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Synthesis of chiral ferrocenyl aziridino alcohols and use in the catalytic asymmetric addition of diethylzinc to aldehydes

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Abstract—A series of novel chiral ferrocenyl aziridino alcohols **5a–i** were conveniently synthesized from L-serine and ferrocenecarboxaldehyde. These compounds have been used as chiral catalysts in the asymmetric addition of diethylzinc to aldehydes and the effects of the ligand structures on the enantioselectivity was studied. Enantioselectivities up to 98.8% have been obtained.

1. Introduction

Asymmetric addition of dialkylzincs to aldehydes catalyzed by various chiral ligands is a convenient method for the preparation of optically active secondary alcohols.[1] Extensive studies of the addition of diethylzinc to aldehydes have revealed that the β-amino alcohols are suitable chiral catalyst for such transformation because of their easy availability, simple preparation conditions and high asymmetric induction efficiency.[2] In this context, diverse chiral ferrocenylamino alcohols possessing either only central chirality in the side chain,[3] or only planar chirality on the substituted ferrocene moiety[4] or a combination of both,[5] have also proven to be highly enantioselective addition catalysts, while ferrocenyl amino alcohols possessing only one single stereogenic centre were found to provide modest degrees of induction.[3a,6] Moreover, Watanabe et al. reported that the presence of a ferrocenyl moiety on the nitrogen atom of ephedrine and norephedrine-based ligands plays an important role in the enantiodifferentiation occurring during this alkylation reaction.[7] On the basis of the above-mentioned data, we sought to design new enantiomerically pure ligands possessing both the ferrocenyl skeleton and the aziridine unit expecting a synergy of the characteristics of both moieties. In a previous article, we reported an improved procedure for the synthesis of enantiopure (2*S*)-1-ferrocenylmethylaziridin-2-yl(diphenyl)methanol **5j**, its crystal structure and its use in the enantioselective addition of diethylzinc to benzaldehyde.[8] Moreover, it was demonstrated that the replacement of the phenyl group on the nitrogen atom of aziridine-based skeleton by a ferrocenyl unit led to a dramatic improvement in the enantioselectivity when used as the catalyst in the addition of diethylzinc to benzaldehyde. Herein, we report the synthesis of a series of ferrocenyl aziridino alcohols and their structural-efficiency relationships for the asymmetric addition of diethylzinc to aldehydes.

2. Results and discussion

2.1. Synthesis of ligands

The starting materials for the synthesis of the aziridino alcohols were the readily available amino acids L-serine. The preparation of aziridino alcohols **5a–j** is shown in Scheme 1. The reaction of L-serine **1** with excess MeOH in the presence of $SOCl_2$ at −15 °C gave methyl L-serine ester hydrochloride **2**.[9] Ferrocenecarboxaldehyde was first condensed with **2** in MeOH in the presence of Et_3N, then reduced by $NaBH_4$, to afford the methyl *N*-ferrocenylmethyl-L-serine ester **3**.[10] Cyclization of **3** was performed in THF using triethylamine (2.1 equiv) and *p*-toluenesulfonyl chloride (1.1 equiv) at reflux temperature for 48 h to yield *N*-ferrocenylmethylaziridine-2-carboxylic esters **4**.[8] Compound **4** was reduced with $LiAlH_4$ to give the aziridino alcohol **5a** in 85% yield. Treatment of **4** with excess of CH_3MgI, C_2H_5MgBr, *n*-C_3H_7MgBr, *i*-C_3H_7MgBr, *n*-C_4H_9MgBr, *i*-C_4H_9MgBr, *n*-$C_5H_{11}MgBr$ *i*-$C_5H_{11}MgBr$ or PhMgBr afforded the ligands **5b** (88%), **5c** (80%), **5d** (69%), **5e** (72%), **5f** (71%), **5g** (61%), **5h** (80%), **5i** (70%) and **5j** (95%), respectively.

