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Organocatalytic Chemo-, (*E*/*Z*)- and Enantioselective Formal Alkenylation of Indole-Derived Hydroxylactams Using *o*-Hydroxystyrenes as a Source of Alkenyl Group

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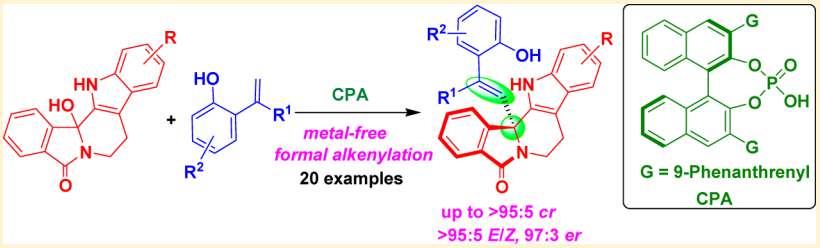
Supporting Information



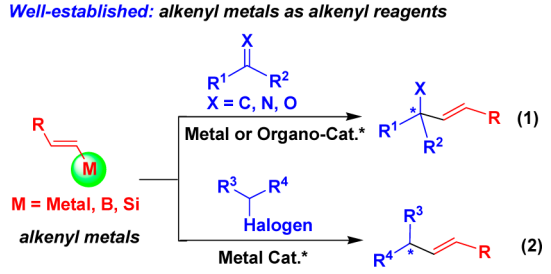
ABSTRACT: The first organocatalytic asymmetric formal alkenylation of multicyclic alcohols using non-metal-based alkenes instead of alkenyl metals as a source of an alkenyl group has been established via chiral phosphoric acid catalyzed tandem reactions. This transformation directly assembles isoindolo-*β*-carboline-derived hydroxylactams with *o*-hydroxystyrenes via an asymmetric cascade vinylogous addition/hydrogen elimination reaction sequence, offering an easy access to functionalized chiral isoindolo-*β*-carbolines with one quaternary stereogenic center in high chemo-, (*E*/*Z*)-, and enantioselectivities (up to >95:5 cr, >95:5 *E*/*Z*, 97:3 er). This approach also represents the first catalytic asymmetric formal alkenylation of isoindolo-*β*-carboline-derived hydroxylactams, which provides a useful strategy for functionalization of isoindolo-*β*-carbolines and synthesis of chiral isoindolo-*β*-carboline derivatives. In addition, the investigation on the activating mode revealed that the hydroxyl group in *o*-hydroxystyrene was essentially important for generating a hydrogen-bond interaction with the catalyst. The dual activation mode of hydrogen bond and ion pair between the catalyst and the substrates cooperatively facilitated the desired formal alkenylation reaction in a chemo- and stereoselective way.

INTRODUCTION

Olefin-containing molecules belong to the most prevalent and important organic compounds, so the development of efficient and stereoselective approaches to produce an alkenyl functional group has aroused great concern in the organic community.[1] Among existing methods, catalytic asymmetric alkenylation (CAA) has proven to be a powerful tool to achieve this goal. The established CAAs mainly include two reaction modes (Scheme 1). One is the enantioselective additions of alkenyl reagents to unsaturated C═X bonds in the presence of chiral metal-based catalysts or organocatalysts (eq 1).[2] Another is the enantioselective cross-couplings of alkenyl reagents with secondary alkyl halide catalyzed by transition metal/chiral ligands (eq 2).[3] *Despite the high efficiency and stereoselectivity of these two approaches, both of them relied heavily on alkenyl metals or metalloids such as Zn,*[2i,j] *Zr,*[2k,l,3a] *Sn,*[2m] *Mg,*[2n] *Al,*[2o−q] *B,*[2a−e] *and Si,*[2f−h,3b] *which served as traditional alkenyl reagents but incurred the environmental issue of producing metal and halide wastes.*

As a result, it is highly desirable to develop alternative sustainable alkenylation strategies using non-metal-based alkenes as alkenyl reagents in place of alkenyl metals. In particular, if chiral organocatalysts could promote the desired alkenylation reaction, the metal-free process would provide a favorable strategy on synthesizing medicinal relevant molecules without any metal contamination of the products.[4] In addition, when alcohols were employed as alkenylation components instead of halides, water would be generated as the sole waste. *Nevertheless, the organocatalytic asymmetric alkenylation of alcohols with non-metal-based alkenes still remained unknown*

Scheme 1. Profile of the Catalytic Asymmetric Alkenylation



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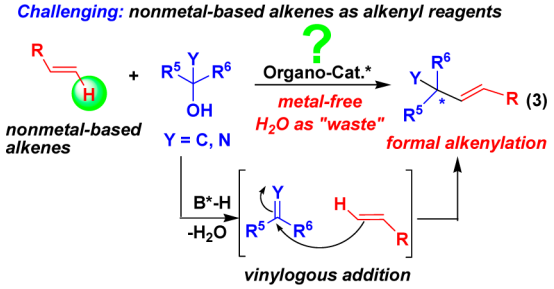
and was full of challenge due to the difficulty in activating both of the substrates during the alkenylation process (eq 3). So, in order to find an alternative strategy, we conceived that multi-substituted alcohols are easily dehydrated in the presence of Brønsted acids (B*-H) to generate unsaturated C═Y bonds, which may undergo enantioselective vinylogous addition with non-metal-based alkenes to achieve asymmetric formal alkenylation of the original alcohols (Sheme 2).

Scheme 2. Formal Alkenylation Strategy Using Non-metal-Based Alkenes as a Source of an Alkenyl Group



Tetrahydro-β-carboline constitutes the key frameworks of many biologically significant man-made compounds or natural products[5] as exemplified by (*R*)-harmicine with antinociceptive activity (Figure 1).[5d] Among them, isoindolo-β-carbolines,

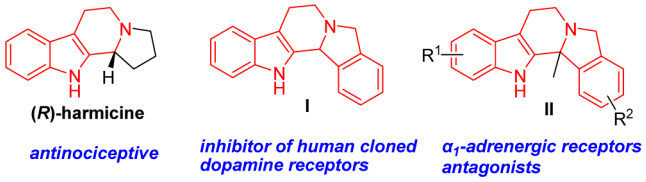
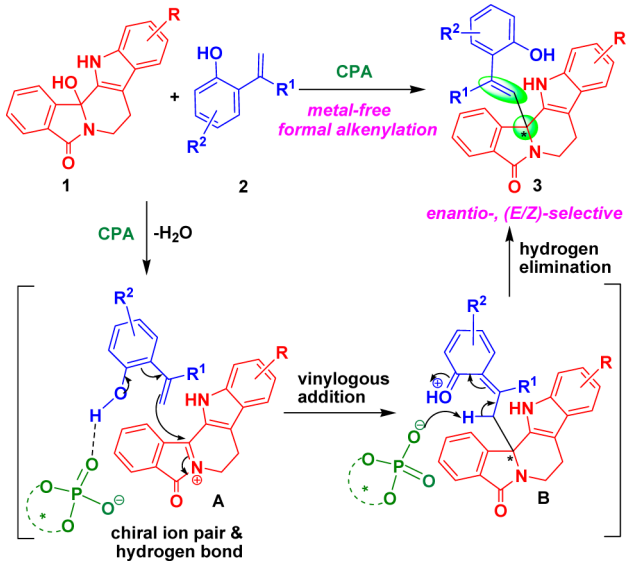


Figure 1. Selected bioactive tetrahydro-β-carbolines and isoindolo-β-carbolines.

which incorporate the two bioactive motifs of tetrahydro-β-carboline and isoindole, exhibit interesting pharmacological activities.[6] For instance, compound **I** possesses the inhibiting action to human cloned dopamine receptors,[6a] and compounds **II** are antagonists of α_1-adrenergic receptors.[6b] Hence, the synthesis and functionalization of isoindolo-β-carbolines such as alkenylation of isoindolo-β-carbolines, particularly the enantioselective transformations, are of certain value in discovery of chiral drugs.[7]

Considering the great challenge in organocatalytic asymmetric alkenylation of alcohols with non-metal-based alkenes and the medicinal relevance of isoindolo-β-carboline framework, we decided to design an organocatalytic stereoselective formal alkenylation of isoindolo-β-carbolines. Recently, chiral phosphoric acids (CPAs) have proven to be a class of robust organocatalysts enabling a wide scope of enantioselective reactions.[8] In the presence of CPA, isoindolo-β-carboline-derived hydroxylactams **1** can be protonated and thereby generate the corresponding *N*-acyliminium ions **A**, which will form ion pair with CPA anions (Scheme 3).[9] Based on this success and our continuous efforts on CPA-catalyzed asymmetric reactions,[10] we envisioned that this intermediate **A** could principally be attacked by *o*-hydroxystyrenes[11] via a vinylogous addition to generate the intermediate **B**, which would subsequently undergo hydrogen elimination to produce the desired formal alkenylation product of isoindolo-β-

Scheme 3. Design of the Organocatalytic Asymmetric Formal Alkenylation of Isoindolo-β-carbolines with *o*-Hydroxystyrenes



carbolines. In this designed metal-free formal alkenylation approach, the two substrates could be simultaneous activated by CPA via chiral ion-pair catalysis[12] and hydrogen-bonding interaction directed by hydroxyl group,[11,13] which would facilitate the desired reaction in an enantio- and (*E*/*Z*)-selective way.

