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Axially Chiral Aryl-Alkene-Indole Framework: A Nascent Member of the Atropisomeric Family and Its Catalytic Asymmetric Construction

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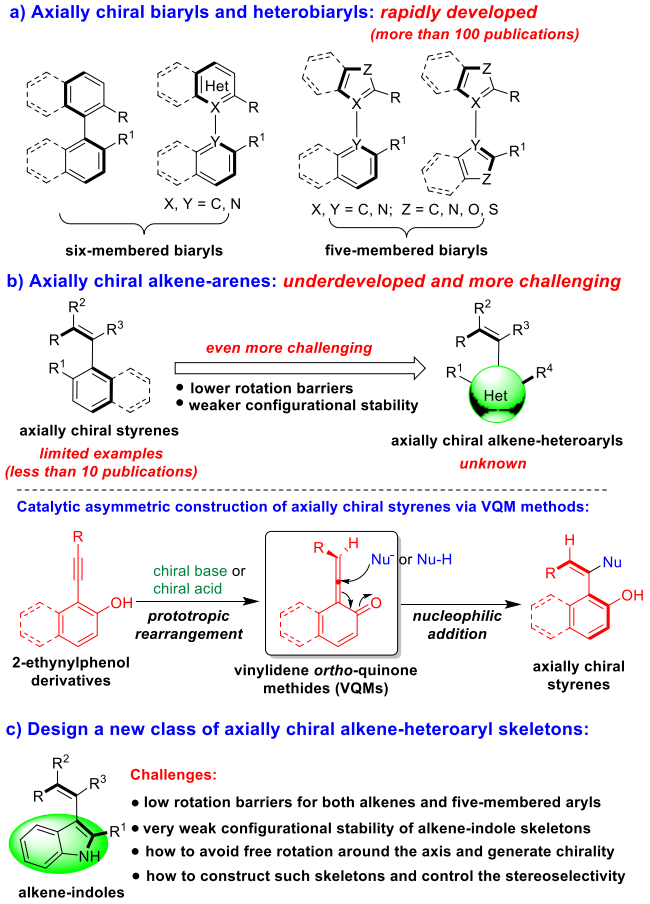
Summary of main observation and conclusion A new class of axially chiral aryl-alkene-indole frameworks has been designed, and the first catalytic asymmetric construction of such scaffolds has been established by the strategy of organocatalytic (*Z*/*E*)-selective and enantioselective (4+3) cyclization of alkynyl-2-indolylmethanols with 2-naphthols or phenols (all >95:5 *E*/*Z*, up to 98% yield, 97% ee). This reaction also represents the first catalytic asymmetric construction of axially chiral alkene-heteroaryl scaffolds, which will add a new member to the atropisomeric family. This approach has not only confronted the great challenges in constructing axially chiral alkene-heteroaryl scaffolds but also provided a powerful strategy for the enantioselective construction of axially chiral aryl-alkene-indole frameworks.

Background and Originality Content

Axial chirality is one important feature of nature because axially chiral frameworks constitute the core structures of many natural products,[1] pharmaceutically relevant molecules[2] and chiral ligands or catalysts.[3] In this context, the catalytic asymmetric construction of axially chiral frameworks has received intensive attention from scientists,[4-5] and many elegant approaches have been developed for the enantioselective construction of axially chiral biaryl[6-9] and heterobiaryl[10-11] frameworks, which have become the majority of the axially chiral frameworks (Scheme 1a).

However, in sharp contrast, axially chiral alkene-arenes, as an important class of atropisomers, have rarely been investigated.[12] This is because the catalytic asymmetric construction of axially chiral alkene-arene frameworks is much more challenging than the construction of axially chiral biaryls due to the low rotational barriers, low configurational stability and difficulty in controlling the (*E*/*Z*)-selectivity and enantioselectivity.[13-14] As a result, there are only limited examples on the catalytic asymmetric construction of axially chiral alkene-arene frameworks, and all of these structures are confined to axially chiral styrene derivatives (Scheme 1b).[13-14] For example, the groups of Yan and Tan utilized the strategy of organocatalytic addition reactions to vinylidene *ortho*-quinone methides (VQMs).[14c-14e] In the presence of a chiral base or acid, 2-ethynylphenol derivatives underwent a prototropic rearrangement to give highly active VQM intermediates, which were readily attacked by nucleophiles such as sulfinate anion, benzenesulfonic acid and naphthols to afford axially chiral styrene derivatives.

In contrast, axially chiral alkene-heteroaryl frameworks have scarcely been discovered in the literature,[15] and the catalytic asymmetric construction of such frameworks is an unknown chemistry, which is challenging because the rotational barrier and conformational stability of heteroaryl scaffolds, especially five-membered scaffolds, are much lower than those of six-membered aryls such as phenyl and naphthyl.[4g-4h] Therefore, it has become an urgent task to design a new class of axially chiral alkene-heteroaryl frameworks and develop innovative methods for the catalytic asymmetric construction of such frameworks.



