



Catalytic atroposelective synthesis of C–N axially chiral 5-pyrazolyl indoles via multicomponent tandem cycloaddition

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Abstract

An organocatalytic asymmetric multicomponent tandem cycloaddition has been established for the construction of C–N axially chiral 5-pyrazolyl indole frameworks, which represent a novel class of five-five-membered indole scaffolds. Utilizing 5-aminopyrazoles, cyclohexanediones, and 2,3-diketoester precursors, this methodology constructs the indole ring *de novo* in a single step, demonstrating high atom- and step-economy with water as the exclusive byproduct. The protocol enabled the efficient and high-enantioselective synthesis of structurally diverse C–N axially chiral 5-pyrazolyl indoles. This achievement not only introduces a new member to the family of axially chiral pyrazolyl indoles but also provides an efficient and novel strategy for their construction.

Keywords: Heterocycle, atropisomer, organocatalysis, cycloaddition, axial chirality

1. Introduction

Atropisomers^[1–8] serve as indispensable components in medicinal chemistry^[9–11], functional materials^[12,13], and diverse industrial chemical applications^[14,15]. Among these, axially chiral indoles constitute a significant class of atropisomers, frequently encountered in numerous natural products, biologically active molecules, and as valuable chiral catalysts and ligands (Figure 1a)^[16–22]. In recent years, the catalytic asymmetric synthesis of axially chiral indoles has evolved into a vibrant research area within the synthetic chemistry community (Figure 1b)^[23–28]. Nevertheless, current methodologies are largely restricted to the construction of six-five-membered axially chiral indoles (spanning C–C^[29–36], C–N^[37–45], and N–N atropisomers^[46–49]). In contrast, the catalytic atroposelective assembly of five-five-membered axially chiral indoles remains underdeveloped^[50–62]. This disparity originates from the inherent low rotational barriers and limited configurational stability characteristic of five-five-membered frameworks, rendering the catalytic asymmetric construction of such scaffolds significantly more challenging^[63–67].

Pyrazolyl indoles represent a distinctive class of five-five-membered indole frameworks, serving as the core structure for numerous biologically active molecules (Figure 2a)^[68–71]. Despite their prevalence and significance, the catalytic asymmetric construction of axially chiral pyrazolyl indoles has only been realized very recently, with merely two reports documented to date (Figure 2b). In 2022, Huang and their co-workers achieved the highly enantioselective synthesis of C–C axially chiral 4-pyrazolyl indoles utilizing a dynamic kinetic resolution strategy^[50]. More recently, in 2025, Feng and their collaborators accomplished the construction of C–N axially chiral 4-pyrazolyl indoles via a central-to-axial chirality transfer strategy^[54]. While these two elegant contributions mark significant progress, there remains an urgent need to design novel axially chiral pyrazolyl indole frameworks and to develop highly efficient strategies for their catalytic asymmetric construction.

To address the aforementioned challenges, and drawing upon our extensive experience in chiral indole chemistry^[72–75], we designed a novel class of axially chiral pyrazolyl indole frameworks: the C–N axially chiral 5-pyrazolyl indole scaffolds (Figure 3a)^[76–79].



Concurrently, we devise the *de novo* ring formation strategy as a novel approach for synthesizing these C–N axially chiral pyrazolyl indoles (Figure 3b). Recently, our group achieved the construction of C–N axially chiral pyrazolyl pyrroles through an organocatalyzed asymmetric Paal–Knorr reaction involving 5-aminopyrazoles (Figure 3c)^[80]. Encouraged by these results, we sought to further utilize 5-aminopyrazole as a platform molecule, aiming to construct our newly designed frameworks through the *de novo* formation of the indole ring^[81–86].

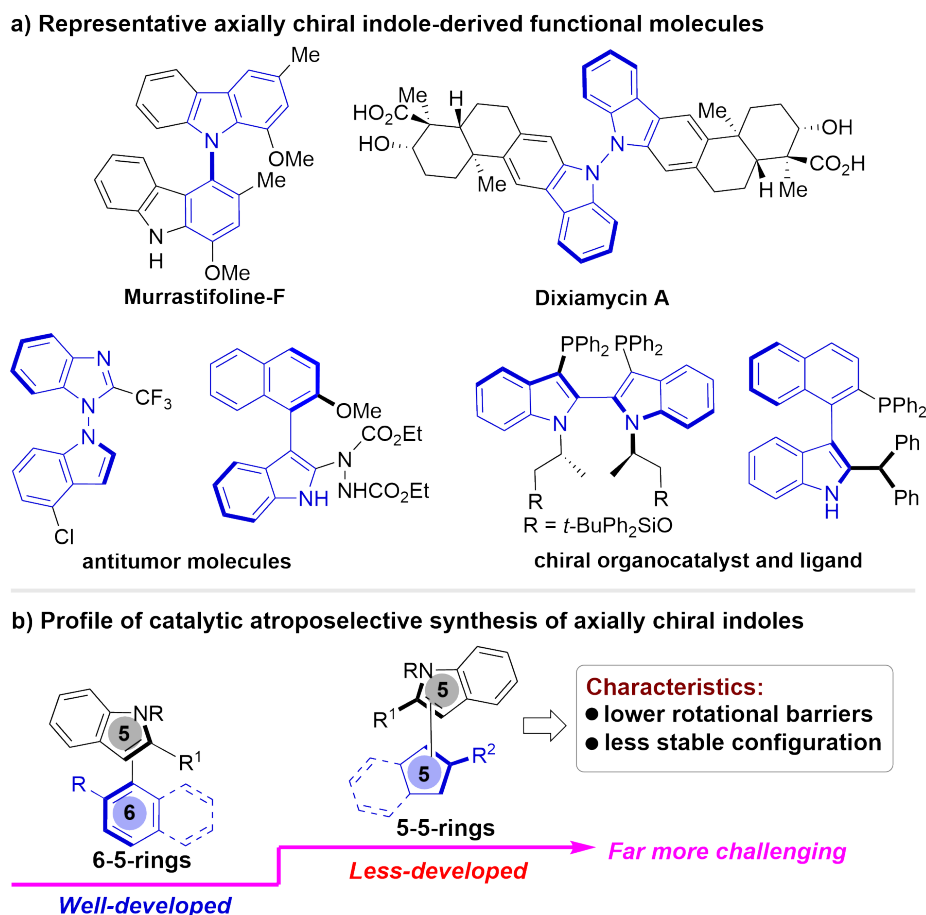


Figure 1. (a) Representative axially chiral indole-derived functional molecules; (b) Profile of catalytic atroposelective synthesis of axially chiral indoles.

