

Supporting Information

Alternating Chiral Selectivity of Aldol Reactions under the Confined Space of Mesoporous Silica

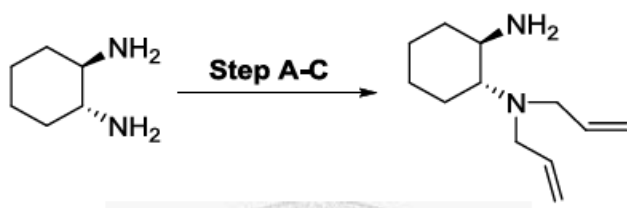
Chewei Yeh,^a Yan-Ru Sun,^a Shing-Jong Huang,^b Yeun-Min Tsai^a and Soofin Cheng^{a*}

^a Department of Chemistry, National Taiwan University, No. 1, Roosevelt Rd. Sec. 4, Taipei 10617, Taiwan.

^b Instrumentation Center, National Taiwan University, No. 1, Roosevelt Rd. Sec. 4, Taipei 10617, Taiwan.

Experimental Procedures

Synthesis of (1*R*,2*R*)-trans-*N,N*-diallyl-trans-1,2-diaminocyclohexane, O₃ [1, 2].



Step A. (1*R*,2*R*)-trans-*N*-phthaloyl-1,2-diaminocyclohexane, O₁ [1]. Monoprotection of (1*R*,2*R*)-trans-1,2-diaminocyclohexane was carried out following the literature procedure of Kaik and Gawroński [148]. A solution of *p*-TsOH·H₂O (3.84 g, 0.02 mol) in xylenes (120 mL) was dehydrated by azeotropic distillation. After cooling to room temperature to the solution was added DACH (2.28 g, 0.02 mol) followed by phthalic anhydride (2.96 g, 0.02 mol). The mixture was heated 8 h with stirring until that the homogeneous solution was obtained and then cooled to room temperature. Next, the product was begun to crystallize. The product was collected by filtration, washed with xylene-hexane and air-dried. A solution of *N*-phthaloyl-1,2-diaminocyclohexane-*p*-TsOH (2 mmol) in dichloromethane (50 mL) was stirred overnight with saturated NaHCO₃ solution (10 mL). The organic solution was separated, dried over MgSO₄ and the solvent removed to give (1*R*,2*R*)-trans-*N*-phthaloyl-1,2-diaminocyclohexane, O₁.

O₁: yield 69%. [α]_{20D} -79.3 (c 1, CHCl₃). ¹H NMR δ 1.1-1.5 (m, 5H), 1.7-1.9 (m, 3H), 2.0-2.1(m, 1H), 2.1-2.3 (m, 1H), 3.42 (dt, 1H), 3.81 (dt, 1H), 7.70-7.75 (m, 2H), 7.80-7.85 (m, 2H).

Step B. (1*R*,2*R*)-trans-*N,N*-Diallyl-*N'*-phthaloyl-1,2-diaminocyclohexane, O₂ [2].

To a solution of (1*R*,2*R*)-trans-*N*-phthaloyl-1,2-diaminocyclohexane (2.00 g, 8.20 mmol) in 40 mL abs. CH₃CN and K₂CO₃ (2.48 g, 18.0 mmol) was added allyl bromide

(2.18 g, 18.0 mmol) and the resulting mixture was heated to reflux for 24 hours. The reaction mixture was cooled to ambient temperature and the solvent was removed in vacuo. The residue was dissolved in dichloromethane (40 mL) and water (40 mL). The organic layer was separated and the aqueous layer (pH ~10) was extracted with dichloromethane (3 × 20 mL). The combined organic layer was dried over anh. MgSO₄ and the solvent was removed in vacuo to obtain pure (*1R,2R*)-*trans-N,N*-diallyl-*N'*-phthaloyl-1,2-diaminocyclohexane as a pale brown solid. **O2**: yield 60%. ¹H NMR δ = 1.14-1.36 (m, 3H), 1.79-1.98 (m, 4H), 2.23-2.43 (m, 1H), 2.78 (m, 2H), 3.16-3.19 (m, 1H), 3.22-3.25 (m, 1H), 3.37 (m, 1H), 4.14 (m, 1H), 4.89-5.00 (m, 4H), 5.29-5.55 (m, 2H), 7.67-7.72 (m, 2H), 7.78-7.83 (m, 2H). ¹³C NMR δ = 24.6, 25.2, 25.8, 29.8, 52.2, 52.5, 58.5, 100.8, 116.0, 122.8, 133.6, 137.4, 168.6.

Step C. (*1R,2R*)-*trans-N,N*-diallyl-1,2-diaminocyclohexane, O3 [2].