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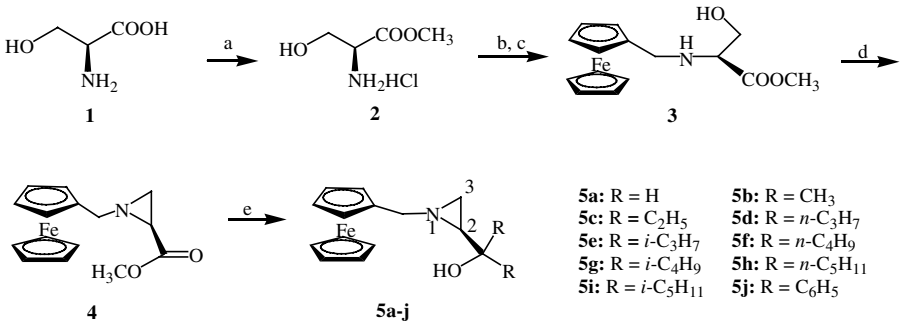
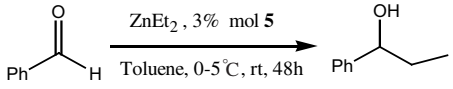


Scheme 1. Synthesis of the aziridino alcohols containing ferrocenyl groups. Reagents and conditions: (a) dry MeOH, $SOCl_2$, −15 °C to rt, 11 h; L-serine, reflux; (b) Et_3N, FcCHO, MeOH, −10 °C to 0 °C; (c) $NaBH_4$; (d) TsCl, Et_3N, THF, reflux; (e) $LiAlH_4$, THF, 0 °C to rt (for compound **5a**); CH_3MgI, Et_2O, 0 °C to reflux (for compound **5b**); RMgX, THF, −20 °C to rt (for compounds **5c**–**j**).

2.2. Asymmetric addition of Et_2Zn to aldehydes

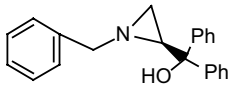
In order to examine the catalytic behaviour of the ligands, the reaction of diethylzinc with benzaldehyde has been first investigated. The reaction of diethylzinc with benzaldehyde was carried out in toluene in 0–20 °C in the presence of 3% ligands **5a**–**j** (Scheme 2). The results are summarized in Table 1 (entries 1–10).



Scheme 2. Addition of diethylzinc to benzaldehyde.

As can be seen from Table 1, the addition of diethylzinc to benzaldehyde led to 1-phenylpropanol in 71–98%

Table 1. Asymmetric addition of diethylzinc to aldehydes using ligand **5**[a]



6 ee = 49%

Entry	ArCHO	Ligands	Mol% (**5**)	Yield[b] (%)	Ee[c] (%)	Config[d]
1	C_6H_5CHO	**5a**	3	77	1.3	*S*
2	C_6H_5CHO	**5b**	3	85	40.4	*S*
3	C_6H_5CHO	**5c**	3	84	50.2	*S*
4	C_6H_5CHO	**5d**	3	59	18.7	*S*
5	C_6H_5CHO	**5e**	3	86	25.2	*S*
6	C_6H_5CHO	**5f**	3	71	13.3	*S*
7	C_6H_5CHO	**5g**	3	90	84.0	*S*
8	C_6H_5CHO	**5h**	3	87	58.1	*S*
9	C_6H_5CHO	**5i**	3	87	62.9	*S*
10	C_6H_5CHO	**5j**	3	97	92.7	*S*
11[e]	C_6H_5CHO	**5j**	5	99	83.5	*S*
12	C_6H_5CHO	**5j**	7	98	90.1	*S*
13	C_6H_5CHO	**5j**	5	98	90.4	*S*
14	C_6H_5CHO	**5j**	1	81	84.1	*S*
15	C_6H_5CHO	**5j**	3[f]	97	92.7	*S*
16	*p*-$MeOC_6H_4CHO$	**5j**	3	99	92.8	*S*
17	*o*-$MeOC_6H_4CHO$	**5j**	3	96	93.5	*S*
18	*m*-ClC_6H_4CHO	**5j**	3	89	98.8	*S*
19	*m*-BrC_6H_4CHO	**5j**	3	91	96.4	*S*
20	Heliotripine	**5j**	3	99	93.7	*S*
21	Ferronenyl aldehyde	**5j**	3	100	92.1	*S*
22	$C_6H_5CH{=}CHCHO$	**5j**	3	88	80.2	*S*
23	$C_6H_5CH_2CH_2CHO$	**5j**	3	33	78.7	*S*

[a] The mol ratio Et_2Zn/aldehyde was 2/1.
[b] Isolated yields.
[c] Determined by HPLC using a chiral OD column.
[d] Absolute configuration assigned by comparison with the sign of specific rotation of known compound and known elution order from a Chiralcel OD column.[14,15]
[e] The reaction proceeded at rt.
[f] The recovered ligand was used.

