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Synthesis of dendrimer-supported ferrocenylmethyl aziridino alcohol ligands and their application in asymmetric catalysis†

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A series of *N*-ferrocenylmethyl aziridino alcohol ligands bearing Fréchet-type dendrimers were synthesized and applied in the asymmetric addition of diethylzinc to aldehydes affording chiral alcohols in excellent yields (up to 99%) and excellent enantioselectivities (ee, up to 98%). The ligands could be recycled and reused eight times for such a reaction with almost the original high reactivity and selectivity.

1. Introduction

Development of highly efficient and recyclable chiral catalysts which meet the requirements of green and sustainable chemistry is crucial for the application of the asymmetric transformations in industry and has been attracting extensive attention of chemists.[1] Although various highly efficient homogeneous chiral catalysts have been developed over the past several decades, they often have disadvantages in aspects such as the separation, recycling of expensive chiral catalysts, as well as contamination of the products by the toxic transition metals, which greatly hamper their industrial application. One of the practical strategies to overcome these problems is the immobilization of the parent homogeneous chiral catalysts to insoluble supports. Most of the conventional heterogeneous catalysts usually exhibit inferior performance than their homogeneous counterparts due to the former being of poor accessibility, random anchoring and disturbed geometry of active sites in insoluble solids.

Recently, soluble polymer- and dendrimer-supported catalysts, with unique features of one-phase catalysis and two-phase catalyst separation (*via* precipitation) after the reaction, have attracted extensive attention.[2,3] While the flexible linear polymer-supported catalysts often give lower reactivity and enantioselectivity than their homogeneous counterparts, most of the dendritic catalysts often exhibit catalytic properties comparable to, or even much better than, those of their parental small molecular catalysts.[3] The fine-tunable catalytic properties of the dendritic chiral catalysts are ascribed to their easily adjustable well-defined structure, size, shape, and solubility of the dendrimers. In addition, the microenvironment created by the attached dendritic wedges sometimes brings positive dendritic effects for the supported catalysts.[3a,b] Since the pioneering work of Knapen *et al.*,[4] a number of chiral dendritic catalysts with different chelating atoms have been developed and applied in asymmetric transformations,[5] which paved a new avenue for a sustainable chemical process.

The catalytic asymmetric addition of organozinc to aldehydes is one of the most reliable methods to obtain synthetically useful chiral secondary alcohols.[6] Chiral catalysts supported on insoluble polymers, inorganic materials and soluble macromolecules have been developed to improve applicability of the transformation.[1a–d] Among these recoverable catalysts, dendritic TADDOLS,[7] BINOLS,[8,9] and those derived from Fréchet-type dendrimers in particular,[10] have proved to be versatile in the asymmetric addition of organozinc to aldehydes. Chiral β-aminoalcohols are undoubtedly the most efficient ligands for such transformations.[6] However, the dendritic Fréchet-type aminoalcohols, which can be prepared by attaching chiral aminoalcohols to Fréchet-type dendrimers, remain less developed.[11] Therefore, syntheses of chiral Fréchet dendrimers supported aminoalcohols and their application in asymmetric catalysis is highly desirable.

When used in asymmetric reactions, the chiral ferrocenyl compounds are very excellent ligands and catalysts because of their rigid structures and outstanding enantioselectivity.[12] Chiral aziridino alcohols, a kind of special β-aminoalcohol possessing a rigid three-member ring moiety, have been proved to be highly effective catalysts for asymmetric additions of organozinc species to aldehydes.[13] In recent years, a series

