JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b01280 • Publication Date (Web): 02 Aug 2019

Just Accepted

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Mechanochemical Pd(II)-Catalyzed Direct and C2-Selective Arylation of Indoles

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Abstract

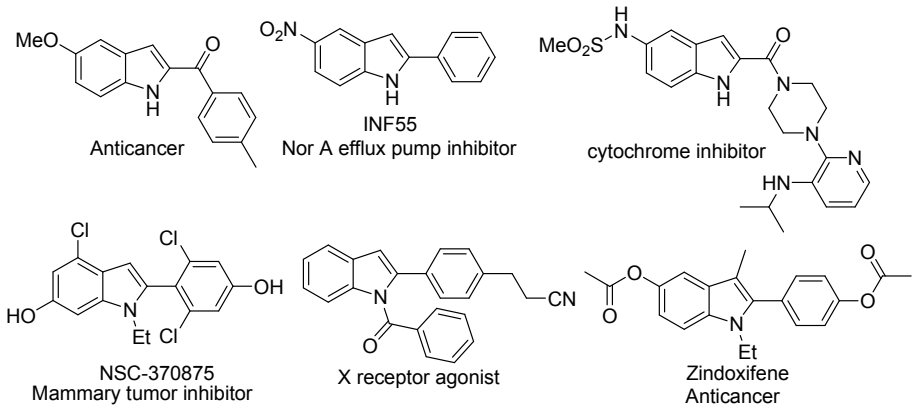
A mechanochemical method for the preparation of synthetically useful 2-arylindoles is developed using Pd(II) as catalyst in the absence of phosphine ligands in a ball-mill. The developed protocol is highly C-2 selective and tolerant of structural variations with electron-rich and electron-deficient substituents both in the indoles and in the iodoarenes. Arylation is possible in both unprotected indoles and *N*-protected indoles with electron donating group with former substrate being relatively slower to react and little less yielding. Indoles with deactivated five-membered ring could also take part in the reaction with ease. The scalability of the reaction was demonstrated by conducting the reaction in gram scale. In general, the reactions were achieved in shorter time than the conventional methods.

Introduction

2-Arylindole substructure is ubiquitous among a large variety of biologically active molecules that are found in many natural products and pharmaceuticals (Fig. 1).[1] Traditional approaches for the synthesis of these compounds involve cross-coupling between a C2-prefunctionalized indole and a functionalized arene derivative, which is not cost effective because of the requirement of pre-activation step.[1a,2] Conversely, focus has been given on the

development of atom economic approaches involving transition metal-catalyzed methods for the direct arylation of indoles via C-H bond functionalization.[3] Typically, several of such arylations involve coupling between an aryl halide and an electron rich indole derivative via a $Pd^{II/0}$ catalytic cycle in the presence of phosphine based ligands.[3a-c] However, the reported methods suffered from one or more disadvantages including low regioselectivity (C2 over C3), high reaction temperatures (>100 °C), toxic organic solvents, long reaction time, *N*-protection of indoles, moderate substrate scope and functional group tolerance. On the other hand, Sanford[4] and Larrosa[5] separately demonstrated phosphine ligands free regioselective C-2 arylation of indoles in the presence of an acid, the chemistry introduced by Gaunt,[6] at much milder condition. Inspired by these works several other groups developed protocols for C-2 arylation,[7-9] in particular, on heterogeneous supports[8] or in green media.[9] However, every protocol has its own scopes and limitations, which indulge researchers to develop new and contemporary methods.

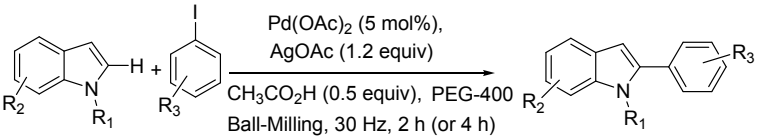
Figure 1. Representative Examples of Biologically Active Molecules and Drug Candidates having 2-Arylindole Substructure.



In recent times, "mechanochemistry" has emerged as one of the better alternatives to conventional solution based reactions in the paradigm of synthetic organic chemistry.[10] Apart

from providing high mechanical force to overcome activation energy barriers to make various chemical transformations possible at ambient temperatures, attributes like solvent-free or solvent-*less* conditions, time efficiency, cleaner and safer reaction profile, easy handling, easy work-up or absence of a work-up step make this technique highly sustainable for future directions. In last few years, the positive effects of mechanochemical conditions have also been well-explored in transition metal-catalysed C-H bond functionalization.[11] For example, Bolm[12] and Stolle[13] developed methods for the syntheses of indoles by cyclo-annulation via C-H bond activation. The directing group assisted allylation,[14] alkynylation[15] at C-2 and asymmetric alkylation[16] or oxidative coupling[17] at C-3 of indole are also reported in recent times. However, the great potential of mechanochemistry demands its further exploration in this area. With our keen interest in mechanochemical reactions,[18] we envisaged, development of a mechanochemical method for synthetically useful 2-arylindoles by Pd(II)-catalysed regioselective direct C-2 arylation. The arylation was achieved by cross-coupling of both *N*-protected and unprotected indoles with iodoarenes under mechanochemical condition in the presence of $Pd(OAc)_2$ as catalyst and PEG-400 as grinding auxiliary (Scheme 1).

Scheme 1: Mechanochemical C-H Bond Arylation of Indoles.



R_1 = Me (**1a**), Bn (**1b**), H (**1c**), Boc (**1d**).
R_2 = 5-CN (**1e**), 5-Br (**1f**), 5-OMe (**1g**).
R_3 = H (**2a**), 4-CN (**2b**), 4-CF_3 (**2c**), 3-CF_3 (**2d**), 4-Br (**2e**), 4-OMe (**2f**), 2-OMe (**2g**), 4-OH (**2h**), 2-Me (**2i**), 3-Me (**2j**), 4-Me (**2k**), 4-*t*-Bu (**2l**), 2-CF_3 (**2m**).

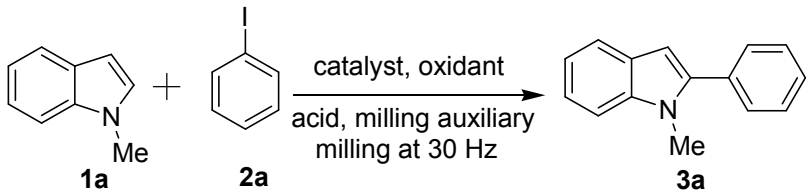
At the outset, we started our investigation by selecting *N*-methylindole (**1a**), an *N*-protected indole derivative with activated ring and iodobenzene (**2a**) as the basic substrates and a model reaction was carried out with 5 mol% of $Pd(OAc)_2$ as the catalyst under milling conditions in

RETSCH mixer mill (MM 400) at 30 Hz. As a silver salt and acidic media usually assist this type of reaction, AgOAc was chosen as the oxidant and the reaction was considered to carry out in the presence of small amount of glacial acetic acid. We first paid our attention in selecting a suitable milling auxiliary and silica gel was chosen for the same. To our delight, TLC revealed complete conversion of the starting materials to product **3a** within 1 h but isolated yield was unexpectedly less (72%, Table 1, entry 1). It is presumed that a part of the product gets adhered in the solid matrix and does not come out even after using polar eluent. The problem was more severe for the C-2 arylation of unprotected indole (**1c**) with iodobenzene (**2a**) to form corresponding product, **3b** as the free base adhere more in acidic silica to drop the yield down to 53%. Whereas, the same reaction between **1a** and **2a** under neat condition did not go to completion even after prolonged milling (4 h) and a lower yield of **3a** was obtained (Table 1, entry 2). This necessitates the requirement of a milling auxiliary for faster reaction. Keeping other condition same, neutral Al_2O_3 was tried in place of silica gel as the milling auxiliary but it was found not useful for the purpose (Table 1, entry 3). Other water soluble salts like Na_2SO_4, NaCl, KCl were also used as milling auxiliaries with a consideration that the matrix can be dissolved in water and the product can be easily extracted in good yield but to our dismay, the reactions became sluggish in the solid ionic media (Table 1, entries 4-6). Considering there are isolation issues with silica or other solid milling auxiliary we chose water soluble PEG-400 as the media for mixing or kneeding purpose. PEG is considered as a useful "green" media for mechanochemical milling because of its biodegradability.[19] The reaction between **1a** and **2a** went well in the presence of 0.3 mL of PEG per mmol of indole derivative to produce 2-phenyl-*N*-methylindole (**3a**) in 91% yield with exclusive C-2 selectivity within 1 h and no trace of 3-phenyl-*N*-methylindole was seen (Table 1, entry 7). With the success in finding suitable milling auxiliary a thorough screening of type and quantity of the catalysts and additives were performed (Table 1, entries 8-27).

