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Rh(III)-Catalyzed C−H Amidation of Indoles with Isocyanates

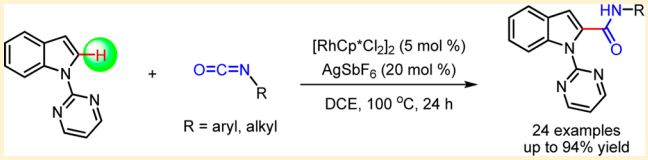
Taejoo Jeong,[†,§] Sangil Han,[†,§] Neeraj Kumar Mishra,[†] Satyasheel Sharma,[†] Seok-Yong Lee,[†] Joa Sub Oh,[‡] Jong Hwan Kwak,[†] Young Hoon Jung,[†] and In Su Kim*[,†]

[†]School of Pharmacy, Sungkyunkwan University, Suwon 440-746, Republic of Korea

[‡]College of Pharmacy, Dankook University, Cheonan 330-714, Republic of Korea

Supporting Information

ABSTRACT: The rhodium(III)-catalyzed direct amidation of indoles and pyrroles with aryl and alkyl isocyanates is described. These transformations provide a facile and efficient construction of C2-amidated N-heterocyclic scaffolds.



Indoles and pyrroles are among the most interesting heterocycles in nature and have been recognized as privileged structural motifs in drug discovery.[1] Consequently, there are many powerful methods for the synthesis and functionalization of these scaffolds.[2] In particular, C2-amidated indoles and pyrroles are known to have diverse biological profiles, including androgen receptor inhibition, protein kinase inhibition, DPP-4 inhibition, allosteric modulation of cannabinoid receptor, and selective inhibition of β-amyloid (Figure 1).[3] The synthetic methods for the formation of C2-amidated indoles and pyrroles rely on traditional approaches such as amidation reactions between carboxylic acid derivatives and amines,[4] coupling reactions of dilithioindoles with isocyanates,[5] Beckmann rearrangement of indoles with an oxime group at the C2-position,[6] and the palladium-catalyzed carbonylation of C2-halogenated indoles using amines and carbon monoxide.[7] However, these protocols have inherent limitations, including the preparation of prefunctionalized indoles, stoichiometric use of metallic reagents, harsh reaction conditions, and the use of hazardous CO gas. In complement with previous protocols, it is desirable to develop more efficient methodologies for synthesizing indole-2-carboxamides and pyrrole-2-carboxamides with fewer synthetic steps that avoid waste formation.

In recent decades, a great deal of effort has been devoted to the transition-metal-catalyzed direct functionalization of inactive C−H bonds with various coupling partners.[8] In this context, there has been recent progress in the area of the transition-metal-catalyzed direct additions of C(sp^2)−H bonds to polarized C−O[9] and C−N[10] multiple bonds. For example, Murai demonstrated the Ir-catalyzed coupling reaction of imidazoles with aldehydes in the presence of trialkylsilanes to quench the C−O bonds and facilitate the catalytic cycle.[9a] Larock disclosed the Pd-catalyzed arene C−H activation and intermolecular carbopalladation of nitriles.[10a,b] Kuninobu and Takai reported the Re-catalyzed intermolecular reaction of aromatic aldimines with alkynes and isocyanates to give indene and phthalimidine derivatives via insertion of unsaturated compounds and an intramolecular annulation reaction.[10c] Ellman and Bergman[11] and Shi[12] independently described the Rh(III)-catalyzed redox-neutral imine insertion of aryl C−H bonds to deliver amine products. In addition, Li,[13] Kim,[14] Shi,[15] and Zhou and Li[16] reported the Rh(III)-catalyzed direct addition of C−H bonds to aldehydes to afford ketones and alcohols. Thus, these protocols represent a catalytic alternative to transcend the barriers imposed by classical Grignard reaction.

Recently, further exploration of this reactivity mode revealed that various directing groups can also facilitate the arylation of the polar C−N π-bond of isocyanates. In this area, acetanilides,[17] phenylpyridines,[18] oximes,[19] and benzoic acid derivatives[20] were efficiently coupled with isocyanates to afford the corresponding *ortho*-amidated products under Rh, Ru, and Re catalysis. Inspired by our recent study on the site-selective functionalization of heterocycles[21] and in consideration of the biological importance of C2-amidated indoles and pyrroles, we herein present the Rh(III)-catalyzed direct C2 addition of indoles and pyrroles to isocyanates via C−H bond activation.

Our study was initiated by examining the coupling of 1-(pyrimidin-2-yl)-1*H*-indole (**1a**) and *n*-butyl isocyanate (**2a**) under rhodium catalysis (Table 1). Initial experiments indicated that the cationic rhodium complex, derived from $[RhCp^*Cl_2]_2$ and $AgSbF_6$, was found to catalyze the coupling of **1a** and **2a** in dichloroethane (DCE) at 100 °C for 24 h to provide C2-amidated indole **3a** in 60% yield (Table 1, entry 1). However, cationic ruthenium and cobalt catalysts were found to be ineffective for this transformation (Table 1, entries 2 and 3). Exclusion of either the Rh catalyst or $AgSbF_6$ additive resulted in no formation of desired product **3a** (Table 1, entries 4 and 5). After screening a range of solvents, DCE was found to exhibit the highest reactivity (Table 1, entries 6−9). Screening silver salts revealed that $AgSbF_6$ additive was the most effective in this coupling reaction (Table 1, entries 10 and 11). Further study revealed that acetate additives failed to facilitate high levels of the conversion reaction (Table 1, entries 12 and 13). To our delight, the optimal result was obtained using an

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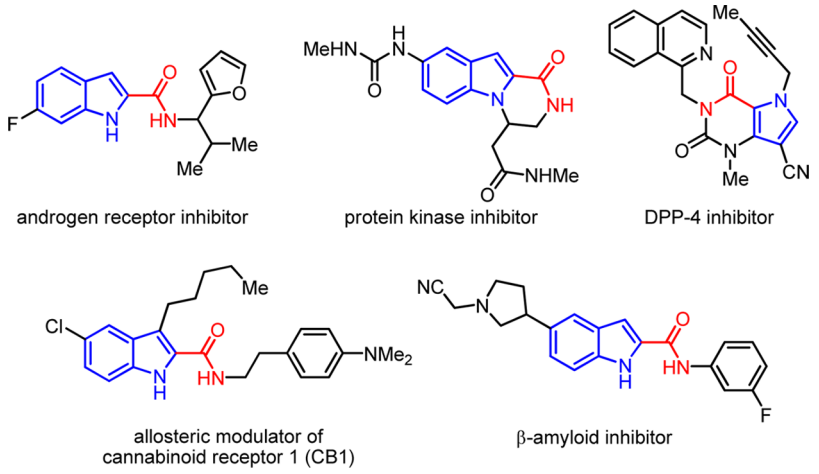
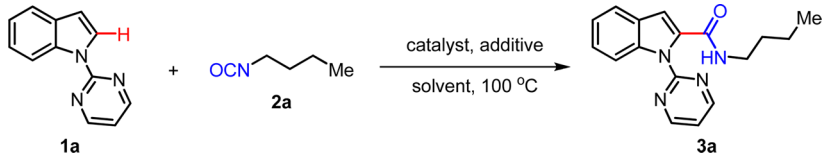


Figure 1. Selected examples for bioactive C2-amidated indoles and pyrroles.

