

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

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## Electronic Supplementary Information

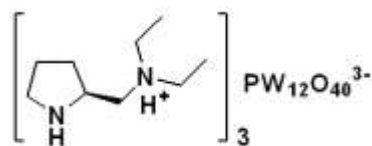
Chemicals and solvents were purchased from commercial suppliers or purified by standard techniques. For preparative thin-layer chromatography (TLC), silica gel plates (GF254) were used. Flash column chromatography was performed using commercial silica gel (200-300 mesh).  $^1\text{H}$  NMR and  $^{13}\text{C}$  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.<sup>[1]</sup> All the cross-aldol products are known compounds and absolute configurations were determined by correlation to literature reported results.<sup>[2a,2b]</sup> The  $^1\text{H}$ NMR spectra of cross-aldol products were in accordance with the literature reports.<sup>[2a,2b]</sup>

### General procedure for the synthesis of chiral diamine/POM catalysts 1-5

**(combination of diamine with POM acids)<sup>3</sup>**: To the mixture of chiral diamine (1 mmol) and 10 mL THF, H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> (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 × 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.

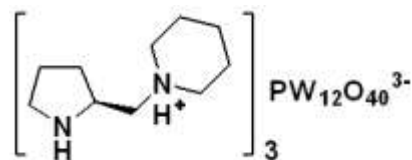
### Characterization data of known catalysts 1<sup>2b</sup>, 2<sup>2b</sup>, 5<sup>2b</sup> and unknown catalysts 3, 4:

#### Catalyst 1:



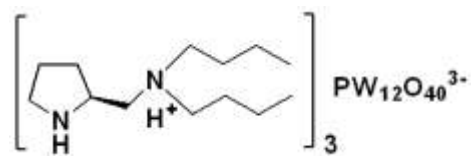
<sup>1</sup>H NMR (500 MHz, DMSO, ppm): δ 0.97-1.01 (6H, m), 1.74-2.00 (4H, m), 2.12 (1H, brs), 2.64-2.70 (4H, m), 3.27-3.29 (1H, m), 3.37-3.46 (2H, m), 3.60-3.62 (2H, m); 3.82 (1H, brs).

#### Catalyst 2:



<sup>1</sup>H NMR (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:**



$^1\text{H}$  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);  $^{13}\text{C}$  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<sup>+</sup>): [M+H] Calcd. for [C<sub>13</sub>H<sub>29</sub>N<sub>2</sub>]: 213.2331. Found: 213.2336;

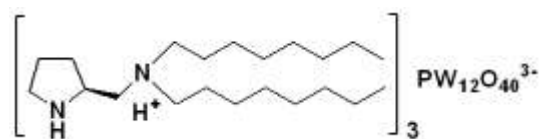
HRMS (TOF MS ES<sup>+</sup>): [M] Calcd. for [O<sub>40</sub>PW<sub>12</sub>]: 2878.1818. Found: 2878.1907;

Elemental Analysis for C<sub>39</sub>H<sub>87</sub>N<sub>6</sub>O<sub>40</sub>PW<sub>12</sub>: Calcd. C 13.31%, H 2.47%, N 2.38%;

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

IR (KBr, cm<sup>-1</sup>): 3442, 2957, 1624, 1459, 1080, 1041, 979, 949, 896, 815.

**Catalyst 4:**



$^1\text{H}$  NMR (500 MHz, DMSO):  $\delta$  0.84-0.87 (6H, m), 1.16-1.130 (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);  $^{13}\text{C}$  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<sup>+</sup>): [M+H] Calcd. for [C<sub>21</sub>H<sub>45</sub>N<sub>2</sub>]: 325.3583. Found: 325.3588;

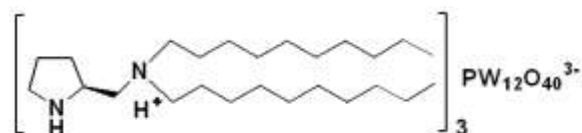
HRMS (TOF MS ES<sup>+</sup>): [M] Calcd. for [O<sub>40</sub>PW<sub>12</sub>]: 2878.1818. Found: 2878.1844;

Elemental Analysis for C<sub>63</sub>H<sub>135</sub>N<sub>6</sub>O<sub>40</sub>PW<sub>12</sub>: Calcd. C 19.62%, H 3.50%, N 2.18%;

Found. C 19.04%, H 3.48%, N 2.16%.

IR (KBr, cm<sup>-1</sup>): 3436, 3942, 1625, 1457, 1080, 1043, 979, 948, 894, 812

### Catalyst 5:



<sup>1</sup>H NMR (500 MHz, DMSO): δ 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 μL, 5.0 mmol), 2-chlorobenzaldehyde (112 μL, 1.0 mmol) and H<sub>2</sub>O (162 μL, 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<sub>4</sub> (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 × 15 mL). The organic phases were combined and washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> 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 (*1R,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),  $t_{\text{R}}$  (major anti isomer) = 33.6 min,  $t_{\text{R}}$ (minor anti isomer) = 36.8 min).

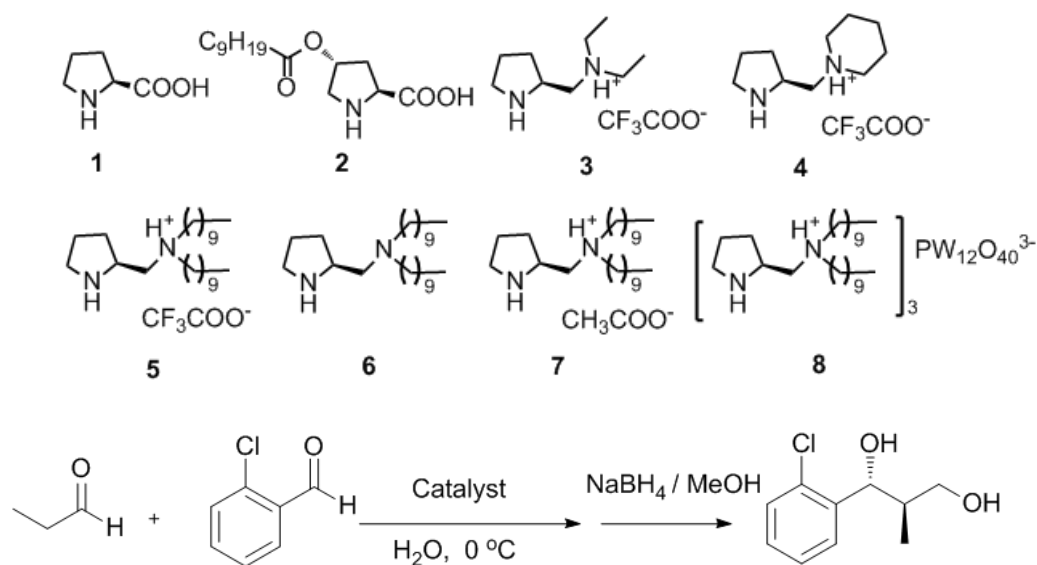
**General procedure for the monobenzoyl protection of the diol:**



To the mixture of (*1R, 2R*)-1-(*o*-chlorophenyl)-2-methylpropane-1,3-diol (0.8 mmol), catalytic amount of 4-dimethylaminopyridine (DMAP) and pyridine (1620  $\mu\text{L}$ ), benzoyl chloride (115  $\mu\text{L}$ ) was added at 0 °C. After stirred for 1 h (from 0 °C to room temperature), the reaction was then quenched with pH=7.0 phosphate buffer solution and extracted with ethyl acetate (3 x 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 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.

