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Harnessing C–H Borylation/Deborylation for Selective Deuteration, Synthesis of Boronate Esters, and Late Stage Functionalization

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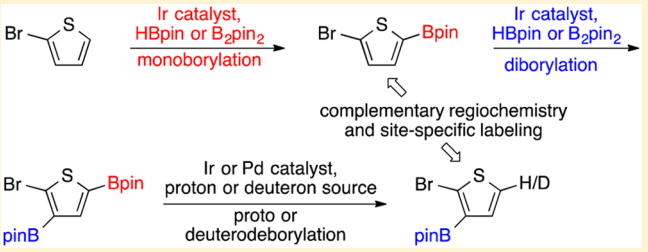
Supporting Information

ABSTRACT: Ir-catalyzed deborylation can be used to selectively deuterate aromatic and heteroaromatic substrates. Combined with the selectivities of Ir-catalyzed C–H borylations, uniquely labeled compounds can be prepared. In addition, diborylation/deborylation reactions provide monoborylated regioisomers that complement those prepared by C–H borylation. Comparisons between Ir-catalyzed deborylations and Pd-catalyzed deborylations of diborylated indoles described by Movassaghi are made. The Ir-catalyzed process is more effective for deborylating aromatics and is generally more effective in the monodeborylation of diborylated thiophenes. These processes can be applied to complex molecules such as clopidogrel.



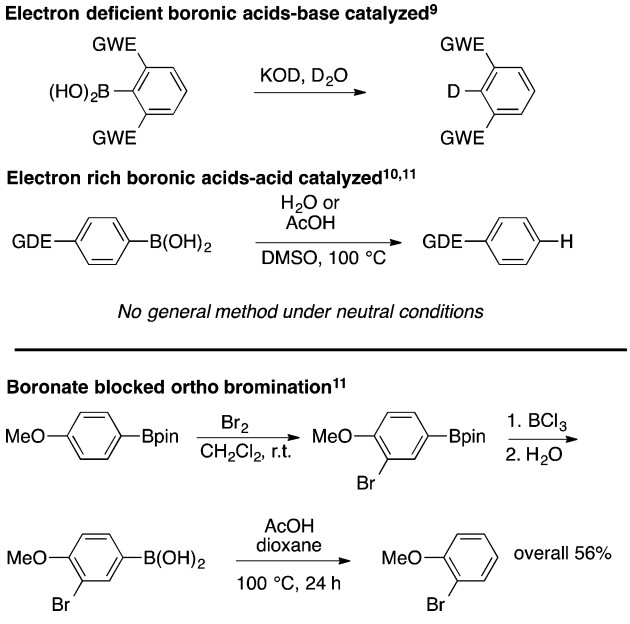
INTRODUCTION

Deuterium and tritium labeled compounds, including those labeled at specific positions, are widely used as probes for spectroscopy, reaction mechanisms, pharmacokinetics, and enzymology.[1] Recently, deuterated molecules have garnered interest as a new class of drug candidates.[2] As the need for specifically labeled compounds grows, reliable methods for incorporating deuterium at specific positions becomes increasingly important.[3] Traditional deuteration methods such as acid, base, or transition metal promoted H/D exchange methods can suffer from harsh conditions, incomplete deuterium incorporation, or poor functional group compatibility.[3] Although some transition metal catalysts exhibit remarkable activities,[4] there are still relatively few examples of selective introduction of one deuterium in an aryl or heteroaryl ring. The most common means of doing so is by metal–halogen exchange, followed by deuterolysis of the organometallic intermediate.[3] More recently, alternatives such as metal catalyzed deuterodecarboxylation have been developed.[5] Both of these approaches require existing functionality to be present. For C–H to C–D transformations, selective examples are limited to ortho deuterations using stoichiometric or catalytic metal organometallic reagents.[3,6,7]

Protolytic deborylations of organoboron compounds are known. For example, benzylic organoboronates undergo stereospecific proto- and deuterodeborylations in the presence of CsF and H_2O/D_2O.[8] It has also recently been shown that extremely electron-deficient aromatic and heteroaromatic boronic acids can be selectively deborylated in 0.2 M hydroxide solutions.[9] Alternatively, electron-rich boronic acids can be deborylated using water or acetic acid as the proton source.[10,11] In these chemistries, the boronic ester or acid can be used for site-specific deuteration or as a blocking group that enables regioselective bromination. These features are summarized in Scheme 1.

In contrast, other boronic acids typically require prolonged reaction times for deborylation.[12] While their rates can be

Scheme 1. Previously Reported Base and Acid Mediated Deborylations Applied to Isotopic Labelling and Synthesis



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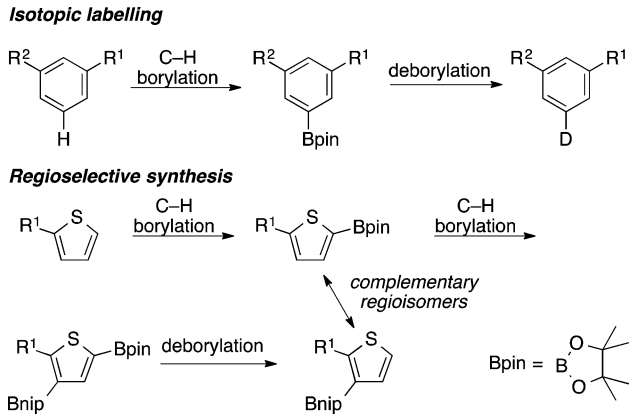
accelerated in highly acidic or basic aqueous solutions and by metal-catalyzed processes,[13,14] many of the conditions employed for deborylation are harsh, and virtually all examples involve boronic acids in aqueous media.

