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Note

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Palladium-Catalyzed Enantioselective Hetero-annulation of 1,3-Dienes by Functionally Substituted Aryl Iodides

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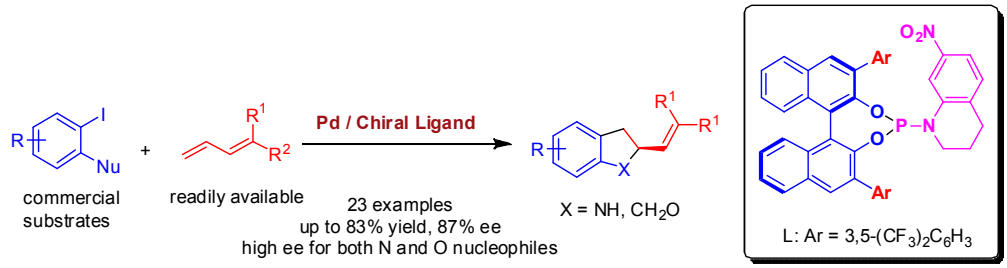


Abstract

The first enantioselective hetero-annulation of 1,3-dienes by 2-iodoanilines and 2-iodobenzylic alcohols is described. The application of a BINOL-derived phosphoramidite ligand bearing electron-withdrawing substituents is the key to obtain high enantioselectivity. This protocol provides an efficient way to access optically active chiral indolines and isochromans from readily available starting materials.

The development of new methods to obtain novel and valuable compounds in an efficient and stereoselective way remains a long-standing challenge for synthetic organic chemistry. Among these procedures are transition-metal-catalyzed cascade reactions feature efficient building up complex molecules from simple and easily available substrates.[1] Palladium catalyzed annulation of 1,3-dienes by functionally substituted aryl halides represents one of the best examples in this category.[2] In this chemistry, pioneered by Dieck[2a] and Larock[2b], readily available iodobenzene derivatives and 1,3-dienes undergoes a palladium-catalyzed tandem Heck[3]/intramolecular Tsuji-Trost allylation[4] process. This methodology provides an ideal approach to access a large range of heterocycles and all-carbon fused cyclic compounds as shown in Figure 1b. These cyclic structures, from indolines, tetrahydroisoquinolines, to dihydrobenzofurans and others, are privileged structural motifs found in numerous naturally bioactive alkaloids, drugs and pharmaceutical agents, as exemplified by oleracein A–D,tremetone, pseudoanguilosporin A, C, et al. (Figure 1c).[5]

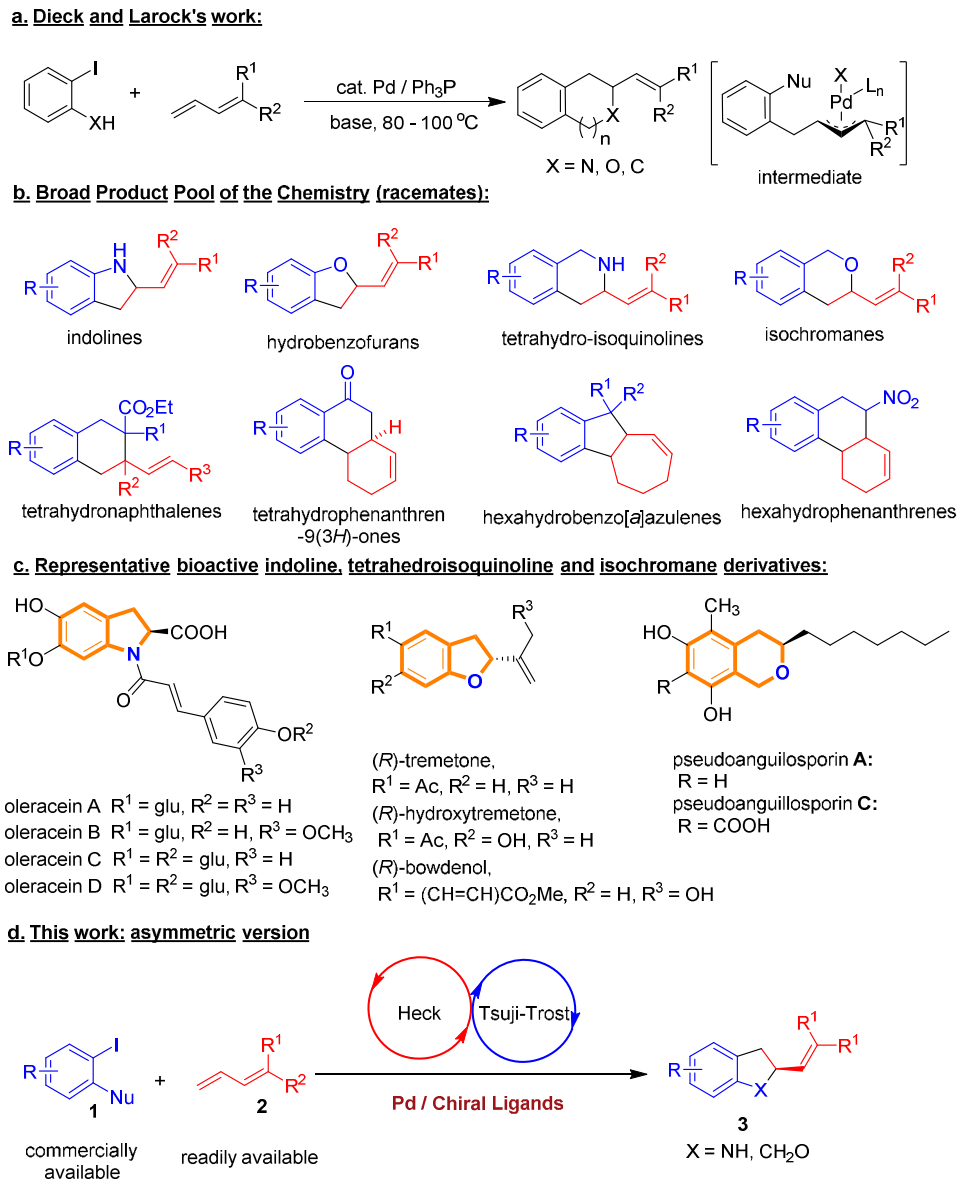


Figure 1. Palladium-catalyzed hetero-annulation of 1,3-dienes and functionally substituted aryl iodides.