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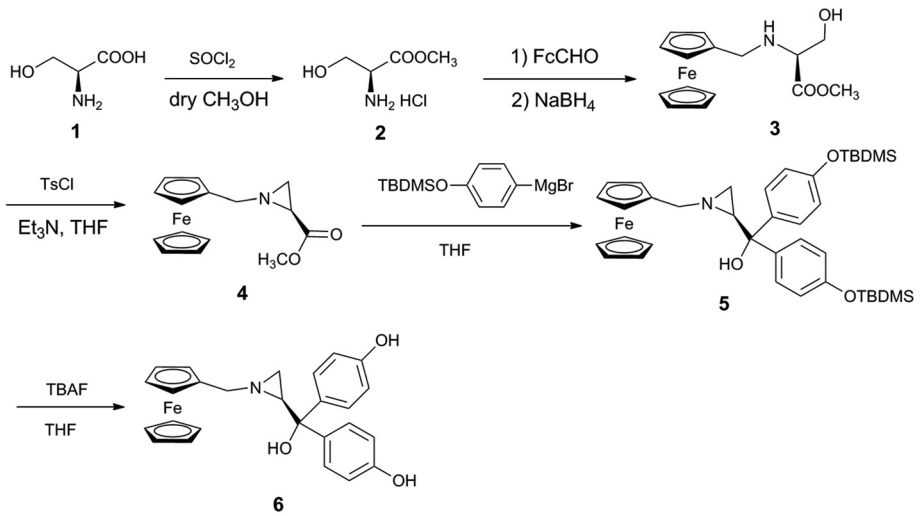
of chiral ferrocenylaziridino alcohols have been synthesized and successfully applied to highly enantioselective addition of organozinc reagents to aldehydes by us.[14] Herein, we would like to report the syntheses of novel recyclable chiral dendritic ligands by coupling the ferrocenylaziridino alcohols with Fréchet-type dendrimers and their preliminary application in asymmetric diethylzinc addition to aldehydes with excellent enantioselectivities (ee).

2. Results and discussion

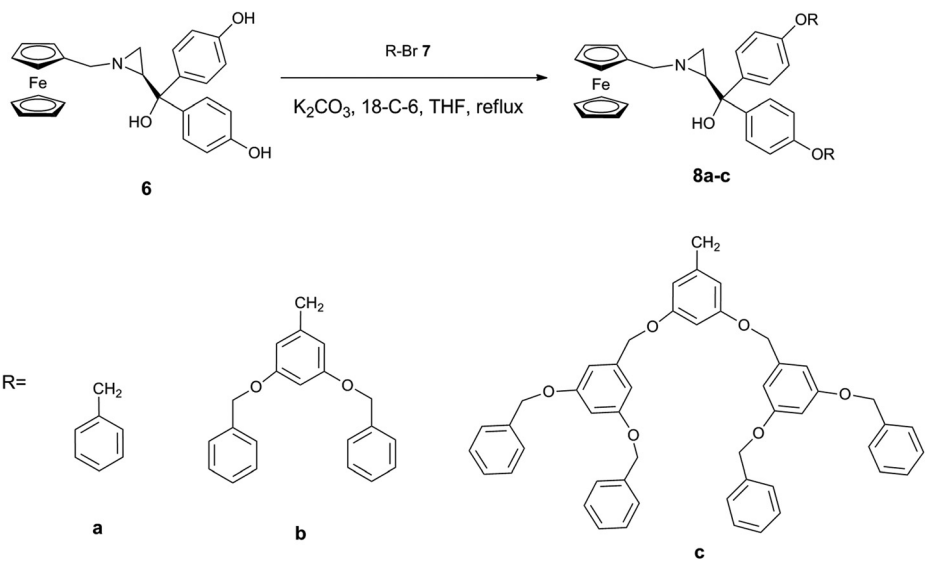
2.1 Synthesis of chiral dendritic ligands

Starting from compound **4** as reported by Wang and coworkers,[14a] compound **6** was synthesized *via* Grignard reaction and followed by the desilylation with TBAF (Scheme 1). With compound **6** in hand, we further synthesized the dendritic wedges **7** according to the procedure in the literature[10] and successfully introduced them into compound **6** (Scheme 2).

The syntheses of *N*-ferrocenyl methyl aziridino alcohol ligands with different dendrimers (**8a–c**) are summarized in Scheme 2. A mixture of compounds **6** and **7(a–c)** was heated at reflux under vigorous stirring for 2 h with 18-crown-6 as the phase-transfer catalyst and K_2CO_3 as the base. The effect of temperature and solvent on the yield of **8b** was studied first. As shown in Table 1, several solvents were chosen and used to optimize the reaction conditions. Almost the same yields were obtained when commercially available THF or anhydrous THF was used (entries 1 and 2). The reactions could finish within two hours in most solvents, except in acetone (entry 4) and

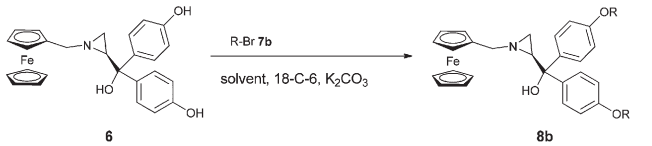


Scheme 1 Synthesis of ferrocenyl β-amino alcohol ligand **6**.