Notably, in 2019, Lin and co-workers reported an elegant approach to the enantioselective synthesis of C–N axially chiral aryl indoles via the *de novo* construction of the indole ring, which involved an organocatalyzed asymmetric tandem cycloaddition of anilines (Figure 3d)^[84]. Inspired by this work, we developed an organocatalyzed asymmetric multicomponent tandem cycloaddition for the efficient construction of C–N axially chiral 5-pyrazolyl indole scaffolds (Figure 3e). In this design, 5-aminopyrazoles **1** and cyclohexanediones **2** are envisioned to initially condense in the presence of the chiral phosphoric acid (CPA)^[87–93] to form enamine intermediates **I**. Simultaneously, 2,3-diketoester precursors **3** undergo dehydration to afford intermediates **II**. Intermediates **I** and **II** then participate in this asymmetric (3+2) cycloaddition to yield intermediates **III**, which subsequently undergo dehydration and aromatization processes, ultimately furnishing the C–N axially chiral 5-pyrazolyl indoles **4**. This work will not only introduce a new member to the family of axially chiral pyrazolyl indoles, but also provide an efficient and novel strategy for their construction.

2. Experimental

¹H NMR spectra (400 MHz), ¹³C NMR spectra (100 MHz), ³¹P NMR spectra (162 MHz) and ¹⁹F NMR spectra (376 MHz) were recorded on commercial instruments. High resolution mass spectra (HRMS) were performed on an AB SCIEX TripleTOF 4600. Enantiomeric excesses (ee) were determined by chiral high-performance liquid chromatography (chiral HPLC). The chiral columns used for the determination of enantiomeric excesses by chiral HPLC were Chiralpak columns. Optical rotation values were measured with instruments operating at $\lambda = 589$ nm, corresponding to the sodium D line at the temperatures indicated. The X-ray source used for the single crystal X-ray diffraction analysis of compound **4aag** was GaK α ($\lambda = 1.34139$), and the thermal ellipsoid was drawn at the 50% probability level. Analytical grade solvents for the column chromatography were distilled before use. Substrates **2** commercially available were used directly. Chiral catalysts, substrates **1** and **3** are known compounds and were synthesized according to the literature procedures (see the [Supplementary materials](#) for details).

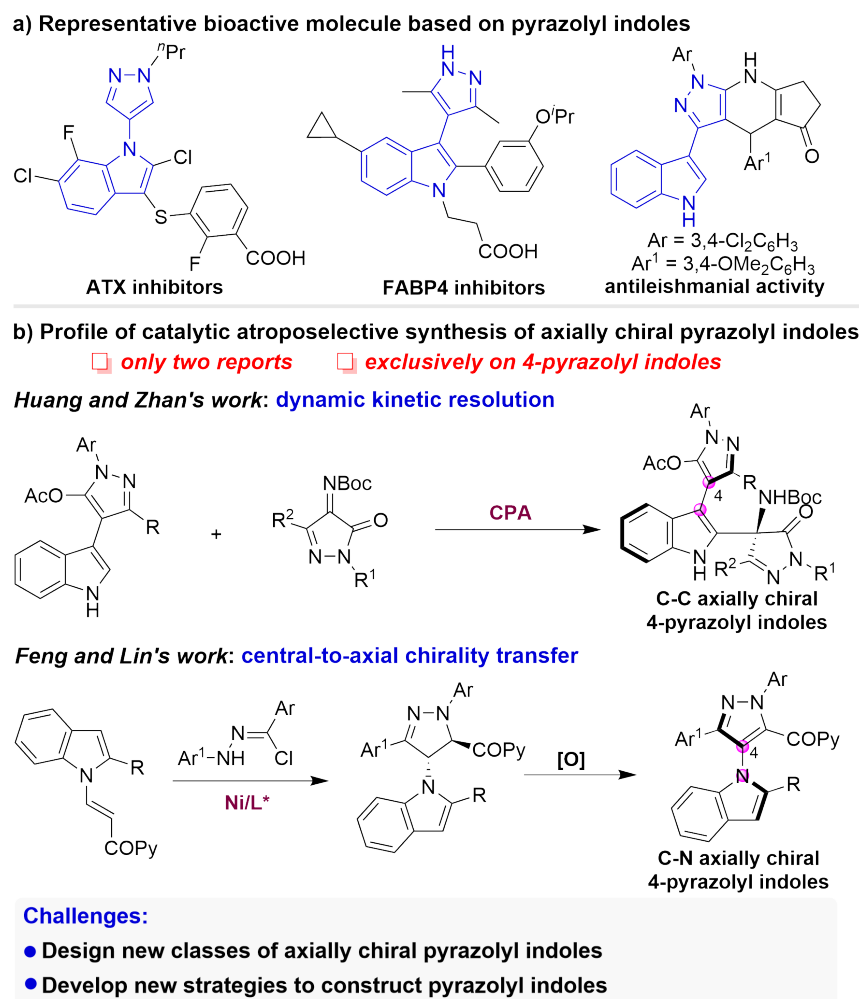


Figure 2. (a) Representative bioactive molecule based on pyrazolyl indoles; (b) Profile of catalytic atroposelective synthesis of axially chiral pyrazolyl indoles.

2.1 Procedure for the synthesis of products 4

In a sealed tube were added 5-aminopyrazole **1** (0.1 mmol), cyclohexanedione **2** (0.1 mmol), 2,3-diketoester precursor **3** (0.1 mmol), chiral phosphoric acid catalyst (*R*)-**5d** (5 mol%), and Na₂SO₄ (50 mg). Subsequently, CHCl₃ (1 mL) was added, and the reaction mixture was stirred at 100 °C for 15 h. The reaction progress was monitored by thin-layer chromatography (TLC). Upon completion of the reaction, the crude mixture was purified by flash column chromatography on silica gel to afford the pure product **4**.

2.2 Synthetic procedure of product 7

Under argon atmosphere, CH₃MgBr (0.2 mL, 3 mol/mL) was added to a Schlenk tube. Then, the solution of **4aab** (51.4 mg, 0.1 mmol) in anhydrous THF (1 mL) was added dropwise to the Schlenk tube at 0 °C. Subsequently, the reaction mixture was stirred at 70 °C for 4 h. After the completion of the reaction indicated by TLC, the reaction mixture was quenched by a saturated ammonium chloride aqueous solution and extracted with ethyl acetate for three times. The combined organic layers were dried and concentrated under reduced pressure to give a residue. Finally, the residue was purified by preparative thin layer chromatography (PE:EA = 4:1) on silica gel to afford pure product **7** in 85% yield (42.5 mg) as a white solid.

