

**Supporting Information for**

**Asymmetric Bifunctional Primary Aminocatalysis on Magnetic Nanoparticles**

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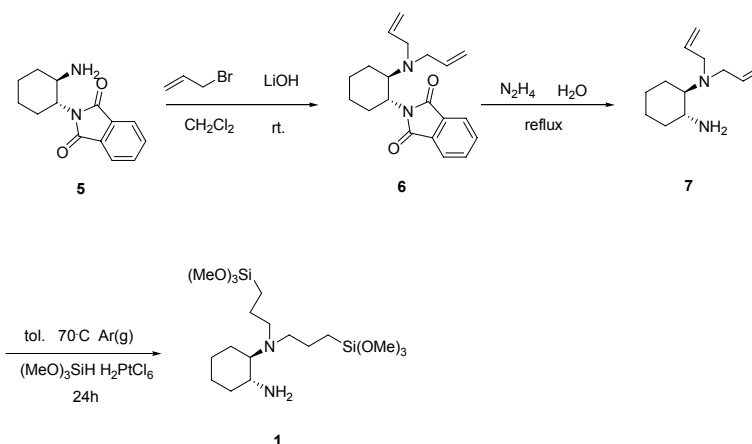
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**General Information:** Commercial reagents were used as received, unless otherwise stated. IR spectrum were obtained from a Jasco FT/IR-480 Plus instrument.

Transmission electron microscope (TEM) images were obtained from a JEOL JEM-2010 instrument. X-ray diffraction (XRD) images were obtained from a Rigaku D/max-2400PC instrument with Cu K $\alpha$  radiation. Elemental analysis (EA) was obtained from ThermoQuest (Flash 1112EA, ITALY). Zeta potential analysis was obtained from Zeta sizer (NANO-ZS, MALVERN). The magnetization curve was obtained by a vibrating sample magnetometer (JDM-13T, CHINA).

## General procedure for the synthesis of catalysts:

### Synthesis of precursor 1:



Compound **6** was prepared according to the procedure of Hitesh Arjan et al<sup>1</sup>. To a stirred solution of **5** (prepared according to the procedure of M. Kaik et al<sup>2</sup>, 4 mmol, 980 mg) in  $\text{CH}_2\text{Cl}_2$  at  $0^\circ\text{C}$ , was added allyl bromide (8 mmol, 690  $\mu\text{L}$ ). After 1 hour, lithium hydroxide monohydrate (8 mmol, 336 mg) was added, and the solution was stirred for 24 h at room temperature. Water (10 mL) was added and the resulting organic layer was separated. The aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  three times, and the combined organic extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated under reduced pressure. The residue was purified by flash column chromatography (petrol ether /ethyl acetate = 8/1) to give product **6** as a yellow solid (714 mg, 55%).  $[\alpha]_{\text{D}}^{20} = +8.1$ , ( $c = 1.0$ , MeOH);  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.20-1.33 (3H, m), 1.79-1.85 (3H, m), 1.95 (1H, m), 2.32 (1H, m), 2.80 (2H, dd,  $J = 8.23$  Hz, 14.27 Hz), 3.20 (2H, m), 3.38 (1H, td,  $J = 3.57$  Hz, 11.25 Hz), 4.14 (1H, td,  $J = 3.57$  Hz, 11.25 Hz), 4.94 (4H, m), 5.44 (2H, m), 7.72( 2H, m), 7.79 (2H, m);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 75 MHz):  $\delta$

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24.7, 25.2, 25.8, 29.8, 52.2, 52.5, 58.5, 116, 122.9, 133.6, 137.4, 168.6; IR spectrum (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{C-H}}$  3451  $\text{cm}^{-1}$ ,  $\nu_{\text{C-H}}$  3076  $\text{cm}^{-1}$ ,  $\nu_{\text{C-H}}$  2929, 2866, 2804  $\text{cm}^{-1}$ ,  $\nu_{\text{C=O}}$  1766, 1706  $\text{cm}^{-1}$ ,  $\nu_{\text{C=C}}$  1650, 1616, 1458  $\text{cm}^{-1}$ ,  $\nu_{\text{C-N}}$  1382  $\text{cm}^{-1}$ ; m.p.: 89 °C; Elemental analysis (EA): calcd. C: 74.04 %, H: 7.46 %, N: 8.64 %, found C: 73.95 %, H: 7.45 %, N: 8.59 %.

Compound **6** (4.69 mmol, 1.52 g) was dissolved in ethanol,  $\text{N}_2\text{H}_4$  (4 mL) was added and the solution was refluxed for 2 hours. The reaction mixture was then filtrated, and the filtrate was diluted by water (20 mL). The aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  three times, and the combined organic extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated to give analytically pure product **7** as a yellow oil, 673 mg, 74%).  $[\alpha]_{\text{D}}^{20} = -67.5$ , ( $c=1.0$ , MeOH);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.15 (4H, m), 1.70-2.05 (4H, m), 2.28 (1H, m), 2.64 (1H, m), 2.89 (2H, dd,  $J = 7.68$  Hz, 11.27 Hz), 3.33 (2H, dd,  $J=5.65$  Hz, 8.67 Hz), 3.26 (2H, m), 5.11 (4H, m), 5.80 (2H, m);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  23.1, 25.0, 25.7, 34.4, 51.3, 52.6, 65.0, 116.3, 137.6. IR spectrum (KBr,  $\text{cm}^{-1}$ ):  $\nu_{\text{C-H}}$  3360, 3302  $\text{cm}^{-1}$ ,  $\nu_{\text{C-H}}$  3075  $\text{cm}^{-1}$ ,  $\nu_{\text{C-H}}$  2927, 2859, 2809  $\text{cm}^{-1}$ ,  $\nu_{\text{C-N}}$  1451, 1359  $\text{cm}^{-1}$ ; HRMS for  $\text{C}_{18}\text{H}_{43}\text{N}_2\text{O}_6\text{Si}_2$  ( $\text{M}^+$ ): calcd. 194.1783, found 194.1782.

Anhydrous toluene (3 mL) and hydrogen hexachloroplatinate (IV) hydrate (catalytic amount, 10 mg) were introduced into a round-bottomed flask containing **7** (1 mmol, 194 mg) under argon. Subsequently, trimethoxysilane (2 mmol, 244 mg) was introduced into the mixture using a hypodermic syringe and the mixture was

heated to 70°C for 24 hours. After cooling to room temperature, the mixture was immediately filtered by applying argon pressure. Compound **1** was unstable and easily polymerized when exposed to air. The toluene solution of **1** was therefore directly used for immobilization without further treatment. For characterization purpose, the solvent was removed under vacuum to afford the desired product **1** as yellow oil with >90% purity as judged by NMR, (438 mg, quant.). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 0.50-0.59 (4H, m), 1.15-1.25 (3H, m), 1.36-1.64 (6H, m), 1.65-1.90 (4H, m) 2.05-2.18 (1H, m), 2.20-2.47 (4H, m), 2.55-2.75 (2H, m), 3.54 (18H, s); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz): δ 6.6, 22.2, 23.7, 24.7, 25.5, 32.9, 50.3, 51.5, 53.0, 65.8; IR spectrum (KBr, cm<sup>-1</sup>): ν<sub>C-H</sub> 3437 cm<sup>-1</sup>, ν<sub>C-H</sub> 2933, 2862 cm<sup>-1</sup>, ν<sub>C-N</sub> 1461, 1386 cm<sup>-1</sup>, ν<sub>Si-O</sub> 1086 cm<sup>-1</sup>; HRMS for C<sub>18</sub>H<sub>43</sub>N<sub>2</sub>O<sub>6</sub>Si<sub>2</sub> (M+1), calcd. 439.2660, found 439.2641. Some minor peaks in NMR spectra may arise from the partially oligomerization of compound **1**, this was proved by the broadening of the <sup>1</sup>H NMR spectra during long standing.

#### **General procedure for the synthesis of PVP-stabilized magnetite nanoparticles:**

Magnetite (Fe<sub>3</sub>O<sub>4</sub>) particles were prepared in a co-precipitation step based on the procedure of Massart et al<sup>3</sup> and T. J. Yoon, et al<sup>4</sup>. FeCl<sub>3</sub>·6H<sub>2</sub>O (22.0 g, 81.4 mmol) and FeCl<sub>2</sub>·4H<sub>2</sub>O (8.0 g, 40.7 mmol) were dissolved in 120mL deionized water under argon with vigorous stirring at 85 °C. the pH value of the solution was adjusted to 9 by concentrated NH<sub>3</sub>·H<sub>2</sub>O. After 4 hours, the magnetite precipitates were washed to pH=7 by deionized water. The black precipitate was collected with a permanent

magnet under the reaction flask, and the supernatant was decanted. The sediment was redispersed in 100 mL of deionized water. The PVP aqueous solution (8.8 mL, 25.6 g/L) was added, and stirred for 1 day at room temperature. The PVP-stabilized magnetite nanoparticles were separated by addition of aqueous acetone ( $\text{H}_2\text{O}/\text{acetone} = 1/10$ , v/v) and centrifugation at 4000 rpm for 10 min. The supernatant solution was removed, and the precipitated particles were washed by ethanol twice. The particles were dried in vacuum.