Scheme 2 Synthesis of **8a–c**.

Table 1 Yield of **8b** in different solvents[a,b,c]



Entry	Solvent	Reaction time (h)	Yield[d] (%)
1	THF	2	76
2	Dry THF	2	73
3	MeCN	2	78
4	Acetone	24	54
5	Dioxane	2	42
6	Dioxane	24	34
7	Toluene	2	53
8	DMF	2	53

[a] All solvents were used as received without further purification except in entry 2. [b] All reactions were carried out at reflux except in entry 6 (75 °C). [c] The volume of all the solvents was 15 mL. [d] Isolated yield.

Table 2 Yields of different chiral ligands in THF and MeCN

Entry	Solvent[a]	Product	Yield[b] (%)
1	THF	**8a**	64
2	MeCN	**8a**	60
3	THF	**8b**	76
4	MeCN	**8b**	78
5	THF	**8c**	67
6	MeCN	**8c**	59

[a] All solvents were used as received without further purification. [b] Isolated yield.

dioxane (entry 6 at 75 °C). Compared to the good yields from using THF and MeCN (entries 1–3), those solvents with a lower or higher boiling point could not achieve a satisfactory result (entries 4–8), indicating that temperature plays an important role in the reaction.

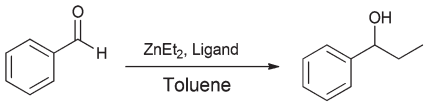
The yield of **8b** was slightly higher (78% *vs.* 76%, Table 1) but the yields of **8a** and **8c** were much lower (60% *vs.* 64% and 59% *vs.* 67% respectively, Table 2) when MeCN instead of THF was used as the solvent. As such, THF was chosen as the most suitable solvent for the reaction.

2.2 Asymmetric addition of Et_2Zn to aldehydes

In order to examine the catalytic behaviour of the chiral dendritic ligands, the reaction of diethylzinc with benzaldehyde was investigated next. The optimal ligand for this reaction was also chosen after optimizing the loading of the ligand and the reaction temperature (Table 3).

As listed in Table 3, although the yield of the product did not change much (Table 3, entries 1–6) when the loading of **8b** as the chiral ligand was increased from 1 mol% to 10 mol%, better enantioselectivity could be obtained with increasing amount of ligand, which was most remarkable when the

Table 3 Optimization of reaction conditions for asymmetric addition of Et_2Zn to benzaldehyde[a]

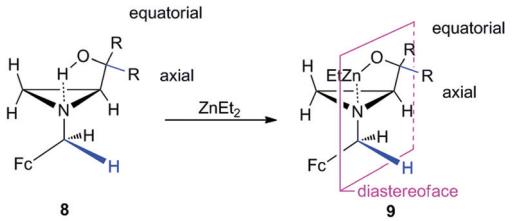


Entry	Ligand	Mol (%)	Temperature (°C)	Yield[b] (%)	ee[c] (%)	Confign.[d]
1	**8b**	1	0, 10 h then 20, 38 h	95	41	*S*
2	**8b**	2	0, 10 h then 20, 38 h	97	80	*S*
3	**8b**	3	0, 10 h then 20, 38 h	96	81	*S*
4	**8b**	5	0, 10 h then 20, 38 h	97	89	*S*
5	**8b**	7	0, 10 h then 20, 38 h	94	82	*S*
6	**8b**	10	0, 10 h then 20, 38 h	96	89	*S*
7	**8b**	5	−20, 48 h	79	88	*S*
8	**8b**	5	0, 48 h	56	81	*S*
9	**8b**	5	20, 48 h	93	92	*S*
10	**8b**	5	40, 48 h	90	81	*S*
11	**6**	5	20, 48 h	49	21	*S*
12	**8a**	5	20, 48 h	95	92	*S*
13	**8c**	5	20, 48 h	56	63	*S*

[a] Reaction was carried out using 0.5 mmol of benzaldehyde in 2 mL of toluene, PhCHO–Et_2Zn = 1 : 4, Et_2Zn (1 M solution in hexane). [b] Isolated yield. [c] Determined by HPLC analysis using DAICEL CHIRALCEL OD-H. [d] Absolute configuration was assigned by comparing the retention time on HPLC with the literature value.[15]

ligand concentration was increased from 1 mol% to 2 mol% (entries 1 and 2, Table 3). It is obvious that the product yield does not depend on the absolute amount of the ligand as long as there is some. Furthermore, we examined the temperature effect on the asymmetric induction in the presence of 5 mol% **8b** (Table 3, entries 7–10). As compared with 20 °C, too low or too high reaction temperature was not conducive to this reaction.

