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Copper-Catalyzed Oxidative C−H Amination of Tetrahydrofuran with Indole/Carbazole Derivatives

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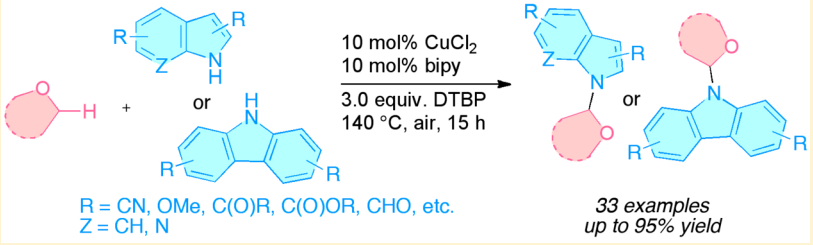
Supporting Information



ABSTRACT: A simple α-C−H amination of cyclic ether with indole/carbazole derivatives has been accomplished by employing copper(II) chloride/bipy as the catalyst system. In the presence of the di-*tert*-butyl peroxide oxidant, cyclic ethers such as tetrahydrofuran, 1,4-dioxane, and tetrahydropyran successfully undergo C−H/N−H cross dehydrogenative coupling (CDC) with various carbazole or indole derivatives in good-to-excellent yields.

N-Alkyl heterocycles are commonly found structural motifs in many materials, biologically active natural products, and pharmaceutical intermediates.[1] In particular, indoles/carbazoles having a *N*-substituted group, where the group is cyclic ether, are important core structures of various medicinally relevant compounds, such as hepatitis C virus (HCV) inhibitor;[2] steroid 17−20 lyase inhibitor;[3] cholecystokinin receptor agonists;[4] and vasopressin antagonists for treating cardiovascular disorders (Figure 1).[5] Therefore, the development of efficient methods for accessing these hemiaminal ethers is vital to the pharmaceutical industry.

The construction of α-substituted cyclic ethers (e.g., five- or six-membered ring) in organic synthesis is always challenging and often requires cumbersome procedures.[6] Traditionally, *N*-alkylated carbazoles/indoles can be synthesized by the most straightforward nucleophilic substitution of alkyl halides under basic conditions.[7] However, the drawback of commercially nonavailable cyclic etheral halides makes the reaction sometimes nonapplicable. In 2009, Kobayashi showed one example of synthesis of *N*-(α-etheral)indole from enol ether and indole under acid-catalyzed conditions.[8] A prolonged reaction time of 6 days was required to afford the product in 45% yield. In the past decade, direct C−H functionalization via a dehydrogenative pathway has emerged as an attractive method to construct C−C, C−O, and C−N bonds.[9] This versatile protocol circumvents the preinstallation of functional groups and also takes advantage of atom economy.[10] Having the background of oxidative coupling, the functionalization of α-C(sp^3)−H bonds of cyclic ether (e.g., THF, THP, 1,4-dioxane) has been made

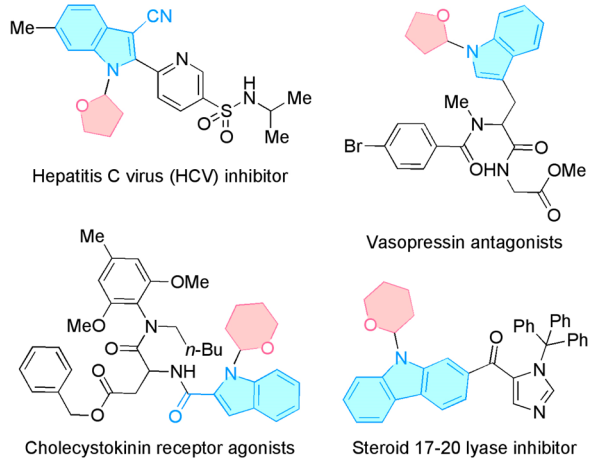


Figure 1. Examples of useful *N*-cyclic ether containing molecules.

successful.[11] Recently, Lei showed the feasibility of C−C bond couplings, i.e. the direct α-arylation, of THF and 1,4-dioxane via a nickel or copper catalyst system using arylboronic acids as the coupling partners.[12] Nevertheless, simple oxidative coupling between the C(sp^3)−H bond of cyclic ethers and N−H bond of azoles remains sporadically studied. In 2010, Li showed the Fe-catalyzed *N*-alkylation of azoles with THF.[13] Hypervalent iodine reagent/tetrabutylammonium iodide (TBAI)-mediated

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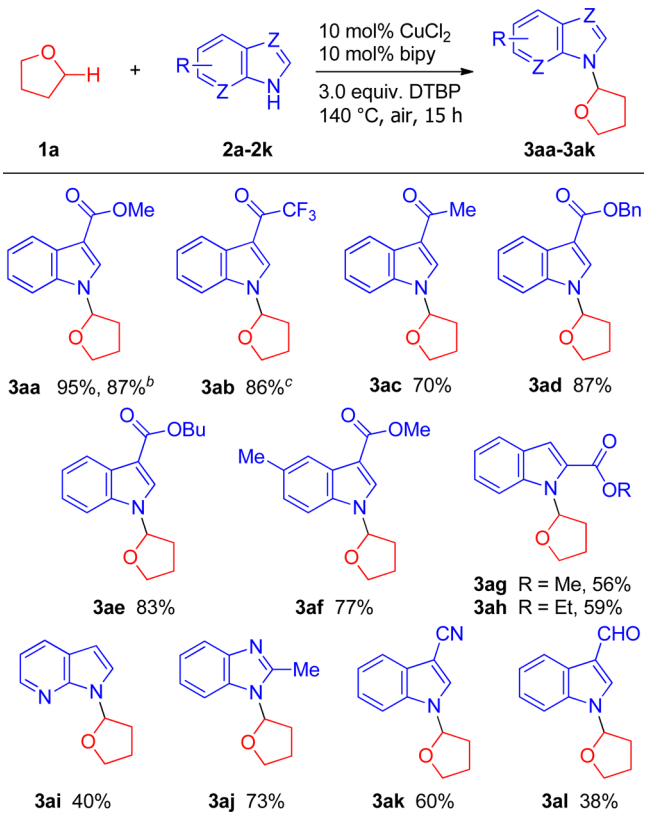
cross dehydrogenative coupling of azoles also offered convergent approach to synthesize hemiaminal ethers.[14] Apart from these developments, there have been very limited examples on C−N bond formation of indole/carbazole derivatives with cyclic ethers. To the best of our knowledge, there are only two examples, reported by Hu recently, showing the α-amination of ethers with free indole and carbazole in moderate yields under the Ph_2IPF_6/NaH system.[15] Cai and co-workers recently applied di-*tert*-butyl peroxide (DTBP) to mediate the oxidative coupling of isochroman and indole derivatives.[16] Interestingly, only the C−C bond-forming process at the indole C-3 position was observed instead of the *N*-position. We envisioned that efficient synthesis of hemiaminal ether with carbazole/indole motifs is in demand.[17] In continuation of our former work on C−H functionalization of heteroarenes[18] and the CDC reaction in *ortho*-acylaniline synthesis,[19] herein we demonstrate the first copper-catalyzed oxidative amination of *ortho*-C−H bond adjacent to the oxygen atom of ethers.