Scheme 1 Profile of catalytic asymmetric construction of axially chiral frameworks and design of a new class of axially chiral alkene-heteroaryl frameworks

Indole-based axially chiral skeletons have recently attracted increasing attention from chemists due to the unique properties of the indole ring and the importance of axially chiral indole-containing scaffolds.[16-17] To fulfill the above-mentioned task, we designed alkene-indoles as a new class of axially chiral

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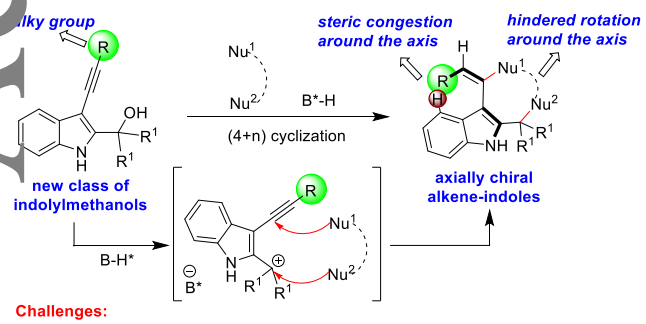
alkene-heteroaryl frameworks (Scheme 1c). Nevertheless, there are great challenges in the catalytic asymmetric construction of axially chiral alkene-indole frameworks. For example, it is well known that both axially chiral alkenes and five-membered biaryls have low rotational barriers.[4g-4h,13-14] Accordingly, the integration of an alkene group with a five-membered indole ring will make the rotational barrier of alkene-indole frameworks extremely low, which will result in the very low configurational stability of such skeletons. Hence, it is a formidable challenge to hinder free rotation around the axis and generate the axial chirality of the alkene-indole framework. More importantly, even if the axial chirality of alkene-indole frameworks can be generated, how to construct such skeletons in a catalytic asymmetric manner and how to control the (*E*/*Z*)-selectivity as well as the enantioselectivity of the alkene-indole structures remain enormous challenges.

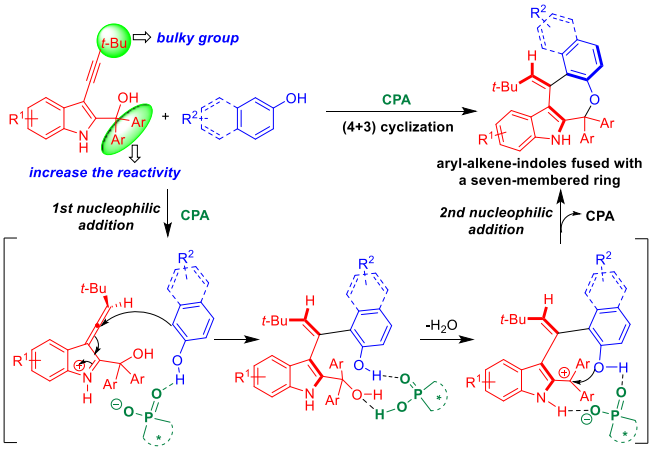
To confront these challenges, we conceived a strategy for the catalytic asymmetric construction of axially chiral alkene-indole frameworks and avoiding free rotation around the axis (Scheme 2). Indolylmethanols have proven to be versatile reactants for constructing indole-containing scaffolds,[18-19] and based on our experience with indolylmethanols,[16c,17a,20] we envision that 3-alkynyl-2-indolylmethanols as a new class of indolylmethanols can serve as building blocks for constructing alkene-indole frameworks. In detail, the incorporation of an alkyne functionality bearing a bulky terminal R group in the structure of 2-indolylmethanol generates the desired C=C bond when using a nucleophile to attack the alkynyl group. In principle, in the presence of a chiral Brønsted acid (B-H*), 3-alkynyl-2-indolylmethanols should act as 1,4-dielectrophiles that can be attacked by nucleophiles. When cyclic dinucleophiles are employed as reaction partners, a (4+n) cyclization will occur to construct the alkene-indole framework with axial chirality. This is because the steric congestion between the R group and the H atom as well as the constructed cyclic framework will lead to hindered rotation around the alkene-indole axis, thus avoiding the free rotation around the axis and generating the axial chirality of the alkene-indole framework. Although this strategy seems feasible, some challenging issues still remain, including (1) the design and synthesis of 3-alkynyl-2-indolylmethanols bearing suitable R/R^1 groups to act as competent 1,4-dielectrophiles; (2) the selection of reactive dinucleophiles that can be easily activated by B*-H; and (3) controlling the regioselectivity of nucleophilic addition, the (*Z*/*E*)-selectivity of the generated alkene geometry and the enantioselectivity of the axially chiral alkene-indole framework.

Scheme 2 Our strategy for constructing axially chiral alkene-indole frameworks



To address these challenging issues, we designed a chiral phosphoric acid[21] (CPA)-catalyzed asymmetric (4+3) cyclization of 3-alkynyl-2-indolylmethanols with 2-naphthols or phenols (Scheme 3). In the design of the 3-alkynyl-2-indolylmethanols, the *t*-Bu group was selected as a terminal bulky group for the alkyne functionality, which will generate steric congestion around the axis. In addition, the installation of two aromatic groups at the benzylic position of the 2-indolylmethanols will increase the reactivity of such reactants by stabilizing the carbocation intermediate. These structural features will make this class of 3-alkynyl-2-indolylmethanols act as competent 1,4-dielectrophiles. In the design of the reaction, the selection of 2-naphthols or phenols as reactive 1,3-dinucleophiles is based on the consideration that these reactants can easily be activated by CPA to perform two nucleophilic additions on 3-alkynyl-2-indolylmethanols, thus accomplishing the (4+3) cyclization to construct the axially chiral aryl-alkene-indole framework. CPA is a suitable B*-H because CPA can generate hydrogen-bonding or ion-pairing interactions with the two reaction partners, therefore controlling the regioselectivity, (*Z*/*E*)-selectivity and enantioselectivity of the reaction.

