Asymmetric transfer hydrogenation catalysed by hydrophobic dendritic DACH–rhodium complex in water

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Hydrophobic Fréchet-type dendritic chiral 1,2-diaminocyclohexane–Rh(III) complexes have been applied in the asymmetric transfer hydrogenation of ketones in water using HCOONa as hydrogen source. The catalysts were found to be finely dissolved in the liquid substrates in the aqueous mixture and exhibited high catalytic activity and enantioselectivity (52–97% ee). The catalytic loading could be decreased to 0.01 mol% and good conversion was still obtained with excellent enantioselectivity. Moreover, the catalyst could be easily precipitated from the mixture by adding hexane and reused several times without affecting the high enantioselectivity.

Introduction

Water has triggered ongoing interest as an alternative solvent in organic synthesis due to its low cost, toxicity and environmental impact.[1] Since more and more metal-catalysed reactions are able to be conducted smoothly in aqueous solution,[2] the recycling of such catalysts is also a task of great environmental importance, especially when expensive and toxic heavy metal complexes are employed. Water-soluble ligands are commonly applied to give hydrophilic metal-catalysts that will be retained in the aqueous phase,[3] however, sometimes reduced catalytic activity is encountered due to the biphasic characteristics of the hydrophilic catalysts and the organic reactants. On the other hand, catalysts immobilised on hydrophobic macromolecules have been rarely investigated in aqueous reactions. This strategy might be applicable in that the hydrophobic complex could be dissolved in the liquid substrate to promote the reaction in a homogeneous fashion, and high catalytic activity would be expected owing to the high catalyst concentration in the substrate solution. Then the catalysts could be recycled by adding inert solvent.

Recently the ruthenium or rhodium complexes of *N*-sulfonated chiral diamines[4,5] have been found to be more active catalysts in the asymmetric transfer hydrogenation of ketones[6] and imines[7] in aqueous solution, in comparison with those in organic solvents. In addition, recyclable *N*-sulfonated 1,2-diphenylethylenediamine (DPEN)–ruthenium catalysts by employing water-soluble ligands[6b,g] or immobilisation on silica gel[6f] have been successfully applied in water. However, the development of recyclable catalysts based on chiral 1,2-diaminocyclohexane (DACH)–metal complexes,[8] especially for the rhodium complexes, has not been well studied yet. Recently we reported the synthesis of dendritic DPEN–ruthenium catalysts and achieved good results in asymmetric transfer hydrogenation reactions in organic solvents.[9,10] It is intriguing to consider that the chiral DACH-metal complexes immobilised on highly hydrophobic Fréchet-type dendrons could be utilised as recyclable transfer hydrogenation catalysts in water. Here, we would like to report our studies on this subject.

Results and discussion

The core-functionalised dendritic ligands based on chiral 1,2-diaminocyclohexane (DACH) were smoothly prepared in a similar way as reported early.[9a,c] As illustrated in Scheme 1, the amino-functionalised intermediate (*R*,*R*)-**4**, which was synthesised in three steps from (*R*,*R*)-DACH, was condensed with Fréchet's polyether dendrons, using $(PhO)_3P$ as the coupling reagent. Then the dendritic ligands **1a–1d** were obtained through the deprotection of the Boc group. The dendritic structures could be established through MS techniques (ESI HRMS or MALDI-TOF MS). All of the MS spectra displayed a very prominent peak corresponding to the dendrimers complexed with proton or potassium cation. MALDI-TOF MS was applied for the analysis of **1d** (Table 1).

With the desired chiral dendritic ligands **1a–1d** in hand, the catalytic activity and enantioselectivity of their ruthenium or rhodium complexes were studied *via* the transfer hydrogenation of acetophenone **7a**, and also compared with the monomeric TsDACH **6**–metal complex. We have conducted the transfer hydrogenation reactions in three different conditions for detailed comparison of the dendritic catalysis at 1 mol% catalyst loading: (A) $[RuCl_2(cymene)]_2$ as the metal precursor in DCM solution,

Table 1 MS data of dendritic ligands

Compound	MW (calcd.)	MW (found)
1a	585.2297	586.2351[a,b]
1b	1009.3972	1010.4095[a,b]
1c	1857.7321	1858.7390[a,b]
1d	3554	3593[c,d]

[a] ESI HRMS. [b] $(M + H)^+$. [c] MALDI-TOF MS. [d] $(M + K)^+$.

