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Aziridine ring-containing chiral ligands as highly efficient catalysts in asymmetric synthesis

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ABSTRACT

Enantiomerically pure bidentate heteroorganic ligands built on an achiral skeleton containing hydroxyl and aziridine moieties as nucleophilic centers, capable of binding various organometallic reagents, have proven to be highly efficient catalysts in the enantioselective addition of diethylzinc and phenylethynylzinc to aryl and alkyl aldehydes to give the desired chiral products in high chemical yields (up to 90%) and with ees of up to 95%. The influence of the stereogenic center located in the carbon atom in the aziridine moiety on the stereochemical course of the reaction is reported.

1. Introduction

Enantiopure compounds are interesting for synthetic organic chemists due to the importance of chirality in industrial sectors (e.g., pharmaceuticals and food). So far, enantioselective carbon–carbon bond formation using organozinc reagents is commonly used in the synthesis of chiral non-racemic compounds.[1–4] As an example, the asymmetric addition of alkynylzinc to carbonyl compounds[5] is very useful in the synthesis of chiral propargyl alcohols, which are important building blocks in the preparation of various natural and biologically active products.[6]

Previously, we have reported on a seven-step synthesis of chiral, diastereomerically pure aminoalcohols,[7] which have proven to be very efficient catalysts in various asymmetric processes, such as asymmetric diethyl- and phenylethynylzinc additions to aldehydes,[8,9] enantioselective conjugate Michael additions of diethylzinc to enones[10] (catalysts bearing chiral aziridinyl moieties), nitroaldol (Henry) reactions,[11] aza-Henry reactions,[12] asymmetric direct aldol condensations[13] and, more recently, asymmetric Mannich reactions[14] (catalysts bearing chiral secondary amines). Moreover, it was possible to access both enantiomeric products of all the reactions using readily available isomers of the catalysts.

In continuation of the aforementioned results[8–10] and having in mind that aziridines are known to efficiently coordinate organozinc compounds,[15–17] we decided to synthesize a series of new ligands built on simple achiral skeletons (salicylic acid and 2-hydroxymethylbenzoic acid) and containing an aziridine moiety as an amino function. We also decided to study the catalytic activity of the ligands in the asymmetric addition of diethylzinc and phenylethynylzinc to aldehydes.

2. Results and discussion

2.1. Synthesis of the ligands

In the first step of the synthesis, phthalide **1** was treated with sodium hydroxide and then with benzoyl chloride to form compound **2**. The chemical yield of this process was low (26%) but similar findings were described previously.[18] The obtained 2-benzoyloxymethylbenzoic acid **2** was then treated with thionyl chloride in benzene at reflux in the presence of pyridine to afford the corresponding acyl chloride **3** in 90% yield (Scheme 1).[19] First, we attempted to synthesize 2-acetoxymethylbenzoic acid but this appeared to be too unstable for isolation (this acetoxy derivative is described in the literature as a co-product formed in only 0.6% yield).[20]

In the next step, 2-benzoyloxymethylbenzoyl chloride **3** and *O*-acetylsalicyloyl chloride **4** (prepared according to the literature[21]) were subjected to reactions with enantiomerically pure aziridines **5a–c** (synthesized as reported previously[22]) in diethyl ether at room temperature in the presence of triethylamine to form the corresponding amides **6a–b** and **7a–c** (Scheme 2). The chemical yields and absolute configuration of the amides are collected in Table 1.

Finally, amides **6a–b** and **7a–c** were reduced to the corresponding aziridine alcohols **8a–b** and **9a–c** using a protocol reported by Das et al.,[23] which employed triethoxysilane in the presence of zinc acetate in boiling THF (Scheme 3). It should be noted that under these reaction conditions, deprotection of the acetyl group occurs spontaneously, whereas deprotection of the benzoyl group requires harsher conditions ($NaBH_4$, THF/MeOH). The chemical

