EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201500304

Palladium-Catalyzed C2-Acylation of Indoles with α-Diketones Assisted by the Removable *N*-(2-Pyrimidyl) Group

Chunpu Li,[a,b] Wei Zhu,[b] Shuangjie Shu,[b] Xiaoming Wu,*[a] and Hong Liu*[a,b]

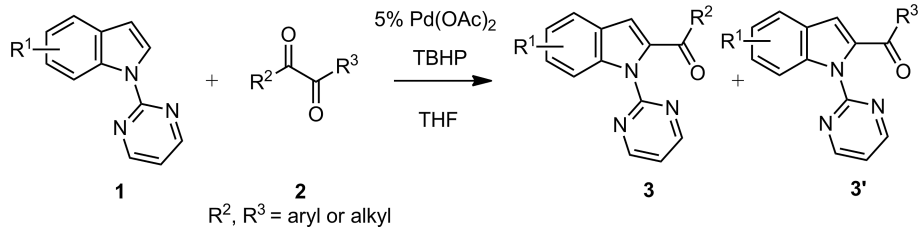
Keywords: Synthetic methods / Acylation / C–H activation / Palladium / Nitrogen heterocycles

An effective and practical palladium-catalyzed C2-acylation method was successfully developed for the synthesis of 2-acylindoles. A variety of 2-acylindoles were readily prepared from *N*-pyrimidyl indoles in moderate to good yields. This methodology offers several advantages, which include ease of handling, mild reaction conditions, and use of an efficient and cheap catalyst. In particular, challenging 2-acetylindoles were synthesized in good yields.

Introduction

C–H functionalization of indoles, such as acylation,[1] alkynylation[2] and alkenylation,[3] occur preferentially at the more reactive C3 position of indoles because of inherent electronic bias.[4] To alter the natural regioselectivity from C3–H to the C2–H of indoles, suitable directing groups are usually introduced into the N1 position of the indole.[5] Transition-metal-catalyzed direct C–H bond functionalization reactions recently emerged as a powerful method of functionalizing indoles at the C2 position. Several transition metal complexes that contain palladium,[6] copper,[7] cobalt,[8] ruthenium,[9] and rhodium,[5c,5d,10] have been explored as active catalysts in these reactions.

2-Acylindole derivatives are found in many natural products and biologically active molecules.[11] The coupling of nitrogen-protected 2-lithioindoles with acyl chloride is a common method for their synthesis,[12] however, this method suffers from air- and moisture-sensitive organolithium reagents. In past decades, innovative methods have been developed to synthesize 2-acylindoles under various catalytic conditions. Beller and co-workers described an efficient ruthenium-catalyzed carbonylative C–H-bond arylation process to provide 2-acylindole derivatives, however, the essential use of carbon monoxide limits the application of this method.[13] Li and co-workers demonstrated oxidative C2 acylation of indoles by using an expensive rhodium catalyst.[14] Recently, Saxena[15] and Zhu[16] reported palladium-catalyzed decarboxylative C2 acylation of indoles by using α-oxocarboxylic acids under different conditions. Therefore, the pursuit of regioselective C–H acylation reactions at the C2 position of indoles remains an extremely attractive and challenging task for organic chemists. Cheng and co-workers described Pd-catalyzed oxidative *ortho*-acylation reactions between arene C–H bonds that bore conventional directing groups and aldehydes as acyl reagents.[17] Such *ortho*-acylation reactions were also realized by using alcohols,[18] carboxylic acids,[19] benzylic ethers,[20] benzylamines,[21] α-diketones,[22] α-oxocarboxylic acids,[23] or toluene derivatives[24] as acylation reagents. Inspired by these strategies, we report herein efficient C2-acylation of indoles that have an easily removable *N*-pyrimidyl group



Scheme 1. Direct C2-acylation reaction of indoles through C–H bond functionalization.

[a] Department of Medicinal Chemistry, China Pharmaceutical University,
24 Tong Jia Xiang, Nanjing 210009, P. R. China
[b] CAS Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences,
555 Zuchongzhi Road, Shanghai 201203, P. R. China
E-mail: hliu@mail.shcnc.ac.cn
http://sourcedb.simm.cas.cn/yw/zjrcyw/201111/t20111121_3399263.html

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201500304.

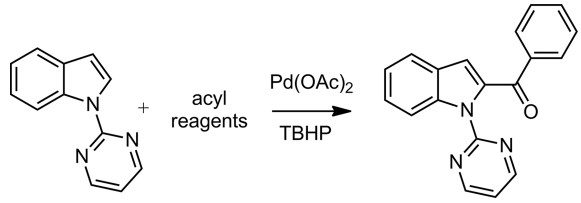
with a versatile palladium catalyst (Scheme 1). Our method proceeds under mild conditions with easy operation and broad substrate scope. In particular, challenging 2-acetylindoles, which are key intermediates for pharmaceutical products, are synthesized in good yields.

Results and Discussion

To begin we focused on the reaction of 1-(pyrimidin-2-yl)-1*H*-indole (**1a**) with toluene in the presence of $Pd(OAc)_2$ and an oxidant (Table 1). To our disappointment, only a low yield of the product was isolated in the presence of *tert*-butyl hydroperoxide (TBHP) as oxidant (Table 1, Entry 1). The optimization process of acylation of 1-(pyrimidin-2-yl)-1*H*-indole (**1a**) with other acylation reagents, such as benzylic ether, benzylamine, benzyl alcohol and benzil, were investigated (Table 1, Entries 2–5). The acylation product could be obtained in 56% yield by reaction of 1-(pyrimidin-2-yl)-1*H*-indole (**1a**) with benzil (**2a**) with TBHP as the oxidant in tetrahydrofuran (THF; Table 1, Entry 5). A systematic screening of the reaction conditions was undertaken. When the catalyst loading was decreased to 3 mol-%, the desired product was obtained at a lower yield of 54% (Table 1, Entry 6). The ratio of 1-(pyrimidin-2-yl)-1*H*-indole (**1a**) to TBHP played a critical role in the reaction efficiency. For example, when this ratio was changed from 1:3 to 1:4 and 1:6, the yields of the desired products changed from 56 to 60 and 48%, respectively (Table 1, Entries 5, 7, and 8). These results indicated that the ratio of 1:4 was the best choice (Table 1, Entry 7). In addition, the ratio of **2a** relative to **1a** was investigated, and two equivalents of **2a** provided the best result (Table 1, Entries 7 and 9). Other solvents were screened, and THF provided the highest yield (Table 1, Entries 9–13). No desired product could be obtained in the absence of $Pd(OAc)_2$ (Table 1, Entry 14). Therefore, the standard conditions for the Pd-catalyzed C2-acylation of indoles are as follows: $Pd(OAc)_2$ (5 mol-%) as catalyst, TBHP (4 equiv.) as oxidant, benzil (**2a**; 2 equiv.) as partner of 1-(pyrimidin-2-yl)-1*H*-indole (**1a**), and reactions were performed at 100 °C in THF without exclusion of air.

