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Dendritic catalysts for asymmetric transfer hydrogenation†

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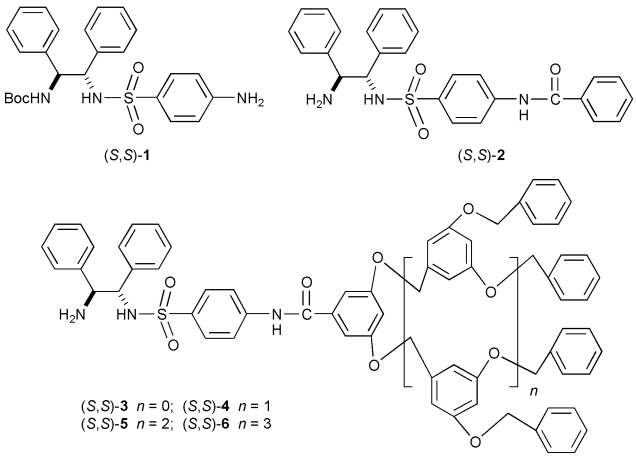
The synthesis of chiral diamine based dendritic ligands and their ruthenium complex catalysed asymmetric transfer hydrogenation is described.

Since the pioneer works reported in 1994,[1] dendritic catalysts with well-defined nanostructures have triggered increasing attention because in principle they have the potential to combine the advantages of homogeneous and heterogeneous catalysts in one system.[2] Although a number of dendritic catalysts have been described,[3] so far, relatively few reports on catalytic asymmetric synthesis are available.[4] Also, chiral ligands and metal catalysts are very expensive and the finding of the recyclable catalysts becomes increasingly important.

Noyori *et al*. discovered an excellent ligand, (*S*,*S*)-*N*-(*p*-tolylsulfonyl)-1,2-diphenylethylenediamine [(*S*,*S*)-TsDPEN], for the ruthenium catalysed transfer hydrogenation reactions.[5] The chiral DPEN is available in our laboratory on the kilogram scale. Moreover, the polymeric catalysts, in which the chiral TsDPEN was incorporated in a polymeric matrix or bound to the insoluble polymers, were reported to be detrimental to the catalytic activity and selectivity in varying degrees.[6] Herein we report the first use of soluble and recyclable dendritic catalysts for the enantioselective transfer hydrogenation of prochiral ketones. The amino-functionalised chiral ligand (*S*,*S*)-**1** was synthesized in three steps from (*S*,*S*)-DPEN, and subsequent condensation with Fréchet's polyether dendritic wedges[7] and the final deprotection of the Boc-group readily gave the dendritic chiral ligands.‡

Asymmetric transfer hydrogenation reactions were studied using acetophenone as the model substrate.§ Compared to the monomer Ru[(*S*,*S*)-**2**] complex, a slightly enhanced reactivity was observed for the dendritic catalysts with the high enantioselectivity (>96% ee), in which the first and third generation catalysts possess higher reactivity (Table 1).

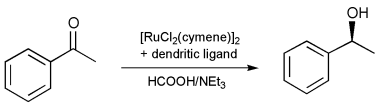
Another unique feature of these dendritic catalysts was that they completely maintained the enantioselectivity with only slight loss of activity in successive use. Using the third and fourth generation catalysts Ru[(*S*,*S*)-**5**] and Ru[(*S*,*S*)-**6**], (*S*)-1-phenylethanol was formed after ~30 h for the fourth use with 88, 85% conversions and 96.4, 96.7% ee, respectively (entries 8 and 12), and high enantioseletivities (>95% ee) remained even for the fifth use (entries 9 and 13). Further addition of $[RuCl_2(cymene)]_2$ into the Ru[(*S*,*S*)-**6**] complex could not regain the reactivity and selectivity (entry 14), and subsequent TLC analysis of the recovered catalyst confirmed that this mostly resulted from the decomposition of the dendritic ligand. For the heterogeneous polymer immobilised catalysts,[6] the reactivity has been mostly lost after the third use. Moreover, the fourth generation catalyst was more active than the third one for the fifth use with 73 *vs*. 52% conversions, respectively (entries 13 and 9), although it is less active than the third generation



catalyst (entries 5 and 4). Thus, we refer the relatively robust activity of the dendritic catalysts to the "dendrimer effects" on stability of the catalytically active complex on the dendron, which had been observed in bis(μ-oxo)dicopper species toward oxidative self-decomposition.[8]

In conclusion, various generations of chiral diamine based dendritic catalysts encapsulated within the matrix have been synthesized and demonstrated good recyclable catalytic activity and enantioselectivity in transfer hydrogenation of an aromatic ketone. Current work is aiming at a detailed insight of the nature

Table 1 Dendritic TsDPEN–Ru(II) complex catalysed asymmetric transfer hydrogenation of acetophenone[a]



Entry	Ligand	*t*/h	Conv.[b] (%)	TOF[c]/h^{-1}	Ee[d] (%)
1	**2**	20	95	8.6	96.5
2	**3**	20	>99	11.9	96.6
3	**4**	20	98	9.5	96.5
4	**5**	20	>99	11.0	96.5
5	**6**	20	98	9.6	96.5
6	**5** (2nd use)[e]	20	93	—	96.7
7	**5** (3rd use)[e]	25	86	—	96.7
8	**5** (4th use)[e]	31	88	—	96.4
9	**5** (5th use)[e]	40	52	—	95.0
10	**6** (2nd use)[e]	20	92	—	96.6
11	**6** (3rd use)[e]	25	87	—	96.8
12	**6** (4th use)[e]	30	85	—	96.7
13	**6** (5th use)[e]	40	73	—	96.3
14	**6** (6th use)[e,f]	40	52	—	87.0

[a] (*S*)-Alcohol was obtained. [b] Based on GC and ^{1}H NMR analysis. [c] Average turn-over frequency calculated over the 5 h reaction time. [d] Determined by GC with a Chrompack CP Chrasil-dex column (25 mm × 0.25 mm). [e] Recovered catalyst was used. [f] Additional $[RuCl_2(cymene)]_2$ was supplemented.

† Electronic supplementary information (ESI) available: synthesis details, recycling procedure and a graph of time-dependent conversion of acetophenone by the catalysts. See http://www.rsc.org/suppdata/cc/b1/b104160f/

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of the dendritic wedge stabilizing effect on the catalyst and the exploration of these catalysts in other asymmetric transfer hydrogenation reactions.

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Notes and references

‡ ESI-HRMS data for the dendritic ligands: (*S*,*S*)-**3** calcd for $C_{41}H_{37}N_3O_5S$ 683.2454, found 684.2429 $[M + H]^+$; (*S*,*S*)-**4** calcd for $C_{69}H_{61}N_3O_9S$ 1107.4129, found 1108.4179 $[M + H]^+$; (*S*,*S*)-**5** calcd for $C_{125}H_{109}N_3O_{17}S$ 1955.7478, found 1956.7929 $[M + H]^+$; (*S*,*S*)-**6** (MALDI-TOF-MS) calcd for $C_{237}H_{205}N_3O_{33}S$ + Na 3675.41, found 3676.03.

§ General procedure: 1 mol% catalyst was prepared *in situ* by mixing 2 equivalents of triethylamine, a dendritic ligand and $[RuCl_2(cymene)]_2$ (1.1 : 0.5 molar ratios) in a 2 M DCM solution for 1 h under argon at 28 °C. Then an acetophenone and formic acid–triethylamine azeotrope (0.5 ml per mmol ketone) was added and the mixture was stirred at 28 °C.

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