Construction of Axially Chiral Compounds via Asymmetric Organocatalysis

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INTRODUCTION

Axial chirality, which refers to stereoisomerism resulting from the nonplanar arrangement of four groups in pairs about a chirality axis (IUPAC), including atropisomerism, chiral allenes, spiranes, spiroindanes, and so on, is ubiquitous in organo- and bioactive molecules, and natural products, as illustrated in Figure 1. Atropisomerism, which is enantiomerism caused by restricted bond rotation and was discovered by Christie and Kenner in 1922, is the most representative subclass of axial chirality. Neglect of the importance of axial chirality changed drastically in 1980 when BINAP was developed as a predominant axially chiral ligand for enantioselective transition-metal-catalyzed reactions. To date, numerous efficient ligands bearing axially chiral backbones have been synthesized and widely applied in transition-metal-mediated asymmetric catalysis, as evidenced by many reviews. The axially chiral unit was also deemed an important...
structural element of many natural products\textsuperscript{11} and bioactive molecules, enantiomers of which usually exhibit different pharmacological activities and metabolic processes in vivo and in vitro.\textsuperscript{8}−\textsuperscript{10} In 2004, Akiyama and Terada first introduced axially chiral BINOL-derived phosphoric acids into asymmetric catalysis, which brought a milestone in the area of axially chiral organocatalysts and asymmetric Brønsted acid catalysis.\textsuperscript{4} Current developments in chiral metal ligands and organo-
catalysts have witnessed wide utilization and growth of axial chirality. The increasing demand for enantioenriched axially chiral compounds in asymmetric catalysis and drug discovery has stimulated the development of efficient methods for these privileged scaffolds.

Although the conventional chiral resolution of racemates and chiral-auxiliary-assisted reactions are generally used for the construction of axially chiral compounds in enantiomerically pure form, asymmetric catalysis meets the demands of high efficiency and economic value. Initial attempts focused on enzymatic and transition-metal-mediated reactions. The development of axially chiral ligands facilitated the discovery of enantioselective metal-catalyzed reactions that are capable of delivering new and more efficient axially chiral ligands, which can be considered to be an evolutionary process. Compared with relatively mature transition-metal-catalyzed reactions, flourishing asymmetric organocatalysis is a rising star.

Organocatalysis has been recognized as a versatile and powerful synthetic tool for the preparation of valuable chiral building blocks. A wide range of chiral organocatalysts, including Bronsted acids, N-heterocyclic carbenes (NHCs), amines, peptides, thiourea catalysts, phosphines, and phase-transfer catalysts, have permitted a large number of enantioselective transformations to proceed smoothly. However, the construction of structurally diverse axially chiral backbones via organocatalysis remains a challenge at the forefront of synthetic chemistry. This Account highlights our efforts to construct axially chiral compounds involving optically active atropisomers and spirobicyclic frameworks through asymmetric organocatalysis.

### (DYNAMIC) KINETIC RESOLUTION STRATEGY

The (dynamic) kinetic resolution of racemic starting materials has been one of the most powerful and reliable strategies for...
the synthesis of enantiopure compounds in past decades. A series of kinetic resolutions for chiral biaryls have been reported,12,14,15 as summarized in detail by Ma and Sibi.13 The present study introduces some organocatalytic examples using the kinetic resolution strategy given its connection to the proposed work.

In 2010, Miller’s group reported the innovative and successful access to axially chiral biaryls (aR)-4 through tripeptide-catalyzed enantioselective bromination involving a dynamic kinetic resolution (Scheme 1).19 The barrier for atropisomer interconversion of rac-1 was low, thereby allowing the dynamic process of the kinetic resolution. Bromines were asymmetrically introduced at the ortho positions and blocked the rotation of the axis, leading to isolation of the enantiomers.

In the proposed mechanism, the spatial configuration of intermediate 5, which was locked by the salt bridge and hydrogen bonds between 1 and the catalyst 2, determined the axial chirality of the products. This work brought a milestone in the organocatalytic enantioselective construction of axially chiral compounds.20 By extension of this strategy to axially chiral arylquinazolinones,21−23 benzamides,24,25 isoquinoline N-oxides,26 and arylquinolines,27 high enantioselectivities were achieved under catalysis by peptides or cinchona-alkaloid-derived bifunctional organocatalysts. In these examples, the hydrogen bonds between the substrates bearing the indispensable hydroxyl group and catalysts (5−8) bearing H-bond acceptors and donors on the chiral scaffolds were critical for chiral induction.

