Supporting information

9-Thiourea Cinchona Alkaloid Supported on Mesoporous Silica as a High Enantioselective, Recycled Heterogeneous Asymmetric Catalyst

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General Methods. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker Avance 600 spectrometer running at 600 and 300 MHz (Bruker, Bremen, Germany), respectively, in $CDCl_3$ as the solvent. Chemical shifts were reported in the δ scale relative to residual $CHCl_3$ (7.26 ppm) for ^{1}H NMR and to the central line of $CDCl_3$ (77.0 ppm) for ^{13}C NMR. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), intergration, coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). The solid state NMR experiments were carried out at 59.6 and 75.5 MHz for ^{29}Si and ^{13}C, respectively, on a Bruker Avance 300M solid-state spectrometer equipped with a commercial 5 mm MAS NMR probe. The chemical shifts were determined usingδ_{TMS}=0 ppm as a reference. The magic-angle spinning frequencies were set to 5 kHz for all experiments. Mass spectra was recorded on a micromass LCT spectrometer using electrspray (ES^+) ionisation techniques. Fourier transform infrared (FTIR) was carried on Bruker Vector 22 spectrometer (resolution 4cm^{-1}) in the range of 4000–400cm^{-1}, using the KBr method. X-ray powder diffraction (XRD) patterns were obtained on a Rigaku D/MAX-2500 X-ray diffractmeter a using Cu Kα radiation (λ=1.5418 Å) at 45 kV and 40 mA. N_2 adsorption-desorption isotherms were measured using Quantachrome Autosorb-1 system at liquid nitrogen temperature. Flash column chromatography (FC) was carried out using silica gel (200-300 mesh, made in Qingdao Haiyang Chemical CO. Ltd.). Optical rotations were measured on a Wzz-1S Automatic polarimeter. The enantiomeric excess (ee) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak OB-H).

Materials. Mesoporous silica SBA-15 was synthesized using pluronic P123 [$EO_{20}PO_{70}EO_{20}$ (EO=ethylene oxide, PO=propyleneoxide), M_{av}=5800 g mol^{-1}, Aldrich] as template and $(EtO)_4Si$ as silica source under acidic conditions.[1] 9-Thiourea epi-quinine was synthesized following the method in literature.[2] N-sulfonyl imines **3b-3e**, were prepared according to literature procedures[3]. quinine, N-sulfonyl imine **3a** and indoles **2a-2c**, were purchased from Aldrich Inc., and used without further purification. The other available solvents and reagents were also used as received.

9-thiourea epi-quinine (amorphous solid, 80–82 % yield), IR (KBr) υ 1622, 1533, 1477, 1382 cm^{-1}; ^{1}H-NMR (600 MHz, CD_3OD, T = 310 K, δ_{TMS} = 0 ppm) δ 8.75 (d, J = 4.6 Hz, 1H), 8.11 (br s, 2H), 8.01 (br d, J = 2.7 Hz, 1H), 7.96 (d, J = 9.3 Hz, 1H), 7.56 (br s, 1H), 7.48 (d, J = 4.6 Hz, 1H), 7.46 (dd, J = 9.3, 2.7 Hz, 1H), 5.62 (ddd, J = 17.1, 10.3, 6.0 Hz, 1H, C*H*=CH_2), 5.05 (dt,

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Reference

1 (a) D. -Y. Zhao, J. Feng, Q. Huo, N. Melosh, G. H. Fredrickson, B. F. Chmelka and G. D. Stucky, *Science* 1998, **279**, 548; (b) D. -Y. Zhao, Q. Huo, J. Feng, B. F. Chmelka and G. D. Stucky, *J. Am. Chem. Soc.* 1998, **120**, 6024

