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Switchable Synthesis of 3-Cyanoindoles and 3-Amidylindoles *via* a Palladium-Catalyzed Reaction of *N,N*-Dimethyl-2-alkynylaniline with Isocyanide

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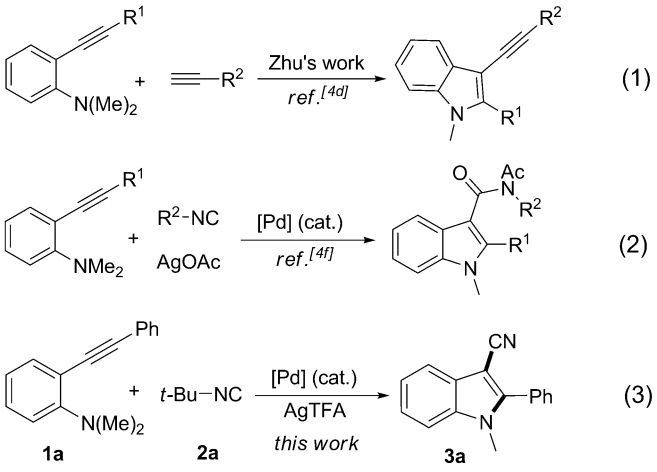
Abstract: A palladium-catalyzed reaction of *N,N*-dimethyl-2-alkynylanilines with isocyanides is reported, leading to the formation of 3-cyanoindoles and 3-amidylindoles. The isocyanide insertion is the key step during the process, and the presence of water is essential for the formation of 3-amidylindoles.

Keywords: 3-amidylindoles; 3-cyanoindoles; *N,N*-dimethyl-2-alkynylanilines; isocyanides; palladium catalysts

Introduction

As a privileged structural motif, indole has been the subject of continuous interest in organic synthesis due to its ubiquity in many bioactive natural products, pharmaceuticals, and agrochemicals.[1] To date, tremendous efforts have been devoted by organic chemists to the development of new synthetic methodologies for the synthesis of diverse indole architectures.[2] Among these achievements, alkynes-based heteroannulations using palladium as catalyst have emerged as excellent representatives.[3] Recently, *N,N*-dimethyl-2-alkynylanilines have been disclosed as a good reaction partner for the formation of indoles by Larock, Zhu, Bertrand, and Liang.[4] For example, Zhu and coworkers found that *N,N*-dimethyl-2-alkynylanilines reacted with alkynes in the presence of palladium catalysis affording to 3-alkynylindoles in moderate to excellent yields [Scheme 1, Eq. (1)].[4d] In the process, a palladium-enabled intramolecular cyclization of the tertiary amine to produce an σ-indolylpalladium(II) was the key step. Recently, we also found that *N,N*-dimethyl-2-alkynylanilines could be involved in a palladium-catalyzed, three-component reaction of isocyanides with silver acetate [Scheme 1, Eq. (2)].[4f] In the reaction process, silver acetate acted as a reagent as well as the oxidant. Surprisingly, during the subsequent library construction, a distinct compound was observed when the oxidant was switched to silver trifluoroacetate. The new compound was identified to be 3-cyano-2-phenyindole after structural determination [Scheme 1, Eq. (3)]. We reasoned that the trifluoroacetate ion might be unfavorable for the reductive elimination compared with the acetate ion, due to its weak coordination to the palladium center and its weak nucleophilicity, thus predominantly leading to the 3-cyanative product with the removal of *tert*-butyl cation.[5] It is well-known that the 3-cyanoin-



Scheme 1. Synthesis of 3-cyanoindole *via* a palladium-catalyzed reaction of *N,N*-dimethyl-2-alkynylanilines with isocyanides.

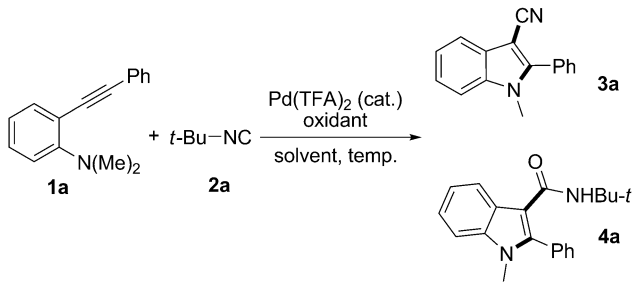
doles are important synthetic targets[6] due to their promising bioactivities and potential for further structural elaboration.[7] Significant contributions have been achieved for the synthesis of 3-cyanoindoles.[6] For instance, Jiao and co-workers disclosed the direct cyanation of indoles using *N,N*-dimethylformamide (DMF) as both reagent and solvent.[6e] Chang described a copper-mediated selective cyanation of indoles with ammonium iodide and DMF.[6g] Based on the above results we obtained, we envisioned that a palladium-catalyzed tandem process starting from *N,N*-dimethyl-2-alkynylanilines and isocyanides would provide a facile access to 3-cyanoindoles.

