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A Scalable Method for Regioselective 3-Acylation of 2-Substituted Indoles under Basic Conditions

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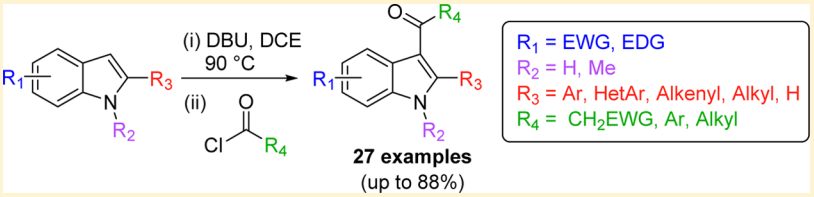
Supporting Information



ABSTRACT: Privileged structures such as 2-arylindoles are recurrent molecular scaffolds in bioactive molecules. We here present an operationally simple, high yielding and scalable method for regioselective 3-acylation of 2-substituted indoles under basic conditions using functionalized acid chlorides. The method shows good tolerance to both electron-withdrawing and donating substituents on the indole scaffold and gives ready access to a variety of functionalized 3-acylindole building blocks suited for further derivatization.

INTRODUCTION

The concept of privileged structures was introduced over 25 years ago to describe molecular scaffolds that show activity at a range of unrelated biological targets.[1] The concept embraces a wide number of structural moieties including spiro-piperidines, 1,1′-biphenyl-2-tetrazoles and 2-arylindoles, that target a variety of receptor families.[2−4] Ligands based on the 2-arylindole scaffold have been attributed diverse biological activities including antimycobacterial properties (**1**, Figure 1), and the scaffold has been used as a starting point for the generation of ligands for several G protein-coupled receptors (GPCRs), e.g., **2** and **3**.[5−7] As part of our medicinal chemistry program targeting GPCRs, we recently reported our synthetic endeavors to access substituted 3-acyl 2-arylindole building blocks (e.g., **4**).[8] Such building blocks are useful intermediates in the synthesis of potentially bioactive ligands, and are as such of general interest to medicinal chemists.

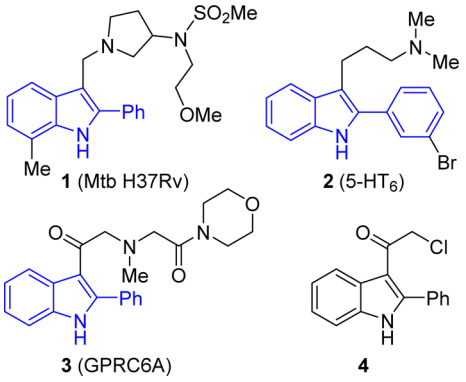


Figure 1. Examples of biologically active compounds based on the 2-arylindole privileged structure: **1** (*Mycobacterium tuberculosis* H37Rv),[5] **2** (5-HT6),[6] and **3** (GPRC6A).[7] Indole **4** is a useful building block that was used in the synthesis of ligand **3**.[7]

We have previously reported the method by Bergman et al.[9] for 3-chloroacetylation of 2-arylindoles (pyridine and chloroacetyl chloride in toluene).[8] However, more recently we have found that the method is unsatisfactory in terms of scope. Thus, we were prompted to investigate alternatives for the acylation of indoles with the aim of finding a simple, more general and scalable synthetic approach. Reports of 3-chloroacetylation of 2-substituted indoles are rare.[10−12] However, a wide range of methods are available for selective 3-acylation of 2-unsubstituted indoles (i.e., 1*H*-indoles). With the exception of the report by Bergman et al.,[9] the use of 1,5-diazabicyclo[4.3.0]-non-5-ene (DBN),[13] and the use of indole zinc salts,[14,15] most acylation methods to date involve the use of Lewis acid catalysis. Ottoni et al. reported successful acylation with acid chlorides, anhydrides and nitriles in good yields using various Lewis acids ($AlCl_3$, $TiCl_4$, $SnCl_4$).[16] Similar findings have been reported by others using acid chlorides and diethyl- or dimethylaluminum chloride,[17,18] $ZrCl_4$,[19] $AlCl_3$ in ionic liquids,[20] or $TiCl_4$-mediated acylation using *N*-acylbenzotriazoles.[21] Slätt et al. reported the use of mixed anhydrides as acylating reagents,[22] while more recent reports make use of transition metal catalysis.[23−26] Collectively, these papers cover electron-rich and poor indoles and acylating reagents. However, the vast majority of reported acylating reagents are non-functionalized with little or no potential for further

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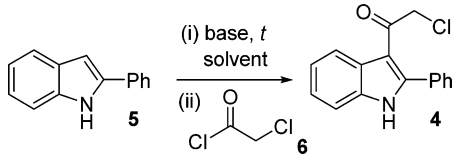
derivatization. Furthermore, several methods suffer from inconvenient reaction conditions, such as reactive or sensitive reagents, laborious workup procedures, or are limited in scope to only *N*-methylated indoles. Ideally, we sought an operationally simple, robust and scalable method that could give us access to multigram quantities of 3-acylated 2-arylindoles. Moreover, the acylating agent should be functionalized to facilitate further derivatization. Of the available methods, we found that of Bergman et al. the most attractive because it provides an operationally very simple procedure, and decided to unravel the potential of this method.

RESULTS AND DISCUSSION

Using indole **5** we screened acylation conditions with chloroacetyl chloride **6** and a series of organic bases with basicity ranging from moderate to strong, and solvents ranging from nonpolar to polar aprotic at varying temperatures and concentrations (Table 1).

Table 1. Reaction Optimization for 3-Chloroacetylation of 2-Phenylindole 5[a]



entry	solvent (conc **5**, M)	base (equiv)	**6** (equiv)	*t* (°C)	yield (%)[b]
1	PhMe (0.2)	py (1.2)	1.1	60	66
2	MeCN (0.2)	py (1.2)	1.1	60	40
3	DCE (0.2)	py (1.2)	1.1	60	68
4	PhMe (0.2)	DBU (1.2)	1.1	60	32
5	MeCN (0.2)	DBU (1.2)	1.1	60	36
6	DCE (0.2)	DBU (1.2)	1.1	60	69
7	DCE (0.2)	DMAP (1.2)	1.1	60	2
8	DCE (0.2)	DBN (1.2)	1.1	60	59
9	DCE (0.2)	–	1.1	60	23
10	DCE (0.2)	DBU (1.6)	1.5	60	70
11	DCE (0.2)	DBU (1.2)	1.1	90	94
12	DCE (0.2)	DBU (1.2)	1.1	95	89
13	DCE (0.2)	DBU (1.2)	1.1	90[c]	60
14	DCE (0.2)	DBU (1.2)	1.1[d]	90	56
15	DCE (0.3)	DBU (1.2)	1.1	90	95
16	DCE (0.3)	DBU (0.15)	1.1	90	79

[a]Reactions were run under argon using **5** (0.3 mmol) in capped 10 mL microwave vials in a heating block (see Supporting Information for details and optimization data). [b]HPLC yield of **4** at 254 nm after 6 h. [c]**6** was added at room temperature and the vial was subsequently heated at 90 °C. [d]Chloroacetic anhydride was used instead of **6**.

We found that the choice of base and solvent had a great effect on the reaction outcome, in particular in terms of reaction rate and side-product formation. When pyridine was employed as the base in nonpolar solvents (e.g., entry 1) fast conversion was achieved but significant side-product formation was also observed. Switching to more polar solvents such as DCE gave a similar result and acetonitrile gave extensive side-product formation (entries 2 and 3). Side-product formation was reduced by employing DBN, and in particular DBU that gave good conversion to indole **4** in most solvents, but most efficiently in DCE (entries 6 and 8). To improve the reaction rate the equivalents of acyl chloride **6** was increased (entry 10), which mainly led to formation of additional side-products. However, raising the concentration and reaction temperature (entries 11 and 15) led to full conversion of the starting material in 6 h. Performing the reaction without base or with catalytic amounts of DBU reduced the reaction rate and caused an increase in side-product formation (entries 9 and 16). Employing chloroacetic anhydride as acylating reagent also led to slower conversion (entry 14). Importantly, we found that the acyl chloride must be added at 90 °C and not at room temperature (followed by heating) as this leads to poor conversion and multiple side-products (entry 13).

With the optimized conditions in hand, we sought to explore the substrate scope. A range of 2-arylindoles bearing electron-withdrawing and donating substituents, and indoles bearing heteroaryl, alkenyl, and alkyl substituents, as well as 1*H*-indole were subjected to chloroacetylation (Scheme 1). Indole starting materials were acquired commercially or synthesized according to literature methods.[27,28]

As shown in Scheme 1, substituted 2-arylindoles were regioselectively acylated in the indole 3-position in good to excellent yields (**4**, **8a**–**o**). The method shows good functional group tolerance with indoles bearing potentially labile groups such as nitriles, esters, and 2-furanyl substituents, as well as a variety of electron withdrawing and donating groups. In addition, the method is applicable to indoles bearing alkenyl and alkyl substituents in the 2-position (**8p**–**q**), and the synthesis of indole **8h** illustrates that this method is equally applicable to *N*-alkylindoles. The reaction conditions proved amenable to scale-up, as illustrated by the synthesis of 11 g of indole **4** after recrystallization. While the stereoelectronic properties of 2-arylindoles do not significantly affect the yield, it does influence the reaction time considerably. Indoles bearing substituents in the 2-position other than aryl groups (**8p**–**q**) were very reactive and full conversion was reached in less than 1 h, with substantial formation of side-products. In an attempt to improve the reaction it was performed at lower temperatures but to no avail (see Supporting Information for details). Next, we explored the use of acylating agents other than **6**, with focus on functionalized acid chlorides that provide handles for further synthesis (Scheme 2).

Electron-deficient acid chlorides **9** produced the highest yields and least side-products (**10a**, **10b**, and **10f**), while nonfunctionalized and electron-rich acid chlorides reacted slowly and produced many side-products (**10d**, **10g**, and **10h**). The synthesis of phthalimide-derivatized indole **10e** also proceeded very slowly, but without significant side-product formation, and for the synthesis of malonic ester derivative **10c** conversion to product was rapid, but resulted in a poor yield due to a challenging purification.

In order to better understand the stereoelectronic properties governing the reaction, we devised a series of experiments where steric bulk and electron density was varied systematically (Scheme 3).

The data shows that increased steric bulk and electron density of the acid chloride retards the reaction (e.g., **4** vs **10a** and **11a**), with pivaloyl chloride being completely unreactive. Taken together, the results presented in Schemes 2 and 3 show that the present method works well for 3-acylation of 2-arylindoles using electron deficient acid chlorides. However, for bulky and/or electron rich acid chlorides the reaction is too slow to be synthetically useful.

With respect to the reaction mechanism we wondered whether DBU is simply a scavenger base or if it plays a more

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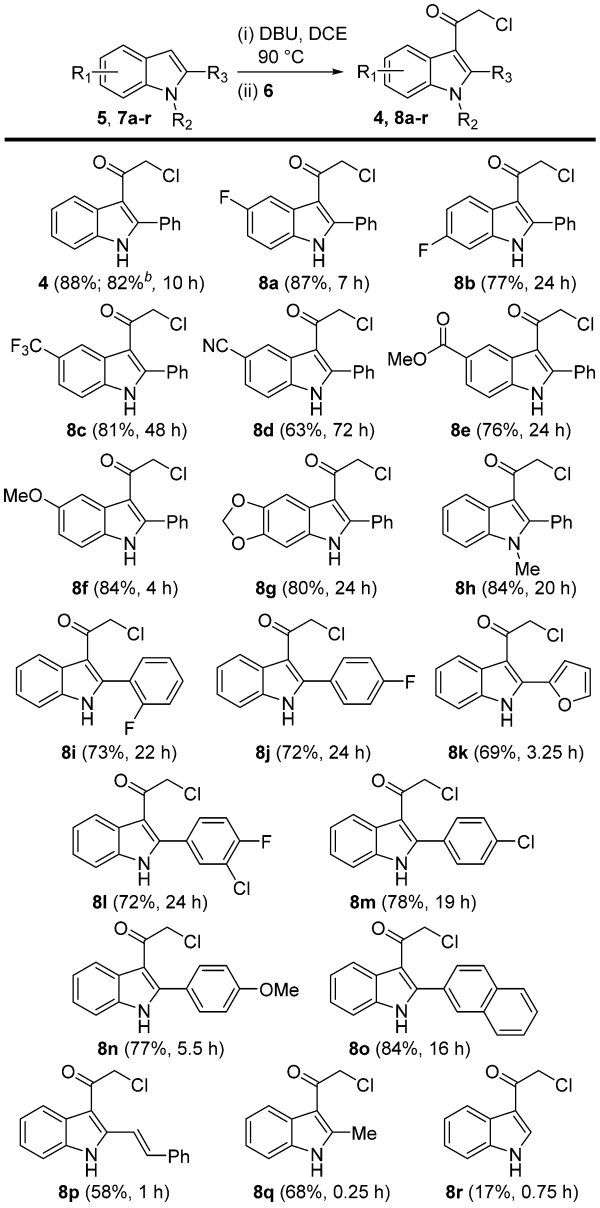
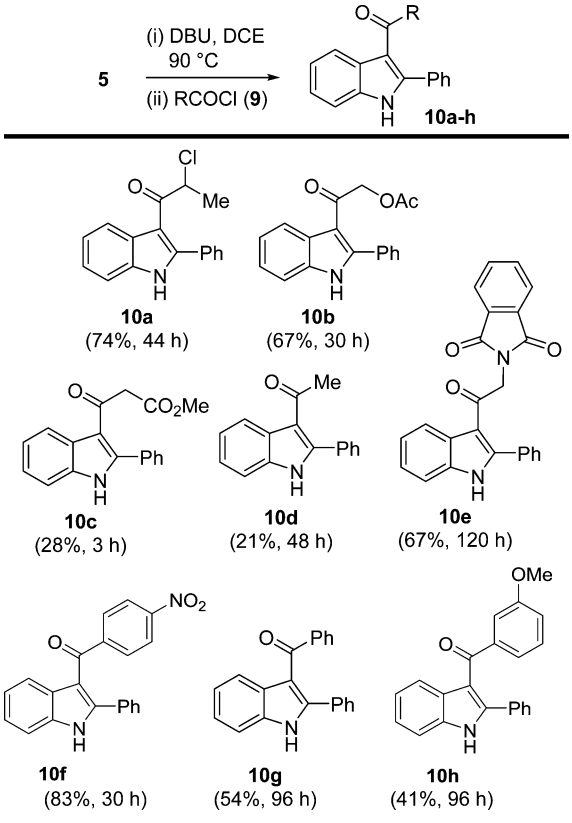
Scheme 1. 3-Chloroacetylation of 2-Substituted Indoles (5, 7a–q) and 1*H*-Indole 7r[a]

