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Syntheses of 3,3-Disubstituted Dihydrobenzofurans, Indolines, Indolinones and Isochromanes by Palladium-Catalyzed Tandem Reaction Using $Pd(PPh_3)_2Cl_2$/(±)-BINAP as a Catalytic System

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Abstract: A general procedure for the tandem arylation reaction of arylbromide with heteroaryl compounds was developed by using $Pd(PPh_3)_2Cl_2$/(±)-BINAP (1,1′-Binaphthalene-2,2′-diylbis (diphenylphosphane)) as catalytic system. Both sulphur- and oxygen-containing heterocycles were also employed as an efficient reagent for arylation, which gave moderate to excellent yields with moderate to good regioselectivities (5:1 to > 20:1 *ir* (isomer ratio)). Except for dihydrobenzofurans, indolines and indolinones, this type of tandem reaction was also expanded to synthesize isochromanes. The synthesized new compounds were well characterized through different spectroscopic techniques, such as ^1H and ^{13}C NMR (nuclear magnetic resonance), and mass spectral analysis.

Keywords: tandem reaction; dihydrobenzofurans; indolines; indolinones; isochromanes

1. Introduction

The benzofuran and indoline scaffold existed extensively in various biologically active molecules, important natural products and also part of different functional materials [1–6]. For example, megapodiol (**I**) is an antileukemic agent [7] and conocarpan (**II**) is toxic to mosquito larvae [8,9]. Coerulescine (**III**) is as an inhibitor of MDM2 (Murine Double Minute 2)-p53 [10,11], where compound **IV** shows antiproliferative activity and may be especially useful for the treatment of cancer [12]. Compound **V** exhibits selective 5-hydroxytryptamine7 (5-HT_7) antagonist activity (K_i = 0.79 nm) [13] and alstonisine (**VI**) also reveals antiplasmodial activity against *Plasmodium falciparum*, with an IC50 (half maximal inhibitory concentration) of 7.6 μM [14] (Figure 1). Therefore, organic chemists around the world made extensive efforts to develop the highly efficient methods of constructing these heterocycles [15–28]. Of these molecules, 3,3-disubsitituted five-membered

heterocycles, including dihydrobenzofurans, indolines and indolinones, have been extensively studied. The domino reactions of the synthesis of them were summarized mainly as follows: (i) the Pd or Ni-catalyzed cyclocarbopalladation/coupling fractions, in which the process was initiated by Heck cyclization of a starter (halide) and a relay (alkene), followed by intermolecular coupling reactions with a terminator (organometallic reagents, alkenes, alkynes, etc.), including Suzuki, Stille, Heck, Sonogashira, C-H activation, carbonylation and amination and so forth [15–17,22,24,25,29–44]; (ii) the C-H oxidative radical coupling reactions, in which these transformations were based on tandem radical addition/cyclization in the presence of oxidants with/without metal catalysts [18–21,23,26,45–55]; and (iii) the other reactions [24,56–61], such as C-H activated cyclization/trapping with the Pd (IV) intermediate or *O*- and *N*-based nucleophiles, Heck/C-H activated cyclization. Among the variety of new synthetic protocols, transition metal-catalyzed reactions are part of the most attractive methodologies, because they can directly lead to complicated molecules with quickness and high efficiency. In particular, palladium-catalyzed domino reactions provide versatile and efficient methods for the assembly of a wide range of these molecules [8].

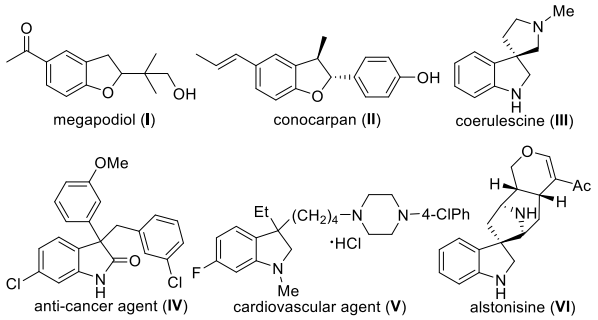


Figure 1. Representatives of natural and artificial bioactive benzofurans and 3,3-disubstituted indoles **I**–**VI**.

In 2009, Fagnou and coworkers [62] reported the X-phos catalytic domino Heck/arylation reaction of arylbromide with sulphur-containing heterocycles (thiazole, thiophene and benzothiophene) to provide 18 products in 41–99% yields (Figure 2). Next, an elegant asymmetric synthesis of 3,3-disubsitituted indolinones via the same domino sequence was presented by Zhu's group [63]. 2-aryl-1,3,4-oxadiazoles were chosen as substrate for the second step and the reaction obtained 24 desired products in 55–75% yields with 82–99% *ee*. However only two other heterocyclic examples (benzothiazole and benzoxazole) were reported in 60–61% yields with 92–97% *ee*. Recently, Xu and Liang also reported an efficient tandem alkylation of electron-deficient polyfluoroarenes with aryl iodides in 51–96% yields [64]. Despite the excellent works mentioned above, the scope of this domino reaction needs to be further expanded with other heterocyclic substrates. Based on our previous studies of reductive Heck cyclization and Suzuki coupling reaction [65–67], synthesis of spiropyrrolidine oxindoles [68,69] and ongoing interest in the highly efficient and atom-economic domino reactions for organic synthesis, we demonstrated herein the synthesis of 3,3-disubstituted hydrobenzofurans, indolines, indolinones and isochromanes using $Pd(PPh_3)_2Cl_2$/(±)-BINAP as a catalytic system and various arylheterocycles as substrates.

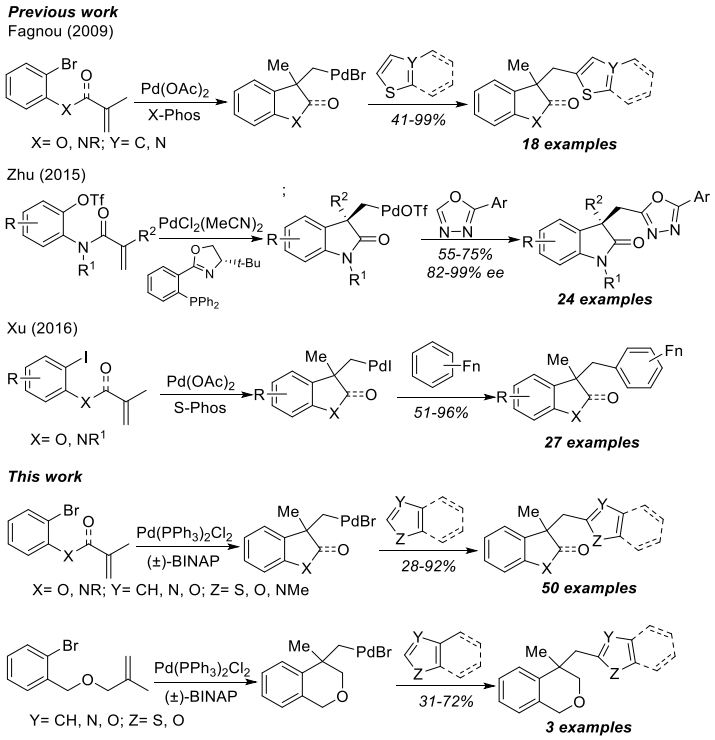


Figure 2. The tandem Heck/arylation for the synthesis of dihydrobenzo-furans, indolines, indolinones and isochromanes.

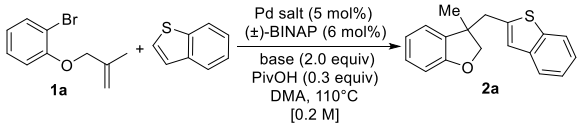
2. Results and Discussion

Initially, we also tried to perform the same reaction with palladium salts and chiral P and *N*,*P*-ligands (for example: (*R*)-BINAP, (*R*)-SDP (spiro-di(1,1′-indanyl)bisphosphine), (*R*)-Segphos and spiro-phosporamidites) and expected to realize an asymmetric synthesis edition in the condition reported by Fagnou's group [62]. Nevertheless, it was unlucky to not obtain satisfying enantioselectivity (0–10% *ee*). We found the (*R*)-BINAP and Pd salts catalyzed the reaction to give the desired product in a satisfying yield, although it could not induce chirally in the process of a reaction. As a common phosphine ligand, the price of (±)-BINAP (162 RMB/mmol from Sigma-Aldrich (Shanghai, China) Trading Co., Shanghai, China) is cheaper than the one of X-phos (348 RMB/mmol from Sigma-Aldrich Sigma-Aldrich (Shanghai) Trading Co.) and other phosphine ligands with more efficiency. Furthermore, BINAP has been widely applied in all kinds of catalyzed symmetric or asymmetric syntheses as a ligand. As a necessary and useful supplement of Fagnou's work, we decided to make our efforts in further developing $Pd(PPh_3)_2$/(±)-BINAP as an efficient catalyst to be used in the synthesis of 3,3-substituted 5 or 6-membered heterocycles, on the basis of the above experimental results.

In the beginning of our study, for the optimization of the reaction conditions, aryl bromide and benzothiophene were chosen as the model substrates. Initially, the reaction was performed in the presence of 5 mol% $Pd(OAc)_2$ as a catalyst, 6 mol% (±)-BINAP as a ligand, 30 mol% PivOH (pivalic acid) as an additive, and 2 equiv. of K_2CO_3 as a base under DMA (*N*,*N*-dimethylacetamide) at 110 °C for 30 h. The desired product was obtained in 61% isolated yield, with 10:1 regioselectivity. The other palladium salts, such as $PdCl_2$, $Pd_2(dba)_3$, $Pd(dppf)_2Cl_2$, $Pd(PPh_3)_2Cl_2$ and Pd/C were tested in the reaction. $Pd(PPh_3)_2Cl_2$ gave the highest yield (80%; Table 1, entry 7), while Pd/C afforded almost no product (Table 1, entry 6). The other palladium salts provided moderate yields (Table 1, entries 2–5). Subsequently, the various bases and solvents were screened by using $Pd(PPh_3)_2Cl_2$ (5 mol%) as a catalyst and (±)-BINAP (6 mol%) as a ligand. In DMA, performing the reaction in the presence of either weak bases (KOAc, K_3PO_4, Na_2CO_3 and Cs_2CO_3) or strong bases (KO*t*Bu, $LiOH{\cdot}H_2O$, NaOH and KOH) resulted in low yields (15–65%) and none of the desired product was formed using an organic

base (TEA (triethylamine)). In DMF (*N*,*N*-dimethylformamide), the reaction gave the light lower yield (76%). The other solvents (e.g., DMSO (dimethyl sulfoxide), 1,4-dioxane, 1,2-DCE (dichloroethane), DME (dimethoxyethane), PhCN (benzonitrile), THF (tetrahydrofuran) and PhH (benzene)) obtained the very lower yields (<10%) or had no predicted product except for toluene and acetonitrile (59% and 44% yields, respectively). The additives were also screened. CsF (cesium fluoride) gave the product in 61% yield, while silver salts (Ag_2CO_3 and $AgNO_3$) furnished one in <20% yields. Furthermore, the yield dropped to 66% without any additive (Table 1, entry 19). Secondly, some common phosphine ligands (PPh_3, PCy_3, P*t*Bu_3, dppe, dppp and dppb) were used to promote the reaction (Table 2). The result was that most ligands gave the poor reactivities in 36%–65% yields. Furthermore, monophosphine ligands (PPh_3, PCy_3 and P*t*Bu_3) at 12 mol% loading only provided slightly increased yields (50%–71%). Finally, the optimal reaction condition (Table 1, entry 6) for the tandem arylation reaction was established as bromide **1a** (1.0 equiv.), benzothiophene (4.0 equiv.), PivOH (0.3 equiv.) and K_2CO_3 (2.0 equiv.) in DMA at 110 °C under $Pd(PPh_3)_2Cl_2$ (5 mmol%) as a catalyst and (±)-BINAP (6 mol%) as a ligand.

Table 1. The condition optimization of the model reaction [a].



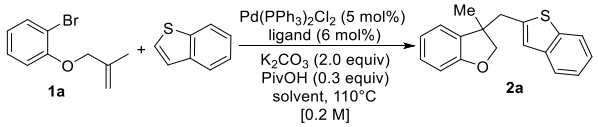
Entry	Pd Salt	Additive	Base	Yield [b]
1	$Pd(OAc)_2$	PivOH	K_2CO_3	61
2	$Pd_2(dba)_3$	PivOH	K_2CO_3	16
3	$Pd(dppf)_2Cl_2$	PivOH	K_2CO_3	39
4	$Pd(PPh_3)_4$	PivOH	K_2CO_3	61
5	$PdCl_2$	PivOH	K_2CO_3	54
6	Pd/C	PivOH	K_2CO_3	- [c]
7	$Pd(PPh_3)_2Cl_2$	PivOH	K_2CO_3	80
8	$Pd(PPh_3)_2Cl_2$	PivOH	KOAc	57
9	$Pd(PPh_3)_2Cl_2$	PivOH	K_3PO_4	15
10	$Pd(PPh_3)_2Cl_2$	PivOH	KO*t*Bu	55
11	$Pd(PPh_3)_2Cl_2$	PivOH	Na_2CO_3	22
12	$Pd(PPh_3)_2Cl_2$	PivOH	Cs_2CO_3	65
13	$Pd(PPh_3)_2Cl_2$	PivOH	$LiOH{\cdot}H_2O$	31
14	$Pd(PPh_3)_2Cl_2$	PivOH	NaOH	25
15	$Pd(PPh_3)_2Cl_2$	PivOH	KOH	42
16	$Pd(PPh_3)_2Cl_2$	PivOH	TEA	- [c]
17	$Pd(PPh_3)_2Cl_2$ (1 mol%)	PivOH	K_2CO_3	59
18	$Pd(PPh_3)_2Cl_2$ (3 mol%)	PivOH	K_2CO_3	75
19	$Pd(PPh_3)_2Cl_2$	- [d]	K_2CO_3	66
20	$Pd(PPh_3)_2Cl_2$	CsF	K_2CO_3	61
21	$Pd(PPh_3)_2Cl_2$	Ag_2CO_3	K_2CO_3	<20%
22	$Pd(PPh_3)_2Cl_2$	$AgNO_3$	K_2CO_3	20%

[a] Reaction conditions: aryl bromide (0.1 mmol), benzothiophene (0.4 mmol), Pd salt (5 mol%), (±)-BINAP (6 mol%), PivOH (0.3 equiv), base (2.0 equiv) and DMA (0.5 mL), 110 °C, 30 h. [b] Isolated by column chromatography with ≥ 10:1 regioselectivity. [c] No product. [d] No additive. PivOH = pivalic acid, TEA = triethylamine, DMA = *N*,*N*-dimethylacetamide, dba = dibenzylideneacetone and dppf = 1,1′-bis(diphenyl phosphino)ferrocene.

