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Pd(0)-Catalyzed Dearomative Diarylation of Indoles

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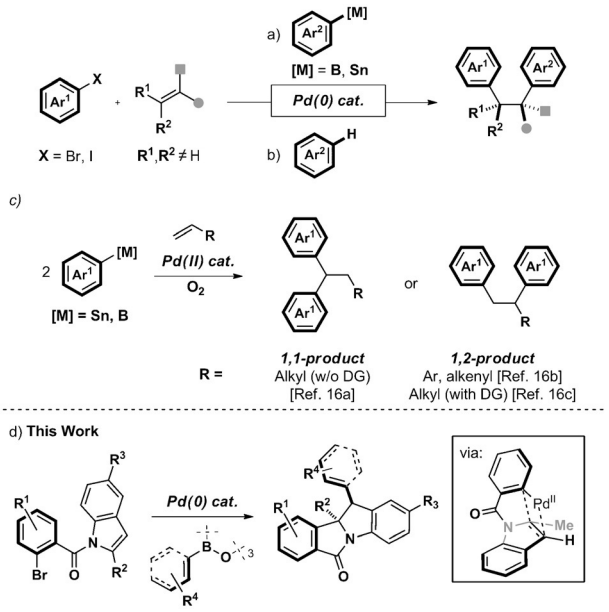
Abstract: We have developed a protocol for a Pd(0)-catalyzed dearomative *syn* 1,2-diarylation of indoles using readily available boroxines (dehydrated boronic acids) as coupling partners. This reaction proceeds efficiently using P*t*Bu$_3$ as the ligand to divergently access to fused indolines while minimizing the extent of direct Suzuki coupling. The scope of the reaction is remarkably broad and all products are obtained as single diastereomers in moderate to excellent yields. We have also compiled data which parallels the steric and electronic properties of both substrate and boroxine with the propensity to undergo the desired dearomative process over direct Suzuki coupling.

Introduction

Easy access to alkenes and alkynes has motivated their extensive use as substrates in transition-metal catalysis. Specifically, much effort has been made to harness their synthetic potential in various Pd-catalyzed difunctionalizations.[1] The ability of Pd to react through multiple oxidation state manifolds has resulted in the development of a remarkably broad range of difunctionalizations wherein most proceed via Pd^0/Pd^{II}[2] or Pd^{II}/Pd^0 cycles.[3] A subset of the former, referred to as Heck-type[4] domino reactions,[5] typically proceed by a catalytic sequence involving oxidative addition to an aryl or vinyl (pseudo)halide, migratory insertion of an unsaturated carbon–carbon moiety, transmetallation/ligand exchange, and reductive elimination. These processes are important as they allow for straightforward formation and functionalization of difficult-to-access organopalladium species,[6] and their utility has been made evident by the large number of reports, which include formal hydroarylations,[6a,b] arylcarbonylations,[6e] aminations,[6d,7] alkenylations,[8] cyanations,[6d,9] halogenations,[10] and borylations.[11]

The 1,2-diarylation involving a terminating Suzuki coupling[12] of arylboronic acids[13,14] is the most widely explored variant to date (Scheme 1 a). This process is mechanistically distinct from the corresponding 1,2-diarylation arising from a terminating C–H functionalization event (Scheme 1 b),[15] or the Pd(II)-catalyzed 1,1- or 1,2-diarylation reactions using arylboron or aryltin reagents (Scheme 1 c).[16] Although numerous examples of Pd(0)-catalyzed 1,2-diarylations[17] of alkenes,[18] alkynes,[19] and allenes[20] have been reported, the majority of examples concern the intramolecular 1,2-diarylation of alkenes[6c,21] and alkynes,[6c,22] with a strong emphasis on the latter. Furthermore, the diarylation of carbon–carbon double bonds has only been explored using both simple and strained bicyclic alkenes wherein diastereoselective examples are rare.[21c,d] Inspired by the recent application of indoles[23] in Pd(0)-catalyzed dearomative Heck,[24a] reductive Heck,[24b] and arylcyanation reactions,[24c] we sought to develop a dearomative 1,2-diarylation as a way to address the above-mentioned shortcomings (Scheme 1 d).[25] The proposed transformation would proceed through a dearomative migratory insertion step of the indole's



Scheme 1. Pd(0)-catalyzed 1,2-diarylation by: a) Heck–Suzuki process; b) Heck/C–H functionalization process; c) Pd(II)-catalyzed oxidative 1,1- and 1,2-diarylation of alkenes; d) diastereoselective Pd(0)-catalyzed dearomative 1,2-diarylation of indoles. DG = directing group.

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enamine functionality, thus fascilitating step economic and divergent access to fused tetracyclic scaffolds.