The focus was to reduce the cost and toxicity of chemicals that were used for the reaction. The cheaper alternative to $Pd(OAc)_2$, the first row transition metal catalyst, $Co(OAc)_2$ was used for the reaction keeping other conditions same but only a faint product spot was visible in the TLC after milling the reaction mixture for 4 h (Table 1, entry 8). Similar results were observed in case of ruthenium and rhodium based catalysts (Table 1, entries 9 and 10). Although $PdCl_2$ can catalyze the reaction with good efficacy a small amount (~5%) of 3-phenylindole was also isolated reducing the final yield of the desired product, **3a** (Table 1, entry 11). The ideal mol% of most suitable catalyst, $Pd(OAc)_2$ was determined by varying the catalyst loading and checking the time and % of yields. As mentioned in table 1, entry 12, 2 mol% of $Pd(OAc)_2$ is capable of converting **1a** and **2a** to **3a** but the reaction becomes slower and the yield drops marginally. The increase in loading of $Pd(OAc)_2$ does not make any difference in terms of yield and time (Table 1, entry 13). A screening of oxidants was done by replacing AgOAc with cheaper variation $Cu(OAc)_2$ or mild bases like K_2CO_3 in place of acid but the yield of **3a** was not promising enough in each case (Table 1, entries 14-16). However, both CsOAc and Cs_2CO_3 as additive produced comparatively better results but in both cases reaction took longer time and yields were not highly satisfactory (Table 1, entries 17,18). Replacement of AgOAc by Ag_2CO_3 slower down the reaction a bit and marginally reduce the yield of the desired product (**3a**) (Table 1, entries 19, 20). The ideal proportion of AgOAc was set as 1.2 equiv only as there is a drop in yield from 91% to 83% as well as the rate of the reaction when 1.0 equiv of AgOAc was used (Table 1, entry 21). However, the reaction gets slower when AcOH is not added (Table 1, entry 22) and the reaction becomes very sluggish in the absence of a silver salt (Table 1, entry 23). An attempt to reduce the amount of costly AgOAc by a combination of 10 mol% of AgOAc and 1 equiv of $Cu(OAc)_2$ did not work well in terms of the yield of the desired product (Table 1, entry 24). It was also observed that the reaction does not provide the best results when mineral acid (conc. HCl) is

used in place of AcOH (Table 1, entries 26,27). Based on above observations, a combination of 5 mol% $Pd(OAc)_2$, AgOAc (1.2 equiv), AcOH (0.5 equiv) in PEG-400 (0.3 mL per mmol of substrate) was set as optimum condition to carry out C-2 arylation of indoles. At the optimized condition, attempted coupling of **1a** with other aromatic substrates (viz. PhBr or PhOTs) did not produce any noticeable amount of product (**3a**) after 4 h of milling at 30 Hz making this method selective for iodoarenes. Next, few reactions were conducted in the solution phase to assess the advantage of milling condition over conventional condition. It was observed that the reaction takes prolonged time with some drop in the yield of the final product (**3a**) when a mixture of **1a** and **2a** is stirred in variable volume of PEG-400 and DMF[5] at room temperature (Table S1). The same reaction in the absence of "milling" in otherwise similar condition took 10 folds more time for completion with 21% drop in the yield of **3a**. However, the solution phase reaction between free indole (**1c**) and iodobenzene (**2a**) produced only negligible amount of product (**3b**) after 24 h of stirring at room temperature. The results clearly explicate the advantage of mechanochemical milling in faster and smoother arylation at C-2 of indole with a broader substrate scope. Notably, the rate of the reaction was much faster for **3a** in PEG-400 than in DMF. Presumably, polar PEG-400 acts as a better medium for both organic substrates and inorganic catalysts and additives to bring all reacting components in contact with each other with ease to afford the product in shorter time. In a separate study, the milling conditions were optimized by changing the milling frequency, the number of balls, the size of the balls and the amount of the reaction mixture (Table 2). All the reactions were carried out in 5 mL stainless steel jars. The best results were obtained by carrying out reactions in 1 mmol quantity of **1a** and with one 10 mm ball. There was not much change in terms of yield of the final product (**3a**) by reducing the milling frequency to 25 Hz but the reaction became really slower at 20 Hz or lower frequency. Thus, the milling frequency was set at 30 Hz for remaining reactions.

Table 1: Optimization of the Reaction Conditions[a]



1a 2a 3a

Entry	Catalyst loading (mol%)	Oxidant (equiv)	Additive (equiv)	Milling auxiliary[b]	Time for formation of 3a (h)	Isolated yield of 3a (%)
1	$Pd(OAc)_2$ (5)	AgOAc (1.2)	AcOH (0.5)	SiO_2	1	72
2	$Pd(OAc)_2$ (5)	AgOAc (1.2)	AcOH (0.5)	Neat	4	52[c]
3	$Pd(OAc)_2$ (5)	AgOAc (1.2)	AcOH (0.5)	Al_2O_3	4	56[c]
4	$Pd(OAc)_2$ (5)	AgOAc (1.2)	AcOH (0.5)	Na_2SO_4	4	54[c]
5	$Pd(OAc)_2$ (5)	AgOAc (1.2)	AcOH (0.5)	KCl	4	25[c]
6	$Pd(OAc)_2$ (5)	AgOAc (1.2)	AcOH (0.5)	NaCl	4	32[c]
7	$Pd(OAc)_2$ (5)	AgOAc (1.2)	AcOH (0.5)	PEG-400	1	91
8	$Co(OAc)_2$ (10)	AgOAc (1.2)	AcOH (0.5)	PEG-400	4	n.d.
9	$[RuCl_2(p\text{-cymene})]_2$ (5)	AgOAc (1.2)	AcOH (0.5)	PEG-400	6	n.d.
10	$[CpRhCl_2]_2$ (2)	AgOAc (1.2)	AcOH (0.5)	PEG-400	4	n.d.
11	$PdCl_2$ (5)	AgOAc (1.2)	AcOH (0.5)	PEG-400	1.5	81[d]
12	$Pd(OAc)_2$ (2)	AgOAc (1.2)	AcOH (0.5)	PEG-400	3	86
13	$Pd(OAc)_2$ (10)	AgOAc (1.2)	AcOH (0.5)	PEG-400	1	88
14	$Pd(OAc)_2$ (5)	$Cu(OAc)_2$ (1.2)	AcOH (0.5)	PEG-400	4	46[c]
15	$Pd(OAc)_2$ (5)	Na_2CO_3 (2)	-	PEG-400	4	25[c]
16	$Pd(OAc)_2$ (5)	K_2CO_3 (2)	-	PEG-400	4	22[c]
17	$Pd(OAc)_2$ (5)	CsOAc (1.2)	AcOH (0.5)	PEG-400	3	68
18	$Pd(OAc)_2$ (5)	Cs_2CO_3 (2)	-	PEG-400	4	61
19	$Pd(OAc)_2$ (5)	Ag_2CO_3 (1.2)	AcOH (0.5)	PEG-400	2	82
20	$Pd(OAc)_2$ (5)	Ag_2CO_3 (1.2)	-	PEG-400	4	76
21	$Pd(OAc)_2$ (5)	AgOAc (1.0)	AcOH (0.5)	PEG-400	1.5	83
22	$Pd(OAc)_2$ (5)	AgOAc (1.2)	-	PEG-400	3	81
23	$Pd(OAc)_2$ (5)	-	AcOH (0.5)	PEG-400	4	24[b]
24	$Pd(OAc)_2$ (5)	AgOAc (0.1)-$Cu(OAc)_2$ (1.0)	AcOH (0.5)	PEG-400	4	29[c]
25	$Pd(OAc)_2$ (5)	AgOAc (1.0)	AcOH (0.5 mL)	--	2	57[c]
26	$Pd(OAc)_2$ (5)	AgOAc (1.2)	HCl (0.1 mL)	PEG-400	1	78

27	$PdCl_2$ (5)	AgOAc (1.2)	HCl (0.1 mL)	PEG-400	1.5	71[d]

[a]1 mmol of **1a** and 1.1 mmol of **2a** were milled together in a RETSCH mixer mill (MM 400) with one 10 mm ball in a 5 ml stainless steel jar at 30 Hz frequency; [b]auxiliary taken was 2-3 times of the weight of **1a**; [c]in each case little to significant amounts of starting materials were recovered; [d]5% of C-3 arylated product was isolated; n.d. not determined.

Table 2. Optimization of the Milling Parameters[a]

Entry	Ball size (& No.)	Operating frequency (Hz)	Amount of 1a (in mmol)	Time (h)	Isolated yield of 3a (%)
1	10 mm (1)	30	1.0	1	91
2	10 mm (1)	30	1.0	2	92
3	10 mm (1)	30	2.0	1	88
4	10 mm (1)	30	0.5	1	86
5	10 mm (1)	25	1.0	1	75
6	10 mm (1)	20	1.0	2	54[b]
7	10 mm (1)	15	1.0	2	46[b]
8	7 mm (1)	30	1.0	2	73[b]
9	7 mm (2)	25	1.0	2	68[b]
10	5 mm (2)	30	1	1	67[b]
11	5 mm (4)	25	1	1	52[b]

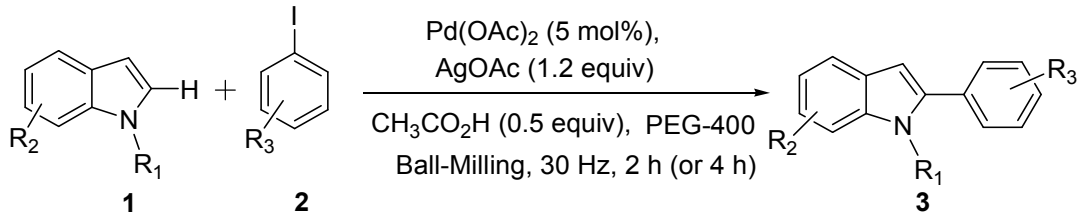
[a] jars and balls are made of stainless steel and all reactions were carried out in 5 mL jars; [b]in each case little to significant amounts of starting materials were recovered.

