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钯催化不对称[3＋4]环加成构建吲哚并环庚烷

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摘要 报道了一种通过钯催化的脱羧方法, 能够以较好的收率、中等至优异的对映选择性, 以及良好的非对映选择性高效地合成吲哚并环庚烷类化合物. 在该方法中, 乙烯基吲哚噁唑酮被钯催化剂活化脱羧形成两性离子中间体, 接着被缺电子双烯所捕获发生不对称[3＋4]环加成反应.

关键词 脱羧; 吲哚并环庚烷; 不对称; 环加成

Palladium-Catalyzed Asymmetric [3＋4] Cycloadditions for the Construction of Cyclohepta[*b*]indoles

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Abstract A Pd-catalyzed decarboxylation strategy for the efficient synthesis of cyclohepta[*b*]indoles in good yields with good to excellent enantioselectivities and moderate diastereoselectivities is reported. In this procedure, viny indoloxazolidones were activated by Pd catalyst to generate zwitterionic intermediates *in situ*, which were then trapped by the electro-deficient diene species via the asymmetric [3＋4] cycloaddition process.

Keywords decarboxylation; cyclohepta[*b*]indoles; asymmetric; cycloadditions

1 Introduction

The novel indolyl delocalized dipoles (IDDPs) derived from the decarboxylation[1] of vinyl indoloxazolidones, which could serve as both all-carbon and aza-1,3-dipoles for the catalyzed asymmetric [3＋2] cycloadditions with 2-atom synthons, were exploited by our group[2] in 2021 (Scheme 1a). Independently, Chen group[3] (all-carbon 1,3-dipoles) and Shi group[4] (aza-1,3-dipoles) also realized [3＋2] cycloadditions, respectively (Scheme 1b). Moreover, Chen group[3] discovered that the vinyl indoloxazolidones could act as all-carbon 1,5-dipoles, and reported the Pd-catalyzed asymmetric [5＋2] cycloadditions of vinyl indoloxazolidones with sulfonyl amines (Scheme 1c). So far, asymmetric cycloadditions of vinyl indoloxazolidones with 2-atom synthons were well-established, but the cycloadditions of vinyl indoloxazolidones as all-carbon 1,3-dipoles with *n*-atom (*n*＞2) synthons remains an unmet challenge (Scheme 1).

Meanwhile, chiral cyclohepta[*b*]indoles are ubiquitous in many natural products and pharmaceutically active molecules, exhibiting significant biological activities.[5-7] Therefore, the enantioselective construction of this skeleton has attracted widespread attention.[8] The catalyzed asymmetric cycloadditions,[9] especially the [3＋4] cycloadditions,[10-11] stand out as important strategies to build this skeleton due to their excellent stereoselective control and substrate applicability.[12] During our previous investigations of [3＋4] cycloadditions,[13] we reasonably envisaged to construct cyclohepta[*b*]indole skeleton by employing vinyl indoloxazolidones as all-carbon 1,3-di- poles and electron-deficient dienes of indole-2,3-quinodimethanes as a 4-atom synthon[13b,14] (Scheme 2). In the reaction, the regioselective controls of vinyl indoloxazolidones and indole-2,3-quinodimethanes to realize [3＋4] cycloadditions are essential. Herein, we reported the Pd- catalyzed asymmetric [3＋4] cycloadditions of vinyl indoloxazolidones with indole-2,3-quinodimethanes, furnishing polysubs-

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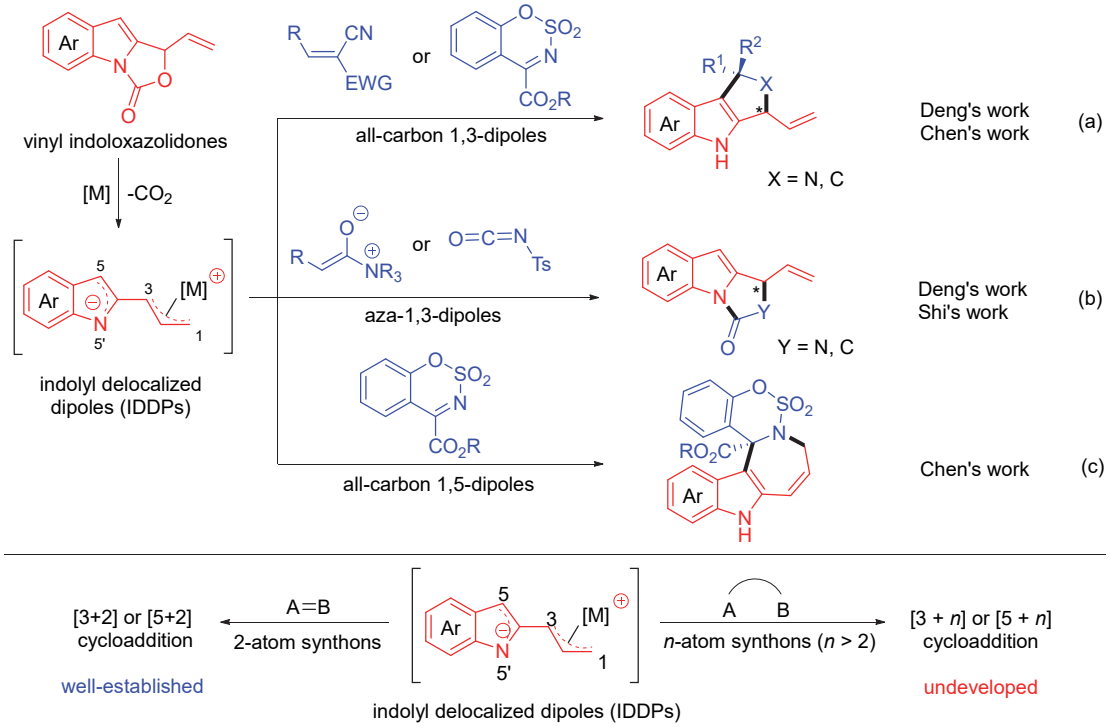
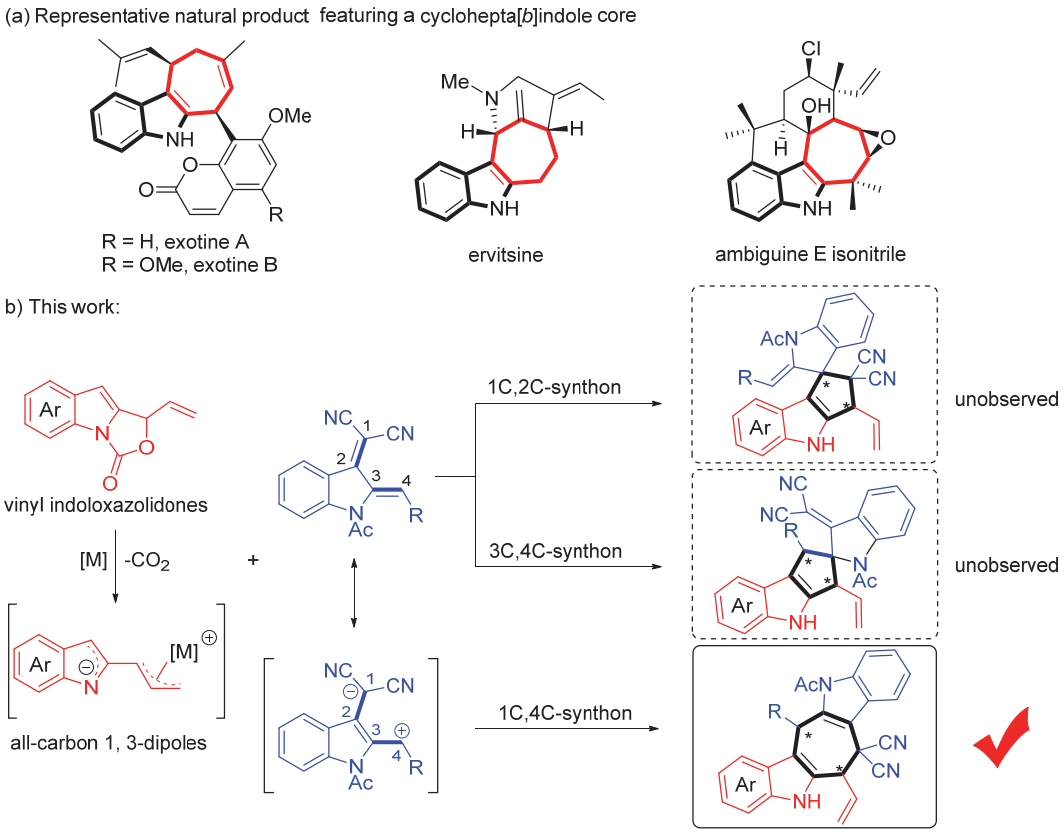


Scheme 1 Transition metal-catalyzed cycloadditions with participation of vinyl indoloxazolidones



Scheme 2 Pd-catalyzed asymmetric cycloadditions for the construction of cyclohepta[*b*]indole core

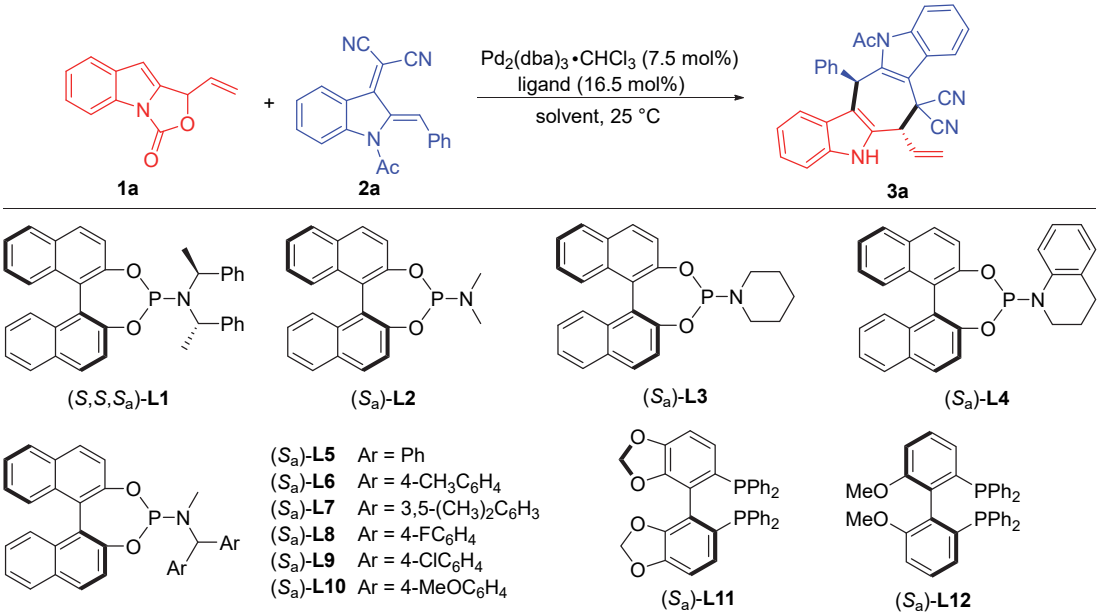
tituted cyclopenta[*b*]indoles in high yields with extreme regioselectivities, high enantioselectivities and moderate diastereoselectivities.

2 Results and discussion

We began our studies by employing vinyl indoloxazoli-

done **1a** and indole-2,3-quinodimethane **2a** as model substrates with $Pd_2(dba)_3$•$CHCl_3$ (7.5 mol%), ligand **L1** (16.5 mol%) in *N*,*N*-dimethylformamide (DMF) (*c* 0.1 mol/L) at 25 °C to test this envision. Gratifyingly, the desired [3+4] cycloaddition reaction proceeded smoothly, producing the target product **3a** in 83% yield with 23% *ee* and 10.2∶1 *dr* (Entry 1, Table 1). Subsequently, following a systematic examination of phosphoramidite-type ligands (Entries 2～5, more details were shown in Supporting Information), we were delighted to find that **L5** could provide **3a** in 59% yield with 75% *ee* and 4.0∶1 *dr* (Entry 5, Table 1). Encouraged by this promising result, more ligands derived from **L5** were utilized in this reaction (Entries 3～7, Table 1). To our delight, when using the phosphoramidite **L10** which bore the methoxy group on the para-position of both phenyl rings, **3a** was achieved in 74% yield with 95% *ee* and 5.2∶1 *dr* (Entry 10, Table 1). Moreover, various of bisphosphine ligands were examined (Entries 11～12, Table 1, more details were shown in Supporting Information), and excellent yield (83%) and diastereoselectivitiy (>20∶1) were achieved with moderate enantioselectivity (67% *ee*) (Entry 12, Table 1), which provided an efficient way for the pure single diastereomer of the product. Further, screening of different solvents (Entries 13～16, Table 1) uncovered that DCM was the optimal. Therefore, the reaction conditions as listed in Entry 10 were selected as the optimal conditions for the cycloadditions. The absolute configuration of **3a** (>99% *ee* after recrystallization) was assigned as *R* by X-ray diffraction analysis.

