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From allylic alcohols to chiral tertiary homoallylic alcohol: palladium-catalyzed asymmetric allylation of isatins

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ABSTRACT

A palladium-catalyzed asymmetric allylation of isatins with allylic alcohols as an allyl donor was developed by using chiral spiro phosphoramidite ligands. A variety of chiral tertiary homoallylic alcohols 3-allyl-3-hydroxy-2-oxindoles were prepared directly from allylic alcohols in one step with excellent yields and moderate enantioselectivities. This represents the first catalytic asymmetric allylation of ketones with allylic alcohol as the allylating agent.

1. Introduction

Transition metal-catalyzed allylation of carbonyl compounds, providing versatile and useful homoallylic alcohols, plays an important role in modern organic synthesis. Over the past decades, many efficient chiral catalysts have been developed for asymmetric allylation of aldehydes with high regioselectivity as well as enantioselectivity.[1] In contrast, the asymmetric allylation of ketones still remains a challenge, due to low reactivity of ketone towards nucleophilic addition of allylating reagents. Only a few transition metal-catalyzed allylations of ketones with allyl metal reagents such as stannanes,[2] boranes,[3] and silanes[4] as nucleophilic allyl sources have afforded high enantioselectivities. However, the allyl metals are air and moisture sensitive and require a multi-step preparation, limiting their wide application in organic synthesis. Thus, the search for more stable and easily available allylating agents will advance the usefulness of this important transformation. Recently, Sigman et al.[5] achieved the chromium-catalyzed asymmetric allylation of aryl ketones with an allylic bromide as allyl donor. This pioneering work has triggered the process of finding better allyl donors instead of allyl metals. In view of the availability and stability, the allylic alcohol is an ideal allylating agent. The direct use of allylic alcohols can avoid the transformation of allylic alcohols to their derivatives bearing a wasteful leaving group, and enhances the synthetic application of the allylation reaction of ketones. However in most cases, the hydroxy group of the allylic alcohol is too unreactive to undergo heterolytic C–O bond cleavage. By using activating reagents such as indium salts,[6] diethyl zinc,[7] and stannous chloride,[8] the palladium-, nickel-, and iridium-catalyzed allylations of ketones with allylic alcohols have been realized. Herein we report the enantioselective palladium-catalyzed allylation of isatin and its derivatives with allylic alcohols in the presence of triethylborane, which is the first example of the asymmetric allylation of ketones with allylic alcohols.[9]

2. Results and discussion

Chiral 3-allyl-3-hydroxy-2-oxindoles **3** are versatile intermediates for the preparation of many natural products and bioactive compounds or potential pharmaceuticals (Fig. 1).[10] Asymmetric allylation of 2,3-indolinediones **1** (isatins) provides an efficient route to generate useful 3-allyl-3-hydroxy-2-oxindole products. By utilizing a chiral titanium complex as a Lewis acid catalyst, Takayama et al.[11] reported the asymmetric addition of allylstannane to isatins with low enantioselectivity (42% ee). The highly enantioselective allylation procedures for the preparation of 3-allyl-3-hydroxy-2-oxindole compounds still remains a challenge.[12] As a continuous effort on the palladium-catalyzed asymmetric allylation of carbonyl compounds,[13] we studied the palladium-catalyzed asymmetric allylation of isatins with allylic alcohols (Scheme 1). By using chiral spiro phosphoramidite ligands, a variety of 3-allyl-3-hydroxy-2-oxindoles were obtained in excellent yields with moderate enantioselectivities.

In our initial studies, the palladium-catalyzed asymmetric allylation of 1-methylindoline-2,3-dione **1a** was carried out with allylic alcohol **2a** in THF at 30 °C with triethylborane as the activating agent (Scheme 1). Firstly, various chiral spiro ligands developed in our laboratory[14] were evaluated in this reaction. The phosphine ligand **4**, which gave good enantioselectivities in palladium-catalyzed allylation of aldehydes with allylic alcohols,[13] was found to be reactive for the allylation reaction, giving the desired product, 3-allyl-3-hydroxy-1-methylindolin-2-one **3aa** in high yield (85%), while the enantioselectivity (35% ee) was low (Table 1, entry 1). The phosphinite ligand **5** and phosphite ligand **6** were very unreactive in the allylation reaction, giving very low yields (<20%) after long reaction times (entries 2 and 3). The reactivity and enantioselectivity of phosphoramidite ligands were quite different according

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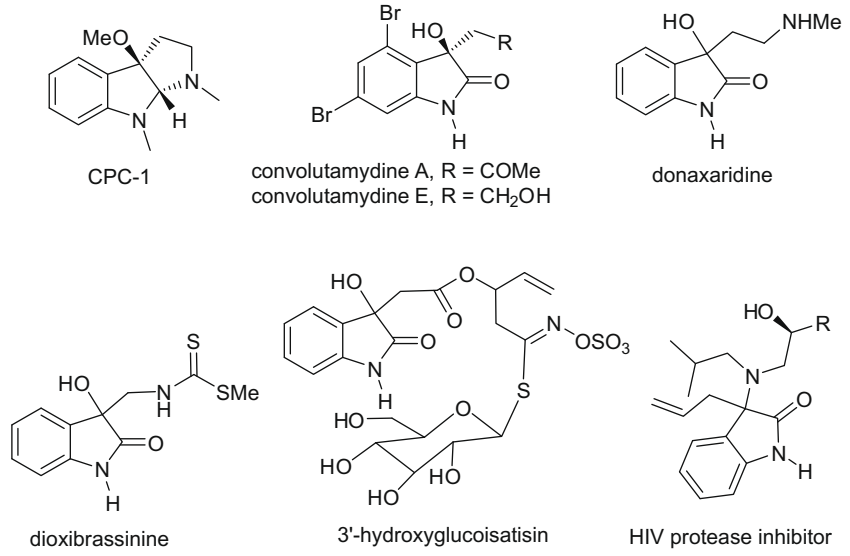
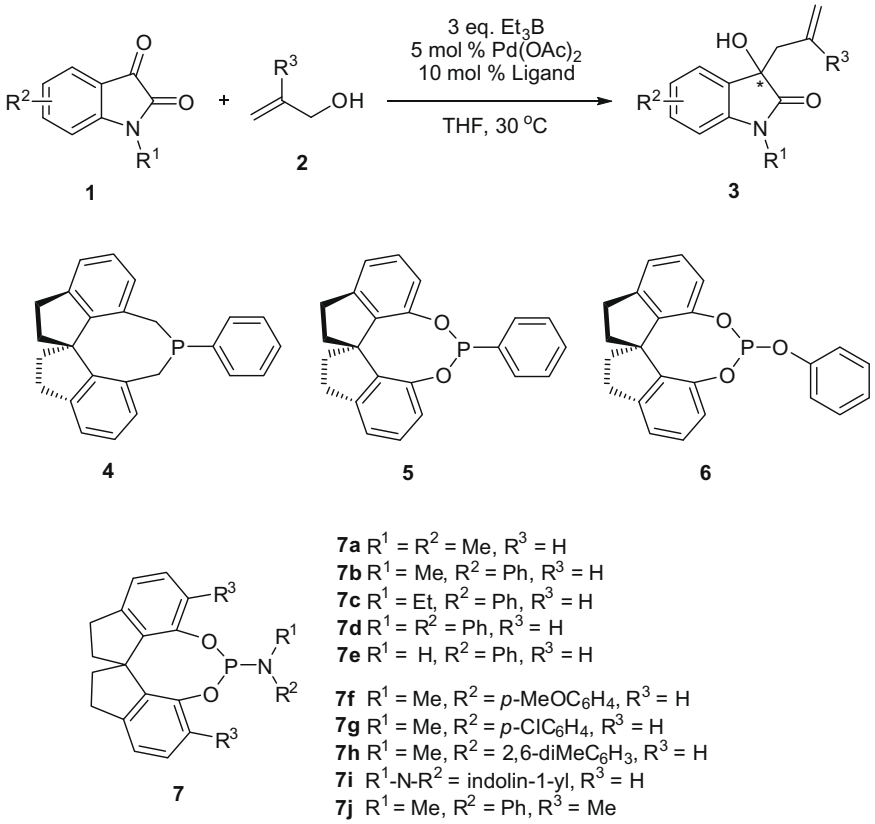