**General procedure for the synthesis of  $\text{SiO}_2$ -coated magnetite nanoparticles:**

$\text{SiO}_2$ -coated magnetite nanoparticles were prepared according to the procedure of Hyeon et al<sup>5</sup>. PVP stabilized magnetite nanoparticles (2.0 g) were dispersed in 400 mL ethanol.  $\text{NH}_3 \cdot \text{H}_2\text{O}$  (12 mL) and tetraethoxysilane (4.0 mL) was added successively. After stirring for 24 hours, the black precipitate was collected with a permanent magnet, and rinsed with ethanol three times. The product was dried and stored in vacuum. The content of nitrogen is less than 0.3 % as determined by elemental analysis.

**Procedure for the synthesis of the Catalyst 2:**

1.0 g of  $\text{SiO}_2$ -coated magnetite nanoparticles were dispersed in 30 mL of dry toluene by sonication for 1 hour. 0.44 g of **1** (1 mmol in toluene) was then added, and the reaction mixture was refluxed for 4 days under argon. After being cooled to room temperature, the products were sedimented on magnet and rinsed thrice with 100 mL

dry toluene and twice with 100 mL of dry acetone. The obtained particles were dried in vacuum. The loading of the catalyst is determined to be 0.39 mmol/g by elemental analysis.

### **General procedure for the synthesis of the Catalyst 3:**

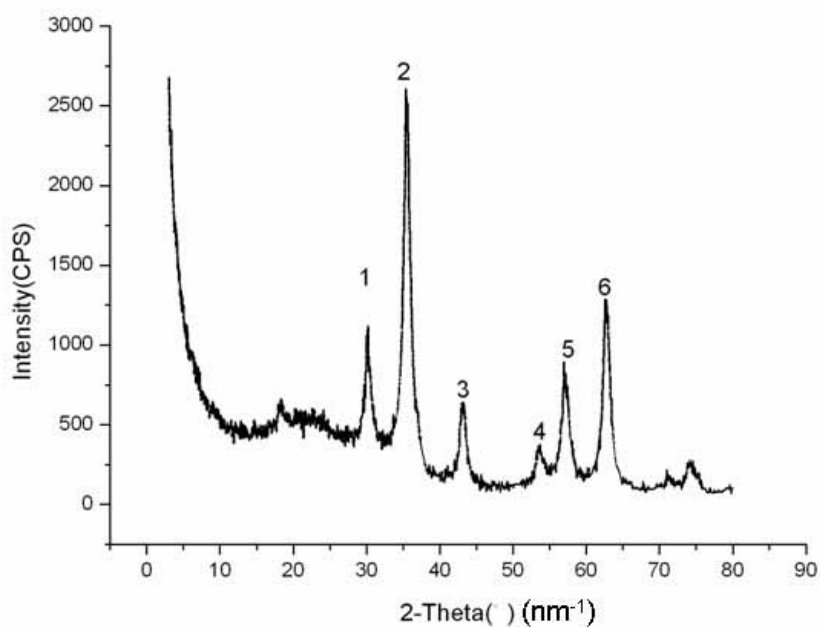
The preparation of catalyst **3** was similar with catalyst **2**. The compound *N*-(triethoxysilyl)propyl-(*-*)-(1*R*,2*R*)-1,2-diaminocyclohexane (**8**) was prepared based on the procedure of A. Adima et al.<sup>6</sup> 1.0 g of PVP-protected MNPs were dispersed in 30 mL dry toluene by sonication for 1 hour. 0.28 g of **8** (1 mmol) was added, and the reaction mixture was refluxed for 4 days under argon. After being cooled to room temperature, the products were sedimented on magnet and rinsed three times with 100 mL dry toluene and twice with 100 mL of dry acetone. The final MNPs were dried in vacuum. The loading of the catalyst is determined to be 1.42 mmol/g by elemental analysis (EA).

### **General procedure for the synthesis of the Catalyst 4:**

The silica we used is commercial amorphous silica (200-300 mesh, about 50-75  $\mu\text{m}$  diameter). 1.0 g of the commercial silica was activated by heating at 120 °C overnight), was dispersed in 30 mL dry toluene by sonication for 1 hour. 0.44 g of **1** (1 mmol in toluene) was added, and the reaction mixture was stirring for 4 days at room temperature under argon. After being cooled to room temperature, the products were precipitated by centrifugation, and rinsed three times with 100 mL dry toluene and twice with 100 mL of dry acetone. The obtained pale yellow powder was dried in

vacuum. The loading of the catalyst **4** is determined to be 0.47 mmol/g by elemental analysis.

**Figure S1** XRD pattern of magnetite nanoparticles.



**Table S1** XRD of magnetite nanoparticles

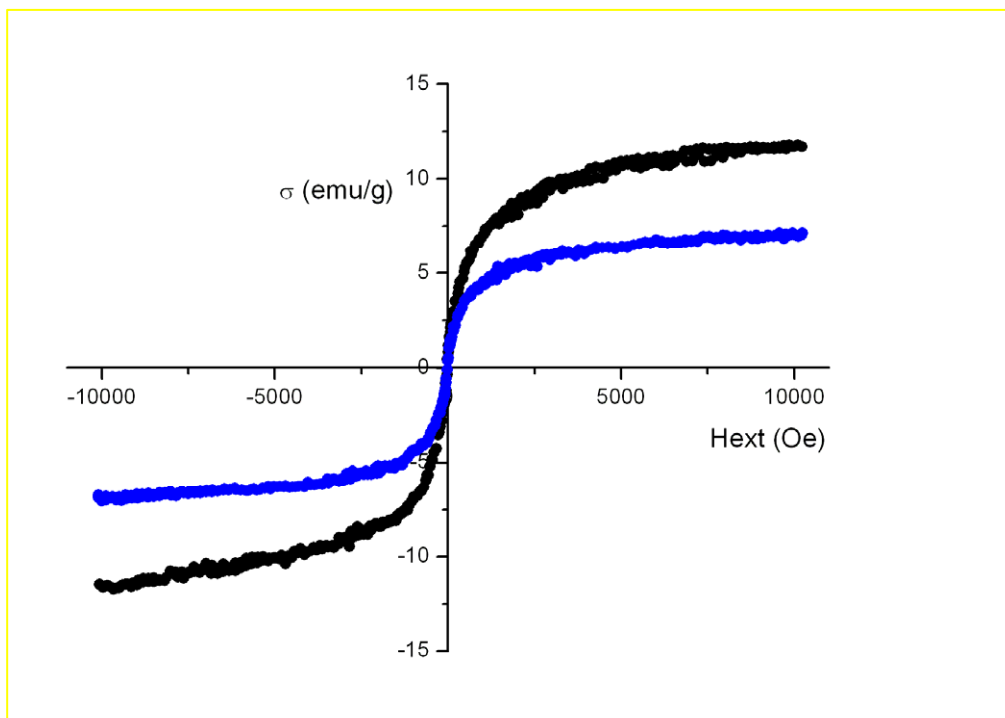
Sample	d (nm)					
Prepared Fe <sub>3</sub> O <sub>4</sub>	0.296	0.252	0.209	0.170	0.161	0.148
Standard Fe <sub>3</sub> O <sub>4</sub>	0.296	0.253	0.209	0.171	0.161	0.148

A dry powder sample of catalyst **2** was used to analyze the XRD pattern of the nanoparticles. The observed diffraction pattern coincides with the JCPDS database for magnetite. The interlayer spacings (d), calculated using the Bragg equation, agree



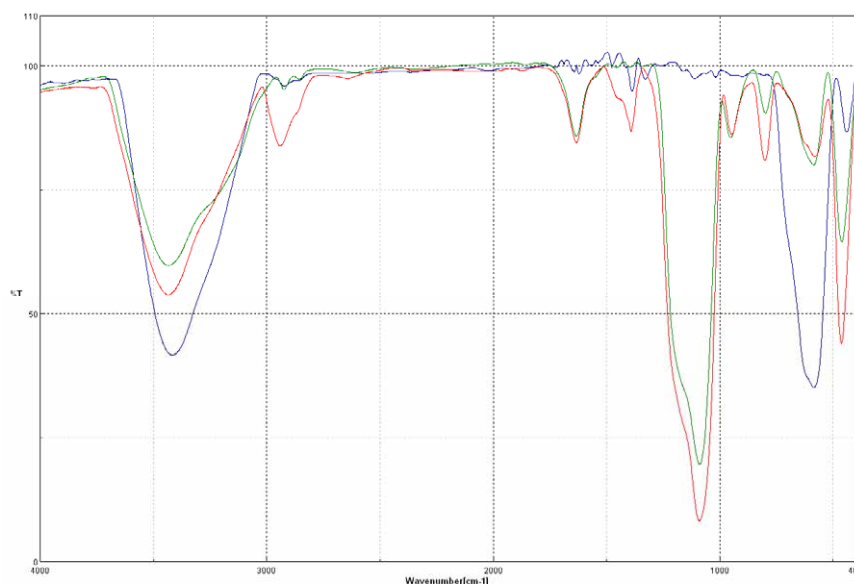
well with the data for standard magnetite (Table S1).

**Figure S2** Magnetic curve of silica-coated magnetite (black) and Catalyst 2 (blue)



The room-temperature magnetization curves of the magnetic nanoparticles before (black line) and after (blue line) functionalization prove that the magnetic nanoparticles are superparamagnetic. The saturation magnetization of samples changed from 11.69 emu/g to 7.00 emu/g because of the functionalization by organic compound **1**.