Recently, the transition metal-catalyzed imidoylative reactions of isocyanides have attracted much attention.[8–10] Among the reports, a palladium-catalyzed cyanation of *N*-heterocycles using isocyanide as the cyano source was highlighted by Zhu and Xu.[5] The transformation proceeded with high efficiency and good regioselectivity in the presence of a stoichiometric amount of copper trifluroacetate as the oxidant. However, no isocyanides other than tertiary amine-derived isocyanides (such as *tert*-butyl isocyanide) could be compatible in these cyanative reactions. Since this method is convenient and safe compared with conventional approaches, it seemed that the generation of 3-cyanoindoles by using isocyanide as the cyano source was feasible. Prompted by the achievement of the *N,N*-dimethyl-2-alkynylaniline chemistry as mentioned above and the attractiveness of isocyanide insertion, we therefore started to explore the possibility of this transformation.

Results and Discussion

Initially, a model reaction of *N,N*-dimethyl-2-aniline **1a** with *tert*-butyl isocyanide **2a** was selected. Some results of the investigation are presented in Table 1. At the outset, the reaction was performed under air in the presence of $Pd(TFA)_2$ (5 mol%) at 70 °C in acetonitrile. Gratifyingly, the expected product **3a** was detected and isolated in 11% yield (Table 1, entry1). Encouraged by this result, the parameters including oxidant, solvent, and temperature were then evaluated. It seemed that silver trifluroacetate was the best choice among the selected oxidants, leading to the desired product **3a** in 52% yield (Table 1, entry 4). By altering the solvent to 1,2-dichloroethane, the yield of the product **3a** was improved dramatically (90%, Table 1, entry 5). The reaction gave a lower yield when the solvent was switched to 1,4-dioxane, toluene, or dimethyl sulfoxide (Table 1, entries 6–8). Interestingly, the reaction afforded the 3-amidylindole **4a** in 44% yield when tetrahydrofuran was employed as the solvent. Under these conditions, the product **3a** was not observed. We assumed that this is probably due to the presence of a trace amount of H_2O in THF (Table 1, entry 9). To verify this hypothesis, 5.0 equivalents of water were added in the reaction mixture. As expected, the product **4a** was furnished in 72% yield (Table 1, entry 10). Reducing the temperature to 50 °C provided the compound **3a** in 62% yield, however, the reaction time was prolonged to 48 h (Table 1, entry 11). An inferior result was obtained when palladium trifluroacetate was replaced by palladium acetate (Table 1, entry 12).

Table 1. Initial studies for the palladium-catalyzed reaction of *N,N*-dimethyl-2-alkynylaniline **1a** with *tert*-butyl isocyanide **2a**.[a]