Catalytic C−H activation/borylations of arenes typically install Bpin with regioselectivities governed by sterics.[15] In addition, borylations of arenes and heterocycles occur under mild conditions and a number of important functional groups are tolerated. If mild deborylation could be accomplished in organic solvents, subsequent deuterodeborylation of these molecules would constitute a labeling method with good functional group tolerance, and whose regioselectivity would complement existing methods.

A second application of the deborylation is more intriguing. Namely, certain substrates, such as 2-substituted thiophenes, undergo selective sequential borylations beginning with the most reactive C−H bonds.[16,17] If the deborylation rates mirror borylation rates, then a simple protocol for preparing complementary borylation regioisomers could be developed.[18−20] These possibilities are outlined in Scheme 2. We note that while this work was in progress a diborylation/monodeborylation route to 7-borylated indoles was reported by Movassaghi and co-workers.[21−23]

Scheme 2. Potential Applications of C−H Borylation/Deborylation

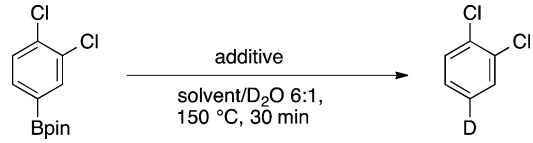


RESULTS AND DISCUSSION

In the course of developing one-pot protocols for Ir-catalyzed C−H borylation and subsequent elaboration of the resulting organoboronate intermediates,[24−26] we noticed that significant quantities of starting substrates were sometimes present at the end of the second reaction, even when the starting materials had been completely consumed during C−H borylation. This indicated that the starting material arose from protolytic deborylation. Moreover, given that Ir-catalyzed additions of aryl boron compounds are known,[27,28] and deborylations have been implicated under the conditions of Ir-catalyzed borylations,[19,29] the deborylations we observed in one-pot reactions were likely Ir-catalyzed.

The fact that pure boronic esters exposed to water under similar conditions did not suffer this problem, and that the ligand used in the borylations, 1,2-bis(dimethylphosphino)ethane (dmpe), failed to promote deborylation (Table 1, entry 2), also supports an Ir-catalyzed process. Indeed, screening of a number of Ir complexes (Table 1) showed that (Ind)Ir(cod) (Ind = η^5-indenyl, cod = 1,5-cyclooctadiene), $[Ir(OMe)(cod)]_2$, and $[Ir(PCy_3)(py)(cod)][PF_6]$ (Crabtree's catalyst, py = pyridine) in the presence of D_2O was very effective in promoting deborylation.[30,31] Some Ir species were less viable at catalyzing this reaction. For example, (dtbpy)Ir(coe) $(BPin)_3$, the catalyst resting state during borylation,[32] was a relatively poor promoter of deborylation, whereas $IrCl_3{\cdot}3H_2O$ and $(\eta^6\text{-}C_6H_6)Ir(Bcat)_3$ did not give detectable deuterated arene. It is noteworthy that, at 150 °C, the crude borylation mixtures are sufficiently active to facilitate deuterodeborylation of arenes to afford reasonably pure compounds labeled at the site of borylation (Supporting Information (SI)).

Table 1. Catalyst Screen for Deuterodeborylation[a]



entry	additive[b]	solvent	conversion[c]
1	crude borylation mixture	THF	>99%
2	dmpe	THF	<1%
3	(Ind)Ir(cod)	THF	95%
4	(Ind)Ir(cod)	DME	97%
5	$[Ir(OMe)(cod)]_2$	THF	98%
6	$[Ir(PCy_3)(py)(cod)][PF_6]$	DME	>99%
7	$[IrCl_3(cod)_2]$	THF	33%
8	$IrCl_3{\cdot}3H_2O$	THF	<1%
9	$(C_6H_6)Ir(Bcat)_3$	THF	<1%
10	(dtbpy)Ir(coe)$(Bpin)_3$	DME	47%
11	none	THF	<1%

[a]All reactions were run in 1 mmol scale in 0.5 mL of D_2O (~23 equiv) and 3−4 mL of solvent, arbitrarily for 30 min. [b]2 mol % Ir in every case. [c]GC area ratio calibrated with corresponding nondeuterated compound.

We next sought lower temperature conditions for deborylation, as they would be synthetically more appealing. Indeed, pure pinacolboronate esters undergo selective deuterodeborylation in THF/D_2O (6:1 by volume) at 80 °C in the presence of 2 mol % $[Ir(\mu\text{-}OMe)(cod)]_2$, a catalyst loading that typically gave complete deborylation after 2 h. Lower catalyst loadings are effective at longer reaction times. The results of deuterodeborylations are given in Table 2. GC analyses indicated clean conversion to products with lower yields in entries 3 and 4 resulting from loss on isolation. Isotopic purity was determined from ^{13}C NMR spectra by integrating the upfield triplet of the deuterated C against the downfield resonance for the residual protonated isotopologue, when detected. The site of deuteration was corroborated by ^2H NMR spectroscopy. The relative reactivities in deborylation mirror the reactivities of the parent arenes toward borylation, with more electron-deficient substrates being more reactive. No deborylation was observed when the substrates in entries 2 and 5 were subjected to Perrin's and Aggarwal's conditions, respectively.[8,9]

A putative catalytic cycle is given in Scheme 3. A generic ligand set is given because from Table 2 we have seen that Ir species without any added ligand are effective. Transmetalation of an Ir hydroxide or alkoxide (vide infra) generates an Ir aryl intermediate. Deuterolysis of the incipient Ir−Ar bond affords the arene and regenerates the Ir hydroxide/alkoxide. While the oxidation state is not defined in Scheme 3, Ir(I) complexes are typically implicated in transmetalations of aryl boron compounds.[27,28] This is consistent with the superior performance of