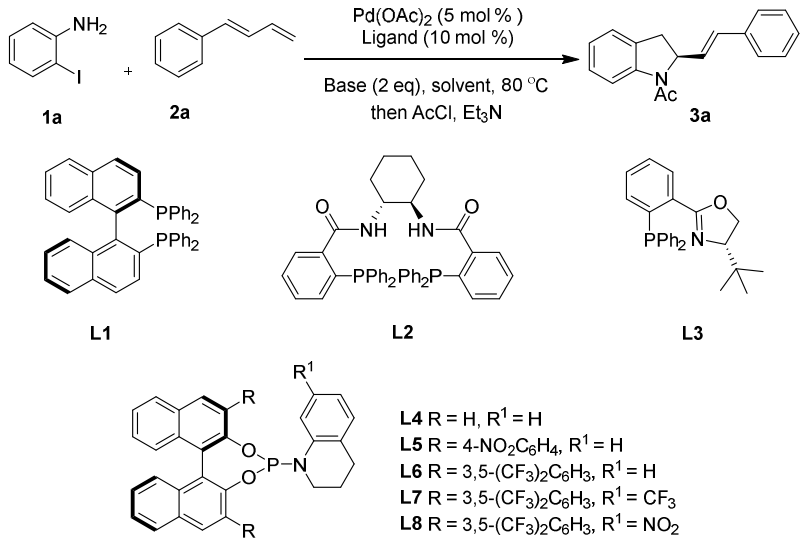
Despite the importance of this versatile methodology, the asymmetric version of this chemistry has not been accomplished up to now, though sporadic reports concerning enantioselective tandem Heck/Tsuji-Trost reaction has been found in the last three decades. Shibasaki's group reported a Pd/BINAP catalyzed intramolecular asymmetric Heck reaction-anion capture process and successfully utilized the methods for the synthesis of a series of natural products.[6] Employing the same catalyst, Overman and co-workers applied a catalytic intramolecular Heck reaction, followed by capture of the resulting

η^3-allylpalladiumintermediate by a tethered diketopiperazine as the key step in the concise total synthesis of several natural products.[7] Using amino group tethered 1,3-dienes and iodobenzenes as substrates, Helmchen reported an tandem Heck/asymmetric Tsuji-Trost reaction catalyzed by Palladium with PHOX as the ligand.[8] In this reaction, besides the limitation of narrow substrate scope, it requires a ten-day reaction time to obtain an up to 80% enantiomeric excess with moderate yield. Very recently, Gong reported a Pd/chiral phosphoramidite catalyzed intermolecular Heck/asymmetric Tsuji-Trost reaction of iodobenzenes, 1,3-dienes and sodium dialkyl malonates.[9] Back to the chemistry of Dieck and Larock[2], the challenging part of the asymmetric version is to search for ideal ligands that are appropriate for both Heck reaction and subsequent asymmetric Tsuji-Trost reaction. Herein, we'll report the first enantioselective hetero-annulation of 1,3-dienes and functionally substituted aryl iodides for the synthesis optically active indolines[10] and isochromans[11] (Figure 1d).

Our study initiated from the screening of chiral ligands for the reaction of 2-iodoaniline (**1a**) and (*E*)-1-phenylbutadiene (**2a**) in the presence of 5 mol% of $Pd(OAc)_2$ and K_2CO_3in THF at 80 ^oC. The resulting reaction mixture was treated with AcCl/Et_3N to convert the product into more stable Ac-protected indoline. (*R*)-BINAP, Trost ligand and chiral phosphinooxazoline-type P, N ligand, which were frequently employed in the asymmetric Tsuji-Trost reaction and asymmetric Heck reaction, were not able to provide good results (Table 1, entries 1-3). Then, BINOL derived chiral phosphoramidite ligands were investigated for the cascade reaction. In the presence of ligand **L4**, synthesized from non-substituted BINOL and tetrahydroquinoline, the desired product **3a** was obtained with 25% yield, but without any enantiomeric excess (entry 4). Introducing electron-withdrawing 4-nitrophenyl groups at the 3,3'-positions of the binaphthyl backbone lead to a drastic increase in the yield albeit still without enantioselectivity (**L5**, entry 5). Replacing the 4-nitrophenyl group with

3,5-$(CF_3)_2C_6H_3$ greatly enhanced the enantioselectivity to 80% ee with a rather poor yield, however (**L6**, entry 6). Further modifying the tetrahydroquinoline moiety revealed that incorporating an electron-withdrawing group at the 7-position could greatly increase the yield without considerable erosion of the enantioselectivity (entries 7–8). **L8** was identified to be the optimal ligand for the reaction, providing **3a** with 78% yield and 80% enantiomeric excess (entry 8). Noteworthy, **L8** was also the optimal ligand for the intermolecular Heck/asymmetric Tsuji-Trost reaction of iodobenzenes, 1,3-dienes and sodium dialkyl malonates.[9] A screening of the solvents found DME (dimethoxyethane) to be the best solvent regarding both yield and enantioselectivity (entries 9–12). The reaction didn't occur at all without a base. While several bases are suitable for the reaction, proving satisfying results, $KHCO_3$ could further increase the optical yield from 80% to 83% *ee* (entries 13–16). Furthermore, tuning the ratio of substrates could slightly increase the enantioselectivity to 84% *ee*.

Table 1. Optimization of the Reaction Conditions



entry	ligand	solvent	base	conversion (%)	yield (%)[b]	ee (%)[c]
1[d]	**L1**	THF	K_2CO_3	50	18	4
2[d]	**L2**	THF	K_2CO_3	<5	trace	4
3	**L3**	THF	K_2CO_3	<5	trace	7
4	**L4**	THF	K_2CO_3	45	25	0
5	**L5**	THF	K_2CO_3	>95	80	0

6	**L6**	THF	K_2CO_3	58	34	80
7	**L7**	THF	K_2CO_3	>95	82	70
8	**L8**	THF	K_2CO_3	>95	78	80
9	**L8**	2-Me-THF	K_2CO_3	>95	85	79
10	**L8**	tBuOMe	K_2CO_3	59	28	79
11	**L8**	1,4-dioxane	K_2CO_3	70	58	27
12	**L8**	DME	K_2CO_3	>95	88	82
13	**L8**	DME	Na_2CO_3	88	54	82
14	**L8**	DME	K_3PO_4	>95	80	82
15	**L8**	DME	DIPEA	>95	70	82
16	**L8**	DME	$KHCO_3$	>95	85	83
17[e]	**L8**	DME	$KHCO_3$	>95	85	83
18[f]	**L8**	DME	$KHCO_3$	>95	77	84

[a]Reaction conditions: **1a** (0.1 mmol), $Pd(OAc)_2$ (5 mol %), **L** (10 mol %), **2a** (1.1 equiv), solvent (1 mL), 80 °C, 15 h, under Ar. [b]Based on ^{1}H-NMR analysis of the crude reaction mixture using trimethyl benzene-1,3,5-tricarboxylate as an internal standard.[c]Determined by HPLC. [d]5 mol% ligand was used. [e]The reaction was carried out with **1a** (0.1mmol) and **2a** (0.2 mmol). [f]The reaction was carried out of **1a** (0.2mmol) and **2a** (0.1 mmol).