We attempted to investigate this reaction by employing tetrahydrofuran (**1a**) and indole **2a** as the model substrates (see Supporting Information, Table S1). In the presence of $CuCl_2$ (10 mol %) and DTBP (2 equiv) in THF (2 mL) at 140 °C for 15 h, the desired product **3aa** was obtained in 23% yield (Table S1, entry 1). Having the initial success of this Cu-catalyzed reaction, a series of copper salts were then screened (Table S1, entries 1−6). $CuCl_2$ gave the best product yields (Table S1, entries 1 vs 2−5). Interestingly, when CuO or $Cu(OAc)_2$ was employed, some side product of dehydrogenative coupling between the C-2 position of indole and α-C−H bond of THF was formed, in 12% or 27% yield, respectively.[20] A control experiment revealed that the reaction did not proceed without the $CuCl_2$ catalyst (Table S1, entry 6). Commonly used oxidants were tested, yet only DTBP was found to promote this direct amination (Table S1, entries 1, 7−9). Among commercially available diamine ligands surveyed, a combination of $CuCl_2$ with 2,2′-bipyridine was found to be the best catalyst of choice for this direct C(sp3)−N bond formation (Table S1, entries 10−18). Increasing the amount of DTBP enhanced the product yield (Table S1, entries 12 vs 19). The optimal stoichiometry of DTBP employed was 3 equiv with respect to **2a**. Lowering either the reaction temperature or catalyst loading led to the decrease of the coupling product yield (Table S1, entries 19 vs 20−21).

With the preliminary optimized reaction conditions in hand, we next tested the generality of this catalyst system for the direct amination of indole derivatives (Table 1). A variety of substituted indoles underwent the coupling smoothly. A slightly lower yield was obtained when this direct amination was performed under a nitrogen atmosphere (e.g., product **3aa**). To the best of our knowledge, there has been no successful example of azoles with ester and cyano groups reported to date in the oxidative amination of cyclic ether. Gratifyingly, under the newly developed $CuCl_2$/bipy catalyst system, functional groups such as ester (e.g., products **3aa**, **3ad**−**h**), keto (e.g., products **3ab**−**c**), and cyano (e.g., product **3ak**) were compatible. Unsubstituted 7-azaindole was a suitable substrate for this amination (e.g., product **3ai**). 2-Methylbenzaimidazole afforded the desired product in good yield (e.g, product **3aj**). Surprisingly, the aldehydo group remained tolerable under these reaction conditions although a poor yield was resulted (e.g., product **3al**).

Table 1. Copper-Catalyzed Direct Amination of THF with Substituted Indoles[a]



[a]Reaction conditions: THF (**1a**) (2 mL), substituted indole **2a**−**2k** (0.5 mmol), $CuCl_2$ (0.05 mmol, 10 mol %), bipy (0.05 mmol, 10 mol %), and DTBP (1.5 mmol, 3 equiv) were stirred at 140 °C under air for 15 h. Isolated yields were reported. Reaction times were not optimized for each substrate. [b]The reaction was performed under nitrogen atmosphere. [c]5 equiv of DTBP was used.

The $CuCl_2$/bipy system was also capable of facilitating the direct amination of THF with a range of carbazole derivatives (Table 2). Good-to-excellent product yields were afforded for electronically neutral substituted carbazoles (e.g., products **5aa**−**ab**, **5ae**, and **5ag**). Bromo and chloro groups remained intact during the course of the reaction (e.g., products **5af**, **5ai**, and **5aj**). These products allow further modification using traditional cross-coupling technology.[21] The reaction of 2-methylcarbazole with tetrahydrofuran showed the steric influence, albeit with a lower yield (e.g., product **5ad**). Keto and ester groups were also compatible substrates under this system to give good-to-excellent yields (e.g., products **5al** and **5am**). In order to demonstrate practicability of this synthetic route, a gram-scale experiment was attempted. To our delight, a comparable product yield was obtained (product **5aj**).

The success of direct amination of tetrahydrofuran drove us to extend this protocol to other cyclic ethers, and the results are compiled in Table 3. Under the previous conditions, 1,4-dioxane coupled well with indole or carbazole derivatives (e.g., products **3ba** and **5ba**). Other cyclic ethers such as tetrahydropyran and isochroman showed excellent reactivity to afford the corresponding products in good-to-excellent yields (e.g., products **3ca**, **3da**, **5ca**, **5da**, **5cf**, and **3bh**). Ethyl 1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-indole-2-carboxylate **3bh**, which is an important analog of cholecystokinin and gastrin antagonists,[22] was obtained in 55% yield. 3-Bromo-9-(tetrahy-

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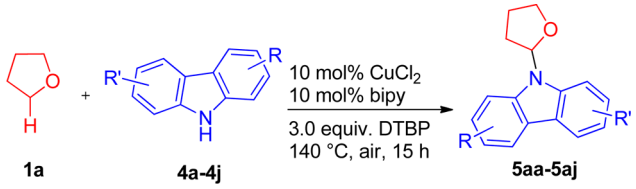
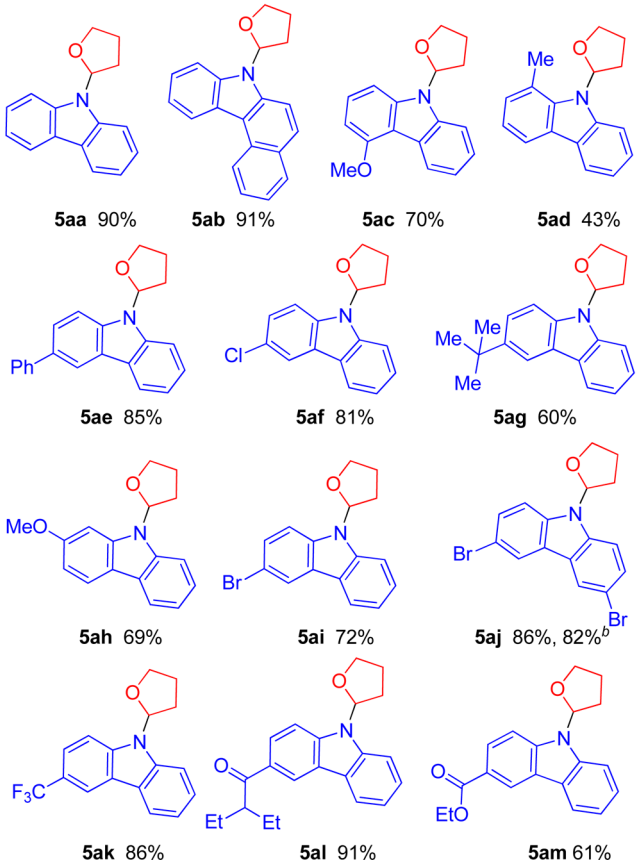
Table 2. Copper-Catalyzed Direct Amination of THF with Substituted Carbazoles[a]



