# Supplementary Information

## The high catalytic activity and reusability of the proline functionalized cage-like mesoporous material SBA-16 for the asymmetric aldol reaction proceeding in methanol/water mixed solvent

Honglei Yang[a], Xueyao Zhang[a], Shuwen Li[a], Xiaoyu Wang[b]* and Jiantai Ma[a]*

[a] State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou, Gansu 730000, P. R. China.

[b] School of Earth Sciences, Lanzhou University, Lanzhou, Gansu, 730000, P. R. China.

*Corresponding author:

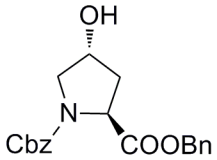
e-mail: majiantai@lzu.edu.cn (J. Ma); wangxiaoyu@lzu.edu.cn (X. Wang).

Tel.: +86-931-8912577;

Fax: +86-931-8912582.

**Table S1. Elemental analysis results of catalysts**

| Catalyst | Content (%) | | |
|---|---|---|---|
| | C | H | N |
| SBA-16-Pro (fresh) | 20.22 | 3.15 | 4.71 |
| SBA-16-Pro (after five runs) | 18.32 | 3.06 | 4.34 |



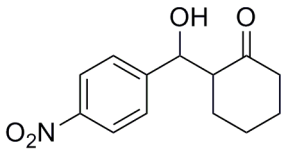

**compound 1**

**Synthesis of compound 1**

In ice bath, benzyl chloroformate (24 mmol, 4.09 g) was added dropwise to a mixture of L-4-hydroxyproline (20 mmol, 2.62 g) and $NaHCO_3$ (60 mmol, 5.04 g) in acetone (20 mL) and distilled water (40 mL) under continuous stirring. The resulting mixture was kept stirring in ice environment for 30 min and followed by reacting at room temperature for 2 h. Then the pH value of the reaction system was adjusted to 3~4 with 1 mol/L HCl. Acetone was removed by vacuum distillation and the aqueous phase was extracted by $CH_2Cl_2$ (4× 30 mL). The organic layer was dried on anhydrous $Na_2SO_4$, filtered and evaporated. (2S,4R)-1-benzyloxycarbonyl-4-hydroxyproline was obtained as colorless oil (4.51 g, yield 85%).

Triethylamine was added to the solution of (2S,4R)-1-benzyloxycarbonyl-4-hydroxyproline (15mmol, 3.98 g) and benzyl bromide (16.5 mmol, 2.82 g) in THF (25 mL) at 0 ℃. After the mixture was stirred for 18 h at room temperature, the solvent was evaporated in vacuo. The residue was dissolved in 50 mL of $CH_2Cl_2$, washed with

HCl (1N), $H_2O$, $Na_2CO_3$ (5%), and $H_2O$, and then dried over $Na_2SO_4$. The solvent was evaporated, and the residue was purified by column chromatography on silica gel (hexane/AcOEt, 2:1) to afford (2S,4R)-1,2-dibenzyloxycarbonyl-4-hydroxy pyrrolidine as pale yellow oil (2.66 g, yield 50%).




$^1$HNMR(400MHz, $CDCl_3$): δ 8.26(d, 2H, J =11.6 Hz), 7.48(d, 2H, J =11.6 Hz), 4.91 (dd, 1H, J =10.8, 4.0 Hz) ,4.12 (d, 1H, J=4.0 Hz), 2.68–2.47 (m, 2H), 2.35 (td, 1H, J =17.6, 7.6 Hz), 2.16–2.06 (m, 1H), 1.90–1.79 (m,1H), 1.71–1.52 (m,3H), 1.45–1.29 (m,1H)

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 1 mL/min, $t_R$= 29, 36, 39, 55 min.

## Optimization for the solvent (20 mol% SBA-16-Pro, 48 h, room temperature)

| | Yield % | | | |
|---|---|---|---|---|
| $t_R$ (min) / solvent | 29 | 36 | 39 | 55 |
| $H_2O$ | - | - | - | - |
| MeOH | 0.79 | 1.02 | 24.97 | 73.22 |
| EtOH | 4.76 | 5.01 | 19.99 | 70.24 |
| $CH_2Cl_2$ | 20.56 | 20.48 | 16.06 | 42.90 |
| $CHCl_3$ | 21.01 | 20.29 | 14.75 | 43.96 |
| no solvent | 1.68 | 1.25 | 18.22 | 78.85 |
| MeOH/$H_2O$ (100:1) | 2.46 | 3.73 | 12.13 | 81.68 |
| MeOH/$H_2O$ (50:1) | 3.01 | 3.60 | 6.56 | 86.83 |
| MeOH/$H_2O$ (10:1) | 1.26 | 1.27 | 8.53 | 88.94 |
| MeOH/$H_2O$ (1:1) | 10.18 | 9.66 | 9.09 | 71.08 |