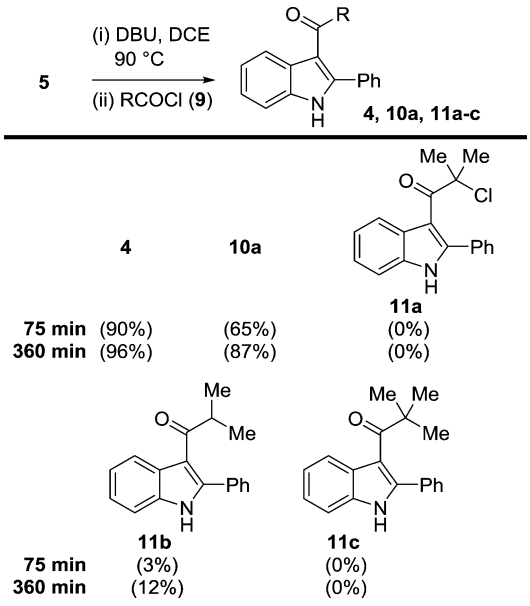


[a]Representative procedure: indole (1 mmol), DCE (3 mL/mmol indole) and DBU (1.2 equiv) were mixed and heated to 90 °C under argon, followed by addition of chloroacetyl chloride (1.1 equiv). Isolated yields. [b]Yield after purification by recrystallization from gram-scale synthesis (11 g isolated).

Scheme 2. Acylation of 2-Phenylindole 5 Using Acid Chlorides 9



Scheme 3. Effect of the Acylating Agent's Stereoelectronic Properties[a]



[a]Yields are based on HPLC analysis at 254 nm.

active role. Taylor et al. have proposed that the closely related base DBN catalyzes 3-acylation of *N*-methylated 1*H*-indoles via nucleophilic catalysis.[13] A similar mechanism may be in play with the present method as the reaction rate drops significantly in the absence of DBU (Table 1, entry 9). However, general base catalysis by concomitant abstraction of the indole N–H and acylation at the 3-position may also play a significant role by markedly increasing the reaction rate. This hypothesis is supported by the fact that the reaction time for the synthesis of *N*-methylated indole **8h** was doubled compared to that of **4** (Scheme 1). Furthermore, the use of catalytic DBU decreased the reaction rate, and resulted in increased side-product formation (Table 1, entry 16). Thus, there is evidence to suggest that DBU has a dual role as a general base catalyst and scavenger base. Possible base-induced haloketene formation as a major reaction pathway is unlikely because nonenolizable acid chlorides undergo facile acylation (**10f–h**, Scheme 2).

Finally, we decided to compare our method to a number of representative literature methods for acylation of free N–H

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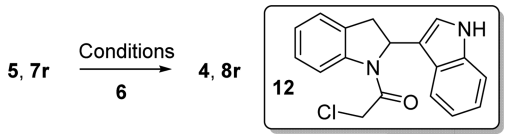
indoles (Table 2). None of the selected methods have previously been reported for the acylation of 2-arylindoles,

Table 2. Comparison of Methods for the 3-Chloroacetylation of Indoles 7r and 5



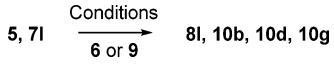
		yield (%)[a]	
method [ref]	conditions	4	8r
Bergman [9]	py, PhMe	56	28
Ottoni [16]	$SnCl_4$, CH_2Cl_2, $MeNO_2$	n.p.	s.p.
Guchhait [19]	$ZrCl_4$, DCE	13	n.p.
Okauchi [17]	Et_2AlCl, CH_2Cl_2	87	29
this work	DBU, DCE	88	17

[a]Isolated yield. n.p. = no product isolated, s.p. = side product **12** isolated (38%).

thus in addition to 2-phenylindole **5**, we included 1*H*-indole **7r** for which these methods were developed.

In our hands, only the methods of Bergman et al.,[9] and Okauchi et al.[17] were viable on both scaffolds. Notably, the method of Ottoni et al.[16] only produced a complex mixture in the case of 2-phenylindole and a major side product **12** in the case of 1*H*-indole. Lewis acid-induced indole dimerization is a known reaction,[29] and thus not a surprising outcome under these conditions. On the basis of the good result with the method by Okauchi et al. we decided to evaluate the generality of the method and compare it to our method (Table 3).

Table 3. Acylation of 2-Arylindoles by the Method of Okauchi et al.[17] and the Method Presented Herein



	yield (%)[a] (time)			
conditions	8l	10b	10d	10g
Et_2AlCl, CH_2Cl_2	78	s.p.	82	92
0 °C	(4 h)	(8 h)	(3.5 h)	(3.5 h)
DBU, DCE	72	67	21	54
90 °C	(24 h)	(30h)	(48 h)	(96 h)

[a]Isolated yield. s.p. = side product.

The results show that the method of Okauchi et al. generally achieves fast conversion to the acylated product in good yields. In comparison with the method presented herein the method of Okauchi et al. appears better for nonfunctionalized acid chlorides (e.g., **10d** and **10g**), while for functionalized and electron deficient acid chloride our method is comparable or better (e.g., **4**, **8l**, and **10b**). In the case of indole **10b** the method of Okauchi et al. resulted in a mixture of side-products (see Supporting Information for details). For substrates that have no functional groups sensitive to Et_2AlCl the method of Okauchi et al. is advantageous in terms of reaction time. However, the use of pyrophoric Et_2AlCl limits the method to small-scale synthesis. Moreover, the workup procedure for this method was found to be laborious.

In conclusion, we present an operationally simple, robust and scalable procedure for regioselective 3-acylation of 2-substituted indoles with electron deficient acid chlorides. The reaction is achieved under basic conditions, which complements existing methods with respect to functional group tolerance. The synthesis of a variety of functionalized 2-substituted 3-acylindoles was demonstrated providing easy access to this class of important building blocks.

EXPERIMENTAL SECTION

General Procedures. *Imine Synthesis (GP-Imine).* A round-bottom flask was charged with an aniline derivative (1 equiv) and a methyl-aryl ketone (1 equiv). Anhydrous toluene (approximately 1 mL/mmol aniline) and 3 Å molecular sieves (approximately 0.7 g/mmol aniline) were added. The mixture was stirred vigorously at ambient temperature under nitrogen or argon until TLC analysis indicated acceptable product formation (1−5.5 days). CH_2Cl_2 (50 mL) was added and the molecular sieves were filtered off through a plug of Celite. The solids were washed thoroughly with EtOAc (30 mL) and the combined organic phases were concentrated in vacuo to afford the crude imine product as an oil or as a solid.

Oxidative Cyclization (GP-Cyclization). According to the procedure by Wei et al.[27] the crude imine (1 equiv), tetra-*n*-butyl ammonium bromide (2 equiv) and $Pd(OAc)_2$ (0.1 equiv) were dissolved in anhydrous DMSO (1 mL/0.2 mmol imine). The flask was evacuated, then fitted with an oxygen balloon and stirred at 60 °C in an oil bath until TLC analysis indicated full consumption of the imine starting material (20−28 h). The reaction mixture was transferred to a separation funnel using sulfate buffer (125 mL) and EtOAc (30 mL). The phases were separated and the aqueous phase was extracted with EtOAc (typically 2 × 30 mL). The combined organic phases were washed with saturated $NaHCO_3$ and brine (typically 75 mL each), dried (Na_2SO_4), filtered and concentrated in vacuo to afford the crude product as a purple to black solid. Purification by column chromatography (EtOAc in *n*-heptane) followed by recrystallization from a suitable solvent gave the indole product.

3-Acylation of Indoles (GP-Acylation). A microwave vial was charged with a 2-arylindole (0.32−1.50 mmol) and a stir bar, and the vial was capped. Anhydrous DCE (3 mL/mmol indole) was added and the vial was flushed with argon for 3−4 min (1 balloon). DBU (1.2 equiv) was added and the mixture was heated in an oil bath or heating block to 90 °C. Once the temperature was reached, the acylating agent (1.1 equiv) was added as a single portion and the solution was stirred until satisfactory conversion of starting material had occurred (0.25 h to 5 days depending on the indole and acid chloride). The heating was stopped and the vial was allowed to cool. The reaction mixture was taken up in EtOAc (125 mL) and sulfate buffer (50 mL). The phases were separated and the organic phase was washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL), dried (Na_2SO_4), filtered and concentrated to give the crude solid product. Purification by column chromatography (mixtures of EtOAc, *n*-heptane, CH_2Cl_2 and MeOH as indicated) gave the indole products.

2-Chloro-1-(2-phenyl-1*H*-indol-3-yl)ethanone (4). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 2-phenylindole (0.29 g, 1.50 mmol), DCE (4.5 mL), DBU (0.27 mL, 1.8 mmol), and chloroacetyl chloride (0.131 mL, 1.65 mmol). The solution was stirred for 10 h. Purification by column chromatography (0.2% MeOH in CH_2Cl_2, v/v) gave indole **4** (0.36 g, 88%) as a light-green solid: TLC R_f = 0.4 (0.2% MeOH in CH_2Cl_2, v/v); HPLC t_R = 6.65 min (A); IR (neat) ν_{max} = 3210, 3063, 1634, 1616, 1147, 1427; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.32 (s, 1H; NH), 8.18−8.16 (m, 1H; indole-H4), 7.68−7.65 (m, 2H; Ph-H2, H2′), 7.60−7.57 (m, 3H; Ph-H3, H3′, H4), 7.47−7.45 (m, 1H; indole-H7), 7.29−7.23 (m, 2H; indole-H6, H5), 4.33 (s, 2H; CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 186.8 (C=O), 145.4 (indole-C2), 135.6 (indole-C7a), 132.1 (Ph-C1), 129.80 (Ph-C2, C2′), 129.79 (Ph-C4), 128.6 (Ph-C3, C3′), 126.9 (indole-C3a), 123.3, 122.2 (indole-C6, C5), 121.3 (indole-C4), 111.8 (indole-C7), 111.6 (indole-C3), 48.1 (CH_2); LRMS (ESI+) *m*/*z* found 270.0 $[M + H]^+$. The analytical data is in agreement with that previously reported by us.[7]

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Large-Scale Synthesis. A dry two-necked 250 mL round-bottom flask was charged with 2-phenylindole (9.66 g, 50.0 mmol) and a stir bar, and the flask was fitted with a condenser. Anhydrous DCE (150 mL) was added and the flask was evacuated and refilled with argon three times. DBU (9.0 mL, 60 mmol), was added and the solution was heated at 90 °C in a heating block for 15 min. Chloroacetyl chloride (4.4 mL, 55 mmol) was then added and the reaction mixture was stirred for 9 h under argon. After cooling, the reaction mixture was taken up in EtOAc (1 L) and sulfate buffer (250 mL). The phases were separated and the organic phase was washed with sulfate buffer (100 mL), saturated $NaHCO_3$ solution (300 mL) and brine (300 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to afford the crude product as brown solid. Recrystallization from absolute EtOH gave indole **4** (11.0 g, 82%) as gray solid in two crops. The analytical data is identical to that reported above for **4**.