yields with 1.3–92.7% ee. It was shown that the enantioselectivity of the reaction was very sensitive to the structure of the chiral catalyst. For example, when the ligands **5a**, **5d**, **5e** and **5f** were employed, (*S*)-1-phenylpropanol was obtained in low ee values (1.3–25.2% ee, Table 1, entries 1, 4, 5, 6), while **5b**, **5c**, **5g**, **5h** and **5i** not only showed high catalytic activity, but also gave the product with moderate to high ee values (40.4–84.0% ee, Table 1, entries 2, 3, 7, 8, 9). Chiral ligands **5j** shows the best asymmetric induction (92.7% ee, Table 1, entry 10). Indeed, the diphenylhydroxymethyl group as a structural unit, although it is not a stereogenic unit, plays a crucial role in various stereoselective reaction or at least lead to an enhancement of enantioselectivity.[11] The 'diarylhydroxymethyl group' is called the 'magic group' in catalyst design and synthesis.[12] This result was remarkable compared to the findings in a recent report where a modest ee of only 49% was obtained for the same reaction, employing *N*-benzylaziridin-2-yldiphenylmethanol **6**.[13]

The effect of the *n*-alkyl chain length on enantioselectivity was observed in the chiral ligands **5b–d**, **5f** and **5h** possessing a di-*n*-alkylhydroxymethyl group. As shown in Figure 1, the ee of (*S*)-1-phenylpropanol varied with the length of the *n*-alkyl chain to form a 'zigzag' curve. A maximum value of 58.1% ee was obtained with the *n*-pentyl group. A similar phenomenon was noted in the chiral oxazolidine-catalyzed addition of Et_2Zn to benzaldehyde.[16] One can assume that this effect originates from the van der Waals interaction and reflects the conformational preference of the *n*-alkyl chain. Meanwhile, we also noted that the chiral ligands possessing a di-*i*-alkylhydroxymethyl group were more enantioselective than their corresponding di-*n*-alkylhydroxymethyl analogues (Table 1, entries 5, 7, 9 vs 4, 6, 8). The results indicated that the bulky substituents could shield the one face of the chelate, which may prohibit the approach of the substrate aldehyde from this face and is responsible for the higher enantio-selectivity.

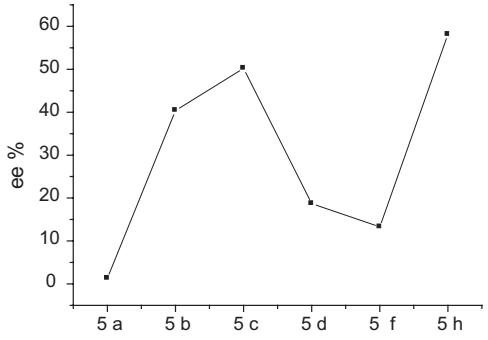


Figure 1.

Furthermore, we examined the effects of the catalytic amount and temperature on the asymmetric induction in the presence of **5j** (Table 1, entries 10–14). We first investigated the effect of reaction temperature on enantioselectivity. Lowering the reaction temperature from room temperature (20–25 °C) to 0 °C led to an enhancement in the addition selectivity from 83.5% to 90.4% (Table 1, entries 11 and 13). We attempted to continue to decrease the reaction temperature for higher enantioselectivity, but there was almost no reaction at −20 °C When increasing the amount of chiral ligand **5j** from 3 to 5 or 7 mol%, even if the overall yield was not significantly affected (Table 1, entries 10, 13 and 12), a slight decrease in product ee was observed. The drop in ee values could be ascribed to lack of ability in forming a soluble complex of **5j** and zinc, because a suspension or a turbid solution was observed as the ligand **5j** loading was increased. However, decreasing the amount of 3–1 mol% was detrimental to the enantioselectivity and the catalytic activity (Table 1, entry 14). We reasoned that the lowering in concentration of **5j** decreased the effective catalyst availability leading to the detrimental effect mentioned above.

The chiral ligand **5j** was recovered in excellent yield (96%) from the reaction mixture by preparative TLC and re-used without any loss of enantiomeric purity of the product (Table 1, entry 15).

Chiral ligand **5j** was then checked for the asymmetric addition of diethylzinc to a series of aromatic aldehydes (Table 1, entries 16–21). The results revealed that **5j** was effective to various aromatic aldehydes, including *ortho*-, *para*- and *meta*-substituted benzaldehydes (Table 1, entries 16–19), Heliotripine (entry 20) and ferrocenecarboxaldehyde (entry 21). The best asymmetric induction as high as 98.8% ee was found by using *m*-chlorobenzaldehyde as substrate (entry 18).