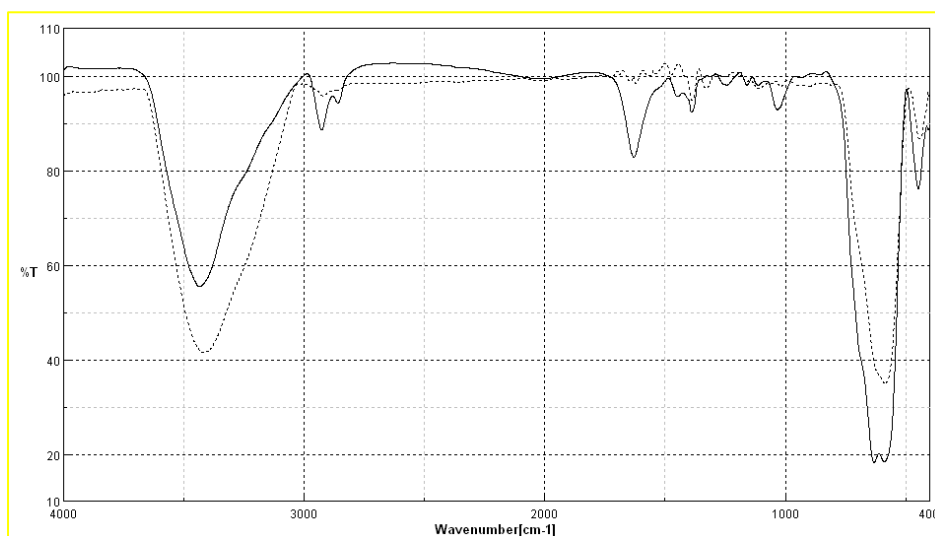
**Figure S3a** FTIR spectra of magnetite nanoparticles (black), silica-coated magnetite (green) and catalyst 2 (red)



The FTIR spectrum for the magnetite nanoparticles alone shows a stretching vibration at 3416 cm<sup>-1</sup> which incorporates the contributions from both symmetrical and asymmetrical modes of the O-H bonds which are attached to the surface iron atoms. The presence of an adsorbed water layer is confirmed by a stretch for the vibrational mode of water found at 1633 cm<sup>-1</sup>. The absorption band at 586 cm<sup>-1</sup> is attributed to the Fe-O bonds. The silica coated particles have stretches at 583, 1088, 1633 and 3434 cm<sup>-1</sup> corresponding to the Fe-O, Si-O-Si, and water stretches respectively. The stretch

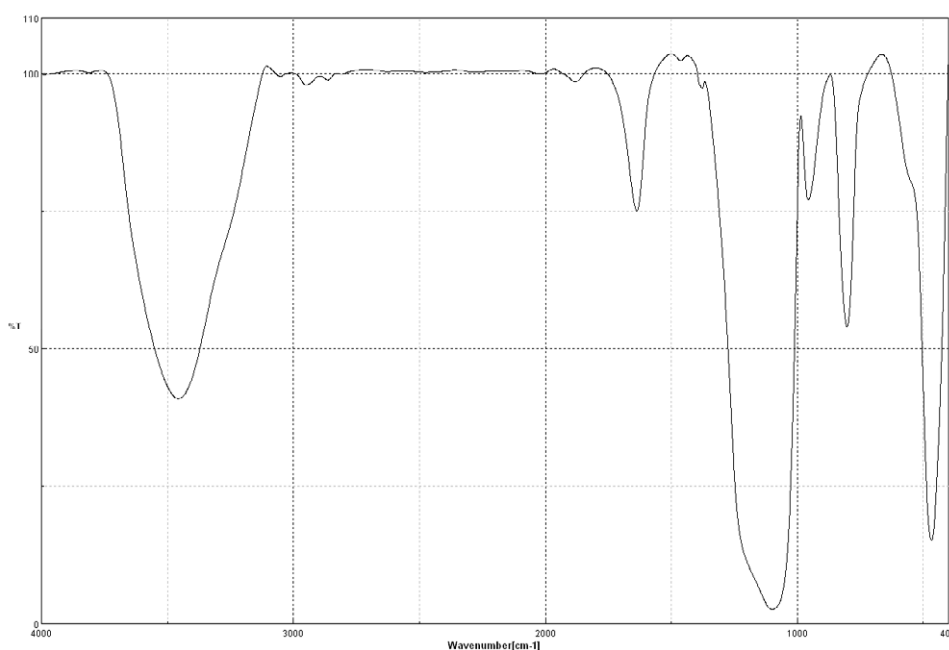
found at  $948\text{ cm}^{-1}$  is due to the presence of Fe-O-Si bonds in the sample. In the spectrum for the catalyst loaded nanoparticles, additional stretches are attributed to the presence of the catalyst. Alkyl C-H stretches are found at  $2941$  and  $2868\text{ cm}^{-1}$ . The amine C-N stretch is found at  $1392\text{ cm}^{-1}$ .

**Figure S3b FTIR spectra of magnetite nanoparticles (dash line), and catalyst 3 (solid line)**



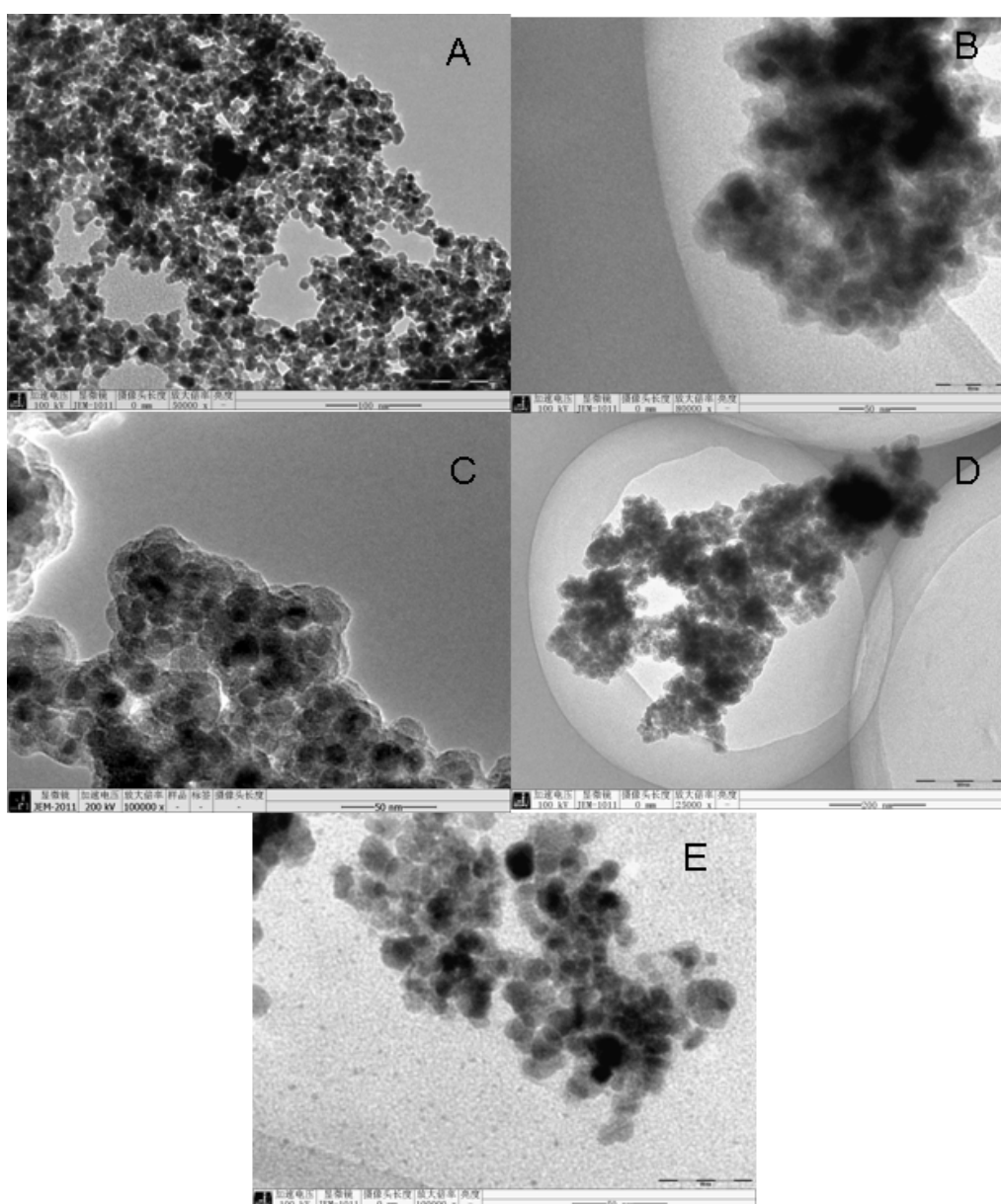
The FTIR spectrum for the magnetite nanoparticles alone shows a stretching vibration at  $3434\text{ cm}^{-1}$  which incorporates the contributions from both symmetrical and asymmetrical modes of the O-H bonds which are attached to the surface iron atoms. The presence of an adsorbed water layer is confirmed by a stretch for the vibrational mode of water found at  $1629\text{ cm}^{-1}$ . The absorption band at  $585\text{ cm}^{-1}$  is attributed to the Fe-O bonds. In the spectrum for the catalyst loaded nanoparticles, additional stretches are attributed to the presence of the catalyst. Alkyl C-H stretches are found at  $2927$  and  $2858\text{ cm}^{-1}$ . The amine C-N stretch is found at  $1390\text{ cm}^{-1}$ .