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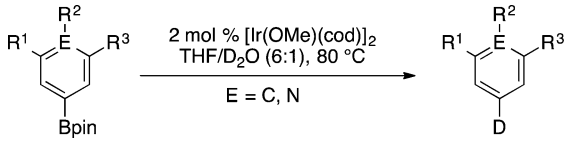
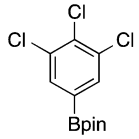
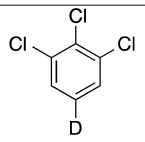
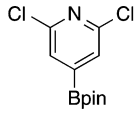
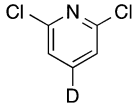
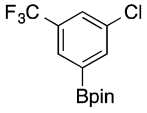
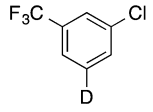
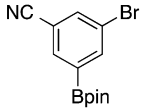
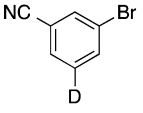
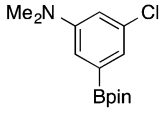
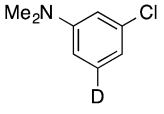
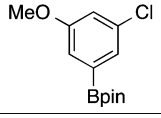
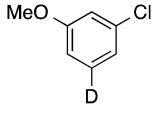
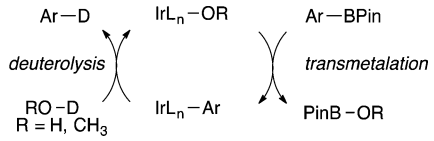
Table 2. Selective Deuterodeborylation Reactions[a]



entry	arene	deuteration time	product	yield[b], %D[c]
1		2 h		80%, >98[d]
2		2 h		82%, 96
3		2 h		65%,[e] >98
4		2 h		60%, >98
5		4.5 h		74%, 96
6		3 h		74%, 93

[a]All reactions were run with 2 mmol of organoboronate. [b]Isolated yields. [c]Determined by integration of ^{13}C NMR spectra; see SI for details for method of calculation. [d]~4% 4-deuterated product was observed due to ~4% 4-borylated isomer in the starting material. [e]Owing to product volatility, solvent impurities were present.

Scheme 3. Proposed Mechanism for Deuterodeborylation

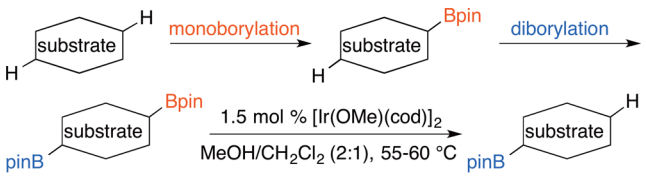


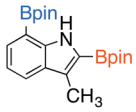
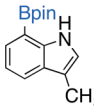
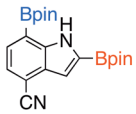
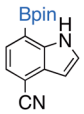
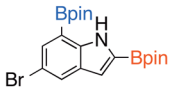
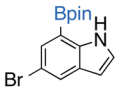
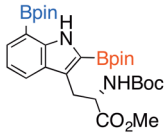
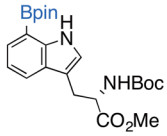
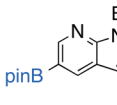
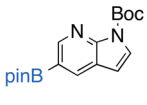
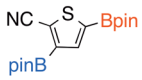
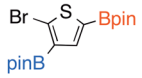
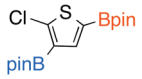
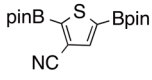
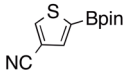
Ir(I) complexes in Table 1. Deborylations using conditions in Table 2 gave clear solutions, and catalysis was not inhibited when a drop of Hg was added to the reaction mixtures, which supports deborylation by homogeneous species.

The fact that the relative reactivities in deborylation reactions parallel the reactivities of the parent arenes toward borylation suggested that, in cases where sequential diborylation is observed, the products would deborylate selectively at the position that was the first site of borylation. If this proved to be the case, the product of diborylation/deborylation would be a different regioisomer of the product of direct C–H borylation.

To test this hypothesis, deborylation of a number of diborylated heterocycles was examined and the results are shown in Table 3. For these more reactive substrates, milder conditions were employed than those used in Table 1 and

Table 3. Synthesis of Monoborylated Compounds via Diborylation/Deborylation[a]



entry	diborylated compound	product	time,[b] yield
1			0.75 h, 68%
2			1 h, 85%
3			1.75h, 83%
4			2 h, 58%
5			4h, 49%
6[c]			5.5 h, 75%
7[c]			10 h, 80%
8[c]			5h, 72%
9[c]			0.5 h, 60%
10[d]			5 h, 58%

[a]Except as where noted, reactions were carried out with pure diborylated starting materials. [b]Time refers to the deborylation step. [c]One-pot synthesis from starting thiophene. [d]Monoborylation of 3-cyanothiophene catalyzed by [IrOMe(cod)]$_2$/dtbpy gives a 1.1:1 ratio of 2- and 5-borylated isomers.

CH_3OH was used as the proton source. For 9 of the 10 substrates, the site of monoborylation in the parent heterocycle is indeed the site of deborylation in the diborylated compounds. The lone exception is 3-cyanothiophene (entry 10), where monoborylation gives a mixture of 2- and 5-borylated compounds. In this case, the high selectivity for deborylation at the 2-position of the diborylated product is the key to synthesizing isomerically pure 5-borylated product.