2,2'-Dihydroxy-1,1'-binaphthyl (BINOL),4,28 2-amino-2'-hydroxy-1,1'-binaphthyl (NOBIN),29 and 1,1'-binaphthyl-2,2'-diamine (BINAM) derivatives are essential axially chiral biaryls in asymmetric catalysis and chiral catalyst preparation. In general, organocatalytic kinetic resolution strategies are used for the construction of these predominant skeletons and exhibited major breakthroughs in this field.13 In 2013, Maruoka’s group reported the kinetic resolution of chiral NOBINs utilizing phase-transfer-catalyzed N-allylation with excellent results.30 Almost simultaneously, we finished the highly enantioselective kinetic resolution of BINAMs through a Bronsted acid-catalyzed imine formation and transfer hydrogenation cascade process (Scheme 2).31 Racemic N-sulfuryl-BINAM (rac-13) and aryl aldehydes were selected as the substrates for this approach, wherein Hantzsch esters 15 were used as the hydride source in the presence of chiral phosphoric acids (CPAs). The initial investigation indicated that the desired sequence of transformations catalyzed by 14 was effective, and the optimization process generated satisfactory results. Under the optimal conditions, a variety of rac-BINAM derivatives produced the corresponding products (aS)-16 with modest to excellent enantiomeric excesses (ee’s) and recovered substrates with excellent enantiomeric excess (ee) (S 7−340). This kinetic resolution exhibited excellent compatibility with different types of N-protecting groups (sulfonyl, aroyl, 2-naphthylmethyl, Fmoc, and amido) and functional groups (Br, Cl, TMS) at the 6- and/or 6'-positions of rac-13.
Control experiments indicated that the transfer hydrogenation process catalyzed by 14 was the enantioselectivity-determining process in the kinetic resolution (Scheme 3), which agrees with the fact that organocatalytic enantioselective reduction of imines through transfer hydrogenation emerged as a powerful synthetic tool for the construction of chiral amines.31 Akiyama and collaborators also introduced enantioselective transfer hydrogenation in the dynamic kinetic resolution of other biaryls.32 Additionally, Zhao’s group successfully accomplished the kinetic resolution of BINOLs and NOBINs through NHC-catalyzed atroposelective acylation.33 These developed methods featured a general strategy that employs prominent reactions for the efficient preparation of useful axially chiral compounds through kinetic resolution.

### DESYMMETRIZATION STRATEGY

The enantioselective desymmetrization of meso- or prochiral precursors is a remarkably valuable transformation in organic synthesis that involves axially chiral skeleton construction13,14 because it breaks the symmetry of the molecule without incorporating new stereogenic centers.34 According to Akiyama, desymmetric bromination, which was catalyzed by CPA 18, afforded axially chiral multisubstituted biaryls (aS)-19 with good to excellent enantioselectivity (Scheme 4).55 In the monobromination process, the CPA controlled the enantioselectivity via a highly organized hydrogen-bonding network among an advantageously configurational substrate, a catalyst, and a brominating reagent (3). The kinetic resolution of rac-19 can also generate good results. In the desymmerization of achiral 17, when a slight excess of 3 (1.1–1.2 equiv) was added, a kinetic resolution process was observed in the further bromination of (aR)-19, which resulted in a slight decrease in the yield and the enhancement of the enantioselectivity. By employing Akiyama’s strategy, Armstrong and Smith36 improved the enantioselectivities of desymmetric nucleophilic aromatic substitution reactions, which delivered axially chiral biaryls with good results.

In 2016, we reported the asymmetric synthesis of axially chiral N-arylurazoles via organocatalytic desymmetrization of 1-aryltriazodiones (ATADs) proceeding without a kinetic resolution process (Scheme 5).37 Urazoles 25 obtained from the tyrosine clicklike reaction were recognized as a type of axially chiral skeleton containing an N–Ar chiral axis in the initial work. However, the strong background reaction and remote axial enantiocontrol were a formidable challenge for the enantioselective desymmetrization of ATADs. The tertiary amine–thiourea bifunctional organocatalyst 24, which could simultaneously activate the nucleophile and electrophile via hydrogen bonding, was finally found to be effective in the remote enantioselective control of the desymmetrization process. A variety of both 2-naphthol derivatives and 4-substituted phenols were deemed to be efficient nucleophiles for this transformation, thereby affording (aS)-25 in good yields with excellent ees under the optimized conditions. The ortho group of the ATADs was not restricted only to the tert-butyl group. In addition, iodo, bromo, and phenyl groups at the ortho position also proved to be compatible with this reaction.