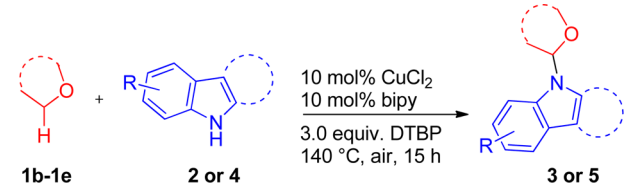


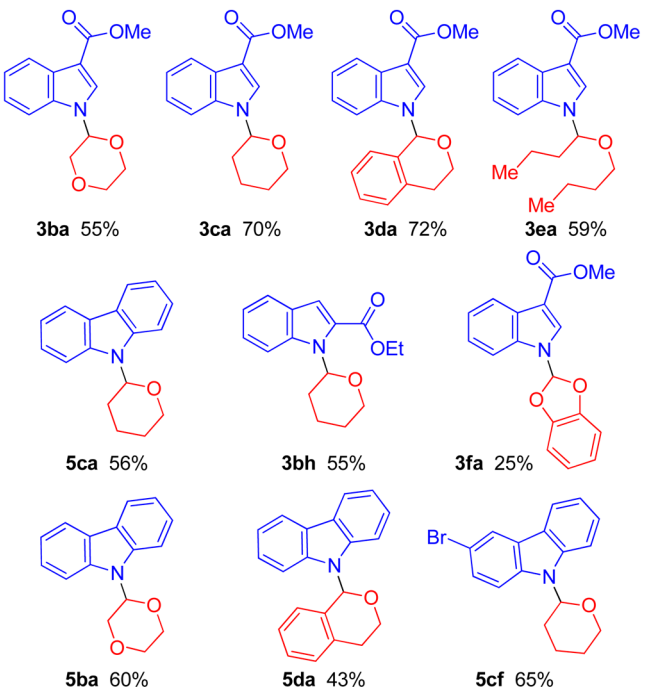
[a]Reaction conditions: THF (**1a**) (2 mL), substituted carbazole **4a**−**4j** (0.5 mmol), $CuCl_2$ (0.05 mmol, 10 mol %), bipy (0.05 mmol, 10 mol %), and DTBP (1.5 mmol, 3 equiv) were stirred at 140 °C under air for 15 h. Isolated yields were reported. Reaction times were not optimized for each substrate. [b]The reaction was scaled up to 5 mmol (gram scale).

dro-2*H*-pyran-2-yl)-9*H*-carbazole, which serves as a precursor for phosphorescent emitters and steroid 17−20 lyase inhibitors,[3,23] was synthesized smoothly (e.g., product **5cf**).

To prove the reaction proceeded through a radical pathway, a radical-trapping experiment was carried out. The addition of 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) in the control experiment essentially suppressed the reaction, and only a trace amount of the desired product **4aa** was detected (Scheme 1a). During the course of this radical-trapping experiment, the THF−TEMPO coupling product was isolated in 30% yield. These results suggested that this reaction proceeds via a free-radical intermediate. A kinetic isotopic effect (KIE) experiment was also conducted, in order to probe the dependence of C−H bond cleavage (Scheme 1b). A KIE of 4.0 was observed from a competition experiment between d_8-THF and THF. This result indicated that the α-C−H bond cleavage of THF is likely to be the kinetically dependent rate-limiting step.

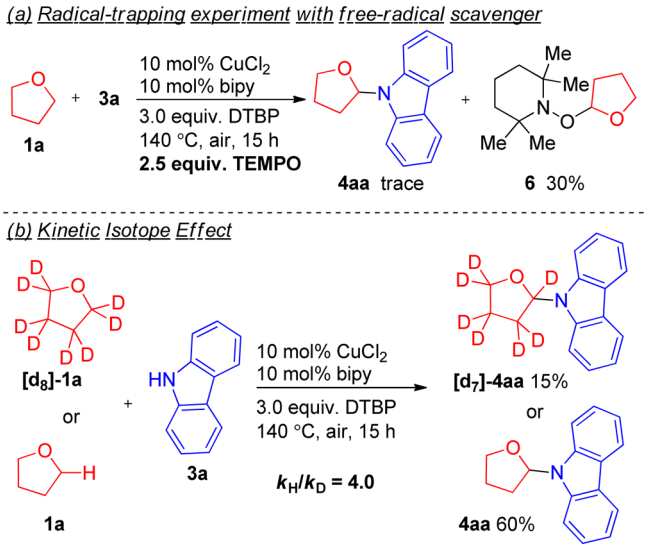
Table 3. Copper-Catalyzed Direct Amination of Alkyl Ethers with Indole or Carbazole Derivatives[a]





[a]Reaction conditions: alkyl ether **1** (2 mL), substituted indoles **2** or substituted carbazoles **4** (0.5 mmol), $CuCl_2$ (0.05 mmol, 10 mol %), bipy (0.05 mmol, 10 mol %), and DTBP (1.5 mmol, 3 equiv) were stirred at 140 °C under air for 15 h. Isolated yields were reported. Reaction times were not optimized for each substrate.

Scheme 1. Control Experiments for the α-Amination of Ether with Carbazole 3a



In conclusion, we have demonstrated the first copper-catalyzed direct α-C−H amination of cyclic ethers with indole/

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carbazole derivatives. Traditional nucleophilic substitution of alkyl halides to access these compounds is difficult due to the commercial nonavailability of α-Br-cyclic ethers and the possible elimination side reaction of α-Br-cyclic ether under basic conditions. Here, with the newly developed Cu-catalyzed C−H/N-H cross dehydrogenative coupling approach, a variety of functionalized *N*-(α-etheral)indoles/carbazoles can be easily afforded.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All the reactions were performed in a Rotaflo (England) resealable screw-cap tube (approximately 10 mL volume) in the presence of a Teflon coated magnetic stirrer bar (4 mm × 10 mm). Dioxane and tetrahydrofuran were freshly distilled over sodium under nitrogen.[24] Thin layer chromatography was performed on precoated silica gel 60 F_{254} plates. Silica gel (230−400 mesh) was used for column chromatography. ^{1}H NMR spectra were recorded on a 400 MHz spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with TMS (δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in the δ scale downfield from TMS. ^{13}C NMR spectra were recorded on a 100 MHz spectrometer, and the spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). Coupling constants (*J*) were reported in hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a mass spectrometer. High-resolution mass spectra (HRMS) were obtained on an ESI-QToF mass spectrometer, in which the ionization method is electrospray ionization (ESI) and the mass analyzer is a quadrupole time-of-flight mass analyzer.

General Procedures for Direct Amination of Tetrahydrofuran and Other Ethers. DTBP was added to a mixture of indole/carbazole (0.50 mmol), $CuCl_2$ (0.05 mmol), 2,2′-bipyridine (0.05 mmol), and ether (2 mL) in a Schlenk tube at room temperature under an air atmosphere. The tube was then placed into a preheated oil bath (140 °C) and stirred for 15 h. After completion of reaction, the reaction tube was allowed to cool to room temperature, quenched with water, and diluted with ethyl acetate. The organic layer was separated, and the aqueous layer was washed with ethyl acetate (∼10 mL × 3). The filtrate was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel (230−400 mesh) to afford the desired product.