A solution of (*1R,2R*)-*trans-N,N*-diallyl-*N'*-phthaloyl-1,2-diaminocyclohexane (3.24 g, 10.0 mmol) in 15 mL ethanol was refluxed with hydrazine monohydrate (1.11 g, 22.0 mmol) for 1 hour. The reaction mixture was then cooled to room temperature and diethyl ether was added to it to precipitate phthaloyl hydrazide completely. The white solid was filtered and the liquid was evaporated to afford (*1R,2R*)-*trans-N,N*-diallyl-1,2-diaminocyclohexane as brown oil. **O3**: yield 82%. ¹H NMR δ = 1.05-1.26 (m, 4H), 1.62-1.99 (m, 6H), 2.15-2.33 (m, 1H), 2.53-2.64 (m, 1H), 2.87 (m, 2H), 3.23-3.30 (m, 2H), 5.05-5.18 (m, 4H), 5.73-5.86 (m, 2H). ¹³C NMR δ = 22.9, 25.1, 25.8, 35.0, 51.3, 52.6, 65.3, 116.2, 137.8.

Material Synthesis. Well-ordered thiol-functionalized mesoporous SBA-15 (SH-SBA-15) materials were prepared by one-pot co-condensation of tetraethyl orthosilicate (TEOS) and 3-mercaptopropyltrimethoxysilane (MPTMS) in 2 M HCl containing Pluronic P123 as the pore-directing agent, following the procedures reported in Reference 15 to achieve homogeneous distribution of the catalytic sites.¹⁵ The reactant molar compositions were 0.017 P123: 1 TEOS: 0.1 MPTMS: 7.9 HCl: 220 H₂O. The chiral diamino catalyst (*trans-N,N*-diallyldiaminocyclohexane, abbreviated DDAC) was anchored on SH-SBA-15 through AIBN-mediated thiol-ene reaction. Thus, 0.59 mmol DDAC was mixed with the 100 °C dried SH-SBA-15 (0.5 g, 1.17 mmol/g) using AIBN (0.059 mmol) as radical initiator in CHCl₃ under Ar atmosphere and refluxed for 24 hours. After washing with CHCl₃, the catalysts DDAC-SH-SBA-15 were obtained.

References:

1. M. Kaik and J. Gawroński, *Tetrahedron: Asymmetry* **2003**, *14*, 1559-1563.
2. A. Berkessel, S. Mukherjee, T. N. Müller, F. Cleemann, K. Roland, M. Brandenburg, Jörg-M. Neudörfel and J. Lex, *Org. Biomol. Chem.* **2006**, *4*, 4319-4330.

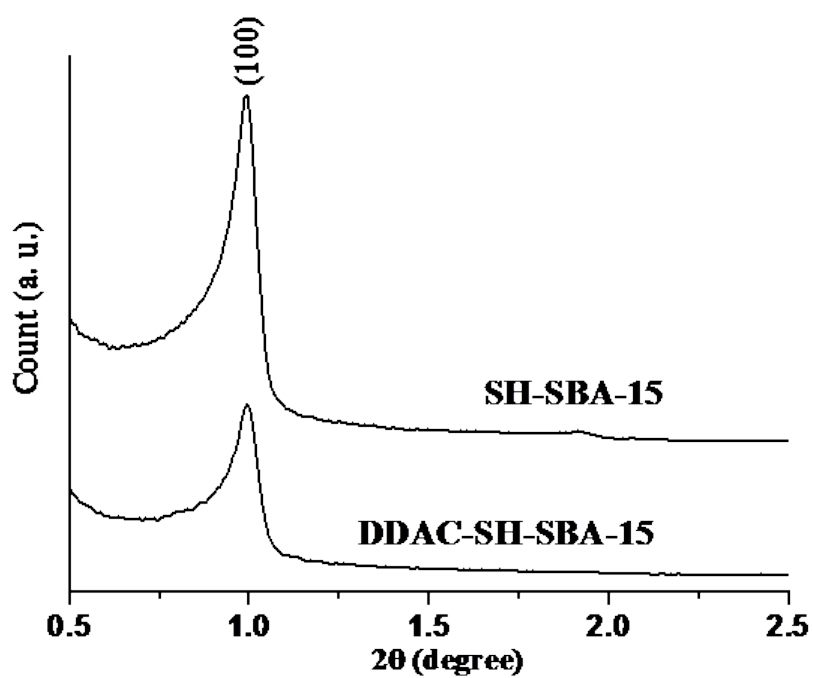


Figure S1 Small angle XRD patterns of SH-SBA-15 and DDAC-SH-SBA-15.