**Figure S3c FTIR spectra of catalyst 4**



The FTIR spectrum shows a stretching vibration at  $3434\text{ cm}^{-1}$  for the contributions from the O-H bonds. The presence of an adsorbed water layer is confirmed by a stretch for the vibrational mode of water found at  $1629\text{ cm}^{-1}$ . Alkyl C-H stretches are found at  $2949$  and  $2864\text{ cm}^{-1}$ . The amine C-N stretch is found at  $1379\text{ cm}^{-1}$  which was covered by a stronger absorption of Si-O bonds at  $1100\text{ cm}^{-1}$ .

**Figure S4** TEM images (all the samples were prepared in water).



**A:** Fe<sub>3</sub>O<sub>4</sub>; the size of the nanoparticles is about 8-10nm. The shape of the nanoparticle

is spherical.

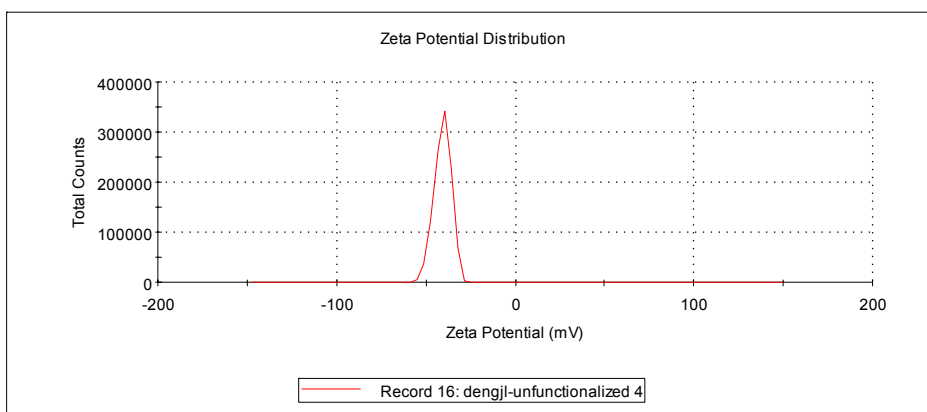
B: SiO<sub>2</sub>@Fe<sub>3</sub>O<sub>4</sub>; the thickness of the SiO<sub>2</sub> layer is about 1-2 nm.

C: Catalyst **2**;

D: Catalyst **2** after 11 recycles

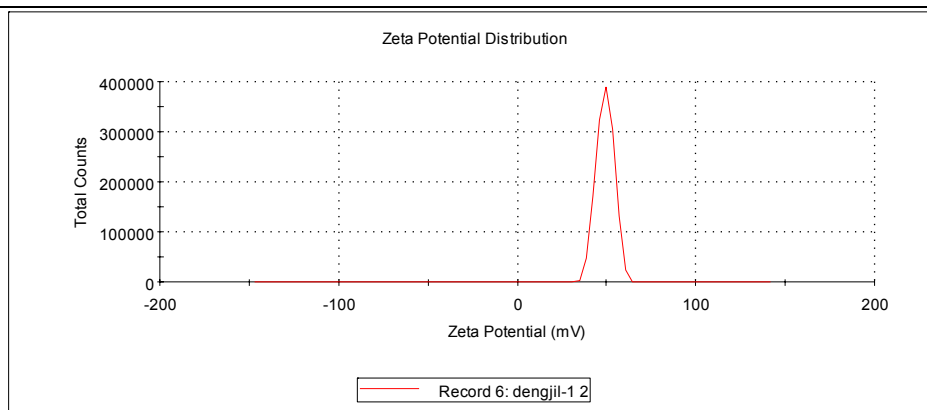
E: Catalyst **3**.

**Figure S5a Zeta potential of SiO<sub>2</sub> coated MNP (before functionalization)**



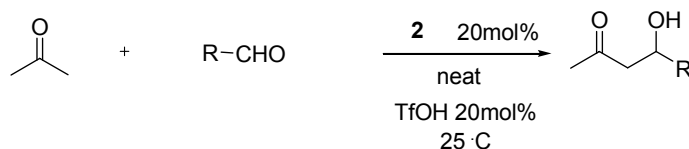
The zeta potential was obtained from silica-coated MNP (0.2 g/L in deionized water pH 6.3 25°C). The zeta potential of this sample is -40.6 mV, suggesting that the particles are dispersed in water very well with good stability. The surface charge is negative.

**Figure S5b Zeta potential of Catalyst 2 (after functionalization)**

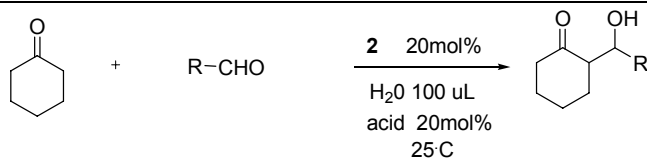


The zeta potential was obtained from Catalyst **2** (0.25 g/L in deionized water pH6.3 25°C). The zeta potential of this sample is +49.0 mV, showing that the particles are with good stability in water after functionalization. The change of surface charge from negative to positive also proves the existence of the attached chiral amines.

#### General Procedure for reactions:



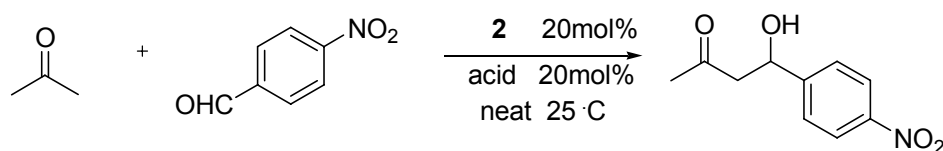
Catalyst **2** (0.05 mmol) was dispersed in 0.2 mL acetone, and the corresponding additive (0.05 mmol) was added. The semi-homogeneous solution was stirred for 10 min, the corresponding aldehyde (0.25 mmol) was added. The resulting solution was stirred at room temperature and monitored by TLC. After the indicated reaction time, ethyl acetate (1 mL) was added, and the extracts were easily decanted by applying a magnet. The extracts were combined and concentrated. The residue was purified by FC on silica gel to afford pure product. All the aldol products are known compounds [7]. We have also reported the characterizations of these products [8].



Catalyst **2** (0.05 mmol) was dispersed in 0.1 mL of cyclohexanone and 0.1 mL of H<sub>2</sub>O, and the corresponding additive (0.05 mmol) was added. The semi-homogeneous solution was stirred for 10 min and the aldehyde (0.25 mmol) was added. The resulting solution was stirred at room temperature and monitored by TLC. After the indicated reaction time, ethyl acetate (1 mL) was added, and the extracts were decanted by applying a magnet. The extracts were combined and concentrated. The residue was purified by FC on silica gel to afford pure product. All the aldol products are known compounds <sup>[7]</sup>. We have also reported the characterizations of these products <sup>[9]</sup>. The diastereoselectivity was determined by <sup>1</sup>H NMR analysis of the crude reaction mixture. The enantioselectivity was determined by chiral HPLC with the purified products. In all the cases examined, the diastereoisomers can be separated using FC.

### Optimization of conditions

**Table S2.** The acid screening<sup>[a]</sup>:



acid	Time (hour)	Yield (%) <sup>[b]</sup>	Ee (%) <sup>[c]</sup>
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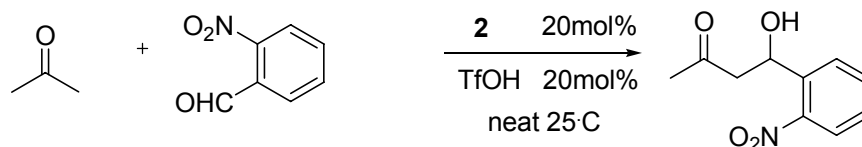


<b>TFA</b>	48	86	66
<b>CF<sub>3</sub>SO<sub>3</sub>H</b>	48	84	73
<b>AcOH</b>	48	81	50
<b>m-NO<sub>2</sub>PhCOOH</b>	48	72	58
<b>PTSA</b>	48	33	63
<b>Camphor sulfonic acid</b>	48	43	57
<b>PhCOOH</b>	48	48	47
<b>Cl<sub>2</sub>CHCOOH</b>	48	81	60
<b>H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub></b>	48	76	67
<b>ZnCl<sub>2</sub></b>	48	48	49

[a] 0.25 mmol aldehyde, 200  $\mu$ L acetone. [b] isolated yields. [c] determined by

HPLC.

**Catalyst recycling<sup>[a]</sup>:**



<b>RUN</b>	<b>Time (hour)</b>	<b>Yield (%)<sup>[b]</sup></b>	<b>Ee (%)<sup>[c]</sup></b>
<b>1</b>	32	92	69
<b>2</b>	32	92	69
<b>3</b>	32	91	69
<b>4</b>	32	92	69
<b>5</b>	32	92	70
<b>6</b>	32	92	69
<b>7</b>	32	92	69
<b>8</b>	32	91	69
<b>9</b>	32	90	69
<b>10</b>	48	90	68
<b>11</b>	48	82	69

[a] 0.25 mmol aldehyde, 200  $\mu$ L acetone. [b] isolated yields. [c] determined by

HPLC.