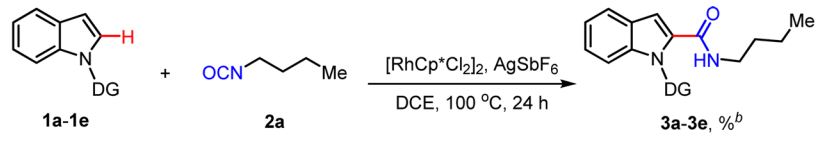
Table 1. Selected Optimization of Reaction Conditions[a]

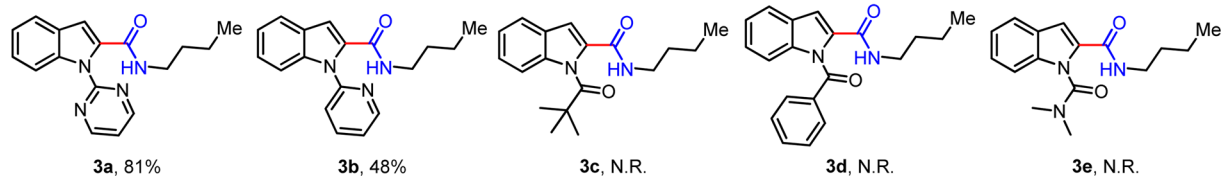


entry	catalyst (mol %)	additive (mol %)	solvent	yield (%)[b]
1	$[RhCp^*Cl_2]_2$ (2.5)	$AgSbF_6$ (10)	DCE	60
2	$[Ru(p\text{-}Cy)Cl_2]_2$ (2.5)	$AgSbF_6$ (10)	DCE	N.R.
3	$CoCp^*(CO)I_2$ (2.5)	$AgSbF_6$ (10)	DCE	12
4	$[RhCp^*Cl_2]_2$ (2.5)		DCE	N.R.
5		$AgSbF_6$ (10)	DCE	N.R.
6	$[RhCp^*Cl_2]_2$ (2.5)	$AgSbF_6$ (10)	THF	54
7	$[RhCp^*Cl_2]_2$ (2.5)	$AgSbF_6$ (10)	MeCN	50
8	$[RhCp^*Cl_2]_2$ (2.5)	$AgSbF_6$ (10)	DMSO	N.R.
9	$[RhCp^*Cl_2]_2$ (2.5)	$AgSbF_6$ (10)	PhCl	35
10	$[RhCp^*Cl_2]_2$ (2.5)	$AgNTf_2$ (10)	DCE	52
11	$[RhCp^*Cl_2]_2$ (2.5)	$AgBF_4$ (10)	DCE	48
12	$[RhCp^*Cl_2]_2$ (2.5)	$AgSbF_6$ (10) + NaOAc (30)	DCE	51
13	$[RhCp^*Cl_2]_2$ (2.5)	$AgSbF_6$ (10) + $Cu(OAc)_2$ (30)	DCE	24
14	**$[RhCp^*Cl_2]_2$ (5)**	**$AgSbF_6$ (20)**	**DCE**	**81**
15[c]	$[RhCp^*Cl_2]_2$ (5)	$AgSbF_6$ (20)	DCE	64
16[d]	$[RhCp^*Cl_2]_2$ (5)	$AgSbF_6$ (20)	DCE	60
17[e]	$[RhCp^*Cl_2]_2$ (5)	$AgSbF_6$ (20)	DCE	52

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), catalyst (quantity noted), additive (quantity noted), solvent (1 mL) under a N_2 atmosphere at 100 °C for 24 h in reaction tubes. [b]Isolated yield by flash column chromatography. [c]**2a** (0.4 mmol, 2 equiv). [d]Under air conditions. [e]60 °C.

Table 2. Screening of Directing Groups[a]





[a]Reaction conditions: **1a−1e** (0.2 mmol), **2a** (0.6 mmol), $[RhCp^*Cl_2]_2$ (5 mol %), $AgSbF_6$ (20 mol %), DCE (1 mL) under a N_2 atmosphere at 100 °C for 24 h in reaction tubes. [b]Isolated yield by flash column chromatography.

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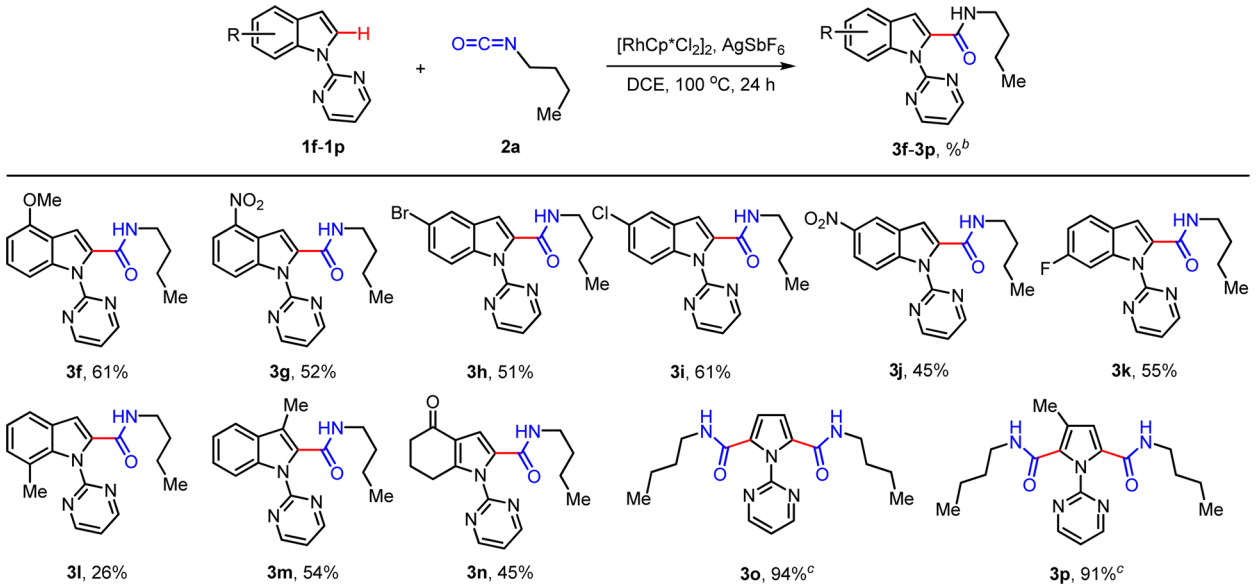
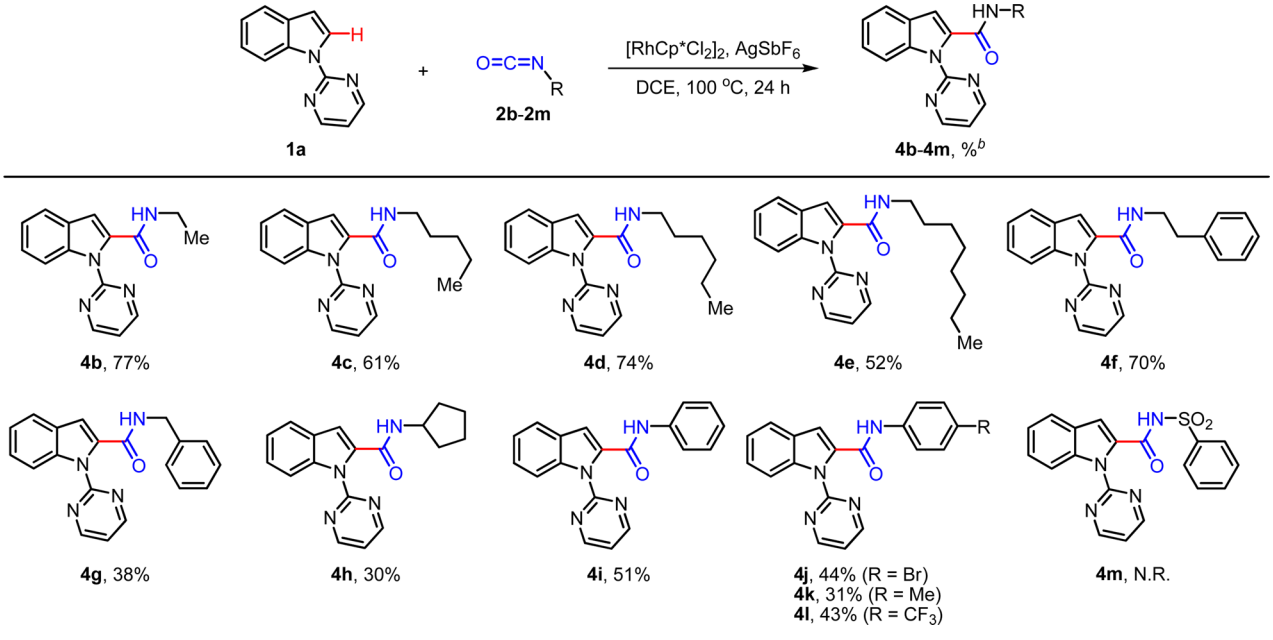
Table 3. Scope of Indoles and Pyrroles[a]



