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Four-Component Synthesis of 9*H*-Pyrimido[4,5-*b*]indoles Using Ammonium Iodide as the Nitrogen Source

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Abstract: A four-component synthesis of 2-phenyl-9*H*-pyrimido[4,5-*b*]indoles was developed using indole-3-carboxaldehydes, aromatic aldehyde and ammonium iodide as the raw materials under transition-metal-free conditions. The pyrimidine ring was formed in one pot through [4+2] annulation reaction. Four C–N bonds were formed in one pot promoted by iodine and iodide additives. This work is highlighted by using two ammonium iodides as the sole nitrogen source.

Keywords: 9*H*-pyrimido[4,5-*b*]indole; aromatic aldehyde; ammonium salt; cycloaddition; transition metal free

1. Introduction

As an important part of nitrogen-containing heterocycles, pyrimidines are widespread in natural products and pharmaceuticals [1–3]. Among them, the 9*H*-pyrimido[4,5-*b*]indole motif has important application in many fields, such as anti-inflammatory, antimicrobial, antimalarial agents and cytotoxic inhibitors [4–6]. Furthermore, the core structure of 9*H*-pyrimido[4,5-*b*]indoles was found in many biologically active molecules, such as HSC*ex* vivo expansion agent, pyruvate dehydrogenase kinases (PDHKs) inhibitors, epidermal growth factor receptor (EGFr) tyrosine kinase inhibitors, and endogenous hormones (Figure 1) [7–11]. Therefore, significant research effort has been focused on the synthesis of 9*H*-pyrimido[4,5-*b*]indole derivatives. According to the reported methods, the synthesis of 9*H*-pyrimido[4,5-b]indoles usually started with highly functionalized materials [12–15]. For example, 4-azido-5-phenylpyrimidine, 1,3,5-triazines, benzamidine, guanidine nitrate and *o*-nitrobiphenyl were successfully used as the starting materials for the synthesis of target products [16–19]. Furthermore, most reactions often use stoichiometric amount of strong acids or bases which do not meet the requirement of green chemistry. For example, Shkurko and co-workers developed a multi-step synthesis of 2-phenyl-9*H*-pyrimido[4,5-*b*]indole from indolin-2-one using sodium ethylate prepared from sodium as the base [20]. Therefore, efficient and green synthetic methods for constructing 9*H*-pyrimido[4,5-*b*]indole derivatives in one pot are highly desirable.

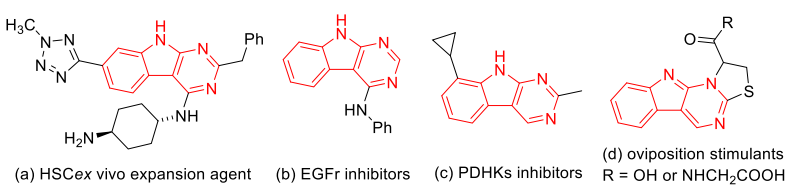


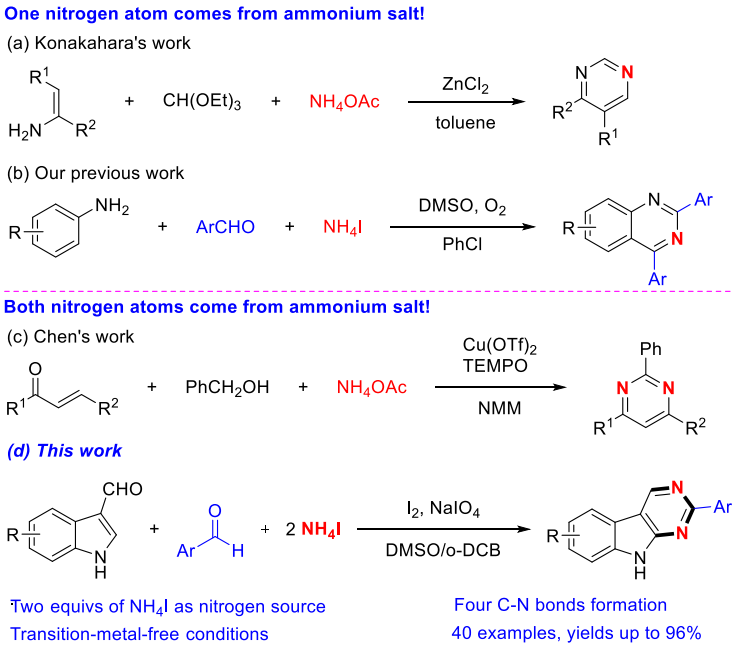
Figure 1. Representative biologically active 9*H*-pyrimido[4,5-*b*]indoles ((**a**) [7], (**b**) [9], (**c**) [8], (**d**) [11]).

Citation: Chen, Y.; Yang, R.; Xiao, F.; Li, T.; Mao, G.; Deng, G.-J. Four-Component Synthesis of 9*H*-Pyrimido[4,5-*b*]indoles Using Ammonium Iodide as the Nitrogen Source. *Catalysts* **2023**, *13*, 623. https://doi.org/10.3390/catal13030623

Academic Editors: Lianghua Zou and Xiaofeng Xia

Received: 20 February 2023
Revised: 17 March 2023
Accepted: 18 March 2023
Published: 20 March 2023

In the last decades, the multi-component reactions (MCRs) have played an increasingly dominant role in the organic synthesis of wide and diverse compounds which provides atom economy, and featured productivity and easy execution [21–29]. MCRs usually start with simple and commercially available materials as the reaction substrates thus providing a shortcut for the synthesis of functional molecules. Meanwhile, ammonium salts are ideal nitrogen sources for the synthesis of nitrogen-containing heterocycles due to their low cost and ease of handling [30–36]. In 2009, Konakahara and coworkers developed a $ZnCl_2$-catalyzed three-component coupling reaction for the synthesis of 4,5-disubstituted pyrimidines from ammonium acetate, enamines and triethyl orthoformate (Scheme 1a) [37]. In recent years, our group also developed several MCRs for the synthesis of nitrogen-containing heterocycles using ammonium salts as the nitrogen source [38–40]. For example, in 2018, we reported a four-component procedure for the synthesis of quinazoline using anilines, aromatic aldehydes and ammonium iodide as starting materials (Scheme 1b) [41]. In 2020, we developed a base-promoted aerobic oxidation approach for the synthesis of benzimidazo[1,2-*a*]-1,3,5-triazines involving 2-aminobenzimidazoles, aromatic aldehydes and ammonium iodide [42]. However, in most cases, ammonium salts only provided a single nitrogen atom source in these multi-component reactions. When two nitrogen atom rings were formed, another organic nitrogen source such as amines is usually required. In 2019, Chen's group demonstrated a three-component reaction of ammonium acetate, chalcone and phenyl-methanol using copper (II) as the catalyst providing tri-substituted pyrimidines in moderate yields (Scheme 1c) [43]. In this process, both nitrogen atoms in the pyrimidine ring come from the ammonium acetate. However, for the synthesis of *N*-heterocycles containing multiple nitrogen atoms which are easy to form a stable complex with the transition metals but encounter difficulties in removing the toxic transition metals, it is particularly important to perform the reaction without the aid of transition-metal catalysts. In the pursuit of research on heterocycle construction using ammonium salts as the nitrogen source under transition-metal-free conditions, herein we describe a general four-component reaction for the synthesis of 2-phenyl-9*H*-pyrimido[4,5-*b*]indole from indole-3-carboxaldehydes, aromatic aldehydes and ammonium salt (Scheme 1d). In this reaction, both nitrogen atoms in the pyrimidine ring come from ammonium salt and four C–N bonds were formed in one pot in the absence of a transition metal catalyst.