Methyl 1-(Tetrahydrofuran-2-yl)-1*H*-indole-3-carboxylate (Table 1, Product 3aa).[8] EA/hexane = 1:5, R_f = 0.3, colorless oil, 95% (116 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20−8.18 (m, 1H), 7.97 (s, 1H), 7.48−7.46 (m, 1H), 7.33−7.28 (m, 2H), 6.25 (q, *J* = 3.12 Hz, 1H), 4.25−4.19 (m, 1H), 4.05 (dd, *J* = 15.64, 7.40 Hz, 1H), 3.94 (s, 3H), 2.48−2.38 (m, 2H), 2.18−2.12 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 135.7, 130.7, 127.1, 122.9, 122.2, 121.8, 110.5, 107.6, 86.3, 69.0, 51.0, 32.1, 24.2. HRMS (ESI) *m*/*z*: calcd for $C_{14}H_{15}NO_3Na$ [M + Na]$^+$ 268.0950, found 268.0948.

2,2,2-Trifluoro-1-(1-(tetrahydrofuran-2-yl)-1*H*-indol-3-yl)-ethanone (Table 1, Product 3ab). EA/hexane = 1:2, R_f = 0.5, colorless oil, 86% (122 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42−8.39 (m, 1H), 8.06−8.05 (m, 1H), 7.45−7.36 (m, 3H), 6.24 (q, *J* = 3.01 Hz, 1H), 4.33−4.28 (m, 1H), 4.11 (dd, *J* = 15.53, 7.85 Hz, 1H), 2.54−2.47 (m, 1H), 2.39−2.33 (m, 1H), 2.19−2.14 (m, 1H), 2.10−2.06 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2 (q, *J* = 36.5 Hz), 135.3, 133.9 (q, *J* = 5.18 Hz), 127.7, 124.6, 124.1, 122.8, 118.5 (d, *J* = 290 Hz), 110.8, 109.6, 87.2, 69.6, 32.6, 24.1. IR (neat): 1650, 1472, 1139 cm^{-1}. HRMS (ESI) *m*/*z*: calcd for $C_{14}H_{13}F_3NO_2$ [M + H]$^+$ 284.0893, found 284.0892.

1-(1-(Tetrahydrofuran-2-yl)-1*H*-indol-3-yl)ethanone (Table 1, Product 3ac). EA/hexane = 1:2, R_f = 0.3, colorless oil, 70% (80 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40−8.38 (m, 1H), 7.89 (s, 1H), 7.44−7.41 (m, 1H), 7.35−7.31 (m, 2H), 6.24 (q, *J* = 3.17 Hz, 1H), 4.31−4.26 (m, 1H), 4.10 (dd, *J* = 15.74, 7.50 Hz, 1H), 2.56 (s, 3H), 2.52−2.45 (m, 1H), 2.40−2.35 (m, 1H), 2.19−2.12 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3, 135.7, 131.0, 126.9, 123.4, 122.8, 122.7, 117.4, 110.3, 86.6, 69.2, 32.4, 27.7, 24.3. IR (neat): 1600, 1415, 1277 cm^{-1}. HRMS (ESI) *m*/*z*: calcd for $C_{14}H_{16}NO_2$ [M + H]$^+$ 230.1176, found 230.1184.

Benzyl 1-(Tetrahydrofuran-2-yl)-1*H*-indole-3-carboxylate (Table 1, Product 3ad). EA/hexane = 1:5, R_f = 0.3, colorless oil, 87% (140 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19−8.17 (m, 1H), 7.98 (s, 1H), 7.50−7.26 (m, 8H), 6.22 (q, *J* = 3.06 Hz, 1H), 5.40 (d, *J* = 2.08 Hz, 1H), 4.22−4.17 (m, 1H), 4.05 (dd, *J* = 15.78, 7.42 Hz, 1H), 2.46−2.35 (m, 2H), 2.15−2.10 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 136.8, 135.7, 130.9, 128.6, 128.1, 128.0, 127.2, 122.9, 122.3, 121.9, 110.6, 107.5, 86.4, 69.0, 65.5, 32.1, 24.3. IR (neat): 1710, 1526, 1429, 1222 cm^{-1}. HRMS (ESI) *m*/*z*: calcd for $C_{20}H_{20}NO_3$ [M + H]$^+$ 322.1438, found 322.1450.

Butyl 1-(Tetrahydrofuran-2-yl)-1*H*-indole-3-carboxylate (Table 1, Product 3ae). EA/hexane = 1:5, R_f = 0.4, colorless oil, 83% (119 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16−8.14 (m, 1H), 7.95 (s, 1H), 7.46−7.37 (m, 1H), 7.30−7.26 (m, 2H), 6.24 (q, *J* = 3.12 Hz, 1H), 4.36−4.232 (m, 2H), 4.23−4.18 (m, 1H), 4.04 (dd, *J* = 15.72, 7.39 Hz, 1H), 2.46−2.35 (m, 2H), 2.17−2.10 (m, 2H), 1.82−1.75 (m, 2H), 1.54−1.48 (m, 2H), 0.99 (t, *J* = 7.39 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 135.7, 130.6, 127.1, 122.9, 122.2, 121.9, 110.6, 108.0, 86.3, 69.0, 63.7, 32.1, 31.0, 24.3, 19.4, 13.8. IR (neat): 1710, 1543, 1228, 1100 cm^{-1}. HRMS (ESI) *m*/*z*: calcd for $C_{17}H_{22}NO_3$ [M + H]$^+$ 288.1600, found 288.1607.

Methyl 5-Methyl-1-(tetrahydrofuran-2-yl)-1*H*-indole-3-carboxylate (Table 1, Product 3af). EA/hexane = 1:5, R_f = 0.3, colorless oil, 77% (100 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (s, 1H), 7.99 (s, 1H), 7.34 (d, *J* = 8.38 Hz, 1H), 7.14−7.11 (m, 1H), 6.25 (q, *J* = 3.13 Hz, 1H), 4.22−4.17 (m, 1H), 4.05 (dd, *J* = 15.68, 7.34 Hz, 1H), 3.94 (s, 3H), 2.51 (s, 3H), 2.45−2.35 (m, 2H), 2.16−2.09 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 134.0, 131.8, 130.7, 127.4, 124.5, 121.4, 110.2, 107.1, 86.4, 68.9, 50.9, 32.0, 24.2, 21.5. IR (neat): 1653, 1426, 1272 cm^{-1}. HRMS (ESI) *m*/*z*: calcd for $C_{15}H_{18}NO_3$ [M + H]$^+$ 260.1281, found 260.1291.

Methyl 1-(Tetrahydrofuran-2-yl)-1*H*-indole-2-carboxylate (Table 1, Product 3ag). EA/hexane = 1:5, R_f = 0.6, colorless oil, 56% (69 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.04 Hz, 1H), 7.61 (d, *J* = 8.42 Hz, 1H), 7.36−7.28 (m, 2H), 7.17−7.09 (m, 2H), 4.39 (dd, *J* = 15.15, 7.00 Hz, 1H), 4.05−4.01 (m, 1H), 3.90 (s, 3H), 2.43−2.38 (m, 1H), 2.36−2.23 (m, 2H), 2.19−2.15 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5, 137.4, 127.5, 127.0, 125.0, 122.8, 120.9, 113.5, 112.4, 87.7, 68.4, 51.8, 31.3, 25.5. IR (neat): 1715, 1500, 1331, 1267 cm^{-1}. HRMS (ESI) *m*/*z*: calcd for $C_{14}H_{16}NO_3$ [M + H]$^+$ 246.1125, found 246.1123.