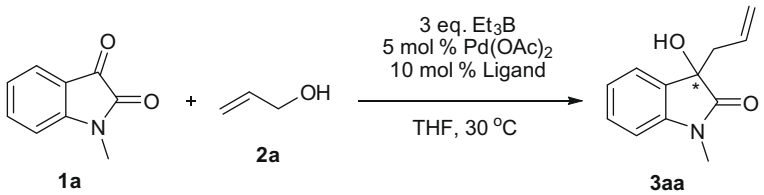
Figure 1. Natural products and bioactive compounds derived from 3-allyl-3-hydroxy-2-oxindoles.



Scheme 1. Palladium-catalyzed asymmetric allylation of isatins with allylic alcohols.

to the amine moiety of the ligand. Ligand **7a** with a dimethylamino group was inert for the reaction (entry 4). Interestingly, ligand **7b** produced by a simple replacement of one methyl group of ligand **7a** with a phenyl afforded the allylation product **3aa** in an almost quantitative yield with 71% ee (entry 5). Noting that the introduction of an aromatic amine into the ligand had a notable effect on the reactivity and enantioselectivity of the catalyst, we then synthesized various phosphoramidite ligands **7c**–**7i** bearing aryl groups on the nitrogen atom. The experiments with those ligands in the allylation reaction showed that the combination of a methyl and a phenyl group on the nitrogen atom of ligand is necessary. Changing the methyl group of ligand **7b** to ethyl **7c**, phenyl **7d** or hydrogen **7e** either lowered the enantioselectivity (entry 6) and reactivity of the reaction (entry 7) or fully prohibited the reaction (entry 8). Modification of ligand **7b** by varying the electronic and steric properties of the *N*-phenyl of the ligand did not improve the enantioselectivity of the reaction (entries 9–12). The steric effect on the spirobiindane scaffold was also examined. When two

Table 1
Palladium-catalyzed asymmetric allylation of **1a** with allylic alcohol: optimizing the reaction conditions[a]



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

Entry	Ligand	Solvent	Time (h)	Yield (%)[b]	ee (%)[c]
1	(*R*)-**4**	THF	12	85	35
2	(*R*)-**5**	THF	48	Trace	—
3	(*R*)-**6**	THF	48	18	38
4	(*R*)-**7a**	THF	48	Trace	—
5	(*S*)-**7b**	THF	4	97	71
6	(*R*)-**7c**	THF	2	96	60
7	(*S*)-**7d**	THF	24	75	65
8	(*S*)-**7e**	THF	48	Trace	—
9	(*S*)-**7f**	THF	3	99	63
10	(*S*)-**7g**	THF	3	99	70
11	(*S*)-**7h**	THF	16	89	47
12	(*S*)-**7i**	THF	3	99	52
13	(*R*)-**7j**	THF	6	95	30
14	(*S*)-**7b**	Et_2O	1.5	80	57
15	(*S*)-**7b**	Dioxane	1.5	99	66
16	(*S*)-**7b**	Diglyme	1.5	99	55
17	(*S*)-**7b**	Toluene	1.5	87	37
18	(*S*)-**7b**	CH_2Cl_2	4	85	53
19[d]	(*S*)-**7b**	THF	20	97	67 (96)[e]

[a] Reaction conditions: $Pd(OAc)_2$/ligand/**1a**/allylic alcohol/Et_3B = 0.0125/0.025/0.25/0.50/0.75 mmol, 2.0 mL solvent at 30 °C.
[b] Isolated yield.
[c] Determined by SFC using a Chiralpak AD-H column.
[d] 1 mol % catalyst was used.
[e] After once recrystallization from ethyl acetate.

methyl groups were introduced onto the 6,6′-position of the spiro backbone of the ligand, the enantioselectivity of the reaction was decreased to 30% ee (entry 13).

With ligand **7b** the reaction conditions including the palladium source, solvent, and reaction temperature were carefully optimized to improve the enantioselectivity; however, no enhancement was observed (entries 14–18). It is worth mentioning that catalyst Pd/**7b** has very high reactivity, the catalyst loading can be reduced to 1 mol %, without diminishing the yield or enantioselectivity. Furthermore, the enantiomeric purity of the allylation product **3aa** was easily enhanced to 96% ee after one recrystallization from ethyl acetate (entry 19).