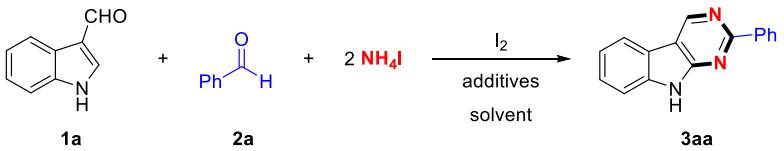


Scheme 1. *N*-heterocycles synthesis through ammonium salts ((**a**) [37], (**b**) [41], (**c**) [43], (**d**) this work).

2. Results

In order to explore the optimized reaction conditions, our study was initiated by using indole-3-carboxaldehyde (**1a**), benzaldehyde (**2a**) and ammonium iodide as model substrates and 20 mol% of iodine as the catalyst under oxygen atmosphere (Table 1). To begin with, potassium iodide was used as an additive to the reaction, affording the target product **3aa** in 45% yield (entry 1). Then, various iodide-containing additives were screened to find the appropriate promotor, among which $NaIO_4$ is the best candidate reagent to provide the product **3aa** in 76% yield (entries 2–5). Moderate yields were obtained when reactions were carried out in PhCl, toluene, mesitylene and $PhCF_3$ (entries 6–9). DMF, CH_3CN, NMP and pyridine as the reaction media completely quenched the reaction (entries 10–13). Furthermore, oxidants screening among others showed that DMSO was superior to others such as H_2O_2, *tert*-butyl hydroperoxide (TBHP), *di*-tert-butyl peroxide (DTBP), $K_2S_2O_8$, and $Na_2S_2O_8$ (entries 14–18). Diminished yield was obtained when the reaction was performed without I_2 (entry 19). Lower yield was obtained when the reaction was carried out in air atmosphere (entry 20). Finally, no desired product was detected when using NH_4Cl instead of NH_4I as nitrogen source for this kind of transformation (entry 21). We believed that iodine, periodate and oxygen were used as the oxidant. The iodine anion could be oxidized to iodine, which could further promote the oxidative aromatization process.

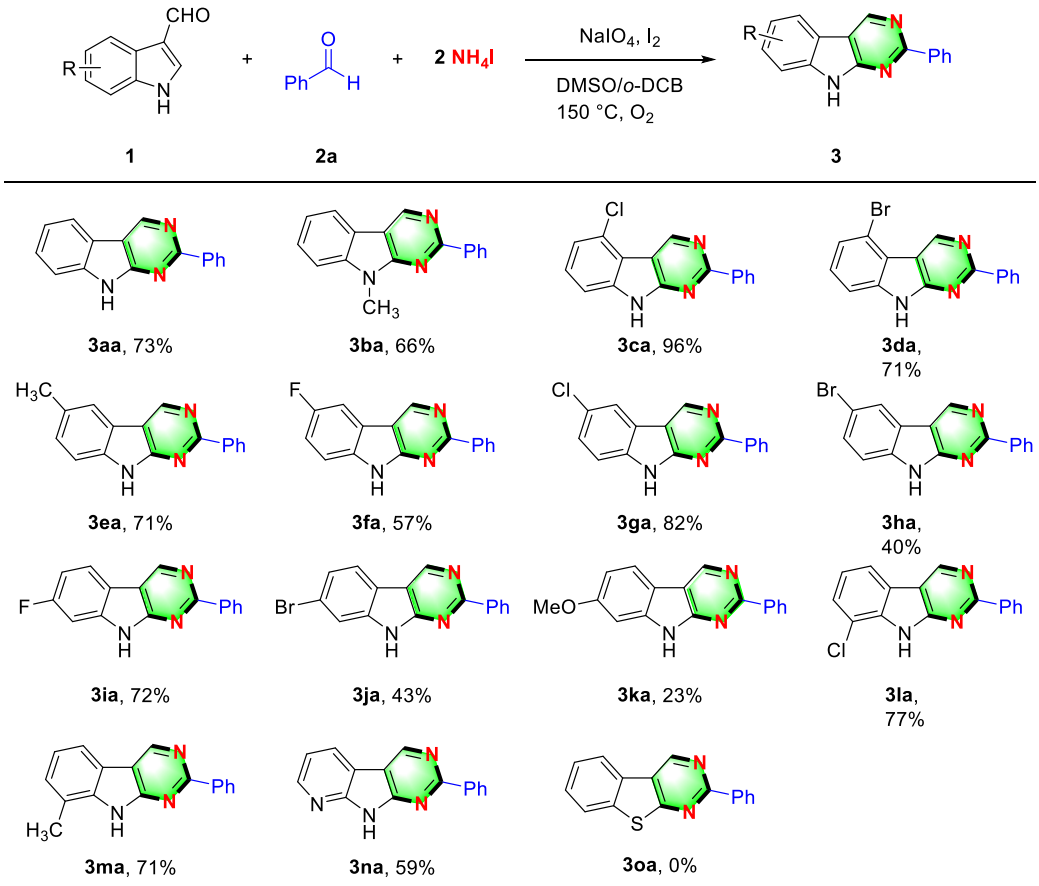
Table 1. Optimization of the reaction conditions [1].



Entry	Additive	Oxidant	Solvent	Yield (%) [2]
1	KI	DMSO	*o*-DCB	45
2	KIO_3	DMSO	*o*-DCB	68
3	$NaIO_4$	DMSO	*o*-DCB	76
4	I_2O_5	DMSO	*o*-DCB	trace
5	NIS	DMSO	*o*-DCB	trace
6	$NaIO_4$	DMSO	PhCl	65
7	$NaIO_4$	DMSO	toluene	53
8	$NaIO_4$	DMSO	mesitylene	40
9	$NaIO_4$	DMSO	$PhCF_3$	39
10	$NaIO_4$	DMSO	DMF	trace
11	$NaIO_4$	DMSO	CH_3CN	trace
12	$NaIO_4$	DMSO	NMP	trace
13	$NaIO_4$	DMSO	Pyridine	trace
14	$NaIO_4$	H_2O_2	*o*-DCB	38
15	$NaIO_4$	TBHP	*o*-DCB	35
16	$NaIO_4$	DTBP	*o*-DCB	30
17	$NaIO_4$	$K_2S_2O_8$	*o*-DCB	trace
18	$NaIO_4$	$Na_2S_2O_8$	*o*-DCB	15
19 [3]	$NaIO_4$	DMSO	*o*-DCB	58
20 [4]	$NaIO_4$	DMSO	*o*-DCB	63
21 [5]	$NaIO_4$	DMSO	*o*-DCB	0

[1] Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), NH_4I (0.6 mmol), I_2 (0.04 mmol), additive (0.2 mmol), oxidant (0.4 mmol), solvent (0.6 mL), 150 °C, 16 h, oxygen. [2] GC yield based on **1a**. [3] Without I_2. [4] Under air. [5] With NH_4Cl (0.6 mmol) instead of NH_4I.