Herein, we report the first organocatalytic asymmetric formal alkenylation of multicyclic alcohols using non-metal-based alkenes instead of alkenyl metals as a source of an alkenyl group, which directly assembles isoindolo-β-carboline-derived hydroxylactams with *o*-hydroxystyrenes via a tandem transformation, leading to functionalized chiral isoindolo-β-carbolines with one quaternary stereogenic center in high chemo-, (*E*/*Z*)- and enantioselectivities (up to >95:5 cr, >95:5 *E*/*Z*, 97:3 er).

RESULTS AND DISCUSSION

The initial experiment to testify our hypothesis started with the reaction of isoindolo-β-carboline-derived hydroxylactam **1a** with *o*-hydroxystyrene **2a** in the presence of CPA **5a** at 30 °C in toluene (Table 1, entry 1). However, the preliminary result was very frustrating because the desired formal alkenylation product **3aa** was generated in an extremely low yield and poor enantioselectivity albeit with a high (*E*/*Z*)-selectivity. In addition, another formal allylation product **4aa** was also produced during the reaction process, which indicated that controlling the chemoselectivity of the reaction was still a great challenge apart from the important issues on the reactivity and the stereoselectivity of reaction. The subsequent screening of BINOL-derived CPAs **5a**−**g** revealed that catalysts **5f** and **5g** with bulky groups at the 3,3′-positions of the BINOL backbone delivered the desired formal alkenylation reaction in a much higher chemo- and enantioselective way than the others (entries 6, 7 vs 1−5), although the yields were still rather low. Among them, 3,3′-(9-phenanthrenyl)-substituted CPA **5g** exhibited the highest capability in controlling both the chemoselectivity (91:9 cr) and the enantioselectivity (92:8 er, entry 7). In order to further improve the reactivity and the enantioselectivity of the reaction, the BINOL backbone of

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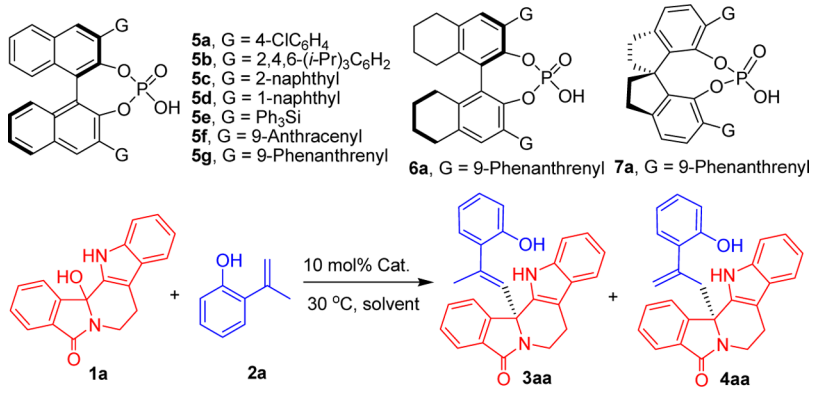
Table 1. Screening of Catalysts and Solvents[a]



entry	solvent	cat.	yield[b] (%)	cr (3aa:4aa)[c]	E/Z of 3aa[d]	er of 3aa[e]
1	toluene	**5a**	13	65:35	>95:5	60:40
2	toluene	**5b**	21	66:34	>95:5	66:34
3	toluene	**5c**	18	64:36	>95:5	64:36
4	toluene	**5d**	24	80:20	>95:5	73:27
5	toluene	**5e**	25	67:33	>95:5	74:26
6	toluene	**5f**	19	90:10	>95:5	90:10
7	toluene	**5g**	28	91:9	>95:5	92:8
8	toluene	**6a**	26	92:8	>95:5	90:10
9	toluene	**7a**	41	94:6	>95:5	78:22
10	CH_2Cl_2	**5g**	49	>95:5	>95:5	70:30
11	EtOAc	**5g**	30	92:8	>95:5	79:21
12	CH_3CN	**5g**	30	91:9	>95:5	87:13
13	*o*-xylene	**5g**	27	92:8	>95:5	92:8
14	*m*-xylene	**5g**	33	91:9	>95:5	91:9
15	*p*-xylene	**5g**	42	90:10	>95:5	90:10
16	F-Ph	**5g**	49	94:6	>95:5	91:9
17	Cl-Ph	**5g**	64	93:7	>95:5	84:16
18	Br-Ph	**5g**	63	95:5	>95:5	75:25

[a]Unless indicated otherwise, the reaction was carried out on a 0.1 mmol scale catalyzed by 10 mol % of **5**−**7** in a solvent (1 mL) at 30 °C for 18 h, and the mole ratio of **1a**:**2a** was 1:1.5. [b]Isolated total yields of **3aa** of **4aa**. [c]The cr of **3aa**:**4aa** was determined by HPLC. [d]The E/Z ratio of **3aa** was determined by HPLC. [e]The er of **3aa** was determined by HPLC.

catalyst **5g** was changed into structurally more rigid H_8-BINOL and SPINOL[14] framework (entries 8 and 9). However, H_8-BINOL-derived CPA **6a** showed catalytic activity similar to that of **5g** (entry 8 vs 7), while SPINOL-derived counterpart **7a** promoted the reaction in a higher yield but with an obviously decreased enantioselectivity (entry 9 vs 7). Thus, BINOL-derived CPA **5g** was finally selected as the most suitable catalyst to further screen different types of solvents (entries 7 and 10−12). Among these representative solvents, toluene as a typical arene-type solvent was much superior to the others with regard to enantioselective control (entry 7 vs 10−12), although dichloromethane afforded the desired reaction in the highest yield (entry 10 vs 7, 11, 12). Then, a series of arene-type solvents such as xylenes and aryl halides were employed to the reaction (entries 13−18), which led to the finding that fluorobenzene could increase the yield to a moderate level with maintained chemo-, (*E*/*Z*)-, and enantioselectivity (entry 16 vs 7). Although chlorobenzene and bromobenzene enhanced the yield to a higher level, the enantioselectivity diminished greatly (entries 17, 18 vs 7, 16). Thus, fluorobenzene was chosen as the optimal reaction media.

With the optimal catalyst and solvent in hand, we then carried out the optimization of other reaction parameters such as additives, temperature, and reagents ratio (Table 2). Nevertheless, the addition of additives including molecular sieves (MS) and sulfates as water absorbers could not benefit the yield of the reaction (entries 2−6 vs 1). Then, in the absence of additives, the reaction temperature was altered (entries 7 and 8). It was found that lowering the reaction temperature was detrimental to both the yield and the chemo- and enantioselectivity (entry 7 vs 1), while elevating the reaction temperature could not further improve the yield and the selectivity of the reaction (entry 8 vs 1). Finally, the reagent ratio was carefully modulated at the optimal reaction temperature of 30 °C (entries 9−12). Increasing the stoichiometry of substrate **1a** led to a decrease of the yield with unvaried chemo-, (*E*/*Z*)-, and enantioselectivity (entry 9). On the contrary, properly raising the stoichiometry of substrate **2a** resulted in a greatly improved yield of 81% with maintained chemo- and stereoselectivity (>95:5 cr, >95:5 *E*/*Z*, 90:10 er, entry 12). Thus, this condition was considered as the most suitable one for its high efficiency and good selectivity in delivering the desired formal alkenylation product.

