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Catalytic Enolate Arylation with 3-Bromoindoles Allows the Formation of β-Carbolines

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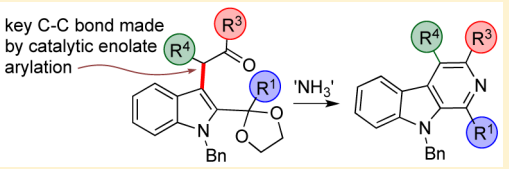
Supporting Information

ABSTRACT: Synthesis of substituted β-carbolines was accomplished by utilizing the catalytic enolate arylation reaction of ketones in conjunction with several 3-bromoindole derivatives. Quenching of the arylation reaction in situ with an electrophile allowed ready incorporation of functionality at the carboline C-4 position in an efficient one-pot protocol.



β-Carbolines are important *N*-heterocyclic aromatic compounds that have been extensively studied for their wide-ranging bioactivity.[1] These compounds are also widely found in natural products extracted from various sources such as the dichotomides,[2] from the roots of *Stellaria dichotoma*; the metatacarbolines,[3] from the fruiting bodies of *Mycena metata*; hirsutaside D,[4] from the leaves of *Uncaria hirsute*, hyrtiocarboline,[5] from the marine sponge *Hyrtios reticulatus*, and stolonines,[6] from the marine tunicate *Cnemidocarpa stolonifera*.

Some of the recently reported methodologies to prepare β-carbolines involve the metal-catalyzed iminoannulation of alkynes,[7] the Rh-catalyzed cycloaddition of yne-ynamides with methylcyanoformate,[8] cascade annulation of alkynols,[9] photocyclization of anilinohalopyridines,[10] coupling of anilines and halopyridines,[11] Pd-catalyzed ring-expansion of azidoalcohols,[12] and cyclization of vinylindoles.[13] While impressive, the main limitations of these methods lie in the formation of regioisomers or the limited accessibility of a variety of substitution patterns in the heterocyclic ring.

We sought a route to these heterocycles that would allow the introduction of many different groups onto the aromatic nucleus but without the complications arising from the formation of regioisomers. In this regard, our approach to the synthesis of carbolines relies on the use of catalytic enolate arylation reaction of ketones,[14] a powerful catalytic reaction still underused in the synthesis of aromatic heterocycles.[15] Previous work from our group has shown that ketones can be easily arylated by reaction of substituted aryl or vinyl halides so that the products are ideally configured (masked 1,4-dicarbonyls) for an aromatization step to furnish substituted isoquinolines[16] or pyridines[17] (Figure 1a).

Herein, we chose a 3-bromoindole partner **A** for the enolate arylation (Figure 1b).[18] The installation of a protected carbonyl at C-2 of the indole bromide partner would provide the functionality required to aromatize the ring after arylation was complete (see **B** → **C**). Moreover, from previous precedent,[15,19] we anticipated that an ability to add an electrophile directly to the catalytic arylation reaction would allow extra functionalization to be added to the product (see R^4 in **B**) that would ultimately allow derivatization at the C-4 position of the carboline without the addition of extra synthetic steps.

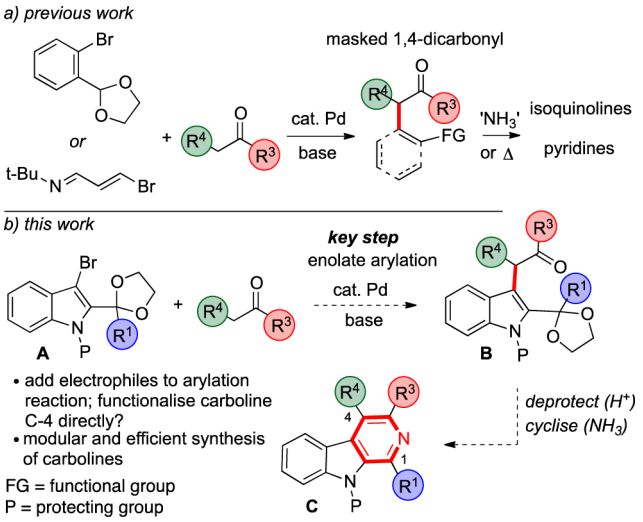


Figure 1. Catalytic enolate arylation route to β-carbolines.

Initially, we selected 1-benzyl-3-bromo-2-(1,3-dioxolan-2-yl)-1*H*-indole (**1**) and acetophenone (**2**) for optimization studies using catalytic palladium (Table 1). Compound **1** was made in high yield from the precursor indole-2-carboxaldehyde via reaction with NBS, followed by *N*-benzylation with base and BnBr and then acetal formation with ethylene glycol and *p*TSA.[20]

We began our screening by treating **1** and acetophenone (**2**) with catalytic Pd(d*t*bpf)Cl_2[21] and NaO*t*Bu in THF (Table 1), which are conditions previously used for related arylations in our laboratory,[15] and they afforded product **3** in an encouraging 52% yield (entry 1). Pleasingly, compound **3** could be isolated

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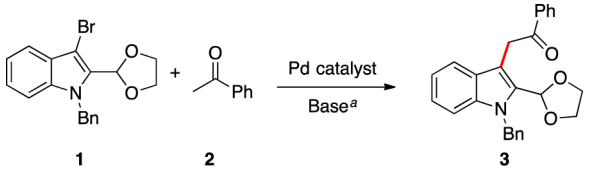
Table 1. Optimization Studies for the Pd-Catalyzed α-Arylation of 1



1 2 3

	catalyst (mol %)	ketone (equiv)	base (2.5 equiv)	T (°C)	yield (%)[b]
1	$Pd(dtbf)Cl_2$ (5)	2	NaOtBu	50	52
2	$Pd(dtbf)Cl_2$ (5)	2	LiHMDS	50	93
3	$Pd(dtbf)Cl_2$ (5)	1.2	LiHMDS	50	80
4	$Pd(dtbf)Cl_2$ (2.5)	2	LiHMDS	50	86
5	$Pd(dtbf)Cl_2$ (2.5)	1.2	LiHMDS	50	70
6	$Pd(dtbf)Cl_2$ (5)	2	LiHMDS	RT	66
7	$Pd(amphos)Cl_2$ (5)	2	LiHMDS	50	17

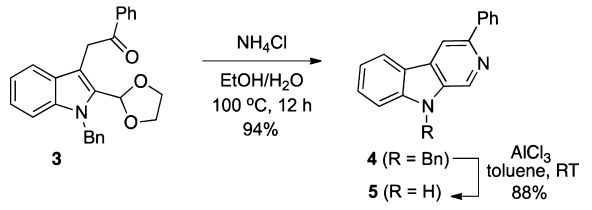
[a]Indole **1** (1.0 equiv),THF, 24 h. [b]Isolated yields.

in 93% yield when the NaO*t*Bu base was replaced by LiHMDS (entry 2).

Further studies showed that the arylation was tolerant of changes to the reaction parameters. For example, lower catalyst loadings and/or ketone equivalents were examined, and these delivered the desired product in good yields (entries 3−5). Moreover, a reasonable yield of **3** (66%) was obtained when the arylation reaction was carried out at room temperature (entry 6). Finally, a different catalyst was screened with $Pd(amphos)_2Cl_2$, (this was also previously very active in our hands), delivering the product in a disappointing 17% yield (entry 7).

Pleasingly, the reaction of arylated product **3** with ammonium chloride in ethanol/water was sufficiently acidic to deprotect the acetal and allow cyclization to give the corresponding carboline **4** in 94% yield (Scheme 1), thus validating our approach to these aromatic heterocycles. Moreover, the *N*-benzyl group was easily removed from the carboline products using $AlCl_3$ (**4** → **5** in 88% yield).[22]

Scheme 1. Cyclization of 3 to Furnish β-Carboline 4



The next stage involved an exploration of the substrate scope, and to do this, we prepared more substituted indole bromides to be coupled with a selection of commercially available ketones (Scheme 2). Our synthesis of the requisite indole bromides began from readily available compound **6**,[23] which was *N*-benzylated (**7**) and then derivatized into two different ketones (**8** and **9**) via reaction with a Grignard reagent. After bromination at C-3 (**10** and **11**), ketone **10** was protected as an acetal (**12**) under standard conditions.

With the key compounds in hand, we explored the substrate scope, and Table 2 shows a set of carbolines (**4**, **14**, **16**, and **18**) that were prepared via this two-step sequence of enolate arylation using the optimized conditions from Table 1, followed

Scheme 2. Synthesis of Substituted Indole Bromides

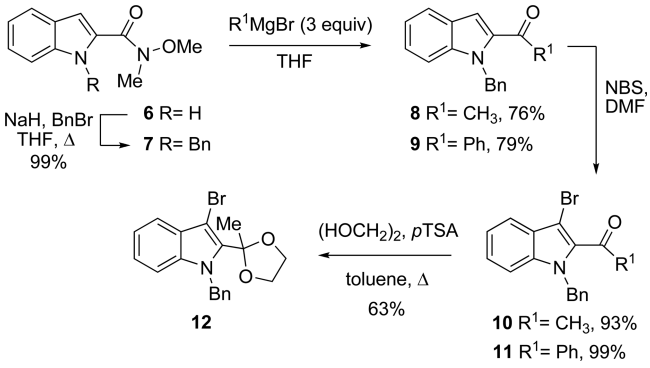
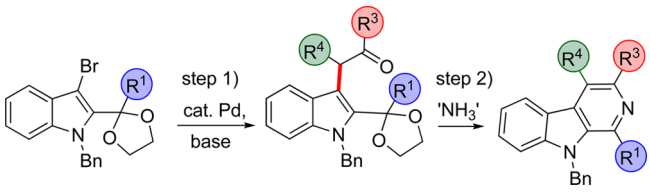
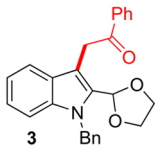
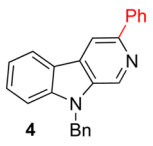
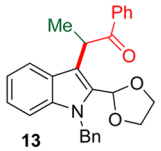
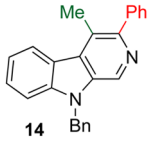
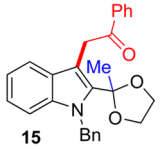
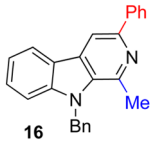
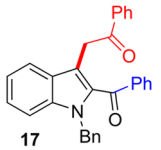
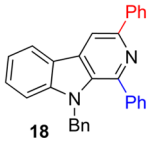


Table 2. Synthesis of Substituted β-Carbolines in Two Steps[a]



arylated ketone	yield[c]	β−carboline	yield[c]
 3	93%	 4	94%
 13	74%	 14	94%
 15	84%	 16	94%[b]
 17	66%	 18	85%[b]

[a]Reaction conditions: (1) indole (1.0 equiv), Pd(d*t*bpf)Cl_2 (5.0 mol %), LiHMDS (2.5 equiv), ketone (2.0 equiv), THF, 50 °C, 24 h; (2) NH_4Cl (10 equiv); EtOH/H_2O 3:1, 100 °C, 12 h. [b]Solvent: EtOH/H_2O/DMF (3:1:2), 110 °C, 12 h. [c]Isolated yields.

by aromatization. Use of this methodology allowed substitution at the carboline C-1, C-3, and C-4 positions simply by using a substituted ketone or altering the substitution pattern of the ketal protected indole bromide in the arylation step. Note that some groups (e.g., Ph) could be introduced at the carboline C-1 position without the need for ketal protection (see **11** → **17** → **18**); in this case, the conjugated nature of the ketone at C-2 of the indole makes it unreactive to competing aldol type side reactions.