With optimized reaction conditions established, the scope of various substrates was examined (Table 2). As shown in Table 2, α-diaryl ketones that bear different substituted groups on the benzene rings, such as methyl, methoxy, fluoro, and chloro, could react with 1-(pyrimidin-2-yl)-1*H*-indole (**1a**) to afford products **3b**–**3f** in moderate to good yields (Table 2, Entries 2–6). α-Diaryl ketones that possess electron-withdrawing groups (**3c** and **3f**) gave higher yields than those with electron-donating groups (**3b**, **3d**, and **3e**). For α-di(aliphatic)ketone derivatives the reaction also proceeded well (Table 2, Entries 7 and 8). Under standard reaction conditions, challenging 2,3-butanedione **2g** and 3,4-hexanedione **2h** also afforded products **3g** and **3h** in 67 and 71% yields, respectively. This provides an efficient route to the synthesis of 2-acetylindoles, which are key intermedi-

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

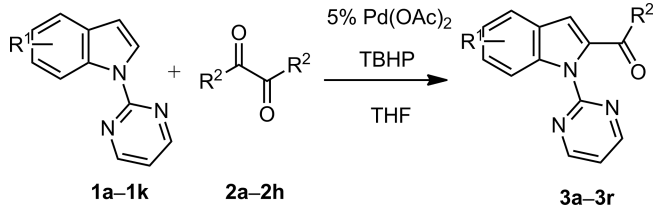


1a **3a**

Entry	Acyl reagents	Acyl reagents [mmol]	TBHP [mmol]	Solvent	Yield [%][b]
1	PhMe	–	1.2	–	20[c]
2	Bn_2O	1.2	1.2	DCE	n.r.
3	$BnNH_2$	1.2	1.2	PhCl	n.r.
4	BnOH	1.2	1.2	PhCl	40[d]
5	benzil (**2a**)	0.5	1.2	THF	56
6	**2a**	0.5	1.2	THF	54[e]
7	**2a**	0.5	1.6	THF	60
8	**2a**	0.5	2.4	THF	48
9	**2a**	0.8	1.6	THF	71
10	**2a**	0.8	1.6	PhCl	n.r.
11	**2a**	0.8	1.6	DME	54
12	**2a**	0.8	1.6	dioxane	25
13	**2a**	0.8	1.6	PhMe	35
14	**2a**	0.8	1.6	THF	n.r.[f]

[a] Reaction conditions: **1a** (0.4 mmol), acyl reagents, TBHP (ca. 5.5 M in decane), $Pd(OAc)_2$ (0.02 mmol), solvent (1.6 mL), 100 °C, 24 h. [b] Isolated yield. [c] Toluene as solvent. [d] $PdCl_2$ (0.02 mmol). [e] $Pd(OAc)_2$ (0.012 mmol). [f] Without Pd. DCE = dichloroethene; DME = dimethoxyethane.

Table 2. Scope of direct C2-acylation of 1-(pyrimidin-2-yl)-1*H*-indoles with α-diketones.[a]



1a–1k **2a–2h** **3a–3r**

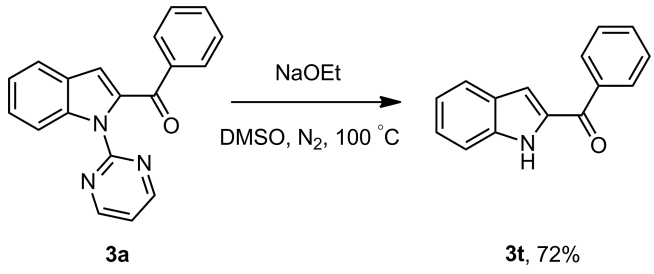
Entry	R^1, **1**	R^2, **2**	**3**	Yield [%][b]
1	H,**1a**	C_6H_5, **2a**	**3a**	71
2	H,**1a**	2-OMe-C_6H_5, **2b**	**3b**	68
3	H,**1a**	2-Cl-C_6H_5, **2c**	**3c**	73
4	H,**1a**	4-OMe-C_6H_5, **2d**	**3d**	55
5	H,**1a**	4-Me-C_6H_5, **2e**	**3e**	75
6	H,**1a**	4-F-C_6H_5, **2f**	**3f**	77
7	H,**1a**	CH_3, **2g**	**3g**	67
8	H,**1a**	CH_3CH_2, **2h**	**3h**	71
9	5-F, **1b**	C_6H_5, **2a**	**3i**	61
10	5-Cl, **1c**	C_6H_5, **2a**	**3j**	70
11	5-Br, **1d**	C_6H_5, **2a**	**3k**	66
12	5-Me, **1e**	C_6H_5, **2a**	**3l**	67
13	5-OMe, **1f**	C_6H_5, **2a**	**3m**	73
14	5-CN, **1g**	C_6H_5, **2a**	**3n**	46
15	5-COOMe, **1h**	C_6H_5, **2a**	**3o**	65
16	6-F, **1i**	C_6H_5, **2a**	**3p**	68
17	7-Me, **1j**	C_6H_5, **2a**	**3q**	70
18	3-CH_2COOEt, **1k**	C_6H_5, **2a**	**3r**	75

[a] Reaction conditions: **1a** (0.4 mmol), **2** (0.8 mmol), TBHP (1.6 mmol, ca. 5.5 M in decane), $Pd(OAc)_2$ (0.02 mmol), THF (1.6 mL), 100 °C, 24 h. [b] Isolated yield.

ates in pharmaceutical products.[25] Subsequently, an investigation into different substituted indoles showed that a number of functional groups could be introduced into the indoles to afford the corresponding products in good yields. The use of electron-donating indoles with methyl (**1e** and **1j**) and methoxy (**1f**) substituents gave corresponding products **3l**, **3q**, and **3m**, respectively, in good yields (Table 2, Entries 12, 13, and 17), whereas indoles with electron-withdrawing groups, such as fluoro, chloro, bromo, nitrile, and methyl ester, provided the corresponding products in moderate to good yields (Table 2, Entries 9–11 and 14–16). The tolerance of the reaction to these active groups in the substrates meant that they could be further transformed into other different functional groups. Steric hindrance on the indole had no effect on the reaction, and the desired product was provided in good yield (Table 2, Entry 18; 75% yield).

The protocol was not limited to indoles as heteroaromatic substrates for C–H bond functionalization, and the results are summarized in Table 3. For example, 2-pyrimidyl-substituted pyrrole was efficiently converted into desired products **3aa** and **3ab** in 41 and 18% yields, respectively. Asymmetric α-diketones, such as 1-phenylpropane-1,2-dione and 1-(4-chlorophenyl)-2-phenylethane-1,2-dione, reacted with 1-(pyrimidin-2-yl)-1*H*-indole (**1a**) smoothly to generate products in good yields and moderate selectivities. A yield of 65% was obtained with a **3g**/**3a** ratio of 1.6:1. 2-Acetylindole product **3g** was obtained as the majority. When the asymmetric aromatic α-diketone with an electron-withdrawing group (Cl) on the benzene ring was investigated, a yield of 55% was obtained with a **3a**/**3s** ratio of 2.7:1.

