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Catalytic Asymmetric Aza-ene Reaction of 3-Indolylmethanols with Cyclic Enaminones: Enantioselective Approach to C3-Functionalized Indoles

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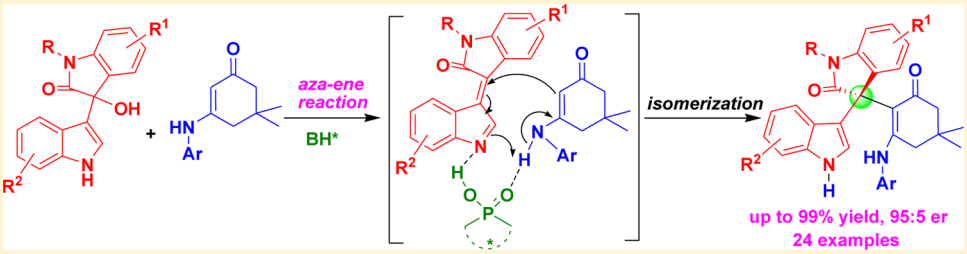
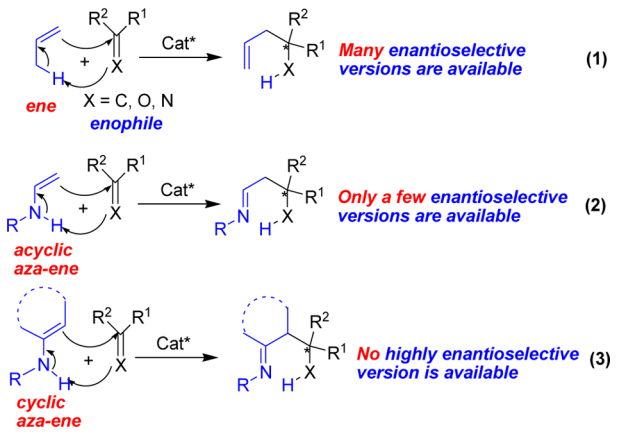
Supporting Information



ABSTRACT: The catalytic asymmetric aza-ene reactions of 3-indolylmethanols with cyclic enaminones and the highly enantioselective aza-ene reactions utilizing cyclic aza-ene components have been established, which directly assemble isatin-derived 3-indolylmethanols and dimedone-derived enaminones into C3-functionalized chiral indoles with one all-carbon quaternary stereogenic center in high yields and excellent enantioselectivities (up to 99% yield, up to 95:5 er).

INTRODUCTION

Aza-ene reaction, a subdivision of ene reaction,[1] is a robust, atom-economic, and simple method to form C−C bond, which has exhibited important synthetic applications.[2] Although enantioselective ene reactions have made tremendous progress in recent years (eq 1),[1a,3] *the enantioselective aza-ene reactions*



have sporadically been described in the literature (eq 2).[4] Among these limited examples of catalytic asymmetric aza-ene reactions, acyclic aza-ene components were employed almost in all cases.[4] On the contrary, *no cyclic aza-ene components were utilized as* reaction *partners to afford highly enantioselective aza-ene reactions* (eq 3),[4f] which may be ascribed to the relatively low reactivity and more rigid structures of cyclic aza-enes compared with acyclic ones. Therefore, it is highly desirable to further develop enantioselective aza-ene reactions, especially cyclic aza-ene-involved transformations despite of the existent great challenge.

Enantioselective functionalization of indole rings and asymmetric synthesis of indoles have been long-lasting goals in the organic community due to the fact that chiral indole skeletons constitute the core structures of numerous natural products, pharmaceuticals, and agrochemicals.[5] In this context, 3-indolylmethanols have proven to be privileged reactants to realize C3-functionalization of indole rings since they can readily transform into carbocation or vinyliminium intermediates catalyzed by Lewis acids (LA) or Brønsted acids (BH).[6]

As a result, elegant developments have been reported in the enantioselective nucleophilic substitutions of 3-indolylmethanols, most of which concentrate on the alkylation of carbonyl compounds (eq 4).[7] *However, in sharp contrast, the catalytic enantioselective aza-ene* reaction *of 3-indolylmethanols were still under developed in spite of its great potential in C−C bond formation and C3-functionalization of indole ring* (eq 5).

Considering the challenge in enantioselective aza-ene reactions, in particular 3-indolylmethanol-involved ones, we decided to design a catalytic asymmetric aza-ene reaction of 3-indolylmethanols with cyclic aza-enes. In the past decades, cyclic enaminones not only served as versatile synthon in organic synthesis[8] but also showed important bioactivities[9] such as anticonvulsant activity,[9b] being phosphodiesterase IV and

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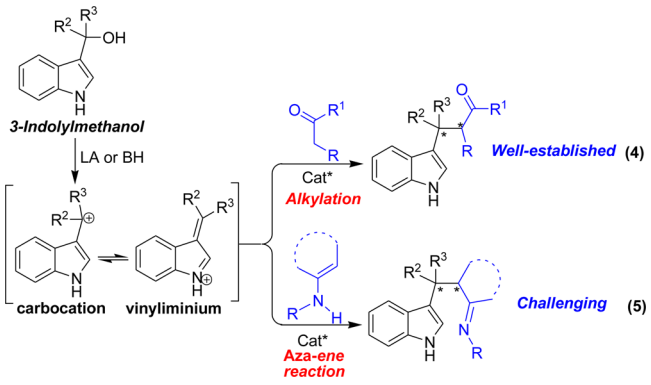


PAI-1inhibitors,[9e] and acting as allosteric modulators of GABAA receptors[9f] (Figure 1). This intriguing class of

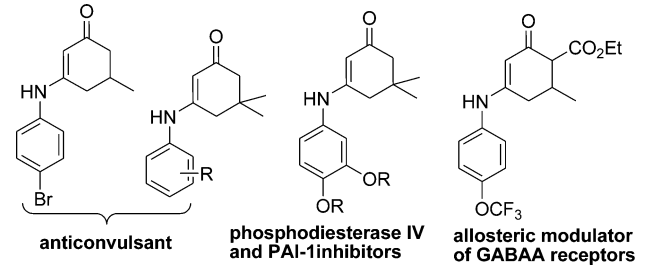
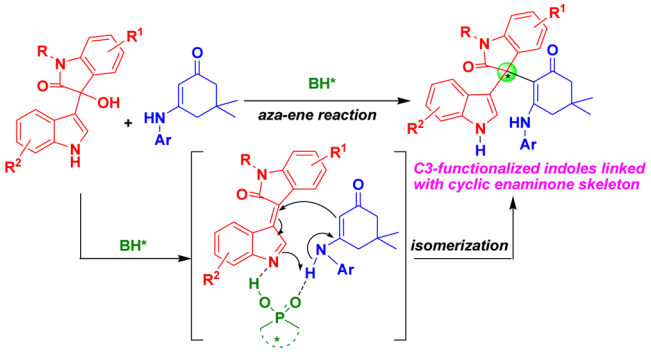


Figure 1. Some bioactive cyclic enaminones.

compounds triggered us to envision that cyclic enaminones would act as aza-ene components to participate in enantioselective aza-ene reactions with isatin-derived 3-indolylmethanols (Scheme 1). More importantly, this type of aza-ene reactions

Scheme 1. Design of Catalytic Asymmetric Aza-ene Reactions of 3-Indolylmethanols with Cyclic Enaminones



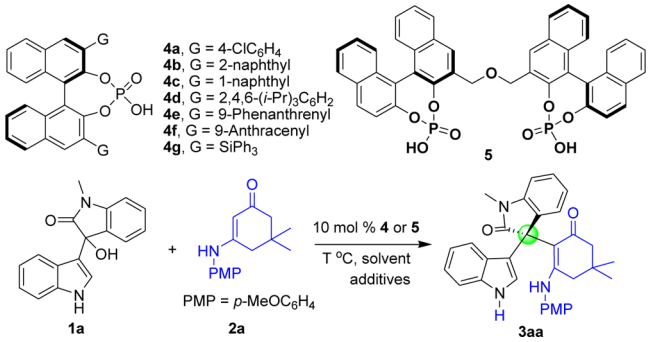
would integrate bioactive indole, isatin, and cyclic enaminone skeletons into a novel type of C3-functionalized indole structure, which may result in enhanced or valuable bioactivities.[10]

Chiral phosphoric acids[11] (CPA) have been recognized as privileged chiral Brønsted acids, and we have realized a series of CPA-catalyzed enantioselective transformations.[12] Inspired by this success, we envisaged that vinyliminium intermediates generated from 3-indolylmethanols and dimedone-derived enaminones could be simultaneously activated by CPA via hydrogen-bonding interactions to undergo enantioselective aza-ene reactions (Scheme 1). Herein, we report the catalytic asymmetric aza-ene reactions of 3-indolylmethanols with cyclic enaminones, which directly assemble isatin-derived 3-indolylmethanols and enaminones of dimedones into C3-functionalized chiral indoles with one all-carbon quaternary stereogenic center in high yields and excellent enantioselectivities (up to 99% yield, up to 95:5 er).