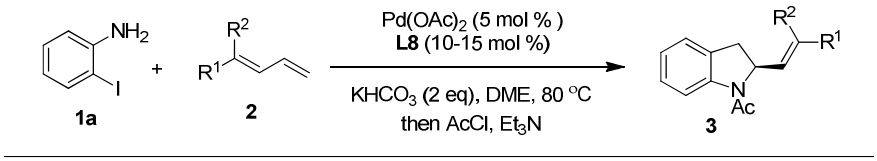
Under the optimized conditions, we next explored the generality of the cascade reaction (Scheme 1). The substrate scope of 1,3-diene was investigated by the reaction of 2-iodoaniline with various substituted 1,3-butadienes. Generally, the reactions underwent smoothly to give the desired indo lines in high enantioselectivities ranging from 75% to 86% ee and up to 78% isolation yield (Scheme 1, **3a**–**3i**).

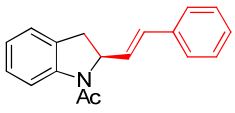
Arylbutadienes with either electron-withdrawing or electron-donating substituents were all tolerable for the protocol. The substitution pattern of arylbutadienes **2** exhibited little effect on the yield and enantioselectivity. Notably, cyclohexyl and diphenyl substituted 1,3-butadienes could also undergo the cascade reaction to afford the desired indoles with high enantioselectivities (80–82% ee) and moderate yields (**3h**, **3i**). Electron-deficient dienyl ester **2s** was

also applicable for the reaction, providing the product **3s** with 40% yield and 79% ee (eq 1).

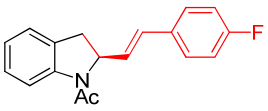
We then moved on to examine the scope of the other substrate **1** by the reaction of a variety of commercially available substituted 2-iodoanilines with1-phenylbutadiene**2a** (**3j**–**3r**). Notably, the position of the substituent on the benzene ring of 2-iodoanilines exhibited significant effect on both enantioselectivity and yield. It could be concluded that 5-substituted 2-iodoanilines provided much higher yield and stereoselectivity than those with substituents at 4-position (**3j**, **3k**, **3l** *vs* **3m**, **3n**, **3o** respectively). Generally, 5-substituted 2-iodoanilines provided the corresponding indolines with high enantioselectivities (84–87% *ee*) and good yields (74–75%) while 4-substituted substrates gave much poorer results (40–83% yield, 58–77% *ee*). On the other hand, the electronic property of the substituents showed obscure influence on the outcome of the reaction.

Scheme 1. Scope of 1,3-dienes[a,b]

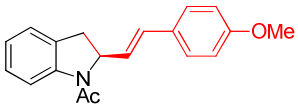




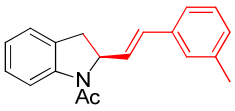
3a
76% yield, 84% *ee*



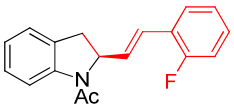
3b
68% yield, 86% ee



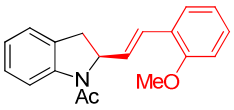
3c
78% yield, 86% ee



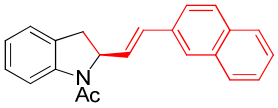
3d
67% yield, 84% ee



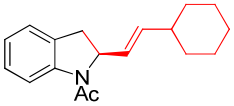
3e
64% yield, 75% ee



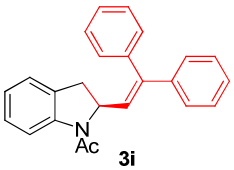
3f
68% yield, 79% ee



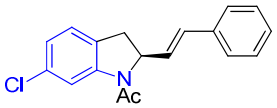
3g
58% yield, 77% ee



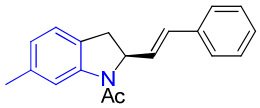
3h
54% yield, 80% ee



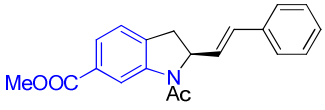
3i
30% yield, 82% ee



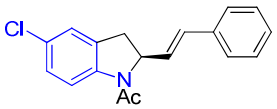
3j
75% yield, 85% ee



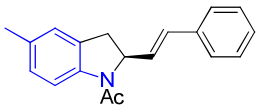
3k
75% yield, 85% ee



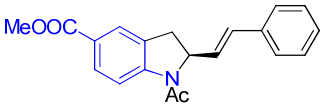
3l
74% yield, 84% ee



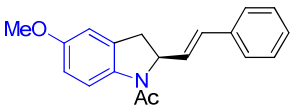
3m
48% yield, 67% ee



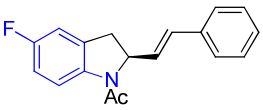
3n
53% yield, 77% ee



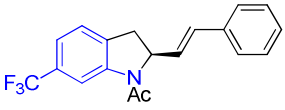
3o
40% yield, 58% ee



3p
83% yield, 67% ee



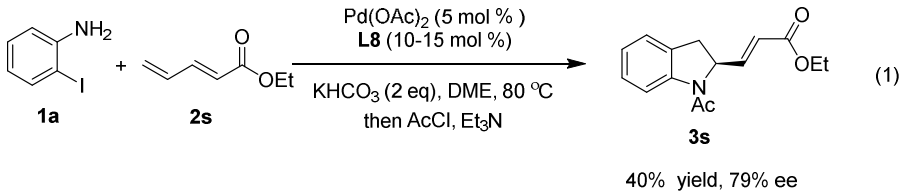
3q
72% yield, 74% ee



3r
75% yield, 87% ee

[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.1 mmol), $Pd(OAc)_2$ (5 mol %), **L8** (15 mol %), DME (1.0 mL), 80 °C, 15 h, under Ar. [b]15 mol% of ligand was used to obtain stable and repeatable