5-Fluoro-2-phenyl-1*H*-indole (7a). *Imine Synthesis.* 4-Fluoroaniline (0.853 mL, 9.00 mmol) and acetophenone (1.052 mL, 9.00 mmol) was dissolved in anhydrous toluene (6 mL) and 3 Å molecular sieves (4 g) were added. The mixture was stirred vigorously at ambient temperature for 23 h under nitrogen. CH_2Cl_2 (50 mL) was added and the molecular sieves were filtered off. The organic phase was concentrated in vacuo to afford the crude product as an orange colored solid. Recrystallization from dry *n*-pentane gave imine (*E*)-4-fluoro-*N*-(1-phenylethylidene)aniline (1.32 g, 69%) as white needles in three crops: TLC R_f = 0.85 (50% EtOAc in *n*-heptane, v/v); HPLC t_R = 5.68 min (A; hydrolyzes on the column); IR (neat) ν_{max} = 2989, 1631, 1498, 1203; mp 87.5−88.5 °C (*n*-pentane; lit.[30] 86−87 °C); ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.98−7.97 (m, 2H; Ph-H2, H2′), 7.53−7.46 (m, 3H; Ph-H3, H3′, H4), 7.20−7.17 (m, 2H; Ar−H3, H3′), 6.83−6.81 (m, 2H; Ar−H2, H2′), 2.21 (s, 3H; CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.8 (d, J = 1 Hz; C═N), 158.5 (d, $^1J_{CF}$ = 237 Hz; CF), 147.6 (d, $^4J_{CF}$ = 3 Hz; aryl-C1), 138.8 (Ph-C1), 130.6 (Ph-C4), 128.3 (Ph-C3, C3′), 127.1 (Ph-C2, C2′), 120.9 (d, $^3J_{CF}$ = 8 Hz; aryl-C2, C2′), 115.5 (d, $^2J_{CF}$ = 22 Hz; aryl-C3, C3′), 17.1 (CH_3). The analytical data is in agreement with that reported by others.[30]

Oxidative Cyclization. A Schlenk flask was charged with imine (1.00 g, 4.69 mmol), *n*-Bu_4NBr (3.02 g, 9.39 mmol), and $Pd(OAc)_2$ (0.105 g, 0.469 mmol). Anhydrous DMSO (24 mL) was added and the flask was evacuated and refilled with oxygen. The flask was stirred at 60 °C under an atmosphere of oxygen for 2 h, then open to atmosphere overnight. Additional $Pd(OAc)_2$ (0.053 g, 0.23 mmol) was added, and a new balloon of oxygen was fitted after 22.5 h to push the reaction to completion. After stirring for a total of 25 h the reaction mixture was transferred to a separation funnel using sulfate buffer (125 mL) and EtOAc (30 mL). The phases were separated and the aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ (75 mL), brine (75 mL), dried (Na_2SO_4), filtered and concentrated in vacuo to afford the crude product as a purple solid. Purification by column chromatography (10% EtOAc in *n*-heptane, v/v) gave indole **7a** (0.80 g, 81%) as an off-white solid: TLC R_f = 0.25 (10% EtOAc in *n*-heptane, v/v); HPLC t_R = 7.18 min (A); IR (neat) ν_{max} = 3435, 2323, 1588, 1457, 1206; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.62 (br s, 1H; NH), 7.87−7.84 (m, 2H; Ph-H2, H2′), 7.49−7.44 (m, 2H; Ph-H3, H3′), 7.38 (dddd, J = 9, 5, 1, 0.5 Hz, 1H; indole-H7), 7.33 (tt, J = 7, 1 Hz, 1H; Ph-H4), 7.28 (ddt, J = 10, 2.5, 0.5 Hz, 1H; indole-H4), 6.93 (ddd, J = 9.5, 9, 2.5 Hz, 1H; indole-H6), 6.89 (dd, J = 2.5, 1.0 Hz, 1H; indole-H3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.1 (d, $^1J_{CF}$ = 230 Hz; CF), 139.5 (indole-C2), 133.8 (indole-C7a), 131.8 (Ph-C1), 128.9 (Ph-C3, C3′), 128.8 (d, $^3J_{CF}$ = 10 Hz; indole-C3a), 127.7 (Ph-C4), 125.1 (Ph-C2, C2′), 112.2 (d, $^3J_{CF}$ = 10 Hz, indole-C7), 109.6 (d, $^2J_{CF}$ = 26 Hz, indole-C6), 104.4 (d, $^2J_{CF}$ = 23 Hz, indole-C4), 98.8 (d, $^4J_{CF}$ = 5 Hz, indole-C3); LRMS (ESI+) m/z found 211.9 $[M + H]^+$. The data is in agreement with that reported by others.[31,32]

6-Fluoro-2-phenyl-1*H*-indole (7b). According to the procedure by Yang et al.[28] a dry 50 mL Schlenk flask was charged with methyl 6-fluoro-1*H*-indole (0.34 g, 2.50 mmol), phenylboronic acid (0.46 g, 3.75 mmol) and $Pd(OAc)_2$ (0.06 g, 0.25 mmol). Acetic acid (25 mL) was added and the flask was flushed with oxygen for 3−4 min. The solution was stirred at ambient temperature under oxygen (1 atm) for 20 h, then concentrated in vacuo. EtOAc (25 mL) was added and the mixture was filtered through a plug of Celite. The solids were washed with EtOAc (50 mL), the combined organic phases were transferred to a separation funnel and washed with sulfate buffer (3 × 30 mL), saturated aqueous $NaHCO_3$ (3 × 30 mL) and brine (3 × 30 mL), dried (Na_2SO_4) and concentrated in vacuo to afford the crude product as a brown solid. Two rounds of purification by column chromatography (30% EtOAc in *n*-heptane, v/v) gave an off-white solid, which was washed with cold *n*-heptane (10 mL) to afford indole **7b** (0.23 g, 44%) as a white solid: TLC R_f = 0.6 (30% EtOAc in *n*-heptane, v/v); HPLC t_R = 7.22 min (A); IR (neat) ν_{max} = 3434, 1593, 1452, 1356, 1225; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.63 (br s, 1H; NH), 7.84−7.81 (m, 2H; Ph-H2, H2′), 7.52 (dd, $^3J_{HH}$ = 9 Hz, $^4J_{HF}$ = 5.5 Hz, 1H; indole-H4), 7.48−7.44 (m, 2H; Ph-H3, H3′), 7.31 (tt, J = 7.5, 1 Hz, 1H; Ph-H4), 7.14 (dd, $^3J_{HF}$ = 10 Hz, $^4J_{HH}$ = 2.5 Hz, 1H; indole-H7), 6.91 (dd, J = 1.5, 1 Hz, 1H; indole-H3), 6.86 (ddd, $^3J_{HF}$ = 10 Hz, $^3J_{HH}$ = 9 Hz, $^4J_{HH}$ = 2.5 Hz, 1H; indole-H5); ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.9 (d, $^1J_{CF}$ = 233 Hz; CF), 138.4 (d, $^5J_{CF}$ = 4 Hz; indole-C2), 137.0 (d, $^3J_{CF}$ = 13 Hz; indole-C7a), 131.9 (Ph-C1), 128.9 (Ph-C3, C3′), 127.4 (Ph-C4), 125.4 (indole-C3a), 124.8 (Ph-C2, C2′), 121.0 (d, $^3J_{CF}$ = 10 Hz; indole-C4), 107.8 (d, $^2J_{CF}$ = 24 Hz; indole-C5), 98.7 (indole-C3), 97.2 (d, $^2J_{CF}$ = 25 Hz; indole-C7); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{14}H_{11}FN^+$ 212.0870, found 212.0879.

2-Phenyl-5-(trifluoromethyl)-1*H*-indole (7c). *Imine Formation.* Synthesized according to **GP-Imine** using 4-trifluoromethylaniline (0.88 mL, 7.0 mmol), acetophenone (0.82 mL, 7.0 mmol), 3 Å molceular sieves (4.9 g) and anhydrous toluene (7 mL). Stirred at ambient temperature for 48 h.

Oxidative Cyclization. Synthesized according to **GP-Cyclization** using the crude imine (1.8 g, 6.8 mmol), *n*-Bu_4NBr (4.41 g, 13.7 mmol), $Pd(OAc)_2$ (0.153 g, 0.68 mmol) and DMSO (34 mL). The mixture was stirred under O_2 at 60 °C for 27 h. Purification by column chromatography (15% EtOAc in *n*-heptane, v/v) and recrystallization from EtOH gave indole **7c** (0.54 g, 30% over 2 steps) as a white solid in two crops: TLC R_f = 0.3 (20% EtOAc in *n*-heptane, v/v); HPLC t_R = 7.55 min (A); IR (neat) ν_{max} = 3433, 3033, 1338, 1102; mp 153.5−154 °C (*n*-heptane; lit.[27] 153−154 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.99 (br s, 1H; NH), 7.93−7.88 (m, 3H; indole-H4, Ph-H2, H2′), 7.58 (dq, J = 8.5, 1 Hz, 1H; indole-H7), 7.52−7.47 (m, 2H; Ph-H3, H3′), 7.40−7.35 (m, 2H; Ph-H4, indole-H6), 7.07−7.06 (m, 1H; indole-H3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 139.9 (C), 138.6 (C), 131.4 (C), 129.0 (Ph-C3, C3′), 128.1 (Ph-C4), 127.9 (C), 125.5 (q, $^1J_{CF}$ = 269 Hz; CF_3), 125.3 (Ph-C2, C2′), 120.2 (q, $^2J_{CF}$ = 31 Hz; indole-C5), 117.8 (q, $^3J_{CF}$ = 3 Hz; indole-C6), 117.5 (q, $^3J_{CF}$ = 4 Hz; indole-C4), 111.9 (indole-C7), 99.5 (indole-C3); LRMS (ESI+) m/z found 262.0 $[M + H]^+$. The data is in agreement with that reported by others.[27]

2-Phenyl-1*H*-indole-5-carbonitrile (7d). *Imine Formation.* Synthesized according to **GP-Imine** using 4-cyanoaniline (0.75 g, 6.35 mmol), acetophenone (0.74 mL, 6.35 mmol), 3 Å molceular sieves (4.5 g) and anhydrous toluene (7 mL). Stirred at ambient temperature for a total of 5.5 days with the addition of additional toluene (3 mL) and molecular sieves (1 g) after 4.5 days.

Oxidative Cyclization. Synthesized according to **GP-Cyclization** using the crude imine (1.25 g, 5.7 mmol), *n*-Bu_4NBr (3.66 g, 11.4 mmol), $Pd(OAc)_2$ (0.128 g, 0.57 mmol) and DMSO (28 mL). The mixture was stirred under O_2 at 60 °C for 28 h. Purification by column chromatography (25% EtOAc in *n*-heptane, v/v) and recrystallization from EtOH gave indole **7d** (0.43 g, 31% over 2 steps) as a white solid in three crops: TLC R_f = 0.35 (30% EtOAc in *n*-heptane, v/v); HPLC t_R = 6.83 min (A); IR (neat) ν_{max} = 3317, 2219, 1452, 1332; mp 201−202.5 °C (EtOH; lit.[33] 194−196 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (br s, 1H; NH), 8.06 (d, J = 1.5 Hz, 1H; indole-H4), 7.91−7.88 (m, 2H; Ph-H2, H2′), 7.56 (dt, J = 8.5, 1 Hz, 1H; indole-H7), 7.52−4.47 (m, 2H; Ph-H3, H3′), 7.45 (dd, J = 8.5, 1.5 Hz, 1H; indole-H6), 7.38 (tt, J = 7.5, 1 Hz, 1H; Ph-H4), 7.05 (d, J = 1.5 Hz, 1H; indole-H3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 140.2 (C), 138.8 (C), 131.1 (C), 129.0 (Ph-C3, C3′), 128.4 (C), 128.2 (Ph-C4), 125.5 (indole-H4), 125.4 (Ph-C2, C2′), 124.2 (indole-H6), 120.6 (C), 112.4

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(indole-H7), 101.5 (C), 99.3 (indole-C3); LRMS (ESI+) m/z found 219.1 $[M + H]^+$. The data is agreement with that reported by others.[33]

Methyl 2-phenyl-1*H*-indole-5-carboxylate (7e). According to the procedure by Yang et al.[28] a dry 50 mL Schlenk flask was charged with methyl 1*H*-indole-5-carboxylate (0.45 g, 2.57 mmol), phenylboronic acid (0.47 g, 3.85 mmol) and $Pd(OAc)_2$ (0.03 g, 0.13 mmol). Acetic acid (25 mL) was added and the flask was flushed with oxygen for 3−4 min. The solution was then stirred at ambient temperature under oxygen (1 atm) for 40 h. The reaction mixture was concentrated in vacuo. EtOAc (15 mL) was added and the mixture was filtered through a plug of Celite. The solids were washed with EtOAc (50 mL), the combined organic phases were transferred to a separation funnel and washed with sulfate buffer (3 × 30 mL), saturated aqueous $NaHCO_3$ (3 × 30 mL) and brine (3 × 30 mL), dried (Na_2SO_4) and concentrated in vacuo to afford the crude product as a brown solid. Purification by column chromatography (30% EtOAc in *n*-heptane, v/v) gave a white solid, which was recrystallized from EtOH to afford **7e** (0.19 g, 29%) as off-white flakes in two crops: TLC R_f = 0.6 (30% EtOAc in *n*-heptane, v/v); HPLC t_R = 6.99 min (A); IR (neat) ν_{max} = 3345, 2945, 1697, 1688, 1610; mp 187.5−188 °C (EtOH; lit.[34] 186−187 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.93 (br s, 1H; NH), 8.25−8.24 (m, 1H; indole-H4), 7.90−7.87 (m, 2H; Ph-H2, H2′), 7.74 (dd, J = 8.5, 1.5 Hz, 1H; indole-H6), 7.51−7.46 (m, 3H; indole-H7, Ph-H3, H3′), 7.38−7.36 (m, 1H; Ph-H4), 7.06 (dd, J = 2, 1 Hz, 1H; indole-H3), 3.85 (s, 3H; CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.1 (C═O), 139.7 (indole-C7a), 139.5 (indole-C2), 131.6 (Ph-C1), 129.0 (Ph-C3, C3′), 128.2 (indole-C3a), 127.9 (Ph-C4), 125.2 (Ph-C2, C2′), 122.54, 122.51 (indole-H6, H4), 120.9 (indole-C5), 111.2 (indole-C7), 99.9 (indole-C3), 51.7 (CH_3); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{16}H_{14}NO_2^+$ 252.1019, found 252.1022.