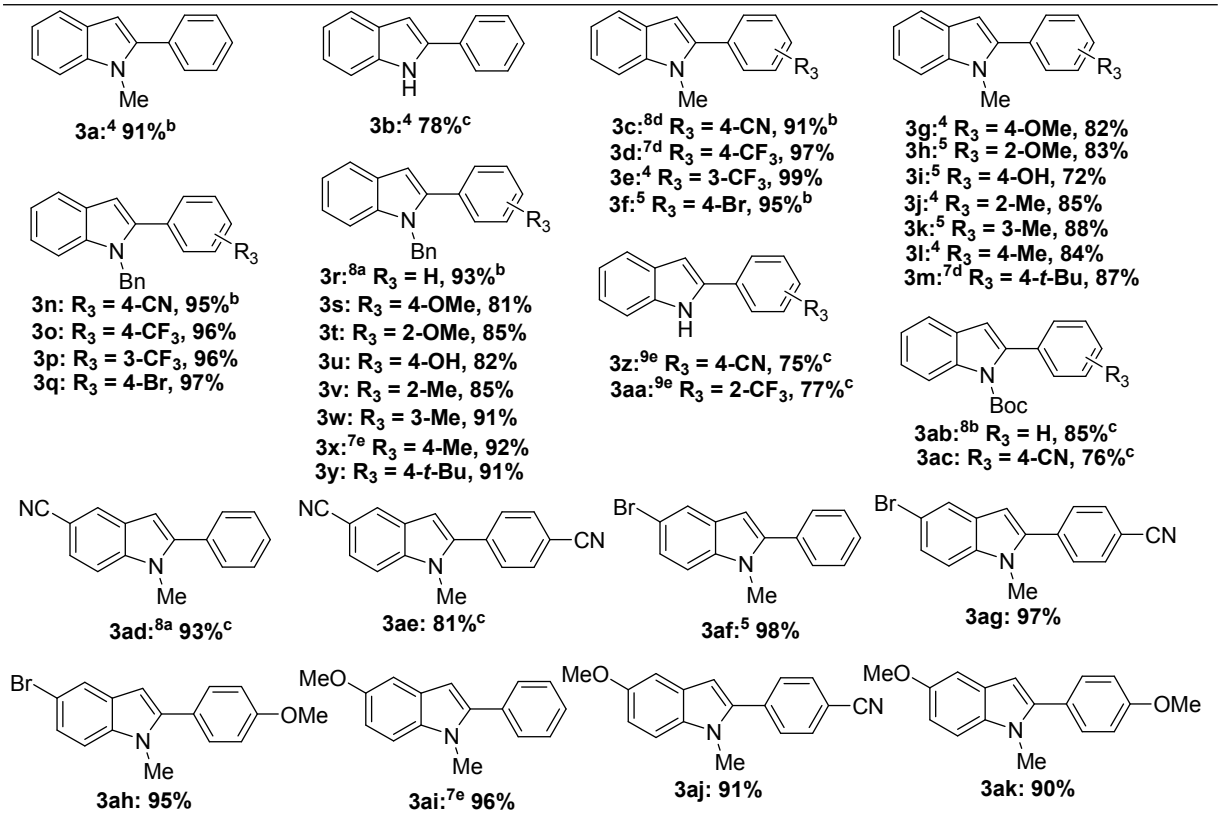
To test the generality of this method, a series of iodoareanes (**2a-m**) was coupled with a variety of indole derivatives at the optimum mechanochemical condition set above to afford C-2 arylated indoles (**3**) in excellent yields (Table 3). Notably, *N*-protected indoles with both electron donating (Me or Bn) and electron withdrawing (viz. Boc) groups were used for this C-H activation reaction along with free indole as the substrate. All the 2-arylindole derivatives were characterized by ^{1}H NMR, ^{13}C NMR, IR and HRMS analysis. The spectra of known compounds were in good agreement with the reported values.[4-9] In all cases the characteristic peak of C-3 H was observed between δ 6.50-6.75 ppm,[4,5] which clearly indicates complete regioselectivity for C-2. In general, the method worked well with a variety of substituents in the iodoarenes. Initially, *N*-methyl and *N*-benzyl indoles (**1a** and **1b**) were

treated with a series of iodoarenes with both electron withdrawing groups (EWG), **2b-e**,**m** and electron donating groups (EDG), **2f-l** to obtain 2-arylindoles, **3(a,c-y)**. Although in few cases the reactions were completed within 1 h, in several other cases it took 2 h for complete conversion. Therefore, the reactions were generally milled for 2 h to afford **3** in high yields. It is worth noting that the substitution with electron-rich groups such as Me, OMe at *o*-, *m*- or *p*-positions and electron-poor groups, such as CN, CF_3, Br at *p*- or *m*-positions of the benzene rings tolerated the mechanochemical reaction condition and these substituents do not pose any significant effect either on the reaction rate or the yields. However, it was observed that the presence of strong EWG (such as –CN) in iodoarene ensures completion of the reaction within 1 h (**3c**, **n**, Table 3); same as in the case iodobenzene (**3a**, Table 3). The rest of the reactions with *N*-alkyl indoles took 2 h for completion. The yield in each case is generally very high for both EWG and EDG but a finer analysis revealed above 90% yields for 2-arlyindoles derived from iodoarenes with EWG (compounds **3c-f**, **3n-q**, Table 3) and just below 90% mark for 2-arlyindoles derived from iodoarenes with EDG (compounds **3g-m**, **3s-y**, Table 3). Only in one case, for the reaction between *N*-methylindole (**1a**) and iodoarene having a phenolic–OH group at *para*-position (**2h**), the yield drops below 80% (**3i**, Table 3). Notably, the steric effect does not play any major role in the reaction as bulky 4-*tert*-butyliodobenzene (**2l)** participated in the reaction to afford corresponding product in about 90% yield in 2 h (**3m**, **3y**, Table 3). Next, a short series of products was synthesized from unprotected indole (**1c**) and *N*-Boc protected indoles (**1d**) to explore the broader substituent scope (compounds **3b**, **3z**, **3aa-ac**, Table 3). It was observed that the course of the reaction was to some extent influenced by *N*-substitution in the indole ring. While an EDG at the nitrogen atom (Me or Bn) helped to carry out the reaction at a faster rate and in high yields of the desired products (**3a, 3c**–**y**, Table 3), an EWG (viz. Boc) at the *N*-atom reduced the rate of the reaction (4 h for complete conversion) as well as the isolated yields were relatively less

than the cases with *N*-alkyl protections (76% yield for **3ac**, Table 3). Also, to our delight, reactions of unprotected indoles were efficiently conducted with some iodoarenes to afford the desired products in good yields (**3b**,**3z**,**3aa**, Table 3). However, as expected, these reactions took little longer time (4 h) than *N*-alkylated indoles because of the reduced electron density in the ring. However, as a whole, the final products involving a deactivated or unprotected indole ring were obtained in shorter time and the yields were good enough to establish a wide substrate scope for this mechanochemical protocol. It is noteworthy to mention that the presence of another halogen atom (such as Br) does not disturb the chemoselectivity as the products **3f** and **3q** were formed as the sole products of the corresponding reactions (Table 3). The same statement holds good for a Br-substituent in the indole ring as well (**3af** and **3ag**, Table 3). Therefore, it can be said that the mechanochemimcal condition is halogen-atom tolerant and transmetalation takes place only at Ar-I bond during the reaction.

Table 3. Substrate Scope of the Mechanochemical Pd(II)-catalyzed C-H Arylation[a]





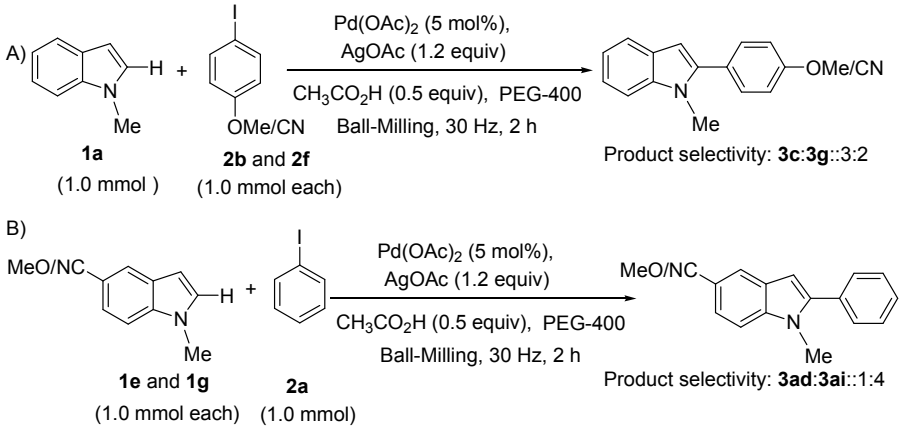
[a]In each case 1 mmol of indole (**1**) and 1.1 mmol of iodoarene (**2**) were milled together for 2 h (unless otherwise stated) in a RETSCH mixer mill (MM 400) with one 10 mm ball in a 5 mL stainless steel jar at 30 Hz frequency; [b]complete conversion took just 1 h; [c] the reaction mixture was milled for 4 h.

