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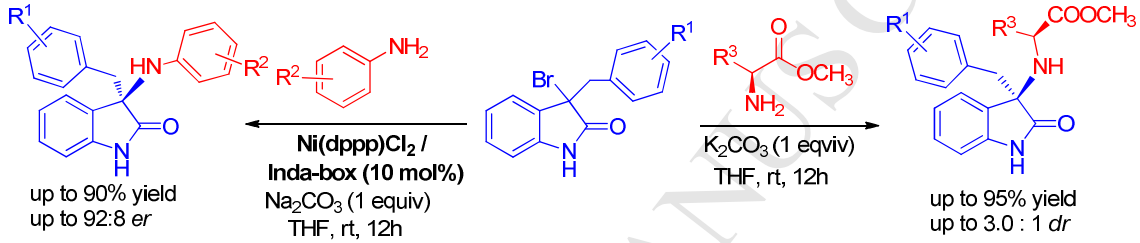
Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123, P. R. China.



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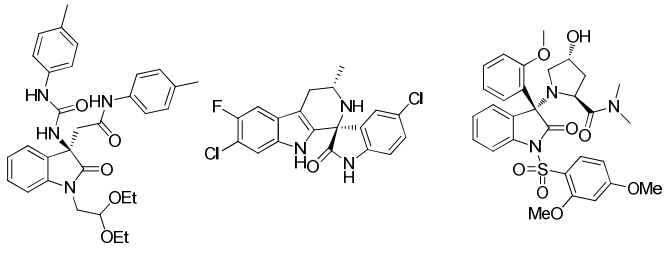
ABSTRACT

The asymmetric amination of anilines to 3-bromooxindoles was developed in the presence of a bis(oxazoline)-Ni(dppp)Cl_2 complex, to provide enantiomerically enriched 3-amino-2-oxindoles with quaternary stereocenters in up to 90% yield with 92:8 *er*. Simultaneously, direct stereoselective amination of α-amino-acid methyl esters to 3-bromooxindoles was also accompolished without any catalysts, which furnished the 3-amino-2-oxindole derivatives in high yields with moderate diastereoselectivities.

1. Introduction

3,3'-Disubstituted chiral oxindoles are privileged skeletons, which present in large amount of alkaloid natural products, pharmaceutical or agrochemical relevant compounds as well as synthetic structural complexities.[1] Because of its importance, more and more catalytic strategies have been developed to efficiently construct the 3,3'-disubstituted oxindole derivatives.[2] In particular, the optically active 3-amino-2-oxindoles, which bear a quarternary stereogenic center at the C3 position,[3] have been recognized as versatile and useful backbones for preparation of some natural products and candidate drugs. For instance, the potent gastrin/CCK-B receptor antagonist AG-041R,[4] the vasopressin VIb receptor antagonist SSR-149415,[5] a drug in clinical trials for treatment of anxiety and depression, as well as the effective anti-malarial drug candidate NITD609[6] (Scheme 1). Therefore, the significance of these structure motifs has attracted considerable attention to synthetic chemists. Over the past several years, several asymmetric methods have been established to synthesize the 3-amino-2-oxindoles, such as the asymmetric Pd/NHC-catalyzed intramolecular α-arylation of amide enolates,[7] the asymmetric addition reaction of isatin derived ketimines,[8] the enantioselective amination of 3-substituted oxindoles with azodicarboxylates,[9] the enantioselective hydroxyamination reaction of oxindoles with nitrosoarenes,[10] and other methods.[11]

Among the developed methodologies of construction of 3-amino-2-oxindole, Wang and co-workers reported a Box-Ni (II) catalyzed directly asymmetric amination reaction of indolines to 3-bromooxindoles, giving a series of 3-amino-2-oxindoles in good yields with excellent enantioselectivities.[12] However, anilines and α-amino-acids, which could incorporate more possible applications into the NH containing adducts, were not taken into consideration. Herein, we developed the direct amination reaction between 3-bromooxindoles and anilines or α-amino-acid esters in the presence of chiral Box-Ni complexes[13] as the catalysts or absence of catalysts, which furnished 3-amino-2-oxindole derivatives in good yields with moderate enantioselectivities and diastereoselectivities.

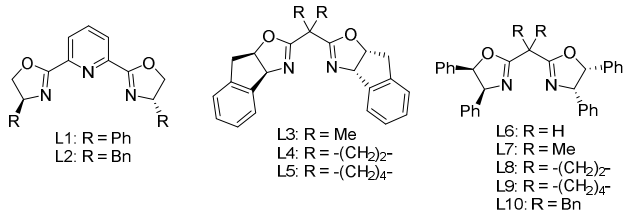


Scheme 1. Bioactive 3,3-disubstituted 3-amino-2-oxindoles.

[a] Corresding auother. Fax: +86-512-65880378
E-mail: wangxw@suda.edu.cn

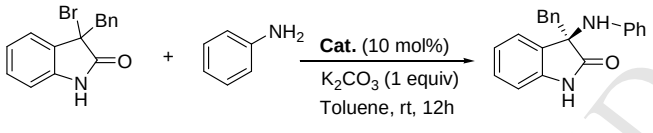
2. Results and discussion

Although background reaction was observed in the absence of chiral catalyst (Table 1, entry 1), the direct asymmetric amination between 3-bromooxindole **1a** and aniline **2a** was still investigated in the presence of 10 mol% of chiral box-nickel catalyst and one equivalent of sodium carbonate in toluene at room temperature. As shown in Scheme 2 and Table 1, the Py-box **L1**/ $Ni(OAc)_2{\cdot}4H_2O$ complex was first used for this reaction and furnished the desired product **3a** in 72% yield, but only with 68:32 *er* (Table 1, entry 2). Then, a series of bis(oxazoline) ligands **L2–L10**/$Ni(OAc)_2{\cdot}4H_2O$ catalysts were investigated, inda-box ligand **L4** was finally proved to be the optimal ligand for this transformation, which provided the desired product **3a** in 80% yield with 70:30 *er* (Table 1, entry 5). On the other hand, more nickel metal sources were tested. To our delight, when 10 mol% of **L4**/$Ni(dppp)Cl_2$ complex was employed, the corresponding enantioselectivity was improved to 79:21 *er* (Table 1, entry 16).



Scheme 2. Screened chiral ligands

Table 1. Optimization of the catalysts

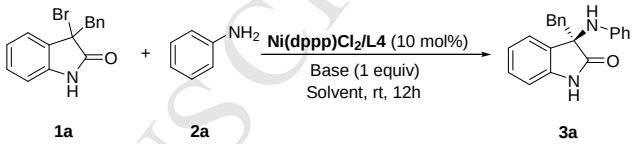


Entry [a]	L*	M	Yield (%) [b]	er [c]
1	--	--	65	--
2	**L1**	$Ni(OAc)_2{\cdot}4H_2O$	72	68:32
3	**L2**	$Ni(OAc)_2{\cdot}4H_2O$	92	57:43
4	**L3**	$Ni(OAc)_2{\cdot}4H_2O$	82	62:38
5	**L4**	$Ni(OAc)_2{\cdot}4H_2O$	80	70:30
6	**L5**	$Ni(OAc)_2{\cdot}4H_2O$	65	60:40
7	**L6**	$Ni(OAc)_2{\cdot}4H_2O$	85	61:39
8	**L7**	$Ni(OAc)_2{\cdot}4H_2O$	90	58:42
9	**L8**	$Ni(OAc)_2{\cdot}4H_2O$	90	62:38
10	**L9**	$Ni(OAc)_2{\cdot}4H_2O$	88	55:45
11	**L10**	$Ni(OAc)_2{\cdot}4H_2O$	93	62:38
12	**L4**	$Ni(acac)_2$	90	63:37
13	**L4**	$Ni(PPh_3)_2Cl_2$	75	71:29
14	**L4**	$NiCl_2$	90	63:37
15	**L4**	$NiCl_2{\cdot}$glyme	88	77:23
16	**L4**	$Ni(dppp)Cl_2$	92	79:21

[a] Unless noted, all reactions were carried out with **1a** (0.10 mmol) **2a** (0.12 mmol) and Cat. (10 mol%) in Toluene (1 mL).
[b] Isolated yield.
[c] Determined by HPLC.

With **L4**/$Ni(dppp)Cl_2$ complex as the optimal catalyst, the effect of the solvent and the base were then investigated and the results are listed in Table 2. After examination of the reaction medium effect, THF turned out to be the optimal solvent for this transformation (Table 2, entry 6). In addition, several bases were surveyed for this reaction. When Na_2CO_3 was used as a base, the enantioselectivity was increased to 88:12 *er* (Table 2, entry 7). In order to improve the enantioselectivity, we further optimized the reaction conditions, such as the reaction temperature, the concentration of reactants, the equivalents of the base, the catalyst loading, and the effect of the metal complexes, the results were listed in Tables **S1–S5**. According to above screening, the optimal reaction conditions were established (Table 2, entry 7).

Table 2. Screening of the solvents and bases for the reaction.