Under the optimal reaction conditions, various isatin derivatives were studied in the allylation reaction with allylic alcohols. The effect of the N-protecting group of isatin on the reactivity and enantioselectivity was evaluated first. With no N-protecting group the isatin facilitates the allylation at both nitrogen and carbonyl group to generate bis-allylation product 1,3-diallyl-3-hydroxyindolin-2-one **3ba** in 90% yield with 63% ee (Table 2, entry 2). Other alkyl and aryl N-protecting groups with different steric and electronic properties all gave the allylation products in slightly lower enantioselectivities (entries 3–5 vs entry 1). When *p*-tolysulfonyl (Ts) was used as the N-protecting group, the allylation reaction became sluggish and the yield as well as the ee value decreased (entry 6). We then investigated the allylation of 1-methylindoline-2,3-dione bearing various substituents at the 5- or 7-position and found that the electronic property of the substituents had a negligible influence on the reactivity of the reaction although the enantioselectivities of reactions were lower than that in the reaction with *N*-methylisatin **1a** (entries 7–11). The allylic alcohols with alkyl or aromatic substituents at 2-position were also suitable allylating agents for this reaction. Under the standard reaction conditions, the corresponding products were generally obtained in excellent yields with moderate enantioselectivities (entries 12–16). The absolute configuration of **3fa** was determined to be (*R*) by comparing the specific rotation of its deprotected product **8** with the literature data $\{[\alpha]_D^{26} = -10$ (*c* 1.3, MeOH) for (*S*)-**8**$\}$[11] (Scheme 2).

3. Conclusion

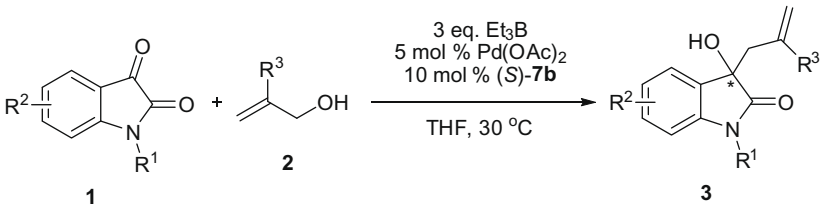
In conclusion, we have reported a palladium-catalyzed asymmetric allylation of isatins with allylic alcohols as the allyl donor. By using chiral spiro phosphoramidite ligands containing an aniline moiety, various homoallylic alcohols such as 3-allyl-3-hydroxy-2-oxindoles were obtained directly from the allylic alcohols in one step with excellent yields and moderate enantioselectivities. This represents the first catalytic asymmetric allylation of ketones with allylic alcohol as the allylating agent.

4. Experimental

4.1. General methods

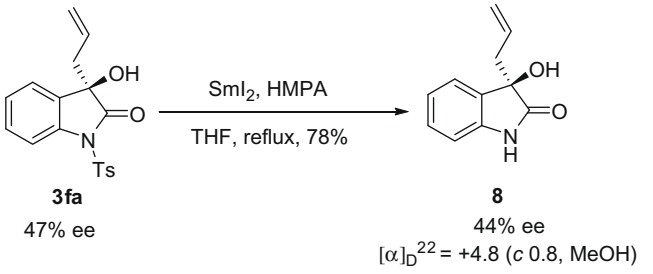
All reactions and manipulations were performed using standard Schlenk techniques. THF, diethyl ether, DME, and toluene, were distilled from sodium benzophenone ketyl. CH_2Cl_2 and Et_3N were distilled over CaH_2 under nitrogen atmosphere. DMSO was distilled over CaH_2 under reduced pressure and stored under nitrogen. $Pd(OAc)_2$, Et_3B, isatin, **1b**, and methallyl alcohol were purchased from Acros or Aldrich Co. Ltd and used as received. The isatin derivatives **1a**, **1c**–**1k** were prepared according to the literature procedures.[15] $Pd_2(dba)_4$ and $Pd_2(dba)_3CHCl_3$ were prepared according to the literature procedure.[16] Chiral spiro phosphorous ligands

Table 2
Palladium-catalyzed asymmetric allylation of isatins with allylic alcohols[a]



Entry	R^1	R^2	R^3	Prod.	Time (h)	Yield (%)	ee (%)
1	Me	H **1a**	H **2a**	**3aa**	4	97	71
2	H	H **1b**	H **2a**	**3ba**[b]	20	90	63
3	$CH_2C(Me)_3$	H **1c**	H **2a**	**3ca**	4	85	62
4	Bn	H **1d**	H **2a**	**3da**	12	99	56
5	Ph	H **1e**	H **2a**	**3ea**	5	93	62
6	Ts	H **1f**	H **2a**	**3fa**	20	74	47
7	Me	5-Cl **1g**	H **2a**	**3ga**	2	98	46
8	Me	5-OMe **1h**	H **2a**	**3ha**	3	96	53
9	Me	5-Me **1i**	H **2a**	**3ia**	3	99	54
10	Me	7-Cl **1j**	H **2a**	**3ja**	2	89	52
11	Me	7-Me **1k**	H **2a**	**3ka**	2	98	64
12	Me	H **1a**	Me **2b**	**3ab**	3	99	48
13	Me	H **1a**	Ph **2c**	**3ac**	5	93	57
14	Me	H **1a**	4-$MeOC_6H_4$ **2d**	**3ad**	5	88	50
15	Me	H **1a**	4-$F_3CC_6H_4$ **2e**	**3ae**	3	99	60
16	Me	H **1a**	Bn **2f**	**3af**	4	98	48

[a] The reaction conditions were the same as those listed out in Table 1, entry 5.
[b] Compound **3ba** is 1,3-diallyl-3-hydroxyindolin-2-one.



Scheme 2. Determination of the absolute configuration of **3fa**.

4,[13] and **5**[17] were prepared according to the previously reported procedures. The chiral phosphite ligand **6** can be purchased from Strem Co. Ltd. Melting points were measured on a RY-I apparatus and are uncorrected. ^1H, ^{13}C and ^{31}P NMR spectra were recorded on Varian Mercury 400 MHz or Bruker 300 MHz spectrometers. Chemical shifts (δ values) were reported in ppm down field from internal Me_4Si (^1H and ^{13}C NMR) and external 85% H_3PO_4 (^{31}P NMR), respectively. Optical rotations were determined using a Perkin Elmer 341 MC polarimeter. Mass spectra were recorded on a VG-7070E or VG ZAB-HS spectrometer. HPLC analyses were performed on a Hewlett Packard Model HP 1100 Series or Waters 2996 instruments and SFC (Supercritical Fluid Chromatography) analyses were performed on a Berger Analytix SFC instrument.

