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Palladium-catalyzed direct desulfitative C2 arylations of 3-halo-*N*-protected indoles using (hetero)arenesulfonyl chlorides

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The direct arylation of *N*-protected 3-haloindole derivatives with benzenesulfonyl chlorides as coupling partners using 5 mol% of bis(acetonitrile)dichloropalladium(II) catalyst and lithium carbonate as base in 1,4-dioxane was investigated. We demonstrated that both iodo and chloro substituents at indolyl C3 position act as temporary blocking groups to allow the formation of 2-arylindoles through a direct desulfitative arylation, followed by *in-situ* dehalogenation. While, from 3-bromoindole derivatives, 2-aryl-3-bromoindoles were obtained without debromination, and could be converted into 2,3-diarylindoles through a second palladium coupling. which are both of interest as potential intermediates in the synthesis of bioactive molecules.

Introduction

The 2-arylindoles derivatives are an important class of molecules because this motif is found in plenty of naturals products and synthetic pharmaceuticals. As examples, Kenpaullone, which contains a bromine substituent at the C5 position, displays inhibition of Cyclin-Dependent Kinase (CDK) activity.[1] Rucaparib, a fluoroindole derivative, is a drug in Phase II for the treatment of patients with ovarian cancers.[2] Diaplasinin is an anti-coagulant and Bazedoxifene is a selective estrogen receptor modulator developed by Pfizer.[3]

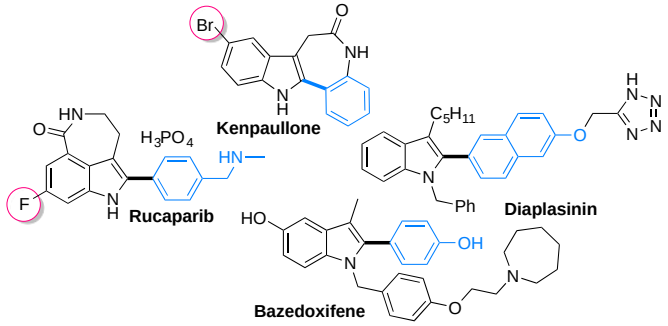

Figure 1. Pharmaceuticals containing a 2-arylindole motif.

Due to the ubiquitousness of this motif, the discovery of environmentally friendly efficient protocols with a high functional group tolerance allowing their preparation remains an important research topic. Stille,[4] Suzuki,[5] or Negishi[6] Pd-catalyzed coupling reactions represent some of the most efficient methods to prepare 2-arylindoles; however, such reactions require the previous preparation of a metallated indole or arene.

In 1985, Ohta *et al.* reported the Pd-catalyzed arylation of heteroarenes *via* a C–H bond activation and, amongst others, indole derivatives has been successfully used as substrates.[7] Since this discovery, this methodology has proven to be a very powerful tool for a simpler and eco-friendly access to a very wide variety of arylated heterocycles, as it saves synthetic steps (*i.e.,* no preparation of metallated derivatives) and as the major by-products of the reaction are a base associated to HX.[8] Several examples of Pd-catalyzed direct arylations of indole derivatives using aryl halides as coupling partners have been reported in recent years.[9] Different coupling partners, such as arylboronic acids,[10] aryl iodonium salts,[11] aryldiazonium salts,[12] arylsiloxanes,[13] carboxylic acids,[14] sodium sulfinates,[15] acid sulfinates,[16] or even simple arenes through a double C–H activation,[17] have been successfully employed in Pd-catalyzed direct C2-arylation of indoles. Among these diverse protocols, only a few of them are tolerant towards the C–Br bonds.

Chemoselective transformations allowing sequential orthogonal transformations, especially involving sequential C–H bond activations,[18] has become a very promising synthetic strategy for the straightforward synthesis of complex structures.[19] As example of chemoselective C2-arylation of indoles, Sanford and co-workers reported the use of bis(4-bromophenyl)iodonium tetrafluoroborate to allow the synthesis of C2-arylated indoles, without the cleavage of the C–Br bond (Figure 1.a).[11a] In 2012, Deng, Luo *et al.* reported a chemoselective desulfitative direct arylation of *N*-methylindole using sodium 4-bromobenzenesulfinate (Figure 1.b).[15] The reaction only involved the sulfinate function and the bromine was untouched. On the other hand, Wang and *al.* extended this coupling to 4-bromobenzenesulfinic acid in acidic conditions and microwave heating (Figure 1c).[16]

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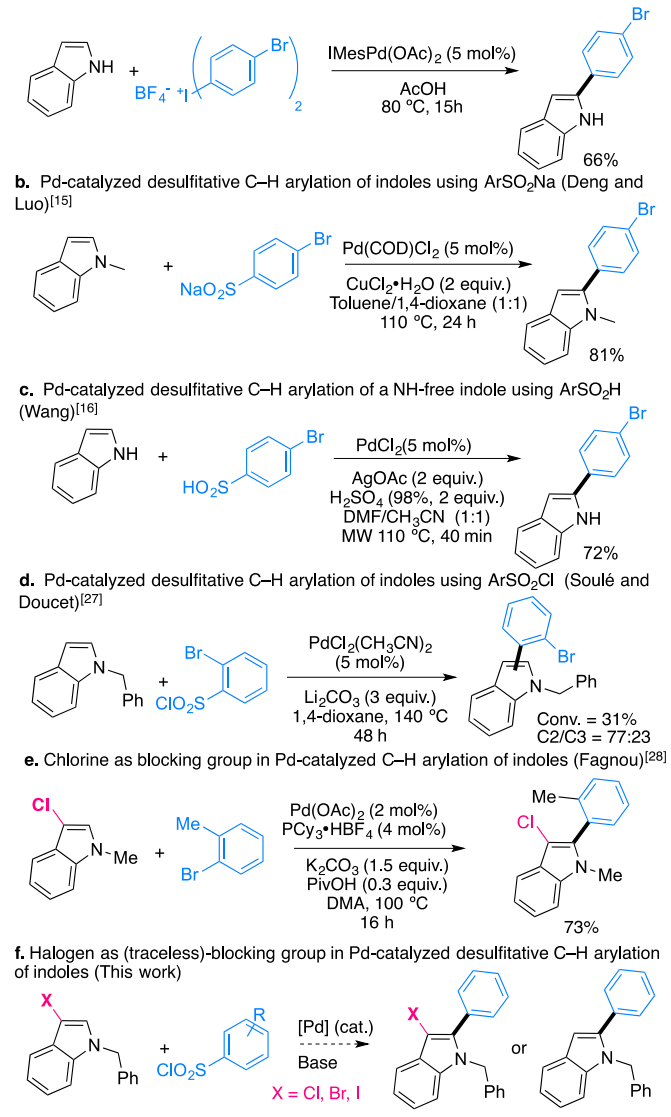


Figure 2. Palladium-catalyzed chemoselective direct arylation of indoles

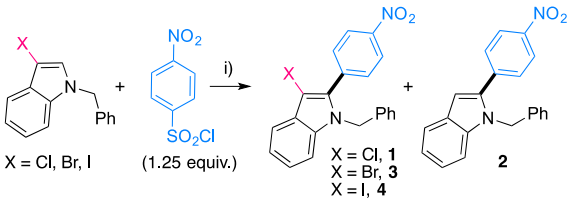
During the last decade, benzenesulfonyl chloride coupling partners have been used for the direct arylation of benzoquinoline,[20] azoles,[21] thiophenes,[22] (benzo)furans[23] and pyrroles.[24] Recently, we reported on Pd-catalyzed chemoselective direct desulfitative arylation of heteroarenes using (poly)halobenzenesulfonyl chlorides,[25] which allowed sequential arylations.[26] It is important to note that in such couplings, even C–I bonds were tolerated by the optimized conditions. However, when we applied our reaction conditions to the desulfitative arylation of indoles, using 2-bromobenzenesulfonyl chloride, a mixture of C2 and C3 arylated products was obtained (Figure 1.d).[24b, 27] Fagnou and coworkers have used 3-chloro-1-methylindole with aryl bromides as starting materials in Pd-catalyzed direct indole C2-arylation (Figure 1.e).[28] The chlorine atom plays the role of blocking group to overcome the regioselectivity issue of this direct coupling. Hence, we decided to investigate the reactivities of 3-chloro-, 3-bromo and 3-iodo-*N*-protected indole derivatives in Pd-catalyzed desulfitative direct arylation (Figure 1.f).