In order to study the effect of dendritic wedges on the catalytic activity and enantioselectivity, compound **6** was used as ligand in the reaction of diethylzinc with benzaldehyde. Under the optimized reaction conditions, it was exciting to find out that both the yield and ee value were much better by using **8a** and **8b** other than ligand **6** when it was linked with dendrimers (Table 3, entries 11–13) with 92% ee from the zero-generation (**8a**) and the first-generation ligand (**8b**) (Table 3, entries 12 and 9). However, further increasing the size of dendritic wedges (**8c**) dramatically decreases the yield and enantioselectivity (Table 3, entry 13). The remarkable dendritic effect was thought to be due to the interaction between the two bulky dendritic wedges. Upon binding of **8** to zinc, chiral catalyst **9** with a rigid framework is formed (Scheme 3). According to the mathematical expression for the enantioselectivity and thermodynamic factors in the conformational equilibrium of catalysts by the addition of diethylzinc to benzaldehyde that we have reported previously,[14f] the bigger steric differentiation of the diastereoface of the five-membered zinc cycle would bring better enantioselectivity. In the case of the zero-generation ligand (**8a**) and the first-generation ligand (**8b**) the steric differentiation caused by equatorial and axial R groups is rela-

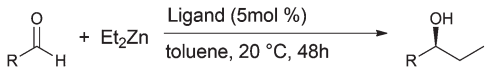


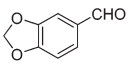
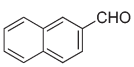
Scheme 3 The structure of chiral catalyst **9**.

tively larger, so excellent enantioselectivities are obtained. In the case of **8c**, the repulsion effect of the bulky equatorial and axial R groups makes the flexible equatorial R group point toward the left side and increases the bulkiness of the left side. Thus, the enantioselectivity decreases with the decreased steric differentiation of the diastereoface.

Ligands **8a** and **8b** were selected for further evaluation on other substrates. As summarized in Table 4, the dendritic ligands were effective to all the aromatic aldehydes tested. In these reactions, all of the aldehyde substrates gave products in excellent yields with good to excellent ee values (88–98% ee). However, *o*-substituted benzaldehydes underwent addition reaction with slightly lower enantioselectivities when compared to their *m*- and *p*-analogues (entries 7, 8 *vs.* 9, 10 or 11, 12).

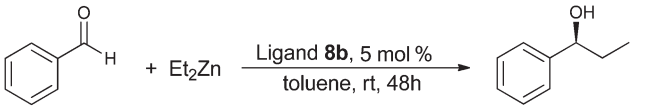
Table 4 Enantioselective diethylzinc addition to aldehydes in the presence of different chiral ligands **8a** and **8b**[a]



Entry	RCHO	Ligand	Yield[b] (%)	ee[c] (%)	Confign.[d]
1	PhCHO	**8a**	95	92	*S*
2		**8b**	93	92	*S*
3	FcCHO	**8a**	98	93	*S*
4		**8b**	>99	94	*S*
5		**8a**	>99	90	*S*
6		**8b**	>99	91	*S*
7	2-CH_3OPhCHO	**8a**	>99	86	*S*
8		**8b**	>99	88	*S*
9	3-CH_3OPhCHO	**8a**	>99	93	*S*
10		**8b**	>99	92	*S*
11	4-CH_3OPhCHO	**8a**	>99	92	*S*
12		**8b**	>99	93	*S*
13	4-CH_3PhCHO	**8a**	98	94[e]	*S*
14		**8b**	>99	98[e]	*S*
15		**8a**	>99	91	*S*
16		**8b**	>99	90	*S*
17		**8a**	>99	95	*S*
18		**8b**	>99	90	*S*
19	2-ClPhCHO	**8a**	97	92[e]	*S*
20		**8b**	97	93[e]	*S*
21	4-ClPhCHO	**8a**	>99	98[e]	*S*
22		**8b**	>99	92[e]	*S*

[a] Unless otherwise stated, reaction was carried out at 20 °C using 0.5 mmol of aldehyde in 2 mL of toluene; RCHO–Et_2Zn = 1 : 4; Et_2Zn (1 M solution in hexane); reaction time: 48 h. [b] Isolated yield. [c] Determined by HPLC analysis using DAICEL CHIRALCEL OD-H. [d] Absolute configuration was assigned by comparing the retention time on HPLC with the literature value.[16] [e] Determined by HPLC analysis using DAICEL CHIRALCEL OB-H.