With the optimal conditions established, the substrate scope of indole-3-carboxaldehydes was explored (Scheme 2). As depicted, various substitutes of indole-3-carboxaldehyde could participate in current reaction regardless of the electronic nature of substituents incorporated on the C4, C5, C6, C7 positions. The model reaction provided product **3aa** in 73% isolated yield. *N*-methylindole-3-carbaldehyde could also be used as the substrate to give product **3ba** in 66% isolated yield. To our surprise, 4-chloro-1*H*-indole-3-carbaldehyde was the best effective substrate that the corresponding product **3ca** was obtained in 96% yield, whereas 4-bromo substituent indole-3-carbaldehyde afforded **3da** in 71% yield. Moreover, when fluoro, chloro and methyl substituents were located at C5, C6 and C7 positions, the counterparts were obtained in moderate to good yields (**3ea**, **3fa**, **3ga**, **3ia**, **3la** and **3ma**). Similarly, bromo substituent at C5 and C6 positions led to lower isolated yields (**3ha** and **3ja**). It was regrettable that 6-methoxy-1*H*-indole-3-carbaldehyde only provided product **3ka** in 23% yield. Further study revealed that 1*H*-pyrrolo[2,3-*b*]pyridine-3-carbaldehyde was also a viable substrate for this kind of reaction, leading to the corresponding product **3na** in 59% yield. Unfortunately, sulfur containing heterocyclic aldehyde such as benzo[*b*]thiophene-3-carbaldehyde was ineffective for this type of cyclization process.

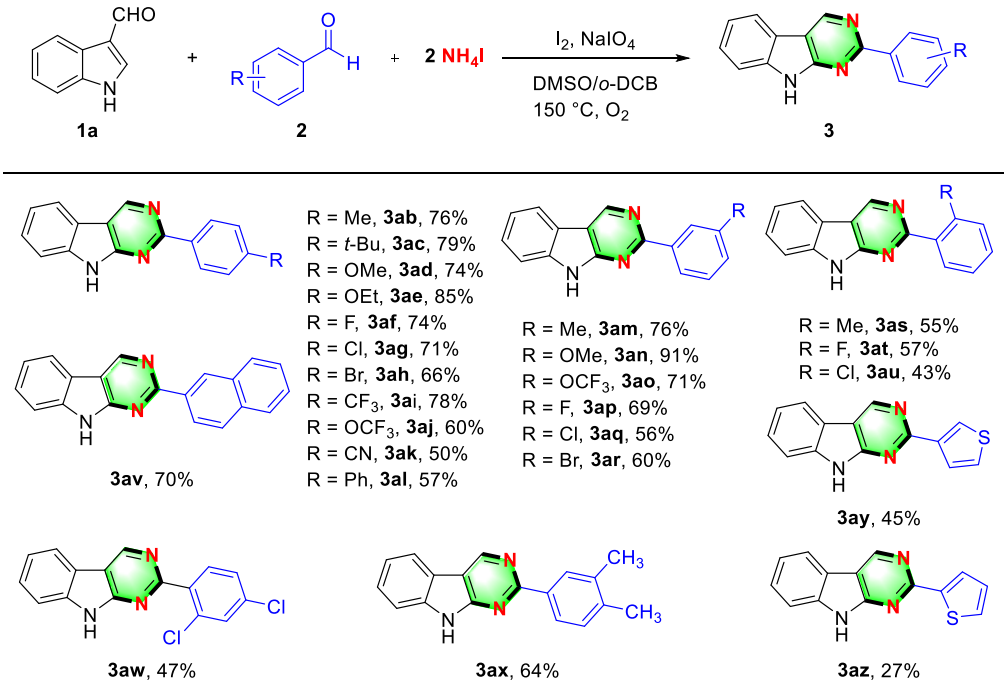


Reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), NH_4I (0.6 mmol), I_2 (0.04 mmol), $NaIO_4$ (0.2 mmol), DMSO (0.4 mmol), 1,2-dichlorobenzene (0.6 mL), 150 °C, 16 h, oxygen atmosphere, isolated yield based on **1**.

Scheme 2. Scope of indole-3-carboxaldehydes.

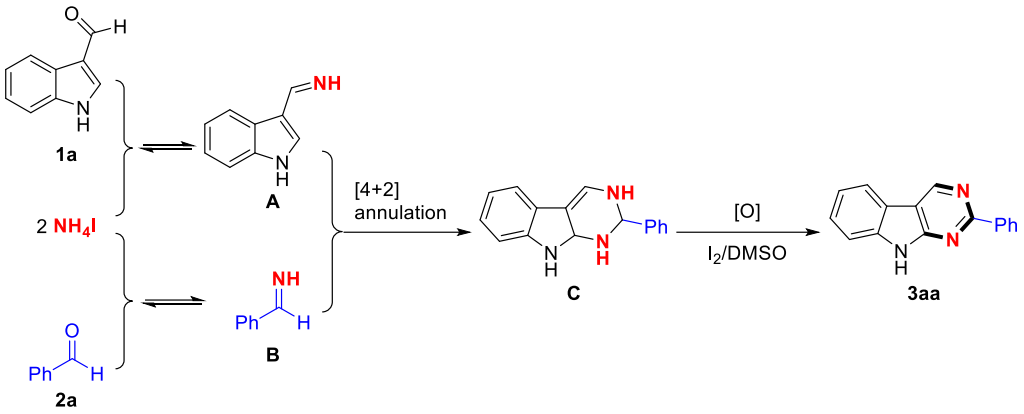
Additional experiments revealed that the current protocol for 2-aryl-9*H*-pyrimido[4,5-*b*]indole synthesis was very effective and efficient, and various aromatic aldehydes derived from **2a** could also react well with indole-3-carboxaldehyde **1a** (Scheme 3). Electron-donating and electron-withdrawing groups decorated on the aryl ring were well tolerated, regardless of the position. A series of *para*-substituted benzaldehydes smoothly

reacted with indole-3-carboxaldehyde **1a** to give the desired products in moderate to good yields (**3ab**–**3al**). It should be noted that other substrates with electron-withdrawing groups at the 4-position on the phenyl ring such as trifluoromethyl, trifluoromethoxy and cyano performed well in the reaction, affording target products **3ai**–**3ak** in good yields. Halogen substituents located at the *para*, *meta* and *ortho* positions were able to smoothly involve the reaction (**3af**–**3ah**, **3ap**–**3ar**, **3at** and **3au**). The steric effect of the reaction is unintelligible. For example, when chloro substituent was located at the *para*, *meta* and *ortho* positions, the corresponding products **3ag**, **3aq** and **3au** were obtained in 71%, 56% and 43% yields, respectively. However, the use of *meta*-methoxybenzaldehyde could afford product **3an** in 91% yield. Benzaldehyde with two functional groups could also react with **1a** and ammonium iodide, affording tricyclic *N*-heterocyclic products **3aw** and **3ax** in 47% and 64% yields, respectively. Moreover, the tolerance of chloro and bromo groups has offered a convenient handle for further transition-metal catalyzed cross-coupling reactions. Analogously, 2-naphthaldehyde was suitable for this cyclization reaction, providing product **3av** in 70% yield. Although picolinaldehyde was not appropriate substrate, thiophene-2-carbaldehyde and thiophene-3-carbaldehyde were also well tolerated under this reaction condition. No desired products were observed when alkyl- or cycloalkyl aldehydes reacted with **1a**.



Scheme 3. Scope of aromatic aldehydes.

Based on the above research and some related literatures [44,45], a plausible reaction pathway is depicted in Scheme 4. Nucleophilic addition of indole-3-carboxaldehyde with ammonium iodide generates animine intermediate **A**. Meanwhile, the nucleophilic addition of benzaldehyde with another ammonium iodide affords an imine intermediate **B**. The [4+2] annulations reaction of **A** and **B** formed an intermediate **C**. Oxidative dehydrogenation of the intermediate **C** in the presence of iodine/DMSO affords the final product 2-phenyl-9*H*-pyrimido[4,5-*b*]indole **3aa**.