2 B. Vakulya, S. Varga, A. Csámpai and T. Soós, *Org Lett.* 2005, **7**, 1967

3 F. Chemla, V. Hebbe and J. -F. Normant, *Synthesis* 2000, **1**, 75

J = 10.3, 1.4 Hz, 1H, CH=C$\underline{H}_2$), 5.03 (dt, J = 17.1, 1.4 Hz, 1H, CH=C$\underline{H}_2$), 4.03 (s, 3H, OCH_3), 3.54 (dddd, J = 15.7, 10.7, 7.8, 2.4 Hz, 1H), 3.36 (br, J = 10.7 Hz, 1H), 3.32 (dd, J = 13.5, 9.8 Hz, 1H), 3.09 (ddd, J = 15.7, 13.6, 4.8 Hz, 1H), 2.51 (ddd, J = 13.6, 4.8, 2.4 Hz, 1H), 2.41 (br m, 1H), 1.71 (overlapping br m, 2H), 1.52 (ddd, J = 13.1, 10.4, 2.7 Hz, 1H), 0.96 (dd, J = 13.1, 10.4 Hz, 1H) ppm.

Preparation of catalyst (1, SBA-15-SQT). Calcined SBA-15 was vacuumed at 373 K for 5 hr (1.0 g), and then treated with 1.5 ml of (3-mercaptopropyl) trimethoxysilane in 20 ml of anhydrous 1:1 pyridine/toluene. The slurry was heated at 388 K for 24 hr. After filtration the solid was subjected to Soxhlet extraction and dried under vacuum for 5 hr, resulting in 1.14 g of a modified SBA-15 containing 2.37 % S, corresponding to 0.74 mmol of S per g of modified SBA-15. This modified SBA-15 (0.96 g) was suspended in chloroform (25ml) under N_2 atmosphere and refluxed with 9-(3,5-bis(trifluoromethyl)phenyl thiourea)-(epi-quinine) (0.42 g) and α,α'-azoisobutyronitrile (AIBN, 50 mg), as radical initiator, for 24 hr. Again, after filtration, the solid was Soxhlet extracted with dichloromethane until the 9-(3,5-bis(trifluoromethyl)phenylthiourea)-(epi-quinine) in excess was completely removed and dried under vacuum. The modified SBA-15 and supported catalyst were characterized by ^{29}Si MAS NMR (Bruker Avance 300M solid-state spectrometer), ^{13}C CP/MAS NMR (δ 185.6 (C=S), 158.2, 143.5, 142.3, 128.2, 124.7, 121.4, 101.7, 58.7, 53.2 (OCH_3), 49.6, 43.2, 39.4, 33.7, 31.5, 25.9, 15.3 (-CH_2-CH_2-), 9.9), FT-IR (Bruker Vector 22 spectrometer), XRD (Shimadzu XRD-6000), and low-temperature N_2 adsorption–desorption (Quantachrome Autosorb-1 system) techniques.

Preparation of N-Sulfonyl imines (3b-3e)

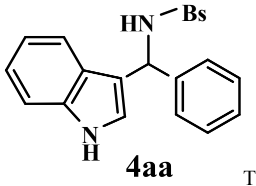
N-Benzylidene-4-methylbenzenesulfonamide (**3b**): 89.0 % yield, ^{1}H NMR (CDC1$_3$, 600 MHz, ppm) δ 9.02 (1 H, s, HC=N), 7.91 (2 H, d, J = 7.9 Hz, o-ArH), 7.87 (2 H, d, J = 8.0 Hz, o-SO_2ArH), 7.60 (1 H, t, J = 7.3 Hz, p-ArH), 7.48 (2 H, t, J= 7.7 Hz, m-ArH), 7.33 (2 H, d, J = 8.0 Hz, m-SO_2ArH), 2.43 (3H, s, CH_3);

N-(2-Chlorobenzylidene)-4-methylbenzenesulfonamide (**3c**): 70.8 % yield, ^{1}H NMR (CDC1$_3$, 600 MHz, ppm) δ 9.49 (1 H, s, HC=N), 8.14 (d, J = 7 Hz, 1 H), 7.88 (d, J = 10 Hz, 2 H), 7.51 (m, 2 H), 7.32 (m, 3 H), 2.44 (s, 3 H);