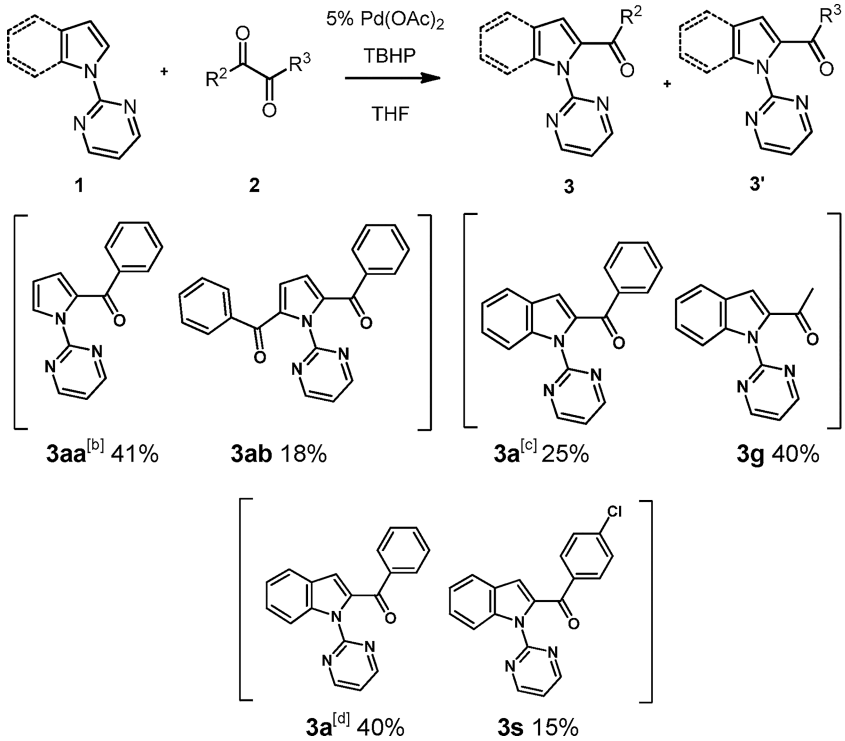
To extend the synthetic practicability of this protocol, removal of the 2-pyrimidyl groups from the acylation products was then conducted (Scheme 2). Upon treatment of **3a** with NaOEt in dimethyl sulfoxide (DMSO) at 100 °C for 24 h, corresponding product **3t** was obtained in 72% yield.



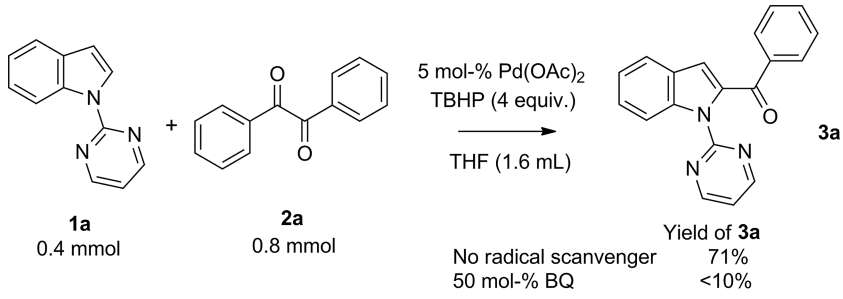
Scheme 2. Deprotection of the 2-pyrimidyl director.

To gain more understanding of this reaction, certain control experiments were performed. When 1-(pyrimidin-2-yl)-1*H*-indole (**1a**) was treated with benzil (**2a**) in the presence of a radical scavenger (1,4-benzoquinone), almost no acylation product was produced, which indicated that a radical was likely involved in the catalytic cycle (Scheme 3). Based

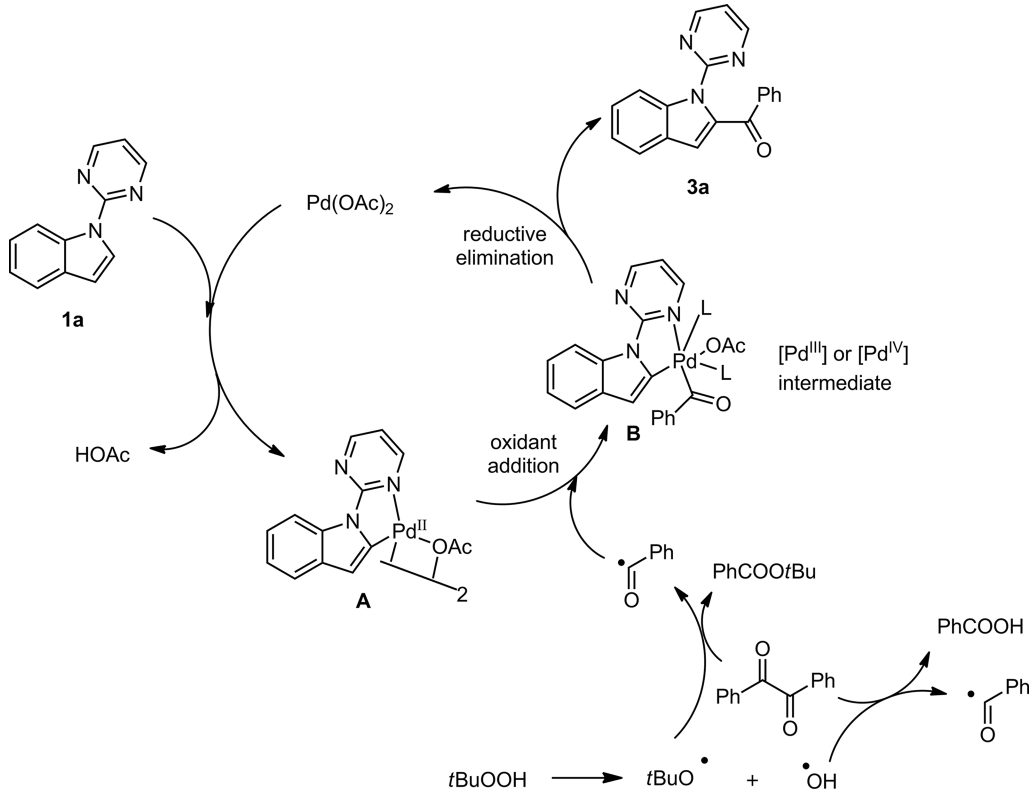
Table 3. Direct C2-acylation of heterocycles with α-diketones or asymmetric α-diketones.[a]



[a] Reaction conditions: **1a** (0.4 mmol), acyl reagents, TBHP (ca. 5.5 M in decane), $Pd(OAc)_2$ (0.02 mmol), solvent (1.6 mL), 100 °C, 24 h, isolated yield. [b] $R^2 = R^3 = Ph$. [c] $R^2 = Ph$, $R^3 = Me$. [d] $R^2 = Ph$, $R^3 = 4\text{-Cl-Ph}$.



Scheme 3. Control experiment.



Scheme 4. A plausible reaction mechanism.

on these observations and previous studies,[16,22] we proposed a possible mechanism, as illustrated in Scheme 4. Coordination of the nitrogen atom of **1a** to Pd^{II} and directed cyclopalladation reaction provide palladacycle, **A**. α-Diphenyl ketone is oxidized to give benzoyl radicals through C–C bond cleavage by TBHP. Then, palladacycle **A** reacts with a benzoyl radical to produce Pd^{III} or Pd^{IV} intermediate **B**, which can undergo reductive elimination to give desired product **3a** and regenerate the Pd^{II} catalyst.

Conclusions

In summary, we have demonstrated a protocol for the synthesis of substituted 2-acylindole derivatives in good yields through palladium-catalyzed C–H bond functionalization. The remarkable features of this methodology include good product yields and wide tolerance of various functional groups, which renders this methodology as a highly versatile and atom-economical alternative to existing methods for building the biologically important 2-acylindole unit. Furthermore, deprotection of the metal-directing pyrimidyl group is very simple and straightforward. The generality, high efficiency, and operational simplicity of this method make it attractive for the alternative construction of 2-acylindoles.

Experimental Section

General Information: Unless otherwise stated, all reagents used were commercially purchased without further purification. THF is commercially available and was used without further evaporation.