Scheme 4. Plausible reaction pathway.

3. Discussion

In summary, we have developed a four-component strategy which can provide an efficient approach to various substituted pyrimido[4,5-*b*]indoles from commercially available indole-3-carboxaldehyde, aromatic aldehydes and ammonium iodide under simple reaction conditions. The C–H bond on the C2 position of indole was directly functionalized and used for a further cyclization process under metal-free conditions. Ammonium iodide was involved in this reaction and was used as two nitrogen sources for the pyrimidine ring construction. The reaction showed good functional group tolerance and wide substrate scope. This four-component mixture could be selectively assembled into the target products in one pot without the use of transition-metal catalyst.

4. Materials and Methods

4.1. General Information

All reactions were carried out under an atmosphere of oxygen unless otherwise noted. Column chromatography was performed using silica gel (200–300 mesh) or neutral alumina. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker-AV (400 and 100 MHz, respectively, Hangzhou, China) instrument internally referenced to tetramethylsilane (TMS) and using chloroform-*d* ($CDCl_3$) and dimethyl sulphoxide-d_6 (DMSO-d_6) as solvent. The obtained spectra can be found in Supplementary Materials. Mass spectra were measured on Agilent 5975 GC-MS instrument (EI) from Agilent Technologies Co., Ltd. (Beijing, China). High-resolution mass spectra (ESI) were obtained with the Thermo Scientific LTQ Orbitrap XL mass spectrometer from Thermo Fisher Scientific (Shanghai, China). Melting points were measured with a YUHUA X-5 melting point instrument from Gongyi Yuhua Instrument Co., Ltd. (Gongyi, China) and were uncorrected. The structures of known compounds were further corroborated by comparing their ^{1}H NMR, ^{13}C NMR data and MS data with those of literature. All reagents were obtained from commercial suppliers and used without further purification unless otherwise noted.

4.2. General Procedure for the Synthesis of 2-Phenyl-9H-pyrimido[4,5-b]indole Derivatives

It was added to an oven-dried reaction vessel with a stir bar including indole-3-carboxaldehyde (0.2 mmol), benzaldehyde (0.4 mmol) and ammonium iodide (0.6 mmol), $NaIO_4$ (0.2 mmol), DMSO (0.4 mmol), I_2 (0.04 mmol), and 1,2-dichlorobenzene (0.6 mL). The reaction vessel was purged with oxygen for three times and then stirred at 150 °C for 16 h. After cooling to room temperature, the volatiles were removed under reduced pressure. The residue was purified by column chromatography on neutral alumina to give the desired product **3aa** in 73% yield.

Characterization of Products are below:

2-Phenyl-*9H*-pyrimido[4,5-*b*]indole (**3aa**, CAS: 1904604-60-9)

Yellow solid (37.3 mg, yield 76%, petroleum ether/ethyl acetate = 15:1), m.p. 295–297 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.35 (s, 1H), 9.53 (s, 1H), 8.51 (d, J = 6.1 Hz, 2H), 8.24 (d, J= 7.8 Hz, 1H), 7.60–7.48 (m, 5H), 7.33 (t, J = 7.3 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 160.1, 156.5, 149.4, 139.5, 138.7, 130.7, 129.1, 128.2, 128.0, 122.1, 121.5, 119.5, 112.8, 112.3.

9-Methyl-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3ba**):

Yellow solid (34.2 mg, yield 66%, petroleum ether/ethyl acetate = 15:1), m.p. 190–192 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.46 (s, 1H), 8.56 (d, J = 5.9 Hz, 2H), 8.22 (d, J = 7.8 Hz, 1H), 7.71–7.48 (m, 5H), 7.36 (t, J = 7.5 Hz, 1H), 3.93 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.0, 155.6, 149.1, 140.6, 138.5, 130.8, 129.0, 128.3, 128.0, 122.0, 121.8, 119.0, 112.5, 110.7, 27.9. HRMS (ESI): m/z calcd. for $C_{17}H_{14}N_3$ $[M + H]^+$ 260.1182, found 260.1185.

5-Chloro-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3ca**):

Yellow solid (53.7 mg, yield 96%, petroleum ether/ethyl acetate = 15:1), m.p. 320–322 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.70 (s, 1H), 9.57 (s, 1H), 8.50 (d, J = 7.1 Hz, 2H), 7.56–7.46 (m, 5H), 7.36 (d, J = 6.4 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 160.6, 156.5, 150.3, 140.6, 138.3, 131.0, 129.1, 129.0, 128.4, 128.3, 121.6, 117.5, 111.8, 111.3. HRMS (ESI): m/z calcd. for $C_{16}H_{11}ClN_3$ $[M + H]^+$ 280.0636, found 280.0632.

5-Bromo-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3da**):

Yellow solid (55.0 mg, yield 71%, petroleum ether/ethyl acetate = 15:1), m.p. 274–276 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.73 (s, 1H), 9.74 (s, 1H), 8.55–8.47 (m, 2H), 7.63–7.43 (m, 6H). ^{13}C NMR (101 MHz, DMSO) δ 160.7, 156.5, 149.9, 140.6, 138.3, 131.0, 129.2, 129.1, 128.4, 124.8, 119.3, 116.6, 112.5, 111.7. HRMS (ESI): m/z calcd. for $C_{16}H_{11}BrN_3$ $[M + H]^+$ 324.0131, found 324.0160.

6-Methyl-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3ea**):

Yellow solid (36.8 mg, yield 71%, petroleum ether/ethyl acetate = 15:1), m.p. 359–361 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.20 (s, 1H), 9.47 (s, 1H), 8.51 (d, J = 6.4 Hz, 2H), 8.02 (s, 1H), 7.58–7.43 (m, 4H), 7.38–7.31 (m, 1H), 2.47 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.0, 156.6, 149.2, 138.8, 137.6, 130.6, 130.4, 129.3, 129.0, 128.2, 121.8, 119.6, 112.7, 112.0, 21.5. HRMS (ESI): m/z calcd. for $C_{17}H_{14}N_3$ $[M + H]^+$ 260.1182, found 260.1181.

6-Fluoro-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3fa**):

Yellow solid (30.0 mg, yield 57%, petroleum ether/ethyl acetate = 15:1), m.p. 317–319 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.40 (s, 1H), 9.54 (s, 1H), 8.51 (d, J = 7.1 Hz, 2H), 8.10 (d, J = 8.1 Hz, 1H), 7.60–7.50 (m, 4H), 7.38 (t, J = 8.0 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 160.6, 158.0 (d, J = 235.0 Hz), 157.1, 150.3, 138.6, 135.9, 130.8, 129.1, 128.3, 120.2 (d, J = 10.5 Hz), 115.8 (d, J = 25.6 Hz), 113.5 (d, J = 9.2 Hz), 112.7 (d, J = 4.5 Hz), 108.0 (d, J = 24.9 Hz). ^{19}F NMR (376 MHz, DMSO) δ −121.9. HRMS (ESI): m/z calcd. for $C_{16}H_{11}FN_3$ $[M + H]^+$ 264.0932, found 264.0929.