2.3 Synthetic procedure of product 8

NaH (60% in oil, 12 mg, 0.3 mmol) and THF (2 mL) were added to a reaction tube at 0 °C. A solution of compound **4aab** (102.7 mg, 0.2 mmol) in THF (1 mL) was then added to the reaction mixture, followed by stirring at room temperature for 30 minutes. Afterward, CH₃I (18.7 μL, 0.3 mmol) was added to the solution at 0 °C, and the reaction mixture was stirred at 0 °C for 12 hours. After the completion of the reaction indicated by TLC, the reaction mixture was quenched by water and extracted with ethyl acetate for three times. The combined organic layers were dried over anhydrous Na₂SO₄ and then concentrated under reduced pressure. The residue was purified through flash column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1) to afford pure product **8** in 86% yield (90.3 mg) as a white solid.

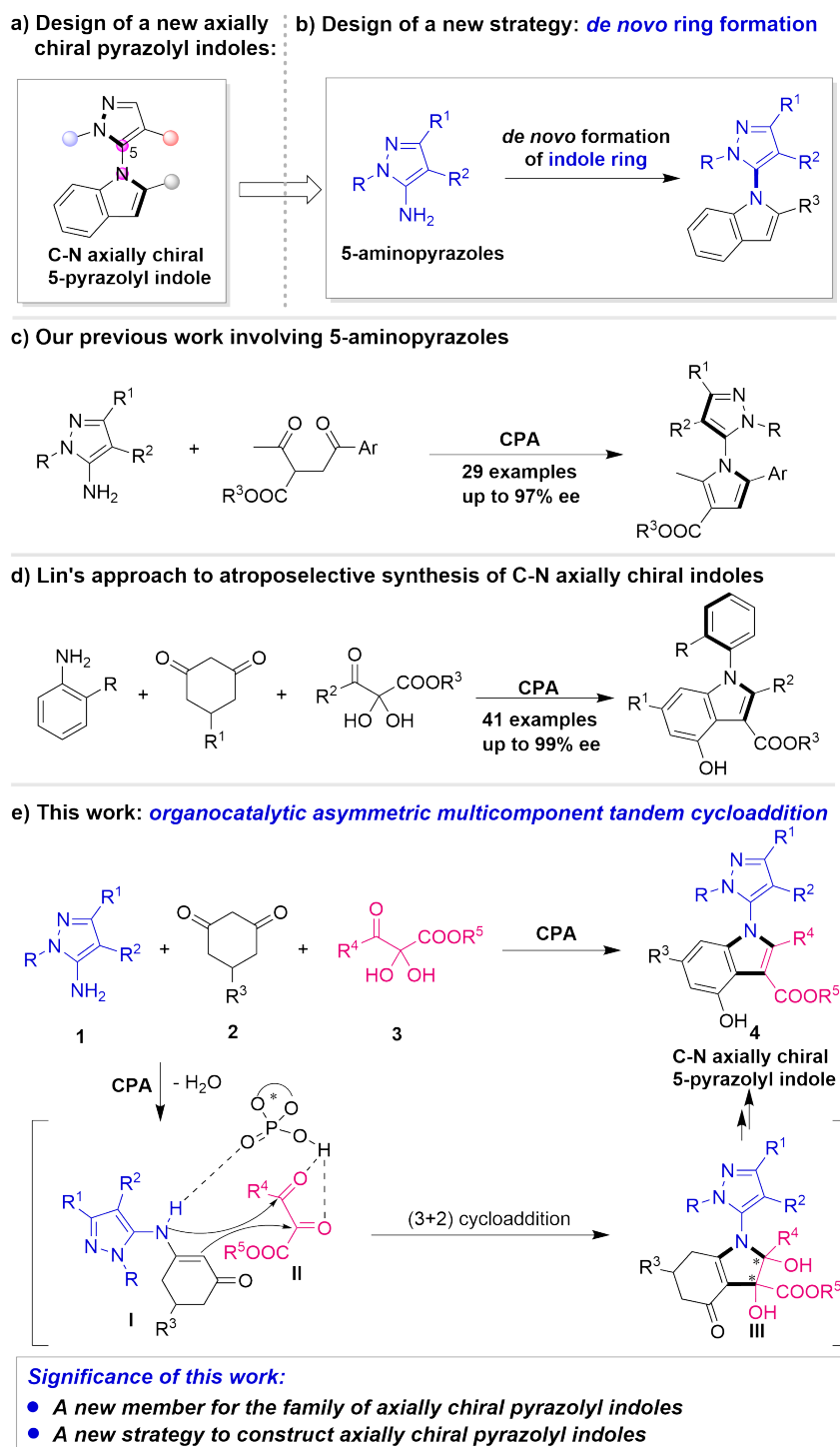


Figure 3. (a) Design of a new axially chiral pyrazolyl indoles; (b) Design of a new strategy; (c) Our previous work involving 5-aminopyrazoles; (d) Lin's approach to atroposelective synthesis of C-N axially chiral indoles; (e) This work.

2.4 Synthetic procedure of product 9

LiAlH₄ (75.9 mg, 2 mmol) and 1.5 mL of THF were added to a reaction tube. Then, the solution of compound 8 (105.5 mg, 0.2 mmol) in 0.5 mL of THF was added to the reaction mixture, which was stirred at 0 °C for 3 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was quenched with 10 mL of H₂O and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over anhydrous Na₂SO₄ and then concentrated under reduced pressure. The residue was purified through flash column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1) to afford pure product 9 in 93% yield (90.3 mg) as a white solid.

