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Graphical Abstract

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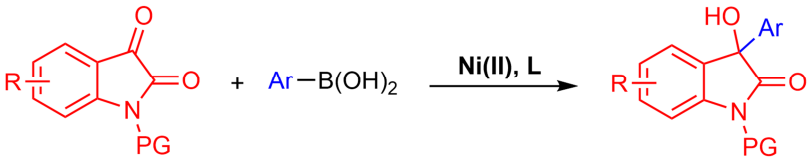

moderate to excellent yield
moderate ee

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ABSTRACT

A Ni-catalyzed addition of arylboronic acids to isatins was first developed. The reaction, driven by $Ni(acac)_2$ and dppp as the phosphine ligand, gave 3-aryl-3-hydroxy-2-oxindoles in up to 97% yield. Scopes of benzyl-protected isatins and arylboronic acids were examined. Substituted phenylboronic acids along with fused-ring and heterocyclic boronic acids reacted with isatins smoothly. Preliminary asymmetric catalysis was investigated as well, showing moderate enantioselectivity. The mechanism was also described.

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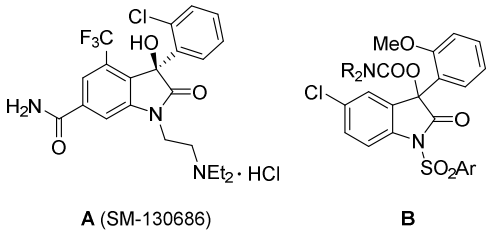
1. Introduction

In these decades, a variety of transition metal-catalyzed C-C bond building methods have been extensively studied [1], in which nickel catalysis, for its inexpensiveness and versatility, is considered as one of the most promising fields.[2] Numerous precursors were used in various reactions such as substitution reactions[3] and addition reactions[4] and outstanding accomplishments have been achieved. Organoboronic acid not only is a class of air and moisture tolerant reagents, but also have less reactivity, better chemoselectivity and suppression of side reactions. Up to date, some nickel-catalyzed reactions with organoboron reagents have been well developed.[5-8]

3-Aryl-3-hydroxy-2-oxindoles are studied as a common motif



A (SM-130686) **B**

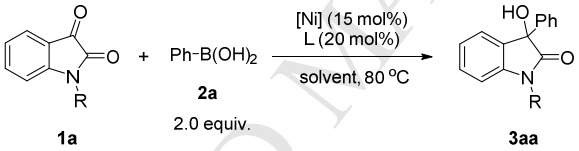
Figure 1. Application examples of 3-aryl-3-hydroxy-2-oxindoles motif.

in several drugs and natural products. For instance, **A** (SM-130686) was found as a potent growth hormone secretagogue and **B** performed high affinity for the arginine-vasopressin receptors and/or the ocytocin receptors (Figure 1).[9] These analogues can be effectively synthesized through addition of precursor isatins with some organometallic reagents such as organosilicon[10] and triorganoaluminium[11]. Reactions of organoboron reagents have been developed as well. Since 2006, pioneered by Minnaard[12a] and Hayashi[12b], rhodium[12], palladium[13], copper[14], ruthenium[15] and iridium[16] have been applied as the catalytic metals, whereas most of them are expensive and sensitive to atmosphere. Compared with the reactions catalyzed by noble metals, the nickel-catalyzed reaction remains challenge due to less stability of C-Ni bonds in the intermediate, which leads to high activation energy and facile decomposition of the intermediate.[17] Encouraged by the fact that nickel catalysts have not yet been applied in this field, we studied and herein report the synthesis of 3-aryl-3-hydroxy-2-oxindoles from isatins and arylboronic acids catalyzed by air-stable nickel(II) salts along with various phosphine ligands.

2. Results and Discussion

Considering that Ni(0) precursors are expensive and very sensitive to air and moisture, we first utilized more practical Ni(II) salt $Ni(acac)_2$ as the metal source. To investigate how ligands influence the metal-catalyzed reactions, *N*-benzyl isatin **1a** and phenylboronic acid **2a** were chosen as the substrates in a primary conditions screening with different ligands to detect the reactivity

Table 1. General Conditions Screening[a]



entry	R	Ni source	ligand	solvent	yield (%)[b]
1	Bn	$Ni(acac)_2$	PPh_3	toluene	38
2	Bn	$Ni(acac)_2$	PCy_3	toluene	34
3	Bn	$Ni(acac)_2$	dppb	toluene	33
4	Bn	$Ni(acac)_2$	dppf	toluene	19
5	Bn	$Ni(acac)_2$	dppp	toluene	84
6	H	$Ni(acac)_2$	dppp	toluene	< 5
7	Boc	$Ni(acac)_2$	dppp	toluene	< 5
8	Me	$Ni(acac)_2$	dppp	toluene	47
9	Bn	$Ni(ClO_4)_2 \cdot 6H_2O$	dppp	toluene	42
10	Bn	$Ni(OAc)_2 \cdot 4H_2O$	dppp	toluene	63
11	Bn	$Ni(dppe)Cl_2$	dppp	toluene	41
12	Bn	$Ni(PPh_3)Cl_2$	dppp	toluene	41
13	Bn	$Ni(cod)_2$	dppp	toluene	39
14[c]	Bn	$Ni(acac)_2$	dppp	toluene	48
15[d]	Bn	$Ni(acac)_2$	dppp	toluene	73
16[e]	Bn	$Ni(acac)_2$	dppp	toluene	54
17	Bn	$Ni(acac)_2$	dppp	DME	64
18	Bn	$Ni(acac)_2$	dppp	1,4-dioxane	52
19	Bn	$Ni(acac)_2$	dppp	MeCN	32
20	Bn	$Ni(acac)_2$	dppp	toluene[f]	77