Entry [a]	Solvent	Base	Yield (%) [b]	er [c]
1	toluene	K_2CO_3	92	79:21
2	MeCN	K_2CO_3	80	66:34
3	DCM	K_2CO_3	70	70:30
4	1,4-Dioxane	K_2CO_3	85	81:19
5	$ClCH_2CH_2Cl$	K_2CO_3	30	61:39
6	THF	K_2CO_3	93	83:17
7	THF	Na_2CO_3	90	88:12
8	THF	Cs_2CO_3	95	71:29
9	THF	$K_3PO_4{\cdot}3H_2O$	90	79:21
10	THF	Et_3N	68	77:23
11	THF	DBU	22	66:34
12	THF	DMAP	56	73:27
13	THF	*i*Pr_2NEt	51	63:37
14	THF	DABCO	10	56:44

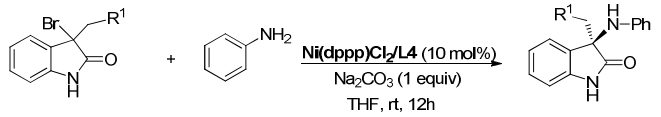
[a] Unless noted, all reactions were carried out with **1a** (0.10 mmol) **2a** (0.12 mmol) and Cat. (10 mol%) in Solvent (1 mL).
[b] Isolated yield.
[c] Determined by HPLC.

With the optimal reaction conditions in hand, we next examined the substrate scope for the synthesis of various optically active 3-amino-2-oxindoles. Firstly, a range of 3-bromooxindole substrates were employed to evaluate, and the results are summarized in Table 3. In general, all the reactions proceeded smoothly to afford the desired products in good yields with moderate enantioselectivities. For 3-bromooxindoles **1b**–**1d** bearing -Me groups onto the phenyl ring, the reactions provided the corresponding products **3b**–**3d** in 80–87% yields with 81:19 to 82:18 *er*s (Table 3, entries 2–4). On the other hand, when electron-withdrawing groups (-Br, -Cl, -F, -CN) were installed onto the phenyl rings, the corresponding reactions also proceeded well and gave the desired products in 80–87% yields

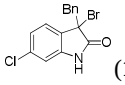
with 75:25 to 84:16 *er*s (Table 3, entries 5–10). It seems that both electronic-donating groups (2-OMe, 4-OMe) and the electronic-withdrawing groups (4-CF_3, 4-Cl) on the phenyl ring, provided the corresponding products in 86–93% yields and 81:19 to 86:14 *er*s (Table 4, entries 2–5), whereas the substrate **2f** containing the strong electronic-withdrawing group (4-NO_2) afforded the desired product **3f** in 65% yield with 80:20 *er* (Table 4, entry 6). Simultaneously, anilines **2g–2j** with bis- or tri-substituted groups (3,5-di-CF_3, 3,5-di-Me, 2,4-di-Cl, 2,4,6-tri-Me) were also compatible with this transformation, and the corresponding products **3t**–3**w** were obtained with 72–87% yields with 77:23 to 81:19 *er*s (Table 4, entries 7–10). In addition, the reactions for 1-naphthylamine **2k** gave the similar results (Table 4, entry 11).

higher enantioselectivity could be obtained when the group was located onto the *para*-position of the phenyl rings. Additionally, the substrates **1k**–**1m** containing fused aromatic rings were also suitable substrates for this reaction, affording the corresponding products **3k**–**3m** in 83–87% yields and 78:22 to 83:17 *er*s (Table 3, entries 11–13). Furthermore, the substrate **1n** containing 6-Cl group on the oxindole core displayed somewhat influence on the reactivity and enantioselectivity of the corresponding reaction, provided the desired products **3n** in 70% yield and 78:22 er (Table 3, entry 14). In order to suppress the background reaction, the aniline **2a** was slowly added into the reaction solution by a syring pump in 12 hours. It was disclosed that the enantioselectivities were obviously improved only for some desired products **3a**, **3d**, **3g** and **3h** (Table 3, entries 1, 4, 7 and 8).

Table 3. Substrate scope for the asymmetric amination of 3-bromooxindole **1** with aniline **2a**.



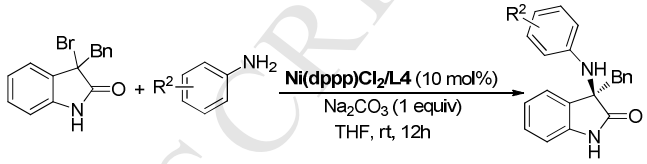
1 **2a** **3**

Entry[a]	Substrate (**R**)	Product	Yield (%)[b]	er (%)[c]
1[d]	Ph (**1a**)	**3a**	90 85	88:12 (92:8)[e]
2	2-MeC_6H_4 (**1b**)	**3b**	80	81:19
3	3-MeC_6H_4 (**1c**)	**3c**	85	82:18
4	4-MeC_6H_4 (**1d**)	**3d**	87 70	82:18 (89:11)[e]
5	2-BrC_6H_4 (**1e**)	**3e**	80	75:25
6	3-BrC_6H_4 (**1f**)	**3f**	85	82:18
7	4-BrC_6H_4 (**1g**)	**3g**	85 75	84:16 (88:12)[e]
8	4-ClC_6H_4 (**1h**)	**3h**	87 74	81:19 (90:10)[e]
9	4-FC_6H_4 (**1i**)	**3i**	86	78:22
10	4-CNC_6H_4 (**1j**)	**3j**	85	83:17
11	2-thienyl (**1k**)	**3k**	83	78:22
12	2-furyl (**1l**)	**3l**	84	83:17
13	1-naphthyl (**1m**)	**3m**	87	80:20
14	 (**1n**)	**3n**	70	78:22

[a] Unless noted, all reactions were carried out with **1a** (0.20 mmol) **2a** (0.24 mmol) and Cat. (10 mol%) in THF (2 mL).
[b] Isolated yield.
[c] Determined by HPLC.
[d] The configuration (*R*) was determined by comparison of the optical rotation **1a** with the literature.[10d]
[e] The aniline **2a** was added by a syring pump to the reaction solution in 12 h.

In order to further explore the scope of the substrates, the electronic and steric effects of the anilines **2** were investigated for this transformation. The aniline derivatives **2b**–**2e** bearing

Table 4. Substrate scope for the asymmetric amination of 3-bromooxindole **1a** with anilines **2**.



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

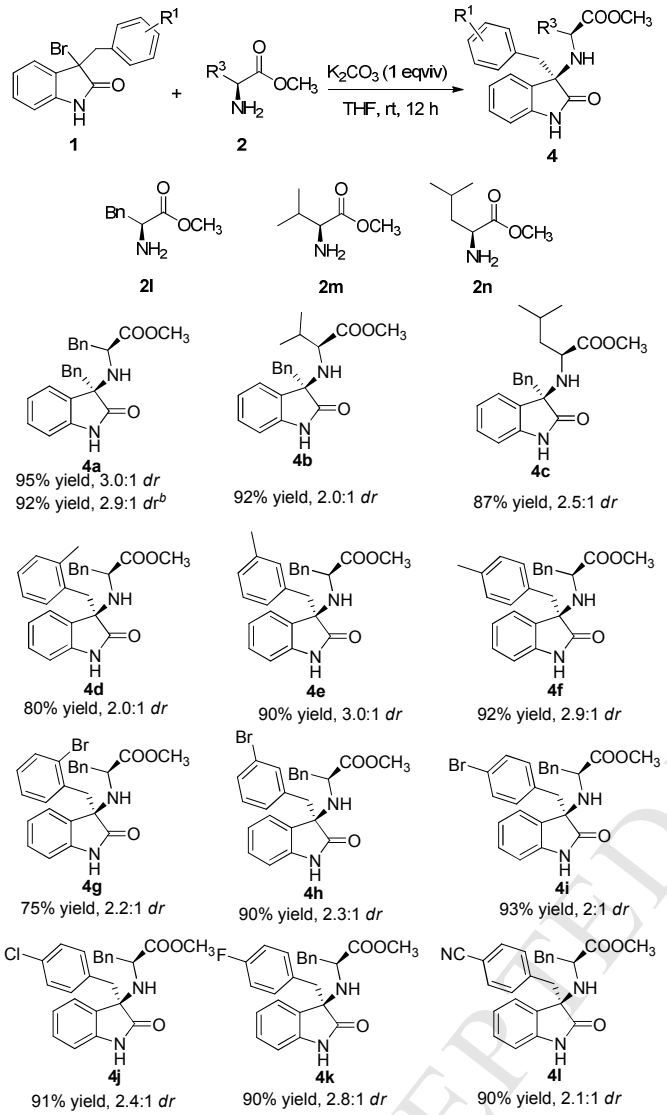
Entry[a]	Substrate (**R**)	Product	Yield (%)[b]	er (%)[c]
1	H (**2a**)	**3a**	90	88:12
2	2-OMe (**2b**)	**3o**	80	83:17
3	4-OMe (**2c**)	**3p**	87	81:19
4	4-CF_3 (**2d**)	**3q**	86	85:15
5	4-Cl (**2e**)	**3r**	93	86:14
6	4-NO_2 (**2f**)	**3s**	65	80:20
7	3,5-di-CF_3 (**2g**)	**3t**	87	79:21
8	3,5-di-Me (**2h**)	**3u**	83	77:23
9	2,4-di-Cl (**2i**)	**3v**	80	80:20
10	2,4,6-tri-Me (**2j**)	**3w**	72	81:19
11	 (**2k**)	**3x**	70	86:14

[a] Unless noted, all reactions were carried out with **1a** (0.20 mmol) **2a** (0.24 mmol) and Cat. (10 mol%) in THF (2 mL).
[b] Isolated yield.
[c] Determined by HPLC.

