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*J. Org. Chem.*, **Just Accepted Manuscript** • Publication Date (Web): 24 Jun 2015

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

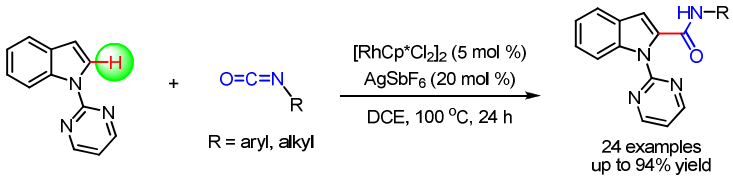
**Taejoo Jeong,[a,†] Sangil Han,[a,†] Neeraj Kumar Mishra,[a] Satyasheel Sharma,[a] Seok-Yong Lee,[a] Joa Sub Oh,[b] Jong Hwan Kwak,[a] Young Hoon Jung,[a] and In Su Kim*[,a]**

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

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

* Corresponding author. Tel.: +82-31-290-7788; fax: +82-31-292-8800; e-mail: insukim@skku.edu

[†] These authors equally contributed.




## Abstract

The rhodium(III)-catalyzed direct amidation of indoles and pyrroles with aryl and alkyl isocyanates is described. These transformations provide the 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, selective inhibition of β-amyloid (Figure 1).[3] The synthetic methods for the formation of C2-amidated indoles and pyrroles relies on the traditional approaches such as amidation reaction 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 as well as the use of hazardous CO gas. In complement to 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.

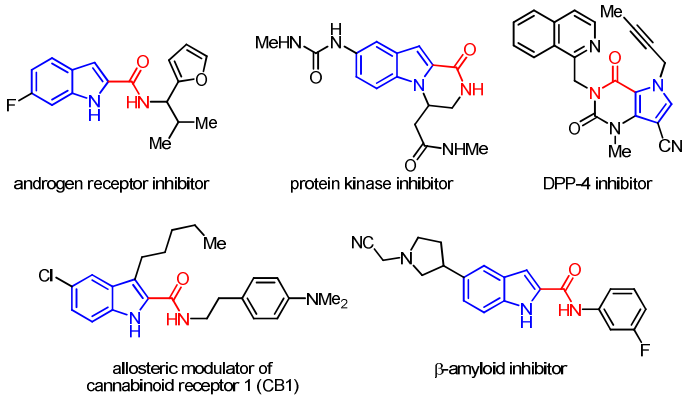



**Figure 1**. Selected examples for bioactive C2-amidated indoles and pyrroles.

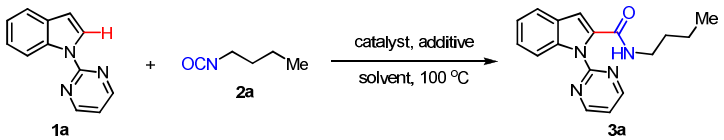
In last decades, a great deal of effort has been devoted to the transition-metal-catalyzed direct functionalization of inactive C–H bonds with various coupling partners.[8] In this context, there has been recent progress in the area of the transition-metal-catalyzed direct additions of C($sp^2$)–H bonds 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 to 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 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 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 are found to be ineffective for this transformation (Table 1, entries 2 and 3). Exclusion of either Rh catalyst or $AgSbF_6$ additive resulted in no formation of the desired product **3a** (Table 1, entries 4 and 5). After screening of a range of solvents, DCE was found to exhibit the highest reactivity (Table 1, entries 6–9). Screening of silver salts revealed that $AgSbF_6$ additive was found to be 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 conversion reaction (Table 1, entries 12 and 13). To our delight, the optimal result was obtained by use of 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 a 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).