[a] The reactions were performed using *N*-substituted isatin (0.2 mmol), phenlyboronic acid (0.4 mmol), Ni precursor (0.03 mmol) and ligand (0.04 mmol) at 80 °C for 22 h under N_2. [b] Isolated yields. [c] The reaction was performed at 60 °C. [d] The reaction was performed at 70 °C. [e] The reaction was performed at 90 °C. [f] Toluene/H_2O = 20/1 (v/v)

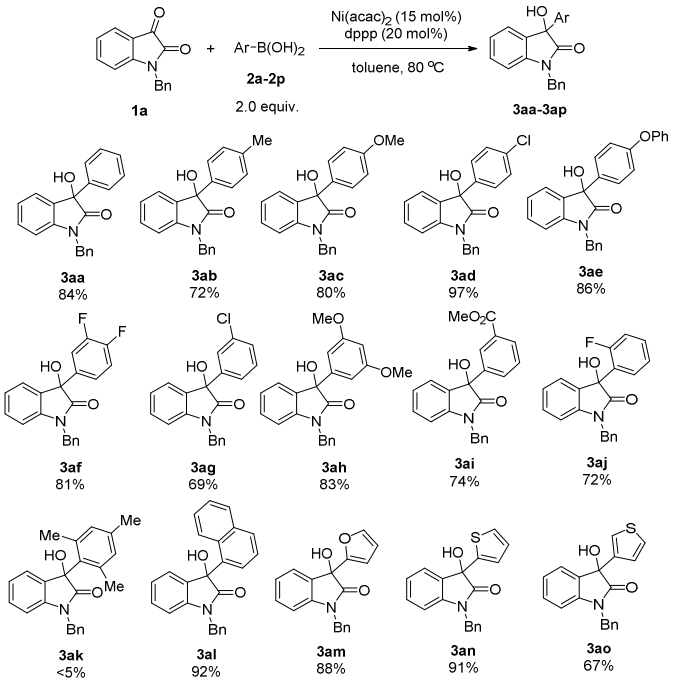
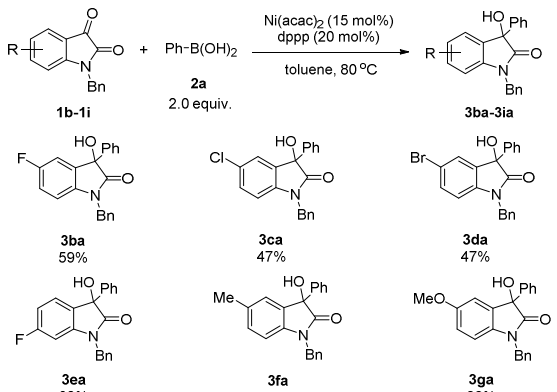


Table 2. Scope of arylboronic acids.[a,b]

[a] The reactions were performed using *N*-benzylisatin (0.2 mmol), arylboronic acids (0.4 mmol), $Ni(acac)_2$ (0.03 mmol) and dppp (0.04 mmol) at 80 °C in toluene for 22 h under N_2. [b] Isolated yield.

(table 1, entries 1-5). Among the selected phosphines, ligand dppp displayed prominent advantage. This is possibly attributed to the appropriate coordination of the ligand with nickel. *N*-substituents on the isatin exerted a great influence on the transformation (table 1, entries 5-8). Among of them, benzyl group showed its superiority. Nickel source was investigated as well (table 1, entries 9-13). Meanwhile, counterion was found to influence the yield. As the result, $Ni(acac)_2$ gave the best yield. In comparsion, employment of zero-valent nickel $Ni(cod)_2$ just acquired a disappoionting result (table 1, entry 13). Temperature screening indicated that the reaction worked best at 80 °C (table 1, entries 14-16). Solvent effect was also nonnegligible on this reaction (table 1, entries 5, 17-20), and toluene is the best choice. Noticeably, addition of water as a common additive also resulted in a slight decrease in the yield (table 1, entry 20).