Ethyl 1-(tetrahydrofuran-2-yl)-1*H*-indole-2-carboxylate (Table 1, Product 3ah). EA/hexane = 1:5, R_f = 0.6, colorless oil, 59% (76.5 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.98 Hz, 1H), 7.61 (d, *J* = 8.45 Hz, 1H), 7.33−7.27 (m, 2H), 7.17−7.09 (m, 2H), 4.40−4.33 (m, 3H), 4.05−4.01 (m, 1H), 2.45−2.38 (m, 1H), 2.36−2.23 (m, 2H), 2.19−2.14 (m, 1H), 1.42 (t, *J* = 7.13 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1, 137.4, 127.9, 127.0, 124.9, 122.7, 120.8, 113.5, 112.2, 87.7, 68.3, 60.7, 31.3, 25.5, 14.3. IR (neat): 1708, 1516, 1292 cm^{-1}. HRMS (ESI) *m*/*z*: calcd for $C_{15}H_{17}NO_3Na$ [M + Na]$^+$ 282.1101, found 282.1104.

1-(Tetrahydrofuran-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (Table 1, Product 3ai). EA/hexane = 1:2, R_f = 0.5, colorless oil, 40% (38 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32−8.30 (m, 1H), 7.89−7.85 (m, 1H), 7.33 (d, *J* = 3.63 Hz, 1H), 7.08−7.05 (m, 1H), 6.68−6.65 (m, 1H), 6.48 (d, *J* = 3.63 Hz, 1H), 4.23−4.18 (m, 1H), 4.03 (dd, *J* = 15.16, 7.19 Hz, 1H), 2.50−2.43 (m, 1H), 2.41−2.33 (m, 1H), 2.22−2.10 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.3, 142.8, 128.8, 124.6, 121.2, 116.2, 100.6, 84.3, 68.7, 32.1, 24.9. IR (neat): 1599, 1228 cm^{-1}. HRMS (ESI) *m*/*z*: calcd for $C_{11}H_{12}N_2ONa$ [M + Na]$^+$ 211.0842, found 211.0847.

2-Methyl-1-(tetrahydrofuran-2-yl)-1*H*-benzo[*d*]imidazole (Table 1, Product 3aj). EA/hexane = 2:1, R_f = 0.3, colorless oil, 73% (74 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68−7.66 (m, 1H), 7.39−7.36 (m, 1H), 7.23−7.17 (m, 2H), 6.08 (t, *J* = 6.53 Hz, 1H), 4.32−4.26 (m, 1H), 4.04−3.98 (m, 1H), 2.62 (s, 3H), 2.38−2.25 (m, 3H), 2.19−2.12 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.0, 142.9,

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133.1, 122.2, 122.0, 119.2, 110.9, 86.4, 68.7, 30.7, 25.5, 14.9. IR (neat): 1570, 1433 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{12}H_{14}N_2ONa$ $[M + Na]^+$ 225.0998, found 225.1007.

1-(Tetrahydrofuran-2-yl)-1*H*-indole-3-carbonitrile (Table 1, Product 3ak). EA/hexane = 1:2, R_f = 0.4, colorless oil, 60% (64 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.76−7.74 (m, 2H), 7.47 (d, J = 7.48 Hz, 1H), 7.36−7.28 (m, 2H), 6.22 (q, J = 2.89 Hz, 1H), 4.24−4.19 (m, 1H), 4.03 (dd, J = 15.80, 7.65 Hz, 1H), 2.50−2.42 (m, 1H), 2.35−2.28 (m, 1H), 2.17−2.04 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.3, 131.4, 128.4, 123.9, 122.5, 12.0, 115.9, 111.1. 86.7, 86.3, 69.3, 32.4, 24.1. IR (neat): 1507, 1216 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{13}H_{13}N_2O$ $[M + H]^+$ 213.1022, found 213.1019.

1-(Tetrahydrofuran-2-yl)-1*H*-indole-3-carbaldehyde (Table 1, Product 3al). EA/hexane = 1:2, R_f = 0.3, yellow oil, 38% (41 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 10.04 (s, 1H), 8.34−8.32 (m, 1H), 7.89 (s, 1H), 7.46−7.44 (m, 1H), 7.38−7.34 (m, 2H), 6.22 (q, J = 2.81 Hz, 1H), 4.324−4.26 (m, 1H), 4.13 (dd, J = 15.52, 7.67 Hz, 1H), 2.53−2.46 (m, 1H), 2.42−2.35 (m, 1H), 2.20−2.08 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.8, 136.0, 134.7, 126.0, 124.1, 123.2, 122.2, 118.4, 110.6, 86.7, 69.4, 32.4, 24.2. IR (neat): 1790, 1677, 1541, 1029 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{13}H_{13}NO_2$ Na $[M + Na]^+$ 238.0838, found 238.0846.

9-(Tetrahydrofuran-2-yl)-9*H*-carbazole (Table 2, Product 5aa).[15] EA/hexane = 1:8, R_f = 0.4, white solid, 90% (107 mg), mp = 122−123 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 7.60 Hz, 2H), 7.54 (d, J = 8.00 Hz, 2H), 7.47−7.43 (m, 2H), 7.26−7.25 (m, 2H), 6.51 (t, J = 6.80 Hz, 1H), 4.44−4.38 (m, 1H), 4.11−4.05 (m, 1H), 2.54−2.47 (m, 1H), 2.36−2.31 (m, 2H), 2.26−2.22 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2, 125.7, 123.9, 120.3, 119.6, 110.4, 86.5, 68.2, 29.4, 25.7. HRMS (ESI) m/z: calcd for $C_{16}H_{16}NO$ $[M + H]^+$ 238.1226, found 238.1235.

7-(Tetrahydrofuran-2-yl)-7*H*-benzo[*c*]carbazole (Table 2, Product 5ab). EA/hexane = 1:8, R_f = 0.35, colorless oil, 91% (131 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.83 (d, J = 8.40 Hz, 1H), 8.63 (d, J = 8.00 Hz, 1H), 8.02 (d, J = 8.00 Hz, 1H), 7.89 (d, J = 9.20 Hz, 1H), 7.79 (d, J = 9.20 Hz, 1H), 7.73−7.67 (m, 2H), 7.51−7.49 (m, 2H), 7.49−7.39 (m, 1H), 6.64 (t, J = 6.80 Hz, 1H), 4.50−4.45 (m, 1H), 4.15−4.09 (m, 1H), 2.54−2.47 (m, 1H), 2.45−2.36 (m, 2H), 2.30−2.24 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.3, 137.0, 129.9, 129.1, 127.1, 126.9, 124.6, 124.1, 123.2, 123.1, 122.2, 120.3, 116.1, 112.1, 110.9, 86.7, 68.2, 30.1, 25.6. IR (neat): 1481, 1378 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{20}H_{18}NO$ $[M + H]^+$ 288.1388, found 288.1371.