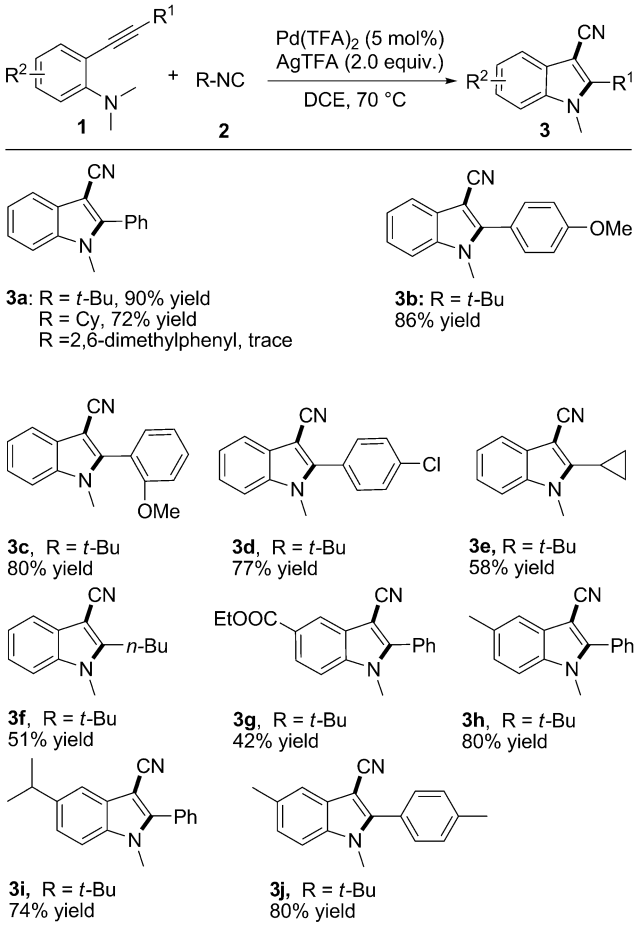


Entry	Oxidant	Solvent	Temp. [°C]	Yield [%][b] 3a	4a
1	air	MeCN	70	11	–
2	O_2	MeCN	70	18	–
3	$Cu(TFA)_2$	MeCN	70	complex	–
4	AgTFA	MeCN	70	52	–
5	AgTFA	DCE	70	90	–
6	AgTFA	dioxane	70	82	–
7	AgTFA	DMSO	70	complex	–
8	AgTFA	toluene	70	81	–
9	AgTFA	THF	70	–	44
10[c]	AgTFA	THF	70	–	72
11[d]	AgTFA	DCE	50	62	–
12[e]	AgTFA	DCE	70	73	–

[a] *Reaction conditions:* *N,N*-dimethyl-2-alkynylaniline **1a** (1.0 equiv.), isocyanide **2a** (2.5 equiv.), palladium trifluroacetate (5 mol%), oxidant (2.0 equiv.), N_2, 70 °C overnight.
[b] Isolated yield based on *N,N*-dimethyl-2-alkynylaniline **1a**.
[c] 5 equivalents of H_2O were added.
[d] After 48 h.
[e] In the presence of 5 mol% of $Pd(OAc)_2$.

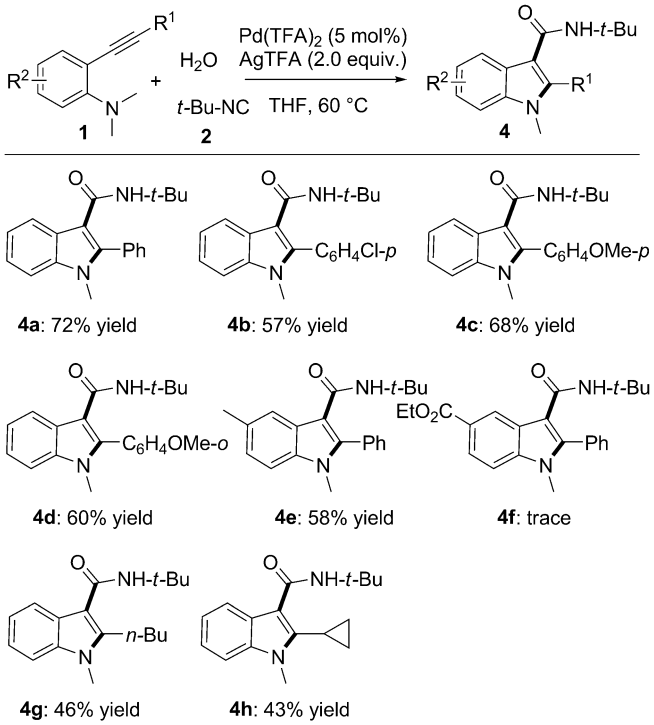
With the above conditions in hand, we then examined the scope and generality of this palladium-catalyzed reaction of 2-alkynylaniline **1** with isocyanide **2**. The reactions occurred in DCE firstly, and the results are illustrated in Table 2. A series of substituted 3-cyanoindoles was constructed as expected. Different 2-alkynylanilines **1** with an aryl or alkyl group at the R^1 position were all good substrates with the formation of the corresponding products **3b**–**3f** (Table 2). Furthermore, variations of the R^2 substituents attached on the aromatic ring of 2-alkynylanilines **1** were also

Table 2. Synthesis of subtituted 3-cyanoindoles *via* a palladium-catalyzed reaction of *N*,*N*-dimethyl-2-alkynylanilines with isocyanides.[a]



[a] Isolated yield based on *N*,*N*-dimethyl-2-alkynylaniline **1**.