In our next study, a series of indole derivatives with substitution at the C-5 position was used as substrates for the reaction to elaborate the scope of this reaction methodology and corresponding electronic effect on the reaction time and on the yield of the final product were also investigated. As shown in last few entries of table 3, the results showed that the substituent at a distant place does not have any significant role to play in terms of the yield of 2-arylindole (**3ad-ak**, Table 3). In all the cases except one the yield was 90% or above. Notably, unlike previous reports[7c,8a] the strong mechanochemical condition enforce indoles with strong electron-withdrawing substituent, –CN at C-5 to take part in the reaction with good efficiency. However, the electronic effect does reduce the rate of the reaction to some extent (reactions require 4 h for complete conversion) as well as the yield drops below 90% at

times (**3ae**, Table 3). The present method was compared with available methods for ligand-free C2-selective arylation of indoles in terms of yields, reaction time, substrate scope etc. and a clear edge on many aspects for the current method has been realized over others conventional methods and several "green" methods (Table S2, SI).

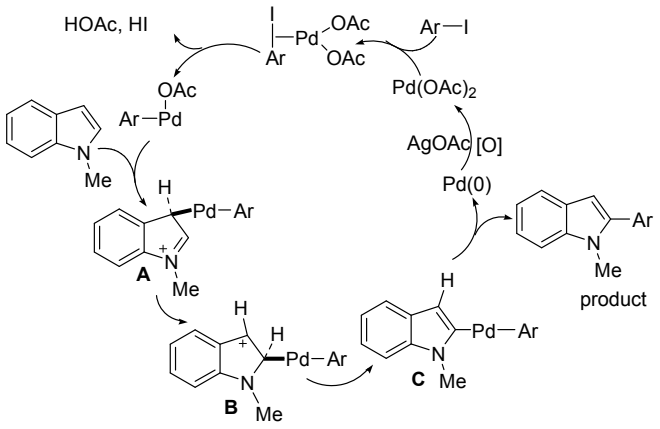
To get a better insight about the substituent effect on the rate of the reaction and product formation couple of kinetic experiments were performed by challenging a strong electron-donating group, -OMe with a strong electro-withdrawing group, -CN both in indole and iodoarenes (Scheme 2). The competing substrates were taken in stoichiometric amounts and the reaction mixtures were subjected to milling at standard condition for 2 h. The desired products and unreacted starting materials were separated by flash chromatography and analysed. TLC revealed complete conversion of the limiting substrates. From the isolated yields of products as shown in scheme 2, it can be understood that the substituent effect is not very significant for iodoarenes as a nominal product selectivity was obtained in favour of –CN derivative (isolated yields are 50% for **3c** and 34% for **3g**). In contrary, electronic effect is quite significant for the substituents present in the benzene ring of indole as the isolated yields were 17% and 69% for **3ad** and **3ai**, respectively.

Scheme 2. Competition Experiments to Study Substituent Effect



On the basis of literature reports of similar kinds of ligand free C-2 arylation reactions of indoles[5,7c,d] a plausible mechanism of a $Pd^{II/0}$ cycle is proposed. The general reaction pathway is represented by the formation of **3a** (Scheme 3). First, the Pd(II) catalyst may get inserted in the Ar-I bond to form an Ar-Pd(II)-X (where X = OAc) complex which undergoes C-H bond insertion at C-3 (intermediate **A**). The palladium from the temporary intermediate, **A** may eventually migrate to the C-2 position to form an intermediate **B**. The intermediate **B** may subsequently undergo an oxidative H-elimination to regain aromaticity (intermediate **C**), which finally release the product and the catalyst at Pd(0) state. The oxidant (here AgOAc) converts Pd(0) to Pd(II) state, which can take part in the next cycle. The presumed mechanistic pathway was further supported by the observation based on a reaction between **1a** and **2a** in the presence of stoichiometric amount of $Pd(OAc)_2$ instead of catalytic amount (5 mol%) without the addition of an oxidant (viz. AgOAc). Although the reaction was not very fair, it produced 2-arylated product (**3a**) as the major product (53%) along with some amount of 3-arylated product (12%) and inseparable polar side products with complete consumption of the starting materials after just 15 min of milling indicating the migration of palladium from metal-complex **A** to **B**.

Scheme 3. Proposed Mechanism



Next, a gram scale experiment was conducted to test the scalability of this mechanochemical procedure. The reaction was carried out with *N*-methylindole (10 mmol), iodobenzene (11 mmol) and 5 mol% $Pd(OAc)_2$ in the presence of AgOAc and AcOH as per the optimum reaction condition. For this purpose 25 mL of SS jar was used with one 15 mm ball. Although the reaction took slightly longer reaction time (1.5 h instead of 1 h), a satisfactory yield of 87% of **3a** was achieved. Therefore, the method can be scaled up by taking the reaction mixture in a bigger jar of adequate volume.

In conclusion, we have developed an efficient mechanochemical method for the direct C-2 selective arylation of indoles with aryl iodides at ambient temperature without the requirement of phosphines or other ligands. $Pd(OAc)_2$ was used as the catalyst and AgOAc as oxidant and the reactions were conducted at mild acidic condition. These mechanochemical conditions permit a broad set of functionalities both in the indole and in the aryl iodide units, and the corresponding 2-arylindoles were obtained up to 99% yields. Arylation is possible in both unprotected indoles and *N*-alkyl indoles with former substrate being relatively slower to react and little less yielding. In addition, indoles with deactivated five-membered ring took part in the reaction to afford high yields of 2-arylindoles. The scalability of the reaction was demonstrated by conducting the reaction in gram scale. The simplicity of this synthetic process, high yields, broad substrate scope, shorter reaction time and environmentally benign reaction conditions make this mechanochemical protocol a more efficient method than several existing methods for direct C-2 selective arylation of indoles.

EXPERIMENTAL SECTION:

General information: All the chemicals were used without further purification as obtained from commercial suppliers unless otherwise mentioned. *N*-Protection of indole derivatives was done by adopting the methods reported in the literature,[20-22] characterized by ^{1}H NMR

and used for the arylation reaction. All the mechanochemical reactions were carried out in 5 mL SS grinding jars with a single 10 mm ball in RETSCH MM 400. Isolation and purification of all the compounds were done by flash chromatography or conventional column chromatography (silica gel, 100–200 mesh) using ethyl acetate-petroleum ether as eluent. NMR spectra were recorded on Bruker Avance (400 MHz) NMR spectrometer and chemical shifts are reported downfield from TMS (= 0) in parts per million (δ) units. HRMS spectra were recorded on Agilent Technologies 6545 Q-TOF LC/MS mass spectrometer with ESI as the ion source. IR Affinity 1, Shimadzu was used to record IR spectra on KBr pellets. Heidolph Hei-Tec stirrer-cum-hot plate was used at 600 rom for *N*-protection of indole derivatives.

Synthetic procedures for *N*-protection of indole.

Preparation of 1-methyl-1*H*-indole (1a):[20] Indole (5 g, 42 mmol) and K_2CO_3 (5.8 g, 42 mmol) were taken in 35 mL of DMF, and 5.5 mL of dimethyl carbonate (65 mmol) was mixed together and the reaction mixture was heated at 130 °C for 2 h in heat-on blocks. At this point TLC showed starting material largely unchanged. The reaction mixture was cooled to about 50 °C and another 5.5 mL of dimethyl carbonate (65 mmol) was added at one portion. The mixture was again heated for another 7 h. The reaction mixture was cooled to room temperature and 150 mL of water was added. The resulting mixture was extracted with EtOAc (2 x 30 mL). The organic layer was washed with water, dried over anhydrous Na_2SO_4 and evaporated under vacuum to get sufficiently pure 1-methylindole (**1a**) as light-yellow oil in 98% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.71 (dt, J_1 = 0.8 Hz, J_2 = 6.8 Hz, 1H), 7.39 (dd, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 1H), 7.30 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 7.18 (td, J_1 = 0.8 Hz, J_2 = 6.8 Hz, 1H), 7.11 (d, J = 2.8 Hz, 1H), 6.56 (dd, J_1 = 1.2 Hz, J_2 = 3.2 Hz, 1H), 3.84 (s, 3H).

Preparation of 1-benzyl-1*H*-indole (1b):[21] A 100 mL round-bottom flask equipped with a magnetic stirring bar was charged with 25 mL of dimethyl sulfoxide and 4.7 g (0.084 mol) of potassium hydroxide. The mixture was stirred at room temperature for 5 min before indole (2 g, 17 mmol) was added. Stirring was continued for 45 min and then benzyl bromide (4.3 g, 34 mmol) was added to the reaction mixture. The reaction mixture was stirred for another 45 min and then diluted with 35 mL of water. The reaction mixture was extracted with diethyl ether (3 x 15 mL), the combined ether layer was washed with brine water, dried over anhydrous Na_2SO_4 and evaporated under vacuum. The crude product was purified by column chromatography to obtain pure product **1b** as colourless oil (3.5 g, 97%).^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.72 (dt, J_1 = 0.8 Hz, J_2 = 7.2 Hz, 1H), 7.46-7.43 (m, 2H), 7.36-7.30 (m, 3H), 7.23 (td, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 7.19-7.14 (m, 3H), 6.62 (dd, J_1 = 1.2 Hz, J_2 = 3.4 Hz, 1H), 5.37 (s, 2H).