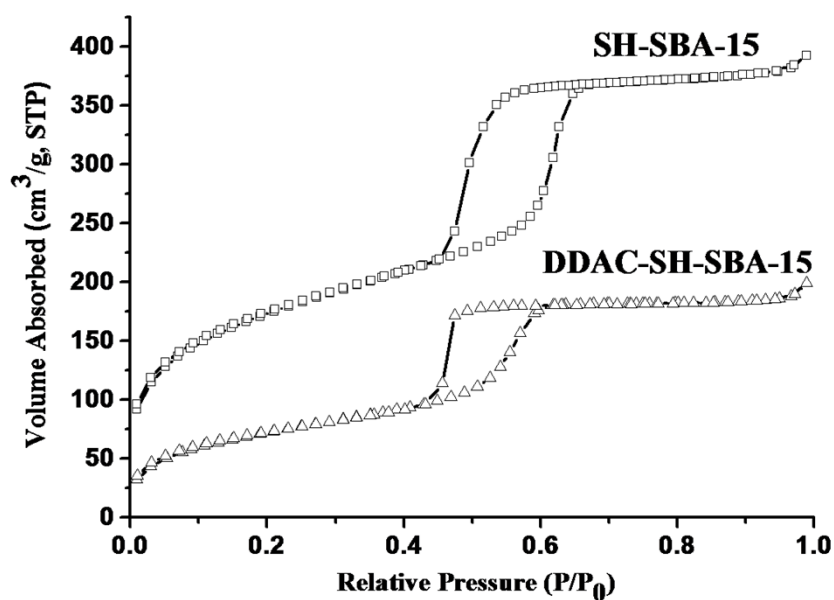


Figure S2 N₂ adsorption-desorption isotherms of SH-SBA-15 and DDAC-SH-SBA-15.

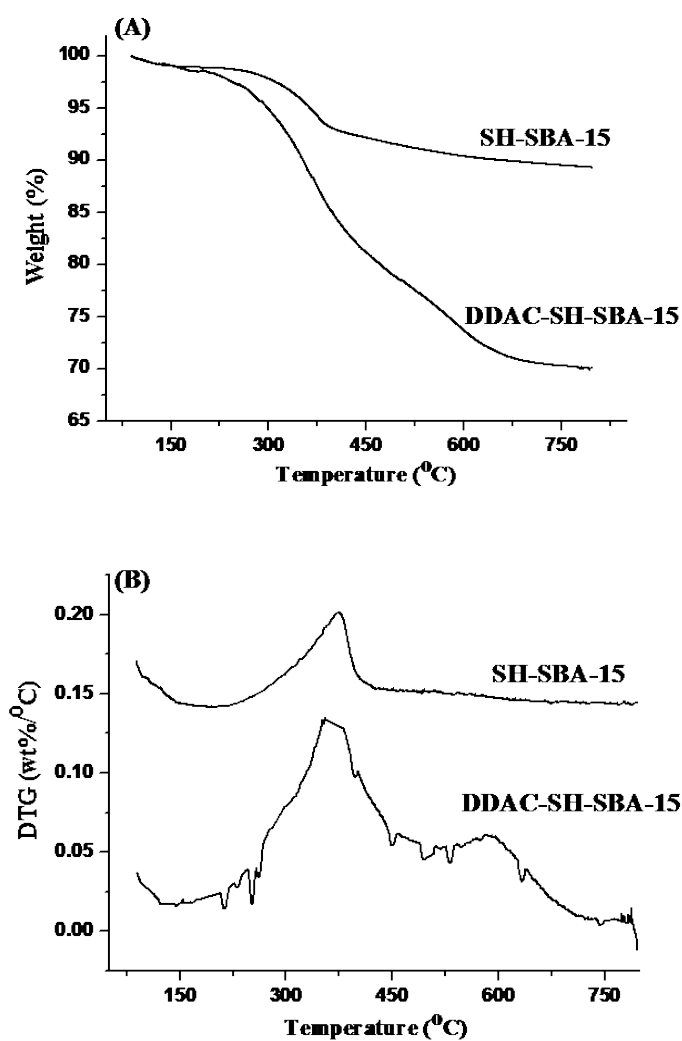
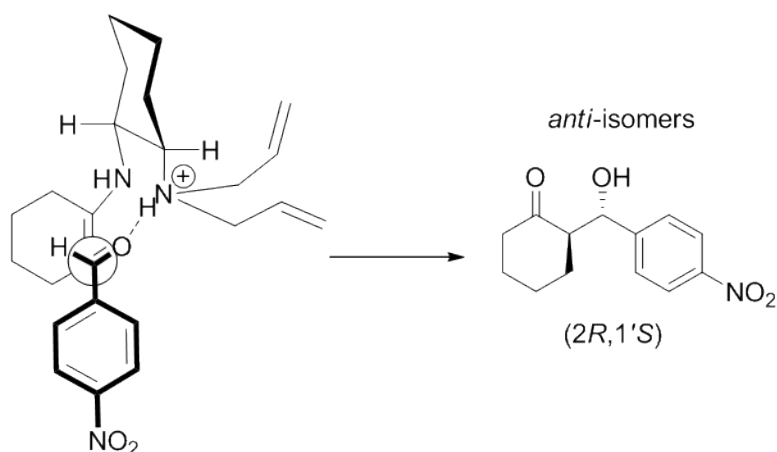