Scheme 3 Design of catalytic asymmetric (4+3) cyclizations to construct axially chiral aryl-alkene-indole frameworks



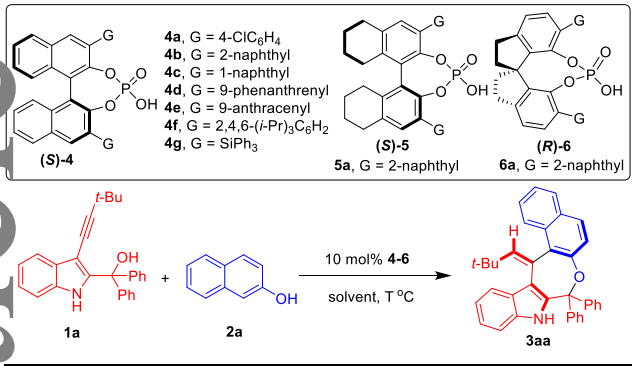
Herein, we report the design of a new class of axially chiral aryl-alkene-indole frameworks and the first catalytic asymmetric construction of such scaffolds by the strategy of organocatalytic (*Z*/*E*)-selective and enantioselective (4+3) cyclization of 3-alkynyl-2-indolylmethanols with 2-naphthols or phenols (all >95:5 *E*/*Z*, up to 98% yield, 97% ee).

Results and Discussion

Initially, the reaction of 3-alkynyl-2-indolylmethanol **1a** with 2-naphthol **2a** was employed to test the possibility of our design (Table 1). Gratifyingly, under the catalysis of CPA **4a** in toluene at 10 °C, the designed (4+3) cyclization smoothly occurred to give axially chiral aryl-alkene-indole product **3aa** in a high yield of 87% and a good enantioselectivity of 86% ee (entry 1). The screening of BINOL-derived CPA **4** (entries 1-7) revealed that CPA **4b** could catalyze the reaction with the highest enantioselectivity (entry 2). Changing the backbone of CPA **4b** to H_8-BINOL and SPINOL (entries 8-9) led to the discovery that H_8-BINOL-derived CPA **5a** was the best catalyst, which promoted the reaction with a higher enantioselectivity of 93% ee (entry 8). The subsequent evaluation of solvents (entries 8 and 10-12) found that the reaction could only occur in toluene and dichloroethane (entries 8 and 10), and toluene was better than dichloroethane in terms of controlling the reactivity and enantioselectivity. The variation in reaction temperature (entries 8 and 13-15) indicated that 30 °C was a more suitable reaction temperature than 10 °C with regard to the yield (entry 14 vs 8). Finally, slightly modulating the molar ratio of the

reactants (entries 16-18) led to the optimal reaction conditions (entry 17), which could offer axially chiral product **3aa** in a high yield of 97% and an excellent enantioselectivity of 95% ee. Notably, in all cases, only the (*E*)-isomer of **3aa** was observed, which implied that this reaction had a complete (*E*/*Z*)-selectivity.

Table 1 Optimization of reaction conditions[a]

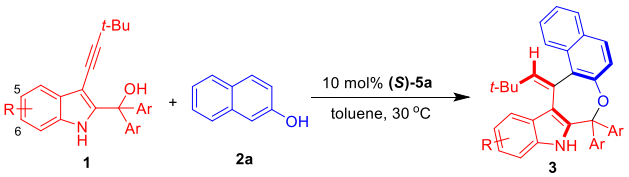


entry	Cat.	solvent	T (°C)	yield (%)[b]	ee (%)[c]
1	**4a**	toluene	10	87	86
2	**4b**	toluene	10	88	88
3	**4c**	toluene	10	trace	-
4	**4d**	toluene	10	69	87
5	**4e**	toluene	10	trace	-
6	**4f**	toluene	10	trace	-
7	**4g**	toluene	10	trace	-
8	**5a**	toluene	10	91	93
9	**6a**	toluene	10	44	50
10	**5a**	DCE	10	69	77
11	**5a**	EtOAc	10	N.R.	-
12	**5a**	CH_3CN	10	N.R.	-
13	**5a**	toluene	-10	62	87
14	**5a**	toluene	30	96	93
15	**5a**	toluene	50	99	76
16[d]	**5a**	toluene	30	90	88
17[e]	**5a**	toluene	30	97	95
18[f]	**5a**	toluene	30	99	93

[a]Unless otherwise indicated, the reaction was carried out on a 0.1 mmol scale and catalyzed by 10 mol% **4-6** in solvent (1 mL) for 12 h, and the molar ratio of **1a**:**2a** was 1:1.2. [b]Isolated yield and only the (*E*)-isomer was observed in all cases. [c]The *ee* value was determined by HPLC. [d]The molar ratio of **1a**:**2a** was 1:2. [e]The molar ratio of **1a**:**2a** was 1.2:1. [f]The molar ratio of **1a**:**2a** was 2:1. DCE = $ClCH_2CH_2Cl$. N.R. = No reaction.

With the optimal reaction conditions known, we then studied the substrate scope of 3-alkynyl-2-indolylmethanols **1** for the construction of axially chiral aryl-alkene-indole frameworks. As listed in Table 2, this catalytic asymmetric (4+3) cyclization was amenable to a series of 3-alkynyl-2-indolylmethanols **1** with various R/Ar substituents at different positions, which gave rise to the axially chiral aryl-alkene-indole derivatives **3** in moderate to high yield, perfect (*E*/*Z*)-selectivity and excellent enantioselectivity.

