Recyclable Enamine Catalysts for Asymmetric Direct Cross-Aldol Reaction of Aldehydes in Emulsion Media

Qiang Gao, Yan Liu, Sheng-Mei Lu, Jun Li and Can Li*

a State Key Laboratory of Catalysis, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, 457 Zhongshan Road, Dalian 116023, China

Tel: 86-411-84379070; Fax: 86-411-84694447; Email: canli@dicp.ac.cn;

b Graduate School of Chinese Academy of Sciences, Beijing, 100049, China

*To whom correspondence should be addressed.

1. Experimental details and characterization of catalysts……………………………………P2

2. Different catalyst screened for the cross-aldol reaction……………………………………P7

3. Photographs of the reaction mixture…………………………………………………P8

5. Microscope images of unstable emulsion system formed with 3………………………..P9

6. HPLC spectra of Aldol Products………………………………………………………P10

7. $^1$HNMR and $^{13}$CNMR spectra of catalyst 3 and 4…………………………………P21
Electronic Supplementary Information

Chemicals and solvents were purchased from commercial suppliers or purified by standard techniques. For preparative thin-layer chromatography (TLC), silica gel plates (GF254) were used. Flash column chromatography was performed using commercial silica gel (200-300 mesh). $^1$H NMR and $^{13}$C NMR spectra were recorded on Bruker AVANCE500HZ at ambient temperature. Elemental analysis was obtained from Elementar Elemental Analyzer Vario EL III; IR spectra were obtained from Thermo Nicolet Nexus 470 FT-IR spectrometer. Mass Spectroscopy was obtained from Micromass UPLC/Q-TOF Micro Mass Spectrometer. Light microscopic images were captured on Nikon TE2000 and Digital Sight DS-U2. HPLC analysis was performed with Agilent HPLC 1200 system equipped with Daicel Chiral AD-H, OD-H, AS-H columns. All the chiral diamines were synthesized according to the published procedure.\textsuperscript{[1]} All the cross-aldol products are known compounds and absolute configurations were determined by correlation to literature reported results.\textsuperscript{[2a,2b]} The $^1$HNMR spectra of cross-aldol products were in accordance with the literature reports.\textsuperscript{[2a,2b]}
General procedure for the synthesis of chiral diamine/POM catalysts 1-5 (combination of diamine with POM acids): To the mixture of chiral diamine (1 mmol) and 10 mL THF, H_{3}PW_{12}O_{40} (1.00 g, 0.33 mmol, dissolved in 10 mL THF) was added in 30 min under Ar atmosphere. After further stirred for 1 hour, the solvent was then removed under vacuum. Then, the obtained solid was washed with ether (3 x 10 mL), and dried under vacuum at 40 °C overnight to give the catalyst as light-yellow powder. The catalysts 1-5 were directly used for the reactions without further purification.

Characterization data of known catalysts 1^{2b}, 2^{2b}, 5^{2b} and unknown catalysts 3, 4:

Catalyst 1:

\[
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{N} \\
\text{N} \\
\text{PW}_{12}O_{40}^{3-}
\end{array}
\]

{^1}H NMR (500 MHz, DMSO, ppm): δ 0.97-1.01 (6H, m), 1.74-2.00 (4H, m), 2.12 (1H, brs), 2.64-2.70 (4H, m), 3.27-3.29 (1H, m), 3.37-3.46 (2H, m), 3.60-3.62 (2H, m); 3.82 (1H, brs).

Catalyst 2:

\[
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{N} \\
\text{H} \\
\text{P}_{12}O_{40}^{3-}
\end{array}
\]

{^1}HNMR (500 MHz, DMSO): δ 1.41-1.42 (2H, m), 1.56-1.58 (4H, m), 1.75-1.76 (2H, m), 1.93-1.98 (2H, m), 2.09-2.13 (1H, m), 2.54-2.74 (2H, brs), 3.24-3.35 (3H, m), 3.59-3.60 (3H, m), 3.83-3.90 (1H, m);
Catalyst 3:

\[ \text{PW}_{12}O_{40}^{3-} \]

