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J. Org. Chem., **Just Accepted Manuscript** • Publication Date (Web): 29 May 2017

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Asymmetric Construction of 3,3-Disubstituted Oxindoles Bearing Vicinal Quaternary-Tertiary Carbon Stereocenters Catalyzed by a Chiral-at-Rhodium Complex

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■ ABSTRACT

A highly diastereo- and enantioselective synthesis of 3,3-disubstituted oxindoles bearing vicinal quaternary-tertiary carbon centers is enabled by a chiral-at-rhodium Lewis acid catalyst, starting from isatin *N*-protected ketimines and 2-acyl imidazoles. The excellent results with 93 to 99% yields, diastereoselectivities of 43:1 to >200:1 dr, and high enantioselectivities of 98.5 to >99% ee confirm the potential of bis-cyclometalated rhodium catalysts for the development of effective asymmetric transformations.

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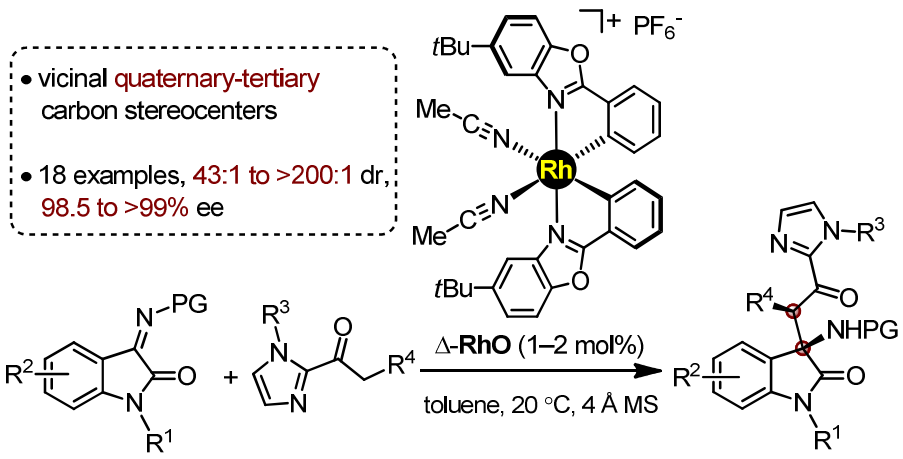


Optical active 3,3-disubstituted oxindoles are highly valuable building blocks for biologically active nature products and pharmaceuticals.[1] Consequently, their synthesis, in particular catalytic asymmetric approaches, have attracted significant attention over the past decades.[2–7] Of them, the Mannich-type reaction of isatin-derived ketimines with different nucleophiles provides an efficient route to chiral 3,3-disubstituted oxindoles containing a 3-amino substituent in addition to adjacent quaternary-tertiary carbon stereocenters.[4] The construction of such stereogenic centers remains a challenging task in organic synthesis, presumably owing to the steric congestion around the stereocenters.[8] For instance, Guo's group developed an enantioselective and solvent-controlled diastereoselective reaction of isatin ketimines with hydroxyacetone by a chiral amino acid catalyst.[4a] Wang and coworkers applied a quinidine-derived organocatalyst to the first direct asymmetric vinylogous Mannich reaction of γ-butenolides with isatin-derived ketimines.[4c] Silvani's group reported the stereoselective addition of trimethylsiloxyfuran to isatin-derived benzhydryl ketimines catalyzed by a chiral phosphoric acid.[4e] In these cases, although the enantioselectivities were good to excellent, only very modest diastereoselectivities were achieved. Recently, Wu *et. al* [4b] and our group[4d] reported the highly diastereoselective and enantioselective Mannich reaction of isatin-derived ketimines to build up vicinal quaternary-tertiary carbon centers on the oxindole scaffold by using a tertiary amine-thiourea catalyst and a metal-templated Brønsted base, respectively. Despite these advances, strategies to gain command of both the absolute and relative configuration in one single chemical transformation are still demanded for the synthesis of such optical active molecules. Herein, we wish to report our progress on utilizing asymmetric catalysts which draw their chirality exclusively from metal-centered chirality[9–11] to catalyze an asymmetric Mannich-type reaction between 2-acyl imidazoles and isatin *N*-protected ketimines (Figure 1). Very high diastereoselectivities (43:1 – >200:1 dr) and enantioselectivities (98.5 – >99% ee) were achieved for a variety of substrates (18 examples).

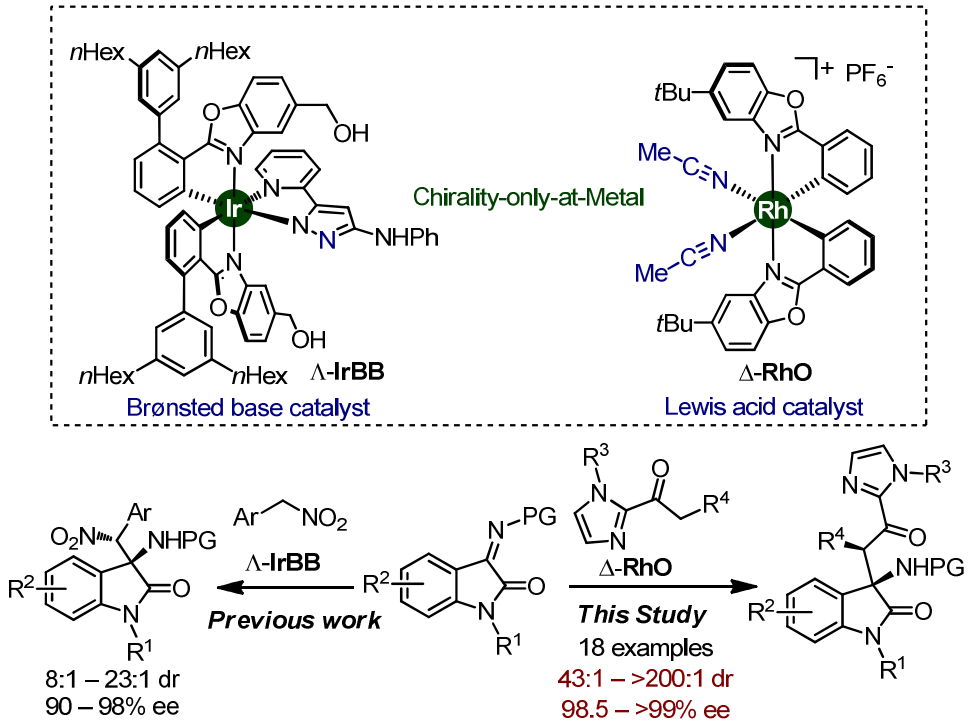
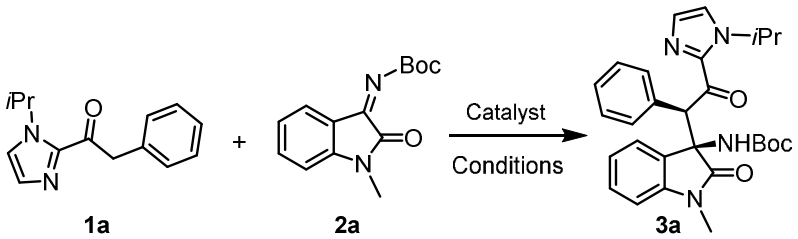


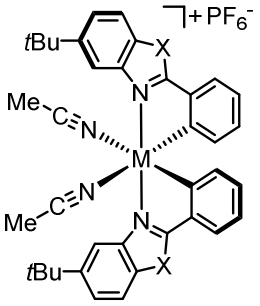
Figure 1. Previous work and this study on stereoselective synthesis of chiral 3,3-disubstituted oxindoles by chiral-at-metal catalysts.

We recently developed highly efficient chiral Lewis acid catalysts based on an octahedral bis-cyclometalated chiral-at-metal scaffold.[10] For example, complex Δ-**RhO**[10c] features exclusive metal-centered chirality which is comprised of a rhodium center, two bidentate benzoxazole ligands and two substitutionally labile acetonitriles in addition to a hexafluorophosphate counterion (Figure 1). It exhibits high catalytic activity and excellent stereocontrol for a range of asymmetric organic transformations.[10] In order to expand our investigations to other challenging transformations which desire a control of both the enantioselectivity and diastereoselectivity, the Mannich-type reaction of 2-acyl imidazole **1a** with isatin *N*-Boc ketimine **2a** was examined in the presence of 5 mol% Δ-**RhO** in dichloromethane. Gratifyingly, the desired product **3a** was generated, although with a sluggish rate and with modest stereoselectivities (70% conversion within 75 h, 5.3:1 dr and 79% ee, Table 1, entry 1). We subsequently optimized the reaction conditions including solvent, catalyst loading, additives, and temperature. As revealed in entries 2–5, toluene served as the best solvent for the transformation **1a**+**2a**→**3a** by providing a 93% conversion in 5 h, 100:1 dr and 97% ee. Further decrease of catalyst loading to 2 mol% and addition of 4 Å molecular sieves (MS) led to the optimal conditions, enabling the reaction to be completed within 14 h to afford **3a** with 49:1 dr and 98% ee (entry 7). Moreover, a rhodium benzothiazole derivative Δ-**RhS**[10e] (entry 10) and an analogous

iridium complex Δ-**IrO**[10a] (entry 11) developed by us previously were also tested in the system. Both of them only provided trace amounts of the desired product at the standard conditions, indicating that the activity of the catalysts in this reaction precisely relied on the chiral environment and inherent character of the metal center.

