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Catalytic Asymmetric Synthesis of 3,3'-Bisindoles Bearing Single Axial Chirality

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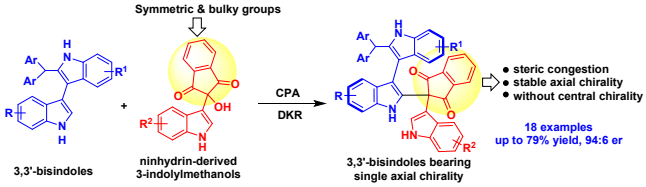


Abstract: A catalytic asymmetric synthesis of 3,3'-bisindoles bearing single axial chirality has been established via chiral phosphoric acid (CPA) catalyzed enantioselective addition reaction of 3,3'-bisindoles with ninhydrin-derived 3-indolylmethanols. The selection of ninhydrin-derived 3-indolylmethanols as suitable electrophiles is based on the consideration that the symmetric and bulky moiety of ninhydrin would increase the steric congestion around the axis to generate stable axial chirality and avoid the generation of central chirality. By this approach, a series of 3,3'-bisindoles bearing single axial chirality were synthesized via dynamic kinetic resolution (DKR) process in generally acceptable yields and considerable enantioselectivities. In addition, an in-depth investigation on the property (stability and rotation barrier) of the synthesized axially chiral 3,3'-bisindoles were carried out, thus providing useful information for this class of axially

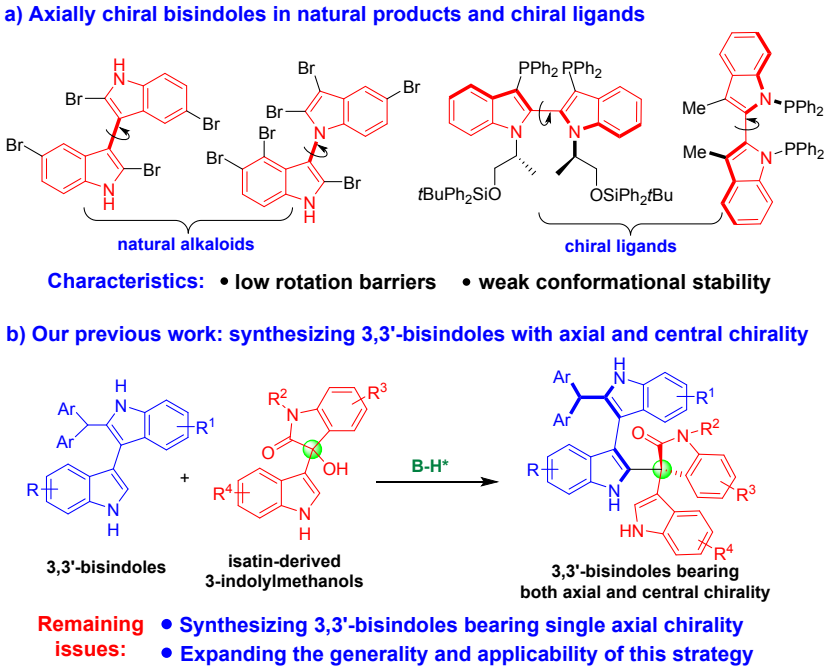
chiral frameworks. This approach makes use of the strategy of dynamic kinetic resolution of 3,3'-bisindoles, therefore expanding the generality and applicability of this strategy for catalytic asymmetric synthesis of 3,3'-bisindoles bearing single axial chirality.

Introduction

Axially chiral indole-containing frameworks have emerged as a new class of family members of atropisomeric hetero-biaryls.[1-2] Consequently, a substantial attention from organic chemists has recently been focused on the catalytic asymmetric construction of axially chiral indole-containing frameworks[3-8] due to the wide occurrence of such frameworks in natural products,[9] bioactive molecules[10] and chiral ligands or catalysts.[11,4a,4d] Among them, axially chiral bisindole scaffolds have gained particular attention from the synthetic community because such scaffolds exist in many natural alkaloids[9] and chiral ligands[11c-d] (Scheme 1a). However, the catalytic asymmetric construction of axially chiral bisindole scaffolds is a challenging task because of the characteristics of five-membered axially chiral skeletons such as low rotation barriers and weak conformational stability.[2]

In our previous work (Scheme 1b),[7a] we devised a strategy to fulfil this task via catalytic asymmetric addition reactions of 3,3'-bisindoles with isatin-derived indolylmethanols in the presence of chiral Brønsted acid (B*-H). By this approach, we accomplished the catalytic asymmetric synthesis of 3,3'-bisindoles bearing both axial and central chirality. However, there are still some remaining issues to be solved regard to this strategy. For example, how to realize the catalytic asymmetric synthesis of 3,3'-bisindoles bearing single axial chirality? Because 3,3'-bisindoles bearing single axial chirality can embody the actual property (stability and rotation

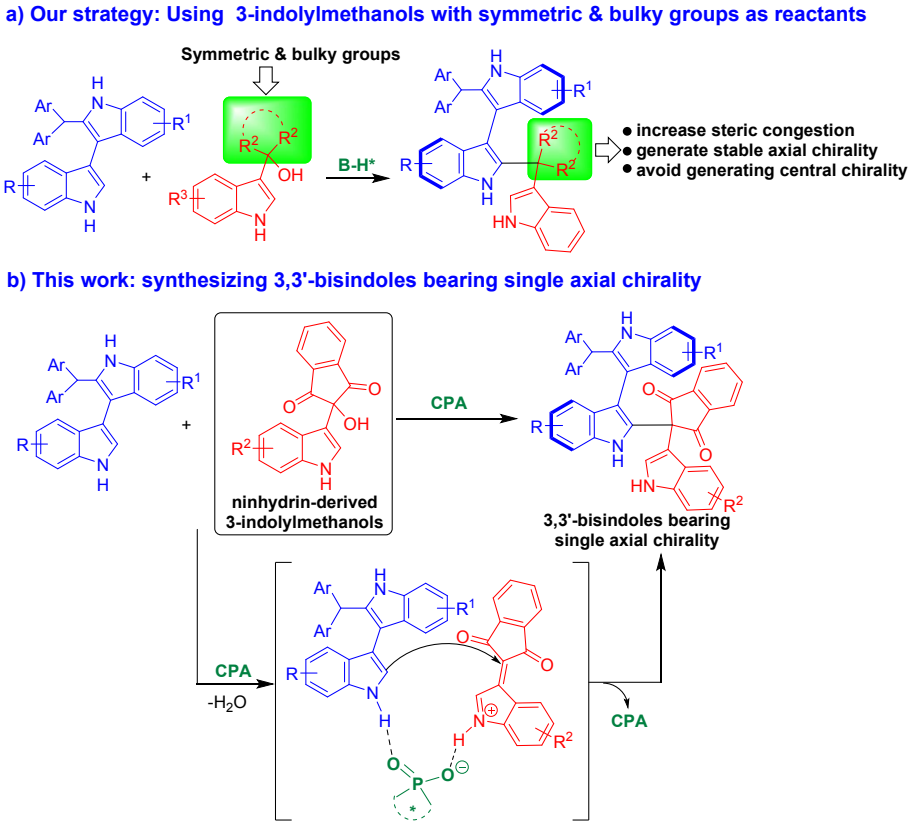
barrier) of axially chiral 3,3'-bisindole frameworks without the effect of central chirality, thus providing useful information for this new class of axially chiral frameworks. In addition, how to expand the generality and applicability of this strategy in synthesizing axially chiral 3,3'-bisindoles? Therefore, it is still valuable to expand the generality and applicability of this strategy for catalytic asymmetric synthesis of 3,3'-bisindoles bearing single axial chirality.



Scheme 1. Axially chiral bisindoles and our previous work for accessing such molecules

To achieve this goal, based on our understanding of 3-indolylmethanols,[12-14] we envisioned if 3-indolylmethanols bearing symmetric and bulky groups were employed as electrophiles to react with 3,3'-bisindoles in the presence of B*-H, 3,3'-bisindoles bearing single axial chirality would be synthesized (Scheme 2a). This is because the existence of symmetric and bulky groups in 3-indolylmethanols would increase the steric congestion around the axis to generate stable axial chirality and avoid the generation of central chirality. Based on this strategy, we considered ninhydrin-derived 3-indolylmethanols could serve as suitable reactants because of the symmetric and bulky moiety of ninhydrin (Scheme 2b). According to this consideration, we designed a chiral

phosphoric acid[15] (CPA) catalyzed asymmetric addition reaction of 3,3'-bisindoles with ninhydrin-derived 3-indolylmethanols. Namely, in the presence of CPA, ninhydrin-derived 3-indolylmethanols would transform into the corresponding carbocations via dehydration. Then, CPA would simultaneously activate 3,3'-bisindoles and the carbocations via hydrogen-bonding and ion-pairing interactions, thus facilitating a nucleophilic addition between them to give 3,3'-bisindoles bearing single axial chirality. On the basis of this design, we carried out an in-depth investigation on this reaction. Herein, we report the details of our investigation.



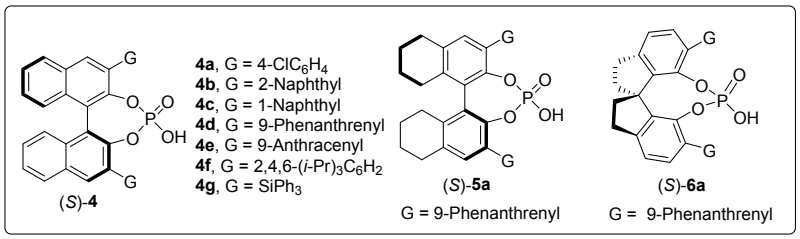
Scheme 2. Design of the reaction for synthesizing 3,3'-bisindoles bearing single axial chirality

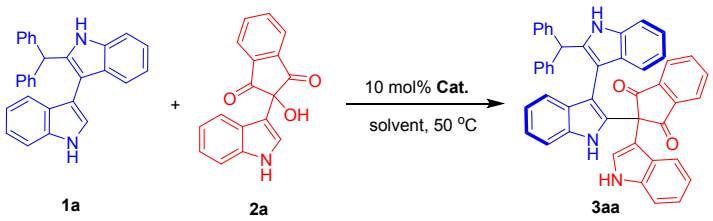
Results and Discussion

At the outset, the reaction of 3,3'-bisindole **1a** with ninhydrin-derived 3-indolylmethanol **2a** in 1,2-dichloroethane (DCE) at 50 °C was employed as a model reaction for the screening of chiral

catalysts (Table 1). However, in the presence of BINOL-derived CPA **4a**-**4g** (entries 1-7), the reactivity of ninhydrin-derived 3-indolylmethanol **2a** was very low, and only CPA **4a**, **4b** and **4d** could catalyze the reaction to afford axially chiral product **3aa** (entries 1-2 and 4). Among them, CPA **4d** bearing 3,3'-di(9-phenanthrenyl) groups displayed the highest catalytic activity in delivering product **3aa** in a moderate enantioselectivity of 80:20 er and an acceptable yield of 42% (entry 4). To improve the enantioselectivity and the yield, we tentatively changed the backbone of CPA **4d** from BINOL to H_8-BINOL and SPINOL (entries 8-9). However, H_8-BINOL-derived CPA **5a** was inferior to CPA **4d** in catalyzing the reaction with regard to the yield and the enantioselectivity of product **3aa** (entry 8 vs entry 4), and SPINOL-derived CPA **6a** failed to catalyze the reaction (entry 9). So, CPA **4d** was selected as the optimal catalyst for this reaction. Then, in the presence of catalyst **4d**, several representative solvents were evaluated (entries 10-14). It was found that only ethyl acetate (entry 10) and acetonitrile (entry 12) could promote the reaction, and no reaction occurred in other solvents including toluene, acetone and tetrahydrofuran (entries 11 and 13-14). However, ethyl acetate and acetonitrile were still inferior to 1,2-dichloroethane in terms of controlling the enantioselectivity (entries 10 and 12 vs entry 4). In order to find more suitable solvents, a series of chloro-containing solvents were further evaluated (entries 15-19). Nevertheless, none of them was better than 1,2-dichloroethane in controlling the enantioselectivity of product **3aa** (entries 15-19 vs entry 4). Thus, 1,2-dichloroethane was chosen as the most suitable solvent for this reaction.