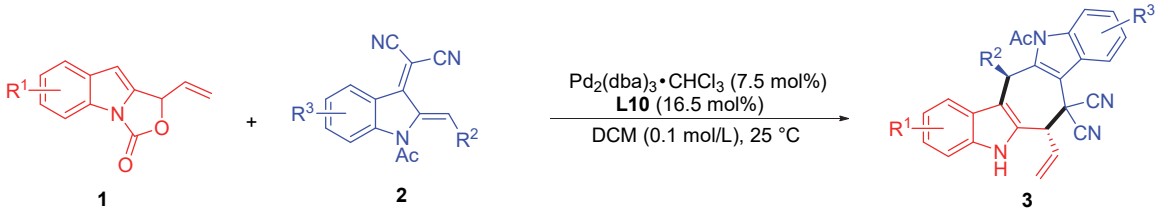
Table 1 Optimization of the reaction conditions[a]



Entry [a]	Ligand	Solvent	Yield[b]/%	*dr*[c]	*ee*[d]/%
1	**L1**	DCM	83	10.2∶1	23
2	**L2**	DCM	73	7.6∶1	68
3	**L3**	DCM	93	10.1∶1	31
4	**L4**	DCM	44	2.9∶1	12
5	**L5**	DCM	59	4.0∶1	75
6	**L6**	DCM	76	3.5∶1	81
7	**L7**	DCM	45	3.4∶1	88
8	**L8**	DCM	70	4.0∶1	87
9	**L9**	DCM	73	3.3∶1	89
10	**L10**	DCM	74	5.2∶1	95
11	**L11**	DCM	43	>20∶1	68
12	**L12**	DCM	83	>20∶1	67
13	**L10**	THF	36	2.8∶1	86
14	**L10**	PhMe	30	1.1∶1	56
15	**L10**	$CHCl_3$	76	5.1∶1	94
16	**L10**	DCE	36	2.9∶1	44

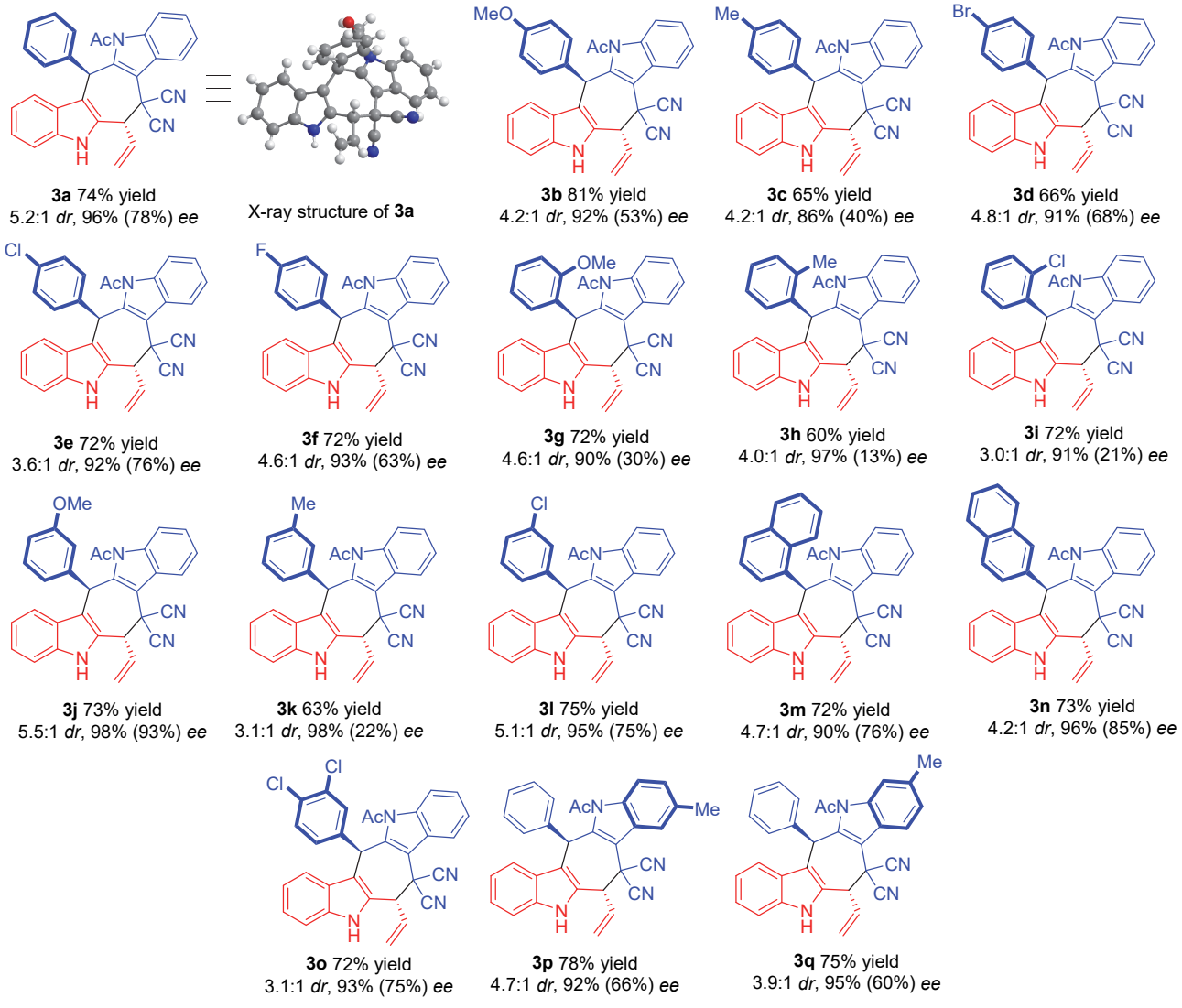
[a] General procedure: **1a** (0.3 mmol), **2a** (0.2 mmol), $Pd_2(dba)_3$•$CHCl_3$ (7.5 mol%), and ligand (16.5 mol%) in 2.0 mL of DCM under N_2 atmosphere at 25 °C. THF, tetrahydrofuran; DCE, 1,2-dichloroethane. [b] Isolated yield of **3a**. [c] The diastereomeric ratio (*dr*) was determined by ^{1}H NMR. [d] *ee* value was determined by chiral HPLC analysis.

Under the optimal reaction conditions (7.5 mol% $Pd_2(dba)_3$•$CHCl_3$, 16.5 mol% (S_a)-**L10**, in 2.0 mL of DCM at 25 °C), the substrate scope was examined (Scheme 3). The limitation of indole-2,3-quinodimethanes **2** was first explored. As summarized in Scheme 3, an array of indole-2,3-quinodimethanes (**2b**～**2l**) possessing either electron-donating or electron-withdrawing groups on the *ortho*- (*o*-OMe, *o*-Me, *o*-Cl), *meta*- (*m*-OMe, *m*-Me, *m*-Cl), and



1 **2** **3**

Variation of indole-2,3-quinodimethanes



3a 74% yield, 5.2:1 *dr*, 96% (78%) *ee*

X-ray structure of **3a**

3b 81% yield, 4.2:1 *dr*, 92% (53%) *ee*

3c 65% yield, 4.2:1 *dr*, 86% (40%) *ee*

3d 66% yield, 4.8:1 *dr*, 91% (68%) *ee*

3e 72% yield, 3.6:1 *dr*, 92% (76%) *ee*

3f 72% yield, 4.6:1 *dr*, 93% (63%) *ee*

3g 72% yield, 4.6:1 *dr*, 90% (30%) *ee*

3h 60% yield, 4.0:1 *dr*, 97% (13%) *ee*

3i 72% yield, 3.0:1 *dr*, 91% (21%) *ee*

3j 73% yield, 5.5:1 *dr*, 98% (93%) *ee*

3k 63% yield, 3.1:1 *dr*, 98% (22%) *ee*

3l 75% yield, 5.1:1 *dr*, 95% (75%) *ee*

3m 72% yield, 4.7:1 *dr*, 90% (76%) *ee*

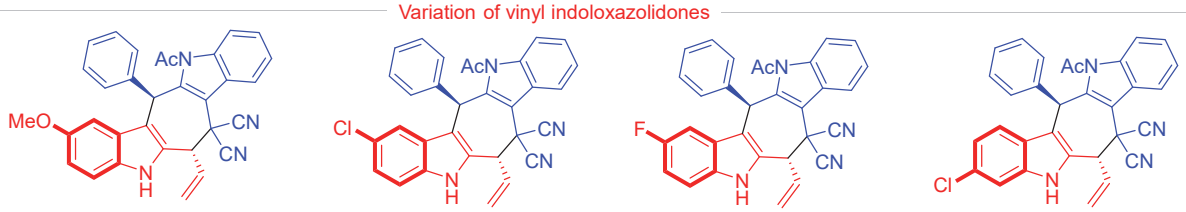
3n 73% yield, 4.2:1 *dr*, 96% (85%) *ee*

3o 72% yield, 3.1:1 *dr*, 93% (75%) *ee*

3p 78% yield, 4.7:1 *dr*, 92% (66%) *ee*

3q 75% yield, 3.9:1 *dr*, 95% (60%) *ee*

Variation of vinyl indoloxazolidones



3r 75% yield, 5.3:1 *dr*, 98% (83%) *ee*

3s 67% yield, 4.3:1 *dr*, 95% (82%) *ee*

3t 72% yield, 4.6:1 *dr*, 94% (63%) *ee*

3u 61% yield, 3.6:1 *dr*, 94% (83%) *ee*

Scheme 3 Substrate scope of Pd-catalyzed asymmetric [3＋4] cycloadditions

para- (*p*-OMe, *p*-Me, *p*-Br, *p*-Cl, *p*-F) positions of phenyl rings were compatible in the reactions, and the corresponding products **3b**～**3l** were obtained in good yields (60%～81%) with good to excellent enantioselectivities (86%～98% *ee*) and moderate diastereoselectivities (3.0∶1 to 5.2∶1 *dr*). As showcased by examples **3m** and **3n**, fused-ring compounds (*α*- or *β*-naphthyl) were also accommodated (**3m**, 72% yield, 90% *ee*, 4.7∶1 *dr*; **3n**, 73% yield, 96% *ee*, 4.2∶1 *dr*). Moreover, the indole-2,3-quinodimethane with disubstituted aryl group (**2o**) also proceeded to afford **3o** in good yields (72%) with excellent enantioselectivity (95% *ee*) and moderate diastereoselectivity (3.1∶1 *dr*). In addition, indole-2,3-quinodimethanes (**2p**～**2q**) containing the methyl group on the C5 or C6 of the indole ring also showed good reactivities, affording products **3p** and **3q** in good yields with excellent enantioselectivities and moderate diastereoselectivities (**3p**, 78% yield, 92% *ee*, 4.7∶1 *dr*; **3q**, 75% yield, 95% *ee*, 3.9∶1 *dr*). Then, the scope of vinyl indoloxazolidones **1** was examined. Vinyl indoloxazolidones (**1b**～**1d**) with either electron-donating or electron-withdrawing groups (5-OMe, 5-Cl, 5-F and 6-Cl) on C5 and C6 presented preferable results, obtaining the corresponding products **3r**～**3u** in good yields (61%～75%) with excellent enantioselectivities (94%～98% *ee*) and moderate diastereoselectivities (4.3∶1 to 5.3∶1 *dr*).