After establishing the optimal reaction conditions, the substrate scope with respect to hydroxylactams **1** was investigated by the reaction with *o*-hydroxystyrene **2a**. As shown in Table 3, this strategy is applicable to a wide range of indole-derived hydroxylactams **1** bearing electronically distinct substituents at different positions of the indole ring, offering

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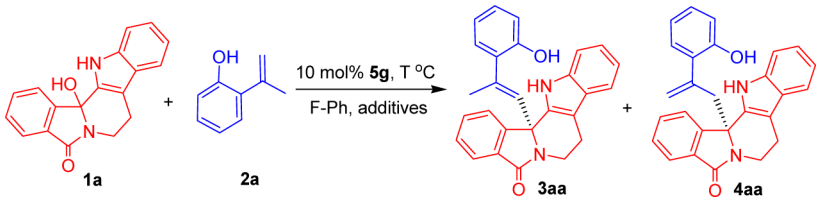
Table 2. Optimization of Other Reaction Parameters[a]



entry	1a:2a	additives	T (°C)	yield[b] (%)	cr (3aa:4aa)[c]	E/Z of 3aa[d]	er of 3aa[e]
1	1:1.5	*f*	30	49	94:6	>95:5	91:9
2	1:1.5	3A	30	18	89:11	>95:5	83:17
3	1:1.5	4A	30	21	88:12	>95:5	90:10
4	1:1.5	5A	30	20	88:12	>95:5	89:11
5	1:1.5	$MgSO_4$	30	37	93:7	>95:5	90:10
6	1:1.5	Na_2SO_4	30	31	95:5	>95:5	92:8
7	1:1.5	*f*	20	19	89:11	>95:5	85:15
8	1:1.5	*f*	40	46	94:6	>95:5	90:10
9	1.5:1	*f*	30	29	94:6	>95:5	91:9
10	1:2.5	*f*	30	51	90:10	>95:5	90:10
11	1:4	*f*	30	63	93:7	>95:5	91:9
12	1:6	*f*	30	81	>95:5	>95:5	90:10

[a]Unless indicated otherwise, the reaction was carried out on a 0.1 mmol scale catalyzed by 10 mol % of **5g** in fluorobenzene (1 mL) for 18 h in the presence of additives (100 mg). [b]Isolated total yields of **3aa** and **4aa**. [c]The cr of **3aa**:**4aa** was determined by HPLC. [d]The E/Z ratio of **3aa** was determined by HPLC. [e]The er of **3aa** was determined by HPLC. [f]In the absence of additives.

the desired formal alkenylation product **3** in generally good to excellent chemo-, (E/Z)-, and enantioselectivities (91:9 to >95:5 cr, all >95:5 E/Z, 83:17 to 97:3 er). Notably, besides C5, C6, or C7-substituted indole-derived hydroxylactams, C4-substituted counterparts **1b**,**c** could also serve as suitable substrates to participate in the reaction with high chemo- and stereoselectivities (entries 2 and 3), which is not very common in indole-related transformations.[10d-e] Furthermore, as exemplified by methyl-substituted substrates **1b**, **1d**, **1h**, and **1k** (entries 2, 4, 8, and 11), C4-methyl-substituted hydroxylactam **1b** afforded higher enantioselectivity than its C5-, C6-, or C7-methyl-substituted analogues (entry 2 vs 4, 8, 11), although the yield of **1b** was not satisfying. Basically, hydroxylactams with electron-donating groups at the indole ring delivered higher enantioselectivity than those with electron-withdrawing ones, while the latter afforded better yields than the former (entry 2 vs 3, entries 4, 5 vs 6, 7). Among the tested hydroxylactams, substrate **1e** with an electron-rich methoxy group provided the formal alkenylation product **3ea** in the highest chemo- and stereoselectivity (>95:5 cr, >95:5 E/Z, 97:3 er) albeit with a moderate yield (entry 5). These results indicated that the electronic nature of the substituents imposed some effect on both the reactivity and the enantioselectivity. Significantly, in all cases, only (E)-isomers were generated with overall high chemoselectivity and good enantioselectivity, which is highly desirable in asymmetric alkenylation and C−C bond formation.

Then, the generality of the reaction for *o*-hydroxystyrenes was studied. As illustrated in Table 4, this method is amenable to a variety of *o*-hydroxystyrene derivatives **2** with different substituents on the phenyl ring or at the vinylic position, producing the formal alkenylation products in good to excellent chemo-, (E/Z)-selectivities (84:16 to >95:5 cr, all >95:5 E/Z), and considerable enantioselectivities (85:15 to 92:8 er). In detail, *o*-hydroxystyrenes bearing electronically neutral, rich or poor substituents on the phenyl moiety could smoothly take part in the designed reaction to chemoselectively afford the (E)-products in good enantioselectivities (entries 1−4). However, electron-neutral or rich *o*-hydroxystyrenes **2a**−**c** exhibited higher capacity than their electron-poor counterpart **2d** in terms of yield, chemoselectivity, and enantioselectivity (entries 1−3 vs 4). Importantly, *o*-hydroxystyrenes with different alkyl groups at the vinylic position proved to be suitable reaction partners, producing the formal alkenylation products with uniformly excellent chemo- and (E/Z)-selectivity (entries 1 and 5, 6), although the reactivity and the enantioselectivity decreased to some extent along with the prolongation of the alkyl group (entries 5, 6 vs 1). In addition, *o*-hydroxystyrenes **2b**,**c** were utilized to react with halogen-substituted hydroxylactams **1c** and **1g**, affording isoindolo-β-carboline derivatives with structural diversity in generally high chemo-, (E/Z)-, and enantioselectivities.

As shown in Scheme 4, the product **3aa** was easily esterified by *p*-chlorobenzoyl chloride to generate compound **8**, which could form a single crystal with 98:2 er after recrystallization. The absolute configuration and the olefin geometry of compound **8** were unambiguously assigned to be (S) and (E) by single-crystal X-ray diffraction analysis.[15] The absolute configuration and the olefin geometry of compound **3aa** were thereby determined to be (S,E), since the esterification step could not affect the absolute configuration of the quaternary stereogenic center and the olefin geometry. In addition, because all products **3** possess similar structures and were synthesized in the presence of the same catalyst **5g**, the absolute configuration and the olefin geometry of these products were also tentatively considered to be (S,E) by analogy with compound **3aa**.

On the basis of the experimental results, possible transition states were proposed to explain the stereochemistry of the reaction (Scheme 5). As mentioned in Scheme 3, *N*-acyliminium ion **A** was initially generated from hydroxylactam **1** via a protonation/dehydration sequence in the presence of CPA. Then, as illustrated in Scheme 5, the *N*-acyliminium ion intermediate A and *o*-hydroxystyrene were simultaneously

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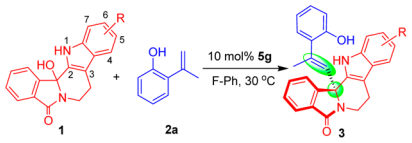
Table 3. Substrate Scope of Hydroxylactams[a]

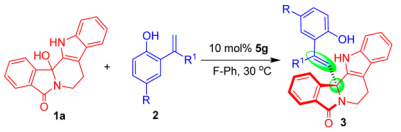


1 2a 3

entry	R (1)	3	yield (%)[b]	cr[c]	E/Z[d]	er[e]
1	H (**1a**)	**3aa**	81	>95:5	>95:5	90:10
2	4-Me (**1b**)	**3ba**	42	93:7	>95:5	93:7
3	4-Cl (**1c**)	**3ca**	72	93:7	>95:5	90:10
4	5-Me (**1d**)	**3da**	50	91:9	>95:5	89:11
5	5-MeO (**1e**)	**3ea**	57	>95:5	>95:5	97:3
6	5-Cl (**1f**)	**3fa**	75	90:10	>95:5	83:17
7	5-Br (**1g**)	**3ga**	83	93:7	>95:5	89:11
8	6-Me (**1h**)	**3ha**	51	95:5	>95:5	90:10
9	6-Cl (**1i**)	**3ia**	62	91:9	>95:5	91:9
10	6-Br (**1j**)	**3ja**	70	91:9	>95:5	89:11
11	7-Me (**1k**)	**3ka**	61	95:5	>95:5	90:10

[a]Unless indicated otherwise, the reaction was carried out on a 0.1 mmol scale catalyzed by 10 mol % of **5g** in fluorobenzene (1 mL) at 30 °C for 18 h, and the mole ratio of **1**:**2a** was 1:6. [b]Isolated total yields of the two chemoselective isomers. [c]The cr was determined by ^{1}H NMR. [d]The *E*/*Z* ratio of **3** was determined by ^{1}H NMR. [e]The er of **3** was determined by HPLC.