Table 2 Substrate scope of 3-alkynyl-2-indolylmethanols **1**[a]

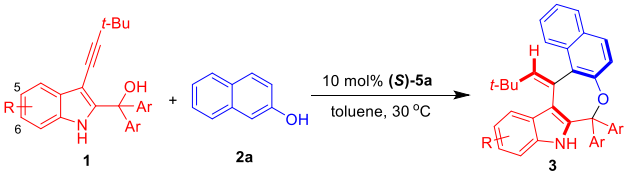


entry	R/Ar (**1**)	**3**	yield (%)[b]	*E*/*Z*[c]	ee (%)[d]
1	H/Ph (**1a**)	**3aa**	97	>95:5	95
2	5-Me/Ph (**1b**)	**3ba**	69	>95:5	91
3	5-OMe/Ph (**1c**)	**3ca**	56	>95:5	90
4	5-Cl/Ph (**1d**)	**3da**	96	>95:5	94
5	5-Br/Ph (**1e**)	**3ea**	87	>95:5	91
6[e]	6-Cl/Ph (**1f**)	**3fa**	87	>95:5	89
7	H/*m*-MeC_6H_4 (**1g**)	**3ga**	72	>95:5	90
8	H/*m*-ClC_6H_4 (**1h**)	**3ha**	61	>95:5	89
9	H/*p*-MeC_6H_4 (**1i**)	**3ia**	64	>95:5	93
10	H/*p*-*t*-BuC_6H_4 (**1j**)	**3ja**	42	>95:5	90
11	H/*p*-FC_6H_4 (**1k**)	**3ka**	83	>95:5	94
12	H/*p*-ClC_6H_4 (**1l**)	**3la**	52	>95:5	90

[a]Unless otherwise indicated, the reaction was carried out on a 0.1 mmol scale in toluene (1 mL) at 30 °C for 12 h, and the molar ratio of **1**:**2a** was 1.2:1. [b]Isolated yield. [c]The *E*/*Z* ratio was determined by ^{1}H NMR. [d]The enantiomeric excess (*ee*) was determined by HPLC. [e]Catalyzed by 40 mol% (*S*)-**5a**.

Then, the generality of the 2-naphthols **2** for the construction of the axially chiral aryl-alkene-indole frameworks was examined. As shown in Table 3, a wide range of 2-naphthols **2** bearing either electron-donating or electron-withdrawing groups at different positions could serve as competent reaction partners to undergo the catalytic asymmetric (4+3) cyclization with 3-alkynyl-2-indolylmethanol **1a**, constructing the axially chiral aryl-alkene-indole scaffolds **3** in overall good yield, complete (E/Z) selectivity and high enantioselectivity.

Table 3 Substrate scope of 2-naphthols **2**[a]



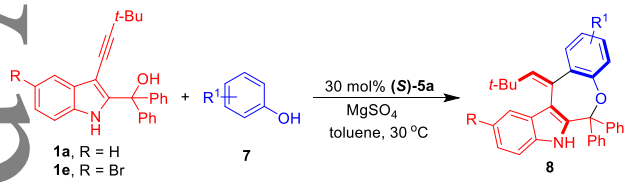
entry	R (**2**)	**3**	yield (%)[b]	*E*/*Z*[c]	ee (%)[d]
1	6-Me (**2b**)	**3ab**	98	>95:5	93
2	6-Et (**2c**)	**3ac**	75	>95:5	94
3	6-OMe (**2d**)	**3ad**	64	>95:5	91
4	6-Br (**2e**)	**3ae**	74	>95:5	92
5[e]	6-CN (**2f**)	***ent*-3af**	76	>95:5	91
6	6-*p*-$OMeC_6H_4$ (**2g**)	**3ag**	68	>95:5	97

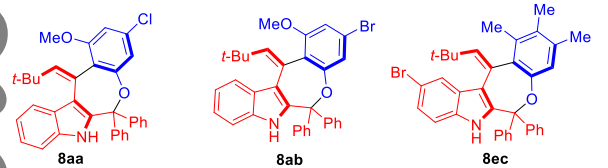
7	7-OMe (**2h**)	**3ah**	84	>95:5	90
8[f]	7-Br (**2i**)	**3ai**	79	>95:5	90
9[g]	7-I (**2j**)	**3aj**	80	>95:5	89
10	7-*p*-OMeC$_6$H$_4$ (**2k**)	**3ak**	97	>95:5	94
11	7-Ph (**2l**)	**3al**	65	>95:5	94
12	8-F (**2m**)	**3am**	55	>95:5	91

[a]Unless otherwise indicated, the reaction was carried out on a 0.1 mmol scale in toluene (1 mL) at 30 °C for 12 h, and the molar ratio of **1a**:**2** was 1.2:1. [b]Isolated yield. [c]The *E*/*Z* ratio was determined by ^{1}H NMR. [d]The enantiomeric excess (*ee*) was determined by HPLC. [e]The reaction was catalyzed by 30 mol% (*R*)-**5a**. [f]The absolute configuration of product **3ai** was determined to be (*S*) by single crystal X-ray diffraction analysis after recrystallization.[22] [g]Catalyzed by 40 mol% (*S*)-**5a**.

Apart from the 2-naphthols, several phenols **7** can also act as suitable 1,3-dinucleophiles to perform the catalytic asymmetric (4+3) cyclization with 3-alkynyl-2-indolylmethanols (Table 4), which afforded axially chiral aryl-alkene-indole derivatives **8** in acceptable yield, perfect (*E*/*Z*)-selectivity and excellent enantioselectivity.