4.2. General procedure for the synthesis of spiro phosphoramidite ligands

A solution of (*S*)-1,1′-spirobiindane-7,7′-diol (SPINOL, 500 mg, 1.98 mmol), and Et_3N (475 mg, 4.4 mmol) in THF (20 mL) was cooled to 0 °C and a freshly distilled PCl_3 (283 mg, 2.06 mmol) was added with stirring. When the addition was over, the reaction mixture was stirred for 0.5 h at 0 °C, and then warmed to room temperature and stirred overnight. The mixture was filtered under nitrogen. The filtrate was evaporated under reduced pressure. The residue was resolved in THF (10 mL), and was cooled to −78 °C, treated with lithium *N*-methyl-*N*-phenylamide prepared from *N*-methylaniline (1.95 mmol) and butyllithium (2.15 M solution in hexane, 0.9 mL, 1.95 mmol) in 5 mL THF at −78 °C. The resulting solution was warmed to room temperature and was stirred for 3 days. The solvent was removed in vacuum and the residue was passed through a silica gel plug with ethyl acetate/petroleum ether (1:25) to afford pure product *N*-methyl-*N*-phenyl-[(*S*)-1,1′-spirobiindane-7,7′-diyl]-phosphoramidite (*S*)-**7b**: 80% yield, white solid. Mp 186–187 °C. $[\alpha]_D^{25} = -25.5$ (*c* 1.0, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 7.23–7.05 (m, 5H), 6.98–6.84 (m, 5H), 6.54–6.49 (m, 1H), 3.02–2.92 (m, 2H), 2.77–2.69 (m, 2H), 2.21–2.11 (m, 5H), 1.98–1.85 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.8, 147.2, 146.8, 146.0, 145.8, 142.4, 140.5, 129.2, 128.7, 128.5, 122.2, 121.7, 121.3, 121.0, 119.3, 119.1, 59.1, 38.7, 38.2, 32.0, 31.1, 30.7. ^{31}P NMR (121 MHz, $CDCl_3$) δ 118.7 (s). EI-HRMS Calcd for $C_{24}H_{22}NO_2P$: 387.1388. Found: 387.1383.

4.2.1. *N*-Ethyl-*N*-phenyl-[(*R*)-1,1′-spirobiindane-7,7′-diyl]-phosphoramidite (*R*)-7c

Ligand (*R*)-**7c** was synthesized from (*R*)-SPINOL and lithium *N*-ethyl-*N*-phenylamide by the same procedure as that for (*S*)-**7b**. 79% yield, white solid, mp 186–188 °C. $[\alpha]_D^{25} = +89.8$ (*c* 1.0, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.20 (m, 5H), 7.15–6.99 (m, 5H), 6.69 (d, *J* = 7.6 Hz, 1H), 3.15–3.05 (m, 2H), 2.90–2.76 (m, 3H), 2.69–2.60 (m, 1H), 2.33–2.23 (m, 2H), 2.09–1.96 (m, 2H), 0.89 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.2, 146.1, 145.5, 145.0, 144.6, 142.4, 140.5, 129.2, 128.7, 128.4, 122.9, 122.2, 122.0, 121.7, 121.4, 120.8, 59.0, 40.1, 38.6, 38.2, 31.1, 30.7, 15.1. ^{31}P NMR (121 MHz, $CDCl_3$) δ 121.1 (s). EI-HRMS Calcd for $C_{25}H_{24}NO_2P$: 401.1545. Found: 401.1547.

4.2.2. *N*,*N*-Diphenyl-[(*S*)-1,1′-spirobiindane-7,7′-diyl]-phosphoramidite (*S*)-7d

Ligand (*S*)-**7d** was synthesized from (*S*)-SPINOL and lithium *N*,*N*-diphenylamide by the same procedure as that for (*S*)-**7b**. 83% yield, white solid, mp 138–140 °C. $[\alpha]_D^{25} = -171$ (*c* 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23–7.02 (m, 10H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.73–6.71 (m, 5H), 3.09–3.01 (m, 2H), 2.89–2.73 (m, 3H), 2.24–2.13 (m, 2H), 2.01–1.93 (m, 1H), 1.78–1.71 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.3, 146.2, 144.8, 144.4, 144.3, 143.5, 143.4, 140.8, 139.6, 128.2, 127.6, 127.3, 124.0, 123.9, 122.7, 120.6, 120.0, 116.7, 58.0, 37.2, 36.9, 29.8, 29.4. ^{31}P NMR (121 MHz, $CDCl_3$) δ 117.0 (s). EI-HRMS Calcd for $C_{29}H_{24}NO_2P$: 449.1545. Found: 449.1544.

4.2.3. *N*-Methyl-*N*-(4-methoxyphenyl)-[(*S*)-1,1′-spirobiindane-7,7′-diyl]-phosphoramidite (*S*)-7f

Ligand (*S*)-**7f** was synthesized from (*S*)-SPINOL and lithium *N*-methyl-*N*-(4-methoxyphenyl)amide by the same procedure as that for (*S*)-**7b**. 68% yield, white solid, mp 132–134 °C. $[\alpha]_D^{25} = -20.4$ (*c* 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23–7.16 (m, 3H), 7.12–7.03 (m, 3H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.69 (d, *J* = 8.0 Hz, 1H), 3.80 (s, 3H), 3.15–3.05 (m, 2H), 2.89–2.83 (m, 2H), 2.33–2.24 (m, 5H), 2.09–1.97 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.7, 147.9, 146.0, 145.9, 145.6, 142.4, 140.6, 140.3, 139.9, 128.7, 122.0, 121.9, 121.6, 121.3, 120.9, 114.6, 59.0, 55.6, 38.6, 38.2, 32.9, 31.1, 30.7. ^{31}P NMR (121 MHz, $CDCl_3$) δ 118.7 (s). EI-HRMS Calcd for $C_{25}H_{24}NO_3P$: 417.1494. Found: 417.1483.