Table 4. Substrate Scope of *o*-Hydroxystyrenes[a]



1a 2 3

entry	R/R^1 (2)	3	yield (%)[b]	cr[c]	E/Z[d]	er[e]
1	H/Me (**2a**)	**3aa**	81	>95:5	>95:5	90:10
2	Me/Me (**2b**)	**3ab**	71	92:8	>95:5	88:12
3	MeO/Me (**2c**)	**3ac**	61	>95:5	>95:5	92:8
4	F/Me (**2d**)	**3ad**	42	84:16	>95:5	88:12
5[f]	H/Et (**2e**)	**3ae**	65	>95:5	>95:5	87:13
6	H/*n*-Pr (**2f**)	**3af**	46	93:7	>95:5	87:13
7[g]	Me/Me (**2b**)	**3cb**	67	89:11	>95:5	85:15
8[g]	MeO/Me (**2c**)	**3cc**	56	>95:5	>95:5	92:8
9[h]	Me/Me (**2b**)	**3gb**	70	93:7	>95:5	90:10
10[h]	MeO/Me (**2c**)	**3gc**	76	84:16	>95:5	86:14

[a]Unless indicated otherwise, the reaction was carried out on a 0.1 mmol scale catalyzed by 10 mol % of **5g** in fluorobenzene (1 mL) at 30 °C for 18 h, and the mole ratio of **1**:**2** was 1:6. [b]Isolated total yields of the two chemoselective isomers. [c]The cr was determined by ^{1}H NMR. [d]The *E*/*Z* ratio was determined by ^{1}H NMR. [e]The er was determined by HPLC. [f]The mole ratio of **1**:**2** was 1:10. [g]Compound **1c** was employed as a substrate instead of **1a**. [h]Compound **1g** was employed as a substrate instead of **1a**.

activated by the catalyst **5g** through the dual action of ion pair and hydrogen bond to undergo an enantioselective vinylogous addition, affording a transient intermediate **B** with fixed (*S*)-

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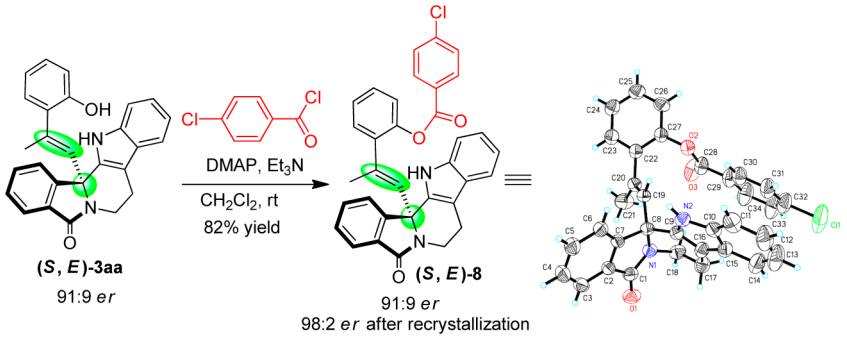
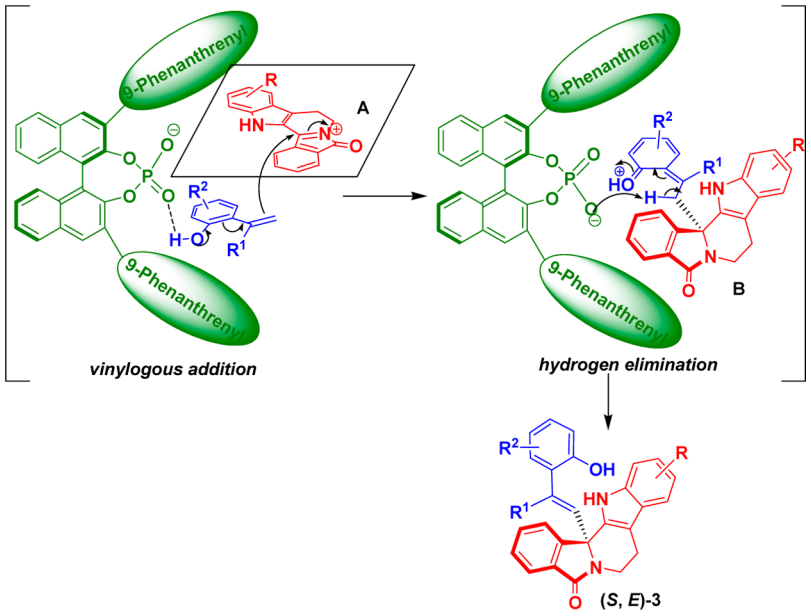
Scheme 4. Esterification of 3aa and X-ray Structure of Compound 8



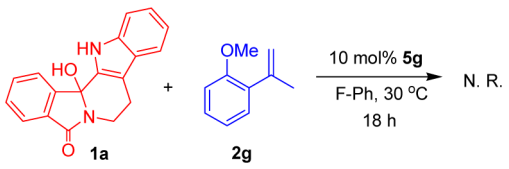
Scheme 5. Proposed Transition States of the Reaction



configuration. Subsequently, again under the promotion of the same catalyst, a regio- and stereoselective hydrogen elimination of the intermediate **B** occurred to give the experimentally observed chemoselective formal alkenylation product **3** with (*S*,*E*)-configuration.

In order to testify the crucial role of the hydroxyl group in *o*-hydroxystyrene, a control experiment was carried out using *o*-methoxystyrene **2g** as a substrate under the optimal reaction conditions (Scheme 6). As expected, no reaction occurred,

Scheme 6. Control Experiment Using *o*-Methoxystyrene 2g as a Substrate



which indicated that the hydroxyl group in *o*-hydroxystyrene was essentially important for producing a hydrogen-bond interaction with the catalyst. This hydrogen-bonding activation together with the ion pair interaction between the catalyst and *N*-acyliminium ion contributed to the success of the desired reaction.

CONCLUSIONS

In summary, we have established the first organocatalytic asymmetric formal alkenylation of multicyclic alcohols using non-metal-based alkenes instead of alkenyl metals as a source of an alkenyl group. In the presence of chiral phosphoric acid, this transformation directly assembles isoindolo-*β*-carboline-derived hydroxylactams with *o*-hydroxystyrenes via an asymmetric cascade vinylogous addition/hydrogen elimination reaction sequence, providing an easy access to functionalized chiral isoindolo-*β*-carbolines with one quaternary stereogenic center in high chemo-, (*E*/*Z*)-, and enantioselectivities (up to >95:5 cr, >95:5 *E*/*Z*, 97:3 er). This approach also represents the first catalytic asymmetric formal alkenylation of isoindolo-*β*-carboline-derived hydroxylactams, which will open a new window for the functionalization of isoindolo-*β*-carbolines and the synthesis of chiral isoindolo-*β*-carboline derivatives. In addition, the investigation on the activating mode revealed that the hydroxyl group in *o*-hydroxystyrene was essentially important for generating a hydrogen-bond interaction with the catalyst. The dual activation mode of hydrogen bond and ion pair between the catalyst and the substrates cooperatively facilitated the desired formal alkenylation reaction in a chemo- and stereoselective way.

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EXPERIMENTAL SECTION

General Information. ^{1}H and ^{13}C NMR spectra were measured at 400 and 100 MHz, respectively. The solvent used for NMR spectroscopy were $CDCl_3$, methanol-d_4, and acetone-d_6 using tetramethylsilane as the internal reference. HRMS spectra were recorded on a LTQ-Orbitrap mass spectrometer. 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 IC, AD-H and Kromasil 5-TBB 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.[9,16]

General Procedure for the Catalytic Asymmetric Formal Alkenylation of Hydroxylactams with *o*-Hydroxystyrenes. Fluorobenzene (0.5 mL) was added to the mixture of isoindolo-β-carboline-derived hydroxylactams **1** (0.1 mmol) and the catalyst **5g** (0.01 mmol). After being stirred at 30 °C for 30 min, *o*-hydroxystyrenes **2** (0.6 mmol) and fluorobenzene (0.5 mL) were added to the reaction mixture, which was stirred at 30 °C for 18 h. Then, the reaction mixture 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**.

(*S*,*E*)-13b-(2-(2-Hydroxyphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3aa). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield 81% (32.9 mg); >95:5 *E*/*Z*; >95:5 cr; pale yellow sticky oil; $[\alpha]^{20}_D$ = −19.0 (*c* 1.42, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.35 (s, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.54−7.48 (m, 1H), 7.47−7.42 (m, 1H), 7.39−7.33 (m, 1H), 7.28 (s, 1H), 7.13−7.02 (m, 4H), 6.89−6.77 (m, 3H), 5.92 (s, 1H), 4.82 (dd, *J* = 13.2, 6.0 Hz, 1H), 3.54 (td, *J* = 12.9, 4.9 Hz, 1H), 3.17−3.03 (m, 1H), 2.84 (dd, *J* = 15.5, 4.6 Hz, 1H), 1.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 152.3, 148.5, 141.4, 136.5, 133.8, 132.7, 131.8, 131.0, 128.8, 128.8, 128.7, 127.6, 126.5, 124.3, 122.5, 122.5, 120.2, 119.9, 118.8, 116.0, 111.3, 108.8, 65.6, 36.6, 21.7, 17.33; IR (KBr) 3271, 3057, 2924, 2852, 1671, 1468, 1447, 1397, 1273, 1197, 746, 713 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{22}N_2O_2\text{-}H)^-$ requires *m*/*z* 405.1597, found *m*/*z* 405.1598; enantiomeric ratio 90:10, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm) t_R = 14.02 min (minor), t_R = 16.28 min (major).