Due to the significance of α-amino-acids, the direct amination was also explored between 3-bromooxindoles and α-amino-acid methyl esters **2l**–**2n**, and the results are illustrated in Scheme 3. For methyl 2-aminopropanoates **2l**–**2n**, the reactions provided the corresponding products **4a**–**4c** in 87–95% yields with 2.0:1 to 3.0:1 *dr*s. Then, **2l** was selected as the nucleophile and a range of the 3-bromooxindoles were investigated. The substrates **1b**–**1d** bearing –Me substituent and **1e**–**1g** bearing –Br substituents furnished the corresponding products in good yields with a range from 2.0:1 to 2.9:1 *dr*s (**4d**–**4i**). These results indicated that the steric hindrance, the position variation of substituents of R^1 showed somewhat influence on the reactivity. In generally, the reactions furnished the expected products in excellent yields when the substituents of R^1 were attatched on the *meta*- or *para*-positions of phenyl rings. So we next examined the reactions by

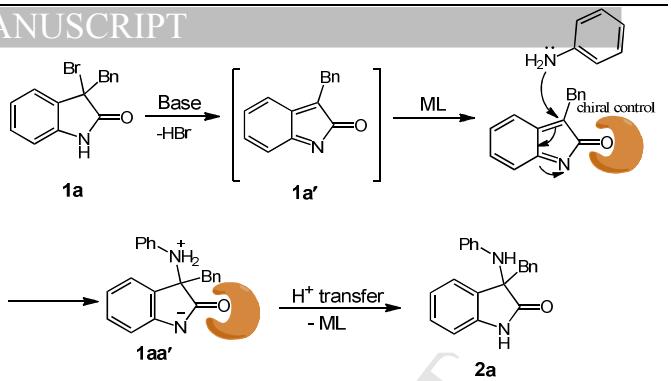
varying the *para*-substituents of R^1. As for the electron-withdrawing groups, such as fluoro-, chloro-, and cyano- groups (**4j**–**4l**), the reaction were carried out smoothly, and these groups were also well tolerated for this transformation.

Scheme 3. Substrate scope for the amination of 3-bromooxindoles **1** with amino-acid esters **2**[a]



[a]All reactions were performed by using **1** (0.20 mmol), **2** (0.24 mmol), and K_2CO_3 (0.20 mmol), in THF (2.0 mL) at room temperature for 12 hours. All yields referred to isolated yields of desired products. The diastereoselectivities were determined by ^{1}H NMR analysis of the crude reaction mixture. [b]**L4**/Ni(dppp)Cl_2 was used as the catalyst.

Based on our experimental results and previous related studies,[2s,12,14] we proposed the possible reaction pathways (Scheme 4). Firstly, the substrate **1a** is transformed into *o*-azaxylylene intermediate **1a'** through the base-mediated dehydrohalogenation process, then the chiral nickel (II) catalyst is coordinated with the *o*-azaxylylene intermediate **1a'**. Simultaneously, aniline attacks the chiral electrophile complex to provide the intermediate **1aa'**. Finally, the target product is obtained by proton transfer and the catalyst is regenerated.



Scheme 4. Proposed reaction pathway.

3. Conclusion

In summary, the box/Ni catalyzed asymmetric amination of anilines to 3-bromooxindoles had been developed to provide enantiomerically enriched 3-amino-2-oxindoles with quaternary stereocenters in good yields with moderate enantioselectivities. Furthermore, the stereoselective amination between 3-bromooxindoles and α-amino-acid methyl esters was also achieved in high yields without the use of chiral metal catalysts.

Experimental Section

4.1 General

Unless otherwise stated, all reactions carried out in flamed dried glassware. All solvents were purified and dried according to standard methods prior to use. The substrates **1** were prepared according to the literature. Organic solutions were concentrated under reduced pressure on an EYELA N-1001 rotary evaporator. Reactions were monitored by thin-layer chromatography (TLC) on silica gel precoated glass plates (0.2 ± 0.03 mm thickness, GF-254, particle size 0.01–0.04 mm). Chromatograms were visualized by fluorescence quenching with UV light at 254 nm. Flash column chromatography was performed using silica gel (particle size 0.04 – 0.05 mm) from Yantai Chemical Industry Research Institute, P. R. China. ^{1}H, ^{13}C NMR spectra were recorded in $CDCl_3$ on Varian Inova (400 MHz, 101 MHz respectively) spectometer. Chemical shifts (δ ppm) are relative to the resonance of the deuterated solvent as the internal standard ($CDCl_3$, δ 7.26 ppm for proton NMR, δ 77.23 ppm for carbon NMR; ^{1}H NMR data are reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. s = broad singlet, dd = double-doublet, td = triple-doublet, ddd = double-double-doublet), coupling constants (J) and assignment. Data for ^{13}C NMR are reported in terms of coupling constants (J) and chemical shift (δ, ppm). IR Spectra were recorded on Thermo Fisher Nicolet 6700. Melting points were performed electrothermal. High-resolution mass spectra were recorded on a commercial apparatus (ESI Source). High performance liquid chromatography (HPLC) was performed on an Agilent 1200 Series chromatographs using Daicel Chiralpak OD-H or AD-H column (0.46cm x 25 cm). Optical rotations are reported as follows: $[\alpha]_D^{20}$ (c in g per 100 mL, solvent).

General procedure for the asymmetric amination reaction of 3-halooxindoles with anilines.

A mixture of **L** (10 mol %), $Ni(dppp)_2Cl_2$ (10 mol%) were stirred in THF (2 mL) at room temperature for 1 hour in the glassware in the glove box. Then the substrate **1**, base and the substrate **2** were added in sequence, and the resulting solution was stirred at room temperature for 12 hours. After the starting material was completely consumed as monitored by TLC, the mixture was concentrated in vacuo. The crude products were purified by flash column chromatography to give **3**.

General procedure the amination reaction of 3-halooxindoles with amino-acid esters.

A mixture of the substrates and K_2CO_3 (1.0 equiv.) were stirred in THF (2 mL) at room temperature for 12 hours. After the starting material was completely consumed as monitored by TLC, the mixture was concentrated in vacuo. The crude products were purified by flash column chromatography to give the major products **4**.

4.2 3-benzyl-3-(phenylamino)indolin-2-one (**3a**): 85% yield, pale yellow solid, m. p. 183 – 185 °C; 92:8 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 17.36, t (minor) = 14.23]; $[\alpha]_D^{20}$ = –4.62 (c 0.43, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.19 – 7.13 (m, 3H), 7.09 (t, *J* = 7.2 Hz, 2H), 7.02 (t, *J* = 7.2 Hz, 1H), 6.96 – 6.88 (m, 4H), 6.66 – 6.62 (m, 2H), 6.28 (d, *J* = 8.0 Hz, 2H), 4.66 (s, 1H), 3.29 (d, *J* = 12.0 Hz, 1H), 3.21 (d, *J* = 12.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.00, 145.32, 140.10, 139.8, 133.30, 130.65, 129.66, 129.26, 128.05, 127.47, 124.78, 122.98, 119.25, 115.09, 110.57, 66.29, 46.63. IR: 3339, 3135, 3080, 3028, 1706, 1601, 1522, 1455, 1318, 1222, 1181, 744, 715, 665 cm^{-1}; ESI-HRMS: Calcd for $[C_{21}H_{18}N_2NaO, M+Na]^+$: 337.1311, found: 337.1303.

4.3 3-(2-methylbenzyl)-3-(phenylamino)indolin-2-one (**3b**): 80% yield, pale yellow solid, m. p. 185 – 187 °C; 81:19 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min–1, λ = 254 nm, t (major) = 10.55, t (minor) = 11.49]; $[\alpha]_D^{20}$ = –7.60 (c 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.21 – 7.16 (m, 1H), 7.13 – 7.09 (m, 1H), 7.04 – 7.01 (m, 3H), 6.96 – 6.91 (m, 4H), 6.75 (d, *J* = 7.6 Hz, 1H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.27 (dd, *J* = 8.4 Hz, *J* = 0.8 Hz, 2H), 4.72 (s, 1H), 3.34 (d, *J* = 13.2 Hz, 1H), 3.26 (d, *J* = 13.6 Hz, 1H), 1.99 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.79, 145.27, 140.09, 138.02, 132.19, 131.19, 130.71, 129.68, 129.25, 129.22, 127.65, 125.69, 125.06, 122.86, 119.22, 115.14, 110.60, 66.05, 42.45, 19.93. IR: 3340, 3140, 3081, 3027, 1706, 1622, 1603, 1470, 1318, 743, 690 cm^{-1}; ESI-HRMS: Calcd for $[C_{22}H_{20}N_2NaO, M+Na]^+$: 351.1468, found: 351.1468.