Figure S3 (A) TG and (B) DTG profiles of SH-SBA-15 and DDAC-SH-SBA-15.



Scheme S1 Proposed transition states for aldol reaction of cyclohexanone with *p*-nitrobenzaldehyde.

Table S1 Textural and Chemical Properties of SH-SBA-15 and DDAC-SH-SBA-15.

Material	a_0 [nm] ^[a]	S_{BET} [m ² /g]	V_{Total} [cm ³ /g]	D_p [nm] ^[b]	W_t [nm] ^[c]	$S^{[d]}$ (mmol/g)	$N^{[d]}$ (mmol/g)
SH-SBA-15	10.6	615	0.59	4.9	5.7	1.17	—
DDAC-SH-SBA-15	10.5	265	0.29	4.1	6.4	1.17	1.08

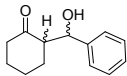
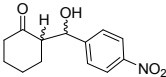
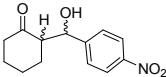
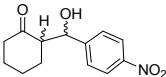
[a] $a_0 = 2d_{100}/(3^{1/2})$.

[b] Pore diameter derived from the BJH adsorption pore size distribution.

[c] Wall thickness calculated by $a_0 - D_p$.

[d] Measured by CHNS elemental analysis.

Table S2 Verification of chiral selectivities of DDAC-SH-SBA-15 catalyst in direct aldol reaction.

Entr	Product	Additive	Conv [%] ^[a]	anti : syn ^[b]	Selectivity [%] ^[c]			
					(2 <i>R</i> ,1' <i>S</i>)	(2 <i>S</i> ,1' <i>R</i>)	(2 <i>S</i> ,1' <i>S</i>)	(2 <i>R</i> ,1' <i>R</i>)
1		H ₂ O	11.1	65 : 35	39(20)	26	6	29(66)
2		H ₂ O	95.2	80 : 20	77(92)	3	4	16
3 ^[d]		TFA	57.6	42 : 58	41(95)	1	30	28
4 ^[e]		H ₂ O	73.1	90 : 10	88(96)	2	2	8

The reactions were carried out with cyclohexanone (2 mmol, 0.2 mL), aldehyde (0.20 mmol, 1 equiv), catalyst DDAC and additive (0.02 mmol, 0.1 equiv) without solvent at RT for 24 h. [a] Determined by HPLC analysis with external standard. [b] Determined by ¹H NMR. [c] The products' configurations determined by chiral-phase HPLC analysis and comparing with reported data; values in parenthesis are e.e. selectivities. [d] The catalyst was recovered from Entry 2 and 0.3 equiv TFA was used as the additive. [e] The catalyst was recovered from Entry 3.

Table S3 Recycling of DDAC-SH-SBA-15 catalyst in direct aldol reaction.

Entry	Run	Conv. [%] ^[a]	anti : syn ^[b]	Selectivity [%] ^[c]			
				(2 <i>R</i> ,1' <i>S</i>)	(2 <i>S</i> ,1' <i>R</i>)	(2 <i>S</i> ,1' <i>S</i>)	(2 <i>R</i> ,1' <i>R</i>)
1	1 ^[d]	67	88 : 12	86.7(97)	1.3	1.6	10.4
2	2 ^[d]	63	86 : 14	84.3(96)	1.7	2.6	11.4
3	3 ^[d]	62	81 : 19	75.3(86)	5.7	7.2	11.8

[a] Determined by HPLC analysis with external standard. [b] Determined by ¹H NMR. [c] The products' configurations determined by chiral-phase HPLC analysis and comparing with reported data; values in parenthesis are e.e. selectivities. [d] The reactions were carried out with cyclohexanone (0.2 mL, 2 mmol), aldehyde (0.20 mmol, 1 equiv), and catalyst DDAC-SH-SBA-15 (0.02 mmol, 0.1 equiv) in H₂O (0.2 mL) at rt for 24 h.