The use of 2-substituted indoles, which are rarely used as nucleophiles in asymmetric organocatalysis with good enantiocontrol, generated only poor results in the presence of catalyst 24. Thus, we turned our focus to chiral phosphoric acid catalysts, as these can perform bifunctional actions to simultaneously activate indoles and ATADs (Scheme 6). As expected, the well-defined CPA 27 smoothly promoted the
reaction to deliver \((aR)-28\) with excellent enantioselectivity. Under the optimized conditions, the reaction was extended to include various 2-substituted indoles with excellent results, thereby demonstrating that the bulkiness and electronic properties of the substituents on the indoles had only a minimal effect on the efficiency and enantioselectivity of this transformation. In summary, this work represented a convenient desymmetric approach to an interesting class of axially chiral urazole derivatives with excellent remote enantiocontrol.

### CYCLIZATION STRATEGY

Axially chiral skeletons are already present in the substrates in the above-mentioned strategies, thereby affording the desired products in the preferred configuration. Cyclization reactions are generally used for the construction of axially chiral compounds because most atropisomers contain at least one aromatic ring stick on the chiral axis.\(^{11,12,14}\) Axially chiral arylpyrroles as essential motifs are widely found in natural products, bioactive entities, and ligands. The direct construction method is highly demanded, whereas the effective synthesis of enantiopure arylpyrroles has always relied on the conventional resolution. The Paal-Knorr reaction, which converts amines into pyrroles with 1,4-diketones through acid-mediated dehydrative annulation, is one of the most common approaches for the construction of pyrroles. However, the asymmetric catalytic Paal-Knorr reaction had been unknown until our present work. A well-defined catalyst 31 smoothly promoted the reaction of 29 and 2-(tert-butyl)aniline to produce axially chiral arylpyrroles \((aR)-32\) with moderate enantioselectivity (Scheme 7).\(^{38}\) To further improve the enantioselectivity, Lewis acids, which activate CPAs to facilitate many challenging transformations in accordance with Yamamoto’s combined-acid\(^ {39}\) and Luo’s binary-acid catalysis principle,\(^ {40}\) were introduced into this catalytic system. Screening of Lewis acids revealed that \(\text{Fe(OTf)}_3\) (10 mol %) was able to promote the CPA-catalyzed Paal-Knorr reaction very well and clearly improved the enantioselectivity. Under the optimized conditions, good results were obtained for all of the tested substrates regardless of the electronic properties and position of the substituents on the aromatic ring of 29 and 30. The rotation-blocking groups at the ortho positions of 30 were not restricted to only tert-butyl groups, as bromo, iodo, and phenyl groups also effectively controlled the enantioselectivity. The products shifted from \((aR)-32\) to their opposite enantiomers following a solvent change from CCl\(_4\)/cyclohexane to CCl\(_4\)/EtOH (Scheme 8). This phenomenon was worth investigating further. The key intermediates 33, which served as the tautomers and were isolated from the transformation, suggested that the desired arylpyrrole formation may go through enamines 33 followed by acid-catalyzed dehydrative cyclization. This work presented a general and efficient method to access enantiomerically pure arylpyrroles through the enantioselective Paal-Knorr reaction.