With the readily obtained optimization conditions in hand, we further investigated the substrate scope for this $Pd(PPh_3)_2Cl_2$/(±)-BINAP-catalyzed tandem arylation reaction. A range of aromatic heterocycles was first screened. As shown in Scheme 1, outside benzothiophene, benzofuran and thiophene worked well in this reaction, thus affording the corresponding products **2ab** and **2ad** in 77% and 65% yields, respectively, with 10:1 and >20:1 regioselectivities. Whereas, *N*-methylindole, substituted thiophenes, thiazole, and furan only obtained moderate yields (35–45%), but with excellent regioselectivities (>20:1 *ir*). However, no products were observed using other bicyclic

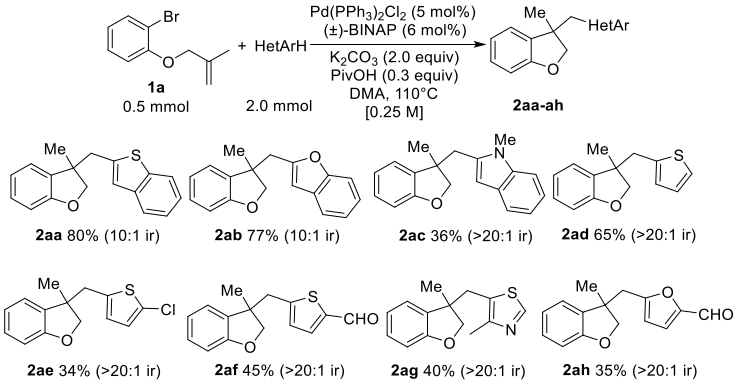
substrates, such as benzoxazole, benzothiazole, 2-bromfuran and 3-bromthiophenes. Unfortunately, (2-phenylallyl)arylether, instead of **1a**, combined with benzothiophene and gave a complex, which showed that the reaction system was not suitable for that kind of substrate.

Table 2. The effect of the ligand and solvent on the model tandem reaction [a].



Entry	Ligand	Solvent	Yield [b]
1	Ph_3P	DMA	36
2	Cy_3P	DMA	56
3	$Cy_3P{\cdot}HBF_4$	DMA	61
4	$tBu_3P{\cdot}HBF_4$	DMA	50
5	dppe	DMA	60
6	dppb	DMA	62
7	dppp	DMA	65
8	(±)-BINAP	DMA	80
9	(±)-BINAP	DMF	76
10	(±)-BINAP	PhMe	59
11	(±)-BINAP	ACN	44
12	(±)-BINAP	PhCN	<10
13	(±)-BINAP	DMSO	-[c]
14	(±)-BINAP	1,4-dioxane	<10
15	(±)-BINAP	DMA (90 °C)	75

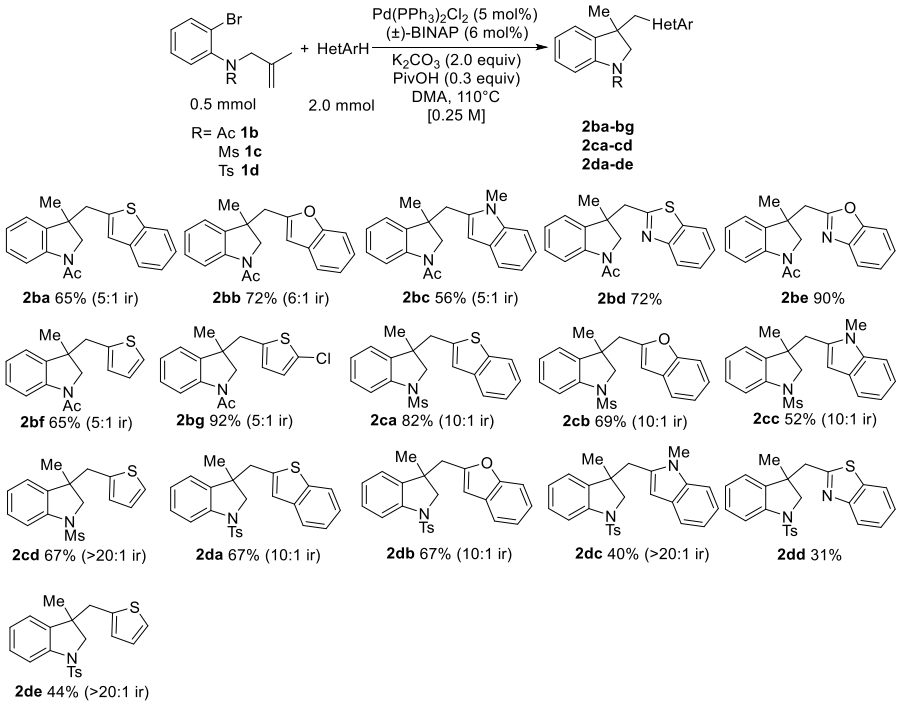
[a] Reaction conditions: aryl bromide (0.1 mmol), benzothiophene (0.4 mmol), $Pd(PPh_3)_2Cl_2$ (5 mol%), ligand (6 mol%), PivOH (0.3 equiv), K_2CO_3 (2.0 equiv) and solvent (0.5 mL), 110 °C, 30 h. [b] Isolated by column chromatography with ≥ 10:1 regioselectivity. [c] No product. DMF = *N*,*N*-dimethylformamide, ACN = acetonitrile, DMSO = dimethyl sulfoxide, dppe = 1,2-bis(diphenylphosphino)ethane, dppb = 1,4-bis(diphenylphosphino)butane and dppp = 1,3-bis(diphenylphosphino)propane.



Scheme 1. Synthesis of 3,3-disubstituted dihydrobenzofruans.

To ascertain further the scope of this method, a variety of *N*- substituted anilines bearing electron-withdrawing groups (Ac, Ms and Ts) were investigated. As summarized in Scheme 2, the reaction is compatible with a wide range of anilines to afford different indoles in moderate to good yields with acceptable to high regioselectivity. *N*-substituted **1b-d**, reacted with benzothiophene smoothly, affording the corresponding α-substituted products **2ba**, **2ca** and **2da** in moderate to high yields (65–82%) with moderate selectivity (5:1–10:1 *ir*). **1b-d** reacted with benzofuran to give similar results (67–72% yields and 6:1–10:1 *ir*). Compared with benzothiophene and benzofuran, the reaction of *N*-methylindole with compounds **1b-d** led to relatively poor results (52–67% yield and 5:1–10:1 *ir*). Meanwhile, in the reaction of thiophene, **1b** coupled with 2-chlorothiophene to produce excellent yield

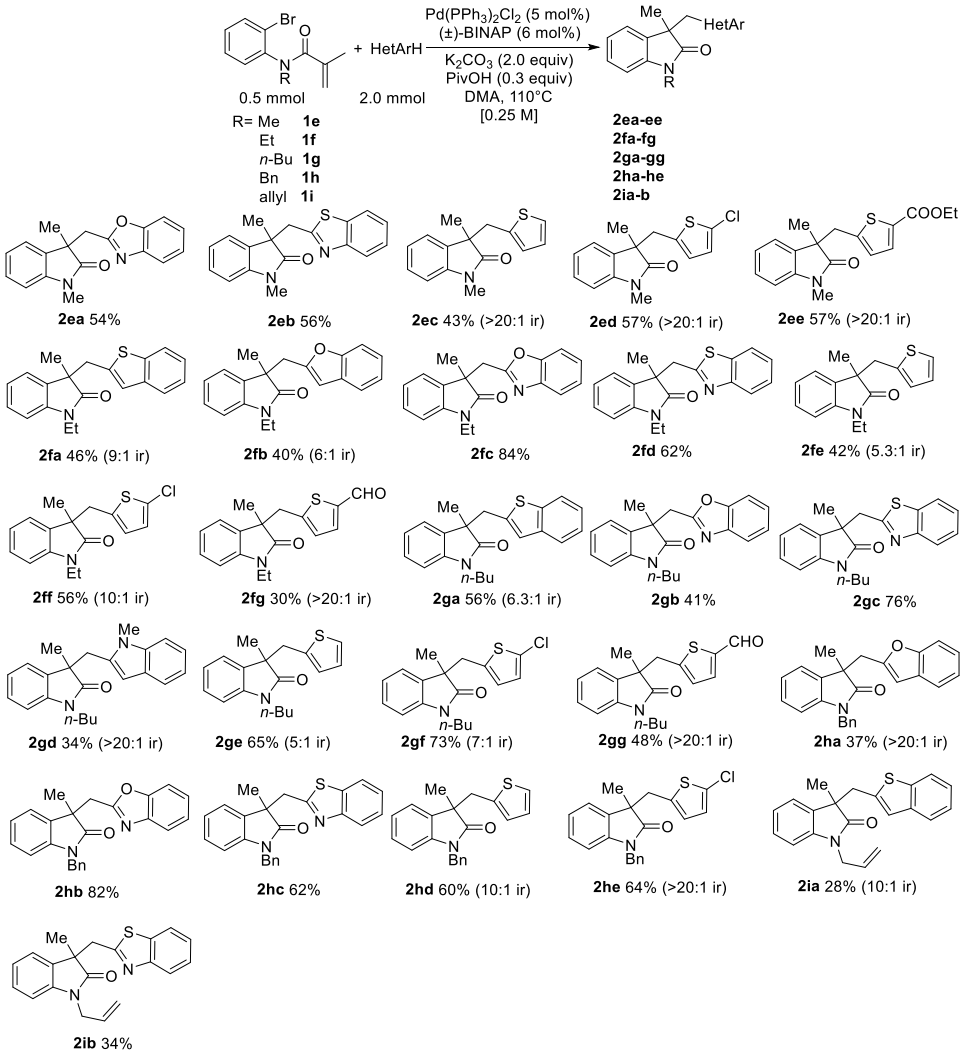
(92%). Finally, the reaction of **1b** with benzothiazole and benzoxazole gave a good result (72% and 90% yields), while **1c**-**d** had unsatisfactory results that only one product **2dd** was obtained in a low yield.



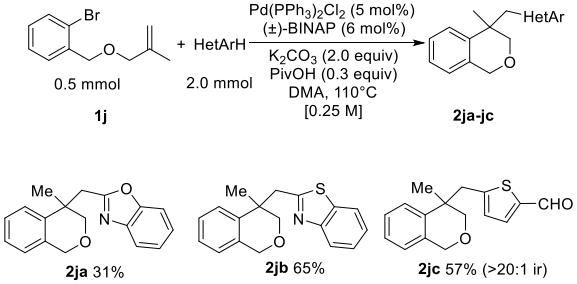
Scheme 2. Synthesis of 3,3-disubstituted indolines.

A scope of the reaction with respect to *N*-heteroarylacrylamides is summarized in Scheme 3. *N*-substituted groups, such as methyl, ethyl, *n*-butyl and benzyl, were well tolerated, providing the desired adducts **2ea**-**2ib** in moderate to excellent yields (28–84%) with moderate to high regioselectivities (5:1 to >20:1 *ir*). Acrylamide with benzyl group **1h** reacted smoothly with heteroarylenes. Among the four compounds **1e**-**h**, both **1f** and **1h** smoothly reacted with benzoxazole, respectively, to get high yields (84% for **2fc** and 82% for **2hb**), if compared to **1e** (54% for **1ea**) and **1g** (41% for **1gb**). Overall, **1e**-**h** performed with benzothiazole and gave the similar results (56–76%). Substituted and unsubstituted thiophenes obtained moderate yields (42–73%), but excellent regioselectivities (>20:1 *ir*) in most cases. However, both benzofuran and *N*-methylindole led to the worst results (40% yield for **2fb** and 37% yield for **2ha**). Finally, the *N*-allyl substrate also proceeded the tandem reaction with benzothiophene and benzothiazole, but in low yields (28% for **2ia** and 34% for **2ib**).

Recently, domino cyclizations of constructing 3,3-disubstituted six-membered heterocycle skeletons also were developed [70–76]. On extending the investigations toward the scope of this transformation, we also studied the reaction of benzylallyl ether or allylbenzyl amines with heteroarenes to form 3,3-disubstituted isochromanes or tetrahydroisoquinolines. As outlined in Scheme 4, ether **1j** also reacted smoothly with heteroarenes, in which it generated the desired products **2ja**-**jc** in 31–65% yields. However, *N*-substituted tetrahydroisoquinolines were not obtained in the standard condition, after many trials.



Scheme 3. Synthesis of 3,3-disubstituted indolinones.



Scheme 4. Synthesis of 4,4-disubstituted isochromanes.

3. Materials and Methods

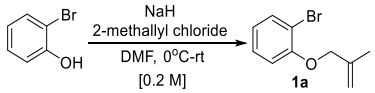
Please see Supplementary Materials.