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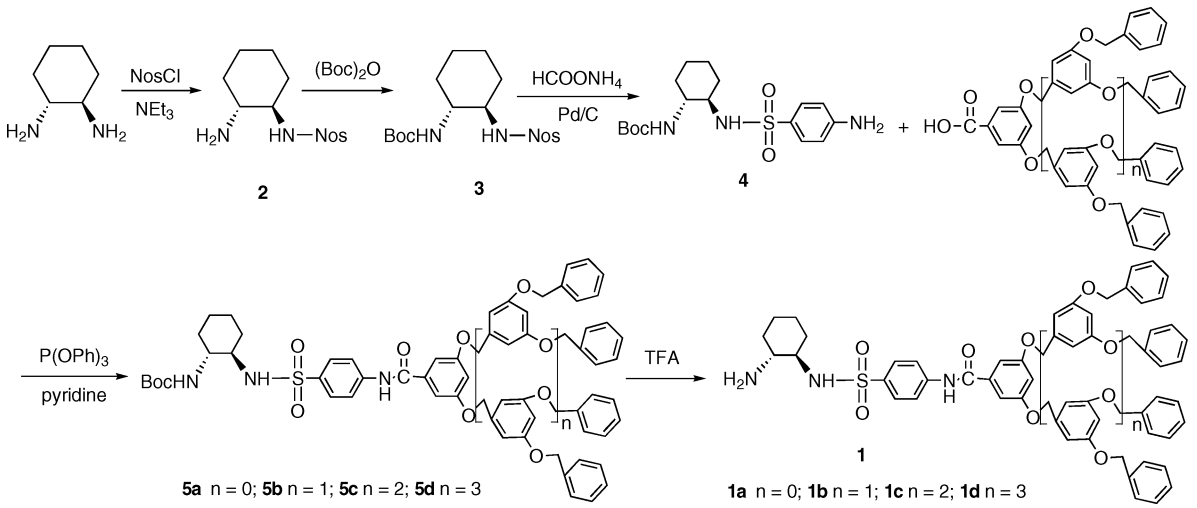


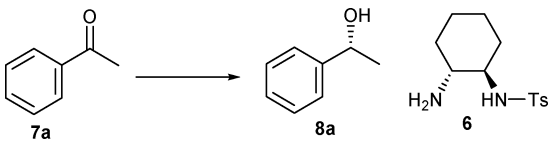
Scheme 1 Synthesis of dendritic DACH ligands.

the azeotrope of HCOOH–NEt_3 as the hydrogen source at 28 °C; (B) $[RuCl_2(cymene)]_2$ as the metal precursor in aqueous solution, HCOONa as the hydrogen source at 35 °C; (C) $[RhCp^*Cl_2]_2$ as the metal precursor in aqueous solution, HCOONa as the hydrogen source at 40 °C. The average turnover frequency (TOFs, in relation to per Ru– or Rh–complex) and enantioselectivity were summarised in Table 2.

Although quite different results were obtained under three reaction conditions, in general, good retention of high enantioselectivity was observed for all dendritic catalysts as compared to the monomeric metal complex of **6**. Much slower catalytic activity was detected for the fourth generation dendritic **1d**–Ru(II) or Rh (III) complex due to its bulky structure, especially in the organic solvent (Table 2, entries 5, 10 and 15).[11] On the other hand, we were pleased to find that all hydrophobic dendritic DACH–Ru(II) or Rh(III) complexes could be finely dissolved in organic acetophenone and maintained the high catalytic activity in water (conditions B, entries 7–10, and conditions C, entries 12–15). Therefore, the asymmetric reactions in the aqueous mixture promoted by the hydrophobic dendritic catalysts still proceeded in a homogeneous way. In addition, much better results were obtained by employing $[RhCp^*Cl_2]_2$ as the metal precursor (conditions C).[6d] Moreover, the catalytic loading could be further decreased under conditions C. The reduction of acetophenone took place smoothly at 0.1 mol% of **1b**–Rh(III), furnishing a >99% conversion with 94% ee in 4 h (entry 16). The reaction was also feasible with S/C ratio up to 10000, though moderate conversion was obtained and a prolonged reaction time was necessary (entry 17).