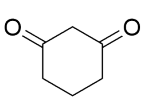
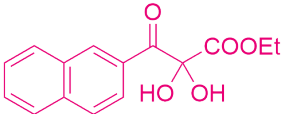
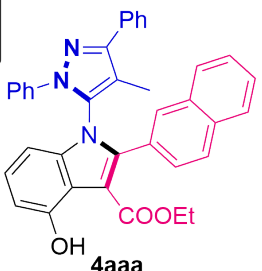
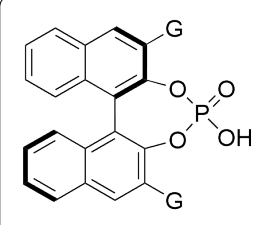
2.5 Synthetic procedure of product 10

Compound **9** (48.6 mg, 0.1 mmol) and EtOAc (2.0 mL) were added to a reaction tube. Then, 2-iodoxybenzoic acid (IBX) (56 mg, 0.2 mmol) was added to the reaction mixture, which was stirred at 80 °C for 7 h. After the completion of the reaction, which was indicated by TLC, the reaction mixture was filtered and concentrated under reduced pressure. The residue was purified through preparative thin layer chromatography on silica gel (petroleum ether/ethyl acetate = 2/1) to afford pure product **10** in 99% yield (48.0 mg) as a white solid.

3. Results and Discussion

To validate the feasibility of our designed organocatalyzed asymmetric multicomponent tandem cycloaddition, we initially attempted the reaction using CPA (*R*)-**5a** as the catalyst and ClCH₂CH₂Cl (DCE) as the solvent (Table 1, entry 1). Encouragingly, we successfully obtained the target C–N axially chiral 5-pyrazolyl indole **4aaa**, albeit with a low yield and moderate enantioselectivity (17% yield, 47% ee). Subsequently, we screened a series of CPAs with different substituents (entries 2–6). The results indicated that CPA (*R*)-**5d** was the most effective (entry 4), delivering excellent enantioselectivity (91% ee). Following this, we evaluated various types of solvents (entries 7–11). It was observed that the reaction exhibited poor solvent compatibility, proceeding efficiently only in DCE and toluene (entries 4 and 7). Moreover, DCE remained the superior solvent for the reaction. We further explored other halogenated solvents (entries 12–13), finding that employing CHCl₃ as the solvent (entry 13) significantly improved the yield to 82% while maintaining excellent enantioselectivity (91% ee). Next, we investigated the effect of reaction temperature (entries 14–15). It was determined that 100 °C (entry 13) still provided the best overall results. Screening of various additives (entries 16–19) revealed that Na₂SO₄ (entry 18) further enhanced both the yield and enantioselectivity (92% yield, 92% ee). We also found that adjusting the stoichiometric ratio of reactants to 1:1:1 (entry 20) led to a marginal improvement in both yield and enantioselectivity (96% yield, 93% ee). Furthermore, the influence of catalyst loading was investigated. Reducing the catalyst loading to 2 mol% (entry 21) led to a significant decrease in yield (66%) and a slight drop in enantioselectivity (91% ee). In contrast, increasing the catalyst amount to 10 mol% showed no impact on either yield or enantioselectivity (entry 22). Finally, the effect of water on the reaction was examined (entries 23–24). Performing the reaction in the absence of Na₂SO₄ resulted in a substantial decrease in yield and a slight reduction in enantioselectivity (entry 23). Besides, the further addition of 10 equiv. of water showed no further impact on either the yield or the enantioselectivity (entry 24). Based on these studies, the reaction conditions outlined in entry 20 were identified as the optimal conditions.

Table 1. Optimization of reaction conditions^a.

 1a +  2a +  3a $\xrightarrow[5\text{ mol\% cat, solvent, additives, } T\text{ }^{\circ}\text{C}]{}$  4aaa  (<i>R</i>)-5a, G = 1-naphthyl (<i>R</i>)-5b, G = 2-naphthyl (<i>R</i>)-5c, G = 9-anthracenyl (<i>R</i>)-5d, G = 9-phenanthrenyl (<i>R</i>)-5e, G = 4-ClC₆H₄ (<i>R</i>)-5f, G = 2,4,6-(<i>i</i>Pr)₃C₆H₂							
entry	Cat.	solvent	T (°C)	additives	1a:2a:3a	yield (%) ^b	ee (%) ^c
1	(<i>R</i>)- 5a	DCE	100	5 Å MS	1:1:2	17	47
2	(<i>R</i>)- 5b	DCE	100	5 Å MS	1:1:2	8	15
3	(<i>R</i>)- 5c	DCE	100	5 Å MS	1:1:2	32	86
4	(<i>R</i>)- 5d	DCE	100	5 Å MS	1:1:2	59	91
5	(<i>R</i>)- 5e	DCE	100	5 Å MS	1:1:2	trace	/
6	(<i>R</i>)- 5f	DCE	100	5 Å MS	1:1:2	25	78
7	(<i>R</i>)- 5d	toluene	100	5 Å MS	1:1:2	25	64

8	(R)- 5d	THF	100	5 Å MS	1:1:2	N.R.	/
9	(R)- 5d	CH ₃ CN	100	5 Å MS	1:1:2	N.R.	/
10	(R)- 5d	acetone	100	5 Å MS	1:1:2	N.R.	/
11	(R)- 5d	EtOAc	100	5 Å MS	1:1:2	N.R.	/
12	(R)- 5d	CCl ₄	100	5 Å MS	1:1:2	29	85
13	(R)- 5d	CHCl ₃	100	5 Å MS	1:1:2	82	91
14	(R)- 5d	CHCl ₃	80	5 Å MS	1:1:2	41	91
15	(R)- 5d	CHCl ₃	120	5 Å MS	1:1:2	81	91
16	(R)- 5d	CHCl ₃	100	3 Å MS	1:1:2	53	90
17	(R)- 5d	CHCl ₃	100	4 Å MS	1:1:2	11	61
18	(R)- 5d	CHCl ₃	100	Na ₂ SO ₄	1:1:2	92	92
19	(R)- 5d	CHCl ₃	100	MgSO ₄	1:1:2	89	92
20	(R)- 5d	CHCl ₃	100	Na ₂ SO ₄	1:1:1	96	93
21 ^d	(R)- 5d	CHCl ₃	100	Na ₂ SO ₄	1:1:1	66	91
22 ^e	(R)- 5d	CHCl ₃	100	Na ₂ SO ₄	1:1:1	95	93
23	(R)- 5d	CHCl ₃	100	/	1:1:1	69	91
24 ^f	(R)- 5d	CHCl ₃	100	/	1:1:1	69	90

^a: Unless indicated otherwise, the reaction was carried out at 0.1 mmol scale and catalyzed by 5 mol% **Cat** in CHCl₃ (1 mL) at T °C with adductives (50 mg) for 15 h; ^b: Isolated yield; ^c: The ee values were determined by HPLC; ^d: 2 mol% **Cat**; ^e: 10 mol% **Cat**; ^f: With water (10.0 equiv.); DCE: ClCH₂CH₂Cl.