Table 5 Reusability of supported ligands for the asymmetric addition of diethylzinc to benzaldehyde[a]



Run	Ligand	Yield[b]	ee[c]	Confign.
1	**8b**	94	92	*S*
2	**8b**	87	93	*S*
3	**8b**	89	92	*S*
4	**8b**	90	91	*S*
5	**8b**	89	91	*S*
6	**8b**	88	90	*S*
7	**8b**	91	90	*S*
8	**8b**	93	87	*S*
9	**8b**	91	88	*S*

[a] Reaction was carried out at 20 °C using 0.5 mmol of aldehyde in 2 mL of toluene; PhCHO–Et_2Zn = 1 : 4; Et_2Zn (1 M solution in hexane); reaction time: 48 h. [b] Isolated yield. [c] Determined by HPLC analysis using DAICEL CHIRALCEL OD-H.

2.3 Recycling of a dendritic catalyst

One major advantage of dendritic ligands is that they may be easily separated from reaction mixtures through precipitation due to the solubility change in different solvents. Having established the efficacy of the dendritic ligands, we then investigated their recyclability (Table 5). After the completion of the reaction, ligand **8b** could be easily recovered by precipitation with *n*-hexane (see the Experimental section). Furthermore, it was found that the recovered catalyst could be reused up to nine runs, without any significant loss of reactivity and enantioselectivity (Table 5, entries 1–9) (Fig. 1).

3. Conclusion

In conclusion, we report here the preparation of three novel *N*-ferrocenylmethyl aziridino alcohol ligands bearing dendrimers. Good yields (more than 99%) and excellent enantioselectivities (up to 98% ee) were achieved by the asymmetric addition of diethylzinc to aldehydes. For all aromatic aldehydes tested, it was found that almost the same level of enantioselectivity could be obtained for ligands **8a** and **8b**. Furthermore, ligand **8b** could be quantitatively recovered by simply adding *n*-hexane to the reaction mixture after being reused 8 times, without significant loss of reactivity and enantioselectivity.

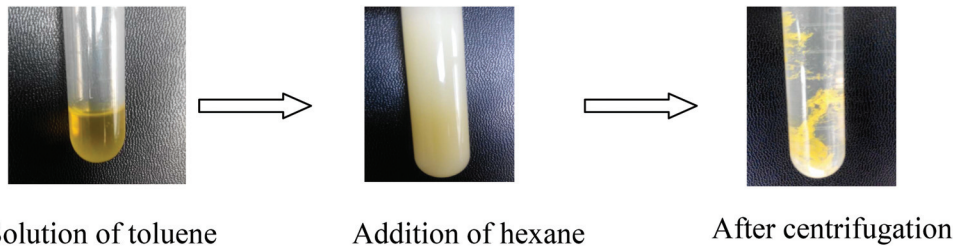


Fig. 1 The recycling of ligand **8b**.

4. Experimental

4.1. General

Oxygen- and moisture-sensitive reactions were carried out under a nitrogen atmosphere. Solvents were purified and dried by standard methods prior to use unless otherwise stated. All commercially available reagents were used without further purification unless otherwise noted. Column chromatography was performed on silica gel (100–200 mesh). Melting points were measured on a BEIJING TECH X-5 melting point apparatus and were uncorrected. Infrared spectra were recorded on a Nicolet-NEXUS 670 FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-400 (400 MHz) spectrometer in $CDCl_3$ with TMS as an internal standard; J values were given in hertz. Mass spectra were recorded using a Bruker esquire-3000 instrument with an electrospray ionization source (ESI-MS). All of the ESI-MS spectra were recorded using MeOH as the solvent. Optical rotations were measured on a Perkin-Elmer model 341 Polarimeter at 20 °C in $CHCl_3$. The ee value was determined by HPLC using a chiral column with hexane-propan-2-ol (ratio as indicated) as the eluent. The chromatographic system was VARIAN PROSTAR, consisting of a UV-VIS detector (model 320) and two pumps (model 320). The column used was a Chiralcel OD-H (250 × 4.6 mm) or Chiralcel OB-H (250 × 4.6 mm) from Daicel Chemical Ind., Ltd (Japan) and operated at ambient temperature.