RESULTS AND DISCUSSION

The initial experiment to test our hypothesis commenced with the reaction of *N*-methylisatin-derived 3-indolylmethanol **1a** and dimedone-derived enaminone **2a** at 35 °C in the presence of CPA **4a**, which afforded the desired aza-ene product **3aa** but in low yield and poor enantioselectivity (Table 1, entry 1). The screening of BINOL-derived CPAs **4** and **5** (entries 2−8) found that bulky groups at the 3,3′-positions of the BINOL backbone were beneficial to the enantioselective control. An exception was CPA **4g** with a bulky −$SiPh_3$ group, which

Table 1. Screening of Catalysts and Optimization of Conditions[a]



entry	cat.	additives	solvent	T (°C)	yield[b] (%)	er[c]
1	**4a**		$CHCl_3$	35	44	57:43
2	**4b**		$CHCl_3$	35	54	65:35
3	**4c**		$CHCl_3$	35	68	85:15
4	**4d**		$CHCl_3$	35	34	81:19
5	**4e**		$CHCl_3$	35	76	88:12
6	**4f**		$CHCl_3$	35	63	91:9
7	**4g**		$CHCl_3$	35	22	61:39
8	**5**		$CHCl_3$	35	88	60:40
9			$CHCl_3$	35		
10	**4f**		CH_2Cl_2	35	69	90:10
11	**4f**		CH_2ClCH_2Cl	35	74	87:13
12	**4f**		CCl_3CH_3	35	40	83:17
13	**4f**		CCl4	35		
14	**4f**		BrPh	35	36	90:10
15	**4f**		THF	35	19	73:27
16	**4f**		1,4-dioxane	35	22	92:8
17	**4f**	3 Å MS	$CHCl_3$	35	88	89:11
18	**4f**	4 Å MS	$CHCl_3$	35	88	89:11
19	**4f**	5 Å MS	$CHCl_3$	35	71	92:8
20	**4f**	$MgSO_4$	$CHCl_3$	35	89	87:13
21	**4f**	Na_2SO_4	$CHCl_3$	35	88	87:13
22[d]	**4f**	5 Å MS	$CHCl_3$	35	88	65:35
23[e]	**4f**	**5 Å MS**	**$CHCl_3$**	**35**	**73**	**93:7**
24[f]	**4f**	5 Å MS	$CHCl_3$	35	88	91:9
25	**4f**	5 Å MS	$CHCl_3$	25	64	93:7
26	**4f**	5 Å MS	$CHCl_3$	45	80	91:9

[a]Unless indicated otherwise, the reaction was carried out in 0.1 mmol scale in a solvent (1 mL) with additives (100 mg) for 16 h, and the mole ratio of **1a**:**2a** was 1:1.5. [b]Isolated yield. [c]The er was determined by HPLC. [d]The mole ratio of **1a**:**2a** was 1:1. [e]The mole ratio of **1a**:**2a** was 1:2.5. [f]The mole ratio of **1a**:**2a** was 1:4.

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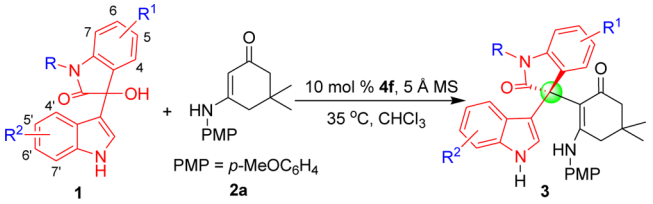
showed low catalytic activity (entry 7). Although bis-CPA **5** delivered the aza-ene reaction in the highest yield of 88%, the enantioselectivity was poor (entry 8). Among the tested catalysts, CPA **4f** substituted with 3,3′-(9-anthracenyl) groups delivered the highest enantioselectivity of 91:9 er (entry 6). The model reaction was also carried out in the absence of the catalyst, but no reaction occurred, which indicated that there was no background reaction (entry 9). The subsequent evaluation of various solvents was performed in the presence of CPA **4f** (entries 6 and 10−16). Among chloro-contained alkanes, chloroform and dichloromethane were much better than the others in terms of enantioselectivity (entry 6 and 10 vs 11−13). Bromobenzene and 1,4-dioxane delivered the reaction in good enantioselectivities but with low yields (entries 14 and 16). Thus, chloroform was still the choice of solvent. Then, different additives including molecular sieves (MS) and anhydrous sulfates as water absorbers were utilized to the reaction (entries 17−21). The results disclosed that 5 Å MS had the highest capability in delivering the best enantioselectivity with a good yield (entry 19), which may largely be ascribed to the action of 5 Å MS in efficiently scavenging the water molecules generated from 3-indolylmethanol. Finally, modulating the mole ratio of the two reactants (entries 22−24) revealed that lowering the stoichiometry of enaminone **2a** was detrimental to the enantioselectivity (entry 22), while properly increasing the stoichiometry of enaminone **2a** led to an improved yield of 73% and a slightly enhanced enantioselectivity of 93:7 er (entry 23). However, lowering or raising the reaction temperature could not ameliorate the enantioselectivity (entries 25 and 26). THus, the most suitable temperature for the reaction was still set at 35 °C.

After establishing the optimal reaction conditions, we then carried out the investigation on the substrate scope of this catalytic asymmetric aza-ene reaction. As shown in Table 2, this approach is applicable to a variety of isatin-derived 3-indolylmethanols **1** with various substituents at different positions, offering the aza-ene products **3** with structural diversity in generally high yields (up to 99%) and good enantioselectivities (up to 94:6 er). In detail, either *N*-alkylisatin-derived 3-indolylmethanol as exemplified by **1a** or *N*-benzylisatin-derived ones (**1b**−**f**) served as suitable substrates to participate in the aza-ene reaction with uniformly good enantioselectivities (93:7 to 94:6 er, entries 1−6), but substrates **1b**−**d** with electron-neutral or -donating substituents linked to the benzyl groups showed higher reactivity (94−99% yield) than the others (entries 2−4 vs 1, 5, 6). It seemed that the position of the substituents at the phenyl ring of isatin skeleton had some effect on the enantioselectivity, since C5-substituted 3-indolylmethanol **1g** was inferior to C6- and C7-substituted ones (**1h**−**k**) in enantioselective control (entry 7 vs 8−11). However, the electronic nature of these substituents had a remarkable influence on the reactivity regardless of their position because C5- or C7-methyl substituted substrates delivered much higher yields than those substituted with electron-poor groups (entries 7, 10 vs 8−9, 11). As for indole core, the position of the substituents did not obviously affect the enantioselectivity, due to the fact that C5′, C6′ or C7′-substituted 3-indolylmethanols could take part in the reaction with generally good enantioselectivities (91:9 to 94:6 er, entries 12−17). Nevertheless, electron-donating groups at different position of the indole moiety afforded much better yields of 89−99% than electron-withdrawing ones (entries 12, 13, 15, 17 vs 14, 16), which indicated that the reactivity of the reaction

Table 2. Substrate Scope of Isatin-Derived 3-Indolylmethanols 1[a]



entry	3	R/R[1]/R[2] (1)	yield[b] (%)	er[c]
1	**3aa**	CH_3/H/H (**1a**)	73	93:7 (>99:1)[d]
2	**3ba**	Bn/H/H (**1b**)	94	94:6
3	**3ca**	*p*-*t*-Bu$C_6H_4CH_2$/H/H (**1c**)	99	94:6
4	**3da**	*m*-$CH_3C_6H_4CH_2$/H/H (**1d**)	99	93:7
5	**3ea**	*m*-$ClC_6H_4CH_2$/H/H (**1e**)	74	94:6
6	**3fa**	*m*,*p*-$Cl_2C_6H_3CH_2$/H/H (**1f**)	62	93:7
7	**3ga**	Bn/5-CH_3/H (**1g**)	71	88:12
8	**3ha**	Bn/6-Cl/H (**1h**)	52	94:6
9	**3ia**	Bn/6-Br/H (**1i**)	50	93:7
10	**3ja**	Bn/7-CH_3/H (**1j**)	85	92:8
11	**3ka**	Bn/7-F/H (**1k**)	51	94:6
12	**3la**	Bn/H/5′-$OCHH_3$ (**1l**)	99	92:8
13	**3ma**	Bn/H/5′-CH_3 (**1m**)	91	93:7
14	**3na**	Bn/H/5′-F (**1n**)	45	91:9
15	**3oa**	Bn/H/6′-CH_3 (**1o**)	99	93:7
16	**3pa**	Bn/H/6′-Br (**1p**)	50	93:7
17	**3qa**	Bn/H/7′-CH_3 (**1q**)	89	94:6

[a]Unless indicated otherwise, the reaction was carried out on a 0.1 mmol scale in $CHCl_3$ (1 mL) with 5 Å MS (100 mg) for 16 h, and the mole ratio of **1**:**2a** was 1:2.5. [b]Isolated yield. [c]The er was determined by HPLC. [d]After recrystallization.

was again dominated by the electronic nature of the substituents. The reactivity of 3-indolylmethanols to take part in the aza-ene reaction may have some effect on the formation and stability of the carboncation or vinyliminium cation intermediate. The stability of the cation intermediate would facilitate its formation and thus increase the reactivity of 3-indolylmethanols. When the substituents of R, R^1, and R^2 in Table 2 were electron-withdrawing groups, they would make the positive charge of the cation intermediate more concentrated, which would decrease the stability of the cation intermediate and therefore resulted in the relatively low reactivity and experimentally observed lower yields of electronically poor 3-indolylmethanols.