4.4 3-(3-methylbenzyl)-3-(phenylamino)indolin-2-one (**3c**): 85% yield, pale yellow solid, m. p. 180 – 182 °C; 82:18 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 12.93, t (minor) = 9.84]; $[\alpha]_D^{20}$ = –3.64 (c 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.19 – 7.15 (m, 2H), 7.03 – 6.91 (m, 5H), 6.72 – 6.67 (m, 3H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.28 (d, *J* = 7.6 Hz, 2H), 4.70 (s, 1H), 3.26 (d, *J* = 12.4 Hz, 1H), 3.26 (d, *J* = 12.4 Hz, 1H), 2.15 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.26, 145.34, 140.18, 137.58, 133.20, 131.47, 129.80, 129.23, 129.17, 128.19, 127.92, 127.67, 124.81, 122.85, 119.14, 115.00, 110.62, 66.19, 46.54, 21.41. IR: 3312, 3142, 3062, 3027, 1705, 1603, 1499, 1470, 1442, 1184, 749, 691 cm^{-1}; ESI-HRMS: Calcd for $[C_{22}H_{20}N_2NaO, M+Na]^+$: 351.1468, found: 351.1468.

4.5 3-(4-methylbenzyl)-3-(phenylamino)indolin-2-one (**3d**): 70% yield, pale yellow solid, m. p. 191 – 193 °C; 89:11 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 15.48, t (minor) = 11.61]; $[\alpha]_D^{20}$ = –4.24 (c 1.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.16 (t, *J* = 7.6 Hz, 2H), 7.01 (t, *J* = 7.6 Hz, 1H), 6.94 – 6.88 (m, 4H), 6.78 (d, *J* = 8.0 Hz, 2H), 6.63 (dd, *J* = 15.2 Hz, *J* = 7.6 Hz, 2H), 6.27 (d, *J* = 8.0 Hz, 2H), 4.73 (s, 1H), 3.26 (d, *J* = 12.4 Hz, 1H), 3.16 (d, *J* = 12.8 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.44, 145.39, 140.17, 137.05, 130.50, 130.18, 129.85, 129.23, 129.14, 128.79, 124.70, 122.90, 119.10, 114.96, 110.71, 66.28, 46.21, 21.24. IR: 3301, 3137, 3027, 2962, 1706, 1602, 1498, 1470, 1257, 1075, 749, 692 cm^{-1}; ESI-HRMS: Calcd for $[C_{22}H_{20}N_2NaO, M+Na]^+$: 351.1468, found: 351.1458.

4.6 3-(2-bromobenzyl)-3-(phenylamino)indolin-2-one (**3e**): 80% yield, pale yellow solid, m. p. 200 – 202 °C; 75:25 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 13.28, t (minor) = 14.59]; $[\alpha]_D^{20}$ = –16.20 (c 0.75, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 7.50 – 7.47 (m, 1H), 7.23 – 7.18 (m, 1H), 7.15 – 7.11 (m, 1H), 7.09 – 7.05 (m, 2H), 6.95 – 6.91 (m, 4H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.26 (dd, *J* = 8.8 Hz, *J* = 1.2 Hz, 2H), 5.03 (s, 1H), 3.63 (d, *J* = 13.6 Hz, 1H), 3.29 (d, *J* = 13.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.68, 145.28, 139.90, 133.92, 133.19, 132.84, 129.38, 129.26, 129.22, 128.99, 127.13, 126.37, 125.85, 122.76, 119.19, 115.07, 110.71, 66.25, 44.39. IR: 3325, 3140, 3082, 1709, 1602, 1470, 1440, 1291, 1219, 1016, 745, 691 cm^{-1}; ESI-HRMS: Calcd for $[C_{21}H_{18}BrN_2O, M+H]^+$: 393.0597, found: 393.0610.

4.7 3-(3-bromobenzyl)-3-(phenylamino)indolin-2-one (**3f**): 85% yield, pale yellow solid, m. p. 166 – 168 °C; 82:18 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 13.59, t (minor) = 10.81]; $[\alpha]_D^{20}$ = –15.5 (c 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.28 – 7.19 (m, 3H), 7.06 (td, *J* = 8.8 Hz, *J* = 0.8 Hz, 1H), 6.98 – 6.92 (m, 4H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.66 (dd, *J* = 15.6 Hz, *J* = 7.6 Hz, 2H), 6.31 – 6.28 (m, 2H), 4.66 (s, 1H), 3.25 (d, *J* = 12.4 Hz, 1H), 3.17 (d, *J* = 12.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.64, 145.20, 140.04, 135.60, 133.51, 130.58, 129.57, 129.52, 129.30, 129.26, 129.24, 124.69, 123.21, 121.93, 119.51, 115.30, 110.77, 66.32, 46.09. IR: 3313, 3140, 3080, 3029, 1709, 1622, 1603, 1471, 1442, 1073, 749, 691 cm^{-1}; ESI-HRMS: Calcd for $[C_{21}H_{18}BrN_2O, M+H]^+$: 393.0597, found: 393.0599.

4.8 3-(4-bromobenzyl)-3-(phenylamino)indolin-2-one (**3g**): 75% yield, pale yellow solid, m. p. 201 – 203 °C; 88:12 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 17.04, t (minor) = 9.33]; $[\alpha]_D^{20}$ = +7.70 (c 0.65, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.25 – 7.18 (m, 4H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.95 (t, *J* = 7.6 Hz, 2H), 6.73 – 6.64 (m, 4H), 6.29 (d, *J* = 7.6 Hz, 2H), 4.64 (s, 1H), 3.24 (d, *J* = 12.4 Hz, 1H), 3.17 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.57, 145.22, 140.04, 132.28, 132.22, 131.15, 129.51, 129.32, 129.30, 124.66, 123.20, 121.71, 119.54, 115.29, 110.73, 66.31, 45.96. IR: 3318, 3300, 3136, 3079, 1704, 1603, 1471, 1123, 1073, 749, 689 cm^{-1}; ESI-HRMS: Calcd for $[C_{21}H_{18}BrN_2O, M+H]^+$: 393.0597, found: 393.0589.

4.9 3-(4-chlorobenzyl)-3-(phenylamino)indolin-2-one (**3h**): 74% yield, pale yellow solid, m. p. 190 – 192 °C; 90:10 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 15.64, t (minor) = 9.74]; $[\alpha]_D^{20}$ = +2.50 (c 1.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.25 – 7.17 (m, 2H), 7.06 – 7.02 (m, 3H), 6.95 (t, *J* = 8.0 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.67 – 6.64 (m, 2H), 6.29 (d, *J* = 7.6 Hz, 2H), 4.65 (s, 1H), 3.25 (d, *J* = 12.4 Hz, 1H), 3.19 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ

179.63, 145.23, 140.05, 133.48, 131.85, 131.76, 129.48, 129.37, 129.30, 128.19, 124.65, 123.19, 119.51, 115.27, 110.71, 66.38, 45.90. IR: 3319, 3302, 3137, 3030, 1704, 1604, 1471, 1354, 1077, 871, 749, 731, 690 cm^{-1}; ESI-HRMS: Calcd for $[C_{21}H_{18}ClN_2O, M+H]^+$: 349.1102, found: 349.1099.

4.10 3-(4-fluorobenzyl)-3-(phenylamino)indolin-2-one (**3i**): 86% yield, pale yellow solid, m. p. 183 – 185 °C; 78:22 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 $mL \cdot min^{-1}$, λ = 254 nm, t (major) = 15.80, t (minor) = 9.78]; $[\alpha]_D^{20}$ = –9.10 (c 0.88, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.70 (s, 1H), 7.25 – 7.15 (m, 2H), 7.04 (t, *J* = 7.2 Hz, 1H), 6.93 (t, *J* = 7.2 Hz, 2H), 6.79 (t, *J* = 5.2 Hz, 2H), 6.73 (t, *J* = 8.4 Hz, 2H), 6.63 (t, *J* = 6.8 Hz, 2H), 6.28 (d, *J* = 7.6 Hz, 2H), 4.79 (s, 1H), 3.26 (d, *J* = 12.4 Hz, 1H), 3.19 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 180.28, 162.28 (d, *J* = 246.8 Hz), 145.33, 140.12, 132.07 (d, *J* = 8.0 Hz), 129.52, 129.40, 129.28, 129.00 (d, *J* = 3.1 Hz), 124.62, 123.16, 119.35, 115.10, 114.88 (d, *J* = 21.3 Hz), 110.75, 66.54, 45.71. IR: 3308, 3136, 3079, 3028, 1704, 1603, 1472, 1417, 1223, 1182, 871,752, 717, 692 cm^{-1}; ESI-HRMS: Calcd for $[C_{21}H_{18}FN_2O, M+H]^+$: 333.1398, found: 333.1399.