With the optimal conditions established, we proceeded to investigate the substrate scope of this catalytic asymmetric multicomponent tandem cycloaddition. We initially focused on exploring the scope of 2,3-diketoester precursors **3** (Figure 4). It was found that 2,3-diketoester precursors **3** bearing various Ar/R substituents were all amenable to this reaction, affording the products **4** in generally high yields (up to 96%) and excellent enantioselectivities (up to 94% ee). Specifically, a phenyl group proved to be a suitable Ar substituent of substrate **3b**, affording the corresponding product **4aab** with 80% yield and 93% ee. Substrates **3c–3i**, bearing either electron-withdrawing or electron-donating groups at the *meta*- or *para*-positions of the phenyl ring, underwent the reaction smoothly to furnish the respective C–N axially chiral 5-pyrazolyl indoles **4aac–4aai** in both high yields and excellent enantioselectivities. Heteroaryl-substituted substrate **3j** also proved to be a suitable substrate for this reaction; however, its performance was marginally lower than that of aryl-substituted substrates **3a–3i**, furnishing product **4aaj** in a moderate yield of 52% and a good enantioselectivity of 85% ee. Furthermore, when the ethyl ester group of substrate **3b** was replaced with a methyl ester group (substrate **3k**), the reaction also proceeded smoothly, yielding the corresponding product **4aak** (57% yield, 91% ee). The moderate yields observed in these cases were attributed to the formation of inseparable mixtures during the reaction. In addition, the absolute configuration of product **4aag** was determined to be (*R*_a) by single-crystal X-ray diffraction analysis (Supplementary materials).

Subsequently, we extended our investigation to evaluate the versatility of 5-aminopyrazoles **1** and cyclohexanediones **2** (Figure 5). In general, a broad array of 5-aminopyrazoles **1** bearing diverse R and Ar groups proved to be compatible with this catalytic asymmetric multicomponent tandem cycloaddition, providing the corresponding C–N axially chiral 5-pyrazolyl indoles **4** in moderate to good yields (67–95%) with high enantioselectivities (85–95% ee). Specifically, 5-aminopyrazoles **1b–1i**, featuring *ortho*-, *meta*-, or *para*-substituted phenyl rings as the R substituent, served as suitable substrates to afford products **4bab–4iab** with high enantioselectivities. Notably, alkyl substituents, such as benzyl, cyclohexyl, and *tert*-butyl groups, also served as effective R substituents for substrates **1j–1l**, undergoing the tandem cyclization to generate the respective products **4jab–4lab** with good enantioselectivity. Furthermore, substrates **1m–1s**, possessing phenyl Ar groups with varying electronic properties at different positions, proceeded smoothly to furnish the corresponding products **4mab–4sab** in good yields and enantioselectivities. To our delight, heteroaromatic motifs, such as the thienyl group (**1t**), were also accommodated, successfully delivering the desired product **4tab**. Regarding the cyclohexanediones **2**, substrate **2b** substituted with an alkyl group served as an effective substrate, delivering the corresponding product **4abb** efficiently.

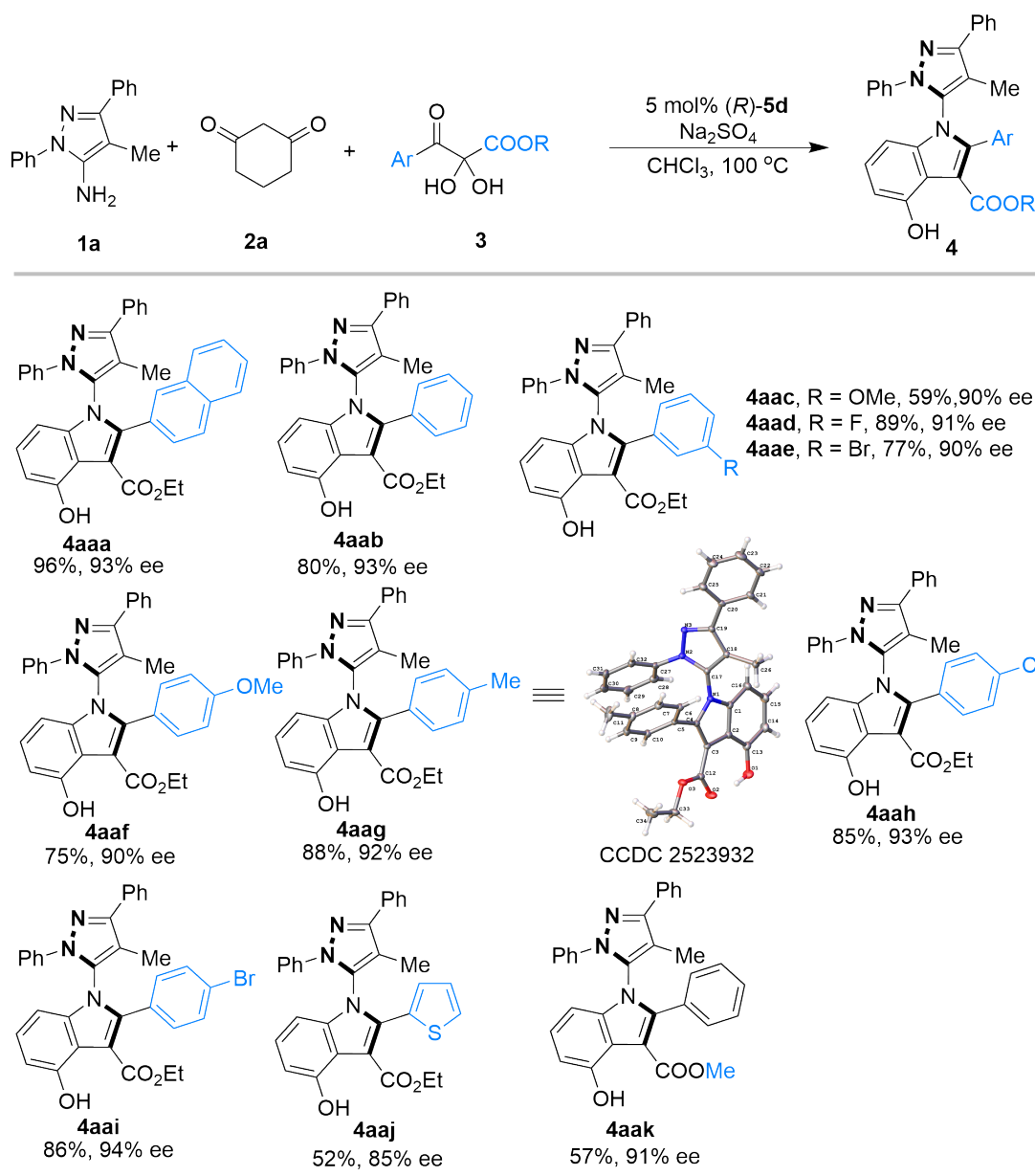


Figure 4. Substrate scope of 2,3-diketoester precursors **3**. *: Unless indicated otherwise, the reaction was carried out at 0.1 mmol scale and catalyzed by 5 mol% (*R*)-**5d** in $CHCl_3$ (1 mL) at 100 °C with Na_2SO_4 (50 mg) as additives for 15 h, and the molar ratio of **1a**:**2a**:**3** was 1:1:1. Isolated yield. The ee values were determined by HPLC. HPLC: high-performance liquid chromatography.