4.2.4. *N*-Methyl-*N*-(4-chlorophenyl)-[(*S*)-1,1′-spirobiindane-7,7′-diyl]-phosphoramidite (*S*)-7g

Ligand (*S*)-**7g** was synthesized from (*S*)-SPINOL and lithium *N*-methyl-*N*-(4-chlorophenyl)amide by the same procedure as that for (*S*)-**7b**. 67% yield, white solid, mp 164–166 °C. $[\alpha]_D^{25} = +8.9$ (*c* 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.21 (m, 3H), 7.16–7.04 (m, 5H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 3.16–3.06 (m, 2H), 2.90–2.83 (m, 2H), 2.33–2.24 (m, 5H), 2.08–1.97 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.5, 146.0, 145.8, 145.6, 142.4, 140.4, 129.1, 128.8, 128.5, 127.2, 121.8, 121.4, 121.1, 120.2, 120.0, 59.0, 38.6, 38.2, 32.0, 31.9, 31.1, 30.7. ^{31}P NMR (121 MHz, $CDCl_3$) δ 117.9 (s). EI-HRMS Calcd for $C_{24}H_{21}NO_2PCl$: 421.0998. Found: 421.0993.

4.2.5. *N*-Methyl-*N*-(2,6-dimethylphenyl)-[(*S*)-1,1′-spirobiindane-7,7′-diyl]-phosphoramidite (*S*)-7h

Ligand (*S*)-**7h** was synthesized from (*S*)-SPINOL and lithium *N*-methyl-*N*-(2,6-dimethylphenyl)amide by the same procedure as that for (*S*)-**7b**. 70% yield, white solid, mp 130–132 °C. $[\alpha]_D^{25} = -105$ (*c* 1.0, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18–7.13 (m, 3H), 7.07–7.00 (m, 5H), 6.93 (d, *J* = 7.8 Hz, 1H), 3.13–3.02 (m, 2H), 2.88–2.76 (m, 2H), 2.57 (s, 3H), 2.42 (s, 3H), 2.30–2.18 (m, 5H), 2.10–1.90 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.0, 147.0, 146.8, 145.7, 145.4, 143.3, 142.9, 142.1, 140.8, 138.6, 129.2, 128.7, 128.2, 127.1, 121.8, 121.3, 120.8, 59.0, 38.4, 34.2, 30.9, 30.6, 19.9, 18.7. ^{31}P NMR (121 MHz, $CDCl_3$) δ 124.0 (s). EI-HRMS Calcd for $C_{26}H_{26}NO_2P$: 415.1701. Found: 415.1709.

4.2.6. (Indolin-1-yl)-[(*S*)-1,1′-spirobiindane-7,7′-diyl]-phosphoramidite [(*S*)-7i]

Ligand (*S*)-**7i** was synthesized from (*S*)-SPINOL and lithium indolinate by the same procedure as that for (*S*)-**7b**. 70% yield, white solid, mp 160–162 °C. $[\alpha]_D^{25} = -144$ (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.22 (m, 1H), 7.11–6.96 (m, 7H), 6.82 (t, *J* = 7.2 Hz, 1H), 6.60 (t, *J* = 4.8 Hz, 1H), 3.58–3.51 (m, 1H), 3.15–3.05 (m, 2H), 2.90–2.80 (m, 3H), 2.73–2.65 (m, 1H), 2.32–2.23 (m, 3H), 2.07–1.97 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.2, 147.8, 147.5, 146.2, 145.9, 145.6, 142.5, 140.7, 131.4, 128.2, 127.3, 125.1, 121.9, 121.7, 121.1, 120.9, 120.3, 109.9, 109.6, 59.0, 46.5, 38.6, 38.2, 31.1, 30.7, 29.1; ^{31}P NMR (121 MHz, $CDCl_3$) δ 120.7 (s); EI-HRMS Calcd for $C_{25}H_{22}NO_2P$: 399.1388. Found: 399.1388.

4.2.7. *N*-Methyl-*N*-phenyl-[(*R*)-1,1′-spirobiindane-6,6′-dimethyl-7,7′-diyl]-phosphoramidite (*R*)-7j

Ligand (*R*)-**7j** was synthesized from (*R*)-SPINOL and lithium *N*-methyl-*N*-phenylamide by the same procedure as that for (*S*)-**7b**. 72% yield, white solid, mp 162–164 °C. $[\alpha]_D^{25} = +219$ (*c* 1.0, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.22 (m, 4H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.01–6.92 (m, 4H), 3.07–2.99 (m, 2H), 2.84–2.77 (m, 2H), 2.33–2.17 (m, 8H), 2.09–1.93 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.4, 147.0, 146.0, 144.9, 143.2, 142.6, 142.4, 140.4, 130.2, 129.2, 121.5, 121.3, 120.6, 118.1, 117.9, 59.0, 38.7, 38.5, 31.0, 30.5, 30.1, 16.7, 16.6, 16.4. ^{31}P NMR (121 MHz, $CDCl_3$) δ 116.0 (s). EI-HRMS Calcd for $C_{26}H_{26}NO_2P$: 415.1701. Found: 415.1703.

4.2.8. *N*-Phenyl-[(*S*)-1,1′-spirobiindane-7,7′-diyl]-phosphoramidite (*S*)-7e

Ligand (*S*)-**7e** was prepared according to the literature procedures. To a mixture of ligand (*S*)-**7a** (520 mg, 1.6 mmol), 1*H*-tetrazole (112 mg, 1.6 mmol) in an argon filled Schlenk tube, aniline (370 mg 4.0 mmol) and toluene (5 mL) were added, the reaction mixture was stirred for 12 h at 120 °C. The solvent was removed in vacuum and the residue was passed through a silica gel plug with ethyl acetate/petroleum ether (1:20) to afford pure product in 40% yield as a white solid, mp 64–66 °C. $[\alpha]_D^{17} = -103$ (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.01 (m, 10H), 6.69 (d, *J* = 6.0 Hz, 1H), 4.87 (s, 1H), 3.20 (br, 2H), 2.98–2.92 (m, 2H), 2.36 (br, 2H), 2.12 (br, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 144.7, 142.2, 142.1, 141.4, 140.9, 140.7, 139.9, 128.4, 127.7, 126.4, 121.3, 120.7, 120.1, 116.1, 116.0, 57.8, 37.5, 36.9, 29.9, 29.5. ^{31}P NMR (162 MHz, $CDCl_3$) δ 117.5 (s). ESI-HRMS Calcd for $[C_{23}H_{20}NO_2PNa, M+Na]^+$: 396.1124. Found: 396.1123.