The ligand **5j** was also tested with α,β-unsaturated aliphatic aldehydes and 3-phenylpropionaldehyde. It was found that this catalyst is also very effective in the enantioselective addition of diethylzinc to these aliphatic aldehydes (Table 1, entries 22 and 23).

In all the examples studied the *S* absolute configuration for the 1-arylpropanol was noted. Based on our results, a plausible mechanism for the enantioselective addition of diethylzinc to arylaldehydes catalyzed by ligand **5j** is proposed (Fig. 2). The diethylzinc coordinates firstly with the ligand **5j** to form a five-membered ring amino alcohol–zinc complex with a chair conformation **7** and then converts to the zinc monoalkoxide–diethylzinc complex **8**. The ethylation reaction can be interpreted in terms of a six-membered cyclic transition state with a chair conformation. Nucleophilic attack of the ethyl group both from the *Si*-face and *Re*-face leads to transition state **9** and **10**, respectively. The transition state **9** should be more stable than **10** because the bulky aryl group is disposed equatorially in **9**. Consequently, the transition state **9** is the favoured structure and leads to (*S*)-1-arylpropanol. On the other hand, the transition state **10** being unstable is the unfavoured structure, which leads to (*R*)-1-arylpropanol.

3. Conclusion

In conclusion, a series of chiral ferrocenyl aziridino alcohols were conveniently synthesized from L-serine and ferrocenecarboxaldehyde. The enantioselective

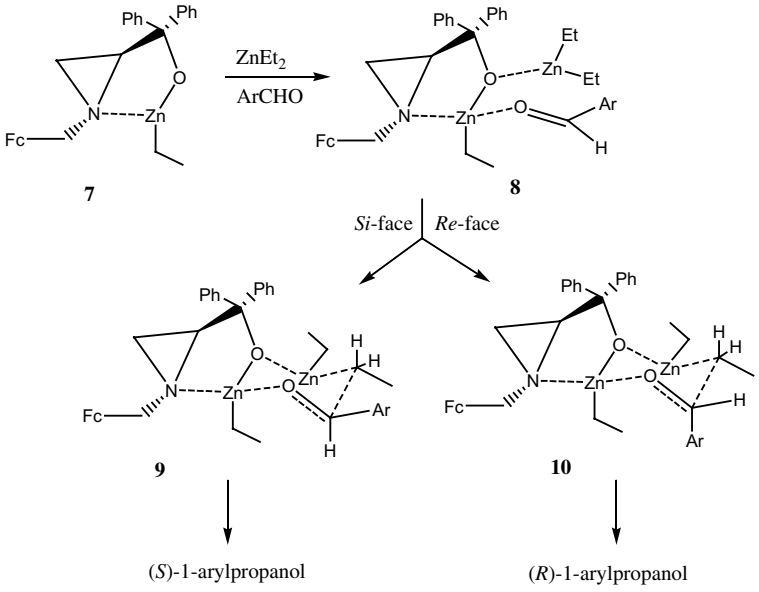


Figure 2. Transition structures derived from amino alcohol.

ethylation of aldehydes with diethylzinc was investigated in the presence of a catalytic amount of the new chiral ligands and the effects of the ligand structures on the enantioselectivity was then examined. We have demonstrated that ferrocenyl amino alcohol **5j** represents an efficient promoter in this catalytic reaction. Further application of chiral compounds **5** for asymmetric synthesis is under investigation in our laboratory.

4. Experimental

4.1. General

Melting points were determined using YRT-3 melting point apparatus, and were uncorrected. Optical rotations were measured with Perkin Elmer, model 341 Polarimeter at 20 °C in $CHCl_3$. The ee was determined by HPLC using a chiral column with hexane-propan-2-ol (ratio as indicated) as the eluent. The chromatographic system consisted of a JASCO model PU-1580 intelligent HPLC pump and a JASCO model UV-1575 intelligent UV/vis detector (254 nm). The injection loop had a 20 L capacity. The column used was a Chiralcel OD (250 × 4.6 mm) from Daicel Chemical Ind., Ltd (Japan). The column was operated at ambient temperature. NMR Spectra (^1H and ^{13}C) were performed on a Bruker DPX 400 (400 MHz) spectrometer using solutions in $CDCl_3$ (referenced internally to Me_4Si); *J* values are given in hertz. IR Spectra were determined on a Therme Nicolet IR 200 spectrophotometer. TLC was performed on dry silica gel plates developed with hexane/ethyl acetate. Mass spectra were obtained using a Bruker esquire-3000 instrument with an electrospray ionization source (ESIMS). All the ESIMS spectra were performed using MeOH as the solvent.