After these positive results, we then developed a one-pot procedure for the arylation/aromatization sequence. This

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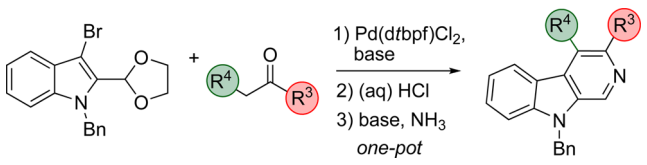
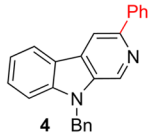
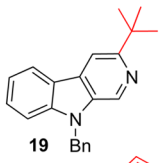
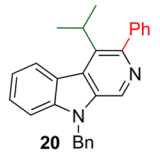
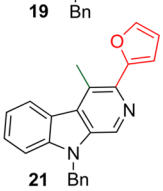
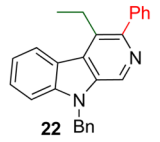
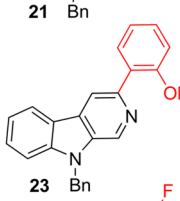
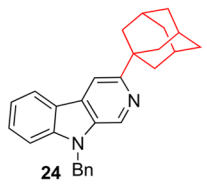
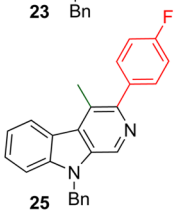
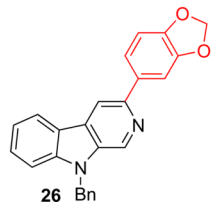
worked well, and starting from **1** and **2**, we quenched the arylation reaction directly with acid and then ammonia to furnish carboline **4** in 68% yield for the one-pot process (Table 3). The one-pot sequence was optimal when it began with an

Table 3. One-Pot Synthesis of Substituted β-Carbolines[a]



β–carboline	yield[c]	β–carboline	yield[c]
 **4**	68%[b]	 **19**	34%[b] 53%
 **20**	42%[b] 73%	 **21**	75%
 **22**	68%	 **23**	74%
 **24**	61%	 **25**	52%
 **26**	61%		

[a]Reaction conditions: (1) indole (1.0 equiv), Pd(d*t*bpf)Cl_2 (5.0 mol %), NaO*t*Bu (2.5 equiv), ketone (2.0 equiv), THF, 75 °C, 24 h; (2) (aq) 1 M HCl; (3) $NaHCO_3$ (20 equiv), NH_3 (20 equiv, 7 M in MeOH), EtOH, DMF, 100 °C, 12 h. [b]LiHMDS (2.5 equiv) as base, 50 °C. [c]Isolated yields.

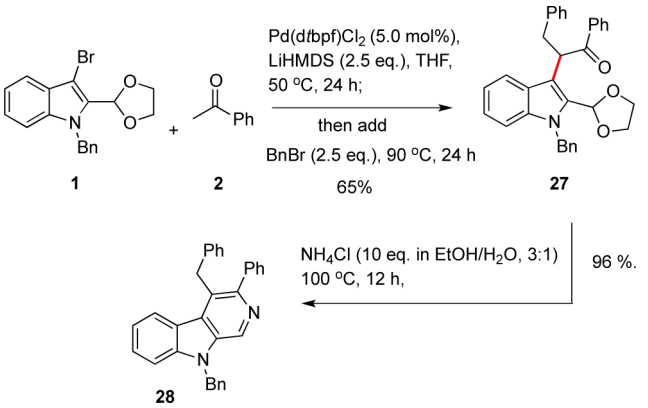
enolate arylation, followed by the sequential addition of acid (to hydrolyze the acetal), neutralization ($NaHCO_3$), and then addition of ammonia (7 M in MeOH) to perform the aromatization.

However, as we switched to more substituted ketone substrates to expand the methodology, we found the arylation conditions that had proved optimal for acetophenone in Table 1 showed poor conversion (see **19** and **20** with 34 and 42% yield, respectively). Therefore, we examined other conditions from Table 1 that had also delivered arylated product and found that a change of base to NaO*t*Bu, together with an increase in the temperature, delivered an arylation reaction that was more reliable across a wider range of ketones (for example, compounds **19** and **20** were now formed in 53 and 73% yield, respectively).

With these new arylation conditions, the one-pot synthesis of various carbolines was then possible in excellent yields. Using this approach, alkyl substituents could be incorporated with ease at either the C-3 or C-4 positions on the carboline nucleus (Table 3). Note that attempts at the one-pot synthesis of C-1 substituted carbolines from bromide **11** were unsuccessful.

Next, we examined the direct functionalization of the arylated products in situ, which was accomplished by quenching the arylation reaction of a methyl ketone with an electrophile (see **1** → **27** with the addition of benzyl bromide, Scheme 3). This

Scheme 3. In Situ Enolate Alkyation to Furnish C-4 Substituted β-Carbolines



protocol works well because the initial arylation reaction requires at least two equivalents of base to reach completion and, therefore, the initial arylation product is actually present in the reaction mixture as an enolate, which can be quenched. As expected, the benzylated compound **27** was then easily aromatized to carboline **28** under standard conditions (Scheme 3).

This precedent then provided the basis for a one-pot arylation/enolate-quench/aromatization sequence starting from **1** and **2**, that provided several C-4 derivatized products in good yields (see **14** and **28**–**31**, Table 4). This chemistry represents a particularly convenient and short route to C-3,4-disubstituted carbolines which installs the desired functionality with complete control of regiochemistry.

To conclude, we extended the enolate arylation/aromatization sequence to accomplish the synthesis of carbolines by using indole-based bromides as coupling partners. A variety of (heterocyclic) substitution patterns were compatible with this approach, either by arylation of a functionalized ketone or by a direct enolate arylation and electrophilic quenching sequence. The ability to combine an enolate arylation with a one-pot aromatization sequence is particularly advantageous. This convenient and modular approach allows access to a wide range of carboline derivatives with many potential uses.

EXPERIMENTAL SECTION

General Methods. All reagents were used as purchased. Solvents were dried using standard laboratory techniques. All reactions requiring dry equipment were carried out in flame-dried glassware under argon atmosphere. Flash column chromatography was performed using Geduran silica gel 60 (40–63 μm). Thin layer chromatography was performed on Merck Kieselgel 60 F254 0.25 mm

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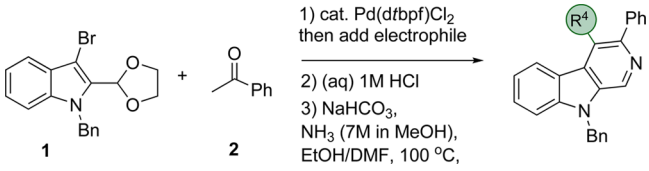
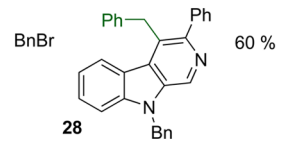
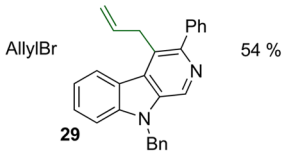
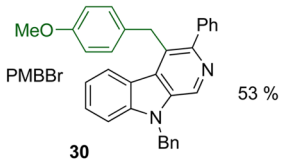
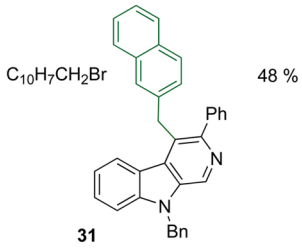
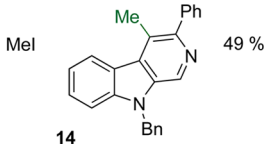
Table 4. One-Pot Synthesis of C-4 Functionalized β-Carbolines[a]



electrophile	β–carboline	yield[b]	electrophile	β–carboline	yield[b]
BnBr		60 %	AllylBr		54 %
PMBBr		53 %	$C_{10}H_7CH_2Br$		48 %
MeI		49 %			

[a]Reaction conditions: (1) indole (1.0 equiv), Pd(dtbpf)Cl_2 (5.0 mol %), LiHMDS (2.5 equiv), ketone (2.0 equiv), THF, 50 °C, 24 h; then electrophile, 90 °C. [b]Isolated yields

precoated aluminum-backed plates. Product spots were visualized under UV light (λ_{max} = 254 nm) and/or by staining with vanillin, phosphomolybdic acid, or basic potassium permanganate solutions. ^{1}H NMR spectra were recorded using a Bruker AVII400, AVIII400, or AVII500 instruments at 400 or 500 MHz. ^{13}C NMR spectra were recorded at 100 or 125 MHz. ^{19}F NMR spectrum was recorded at 376 MHz. Chemical shifts, δ, are reported relative to residual solvent peaks and quoted in parts per million (ppm) to the nearest 0.01 for ^{1}H and to the nearest 0.1 ppm for ^{13}C and ^{19}F. Coupling constants, *J*, are quoted to the nearest 0.1 Hz. Assignments were based upon DEPT, COSY, HSQC, and HMBC experiments. High-resolution mass spectra were acquired using electrospray ionization (ESI) as ionization source and were recorded on a Fisons Platform II with TOF detector. IR spectra were obtained from evaporated films using a Bruker Tensor 27 spectrometer equipped with a PIKE Miracle Attenuated Total Reflectance (ATR) sampling accessory. Absorption maxima are quoted in wavenumbers (cm^{-1}) for the range 3500–600 cm^{-1}. Melting points (mp) were obtained by using a Leica VMTG heated-stage microscope and are uncorrected.