We further explored the scope of different cyclic ketones as substrates **2** (Figure 6). Cyclohexanone (**2c**) was found to be a competent substrate for this catalytic asymmetric multicomponent tandem cycloaddition, providing the corresponding product **4acb** in 50% yield with an acceptable enantioselectivity of 74% ee. However, when 1,3-cyclopentanedione (**2d**) was employed as the substrate, the desired product could not be obtained.

To elucidate the reaction mechanism of this catalytic asymmetric multicomponent tandem cycloaddition, we conducted a series of control experiments (Figure 7a). We directly employed pre-synthesized enamine **6** as a substrate to react with 2,3-diketoester precursor **3b** under optimal conditions. This reaction proceeded smoothly, affording product **4aab** in high yield and excellent enantioselectivity (eq 1). Furthermore, when 5-aminopyrazole **1a** and cyclohexanedione **2a** were reacted under optimal conditions for 8 hours, TLC monitoring indicated complete conversion of both starting materials to enamine **6**. Subsequently, the addition of substrate **3b** and continuation of the reaction for an additional 7 hours afforded product **4aab** in 79% yield and 92% ee (eq 2). These results unequivocally demonstrated that enamine **6** is a crucial intermediate in this reaction. Moreover, as we initially envisioned, in this catalytic asymmetric multicomponent tandem cycloaddition, substrates **1** and **2** first condensed to form the enamine intermediates, which then underwent a cycloaddition reaction with substrates **3**.

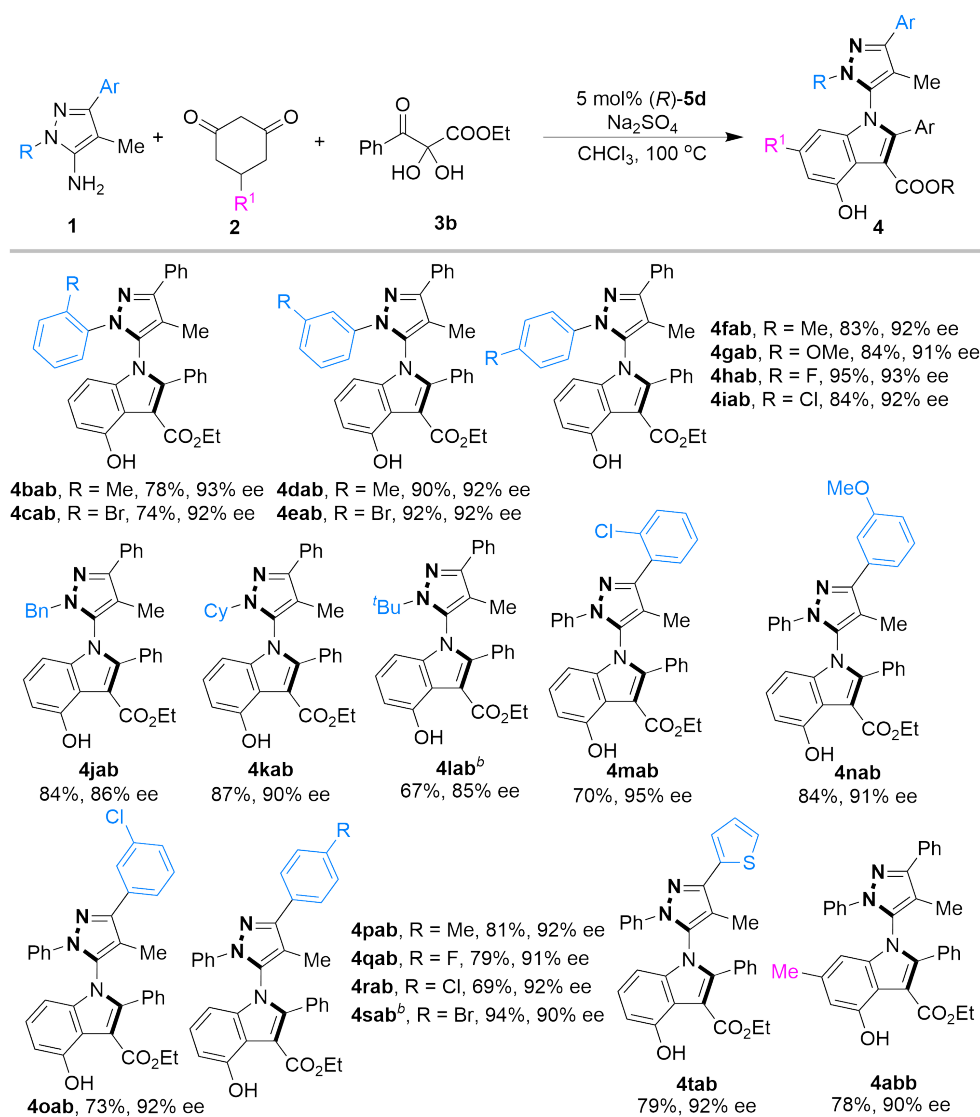


Figure 5. Substrate scope of 5-aminopyrazoles **1** and cyclohexanediones **2**. ^a: Unless indicated otherwise, the reaction was carried out at 0.1 mmol scale and catalyzed by 5 mol% (*R*)-**5d** in CHCl₃ (1 mL) at 100 °C with Na₂SO₄ (50 mg) as additives for 15 h, and the molar ratio of **1:2:3b** was 1:1:1. Isolated yield. The ee values were determined by HPLC; ^b: 30 mol% (*R*)-**5d**; HPLC: high-performance liquid chromatography.