4.11 4-((2-oxe-3-(phenylamino)indolin-3-yl)benzonitrile (**3j**): 85% yield, pale yellow solid, m. p. 190 – 192 °C; 83:17 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 $mL \cdot min^{-1}$, λ = 254 nm, t (major) = 27.44, t (minor) = 10.75]; $[\alpha]_D^{20}$ = +10.0 (c 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.89 (s, 1H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.22 (td, *J* = 8.8 Hz, *J* = 1.2 Hz, 1H), 7.08 (td, *J* = 8.4 Hz, *J* = 0.8 Hz, 1H), 6.99 – 6.94 (m, 4H), 6.68 (dd, *J* = 14.4 Hz, *J* = 7.6 Hz, 2H), 6.31 (dd, *J* = 8.8 Hz, *J* = 0.8 Hz, 2H), 4.59 (s, 1H), 3.33 (d, *J* = 12.4 Hz, 1H), 3.28 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 178.93, 145.02, 139.88, 138.82, 131.69, 131.27, 129.79, 129.34, 128.87, 124.70, 123.41, 119.92, 118.83, 115.62, 111.44, 110.71, 66.40, 46.44. ESI-HRMS: Calcd for $[C_{22}H_{17}N_3NaO, M+Na]^+$: 362.1264, found: 362.1262.

4.12 3-(phenylamino)-3-(thiophen-2-ylmethyl)indolin-2-one (**3k**): 83% yield, pale yellow solid, m. p. 194 – 196 °C; 78:22 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 $mL \cdot min^{-1}$, λ = 254 nm, t (major) = 22.79, t (minor) = 19.53]; $[\alpha]_D^{20}$ = –21.25 (c 0.60, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.64 (s, 1H), 7.24 – 7.19 (m, 2H), 7.07 – 7.02 (m, 2H), 6.95 (t, *J* = 8.0 Hz, 2H), 6.82 – 6.79 (m, 1H), 6.75 (d, *J* = 7.6 Hz, 1H), 6.67 – 6.63 (m, 2H), 6.31 (d, *J* = 7.6 Hz, 2H), 4.69 (s, 1H), 3.50 (d, *J* = 13.6 Hz, 1H), 3.44 (d, *J* = 13.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 179.96, 145.23, 140.53, 134.81, 129.54, 129.27, 128.51, 126.73, 125.61, 124.82, 123.20, 119.50, 115.36, 110.78, 65.94, 40.66. IR: 3310, 3139, 3079, 3028, 1706, 1603, 1470, 1259, 1218, 1080, 747, 689, 652 cm^{-1}; ESI-HRMS: Calcd for $[C_{19}H_{17}N_2OS, M+H]^+$: 321.1056, found: 321.1065.

4.13 (3-(furan-2-ylmethyl)-3-(phenylamino)indolin-2-one (**3l**): 84% yield, pale yellow solid, m. p. 160 – 162 °C; 83:17 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 $mL \cdot min^{-1}$, λ = 254 nm, t (major) = 16.34, t (minor) = 62.99]; $[\alpha]_D^{20}$ = –16.36 (c 0.825, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) *δ* 9.20 (s, 1H), 7.32 (d, *J* = 1.2 Hz, 1H), 7.21 – 7.17 (m, 1H), 6.98 – 6.92 (m, 4H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.30 – 6.25 (m, 3H), 5.97 (d, *J* = 3.2 Hz, 1H), 4.97 (s, 1H), 3.38 (d, *J* = 14.4 Hz, 1H), 3.11 (d, *J* = 14.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 180.44, 149.03, 145.16, 142.66, 139.95, 129.63, 129.26, 129.23, 124.81, 122.98, 119.08, 114.76, 110.87, 110.64, 109.89, 64.89, 38.55. IR: 3136, 3143, 3079, 3031, 1705, 1602, 1469, 1387, 1078, 738, 690, 663cm^{-1}; ESI-HRMS: Calcd for $[C_{19}H_{17}N_2O_2, M+H]^+$: 305.1285, found: 305.1289.

4.14 3-(naphthalen-1-ylmethyl)-3-(phenylamino)indolin-2-one (**3m**): 84% yield, pale yellow solid, m. p. 210 – 212 °C; 80:20 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 $mL \cdot min^{-1}$, λ = 254 nm, t(major) = 12.49, t (minor) = 13.54]; $[\alpha]_D^{20}$ = +13.41 (c 1.23, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.28 (s, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.79 – 7.76 (m, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.41 – 7.34 (m, 2H), 7.30 – 7.26 (t, *J* = 7.2 Hz, 1H), 7.16 – 7.11 (m, 2H), 6.95 – 6.89 (m, 3H), 6.86 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 6.72 (d, *J* = 7.6 Hz, 1H), 6.60 (t, *J* = 7.4 Hz, 1H), 6.20 (dd, *J* = 8.4 Hz, *J* = 0.8 Hz, 2H), 4.76 (s, 1H), 3.78 (d, *J* = 13.6 Hz, 1H), 3.67 (d, *J* = 13.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 180.27, 145.12, 139.93, 133.94, 133.04, 129.88, 129.76, 129.62, 129.20, 129.16, 128.83, 128.54, 126.07, 125.75, 125.34, 125.02, 124.22, 122.77, 119.16, 114.95, 110.57, 66.13, 41.97. IR: 3313, 3145, 3089, 3032, 1704, 1602, 1471, 1257, 773, 752,715 cm^{-1}; ESI-HRMS: Calcd for $[C_{25}H_{20}N_2NaO, M+Na]^+$: 387.1473, found: 387.1467.

4.15 3-benzyl-6-chloro-3-(phenylamino)indolin-2-one (**3n**): 84% yield, pale yellow solid, m. p. 230 – 232 °C; 78:22 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 $mL \cdot min^{-1}$, λ = 254 nm, t (major) = 12.49, t (minor) = 13.54]; $[\alpha]_D^{20}$ = +14.1 (c 1.06, $CHCl_3$); ^1H NMR (400 MHz, DMSO) *δ* 10.50 (s, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.14 – 7.07 (m, 3H), 6.99 (dd, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H), 6.93 (t, *J* = 8.0 Hz, 2H), 6.81 – 6.77 (m, 2H), 6.61 (d, *J* = 2.0 Hz, 1H), 6.52 – 6.48 (m, 2H), 6.22 (d, *J* = 7.6 Hz, 2H), 3.26 (d, *J* = 12.4 Hz, 1H), 3.17 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) *δ* 178.24, 146.21, 142.74, 133.60, 132.71, 130.09, 128.67, 128.46, 127.45, 126.82, 125.40, 121.33, 116.95, 113.38, 109.56, 65.22, 44.90. IR: 3310, 3107, 3029, 2918, 1713, 1667, 1600, 1484, 1264, 1066, 744, 699 cm^{-1}; ESI-HRMS: Calcd for $[C_{21}H_{17}ClN_2NaO, M+Na]^+$: 371.0922, found: 371.0922.

4.16 3-benzyl-3-((2-methoxyphenyl)amino)indolin-2-one (**3o**): 86% yield, pale yellow solid, m. p. 200 – 202 °C; 83:17 er. [Daicel Chiralcel OD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 $mL \cdot min^{-1}$, λ = 254 nm, t (major) = 6.16 , t (minor) = 14.92; $[\alpha]_D^{20}$ = +11.63 (c 0.22, $CHCl_3$); *δ* 7.93 (s, 1H), 7.19 – 7.08 (m, 5H), 7.00 (td, *J* = 7.6 Hz, *J* = 0.8 Hz, 1H), 6.92 – 6.89 (m, 2H), 6.72 (dd, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.59 (td, *J* = 7.6 Hz, 1.6 Hz, 1H), 6.45 (td, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 5.82 (dd, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H), 5.19 (s, 1H), 3.87 (s, 3H), 3.34 (d, *J* = 12.4 Hz, 1H), 3.26 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 179.59, 147.48, 140.00, 135.11, 133.41, 130.68, 129.81, 129.15, 127.97, 127.38, 124.73, 122.92, 121.14, 118.27, 111.92, 110.34, 109.79, 65.69, 55.74, 46.69. IR: 3354, 3134, 3083, 2919, 2360, 1724, 1601, 1523, 1471, 1305, 1260, 1180, 1089, 804, 774, 719 cm^{-1}; ESI-HRMS: Calcd for $[C_{22}H_{20}N_2NaO_2, M+Na]^+$: 367.1417, found: 367.1417.

4.17 3-benzyl-3-((4-methoxyphenyl)amino)indolin-2-one (**3p**): 87% yield, pale yellow solid, m. p. 190 – 192 °C; 81:19 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 $mL \cdot min^{-1}$, λ = 254 nm, t (major) = 13.86, t (minor) = 17.27]; $[\alpha]_D^{20}$ = –34.0 (c 0.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) *δ* 8.59 (s, 1H), 7.25 (d, *J* = 2.4 Hz, 1H), 7.17 – 7.02 (m, 5H), 6.89 (d, *J* = 7.2 Hz, 2H), 6.58 (d, *J* = 7.6 Hz, 1H), 6.46 (d, *J* = 8.8 Hz, 2H), 6.31 (d, *J* = 8.8 Hz, 2H), 4.45 (s, 1H), 3.54 (s, 3H), 3.29 (d, *J* = 12.4 Hz, 1H), 3.18 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 180.57, 153.68, 140.40, 139.01, 133.63, 130.62, 129.86, 129.19, 127.98, 127.31, 124.99, 122.85, 118.22, 114.54, 110.55, 67.57, 55.52, 46.21. IR: 3301, 3137, 3079, 2833, 1707, 1624, 1510, 1474, 1453, 1244, 1177, 832, 790, 698, 657, 639 cm^{-1}; ESI-HRMS: Calcd for $[C_{22}H_{21}N_2O_2, M+H]^+$: 345.1598, found: 345.1588.