3.1. General Methods

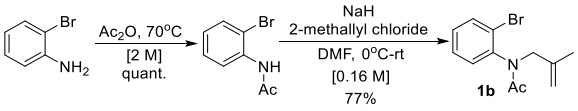
All non-aqueous reactions were carried out using flame-dried round-bottomed flasks and Schlenk tubes under an inert atmosphere of argon with dry solvents. All reagents were obtained from commercial suppliers unless otherwise stated. *N*, *N*-dimethylformamide (DMF), *N*, *N*-dimethylacetamide (DMA), dimethyl sulfoxide (DMSO), acetonitrile (ACN), benzonitrile, dichloromethane (DCM), triethylamine

(TEA) and pyridine were distilled from calcium hydride under argon; toluene and dioxane were distilled from Na/benzophenone under argon; and methanol (MeOH) was distilled from Mg/I_2 under argon. Flash chromatography was performed using silica gel (300–400 mesh). Reactions were monitored by TLC (thin-layer chromatography). Visualization was achieved under a UV (Ultraviolet) lamp (254 nm and 365 nm), I_2 and by developing the plates with para-anisaldehyde, phosphomolybdic acid, or potassium permanganate. ^{1}H and ^{13}C NMR were recorded on a 400 MHz NMR spectrometer with tetramethylsilane (TMS) as the internal standard and were calibrated using a residual nondeuterated solvent as an internal reference ($CDCl_3$: ^{1}H NMR δ = 7.26, ^{13}C NMR δ = 77.16; DMSO-d_6: ^{1}H NMR δ = 2.54, ^{13}C NMR δ = 40.45). High-resolution mass spectra were obtained using electrospray ionization (ESI). The following abbreviations were used for the multiplicities: *s*: singlet, *d*: doublet, *t*: triplet, *m*: multiplet and *br s*: broad singlet for proton spectra. Coupling constants (*J*) are reported in Hertz (Hz).

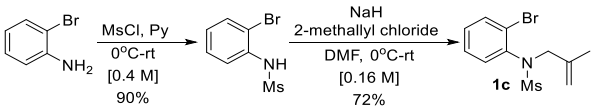
3.2. General Procedure A for the Preparation of O or N-methylallyl Arylbromides



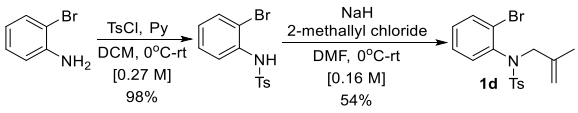
To a solution of 2-bromophenol (1.73 g, 10 mmol, 1.0 equiv.) in dry DMF (50 mL), NaH (60%, 440 mg, 11.0 mmol, 1.1 equiv.) was added in three portions at 0 °C, and the mixture was stirred for 30 min. 2-Methallyl chloride (1.08 g, 12.0 mmol, 1.2 equiv.) was added and then the mixture was stirred at rt (room temperature) until the reaction was judged to be completed by TLC analysis. After the completion of the reaction, saturated NH_4Cl solution (10 mL) and brine (100 mL) was added, and then extracted with petroleum ether/EtOAc (*V*/*V* = 10:1, 3 × 30 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to afford **1a** as a colorless oil (1.86 g, 82%) [62]. (CAS: 10178-53-7); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.25–7.21 (m, 1 H), 6.87 (dd, *J* = 8.0, 1.2 Hz, 1 H), 6.82 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1 H), 5.17 (dd, *J* = 1.6, 0.8 Hz, 1 H), 5.02 (dd, *J* = 2.8, 1.2 Hz, 1 H), 4.49 (s, 2 H), 1.86 (d, *J* = 0.4 Hz, 3 H).



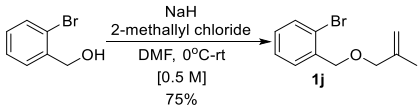
A solution of 2-bromoaniline (1.72 g, 10 mmol) in Ac_2O (5 mL) was stirred at 70 °C for 1 h. The mixture was added dropwise to a saturated $NaHCO_3$ solution (50 mL) at 0 °C and then extracted with EtOAc (4 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford the *N*-Ac product as a white solid (2.30 g, quantitative yield). The above product (0.85 g, 4.0 mmol, 1 equiv.) was dissolved in dry DMF (25 mL) and NaH (60%, 192 mg, 4.8 mmol, 1.2 equiv.) was added in two portions at 0 °C. The mixture was stirred for 30 min and then 2-methallyl chloride (0.43 mL, 4.4 mmol, 1.1 equiv.) was added. The resulting mixture was stirred at rt overnight, before it was quenched with saturated NH_4Cl solution (20 mL) and brine (20 mL) and then extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to provide **1b** (0.83 g, 77%) as a pale yellow solid [70]. (CAS: 115802-65-8); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.37–7.33 (m, 1 H), 7.27 (d, *J* = 4.0 Hz, 1 H), 7.24–7.20 (m, 1 H), 4.94 (d, *J* = 4.8 Hz, 1 H), 4.83 (s, 1 H), 4.67 (s, 1 H), 3.68 (d, *J* = 15.0 Hz, 1 H), 1.84 (s, 3 H), 1.80 (s, 3 H).



To a solution of 2-bromoaniline (1.37 g, 8 mmol, 1 equiv.) in pyridine (20 mL) at 0 °C, MsCl (0.74 mL, 9.6 mmol, 1.2 equiv.) was added dropwise. The mixture was stirred at rt for 48 h, before it was quenched with 10% hydrochloric acid at 0 °C and up to pH = 5. The mixture was extracted with EtOAc (4 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford the *N*-Ms product as a brown solid (1.80 g, 90%). The above crude product (1.00 g, 4.0 mmol, 1.0 equiv.) was dissolved in dry DMF (25 mL) and NaH (60%, 192 mg, 4.8 mmol, 1.2 equiv.) was added in two portions at 0 °C. The mixture was stirred for 30 min and then 2-methallyl chloride (0.40 g, 4.4 mmol, 1.1 equiv.) was added. The resulting mixture was stirred at rt for 38 h, before it was quenched with saturated NH_4Cl solution (20 mL) and brine (20 mL) and then extracted with EtOAc (4 × 15 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to provide **1c** (0.89 g, 72%) as a pale yellow solid [77]. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.44 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.36–7.32 (m, 1 H), 7.24–7.20 (m, 1 H), 4.82 (s, 1 H), 4.78 (s, 1 H), 4.38 (s, 1 H), 4.15 (s, 1 H), 3.06 (s, 3 H), 1.84 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.9, 137.3, 134.0, 134.0, 1333.9, 130.0, 128.3, 123.8, 115.9, 56.6, 40.9, 20.4; HRMS (high resolution mass spectrometer) *m/z* Calcd for $C_{11}H_{14}O_2NSBrNa$ $[M+Na]^+$ 325.9826, found 325.9835.

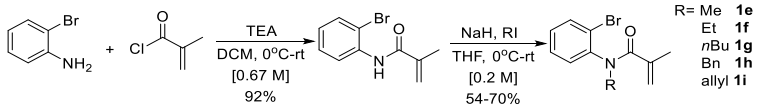


A solution of 2-bromoaniline (1.38 g, 8 mmol, 1 equiv.), TsCl (1.83 g, 9.6 mmol, 1.2 equiv.), and pyridine (1.93 mL, 24 mmol, 3.0 equiv.) in dry DCM (30 mL) was stirred at rt for 24 h. Then it was quenched with 10% hydrochloric acid at 0 °C and up to pH = 5. The mixture was extracted with DCM (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford the *N*-Ts product as a white solid (2.56 g, 98%). The above product (1.30 g, 4.0 mmol, 1 equiv.) was dissolved in dry DMF (25 mL) and NaH (60%, 192 mg, 4.8 mmol, 1.2 equiv.) was added in two portions at 0 °C. The mixture was stirred for 30 min and then 2-methallyl chloride (0.43 mL, 4.4 mmol, 1.1 equiv.) was added. The resulting mixture was stirred at rt overnight, before it was quenched with saturated NH_4Cl solution (20 mL) and brine (20 mL) and then extracted with EtOAc (4 × 15 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc 5:1) to provide **1d** (0.85 g, 54%) as a pale yellow solid [78]. (CAS: 1191913-83-3); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.4 Hz, 2 H), 7.56 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.28–7.24 (m, 3 H), 7.18–7.13 (m, 2 H), 4.74 (s, 1 H), 4.66 (s, 1 H), 4.15 (d, 2 H), 2.43 (s, 3 H), 1.81 (s, 3 H).



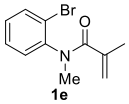
To a solution of 2′-bromobenzyl alcohol (3.74 g, 20 mmol, 1.0 equiv.) in DMF (40 mL), NaH (60%, 960 mg, 24 mmol, 1.2 equiv.) was added in three portions at 0 °C, and the mixture was stirred for 30 min. 2-Methallyl chloride (2.35 mL, 22 mmol, 1.1 equiv.) was added and then the mixture was stirred at rt until the reaction was judged to be completed by the TLC analysis. After the completion of the reaction, saturated NH_4Cl solution and brine was added, and then extracted with EtOAc (ethyl acetate; 4 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to afford **1j** as a colorless oil (3.90 g, 75%) [79]. (CAS: 935742-52-2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.49 (m, 2 H), 7.30–7.28 (m, 1 H), 7.14–7.10 (m, 1 H), 5.03 (d, *J* = 0.6 Hz, 1 H), 4.94 (d, *J* = 0.6 Hz, 1 H), 4.55 (s, 2 H), 4.00 (s, 2 H), 1.78 (s, 3 H).

3.3. General Procedure B for the Preparation of Starting Materials



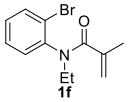
To a solution of 2-bromoaniline (3.40 g, 20 mmol, 1.0 equiv.) and TEA (3.60 mL, 26 mmol, 1.3 equiv.) in dry DCM (30 mL), methacryloyl chloride (2.52 mL, 26 mmol, 1.3 equiv.) was slowly added. The mixture was stirred at rt for 12 h and extra methacryloyl chloride (0.5 g, 4.78 mmol, 0.24 equiv.) was added. After 18 h, brine (15 mL) was added and the mixture was concentrated, followed by extraction with EtOAc (3 × 30 mL). The organic layer was dried over Mg_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to afford *N*-substituted product as a yellow oil (4.42 g, 92%).

To a solution of the above oil (2.40 g, 10 mmol, 1.0 equiv.) in dry THF (50 mL), NaH (60%, 0.50 g, 12.5 mmol, 1.2 equiv.) was added and the mixture was stirred at rt for 30 min. Alkyl iodide (1.2 equiv.) was added slowly and the mixture was stirred until the reaction was judged to be completed by the TLC analysis. After the completion of the reaction, brine was added and the mixture was extracted with EtOAc (4 × 30 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography to afford the corresponding product **1e-I** [80].



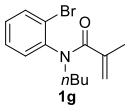
1e

(CAS: 102804-50-2); 62% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63–6.61 (m, 1 H), 7.34–7.30 (m, 1 H), 7.20–7.16 (m, 2 H), 5.00 (d, *J* = 17.2 Hz, 2 H), 3.26 (s, 3 H), 1.82 (s, 3 H).



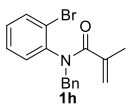
1f

(CAS: 1638143-30-2); 65% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 8.0 Hz, 1 H), 7.26–7.23 (m, 1 H), 7.13–7.07 (m, 2 H), 4.92 (s, 1 H), 4.88 (s, 1 H), 4.08 (m, 1 H), 3.55 (m, 1 H), 1.75 (s, 3 H), 1.07 (t, *J* = 5.6 Hz, 3 H).



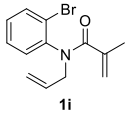
1g

54% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.62 (m, 1 H), 7.34–7.29 (m, 1 H), 7.20–7.16 (m, 2 H), 4.95 (d, *J* = 11.8 Hz, 2 H), 4.15–4.08 (m, 1 H), 3.33–3.26 (m, 1 H), 1.82 (s, 3 H), 1.61–1.56 (m, 1 H), 1.51–1.45 (m, 1 H), 1.36–1.26 (m, 2 H), 0.90 (t, *J* = 7.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4, 142.0, 140.5, 133.8, 131.1, 129.1, 128.1, 123.6, 118.1, 48.4, 29.4, 20.4, 20.2, 13.8; HRMS *m/z* Calcd for $C_{14}H_{19}NOBr$ $[M+H]^+$ 296.0650, found 296.0602.



1h

(CAS: 151502-76-0); 67% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.59 (m, 1 H), 7.26 (d, *J* = 2.8 Hz, 1 H), 7.24 (d, *J* = 1.8 Hz, 2 H), 7.21–7.19 (m, 2 H), 7.14–7.10 (m, 2 H), 5.64 (d, *J* = 14.4 Hz, 1 H), 5.01 (s, 1 H), 4.97 (s, 1 H), 4.18 (d, *J* = 14.4 Hz, 1 H), 1.83 (s, 1 H).



1i

(CAS: 146499-16-3); 70% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.31–7.27 (m, 1 H), 7.18 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.16–7.12 (m, 1 H), 5.94–5.96 (m, 1 H), 5.13–5.06 (m, 2 H), 5.05–4.98 (m, 2 H), 4.81 (dd, *J* = 14.4, 4.4 Hz, 1 H), 3.85–3.80 (m, 1 H), 1.83 (s, 3 H).

3.4. General Procedure for Condition Optimization of the Tandem Reaction

In an argon-filled glove bag, base (0.2 mmol, 2.0 equiv.), Pd salt (0.005 mmol, 0.05 equiv.), ligand (0.006 mmol, 0.06 equiv.), additive (0.03 mmol, 0.3 equiv.), **1a** (0.1 mmol, 1.0 equiv.), benzothiophene (0.4 mmol, 4.0 equiv.) and solvent (0.5 mL) were successively added to a 10 mL Schlenk tube. The tube was vigorously stirred in an oil bath for 30 h.