4.3. General procedure for the palladium-catalyzed asymmetric allylation of isatins and analytical data for homoallylic alcohols

A mixture of $Pd(OAc)_2$ (2.8 mg, 12.5 μmol), (*S*)-**7b** (9.7 mg, 25 μmol) in THF (2.0 mL) in an argon filled Schlenk tube was stirred at 30 °C for 10 min. The 1-methylindoline-2,3-dione (41 mg, 0.25 mmol), allyl alcohol (30 mg, 0.5 mmol), and Et_3B (0.75 mL, 1.0 M in hexane, 0.75 mmol) were added sequentially. The resulting mixture was stirred at 30 °C until no more changes were observed (monitored by TLC). The reaction mixture was diluted with ethyl acetate (20 mL) and quenched by adding 3 g of silica gel. After concentrated under reduced pressure, the crude product was purified by a flash chromatography with ethyl acetate/petroleum ether (1:1.5) to afford (+)-3-allyl-3-hydroxy-1-methylindolin-2-one as a pale yellow solid. The analytical data for homoallylic alcohols are listed below.

4.3.1. (+)-3-Allyl-3-hydroxy-1-methylindolin-2-one 3aa

Pale yellow solid, 97% yield, 71% ee. Mp: 109–110 °C. $[\alpha]_D^{29} = +21.4$ (*c* 1.05, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 5.69–5.59 (m, 1H), 5.12–5.07 (m, 2H), 3.17 (s, 3H), 2.74 (dd, *J* = 13.6, 6.4 Hz, 1H), 2.60 (dd, *J* = 13.2, 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.9, 143.2, 130.6, 129.8, 129.6, 124.1, 123.0, 120.2, 108.3, 75.9, 42.9, 26.1. EI-HRMS Calcd for $C_{12}H_{13}NO_2$: 203.0946. Found: 203.0949. SFC condition: Chiralpak AD-H column, CO_2/2-propanol = 90:10, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 210 nm, t_R = 8.9 min (major), and t_R = 9.9 min (minor).

4.3.2. (+)-1,3-Diallyl-3-hydroxyindolin-2-one 3ba

Pale yellow solid, 90% yield, 63% ee. Mp: 112–114 °C. $[\alpha]_D^{29} = +18.9$ (*c* 0.98, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.2 Hz, 1H), 7.31 (t, *J* = 8.1 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 7.5 Hz, 1H), 5.87–5.74 (m, 1H), 5.67–5.51 (m, 1H), 5.26–5.19 (m, 2H), 5.13–5.05 (m, 2H), 4.47–4.38 (m, 1H), 4.21–4.12 (m, 1H), 3.77 (s, 1H), 2.84–2.77 (m, 1H), 2.72–2.65 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.7, 142.5, 131.1, 130.6, 129.8, 129.5, 124.1, 123.0, 120.3, 117.6, 109.3, 76.0, 43.0, 42.3. ESI-HRMS Calcd for $[C_{14}H_{15}NO_2Na, M+Na]^+$: 252.0995. Found: 252.1002. SFC condition: Chiralpak AD-H column, CO_2/2-propanol = 90:10, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 210 nm, t_R = 10.4 min (major), and t_R = 11.6 min (minor).

4.3.3. (+)-3-Allyl-3-hydroxy-1-neopentylindolin-2-one 3ca

White solid, 85% yield, 62% ee. Mp: 98–100 °C. $[\alpha]_D^{29} = +37.3$ (*c* 1.35, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.6 Hz, 1H), 7.29–7.26 (m, 1H), 7.06 (t, *J* = 7.2 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 5.64–5.54 (m, 1H), 5.12–5.05 (m, 2H), 3.74 (d, *J* = 4.4 Hz, 1H), 3.65 (d, *J* = 14.0 Hz, 1H), 3.24 (d, *J* = 14.0 Hz, 1H), 2.81–2.75 (m, 1H), 2.69–2.64 (m, 1H), 0.99 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.4, 144.4, 130.7, 129.9, 129.2, 124.0, 122.7, 120.3, 109.6, 75.7, 51.9, 43.3, 34.5, 28.5. ESI-HRMS Calcd for $[C_{16}H_{21}NO_2Na, M+Na]^+$: 282.1465. Found: 282.1466. HPLC condition: Chiralpak AD-H column, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 6.2 min (major), t_R = 7.0 min (minor).

4.3.4. (+)-3-Allyl-1-benzyl-3-hydroxyindolin-2-one 3da

Pale yellow solid, 99% yield, 56% ee. Mp: 146–148 °C. $[\alpha]_D^{29} = +5.2$ (*c* 1.55, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.40 (d, *J* = 7.2 Hz, 1H), 7.34–7.22 (m, 5H), 7.21–7.17 (t, *J* = 7.6 Hz, 1H), 7.08–7.03 (t, *J* = 7.6 Hz, 1H), 6.70–6.67 (d, *J* = 8.0 Hz, 1H), 5.65–5.54 (m, 1H), 5.16–5.00 (m, 3H), 4.73–4.68 (d, *J* = 16.0 Hz, 1H), 3.99 (br, 1H), 2.87–2.82 (dd, *J* = 13.2, 6.4 Hz, 1H), 2.76–2.70 (dd, *J* = 13.2, 8.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.1, 142.4, 135.5, 130.6, 129.8, 129.5, 128.8, 127.7, 127.3, 124.2, 123.1, 120.5, 109.5, 76.1, 43.8, 43.0. ESI-HRMS Calcd for $[C_{18}H_{17}NO_2Na, M+Na]^+$: 302.1151. Found: 302.1147. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 88:12, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 210 nm, t_R = 8.7 min (major), and t_R = 9.6 min (minor).

4.3.5. (+)-3-Allyl-3-hydroxy-1-phenylindolin-2-one 3ea

Pale yellow solid, 93% yield, 62% ee. Mp: 110 °C. $[\alpha]_D^{29} = +23.3$ (*c* 1.25, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.52–7.35 (m, 6H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 5.66–5.56 (m, 1H), 5.15–5.08 (m, 2H), 4.02 (s, 1H), 2.88–2.74 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.3, 143.3, 134.0, 130.5, 129.6, 129.5, 129.4, 128.2, 126.5, 124.4, 123.5, 120.5, 109.7, 76.2, 43.5. ESI-HRMS Calcd for $[C_{17}H_{15}NO_2Na, M+Na]^+$: 288.0995. Found: 288.1001. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 85:15, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 210 nm, t_R = 5.0 min (major), and t_R = 6.8 min (minor).