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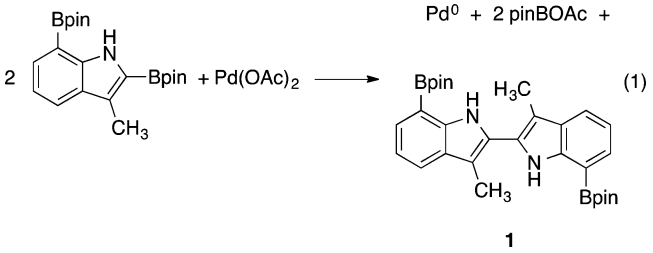
Several of the results in Table 3 merit comment. For the indole substrates, diborylation/deborylation affords the 7-borylated products, which have previously been prepared by a relay-directed reaction of N-silylated indoles, which are in turn prepared in a Ru-catalyzed reaction from the parent indole and a disilane.[33] After Ir-catalyzed C−H borylation, the silane deprotection yields the 7-borylated product. Diborylation/deborylation obviates the need for N-protection/deprotection. Entries 4 and 5 utilize Boc protected compounds and demonstrate that, as is the case for Ir-catalyzed C−H borylation, Boc protecting groups are compatible with Ir-catalyzed deborylation. Diborylation/deborylation of 2-halogenated thiophenes provide unique halogenated building blocks. Synthesis of these compounds by lithiation would not be feasible because halogenated heteroaryl lithium compounds undergo "halogen dance" rearrangements.[34] The fact that 3- or 5-borylated isomers of 2-halogenated thiophenes can be accessed is a testament to the mild conditions of these Ir-catalyzed processes. We note that reaction times for Table 3, entry 1 were particularly sensitive to the quality of the MeOH used in the deborylation, with lower grade reagent requiring substantially longer reaction times.

In Movassaghi and co-worker's recent report, a mechanism involving indole protonation is proposed with no role invoked for the metal.[21] Three procedures were described in their paper. In the first (condition **A**), diborylation of 3-substituted indoles is carried out with 5.0 equiv of HBpin catalyzed by 2.5 mol % $[Ir(OMe)(cod)]_2$ and 5 mol % dtbpy in THF. After diborylation is completed, the reaction is diluted with CH_2Cl_2 and trifluoroacetic acid (TFA) is added at 0 °C. The reaction is allowed to warm to 23 °C and quenched when the monoborylated product is maximized. In the second procedure (condition **B**), *N*-2-(1*H*-Indol-3-yl)ethyl)-*N*,2,4,6-tetramethylbenzenesulfonamide was diborylated under Ir-catalyzed conditions. The crude product was purified by flash chromatography. The pure material was then dissolved in CH_2Cl_2 and deborylation was carried out with TFA. In the third set of conditions (condition **C**), diborylation is carried out under Ir-catalyzed conditions. Afterward, volatile materials are removed, the crude mixture is dissolved in acetic acid, and 5 mol % $Pd(OAc)_2$ is added to effect deborylation. It is important to note that metal (Ir and/or Pd) is present during the deborylation.

To assess the role of the metal, we carried out a set of experiments. First we repeated Movassaghi and co-worker's synthesis of 7-borylated 3-methylindole using condition **A** and obtained similar results. Next, we attempted metal-free deborylation of pure 2,7-diborylated 3-methylindole with TFA in CH_2Cl_2. After the same reaction time as the procedure with conditions **A** called for, an aliquot was taken and volatile materials were removed. In contrast to the case for condition **A**, ^{1}H NMR spectra revealed a complex mixture with multiple resonances in the aromatic region. Next, we compared deborylations of isolated 2,7-diborylated 3-methylindole with acetic acid catalyzed by either 2.5 mol % $[Ir(OMe)(cod)]_2$ or 5 mol % $Pd(OAc)_2$. After 8 h at 30 °C, aliquots from the reactions were analyzed by ^{1}H NMR spectroscopy by integrating the NH resonances that are resolved and shifted downfield from the NH resonance of 3-methylindole. For the Ir-catalyzed reaction the ratio of 7-borylated to 2,7-diborylated species was 75:25. For the Pd-catalyzed reaction, a third species was observed with an NH resonance at δ 9.38 ppm. This product increased when the $Pd(OAc)_2$ loading was increased. In the ^{1}H NMR spectrum, the NH chemical shift is consistent with an indole whose NH is flanked by one or two Bpin groups and the splitting pattern of the C6 ring protons is similar to that for the diborylated indole. LC/MS spectra revealed a molecular ion at m/z = 513.064, which is consistent with a homocoupled bisindole. In conjunction with the NMR data, we assign this byproduct to structure **1** (eq 1).



1

Attempts to separate **1** from the indole products were unsuccessful. At a 5% loading of $Pd(OAc)_2$, in deborylation with acetic acid at 30 °C for 8 h, the ratio of 7-borylated, 2,7-diborylated, to the homocoupled bisindole species was 95:2:3 (average of three runs). This suggests that the first step in the deborylation reaction is homocoupling of the indole to generate Pd^0. For Pd-catalyzed deborylation of the crude diborylated indole that results from Ir-catalyzed C−H borylation, only traces of the homocoupled bisindole are found in ^{1}H NMR spectra. This is an added advantage of the one-pot transformation.

To complete the comparison of Pd- and Ir-catalyzed chemistries, deborylation of the diborylated product of 3-methylindole was carried out with 3 mol % $Pd(OAc)_2$ in MeOH/CH_2Cl_2 (2:1) at 60 °C for 3 h. Conversion to 7-borylated 3-methylindole (17%), along with 3% 3-methylindole, shows that under these conditions Pd is less efficient than Ir at facilitating deborylation. The superior performance of the Ir-catalyzed reactions under these conditions makes them better suited for molecules with acid sensitive groups.