Table 1. Screening of catalysts and solvents[a]





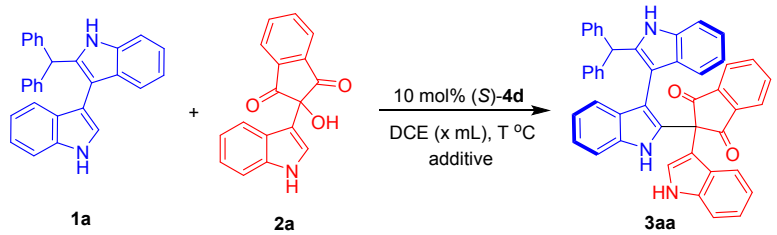
entry	Cat.	solvent	yield (%)[b]	er[c]
1	(*S*)-**4a**	DCE	50	50:50
2	(*S*)-**4b**	DCE	47	63:27
3	(*S*)-**4c**	DCE	N.R.	-
4	(*S*)-**4d**	DCE	42	80:20
5	(*S*)-**4e**	DCE	N.R.	-
6	(*S*)-**4f**	DCE	N.R.	-
7	(*S*)-**4g**	DCE	N.R.	-
8	(*S*)-**5a**	DCE	38	74:26
9	(*S*)-**6a**	DCE	N.R.	-
10	(*S*)-**4d**	EtOAc	41	72:28
11	(*S*)-**4d**	toluene	N.R.	-
12	(*S*)-**4d**	MeCN	30	72:28
13	(*S*)-**4d**	acetone	N.R.	-
14	(*S*)-**4d**	THF	N.R.	-
15	(*S*)-**4d**	CH_2Cl_2	20	77:23
16	(*S*)-**4d**	$CHCl_3$	39	76:24
17	(*S*)-**4d**	Cl_2CHCH_2Cl	28	82:14
18	(*S*)-**4d**	Cl_3CCH_3	43	53:47
19	(*S*)-**4d**	$Cl_2CHCHCl_2$	22	77:23

[a]Unless indicated otherwise, the reaction was carried out in 0.05 mmol scale in a solvent (0.5 mL) at 50 °C for 12 h, and the molar ratio of **1a**:**2a** was 1:1.2. [b]Isolated yields. [c]The enantiomeric ratio (*er*) was determined by HPLC. DCE = $ClCH_2CH_2Cl$. N.R. = No Reaction.

Subsequently, other reaction conditions were further optimized to increase the yield and the enantioselectivity (Table 2). At first, some additives such as molecular sieves (MS) and anhydrous sulfates were added to the reaction system (entries 2-6), and it was revealed that the addition of

sodium sulfate could increase the yield and the enantioselectivity of **3aa** to some extent (entry 6 vs entry 1). Then, the concentration of the reaction was modulated by altering the volume of solvent (entries 7-10). However, increasing the concentration had no evident effect on the reaction (entry 7 vs entry 6), while lowering the concentration led to a sharply decreased yield of **3aa** (entries 8-10 vs entry 6). Next, the reaction temperature was either elevated or lowered (entries 11-13), and it was discovered that the enantioselectivity could be improved from 84:16 er to 87:13 er when lowering the reaction temperature from 50 °C to 30 °C (entry 6 vs entry 12). Because it was reported that the addition of hexafluoroisopropanol (HFIP) could benefit the reaction in some cases,[16] we tentatively added some quantity of HFIP to the reaction (entries 14-16). Gratifyingly, the addition of proper amount of HFIP could indeed improve the enantioselectivity of **3aa** to 91:9 er (entry 15 vs entry 12). The subsequent decreasing of the reaction temperature to 10 °C led a further enhanced enantioselectivity of 93:7 er but with a decreased yield of 42% (entry 17). Finally, performing the reaction in a prolonged time resulted in a greatly increased yield of 75% with a nearly retained enantioselectivity of 91:9 er (entry 18). Therefore, the optimal conditions for this reaction were set as what entry 18 illustrated.

Table 2. Optimization of other reaction conditions[a]



1a 2a 3aa

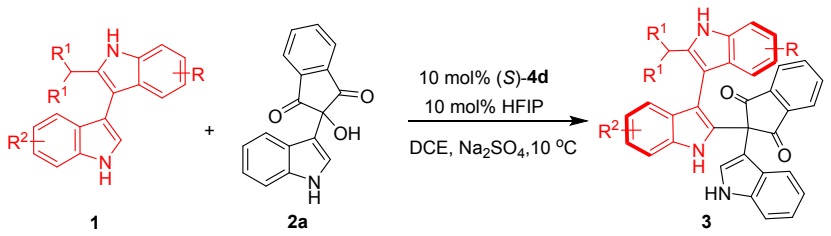
entry	x (mL)	T (°C)	additive	yield (%)[b]	er[c]
1	0.5	50	-	42	80:20
2	0.5	50	3 Å MS	20	81:19
3	0.5	50	4 Å MS	N.R.	-
4	0.5	50	5 Å MS	22	79:21
5	0.5	50	$MgSO_4$	48	83:17
6	0.5	50	Na_2SO_4	54	84:16

7	0.25	50	Na_2SO_4	53	84:16
8	1	50	Na_2SO_4	36	84:16
9	2	50	Na_2SO_4	33	84:16
10	4	50	Na_2SO_4	29	84:16
11	0.5	70	Na_2SO_4	51	80:20
12	0.5	30	Na_2SO_4	52	87:13
13	0.5	20	Na_2SO_4	42	87:13
14[d]	0.5	30	Na_2SO_4	48	90:10
15[e]	0.5	30	Na_2SO_4	49	91:9
16[f]	0.5	30	Na_2SO_4	46	90:10
17[e]	0.5	10	Na_2SO_4	42	93:7
18[e,g]	0.5	10	Na_2SO_4	75	91:9

[a]Unless indicated otherwise, the reaction was carried out at 0.05 mmol scale with additives (50 mg) for 12 h, and the molar ratio of **1a**:**2a** was 1:1.2. [b]Isolated yield. [c]The enantiomeric ratio (*er*) was determined by HPLC. [d]Adding 5 mol% hexafluoroisopropanol (HFIP). [e]Adding 10 mol% HFIP. [f]Adding 20 mol% HFIP. [g]The reaction was performed at 0.1 mmol scale for 48 h.

After establishing the optimal reaction conditions, we carried out the investigation on the substrate scope of 3,3'-bisindoles **1** by the reaction with ninhydrin-derived 3-indolylmethanol **2a**. As shown in Table 3, this protocol could be applicable to a range of 3,3'-bisindoles **1** bearing different R, R^1 and R^2 groups, and these substrates **1** smoothly participated in the catalytic asymmetric addition reaction to afford 3,3'-bisindole products **3** bearing single axial chirality in overall moderate yields (40%-79%) and good enantioselectivities (88:12 er to 94:6 er). Specifically, both R^2 (entries 2-6) and R (entries 7-9) groups could be different halogen and electron-donating groups such as methyl and methoxyl. In addition, R^1 groups could be phenyl groups bearing electronically distinct substituents at different positions (entries 10-12).

Table 3. Substrate scope of 3,3'-bisindoles **1**[a]



1 **2a** **3**

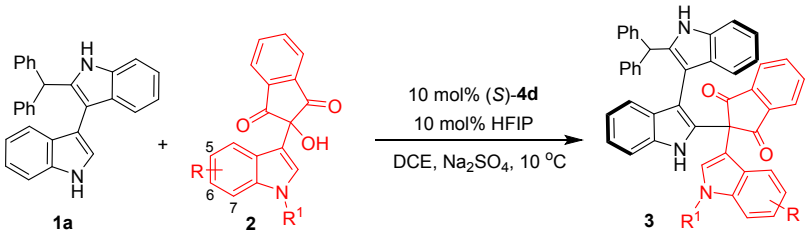
entry	**3**	R\R[1]\R[2] (**1**)	yield (%)[b]	er[c]
1	**3aa**	H\Ph\H (**1a**)	75	91:9
2	**3ba**	H\Ph\5-F (**1b**)	62	93:7
3	**3ca**	H\Ph\5-Cl (**1c**)	43	92:8
4	**3da**	H\Ph\5-Br (**1d**)	40	91:9
5	**3ea**	H\Ph\5-Me (**1e**)	75	91:9
6	**3fa**	H\Ph\5-OMe (**1f**)	63	89:11
7	**3ga**	5'-Br\Ph\H (**1g**)	79	94:6
8	**3ha**	5'-Me\Ph\H (**1h**)	45	93:7
9	**3ia**	5'-OMe\Ph\H (**1i**)	41	93:7
10	**3ja**	H*m*-MeOC$_6$H$_4$\H (**1j**)	43	88:12
11	**3ka**	H*m*-FC$_6$H$_4$\H (**1k**)	54	90:10
12	**3la**	H*p*-FC$_6$H$_4$\H (**1l**)	65	88:12

[a]Unless indicated otherwise, the reaction was carried out at 0.1 mmol scale and catalyzed by 10 mol% (*S*)-**4d** in DCE (0.5 mL) at 10 °C with 10 mol% HFIP and Na_2SO_4 (100 mg) as additives for 48 h, and the molar ratio of **1**:**2a** was 1:1.2. [b]Isolated yield. [c]The *er* value was determined by HPLC.

Next, we investigated the substrate scope of ninhydrin-derived 3-indolylmethanols **2** by the reactions with **1a** under standard conditions (Table 4). As shown in entries 1-6, this approach could be amenable to a series of ninhydrin-derived 3-indolylmethanols **2** bearing different substituents at C5, C6 and C7-positions of the indole ring, and these substrates **2** took part in the reaction to give axially chiral 3,3'-bisindoles **3** in acceptable yields (40%-76%) and considerable enantioselectivities (85:15 er to 94:6 er). In addition, *N*-methyl-protected substrate **2g** could also smoothly take part in the reaction to generate axially chiral product **3ag** albeit with a much lower yield of 43% and a slightly decreased enantioselectivity of 88:12 er compared with product **3aa** (entry 7 vs entry 1), which was generated from *N*-H unprotected substrate **2a**. In general, the

unsatisfying yields of products **3** should be largely ascribed to the low reactivity of ninhydrin-derived 3-indolylmethanols **2** because there were many remaining substrates in the reaction system after a substantial reaction time of 48 hours.