Preparation of *tert*-butyl 1*H*-indole-1-carboxylate (1d):[22] To a stirred solution of indole (1 g, 8.55 mmol) in CH_3CN (12 mL) and DMAP (0.104 g, 0.85 mmol) in a round-bottom flask was added Boc_2O (2.79 g, 12.82 mmol) and the reaction mixture was stirred at room temperature for 2 h. The solvent was evaporated, diluted with 10 mL EtOAc, washed with H_2O (50 mL), aq sat. $NaHCO_3$ (25 mL), brine (25 mL), and dried over anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by column chromatography to obtain pure *N*-Boc indole, **1d** as colourless oil (1.8 g, 97%). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.20 (d, J = 8.4 Hz, 1H), 7.63 (d, J = 3.6 Hz, 1H), 7.60 (dt, J_1 = 0.8 Hz, J_2 = 6.8 Hz, 1H), 7.34 (td, J_1 = 1.6 Hz, J_2 = 7.6 Hz, 1H), 7.26 (td, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 6.60 (dd, J_1 = 0.8 Hz, J_2 = 3.6 Hz, 1H), 1.71 (s, 9H).

General Procedure for the Synthesis of Compound 3.

Indole derivative, **1** (1 mmol), iodoarene **2** (1.1 mmol), $Pd(OAc)_2$ (0.05 mmol, 5 mol%), AgOAc (1.2 mmol) and CH_3COOH (0.5 mmol) were taken in a 5 mL stainless steel milling

jar containing PEG-400 (0.3 mL) and a stainless steel ball (10 mm diameter). The jar was capped properly and the reaction mixture was subjected to milling in MM 400 for 2 h (or 4 h) at 30 Hz. After completion of reaction, the crude mixture was transferred to a beaker and stirred in the presence of 5 mL of EtOAc and 10 mL of water to take up the product in the organic layer and PEG-400 in water. After separating the organic layer, the aqueous layer was extracted with EtOAc (1 × 5 mL); organic fractions were combined, filtered through a celite bed, washed with brine and then dried over anhydrous Na_2SO_4. The solvent was evaporated in vacuum and the crude product was purified by flash chromatography or conventional column chromatography (silica gel, 100–200 mesh) to afford 72-99% of respective pure product (**3**).

1-Methyl-2-phenyl-1*H*-indole (3a):[4] White solid, 189 mg (91%), m.p. 95-97 °C (lit. m.p. 99-102 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.63 (d, J = 7.6 Hz, 1H), 7.51-7.43 (m, 4H), 7.39 (dt, J_1 = 1.2 Hz, J_2 = 4.8 Hz, 1H), 7.35 (d, J = 8.4 Hz, 1H), 7.24 (td, J_1 = 0.8 Hz, J_2 = 6.8 Hz, 1H), 7.14 (td, J_1 = 1.2 Hz, J_2 = 8.0 Hz, 1H), 6.56 (s, 1H), 3.72 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 141.6, 138.4, 132.9, 129.4, 128.5, 128.0, 127.9, 121.7, 120.5, 119.9, 109.7, 101.7, 31.2; IR (KBr): ṽ 3055, 2935, 1600, 1465, 766 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{13}N$ 208.1121; Found 208.1099.

2-Phenyl-1*H*-indole (3b):[4] White solid, 151 mg (78%), m.p. 185-186 °C (lit. m.p. 188-189 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.24 (br s, 1H), 7.60-7.55 (m, 3H), 7.38-7.33 (m, 3H), 7.25 (t, J = 7.2 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 7.05 (t, J = 7.2 Hz, 1H), 6.76 (s, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 137.9, 136.8, 132.4, 129.3, 129.1, 127.7, 125.2, 122.4, 120.7, 120.3, 110.9, 100.0; IR (KBr): ṽ 3446, 3049, 2922, 1647, 1458, 742 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{11}N$ 194.0964; Found 194.0942.

4-(1-Methyl-1*H*-indol-2-yl)benzonitrile (3c):[8d] Light brown solid, 212 mg (91%), m.p. 156-158 °C (lit. m.p. 161-162 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.76-7.73 (m, 2H), 7.66-7.60 (m, 3H), 7.38 (d, J_1 = 8.4 Hz, 1H), 7.30 (td, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 7.17 (td, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 6.65 (s, 1H), 3.76 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 139.3, 139.1, 137.4, 132.3, 129.5, 127.8, 122.8, 121.0, 120.4, 118.7, 111.3, 109.9, 103.6, 31.5; IR (KBr): ṽ 3070, 2939, 2221, 1928, 1602, 1465, 844, 796, 754 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{12}N_2$ 233.1073; Found 233.1061.

1-Methyl-2-(4-(trifluoromethyl)phenyl)-1*H*-indole (3d):[7d] White solid, 267 mg (97%), m.p. 56-59 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.73 (d, J = 8.4 Hz, 2H), 7.64 (t, J = 8.8 Hz, 3H), 7.38 (d, J = 8.4 Hz, 1H), 7.28 (td, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 7.17 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 6.63 (s, 1H), 3.76 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 139.9, 138.8, 136.4, 129.8 (q, $^2J_{C\text{-}F}$ = 32.4 Hz), 129.4, 128.2, 127.8, 125.5 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 123.9 (q, $^1J_{C\text{-}F}$ = 272.0 Hz), 122.4, 120.8, 120.2, 109.8, 102.9, 31.3; IR (KBr): ṽ 3059, 2945, 1614, 1465, 1323, 748 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{12}F_3N$ 276.0995; Found 276.0965.

1-Methyl-2-(3-(trifluoromethyl)phenyl)-1*H*-indole (3e):[4] Pale yellow solid, 273 mg (99%), m.p. 55-57 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.77 (s, 1H), 7.70-7.57 (m, 4H), 7.38 (d, J = 8.4 Hz, 1H), 7.28 (td, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 7.16 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 6.62 (s, 1H), 3.75 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 139.8, 138.6, 133.7, 132.5 (q, $^4J_{C\text{-}F}$ = 1.2 Hz), 131.2 (q, $^2J_{C\text{-}F}$ = 32 Hz), 129.1, 127.8, 126.0 (q, $^3J_{C\text{-}F}$ = 3.7 Hz), 124.51 (q, $^3J_{C\text{-}F}$ = 3.7 Hz), 124.49 (q, $^1J_{C\text{-}F}$ = 273.0 Hz), 122.3, 120.8, 120.2, 109.8, 102.6, 31.3; IR (KBr): ṽ 3062, 2949, 1606, 1325, 752 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{12}F_3N$ 276.0995; Found 276.0968.

2-(4-Bromophenyl)-1-methyl-1*H*-indole (3f):[5] White solid, 271 mg (95%), m.p. 99-102 °C (lit. m.p. 113–114 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.63 (d, J = 7.6 Hz, 1H), 7.59

(dt, J_1 = 2.4 Hz, J_2 = 6.4 Hz, 2H), 7.38-7.34 (m, 3H), 7.26 (td, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 7.15 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 6.56 (d, J = 0.8 Hz, 1H), 3.73 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 140.3, 138.5, 131.7, 130.8, 127.9, 122.2, 122.0, 120.6, 120.1, 109.7, 102.0, 31.2; IR (KBr): ṽ 3047, 2945, 1527, 1465, 1315, 779 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{12}BrN$ 286.0226 (for ^{79}Br) and 288.0207 (for ^{81}Br); Found 286.0233 (for ^{79}Br) and 288.0214 (for ^{81}Br).

2-(4-Methoxyphenyl)-1-methyl-1*H*-indole (3g):[4] Off-white solid, 195 mg (82%), m.p. 115-117 °C (lit. m.p. 117-120 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.62 (d, J = 8.0 Hz, 1H), 7.43 (dt, J_1 = 3.2 Hz, J_2 = 6.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 1H), 7.23 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 7.13 (td, J_1 = 0.8 Hz, J_2 = 8.0 Hz, 1H), 7.00 (dt, J_1 = 2.8 Hz, J_2 = 6.8 Hz, 2H), 6.50 (s, 1H), 3.86 (s, 3H), 3.71 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 159.5, 141.5, 138.2, 130.7, 128.0, 125.3, 121.4, 120.3, 119.8, 114.0, 109.6, 101.0, 55.4, 31.1; IR (KBr): ṽ 3051, 2937, 1919, 1610, 1496, 1246, 842 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{15}NO$ 238.1226; Found 238.1222.

2-(2-Methoxyphenyl)-1-methyl-1*H*-indole (3h):[5] Pale yellow solid, 196 mg (83%), m.p. 75-77 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.63 (d, J = 8.0 Hz, 1H), 7.42 (td, J_1 = 1.6 Hz, J_2 = 7.2 Hz, 1H), 7.35 (td, J_1 = 2.0 Hz, J_2 = 7.6 Hz, 2H), 7.22 (td, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 7.11 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 7.05 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 6.49 (s, 1H), 3.80 (s, 3H), 3.58 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 157.5, 138.6, 137.7, 132.6, 130.1, 128.0, 122.1, 121.3, 120.7, 120.5, 119.4, 110.9, 109.3, 101.7, 55.5, 30.7; IR (KBr): ṽ 3050, 2950, 1609, 1470, 1255, 1106, 785 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{15}NO$ 238.1226; Found 238.1204.