4-Methoxy-9-(tetrahydrofuran-2-yl)-9*H*-carbazole (Table 2, Product 5ac). EA/hexane = 1:8, R_f = 0.4, colorless oil, 70% (94 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, J = 7.73 Hz, 1H), 7.53 (d, J = 8.24 Hz, 1H), 7.45−7.37 (m, 2H), 7.30−7.28 (m, 1H), 7.17 (d, J = 8.24 Hz, 1H), 6.74 (d, J = 7.94 Hz, 1H), 6.50 (t, J = 6.80 Hz, 1H), 4.45−4.40 (m, 1H), 4.12−4.07 (m, 4H), 2.54−2.47 (m, 1H), 2.41−2.31 (m, 2H), 2.29−2.21 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 140.7, 138.4, 126.4, 124.7, 123.3, 119.7, 113.0, 109.8, 103.3, 100.7, 86.6, 68.1, 55.4, 29.4, 25.6. IR (neat): 1491, 1329 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{17}H_{18}NO_2$ $[M + H]^+$ 268.1338, found 268.1337.

1-Methyl-9-(tetrahydrofuran-2-yl)-9*H*-carbazole (Table 2, Product 5ad). EA/hexane = 1:8, R_f = 0.5, white solid, 43% (54 mg), mp = 105−106 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 8.74 Hz, 1H), 8.02 (d, J = 7.34 Hz, 1H), 7.68 (d, J = 8.28 Hz, 1H), 7.49−7.45 (m, 1H), 7.34−7.20 (m,3H), 6.94 (t, J = 6.72 Hz, 1H), 4.49−4.44 (m, 1H), 4.12−4.06 (m, 1H), 2.85 (s, 3H), 2.55−2.49 (m, 1H), 2.40−2.35 (m, 1H), 2.32−2.22 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 138.9, 129.7, 125.4, 125.0, 124.5, 120.2, 120.0, 119.8, 118.1, 112.7, 87.7, 67.8, 29.9, 25.6, 21.5. IR (neat): 1459, 1327 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{17}H_{18}NO$ $[M + H]^+$ 252.1338, found 252.1337.

3-Phenyl-9-(tetrahydrofuran-2-yl)-9*H*-carbazole (Table 2, Product 5ae). EA/hexane = 1:8, R_f = 0.4, colorless oil, 85% (133 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, J = 1.44 Hz, 1H), 8.16 (d, J = 7.78 Hz, 1H), 7.75−7.70 (m, 3H), 7.61−7.45 (m, 5H), 7.39−7.35 (m, 1H), 7.31−7.27 (m, 1H), 6.54 (t, J = 6.72 Hz, 1H), 4.48−4.42 (m, 1H), 4.15−4.09 (m, 1H), 2.57−2.51 (m, 1H), 2.45−2.37 (m, 2H), 2.32−2.24 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.0, 139.7, 138.7, 133.1, 128.8, 127.3, 126.6, 125.9, 125.3, 124.5, 124.0, 120.4, 119.8, 118.8, 110.7, 110.5, 86.6, 68.2, 29.6, 25.7. IR (neat): 1450, 1222 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{22}H_{20}NO$ $[M + H]^+$ 314.1545, found 314.1555.

3-Chloro-9-(tetrahydrofuran-2-yl)-9*H*-carbazole (Table 2, Product 5af). EA/hexane = 1:8, R_f = 0.4, white solid, 81% (110 mg), mp = 119−120 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05−8.04 (m, 2H), 7.53−7.38 (m, 4H), 7.29−7.29 (m, 1H), 6.47 (t, J = 6.60 Hz, 1H), 4.44−4.39 (m, 1H), 4.13−4.07 (m, 1H), 2.48−2.37 (m, 3H), 2.36−2.25 (m, 1H. ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.7, 137.5, 126.4, 125.7, 125.1, 122.9, 120.5, 120.0, 119.9, 111.5, 110.5, 110.4, 86.6, 68.2, 29.6, 25.6. IR (neat): 1455, 1210 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{16}H_{15}NOCl$ $[M + H]^+$ 272.0837, found 272.0837.

3-(*tert*-Butyl)-9-(tetrahydrofuran-2-yl)-9*H*-carbazole (Table 2, Product 5ag). EA/hexane = 1:8, R_f = 0.5, colorless oil, 60% (88 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.18−8.16 (m, 2H), 7.60−7.468 (m, 4H), 7.32−7.26 (m, 1H), 6.527 (t, J = 6.78 Hz, 1H), 4.46−4.41 (m, 1H), 4.13−4.07 (m, 1H), 2.578−2.51 (m, 1H), 2.42−2.31 (m, 2H), 2.29−2.19 (m, 1H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6, 139.7, 137.4 125.5, 124.2, 123.7, 120.2, 119.4, 116.4, 110.3, 110.0, 86.6, 68.2, 34.7, 32.0, 29.4, 25.7. IR (neat): 1437, 1269 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{20}H_{24}NO$ $[M + H]^+$ 294.1858, found 294.1845.

2-Methoxy-9-(tetrahydrofuran-2-yl)-9*H*-carbazole (Table 2, Product 5ah). EA/hexane = 1:8, R_f = 0.3, colorless oil, 69% (92 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.05−7.99 (m, 2H), 7.53 (d, J = 8.18 Hz, 1H), 7.44−7.41 (m, 1H), 7.30−7.26 (m, 1H), 7.07 (s, 1H), 6.94−6.92 (m, 1H), 6.48 (t, J = 6.74 Hz, 1H), 4.46−4.41 (m, 1H), 4.13−4.07 (m, 1H), 3.97 (s, 3H), 2.55−2.49 (m, 1H), 2.39−2.33 (m, 2H), 2.27−2.23 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 140.6, 139.4, 124.5, 124.1, 120.9, 119.7, 119.5, 117.9, 110.2, 107.7, 95.4, 86.5, 68.7, 55.7, 29.2, 25.7. IR (neat): 1519, 1261 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{17}H_{18}NO_2$ $[M + H]^+$ 268.1338, found 268.1333.

3-Bromo-9-(tetrahydrofuran-2-yl)-9*H*-carbazole (Table 2, Product 5ai). EA/hexane = 1:8, R_f = 0.4, white solid, 72% (114 mg), mp =115−116 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.21 (d, J = 1.76 Hz, 1H), 8.05 (d, J = 7.80 Hz, 1H), 7.54−7.46 (m, 3H), 7.42 (d, J = 8.76 Hz, 1H), 6.304−6.26 (m, 1H), 6.47 (t, J = 6.54 Hz, 1H), 4.44−4.38 (m, 1H), 2.47−2.43 (m, 1H), 2.41−2.33 (m, 2H), 2.28−2.26 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.5, 137.8, 128.3, 126.4, 125.7, 123.0, 122.8, 120.5, 120.0, 112.5, 111.9, 110.5, 86.6, 68.2, 29.6, 25.6. IR (neat): 1462, 1280 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{16}H_{15}NOBr$ $[M + H]^+$ 316.0332, found 316.0333.