\(^1\)H NMR (500 MHz, DMSO): \( \delta \) 0.87-0.89 (6H, m), 1.26-1.29 (4H, m), 1.59-1.63 (1H, m), 1.94-1.97 (2H, m), 2.07-2.09 (1H, m), 2.45-2.47 (4H, m), 2.60-2.70 (2H, m), 3.27-3.44 (2H, m), 3.76-3.79 (1H, m); \(^{13}\)C NMR (125 MHz, DMSO): \( \delta \) 13.91, 19.96, 25.09, 22.64, 27.96, 28.14, 44.97, 52.95, 54.73, 57.41;

HRMS (TOF MS ES+): [M+H] Calcd. for [C\(_{13}\)H\(_{29}\)N\(_2\)]: 213.2331. Found: 213.2336;


Elemental Analysis for C\(_{39}\)H\(_{87}\)N\(_6\)O\(_{40}\)PW\(_{12}\): Calcd. C 13.31%, H 2.47%, N 2.38%;

Found. C 13.64%, H 2.60%, N 2.28%.

IR (KBr, cm\(^{-1}\)): 3442, 2957, 1624, 1459, 1080, 1041, 979, 949, 896, 815.

Catalyst 4:

\[ \text{PW}_{12}O_{44}^{2-} \]

\(^1\)H NMR (500 MHz, DMSO): \( \delta \) 0.84-0.87 (6H, m), 1.16-1.1.30 (20H, m), 1.36-1.38 (4H, m), 1.59-1.62 (1H, m), 1.92-1.95 (2H, m), 2.00-2.08 (2H, m), 2.40-2.46 (4H, m), 2.58-2.64 (2H, m), 3.25-3.27 (2H, m); 3.36-3.38 (2H, m), 3.73-3.76 (1H,m); \(^{13}\)C NMR (125 M Hz, DMSO): \( \delta \) 13.88, 20.03, 22.63, 26.03, 26.77, 27.94, 28.67, 28.93, 31.22, 44.90, 53.21, 54.80, 57.40;
HRMS (TOF MS ES+): [M+H] Calcd. for [C_{21}H_{45}N_2]: 325.3583. Found: 325.3588;
HRMS (TOF MS ES+): [M] Calcd. for [O_{40}PW_{12}]: 2878.1818. Found: 2878.1844;
Elemental Analysis for C_{63}H_{135}N_6O_{40}PW_{12}: Calcd. C 19.62%, H 3.50%, N 2.18%;
Found. C 19.04%, H 3.48%, N 2.16%.
IR (KBr, cm\(^{-1}\)): 3436, 3942, 1625, 1457, 1080, 1043, 979, 948, 894, 812

Catalyst 5:

\[
\begin{array}{c}
\text{P}_{\text{W}_{12}\text{O}_{46}^{3-}} \\
\text{H}_2
\end{array}
\]

\(^1\)H NMR (500 MHz, DMSO): \(\delta\) 0.84-0.87 (6H, m), 1.15-1.1.30 (28H, m), 1.32-1.46 (4H, m), 1.54-1.59 (1H, m), 1.88-1.95 (2H, m), 2.02-2.08 (2H, m), 2.38-2.50 (4H, m), 2.53-2.65 (2H, m), 3.15-3.24 (2H, m); 3.58-3.63 (1H, m).

**General procedure for the asymmetric cross-aldol reaction of two aldehydes catalyzed by 5 in water** (Table 1, entry 5): To the mixture of catalyst 5 (66 mg, 0.025 mmol) and propionaldehyde (360 \(\mu\)L, 5.0 mmol), 2-chlorobenzaldehyde (112 \(\mu\)L, 1.0 mmol) and \(\text{H}_2\text{O}\) (162 \(\mu\)L, 9 equiv.) were added at 0 °C. Emulsion was formed after vigorous stirring (See page 8, photograph b ). After stirring the mixture at 0 °C for 72 hrs, MeOH (6 mL) and NaBH\(_4\) (400 mg) were added. The mixture was stirred for 30 mins at 0 °C. The reaction was then quenched with pH=7.0 phosphate buffer solution and extracted with DCM (3 \(\times\) 15 mL). The organic phases were combined and washed with brine, dried over anhydrous Na\(_2\)SO\(_4\) and concentrated in vacuo after filtration. The residue was directly purified by flash column chromatography carefully to
afford the aldol adducts (silica gel, petroleum ether/AcOEt from 20:1 to 3:1), giving the cross-aldol product \((\text{IR},\text{2R})\)−1-(o-chlorophenyl)-2-methylpropane-1,3-diol (196 mg, 0.98 mmol, 98%) as a colorless oil: anti/syn >20:1 (by \(^1\text{H}\) NMR spectroscopy of the crude mixture).