6-Chloro-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3ga**):

Yellow solid (45.7 mg, yield 82%, petroleum ether/ethyl acetate = 15:1), m.p. 290–292 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.52 (s, 1H), 9.58 (s, 1H), 8.51 (d, J = 7.9 Hz, 2H), 8.38 (s, 1H), 7.61–7.49 (m, 5H). ^{13}C NMR (101 MHz, DMSO) δ 160.8, 156.9, 150.4, 138.5, 138.0, 130.9, 129.1, 128.3, 127.9, 125.8, 121.8, 120.9, 113.9, 112.2. HRMS (ESI): m/z calcd. for $C_{16}H_{11}ClN_3$ $[M + H]^+$ 280.0636, found 280.0632.

6-Bromo-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3ha**):

Yellow solid (25.9 mg, yield 40%, petroleum ether/ethyl acetate = 15:1), m.p. 292–294 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.54 (s, 1H), 9.59 (s, 1H), 8.55–8.48 (m, 3H), 7.67 (d, J = 8.5 Hz, 1H), 7.54 (d, J = 6.9 Hz, 4H). ^{13}C NMR (101 MHz, DMSO) δ 160.8, 156.7, 150.5, 138.5, 138.2, 130.9, 130.5, 129.1, 128.3, 124.8, 121.5, 114.3, 113.6, 112.0. HRMS (ESI): m/z calcd. for $C_{16}H_{11}BrN_3$ $[M + H]^+$ 324.0131, found 324.0155.

7-Fluoro-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3ia**):

Yellow solid (37.9 mg, yield 72%, petroleum ether/ethyl acetate = 15:1), m.p. 286–288 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.50 (s, 1H), 9.52 (s, 1H), 8.50 (d, J = 6.4 Hz, 2H), 8.27 (dd, J = 8.6, 5.5 Hz, 1H), 7.59–7.48 (m, 3H), 7.34 (d, J = 7.3 Hz, 1H), 7.19 (t, J = 9.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.4 (d, J = 242.0 Hz), 159.9, 157.2, 149.3, 140.4 (d, J = 12.5

Hz), 138.5, 130.7, 129.1, 128.2, 123.8 (d, *J* = 10.6 Hz), 116.2, 112.5, 109.6 (d, *J* = 24.2 Hz), 99.1 (d, *J* = 26.7 Hz). HRMS (ESI): *m*/*z* calcd. for $C_{16}H_{11}FN_3$ $[M + H]^+$ 264.0932, found 264.0930.

7-Bromo-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3ja**)**:**

Yellow solid (27.6 mg, yield 43%, petroleum ether/ethyl acetate = 15:1), m.p. 291–293 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.52 (s, 1H), 9.57 (s, 1H), 8.50 (d, *J* = 8.1 Hz, 2H), 8.21 (d, *J* = 8.3 Hz, 1H), 7.72 (s, 1H), 7.57–7.46 (m, 4H). ^{13}C NMR (101 MHz, DMSO) δ 160.6, 156.8, 150.0, 140.4, 138.5, 130.9, 129.1, 128.3, 124.4, 123.9, 120.7, 118.7, 115.0, 112.3. HRMS (ESI): *m*/*z* calcd. for $C_{16}H_{11}BrN_3$ $[M + H]^+$ 324.0131, found 324.0160.

7-Methoxy-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3ka**):

Yellow solid (12.4 mg, yield 23%, petroleum ether/ethyl acetate = 10:1), m.p. 244–246 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.27 (s, 1H), 9.39 (s, 1H), 8.49 (d, *J* = 6.5 Hz, 2H), 8.10 (d, *J* = 8.6 Hz, 1H), 7.57–7.46 (m, 3H), 7.05–6.90 (m, 1H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.2, 158.9, 156.8, 147.9, 141.1, 138.8, 130.4, 129.0, 128.0, 123.0, 113.1, 112.8, 110.5, 95.9, 55.9. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{14}N_3O$ $[M + H]^+$ 276.1131, found 276.1137.

8-Chloro-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3la**):

Yellow solid (42.9 mg, yield 77%, petroleum ether/ethyl acetate = 15:1), m.p. 247–249 °C. 1H NMR (400 MHz, DMSO-d_6) δ 12.81 (s, 1H), 9.57 (s, 1H), 8.51 (d, *J* = 7.1 Hz, 2H), 8.20 (d, *J* = 7.7 Hz, 1H), 7.61–7.50 (m, 4H), 7.31 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 160.9, 156.9, 150.4, 138.5, 136.7, 130.9, 129.1, 128.3, 127.4, 122.5, 121.6, 120.8, 116.8, 112.9. HRMS (ESI): *m*/*z* calcd. for $C_{16}H_{11}ClN_3$ $[M + H]^+$ 280.0636, found 280.0632.

8-Methyl-2-phenyl-*9H*-pyrimido[4,5-*b*]indole (**3ma**):

Yellow solid (36.8 mg, yield 71%, petroleum ether/ethyl acetate = 15:1), m.p. 189–191 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.38 (s, 1H), 9.49 (s, 1H), 8.52 (d, *J* = 7.4 Hz, 2H), 8.02 (d, *J* = 7.7 Hz, 1H), 7.53 (q, *J* = 9.8, 8.5 Hz, 3H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 2.56 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.0, 156.7, 149.4, 138.8, 138.8, 130.6, 129.1, 128.6, 128.2, 121.9, 121.6, 119.3, 119.2, 113.2, 17.5. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{14}N_3$ $[M + H]^+$ 260.1182, found 260.1181.

2-Phenyl-9*H*-pyrido[3′,2′:4,5]pyrrolo[2,3-*d*]pyrimidine (**3na**):

Yellow solid (29.0 mg, yield 59%, petroleum ether/ethyl acetate = 10:1), ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.92 (s, 1H), 9.57 (s, 1H), 8.63 (d, *J* = 7.7 Hz, 1H), 8.57–8.48 (m, 3H), 7.59–7.50 (m, 3H), 7.39 (dd, *J* = 7.8, 4.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 160.8, 156.3, 152.0, 150.6, 148.3, 138.4, 131.0, 130.6, 129.1, 128.3, 117.9, 112.8, 111.3. HRMS (ESI): *m*/*z* calcd. for $C_{15}H_{11}N_4$ $[M + H]^+$ 247.0978, found 247.0972.

2-(*p*-Tolyl)-*9H*-pyrimido[4,5-*b*]indole (**3ab**):

Yellow solid (39.4 mg, yield 76%, petroleum ether/ethyl acetate = 15:1), m.p. 277–279 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.29 (s, 1H), 9.49 (s, 1H), 8.40 (d, *J* = 7.9 Hz, 2H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.61–7.45 (m, 2H), 7.36–7.27 (m, 3H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.3, 156.6, 149.4, 140.3, 139.4, 136.1, 129.7, 128.2, 127.9, 122.0, 121.4, 119.6, 112.6, 112.3, 21.5. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{14}N_3$ $[M + H]^+$ 260.1182, found 260.1181.

2-(4-(*tert*-Butyl)phenyl)-*9H*-pyrimido[4,5-*b*]indole (**3ac**):

Yellow solid (47.6 mg, yield 79%, petroleum ether/ethyl acetate = 15:1), m.p. 171–173 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.36 (s, 1H), 9.50 (s, 1H), 8.43 (d, *J* = 8.5 Hz, 2H), 8.22 (d, *J* = 7.6 Hz, 1H), 7.58–7.49 (m, 4H), 7.36–7.28 (m, 1H), 1.33 (s, 9H). ^{13}C NMR (101 MHz, DMSO) δ 160.2, 156.6, 153.4, 149.3, 139.4, 136.0, 128.1, 128.0, 125.9, 122.0, 121.4, 119.5, 112.6, 112.3, 35.0, 31.5. HRMS (ESI): *m*/*z* calcd. for $C_{20}H_{20}N_3$ $[M + H]^+$ 302.1652, found 302.1635.