4-(1-Methyl-1*H*-indol-2-yl)phenol (3i):[5] Brown solid, 160 mg (72%), m.p. 98-100 °C (lit. m.p. 106–107 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.62 (d, J = 8.0 Hz, 1H), 7.39-7.33 (m, 3H), 7.25-7.21 (m, 1H), 7.13 (td, J_1 = 0.8 Hz, J_2 = 6.8 Hz, 1H), 6.92 (dt, J_1 = 2.4 Hz, J_2 =

6.4 Hz, 2H), 6.49 (s, 1H), 3.71 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 155.5, 141.4, 138.2, 130.9, 128.0, 125.5, 121.4, 120.3, 119.8, 115.4, 109.5, 101.0, 31.1; IR (KBr): ṽ 3447, 3065, 2936, 1750, 1603, 1069, 740 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{13}NO$ 224.107; Found 224.1066.

1-Methyl-2-*o*-tolyl-1*H*-indole (3j):[4] White solid, 188 mg (85%), m.p. 88-90 °C (lit. m.p. 90-92 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.64 (d, J = 8.0 Hz, 1H), 7.36-7.24 (m, 6H), 7.14 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 6.43 (s, 1H), 3.50 (s, 3H), 2.20 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 140.5, 138.1, 137.3, 132.6, 131.2, 130.1, 128.7, 128.1, 125.6, 121.3, 120.4, 119.7, 109.4, 101.6, 30.4, 20.1; IR (KBr): ṽ 3053, 2951, 1913, 1465, 1336, 767 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{15}N$ 222.1277; Found 222.1283.

1-Methyl-2-*m*-tolyl-1*H*-indole (3k):[5] White solid, 194 mg (88%), m.p. 35-37 °C (lit. colourless oil); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.63 (d, J = 8.0 Hz, 1H), 7.37-7.29 (m, 4H), 7.26-7.20 (m, 2H), 7.13 (t, J = 7.6 Hz, 1H), 6.54 (s, 1H), 3.73 (s, 3H), 2.42 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 141.8, 138.4, 138.2, 132.8, 130.1, 128.7, 128.4, 128.1, 126.5, 121.6, 120.5, 119.8, 109.6, 101.6, 31.2, 21.5; IR (KBr): ṽ 3049, 2914, 1604, 1465, 1340, 750 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{15}N$ 222.1277; Found 222.1272.

1-Methyl-2-*p*-tolyl-1*H*-indole (3l):[4] White solid, 186 mg (84%), m.p. 95-97 °C (lit. m.p. 96-98 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.62 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 8.0 Hz, 1H), 7.28-7.21 m, 3H), 7.13 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 6.53 (s, 1H), 3.73 (s, 3H), 2.42 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 141.7, 138.3, 137.8, 130.0, 129.3, 129.2, 128.1, 121.5, 120.4, 119.8, 109.6, 101.4, 31.1, 21.3; IR (KBr): ṽ 3024, 2914, 1604, 1462, 1338, 775 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{15}N$ 222.1277; Found 222.1270.

2-(4-*tert*-Butylphenyl)-1-methyl-1*H*-indole (3m):[7d] White solid, 229 mg (87%), m.p. 55-60 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.63 (d, J = 8.0 Hz, 1H), 7.50-7.44 (m, 4H), 7.35 (d, J = 7.6 Hz, 1H), 7.23 (td, J_1 = 1.2 Hz, J_2 = 8.0 Hz, 1H), 7.13 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 6.54 (s, 1H), 3.75 (s, 3H), 1.38 (s, 9H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 150.9, 141.7, 138.3, 129.9, 129.1, 128.0, 125.4, 121.5, 120.4, 119.8, 109.5, 101.4, 34.7, 31.4, 31.2; IR (KBr): ṽ 3047, 2964, 1498, 1465, 736 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{19}H_{21}N$ 264.1747; Found 264.1724.

4-(1-Benzyl-1*H*-indol-2-yl)benzonitrile (3n): White solid, 293 mg (95%), m.p. 155-156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.69 (dt, J_1 = 1.2 Hz, J_2 = 6.4 Hz, 1H), 7.64 (dt, J_1 = 2.0 Hz, J_2 = 6.4 Hz, 2H), 7.51 (dt, J_1 = 1.6 Hz, J_2 = 6.4 Hz, 2H), 7.31-7.25 (m, 3H), 7.22-7.15 (m, 3H), 7.01 (d, J = 6.8 Hz, 2H), 6.72 (s, 1H), 5.36 (s, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 139.6, 138.8, 137.6, 137.3, 132.4, 129.4, 129.0, 128.1, 127.5, 125.8, 123.0, 121.1, 120.7, 118.7, 111.4, 110.7, 104.2, 48.0; IR (KBr): ṽ 3055, 2223, 1932, 1604, 1458, 1348, 856, 798, 725 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{22}H_{16}N_2$ 309.1386; Found 309.1395.

1-Benzyl-2-(4-(trifluoromethyl)phenyl)-1*H*-indole (3o): White solid, 337 mg (96%), m.p. 65-68 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.70-7.68 (m, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.53 (d, J= 8.4 Hz, 2H), 7.29-7.26 (m, 3H), 7.21-7.16 (m, 3H), 7.02 (dd, J_1 = 1.6 Hz, J_2 = 7.6 Hz, 2H), 6.72 (s, 1H), 5.36 (s, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 140.1, 138.5, 137.8, 136.3, 129.9 (q, $^2J_{C\text{-}F}$ = 32.6 Hz), 129.3, 128.9, 128.1, 127.4, 125.8, 125.5 (q, $^3J_{C\text{-}F}$ = 3.7 Hz), 124.1 (q, $^1J_{C\text{-}F}$ = 270.0 Hz), 122.6, 120.9, 120.5, 110.6, 103.5, 47.9; IR (KBr): ṽ 3057, 2933, 1616, 1458, 1325, 1068, 786 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{22}H_{16}F_3N$ 352.1308; Found 352.1278.

1-Benzyl-2-(3-(trifluoromethyl)phenyl)-1*H*-indole (3p): Colourless oil, 336 mg (96%), ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.62-7.59 (m, 2H), 7.50 (t, J = 8.8 Hz, 2H), 7.39 (t, J = 7.6

Hz, 1H), 7.22-7.07 (m, 6H), 6.92 (dd, J_1 = 1.6 Hz, J_2 = 7.6 Hz, 2H), 6.63 (s, 1H) 5.26 (s, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 140.0, 138.4, 137.9, 133.5, 132.2, 131.0 (q, $^2J_{C-F}$ = 32.2 Hz), 129.1, 128.9, 128.1, 127.4, 126.0 (q, $^3J_{C-F}$ = 3.9 Hz), 125.9, 124.7 (q, $^3J_{C-F}$ = 3.7 Hz), 123.9 (q, $^1J_{C-F}$ = 271.0 Hz), 122.6, 120.9, 120.5, 110.6, 103.3, 47.8; IR (KBr): ṽ 3061, 2927, 1496, 1452, 1325, 1124, 700 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{22}H_{16}F_3N$ 352.1308; Found 352.1278.

1-benzyl-2-(4-bromophenyl)-1*H*-indole (3q): White solid, 349 mg (97%), m.p. 103-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.67-7.65 (m, 1H), 7.48 (dt, J_1 = 2.8 Hz, J_2 = 6.4 Hz, 2H), 7.28-7.23 (m, 5H), 7.18-7.13 (m, 3H), 6.99 (d, J = 6.8 Hz, 2H), 6.64 (s, 1H), 5.32 (s, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 140.5, 138.2, 138.0, 131.8, 131.7, 130.7, 128.9, 128.3, 127.3, 125.9, 122.4, 122.3, 120.7, 120.4, 110.6, 102.8, 47.8; IR (KBr): ṽ 3028, 2916, 1602, 1460, 1344, 754 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{21}H_{16}BrN$ 362.0539 (for ^{79}Br) and 364.0521 (for ^{81}Br); Found 362.0552 (for ^{79}Br) and 364.0531 (for ^{81}Br).

1-Benzyl-2-phenyl-1*H*-indole (3r):[8a] Off white solid, 263 mg (93%), m.p. 35-40 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.68-7.65 (m, 1H), 7.44-7.42 (m, 2H), 7.39-7.34 (m, 3H), 7.28-7.23 (m, 3H), 7.18-7.12 (m, 3H), 7.02 (d, J = 6.8 Hz, 2H), 6.65 (s, 1H), 5.35 (s, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 141.9, 138.3, 138.0, 132.7, 129.3, 128.85, 128.79, 128.6, 128.3, 128.1, 126.0, 122.0, 120.6, 120.2, 110.6, 102.4, 47.8; IR (KBr): ṽ 3043, 3015, 1780, 1602, 1462, 1344, 748 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{21}H_{17}N$ 284.1434; Found 284.1441.