Results

Using our previous optimized reaction conditions for Pd-catalyzed direct desulfitative arylation with heteroarenes – namely, 5 mol% of $PdCl_2(CH_3CN)_2$ catalyst associated to 3 equivalents of Li_2CO_3 as base in 1,4-dioxane at 140 ºC over 48 h– we evaluated the reactivity of 1-benzyl-3-chloroindole in the presence of 4-nitrobenzenesulfonyl chloride (Table 1, entry 1). To our surprise, the desulfitative C2-arylation and the dechlorination of the C3 position occurred at the same time to afford directly the 2-arylindole **2** in 74% yield. The fact that no indole C3-arylation was observed suggests that the arylation occurred first followed by dehalogenation. Hence, the chlorine atom at indole C3-position acts as a trace-less blocking group. Next, we investigated the reactivity of 1-benzyl-3-bromoindole. In contrast to 3-chloroindole derivative, the C–Br bond was only partially cleaved under these reaction conditions, as the 3-bromo-2-arylindole **3** was isolated in 64% yield, although the debrominated 2-arylindole **2** was also formed in 28% yield (Table 1, entry 2). Hence, we decided to investigate a few reaction parameters in order to improve the yield in **3** (Table 1, entries 3-11). When the reaction was performed at a lower temperature of 100 ºC, no reaction occurred (Table 1, entry 3). The change of solvent to diethylcarbonate (DEC) or cyclopentyl methyl ether (CPME) did not allowed to improve the yield of **3**. In addition, neat condition did not afford any desired arylated product, but only side products (Table 1, entries 4-6). The use of other palladium sources, such as $Pd(OAc)_2$ or $Pd_2(dba)_3$, only gave the debrominated coupling product **2** in low yields (Table 1, entries 7 and 8). The use of 0.5 equivalent of CuBr as additive also gave only the undesired product **2** in 65% yield (Table 1, entry 9). Finally, a shorter reaction time of 18 h allowed to reach a high **3**:**2** selectivity, and the desired 2-aryl-3-bromoindole **3** was isolated in 83% yield (Table 1, entry 10). A reaction time of 5 h lead to a poor yield in **3**, but without any formation of **2** (Table 1, entry 11). Finally, we evaluated the reactivity of 1-benzyl-3-iodoindole under the same reaction conditions. Similarly to the chloro substituent, an iodo substituent at indolyl C3-position acts as a trace-less blocking group. Indeed, only the dehalogenated C-2-arylated indole **2** was obtained in 84% yield (Table 1, entry 12).

In summary, we found that both Cl and I substituents at the indolyl C3 position are cleaved under our reaction conditions and play the role of temporary blocking group, allowing the regioselective C2-arylation of indoles. In contrast, 1-benzyl-3-bromoindole was arylated at C2 position without the cleavage of the C–Br bond.

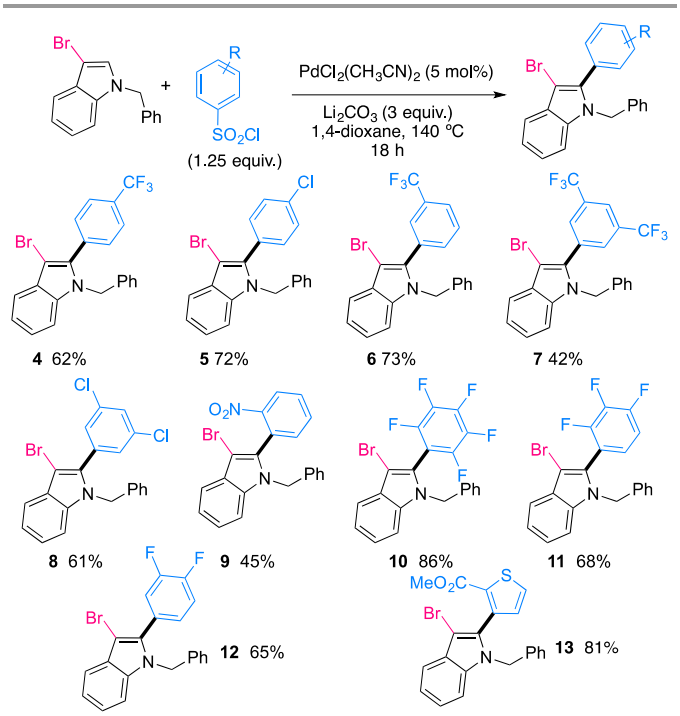
Table 1. Reactivity of 1-Benzyl-3-haloindoles in Palladium-Catalyzed Desulfitative Arylation with 4-Nitrobenzenesulfonyl Chloride.



Entry	X	Modifications to conditions	Conv.	Yield of **1, 3** or **4**	Yield of **2**
1	Cl	–	100%	**1,** traces	73%
2	Br	–	100%	**3**, 64%	28%
3	Br	100 ºC	0%	0%	0%
4	Br	DEC as solvent	52%	**3**, 22%	30%
5	Br	CPME as solvent	25%	**3**, traces	24%
6	Br	neat, 18 h	75%	**3**, traces	
7	Br	$Pd(OAc)_2$	15%	**3**, traces	15%
8	Br	$Pd_2(dba)_3$	15%	**3**, traces	15%
9	Br	CuBr (50 mol%)	69%	**3**, traces	65%
10	Br	18 h	100%	**3**, 83%	5%
11	Br	5 h	28%	**3**, 28%	0%
12	I	–	100%	**4**, traces	84%

i) $PdCl_2(CH_3CN)_2$ (5 mol%), Li_2CO_3 (3 equiv.), 1,4-dioxane, 140 ºC, 48 h. DEC = diethylcarbonate; CPME = cyclopentyl methyl ether.

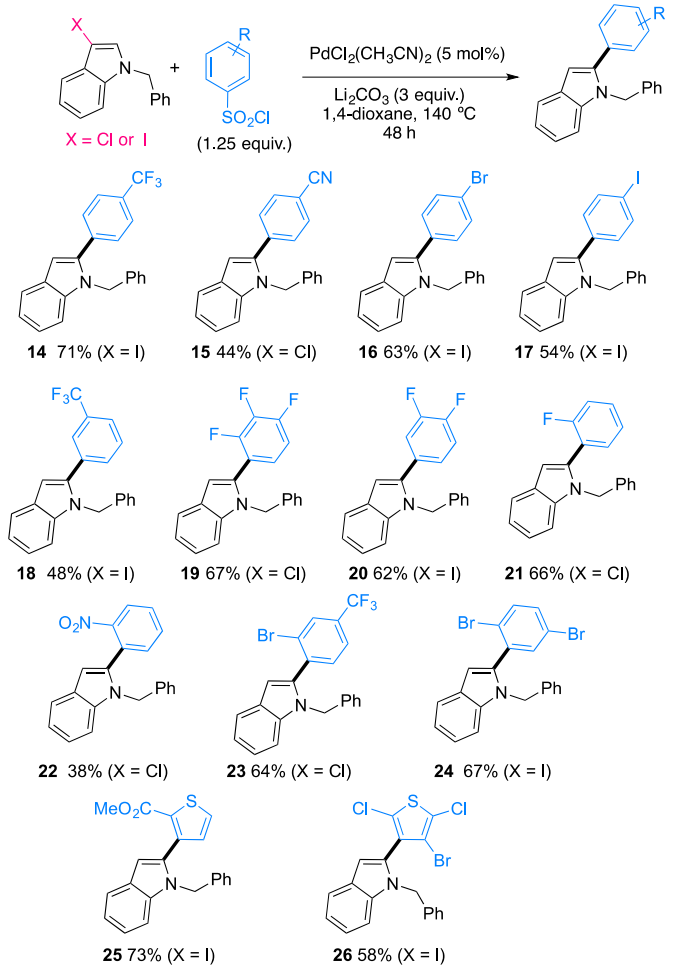
Then, we studied the scope of the benzenesulfonyl chlorides in Pd-catalyzed desulfitative arylation of 1-benzyl-3-bromoindole using 5 mol% of $PdCl_2(CH_3CN)_2$ catalyst associated to 3 equivalents of Li_2CO_3 as base in 1,4-dioxane at 140ºC over 18h (Scheme 1). Benzenesulfonyl chlorides substituted at *para*-position by an electron-withdrawing group, such as trifluoromethyl or chloro, allowed the formation of desired C2-arylated indoles **4** and **5** in 62% and 72% yields, respectively, without cleavage of the C–Br bonds. A *meta*-substituent on the benzenesulfonyl chloride has no influence on the yield, as the coupling product **6** was isolated in 73% yield. In contrast, 3,5-bis(trifluoromethyl)benzenesulfonyl chloride displayed a moderate reactivity, as the 2-arylated 3-bromoindole derivative **7** was obtained in only 42% yield. However, the coupling product **8**, resulting from the use of 3,5-dichlorobenzenesulfonyl chloride as aryl source, was isolated in 61%. The reaction seems to be sensitive to steric hindrance, as the reaction between 2-nitrobenzenesulfonyl chloride and 1-benzyl-3-bromoindole afforded the desired indole **9** in only 45% yield. Polyfluorinated molecules are ubiquitous in medicinal chemistry as well as in materials owing to fluorine atom properties (*i.e.*, electronegativity, size, lipophilicity, and electrostatic interactions), which induces a dramatic change in the molecules behavior.[29] Hence, we studied the reactivity of a couple of polyfluorinated benzenesulfonyl chlorides as coupling partners with 1-benzyl-3-bromoindole under the same reaction conditions.[18c] We were pleased to find that arylation occurred again at the indolyl C2 position without the cleavage of both C–Br and C–F bonds to afford the penta-, tri- and difluophenylindoles **10**-**12** in 65-86% yields. Finally, methyl 3-(chlorosulfonyl)thiophene-2-carboxylate was also tolerated affording methyl 3-(1-benzyl-3-bromoindol-2-yl)thiophene-2-carboxylate (**13**) in 81% yield.[30]