Table 4 Utilizing phenols **7** as substrates for the construction of axially chiral aryl-alkene-indole frameworks[a]





80% (46%[b]), >95:5 *E*/*Z*
91% ee

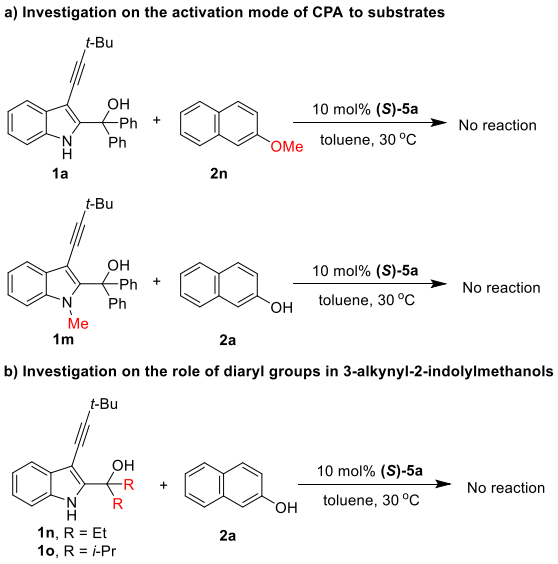
61% (40%[b]), >95:5 *E*/*Z*
94% ee

41%[c], >95:5 *E*/*Z*
93% ee

[a]Unless otherwise indicated, the reaction was carried out on a 0.1 mmol scale in toluene (1 mL) with $MgSO_4$ (100 mg) at 30 °C for 12 h, and the molar ratio of **1**:**7** was 4:1. The yield refers to the isolated yield. The *E*/*Z* ratio was determined by ^{1}H NMR, and the *ee* value was determined by HPLC. [b]The molar ratio of **1**:**7** was 1.2:1 for 24 h. [c]The molar ratio of **1e**:**7c** was 2:1.

To gain some insights into the catalytic asymmetric (4+3) cyclization, we performed some control experiments (Scheme 4). First, to investigate the possible activation mode of the chiral phosphoric acid on the two substrates, we employed the *O*-methyl-protected substrate **2n** and *N*-methyl-protected substrate **1m** for the reaction under standard conditions (Scheme 4a). In both cases, no reaction occurred, and no one-step addition reaction to the alkynyl group of substrates **1** was observed. These results demonstrated that the OH group of substrates **2** and the NH group of substrates **1** played a crucial role in promoting the reaction, which might form hydrogen-bonding interactions with CPA during the reaction process. Second, to study the role of the diaryl groups in 3-alkynyl-2-indolylmethanols, substrates **1n** and **1o**, bearing two aliphatic groups, were engaged in the reaction, and no reaction occurred (Scheme 4b). This outcome indicated that the two aromatic groups at the benzylic position are necessary for the high reactivity of the 3-alkynyl-2-indolylmethanols, which might play an important role in stabilizing the carbocation intermediate (see page S190 of the Supporting Information for theoretical calculations). Therefore, these control experiments verified the structural features necessary when we began to design this new class of indolylmethanols for constructing axially chiral alkene-indole frameworks.