1-Benzyl-2-(4-methoxyphenyl)-1*H*-indole (3s): White solid, 255 mg (81%), m.p. 99-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.66-7.64 (m, 1H), 7.34 (dt, J_1 = 2.8 Hz, J_2 = 6.4 Hz, 2H), 7.29-7.22 (m, 3H), 7.16-7.11 (m, 3H), 7.02 (d, J = 6.8 Hz, 2H), 6.90 (dt, J_1 = 2.8 Hz, J_2 = 6.8 Hz, 2H), 6.59 (s, 1H), 5.32 (s, 2H), 3.81 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz,

$CDCl_3$): δ (ppm) 159.6, 141.7, 138.3, 137.8, 130.5, 128.8, 128.4, 127.2, 126.0, 125.1, 121.7, 120.4, 120.1, 114.0, 110.5, 101.7, 55.4, 47.7; IR (KBr): ṽ 3026, 2958, 2345, 1610, 1498, 1253, 788, 725 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{22}H_{19}NO$ 314.1539; Found 314.1550.

1-Benzyl-2-(2-methoxyphenyl)-1*H*-indole (3t): Colourless thick oil, 267 mg (85%); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.66-7.64 (m, 1H), 7.38-7.31 (m, 3H), 7.20-7.15 (m, 3H), 7.12-7.09 (m, 2H), 7.00-6.92 (m, 4H), 6.56 (s, 1H), 5.18 (s, 2H), 3.60 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$): δ (ppm) 157.5, 138.6, 138.3, 137.2, 132.8, 130.2, 128.4, 128.3, 127.8, 127.7, 126.8, 126.4, 121.8, 121.5, 120.6, 120.5, 119.6, 110.7, 110.5, 102.6, 55.1, 48.0; IR (KBr): ṽ 3049, 2941, 1606, 1458, 1246, 736 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{22}H_{19}NO$ 314.1539; Found 314.1516.

4-(1-Benzyl-1*H*-indol-2-yl)phenol (3u): Light brown solid, 264 mg (82%), m.p. 80-82 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.66-7.63 (m, 1H), 7.29-7.21 (m, 5H), 7.12-7.11 (m, 3H), 7.01 (d, J = 6.8 Hz, 2H), 6.81 (dt, J_1 = 3.2 Hz, J_2 = 6.4 Hz, 2H), 6.57 (s, 1H), 5.32 (s, 2H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$): δ (ppm) 155.6, 141.6, 138.3, 137.8, 130.7, 128.8, 128.3, 127.2, 126.0, 125.3, 121.7, 120.4, 120.1, 110.5, 101.8, 47.6; IR (KBr): ṽ 3491, 3028, 2933, 1610, 1166, 754 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{21}H_{17}NO$ 300.1383; Found 300.1390.

1-Benzyl-2-*o*-tolyl-1*H*-indole (3v): Colourless thick oil, 252 mg (85%), ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.67-7.65 (m, 1H), 7.30-7.22 (m, 4H), 7.19-7.13 (m, 6H), 6.87-6.84 (m, 2H), 6.50 (s, 1H), 5.13 (s, 2H), 2.12 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$): δ (ppm) 140.3, 138.2, 137.9, 136.9, 132.3, 131.1, 130.2, 128.7, 128.5, 128.4, 127.1, 126.4, 125.5, 121.5, 120.5, 119.9, 110.5, 102.5, 47.3, 20.1; IR (KBr): ṽ 3024, 2908, 1602, 1460, 723 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{22}H_{19}N$ 298.159; Found 298.1599.

1-Benzyl-2-*m*-tolyl-1*H*-indole (3w): White solid, 271 mg (91%), m.p. 75-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.67-7.65 (m, 1H), 7.28-7.22 (m, 6H), 7.19-7.12 (m, 4H), 7.02 (d, J = 6.8 Hz, 2H), 6.63 (s, 1H), 5.35 (s, 2H), 2.32 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 142.1, 138.4, 138.2, 138.0, 132.7, 130.1, 128.8, 128.7, 128.4, 127.1, 126.3, 126.1, 121.8, 120.5, 120.1, 110.5, 102.2, 47.8, 21.4; IR (KBr): ṽ 3024, 2918, 1604, 1462, 1354, 727 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{22}H_{19}N$ 298.159; Found 298.1604.

1-Benzyl-2-*p*-tolyl-1*H*-indole (3x):[7e] White solid, 273 mg (92%), m.p. 79-82 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.66-7.64 (m, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.28-7.21 (m, 3H), 7.19-7.11 (m, 5H), 7.02 (d, J = 6.8 Hz, 2H), 6.62 (s, 1H), 5.35 (s, 2H), 2.37 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 142.0, 138.3, 138.0, 137.9, 129.8, 129.3, 129.2, 128.8, 128.4, 127.1, 126.0, 121.8, 120.5, 120.1, 110.5, 102.0, 47.7, 21.3; IR (KBr): ṽ 3028, 2914, 1602, 1460, 752 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{22}H_{19}N$ 298.159; Found 298.1604

1-Benzyl-2-(4-*tert*-butylphenyl)-1*H*-indole (3y): White solid, 310 mg (91%), m.p. 120-125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.67-7.64 (m, 1H), 7.41-7.36 (m, 4H), 7.30-7.23 (m, 3H), 7.15-7.11 (m, 3H), 7.04 (d, J = 7.2 Hz, 2H), 6.63 (s, 1H), 5.34 (s, 2H), 1.33 (s, 9H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 151.1, 141.9, 138.4, 137.9, 129.7, 128.8, 128.7, 128.4, 127.1, 126.0, 125.5, 121.7, 120.4, 120.1, 110.5, 102.0, 47.8, 34.7, 31.3; IR (KBr): ṽ 3055, 2964, 1496, 1460, 1348, 727 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{25}H_{25}N$ 340.206; Found 340.2031.

4-(1*H*-Indol-2-yl)benzonitrile (3z):[9e] Pale green solid, 163 mg (75%), m.p. 170-174 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.38 (br s, 1H), 7.67-7.57 (m, 5H), 7.35 (dd, J_1 = 0.8 Hz, J_2 = 8.0 Hz, 1H), 7.18 (td, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 7.08 (td, J_1 = 1.2 Hz, J_2 = 7.0 Hz, 1H), 6.88 (dd, J_1 = 0.8 Hz, J_2 = 2.0 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm)

137.4, 136.6, 135.5, 132.9, 128.9, 125.3, 123.7, 121.2, 120.8, 118.9, 111.2, 110.6, 102.7; IR (KBr): ṽ 3408, 3055, 2922, 2221, 1425, 804, 754 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{10}N_2$ 219.0917; Found 219.0899.

2-(2-(Trifluoromethyl)phenyl)-1*H*-indole (3aa):[9e] White solid, 191 mg (77%), m.p. 88-90 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.27 (br s, 1H), 7.81-7.80 (m, 1H), 7.75-7.72 (m, 1H), 7.57 (dd, J_1 = 0.8 Hz, J_2 = 7.6 Hz, 1H), 7.49-7.47 (m, 2H), 7.34 (dd, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 1H), 7.16 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 7.07 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 6.82 (dd, J_1 = 1.2 Hz, J_2 = 2.4 Hz, 1H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$): δ (ppm) 137.1, 136.2, 133.2, 131.4 (q, $^2J_{C-F}$ = 32.2 Hz), 129.6, 129.1, 128.3, 124.2 (q, $^3J_{C-F}$ = 3.8 Hz), 124.0 (q, $^1J_{C-F}$ = 273 Hz), 123.1, 121.7 (q, $^3J_{C-F}$ = 3.8 Hz), 121.0, 120.6, 111.1, 101.3; IR (KBr): ṽ 3442, 3045, 2920, 1602, 1455, 1350, 735 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{10}F_3N$ 262.0838; Found 262.0802.

***tert*-Butyl-2-phenyl-1*H*-indole-1-carboxylate (3ab):**[8b] White solid, 250 mg (85%), m.p. 73-75 °C (lit. m.p. 75-76 °C); ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.14 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 7.2 Hz, 1H), 7.35-7.24 (m, 6H), 7.18 (td, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 6.48 (s, 1H), 1.23 (s, 9H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$): δ (ppm) 150.2, 140.5, 137.4, 135.0, 129.2, 128.7, 127.8, 127.6, 124.3, 122.9, 120.5, 115.2, 109.9, 83.4, 27.6; IR (KBr): ṽ 3053, 2980, 1730, 1540, 1338, 752 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{19}H_{19}NO_2$ 294.1489; Found 294.1484.

***tert*-Butyl-2-(4-cyanophenyl)-1*H*-indole-1-carboxylate (3ac):** White solid, 241 mg (76%), m.p. 73-75 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.12 (d, J = 9.2 Hz, 1H), 7.62 (dt, J_1 = 1.6 Hz, J_2 = 6.8 Hz, 2H), 7.51 (d, J = 7.6 Hz, 1H), 7.46 (dt, J_1 = 2.0 Hz, J_2 = 6.4 Hz, 2H), 7.30 (td, J_1 = 1.2 Hz, J_2 = 7.2 Hz, 1H), 7.21 (td, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 6.57 (s, 1H), 1.30 (s, 9H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$): δ (ppm) 149.9, 139.5, 138.3, 137.7, 131.6, 129.3, 128.9, 125.2, 123.4, 120.9, 118.9, 115.5, 111.7, 111.1, 84.3, 27.7; IR (KBr): ṽ 3053,

2983, 2227, 1728, 1452, 1340, 752 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{18}N_2O_2$ 319.1441; Found 319.1458.