Subsequently, a scale-up experiment between **1a** (896.4 mg) and **2a** (934.0 mg) was also conducted, affording **3a** (895.7 mg) in slightly lower yield (64%) with maintained enantiopurity (95% *ee*, 5.6∶1 *dr*). To demonstrate the synthetic utility of the catalytic asymmetric [3+4] cycloadditions, further transformations of **3a** were explored (Scheme 4). The stereoselective hydrolysis of **3a** occurred smoothly with NaOH and provided amide derivative **4** bearing three contiguous stereogenic centers in 65% yield with excellent enantioselectivity (95% *ee*) and diastereoselectivity (>20∶1 *dr*). An addition of *n*-Bu_3SnH to **3a** at 55 ℃ furnished the deprotected cyclohepta[*b*]indole **5** in 94% yield without erosion of enantiopurity (95% *ee*, > 20∶1 *dr*).

To better explain the formation of the products. A putative mechanism was proposed as shown in Scheme 5 by utilizing the formation of product **3a** as an example. First, coordination of *in situ* generated Pd catalyst to vinyl indoloxazolidone **1a** gives Pd-π-allyl intermediate **A**. Then, the nucleophilic addition of Pd-π-allyl intermediate **A** to indole-2,3-quinodimethane **2a** was favored from the *Si*-face, followed by intramolecular allylic substitution. The **3a** was furnished with high enantioselectivities and the Pd catalyst was regenerated.

3 Conclusions

In summary, we have demonstrated the first Pd-catalyzed asymmetric [3+4] cycloadditions of vinyl indoloxazolidones with indole-2,3-quinodimethanes to afford cyclohepta[*b*]indoles in good yields (60%～81%) with good to excellent enantioselectivities (86%～98% *ee*) and moderate diastereoselectivities (3.0∶1 to 5.5∶1 *dr*). The diastereomers were easily to be isolated, which provided a convenient way to obtain all four stereoconfigurations of the products. This approach represents the first example of the catalytic asymmetric [3+4] cycloadditions of vinyl indoloxazolidones. In addition, a range of [3+4] cycloadditions between vinyl indoloxazolidones and oxa- or aza-dienes are ongoing in our laboratory.

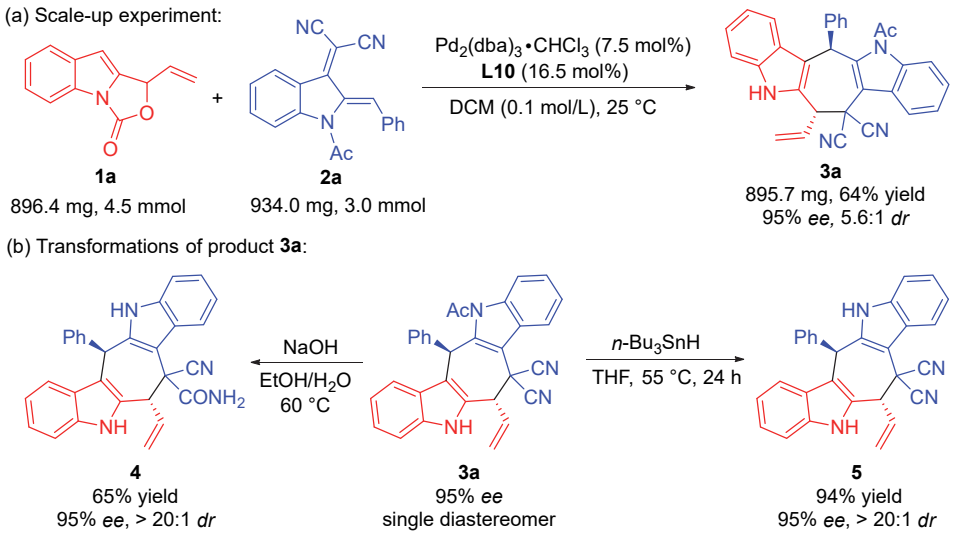
4 Experimental section

4.1 General procedure for the synthesis of 1 and 2

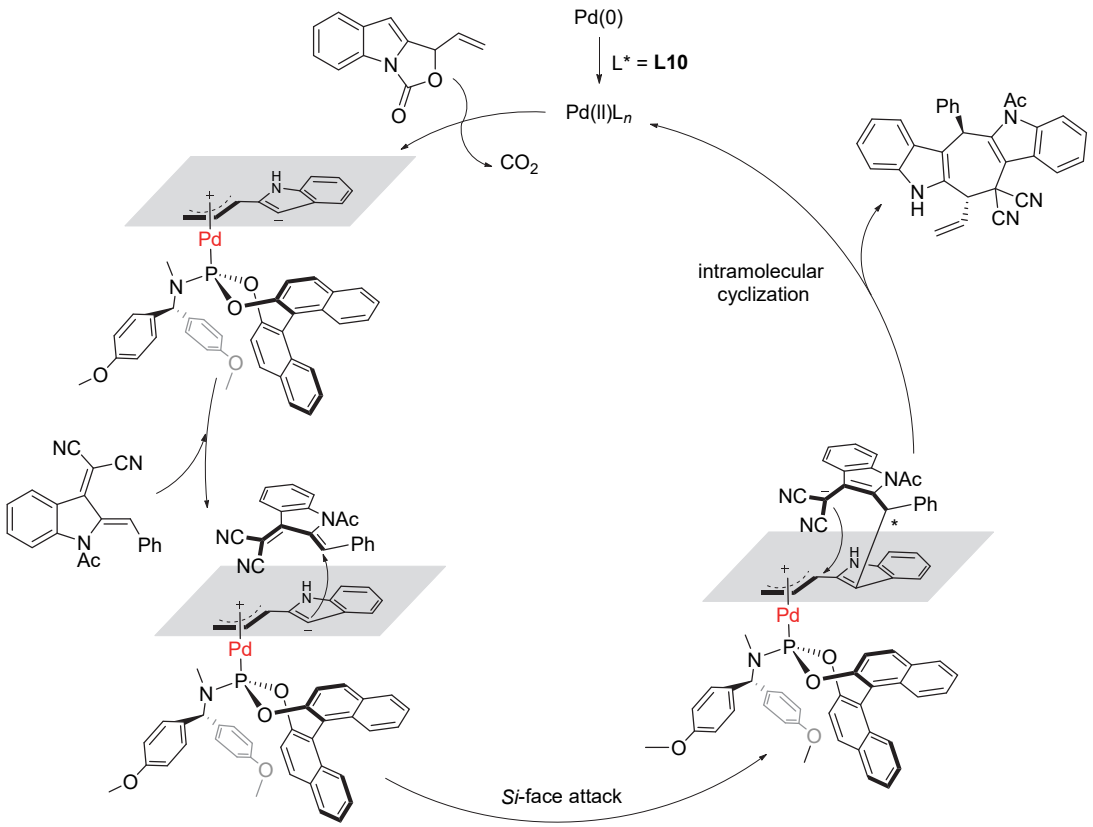
Substrates **1a** and **1r**～**1u** were prepared according to the reported procedures.[2] Substrates **2a**～**2** were prepared according to the reported procedures.[14]

4.2 General procedure for the synthesis of the 3

Under nitrogen atmosphere, $Pd_2(dba)_3$•$CHCl_3$ (15.4 mg, 0.015 mmol) and (S_a)-**L10** (18.8 mg, 0.033 mmol) were



Scheme 4 Scale-up experiment and transformations



Scheme 5 Proposed mechanism for Pd-catalyzed asymmetric [3+4] cycloadditions

added sequentially into a flame-dried Schlenk tube equipped with a magnetic stirring bar. The tube was evacuated and back-filled with nitrogen for three times. Then the anhydrous dichloromethane (2.0 mL) was added via syringe sequentially and the resulting mixture stirred at 25 ℃ for 30 min. Then, vinyl indoloxazolidones **1** (0.3 mmol) and indole-2,3-quinodimethanes **2** (0.2 mmol) were added sequentially. Once starting material **2** was consumed (24～72 h, monitored by TLC), the mixture was concentrated and purified by column chromatography (petroleum ether/dichloromethane, *V*∶*V*=1∶1) to give the corresponding cycloadducts **3**.

(6*R*,12*S*)-5-Acetyl-6-phenyl-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3a**): White solid, 74% yield (69.0 mg), 5.2∶1 *dr*. Major diastereomer: 96% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol)=96/4, flow rate=1.0 mL/min, λ=254 nm), t_R=19.223 min (minor), 23.012 min (major). $[\alpha]_D^{25}$ −178.5 (*c* 0.10, CH_2Cl_2); m.p. 196～198 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.30 (s, 1H), 8.03～7.93 (m, 1H), 7.88～7.80 (m, 1H), 7.78～7.71 (m, 1H), 7.50～7.41 (m, 2H), 7.41～7.35 (m, 1H), 7.29～7.17 (m, 5H), 7.10 (m, 2H), 6.73 (s, 1H), 6.49 (m, 1H), 5.76 (d, *J*=10.3 Hz, 1H), 5.51 (d, *J*=16.9 Hz, 1H), 4.55 (d, *J*=9.2 Hz, 1H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.0, 141.8, 139.5, 134.8, 134.5, 128.8, 128.7 (2C), 128.6, 127.4(0), 127.3(7), 127.0 (2C) 126.9, 126.3, 125.7, 124.0, 123.0, 120.9, 119.6, 118.4, 117.9, 114.4, 114.2, 113.2, 111.8, 110.1, 46.8, 39.9, 37.7, 28.3; HRMS (ESI-TOF) calcd for $C_{31}H_{23}N_4O$ $[M+H]^+$: 467.1866, found 467.1869.

Minor diastereomer: 78% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol)=96/4, flow rate=1.0 mL/min, λ=254 nm), t_R=14.701 min (major), 17.749 min (minor). $[\alpha]_D^{25}$ −143.8 (*c* 0.10, CH_2Cl_2); m.p. 212～214 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.2～8.1 (m, 2H), 7.7～7.7 (m, 1H), 7.6～7.6 (m, 1H), 7.4～7.3 (m, 3H), 7.2～7.1 (m, 3H), 7.1 (m, 2H), 7.0～6.9 (m, 2H), 6.9 (s, 1H), 5.8 (ddd, *J*=16.7, 10.0, 8.7 Hz, 1H), 5.2 (d, *J*=16.7 Hz, 1H), 5.0 (d, *J*=10.1 Hz, 1H), 4.3 (d, *J*=8.7 Hz, 1H), 2.7 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 171.6, 142.8, 139.2, 134.9, 134.8, 130.7, 129.3, 128.8, 128.5 (2C), 127.4 (2C), 127.3, 126.8, 125.5, 123.8, 123.3, 123.1, 121.0, 119.9, 118.8, 114.5, 114.4, 114.0, 113.9, 111.5, 107.5, 52.1, 39.3, 38.1, 28.1; HRMS (ESI-TOF) calcd for $C_{31}H_{23}N_4O$ $[M+H]^+$: 467.1866, found 467.1868.

(6*R*,12*S*)-5-Acetyl-6-(4-methoxyphenyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3b**): White solid, 81% yield (80.4 mg), 4.2∶1 *dr*. Major diastereomer: 92% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 93/7, flow rate = 1.0 mL/min, λ=254 nm), t_R=16.453 min (minor), 17.966 min (major). $[\alpha]_D^{25}$ −120.5 (*c* 0.10, CH_2Cl_2); m.p. 177～179 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.26 (s, 1H), 8.01～7.93 (m, 1H), 7.81 (m, 1H), 7.77～7.72 (m, 1H), 7.47～7.40 (m, 2H), 7.38 (m, 1H), 7.25～7.22 (m, 2H), 7.01 (m, 2H), 6.77 (m, 2H), 6.64 (s, 1H), 6.50 (m, 1H), 5.78 (d, *J*=10.3 Hz, 1H), 5.55 (d, *J*=16.9 Hz, 1H), 4.57 (d, *J*=9.2 Hz, 1H), 3.75 (s, 3H), 2.84 (s, 3H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ: 171.0, 158.4, 139.8, 134.8, 134.5, 133.8, 128.7(0), 128.6(9), 128.1 (2C), 127.4, 127.3, 126.3, 125.7, 124.0, 123.0, 120.9, 119.6, 118.6, 117.9, 114.4, 114.2, 114.1 (2C), 113.2, 111.8, 109.9, 55.4, 46.8, 39.9, 37.0, 28.3; HRMS (ESI-TOF) calcd for $C_{32}H_{24}N_4NaO_2$ $[M+Na]^+$: 519.1791, found 519.1794.