Having demonstrated that the dendritic DACH–Rh(III) catalysts have high catalytic efficacy in water, we then tested the recyclability of these dendritic catalysts *via* the solvent precipitation method. We employed the second generation dendritic **1b**–Rh(III) complex at 1 mol% loading as the example. After a specific reaction time, hexane was added to precipitate the **1b**–Rh catalyst, and then the organic phase containing the product was removed. Before the next reaction could be conducted, 1 equiv. HCOOH was added to adjust the pH value to about 7. As shown in Table 3, the recycling use of dendritic **1b**–Rh(III) catalyst was

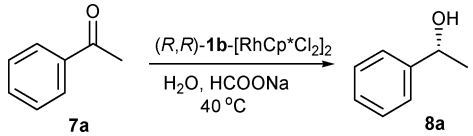
Table 2 Comparison of the catalytic efficiency of dendritic catalysts in different conditions in the asymmetric transfer hydrogenation of acetophenone[a]



Entry	Ligand	Conditions	TOF/h^{-1}	Conv. (%)	Ee[b] (%)
1	**6**	A	3.6	>99	94
2	**1a**	A	3.5	>99	93
3	**1b**	A	3.3	>99	94
4	**1c**	A	3.8	>99	93
5	**1d**	A	0.3	80	93
6	**6**	B	41	>99	88
7	**1a**	B	37	>99	88
8	**1b**	B	36	>99	88
9	**1c**	B	37	>99	87
10	**1d**	B	20	95	85
11	**6**	C	384	>99	95
12	**1a**	C	344	>99	96
13	**1b**	C	364	>99	96
14	**1c**	C	324	>99	96
15	**1d**	C	236	99	95
16[c]	**1b**	C		>99	94
17[d]	**1b**	C		61	95

[a] Conditions A: $[RuCl_2(cymene)]_2$ (0.002 mmol), diamine ligand (0.0044 mmol), acetophenone (0.4 mmol) and HCOOH–NEt_3 (0.2 mL) were stirred in DCM (0.5 mL) at 28 °C. The average TOFs were calculated over 5 h reaction time. Conversions were determined by GC analysis after 30 h; Conditions B: $[RuCl_2(cymene)]_2$ (0.002 mmol), diamine ligand (0.0044 mmol), acetophenone (0.4 mmol) and HCOONa (2.4 mmol) were stirred in water (1 mL) at 35 °C. The average TOFs were calculated over 2 h reaction time. Conversions were determined by GC analysis after 4 h; Conditions C: $[RhCp^*Cl_2]_2$ (0.002 mmol), diamine ligand (0.0044 mmol), acetophenone (0.4 mmol) and HCOONa (2.4 mmol) were stirred in water (1 mL) at 40 °C. The average TOFs were calculated over 15 min reaction time. Conversions were determined by GC analysis after 40 min. [b] Determined by GC analysis on a Chrompack CP Chirasil-dex column. The absolute configuration was *R*. [c] Under conditions C at 4 mmol scale, S/C = 1000, 4 h. [d] Under conditions C at 40 mmol scale, S/C = 10000, 72 h.

Table 3 Recycling use of dendritic **1b**–Rh in the asymmetric transfer hydrogenation of acetophenone in water[a]



Run	*t*/min	Conv.[b] (%)	Ee[c] (%)
1	40	>99	96
2	40	>99	95
3	40	98	94
4	60	99	95
5	60	85	95
6	90	97	95

[a] Conditions: $[RhCp^*Cl_2)]_2$ (0.01 mmol), ligand **1b** (0.022 mmol), acetophenone (2.0 mmol) and HCOONa (12 mmol) were stirred in water (5 mL) at 40 °C. [b] Determined by GC analysis. [c] Determined by GC analysis on a Chrompack CP Chirasil-dex column.