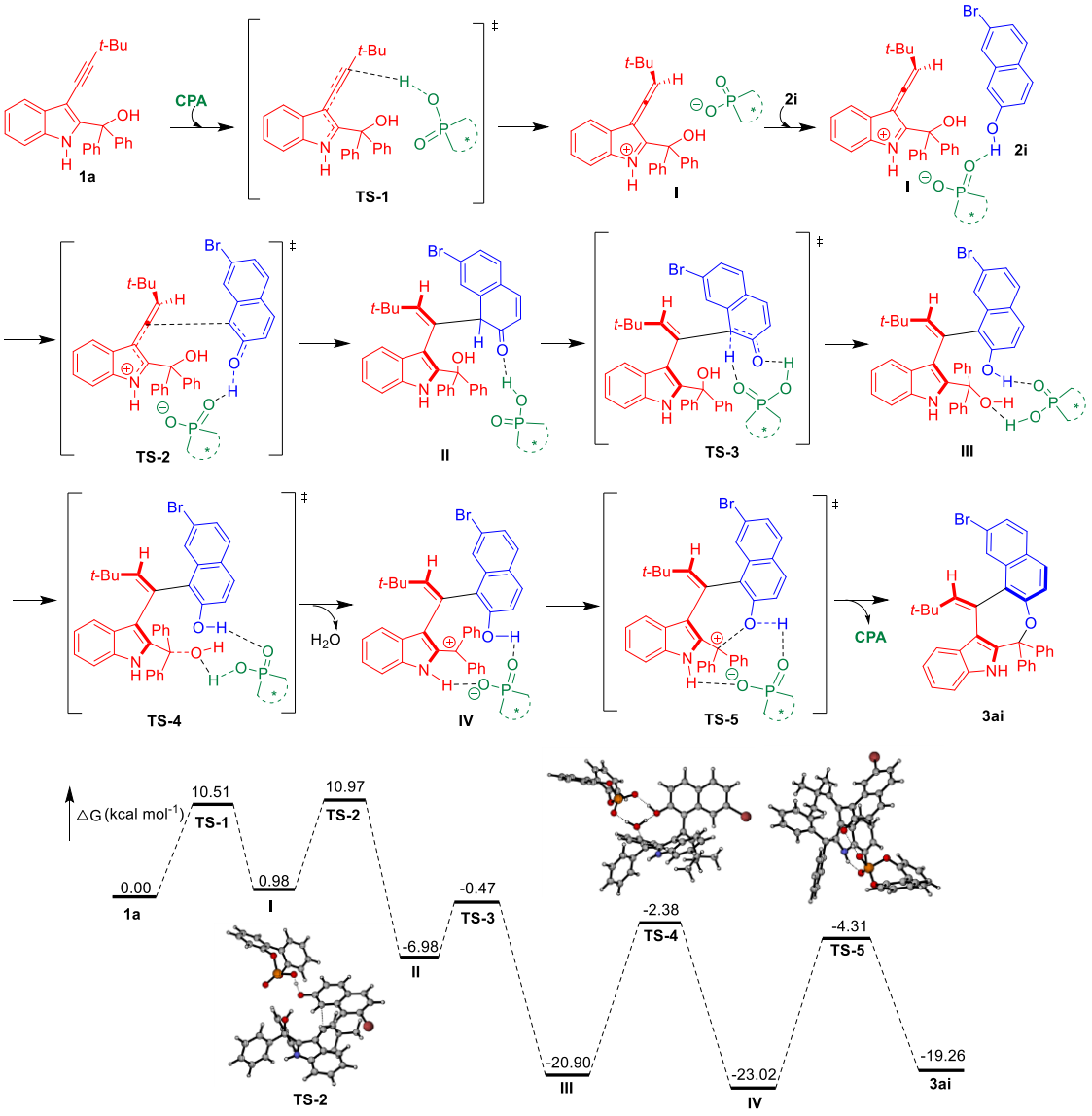
Scheme 4 Control experiments



From the point of the reaction mechanism, the (4+3) cyclization involves two nucleophilic additions of the 1,3-dinucleophile to the 3-alkynyl-2-indolylmethanol. Therefore, in principle, there are two possible reaction pathways based on different sequences of the two nucleophilic additions. To better understand the reaction pathways and find the more possible one, we performed DFT calculations on the reaction and found two possible reaction pathways, A and B (Schemes 5 and 6), for the CPA-catalyzed (4+3) cyclization of 3-alkynyl-2-indolylmethanol **1a** with 2-naphthol **2i** (see page S132 of the Supporting Information) based on the previously reported theoretical calculations of CPA-catalyzed reactions.[23]

In possible reaction pathway A (Scheme 5), 3-alkynyl-2-indolylmethanol **1a** is suggested to transform into allene-iminium intermediate **I** via a transition state (**TS-1**) with an energy barrier of 10.51 kcal mol^{-1}. Then, the CPA anion simultaneously activates both 2-naphthol **2i** and intermediate **I** by hydrogen-bonding and ion-pairing interactions to promote the nucleophilic addition between them (**TS-2**), thus generating intermediate **II** with axial chirality. Intermediate **II** can easily isomerize into another intermediate, **III**, via **TS-3** with a low energy barrier of 6.51 kcal mol^{-1} due to the force of rearomatization of the naphthol ring. Subsequently, CPA forms two hydrogen bonds with the two OH groups of intermediate **III** (**TS-4**) to generate carbocation intermediate **IV** via dehydration. Finally, activated again by the CPA anion, the intramolecular nucleophilic addition of intermediate **IV** (**TS-5**) gives rise to axially chiral product **3ai** with the regeneration of the CPA catalyst.

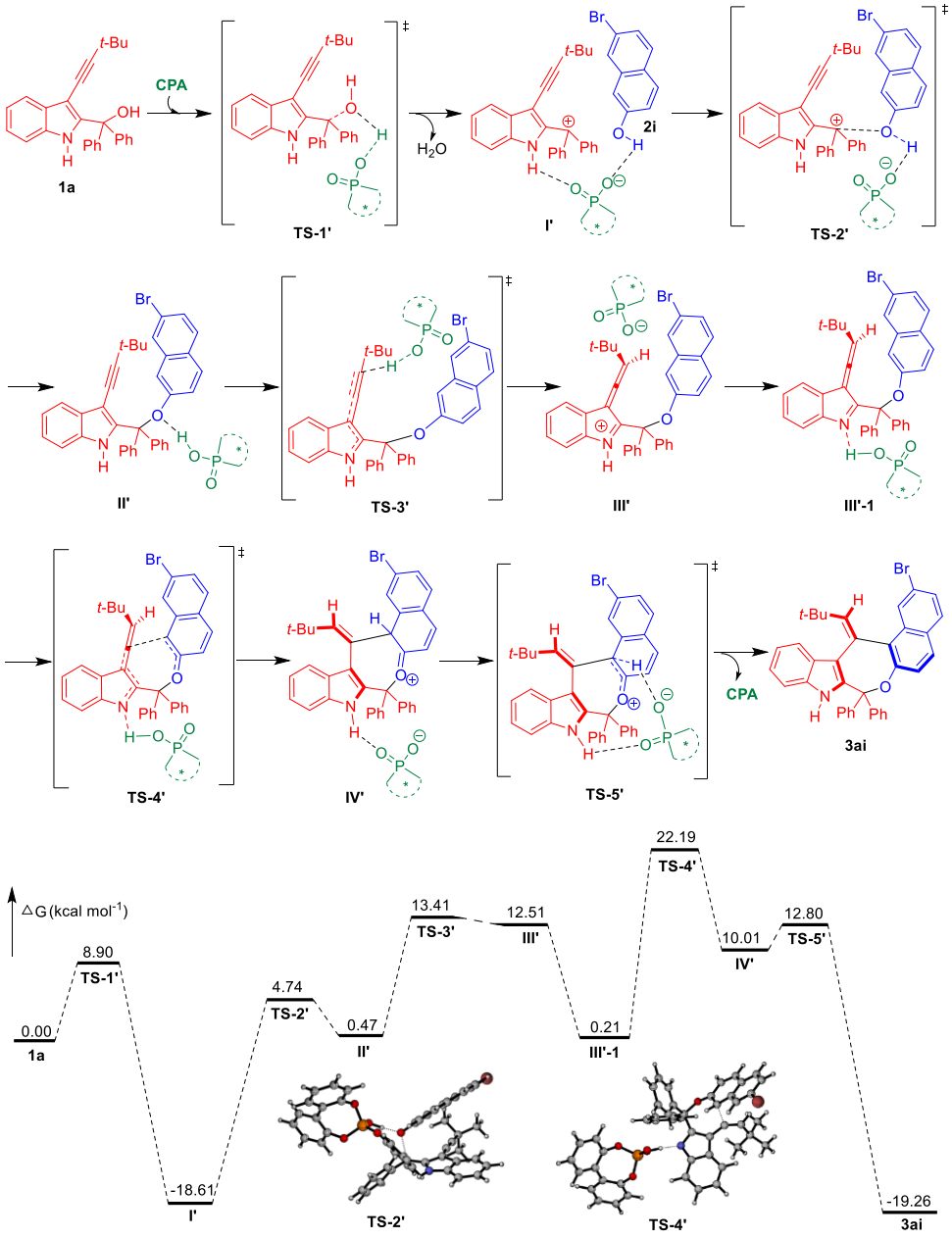
Scheme 5 Possible reaction pathway A and calculated free energy profile