Minor diastereomer: 53% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol)=93/7, flow rate=1.0 mL/min, λ=254 nm), t_R=22.047 min (minor), 24.894 min (major). $[\alpha]_D^{25}$ −116.2 (*c* 0.10, CH_2Cl_2); m.p. 201～203 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.28～8.20 (m, 2H), 7.77～7.72 (m, 1H), 7.70～7.65 (m, 1H), 7.48～7.40 (m, 2H), 7.40～7.36 (m, 1H), 7.32～7.15 (m, 2H), 6.99～6.90 (m, 2H), 6.88 (s, 1H), 6.75～6.65 (m, 2H), 5.92 (ddd, *J*=16.6, 10.0, 8.7 Hz, 1H), 5.36～5.26 (d, *J*=16.6 Hz 1H), 5.14 (d, *J*=10.0 Hz, 1H), 4.38 (d, *J*=8.8 Hz, 1H), 3.72 (s, 3H), 2.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.7, 158.3, 139.4, 135.4, 134.9, 134.8, 130.7, 129.2, 128.7, 128.5 (2C), 127.3, 125.5, 123.7, 123.3, 123.2, 121.0, 119.9, 118.8, 114.5(1), 114.5(0), 114.1, 113.9, 113.8 (2C), 111.5, 107.3, 55.3, 52.2, 39.4, 37.5, 28.1; HRMS (ESI-TOF) calcd for $C_{32}H_{24}N_4NaO_2$ $[M+Na]^+$: 519.1791, found 519.1793.

(6*R*,12*S*)-5-Acetyl-6-(p-tolyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3c**): White solid, 65% yield (62.4 mg), 4.2∶1 *dr*. Major diastereomer: 86% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol)=96/4, flow rate=1.0 mL/min, λ=254 nm), t_R=17.328 min (minor), 20.618 min (major). $[\alpha]_D^{25}$ −275.2 (*c* 0.10, CH_2Cl_2); m.p. 165～167 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.59 (s, 1H), 8.07～7.94 (m, 1H), 7.83 (m, 2H), 7.47 (m, 3H), 7.16 (m, 2H), 7.09 (m, 2H), 6.93 (m, 2H), 6.66 (m, 1H), 6.57 (s, 1H), 5.74 (d, *J*=10.3 Hz, 1H), 5.38 (d, *J*=16.7 Hz, 1H), 4.41 (d, *J*=9.8 Hz, 1H), 2.85 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 171.8, 139.5, 138.9, 135.6, 134.9, 134.2, 129.3, 129.1 (2C), 128.8, 126.6 (2C), 126.5, 126.2, 125.4(3), 125.4(0), 123.5, 122.0, 119.9, 118.2, 117.8, 117.0, 115.4, 114.1, 113.2, 111.9, 108.3, 47.1, 40.0, 36.9, 28.1, 20.6; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O$ $[M+H]^+$: 481.2023, found 481.2029.

Minor diastereomer: 40% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol)=96/4, flow rate=1.0 mL/min, λ=254 nm), t_R=24.626 min (minor), 30.847 min (major). $[\alpha]_D^{25}$ −188.4 (*c* 0.10, CH_2Cl_2); m.p. 188～190 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.3～8.2 (m, 2H), 7.8 (d, *J*=7.7 Hz, 1H), 7.7 (d, *J*=7.8 Hz, 1H), 7.4 (m, 2H), 7.4 (d, *J*=7.9 Hz, 1H), 7.3 (m, 2H), 7.0 (d, *J*=7.9 Hz, 2H), 6.9～6.9 (m, 3H), 6.0～5.9 (m, 1H), 5.3 (d, *J*=16.7 Hz, 1H), 5.1 (d, *J*=10.0 Hz, 1H), 4.4 (d, *J*=8.8 Hz, 1H), 2.8 (s, 3H), 2.2 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.7, 139.7, 139.3, 136.3, 134.9, 134.8, 130.7, 129.3, 129.2 (2C), 128.7, 127.3, 127.2 (2C), 125.5, 123.7, 123.2, 123.1, 121.0, 119.9, 118.8, 114.5, 114.4, 114.1, 113.9, 111.4, 107.3, 52.2, 39.4, 37.8, 28.1, 21.1; HRMS (ESI-TOF) calcd for $C_{32}H_{24}N_4NaO$ $[M+Na]^+$: 503.1842, found 503.1847.

(6*R*,12*S*)-5-Acetyl-6-(4-bromophenyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3d**): White solid, 66% yield (72.0 mg), 4.8∶1 *dr*. Major diastereomer: 91% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=5.199 min (major), 6.321 min (minor). $[\alpha]_D^{25}$ −150.5 (*c* 0.10, CH_2Cl_2); m.p. 114～116 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.35 (s, 1H), 8.10～7.94 (m, 1H), 7.85～7.77 (m, 1H), 7.75～7.66 (m, 1H), 7.50～7.42 (m, 2H), 7.40～7.31 (m, 3H), 7.30～7.17 (m, 2H), 7.06～6.91 (m, 2H), 6.65 (s, 1H), 6.49 (ddd, *J*=16.9, 10.3, 9.1 Hz, 1H), 5.77 (d, *J*=10.3 Hz, 1H), 5.56 (d, *J*=16.8 Hz, 1H), 4.48 (d, *J*=9.1 Hz, 1H), 2.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.0, 141.0, 139.0, 134.8, 134.4, 131.8 (2C), 128.8 (2C), 128.7, 128.4, 127.3, 127.2, 126.5, 125.9, 124.1, 123.2, 121.0, 120.8, 119.7, 117.7(8), 117.7(7), 114.3, 114.0, 113.0, 111.8, 110.4, 46.8, 39.9, 37.4, 28.3; HRMS (ESI-TOF) calcd for $C_{31}H_{21}Br^{79}N_4NaO$ $[M+Na]^+$: 567.0791, found 567.0792; calcd for $C_{31}H_{21}Br^{81}N_4NaO$ $[M+Na]^+$: 569.0770, found 569.0776.

Minor diastereomer: 68% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=4.910 min (major), 5.764 min (minor). $[\alpha]_D^{25}$ −177.7 (*c* 0.10, CH_2Cl_2); m.p. 154～156 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.26 (s, 1H), 8.21～8.15 (m, 1H), 7.69 (m, 1H), 7.65～7.58 (m, 1H), 7.43～7.35 (m, 2H), 7.35～7.28 (m, 1H), 7.24～7.13 (m, 4H), 6.86～6.82 (m, 2H), 6.81 (s, 1H), 5.78 (ddd, *J*=16.8, 10.0, 8.4 Hz, 1H), 5.19 (d, *J*=16.7, 1H), 5.05 (d, *J*=9.8, Hz, 1H), 4.31 (d, *J*=8.5 Hz, 1H), 2.73 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.5, 141.9, 138.7, 134.8(5), 134.8(0), 132.1, 131.5 (2C), 130.4, 129.1 (2C), 128.9, 127.3, 125.7, 123.9, 123.4(4), 123.4(1), 121.2, 120.6, 120.0, 118.5, 114.4, 114.1, 113.9, 113.8, 111.6, 107.8, 51.8, 39.2, 37.8, 28.2; HRMS (ESI-TOF) calcd for $C_{31}H_{21}Br^{79}N_4NaO$ $[M+Na]^+$: 567.0791, found 567.0790; calcd for $C_{31}H_{21}Br^{81}N_4NaO$ $[M+Na]^+$: 569.0770, found 569.0774.

(6*R*,12*S*)-5-Acetyl-6-(4-chlorophenyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3e**): White solid, 72% yield (72.1 mg), 3.6∶1 *dr*. Major diastereomer: 92% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=5.062 min (major), 5.970 min (minor). $[\alpha]_D^{25}$ −133.0 (*c* 0.10, CH_2Cl_2); m.p. 208～210 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.33 (s, 1H), 8.02～7.94 (m, 1H), 7.80 (m, 1H), 7.75～7.68 (m, 1H), 7.49～7.40 (m, 2H), 7.37 (m, 1H), 7.29～7.14 (m, 4H), 7.03 (m, 2H), 6.67 (s, 1H), 6.49 (m, 1H), 5.78 (d, *J*=10.3 Hz, 1H), 5.56 (d, *J*=16.9 Hz, 1H), 4.48 (d, *J*=9.1 Hz, 1H), 2.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.0, 140.5, 139.1, 134.8, 134.4, 132.7, 128.8(2) (2C), 128.8(0), 128.4(3), 128.4(0) (2C), 127.4, 127.2, 126.5, 125.9, 124.1, 123.2, 121.0, 119.7, 117.9, 117.8, 114.3, 114.1, 113.0, 111.8, 110.4, 46.8, 39.9, 37.4, 28.3; HRMS (ESI-TOF) calcd for $C_{31}H_{21}ClN_4NaO$ $[M+Na]^+$: 523.1296, found 523.1300.

Minor diastereomer: 76% *ee*; HPLC (Chiralpak IF,

V(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 4.810 min (major), 5.493 min (minor). $[\alpha]_D^{25}$ −98.0 (*c* 0.10, CH_2Cl_2); m.p. 190～192 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.29～8.24 (m, 2H), 7.79～7.73 (m, 1H), 7.71～7.65 (m, 1H), 7.50～7.41 (m, 2H), 7.42～7.34 (m, 1H), 7.26 (m, 2H), 7.13 (m, 2H), 6.96 (m, 2H), 6.90 (s, 1H), 5.86 (ddd, *J* = 16.6, 10.0, 8.5 Hz, 1H), 5.26 (d, *J* = 16.7 Hz, 1H), 5.12 (d, *J* = 10.1 Hz, 1H), 4.37 (d, *J* = 8.5 Hz, 1H), 2.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 141.4, 138.8, 134.9, 134.8, 132.5, 130.4, 129.1, 128.9, 128.7 (2C), 128.5 (2C), 127.3, 125.7, 123.9, 123.5, 123.4, 121.2, 120.0, 118.5, 114.4, 114.1, 113.9, 113.8, 111.6, 107.8, 51.8, 39.2, 37.7, 28.2; HRMS (ESI-TOF) calcd for $C_{31}H_{21}ClN_4NaO$ $[M+Na]^+$: 523.1296, found 523.1298.

(6*R*,12*S*)-5-Acetyl-6-(4-fluorophenyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3f**): White solid, 72% yield (69.7 mg), 4.6∶1 *dr*. Major diastereomer: 93% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 96/4, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 19.969 min (minor), 22.549 min (major). $[\alpha]_D^{25}$ −162.5 (*c* 0.10, CH_2Cl_2); m.p. 178～180 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.38 (s, 1H), 8.01～7.95 (m, 1H), 7.83～7.77 (m, 1H), 7.73～7.68 (m, 1H), 7.47～7.42 (m, 2H), 7.38～7.33 (m, 1H), 7.26～7.19 (m, 2H), 7.05 (m, 2H), 6.91 (m, 2H), 6.67 (s, 1H), 6.53～6.44 (m, 1H), 5.75 (d, *J* = 10.4 Hz, 1H), 5.52 (d, *J* = 16.9 Hz, 1H), 4.48 (d, *J* = 9.2 Hz, 1H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.1, 161.6 (d, *J* = 245.7 Hz), 139.4, 137.6 (d, *J* = 3.2 Hz), 134.8, 134.4, 128.7, 128.5(5) (d, *J* = 8.0 Hz) (2C), 128.5(0), 127.3, 127.2, 126.4, 125.8, 124.1, 123.1, 121.0, 119.6, 118.2, 117.8, 115.5 (d, *J* = 21.6 Hz) (2C), 114.3, 114.1, 113.1, 111.8, 110.2, 46.9, 39.9, 37.1, 28.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −115.98; HRMS (ESI-TOF) calcd for $C_{31}H_{21}FN_4NaO$ $[M+Na]^+$: 507.1592, found 507.1598.