Next, the substrate scope with respect to dimedone-derived enaminone **2** was examined by the aza-ene reactions with 3-indolylmethanol **1b** under the optimal reaction conditions. As listed in Table 3, a series of aniline-derived enaminones bearing electron-rich, -neutral, or -poor groups on the phenyl ring were utilized to the reaction, giving chiral aza-ene products **3** with one quaternary stereogenic center in excellent yields (86−99%) and generally high enantioselectivities (86:14 to 94:6 er). Basically, the electronic nature of aniline moieties imposed an evident impact on the enantioselectivity because enaminones substituted with electron-donating groups delivered higher enantioselectivities than those substituted with electron-neutral or -withdrawing groups (entries 1−5 vs 6−8). Furthermore, monosubstituted enaminone was superior to disubstituted enaminone in enantioselective control as exemplified by substrates **2a** and **2e** (entry 1 vs 5). However, the reactivity

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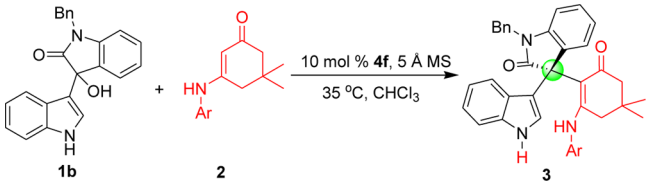
Table 3. Substrate Scope of Dimedone-Derived Enaminones 2[a]



entry	3	Ar (2)	yield[b] (%)	er[c]
1	**3ba**	4-MeOC$_6$H$_4$ (**2a**)	94	94:6
2	**3bb**	4-EtOC$_6$H$_4$ (**2b**)	99	93:7
3	**3bc**	4-*i*-PrOC$_6$H$_4$ (**2c**)	99	93:7
4	**3bd**	4-*i*-PrC$_6$H$_4$ (**2d**)	92	90:10
5	**3be**	3,4-(MeO)$_2$C$_6$H$_3$ (**2e**)	99	88:12
6	**3bf**	Ph (**2f**)	99	86:14
7	**3bg**	4-FC$_6$H$_4$ (**2g**)	99	87:13
8[d]	**3ah**	4-ClC$_6$H$_4$ (**2h**)	86	87:13 (99:1)[e]

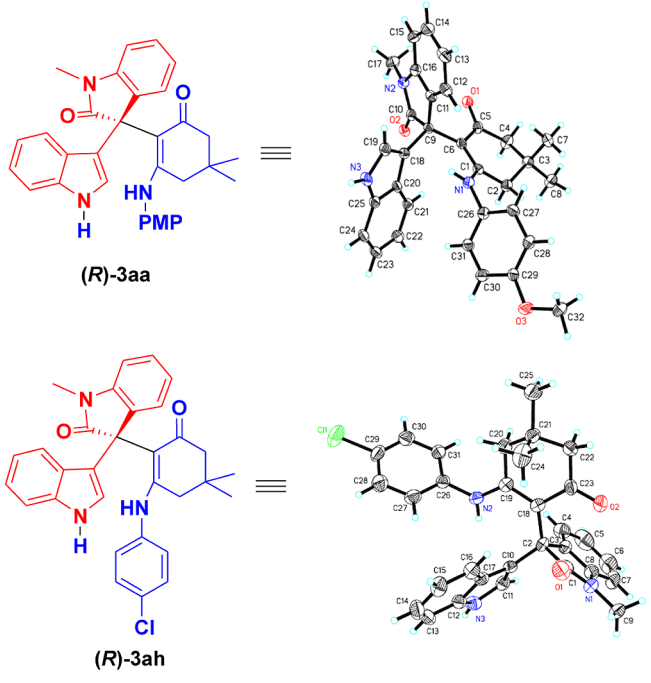
[a]Unless indicated otherwise, the reaction was carried out on a 0.1 mmol scale in $CHCl_3$ (1 mL) with 5 Å MS (100 mg) for 16 h, and the mole ratio of **1b**:**2** was 1:2.5. [b]Isolated yield. [c]The er was determined by HPLC. [d]Using 3-indolylmethanol **1a** instead of **1b**. [e]After recrystallization.

of different substrates was extremely high in all cases, most of which delivered the aza-ene reaction in quantitative yields (entries 2, 3, and 5–7).

The absolute configurations of products **3aa** (>99:1 er after recrystallization) and **3ah** (99:1 er after recrystallization) were unambiguously determined to be (*R*) by single-crystal X-ray diffraction analysis (Scheme 2).[13] The absolute configuration of other products **3** was assigned by analogy.

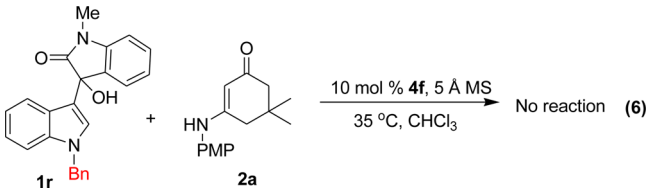
On the basis of the experimental results, we suggested a possible transition state to explain the stereochemistry of this catalytic asymmetric aza-ene reaction. As illustrated in Scheme 3, both enophiles generated from vinyliminium intermediates

Scheme 2. X-ray Structures of 3aa and 3ah

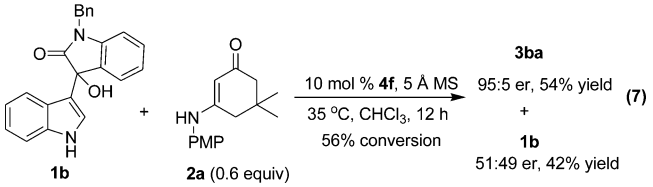


by deprotonation and dimedone-derived enaminones were simultaneously activated by CPA **4f** via hydrogen-bonding interactions. In this transition state, CPA **4f** acted as a Brønsted acid/Lewis base bifunctional catalyst to realize dual hydrogen-bonding activation mode. With the help of hydrogen bonds formed between the catalyst and the two reactants, the chiral environment generated by (*R*)-BINOL backbone, and the bulky 3,3′-(9-anthracenyl)-substituents of CPA **4f**, an efficient and enantioselective aza-ene reaction proceeded to afford intermediate **6**, which was easily isomerized to final product **3** with experimentally observed (*R*)-configuration.

In our proposed reaction pathway, the N–H group of the indole moiety was essentially important for generating the corresponding enophile via deprotonation of the vinyliminium intermediate and thus creating hydrogen bond with the hydroxyl group of CPA **4f**. To testify this activation mode and the role of indole N–H group, a control experiment using *N*-benzyl-protected 3-indolylmethanol **1r** as a substrate was performed under the optimal reaction conditions (eq 6). As expected, no reaction occurred, which demonstrated that the indole N–H group indeed played a crucial role in the designed aza-ene reaction.



To investigate whether there was a kinetic resolution of 3-indolylmethanol during the process of aza-ene reaction, racemic substrate **1b** was reacted with 0.6 equiv of enaminone **2a** under the optimized reaction conditions (eq 7). After completion of



the reaction, the desired aza-ene product **3ba** was obtained in an excellent enantioselectivity of 95:5 er, but the recovered 3-indolylmethanol **1b** was almost a racemate (51:49 er), which implied that there was no obvious kinetic resolution during the reaction process. This result indicated that the first step of protonation and dehydration of 3-indolylmethanol **1** to form planar enophilic intermediate was very fast and the two enantiomers of 3-indolylmethanol **1** did not exhibit obvious difference with regard to reactivity in this step.

CONCLUSIONS

In summary, we have established the catalytic asymmetric aza-ene reactions of 3-indolylmethanols with cyclic enaminones, which directly assemble isatin-derived 3-indolylmethanols and enaminones of dimedones into C3-functionalized chiral indoles with one all-carbon quaternary stereogenic center in high yields and excellent enantioselectivities (up to 99% yield, up to 95:5 er). This transformation also represents highly enantioselective aza-ene reactions utilizing cyclic aza-ene components; it not only overcomes, the great challenge of relatively low reactivity

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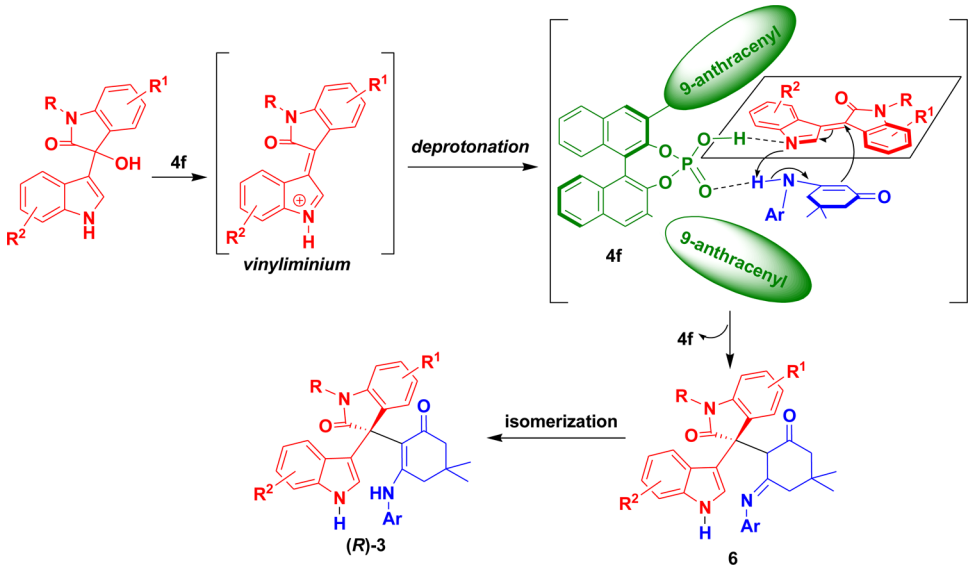
Scheme 3. Proposed Transition State



and rigid structure inherent in cyclic aza-enes but also makes progress toward catalytic asymmetric aza-ene reactions for its high efficiency and enantioselectivity in C−C bond formation and C3-functionalization of indole ring. More importantly, these protocol-integrated bioactive indole, isatin, and cyclic enaminone skeletons change into a novel type of C3-functionalized indole structure, leading to a variety of chiral indole derivatives with structural complexity and diversity, which may find medicinal applications after bioassay.