2-(4-Methoxyphenyl)-*9H*-pyrimido[4,5-*b*]indole (**3ad**):

White solid (40.7 mg, yield 74%, petroleum ether/ethyl acetate = 10:1), m.p. 256–258 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.35 (s, 1H), 9.47 (s, 1H), 8.45 (d, *J* = 8.9 Hz, 2H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.54–7.46 (m, 1H), 7.35–7.26 (m, 1H), 7.08 (d, *J* = 8.9 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 161.5, 160.2, 156.6, 149.4, 139.3, 131.3, 129.8, 127.8, 121.8, 121.4, 119.6, 114.4, 112.3, 112.2, 55.8. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{14}N_3O$ $[M + H]^+$ 276.1131, found 276.1133.

2-(4-Ethoxyphenyl)-*9H*-pyrimido[4,5-*b*]indole (**3ae**):

Yellow solid (49.1 mg, yield 85%, petroleum ether/ethyl acetate = 10:1), m.p. 244–246 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.26 (s, 1H), 9.46 (s, 1H), 8.44 (d, J = 8.9 Hz, 2H), 8.20 (d, J = 7.8 Hz, 1H), 7.58–7.47 (m, 2H), 7.34–7.26 (m, 1H), 7.05 (d, J = 8.9 Hz, 2H), 4.09 (q, J = 6.9 Hz, 2H), 1.35 (t, J= 6.9 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.8, 160.2, 156.6, 149.4, 139.3, 131.1, 129.8, 127.8, 121.8, 121.4, 119.6, 114.8, 112.2, 112.2, 63.7, 15.1. HRMS (ESI): m/z calcd. for $C_{18}H_{16}N_3O$ $[M + H]^+$ 290.1288, found 290.1289.

2-(4-Fluorophenyl)-*9H*-pyrimido[4,5-*b*]indole (**3af**):

Yellow solid (38.9 mg, yield 74%, petroleum ether/ethyl acetate = 15:1), m.p. 247–249 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 12.36 (s, 1H), 9.51 (s, 1H), 8.58–8.50 (m, 2H), 8.23 (d, J = 7.8 Hz, 1H), 7.60–7.48 (m, 2H), 7.40–7.28 (m, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.1 (d, J = 247.4 Hz), 159.2, 156.5, 149.4, 139.4, 135.2 (d, J = 2.9 Hz), 130.5 (d, J = 8.6 Hz), 128.1, 122.1, 121.5, 119.5, 116.0 (d, J = 21.6 Hz), 112.7, 112.3. ^{19}F NMR (376 MHz, DMSO) δ −111.5. HRMS (ESI): m/z calcd. for $C_{16}H_{11}FN_3$ $[M + H]^+$ 264.0932, found 264.0929.

2-(4-Chlorophenyl)-*9H*-pyrimido[4,5-*b*]indole (**3ag**):

Yellow solid (39.7 mg, yield 71%, petroleum ether/ethyl acetate = 15:1), m.p. 288–290 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.39 (s, 1H), 9.53 (s, 1H), 8.50 (d, J= 8.6 Hz, 2H), 8.24 (d, J = 7.8 Hz, 1H), 7.63–7.51 (m, 4H), 7.36–7.31 (m, 1H). ^{13}C NMR (101 MHz, DMSO) δ 159.1, 156.4, 149.4, 139.5, 137.6, 135.5, 129.9, 129.2, 128.2, 122.1, 121.6, 119.4, 113.0, 112.4. HRMS (ESI): m/z calcd. for $C_{16}H_{11}ClN_3$ $[M + H]^+$ 280.0636, found 280.0632.

2-(4-Bromophenyl)-*9H*-pyrimido[4,5-*b*]indole (**3ah**):

Yellow solid (42.8 mg, yield 66%, petroleum ether/ethyl acetate = 15:1), m.p. 284–286 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.37 (s, 1H), 9.52 (s, 1H), 8.43 (d, J = 8.6 Hz, 2H), 8.24 (d, J = 7.8 Hz, 1H), 7.73 (d, J = 8.6 Hz, 2H), 7.61–7.50 (m, 2H), 7.38–7.29 (m, 1H). ^{13}C NMR (101 MHz, DMSO) δ 159.2, 156.4, 149.4, 139.5, 137.9, 132.1, 130.2, 128.2, 124.4, 122.2, 121.6, 119.4, 113.0, 112.4. HRMS (ESI): m/z calcd. for $C_{16}H_{11}BrN_3$ $[M + H]^+$ 324.0131, found 324.0160.

2-(4-(Trifluoromethyl)phenyl)-*9H*-pyrimido[4,5-*b*]indole (**3ai**):

Yellow solid (48.3 mg, yield 78%, petroleum ether/ethyl acetate = 10:1), m.p. 290–292 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.48 (s, 1H), 9.58 (s, 1H), 8.69 (d, J = 8.1 Hz, 2H), 8.27 (d, J = 7.8 Hz, 1H), 7.90 (d, J = 8.2 Hz, 2H), 7.63–7.51 (m, 2H), 7.39–7.31 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.6, 156.4, 149.5, 142.5, 139.7, 130.5 (q, J = 31.6 Hz), 128.8, 126.0 (q, J = 4.0 Hz), 124.8 (q, J = 272.1 Hz), 122.3, 121.7, 119.3, 113.4, 112.4. ^{19}F NMR (376 MHz, DMSO) δ −61.1. HRMS (ESI): m/z calcd. for $C_{17}H_{11}F_3N_3$ $[M + H]^+$ 314.0900, found 314.0930.

2-(4-(Trifluoromethyl)phenyl)-*9H*-pyrimido[4,5-*b*]indole (**3aj**):

Yellow solid (37.6 mg, yield 60%, petroleum ether/ethyl acetate = 10:1), m.p. 285–287 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.42 (s, 1H), 9.52 (s, 1H), 8.59 (d, J = 8.9 Hz, 2H), 8.24 (d, J= 7.8 Hz, 1H), 7.59–7.48 (m, 4H), 7.37–7.29 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.8, 156.4, 150.3, 149.4, 139.5, 137.8, 130.2, 128.2, 122.2, 121.6, 121.4, 120.6 (q, J = 256.8 Hz), 119.4, 113.0, 112.4.19F NMR (376 MHz, $CDCl_3$) δ −51.9. HRMS (ESI): m/z calcd. for $C_{17}H_{11}F_3N_3O$ $[M + H]^+$ 330.0849, found 330.0876.

4-(9*H*-Pyrimido[4,5-*b*]indol-2-yl)benzonitrile (**3ak**):

Yellow solid (27.0 mg, yield 50%, petroleum ether/ethyl acetate = 10:1), m.p. 298–300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.47 (s, 1H), 9.56 (s, 1H), 8.62 (d, J = 8.2 Hz, 2H), 8.25 (d, J = 7.8 Hz, 1H), 7.98 (d, J = 8.1 Hz, 2H), 7.62–7.51 (m, 2H), 7.38–7.30 (m, 1H). ^{13}C NMR (101 MHz, DMSO) δ 158.2, 156.3, 149.4, 142.8, 139.7, 133.1, 128.7, 128.5, 122.3, 121.7, 119.3, 119.3, 113.5, 112.8, 112.4. HRMS (ESI): m/z calcd. for $C_{17}H_{11}N_4$ $[M + H]^+$ 271.0978, found 271.0976.