Table 1. Initial Experiments and Optimization[a]





Catalyst	M	X
Δ-**RhO**	Rh	O
Δ-**RhS**	Rh	S
Δ-**IrO**	Ir	O

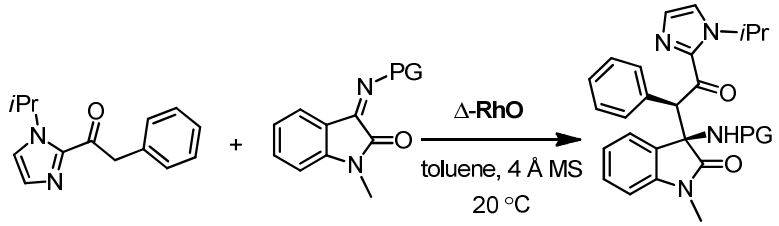
entry	cat. (mol%)	solvent	additives	T (°C)	t (h)	conv. (%)[b]	ee (%)[c]	dr[d]
1	Δ-**RhO**(5)	CH_2Cl_2	none	20	75	70	79	5.3:1
2	Δ-**RhO**(5)	THF	none	20	72	59	77	18:1
3	Δ-**RhO**(5)	MTBE	none	20	3	99	46	1:1.9
4	Δ-**RhO**(5)	DMF	none	20	72	11	–[e]	–[e]
5	Δ-**RhO**(5)	toluene	none	20	5	93	97	100:1
6	Δ-**RhO**(2)	toluene	none	20	14	99	96	80:1
7	Δ-**RhO**(2)	toluene	4Å MS	20	14	96	98	49:1
8	Δ-**RhO**(2)	toluene	4Å MS	40	4	96	96	80:1
9	Δ-**RhO**(2)	toluene	4Å MS	0	96	99	99	12:1
10	Δ-**RhS**(2)	toluene	4Å MS	20	14	<5	n.d.[e]	n.d.[e]
11	Δ-**IrO**(2)	toluene	4Å MS	20	14	<5	n.d.[e]	n.d.[e]
12	none	toluene	4Å MS	20	14	<5	n.d.[e]	n.d.[e]

[a]Reaction conditions: 2-acyl imidazole **1a** (0.10 mmol), isatin *N*-Boc ketimine **2a** (0.15 mmol), the metal catalyst (2–5 mol%), in the indicated solvent (1 mL) and at the indicated temperature in air.

[b]Conversion determined by ^{1}H NMR analysis. [c]Ee values of the major diastereomer determined by HPLC analysis on a chiral stationary phase. [d]Dr values determined by HPLC analysis on a chiral stationary phase. [e]Not determined.

We next examined the influence of protection groups of the isatin-derivated ketimines on the catalytic outcomes. As summarized in Table 2, the reaction was strongly dependent on steric and electronic effects of the *N*-protection group. For example, the benzyloxy carbamate (Cbz protection group) provided a slightly faster reaction rate and higher enantioselectivity (entry 2), while the electron-rich *p*-methoxyphenyl group (PMP) prevented a conversion to the desired product (entry 3). Most interestingly, the sterically less demanding methyloxy carbamate led to a significantly improvement of the reaction rate (94% yield in 2 h) as well as diastereo- and enantioselectivity (>200:1 dr, >99% ee, entry 4). We found that for substrate **2d**, the catalyst loading could be reduced to 1 mol% while still providing a satisfactory reaction time of 4 hours for 95% yield, 200:1 dr and >99% ee (entry 5). A further reduction of the catalyst loading to 0.5 and 0.2 mol% resulted in slightly lower stereoselectivities (entries 6–8).

Table 2. Comparison of Protection Groups (PG) for the Isatin-Derivated Ketimines[a]

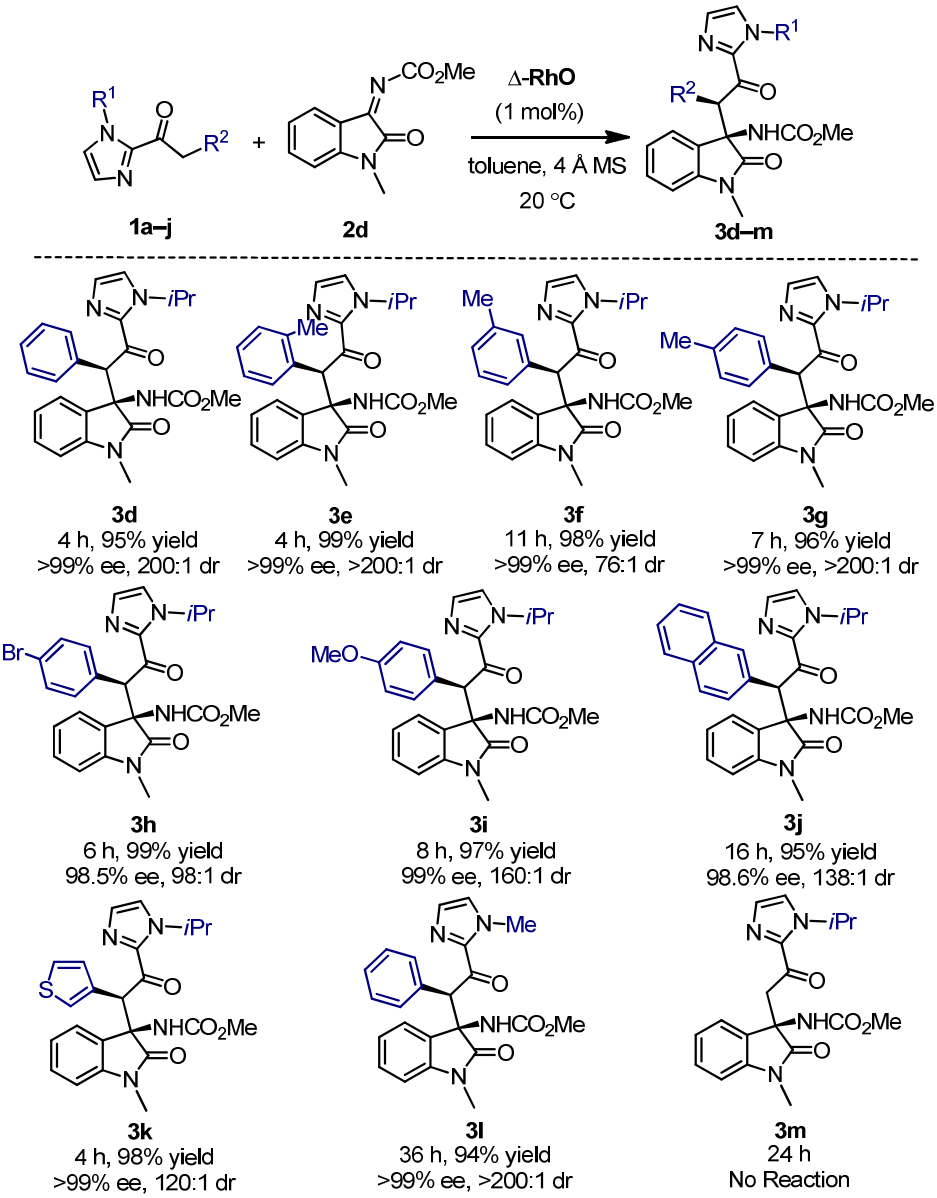


1a **2a-d** **3a-d**

entry	PG	cat. (mol%)	t(h)	yield (%)	ee (%)[b]	dr[c]
1[d]	Boc(**2a**)	2	14	88	98	49:1
2	Cbz(**2b**)	2	12	96	>99	48:1
3	PMP(**2c**)	2	12	0	n.a.[e]	n.a.[e]
4	COOMe(**2d**)	2	2	94	>99	> 200:1
5	COOMe(**2d**)	1	4	95	>99	200:1
6	COOMe(**2d**)	0.5	20	93	99	55:1
7	COOMe(**2d**)	0.2	64	46	92	2.4:1
8[f]	COOMe(**2d**)	0.2	24	94	98	29:1

[a]Reaction conditions: 2-acyl imidazole **1a** (0.10 mmol), isatin *N*-protected ketimine **2a–d** (0.15 mmol), metal catalyst (0.2–2 mol%), 4Å MS (5.0 mg), toluene (1 mL) in air. [b]Ee values of the major diastereomer determined by HPLC analysis on a chiral stationary phase. [c]Dr values determined by HPLC analysis on a chiral stationary phase. [d]Taken from entry 7 of Table 1. [e]Not applicable. [f]Carried out at 40 °C.

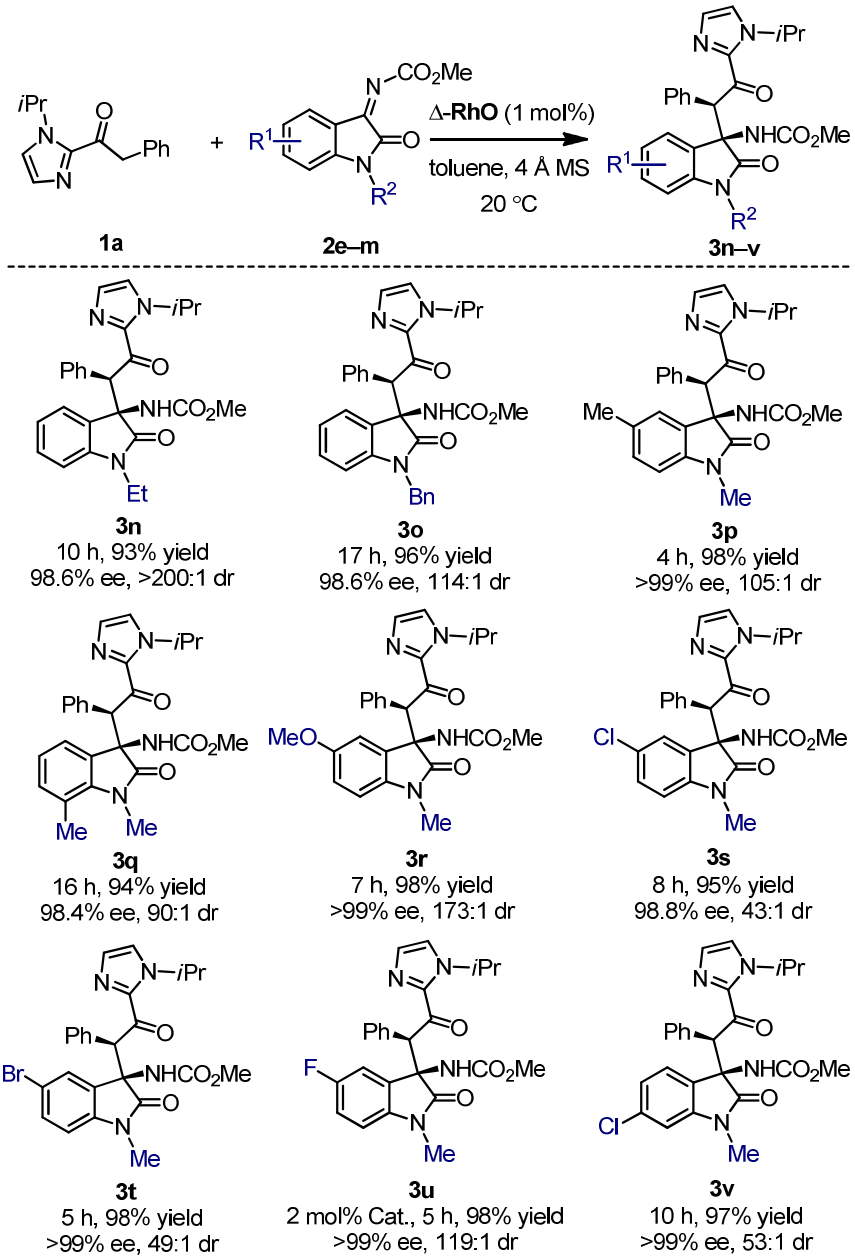
Scheme 1. Scope Regarding 2-Acyl Imidazoles.