**Reference:**

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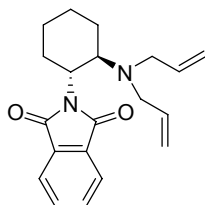
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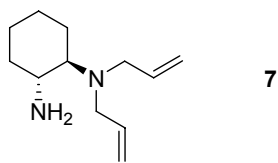
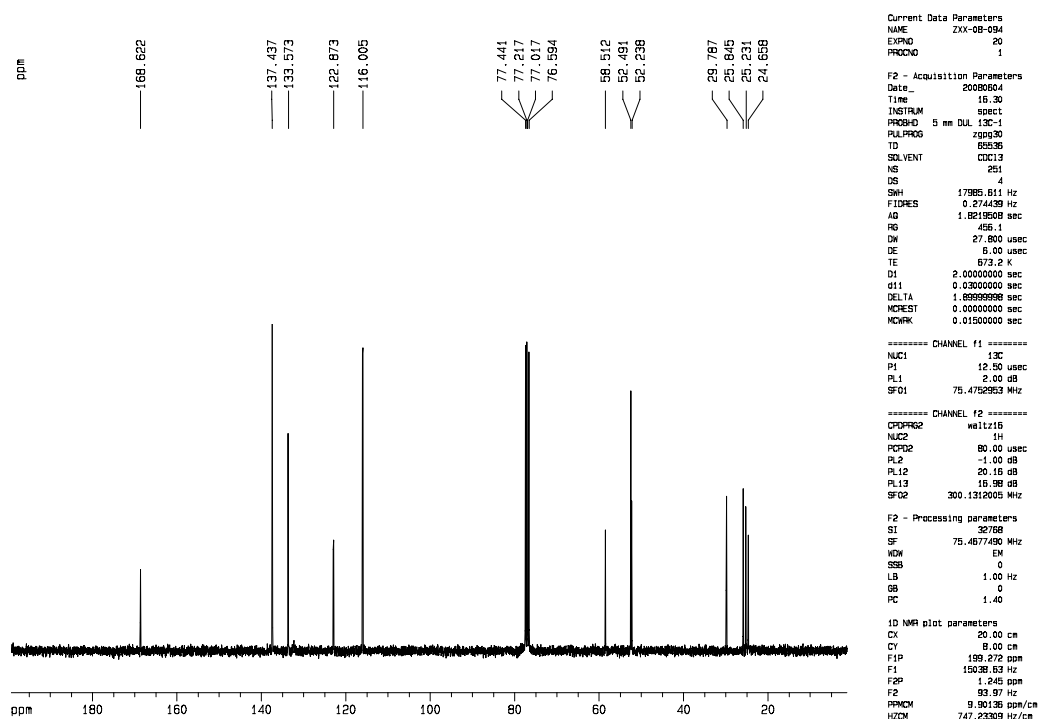
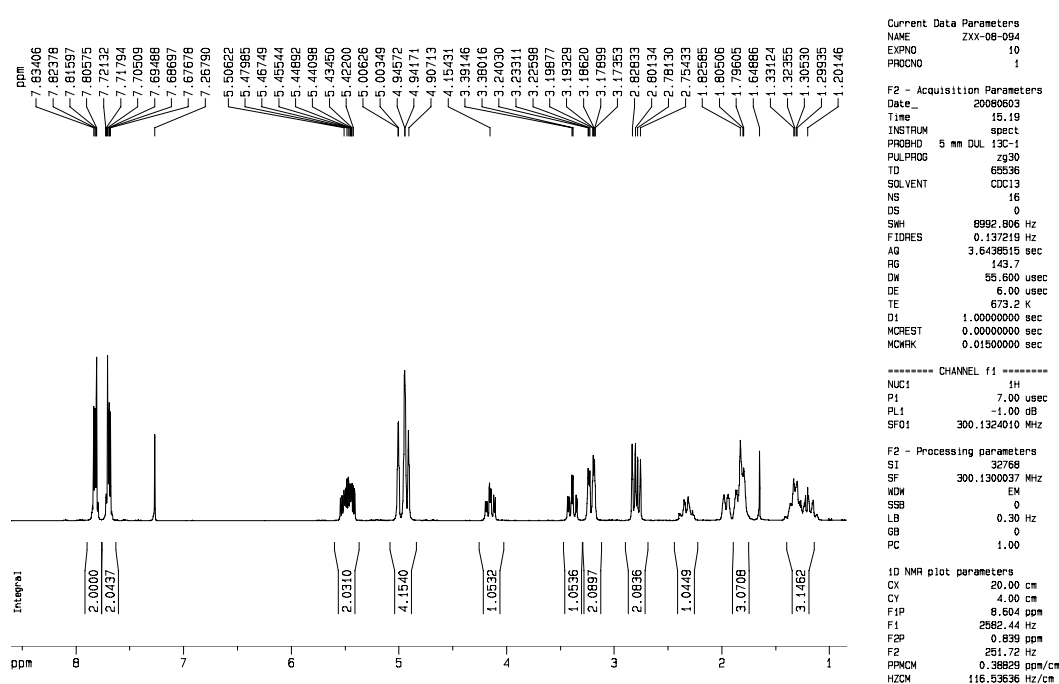
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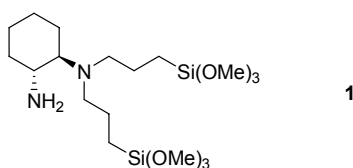
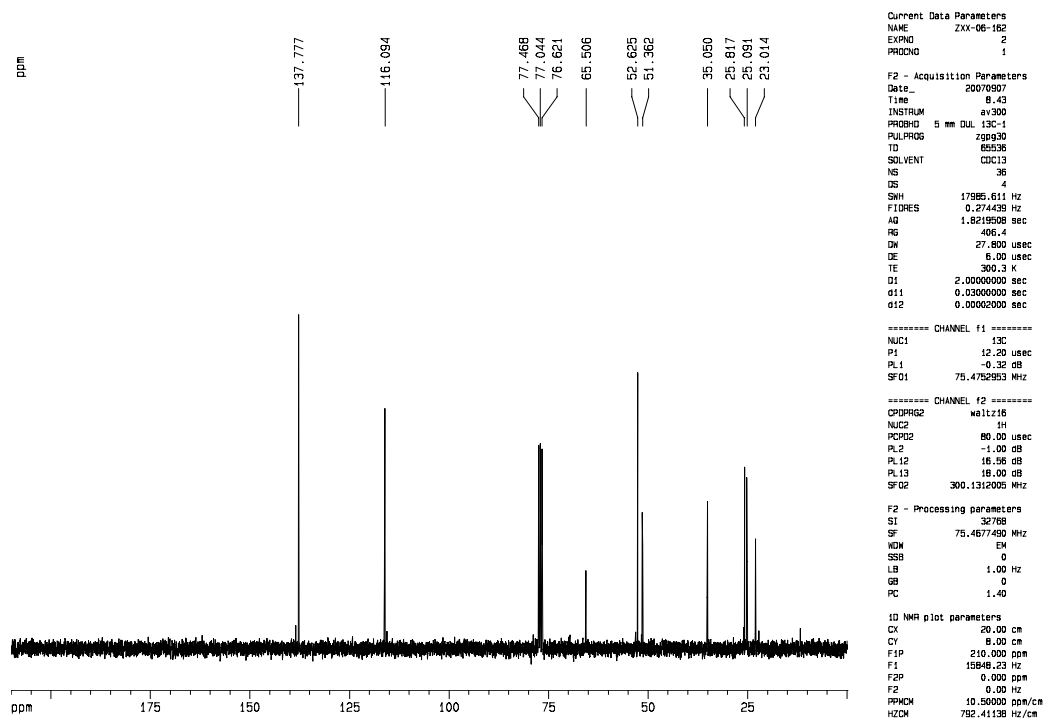
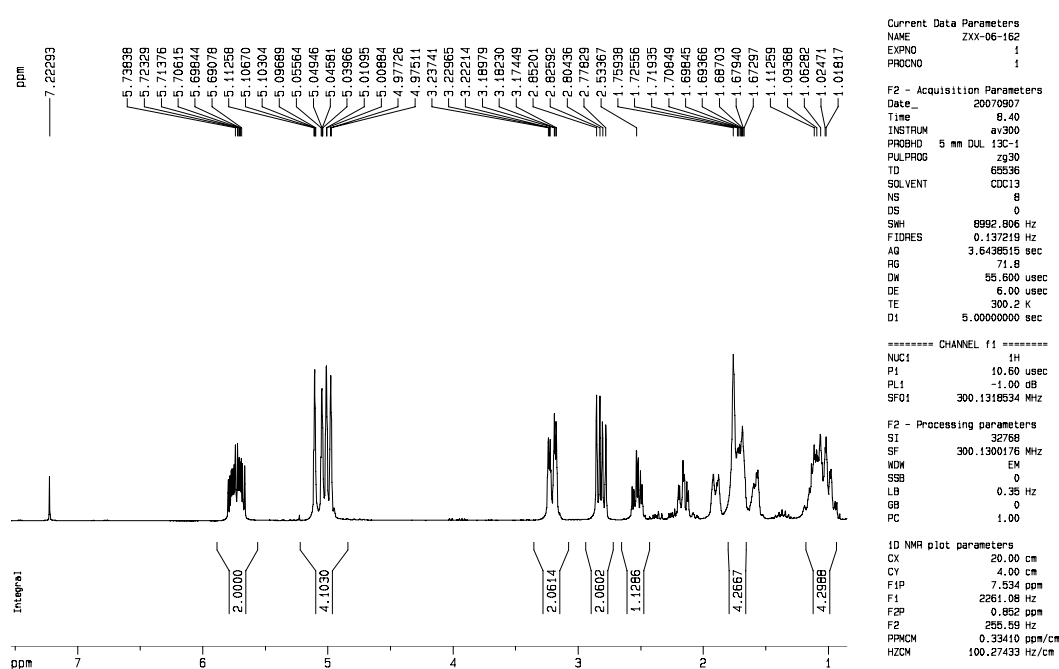
[9] S. Z. Luo, H. Xu, L. Zhang, J. Y. Li and J.-P. Cheng, *Org. Lett.*, 2008, **10**, 653-656