Minor diastereomer: 63% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 96/4, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 12.178 min (major), 15.327 min (minor). $[\alpha]_D^{25}$ −212.5 (*c* 0.10, CH_2Cl_2); m.p. 172～174 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.30 (s, 1H), 8.28～8.23 (m, 1H), 7.75 (m, 1H), 7.71～7.65 (m, 1H), 7.48～7.43 (m, 2H), 7.39 (m, 1H), 7.32～7.22 (m, 2H), 7.03～6.95 (m, 2H), 6.92～6.82 (m, 3H), 5.86 (ddd, *J* = 16.6, 10.0, 8.5 Hz, 1H), 5.27 (d, *J* = 16.7 Hz, 1H), 5.12 (d, *J* = 10.1 Hz, 1H), 4.38 (d, *J* = 8.6 Hz, 1H), 2.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 161.5 (d, $J_{C\text{-}F}$ = 245.6 Hz), 139.1, 138.6 (d, $J_{C\text{-}F}$ = 3.2 Hz), 134.9, 134.8, 130.5, 129.1, 128.9(3) (d, $J_{C\text{-}F}$ = 8.1 Hz) (2C), 128.9(0), 127.3, 125.7, 123.9, 123.4, 123.2, 121.1, 120.0, 118.5, 115.2 (d, $J_{C\text{-}F}$ = 21.4 Hz) (2C), 114.4, 114.1, 114.0, 113.9, 111.6, 107.6, 51.8, 39.2, 37.5, 28.2; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −116.18; HRMS (ESI-TOF) calcd for $C_{31}H_{21}FN_4NaO$ $[M+Na]^+$: 507.1592, found 507.1593.

(6*S*,12*S*)-5-Acetyl-6-(2-methoxyphenyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3g**): White solid, 72% yield (71.5 mg), 4.6∶1 *dr*. Major diastereomer: 90% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 4.981 min (major), 5.474 min (minor). $[\alpha]_D^{25}$ +112.5 (*c* 0.10, CH_2Cl_2); m.p. 156～158 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.17 (s, 1H), 8.00～7.88 (m, 2H), 7.79～7.71 (m, 1H), 7.45～7.39 (m, 2H), 7.32～7.27 (m,1H), 7.24～7.10 (m, 4H), 6.94～6.83 (m, 2H), 6.79 (s, 1H), 6.59～6.45 (m, 1H), 5.78 (d, *J* = 10.3 Hz, 1H), 5.61 (d, *J* = 16.9 Hz, 1H), 4.99 (d, *J* = 9.1 Hz, 1H), 3.66 (s, 3H), 2.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.9, 156.9, 138.8, 134.7, 134.6, 129.3, 128.8, 128.7, 128.5, 127.5, 127.3, 126.7, 126.2, 125.7, 123.9, 122.5, 120.1(2), 120.1(0), 119.8, 119.3, 116.6, 114.6, 114.5, 113.2, 111.4(0), 111.3(7), 111.0, 55.3, 46.3, 40.0, 34.1, 28.0; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O_2$ $[M+H]^+$: 497.1972, found 497.1972.

Minor diastereomer: 30% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 5.963 min (major), 7.046 min (minor). $[\alpha]_D^{25}$ +168.4 (*c* 0.10, CH_2Cl_2); m.p. 187～189 ℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 11.39 (s, 1H), 8.04～8.00 (m, 1H), 7.89～7.83 (m, 1H), 7.49～7.44 (m, 3H), 7.39 (m, 1H), 7.23 (m, 1H), 7.10 (m, 1H), 7.03 (m, 1H), 6.95 (m, 1H), 6.88 (s, 1H), 6.82 (m, 1H), 6.74 (m, 1H), 6.21 (ddd, *J* = 16.7, 10.1, 9.5 Hz, 1H), 5.45 (d, *J* = 16.7 Hz, 1H), 5.22 (d, *J* = 10.1 Hz, 1H), 4.97 (d, *J* = 9.0 Hz, 1H), 3.56 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 172.2, 156.8, 139.4, 134.5, 134.4, 131.5, 130.2(1), 130.2(0), 129.1, 128.6, 128.3, 126.1, 125.2, 123.1, 123.0, 121.5, 120.0, 119.8, 118.9, 118.4, 114.6, 114.3(5), 114.3(0), 111.6, 111.4, 111.3, 107.5, 55.0, 49.6, 39.0, 34.7, 27.4; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O_2$ $[M+H]^+$: 497.1972, found 497.1979.

(6*R*,12*S*)-5-Acetyl-6-(*o*-tolyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3h**): White solid, 60% yield (57.6 mg), 4.0∶1 *dr*. Major diastereomer: 97% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 96/4, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 11.953 min (major), 14.796 min (minor). $[\alpha]_D^{25}$ −137.4 (*c* 0.10, CH_2Cl_2); m.p. 175～177 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.30 (s, 1H), 7.98～7.93 (m, 1H), 7.83 (m, 1H), 7.76～7.69 (m, 1H), 7.46～7.40 (m, 2H), 7.33～7.30 (m, 1H), 7.17 (m, 6H), 6.78 (s, 1H), 6.50 (ddd, *J* = 16.9, 10.3, 8.9 Hz, 1H), 5.77 (d, *J* = 10.3 Hz, 1H), 5.57 (d, *J* = 16.9 Hz, 1H), 5.02 (d, *J* = 8.9 Hz, 1H), 2.77 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.0, 139.8, 138.5, 137.4, 134.6, 134.5, 131.9, 129.4, 128.4, 127.3(8), 127.3(6), 127.1, 126.7, 126.3, 125.7(3), 125.7(0), 124.0, 122.8, 120.6, 119.3, 118.8, 116.3, 114.5, 114.3, 113.1, 111.8, 110.9, 46.0, 39.9, 36.5, 28.2, 21.5; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O$ $[M+H]^+$: 481.2023, found 481.2027.

Minor diastereomer: 13% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 96/4, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 16.140 min (minor), 28.878 min (major). $[\alpha]_D^{25}$ −164.3 (*c* 0.10, CH_2Cl_2); m.p. 220～222 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.34 (s, 1H), 8.08～8.01 (m,

1H), 7.39 (m, 3H), 7.34～7.22 (m, 3H), 7.16 (m, 2H), 7.04 (m, 2H), 6.70 (m, 1H), 6.55 (m, 1H), 6.38 (s, 1H), 5.85 (d, J=10.5 Hz, 1H), 5.80 (d, J=17.1 Hz, 1H), 4.92 (d, J=9.2 Hz, 1H), 2.10 (s, 3H), 1.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.7, 142.4, 141.3, 141.1, 139.2, 135.3, 134.6, 132.9, 131.2, 130.0, 129.3, 128.0, 127.6, 126.2, 126.1, 125.7, 125.5, 123.0, 122.6, 120.3, 120.0, 120.0, 113.9, 113.1, 112.3, 111.8, 111.7, 111.3, 49.7, 40.1, 26.5, 19.7; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O$ $[M+H]^+$: 481.2023, found 481.2016.

(6*S*,12*S*)-5-Acetyl-6-(2-chlorophenyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3i**): White solid, 72% yield (72.1 mg), 3.0∶1 *dr*. Major diastereomer: 91% *ee*; $[\alpha]_D^{25}$ +100.2 (*c* 0.10, CH_2Cl_2); m.p. 155～157 ℃; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=5.335 min (major), 5.725 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.29 (s, 1H), 7.95 (m, 2H), 7.81～7.63 (m, 1H), 7.46～7.38 (m, 3H), 7.29 (m, 2H), 7.23～7.14 (m, 4H), 6.85 (s, 1H), 6.51 (ddd, J=16.9, 10.3, 8.8 Hz, 1H), 5.77 (d, J=10.3, Hz, 1H), 5.58 (d, J=16.9 Hz, 1H), 4.95 (d, J=8.8 Hz, 1H), 2.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.8, 138.6, 138.0, 134.8, 134.6, 134.4, 131.2, 129.1, 128.6, 128.4, 128.2, 127.2(4), 127.2(0), 126.5, 126.3, 125.9, 124.1, 122.8, 120.4, 119.9, 119.4, 115.7, 114.5, 114.3, 112.9, 111.6, 111.4, 46.2, 39.9, 37.2, 28.1; HRMS (ESI-TOF) calcd for $C_{31}H_{22}ClN_4O$ $[M+H]^+$: 501.1477, found 501.1468.

Minor diastereomer: 21% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=8.181 min (major), 9.636 min (minor). $[\alpha]_D^{25}$ +91.4 (*c* 0.10, CH_2Cl_2); m.p. 132～134 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.33 (s, 1H), 8.23～8.07 (m, 1H), 7.55～7.48 (m, 1H), 7.43～7.38 (m, 3H), 7.33 (m, 1H), 7.31～7.26 (m, 2H), 7.19 (m, 1H), 7.11 (m, 1H), 7.07 (m, 1H), 6.84 (m, 1H), 6.75 (s, 1H), 6.47 (ddd, J=16.8, 10.3, 8.7 Hz, 1H), 5.80～5.65 (m, 2H), 4.84 (d, J=8.7 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.8, 140.3, 140.1, 135.5, 135.1, 134.8, 133.0, 130.3, 130.2, 129.1(3), 129.1(0), 127.8, 127.0, 126.7, 125.7, 125.3, 123.4, 122.8, 120.5, 120.0, 119.8, 114.1, 113.2, 112.6, 112.2, 112.0, 111.4, 50.0, 41.0, 39.9, 27.2; HRMS (ESI-TOF) calcd for $C_{31}H_{22}ClN_4O$ $[M+H]^+$: 501.1477, found 501.1471.

(6*R*,12*S*)-5-Acetyl-6-(3-methoxyphenyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3j**): White solid, 73% yield (72.5 mg), 5.5∶1 *dr*. Major diastereomer: 98% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 96/4, flow rate = 1.0 mL/min, λ=254 nm), t_R=25.980 min (minor), 31.995 min (major). $[\alpha]_D^{25}$ −126.5 (*c* 0.10, CH_2Cl_2); m.p. 235～237 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.60 (s, 1H), 8.05～7.96 (m, 1H), 7.84 (m, 2H), 7.48 (m, 3H), 7.26～7.13 (m, 3H), 6.85～6.78 (m, 1H), 6.74～6.61 (m, 2H), 6.57 (m, 2H), 5.76 (d, J=10.0 Hz, 1H), 5.41 (d, J=16.6 Hz, 1H), 4.49 (d, J=10.1, 1H), 3.62 (s, 3H), 2.85 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 171.7, 159.3, 143.4, 139.0, 134.9, 134.2, 129.7, 129.3, 128.8, 126.4, 126.1, 125.4(7), 125.4(6), 123.5, 122.1, 119.9, 119.0, 118.2, 117.8, 116.8, 115.4, 114.1, 113.3, 113.1, 111.9, 111.2, 108.6, 55.0, 47.1, 40.0, 37.3, 28.1; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O_2$ $[M+H]^+$: 497.1972, found 497.1973.

Minor diastereomer: 93% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol)=96/4, flow rate=1.0 mL/min, λ=254 nm), t_R=38.758 min (minor), 48.078 min (major). $[\alpha]_D^{25}$ −97.5 (*c* 0.10, CH_2Cl_2); m.p. 211～213 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 11.53 (s, 1H), 8.05 (m, 1H), 8.01～7.96 (m, 1H), 7.76～7.71 (m, 1H), 7.50 (m, 3H), 7.21 (m, 2H), 7.14 (m, 1H), 6.86 (s, 1H), 6.76 (m, 1H), 6.52～6.42 (m, 2H), 5.70 (m, 1H), 5.32 (d, J=16.6 Hz, 1H), 4.95 (d, J=10.0 Hz, 1H), 4.83 (d, J=9.2 Hz, 1H), 3.57 (s, 3H), 2.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 172.4, 159.2, 144.8, 138.0, 134.4(9), 134.4(8), 130.8, 130.0, 129.5, 128.4, 126.4, 125.4, 123.3, 122.3, 122.2, 120.1, 118.9, 118.6, 117.7, 115.2, 114.6, 114.2, 113.8, 112.9, 111.9, 110.7, 106.3, 54.9, 49.7, 38.7, 37.1, 28.0; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O_2$ $[M+H]^+$: 497.1972, found 497.1973.