With the optimal conditions in hand, we set about expanding the scope of substrates. Firstly, different arylboronic acids were employed (Table 2). As the para substituents, functional groups with different electron effects reasonably influenced the reaction yields (**3ab**-**3af**, 72%-97%), and remarkably *p*-chlorophenylboronic acid gave an excellent yield (**3ad**, 97%). This result is consistent with Hu's report[8e]. Meta substituents with electron withdrawing effect could somewhat decrease the yields and those having electron donating effect was beneficial to the reaction in some degree (**3ag**-**3ai**, 69%-83%). In contrast, ortho substituents of arylboronic acids showed significant steric hindrance and dropped the product yields fiercely (**3aj**, 72%, and



3ak). Satisfactorily, fused-ring and electron-rich heterocyclic arylboronic acids also gave the products in reasonable yields respectively (**3al**-**3an**, 88%-92%). This is scarce in most cases with other metals, though 3-thiophenyl arylboronic acid performed moderately (**3ao**, 67%).

Table 3. Scope of *N*-benzylisatins.[a,b]

[a] The reactions were performed using *N*-benzylisatins (0.2 mmol), phenlyboronic acid (0.4 mmol), $Ni(acac)_2$ (0.03 mmol) and dppp (0.04 mmol) at 80 °C in toluene for 22 h under N_2. [b] Isolated yield.

Studies on the scope of benzyl-protected isatins showed that electronic effect played an important role in the reaction (Table 3). 5-Haloisatin afforded lower yields as atomic weight rises (**3ba**-**3da**, 47%-59%) due to increasing steric hindrance and electron withdrawing effect in substrates isatins. Fluoro-substituent in other position affected the yields similarly (**3ea**, 62%). In contrast, 5-methyl and 5-methoxylisatin bearing electron donating groups facilitated the reaction (**3fa** and **3ga**, 77% and 88%).

The preliminary investigation of the addition reaction in asymmetric way was also performed. After examining an array of chiral ligands instead of dppp, the best enantioselectivity (50% ee and 29% yield) for the product was obtained using Me-Duphos **L1** as the ligand (Scheme 1). The experiments further indicate that the six-membered ring chelate similar to the Ni-dppp skeleton is crucial to the high reactivity, while ligands with longer or shorter chains remain relatively inert to the reaction. Chiral ligands with appropriate stereoscopic effect are expected to acquire good yield and enantioselectivity.

The mechanism of the catalytic cycle was considered preliminarily (Figure 2).[8c,18] Ni(0) species is first generated plausibly by reduction of Ni(II) precursor with arylboronic acids. Coordinating with phosphine ligand, the complex interacts with isatins leading to the η^2-coordinate intermediate **4**, which can be interconverted into its resonance **5**. After transmetalation of the intermediate with arylboronic acid, Ni(II) compound **6** is formed.

Scheme 1. Preliminary investigation of asymmetric reaction.

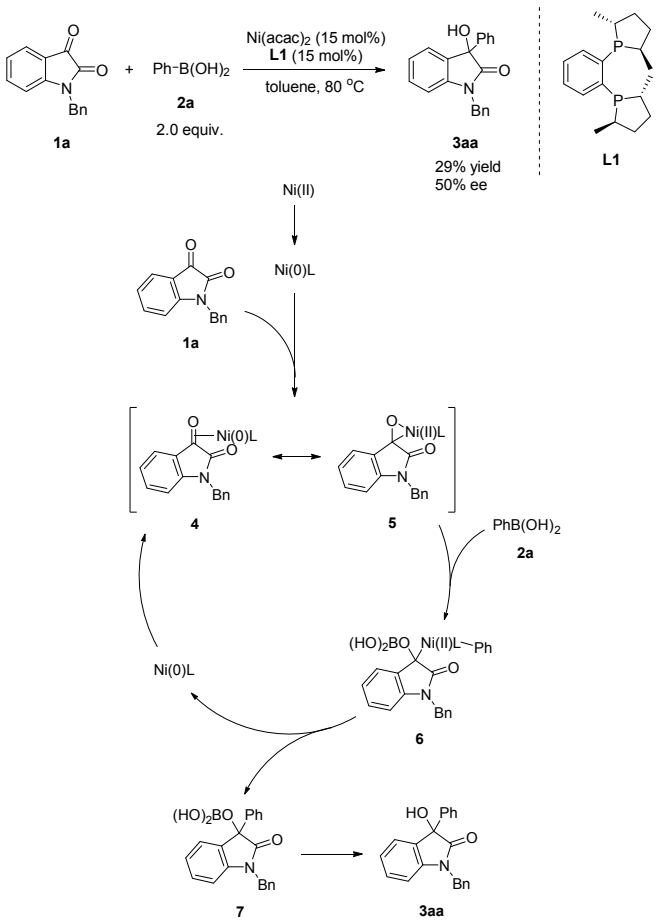


Figure 2. Plausible mechanism of the nickel-catalyzed addition reaction.

Via a subsequent reductive elimination, compound **7** is given, which affords product **3aa** upon workup. Furthermore, the regenerated Ni(0) species goes on the catalytic cycle ceaselessly.