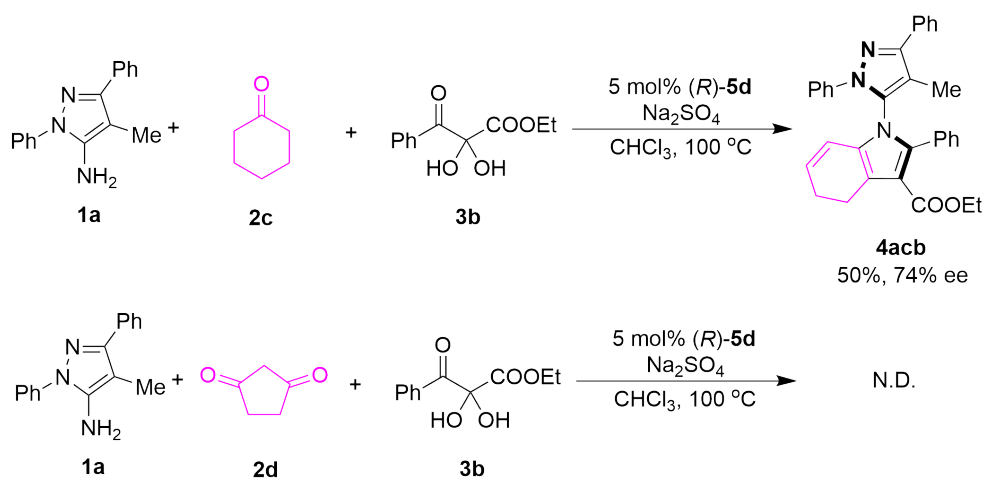
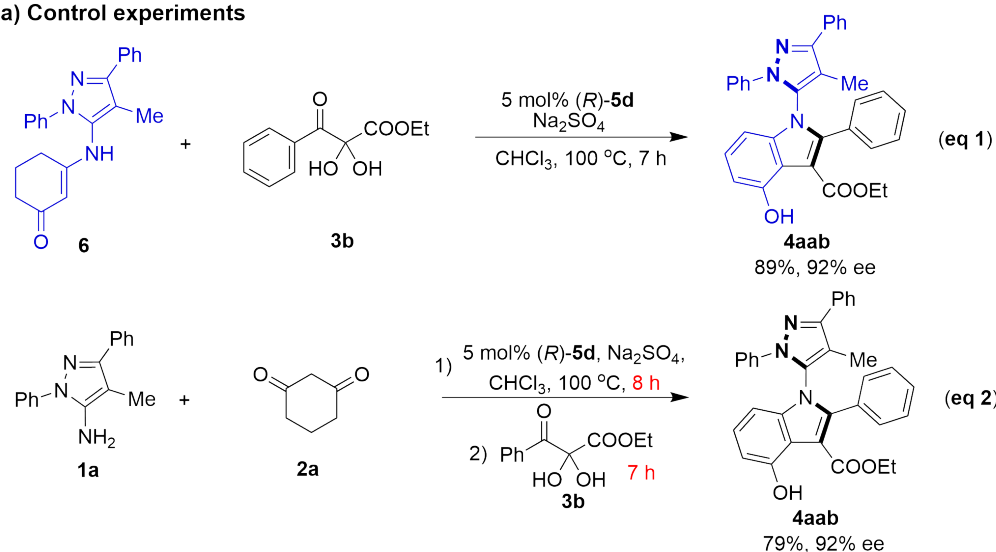


Figure 6. Investigation on using different cyclic ketones as substrates **2**.

a) Control experiments



b) Proposed reaction pathway

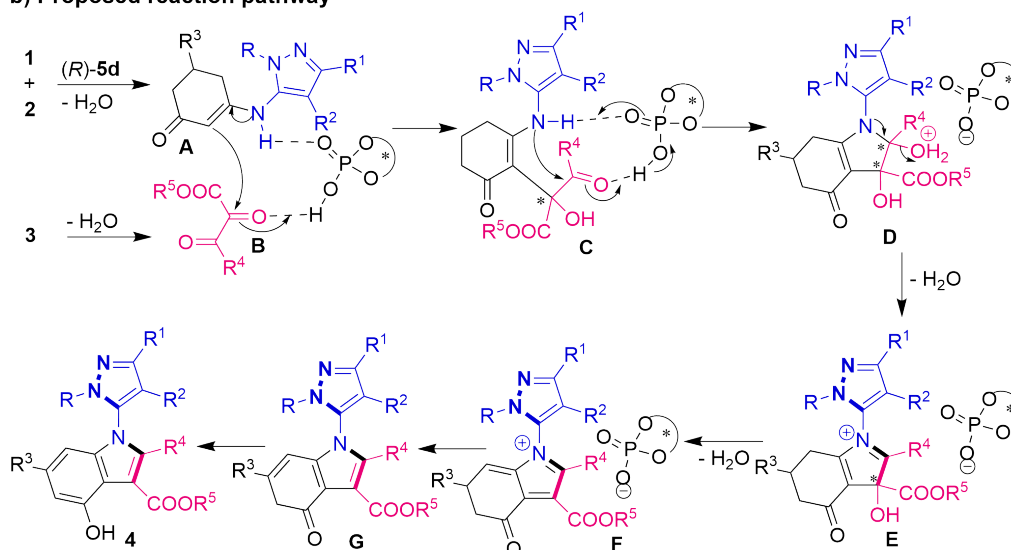


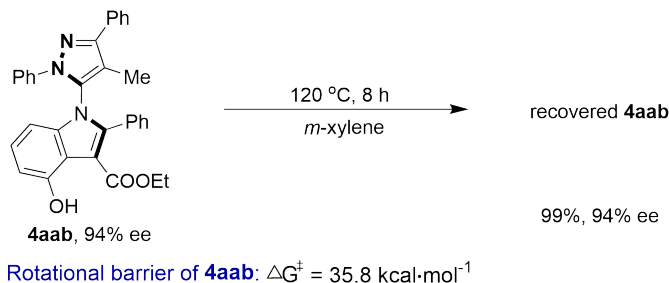
Figure 7. (a) Control experiments; (b) Suggested reaction pathway.