Substrates **1a**–**1k** and 2-(1*H*-pyrrol-1-yl)pyrimidine were prepared according to literature procedures.[6c,7b,9a,10a,16] Analytical TLC was performed with HSGF 254 (0.15–0.2 mm thickness). Compound spots were visualized by UV light (254 nm). Column chromatography was performed with silica gel FCP 200–300. NMR spectra were recorded with a 400 or 500 MHz instrument. Chemical shifts are reported relative to tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br.). HRMS was measured with a Micromass Ultra Q-TOF spectrometer.

General Procedure for the Synthesis of Phenyl[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]methanone (3a): To a dry sealed tube was added 1-(pyrimidin-2-yl)-1*H*-indole (**1a**; 78 mg, 0.40 mmol), benzil (168 mg, 0.80 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), and TBHP (290 μL, 1.6 mmol, ca. 5.5 M in decane) and dissolved in THF (1.6 mL). The resulting mixture was stirred for 24 h at 100 °C. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure, and the obtained residue was purified by column chromatography (silica gel) to give **3a**; yield: 85 mg (71%).

Phenyl[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]methanone (3a):[16] White solid, yield 85 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.64 (d, J = 4.8 Hz, 2 H), 8.40 (d, J = 8.5 Hz, 1 H), 7.98 (d, J = 8.0 Hz, 2 H), 7.71 (d, J = 7.9 Hz, 1 H), 7.59–7.52 (m, 1 H), 7.49–7.40 (m, 3 H), 7.33–7.27 (m, 1 H), 7.14 (s, 1 H), 7.06 (t, J = 4.8 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 187.70, 158.09, 157.40, 138.40, 138.08, 137.29, 132.82, 129.67, 128.46, 128.12, 126.64, 122.95, 122.62, 117.50, 115.56, 114.34 ppm. MS (ESI): m/z = 300.0 $[M + H]^+$.

(2-Methoxyphenyl)[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]methanone (3b): White solid, yield 89 mg (68%), m.p. 94–96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.65 (d, J = 4.8 Hz, 2 H), 8.39 (d, J = 8.5 Hz, 1 H), 7.71 (d, J = 7.9 Hz, 1 H), 7.58–7.52 (m, 2 H), 7.45 (t, J = 7.8 Hz, 1 H), 7.37–7.27 (m, 2 H), 7.15 (s, 1 H), 7.13–7.06 (m, 2 H), 3.85 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.41, 159.75, 158.11, 157.44, 139.38, 138.43, 137.26, 129.45, 128.10, 126.66, 122.95, 122.65, 119.66, 117.52, 115.62, 114.34, 113.51, 55.59 ppm. MS (ESI): m/z = 330.0 $[M + H]^+$. HRMS (ESI): calcd. for $C_{20}H_{16}N_3O_2$ $[M + H]^+$ 330.1243; found 330.1236.

(2-Chlorophenyl)[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]methanone (3c): White solid, yield 97 mg (73%), m.p. 91–93 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.70 (d, J = 4.8 Hz, 2 H), 8.29 (d, J = 8.5 Hz, 1 H), 7.69 (d, J = 7.9 Hz, 1 H), 7.54 (d, J = 7.6 Hz, 1 H), 7.47–7.39 (m, 2 H), 7.35 (t, J = 7.7 Hz, 1 H), 7.31–7.20 (m, 2 H), 7.15 (s, 1 H), 7.09 (t, J = 4.8 Hz, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 185.69, 158.14, 157.37, 138.99, 137.92, 137.65, 133.04, 131.89, 130.78, 130.70, 127.83, 127.26, 126.30, 123.02, 122.96, 117.79, 117.17, 114.20 ppm. MS (ESI): m/z = 334.0 $[M + H]^+$. HRMS (ESI): calcd. for $C_{19}H_{13}ClN_3O$ $[M + H]^+$ 334.0747; found 334.0756.

(4-Methoxyphenyl)[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]methanone (3d):[16] White solid, yield 72 mg (55%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.64 (d, J = 4.8 Hz, 2 H), 8.40 (d, J = 8.5 Hz, 1 H), 7.99 (d, J = 8.7 Hz, 2 H), 7.70 (d, J = 7.8 Hz, 1 H), 7.43 (t, J = 7.7 Hz, 1 H), 7.34–7.24 (m, 1 H), 7.15–7.03 (m, 2 H), 6.94 (d, J = 8.8 Hz, 2 H), 3.87 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 186.63, 163.51, 158.09, 157.48, 138.25, 137.46, 132.06, 130.93, 128.20, 126.36, 122.87, 122.46, 117.46, 114.78, 114.33, 113.75, 55.62 ppm. MS (ESI): m/z = 330.0 $[M + H]^+$.

[1-(Pyrimidin-2-yl)-1*H*-indol-2-yl](*p*-tolyl)methanone (3e):[16] White solid, yield 94 mg (75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.66 (d, J = 4.4 Hz, 2 H), 8.42 (d, J = 8.5 Hz, 1 H), 7.92 (d, J = 7.7 Hz, 2 H), 7.73 (d, J = 7.8 Hz, 1 H), 7.47 (t, J = 7.8 Hz, 1 H), 7.35–7.25 (m, 3 H), 7.13 (s, 1 H), 7.11–7.06 (m, 1 H), 2.44 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.48, 158.08, 157.44, 143.67, 138.31, 137.43, 135.45, 129.88, 129.18, 128.14, 126.47, 122.88, 122.53, 117.47, 115.16, 114.31, 21.82 ppm. MS (ESI): m/z = 314.0 $[M + H]^+$.

(4-Fluorophenyl)[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]methanone (3f): Yellow solid, yield 97 mg (77%), m.p. 113–114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.64 (d, J = 4.8 Hz, 2 H), 8.42 (d, J = 8.5 Hz, 1 H), 8.06–7.94 (m, 2 H), 7.71 (d, J = 7.9 Hz, 1 H), 7.46 (t, J = 7.8 Hz, 1 H), 7.31 (t, J = 7.5 Hz, 1 H), 7.16–7.04 (m, 4 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 186.27, 165.65 (d, J = 254.8 Hz), 158.11, 157.32, 138.37, 136.96, 134.45 (d, J = 2.9 Hz), 132.22, 132.15, 128.07, 126.73, 123.05, 122.62, 117.55, 115.72, 115.54, 115.43, 114.42 ppm. MS (ESI): m/z = 318.0 $[M + H]^+$. HRMS (ESI): calcd. for $C_{19}H_{13}FN_3O$ $[M + H]^+$ 318.1043; found 318.1037.

1-[1-(Pyrimidin-2-yl)-1*H*-indol-2-yl]ethanone (3g): Yellow solid, yield 64 mg (67%), m.p. 155–158 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.79 (d, J = 4.8 Hz, 2 H), 7.98 (d, J = 8.5 Hz, 1 H), 7.71 (d, J = 7.9 Hz, 1 H), 7.43–7.36 (m, 1 H), 7.34 (s, 1 H), 7.29–7.19 (m, 2 H), 2.60 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 190.72, 158.43, 157.97, 139.47, 137.93, 127.49, 127.08, 122.91, 122.73, 118.45, 114.62, 113.24, 28.17 ppm. MS (ESI): m/z = 238.0 $[M + H]^+$. HRMS (ESI) calcd. for $C_{14}H_{12}N_3O$ $[M + H]^+$ 238.0980; found 238.0982.