3. Conclusions

In conclusion, the nickel(II)-catalyzed addition of arylboronic acids to isatins was developed successfully, giving 3-aryl-3-hydroxy-2-oxindoles in up to 97% yield. To our knowledge, this is the first example using nickel catalysts in this kind of reactions. Counterion was effective and H_2O was unnecessary in the catalytic system. Substrate investigations demonstrate that steric hindrance of arylboronic acids has significant influence on the yield, whereas electron-rich isatins are beneficial to get higher yields. Reaction mechanism was also considered and described as a Ni-catalytic cycle. Further exploration of the nickel-catalyzed reactions is ongoing in our laboratory.

4. Experimental section

4.1. General information

Anhydrous toluene was distilled from sodium and benzophenone before use and other solvents were dried through standard method. Reagents were obtained from commercial sources and used directly without further purification unless otherwise specified. Column chromatography was performed with silica gel (200-300 mesh). NMR spectra were recorded on a Brucker Avance III 400 MHz instrument with chemical shifts reported relative to Tetramethylsilane (TMS).

4.2. General procedure

N-benzylisatins (0.2 mmol) and arylboronic acids (0.4 mmol) were placed in a seal tube, in which $Ni(acac)_2$ (0.03 mmol) and dppp (0.04 mmol) were subsequently added under N_2 atmosphere. Using toluene (2 mL) as solvent, the reaction proceeded for 22 h at 80 ^{o}C with stirring. After concentrating solvent under reduced pressure, the mixture was purified by column chromatography on silica gel with petroleum ether and ethyl acetate. Eluent was removed to give the product.

*4.2.1. 1-benzyl-3-hydroxy-3-phenylindolin-2-one (**3aa**)*[16]

White solid, 53.0 mg, 84% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.0 Hz, 2H), 7.40 – 7.29 (m, 9H), 7.25 (td, *J* = 7.8, 1.1 Hz, 1H), 7.07 (dd, *J* = 11.1, 4.0 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 5.07 (d, *J* = 15.7 Hz, 1H), 4.85 (d, *J* = 15.7 Hz, 1H), 3.67 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.59, 142.67, 140.15, 135.41, 131.57, 129.82, 128.90, 128.69, 128.37, 127.81, 127.30, 125.30, 125.01, 123.58, 109.78, 77.99, 44.08.

*4.2.2. 1-benzyl-3-hydroxy-3-(p-tolyl)indolin-2-one (**3ab**)*[16]

White solid, 47.4 mg, 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 8H), 7.24 (td, *J* = 7.8, 1.1 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.06 (dd, *J* = 11.0, 4.0 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 5.06 (d, *J* = 15.7 Hz, 1H), 4.84 (d, *J* = 15.7 Hz, 1H), 3.61 (s, 1H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.78, 142.63, 138.16, 137.24, 135.47, 131.75, 129.69, 129.37, 128.87, 127.76, 127.29, 125.26, 124.95, 123.53, 109.72, 77.90 44.04, 21.13.

*4.2.3. 1-benzyl-3-hydroxy-3-(4-methoxyphenyl)indolin-2-one (**3ac**)*[15]

White solid, 55.3 mg, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 8H), 7.24 (t, *J* = 7.4 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.79 (d, *J* = 7.8 Hz, 1H), 5.04 (d, *J* = 15.7 Hz, 1H), 4.81 (d, *J* = 15.7 Hz, 1H), 3.88 (s, 1H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.83, 159.61, 142.55, 135.48, 132.26, 131.77, 129.65, 128.87, 127.74, 127.28, 126.87, 124.97, 123.51, 114.04, 109.73, 77.66, 55.30, 44.00.

*4.2.4. 1-benzyl-3-(4-chlorophenyl)-3-hydroxyindolin-2-one (**3ad**)*[16]

White solid, 67.9 mg, 97% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 9H), 7.26 (t, *J* = 7.2 Hz, 2H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 5.04 (d, *J* = 15.6 Hz, 1H), 4.82 (d, *J* = 15.6 Hz, 1H), 3.87 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.29, 142.53, 138.70, 135.27, 134.31, 131.29, 130.02, 128.94, 128.82, 127.90, 127.31, 126.90, 124.94, 123.75, 109.91, 77.62, 44.11.

*4.2.5. 1-benzyl-3-hydroxy-3-(4-phenoxyphenyl)indolin-2-one (**3ae**)*[16]

White solid, 70.1 mg, 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.22 (m, 11H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.08 (t, *J* = 7.3 Hz, 1H), 7.03 (d, *J* = 7.8 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 6.81 (d, *J* = 7.8 Hz, 1H), 5.05 (d, *J* = 15.7 Hz, 1H), 4.84 (d, *J* = 15.7 Hz, 1H), 3.70 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.67, 157.52, 156.75, 142.57, 135.38, 134.75, 131.58, 129.83, 129.80, 128.91, 127.82, 127.29, 127.08, 125.01, 123.61, 123.58, 119.24, 118.64, 109.83, 77.71, 44.07.