Herein, we report the development and application of the first dearomative indole 1,2-diarylation, which proceeds efficiently using aryl and vinyl boroxines as coupling partners. Despite the challenging nature of the crucial dearomative migratory insertion, the *syn* 1,2-diarylation products are obtained in preference to the direct Suzuki coupling when the bulky Pd(0) precatalyst [Pd(P*t*Bu$_3$)$_2$] is used. Furthermore, key trends correlating the steric and electronic properties of both the substrate and boroxine with this observed selectivity have been outlined for this class of reaction.

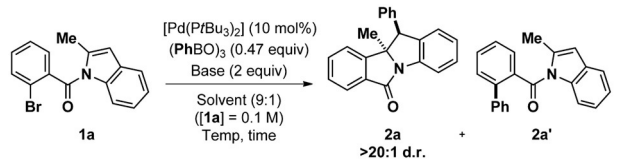
Results and Discussion

Reaction Optimization

To optimize the dearomative 1,2-diarylation reaction using aryl boron reagents, *N*-benzoylated indole **1a** was investigated under various reaction conditions (Table 1). Initially, **1a** was treated with [Pd(P*t*Bu$_3$)$_2$] (10 mol%), K$_2$CO$_3$ (2 equiv), phenyl boroxine (0.47 equiv)[26] in PhMe at 110 °C for 18 h (entry 1). This led to the formation of the desired 1,2-diarylation product **2a** in 20% yield in >20:1 d.r., albeit with 63% of the direct Suzuki coupling product **2a′**. The use of an aqueous solvent mixture lead to a decrease in the amount of **2a′** formed (entry 2). However, the presence of 2-methylindole in the crude reaction mixture suggested that decomposition of **1a** and/or **2a′** by hydrolysis of the weak amide C–N bond was occurring.[27] Changing the organic component of the solvent from PhMe to dioxane or DMF led to decreased conversion and yields (entries 3 and 4). A switch in the reaction's selectivity was observed when a 9:1 MeCN:H$_2$O mixture was used, wherein **2a** was obtained in 61% yield (entry 5). Lowering the reaction temperature to 100 °C led to better overall mass recovery and a slight increase in the yield of **2a** to 64% (entry 6), whereas deviating from a 0.1 M concentration of **1a** only led to inferior results (entries 7 and 8). Decreasing the reaction time to 2.5 h led to an increase in yield of **2a** to 71% (entry 9), and nearly quantitative mass recovery. The use of other potassium-containing bases, such as KOH, KOAc, or K$_3$PO$_4$, all lead to marked decreases in yield and/or conversions (entries 10–12). In the case of KOH, severe decomposition was observed. Furthermore, although the use of Na$_2$CO$_3$ did not lead to better results (entry 13), Cs$_2$CO$_3$ provided **2a** in 75% yield (entry 14). To further explore the effect of Cs counterions on the reaction, CsF was tested. To our surprise, **2a** was obtained in 80% yield with 10% of **2a′** after only one hour (entry 15). By lowering the catalyst loading to 2.5 mol%, **2a** could to be isolated in 88% yield with only 7% of **2a′** (entry 16). The final optimal conditions were found to be [Pd(P*t*Bu$_3$)$_2$] (2.5 mol%), CsF (2 equiv), phenyl boroxine (0.47 equiv) in MeCN:H$_2$O (9:1) at 100 °C for one hour, and will be referred to as the standard conditions.

The effect of altering various reaction parameters on the efficacy of the 1,2-diarylation was also investigated (Table 2). When the dinuclear bromine-bridged complex [{Pd(P*t*Bu$_3$)(μ-Br)}$_2$] was employed as the precatalyst instead, almost identical results were obtained (entry 2). The similarity in the reaction

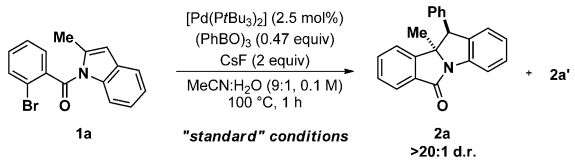
Table 1. Indole bisfunctionalization by Pd-catalyzed diarylation: Reaction optimization.[a]



Entry	Base	Solvent	*T* [°C]	*t* [h]	Conv [%][b]	**2a** [%][b]	**2a′** [%][b]
1	K$_2$CO$_3$	PhMe	110	18	>95	20	63
2	K$_2$CO$_3$	PhMe:H$_2$O	110	18	>95	20	43
3	K$_2$CO$_3$	Dioxane:H$_2$O	110	18	89	34	21
4	K$_2$CO$_3$	DMF:H$_2$O	110	18	83	10	9
5	K$_2$CO$_3$	MeCN:H$_2$O	110	18	>95	61	20
6	K$_2$CO$_3$	MeCN:H$_2$O	100	18	>95	64	29
7[c]	K$_2$CO$_3$	MeCN:H$_2$O	100	18	>95	64	26
8[d]	K$_2$CO$_3$	MeCN:H$_2$O	100	18	>95	47	44
9	K$_2$CO$_3$	MeCN:H$_2$O	100	2.5	>95	71	28
10	KOH	MeCN:H$_2$O	100	1	>95	28	8
11	KOAc	MeCN:H$_2$O	100	1	53	29	4
12	K$_3$PO$_4$	MeCN:H$_2$O	100	1	>95	58	29
13	Na$_2$CO$_3$	MeCN:H$_2$O	100	1	>95	67	16
14	Cs$_2$CO$_3$	MeCN:H$_2$O	100	1	>95	75	25
15	CsF	MeCN:H$_2$O	100	1	>95	80	10
16[e–g]	**CsF**	**MeCN:H$_2$O**	**100**	**1**	**>95**	**(88)**	**7**