EXPERIMENTAL SECTION

General Information. NMR spectra were measured respectively at 400 and 100 MHz, respectively. The solvent used for NMR spectroscopy was $CDCl_3$, using tetramethylsilane as the internal reference. HRMS spectra were recorded on a LTQ-Orbitrap mass spectrometer (ionization mode: ESI+). Enantiomeric ratios (er) were determined by chiral high-performance liquid chromatography (chiral HPLC). The chiral columns used for the determination of Enantiomeric ratios by chiral HPLC were Chiralpak IA, OD-H, and AD-H columns. Optical rotation values were measured with instruments operating at λ = 589 nm, corresponding to the sodium D line at the temperatures indicated.

Analytical-grade solvents for the column chromatography and commercially available reagents were used as received. All starting materials commercially available were used directly. Substrates **1** and **2** were synthesized according to the literature methods.[7a,f,14]

General Procedure for the Catalytic Asymmetric Aza-ene Reactions of Isatin-Derived 3-Indolylmethanols with Enaminones of Dimedones. Chloroform (1 mL) was added to the mixture of isatin-derived 3-indolylmethanols **1** (0.1 mmol), enaminones of dimedones **2** (0.25 mmol), the catalyst **4f** (0.01 mmol), and 5 Å molecular sieves (100 mg). After being stirred at 35 °C for 16 h, the reaction mixture was filtered to remove molecular sieves, and the solid powder was washed with ethyl acetate. The resultant solution was concentrated under the reduced pressure to give the residue, which was purified through flash column chromatography on silica gel to afford pure products **3**.

Compound 3aa: flash column chromatography eluent, petroleum ether/ethyl acetate = 1/2; reaction time = 16 h; yield: 73% (36.9 mg); white solid; mp 152−153 °C; $[\alpha]^{20}_D$ = +122.9 (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 1.9 Hz, 1H), 8.32 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 7.1 Hz, 2H), 7.27−7.24 (m, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.19−7.14 (m, 1H), 7.14−7.08 (m, 1H), 7.04−6.98 (m, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 6.61 (d, *J* = 8.9 Hz, 2H), 6.40 (d, *J* = 2.6 Hz, 1H), 6.03 (d, *J* = 8.8 Hz, 2H), 3.70 (s, 3H), 3.06 (s, 3H), 2.31−2.27 (m, 1H), 2.19−2.02 (m, 3H), 1.13 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 178.8, 161.7, 158.0, 144.6, 137.7, 133.1, 131.0, 128.1, 127.9, 126.5, 123.2, 123.1, 122.6, 121.8, 120.2, 114.5, 114.2, 112.0, 108.6, 108.1, 55.5, 52.4, 50.2, 41.3, 31.9, 29.0, 27.8, 26.6; IR (KBr) ν 3552, 3415, 2953, 2039, 1696, 1638, 1616, 1566, 1510, 1396, 1246, 1168, 1075, 1032, 904, 618 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{31}N_3O_3 + Na)^+$ requires *m*/*z* 528.2258, found *m*/*z* 528.2271; enantiomeric ratio 93:7, determined by HPLC (Daicel Chirapak AD-H, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm) t_R = 5.920 min (minor), t_R = 9.12 min (major).

Compound 3ba: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 94% (54.4 mg); white solid; mp 185−187 °C; $[\alpha]^{20}_D$ = +416.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, *J* = 2.0 Hz, 1H), 8.35 (d, *J* = 7.9 Hz, 1H), 7.35−7.29 (m, 2H), 7.27−7.25 (m, 1H), 7.25−7.24 (m, 2H), 7.20−7.15 (m, 1H), 7.15−7.06 (m, 5H), 6.96 (t, *J* = 7.1 Hz, 1H), 6.65−6.56 (m, 3H), 6.38 (d, *J* = 2.5 Hz, 1H), 6.04 (d, *J* = 8.8 Hz, 2H), 4.91 (d, *J* = 16.1 Hz, 1H), 4.76 (d, *J* = 16.1 Hz, 1H), 3.69 (s, 3H), 2.34 (d, *J* = 16.3 Hz, 1H), 2.22−2.05 (m, 3H), 1.11 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 178.4, 161.6, 157.9, 143.5, 137.6, 136.9, 133.1, 130.9, 128.4, 127.8, 127.8, 127.2, 126.9, 126.5, 123.2, 123.1, 123.0, 122.5, 121.8, 120.2, 114.9, 114.1, 111.9, 109.3, 108.4, 55.4, 52.5, 50.1, 44.1, 41.2, 31.9, 29.0, 27.8; IR (KBr) ν 3552, 3415, 3055, 2951, 2036, 1698, 1681, 1638, 1616, 1566, 1511, 1396, 1384, 1247, 1173, 1011, 752 cm^{-1}; ESI FTMS exact mass calcd for $(C_{38}H_{35}N_3O_3 + Na)^+$ requires *m*/*z* 604.2571, found *m*/*z* 604.2615; enantiomeric ratio 94:6, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm) t_R = 7.513 min (minor), t_R = 9.247 min (major).

Compound 3ca: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield: 99% (63 mg); white solid; mp 159−160 °C; $[\alpha]^{20}_D$ = +477.1 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 1.9 Hz, 1H), 8.39 (d, *J* = 7.8 Hz, 1H), 7.34−7.27 (m, 3H), 7.23 (s, 4H), 7.22−7.14 (m, 2H), 7.10 (dd, *J* = 7.7, 1.0 Hz, 1H), 6.97 (t, *J* = 7.2 Hz, 1H), 6.66−6.59 (m, 3H), 6.43 (d, *J* = 2.5 Hz, 1H), 6.05 (d, *J* = 8.8 Hz, 2H), 4.87 (d, *J* = 16.0 Hz, 1H), 4.78 (d, *J* = 16.0 Hz, 1H), 3.69 (s, 3H), 2.36 (d, *J* = 16.3 Hz, 1H), 2.22−2.06 (m, 3H), 1.23 (s, 9H), 1.15 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 178.3, 161.4, 157.9, 149.6, 143.7, 137.6, 133.9, 133.1, 131.0, 127.8, 126.9, 126.6, 125.4, 123.2, 123.0, 122.8, 122.7, 121.7, 120.3, 115.3, 114.1, 111.8, 109.3, 108.5, 55.4, 52.4, 50.2, 43.8, 41.3, 34.4, 31.9, 31.4, 29.0, 27.9; IR (KBr) ν 3552, 3415, 3302, 3054, 2960, 2867, 2835, 2246, 2059, 1698, 1617, 1565, 1510, 1383, 1248, 1179, 1106, 899, 840, 619 cm^{-1}; ESI FTMS exact mass calcd for

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$(C_{42}H_{43}N_3O_3+Na)^+$ requires m/z 660.3197, found m/z 660.3201; enantiomeric ratio 94:6, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 5.900 min (minor), t_R = 7.523 min (major).

Compound 3da: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield: 99% (59 mg); white solid; mp 162−163 °C; $[\alpha]^{20}_D$ = +67.6 (c 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 2.0 Hz, 1H), 8.36 (d, J = 7.9 Hz, 1H), 7.36−7.28 (m, 2H), 7.27−7.25 (m, 1H), 7.22−7.16 (m, 1H), 7.12 (td, J = 7.8, 1.0 Hz, 2H), 7.05−6.93 (m, 4H), 6.89 (d, J = 6.3 Hz, 1H), 6.62 (t, J = 8.4 Hz, 3H), 6.40 (d, J = 2.5 Hz, 1H), 6.05 (d, J = 8.8 Hz, 2H), 4.95 (d, J = 16.0 Hz, 1H), 4.65 (d, J = 16.0 Hz, 1H), 3.69 (s, 3H), 2.34 (d, J = 16.4 Hz, 1H), 2.27−2.22 (m, 1H), 2.15 (s, 3H), 2.14−2.12 (m, 1H), 2.07 (d, J = 16.7 Hz, 1H), 1.13 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 178.4, 161.6, 157.9, 143.5, 137.9, 137.6, 136.8, 133.1, 130.9, 128.3, 127.9, 127.8, 127.8, 127.7, 126.5, 124.3, 123.1, 123.0, 122.5, 121.7, 120.2, 114.8, 114.1, 111.9, 109.2, 108.3, 55.4, 52.5, 50.1, 43.9, 41.2, 31.9, 29.0, 27.8, 21.4; IR (KBr) ν 3552, 3478, 3413, 3302, 3053, 2953, 2925, 2866, 1698, 1637, 1566, 1510, 1396, 1246, 1222, 1171, 1038, 907, 743, 617 cm^{-1}; ESI FTMS exact mass calcd for $(C_{39}H_{37}N_3O_3 + Na)^+$ requires m/z 618.2727, found m/z 618.2747; enantiomeric ratio 93:7, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 6.717 min (minor), t_R = 8.590 min (major).