Table 3. Synthesis of subtituted 3-amidylindoles *via* a palladium-catalyzed reaction of *N*,*N*-dimethyl-2-alkynylanilines, isocyanides, and H_2O.[a]



[a] Isolated yield based on *N*,*N*-dimethyl-2-alkynylaniline **1**.

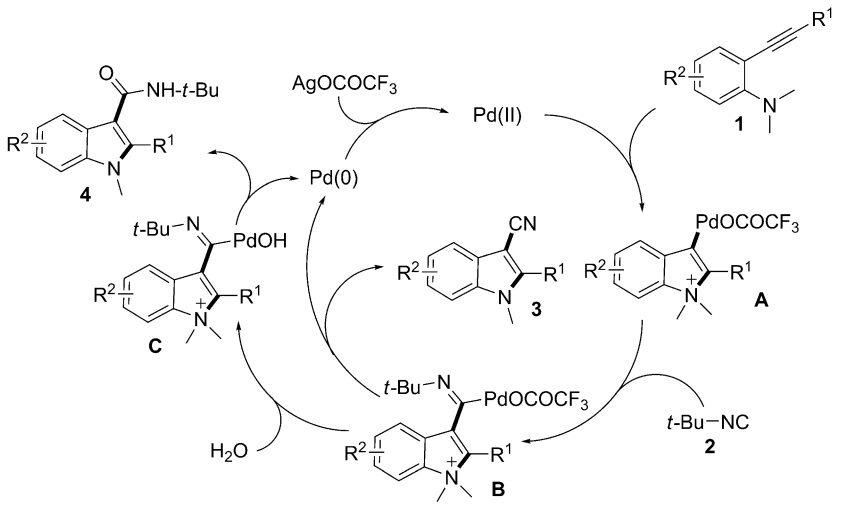
explored. It is noteworthy that the ester group could be compatible as well under the standard conditions. Additionally, not only *tert*-butyl isocyanide **2a** but also cyclohexyl isocyanide **2b** could be tolerated in the reaction, leading to 3-cyanated indole **3a** in good yields, which to some extent overcame the drawback that *tert*-butyl isocyanide was the only appropriate type of isocyanide in the procedures developed by Zhu and Xu.[5]

To expand the scope of this tandem reaction, we subsequently explored the 3-amidylindole formation under the conditions highlighted in Table 1, entry 10. The results are presented in Table 3. For most of the cases, the corresponding 3-amidylindoles were afforded in reasonable yields. For instance, 2-[2-(4-chlorophenyl)ethynyl]-*N*,*N*-dimethylaniline **1b** reacted with *tert*-butyl isocyanide and H_2O, providing the product **4b** in 57% yield, while the reactions of 4-methoxy-substituted and 2-methoxy-subtituted 2-alkynylanilines gave rise to the products **4c** and **4d** in 68% and 60% yields, respectively. 2-(Hex-1-ynyl)-*N*,*N*-dimethylaniline was a good partner as well in the transformation, resulting in the 3-amidylindole **4g** in 46% yield.

In the light of these results, a plausible mechanism was proposed which is shown in Scheme 2. The possible intermediate **A**, which was generated through $Pd(TFA)_2$-catalyzed cyclization of 2-alkynylaniline, would undergo isocyanide insertion, producing the intermediate **B**. The intermediate **B** might go through two pathways: a) cleavage of C–N bond and removal of tertiary carbon cation would occur to generate the 3-cyanoindoles **3**, with the formation of Pd(0); b) the intermediate **B** would react with water if water was presented in the reaction, producing the intermediate **C**. The subsequent reductive elimination and isomerization would provide the 3-amidated indole **4**. Meantime, Pd(0) would be re-oxidized to Pd(II) to trigger the catalytic cycle again.

Conclusions

In conclusion, we have described a switchable synthesis of 3-cyanoindoles and 3-amidylindoles *via* a palladium-catalyzed reaction of *N*,*N*-dimethyl-2-alkynylanilines and isocyanide. The isocyanide insertion is the key step during the process. The presence of water is



Scheme 2. A plausible mechanism for the palladium-catalyzed reaction of *N,N*-dimethyl-2-alkynylanilines **1** with isocyanides **2**.

essential for the formation of 3-amidylindoles. The different outcome could provide a new insight for the chemistry of isocyanide insertion. Currently, exploration of isocyanide insertion in other transformations is ongoing in our laboratory, and the results will be reported in due course.