4.2. General procedure for the synthesis of compound 4

The compound **4** was prepared according to the literature procedures.[14a]

4.3. General procedure for the synthesis of compound 5

A Grignard reagent was prepared from 133 mg (5.5 mmol) magnesium and 1.55 g (4-bromophenoxy)(*tert*-butyl)dimethylsilane (5.4 mmol) in dry THF (15 mL). After adding a small crystal of iodine to initiate the reaction, the reaction mixture was heated to reflux for 2 h. The solution was cooled to 0 °C before adding 0.25 g (0.84 mmol) of compound **4**. The reaction was quenched with saturated aqueous NH_4Cl at 0 °C after completion at room temperature. The phases were separated and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with brine (15 mL), dried over Na_2SO_4 and after filtration, the solvent was removed under reduced pressure. The resulting residue was purified by preparative TLC with petroleum (60–90 °C)–EtOAc (v/v, 6 : 1) as an eluant to give a yellow solid: mp 85–87 °C, yield 70%. $[\alpha]_D^{20}$ = −28 (c 0.5, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.13 (m, 4H, Ar–*H*), 6.78–6.70 (m, 4H, Ar–*H*), 4.12–4.03 (m, 9H, Fc*H*), 3.71 (s, 1H, –O*H*), 3.51 (d, J = 13.0 Hz, 1H, Fc*CH′H*N), 3.22 (d, J = 13.0 Hz, 1H, Fc*CH′H*N), 2.31 (dd, J = 6.3, 3.5 Hz, 1H, –N–*CH*), 1.90 (d, J = 3.5 Hz, 1H, –N–*CH′H*), 1.48 (d, J = 6.3 Hz, 1H, –N–*CH′H*), 0.99 (s, 9H, –C(*CH*$_3$)$_3$), 0.96 (s, 9H, –C(*CH*$_3$)$_3$), 0.20 (d, J = 0.7 Hz, 6H, –C*H*$_3$), 0.18 (d, J = 3.3 Hz, 6H, –C*H*$_3$).^{13}C NMR (100 MHz, $CDCl_3$) δ 154.39, 140.73, 137.89, 127.55, 119.33, 83.88, 73.56, 68.91, 68.47, 68.08, 58.14, 45.77, 30.15, 25.66. IR (KBr) 3429, 3084, 2939, 2858, 1607, 1507, 1465, 1404, 1357, 1258, 1171, 1091, 1006, 916, 833, 558, 479. HRMS (ESI): calcd for $C_{38}H_{53}FeNO_3Si_2$ $[M]^+$ 683.2913, found 683.2944 $[M + H]^+$ 684.2947, found 684.2990.

4.4. General procedure for the synthesis of compound 6

0.31 g (0.45 mmol) of compound **5** (in 10 mL dry THF) was dropped into a solution of 1 mL TBAF (1 M in THF) in dry THF (5 mL) at room temperature in half an hour. The resulting solution was stirred at room temperature for half an hour and the solution was quenched with pure water. The phases were separated and the aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with brine (20 mL), dried over Na_2SO_4 and after filtration, the solvent was removed under reduced pressure. The resulting residue was purified by preparative TLC with CH_2Cl_2–CH_3OH (v/v, 20 : 1) as the eluant to give a yellow solid: mp 117–118.3 °C, yield 93%. $[\alpha]_D^{20}$ = −54 (c 0.724, in CH_3OH). ^{1}H NMR (400 MHz, DMSO) δ 7.12 (dd, J = 25.7, 8.6 Hz, 4H, Ar–*H*), 6.62 (dd, J = 8.6, 1.9 Hz, 4H, Ar–*H*), 5.76 (s, 2H, Ar–O*H*), 4.38 (s, 1H, –O*H*), 4.20–4.00 (m, 9H, Fc*H*), 3.56 (d, J = 13.0 Hz, 1H, Fc*CH′H*N), 3.00 (d, J = 13.0 Hz, 1H, Fc*CH′H*N), 2.36 (dd, J = 6.1, 3.3 Hz, 1H, –N–*CH*), 1.52 (d, J = 3.0 Hz, 1H, –N–*CH′H*), 1.33 (d, J = 6.2 Hz, 1H, –N–*CH′H*). ^{13}C NMR (100 MHz, DMSO) δ 155.88, 138.26, 137.56, 127.93, 127.48, 114.36, 84.92, 74.17, 69.05, 68.51, 67.69, 58.51, 55.13, 46.38, 29.45. IR (KBr) 3460, 2927, 1601, 1509, 1446, 1369, 1236, 1169, 1031, 829, 587, 488. HRMS (ESI): calcd for $C_{26}H_{25}FeNO_3$ $[M + H]^+$ 456.1217, found 456.1258 $[M + Na]^+$ 478.1082, found 478.1126.