Table 4 Asymmetric transfer hydrogenation of ketones catalysed by dendritic **1b**–Rh in H_2O–HCOONa[a]

Entry	Substrate	*t*/h	Conv.[b] (%)	Ee[c] (%)
1	**7a**	0.7	>99	96
2	**7b**	0.5	99	93
3	**7c**	0.8	97	92
4	**7d**	1	95	94
5	**7e**	1.5	>99	81
6	**7f**	0.8	99	97
7	**7g**	0.5	98	96
8	**7h**	5	70[d]	91[e]
9	**7i**	9	69[d]	57
10	**7j**	4	97[d]	72[e]
11	**7k**	1.3	94[d]	52[e]

[a] Conditions: $[RhCp^*Cl_2)]_2$ (0.002 mmol), ligand **1b** (0.0044 mmol), ketone **7** (0.4 mmol) and HCOONa (2.4 mmol) were stirred in water (1 mL) at 40 °C. [b] Determined by GC analysis. [c] Determined by GC analysis on a Chrompack CP Chirasil-dex column. [d] Isolated yield. [e] Determined by HPLC analysis on OD or AS column.

quite successful (Table 3, runs 1–6). Excellent conversion (97%) and enantioselectivity (95%) were obtained even in the sixth run with some extension of the reaction time. On the other hand, it should be noted that, in contrast to the previously reported dendritic DPEN–Ru(II) catalysts,[9] the dendritic DACH–Rh(III) or Ru(II) complexes exhibited very limited recyclability in organic solution.[12]

Subsequently, we extended this protocol to a range of aromatic, heteroaromatic and functionalised ketones (Fig. 1), aiming to determine the potential applicability of the dendritic catalytic system in the asymmetric transfer hydrogenation in water. The results are summarised in Table 4. In the case of acetophenone derivatives, excellent conversions and high ees could be obtained irrespective of the substitution on the aryl ring (Table 4, entries 1–5), however, a lower ee was observed for the *ortho*-substituted ketone **7e** (entry 5). 1-Tetralone **7f** was completely converted to the corresponding alcohol with excellent ee (entry 6). The heteroaromatic ketones were also tested. 2-Acetylthiophene **7g** was successfully reduced in 98% conversion and 96% ee in 0.5 h (entry 7). On the other hand, the transfer hydrogenation of pyridyl ketones **7h** and **7i** in homogenous DCM–HCOOH–NEt_3 conditions seemed unfeasible, in sharp contrast, both substrates were smoothly reduced in the H_2O–HCOONa system, affording good isolated yields, while much higher reactivity and ee were obtained for 2-acetylpyridine **7h** than those of 3-acetylpyridine **7i** (entry 8 *vs.* entry 9).[13] α-Ketoester **7j** could be smoothly transfer hydrogenated in moderate enantioselectivity (entry 10). In addition, α,β-unsaturated ketone **7k** was chemoselectively reduced to the corresponding allylic alcohol in high yield, while the ee was not satisfying (entry 11).[9c]

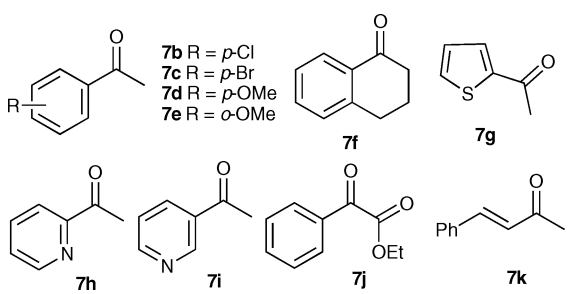


Fig. 1 Structures of the various ketones.

Conclusions

In conclusion, dendritic chiral monosulfonylated DACH ligands supported on the core of Fréchet-type dendrons have been synthesised. Their ruthenium(II) and rhodium(III) complexes have been tested in the transfer hydrogenation of ketones in organic or aqueous solution, and much better catalytic efficacy has been noted in an aqueous system using HCOONa as the hydrogen source. The highly hydrophobic dendritic rhodium(III) complexes were found to be finely dissolved in the liquid substrates in the reaction mixture and exhibited high catalytic activity and enantioselectivity for a range of ketones. The catalytic loading could be decreased to 0.01 mol% and good conversion was still obtained with excellent enantioselectivity. Moreover, the catalyst could be easily precipitated from the mixture by adding hexane and reused several times without affecting the high enantioselectivity. We believe that the application of other immobilised hydrophobic catalysts in aqueous catalysis could be also desirable.