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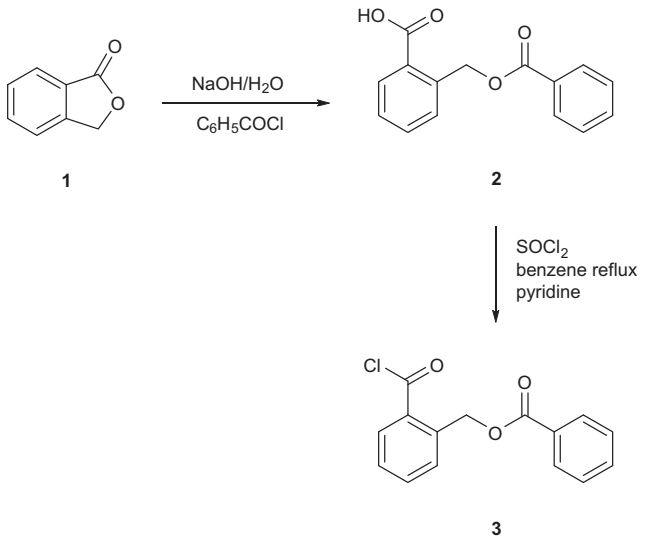


Scheme 1. Synthesis of 2-benzoyloxymethylbenzoyl chloride **3**.

yields, specific rotation values, and absolute configurations are shown in Table 2.

2.2. Screening of the ligands

In order to determine the ability of ligands **8a**–**b** and **9a**–**c** to catalyze the enantioselective addition of diethyl- and alkynylzinc to aldehydes, we chose the addition of diethyl- and phenylethynylzinc to benzaldehyde as reference transformations. The reactions were performed under standard conditions (Scheme 4) and the results are shown in Table 3.

From Table 3 it can be seen that chiral products **10a** and **11a** were formed in good chemical yields and with high ees. The best results were obtained using ligand **8b** built on the skeleton of 2-hydroxymethylbenzoic acid bearing an (*S*)-2-isopropylaziridine moiety as the amino function. Moreover, the reactions promoted by two enantiomeric catalysts **9b** and **9c** led to formation of the opposite enantiomers of the products **10a** and **11a**. From these results it can be seen that the stereogenic center located in the aziridine moiety has a decisive influence on the stereochemistry of both additions and hence on the absolute configuration of the products.

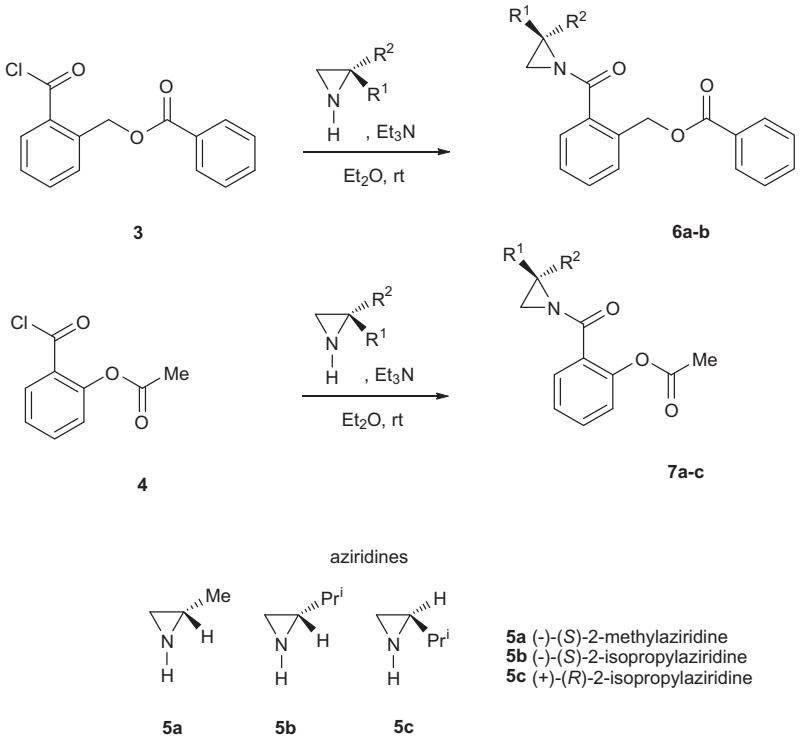
Table 1
Synthesis of amides **6a**–**b** and **7a**–**c**