Scheme 1. Scope of Benzenesulfonyl Chlorides in Pd-Catalyzed Desulfitative C2-Arylation of 1-Benzyl-3-bromoindole.

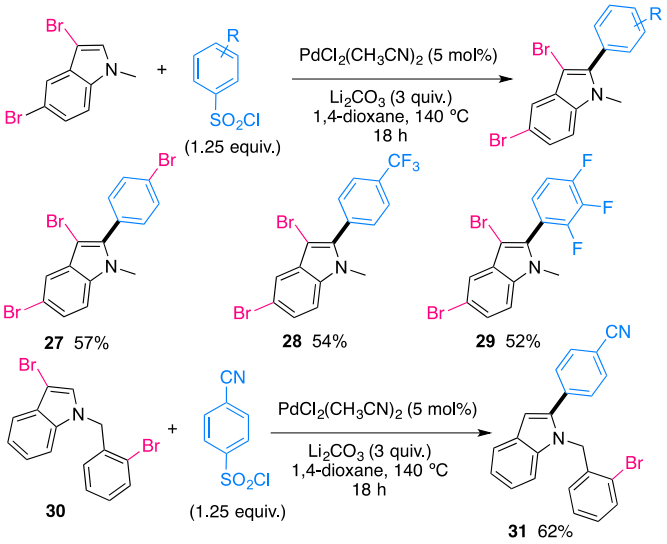
Next, we employed 1-benzyl-3-chloroindole or 1-benzyl-3-iodoindole, in which the halo substituents were used as traceless blocking groups, with a wide range of benzenesulfonyl chlorides for the one-step synthesis of 2-arylindole derivatives (Scheme 2). Overall, better yields in favor of the desired C2-arylated indole derivatives were obtained when the reaction was performed from 1-benzyl-3-iodoindole. Benzenesulfonyl chlorides substituted at *para*-position by an electron-withdrawing group such as trifluoromethyl or cyano allowed the formation of the desired C2-arylated indoles **14** and **15** in 71% and 44% yields, with the cleavage of C–X bonds. Then, we investigated the reactivity of benzenesulfonyl chlorides bearing a C–X bond. 4-bromo- and 4-iodo-benzenesulfonyl chlorides smoothly reacted with 1-benzyl-3-iodoindole to afford the C2-arylated products **16** and **17** in 63% and 54% yields, respectively. It is important to note that, unlike indolyl C–I bond, both phenyl C–Br and C–I bonds remained untouched at the end of the reactions, allowing further Pd-catalyzed orthogonal transformations. A *meta*-trifluoromethyl group on the benzenesulfonyl chloride resulted in a moderate reactivity; as from 1-benzyl-3-chloroindole, the arylated product **18** was obtained in moderate yield. Again, polyfluorinated benzenesulfonyl chlorides smoothly reacted, whatever the coupling partners, to deliver the tri-, di- and mono-fluorophenylindoles **19**-**21** in 62-67% yields. As seen previously, an *ortho*-substituent on the benzenesulfonyl chloride resulted in a moderate reactivity in desulfitative coupling with 3-haloindoles. Indeed, the reaction between 1-benzyl-3-chloroindole and 2-nitrobenzenesulfonyl

chloride afforded the arylated product **22** in only 38% yield. As one of the major advantage of the desulfitative coupling is the chemoselectivity in the presence of halo-benzenesulfonyl chlorides, we investigated other (poly)bromobenzenesulfonyl chlorides as aryl sources. The reaction between 2-bromo-4-(trifluoromethyl)benzenesulfonyl chloride and 1-benzyl-3-chloroindole afforded the 2-arylindole **23** in 64% yield, without cleavage of the C–Br bond. A similar result was observed in the case of 2,5-dibromobenzenesulfonyl chloride affording **24** in 67% yield. Thiophene-3-sulfonyl chloride derivatives were also used as coupling partners giving the heteroarenes diads **25** and **26** in 73% and 58% yields. Importantly, the thienyl C–Br and C–Cl bonds were untouched.



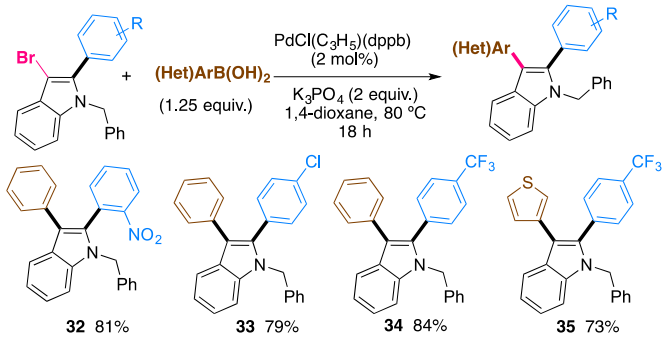
Scheme 2. Scope of Benzenesulfonyl Chlorides in Pd-Catalyzed Desulfitative C2-Arylation of 1-Benzyl-3-chloroindole or 1-Benzyl-3-iodoindole.

Polybrominated indoles are important building blocks in pharmaceutical synthesis, as C–Br bonds provide complementary platforms for further elaboration *via,* among others, Pd-catalyzed cross-coupling reactions. Therefore, we investigated the reactivity of polybrominated indoles in such desulfitative couplings. Under the previous optimized reaction conditions, 3,5-dibromo-1-methylindole was arylated at C2-position using 4-bromobenzenesulfonyl chloride to give the tribromoindole **27** in 57% yield, without the cleavage of the three C–Br bonds. Two other benzenesulfonyl chlorides were also coupled to 3,5-dibromo-1-methylindole affording the 3,5-dibromoindoles **28** and **29** in 54% and 52% yields, respectively. In addition, we evaluated the reactivity of 3-bromo-1-(2-bromobenzyl)indole **30** in the presence of 4-cyanobenzenesulfonyl chloride. The 2-arylindole **31** was obtained in good yield, albeit we observed the cleavage of the indolyl C–Br bond, whereas the benzyl C–Br was untouched.



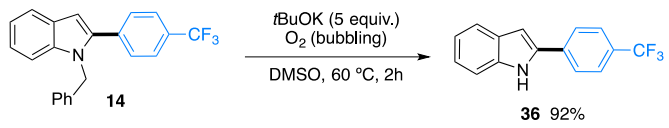
Scheme 3. Scope of Benzenesulfonyl chlorides in Pd-Catalyzed Desulfitative Arylation of 3,5-dibromo-1-methylindole and 3-Bromo-1-(2-bromobenzyl)indole.

We further demonstrated the potential of this methodology with the introduction of a second aryl group, for the two steps synthesis of 2,3-diarylindole derivatives containing two different aryl units (Scheme 4). From a mixture of 2-aryl-3-bromoindole **9** and phenylboronic acid (1.2 equivalents) in the presence of 2 mol% of a diphosphine-palladium catalyst and 2 equivalent of K_3PO_4 in dioxane at 80 ºC over 18h, the 2,3-diarylindole **32** was obtained in 81% yield. Other 2,3-diarylindoles, with different substituents (*e.g.*, Cl, CF_3) on the C2-aryl group, were subjected to the same reaction conditions and allowed the formation of the desired coupling products **33** and **34** in similar yields. Finally, an heteroarylboronic acid, such as thiophen-3-ylboronic acid, was coupled with **4** to afford the 2,3-diarylindole **35** in 73% yield.