Experimental

General methods

Melting points were determined in open capillaries and are uncorrected. TLC was performed on glass-backed silica plates. Column chromatography was performed using silica gel (200–300 mesh) eluting with ethyl acetate and petroleum ether. NMR was recorded on Bruker 300 or 400 MHz spectrometers. Chemical shifts are reported in ppm down field from tetramethylsilane with the solvent resonance as the internal standard. Enantiomeric excess was determined by GC analysis on a CP CHIPASIL-DEX column and HPLC analysis on Chiralpak OD or AS column. DCM was distilled from CaH_2. All other reagents were used without purification as commercially available.

(*R*,*R*)–*N*-(4′-Nitrophenylsulfonyl)-1,2-diaminocyclohexane (2). To a solution of (*R*,*R*)-1,2-diaminocyclohexane (0.9 g, 16.7 mmol) and NEt_3 (3 mL, 21 mmol) in DCM (40 mL) was added a solution of 4-nitrobenzenesulfonyl chloride (3.7 g, 16.7 mmol) in DCM (10 mL) in an ice bath. The mixture was stirred overnight at room temperature and concentrated under reduced pressure. The residue was acidified with dilute HCl and extracted with EtOAc–ether (1 : 20 v/v, 20 mL). Then the aqueous phase was neutralised with ammonia. The solid was collected, washed with water, and air dried. Yield 3.6 g (72%), mp = 177.5–178 °C. $[\alpha]_D^{23}$ +32.1 ($c = 0.49$, C_2H_5OH). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.05–2.06 (m, 8H), 2.40–2.48 (m, 1H), 2.70–2.92 (m, 3H), 8.11 (d, $J = 8.7$ Hz, 2H), 8.37 (d, $J = 8.7$ Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$ + DMSO, 75 MHz) δ 19.1, 19.6, 27.2, 28.4, 49.0, 54.9, 118.9, 122.9, 142.8, 144.3 ppm. IR (KBr) ν (cm^{-1}): 3429, 3297, 1529, 1354, 1165, 1090. ESI MS *m*/*z*: 300.1 $[M + H]^+$ (100).

(*R*,*R*)–*N*-Boc-*N*′-(4′-nitrophenylsulfonyl)-1,2-diaminocyclohexane (3). Compound **2** (2.0 g, 6.7 mmol), $(Boc)_2O$ (1.7 g, 7.8 mmol) and DIPEA (1.5 mL, 8.6 mmol) were stirred in DCM (30 mL) at room temperature for 20 hours. The solution was washed successively with 0.5 mol L^{-1} citric acid, water, saturated sodium bicarbonate and brine, and dried over Na_2SO_4. Concentrating the solvent gave **3** as a pale yellow solid. Yield 2.6 g (99%), mp = 159–162 °C. $[\alpha]_D^{23}$ +42.1 ($c = 0.42$, C_2H_5OH). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.12–2.03 (m, 8 H), 1.45 (s, 9H), 2.93–2.96 (m, 1H), 3.34–3.37 (m, 1H), 4.40 (d, $J = 7.5$ Hz, 1H), 6.23 (d, $J = 5.4$ Hz, 1H), 8.06 (d, $J = 7.8$ Hz, 2H), 8.34 (d, $J = 8.1$ Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.3, 24.5, 28.2, 32.5, 33.6, 53.4, 59.8, 80.2, 124.1, 128.0, 147.4, 149.6, 157.0 ppm. IR (KBr) ν (cm^{-1}): 3386, 3349, 1678. ESI MS *m*/*z*: 438.1 $[M + K]^+$, 422.1 $[M + Na]^+$. Calcd. for $C_{17}H_{25}N_3O_6S$: C 51.10, H 6.31, N 10.52, S 8.03, found C 51.30, H 6.36, N 10.57, S 7.79%.