[a]Reaction conditions: **1f−1p** (0.2 mmol), **2a** (0.6 mmol), $[RhCp^*Cl_2]_2$ (5 mol %), $AgSbF_6$ (20 mol %), DCE (1 mL) under a N_2 atmosphere at 100 °C for 24 h in reaction tubes. [b]Isolated yield by flash column chromatography. [c]60 °C, 1 h.

Table 4. Scope of Isocyanates[a]



[a]Reaction conditions: **1a** (0.2 mmol), **2a−2m** (0.6 mmol), $[RhCp^*Cl_2]_2$ (5 mol %), $AgSbF_6$ (20 mol %), DCE (1 mL) under a N_2 atmosphere at 100 °C for 24 h in reaction tubes. [b]Isolated yield by flash column chromatography.

increased amount of Rh catalyst and Ag additive to afford our desired product **3a** in 81% yield (Table 1, entry 14). However, a decreased loading of isocyanate **2a** under otherwise identical conditions led to decreased formation of **3a** (Table 1, entry 15). In addition, this reaction can proceed under air conditions or at lower temperature (60 °C) to give **3a**, albeit in relatively low yields (Table 1, entries 16 and 17).

With the optimal reaction conditions in hands, various directing groups on indoles **1b−1e** were examined for C2-amidation with *n*-butyl isocyanate (**2a**), as shown in Table 2. Indole **1b** containing a pyridinyl directing group provided our desired product **3b** in 48% yield. However, indoles **1c−1e** with carbonyl directing groups, such as pivaloyl, benzoyl, and *N*,*N*-dimethylcarbamoyl groups, did not deliver the coupling product. These results suggest that nitrogen-containing heterocyclic directing groups are very crucial for this transformation.

To evaluate the scope and limitation of this process, various indoles **1f−1n** were screened under the optimal reaction conditions, as shown in Table 3. Indoles **1f−1k** bearing electron-rich and -deficient groups (OMe, NO_2, Br, Cl, and F) at the C4-, C5-, and C6-positions were found to undergo coupling with *n*-butyl isocyanate (**2a**), affording corresponding products **3f−3k**, whereas C7-substituted indole **1l** was found to

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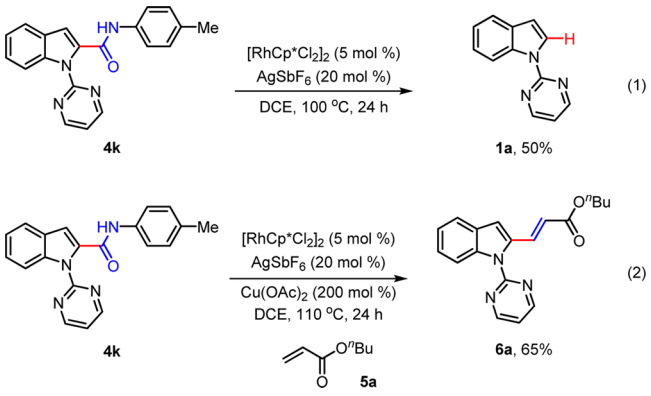
be less reactive under these conditions. Notably, the bromo and chloro moieties on amidated indoles **3h** and **3i** offer the opportunity for further transformations by empolying other traditional cross-coupling reactions. In addition, sterically congested C3-substituted indole **1m** and 2,3-disubstituted pyrrole **1n** also participated in this catalytic amidation reaction to furnish **3m** and **3n** in moderate yields. Finally, 2-(1*H*-pyrrol-1-yl)pyrimidine (**1o**) and 2-(3-methyl-1*H*-pyrrol-1-yl)-pyrimidine (**1p**) underwent bis-amidation under slightly modified reaction conditions to afford **3o** and **3p** in high yields, respectively.

To further explore the scope of this transformation, the optimal reaction conditions were applied to a range of alkyl-, aryl-, and arylsulfonyl isocyanates **2b**−**2m** (Table 4). In the case of alkyl isocyanates **2b**−**2f**, the desired indolic C2-amidation adducts were obtained in moderate to good yields. Benzyl isocyanate (**2g**) and cyclopentyl isocyanate (**2h**), however, exhibited slightly decreased reactivity. In addition, aryl isocyanates **2i**−**2l** with electron-rich and -deficient groups (Me, Br, and CF_3) were tolerated under the current reaction conditions to afford the corresponding products **4i**−**4l**. However, highly electron-deficient phenylsulfonyl isocyanate (**2m**) did not deliver the corresponding coupling product.