[a] All reactions were run on a 0.2 mmol scale. [b] Determined by ^{1}H NMR analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as an internal standard. [c] [**1a**] = 0.05 M. [d] [**1a**] = 0.2 M. [e] Average value over three runs. [f] Value in parentheses represents the average isolated yield over three runs. [g] Reaction was run using [Pd(P*t*Bu$_3$)$_2$] (2.5 mol%).

Table 2. Dearomative indole bisfunctionalization by Pd-catalyzed diarylation: Effect of reaction parameters.[a]



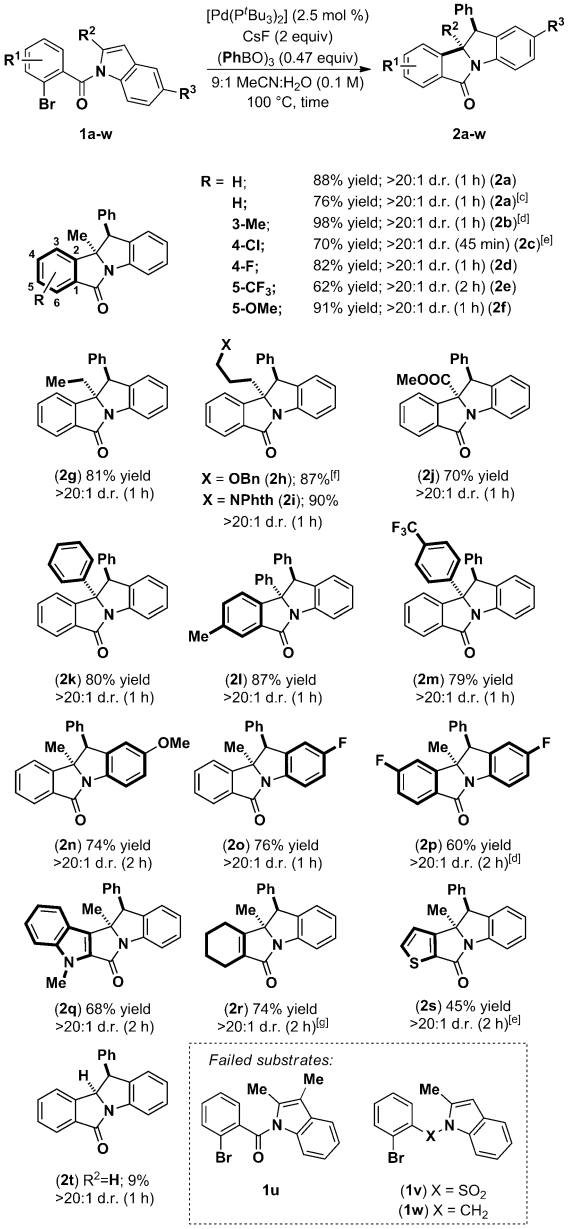
Entry	Variation from the standard conditions	Yield **2a** [%][b–c]	Yield **2a′** [%][b]
1	**none**	**88 (88)**[d]	**7**
2	[{Pd(P*t*Bu$_3$)(μ-Br)}$_2$][e]	93(88)[d]	5
3	[Pd{P(*o*-Tol)$_3$}$_2$]	69	3
4	[Pd(PhP*t*Bu$_2$)$_4$]	42	22
5	[Pd(PPh$_3$)$_4$]	5	17
6	90 °C instead of 100 °C	79	10
7	ArCl instead of ArBr	63	17
8	0.33 equiv of (PhBO)$_3$	67	8
9[f,g]	PhB(OH)$_2$ instead of (PhBO)$_3$	83	6
10[g]	PhBF$_3$K instead of (PhBO)$_3$	45	0

[a] Reactions were run on a 0.2 mmol scale. [b] Determined by ^{1}H NMR analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as an internal standard. [c] Value in parentheses represents isolated yields. [d] Average value over three experiments. [e] 1.25 mol% was used. [f] Freshly recrystallized phenylboronic acid was used. [g] 1.4 equivalents of the aryl boron reagent were used.