(*S*,*E*)-13b-(2-(2-Hydroxyphenyl)prop-1-en-1-yl)-9-methyl-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ba). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time =18 h; yield: 42% (17.8 mg); >95:5 *E*/*Z*; 93:7 cr; pale yellow sticky oil; $[\alpha]^{20}_D$ = +43.3 (*c* 0.10, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dt, *J* = 7.8, 0.9 Hz, 1H), 7.80 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.55 (td, *J* = 7.6, 1.2 Hz, 1H), 7.40 (td, *J* = 7.5, 1.0 Hz, 1H), 7.22−7.18 (m, 1H), 7.08−7.01 (m, 1H), 6.99−6.94 (m, 3H), 6.78−6.73 (m, 2H), 5.65 (d, *J* = 1.3 Hz, 1H), 4.71−4.64 (m, 1H), 3.49−3.39 (m, 1H), 3.36−3.22 (m, 2H), 2.86 (s, 3H), 1.48 (d, *J* = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, methanol-d_4/$CDCl_3$) δ 168.2, 151.9, 148.10, 141.2, 135.7, 132.3, 131.7, 131.6, 129.8, 129.7, 128.1, 127.6, 127.4, 126.1, 124.5, 122.7, 122.1, 121.1, 119.6, 118.8, 114.5, 108.1, 107.5, 64.6, 35.7, 23.3, 18.7, 15.7; IR (KBr) 3246, 3056, 2948, 1659, 1602, 1470, 1448, 1408, 1343, 1321, 1296, 1126, 1085, 1037, 753, 707 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{24}N_2O_2\text{-}H)^-$ requires *m*/*z* 419.1754, found *m*/*z* 419.1775; enantiomeric ratio 93:7, determined by HPLC (Daicel Chirapak AD-H, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm) t_R = 10.68 min (minor), t_R = 40.66 min (major).

(*S*,*E*)-9-Chloro-13b-(2-(2-hydroxyphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ca). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield: 72% (31.9 mg); >95:5 *E*/*Z*; 93:7 cr; white solid, mp 227.2−228.9 °C; $[\alpha]^{20}_D$ = −80.1 (*c* 0.55, acetone); ^{1}H NMR (400 MHz, Methanol-d_4/$CDCl_3$) δ 7.95 (d, *J* = 7.7 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.56−7.46 (m, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 1H), 7.00−6.95 (m, 1H), 6.95−6.88 (m, 2H), 6.74−6.62 (m, 3H), 5.61 (s, 1H), 4.59 (dd, *J* = 13.3, 5.8 Hz, 1H), 3.50−3.40 (m, 1H), 3.29−3.17 (m, 1H), 3.16−3.05 (m, 1H), 1.43 (d, *J* = 1.6 Hz, 3H); ^{13}C NMR (100 MHz, methanol-d_4/$CDCl_3$) δ 168.9, 152.4, 148.6, 141.9, 137.7, 134.6, 132.5, 132.4, 130.9, 129.0, 128.7, 128.4, 127.1, 126.2, 123.9, 123.9, 122.87, 122.5, 120.0, 119.9, 115.5, 109.9, 108.4, 65.2, 36.5, 23.6, 16.7; IR (KBr) 3254, 3056, 2931, 2361, 1669, 1470, 1449, 1409, 1296, 1194, 1121, 1037, 744 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{21}ClN_2O_2\text{-}H)^-$ requires *m*/*z* 439.1208, found *m*/*z* 439.1229; enantiomeric ratio: 90:10, determined by HPLC (Kromasil 5-TBB, hexane/2-propanol = 90/10, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 53.00 min (minor), t_R = 47.72 min (major).

(*S*,*E*)-13b-(2-(2-Hydroxyphenyl)prop-1-en-1-yl)-10-methyl-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3da). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield: 50% (21.2 mg); >95:5 *E*/*Z*; 91:9 cr; white solid, mp 235.4−237.1 °C; $[\alpha]^{20}_D$ = −16.8 (*c* 0.10, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.89 (d, *J* = 7.5 Hz, 1H), 7.58−7.54 (m, 1H), 7.45−7.39 (m, 1H), 7.25−7.22 (m, 1H), 7.15−7.07 (m, 2H), 7.05−7.01 (m, 1H), 6.96−6.91 (m, 1H), 6.86−6.80 (m, 2H), 6.25 (s, 1H), 5.90 (d, *J* = 1.4 Hz, 1H), 4.85−4.76 (m, 1H), 3.56−3.46 (m, 1H), 3.12−3.01 (m, 1H), 2.88−2.79 (m, 1H), 2.40 (s, 3H), 1.60 (d, *J* = 1.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 152.0, 148.4, 140.9, 134.8, 133.8, 132.6, 131.7, 131.2, 129.2, 128.8, 128.7, 128.7, 128.0, 126.8, 124.4, 124.1, 122.2, 120.3, 118.5, 115.9, 110.9, 108.6, 65.3, 36.5, 21.6, 21.4, 17.3; IR (KBr) 3278, 3053, 2924, 2853, 2360, 1672, 1602, 1469, 1404, 1299, 1236, 1038, 797, 752 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{24}N_2O_2\text{-}H)^-$ requires *m*/*z* 419.1754, found *m*/*z* 419.1765; enantiomeric ratio: 89:11, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 90/10, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 29.12 min (minor), t_R = 34.95 min (major).

(*S*,*E*)-13b-(2-(2-Hydroxyphenyl)prop-1-en-1-yl)-10-methoxy-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ea). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield 57% (24.9 mg); >95:5 *E*/*Z*; >95:5 cr; pale yellow sticky oil; $[\alpha]^{20}_D$ = +5.3 (*c* 0.73, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 7.95 (d, *J* = 7.7 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.54 (td, *J* = 7.6, 1.0 Hz, 1H), 7.42−7.36 (m, 1H), 7.17−7.13 (m, 1H), 7.12−7.06 (m, 1H), 7.05−7.01 (m, 1H), 6.89 (d, *J* = 2.4 Hz, 1H), 6.85−6.79 (m, 2H), 6.79−6.74 (m, 1H), 6.40 (s, 1H), 5.90 (d, *J* = 1.4 Hz, 1H), 4.81 (dd, *J* = 13.3, 6.1 Hz, 1H), 3.81 (s, 3H), 3.57−3.48 (m, 1H), 3.11−3.00 (m, 1H), 2.85−2.76 (m, 1H), 1.59 (d, *J* = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 154.2, 152.1, 134.6, 132.6, 131.7, 131.5, 131.1, 128.8, 128.7, 127.8, 122.3, 120.3, 115.9, 112.6, 112.0, 108.7, 100.7, 65.4, 55.8, 36.5, 21.7, 17.3; IR (KBr) 3201, 3058, 2964, 2930, 1666, 1487, 1469, 1449, 1409, 1214, 1119, 1070, 1040, 749 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{24}N_2O_3\text{-}H)^-$ requires *m*/*z* 435.1703, found *m*/*z* 435.1724; enantiomeric ratio: 97:3, determined by HPLC (Daicel Chirapak AD-H, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm): t_R = 13.48 min (minor), t_R = 16.28 min (major).

(*S*,*E*)-10-Chloro-13b-(2-(2-hydroxyphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3fa). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield: 75% (32.9 mg); >95:5 *E*/*Z*; 90:10 cr; pale yellow sticky oil; $[\alpha]^{20}_D$ = −26.7 (*c* 0.56, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 8.03 (d, *J* = 7.7 Hz, 1H), 7.89−7.83 (m, 1H), 7.55−7.47 (m, 1H), 7.40−7.34 (m, 2H), 7.15−7.07 (m, 2H), 7.06−6.99 (m, 2H), 6.87−6.79 (m, 2H), 5.94−5.85 (m, 1H), 4.83−4.73 (m, 1H), 3.51 (td, *J* = 13.3, 5.0 Hz, 1H), 3.07−2.94 (m, 1H), 2.80−2.71 (m, 1H), 1.58 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 148.1, 141.4, 135.3, 134.8, 132.8, 131.6, 131.0, 129.0, 128.8, 128.7, 127.6, 127.4, 125.5, 124.4, 122.8, 122.3, 120.4, 118.3, 116.0, 112.2, 108.6, 65.3, 36.4, 21.5, 17.3; IR (KBr) 3270, 3055, 2929, 2850, 1672, 1602, 1469, 1446,

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1291, 1264, 1233, 1038, 798, 755, 713 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{21}ClN_2O_2\text{-}H)^-$ requires m/z 439.1208, found m/z 439.1208; enantiomeric ratio: 83:17, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 26.88 min (minor), t_R = 42.89 min (major).