(*R*,*R*)–*N*-Boc-*N*′-(4′-aminophenylsulfonyl)-1,2-diaminocyclohexane (4). Compound **3** (2.5 g, 6.3 mmol), ammonium formate (2 g, 32 mmol) and 10% Pd/C (400 mg) were stirred in methanol (50 mL) for 20 min. The mixture was filtered through Celite. The filtrate was concentrated and water (20 mL) was added, and then the resultant precipitate was filtered, washed with water, and air dried to give **4** as a white solid. Yield 2.3 g (95%), mp 176–177 °C. $[\alpha]_D^{23}$ +69.6 ($c = 0.39$, C_2H_5OH). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.10–2.05 (m, 8 H), 1.46 (s, 9 H, CH_3), 2.79–2.82 (m, 1H), 3.27–3.31 (m, 1H, NCH), 3.94 (br s, 2H), 4.53 (d, $J = 7.8$ Hz, 1H), 5.43 (d, $J = 5.7$ Hz, 1H), 6.70 (d, $J = 8.7$ Hz, 2H), 7.63 (d, $J = 8.1$ Hz, 2H) ppm. ^{13}C NMR (DMSO + $CDCl_3$, 75 MHz) δ 24.4, 24.6, 28.4, 32.4, 33.0, 53.9, 57.4, 78.7, 113.4, 127.6, 128.6, 151.7, 156.6 ppm. IR (KBr) ν (cm^{-1}): 3477, 3381, 3295, 1689. ESI MS *m*/*z*: 392.2 $[M + Na]^+$. Calcd. for $C_{17}H_{27}N_3O_4S$: C 55.26, H 7.37, N 11.73, S 8.68, found C 55.35, H 7.37, N 11.56, S 8.48%.

General procedure for condensation of Frechét-type acid with (*R*,*R*)-4

(*R*,*R*)-**4** (150 mg, 0.41 mmol), dendritic acid (1.05 equiv.) and triphenyl phosphate (370 mg, 1.1 mmol) were stirred in pyridine (2 mL) at 95 °C for 24 h. The solution was poured into water (30 mL) and extracted with EtOAc (40 mL). The organic layer was washed successively with 0.5 mol L^{-1} citric acid, water, saturated sodium bicarbonate and brine, and dried (Na_2SO_4). Flash chromatography on silica gel gave the Boc-protected dendrimers **5a–5d**.

(*R*,*R*)-5a. Yield 86%, mp = 185–187 °C. $[\alpha]_D^{23}$ +30.6 ($c = 0.35$, THF). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.08–2.05 (m, 8H), 1.46 (s, 9H), 2.82–2.86 (m, 1H), 3.30–3.33 (m, 1H), 4.45–4.47 (m, 1H), 5.10 (s, 4H), 5.72 (s, 1H), 6.81 (s, 1H), 7.10 (s, 2H), 7.34–7.43 (m, 10H), 7.76 (d, $J = 7.8$ Hz, 2H), 7.83 (d, $J = 7.8$ Hz, 2H), 8.04 (s, 1H) ppm. ^{13}C NMR (DMSO + $CDCl_3$, 75 MHz) δ 23.5, 24.6, 28.5, 32.3, 32.9, 53.6, 57.0, 70.0, 105.2, 107.2, 120.0, 127.4, 127.8, 128.1, 128.4, 128.6, 136.7, 142.7, 156.2, 159.7, 165.7 ppm. IR (KBr) ν (cm^{-1}): 3409, 3361, 1680, 1592, 1524, 1318, 1159. ESI HRMS calcd. for $C_{38}H_{43}N_3O_7S$ + Na 708.2720, found 708.2697.