outcome suggests that this Pd^{I} source may be converting to the corresponding mononuclear Pd^{0} catalyst under the reaction conditions.[28] In all cases, decreasing the size of the ligand led to a decrease in yield of **2a** (entries 3–5).[29] We hypothesize that when extremely bulky ligands (such as P*t*Bu$_3$) are used, only one ligand can be accommodated in the coordination sphere of the ArPd^{II}Br species resulting from the oxidative addition. This translates to a vacant coordination site for easier binding of the indole olefin moiety, and presumably a more facile migratory insertion. Conversely, the coordination sphere can reach saturation easier when less bulky ligands (such as PhP*t*Bu$_2$) are used, therefore decreasing propensity of the Pd^{II} species to undergo olefin insertion, which manifests itself in the form of a higher degree of the undesired direct Suzuki coupling process. Both decreasing the reaction temperature below 100 °C and employing the aryl chloride analog of **1a**, led to a higher amount of **2a'** being formed (entries 6 and 7). Decreasing the amount of phenyl boroxine to 0.33 equivalents (≈one equivalents of ArB) led to decreased efficiency of the 1,2-diarylation process (entry 8). The use of freshly prepared PhB(OH)$_2$ lead to a slight decrease in yield of **2a**, whereas the use of PhBF$_3$K inhibited the formation of **2a'** at the expense of overall conversion and yield of **2a** (entries 9 and 10).

Substrate Scope

With the optimized conditions in hand, the generality of this catalytic process was evaluated. We first sought to determine the effects of various steric and electron perturbations on the 1,2-diarylation reaction using a series of substituted *N*-protected indoles **1a**–**1w** (Scheme 2). Sterically hindered aryl bromide **1b** was found to function exceptionally well in this reaction, and **2b** was obtained in 98% yield with only trace amounts of the direct Suzuki coupling. Chloro- and fluoro-bromobenzoyl analogs **1c** and **1d** could be converted to the corresponding diarylated products in 70% (**2c**) and 82% yield (**2d**), respectively. In the case **1c**, the boroxine loading was lowered to 0.4 equivalents to inhibit the direct Suzuki coupling of the aryl chloride in the product at higher conversions. Electron-deficient and -rich aryl bromides could be converted to the corresponding products in moderate to excellent yields (**2e** and **2f**). Various 2-alkyl (**1g**–**1i**) -carbonyl (**1j**) and -aryl indoles (**1k**–**1m**) were well tolerated under the reaction conditions and the corresponding products (**2g**–**2m**) could be obtained in good to excellent yields. Both electron-rich (**1n**) and -poor (**1o** and **1p**) indoles led to the desired products (**2n**–**2p**), albeit in slightly lower yield than the parent substrate. In the case of the difluorinated **1p**, a catalyst loading of 3.5 mol% was required to reach full conversion. *N*-Methyindolyl (**1q**) and cyclohexenyl (**1r**) substrates were found to undergo the desired transformation, and the corresponding indolines could be obtained in moderate yields. 3-bromothiophene derivative **1s** converted cleanly under the reaction conditions, yet the desired product **2s** could only be obtained in 45% yield on account of a more efficient direct Suzuki coupling reaction (vide infra).

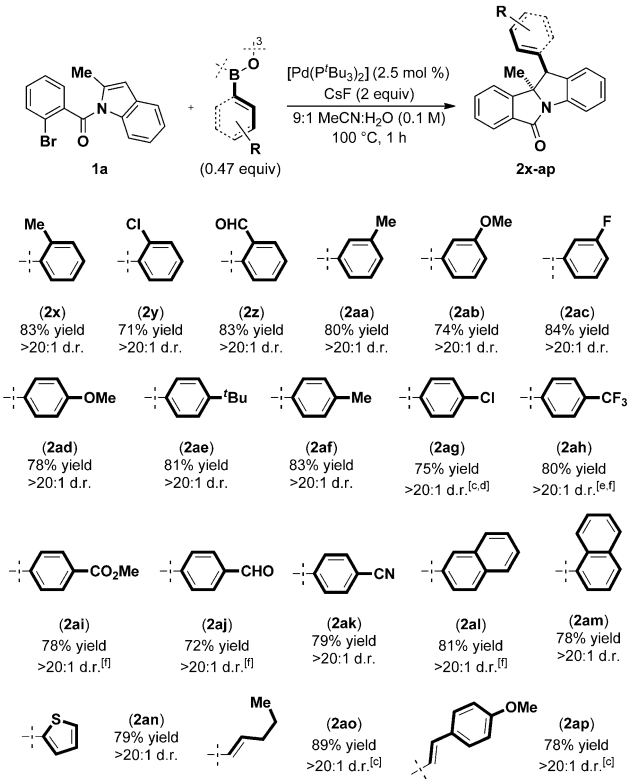


Scheme 2. Pd(0)-catalyzed dearomative indole diarylation: Scope of *N*-benzoyl indoles. [a] All reactions were run on a 0.2 mmol scale unless otherwise stated; [b] diastereomeric ratios were determined by ^{1}H NMR analysis of the crude reaction mixture; [c] 1 gram (3.20 mmol) scale using [Pd(P*t*Bu$_3$)$_2$] (1.25 mol%); [d] [Pd(P*t*Bu$_3$)$_2$] (3.5 mol%); [e] (PhBO)$_3$ (0.4 equiv); [f] reaction was run on a 0.13 mmol scale; [g] [Pd(P*t*Bu$_3$)$_2$] (5 mol%).