**Optimization for the catalyst loading (MeOH/$H_2O$=10:1, 48 h, room temperature)**

| | Yield % | | | |
|---|---|---|---|---|
| $t_R$ (min) / loading (mol%) | 29 | 36 | 39 | 55 |
| - | - | - | - | - |
| SBA-16 | - | - | - | - |
| L-4-hydroxyproline | 9.67 | 8.57 | 13.24 | 68.52 |
| 20* | 1.89 | 2.77 | 11.65 | 83.69 |
| 5 | 2.31 | 2.53 | 7.56 | 87.60 |
| 10 | 4.21 | 4.22 | 8.85 | 82.72 |
| 30 | 8.15 | 9.57 | 9.18 | 73.10 |
| 40 | 10.06 | 10.47 | 7.23 | 72.24 |

* After the reaction proceeded for 24 h, the catalyst SBA-16-Pro was separated from the system by filtration and the left reaction mixture kept being stirring for another 24 h.

**Optimization for the reaction temperature (20 mol% SBA-16-Pro, MeOH/$H_2O$=10:1, 48 h)**

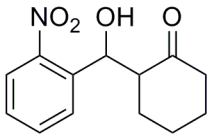
| | Yield % | | | |
|---|---|---|---|---|
| $t_R$ (min) / Temperature (℃) | 29 | 36 | 39 | 55 |
| 40 | 0.00 | 0.00 | 19.26 | 80.74 |
| 60 | 0.51 | 0.34 | 40.64 | 58.51 |

**Optimization for the reaction time (20 mol% SBA-16-Pro, MeOH/$H_2O$=10:1, room temperature)**

| | Yield % | | | |
|---|---|---|---|---|
| $t_R$ (min) / Time (h) | 29 | 36 | 39 | 55 |
| 12 | 0 | 0 | 11.43 | 88.57 |
| 24 | 1.38 | 2.19 | 12.21 | 84.21 |
| 72 | 5.93 | 4.56 | 9.67 | 79.85 |
| 96 | 0.04 | 0.08 | 11.72 | 88.16 |

**Recycling experiments of the catalyst SBA-16-Pro for the aldol reaction between 4-nitrobenzaldehyde and cyclohexanone**

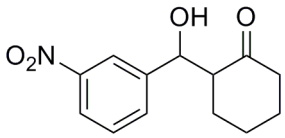
| | Yield % | | | |
|---|---|---|---|---|
| $t_R$ (min) / Run | 29 | 36 | 39 | 55 |
| 1 | 1.26 | 1.27 | 8.53 | 88.94 |
| 2 | 1.20 | 0.43 | 11.12 | 87.25 |
| 3 | 0.62 | 0.51 | 10.71 | 88.17 |
| 4 | 2.37 | 2.84 | 9.01 | 85.78 |
| 5 | 4.21 | 4.22 | 8.85 | 82.72 |




$^1$HNMR (400 MHz, $CDCl_3$): δ 7.91 (d, 1H, J = 10.08 Hz), 7.83 (d, 1H, J = 10.4 Hz), 7.62 (t, 1H, J = 10.0 Hz), 7.44 (t, 1H, J = 10.4 Hz), 5.51 (d, 1H, J = 8.8 Hz), 3.98 (br, 1H), 2.83–2.69 (m, 1H), 2.48–2.40 (m, 1H), 2.41 (td, 1H, J = 16.4, 7.6 Hz), 2.15– 2.06 (m, 1H), 1.90–1.64 (m, 5H).

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 0.5 mL/min, $t_R$= 22, 28, 45, 49 min.

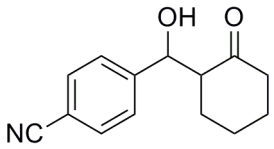
| $t_R$ (min) | 22 | 28 | 45 | 49 |
|---|---|---|---|---|
| Yield % | 7.55 | 4.04 | 86.34 | 2.07 |




$^1$HNMR (400MHz, $CDCl_3$): δ 8.26 (d, 2H, J =11.6 Hz), 7.49 (d, 2H, J =11.6 Hz), 4.90 (dd, 1H, J =11.2, 4.0 Hz) ,4.10 (d, 1H, J =4.0 Hz), 2.65–2.42 (m, 2H), 2.35 (td, 1H, J =17.6, 7.6 Hz) ,2.17–2.08 (m, 1H), 1.90–1.81 (m, 1H), 1.65–1.52 (m, 3H), 1.44–1.29 (m, 1H).