N-(2-Nitrobenzylidene)-4-methylbenzenesulfonamide (**3d**): 73.8 % yield, ^{1}H NMR (CDC1$_3$, 600 MHz, ppm) δ 9.09 (1 H, s, HC=N), 8.32 (d, J = 7 Hz, 2 H), 8.10 (d, J = 10 Hz, 2 H), 7.90 (m, 2 H), 7.37 (m, 2 H), 2.44 (s, 3 H);

N-isobutylidene-4-methylbenzenesulfonamide (**3e**): 64.8 % yield, ^{1}H NMR (CDC1$_3$, 600 MHz, ppm) δ 8.60 (1 H, t, HC=N), 8.00 (m, 2 H), 6.92 (m, 2 H), 2.00 (s, 3 H), 1.92 (bs, 2 H), 1.72(m, 1 H), 0.71(d, J = 6.5 Hz, 6 H);

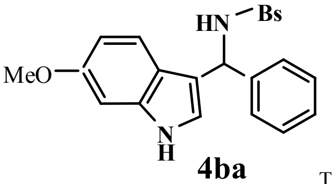
General procedure for the asymmetric addition of indoles to N-Sulfonyl imines. In a test tube, to a mixture of N-sulfonyl imines **3** (0.1 mmol) and supported catalyst **1** (1 mol %) in EtOAc (0.3 mL) was added indoles **2** (0.2 mmol) in one portion. The resulting mixture was kept at 40℃ for 5 days (as indicated in Tables 1 and 2). The reaction mixture was filtered and the filtrate was subjected to flash chromatography to afford the desired product **4**.



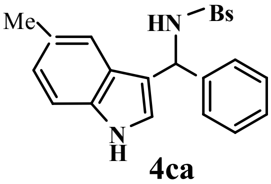
4aa

This product was obtained as a greenish foam in 76.8 % yield after flash chromatography (silica gel: Ethyl acetate/Hexane=1/3) and in 99.2 % ee as determined by HPLC [Daicel Chiralcel OB-H, Hexane/IPA=80/20, 0.5 ml/min^{-1}, λ=254 nm, t (major) =34.0 min., t (minor) = 19.5 min.] from a reaction catalyzed by 1 (1 mol%) at 40℃ for 5 days. $[\alpha]_{25}^{D}$ = -17.0 (c 0.004, Acetone); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.34 (d, J = 7.2 Hz, 1H), 5.86 (d, J = 7.2 Hz, 1H), 6.61 (s, 1H), 6.99 (t, J

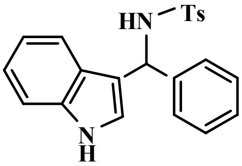
= 7.6 Hz, 1H), 7.14-7.20 (m, 6H), 7.25-7.28 (m, 4H). 7.44 (t, J = 7.4 Hz, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.87 (br, 1H); ^{13}C NMR (600 MHz, CDCl$_3$) δ 55.1, 111.3, 116.2, 119.2, 119.9, 122.5, 123.8, 125.3, 127.1, 127.2, 127.4, 128.3, 128.6, 132.2, 136.5, 140.0, 140.4; IR (neat) ν 1456, 1448, 1158; ESIMS m/z 363 [M + H$^+$];



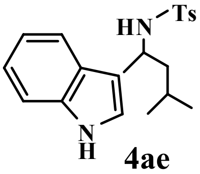
4ba This product was obtained as a gray foam in 68.5 % yield after flash chromatography (silica gel: Ethyl acetate/Hexane=1/3) and in 98.9 % ee as determined by HPLC [Daicel Chiralcel OB-H, Hexane/IPA=80/20, 0.5 ml/min^{-1}, λ=254 nm, t (major) =32.8 min., t (minor) = 19.0 min.] from a reaction catalyzed by 1 (1 mol%) at 40℃ for 5 days. [α]$_{25}^{D}$ = -18.2 (c 0.004, Acetone); ^{1}H NMR (600 MHz, CDCl$_3$) δ 3.79 (s, 3H), 5.82 (d, J = 7.6 Hz, 1H), 6.52 (s, 1H), 6.66 (d, J = 2.0 Hz, 1H), 6.77 (s, 1H), 7.17-7.19 (m, 5H), 7.29-7.31 (t, J = 8.0 Hz, 4H), 7.57 (t, J = 7.6 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H); ^{13}C NMR (600 MHz, CDCl$_3$) δ 55.1, 55.6, 94.7, 109.9, 116.3, 119.7, 119.9, 122.6, 126.4.0, 127.1, 127.4, 128.3, 128.6,128.6, 129.1, 130.9, 132.2, 132.8, 137.4, 140.0,140.4,141.9, 156.8; IR (neat) ν 2963, 1448, 1334, 1158; ESIMS m/z 393 [M + H$^+$];