The theoretical calculations rationalized our observations on the control experiments in Scheme 4. Namely, the OH group in substrates **2** and the NH group in substrates **1** could form hydrogen-bonding and ion-pairing interactions with CPA during the reaction process. In addition, the two aromatic groups at the benzylic position of 3-alkynyl-2-indolylmethanols **1** would stabilize the carbocation in intermediate **IV**, which is crucial for the reactivity of this new class of indolylmethanols. Overall, the calculated free energy profile of possible reaction pathway A is reasonable and feasible, which could explain the chemistry of the catalytic asymmetric (4+3) cyclization. Moreover, additional theoretical calculations and experiments also supported the role of the two aryl groups at the benzylic position and the possible reaction pathway A (see page S190 of the Supporting Information for details).

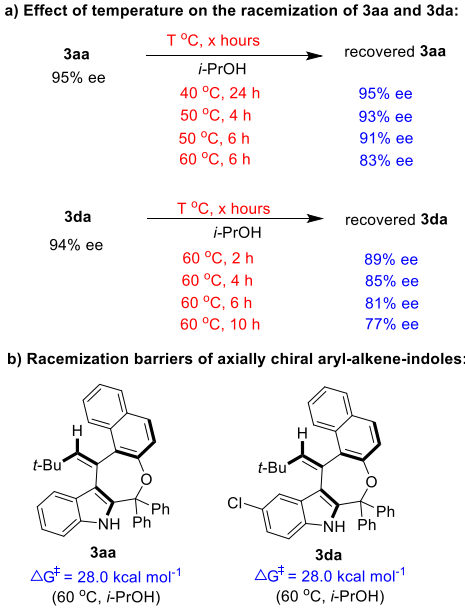
However, in possible reaction pathway B (Scheme 6), the free energies of some steps are much higher than those in pathway A (see page S134 of the Supporting Information for detailed discussion). Therefore, these calculation results suggest that reaction pathway A has a higher probability than reaction pathway B.

Scheme 6 Possible reaction pathway B and calculated free energy profile



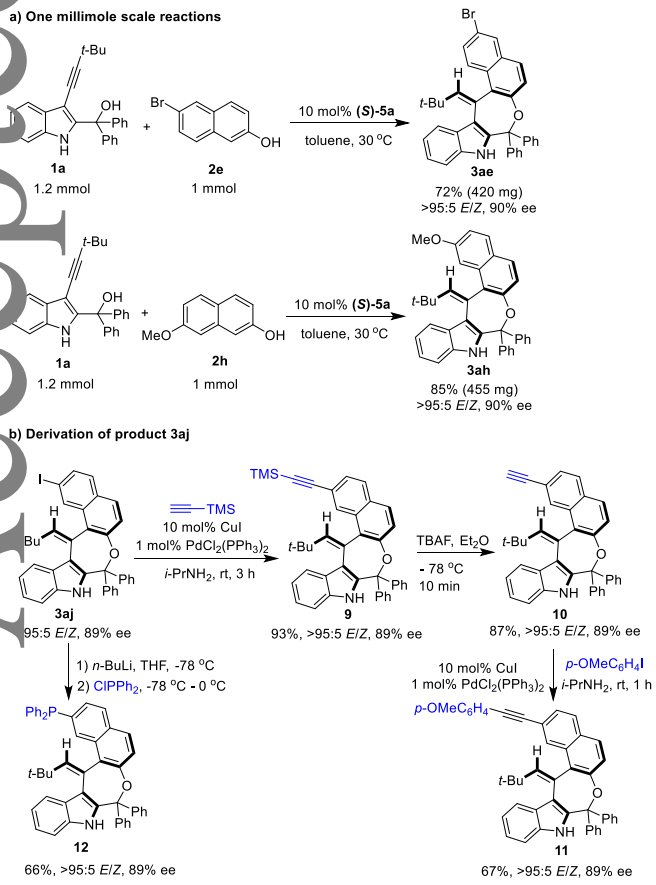
To better understand the conformational stability of this new class of axially chiral aryl-alkene-indole scaffolds, we performed racemization studies on representative aryl-alkene-indoles **3aa** and **3da** (see page S38 of the Supporting Information for details). First, we investigated the effect of temperature on the racemization of **3aa** and **3da** (Scheme 7a), which indicated that this class of axially chiral aryl-alkene-indole scaffolds underwent the racemization process slowly at 40 °C or 50 °C. Second, we experimentally calculated the racemization barriers of **3aa** and **3da** (Scheme 7b). It was found that their racemization barriers (28.0 kcal mol^{-1}) are just slightly greater than 24 kcal mol^{-1}, which is the required racemization barrier for isolating the individual atropisomers.[1f] Therefore, these results verified the formidable challenges in generating the axial chirality of aryl-alkene-indole frameworks due to the extremely low racemization barrier and the very low configurational stability of such skeletons. More importantly, the efficient control of the (*Z*/*E*)-selectivity and the enantioselectivity of products **3** manifested the superiority of our strategy for constructing axially chiral aryl-alkene-indole frameworks.