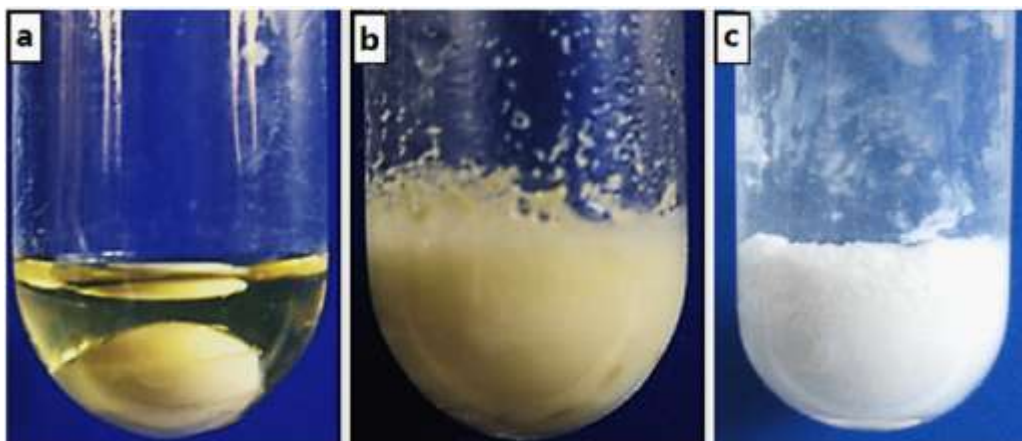
**Table S1.** Different protonic acids and diamines used to screen the reaction condition.



| Entry | Catalyst       | Yield <sup>b</sup> (%) | Anti/Syn | ee <sup>c</sup> (%) |
|-------|----------------|------------------------|----------|---------------------|
| 1     | 1              | <5                     | -        | -                   |
| 2     | 2              | 95                     | 16:1     | 98                  |
| 3     | 3              | 37                     | 5:1      | 87                  |
| 4     | 4              | 49                     | 6:1      | 84                  |
| 5     | 5              | 93                     | >20:1    | 96                  |
| 6     | 6              | 70                     | 3:1      | 30                  |
| 7     | 7              | 76                     | 10:1     | 95                  |
| 8     | 8 <sup>d</sup> | 98                     | >20:1    | 96                  |

<sup>a</sup> Reaction performed in 360  $\mu\text{L}$  propionaldehyde, 112  $\mu\text{L}$  2-chlorobenzaldehyde (1.0 mmol), 7.5 mol% catalyst, 162  $\mu\text{L}$  water,  $0\text{ }^\circ\text{C}$ , 72 h; <sup>b</sup> isolated yield; <sup>c</sup> ee value of *anti*-isomer, determined by chiral HPLC after conversion into the monobenzoyl ester; <sup>d</sup> 2.5 mol% catalyst used.

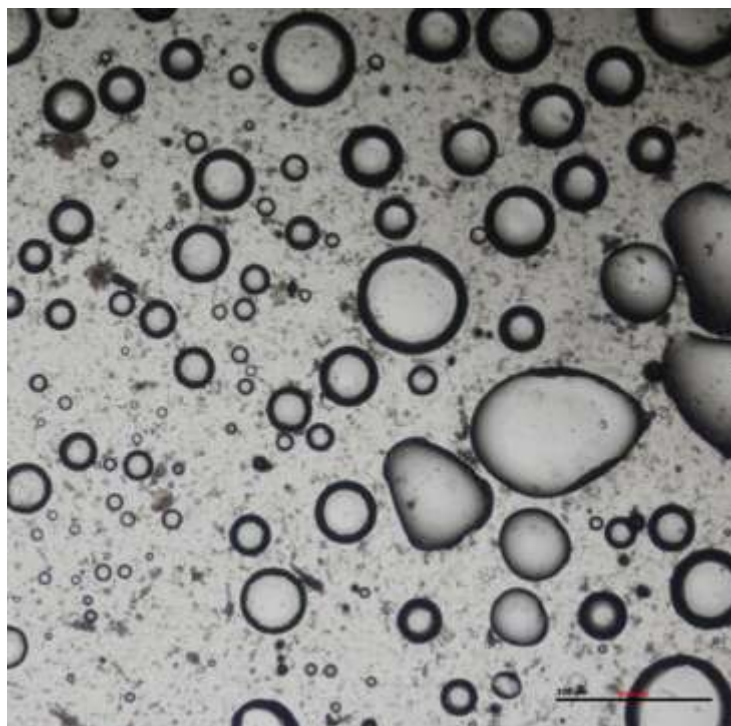
**Figure S1.** Photographs of the reaction mixture



- a) Mixture of 360  $\mu\text{L}$  propionaldehyde, 112  $\mu\text{L}$  2-chlorobenzaldehyde (1.0 mmol), 2.5 mol% catalyst **5**, homogeneous reaction; b) Mixture of 360  $\mu\text{L}$  propionaldehyde, 112  $\mu\text{L}$  2-chlorobenzaldehyde (1.0 mmol), 2.5 mol% catalyst **5**, 162  $\mu\text{L}$  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**



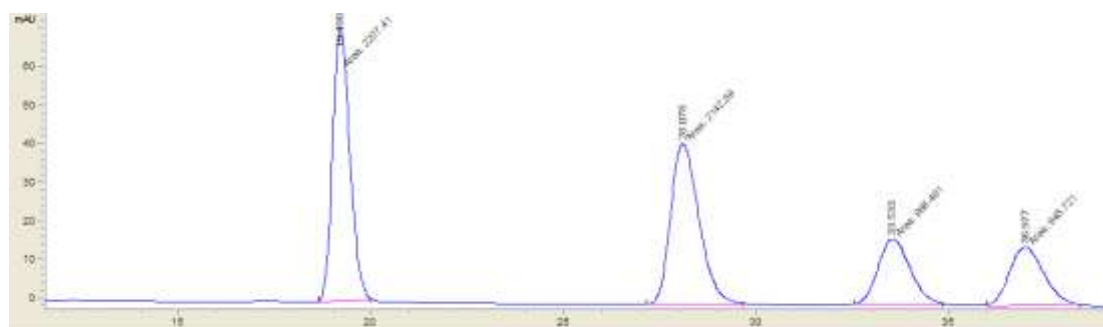
Light microscopic image was taken after the mixture of 360  $\mu\text{L}$  propionaldehyde, 112  $\mu\text{L}$  2-chlorobenzaldehyde (1.0 mmol), 2.5 mol% catalyst **3** and 162  $\mu\text{L}$  water (9 mmol) was stirred for 1 h. The emulsion was unstable. Even while taking the microscopic images, the aggregation of little droplets to big droplets ( $>300\mu\text{m}$ ) were observed, and finally, oil phase and aqueous phase were separated.