1-[1-(Pyrimidin-2-yl)-1*H*-indol-2-yl]propan-1-one (3h): Yellow solid, yield 71 mg (67%), m.p. 76–78 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.82–8.75 (m, 2 H), 8.01 (d, J = 8.5 Hz, 1 H), 7.71 (d, J = 7.9 Hz, 1 H), 7.39 (t, J = 7.8 Hz, 1 H), 7.29 (s, 1 H), 7.28–7.20 (m, 2 H), 2.97 (q, J = 7.3 Hz, 2 H), 1.23 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 194.57, 158.43, 158.03, 139.18, 137.81, 127.69, 126.81, 122.79, 122.71, 118.36, 113.39, 33.90, 8.71 ppm. MS (ESI): m/z = 252.1 $[M + H]^+$. HRMS (ESI): calcd. for $C_{15}H_{14}N_3O$ $[M + H]^+$ 252.1137; found 252.1134.

[5-Fluoro-1-(pyrimidin-2-yl)-1*H*-indol-2-yl](phenyl)methanone (3i): White solid, yield 77 mg (61%), m.p. 146–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.61 (d, J = 4.8 Hz, 2 H), 8.42 (dd, J = 9.2, 4.5 Hz, 1 H), 7.95 (d, J = 7.9 Hz, 2 H), 7.55 (t, J = 7.2 Hz, 1 H), 7.44 (t, J = 7.6 Hz, 2 H), 7.34 (dd, J = 8.6, 2.3 Hz, 1 H), 7.18 (td, J = 9.0, 2.4 Hz, 1 H), 7.11–6.99 (m, 2 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.69, 159.34 (d, J = 239.8 Hz), 158.11, 157.14, 138.62, 137.88, 134.59, 133.00, 129.62, 128.81 (d, J = 10.2 Hz), 128.54, 117.58, 115.81 (d, J = 8.9 Hz), 114.75 (d, J = 25.6 Hz), 114.40 (d, J = 4.4 Hz), 107.31 (d, J = 23.7 Hz) ppm. MS (ESI): m/z = 318.0 $[M + H]^+$. HRMS (ESI): calcd. for $C_{19}H_{13}FN_3O$ $[M + H]^+$ 318.1043; found 318.1034.

[5-Chloro-1-(pyrimidin-2-yl)-1*H*-indol-2-yl](phenyl)methanone (3j): White solid, yield 94 mg (70%), m.p. 109–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (d, J = 4.8 Hz, 2 H), 8.38 (d, J = 9.0 Hz, 1 H), 7.95 (d, J = 7.7 Hz, 2 H), 7.71–7.64 (m, 1 H), 7.56 (t, J = 7.4 Hz, 1 H), 7.45 (t, J = 7.7 Hz, 2 H), 7.39 (dd, J = 8.9, 1.9 Hz, 1 H), 7.07 (t, J = 4.8 Hz, 1 H), 7.03 (s, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.61, 158.14, 157.07, 138.34, 137.81, 136.47, 133.06, 129.64, 129.27, 128.56, 128.46, 126.69, 121.78, 117.71, 115.81, 113.92 ppm. MS (ESI): m/z = 334.0 $[M + H]^+$. HRMS (ESI): calcd. for $C_{19}H_{13}ClN_3O$ $[M + H]^+$ 334.0747; found 334.0739.

[5-Bromo-1-(pyrimidin-2-yl)-1*H*-indol-2-yl](phenyl)methanone (3k):[16] White solid, yield 100 mg (66%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (d, J = 4.8 Hz, 2 H), 8.33 (d, J = 8.9 Hz, 1 H),

7.95 (d, J = 7.8 Hz, 2 H), 7.83 (d, J = 1.8 Hz, 1 H), 7.59–7.49 (m, 2 H), 7.44 (t, J = 7.6 Hz, 2 H), 7.08 (t, J = 4.8 Hz, 1 H), 7.03 (s, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.59, 158.14, 157.06, 138.18, 137.80, 136.78, 133.07, 129.86, 129.64, 129.28, 128.56, 124.90, 117.73, 116.19, 116.05, 113.77 ppm. MS (ESI): m/z = 378.0 $[M + H]^+$.

[5-Methyl-1-(pyrimidin-2-yl)-1*H*-indol-2-yl](phenyl)methanone (3l): Yellow solid, yield 84 mg (67%), m.p. 136–138 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.65–8.58 (m, 2 H), 8.29 (d, J = 8.6 Hz, 1 H), 8.00–7.92 (m, 2 H), 7.57–7.50 (m, 1 H), 7.47 (s, 1 H), 7.43 (t, J = 7.6 Hz, 2 H), 7.29–7.24 (m, 1 H), 7.07–7.00 (m, 2 H), 2.47 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.78, 158.04, 157.43, 138.20, 137.33, 136.77, 132.75, 132.43, 129.63, 128.44, 128.38, 128.29, 122.17, 117.29, 115.35, 114.11, 21.48 ppm. MS (ESI): m/z = 314.0 $[M + H]^+$. HRMS (ESI): calcd. for $C_{20}H_{16}N_3O$ $[M + H]^+$ 314.1293; found 314.1286.

[5-Methoxy-1-(pyrimidin-2-yl)-1*H*-indol-2-yl](phenyl)methanone (3m):[16] White solid, yield 96 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.60 (d, J = 4.8 Hz, 2 H), 8.34 (d, J = 9.1 Hz, 1 H), 7.95 (d, J = 7.8 Hz, 2 H), 7.54 (t, J = 7.3 Hz, 1 H), 7.43 (t, J = 7.6 Hz, 2 H), 7.14–7.11 (m, 1 H), 7.11–7.06 (m, 1 H), 7.05 (s, 1 H), 7.02 (t, J = 4.8 Hz, 1 H), 3.88 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.75, 158.01, 157.32, 156.11, 138.20, 137.75, 133.33, 132.76, 129.59, 128.85, 128.44, 117.25, 116.61, 115.56, 115.03, 103.59, 55.83 ppm. MS (ESI): m/z = 330.0 $[M + H]^+$.

2-Benzoyl-1-(pyrimidin-2-yl)-1*H*-indole-5-carbonitrile (3n): Yellow solid, yield 60 mg (46%), m.p. 152–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.66 (d, J = 4.8 Hz, 2 H), 8.51 (d, J = 8.8 Hz, 1 H), 8.05 (s, 1 H), 7.96 (d, J = 8.2 Hz, 2 H), 7.65 (d, J = 8.8 Hz, 1 H), 7.59 (t, J = 7.4 Hz, 1 H), 7.47 (t, J = 7.6 Hz, 2 H), 7.19–7.09 (m, 2 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.30, 158.32, 156.72, 139.47, 139.11, 137.36, 133.39, 129.69, 128.90, 128.68, 128.01, 127.70, 119.80, 118.37, 115.58, 113.84, 106.27 ppm. MS (ESI): m/z = 325.0 $[M + H]^+$. HRMS (ESI): calcd. for $C_{20}H_{13}N_4O$ $[M + H]^+$ 325.1089; found 325.1081.

Methyl 2-Benzoyl-1-(pyrimidin-2-yl)-1*H*-indole-5-carboxylate (3o):[16] Yellow solid, yield 93 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.65 (d, J = 4.8 Hz, 2 H), 8.45 (s, 1 H), 8.41 (d, J = 8.9 Hz, 1 H), 8.12 (d, J = 8.9 Hz, 1 H), 7.97 (d, J = 7.4 Hz, 2 H), 7.57 (t, J = 7.4 Hz, 1 H), 7.45 (t, J = 7.6 Hz, 2 H), 7.17 (s, 1 H), 7.11 (t, J = 4.8 Hz, 1 H), 3.95 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.44, 167.48, 158.26, 157.07, 140.65, 138.45, 137.69, 133.16, 129.73, 128.60, 127.79, 127.56, 125.26, 124.96, 118.07, 115.53, 114.13, 52.27 ppm. MS (ESI): m/z = 358.0 $[M + H]^+$.