(6*R*,12*S*)-5-Acetyl-6-(*m*-tolyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3k**): White solid, 63% yield (60.5 mg), 3.1∶1 *dr*. Major diastereomer: 98% *ee*; HPLC (Chiralpak IA, *V*(*n*- hexane)/*V*(*i*-propanol)=96/4, flow rate=1.0 mL/min, λ=254 nm), t_R=16.505 min (minor), 18.962 min (major). $[\alpha]_D^{25}$ −134.4 (*c* 0.10, CH_2Cl_2); m.p. 180～182 ℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 11.62 (s, 1H), 8.04～7.96 (m, 1H), 7.89～7.81 (m, 2H), 7.53～7.41 (m, 3H), 7.17 (m, 3H), 7.03 (m, 1H), 6.89 (s, 1H), 6.85 (m, 1H), 6.68 (m, 1H), 6.59 (s, 1H), 5.86～5.61 (d, J=10.2 Hz 1H), 5.38 (d, J=16.7 Hz, 1H), 4.46 (d, J=10.1 Hz, 1H), 2.85 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 171.8, 141.8, 139.3, 137.7, 134.9, 134.2, 129.3, 128.8, 128.5, 127.3, 127.2, 126.5, 126.2, 125.5, 125.4, 123.8, 123.5, 122.0, 119.9, 118.2, 117.8, 117.0, 115.4, 114.1, 113.2, 111.9, 108.5, 47.1, 40.0, 37.3, 28.1, 21.2; HRMS (ESI-TOF) calcd for $C_{32}H_{24}N_4NaO$ $[M+Na]^+$: 503.1842, found 503.1829.

Minor diastereomer: 22% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol)=96/4, flow rate=1.0 mL/min, λ=254 nm), t_R=17.818 min (minor), 20.511 min (major). $[\alpha]_D^{25}$ −168.2 (*c* 0.10, CH_2Cl_2); m.p. 175～177 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.30 (s, 1H), 8.25 (m, 1H), 7.78 (m, 1H), 7.67 (m, 1H), 7.47～7.40 (m, 2H), 7.39～7.34 (m, 1H), 7.28～7.18 (m, 2H), 7.05 (m, 1H), 6.95 (m, 2H), 6.85 (s, 1H), 6.82～6.78 (m, 1H), 5.91 (ddd, J=16.7, 10.1, 8.8 Hz, 1H), 5.27 (d, J=16.7 Hz, 1H), 5.08 (d, J=10.1, 1H), 4.37 (d, J=8.7, 1H), 2.75 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.7, 142.6, 139.2, 138.2, 134.9, 134.8, 130.7, 129.3, 128.7, 128.3, 128.1, 127.6, 127.3, 125.5, 124.4, 123.7, 123.2, 123.0, 121.0, 119.9, 118.8, 114.5, 114.4, 114.1, 113.9, 111.5, 107.3, 52.1, 39.3, 38.0, 28.0, 21.7; HRMS (ESI-TOF) calcd for $C_{32}H_{24}N_4NaO$ $[M+Na]^+$: 503.1842, found 503.1825.

(6*R*,12*S*)-5-Acetyl-6-(3-chlorophenyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3l**): White solid, 75% yield (75.1 mg), 5.1∶1 *dr*. Major diastereomer: 95% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=5.007 min (major), 5.420 min (minor). $[\alpha]_D^{25}$ −187.5 (*c* 0.10, CH_2Cl_2); m.p. 230～232 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.30 (s, 1H), 8.01～7.96 (m, 1H), 7.80 (m, 1H), 7.75～7.70 (m, 1H), 7.48～7.44 (m, 2H), 7.39 (m, 1H), 7.28～7.23 (m, 2H), 7.20～7.16 (m, 2H), 7.09 (m, 1H), 6.98 (m, 1H), 6.69 (s, 1H), 6.50 (ddd, *J*=16.9, 10.3, 9.1 Hz, 1H), 5.80 (d, *J*=10.3 Hz, 1H), 5.57 (d, *J*=16.9 Hz, 1H), 4.51 (d, *J*=9.1 Hz, 1H), 2.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.0, 143.9, 138.8, 134.8(5), 134.8(2), 134.4, 129.8, 128.8, 128.4, 127.4, 127.4, 127.2(5), 127.2(1), 126.5, 125.9, 125.1, 124.1, 123.2, 121.1, 119.7, 117.8, 117.7, 114.4, 114.0, 113.1, 111.9, 110.5, 46.8, 39.9, 37.6, 28.4; HRMS (ESI-TOF) calcd for $C_{31}H_{22}ClN_4O$ $[M+H]^+$: 501.1477, found 501.1482.

Minor diastereomer: 75% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 90/10, flow rate = 1.0 mL/min, λ=254 nm), t_R=10.370 min (minor), 11.726 min (major). $[\alpha]_D^{25}$ −110.0 (*c* 0.10, CH_2Cl_2); m.p. 175～177 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.32 (s, 1H), 8.29～8.24 (m, 1H), 7.81～7.73 (m, 1H), 7.71～7.64 (m, 1H), 7.46 (m, 2H), 7.41～7.35 (m, 1H), 7.32～7.21 (m, 2H), 7.16～7.07 (m, 2H), 7.01 (s, 1H), 6.92 (m, 2H), 5.88 (ddd, *J*=16.6, 10.1, 8.3 Hz, 1H), 5.24 (d, *J*=16.7 Hz, 1H), 5.12 (d, *J*=10.1 Hz, 1H), 4.38 (d, *J*=8.3 Hz, 1H), 2.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 144.8, 138.6, 134.8(5), 134.8(0), 134.4, 130.5, 129.6, 129.1, 129.0, 127.5, 127.3, 126.9, 125.7, 125.6, 123.9, 123.5, 123.3, 121.2, 120.0, 118.5, 114.4, 114.1, 113.9, 113.6, 111.6, 107.8, 51.7, 39.2, 37.8, 28.2; HRMS (ESI-TOF) calcd for $C_{31}H_{22}ClN_4O$ $[M+H]^+$: 501.1477, found 501.1476.

(6*R*,12*S*)-5-Acetyl-6-(naphthalen-1-yl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3m**): White solid, 72% yield (74.4 mg), 4.7∶1 *dr*. Major diastereomer: 90% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 96/4, flow rate = 1.0 mL/min, λ=254 nm), t_R=22.465 min (major), 25.326 min (minor). m.p. 223～225 ℃; $[\alpha]_D^{25}$ −100.0 (*c* 0.10, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.47 (m, 1H), 8.26 (s, 1H), 8.11 (m, 1H), 7.97 (m, 1H), 7.84～7.80 (m, 1H), 7.79～7.72 (m, 2H), 7.50～7.27 (m, 9H), 7.26～7.13 (m, 1H), 6.43 (ddd, *J*=16.9, 10.3, 8.9 Hz, 1H), 5.66 (d, *J*=10.3 Hz, 1H), 5.43 (d, *J*=16.9 Hz, 1H), 5.04 (d, *J*=8.8 Hz, 1H), 2.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.0, 139.5, 136.2, 134.9, 134.7, 134.6, 131.5, 129.6, 129.0, 128.6, 128.3, 127.4, 126.6(3), 126.6(0), 126.3, 126.1, 125.8, 124.9, 124.7, 124.3, 124.1, 122.9, 121.0, 119.3, 118.2, 117.2, 114.6, 114.3, 113.1, 112.1, 111.2, 45.8, 39.9, 36.2, 28.1; HRMS (ESI-TOF) calcd for $C_{35}H_{24}N_4NaO$ $[M+Na]^+$: 539.1842, found 539.1845.

Minor diastereomer: 76% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=7.565 min (minor), 8.609 min (major). $[\alpha]_D^{25}$ −86.7 (*c* 0.10, CH_2Cl_2); m.p. 200～202 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.30 (s, 1H), 8.13 (m, 1H), 8.00～7.89 (m, 1H), 7.83 (m, 2H), 7.44～7.29 (m, 5H), 7.29～7.18 (m, 4H), 7.07 (s, 1H), 7.01 (m, 1H), 6.63 (m, 1H), 6.47 (m, 1H), 5.77～5.59 (m, 2H), 4.90 (d, *J*=9.0 Hz, 1H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.5, 141.4, 138.9, 135.2, 134.8, 133.9, 132.3, 130.4, 130.1, 128.9, 128.8(6), 128.8(0), 127.7, 126.8, 126.5, 126.0, 125.5, 125.2, 124.2, 123.5, 123.1, 122.6, 120.3, 120.0(4), 120.0(1), 114.1, 113.4, 113.3, 112.2, 111.3, 111.0, 50.4, 40.2, 29.8, 26.9; HRMS (ESI-TOF) calcd for $C_{35}H_{24}N_4NaO$ $[M+Na]^+$: 539.1842, found 539.1835.

(6*R*,12*S*)-5-Acetyl-6-(naphthalen-2-yl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3n**): White solid, 73% yield (75.4 mg), 4.2∶1 *dr*. Major diastereomer: 96% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 90/10, flow rate = 1.0 mL/min, λ=254 nm), t_R=8.713 min (major), 10.826 min (minor). $[\alpha]_D^{25}$ −275.2 (*c* 0.10, CH_2Cl_2); m.p. 220～222 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.27 (s, 1H), 8.06～7.97 (m, 1H), 7.94～7.88 (m, 1H), 7.81～7.74 (m, 2H), 7.74～7.64 (m, 2H), 7.51～7.44 (m, 3H), 7.44～7.36 (m, 3H), 7.33～7.21 (m, 3H), 6.88 (s, 1H), 6.46 (ddd, *J*=16.9, 10.3, 9.0 Hz, 1H), 5.70 (d, *J*=10.3 Hz, 1H), 5.43 (d, *J*=16.9 Hz, 1H), 4.63 (d, *J*=9.1 Hz, 1H), 2.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.0, 139.2(3), 139.2(0), 134.8, 134.6, 133.2, 132.4, 129.0, 128.9, 128.5, 128.1, 127.7, 127.5, 127.4, 126.5, 126.4, 126.1, 126.0, 125.8, 124.6, 124.1, 123.1, 121.0, 119.7, 118.0, 117.9, 114.5, 114.2, 113.2, 111.8, 110.4, 46.6, 40.0, 38.0, 28.3; HRMS (ESI-TOF) calcd for $C_{35}H_{24}N_4NaO$ $[M+Na]^+$: 539.1842, found 539.1844.

Minor diastereomer: 85% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=7.875 min (major), 9.433 min (minor). $[\alpha]_D^{25}$ −186.8 (*c* 0.10, CH_2Cl_2); m.p. 210～212 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.32～8.24 (m, 2H), 7.89～7.84 (m, 1H), 7.76～7.72 (m, 1H), 7.71～7.67 (m, 1H), 7.63 (m, 2H), 7.50～7.44 (m, 2H), 7.42～7.33 (m, 4H), 7.31～7.24 (m, 3H), 7.14 (s, 1H), 5.93 (ddd, *J*=16.7, 10.0, 8.5 Hz, 1H), 5.18 (d, *J*=16.7 Hz, 1H), 4.90 (d, *J*=10.1 Hz, 1H), 4.39 (d, *J*=8.5 Hz, 1H), 2.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.7, 140.3, 138.9, 134.9(3), 134.9(1), 133.2, 132.2, 130.4, 129.3, 129.1, 128.5, 128.0, 127.7, 127.4, 126.3, 126.0, 125.9, 125.6, 125.4, 123.8, 123.3, 123.2, 121.1, 120.0, 118.8, 114.5, 114.2, 114.1, 114.0, 111.6, 107.7, 52.0, 39.4, 38.4, 28.0; HRMS (ESI-TOF) calcd for $C_{35}H_{24}N_4NaO$ $[M+Na]^+$: 539.1842, found 539.1847.