(*S*,*E*)-10-Bromo-13b-(2-(2-hydroxyphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ga). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield: 83% (40.2 mg); >95:5 *E*/*Z*; 93:7 cr; off-white sticky oil; $[\alpha]^{20}_D$ = −26.6 (*c* 0.73, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 5.90−5.84 (m, 1H), 8.02 (d, *J* = 7.7 Hz, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.56−7.48 (m, 2H), 7.40−7.32 (m, 1H), 7.15−7.11 (m, 1H), 7.11−7.06 (m, 2H), 7.06−7.01 (m, 1H), 6.88−6.84 (m, 1H), 6.82−6.79 (m, 1H), 5.88 (s, 1H), 4.78 (dd, *J* = 13.2, 6.2 Hz, 1H), 3.60−3.41 (m, 1H), 3.09−2.93 (m, 1H), 2.75 (dd, *J* = 15.4, 4.7 Hz, 1H), 1.58 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 152.2, 148.3, 141.7, 135.1, 135.1, 132.9, 131.7, 130.8, 129.0, 128.8, 128.8, 128.2, 127.2, 125.3, 124.3, 122.6, 121.4, 120.3, 116.0, 113.0, 112.8, 108.4, 65.5, 36.5, 21.6, 17.2; IR (KBr) 3271, 3056, 2925, 2851, 1671, 1602, 1469, 1446, 1397, 1289, 1263, 1235, 1109, 1045, 994, 796, 756 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{21}BrN_2O_2\text{-}H)^-$ requires m/z 483.0703, found m/z 483.0733; enantiomeric ratio: 89:11, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 13.31 min (minor), t_R = 21.72 min (major).

(*S*,*E*)-13b-(2-(2-Hydroxyphenyl)prop-1-en-1-yl)-11-methyl-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ha). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield 51% (21.5 mg); >95:5 *E*/*Z*; 95:5 cr; brownish red solid, mp 237.0−238.9 °C; $[\alpha]^{20}_D$ = −40.3 (*c* 0.22, acetone); ^{1}H NMR (400 MHz, Acetone-d_6) δ 10.43 (s, 1H), 8.31 (s, 1H), 8.22 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.70 (td, *J* = 7.6, 1.2 Hz, 1H), 7.52 (td, *J* = 7.5, 0.9 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.15−7.12 (m, 1H), 7.10−7.04 (m, 2H), 6.86−6.80 (m, 2H), 6.75 (td, *J* = 7.4, 1.1 Hz, 1H), 5.93 (d, *J* = 1.4 Hz, 1H), 4.72−4.64 (m, 1H), 3.56−3.47 (m, 1H), 2.94−2.88 (m, 1H), 2.87−2.81 (m, 1H), 2.35 (s, 3H), 1.61 (d, *J* = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ 167.7, 153.9, 148.9, 141.4, 137.3, 134.3, 132.2, 131.4, 131.3, 129.3, 128.4, 128.4, 127.1, 124.5, 123.2, 123.2, 120.9, 119.4, 118.1, 115.5, 111.1, 107.7, 65.2, 36.0, 21.3, 20.9, 16.0; IR (KBr) 3082, 2920, 2850, 1665, 1600, 1470, 1449, 1413, 1303, 1228, 1153, 1087, 1035, 918, 813, 750, 700 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{24}N_2O_2\text{-}H)^-$ requires m/z 419.1754, found m/z 419.1764; enantiomeric ratio: 90:10, determined by HPLC (Daicel Chirapak AD-H, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 10.23 min (minor), t_R = 31.40 min (major).

(*S*,*E*)-11-Chloro-13b-(2-(2-hydroxyphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ia). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield 62% (27.5 mg); >95:5 *E*/*Z*; 91:9 cr; pale yellow oil; $[\alpha]^{20}_D$ = −27.2 (*c* 0.71, acetone); ^{1}H NMR (400 MHz, acetone-d_6) δ 10.80 (s, 1H), 8.20 (d, *J* = 7.7 Hz, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.72 (td, *J* = 7.6, 1.1 Hz, 1H), 7.54 (td, *J* = 7.5, 0.8 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.39−7.34 (m, 1H), 7.10−7.00 (m, 3H), 6.82 (d, *J* = 7.7 Hz, 1H), 6.75 (td, *J* = 7.5, 1.1 Hz, 1H), 5.92 (d, *J* = 1.4 Hz, 1H), 4.73−4.64 (m, 1H), 3.57−3.46 (m, 1H), 2.95−2.83 (m, 2H), 1.60 (d, *J* = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ 167.7, 153.9, 148.5, 137.2, 136.1, 132.4 131.4, 129.3, 128.6, 128.4, 127.2, 126.7, 123.3, 123.2, 119.7, 119.4, 115.5, 111.0, 65.0, 35.9, 21.1, 16.1; IR (KBr) 3272, 3058, 2931, 2849, 1672, 1604, 1468, 1449, 1402, 1282, 1227, 1062, 915, 802, 751 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{21}ClN_2O_2\text{-}H)^-$ requires m/z 439.1208, found m/z 439.1203; enantiomeric ratio: 91:9, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 23.73 min (minor), t_R = 25.60 min (major).

(*S*,*E*)-11-Bromo-13b-(2-(2-hydroxyphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ja). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield: 70% (34.0 mg); >95:5 *E*/*Z*; 91:9 cr; off-white sticky oil; $[\alpha]^{20}_D$ = −34.0 (*c* 0.71, acetone); ^{1}H NMR (400 MHz, methanol-d_4/$CDCl_3$) δ 7.98 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.49−7.27 (m, 3H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.11−6.86 (m, 3H), 6.71−6.60 (m, 1H), 5.64−5.57 (m, 1H), 4.62 (dd, *J* = 13.2, 6.0 Hz, 1H), 3.56−3.31 (m, 1H), 3.02−2.85 (m, 1H), 2.77 (dd, *J* = 15.4, 4.3 Hz, 1H), 1.41 (d, *J* = 1.6 Hz, 3H); ^{13}C NMR (100 MHz, methanol-d_4/$CDCl_3$) δ 168.3, 152.1, 147.8, 141.6, 136.6, 133.7, 131.7, 131.6, 129.8, 128.1, 127.7, 127.5, 125.6, 124.3, 122.7, 122.1, 121.5, 118.8, 118.8, 114.5, 114.4, 113.3, 107.2, 64.7, 35.4, 20.7, 15.5; IR (KBr) 3298, 1651, 1672, 1469, 1447, 1402, 1343, 1289, 1150, 798, 757, 714 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{21}BrN_2O_2\text{-}H)^-$ requires m/z 483.0703, found m/z 483.0703; enantiomeric ratio: 89:11, determined by HPLC (Kromasil 5-TBB, hexane/2-propanol =90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 49.53 min (minor), t_R = 43.42 min (major).

(*S*,*E*)-13b-(2-(2-Hydroxyphenyl)prop-1-en-1-yl)-12-methyl-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ka). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield: 61% (25.5 mg); >95:5 *E*/*Z*; 95:5 cr; pale yellow sticky oil; $[\alpha]^{20}_D$ = −29.5 (*c* 0.45, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.06 (d, *J* = 7.7 Hz, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.61 (td, *J* = 7.6, 1.1 Hz, 1H), 7.47−7.41 (m, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.11−7.06 (m, 1H), 7.05−7.01 (m, 2H), 6.97−6.92 (m, 1H), 6.83−6.77 (m, 2H), 5.99 (d, *J* = 1.4 Hz, 1H), 4.80 (dd, *J* = 13.3, 6.2 Hz, 1H), 3.54−3.47 (m, 1H), 3.14−3.05 (m, 1H), 2.87 (dd, *J* = 15.6, 4.6 Hz, 1H), 2.43 (s, 3H), 1.61 (d, *J* = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, methanol-d_4/$CDCl_3$) δ 169.0, 152.4, 141.7, 132.5, 129.0, 128.5, 128.3, 127.3, 123.8, 123.0, 122.9, 122.8, 119.9, 119.7, 116.1, 115.4, 65.6, 36.5, 22.6, 21.9, 16.6; IR (KBr) 3273, 3052, 2924, 2853, 1669, 1602, 1448, 1469, 1402, 1280, 1087, 1037, 917, 837, 778, 749 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{24}N_2O_2\text{-}H)^-$ requires m/z 419.1754, found m/z 419.1777; enantiomeric ratio: 90:10, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 32.72 min (minor), t_R = 40.54 min (major).

(*S*,*E*)-13b-(2-(2-Hydroxy-5-methylphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ab). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield: 71% (30.1 mg); >95:5 *E*/*Z*; 92:8 cr; pale yellow sticky oil; $[\alpha]^{20}_D$ = −24.9 (*c* 0.47, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 7.99 (d, *J* = 7.6 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.55−7.50 (m, 1H), 7.47−7.44 (m, 1H), 7.41−7.36 (m, 1H), 7.26−7.23 (m, 1H), 7.12−7.07 (m, 2H), 6.92−6.89 (m, 1H), 6.87−6.85 (m, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 5.92 (d, *J* = 1.6 Hz, 1H), 4.83 (dd, *J* = 13.3, 6.2 Hz, 1H), 3.58−3.48 (m, 1H), 3.14−3.03 (m, 1H), 2.91−2.80 (m, 1H), 2.23 (s, 3H), 1.60 (d, *J* = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 149.8, 148.5, 141.3, 136.5, 133.9, 133.9, 132.6, 131.5, 131.1, 129.5, 129.2, 129.1, 128.8, 127.6, 126.5, 124.3, 122.5, 122.4, 119.8, 118.8, 115.8, 111.3, 108.8, 65.4, 36.6, 21.7, 20.4, 17.3; IR (KBr) 3271, 3057, 2924, 2852, 1671, 1468, 1447, 1397, 1273, 1197, 746, 713 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{24}N_2O_2\text{-}H)^-$ requires m/z 419.1754, found m/z 419.1784; enantiomeric ratio 88:12, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 14.94 min (minor), t_R = 16.69 min (major).