1-Methyl-2-phenyl-1*H*-indole-5-carbonitrile (3ad):[8a] White solid, 216 mg (93%), m.p. 166-170 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.88 (s, 1H), 7.45-7.40 (m, 4H), 7.39-7.36 (m, 2H), 7.31 (dt, J_1 = 0.8 Hz, J_2 = 8.0 Hz, 1H), 6.54 (s, 1H), 3.69 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$): δ (ppm) 143.9, 139.7, 131.6, 129.4, 128.75, 128.68, 127.7, 125.9, 124.6, 120.9, 110.5, 102.8, 102.3, 31.5; IR (KBr): ṽ 2925, 2217, 1610, 1330, 770 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{12}N_2$ 233.1073; Found 233.1067.

2-(4-Cyanophenyl)-1-methyl-1*H*-indole-5-carbonitrile (3ae): White solid, 208 mg (81%), m.p. 206-211 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.00 (s, 1H), 7.82 (dt, J_1 = 1.6 Hz, J_2 = 6.8 Hz, 2H), 7.66 (dt, J_1 = 2.0 Hz, J_2 = 6.4 Hz, 2H), 7.52 (dd, J_1 = 1.6 Hz, J_2 = 8.4 Hz, 1H), 7.46 (dt, J_1 = 0.8 Hz, J_2 = 7.6 Hz, 1H), 6.74 (s, 1H), 3.83 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$): δ (ppm) 141.6, 140.2, 136.1, 132.5, 129.8, 127.4, 126.4, 125.4, 120.5, 118.5, 112.2, 110.8, 104.0, 103.4, 31.7; IR (KBr): ṽ 3076, 2957, 2230, 2217, 1608, 1472, 798 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{11}N_3$ 258.1026; Found 258.1022.

5-Bromo-1-methyl-2-phenyl-1*H*-indole (3af):[5] White solid, 280 mg (98%), m.p. 108-110 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.79 (d, J = 2.0 Hz, 1H), 7.55-7.44 (m, 5H), 7.35 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 1H), 7.26 (dt, J_1 = 0.8 Hz, J_2 = 8.0 Hz, 1H), 6.53 (s, 1H), 3.76 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$): δ (ppm) 142.7, 137.0, 132.3, 129.6, 129.4, 128.6, 128.2, 124.4, 122.9, 113.1, 111.1, 101.1, 31.3; IR (KBr): ṽ 3076, 2968, 1602, 1467, 1329, 758, 659 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{12}BrN$ 286.0226 (for ^{79}Br) and 288.0207 (for ^{81}Br); Found 286.022 (for ^{79}Br) and 288.0201 (for ^{81}Br).

4-(5-Bromo-1-methyl-1*H*-indol-2-yl)benzonitrile (3ag): White solid, 300 mg (97%), m.p. 158-160 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.80-7.77 (m, 3H), 7.64 (dt, J_1 = 2.0 Hz, J_2 = 6.4 Hz, 2H), 7.38 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 1H), 7.27 (dt, J_1 = 0.8 Hz, J_2 = 8.4 Hz,

1H), 6.61 (s, 1H), 3.77 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 140.4, 137.6, 136.8, 132.4, 129.6, 129.3, 125.5, 123.3, 118.6, 113.6, 111.6, 111.3, 102.9, 31.6; IR (KBr): ṽ 3080, 2927, 2225, 1610, 1470, 789 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{16}H_{11}BrN_2$ 311.0178 (for ^{79}Br) and 313.0163 (for ^{81}Br); Found 311.0174 (for ^{79}Br) and 313.0158 (for ^{81}Br).

5-Bromo-2-(4-methoxyphenyl)-1-methyl-1*H*-indole (3ah): Yellowish solid, 301 mg (95%), m.p. 98-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.76 (d, J = 1.6, 1H), 7.44 (dt, J_1 = 2.8 Hz, J_2 = 6.4 Hz, 2H), 7.33 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 1H), 7.23 (dt, J_1 = 0.8 Hz, J_2 = 8.0 Hz, 1H), 7.04 (dt, J_1 = 2.8 Hz, J_2 = 6.8 Hz, 2H), 6.46 (s, 1H), 3.90 (s, 3H), 3.73 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 159.7, 142.6, 136.8, 130.6, 129.6, 124.7, 124.1, 122.7, 114.1, 113.0, 111.0, 100.5, 55.4, 31.2; IR (KBr): ṽ 3074, 2958, 2836, 1609, 1468, 1244 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{16}H_{14}BrNO$ 316.0332 (for ^{79}Br) and 318.0312 (for ^{81}Br); Found 316.0326 (for ^{79}Br) and 318.0307 (for ^{81}Br).

5-Methoxy-1-methyl-2-phenyl-1*H*-indole (3ai):[7e] Yellowish solid, 228 mg (96%), m.p. 90-96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.43-7.35 (m, 4H), 7.33-7.29 (m, 1H), 7.17 (d, J = 8.8 Hz, 1H), 7.02 (d, J = 2.4 Hz, 1H), 6.83 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H), 6.41 (s, 1H), 3.78 (s, 3H), 3.63 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 154.4, 142.2, 133.8, 132.9, 129.3, 128.5, 128.3, 127.8, 111.9, 110.4, 102.2, 101.3, 56.0, 31.3; IR (KBr): ṽ 3074, 2986, 1854, 1616, 1475, 1220, 801 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{16}H_{15}NO$ 238.1226; Found 238.1222.

4-(5-Methoxy-1-methyl-1*H*-indol-2-yl)benzonitrile (3aj): Light pink solid, 238 mg (91%), m.p. 118-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.77 (dt, J_1 = 1.6 Hz, J_2 = 6.8 Hz, 2H), 7.63 (dt, J_1 = 1.6 Hz, J_2 = 6.8 Hz, 2H), 7.30 (d, J = 8.8 Hz, 1H), 7.13 (d, J = 2.4 Hz, 1H), 6.99 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H), 6.61 (s, 1H), 3.90 (s, 3H), 3.77 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 154.6, 139.8, 137.4, 134.5, 132.3, 129.4, 128.1, 118.8,

113.3, 111.1, 110.7, 103.2, 102.2, 55.9, 31.7; IR (KBr): ṽ 3057, 2924, 2834, 2232, 1607, 1474, 1221, 840, 574 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{14}N_2O$ 263.1179; Found 263.1175.

5-Methoxy-2-(4-methoxyphenyl)-1-methyl-1*H*-indole (3ak): Yellowish solid, 241 mg (90%), m.p. 78-80 °C; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.34 (dt, J_1 = 3.0 Hz, J_2 = 6.4 Hz, 2H), 7.15 (d, J = 8.8 Hz, 1H), 7.01 (d, J = 2.4 Hz, 1H), 6.91 (dt, J_1 = 2.0 Hz, J_2 = 6.8 Hz, 2H), 6.81 (dd, J_1 = 2.8 Hz, J_2 = 9.2 Hz, 1H), 6.35 (s, 1H), 3.78 (s, 6H), 3.61 (s, 3H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$): δ (ppm) 159.4, 154.3, 142.0, 133.6, 130.6, 128.3, 125.4, 114.0, 111.6, 110.3, 102.1, 100.7, 56.0, 55.4, 31.2; IR (KBr): ṽ 2957, 1613, 1476, 1216, 1173 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{17}NO_2$ 268.1332; Found 268.1324.

Scale-up synthesis of compound 3a

For scale-up synthesis of **3a** all the substrates, reagents and catalyst were taken 10 times of the usual quantity (i.e. 10 mmol of **1a** and rest in appropriate proportions) and the reaction was conducted in a 25 mL SS jar with one 15 mm ball and reaction was milled for 1.5 h for complete conversion. The rest of the procedure remained same. After purification by flash chromatography 1.81 g (87%) of **3a** was obtained.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Information on solution phase reactions, a comparative table, copies of ^1H NMR and ^{13}C NMR spectra.

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ACKNOWLEDGEMENTS

M. B. thanks DST-SERB (project No. EMR/2016/002253) for financial support and D. D. is indebted to SERB for JRFship. Z. T. B thanks DST-INSPIRE for INSPIRE Fellowship. We acknowledge central instrumentation facility of BITS-Pilani, Pilani campus for NMR and HRMS analysis.

Declaration of interest

The authors declare no personal, financial or organizational conflict of interests.

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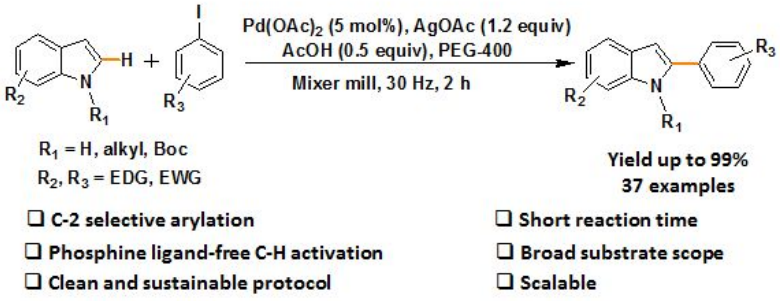
Graphical Abstract/TOC



R_1 = H, alkyl, Boc
R_2, R_3 = EDG, EWG

Yield up to 99%
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- ❑ C-2 selective arylation
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