[6-Fluoro-1-(pyrimidin-2-yl)-1*H*-indol-2-yl](phenyl)methanone (3p):[16] White solid, yield 87 mg (68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.64 (d, J = 4.8 Hz, 2 H), 8.14 (dd, J = 10.5, 2.1 Hz, 1 H), 7.97 (d, J = 7.5 Hz, 2 H), 7.63 (dd, J = 8.7, 5.5 Hz, 1 H), 7.56 (t, J = 7.4 Hz, 1 H), 7.45 (t, J = 7.7 Hz, 2 H), 7.12–7.02 (m, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.23, 162.41 (d, J = 243.2 Hz), 158.16, 157.23, 138.83 (d, J = 13.0 Hz), 137.94, 137.86 (d, J = 3.9 Hz), 132.92, 129.68, 128.52, 124.50, 123.59 (d, J = 10.3 Hz), 117.72, 115.48, 111.90 (d, J = 24.9 Hz), 101.41 (d, J = 28.6 Hz) ppm. MS (ESI): m/z = 318.0 $[M + H]^+$.

[7-Methyl-1-(pyrimidin-2-yl)-1*H*-indol-2-yl](phenyl)methanone (3q):[16] White solid, yield 88 mg (70%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.88 (d, J = 4.9 Hz, 2 H), 7.96–7.91 (m, 2 H), 7.63–7.56 (m, 2 H), 7.51–7.46 (m, 2 H), 7.42 (t, J = 4.9 Hz, 1 H), 7.21 (s, 1 H), 7.15–7.12 (m, 2 H), 1.98 (s, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 187.19, 159.86, 158.30, 138.54, 138.37, 136.13, 132.56, 129.81, 129.40, 128.41, 127.36, 122.64, 122.05, 121.25, 120.34, 116.61, 19.52 ppm. MS (ESI): m/z = 314.0 $[M + H]^+$.

Ethyl 2-[2-Benzoyl-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]acetate (3r): Yellow solid, yield 116 mg (75%), m.p. 129–131 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.65 (d, J = 8.4 Hz, 1 H), 8.45 (dd, J = 4.8, 1.1 Hz, 2 H), 7.80–7.73 (m, 2 H), 7.71 (d, J = 7.9 Hz, 1 H), 7.51–7.45 (m, 1 H), 7.43–7.38 (m, 1 H), 7.37–7.32 (m, 1 H), 7.29 (t, J = 7.7 Hz, 2 H), 6.90–6.83 (m, 1 H), 4.04 (q, J = 7.1 Hz, 2 H), 3.91 (s, 2 H), 1.09 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 189.32, 170.61, 157.73, 157.00, 139.24, 136.28, 134.73, 132.44, 129.36, 128.62, 128.38, 126.38, 123.10, 120.42, 118.16, 116.59, 115.43, 61.08, 30.40, 14.14 ppm. MS (ESI): m/z = 386.1 $[M + H]^+$. HRMS (ESI): calcd. for $C_{23}H_{20}N_3O_3$ $[M + H]^+$ 386.1505; found 386.1498.

(4-Chlorophenyl)[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]methanone (3s):[16] White solid, yield 20 mg (15%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.63 (d, J = 4.8 Hz, 2 H), 8.42 (dd, J = 8.5, 0.6 Hz, 1 H), 7.95–7.87 (m, 2 H), 7.71 (d, J = 7.9 Hz, 1 H), 7.49–7.43 (m, 1 H), 7.43–7.39 (m, 2 H), 7.33–7.28 (m, 1 H), 7.12 (s, 1 H), 7.07 (t, J = 4.8 Hz, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 186.51, 158.11, 157.30, 139.19, 138.37, 136.85, 136.50, 130.96, 128.81, 128.09, 126.80, 123.09, 122.65, 117.55, 115.48, 114.49 ppm. MS (ESI): m/z = 334.0 $[M + H]^+$.

Phenyl[1-(pyrimidin-2-yl)-1*H*-pyrrol-2-yl]methanone (3aa): Yellow solid, yield 41 mg (41%), m.p. 105–107 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.60 (d, J = 4.8 Hz, 2 H), 7.98–7.91 (m, 2 H), 7.75–7.69 (m, 1 H), 7.56–7.50 (m, 1 H), 7.46–7.40 (m, 2 H), 7.11 (t, J = 4.8 Hz, 1 H), 6.83 (dd, J = 3.6, 1.6 Hz, 1 H), 6.39–6.34 (m, 1 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 186.01, 158.34, 156.95, 138.35, 132.50, 132.33, 129.75, 128.33, 128.04, 122.77, 118.56, 110.56 ppm. MS (ESI): m/z = 250.0 $[M + H]^+$. HRMS (ESI): calcd. for $C_{15}H_{12}N_3O$ $[M + H]^+$ 250.0980; found 250.0987.

[1-(Pyrimidin-2-yl)-1*H*-pyrrole-2,5-diyl]bis(phenylmethanone) (3ab): Yellow solid, yield 25 mg (18%), m.p. 139–142 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.77 (d, J = 4.9 Hz, 2 H), 7.98–7.89 (m, 4 H), 7.63–7.55 (m, 2 H), 7.52–7.45 (m, 4 H), 7.39–7.33 (m, 1 H), 6.84 (s, 2 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 185.84, 158.54, 158.32, 137.60, 136.27, 133.02, 129.79, 128.54, 120.22, 119.35 ppm. MS (ESI): m/z = 354.0 $[M + H]^+$. HRMS (ESI): calcd. for $C_{22}H_{16}N_3O_2$ $[M + H]^+$ 354.1243; found 354.1233.

The Procedure of Removal of the 2-Pyrimidyl Directing Group: Based on literature reports,[16] the procedure for removal of the 2-pyrimidyl directing group is as follows: a mixture of **3a** (30 mg, 0.1 mmol), NaOEt (20 mg, 0.3 mmol) and DMSO (3 mL) was stirred in a reaction tube at 100 °C under an argon atmosphere for 24 h. The resulting mixture was then quenched with water. The mixture was extracted with ethyl acetate, and the combined organic layer was dried with sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (silica gel) to give product **3t** as a yellow solid (16 mg, yield 72%).

(1*H*-Indol-2-yl)(phenyl)methanone (3t):[16] Yellow solid, yield 16 mg (72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.41 (s, 1 H), 8.01 (d, J = 7.4 Hz, 2 H), 7.73 (d, J = 8.1 Hz, 1 H), 7.67–7.60 (m, 1 H), 7.58–7.46 (m, 3 H), 7.43–7.35 (m, 1 H), 7.22–7.13 (m, 2 H) ppm.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H and ^{13}C NMR spectra for all final products.

Acknowledgments

The authors gratefully acknowledge financial support from the National Natural Science Foundation of China (NSFC) (grant

numbers 21021063, 91229204, and 81025017) and National S&T Major Projects (grant numbers 2012ZX09103101-072, 2012ZX09301001-005, 2013ZX09507-001, and 2014ZX09507002-001).