Entry	Amide	Yield (%)	Absolute configuration
1	**6a**	92	(*S*)
2	**6b**	96	(*S*)
3	**7a**	89	(*S*)
4	**7b**	89	(*S*)
5	**7c**	94	(*R*)

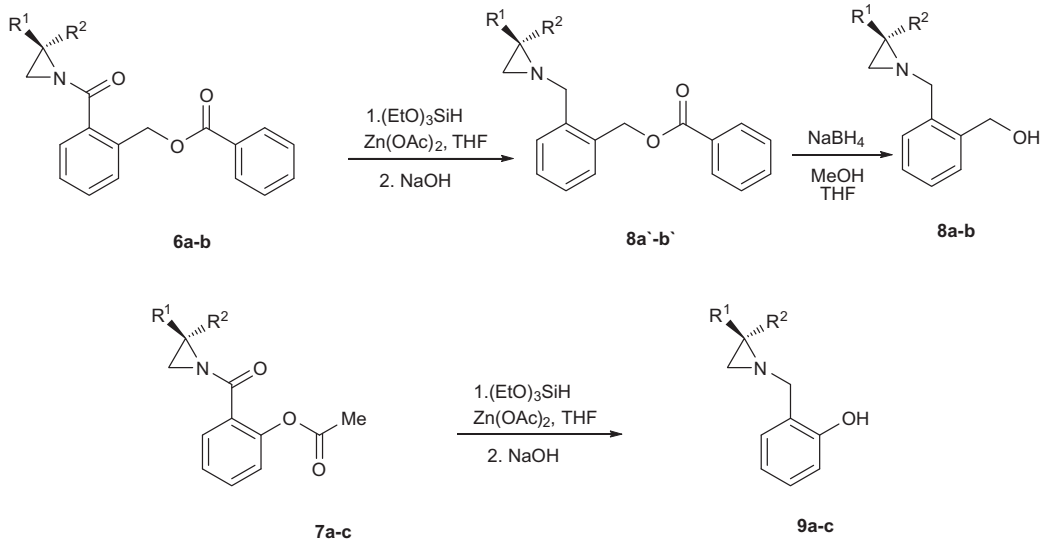
2.3. Asymmetric addition of diethyl- and phenylethynylzinc to various aldehydes in the presence of ligand 8b

Having obtained the best results with ligand **8b**, we then decided to determine the scope of its activity. To this end, it was used to catalyze the title transformations performed with a series of aldehydes (Scheme 5). The results are shown in Table 4.

The results shown in Tables 3 and 4 clearly indicate that the selected ligand **8b** is an effective catalyst for the title reactions and give the appropriate chiral products in good chemical yields and ees. As mentioned earlier, each enantiomeric ligand is easily accessible and leads to the formation of the opposite enantiomer of the addition product. This means that the desired enantiomer of the product can be obtained by choosing the appropriate enantiomeric aziridine to synthesize an enantiomeric ligand starting from the same achiral precursor.



Scheme 2. Synthesis of amides **6a**–**b** and **7a**–**c**.

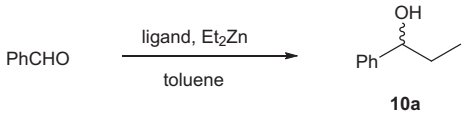


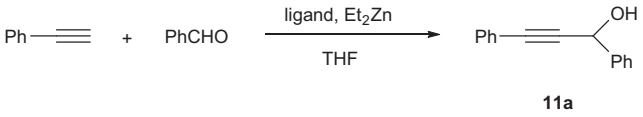
Scheme 3. Reduction of amides to form ligands **8a–b** and **9a–c**.