With the optimal conditions and the best protection group for ketimine substrates in hand, we evaluated the generality of the catalytic reaction with respect to 2-acyl imidazoles and isatin derivated ketimines. First, a range of 2-acyl imidazoles containing phenyl groups with methyl substituents at *meta*-, *ortho*- or *para*-position (products **3e–g**), electron withdrawing (product **3h**) or donating (products **3i**) groups, a naphthyl moiety (product **3j**), and a heteroaromatic ring (product **3k**) at the β-position to the 2-acyl imidazoles moiety were established to be nicely compatible in this reaction (Scheme 1). The products **3d–k** were provided in 95 – 99% yield with 76:1 – >200:1 dr and 98.5 – >99% ee. Notably, an *N*-methyl protected imidazole (product **3l**) required a longer

reaction time of 36 h, but still provided excellent stereoselectivities. However, the substrate **1j** without an aromatic substituent at the β-position of the 2-acyl imidazole moiety failed to provide the desired product. Furthermore, Scheme 2 reveals that different aryl substituents were also well tolerated for the isatin-derivated ketimines. In all of the nine examples, the desired products **3n–v** were generated with excellent yields, dr, and ee values.

Scheme 2. Scope Regarding Isatin-Derivated Ketimines.

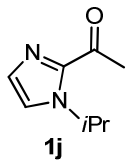


In summary, we have developed a highly diastereo- and enantioselective synthesis of 3,3-disubstituted oxindoles bearing vicinal quaternary-tertiary carbon centers by using a chiral-at-rhodium catalyst. Chiral oxindoles were obtained in 93 – 99% yield, and with 43:1 – >200:1 dr and 98.5 – >99% ee (18 examples), thereby confirming the versatility of our bis-cyclometalated chiral-at-metal Lewis acids for asymmetric catalysis.

■ EXPERIMENTAL SECTION

General Information. Catalyst Δ-**RhO**,[10c] Δ-**RhS**,[10e] Δ-**IrO**,[10a] 2-acyl imidazoles[12] and *N*-alkoxycarbonyl ketimines[13] were prepared according to published procedures. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra (proton decoupled) were recorded on a Bruker AM (400 MHz or 500 MHz) spectrometer at ambient temperature. NMR standards were used as follows: ^{1}H NMR spectroscopy: δ = 7.26 ppm ($CDCl_3$), 3.31 ppm (CD_3OD), 2.05 ppm (CD_3COCD_3); $^{13}C\{^{1}H\}$ NMR spectroscopy: δ = 77.0 ppm ($CDCl_3$), 49.0 ppm (CD_3OD), 29.8 ppm (CD_3COCD_3). High-resolution mass spectra were recorded on a Bruker En Apex Ultra 7.0T FT-MS instrument using ESI technique (ICR：ion cyclotron resonance). Elemental analysis was performed on a Vario EL III (Germany).

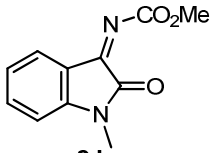
General Procedure for the Synthesis of 2-Acyl Imidazoles.[12] To a solution of *N*-methylimidazole or *N*-isopropylimidazole (1.2 eq) in anhydrous THF (0.6 M) at –78 °C was added *n*-BuLi (1.2 eq, 2.4 M in hexanes) dropwise. The reaction mixture was stirred at this temperature for 30 min, and then stirred at room temperature for 30 min. The corresponding Weinreb amide in THF (2.0 M) was added dropwise to the flask after the reaction mixture was cooled to –78 °C. The reaction mixture was allowed to warm to room temperature slowly and stirred overnight. The reaction was quenched with AcOH (6.0 eq) at room temperature and extracted with EtOAc. The organic phase was washed with aqueous saturated $NaHCO_3$, brine, dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude product was subjected to a silica gel flash chromatography (*n*-hexane/EtOAc = 5:1 to 3:1) to afford the pure substrates.



1j

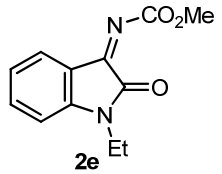
*1-(1-Isopropyl-1H-imidazol-2-yl)ethan-1-one (**1j**).* 1.25 g, 82% yield, colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.15 (d, J = 0.7 Hz, 1H), 7.04 (d, J = 0.5 Hz, 1H), 5.43 (hept, J = 6.7 Hz, 1H), 2.55 (s, 3H), 1.32 (d, J = 6.7 Hz, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 190.7, 142.4, 129.4, 121.0, 49.1, 27.8, 23.4; IR (film): ν (cm^{-1}) 2982, 2934, 2866, 1675, 1463, 1454, 1393, 1371, 1353, 1333, 1258, 1212, 1158, 1134, 1101, 1088, 1051, 953, 916, 770, 716, 666, 624; HRMS (ESI) *m/z* calcd for $C_8H_{12}N_2ONa$ $(M+Na)^+$ 175.0847, found: 175.0851.

Preparation of ketimines. In an oven-dried Schlenk tube under argon atmosphere, isatin (2.00 mmol) and *N*-carbomethoxy-triphenylphosphinimine (2.20 mmol) were placed. After an addition of anhydrous 1,4-dioxane (2.00 mL), the mixture was heated at 120 °C for 5 h. After that, additional *N*-carbomethoxy-triphenylphosphinimine (1.32 mmol) was added into the reaction mixture at room temperature, and the system was degassed *via* freeze-pump-thaw for three cycles. After the mixture was thoroughly degassed, the mixture was sealed and heated at 120 °C for additional 8 h, then cooled down to room temperature. After evaporation of the volatile organic solvent, the crude residue was purified by flash chromatography (silica gel, *n*-hexane/EtOAc = 3:1), and then recrystallized from *n*-hexane/EtOAc.



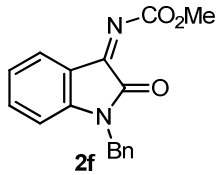
2d

*Methyl (Z)-(1-methyl-2-oxoindolin-3-ylidene)carbamate (**2d**).* 218 mg, 50% yield, orange solid, mp 128–130 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.61 (s, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.09 (t, J = 7.2 Hz, 1H), 6.84 (d, J = 7.8 Hz, 1H), 3.93 (s, 3H), 3.18 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 162.5, 157.2, 154.5, 148.1, 135.8, 124.5, 123.6, 118.8, 109.4, 53.8, 26.1; IR (film): ν (cm^{-1}) 2957, 2359, 1959, 1738, 1721, 1612, 1471, 1434, 1372, 1333, 1277, 1260, 1240, 1185, 1155, 1123, 1097, 1016, 982, 895, 879, 792, 751; HRMS (ESI) *m/z* calcd for $C_{11}H_{10}N_2O_3Na$ $(M+Na)^+$ 241.0584, found: 241.0583.



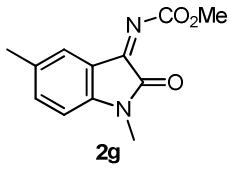
2e

*Methyl (Z)-(1-ethyl-2-oxoindolin-3-ylidene)carbamate (**2e**).* 200 mg, 43% yield, red solid, mp 114–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.56 (s, 1H), 7.45 (t, J = 7.6 Hz, 1H), 7.03 (t, J = 6.8 Hz, 1H), 6.83 (d, J = 7.7 z, 1H), 3.90 (s, 3H), 3.68 (d, J = 6.8 Hz, 2H), 1.22(t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm) 162.5, 156.7, 154.7, 147.2, 135.7, 124.5, 123.2, 118.7, 109.4, 53.6, 34.8, 12.3; IR (film): v (cm^{-1}) 2086, 1736, 1615, 1470, 1358, 1253, 1185, 1100, 987,751, 462; HRMS (ESI) *m/z* calcd for $C_{12}H_{12}N_2O_3Na$ $(M+Na)^+$ 255.0740, found: 255.0738.



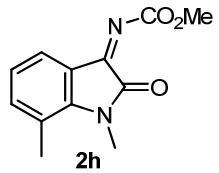
2f

*Methyl (E)-(1-benzyl-2-oxoindolin-3-ylidene)carbamate (**2f**).* 324 mg, 55% yield, orange solid, mp 102–104 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.54 (s, 1H), 7.29 (t, J = 7.7 Hz, 1H), 7.26–7.13 (m, 5H), 6.96 (t, J = 7.3 Hz, 1H), 6.65 (d, J = 7.9 Hz, 1H), 4.78 (s, 2H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 162.5, 157.3, 154.5, 147.4, 135.7, 134.4, 128.9, 128.0, 127.4, 124.6, 123.6, 118.9, 110.4, 53.9, 44.0; IR (film): v (cm^{-1}) 2069, 1737, 1616, 1470, 1435, 1354, 1250, 1182, 1100, 1002, 462; HRMS (ESI) *m/z* calcd for $C_{17}H_{15}N_2O_3$ $(M+H)^+$ 295.1077, found: 295.1077.