## HPLC Conditions :

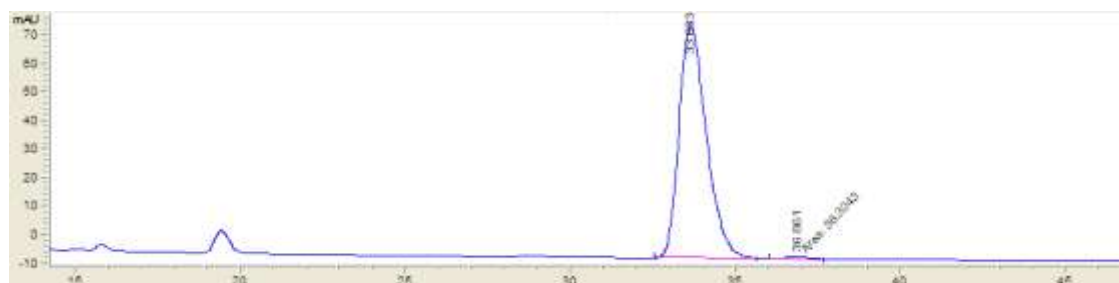
(1*R*, 2*R*)-1-(*o*-Chlorophenyl)-2-methylpropane-1, 3-diol (Table 1, entry 5, known compound<sup>2a</sup>)

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 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<sub>R</sub>* (major) = 33.6 min, *t<sub>R</sub>* (minor) = 36.8 min; after conversion to the monobenzoyl ester.



| # | Time   | Area   | Height | Width  | Area%  | Symmetry |
|---|--------|--------|--------|--------|--------|----------|
| 1 | 19.198 | 2207.4 | 71     | 0.518  | 35.250 | 0.788    |
| 2 | 28.078 | 2142.6 | 41.7   | 0.8555 | 34.215 | 0.703    |
| 3 | 33.533 | 966.5  | 16.8   | 0.9592 | 15.433 | 0.826    |
| 4 | 36.977 | 945.7  | 15.1   | 1.043  | 15.102 | 0.846    |



| # | Time   | Area   | Height | Width  | Area%  | Symmetry |
|---|--------|--------|--------|--------|--------|----------|
| 1 | 33.633 | 4699.9 | 81.8   | 0.8902 | 98.816 | 0.683    |
| 2 | 36.861 | 56.3   | 9.1E-1 | 1.0262 | 1.184  | 1.057    |

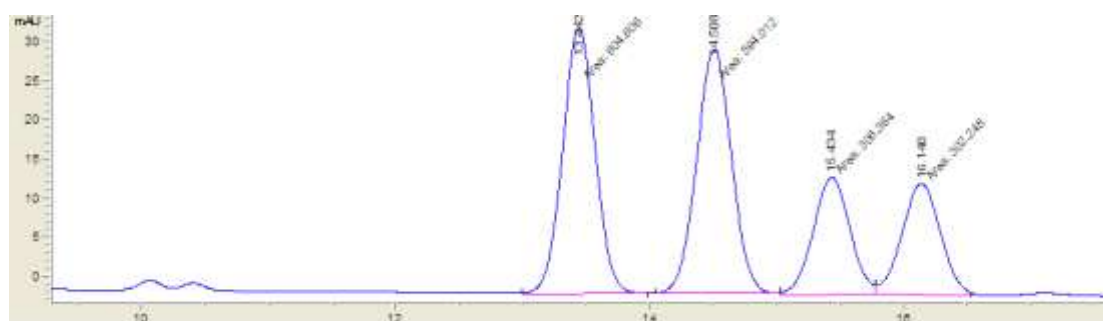
(1*R*, 2*R*)-1-(*p*-Nitrophenyl)-2-methylpropane-1, 3-diol (Table 2, entry 1, known compound<sup>2b</sup>)

<sup>1</sup>HNMR(500MHz,CDCl<sub>3</sub>): δ 0.77 (3H, d, *J*=7.0 Hz), 2.02 (1H,m), 2.80 (2H, br), 3.69

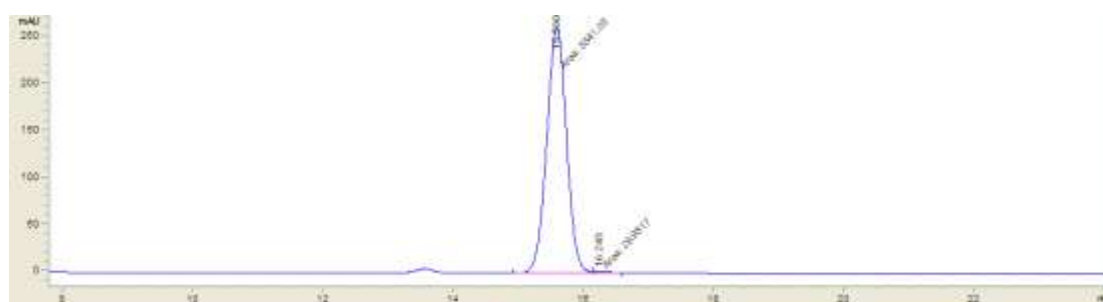
(1H, m), 3.80 (1H, m), 4.70 (1H, d, *J*=7.5 Hz), 7.51-7.53 (2H, m), 8.19-8.22 (2H, m).

Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (*n*-hexane :

*i*-PrOH = 90:10, λ=254 nm, 1.0 mL/min, 25 °C); *t*<sub>R</sub> (major) = 15.6 min, *t*<sub>R</sub> (minor) = 16.2 min.



| # | Time   | Area  | Height | Width  | Area%  | Symmetry |
|---|--------|-------|--------|--------|--------|----------|
| 1 | 13.442 | 604.6 | 34     | 0.2964 | 33.455 | 0.986    |
| 2 | 14.508 | 594   | 31.1   | 0.3181 | 32.869 | 0.987    |
| 3 | 15.434 | 306.4 | 15.1   | 0.3387 | 16.952 | 1.007    |
| 4 | 16.14  | 302.2 | 14.3   | 0.3527 | 16.724 | 0.99     |

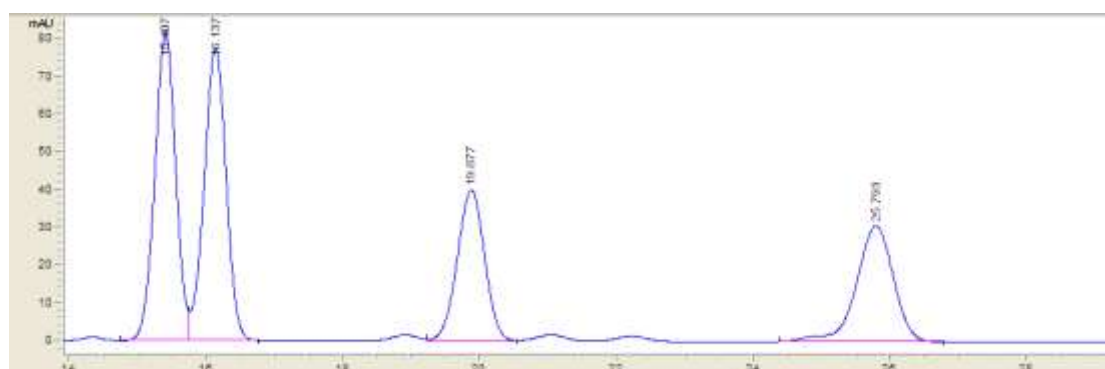


| # | Time   | Area | Height | Width  | Area%  | Symmetry |
|---|--------|------|--------|--------|--------|----------|
| 1 | 15.59  | 5541 | 261.3  | 0.3534 | 99.462 | 1.002    |
| 2 | 16.243 | 30   | 1.8    | 0.2514 | 0.538  | 0.338    |