Enantioselectivity was determined after conversion into the corresponding monobenzoyl ester: 97% ee (Chiralcel AS-H column, \(n\)-Hexane:i-PrOH =99:1, \(\lambda= 230\) nm, 1.2 mL/min, 25 °C), \(t_R\) (major anti isomer) = 33.6 min, \(t_R\) (minor anti isomer) = 36.8 min.

**General procedure for the monobenzoyl protection of the diol:**

![Chemical structure](image)

To the mixture of \((\text{1R, 2R})\)−1-(o-chlorophenyl)-2-methylpropane-1,3-diol (0.8 mmol), catalytic amount of 4-dimethylaminopyridine (DMAP) and pyridine (1620 \(\mu\)L), benzoyl chloride (115 \(\mu\)L) was added at 0 °C. After stirred for 1 h (from 0 °C to room temperature), the reaction was then quenched with \(\text{pH}=7.0\) phosphate buffer solution and extracted with ethyl acetate (3 × 10 mL). The combined organic phase were washed with 1N-HCl solution and brine, dried over anhydrous \(\text{Na}_2\text{SO}_4\), concentrated in vacuo after filtration, and purified by preparative TLC (petroleum ether:ethyl acetate= 6:1).

**General procedure for the recycle of catalyst 5 (Table 3):** After reaction, \(\text{CH}_3\text{OH}(4\text{ mL})\) was added at 0 °C, the chiral diamine/POM catalyst 5 was then precipitated. The reaction solution was centrifuged at 4200 rpm for 5 mins. After removing the liquid, remained solid catalyst was dried in vacuum for 10 hrs and ready for the next recycle.
Table S1. Different protonic acids and diamines used to screen the reaction condition.

![Chemical structures](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Yield(^\text{b}(%)))</th>
<th>Anti/Syn</th>
<th>ee(^\text{c}(%)))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>&lt;5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>95</td>
<td>16:1</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>37</td>
<td>5:1</td>
<td>87</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>49</td>
<td>6:1</td>
<td>84</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>93</td>
<td>&gt;20:1</td>
<td>96</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>70</td>
<td>3:1</td>
<td>30</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
<td>76</td>
<td>10:1</td>
<td>95</td>
</tr>
<tr>
<td>8</td>
<td>8(^\text{d}))</td>
<td>98</td>
<td>&gt;20:1</td>
<td>96</td>
</tr>
</tbody>
</table>

\(^a\) Reaction performed in 360 \text{ uL} propionaldehyde, 112 \text{ uL} 2-chlorobenzaldehyde (1.0 mmol), 7.5 mol\% catalyst, 162 \text{ uL} water, 0 °C, 72 h; \(^b\) isolated yield; \(^c\) ee value of anti-isomer, determined by chiral HPLC after conversion into the monobenzoyl ester; \(^d\) 2.5 mol\% catalyst used.
**Figure S1.** Photographs of the reaction mixture

(a) Mixture of 360 μL propionaldehyde, 112 μL 2-chlorobenzaldehyde (1.0 mmol), 2.5 mol% catalyst 5, homogeneous reaction; (b) Mixture of 360 μL propionaldehyde, 112 μL 2-chlorobenzaldehyde (1.0 mmol), 2.5 mol% catalyst 5, 162 μL water, emulsion formed after stirred for 1 hour; (c) After reaction, catalyst was precipitated when methanol was added.
**Figure S2. Microscope images of emulsion system formed with catalyst 3**

Light microscopic image was taken after the mixture of 360 μL propionaldehyde, 112 μL 2-chlorobenzaldehyde (1.0 mmol), 2.5 mol% catalyst 3 and 162 μL water (9 mmol) was stirred for 1 h. The emulsion was unstable. Even while taking the microscopic images, the aggregation of little droplets to big droplets (>300μm) were observed, and finally, oil phase and aqueous phase were separated.
HPLC Conditions:

(1R, 2R)-1-(o-Chlorophenyl)-2-methylpropane-1, 3-diol (Table 1, entry 5, known compound$^{2a}$)