General Procedure A for α-Arylation of Ketones. A fresh solution of LiHMDS was prepared in a dry vial adding sequentially dry THF (2 mL), HMDS (80 μL, 0.38 mmol, 2.5 equiv), a 2.5 M solution of *n*BuLi (0.15 mL, 0.38 mmol 2.5 equiv) and stirring at −78 °C for 10 min. The ketone (0.31 mmol, 2.0 equiv) was then added at 0 °C and stirred for 15 min. In a second dry vial were added bromo indole (0.15 mmol) and Pd(dtbpf)Cl_2 (5 mg, 8 μmol, 5 mol %). The flask was sealed, evacuated, and backfilled with argon. The freshly formed enolate solution was then transferred via syringe to the flask. The mixture was stirred at 50 °C for 24 h in an oil bath. The resulting mixture was filtered through a plug of silica and concentrated in vacuo. The crude product was purified by flash column chromatography (eluted with a mixture of petroleum ether:EtOAc) to afford the ketone product.

General Procedure B for the Cyclization of α-Arylated Ketones. To a reaction flask were added the arylated ketone (4.15 mmol) and a 1 M solution of NH_4Cl (4.1 mL, 10 equiv) in EtOH:H_2O 3:1. The mixture was stirred at 90 °C for 12 h. NH_4HCO_3 (6.97 g, 83.0 mmol, 20 equiv) was then added to the flask, and the solution was stirred at 90 °C for 3 h. The crude product was concentrated in vacuo, redissolved in pure EtOAc, and mixed with water. The aqueous layer was extracted twice with EtOAc; the organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting solid was purified by flash column chromatography (eluted with a mixture of petroleum ether:EtOAc) to afford the β-carboline product.

General Procedure C for the Synthesis of Ketones from Weinreb Amide 7. To a dry reaction flask were added indole **7** (2.00 g, 6.79 mmol) and dry THF (68 mL). A 3 M solution of the appropriate Grignard reagent (6.8 mL, 20 mmol, 3 equiv) was slowly added over 30 min at −78 °C and then allowed to stir at 0 °C for 1 h. The mixture was then quenched at 0 °C with $NH_4Cl_{(aq)}$, and the aqueous layer was extracted twice with EtOAc. The organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting solid was purified by flash column chromatography (eluted with a mixture of petroleum ether:EtOAc) to afford the product ketone.

General Procedure D for the One-Pot Synthesis of β-Carbolines. To a dry vial were added bromo indole **1** (110 mg, 307 μmol), Pd(dtbpf)Cl_2 (10 mg, 15 μmol, 5 mol %), and NaO*t*Bu (74 mg, 0.77 mmol, 2.5 equiv). The flask was sealed, evacuated, and backfilled with argon twice and then dry THF (4 mL), and the corresponding ketones (0.61 mmol, 2 equiv) were added in sequence. The mixture was stirred for 24 h at 75 °C. After cooling to room temperature, $HCl_{(aq)}$ (1 M, 10 equiv) was added, and the mixture was stirred for 12 h at 90 °C. After cooling to room temperature, DMF (2 mL), EtOH (4 mL), $NaHCO_3$ (516 mg, 6.14 mmol, 20 equiv), and NH_3 (7 M solution in MeOH, 0.88 mL, 6.1 mmol, 20 equiv) were added, and the mixture was stirred at 110 °C for 24 h. The crude product was concentrated in vacuo, redissolved in pure EtOAc, and mixed with water. The aqueous layer was extracted twice with EtOAc, and the organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting solid was purified by flash column chromatography (eluted with a mixture of petroleum ether:EtOAc) to afford the β-carboline product.

General Procedure E for the Bromination of Keto-Indoles. To a dry reaction flask were added the appropriate ketone (5.45 mmol) and DMF (3.9 mL). A solution of NBS (1.11 g, 6.27 mmol, 1.15 equiv) in DMF (3.9 mL) was added over 30 min at 0 °C, and the resulting mixture was then stirred at room temperature for 2 h. H_2O (70 mL) was added, and the resulting slurry was extracted three times with EtOAc; the organic extracts were combined and washed five times with H_2O, dried over $MgSO_4$, filtered, and concentrated in vacuo, affording the bromo indole product or, alternatively, were purified by flash column chromatography (eluted with a mixture of petroleum ether:EtOAc) to afford the bromo indole product.

General Procedure F for the One-Pot Synthesis of β-Carboline with Addition of Electrophiles. A fresh solution of LiHMDS was prepared in a dry vial adding sequentially dry THF (4 mL), HMDS (0.16 mL, 0.77 mmol, 2.5 equiv), and a 2.5 M solution of *n*BuLi (0.31 mL, 0.77 mmol, 2.5 equiv) and stirring at −78 °C for 10 min. Acetophenone (72 μL, 0.61 mmol, 2.0 equiv) was then added at 0 °C and stirred for 15 min. In a second dry vial were added bromo indole **1** (110 mg, 307 μmol) and Pd(dtbpf)Cl_2 (10 mg, 15 μmol, 5 mol %). The flask was sealed, evacuated, and backfilled with argon. The freshly formed enolate solution was then transferred via syringe to the flask. The mixture was stirred at 50 °C for 24 h in an oil bath. After cooling to room temperature, the appropriate electrophile (0.77 mmol, 2.5 equiv) was added, and the mixture was stirred at 90 °C for 24 h. After cooling to room temperature, 1 M $HCl_{(aq)}$ (3.1 mL, 10 equiv) was added, and the mixture was stirred for 12 h at 90 °C. After cooling to room temperature, DMF (2 mL), EtOH (4 mL), $NaHCO_3$ (516 mg, 6.14 mmol, 20 equiv), and NH_3 (7 M solution in MeOH, 0.88 mL, 6.1 mmol, 20 equiv) were added, and the mixture was stirred at 110 °C for 24 h. The crude product was concentrated in vacuo, redissolved in pure EtOAc, and mixed with water. The aqueous layer

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was extracted twice with EtOAc and the organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting solids were purified by flash column chromatography (eluted with a mixture of petroleum ether:EtOAc) to afford the β-carboline product.

Synthesis of 1-Benzyl-3-bromo-2-(1,3-dioxolan-2-yl)-1*H*-indole (1). To a dry reaction flask connected to a Dean−Stark apparatus were added 1-benzyl-3-bromo-1*H*-indole-2-carbaldehyde (330 mg, 1.05 mmol), ethylene glycol (116 μL, 2.09 mmol, 2 equiv), *p*-toluenesulfonic acid monohydrate (20 mg, 105 μmol, 10 mol %), and toluene (10 mL). The resulting mixture was heated at reflux for 14 h and then cooled to room temperature and quenched with $NaHCO_{3(aq)}$. The aqueous layer was extracted twice with EtOAc, and the organic extracts combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting solid was purified by flash column chromatography (eluted with 9:1 petroleum ether:EtOAc), affording **1** (350 mg, 93%) as a yellow solid. Mp: 64−67 °C. IR ν_{max} (thin film): 3060, 2888, 1075 cm^{-1}. HRMS: calcd for $C_{18}H_{17}BrNO_2$, 358.04372 $[M + H]^+$, found *m/z* 358.04379, Δ = 0.20 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.62−7.55 (1H, m, HC_{Ar}), 7.30−7.00 (8H, m, 8 × HC_{Ar}), 6.21 (1H, s, $CH(OR)_2$), 5.46 (1H, s, $PhCH_2R$), 4.06−3.86 (4H, m, $(OCH_2)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 137.9, 137.4, 129.3 (3 × C_{Ar}), 128.6 (HC_{Ar}), 127.3 (HC_{Ar}), 126.7 (C_{Ar}), 126.3, 124.3, 120.7, 120.0, 110.6 (5 × HC_{Ar}), 98.7 ($CH(OR)_2$), 94.5 (C(3)), 65.2 ($(OCH_2)_2$), 48.5 ($PhCH_2R$).

*2-(1-Benzyl-2-(1,3-dioxolan-2-yl)-1H-indol-3-yl)-1-phenylethan-1-one (**3**).* This compound was prepared according to general procedure A, affording **3** (57 mg, 93%) as a brown solid. Mp: 100−102 °C. IR ν_{max} (thin film): 3368, 3060, 2925, 1613, 1082, 745 cm^{-1}. HRMS: calcd for $C_{26}H_{24}O_3N$, 398.17507 $[M + H]^+$, found *m/z* 398.17496, Δ = −0.30 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.15−8.10 (2H, m, 2 × HC_{Ar}), 7.63−7.54 (2H, m, 2 × HC_{Ar}), 7.48 (2H, t, *J* = 7.4 Hz, 2 × HC_{Ar}), 7.33−7.03 (9H, m, 9 × HC_{Ar}), 6.13 (1H, s, $CH(OR)_2$), 5.54 (1H, s, $PhCH_2R$), 4.65 (2H, s, $CH_2C(O)$), 4.05−3.90 (4H, m, $(OCH_2)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 196.7 (C(O)), 137.1, 136.4, 135.9 (3 × C_{Ar}), 131.8 (HC_{Ar}), 129.8 (C_{Ar}), 127.5, 127.5, 127.4 (3 × HC_{Ar}), 126.6 (C_{Ar}), 126.0, 125.0, 121.9, 118.7, 118.2, 109.0 (6 × HC_{Ar}), 108.2 (C_{Ar}), 97.9 ($CH(OR)_2$), 63.9 ($(OCH_2)_2$), 46.7 (RCH_2Ph), 34.0 ($CH_2C(O)$).