Compound 3ea: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield: 74% (44.2 mg); white solid; mp 180−182 °C; $[\alpha]^{20}_D$ = +468.5 (c 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 7.8 Hz, 1H), 8.25 (s, 1H), 7.34−7.28 (m, 4H), 7.25−7.20 (m, 2H), 7.16 (d, J = 8.6 Hz, 1H), 7.14−7.07 (m, 3H), 7.00 (t, J = 7.3 Hz, 1H), 6.63−6.58 (m, 3H), 6.46 (d, J = 2.4 Hz, 1H), 6.07 (d, J = 8.8 Hz, 2H), 4.97 (d, J = 16.3 Hz, 1H), 4.74 (d, J = 16.3 Hz, 1H), 3.71 (s, 3H), 2.39 (d, J = 16.4 Hz, 1H), 2.24−2.08 (m, 3H), 1.19 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ 193.1, 178.2, 161.6, 159.0, 144.3, 141.1, 139.0, 134.8, 134.6, 132.1, 130.8, 128.7, 128.5, 128.2, 127.9, 127.8, 126.8, 124.4, 124.0, 123.5, 122.5, 120.1, 115.9, 114.9, 112.8, 109.4, 109.0, 55.8, 53.4, 51.0, 43.5, 41.9, 32.6, 28.2; IR (KBr) ν 3552, 3479, 3414, 3308, 3237, 3118, 2956, 2933, 2836, 1688, 1574, 1512, 1487, 1396, 1251, 1169, 1038, 682 cm^{-1}; ESI FTMS exact mass calcd for $(C_{38}H_{34}ClN_3O_3$ + Na)$^+$ requires m/z 638.2181, found m/z 638.2172; enantiomeric ratio 94:6, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 7.670 min (minor), t_R = 9.513 min (major).

Compound 3fa: Flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 62% (40.2 mg); white solid; mp 170−171 °C; $[\alpha]^{20}_D$ = +398.3 (c 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 1.9 Hz, 1H), 8.37 (d, J = 7.9 Hz, 1H), 7.32 (dd, J = 7.3, 3.5 Hz, 2H), 7.29 (s, 1H), 7.26−7.24 (m, 2H), 7.22 (dd, J = 6.2, 1.3 Hz, 1H), 7.19 (dd, J = 8.4, 2.0 Hz, 2H), 7.14 (dd, J = 7.7, 1.1 Hz, 1H), 7.03−6.99 (m, 1H), 6.64−6.59 (m, 2H), 6.56 (d, J = 7.7 Hz, 1H), 6.43 (d, J = 2.5 Hz, 1H), 6.06 (d, J = 8.8 Hz, 2H), 4.83 (d, J = 16.3 Hz, 1H), 4.72 (d, J = 16.3 Hz, 1H), 3.71 (s, 3H), 2.36 (d, J = 16.5 Hz, 1H), 2.19 (t, J = 17.6 Hz, 2H), 2.10 (d, J = 16.7 Hz, 1H), 1.17 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 178.1, 161.7, 158.0, 142.8, 137.6, 137.3, 133.0, 132.3, 130.9, 130.8, 130.5, 129.0, 127.9, 127.8, 126.8, 126.4, 123.5, 123.2, 122.8, 122.6, 122.1, 120.4, 115.1, 114.1, 111.8, 108.9, 108.1, 55.4, 52.5, 50.1, 42.7, 41.2, 31.9, 29.0, 27.8; IR (KBr) ν 3553, 3413, 3231, 3035, 2958, 2881, 1688, 1638, 1609, 1572, 1397, 1330, 1272, 1168, 1047, 940, 829, 684 cm^{-1}; ESI FTMS exact mass calcd for $(C_{38}H_{33}Cl_2N_3O_3$ + Na)$^+$ requires m/z 672.1791, found m/z 672.1778; enantiomeric ratio 93:7, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 7.777 min (minor), t_R = 10.300 min (major).

Compound 3ga: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 70.5% (42 mg); white solid; mp 249−250 °C; $[\alpha]^{20}_D$ = +22.4 (c 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 1.7 Hz, 1H), 8.37 (d, J = 7.9 Hz, 1H), 7.31−7.23 (m, 4H), 7.21−7.16 (m, 1H), 7.16−7.04 (m, 5H), 6.92 (d, J = 7.8 Hz, 1H), 6.61 (d, J = 8.8 Hz, 2H), 6.47 (dd, J = 16.5, 5.2 Hz, 2H), 6.04 (d, J = 8.7 Hz, 2H), 4.90 (d, J = 16.1 Hz, 1H), 4.75 (d, J = 16.1 Hz, 1H), 3.70 (s, 3H), 2.33 (d, J = 16.6 Hz, 1H), 2.29 (s, 3H), 2.24−2.13 (m, 2H), 2.07 (d, J = 16.7 Hz, 1H), 1.15 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 178.6, 161.5, 158.0, 141.4, 137.8, 137.2, 133.3, 131.2, 131.2, 128.6, 128.3, 127.9, 127.4, 127.0, 126.8, 124.0, 123.3, 122.8, 120.4, 115.3, 114.3, 112.1, 109.2, 108.7, 55.6, 52.8, 50.3, 44.3, 41.5, 31.9, 29.5, 27.7, 21.6; IR (KBr) ν 3551, 3414, 3312, 3057, 2958, 2927, 2053, 1868, 1688, 1616, 1561, 1510, 1395, 1382, 1247, 1188, 1031, 1009, 823, 733, 698 cm^{-1}; ESI FTMS exact mass calcd for $(C_{39}H_{37}N_3O_3$ + Na)$^+$ requires m/z 618.2727, found m/z 618.2721; enantiomeric ratio 88:12, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 7.217 min (minor), t_R = 9.113 min (major).

Compound 3ha: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield: 52% (32.2 mg); white solid; mp 135−136 °C; $[\alpha]^{20}_D$ = +22.3 (c 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 7.9 Hz, 1H), 8.24 (s, 1H), 7.34 (d, J = 8.1 Hz, 1H), 7.28 (d, J = 7.0 Hz, 1H), 7.26−7.25 (m, 2H), 7.24−7.18 (m, 5H), 7.18−7.13 (m, 1H), 6.96 (dd, J = 7.8, 1.8 Hz, 1H), 6.63−6.60 (m, 3H), 6.51 (d, J = 2.5 Hz, 1H), 6.05 (d, J = 8.8 Hz, 2H), 4.98 (d, J = 16.1 Hz, 1H), 4.75 (d, J = 16.1 Hz, 1H), 3.71 (s, 3H), 2.40 (d, J = 16.4 Hz, 1H), 2.20 (dd, J = 16.6, 5.7 Hz, 2H), 2.10 (d, J = 16.7 Hz, 1H), 1.18 (s, 3H), 0.97 (s, 3H; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 158.0, 144.9, 137.5, 136.3, 133.4, 131.4, 130.7, 128.6, 127.8, 127.2, 127.1, 126.4, 123.8, 123.6, 122.7, 122.6, 121.6, 120.6, 115.0, 114.2, 111.6, 109.8, 108.0, 55.4, 52.1, 50.0, 44.1, 41.3, 31.9, 29.0, 27.8; IR (KBr) ν 3443, 3383, 2958, 2925, 1705, 1650, 1607, 1510, 1398, 1329, 1248, 1221, 1103, 913, 803, 745, 699 cm^{-1}; ESI FTMS exact mass calcd for $(C_{38}H_{34}ClN_3O_3$ + H)$^+$ requires m/z 616.2376, found m/z 616.2343; enantiomeric ratio 94:6, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 6.717 min (minor), t_R = 9.007 min (major).

Compound 3ia: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 50% (33.2 mg); white solid; mp 136−137 °C; $[\alpha]^{20}_D$ = +428.6 (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 7.8 Hz, 1H), 8.21 (s, 1H), 7.37 (d, J = 8.1 Hz, 1H), 7.33−7.30 (m, 1H), 7.29−7.27 (m, 1H), 7.26−7.22 (m, 5H), 7.22−7.17 (m, 2H), 7.14 (dd, J = 7.8, 1.7 Hz, 1H), 6.79 (d, J = 1.6 Hz, 1H), 6.64 (d, J = 8.9 Hz, 2H), 6.54 (d, J = 2.5 Hz, 1H), 6.07 (d, J = 8.8 Hz, 2H), 5.00 (d, J = 16.1 Hz, 1H), 4.77 (d, J = 16.1 Hz, 1H), 3.74 (s, 3H), 2.42 (d, J = 16.5 Hz, 1H), 2.25−2.10 (m, 3H), 1.21 (s, 3H), 0.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 177.9, 161.6, 158.0, 145.1, 137.5, 136.3, 132.0, 130.7, 128.6, 127.8, 127.2, 126.4, 124.5, 124.2, 123.6, 122.7, 122.5, 121.3, 120.6, 114.9, 114.2, 112.5, 111.6, 107.9, 55.4, 52.1, 50.0, 44.1, 41.3, 31.9, 29.0, 27.8; IR (KBr) ν 3552, 3414, 3236, 2955, 2036, 1705, 1638, 1617, 1566, 1510, 1487, 1397, 1329, 1247, 1221, 1104, 1034, 767, 743, 620 cm^{-1}; ESI FTMS exact mass calcd for $(C_{38}H_{34}BrN_3O_3$ + Na)$^+$ requires m/z 684.1663, found m/z 684.1635; enantiomeric ratio 93:7, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 6.700 min (minor), t_R = 9.123 min (major).