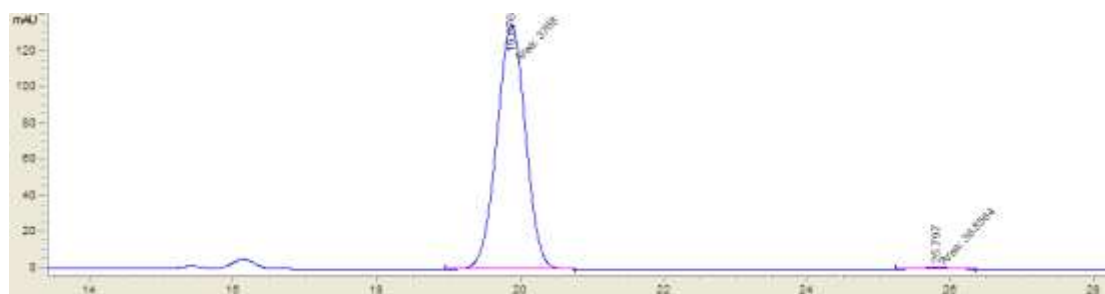
**(1R, 2R)-1-(*m*-Nitrophenyl)-2-methylpropane-1, 3-diol (Table 2, entry 2, known compound<sup>2b</sup>)**

<sup>1</sup>HNMR(500MHz, CDCl<sub>3</sub>): δ 0.75 (3H, d, *J*=7.0 Hz), 2.02 (1H,m), 3.2 (2H, br), 3.69 (1H, m), 3.80 (1H, m), 4.68 (1H, d, *J*=8.0 Hz), 7.52 (1H, t, *J*=8.0 Hz), 7.67 (1H, d, *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 (*n*-hexane : *i*-PrOH =80:20, λ= 254 nm, 1.0 mL/min, 25 °C); *t<sub>R</sub>* (major) = 19.9 min, *t<sub>R</sub>* (minor) = 25.8 min. after conversion to the monobenzoyl ester.



| # | Time   | Area   | Height | Width  | Area%  | Symmetry |
|---|--------|--------|--------|--------|--------|----------|
| 1 | 15.407 | 1741.5 | 81.5   | 0.3309 | 30.289 | 1.025    |
| 2 | 16.137 | 1726.8 | 77.4   | 0.3463 | 30.033 | 1.029    |
| 3 | 19.877 | 1118.8 | 40     | 0.4354 | 19.457 | 1.024    |
| 4 | 25.793 | 1162.7 | 30.7   | 0.583  | 20.221 | 1.131    |

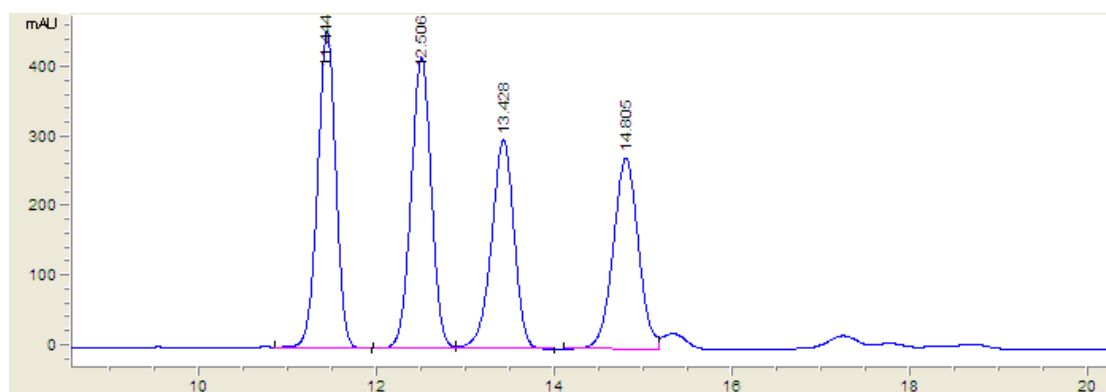


| # | Time   | Area | Height | Width  | Area%  | Symmetry |
|---|--------|------|--------|--------|--------|----------|
| 1 | 19.876 | 3768 | 134.6  | 0.4664 | 99.031 | 1.021    |
| 2 | 25.797 | 36.9 | 1      | 0.5886 | 0.969  | 0.955    |

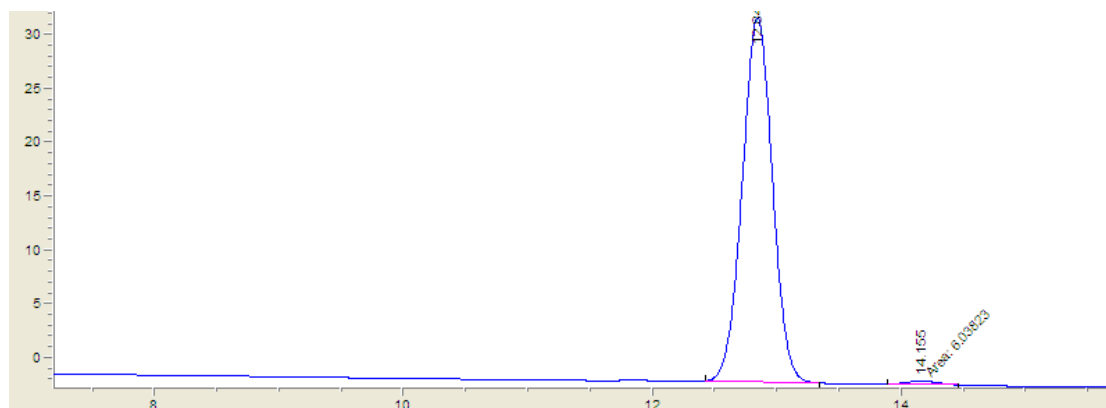
(1*R*, 2*R*)-1-(*o*-Nitrophenyl)-2-methylpropane-1, 3-diol (Table 2, entry 3, known compound<sup>2b</sup>)

<sup>1</sup>HNMR(500MHz, CDCl<sub>3</sub>): δ 0.87 (3H, d, *J*=7.0 Hz), 2.03 (1H, br), 2.09-2.14 (1H, m),  
3.67-3.79 (2H, m), 3.90 (1H, m), 5.21 (1H, d, *J*=7.0 Hz), 7.41-7.44 (1H, m), 7.63-7.66  
(1H, m), 7.84-7.86 (2H, m)

Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (*n*-hexane :  
*i*-PrOH =90:10, λ= 254 nm, 1.0 mL/min, 25 °C); *t*<sub>R</sub> (major) = 12.8 min, *t*<sub>R</sub> (minor) = 14.2 min.