3,6-Dibromo-9-(tetrahydrofuran-2-yl)-9*H*-carbazole (Table 2, Product 5aj). EA/hexane = 1:8, R_f = 0.3, white solid, 86% (169 mg), mp 146−147 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.11 (s, 2H), 7.52 (d, J = 8.74 Hz, 2H), 7.37 (d, J = 8.56 Hz, 2H), 6.36 (s, 1H), 4.39−4.36 (m, 1H), 4.08−4.05 (m, 1H), 2.36−2.29 (m, 3H), 2.25−2.23 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1, 129.1, 124.5, 123.2, 112.8, 112.1, 86.7, 68.3, 29.9, 25.5. IR (KBr): 1471, 1434, 1282 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{16}H_{14}NOBr_2$ $[M + H]^+$ 393.9437, found 393.9443.

9-(Tetrahydrofuran-2-yl)-3-(trifluoromethyl)-9*H*-carbazole (Table 2, Product 5ak). EA/hexane = 1:10, R_f = 0.3, yellow oil, 86% (131 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 8.15 (d, J = 7.82 Hz, 1H), 7.71 (d, J = 8.56 Hz, 1H), 7.62−7.50 (m, 3H), 7.30 (t, J = 7.08 Hz, 1H), 6.51 (t, J = 6.56 Hz, 1H), 4.47−4.42 (m, 1H), 4.15−4.10 (m, 1H), 2.51−2.36 (m, 3H), 2.31−2.24 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.7, 139.8, 126.7, 123.9, 123.6, 123.4, 122.5 (q, J = 3.56 Hz), 121.9 (q, J = 32.6 Hz), 120.6, 120.4, 117.8 (q, J = 3.6 Hz), 110.8, 110.5, 86.7, 68.4, 29.8, 25.5. IR (neat): 1429, 1268 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{17}H_{15}F_3NO$ $[M + H]^+$ 306.1106, found 306.1096.

2-Ethyl-1-(9-(tetrahydrofuran-2-yl)-9*H*-carbazol-3-yl)butan-1-one (Table 2, Product 5al). EA/hexane = 1:5, R_f = 0.4, yellow oil, 91% (152.5 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 8.81 (d, J = 1.60 Hz, 1H), 8.20−8.15 (m, 2H), 7.58−7.54 (t, J = 8.0 Hz, 2H), 7.51−7.49 (m, 1H), 7.35 (t, J = 7.2 Hz, 1H), 6.49 (t, J = 6.6 Hz, 1H), 4.43−4.39 (m, 1H), 4.11−4.05 (m, 1H), 3.56−3.49 (m, 1H), 2.47−2.30 (m, 3H),

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2.25−2.20 (m, 1H), 1.95−1.88 (m, 2H), 1.71−1.65 (m, 2H), 0.97 (t, J = 7.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.0, 141.9, 139.8, 130.1, 126.5, 126.4, 124.1, 123.8, 121.3, 120.6, 120.5, 110.9, 110.1, 86.6, 68.4, 48.9, 29.9, 25.6, 25.4, 12.1. IR (neat): 1694, 1460, 1212 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{22}H_{26}NO_2$ [M + H]$^+$ 336.1964, found 336.1955.

Ethyl 9-(Tetrahydrofuran-2-yl)-9*H*-carbazole-3-carboxylate (Table 2, Product 5am). EA/hexane = 1:5, R_f = 0.4, yellow oil, 61% (94 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.83 (d, J = 1.2 Hz, 1H), 8.18 (d, J = 8.4 Hz, 2H), 7.56−7.47 (m, 3H), 7.32 (t, J = 3.6 Hz, 1H), 6.49 (t, J = 6.6 Hz, 1H), 4.49−4.41 (m, 3H), 4.11−4.08 (m, 1H), 2.52−2.34 (m, 3H), 2.25−2.10 (m, 1H), 1.49 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 141.9, 139.7, 127.3, 126.4, 123.9, 123.6, 122.6, 121.8, 120.6, 120.4, 110.8, 109.8, 86.6, 68.4, 60.8, 29.8, 25.6, 14.5. IR (neat): 1739, 1498, 1222 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{19}H_{20}NO_3$ [M + H]$^+$ 310.1443, found 310.1434.

Methyl 1-(1,4-Dioxan-2-yl)-1*H*-indole-3-carboxylate (Table 3, Product 3ba). EA/hexane = 1:5, R_f = 0.2, white solid, 55% (72 mg), mp = 120−121 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20−8.18 (m, 2H), 7.49−7.47 (m, 1H), 7.33−7.28 (m, 2H), 6.48 (t, J = 4.16 Hz, 1H), 4.12−4.10 (m, 2H), 3.92 (s, 3H), 3.91−3.79 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 136.4, 132.4, 126.6, 123.3, 122.6, 121.8, 110.6, 108.6, 68.3, 66.4, 63.8, 51.1. IR (neat): 1634, 1470, 1135 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{14}H_{16}NO_4$ [M + H]$^+$ 262.1074, found 262.1082.

Methyl 1-(Tetrahydro-2*H*-pyran-2-yl)-1*H*-indole-3-carboxylate (Table 3, Product 3ca). EA/hexane = 1:5, R_f = 0.4, colorless oil, 70% (91 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20−8.18 (m, 1H), 8.06 (s, 1H), 7.51−7.49 (m, 1H), 7.33−7.28 (m, 2H), 5.54 (dd, J = 8.82, 2.84 Hz, 1H), 4.15−4.12 (m, 1H), 3.94 (s, 3H), 3.81−3.74 (m, 1H), 2.15−2.07 (m, 3H), 1.79−1.72 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 136.2, 131.1, 126.7, 123.0, 122.3, 121.7, 110.7, 108.1, 83.7, 68.1, 51.0, 30.7, 25.1, 22.9. IR (neat): 1656, 1468, 1122 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{15}H_{18}NO_3$ [M + H]$^+$ 260.1281, found 260.1291.

Methyl 1-(Isochroman-1-yl)-1*H*-indole-3-carboxylate (Table 3, Product 3da). EA/hexane = 1:5, R_f = 0.4, white solid, 72% (111 mg), mp = 114−115 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26−8.24 (m, 1H), 7.68−7.66 (m, 1H), 7.51 (s, 1H), 7.43−7.36 (m, 3H), 7.34−7.28 (m, 2H), 7.08 (d, J = 7.66 Hz, 1H), 7.00 (s, 1H), 3.99−3.95 (m, 1H), 3.89 (s, 3H), 3.86−3.80 (m, 1H), 3.19−3.11 (m, 1H), 2.89−2.84 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 137.1, 135.1, 133.5, 130.5, 129.3, 129.1, 127.4, 127.1, 127.0, 123.3, 122.6, 121.8, 111.3, 107.8, 80.7, 59.9, 51.1, 27.7. IR (neat): 1653, 1459, 1161 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{19}H_{18}NO_3$ [M + H]$^+$ 308.1287, found 308.1297.