$^1$H NMR (400 MHz, CDCl$_3$): δ 0.87 (3H, m), 2.09–2.13 (1H, m), 2.58 (2H, brs), 3.68–3.76 (2H, m), 5.11–5.13 (1H, d, $J$=7.2 Hz), 7.21–7.24 (1H, m), 7.30–7.34 (2H, m), 7.56–7.58 (1H, d, $J$=7.6 Hz);

Enantiomeric excess was determined by HPLC with a Chiralcel AS-H column ($n$-hexane : i-PrOH =99:1, λ= 230 nm, 1.2 mL/min, 25 °C), $t_R$ (major) = 33.6 min, $t_R$ (minor) = 36.8 min; after conversion to the monobenzoyl ester.
(1R, 2R)-1-(p-Nitrophenyl)-2-methylpropane-1, 3-diol (Table 2, entry 1, known compound)

$^1$HNMR(500MHz,CDCl$_3$): $\delta$ 0.77 (3H, d, $J$=7.0 Hz), 2.02 (1H,m), 2.80 (2H, br), 3.69 (1H, m), 3.80 (1H, m), 4.70 (1H, d, $J$=7.5 Hz), 7.51-7.53 (2H, m), 8.19-8.22 (2H, m).

Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column ($n$-hexane : $i$-PrOH = 90:10, $\lambda$=254 nm, 1.0 mL/min, 25 °C); $t_R$ (major) = 15.6 min, $t_R$ (minor) = 16.2 min.

<table>
<thead>
<tr>
<th>#</th>
<th>Time</th>
<th>Area</th>
<th>Height</th>
<th>Width</th>
<th>Area%</th>
<th>Symmetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13.44</td>
<td>604.6</td>
<td>34</td>
<td>0.2964</td>
<td>33.455</td>
<td>0.996</td>
</tr>
<tr>
<td>2</td>
<td>14.50</td>
<td>594</td>
<td>31.1</td>
<td>0.3181</td>
<td>32.869</td>
<td>0.987</td>
</tr>
<tr>
<td>3</td>
<td>15.43</td>
<td>305.4</td>
<td>15.1</td>
<td>0.3387</td>
<td>16.952</td>
<td>1.007</td>
</tr>
<tr>
<td>4</td>
<td>16.14</td>
<td>302.2</td>
<td>14.3</td>
<td>0.3527</td>
<td>16.724</td>
<td>0.99</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>#</th>
<th>Time</th>
<th>Area</th>
<th>Height</th>
<th>Width</th>
<th>Area%</th>
<th>Symmetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.59</td>
<td>5541</td>
<td>261.3</td>
<td>0.3534</td>
<td>99.462</td>
<td>1.002</td>
</tr>
<tr>
<td>2</td>
<td>16.24</td>
<td>30</td>
<td>1.8</td>
<td>0.2514</td>
<td>0.533</td>
<td>0.338</td>
</tr>
</tbody>
</table>
(1R, 2R)-1-(m-Nitrophenyl)-2-methylpropane-1, 3-diol (Table 2, entry 2, known compound\textsuperscript{2b})

\textsuperscript{1}HNMR(500MHz, CDCl\textsubscript{3}): δ 0.75 (3H, d, \textit{J}=7.0 Hz), 2.02 (1H, m), 3.2 (2H, br), 3.69 (1H, m), 3.80 (1H, m), 4.68 (1H, d, \textit{J}=8.0 Hz), 7.52 (1H, t, \textit{J}=8.0 Hz), 7.67 (1H, d, \textit{J}=7.5 Hz), 8.12-8.14 (1H, m), 8.21 (1H, m).

Enantiomeric excess was determined by HPLC with a Chiralpak AS-H column (\textit{n}-hexane : \textit{i}-PrOH =80:20, \textit{\lambda}= 254 nm, 1.0 mL/min, 25 °C); \textit{t}\textsubscript{R} (major) = 19.9 min, \textit{t}\textsubscript{R} (minor) = 25.8 min. after conversion to the monobenzoyl ester.
(1R, 2R)-1-(o-Nitrophenyl)-2-methylpropane-1, 3-diol (Table 2, entry 3, known compound\textsuperscript{2b})

\[^1\text{H}NMR(500\text{MHz, CDCl}_3): \delta 0.87 (3\text{H, d, } J=7.0 \text{ Hz}), 2.03 (1\text{H, br}), 2.09-2.14 (1\text{H, m}), 3.67-3.79 (2\text{H, m}), 3.90 (1\text{H, m}), 5.21 (1\text{H, d, } J=7.0 \text{ Hz}), 7.41-7.44 (1\text{H, m}), 7.63-7.66 (1\text{H, m}), 7.84-7.86 (2\text{H, m})\]

Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (\textit{n}-hexane : \textit{i}-PrOH =90:10, \lambda= 254 \text{ nm, } 1.0 \text{ mL/min, } 25 \text{ °C}; t_R (major) = 12.8 \text{ min, } t_R (minor) = 14.2 \text{ min.}
(1R, 2R)-1-(o-Methoxyphenyl)-2-methylpropane-1, 3-diol (Table 2, entry 4, known compound\textsuperscript{3a})

\[ ^1H \text{NMR (500 MHz, CDCl}_3\text{)}: \delta 0.73 \text{ (3H, d, } J=7.0 \text{ Hz), 2.15-2.18 \text{ (1H, m), 3.46 (2H, brs), 3.63-3.73 \text{ (2H, m), 3.83 (3H, s), 4.84 (1H, d, } J=8.0 \text{ Hz), 6.87-6.89 \text{ (1H, m), 6.95-6.98 (1H, m), 7.23-7.27 (1H, m), 7.31-7.33 \text{ (1H, m).}} \]

Enantiomeric excess was determined by HPLC with a Chiralpak OD-H column (n-hexane : i-PrOH =99:1, \( \lambda = 230 \text{ nm, } 1.0 \text{ mL/min, 25} \circ \text{C); } t_R \text{ (major)} = 9.4 \text{ min, } t_R \text{ (minor)} = 11.7 \text{ min. after conversion to the dibenzoyl ester (the anti-isomers were isolated through preparative TLC).} \]
(1R, 2R)-1-Phenyl-2-methylpropane-1, 3-diol (Table 2, entry 5, known compound\textsuperscript{2a})

$^1$H NMR (500 MHz, CDCl$_3$): δ 0.75 (3H, d, $J=6.5$ Hz), 1.97-2.06 (1H, m), 3.48 (2H, brs), 3.87-4.02 (2H, m), 4.60 (1H, d, $J=9.5$ Hz), 7.27-7.36 (4H, m).

Enantiometric excess was determined by HPLC with a Chiralpak AD-H column (n-hexane : i-PrOH =97:3, $\lambda$= 230 nm, 1.2 mL/min, 25 °C); $t_R$ (major) = 37.9 min, $t_R$ (minor) = 62.1 min; after conversion to the monobenzoyl ester.
(1R, 2R)-1-(Naphthalen-1-yl)-2-methylpropane-1, 3-diol (Table 2, entry 6, known compound\textsuperscript{2a})

\(^1\)H NMR (500 MHz, CDCl\textsubscript{3}): \(\delta\) 0.78 (3H, d, \(J=7.0\) Hz), 2.35-2.36 (1H, m), 2.93 (2H, brs), 3.67-3.81 (2H, m), 5.30 (1H, d, \(J=7.5\) Hz), 7.45-7.50 (3H, m), 7.58-7.59 (1H, m), 7.78-7.80 (1H, m), 7.85-7.87 (1H, m), 8.18-8.20 (1H, m).

Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (n-hexane : i-PrOH =99:1, \(\lambda=230\) nm, 0.5 mL/min, 25 °C); \(t_R\) (major) = 13.5 min, \(t_R\) (minor) = 17.2 min; after conversion to the dibenzoyl ester.
(1R, 2R)-1-(p-Tolyl)-2-methylpropane-1, 3-diol  (Table 2, entry 7, known compound\textsuperscript{25})

\[^1\text{H} \text{NMR (500 MHz, CDCl}_3\text{): } \delta 0.69 (3H, d, J=7.0 \text{ Hz}), 2.01\text{-}2.07 (1H, m), 2.35 (3H, s), 2.88 (2H, brs), 3.68\text{-}3.77 (2H, m), 4.50 (1H, d, J=8.5 \text{ Hz}), 7.15\text{-}7.17 (2H, m), 7.21\text{-}7.23 (2H, m).\]

Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (\(n\)-hexane : \(i\)-PrOH =99:1, \(\lambda\) = 230 nm, 1.0 mL/min, 25 °C); \(t_R\) (major) = 7.6 min, \(t_R\) (minor) = 9.8 min; after conversion to the dibenzoyl ester.