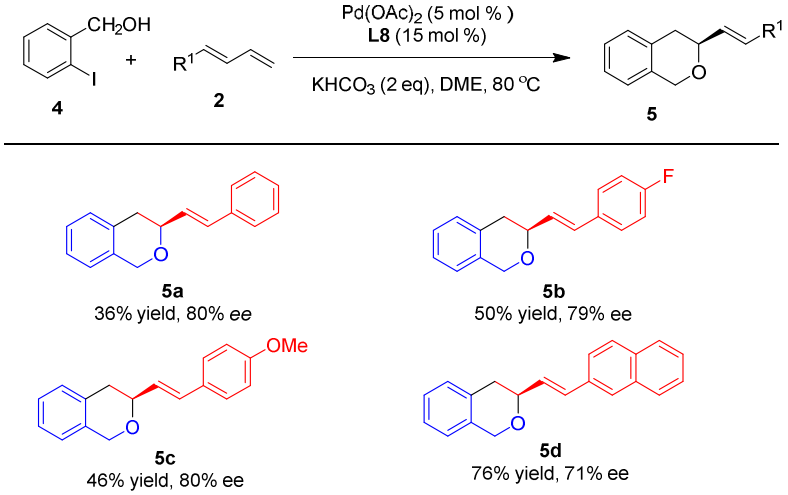
results except **3a**.



40% yield, 79% ee

In the meantime, we altered the nucleophile from *o*-iodolanilines to *o*-iodobenzyl alcohol under the same reaction condition. To our delight, upon the reactions with several arylbutadienes, chiral isochromans could also be obtained with high enantioselectivities and moderate yields (Scheme 2, **5a**–**5d**).

Scheme 2. Synthesis of Isochromanes



[a]Reaction conditions: **4**(0.2 mmol), **2** (0.1 mmol), $Pd(OAc)_2$ (5 mol %), **L8** (15 mol %), DME (1.0 mL), 80 °C, 48 h, under Ar.

In summary, we have developed, to the best of our knowledge, the first palladium-catalyzed enantioselective hetero-annulation of 1,3-dienes by 2-iodoanilines and 2-iodobenzylic alcohols. The employment of a BINOL-derived phosphoramidite ligand bearing electron-withdrawing substituents is crucial for the stereo control of the reaction. With the same ligand, both 2-iodoanilines and 2-iodobenzyl alcohol were well tolerated for this

cascade reaction. This protocol provides an efficient way to access optically active chiral indolines and isochromans from readily available starting materials.

■ EXPERIMENTAL SECTION

General Method. NMR spectra were recorded on a 400 MHz spectrometer. HRMS spectra were recorded on a TOF-Q mass spectrometer. The enantiomeric excess of the compounds was determined by chiral HPLC using racemic compounds as references. All solvents were purified and dried according to standard methods prior to use, unless stated otherwise.

For the synthesis procedure and the Determination of the absolute configuration, see supporting information.

General Reaction Procedures. To a flame-dried and Ar-purged Schlenk tube (10 mL) were added $Pd(OAc)_2$ (0.05 equiv.), phosphoramidite **L8** (0.15 equiv.), potassium bicarbonate (2.0 equiv.), 2-iodoaniline (2.0 equiv.) and a stir bar. The Schlenk tube was then evacuated and filled with argon. This cycle was repeated three times and followed by addition of aryl butadiene (0.1 mmol) and DME (1 mL) via syringe. The mixture was stirred at 80 °C for 15 h, and then was cooled down to 0 °C. To the reaction mixture at 0 °C was slowly added Et_3N (15 equiv.) and acetyl chloride (10 equiv.). The resulting mixture was stirred at room temperature for 30 min, and then filtered through silica gel, and washed with ethyl acetate. The organic phase was concentrated in vacuo. The product was purified by column chromatography on silica gel (Eluent, PE/EA = 10:1 or PE/t-BuOH = 20:1).

Characterization of the product 3 and 5.

(*S,E*)-1-(2-styrylindolin-1-yl)ethanone(3a)

Colorless oil. Yield: 76%, 20.0mg. $[\alpha]_D^{20}$ = -56.0 (c 0.16, $CHCl_3$). Enantiomeric excess: 84%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 13.35 min (minor), t_R = 14.90 min (major).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 6.4 Hz, 1H), 7.34 – 7.15 (m, 7H),

7.09 – 6.98 (m, 1H), 6.50 (d, *J* = 15.9 Hz, 1H), 6.20 (dd, *J* = 15.9, 7.1 Hz, 1H), 5.02 – 4.92 (m, 1H), 3.59 (dd, *J* = 14.5, 10.2 Hz, 1H), 2.92 (d, *J* = 15.9 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 142.3, 135.8, 130.6, 129.5, 128.6, 128.4, 128.0, 127.6, 126.5, 124.7, 123.9, 117.5, 62.2, 36.1, 23.9.IR (KBr) γ 2955, 2921, 2850, 1658, 1460, 1396, 1021, 755, 694 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{18}H_{18}ON$: 264.1383, observed: 264.1378. For the absolute configuration determination process of **3a**, see supporting information.

(*S,E*)-1-(2-(4-fluorostyryl)indolin-1-yl)ethanone(3b)

Colorless oil. Yield: 68%, 19.1mg. $[\alpha]_D^{20}$ = -45.6 (c 0.15, $CHCl_3$). Enantiomeric excess: 86%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 13.29 min (minor), t_R = 14.98 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 6.6 Hz, 1H), 7.30 – 7.15 (m, 4H), 7.04 (dd, *J* = 8.2, 7.5 Hz, 1H), 6.97 (t, *J* = 8.5 Hz, 2H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.11 (dd, *J* = 15.9, 7.0 Hz, 1H), 5.08 – 4.84 (m, 1H), 3.75 – 3.33 (m, 1H), 2.91 (d, *J* = 15.9 Hz, 1H), 2.26 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 162.5 (d, *J* = 247.6 Hz), 142.3, 132.0, 129.5, 129.3, 128.2, 128.0 (d, *J* = 8.1 Hz), 127.7, 124.8, 123.9, 117.5, 115.5 (d, *J* = 21.6 Hz), 62.1, 36.1, 23.9. IR (KBr) γ 2955, 2921, 2851, 1659, 1460, 1379, 1226, 1091, 1020, 756 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{18}H_{17}ONF$: 282.1289, observed: 282.1282.