Table 4. Substrate scope of ninhydrin-derived 3-indolylmethanols **2**[a]



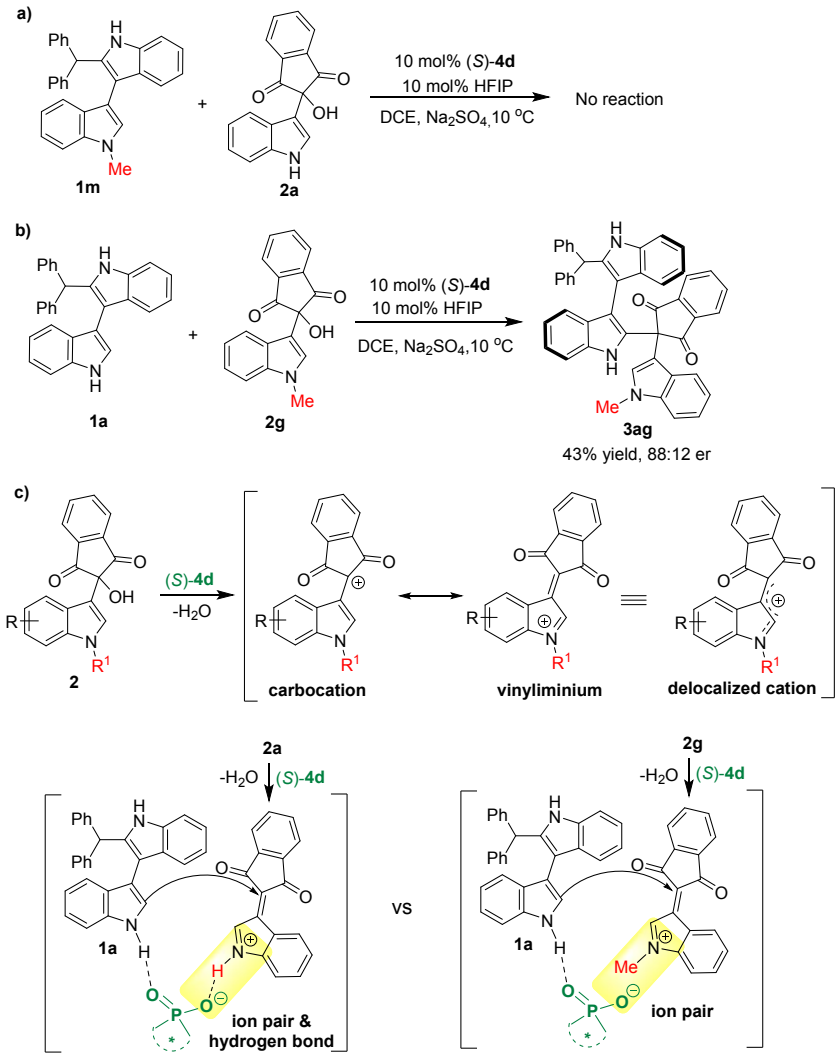
entry	**3**	R\R[1] (**2**)	yield (%)[b]	er[c]
1	**3aa**	H\H (**2a**)	75	91:9
2	**3ab**	5-Cl\H (**2b**)	47	88:12
3	**3ac**	5-Me\H (**2c**)	46	94:6
4	**3ad**	5-OMe\H (**2d**)	43	92:8
5	**3ae**	6-Br\H (**2e**)	40	85:15
6	**3af**	7-Me\H (**2f**)	76	87:13
7	**3ag**	H\Me (**2g**)	43	88:12

[a]Unless indicated otherwise, the reaction was carried out at 0.1 mmol scale and catalyzed by 10 mol% (*S*)-**4d** in DCE (0.5 mL) at 10 °C with 10 mol % HFIP and Na_2SO_4 (100 mg) as additives for 48 h, and the molar ratio of **1a**:**2** was 1:1.2. [b]Isolated yield. [c]The *er* value was determined by HPLC.

The absolute configuration of axially chiral product **3ba** (99:1 er after recrystallization) was determined to be (R_a) by the analysis on its single-crystal structure.[17] Because all products **3** were synthesized in the presence of the same CPA (*S*)-**4d**, the absolute configurations of other axially chiral products **3** were assigned to be (R_a) by analogy.

To investigate the possible activation mode of CPA (*S*)-**4d** to substrates **1** and **2**, we performed control experiments (Scheme 3). Firstly, *N*-methyl-protected substrate **1m** was utilized in the reaction with **2a** under standard conditions (Scheme 3a). In this case, no reaction occurred, and the outcome demonstrated the *N*-H group of substrates **1** played a crucial role in carrying out

the addition reaction with substrates **2** possibly by forming a hydrogen bond with CPA (*S*)-**4d**.

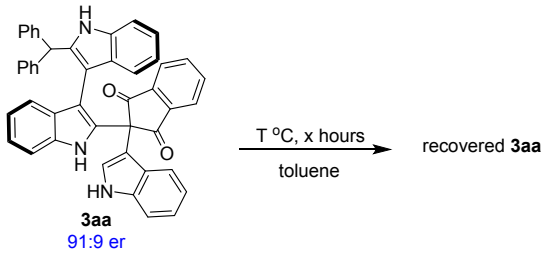


Scheme 3. Control experiments and suggested activation mode

Secondly, instead of *N*-unprotected substrate **2a**, *N*-methyl-protected substrate **2g** was employed to the reaction (Scheme 3b). Compared to the reaction of **2a** (Table 4, entry 1), the reaction of **2g** could still occur to give product **3ag** but with a much lower yield and a decreased enantioselectivity. This result showed that the *N*-H group of ninhydrin-derived 3-indolylmethanols **2** was helpful for increasing the reactivity and the enantioselectivity, but it was not crucial for substrates **2** to undergo the addition reaction, which indicated that substrates **2** might generate ion-pairing interaction with CPA (*S*)-**4d** apart from hydrogen-bonding interaction. Based on the

control experiments, we suggested a possible activation mode of CPA (*S*)-**4d** to the substrates. As illustrated in Scheme 3c, in the presence of (*S*)-**4d**, ninhydrin-derived 3-indolylmethanols **2** underwent dehydration to transform into carbocation and vinyliminium intermediates, which could be described as delocalized cation. In the reaction of **1a** with **2a**, the anion of CPA (*S*)-**4d** could form hydrogen-bonding and ion-pairing interactions with the two reaction partners. While in the reaction of **1a** with **2g**, CPA anion could not form hydrogen-bonding interaction with **2g**. Instead, an ion-pairing interaction between them was generated, which could also promote the addition reaction.

Table 5. Investigation on the stability of axially chiral product **3aa**[a]



3aa
91:9 er

entry	T (°C)	x (hour)	recovery yield of **3aa** (%)[b]	er of recovered **3aa**[c]
1	60	2	98	91:9
2	60	4	96	91:9
3	60	6	97	91:9
4	60	8	98	91:9
5	60	10	97	91:9
6	60	24	97	91:9
7	80	2	98	91:9
8	80	4	96	91:9
9	80	6	98	91:9
10	80	8	96	91:9
11	80	10	98	91:9
12	80	24	96	91:9
13	120	24	96	91:9
14	130	24	97	91:9

[a]Unless indicated otherwise, the reaction was carried out at 0.1 mmol scale in toluene (1 mL) under argon atmosphere. [b]Isolated yield. [c]The enantiomeric ratio (*er*) was determined by HPLC.

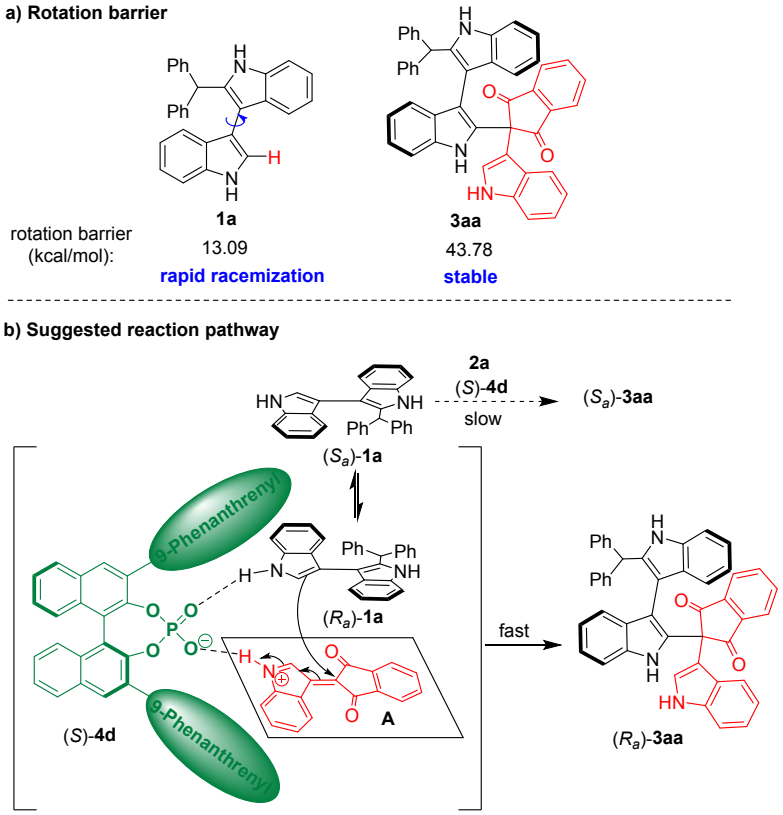
In order to get some information on this class of 3,3'-bisindole frameworks bearing single

axial chirality, we performed the investigation on the stability of axially chiral product **3aa** (91:9 er) at different temperatures. As listed in Table 5, after being stirred at 60 °C (entries 1-6) or 80 °C (entries 7-12) from 2 hours to 24 hours, no racemization was observed in the recovered **3aa**. Notably, the enantioselectivity of the recovered **3aa** could still be retained even after being stirred at a much higher temperature of 120 °C or 130 °C for 24 hours (entries 13-14). These experiments demonstrated that this class of 3,3'-bisindole frameworks bearing single axial chirality has a high stability even at a high temperature.

Furthermore, we theoretically calculated the rotation barrier of compound **3aa** (Scheme 4a), and it was found that the rotation barrier of compound **3aa** was very high (43.78 kcal mol^{-1}), which was in accordance with its high stability at high temperature (Table 5). The high rotation barrier and stability of compound **3aa** might be ascribed to the bulky moiety of ninhydrin. In contrast, the rotation barrier of substrate **1a** was very low (13.09 kcal mol^{-1}),[7] which was much lower than the energy required for isolating the individual atropisomers (24 kcal mol^{-1}).[1a] So, substrate **1a** could undergo rapid racemization during the reaction process, thus providing an opportunity for the synthesis of axially chiral product **3aa** in an enantioselective manner via the process of dynamic kinetic resolution (DKR).

Based on the experimental results, we suggested a possible reaction pathway for the generation of axially chiral product **3aa**. As illustrated in Scheme 4b, (R_a)-**1a** was matched with chiral catalyst (*S*)-**4d**. So, under the activation of (*S*)-**4d** via hydrogen-bonding and ion-pairing interaction, a fast nucleophilic addition between (R_a)-**1a** and vinyliminium intermediate **A** (generated from substrate **2a**) occurred to give product (R_a)-**3aa**. In contrast, due to the mismatched interaction between (S_a)-**1a** and catalyst (*S*)-**4d**, the reaction between (S_a)-**1a** and **2a**

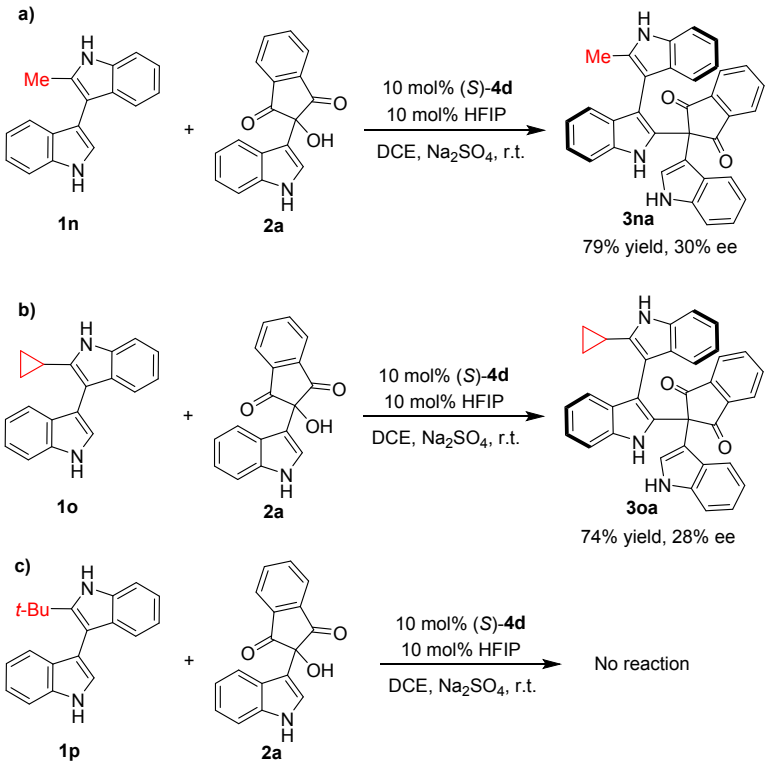
was very slow. So, owing to the low rotation barrier of substrate **1a**, (S_a)-**1a** continuously transformed into (R_a)-**1a** to react with vinyliminium **A**, thus realizing the process of DKR and the synthesis of axially chiral 3,3'-bisindole **3aa** with (R_a)-configuration.