4.18 3-benzyl-3-((4-(trifluoromethyl)phenyl)amino)indolin-2-one (**3q**): 86% yield, pale yellow solid, m. p. 200 – 202 °C; 85:15 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 6.22, t (minor) = 13.75; $[\alpha]_D^{20}$ = –16.0 (c 0.53, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (s, 1H), 7.20 – 7.12 (m, 5H), 7.08 – 7.06 (m, 3H), 6.86 (d, *J* = 7.2 Hz, 2H), 6.65 (d, *J* = 7.6 Hz, 1H), 6.24 (d, *J* = 8.8 Hz, 2H), 5.36 (s, 1H), 3.33 (d, *J* = 12.4 Hz, 1H), 3.25 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.33, 148.05, 139.99, 132.75, 130.57, 129.69, 128.89, 128.13, 127.70, 126.66 (q, *J* = 3.7 Hz), 124.78 (d, *J* = 269.1 Hz), 124.61, 123.39, 120.52 (q, *J* = 32.3 Hz), 113.72, 110.99, 66.18, 46.51. IR: 3322, 3083, 3030, 1709, 1619, 1533, 1454, 1266, 1068, 827, 749, 698, 644 cm^{-1}; ESI-HRMS: Calcd for $[C_{22}H_{17}F_3N_2NaO, M+Na]^+$: 405.1185, found: 405.1173.

4.19 3-benzyl-3-((4-chlorophenyl)amino)indolin-2-one (**3r**): 93% yield, pale yellow solid, m. p. 202 – 204 °C; 86:14 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 10.16, t (minor) = 18.57; $[\alpha]_D^{20}$ = –14.75 (c 1.39, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.22 – 7.15 (m, 3H), 7.10 (t, *J* = 7.2 Hz, 2H), 7.05 (t, *J* = 7.6 Hz, 1H) 6.89 – 6.87 (m, 4H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.20 (d, *J* = 8.4 Hz, 2H), 4.67 (s, 1H), 3.28 (d, *J* = 12.4 Hz, 1H), 3.20 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.58, 143.91, 140.00, 133.06, 130.61, 129.51, 129.19, 129.16, 128.12, 127.58, 124.79, 124.14, 123.16, 116.34, 110.65, 66.34, 46.54. IR: 3300, 3140, 3083, 3030, 1705, 1624, 1541, 1492, 1472, 1302, 829, 795, 714, 667, 650 cm^{-1}; ESI-HRMS: Calcd for $[C_{21}H_{17}ClN_2NaO, M+Na]^+$: 371.0922, found: 371.0915.

4.20 3-benzyl-3-((4-nitrophenyl)amino)indolin-2-one (**3s**): 65% yield, pale yellow solid, m. p. 219 – 221 °C; 80:20 er. [Daicel Chiralcel OD-H, hexanes/*i*-PrOH = 90/10, flow rate: 1.0 mL·min^{-1}, λ = 210.8 nm, t (major) = 21.28, t (minor) = 17.03; $[\alpha]_D^{20}$ = –24.1 (c 0.34, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.84 (d, *J* = 9.2 Hz, 2H), 7.24 – 7.17 (m, 2H), 7.14 – 7.10 (m, 3H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 7.2 Hz, 2H), 6.75 (d, *J* = 7.6 Hz, 1H), 6.22 (d, *J* = 9.2 Hz, 2H), 5.54 (s, 1H), 3.33 (d, *J* = 12.4 Hz, 1H), 3.25 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.68, 150.72, 139.82, 139.49, 132.33, 130.54, 130.02, 128.31, 128.13, 127.93, 126.10, 124.62, 123.52, 113.18, 111.02, 65.74, 46.37. IR: 3314, 3143, 3083, 2816, 1704, 1601, 1507, 1492, 1470, 1339, 1115, 831, 751, 698, 664 cm^{-1}; ESI-HRMS: Calcd for $[C_{21}H_{18}N_3O_3, M+H]^+$: 360.1343, found: 360.1339.

4.21 3-benzyl-3-((3,5-bis(trifluoromethyl)phenyl)amino)indolin-2-one (**3t**): 87% yield, pale yellow solid, m. p. 189 – 191 °C; 79:21 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 90/10, flow rate: 1.0 mL·min^{-1}, λ = 210.8 nm, t (major) = 7.09, t (minor) = 10.20; $[\alpha]_D^{20}$ = –22.1 (c 0.52, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.24 (td, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H), 7.20 – 7.16 (m, 1H), 7.13 – 7.09 (m, 3H), 7.07 – 7.04 (m, 2H), 6.90 (d, *J* = 7.2 Hz, 2H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.63 (s, 2H), 5.30 (s, 1H), 3.33 (d, *J* = 12.4 Hz, 1H), 3.21 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.15, 146.08, 139.96, 132.53, 132.38 (q, *J* = 32.6 Hz), 130.63, 130.13, 128.25, 127.84, 127.82, 124.88, 123.50, 123.39 (d, *J* = 271 Hz), 114.03, 112.08 (d, *J* = 4 Hz), 110.93, 65.90, 46.11. IR: 3302, 3144, 3089, 3030, 1704, 1623, 1554, 1219, 1120, 950, 852, 750, 699, 681, 656 cm^{-1}; ESI-HRMS: Calcd for $[C_{23}H_{16}F_6N_2NaO, M+Na]^+$: 473.1059, found: 473.1042.

4.22 3-benzyl-3-((3,5-dimethylphenyl)amino)indolin-2-one (**3u**): 83% yield, pale yellow solid, m. p. 199 – 201 °C; 77:23 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 29.26, t (minor) = 9.85; $[\alpha]_D^{20}$ = –11.86 (c 0.97, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.20 – 7.08 (m, 5H), 7.02 (td, *J* = 7.2 Hz, *J* = 0.8 Hz, 1H), 6.91 – 6.88 (m, 2H), 6.69 – 6.67 (m, 1H), 6.30 (s, 1H), 5.92 (s, 2H), 4.46 (s, 1H), 3.27 (d, *J* = 12.4 Hz, 1H), 3.18 (d, *J* = 12.4 Hz, 1H), 2.02 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.80, 145.26, 140.06, 138.71, 133.41, 130.67, 129.91, 129.18, 128.02, 127.41, 124.87, 122.93, 121.39, 113.13, 110.25, 66.17, 46.62, 21.60. IR: 3340, 3148, 3086, 3027, 1715, 1668, 1603, 1507, 1471, 1338, 1222, 1191, 812, 749, 711, 683, 661 cm^{-1}; ESI-HRMS: Calcd for $[C_{23}H_{22}N_2NaO, M+Na]^+$: 365.1624, found: 365.1609.

4.23 3-benzyl-3-((2,4-dichlorophenyl)amino)indolin-2-one (**3v**): 80% yield, pale yellow solid, m. p. 195 – 197 °C; 80:20 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 90/10, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 11.80, t (minor) = 10.50; $[\alpha]_D^{20}$ = +9.30 (c 0.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.24 – 7.13 (m, 5H), 7.03 – 6.96 (m, 4H), 6.75 (d, *J* = 7.7 Hz, 1H), 6.66 (dd, *J* = 8.8 Hz, *J* = 2.0 Hz, 1H), 5.78 (d, *J* = 8.8 Hz, 1H), 5.15 (s, 1H), 3.35 (d, *J* = 12.4 Hz, 1H), 3.21 (d, *J* = 12.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.29, 139.94, 139.88, 132.82, 130.78, 129.67, 129.07, 128.57, 128.31, 127.86, 127.77, 124.78, 123.15, 123.09, 120.93, 113.64, 110.84, 65.44, 46.41. IR: 3318, 3140, 3030, 2829, 1714, 1679, 1595, 1471, 1393, 1266, 1219, 1181, 1044, 743, 718, 667, 649 cm^{-1}; ESI-HRMS: Calcd for $[C_{21}H_{16}Cl_2N_2NaO, M+Na]^+$: 405.0532, found: 405.0534.

4.24 3-benzyl-3-(mesitylamino)indolin-2-one (**3w**): 72% yield, pale yellow solid, m. p. 175 – 177 °C; 81:19 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 80/20, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 8.27, t (minor) = 7.66; $[\alpha]_D^{20}$ = +65.2 (c 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.11 – 7.01 (m, 4H), 6.85 – 6.80 (m, 3H), 6.70 – 6.67 (m, 3H), 6.57 (d, *J* = 7.6 Hz, 1H), 3.59 (s, 1H), 3.42 (d, *J* = 12.4 Hz, 1H), 3.36 (d, *J* = 12.0 Hz, 1H), 2.15 (s, 3H), 2.02 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.55, 140.62, 139.75, 134.20, 133.27, 132.94, 130.51, 129.30, 129.10, 128.82, 127.95, 127.13, 126.00, 121.98, 109.84, 68.89, 48.02, 20.79, 19.36. IR: 3360, 3209, 3029, 2942, 1716, 1672, 1601, 1436, 1339, 1221, 1163, 1009, 860, 748, 697 cm^{-1}; ESI-HRMS: Calcd for $[C_{24}H_{24}N_2NaO, M+Na]^+$: 379.1781, found: 379.1776.