On the basis of these results, we considered that the moderate to low yields obtained from aryl isocyanates **2i**−**2l** might be possibly attributed to a reversibility of the amidation. Thus, we performed a reversibility experiment using **4k** under the standard reaction conditions, which provided **1a** in 50% yield (Scheme 1, eq 1). Previously, a similar reversible process

Scheme 1. Reversibility Experiments

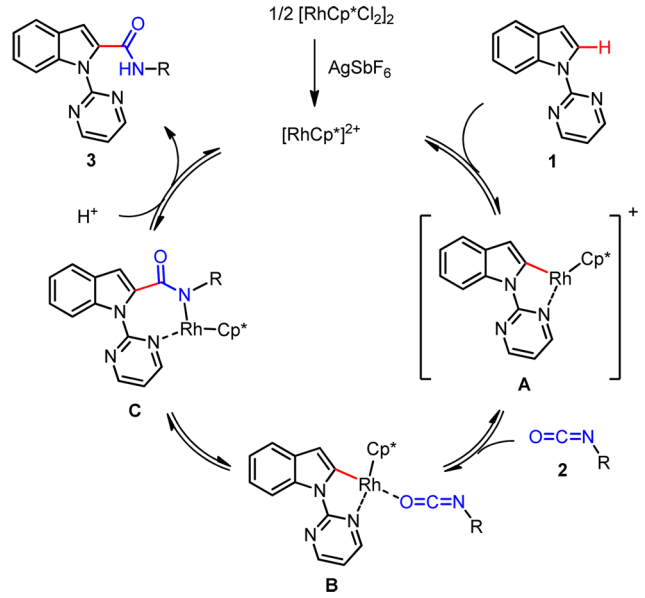


was observed by Bergman and Ellman in the Rh(III)-catalyzed coupling reaction between 2-phenylpyridines and N-Boc-imines.[11a] In addition, this reversible reaction was further confirmed by treatment with *n*-butyl acrylate (**5a**), which afforded C2-alkenylated indole **6a** in 65% yield (Scheme 1, eq 2).[22]

Meanwhile, the deprotection of a pyrimidyl directing group on C2-amidated indoles **3a** and **4k** was carried out, as shown in Scheme 2. First, treatment of **3a** under the standard reaction conditions (NaOEt, DMSO, 100 °C)[23] afforded desired product **7a** in low yield (16%). After further optimization, cleavage of the pyrimidinyl directing group was found to increase by additional use of EtOH, affording C2-amidated free-(NH)-indoles **7a** (42%) and **7b** (52%).[24]

A plausible reaction mechanism for the Rh(III)-catalyzed amidation reaction of indoles with isocyanates is depicted in Scheme 3. Cationic Rh(III) catalyst,[25] derived from

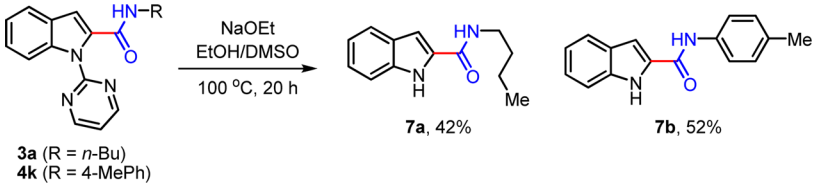
Scheme 3. Proposed Reaction Mechanism



$[RhCp^*Cl_2]_2$ and $AgSbF_6$, can coordinate to the pyrimidinyl nitrogen atom, which can reversibly activate the C−H bond at the indolic C2-position, providing cyclorhodated intermediate **A**[26] (see Supporting Information for H/D exchange experiment) and releasing 1 equiv of proton (H^+). Subsequent coordination of isocyanate furnishes intermediate **B**, which, on migratory insertion into the Rh−C bond, delivers complex **C**. Finally, protonation of **C** affords our desired product and the regeneration of active Rh(III) catalyst.

In conclusion, we disclosed a selective C2-amidation of indoles and pyrroles with isocyanates under rhodium catalysis. These transformations have been applied to a wide range of substrates and typically proceed with excellent levels of chemoselectivity as well as with high functional group tolerance.

Scheme 2. Removal of the Directing Group on Indoles



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EXPERIMENTAL SECTION

General Procedure for the Synthesis of Heteroarenes Substrates (1a, 1b, and 1f−1p). Indoles and pyrroles containing 2-pyrimidinyl and 2-pyridinyl directing groups were prepared as described previously.[27]

Typical Procedure for C2-Amidation of Indoles and Pyrrole 1a−1p with Isocyanates 2a−2m. To an oven-dried sealed tube charged with 1-(pyrimidin-2-yl)-1*H*-indole (**1a**) (39.1 mg, 0.2 mmol, 100 mol %), $[RhCp^*Cl_2]_2$ (6.2 mg, 0.01 mmol, 5 mol %), and $AgSbF_6$ (13.7 mg, 0.04 mmol, 20 mol %) were added *n*-butyl isocyanate (**2a**) (67.5 μL, 0.6 mmol, 300 mol %) and DCE (1 mL) under a N_2 atmosphere. The reaction mixture was allowed to stir at 100 °C for 24 h and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 2:1) to afford 48 mg of **3a** in 81% yield.

***N*-Butyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (3a).** 48.0 mg (81%); brown solid; mp = 241.7−244.6 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.2 Hz, 2H), 8.26 (d, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 8.4 Hz, 1H), 7.21 (t, *J* = 7.0 Hz, 1H), 7.10 (t, *J* = 4.9 Hz, 1H), 6.89 (s, 1H), 6.34 (s, 1H), 3.38 (q, *J* = 7.0 Hz, 2H), 1.57−1.55 (m, 2H), 1.42−1.38 (m, 2H), 0.94 (t, *J* = 7.7 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.8, 157.9, 157.2, 137.5, 134.7, 127.8, 125.2, 122.3, 121.5, 117.5, 113.8, 109.1, 39.4, 31.5, 19.9, 13.7; IR (KBr) υ 3249, 2927, 2870, 1637, 1556, 1417, 1344, 1286, 1233, 1192, 1145, 1058, 977, 817, 742 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{17}H_{18}N_4O$ $[M]^+$, 294.1481; found, 294.1479.

***N*-Butyl-1-(pyridin-2-yl)-1*H*-indole-2-carboxamide (3b).** 28.2 mg (48%); white solid; mp = 96.5−99.4 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.2 Hz, 1H), 7.87 (t, *J* = 7.7 Hz, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.33 (t, *J* = 6.3 Hz, 1H), 7.27 (t, *J* = 7.0 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 6.44 (s, 1H), 3.35 (q, *J* = 7.0 Hz, 2H), 1.52−1.50 (m, 2H), 1.36−1.32 (m, 2H), 0.92 (t, *J* = 7.7 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.7, 151.5, 149.1, 138.5, 138.2, 134.0, 127.0, 124.8, 122.5, 121.9, 121.6, 121.3, 111.1, 107.4, 39.3, 31.5, 20.0, 13.7; IR (KBr) υ 3284, 3054, 2924, 2855, 1641, 1546, 1467, 1447, 1387, 1350, 1273, 1225, 1148, 809, 739 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{18}H_{19}N_3O$ $[M]^+$, 293.1528; found, 293.1522.

***N*-Butyl-4-methoxy-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (3f).** 39.6 mg (61%); light yellow solid; mp = 142.5−147.5 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.2 Hz, 2H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.27 (t, *J* = 7.7 Hz, 1H), 7.16 (t, *J* = 4.9 Hz, 1H), 7.07 (s, 1H), 6.64 (d, *J* = 8.4 Hz, 1H), 6.17 (s, 1H), 3.96 (s, 3H), 3.44−3.41 (m, 2H), 1.62−1.59 (m, 2H), 1.45−1.42 (m, 2H), 0.96 (t, *J* = 7.7 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.6, 158.0, 157.5, 153.6, 139.0, 133.3, 126.3, 118.4, 117.8, 106.6, 106.4, 102.2, 55.4, 39.4, 31.6, 20.2, 13.8; IR (KBr) υ 3297, 2923, 2854, 1637, 1541, 1432, 1360, 1296, 1255, 1227, 1183, 1109, 1080, 985, 853, 822, 757, 722 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{18}H_{20}N_4O_2$ $[M]^+$, 324.1586; found, 324.1586.