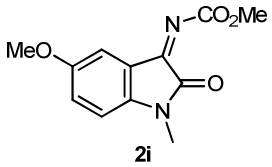
2g

*Methyl (E)-(1,5-dimethyl-2-oxoindolin-3-ylidene)carbamate (**2g**).* 162 mg, 35% yield, red solid, mp 142–144 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.34 (s, 1H), 7.22 (d, J = 7.9 Hz, 1H), 6.66 (d, J = 7.9 Hz, 1H), 3.87 (s, 3H), 3.09 (s, 3H), 2.24 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 162.6, 157.3, 154.8, 145.9, 136.2, 133.3, 124.9, 118.7, 109.2, 53.7, 26.1, 20.7; IR (film): v (cm^{-1}) 2922, 1959, 1729, 1676, 1620, 1601, 1494, 1422, 1359,1334, 1269, 1241, 1212, 1150, 1113, 1013, 914, 880, 820, 757, 727, 546, 458; HRMS (ESI) *m/z* calcd for $C_{12}H_{12}N_2O_3Na$ $(M+Na)^+$ 255.0740, found: 255.0740.



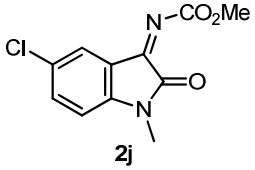
2h

*Methyl (E)-(1,7-dimethyl-2-oxoindolin-3-ylidene)carbamate (**2h**).* 214 mg, 46% yield, red solid, mp 148–150 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.40 (s, 1H), 7.17 (d, J = 7.7 Hz, 1H), 6.90 (t, J = 7.5 Hz, 1H), 3.88 (s, 3H), 3.38 (s, 3H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 162.5, 157.8, 154.5, 145.6, 139.5, 123.4, 122.2, 121.2, 119.3, 53.58, 29.30, 18.40; IR (film): ν (cm^{-1}) 2953, 1737, 1682, 1604, 1453, 1364, 1326, 1265, 1211, 1125,1084, 1040, 918, 875, 854, 790, 771, 734, 604, 534, 511; HRMS (ESI) *m/z* calcd for $C_{12}H_{12}N_2O_3Na$ $(M+Na)^+$ 255.0740, found: 255.0736.



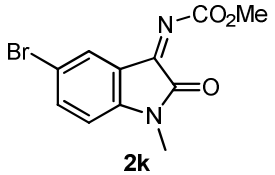
2i

*Methyl (E)-(5-methoxy-1-methyl-2-oxoindolin-3-ylidene)carbamate (**2i**).* 238 mg, 48% yield, maroon solid, mp 174–176 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.20 (s, 1H), 7.05 (d, J = 7.3 Hz, 1H), 6.75 (d, J = 8.5 Hz, 1H), 3.95 (s, 3H), 3.80 (s, 3H), 3.17 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 162.4, 157.3, 156.4, 155.0, 141.9, 121.7, 119.4, 110.2, 109.3, 55.8, 53.8, 26.1; IR (film): ν (cm^{-1}) 2360, 1787, 1743, 1722, 1676, 1640, 1631, 1552, 1530,1491, 1468, 1433, 1414, 1383, 1359, 1290, 1268, 1239, 1222, 1195, 1163, 1113, 1027, 998, 897, 878, 824, 805, 572, 460; HRMS (ESI) *m/z* calcd for $C_{12}H_{12}N_2O_4Na$ $(M+Na)^+$ 271.0689, found: 271.0687.



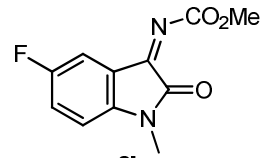
2j

*Methyl (E)-(5-chloro-1-methyl-2-oxoindolin-3-ylidene)carbamate (**2j**).* 162 mg, 32% yield, red solid, mp 149–151 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.53 (s, 1H), 7.41 (dd, J = 8.3, 1.9 Hz, 1H), 6.74 (d, J = 8.4 Hz, 1H), 3.88 (s, 3H), 3.13 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 161.9, 156.7, 153.6, 146.4, 135.2, 129.2, 124.3, 120.0, 110.6, 53.9, 26.2; IR (film): ν (cm^{-1}) 2921, 1959, 1741, 1683, 1613, 1483, 1462, 1434, 1356, 1240, 1198, 1179, 1113, 1074, 1013, 905, 879, 825, 807, 727, 662, 559, 538, 460; HRMS (ESI) *m/z* calcd for $C_{11}H_9ClN_2O_3Na$ $(M+Na)^+$ 275.0194, found: 275.0194.



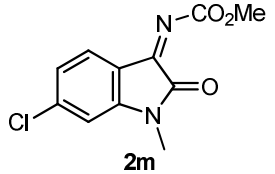
2k

*Methyl (E)-(5-bromo-1-methyl-2-oxoindolin-3-ylidene)carbamate (**2k**).* 238 mg, 40% yield, red solid, mp 140–142 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.67 (s, 1H), 7.59 (dd, J = 8.3, 1.9 Hz, 1H), 6.74 (d, J = 8.3 Hz, 1H), 3.91 (s, 3H), 3.16 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 161.9, 156.5, 153.4, 146.8, 138.1, 127.1, 120.3, 116.2, 111.0, 53.9, 26.2; IR (film): ν (cm^{-1}) 2922, 2851, 1958, 1741, 1683, 1611, 1552, 1531, 1481, 1463, 1434, 1354, 1324, 1267, 1242, 1197, 1178, 1111, 1013, 901, 877, 457; HRMS (ESI) *m/z* calcd for $C_{11}H_9BrN_2O_3Na$ $(M+Na)^+$ 318.9689, found: 318.9687.



2l

*Methyl (E)-(5-fluoro-1-methyl-2-oxoindolin-3-ylidene)carbamate (**2l**).* 165 mg, 35% yield, red solid, mp 122–124 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.34 (s, 1H), 7.21 (td, J = 8.7, 2.6 Hz, 1H), 6.80 (dd, J = 8.6, 3.7 Hz, 1H), 3.94 (s, 3H), 3.19 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 162.1, 160.3, 158.3, 154.1, 144.2, 122.1 (d, J = 24.3 Hz), 119.9, 111.8 (d, J = 24.1 Hz), 110.3 (d, J = 7.5 Hz), 53.9, 26.2; IR (film): ν (cm^{-1}) 3067, 2957, 1739, 1682, 1622, 1489, 1437, 1360, 1336, 1276, 1243, 1210, 1159, 1108, 1055, 1013, 922, 882, 835, 795, 761, 723, 680, 548, 506, 461; HRMS (ESI) *m/z* calcd for $C_{11}H_9FN_2O_3Na$ $(M+Na)^+$ 259.0489, found: 259.0489.

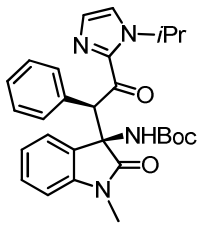


2m

*Methyl (E)-(6-chloro-1-methyl-2-oxoindolin-3-ylidene)carbamate (**2m**).* 212 mg, 42% yield, yellow solid, mp 146–148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.53 (s, 1H), 7.05 (d, J = 7.7 Hz, 1H), 6.84 (d, J = 1.6 Hz, 1H), 3.92 (s, 3H), 3.17 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 162.1, 157.1, 153.3, 149.1, 141.9, 125.4, 123.7, 117.1, 110.2, 53.8, 26.2; IR (film): ν (cm^{-1}) 2921, 1959, 1740, 1679, 1611, 1491, 1434, 1370, 1310, 1265, 1237, 1201, 1185, 1104, 1077, 1012,

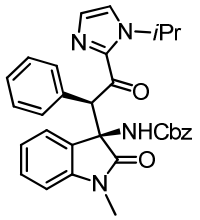
984, 911, 884, 852, 827, 805, 731, 602, 577, 468; HRMS (ESI) *m/z* calcd for $C_{11}H_9ClN_2O_3Na$ $(M+Na)^+$ 275.0194, found: 275.0195.

General Procedure for the Catalytic Reaction of 2-Acyl Imidazoles with Ketimines. To a solution of Δ-**RhO** catalyst (0.2–2.0 mol%) in anhydrous toluene was added 2-acyl imidazole **1a–j** (0.100 mmol) and 4Å MS (5.00 mg) in a brown glass vial. The mixture was stirred at 20 ℃ for 30 min, then ketimine **2a–m** (0.150 mmol) was added. The reaction mixture was stirred at 20 ℃ for the indicated time. Upon completion, the mixture was purified by flash chromatography on silica gel (*n*-hexane/EtOAc = 4:1 to 1:1) to afford product **3a–v**.



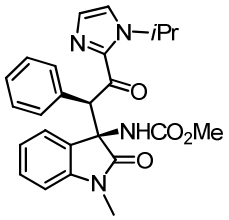
3a

*tert-Butyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (**3a**).* 43.0 mg, 88% yield, white solid, mp 147–149 °C; 98% ee, 49:1 dr (HPLC: Chiralpak IB, *n*-hexane/*i*-PrOH = 85:15–75:25 in 15 min with a linear gradient elution, flow rate: 0.80–0.50 mL/min in 15 min, 30 °C, 254 nm, major diastereomer: t_r(major) = 12.4 min, t_r(minor) = 16.1 min); $[\alpha]_D^{20}$ = –17.1 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.19 (s, 1H), 7.18–7.04 (m, 8H), 6.86 (t, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 7.1 Hz, 1H), 6.55 (d, *J* = 7.7 Hz, 1H), 5.53 (s, 1H), 5.38 (hept, 1H), 2.82 (s, 3H), 1.43 (d, *J* = 6.6 Hz, 3H), 1.27 (d, *J* = 6.7 Hz, 3H), 1.11 (s, 9H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 189.1, 175.6, 154.2, 143.9, 143.0, 132.5, 130.8, 130.0, 128.8, 127.9, 127.6, 125.0, 122.1, 121.7, 107.6, 79.9, 64.9, 55.2, 49.6, 28.0, 25.9, 23.7, 23.4. IR(film): *v* (cm^{-1}) 2966, 2924, 1722, 1691, 1678, 1613, 1493, 1469, 1454, 1392, 1255, 1165, 1090, 1023, 799, 750, 701; HRMS (ESI) *m/z* calcd for $C_{28}H_{32}N_4O_4Na$ $(M+Na)^+$ 511.2316, found: 511.2316.