4.3.6. (*R*)-3-Allyl-3-hydroxy-1-tosylindolin-2-one 3fa

Pale yellow solid, 74% yield, 47% ee. Mp: 90–92 °C. $[\alpha]_D^{29} = +5.2$ (*c* 1.33, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.92–7.86 (m, 3H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 5.34–5.23 (m, 1H), 4.91–4.83 (m, 2H), 3.50 (s, 1H), 2.64–2.51 (m, 2H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 146.1, 138.8, 135.0, 130.6, 130.1, 129.3, 128.9, 128.2, 125.5, 124.7, 121.4, 113.8, 76.2, 43.8, 22.0. ESI-HRMS Calcd for $[C_{18}H_{17}NO_4SNa, M+Na]^+$: 366.0770. Found: 366.0776. HPLC condition: Chiralcel OD-H column, *n*-hexane/2-propanol = 90:10, flow rate = 1.0 mL/min, wavelength = 254 nm, t_R = 13.2 min (*R*), t_R = 15.3 min (*S*).

4.3.7. (+)-3-Allyl-5-chloro-3-hydroxy-1-methylindolin-2-one 3ga

Pale yellow solid, 98% yield, 46% ee. Mp: 132–134 °C. $[\alpha]_D^{29} = +2.7$ (*c* 0.98, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 2.0 Hz, 1H), 7.28 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 5.62–5.51 (m, 1H), 5.10–5.06 (m, 2H), 4.16 (s, 1H), 3.14 (s, 3H), 2.74 (dd, *J* = 13.2, 6.4 Hz, 1H), 2.60 (dd, *J* = 9.2, 8.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.7, 141.7, 131.5, 130.0, 129.4, 128.5, 124.7, 120.7, 109.3, 76.0, 42.8, 26.3. EI-HRMS Calcd for $C_{12}H_{12}NO_2Cl$: 237.0557. Found: 237.0556. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 85:15, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 254 nm, t_R = 3.8 min (major), and t_R = 5.0 min (minor).

4.3.8. (+)-3-Allyl-3-hydroxy-5-methoxy-1-methylindolin-2-one 3ha

Pale yellow solid, 96% yield, 53% ee. Mp: 142–144 °C. $[\alpha]_D^{29} = +8.0$ (*c* 1.33, CH_2Cl_2). ^1H NMR (400 MHz, D_6-DMSO) δ 6.94 (d, *J* = 2.0 Hz, 1H), 6.87–6.82 (m, 1H), 6.06 (s, 1H), 5.44–5.34 (m, 1H), 4.94–4.89 (m, 2H), 3.71 (s, 3H), 3.48 (s, 1H), 3.03 (s, 3H), 2.64–2.59 (m, 1H), 2.47–2.42 (m, 1H). ^{13}C NMR (75 MHz, D_6-DMSO) δ 176.6, 155.4, 136.4, 132.1, 131.6, 118.9, 113.1, 111.1, 108.6, 75.4, 55.5, 42.0, 25.7. ESI-HRMS Calcd for $[C_{13}H_{15}NO_3Na, M+Na]^+$: 256.0944. Found: 256.0943. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 85:15, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 254 nm, t_R = 3.9 min (major), and t_R = 5.0 min (minor).

4.3.9. (+)-3-Allyl-3-hydroxy-1,5-dimethylindolin-2-one 3ia

Pale yellow solid, 99% yield, 54% ee. Mp: 138–140 °C. $[\alpha]_D^{29} = +7.0$ (*c* 1.33, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (s, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 5.61–5.50 (m, 1H), 5.08–5.00 (m, 2H), 4.35 (s, 1H), 3.11 (s, 3H), 2.77–2.72 (m, 1H), 2.65–2.59 (m, 1H), 2.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.1, 140.8, 132.6, 130.8, 130.0, 129.7, 124.9, 119.9, 108.1, 76.2, 42.8, 26.1, 21.1. ESI-HRMS Calcd for $[C_{13}H_{15}NO_2Na, M+Na]^+$: 240.0995. Found: 240.1001. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 85:15, flow rate = 2.0 mL/min, pressure = 100 -bar, wavelength = 254 nm, t_R = 3.2 min (major), and t_R = 3.8 min (minor).

4.3.10. (+)-3-Allyl-7-chloro-3-hydroxy-1-methylindolin-2-one 3ja

Pale yellow solid, 89% yield, 52% ee. Mp: 104–106 °C. $[\alpha]_D^{29} = +11.3$ (*c* 1.40, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 7.2 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 6.98 (t, *J* = 8.0 Hz, 1H), 5.57–5.46 (m, 1H), 5.05–5.02 (m, 2H), 4.39 (d, *J* = 3.2 Hz, 1H), 3.50 (s, 3H), 2.74–2.69 (m, 1H), 2.64–2.58 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.5, 139.0, 132.8, 131.8, 130.1, 123.9, 122.7, 120.5, 115.8, 75.6, 43.1, 29.5. EI-HRMS Calcd for $C_{12}H_{12}NO_2Cl$: 237.0557. Found: 237.0558. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 85:15, flow rate = 2.0 mL/min, pressure = 100 -bar, wavelength = 254 nm, t_R = 3.4 min (major), and t_R = 3.8 min (minor).

4.3.11. (+)-3-Allyl-3-hydroxy-1,7-dimethylindolin-2-one 3ka

Pale yellow solid, 98% yield, 64% ee. Mp: 116–118 °C. $[\alpha]_D^{29} = +15.8$ (*c* 1.33, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 7.2 Hz, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 6.97 (t, *J* = 7.6 Hz, 1H), 5.65–5.55 (m, 1H), 5.11–5.06 (m, 2H), 3.44 (s, 4H), 2.73–2.68 (m, 1H), 2.63–2.57 (m, 1H), 2.54 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.5, 161.3, 139.9, 132.4, 129.6, 122.0, 121.0, 119.2, 74.1, 42.2, 28.5, 18.0. ESI-HRMS Calcd for $[C_{13}H_{15}NO_2Na, M+Na]^+$: 240.0995. Found: 240.1003. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 85:15, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 254 nm, t_R = 4.0 min (major), and t_R = 4.5 min (minor).