Scheme 4. Pd-Catalyzed Functionalizations of the 2-Aryl-3-bromoindole Derivatives Through Suzuki Coupling Reaction.

As a lot of natural products and pharmaceuticals contain NH-free indole motifs, we demonstrated that the *N*-benzyl substituent of indole derivative **14** could be deprotected (Scheme 5). We used slightly modified conditions described by Deaton-Rewolinski,[31] namely large excess of *t*BuOK (5 equiv.) in DMSO at 60 ºC under oxygen bubbling. Using these conditions, the indole derivative **14** was deprotected into the NH-free indole **36** in 92% yield.



Scheme 5. Debenzylation of the indole derivative **14**.

Conclusions

In summary, we reported herein on the reactivity of 3-halo-*N*-protected-indoles in Pd-catalyzed desulfitative arylation using benzenesulfonyl chlorides as aryl sources. We shown that a bromo substituent at indolyl C3 position can be used as a blocking group and then used in further chemical transformation in orthogonal synthesis of 2,3-diarylindoles containing two different aryl groups. On the contrary, both indolyl chloro or iodo C3-substituents act as traceless blocking groups to regioselectively afford the dehalogenated C2-arylated indoles in good yields. A wide range of benzenesulfonyl chloride was tolerated by the optimized reaction conditions including those bearing C–Br and C–I bonds. Thanks to this chemoselectivity, this Pd-catalyzed orthogonal transformation scheme could have the potential to streamline pharmaceutical development, providing a new rapid and efficient method to discover drug candidates.

Experimental Section

General: All reactions were carried out under argon atmosphere with standard Schlenk-tube techniques. HPLC grade 1,4-dioxane was stored under argon and used without further purification. ^{1}H NMR spectra were recorded on Bruker GPX (400 MHz or 300 MHz) spectrometer. Chemical shifts (d) were reported in parts per million relative to residual chloroform (7.26 ppm for ^{1}H ; 77.0 ppm for ^{13}C), constants were reported in Hertz. ^{1}H NMR assignment abbreviations were the following: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), and multiplet (m). ^{13}C NMR spectra were recorded at 100 MHz on the same spectrometer and reported in ppm. All reagents were weighed and handled in air.

Preparation of the $PdCl(C_3H_5)(dppb)$ catalyst:[32] An oven-dried 40 mL Schlenk tube equipped with a magnetic stirring bar under argon atmosphere, was charged with $[Pd(C_3H_5)Cl]_2$ (182 mg, 0.5 mmol) and dppb (426 mg, 1 mmol). 10 mL of anhydrous dichloromethane were added, then, the solution was stirred at room temperature for twenty minutes. The solvent was removed in vacuum. The powder was used without purification. (^{31}P NMR 381 MHz, $CDCl_3$) δ = 19.3 (s).

General procedure for synthesis of heteroarylated heteroarenes: To a 25 mL oven dried Schlenk tube, arylsulfonyl chloride (1.25 mmol), 3-haloindole derivative (1 mmol), Li_2CO_3 (0.222 g, 3 mmol), 1,4-dioxane (2 mL) and $PdCl_2(CH_3CN)_2$ (12.9 mg, 0.05 mmol) were successively added. The reaction mixture was evacuated by vacuum-argon cycles (5 times) and stirred at 140 ºC (oil bath temperature) for 18-48 h (see tables and schemes). After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography to afford the 2-arylated indoles.

1-Benzyl-2-(4-nitrophenyl)indole (2): 1-Benzyl-3-chloroindole (0.241 g, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.277 g, 1.25 mmol) affords **2** in 73 % (0.241 g) or 84% (0.276 g) from 1-benzyl-3-iodoindole (0.333 g, 1 mmol) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.23 (d, *J* = 8.7 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 2H), 7.33-7.22 (m, 5H), 7.22-7.16 (m, 1H), 7.03 (dd, *J* = 1.9 and 7.3 Hz, 2H), 6.80 (s, 1H), 5.39 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 147.1, 139.2, 139.0, 137.5, 129.4, 129.0, 128.0, 127.6, 125.8, 123.9, 123.3, 121.2, 120.8, 110.7, 104.8, 48.1. Elemental analysis: calcd (%) for $C_{21}H_{16}N_2O_2$ (328.37): C 76.81, H 4.91; found: C 77.13, H 4.82.

1-Benzyl-3-bromo-2-(4-nitrophenyl)indole (**3**): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.277 g, 1.25 mmol) affords **3** in 83% (0.338 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.28 (d, *J* = 8.7 Hz, 2H), 7.70-7.66 (m, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.307.24 (m, 7H), 6.95-6.90 (m, 1H), 5.30 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 147.7, 137.2, 137.0, 135.6, 131.4, 131.2, 129.0, 127.7, 127.5, 125.8, 124.3, 123.7, 121.4, 120.0, 110.8, 92.9, 48.6. Elemental analysis: calcd (%) for $C_{21}H_{15}BrN_2O_2$ (407.27): C 61.93, H 3.71; found: C 61.69, H 3.79.

1-Benzyl-3-bromo-2-(4-(trifluoromethyl)phenyl)indole (**4**): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 4-(trifluoromethyl)benzenesulfonyl chloride (0.305 g, 1.25 mmol) affords **4** in 62% (0.267 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.70-7.66 (m, 3H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.33-7.24 (m, 6H), 6.97-6.93 (m, 2H), 5.28 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.3, 136.8, 136.5, 134.1, 131.0, 130.9 (q, *J* = 21.9 Hz), 128.9, 127.6, 127.5, 125.9, 125.5 (q, *J* = 3.2 Hz), 124.0 (q, *J* = 271.0 Hz), 123.8, 121.2, 119.8, 110.7, 92.0, 48.4. Elemental analysis: calcd (%) for $C_{22}H_{15}BrF_3N$ (430.27): C 61.41, H 3.51; found: C 61.28, H 3.83.

1-Benzyl-3-bromo-2-(4-chlorophenyl)indole (**5**): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 4-chlorobenzenesulfonyl chloride (0.264 g, 1.25 mmol) affords **5** in 72% (0.286 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.70-7.66 (m, 1H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 7.31-7.23 (m, 6H), 6.99-6.94 (m, 2H), 5.30 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.4, 136.9, 136.6, 135.0, 131.9, 131.7, 128.8, 127.5, 125.9, 123.4, 121.0, 120.9, 119.6, 118.5, 110.7, 91.5, 48.3. Elemental analysis: calcd (%) for $C_{21}H_{15}BrClN$ (396.71): C 63.58, H 3.81; found: C 63.73, H 3.89.

1-Benzyl-3-bromo-2-(3-(trifluoromethyl)phenyl)indole (**6**): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 3-(trifluoromethyl)benzenesulfonyl chloride (0.305 g, 1.25 mmol) affords **6** in 73% (0.314 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.68-7.65 (m, 1H), 7.65-6.61 (m, 2H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.53 (t, *J* = 7.0 Hz, 1H), 7.28-7.21 (m, 6H), 6.94-6.88 (m, 2H), 5.26 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.2, 136.7, 136.4, 133.8, 131.2, 130.9 (q, *J* = 33.0 Hz), 129.0, 128.8, 127.5 (q, *J* = 3.0 Hz), 125.9, 125.5 (q, *J* = 3.0 Hz), 123.8 (q, J = 262.7 Hz), 123.6, 121.1, 120.9, 119.7, 118.7, 110.6, 91.9, 48.4. Elemental analysis: calcd (%) for $C_{22}H_{15}BrF_3N$ (430.27): C 61.41, H 3.51; found: C 61.67, H 3.29.

1-Benzyl-3-bromo-2-(3,5-bis(trifluoromethyl)phenyl)indole (**7**): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 3,5-bis(trifluoromethyl)benzenesulfonyl chloride (0.391 g, 1.25 mmol) affords **7** in 42% (0.209 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.89 (brs, 1H), 7.81 (brs, 2H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.36-7.32 (m, 2H), 7.32-7.27 (m, 1H), 7.27-7.23 (m, 3H), 6.92-6.88 (m, 2H), 5.27 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.2, 137.0, 134.6, 132.6, 132.1, 131.7, 130.7 (m), 129.0, 127.9, 127.2, 125.8, 124.4, 122.9 (q, *J* = 262.7 Hz), 122.3 (m), 120.0, 110.5, 92.9, 48.6. Elemental analysis: calcd (%) for $C_{23}H_{14}BrF_6N$ (498.27): C 55.44, H 2.83; found: C 55.42, H 2.81.