Scheme 7 Racemization studies on axially chiral aryl-alkene-indole scaffolds



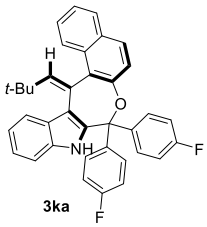
In addition, one millimole scale synthesis of axially chiral aryl-alkene-indoles **3ae** and **3ah** demonstrated that this reaction could be scaled up (Scheme 8a). Moreover, product **3aj** can be derived into compounds **9**-**12** with retained excellent (*E*/*Z*)-selectivity and good enantioselectivity (Scheme 8b).

Scheme 8 One millimole scale reactions and derivation of product **3aj**



Finally, to investigate the potential bioactivity of this class of axially chiral aryl-alkene-indoles, compound **3ka** was subjected to the evaluation of its cytotoxicity (Scheme 9, see page S41 of the Supporting Information for details). This compound displayed potent cytotoxicity toward several cancer cell lines, with IC_{50} values ranging from 39.29 to 50.85 μg mL^{-1}, which implied that this class of axially chiral aryl-alkene-indoles is promising to discover an application in medicinal chemistry.

Scheme 9 Cytotoxicity of the axially chiral product **3ka**



Cancer cell line	IC_{50} (μg mL^{-1})[a]
MCF-7	41.85
MKN-45	41.07
BGC-823	39.29
ECA-109	50.85

[a]The IC_{50} value corresponds to the compound concentration causing 50% mortality in cancer cells.

Conclusions

In summary, we have accomplished the design of a new class of axially chiral aryl-alkene-indole frameworks and the first catalytic asymmetric construction of such scaffolds by the strategy of organocatalytic (*Z*/*E*)-selective and enantioselective (4+3) cyclization of 3-alkynyl-2-indolylmethanols with 2-naphthols or phenols (all >95:5 *E*/*Z*, up to 98% yield, 97% ee). This reaction also represents the first catalytic asymmetric construction of axially chiral alkene-heteroaryl scaffolds, which will add a new member to the atropisomeric family. This approach has not only confronted the great challenges in constructing axially chiral alkene-heteroaryl scaffolds but also provided a powerful strategy for the construction of axially chiral aryl-alkene-indole frameworks in an enantioselective manner. In addition, this approach has realized the design and synthesis of 3-alkynyl-2-indolylmethanols as a new kind of indolylmethanols and has accomplished the first application of such reactants in catalytic asymmetric reactions. This reaction will not only contribute greatly to the chemistry of axial chirality and indolylmethanols but also serve as a robust protocol for constructing seven-membered heterocycles bearing axial chirality.

Experimental

General Procedure for the synthesis of products 3:

To the mixture of 3-alkynyl-2-indolylmethanol **1** (0.12 mmol), 2-naphthol **2** (0.1 mmol), catalyst **(*S*)-5a** (6.1 mg, 0.01 mmol) was added toluene (1 mL). Then, the reaction mixture was stirred at 30 °C for 12 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was directly purified through preparative thin layer chromatography on silica gel to afford pure product **3**.

General Procedure for the synthesis of products 8:

To the mixture of 3-alkynyl-2-indolylmethanol **1** (0.4 mmol), phenol **7** (0.1 mmol), $MgSO_4$ (100 mg), catalyst **(*S*)-5a** (18.3 mg, 0.03 mmol) was added toluene (1 mL). Then, the reaction mixture was stirred at 30 °C for 12 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was directly purified through preparative thin layer chromatography on silica gel to afford pure product **8**.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.2018xxxxx.

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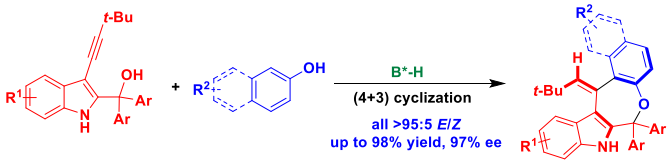

Cheng-Shuai Wang, Tian-Zhen Li, Si-Jia Liu, Yu-Chen Zhang, Shuang Deng, Yinchun Jiao* and Feng Shi*

The first catalytic asymmetric construction of axially chiral aryl-alkene-indole scaffolds has been established by (4+3) cyclization of 3-alkynyl-2-indolylmethanols with 2-naphthols or phenols.