*9-Benzyl-3-phenyl-9H-pyrido[3,4-b]indole (**4**).* This compound was prepared according to general procedure B on a 4.15 mmol scale, affording **4** (1.30 g, 94%) as a light brown solid. Mp: 143−146 °C. IR ν_{max} (thin film): 3059, 3030, 1460, 733, 694 cm^{-1}. HRMS: calcd for $C_{24}H_{19}N_2$, 335.15428 $[M + H]^+$, found *m/z* 335.15350, Δ = −2.3 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.82 (1H, s, C(1)), 8.33 (1H, s, C(4)), 8.13 (1H, d, *J* = 7.8 Hz, HC_{Ar}), 8.08 (2H, d, *J* = 7.5 Hz, HC_{Ar}), 7.55−7.43 (3H, m, 3 × HC_{Ar}), 7.40−7.31 (2H, m, 2 × HC_{Ar}), 7.30−7.15 (4H, m, 4 × HC_{Ar}), 7.14−7.05 (2H, m, 2 × HC_{Ar}), 5.41 (2H, s, $PhCH_2Ar$); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 147.9, 141.9, 140.6, 136.5, 136.0 (5 × C_{Ar}), 131.9 (HC(1)), 129.8 (C_{Ar}), 129.0, 128.8, 128.6, 127.9, 127.8, 126.9, 126.7, 122.0 (8 × HC_{Ar}), 121.7 (C_{Ar}), 120.0, 111.4, 109.9 (3 × HC_{Ar}), 47.0 ($PhCH_2Ar$). ^1H and ^{13}C NMR data were consistent with those previously reported.[7c]

Synthesis of 3-Phenyl-9*H*-pyrido[3,4-*b*]indole (5). To a dry reaction flask were added freshly sublimed $AlCl_3$ (287 mg, 2.15 mmol, 6 equiv) and toluene (1.8 mL). A solution of β-carboline **4** (120 mg, 359 μmol) in toluene (1.8 mL) was added at 0 °C over 10 min and stirred at room temperature for 2 h. The resulting mixture was quenched with $NaHCO_{3(aq)}$, and the aqueous layer was extracted twice with EtOAc. The organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting solids were purified by flash column chromatography (eluted with a 19:1 mixture of $CHCl_3$:MeOH) to afford the β-carboline product **5** (71 mg, 88%) as a white solid. Mp: 226−229 °C. IR ν_{max} (thin film): 3125, 3018, 2923, 2755, 1137, 738, 696 cm^{-1}. HRMS: calcd for $C_{17}H_{13}N_2$, 245.10732 $[M + H]^+$, found *m/z* 245.10730, Δ = −0.10 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.99 (1H, s, HC_{Ar}), 8.57 (1H, bs, NH), 8.40 (1H, s, HC_{Ar}), 8.20 (1H, d, *J* = 7.8 Hz, HC_{Ar}), 8.12−8.07 (2H, m, 2 × HC_{Ar}), 7.59−7.46 (4H, m, 4 × HC_{Ar}), 7.43−7.36 (1H, m, HC_{Ar}), 7.32 (1H, dd, *J* = 8.1, 7.0 Hz, HC_{Ar}). ^1H NMR (400 MHz, DMSO-d_6) δ_H: 11.69 (1H, s, NH), 9.00 (1H, s, HC(1)), 8.77 (1H, s, HC(4)), 8.36 (1H, d, *J* = 7.9 Hz, HC_{Ar}), 8.22 (2H, ddd, *J* = 8.3, 1.2, 1.0 Hz, 2 × HC_{Ar}), 7.66−7.60 (1H, m, HC_{Ar}), 7.58 (1H, dd, *J* = 6.9, 1.2 Hz, HC_{Ar}), 7.54−7.48 (2H, m, 2 × HC_{Ar}), 7.41−7.35 (1H, m, HC_{Ar}), 7.28 (1H, ddd, *J* = 8.0, 6.9, 1.0 Hz, HC_{Ar}); ^{13}C NMR (100 MHz, $CDCl_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 146.0, 141.6, 140.6, 135.9 (4 × C_{Ar}), 134.0 (HC(1)), 129.3 (C_{Ar}), 129.1, 128.7, 127.9, 126.6 122.5, (5 × HC_{Ar}), 121.5 (C_{Ar}), 119.8, 112.5 (2 × HC_{Ar}), 111.6 (HC(4)). ^1H NMR data were consistent with those previously reported.[24]

Synthesis of 1-Benzyl-*N*-methoxy-*N*-methyl-1*H*-indole-2-carboxamide (7). To a dry reaction flask equipped with a reflux condenser were added indole **6** (12.0 g, 58.7 mmol) and dry THF (590 mL). NaH (60% in mineral oil, 2.82 g, 70.5 mmol, 1.2 equiv) was added slowly at 0 °C over 10 min, and the resulting mixture was heated at reflux for 30 min. After cooling to room temperature, benzyl bromide (8.4 mL, 70 mmol, 1.2 equiv) was added, and the solution was heated at reflux for 2 h and then cooled to 0 °C, when it was quenched using $NH_4Cl_{(aq)}$. The aqueous layer was extracted twice with EtOAc, and the organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting solid was purified by flash column chromatography (eluted with 4:1 petroleum ether:-EtOAc) to afford protected indole **7** (17.1 g, 99%) as a white solid. Mp: 34−37 °C. IR ν_{max} (thin film): 3060, 3030, 2931, 1632, 1453, 739 cm^{-1}. HRMS: calcd for $C_{18}H_{18}O_2N_2$, 295.14410 $[M + H]^+$, found *m/z* 295.14398, Δ = −0.41 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.79−7.40 (1H, m, HC_{Ar}), 7.44 (1H, dd, *J* = 8.4, 0.8 Hz, HC_{Ar}), 7.33 (1H, ddd, *J* = 8.3, 7.0, 1.2 Hz, HC_{Ar}), 7.31−7.19 (5H, m, 6 × HC_{Ar}), 7.13 (2H, d, *J* = 6.6 Hz, 2 × HC_{Ar}), 5.77 (2H, s, $PhCH_2R$), 3.53 (3H, s, OCH_3), 3.34 (3H, s, NCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 162.8 (C(O)), 138.6, 138.4, 129.6 (3 × C_{Ar}), 128.6, 127.3, 126.8 (3 × HC_{Ar}), 126.7 (C_{Ar}), 124.4, 122.3, 120.6, 110.6, 108.1 (5 × HC_{Ar}), 61.2 (OCH_3), 47.9 (RCH_2Ph), 33.9 (NCH_3).

*1-(1-Benzyl-1H-indol-2-yl)ethan-1-one (**8**).* This compound was prepared according to general procedure C, affording **8** (1.28 g, 76%) as a white solid. Mp: 125−126 °C. IR ν_{max} (thin film): 3061, 3031, 2924, 1657, 725 cm^{-1}. HRMS: calcd for $C_{17}H_{16}ON$, 250.12264 $[M + H]^+$, found *m/z* 250.12302, Δ = 1.50 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.81−7.77 (1H, m, HC_{Ar}), 7.45−7.36 (3H, m, 3 × HC_{Ar}), 7.32−7.20 (4H, m, 4 × HC_{Ar}), 7.14−7.08 (2H, m, 2 × HC_{Ar}), 5.91 (s, 2H, NCH_2Ph), 2.66 (s, 3H, $C(O)CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 191.3 (C(O)), 140.0, 138.4, 134.4 (3 × C_{Ar}), 128.5, 127.1, 126.5, 126.3 (4 × HC_{Ar}), 126.0 (C_{Ar}), 123.0, 121.1, 113.0, 111.0 (4 × HC_{Ar}), 48.2 ($PhCH_2N$), 28.1 ($C(O)CH_3$). ^1H NMR data were consistent with those previously reported.[25]

*(1-Benzyl-1H-indol-2-yl)(phenyl)methanone (**9**).* This compound was prepared according to general procedure C on a 10.2 mmol scale, affording **9** (2.51 g, 79%) as a white solid. Mp: 107−110 °C. IR ν_{max} (thin film): 3060, 3030, 2923, 1633, 718, 694 cm^{-1}. HRMS: calcd for $C_{22}H_{17}ONNa$, 334.12024 $[M + Na]^+$, found *m/z* 334.12023, Δ = −0.02 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.95−7.90 (2H, m, 2 × HC_{Ar}), 7.73 (1H, d, *J* = 8.0, HC_{Ar}), 7.65−7.58 (1H, m, HC_{Ar}), 7.54−7.48 (2H, m, 2 × HC_{Ar}), 7.44 (1H, dd, *J* = 8.5, 0.7 Hz, HC_{Ar}), 7.38 (1H, ddd, *J* = 8.4, 6.9, 1.1 Hz, HC_{Ar}), 7.31−7.18 (4H, m, 4 × HC_{Ar}), 7.18−7.14 (2H, m, 2 × HC_{Ar}), 7.12 (1H, d, *J* = 0.6 Hz, C(3)), 5.91 (2H, s, $PhCH_2R$); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 188.6 (C(O)), 140.2, 139.4, 138.4, 134.7 (4 × C_{Ar}), 132.2, 129.8, 128.6, 128.2, 127.2, 126.6, 126.2 (7 × HC_{Ar}), 126.1 (C_{Ar}), 123.1,121.1,115.8, 111.1 (4 × HC_{Ar}), 48.1 ($PhCH_2R$). ^1H NMR data were consistent with those previously reported.[26]

*1-(1-Benzyl-3-bromo-1H-indol-2-yl)ethan-1-one (**10**).* This compound was prepared according to general procedure E, affording **10** (1.66 g, 93%) as a white solid. Mp: 118−120 °C. IR ν_{max} (thin film): 3061, 3032, 2921, 16511, 726 cm^{-1}. HRMS: calcd for $C_{17}H_{15}ONBr$, 328.03315 $[M + H]^+$, found *m/z* 328.03348, Δ = 0.99 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.80−7.74 (1H, m, HC_{Ar}), 7.43−7.39 (2H, m, 2 × HC_{Ar}), 7.32−7.22 (4H, m, 4 × HC_{Ar}), 7.08−7.03 (2H, m, 2 × HC_{Ar}), 5.80 (2H, s, $PhCH_2N$), 2.83 (3H, s, $C(O)CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 192.0 (C(O)), 138.4, 138.0, 132.6 (3 × C_{Ar}), 128.6, 127.3, 127.1 (3 × HC_{Ar}), 126.8 (C_{Ar}), 126.3, 121.9, 121.8, 111.0 (4 × HC_{Ar}), 100.0 (C_{Ar}), 48.9 ($PhCH_2N$), 31.9 ($C(O)CH_3$).