| # | Time   | Area   | Height | Width  | Area%  | Symmetry |
|---|--------|--------|--------|--------|--------|----------|
| 1 | 11.444 | 6616.9 | 457.1  | 0.2243 | 27.469 | 1.066    |
| 2 | 12.506 | 6637.6 | 420.1  | 0.2456 | 27.555 | 1.023    |
| 3 | 13.428 | 5355.5 | 301.1  | 0.2731 | 22.233 | 1.117    |
| 4 | 14.805 | 5478.6 | 275.5  | 0.3063 | 22.743 | 1.002    |

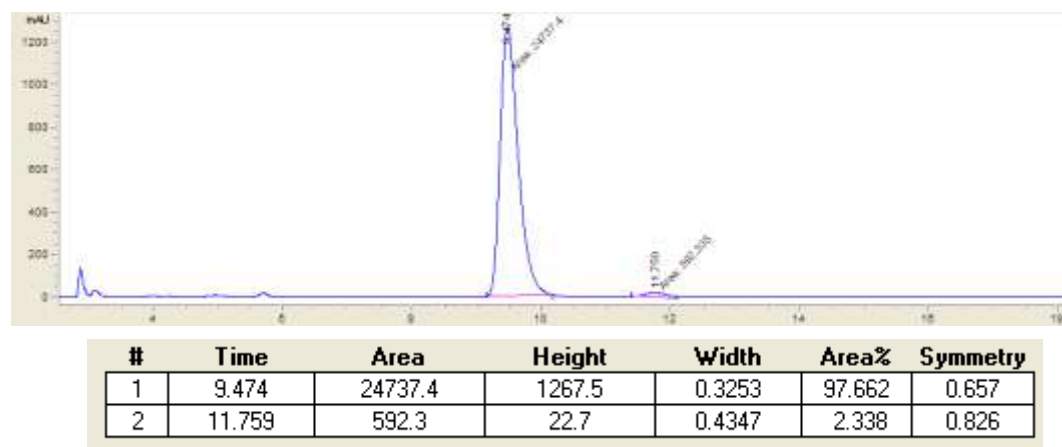
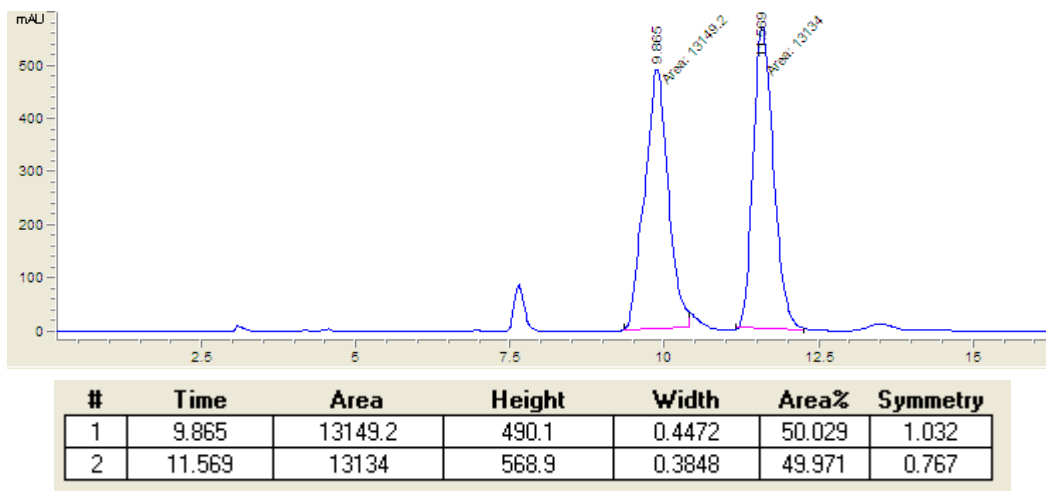


| # | Time   | Area  | Height | Width  | Area%  | Symmetry |
|---|--------|-------|--------|--------|--------|----------|
| 1 | 12.841 | 572.1 | 33.9   | 0.2627 | 98.956 | 1        |
| 2 | 14.155 | 6     | 3.4E-1 | 0.2965 | 1.044  | 0.876    |

(1*R*, 2*R*)-1-(*o*-Methoxyphenyl)-2-methylpropane-1, 3-diol (Table 2, entry 4, known compound<sup>2a</sup>)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 0.73 (3H, d, *J*=7.0 Hz), 2.15-2.18 (1H, m), 3.46 (2H, brs), 3.63-3.73 (2H, m), 3.83 (3H, s), 4.84 (1H, d, *J*=8.0 Hz), 6.87-6.89 (1H, m), 6.95-6.98 (1H, m), 7.23-7.27 (1H, m), 7.31-7.33 (1H, m).

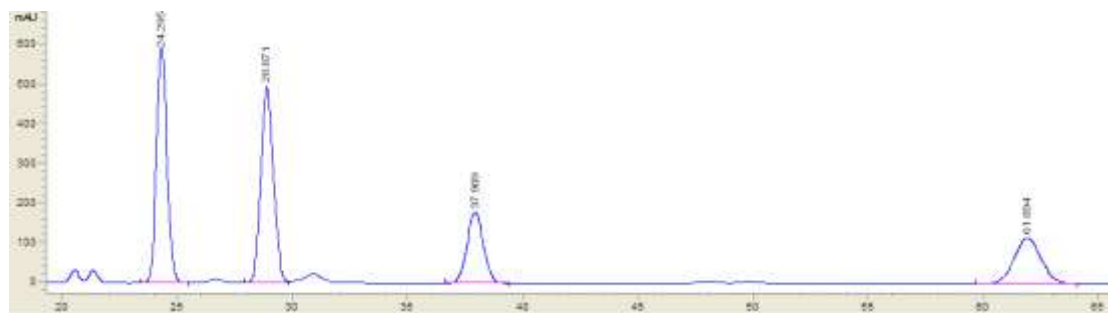
Enantiomeric excess was determined by HPLC with a Chiralpak OD-H column (n-hexane : i-PrOH =99:1, λ= 230 nm, 1.0 mL/min, 25 °C); *t<sub>R</sub>* (major) = 9.4 min, *t<sub>R</sub>* (minor) = 11.7 min., after conversion to the dibenzoyl ester (the anti-isomers were isolated through preparative TLC).



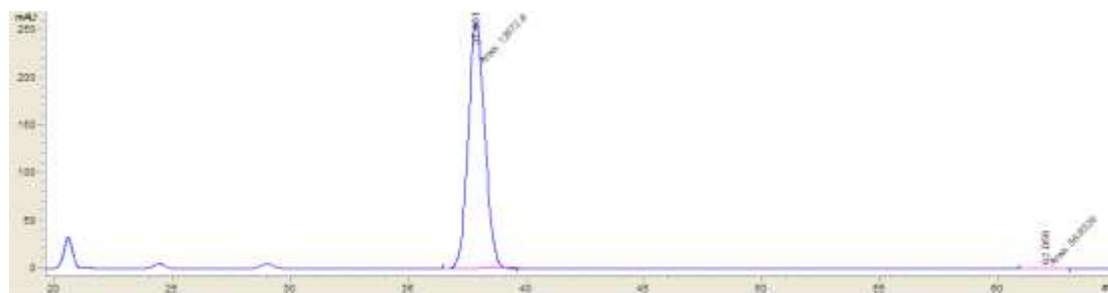
**(1R, 2R)-1-Phenyl-2-methylpropane-1, 3-diol** (Table 2, entry 5, known compound<sup>2a</sup>)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): 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, λ= 230 nm, 1.2 mL/min, 25 °C); *t<sub>R</sub>* (major) = 37.9 min, *t<sub>R</sub>* (minor) = 62.1 min; after conversion to the monobenzoyl ester.