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 1 mL/min, $t_R$= 25, 27, 31, 40 min.

| $t_R$ (min) | 25 | 27 | 31 | 40 |
|---|---|---|---|---|
| Yield % | 1.79 | 2.12 | 86.58 | 9.52 |

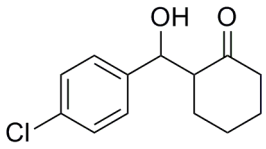



$^1$HNMR (400 MHz, $CDCl_3$): δ 7.76 (d, 2H, J = 10.8 Hz), 7.53 (d, 2H, J = 10.8 Hz), 4.90 (dd, 1H, J = 10.8, 4.0 Hz), 4.09 (d, 1H, J = 4.0 Hz), 2.65–2.44 (m, 2H), 2.38 (td, 1H, J = 17.2, 8.0 Hz), 2.15–2.06 (m, 1H), 1.90–1.79 (m, 1H), 1.75–1.51 (m, 3H), 1.42–1.29 (m, 1H).

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 1 mL/min, $t_R$=

27, 33, 39, 50 min.

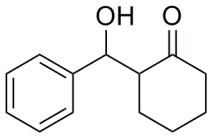
| $t_R$ (min) | 27 | 33 | 39 | 50 |
|---|---|---|---|---|
| Yield % | 9.47 | 10.76 | 7.34 | 72.43 |




$^1$HNMR (400 MHz, $CDCl_3$): δ 7.34 (dd, 4H, J = 25.5, 11.2 Hz), 4.81 (dd, 1H, J = 11.6, 3.6 Hz), 4.01 (d, 1H, J = 4.0 Hz), 2.59–2.43 (m, 2H), 2.37 (td, 1H, J = 17.2, 7.2 Hz), 2.17–2.06 (m, 1H), 1.88–1.78 (m, 1H), 1.72–1.53 (m, 3H), 1.35– 1.19 (m, 1H).

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 1 mL/min, $t_R$= 11, 13, 19, 22 min.

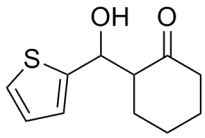
| $t_R$ (min) | 11 | 13 | 19 | 22 |
|---|---|---|---|---|
| Yield % | 5.81 | 5.59 | 6.84 | 81.76 |




$^1$HNMR (400 MHz, $CDCl_3$): δ 7.41–7.28 (5H, m), 4.78 (d, 1H, *J* = 12.0 Hz), 4.05 (m, 1H), 2.72–2.43 (m, 2H), 2.38 (td, 1H, *J* = 16.4, 7.2 Hz), 2.17–2.07 (m, 1H), 1.90–1.51 (m, 4H), 1.39–1.20 (m, 1H).

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 1 mL/min, $t_R$= 17, 19, 21, 26 min.

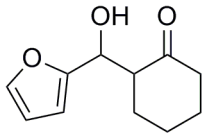
| $t_R$ (min) | 17 | 19 | 21 | 26 |
|---|---|---|---|---|
| Yield % | 89.14 | 3.35 | 4.83 | 2.69 |




$^1$HNMR (400 MHz, $CDCl_3$): $\delta$ 7.28 (m, 1H), 6.97–6.93 (m, 2H), 5.11 (d, 1H, J = 10.8 Hz), 4.11 (s, 1H), 2.69–2.35 (m, 3H), 2.13–2.09 (m, 1H), 1.85–1.67 (m, 4H), 1.39–1.35 (m, 1H).

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 1 mL/min, $t_R$= 26, 28, 34, 41 min.

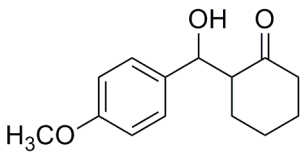
| $t_R$ (min) | 26 | 28 | 34 | 41 |
|---|---|---|---|---|
| Yield % | 5.53 | 6.28 | 84.5 | 3.69 |




$^1$HNMR (400 MHz, $CDCl_3$): $\delta$ 7.38 (d, 1H, J = 0.8 Hz), 6.35 (dd, 1H, J = 4.0, 2.4 Hz), 6.28 (d, 1H, J = 4.0 Hz), 4.84 (dd, 1H, J = 11.2, 5.2 Hz), 3.88 (d, 1H, J = 5.2 Hz), 2.95-2.87 (m,1H), 2.50-2.30 (m, 2H), 2.16-2.02 (m, 1H), 1.88-1.79 (m,1H), 1.75-1.55 (m, 3H), 1.43-1.29 (m,1H).

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 1 mL/min, $t_R$= 16, 18, 26, 31 min.