4.3.12. (+)-3-Hydroxy-1-methyl-3-(2-methylallyl)indolin-2-one 3ab

Pale yellow solid, 99% yield, 48% ee. Mp: 92–94 °C. $[\alpha]_D^{29} = +15.1$ (*c* 1.18, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.2 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 4.75 (s, 1H), 4.61 (s, 1H), 3.16 (d, *J* = 1.6 Hz, 3H), 2.70 (s, 2H), 1.52 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.5, 143.6, 139.4, 130.1, 129.8, 124.7, 123.2, 116.0, 108.6, 76.8, 46.3, 26.3, 24.2. ESI-HRMS Calcd for $[C_{13}H_{15}NO_2Na, M+Na]^+$: 240.0995. Found: 240.0996. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 85:15, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 254 nm, t_R = 3.5 min (major), and t_R = 4.1 min (minor).

4.3.13. (+)-3-Hydroxy-1-methyl-3-(2-phenylallyl)indolin-2-one 3ac

Pale yellow solid, 93% yield, 57% ee. Mp: 137–139 °C. $[\alpha]_D^{29} = +6.0$ (*c* 1.55, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.22–7.15 (m, 5H), 7.02–6.99 (m, 2H), 6.90 (t, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 5.05 (s, 1H), 4.97 (s, 1H), 4.14 (s, 1H), 3.32–3.21 (m, 2H), 2.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 143.5, 141.1, 129.6, 129.4, 128.0, 127.5, 126.6, 124.9, 123.0, 122.9, 118.3, 108.3, 77.0, 44.6, 26.0. ESI-HRMS Calcd for $[C_{18}H_{17}NO_2Na, M+Na]^+$: 302.1151. Found: 302.1149. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 85:15, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 254 nm, t_R = 6.5 min (major), and t_R = 7.6 min (minor).

4.3.14. (+)-3-Hydroxy-3-(2-(4-methoxyphenyl)allyl)-1-methylindolin-2-one 3ad

Pale yellow solid, 88% yield, 50% ee. Mp: 126–128 °C. $[\alpha]_D^{29} = +1.1$ (*c* 1.70, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.21–7.16 (m, 2H), 6.93–6.88 (m, 3H), 6.68–6.61 (m, 3H), 4.94 (dd, *J* = 9.2, 1.2 Hz, 1H), 4.85 (d, *J* = 4.4 Hz, 1H), 3.73 (s, 3H), 3.34–3.29 (m, 1H), 3.18 (d, *J* = 13.2 Hz, 1H), 2.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 159.0, 143.4, 142.8, 133.6, 129.5, 127.8, 124.9, 123.0, 122.9, 117.0, 113.4, 108.2, 77.0, 55.5, 44.6, 26.0. ESI-HRMS Calcd for $[C_{19}H_{19}NO_3Na, M+Na]^+$: 332.1257. Found: 332.1261. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 85:15, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 254 nm, t_R = 8.1 min (major), and t_R = 9.5 min (minor).

4.3.15. (+)-3-Hydroxy-1-methyl-3-(2-(4-(trifluoromethyl)phenyl) allyl)indolin-2-one 3ae

Pale yellow solid, 99% yield, 60% ee. Mp: 154–156 °C. $[\alpha]_D^{29} = +3.0$ (*c* 1.90, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.6 Hz, 2H), 7.21–7.13 (m, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 1H), 5.10 (s, 1H), 5.08 (s, 1H), 3.32 (d, *J* = 13.2, 1H), 3.25 (d, *J* = 13.2 Hz, 1H), 2.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 144.8, 143.2, 142.5, 129.8, 129.4, 129.2, 129.1, 127.0, 125.7, 124.9, 123.1, 120.0, 108.4, 77.0, 44.5, 26.0. ESI-HRMS Calcd for $[C_{19}H_{16}F_3NO_2Na, M+Na]^+$: 370.1025. Found: 370.1028. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 85:15, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 254 nm, t_R = 4.2 min (major), and t_R = 5.0 min (minor).

4.3.16. (+)-3-(2-Benzylallyl)-3-hydroxy-1-methylindolin-2-one 3af

Pale yellow solid, 98% yield, 48% ee. Mp: 144–146 °C. $[\alpha]_D^{29} = +9.7$ (*c* 1.80, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.2 Hz, 1H), 7.38–7.34 (m, 1H), 7.24 (t, *J* = 7.2 Hz, 2H), 7.19–7.12 (m, 2H), 6.98 (d, *J* = 6.8 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 4.78 (s, 1H), 4.67 (d, *J* = 1.2 Hz, 1H), 4.07 (s, 1H), 3.15 (s, 3H), 3.10 (d, *J* = 15.2 Hz, 1H), 2.95 (d, *J* = 15.6 Hz, 1H), 2.70 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 143.7, 142.5, 139.3, 130.1, 130.0, 129.4, 128.5, 126.3, 124.7, 123.3, 117.2, 108.7, 77.0, 43.8, 43.6, 26.4. ESI-HRMS Calcd for $[C_{19}H_{19}NO_2Na, M+Na]^+$: 316.1308. Found: 316.1314. SFC condition: Chiralcel OD-H column, CO_2/2-propanol = 85:15, flow rate = 2.0 mL/min, pressure = 100 bar, wavelength = 254 nm, t_R = 7.0 min (major), and t_R = 8.6 min (minor).

4.4. Deprotection of 3fa with SmI_2/HMPA)[18]

A 0.1 M solution of SmI_2 in THF (4.2 mL, 0.42 mmol) and HMPA (0.15 mL, 0.88 mmol) were added to **3fa** (70 mg, 0.21 mmol) at room temperature. After refluxing for 5 h, the reaction mixture was quenched with 10% HCl, and then extracted with EtOAc. The organic layer was concentrated under reduced pressure. The crude product was purified by a flash chromatography with ethyl acetate/petroleum ether (1:1) to afford (*R*)-3-allyl-3-hydroxyindolin-2-one (**8**) as a pale yellow solid with 78% yield and 44% ee. Mp: 132–134 °C. $[\alpha]_D^{22} = +4.8$ (*c* 0.8, MeOH). ^1H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.30 (d, *J* = 7.2 Hz, 1H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 2H), 5.65–5.54 (m, 1H), 5.06 (d, *J* = 8.8 Hz, 1H), 5.02 (s, 1H), 3.38 (s, 1H), 2.71–2.64 (dd, *J* = 13.2, 6.4 Hz, 1H), 2.58–2.51 (dd, *J* = 13.2, 8.4 Hz, 1H). HPLC condition: Chiralpak AD-H column, *n*-hexane/2-propanol = 90:10, flow rate = 1.0 mL/min, wavelength = 210 nm, t_R = 10.5 min (*S*), t_R = 16.3 min (*R*).

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