**Table 1.** Selected optimization of reaction conditions.[a]



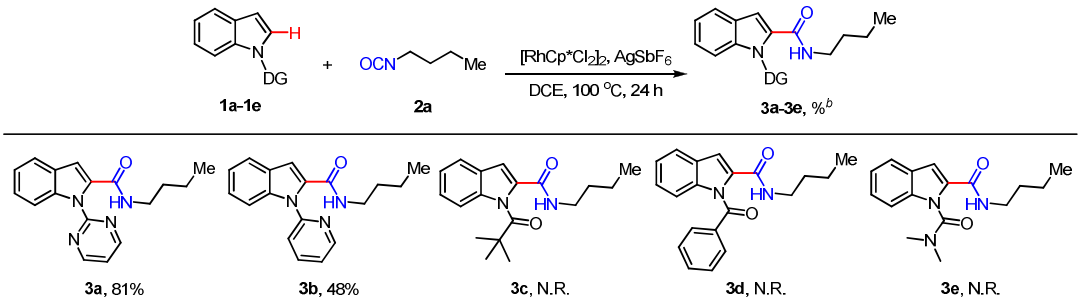

| Entry | Catalyst (mol %) | Additive (mol %) | Solvent | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $[RhCp^*Cl_2]_2$ (2.5) | $AgSbF_6$ (10) | DCE | 60 |
| 2 | $[Ru(p\text{-}Cy)Cl_2]_2$ (2.5) | $AgSbF_6$ (10) | DCE | N.R. |
| 3 | $CoCp^*(CO)I_2$ (2.5) | $AgSbF_6$ (10) | DCE | 12 |
| 4 | $[RhCp^*Cl_2]_2$ (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 $N_2$ 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.

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.

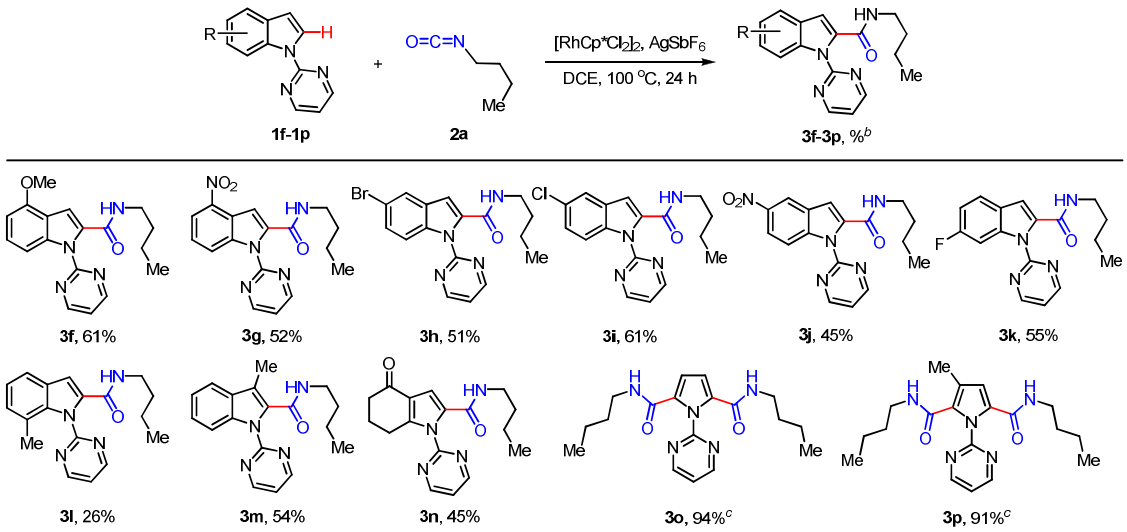
**Table 2.** Screening of directing groups.[a]




[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 $N_2$ atmosphere at 100 °C for 24 h in reaction tubes. [b] Isolated yield by flash column chromatography.