[1] a) D. M. Ketcha, G. W. Gribble, *J. Org. Chem.* **1985**, *50*, 5451–5457; b) T. Okauchi, M. Itonaga, T. Minami, T. Owa, K. Kitoh, H. Yoshino, *Org. Lett.* **2000**, *2*, 1485–1487; c) O. Ottoni, A. V. Neder, A. K. Dias, R. P. Cruz, L. B. Aquino, *Org. Lett.* **2001**, *3*, 1005–1007; d) A. R. Katritzky, K. Suzuki, S. K. Singh, H. Y. He, *J. Org. Chem.* **2003**, *68*, 5720–5723; e) J. Chen, B. Liu, D. Liu, S. Liu, J. Cheng, *Adv. Synth. Catal.* **2012**, *354*, 2438–2442; f) E. Kianmehr, S. Kazemi, A. Foroumadi, *Tetrahedron* **2014**, *70*, 349–354; g) Y. Ma, J. You, F. Song, *Chem. Eur. J.* **2013**, *19*, 1189–1193; h) C. Wang, S. Wang, H. Li, J. Yan, H. Chi, X. Chen, Z. Zhang, *Org. Biomol. Chem.* **2014**, *12*, 1721–1724; i) W. Wu, W. Su, *J. Am. Chem. Soc.* **2011**, *133*, 11924–11927; j) Q. Xing, P. Li, H. Lv, R. Lang, C. Xia, F. Li, *Chem. Commun.* **2014**, *50*, 12181–12184.

[2] a) J. P. Brand, J. Charpentier, J. Waser, *Angew. Chem. Int. Ed.* **2009**, *48*, 9346–9349; *Angew. Chem.* **2009**, *121*, 9510–9513; b) J. P. Brand, C. Chevalley, R. Scopelliti, J. Waser, *Chem. Eur. J.* **2012**, *18*, 5655–5666; c) Y. Gu, X.-M. Wang, *Tetrahedron Lett.* **2009**, *50*, 763–766; d) J. L. Ruano, J. Aleman, L. Marzo, C. Alvarado, M. Tortosa, S. Diaz-Tendero, A. Fraile, *Angew. Chem. Int. Ed.* **2012**, *51*, 2712–2716; *Angew. Chem.* **2012**, *124*, 2766–2770.

[3] a) N. P. Grimster, C. Gauntlett, C. R. Godfrey, M. J. Gaunt, *Angew. Chem. Int. Ed.* **2005**, *44*, 3125–3129; *Angew. Chem.* **2005**, *117*, 3185–3189; b) H. Yu, Z. Yu, *Angew. Chem. Int. Ed.* **2009**, *48*, 2929–2933; *Angew. Chem.* **2009**, *121*, 2973–2977; c) S. K. Xiang, B. Zhang, L. H. Zhang, Y. Cui, N. Jiao, *Chem. Commun.* **2011**, *47*, 8097–8099; d) Q. Yang, L. Wang, T. Guo, Z. Yu, *J. Org. Chem.* **2012**, *77*, 8355–8361; e) Q. Huang, Q. Song, J. Cai, X. Zhang, S. Lin, *Adv. Synth. Catal.* **2013**, *355*, 1512–1516; f) Y. P. Shang, X. M. Jie, J. Zhou, P. Hu, S. J. Huang, W. P. Su, *Angew. Chem. Int. Ed.* **2013**, *52*, 1299–1303; *Angew. Chem.* **2013**, *125*, 1337–1341; g) W. L. Chen, Y. R. Gao, S. Mao, Y. L. Zhang, Y. F. Wang, Y. Q. Wang, *Org. Lett.* **2012**, *14*, 5920–5923.

[4] a) S. Lakhdar, M. Westermaier, F. Terrier, R. Goumont, T. Boubaker, A. R. Ofial, H. Mayr, *J. Org. Chem.* **2006**, *71*, 9088–9095; b) R. J. Sundberg, *Indoles*; Academic Press: San Diego, **1996**; p. 190; c) R. J. Sundberg, *Comprehensive Heterocyclic Chemistry:* (Eds.: A. R. Katritzky, C. W. Rees), Pergamon, Oxford, UK, **1984**; vol. 4, p. 313–376.

[5] a) E. Capito, J. M. Brown, A. Ricci, *Chem. Commun.* **2005**, 1854–1856; b) A. Garcia-Rubia, R. Gomez Arrayas, J. C. Carretero, *Angew. Chem. Int. Ed.* **2009**, *48*, 6511–6515; *Angew. Chem.* **2009**, *121*, 6633–6637; c) B. Li, J. Ma, W. Xie, H. Song, S. Xu, B. Wang, *Chem. Eur. J.* **2013**, *19*, 11863–11868; d) S. Sharma, S. Han, M. Kim, N. K. Mishra, J. Park, Y. Shin, J. Ha, J. H. Kwak, Y. H. Jung, I. S. Kim, *Org. Biomol. Chem.* **2014**, *12*, 1703–1706; e) S. Yu, X. Li, *Org. Lett.* **2014**, *16*, 1200–1203.

[6] a) A. Garcia-Rubia, B. Urones, R. Gomez Arrayas, J. C. Carretero, *Chem. Eur. J.* **2010**, *16*, 9676–9685; b) Z.-L. Yan, W.-L. Chen, Y.-R. Gao, S. Mao, Y.-L. Zhang, Y.-Q. Wang, *Adv. Synth. Catal.* **2014**, *356*, 1085–1092; c) S. Xu, X. Huang, X. Hong, B. Xu, *Org. Lett.* **2012**, *14*, 4614–4617.

[7] a) X. Kou, M. Zhao, X. Qiao, Y. Zhu, X. Tong, Z. Shen, *Chem. Eur. J.* **2013**, *19*, 16880–16886; b) M. Nishino, K. Hirano, T. Satoh, M. Miura, *Angew. Chem. Int. Ed.* **2012**, *51*, 6993–6997; *Angew. Chem.* **2012**, *124*, 7099–7103; c) C. Pan, H. Jin, P. Xu, X. Liu, Y. Cheng, C. Zhu, *J. Org. Chem.* **2013**, *78*, 9494–9498; d) H. Xu, X. Qiao, S. Yang, Z. Shen, *J. Org. Chem.* **2014**, *79*, 4414–4422.

[8] a) Z. Ding, N. Yoshikai, *Beilstein J. Org. Chem.* **2012**, *8*, 1536–1542; b) Z. Ding, N. Yoshikai, *Angew. Chem. Int. Ed.* **2012**, *51*, 4698–4701; *Angew. Chem.* **2012**, *124*, 4776–4779; c) H. Ikemoto, T. Yoshino, K. Sakata, S. Matsunaga, M. Kanai, *J. Am. Chem. Soc.* **2014**, *136*, 5424–5431; d) B. Punji, W. Song, G. A. Shevchenko, L. Ackermann, *Chem. Eur. J.* **2013**, *19*, 10605–10610; e) W. Song, L. Ackermann, *Angew. Chem. Int. Ed.* **2012**, *51*, 8251–8254; *Angew. Chem.* **2012**, *124*, 8376–8379; f) B. Sun, T. Yoshino, S. Matsunaga, M. Kanai, *Adv. Synth. Catal.* **2014**, *356*, 1491–1495; g) T. Yoshino, H. Ikemoto, S. Matsunaga, M. Kanai, *Chem. Eur. J.* **2013**, *19*, 9142–9146.