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*(1-Benzyl-3-bromo-1H-indol-2-yl)(phenyl)methanone (**11**).* This compound was prepared according to general procedure E on a 4.17 mmol scale, affording **11** (1.62 g, 99%) as a white solid. Mp: 87−89 °C. IR ν_{max} (thin film): 3060, 3030, 1719, 722, 692 cm^{-1}. HRMS: calcd for $C_{22}H_{17}ONBr$, 390.04880 $[M + H]^+$, found m/z 390.04959, Δ = 2.02 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.82−7.78 (2H, m, 2 × HC_{Ar}), 7.68 (1H, d, J = 8.0 Hz, HC_{Ar}), 7.62−7.56 (1H, m, HC_{Ar}), 7.46−7.34 (4H, m, 4 × HC_{Ar}), 7.27 (1H, ddd, J = 8.0, 6.6, 1.3 Hz, HC_{Ar}), 7.24−7.14 (3H, m, 3 × HC_{Ar}), 7.08−7.03 (2H, m, HC_{Ar}), 5.60 (2H, s, PhCH_2R); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 189.4 (C(O)), 138.0, 138.0, 137.5, 133.5 (4 × C_{Ar}), 133.3, 130.2, 128.7, 128.5, 127.6 (5 × HC_{Ar}), 126.8 (C_{Ar}), 126.7, 126.2, 121.6, 121.3, 110.9 (5 × HC_{Ar}), 98.1 (C_{Ar}), 48.3 (PhCH_2R).

Synthesis of 1-Benzyl-3-bromo-2-(2-methyl-1,3-dioxolan-2-yl)-1*H*-indole (12). To a dry reaction flask connected to a Dean−Stark apparatus were added bromo indole **10** (3.00 g, 9.14 mmol), ethylene glycol (5.1 mL, 91 mmol, 10 equiv), *p*-toluenesulfonic acid monohydrate (175 mg, 914 μmol, 10 mol %), and toluene (91 mL). The resulting mixture was heated at 120 °C for 60 h and then cooled to room temperature and quenched with $NaHCO_{3(aq)}$. The aqueous layer was extracted twice with EtOAc, and the organic extracts combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting solid was purified by flash column chromatography (eluted with 1:0.8 petroleum ether:$CHCl_3$), affording **12** (2.14 g, 63%) as a white solid. Mp: 89−90 °C. IR ν_{max} (thin film): 3031, 2990, 2892 cm^{-1}. HRMS: calcd for $C_{19}H_{18}O_2NBr$, 372.05937 $[M + H]^+$, found m/z 372.05930, Δ = −0.19 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.59−7.53 (1H, m, HC_{Ar}), 7.20−7.05 (6H, m, 6 × HC_{Ar}), 7.85−6.79 (2H, m, 2 × HC_{Ar}), 5.60 (2H, s, PhCH_2N), 3.95−3.83 (2H, m C$H_a$$H_bCH_a$$H_b$), 3.65−3.53 (2H, m, CH$_a$$H_bCH_a$$H_b$); 1.60 (3H, s, CC$H_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 138.4, 137.1, 135.4 (3 × C_{Ar}), 128.6 (HC_{Ar}), 127.4 (C_{Ar}), 127.0, 125.7, 123.6, 120.7, 119.8, 110.3 (6 × HC_{Ar}), 106.4, 89.6 (2 × C_{Ar}), 64.6 (OCH_2)$_2$), 48.6 (PhCH_2N), 26.4 (CCH_3).

*2-(1-Benzyl-2-(1,3-dioxolan-2-yl)-1H-indol-3-yl)-1-phenylpropan-1-one (**13**).* This compound was prepared according to general procedure A, affording **13** (47 mg, 74%) as a yellow solid. Mp: 159−164 °C. IR ν_{max} (thin film): 3061, 2974, 2930, 2890, 1680, 1079, 745 cm^{-1}. HRMS: calcd for $C_{27}H_{25}O_3N$, 412.19072 $[M + H]^+$, found m/z 412.19196, Δ = 3.0 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.01 (2H, d, J = 7.40 Hz, 2 × HC_{Ar}), 7.64 (1H, d, J = 7.6 Hz, HC_{Ar}), 7.34 (1H, t, J = 7.4 Hz, HC_{Ar}), 7.24 (2H, t, J = 7.4 Hz, 2 × HC_{Ar}), 7.21−7.13 (3H, m,3 × HC_{Ar}), 7.08−6.99 (3H, m, 3 × HC_{Ar}), 6.90−6.84 (2H, m, 2 × HC_{Ar}), 6.18 (1H, s, CH(OR)$_2$), 5.42 (1H, s, PhC$H_a$$H_b$R), 5.41 (1H, s, PhCH$_a$$H_b$R), 5.15 (1H, q, J = 6.8, CHCH$_3$), 4.12−3.92 (4H, m, (OCH_2)$_2$), 1.66 (3H, d, CH_3CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 201.1 (C(O)), 138.1, 137.64, 137.0 (3 × CAr), 132.4, 128.8 (2 × HC_{Ar}), 128.7 (C_{Ar}), 128.6, 128.2, 127.1, 125.9 (4 × HC_{Ar}), 125.8 (C_{Ar}), 123.1, 120.2, 119.9 (3 × HC_{Ar}), 116.7 (C_{Ar}), 110.1 (HC_{Ar}), 98.6 (CH(OR_2)$_2$), 65.2 (CHO$_2$C$_a$H$_2$C$_b$H$_2$), 65.0 (CHO$_2$C$_a$H$_2$C$_b$H$_2$), 47.7 (PhCH_2R), 39.8 (CHCH$_3$), 18.0 (CHCH_3).

*9-Benzyl-4-methyl-3-phenyl-9H-pyrido[3,4-b]indole (**14**).* This compound was prepared according to general procedure B on a 0.15 mmol scale, affording **14** (50 mg, 94%) as a yellow solid. Mp: 164−167 °C. IR ν_{max} (thin film): 3055, 3030, 2924, 1454, 737, 701 cm^{-1}. HRMS: calcd for $C_{25}H_{21}N_2$, 349.16993 $[M + H]^+$, found m/z 349.16946, Δ = −1.3 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.82 (1H, s, HC(1)), 8.33 (1H, d, J = 8.0 Hz, HC_{Ar}), 7.65−7.60 (2H, m, 2 × HC_A), 7.59 (1H, ddd, J = 8.3, 7.1, 1.2 Hz, HC_A), 7.54−7.47 (3H, m, 3 × HC_A), 7.45−7.39 (1H, m, HC_{Ar}) 7.34 (1H, t, J = 8.0 Hz, HC(6)), 7.32−7.25 (3H, m, 3 × HC_{Ar}), 7.22−7.17 (2H, m, 2 × HC_{Ar}), 5.58 (2H, s, PhCH_2R), 2.91 (3H, s, RCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 149.2, 141.7, 141.2, 136.6, 135.6 (5 × C_{Ar}), 130.0, 129.3 (2 × HC_{Ar}), 129.0 (C(1)), 128.4 (C_{Ar}), 128.1, 127.8, 127.8, 127.2, 126.6 (5 × HC_{Ar}), 124.9 (C_{Ar}), 124.2 (C(5)), 122.4 (C_{Ar}), 119.9 (C(6)), 109.6 (HC_{Ar}), 46.9 (PhCH_2R), 17.6 (RCH_3).

*2-(1-Benzyl-2-(2-methyl-1,3-dioxolan-2-yl)-1H-indol-3-yl)-1-phenylethan-1-one (**15**).* This compound was prepared according to general procedure A on 0.15 mmol scale, affording **15** (50 mg, 84%) as an off-white solid. Mp: 128−131 °C. IR ν_{max} (thin film): 3058, 3029, 2989, 2891, 1691, 1197, 742 cm^{-1}. HRMS: calcd for $C_{27}H_{25}O_3NNa$, 434.17266 $[M + Na]^+$, found m/z 434.17270, Δ = 0.08 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.15−8.11 (2H, m, 2 × HC_{Ar}), 7.63−7.56 (1H, m, HC_{Ar}), 7.55−7.46 (3H, m, 3 × HC_{Ar}), 7.30−7.12 (6H, m, 6 × HC_{Ar}), 6.98−6.93 (2H, m, 2 × HC_{Ar}), 5.67 (2H, s, PhCH_2N), 4.72 (2H, s, ArCH_2C(O)), 3.88−3.80 (2H, m C$H_a$$H_bCH_a$$H_b$), 3.68−3.62 (2H, m, CH$_a$$H_bCH_a$$H_b$), 1.65 (3H, s, CCH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 198.2 (C(O)), 139.0,137.5, 137.4, 136.6 (4 × C_{Ar}), 132.8, 128.6, 128.5 (3 × HC_{Ar}), 128.4 (C_{Ar}), 128.3, 126.7, 125.8, 122.5, 119.8, 118.6, 110.3 (7 × HC_{Ar}), 107.3, 106.8 (C_{Ar} + CCH$_3$), 64.8 (OCH_2)$_2$), 48.0 (PhCH$_2$N), 35.2 (ArCH$_2$C(O)), 27.2 (CCH_3).