In addition to the direct aromatic ring formation, a stepwise method involving cyclization and subsequent aromatization for axial chirality was also deemed efficient and applicable. According to Rodriguez and Bonne, the organocatalytic 1,4-addition of carbon nucleophiles to 37 triggered an intramolecular O-alkylation resulting in trans-dihydrofurans, which
delivered the final axially chiral furans through oxidative central-to-axial chirality conversion. Numerous 1,3-cyclohexanones 35 and 2-naphthols 36 as C₂O-dinucleophiles proved to be compatible with the sequential transformation, by which enantiopure \((\alphaS)\)-39 and \((\alphaS)\)-40, respectively, were produced with great efficiencies (Scheme 9). Various functional groups at the ortho position of the nitrostyrene were well-tolerated in the reaction with 2-naphthol. Notably, the authors clearly proposed the highly efficient central-to-axial chirality transfer mechanism, which demonstrated that the oxidants phenyliodine diacetate (PIDA, \(\text{cp} = 84−92\%\)) and \(\text{MnO}_2\) (\(\text{cp} = 89−100\%\)) proceeded with opposite chirality transfer manners in the oxidation process. Following the application of this strategy, Rodriguez and Bonne also successfully developed an enantioselective approach for axially chiral 4-arylpyridines. These excellent works shed light on the research of atropisomer construction through central-to-axial chirality transfer.
Similar to arylpyrroles, axially chiral arylquinazolinones constitute a privileged structural scaffold found in a large number of natural products, bioactive compounds, and chiral ligands. Miller’s work involving dynamic kinetic resolution through peptide-catalyzed bromination yielded several axially chiral arylquinazolinones with good results. However, the organocatalytic direct construction approach to access enantiopure arylquinazolinones remained underexplored until our present work. N-Arylanthranilamides were able to react with aldehydes catalyzed by chiral Brønsted acids to generate centrally chiral 2,3-dihydroquinazolinones, which could be converted to axially chiral N-arylquinazolinones with central-to-axial chirality transfer upon dehydrogenation with oxidants. DDQ was identified as a suitable oxidant for this cascade reaction, which proceeds smoothly with 41 and aryl aldehydes to afford highly enantiopure arylquinazolinones under the catalysis of CPA 43 (Scheme 10). Compared with Rodriguez and Bonne’s stepwise method, this transformation performed well regardless of when the oxidant was added, thereby allowing its use in multicomponent processes. Under the standard conditions, 41 and 42 with different functional groups were well-tolerated. The ortho group, which blocked the rotation of the axes, was not restricted only to the tert-butyl group, as I, Br, Ph, and POPh2 also exhibited efficiency. Several control experiments demonstrated that the introduction of chirality into the catalytic cyclization process and the oxide hydrogenation were responsible for the central-to-axial chirality transfer. Following the application of our developed methodology, the first enantioselective total synthesis of eupolyphagin was achieved in six steps in an overall yield of 32%. Interestingly, in the case of cyclohexanal, the 2-cyclohexyl ((aR)-44b) or 2-H ((aR)-44c) arylquinazolinone was obtained slightly.
when DDQ or PIDA, respectively, was added following the catalytic cyclization. However, acyclic aliphatic aldehydes afforded only poor results in this transformation.

To tackle this problem, a new direct construction approach using the Brønsted acid-catalyzed carbon–carbon bond cleavage strategy was developed. The reaction of N-arylanthranilamides with acetylacetone catalyzed by the Brønsted acid produced 2-methylarylquinazolinones. A deep investigation found that 4-methoxypentenone was more reactive than acetylacetone and that N-triflylphosphoramides could well control the enantioselectivity of the axially chiral products (aS)-49 (Scheme 11). The subsequent transformations of (aS)-49a to (aS)-50 further enlarged the scope of axially chiral arylquinazolinones.

### ADDITION STRATEGY

Modification of alkynyl groups is one of the most common methods for the synthesis of alkenes. Styrenes 52, which were obtained from 3-aryllkynals 51 through 1,4-addition, exhibited a relatively high computed rotational barrier, thereby indicating that the atropisomers of the substituted styrenes might be stable enough for isolation and application (Scheme 12). Simple styrenes are the predominant principal building blocks for chemical synthesis and catalysis. Thus, they are very attractive and highly desirable for the development of the enantioselective synthetic approach to axially chiral styrenes, which remains underexplored.

We first focused on evaluating the addition reaction between nucleophilic 1,3-diones and 2-iodophenylpropiolaldehyde for the enantioselective construction of axially chiral styrenes. However, only a few organocatalytic enantioselective transformations involving alkynals have been exploited. After deep research, chiral secondary amine was deemed a suitable catalyst for the transformation to yield axially chiral styrenes (aR)-56 with complete Z/E selectivity (>20:1) and moderate ee (Scheme 13). Under the optimized conditions, a series of 3-arylalkynals 54 bearing different substituents on the phenyl ring smoothly produced axially chiral styrenes with moderate to good results. In addition to 1,3-diones, 1,3-keto esters and malononitriles as nucleophiles also efficiently generated (aR)-56 with good to excellent results. The subsequent transformations to several complex chiral compounds, including 57a and 57b, without a decrease in the enantioselectivities demonstrated the synthetic utility of the axially chiral styrenes. Inspired by this work, the discovery of other promising strategies for enantiopure styrenes is in high demand, considering the importance of axially chiral styrenes.