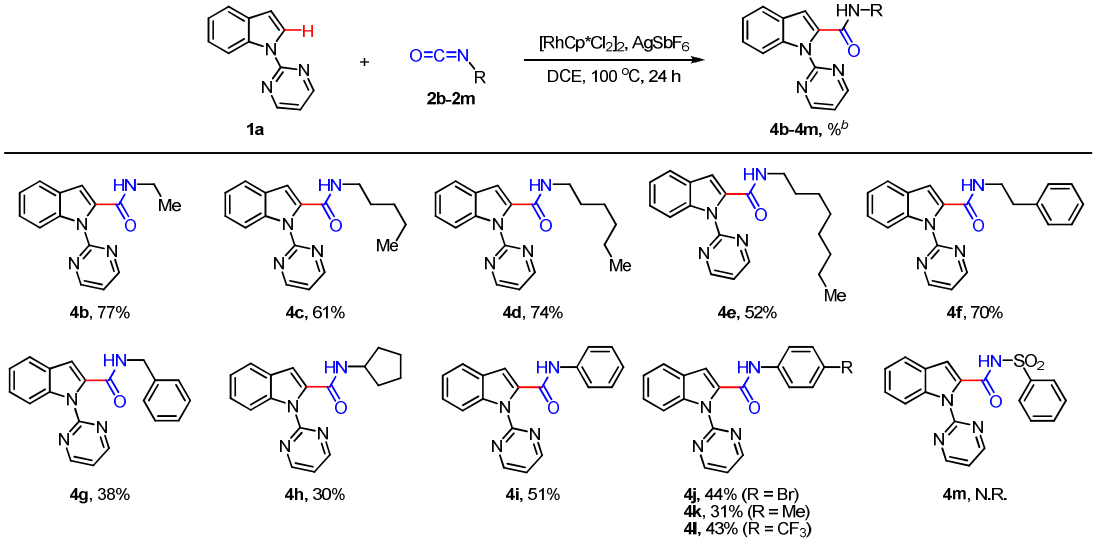
To evaluate the scope and limitation of this process, various indoles **1f–1n** were screened under the optimal reaction conditions, as shown in Table 3. Indoles **1f–1k** bearing electron-rich and electron-deficient groups (OMe, $NO_2$, Br, Cl and F) at the C4-, C5- and C6-positions were found to undergo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

**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 $N_2$ 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]

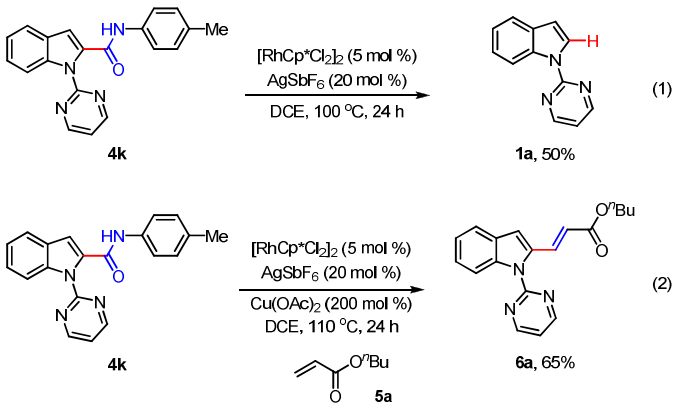



[a] *Reaction conditions*: **1a** (0.2 mmol), **2a–2m** (0.6 mmol), $[RhCp^*Cl_2]_2$ (5 mol %), $AgSbF_6$ (20 mol %), DCE (1 mL) under $N_2$ atmosphere at 100 °C for 24 h in reaction tubes. [b] Isolated yield by flash column chromatography.

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 case of alkyl isocyanates **2b–2f**, the desired indolic C2-amidation adducts were obtained in moderate to good yields. Exceptionally, benzyl isocyanate (**2g**) and cyclopentyl isocyanate (**2h**) exhibited the slightly decreased reactivity. In addition, aryl isocyanates **2i–2l** with electron-rich and electron-deficient groups (Me, Br and $CF_3$) were tolerated

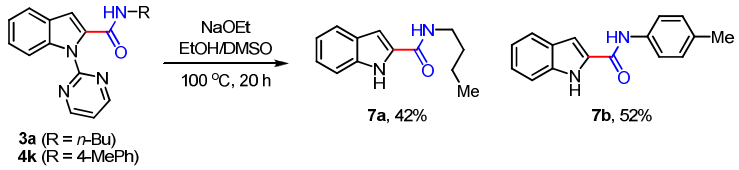
under current reaction conditions to afford the corresponding products **4i**–**4l**. However, highly electron-deficient phenylsulfonyl isocyanate (**2m**) did not deliver the corresponding coupling product.