3b

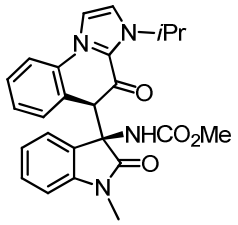
*Benzyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-1-methyl-2-oxoindol in-3-yl)carbamate (**3b**).* 50.2 mg, 96% yield, white solid, mp 141–143 °C; >99% ee, 48:1 dr (HPLC: Chiralpak IB, *n*-hexane/*i*-PrOH = 60:40–80:20 in 15 min with a linear gradient elution, flow rate: 0.40 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 21.2 min, t_r(major) = 24.1 min); $[\alpha]_D^{20}$ = –43.3 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.65 (s, 1H), 7.18 (s, 6H), 7.15–6.96 (m, 6H), 6.85 (t, *J* = 7.4 Hz, 1H), 6.74 (d, *J* = 7.0 Hz, 1H), 6.55 (s, 1H), 5.52 (s, 1H), 5.38 (hept, *J* = 6.5 Hz, 1H), 4.84 (s, 2H), 2.83 (s, 3H), 1.42 (d, *J* = 6.4 Hz, 3H), 1.26 (d, *J* = 6.5 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 189.1, 175.3, 155.0, 144.0, 142.8, 132.4, 130.7, 130.0, 129.1, 128.3, 128.0, 128.0, 127.9, 127.7, 127.0, 125.1, 122.2, 121.8, 107.8, 66.9, 64.9, 55.0, 49.6, 26.0, 23.6, 23.3; IR(film): ν (cm^{-1}) 3347, 2962, 2924, 2852, 1723, 1675, 1613, 1493, 1470, 1765, 1394, 1374, 1317, 1257, 1127, 1091, 1026, 828, 745, 698, 560; HRMS (ESI) *m*/*z* calcd for $C_{31}H_{30}N_4O_4Na$ $(M+Na)^+$ 545.2159, found: 545.2161.



3d

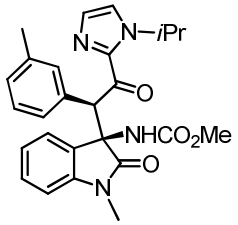
*Methyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-1-methyl-2-oxoindol in-3-yl)carbamate (**3d**).* 42.4 mg, 95% yield, white solid, mp 135–137 °C; >99% ee, >200:1 dr (HPLC: Chiralpak IB, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 12.6 min, t_r(major) = 14.5 min); $[\alpha]_D^{20}$ = –40.0 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.73 (s, 1H), 7.21 (s, 1H), 7.20–7.16 (m, 1H), 7.16–7.12 (m, 2H), 7.12–7.04 (m, 4H), 6.85 (t, *J* = 7.5 Hz, 1H), 6.70 (d, *J* = 7.3 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 5.50 (s, 1H), 5.38 (hept, *J* = 6.6 Hz, 1H), 3.45 (s, 3H), 2.86 (s, 3H), 1.43 (d, *J* = 6.6 Hz, 3H), 1.28 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 189.1, 175.4, 155.5, 144.0, 142.9, 132.4, 130.7, 130.0, 129.2, 128.0, 127.7, 126.9, 124.9, 122.3, 121.8, 107.7, 64.8, 54.9, 52.1, 49.6, 26.1, 23.7, 23.3;

IR(film): ν (cm^{-1}) 3350, 2962, 2925, 1724, 1676, 1614, 1493, 1470, 1456, 1394, 1375, 1318, 1256, 1195, 1128, 1090, 1025, 917, 798, 750, 700, 630, 540, 518; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{26}N_4O_4Na$ $(M+Na)^+$ 469.1846, found: 469.1847.



3e

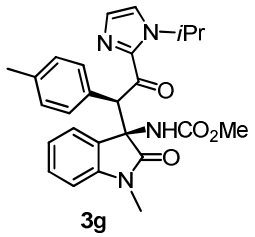
*Methyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-(o-tolyl)ethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (**3e**).* 45.6 mg, 99% yield, white solid, mp 132–134 °C; >99% ee, >200:1 dr (HPLC: Chiralpak IB, *n*-hexane/*i*-PrOH = 90:10, flow rate: 0.80 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 16.1 min, t_r(major) = 17.7 min); $[\alpha]_D^{20}$ = –32.3 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, CD_3OD) δ (ppm) 7.53 (s, 1H), 7.27 (dd, *J* = 16.5, 8.0 Hz, 2H), 7.16–7.06 (m, 2H), 7.05–6.93 (m, 2H), 6.86 (t, *J* = 7.3 Hz, 2H), 6.63 (d, *J* = 7.3 Hz, 1H), 5.82 (s, 1H), 5.46 (hept, *J* = 6.6 Hz, 1H), 3.50 (s, 3H), 3.02 (s, 3H), 2.03 (s, 3H), 1.50 (d, *J* = 6.7 Hz, 3H), 1.30 (d, *J* = 6.7 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, CD_3OD) δ (ppm) 191.0, 178.3, 157.6, 145.1, 143.9, 140.6, 132.2, 131.6, 131.0, 130.3, 130.1, 129.2, 129.0, 126.2, 126.1, 124.4, 123.2, 109.4, 66.4, 52.7, 50.9, 50.4, 26.6, 23.6, 23.5, 20.1; IR(film): ν (cm^{-1}) 3354, 3110, 3055, 2961, 2926, 1724, 1664, 1613, 1493, 1470, 1394, 1311, 1254, 1194, 1163, 1128, 1091, 1055, 1023, 962, 937, 917, 837, 783, 753, 689, 629, 560, 540, 500; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{29}N_4O_4$ $(M+H)^+$ 461.2183, found: 461.2183.



3f

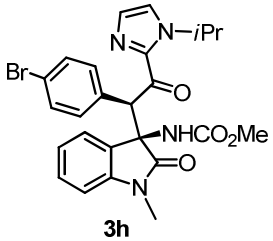
*Methyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-(m-tolyl)ethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (**3f**).* 45.1 mg, 98% yield, white solid, mp 163–165 °C; >99% ee, 76:1 dr (HPLC: Chiralpak IA, *n*-hexane/*i*-PrOH = 70:30, flow rate: 0.80 mL/min, 30 °C, 254 nm, major diastereomer: t_r(major) = 9.4 min, t_r(minor) = 18.9 min); $[\alpha]_D^{20}$ = –30.0 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, CD_3COCD_3) δ (ppm) 7.63 (s, 1H), 7.61 (s, 1H), 7.25 (t, *J* = 7.8 Hz, 2H), 7.15 (s, 1H),

7.05–6.93 (m, 3H), 6.93–6.87 (m, 1H), 6.86 (s, 1H), 6.73 (d, J = 7.7 Hz, 1H), 5.68 (s, 1H), 5.46 (hept, J = 6.6 Hz, 1H), 3.43 (s, 3H), 2.85 (s, 3H), 2.13 (s, 3H), 1.50 (d, J = 6.6 Hz, 3H), 1.37 (d, J = 6.7 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, CD_3COCD_3) δ (ppm) 189.5, 175.8, 155.8, 145.5, 143.6, 137.6, 133.5, 132.1, 130.5, 129.6, 129.2, 128.6, 128.5, 128.1, 126.3, 123.7, 122.1, 108.3, 65.5, 57.1, 52.0, 50.3, 26.1, 23.6, 23.4, 21.3; IR(film): ν (cm^{-1}) 3348, 2961, 2925, 1724, 1675, 1614, 1493, 1469, 1394, 1374, 1315, 1256, 1195, 1128, 1091, 1030, 907, 868, 799, 777, 754, 734, 699, 632, 540, 503; HRMS (ESI) m/z calcd for $C_{26}H_{28}N_4O_4Na$ $(M+Na)^+$ 483.2003, found: 483.2004.



3g

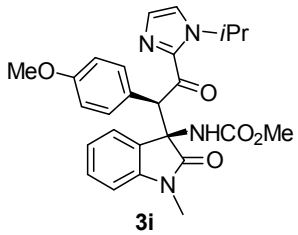
*Methyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-(p-tolyl)ethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (**3g**).* 44.2 mg, 96% yield, white solid, mp 165–167 °C; >99% ee, >200:1 dr (HPLC: Chiralpak IB, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 13.5 min, t_r(major) = 15.0 min); $[\alpha]_D^{20}$ = –40.1 (c = 1.0, CH_2Cl_2); ^1H NMR (500 MHz, CD_3COCD_3) δ (ppm) 7.76–7.51 (m, 2H), 7.25 (t, J = 7.2 Hz, 2H), 7.14 (s, 1H), 7.01–6.87 (m, 5H), 6.73 (d, J = 7.9 Hz, 1H), 5.69 (s, 1H), 5.46 (hept, J = 6.6 Hz, 1H), 3.43 (s, 3H), 2.87 (s, 3H), 2.20 (s, 3H), 1.49 (d, J = 6.6 Hz, 3H), 1.36 (d, J = 6.7 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, CD_3COCD_3) δ (ppm) 189.7, 175.9, 155.8, 145.5, 143.6, 138.2, 131.3, 130.6, 130.5, 129.6, 128.9, 128.6, 126.3, 123.7, 122.1, 108.4, 65.6, 56.8, 52.0, 50.3, 26.1, 23.6, 23.4, 20.9; IR(film): ν (cm^{-1}) 3348, 2962, 2924, 1725, 1675, 1613, 1493, 1469, 1394, 1374, 1317, 1257, 1194, 1127, 1091, 1024, 917, 834, 752, 703, 686, 601, 560, 539, 489; HRMS (ESI) m/z calcd for $C_{26}H_{29}N_4O_4$ $(M+H)^+$ 461.2183, found: 461.2192.