3.5. General Procedure for the Typical Procedure for Tandem Reactions

In an argon-filled glove bag, bromides (0.5 mmol, 1.0 equiv.), arylheterocycles (2.0 mmol, 4.0 equiv.), K_2CO_3 (138.2 mg, 1.0 mmol, 2.0 equiv.), PivOH (15.3 mg, 0.15 mmol, 0.3 equiv.), (±)-BINAP (18.7 mg, 0.03 mmol, 6 mmol%), $Pd(PPh_3)_2Cl$ (17.5 mg, 0.025 mmol, 5 mmol%) and DMA (2.0 mL) were added successively to a 25 mL Schlenk tube. The tube was vigorously stirred in an oil bath at 110 °C for 30 h. At the end of the reaction, the mixture cooled to room temperature and then was directly purified by silica gel column chromatography to afford the corresponding product.

*(±)-3-(benzothiophen-2-ylmethyl)-3-methyl-2,3-dihydrobenzofuran (**2aa**)*

(CAS: 1191913-87-7); 80% yield, an inseparable pale yellow solid, isomers ratio = 10:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 7.8 Hz, 1 H), 7.66 (d, *J* = 7.2 Hz, 1 H), 7.33–7.29 (m, 1 H), 7.28–7.24 (m, 1 H), 7.19–7.15 (m, 1 H), 7.11 (dd, *J* = 7.6, 0.8 Hz, 1 H), 6.93 (s, 1 H), 6.92–6.88 (m, 1 H), 6.78 (d, *J* = 8.0 Hz, 1 H), 4.59 (d, *J* = 8.8 Hz, A of AB, 1 H), 4.17 (d, *J* = 8.8 Hz, B of AB, 1 H), 3.22 (d, *J* = 14.4 Hz, A′ of A′B′, 1 H), 3.17 (d, *J* = 14.4 Hz, B′ of A′B′, 1 H), 1.47 (s, 3 H); HRMS *m/z* Calcd for $C_{18}H_{16}OS$ $[M+H]^+$ 281.1000, found 281.0953. Minor isomer: (±)-3-(benzothiophen-3-ylmethyl)-3-methyl-2,3-dihydrobenzofuran.

*(±)-2-((3-methyl-2,3-dihydrobenzofuran-3-yl)methyl) benzofuran (**2ab**)*

77% yield, an inseparable colorless oil, isomers ratio = 10:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.47 (m, 1 H), 7.412 (d, *J* = 8.4 Hz, 1 H), 7.23–7.20 (m, 1 H), 7.18–7.13 (m, 2 H), 7.08 (dd, *J* = 7.4, 0.8 Hz, 1 H), 6.89 (td, *J* = 7.4, 0.8 Hz, 1 H), 6.81 (d, *J* = 8.0 Hz, 1 H), 6.35 (s, 1 H), 4.67 (d, *J* = 8.8 Hz, A of AB, 1 H), 4.19 (d, *J* = 8.8 Hz, B of AB, 1 H), 3.09 (d, *J* = 14.4 Hz, A′ of A′B′, 1 H), 3.05 (d, *J* = 14.4 Hz, B′ of A′B′, 1 H), 1.42 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 155.6, 154.8, 134.6, 128.6, 128.5, 123.6, 122.9, 122.6, 120.6, 120.5, 110.9, 109.9, 105.0, 82.2, 45.7, 39.1, 24.9; HRMS *m/z* Calcd for $C_{18}H_{16}O_2$ $[M+H]^+$ 265.1229, found 265.1185. Minor isomer: (±)-3-((3-methyl-2,3-dihydrobenzofuran-3-yl)methyl) benzofuran.

*(±)-1-methyl-2-((3-methyl-2,3-dihydrobenzofuran-3-yl)methyl)-1H-indole (**2ac**)*

36% yield, a colorless oil, isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.17–7.01 (m, 4 H), 6.75 (d, *J* = 8.0 Hz, 1 H), 6.69 (td, *J* = 7.2, 0.8 Hz, 1 H), 6.59 (d, *J* = 7.6 Hz, 1 H), 6.25 (s, 1 H), 4.45 (dd, *J* = 8.8, 1.6 Hz, A of AB, 1 H), 4.12 (d, *J* = 8.8 Hz, B of AB, 1 H), 3.12 (s, 3 H), 3.03 (d, *J* = 14.8 Hz, A′ of A′B′, 1 H), 2.93 (d, *J* = 14.8 Hz, B′ of A′B′, 1 H), 1.41 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.6, 137.2, 136.6, 134.3, 128.6, 123.4, 120.9, 120.7, 120.0, 119.6, 109.9, 109.7, 109.3, 101.8, 82.9, 46.2, 36.9, 29.3, 26.0; HRMS m/z Calcd for $C_{19}H_{20}NO$ $[M+H]^+$ 278.1545, found.278.15744.

*(±)-3-methyl-3-(thiophen-2-ylmethyl)-2,3-dihydro benzofuran (**2ad**)*

65% yield, a colorless oil; isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17–7.15 (m, 2 H), 7.06 (d, *J* = 7.4 H z, 1 H), 6.91–6.87 (m, 2 H), 6.77 (d, *J* = 8.0 Hz, 1 H), 6.68 (dd, *J* = 3.2, 0.8 Hz, 1 H), 4.52 (d, *J* = 8.8 Hz, A of AB, 1 H), 4.12 (d, *J* = 8.8 Hz, B of AB, 1 H), 3.13 (d, *J* = 14.8 Hz, A′ of A′B′, 1 H), 3.09 (d, *J* = 14.8 Hz, B′ of A′B′, 1 H), 1.42 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7, 139.4,

134.4, 128.4, 127.1, 126.6, 124.3, 123.0, 120.5, 109.8, 81.7, 46.2, 40.7, 25.3; HRMS *m/z* Calcd for $C_{14}H_{14}OS$ $[M+H]^+$ 231.0844, found 231.0809.

*(±)-3-((5-chlorothiophen-2-yl)methyl)-3-methyl-2,3-dihydrobenzofuran (**2ae**)*

(CAS: 1191913-90-2); 34% yield, a yellow oil; isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–7.14 (m, 1 H), 7.05(d, *J* = 7.4 Hz, 1 H), 6.90 (t, *J* = 7.2 Hz, 1 H), 6.77 (d, *J* = 8.0 Hz, 1 H), 6.70 (d, *J* = 3.6 Hz, 1 H), 6.44 (d, *J* = 3.6 Hz, 1 H), 4.46 (d, *J* = 8.8 Hz, A of AB, 1 H), 4.14 (d, *J* = 8.8 Hz, B of AB, 1 H), 3.03 (d, *J* = 14.4 Hz, A′ of A′B′, 1 H), 2.97 (d, *J* = 14.4 Hz, B′ of A′B′, 1 H), 1.42 (s, 3 H); HRMS *m/z* Calcd for $C_{14}H_{14}OSCl$ $[M+H]^+$ 265.0454, found 265.0463.

*(±)-5-((3-methyl-2,3-dihydrobenzofuran-3-yl)methyl) thiophene-2-carbaldehyde (**2af**)*

(CAS: 1191913-92-4); 45% yield, a yellow oil; isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.79 (s, 1 H), 7.56 (d, *J* = 3.6 Hz, 1 H), 7.19–7.14 (m, 1 H), 7.04 (d, *J* = 7.2 Hz, 1 H), 6.90 (t, *J* = 7.4 Hz, 1 H), 6.76 (t, *J* = 8.0 Hz, 1 H), 6.70 (d, *J* = 3.6 Hz, 1 H), 4.48 (d, *J* = 8.8 Hz, A of AB, 1 H), 4.15 (d, *J* = 8.8 Hz, B of AB, 1 H), 3.17 (d, *J* = 15.2 Hz, A′ of A′B′, 1 H), 3.13 (d, *J* = 15.2 Hz, B′ of A′B′, 1 H), 1.46 (s, 3 H); HRMS *m/z* Calcd for $C_{15}H_{14}O_2SNa$ $[M+Na]^+$ 281.0612, found 281.0578.

*(±)-4-methyl-5-((3-methyl-2,3-dihydrobenzofuran-3-yl)methyl)thiazole (**2ag**)*

(CAS: 1191913-85-5); 40% yield, a yellow oil; isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.55 (s, 1 H), 7.19–7.14 (m, 1 H), 6.93 (dd, *J* = 7.4, 1.2 Hz, 1 H), 6.87 (td, *J* = 7.2, 0.8 Hz, 1 H), 6.77 (d, *J* = 8.0 Hz, 1 H), 4.40 (d, *J* = 8.8 Hz, A of AB, 1 H), 4.15 (d, *J* = 8.8 Hz, B of AB, 1 H), 3.10 (d, *J* = 14.4 Hz, A′ of A′B′, 1 H), 3.00 (d, *J* = 14.4 Hz, B′ of A′B′, 1 H), 2.18 (s, 3 H), 1.45 (s, 3 H); HRMS *m/z* Calcd for $C_{14}H_{16}NOS$ $[M+H]^+$ 246.0953, found 246.0866.

*(±)-5-((3-methyl-2,3-dihydrobenzofuran-3-yl)methyl) furan-2-carbaldehyde (**2ah**)*

31% yield, a yellow oil; isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.54 (s, 1 H), 7.18–7.15 (m, 1 H), 7.13 (d, *J* = 7.6 Hz, 1 H), 7.03 (dd, *J* = 7.4, 1.2 Hz, 1 H), 6.89 (td, *J* = 7.2, 0.8 Hz, 1 H), 6.78 (d, *J* = 8.0 Hz, 1 H), 6.05 (d, *J* = 3.6 Hz, 1 H), 4.54 (d, *J* = 9.0 Hz, A of AB, 1 H), 4.17 (d, *J* = 9.0 Hz, B of AB, 1 H), 3.02 (ψs, 2 H), 1.42 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.1, 159.7, 159.4, 152.3, 133.7, 130.9, 128.7, 122.8, 120.7, 111.2, 110.0, 81.9, 45.8, 39.2, 24.9; HRMS *m/z* Calcd for $C_{15}H_{14}O_3Na$ $[M+Na]^+$ 265.0841, found 265.0811.

*(±)-1-(3-(benzothiophen-2-ylmethyl)-3-methylindolin-1-yl)ethan-1-one (**2ba**)*

65% yield, an inseparable yellow solid, isomers ratio = 5:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 8.0 Hz, 1 H), 7.72 (d, *J* = 7.6 Hz, 1 H), 7.66 (d, *J* = 7.2 Hz, 1 H), 7.33–7.31 (m, 1 H), 7.30–7.27 (m, 2 H), 7.20–7.18 (m, 1 H), 7.12–7.08 (m, 1 H), 6.90 (s, 1 H), 4.10 (d, *J* = 10.4 Hz, A of AB, 1 H), 3.66 (d, *J* = 10.4 Hz, B of AB, 1 H), 3.21 (d, *J* = 10.2 Hz, A′ of A′B′, 1 H), 3.18 (d, *J* = 10.2 Hz, B′ of A′B′, 1 H), 2.17 (s, 3 H), 1.50 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 142.3, 140.2, 139.8, 139.6, 138.2, 128.4, 124.3, 124.0, 123.9, 123.8, 123.0, 122.4, 122.1, 117.2, 60.4, 44.5, 42.1, 26.9, 24.3; HRMS *m/z* Calcd for $C_{20}H_{19}NOS$ $[M+H]^+$ 322.1266, found 322.1253. Minor isomer: (±)-1-(3-(benzothiophen-3-ylmethyl)-3-methylindolin -1-yl)ethan-1-one.

*(±)-1-(3-(benzofuran-2-ylmethyl)-3-methylindolin-1-yl)ethan-1-one (**2bb**)*

72% yield, an inseparable yellow solid, isomers ratio = 6:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 8.0 Hz, 1 H), 7.48 (d, *J* = 7.2 Hz, 1 H), 7.42 (d, *J* = 8.0 Hz, 1 H), 7.25–7.22 (m, 1 H), 7.21–7.17 (m, 2 H), 7.14 (d, *J* = 7.2 Hz, 1 H), 7.06 (td, *J* = 7.2, 0.8 Hz, 1 H), 6.31 (s, 1 H), 4.22 (d, *J* = 10.6 Hz, A of AB, 1 H), 3.70 (d, *J* = 10.6 Hz, B of AB, 1 H), 3.05 (ψs, 2 H), 2.23 (s, 3 H), 1.46 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 155.2, 154.8, 142.0, 138.5, 128.4, 128.3, 123.9, 123.8, 122.8, 122.2, 120.6, 117.1, 110.0, 105.2, 61.0, 44.3, 39.8, 26.1, 24.2; HRMS *m/z* Calcd for $C_{20}H_{19}NO_2$ $[M+H]^+$ 306.1494, found 306.1483. Minor isomer: (±)-1-(3-(benzofuran-3-ylmethyl)-3-methylindolin-1-yl)ethan-1-one.

*(±)-1-(3-methyl-3-((1-methyl-1H-indol-2-yl)methyl)indolin-1-yl)ethan-1-one (**2bc**)*

56% yield, an inseparable pale yellow solid, isomer ratio = 5:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 8.0 Hz, 1 H), 7.57 (d, *J* = 7.6 Hz, 1 H), 7.24–7.22 (m, 1 H), 7.20–7.16 (m, 2 H), 7.12–7.08 (m, 1 H), 6.94 (t, *J* = 7.6 Hz, 1 H), 6.74 (d, *J* = 7.4 Hz, 1 H), 6.31 (s, 1 H), 4.07 (d, *J* = 10.4 Hz, A of AB, 1 H), 3.76 (d, *J* = 10.4 Hz, B of AB, 1 H), 3.16 (s, 3 H), 3.07 (d, *J* = 14.8 Hz, A′ of A′B′, 1 H), 3.02 (d, *J* = 14.8 Hz, B′ of A′B′, 1 H), 2.23 (s, 3 H), 1.52 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8,

142.1, 137.9, 136.1, 128.4, 127.5, 123.8, 122.7, 123.8, 122.7, 121.1, 119.9, 119.6, 117.1, 109.3, 101.8, 61.9, 44.3, 37.7, 29.3, 25.0, 24.3; HRMS *m/z* Calcd for $C_{21}H_{22}N_2O$ $[M+H]^+$ 319.1810, found 319.1803. Minor isomer: (±)-1-(3-methyl-3-((1-methyl-1H-indol-3-yl)methyl)indolin-1-yl)ethan-1-one.