***N*-Butyl-4-nitro-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (3g).** 35.3 mg (52%); dark brown solid; mp = 160.5−164.2 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.2 Hz, 2H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.16 (d, *J* = 7.7 Hz, 1H), 7.60 (s, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.27 (t, *J* = 4.9 Hz, 1H), 6.54 (s, 1H), 3.46 (q, *J* = 7.0 Hz, 2H), 1.67−1.64 (m, 2H), 1.48−1.45 (m, 2H), 0.99 (t, *J* = 7.7 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.7, 158.3, 156.7, 140.8, 138.9, 138.3, 124.2, 122.1, 120.6, 119.6, 118.8, 107.5, 39.7, 31.6, 20.0, 13.7; IR (KBr) υ 3291, 2928, 1644, 1549, 1505, 1420, 1333, 1286, 1226, 991, 824, 760, 733 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{17}H_{17}N_5O_3$ $[M]^+$, 339.1331; found, 339.1326.

5-Bromo-*N*-butyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (3h). 38.1 mg (51%); light yellow solid; mp = 180.0−182.5 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.72 (d, *J* = 3.5 Hz, 2H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.71 (s, 1H), 7.41 (d, *J* = 9.1 Hz, 1H), 7.17 (t, *J* = 3.5 Hz, 1H), 6.82 (s, 1H), 6.21 (s, 1H), 3.43 (q, *J* = 5.6 Hz, 2H), 1.63−1.59 (m, 2H), 1.46−1.42 (m, 2H), 0.97 (t, *J* = 6.3 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.5, 158.0, 157.0, 136.1, 135.8, 129.6, 128.1, 124.0, 117.9, 115.6, 115.5, 108.1, 39.5, 31.5, 20.0, 13.8; IR (KBr) υ 3265, 2921, 2852, 1637, 1554, 1426, 1378, 1333, 1290, 1210, 1051, 863, 801, 754, 717 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{17}H_{17}BrN_4O$ $[M]^+$, 372.0586; found, 372.0580.

***N*-Butyl-5-chloro-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (3i).** 40.1 mg (61%); light yellow solid; mp = 167.4−171.8 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.9 Hz, 2H), 8.23 (d, *J* = 9.1 Hz, 1H), 7.54 (s, 1H), 7.28 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.16 (t, *J* = 4.9 Hz, 1H), 6.82 (s, 1H), 6.23 (s, 1H), 3.43 (q, *J* = 7.0 Hz, 2H), 1.63−1.59 (m, 2H), 1.46−1.41 (m, 2H), 0.97 (t, *J* = 7.7 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.6, 158.0, 157.0, 136.0, 135.8, 129.0, 127.9, 125.5, 120.9, 117.8, 115.2, 108.2, 39.5, 31.5, 20.0, 13.8; IR (KBr) υ 3276, 2927, 2871, 1642, 1556, 1425, 1335, 1290, 1229, 1067, 879, 804, 713, 656 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{17}H_{17}ClN_4O$ $[M]^+$, 328.1091; found, 328.1092.

***N*-Butyl-5-nitro-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (3j).** 30.5 mg (45%); light brown solid; mp = 205.0−206.8 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.9 Hz, 2H), 8.50 (s, 1H), 8.31 (d, *J* = 9.1 Hz, 1H), 8.18 (d, *J* = 9.1 Hz, 1H), 7.26 (t, *J* = 4.9 Hz, 1H), 7.0 (s, 1H), 6.30 (s, 1H), 3.45 (q, *J* = 7.0 Hz, 2H), 1.65−1.63 (m, 2H), 1.48−1.44 (m, 2H), 0.98 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.9, 158.2, 156.6, 143.5, 140.0, 137.8, 127.5, 120.3, 118.7, 118.2, 114.3, 109.2, 39.7, 31.5, 20.0, 13.7; IR (KBr) υ 3271, 2926, 1642, 1565, 1511, 1422, 1332, 1296, 1280, 1072, 896, 812, 731, 655 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{17}H_{17}N_5O_3$ $[M]^+$, 339.1331; found, 339.1333.

***N*-Butyl-6-fluoro-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (3k).** 34.4 mg (55%); light yellow solid; mp = 146.3−148.1 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.9 Hz, 2H), 8.05 (d, *J* = 10.5 Hz, 1H), 7.53 (t, *J* = 8.4 Hz, 1H), 7.17 (t, *J* = 4.2 Hz, 1H), 6.99 (td, *J* = 9.8, 2.1 Hz, 1H), 6.89 (s, 1H), 6.15 (s, 1H), 3.43 (q, *J* = 7.0 Hz, 2H), 1.63−1.59 (m, 2H), 1.46−1.43 (m, 2H), 0.97 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.6, 161.5 (d, J_{C-F} = 239.4 Hz), 158.0, 157.1, 137.9, 135.3 (d, J_{C-F} = 4.2 Hz), 124.2, 122.4 (d, J_{C-F} = 10.1 Hz), 117.8, 111.2 (d, J_{C-F} = 24.3 Hz), 109.0, 101.1 (d, J_{C-F} = 28.3 Hz), 39.5, 31.6, 20.0, 13.8; IR (KBr) υ 3272, 2927, 2869, 1644, 1617, 1552, 1473, 1423, 1357, 1291, 1234, 1211, 1134, 977, 858, 834, 736, 673 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{17}H_{17}FN_4O$ $[M]^+$, 312.1386; found, 312.1383.

***N*-Butyl-7-methyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (3l).** 16.1 mg (26%); light yellow solid; mp = 130.2−131.6 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 9.11 (d, *J* = 4.9 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.66 (t, *J* = 4.9 Hz, 1H), 7.52 (s, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.28 (t, *J* = 7.0 Hz, 1H), 6.53 (s, 1H), 3.57 (q, *J* = 7.0 Hz, 2H), 2.15 (s, 3H), 1.80−1.78 (m, 2H), 1.64−1.60 (m, 2H), 1.18 (t, *J* = 7.7 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.4, 159.8, 158.0, 137.5, 133.5, 127.4, 127.3, 122.3, 121.6, 120.2, 119.9, 106.2, 39.3, 31.6, 20.0, 19.1, 13.7; IR (KBr) υ 3327, 2924, 1636, 1549, 1421, 1282, 1243, 911, 829, 772, 728 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{18}H_{20}N_4O$ $[M]^+$, 308.1637; found, 308.1632.