3h

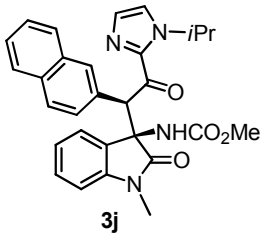
*Methyl((R)-3-((R)-1-(4-bromophenyl)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxoethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (**3h**).* 52.0 mg, 99% yield, white solid, mp 134–136 °C; 98.5% ee,

98:1 dr (HPLC: Chiralpak IA, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, 254 nm, major diastereomer: t_r(major) = 10.9 min, t_r(minor) = 13.5 min); $[\alpha]_D^{20}$ = –73.1 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.69 (s, 1H), 7.24 (s, 1H), 7.21 (t, *J* = 8.2 Hz, 3H), 7.15 (s, 1H), 6.94 (d, *J* = 8.3 Hz, 2H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 7.3 Hz, 1H), 6.61 (d, *J* = 7.8 Hz, 1H), 5.51 (s, 1H), 5.36 (hept, *J* = 6.6 Hz, 1H), 3.45 (s, 3H), 2.86 (s, 3H), 1.43 (d, *J* = 6.6 Hz, 3H), 1.29 (d, *J* = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 188.4, 175.2, 155.5, 144.1, 142.8, 132.3, 131.4, 130.8, 130.1, 129.4, 126.5, 124.9, 122.5, 122.4, 122.0, 107.9, 64.5, 54.5, 52.2, 49.7, 26.1, 23.7, 23.3; IR(film): ν (cm^{-1}) 3338, 3055, 2962, 2926, 2853, 1725, 1675, 1614, 1489, 1470, 1413, 1393, 1374, 1354, 1313, 1258, 1194, 1148, 1128, 1090, 1028, 1012, 918, 791, 753, 735, 702, 637, 617, 579, 540, 529, 488; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{25}BrN_4O_4Na$ $(M+Na)^+$ 547.0951, found: 547.0952.



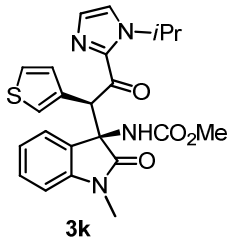
3i

*Methyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-1-(4-methoxyphenyl)-2-oxoethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (**3i**).* 46.2 mg, 97% yield, white solid, mp 162–164 °C; 99% ee, 160:1 dr (HPLC: Chiralpak AS-H, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, 254 nm, major diastereomer: t_r(major) = 22.5 min, t_r(minor) = 42.4 min); $[\alpha]_D^{20}$ = –50.4 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, CD_3COCD_3) δ (ppm) 7.62 (d, *J* = 5.8 Hz, 2H), 7.25 (dd, *J* = 9.9, 4.5 Hz, 2H), 7.15 (s, 1H), 7.00 (d, *J* = 8.7 Hz, 2H), 6.96 (t, *J* = 7.3 Hz, 1H), 6.75 (t, *J* = 12.0 Hz, 1H), 6.67 (d, *J* = 8.8 Hz, 2H), 5.67 (s, 1H), 5.46 (hept, *J* = 6.6 Hz, 1H), 3.69 (s, 3H), 3.43 (s, 3H), 2.88 (s, 3H), 1.49 (d, *J* = 6.6 Hz, 3H), 1.35 (t, *J* = 10.1 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, CD_3COCD_3) δ (ppm) 189.7, 176.0, 160.3, 155.9, 145.6, 143.6, 132.5, 130.5, 129.7, 128.6, 126.3, 125.4, 123.7, 122.1, 113.7, 108.4, 65.4, 56.3, 55.4, 52.0, 50.3, 26.2, 23.6, 23.4; IR(film): ν (cm^{-1}) 2917, 1959, 1724, 1674, 1612, 1511, 1468, 1394, 1255, 1180, 1091, 1029, 830, 560; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{28}N_4O_5Na$ $(M+Na)^+$ 499.1952, found: 499.1958.



3j

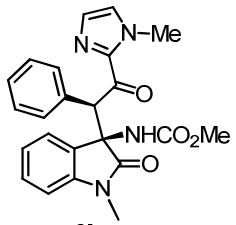
*Methyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-1-(naphthalen-2-yl)-2-oxoethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (**3j**).* 47.2 mg, 95% yield, white solid, mp 137–139 °C; 98.6% ee, 138:1 dr (HPLC: Chiralpak IA, *n*-hexane/*i*-PrOH = 70:30, flow rate: 0.80 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 9.9 min, t_r(major) = 11.7 min); $[\alpha]_D^{20}$ = –40.1 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.74 (s, 1H), 7.65 (d, *J* = 7.4 Hz, 1H), 7.57 (dd, *J* = 19.3, 9.3 Hz, 3H), 7.39–7.27 (m, 2H), 7.27–7.15 (m, 3H), 7.12 (s, 1H), 6.83 (t, *J* = 7.4 Hz, 1H), 6.74 (d, *J* = 7.1 Hz, 1H), 6.55 (d, *J* = 7.7 Hz, 1H), 5.69 (s, 1H), 5.39 (hept, *J* = 6.5 Hz, 1H), 3.45 (s, 3H), 2.80 (s, 3H), 1.42 (d, *J* = 6.5 Hz, 3H), 1.24 (d, *J* = 6.6 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 189.1, 175.4, 155.6, 144.0, 142.8, 132.8, 132.7, 130.2, 130.0, 129.9, 129.2, 128.3, 128.2, 127.3, 127.1, 127.0, 126.1, 125.8, 125.0, 122.3, 121.9, 107.8, 64.8, 55.1, 52.1, 49.6, 26.1, 23.6, 23.3; IR(film): ν (cm^{-1}) 2917, 1959, 1724, 1674, 1612, 1511, 1468, 1394, 1255, 1180, 1091, 1029, 830, 560, 439; HRMS (ESI) *m*/*z* calcd for $C_{29}H_{28}N_4O_4Na$ $(M+Na)^+$ 519.2003, found: 519.2004.



3k

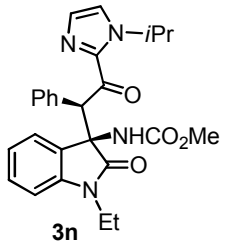
*Methyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-(thiophen-3-yl)ethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (**3k**).* 44.3 mg, 98% yield, white solid, mp 161–163 °C; >99% ee, 120:1 dr (HPLC: Chiralpak IA, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 9.4 min, t_r(major) = 13.0 min); $[\alpha]_D^{20}$ = –96.3 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, CD_3COCD_3) δ (ppm) 7.82 (s, 1H), 7.68 (s, 1H), 7.28 (td, *J* = 7.7, 1.0 Hz, 1H), 7.25–7.16 (m, 2H), 7.07 (t, *J* = 5.8 Hz, 2H), 6.96 (t, *J* = 7.4 Hz, 1H), 6.84–6.69 (m, 2H), 5.85 (s, 1H), 5.45 (hept, *J* = 6.6 Hz, 1H), 3.43 (s, 3H), 2.90 (s, 3H), 1.50 (d, *J* = 6.6 Hz, 3H), 1.39 (d, *J* = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, CD_3COCD_3) δ (ppm) 188.8, 175.7, 155.8, 145.6, 143.7, 133.6, 130.6, 130.2, 129.8, 128.3, 126.3, 125.7, 124.6, 124.1, 122.1, 108.5, 65.1, 52.5, 52.1, 50.4, 26.2, 23.7, 23.2;

IR(film): ν (cm^{-1}) 3343, 3110, 2962, 2926, 1724, 1676, 1614, 1494, 1469, 1395, 1374, 1355, 1323, 1259, 1195, 1149, 1128, 1090, 1029, 914, 829, 754, 734, 701, 679, 647, 560, 540, 509; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{25}N_4O_4S$ $(M+H)^+$ 453.1591, found: 453.1593.



3l

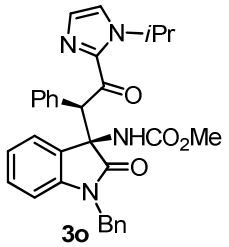
Methyl((R)-1-methyl-3-((R)-2-(1-methyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-2-oxoindolin-3-yl)carbamate ***(3l)***. 39.3 mg, 94% yield, white solid, mp 149–151 °C; >99% ee, >200:1 dr (HPLC: Chiralpak AS-H, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 28.5 min, t_r(major) = 35.2 min); $[\alpha]_D^{20}$ = –60.7 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, CD_3COCD_3) δ (ppm) 7.67 (s, 1H), 7.37 (s, 1H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.25 (td, *J* = 7.7, 0.9 Hz, 1H), 7.16 (t, *J* = 7.1 Hz, 1H), 7.13–7.02 (m, 5H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 5.68 (s, 1H), 4.00 (s, 3H), 3.43 (s, 3H), 2.82 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, CD_3COCD_3) δ (ppm) 189.1, 175.8, 155.8, 145.5, 144.4, 133.5, 131.4, 129.9, 129.7, 129.5, 128.6, 128.4, 128.2, 126.4, 122.2, 108.4, 65.5, 56.7, 52.0, 36.5, 26.1; IR(film): ν (cm^{-1}) 3338, 2960, 2921, 2850, 1959, 1723, 1676, 1613, 1493, 1471, 1402, 1374, 1321, 1259, 1158, 1127, 1091, 1026, 916, 828, 752, 700, 633, 604, 560, 540, 522; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{22}N_4O_4Na$ $(M+Na)^+$ 441.1533, found: 441.1534.