Experimental Section

General Procedure for the Synthesis of Subtituted 3-Cyanoindoles 3 *via* a Palladium-Catalyzed Reaction of *N,N*-Dimethyl-2-alkynylaniline and Isocyanide

$Pd(TFA)_2$ (5 mol%) and AgTFA (2.0 equiv.) were added to a solution of 2-alkynylaniline **1** (0.2 mmol) in DCE (2.0 mL). Then isocyanide (2.5 equiv.) was added. The reaction mixture was stirred at 70 °C. After completion of the reaction as indicated by TLC, the solvent was evaporated and the residue was purified on silica gel to provide the desired product **3**.

1-Methyl-2-phenyl-1*H*-indole-3-carbonitrile (3a):[5a] ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.75$ (s, 3H), 7.30–7.43 (m, 3H), 7.53–7.56 (m, 5H), 7.77 (d, $J = 7.6$ Hz, 1H).

2-(4-Methoxyphenyl)-1-methyl-1*H*-indole-3-carbonitrile (3b): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.75$ (s, 3H), 3.89 (s, 3H), 7.08 (d, $J = 8.4$ Hz, 2H), 7.31–7.40 (m, 3H), 7.51 (d, $J = 8.8$ Hz, 2H), 7.76 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 31.7$, 55.5, 110.5, 114.5, 116.9, 119.4, 120.9, 122.3, 123.7, 127.6, 131.2, 136.8, 148.2, 160.8; HR-MS (ESI): $m/z = 263.1169$, calcd. for $C_{17}H_{15}N_2O^+$ ($M+H^+$): 263.1179.

2-(2-Methoxyphenyl)-1-methyl-1*H*-indole-3-carbonitrile (3c): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.63$ (s, 3H), 3.84 (s, 3H), 7.07 (d, $J = 8.0$ Hz, 1H), 7.12–7.16 (m, 1H), 7.30–7.47 (m, 4H), 7.51–7.55 (m, 1H), 7.79 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 31.5$, 55.8, 110.4, 110.9, 116.7, 117.7, 119.5, 121.1, 122.0, 123.5, 127.6, 131.9, 132.3, 136.6, 145.9, 157.4; HR-MS (ESI): $m/z = 263.1187$, calcd. for $C_{17}H_{15}N_2O^+$ ($M+H^+$): 263.1179.

2-(4-Chlorophenyl)-1-methyl-1*H*-indole-3-carbonitrile (3d): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.76$ (s, 3H), 7.32–7.46 (m, 3H), 7.51–7.57 (m, 4H), 7.77 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 31.7$, 110.6, 116.4, 119.6, 122.6, 124.2, 127.1, 127.4, 129.4, 131.1, 136.3, 136.9, 146.7; HR-MS (ESI): $m/z = 267.0668$, calcd. for $C_{16}H_{12}ClN_2^+$ ($M+H^+$): 267.0684.

2-Cyclopropyl-1-methyl-1*H*-indole-3-carbonitrile (3e): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.11$–1.15 (m, 2H), 1.17–1.22 (m, 2H), 1.93–1.98 (m, 1H), 3.84 (s, 3H), 7.23–7.33 (m, 3H), 7.66 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 6.34$, 7.42, 30.2, 109.7, 114.6, 116.5, 119.1, 121.9, 123.3, 127.3, 136.0, 149.2; HR-MS (ESI): $m/z = 197.1070$, calcd. for $C_{13}H_{13}N_2^+$ ($M+H^+$): 197.1073.

2-Butyl-1-methyl-1*H*-indole-3-carbonitrile (3f): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.98$ (t, $J = 7.2$ Hz, 3H), 1.43–1.49 (m, 2H), 1.66–1.74 (m, 2H), 2.93–2.97 (m, 2H), 3.73 (s, 3H), 7.24–7.35 (m, 3H), 7.67 (d, $J = 7.2$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 13.7$, 22.3, 25.9, 30.2, 31.2, 109.8, 116.7, 119.1, 121.9, 122.9, 127.1, 136.4, 149.9; HR-MS (ESI): $m/z = 213.1380$, calcd. for $C_{14}H_{17}N_2^+$ ($M+H^+$): 213.1386.