Table 2
Reduction of amides **6a–b** and **7a–c** to form ligands **8a–b** and **9a–c**

Entry	Ligand	Yield (%)	$[\alpha]_D$[a]	Absolute configuration
1	**8a**	96	+21.8	(*S*)
2	**8b**	94	−38.4	(*S*)
3	**9a**	94	+4.5	(*S*)
4	**9b**	92	−42.0	(*S*)
5	**9c**	90	+42.0	(*R*)

[a] In chloroform (*c* 1).

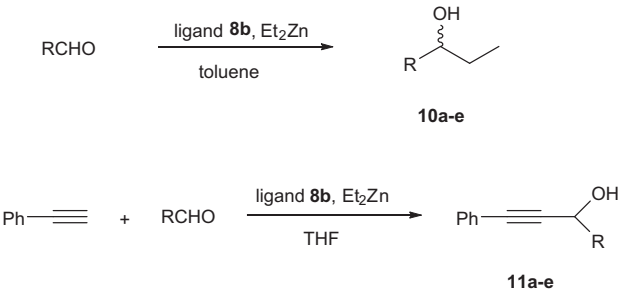




Scheme 4. Asymmetric addition of diethyl- and phenylethynylzinc to benzaldehyde.

3. Conclusion

Chiral bidentate ligands containing one stereogenic center located in the carbon atom in the aziridine moiety were found to be efficient catalysts for the enantioselective addition of diethyl- and phenylethynylzinc to aldehydes. The stereogenic centers located in the amine moieties exerted a decisive influence on the stereochemistry of the reaction and the absolute configuration of the products. Each enantiomer of the product can be obtained by using easily available ligands. Moreover, it should be noted that all the ligands were built on the achiral skeletons of salicylic acid and 2-hydroxymethylbenzoic acid.



Scheme 5. Addition of diethyl- and phenylethynylzinc to aldehydes in the presence of ligand **8b**.

4. Experimental

4.1. General

Unless otherwise specified, all reagents were purchased from commercial suppliers and used without further purification. Tetrahydrofuran and benzene were distilled from sodium benzophe-

Table 3
Screening of ligands **8a–b** and **9a–c**

Entry	Ligand	Product **10a**				Product **11a**			
		Yield (%)	$[\alpha]_D$[a]	ee (%)[b]	Absolute configuration	Yield (%)	$[\alpha]_D$[a]	ee (%)[b]	Absolute configuration[c]
1	**8a**	90	−42.7	95	(*S*)	86	−4.8	93	(*S*)
2	**8b**	93	−44.1	96	(*S*)	95	−4.9	95	(*S*)
3	**9a**	76	−36.0	80	(*S*)	82	−3.9	76	(*S*)
4	**9b**	85	−40.2	92	(*S*)	88	−4.8	93	(*S*)
5	**9c**	82	+38.8	86	(*R*)	80	+4.3	84	(*R*)

[a] In chloroform (*c* 1).
[b] Determined using chiral HPLC.
[c] Taken from the literature.[24]

Table 4
Addition of diethyl- and phenylethynylzinc to aldehydes in the presence of ligand **8b**

Entry	R	Products **10a–e**				Products **11a–e**			
		Yield (%)	$[\alpha]_D$[a]	ee (%)[b]	Absolute configuration[c]	Yield (%)	$[\alpha]_D$[a]	ee (%)[b]	Absolute configuration[c]
1	Ph	93	−44.1	92	(*S*)	95	−4.9	95	(*S*)
2	2-$MeOC_6H_4$	91	−47.6	91	(*S*)	92	−7.5	90	(*R*)
3	*n*-Pr	82	+6.0	85	(*S*)	89	−3.0	86	(*S*)
4	4-BrC_6H_4	89	−7.9	90	(*S*)	82	+3.7	86	(*R*)
5	2-MeC_6H_4	80	−39.8	89	(*S*)	91	−11.0	88	(*R*)