3n

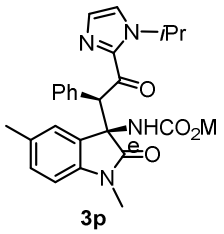
Methyl((R)-1-ethyl-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-2-oxoindolin-3-yl)carbamate ***(3n)***. 42.8 mg, 93% yield, white solid, mp 115–117 °C; 98.6% ee, >200:1 dr (HPLC: Chiralpak OD-H, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 14.1 min, t_r(major) = 19.3 min); $[\alpha]_D^{20}$ = –62.9 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.79 (s, 1H), 7.23 (s, 1H), 7.19 (dd, *J* = 8.8, 6.6 Hz, 1H), 7.16 (s,

1H), 7.15–7.08 (m, 1H), 7.04 (d, J = 4.3 Hz, 4H), 6.88 (t, J = 7.5 Hz, 1H), 6.82 (d, J = 7.3 Hz, 1H), 6.60 (d, J = 7.8 Hz, 1H), 5.54 (s, 1H), 5.36 (hept, J = 6.7 Hz, 1H), 3.59 (dq, J = 14.2, 7.0 Hz, 1H), 3.44 (s, 3H), 3.26 (dq, J = 14.2, 7.1 Hz, 1H), 1.44 (d, J = 6.6 Hz, 3H), 1.28 (d, J = 6.7 Hz, 3H), 0.70 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ (ppm) 188.8, 174.7, 155.4, 143.3, 143.2, 132.3, 130.9, 130.0, 129.1, 128.0, 127.6, 126.9, 125.1, 122.2, 121.6, 107.8, 64.5, 55.2, 52.1, 49.6, 34.4, 23.8, 23.3, 11.8; IR(film): ν (cm^{-1}) 3348, 2964, 2932, 1721, 1676, 1613, 1489, 1467, 1456, 1393, 1372, 1321, 1259, 1236, 1195, 1133, 1096, 1039, 990, 918, 798, 744, 700, 631, 551, 524, 490, 434; HRMS (ESI) m/z calcd for $C_{26}H_{28}N_4O_4Na$ $(M+Na)^+$ 483.2003, found: 483.2000.



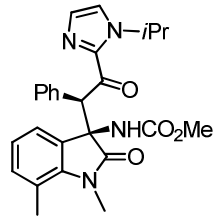
3o

Methyl((R)-1-benzyl-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-2-oxoindol in-3-yl)carbamate ***(3o)***. 50.2 mg, 96% yield, white solid, mp 163–165 °C; 98.6% ee, 114:1 dr (HPLC: Chiralpak IA, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 13.3 min, t_r(major) = 25.5 min); $[\alpha]_D^{20}$ = –86.2 (c = 1.0, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.79 (s, 1H), 7.23 (s, 1H), 7.21–7.16 (m, 2H), 7.16–7.07 (m, 7H), 7.04 (td, J = 7.7, 1.2 Hz, 1H), 6.93–6.73 (m, 4H), 6.39 (d, J = 7.8 Hz, 1H), 5.64 (s, 1H), 5.38 (hept, 1H), 4.76 (d, 1H), 4.48 (d, J = 16.1 Hz, 1H), 3.46 (s, 3H), 1.44 (d, J = 6.6 Hz, 3H), 1.29 (d, J = 6.7 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ (ppm) 189.1, 175.7, 155.5, 143.5, 143.1, 135.5, 132.4, 131.0, 130.1, 129.1, 128.5, 128.1, 127.9, 127.1, 126.9, 126.8, 125.0, 122.4, 121.9, 109.1, 64.7, 55.1, 52.2, 49.7, 44.1, 23.8, 23.3; IR(film): ν (cm^{-1}) 3338, 2960, 2921, 2850, 1723, 1676, 1613, 1493, 1471, 1402, 1374, 1321, 1259, 1158, 1127, 1091, 1026, 916, 828, 752, 700, 560; HRMS (ESI) m/z calcd for $C_{31}H_{30}N_4O_4Na$ $(M+Na)^+$ 545.2159, found: 545.2160.



3p

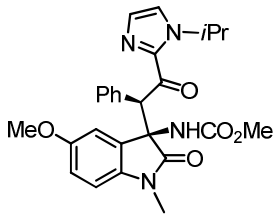
*Methyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-1,5-dimethyl-2-oxoindolin-3-yl)carbamate (**3p**).* 45.1 mg, 98% yield, white solid, mp 179–181 °C; >99% ee, 105:1 dr (HPLC: Chiralpak IB, *n*-hexane/*i*-PrOH = 80:20, flow rate: 0.50 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 24.3 min, t_r(major) = 26.3 min); $[\alpha]_D^{20}$ = –78.7 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.79 (s, 1H), 7.21 (s, 1H), 7.18–7.13 (m, 1H), 7.12 (s, 1H), 7.11–7.06 (m, 3H), 6.97 (d, *J* = 7.8 Hz, 1H), 6.49 (d, *J* = 7.9 Hz, 1H), 6.40 (s, 1H), 5.45 (s, 1H), 5.39 (hept, *J* = 13.2, 6.8 Hz, 1H), 3.46 (s, 3H), 2.86 (s, 3H), 2.13 (s, 3H), 1.44 (d, *J* = 6.6 Hz, 3H), 1.29 (d, *J* = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 189.2, 175.3, 155.6, 142.9, 141.6, 132.6, 131.0, 130.8, 129.9, 129.4, 128.0, 127.6, 126.8, 125.9, 122.2, 107.4, 64.9, 54.9, 52.1, 49.6, 26.1, 23.7, 23.3, 21.1; IR(film): ν (cm^{-1}) 3356, 2962, 2922, 2852, 1722, 1675, 1622, 1604, 1499, 1455, 1393, 1366, 1316, 1258, 1196, 1136, 1090, 1026, 918, 853, 804, 742, 700, 672, 623, 552, 520; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{28}N_4O_4Na$ $(M+Na)^+$ 483.2003, found: 483.2000. Anal. Calcd (%) for $C_{26}H_{28}N_4O_4$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.85; H, 6.30; N, 11.92.



3q

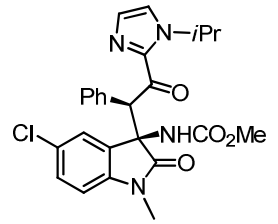
*Methyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-1,7-dimethyl-2-oxoindolin-3-yl)carbamate (**3q**).* 43.3 mg, 94% yield, white solid, mp 142–144 °C; 98.4% ee, 90:1 dr (HPLC: Chiralpak OD-H, *n*-hexane/*i*-PrOH = 70:30, flow rate: 0.50 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 14.1 min, t_r(major) = 22.5 min); $[\alpha]_D^{20}$ = –34.6 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.79 (s, 1H), 7.21 (s, 1H), 7.18–7.14 (m, 1H), 7.13 (s, 1H), 7.12–7.05 (m, 4H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.70 (t, *J* = 7.6 Hz, 1H), 6.44 (d, *J* = 7.3 Hz, 1H), 5.43 (s, 1H), 5.38 (hept, *J* = 13.3, 6.7 Hz, 1H), 3.46 (s, 3H), 3.13 (s, 3H), 2.36 (s, 3H), 1.43 (d, *J* = 6.6 Hz, 3H), 1.28 (d, *J* = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 189.1, 176.3, 155.6, 142.9,

141.7, 132.9, 132.5, 130.9, 129.9, 128.0, 127.6, 127.5, 122.7, 122.2, 121.6, 119.3, 64.4, 55.1, 52.1, 49.6, 29.6, 23.7, 23.3, 18.9; IR(film): ν (cm^{-1}) 3349, 2962, 2926, 1720, 1676, 1603, 1491, 1456, 1394, 1367, 1343, 1317, 1259, 1196, 1149, 1122, 1073, 1052, 1035, 919, 821, 777, 744, 702, 636, 597, 560, 542, 507; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{28}N_4O_4Na$ $(M+Na)^+$ 483.2003, found: 483.2004.



3r

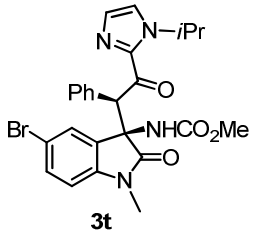
Methyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-5-methoxy-1-methyl -2-oxoindolin-3-yl)carbamate ***(3r)***. 46.7 mg, 98% yield, white solid, mp 133–135 °C; >99% ee, 173:1 dr (HPLC: Chiralpak IA, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 11.1 min, t_r(major) = 14.5 min); $[\alpha]_D^{20}$ = –81.8 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.76 (s, 1H), 7.21 (s, 1H), 7.18–7.05 (m, 6H), 6.71 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.51 (d, *J* = 8.4 Hz, 1H), 6.22 (s, 1H), 5.45 (s, 1H), 5.39 (hept, *J* = 13.2, 6.6 Hz, 1H), 3.54 (s, 3H), 3.47 (s, 3H), 2.87 (s, 3H), 1.43 (d, *J* = 6.6 Hz, 3H), 1.29 (d, *J* = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 189.3, 175.2, 155.7, 155.1, 142.8, 137.5, 132.6, 130.8, 130.0, 128.1, 128.0, 127.8, 122.3, 114.1, 111.9, 108.1, 65.1, 55.4, 54.6, 52.16, 49.6, 26.2, 23.7, 23.3; IR(film): ν (cm^{-1}) 3349, 2961, 1721, 1673, 1603, 1496, 1467, 1456, 1435, 1394, 1369, 1288, 1258, 1208, 1130, 1088, 1037, 918, 852, 803, 741, 700, 648, 523; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{28}N_4O_5Na$ $(M+Na)^+$ 499.1952, found: 499.1948.