4.5. General procedure for the synthesis of chiral ligands bearing dendrimers

4.5.1. Compound 8a. A mixture 0.1 g (0.22 mmol) of compound **6**, the corresponding benzyl bromide (53 μL), 0.12 g (0.87 mmol) K_2CO_3 and 0.001 g (0.004 mmol) 18-C-6 in THF was heated at reflux and stirred vigorously for one hour. After most of the organic solvent was removed under reduced pressure, CH_2Cl_2 (20 mL) and water (20 mL) were added to the mixture. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were washed with brine (20 mL), dried over Na_2SO_4 and after filtration, the solvent was removed under reduced pressure. The resulting residue was purified by preparative TLC with petroleum (60–90 °C)–EtOAc (v/v, 4 : 1) as the eluant to give a yellow foam: mp 39–41 °C, yield 64%. $[\alpha]_D^{20}$ = −14 (*c* 1.05, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.30 (m, 10H, Ar–*H*), 7.30–7.22 (m, 4H, Ar–*H*), 6.89 (td, *J* = 9.4, 2.5 Hz, 4H, Ar–*H*), 5.04 (d, *J* = 8.2 Hz, 4H, Ar–O–C*H*$_2$), 4.17–3.96 (m, 9H, Fc*H*), 3.71 (d, *J* = 3.6 Hz, 1H, –O*H*), 3.49 (d, *J* = 12.9 Hz, 1H, FcC*H*′*H*N), 3.25 (dd, *J* = 12.9, 1.9 Hz, 1H, FcC*H*′*H*N), 2.34 (dd, *J* = 5.9, 3.1 Hz, 1H, –N–*CH*), 1.90 (d, *J* = 2.8 Hz, 1H, –N–*CH*′*H*), 1.48 (d, *J* = 6.3 Hz, 1H, –N–*CH*′*H*). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.71, 157.56, 140.43, 137.69, 137.08, 137.03, 128.56, 128.54, 127.93, 127.59, 127.47, 114.21, 114.17, 83.82, 73.48, 69.93, 69.00, 68.83, 68.46, 68.15, 68.08, 58.20, 45.63, 30.10. IR (KBr) 3429, 3035, 2921, 1607, 1505, 1456, 1381, 1317, 1236, 1170, 1105, 1024, 820, 737, 694, 635, 486. HRMS (ESI): calcd for $C_{40}H_{37}FeNO_3$ $[M]^+$ 635.2123, found 635.2088 $[M + H]^+$ 636.2156, found 636.2204.

4.5.2. Compound 8b. A mixture 0.1 g (0.22 mmol) compound **4**, the corresponding 0.17 g (0.44 mmol) of compound **7b**, 0.3 g (2.17 mmol) K_2CO_3 and 0.003 g (0.011 mmol) 18-C-6 in THF was heated at reflux and stirred vigorously for two hours. The following procedure is the same as that of compound **8a**. The resulting residue was purified by preparative TLC with petroleum (60–90 °C)–CH_2Cl_2–EtOAc (v/v/v, 6 : 4 : 1) as the eluant to give a yellow foam: mp 43–45 °C; yield 76%. $[\alpha]_D^{20}$ = −15 (*c* 0.412, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.20 (m, 24H, Ar–*H*), 6.87 (dd, *J* = 10.6, 8.9 Hz, 4H, Ar–*H*), 6.69 (dd, *J* = 10.4, 2.2 Hz, 4H, Ar–*H*), 6.58 (dt, *J* = 7.7, 2.2 Hz, 2H, Ar–*H*), 5.01 (dd, *J* = 24.6, 7.3 Hz, 12H, Ar–O–C*H*$_2$), 4.16–3.97 (m, 9H, Fc*H*), 3.71 (s, 1H, –O*H*), 3.49, 3.27 (d, *J* = 12.9 Hz, 2H, FcC*HH*′N), 2.34 (dd, *J* = 6.2, 3.4 Hz, 1H, –N–*CH*), 1.91 (d, *J* = 3.3 Hz, 1H, –N–*CH*′*H*), 1.49 (d, *J* = 6.3 Hz, 1H, –N–*CH*′*H*). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.14, 157.56, 139.57, 137.77, 136.75, 128.60, 128.03, 127.58, 114.26, 106.34, 101.45, 83.86, 73.47, 70.12, 69.89, 68.93, 68.48, 68.13, 58.24, 45.62, 30.15, 29.70. IR (KBr) 3420, 3033, 2921, 2860, 1598, 1504, 1452, 1376, 1299, 1234, 1154, 1019, 824, 738, 691, 581, 485. HRMS (ESI): calcd for $C_{68}H_{61}FeNO_7$ $[M]^+$ 1059.3797, found 1059.3811; $[M + H]^+$ 1060.3831, found 1060.3877; $[M + K]^+$ 1098.3434, found 1098.3487.