Pd-catalyzed deborylations of the diborylated thiophenes in entries 6, 8, and 10 of Table 3 were carried out in acetic acid with 5 mol % $Pd(OAc)_2$ at 30 °C, to compare to Movassaghi's conditions, and with 3 mol % $Pd(OAc)_2$ in MeOH/CH_2Cl_2 (2:1) at 55 °C, to compare to Ir-catalyzed reactions in Table 3. The results are shown in Table 4. While the reactions in MeOH/CH_2Cl_2 gave the highest conversions for the Pd-catalyzed reactions, they were less efficient and, in the case of the diborylated product of 3-cyanothiophene, less selective than the corresponding deborylations with Ir (Table 3).

The conditions for C−H activation/borylation are sufficiently mild for late stage functionalization of advanced molecules such as pharmaceuticals. This is illustrated in Scheme 4 where clopidogrel (**2**), the active ingredient of Plavix, is selectively borylated at the 5-position of its thiophene ring to afford (**3**).[35] Deuterodeborylation of borylated clopidogrel confirms the site of borylation and provides a probe for the stereospecificity of the borylation (and deborylation) reactions. As shown in Scheme 4, Ir-catalyzed deuterodeborylation can be achieved at 55 °C in 2:1 $CD_3OD/CDCl_3$ with 92% deuteration at the 5-position of the thiophene ring, confirming the site of borylation. Moreover, the 5-deuterated clopidogrel showed no loss of optical rotation when compared to unlabeled clopidogrel.[36] Thus, both the borylation and deborylation proceed with a high degree of stereospecificity. This is significant, as synthesis of borylated clopidogrel by ortholithiation and subsequent trapping with boron electrophiles gives a racemic product.[37]

To demonstrate the potential for diborylation/deborylation in complex substrates, we return again to clopidogrel (Scheme 5). With a moderate excess of HBpin, clopidogrel is smoothly

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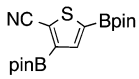
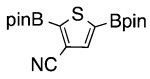
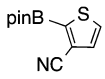
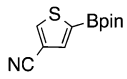
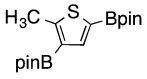
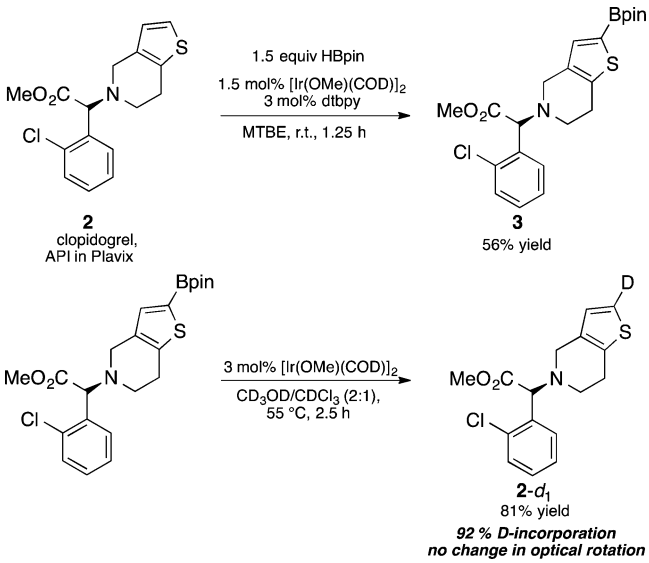
Table 4. Pd-Catalyzed Deborylation of Diborylated Thiophenes

entry	reactant	$Pd(OAc)_2$ loading, T, solvent, time	product (% conversion)
1			
		5 mol %, 30 °C, AcOH, 23 h	11%
		3mol %, 55 °C, $MeOH/CH_2Cl_2$, 5.5 h	15%
2[a]			 
		5 mol %, 30 °C, AcOH, 23 h	8% 14%
		3mol %, 55 °C, $MeOH/CH_2Cl_2$, 5 h	7% 42%
3			
		5 mol %, 30 °C, AcOH, 23 h	59%
		3mol %, 55 °C, $MeOH/CH_2Cl_2$, 5.5 h	39%

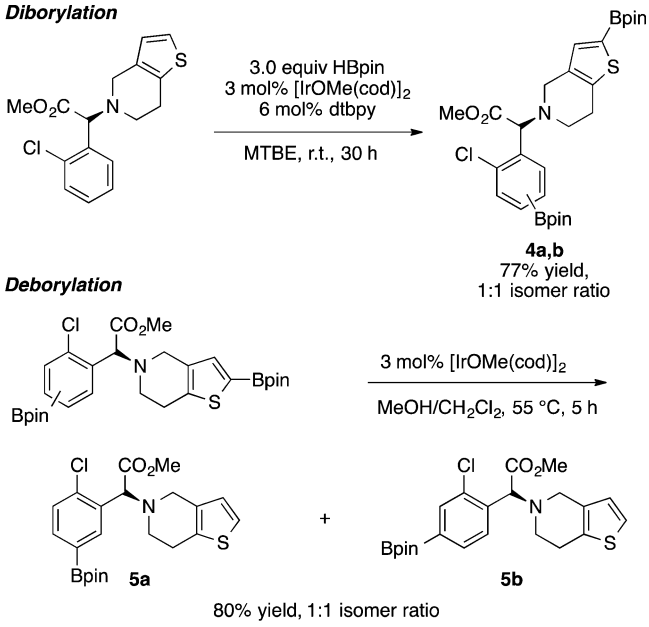
[a]The diborylated thiophene rapidly deborylates to the 5-borylated product when washed with saturated $NaHCO_3$ solutions.