Scheme 4. Calculated rotation barrier and suggested reaction pathway

To further investigate the scope of substrates **1**, we tried using other groups to replace the bisphenylmethyl group at the C2-position of substrates **1** (Scheme 5). When substrate **1n** bearing a small methyl group was employed to the reaction with **2a** (Scheme 5a), the reaction could smoothly occur to generate axially chiral product **3na** in a good yield of 79% with some extent of enantioselectivity (30% ee). When using substrate **1o** bearing a cyclopropyl group at the C2-position (Scheme 5b), the reaction still occurred to give product **3oa** with axially chirality in a considerable yield (74%) albeit with no improvement on the enantioselectivity (28% ee). To further increase the size of the C2-substituent, substrate **1p** bearing a bulky tertiary-butyl (*t*-Bu)

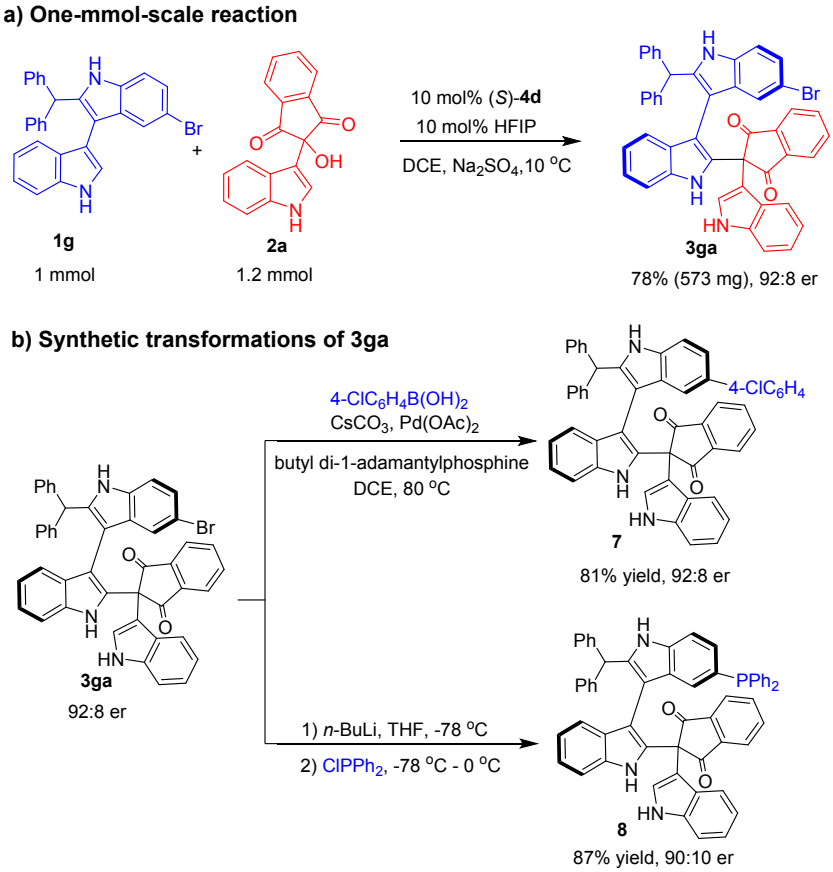
group was employed to the reaction (Scheme 5c). However, in this case, no reaction occurred, which indicated that the introduction of *t*-Bu group to the structure of substrates **1** greatly affected the reactivity of substrates **1**. From these results, it seemed that the bisphenylmethyl group at the C2-position of substrates **1** was necessary for controlling the enantioselectivity with a suitable reactivity.



Scheme 5. Further investigation on the scope of substrates **1**

Finally, to demonstrate the practical utility of this synthetic method, a one-mmol-scale reaction of substrates **1g** and **2a** was carried out (Scheme 6a). This larger-scale reaction smoothly occurred to afford product **3ga** in a good yield of 78% and a high enantioselectivity of 92:8 er, which indicated that this reaction could be utilized for larger-scale synthesis of axially chiral 3,3'-bisindoles. In addition, some synthetic transformations of product **3ga** were performed. As illustrated in Scheme 6b, product **3ga** underwent a Suzuki coupling with 4-chlorophenylboronic acid to give compound **7** in a high yield of 81% with a retained enantioselectivity of 92:8 er. More

importantly, product **3ga** could transform into axially chiral phosphine **8** in a high yield (81%) with a nearly maintained good enantioselectivity (90:10 er).



Scheme 6. One-mmol-scale reaction and synthetic transformations

Conclusion

In summary, we have established the atroposelective synthesis of 3,3'-bisindoles bearing single axial chirality via chiral phosphoric acid-catalyzed asymmetric addition reaction of3,3'-bisindoles with ninhydrin-derived 3-indolylmethanols. The selection of ninhydrin-derived 3-indolylmethanols as suitable electrophiles is based on the consideration that the symmetric and bulky moiety of ninhydrin would increase the steric congestion around the axis to generate stable axial chirality and avoid the generation of central chirality. By this approach, a series of

3,3'-bisindoles bearing single axial chirality were synthesized via dynamic kinetic resolution process in generally acceptable yields and considerable enantioselectivities. In addition, we carried out an in-depth investigation on the property (stability and rotation barrier) of the synthesized axially chiral 3,3'-bisindoles, thus providing useful information for this class of axially chiral frameworks. This approach makes use of the strategy of dynamic kinetic resolution of 3,3'-bisindoles, therefore expanding the generality and applicability of this strategy for catalytic asymmetric synthesis of 3,3'-bisindoles bearing single axial chirality.

Experimental Section

^{1}H and ^{13}C NMR spectra were measured at 400 and 100 MHz, respectively. The solvents used for NMR spectroscopy were DMSO-d_6 and $CDCl_3$, using tetramethylsilane as the internal reference. HR MS (ESI) was determined by a HR MS/MS instrument. The X-ray source used for the single crystal X-ray diffraction analysis of compound **3ba** was GaKα (λ = 1.34139), and the thermal ellipsoid was drawn at the 30% probability level. Analytical grade solvents for the column chromatography were used after distillation, and commercially available reagents were used as received.

Methods for the synthesis of substrates 1:

Substrates **1a-1m** could be conveniently synthesized according to the known literature procedures.[18] Among them, **1a-1b**, **1d-1g**, **1k**, **1l-1m** are known compounds, and the identities of these compounds were confirmed by comparing the measured spectroscopic and physical data with the literature data.[18] Substrates **1n-1p** could be conveniently synthesized according to the known literature procedures.[19] Among them, **1n** is a known compound, and the identity of this

compound was confirmed by comparing the measured spectroscopic and physical data with the literature data.[19]

2-benzhydryl-5'-chloro-1*H*,1'*H*-3,3'-biindole (1c): Flash column chromatography (petroleum ether/ethyl acetate = 5/1); 44% yield (1.9 g); white solid; m.p. 213-214 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.46 (s, 1H), 10.99 (s, 1H), 7.49 – 7.39 (m, 2H), 7.34 (s, 1H), 7.32 (s, 2H), 7.30 (s, 3H), 7.27 – 7.21 (m, 4H), 7.20 – 7.13 (m, 4H), 7.11 – 7.05 (m, 1H), 7.01 – 6.93 (m, 1H), 5.68 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 143.2, 137.3, 136.8, 135.3, 129.2, 128.9, 128.2, 126.9, 126.1, 123.7, 121.6, 121.5, 119.4, 119.3, 119.0, 113.7, 111.9, 108.7, 108.6, 107.1, 107.0, 48.4; IR (KBr): 3448, 3055, 3021, 1450, 785, 746, 699 cm^{-1}; HRMS (ESI-TOF) m/z: [M - H]$^-$ Calcd for $C_{29}H_{20}ClN_2$ 431.1320, found 431.1322.

2-benzhydryl-5-methyl-1*H*,1'*H*-3,3'-biindole (1h): Flash column chromatography (petroleum ether/ethyl acetate = 5/1); 70% yield (2.9 g); white solid; m.p. 218-219 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.19 (s, 1H), 10.77 (s, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.35 – 7.26 (m, 6H), 7.23 (d, J = 7.2 Hz, 2H), 7.21 – 7.14 (m, 4H), 7.13 – 7.09 (m, 2H), 7.08 (s, 1H), 6.97 – 6.86 (m, 2H), 5.69 (s, 1H), 2.30 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 143.4, 137.1, 136.8, 135.2, 129.2, 128.9, 128.7, 128.1, 127.5, 126.8, 124.2, 122.9, 121.6, 120.0, 119.3, 119.1, 112.1, 111.6, 109.0, 107.4, 48.4, 21.8; IR (KBr): 3456, 3430, 3048, 3025, 1482, 1454, 748, 706, 602 cm^{-1}; HRMS (ESI-TOF) m/z: [M - H]$^-$ Calcd for $C_{30}H_{23}N_2$ 411.1866, found 411.1863.

2-benzhydryl-5-methoxy-1*H*,1'*H*-3,3'-biindole (1i): Flash column chromatography (petroleum ether/ethyl acetate = 5/1); 75% yield (3.2 g); white solid; m.p. 130-131 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.20 (s, 1H), 10.74 (s, 1H), 7.47 (d, J = 8.1 Hz, 1H), 7.36 – 7.27 (m, 6H), 7.26 – 7.20 (m, 2H), 7.19 – 7.03 (m, 6H), 6.98 – 6.91 (m, 1H), 6.80 – 6.71 (m, 2H), 5.70 (s, 1H),

3.62 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 153.6, 143.3, 137.6, 136.8, 131.9, 129.1, 128.8, 128.6, 127.8, 126.8, 124.0, 121.5, 119.9, 118.9, 112.4, 112.1, 111.3, 108.8, 107.7, 101.5, 55.7, 48.4; IR (KBr): 3409, 3055, 3023, 1618, 1482, 1088, 798, 743, 701 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{30}H_{23}N_2O$ 427.1816, found 427.1810.

2-(bis(3-methoxyphenyl)methyl)-1*H*,1'*H*-3,3'-biindole (1j): Flash column chromatography (petroleum ether/ethyl acetate = 5/1); 44% yield (2.0 g); white solid; m.p.138-140 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.21 (s, 1H), 10.91 (s, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.40 (d, J = 8.1 Hz, 1H), 7.29 (d, J = 7.9 Hz, 2H), 7.26 – 7.21 (m, 2H), 7.15 – 7.13 (m, 1H), 7.11 – 7.08 (m, 1H), 7.06 (d, J = 7.8 Hz, 1H), 6.96 – 6.92 (m, 2H), 6.84 – 6.80 (m, 2H), 6.75 (d, J = 7.5 Hz, 2H), 6.70 (s, 2H), 5.65 (s, 1H), 3.67 (s, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 159.7, 144.6, 136.7, 129.8, 128.3, 128.0, 124.1, 121.5, 121.3, 119.9, 119.6, 119.0, 115.4, 112.1, 111.7, 108.7, 107.8, 55.4, 48.2; IR (KBr): 3411, 3052, 2833, 1579, 1455, 1486, 1047, 742, 697 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{31}H_{25}N_2O_2$ 457.1921, found 457.1929.

2-cyclopropyl-1*H*,1'*H*-3,3'-biindole (1o): Flash column chromatography (petroleum ether/ethyl acetate = 10/1); 81% yield (2.2 g); white solid; m.p. 80-81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.72 (s, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.53 (d, J = 7.8 Hz, 1H), 7.47 (d, J = 8.1 Hz, 1H), 7.37 – 7.35 (m, 1H), 7.35 – 7.31 (m, 1H), 7.27 – 7.25 (m, 1H), 7.19 – 7.11 (m, 2H), 7.10 – 7.05 (m, 1H), 2.28 – 2.16 (m, 1H), 1.00 – 0.92 (m, 2H), 0.81 – 0.75 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 136.9, 136.2, 134.9, 129.3, 127.8, 123.0, 122.0, 121.3, 120.9, 119.6, 119.4, 119.3, 111.1, 110.4, 110.3, 107.6, 8.6, 7.7; IR (KBr): 3568, 3013, 1786, 1577, 1458, 1070, 897, 742, 669 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{19}H_{15}N_2$ 271.1240, found 271.1255.