4.2. Reagents and solvents

Tetrahydrofuran (THF) was pre-dried over calcium chloride, then distilled from $LiAlH_4{\cdot}Et_3N$ was dried with KOH pellets, then refluxed for 2 h with *p*-toluenesulfonyl chloride and distilled. *p*-Toluenesulfonyl chloride was purified by dissolving (10 g) in the minimum volume of $CHCl_3$ (ca. 25 mL) filtered, and diluted with five volumes (i.e., 125 mL) of petroleum ether (bp 30–60 °C) to precipitate impurities. The solution was filtered, clarified with charcoal, concentrated to 15 mL by evaporation and gave 7 g of white crystals. All other reagents are commercially available and were used as received.

4.3. Synthesis of (*S*)-methyl *N*-ferrocenylmethyl-L-serine ester 3

Methyl L-serine ester hydrochloride **2** was synthesized following a literature procedure.[13] Compound **2** (9.6 g, 62.4 mmol) was dissolved in 80 mL of anhydrous methanol and cooled to 0 °C. Triethylamine (10 mL, 79 mmol) was added, and the reaction was stirred for 10 min ferrocenecarboxaldehyde (13.3 g, 62.2 mmol) was added, and the reaction mixture was stirred for 2 h, at which time sodium borohydride (4.8 g, 130 mmol) was added portionwise to the reaction mixture over a period of 0.5 h. The solution was carefully neutralized with 5% HCl to pH = 7–8, and extracted three times with 40 mL portion of diethyl ether. The combined ether extract was washed with brine, dried over Na_2SO_4 and evaporated under the reduced pressure. the resulting residue was purified by the preparative TLC with petroleum (60–90 °C)/EtOAc (1:2) as developing solvent to give **3** in 70.2% yield (13.2 g). Mp 65–66 °C. $[\alpha]_D^{20} = -32.6$ (*c* 0.998, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 2.69 (br s, 2H, *OH*, *NH*), 3.43 (d, $J = 8$ Hz, 1H, CO*CH*), 3.45, 3.54 (d, $J = 12.8$ Hz, each 1H, N*CHH′*), 3.74 (s, 3H, OCH_3), 3.60, 3.76 (dd, $J_1 = 4.4$ Hz, $J_2 = 6.4$ Hz, each 1H, HO*CHH′*), 4.11–4.20 (m, 9H, Fc*H*). IR (KBr pellet): 3301, 3174, 2946, 2911, 2853, 1725, 1433, 1401, 1331, 1267, 1233, 1196, 1170, 1114, 1030, 986, 874, 811. MS *m/z* (ESI) 318 (M^++H), 340 (M^++Na). Anal. Calcd for $C_{15}H_{19}FeNO_3$: C,

56.80; H, 6.04; N, 4.42. Found: C, 56.73; H, 6.14; N, 4.44.

4.4. (2*S*)-Methyl 1-ferrocenylmethylaziridine-2-carboxylate 4

Compound **4** was prepared by our improved procedure.[8]

4.5. Synthesis of (2*S*)-1-ferrocenylaziridin-2-ylmethanol 5a

To a stirred suspension of $LiAlH_4$ (83 mg, 2.1 mmol) in dry THF (4 mL), under N_2, cooled to 0 °C, a solution of compound **4** (210 mg, 0.7 mmol) in dry THF (2 mL) was added dropwise during 15 min. After the reaction mixture was stirred for 8 h, wet Et_2O (10 mL) and saturated aqueous NH_4Cl (10 mL) was added carefully at 0 °C. The resultant gel was filtered through glass wool and washed carefully with Et_2O. The filtrate was dried over Na_2SO_4, and the solvents were removed under reduced pressure giving an orange red oil. This was further purified by the preparative TLC with hexane/EtOAc (1:2) as developing solvent to give an orange red solid (164 mg, 85%). Mp 87–88.5 °C. $[\alpha]_D^{20} = -0.8$ (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (d, $J = 6.4$ Hz, 1H, H–C(3)), 1.72–1.76 (m, 2H, H–C(2), H–C(3)), 2.35 (br, 1H, *OH*), 3.20 (d, $J = 12.8$ Hz, 1H, Fc*CHH*′N), 3.28–3.33 (m, 2H, *CHH*′OH, Fc*CHH*′N), 3.75 (dd, $J_1 = 11.6$ Hz, $J_2 = 3.2$ Hz, 1H, *CHH*′OH), 4.09–4.21 (m, 9H, Fc*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.90, 39.72, 59.54, 62.82, 68.18, 68.21, 68.52, 68.71, 68.80, 84.46. IR (KBr pellet): 3185 (O–H, br); 3089 (C_5H_5); 2982, 2921 (C H, s); 1641 (C=C); 1444, 11405, 1331 (CH); 1153 (C–O); 1056, 1026 (C–N); 1103, 1000; 828. MS: *m*/*z* (ESI) 272 (M^++1), 294 (M^++Na). Anal. Calcd for $C_{14}H_{17}FeNO$: C, 62.02; H, 6.32; N, 5.17. Found: C, 62.18; H, 6.21; N, 4.94.