(*R*,*R*)-5b. Yield 88%, mp 173–174 °C. $[\alpha]_D^{23}$ +17.6 ($c = 0.49$, THF). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.08–2.00 (m, 8H), 1.46 (s, 9H), 2.75–2.87 (m, 1H), 3.20–3.35 (m, 1H), 5.04, 5.10 (s × 2, 12H), 6.59–6.69 (m, 7H), 7.06 (s, 2H), 7.30–7.43 (m, 20H), 7.75–7.95 (m, 4H) ppm. Partial ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.9, 25.0, 28.3, 38.0, 39.5, 54.8, 59.5, 66.0, 70.1, 80.2, 101.5, 106.3, 106.4, 119.9, 127.5, 128.0, 128.5, 136.4, 136.6, 138.7, 160.0, 160.1, 165.7 ppm. IR (KBr) ν (cm^{-1}): 3409, 3362, 1683, 1593, 1320, 1159, 1049. ESI MS *m*/*z*: 1131.8 $[M + Na]^+$. Calcd. for $C_{66}H_{67}N_3O_{11}S$ C 71.39, H 6.08, N 3.78, S 2.89, found C 71.02, H 6.13, N 3.68, S 2.89%.

(*R*,*R*)-5c. Yield 74%, mp 131–133 °C. $[\alpha]_D^{23}$ +15.8 ($c = 0.35$, THF). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86–2.01 (m, 8H), 1.46 (s, 9H), 2.84–2.86 (m, 1H), 3.30–3.33 (m, 1H), 4.90–5.01 (m, 28H), 6.57–6.68 (m, 19H), 7.02 (s, 2H), 7.28–7.41 (m, 40H), 7.65–7.80 (m, 4H) ppm. Partial ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.4, 26.9, 28.3, 34.9, 35.4, 53.8, 59.8, 69.9, 70.0, 80.3, 101.5, 101.6, 106.4, 119.7, 127.5, 127.9, 128.1, 128.2, 128.3, 128.5, 136.4, 136.7, 138.7, 139.1, 160.0, 160.1, 165.5 ppm. IR (KBr) ν (cm^{-1}): 3509, 3407, 3316, 1680, 1595, 1158, 1051. Calcd. for $C_{122}H_{115}N_3O_{19}S$ C 74.79, H 5.92, N 2.14, S 1.64, found C 74.76, H 5.94, N 2.09, S 1.26%.

(*R*,*R*)-5d. Yield 55%, mp 93–98 °C. $[\alpha]_D^{23}$ +4.6 ($c = 0.37$, THF). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89–1.95 (m, 8H), 1.46 (s, 9H), 2.82–2.86 (m, 1H), 3.31–3.32 (m, 1H), 4.75–4.98 (m, 60H), 6.55–6.83 (m, 45H), 7.14–7.37 (m, 80H), 7.72–7.78 (m, 4H) ppm. IR (KBr) ν (cm^{-1}): 3527, 3500, 3415, 3031, 1685, 1595, 1449, 1156, 1050. Calcd. for $C_{242}H_{211}N_3O_{35}S$ C 76.85, H 5.82, N 1.15, S 0.88, found C 76.56, H 5.77, N 1.14, S 0.54%.

General procedure for deprotection of Boc-group

Boc-protected dendrimer **5a–5d** (0.42 mmol) was dissolved in DCM (1 mL) and cooled in ice water. TFA (2 mL) was added and the solution was stirred for 1 h (HCl–EtOAc solution was used to deprotect Boc-group of dendrimer **5d**). The solvent was removed under vacuum. The mixture was neutralised with ammonia and then extracted with EtOAc (20 mL). The organic layer was washed with water, dried and concentrated to give the desired product **1a–1d** as a white solid.

(*R*,*R*)-1a. Yield 92%, mp 212–214 °C. $[\alpha]_D^{23}$ −8.0 ($c = 0.34$, THF). ^{1}H NMR (DMSO, 300 MHz) δ 1.05–1.80 (m, 8H), 2.58–2.75 (m, 2H), 5.18 (s, 4H), 6.94 (s, 1H), 7.22 (d, $J = 2.1$ Hz, 2H), 7.35–7.49 (m, 10H), 7.80 (d, $J = 8.7$ Hz, 2H), 7.97 (d, $J = 8.7$ Hz, 2H) ppm. ^{13}C NMR (DMSO, 75 MHz) δ 29.2, 29.6, 37.0, 38.3, 59.0, 64.6, 74.8, 110.3, 112.1, 125.2, 132.5, 132.6, 132.9, 133.1, 133.6, 141.6, 141.8, 147.6, 164.6, 170.5 ppm. IR (KBr) ν (cm^{-1}):

3432, 3303, 1655, 1591, 1522, 1322, 1159, 1059. ESI HRMS calcd. for $C_{33}H_{35}N_3O_5S$ + H 586.2375, found 586.2351.