1-Benzyl-3-bromo-2-(3,5-dichlorophenyl)indole (**8**): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 3,5-dichlorobenzenesulfonyl chloride (0.307 g, 1.25 mmol) affords **8** in 61% (0.263 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.68-7.65 (m, 1H), 7.42 (t, *J* = 2.1 Hz, 1H), 7.29-7.26 (m, 5H), 7.26-7.24 (m, 3H), 6.94-6.90 (m, 2H), 5.28 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.2, 136.8, 135.2, 135.1, 133.3, 129.0, 128.9, 128.8, 127.7, 127.3, 126.0, 123.9, 121.2, 119.9, 110.7, 92.3, 48.5. Elemental analysis: calcd (%) for $C_{21}H_{14}BrCl_2N$ (431.15): C 58.50, H 3.27; found: C 58.21, H 3.14.

1-Benzyl-3-bromo-2-(2-nitrophenyl)indole (**9**): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 2-nitrobenzenesulfonyl chloride (0.277 g, 1.25 mmol) affords **9** in 45% (0.183 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.15-8.12 (m, 1H), 7.65-7.59 (m, 3H), 7.35-7.30 (m, 1H), 7.28-7.25 (m, 3H), 7.23-7.19 (m, 3H), 6.94-6.90 (m, 2H), 5.36 (d, *J* = 16.8 Hz, 1H), 5.05 (d, *J* = 16.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 149.7, 137.0, 136.5, 133.5, 132.9, 130.5, 128.7, 127.6, 127.1, 126.3, 125.7, 124.8, 123.5, 120.9, 119.6, 118.6, 110.6, 92.0, 48.8. Elemental analysis: calcd (%) for $C_{21}H_{15}BrN_2O_2$ (407.27): C 61.93, H 3.71; found: C 62.12, H 3.58.

1-Benzyl-3-bromo-2-(perfluorophenyl)indole (**10**): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 2,3,4,5,6-pentafluorobenzenesulfonyl chloride (0.333 g, 1.25 mmol) affords **10** in 86% (0.388 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.68 (d, *J* = 7.4 Hz, 1H), 7.33-7.29 (m, 2H), 7.29-7.24 (m, 1H), 7.23-7.19 (m, 3H), 6.86 (ddd, *J* = 1.5, 3.1 and 5.9 Hz, 2H), 5.23 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 144.9 (md, *J* = 251.2 Hz), 142.2 (md, *J* = 266.8 Hz), 137.8 (md, *J* = 251.2 Hz), 137.1, 136.2, 128.8, 127.8, 127.0, 126.0, 124.3, 122.6, 121.1, 120.0, 110.6, 105.9 (t, *J* = 18.9 Hz), 95.7, 48.6. Elemental analysis: calcd (%) for $C_{21}H_{11}BrF_5N$ (452.22): C 55.78, H 2.45; found: C 55.98, H 2.38.

1-Benzyl-3-bromo-2-(2,3,4-trifluorophenyl)indole (**11**): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 2,3,4-trifluorobenzenesulfonyl chloride (0.288 g, 1.25 mmol) affords **11** in 68% (0.283 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 77.71-7.66 (m, 1H), 7.33-7.25 (m, 4H), 7.24-7.20 (m, 2H), 7.04 (dquint., *J* = 2.4 and 5.3 Hz, 2H), 6.88 (dd, *J* = 2.7 and 5.5 Hz, 2H), 5.34 (d, *J* = 16.8 Hz, 1H), 5.16 (d, *J* = 16.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 151.9 (ddd, *J* = 3.9, 10.2 and 256.3 Hz), 149.6 (ddd, *J* = 3.9, 10.2 and 256.3 Hz), 140.3 (td, *J* = 14.7 and 247.9 Hz), 136.8, 136.6, 130.2, 128.7, 127.6, 127.2, 126.7 (m), 126.0, 123.8, 121.0, 119.7, 116.1 (dd, *J* = 2.8 and 12.0 Hz), 112.4 (dd, *J* = 3.2 and 17.4 Hz), 110.6, 93.5, 48.4. Elemental analysis: calcd (%) for $C_{21}H_{13}BrF_3N$ (416.24): C 60.60, H 3.15; found: C 60.84, H 3.29.

1-Benzyl-3-bromo-2-(3,4-difluorophenyl)indole (**12**): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and 3,4-difluorobenzenesulfonyl chloride (0.266 g, 1.25 mmol) affords **12** in 65% (0.259 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.90 (dddd, *J* = 2.4, 6.7, 9.0 and 15.5 Hz, 1H), 7.69-7.65 (m, 1H), 7.44 (dt, *J* = 7.1 and 9.3 Hz, 1H), 7.34-7.19 (m, 6H), 7.17-7.13 (m, 1H), 6.97-6.89 (m, 2H), 5.29 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 150.6 (dd, *J* = 17.7 and 148.8 Hz), 150.0 (dd, *J* = 17.7 and 148.8 Hz), 137.2, 136.5, 135.8, 129.8, 127.5, 127.2, 127.0 (m), 125.8, 123.6, 121.0, 119.8 (d, *J* = 18.5 Hz), 119.6, 117.5 (d, *J* = 16.2 Hz), 110.6, 91.8, 48.2. Elemental analysis: calcd (%) for $C_{21}H_{14}BrF_2N$ (398.25): C 63.33, H 3.54; found: C 63.67, H 3.91.

Methyl 3-(1-benzyl-3-bromoindol-2-yl)thiophene-2-carboxylate (**13**): 1-Benzyl-3-bromoindole (0.286 g, 1 mmol) and methyl 3-(chlorosulfonyl)thiophene-2-carboxylate (0.301 g, 1.25 mmol) affords **13** in 81% (0.345 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.63-7.60 (m, 1H), 7.54 (d, *J* = 5.3 Hz, 1H), 7.51 (d, *J* = 5.3 Hz, 1H), 7.27-7.23 (m, 1H), 7.23-7.19 (m, 1H), 7.19-7.15 (m, 2H), 7.05 (d, *J* = 4.9 Hz, 1H), 6.98 (d, *J* = 4.9 Hz, 1H), 6.89 (dd, *J* = 2.8 and 5.5 Hz, 2H), 5.27 (d, *J* = 16.5 Hz, 1H), 5.15 (d, *J* = 16.4 Hz, 1H), 3.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 161.6, 137.4, 136.3, 135.7, 132.3, 132.0, 131.8, 130.7, 128.6, 127.4, 127.2, 126.4, 123.1, 120.6, 119.5, 110.4, 92.3, 52.3, 48.5. Elemental analysis: calcd (%) for $C_{21}H_{16}BrNO_2S$ (426.32): C 59.16, H 3.78; found: C 59.36, H 4.02.

1-Benzyl-2-(4-(trifluoromethyl)phenyl)indole (14): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 4-(trifluoromethyl)benzenesulfonyl chloride (0.305 g, 1.25 mmol) affords **14** in 71% (0.249 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.15 (ddd, *J* = 1.3, 4.6 and 6.8 Hz, 1H), 8.09 (ddd, *J* = 1.7, 5.0 and 7.9 Hz, 2H), 8.03-7.98 (m, 2H), 7.75-7.70 (m, 3H), 7.69-7.62 (m, 3H), 7.48 (dd, *J* = 4.7 and 7.2 Hz, 2H), 7.17 (s, 1H), 5.28 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 140.1, 138.4, 137.8, 136.2, 129.9 (q, *J* = 33.0 Hz), 129.2, 128.8, 129.1, 127.4, 125.8, 125.5 (q, *J* = 2.1 Hz), 124.1 (q, *J* = 279.8 Hz), 122.6, 120.8, 120.5, 110.6, 103.5, 47.8. Elemental analysis: calcd (%) for $C_{22}H_{16}F_3N$ (362.26): C 75.20, H 4.59; found: C 75.64, H 4.89.