Some limitations with the reaction were noted. When non-substituted indole **1t** was subjected to the reaction conditions, only 9% of the desired indoline product **2t** could be isolated in addition to 91% of the product resulting from a direct cyclizative C–H functionalization at the C2-position of indole.[30] 2,3-Dialkylated indole **1u** did not lead to any desired product containing a quaternary benzylic position. Instead, the corresponding dearomative Heck reaction was found to occur, and the corresponding product containing an exomethylene could be isolated in 92% yield.[24a] Exchanging the amide functionality of **1a** for a sulfonamide (**1v**) negatively impacted the reac-

tion and no dearomative cyclization was observed. Instead, only the direct Suzuki coupled product was obtained, which was accompanied by recovered starting material. *N*-benzyl analog **1w** was fully consumed when subjected to the reaction conditions; however, no desired product was observed and 91% of the direct Suzuki was isolated instead. Finally, when the reaction was run on a gram scale, **2a** could be obtained in 76% yield and >20:1 d.r. when the catalyst loading was decreased to 1.25 mol%.

Next, the effect of various sterically and electronically diverse boroxines on the 1,2-diarylation reaction was explored (Scheme 3). Overall, the reaction was quite tolerant to many



Scheme 3. Pd(0)-catalyzed dearomative indole diarylation: Scope of boroxines. [a] All reactions were run on a 0.2 mmol scale; [b] diastereomeric ratios were determined by ^{1}H NMR analysis of the crude reaction mixture; [c] 0.4 equivalents of the corresponding boroxine; [d] reaction time = 50 min; [e] run using [Pd(P*t*Bu$_3$)$_2$] (3.5 mol%); [f] reaction time = 2 h.

types of aryl boroxines with varying ratios of 1,2-diarylation to direct Suzuki coupling being observed. Aryl groups bearing *ortho*-methyl, -chloro, and -formyl substituents could be incorporated into the tetracyclic indole scaffold in moderate to good yields (**2x**–**2z**). No Suzuki coupling of the product arylchloride was observed in the case of **2y** even when using 0.47 equivalents of the boroxine. Aryl boroxines bearing *meta* substituents, such as methyl, methoxy, and fluoro, were also well tolerated (**2aa**–**2ac**). The reaction also performed well when various electronically diverse *para*-substituted boroxines were employed (**2ad**–**2ak**). In some instances (**2ah**–**2ak**), reaction times had to be increased to 2 h in order to obtain full conversion of the starting material. Suzuki coupling of the aryl chloride of **2ag** was initially observed under the standard conditions; however, decreasing the boroxine loading to 0.4 equivalents eradicated this undesired process. We were able to unambiguously confirm the relative stereochemistry of the diarylation to be *syn* by X-ray crystallographic analysis of **2ah** (Figure 1). 1- and 2-napthylene boroxines were well tolerated

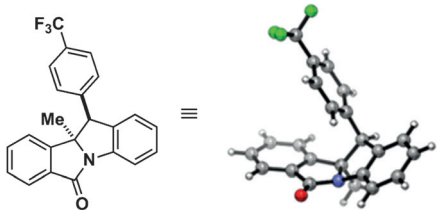


Figure 1. X-ray structure of **2ah** showing relative stereochemistry.[37]

under the reaction conditions and the corresponding products **2al** and **2am** could be obtained in 81% and 78% yield, respectively. 2-Thiophene boroxine could also be incorporated into the indoline scaffold in 79% yield, whereas *E*-pentenyl (**2ao**) and styrenyl (**2ap**) boroxines were also capable of undergoing the desired tranformation in 89% and 78% yields, respectively. When alkylboronic acids were used in the reaction, none of the desired 1,2-diarylation was observed, and only traces of the direct Suzuki coupling as the sole product were observed.

Analysis of Selectivity

The undesired biaryl product **2′** arising from the direct Suzuki coupling of the aryl bromide occurred to some extent in all instances during the substrate scope determination. By ^{1}H NMR analysis of the crude reaction mixtures, trends could be observed that relate steric and electronic perturbation of both **1** and the boroxine reagents to the ratio of **2**:**2′**. Figure 2 displays the ratios of 1,2-diarylation/direct Suzuki coupling from reactions of various *N*-benzoylated indoles bearing substitution on the aryl bromide fragment, and both the indole C2- and C5-positions, respectively.