2-(tert-butyl)-1*H*,1'*H*-3,3'-biindole (1p): Flash column chromatography (petroleum ether/ethyl acetate = 10/1); 63% yield (1.8 g); white solid; m.p. 88-89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 8.14 (s, 1H), 7.47 – 7.43 (m, 1H), 7.41 – 7.34 (m, 2H), 7.26 – 7.21 (m, 1H), 7.20 – 7.12 (m, 3H), 7.10 – 7.05 (m, 1H), 7.02 – 6.96 (m, 1H), 1.35 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.6, 135.9, 133.8, 131.6, 129.4, 124.3, 121.9, 121.2, 120.5, 119.5, 119.4, 111.4, 110.9, 110.1, 104.4, 33.2, 30.7; IR (KBr): 3568, 3052, 2962, 1735, 1458, 1265, 741, 705 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{20}N_2Na$ 311.1519, found 311.1528.

Methods for the synthesis of substrates 2:

To the mixture of indole (10 mmol), ninhydrin (10 mmol) was added AcOH (10 mL). Then, the reaction mixture was stirred at room temperature for 2 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was filtered to obtain a crude product, and the residue was recrystallized from hot ethanol (water bath) to afford substrates **2**.

2-hydroxy-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (2a): The product was recrystallized from hot ethanol (water bath); 94% yield (2.6 g); yellow solid; m.p. 209-210 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.20 (s, 1H), 8.04 – 7.97 (m, 4H), 7.79 (d, J = 7.9 Hz, 1H), 7.33 (d, J = 8.1 Hz, 1H), 7.11 – 7.05 (m, 1H), 7.03 – 6.95 (m, 2H), 6.62 – 6.56 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 199.7, 139.6, 137.2, 137.0, 125.6, 125.4, 124.0, 122.1, 121.5, 119.6, 112.1, 110.8, 77.8; IR (KBr): 3353, 3129, 1743, 1703, 1585, 1119, 983, 853, 778, 665 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{12}NO_3$ 278.0812, found 278.0810.

2-(5-chloro-1*H*-indol-3-yl)-2-hydroxy-1*H*-indene-1,3(2*H*)-dione (2b): The product was recrystallized from hot ethanol (water bath); 93% yield (2.9 g); yellow solid; m.p. 187-188 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.33 (s, 1H), 8.07 – 7.96 (m, 4H), 7.81 (d, J = 8.4 Hz, 1H), 7.52 (s,

1H), 7.16 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.03 (d, *J* = 2.8 Hz, 1H), 6.66 (s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 199.5, 139.4, 137.4,135.5, 127.0, 126.9, 124.2, 124.1, 122.2, 120.9, 113.7, 110.6, 77.5; IR (KBr): 3506, 3279, 1747, 1707, 1464, 1354, 1140 , 976, 804, 652 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{11}ClNO_3$ 312.0422, found 312.0418.

2-hydroxy-2-(5-methyl-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (2c): The product was recrystallized from hot ethanol (water bath); 89% yield (2.6 g); yellow solid; m.p. 208−209 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.06 (s, 1H), 8.03 – 7.94 (m, 4H), 7.62 (s, 1H), 7.21 (d, *J* = 8.3 Hz, 1H), 6.95 – 6.87 (m, 2H), 6.53 (s, 1H), 2.35 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 199.6, 153.7, 139.6, 137.2, 132.2, 126.0, 125.9, 123.9, 112.7, 112.2, 110.3, 103.3, 77.9, 55.6; IR (KBr): 3472, 3265, 1743, 1705, 1590, 1147, 1078, 974, 865, 662, 589 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{14}NO_3$ 292.0968, found 292.0972.

2-hydroxy-2-(5-methoxy-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (2d): The product was recrystallized from hot ethanol (water bath); 92% yield (2.8 g); yellow solid; m.p. 207−208 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.07 (s, 1H), 8.00 (s, 4H), 7.63 (s, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 6.96 – 6.88 (m, 2H), 6.54 (d, *J* = 6.0 Hz, 1H), 2.35 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 199.7, 139.5, 137.2, 135.4, 128.0, 125.9, 125.4, 123.9, 123.7, 121.2, 111.7, 110.2, 78.0, 21.8; IR (KBr): 3342, 3055, 1748, 1710, 1487, 1166, 1075, 1018, 864, 710, 660 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{14}NO_4$ 308.0918, found 308.0915.

2-(6-bromo-1*H*-indol-3-yl)-2-hydroxy-1*H*-indene-1,3(2*H*)-dione (2e): The product was recrystallized from hot ethanol (water bath); 90% yield (3.2 g); yellow solid; m.p. 192−193 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.32 (s, 1H), 8.04 – 7.99 (m, 4H), 7.81 (d, *J* = 8.6 Hz, 1H), 7.53 (s, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.03 (d, *J* = 2.4 Hz, 1H), 6.65 (s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz,

DMSO-d_6) δ 199.5, 139.5, 137.9, 137.4, 126.3, 124.8, 124.1, 123.4, 122.5, 114.9, 114.6, 111.1, 77.5; IR (KBr): 3503, 3280, 1750, 1713, 1474, 1360, 1139 , 983, 795, 649 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{11}BrNO_3$ 355.9917, found 355.9920.

2-hydroxy-2-(7-methyl-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (2f): The product was recrystallized from hot ethanol (water bath); 93% yield (2.7 g); yellow solid; m.p. 185−186 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.18 (s, 1H), 8.06 – 7.97 (m, 4H), 7.60 – 7.53 (m, 1H), 6.99 (d, *J* = 2.8 Hz, 1H), 6.91 – 6.85 (m, 2H), 6.63 – 6.37 (m, 1H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 199.7, 139.6, 137.2, 136.5, 125.2, 125.0, 124.0, 122.5, 121.2, 119.8, 119.0, 111.3, 77.9, 17.1; IR (KBr): 3440, 2630, 2602, 2192, 1749, 1709, 1026, 665, 583 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{14}NO_3$ 292.0968, found 292.0971.

2-hydroxy-2-(1-methyl-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (2g): The product was recrystallized from hot ethanol (water bath); 48% yield (1.4 g); yellow solid; m.p. 209-210 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.04 – 7.98 (m, 4H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.18 – 7.12 (m, 1H), 7.06 – 7.01 (m, 2H), 6.58 (s, 1H), 3.67 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 199.6, 139.5, 137.5, 137.3, 129.5, 126.0, 124.0, 122.2, 121.7, 119.7, 110.3, 109.8, 77.7, 32.8; IR (KBr): 3481, 3112, 1766, 1706, 1525, 1329, 1146, 957, 766, 651, 604 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{14}NO_3$ 292.0968, found 292.0972.

General procedure for the synthesis of products 3

To the mixture of 3,3'-bisindoles **1** (0.1 mmol), ninhydrin-derived 3-indolylmethanols **2** (0.12 mmol), catalyst (*S*)-**4d** (7.0 mg, 0.01 mmol), hexafluoroisopropanol (1 μL, 0.01 mmol) and Na_2SO_4 (100 mg) was added DCE (0.5 mL). Then, the reaction mixture was stirred at 10 °C for 48 h. Then, the reaction mixture was directly purified through preparative thin layer chromatography

or flash column chromatography to afford products **3**.

(R_a)-2-(2'-benzhydryl-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (3aa): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 75% yield (49.3 mg); yellow solid; m.p. 175-176 °C; $[\alpha]_D^{20}$ = -335.0 (c 0.38, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.31 – 8.26 (m, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 7.4 Hz, 2H), 7.59 (s, 1H), 7.47 – 7.40 (m, 2H), 7.40 – 7.30 (m, 3H), 7.30 – 7.26 (m, 1H), 7.26 – 7.22 (m, 3H), 7.21 – 7.16 (m, 1H), 7.15 – 7.06 (m, 5H), 7.04 – 6.99 (m, 2H), 6.97 – 6.92 (m, 1H), 6.90 – 6.82 (m, 2H), 6.79 – 6.72 (m, 2H), 6.59 – 6.48 (m, 1H), 6.36 (d, *J* = 8.0 Hz, 1H), 5.57 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.3, 143.3, 141.8, 140.4, 140.2, 139.4, 137.0, 134.9, 134.8, 134.1, 133.9, 133.2, 130.6, 130.0, 129.7, 129.0, 128.8, 128.2, 127.0, 126.3, 126.1, 124.9, 123.1, 123.0, 122.6, 121.8, 121.4, 120.8, 120.7, 120.3, 120.2, 119.5, 119.0, 111.4, 110.4, 109.8, 109.2, 106.1, 105.6, 59.0, 48.8; IR (KBr): 3567, 1717, 1662, 1398, 791, 743, 697 cm^{-1}; HRMS (ESI-TOF) m/z: [M - H]$^-$ Calcd for $C_{46}H_{30}N_3O_2$ 656.2343, found 656.2315; Enantiomeric ratio = 91:9, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.257 min (major), t_R = 41.357 min (minor).

(R_a)-2-(2'-benzhydryl-5-fluoro-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (3ba): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 62% yield (41.6 mg); yellow solid; m.p. 191-192 °C; $[\alpha]_D^{20}$ = -404.8 (c 0.46, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 – 8.31 (m, 1H), 8.28 (s, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.67 (d, *J* = 7.3 Hz, 2H), 7.59 (s, 1H), 7.49 – 7.41 (m, 2H), 7.40 – 7.31 (m, 3H), 7.31 – 7.26 (m, 3H), 7.26 – 7.18 (m, 2H), 7.17 – 7.08 (m, 4H), 7.04 – 6.99 (m, 2H), 6.99 – 6.94 (m, 1H), 6.92 – 6.74 (m, 4H), 6.71 – 6.63 (m, 1H), 5.93 – 5.85 (m, 1H), 5.53 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.3,

197.2, 157.3 (J = 233 Hz), 143.1, 141.5, 141.0, 140.1, 139.3, 137.0, 135.0, 134.2, 133.8, 131.2, 130.6, 130.5, 130.4, 129.6, 128.9 (J = 10.6 Hz), 128.3, 127.1, 126.6, 126.1, 124.9, 123.1, 123.0, 122.5, 121.8, 120.9, 120.8, 120.0, 119.6, 111.5, 111.0 (J = 9.4 Hz), 110.0, 109.9, 109.7, 108.9, 106.1 (J = 4.7 Hz), 104.9, 104.7, 58.9, 48.9; IR (KBr): 3445, 3058, 1741, 1705, 1485, 1456, 744, 701 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{46}H_{29}FN_3O_2$ 674.2249, found 674.2248; Enantiomeric ratio = 93:7, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.737 min (major), t_R = 47.387 min (minor).

(R_a)-2-(2'-benzhydryl-5-chloro-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (3ca): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 43% yield (29.5 mg); yellow solid; m.p. 188-190 °C; $[\alpha]_D^{20}$ = -281.8 (c 0.440, Acetone); ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 – 8.33 (m, 1H), 8.30 (s, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 7.4 Hz, 2H), 7.58 (s, 1H), 7.46 – 7.32 (m, 5H), 7.31 – 7.26 (m, 3H), 7.26 – 7.19 (m, 2H), 7.18 – 7.10 (m, 4H), 7.05 – 6.94 (m, 3H), 6.91 – 6.82 (m, 3H), 6.82 – 6.76 (m, 1H), 6.74 (d, J = 7.8 Hz, 1H), 6.20 (d, J = 2.0 Hz, 1H), 5.52 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.3, 197.2, 142.8, 141.4, 141.2, 140.2, 139.4, 137.1, 135.1, 134.8, 134.2, 133.8, 133.0, 131.0, 130.5, 129.7, 129.0, 128.9, 128.3, 127.1, 126.9, 126.1, 124.9, 123.2, 123.1, 122.5, 121.9, 121.8, 121.0, 120.9, 120.0, 119.7, 119.6, 111.6, 111.5, 109.9, 108.9, 105.8, 104.7, 58.9, 49.0; IR (KBr): 3026, 2917, 2351, 1704, 1557, 1455, 743, 701 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{46}H_{29}ClN_3O_2$ 690.1954, found 690.1951; Enantiomeric ratio = 92:8, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.783 min (major), t_R = 46.193 min (minor).