Scheme 4. Borylation/Deuterodeborylation of Clopidogrel



borylated at the thiophene and arene rings affording diborylated isomers **4a,b** due to competitive borylation at the 4 and 5-positions of the arene ring. This isomer mixture undergoes regioselective deborylation at the thiophene moiety to produce the monoborylated isomers **5a,b** in Scheme 5 in excellent yield. The results in Schemes 4 and 5 further demonstrate the potential for Ir-catalyzed borylations and deborylations in the late stage functionalization of complex molecules.[29]

Scheme 5. Diborylation/Deborylation of Clopidogrel



CONCLUSIONS

In summary, we have shown that Ir-catalyzed deborylation can be utilized to isotopically label unactivated C−H positions of arenes selectively. In addition, deborylation can be coupled to diborylation to prepare monoborylated compounds where the regioselectivities complement those found for monoborylation of the parent substrates. The Ir-catalyzed deborylations of 2-borylated indoles are slower than Pd-catalyzed reactions reported by Movassaghi, but are superior for deborylations of arenes and thiophenes. In contrast to Brønsted acid and base mediated deborylations, the Ir-catalyzed deborylations are not limited by substrate electronics. The mild conditions of Ir-catalyzed borylations and deborylations make applications to complex substrates possible, where other methods for deborylation would result in unwanted side reactions.[38]

EXPERIMENTAL SECTION

Pinacolborane (HBPin) and B_2pin_2 were generously supplied by BoroPharm, Inc. (η^5-Indenyl)(η^4-1,5-cyclooctadiene)iridium ((Ind)Ir(cod)),[39] Bis(η^4-1,5-cyclooctadiene)-di-μ-methoxy-diiridium(I) ([Ir(OMe)(cod)]$_2$),[40] (dtbpy)Ir(coe)(Bpin)$_3$,[32] and (η^6-C_6H_6)Ir(Bcat)$_3$[41] were prepared per the literature procedures. 4,4′-Di-*tert*-butyl-2,2′-bipyridine (dtbpy) was purchased from Aldrich. $IrCl_3\cdot(H_2O)_x$ was purchased from Pressure Chemical Co., and [Ir((PCy$_3$)(py)(cod)]-[PF_6^-] was purchased from Strem Chemicals, Inc. Diborylated *N*-Boc-7-azaindole and diborylated *N*-Boc-L-tryptophan methyl were prepared according to the literature procedure.[42] All substrates were purified by column chromatography or passing through a plug of alumina. Pinacolborane (HBPin) was distilled before use. *n*-Hexane, cyclohexane, and MTBE were refluxed over sodium, distilled, and degassed. Tetrahydrofuran and CH_2Cl_2 were obtained from a dry still packed with activated alumina and degassed before use. Silica gel was purchased from EMD (230−400 Mesh).

All reactions were monitored by GC-FID (column type: Fused silica 30 m × 0.25 mm ID coating CP-SIL 8 CB). GC-FID method: 70 °C, 2 min; 20 °C/min, 9 min; 250 °C, 10 or 20 min. All reported yields are for isolated materials unless otherwise stated.

^{1}H and ^{13}C NMR spectra were recorded at 300.11 and 75.47 MHz, respectively, or 499.74 and 125.67 MHz, respectively, and referenced to residual solvent signals (7.24 and 77.0 ppm for $CDCl_3$, respectively). ^{11}B spectra were recorded at 96.29 MHz and were referenced to neat $BF_3\cdot$

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Et_2O as the external standard. All coupling constants are apparent J values measured at the indicated field strengths. All two-dimensional experiments were run using z-axis pulse field gradients. GC-MS data were obtained using fused silica 30 m × 0.25 mm ID columns coated with CP-SIL 8 CB. Melting points were measured on a capillary melting apparatus and are uncorrected. Optical rotations were recorded at the sodium D line.

General Procedure for C−H Borylation with Diphosphine Ligands. In the glovebox, arene, HBpin (1.5−2.5 equiv), (Ind)Ir(cod) (2 mol %), and dmpe/dppe (2 mol %) were transferred into an air-free flask equipped with a stirrer bar in the following order: HBpin with Ir calatyst, followed by ligand, followed by arene. A 0.5−2 mL aliquot (per mmol of arene) of solvent (cyclohexane, *n*-hexane, heptane, or octane) could be used to help dissolution and transfer. The flask was sealed and brought out of the glovebox and placed in an oil bath heated to 150 °C (for (Ind)Ir(cod)/dmpe) or 100 °C (for (Ind)Ir(cod)/dppe) until the reaction was judged complete by GC-FID. (*Note: in the cases of multiple borylations and borylations of sluggish substrates, periodic cooling and purging of the H_2 gas help to maintain an effective rate of reaction.*) At that time the reaction was allowed to cool to room temperature. Upon stirring, the residue was quenched by dropwise addition of MeOH until gas evolution ceased. The mixture was concentrated by a gentle nitrogen flow, and the resultant syrup was passed through a silica plug (10−15 cm long, 2 cm wide for 1−2 mmol scale, CH_2Cl_2 or hexanes/CH_2Cl_2) to give the desired boronic ester.