Compound 3ja: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 85% (50.7 mg); white solid; mp 141−142 °C; $[\alpha]^{20}_D$ = +410.9 (c 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.38 (d, J = 7.9 Hz, 1H), 7.28 (d, J = 7.9 Hz, 2H), 7.25−7.14 (m, 3H), 7.12−7.11 (m, 4H), 7.08−6.99 (m, 1H), 6.94−6.90 (m, 2H), 6.65−6.58 (m, 2H), 6.45 (d, J = 2.5 Hz, 1H), 6.05 (d, J = 8.8 Hz, 2H), 5.22 (d, J = 16.4 Hz, 1H), 4.99 (d, J = 16.4 Hz, 1H), 3.71 (s, 3H), 2.42−2.30 (m, 2H), 2.24 (s, 3H), 2.18−2.11 (m, 1H), 1.15 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 179.2, 161.5, 157.9, 141.6, 139.4, 137.6, 133.8, 131.8, 131.0, 128.9, 128.4, 127.8, 126.6, 126.4, 125.9, 125.8, 123.2, 123.1, 122.7, 121.9, 121.1, 120.3, 119.6, 115.7, 114.1, 111.7, 108.6, 55.4, 52.1, 50.1, 45.1, 41.2, 31.9, 28.9, 27.9, 19.0; IR (KBr) ν 3351, 3414, 3236, 2953, 2867, 2037, 1715, 1694, 1638, 1616, 1510, 1418, 1395, 1248, 1182, 1036, 1010, 846, 766, 617 cm^{-1}; ESI FTMS exact mass calcd for $(C_{39}H_{37}N_3O_3$ + H)$^+$ requires m/z 596.2913, found m/z 596.2935;

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enantiomeric ratio 92:8, determined by HPLC (Daicel Chirapak OD-H, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 4.803 min (minor), t_R = 7.747 min (major).

Compound 3ka: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 51% (30.5 mg); white solid; mp 146−147 °C; $[\alpha]^{20}_D$ = +384.0 (c 0.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 7.9 Hz, 1H), 8.21 (s, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.31 (dd, J = 7.0, 1.1 Hz, 1H), 7.25 (d, J = 6.7 Hz, 2H), 7.21 (d, J = 8.3 Hz, 2H), 7.19−7.11 (m, 4H), 6.98−6.90 (m, 2H), 6.69−6.58 (m, 2H), 6.44 (d, J = 2.6 Hz, 1H), 6.08 (d, J = 8.8 Hz, 2H), 5.16 (d, J = 15.8 Hz, 1H), 4.93 (d, J = 15.9 Hz, 1H), 3.73 (s, 3H), 2.43 (d, J = 16.4 Hz, 1H), 2.25−2.11 (m, 3H), 1.21 (s, 3H), 0.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 177.8, 177.0, 161.7, 158.0, 148.7, 146.3, 138.3, 137.5, 136.1, 130.7, 130.3, 130.3, 128.6, 128.1, 127.8, 127.7, 127.2, 126.7, 126.4, 123.4, 123.3, 122.9, 122.6, 122.3, 122.2, 120.5, 120.1, 118.9, 116.1, 115.9, 114.7, 114.2, 111.7, 111.6, 108.0, 55.4, 52.8, 50.0, 45.3, 41.2, 31.9, 28.9, 27.8; IR (KBr) ν 3553, 3478, 3414, 3305, 2925, 2853, 1722, 1617, 1566, 1510, 1397, 1246, 1183, 1033, 853, 735, 619 cm^{-1}; ESI FTMS exact mass calcd for $(C_{38}H_{34}FN_3O_3 + H)^+$ requires m/z 600.2662, found m/z 600.2680; enantiomeric ratio 94:6, determined by HPLC (Daicel Chirapak AD-H, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 6.850 min (minor), t_R = 8.237 min (major).

Compound 3la: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 99% (60.5 mg); white solid; mp 164−165 °C; $[\alpha]^{20}_D$ = +440.7 (c 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 2.3 Hz, 1H), 7.85 (d, J = 2.4 Hz, 1H), 7.42 (s, 1H), 7.28 (s, 1H), 7.24 (s, 1H), 7.17−7.11 (m, 3H), 7.09−7.05 (m, 2H), 6.96−6.93 (m, 1H), 6.87 (dd, J = 8.9, 2.5 Hz, 1H), 6.66−6.61 (m, 2H), 6.56 (d, J = 7.7 Hz, 1H), 6.32 (d, J = 2.6 Hz, 1H), 6.08 (d, J = 8.8 Hz, 2H), 4.89 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 16.0 Hz, 1H), 3.79 (s, 3H), 3.70 (s, 3H), 2.29 (dd, J = 16.4, 12.8 Hz, 2H), 2.17−2.05 (m, 2H), 1.21 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 178.6, 161.5, 157.9, 154.3, 143.4, 136.8, 133.1, 132.7, 130.9, 128.4, 127.8, 127.6, 127.1, 126.9, 126.8, 123.6, 123.1, 121.8, 114.4, 114.2, 114.1, 112.7, 109.3, 108.0, 103.2, 55.7, 55.4, 52.5, 49.9, 44.0, 41.4, 31.5, 29.7, 27.4; IR (KBr) ν 3352, 3416, 3056, 2953, 2038, 1698, 1637, 1616, 1567, 1510, 1448, 1464, 1397, 1384, 1292, 1246, 1176, 1041, 803, 750, 626 cm^{-1}; ESI FTMS exact mass calcd for $(C_{39}H_{37}N_3O_4 + Na)^+$ requires m/z 634.2676, found m/z 634.2672; enantiomeric ratio 92:8, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 7.007 min (minor), t_R = 10.213 min (major).

Compound 3ma. Flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 91% (54.2 mg); white solid; mp 157−158 °C; $[\alpha]^{20}_D$ = +468.8 (c 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, J = 2.1 Hz, 1H), 8.17 (s, 1H), 7.36 (s, 1H), 7.28 (d, J = 6.4 Hz, 2H), 7.25 (s, 1H), 7.18−7.11 (m, 3H), 7.09−7.04 (m, 2H), 7.02 (dd, J = 8.4, 1.3 Hz, 1H), 6.93 (t, J = 7.2 Hz, 1H), 6.62 (d, J = 8.8 Hz, 2H), 6.58 (d, J = 7.6 Hz, 1H), 6.29 (d, J = 2.6 Hz, 1H), 6.03 (d, J = 8.8 Hz, 2H), 4.90 (d, J = 16.0 Hz, 1H), 4.77 (d, J = 16.0 Hz, 1H), 3.70 (s, 3H), 2.40 (s, 3H), 2.33 (d, J = 16.3 Hz, 1H), 2.23 (d, J = 16.9 Hz, 1H), 2.14 (d, J = 16.6 Hz, 1H), 2.06 (d, J = 16.7 Hz, 1H), 1.19 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 178.5, 161.6, 157.8, 143.5, 136.9, 136.0, 133.2, 131.0, 129.2, 128.4, 127.8, 127.6, 127.2, 126.9, 126.7, 124.8, 123.1, 123.1, 122.0, 121.8, 114.1, 114.0, 111.6, 109.2, 108.4, 55.4, 52.4, 50.0, 44.0, 41.3, 31.7, 29.5, 27.3, 21.6; IR (KBr) ν 3551, 3413, 3298, 3031, 2953, 2867, 1699, 1610, 1567, 1510, 1396, 1384, 1345, 1247, 1222, 1168, 1037, 798, 750, 698 cm^{-1}; ESI FTMS exact mass calcd for $(C_{39}H_{37}N_3O_3 + H)^+$ requires m/z 596.2913, found m/z 596.2880; enantiomeric ratio 93:7, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 7.007 min (minor), t_R = 8.247 min (major).

Compound 3na: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 45% (25.6 mg); white solid; mp 146−148 °C; $[\alpha]^{20}_D$ = +51.0 (c 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.09−8.06 (m, 1H), 7.31 (d, J = 7.5 Hz, 1H), 7.27 (s, 1H), 7.24 (s, 2H), 7.24−7.21 (m, 1H), 7.19 (t, J = 7.2 Hz, 2H), 7.16−7.09 (m, 2H), 7.05−6.94 (m, 2H), 6.66−6.62 (m, 3H), 6.50 (d, J = 2.0 Hz, 1H), 6.16 (d, J = 8.3 Hz, 2H), 4.97 (d, J = 16.1 Hz, 1H), 4.80 (d, J = 16.1 Hz, 1H), 3.72 (s, 3H), 2.39 (d, J = 16.2 Hz, 1H), 2.24−2.10 (m, 3H), 1.18 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 178.3, 158.0, 143.5, 136.8, 134.0, 132.7, 130.7, 128.5, 128.0, 127.8, 127.2, 127.0, 124.3, 123.0, 121.8, 114.2, 112.2, 112.0, 109.4, 108.1, 107.8, 55.4, 52.3, 50.1, 44.1, 41.3, 32.0, 28.8, 28.0; IR (KBr) ν 3313, 2955, 1697, 1610, 1566, 1510, 1489, 1397, 1384, 1247, 1177, 939, 750, 697, 626 cm^{-1}; ESI FTMS exact mass calcd for $(C_{38}H_{34}FN_3O_3 + H)^+$ requires m/z 600.2662, found m/z 600.2670; enantiomeric ratio: 91:9, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 14.360 min (minor), t_R = 18.310 min (major).