4.6. (2*S*)-1-Ferrocenylmethylaziridin-2-yl(dimethyl)methanol 5b

A Grignard reagent was prepared in the usual way from 96 mg (4 mmol) magnesium and methyl iodide (0.25 mL, 4 mmol) in Et_2O (10 mL). The solution was cooled to 0 °C before addition of a solution of **4** (165 mg, 5.5 mmol) in Et_2O (2 mL). The reaction mixture was stirred for 2 h at 0 °C, then was heated to reflux for 5 h. The reaction was quenched with saturated aqueous NH_4Cl (10 mL) at 0 °C. 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 the preparative TLC with hexane/EtOAc (2:1) as developing solvent to give **5b** (145 mg, 88%). $[\alpha]_D^{20} = -42.3$ (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.10 (s, 6H, $2 \times CH_3$), 1.32 (d, $J = 6.4$ Hz, 1H, H–C(3)), 1.48 (dd, $J_1 = 6.4$ Hz, $J_2 = 3.6$ Hz, 1H, H–C(2)), 1.79 (d, $J = 3.6$ Hz, 1H, H–C(3)), 2.35 (br, 1H, *OH*), 3.11, 3.42 (d, $J = 12.8$ Hz, each 1H, Fc*CHH*′N), 4.09–4.22 (m, 9H, Fc*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.86, 29.25, 30.09, 46.56, 59.43, 66.92, 68.03, 68.31, 68.49, 69.01, 69.09, 84.51. IR (KBr pellet): 3438 (O–H, br); 3092 (C_5H_5); 2971, 2926 (CH, s); 1634 (C=C); 1462, 1363 (CH); 1151 (C–O); 1026 (C–N); 1104, 1000; 819. MS: *m*/*z* (ESI) 300 (M^++1), 322 (M^++Na). HRMS (MALDI): calcd for $C_{16}H_{21}FeNO$ M^+ 299.0967, found: 299.0984.

4.7. General procedure for the synthesis of aziridine alcohols 5c–j

A Grignard reagent was prepared in the usual way from 135 mg (5.6 mmol) magnesium and alkyl bromide 5.6 mmol in THF (5 mL). The solution was cooled to −20 °C before addition of a solution of **4** 210 mg (0.7 mmol) in THF (1 mL). The mixture was allowed to reach the room temperature. After stirring for 24 h the reaction was quenched with saturated aqueous NH_4Cl (6 mL) at 0 °C. 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 the preparative TLC with hexane/EtOAc as developing solvent to give **5c–j**.

4.7.1. (2*S*)-1-Ferrocenylmethylaziridin-2-yl(diethyl)methanol 5c. Following the general procedure gave compound **5c** as an orange red oil (184 mg, 80%). $[\alpha]_D^{20} = -35.4$ (*c* 1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (m, 6H, $2 \times CH_3$), 1.33 (d, $J = 6.4$ Hz, 1H, H–C(3)), 1.40–1.47 (m, 4H, $2 \times CH_2CH_3$), 1.54 (dd, $J_1 = 6.4$ Hz, $J_2 = 4$ Hz, 1H, H–C(2)), 1.82 (d, $J = 3.6$ Hz, 1H, H–C(3)), 2.44 (br, 1H, *OH*), 3.24, 3.38 (d, $J = 12.8$ Hz, each 1H, Fc*CHH*′N), 4.11–4.21 (m, 9H, Fc*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 7.78, 7.89, 29.27, 29.35, 31.95, 43.65, 58.75, 68.05, 68.27, 68.49, 68.98, 69.05, 84.10. IR (KBr pellet): 3438, 3092, 2968, 2930, 1642, 1459, 1370, 1326, 1144, 1104, 1028, 964, 818. MS: *m*/*z* (ESI) 328 (M^++1), (M^++Na). HRMS (MALDI): calcd for $C_{18}H_{25}FeNO$ M^+ 327.1280, found: 327.1302.