General Procedure for Borylation with [Ir(OMe)(cod)]$_2$ and dtbpy. Two separate test tubes were charged with $[Ir(OMe)(cod)]_2$ and dtbpy. Excess HBPin was added to the $[Ir(OMe)(cod)]_2$ test tube. In cases where B_2pin_2 was used as the borylating agent, HBPin (3 × Ir mol %) was used to generate an active catalyst. *n*-Hexane or cyclohexane or MTBE (1 mL) was added to the dtbpy containing test tube in order to dissolve the dtbpy. The dtbpy solution was then mixed with the $[Ir(OMe)(cod)]_2$ and HBPin mixture. After mixing for 1 min, the resulting solution was transferred to a Schlenk flask equipped with a magnetic stirring bar. Additional *n*-hexane or cyclohexane or MTBE (2 × 1 mL) was used to wash the test tubes, and the washings were transferred to the Schlenk flask. Substrate (1 mmol, 1 equiv) was added to the Schlenk flask. The flask was stoppered, brought out of the glovebox, and attached to the Schlenk line in a fume hood. The Schlenk flask was placed under N_2, and the reaction was carried out at the specified temperature. The reaction was monitored by GC-FID/MS. After completion of the reaction, the volatile materials were removed on a rotary evaporator. The crude material was purified by column chromatography or dissolved in CH_2Cl_2 and passed through a plug of silica.

General Procedure for the Borylation of Arenes. In a glovebox, in an air-free flask, $[Ir(OMe)COD]_2$ (1 mol %), dtbpy (2 mol %), HBPin (1.8 equiv), and the substrate (11 mmol) were combined neat or in cyclohexane. The flask was sealed, brought out of the drybox, and heated to a temperature depending on the substrate until GC/MS indicated a complete reaction. The reaction was pumped down to obtain the crude product, which was purified by column chromatography (CH_2Cl_2) to afford the pure product.

General Procedure for Preparation of Deuterated Aromatics via C−H Borylation/Deuteration with D_2O. A borylation reaction with 2 mmol of arene was set up and monitored by GC-FID until judged complete. Solvent for this borylation, if any, was removed by a gentle nitrogen flow. The residue was placed under high vacuum for a few hours, and the flask was backfilled with nitrogen. To the reaction were added 0.5 mL of D_2O and 3−4 mL of dry THF or DME. The flask was resealed and heated in an oil bath to 150 °C until the reaction was judged complete by GC-FID. Upon completion, the mixture was poured into water and extracted with pentane (or CH_2Cl_2 if the product has low solubility in pentane), dried over $MgSO_4$, filtered, and evaporated. Column chromatography (pentane or CH_2Cl_2) afforded the product.

For deuteration of isolated boronic acids/esters, 2 mmol of aryl boronic acid/ester and the Ir catalyst (0.02 mmol, 2 mol %) were dissolved in 3−4 mL of THF or DME in the glovebox and transferred into an air-free flask equipped with a stirrer bar. The flask was sealed and brought out of the drybox and charged with 0.5 mL of D_2O. It was resealed and heated in an oil bath to 150 °C until the reaction was judged complete by GC-FID and worked up as described in the general procedure.

General Procedure for the Deuteration of Aryl Boronic Esters with D_2O. In the glovebox, in an air-free flask, $[Ir(OMe)(cod)]_2$ (2 mol %) and the aryl boronic ester (2 mmol) were combined in THF (3 mL). The flask was sealed and brought out of the box where it was charged with D_2O (0.5 mL). The flask was resealed and heated at 80 °C until the reaction was judged to be complete by GC/MS. When the reaction was complete, it was poured into water and extracted with CH_2Cl_2, Et_2O, or pentane, dried over $MgSO_4$, filtered, and concentrated. Purification by Kugelrohr distillation, sublimation, or column chromatography afforded the pure product.

General Procedure for Deborylation with MeOH. A Schlenk flask equipped with a magnetic stirring bar and condenser was charged with substrate (1.0 mmol, 1.0 equiv) and $[Ir(OMe)(cod)]_2$ (10 mg, 0.015 mmol, 3 mol % Ir). The Schlenk flask was then evacuated and backfilled with nitrogen (this sequence was carried out two times). Solvent mixture (methanol/dichloromethane 2:1, 5 mL) was added to the Schlenk flask and flushed under nitrogen twice as mentioned previously. The Schlenk flask was placed under N_2, and the reaction was carried out at the specified temperature. The reaction was monitored by GC-FID/MS. After completion of the reaction, the volatile materials were removed on a rotary evaporator. The crude material was purified by column chromatography or dissolved in CH_2Cl_2 and passed through a plug of silica.

General Procedure for One-Pot Diborylation/Deborylation. The Ir-catalyst was generated as follows: in a glovebox, two separate test tubes were charged with $[Ir(OMe)(cod)]_2$ (10 mg, 0.015 mmol, 3 mol % Ir) and dtbpy (8 mg, 0.03 mmol, 3 mol %). Excess HBPin (2.5 to 3 equiv) was added to the $[Ir(OMe)(cod)]_2$ test tube. *n*-Hexane (1 mL) was added to the dtbpy containing test tube in order to dissolve the dtbpy. The dtbpy solution was then mixed with the $[Ir(OMe)(cod)]_2$ and HBPin mixture. After mixing for 1 min, the resulting solution was transferred to a Schlenk flask equipped with a magnetic stirring bar. Additional *n*-hexane (2 × 1 mL) was used to wash the test tubes, and the washings were transferred to the Schlenk flask. Substituted thiophene (1 mmol, 1 equiv) was added to the Schlenk flask. The reaction was stirred at room temperature and was monitored by GC-FID/MS. After completion of the reaction, the volatile materials were removed and 5 mL of CH_3OH/CH_2Cl_2 mixture (2:1) were added and heated at 55 °C. The reaction was monitored by GC-FID/MS, and after completion of the reaction, the volatile materials were removed on a rotary evaporator. The crude material was purified by column chromatography or dissolved in CH_2Cl_2 and passed through a plug of silica. Small amounts of impurities, if present, were removed by crystallization.