*(±)-1-(3-(benzo[d]thiazol-2-ylmethyl)-3-methylindolin-1-yl)ethan-1-one (**2bd**)*

72% yield, a yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.0 Hz, 1 H), 7.88 (d, *J* = 8.0 Hz, 1 H), 7.76 (d, *J* = 8.0 Hz, 1 H), 7.47–7.43 (m, 1 H), 7.36–7.32 (m, 1 H), 7.27–7.23 (m, 2 H), 7.13–7.09 (m, 1 H), 4.42 (d, *J* = 10.8 Hz, A of AB, 1 H), 3.73 (d, *J* = 10.8 Hz, B of AB, 1 H), 3.42 (d, *J* = 14.4 Hz, A′ of A′B′, 1 H), 3.34 (d, *J* = 14.4 Hz, B′ of A′B′, 1 H), 2.16 (s, 3 H), 1.54 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 166.8. 152.9, 142.4, 137.6, 135.4, 128.6, 126.1, 125.1, 123.9, 122.7, 122.2, 121.5, 117.3, 60.1, 45.1, 44.3, 26.9, 24.2; HRMS *m/z* Calcd for $C_{19}H_{18}N_2OSNa$ $[M+Na]^+$ 345.1038, found 344.1048.

*(±)-1-(3-(benzo[d]oxazol-2-ylmethyl)-3-methylindolin-1-yl)ethan-1-one (**2be**)*

90% yield, a yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 8.0 Hz, 1 H), 7.71–7.69 (m, 1 H), 7.50–7.47 (m, 1 H), 7.33 (dd, *J* = 5.6, 3.6 Hz, 2 H), 7.25–7.23 (m, 1 H), 7.22–7.20 (m, 1 H), 7.08 (t, *J* = 7.2 Hz, 1 H), 4.45 (d, *J* = 10.8 Hz, A of AB, 1 H), 3.81 (d, *J* = 10.8 Hz, B of AB, 1 H), 3.24 (d, *J* = 14.8 Hz, A′ of A′B′, 1 H), 3.22 (d, *J* = 14.8 Hz, B′ of A′B′, 1 H), 2.27 (s, 3 H), 1.50 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 163.6, 150.7, 141.8, 141.1, 137.8, 128.6, 125.0, 124.4, 124.0, 122.1, 119.8, 117.2, 110.5, 60.7, 43.6, 39.7, 25.9, 24.3; HRMS *m/z* Calcd for $C_{19}H_{18}N_2O_2Na$ $[M+Na]^+$ 329.1266, found 329.1270.

*(±)-1-(3-methyl-3-(thiophen-2-ylmethyl)indolin-1-yl)ethan-1-one (**2bf**)*

65% yield, an inseparable yellow oil, isomers ratio = 5:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.0 Hz, 1 H), 7.25–7.21 (m, 1 H), 7.13 (d, *J* = 7.2 Hz, 1 H), 7.10–7.06 (m, 2 H), 6,87 (dd, *J* = 4.8, 3.6 Hz, 1 H), 6.60 (d, *J* = 3.2 Hz, 1 H), 4.03 (d, *J* = 10.4 Hz, A of AB, 1 H), 3.62 (d, *J* = 10.4 Hz, B of AB, 1 H), 3.11 (d, *J* = 14.8, A′ of A′B′, 1 H), 3.06 (d, *J* = 14.8 Hz, B′ of A′B′, 1 H), 2.14 (s, 3 H), 1.45 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5, 142.4, 138.9, 138.2, 128.3, 127.0, 126.7, 124.4, 123.8, 122.4, 117.1, 60.3, 44.8, 41.6, 26.5, 24.2; HRMS *m/z* Calcd for $C_{16}H_{17}NOSNa$ $[M+Na]^+$ 294.0929, found 294.0909. Minor isomer: (±)-1-(3-methyl-3-(thiophen-3-ylmethyl)indolin-1-yl)ethan-1-one.

*(±)-1-(3-((5-chlorothiophen-2-yl)methyl)-3-methylindolin-1-yl)ethan-1-one (**2bg**)*

92% yield, an inseparable yellow solid, isomers ratio = 5:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.0 Hz, 1 H), 7.28–7.23 (m, 1 H), 7.12–7.05 (m, 2 H), 6.90 (d, *J* = 3.6 Hz, 1 H), 6.39 (d, *J* = 3.6 Hz, 1 H), 3.98 (d, *J* = 10.8 Hz, A of AB, 1 H), 3.66 (d, *J* = 10.8 Hz, B of AB, 1 H), 3.03 (d, *J* = 14.6 Hz, A′ of A′B′, 1 H), 2.97 (d, *J* = 14.6 Hz, B′ of A′B′, 1 H), 2.17 (s, 3 H), 1.45 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5, 142.4, 137.9, 137.7, 128.5, 128.3, 126.5, 125.7, 123.8, 122.4, 117.1, 60.3, 44.4, 42.0, 26.6, 24.2; HRMS *m/z* Calcd for $C_{16}H_{16}ClNOS$ $[M+H]^+$ 306.0719, found 306.0710. Minor isomer: (±)-1-(3-((5-chlorothiophen-3-yl)methyl)-3-methylindolin-1-yl)ethan-1-one.

*(±)-3-(benzothiophen-2-ylmethyl)-3-methyl-1-(methylsulfonyl)indoline (**2ca**)*

82% yield, an inseparable pale yellow solid, isomers ratio = 10:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (t, *J* = 8.0 Hz, 2 H), 7.36 (d, *J* = 8.0 Hz, 1 H), 7.26–7.25 (m, 2 H), 7.24–7.20 (m, 2 H), 7.10 (t, *J* = 7.4 Hz, 1 H), 6.90 (s, 1 H), 4.01 (d, *J* = 10.4 Hz, A of AB, 1 H), 3.67 (d, *J* = 10.4 Hz, B of AB, 1 H), 3.25 (d, *J* = 14.6 Hz, A′ of A′B′, 1 H), 3.16 (d, *J* = 14.6 Hz, B′ of A′B′, 1 H), 2.44 (s, 3 H), 1.52 (s, 3 H); ^{13}CNMR (100 MHz, $CDCl_3$): δ = 141.6, 140.3, 139.8, 139.4, 137.6, 128.9, 124.4, 124.2, 124.1, 123.7, 123.6, 123.0, 121.9, 113.2, 60.8, 44.5, 41.9, 34.2, 27.4; HRMS *m/z* Calcd for $C_{19}H_{19}NO_2S_2Na$ $[M+Na]^+$ 380.0755, found 380.0709. Minor isomer: (±)-3-(benzothiophen-3-ylmethyl)-3-methyl-1-(methylsulfonyl)indoline.

*(±)-3-(benzofuran-2-ylmethyl)-3-methyl-1-(methylsulfonyl)indoline (**2cb**)*

69%, yield, an inseparable pale yellow solid, isomers ratio = 10:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.45 (m, 1 H), 7.41–7.38 (m, 2 H), 7.26–7.20 (m, 2 H), 7.18 (dd, *J* = 7.6, 0.8 Hz, 1 H), 7.15 (dd, *J* = 7.2, 0.8 Hz, 1H), 7.06 (td, *J* = 7.2, 0.8 Hz, 1 H), 6.32 (s, 1 H), 4.13 (d, *J* = 10.4 Hz, A of AB, 1 H), 3.66 (d, *J* = 10.4 Hz, A of AB, 1 H), 3.10 (d, *J* = 14.8 Hz, A′ of A′B′, 1 H), 3.05 (d, *J* = 14.8 Hz, B′ of A′B′, 1 H), 2.75 (s, 3 H), 1.45 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.0, 154.8, 141.1, 138.1, 128.7, 128.4, 123.8, 123.6, 123.4, 122.8, 120.6, 113.2, 111.0, 105.4, 61.8, 44.0, 39.3, 34.5, 26.1; HRMS *m/z* Calcd for $C_{19}H_{19}NO_3S$ $[M+H]^+$ 342.1164, found 342.1104. Minor isomer: (±)-3-(benzofuran-3-ylmethyl)-3-methyl-1-(methylsulfonyl)indoline.

*(±)-1-methyl-2-((3-methyl-1-(methylsulfonyl)indolin-3-yl)methyl)-1H-indole (**2cc**)*

52% yield, an inseparable pale yellow solid, isomers ratio = 10:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 7.6 Hz, 1 H), 7.40 (d, *J* = 8.0 Hz, 1 H), 7.26–7.22 (m, 1 H), 7.19–7.13 (m, 2 H), 7.09–7.06 (m, 1 H), 6.95 (td, *J* = 7.6, 0.8 Hz, 1 H), 6.78 (dd, *J* = 7.6, 0.8 Hz, 1 H), 6.25 (s, 1 H), 4.01 (d, *J* = 10.0 Hz, A of AB, 1 H), 3.55 (d, *J* = 10.0 Hz, A of AB, 1 H), 3.18 (s, 3 H), 3.11 (d, *J* = 14.8 Hz, A′ of A′B′, 1 H), 3.02 (d, *J* = 14.8 Hz, B′ of A′B′, 1 H), 2.72 (s, 3 H), 1.53 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.4, 137.6, 137.2, 135.9, 128.7, 127.5, 123.8, 123.6, 121.1, 119.9, 119.6, 113.0, 109.3, 102.1, 62.4, 44.3, 36.8, 34.2, 29.3, 24.7, HRMS *m/z* Calcd for $C_{20}H_{22}N_2O_2S$ $[M+H]^+$ 355.1480, found 355.1449. Minor isomer: (±)-1-methyl-3-((3-methyl-1-(methylsulfonyl)indolin-3-yl)methyl)-1H-indole.

*(±)-3-methyl-1-(methylsulfonyl)-3-(thiophen-2-ylmethyl)indoline (**2cd**)*

67% yield, a pale yellow oil, isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 8.0 Hz, 1 H), 7.27–7.23 (m, 1 H), 7.19 (dd, *J* = 7.4, 0.8 Hz, 1 H), 7.11–7.07 (m, 1 H), 7.06 (dd, *J* = 5.2, 0.8 Hz, 1 H), 6.86 (dd, *J* = 5.2, 3.4 Hz, 1 H), 6.65 (d, 3.2 Hz, 1 H), 3.93 (d, *J* = 10.4 Hz, A of AB, 1 H), 3.64 (d, *J* = 10.4 Hz, B of AB, 1 H), 3.19 (d, *J* = 14.6 Hz, A′ of A′B′, 1 H), 3.10 (d, *J* = 14.6 Hz, B′ of A′B′, 1 H), 2.49 (s, 3 H), 1.48 (s, 3 H); ^{13}CNMR (100 MHz, $CDCl_3$): δ = 141.7, 139.2, 137.6, 128.8, 127.4, 126.7, 124.8, 123.6, 123.5, 113.1, 60.6, 44.4, 41.2, 34.1, 27.5; HRMS *m/z* Calcd for $C_{15}H_{17}NO_2S_2$ $[M+H]^+$ 308.0779 found 308.0723.

*(±)-3-(benzothiophen-2-ylmethyl)-3-methyl-1-tosylindoline (**2da**)*

(CAS: 1191913-95-7); 67% yield, an inseparable white solid, isomer ratio = 10:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65–7.59 (m, 4 H), 7.56 (d, *J* = 8.4 Hz, 2 H), 7.33–7.29 (m, 1 H), 7.28–7.23 (m, 1 H), 7.08–7.02 (m, 2 H), 7.01–6.97 (m, 2 H), 6.82 (s, 1 H), 3.98 (d, *J* = 10.4 Hz, A of AB, 1 H), 3.60 (d, *J* = 10.4 Hz, B of AB, 1 H), 3.07 (d, *J* = 14.4 Hz, A′ of A′B′, 1 H), 3.00 (d, *J* = 14.4 Hz, B′ of A′B′, 1 H), 2.24 (s, 3 H), 1.30 (s, 3H); HRMS *m/z* Calcd for $C_{25}H_{23}NO_2S_2$ $[M+H]^+$ 434.1248, found 434.1192. Minor isomer: (±)-3-(benzothiophen-3-ylmethyl)-3-methyl-1-tosylindoline.