(*S,E*)-1-(2-(4-methoxystyryl)indolin-1-yl)ethanone(3c)

Colorless oil. Yield: 78%, 22.8mg. $[\alpha]_D^{20}$ = -56.6 (c 0.24, $CHCl_3$). Enantiomeric excess: 86%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 20.50 min (minor), t_R = 22.65 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 6.8 Hz, 1H), 7.27 – 7.14 (m, 4H), 7.03 (td, *J* = 7.5, 0.7 Hz, 1H), 6.88 – 6.72 (m, 2H), 6.43 (d, *J* = 15.8 Hz, 1H), 6.05 (dd, *J* = 15.9, 7.2 Hz, 1H), 5.03 – 4.80 (m, 1H), 3.77 (s, 3H), 3.56 (dd, *J* = 14.7, 9.9 Hz, 1H), 2.90 (d, *J* = 15.9 Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 159.5, 142.4, 130.0, 129.7, 128.5, 127.7, 127.6, 126.2, 124.7, 123.8, 117.4, 114.0,

62.3, 55.2, 36.2, 23.9. IR (KBr) γ 2955, 2922, 2852, 1658, 1510, 1460, 1395, 1249, 1027cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{19}H_{20}O_2N$: 294.1489, observed: 294.1483.

(*S,E*)-1-(2-(3-methylstyryl)indolin-1-yl)ethanone(3d)

Colorless oil. Yield: 67%, 18.6mg. $[\alpha]_D^{20}$ = -54.4 (c 0.26, $CHCl_3$). Enantiomeric excess: 84%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 11.06 min (minor), t_R = 13.04 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 7.0 Hz, 1H), 7.25 – 6.99 (m, 7H), 6.47 (d, *J* = 15.9 Hz, 1H), 6.19 (dd, *J* = 15.9, 7.2 Hz, 1H), 5.10 – 4.84 (m, 1H), 3.59 (dd, *J* = 15.0, 10.1 Hz, 1H), 2.92 (d, *J* = 15.9 Hz, 1H), 2.31 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 142.4, 138.2, 135.8, 130.7, 129.6, 128.8, 128.5, 128.2, 127.6, 127.1, 124.7, 123.9, 123.7, 117.5, 62.3, 36.2, 23.9, 21.3. IR (KBr) γ 2954, 2921, 2851, 1660, 1460, 1395, 1021, 756 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{19}H_{20}ON$: 278.1539, observed: 278.1535.

(*S,E*)-1-(2-(2-fluorostyryl)indolin-1-yl)ethanone(3e)

Colorless oil. Yield: 64%, 18.0mg. $[\alpha]_D^{20}$ = -37.8 (c 0.28, $CHCl_3$). Enantiomeric excess: 75%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 11.37 min (minor), t_R = 19.42 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 6.7 Hz, 1H), 7.35 (td, *J* = 7.7, 1.6 Hz, 1H), 7.25 – 7.12 (m, 3H), 7.10 – 6.94 (m, 3H), 6.66 (d, *J* = 16.1 Hz, 1H), 6.29 (dd, *J* = 16.1, 7.3 Hz, 1H), 5.07 – 4.88 (m, 1H), 3.60 (dd, *J* = 14.6, 10.3 Hz, 1H), 2.92 (d, *J* = 16.0 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 160.3 (d, *J* = 249.8 Hz), 142.3, 131.1 (d, *J* = 3.9 Hz), 129.5, 129.3 (d, *J* = 8.4 Hz), 127.7, 127.5 (d, *J* = 3.6 Hz), 124.7, 124.1 (d, *J* = 2.5 Hz), 123.9, 123.7 (d, *J* = 12.7 Hz), 123.3 (d, *J* = 2.1 Hz), 117.5, 115.8 (d, *J* = 22.1 Hz), 62.5, 36.1, 23.9. IR (KBr) γ 2955, 2922, 2851, 1660, 1482, 1460, 1395, 756 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{18}H_{17}ONF$: 282.1289, observed: 282.1283.

(*S,E*)-1-(2-(2-methoxystyryl)indolin-1-yl)ethanone(3f)

Colorless oil. Yield: 68%, 19.9mg. $[\alpha]_D^{20}$ = -19.7 (c 0.20, $CHCl_3$). Enantiomeric excess: 79%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 13.20 min (minor), t_R = 15.06 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 6.8 Hz, 1H), 7.34 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.24 – 7.11 (m, 3H), 7.08 – 6.96 (m, 1H), 6.92 – 6.80 (m, 3H), 6.21 (dd, *J* = 16.0, 7.8 Hz, 1H), 5.12 – 4.78 (m, 1H), 3.81 (s, 3H), 3.58 (dd, *J* = 15.5, 10.0 Hz, 1H), 2.92 (d, *J* = 16.0 Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 156.8, 142.4, 129.8, 129.1, 129.0, 127.5, 126.9, 125.9, 124.8, 124.7, 123.7, 120.6, 117.5, 110.9, 62.9, 55.4, 36.3, 24.0. IR (KBr) γ 2955, 2920, 2850, 1657, 1461, 1395, 1247, 1023, 754 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{19}H_{20}O_2N$: 294.1489, observed: 294.1484.

(*S,E*)-1-(2-(2-(naphthalen-2-yl)vinyl)indolin-1-yl)ethanone(3g)

Colorless oil. Yield: 58%, 18.1mg. $[\alpha]_D^{20}$ = +17.9 (c 0.07, $CHCl_3$). Enantiomeric excess: 77%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 16.88 min (minor), t_R = 18.51 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 6.8 Hz, 1H), 7.84 – 7.63 (m, 4H), 7.54 – 7.36 (m, 3H), 7.27 – 7.16 (m, 2H), 7.05 (td, *J* = 7.4, 0.9 Hz, 1H), 6.64 (d, *J* = 15.8 Hz, 1H), 6.31 (dd, *J* = 15.9, 7.1 Hz, 1H), 5.10 – 4.91 (m, 1H), 3.60 (dd, *J* = 14.7, 10.1 Hz, 1H), 2.95 (d, *J* = 15.9 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 142.4, 133.4, 133.2, 133.1, 130.7, 129.6, 128.7, 128.3, 127.9, 127.7, 127.6, 126.7, 126.4, 126.1, 124.8, 123.9, 123.3, 117.5, 62.3, 36.2, 23.9. IR (KBr) γ 2955, 2921, 2850, 1459, 1376, 1093, 1022, 756 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{22}H_{20}ON$: 314.1539, observed: 314.1534.