***N*-Butyl-3-methyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (3m).** 33.4 mg (54%); yellow solid; mp = 176.4−181.3 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.9 Hz, 2H), 8.45 (d, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.0 Hz, 1H), 7.26 (t, *J* = 9.1 Hz, 1H), 7.06 (t, *J* = 4.9 Hz, 1H), 5.84 (s, 1H), 3.47 (q, *J* = 7.0 Hz, 2H), 2.44 (s, 3H), 1.63−1.60 (m, 2H), 1.45−1.41 (m, 2H), 0.97 (t, *J* = 7.7 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 163.7, 157.8, 157.5, 136.6, 131.3, 129.9, 125.4, 122.2, 119.6, 117.7, 116.7, 114.6, 39.6, 31.6, 20.1, 13.8, 9.3; IR (KBr) υ 3285, 2926, 2868, 2363, 1698, 1623, 1558, 1424, 1348, 1280, 1224, 1159, 1074, 947, 759, 744, 700 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{18}H_{20}N_4O$ $[M]^+$, 308.1637; found, 308.1642.

***N*-Butyl-4-oxo-1-(pyrimidin-2-yl)-4,5,6,7-tetrahydro-1*H*-indole-2-carboxamide (3n).** 28.2 mg (45%); yellow oil; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.9 Hz, 2H), 7.34 (t, *J* = 4.9 Hz, 1H), 6.98 (s, 1H), 6.11 (s, 1H), 3.30 (q, *J* = 7.0 Hz, 2H), 2.87 (t, *J* = 5.6 Hz, 2H), 2.52 (t, *J* = 6.3 Hz, 2H), 2.14 (t, *J* = 6.3 Hz, 2H), 1.54−1.52 (m, 2H), 1.39−1.35 (m, 2H), 0.92 (t, *J* = 7.7 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 194.6, 160.8, 158.4, 156.8, 147.7, 130.0, 120.9, 120.0, 109.1, 39.2, 37.8, 31.6, 23.3, 22.9, 20.0, 13.7; IR (KBr) υ 3298, 2923, 2854, 2139, 1640, 1554, 1416, 1296, 1223, 1129, 1087, 997, 898,

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817, 751, 718 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{17}H_{20}N_4O_2$ $[M]^+$, 312.1586; found, 312.1585.

***N,N′*-Dibutyl-1-(pyrimidin-2-yl)-1*H*-pyrrole-2,5-dicarboxamide (3o).** 64.5 mg (94%); white solid; mp = 244.7−246.2 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.78 (d, J = 4.9 Hz, 2H), 7.35 (t, J = 4.9 Hz, 1H), 6.60 (s, 2H), 6.17 (br s, 2H), 3.26 (q, J = 7.0 Hz, 4H), 1.51−1.46 (m, 4H), 1.34−1.31 (m, 4H), 0.90 (t, J = 7.0 Hz, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 160.2, 158.5, 158.0, 131.6, 120.2, 111.1, 39.2, 31.6, 20.6, 13.7; IR (KBr) υ 3322, 3301, 2924, 1643, 1542, 1414, 1283, 822, 739 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{18}H_{25}N_5O_2$ $[M]^+$, 343.2008; found, 343.2009.

***N,N′*-Dibutyl-3-methyl-1-(pyrimidin-2-yl)-1*H*-pyrrole-2,5-dicarboxamide (3p).** 65.0 mg (91%); light yellow oil; ^1H NMR (700 MHz, $CDCl_3$) δ 8.68 (d, J = 4.9 Hz, 2H), 7.27 (t, J = 4.9 Hz, 1H), 6.87 (br s, 1H), 6.33 (s, 1H), 6.30 (br s, 1H), 3.24−3.21 (m, 2H), 3.18−3.15 (m, 2H), 2.15 (s, 3H), 1.46−1.40 (m, 4H), 1.31−1.26 (m, 4H), 0.88−0.84 (m, 6H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.2, 160.5, 158.2, 157.7, 129.7, 129.0, 121.5, 119.7, 114.2, 39.1, 39.0, 31.5, 20.0, 19.9, 13.6, 12.3; IR (KBr) υ 3309, 3203, 1708, 1636, 1561, 1520, 1428, 1413, 1255, 1147, 817, 756 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{19}H_{27}N_5O_2$ $[M]^+$, 357.2165; found, 357.2166.

***N*-Ethyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (4b).** 41.0 mg (77%); yellow sticky solid; ^1H NMR (700 MHz, $CDCl_3$) δ 8.76 (br s, 2H), 8.28 (d, J = 7.7 Hz, 1H), 7.62 (d, J = 7.0 Hz, 1H), 7.36 (t, J = 7.0 Hz, 1H), 7.26−7.23 (m, 1H), 7.17 (s, 1H), 6.94 (s, 1H), 6.20 (s, 1H), 3.47 (s, 2H), 1.26 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.8, 157.9, 157.3, 137.6, 134.7, 127.9, 125.3, 122.4, 121.6, 117.7, 113.9, 109.3, 34.7, 14.7; IR (KBr) υ 3283, 2924, 1642, 1556, 1419, 1345, 1284, 1231, 1148, 931, 810, 741, 657 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{15}H_{14}N_4O$ $[M]^+$, 266.1168; found, 266.1174.

***N*-Pentyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (4c).** 37.6 mg (61%); yellow oil; ^1H NMR (700 MHz, $CDCl_3$) δ 8.74 (d, J = 4.2 Hz, 2H), 8.28 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.34 (t, J = 7.0 Hz, 1H), 7.24 (t, J = 7.7 Hz, 1H), 7.16 (t, J = 4.9 Hz, 1H), 6.94 (s, 1H), 6.17 (s, 1H), 3.43 (q, J = 7.0 Hz, 2H), 1.64−1.62 (m, 2H), 1.40−1.37 (m, 4H), 0.93 (t, J = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.9, 158.0, 157.4, 137.6, 134.8, 127.9, 125.3, 122.4, 121.6, 117.6, 113.9, 109.2, 39.8, 29.2, 29.0, 22.4, 14.0; IR (KBr) υ 3272, 2925, 2856, 1639, 1548, 1146, 1426, 1348, 1290, 1266, 1233, 1149, 1026, 817, 739, 708 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{18}H_{20}N_4O$ $[M]^+$, 308.1637; found, 308.1638.

***N*-Hexyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (4d).** 47.7 mg (74%); yellow solid; mp = 117.6−120.4 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.73 (d, J = 4.9 Hz, 2H), 8.28 (d, J = 8.4 Hz, 1H), 7.61 (d, J = 7.7 Hz, 1H), 7.35 (t, J = 7.7 Hz, 1H), 7.23 (t, J = 7.0 Hz, 1H), 7.15 (t, J = 4.9 Hz, 1H), 6.93 (s, 1H), 6.15 (s, 1H), 3.43 (q, J = 6.3 Hz, 2H), 1.64−1.62 (m, 2H), 1.42−1.40 (m, 2H), 1.34−1.33 (m, 4H), 0.91 (t, J = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.9, 158.0, 157.4, 137.7, 134.9, 128.0, 125.3, 122.5, 121.6, 117.6, 113.9, 109.2, 39.8, 31.5, 29.5, 26.6, 22.6, 14.0; IR (KBr) υ 3274, 2924, 2855, 1643, 1558, 1419, 1347, 1287, 1233, 1149, 807, 744, 657 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{19}H_{22}N_4O$ $[M]^+$, 322.1794; found, 322.1795.

