\ 5^\circ \text{C} \end{array} \]

![NMR spectrum](image)

Figure S1 Full $^1$H NMR spectrum corresponding to Fig.1 in the main text.
In situ Raman spectra of reaction mixture with 1,2-dichlorobenzene internal reference. Showing decrease of the signals at 1648, 1664 and 1730 cm\(^{-1}\) and the appearance of the products at ca. 1753 cm\(^{-1}\). at 40 min intervals between 0 and 7.5 h and after 21 h. The Raman spectrum of diethyl maleate overlaps with that of diethyl fumarate precluding detailed analysis. Nevertheless the decrease in the intensity of the diethyl fumarate bands is consistent with the conversion determined by NMR spectroscopy.

6.2 Oxidation of diethyl fumarate and in the presence of d/l- and meso-diethyltartrate

A stock solution containing both Mn(ClO\(_4\))\(_2\) \(\cdot\) 6H\(_2\)O (7.2 mg, 19.9 \(\mu\)mol) and pyridine-2-carboxylic acid (7.4 mg, 60.0 \(\mu\)mol) in acetone (10 mL) was prepared prior to the experiment. 0.5 mL of this stock solution (1.0 \(\mu\)mol Mn(ClO\(_4\))\(_2\) \(\cdot\) 6H\(_2\)O, 0.1 mol\%, and 3.0 \(\mu\)mol pyridine-2-carboxylic acid, 0.3 mol\%) was added to the solution of diethyl fumarate (92 mg, 0.5 mmol), d/l-diethyl tartrate (109 mg, 0.5 mmol) and 1,2-dichlorobenzene (56 \(\mu\)L, 0.5 mmol) in acetone (1 mL). After addition of 50.0 \(\mu\)L of a 0.6 M stock (aqueous) of NaOAc (30.0 \(\mu\)mol, 3.0 mol\%), the mixture was cooled to 5 °C and 1.5 equiv. \(\text{H}_2\text{O}_2\) was added in one portion. The reaction was monitored in situ by Raman spectroscopy for 16 h to follow conversion. Excess solid NaHSO\(_3\) was added to the reaction mixture to remove residual peroxides if present (verified using peroxide test-strips). With meso-diethyl tartrate essentially identical results were obtained.
In situ Raman spectra of reaction mixture with 1,2-dichlorobenzene internal reference. Showing decrease of the signals at 1648, 1664 and 1730 cm$^{-1}$ and the appearance of the products at ca. 1753 cm$^{-1}$ at 10 min intervals over 2 h 20 min. The bands of the diethyl fumarate are completely gone by decrease in the intensity of the diethyl fumarate bands is consistent with the conversion determined by $^1$H NMR spectroscopy.

The time course of the reaction shows that full conversion is achieved within 90 min.

6.2 Oxidation of diethyl fumarate with addition of acetic acid after 1 h
In situ monitoring by Raman spectroscopy before (blue) and after 95 min (green), 195 min (pink), 300 min (red) and at 460, 560 and 620 min. The reaction is retarded by the addition of acetic acid which was added after 60 min. but still proceeds to > 85% conversion (confirmed by \(^1\)H NMR spectroscopy). This is in contrast to the situation where acetic acid is added prior to addition of \(\text{H}_2\text{O}_2\). See Table 4 in main text.