### DIRECTARYLATION STRATEGY

Direct construction of the chiral axis through metal-catalyzed cross-coupling and oxidation has been the most common
approach for the asymmetric synthesis of atropisomers. In comparison, only a few organocatalytic examples have been reported. In 2013, the groups of Kürti and List independently reported the asymmetric synthesis of enantio- pure \((aS)-\text{BINAM}\) derivatives through the CPA-catalyzed [3,3]-rearrangement of \(N,N'\)-diarylhydrazines, which was a significant improvement of Sannicolo’s work (Scheme 14). The enantioselectivity determined by the C−C bond-forming step was notably affected by both the steric and electronic effects of the substituents on 58. These two prominent works paved the way for the practicable construction of biaryls through the direct formation of chiral axes promoted by organocatalysts.

In addition to intramolecular rearrangement, intermolecular nucleophilic aromatic substitution is another direct arylation approach to atropisomers. The combination of readily available carbon-nucleophilic 2-naphthols and carbon-electrophilic quinones allowed the development of a direct enantioselective arylation strategy to construct non-\(C_2\)-symmetric axially chiral biaryldiols. In our work, an ester group was incorporated into the quinone skeleton to address the challenges involving enantioselectivity control and product axial rotation restriction. CPAs were deemed suitable catalysts for this transformation. BINOL-derived CPA 64 was found to be the catalyst of choice to produce \((aR)-65\) with 93% ee under the optimal conditions (Scheme 15). In this catalytic system, different quinone esters and various substituents at different positions of the 2-naphthol were well-tolerated. Changing the ester group to a useful halogen group at the quinone moiety had almost no negative influence on the reaction efficiency and stereoselectivity. The obtained axially chiral biaryldiols were verified as excellent ligands for the titanium-catalyzed enantioselective addition of diethylzinc to aldehydes, thereby indicating the potential utility of the products. In the proposed mechanism, 64 performed as a bifunctional organocatalyst to promote the enantioselective conjugate addition of the 2-naphthol to the quinone derivative to form centrally chiral intermediate 66 through multiple-hydrogen-bonding activation. The subsequent aromatization of 66 to form \((aR)-75\) efficiently transferred the chirality from central to axial. Xu, Kürti, Sun, and co-workers found that \(N\)-sulfonyl-protected iminoquinones also smoothly reacted with phenols to afford BINOL analogues with good enantioselectivity.

To construct enantiomerically enriched NOBIN analogues with this strategy, 2-naphthylamines were selected as nucleophiles instead of 2-naphthols. Readily available 2-naphthylamines had scarcely been investigated prior to our work. Under the above-mentioned conditions, the reaction of 2-naphthylamines and quinone esters afforded the desired NOBIN analogues \((aS)-69\) with good results considering the yield and ee (Scheme 16). Under the optimized conditions, numerous 2-naphthylamines smoothly yielded \((aS)-69\) in moderate to good yields with excellent enantioselectivities. The electronic properties of the substituents on the aromatic ring of the 2-naphthylamine exhibited significant effects on the chemical yield rather than on the enantioselectivity. Additionally, various substituents on 67 and the amino groups of 68 were well-tolerated in this catalytic
system. This work presented a rare example of 2-naphthylamines acting as carbon nucleophiles in the organocatalytic enantioselective transformation, which gave effective access to enantiopure NOBIN analogues.

In the above-mentioned reactions, quinones and iminoquinones acted as arylation reagents through conjugate addition. Electrophilic and nucleophilic aromatic substitutions as textbook organic reactions were alternative, more straightforward arylation methods. In contrast, nucleophilic aromatic substitution with cleavage of the electrophilic aryl C–H bond was merely developed in recent years through transition-metal-catalyzed aryl C–H activation or a radical process; the organocatalytic one via a nonradical process is an enormous challenge in organic synthesis. As the present study sought suitable activating and directing groups, the azo group was identified as a useful moiety that could effectively activate an aromatic ring in the presence of a Brønsted acid for formal nucleophilic aromatic substitution resulting in the cleavage of the aryl C–H bond and the direct arylation of the nucleophile.