*9-Benzyl-1-methyl-3-phenyl-9H-pyrido[3,4-b]indole (**16**).* This compound was prepared according to a modification of general procedure B on a 85 μmol scale, affording **16** (28 mg, 94%) as a brown solid. A mixture of EtOH:H_2O:DMF (3:1:2) was used as solvent, and the temperature was kept at 110 °C for this cyclization. Mp: 127−129 °C. IR ν_{max} (thin film): 3060, 3030, 1472, 734, 694 cm^{-1}. HRMS: calcd for $C_{25}H_{21}N_2$, 349.16993 $[M + H]^+$, found m/z 349.16943, Δ = −1.41 ppm. ^1H NMR (500 MHz, $CDCl_3$) δ_H: 8.31 (1H, s, HC(4)), 8.22 (1H, d, J = 7.7 Hz, HC_{Ar}), 8.16−8.12 (2H, m, 2 × HC_{Ar}), 7.56−7.48 (3H, m, 3 × HC_{Ar}), 7.41−7.35 (2H, m, 2 × HC_{Ar}), 7.34−7.22 (4H, m, 5 × HC_{Ar}), 7.05−7.00 (2H, m, 2 × HC_{Ar}), 5.81 (2H, s, PhCH_2N), 2.95 (3H, s, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C: 145.9, 141.3, 140.2, 139.4, 137.0, 133.9, 129.2 (7 × C_{Ar}), 127.9, 127.6, 127.3, 126.5, 126.5, 125.7, 124.4 (7 × HC_{Ar}), 120.7 (C_{Ar}), 120.4, 119.0, 108.9 (3 × HC_{Ar}), 108.5 (C(4)), 47.2 (PhCH$_2$N), 22.4 (CH$_3$).

*2-(2-Benzoyl-1-benzyl-1H-indol-3-yl)-1-phenylethan-1-one (**17**).* This compound was prepared according to general procedure A on a 6.36 mmol scale, affording **17** (1.75 g, 64%) as a yellow solid. Mp: 132−134 °C. IR ν_{max} (thin film): 3059, 3030, 1689, 1637, 745, 729 cm^{-1}. HRMS: calcd for $C_{30}H_{23}O_2NNa$, 452.16210 $[M + Na]^+$, found m/z 452.16183, Δ = −0.59 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 7.78 (2H, ddd, J = 8.0, 1.3, 0.9 Hz, 2 × HC_{Ar}), 7.74−7.69 (2H, m, 2 × HC_{Ar}), 7.58 (1H, d, J = 8.0 Hz, HC_{Ar}), 7.54−7.48 (1H, m, HC_{Ar}), 7.43−7.13 (11H, m, 11 × HC_{Ar}), 7.05−7.00 (2H, m, 2 × HC_{Ar}), 5.59 (2H, s, PhCH_2Ar), 4.26 (2H, s, CH_2C(O)); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 196.4, 190.2 (2 × C(O)), 139.6, 138.8, 138.0, 136.6, 134.5 (5 × C_{Ar}), 133.0, 132.8, 129.4, 128.6, 128.6, 128.5, 128.1 (7 × HC_{Ar}), 127.5 (C_{Ar}), 127.3, 126.5, 125.6, 121.1, 120.9 (5 × HC_{Ar}), 116.1 (C_{Ar}), 110.9 (HC_{Ar}), 48.1 (PhCH$_2$Ar), 36.0 (CH$_2$C(O)).

*9-Benzyl-1,3-diphenyl-9H-pyrido[3,4-b]indole (**18**).* This compound was prepared according to a modification of general procedure B on a 0.17 mmol scale, affording **18** (61 mg, 85%) as a yellow solid. A mixture of EtOH:H_2O:DMF (3:1:2) was used as solvent, and the temperature was kept at 110 °C for this cyclization. Mp: 170−174 °C. IR ν_{max} (thin film): 3058, 3031, 1468, 1450, 737, 694 cm^{-1}. HRMS: calcd for $C_{30}H_{22}N_2$, 411.18558 $[M + H]^+$, found m/z 411.18452, Δ = −2.57 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.48 (1H, s, HC(4)), 8.30 (1H, ddd, J = 7.8, 1.2, 0.8 Hz, HC_{Ar}), 8.23−8.18 (2H, m, 2 × HC_{Ar}), 7.58−7.47 (5H, m, 5 × HC_{Ar}), 7.45−7.30 (6H, m, 6 × HC_{Ar}), 7.20−7.10 (3H, m, 3 × HC_{Ar}), 6.68−6.62 (2H, m, 2 × HC_{Ar}), 5.25 (2H, s, PhCH_2N); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 147.1, 144.0, 143.2, 140.3, 139.9, 137.1, 134.0, 131.8 (8 × C_{Ar}), 129.6, 128.7, 128.6, 128.4, 128.3, 128.0, 127.8, 127.1, 127.0, 125.8 (10 × HC_{Ar}), 122.0 (C_{Ar}), 121.6, 120.3 (2 × HC_{Ar}), 110.8 (C(3)), 110.2 (HC_{Ar}), 48.2 (PhCH_2N).

*9-Benzyl-3-(tert-butyl)-9H-pyrido[3,4-b]indole (**19**).* This compound was prepared according to general procedure D, affording **19** (51 mg, 53%) as a brown solid. Mp: 132−134 °C. IR ν_{max} (thin film): 3030, 2956, 2864, 1468, 740, 698 cm^{-1}. HRMS: calcd for $C_{22}H_{23}N_2$, 315.18558 $[M + H]^+$, found m/z 315.18530, Δ = −0.86 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.82 (1H, d, J = 0.9 Hz, HC(1)), 8.19 (1H, d, J = 7.8 Hz, HC_{Ar}), 8.19 (1H, d, J = 0.9 Hz, HC(4)), 7.55 (1H, ddd, J = 8.3, 7.1, 1.2 Hz, HC_{Ar}), 7.43 (1H, d, J = 8.3 Hz, HC_{Ar}), 7.32−7.18 (6H, m, 6 × HC_{Ar}), 5.53 (2H, s, PhCH_2N), 1.51 (9*H*, s, (CH_3)$_3$C); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 159.0, 141.8, 136.7, 135.0 (4 × C_{Ar}), 130.8 (C(1)), 129.3 (C_{Ar}), 128.9, 128.2, 127.8, 126.7, 121.8 (5 × HC_{Ar}), 121.6 (C_{Ar}), 119.6, 109.6 (2 × H_{Ar}), 109.4 ((4)), 47.1 (PhCH$_2$N), 37.2 ((CH$_3$)$_3$C), 30.9 ((CH$_3$)$_3$C).

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*9-Benzyl-4-isopropyl-3-phenyl-9H-pyrido[3,4-b]indole (**20**).* This compound was prepared according to general procedure D, affording **20** (84 mg, 73%) as a brown solid. Mp: 170−171 °C. IR ν_{max} (thin film): 3055, 3030, 2990, 2958, 2929, 2872, 1439, 741, 701 cm^{-1}. HRMS: calcd for $C_{27}H_{24}N_2$, 377.20123 $[M + H]^+$, found m/z 377.20139, Δ = 0.42 ppm. ^1H NMR (500 MHz, $CDCl_3$) δ_H: 8.89 (1H, s, $HC(1)$), 7.62−7.53 (3H, m, 3 × HC_{Ar}), 7.46−7.37 (4H, m, 4 × HC_{Ar}), 7.33−7.23 (5H, m, 5 × HC_{Ar}), 6.95 (1H, dd, J = 8.0, 6.9 Hz, HC_{Ar}), 6.83 (1H, d, J = 8.0 Hz, HC_{Ar}) 5.53 (2H, s, PhCH_2N), 3.18 (1H, hept, J = 6.8 Hz, CH(CH_3)$_2$), 1.29 (6H, d, J = 6.8 Hz, CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 153.9, 141.8, 138.6, 136.7, 134.9 (5 × C_{Ar}), 130.9, 129.3, 128.9, 128.9 (4 × HC_{Ar}), 128.9 128.8 (2 × C_{Ar}), 127.8, 127.8, 127.8, 126.8, 123.5 (5 × HC_{Ar}), 121.6 (C_{Ar}), 119.4, 109.3 (2 × HC_{Ar}), 47.0 (PhCH_2N), 30.9 (CH(CH_3)$_2$), 23.2 (CH(CH_3)$_2$).

*9-Benzyl-3-(furan-2-yl)-4-methyl-9H-pyrido[3,4-b]indole (**21**).* This compound was prepared according to general procedure D, affording **21** (78 mg, 75%) as a brown solid. Mp: 156−159 °C. IR ν_{max} (thin film): 3141, 2918, 1488, 1301, 733, 696 cm^{-1}. HRMS: calcd for $C_{23}H_{19}ON_2$, 339.14919 $[M + H]^+$, found m/z 339.14883, Δ = −1.05 ppm. ^1H NMR (500 MHz, $CDCl_3$) δ_H: 8.63 (1H, s, $HC(1)$), 8.19 (1H, d, J = 8.0 Hz, HC_{Ar}), 7.50 (1H, dd, J = 1.9, 0.7 Hz, OCH), 7.44 (1H, ddd, J = 8.2, 7.2, 1.1 Hz, HC_{Ar}), 7.33 (1H, d, J = 8.3 Hz, HC_{Ar}), 7.20 (1H, ddd, J = 8.0, 7.3, 0.6 Hz, HC_{Ar}), 7.16−7.09 (3H, m, 3 × HC_{Ar}), 7.03−6.99 (2H, m, 2 × HC_{Ar}), 6.67 (1H, dd, J = 3.3, 0.7 Hz, OCCH), 6.46 (1H, dd, J = 3.3, 1.9 Hz, OCHCH), 5.39 (2H, s, PhCH_2N), 2.89 (3H, s, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C: 154.1 (C_{Ar}), 142.2 (OCH), 141.6, 139.1, 136.4, 135.3 (4 × C_{Ar}), 129.6 ($C(1)$), 128.9 (HC_{Ar}), 128.3 (C_{Ar}), 127.8, 127.8, 126.5 (3 × HC_{Ar}), 125.4 (C_{Ar}), 124.2 (HC_{Ar}), 122.4 (C_{Ar}), 120.1 (HC_{Ar}), 111.2 (OCHCH), 109.7 (HC_{Ar}), 109.6 (OCCH), 46.8 (PhCH_2N), 16.8 (CH_3).