The introduction of local steric effects (*o*-Me, **1b**) around the carbon–bromine bond led to the lowest amount of Suzuki coupling (**2**:**2′** = 31:1). The presence of electron donating OMe group *para* to the carbon–bromine (**1f**) bond also helped suppress the direct Suzuki coupling (**2**:**2′** = 28:1), whereas *p*-CF$_3$ group (**2e**) had the opposite effect (**2**:**2′** = 3.4:1). The presence of activating Cl or F atoms (**1c** and **1d**) led to a similar increase in Suzuki coupling (**2**:**2′** = ≈5:1). In general, heteroaryl bromides exhibited the lowest ability to undergo the desired dearomative 1,2-diarylation reaction across all substrates. For example, 3-bromothiophene derivative **1s** led to the Suzuki coupling being the major pathway (**2**:**2′** = 0.8:1). Generally, both sterically hindered and electron-rich aryl bromides led to the largest suppression of the Suzuki pathway, whereas the opposite effect was observed across all electron-deficient aryl bro-

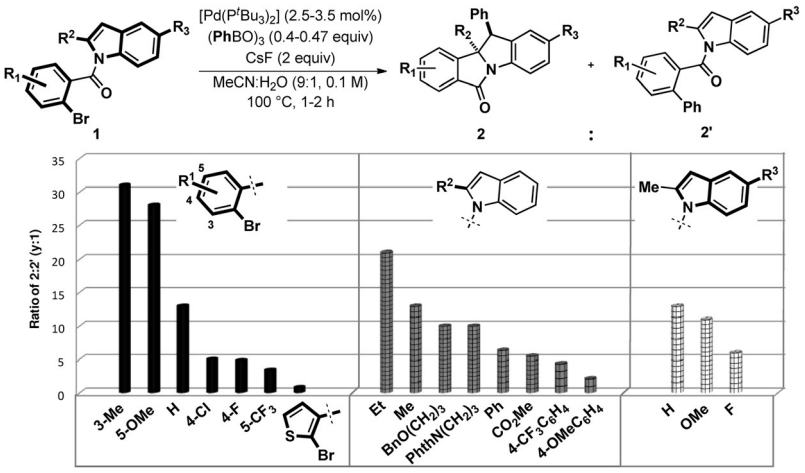


Figure 2. Effect of steric and electronic perturbation of **1** on the ratio of **2**:**2**′.

mides. Varying the indole C2 substitution had similar effects on the reaction outcome. Interestingly, 2-Et (**1 g**) led to a decrease in the Suzuki coupling amount with respect to **1 a** (**2**:**2**′ = 21:1), other larger alkyl substituents (**1 h** and **1 i**) also led to a similar decrease (**2**:**2**′ = 10:1). A 2-Ph group (**1 k**) decreased the ability to undergo dearomatization (**2**:**2**′ = 6.4:1), whereas a further *para*-CF_3 (**2 m**) and -OMe[32] substitution of this aryl group further magnified this effect (**2**:**2**′ = 4.4:1 and 2.1:1). Perturbation of the indole backbone at C5 with electron-donating (OMe, **1 n**) and -withdrawing (CF_3, **1 m**) substituents led to a decrease in the efficiency of the dearomative diarylation (**2**:**2**′ = 11:1 and 6:1), which echo our previous discussion concerning *N*-substitution on the efficacy of the reaction, as it appears to be very sensitive to the electronics of the enamine component.

Figure 3 displays the ratios of 1,2-diarylation/direct Suzuki coupling from reactions of aryl and alkenyl boroxines possessing various steric and electronic properties. Although differences can be seen within this data set, the trends within groups possessing different substituents are less obvious. An *o*-Me-substituted boroxine led to no change in the ratio of **2**:**2**′, which suggests that some groups at this position do not have a significant impact. However, electron-withdrawing *ortho*-CHO and -Cl substituents produce marked increases in the amount of Suzuki coupling (**2**:**2**′ = 6.7:1 and 3.8:1).

Boroxines substituted with electron-donating and -withdrawing groups at the *meta*-position appeared to have no effect on the ratio of **2**:**2′** with respect to phenyl boroxine. Furthermore, although a *p*-CHO group positively impact the ratio of **2**:**2′** (15:1), other electron-withdrawing groups had either no impact (*p*-CN and *p*-Cl) or a negative impact on the diarylation reaction. Alkyl groups, such as *t*Bu and Me, at the *para*-position led to slightly more Suzuki coupling (**2**:**2**′ = 12:1 and 11:1), while *para* electron-withdrawing groups, such as CO_2Me and CF_3, produce a similar effect. Finally, the use of vinyl boroxine derivatives, such as (*E*)-penten-1-ylboroxine (**A1**) and (*E*)-2-(4-methoxyphenyl)vinylboroxine (**A2**), led to an increase in the amount of observed Suzuki product (**2**:**2**′ = 6:1 and 5:1). Despite the fact that boronic acids containing electron-donating