4.5.3. Compound 8c. A mixture 0.1 g (0.22 mmol) of compound **6**, the corresponding 0.355 g (0.44 mmol) of compound **7c**, 0.414 g (3 mmol) K_2CO_3 and 0.024 g (0.09 mmol) 18-C-6 in THF was heated at reflux and stirred vigorously for four hours. The following procedure is the same as that of compound **8a**. The resulting residue was purified by preparative TLC with petroleum (60–90 °C)–CH_2Cl_2–EtOAc (v/v/v, 6 : 4 : 1) as the eluant to give a yellow foam: mp 49–51 °C; yield 67%. $[\alpha]_D^{20}$ = −5.9 (*c* 0.994, in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.27 (m, 40H, Ar–*H*), 7.22 (t, *J* = 4.4 Hz, 4H, Ar–*H*), 6.86 (t, *J* = 9.2 Hz, 4H, Ar–*H*), 6.72–6.58 (m, 12H, Ar–*H*), 6.58–6.46 (m, 6H, Ar–*H*), 5.05–4.85 (m, 28H, Ar–O–C*H*$_2$), 4.17–3.94 (m, 9H, Fc*H*), 3.68 (s, 1H, –O*H*), 3.46 (d, *J* = 13.0 Hz, 1H, FcC*HH*′N), 3.23 (d, *J* = 12.9 Hz, 1H, FcC*HH*′N), 2.30 (dd, *J* = 6.0, 3.4 Hz, 1H, –N–*CH*), 1.88 (d, *J* = 3.1 Hz, 1H, –N–*CH*′*H*), 1.45 (d, *J* = 6.3 Hz, 1H, –N–*CH*′*H*). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.17, 160.08, 160.05, 157.68, 157.53, 140.54, 139.61, 139.56, 139.23, 137.83, 136.78, 128.57, 127.99, 127.63, 127.54, 114.28, 106.43, 106.41, 101.62, 101.54, 101.48, 83.89, 73.49, 70.11, 70.00, 69.92, 69.01, 68.83, 68.48, 68.16, 68.07, 58.22, 45.65, 30.17. IR (KBr) 3433, 3021, 2869, 1598, 1504, 1452, 1375, 1301, 1235, 1154, 1047, 830, 740, 693, 489. HRMS (ESI): calcd for $C_{124}H_{109}FeNO_{15}$; $[M]^+$ 1907.7147, found 1907.6949; $[M + H]^+$ 1908.7180, found 1908.7228.

4.6 General procedure for the asymmetric diethylzinc addition to aldehydes

A mixture of 0.025 mmol chiral ligand and 2.0 mmol Et_2Zn (1 M, in hexane) was stirred in 2.0 mL toluene at 0 °C for half an hour. Then 0.5 mmol freshly distilled aldehyde was added dropwise *via* a syringe. After that, the vessel was taken out of the cooling bath. After stirring for 2 days, the reaction was quenched with 4 mL of saturated NH_4Cl aqueous solution and was extracted with 10 mL of diethyl ether three times. The combined organic phase was washed with brine, and was dried with anhydrous Na_2SO_4. The solvent was evaporated and the crude residue was transferred into a centrifugal tube containing 0.5 mL toluene. To the centrifugal tube 10 mL *n*-hexane was added. The precipitation (ligand) was separated, collected by centrifugation and dried for the next run. The mother liquid was concentrated and purified by thin layer chromatography to afford the final products (petroleum ether–EtOAc).

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