Based on these experimental results, we proposed a plausible mechanism and the activation mode for this reaction (Figure 7b). Under the action of CPA (*R*)-5d, 5-aminopyrazoles **1** and cyclohexanediones **2** underwent dehydration–condensation to form enamine intermediates **A**. Concurrently, 2,3-diketoester precursors **3** underwent dehydration to form 2,3-diketoester intermediates **B**. CPA (*R*)-5d then activated both intermediates **A** and intermediates **B** simultaneously through hydrogen bonding, promoting the asymmetric addition to generate intermediates **C** with a newly formed stereocenter. Subsequently, intermediates **C**, activated by CPA (*R*)-5d, underwent intramolecular cycloaddition via amine attack on the carbonyl group, leading to intermediates **D** containing two stereocenters. During the subsequent dehydration and aromatization steps involving intermediates **E**, **F**, and **G**, the established central chirality was efficiently transferred to axial chirality. Finally, a subsequent isomerization process delivered the C–N axially chiral 5-pyrazolyl indoles **4**.

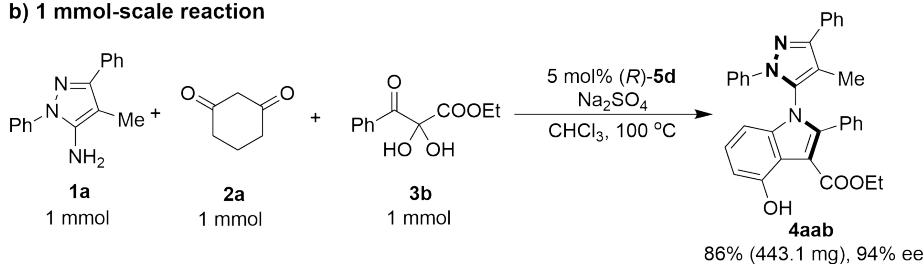
To assess the configurational stability of the newly designed C–N axially chiral 5-pyrazolyl indoles, a racemization experiment was conducted (Figure 8a). Product **4aab**, after stirring at 120 °C for 8 hours, maintained excellent chemical and configurational stability, being recovered with quantitative recovery (99% recovery) and retaining enantioselectivity (94% ee). In addition, the rotational barrier of product **4aab** was theoretically calculated as 35.8 kcal mol^{−1}, further supporting the high configurational stability of these C–N axially chiral 5-pyrazolyl indoles. To demonstrate the synthetic utility of this methodology, a 1 mmol scale-up reaction was performed (Figure 8b). The transformation proved to be highly robust upon scaling, delivering product **4aab** in 86% yield with 94% ee, which was consistent with the results obtained on a 0.1 mmol scale. Furthermore, several synthetic transformations of the obtained products were also explored (Figure 8c). Product **4aab** underwent nucleophilic addition with a Grignard reagent to afford the

corresponding tertiary alcohol derivative **7** with preservation of enantiopurity. Additionally, the phenolic hydroxyl group of product **4aab** could be methylated to afford compound **8** in 86% yield. Subsequent reduction of the ester group in compound **8** with LiAlH_4 efficiently furnished the C–N axially chiral benzylic alcohol derivative **9**, which was further oxidized to access the axially chiral indole-3-carboxaldehyde derivative **10**. Notably, the enantioselectivity was well-maintained throughout this sequence of transformations.

a) Study on the configurational stability



b) 1 mmol-scale reaction



c) Synthetic transformation

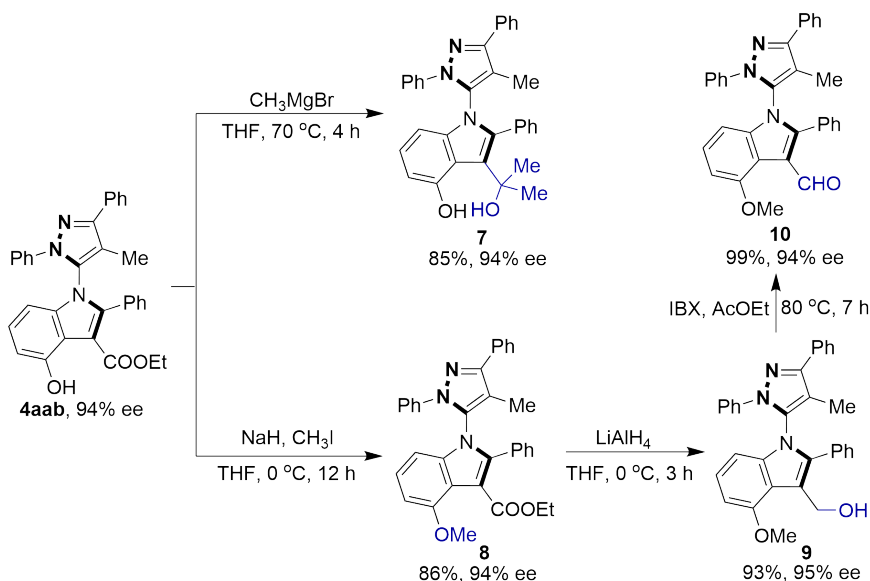


Figure 8. (a) Study on the configurational stability; (b) One mmol scale reaction; (c) Synthetic transformation.

4. Conclusion

In summary, we have established an organocatalytic asymmetric multicomponent tandem cycloaddition for the construction of C–N axially chiral 5-pyrazolyl indole frameworks, representing a novel class of five-five-membered indole scaffolds. Utilizing 5-aminopyrazoles, cyclohexanediones, and 2,3-diketoeester precursors, this methodology constructs the indole ring de novo in a single step, demonstrating high atom- and step-economy with water as the exclusive byproduct. The protocol enabled the efficient and high-enantioselective synthesis of structurally diverse C–N axially chiral 5-pyrazolyl indoles (up to 96% yield, 95% ee). Mechanistic insights were gained through control experiments, and the resulting products demonstrated outstanding configurational stability. Further validation of the practical utility of this reaction was achieved through scale-up experiments and exploration of synthetic transformations. This achievement not only introduces a new member to the family of axially chiral pyrazolyl indoles but also provides an efficient and novel strategy for their construction.

Supplementary materials

The supplementary material for this article is available at: [Supplementary materials](#).

Declarations

Authors contribution

Chen YY, Xue J: Investigation, formal analysis.

Zhang YC, Shi F: Conceptualization, methodology, writing-original draft, writing-review & editing.

Conflicts of interest

Feng Shi is an Editorial Board Member of *Chiral Chemistry*. Other authors declared that there are no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

The data reported in this paper are available in the main text or [Supplementary materials](#), including methods, NMR data, HRMS data, HPLC spectra Crystal data and NMR spectra. Crystallographic data for the structures reported in this article have been deposited at the Cambridge Crystallographic Data Centre, under deposition numbers CCDC 2523932 (**4aag**).

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