(6*R*,12*S*)-5-Acetyl-6-(3,4-dichlorophenyl)-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3o**): White solid, 72% yield (77.1 mg), 3.1∶1 *dr*. Major diastereomer: 93% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=4.943 min (major), 5.466 min (minor). $[\alpha]_D^{25}$ −205.2 (*c* 0.10, CH_2Cl_2); m.p. 177～

179 ℃; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 11.67 (s, 1H), 8.04～7.96 (m, 1H), 7.91～7.85 (m, 1H), 7.81 (m, 1H), 7.58～7.43 (m, 4H), 7.24～7.13 (m, 3H), 7.02 (m, 1H), 6.66 (m, 1H), 6.53 (s, 1H), 5.78 (d, J=10.3 Hz, 1H), 5.56 (d, J=16.7 Hz, 1H), 4.39 (d, J=9.8 Hz, 1H), 2.88 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 171.7, 143.3, 138.2, 135.0, 134.1, 131.1, 130.7, 129.1(3), 129.1(3), 129.1(1), 129.1(1), 128.5, 126.9, 126.4, 126.1, 125.9, 123.5, 122.2, 120.1, 118.4, 117.8, 115.7, 115.5, 114.0, 113.1, 112.0, 109.0, 47.0, 40.0, 37.1, 28.3; HRMS (ESI-TOF) calcd for $C_{31}H_{20}Cl_2N_4NaO$ [M+Na]$^+$: 557.0906, found 557.0918.

Minor diastereomer: 75% *ee*; HPLC (Chiralpak IF, V(*n*-hexane)/V(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=4.669 min (major), 5.018 min (minor). $[\alpha]_D^{25}$ −148.7 (*c* 0.10, CH_2Cl_2); m.p. 155～157 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.36 (s, 1H), 8.32～8.24 (m, 1H), 7.74 (m, 1H), 7.70 (m, 1H), 7.47 (m, 2H), 7.41～7.36 (m, 1H), 7.32～7.20 (m, 3H), 7.11 (m, 1H), 6.91～6.85 (m, 2H), 5.88 (ddd, J=16.7, 9.5, 8.2, Hz, 1H), 5.28～5.23 (d, J=16.7 Hz, 1H), 5.17 (d, J=10.1, Hz, 1H), 4.42～4.36 (d, J=8.2 Hz,1H), 2.83 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.4, 143.0, 138.3, 134.8, 134.7, 132.5, 130.7, 130.4, 130.2, 129.4, 129.0, 128.9, 127.2, 126.9, 125.9, 124.1, 123.6(2), 123.6(0), 121.3, 120.0, 118.3, 114.3, 114.2, 113.8, 113.1, 111.6, 108.0, 51.5, 39.1, 37.6, 28.3; HRMS (ESI-TOF) calcd for $C_{31}H_{20}Cl_2N_4NaO$ [M+Na]$^+$: 557.0906, found 557.0908.

(6*R*,12*S*)-5-Acetyl-2-methyl-6-phenyl-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3p**): White solid, 78% yield (74.9 mg), 4.7∶1 *dr*. Major diastereomer: 92% *ee*; HPLC (Chiralpak IF, V(*n*-hexane)/V(*i*-propanol) = 85/15, flow rate = 1.0 mL/min, λ=254 nm), t_R=5.699 min (major), 6.352 min (minor). $[\alpha]_D^{25}$ −101.5 (*c* 0.10, CH_2Cl_2); m.p. 134～136 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.28 (s, 1H), 7.84 (m, 2H), 7.53 (s, 1H), 7.36 (m, 1H), 7.31～7.16 (m, 6H), 7.14～7.07 (m, 2H), 6.69 (s, 1H), 6.47 (m, 1H), 5.74 (d, J=10.4 Hz, 1H), 5.50 (d, J=16.9 Hz, 1H), 4.52 (d, J=9.2 Hz, 1H), 2.82 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.1, 141.9, 138.6, 135.9, 134.9, 134.8, 128.7(3), 128.7(0) (2C), 128.6, 127.3, 127.0 (2C), 126.8, 126.3, 125.4, 125.2, 123.0, 120.9, 119.1, 118.4, 117.9, 114.6, 114.2, 113.2, 111.8, 110.0, 46.7, 39.9, 37.7, 28.3, 22.3; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O$ [M + H]$^+$: 481.2023, found 481.2027.

Minor diastereomer: 66% *ee*; HPLC (Chiralpak IF, V(*n*-hexane)/V(*i*-propanol) = 90/10, flow rate = 1.0 mL/min, λ=254 nm), t_R=6.637 min (major), 7.571 min (minor). $[\alpha]_D^{25}$ −87.0 (*c* 0.10, CH_2Cl_2); m.p. 153～155 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.26 (s, 1H), 8.13～8.10 (m, 1H), 7.78 (m, 1H), 7.46 (s, 1H), 7.39～7.32 (m, 1H), 7.30～7.21 (m, 3H), 7.15 (m, 3H), 7.05～7.01 (m, 2H), 6.94 (s, 1H), 5.86 (ddd, J=16.7, 10.0, 8.7 Hz, 1H), 5.25 (d, J=16.7 Hz, 1H), 5.05 (d, J=10.1 Hz, 1H), 4.34 (d, J=8.7 Hz, 1H), 2.76 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 171.7, 142.9, 138.4, 135.7, 135.2, 134.8, 130.7, 129.3, 128.8, 128.5 (2C), 127.3 (2C), 126.7, 125.2, 125.1, 123.2, 123.0, 120.9, 119.5, 118.8, 114.5, 114.4, 114.1, 114.0, 111.5, 107.4, 52.0, 39.3, 38.1, 28.1, 22.2; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O$ [M + H]$^+$: 481.2023, found 481.2015.

(6*R*,12*S*)-5-Acetyl-3-methyl-6-phenyl-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3q**): White solid, 75% yield (72.0 mg), 3.9∶1 *dr*. Major diastereomer: 95% *ee*; HPLC (Chiralpak IF, V(*n*-hexane)/V(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=4.628 min (major), 5.151 min (minor). $[\alpha]_D^{25}$ −133.6 (*c* 0.10, CH_2Cl_2); m.p. 117～119 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.24 (s, 1H), 7.83 (m, 1H), 7.73 (s, 1H), 7.61 (m, 1H), 7.38 (m, 1H), 7.29～7.17 (m, 6H), 7.12～7.04 (m, 2H), 6.75 (s, 1H), 6.49 (m, 1H), 5.76 (d, J=10.3 Hz, 1H), 5.50 (d, J=16.9 Hz, 1H), 4.54 (d, J=9.1 Hz, 1H), 2.82 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.9, 141.8, 139.5, 134.8, 133.8, 132.8, 128.8, 128.7(2) (2C), 128.7(0), 127.7, 127.4, 127.1, 127.0 (2C), 126.8, 126.3, 123.0, 120.9, 119.4, 118.5, 118.0, 114.2, 114.1, 113.2, 111.8, 109.9, 46.8, 39.9, 37.7, 28.3, 21.6; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O$ [M+H]$^+$: 481.2023, found 481.2025.

Minor diastereomer: 60% *ee*; HPLC (Chiralpak IA, V(*n*-hexane)/V(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ=254 nm), t_R=5.484 min (major), 6.093 min (minor). $[\alpha]_D^{25}$ −97.4 (*c* 0.10, CH_2Cl_2); m.p. 144～146 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.23 (s, 1H), 8.01 (s, 1H), 7.83～7.76 (m, 1H), 7.56 (m, 1H), 7.41～7.34 (m, 1H), 7.31～7.21 (m, 3H), 7.15 (m, 3H), 7.07～6.94 (m, 3H), 5.84 (ddd, J=16.6, 10.0, 8.7 Hz, 1H), 5.24 (d, J=16.7 Hz, 1H), 5.03 (d, J=10.0 Hz, 1H), 4.35 (d, J=8.7 Hz, 1H), 2.76 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 142.9, 139.2, 134.8, 133.6, 133.1, 130.7, 129.4, 128.9, 128.5 (2C), 127.6, 127.3 (2C), 126.9, 126.7, 123.3, 122.9, 121.0, 119.7, 118.7, 114.6(0), 114.6(0), 114.0, 113.8, 111.5, 107.2, 52.1, 39.3, 38.0, 28.1, 21.7; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O$ [M + H]$^+$: 481.2023, found 481.2028.

(6*R*,12*S*)-5-Acetyl-8-methoxy-6-phenyl-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3r**): White solid, 75% yield (74.4 mg), 5.3∶1 *dr*. Major diastereomer: 98% *ee*; HPLC (Chiralpak IA, V(*n*-hexane)/V(*i*-propanol) = 96/4, flow rate = 1.0 mL/min, λ=254 nm), t_R=24.841 min (minor), 28.923 min (major). $[\alpha]_D^{25}$ −139.2 (*c* 0.10, CH_2Cl_2); m.p. 220～222 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.18 (s, 1H), 8.04～7.92 (m, 1H), 7.85～7.66 (m, 1H), 7.48～7.37 (m, 2H), 7.22 (m, 5H), 7.10 (m, 2H), 6.88 (m, 1H), 6.67 (s, 1H), 6.46 (m, 1H), 5.74 (d, J=10.4 Hz, 1H), 5.49 (d, J=16.9 Hz, 1H), 4.51 (d, J=9.2 Hz, 1H), 3.90 (s, 3H), 2.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.1, 155.2, 141.9, 139.6, 134.5, 130.0, 129.4, 128.7 (2C), 128.6, 127.8, 127.4, 127.0 (2C), 126.9, 126.2, 125.7, 124.0, 119.6, 118.2, 114.3, 114.2, 113.3, 113.2, 112.6, 110.2, 99.5, 56.2, 46.8, 39.9, 37.8, 28.4; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O_2$ [M+H]$^+$: 497.1972, found 497.1976.

Minor diastereomer: 83% *ee*; HPLC (Chiralpak AD,

V(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 6.686 min (major), 7.399 min (minor). $[\alpha]_D^{25}$ −147.5 (*c* 0.10, CH_2Cl_2); m.p. 189～191 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.27～8.22 (m, 1H), 8.15 (s, 1H), 7.71～7.63 (m, 1H), 7.50～7.41 (m, 2H), 7.27 (m, 1H), 7.20～7.15 (m, 3H), 7.13 (m, 1H), 7.07～7.01 (m, 2H), 6.92 (m, 1H), 6.90 (s, 1H), 5.85 (ddd, *J* = 16.6, 10.0, 8.7 Hz, 1H), 5.27 (d, *J* = 16.7 Hz, 1H), 5.07 (d, *J* = 10.1 Hz, 1H), 4.35 (d, *J* = 8.8 Hz, 1H), 3.87 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.7, 155.2, 142.9, 139.3, 134.8, 130.6, 129.9, 129.7, 129.4, 128.5 (2C), 127.4 (2C), 127.3, 126.8, 125.5, 123.8, 123.1, 120.0, 114.5, 114.2, 114.0, 113.9, 113.6, 112.3, 107.6, 100.3, 56.1, 52.1, 39.3, 38.3, 28.1; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_4O_2$ $[M+H]^+$: 497.1972, found 497.1949.

(6*R*,12*S*)-5-Acetyl-8-chloro-6-phenyl-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3s**): White solid, 67% yield (67.1 mg), 4.3∶1 *dr*. Major diastereomer: 95% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 5.193 min (minor), 6.122 min (major). $[\alpha]_D^{25}$ −125.5 (*c* 0.10, CH_2Cl_2); m.p. 153～155 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.30 (s, 1H), 8.04～7.94 (m, 1H), 7.78 (m, 1H), 7.77～7.73 (m, 1H), 7.49～7.42 (m, 2H), 7.28～7.19 (m, 4H), 7.15 (m, 1H), 7.07 (m, 2H), 6.66 (s, 1H), 6.47 (m, 1H), 5.77 (d, *J* = 10.4 Hz, 1H), 5.51 (d, *J* = 16.9 Hz, 1H), 4.52 (d, *J* = 9.1 Hz, 1H), 2.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.0, 141.4, 139.2, 134.5, 133.1, 130.3, 128.8 (2C), 128.3(4), 128.3(0), 127.3, 127.0(2), 127.0(0) (2C), 126.8, 126.6, 125.8, 124.1, 123.4, 119.6, 118.1, 117.5, 114.4, 114.0, 113.1, 112.8, 110.1, 46.7, 39.9, 37.7, 28.4; HRMS (ESI-TOF) calcd for $C_{31}H_{21}ClN_4NaO$ $[M+Na]^+$: 523.1296, found 523.1297.