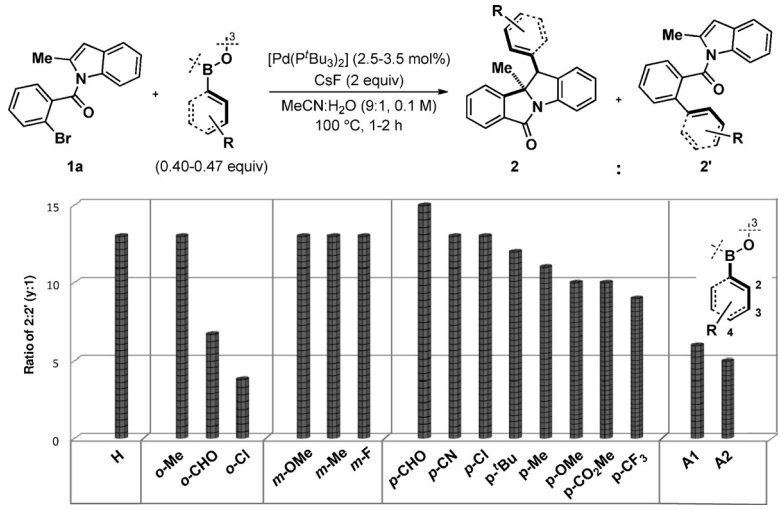


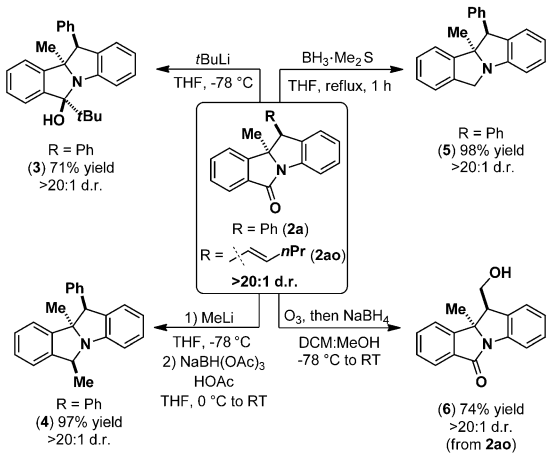
Figure 3. Effect of steric and electronic perturbation of the boroxine reagent on the ratio of **2**:**2**′. **A1** = (*E*)-penten-1-ylboroxine, **A2** = (*E*)-2-(4-methoxyphenyl)vinylboroxine.

groups are known to undergo faster transmetallation with Pd^{II} species than those containing electron-withdrawing group,[26b] this is not reflected in the ratio of **2**:**2′**.

Although reports have appeared in which boroxines are active transmetallation species under anhydrous conditions,[33] it is reasonable to suggest that under our standard conditions involving an aqueous biphase (MeCN:H_2O and CsF), aryl boronic acid can present in the bulk organic phase as a result of aryl boroxine hydrolysis. While we understand that the factors behind boron reagent activation and subsequent reactivity is nontrivial, it is likely that the ability of the dearomative diarylation to outperform the undesired Suzuki pathway is dependent on a balance between hydrolytic susceptibility of the boroxine in question and the transmetallation aptitude of the resulting aryl boronic acid. Nevertheless, the studies depicted in Figures 1 and 2 reveal that structural variations of the *N*-benzoyl indole generally appear to have a more pronounced effect than those of the boroxine component on the product distribution.

Derivatization of Products

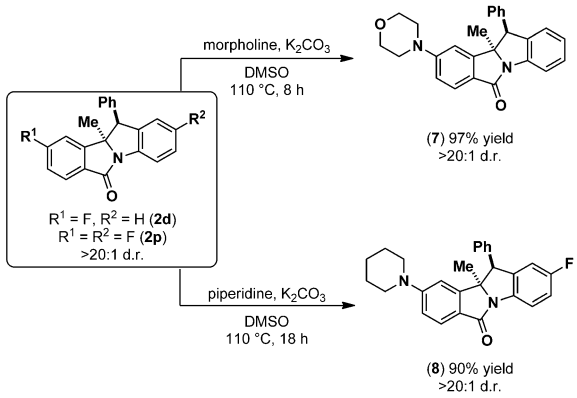
The tetracyclic indoline products were subjected to various conditions to probe their synthetic utility (Scheme 4). In an effort to forge an all-carbon benzylic quaternary carbon by a deprotonation/alkylation strategy, **2a** was treated with *t*BuLi



Scheme 4. Product derivatization.

at −78 °C. Deprotonation did not result under these conditions,[34] and instead hemiaminal **3** was formed in 71% as a single diastereomer. The relative stereochemistry of **3** was unambiguously determined by X-ray crystallographic analysis. The unexpected reactivity of the lactam leaves it prone to nucleophilic attack of the organolithium reagent at the carbonyl from the face opposite to the flanking benzylic Ph group.[31] Nucleophilic addition of organolithium reagents appeared to be quite general[35] as MeLi could also be added. Subsequent dehydration formed the enamine,[31] which could be stereoselectively reduced using $NaBH(OAc)_3$ under acidic conditions to generate amine **4** in 97% yield and >20:1 d.r. over two steps. The amide functionality could be reduced to generate amine **5** in 98% yield by using $BH_3{\cdot}SMe_2$ in refluxing THF.[36] The use of alkenyl boroxines facilitates the introduction of benzylic alkenes, and **2ao** could undergo oxonolysis using a reductive workup to produce homobenzylic alcohol **6** in good yield.