Ethyl 3-cyano-1-methyl-2-phenyl-1*H*-indole-5-carboxylate (3g): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.44$ (t, $J = 7.2$ Hz, 3H), 3.79 (s, 3H), 4.40–4.45 (m, 2H), 7.45 (d, $J = 8.8$ Hz, 1H), 7.56–7.59 (m, 5H), 8.08 (d, $J = 8.8$ Hz, 2H), 8.51 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.2$, 32.0, 61.1, 110.3, 115.9, 121.9, 124.8, 125.3, 127.0, 128.2, 129.1, 129.8, 130.4, 139.2, 149.7, 166.8; HR-MS (ESI): $m/z = 305.1268$, calcd. for $C_{19}H_{17}N_2O_2^+$ ($M+H^+$): 305.1285.

1,5-Dimethyl-2-phenyl-1*H*-indole-3-carbonitrile (3h): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.62$ (s, 3H), 3.74 (s, 3H), 7.20 (d, $J = 8.0$ Hz, 1H), 7.32 (d, $J = 8.4$ Hz, 1H), 7.51–7.57 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.5$, 31.8, 110.2, 116.9, 119.2, 125.5, 127.8, 129.0, 129.8, 132.1, 136.3, 147.8; HR-MS (ESI): $m/z = 247.1228$, calcd. for $C_{17}H_{15}N_2^+$ ($M+H^+$): 247.1230.

5-Isopropyl-1-methyl-2-phenyl-1*H*-indole-3-carbonitrile (3i): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.35$ (d, $J = 6.8$ Hz,

6H), 3.04–3.12 (m, 1H), 3.75 (s, 3H), 7.28 (d, $J=7.2$ Hz, 1H), 7.36 (d, $J=8.4$ Hz, 1H), 7.53–7.57 (m, 5H), 7.64 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=24.5$, 31.7, 34.2, 110.4, 116.5, 116.9, 123.3, 127.8, 128.9, 129.0, 129.8, 135.6, 143.6, 148.0; HR-MS (ESI): $m/z=275.1544$, calcd. for $C_{19}H_{19}N_2^+$ ($M+H^+$): 275.1543.

1,5-Dimethyl-2-*p*-tolyl-1*H*-indole-3-carbonitrile (3j): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=2.46$ (s, 3H), 2.51 (s, 3H), 3.73 (s, 3H), 7.18 (d, $J=8.4$ Hz, 1H), 7.30 (d, $J=8.4$ Hz, 1H), 7.36 (d, $J=8.0$ Hz, 2H), 7.46 (d, $J=8.0$ Hz, 2H), 7.56 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=21.4$, 31.7, 110.1, 116.9, 119.1, 125.3, 125.9, 127.9, 129.7, 132.0, 135.2, 139.9, 148.2; HR-MS (ESI): $m/z=$ calcd. for $C_{18}H_{17}N_2^+$ ($M+H^+$): 261.1386.

General Procedure for the Synthesis of Subtituted 3-Amidylindole 4 *via* a Palladium-Catalyzed Reaction of *N*,*N*-Dimethyl-2-alkynylaniline, Isocyanide, and H_2O

$Pd(TFA)_2$ (5 mol%) and AgTFA (2.0 equiv.) were added to a solution of 2-alkynylaniline **1** (0.2 mmol) in THF (2.0 mL). Then H_2O (5.0 equiv.) and isocyanide (2.5 equiv.) was added. The reaction was stirred at 60 °C. After completion of the reaction as indicated by TLC (8–12 h), the solvent was evaporated and the residue was purified on silica gel to provide the desired product **4**.

***N*-*tert*-Butyl-1-methyl-2-phenyl-1*H*-indole-3-carboxamide (4a):**[8g] ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.14$ (s, 9H), 3.54 (s, 3H), 5.00 (s, 1H), 7.25–7.35 (m, 3H), 7.46–7.48 (m, 2H), 7.57–7.58 (m, 3H), 8.39 (d, $J=7.6$ Hz, 1H).

***N*-*tert*-Butyl-2-(4-chlorophenyl)-1-methyl-1*H*-indole-3-carboxamide (4b):** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.22$ (s, 9H), 3.53 (s, 3H), 5.10 (s, 1H), 7.25–7.35 (m, 3H), 7.42 (d, $J=8.4$ Hz, 2H), 7.55 (d, $J=8.4$ Hz, 2H), 8.26 (d, $J=7.6$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=28.8$, 30.7, 50.9, 109.5, 110.9, 121.6, 122.9, 126.6, 129.3, 129.7, 132.1, 135.9, 136.8, 139.2, 164.4; HR-MS (ESI): $m/z=341.1401$, calcd. for $C_{20}H_{22}ClN_2O^+$ ($M+H^+$): 341.1415.