[a] In chloroform (*c* 1).
[b] Determined using chiral HPLC.
[c] Taken from the literature.[4,8,9,25]

none ketyl radical. NMR spectra were recorded on a Bruker instrument at 600 MHz with $CDCl_3$ as solvent and relative to TMS as internal standard. Data are reported as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and b = broad. Optical rotations were measured on a Perkin–Elmer 241 MC polarimeter with a sodium lamp at room temperature (*c* 1). Melting points were measured on a MELTEMP apparatus and are uncorrected. Column chromatography was carried out using Merck 60 silica gel. TLC was performed on Merck 60 F_{254} silica gel plates. Visualization was accomplished with UV light. The enantiomeric excess (ee) values were determined by chiral HPLC (Knauer, Chiralcel OD). The enantiomerically pure aziridines **5a–c** were prepared according to the literature.[22]

4.2. Synthesis of ligands 8a–b and 9a–c

4.2.1. Synthesis of 2-benzoyloxymethylbenzoyl chloride 3[19]

Phthalide **1** (10 g, 0,074 mol) was dissolved in 20% NaOH (54 mL, 0.26 mol) and the solution was heated at 60 °C for 30 min. Next, water (440 mL) was added and after 10 min of vigorous stirring, benzoyl chloride (11.2 mL, 0.096 mol) was added. The mixture was stirred and after 1 h was diluted with water (440 mL). Next, 10% HCl was added to reach pH 2 (around 70 mL). The white precipitate was filtered off under reduced pressure and crystallized from the mixture of ethanol and water to afford 2-benzoyloxymethylbenzoic acid **2** in 26% yield (5.6 g) as colorless crystals, mp = 130–131 °C; ^{1}H NMR ($CDCl_3$)[19]: δ = 5.71 (s, 2H), 7.48–7.56 (m, 3H), 7.60–7.66 (m, 1H), 7.66–7.70 (m, 2H), 8.12–8.14 (m, 2H), 8.33 (s, 1H).

To a suspension of 2-benzoyloxymethylbenzoic acid **2** (2.41 g, 9.4 mmol) in toluene (4 mL), pyridine (0.74 g, 9.4 mmol) and thionyl chloride (10 mL) were added. The mixture was heated at 80 °C on an oil bath for 20 min after which it was cooled to room temperature and concentrated in vacuo. The solid residue was extracted with dry hexane (3 × 25 mL) and, after concentration in vacuo, the crude product was recrystallized from petroleum ether to yield 2-benzoyloxymethylbenzoyl chloride **3** as colorless crystals (1.44 g, 56%), mp = 50–52 °C; ^{1}H NMR ($CDCl_3$): δ = 5.71 (s, 2H), 7.48–7.56 (m, 3H), 7.60–7.66 (m, 1H), 7.66–7.70 (m, 2H), 8.12–8.14 (m, 2H), 8.33 (s, 1H).

4.2.2. Synthesis of amides 6a–b and 7a–c—general procedure

In a round-bottomed flask aziridine (3 mmol), triethylamine (3 mmol), and diethyl ether (30 mL) were placed. The mixture was cooled to 0 °C using an ice bath and the corresponding acyl chloride (3 mmol) in Et_2O was added dropwise. After 30 min of stirring at room temperature, the precipitate was filtered off and the filtrate was concentrated on a rotary evaporator to yield the corresponding amides **6a–b** and **7a–c**.

Amide **6a** (colorless oil, 1.007 g, 92%); ^{1}H NMR ($CDCl_3$): δ = 1.35 (d, *J* = 5.5 Hz, 3H), 2.13 (d, *J* = 3.6 Hz, 1H), 2.53 (d, *J* = 5.8 Hz, 1H), 2.53–2.61 (s, 1H), 5.70 (d, *J* = 13.8 Hz, 1H), 5.78 (d, *J* = 13.8 Hz, 1H), 7.42–7.48 (m, 3H), 7.52–7.59 (m, 1H), 7.57–7.61 (m, 2H), 8.01–8.02 (m, 1H), 8.08–8.09 (m, 2H).