5-Methoxy-2-phenyl-1*H*-indole (7f). *Imine Formation.* Synthesized according to **GP-Imine** using 4-methoxyaniline (0.75 g, 8.1 mmol), acetophenone (0.95 mL, 8.1 mmol), 3 Å molecular sieves (5.6 g) and anhydrous toluene (7 mL). Stirred at ambient temperature for 42 h.

Oxidative Cyclization. Synthesized according to **GP-Cyclization** using the crude imine (1.25 g, 5.6 mmol), *n*-Bu_4NBr (3.58 g, 11.1 mmol), $Pd(OAc)_2$ (0.125 g, 0.56 mmol) and DMSO (28 mL). The mixture was stirred under O_2 at 60 °C for 28 h. Purification by column chromatography (20% EtOAc in *n*-heptane, v/v) and recrystallization from EtOH gave indole **7f** (0.68 g, 38% over 2 steps) as a white solid in three crops: TLC R_f = 0.3 (20% EtOAc in *n*-heptane, v/v); HPLC t_R = 6.97 min (A); IR (neat) ν_{max} = 3425, 3002, 1620, 1477, 1216; mp 170−171 °C (EtOH; lit.[27] 169−170 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.35 (br s, 1H; NH), 7.84−7.81 (m, 2H; Ph-H2, H2′), 7.46−7.42 (m, 2H; Ph-H3, H3′), 7.32−7.27 (m, 2H; Ph-H4, indole-H7), 7.02 (d, J = 2.5 Hz, 1H; indole-H4), 6.81 (dd, J = 2, 1 Hz, 1H, indole-H3), 6.74 (dd, J = 9, 2.5 Hz, 1H; indole-H6), 3.76 (s, 3H; CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.6 (indole-C5), 138.1, 132.3, 132.2, 129.0 (4 × C), 128.8 (Ph-C3, C3′), 127.2 (Ph-C4), 124.8 (Ph-C2, C2′), 111.9, 111.8 (indole-H6, H7), 101.6 (indole-H4), 98.5 (indole-H3), 55.2 (CH_3); LRMS (ESI+) m/z found 224.1 $[M + H]^+$. The data is in agreement with that reported by others.[27]

2-(2-Fluorophenyl)-1*H*-indole (7i). *Imine Formation.* Synthesized according to **GP-Imine** using aniline (0.73 mL, 8.0 mmol), 2-fluoroacetophenone (0.98 mL, 8.0 mmol), 3 Å molecular sieves (5.6 g) and anhydrous toluene (7 mL). Stirred at ambient temperature for 25 h. The crude imine (1.49 g) was isolated as a yellow to green oil.

Oxidative Cyclization. Synthesized according to **GP-Cyclization** using the crude imine (1.49 g, 7.0 mmol), *n*-Bu_4NBr (4.50 g, 14.0 mmol), $Pd(OAc)_2$ (0.157 g, 0.70 mmol) and DMSO (35 mL). The mixture was stirred under O_2 at 60 °C for 20 h. Purification by column chromatography (10% EtOAc in *n*-heptane, v/v) and recrystallization from MeOH gave indole **7i** (0.79 g, 47% over 2 steps) as white needles in three crops: TLC R_f = 0.25 (10% EtOAc in *n*-heptane, v/v); HPLC t_R = 7.23 min (A); IR (neat) ν_{max} = 3476, 3053, 1460, 1209, 754; mp 99−100 °C (MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.48 (br s, 1H; NH), 7.95−7.90 (m, 1H; ArH), 7.58 (ddt, J = 8, 1.2, 0.8 Hz, 1H; indole-H4), 7.45 (ddt, J = 8.5, 1.2, 0.8 Hz, 1H; indole-H7), 7.41−7.31 (m, 3H; ArH), 7.14 (ddd, J = 8.5, 7, 1 Hz, 1H; indole-H6), 7.02 (ddd, J = 8, 7, 1 Hz, 1H; indole-H5), 6.92 (ddd, J = 3, 2, 1 Hz, 1H; indole-H3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.9 (d, $^1J_{CF}$ = 247 Hz; CF), 136.7 (C), 131.3 (d, J_{CF} = 2 Hz; C), 129.0 (d, J_{CF} = 8 Hz; Ar−CH), 128.3 (C), 127.7 (d, J_{CF} = 4 Hz; Ar−CH), 124.9 (d, J_{CF} = 3 Hz; Ar−CH), 122.0 (indole-C6), 120.3 (indole-C4), 120.1 (d, J_{CF} = 12 Hz; C), 119.4 (indole-C5), 116.4 (d, $^2J_{CF}$ = 22 Hz; Ar−C3), 111.4 (indole-C7), 102.5 (d, $^4J_{CF}$ = 9 Hz, indole-C3); LRMS (ESI+) m/z found 212.1 $[M + H]^+$. The data is in agreement with that reported by others.[35]

2-(Furan-2-yl)-1*H*-indole (7k). *Imine Formation.* Synthesized according to **GP-Imine** using aniline (0.73 mL, 8.0 mmol), 2-acetylfuran (0.81 mL, 8.0 mmol), 3 Å molecular sieves (5.6 g) and anhydrous toluene (7 mL). Stirred at ambient temperature for 4.5 days.

Oxidative Cyclization. Synthesized according to **GP-Cyclization** using the crude imine (1.28 g, 6.9 mmol), *n*-Bu_4NBr (4.45 g, 13.8 mmol), $Pd(OAc)_2$ (0.155 g, 0.69 mmol) and DMSO (35 mL). The mixture was stirred under O_2 at 60 °C for 23 h. Purification by column chromatography (10% EtOAc in *n*-heptane, v/v) and recrystallization from *n*-heptane gave indole **7k** (0.39 g, 31% over 2 steps) as off-white flakes in two crops: TLC R_f = 0.65 (50% EtOAc in *n*-heptane, v/v); HPLC t_R = 6.85 min (A); IR (neat) ν_{max} = 3425, 3051, 1602, 1347; mp 129−129.5 °C (*n*-heptane; lit.[36] 120−123 °C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.52 (br s, 1H; NH), 7.76 (dd, J = 1.5, 0.5 Hz, 1H; furan-H5), 7.52 (ddt, J = 7, 1.2, 0.8 Hz, 1H; indole-H4), 7.38 (ddd, J = 8.5, 2, 1 Hz, 1H; indole-H7), 7.10 (ddd, J = 8, 7, 1 Hz, 1H; indole-H6), 7.00 (ddd, J = 8, 7, 1 Hz, 1H; indole-H5), 6.86 (ddd, J = 3, 1, 0.5 Hz, 1H; furan-H3), 6.69 (dd, J = 2, 1 Hz, 1H; indole-H3), 6.62 (dd, J = 3, 1.5 Hz, 1H; furan-H4); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.7 (furan-C2), 142.6 (furan-C5), 136.6 (indole-C7a), 129.3 (indole-C2), 128.2 (indole-C3a), 121.7 (indole-C6), 120.0 (indole-C4), 119.4 (indole-C5), 111.9 (furan-C4), 111.2 (indole-C7), 105.8 (furan-C3), 97.6 (indole-C3); LRMS (ESI+) m/z found 184.0 $[M + H]^+$. The data is in agreement with that reported by others.[36]

2-(4-Methoxyphenyl)-1*H*-indole (7n). According to the procedure of Yang et al.[28] a dry 50 mL Schlenk flask was charged with 1*H*-indole (0.30 g, 2.56 mmol), 4-methoxyphenylboronic acid (0.58 g, 3.84 mmol) and $Pd(OAc)_2$ (0.03g, 0.13 mmol). Acetic acid (25 mL) was added and the flask was flushed with oxygen for 3−4 min. The solution was stirred at ambient temperature under oxygen (1 atm) for 23 h. The reaction mixture was concentrated in vacuo and the afforded solids were suspended in EtOAc (20 mL) and filtered off through a plug of Celite. The solids were further washed with EtOAc (50 mL), and the combined organic phases were transferred to a separation funnel, washed with sulfate buffer (3 × 30 mL), saturated aqueous $NaHCO_3$ (3 × 30 mL) and brine (3 × 30 mL), dried (Na_2SO_4) and concentrated in vacuo to afford the crude product as a brown solid. Purification by column chromatography (10% EtOAc in *n*-heptane, v/v) gave a white solid, which was recrystallized from EtOH to give indole **7n** (0.13 g, 22%) as a white solid in two crops: TLC R_f = 0.5 (30% EtOAc in *n*-heptane, v/v); HPLC t_R = 7.07 min (A); IR (neat) ν_{max} = 3430, 1500, 1431, 1397; mp 224−229 °C (EtOH; lit.[37] 227.4−230.8 °C); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.38 (br s, 1H; NH), 7.80−7.78 (m, 2H; Ph-H2, H2′), 7.49 (ddt, J = 8, 1, 0.5 Hz, 1H; indole-H4), 7.36 (ddt, J = 8, 1, 0.5 Hz, 1H; indole-H7), 7.07−7.02 (m, 3H; indole-H6, Ph-H3, H3′), 6.97 (ddd, J = 8, 7, 1 Hz, 1H; indole-H5), 6.75 (dd, J = 2, 0.5 Hz, 1H; indole-H3), 3.81 (s, 3H; CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 158.8 (Ph-C4), 137.7 (indole-C2), 136.9 (indole-C7a), 128.8 (indole-C3a), 126.3 (Ph-C2, C2′), 124.9 (Ph-C1), 121.0 (indole-C6), 119.6 (indole-C4), 119.2 (indole-C5), 114.3 (Ph-C3, C3′), 111.0 (indole-C7), 97.3 (indole-C3), 55.2 (CH_3); LRMS (ESI+) m/z found 224.1 $[M + H]^+$. The analytical data is in agreement will that reported by others.[37]

(*E*)-2-Styryl-1*H*-indole (7p). *Imine Formation.* A 50 mL round-bottom flask was charged with (*E*)-4-phenylbut-3-en-2-one (1.46 g, 10.0 mmol), 3 Å molecular sieves (5 g), anhydrous toluene (10 mL) and aniline (0.91 mL, 10.0 mmol). The mixture was stirred under argon at ambient temperature for 3 days, then heated at 60 °C for 25 h. CH_2Cl_2 (50 mL) was added and the mixture was filtered through a plug of Celite. The solids were washed with EtOAc (50 mL) and the

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combined organic phases were concentrated in vacuo to give the crude imine intermediate as a yellow solid.

Oxidative Cyclization. The crude imine (2.2 g), *n*-Bu_4NBr (6.35 g, 19.7 mmol), and $Pd(OAc)_2$ (0.22 g, 0.98 mmol) were dissolved in anhydrous DMSO (50 mL) and the flask was pump-filled with O_2 four times. The reaction mixture was heated at 60 °C under O_2 for 20 h. Sulfate buffer (150 mL) was added and the aqueous mixture was extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to afford the crude product as a green solid crude. Purification by column chromatography (50% *n*-heptane in CH_2Cl_2, v/v) followed by recrystallization from 2-propanol gave indole **7p** (0.91 g, 42% over 2 steps) as an off-white solid that was washed with cold *n*-heptane and dried under vacuum: TLC R_f = 0.4 (50% *n*-heptane in CH_2Cl_2, v/v); HPLC t_R = 7.43 min (A); IR (neat) ν_{max} = 3407, 2988, 2901, 1417; mp 207−208.5 °C (*i*-PrOH; lit.[36] 202−204 °C) ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.37 (br s, 1H; NH), 7.57−7.55 (m, 2H; Ph-H2, H2′), 7.49 (d, J = 8 Hz, 1H; indole-H4), 7.40−7.38 (m, 2H; Ph-H3, H3′), 7.35 (ddt, J = 8.5, 1, 0.5 Hz, 1H; indole-H7), 7.28−7.24 (m, 2H; Ph-H4, *H*C═CH-Ph), 7.20 (d, J = 16 Hz, 1H; HC═C*H*-Ph), 7.10 (ddd, J = 8.5, 7, 1 Hz, 1H; indole-H6), 6.97 (ddd, J = 8, 7, 1 Hz, 1H; indole-H5), 6.58 (d, J = 1 Hz, 1H; indole-H3), ^{13}C NMR (150 MHz, DMSO-d_6) δ 137.2 (indole-C7a), 136.9, 136.7 (indole-C2, Ph-C1), 128.8 (Ph-C3, C3′), 128.4 (indole-C3a), 127.5 (Ph-C4), 127.1 (HC═*C*H-Ph), 126.1 (Ph-C2, C2′), 122.0 (indole-C6), 120.0 (indole-C4), 119.5 (HC═CH-Ph), 119.2 (indole-C5), 110.9 (indole-C7), 102.9 (indole-C3); LRMS (ESI+) m/z found 220.1 $[M + H]^+$. The data is in agreement with that reported by others.[36]

2-Chloro-1-(5-fluoro-2-phenyl-1*H*-indol-3-yl)ethanone (8a). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, indole **7a** (0.126 g, 0.60 mmol), DCE (1.8 mL), DBU (0.107 mL, 0.72 mmol), and chloroacetyl chloride (0.052 mL, 0.66 mmol). The solution was stirred for 7 h. Purification by column chromatography (30 to 25% *n*-heptane in CH_2Cl_2, v/v) gave indole **8a** (0.15 g, 87%) as a white solid: TLC R_f = 0.2 (30% *n*-heptane in CH_2Cl_2, v/v); HPLC t_R = 6.76 min (A); IR (neat) ν_{max} = 3177, 2972, 1615, 1447; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.44 (s, 1H; NH), 7.88 (ddd, $^3J_{HF}$ = 10 Hz, $^4J_{HH}$ = 3 Hz, $^5J_{HH}$ = 0.5 Hz, 1H; indole-H4), 7.69−7.66 (m, 2H; Ph-H2, H2′), 7.62−7.56 (m, 3H; Ph-H3, H3′, H4), 7.46 (ddd, $^3J_{HH}$ = 9 Hz, $^4J_{HF}$ = 4.5 Hz, $^5J_{HH}$ = 0.5 Hz, 1H; indole-H7), 7.13 (ddd, $^3J_{HF}$ = 9.5 Hz, $^3J_{HH}$ = 9 Hz, $^4J_{HH}$ = 3 Hz, 1H; indole-H6), 4.31 (s, 2H; CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 186.7 (C═O), 158.8 (d, J = 233 Hz; CF), 146.9 (indole-C2), 132.2 (indole-C7a), 131.8 (Ph-C1), 130.0 (Ph-C4), 129.8 (Ph-C2, C2′), 128.7 (Ph-C3, C3′), 127.5 (d, $^3J_{CF}$ = 11 Hz; indole-C3a), 113.1 (d, $^3J_{CF}$ = 10 Hz; indole-C7), 111.7 (d, $^4J_{CF}$ = 4 Hz; indole-C3), 111.4 (d, $^2J_{CF}$ = 26 Hz; indole-C6), 106.4 (d, $^2J_{CF}$ = 25 Hz; indole-C4), 47.9 (CH_2); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{16}H_{12}ClFNO^+$ 288.0586, found 288.0562.