(R_a)-2-(2'-benzhydryl-5-bromo-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1, 3(2*H*)-dione (3da): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 40% yield (29.5 mg); yellow solid; m.p. 190-192 °C; $[\alpha]_D^{20}$ = -148.1 (c 0.87, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 – 8.25 (m, 2H), 8.04 (d, *J* = 7.9 Hz, 1H), 7.67 (d, *J* = 7.4 Hz, 2H), 7.60 (s, 1H), 7.49 – 7.41 (m, 2H), 7.40 – 7.32 (m, 3H), 7.31 – 7.26 (m, 3H), 7.26 – 7.13 (m, 5H), 7.12 (d, *J* = 2.7 Hz, 1H), 7.03 – 6.98 (m, 3H), 6.94 – 6.83 (m, 3H), 6.82 – 6.72 (m, 2H), 6.42 – 6.35 (m, 1H), 5.54 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.3, 197.2, 142.7, 141.5, 141.2, 140.2, 139.4, 137.1, 135.1, 134.7, 134.3, 133.8, 133.3, 131.6, 130.5, 129.7, 128.9, 128.4, 127.2, 127.0, 126.1, 124.9, 124.4, 123.2, 123.1, 122.6, 122.5, 121.8, 121.0, 120.9, 120.0, 119.7, 112.7, 112.0, 111.6, 110.0, 108.9, 105.8, 104.7, 58.9, 49.0; IR (KBr): 3026, 2917, 1557, 1455, 1417, 795, 701 cm^{-1}; HRMS (ESI-TOF) m/z: [M - H]$^-$ Calcd for $C_{46}H_{29}BrN_3O_2$ 734.1448, found 734.1440; Enantiomeric ratio = 91:9, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.773 min (major), t_R = 44.803 min (minor).

(R_a)-2-(2'-benzhydryl-5-methyl-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1, 3(2*H*)-dione (3ea): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 75% yield (50.4 mg); yellow solid; m.p. 195-196 °C; $[\alpha]_D^{20}$ = -542.4 (c 0.58, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 – 8.25 (m, 1H), 8.23 (s, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 7.4 Hz, 2H), 7.61 (s, 1H), 7.50 – 7.41 (m, 2H), 7.40 – 7.31 (m, 3H), 7.30 – 7.26 (m, 2H), 7.26 – 7.22 (m, 2H), 7.22 – 7.17 (m, 1H), 7.16 – 7.12 (m, 3H), 7.10 (d, *J* = 2.7 Hz, 1H), 7.06 – 7.00 (m, 2H), 6.98 (d, *J* = 8.3 Hz, 1H), 6.92 – 6.83 (m, 2H), 6.82 – 6.75 (m, 3H), 6.08 (s, 1H), 5.57 (s, 1H), 1.98 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.7, 197.6, 143.3, 141.9, 140.6, 140.3, 139.4,

137.0, 134.9, 134.2, 133.9, 133.3, 133.1, 130.6, 130.3, 129.7, 129.2, 128.8, 128.2, 128.1, 127.0, 126.3, 126.2, 124.9, 123.2, 123.1, 123.0, 122.7, 121.9, 120.9, 120.1, 120.4, 120.0, 119.5, 111.5, 110.1, 109.8, 109.3, 105.8, 105.5, 59.0, 48.8, 21.0; IR (KBr): 3402, 3056, 2996, 1705, 1593, 1451, 777, 743, 598 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{47}H_{32}N_3O_2$ 670.2500, found 670.2496; Enantiomeric ratio = 91:9, determined by HPLC (Daicel Chiralpak IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 4.017 min(major), t_R = 4.660 min (minor).

(*R*$_a$)-2-(2'-benzhydryl-5-methoxy-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (3fa): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 63% yield (43.6 mg); yellow solid; m.p. 178-180 °C; $[\alpha]_D^{20}$ = -227.9 (c 1.08, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 – 8.33 (m, 1H), 8.27 (s, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.71 – 7.60 (m, 3H), 7.48 – 7.39 (m, 2H), 7.38 – 7.31 (m, 3H), 7.30 – 7.27 (m, 1H), 7.26 – 7.23 (m, 3H), 7.23 – 7.18 (m, 1H), 7.17 – 7.10 (m, 3H), 7.10 – 7.08 (m, 1H), 7.07 – 7.02 (m, 2H), 6.99 (d, *J* = 8.8 Hz, 1H), 6.94 – 6.77 (m, 4H), 6.67 – 6.58 (m, 1H), 5.95 – 5.82 (m, 1H), 5.60 (s, 1H), 3.29 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.6, 197.5, 153.6, 143.7, 142.0, 140.2, 139.3, 137.1, 134.9, 134.2, 134.0, 130.7, 130.6, 129.9, 129.7, 129.0, 128.8, 128.3, 127.0, 126.4, 126.2, 125.0, 123.1, 122.9, 122.7, 122.0, 121.0, 120.8, 120.6, 119.5, 112.8, 111.6, 111.5, 109.9, 109.2, 105.8, 105.7, 100.9, 59.0, 55.4, 48.7; IR (KBr): 3397, 3056, 2965, 2360, 1705, 1456, 842, 797, 744 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{47}H_{32}N_3O_3$ 686.2449, found 686.2450; Enantiomeric ratio = 89:11, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 7.397 min (major), t_R = 38.140 min (minor).

(*R*$_a$)-2-(2'-benzhydryl-5'-bromo-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,

3(2*H*)-dione (3ga): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 79% yield (58.4 mg); yellow solid; m.p. 198-200 °C; $[\alpha]_D^{20}$ = -804.0 (c 0.40, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.34 – 8.28 (m, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.74 – 7.60 (m, 4H), 7.47 – 7.30 (m, 5H), 7.27 (s, 2H), 7.21 – 7.15 (m, 2H), 7.15 – 7.06 (m, 5H), 7.04 – 6.99 (m, 2H), 6.98 – 6.91 (m, 2H), 6.81 – 6.70 (m, 2H), 6.59 – 6.48 (m, 1H), 6.32 (d, *J* = 8.0 Hz, 1H), 5.61 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.4, 197.1, 142.7, 142.1, 141.4, 140.3, 139.6, 136.9, 135.2, 134.9, 134.6, 132.9, 132.4, 132.2, 129.8, 129.6, 129.0, 128.9, 128.3, 127.1, 126.5, 126.1, 124.9, 123.6, 123.3, 123.0, 122.4, 122.2, 121.9, 121.7, 120.7, 120.0, 119.2, 113.0, 111.5, 111.4, 110.5, 109.4, 105.4, 59.1, 48.8; IR (KBr): 3057, 2953, 1741, 1701, 1451, 1412, 837, 744, 699 cm^{-1}; HRMS (ESI-TOF) m/z: [M - H]$^-$ Calcd for $C_{46}H_{29}BrN_3O_2$ 734.1448, found 734.1428; Enantiomeric ratio = 94:6, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.083 min (major), t_R = 84.883 min (minor).

(*R*$_a$)-2-(2'-benzhydryl-5'-methyl-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1, 3(2*H*)-dione (3ha): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 45% yield (30.3 mg); yellow solid; m.p. 197-199 °C; $[\alpha]_D^{20}$ = -205.1 (c 0.81, Acetone); ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 11.27 (d, *J* = 2.4 Hz, 1H), 10.59 (s, 1H), 10.34 (s, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.63 – 7.59 (m, 1H), 7.54 (d, *J* = 8.1 Hz, 1H), 7.50 – 7.44 (m, 1H), 7.42 – 7.30 (m, 5H), 7.27 – 7.22 (m, 2H), 7.22 – 7.15 (m, 3H), 7.14 – 7.06 (m, 3H), 7.03 – 6.94 (m, 3H), 6.93 – 6.82 (m, 2H), 6.58 – 6.52 (m, 1H), 6.44 – 6.36 (m, 1H), 6.14 (d, *J* = 4.7 Hz, 2H), 5.43 (s, 1H), 2.04 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.4, 197.2, 142.7, 142.2, 141.5, 140.4, 139.7, 137.0, 135.3, 135.0, 134.7, 133.0, 132.5, 132.2, 129.8, 129.7, 129.0, 128.9, 128.4, 127.2, 126.5, 126.2,

125.0, 123.6, 123.4, 123.1, 122.4, 122.3, 121.9, 121.7, 120.8, 120.0, 119.2, 113.1, 111.5, 111.5, 110.6, 109.4, 105.4, 59.1, 48.9; IR (KBr): 3056, 2964, 1558, 1449, 1417, 793, 743, 698, 599 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{47}H_{32}N_3O_2$ 670.2500, found 670.2473; Enantiomeric ratio = 93:7, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 5.980 min (major), t_R = 64.023 min (minor).

(*R*$_a$)-2-(2'-benzhydryl-5'-methoxy-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (3ia): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 41% yield (28.1 mg); yellow solid; m.p. 197-199 °C; $[\alpha]_D^{20}$ = -314.8 (c 0.50, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 – 8.27 (m, 2H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 7.4 Hz, 2H), 7.51 – 7.36 (m, 5H), 7.36 – 7.26 (m, 4H), 7.26 – 7.18 (m, 2H), 7.17 – 7.05 (m, 5H), 7.03 – 6.98 (m, 2H), 6.98 – 6.90 (m, 1H), 6.69 (d, *J* = 8.7 Hz, 1H), 6.57 – 6.47 (m, 2H), 6.32 (d, *J* = 8.0 Hz, 1H), 6.24 – 6.19 (m, 1H), 5.52 (s, 1H), 3.72 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.7, 197.5, 154.0, 143.4, 141.8, 141.3, 140.3, 139.2, 137.1, 134.9, 134.8, 134.2, 133.6, 131.2, 130.0, 129.7, 129.1, 128.8, 128.7, 128.3, 127.0, 126.4, 126.2, 124.9, 123.2, 122.7, 121.8, 121.4, 120.9, 120.3, 119.1, 111.7, 111.5, 110.7, 110.5, 109.1, 106.0, 105.5, 101.0, 58.9, 55.5, 48.9; IR (KBr): 3056, 2360, 2342, 1702, 1589, 1485, 1449, 837, 797, 743 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{47}H_{32}N_3O_3$ 686.2449, found 686.2424; Enantiomeric ratio = 93:7, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.483 min (major), t_R = 38.367 min (minor).

(*R*$_a$)-2-(2'-(bis(3-methoxyphenyl)methyl)-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (3ja): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 43% yield (30.9 mg); yellow solid; m.p. 170-172 °C; $[\alpha]_D^{20}$ = -146.1 (c 0.74, Acetone); ^{1}H

NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.30 – 8.24 (m, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.66 (s, 1H), 7.43 – 7.30 (m, 4H), 7.29 – 7.27 (m, 1H), 7.26 – 7.20 (m, 3H), 7.20 – 7.13 (m, 2H), 7.12 – 7.08 (m, 2H), 7.06 – 7.00 (m, 1H), 6.99 – 6.91 (m, 1H), 6.90 – 6.84 (m, 3H), 6.79 – 6.70 (m, 2H), 6.66 – 6.59 (m, 2H), 6.59 – 6.53 (m, 1H), 6.53 – 6.49 (m, 1H), 6.41 (d, *J* = 8.0 Hz, 1H), 5.47 (s, 1H), 3.81 (s, 3H), 3.57 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.4, 197.3, 160.0, 159.5, 144.6, 143.2, 140.2, 140.1, 139.7, 137.0, 135.0, 134.9, 134.2, 134.0, 133.1, 130.5, 130.1, 129.7, 129.1, 126.2, 124.9, 123.0, 122.6, 121.9, 121.8, 121.6, 121.5, 120.8, 120.7, 120.3, 120.2, 119.4, 119.0, 115.8, 115.3, 112.3, 111.6, 111.4, 110.4, 109.9, 109.4, 106.2, 105.7, 59.0, 55.4, 55.2, 49.0 cm^{-1}; IR (KBr): 3567, 3055, 1701, 1488, 1456, 1418, 836, 743, 695 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{48}H_{34}N_3O_4$ 716.2555, found 716.2532; Enantiomeric ratio = 88:12, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.207 min (major), t_R = 64.257 min (minor).