4ca This product was obtained as a greenish foam in 65.8 % yield after flash chromatography (silica gel: Ethyl acetate/Hexane=1/3) and in 93.2 % ee as determined by HPLC [Daicel Chiralcel OB-H, Hexane/IPA=80/20, 0.5ml/min^{-1} λ=254 nm, t (major) =37.3 min, t (minor) =21.3min.] from a reaction catalyzed by 1 (1 mol%) at 40℃ for 5 days. [α]$_{25}^{D}$ = -18.4 (c 0.004, Acetone); ^{1}H NMR (600 MHz, CD$_3$OD) δ 2.31 (s, 3H), 5.81 (s, 1H), 6.56 (s, 1H), 6.90 (d, J = 8.0 Hz, 1H), 7.00 (s, 1H), 7.08-7.20 (m, 4H), 7.15-7.20 (m, 4H), 7.45 (t, J = 7.6 Hz, 1H), 7.68 (dd, J = 8.8 Hz, 2H); ^{13}C NMR (600 MHz, CD$_3$OD) δ 20.3, 54.8, 110.5, 114.9, 118.2, 122.8, 123.8, 126.0, 126.6, 127.1, 127.7, 128.2, 131.6, 135.2, 141.4, 141.5; IR (neat) ν 1447, 1321, 1157; ESIMS m/z 377 [M + H$^+$];



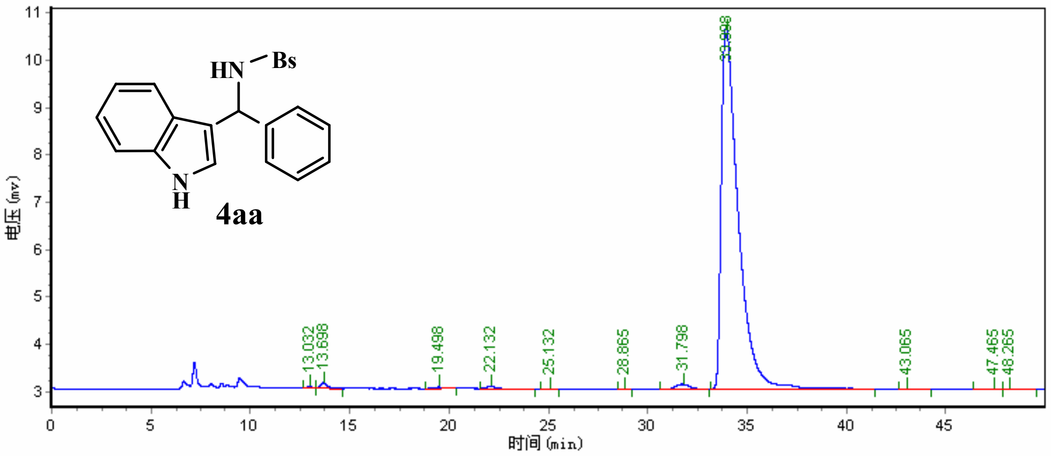
4ab This product was obtained as a colorless solid in 68.2 % yield after flash chromatography (silica gel: Ethyl acetate/Hexane=1/3) and in 89.5 % ee as determined by HPLC [Daicel Chiralcel OB-H, Hexane/IPA=80/20, 0.5 ml/min^{-1}, λ=254 nm, t (major)=20.3 min., t (minor) = 38.6 min.] from a reaction catalyzed by 1 (1 mol%) at 40℃ for 5 days; [α]$_{25}^{D}$ = -16.5 (c 0.004, CHCl$_3$); ^{1}H NMR (600 MHz, CDCl$_3$) δ 2.36 (s, 3H), 4.98 (d, J = 7.2 Hz, 1H), 5.83 (d, J = 7.2 Hz, 1H), 6.63 (s, 1H), 6.99 (t, J = 7.6 Hz, 1H), 7.06 (d, J = 8.0 Hz, 2H), 7.10-7.27 (m, 8H), 7.53 (d, J = 8.0 Hz, 2H), 8.04 (br, 1H); ^{13}C NMR (600 MHz, CDCl$_3$) δ 21.4, 55.0, 111.3, 116.2, 119.5, 122.4, 123.9, 125.4, 126.4, 127.1, 127.2, 127.3, 128.3, 129.2, 129.7, 136.5, 137.4, 140.3, 143.5; IR (neat) ν 2963, 1457, 1315, 1157, 1098, 744, 669 cm^{-1}; ESIMS m/z 377 [M + H$^+$];