2-Chloro-1-(6-fluoro-2-phenyl-1*H*-indol-3-yl)ethanone (8b). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, indole **7b** (0.208 g, 0.98 mmol), DCE (3.0 mL), DBU (0.176 mL, 1.18 mmol), and chloroacetyl chloride (0.086 mL, 1.08 mmol). The solution was stirred for 24 h. Purification by column chromatography (30% *n*-heptane in CH_2Cl_2, v/v) gave a yellow solid, which was washed with cold EtOAc (1 mL) to give indole **8b** (0.22 g, 77%) as a white solid: TLC R_f = 0.4 (30% EtOAc in *n*-heptane, v/v); HPLC t_R = 6.78 min (A); IR (neat) ν_{max} = 3200, 1625, 1450, 1420, 1100; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.40 (br s, 1H; NH), 8.17 (dd, $^3J_{HH}$ = 9 Hz, $^4J_{HF}$ = 5.5 Hz, 1H; indole-H4), 7.68−7.64 (m, 2H; Ph-H2, H2′), 7.61−7.57 (m, 3H; Ph-H3, H3′, H4), 7.22 (dd, $^3J_{HF}$ = 9.5 Hz, $^4J_{HH}$ = 2.5 Hz, 1H; indole-H7), 7.12 (ddd, $^3J_{HF}$ = 9.5 Hz, $^3J_{HH=}$ 9 Hz, $^4J_{HH}$ = 2.5 Hz, 1H; indole-H5), 4.30 (s, 2H; CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 186.9 (C═O), 159.4 (d, $^1J_{CF}$ = 236 Hz; CF), 146.0 (d, $^5J_{CF}$ = 2 Hz; indole-C2), 135.7 (d, $^3J_{CF}$ = 12 Hz; indole-C7a), 131.8 (Ph-C1), 129.9 (Ph-C4), 129.8 (Ph-C2, C2′), 128.7 (Ph-C3, C3′), 123.6 (indole-C3a), 122.7 (d, $^3J_{CF}$ = 10 Hz; indole-C4), 111.5 (indole-C3), 110.5 (d, $^2J_{CF}$ = 24 Hz; indole-C5), 98.0 (d, $^2J_{CF}$ = 26 Hz; indole-C7), 47.9 (CH_2); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{16}H_{12}ClFNO^+$ 288.0586, found 288.0593.

2-Chloro-1-(2-phenyl-5-(trifluoromethyl)-1*H*-indol-3-yl)-ethanone (8c). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, indole **7c** (0.19 g, 0.73 mmol), DCE (2.2 mL), DBU (0.133 mL, 0.87 mmol), and chloroacetyl chloride (0.64 mL, 0.81 mmol). The solution was stirred for 48 h. Purification by column chromatography (30% *n*-heptane in CH_2Cl_2, v/v) gave indole **8c** (0.20 g, 81%) as a white solid: TLC R_f = 0.3 (30% *n*-heptane in CH_2Cl_2, v/v); HPLC t_R = 7.13 min; IR (neat) ν_{max} = 3151, 1622, 1592, 1447, 1439; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.73 (s, 1H; NH), 8.52 (br m, 1H; indole-H4), 7.72−7.70 (m, 2H; Ph-H2, H2′), 7.66−7.58 (m, 5H; indole-H6, H7, Ph-H3, H3′, H4), 4.33 (s, 2H; CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 187.2 (C═O), 147.4 (indole-C2), 137.3 (indole-C7a), 131.4 (Ph-C1), 130.2 (Ph-C4), 129.8 (Ph-C2, C2′), 128.8 (Ph-C3, C3′), 126.4 (indole-C3a), 125.2 (q, $^1J_{CF}$ = 268 Hz; CF_3), 122.9 (q, $^2J_{CF}$ = 30 Hz; indole-C5), 119.9 (q, $^3J_{CF}$ = 3 Hz; indole-C6), 118.7 (q, $^3J_{CF}$ = 3 Hz; indole-C4), 112.8 (indole-C7), 112.0 (indole-C3), 47.9 (CH_2); HRMS (ESI+) m/z $[M + Na]^+$ Calcd for $C_{17}H_{11}ClF_3NNaO^+$ 360.0373, found 360.0373.

3-(2-Chloroacetyl)-2-phenyl-1*H*-indole-5-carbonitrile (8d). Synthesized according to **GP-Acylation** using a 10 mL microwave vial, indole **7d** (0.071 g, 0.32 mmol), DCE (1 mL), DBU (0.058 mL, 0.39 mmol), and chloroacetyl chloride (0.029 mL, 0.36 mmol). The solution was stirred for 72 h. Two consecutive rounds of purification by column chromatography (0.5% MeOH in CH_2Cl_2, v/v) gave indole **8d** (0.061 g, 63%) as a white solid: TLC R_f = 0.35 (0.75% MeOH in CH_2Cl_2, v/v); HPLC t_R = 6.53 min; IR (neat) ν_{max} = 3141, 2988, 2905, 2219, 1610, 1449; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.83 (s, 1H; NH), 8.56 (dd, J = 1, 0.5 Hz, 1H; indole-H4), 7.71−7.69 (m, 2H; Ph-H2, H2′), 7.66 (dd, J = 8.5, 1 Hz, 1H; indole-H6), 7.64−7.59 (m, 4H; indole-H7, Ph-H3, H3′, H4), 4.40 (s, 2H; CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 187.1 (C═O), 147.5 (indole-C2), 137.5 (indole-C7a), 131.1 (Ph-C1), 130.3 (Ph-C4), 129.8 (Ph-C2, C2′), 128.7 (Ph-C3, C3′), 126.6 (indole-C3a), 126.4 (indole-C4), 126.2 (indole-C6), 120.1 (CN), 113.3 (indole-C7), 111.6 (indole-C3), 104.4 (indole-C5), 48.2 (CH_2); HRMS (ESI+) m/z $[M + Na]^+$ Calcd for $C_{17}H_{11}ClN_2NaO^+$ 317.0452, found 317.0457.

Methyl 3-(2-chloroacetyl)-2-phenyl-1*H*-indole-5-carboxylate (8e). Synthesized according to **GP-Acylation** using a 10 mL microwave vial, indole **7e** (0.155 g, 0.62 mmol), DCE (1.8 mL), DBU (0.11 mL, 0.74 mmol), and chloroacetyl chloride (0.054 mL, 0.68 mmol). The solution was stirred for 24 h. Purification by column chromatography (30% EtOAc in *n*-heptane, v/v) gave a pale brown solid, which was washed with cold EtOAc (8 mL) to give indole **8e** (0.15 g, 76%) as a white solid: TLC R_f = 0.2 (30% EtOAc in *n*-heptane, v/v); HPLC t_R = 6.57 min (A); IR (neat) ν_{max} = 3119, 1702, 1614, 1439; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.65 (br s, 1H; NH), 8.88−8.87 (m, 1H; indole-H4), 7.90 (dd, J = 8.5, 2 Hz, 1H; indole-H6), 7.71−7.70 (m, 2H; Ph-H2, H2′), 7.63−7.59 (m, 3H; Ph-H3, H3′, H4), 7.55 (dd, J = 8.5, 0.5 Hz, 1H; indole-H7), 4.31 (s, 2H; CH_2), 3.89 (s, 3H; CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 187.1 (ketone-C═O), 166.9 (ester-C═O), 147.0 (indole-C2), 138.2 (indole-C7a), 131.5 (Ph-C1), 130.2 (Ph-C4), 129.8 (Ph-C2, C2′), 128.8 (Ph-C3, C3′), 126.6 (indole-C3a), 124.3 (indole-C6), 123.7 (indole-C4), 123.5 (indole-C5), 112.3 (indole-C3), 111.9 (indole-C7), 51.9 (CH_3), 47.9 (CH_2); HRMS (ESI+) m/z $[M + Na]^+$ Calcd for $C_{18}H_{14}ClNNaO_3^+$ 350.0554, found 350.0547.

2-Chloro-1-(5-methoxy-2-phenyl-1*H*-indol-3-yl)ethanone (8f). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, indole **7f** (0.223 g, 1.00 mmol), DCE (3 mL), DBU (0.18 mL, 1.2 mmol), and chloroacetyl chloride (0.88 mL, 1.1 mmol). The solution was stirred for 4 h. Purification by column chromatography (0.2% MeOH in CH_2Cl_2, v/v) gave indole **8f** (0.25 g, 84%) as a yellow solid: TLC R_f = 0.4 (0.2% MeOH in CH_2Cl_2, v/v); HPLC t_R = 6.60 min; IR (neat) ν_{max} = 3193, 2988, 2901, 1623, 1600, 1572; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.20 (s, 1H; NH), 7.69 (d, J = 2.5 Hz, 1H; indole-H4), 7.66−7.64 (m, 2H; Ph-H2, H2′), 7.60−7.57 (m, 3H; Ph-H3, H3′, H4), 7.35 (d, J = 8.5 Hz, 1H; indole-H7), 6.90 (dd, J = 8.5, 2.5 Hz, 1H; indole-H6), 4.27 (s, 2H; CH_2), 3.81 (s, 3H; CH_3); ^{13}C

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NMR (150 MHz, DMSO-d_6) δ 186.7 (C═O), 155.7 (indole-C5), 145.6 (indole-C2), 132.2 (Ph-C1), 130.5 (indole-C7a), 129.7 (Ph-C2, C2′, C4), 128.6 (Ph-C3, C3′), 127.8 (indole-C3a), 113.0 (indole-C6), 112.6 (indole-C7), 111.6 (indole-C3), 103.2 (indole-C4), 55.3 (CH_3), 47.9 (CH_2); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{17}H_{15}ClNO_2^+$ 300.0786, found 300.0769.

2-Chloro-1-(6-phenyl-5*H*-[1,3]dioxolo[4,5-*f*]indol-7-yl)-ethanone (8g). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 6-phenyl-5*H*-[1,3]dioxolo[4,5-*f*]indole (0.230 g, 0.97 mmol), DCE (3.0 mL), DBU (0.174 mL, 1.16 mmol), and chloroacetyl chloride (0.085 mL, 1.07 mmol). The solution was stirred for 24 h. Purification by column chromatography (30% *n*-heptane in CH_2Cl_2, v/v) gave an orange solid, which was washed with cold EtOAc (10 mL) to yield indole **8g** (0.24 g, 80%) as a yellow solid: TLC R_f = 0.3 (30% EtOAc in *n*-heptane, v/v); HPLC t_R = 6.56 min (A); IR (neat) ν_{max} = 3190, 1591, 1450, 1422, 1035. ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.15 (br s, 1H; NH), 7.63−7.61 (m, 2H; Ph-H2, H2′), 7.59 (d, J = 0.5 Hz, 1H; indole-H4), 7.58−7.55 (m, 3H; Ph-H3, H3′, H4), 6.94 (d, J = 0.5 Hz, 1H; indole-H7), 6.03 (s, 2H; OCH_2O), 4.26 (s, 2H; CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 186.8 (C═O), 145.1 (indole-C5), 144.4 (indole-C6), 143.6 (indole-C2), 132.2 (Ph-C1), 130.5 (indole-C7a), 129.7 (Ph-C2, C2′), 129.6 (Ph-C4), 128.6 (Ph-C3, C3′), 121.0 (indole-C3a), 112.0 (indole-C3), 100.8 (OCH_2O), 100.0 (indole-C4), 92.4 (indole-C7), 47.8 (CH_2); LRMS (ESI+) m/z found 314.0 $[M + H]^+$. The analytical data is in agreement with that previously reported by us.[8]

2-Chloro-1-(1-methyl-2-phenyl-1*H*-indol-3-yl)ethanone (8h). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 1-methyl-2-phenylindole (0.207 g, 1.00 mmol), DCE (3 mL), DBU (0.18 mL, 1.2 mmol), and chloroacetyl chloride (0.087 mL, 1.1 mmol). The solution was stirred for 20 h. Purification by column chromatography (30% *n*-heptane in CH_2Cl_2, v/v) gave indole **8h** (0.24 g, 84%) as a yellow solid: TLC R_f = 0.2 (30% *n*-heptane in CH_2Cl_2, v/v); HPLC t_R = 7.08 min (A); IR (neat) ν_{max} = 3053, 2946, 1646, 1466, 1395; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 (ddd, J = 8, 1.5, 0.5 Hz, 1H; indole-H4), 7.67−7.58 (m, 6H; PhH, indole-H7), 7.36 (ddd, J = 8, 7, 1.5 Hz, 1H; indole-H6), 7.32 (ddd, J = 8, 7, 1.5 Hz, 1H; indole-H5), 4.05 (s, 2H; CH_2), 3.52 (s, 3H; CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 185.9 (C═O), 146.7 (indole-C2), 136.6 (indole-C7a), 130.9 (Ph-C1), 130.3, 130.1, 128.9 (5 × Ph-CH), 126.1 (indole-C3a), 123.4 (indole-C6), 122.8 (indole-C5), 121.5 (indole-C4), 112.2 (indole-C3), 110.9 (indole-C7), 48.0 (CH_2), 31.0 (CH_3); HRMS (ESI+) m/z $[M + Na]^+$ Calcd for $C_{17}H_{14}ClNNaO^+$ 306.0656, found 306.0664.