Minor diastereomer: 82% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 90/10, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 10.423 min (minor), 11.396 min (major). $[\alpha]_D^{25}$ −89.2 (*c* 0.10, CH_2Cl_2); m.p. 167～169 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.34 (s, 1H), 8.28～8.21 (m, 1H), 7.73 (m, 1H), 7.71～7.65 (m, 1H), 7.45 (m, 2H), 7.30～7.22 (m, 1H), 7.22～7.13 (m, 4H), 7.04～6.96 (m, 2H), 6.89 (s, 1H), 5.84 (m, 1H), 5.26 (d, *J* = 16.7 Hz, 1H), 5.07 (d, *J* = 10.0 Hz, 1H), 4.35 (d, *J* = 8.7 Hz, 1H), 2.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.6, 142.4, 138.8, 134.8, 133.1, 130.4, 130.3(0), 130.2(6), 128.6 (2C), 127.3 (2C), 127.2, 126.9, 126.9, 125.6, 123.8, 123.7, 123.4, 119.9, 118.2, 114.4, 114.1, 113.9(4), 113.9(0), 112.6, 107.4, 52.0, 39.2, 38.1, 28.1; HRMS (ESI-TOF) calcd for $C_{31}H_{22}ClN_4O$ $[M+H]^+$: 501.1477, found 501.1470.

(6*R*,12*S*)-5-Acetyl-8-fluoro-6-phenyl-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3t**): White solid, 72% yield (69.7 mg), 4.6∶1 *dr*. Major diastereomer: 94% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 5.308 min (minor), 5.891 min (major). $[\alpha]_D^{25}$ −162.5 (*c* 0.10, CH_2Cl_2); m.p. 186～188 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.29 (s, 1H), 8.05～7.96 (m, 1H), 7.80～7.70 (m, 1H), 7.50～7.42 (m, 3H), 7.31～7.16 (m, 4H), 7.13～7.04 (m, 2H), 6.97 (m, 1H), 6.65 (s, 1H), 6.46 (ddd, *J* = 16.9, 10.4, 9.8 Hz, 1H), 5.76 (d, *J* = 10.4, Hz, 1H), 5.51 (d, *J* = 16.9 Hz, 1H), 4.53 (d, *J* = 9.2 Hz, 1H), 2.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.0, 158.7 (d, *J* = 236.6 Hz), 141.5, 139.3, 134.5, 131.3, 130.6, 128.8 (2C), 128.4, 127.7 (d, *J* = 9.8 Hz), 127.3, 127.0, 126.9 (2C), 126.5, 125.8, 124.0, 119.6, 118.5 (d, *J* = 4.6 Hz), 114.4, 114.1, 113.2, 112.6 (d, *J* = 9.2 Hz), 111.6 (d, *J* = 26.5 Hz), 110.0, 103.0 (d, *J* = 23.9 Hz), 46.8, 39.9, 37.8, 28.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −122.43; HRMS (ESI-TOF) calcd for $C_{31}H_{22}FN_4O$ $[M+H]^+$: 485.1772, found 485.1773.

Minor diastereomer: 63% *ee*; HPLC (Chiralpak AD, *V*(*n*-hexane)/*V*(*i*-propanol) = 90/10, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 12.938 min (major), 14.328 min (minor). $[\alpha]_D^{25}$ −144.0 (*c* 0.10, CH_2Cl_2); m.p. 146～148 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.29 (s, 1H), 8.27～8.22 (m, 1H), 7.71～7.63 (m, 1H), 7.50～7.41 (m, 2H), 7.38 (m, 1H), 7.25 (s, 1H), 7.23～7.13 (m, 3H), 7.10～6.92 (m, 3H), 6.87 (s, 1H), 5.86 (ddd, *J* = 16.7, 10.1, 8.7 Hz, 1H), 5.26 (d, *J* = 16.7 Hz, 1H), 5.07 (d, *J* = 10.0 Hz, 1H), 4.36 (d, *J* = 8.7 Hz, 1H), 2.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.7, 158.7 (d, *J* = 236.8 Hz), 142.5, 138.9, 134.8, 131.3, 130.7, 130.4, 129.7 (d, *J* = 9.4 Hz), 128.6 (2C), 127.3 (2C), 127.2, 126.9, 125.6, 123.8, 123.3, 119.9, 114.5 (d, *J* = 5.0 Hz), 114.4, 113.9(2), 113.9(0), 112.4 (d, *J* = 9.7 Hz), 111.9 (d, *J* = 26.3 Hz), 107.5, 103.8 (d, *J* = 24.2 Hz), 52.0, 39.3, 38.3, 28.1; ^{19}F NMR (377 MHz, $CDCl_3$) δ: −122.29; HRMS (ESI-TOF) calcd for $C_{31}H_{21}FN_4NaO$ $[M+Na]^+$: 507.1592, found 507.1599.

(6*R*,12*S*)-5-Acetyl-9-chloro-6-phenyl-12-vinyl-5,6,11,12-tetrahydro-13*H*-cyclohepta[1,2-*b*:4,5-*b*′]diindole-13,13-dicarbonitrile (**3u**): White solid, 61% yield (61.1 mg), 3.6∶1 *dr*. Major diastereomer: 94% *ee*; HPLC (Chiralpak IA, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 13.518 min (minor), 14.665 min (major). $[\alpha]_D^{25}$ −113.0 (*c* 0.10, CH_2Cl_2); m.p. 234～236 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.35 (s, 1H), 7.99 (m, 1H), 7.81～7.65 (m, 2H), 7.46 (m, 2H), 7.31～7.13 (m, 4H), 7.12 (s, 1H), 7.08～7.03 (m, 2H), 6.70 (m, 1H), 6.55～6.34 (m, 1H), 5.75 (d, *J* = 10.0 Hz, 1H), 5.49 (d, *J* = 16.9 Hz, 1H), 4.50 (d, *J* = 9.3 Hz, 1H), 2.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.0, 141.5, 139.3, 134.9, 134.5, 129.4, 128.8 (2C), 128.3, 127.3, 127.0, 126.9 (2C), 126.7, 125.9, 125.8, 124.1, 121.8, 119.6, 118.9, 118.4, 114.4, 114.0, 113.3, 111.7, 111.5, 110.1, 46.7, 39.9, 37.7, 28.4; HRMS (ESI-TOF) calcd for $C_{31}H_{21}ClN_4NaO$ $[M+Na]^+$: 523.1296, found 523.1289.

Minor diastereomer: 83% *ee*; HPLC (Chiralpak IF, *V*(*n*-hexane)/*V*(*i*-propanol) = 80/20, flow rate = 1.0 mL/min, λ = 254 nm), t_R = 6.373 min (major), 7.392 min (minor). $[\alpha]_D^{25}$ −86.7 (*c* 0.10, CH_2Cl_2); m.p. 212～214 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.31 (s, 1H), 8.28～8.21 (m, 1H), 7.73～7.61 (m, 2H), 7.49～7.42 (m, 2H), 7.38 (m, 1H), 7.24～7.13 (m, 4H), 7.02～6.98 (m, 2H), 6.94 (s, 1H),

5.86 (ddd, J=16.7, 10.0, 8.7 Hz, 1H), 5.29 (d, J=16.6 Hz, 1H), 5.10 (d, J=10.0 Hz, 1H), 4.37 (d, J=8.7 Hz, 1H), 2.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.7, 142.4, 138.9, 135.1, 134.8, 130.3, 129.5, 129.2, 128.6 (2C), 127.9, 127.3 (2C), 127.2, 126.9, 125.6, 123.8, 123.5, 121.9, 119.9, 119.8, 114.4(5), 114.4(0), 113.8(9), 113.8(5), 111.4, 107.5, 51.9, 39.2, 38.1, 28.1; HRMS (ESI-TOF) calcd for $C_{31}H_{21}ClN_4NaO$ $[M+Na]^+$: 523.1296, found 523.1290.

4.3 General procedure for the synthesis of the **4**

A reaction tube equipped with a magnetic stirring bar was charged compound **3a** (46.6 mg, 0.1 mmol), EtOH/H_2O (V/V=1/1, 2 mL) was added via syringe to the reaction tube, then NaOH (8.0 mg, 0.2 mmol) was added, the reaction mixture was stirred at 60 ℃ for 4 h until completion. The reaction mixture was diluted with ethyl acetate, washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, V/V=2/1) to give product **4** as a white solid, 65% yield (28.7 mg), 95% *ee*. HPLC (Chiralpak IF, V(*n*-hexane)/V(*i*-propanol) = 80/20, flow rate=1.0 mL/min, λ=254 nm), t_R=7.384 min (major), 8.017 min (minor). $[\alpha]_D^{25}$ −128.2 (*c* 0.10, CH_2Cl_2); m.p. 122～124 ℃; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.42 (s, 1H), 8.37 (s, 1H), 7.83 (m, 1H), 7.32～7.22 (m, 7H), 7.18 (m, 2H), 7.12 (m, 2H), 7.02 (m, 1H), 6.34 (m, 1H), 5.83～5.71 (m, 3H), 5.36 (d, J=10.2 Hz, 1H), 5.19 (d, J=16.9 Hz, 1H), 4.53 (d, J=8.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 169.3, 142.6, 137.3, 135.3, 134.9, 131.7, 131.0, 129.1 (2C), 129.0, 127.9, 127.6, 127.5, 127.3, 127.2, 123.3, 122.3(2), 122.3(0), 121.2, 120.2, 119.2, 118.4(1), 118.4(0), 111.7, 111.1, 104.8, 53.2, 48.7, 41.6; HRMS (ESI-TOF) calcd for $C_{29}H_{23}N_4O$ $[M+H]^+$: 443.1866, found 443.1871.

4.4 General procedure for the synthesis of the **5**

Under nitrogen atmosphere, compound **3a** (46.6 mg, 0.1 mmol) was added into a flame-dried Schlenk tube equipped with a magnetic stirring bar. Anhydrous THF (1.0 mL) was added via syringe to the reaction tube. Then *n*-Bu_3SnH (145 mg, 0.5 mmol) was added, and the reaction mixture was stirred at 55 ℃ for 24 h until completion. The reaction mixture was diluted with ethyl acetate, washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate, V/V=4/1) to give product **5** as a white solid, 94% yield (40.0 mg), 95% *ee*. HPLC (Chiralpak IA, V(*n*-hexane)/V(*i*-propanol) = 80/20, flow rate=1.0 mL/min, λ=254 nm), t_R=10.653 min (major), 11.310 min (minor). $[\alpha]_D^{25}$ −79.8 (*c* 0.10, CH_2Cl_2); m.p. 178～180 ℃; ^{1}H NMR (600 MHz, CD_2Cl_2) δ: 8.61 (s, 1H), 8.43 (s, 1H), 8.01～7.95 (m, 1H), 7.73 (m, 1H), 7.47～7.41 (m, 2H), 7.33～7.15 (m, 9H), 6.53 (m, 1H), 5.87 (s, 1H), 5.80 (d, J=10.4 Hz, 1H), 5.61 (d, J=16.9 Hz, 1H), 4.64 (d, J=9.2 Hz, 1H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ: 141.8, 136.5, 135.2, 135.0, 129.9, 129.3 (2C), 129.1, 127.5(5), 127.5(0), 127.4 (2C), 126.7, 125.7, 123.9, 123.2, 121.5, 121.0, 119.0, 118.3, 116.3, 115.0, 114.3, 112.0, 111.6, 102.3, 48.4, 40.4, 39.7; HRMS (ESI-TOF) calcd for $C_{29}H_{20}N_4Na$ $[M+Na]^+$: 447.1564, found 447.1586.

Supporting Information The HPLC, ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of products **3a**～**3u**, and crystallographic data for the compound **3a**. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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