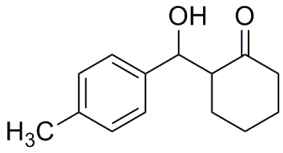
| $t_R$ (min) | 16 | 18 | 26 | 31 |
|---|---|---|---|---|
| Yield % | 1.28 | 1.35 | 7.56 | 89.81 |




$^1$HNMR (400 MHz, $CDCl_3$): $\delta$ 7.21 (dd, 4H, *J* = 22.8, 11.2 Hz), 4.73 (dd, 1H, *J* = 12.0, 3.6 Hz), 3.97 (d, 1H, *J* = 3.6 Hz), 2.66-2.55 (m, 1H), 2.49-2.41 (m, 1H), 2.39 (td, 1H, *J* = 17.6, 8.0 Hz), 2.35 (s, 3H), 2.15-2.05 (m, 1H), 1.85–1.77 (m, 1H), 1.68–1.51 (m, 3H), 1.38–1.15 (m, 1H).

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 1 mL/min, $t_R$= 19, 23, 29, 35 min.

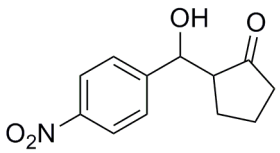
| $t_R$ (min) | 19 | 23 | 29 | 35 |
|---|---|---|---|---|
| Yield % | 2.56 | 2.73 | 8.21 | 86.50 |




$^1$HNMR (400 MHz, $CDCl_3$): $\delta$ 7.21 (dd, 4H, J = 22.8, 11.2 Hz), 4.74 (dd, 1H, J = 12.0, 3.6 Hz), 3.96 (d, 1H, J = 3.6 Hz), 2.65–2.55 (m, 1H), 2.51–2.43 (m, 1H), 2.37 (td, 1H, J = 17.6, 8.0 Hz), 2.35 (s, 3H), 2.15–2.05 (m, 1H), 1.85–1.75 (m, 1H), 1.70–1.51 (m, 3H), 1.37–1.18 (m, 1H).

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 1 mL/min, $t_R$= 18, 22, 30, 34 min.

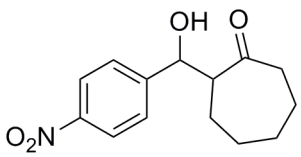
| $t_R$ (min) | 18 | 22 | 30 | 34 |
|---|---|---|---|---|
| Yield % | 1.71 | 1.06 | 4.58 | 92.65 |




$^1$HNMR (400 MHz, $CDCl_3$): $\delta$ 8.23 (d, 2H, *J* = 11.6 Hz), 7.58 (d, 2H, *J* = 12.0 Hz), 4.86 (d, 1H, *J* = 12.0 Hz), 4.77 (s, 1H), 2.53–2.19 (m, 3H), 2.10–1.95 (m, 1H), 1.79–1.47 (m, 3H).

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 1 mL/min, $t_R$= 37, 51, 69, 71 min.

| $t_R$ (min) | 37 | 51 | 69 | 71 |
|---|---|---|---|---|
| Yield % | 21.87 | 22.14 | 55.98 | 0.01 |

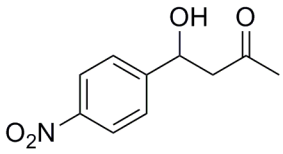



$^1$HNMR (400 MHz, $CDCl_3$): $\delta$ 8.31 (d, 2H, *J* = 12.0 Hz), 7.58 (d, 2H, *J* = 10.8 Hz), 4.89 (dd, 1H,

*J* = 9.2, 6.8 Hz), 3.77 (d, 1H, *J* = 6.4 Hz), 3.01 (m, 1H), 2.51-2.43 (m, 2H), 1.90-1.63 (m, 4H), 1.44-1.22 (m, 4H).

HPLC Column: Chiralpak AD-H, mobile phase: 95:5 hexanes:i-PrOH, flow rate: 0.5 mL/min, $t_R$= 21, 33, 40, 88 min.

| $t_R$ (min) | 21 | 33 | 40 | 88 |
|---|---|---|---|---|
| Yield % | 22.94 | 24.40 | 11.14 | 41.53 |




$^1$HNMR (400 MHz, CDCl3): $\delta$ 8.31 (d, 2H, *J* = 11.6 Hz), 7.63 (d, 2H, *J* = 11.6 Hz), 5.34 (t, 1H, *J* = 8.0 Hz), 3.99 (s, 1H), 2.90 (d, 2H, *J* = 8.8 Hz), 2.18 (s, 3H).

HPLC Column: Chiralpak OB-H, mobile phase: 85:15 hexanes:i-PrOH, flow rate: 1 mL/min, $t_R$= 20, 23 min.

| $t_R$ (min) | 20 | 23 |
|---|---|---|
| Yield % | 69.05 | 30.95 |