Methyl 1-(1-Butoxybutyl)-1*H*-indole-3-carboxylate (Table 3, Product 3ea). EA/hexane = 1:5, R_f = 0.5, colorless oil, 59% (89 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24−8.22 (m, 1H), 7.98 (s, 1H), 7.59−7.56 (m, 1H), 7.31−7.28 (m, 2H), 5.47 (t, J = 6.52 Hz, 1H), 3.95 (s, 3H), 3.36−3.26 (m, 2H), 2.16−2.08 (m, 1H), 2.04−1.96 (m, 1H), 1.55−1.49 (m, 2H), 1.42−1.29 (m, 4H), 0.95 (t, J = 7.29 Hz, 3H), 0.89 (t, J = 7.29 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 136.0, 131.7, 127.0, 122.9, 122.1, 121.8, 110.9, 107.9, 87.9, 68.5, 51.0, 37.9, 31.4, 19.2, 18.3, 13.7, 13.6. IR (neat): 1478, 1279 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{18}H_{25}NO_3Na$ [M + Na]$^+$ 326.1727, found 326.1736.

9-(Tetrahydro-2*H*-pyran-2-yl)-9*H*-carbazole (Table 3, Product 5ca).[25] EA/hexane = 1:8, R_f = 0.6, white solid, 56% (70 mg), mp = 118−119 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 7.74 Hz, 2H), 7.69 (d, J = 8.24 Hz, 2H), 7.48−7.43(m, 2H), 7.28−7.24 (m, 2H), 5.84 (dd, J = 11.20, 2.40 Hz, 1H), 4.36−4.33 (m, 1H), 3.86−3.80 (m, 1H), 2.54−2.01 (m, 1H), 2.15−2.11 (m, 1H), 1.92−1.81 (m, 3H), 1.74−1.71 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.1, 125.6, 123.6, 120.2, 119.4, 110.9, 84.4, 69.4, 29.6, 25.4, 23.6. HRMS (ESI) m/z: calcd for $C_{17}H_{18}NO$ [M + H]$^+$ 252.1383, found 252.1388.

Ethyl 1-(tetrahydro-2*H*-pyran-2-yl)-1*H*-indole-2-carboxylate (Table 3, Product 3bh).[22] EA/hexane = 1:5, R_f = 0.6, colorless oil, 55% (75 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 8.56 Hz, 1H), 7.67 (d, J = 8.09 Hz, 1H), 7.34−7.30 (m, 2H), 7.17 (t, J = 7.56 Hz, 1H), 6.64 (dd, J = 10.80, 2.40 Hz, 1H), 4.41−4.36 (m, 2H), 4.29−4.26 (m, 1H), 3.81−3.75 (m, 1H), 2.38−2.32 (m, 1H), 2.06−2.04 (m, 1H), 1.95 (d, J = 13.12 Hz, 1H), 1.86−1.81 (m, 2H), 1.67−1.65 (m, 1H), 1.45 (t, J = 7.12 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1, 137.9, 126.8, 126.7, 124.8, 122.5, 120.8, 115.0, 111.8, 85.2, 69.2, 60.7, 30.6, 25.5, 23.4, 14.3. HRMS (ESI) m/z: calcd for $C_{16}H_{19}NO_3Na$ [M + Na]$^+$ 296.1257, found 296.1263.

Methyl 1-(benzo[*d*][1,3]dioxol-2-yl)-1*H*-indole-3-carboxylate (Table 3, Product 3fa). EA/hexane = 1:5, R_f = 0.5, colorless oil, 25% (37 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23−8.21 (m, 1H), 8.00 (s, 1H), 7.89 (s, 1H), 7.42−7.40 (m, 1H), 7.35−7.31 (m, 2H), 7.02 (s, 4H), 3.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 145.5, 134.7, 130.3, 127.3, 124.0, 123.1, 122.8, 122.1, 110.8, 110.2, 109.1, 108.1, 51.3. IR (neat): 1468, 1292 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{17}H_{14}NO_4$ [M + H]$^+$ 296.0923, found 296.0932.

9-(1,4-Dioxan-2-yl)-9*H*-carbazole (Table 3, Product 5ba). EA/hexane = 1:8, R_f = 0.35, white solid, 60% (76 mg), mp = 99−100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 7.72 Hz, 2H), 7.72 (d, J = 8.28 Hz, 2H), 7.49−7.45 (m, 2H), 7.30−7.26 (m, 2H), 6.06 (dd, J = 9.91, 3.13 Hz, 1H), 4.35−4.29 (m, 1H), 4.22−4.11 (m, 2H), 3.95−3.87 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.1, 125.9, 123.8, 120.3, 119.9, 110.8, 81.1, 67.7, 67.3, 66.0. HRMS (ESI) m/z: calcd for $C_{16}H_{16}NO_2$ [M + H]$^+$ 254.1176, found 254.1176.

9-(Isochroman-1-yl)-9*H*-carbazole (Table 3, Product 5da). EA/hexane = 1:5, R_f = 0.4, white solid, 43% (64 mg), mp = 165−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 7.64 Hz, 2H), 7.37−7.33 (m, 4H), 7.28−7.25 (m, 2H), 7.23−7.10 (m, 4H), 6.91 (d, J = 7.76 Hz, 1H), 4.35−4.29 (m, 1H), 4.23−4.16 (m, 1H), 3.34−3.26 (m, 1H), 3.06−2.99 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ140.3, 135.0, 133.4, 129.0, 128.4, 127.1, 126.3, 125.8, 125.8, 124.0, 120.3, 120.2, 119.9, 119.4, 110.8, 110.6, 81.0, 63.8, 28.4. IR (neat): 1476, 1277 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{21}H_{18}NO$ [M + H]$^+$ 300.1388, found 300.1402.

3-Bromo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-carbazole (Table 3, Product 5cf). EA/hexane = 1:8, R_f = 0.4, colorless oil, 65% (107 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (d, J = 1.70 Hz, 1H), 8.05 (d, J = 7.74 Hz, 1H), 7.66 (d, J = 8.18 Hz, 1H), 7.58−7.46 (m, 3H), 7.28−7.25 (m, 1H), 5.79 (dd, J = 11.18, 2.32 Hz, 1H), 4.35−4.31 (m, 1H), 3.84−3.78 (m, 1H), 2.46−2.42 (m, 1H), 2.13−2.10 (m, 1H), 1.91−1.79 (m, 3H), 1.74−1.71 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.4, 137.7, 128.2, 126.3, 125.5, 122.9, 122.5, 120.4, 119.8, 112.6, 112.3, 110.9, 84.4, 69.4, 29.6, 25.4, 23.5. IR (neat): 1479, 1276 cm^{-1}. HRMS (ESI) m/z: calcd for $C_{17}H_{17}NOBr$ [M + H]$^+$ 330.0488, found 330.0485.

2,2,6,6-Tetramethyl-1-(tetrahydrofuran-2-yloxy)piperidine (Scheme 1, Product 6).[12b] Yellow oil, 30% (85 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.37 (dd, J = 5.60, 2.00 Hz, 1H), 3.90−3.79 (m, 2H), 2.01−1.91 (m, 3H), 1.90−1.78 (m, 1H), 1.77−1.46 (m, 5H), 1.33−1.30 (m, 1H), 1.22 (s, 3H), 1.10 (s, 3H), 1.07 (s, 3H), 1.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 109.6, 66.6, 60.1, 58.6, 40.16, 39.7, 33.9, 33.3, 31.2, 23.9, 20.4, 20.0, 17.2.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01990.

Copies of ^{1}H NMR and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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