Fluorinated analogs **2d** and **2p** were found to react with cyclic secondary amines to afford various aniline derivatives by S_NAr reactions (Scheme 5). When monofluorinated **2d** was



Scheme 5. S_NAr reactions of indoline products containing reactive C–F bonds.

treated with excess morpholine in the presence of K_2CO_3, adduct **7** could be obtained in 97% yield. Furthermore, due to the different electronic densities of the two aromatic rings in the diarylation products, it seemed likely that a selective S_NAr reaction could occur on the more electron-deficient of the two. When difluorinated **2p** was treated with excess piperidine under similar conditions, a highly selective substitution of the isoindoline fluorine over the indoline fluorine could be achieved, yielding **8** in 90% yield.

Conclusion

We have developed and applied a fully *syn*-selective Pd(0)-catalyzed dearomative indole 1,2-diarylation using boroxines as coupling partners. This reaction employs indoles as nontraditional Heck acceptors, and proceeds using relatively low catalyst loadings and short reaction times. The complex indoline-containing products generated possess a unique stereogenic arrangement consisting of a tetrasubstituted tertiary stereocenter vicinal to a tertiary benzylic stereocenter. The scope of this transformation is remarkably broad, and many substrate perturbations are well tolerated under the standard conditions or slight variants thereof. Furthermore, the catalytic reaction conditions were tailored to minimize the amount of undesired (yet separable) direct Suzuki coupling product. However, due to the challenging nature of the migratory insertion step, the Suzuki product forms to some extent in all substrates. The diverse heterocyclic scaffolds generated rapidly with our method are quite amenable to derivatization, which should encourage their use as complex synthetic building blocks. We are currently investigating the development of an enantioselective var-

iant, and the application of the reported transformation in natural product synthesis.

Experimental Section

Methods and Characterization: All catalytic reactions were carried out under an inert atmosphere of dry argon utilizing glassware that was oven (120 °C) or flame dried and cooled under argon. Reactions were monitored using thin-layer chromatography (TLC) on EMD Silica Gel 60 F254 plates. Visualization of the developed plates was performed under UV light (254 nm) or using $KMnO_4$. MeCN was distilled over CaH_2. Flash column chromatography was performed on Silicycle 230–400 mesh silica gel. NMR characterization data was collected at 296 K on a Varian Mercury 300, Varian Mercury 400, Bruker Avance III, Agilent 500, or a Varian 600 operating at 300, 400, 500, or 600 MHz for ^{1}H NMR, and 75, 100, 125, or 150 MHz for ^{13}C NMR. ^{1}H NMR spectra were internally referenced to the residual solvent signal ($CDCl_3$ = 7.26 ppm) or TMS. ^{13}C NMR spectra were internally referenced to the residual solvent signal ($CDCl_3$ = 77.0 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration. Coupling constants have been rounded to the nearest 0.5 Hz. All reported diastereomeric ratios in data section are those obtained from ^{1}H NMR analysis of the crude reaction mixtures using a 5 second relaxation delay.

Typical procedure for the diastereoselective Pd(0)-catalyzed dearomative diarylation of *N*-(*o*-bromobenzoyl)indoles with boroxines: A dry 2 dram vial containing a magnetic stir bar was charged with anhydrous CsF (61.8 mg, 0.4 mmol, 2 equiv) using a flame-dried spatula followed by the *N*-(*o*-bromobenzoyl)indole derivative **1** (0.2 mmol, 1 equiv), [Pd(P*t*Bu$_3$)$_2$] (2.55 mg, 0.005 mmol, 2.5 mol%), and the boroxine (0.08 mmol or 0.094 mmol, 0.4 or 0.47 equiv) and was purged with argon for 10 min. The contents of the vial were taken up in MeCN:H_2O (9:1, 2 mL), and the vial was sealed with a Teflon® lined screw-cap and then placed in an oil bath pre-heated to 100 °C where it was stirred for 1 or 2 h. The vial was then cooled to room temperature and anhydrous Na_2SO_4 (50 mg) was added to remove the aqueous component of the solvent. The remaining solution was passed through a short pad of silica gel eluting with 100% EtOAc (5 mL). The diastereomeric ratio was determined by ^{1}H NMR analysis of a homogeneous aliquot of the crude reaction mixture, which was subsequently purified via silica gel flash column chromatography using hexanes/EtOAc as the mobile phase to afford the corresponding indolines **2**. Isolated yields were calculated based on the obtained masses and all isolated products were identified by ^{1}H NMR, ^{13}C NMR, IR, and HRMS analysis.

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[37] CCDC 1456617 (**2 ah**) and 1456618 (**3**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

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