*9-Benzyl-4-ethyl-3-phenyl-9H-pyrido[3,4-b]indole (**22**).* This compound was prepared according to general procedure D, affording **22** (76 mg, 68%) as a brown solid. Mp: 136−138 °C. IR ν_{max} (thin film): 3056, 2969, 2933, 2873, 1441, 730, 700 cm^{-1}. HRMS: calcd for $C_{26}H_{23}N_2$, 363.18558 $[M + H]^+$, found m/z 363.18530, Δ = −0.75 ppm. ^1H NMR (500 MHz, $CDCl_3$) δ_H: 8.81 (1H, s, $C(1)$), 8.28 (1H, d, J = 8.0 Hz, HC_{Ar}), 7.61−7.55 (3H, m, 3 × HC_{Ar}), 7.52−7.46 (3H, m, 3 × HC_{Ar}), 7.44−7.39 (1H, m, HC_{Ar}), 7.35 (1H, ddd, J = 8.0, 7.1, 1.0 Hz, HC_{Ar}), 7.32−7.26 (3H, m, 3 × HC_{Ar}), 7.24−7.20 (2H, m, 2 × HC_{Ar}), 5.60 (2H, s, PhCH_2N), 3.26 (2H, q, J = 7.5 Hz, CH_2CH$_3$), 1.44 (3H, t, J = 7.5 Hz, CH$_2$CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C: 149.1, 141.7, 141.5, 136.6, 136.2 131.2 (6 × C_{Ar}), 129.5 ($C(1)$), 129.4, 129.0, 128.1, 127.8, 127.8 (5 × HC_{Ar}), 127.4 (C_{Ar}), 127.2, 126.6, 124.2 (3 × HC_{Ar}), 121.5 (C_{Ar}), 120.1, 109.7 (2 × HC_{Ar}), 46.9 (PhCH_2N), 23.4 (CH_2CH$_3$), 14.5 (CH$_2$CH_3).

*9-Benzyl-3-(2-methoxyphenyl)-9H-pyrido[3,4-b]indole (**23**).* This compound was prepared according to general procedure D, affording **23** (83 mg, 74%) as a yellow solid. Mp: 95−97 °C. IR ν_{max} (thin film): 3030, 2935, 2834, 1491, 727, 700 cm^{-1}. HRMS: calcd for $C_{25}H_{20}N_2O$, 365.16484 $[M + H]^+$, found m/z 365.16464, Δ = −0.54 ppm. ^1H NMR (500 MHz, $CDCl_3$) δ_H: 8.94 (1H, d, J = 1.0 Hz, $HC(1)$), 8.51 (1H, d, J = 1.0 Hz, $HC(4)$), 8.22 (1H, ddd, J = 7.8, 1.2, 0.7 Hz, HC_{Ar}), 7.84, (1H, dd, J = 7.6, 1.8 Hz, HC_{Ar}), 7.57 (1H, ddd, J = 8.3, 7.1, 1.2 Hz, HC_{Ar}), 7.46−7.42 (1H, m, HC_{Ar}), 7.38 (1H, ddd, J = 8.3, 7.4, 1.8 Hz, HC_{Ar}), 7.34−7.18 (6H, m, 6 × HC_{Ar}), 7.14−7.09 (1H, m, HC_{Ar}), 7.06 (1H, dd, J = 8.3, 1.0 Hz, HC_{Ar}), 5.58 (2H, s, PhCH_2N), 3.91 (3H, s, CH_3O); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C: 156.8, 146.0, 141.8, 136.6, 135.7 (5 × C_{Ar}), 131.6 (HC_{Ar}), 131.5 ($C(1)$), 130.2, 129.0 (2 × C_{Ar}), 128.9, 128.9, 128.4, 127.8, 126.7, 122.0 (6 × HC_{Ar}), 121.7 (C_{Ar}), 121.1, 119.8 (2 × HC_{Ar}), 115.9 ($C(4)$), 111.5, 109.7 (2 × HC_{Ar}), 55.8 (CH_3O), 47.0 (PhCH_2N).

*3-((3r,5r,7r)-Adamantan-1-yl)-9-benzyl-9H-pyrido[3,4-b]indole (**24**).* This compound was prepared according to general procedure D, affording **24** (73 mg, 61%) as a brown solid. Mp: 241−243 °C. IR ν_{max} (thin film): 2901, 2846, 1464, 1452, 738, 698 cm^{-1}. HRMS: calcd for $C_{28}H_{30}N_2$, 393.23253 $[M + H]^+$, found m/z 393.23257, Δ = 0.12 ppm. ^1H NMR (500 MHz, $CDCl_3$) δ_H: 8.82 (1H, d, J = 1.0 Hz, $HC(1)$), 8.17 (1H, d, J = 7.8 Hz, HC_{Ar}), 7.96 (1H, d, J = 1.0 Hz, $HC(4)$), 7.54 (1H, ddd, J = 8.3, 7.2, 1.1 Hz, HC_{Ar}), 7.43 (1H, d, J = 8.3 Hz, HC_{Ar}), 7.30−7.23 (4H, m, 4 × HC_{Ar}), 7.22−7.18 (2H, m, 2 × HC_{Ar}), 5.53 (2H, s, PhCH_2N), 2.19−2.15 (3H, m, 3 × CH), 2.14 (6H, d, J = 2.9 Hz, RC(CH_2)$_3$), 1.84 (6H, t, J = 3.1, 3 × CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C: 158.0, 140.7, 135.7, 134.0 (4 × C_{Ar}), 129.9 ($C(1)$), 128.3 (C_{Ar}), 127.8, 127.1, 126.7, 125.7, 120.7 (5 × HC_{Ar}), 120.6 (C_{Ar}), 118.5 (HC_{Ar}), 108.5 ($C(4)$), 108.2 (HC_{Ar}), 46.0 (PhCH_2N), 41.6 (RC-(CH_2)$_3$), 37.6 (RC(CH$_2$)$_3$), 35.9 (CH$_2$), 28.0 (CH).

*9-Benzyl-3-(4-fluorophenyl)-4-methyl-9H-pyrido[3,4-b]indole (**25**).* This compound was prepared according to general procedure D, affording **25** (58 mg, 52%) as a brown solid. Mp: 183−185 °C. IR ν_{max} (thin film): 3056, 1455 1219, 731, 699 cm^{-1}. HRMS: calcd for $C_{25}H_{19}FN_2$, 367.16050 $[M + H]^+$, found m/z 367.16034, Δ = −0.45 ppm. ^1H NMR (500 MHz, $CDCl_3$) δ_H: 8.78 (1H, s, $HC(1)$), 8.32 (1H, d, J = 7.8 Hz, HC_{Ar}), 7.62−7.54 (3H, m, 3 × HC_{Ar}), 7.49 (1H, d, J = 8.2, HC_{Ar}), 7.35 (1H, t, J = 7.6 Hz, HC_{Ar}), 7.37−7.24 (3H, m, 3 × HC_{Ar}), 7.21−7.14 (4H, m, 4 × HC_{Ar}), 5.59 (2H, s, PhCH_2N), 2.89 (3H, s, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C: 161.2 (d, J = 246 Hz, CF), 147.0, 140.6 (2 × C_{Ar}), 136.1 (d, J = 3.3 Hz, $CCHCHCF$), 135.4, 134.6 (2 × C_{Ar}) 130.5 (d, J = 8.1 Hz, $CHCF$), 128.2 (HC_{Ar}), 127.9 ($HC(1)$), 127.4 (C_{Ar}), 126.8 (d, J = 6.2 Hz, $CHCHF$), 125.5 (HC_{Ar}), 123.8 (C_{Ar}), 123.1 (HC_{Ar}), 121.2 (C_{Ar}), 118.9, 114.0, 113.8, 108.6 (4 × HC_{Ar}), 45.8 (PhCH_2N), 16.5 (CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F: 115.4 (tt, J = 8.8, 5.5 Hz).

*3-(Benzo[d][1,3]dioxol-5-yl)-9-benzyl-4-methyl-9H-pyrido[3,4-b]-indole (**26**).* This compound was prepared according to general procedure D, affording **26** (71 mg, 61%) as a brown solid. Mp: 152−155 °C. IR ν_{max} (thin film): 2890, 1459, 725 cm^{-1}. HRMS: calcd for $C_{25}H_{19}N_2$, 379.14410 $[M + H]^+$, found m/z 379.14352, Δ = −1.53 ppm. ^1H NMR (500 MHz, $CDCl_3$) δ_H: 8.84 (1H, d, J = 0.9 Hz, $HC(1)$), 8.30 (1H, d, J = 0.9 Hz, $HC(4)$), 8.20 (1H, d, J = 7.8 Hz, HC_{Ar}), 7.64−7.54 (3H, m, 3 × HC_{Ar}), 7.43 (1H, d, J = 8.3 Hz, HC_{Ar}), 7.34−7.22 (4H, m, 4 × HC_{Ar}), 7.20−7.16 (2H, m, 2 × HC_{Ar}), 6.94 (1H, d, J = 8.1 Hz, HC_{Ar}), 6.01 (2H, s, O_2CH_2), 5.54 (2H, s, PhCH_2N); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C: 148.2, 147.5, 147.5, 141.9, 136.5, 135.8, 135.1 (7 × C_{Ar}), 131.6 ($HC(1)$), 129.8 (C_{Ar}), 129.0, 128.6, 127.9, 126.6, 121.9 (5 × HC_{Ar}), 121.6 (C_{Ar}), 120.4, 120.0 (2 × HC_{Ar}), 110.8 ($HC(4)$), 109.8, 108.5, 107.4 (3 × HC_{Ar}), 101.2 (O_2CH_2), 47.0 (PhCH_2N).