4ae This product was obtained as a colorless gum in 79.7 % yield after flash chromatography (silica gel: Ethyl acetate/Hexane=1/3) and in 95.6 % ee as determined by HPLC [Daicel Chiralcel OB-H, Hexane/IPA=80/20, 0.5 ml/min^{-1} , λ=254 nm, t (major) = 30.0 min., t (minor) = 18.8 min.] from a reaction catalyzed by 1 (1mol%) at 40℃ for 5 days; ^{1}H NMR

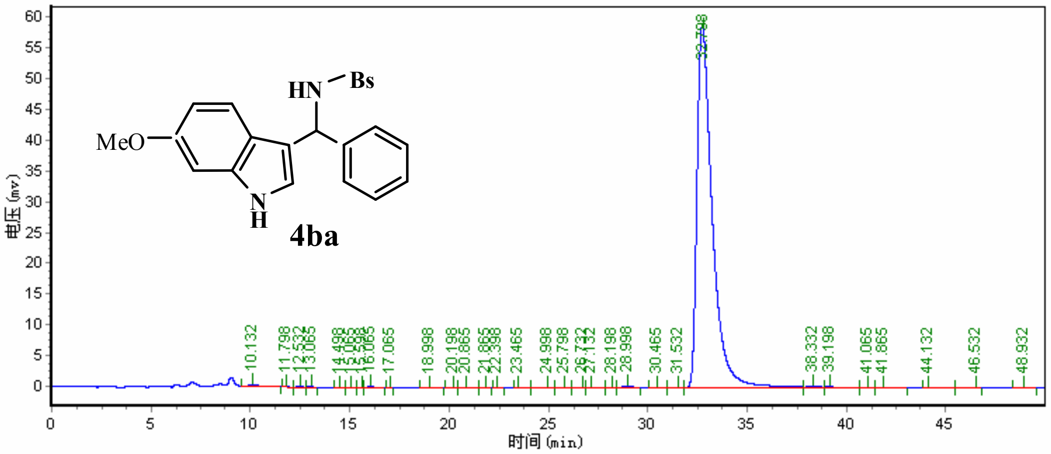
(600 MHz, $CDCl_3$) δ 0.83 – 0.98 (m, 6H), 1.56 (m, 1H), 1.82-1.89 (m, 2H), 2.30 (s, 3H), 4.66 (m, 1H), 4.74 (m, 1 H), 6.87 (s, 1H), 6.97-7.02 (m, 3H), 7.12 (t, J = 7.6 Hz, 1H), 7.23 (d, J = 9.2 Hz, 1H), 7.28-7.31 (d, J = 7.6 Hz, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.80 (br, 1H); ^{13}C NMR (600 MHz, $CDCl_3$) δ 21.4, 22.0, 22.7, 25.0, 45.4, 50.1, 111.2, 115.8, 119.0, 119.6, 122.1, 122.2, 125.2, 126.7, 129.3 , 136.4, 137.5, 143.6; IR (neat) ν 2963, 1457, 1315, 1157, 744 cm^{-1} ; ESIMS m/z 357 [M + H^+].