4.7.2. (2*S*)-1-Ferrocenylmethylaziridin-2-yl(di-*n*-propyl)methanol 5d. Following the general procedure gave compound **5d** as an orange red oil (171 mg, 69%). $[\alpha]_D^{20} = -28.4$ (*c* 1.094, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (m, 6H, $2 \times CH_3$), 1.28–1.39 (m, 9H, H–C(3), $2 \times CH_2CH_3$), 1.54 (dd, $J_1 = 6.0$ Hz, $J_2 = 4$ Hz, 1H, H–C(2)), 1.82 (d, $J = 3.6$ Hz, 1H, H–C(3)), 2.44 (br, 1H, *OH*), 3.27, 3.33 (d, $J = 12.8$ Hz, each 1H, Fc*CHH*′N), 4.11–4.21 (m, 9H, Fc*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.72, 14.80, 16.62, 16.84, 29.53, 39.72, 42.66, 44.19, 58.79, 68.05, 68.31, 68.49, 68.98, 69.04, 70.03, 84.10. IR (KBr pellet): 3440, 3093, 2958, 2930, 1635, 1460, 1374, 1330, 1349, 1102, 1029, 1000, 819. MS: *m*/*z* (ESI) 356 (M^++1), 378 (M^++Na). HRMS (MALDI): calcd for $C_{20}H_{29}FeNO$ M^+ 355.1593, found: 355.1615.

4.7.3. (2*S*)-1-Ferrocenylmethylaziridin-2-yl(di-*i*-propyl)methanol 5e. Following the general procedure gave compound **5e** as an orange red crystal (179 mg, 72%). All the physical and spectroscopic data for

compound **5e** were in complete agreement with the reported data.[8]

4.7.4. (2*S*)-1-Ferrocenylmethylaziridin-2-yl(di-*n*-butyl)methanol 5f. Following the general procedure gave compound **5f** as an orange red oil (200 mg, 71%). $[\alpha]_D^{20} = -27.1$ (*c* 1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (m, 6H, $2 \times CH_3$), 1.22–1.41 (m, 13H, H–C(3), $2 \times CH_2CH_2CH_2CH_3$), 1.53 (dd, $J_1 = 6.0$ Hz, $J_2 = 3.6$ Hz, 1H, H–C(2)), 1.82 (d, $J = 3.2$ Hz, 1H, H–C(3)), 2.40 (br, 1H, *OH*), 3.27, 3.33 (d, $J = 12.8$ Hz, each 1H, Fc*CHH*′N), 4.11–4.22 (m, 9H, Fc*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.08, 23.28, 23.41, 25.53, 25.70, 29.66, 37.04, 39.97, 44.25, 58.89, 67.96, 68.30, 68.48, 68.97, 69.05, 70.00, 84.11. IR (KBr pellet): 3446, 3093, 2932, 2864, 1634, 1461, 1409, 1376, 1329, 1153, 1032, 1001, 818. MS: *m*/*z* (ESI) 384 (M^++1), 406 (M^++Na). HRMS (MALDI): calcd for $C_{22}H_{33}FeNO$ M^+ 383.1906, found: 383.1929.

4.7.5. (2*S*)-1-Ferrocenylmethylaziridin-2-yl(di-*i*-butyl)-methanol 5g. Following the general procedure gave compound **5g** as an orange red oil (163 mg, 61%). $[\alpha]_D^{20} = -30.7$ (*c* 1.274, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 0.92 (m, 12 H, $4 \times CH_3$), 1.34 (m, 4H, $2 \times CH_2CH_3$), 1.39 (d, $J = 6.0$ Hz, 1H, H–C(3)), 1.52 (dd, $J_1 = 6.4$ Hz, $J_2 = 3.6$ Hz, 1H, H–C(2)), 1.75–1.85 (m, 3H, H–C(3), $2 \times$ CH), 2.41 (br, 1H, *OH*), 3.14, 3.49 (d, $J = 12.8$ Hz, each 1H, Fc*CHH*′N), 4.10–4.20 (m, 9H, Fc*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.77, 23.86, 24.76, 24.81, 24.88, 29.79, 45.29, 46.62, 49.51, 58.69, 67.97, 68.18, 68.47, 68.80, 68.99, 71.24, 84.14. IR (KBr pellet): 3373, 3098, 2949, 2866, 1638, 1465, 1410, 1365, 1325, 1236, 1106, 1039, 1013, 817. *m*/*z* (ESI) 384 (M^++1), 406 (M^++Na). HRMS (MALDI): calcd for $C_{22}H_{33}FeNO$ M^+ 383.1906, found: 383.1928.