Amide **6b** (colorless oil, 1.365 g, 96%); ^{1}H NMR ($CDCl_3$): δ = 0.96 (d, *J* = 7.2 Hz, 3H), 1.08 (d, *J* = 7.2 Hz, 3H), 1.67–1.73 (m, 1H), 2.18 (d, *J* = 3.6 Hz, 1H), 2.40–2.43 (m, 2H), 5.70 (d, *J* = 13.8 Hz, 1H), 5.78 (d, *J* = 13.8 Hz, 1H), 7.40–7.43 (m, 1H), 7.45–7.48 (m, 2H), 7.50–7.53 (m, 1H), 7.57–7.60 (m, 2H), 7.97–7.99 (m, 1H), 8.07–8.09 (m, 2H).

Amide **7a** (colorless oil, 1.212 g, 89%); ^{1}H NMR ($CDCl_3$): δ = 1.35 (d, *J* = 5.5 Hz, 3H), 2.09 (d, *J* = 3.6 Hz, 1H), 2.30 (s, 3H), 2.51 (d, *J* = 5.8 Hz, 1H), 2.61–2.66 (m, 1H), 7.10–7.11 (m, 1H), 7.32–7.35 (m, 1H), 7.53–7.59 (m, 1H), 7.96–7.97 (m, 1H).

Amide **7b** (1.212 g, 89%); ^{1}H NMR ($CDCl_3$): δ = 0.96 (d, *J* = 6.8 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 1.65–1.71 (m, 1H), 2.12 (d, *J* = 3.6 Hz, 1H), 2.26 (s, 3H), 2.37 (d, *J* = 6.0 Hz, 1H), 2.44–2.46 (m, 1H), 7.07–7.08 (m, 1H), 7.28–7.31 (m, 1H), 7.49–7.52 (m, 1H), 7.93–7.94 (m, 1H).

Amide **7c** (colorless oil, 1.28 g, 94%); ^{1}H NMR ($CDCl_3$): δ = 0.96 (d, *J* = 6.8 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 1.65–1.71 (m, 1H), 2.12 (d, *J* = 3.6 Hz, 1H), 2.26 (s, 3H), 2.37 (d, *J* = 6.0 Hz, 1H), 2.44–2.46 (m, 1H), 7.07–7.08 (m, 1H), 7.28–7.31 (m, 1H), 7.49–7.52 (m, 1H), 7.93–7.94 (m, 1H).

4.2.3. Reduction of amides 6a–b and 7a–c to form chiral ligands 8a–b and 9a–c—general procedure

In a round-bottomed flask, zinc acetate (0.64 g, 3.5 mmol), triethoxysilane (2.296 g, 14 mmol), and freshly distilled dry THF (10 mL) were mixed. The mixture was stirred for 30 min under argon followed by the addition of the corresponding amide (3.5 mmol) in THF (6 mL). The mixture was refluxed on an oil bath and after 6 h was cooled to room temperature and treated with 1 M NaOH (10 mL). After 3 h of stirring, the mixture was extracted with ethyl acetate (4×), and the combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford the crude products which after recrystallization from a mixture of diethyl ether and hexane gave the final ligand structures **9a–c**. In order to reduce amides **6a–b** to aziridine alcohols **8a–b**, an additional protocol was required, which included deprotection of the hydroxymethyl group. The crude products **8a′–b′** were dissolved in THF (4 mL) and $NaBH_4$ (0.11 g, 2.89 mmol) was added. The mixture was heated at reflux and dry methanol was added carefully. After heating for 2 h, the mixture was cooled to room temperature and water was added, THF was evaporated and the residue was extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed in vacuo. The resulting oil was dissolved in methanol (3 mL), after which sodium methoxide (3 mL) was added and the mixture was refluxed for 2 h. Then, methanol was removed in vacuo, water was added and the mixture was extracted with ethyl acetate, dried over anhydrous Na_2SO_4 and after concentration on a rotary evaporator the final ligands **8a–b** were obtained. Chemical yields, specific rotation values, and absolute configurations of all of the ligands **8a–b** and **9a–c** are shown in Table 2.