2-([1,1′-Biphenyl]-4-yl)-*9H*-pyrimido[4,5-*b*]indole (**3al**):

Yellow solid (36.6 mg, yield 57%, petroleum ether/ethyl acetate = 15:1), m.p. 298–300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.38 (s, 1H), 9.55 (s, 1H), 8.60 (d, J = 8.4 Hz, 2H), 8.25 (d, J = 7.8 Hz, 1H), 7.85 (d, J = 8.2 Hz, 2H), 7.77 (d, J = 7.2 Hz, 2H), 7.60–7.47 (m, 4H), 7.41 (t, J = 7.4 Hz, 1H), 7.34 (t, J = 7.1 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 159.9, 156.5, 149.5, 142.1, 140.0, 139.5, 137.8, 129.5, 128.8, 128.3, 128.1, 127.3, 127.2, 122.1, 121.5, 119.5, 112.8, 112.3. HRMS (ESI): m/z calcd. for $C_{22}H_{16}N_3$ $[M + H]^+$ 322.1339, found 322.1325.

2-(*m*-Tolyl)-9*H*-pyrimido[4,5-*b*]indole (**3am**):

Yellow solid (39.4 mg, yield 76%, petroleum ether/ethyl acetate = 15:1), m.p. 247–249 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.35 (s, 1H), 9.51 (s, 1H), 8.34 (s, 1H), 8.30 (d, J = 7.8 Hz, 1H), 8.23 (d, J = 7.8 Hz, 1H), 7.60–7.48 (m, 2H), 7.41 (t, J = 7.6 Hz, 1H), 7.36–7.28 (m, 2H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.3, 156.5, 149.3, 139.4, 138.6, 138.1, 131.3, 129.0, 128.8, 128.0, 125.5, 122.0, 121.5, 119.5, 112.8, 112.3, 21.6. HRMS (ESI): m/z calcd. for $C_{17}H_{14}N_3$ [M + H]$^+$ 260.1182, found 260.1185.

2-(3-Methoxyphenyl)-9*H*-pyrimido[4,5-*b*]indole (**3an**):

Yellow solid (50.0 mg, yield 91%, petroleum ether/ethyl acetate = 10:1), m.p. 265–267 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.34 (s, 1H), 9.51 (s, 1H), 8.23 (d, J = 7.8 Hz, 1H), 8.11 (d, J = 7.8 Hz, 1H), 8.06 (s, 1H), 7.60–7.49 (m, 2H), 7.45 (t, J = 7.9 Hz, 1H), 7.33 (t, J = 7.3 Hz, 1H), 7.13–7.04 (m, 1H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.0, 159.9, 156.5, 149.3, 140.2, 139.5, 130.1, 128.1, 122.1, 121.5, 120.7, 119.5, 116.7, 113.0, 112.9, 112.3, 55.6. HRMS (ESI): m/z calcd. for $C_{17}H_{14}N_3O$ [M + H]$^+$ 276.1131, found 276.1137.

2-(3-(Trifluoromethoxy)phenyl)-9*H*-pyrimido[4,5-*b*]indole (**3ao**):

Yellow solid (46.7 mg, yield 71%, petroleum ether/ethyl acetate = 10:1), m.p. 280–282 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.47 (s, 1H), 9.56 (s, 1H), 8.53 (d, J = 7.8 Hz, 1H), 8.39 (s, 1H), 8.26 (d, J = 7.8 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.61–7.48 (m, 3H), 7.35 (t, J = 7.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.4, 156.4, 149.5, 149.3, 141.1, 139.6, 131.3, 128.4, 127.1, 123.1, 122.2, 121.6, 120.7 (q, J = 256.4 Hz), 119.9, 119.4, 113.4, 112.4. ^{19}F NMR (376 MHz, DMSO) δ −56.6. HRMS (ESI): m/z calcd. for $C_{17}H_{11}F_3N_3O$ [M + H]$^+$ 330.0849, found 330.0844.

2-(3-Fluorophenyl)-9*H*-pyrimido[4,5-*b*]indole (**3ap**):

Yellow solid (36.3 mg, yield 69%, petroleum ether/ethyl acetate = 15:1), m.p. 210–212 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.53 (s, 1H), 9.54 (s, 1H), 8.35 (d, J = 7.8 Hz, 1H), 8.25 (d, J = 7.8 Hz, 1H), 8.22–8.15 (m, 1H), 7.64–7.49 (m, 3H), 7.39–7.29 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.01 (d, J = 242.5 Hz),158.77 (d, J = 3.3 Hz), 156.32, 149.39, 141.32 (d, J = 7.8 Hz), 139.64, 131.15 (d, J = 8.3 Hz), 128.25, 124.20 (d, J = 2.6 Hz), 122.18, 121.56, 119.36, 117.41 (d, J = 21.1 Hz), 114.47 (d, J = 23.1 Hz), 113.20, 112.47. HRMS (ESI): m/z calcd. for $C_{16}H_{11}FN_3$ [M + H]$^+$ 264.0932, found 264.0930.

2-(3-Chlorophenyl)-9*H*-pyrimido[4,5-*b*]indole (**3aq**):

Yellow solid (31.3 mg, yield 56%, petroleum ether/ethyl acetate = 15:1), m.p. 201–203 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.49 (s, 1H), 9.55 (s, 1H), 8.48 (s, 1H), 8.47–8.42 (m, 1H), 8.25 (d, J = 7.8 Hz, 1H), 7.63–7.50 (m, 4H), 7.38–7.30 (m, 1H). ^{13}C NMR (101 MHz, DMSO) δ 158.6, 156.4, 149.4, 140.8, 139.6, 134.0, 131.1, 130.4, 128.3, 127.8, 126.7, 122.2, 121.6, 119.4, 113.3, 112.4. HRMS (ESI): m/z calcd. for $C_{16}H_{11}ClN_3$ [M + H]$^+$ 280.0636, found 280.0632.

2-(3-Bromophenyl)-9*H*-pyrimido[4,5-*b*]indole (**3ar**):

Yellow solid (38.9 mg, yield 60%, petroleum ether/ethyl acetate = 15:1), m.p. 213–215 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.54 (s, 1H), 9.54 (s, 1H), 8.63 (s, 1H), 8.49 (d, J = 7.8 Hz, 1H), 8.25 (d, J = 7.8 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 8.1 Hz, 1H), 7.58–7.47 (m, 2H), 7.33 (t, J = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 158.4, 156.3, 149.4, 141.0, 139.6, 133.2, 131.4, 130.7, 128.3, 127.1, 122.5, 122.2, 121.6, 119.4, 113.2, 112.5. HRMS (ESI): m/z calcd. for $C_{16}H_{11}BrN_3$ [M + H]$^+$ 324.0131, found 324.0160.

2-(*o*-Tolyl)-9*H*-pyrimido[4,5-*b*]indole (**3as**):

Yellow solid (28.5 mg, yield 55%, petroleum ether/ethyl acetate = 15:1), m.p. 235–237 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.04 (s, 1H), 9.73 (s, 1H), 8.36 (d, J = 7.8 Hz, 1H), 7.79 (d, J = 7.2 Hz, 1H), 7.71–7.61 (m, 2H), 7.52–7.37 (m, 4H), 2.53 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 156.2, 140.2, 137.5, 131.7, 131.0, 130.7, 129.5, 126.5, 122.9, 122.8, 119.4, 113.1, 112.4, 20.8. HRMS (ESI): m/z calcd. for $C_{17}H_{14}N_3$ [M + H]$^+$ 260.1182, found 260.1181.