3s

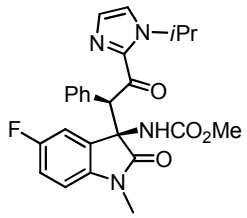
Methyl((R)-5-chloro-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-1-methyl-2 -oxoindolin-3-yl)carbamate ***(3s)***. 45.7 mg, 95% yield, white solid, mp 136–138 °C; 98.8% ee, 43:1 dr (HPLC: Chiralpak IA, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, 254 nm,

major diastereomer: t_r(minor) = 9.3 min, t_r(major) = 14.2 min); $[\alpha]_D^{20}$ = –64.8 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.67 (s, 1H), 7.22 (s, 1H), 7.18–7.14 (m, 2H), 7.12 (s, 1H), 7.10 (d, J = 4.8 Hz, 3H), 6.68 (s, 1H), 6.51 (d, J = 8.3 Hz, 1H), 5.48 (s, 1H), 5.39 (hept, 1H), 3.47 (s, 3H), 2.84 (s, 3H), 1.45 (d, J = 6.6 Hz, 3H), 1.29 (d, J = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 188.8, 175.1, 155.6, 142.7, 142.6, 132.0, 130.6, 130.1, 129.0, 128.7, 128.2, 127.8, 127.2, 125.6, 122.4, 108.6, 64.9, 54.8, 52.3, 49.7, 26.2, 23.6, 23.4; IR(film): ν (cm^{-1}) 3342, 2962, 2925, 1727, 1674, 1611, 1490, 1465, 1394, 1365, 1299, 1260, 1195, 1132, 1103, 1026, 973, 918, 836, 738, 700, 642, 621, 560, 546, 522; HRMS (ESI) m/z calcd for $C_{25}H_{25}N_4O_4ClNa$ $(M+Na)^+$ 503.1457, found: 503.1456.



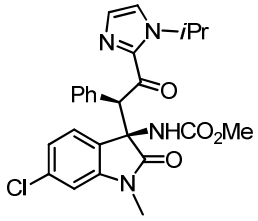
3t

Methyl((R)-5-bromo-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-1-methyl-2-oxoindolin-3-yl)carbamate ***(3t)***. 51.5 mg, 98% yield, white solid, mp 159–161 °C; >99% ee, 49:1 dr (HPLC: Chiralpak IA, *n*-hexane/*i*-PrOH = 70:30, flow rate: 0.80 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 8.1 min, t_r(major) = 11.5 min); $[\alpha]_D^{20}$ = –67.4 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.68 (s, 1H), 7.30 (d, J = 8.2 Hz, 1H), 7.22 (s, 1H), 7.18–7.14 (m, 1H), 7.14–6.98 (m, 5H), 6.79 (s, 1H), 6.47 (d, J = 8.2 Hz, 1H), 5.47 (s, 1H), 5.39 (hept, J = 13.1, 6.5 Hz, 1H), 3.47 (s, 3H), 2.84 (s, 3H), 1.45 (d, J = 6.6 Hz, 3H), 1.29 (d, J = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 188.7, 174.9, 155.6, 143.1, 142.7, 132.0, 131.9, 130.6, 130.1, 129.0, 128.3, 128.2, 127.8, 122.4, 114.6, 109.1, 64.8, 54.8, 52.3, 49.7, 26.2, 23.6, 23.3; IR(film): ν (cm^{-1}) 3343, 2962, 2926, 1727, 1675, 1609, 1488, 1466, 1456, 1394, 1363, 1298, 1260, 1195, 1133, 1101, 1053, 1026, 971, 918, 858, 808, 740, 700, 638, 620, 565, 533; HRMS (ESI) m/z calcd for $C_{25}H_{25}N_4O_4BrNa$ $(M+Na)^+$ 547.0951, found: 547.0952.



3u

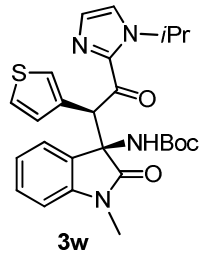
*Methyl((R)-5-fluoro-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (**3u**).* 45.5 mg, 98% yield, white solid, mp 154–156 °C; >99% ee, 119:1 dr (HPLC: Chiralpak AS-H, *n*-hexane/*i*-PrOH = 80:20, flow rate: 1.0 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 20.2 min, t_r(major) = 33.3 min); $[\alpha]_D^{20}$ = –19.3 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.65 (s, 1H), 7.22 (s, 1H), 7.18–7.04 (m, 6H), 6.88 (td, *J* = 8.9, 2.5 Hz, 1H), 6.50 (dd, *J* = 8.4, 3.8 Hz, 2H), 5.50 (s, 1H), 5.39 (hept, 1H), 3.47 (s, 3H), 2.85 (s, 3H), 1.45 (d, *J* = 6.6 Hz, 3H), 1.29 (d, *J* = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 188.9, 175.2, 159.5, 157.6, 155.6, 142.7, 140.0, 132.1, 130.6, 130.1, 128.2, 127.8, 122.4, 115.3 (d, *J* = 23.6 Hz), 113.4 (d, *J* = 25.5 Hz), 108.1 (d, *J* = 8.0 Hz), 65.0, 54.8, 52.2, 49.7, 26.2, 23.7, 23.4; IR(film): ν (cm^{-1}) 3344, 2963, 2926, 1725, 1674, 1621, 1494, 1467, 1455, 1394, 1370, 1298, 1259, 1197, 1165, 1122, 1088, 1026, 979, 917, 812, 741, 701, 674, 625, 559, 524, 440; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{25}N_4O_4FNa$ $(M+Na)^+$ 487.1752, found: 487.1753.



3v

*Methyl((R)-6-chloro-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-phenylethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (**3v**).* 46.7 mg, 97% yield, white solid, mp 105–107 °C; >99% ee, 53:1 dr (HPLC: Chiralpak IA, *n*-hexane/*i*-PrOH = 70:30, flow rate: 0.90 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 6.8 min, t_r(major) = 8.9 min); $[\alpha]_D^{20}$ = –33.2 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.68 (s, 1H), 7.22 (d, *J* = 0.6 Hz, 1H), 7.18–7.04 (m, 6H), 6.83 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.64 (d, *J* = 7.9 Hz, 1H), 6.60 (d, *J* = 1.8 Hz, 1H), 5.49 (s, 1H), 5.37 (hept, 1H), 3.46 (s, 3H), 2.85 (s, 3H), 1.44 (d, *J* = 6.6 Hz, 3H), 1.28 (d, *J* = 6.7 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm) 188.9, 175.4, 155.6, 145.3, 142.8, 135.0, 132.1, 130.6, 130.1, 128.2, 127.9,

125.9, 125.4, 122.4, 121.8, 108.5, 64.5, 54.8, 52.24, 49.7, 26.2, 23.7, 23.4.; IR(film): ν (cm^{-1}) 3346, 2962, 2926, 1729, 1675, 1610, 1495, 1465, 1394, 1371, 1296, 1260, 1195, 1133, 1074, 1026, 967, 917, 892, 842, 796, 737, 701, 647, 620, 577, 518; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{25}N_4O_4ClNa$ $(M+Na)^+$ 503.1457, found: 503.1455.



3w

*tert-Butyl((R)-3-((R)-2-(1-isopropyl-1H-imidazol-2-yl)-2-oxo-1-(thiophen-3-yl)ethyl)-1-methyl-2-oxoindolin-3-yl)carbamate (**3w**, for crystallization).* 48.5 mg, 98% yield, white solid, mp 161–163 °C; >99% ee, 30:1 dr (HPLC: Chiralpak IB, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min, 25 °C, 254 nm, major diastereomer: t_r(major) = 16.7 min, t_r(minor) = 24.7 min); $[\alpha]_D^{20}$ = –92.3 (c = 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.36 (s, 1H), 7.23 (s, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 7.14 (s, 1H), 7.00 (dd, *J* = 4.5, 3.1 Hz, 1H), 6.96 (s, 1H), 6.87 (t, *J* = 7.5 Hz, 1H), 6.82–6.69 (m, 2H), 6.57 (d, *J* = 7.7 Hz, 1H), 5.67 (s, 1H), 5.38 (hept, *J* = 6.6 Hz, 1H), 2.84 (s, 3H), 1.44 (d, *J* = 6.6 Hz, 3H), 1.29 (d, *J* = 6.7 Hz, 3H), 1.09 (s, 9H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ (ppm) 188.3, 175.5, 154.1, 143.8, 142.9, 132.4, 130.0, 129.4, 128.8, 127.6, 125.6, 124.6, 123.7, 122.3, 121.6, 107.5, 79.8, 64.7, 50.9, 49.5, 27.9, 25.9, 23.6, 23.3; IR(film): ν (cm^{-1}) 3357, 3111, 3055, 2975, 2928, 1721, 1675, 1614, 1494, 1470, 1393, 1373, 1353, 1322, 1256, 1165, 1126, 1090, 1023, 962, 918, 829, 752, 726, 701, 679, 648, 560, 540, 514, 488, 463; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{30}N_4O_4SNa$ $(M+Na)^+$ 517.1880, found: 517.1880.

Catalytic Asymmetric Reaction in 0.8 mmol Scale. To a solution of Δ-**RhO** catalyst (6.64 mg, 0.00800 mmol, 1.0 mol%) in anhydrous toluene was added 2-acyl imidazole **1b** (194 mg, 0.800 mmol) and 4Å MS (40.0 mg) in a brown glass vial. The mixture was stirred at 20 °C for 30 min, then ketimine **2d** (262 mg, 1.20 mmol) was added. The reaction mixture was stirred at 20 °C for 5 h. After that, the resulting mixture was purified by flash chromatography on silica gel (*n*-hexane/EtOAc= 4:1 to 1:1) to afford product **3e** (361 mg, 98% yield) as a white solid. Enantiomeric excess and diasteromeric ratio were established by HPLC analysis, >99% ee, >200:1

dr (HPLC: Chiralpak IB, *n*-hexane/*i*-PrOH = 90:10, flow rate: 0.80 mL/min, 30 °C, 254 nm, major diastereomer: t_r(minor) = 17.5 min, t_r(major) = 18.8 min); $[\alpha]_D^{20}$ = –32.3 (c =1.0, CH_2Cl_2).

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■ ACKNOWLEDGMENT

We are grateful for financial support from the National Natural Science Foundation of China (grant nos. 21572184 and 21472154), the Natural Science Foundation of Fujian Province of China (grant no. 2017J06006), and the Fundamental Research Funds for the Central Universities (grant no. 20720160027).

■ ASSOCIATED CONTENT

Supporting Information. NMR spectra, HPLC traces and X-ray crystal structure. This material is available free of charge via the Internet at http://pubs.acs.org. Crystallographic data for compound **3w** has been deposited with the Cambridge Crystallographic Data Centre (CCDC) under deposition number 1541214.

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