***N*-Octyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (4e).** 36.4 mg (52%); yellow solid; mp = 103.3−105.4 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.74 (d, J = 4.9 Hz, 2H), 8.28 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.35 (t, J = 7.7 Hz, 1H), 7.24 (t, J = 7.7 Hz, 1H), 7.15 (t, J = 4.9 Hz, 1H), 6.94 (s, 1H), 6.14 (s, 1H), 3.43 (q, J = 7.0 Hz, 2H), 1.64−1.61 (m, 2H), 1.42−1.38 (m, 2H), 1.35−1.27 (m, 8H), 0.89 (t, J = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.9, 158.0, 157.5, 137.7, 134.9, 128.0, 125.3, 122.5, 121.6, 117.6, 113.9, 109.2, 39.9, 31.8, 29.7, 29.6, 29.2, 26.9, 22.6, 14.0; IR (KBr) υ 3273, 2921, 2851, 1644, 1557, 1420, 1347, 1288, 1234, 1213, 1150, 804, 744, 720 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{21}H_{26}N_4O$ $[M]^+$, 350.2107; found, 350.2106.

***N*-Phenethyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (4f).** 47.9 mg (70%); yellow oil; ^1H NMR (700 MHz, $CDCl_3$) δ 8.73 (d, J = 4.9 Hz, 2H), 8.28 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 7.7 Hz, 1H), 7.37−7.32 (m, 3H), 7.28 (d, J = 7.0 Hz, 2H), 7.26−7.22 (m, 2H), 7.15 (t, J = 4.9 Hz, 1H), 6.84 (s, 1H), 6.26 (s, 1H), 3.69 (q, J = 6.3 Hz, 2H), 2.95 (t, J = 7.0 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.8, 158.0, 157.3, 139.0, 137.6, 134.6, 128.9, 128.6, 127.8, 126.5, 125.4, 122.5, 121.6, 117.6, 113.9, 109.4, 41.0, 35.5; IR (KBr) υ 3285, 2923, 2854, 1642, 1556, 1421, 1346, 1284, 1231, 1151, 809, 742, 697 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{21}H_{18}N_4O$ $[M]^+$, 342.1481; found, 342.1485.

***N*-Benzyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (4g).** 24.9 mg (38%); light yellow solid; mp = 175.2−176.9 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.70 (d, J = 4.9 Hz, 2H), 8.31 (d, J = 8.4 Hz, 1H), 7.61 (d, J = 7.7 Hz, 1H), 7.43 (d, J = 7.7 Hz, 2H), 7.38−7.35 (m, 3H), 7.31 (t, J = 6.3 Hz, 1H), 7.24 (dt, J = 7.7, 1.4 Hz, 1H), 7.14 (t, J = 4.9 Hz, 1H), 6.98 (s, 1H), 6.52 (s, 1H), 4.64 (d, J = 5.6 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.8, 158.0, 157.3, 138.2, 137.7, 134.4, 128.6, 127.9, 127.8, 127.5, 125.5, 122.5, 121.7, 117.6, 114.0, 109.6, 43.7; IR (KBr) υ 3315, 2919, 1649, 1552, 1421, 1338, 1240, 1078, 975, 836, 754, 695 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{20}H_{16}N_4O$ $[M]^+$, 328.1324; found, 328.1319.

***N*-Cyclopentyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (4h).** 18.3 mg (30%); light yellow solid; mp = 185.0−190.0 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.75 (d, J = 4.9 Hz, 2H), 8.29 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.35 (t, J = 8.4 Hz, 1H), 7.24 (t, J = 7.7 Hz, 1H), 7.16 (t, J = 4.2 Hz, 1H), 6.94 (s, 1H), 6.08 (s, 1H), 4.38−4.35 (m, 1H), 2.09−2.04 (m, 2H), 1.73−1.70 (m, 2H), 1.68−1.64 (m, 2H), 1.58−1.57 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 162.6, 158.0, 157.4, 137.5, 134.9, 128.0, 125.3, 122.5, 121.6, 117.6, 113.9, 109.1, 51.6, 32.9, 23.7; IR (KBr) υ 3319, 3046, 2953, 2865, 1626, 1557, 1425, 1350, 1295, 1150, 1079, 823, 803, 740, 664 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{18}H_{18}N_4O$ $[M]^+$, 306.1481; found, 306.1476.

***N*-Phenyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (4i).** 32.1 mg (51%); light yellow solid; mp = 173.9−176.0 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.74 (d, J = 4.9 Hz, 2H), 8.28 (d, J = 8.4 Hz, 1H), 8.11 (br s, 1H), 7.61−7.59 (m, 3H), 7.38 (t, J = 8.4 Hz, 1H), 7.33 (t, J = 7.7 Hz, 2H), 7.24−7.23 (m, 1H), 7.16 (t, J = 4.2 Hz, 1H), 7.13 (t, J = 7.0 Hz, 1H), 7.08 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 160.5, 158.1, 157.3, 138.0, 137.9, 134.4, 129.0, 127.7, 125.8, 124.4, 122.7, 121.9, 119.9, 117.8, 113.9, 110.3; IR (KBr) υ 3016, 1653, 1600, 1564, 1538, 1444, 1425, 1353, 1310, 1236, 1191, 1150, 819, 744, 690 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{19}H_{14}N_4O$ $[M]^+$, 314.1168; found, 314.1173.

***N*-(4-Bromophenyl)-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (4j).** 34.6 mg (44%); light yellow solid; mp = 223.3−225.9 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.74 (d, J = 4.9 Hz, 2H), 8.29 (d, J = 8.4 Hz, 1H), 8.10 (br s, 1H), 7.60 (d, J = 7.7 Hz, 1H), 7.49−7.48 (m, 2H), 7.43 (d, J = 9.1 Hz, 2H), 7.39 (t, J = 8.4 Hz, 1H), 7.26−7.24 (m, 1H), 7.17 (t, J = 4.9 Hz, 1H), 7.08 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 160.5, 158.2, 157.2, 137.9, 137.0, 134.0, 132.0, 127.6, 126.0, 122.8, 121.9, 121.4, 117.8, 117.0, 113.9, 110.5; IR (KBr) υ 3292, 2920, 2850, 1659, 1588, 1538, 1184, 1424, 1396, 1305, 1239, 1194, 1069, 938, 819, 737, 655 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{19}H_{13}BrN_4O$ $[M]^+$, 392.0273; found, 392.0269.

1-(Pyrimidin-2-yl)-*N*-(*p*-tolyl)-1*H*-indole-2-carboxamide (4k). 20.3 mg (31%); colorless oil; ^1H NMR (700 MHz, $CDCl_3$) δ 8.75 (d, J = 4.9 Hz, 2H), 8.31 (d, J = 8.4 Hz, 1H), 7.96 (br s, 1H), 7.64 (d, J = 7.7 Hz, 1H), 7.49 (br s, 2H), 7.39 (t, J = 7.7 Hz, 1H), 7.28−7.26 (m, 2H), 7.16−7.15 (m, 2H), 7.09 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 158.1, 157.4, 137.9, 135.5, 134.7, 134.1, 129.5, 127.9, 125.7, 122.7, 121.8, 120.0, 117.7, 114.0, 110.1, 20.8; IR (KBr) υ 3256, 2921, 1660, 1602, 1564, 1534, 1422, 1348, 1313, 1240, 1191, 1149, 814, 734 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{20}H_{16}N_4O$ $[M]^+$, 328.1324; found, 328.1328.