(*R*$_a$)-2-(2'-(bis(3-fluorophenyl)methyl)-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (3ka): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 54% yield (37.2 mg); yellow solid; m.p. 183-185 °C; $[\alpha]_D^{20}$ = -238.1 (c 0.88, Acetone); ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.33 – 8.28 (m, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.53 (s, 1H), 7.47 – 7.41 (m, 1H), 7.41 – 7.31 (m, 4H), 7.31 – 7.28 (m, 3H), 7.27 – 7.24 (m, 1H), 7.23 – 7.16 (m, 1H), 7.14 – 7.02 (m, 4H), 7.01 – 6.94 (m, 1H), 6.93 – 6.87 (m, 2H), 6.85 – 6.75 (m, 4H), 6.74 – 6.68 (m, 1H), 6.64 – 6.57 (m, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 5.55 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.6, 197.2, 163.2 (*J* = 245 Hz), 162.9 (*J* = 245 Hz), 145.1(*J* = 6.8 Hz), 143.8 (*J* = 7.1 Hz), 140.3, 139.4, 138.9, 137.0, 135.1, 134.9, 133.3, 130.4, 130.3, 129.9, 129.8, 126.1, 125.2, 124.9, 123.2, 122.5, 121.9, 121.3, 120.8, 120.4, 119.9, 119.8, 119.5, 116.8 (*J* = 21.9

Hz), 116.0 (J = 21.7 Hz), 114.3 (J = 20.9 Hz), 113.6 (J = 20.9 Hz), 111.5, 110.7, 110.0, 109.1, 106.3, 105.6, 59.0, 48.2; IR (KBr): 3566, 3446, 1700, 1611, 1507, 1456, 792, 743, 691, 522 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{46}H_{28}F_2N_3O_2$ 692.2155, found 692.2149; The enantiomeric ratio = 90:10, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 5.783 min (major), t_R = 49.453 min (minor).

(*R*$_a$)-2-(2'-(bis(4-fluorophenyl)methyl)-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (3la): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 65% yield (44.9 mg); yellow solid; m.p. 195-198 °C; $[\alpha]_D^{20}$ = -420.0 (c 0.61, Acetone); ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.33 – 8.27 (m, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.71 – 7.56 (m, 2H), 7.51 (s, 1H), 7.44 – 7.34 (m, 2H), 7.31 – 7.27 (m, 2H), 7.26 – 7.25 (m, 1H), 7.24 – 7.16 (m, 2H), 7.15 – 7.05 (m, 4H), 7.00 – 6.91 (m, 3H), 6.90 – 6.84 (m, 2H), 6.84 – 6.72 (m, 4H), 6.66 – 6.52 (m, 1H), 6.35 (d, J = 8.0 Hz, 1H), 5.53 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 197.7, 197.1, 161.5 (J = 241.1 Hz), 161.3 (J = 241.1 Hz), 140.3, 140.1, 139.9, 139.6, 138.4, 137.6, 136.2, 136.0, 135.6, 134.0, 131.6 (J = 7.9 Hz), 131.1(J = 8.0 Hz), 130.0, 129.8, 126.7, 126.0, 123.5, 122.7, 122.0, 121.0, 120.5, 119.5, 119.3, 119.2, 118.6, 118.3, 115.5 (J = 3.9 Hz), 115.2 (J = 3.7 Hz), 112.2, 111.9, 111.2, 109.1, 105.6, 105.3, 59.7, 47.4; IR (KBr): 3055, 2359, 1501, 1601, 1506, 1456, 1417, 1157, 836, 742, 564 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{46}H_{28}F_2N_3O_2$ 692.2155, found 692.2136; Enantiomeric ratio = 88:12, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.863 min (major), t_R = 33.497 min (minor).

(*R*$_a$)-2-(2'-benzhydryl-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(5-chloro-1*H*-indol-3-yl)-1*H*-indene-1,3

(2*H*)-dione (3ab): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 47% yield (32.4 mg); yellow solid; m.p. 197-199 °C; $[\alpha]_D^{20}$ = -171.8 (c 0.99, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 – 8.28 (m, 1H), 8.20 (s, 1H), 8.05 – 8.01 (m, 1H), 7.65 (d, *J* = 7.3 Hz, 2H), 7.61 (s, 1H), 7.48 – 7.39 (m, 3H), 7.37 – 7.27 (m, 3H), 7.26 – 7.19 (m, 3H), 7.17 (d, *J* = 2.7 Hz, 1H), 7.16 – 7.06 (m, 4H), 7.06 – 6.99 (m, 2H), 6.99 – 6.93 (m, 1H), 6.90 – 6.81 (m, 2H), 6.74 – 6.62 (m, 2H), 6.58 – 6.49 (m, 1H), 6.36 (d, *J* = 8.0 Hz, 1H), 5.56 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.1, 196.9, 143.2, 141.7, 140.5, 140.2, 139.6, 135.4, 135.1, 135.0, 134.3, 133.9, 132.5, 130.5, 130.0, 129.7, 129.0, 128.9, 128.3, 127.3, 127.0, 126.5, 126.3, 126.1, 123.7, 123.2, 121.9, 121.8, 121.7, 120.9, 120.3, 120.1, 119.5, 119.1, 112.5, 110.5, 109.9, 109.3, 106.5, 105.5, 58.7, 49.0; IR (KBr): 3056, 2967, 1700, 1450, 743, 653 cm^{-1}; HRMS (ESI-TOF) m/z: [M - H]$^-$ Calcd for $C_{46}H_{29}ClN_3O_2$ 690.1954, found 690.1925; Enantiomeric ratio = 88:12, determined by HPLC (Daicel Chiralpak IB, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 10.147 min (major), t_R = 11.763 min (minor).

(R_a)-2-(2'-benzhydryl-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(5-methyl-1*H*-indol-3-yl)-1*H*-indene-1, 3(2*H*)-dione (3ac): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 46% yield (30.7 mg); yellow solid; m.p. 189-191 °C; $[\alpha]_D^{20}$ = -227.4 (c 0.81, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.25 – 8.18 (m, 1H), 7.88 (s, 1H), 7.71 – 7.57 (m, 3H), 7.47 – 7.40 (m, 2H), 7.40 – 7.31 (m, 2H), 7.31 – 7.26 (m, 2H), 7.26 – 7.19 (m, 2H), 7.15 – 7.06 (m, 6H), 7.04 – 6.98 (m, 2H), 6.98 – 6.92 (m, 1H), 6.91 – 6.84 (m, 2H), 6.81 – 6.74 (m, 2H), 6.59 – 6.49 (m, 1H), 6.35 (d, *J* = 8.0 Hz, 1H), 5.57 (s, 1H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.5, 197.2, 143.4, 141.9, 140.4, 140.2, 139.6, 135.4, 135.0, 134.9, 134.2, 134.0, 133.4, 130.5, 130.1, 130.0, 129.7, 129.0, 128.9, 128.2, 127.0, 126.4, 126.3, 125.0, 124.8, 123.0, 122.0, 121.9,

121.4, 120.9, 120.4, 120.3, 119.5, 119.0, 111.2, 110.5, 109.8, 108.6, 106.0, 105.7, 59.0, 48.9, 21.9; IR (KBr): 3056, 2971, 1701, 1540, 1456, 1418, 744, 700 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{47}H_{32}N_3O_2$ 670.2500, found 670.2478; Enantiomeric ratio = 94:6, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R =6.340 min (major), t_R = 48.317 min (minor).

(*R*$_a$)-2-(2'-benzhydryl-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(5-methoxy-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (3ad): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 43% yield (29.4 mg); yellow solid; m.p. 184-186 °C; $[\alpha]_D^{20}$ = -351.2 (c 0.48, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.27 – 8.17 (m, 1H), 7.66 (d, *J* = 7.5 Hz, 2H), 7.60 – 7.52 (m, 2H), 7.49 – 7.30 (m, 5H), 7.30 – 7.26 (m, 2H), 7.21 – 6.99 (m, 6H), 6.98 – 6.90 (m, 4H), 6.89 – 6.83 (m, 2H), 6.81 – 6.73 (m, 2H), 6.55 – 6.43 (m, 1H), 6.30 (d, *J* = 8.0 Hz, 1H), 5.52 (s, 1H), 3.78 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.5, 197.2, 154.6, 143.3, 141.8, 140.4, 139.5, 138.3, 134.9, 133.9, 132.2, 131.1, 130.6, 130.1, 129.0, 128.8, 127.0, 126.7, 125.4, 123.1, 121.8, 120.8, 120.2, 119.5, 119.0, 117.3, 113.7, 112.1, 110.4, 109.8, 109.0, 105.9, 105.7, 104.0, 58.9, 55.8, 48.9; IR (KBr): 3650, 2347, 1705, 1559, 1452, 1417, 925, 743, 700 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{47}H_{32}N_3O_3$ 686.2449, found 686.2425; Enantiomeric ratio: 92:8, determined by HPLC (Daicel Chiralpak IB, hexane/isopropanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 11.997 min (minor), t_R = 14.497 min (major).

(*R*$_a$)-2-(2'-benzhydryl-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(6-bromo-1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (3ae): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 40% yield (29.5 mg); yellow solid; m.p. 189-190 °C; $[\alpha]_D^{20}$ = -59.4 (c 1.04, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.25 (m, 1H), 8.22 (s, 1H), 7.86 (d, *J* = 8.6 Hz, 1H), 7.71 – 7.56 (m,

3H), 7.54 – 7.49 (m, 1H), 7.48 – 7.31 (m, 4H), 7.30 – 7.26 (m, 2H), 7.25 – 7.21 (m, 2H), 7.15 – 7.08 (m, 4H), 7.07 (d, *J* = 2.7 Hz, 1H), 7.03 – 6.97 (m, 2H), 6.97 – 6.92 (m, 1H), 6.91 – 6.82 (m, 2H), 6.80 – 6.69 (m, 2H), 6.58 – 6.51 (m, 1H), 6.37 (d, *J* = 8.0 Hz, 1H), 5.53 (s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 197.3, 197.1, 143.2, 141.8, 140.4, 140.2, 139.4, 137.8, 135.1, 134.9, 134.3, 133.9, 132.8, 130.6, 130.0, 129.7, 129.0, 128.9, 128.3, 127.1, 126.4, 125.4, 125.2, 124.1, 123.9, 123.1, 121.8, 121.7, 121.0, 120.3, 120.1, 119.6, 119.2, 116.8, 114.4, 110.5, 109.9, 109.7, 106.4, 105.6, 58.8, 48.9; IR (KBr): 3056, 2965, 1740, 1701, 1450, 1416, 743, 698, 472 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{46}H_{29}BrN_3O_2$ 734.1448, found 734.1430; Enantiomeric ratio = 85:15, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 5.780 min (major), t_R =74.007 min (minor).

(*R*$_a$)-2-(2'-benzhydryl-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(7-methyl-1*H*-indol-3-yl)-1*H*-indene-1, 3(2*H*)-dione (3af): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 76% yield (51.1 mg); yellow solid; m.p. 188-189 °C; $[\alpha]_D^{20}$ = -392.5 (c 0.44, Acetone); ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.28 – 8.19 (m, 1H), 7.87 (d, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 7.3 Hz, 2H), 7.58 (s, 1H), 7.47 – 7.39 (m, 2H), 7.39 – 7.30 (m, 2H), 7.30 – 7.26 (m, 1H), 7.26 – 7.23 (m, 2H), 7.15 (d, *J* = 2.7 Hz, 1H), 7.14 – 7.03 (m, 6H), 7.03 – 6.98 (m, 2H), 6.97 – 6.91 (m, 1H), 6.90 – 6.82 (m, 2H), 6.81 – 6.74 (m, 2H), 6.58 – 6.47 (m, 1H), 6.34 (d, *J* = 8.0 Hz, 1H), 5.56 (s, 1H), 2.50 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 197.4, 197.3, 143.4, 141.9, 140.4, 140.2, 139.5, 136.7, 135.0, 134.9, 134.1, 133.9, 133.3, 130.6, 130.1, 129.7, 129.0, 128.8, 128.2, 127.0, 126.3, 125.8, 124.5, 123.6, 123.0, 121.9, 121.4, 121.0, 120.9, 120.5, 120.4, 120.3, 120.2, 119.5, 119.0, 110.4, 109.9, 109.8, 106.1, 105.7, 59.0, 48.8, 16.6; IR (KBr): 3054, 2360, 1700, 1450, 1417, 1253, 743, 698 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{47}H_{32}N_3O_2$ 670.2500,

found 670.2491; Enantiomeric ratio = 87:13, determined by HPLC (Daicel Chiralpak IB, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.123 min (minor), t_R = 7.960 min (major).