(*S,E*)-1-(2-(2-cyclohexylvinyl)indolin-1-yl)ethanone(3h)

Colorless oil. Yield: 54%, 14.5mg. $[\alpha]_D^{20}$ = -12.4 (c 0.26, $CHCl_3$). Enantiomeric excess: 80%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 10.33 min (minor), t_R = 12.10 min

(major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (t, *J* = 12.9 Hz, 1H), 7.24 – 7.10 (m, 2H), 7.01 (t, *J* = 7.4 Hz, 1H), 5.57 (dd, *J* = 15.5, 6.4 Hz, 1H), 5.41 (dd, *J* = 15.6, 7.3 Hz, 1H), 4.73 (t, *J* = 8.0 Hz, 1H), 3.50 (dd, *J* = 15.6, 9.9 Hz, 1H), 2.80 (d, *J* = 15.9 Hz, 1H), 2.22 (s, 3H), 1.99 – 1.85 (m, 1H), 1.75 – 1.55 (m, 4H). 1.38 – 0.86 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 142.4, 138.0, 129.8, 127.5, 126.6, 124.6, 123.7, 117.4, 62.4, 40.0, 36.3, 32.7, 32.6, 26.0, 25.9, 23.9.IR (KBr) γ 2954, 2923, 2852, 1662, 1459, 1396, 1022, 755 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{18}H_{24}ON$: 270.1852, observed: 270.1849.

(*S*)-1-(2-(2,2-diphenylvinyl)indolin-1-yl)ethanone(3i)

Colorless oil. Yield: 30%, 10.1mg. $[\alpha]_D^{20}$ = -143.5 (c 0.12, $CHCl_3$). Enantiomeric excess: 82%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 11.07 min (major), t_R = 12.59 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 7.3 Hz, 1H), 7.53 – 7.35 (m, 3H), 7.26 – 7.14 (m, 9H), 7.03 (td, *J* = 7.4, 1.0 Hz, 1H), 6.14 (d, *J* = 9.5 Hz, 1H), 4.84 (t, *J* = 8.6 Hz, 1H), 3.59 (dd, *J* = 15.2, 10.1 Hz, 1H), 3.09 (d, *J* = 15.8 Hz, 1H), 1.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 142.7, 142.2, 140.8, 138.7, 129.8, 129.7, 128.6, 128.3, 128.2, 128.0, 127.9, 127.7, 127.4, 124.6, 123.8, 117.5, 59.3, 37.0, 23.7. IR (KBr) γ 2955, 2921, 2851, 1460, 1378, 1093, 1023, 762 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{24}H_{22}ON$: 340.1696, observed: 340.1687.

(*S,E*)-1-(6-chloro-2-styrylindolin-1-yl)ethanone(3j)

Colorless oil. Yield: 75%, 22.3mg. $[\alpha]_D^{20}$ = -64.7 (c 0.10, $CHCl_3$). Enantiomeric excess: 85%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 10.72 min (minor), t_R = 12.30 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.34 – 7.23 (m, 5H), 7.06 (d, *J* = 7.9 Hz, 1H), 6.99 (dd, *J* = 7.9, 1.9 Hz, 1H), 6.47 (d, *J* = 15.9 Hz, 1H), 6.17 (dd, *J* = 15.9, 7.1 Hz, 1H), 5.09 – 4.88 (m, 1H), 3.52 (dd, *J* = 15.7, 9.8 Hz, 1H), 2.87 (d, *J* = 16.0 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 143.3, 135.6, 133.1, 130.8, 128.6, 128.1, 128.0, 127.9, 126.5, 125.4, 123.8, 117.7, 62.7, 35.6, 23.8. IR (KBr) γ

2955, 2921, 2851, 1664, 1474, 1418, 1390, 1093, 1022 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{18}H_{17}ONCl$: 298.0993, observed: 298.0987.

(*S,E*)-1-(6-methyl-2-styrylindolin-1-yl)ethanone(3k)

Colorless oil. Yield: 75%, 20.9mg. $[\alpha]_D^{20}$ = -72.9 (c 0.14, $CHCl_3$). Enantiomeric excess: 85%, determined by HPLC (CHIRALPAK IC-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 10.47 min (minor), t_R = 11.67 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.33 – 7.19 (m, 5H), 7.04 (d, *J* = 7.3 Hz, 1H), 6.85 (d, *J* = 7.5 Hz, 1H), 6.47 (d, *J* = 15.9 Hz, 1H), 6.18 (dd, *J* = 15.9, 7.1 Hz, 1H), 5.02 – 4.86 (m, 1H), 3.52 (dd, *J* = 14.5, 10.2 Hz, 1H), 2.85 (d, *J* = 15.8 Hz, 1H), 2.36 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 142.4, 137.5, 135.9, 130.4, 128.6, 128.5, 128.0, 126.6, 126.4, 124.6, 124.3, 118.2, 62.5, 35.8, 23.9, 21.6. IR (KBr) γ2955, 2921, 2850, 1658, 1460, 1378, 1022, 755 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{19}H_{20}ON$: 278.1539, observed: 278.1534.

(*S,E*)-methyl 1-acetyl-2-styrylindoline-6-carboxylate(3l)

Colorless oil. Yield: 74%, 23.8mg. $[\alpha]_D^{20}$ = -97.8 (c 0.50, $CHCl_3$). Enantiomeric excess: 84%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 56.31 min (minor), t_R = 61.99 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (s, 1H), 7.78 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.32 – 7.20 (m, 6H), 6.50 (d, *J* = 15.9 Hz, 1H), 6.19 (dd, *J* = 15.9, 7.0 Hz, 1H), 5.14 – 4.92 (m, 1H), 3.91 (s, 3H), 3.62 (dd, *J* = 15.0, 9.6 Hz, 1H), 2.97 (d, *J* = 16.6 Hz, 1H), 2.23 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 167.0, 142.5, 135.7, 134.9, 130.8, 130.0, 128.6, 128.2, 127.9, 126.5, 125.9, 124.6, 118.2, 62.3, 52.1, 36.2, 23.9. IR (KBr) γ 2922, 1717, 1663, 1433, 1392, 1277, 1088, 758 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for$C_{20}H_{20}O_3N$: 322.1438, observed: 322.1434.