| # | Time   | Area    | Height | Width  | Area%  | Symmetry |
|---|--------|---------|--------|--------|--------|----------|
| 1 | 24.295 | 18859.1 | 592.9  | 0.4906 | 33.721 | 0.853    |
| 2 | 28.871 | 18896.2 | 496.1  | 0.5901 | 33.787 | 0.872    |
| 3 | 37.909 | 8867.8  | 178.1  | 0.7764 | 15.856 | 0.926    |
| 4 | 61.894 | 9304.1  | 114.9  | 1.2569 | 16.636 | 0.956    |

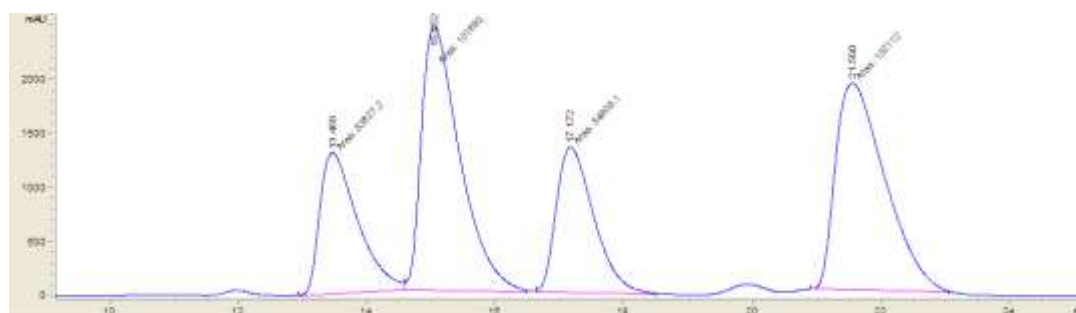


| # | Time   | Area    | Height | Width  | Area%  | Symmetry |
|---|--------|---------|--------|--------|--------|----------|
| 1 | 37.881 | 12672.9 | 256.9  | 0.822  | 99.553 | 0.887    |
| 2 | 62.058 | 56.9    | 7E-1   | 1.3541 | 0.447  | 1.274    |

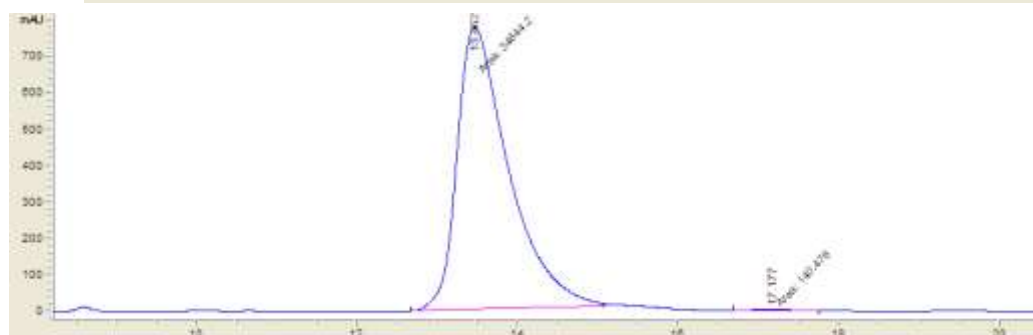
(1*R*, 2*R*)-1-(Naphthalen-1-yl)-2-methylpropane-1, 3-diol (Table 2, entry 6, known compound<sup>2a</sup>)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 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, λ= 230 nm, 0.5 mL/min, 25 °C); *t<sub>R</sub>* (major) = 13.5 min, *t<sub>R</sub>* (minor) = 17.2 min; after conversion to the dibenzoyl ester.



| # | Time   | Area     | Height | Width  | Area%  | Symmetry |
|---|--------|----------|--------|--------|--------|----------|
| 1 | 13.468 | 53827.2  | 1307.9 | 0.6859 | 17.211 | 0.49     |
| 2 | 15.052 | 101892.7 | 2440.9 | 0.6957 | 32.580 | 0.488    |
| 3 | 17.172 | 54909.1  | 1343.4 | 0.6812 | 17.557 | 0.589    |
| 4 | 21.56  | 102112.4 | 1910.9 | 0.8906 | 32.651 | 0.507    |



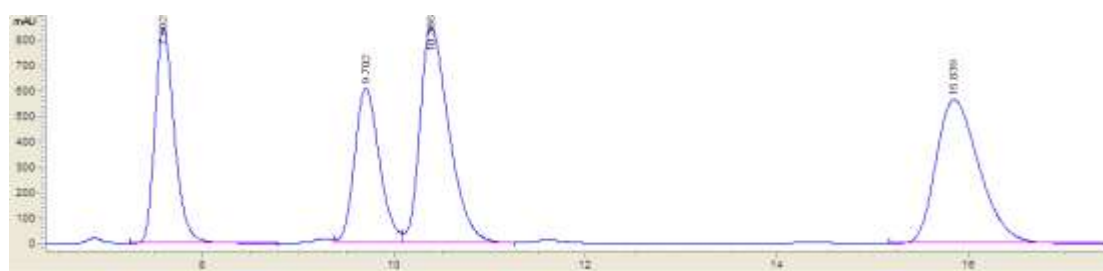
| # | Time   | Area    | Height | Width  | Area%  | Symmetry |
|---|--------|---------|--------|--------|--------|----------|
| 1 | 13.462 | 34644.2 | 771.4  | 0.7486 | 99.596 | 0.506    |
| 2 | 17.177 | 140.5   | 3.9    | 0.5981 | 0.404  | 0.741    |



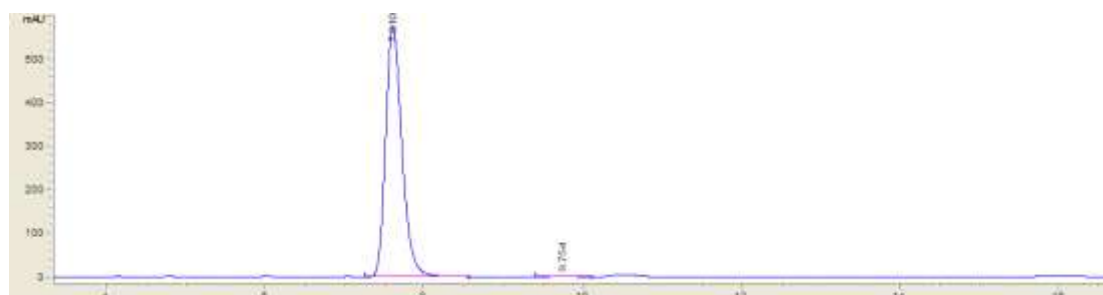
**(1R, 2R)-1-(*p*-Tolyl)-2-methylpropane-1, 3-diol** (Table 2, entry 7, known compound<sup>2a</sup>)

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 0.69 (3H, d, *J*=7.0 Hz), 2.01-2.07 (1H, m), 2.35 (3H, s), 2.88 (2H, brs), 3.68-3.77 (2H, m), 4.50 (1H, d, *J*=8.5 Hz), 7.15-7.17 (2H, m), 7.21-7.23 (2H, m).