1-(Pyrimidin-2-yl)-*N*-(4-(trifluoromethyl)phenyl)-1*H*-indole-2-carboxamide (4l). 32.9 mg (43%); light yellow solid; mp = 241.7−244.6 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.75 (d, J = 4.2 Hz, 2H), 8.30 (d, J = 8.4 Hz, 1H), 8.23 (s, 1H), 7.70 (d, J = 7.7 Hz, 2H), 7.62 (d, J = 8.4 Hz, 1H), 7.58 (d, J = 8.4 Hz, 2H), 7.41 (dt, J = 7.7, 1.4 Hz, 1H), 7.27−7.25 (m, 1H), 7.18 (t, J = 4.9 Hz, 1H), 7.12 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 160.7, 158.2, 157.2, 141.0, 138.0, 133.8, 127.6, 126.4 (q, J_{C-F} = 2.6 Hz), 126.3 (q, J_{C-F} = 32.2 Hz), 126.2, 124.0 (q, J_{C-F} = 269.3 Hz), 122.9, 122.0, 119.5, 117.9, 114.0, 110.8; IR

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(KBr) υ 3261, 2918, 2359, 1666, 1602, 1542, 1423, 1315, 1249, 1158, 1107, 1065, 937, 835, 739 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{20}H_{13}F_3N_4O$ $[M]^+$, 382.1041; found, 382.1039.

Experimental Procedure for Reversibility Experiment of 4k. To a mixture of 1-(pyrimidin-2-yl)-*N*-(*p*-tolyl)-1*H*-indole-2-carboxamide (**4k**) (65.6 mg, 0.2 mmol, 100 mol %), $[RhCp^*Cl_2]_2$ (6.2 mg, 0.01 mmol, 5 mol %), and $AgSbF_6$ (13.7 mg, 0.04 mmol, 20 mol %) was added DCE (1 mL) under a N_2 atmosphere. The reaction mixture was allowed to stir at 100 °C for 24 h and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 10:1) to afford 19.6 mg of **1a** in 50% yield.

Reaction of 4k with *n*-Butyl Acrylate (5a). To a stirred solution of 1-(pyrimidin-2-yl)-*N*-(*p*-tolyl)-1*H*-indole-2-carboxamide (**4k**) (65.6 mg, 0.2 mmol, 100 mol %), $[RhCp^*Cl_2]_2$ (6.2 mg, 0.01 mmol, 5 mol %), $AgSbF_6$ (13.7 mg, 0.04 mmol, 20 mol %), and $Cu(OAc)_2$ (72.6 mg, 0.4 mmol, 200 mol %) in DCE (1 mL) was added *n*-butyl acrylate (**5a**) (57.3 μL, 0.4 mmol, 200 mol %). The reaction mixture was allowed to stir at 110 °C for 24 h and cooled to room temperature. The reaction mixture was diluted with EtOAc (3 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 4:1) to afford 42 mg of **6a** in 65% yield.

(*E*)-Butyl 3-(1-(Pyrimidin-2-yl)-1*H*-indol-2-yl)acrylate (6a). Light yellow solid; mp = 85.1−88.3 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.82 (d, J = 4.9 Hz, 2H), 8.34 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 16.1 Hz, 1H), 7.62 (d, J = 7.7 Hz, 1H), 7.33 (dt, J = 7.7, 1.4 Hz, 1H), 7.24 (dt, J = 7.7, 1.4 Hz, 1H), 7.19 (t, J = 4.9 Hz, 1H), 7.13 (s, 1H), 6.47 (d, J = 16.1 Hz, 1H), 4.10 (t, J = 6.3 Hz, 2H), 1.71−1.66 (m, 2H), 1.46−1.43 (m, 2H), 0.96 (t, J = 7.7 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 167.1, 158.3, 157.5, 137.8, 136.2, 135.4, 128.6, 124.9, 122.6, 121.1, 117.8, 117.4, 114.2, 108.8, 64.3, 30.7, 19.1, 13.7; IR (KBr) υ 2956, 2926, 2870, 1703, 1624, 1561, 1447, 1419, 1340, 1302, 1261, 1223, 1159, 964, 806, 739 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{19}H_{19}N_3O_2$ $[M]^+$, 321.1477; found, 321.1477.

General Procedure and Characterization for Deprotection of 3a and 4k. To a stirred solution of *N*-butyl-1-(pyrimidin-2-yl)-1*H*-indole-2-carboxamide (**3a**) (58.8 mg, 0.2 mmol, 100 mol %) in DMSO (1.5 mL) was added NaOEt (40.8 mg, 0.6 mmol, 300 mol %) in EtOH (0.3 mL) at room temperature. The reaction mixture was allowed to stir for 20 h at 100 °C under a N_2 atmosphere. The reaction mixture was diluted with EtOAc (10 mL) and washed with H_2O (2 × 25 mL). The aqueous layer was extracted with EtOAc (2 × 25 mL). The combined organic layer was dried over Mg_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexanes/EtOAc = 10:1) to afford 18.1 mg of **7a** in 42% yield.

***N*-Butyl-1*H*-indole-2-carboxamide (7a).** 18.2 mg (42%); light yellow solid; mp = 164.8−167.8 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.63 (d, J = 7.7 Hz, 1H), 7.44 (d, J = 7.7 Hz, 1H), 7.28 (t, J = 7.7 Hz, 1H), 7.13 (t, J = 7.7 Hz, 1H), 6.81 (s, 1H), 6.18 (s, 1H), 3.50 (q, J = 7.0 Hz, 2H), 1.66−1.61 (m, 2H), 1.46−1.42 (m, 2H), 0.97 (t, J = 7.0 Hz, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 161.6, 136.2, 130.8, 127.6, 124.3, 121.8, 120.6, 111.9, 101.4, 39.4, 31.8, 20.1, 13.7; IR (KBr) υ 3333, 3266, 2922, 2852, 1610, 1551, 1416, 1338, 1252, 1216, 1154, 842, 811, 776, 714 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{13}H_{16}N_2O$ $[M]^+$, 216.1263; found, 216.1267.

***N*-(*p*-Tolyl)-1*H*-indole-2-carboxamide (7b).** 26.1 mg (52%); light yellow solid; mp = 235.6−237.4 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 9.27 (s, 1H), 7.81 (s, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.4 Hz, 1H), 7.32 (t, J = 7.7 Hz, 1H), 7.20−7.16 (m, 3H), 6.98 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 159.3, 136.4, 134.8, 134.3, 130.8, 129.7, 127.6, 124.9, 122.0, 120.9, 120.1, 111.9, 102.3, 20.9; IR (KBr) υ 3406, 3332, 3050, 2916, 2851, 1729, 1644, 1593, 1512, 1403, 1301, 1233, 934, 883, 809, 740 cm^{-1}; HRMS (quadrupole, EI) calcd for $C_{16}H_{14}N_2O$ $[M]^+$, 250.1106; found, 250.1108.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectroscopic data for all compounds and deuterium exchange experiments. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00763.

■ AUTHOR INFORMATION

Corresponding Author

*Tel.: +82-31-290-7788; Fax: +82-31-292-8800; E-mail: insukim@skku.edu.

Author Contributions

§T.J. and S.H. contributed equally to this work.

Notes

The authors declare no competing financial interest.

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