(*S,E*)-1-(5-chloro-2-styrylindolin-1-yl)ethanone(3m)

Colorless oil. Yield: 48%, 14.3mg. $[\alpha]_D^{20}$ = +7.6 (c 0.18, $CHCl_3$). Enantiomeric excess: 67%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 85/15,

flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 16.81 min (minor), t_R = 18.29 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 7.7 Hz, 1H), 7.32 – 7.11 (m, 7H), 6.47 (d, *J* = 15.9 Hz, 1H), 6.16 (dd, *J* = 15.9, 7.1 Hz, 1H), 5.04 – 4.82 (m, 1H), 3.54 (dd, *J* = 15.6, 9.9 Hz, 1H), 2.87 (d, *J* = 16.2 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 141.0, 135.6, 131.5, 130.8, 128.7, 128.6, 128.4, 128.1, 127.8, 127.5, 126.5, 124.9, 118.3, 62.3, 35.9, 23.8. IR (KBr) γ 2955, 2921, 2851, 1661, 1468, 1392, 1091, 1021 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{18}H_{17}ONCl$: 298.0993, observed: 298.0989.

(*S,E*)-1-(5-methyl-2-styrylindolin-1-yl)ethanone(3n)

Colorless oil. Yield: 53%, 14.9mg. $[\alpha]_D^{20}$ = -29.1 (c 0.14, $CHCl_3$). Enantiomeric excess: 77%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 13.26 min (minor), t_R = 16.14 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.8 Hz, 1H), 7.33 – 7.20 (m, 5H), 7.10 – 6.89 (m, 2H), 6.47 (d, *J* = 15.9 Hz, 1H), 6.18 (dd, *J* = 15.9, 7.1 Hz, 1H), 4.93 (t, *J* = 7.3 Hz, 1H), 3.54 (dd, *J* = 15.4, 9.9 Hz, 1H), 2.85 (d, *J* = 15.9 Hz, 1H), 2.30 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 140.1, 135.8, 133.5, 130.4, 129.6, 128.6, 128.5, 128.0, 128.0, 126.4, 125.4, 117.2, 62.2, 36.1, 23.8, 20.9. IR (KBr) γ 2955, 2921, 2851, 1460, 1378, 1093, 1022, 761 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{19}H_{20}ON$: 278.1539, observed: 278.1535.

(*S,E*)-methyl 1-acetyl-2-styrylindoline-5-carboxylate(3o)

Colorless oil. Yield: 40%, 12.8mg. $[\alpha]_D^{20}$ = +24.0 (c 0.28, $CHCl_3$). Enantiomeric excess: 58%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 21.70 min (major), t_R = 24.53 min (minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 – 8.14 (m, 1H), 7.98 – 7.93 (m, 1H), 7.86 (s, 1H), 7.36 – 7.20 (m, 5H), 6.50 (d, *J* = 15.9 Hz, 1H), 6.20 (dd, *J* = 15.9, 7.2 Hz, 1H), 5.25 – 4.91 (m, 1H), 3.89 (s, 3H), 3.61 (dd, *J* = 15.6, 10.0 Hz, 1H), 2.97 (d, *J* = 16.1 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 166.7, 146.2, 135.6, 131.0, 130.3, 129.8, 128.7, 128.2, 127.9, 126.5, 126.3, 125.6, 116.7, 62.6, 51.9, 35.7, 24.1.

IR (KBr) γ 2955, 2922, 2851, 1716, 1669, 1448, 1382, 1261, 1212 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{20}H_{20}O_3N$: 322.1438, observed: 322.1429.

(*S,E*)-1-(5-methoxy-2-styrylindolin-1-yl)ethanone(3p)

Brown oil. Yield: 83%, 24.3mg. $[\alpha]_D^{20}$ = -28.7 (c 0.44, $CHCl_3$). Enantiomeric excess: 67%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 21.55 min (minor), t_R = 24.83 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.6 Hz, 1H), 7.34 – 7.20 (m, 5H), 6.86 – 6.67 (m, 2H), 6.48 (d, *J* = 15.9 Hz, 1H), 6.20 (dd, *J* = 15.9, 7.1 Hz, 1H), 4.97 (t, *J* = 8.1 Hz, 1H), 3.78 (s, 3H), 3.59 (dd, *J* = 16.0, 9.7 Hz, 1H), 2.89 (d, *J* = 16.1 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 156.5, 136.1, 135.8, 131.2, 130.5, 128.6, 128.3, 128.1, 126.5, 118.1, 112.1, 111.0, 62.4, 55.6, 36.3, 23.7. IR (KBr) γ 2956, 2924, 2852, 1652, 1487, 1460, 1395, 1272, 1192, 1033 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{19}H_{20}O_2N$: 294.1489, observed: 294.1486.

(*S,E*)-1-(5-fluoro-2-styrylindolin-1-yl)ethanone(3q)

Colorless oil. Yield: 72%, 20.2mg. $[\alpha]_D^{20}$ = -52.5 (c 0.34, $CHCl_3$). Enantiomeric excess: 74%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 95/5, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 50.12 min (minor), t_R = 54.70 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 4.7 Hz, 1H), 7.34 – 7.21 (m, 5H), 7.00 – 6.72 (m, 2H), 6.48 (d, *J* = 15.9 Hz, 1H), 6.18 (dd, *J* = 15.9, 7.1 Hz, 1H), 4.98 (t, *J* = 7.6 Hz, 1H), 3.57 (dd, *J* = 15.9, 9.8 Hz, 1H), 2.89 (d, *J* = 16.2 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 159.4 (d, *J* = 242.4 Hz), 138.5, 135.7, 131.6 (d, *J* = 8.3 Hz), 130.8, 128.6, 128.1, 128.0, 126.5, 118.2 (d, *J* = 7.8 Hz), 113.9 (d, *J* = 22.6 Hz), 112.0 (d, *J* = 24.0 Hz),111.9, 62.4, 36.0, 23.7. IR (KBr) γ 2955, 2924, 1659, 1481, 1393, 1356, 1259, 1180, 751 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{18}H_{17}ONF$: 282.1289, observed: 282.1285.

(*S,E*)-1-(2-styryl-6-(trifluoromethyl)indolin-1-yl)ethanone(3r)

Brown oil. Yield: 75%, 24.8mg. $[\alpha]_D^{20}$ = -57.5 (c 0.48, $CHCl_3$). Enantiomeric

excess: 87%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 95/5, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 27.32 min (minor), t_R = 29.43 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.35 – 7.23 (m, 7H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.19 (dd, *J* = 15.9, 7.1 Hz, 1H), 5.14 – 4.89 (m, 1H), 3.62 (dd, *J* = 16.0, 10.0 Hz, 1H), 2.98 (d, *J* = 16.5 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 142.8, 135.5, 133.5, 131.1, 130.2 (q, *J* = 32.0 Hz), 128.7, 128.3, 127.7, 126.5, 124.9, 124.2 (q, *J* = 272.4 Hz), 120.9 (q, *J* = 3.8 Hz), 114.4, 62.4, 36.1, 23.9. IR (KBr) γ 2955, 2922, 2852, 1667, 1438, 1395, 1324, 1290, 1162, 1122, 1060, 1022, 751 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{19}H_{17}ONF_3$: 332.1257, observed: 332.1251.