(*S*,*E*)-13b-(2-(2-Hydroxy-5-methoxyphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ac). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield 61% (26.7 mg); >95:5 *E*/*Z*; >95:5 cr; pale yellow sticky oil; $[\alpha]^{20}_D$ = −50.5 (*c* 0.48, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 7.97 (d, *J* = 7.6 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.58−7.49 (m, 1H), 7.48−7.35 (m, 2H), 7.30−7.25 (m, 1H), 7.15−7.03 (m, 2H), 6.77 (d, *J* = 8.7 Hz, 1H), 6.71−6.63 (m, 1H), 6.63−6.58 (m, 1H), 5.94 (d, *J* = 1.5 Hz, 1H), 4.91−4.69 (m, 1H), 3.72 (s, 3H), 3.57−3.45 (m, 1H), 3.14−3.04 (m, 1H), 2.93−2.80 (m, 1H), 1.59 (d, *J* = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 152.1, 147.3, 144.9, 139.9, 135.4, 132.7, 131.6, 131.4, 130.0, 127.8, 126.9, 125.5, 123.3, 121.5, 121.3,

118.8, 117.7, 115.6, 113.1, 112.7, 110.2, 107.9, 64.3, 54.7, 35.5, 20.6, 16.21; IR (KBr) 3272, 2963, 2929, 2851, 1670, 1493, 1467, 1423, 1345, 1262, 1208, 1100, 1038, 804 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{24}N_2O_3\text{-}H)^-$ requires m/z 435.1703, found m/z 435.1708; enantiomeric ratio: 92:8, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 19.04 min (minor), t_R = 21.96 min (major).

(*S,E*)-13b-(2-(5-Fluoro-2-hydroxyphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ad). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield 42% (17.6 mg); >95:5 *E/Z*; 84:16 cr; yellow sticky oil; $[\alpha]^{20}_D$ = −1.2 (*c* 0.41, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (s, 1H), 7.97 (d, J = 7.6 Hz, 1H), 7.90−7.87 (m, 1H), 7.59−7.56 (m, 1H), 7.47−7.42 (m, 2H), 7.29−7.27 (m, 1H), 7.14−7.07 (m, 2H), 6.80−6.73 (m, 3H), 6.34 (s, 1H), 5.96−5.94 (m, 1H), 4.81 (dd, J = 13.3, 6.2 Hz, 1H), 3.56−3.47 (m, 1H), 3.09 (d, J = 15.7, 11.7, 6.4 Hz, 1H), 2.87 (dd, J = 15.5, 4.7 Hz, 1H), 1.58 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 148.2, 136.5, 133.8, 133.7, 132.6, 131.1, 128.89, 128.5, 126.5, 124.3, 123.1, 122.9, 122.6, 122.3, 119.9, 118.8, 111.3, 109.0, 65.2, 36.5, 21.6, 17.0; IR (KBr) 3698, 3686, 3666, 3645, 3626, 2926, 2359, 1712, 1667, 1443, 1263, 1185 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{21}FN_2O_2\text{-}H)^-$ requires m/z 423.1503, found m/z 423.1531; enantiomeric ratio: 88:12, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 95/5, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 8.49 min (minor), t_R = 9.44 min (major).

(*S,E*)-13b-(2-(2-Hydroxyphenyl)but-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3ae). Flash column chromatography eluent, dichloromethane/ethyl acetate =15/1; reaction time = 18 h; yield 65% (27.4 mg); >95:5 *E/Z*; >95:5 cr; pale yellow sticky oil; $[\alpha]^{20}_D$ = +8.1 (*c* 0.30, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.91 (d, J = 7.5 Hz, 1H), 7.60−7.53 (m, 1H), 7.48−7.36 (m, 2H), 7.29−7.26 (m, 1H), 7.16−7.05 (m, 3H), 7.01 (dd, J = 7.6, 1.6 Hz, 1H), 6.89−6.80 (m, 2H), 6.17 (s, 1H), 5.92 (s, 1H), 4.85 (dd, J = 13.3, 6.1 Hz, 1H), 3.62−3.48 (m, 1H), 3.19−3.03 (m, 1H), 2.86 (dd, J = 15.6, 4.7 Hz, 1H), 2.10−1.91 (m, 2H), 0.60 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 152.5, 148.9, 147.1, 136.5, 134.1, 132.7, 130.9, 129.5, 129.1, 128.9, 128.7, 127.5, 126.5, 124.5, 122.6, 122.3, 120.1, 119.9, 118.8, 115.7, 111.2, 108.8, 65.3, 36.7, 23.8, 21.7, 12.2; IR (KBr) 3646, 3290, 3057, 2931, 1673, 1469, 1449, 1374,1397, 1346, 1276, 1238, 1038, 886, 752 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{24}N_2O_2\text{-}H)^-$ requires m/z 419.1754, found m/z 419.1783; enantiomeric ratio: 87:13, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 11.51 min (minor), t_R = 13.35 min (major).

(*S,E*)-13b-(2-(2-Hydroxyphenyl)pent-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3af). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield 46% (20.1 mg); >95:5 *E/Z*; 93:7 cr; pale yellow sticky oil; $[\alpha]^{20}_D$ = −44.5 (*c* 0.27, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.00 (d, J = 7.6 Hz, 1H), 7.93−7.88 (m, 1H), 7.61−7.54 (m, 1H), 7.48−7.41 (m, 2H), 7.30−7.26 (m, 1H), 7.15−7.05 (m, 3H), 7.03−6.98 (m, 1H), 6.89−6.79 (m, 2H), 5.95 (s, 1H), 4.89−4.77 (m, 1H), 3.60−3.49 (m, 1H), 3.16−3.04 (m, 1H), 2.92−2.80 (m, 1H), 1.99−1.92 (m, 2H), 1.15−1.05 (m, 1H), 0.98−0.86 (m, 1H), 0.45 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 152.5, 146.0, 136.5, 134.1, 132.6, 131.1, 129.7, 128.9, 128.9, 128.6, 126.5, 124.4, 122.6, 120.1, 119.9, 118.8, 115.7, 111.2, 65.2, 36.6, 32.6, 21.7, 21.2, 13.9; IR (KBr) 3280, 2956, 2930, 2869, 1672, 1602, 1448, 1400, 1297, 1235, 1037, 745, 712 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{26}N_2O_2\text{-}H)^-$ requires m/z 433.1910, found m/z 433.1923; enantiomeric ratio: 87:13, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 18.21 min (minor), t_R = 22.34 min (major).

(*S,E*)-9-Chloro-13b-(2-(2-hydroxy-5-methylphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]-indol-5-one (3cb). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield: 67% (30.3 mg); >95:5 *E/Z*; 89:11 cr; off-white sticky oil; $[\alpha]^{20}_D$ = −28.3 (*c* 0.49, acetone); ^{1}H NMR (400 MHz, acetone-d_6) δ 10.94 (s, 1H), 8.23 (d, J = 7.7 Hz, 1H), 7.79 (d, J = 7.5 Hz, 1H), 7.70 (td, J = 7.6, 1.2 Hz, 1H), 7.54 (td, J = 7.5, 0.8 Hz, 1H), 7.31 (dd, J = 7.9, 1.1 Hz, 1H), 7.02 (t, J = 7.8 Hz, 1H), 7.01−6.93 (m, 1H), 6.94−6.83 (m, 2H), 6.72 (d, J = 8.1 Hz, 1H), 5.92 (d, J = 1.4 Hz, 1H), 4.70−4.64 (m, 1H), 3.57−3.47 (m, 1H), 3.35−3.29 (m, 1H), 3.22−3.13 (m, 1H), 2.16 (s, 3H), 1.60 (d, J = 1.4 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ 167.6, 151.6, 148.5, 142.1, 138.1, 136.4, 132.4, 132.1, 131.4, 129.7, 128.8, 128.6, 128.2, 126.5, 125.6, 123.8, 123.3, 123.3, 122.5, 119.7, 115.5, 110.3, 107.7, 65.0, 36.0, 23.3, 19.5, 16.1; IR (KBr) 3205, 3054, 2980, 2940, 1649, 1495, 1470, 1409, 1342, 1296, 1194, 1121, 813, 774, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{23}ClN_2O_2\text{-}H)^-$ requires m/z 453.1364, found m/z 453.1366; enantiomeric ratio: 85:15, determined by HPLC (Daicel Chirapak AD-H, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 9.41 min (minor), t_R = 20.52 min (major).