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



| # | Time   | Area    | Height | Width  | Area%  | Symmetry |
|---|--------|---------|--------|--------|--------|----------|
| 1 | 7.592  | 12058.2 | 850.7  | 0.2179 | 20.443 | 0.713    |
| 2 | 9.702  | 11051.6 | 613.7  | 0.2786 | 18.736 | 0.782    |
| 3 | 10.386 | 18094   | 857.2  | 0.3206 | 30.675 | 0.597    |
| 4 | 15.839 | 17781.8 | 567.2  | 0.4868 | 30.146 | 0.692    |



| # | Time  | Area   | Height | Width  | Area%  | Symmetry |
|---|-------|--------|--------|--------|--------|----------|
| 1 | 7.61  | 8280.8 | 576.2  | 0.2216 | 99.393 | 0.73     |
| 2 | 9.754 | 50.6   | 2.9    | 0.2702 | 0.607  | 0.872    |

(1*R*, 2*R*)-1-(*p*-Fluorophenyl)-2-methylpropane-1, 3-diol (Table 2, entry 8, known compound<sup>2a</sup>)

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<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): 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*<sub>R</sub> (major) = 30.2 min, *t*<sub>R</sub> (minor) = 44.6 min; after conversion to the monobenzoyl ester(the anti-isomers were isolated through preparative TLC).



| # | Time   | Area   | Height | Width  | Symmetry |
|---|--------|--------|--------|--------|----------|
| 1 | 30.478 | 2499.2 | 47.5   | 0.8151 | 0.697    |
| 2 | 45.48  | 2477   | 30     | 1.2145 | 0.649    |

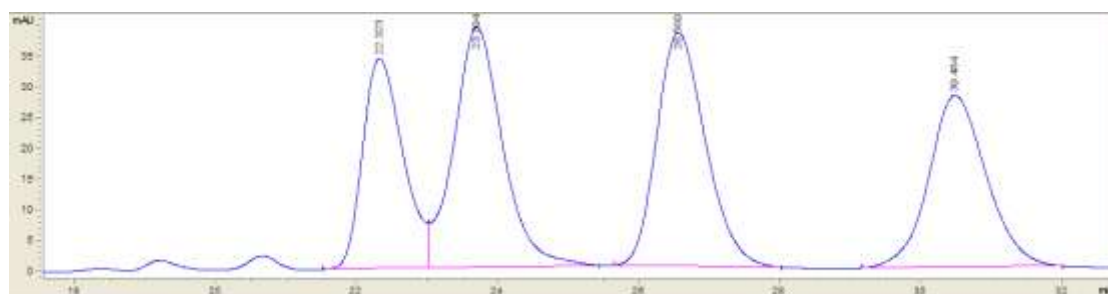


| # | Time   | Area   | Height | Width  | Area%  | Symmetry |
|---|--------|--------|--------|--------|--------|----------|
| 1 | 30.209 | 2869.8 | 49.9   | 0.9593 | 99.811 | 0.533    |
| 2 | 44.582 | 5.4    | 8.4E-2 | 1.0751 | 0.189  | 0.749    |

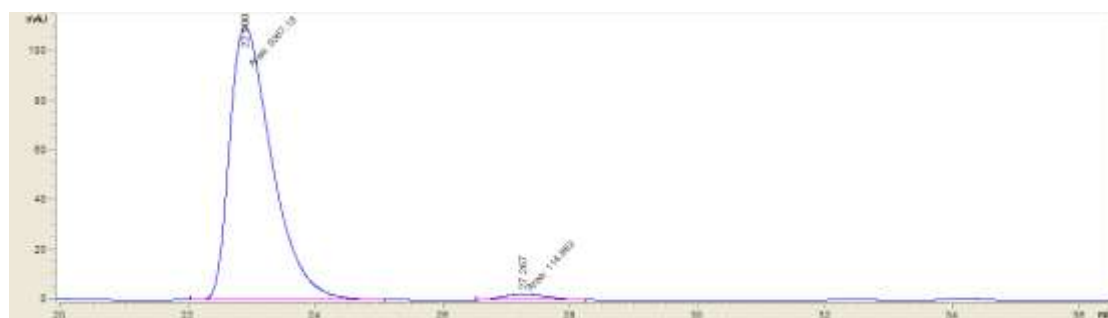
**(1*R*, 2*R*)-1-(*p*-Chlorophenyl)-2-methylpropane-1, 3-diol (Table 2, entry 9, known compound<sup>2a</sup>)**

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 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 (*n*-hexane : *i*-PrOH =99:1, λ= 254 nm, 0.5 mL/min, 25 °C); t<sub>R</sub> (major) = 22.9 min, t<sub>R</sub> (minor) = 27.3 min; after conversion to the dibenzoyl ester.



| # | Time   | Area   | Height | Width  | Area%  | Symmetry |
|---|--------|--------|--------|--------|--------|----------|
| 1 | 22.323 | 1366.5 | 34.1   | 0.6143 | 20.497 | 0.683    |
| 2 | 23.704 | 1880.1 | 39     | 0.7163 | 28.202 | 0.841    |
| 3 | 26.56  | 1829.3 | 38     | 0.7408 | 27.440 | 0.747    |
| 4 | 30.484 | 1590.7 | 28     | 0.8658 | 23.861 | 0.819    |



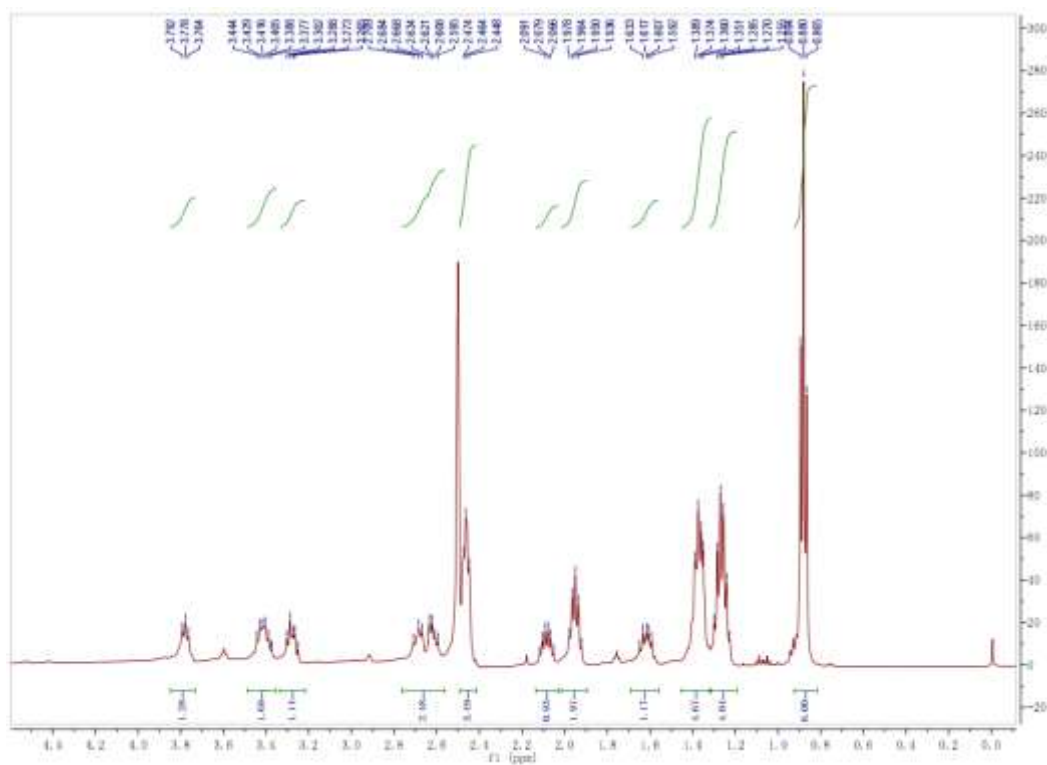
| # | Time   | Area   | Height | Width  | Area%  | Symmetry |
|---|--------|--------|--------|--------|--------|----------|
| 1 | 22.9   | 5067.2 | 110    | 0.7677 | 97.781 | 0.556    |
| 2 | 27.267 | 115    | 2.4    | 0.7927 | 2.219  | 0.85     |