*(±)-3-(benzofuran-2-ylmethyl)-3-methyl-1-tosylindoline (**2db**)*

67% yield, an inseparable yellow solid, isomer ratio = 10:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.0 Hz, 2 H), 7.65 (d, *J* = 8.0 Hz, 1 H), 7.43 (dd, *J* = 6.8, 0.8 Hz, 1 H), 7.39 (d, *J* = 8.0 Hz, 1 H), 7.24–7.20 (m, 2 H), 7.19–7.15 (m, 3 H), 7.02–7.00 (m, 2 H), 6.22 (s, 1 H), 4.10 (d, *J* = 10.4 Hz, A of AB, 1 H), 3.57 (d, *J* = 10.4 Hz, B of AB, 1 H), 2.85 (d, *J* = 14.4 Hz, A′ of A′B′, 1 H), 2.82 (d, *J* = 14.4 Hz, B′ of A′B′, 1 H), 2.32 (s, 3 H), 1.21 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.1, 154.7, 144.1 141.0, 138.6, 134.0, 129.6, 128.5, 128.4, 127.3, 123.1, 122.6, 120.5, 114.5, 111.0, 105.2, 101.3, 61.3, 43.9, 39.1, 26.0, 21.6; HRMS *m/z* Calcd for $C_{25}H_{23}NO_3S$ $[M+H]^+$ 418.1477 found 418.1418. Minor isomer: (±)-3-(benzofuran-3-ylmethyl)-3-methyl-1-tosylindoline

*(±)-1-methyl-2-((3-methyl-1-tosylindolin-3-yl)methyl)-1H-indole (**2dc**)*

40% yield, a pale yellow solid; isomer ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.4 Hz, 2 H), 7.67 (d, *J* = 8.0 Hz, 1 H), 7.50 (dd, *J* = 7.6, 0.8 Hz, 1 H), 7.21–7.19 (d, *J* = 8.0 Hz, 2 H), 7.17–7.15 (m, 3 H), 7.10–7.08 (m, 1 H), 6.85 (t, *J* = 7.4 Hz, 1 H), 6.56 (d, *J* = 7.6 Hz, 1 H), 6.21 (s, 1 H), 4.00 (d, *J* = 10.0 Hz, A of AB, 1 H), 3.47 (d, *J* = 10.0 Hz, B of AB, 1 H), 3.04 (s, 3 H), 2.88 (ψs, 2 H), 2.35 (s, 3 H), 1.35 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.3, 141.2, 147.9, 137.1, 135.9, 133.7, 129.7, 128.4, 127.5, 127.4, 123.5, 123.4, 121.0, 119.5, 114.1, 109.0, 101.9, 62.1, 44.2, 36.8, 29.1, 24.4, 21.6; HRMS *m/z* Calcd for $C_{26}H_{26}N_2O_2S$ $[M+H]^+$ 431.1793, found 431.1740.

*(±)-2-((3-methyl-1-tosylindolin-3-yl)methyl)benzo[d]thiazole (**2dd**)*

31% yield, a white solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.0 Hz, 1 H), 7.71(d, *J* = 8.0 Hz, 1 H), 7.65–7.60 (m, 3 H), 7.47 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.35(td, *J* = 7.6, 0.8 Hz, 1 H), 7.28–7.24 (m, 1 H), 7.09 (dd, *J* = 7.2, 0.8 Hz, 1 H), 7.06–7.01 (m, 3 H), 4.14 (d, *J* = 10.8 Hz, A of AB, 1 H), 3.68 (d, *J* = 10.8 Hz, B of AB, 1 H), 3.27 (d, *J* = 14.4 Hz, A′ of A′B′, 1 H), 3.17 (d, *J* = 14.4 Hz, B′ of A′B′, 1 H), 2.25 (s, 3 H), 1.33 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.7, 153.0, 141.5, 137.2, 135.3, 130.9, 129.7, 129.0, 126.2, 125.2, 123.7, 123.4, 122.8, 121.4, 120.8, 113.4, 60.9, 44.3, 44.2, 27.1, 22.7; HRMS *m/z* Calcd for $C_{24}H_{22}N_2O_2S_2$ $[M+H]^+$ 435.1201, found 435.1197.

*(±)-3-methyl-3-(thiophen-2-ylmethyl)-1-tosylindoline (**2de**)*

50% yield, a colorless oil; isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.0 Hz, 2 H), 7.62 (d, *J* = 8.0 Hz, 1 H), 7.25–7.22 (m, 1 H), 7.20 (d, *J* = 8.0 Hz, 2 H), 7.05–7.04 (m, 1 H), 7.01–6.98 (m, 2 H), 6.84 (dd, *J* = 5.2, 3.6 Hz, 1 H), 6.57 (d, *J* = 3.6 Hz, 1 H), 3.93 (d, *J* = 10.4 Hz, A of AB, 1 H), 3.49 (d, *J* = 10.4 Hz, B of AB, 1 H), 2.93 (d, *J* = 14.4 Hz, A′ of A′B′, 1 H), 2.90 (d, *J* = 14.4 Hz, B′ of A′B′, 1 H), 2.36 (s, 3 H), 1.22 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.0, 141.3, 138.9, 138.3, 134.0, 129.7, 128.4, 127.3, 126.6, 124.4, 123.5, 123.3, 114.3, 60.7, 44.4, 40.5, 26.3, 21.6; HRMS *m/z* Calcd for $C_{21}H_{21}NO_2S_2$ $[M+H]^+$ 384.1092, found 384.1088.

*(±)-3-(benzo[d]oxazol-2-ylmethyl)-1,3-dimethylindolin-2-one (**2ea**)*

54% yield, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (dd, *J* = 6.0, 3.2 Hz, 1 H), 7,21–7.28 (m, 1 H), 7.148–7.14 (m, 2 H), 7.13–7.10 (m, 1 H). 7.04 (d, *J* = 7.2 Hz, 1 H), 6.91–6.87 (m, 1 H), 6.69 (d, *J* = 7.6 Hz, 1 H), 3.35 (d, *J* = 14.4 Hz, A of AB, 1 H), 3.32 (d, *J* = 14.4 Hz, B of AB, 1 H), 3.17 (s, 3 H), 1.49 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.3, 161.9, 149.6, 142.0, 140.0, 131.1, 127.3, 123.6, 123.1, 122.1, 121.6, 118.8, 109.2, 107.1, 46.1, 35.4, 25.4, 22.5; HRMS *m/z* Calcd for $C_{18}H_{16}N_2O_2$ $[M+H]^+$ 293.1290, found 293.1296 $[M+Na]^+$ 315.1109, found 315.1118.

*(±)-3-(benzo[d]thiazol-2-ylmethyl)-1,3-dimethylindolin-2-one (**2eb**)*

56% yield, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.0 Hz, 1 H), 7.70 (d, *J* = 8.0 Hz, 1 H), 7.39–7.35 (m, 1 H), 7.30–7.28 (m, 1 H), 7.23 (d, *J* = 7.6 Hz, 1 H), 7.21–7.19 (m, 1 H), 7.01 (t, *J* = 7.4 Hz, 1 H), 6.74 (d, *J* = 7.6 Hz, 1 H), 3.70 (d, *J* = 14.4 Hz, A of AB, 1 H), 3.60 (d, *J* = 14.4 Hz, B of AB, 1 H), 3.19 (s, 3 H), 1.56 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.3, 165.8, 152.7, 143.3, 135.4, 132.1, 128.3, 125.8, 124.8, 123.3, 122.9, 122.6, 121.3, 108.2, 48.4, 41.8, 26.4, 24.2; HRMS *m/z* Calcd for $C_{18}H_{16}N_2OS$ $[M+H]^+$ 309.1062, found 309.1081.

*(±)-1,3-dimethyl-3-(thiophen-2-ylmethyl)indolin-2-one (**2ec**)*

43% yield yellow solid, isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.22 (m, 1 H), 7.18 (dd, *J* = 7.4, 0.8 Hz, 1 H), 7.09–7.05 (m, 1 H), 6.94 (dd, *J* = 5.2, 1.2 Hz, 1 H), 6.72 (dd, *J* = 5.2, 3.4 Hz, 1 H), 6.70 (d, *J* = 7.6 Hz, 1 H), 6.56–6.55 (m, 1 H), 3.39 (d, *J* = 14.4 Hz, A of AB, 1 H), 3.22 (d, *J* = 14.4 Hz, B of AB, 1 H), 3.05 (s, 3 H), 1.48 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.7, 143.5, 138.0, 132.9, 128.1, 126.7, 126.1, 124.0, 123.1, 122.3, 107.9, 49.8, 38.5, 26.0, 23.0; HRMS *m/z* Calcd for $C_{15}H_{15}NOS$ $[M+H]^+$ 258.0953 found 258.0942 $[M+Na]^+$ 280.0772 found 280.0757.

*(±)-3-((5-chlorothiophen-2-yl)methyl)-1,3-dimethylindolin-2-one (**2ed**)*

57% yield, yellow solid, isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 (dd, *J* = 7.2, 0.8 Hz, 1 H), 7.28–7.24 (m, 1 H), 7.09–7.05 (m, 1 H), 6.91 (d, *J* = 7.6 Hz, 1 H), 6.71 (d, *J* = 3.6 Hz, 1 H), 6.38 (d, *J* = 3.6 Hz, 1 H), 3.31 (d, *J* = 14.8 Hz, A of AB, 1 H), 3.21 (d, *J* = 14.8 Hz, B of AB, 1 H), 3.00 (s, 3 H), 1.35 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.4, 143.6, 137.0, 132.5, 128.4, 127.8, 126.1, 125.2, 122.9, 122.5, 108.2, 49.6, 38.9, 26.1, 23.1; HRMS *m/z* Calcd for $C_{15}H_{14}ClNOSNa$ $[M+Na]^+$ 314.0382, found 314.0288.

*(±)-ethyl 5-((1,3-dimethyl-2-oxoindolin-3-yl)methyl)thiophene-2-carboxylate (**2ee**)*

56% yield, yellow oil, isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 1.2 Hz, 1 H), 7.27–7.23 (m, 1 H), 7.20 (dd, *J* = 7.2, 0.8 Hz, 1 H), 7.08 (td, *J* = 7.6, 1.2 Hz, 1 H), 6.99–6.98 (d, *J* = 1.2 Hz, 1 H), 6.71 (d, *J* = 7.6 Hz, 1 H), 4.26–4.21 (m, 2 H), 3.38 (d, *J* = 14.4 Hz, A of AB, 1 H), 3.18 (d, *J* = 14.4 Hz, B of AB, 1 H), 3.06 (s, 3 H), 1.48 (s, 3 H), 1.30 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.3, 162.7, 143.5, 138.9, 132.8, 132.4, 131.5, 128.3, 127.2, 123.0, 122.6, 108.1, 60.5, 49.6, 38.5, 26.1, 23.1, 14.3; HRMS m/z Calcd for $C_{18}H_{19}NO_3S$ $[M+H]^+$ 330.1164, found 330.1165.

*(±)-3-(benzothiophen-2-ylmethyl)-1-ethyl-3-methylindolin-2-one (**2fa**)*

46% yield, an inseparable yellow solid; isomers ratio = 9:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.0 Hz, 1 H), 7.69 (d, *J* = 8.0 Hz, 1 H), 7.37–7.35 (m, 1 H), 7.29–7.23 (m, 2 H), 7.22–7.18 (m, 1 H), 7.03–6.99 (m, 1 H), 6.74 (d, *J* = 8.0 Hz, 1 H), 3.85–3.80 (m, 1 H), 3.72 (d, *J* = 14.4 Hz, A of AB, 1 H), 3.67–3.60 (m, 1 H), 3.55 (d, *J* = 14.4 Hz, B of AB, 1 H), 1.55 (s, 3 H), 1.13 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.8, 165.7, 152.8, 142.5, 135.4, 132.3, 128.2, 125.7, 124.7, 123.4, 122.8, 122.3, 121.2, 108.3, 48.3, 41.7, 34.7, 24.3, 12.4; HRMS m/z Calcd for $C_{20}H_{19}NOS$ $[M+H]^+$ 345.1266, found 322.1210. Minor isomer: (±)-3-(benzothiophen-3-ylmethyl)-1-ethyl-3-methylindolin-2-one.

*(±)-3-(benzofuran-2-ylmethyl)-1-ethyl-3-methylindolin-2-one (**2fb**)*

37% yield, an inseparable yellow oil; isomers ratio = 6:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 7.2 Hz, 1 H), 7.25–7.27 (m, 1 H), 7.21–7.15 (m, 2 H), 7.13–7.09 (m, 2 H), 7.00 (t, *J* = 7.6 Hz, 1 H), 6.73 (d, *J* = 7.2 Hz, 1 H), 6.17 (s, 1 H), 3.82 (m, 1 H), 3.59 (m, 1 H), 3.27 (d, *J* = 14.8 Hz, A of AB, 1 H), 3.24 (d, *J* = 14.8 Hz, B of AB, 1 H), 1.50 (s, 3 H), 1.10 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.6, 154.5, 142.7, 131.1, 128.0, 126.7, 123.4, 122.4, 122.2, 121.8, 120.4, 118.4, 110.8, 108.1, 104.5, 48.1, 35.0, 27.1, 19.2, 13.0; HRMS *m/z* Calcd for $C_{20}H_{19}NO_2Na$ $[M+Na]^+$ 328.1313, found 328.1342. Minor isomer: (±)-3-(benzofuran-3-ylmethyl)-1-ethyl-3-methylindolin-2-one.

*(±)-3-(benzo[d]oxazol-2-ylmethyl)-1-ethyl-3-methylindolin-2-one (**2fc**)*

84% yield, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (dd, *J* = 6.0, 3.2 Hz 1H), 7.34 (dd, *J* = 6.0, 3.2 Hz, 1 H), 7.24–7.19 (m, 2 H), 7.17 (dd, *J* = 7.6, 4.0 Hz, 2 H), 6.96 (t, *J* = 7.6 Hz, 1 H), 6.77 (d, *J* = 8.0 Hz, 1 H), 3.99–3.89 (m, 1 H), 3.71–3.62 (m, 1 H), 3.47 (d, *J* = 14.8 Hz, A of AB, 1 H), 3.42 (d, *J* = 14.8 Hz, B of AB, 1 H), 1.56 (s, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H); ^{13}CNMR (100 MHz, $CDCl_3$): δ = 178.8, 162.9, 150.6, 142.1, 141.0, 132.3, 128.2, 124.6, 124.0, 123.2, 122.3, 119.8, 110.2, 108.3, 47.1, 36.4, 34.7, 23.9, 12.3; HRMS *m/z* Calcd for $C_{19}H_{18}N_2O_2$ $[M+H]^+$ 307.1447 found 307.1369 $[M+Na]^+$ 329.1266 found 326.1274.