HPLC Conditions: Daicel chiralpak OB-H, Hexane:IPA=80:20 0.5 mL/min, λ 254 nm



4aa

HPLC Conditions: Daicel chiralpak OB-H, Hexane:IPA=80:20 0.5 mL/min, λ 254 nm



4ba

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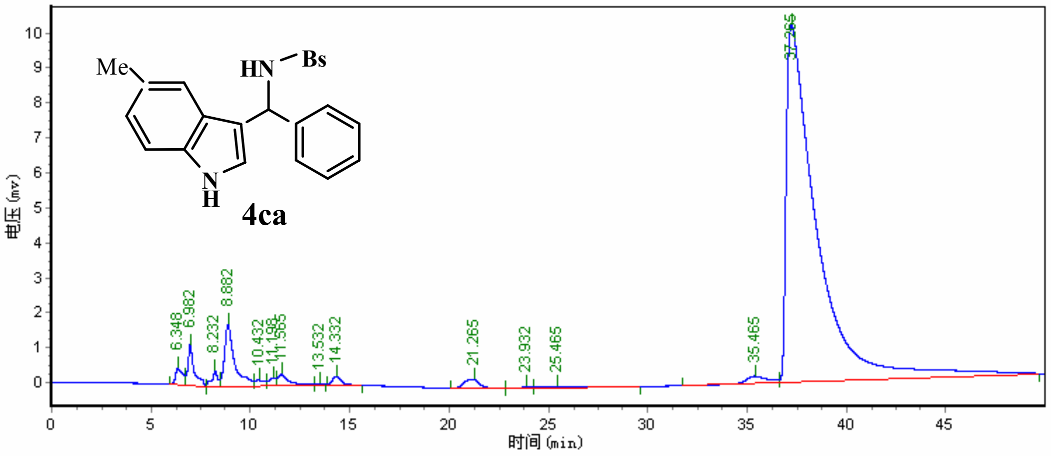
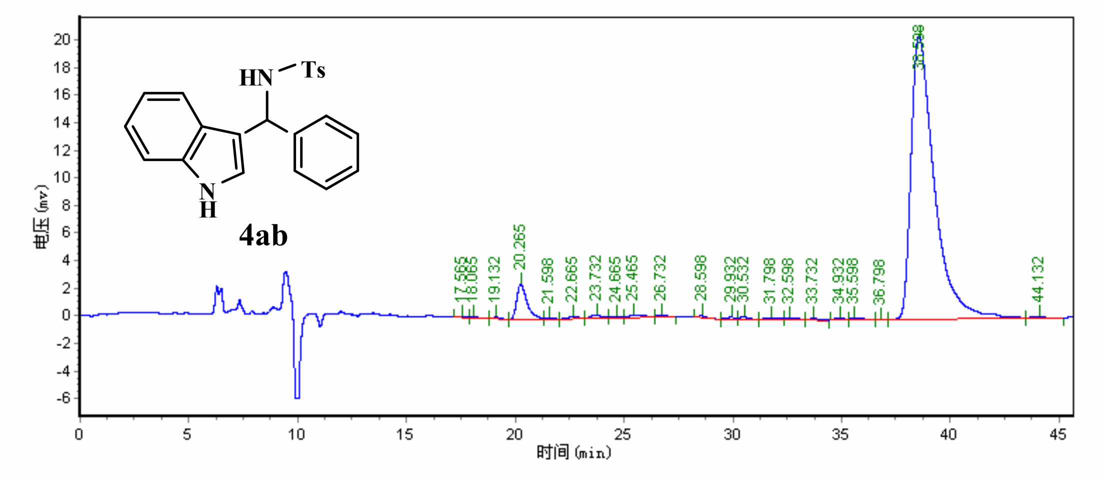


4ca

HPLC Conditions: Daicel chiralpak OB-H, Hexane:IPA=80:20 0.5 mL/min, λ 254 nm



HPLC Conditions: Daicel chiralpak OB-H, Hexane:IPA=80:20 0.5 mL/min, λ 254 nm