4.25 3-benzyl-3-(naphthalen-1-ylamino)indolin-2-one (**3x**): 70% yield, pale yellow solid, m. p. 193 – 195 °C; 86:14 er. [Daicel Chiralcel AD-H, hexanes/*i*-PrOH = 70/30, flow rate: 1.0 mL·min^{-1}, λ = 254 nm, t (major) = 35.68, t (minor) = 6.70; $[\alpha]_D^{20}$ = +77.7 (c 0.53, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.70 (dd, *J* = 7.6 Hz, *J* = 0.8 Hz, 1H), 7.48 – 7.40 (m, 2H), 7.23 – 7.13 (m, 5H), 7.05 – 7.03 (m, 3H), 6.95 (td, *J* = 8.4 Hz, *J* = 0.8 Hz, 1H), 6.89 (t, *J* = 7.6 Hz, 1H) 6.73 (d, *J* = 7.6 Hz, 1H), 5.85 (d, *J* = 7.2 Hz, 1H), 5.26 (s, 1H), 3.46 (d, *J* = 12.4Hz, 1H), 3.31 (d, *J* = 12.4Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.21, 140.03, 139.92, 134.47, 133.40, 130.85, 129.35, 129.23, 128.85, 128.25, 127.73, 126.27, 125.86, 125.23, 124.68, 124.44, 122.90, 120.31, 119.15, 110.68, 107.39, 65.58, 46.98. IR: 3618, 3153, 3084, 3030, 2922, 2360, 1708, 1647, 1507, 1471, 1219, 1172, 803, 785, 714, 698 cm^{-1}; ESI-HRMS: Calcd for $[C_{25}H_{21}N_2O, M+H]^+$: 365.1648, found: 365.1640.

4.26 methyl 2-((3-benzyl-2-oxoindolin-3-yl)amino)-3-phenylpropanoate (**4a**): 95% yield, white solid, m. p. 150 – 152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.24 – 7.19 (m, 4H), 7.15 – 7.10 (m, 3H), 7.07 – 6.99 (m, 4H), 6.81 (dd, *J* = 8.4 Hz, *J* = 1.6 Hz, 2H), 6.60 (d, *J* = 7.6 Hz, 1H), 3.47 (t, *J* = 7.2 Hz, 1H), 3.25 (s, 3H), 3.04 (dd, *J* = 18.0 Hz, *J* = 12.8 Hz, 2H),

2.92 (dd, *J* = 7.2 Hz, *J* = 2.8 Hz, 2H), 2.50 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.72, 175.11, 140.89, 136.74, 134.28, 130.48, 129.52, 129.32, 128.79, 128.57, 127.85, 127.03, 126.91, 126.08, 122.31, 110.03, 67.73, 59.05, 51.68, 44.29, 40.82. IR: 3279, 3166, 3085, 3060, 3030, 2948, 1743, 1706, 1619, 1472, 1213, 1177, 785, 697, 653 cm^{-1}; ESI-HRMS: Calcd for $[C_{25}H_{25}N_2O_3, M+H]^+$: 401.1860, found: 401.1861.

4.27 methyl 2-((3-benzyl-2-oxoindolin-3-yl)amino)-3-methylbutanoate (**4b**): 92% yield, white solid, m. p. 195 – 197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.13 (td, *J* = 8.8 Hz, *J* = 1.2 Hz, 1H), 7.08 – 6.99 (m, 4H), 6.88 (dd, *J* = 7.6 Hz, *J* = 1.2 Hz, 2H), 6.65 (d, *J* = 8.0 Hz, 1H), 3.34 (s, 3H), 3.17 (dd, *J* = 14.8 Hz, *J* = 12.8 Hz, 2H), 2.92 (d, *J* = 6.0 Hz, 1H), 2.47 (br. s, 1H), 1.91 – 1.82 (m, 1H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.04, 175.82, 141.01, 134.43, 130.45, 129.19, 129.17, 127.86, 126.87, 125.95, 122.09, 110.14, 67.86, 62.87, 51.48, 44.04, 32.27, 19.13, 18.77. IR: 3284, 3147, 3084, 3029, 2975, 2947, 2921, 2853, 1732, 1705, 1669, 1624, 1605, 1485, 1471, 1450, 1432, 1303, 1227, 1169, 1080, 794, 750, 739, 695, 655 cm^{-1}; ESI-HRMS: Calcd for $[C_{21}H_{25}N_2O_3, M+H]^+$: 353.1860, found: 353.1863.

4.28 methyl 2-((3-benzyl-2-oxoindolin-3-yl)amino)-4-methylpentanoate (**4c**): 87% yield, white solid, m. p. 138 – 140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.14 (td, *J* = 8.8 Hz, *J* = 1.2 Hz, 1H), 7.08 – 6.99 (m, 4H), 6.88 – 6.86 (m, 2H), 6.67 (d, *J* = 7.6 Hz, 1H), 3.31 (s, 3H), 3.20 – 3.12 (m, 3H), 2.23 (br. s, 1H), 1.72 – 1.69 (m, 1H), 1.49 – 1.39 (m, 2H), 0.87 (dd, *J* = 6.8 Hz, *J* = 5.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.28, 176.48, 141.06, 134.30, 130.43, 129.24, 128.72, 127.85, 126.91, 126.12, 122.13, 110.16, 68.16, 56.02, 51.66, 44.42, 43.81, 24.82, 22.92, 22.38. IR: 3292, 3152, 3087, 3030, 2951, 2867, 1729, 1707, 1669, 1604, 1473, 1436, 1336, 1278, 1226, 1128, 1081, 934, 854, 795, 749, 679 cm^{-1}; ESI-HRMS: Calcd for $[C_{22}H_{27}N_2O_3, M+H]^+$: 367.2016, found: 367.2020.

4.29 methyl 2-((3-(2-methylbenzyl)-2-oxoindolin-3-yl)amino)-3-phenylpropanoate (**4d**): 80% yield, white solid, m. p. 95 – 97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.23 – 7.12 (m, 6H), 7.05 – 7.01 (m, 1H), 6.97 – 6.87 (m, 5H), 6.71 (d, *J* = 7.6 Hz, 1H), 3.46 (t, *J* = 6.8 Hz, 1H), 3.22 (s, 3H), 3.12 (d, *J* = 13.6 Hz, 1H), 3.02 (d, *J* = 13.6 Hz, 1H), 2.93 (d, *J* = 7.2 Hz, 2H), 2.53 (br. s, 1H), 1.98 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.71, 175.12, 140.88, 137.69, 136.81, 133.07, 130.95, 130.39, 129.53, 129.28, 129.06, 128.51, 127.08, 126.94, 126.22, 125.45, 122.13, 110.14, 67.33, 59.03, 51.60, 40.85, 40.11, 20.05. IR: 3277, 3155, 3059, 3024, 2954, 2917, 1734, 1702, 1619, 1602, 1490, 1436, 1262, 1127, 1081, 1028, 983, 839, 729, 662 cm^{-1}; ESI-HRMS: Calcd for $[C_{26}H_{27}N_2O_3, M+H]^+$: 415.2016, found: 415.2013.

4.30 methyl 2-((3-(3-methylbenzyl)-2-oxoindolin-3-yl)amino)-3-phenylpropanoate (**4e**): 90% yield, white solid, m. p. 90 – 92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.22 – 7.16 (m, 4H), 7.14 – 7.11 (m, 3H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.91 – 6.85 (m, 2H), 6.65 – 6.21 (m, 3H), 3.45 (t, *J* = 7.2 Hz, 1H), 3.21 (s, 3H), 3.02 (dd, *J* = 27.6 Hz, *J* = 12.6 Hz, 2H), 2.91 (d, *J* = 7.2 Hz, 2H), 2.50 (br. s, 1H), 2.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.24, 175.08, 141.13, 137.21, 136.62, 134.10, 131.26, 129.40, 129.17, 128.82, 128.45, 127.63, 127.55, 127.42, 126.89, 126.00, 122.05, 110.21, 67.75, 59.05, 51.55, 44.11, 40.67, 21.28. IR: 3286, 3143, 3082, 3025, 2952, 2920, 1740, 1705, 1671, 1620, 1472, 1438, 1333, 1290, 1253, 1179, 1094, 838, 746, 696 cm^{-1}; ESI-HRMS: Calcd for $[C_{26}H_{27}N_2O_3, M+H]^+$: 415.2016, found: 415.2013.