*(±)-3-(benzo[d]thiazol-2-ylmethyl)-1-ethyl-3-methylindolin-2-one (**2fd**)*

62% yield, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.0 Hz, 1 H), 7.69 (d, *J* = 8.0 Hz, 1 H), 7.37–7.35 (m, 1 H), 7.29–7.23 (m, 2 H), 7.22–7.18 (m, 1 H), 7.03–6.99 (m, 1 H), 6.74 (d, *J* = 8.0 Hz, 1 H), 3.85–3.80 (m, 1 H), 3.72 (d, *J* = 14.4 Hz, A of AB, 1 H), 3.67–3.60 (m, 1 H), 3.55 (d, *J* = 14.4 Hz, B of AB, 1 H), 1.55 (s, 3 H), 1.13 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.8, 165.7, 152.8, 142.5, 135.4, 132.3, 128.2, 125.7, 124.7, 123.4, 122.8, 122.3, 121.2, 108.3, 48.3, 41.7, 34.7, 24.3, 12.4; HRMS m/z Calcd for $C_{19}H_{18}N_2OS$ $[M+H]^+$ 323.1218, found 323.1169.

*(±)-1-ethyl-3-methyl-3-(thiophen-2-ylmethyl)indolin-2-one (**2fe**)*

42% yield, an inseparable yellow oil; isomers ratio = 5.3:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (d, *J* = 7.6 Hz, 2 H), 7.08 (t, *J* = 7.6 Hz, 1 H), 6.92 (d, *J* = 5.2 Hz, 1 H), 6.72–6.70 (m, 2 H), 6.54 (d, *J* = 2.8 Hz, 1 H), 3.78–3.70 (m, 1 H), 3.46–3.99 (m, 1 H), 3.42 (d, *J* = 14.4 Hz, A of AB, 1 H), 3.22 (d, *J* = 14.4 Hz, B of AB, 1 H), 1.48 (s, 3 H), 0.92 (t, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.1, 142.8, 137.9, 133.2, 128.1, 126.7, 124.0, 123.2, 121.8, 118.4, 108.1, 49.7, 38.7, 22.9, 19.2, 12.2; HRMS *m/z* Calcd for $C_{16}H_{17}NOS$ $[M+H]^+$ 272.1109, found 272.1040. Minor isomer: (±)-1-ethyl-3-methyl-3-(thiophen-3-ylmethyl)indolin-2-one.

*(±)-3-((5-chlorothiophen-2-yl)methyl)-1-ethyl-3-methylindolin-2-one (**2ff**)*

63% yield, an inseparable yellow oil; isomers ratio = 10:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.25 (m, 1 H), 7.24–7.22 (m, 1 H), 7.11–7.07 (m, 1 H), 6.75 (d, *J* = 7.6 Hz, 1 H), 6.52 (d, *J* = 3.6 Hz, 1 H), 6.32 (d, *J* = 3.6 Hz, 1 H), 3.79–3.72 (m, 1 H), 3.52–3.43 (m, 1 H), 3.30 (d, *J* = 14.4 Hz, A of AB, 1 H), 3.10 (d, *J* = 14.4 Hz, B of AB, 1 H), 1.45 (s, 3 H), 0.98 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.8, 142.8, 136.8, 132.8, 128.6, 127.8, 126.1, 125.1, 123.0, 122.3, 108.3, 49.5, 38.2, 34.4, 22.9, 12.2; HRMS *m/z* Calcd for $C_{16}H_{16}ClNOS$ $[M+H]^+$ 306.0719 found 306.0741. Minor isomer: (±)-3-((5-chlorothiophen-3-yl)methyl)-1-ethyl-3-methylindolin-2-one.

*(±)-5-((1-ethyl-3-methyl-2-oxoindolin-3-yl)methyl)thiophene-2-carbaldehyde (**2fg**)*

30% yield, yellow oil; isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.67 (s, 1 H), 7.41 (d, *J* = 3.8 Hz, 1 H), 7.28–7.24 (m, 1 H), 7.11–7.08 (m, 1 H), 6.72 (d, *J* = 8.4 Hz, 1 H), 6.70 (d, *J* = 3.8 Hz, 1 H), 3.78–3.68 (m, 1 H), 3.49–3.42 (m, 1 H), 3.48 (d, *J* = 14.0 Hz, A of AB, 1 H), 3.24 (d, *J* = 14.0 Hz, B of AB, 1 H), 1.50 (s, 3 H), 0.94 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.6, 178.5, 149.6, 142.5, 135.8, 132.2, 128.3, 123.1, 122.6, 108.4, 49.5, 47.7, 39.3, 34.4, 23.3, 12.2; HRMS *m/z* Calcd for $C_{17}H_{18}NO_2S$ $[M+H]^+$ 300.1058, found 300.1032.

*(±)-3-(benzothiophen-2-ylmethyl)-1-butyl-3-methylindolin-2-one (**2ga**)*

56% yield, an inseparable yellow solid; isomers ratio = 6.3:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (ψt, *J* = 8.4 Hz, 2 H), 7.32 (dd, *J* = 7.4, 1.0 Hz, 1 H), 7.28–7.16 (m, 3 H), 7.13 (td, *J* = 7.6, 0.8 Hz, 1 H), 6.87 (s, 1 H), 6.72 (d, *J* = 7.6 Hz, 1 H), 3.68 (td, *J* = 14.0, 7.2 Hz, A of AB, 1 H), 3.33 (d, *J* = 14.0 Hz, B of AB, 1 H), 1.54 (s, 3 H), 1.29–1.21 (m, 2 H), 0.58 (t, *J* = 7.2 Hz, 3 H); ^{13}CNMR (100 MHz, $CDCl_3$): δ = 179.2, 143.3, 139.8, 139.2, 133.0, 128.2, 123.8, 123.6, 123.5, 123.1, 122.9, 122.2, 121.8, 108.5,

108.3, 46.5, 39.6, 39.4, 29.3, 23.7, 19.9, 13.5; HRMS *m/z* Calcd for $C_{22}H_{24}NOS$ $[M+H]^+$ 350.1579 found 350.1596. Minor isomer: (±)-3-(benzothiophen-3-ylmethyl)-1-butyl-3-methylindolin-2-one.

*(±)-3-(benzo[d]oxazol-2-ylmethyl)-1-butyl-3-methylindolin-2-one (**2gb**)*

41% yield, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57–7.54 (m, 1 H), 7.37–7.33 (m, 1 H), 7.25–7.19 (m, 2 H), 7.18–7.14 (m, 2 H), 6.98–6.94 (m, 1 H), 6.77 (d, *J* = 7.8 Hz, 1 H), 3.87–3.80 (m, 1 H), 3.66–3.59 (m, 1 H), 3.46 (d, *J* = 5.0 Hz, A of AB, 1 H), 3.45 (d, *J* = 5.0 Hz, B of AB, 1 H), 1.71–1.61 (m, 2 H), 1.56 (s, 3 H), 1.43–1.34 (m, 2 H), 0.95 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.1, 161.9, 149.6, 141.5, 140.0, 131.2, 127.2, 123.6, 123.0, 122.2, 121.3, 118.8, 109.2, 107.4, 46.1, 38.8, 35.2, 28.3, 23.0, 19.2, 12.8; HRMS *m/z* Calcd for $C_{21}H_{22}N_2O_2$ $[M+H]^+$ 335.1760, found 335.1726.

*(±)-3-(benzo[d]thiazol-2-ylmethyl)-1-butyl-3-methylindolin-2-one (**2gc**)*

76% yield, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (dd, *J* = 8.0, 0.4 Hz, 1 H), 7.70–7.68 (m, 1 H), 7.38–7.24 (m, 1 H), 7.28–7.24 (m, 2 H), 7.20 (td, *J* = 7.8, 1.2 Hz, 1 H), 7.02 (td, *J* = 7.6, 0.8 Hz, 1 H), 6.74 (d, *J* = 7.8 Hz, 1 H), 3.76–3.69 (m, 1 H), 3.72 (d, *J* = 14.4 Hz, A of AB, 1 H), 3.60–3.53 (m, 1 H), 3.55 (d, *J* = 14.4 Hz, B of AB, 1 H), 1.55 (s, 3 H), 1.53–1.44 (m, 2 H), 1.24–1.21 (m, 1 H), 1.19–1.15 (m, 1 H), 0.78 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.0, 164.7, 151.6, 141.9, 134.3, 131.2, 127.2, 124.7, 123.7, 122.3, 121.8, 121.3, 120.2, 107.4, 47.3, 40.8, 38.8, 28.3, 23.3, 19.0, 12.6; HRMS *m/z* Calcd for $C_{21}H_{22}N_2OSNa$ $[M+Na]^+$ 373.1351, found 373.1340.

*(±)-1-butyl-3-methyl-3-((1-methyl-1H-indol-2-yl)methyl)indolin-2-one (**2gd**)*

34% yield, yellow oil; isomers ratio > 20:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.38 (m, 1 H), 7.25–7.21 (m, 1 H), 7.16 (d, *J* = 7.8 Hz, 1 H), 7.12–7.08 (m, 1 H), 7.05–6.99 (m, 3 H), 6.73 (d, *J* = 7.8 Hz, 1 H), 5.86 (s, 1 H), 3.70–3.63 (m, 1 H), 3,48–3.41 (m, 1 H), 3.45 (s, 3 H), 3.26 (d, *J* = 14.8 Hz, A of AB, 1 H), 3.23 (d, *J* = 14.8 Hz, B of AB, 1 H), 1.52 (s, 3 H), 1.35–1.27 (m, 2 H), 1.09–1.02 (m, 2 H), 0.69 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.8, 142.9, 137.0, 135.2, 128.1, 126.0, 127.5, 123.3, 122.1, 120.8, 119.9, 119.2, 109.1, 108.4, 101.6, 48.9, 39.6, 34.2, 29.7, 29.3, 23.2, 19.9, 13.6; HRMS *m/z* Calcd for $C_{23}H_{26}N_2O$ $[M+H]^+$347.2123, found 347.2124.

*(±)-1-butyl-3-methyl-3-(thiophen-2-ylmethyl)indolin-2-one (**2ge**)*

65% yield, an inseparable yellow solid; isomers ratio = 5:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22 (d, *J* = 7.6 Hz, 2 H), 7.09–7.05 (m, 1 H), 6.91 (dd, *J* = 5.6, 1.0 Hz, 1 H), 6.73–6.70 (m, 2 H), 6.56 (d, *J* = 3.2 Hz, 1 H), 3.69–3.62 (m, 1 H), 3.44–3.37 (m, 1 H), 3.40 (d, *J* = 14.2 Hz, A of AB, 1 H), 3.21 (d, *J* = 14.2 Hz, B of AB, 1 H), 1.47 (s, 3 H), 1.41–1.31 (m, 2 H), 1.16–1.07 (m, 2 H), 0.86 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.3, 143.3, 137.9, 133.2, 128.0, 126.8, 126.1, 124.0, 123.2, 122.1, 108.2, 49.7, 39.5, 38.5, 29.3. 23.3, 20.0, 13.8; HRMS *m/z* Calcd for $C_{18}H_{21}NOS$ $[M+H]^+$300.1422, found 300.1429. Minor isomer: (±)-1-butyl-3-methyl-3-(thiophen-3-ylmethyl)indolin-2-one.

*(±)-1-butyl-3-((5-chlorothiophen-2-yl)methyl)-3-methylindolin-2-one (**2gf**)*

73% yield, an inseparable yellow oil; isomers ratio = 7:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.22 (m, 2 H), 7.10–7.06 (m, 1 H), 6.75(d, *J* = 7.6 Hz, 1 H), 6.52 (d, *J* = 3.6 Hz, 1 H), 6.33(d, *J* = 3.6 Hz, 1 H), 3.73–3.66 (m, 1 H), 3.45–3.38 (m, 1 H), 3.30 (d, *J* = 14.4 Hz, A of AB, 1 H), 3.10 (d, *J* = 14.4 Hz, B of AB, 1 H), 1.44 (s, 3 H), 1.42–1.32 (m, 2 H), 1.18–1.08 (m, 2 H), 0.86 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.1, 143.3, 136.9, 132.9, 128.4, 127.8, 126.2, 125.1, 123.0, 122.3, 108.5, 49.5, 39.6, 39.1, 29.4, 23.3, 20.0, 13.8; HRMS *m/z* Calcd for $C_{18}H_{20}ClNOSNa$ $[M+Na]^+$ 357.1579, found 357.1545. Minor isomer: (±)-1-butyl-3-((5-chlorothiophen-3-yl)methyl)-3-methylindolin-2-one.

*(±)-5-((1-butyl-3-methyl-2-oxoindolin-3-yl)methyl)thiophene-2-carbaldehyde (**2gg**)*

48% yield, yellow oil; isomers ratio >20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.67 (s, 1 H), 7.41 (d, *J* = 3.6 Hz, 1 H), 7.28–7.25 (m, 2 H), 7.10 (td, *J* = 7.2, 0.8 Hz, 1H), 6.73–6.72 (m, 1 H), 6.70 (d, *J* = 3.8 Hz, 1 H), 3.68–3.61 (m, 1 H), 3.48 (d, *J* = 14.0 Hz, A of AB, 1 H), 3.46–3.39 (m, 1 H), 3.24 (d, *J* = 14.0 Hz, B of AB, 1 H), 1.50 (s, 3 H), 1.40–1.30 (m, 2 H), 1.13–1.07 (m, 2 H), 0.82 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.5, 177.7, 148.6, 142.0, 141.5, 134.8, 131.1, 127.6, 127.4, 122.0, 121.5, 107.6, 48.5, 38.6, 38.1, 28.3, 22.6, 18.9, 12.7; HRMS *m/z* Calcd for $C_{19}H_{21}NO_2S$ $[M+H]^+$ 328.1371, found 328.1360.

