A new class of chiral zirconium complexes supported by chiral tridentate \([\text{O}^+\text{N}^-\text{O}^-]\)-type of ligands derived from amino acids were synthesized and structurally characterized. They catalyzed asymmetric hydroamination/cyclization of primary aminoalkenes to give five- and six-membered N-heterocyclic amines with up to 94% ee.

Hydroamination as a highly atom-economic reaction for efficient synthesis of nitrogen containing compounds has received great attention. In particular, chiral intramolecular hydroamination provides a convenient way to obtain chiral N-heterocycles, which plays an important role in pharmaceuticals. Since the first report on asymmetric hydroamination in 1992 based on chiral ansa-lanthanocenes, several chiral catalyst systems have been developed, including group 4 metals, alkaline earth metals, alkali metals, late transition metals, rare earth metals, and chiral Bronsted acids. Though significant progress has been made in the past decade in this field, the reported enantioselective systems remain very limited. In view of the recent progress in asymmetric catalysis, it is envisioned that new ligand design, new catalyst synthesis, and mechanism tests may offer strategies for addressing challenging issues in asymmetric olefin hydroamination, thus further advancing this field.

Very recently, we reported a highly active cationic zirconium system based on a tridentate \([\text{O}^-\text{N}^-\text{S}]^+\) ligand for catalytic hydroamination with a broad substrate scope from primary amines to secondary amines, and from terminal alkenes to much less reactive internal alkenes. This system also catalyzed tandem intramolecular hydroamination of primary aminoalkenes to give bicyclic amines, and was tolerant of many functional groups.

We wondered if chiral ligands derived from such a tridentate backbone system would offer both high catalytic activity and enantioselectivity in asymmetric hydroamination. Here we report the new chiral catalyst systems for asymmetric hydroamination of aminoalkenes with up to 94% ee and ≥95% conversion. The reaction mechanism is also discussed.

Initially, a series of new chiral auxiliary \([\text{O}^-\text{N}^-\text{O}]^+\) ligands were synthesized via the condensation of salicylaldehyde with \(O\)-alkylated chiral aminoalcohol, followed by reduction with \(\text{LiAlH}_4\) (see ESI†). They were treated with 1 equiv. of tetrabenzyldizirconium in toluene to give new chiral dibenzyl zirconium complexes 1–4 (Chart 1).

Screening results on catalytic hydroamination of 2,2-diphenyl-4-pentenamine \((5\text{a}–\text{f})\) indicated that \(4\text{b}\) offered the best ee value and the lability of the OR\(^2\) group disfavored the chiral induction (Table S3 in ESI†). To fix this problem, a covalent bond between the Zr atom and O(2) was desirable, which led to the design of a new ligand backbone. Subsequently, a series of new ligands with a \([\text{O}^-\text{N}^-\text{O}]^+\) backbone were prepared. Their Zr complexes 5a–f were also synthesized and characterized by various spectroscopic data and single-crystal X-ray analyses (Fig. S8–S11 in ESI†).

We identified \(5\text{b}\) as the best catalyst for hydroamination of \(6\text{a}\), the effect of reaction temperature on enantioselectivity was examined and the results are listed in Table S4 (ESI†). Under the optimal reaction conditions, several substrates were examined, and the results are summarized in Table 1. Both five- and six-membered N-heterocyclic ring products were generated with up

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**Chart 1** Chiral Zr complexes 1–4.

| complex | \(R^1\) | \(R^2\) | 1 | 2 | 3a | 4a | 4b | 4c | 4d |
|---------|-----|-----|---|---|---|---|---|---|---|
| \(\text{Bu}\) | \(\text{adm}\) | \(\text{PhSiPh}_2\text{PhCPhCPhCPhCPhC}\) | Et | Et | Et | Et | Et | Bn | \(\text{Bu}\) |
| \(\text{adm} = \text{adamantane}\) | | | | | | | | | |

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**Table 1** Screening results on catalytic hydroamination of 2,2-diphenyl-4-pentenamine. Values are expressed as the mean of three individual experiments.

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to 94% ee. The substrate 6B gave spiro[4,5] product 7B in 93% ee (entry 2), and the substrate 6C offered spiro[4,4] product 7C in 87% ee (entry 3). Desymmetrization with the two allyl groups in aminodiene 6F produced both diastereomers with 88% ee and 92% ee, respectively, whereas the diastereoselectivity was low (1 : 1.7) (entry 6). Upon replacing phenyl in 6F with methyl, even higher ee values of 90% and 93% were achieved (entry 5). The gem-dialyl effect was also observed. As anticipated, replacement of gem-diphenyl substituents in 6A by gem-dimethyl-ones resulted in a much lower activity (entry 4). Complex 5e was found to give 7G in 66% ee, which represents the best enantioselectivity so far observed for the hydroamination of 6G (entry 7).