2-(2-Fluorophenyl)-9*H*-pyrimido[4,5-*b*]indole (**3at**):

Yellow solid (30.0 mg, yield 57%, petroleum ether/ethyl acetate = 15:1), m.p. 271–273 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.46 (s, 1H), 9.57 (s, 1H), 8.27 (d, J = 7.8 Hz, 1H), 8.11 (t, J = 7.9 Hz, 1H), 7.61–7.49 (m, 3H), 7.40–7.31 (m, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ

162.1, 159.6, 158.7 (d, *J* = 4.3 Hz), 149.3, 139.4, 132.5 (d, *J* = 2.1 Hz), 131.9 (d, *J* = 8.5 Hz), 128.3, 127.7 (d, *J* = 9.7 Hz), 124.8 (d, *J* = 3.7 Hz), 122.3, 121.5, 119.2, 117.2 (d, *J* = 22.3 Hz), 112.6, 112.4. ^{19}F NMR (376 MHz, DMSO) δ −114.4. HRMS (ESI): *m*/*z* calcd. for $C_{16}H_{11}FN_3$ $[M + H]^+$ 264.0932, found 264.0929.

2-(2-Chlorophenyl)-9*H*-pyrimido[4,5-*b*]indole (**3au**):

Yellow solid (30.0 mg, yield 43%, petroleum ether/ethyl acetate = 15:1), m.p. 261–263 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.43 (s, 1H), 9.57 (s, 1H), 8.28 (d, *J* = 7.5 Hz, 1H), 7.82–7.76 (m, 1H), 7.63–7.45 (m, 5H), 7.37 (t, *J* = 6.1 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 161.0, 155.9, 149.1, 139.4, 139.2, 132.4, 132.1, 130.7, 130.6, 128.3, 127.5, 122.3, 121.6, 119.2, 112.6, 112.4. HRMS (ESI): *m*/*z* calcd. for $C_{16}H_{11}ClN_3$ $[M + H]^+$ 280.0636, found 280.0632.

2-(Naphthalen-2-yl)-9*H*-pyrimido[4,5-*b*]indole (**3av**):

Yellow solid (41.2 mg, yield 70%, petroleum ether/ethyl acetate = 15:1), m.p. 304–306 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.35 (s, 1H), 9.56 (s, 1H), 9.06 (s, 1H), 8.63 (d, *J* = 8.6 Hz, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 8.12–8.07 (m, 1H), 8.05 (d, *J* = 8.7 Hz, 1H), 8.00–7.94 (m, 1H), 7.62–7.51 (m, 4H), 7.33 (t, *J* = 6.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 160.1, 156.6, 149.4, 139.5, 136.1, 134.4, 133.4, 129.4, 128.5, 128.1, 128.1, 127.6, 127.0, 125.5, 122.1, 121.6, 119.5, 112.9, 112.4. HRMS (ESI): *m*/*z* calcd. for $C_{20}H_{14}N_3$ $[M + H]^+$ 296.1182, found 296.1170.

2-(2,4-Dichlorophenyl)-9*H*-pyrimido[4,5-*b*]indole (**3aw**):

Yellow solid (29.5 mg, yield 47%, petroleum ether/ethyl acetate = 15:1), m.p. 212–214 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.49 (s, 1H), 9.58 (s, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.77 (s, 1H), 7.63–7.55 (m, 3H), 7.37 (t, *J* = 6.4 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 160.0, 155.8, 149.1, 139.5, 138.0, 134.5, 133.8, 133.2, 130.1, 128.5, 127.8, 122.4, 121.7, 119.1, 112.8, 112.4. HRMS (ESI): *m*/*z* calcd. for $C_{16}H_{10}Cl_2N_3$ $[M + H]^+$ 314.0246, found 314.0273.

2-(3,4-Dimethylphenyl)-9*H*-pyrimido[4,5-*b*]indole (**3ax**):

Yellow solid (35.0 mg, yield 64%, petroleum ether/ethyl acetate = 15:1), m.p. 299–301 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.30 (s, 1H), 9.49 (s, 1H), 8.30 (s, 1H), 8.22 (d, *J* = 7.9 Hz, 2H), 7.58–7.47 (m, 2H), 7.35–7.25 (m, 2H), 2.34 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.4, 156.6, 149.3, 139.4, 139.1, 136.7, 136.4, 130.2, 129.3, 127.9, 125.8, 121.9, 121.4, 119.6, 112.5, 112.3, 20.1, 19.9. HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{16}N_3$ $[M + H]^+$ 274.1339, found 274.1338.

2-(Thiophen-3-yl)-9*H*-pyrimido[4,5-*b*]indole (**3ay**):

Yellow solid (22.6 mg, yield 45%, petroleum ether/ethyl acetate = 15:1), m.p. 283–285 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.33 (s, 1H), 9.46 (s, 1H), 8.39 (s, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.91 (d, *J* = 5.0 Hz, 1H), 7.70–7.63 (m, 1H), 7.58–7.47 (m, 2H), 7.32 (t, *J* = 6.4 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 157.8, 156.4, 149.5, 142.7, 139.3, 127.9, 127.7, 127.7, 127.4, 121.9, 121.5, 119.6, 112.4, 112.3. HRMS (ESI): *m*/*z* calcd. for $C_{14}H_{10}N_3S$ $[M + H]^+$ 252.0590, found 252.0588.

2-(Thiophen-2-yl)-9*H*-pyrimido[4,5-*b*]indole (**3az**):

Yellow solid (13.6 mg, yield 27%, petroleum ether/ethyl acetate = 15:1), m.p. 272–274 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.38 (s, 1H), 9.42 (s, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 8.02–7.96 (m, 1H), 7.73 (d, *J* = 4.1 Hz, 1H), 7.57–7.47 (m, 2H), 7.36–7.28 (m, 1H), 7.25–7.18 (m, 1H). ^{13}C NMR (101 MHz, DMSO) δ 157.2, 156.2, 149.4, 144.7, 139.3, 130.3, 128.9, 128.4, 128.0, 121.9, 121.6, 119.6, 112.5, 112.3. HRMS (ESI): *m*/*z* calcd. for $C_{14}H_{10}N_3S$ $[M + H]^+$ 252.0590, found 252.0588.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/catal13030623/s1, ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of products **3aa**–**3az**.

Author Contributions: Conceptualization, Y.C., F.X. and G.-J.D.; Methodology, Y.C.; data curation, Y.C., R.Y. and T.L.; validation, Y.C., R.Y., F.X., T.L. and G.-J.D.; investigation, Y.C.; writing—original draft preparation, Y.C.; writing—review and editing, Y.C. F.X. and G.-J.D.; supervision, F.X. and G.-J.D.; funding acquisition, G.M. and G.-J.D. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the National Natural Science Foundation of China (22271244, 21871226), the Undergraduate Investigated Study and Innovated Experiment Plan from Ministry of Education of China and Hunan Province, and the Open Research Fund of School of Chemistry and Chemical Engineering, Henan Normal University (2022C02).

Data Availability Statement: The authors declare that the raw data supporting the findings and conclusions of this research are available from the corresponding author upon request.

Conflicts of Interest: The authors declare no conflict of interest.

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