Synthesis of 2-(1-Benzyl-2-(1,3-dioxolan-2-yl)-1*H*-indol-3-yl)-1,3-diphenylpropan-1-one (27). A fresh solution of LiHMDS was prepared in a dry vial, adding sequentially dry THF (7.3 mL), HMDS (290 μL, 1.39 mmol, 2.5 equiv), and a 2.5 M solution of *n*BuLi (1.39 mmol, 558 μL, 2.5 equiv) and stirring at −78 °C for 10 min. Acetophenone (130 μL, 1.07 mmol, 2 equiv) was then added at 0 °C and stirred for 15 min. In a second dry vial were added bromo indole **1** (200 mg, 558 μmol) and Pd(d*t*bpf)Cl$_2$ (18 mg, 27.9 μmol, 5 mol %). The flask was sealed, evacuated, and backfilled with argon twice. The freshly formed enolate solution was then transferred via syringe to the flask. The mixture was stirred at 50 °C for 24 h in an oil bath. After cooling to room temperature, benzyl bromide (166 μL, 1.39 mmol, 2.5 equiv) was added, and the mixture was stirred at 90 °C for 24 h. The resulting mixture was filtered through a plug of silica and concentrated in vacuo. The crude product was purified by flash column chromatography (eluted with 9:1 petroleum ether:EtOAc) to afford product **27** (177 mg, 65%) as a brown solid. Mp: 134−135 °C. IR ν_{max} (thin film): 3060, 3027, 2924, 1679, 1083, 742, 697 cm^{-1}. HRMS: calcd for $C_{33}H_{30}O_3N$, 488.22202 $[M + H]^+$, found m/z 488.22195, Δ = −0.14 ppm. ^1H NMR (400 MHz, C_6D_6) δ_H: 8.24 (2H, ddd, J = 8.2, 1.9, 1.5 Hz, HC_{Ar}), 8.05 (1H, d, J = 8.05 Hz, HC_{Ar}), 7.17−7.14 (1H, m, HC_{Ar}), 7.12−6.89 (12H, m, HC_{Ar}), 6.86 (1H, d, J = 8.2 Hz, HC_{Ar}), 6.72 (2H, ddd, J = 7.6, 1.9, 1.3 Hz, 2 × HCAr), 5.92 (1H, s, CH(OR)$_2$), 5.39 (1H, dd, J = 8.4, 6.0 Hz, CH$_2$CHC(O)), 5.15 (1H, d, J = 17.1 Hz, PhCH_aH$_b$Ar), 5.09 (1H, d, J = 17.1 Hz, PhCH$_a$$H_b$Ar), 3.99 (1H, dd, J = 13.5, 6.0 Hz, PhCH_aH$_b$CH), 3.59 (1H, dd, J = 13.5, 8.4 Hz, PhCH$_a$CH_bCH), 3.36−3.13 (4H, m, (OCH_2)$_2$); ^{13}C NMR (100 MHz, C_6D_6) δ_C: 198.9 (C(O)), 140.8, 138.3, 137.6, 137.3 (4 × C_{Ar}), 132.0 (HC_{Ar}), 129.9, (C_{Ar}), 129.4, 128.8, 128.3, 128.0, 128.0, 126.7 (6 × HC_{Ar}), 126.3 (C_{Ar}), 125.9, 125.8, 123.1, 120.5, 120.3 (5 × HC_{Ar}), 113.9 (C_{Ar}), 110.3 (HC_{Ar}), 99.5 (CH(OR)$_2$), 64.6

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($O_2C_aH_2C_bH_2$), 64.3 ($O_2C_aH_2C_bH_2$), 48.0 ($CH_2CHC(O)$), 47.5 ($PhCH_2Ar$), 38.2 (CH_2CH)

*4,9-Dibenzyl-3-phenyl-9H-pyrido[3,4-b]indole (**28**).* This compound was prepared according to general procedure B on a 0.18 mmol scale, affording **28** (75 mg, 96%) as an off-white solid. Mp: 201−204 °C. IR ν_{max} (thin film): 3056, 3026, 1448, 740, 728, 699 cm^{-1}. HRMS: calcd for $C_{31}H_{25}N_2$, 425.20123 $[M + H]^+$, found m/z 425.20102, Δ = −0.48 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.95 (1H, s, $HC(1)$), 7.89 (1H, d, J = 8.0 Hz, HC_{Ar}), 7.55−7.44 (4H, m, 4 × HC_{Ar}), 7.42−7.10 (14H, m, 14 × HC_{Ar}), 5.64 (2H, s, $PhCH_2N$), 4.68 (2H, s, $PhCH_2Ar$); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 150.3, 141.8, 141.0, 139.7, 136.5, 136.0 (6 × C_{Ar}), 130.3 ($HC(1)$), 129.5, 129.0 (2 × HC_{Ar}), 128.9 (C_{Ar}), 128.7, 128.2, 128.0, 128.0, 127.9, 127.4, 126.7, 126.1 (8 × HC_{Ar}), 126.0 (C_{Ar}), 124.4 (HC_{Ar}), 121.5 (C_{Ar}), 120.1, 109.6 (2 × HC_{Ar}), 47.0 ($PhCH_2N$), 36.4 ($PhCH_2Ar$).

*4-Allyl-9-benzyl-3-phenyl-9H-pyrido[3,4-b]indole (**29**).* This compound was prepared according to general procedure F, affording **29** (62 mg, 54%) as an off-white solid. Mp: 156−158 °C. IR ν_{max} (thin film): 3056, 2926, 1487, 739, 700 cm^{-1}. HRMS: calcd for $C_{27}H_{23}N_2$, 375.18558 $[M + H]^+$, found m/z 375.18552, Δ = −0.16 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.75 (1H, s, $HC(1)$), 8.09 (1H, d, J = 8.0 Hz, HC_{Ar}), 7.52 (2H, d, J = 7.0 Hz, 2 × HC_{Ar}), 7.44 (1H, t, J = 7.5 Hz, HC_{Ar}), 7.39−7.25 (4H, m, 4 × HC_{Ar}), 7.23−7.05 (6H, m, 6 × HC_{Ar}), 6.23−6.10 (1H, m, $ArCH_2CHCH_2$), 5.48 (2H, s, $PhCH_2N$), 5.08 (1H, dd, J = 10.3, 1.3 Hz, $CH_{cis}H_{trans}CHAr$), 4.87 (1H, dd, J = 17, 1.3 Hz, $CH_{cis}H_{trans}CHAr$), 3.92−3.84 (2H, m, $ArCH_2CHCH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 149.8, 141.8, 141.1, 136.5, 135.9 (5 × C_{Ar}), 135.6 ($ArCH_2CHCH_2$), 130.0, 129.5, 129.0 (3 × HC_{Ar}), 128.4 (C_{Ar}), 128.0, 128.0, 127.9, 127.4, 126.6 (5 × HC_{Ar}), 125.9 (C_{Ar}), 124.6 (HC_{Ar}), 121.4 (C_{Ar}), 120.0 (HC_{Ar}), 116.8 ($ArCH_2CHCH_2$), 109.7 (HC_{Ar}), 47.0 ($PhCH_2N$), 34.5 ($ArCH_2CHCH_2$).

*9-Benzyl-4-(4-methoxybenzyl)-3-phenyl-9H-pyrido[3,4-b]indole (**30**).* This compound was prepared according to general procedure F, affording **30** (74 mg, 53%) as a yellow solid. Mp: 208−209 °C. IR ν_{max} (thin film): 3058, 2932, 2835, 1244, 735, 699 cm^{-1}. HRMS: calcd for $C_{32}H_{26}N_2O$, 455.21179 $[M + H]^+$, found m/z 455.21158, Δ = −0.46 ppm. ^1H NMR (400 MHz, $CDCl_3$) δ_H: 8.80 (1H, s, $HC(1)$), 7.78 (1H, d, J = 8.0 Hz, HC_{Ar}), 7.42−7.30 (4H, m, 4 × HC_{Ar}), 7.28−7.08 (8H, m, 8 × HC_{Ar}), 7.05−6.98 (1H, m, HC_{Ar}), 6.94 (2H, d, J = 8.6 Hz, 2 × HC_{Ar}), 6.70−6.65 (2H, m, 2 × HC_{Ar}), 5.49 (2H, s, $PhCH_2N$), 4.47 (2H, s, $PMBCH_2Ar$), 3.63 (3H, s, CH_3O); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 157.9, 150.2, 141.8, 141.0, 136.5, 136.0, 131.7 (7 × C_{Ar}), 130.3 ($C(1)$), 129.5, 129.1, 129.0 (3 × HC_{Ar}), 128.9 (C_{Ar}), 128.0, 128.0, 127.9, 127.4, 126.7 (5 × HC_{Ar}), 126.4 (C_{Ar}), 124.5 (HC_{Ar}), 121.5 (C_{Ar}), 120.1, 114.1, 109.6 (3 × HC_{Ar}), 55.2 (CH_3O), 47.0 ($PhCH_2N$), 35.6 ($PMBCH_2Ar$).

*9-Benzyl-4-(naphthalen-2-ylmethyl)-3-phenyl-9H-pyrido[3,4-b]-indole (**31**).* This compound was prepared according to general procedure F, affording **31** as a brown solid (70 mg, 48%). Mp: 181−183 °C. IR ν_{max} (thin film): 3052, 734, 699 cm^{-1}. HRMS: calcd for $C_{35}H_{27}N_2$, 475.21688 $[M + H]^+$, found m/z 475.21644, Δ = −0.91 ppm. ^1H NMR (500 MHz, $CDCl_3$) δ_H: 9.01 (1H, s, $HC(1)$), 7.88 (1H, d, J = 8.1 Hz, HC_{Ar}), 7.85−7.81 (2H, m, 2 × HC_{Ar}), 7.61 (1H, d, J = 7.8 Hz, HC_{Ar}), 7.57−7.52 (2H, m, 2 × HC_{Ar}), 7.51−7.46 (3H, m, 3 × HC_{Ar}), 7.45−7.25 (11H, m, 11 × HC_{Ar}), 7.09−7.03 (1H, m, HC_{Ar}), 5.66 (2H, s, $PhCH_2N$), 4.84 (2H, s, $C_{10}H_7CH_2Ar$); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C: 150.3, 141.9, 140.9, 137.4, 136.5, 136.1, 133.8, 132.2 (8 × C_{Ar}), 130.5 ($C(1)$), 129.5, 129.0 (2 × HC_{Ar}), 129.0 (C_{Ar}), 128.5, 128.1, 128.0, 127.9, 127.8, 127.6, 127.5, 127.0, 126.7, 126.3, 126.0 (11 × HC_{Ar}), 125.8 (C_{Ar}), 125.4, 124.4 (2 × HC_{Ar}), 121.5 (C_{Ar}), 120.5, 109.6 (2 × HC_{Ar}), 47.1 ($PhCH_2N$), 36.8 ($C_{10}H_7CH_2Ar$).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00299.

Spectroscopic data for all new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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