*(±)-3-(benzofuran-2-ylmethyl)-1-benzyl-3-methylindolin-2-one (**2ha**)*

37% yield, yellow solid; isomer rate >20:1, ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 7.2 Hz, 1 H), 7.30 (d, *J* = 8.0 Hz, 1 H), 7.24 (d, *J* = 7.2 Hz, 1 H), 7.21–7.11 (m, 3 H), 3.07–6.96 (m, 5 H), 6.59 (d, *J* = 7.6 Hz, 1 H), 6.19 (s, 1 H), 5.11 (d, *J* = 16.0 Hz, 1 H), 4.68 (d, *J* = 16.0 Hz, 1 H), 3.42 (d, *J* = 14.6 Hz, A of AB, 1 H), 3.36 (d, *J* = 14.6 Hz, B of AB, 1 H), 1.60 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.6, 154.5, 154.3, 142.2, 135.5, 132.9, 128.6, 128.5, 128.0, 127.3, 126.9, 123.6, 123.2, 122.5 (2 C), 120.6, 111.0, 109.2, 104.8, 48.4, 43.7, 36.6, 24.1, 19.5; HRMS *m/z* Calcd for $C_{25}H_{22}NO_2$ $[M+H]^+$ 368.1651, found 368.1660.

*(±)-3-(benzo[d]oxazol-2-ylmethyl)-1-benzyl-3-methylindolin-2-one (**2hb**)*

82% yield, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.56 (m, 1 H), 7.33–7.31 (m, 1 H), 7.25–7.22 (m, 2 H), 7.16 (d, *J* = 7.2 Hz, 1 H), 7.09–7.04 (m, 1 H), 6.96–6.92 (m, 1 H), 6.62 (d, *J* = 7.6 Hz, 1 H), 5.09 (d, *J* = 15.6 Hz, 1 H), 4.81 (d, *J* = 15.6 Hz, 1 H), 3.55 (d, *J* = 15.0 Hz, A of AB, 1 H), 3.50 (d, *J* = 15.0 Hz, B of AB, 1 H), 1.62 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.3, 162.8, 150.6, 142.2, 141.0, 135.8, 132.1, 128.7, 128.2, 127.5, 127.2, 124.7, 124.1, 123.1, 122.6, 119.9, 110.4, 109.3, 47.3, 44.0, 36.1, 24.7; HRMS *m/z* Calcd for $C_{24}H_{20}N_2O_2$ $[M+H]^+$ 369.1603, found 369.1604.

*(±)-3-(benzo[d]thiazol-2-ylmethyl)-1-benzyl-3-methylindolin-2-one (**2hc**)*

62% yield, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.0 Hz, 1 H). 7.66 (d, *J* = 8.0 Hz, 1 H), 7.42–7.38 (m, 1 H), 7.32–7.28 (m, 1 H), 7.13–7.08 (m, 2 H), 7.07–7.02 (m, 1 H), 6.58 (d, *J* = 7.6 Hz, 1 H), 5.03 (d, *J* = 15.6 Hz, 1 H), 4.67 (d, *J* = 15.6 Hz, A of AB, 1 H), 3.83 (d, *J* = 14.4 Hz, B of AB, 1 H), 3.61 (d, *J* = 14.4 Hz, 1 H), 1.62 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.1, 165.7, 152.7, 142.6, 135.5, 132.1, 128.5, 128.4, 127.3, 127.0, 125.8, 124.9, 123.3, 123.1, 122.7, 121.4, 109.4, 48.6, 43.8, 41.9, 24.8; HRMS *m/z* Calcd for $C_{24}H_{20}N_2OS$ $[M+H]^+$ 385.1375 found 385.1367 $[M+Na]^+$ 407.1194 found 407.1187.

*(±)-1-benzyl-3-methyl-3-(thiophen-2-ylmethyl)indolin-2-one (**2hd**)*

60% yield, an inseparable white solid; isomers ratio = 10:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.26 (m, 4 H), 7.17–7.05 (m, 2 H), 6.96 (dd, *J* = 5.2, 0.8 Hz, 1 H), 6.80–6.72 (m, *3* H), 6.62 (d, *J* = 3.2 Hz, 1H), 6.50 (d, *J* = 7.6 Hz, 1 H), 5.04 (d, *J* = 16.0 Hz, A of AB, 1 H), 4.52 (d, *J* = 16.0 Hz, B of AB, 1 H), 3.52 (d, *J* = 14.4 Hz, 1 H), 3.30 (d, *J* = 14.4 Hz, 1 H), 1.54 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.5, 142.8, 138.0, 133.0, 128.6, 128.1, 127.4, 127.2, 127.1, 126.7, 126.3, 124.3, 123.0, 122.4, 109.3, 50.3, 43.5, 38.4, 19.5; HRMS *m/z* Calcd for $C_{21}H_{20}NOSK$ $[M+K]^+$ 356.1053, found 356.1094. Minor isomer: (±)-1-benzyl-3-methyl-3-(thiophen-3-ylmethyl)indolin-2-one.

*(±)-1-benzyl-3-((5-chlorothiophen-2-yl)methyl)-3-methylindolin-2-one (**2he**)*

64% yield, yellow oil; isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.30 (m, 1 H), 7.27 (dd, *J* = 7.2, 0.8 Hz, 1 H), 7.23–7.18 (m, 2 H), 7.14 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.09–7.05 (m, 1 H), 6.80–6.76 (m, 2 H), 6.57–6.54 (m, 2 H), 6.39 (d, *J* = 3.6 Hz, 1 H), 5.11 (d, *J* = 16.0 Hz, A of AB, 1 H), 4.48 (d, *J* = 16.0 Hz, B of AB, 1 H), 3.41 (d, *J* = 14.4 Hz, 1 H), 3.18 (d, *J* = 14.4 Hz, 1 H), 1.52 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.2, 142.9, 137.0, 135.3, 132.5, 128.8, 128.6, 128.5, 127.4, 126.7, 126.5, 125.4, 122.8, 122.6, 109.5, 49.8, 43.6, 39.0, 23.9; HRMS *m/z* Calcd for $C_{21}H_{18}ClNOS$ $[M+H]^+$ 368.0876, found 368.0907.

*(±)-1-allyl-3-(benzothiophen-2-ylmethyl)-3-methylindolin-2-one (**2ia**)*

28% yield, an inseparable yellow solid; isomers ratio = 10:1; major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 8.0 Hz, 1 H), 7.56–7.54 (m, 1 H), 7.30 (dd, *J* = 7.2, 0.8 Hz, 1 H), 7.24–7.20 (m, 2 H), 7.19–7.15 (m, 1 H), 7.12–7.08 (m, 1 H), 6.84 (s, 1 H), 6.65 (d, *J* = 7.2 Hz, 1 H), 5.49–5.42 (m, 1 H), 4.75–4.73 (m, 1 H), 4.65–4.60 (m, 1 H), 4.33–4.27 (m, 1 H), 4.07–4.01 (m, 1 H), 3.53 (d, *J* = 14.2 Hz, A of AB, 1 H), 3.31 (d, *J* = 14.2 Hz, B of AB, 1 H), 1.54 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.2, 142.8, 139.7, 139.5, 139.1, 132.8, 130.9, 128.2, 123.8, 123.6, 123.1, 123.0, 124.4, 121.8, 118.3, 116.7, 109.1, 49.7, 42.0, 39.2, 23.8; HRMS *m/z* Calcd for $C_{21}H_{19}NOS$ $[M+Na]^+$ 356.1058, found 356.1076. Minor isomer: (±)-1-allyl-3-(benzothiophen-3-ylmethyl)-3-methylindolin-2-one.

*(±)-1-allyl-3-(benzo[d]thiazol-2-ylmethyl)-3-methylindolin-2-one (**2ib**)*

34% yield, an inseparable yellow solid; isomers ratio = 5:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 7.6 Hz, 1 H), 7.69 (dd, *J* = 8.0, 0.4 Hz, 1 H), 7.38–7.34 (m, 1 H), 7.28–7.24 (m, 2 H), 7.17 (td, *J* = 8.0, 1.2 Hz, 1 H), 7.01 (td, *J* = 7.6, 0.8 Hz, 1 H), 6.72 (d, *J* = 7.6 Hz, 1 H), 5.74–5.65 (m, 1 H), 5.05–5.01 (m, 2 H), 4.40–4.34 (m, 1 H), 4.27–4.21 (m, 1 H), 3.74 (d, *J* = 14.4 Hz, A of AB, 1 H), 3.58 (d, *J* = 14.4 Hz, B of AB, 1 H), 1.58 (s, 3 H); ^{3}C NMR (100 MHz, $CDCl_3$): δ = 178.9, 165.6, 152.8, 142.6, 135.4, 132.1,

131.3, 128.2, 125.7, 124.8, 123.3, 122.9, 122.5, 121.3, 117.4, 109.1, 48.4, 42.4, 41.7, 24.5; HRMS *m/z* Calcd for $C_{20}H_{18}N_2OS$ $[M+H]^+$ 335.1218, found 335.1219.

*(±)-2-((4-methylisochroman-4-yl)methyl)benzo[d] oxazole (**2ja**)*

31% yield, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.68 (m, 1 H), 7.47–7.45 (m, 1 H), 7.30 (td, *J* = 3.6, 1.2 Hz, 2 H), 7.26–7.24 (m, 1 H), 7.19–7.16 (m, 2 H), 7.00–6.98 (m, 1 H), 4.87 (d, *J* = 15.0 Hz, A of AB, 1 H), 4.82 (d, *J* = 15.0 Hz, B of AB, 1 H), 4.09 (d, *J* = 11.6 Hz, A′ of A′B′, 1 H), 3.57 (d, *J* = 11.6 Hz, B′ of A′B′, 1 H), 3.37 (d, *J* = 14.0 Hz, A′′ of A′′B′′, 1 H), 3.25 (d, *J* = 14.0 Hz, B′′ of A′′B′′, 1 H), 1.38 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.5, 150.8, 141.3, 140.4, 133.7, 126.9, 126.6, 125.8, 124.6, 124.3, 124.2, 119.8, 110.4, 73.7, 69.0, 39.3, 37.2, 22.8; HRMS *m/z* Calcd for $C_{18}H_{17}NO_2$ $[M+H]^+$ 280.1338, found 280.1337.

*(±)-2-((4-methylisochroman-4-yl)methyl)benzo[d] thiazole (**2jb**)*

65% yield, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.0 Hz, 1 H), 7.75 (dd, *J* = 8.0, 0.4 Hz, 1 H), 7.47–7.43 (m, 1 H), 7.36–7.31 (m, 1 H), 7.22–7.18 (m, 2 H), 7.01–6.99 (m, 1 H), 4.80 (ψs, 2 H), 4.04 (d, *J* = 11.6 Hz, A of AB, 1 H), 3.58 (d, *J* = 11.6 Hz, B of AB, 1 H), 3.57 (d, *J* = 14.0 Hz, A′ of A′B′, 1 H), 3.42 (d, *J* = 14.0 Hz, B′ of A′B′, 1 H), 1.41 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.8, 153.0, 140.4, 135.6, 134.2, 126.9, 126.1, 125.9, 124.8, 124.4, 122.8, 121.3, 73.6, 69.0, 44.4, 37.6, 23.9; HRMS *m/z* Calcd for $C_{18}H_{17}NOS$ $[M+H]^+$ 296.1109, found 296.1105.

*(±)- 5-((4-methylisochroman-4-yl)methyl)thiophene-2-carbaldehyde (**2jc**)*

57% yield, yellow solid; isomers ratio > 20:1; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.78 (s, 1 H), 7.83 (d, *J* = 3.6 Hz, 1 H), 7.39 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.25–7.17 (m, 2 H), 7.02 (dd, *J* = 7.2, 1.2 Hz, 1 H), 6.96 (d, *J* = 3.6 Hz, 1 H), 4.69 (d, *J* = 8.8 Hz, A of AB, 1 H), 4.66 (d, *J* = 8.8 Hz, B of AB, 1 H), 3.70 (d, *J* = 11.6 Hz, A′ of A′B′, 1 H), 3.48 (d, *J* = 11.6 Hz, B′ of A′B′, 1 H), 3.31 (d, *J* = 14.4 Hz, A′′ of A′′B′′, 1 H), 3.17 (d, *J* = 14.4 Hz, B′′ of A′′B′′, 1 H), 1.24 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.6, 151.8, 142.6, 140.2, 136.4, 133.9, 128.9, 126.8, 126.6, 126.0, 124.3, 73.4, 68.9, 41.5, 37.5, 23.3; HRMS *m/z* Calcd for $C_{16}H_{16}O_2S$ $[M+H]^+$ 273.0949, found 273.0943.

4. Conclusions

In summary, we developed a palladium-catalyzed domino arylation reaction for the formation of biologically relevant 3,3-disubstituted dihydrobenzofurans, indolines, indolinones and isochromanes in moderate to excellent yields (28–92%) with moderate to good regioselectivities (5:1 to > 20:1 *ir*) using $Pd(PPh_3)_2Cl_2$/(±)-BINAP as the catalyst. We employed not only sulphur-containing heterocycles, but also oxygen-containing ones as efficient reagents for the tandem arylation, compared with Fagnou's work (they just developed sulphur-containing heterocycles as coupling reagents). In addition, our catalytic system was also expanded to synthesize isochromanes. Generally, substituted or unsubstituted thiophenes, reacted with 2-substituted phenylbromides, afforded the products with high regioselectivities (>20:1 *ir*). The synthesized new compounds were well characterized through different spectroscopic techniques, such as ^{1}H and ^{13}C NMR, and mass spectral analysis.

Supplementary Materials: The following are available online at http://www.mdpi.com/2073-4344/10/9/1084/s1. Copies of ^{1}H and ^{13}C NMR spectra for the new compounds.

Author Contributions: G.Y. and C.L. conceived the experiments and wrote the main manuscript. S.L., D.J., G.D., J.F. and X.W. conducted the experiments. G.Y., C.L. and L.Z. supervised the experimental works. C.L. was responsible for mass spectrometry of all compounds. H.C., C.Y., Z.Y., X.S. and X.L. analyzed the results. All authors have read and agreed to the published version of the manuscript.

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