Ligand **8a** (colorless crystals, 0.58 g, 96%), mp = 54–55 °C; ^{1}H NMR ($CDCl_3$): δ = 1.14 (d, J = 5.4 Hz, 3H), 1.47 (d, J = 6.4 Hz, 1H), 1.58 (d, J = 3.8 Hz, 1H), 1.65–1.69 (m, 1H), 3.46 (d, J = 12.6 Hz, 1H), 3.57 (d, J = 12.6 Hz, 1H), 4.70 (d, J = 12.0 Hz, 1H), 4.73 (d, J = 12.0 Hz, 1H), 7.13–7.15 (m, 1H), 7.26–7.29 (m, 1H), 7.32–7.34 (m, 1H), 7.39–7.41 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 17.9 (CH_3), 34.5 (CH), 35.0 (CH_2), 63.7 (CH_2), 64.5 (CH_2), 127.9 (CH_{ar}), 128.3 (CH_{ar}), 129.8 (CH_{ar}), 130.2 (CH_{ar}), 137.7 ($C_{q\ ar}$), 141.4 ($C_{q\ ar}$); MS (CI): m/z 177 (M+H); HRMS (CI): calcd for $C_{11}H_{15}NO$: 177.0429; found 177.0428.

Ligand **8b** (colorless crystals, 0.574 g, 94%), mp = 70–71 °C; ^{1}H NMR ($CDCl_3$): δ = 0.75 (d, J = 6.8 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H), 1.21–1.27 (m, 1H), 1.37–1.40 (m, 1H), 1.47 (d, J = 6.6 Hz, 1H), 1.69 (d, J = 3.8 Hz, 1H), 3.34 (d, J = 12.2 Hz, 1H), 3.67 (d, J = 12.2 Hz, 1H), 4.68 (d, J = 12.0 Hz, 1H), 4.77 (d, J = 12.0 Hz, 1H), 7.13–7.14 (m, 1H), 7.26–7.29 (m, 1H), 7.31–7.34 (m, 1H), 7.40–7.41 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 19.4 (CH_3), 19.8 (CH_3), 30.9 (CH), 32.7 (CH_2), 46.7 (CH), 63.9 (CH_2), 64.6 (CH_2), 127.8 (CH_{ar}), 128.3 (CH_{ar}), 129.9 (CH_{ar}), 130.2 (CH_{ar}), 137.8 ($C_{q\ ar}$), 141.3 ($C_{q\ ar}$); MS (CI): m/z 206 (M+H); HRMS (CI): calcd for $C_{13}H_{19}NO$: 206.0358; found 206.0357.

Ligand **9a** (colorless crystals, 0.54 g, 94%), mp = 42–43 °C; ^{1}H NMR ($CDCl_3$): δ = 1.23 (d, J = 5.4 Hz, 3H), 1.47 (d, J = 6.4 Hz, 1H), 1.63–1.67 (m, 1H), 1.70 (d, J = 4.2 Hz, 1H), 3.60 (d, J = 13.8 Hz, 1H), 3.63 (d, J = 13.8 Hz, 1H), 6.78–6.81 (m, 1H), 6.88–6.92 (m, 2H), 7.18–7.21 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 17.7 (CH_3), 34.8 (CH), 35.3 (CH_2), 63.1 (CH_2), 116.6 (CH_{ar}), 118.9 (CH_{ar}), 122.9 (CH_{ar}), 127.9 (CH_{ar}), 128.6 (CH_{ar}), 157.6 ($C_{q\ ar}$); MS (CI): m/z 164 (M+H); HRMS (CI): calcd for $C_{10}H_{13}NO$: 164.1163; found 164.1161.