4.31 methyl 2-((3-(4-methylbenzyl)-2-oxoindolin-3-yl)amino)-3-phenylpropanoate (**4f**): 92% yield, white solid, m. p. 120 – 122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.24 – 7.16 (m, 4H), 7.14 – 7.10 (m, 3H), 6.99 (td, *J* = 7.6 Hz, *J* = 0.4 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 2H), 6.72 (d, *J* = 8.0 Hz, 2H), 6.63 (d, *J* = 7.6 Hz, 1H), 3.45 (t, *J* = 7.2 Hz, 1H), 3.21 (s, 3H), 3.00 (dd, *J* = 22.8 Hz, *J* = 12.8 Hz, 2H), 2.91 (d, *J* = 7.2 Hz, 2H), 2.53 (s, 1H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.14, 175.11, 141.07, 136.69, 136.34, 131.12, 130.33, 129.45, 129.18, 128.90, 128.55, 128.50, 126.94, 126.00, 122.15, 110.18, 67.78, 59.11, 51.59, 43.84, 40.76, 21.15. IR: 3275, 3140, 3072, 3013, 2950, 2917, 1741, 1706, 1617, 1513, 1497, 1435, 1374, 1286, 1214, 1074, 971, 867, 819, 749, 695 cm^{-1}; ESI-HRMS: Calcd for $[C_{26}H_{27}N_2O_3, M+H]^+$: 415.2016, found: 415.2007.

4.32 methyl 2-((3-(2-bromobenzyl)-2-oxoindolin-3-yl)amino)-3-phenylpropanoate (**4g**): 75% yield, white solid, m. p. 112 – 114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.25 – 7.20 (m, 3H), 7.16 – 7.12 (m, 3H), 7.07 (d, *J* = 4.0 Hz, 2H), 7.00 – 6.95 (m, 2H), 6.90 (t, *J* = 7.6 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 3.53 (t, *J* = 6.8 Hz, 1H), 3.33 (d, *J* = 13.6 Hz, 1H), 3.28 (s, 3H), 3.19 (d, *J* = 14.0 Hz, 1H), 2.92 (ddd, *J* = 29.6, 13.3, 6.8 Hz, 2H), 2.52 (br. s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.14, 175.08, 140.61, 136.84, 134.71, 132.86, 131.94, 129.59, 129.37, 128.60, 128.58, 128.43, 127.04, 127.01, 126.73, 126.49, 122.22, 109.94, 66.76, 58.81, 51.70, 42.07, 40.81. IR: 3324, 3170, 3086, 3058, 2921, 2850, 1727, 1707, 1669, 1623, 1470, 1335, 1228, 1195, 1083, 917, 794, 751, 697, 654 cm^{-1}; ESI-HRMS: Calcd for $[C_{25}H_{24}BrN_2O_3, M+H]^+$: 479.0965, found: 479.0975.

4.33 methyl 2-((3-(3-bromobenzyl)-2-oxoindolin-3-yl)amino)-3-phenylpropanoate (**4h**): 90% yield, white solid, m. p. 95 – 97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.25 – 7.19 (m, 5H), 7.16 – 7.13 (m, 3H), 7.03 (t, *J* = 7.2 Hz, 1H), 6.96 (s, 1H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.75 (d, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 1H), 3.50 (t, *J* = 7.2 Hz, 1H), 3.28 (s, 3H), 2.98 – 2.85 (m, 4H), 2.42 (br. s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.47, 175.05, 140.85, 136.64, 133.39, 130.05, 129.60, 129.51, 129.37, 129.13, 128.65, 128.59, 128.40, 127.07, 125.93, 122.49, 121.79, 110.27, 67.41, 58.90, 51.76, 43.63, 40.70. IR: 3287, 3059, 3027, 2918, 2849, 1711, 1619, 1567, 1471, 1330, 1285, 1208, 1072, 1019, 797, 750, 715, 699 cm^{-1}; ESI-HRMS: Calcd for $[C_{25}H_{24}BrN_2O_3, M+H]^+$: 479.0965, found: 479.0960.

4.34 methyl 2-((3-(4-bromobenzyl)-2-oxoindolin-3-yl)amino)-3-phenylpropanoate (**4i**): 93% yield, white solid, m. p. 65 – 67 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.23 – 7.17 (m, 4H), 7.15 – 7.12 (m, 5H), 7.01 (td, *J* = 7.6 Hz, *J* = 0.4 Hz, 1H), 6.68 – 6.63 (m, 3H), 3.48 (t, *J* = 7.2 Hz, 1H), 3.25 (s, 3H), 2.98 (d, *J* = 2.0 Hz, 2H), 2.90 (dd, *J* = 10.4 Hz, *J* = 6.8 Hz, 2H), 2.50 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.80, 175.05, 141.00, 136.61, 133.30, 132.14, 130.89, 129.49, 129.45, 128.54, 128.47, 127.02, 125.83, 122.37, 121.05, 110.36, 67.44, 58.95, 51.70, 43.37, 40.68. IR: 3276, 3060, 3027, 2948, 2919, 1704, 1618, 1486, 1471, 1434, 1325, 1260, 1215, 1072, 939, 820, 750, 698, 655 cm^{-1}; ESI-HRMS: Calcd for $[C_{25}H_{24}BrN_2O_3, M+H]^+$: 479.0965, found: 479.0963.

4.35 methyl 2-((3-(4-chlorobenzyl)-2-oxoindolin-3-yl)amino)-3-phenylpropanoate (**4j**): 91% yield, white solid, m. p. 91 – 93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.23 – 7.21 (m, 3H), 7.13 (td, *J* = 8.4 Hz, *J* = 0.8 Hz, 1H), 7.03 – 6.99 (m, 4H), 6.83 (td, *J* = 7.2 Hz, *J* = 0.4 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 2H), 6.66 (d, *J* = 8.0 Hz, 1H), 6.41 (d, *J* = 7.2 Hz, 1H), 3.54 (s, 3H). 3.01 (t, *J* = 12.8 Hz, 2H), 2.89 (d, *J* = 12.8 Hz, 1H), 2.81 –

2.69 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.38, 174.79, 141.09, 137.51, 132.88, 132.86, 131.93, 129.82, 129.31, 128.30, 127.87, 127.85, 126.68, 125.36, 122.57, 110.10, 67.90, 58.83, 51.84, 44.67, 41.09. IR: 3296, 3189, 3086, 3024, 2951, 2925, 1736, 1704, 1668, 1621, 1491, 1472, 1334, 1287, 1228, 1182, 1090, 1026, 931, 861, 750, 733, 695 cm^{-1}; ESI-HRMS: Calcd for $[C_{25}H_{24}ClN_2O_3, M+H]^+$: 435.1470, found: 435.1486.

4.36 methyl 2-((3-(4-fluorobenzyl)-2-oxoindolin-3-yl)amino)-3-phenylpropanoate (**4k**): 90% yield, white solid, m. p. 115 – 117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.24 – 7.18 (m, 4H), 7.16 – 7.12 (m, 3H), 7.01 (t, J = 7.2 Hz, 1H), 6.78 – 6.74 (m, 2H), 6.69 (t, J = 8.8 Hz, 2H), 6.63 (d, J = 7.6 Hz, 1H), 3.48 (t, J = 7.2 Hz, 1H), 3.27 (s, 3H), 3.04 – 2.96 (m, 2H), 2.95 – 2.86 (m, 2H), 2.49 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.73, 175.08, 161.97 (d, J = 246.1 Hz), 140.93, 136.70, 131.94 (d, J = 8.0 Hz), 130.00 (d, J = 3.2 Hz), 129.51, 129.46, 128.64, 128.58, 127.05, 125.93, 122.41, 114.68 (d, J = 21.2 Hz), 110.17, 67.66, 59.00, 51.70, 43.31, 40.77. IR: 3293, 3142, 3081, 3026, 2954, 2923, 1738, 1702, 1672, 1620, 1472, 1437, 1364, 1337, 1214, 1184, 1132, 1081, 1020, 942, 860, 828, 751, 700, 664 cm^{-1}; ESI-HRMS: Calcd for $[C_{25}H_{24}FN_2O_3, M+H]^+$: 419.1765, found: 419.1764.

4.37 methyl 2-((3-(4-cyanobenzyl)-2-oxoindolin-3-yl)amino)-3-phenylpropanoate (**4l**): 90% yield, white solid, m. p. 99 – 101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.23 – 7.20 (m, 3H), 7.12 (td, J = 7.6 Hz, J = 1.2 Hz, 1H), 7.03 (dd, J = 7.2 Hz, J = 3.6 Hz, 2H), 6.84 (td, J = 8.0 Hz, J = 0.8 Hz, 1H), 6.77 – 6.68 (m, 4H), 6.62 (d, J = 7.6 Hz, 1H), 6.45 (d, J = 7.2 Hz, 1H), 3.58 (s, 3H). 3.03 – 2.99 (m, 2H), 2.91 (d, J = 12.8 Hz, 1H), 2.81 – 2.70 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.55, 174.68, 140.83, 140.09, 137.50, 131.49, 131.37, 129.83, 129.60, 128.35, 127.32, 126.77, 125.41, 122.80, 119.02, 110.89, 110.09, 67.64, 58.80, 51.92, 45.36, 41.09. IR: 3312, 3200, 3023, 2954, 2921, 2850, 1734, 1704, 1667, 1622, 1606, 1494, 1471, 1451, 1428, 1413, 1335, 1227, 1134, 1087, 1016, 970, 930, 861, 784, 751, 740, 696 cm^{-1}; ESI-HRMS: Calcd for $[C_{26}H_{24}N_2O_3, M+H]^+$: 426.1812, found: 426.1819.

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