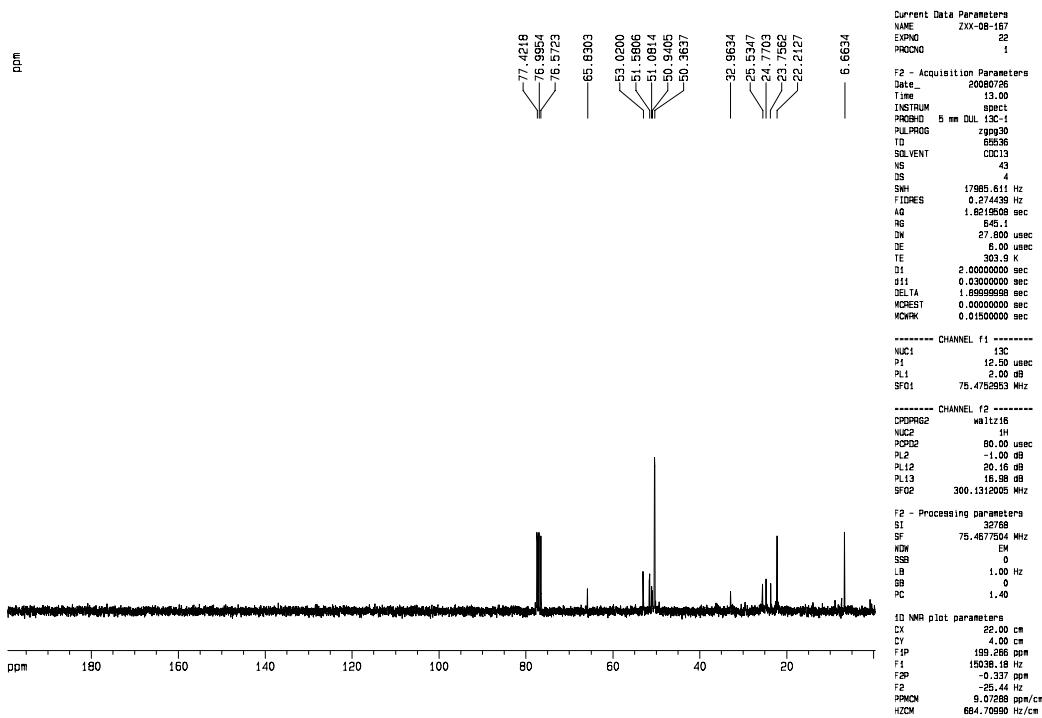
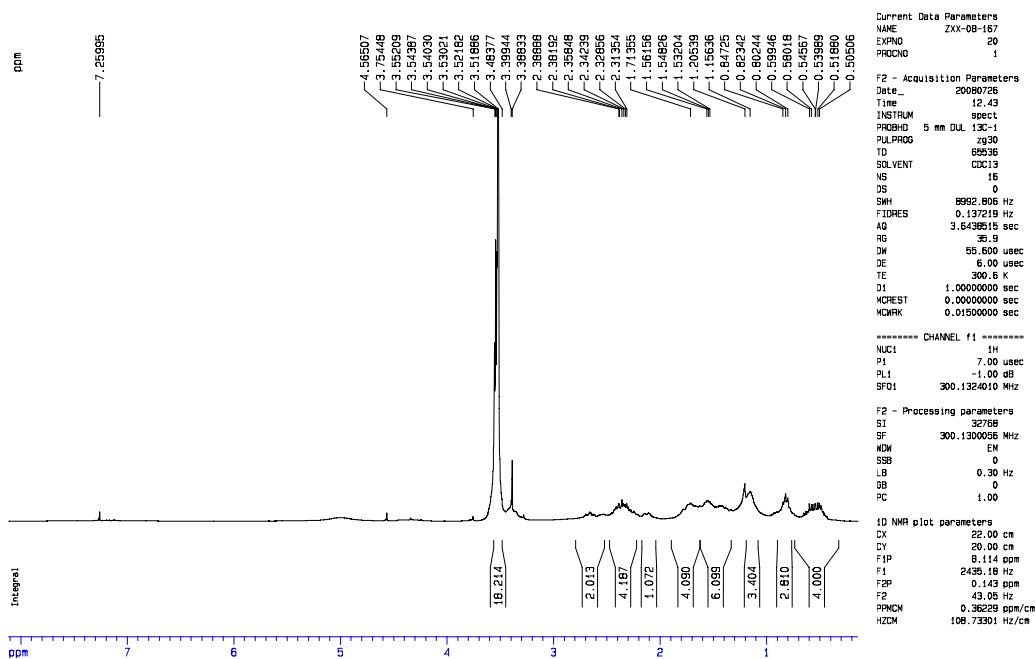
**NMR & HR-MS spectra:**



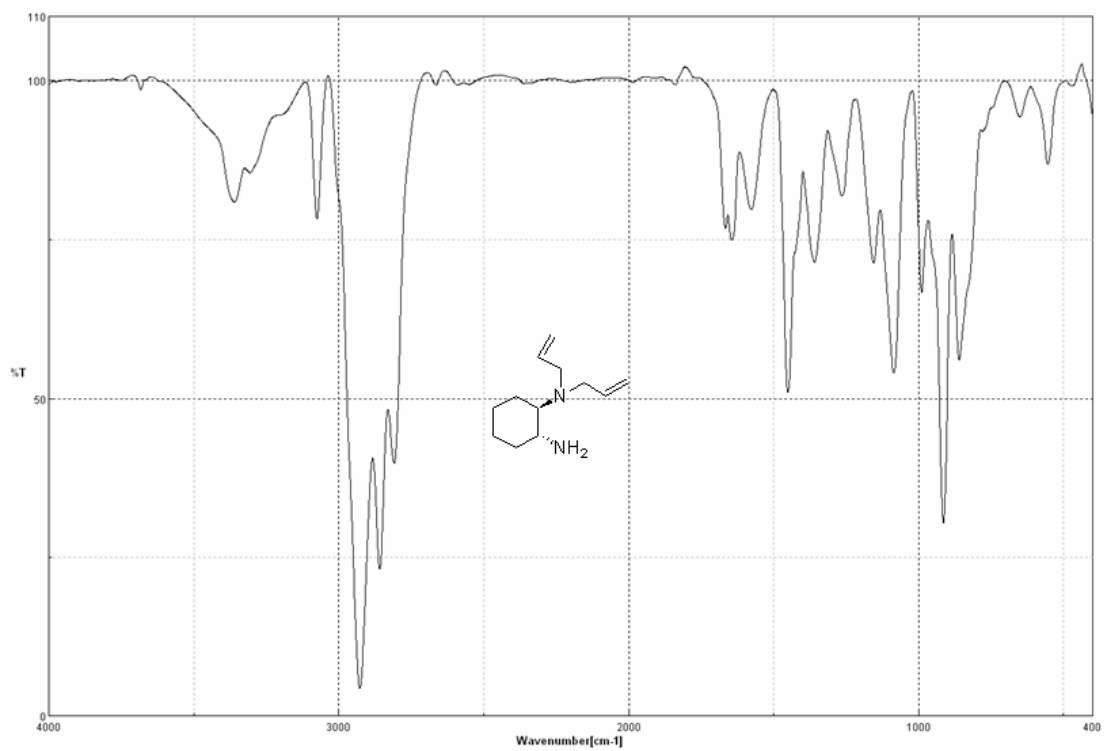
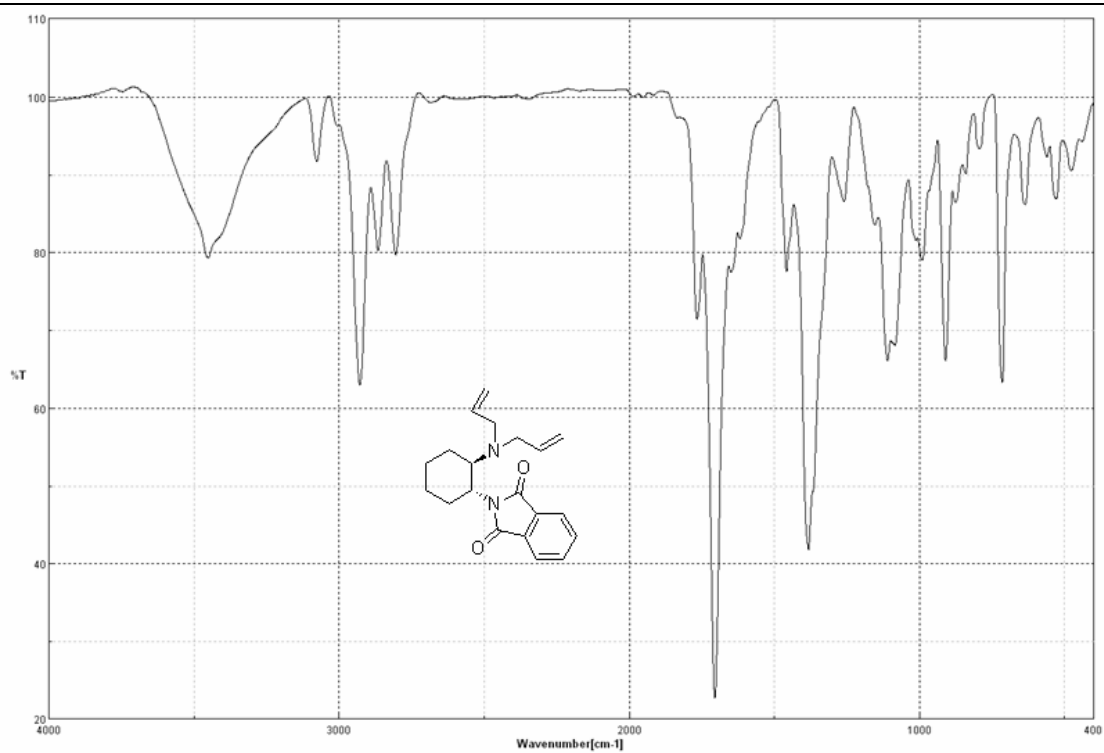
**6**