Following the introduction of 2,3-disubstituted indoles, the products shifted from axially chiral to centrally chiral polycyclic pyrroloindole derivatives bearing two contiguous quaternary chiral centers in excellent yields and ee’s (Scheme 19). Among these three types of transformations, the initial stereoselective nucleophilic addition promoted by a Brønsted acid and primary rearomatization was the common step that thermodynamically produced more stable arylhydrazine intermediates (Scheme 19). Several control experiments suggested that axially chiral and polycyclic pyrroloindoles came from the same intermediate, which was obtained from intermediate through the intramolecular cyclization process. In the case of 2-substituted indoles bearing a bulky group, the cyclization was blocked by the bulky substituent, thereby resulting in the further rearomatization of intermediate to preferentially produce with central-to-axial chirality transfer. This work represented an unprecedented arylation approach involving organocatalytic formal nucleophilic aromatic substitution and aryl C–H bond cleavage. In addition to affording structurally diverse axially...
and centrally chiral indole derivatives, this strategy provides an opportunity for the direct construction of many other prominent axially chiral backbones and will foster the development of many other organocatalytic enantioselective arylation methods.

**OTHERS**

1,1′-Spirobiindane as a privileged C₂-symmetric spirobicyclic framework has served as one of the most essential backbones of axially chiral organocatalysts and ligands. The two rings of 1,1′-spirobiindanes lie in perpendicular planes and are rigidly connected at a quaternary center through a σ bond. This structural feature makes racemization of axially chiral 1,1′-spirobiindanes impossible, and the asymmetric synthesis of this spirobicyclic framework difficult. Similar to atropisomers, chiral resolution of these racemates was previously the sole method for the enantioselective preparation of versatile axially chiral 1,1′-spirobiindane-7,7′-diols (SPINOLs), which are fundamental synthetic precursors for the construction of chiral catalysts and ligands containing 1,1′-spirobiindane scaffolds. Until our study, no reports tackled the challenge involving the direct construction of SPINOLs through asymmetric catalysis. Our group developed a CPA-catalyzed cyclization reaction for the asymmetric synthesis of SPINOLs in an enantiomerically pure form (Scheme 20). In the presence of SPINOL-derived CPA 82, the cyclization of 81 did not proceed at room temperature. However, (aS)-83 was produced in satisfactory yield and enantioselectivity when the temperature was raised to 120 °C. Under the optimized conditions, electron-donating alkyl and aryl groups on the aryl group were well-tolerated, whereas substrates bearing electron-withdrawing groups generated poor results with respect to yield.

To expand the scope of the substrates, ketal 84 was evaluated under modified conditions. Under the optimal conditions, a broad scope of ketals bearing either electron-rich or electron-deficient substituents at the para position of the phenol performed smoothly to afford C₂-symmetric and non-C₂-symmetric SPINOLs with high enantioselectivities in good to excellent isolated yields (Scheme 20). However, the reaction rate and enantiocontrol were obviously retarded following the introduction of an aryl group at the ortho position of the phenol (Scheme 21). Further screening of the catalysts indicated that (aR)-74 instead of (aS)-82 was the optimal catalyst, which smoothly promoted the reaction with over 90% ee in good yield. The optimal conditions were compatible with different electronic properties of the o-aryl group.

**CONCLUSION**

Axially chiral compounds have received significant attention in recent years because of their wide applications in the total synthesis of natural products, drug discovery, and asymmetric catalysis. Axially chiral biaryl and 1,1′-spirobiindane-derived catalysts and ligands have specifically been the main force in high-performance organic and transition-metal-mediated asymmetric reactions. In addition to the chiral resolution and transition-metal-catalyzed reactions, diverse organocatalytic reactions, which include hydrogen-bonding catalysis and covalent catalysis, are powerful and economically feasible tools for the enantioselective construction of chiral skeletons. Attempts to construct enantiopure axially chiral compounds via asymmetric organocatalysis have achieved fruitful results. Many efficient and applicable enantioselective approaches for axial chirality have been developed, including several completely new organocatalytic strategies. However, a large number of axially chiral backbones still lack efficient preparation methods, especially asymmetric organocatalytic approaches, given their importance and difficulty for chemists. Additionally, numerous potentially useful axially chiral skeletons have yet to be discovered. Our group has been concentrating on the development of efficient methods for the asymmetric
construction of known and unknown useful axially chiral compounds via the use of chiral organocatalysts. We hope to discover some new reactions involving conceptually new synthetic chemistry such as organocatalytic enantioselective aryl C–H functionalization. In the meanwhile, we aim to develop some novel skeletons bearing axial chirality as useful chiral ligands/organocatalysts in the field of asymmetric catalysis or leading compounds in the field of drug discovery. We speculate that the mutual promotion present between organocatalysis and axial chirality will result in an evolutionary step in their development.

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**Notes**

The authors declare no competing financial interest.

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