Ligand **9b** (colorless crystals, 0.526 g, 92%), mp = 28–29 °C; ^{1}H NMR ($CDCl_3$): δ = 0.92 (d, J = 3.6 Hz, 3H), 0.93 (d, J = 3.6 Hz, 3H), 1.38–1.44 (m, 3H), 1.79 (d, J = 3.6 Hz, 1H), 3.74 (d, J = 13.8 Hz, 1H), 3.82 (d, J = 13.8 Hz, 1H), 6.78–6.81 (m, 1H), 6.88–6.92 (m, 2H), 7.18–7.21 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 19.3 (CH_3), 19.9 (CH_3), 30.6 (CH), 32.5 (CH_2), 46.9 (CH), 63.4 (CH_2), 116.6 (CH_{ar}), 118.9 (CH_{ar}), 123.1 (CH_{ar}), 127.9 (CH_{ar}), 128.6 (CH_{ar}), 157.6 ($C_{q\ ar}$); MS (CI): m/z 192 (M+H); HRMS (CI): calcd for $C_{12}H_{17}NO$: 192.0256; found 192.0257.

Ligand **9c** (colorless crystals, 0.496 g, 86%), mp = 28–29 °C; ^{1}H NMR ($CDCl_3$): δ = 0.92 (d, J = 3.6 Hz, 3H), 0.93 (d, J = 3.6 Hz, 3H), 1.38–1.44 (m, 3H), 1.79 (d, J = 3.6 Hz, 1H), 3.74 (d, J = 13.8 Hz, 1H), 3.82 (d, J = 13.8 Hz, 1H), 6.78–6.81 (m, 1H), 6.88–6.92 (m, 2H), 7.18–7.21 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 19.3 (CH_3), 19.9 (CH_3), 30.6 (CH), 32.5 (CH_2), 46.9 (CH), 63.4 (CH_2), 116.6 (CH_{ar}), 118.9 (CH_{ar}), 123.1 (CH_{ar}), 127.9 (CH_{ar}), 128.6 (CH_{ar}), 157.6 ($C_{q\ ar}$); MS (CI): m/z 192 (M+H); HRMS (CI): calcd for $C_{12}H_{17}NO$: 192.0256; found 192.0257.

4.3. Asymmetric addition of diethylzinc to aldehydes—general procedure[8]

Chiral catalysts **8a**–**b** or **9a**–**c** (0.1 mmol) in dry toluene (5 mL) were placed in a round-bottomed flask. The mixture was cooled to 0 °C and a solution of diethylzinc (1.0 M solution in hexane, 3 mmol) was then added under argon. After stirring for 30 min, an aldehyde (1 mmol) was added at 0 °C and the mixture was stirred at room temperature overnight. Next, 5% aqueous solution of HCl was added, the layers were separated and the aqueous phase was extracted with diethyl ether (4×). The combined organic layers were washed with brine (10 mL) and dried over anhydrous $MgSO_4$. The solvents were evaporated to afford the crude alcohols **10a**–**e**, which were purified via column chromatography on silica gel (ethyl acetate with hexane in gradient). Yields, specific rotations, enantiomeric excess values, and absolute configurations of the products **10a**–**e** are shown in Table 4. The spectroscopic data are in full agreement with those reported in the literature.[4,8,9,24]

4.4. Asymmetric addition of phenylethynylzinc to aldehydes—general procedure[9]

To a solution of ligand **8a**–**b** or **9a**–**c** (0.2 mmol) in THF (5 mL), was added a solution of diethylzinc (1.4 mL, 1.4 mmol, 1.0 M in hexane) at room temperature under argon. After the mixture was stirred at ambient temperature for 30 min, phenylacetylene (0.154 mL, 1.4 mmol) was added, and stirring was continued for another 30 min. The solution was cooled to 0 °C (ice bath) and treated with the corresponding aldehyde (1 mmol). The resultant mixture was stirred for 2 h at 0 °C and then overnight at room temperature. After completion of the reaction (TLC), it was quenched by 5% aqueous HCl. The resulting mixture was extracted with diethyl ether and the combined organic phases were washed with brine, dried over anhydrous $MgSO_4$ and the solvent was removed in vacuo. The residue was purified by column chromatography (silica gel, ethyl acetate with hexane in gradient) to afford the corresponding products **11a**–**e**. Yields, specific rotations, enantiomeric excess values, and absolute configurations of the products **11a**–**e** are shown in Table 4. The spectroscopic data are in full agreement with those reported in the literature.[4,8,9,24]

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