(*S,E*)-ethyl 3-(1-acetylindolin-2-yl)acrylate(3s)[12]

Yellow oil. Yield: 40%, 10.3mg. $[\alpha]_D^{20}$ = -77.1 (c 0.14, $CHCl_3$). Enantiomeric excess: 79%, determined by HPLC (CHIRALPAK IC, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 16.97 min (minor), t_R = 20.55 min (major). ^{1}H NMR (400 MHz, DMSO) δ 8.04 (d, *J* = 7.0 Hz, 1H), 7.30 – 7.12 (m, 2H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.88 (dd, *J* = 15.5, 5.1 Hz, 1H), 5.77 (dd, *J* = 15.7, 1.0 Hz, 1H), 5.29 (dd, *J* = 9.6, 5.5 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.53 (dd, *J* = 16.4, 9.3 Hz, 1H), 2.89 (d, *J* = 16.2 Hz, 1H), 2.12 (s, 3H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 168.52, 165.14, 146.97, 142.04, 129.61, 127.30, 125.12, 123.76, 120.02, 116.44, 60.23, 59.78, 39.52, 34.22, 23.40, 14.00.

(*S,E*)-3-styrylisochroman(5a)

Colorless oil. Yield: 36%, 8.5mg. $[\alpha]_D^{20}$ = -91.0 (c 0.13, $CHCl_3$). Enantiomeric excess: 80%, determined by HPLC (CHIRALCEL OD-H, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 6.70 min (minor), t_R = 11.47 min (major). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.3 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.27 – 7.14 (m, 4H), 7.07– 6.98 (m, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 6.36 (dd, *J* = 16.0, 5.9 Hz, 1H), 5.01 – 4.84 (m, 2H), 4.46 – 4.31 (m, 1H), 2.96 (dd, *J* = 16.2, 10.4 Hz, 1H), 2.87 (dd, *J* = 16.2, 3.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.7, 134.5, 132.9, 131.0, 129.4, 128.8, 128.5, 127.7, 126.5, 126.5, 126.1, 124.2, 75.1, 68.0,

34.2. IR (KBr) γ 2955, 2921, 2851, 1460, 1377, 1271, 1023, 750 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{17}H_{17}O$: 237.1274, observed: 237.1272.

(*S,E*)-3-(4-fluorostyryl)isochroman(5b)

Colorless oil. Yield: 50%, 12.7mg. $[\alpha]_D^{20}$ = -102.0 (c 0.20, $CHCl_3$). Enantiomeric excess: 79%, determined by HPLC (CHIRALPAK ID, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 5.16 min (minor), t_R = 6.05 min (major). ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 – 6.96 (m, 8H), 6.68 (d, *J* = 16.0 Hz, 1H), 6.27 (dd, *J* = 15.9, 5.4 Hz, 1H), 5.01 – 4.81 (m, 2H), 4.44 – 4.27 (m, 1H), 3.02 – 2.72 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ162.4 (d, *J* = 246.9 Hz), 134.4, 132.9, 132.8, 129.8, 129.2 (d, *J* = 2.2 Hz), 128.8, 128.0 (d, *J* = 8.0 Hz), 126.5, 126.2, 124.2, 115.5 (d, *J* = 21.6 Hz), 75.0, 68.0, 34.2. IR (KBr) γ 2922, 2849, 1507, 1276, 1261, 1227, 1088, 965, 748 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{17}H_{16}OF$: 255.1180, observed: 255.1176.

(*S,E*)-3-(4-methoxystyryl)isochroman(5c)

Colorless oil. Yield: 46%, 12.2mg. $[\alpha]_D^{20}$ = -39.2 (c 0.24, $CHCl_3$). Enantiomeric excess: 80%, determined by HPLC (CHIRALPAK ID, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 7.36 min (minor), t_R = 8.18 min (major). ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.4 Hz, 2H), 7.22 – 7.09 (m, 3H), 7.07 – 6.95 (m, 1H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.66 (d, *J* = 16.0 Hz, 1H), 6.22 (dd, *J* = 16.0, 6.0 Hz, 1H), 5.00 – 4.81 (m, 2H), 4.41 – 4.27 (m, 1H), 3.81 (s, 3H), 3.05 – 2.74 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 134.5, 133.1, 130.7, 129.4, 128.8, 127.7, 127.2, 126.4, 126.1, 124.23, 114.0, 75.3, 68.0, 55.3, 34.3. IR (KBr) γ2922, 2849, 1507, 1276, 1261, 1227, 1088, 748cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{18}H_{19}O_2$: 267.1380, observed: 267.1380.

(*S,E*)-3-(2-(naphthalen-2-yl)vinyl)isochroman(5d)

Colorless oil. Yield: 76%, 21.7mg. $[\alpha]_D^{20}$ = -63.3 (c 0.45, $CHCl_3$). Enantiomeric excess: 71%, determined by HPLC (CHIRALPAK ID, hexane/isopropanol = 70/30, flow rate 1.0 mL/min, T = 30°C, 254 nm): t_R = 6.32 min (minor), t_R = 7.01 min (major). ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.72 (m, 4H), 7.63 (dd, *J* = 8.6, 1.4

Hz, 1H), 7.49 – 7.36 (m, 2H), 7.22 – 7.12 (m, 3H), 7.07 – 6.99 (m, 1H), 6.87 (d, *J* = 16.0 Hz, 1H), 6.48 (dd, *J* = 16.0, 5.9 Hz, 1H), 5.03 – 4.86 (m, 2H), 4.49 – 4.34 (m, 1H), 3.08 – 2.80 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.5, 134.2, 133.6, 133.1, 133.0, 131.1, 129.8, 128.9, 128.2, 128.0, 127.7, 126.6, 126.5, 126.3, 126.2, 125.9, 124.2, 123.5, 75.2, 68.1, 34.3. IR (KBr) γ 2922, 2849, 1507, 1276, 1261, 1227, 1088, 748 cm^{-1}. HRMS (ESI) m/z $(M+H)^+$ calculated for $C_{21}H_{19}O$: 287.1430, observed: 287.1429.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/

Complete description of methods and additional results;
spectroscopic data for all new compounds; synthesis procedures for substrates (PDF)

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Notes

The authors declare no competing financial interest.

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