*4.2.6. 1-benzyl-3-(3,4-difluorophenyl)-3-hydroxyindolin-2-one (**3af**)*[16]

White solid, 56.9 mg, 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 8H), 7.14 – 7.03 (m, 3H), 6.83 (d, *J* = 7.8 Hz, 1H), 5.01 (d, *J* = 15.6 Hz, 1H), 4.81 (d, *J* = 15.6 Hz, 1H), 4.59 – 4.36 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.21, 151.59, 151.53, 151.46, 151.40, 149.12, 149.05, 148.99, 148.92, 142.39, 137.30, 135.16, 131.18, 130.13, 128.96, 127.95, 127.30, 124.92, 123.89, 121.72, 121.69, 121.66, 121.62, 117.45, 117.28, 115.25, 115.06, 110.01, 77.32, 44.13.

*4.2.7. 1-benzyl-3-(3-chlorophenyl)-3-hydroxyindolin-2-one (**3ag**)*[16]

White solid, 48.3 mg, 69% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.39 – 7.23 (m, 10H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 5.04 (d, *J* = 15.6 Hz, 1H), 4.83 (d, *J* = 15.6 Hz, 1H), 4.17 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.30, 142.45, 142.30, 135.25, 134.62, 131.34, 130.03, 129.94, 128.96, 128.49, 127.91, 127.35, 125.68, 124.95, 123.83, 123.56, 109.95, 77.69, 44.13.

*4.2.8. 1-benzyl-3-(3,5-dimethoxyphenyl)-3-hydroxyindolin-2-one (**3ah**)*

White solid, 62.3 mg, 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 6H), 7.25 (td, *J* = 11.2, 4.4 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.58 (d, *J* = 2.2 Hz, 2H), 6.41 (t, *J* = 2.1 Hz, 1H), 5.09 (d, *J* = 15.6 Hz, 1H), 4.82 (d, *J* = 15.6 Hz, 1H), 3.75 (s, 6H), 3.48 – 3.33 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.34, 161.00, 142.58, 135.51, 131.49, 129.84, 128.88, 127.81, 127.36, 124.86, 123.59, 109.70, 103.32, 100.36, 77.98, 55.33, 44.06.

*4.2.9. methyl 3-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)benzoate (**3ai**)*[16]

White solid, 55.3 mg, 74% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.38 – 7.30 (m, 5H), 7.25 (t, *J* = 7.7 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 5.07 (d, *J* = 15.6 Hz, 1H), 4.85 (d, *J* = 15.6 Hz, 1H), 3.90 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.32, 166.68, 142.59, 140.79, 135.29, 131.35, 130.61, 130.04, 129.85, 129.55, 128.94, 128.81, 127.86, 127.33, 126.48, 124.93, 123.76, 109.97, 77.79, 52.20, 44.14.

*4.2.10. 1-benzyl-3-(2-fluorophenyl)-3-hydroxyindolin-2-one (**3aj**)*[15]

White solid, 48.0 mg, 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (td, *J* = 7.8, 1.6 Hz, 1H), 7.44 – 7.30 (m, 6H), 7.28 – 7.20 (m, 2H), 7.16 (d, *J* = 7.3 Hz, 1H), 7.04 – 6.94 (m, 2H), 6.77 (d, *J* = 7.8 Hz, 1H), 5.11 (d, *J* = 15.8 Hz, 1H), 4.89 (d, *J* = 15.8 Hz, 1H), 3.94 – 3.76 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.92, 160.31, 157.86, 143.04, 135.34, 130.18, 130.09, 130.00, 128.83, 127.71, 127.52, 127.49, 127.34, 127.33, 124.58, 124.37, 124.34, 123.36, 115.79, 115.58, 109.82, 75.33, 44.25.

*4.2.11. 1-benzyl-3-hydroxy-3-(naphthalen-1-yl)indolin-2-one (**3al**)*[19]

White solid, 67.2 mg, 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 5.3 Hz, 1H), 7.87 (d, *J* = 8.2 Hz, 2H), 7.67 – 7.47 (m, 4H), 7.39 (dt, *J* = 14.1, 7.6 Hz, 4H), 7.27 (td, *J* = 7.8, 1.0 Hz, 1H), 7.18 (t, *J* = 7.0 Hz, 2H), 6.96 (dd, *J* = 12.8, 7.6 Hz, 2H), 5.23 (d, *J* = 15.4 Hz, 1H), 4.90 (d, *J* = 15.4 Hz, 1H), 3.85 – 3.74 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.47, 142.62, 135.45, 134.97, 134.27, 131.68, 130.03, 129.64, 129.05, 128.95, 128.03, 127.98, 126.26, 125.55, 125.07, 124.97, 124.77, 124.33, 123.59, 109.98, 78.41, 44.37.

*4.2.12. 1-benzyl-3-(furan-2-yl)-3-hydroxyindolin-2-one (**3am**)*

White solid, 53.7 mg, 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.3 Hz, 1H), 7.48 (d, *J* = 0.6 Hz, 1H), 7.38 – 7.22 (m, 6H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.43 – 6.33 (m, 2H), 5.04 (d, *J* = 15.8 Hz, 1H), 4.85 (d, *J* = 15.8 Hz, 1H), 4.09 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.33, 151.44, 143.92, 142.57, 135.15, 130.15, 128.86, 128.37, 127.73, 127.09, 125.48, 123.42, 110.42, 109.77, 108.87, 73.64, 43.95.