Compound 3oa: Flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 99% (59 mg); white solid; mp 127−129 °C; $[\alpha]^{20}_D$ = +475.4 (c 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.2 Hz, 1H), 8.08 (s, 1H), 7.36 (s, 1H), 7.33−7.27 (m, 3H), 7.20 (t, J = 7.3 Hz, 2H), 7.16−7.08 (m, 3H), 7.04 (d, J = 8.2 Hz, 1H), 6.96 (t, J = 7.2 Hz, 1H), 6.61 (t, J = 8.3 Hz, 3H), 6.38 (d, J = 1.8 Hz, 1H), 6.11 (d, J = 8.2 Hz, 2H), 4.96 (d, J = 16.1 Hz, 1H), 4.81 (d, J = 16.0 Hz, 1H), 3.72 (s, 3H), 2.46 (s, 3H), 2.40−2.34 (m, 1H), 2.24−2.08 (m, 3H), 1.18 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.5, 178.2, 157.8, 143.6, 138.0, 137.0, 133.2, 133.0, 131.1, 128.4, 127.8, 127.3, 126.9, 124.4, 123.0, 122.4, 122.3, 122.0, 121.6, 115.5, 114.1, 111.3, 109.2, 108.6, 55.4, 52.4, 50.1, 44.1, 41.3, 31.9, 29.1, 27.8, 21.8; IR (KBr) ν 3351, 3412, 3295, 3058, 3030, 2952, 2866, 2050, 1886, 1698, 1611, 1567, 1510, 1464, 1344, 1246, 1170, 1031, 891, 753, 697 cm^{-1}; ESI FTMS exact mass calcd for $(C_{39}H_{37}N_3O_3$+Na)$^+$ requires m/z 618.2727, found m/z 618.2743; enantiomeric ratio 93:7, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 6.573 min (minor), t_R = 10.223 min (major).

Compound 3pa. Flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield: 50% (33 mg); white solid; mp 137−138 °C; $[\alpha]^{20}_D$ = +7.9 (c 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67−8.64 (m, 1H), 8.25 (d, J = 8.5 Hz, 1H), 7.45 (d, J = 1.3 Hz, 1H), 7.34−7.27 (m, 2H), 7.26−7.25 (m, 1H), 7.24−7.22 (m, 2H), 7.16 (t, J = 7.3 Hz, 2H), 7.11−7.08 (m, 2H), 6.97 (t, J = 7.2 Hz, 1H), 6.71−6.58 (m, 3H), 6.44−6.35 (m, 1H), 6.16 (d, J = 8.4 Hz, 2H), 4.92−4.87 (m, 1H), 4.78 (d, J = 16.0 Hz, 1H), 3.72 (s, 3H), 2.34 (d, J = 16.1 Hz, 1H), 2.21−2.07 (m, 3H), 1.12 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 178.2, 161.5, 158.1, 143.4, 138.4, 136.7, 132.6, 130.6, 128.5, 128.1, 127.8, 127.2, 127.0, 125.4, 123.9, 123.6, 123.4, 123.0, 121.9, 116.9, 115.8, 114.7, 114.3, 109.4, 108.4, 55.4, 52.3, 44.1, 41.3, 31.9, 28.9, 27.9; IR (KBr) ν 3419, 2961, 2927, 1697, 1610, 1567, 1510, 1488, 1465, 1455, 1396, 1247, 1171, 1028, 804, 752, 698 cm^{-1}; ESI FTMS exact mass calcd for $(C_{38}H_{34}BrN_3O_3 + H)^+$ requires m/z 660.1862, found m/z 660.1845; enantiomeric ratio: 93:7, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 5.763 min (minor), t_R = 10.560 min (major).

Compound 3qa: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield: 89% (53.2 mg); white solid; mp 152−153 °C; $[\alpha]^{20}_D$ = +5.1 (c 1.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.20 (d, J = 7.9 Hz, 1H), 7.33−7.28 (m, 3H), 7.26 (s, 1H), 7.15 (t, J = 7.4 Hz, 2H), 7.11−7.02 (m, 3H), 7.02−6.93 (m, 2H), 6.63−6.56 (m, 3H), 6.43 (d, J = 2.5 Hz, 1H), 6.06 (d, J = 8.8 Hz, 2H), 4.92 (d, J = 16.1 Hz, 1H), 4.77 (d, J = 16.1 Hz, 1H), 3.71 (s, 3H), 2.36 (s, 1H), 2.33 (s, 3H), 2.21−2.12 (m, 2H), 2.08 (d, J = 16.6 Hz, 1H), 1.14 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (100 MHz, MeOD) δ 195.8, 180.6, 165.1, 159.8, 144.4, 138.8, 138.0, 134.6, 131.5, 129.5, 128.9, 128.1, 127.5, 124.5, 124.3, 124.3, 123.4, 122.6, 121.2, 120.9, 115.3, 115.2, 110.5, 108.4, 55.8, 50.9, 44.6, 42.1, 33.0, 28.9, 28.3, 16.9; IR (KBr) ν 3418, 3053, 2953, 2039, 1699, 1614, 1566, 1510, 1488, 1383, 1346, 1246, 1170, 1030, 743, 697, 617 cm^{-1}; ESI FTMS exact mass calcd for $(C_{39}H_{37}N_3O_3 + Na)^+$ requires m/z 618.2727, found m/z 618.2745; enantiomeric ratio 94:6, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm) t_R = 9.357 min (minor), t_R = 7.133 min (major).

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Compound 3bb: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield: 99% (59 mg); white solid; mp 171−173 °C; $[\alpha]^{20}_{D}$ = +357.8 (*c* 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 1.9 Hz, 1H), 8.37 (d, *J* = 7.8 Hz, 1H), 7.31−7.26 (m, 3H), 7.24 (s, 1H), 7.22−7.17 (m, 1H), 7.17−7.12 (m, 3H), 7.11−7.07 (m, 2H), 6.96 (t, *J* = 7.1 Hz, 1H), 6.60 (d, *J* = 8.8 Hz, 3H), 6.38 (d, *J* = 2.5 Hz, 1H), 6.03 (d, *J* = 8.8 Hz, 2H), 4.93 (d, *J* = 16.1 Hz, 1H), 4.77 (d, *J* = 16.1 Hz, 1H), 3.90 (q, *J* = 7.0 Hz, 2H), 2.35 (d, *J* = 16.3 Hz, 1H), 2.22−2.06 (m, 3H), 1.35 (t, *J* = 7.0 Hz, 3H), 1.14 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 178.4, 161.6, 157.3, 143.5, 137.6, 136.9, 133.1, 130.7, 128.4, 127.8, 127.2, 126.9, 126.5, 123.2, 123.1, 122.9, 122.6, 121.7, 120.2, 115.0, 114.6, 111.8, 109.2, 108.4, 63.6, 52.5, 50.1, 44.1, 41.2, 31.9, 29.0, 27.8, 14.8; IR (KBr) ν 3415, 2978, 2037, 1699, 1638, 1616, 1510, 1397, 1242, 1172, 1115, 1048, 739, 619 cm^{-1}; ESI FTMS exact mass calcd for $(C_{39}H_{37}N_3O_3+Na)^+$ requires *m*/*z* 618.2727, found *m*/*z* 618.2736; enantiomeric ratio: 93:7, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 7.303 min (minor), t_R = 9.537 min (major).

Compound 3bc. Flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 99% (60.5 mg); white solid; mp 187−188 °C; $[\alpha]^{20}_{D}$ = +437.8 (*c* 0.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 2.0 Hz, 1H), 8.36 (d, *J* = 7.9 Hz, 1H), 7.31 (s, 1H), 7.30−7.26 (m, 2H), 7.25 (d, *J* = 1.1 Hz, 1H), 7.24 (s, 1H), 7.17 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.15−7.10 (m, 3H), 7.09−7.03 (m, 2H), 6.96 (d, *J* = 7.1 Hz, 1H), 6.59 (d, *J* = 8.7 Hz, 3H), 6.36 (d, *J* = 2.5 Hz, 1H), 6.02 (d, *J* = 8.8 Hz, 2H), 4.92 (d, *J* = 16.1 Hz, 1H), 4.77 (d, *J* = 16.1 Hz, 1H), 4.43−4.37 (m, 1H), 2.34 (d, *J* = 16.4 Hz, 1H), 2.25−2.04 (m, 3H), 1.26 (d, *J* = 6.0 Hz, 6H), 1.13 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 178.4, 161.6, 156.2, 143.5, 137.6, 136.9, 133.1, 130.6, 128.4, 127.8, 127.8, 127.2, 126.9, 126.5, 123.1, 123.1, 123.0, 122.5, 121.8, 120.2, 115.9, 114.8, 111.9, 109.2, 108.3, 70.1, 52.5, 50.1, 44.1, 41.2, 31.9, 29.0, 27.8, 22.0, 22.0; IR (KBr) ν 3353, 3479, 3413, 3302, 3055, 2955, 2926, 1716, 1610, 1562, 1508, 1384, 1344, 1242, 1167, 1117, 1010, 741, 697 cm^{-1}; ESI FTMS exact mass calcd for $(C_{40}H_{39}N_3O_3 + Na)^+$ requires *m*/*z* 632.2884, found *m*/*z* 632.2894; enantiomeric ratio 93:7, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 6.970 min (minor), t_R = 8.747 min (major).