2-Chloro-1-(2-(2-fluorophenyl)-1*H*-indol-3-yl)ethanone (8i). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, indole **7i** (0.211 g, 1.00 mmol), DCE (3 mL), DBU (0.18 mL, 1.2 mmol), and chloroacetyl chloride (0.88 mL, 1.1 mmol). The solution was stirred for 22 h. Purification by column chromatography (30% *n*-heptane in CH_2Cl_2, v/v) gave indole **8i** (0.21 g, 73%) as an off-white solid: TLC R_f = 0.25 (30% *n*-heptane in CH_2Cl_2, v/v); HPLC t_R = 6.62 min; IR (neat) ν_{max} = 3145, 2988, 1619, 1581, 1436; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.46 (br s, 1H; NH), 8.15−8.13 (m, 1H; indole-H4), 7.69−7.63 (m, 2H; aryl-H), 7.48 (ddd, J = 7, 1, 0.5 Hz, 1H; indole-H7), 7.46−7.43 (m, 1H; aryl-H3), 7.41 (dt, J = 8, 1 Hz, 1H; aryl-H), 7.29 (ddd, J = 8, 7, 1 Hz, 1H; indole-H6), 7.29 (ddd, J = 8, 7, 1 Hz, 1H; indole-H5), 4.44 (s, 2H; CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 186.4 (C═O), 159.4 (d, $^1J_{CF}$ = 246 Hz; CF), 138.1 (indole-C2), 135.8 (indole-C7a), 132.2 (d, J = 8 Hz), 132.1 (d, J = 2 Hz) (2 × aryl-CH), 126.2 (indole-C3a), 124.7 (d, J = 3 Hz, aryl-CH), 123.4 (indole-C6), 122.2 (indole-C5), 121.3 (indole-C4), 120.1 (d, $^2J_{CF}$ = 15 Hz, aryl-C1), 116.0 (d, $^2J_{CF}$ = 21 Hz, aryl-C3), 112.6 (indole-C3), 112.0 (indole-C7), 48.0 (CH_2); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{16}H_{12}ClFNO^+$ 288.0586, found 288.0587.

2-Chloro-1-(2-(4-fluorophenyl)indol-3-yl)ethanone (8j). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 2-(4-fluorophenyl)indole (0.220 g, 1.04 mmol), DCE (3.0 mL), DBU (0.19 mL, 1.25 mmol), and chloroacetyl chloride (0.091 mL, 1.15 mmol). The solution was stirred for 24 h. Purification by column chromatography (30% *n*-heptane in CH_2Cl_2, v/v) gave indole **8j** (0.22 g, 72%) as an off-white solid: TLC R_f = 0.4 (30% EtOAc in *n*-heptane, v/v); HPLC t_R = 6.68 min (A); IR (neat) ν_{max} = 3214, 1632, 1611, 1432, 1099; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.33 (br s, 1H; NH), 8.15 (ddd, J = 8.5, 2, 1 Hz, 1H; indole-H4), 7.75−7.71 (m, 2H; Ph-H2, H2′), 7.46 (ddd, J = 8, 2, 1 Hz, 1H; indole-H7), 7.44−7.40 (m, 2H; Ph-H3, H3′), 7.29−7.23 (m, 2H; indole-H5, H6), 4.38 (s, 2H; CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 186.7 (C═O), 162.9 (d, $^1J_{CF}$ = 246 Hz; CF), 144.3 (indole-C2), 135.6 (indole-C7a), 132.2 (d, $^3J_{CF}$ = 8 Hz; Ph-C2, C2′), 128.5 (d, $^4J_{CF}$ = 3 Hz; Ph-C1), 126.7 (indole-C3a), 123.3, 122.2 (indole-C6, C5), 121.3 (indole-C4), 115.6 (d, $^2J_{CF}$ = 22 Hz; Ph-C3, C3′), 111.9 (indole-C7), 111.6, (indole-C3), 48.3 (CH_2); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{16}H_{12}ClFNO^+$ 288.0586, found 288.0577.

2-Chloro-1-(2-(furan-2-yl)-1*H*-indol-3-yl)ethanone (8k). Synthesized according to **GP-Acylation** using a 10 mL microwave vial, indole **7k** (0.090 g, 0.49 mmol), DCE (1.5 mL), DBU (0.088 mL, 0.59 mmol), and chloroacetyl chloride (0.043 mL, 0.54 mmol). The solution was stirred for 3 h 15 min. Purification by column chromatography (40% *n*-heptane in CH_2Cl_2, v/v) gave indole **8k** (0.088 g, 69%) as a yellow solid: TLC R_f = 0.25 (40% *n*-heptane in CH_2Cl_2, v/v); HPLC t_R = 6.56 min; IR (neat) ν_{max} = 3222, 2988, 1610, 1582, 1410; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.50 (br s, 1H; NH), 8.02 (dd, J = 2, 0.5 Hz, 1H; furan-H5), 7.97−7.96 (m, 1H; indole-H4), 7.66 (dd, J = 3.5, 1 Hz, 1H; furan-H3), 7.53 (ddd, J = 8, 1, 0.5 Hz, 1H; indole-H7), 7.28 (ddd, J = 8, 7, 1 Hz, 1H; indole-H6), 7.24 (ddd, J = 8.5, 7, 1 Hz, 1H; indole-H5), 6.77 (dd, J = 3.5, 2 Hz, 1H; furan-H4), 4.92 (s, 2H; CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 186.5 (C═O), 145.1 (furan-C2), 144.9 (furan-C5), 135.8 (indole-C7a), 133.6 (indole-C2), 125.8 (indole-C3a), 123.4 (indole-C6), 122.2 (indole-C5), 121.2 (indole-C4), 114.4 (furan-C3), 112.5 (furan-C4), 112.3 (indole-C7), 110.2 (indole-C3), 49.4 (CH_2); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{14}H_{11}ClNO_2^+$ 260.0473, found 260.0459.

2-Chloro-1-(2-(3-chloro-4-fluorophenyl)-1*H*-indol-3-yl)-ethanone (8l). Synthesized according to **GP-Acylation** using 2-(3-chloro-4-fluorophenyl)-1*H*-indole (0.246 g, 1.00 mmol), DCE (3.0 mL), DBU (0.18 mL, 1.2 mmol), and chloroacetyl chloride (0.087 mL, 1.1 mmol). The solution was stirred for 24 h. Purification by column chromatography (Gradient; 33% *n*-heptane in CH_2Cl_2, v/v to 100% CH_2Cl_2) gave indole **8l** (0.23 g, 72%) as a light-yellow solid: TLC R_f = 0.2 (33% *n*-heptane in CH_2Cl_2, v/v); HPLC t_R = 6.94 min (A); IR (neat) ν_{max} = 3149, 2984, 1618, 1441; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.40 (br s, 1H; NH), 8.13−8.11 (m, 1H; indole-H4), 7.96 (dd, $^4J_{HF}$ = 7 Hz, $^4J_{HH}$ = 2 Hz, 1H; aryl-H2), 7.71 (ddd, $^3J_{HH}$ = 9 Hz, $^4J_{HF}$ = 5 Hz, $^4J_{HH}$ = 2 Hz, 1H; aryl-H6), 7.62 (dd, $^3J_{HF}$ = 9 Hz, $^3J_{HH}$ = 9 Hz; 1H; aryl-H5), 7.49−7.46 (m, 1H; indole-H7), 7.31−7.24 (m, 2H; indole-H6, H5), 4.51 (s, 2H; CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 186.7 (C═O), 157.9 (d, $^1J_{CF}$ = 248 Hz, aryl-C4), 142.5 (indole-C2), 135.6 (indole-C7a), 132.0 (Aryl-C2), 131.0 (d, $^3J_{CF}$ = 8 Hz, aryl-C6), 129.8 (d, $^4J_{CF}$ = 4 Hz; aryl-C1), 126.4 (indole-C3a), 123.4 (indole-C6), 122.3 (indole-C5), 121.4 (indole-C4), 119.6 (d, $^2J_{CF}$ = 18 Hz, aryl-C3), 117.0 (d, $^2J_{CF}$ = 21 Hz, aryl-C5), 112.0 (indole-C7), 111.7 (indole-C3), 48.6 (CH_2); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{16}H_{11}Cl_2FNO^+$ 322.0196, found 322.0199.

2-Chloro-1-(2-(4-chlorophenyl)-1*H*-indol-3-yl)ethanone (8m). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 2-(4-chlorophenyl)-1*H*-indole (0.23 g, 1.01 mmol), DCE (3.0 mL), DBU (0.18 mL, 1.21 mmol), and chloroacetyl chloride (0.088 mL, 1.11 mmol). The solution was stirred for 19 h. Purification by column chromatography (30% *n*-heptane in CH_2Cl_2, v/v) gave a yellow solid (0.25 g), which was washed with cold EtOAc (10 mL) to give indole **8m** (0.24 g, 78%) as an off-white solid: TLC R_f = 0.45 (30% EtOAc in *n*-heptane, v/v); HPLC t_R = 6.92 min.; IR (neat) ν_{max} = 3398, 1634, 1434, 1090; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.36 (br s, 1H; NH), 8.14−8.12 (m, 1H; indole-H4), 7.72−7.68 (m, 2H; Ph-H2, H2′), 7.66−7.63 (m, 2H; Ph-H3, H3′), 7.48−7.46 (m, 1H; indole-H7), 7.30−7.23 (m, 2H; indole-H5, H6), 4.43 (s, 2H; CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 186.8 (C═O), 143.8 (indole-C2), 135.6 (indole-C7a), 134.6 (Ph-C4), 131.7 (Ph-C2, C2′), 130.9 (Ph-C1), 128.6 (Ph-C3, C3′), 126.6 (indole-C3a), 123.3, 122.3 (indole-C6, C5), 121.3 (indole-C4), 111.9 (indole-C7), 111.6 (indole-C3), 48.4

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(CH_2); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{16}H_{12}Cl_2NO^+$ 304.0290, found 304.0298.

2-Chloro-1-(2-(4-methoxyphenyl)-1*H*-indol-3-yl)ethanone (8n). Synthesized according to **GP-Acylation** using a 10 mL microwave vial, indole **7n** (0.130 g, 0.58 mmol), DCE (1.8 mL), DBU (0.105 mL, 0.70 mmol), and chloroacetyl chloride (0.051 mL, 0.64 mmol). The solution was stirred for 5.5 h. Purification by column chromatography (30% EtOAc in *n*-heptane, v/v) gave the crude product as a brown solid, which was washed with cold EtOAc (10 mL) to afford indole **7n** (0.13 g, 77%) as off-white solid: TLC R_f = 0.3 (30% EtOAc in *n*-heptane, v/v); HPLC t_R = 6.65 min (A); IR (neat) ν_{max} = 3180, 1611, 1437, 1254; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.20 (br s, 1H; NH), 8.16−8.14 (m, 1H; indole-H4), 7.62−7.59 (m, 2H; Ph-H2, H2′), 7.44 (m, 1H; indole-H7), 7.26−7.21 (m, 2H; indole-H5, H6), 7.15−7.12 (m, 2H; Ph-H3, H3′), 4.34 (s, 2H; CH_2), 3.86 (s, 3H; CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 186.8 (C═O), 160.4 (Ph-C4), 145.5 (indole-C2), 135.5 (indole-C7a), 131.2 (Ph-C2, C2′), 127.0 (indole-C3a), 124.0 (Ph-C1), 123.1, 122.1 (indole-C6, C5), 121.2 (indole-C4), 114.1 (Ph-C3, C3′), 111.7 (indole-C7), 111.4 (indole-C3), 55.4 (CH_3), 48.0 (CH_2); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{17}H_{15}ClNO_2^+$ 300.0786, found 300.0786.