*4.2.13. 1-benzyl-3-hydroxy-3-(thiophen-2-yl)indolin-2-one (**3an**)*

White solid, 58.5 mg, 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.4 Hz, 1H), 7.37 – 7.24 (m, 7H), 7.12 (t, *J* = 7.3 Hz, 1H), 7.05 (dd, *J* = 3.6, 1.0 Hz, 1H), 6.98 (dd, *J* = 4.9, 3.7 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 5.05 (d, *J* = 15.7 Hz, 1H), 4.84 (d, *J* = 15.8 Hz, 1H), 3.77 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.27, 143.53, 142.23, 135.19, 130.53, 130.13, 128.93, 128.89, 128.85, 127.79, 127.22, 127.18, 127.13, 126.90, 126.75, 125.82, 125.03, 123.50, 109.90, 75.58, 44.07.

*4.2.14. 1-benzyl-3-hydroxy-3-(thiophen-3-yl)indolin-2-one (**3ao**)*

White solid, 43.1 mg, 67% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.4 Hz, 1H), 7.37 – 7.22 (m, 8H), 7.17 (dd, *J* = 4.8, 1.1 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 5.04 (d, *J* = 15.7 Hz, 1H), 4.84 (d, *J* = 15.7 Hz, 1H), 3.83 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.03, 142.34, 140.98, 135.34, 130.81, 129.86, 128.89, 127.78, 127.21, 126.87, 125.62, 124.87, 123.49, 122.96, 109.80, 75.98, 44.00.

*4.2.15. 1-benzyl-5-fluoro-3-hydroxy-3-phenylindolin-2-one (**3ba**)*[16]

White solid, 39.3 mg, 59% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.29 (m, 10H), 7.04 (dd, *J* = 7.6, 2.5 Hz, 1H), 6.93 (td, *J* = 8.8, 2.6 Hz, 1H), 6.71 (dd, *J* = 8.6, 4.0 Hz, 1H), 5.05 (d, *J* = 15.7 Hz, 1H), 4.83 (d, *J* = 15.7 Hz, 1H), 3.94 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.63, 160.86, 158.45, 139.72, 138.38, 135.08, 133.40, 133.32, 128.97, 128.79, 128.74, 128.56, 127.93, 127.26, 125.20, 116.15, 115.92, 113.25, 113.00, 110.54, 110.46, 78.18, 44.23.

*4.2.16. 1-benzyl-5-chloro-3-hydroxy-3-phenylindolin-2-one (**3ca**)*[16]

White solid, 32.9 mg, 47% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.26 (m, 11H), 7.20 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 5.04 (d, *J* = 15.7 Hz, 1H), 4.83 (d, *J* = 15.7 Hz, 1H), 3.96 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.38, 141.05, 139.59, 134.95, 133.34, 129.65, 129.04, 128.99, 128.82, 128.60, 127.97, 127.25, 125.54, 125.20, 110.82, 78.01, 44.19.

*4.2.17. 1-benzyl-5-bromo-3-hydroxy-3-phenylindolin-2-one (**3da**)*[15]

White solid, 37.1 mg, 47% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.29 (m, 12H), 6.67 (d, *J* = 8.3 Hz, 1H), 5.03 (d, *J* = 15.7 Hz, 1H), 4.83 (d, *J* = 15.7 Hz, 1H), 3.89 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.28, 141.55, 139.57, 134.91, 133.68, 132.56, 128.99, 128.83, 128.61, 128.27, 127.98, 127.25, 125.19, 116.32, 111.30, 77.95, 44.17.

*4.2.18. 1-benzyl-6-fluoro-3-hydroxy-3-phenylindolin-2-one (**3ea**)*

White solid, 41.3 mg, 62% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.29 (m, 10H), 7.24 (dd, *J* = 8.2, 5.4 Hz, 1H), 6.77 – 6.70 (m, 1H), 6.54 (dd, *J* = 8.8, 2.1 Hz, 1H), 5.03 (d, *J* = 15.7 Hz, 1H), 4.80 (d, *J* = 15.7 Hz, 1H), 3.84 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.93, 164.95, 162.49, 144.32, 144.21, 139.92, 134.90, 129.03, 128.74, 128.47, 128.02, 127.28, 126.41, 126.31, 125.35, 125.26, 109.89, 109.67, 98.78, 98.50, 77.61, 44.22.

*4.2.19. 1-benzyl-3-hydroxy-5-methyl-3-phenylindolin-2-one (**3fa**)*[15]

White solid, 50.7 mg, 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 7.9, 1.2 Hz, 2H), 7.40 – 7.29 (m, 8H), 7.12 (s, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.04 (d, *J* = 15.6 Hz, 1H), 4.83 (d, *J* = 15.6 Hz, 1H), 3.82 (s, 1H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.71, 140.41, 140.17, 135.55, 133.28, 131.76, 130.00, 128.85, 128.64, 128.24, 127.73, 127.30, 125.69, 125.30, 109.54, 78.16, 44.08, 21.00.