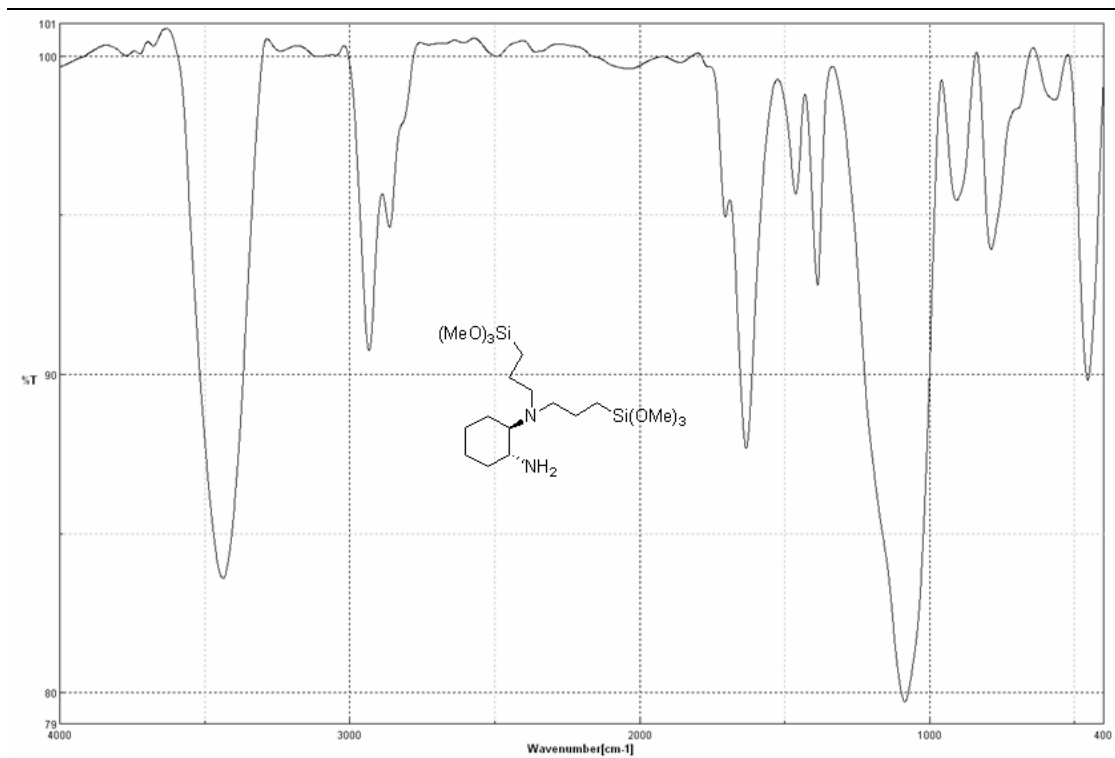






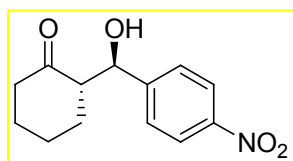
IR spectra of the compound:



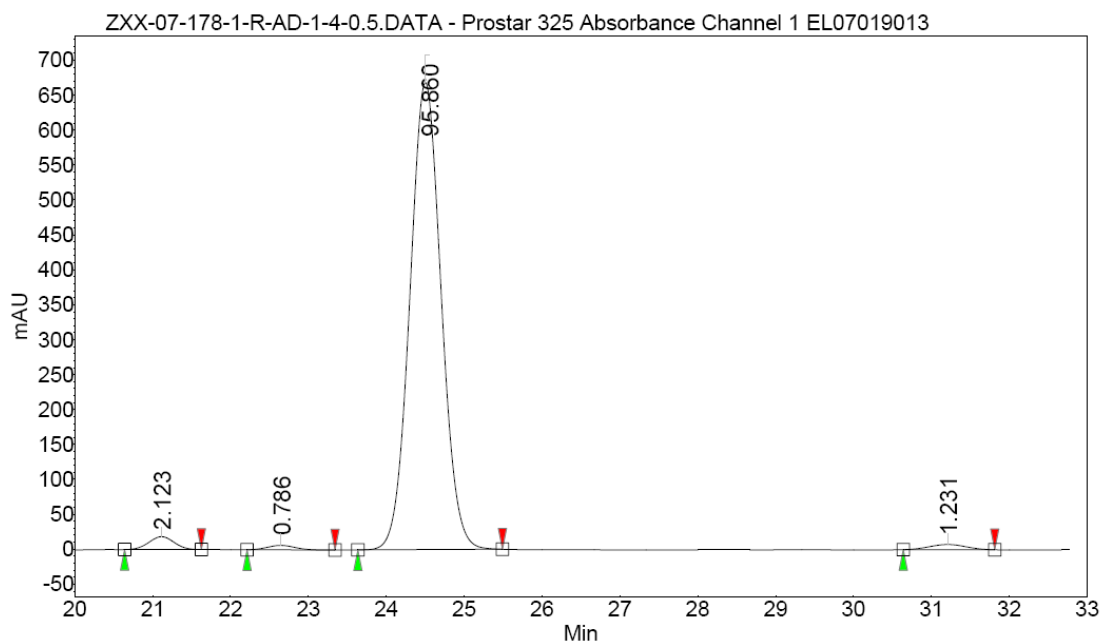
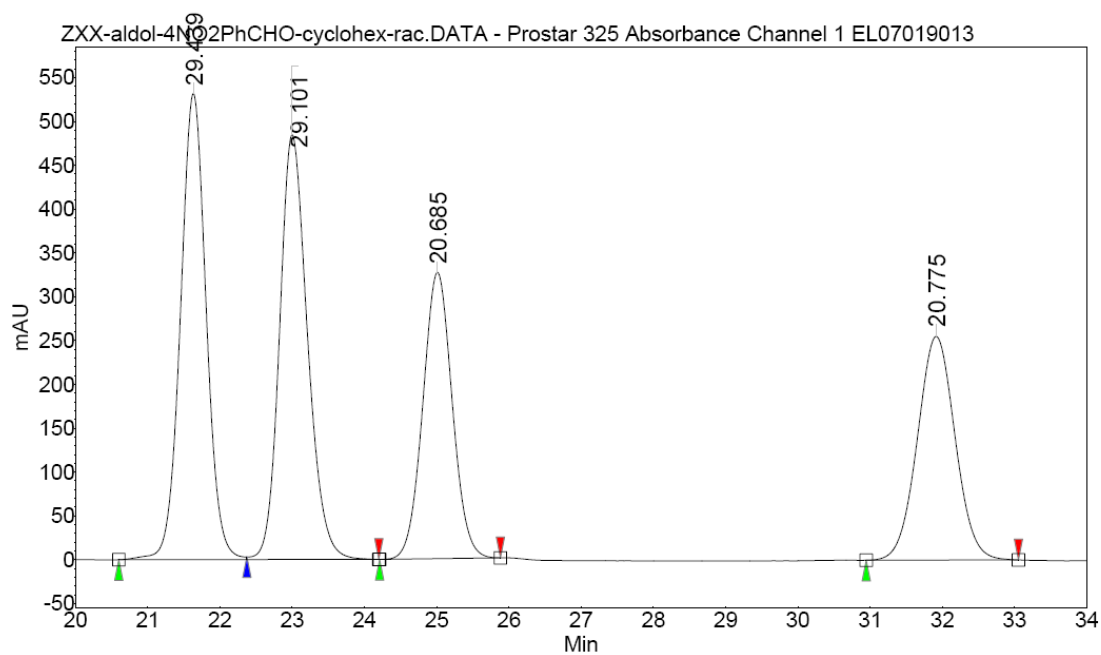


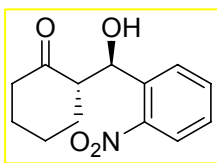


## HPLC conditions

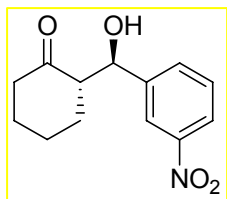


The enantiomeric excess was determined by HPLC with an AD-H column at 254 nm (2-propanol: Hexane = 20:80), 25 °C, 0.5 mL/min; anti:  $t_R = 24.50$  (major),  $t_R = 31.21$  (minor); syn:  $t_R = 21.11$  (major),  $t_R = 22.65$  (minor).