4.7.6. (2*S*)-1-Ferrocenylmethylaziridin-2-yl(di-*n*-pentyl)-methanol 5h. Following the general procedure gave compound **5h** as an orange red oil (233 mg, 80%). $[\alpha]_D^{20} = -24.2$ (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (m, 6H, $2 \times CH_3$), 1.16–1.38 (m, 17H, H–C(3), $2 \times CH_2CH_2CH_2CH_2CH_3$), 1.53 (dd, $J_1 = 6.4$ Hz, $J_2 = 4.0$ Hz, 1H, H–C(2)), 1.81 (d, $J = 4.4$ Hz, 1H, H–C(3)), 2.42 (br, 1H, *OH*), 3.26, 3.31 (d, $J = 12.8$ Hz, each 1H, Fc*CHH*′N), 4.10–4.22 (m, 9H, Fc*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.11, 22.65, 23.01, 23.21, 29.62, 32.42, 32.57, 37.24, 40.15, 44.21, 58.90, 67.99, 68.32, 68.47, 68.97, 69.06, 70.04, 84.19. IR (KBr pellet): 3447, 3094, 2931, 2862, 1635, 1461, 1409, 1375, 1330, 1237, 1150, 1102, 1028, 1105, 818. MS: *m*/*z* (ESI) 412 (M^++1), 434 (M^++Na). HRMS (MALDI): calcd for $C_{24}H_{37}FeNO$ M^+ 411.2219, found: 411.2244.

4.7.7. (2*S*)-1-Ferrocenylmethylaziridin-2-yl(di-*i*-pentyl)-methanol 5i. Following the general procedure gave compound **5i** as an orange red oil (204 mg, 70%). $[\alpha]_D = -23.6$ (*c* 0.958, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 0.86 (m, 12H, $4 \times CH_3$), 1.13–1.21 (m, 5H, H–C(3), $2 \times CH_2$), 1.32–1.46 (m, 6H,$2 \times CH_2CH$), 1.53 (dd, $J_1 = 6.4$ Hz, $J_2 = 3.6$ Hz, 1H, H–C(2)), 1.83 (d, $J = 3.2$ Hz, 1H, H–C(3)), 2.41 (br, 1H, *OH*), 3.24, 3.36 (d, $J = 12.8$ Hz, each 1H, Fc*CHH*′N), 4.11–4.22 (m, 9H, Fc*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.54, 22.63,22.75, 28.54, 28.62, 29.72, 32.24, 32.30, 34.85, 37.78, 44.34, 58.88, 68.01, 68.38, 68.48, 68.98, 69.10, 70.04, 84.14. IR (KBr pellet): 3440, 3259, 3096, 2954, 2866, 1635, 1463, 1409, 1374, 1328, 1327, 1157, 1099, 1031, 1002, 817. MS: *m*/*z* (ESI) 412 (M^++1), 434 (M^++Na). HRMS (MALDI): calcd for $C_{24}H_{37}FeNO$ M^+ 411.2219, found: 411.2242.

4.7.8. (2*S*)-1-Ferrocenylmethylaziridin-2-yl(diphenyl)-methanol 5j. Following the general procedure to give compound **5j** as an orange red crystal. All the physical and spectroscopic data for compound **5e** were in complete agreement with the reported data.[8]

4.8. General procedure for the enantioselective addition of Et_2Zn to arylaldehydes

A solution of diethylzinc (1 M in *n*-hexane, 1.1 mL) was added to a solution of a chiral catalyst (0.015 mmol, 6.3 mg, 3 mol%) in dry toluene under a nitrogen atmosphere. The mixture was cooled to 0 °C, and stirred for 30 min. Freshly distilled benzaldehyde (0.05 mL, 0.5 mmol) was added to the mixture. The resulting mixture was stirred for 10 h in 0–5 °C and was allowed to warm to room temperature, and kept stirring for another 38 h at the same temperature. The reaction was quenched by the addition of saturated aqueous NH_4Cl (4 mL). The mixture was extracted with Et_2O (3×8 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. Purification of the residue by the preparative silica gel TLC plate (hexane/EtOAc = 4/1) afforded the (*S*)-1-phenyl-1-propanol in 97% yield. The ee was determined by HPLC analyses using a chiral column.

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