*4.2.20. 1-benzyl-3-hydroxy-5-methoxy-3-phenylindolin-2-one (**3ga**)*

White solid, 60.8 mg, 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.40 – 7.29 (m, 8H), 6.91 (d, *J* = 2.4 Hz, 1H), 6.76 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.70 (d, *J* = 8.5 Hz, 1H), 5.04 (d, *J* = 15.7 Hz, 1H), 4.82 (d, *J* = 15.7 Hz, 1H), 3.93 – 3.76 (m, 1H), 3.72 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.62, 156.64, 140.24, 135.84, 135.50, 132.95, 128.89, 128.69, 128.33, 127.79, 127.32, 125.31, 114.65, 111.71, 110.40, 78.42, 55.77, 44.17.

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Reference

1. General reviews: (a) de Meijere, A.; Diederich, F. *Metal-catalyzed Cross-coupling Reactions, 2nd ed.*, Wiley-VCH: Weinheim, Germany, **2004**; (b) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417-1492.

2. Recent progresses: (a) Y. Tamaru, *Modern Organonickel Chemistry*, Wiley-VCH: New York, **2005**; (b) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, V. *Chem. Rev.* **2011**, *111*, 1346-1416; (c) Tasker, S. Z.; Standley, E. A.; Jamison, T. F.; *Nature* **2014**, *509*, 299-309; (d) Henrion, M.; Ritleng, V.; Chetcuti, M. J. *ACS Catal.* **2015**, *5*, 1283-1302; (e) Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. *Chem. Rev.* **2015**, *115*, 9587-9652; (f) Yang, H.; Yang, X.; Tang, W. *Tetrahedron* **2016**, *72*, 6143-6174.
3. (a) Rudolph, A.; Lautens, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 2656-2670; (b) Swift, E. C.; Jarvo, E. R. *Tetrahedron* **2013**, *69*, 5799-5817; (c) Haas, D.; Hammann, J. M.; Greiner, R.; Knochel, P. *ACS Catal.* **2016**, *6*, 1540-1552.
4. (a) RajanBabu, T. V. *Chem. Rev.* **2003**, *103*, 2845-2860; b) RajanBabu, T. V. *Synlett.* **2009**, 853-885; (c) Hilt, G. *Eur. J. Org. Chem.* **2012**, 4441-4451; (d) Pellissier, H. *Adv. Synth. Catal.* **2015**, *357*, 2745-2780; (e) Moslin, R. M.; Miller-Moslin, K.; Jamison, T. F. *Chem. Commun.* **2007**, *43*, 4441-4449.
5. Selected reports for reactions of organoboron reagents: (a) Saito, B.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 6694-6695; (b) Lundin, P. M.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 11027-11029; c) Zultanski, S. L.; Fu, G. C. *J. Am. Chem. Soc.* **2011**, *133*, 15362-15364; (d) Owston, N. A.; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 11908-11909; (e) Lu, Z.; Wilsily, A.; Fu, G. C. *J. Am. Chem. Soc.* **2011**, *133*, 8154-8157; (f) Wilsily, A.; Tramutola, F.; Owston, N. A.; Fu, G. C.; *J. Am. Chem. Soc.* **2012**, *134*, 5794-5797; (g) Jiang, X.; Sakthivel, S.; Kulbitski, K.; Nisnevich, G.; Gandelman, M. *J. Am. Chem. Soc.* **2014**, *136*, 9548-9551; (h) Jiang, X.; Gandelman, M. *J. Am. Chem. Soc.* **2015**, *137*, 2542-2547; (i) Shields, J. D.; Ahneman, D. T.; Graham, T. J. A.; Doyle, A. G. *Org. Lett.* **2014**, *16*, 142-145.
6. Review for nickel-catalyzed Suzuki-Miyaura reaction: (a) Han, F. S. *Chem. Soc. Rev.* **2013**, *42*, 5270-5298; (b) Yamaguchi, J.; Muto, K.; Itami, K. *Eur. J. Org. Chem.* **2013**, 19-30.
7. Reports for addition reaction to electron-deficient olefins: (a) Lin, P.-S.; Jeganmohan, M.; Cheng, C.-H. *Chem. - Asian J.* **2007**, *2*, 1409-1416; b) Chen, W.; Sun, L.; Huang, X.; Wang, J.; Peng, Y.; Song, G. *Adv. Synth. Catal.* **2015**, *357*, 1474-1482.