Compound 3bd: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield: 92% (56 mg); white solid; mp 162−163 °C; $[\alpha]^{20}_{D}$ = +115.8 (*c* 1.7, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, *J* = 2.0 Hz, 1H), 8.35 (d, *J* = 8.0 Hz, 1H), 7.52 (s, 1H), 7.31−7.27 (m, 3H), 7.25 (s, 1H), 7.21−7.17 (m, 1H), 7.12 (t, *J* = 7.8 Hz, 5H), 7.09−7.05 (m, 2H), 6.94 (t, *J* = 7.2 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 6.38 (d, *J* = 2.6 Hz, 1H), 6.02 (d, *J* = 8.5 Hz, 2H), 4.93 (d, *J* = 16.1 Hz, 1H), 4.78 (d, *J* = 16.1 Hz, 1H), 2.39−2.32 (m, 2H), 2.18−2.12 (m, 2H), 1.23 (s, 9H), 1.14 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 178.4, 160.9, 148.9, 143.5, 137.7, 136.9, 135.4, 133.1, 128.4, 127.8, 127.2, 126.9, 126.5, 125.9, 125.3, 123.2, 123.1, 123.1, 122.4, 121.8, 120.2, 114.5, 112.0, 109.2, 108.7, 52.5, 50.1, 44.1, 41.2, 34.4, 31.8, 31.3, 29.4, 27.3; IR (KBr) ν 3552, 3414, 3299, 3055, 2957, 2867, 2037, 1888, 1699, 1637, 1613, 1561, 1514, 1489, 1383, 1270, 1223, 1010, 741, 697 cm^{-1}; ESI FTMS exact mass calcd for $(C_{41}H_{41}N_3O_2 + H)^+$ requires *m*/*z* 608.3277, found *m*/*z* 608.3277; enantiomeric ratio 90:10, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm) t_R = 5.663 min (minor), t_R = 7.153 min (major).

Compound 3be: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 99% (60.5 mg); white solid; mp 152−153 °C; $[\alpha]^{20}_{D}$ = +113.6 (*c* 1.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.39 (dd, *J* = 6.3, 2.9 Hz, 1H), 7.36−7.30 (m, 2H), 7.28 (d, *J* = 3.1 Hz, 1H), 7.24 (s, 2H), 7.17−7.13 (m, 4H), 7.09 (d, *J* = 8.2 Hz, 2H), 6.97 (t, *J* = 7.4 Hz, 1H), 6.61 (t, *J* = 7.8 Hz, 2H), 6.42 (d, *J* = 2.5 Hz, 1H), 6.12 (dd, *J* = 8.4, 1.8 Hz, 1H), 5.20 (d, *J* = 1.9 Hz, 1H), 4.92 (d, *J* = 16.1 Hz, 1H), 4.78 (d, *J* = 16.1 Hz, 1H), 3.79 (s, 3H), 3.51 (s, 3H), 2.34 (d, *J* = 16.4 Hz, 1H), 2.25−2.08 (m, 3H), 1.15 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 178.3, 149.0, 147.5, 143.5, 137.6, 136.8, 133.0, 131.0, 128.4, 127.9, 127.2, 126.9, 126.5, 123.2, 123.2, 122.7, 121.8, 120.2, 119.2, 115.0, 111.8, 110.6, 109.9, 109.3, 108.3, 56.1, 56.0, 52.4, 50.0, 44.1, 41.2, 31.8, 29.7, 29.1, 27.7; IR (KBr) ν 3552, 3413, 3305, 3057, 2953, 2867, 2038, 1698, 1611, 1568, 1512, 1465, 1383, 1168, 1026, 743, 697 cm^{-1}; ESI FTMS exact mass calcd for $(C_{39}H_{37}N_3O_4 + Na)^+$ requires *m*/*z* 634.2676, found *m*/*z* 634.2720; enantiomeric ratio 88:12, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 7.127 min (minor), t_R = 10.587 min (major).

Compound 3bf: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 99% (55 mg); white solid; mp 142−144 °C; $[\alpha]^{20}_{D}$ = +15.5 (*c* 1.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.36 (d, *J* = 7.9 Hz, 1H), 7.51 (s, 1H), 7.29 (d, *J* = 8.5 Hz, 3H), 7.25 (s, 1H), 7.23−7.18 (m, 1H), 7.18−7.13 (m, 3H), 7.08 (dt, *J* = 10.0, 7.1 Hz, 5H), 6.96 (t, *J* = 7.4 Hz, 1H), 6.60 (d, *J* = 7.8 Hz, 1H), 6.41−6.39 (m, 1H), 6.11 (d, *J* = 7.0 Hz, 2H), 4.93 (d, *J* = 16.1 Hz, 1H), 4.79 (d, *J* = 16.1 Hz, 1H), 2.38−2.31 (m, 2H), 2.21−2.10 (m, 2H), 1.16 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 178.3, 160.5, 143.5, 138.2, 137.6, 136.9, 133.0, 129.0, 128.4, 127.9, 127.2, 126.9, 126.4, 125.9, 125.8, 123.3, 123.1, 122.5, 121.8, 120.4, 114.8, 111.8, 109.3, 109.1, 52.5, 50.1, 44.1, 41.4, 31.9, 29.2, 27.5; IR (KBr) ν 3413, 3296, 3055, 2953, 2925, 2866, 2037, 1698, 1612, 1567, 1489, 1465, 1383, 1344, 1272, 1222, 1170, 1010, 741, 699 cm^{-1}; ESI FTMS exact mass calcd for $(C_{37}H_{33}N_3O_2 + H)^+$ requires *m*/*z* 552.2651, found *m*/*z* 552.2670; enantiomeric ratio 86:14, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 6.383 min (minor), t_R = 8.337 min (major).

Compound 3bg: flash column chromatography eluent, petroleum ether/ethyl acetate = 2/1; reaction time = 16 h; yield 99% (56.5 mg); white solid; mp 153−154 °C; $[\alpha]^{20}_{D}$ = +374.3 (*c* 0.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.12−8.96 (m, 1H), 8.35 (d, *J* = 7.9 Hz, 1H), 7.37 (s, 1H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.28−7.23 (m, 3H), 7.21−7.07 (m, 6H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.79 (t, *J* = 8.3 Hz, 2H), 6.63−6.60 (m, 1H), 6.41−6.38 (m, 1H), 6.08−6.05 (m, 2H), 4.90 (d, *J* = 16.1 Hz, 1H), 4.78 (d, *J* = 16.1 Hz, 1H), 2.34 (d, *J* = 16.4 Hz, 1H), 2.25−2.06 (m, 3H), 1.13 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 178.4, 162.0, 160.9, 159.5, 143.4, 137.7, 136.7, 134.2, 134.1, 132.9, 128.4, 128.1, 128.0, 127.9, 127.2, 126.9, 126.4, 123.3, 123.1, 123.1, 122.3, 121.9, 120.2, 115.9, 115.7, 114.4, 114.3, 112.1, 109.3, 109.0, 52.5, 50.1, 44.1, 41.3, 31.9, 29.0, 27.7; IR (KBr) ν 3552, 3478, 3413, 3057, 2956, 2029, 1697, 1615, 1573, 1508, 1383, 1211, 1010, 742, 696, 618 cm^{-1}; ESI FTMS exact mass calcd for $(C_{37}H_{32}FN_3O_2 + Na)^+$ requires *m*/*z* 592.2371, found *m*/*z* 592.2394; enantiomeric ratio 87:13, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm) t_R = 7.487 min (minor), t_R = 9.440 min (major).

Compound 3ah: flash column chromatography eluent, petroleum ether/ethyl acetate = 1/2; reaction time = 16 h; yield 86% (43.8 mg); white solid; mp 172−173 °C; $[\alpha]^{20}_{D}$ = +326 (*c* 0.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.32 (d, *J* = 7.9 Hz, 1H), 7.37 (s, 1H), 7.28 (d, *J* = 7.6 Hz, 2H), 7.26−7.25 (s, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.15−7.12 (m, 1H), 7.06−7.00 (m, 3H), 6.84−6.81 (m, 1H), 6.46−6.44 (m, 1H), 6.02−5.99 (m, 2H), 3.12 (s, 3H), 2.33−2.22 (m, 2H), 2.14−2.08 (m, 2H), 1.16 (s, 3H), 0.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 178.4, 159.9, 144.5, 137.5, 136.8, 132.7, 131.5, 129.1, 128.1, 127.1, 126.3, 123.4, 122.9, 122.6, 121.7, 120.4, 114.6, 111.8, 109.8, 108.1, 52.3, 50.1, 41.4, 31.9, 29.1, 27.5, 26.6. IR (KBr) ν 3290, 2924, 2853, 1717, 1698, 1609, 1584, 1561, 1492, 1381, 1326, 1241, 1127, 1089, 1013, 742 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{28}ClN_3O_2 + Na)^+$ requires *m*/*z* 532.1762, found *m*/*z* 532.1755; enantiomeric ratio 87:13, determined by HPLC (Daicel Chirapak IA, hexane/2-propanol = 70/30, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm) t_R = 5.397 min (minor), t_R = 7.057 min (major).

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■ ASSOCIATED CONTENT

Supporting Information

Characterization data (including ^{1}H and ^{13}C NMR and HPLC spectra) for all products **3** and crystal data of compounds **3aa** and **3ah**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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