<table>
<thead>
<tr>
<th>#</th>
<th>Time</th>
<th>Area</th>
<th>Height</th>
<th>Width</th>
<th>Area%</th>
<th>Symmetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.592</td>
<td>12058.2</td>
<td>850.7</td>
<td>0.2179</td>
<td>20.443</td>
<td>0.713</td>
</tr>
<tr>
<td>2</td>
<td>9.702</td>
<td>11051.6</td>
<td>613.7</td>
<td>0.2786</td>
<td>13.736</td>
<td>0.732</td>
</tr>
<tr>
<td>3</td>
<td>10.386</td>
<td>16094</td>
<td>857.2</td>
<td>0.3206</td>
<td>30.675</td>
<td>0.537</td>
</tr>
<tr>
<td>4</td>
<td>15.839</td>
<td>17781.8</td>
<td>557.2</td>
<td>0.4888</td>
<td>30.146</td>
<td>0.632</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>#</th>
<th>Time</th>
<th>Area</th>
<th>Height</th>
<th>Width</th>
<th>Area%</th>
<th>Symmetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.61</td>
<td>8290.8</td>
<td>576.2</td>
<td>0.2216</td>
<td>99.393</td>
<td>0.73</td>
</tr>
<tr>
<td>2</td>
<td>9.754</td>
<td>50.6</td>
<td>2.9</td>
<td>0.2702</td>
<td>0.607</td>
<td>0.672</td>
</tr>
</tbody>
</table>
(1R, 2R)-1-(p-Fluorophenyl)-2-methylpropane-1, 3-diol (Table 2, entry 8, known compound2a)

1H NMR (500 MHz, CDCl₃): δ 0.65 (3H, d, J=7.0 Hz), 1.93-1.98 (1H, m), 3.52 (2H, brs), 3.62-3.74 (2H, m), 4.48 (1H, d, J=8.0 Hz), 7.00-7.04 (2H, m), 7.27-7.30 (2H, m).

Enantiomeric excess was determined by HPLC with a Chiralpak AS-H column (n-hexane : i-PrOH =99:1, λ= 254 nm, 1.0 mL/min, 25 °C); t_R (major) = 30.2 min, t_R (minor) = 44.6 min; after conversion to the monobenzoyl ester (the anti-isomers were isolated through preparative TLC).

<table>
<thead>
<tr>
<th>#</th>
<th>Time</th>
<th>Area</th>
<th>Height</th>
<th>Width</th>
<th>Symmetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30.478</td>
<td>2499.2</td>
<td>47.5</td>
<td>0.8151</td>
<td>0.697</td>
</tr>
<tr>
<td>2</td>
<td>45.43</td>
<td>2477</td>
<td>30</td>
<td>1.2145</td>
<td>0.649</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>#</th>
<th>Time</th>
<th>Area</th>
<th>Height</th>
<th>Width</th>
<th>Area%</th>
<th>Symmetry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30.209</td>
<td>2869.8</td>
<td>49.9</td>
<td>0.9593</td>
<td>99.311</td>
<td>0.533</td>
</tr>
<tr>
<td>2</td>
<td>44.582</td>
<td>5.4</td>
<td>8.4E-2</td>
<td>1.0751</td>
<td>0.189</td>
<td>0.749</td>
</tr>
</tbody>
</table>
(1R, 2R)-1-(p-Chlorophenyl)-2-methylpropane-1, 3-diol (Table 2, entry 9, known compound\textsuperscript{2a})

\(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 0.66 (3H, d, J= 7.0 Hz), 1.92-1.98 (1H, m), 3.47 (2H, brs), 3.61-3.67 (2H, m), 4.47 (1H, d, J=8.0 Hz), 7.23-7.28 (2H, m), 7.30-7.30 (2H, m).

Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (\textit{n}-hexane : i-PrOH =99:1, \(\lambda = 254\) nm, 0.5 mL/min, 25 °C); \(t_R\) (major) = 22.9 min, \(t_R\) (minor) = 27.3 min; after conversion to the dibenzoyl ester.
References:


NMR of Catalyst 3:

$^1$HNMR

$^{13}$CNMR
NMR of Catalyst 4:

$^1$HNMR

$^{13}$CNMR