8. Selected reports for addition to carbonyl compounds: (a) Takahashi, G.; Shirakawa, E.; Tsuchimoto, T.; Kawakami, Y. *Chem. Commun.* **2005**, 1459-1461; (b) Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2005**, *7*, 4689-4691; (c) Sakurai, F.; Kondo, K.; Aoyama, T. *Tetrahedron Lett.* **2009**, *50*, 6001-6003; (d) Bouffard, J.; Itami, K. *Org. Lett.* **2009**, *11*, 4410-4413; (e) Xing, C.-H.; Hu, Q.-S. *Tetrahedron Lett.* **2010**, *51*, 924-927; (f) Quan, M.; Tang, L.; Shen, J.; Yang, G.; Zhang, W. *Chem. Commun.* **2017**, *53*, 609-612.
9. (a) Tokunaga, T.; Hume, W. E.; Nagamine, J.; Kawamura, T.; Taiji, M.; Nagata, R. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1789-1792; (b) Nagamine, J.; Nagata, R.; Seki, H.; Nomura-Akimaru, N.; Ueki, Y.; Kumagai, K.; Taiji, M.; Noguchi, H. *J. Endocrinol.* **2001**, *171*, 481-489; (c) Tokunaga, T.; Hume, W. E.; Umezome, T.; Okazaki, K.; Ueki, Y.; Kumagai, K.; Hourai, S.; Nagamine, J.; Seki, H.; Taiji, M.; Noguchi, H.; Nagata, R. *J. Med. Chem.* **2001**, *44*, 4641-4649; (d) Marti, C.; Carreira, E. M. *Eur. J. Org. Chem.* **2003**, 2209-2219. (e) Raunak; Kumar, V.; Mukherjee, S.; Poonam; Prasad, A. K.; Olsen, C. E.; Schaffer, S. J. C.; Sharma, S. K.; Watterson, A. C.; Errington, W.; Parmar, V. S. *Tetrahedron* **2005**, *61*, 5687-5697; (f) Khuzhaev, V. U.; Zhalolov, I.; Turgunov, K. K.; Tashkhodzhaev, B.; Levkovich, M. G.; Aripova, S. F.; Shashkov, A. S. *Chem. Nat. Compd.* **2004**, *40*, 269-272; (g) Di Malta, A.; Garcia, G.; Roux, R.; Schoentjes, B.; Serradeil-le Gal, C.; Tonnerre, B.; Wagnon, J. PCT Int. Appl. No. WO2003008407, **2003**.
10. (a) Yamasaki, S.; Fujii, K.; Wada, R.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2002**, *124*, 6536-6537; (b) Tomita, D.; Wada, R.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 4138-4139; (c) Motoki, R.; Tomita, D.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2006**, *47*, 8083-8086; (d) Tomita, D.; Yamatsugu, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 6946-6948.
11. (a) Yamada, K.; Tomioka, K. *Chem. Rev.* **2008**, *108*, 2874-2886; (b) Alexakis, A.; Bäckvall, J. E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796-2823; (c) Kumar, G. S.; Ramesh, P.; Kumar, A. S. Swetha, A.; Meshram, H. M. *Tetrahedron Lett.* **2013**, *54*, 5048-5051.
12. (a) Toullec, P. Y.; Jagt, R. B. C.; de Vries, J. G.; Feringa, B. L.; Minnaard, A. J. *Org. Lett.* **2006**, *8*, 2715-2718; (b) Shintani, R.; Inoue, M.; Hayashi, T. *Angew. Chem. Int. Ed.* **2006**, *45*, 3353-3356; (c) Gui, J.; Chen, G.; Cao, P.; Liao, J. *Tetrahedron: Asymmetry* **2012**, *23*, 554-563; (d) Feng, X.; Nie, Y.; Zhang, L.; Yang, J.; Du, H. *Tetrahedron Lett.* **2014**, *55*, 4581-4584.
13. (a) Lai, H.; Huang, Z.; Wu, Q.; Qin, Y. *J. Org. Chem.* **2009**, *74*, 283-288; (b) Liu, Z.; Gu, P.; Shi, M.; McDowell, P.; Li, G. *Org. Lett.* **2011**, *13*, 2314-2317; (c) Li, Q.; Wan, P.; Wang, S.; Zhuang, Y.; Li, L.; Zhou, Y.; He, Y.; Cao, R.; Qiu, L.; Zhou, Z. *Appl. Catal. A-Gen.* **2013**, *458*, 201-206.
14. (a) Shintani, R.; Takatsu, K.; Hayashi, T. *Chem. Commun.* **2010**, *46*, 6822-6824; (b) Zhang, J.; Chen, J.; Ding, J.; Liu, M.; Wu, H. *Tetrahedron* **2011**, *67*, 9347-9351.
15. Yamamoto, Y.; Yohda, M.; Shirai, T.; Ito, H.; Miyaura, N. *Chem. Asian J.* **2012**, *7*, 2446-2449.
16. Zhuang, Y.; He, Y.; Zhou, Z.; Xia, W.; Cheng, C.; Wang, M.; Chen, B.; Zhou, Z.; Pang, J.; Qiu, L. *J. Org. Chem.* **2015**, *80*, 6968-6975.
17. Uddin, J.; Morales, C. M.; Maynard, J. H.; Landis, C. R.; *Organometallics* **2006**, *25*, 5566-5581.
18. Arao, T.; Kondo, K.; Aoyam, T. *Tetrahedron Lett.* **2007**, *48*, 4115-4117.
19. Tan, J.; Kuang, Y.; Wang, Y.; Huang, Q.; Zhu, J.; Wang, Y. *Organometallics* **2016**, *35*, 3139-3147.