2-Chloro-1-(2-(naphthalen-2-yl)-1*H*-indol-3-yl)ethanone (8o). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 2-(2-naphthyl)-indole (0.243 g, 1.00 mmol), DCE (3 mL), DBU (0.18 mL, 1.2 mmol), and chloroacetyl chloride (0.087 mL, 1.1 mmol). The solution was stirred for 16 h. Purification by column chromatography (40 to 30% *n*-heptane in CH_2Cl_2, v/v) gave indole **8o** (0.27 g, 84%) as a light-yellow solid: TLC R_f = 0.3 (40% *n*-heptane in CH_2Cl_2, v/v); HPLC t_R = 7.08 min; IR (neat) ν_{max} = 3138, 2967, 1611, 1439; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.42 (br s, 1H; NH), 8.27 (br d, J = 1 Hz, 1H; naphthyl-H1), 8.19−8.18 (m, 1H; indole-H4), 8.12 (d, J = 8.5 Hz, 1H; naphthyl-H4), 8.08−8.05 (m, 2H; naphthyl-H), 7.77 (dd, J = 8.5, 2 Hz, 1H; naphthyl-H3), 7.67−7.63 (m, 2H; naphthyl-H), 7.50−7.49 (m, 1H; indole-H7), 7.30 (ddd, J = 8, 7, 1 Hz, 1H; indole-H6), 7.27 (ddd, J = 8, 7, 1 Hz, 1H; indole-H5), 4.39 (s, 2H; CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 187.0 (C═O), 145.3 (indole-C2), 135.8 (indole-C7a), 133.1 (naphthyl-C4a), 132.4 (naphthyl-C8a), 129.5 (naphthyl-C2), 129.4 (naphthyl-C1), 128.3, 128.1, 127.8 (naphthyl-C4, 2 × naphthyl-CH), 127.3, 127.03, 126.97 (2 × naphthyl-CH, naphthyl-C3), 126.93 (indole-C3a), 123.3 (indole-C6), 122.3 (indole-C5), 121.4 (indole-C4), 111.9 (indole-C7), 111.8 (indole-C3), 48.2 (CH_2); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{20}H_{15}ClNO^+$ 320.0837, found 320.0820.

(*E*)-2-Chloro-1-(2-styryl-1*H*-indol-3-yl)ethanone (8p). Synthesized according to **GP-Acylation** using indole **7p** (0.219 g, 1.00 mmol), DCE (3.0 mL), DBU (0.18 mL, 1.2 mmol), and chloroacetyl chloride (0.087 mL, 1.1 mmol). The solution was stirred for 1 h. Purification by column chromatography (30% *n*-heptane in CH_2Cl_2, v/v) gave indole **8p** (0.17 g, 58%) as a yellow solid: TLC R_f = 0.3 (30% *n*-heptane in CH_2Cl_2, v/v); HPLC t_R = 7.10 min (A); IR (neat) ν_{max} = 3304, 3061, 3023, 1642, 1626, 1577, 1439; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.39 (br s, 1H; NH), 7.97 (d, J = 17 Hz, 1H; *H*C═CH-Ph), 7.95 (d, J = 8 Hz, 1H; indole-H4), 7.66−7.64 (m, 2H; Ph-H2, H2′), 7.54 (d, J = 16 Hz, 1H; HC═C*H*-Ph), 7.49−7.46 (m, 3H; indole-H7, Ph-H3, H3′), 7.38 (tt, J = 7, 1 Hz, 1H; Ph-H4), 7.27 (ddd, J = 8.5, 7, 1 Hz, 1H; indole-H6), 7.21 (ddd, J = 8, 7, 1 Hz, 1H; indole-H5), 5.07 (s, 2H; CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 187.2 (C═O), 142.3 (indole-C2), 136.3 (indole-C7a), 136.1 (Ph-C1), 134.1 (HC═*C*H-Ph), 129.1 (Ph-C3, C3′), 128.9 (Ph-C4), 126.9 (Ph-C2, C2′), 125.9 (indole-C3a), 123.5 (indole-C6), 121.9 (indole-C5), 121.2 (indole-C4), 118.1 (HC═CH-Ph), 111.7 (indole-C7), 111.6 (indole-C3), 50.1 (CH_2); HRMS (ESI+) m/z $[M + Na]^+$ Calcd for $C_{18}H_{14}ClNNaO^+$ 318.0656, found 318.0663.

2-Chloro-1-(2-methyl-1*H*-indol-3-yl)ethanone (8q). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 2-methylindole (0.164 g, 1.25 mmol), DCE (3.8 mL), DBU (0.224 mL, 1.50 mmol), and chloroacetyl chloride (0.109 mL, 1.38 mmol). The solution was stirred for 0.25 h. Purification by column chromatography (CH_2Cl_2) gave indole **8q** (0.18 g, 68%) as white solid: TLC R_f = 0.3 (CH_2Cl_2); HPLC t_R = 5.96 min (A); IR (neat) ν_{max} = 3259, 3062, 2991, 1638, 1614, 1432; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.01 (s, 1H; NH), 8.01−7.98 (m, 1H; indole-H4), 7.40−7.38 (m, 1H; indole-H7), 7.18−7.15 (m, 2H; indole-H6, H5), 4.92 (s, 2H; CH_2), 2.71 (s, 3H; CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 186.0 (C═O), 145.3 (C2), 134.8 (C7a), 126.5 (C3a), 122.1, 121.7 (C6, C5), 120.6 (C4), 111.4 (C7), 110.9 (C3), 49.5 (CH_2), 15.0 (CH_3); HRMS (ESI+) m/z $[M + Na]^+$ Calcd for $C_{11}H_{10}ClNNaO^+$ 230.0343, found 230.0340.

2-Chloro-1-(1*H*-indol-3-yl)ethanone (8r). Synthesized according to **GP-Acylation** using 1*H*-indole (0.117 g, 1.00 mmol), DCE (3.0 mL), DBU (0.18 mL, 1.2 mmol), and chloroacetyl chloride (0.087 mL, 1.1 mmol). The solution was stirred for 45 min. Two sequential rounds of purification by column chromatography (0.4% MeOH in CH_2Cl_2, v/v, and 40% EtOAc in *n*-heptane, v/v) gave indole **8r** (0.033 g, 17%) as a white solid: TLC R_f = 0.25 (40% EtOAc in *n*-heptane, v/v); HPLC t_R = 5.71 min (A); IR (neat) ν_{max} = 3184, 3050, 2943, 1644, 1432; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (br s, 1H; NH), 8.43 (d, J = 3 Hz, 1H; indole-H2), 8.17−8.15 (m, 1H; indole-H4), 7.51−7.49 (m, 1H; indole-H7), 7.25 (ddd, J = 7.5, 7, 2 Hz, 1H; indole-H6), 7.23 (ddd, J = 7.5, 7, 1.5 Hz, 1H; indole-H5), 4.87 (s, 2H; CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 186.1 (C═O), 136.6 (C7a), 134.7 (C2), 125.4 (C3a), 123.1 (C6), 122.1 (C5), 121.1 (C4), 113.6 (C3), 112.3 (C7), 46.4 (CH_2); HRMS (ESI+) m/z $[M + H]^+$ Calcd for $C_{10}H_9ClNO^+$ 194.0367, found 194.0349.

2-Chloro-1-(2-phenyl-1*H*-indol-3-yl)propan-1-one (10a). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 2-phenylindole (0.193 g, 1.00 mmol), DCE (3.0 mL), DBU (0.18 mL, 1.20 mmol) and 2-chloropropionyl chloride (0.107 mL, 1.10 mmol). The solution was stirred for 44 h. Purification by column chromatography (30% *n*-heptane in CH_2Cl_2, v/v) gave indole **10a** (0.21 g, 74%) as an off-white solid: TLC R_f = 0.4 (30% EtOAc in *n*-heptane, v/v); HPLC t_R = 6.91 min (A); IR (neat) ν_{max} = 3251, 1612, 1449, 1425; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.35 (br s, 1H; NH), 8.15 (ddd, J = 8, 2, 1 Hz, 1H; indole-H4), 7.68−7.65 (m, 2H; Ph-H2, H2′), 7.61−7.57 (m, 3H; Ph-H3, H3′, H4), 7.46 (ddd, J = 8, 2, 1 Hz, 1H; indole-H7), 7.28 (ddd, J = 8, 7, 1 Hz, 1H; indole-H6), 7.25 (ddd, J = 8, 7, 1 Hz, 1H; indole-H5), 4.71 (q, J = 6.5 Hz, 1H; CHCl), 1.46 (d, J = 6.5 Hz, 3H; CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 190.1 (C═O), 145.4 (indole-C2), 135.7 (indole-C7a), 132.0 (Ph-C1), 129.8 (Ph-C4), 129.7 (Ph-C2, C2′), 128.6 (Ph-C3, C3′), 127.2 (indole-C3a), 123.3 (indole-C6), 122.2 (indole-C5), 121.3 (indole-C4), 111.9 (indole-C7), 110.8 (indole-C3), 55.5 (CHCl), 20.4 (CH_3); HRMS (ESI+) m/z $[M + Na]^+$ Calcd for $C_{17}H_{14}ClNNaO^+$ 306.0656, found 306.0668.

2-Oxo-2-(2-phenyl-1*H*-indol-3-yl)ethyl acetate (10b). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 2-phenylindole (0.193 g, 1.00 mmol), DCE (3 mL), DBU (0.18 mL, 1.2 mmol), and acetoxyacetyl chloride (0.12 mL, 1.1 mmol). The solution was stirred for 30 h. Purification by column chromatography (0.5% MeOH in CH_2Cl_2, v/v) gave indole **10b** (0.20 g, 67%) as an off-white solid: TLC R_f = 0.25 (0.5% MeOH in CH_2Cl_2, v/v); HPLC t_R = 6.32 min (A); IR (neat) ν_{max} = 3280, 3060, 1744, 1637, 1449; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.26 (s, 1H; NH), 8.14 (ddd, J = 8, 2, 0.5 Hz, 1H; indole-H4), 7.70−7.67 (m, 2H; Ph-H2, H2′), 7.58−7.56 (m, 3H; Ph-H3, H3′, H4), 7.45 (ddd, J = 8, 2, 0.5 Hz, 1H; indole-H7), 7.26 (ddd, J = 8, 7, 2 Hz, 1H; indole-H6), 7.23 (ddd, J = 8, 7, 2 Hz, 1H; indole-H5), 4.68 (s, 2H; CH_2), 2.04 (s, 3H; CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 188.2 (ketone-C═O), 169.9 (ester-C═O), 145.0 (indole-C2), 135.6 (indole-C7a), 132.4 (Ph-C1), 129.7 (Ph-C2, C2′, C4), 128.6 (Ph-C3, C3′), 126.7 (indole-C3a), 123.1 (indole-C6), 122.1 (indole-C5), 121.3 (indole-C4), 111.8 (indole-C7), 111.1 (indole-C3), 67.2 (CH_2), 20.3 (CH_3); LRMS (ESI+) m/z found 294.0 $[M + H]^+$. The analytical data is in agreement with that previously reported by us.[8]

Methyl 3-oxo-3-(2-phenyl-1*H*-indol-3-yl)propanoate (10c). Synthesized according to **GP-Acylation** using 2-phenylindole (0.193 g, 1.00 mmol), DCE (3.0 mL), DBU (0.18 mL, 1.2 mmol), and methyl 3-chloro-3-oxopropanoate (0.118 mL, 1.10 mmol). The solution was stirred for 3 h 10 min. Purification by two consecutive rounds of column chromatography (0.5% MeOH in CH_2Cl_2, v/v) gave indole **10c** (0.081 g, 28%) as a light yellow solid: TLC R_f = 0.3 (0.5% MeOH

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in CH_2Cl_2, v/v); HPLC t_R = 6.29 min (A); IR (neat) ν_{max} = 3178, 2982, 1732, 1613, 1436; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.26 (br s, 1H; NH), 8.20−8.18 (ddd, J = 8, 1, 0.5 Hz, 1H; indole-H4), 7.65−7.62 (m, 2H; Ph-H2, H2′), 7.58−7.56 (m, 3H; Ph-H3, H3′, H4), 7.44 (ddd, J = 8, 1, 0.5 Hz, 1H; indole-H7), 7.26 (ddd, J = 8, 7, 1 Hz, 1H; indole-H6), 7.23 (ddd, J = 8, 7, 1 Hz, 1H; indole-H5), 3.53 (s, 3H; CH_3), 3.48 (s, 2H; CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 188.1 (ketone-C═O), 168.2 (ester-C═O), 145.7 (indole-C2), 135.4 (indole-C7a), 132.1 (Ph-C1), 129.9 (Ph-C2, C2′), 129.7 (Ph-C4), 128.5 (Ph-C3, C3′), 126.9 (indole-C3a), 123.2 (indole-C6), 122.2 (indole-C5), 121.4 (indole-C4), 113.4 (indole-C3), 111.7 (indole-C7), 51.6 (CH_3), 47.6 (CH_2); HRMS (ESI+) m/z [M + Na]$^+$ Calcd for $C_{18}H_{15}NNaO_3^+$ 316.0944, found 316.0953.