## References:

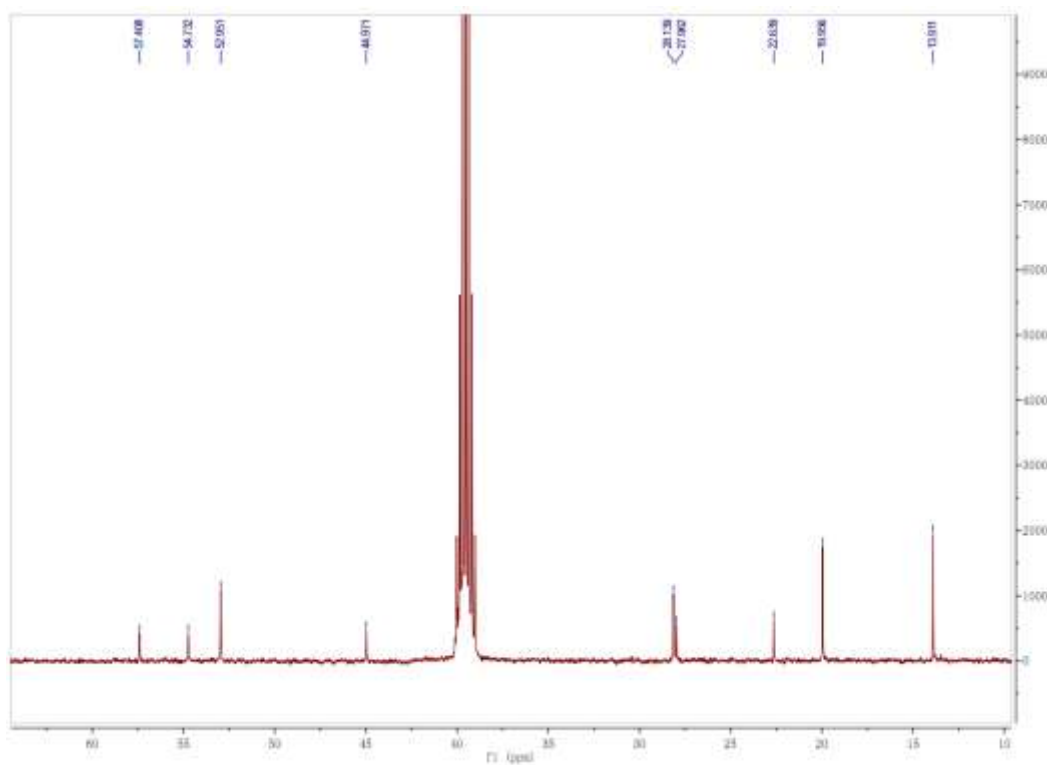
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2. (a) Y. Hayashi, S. Aratake, T. Okano, J. Takahashi, T. Sumiya and M. Shoji, *Angew. Chem. Int. Ed.* 2006, **45**, 5527; (b) J. Li, N. Fu, X. Li, S. Luo and J.-P. Cheng, *J. Org. Chem.*, 2010, **75**, 4501.
3. (a) S. Luo, J. Li, H. Xu, L. Zhang and J.-P. Cheng, *Org. Lett.* 2007, **9**, 3675; (b) J. Li, S. Hu, S. Luo and J.-P. Cheng, *Eur. J. Org. Chem.* 2009, 132.

### NMR of Catalyst 3:

#### $^1\text{H}$ NMR

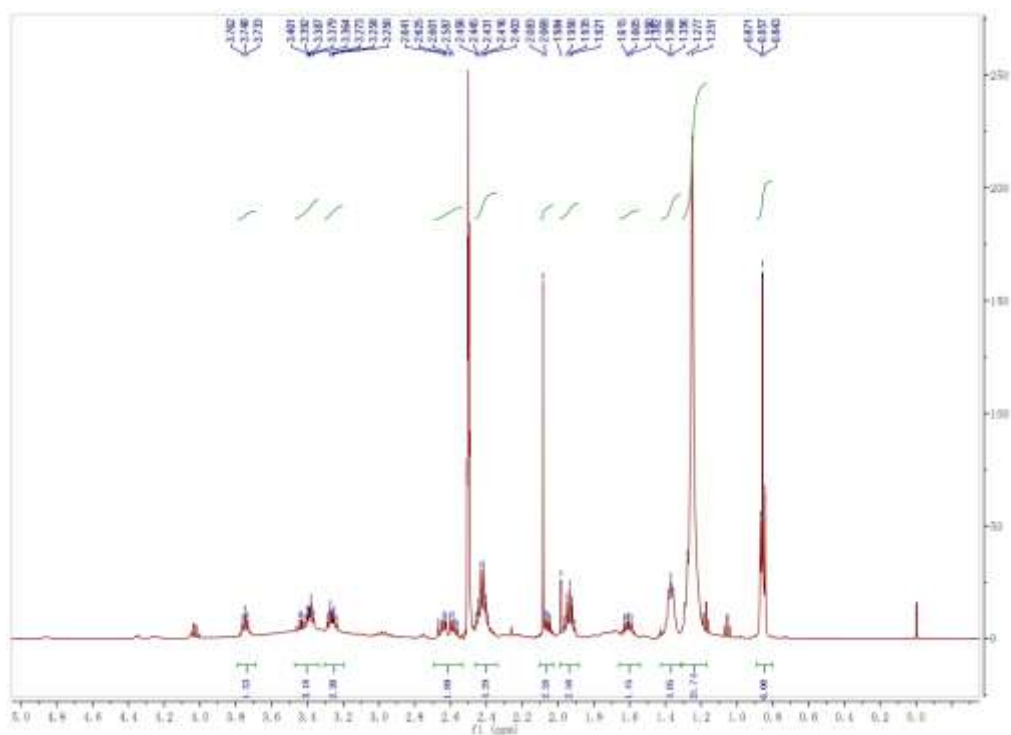


#### $^{13}\text{C}$ NMR



## NMR of Catalyst 4:

### $^1\text{H}$ NMR



### $^{13}\text{C}$ NMR