4-(1-Benzylindol-2-yl)benzonitrile (15): 1-Benzyl-3-chloroindole (0.242 g, 1 mmol) and 4-cyanobenzenesulfonyl chloride (0.252 g, 1.25 mmol) affords **15** in 44% (0.136 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.70-7.63 (m, 3H), 7.51(d, *J* = 8.1 Hz, 2H), 7.29-7.15 (m, 6H), 7.00 (d, *J* = 7.2 Hz, 2H), 6.74 (s, 1H), 5.35 (s, 2H). This is a known compound and the spectral data are identical to those reported in literature.[33]

1-Benzyl-2-(4-bromophenyl)indole (16): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 4-bromobenzenesulfonyl chloride (0.319 g, 1.25 mmol) affords **16** in 63% (0.228 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.71-7.67 (m, 1H), 7.53 (d, *J* = 8.5 Hz, 2H), 7.35-7.28 (m, 4H), 7.26-7.24 (m, 1H), 7.22-7.18 (m, 2H), 7l.18-7.14 (m, 1H), 7.03 (dd, *J* = 2.1 and 7.3 Hz, 2H), 6.67 (s, 1H), 5.36 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 140.5, 138.2, 138.0, 131.7, 131.6, 130.7, 128.8, 128.2, 127.3, 125.9, 122.4, 122.3, 120.7, 120.4, 110.5, 102.7, 47.8. Elemental analysis: calcd (%) for $C_{21}H_{16}BrN$ (351.37): C 69.63, H 4.45; found: C 69.27, H 4.78.

1-Benzyl-2-(4-iodophenyl)indole (17): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 4-iodobenzenesulfonyl chloride (0.378 g, 1.25 mmol) affords **17** in 54% (0.221 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.72 (d, *J* = 8.2 Hz, 2H), 7.70-7.68 (m, 1H), 7.32-7.24 (m, 3H), 7.21-7.13 (m, 5H), 7.02 (d, *J* = 7.4 Hz, 2H), 6.66 (s, 1H), 5.35 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 140.5, 138.2, 137.9, 137.7, 132.1, 130.8, 128.8, 128.2, 127.3, 125.8, 122.2, 120.6, 120.3, 110.5, 102.7, 93.9, 47.7. Elemental analysis: calcd (%) for $C_{21}H_{16}IN$ (409.27): C 61.63, H 3.94; found: C 69.89, H 4.13.

1-Benzyl-2-(3-(trifluoromethyl)phenyl)indole (18): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 3-(trifluoromethyl)benzenesulfonyl chloride (0.305 g, 1.25 mmol) affords **18** in 48% (0.169 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.71-7.66 (m, 2H), 7.59 (dd, *J* = 7.9 and 10.2 Hz, 2H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.31-7.22 (m, 5H), 7.19 (d quint., *J* = 2.2 and 7.3 Hz, 2H), 7.01 (d, *J* = 7.1

Hz, 2H), 6.71 (s, 1H), 5.35 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 140.0, 138.3, 137.8, 133.5, 132.2, 131.0 (q, *J* = 31.5 Hz), 129.0, 128.8, 128.1, 127.4, 126.0 (q, *J* = 3.0 Hz), 125.8, 124.6 (q, *J* = 3.0 Hz), 123.9 (q, *J* = 266.9 Hz), 122.5, 120.8, 120.4, 110.5, 103.3, 47.8. Elemental analysis: calcd (%) for $C_{22}H_{16}F_3N$ (351.37): C 75.20, H 4.59; found: C 75.59, H 4.42.

1-Benzyl-2-(2,3,4-trifluorophenyl)indole (**19**): 1-Benzyl-3-chloroindole (0.242 g, 1 mmol) and 2,3,4-trifluorobenzenesulfonyl chloride (0.288 g, 1.25 mmol) affords **19** in 67% (0.226 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69 (dd, *J* = 1.5 and 7.7 Hz, 1H), 7.24-7.18 (m, 5H), 7.15 (t, *J* = 8.2 Hz, 1H), 7.07-6.98 (m, 1H), 6.98-6.92 (m, 1H), 6.9 (dd, *J* = 2.3 and 6.9 Hz, 2H), 6.68 (s, 1H), 5.27 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 151.2 (md, *J* = 256.3 Hz), 149.3 (md, *J* = 256.3 Hz), 140.2 (md, *J* = 256.3 Hz), 137.7, 137.4, 132.6, 128.6, 128.0, 127.3, 126.0, 125.6 (m), 122.6, 120.9, 120.3, 118.4 (dd, *J* = 3.8 and 12.4 Hz), 112.1 (dd, *J* = 4.0 and 17.9 Hz), 110.6, 104.7, 47.9. Elemental analysis: calcd (%) for $C_{21}H_{14}F_3N$ (337.35): C 74.77, H 4.18; found: C 74.96, H 4.36.

1-Benzyl-2-(3,4-difluorophenyl)indole (**20**): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 3,4-difluorobenzenesulfonyl chloride (0.266 g, 1.25 mmol) affords **20** in 62% (0.198 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69-7.65 (m, 1H), 7.31-7.21 (m, 5H), 7.21-7.10 (m, 4H), 6.99 (d, *J* = 7.5 Hz, 2H), 6.63 (s, 1H), 5.34 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 150.3 (dm, *J* = 253.1 Hz), 150.5 (dm, *J* = 253.1 Hz), 139.4, 138.1, 137.7, 129.7 (t, *J* = 6.8 Hz), 128.9, 128.0, 127.4, 125.8, 125.3 (dd, *J* = 3.0 and 6.0 Hz), 122.4, 120.7, 120.4, 118.2 (d, *J* = 17.7 Hz), 117.4 (d, *J* = 17.3 Hz), 110.5, 103.0, 47.7. Elemental analysis: calcd (%) for $C_{21}H_{15}F_2N$ (319.35): C 78.98, H 4.73; found: C 79.24, H 5.01.

1-Benzyl-2-(2-fluorophenyl)indole (**21**): 1-Benzyl-3-chloroindole (0.242 g, 1 mmol) and 2-fluorobenzenesulfonyl chloride (0.243 g, 1.25 mmol) affords **21** in 66% (0.199 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.71-7.68 (m, 1H), 7.42-7.34 (m, 2H), 7.25-7.14 (m, 8H), 6.95 (d, *J* = 7.5 Hz, 2H), 6.69 (s, 1H), 5.30 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 160.2 (d, *J* = 250.9 Hz), 137.9, 137.6, 135.0, 132.4, 130.4 (d, *J* = 8.5 Hz), 128.6, 128.3, 127.1, 126.2, 124.2 (d, *J* = 2.8 Hz), 122.1, 120.7, 120.6, 120.1, 116.0 (d, *J* = 22.0 Hz), 110.6, 104.0, 47.9. Elemental analysis: calcd (%) for $C_{21}H_{16}FN$ (301.36): C 83.70, H 5.35; found: C 83.99, H 5.18.

1-Benzyl-2-(2-nitrophenyl)indole (**22**): 1-Benzyl-3-chloroindole (0.242 g, 1 mmol) and 2-nitrobenzenesulfonyl chloride (0.277 g, 1.25 mmol) affords **22** in 38% (0.125 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.99-7.86 (m, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.57-7.51 (m, 2H), 7.37-7.33 (m, 1H), 7.25-7.12 (m, 6H), 6.92 (dd, *J* = 2.9 and 5.5 Hz, 2H), 6.55 (s, 1H), 5.21 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 150.0, 137.6, 137.5, 135.3, 133.5, 132.2, 129.6, 128.6, 128.0, 127.3, 126.3, 124.1, 122.4, 120.9, 120.2, 110.5, 103.3, 48.0. Elemental analysis: calcd (%) for $C_{21}H_{16}N_2O_2$ (328.37): C 76.81, H 4.91; found: C 77.2, H 5.12.

1-Benzyl-2-(2-bromo-4-(trifluoromethyl)phenyl)indole (**23**): 1-Benzyl-3-chloroindole (0.242 g, 1 mmol) and 2-bromo-4-(trifluoromethyl)benzenesulfonyl chloride (0.404 g, 1.25 mmol) affords **23** in 64% (0.275 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.96 (s, 1H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.3 (d, *J* = 7.3 Hz, 1H), 7.23 (dt, *J* = 0.9 and 7.1 Hz, 1H), 7.21-7.16 (m, 4H), 6.88-6.84 (m, 2H), 6.65 (s, 1H), 5.22 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.8, 137.5, 137.1, 133.1, 132.1 (q, *J* = 32.1 Hz), 129.8 (m), 128.6, 127.8, 127.3, 126.2, 125.4, 123.9 (m), 123.0 (q, *J* = 276.5 Hz), 122.5, 121.0, 120.3, 110.5, 104.0, 47.8. Elemental analysis: calcd (%) for $C_{22}H_{15}BrF_3N$ (430.26): C 61.41, H 3.51; found: C 61.75, H 3.87.