***N*-*tert*-Butyl-2-(4-methoxyphenyl)-1-methyl-1*H*-indole-3-carboxamide (4c):** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.18$ (s, 9H), 3.51 (s, 3H), 3.90 (s, 3H), 5.17 (s, 1H), 7.09 (d, $J=8.8$ Hz, 2H), 7.24–7.33 (m, 3H), 7.38 (d, $J=8.8$ Hz, 2H), 8.39 (d, $J=6.4$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=28.3$, 30.6, 50.6, 55.5, 109.3, 110.2, 114.6, 121.4, 122.0, 122.6, 123.0, 127.0, 132.1, 136.6, 140.3, 160.7, 164.9; HR-MS (ESI): $m/z=337.1873$, calcd. for $C_{21}H_{25}N_2O_2^+$ ($M+H^+$): 337.1911.

***N*-*tert*-Butyl-2-(2-methoxyphenyl)-1-methyl-1*H*-indole-3-carboxamide (4d):** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.15$ (s, 9H), 3.48 (s, 3H), 3.80 (s, 3H), 5.28 (s, 1H), 7.08–7.18 (m, 2H), 7.22–7.53 (m, 4H), 7.55–7.57 (m, 1H), 8.38 (d, $J=8.4$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=28.8$, 30.4, 50.4, 55.6, 109.2, 110.6, 111.4, 119.9, 121.1, 121.2, 122.0, 122.4, 127.1, 131.7, 132.8, 136.7, 137.3, 157.9, 164.9; HR-MS (ESI): $m/z=337.1899$, calcd. for $C_{21}H_{25}N_2O_2^+$ ($M+H^+$): 337.1911.

***N*-*tert*-Butyl-1,5-dimethyl-2-phenyl-1*H*-indole-3-carboxamide (4e):** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.13$ (s, 9H), 2.49 (s, 3H), 3.50 (s, 3H), 5.03 (s, 1H), 7.11–7.26 (m, 2H), 7.46–7.47 (m, 2H), 7.55–7.57 (m, 3H), 8.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=21.5$, 28.7, 30.7, 50.6, 108.9, 121.7, 124.3, 127.3, 129.2, 129.7, 130.8, 131.0, 131.5, 135.1, 140.3, 164.9; HR-MS (ESI): $m/z=321.1907$, calcd. for $C_{21}H_{25}N_2O^+$ ($M+H^+$): 321.1961.

***N*-*tert*-Butyl-2-butyl-1-methyl-1*H*-indole-3-carboxamide (4g):** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.96$ (t, $J=7.2$ Hz, 3H), 1.43–1.49 (m, 2H), 1.52 (s, 9H), 1.60–1.68 (m, 2H), 3.14–3.18 (m, 2H), 3.70 (s, 3H), 5.82 (s, 1H), 7.18–7.23 (m, 2H), 7.32 (d, $J=8.8$ Hz, 1H), 7.69 (d, $J=8.4$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=13.9$, 22.6, 24.8, 29.3, 29.5, 31.9, 51.2, 109.5, 118.4, 120.8, 121.4, 125.2, 136.4, 145.4, 165.6; HR-MS (ESI): $m/z=287.2101$, calcd. for $C_{18}H_{27}N_2O^+$ ($M+H^+$): 287.2118.

***N*-*tert*-Butyl-2-cyclopropyl-1-methyl-1*H*-indole-3-carboxamide (4h):** ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=0.82$–0.86 (m, 2H), 1.18–1.23 (m, 2H), 1.52 (s, 9H), 1.88–1.93 (m, 1H), 3.80 (s, 3H), 5.95 (s, 1H), 7.15–7.25 (m, 3H), 8.05 (d, $J=7.6$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=6.64$, 8.17, 29.1, 30.1, 51.1, 108.8, 111.1, 120.6, 120.8, 122.2, 126.2, 136.0, 141.1, 165.0; HR-MS (ESI): $m/z=271.1808$, calcd. for $C_{17}H_{23}N_2O^+$ ($M+H^+$): 271.1805.

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