(*S,E*)-9-Chloro-13b-(2-(2-hydroxy-5-methoxyphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]-indol-5-one (3cc). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield 56% (26.6 mg); >95:5 *E/Z*; >95:5 cr; off-white sticky oil; $[\alpha]^{20}_D$ = −62.6 (*c* 0.37, acetone); ^{1}H NMR (400 MHz, acetone-d_6) δ 11.00 (s, 1H), 8.26 (d, J = 7.7 Hz, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.70 (td, J = 7.6, 1.1 Hz, 1H), 7.53 (td, J = 7.5, 0.8 Hz, 1H), 7.33−7.29 (m, 1H), 7.04−6.99 (m, 1H), 6.99−6.93 (m, 1H), 6.78−6.74 (m, 1H), 6.70−6.65 (m, 2H), 5.96 (d, J = 1.4 Hz, 1H), 4.67 (dd, J = 13.4, 5.5 Hz, 1H), 3.67 (s, 3H), 3.57−3.49 (m, 1H), 3.31 (dd, J = 16.0, 4.2 Hz, 1H), 3.23−3.15 (m, 1H), 1.61 (d, J = 1.5 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ 167.7, 152.9, 148.5, 147.7, 141.8, 138.1, 136.3, 133.0, 132.4, 131.3, 128.6, 126.8, 125.6, 123.7, 123.4, 122.5, 119.7, 116.2, 114.9, 113.1, 110.3, 107.7, 65.0, 55.0, 36.0, 23.3, 16.1; IR (KBr) 3210, 2939, 1648, 1495, 1416, 1197, 1041, 775, 741, 700 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{23}ClN_2O_3\text{-}H)^-$ requires m/z 469.1313, found m/z 469.1325; enantiomeric ratio: 92:8, determined by HPLC (Daicel Chirapak AD-H, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 12.45 min (minor), t_R = 24.49 min (major).

(*S,E*)-10-Bromo-13b-(2-(2-hydroxy-5-methylphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]-indol-5-one (3gb). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield: 70% (35.0 mg); >95:5 *E/Z*; 93:7 cr; off-white sticky oil; $[\alpha]^{20}_D$ = −20.2 (*c* 0.59, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 8.02 (d, J = 7.7 Hz, 1H), 7.87 (d, J = 7.6 Hz, 1H), 7.57−7.48 (m, 2H), 7.41−7.33 (m, 1H), 7.17−7.11 (m, 1H), 7.10−7.06 (m, 1H), 6.90 (dd, J = 8.2, 1.7 Hz, 1H), 6.87−6.83 (m, 1H), 6.75 (dd, J = 8.1, 2.9 Hz, 1H), 6.47 (s, 1H), 5.87 (d, J = 1.4 Hz, 1H), 4.85−4.72 (m, 1H), 3.59−3.45 (m, 1H), 3.09−2.94 (m, 1H), 2.77 (dd, J = 15.5, 4.7 Hz, 1H), 2.22 (s, 3H), 1.57 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 149.8, 148.3, 141.8, 135.1, 132.8, 131.5, 130.9, 129.5, 129.3, 129.1, 128.2, 127.2, 125.3, 124.3, 122.5, 121.4, 115.9, 113.0, 112.7, 108.5, 65.4, 36.5, 21.6, 20.4, 17.3; IR (KBr) 3435, 3282, 2922, 1672, 1469, 1441, 1292, 1235, 1131, 813, 796, 745 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{23}BrN_2O_2\text{−}H)^-$ requires m/z 497.0859, found m/z 497.0859; enantiomeric ratio: 90:10, determined by HPLC (Daicel Chirapak AD-H, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 14.30 min (minor), t_R = 16.20 min (major).

(*S,E*)-10-Bromo-13b-(2-(2-hydroxy-5-methoxyphenyl)prop-1-en-1-yl)-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]indolizino[8,7-*b*]indol-5-one (3gc). Flash column chromatography eluent, dichloromethane/ethyl acetate = 15/1; reaction time = 18 h; yield: 76% (38.9 mg); >95:5 *E/Z*; 84:16 cr; off-white sticky oil; $[\alpha]^{20}_D$ = −20.0 (*c* 0.60, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 8.00 (d, J = 7.7 Hz, 1H), 7.87 (d, J = 7.6 Hz, 1H), 7.57−7.50 (m, 2H), 7.39 (t, J = 7.5 Hz, 1H), 7.14 (dd, J = 8.6, 1.8 Hz, 1H), 7.10−7.05 (m, 1H), 6.77 (d, J = 8.7 Hz, 1H), 6.66 (dd, J = 8.8, 3.0 Hz, 1H), 6.61 (d, J = 3.0 Hz, 1H), 6.20 (s, 1H), 5.89 (d, J = 1.4 Hz, 1H), 4.78 (dd, J = 13.3, 6.3 Hz, 1H), 3.72 (s, 3H), 3.54−3.43 (m, 1H), 3.06−2.94 (m, 1H), 2.76 (dd, J = 15.5, 4.7 Hz, 1H), 1.57 (d, J = 1.2

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Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 153.2, 148.2, 146.0, 141.5, 135.1, 135.0, 132.8, 132.5, 129.0, 128.2, 127.6, 125.4, 124.4, 122.5, 121.4, 116.7, 114.4, 113.7, 113.0, 112.7, 108.5, 65.3, 55.8, 36.5, 21.6, 17.1; IR (KBr) 3325, 2938, 1662, 1504, 1469, 1425, 1289, 1208, 1045, 806, 792, 738, 768 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{23}BrN_2O_3-H)^-$ requires m/z 513.0808, found m/z 513.0805; enantiomeric ratio: 86:14, determined by HPLC (Daicel Chirapak IC, hexane/2-propanol = 85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm): t_R = 18.53 min (minor), t_R = 30.59 min (major).

Procedure for the Synthesis of Compound 8. A newly distilled dichloromethane (8 mL) was added to the mixture of compound **3aa** (0.2 mmol) and DMAP (0.04 mmol) in a dried reaction bottle. After Et_3N (1.2 mmol) was added, the reaction mixture was stirred at room temperature for 15 min. Then, *p*-chlorobenzoyl chloride (0.8 mmol) and distilled dichloromethane (2 mL) were added to the reaction mixture, which was stirred at room temperature for 2 h. After the completion of the reaction as indicated by TLC, 1 M HCl was added to the reaction mixture, which was further extracted by dichloromethane and dried by anhydrous Na_2SO_4. The resultant organic layer was concentrated under the reduced pressure to give the residue, which was purified through flash column chromatography on silica gel to afford pure product **8**.

(*S*,*E*)-2-(1-(5-Oxo-7,8,13,13b-tetrahydro-5*H*-benzo[1,2]-indolizino[8,7-*b*]indol-13b-yl)prop-1-en-2-yl)phenyl 4-Chlorobenzoate (8). Flash column chromatography eluent, petroleum ether/ethyl acetate = 4/1; reaction time = 2 h; yield 82% (89.2 mg); colorless solid, mp 261.0−261.6 °C; $[\alpha]^{20}_D$ = −29.0 (*c* 0.67, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.86 (d, J = 8.5 Hz, 2H), 7.83−7.77 (m, 1H), 7.53 (dd, J = 5.6, 2.3 Hz, 1H), 7.39−7.33 (m, 3H), 7.31−7.27 (m, 3H), 7.24 (s, 1H), 7.22−7.17 (m, 2H), 7.17−7.13 (m, 1H), 7.10 (t, J = 7.9 Hz, 2H), 6.08−6.01 (s, 1H), 4.56 (dd, J = 13.2, 6.2 Hz, 1H), 3.14 (td, J = 13.0, 12.5, 4.9 Hz, 1H), 2.96−2.84 (m, 1H), 2.45 (dd, J = 15.6, 4.6 Hz, 1H), 1.62−1.54 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 164.2, 147.5, 147.1, 140.3, 138.4, 138.0, 136.3, 134.0, 132.2, 131.1, 129.1, 129.0, 128.6, 128.5, 128.0, 127.4, 126.5, 126.4, 124.3, 123.1, 122.6, 122.6, 121.6, 120.0, 118.9, 111.0, 109.0, 64.9, 36.0, 21.2, 17.2; IR (KBr) 3522, 3443, 3323, 3209, 2963, 2852, 1668, 1593, 1488, 1262, 1091, 1014, 750 cm^{-1}; ESI FTMS exact mass calcd for $(C_{34}H_{25}ClN_2O_3-H)^-$ requires m/z 543.1476, found m/z 543.1503; enantiomeric ratio: 91:9, 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 = 5.53 min (minor), t_R = 10.38 min (major).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Characterization data (including ^{1}H, ^{13}C NMR and HPLC spectra) for all products **3** and **8**; crystal data of compound **8** (CIF). 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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