Since 5b did not show catalytic activity toward secondary aminodienes, it seemed that the above [ONO]Zr(CH2Ph)2 system might offer spiro[4,4] product 7A in a similar activity to that of 6A. Single-crystal X-ray analyses reveal that 9 is a dimer with bridging imido 1BuN and alkoxy units, respectively (Scheme 2). One of the Zr atoms is five coordinated, and the other is six coordinated. In addition, each Zr atom is σ-bonded to one amido unit 1BuNH, and the two 1BuNH moieties are oriented in trans positions (Fig. S13 in ESI†).

To gain further insight into the reaction mechanism, a kinetic analysis of hydroamination/cyclization of aminodiene 6A catalyzed by 5b was performed for the determination of an empirical rate law using in situ 1H NMR monitoring. Ferrocene was employed as an internal 1H NMR integration standard, as it was readily differentiated from the substrate, product, and catalyst resonances in deuterated toluene. The appearance of the product 7A CH2CH2 signal was monitored as a function of time and normalized versus the internal standard. The results show that there is a first-order dependence on both catalyst and substrate concentration, giving the empirical rate law in the following equation on the basis of initial rate measurements: rate = k(obs)[catalyst][substrate].

To gauge the effect of N-deuteration on the reaction catalyzed by 5b, the conversion of d2-6A was studied (Scheme 3). It was found that the cyclization of N-deuterated d2-6A was much slower than for the protonic counterpart 6A, giving kH/kD = 5.2 at 60 °C (see Fig. S19 in ESI†).

To further probe the nature of the turnover-limiting step, the temperature dependence of the cyclization rate of 6A was investigated by determining the kobs values at 50 °C, 60 °C, 70 °C and 80 °C (see Fig. S20 in ESI†). The Eyring plot generated from these data is shown in Fig. S21 in ESL†. The calculated thermodynamic parameters are ΔH° = 9.9 ± 0.3 kcal mol−1 and ΔS° = −53.4 ± 0.9 cal K−1 mol−1, which are very comparable to ΔH° = 6.7 ± 0.2 kcal mol−1 and ΔS° = −43 ± 7 cal K−1 mol−1 observed for the [PhB(C6H4)[OX]2Zr(NMe2)2] system.† These values may also be compared to ΔH° = 17 to 21 kcal mol−1 and ΔS° = −13 to −23 cal K−1 mol−1 in the salicyloxazoline zirconium system17 and ΔH° = 20.1 ± 0.5 kcal mol−1 and ΔS° = −21 ± 1 cal K−1 mol−1 in

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**Table 1** Substrate scope of hydroamination catalyzed by 5b

| Entry | Substrate | Product | Time (h) | Yield/ee (%) |
|-------|-----------|---------|----------|--------------|
| 1a    | 6A        | 7A      | 19       | 84/94        |
| 2c    | 6B        | N-Ts-7B | 21       | 97/93        |
| 3c    | 6C        | N-Ts-7C | 72       | 91/87        |
| 4c    | 6D        | N-Ts-7D | 120      | 96/89        |
| 5c    | 6E        | N-Ts-7E | 89       | 90/93, 91    |
| 6c    | 6F        | N-Ts-7F | 24       | 91/88, 92    |
| 7b    | 7F        | 7G      | 2        | 91/66        |

a Temp. = 85 °C. b Using 10 mol% 5e at 130 °C. c Temp. = 70 °C. d The ee value measured by chiral HPLC. e Products were converted to N-Ts compounds and the ee value was measured by chiral HPLC, the dr value was determined by the analyses of the 1H NMR spectrum of the crude product. f Isolated yield.

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**Scheme 2** Reaction of 8 with t-BuNH2.

**Scheme 3** Primary kinetic isotopic effect observed in the cyclization of 6A (E = H/D).
trium showed that through systematic studies, we have developed a class of new pincer-chiral zirconium catalysts for asymmetric hydroamination/cyclization. In addition, experiments on the non-linear effect were carried out. A strict linear turnover-limiting step of the catalytic cycle. Such a mechanism is similar to those of precatalyst 5b observed (see Fig. S22 in the ESI). Such effects show that an N–H (or N–D) bond is involved in the reaction mechanism and those of precatalyst 5a displayed a similar catalytic activity to that of J. Am. Chem. Soc. 

the parameters obtained in the current study show a highly organized transition state. Though 9 displayed a similar catalytic activity to that of 8 and 5b, it was not clear whether a dinuclear species was involved in the turnover-limiting step of the catalytic cycle as the first-order dependence on precatalyst concentration was observed. Accordingly, experiments on the non-linear effect were carried out. A strict linear relationship between the ee values of 7a and those of precatalyst 5b was observed (see Fig. S22 in the ESI†). Such effects show that an N–H (or N–D) bond is involved in the reaction mechanism and those of precatalyst 5a displayed a similar catalytic activity to that of J. Am. Chem. Soc.

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