Based on the above results, we considered that the moderate to low yields obtained from aryl isocyanates **2i**–**2l** might be possibly attributed to the reversibility of amidation. Thus we performed the reversibility experiment using **4k** under the standard reaction conditions, which provided **1a** in 50% yield (Scheme 1, eq. 1). Previously, the similar reversible process 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 the treatment of *n*-butyl acrylate (**5a**) to afford C2-alkenylated indole **6a** in 65% yield (Scheme 1, eq. 2).[22]




**Scheme 1**. Reversibility experiments.

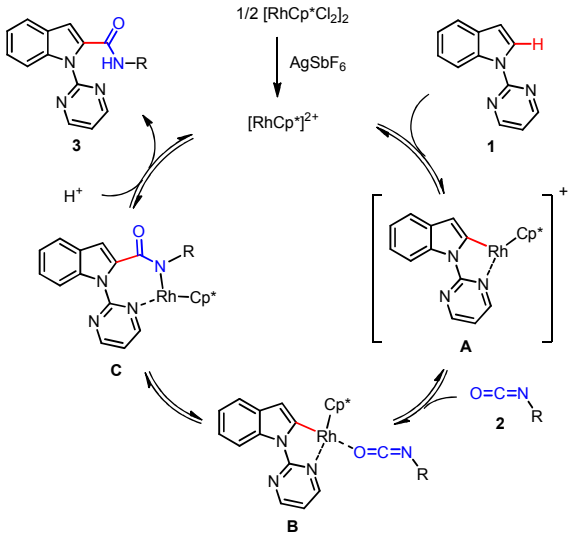
Meanwhile, the deprotection of a pyrimidyl directing group on C2-amidated indoles **3a** and **4k** was carried out, as shown in Scheme 2. First, treatment of **3a** under the standard reaction condition (NaOEt, DMSO, 100 °C)[23] afforded the desired product **7a** in low yield (16%). After further optimization,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




**Scheme 2**. Removal of directing group on indoles.

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 $[RhCp^*Cl_2]_2$ and $AgSbF_6$,

can coordinate to 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 the release of one equivalent of proton ($H^+$). Subsequent coordination of isocyanate furnishes intermediate **B**, which on migratory insertion into the Rh–C bond deliver the complex **C**. Finally, protonation of **C** affords our desired product and the regeneration of active Rh(III) catalyst.




**Scheme 3**. Proposed reaction mechanism.

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.

## Experimental Section

**General procedure for the synthesis of heteroarenes substrates (1a, 1b and 1f–1p):** Indoles and pyrroles containing a 2-pyrimidinyl and 2-pyridinyl directing groups were prepared as described in previous literatures.[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 $N_2$ atmosphere. The reaction mixture was allowed to stir at 100 $^oC$ 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, $J_{C\text{-}F}$ = 239.4 Hz), 158.0, 157.1, 137.9, 135.3 (d, $J_{C\text{-}F}$ = 4.2 Hz), 124.2, 122.4 (d, $J_{C\text{-}F}$ = 10.1 Hz), 117.8, 111.2 (d, $J_{C\text{-}F}$ = 24.3 Hz), 109.0, 101.1 (d, $J_{C\text{-}F}$ = 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, 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; $^1$H 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; $^1$H 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; $^1$H 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; $^1$H 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; $^1$H 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; $^1$H 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; $^1$H 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; $^1$H 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, $J_{C\text{-}F}$ = 2.6 Hz), 126.3 (q, $J_{C\text{-}F}$ = 32.2 Hz), 126.2, 124.0 (q, $J_{C\text{-}F}$ = 269.3 Hz), 122.9, 122.0, 119.5, 117.9, 114.0, 110.8; IR (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 $N_2$ 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; $^1$H 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 nitrogen 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; $^1$H 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; $^1$H 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.

## Acknowledgment

This research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea Government (MSIP) (Nos. 2013R1A2A2A01005249 and 2013R1A1A2058800).

**Supporting Information Available:** Spectroscopic data for all compounds and deuterium exchange experiments. This material is available free of charge via the internet at http://pubs.acs.org.

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