(*R*,*R*)-1b. Yield 91%. $[\alpha]_D^{23}$ +11.3 (c = 0.24, THF). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.87–2.14 (m, 8H), 2.75–2.87 (m, 1H), 3.20–3.35 (m, 1H), 4.89, 5.05 (s × 2, 12H), 6.49–6.74 (m, 9H), 7.28–7.45 (m, 20H), 7.89–8.04 (m, 4H) ppm. Partial ^{13}C NMR ($CDCl_3$ + DMSO, 75 MHz) δ 29.2, 29.7, 31.5, 36.8, 37.8, 59.1, 63.8, 74.6, 106.2, 110.2, 111.2, 111.8, 112.0, 125.0, 132.3, 132.7, 133.3, 140.9, 141.5, 143.8, 147.7, 164.4, 164.8, 170.8 ppm. IR (KBr) ν (cm^{-1}): 3437, 1658, 1594, 1321, 1157, 1054. ESI HRMS calcd. for $C_{61}H_{59}N_3O_9S$ + H 1010.4050, found 1010.4095.

(*R*,*R*)-1c. Yield 90%. $[\alpha]_D^{23}$ +3.4 (c = 0.30, THF). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89–1.72 (m, 8H), 2.94–2.99 (m, 1H), 3.32–3.42 (m, 1H), 4.79–5.03 (m, 28H), 6.48–6.67 (m, 21H), 7.13–7.38 (m, 40H), 7.75–7.90 (m, 4H) ppm. IR (KBr) ν (cm^{-1}): 3433, 3031, 1599, 1450, 1321, 1157, 1053. ESI HRMS calcd. for $C_{117}H_{107}N_3O_{17}S$ + H 1858.7395, found 1858.7390.

(*R*,*R*)-1d. Yield 85%. $[\alpha]_D^{23}$ +1.3 (c = 0.31, THF). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.79–5.0 (m, 60H), 6.48–6.67 (m, 45H), 7.25–7.38 (m, 84H) ppm. The signal of the DACH moiety is too small to be detected. IR (KBr) ν (cm^{-1}): 3411, 3032, 1595, 1449, 1374, 1157, 1052. MALDI-TOF MS calcd. for $C_{229}H_{203}N_3O_{33}S$ + K 3593, found 3593.

General procedure for asymmetric transfer hydrogenation of ketone compounds

$[Cp^*RhCl_2]_2$ (1.3 mg, 0.002 mmol), dendritic ligand **1** (0.0044 mmol) and NEt_3 (2 μL, 0.013 mmol) were stirred in DCM at 40 °C for 1 h. After removal of DCM under reduced pressure, ketone **7** (0.4 mmol), HCOONa (250 mg, 6 equiv.) and water (1 mL) were added. After the reaction was completed (monitored by TLC), the reaction mixture was extracted with ether. The organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The product was directly used for GC analysis. Products from **7h**, **7j** and **7k** were purified by flash chromatography on silica gel and the ees were determined by HPLC analysis on OD or AS column.

General procedure for recycling of dendritic catalyst in asymmetric transfer hydrogenation of acetophenone

$[Cp^*RhCl_2]_2$ (6.5 mg, 0.01 mmol), dendritic ligand **1b** (0.022 mmol) and NEt_3 (10 μL, 0.065 mmol) were stirred in DCM at 40 °C for 1 h. After removal of DCM under reduced pressure, acetophenone (0.24 mL, 2 mmol), HCOONa (1.25 g, 12 mmol) and water (5 mL) were added. After a specific reaction time, *n*-hexane (5 mL) was added to precipitate the dendritic catalyst, and the organic phase containing the chiral alcohol was carefully removed. Before the next reaction could be conducted, HCOOH (80 μL, 2 mmol) was added to adjust the pH value of aqueous solution to about 7. Then acetophenone (2 mmol) were added and the mixture was stirred at 40 °C.

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