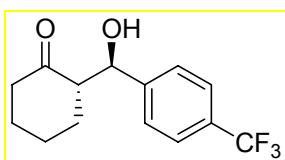




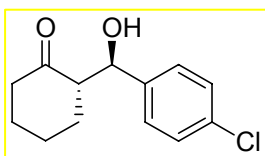
The enantiomeric excess was determined by HPLC with an AD-H column at 254 nm (2-propanol: Hexane = 5:95), 25°C, 1.0 mL/min; anti:  $t_R = 34.84$  (major),  $t_R = 36.38$  (minor); syn:  $t_R = 21.14$  (minor),  $t_R = 24.75$  (major).



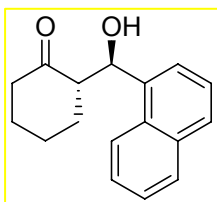
The enantiomeric excess was determined by HPLC with an AS-H column at 254 nm (2-propanol: Hexane = 5:95), 25°C, 0.8 mL/min; anti:  $t_R = 61.74$  (major),  $t_R = 68.76$  (minor); syn:  $t_R = 41.30$  (minor),  $t_R = 51.59$  (major).



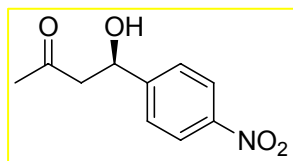
The enantiomeric excess was determined by HPLC with an AD-H column at 254 nm (2-propanol: Hexane = 20:80), 25°C, 0.5 mL/min; anti:  $t_R = 14.22$  (minor),  $t_R = 16.61$  (major); syn:  $t_R = 10.24$  (minor),  $t_R = 11.78$  (major).



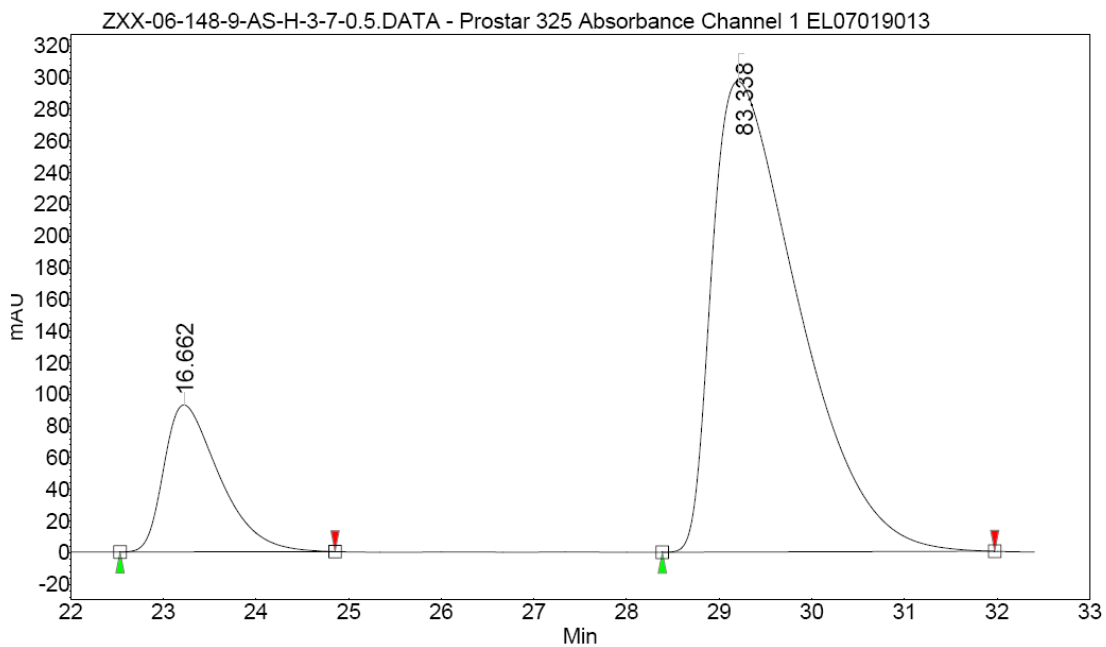
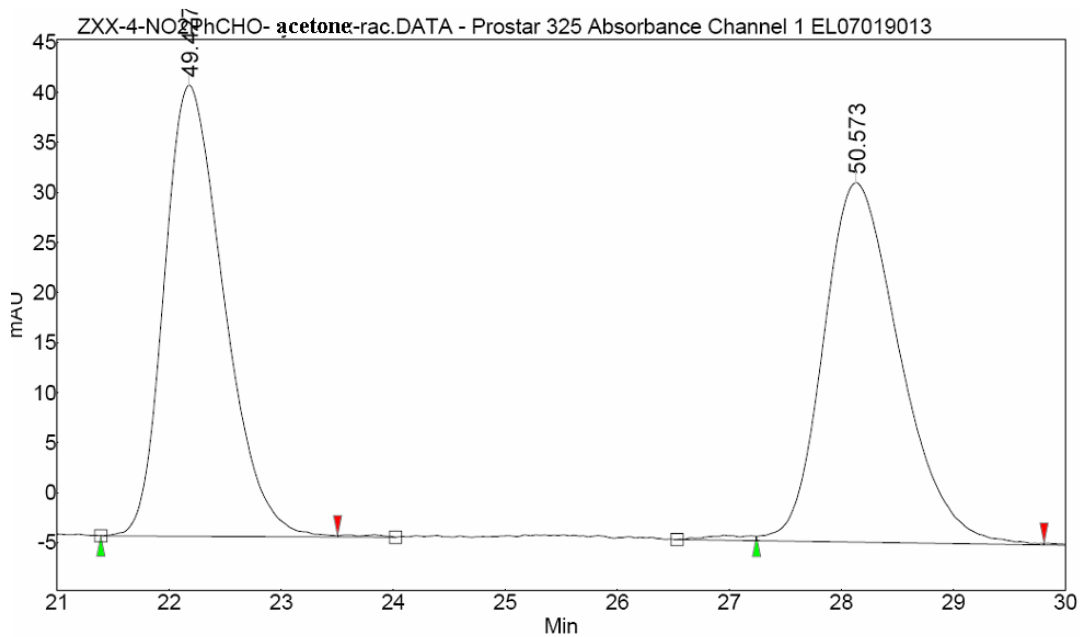
The enantiomeric excess was determined by HPLC with an AD-H column at 254 nm (2-propanol: Hexane = 10:90), 25°C, 0.5 mL/min; anti:  $t_R = 27.21$  (minor),  $t_R = 31.04$  (major); syn:  $t_R = 18.02$  (minor),  $t_R = 20.79$  (major).

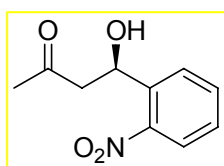


The enantiomeric excess was determined by HPLC with an AD-H column at 254 nm (2-propanol: Hexane = 5:95), 25°C, 0.8 mL/min; anti:  $t_R = 39.71$  (minor),  $t_R = 51.12$  (major); syn:  $t_R = 18.22$  (minor),  $t_R = 22.47$  (major).

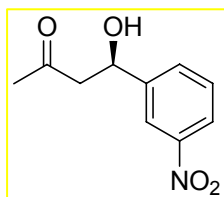


The enantiomeric excess was determined by HPLC with an AS-H column at 254 nm (2-propanol: Hexane = 30:70), 25 °C, 0.5 mL/min;  $t_R = 23.22$  (minor),  $t_R = 29.20$  (major).

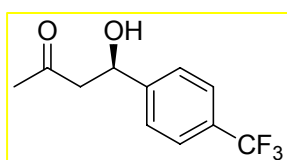




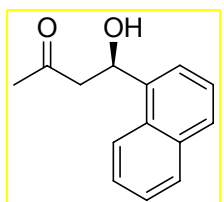
The enantiomeric excess was determined by HPLC with an AS-H column at 254 nm (2-propanol: Hexane = 30:70), 25°C, 0.8 mL/min;  $t_R = 16.63$  (major),  $t_R = 22.70$  (minor).



The enantiomeric excess was determined by HPLC with an OJ-H column at 254 nm (2-propanol: Hexane = 30:70), 25°C, 0.5 mL/min;  $t_R = 30.05$  (minor),  $t_R = 33.06$  (major).



The enantiomeric excess was determined by HPLC with an AS-H column at 254 nm (2-propanol: Hexane = 20:80), 25°C, 0.5 mL/min;  $t_R = 12.96$  (major),  $t_R = 14.25$  (minor).



The enantiomeric excess was determined by HPLC with an AS-H column at 254 nm (2-propanol: Hexane = 15:85), 25°C, 0.5 mL/min;  $t_R = 13.69$  (major),  $t_R = 14.94$  (minor).