1-Benzyl-2-(2,5-dibromophenyl)indole (**24**): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 2,5-dibromobenzenesulfonyl chloride (0.418 g, 1.25 mmol) affords **24** in 67% (0.296 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.72 (d, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 9.3 Hz, 1H), 7.43 (s, 1H), 7.32-7.27 (m, 4H), 7.27-7.17 (m, 4H), 6.92-6.88 (m, 2H), 5.24 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.8, 137.5, 136.9, 135.9, 135.6, 134.0, 133.0, 128.5, 127.8, 127.3, 126.3, 123.8, 122.3, 121.0, 120.8, 120.1, 110.4, 103.7, 47.8. Elemental analysis: calcd (%) for $C_{21}H_{15}Br_2N$ (441.17): C 57.17, H 3.43; found: C 57.39, H 3.91.

1-Methyl 3-(1-benzylindol-2-yl)thiophene-2-carboxylate (**25**): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and methyl 3-(chlorosulfonyl)thiophene-2-carboxylate (0.301 g, 1.25 mmol) affords **25** in 73% (0.254 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.69 (d, *J* = 7.7 Hz, 1H), 7.50 (d, *J* = 5.2 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.25-7.11 (m, 4H), 7.01 (d, *J* = 5.0 Hz, 1H), 6.93 (d, *J* = 2.8 Hz, 2H), 6.66 (s, 1H), 5.26 (s, 2H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 161.8, 138.4, 137.9, 137.2, 134.1, 132.2, 130.3, 128.4, 127.9, 127.1, 126.3, 121.9, 120.7, 119.8, 110.4, 110.3, 103.4, 52.1, 47.7. Elemental analysis: calcd (%) for $C_{21}H_{17}NO_2S$ (347.43): C 72.60, H 4.93; found: C 72.99, H 5.13.

1-Benzyl-2-(4-bromo-2,5-dichlorothiophen-3-yl)indole (**26**): 1-Benzyl-3-iodoindole (0.333 g, 1 mmol) and 4-bromo-2,5-dichlorothiophene-3-sulfonyl chloride (0.301 g, 1.25 mmol) affords **26** in 58% (0.253 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.77 (d, *J* = 7.7 Hz, 1H), 7.36 (dd, *J* = 1.6 and 7.5 Hz, 1H), 7.32-7.20 (m, 5H), 7.02-6.98 (m, 2H), 6.70 (s, 1H), 5.32 (d, *J* = 16.3 Hz, 1H), 5.23 (d, *J* = 16.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.2, 137.1, 131.3, 130.5, 128.5, 127.8, 127.7, 127.4, 126.5, 123.6, 122.6, 121.2, 120.1, 113.4, 110.5, 105.4, 48.0. Elemental analysis: calcd (%) for $C_{19}H_{12}BrCl_2NS$ (437.17): C 52.20, H 2.77; found: C 52.45, H 3.14.

3,5-Dibromo-2-(4-bromophenyl)-1-methylindole (27): 3,5-Dibromo-1-methylindole (0.289 g, 1 mmol) and 4-bromobenzenesulfonyl chloride (0.319 g, 1.25 mmol) affords **27** in 57% (0.253 g) yield. ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 8.11 (s, 1H), 7.45 (dd, *J* = 2.0 and 8.7 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 6.66 (d, *J* = 8.7 Hz, 1H) , 2.73 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ (ppm) 138.2, 136.2, 132.7, 132.2, 129.7, 129.0, 126.6, 123.9, 122.8, 114.9, 112.0, 90.2, 31.2. Elemental analysis: calcd (%) for $C_{15}H_{10}Br_3N$ (443.96): C 40.58, H 2.27; found: C 40.75, H 2.12.

3,5-Dibromo-1-methyl-2-(4-(trifluoromethyl)phenyl)indole (28): 3,5-Dibromo-1-methylindole (0.289 g, 1 mmol) and 4-(trifluoromethyl)benzenesulfonyl chloride (0.305 g, 1.25 mmol) affords **28** in 54% (0.234 g) yield. ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 8.02 (s, 1H), 7.38-7.31 (m, 3H), 6.98 (d, *J* = 7.8 Hz, 2H), 6.56 (d, *J* = 8.9 Hz, 1H), 2.60 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ (ppm) 137.7, 136.3, 134.1, 131.5, 130.8 (q, *J* = 29.8 Hz), 129.6, 126.9, 125.8 (q, *J* = 4.0 Hz), 122.9, 120.6 (q, *J* = 259.1 Hz), 115.0, 112.1, 90.7, 31.5. Elemental analysis: calcd (%) for $C_{16}H_{10}Br_2F_3N$ (433.07): C 44.38, H 2.33; found: C 44.19, H 2.61.

3,5-Dibromo-1-methyl-2-(2,3,4-trifluorophenyl)indole (29): 3,5-Dibromo-1-methylindole (0.289 g, 1 mmol) and 2,3,4-trifluorobenzenesulfonyl chloride (0.288 g, 1.25 mmol) affords **29** in 52% (0.218 g) yield. ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 7.97 (s, 1H), 7.32 (dd, *J* = 1.9 and 8.7 Hz, 1H), 6.52 (d, *J* = 8.7 Hz, 1H), 6.50-6.45 (m, 1H), 6.34 (ddt, *J* = 1.9, 7.1 and 9.3 Hz, 1H), 2.65 (s,

3H). ^{13}C NMR (100 MHz, C_6D_6) δ (ppm) 152.4 (md, *J* = 249.1 Hz), 150.0 (md, *J* = 249.1 Hz), 141.0 (td, *J* = 8.0 and 252.8 Hz), 136.2, 131.7, 129.4, 127.3 (m), 127.1, 123.0, 116.4 (dd, *J* = 4.8 and 12,1 Hz), 115.0, 112.8 (dd, *J* = 3.6 and 17.5 Hz), 112.1, 91.9, 31.0. Elemental analysis: calcd (%) for $C_{15}H_8Br_2F_3N$ (419.04): C 42.99, H 1.92; found: C 43.26, H 2.27.

3-Bromo-1-(2-bromobenzyl)indole (30): To a solution of 3-bromoindole (1 g, 5.15 mmol, 1 equiv.) in DMF (10 ml) was added in small portions 60% oil NaH (0.25 g, 6.43 mmol, 1.25 mmol) at 0 ºC. The resulting mixture was stirred at room temperature over 1 h before adding 2-bromobenzyl bromide (1.60 g, 6.43 mmol, 1.25 mmol). Then, the mixture was stirred at room temperature for 4 h. The resulting solution was pourred in NH_4Cl aqueous solution (100 ml). The mixture was extracted with three 100-ml. portions of diethyl ether, and each ether layer was washed with three 50-ml. portions of water. The combined ether layers were dried over $MgSO_4$, and the solvent was removed under slightly reduced pressure. The crude mixture was purified by silica column chromatography to afford **30** in 89% yield (1.87 g). ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 7.76 (d, *J* = 7.9 Hz, 1H), 7.26 (dd, *J* = 1.6 and 7.7 Hz, 1H), 7.12 (dd, *J* = 6.8 and 8.0 Hz, 1H), 7.03 (dd, *J* = 6.8 and 8.3 Hz, 1H), 6.79 (d, *J* = 8.3 Hz, 1H), 6.59-6.49 (m, 2H), 6.47 (s, 1H), 6.14 (dd, *J* = 1.9 and 7.5 Hz, 1H), 4.70 (s, 2H). ^{13}C NMR (100 MHz, C_6D_6) δ (ppm) 136.9, 136.6, 133.1, 129.5, 129.0, 127.9, 123.8, 122.5, 121.4, 120.2, 110.5, 91.4, 50.5. Elemental analysis: calcd (%) for $C_{15}H_{11}Br_2N$ (365.06): C 49.35, H 3.04; found: C 49.59, H 2.81.