1-(2-Phenyl-1*H*-indol-3-yl)ethanone (10d). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 2-phenylindole (0.193 g, 1.00 mmol), DCE (3 mL), DBU (0.18 mL, 1.2 mmol), and acetyl chloride (0.078 mL, 1.1 mmol). The solution was stirred for 48 h. Purification by column chromatography (CH_2Cl_2) gave indole **10d** (0.049 g, 21%) as an orange colored solid: TLC R_f = 0.25 (CH_2Cl_2); HPLC t_R = 6.35 min (A); IR (neat) ν_{max} = 3176, 2988, 1614, 1412, 745; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.08 (br s, 1H; NH), 8.19 (ddd, J = 8, 2, 0.5 Hz, 1H; indole-H4), 7.65−7.63 (m, 2H; Ph-H2, H2′), 7.58−7.55 (m, 3H; Ph-H3, H3′, H4), 7.42 (ddd, J = 8, 1, 0.5 Hz, 1H; indole-H7), 7.23 (ddd, J = 8, 7, 2 Hz, 1H; indole-H6), 7.19 (ddd, J = 8, 7, 1 Hz, 1H; indole-H5), 2.07 (s, 3H; CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 193.5 (C═O), 144.9 (indole-C2), 135.4 (indole-C7a), 132.7 (Ph-C1), 130.0 (Ph-C2, C2′), 129.3 (Ph-C4), 128.4 (Ph-C3, C3′), 127.0 (indole-C3a), 122.8 (indole-C6), 121.7 (indole-C5), 121.5 (indole-C4), 114.2 (indole-C3), 111.5 (indole-C7), 30.1 (CH_3); LRMS (ESI+) m/z Found 236.0 [M + H]$^+$. The data is in agreement with that reported by others.[38]

2-(2-Oxo-2-(2-phenyl-1*H*-indol-3-yl)ethyl)isoindoline-1,3-dione (10e). A 20 mL microwave vial was charged with 2-phenylindole (0.193 g, 1.00 mmol) and DCE (3 mL). The flask was flushed with argon for approximately 5 min, DBU (0.18 mL, 1.2 mmol) was added and the mixture was heated at 90 °C. Meanwhile, a separate vial was charged with 2-(1,3-dioxoisoindolin-2-yl)acetyl chloride (0.246 g, 1.1 mmol). Addition of DCE (1.5 mL) gave a slurry that was transferred to the reaction mixture using a syringe. The resulting solution was stirred for 5 d. Purification by column chromatography (0.25% MeOH in CH_2Cl_2, v/v) gave indole **10e** (0.25 g, 67%) as an off-white solid: TLC R_f = 0.3 (0.25% MeOH in CH_2Cl_2, v/v); HPLC t_R = 6.80 min (A); IR (neat) ν_{max} = 3303, 2988, 1771, 1709, 1649, 1424; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.39 (s, 1H; NH), 8.14 (ddd, J = 8.5, 1, 0.5 Hz, 1H; indole-H4), 7.91−7.85 (m, 4H; 4 × phthalimide-H), 7.78−7.76 (m, 2H; Ph-H2, H2′), 7.64−7.58 (m, 3H; Ph-H3, H3′, H4), 7.48 (ddd, J = 8, 1, 0.5 Hz, 1H; indole-H7), 7.28 (ddd, J = 8, 7, 1 Hz, 1H; indole-H6), 7.23 (ddd, J = 8.5, 7, 1 Hz, 1H; indole-H5), 4.44 (s, 2H; CH_2); ^{13}C NMR (150 MHz, DMSO-d_6) δ 186.9 (C═O), 167.5 (N(C═O)$_2$), 145.8 (indole-C2), 135.6 (indole-C7a), 134.6 (phthalimide-CH), 132.4 (Ph-C1), 131.6 (phthalimide-C), 129.89 (Ph-C2, C2′), 129.86 (Ph-C4), 128.7 (Ph-C3, C3′), 126.7 (indole-C3a), 123.3 (indole-C6), 123.2 (phthalimide-CH), 122.3 (indole-C5), 121.3 (indole-C4), 111.9 (indole-C7), 111.4 (indole-C3), 45.8 (CH_2); HRMS (ESI+) m/z [M + Na]$^+$ Calcd for $C_{24}H_{16}N_2NaO_3^+$ 403.1053, found 403.1041.

(2-Methyl-1*H*-indol-3-yl)(4-nitrophenyl)methanone (10f). A 20 mL microwave vial was charged with 2-phenylindole (0.145 g, 0.75 mmol) and DCE (1.25 mL). The flask was flushed with argon for approximately 5 min, DBU (0.135 mL, 0.9 mmol) was added and the mixture was heated at 90 °C. Meanwhile, a separate vial was charged with 4-nitrobenzoyl chloride (0.153 g, 0.82 mmol). Addition of DCE (1 mL) gave a slurry that was transferred to the reaction mixture using a syringe. The resulting solution was stirred for 30 h, then allowed to cool. CH_2Cl_2 (75 mL) and sulfate buffer (60 mL) was added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (8 × 30 mL) and the combined organic phases were washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to afford the crude product as a gray solid. Purification by column chromatography (10% n-heptane in CH_2Cl_2, v/v) gave indole **10f** (0.18 g, 83%) as a light-yellow solid: TLC R_f = 0.45 (10% n-heptane in CH_2Cl_2, v/v); HPLC t_R = 6.98 min (A); IR (neat) ν_{max} = 3167, 3104, 1565, 1518, 1517; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.38 (br s, 1H; NH), 7.98 (ddd, J = 8, 1, 0.5 Hz, 1H; indole-H4), 7.97−7.94 (m, 2H; Ar−H3, H3′), 7.66−7.63 (m, 2H; Ar−H2, H2′), 7.53 (ddd, J = 8, 1, 0.5 Hz, 1H; indole-H7), 7.34−7.32 (m, 2H; Ph-H2, H2′), 7.30 (ddd, J = 8, 7, 1 Hz, 1H; indole-H6), 7.26−7.19 (m, 4H; indole-H5, Ph-H3, H3′, H4); ^{13}C NMR (150 MHz, DMSO-d_6) δ 190.2 (C═O), 148.1 (Ar−C4), 146.1 (indole-C2), 145.8 (Ar−C1), 135.9 (indole-C7a), 131.2 (Ph-C1), 130.02 (Ar−C2, C2′), 129.97 (Ph-C2, C2′), 128.7 (Ph-C4), 127.92 (Ph-C3, C3′), 127.85 (indole-C3a), 123.3 (indole-C6), 122.7 (Ar−C3, C3′), 122.1 (indole-C5), 120.8 (indole-C4), 112.0 (indole-C7), 111.9 (indole-C3); HRMS (ESI+) m/z [M + H]$^+$ Calcd for $C_{21}H_{15}N_2O_3^+$ 343.1077, found 343.1088.

Phenyl(2-phenyl-1*H*-indol-3-yl)methanone (10g). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 2-phenylindole (0.19 g, 1.00 mmol), DCE (3.0 mL), DBU (0.179 mL, 1.20 mmol), and benzoyl chloride (0.13 mL, 1.10 mmol). The solution was stirred for 4 days. Purification by column chromatography (30% EtOAc in n-heptane, v/v) gave a yellow solid (0.17 g) that was washed with cold EtOAc (1 mL) to give indole **10g** (0.16 g, 54%) as an off-white solid: TLC R_f = 0.45 (30% EtOAc in n-heptane, v/v); HPLC t_R = 6.97 min (A); IR (neat) ν_{max} = 3055, 2976, 1591, 1563, 1450, 1422; ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.18 (br s, 1H, NH), 7.73 (ddd, J = 8, 1, 0.5 Hz, 1H; indole-H4), 7.53−7.50 (m, 3H; indole-H7, 2 × Ph-H), 7.40−7.34 (m, 3H; 3 × Ph-H), 7.27−7.19 (m, 6H; 5 × Ph-H, indole-H6), 7.15 (ddd, J = 8, 7, 1 Hz, 1H; indole-H5); ^{13}C NMR (150 MHz, DMSO-d_6) δ 192.1 (C═O), 144.0 (indole-C2), 139.8 (Ph-C), 135.8 (indole-C7a), 131.5 (Ph-C), 131.3, 129.5, 129.0, 128.4 (6 × Ph-CH), 128.1 (indole-C3a), 128.0, 127.7 (4 × Ph-CH), 122.8 (indole-C6), 121.4 (indole-C5), 120.5 (indole-C4), 112.1 (indole-C3), 111.8 (indole-C7); LRMS (ESI+) m/z found 298.0 [M + H]$^+$. The analytical data is in agreement with that reported by others.[39]

(3-Methoxyphenyl)(2-phenyl-1*H*-indol-3-yl)methanone (10h). Synthesized according to **GP-Acylation** using a 20 mL microwave vial, 2-phenylindole (0.19 g, 1.0 mmol), DCE (3.0 mL), DBU (0.179 mL, 1.20 mol), and 3-methoxybenzoyl chloride (0.15 mL, 1.10 mmol). The solution was stirred for 4 days. Purification by column chromatography (30% EtOAc in n-heptane, v/v) gave a yellow solid, which was washed with cold EtOAc (1 mL) to afford indole **10h** (0.13 g, 41%) as an off-white solid: TLC R_f = 0.4 (30% EtOAc in n-heptane, v/v); HPLC t_R = 6.91 min (A); IR (neat) ν_{max} = 3219, 3061, 1595, 1575, 1449; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.18 (br s, 1H, NH), 7.79 (ddd, J = 8, 1.2, 0.8 Hz, 1H; indole-H4), 7.51 (ddd, J = 8, 1.1, 0.8 Hz, 1H; indole-H7), 7.40−7.37 (m, 2H, Ph-C2, C2′), 7.28−7.23 (m, 4H; Ph-H3, H3′, H4, indole-H6), 7.18−7.11 (m, 3H; indole-H5, Ar−H5, H6), 7.02−7.01 (m, 1H, Ar−H2), 6.92−6.89 (m, 1H, Ar−H4), 3.60 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.7 (C═O), 158.6 (Ar−C3), 144.1 (indole-C2), 141.2 (Ar−C1), 135.8 (indole-C7a), 131.6 (Ph-C1), 129.5 (Ph-C2, C2′), 128.9 (Ar−C5), 128.5 (Ph-C4), 128.2 (indole-C3a), 128.0 (Ph-C3, C3′), 122.9 (indole-C6), 121.5 (Ar−C6), 121.4 (indole-C5), 120.6 (indole-C4), 117.7 (Ar−C4), 113.5 (Ar−C2), 112.1 (indole-C3), 111.8 (indole-C7), 55.0 (CH_3); HRMS (ESI+) m/z [M + Na]$^+$ Calcd for $C_{22}H_{17}NNaO_2^+$ 350.1151, found 350.1155.

1-(2-(1*H*-Indol-3-yl)indolin-1-yl)-2-chloroethan-1-one (12). A dry 20 mL microwave vial was charged with 1*H*-indole (0.234 g, 2.00 mmol) and a stir bar and the vial was capped. Anhydrous CH_2Cl_2 (4 mL) was added and the vial was flushed with argon for 3−4 min, then cooled to 0 °C in an ice−water bath. $SnCl_4$ (1 M in CH_2Cl_2, 2.4 mL, 2.4 mmol) was added in a single portion to give a gray precipitate. After 5 min the temperature was raised to room temperature and the mixture was stirred for 30 min. Chloroacetyl chloride (0.160 mL, 2.00 mmol) and $MeNO_2$ (3 mL) were added and the resulting solution was stirred at room temperature for 5.25 h. The reaction mixture was poured into ice water (10 mL) and saturated aqueous $NaHCO_3$ (50 mL) was added. The aqueous phase was extracted with EtOAc (50 + 2 × 25 mL) and the combined organic phases were washed with brine (50 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to

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afford a crude solid product. Purification by column chromatography (0.5% MeOH in CH_2Cl_2, v/v) gave indole **12** (0.12 g, 38%) as a white solid: TLC R_f = 0.4 (0.5% MeOH in CH_2Cl_2, v/v); HPLC t_R = 6.76 min (A); IR (neat) ν_{max} = 3313, 3050, 1655, 1648, 1480; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.06 (br s, 1H; NH), 8.18−8.15 (br m, 1H; indoline-H7), 7.37 (d, J = 8 Hz, 1H; indole-H7), 7.32−7.22 (m, 3H; indoline-H4, H6, indole-H2), 7.12 (dt, J = 7.5, 1 Hz, 1H; indoline-H5), 7.09−7.05 (m, 1H; indole-H6), 7.01 (br d, J = 8 Hz, 1H; indole-H4), 6.89−6.85 (m, 1H; indole-H5), 5.98 (dd, J = 10, 2.5 Hz, 1H; indoline-C2), 4.71 (d, $^2J_{HH}$ = 14.5 Hz, 1H; CH_aH$_b$Cl), 4.06 (br d, $^2J_{HH}$ = 14.5 Hz, 1H; CH$_a$$H_b$Cl), 3.80 (dd, $^2J_{HH}$ = 16.5 Hz, $^3J_{HH}$ J = 10 Hz, 1H; indoline-H3$_{syn}$), 3.04 (dd, $^2J_{HH}$ = 16.5 Hz, $^3J_{HH}$ J = 2.5 Hz, 1H; indoline-H3$_{anti}$); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.4 (C═O), 142.5 (indoline-C7a), 136.9 (indole-C7a), 130.9 (indoline-C3a), 127.4, 125.0 (indoline-C4, C6), 124.3 (indoline-C5), 123.9 (indole-C3a), 122.8 (indole-C2), 121.5 (indole-C6), 119.0 (indole-C5), 118.4 (indole-C4), 116.3 (indoline-C7), 116.0 (indole-C3), 111.9 (indole-C7), 56.4 (indoline-C2), 43.4 (CH_2Cl), 37.4 (indoline-C3); HRMS (ESI+) m/z $[M + Na]^+$ Calcd for $C_{18}H_{15}ClN_2NaO^+$ 333.0765, found 333.0769.

■ ASSOCIATED CONTENT

Supporting Information

General experimental procedures and reaction optimization, ^{1}H and ^{13}C NMR spectra and HPLC chromatograms for all synthesized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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