[9] a) L. Ackermann, A. V. Lygin, *Org. Lett.* **2011**, *13*, 3332–3335; b) B. Li, J. Ma, W. Xie, H. Song, S. Xu, B. Wang, *J. Org. Chem.* **2013**, *78*, 9345–9353; c) J. Pospech, A. Tlili, A. Spannenberg, H. Neumann, M. Beller, *Chem. Eur. J.* **2014**, *20*, 3135–3141; d) M. Schinkel, I. Marek, L. Ackermann, *Angew. Chem. Int. Ed.* **2013**, *52*, 3977–3980; *Angew. Chem.* **2013**, *125*, 4069–4072; e) L. Q. Zhang, S. Yang, X. Huang, J. You, F. Song, *Chem. Commun.* **2013**, *49*, 8830–8832; f) V. Lanke, K. R. Prabhu, *Org. Lett.* **2013**, *15*, 2818–2821.

[10] a) B. Gong, J. Shi, X. Wang, Y. Yan, Q. Li, Y. Meng, H. E. Xu, W. Yi, *Adv. Synth. Catal.* **2014**, *356*, 137–143; b) X. Hong, H. Wang, G. Qian, Q. Tan, B. Xu, *J. Org. Chem.* **2014**, *79*, 3228–3237; c) M. Kim, J. Park, S. Sharma, S. Han, S. H. Han, J. H. Kwak, Y. H. Jung, I. S. Kim, *Org. Biomol. Chem.* **2013**, *11*, 7427–7434; d) X. Li, S. Yu, F. Wang, B. Wan, X. Yu, *Angew. Chem. Int. Ed.* **2013**, *52*, 2577–2580; *Angew. Chem.* **2013**, *125*, 2637–2640; e) M. Z. Lu, P. Lu, Y. H. Xu, T. P. Loh, *Org. Lett.* **2014**, *16*, 2614–2617; f) K. Parthasarathy, A. R. Azcargorta, Y. Cheng, C. Bolm, *Org. Lett.* **2014**, *16*, 2538–2541; g) J. Ryu, K. Shin, S. H. Park, J. Y. Kim, S. Chang, *Angew. Chem. Int. Ed.* **2012**, *51*, 9904–9908; *Angew. Chem.* **2012**, *124*, 10042–10046.

[11] a) A. Brancale, R. Silvestri, *Med. Res. Rev.* **2007**, *27*, 209–238; b) E. Yamuna, R. A. Kumar, M. Zeller, K. J. Rajendra Prasad, *Eur. J. Med. Chem.* **2012**, *47*, 228–238; c) S. Mahboobi, S. Teller, H. Pongratz, H. Hufsky, A. Sellmer, A. Botzki, A. Uecker, T. Beckers, S. Baasner, C. Schachtele, F. Uberall, M. U. Kassack, S. Dove, F. D. Bohmer, *J. Med. Chem.* **2002**, *45*, 1002–1018; d) M. A. Tarselli, K. M. Raehal, A. K. Brasher, J. M. Streicher, C. E. Groer, M. D. Cameron, L. M. Bohn, G. C. Micalizio, *Nat. Chem.* **2011**, *3*, 449–453; e) F. Yu, R. L. Wolin, J. Wei, P. J. Desai, P. M. McGovern, P. J. Dunford, L. Karlsson, R. L. Thurmond, *J. Receptor Ligand Channel Res.* **2010**, *3*, 37–49.

[12] a) M. G. Saulnier, G. W. Gribble, *J. Org. Chem.* **1982**, *47*, 757–761; b) R. J. Sundberg, H. F. Russell, *J. Org. Chem.* **1973**, *38*, 3324–3330.

[13] J. Pospech, A. Tlili, A. Spannenberg, H. Neumann, M. Beller, *Chem. Eur. J.* **2014**, *20*, 3135–3141.

[14] B. Zhou, Y. X. Yang, Y. C. Li, *Chem. Commun.* **2012**, *48*, 5163–5165.

[15] S. Sharma, I. A. Khan, A. K. Saxena, *Adv. Synth. Catal.* **2013**, *355*, 673–678.

[16] C. Pan, H. Jin, X. Liu, Y. Cheng, C. Zhu, *Chem. Commun.* **2013**, *49*, 2933–2935.

[17] X. Jia, S. Zhang, W. Wang, F. Luo, J. Cheng, *Org. Lett.* **2009**, *11*, 3120–3123.

[18] F. H. Xiao, S. A. Qi, F. Zhao, O. Basle, G. J. Deng, C. J. Li, *Org. Lett.* **2011**, *13*, 1614–1617.

[19] J. Lu, H. Zhang, X. Chen, H. Liu, Y. Jiang, H. Fu, *Adv. Synth. Catal.* **2013**, 529–536.

[20] S. Han, S. Sharma, J. Park, M. Kim, Y. Shin, N. K. Mishra, J. J. Bae, J. H. Kwak, Y. H. Jung, I. S. Kim, *J. Org. Chem.* **2014**, *79*, 275–284.

[21] Q. Zhang, F. Yang, Y. Wu, *Chem. Commun.* **2013**, *49*, 6837–6839.

[22] W. Zhou, H. J. Li, L. Wang, *Org. Lett.* **2012**, *14*, 4594–4597.

[23] M. Li, H. Ge, *Org. Lett.* **2010**, *12*, 3464–3467.

[24] a) Z. Xu, B. Xiang, P. Sun, *RSC Adv.* **2013**, *3*, 1679; b) S. Guin, S. K. Rout, A. Banerjee, S. Nandi, B. K. Patel, *Org. Lett.* **2012**, *14*, 5294–5297.

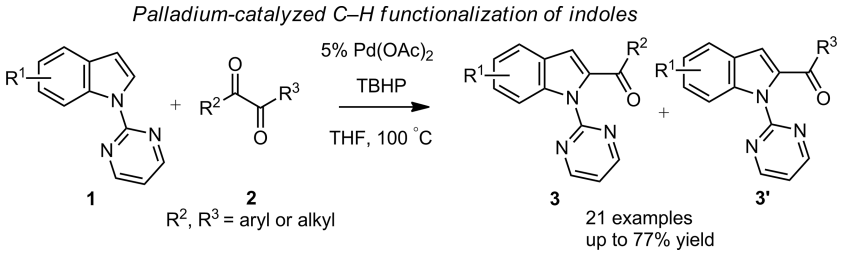
[25] a) N. S. Kumar, E. A. Amandoron, A. Cherkasov, B. B. Finlay, H. Gong, L. Jackson, S. Kaur, T. Lian, A. Moreau, C. Labriere, N. E. Reiner, R. H. See, N. C. Strynadka, L. Thorson, E. W.

Wong, L. Worrall, R. Zoraghi, R. N. Young, *Bioorg. Med. Chem.* **2012**, *20*, 7069–7082; b) R. K. Tiwari, D. Singh, J. Singh, V. Yadav, A. K. Pathak, R. Dabur, A. K. Chhillar, R. Singh, G. L. Sharma, R. Chandra, A. K. Verma, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 413–416; c) H. Zhao, A. C. Donnelly, B. R. Kuszuma, G. E. Brandt, D. Brown, R. A. Rajewski, G. Vielhauer, J. Holzbeierlein, M. S. Cohen, B. S. Blagg, *J. Med. Chem.* **2011**, *54*, 3839–3853.

Received: March 6, 2015
Published Online: ■

EurJOC European Journal of Organic Chemistry

C–H Functionalization



A variety of 2-acylindoles were readily prepared from *N*-pyrimidyl-substituted indoles in moderate to good yields by an effective palladium-catalyzed C2-acylation method. The remarkable features of this methodology include good product yields and wide tolerance of various functional groups.

Keywords: Synthetic methods / Acylation / C–H activation / Palladium / Nitrogen heterocycles