4-(1-(2-Bromobenzyl)indol-2-yl)benzonitrile (31): 3-bromo-1-(2-bromobenzyl)indole (**30**) (0.365 g, 1 mmol) and 4-cyanobenzenesulfonyl chloride (0.252 g, 1.25 mmol) affords **31** in 62% (0.240 g) yield. ^{1}H NMR (400 MHz, C_6D_6) δ (ppm) 7.71 (d, *J* = 7.9 Hz, 1H), 6.32-7.29 (m, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.1 (dd, *J* = 6.9 and 8.5 Hz, 1H), 6.92 (d, *J* = 8.3 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 1H), 6.77 (d, *J* = 8.3 Hz, 2H) 6.67-6.54 (m, 2H), 6.54 (s, 1H), 6.46-6.40 (m, 1H), 5.00 (s, 2H). ^{13}C NMR (100 MHz, C_6D_6) δ (ppm) 140.0, 139.5, 137.3, 136.7, 133.4, 132.7, 129.5, 129.1, 129.0, 128.5, 128.0, 124.0, 122.1, 121.8, 121.7, 118.9, 112.3, 111.2, 105.0, 49.0. Elemental analysis: calcd (%) for $C_{22}H_{15}BrN_2$ (387.28): C 68.23, H 3.90; found: C 68.37, H 4.15.

1-Benzyl-2-(2-nitrophenyl)-3-phenylindole (32): The reaction of 1-benzyl-3-bromo-2-(2-nitrophenyl)indole (**9**) (0.204 g, 0.5 mmol), phenylboronic acid (0.073 g, 0.6 mmol) and K_3PO_4 (0.212 g, 1 mmol) at 80°C over 15 h in 1,4-dioxane (1 mL) in the presence of $PdCl(C_3H_5)$(dppb) (6 mg, 0.01 mmol) under argon affords, after evaporation of the solvent and purification on silica gel, product **32** in 81% (0.164 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.98 (dd, *J* = 1.8 and 7.8 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.55-5.45 (m, 2H), 7.34-7.17 (m, 12H), 7.00-6.97 (m, 2H), 5.39 (d, *J* = 16.7 Hz, 1H), 5.08 (d, *J* = 16.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 150.3, 137.4, 134.5, 134.1, 132.6, 132.3, 129.7, 129.4, 128.6, 128.3, 127.3, 127.1, 127.0, 126.3, 126.0, 124.4, 122.8, 120.5, 119.9, 117.0, 110.4, 102.9, 48.0. Elemental analysis: calcd (%) for $C_{27}H_{20}N_2O_2$ (404.47): C 80.18, H 4.98; found: C 80.35, H 5.17.

1-Benzyl-2-(4-chlorophenyl)-3-phenylindole (33): The reaction of 1-benzyl-3-bromo-2-(4-chlorophenyl)indole (**5**) (0.198 g, 0.5 mmol), phenylboronic acid (0.073 g, 0.6 mmol) and K_3PO_4 (0.212 g, 1 mmol) at 80°C over 15 h in 1,4-dioxane (1 mL) in the presence of $PdCl(C_3H_5)$(dppb) (6 mg, 0.01 mmol) under argon affords, after evaporation of the solvent and purification on silica gel, product **33** in 79% (0.156 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.81 (dd, *J* = 1.7 and 7.5 Hz, 1H), 7.32-7.28 (m, 4H), 7.28-7.19 (m, 7H), 7.23-7.18 (m, 2H), 7.16 (d, *J* = 8.5 Hz, 2H), 7.00 (dd, *J* = 2.1 and 7.4 Hz, 2H), 5.38 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.9, 137.2, 136.5, 135.8, 134.8, 134.3, 132.3, 130.3, 129.9, 129.3, 128.8, 128.7, 128.3, 127.3, 126.0, 125.8, 122.7, 120.6, 119.8, 110.5, 47.6. Elemental analysis: calcd (%) for $C_{27}H_{20}ClN$ (393.91): C 82.33, H 5.12; found: C 82.58, H 5.29.

1-Benzyl-3-phenyl-2-(4-(trifluoromethyl)phenyl)indole (34): The reaction of 1-benzyl-3-bromo-2-(4-(trifluoromethyl)phenyl)indole (**4**) (0.215 g, 0.5 mmol), phenylboronic acid (0.073 g, 0.6 mmol) and K_3PO_4 (0.212 g, 1 mmol) at 80°C over 15 h in 1,4-dioxane (1 mL) in the presence of $PdCl(C_3H_5)$(dppb) (6 mg, 0.01 mmol) under argon affords, after evaporation of the solvent and purification on silica gel, product **34** in 84% (0.180 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.81 (d, *J* = 7.7 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H), 7.32-7.29 (m, 4H), 7.28-7.24 (m, 5H) 7.24-7.18 (2H), 7.01 (d, *J* = 7.4 Hz, 2H), 5.29 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.8, 137.3, 136.0, 134.5, 133.3 (q, *J* = 34.7 Hz), 131.2, 130.0, 128.8, 128.4, 128.1, 127.4, 127.3, 126.0, 125.9, 125.3 (q, *J* = 1.8 Hz), 123.6 (q, *J* = 275.1 Hz), 123.0, 120.7, 119.9, 116.8, 110.5, 47.7. Elemental analysis: calcd (%) for $C_{28}H_{20}F_3N$ (427.47): C 78.67, H 4.72; found: C 78.98, H 4.49.

1-Benzyl-3-(thiophen-3-yl)-2-(4-(trifluoromethyl)phenyl)indole (35): The reaction of 1-benzyl-3-bromo-2-(4-(trifluoromethyl)phenyl)indole (**4**) (0.215 g, 0.5 mmol), thiophen-3-ylboronic acid (0.077 g, 0.6 mmol) and K_3PO_4 (0.212 g, 1 mmol) at 80°C over 15 h in 1,4-dioxane (1 mL) in the presence of $PdCl(C_3H_5)$(dppb) (6 mg, 0.01 mmol) under argon affords, after evaporation of the solvent and purification on silica gel, product **35** in 73% (0.158 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.87 (d, *J* = 7.2 Hz, 1H), 7.59 (d, *J* = 8.2 Hz, 2H), 7.4 (d, *J* = 8.2 Hz, 2H), 7.30-7.22 (m, 7H), 7.16 (d, *J* = 3.1 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 5.2 Hz, 1H), 5.38 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.7, 137.2, 136.0, 135.7, 134.6, 131.2, 130.3 (q, *J* = 32.1 Hz), 128.8, 128.6, 127.4, 125.9, 125.8, 125.3 (m), 125.0, 123.9 (q, *J* = 279.5 Hz), 123.0, 121.7, 120.7, 120.0, 111.8, 110.5, 47.7. Elemental analysis: calcd (%) for $C_{26}H_{18}F_3NS$ (433.49): C 72.04, H 4.19; found: C 71.89, H 3.96.

2-(4-(Trifluoromethyl)phenyl)indole (36): **1**-Benzyl-2-(4-(trifluoromethyl)phenyl)indole (**14**) (0.181 g, 0.5 mmol) was dissolved in DMSO (5 mL) and added to a flame-dried flask. While stirring the solution at room temperature, *t*BuOK (0.280 g, 2.5 mmol) was added. The solution was heated at 60 ºC, then oxygen was then bubbled into the solution over 2 h. The reaction was quenched with saturated ammonium chloride. The product was extracted three times with EtOAc. The organics were combined, dried over Na_2SO_4 and concentrated. The crude mixtuire was purified on silica gel to afford the product **36** in 92% (0.120 g) yield. ^{1}H NMR (400 MHz, d^6-DMSO) δ (ppm) 11.72 (br, 1H), 8.07 (d, *J* = 8.3 Hz, 2H), 7.81 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 8.2 Hz, 1H), 7.17-7.13 (m, 1H), 7.07 (s, 1H), 7.05-7.01 (m, 1H). This is a known compound and the spectral data are identical to those reported in literature.[34]

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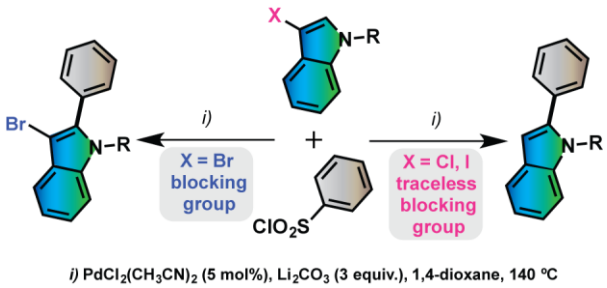

i) $PdCl_2(CH_3CN)_2$ (5 mol%), Li_2CO_3 (3 equiv.), 1,4-dioxane, 140 °C