(*R*$_a$)-2-(2'-benzhydryl-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1-methyl-1*H*-indol-3-yl)-1*H*-indene-1, 3(2*H*)-dione (3ag): Preparative thin layer chromatography (petroleum ether/ethyl acetate = 2:1); 43% yield (28.9 mg); yellow solid; m.p. 192-193 °C; $[\alpha]_D^{20}$ = -571.2 (c 0.16, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.03 (d, *J* = 8.1 Hz, 1H), 7.65 (d, *J* = 7.3 Hz, 2H), 7.55 (s, 1H), 7.45 – 7.40 (m, 2H), 7.39 – 7.29 (m, 4H), 7.29 – 7.26 (m, 1H), 7.26 – 7.16 (m, 4H), 7.15 – 7.06 (m, 4H), 7.03 (s, 1H), 7.02 – 6.97 (m, 2H), 6.96 – 6.91 (m, 1H), 6.86 – 6.83 (m, 1H), 6.81 – 6.76 (m, 2H), 6.57 – 6.47 (m, 1H), 6.33 (d, *J* = 8.0 Hz, 1H), 5.54 (s, 1H), 3.77 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.6, 197.5, 153.6, 143.7, 142.0, 140.2, 139.3, 137.1, 134.9, 134.2, 134.0, 130.7, 130.6, 129.9, 129.7, 129.0, 128.8, 128.3, 127.0, 126.4, 126.2, 125.0, 123.1, 122.9, 122.7, 122.0, 121.0, 120.8, 120.6, 119.5, 112.8, 111.6, 111.5, 109.9, 109.2, 105.8, 105.7, 100.9, 59.0, 55.4, 48.7; IR (KBr): 3567, 3056, 2361, 1710, 1436, 1418, 1256, 741, 702 cm^{-1}; HRMS (ESI-TOF) m/z: [M - H]$^-$ Calcd for $C_{47}H_{32}N_3O_2$ 670.2500, found 670.2485; Enantiomeric ratio = 88:12, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.240 min (major), t_R = 23.057 min (minor).

(*R*$_a$)-2-(1*H*-indol-3-yl)-2-(2'-methyl-1*H*,1'*H*-[3,3'-biindol]-2-yl)-1*H*-indene-1,3(2*H*)-dione (3na): Flash column chromatography (petroleum ether/ethyl acetate = 2/1); 79% yield (39.9 mg); yellow solid; m.p. 208-209 °C; $[\alpha]_D^{20}$ = -51.1 (c 0.18, Acetone); ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 11.27 (s, 1H), 10.67 (s, 1H), 10.59 (s, 1H), 7.54 (m, 3H), 7.49 – 7.24 (m, 4H), 7.24 – 7.01 (m, 3H), 7.01 – 6.70 (m, 5H), 6.69 – 6.44 (m, 2H), 1.92 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-*d*$_6$)

δ 197.1, 196.7, 140.1, 139.5, 137.5, 136.0, 135.9, 135.4, 135.2, 134.7, 130.1, 129.9, 126.7, 125.7, 122.9, 122.2, 122.0, 121.9, 121.2, 119.9, 119.3, 119.1, 118.8, 118.6, 118.4, 112.1, 112.0, 110.1, 108.7, 106.1, 104.5, 59.3, 12.1; IR (KBr): 3568, 3033, 1735, 1685, 1560, 1458, 1070, 742, 669 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{34}H_{22}N_3O_2$ 504.1717, found 504.1707; Enantiomeric ratio = 65:35, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 7.857 min (major), t_R = 29.837 min (minor).

(*R*$_a$)-2-(2'-cyclopropyl-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (3oa): Flash column chromatography (petroleum ether/ethyl acetate = 2/1); 74% yield (39.5 mg); yellow solid; m.p. 300-301 °C; $[\alpha]_D^{20}$ = -42.9 (c 0.28, Acetone); ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 – 8.31 (m, 2H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.41 (s, 1H), 7.40 – 7.35 (m, 1H), 7.34 – 7.27 (m, 3H), 7.25 – 7.18 (m, 3H), 7.17 – 7.10 (m, 2H), 7.09 (d, *J* = 2.6 Hz, 1H), 7.04 – 6.98 (m, 1H), 6.94 – 6.80 (m, 4H), 1.80 – 1.70 (m, 1H), 0.95 – 0.84 (m, 1H), 0.82 – 0.70 (m, 1H), 0.65 – 0.51 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.9, 196.6, 140.4, 140.2, 139.7, 136.9, 135.1, 134.8, 134.2, 134.0, 130.5, 130.1, 126.2, 124.7, 122.9, 122.8, 122.6, 121.9, 120.7, 120.5, 119.7, 119.5, 119.4, 111.3, 111.0, 109.3, 109.1, 106.9, 105.5, 58.8, 8.1, 7.0, 6.8; IR (KBr): 3568, 3067, 1751, 1560, 1458, 1069, 896, 741, 669, 463 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{36}H_{24}N_3O_2$ 530.1874, found 530.1867; Enantiomeric ratio = 64:36, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 8.977 min (major), t_R = 24.863 min (minor).

Procedure for one-mmol-scale synthesis of product 3ga

To the mixture of 3,3'-bisindole **1g** (476 mg, 1 mmol), ninhydrin-derived 3-indolylmethanol

2a (332 mg, 1.2 mmol,), catalyst (*S*)-**4d** (70 mg, 0.1 mmol), hexafluoroisopropanol (10 μL, 0.1 mmol) and Na_2SO_4 (200 mg) was added DCE (5 mL). Then, the reaction mixture was stirred at 10 ^oC for 72 h. Then, the reaction mixture was directly purified through flash column chromatography (petroleum ether/ethyl acetate = 5:1) to afford product **3ga** in 78% yield (573 mg) with 92:8 er.

Procedure for the synthesis of product 7

Under argon atmosphere, compound **3ga** (73.5 mg, 0.1 mmol), 4-chlorophenylboronic acid (23.4 mg, 0.15 mmol), Cs_2CO_3 (65.2 mg, 0.2 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and butyl di-1-adamantylphosphine (2.1 mg, 0.006 mmol) were added to a dried tube. After adding DCE (1.2 mL) to the reaction system, the reaction mixture was stirred at 80 ^oC (oil bath) for 6 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was directly purified by flash column chromatography (petroleum ether/ethyl acetate = 2/1) to give pure product **7** as a yellow solid.

(R_a)-2-(2'-benzhydryl-5'-(4-chlorophenyl)-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (7): Flash column chromatography (petroleum ether/ethyl acetate = 2/1); 81% yield (62.1 mg); yellow solid; m.p. 202-203 ^oC; $[\alpha]_D^{20}$ = -320.5 (c 0.52, Acetone); ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.29 (s, 1H), 8.14 – 8.04 (m, 1H), 7.74 – 7.69 (m, 2H), 7.65 (s, 1H), 7.62 – 7.56 (m, 2H), 7.48 – 7.43 (m, 2H), 7.42 – 7.32 (m, 4H), 7.31 – 7.26 (m, 2H), 7.26 – 7.18 (m, 4H), 7.18 – 7.11 (m, 5H), 7.10 (s, 1H), 7.07 – 7.01 (m, 2H), 7.00 – 6.91 (m, 2H), 6.91 – 6.85 (m, 1H), 6.56 – 6.48 (m, 1H), 6.36 – 6.29 (m, 1H), 5.60 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.9, 197.3, 143.2, 141.7, 141.6, 140.7, 140.2, 139.1, 137.0, 134.9, 134.8, 134.1, 133.5, 132.1, 131.5, 131.2, 130.0, 129.7, 129.0, 128.8, 128.7, 128.4, 128.3, 127.6, 127.2, 127.1, 126.4,

126.1, 124.8, 123.1, 122.7, 122.6, 121.9, 121.5, 120.8, 120.2, 120.1, 119.1, 118.6, 111.4, 110.5, 110.3, 109.1, 106.1, 105.6, 58.9, 48.8; IR (KBr): 3592, 3444, 1703, 1659, 1469, 1262, 1091, 741, 705, 611, 549 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{52}H_{33}ClN_3O_2$ 766.2267, found 766.2258; Enantiomeric ratio = 92:8, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 6.146 min (major), t_R = 43.966 min (minor).

Procedure for the synthesis of product 8

Under argon atmosphere, *n*-BuLi (2.5 M in *n*-hexane, 40 μL) was added dropwise to the solution of compound **3ga** (73.5 mg, 0.1 mmol) in THF (1.0 mL) at -78 °C, and the reaction mixture was stirred at this temperature for 1 h. After the addition of $ClPPh_2$ (17.9 μL, 0.1 mmol), the reaction mixture was allowed to warm up to room temperature for 1 h. After the completion of the reaction which was indicated by TLC, the reaction mixture was directly purified through flash column chromatography (petroleum ether/ethyl acetate = 2/1) to give pure product **8** as a yellow solid.

(*R*$_a$)-2-(2'-benzhydryl-5'-(diphenylphosphino)-1*H*,1'*H*-[3,3'-biindol]-2-yl)-2-(1*H*-indol-3-yl)-1*H*-indene-1,3(2*H*)-dione (8): Flash column chromatography (petroleum ether/ethyl acetate = 2/1); 87% yield (73.1 mg); yellow solid; m.p. 165-166 °C; $[\alpha]_D^{20}$ = -204.1 (c 0.82, Acetone); ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.79 – 7.72 (m, 2H), 7.71 (s, 1H), 7.68 – 7.65 (m, 1H), 7.64 – 7.59 (m, 2H), 7.49 – 7.38 (m, 5H), 7.38 – 7.33 (m, 5H), 7.33 – 7.26 (m, 5H), 7.26 – 7.19 (m, 2H), 7.18 – 7.14 (m, 1H), 7.13 – 7.04 (m, 6H), 6.99 – 6.91 (m, 4H), 6.83 – 6.77 (m, 1H), 6.61 (s, 1H), 6.58 – 6.51 (m, 1H), 6.32 (d, *J* = 8.0 Hz, 1H), 5.58 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.7, 196.6, 142.5, 142.2, 142.0, 141.4, 140.2, 140.0, 135.8, 135.7, 135.6, 135.4, 135.2,

135.0, 134.7, 132.5, 132.3, 132.2, 132.1, 132.0, 131.5, 130.1, 129.9, 129.7, 129.6, 129.0, 128.9, 128.8, 128.7, 128.3, 127.2, 126.4, 123.6, 123.5, 123.1, 122.1, 122.0, 121.9, 121.5, 120.0, 119.2, 113.7, 113.1, 113.0, 112.9, 111.5, 110.5, 106.0, 105.3, 59.5, 49.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 39.5; IR (KBr): 3440, 3055, 1704, 1557, 1448, 1255, 742, 596, 487 cm^{-1}; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{58}H_{39}N_3O_2P$ 840.2785, found 840.2767; Enantiomeric ratio = 90:10, determined by HPLC (Daicel Chiralpak IA, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 5.456 min (major), t_R = 14.903 min (minor).

Supporting Information:

^{1}H and ^{13}C NMR spectra of substrates **1c**, **1h-1j**, **1o-1p**, **2** and products **3**, **7-8**, HPLC spectra of products **3** and **7-8**, X-ray single-crystal data for product **3ba**, theoretical calculation on the rotation barrier (PDF)

Single-crystal data of product **3ba** (CIF)

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