1,2-Dichlorobenzene-4-*d*. The borylation step was carried out neat with 295 mg of 1,2-dichlorobenzene (2 mmol) and 365 mg of HBpin (2.85 mmol, 1.4 equiv), 16.6 mg of (Ind)Ir(cod) (0.04 mmol, 2 mol %), and 6.0 mg of dmpe (0.04 mmol, 2 mol %) at 150 °C for 3.5 h. The crude borylation mixture was pumped down under a high vacuum and charged with 0.5 mL of D_2O and 3 mL of THF. The deuteration step was then carried out at 150 °C for 30 min and worked up as described in the general procedure, after which the crude material was purified with silica gel chromatography (pentane) to afford 220 mg of the deuterated compound (74%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41−7.44 (m, 2 H), 7.16−7.20 (m, 1 H); ^{2}H NMR (76.75 MHz, pentane): δ 7.21; ^{13}C NMR (125 MHz, $CDCl_3$): δ 132.6, 130.5, 130.4, 127.6, 127.4 (t, $J_{C\text{-}D}$ = 25 Hz); IR (neat): 3063, 1564, 1455, 1385, 1125, 1034, 901, 835, 731, 648 cm^{-1}; LRMS (EI): m/e 147 (M^+), 112, 76. HRMS (EI) m/e calcd for $[C_6H_3DCl_2]^+$ 146.9753, found 146.9759.

Synthesis of 5-Bpin-1,2,3-trichlorobenzene.[43] The reaction was carried out neat with 1,2,3-trichlorobenzene (11 mmol, 2.00 g), $[Ir(OMe)(cod)]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBPin (19.8 mmol, 2.5 g). The reaction stirred at 80 °C for 2 h. The crude product was purified as outlined in the general procedure to afford the pure product (3.07 g, 91%) as a white solid; mp 94−97 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 (s, 2H), 1.34 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.4, 134.1, 133.9, 84.7, 24.8; ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.1; FT-IR (KBr): 2989, 2931, 1583,

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1533, 1450, 1370, 1342, 1147, 1121, 965, 882, 847, 799, 703, 673, 555 cm^{-1}; HRMS (ESI) *m/z* Calcd for $C_{12}H_{15}BCl_3O_3$ $[M+ {}^{-}OH]^{-}$ 323.0182, found 323.0185.

1,2,3-Trichlorobenzene-5-*d*. The borylation step was carried out neat with 364 mg of 1,2,3-trichlorobenzene (2 mmol) and 450 mg of HBpin (3.6 mmol, 1.8 equiv), 16.6 mg of (Ind)Ir(cod) (0.04 mmol, 2 mol %), and 6.0 mg of dmpe (0.04 mmol, 2 mol %) at 150 °C for 3.25 h. The crude borylation mixture was pumped down under high vacuum and charged with 0.5 mL of D_2O and 3 mL of THF. The deuteration step was then carried out at 150 °C for 60 min and worked up as described in the general procedure, after which the crude material was purified with silica gel chromatography (pentane) to afford 343 mg of the deuterated compound (94%) as a white solid; mp 52−53 °C (53−55 °C for commercial nondeuterated compound). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (t, $J_{H\text{-}D}$ = 1.1 Hz); ^{2}H NMR (76.75 MHz, pentane): δ 7.14; ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.3, 131.6, 128.6, 127.2 (t, $J_{C\text{-}D}$ = 25 Hz); IR (neat): 3071, 1553, 1412, 1385, 1196, 1159, 899, 768, 666 cm^{-1}; LRMS (EI): *m/e* 181 (M^+), 146, 110. Anal. Calcd for $C_6H_2DCl_3$: C, 39.50. Found: C, 39.06.

1,2,3-Trichlorobenzene-5-*d* (Alternative Procedure). The deuteration was carried out in THF and D_2O as outlined in the general procedure with 5-Bpin-1,2,3-trichlorobenzene (2 mmol, 614 mg) and $[Ir(OMe)(cod)]_2$ (2 mol %, 0.04 mmol, 26.4 mg). The reaction was heated at 80 °C for 2 h. When the reaction was complete, it was poured into water and 1 M NaOH. The product was extracted into CH_2Cl_2, dried over $MgSO_4$, and concentrated. The crude product was purified by passing it through a short silica column ($CHCl_3$) to afford the deuterated compound as a white solid (292 mg, 80%); mp 52−54 °C. Approximately 3−4% of the isolated deuterium compound was 1,2,3-trichlorobenzene-4-*d* as determined by ^{1}H NMR and confirmed by ^{2}H NMR. Due to spectral overlap, deconvolution of the spectra was necessary to extract accurate integration. There was also approximately 3−4% of 4-Bpin-1,2,3-trichlorobenzene observed in the isolated borylated starting material. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (apparent t, $J_{H\text{-}D}$ = 1.0 Hz, 2H); ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.18; ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.3 (t, $^3J_{C\text{-}D}$ = 1.76 Hz), 131.5, 128.6, 127.2 (t, $J_{C\text{-}D}$ = 25 Hz); LRMS (EI): *m/z* 181 (M^+); HRMS (EI): *m/z* calculated for $[C_6H_2DCl_3]^+$ 180.9363, found 180.9365. Percent D incorporation (based on quantitative ^{13}C NMR): >98.1%

Synthesis of 4-Bpin-2,6-dichloropyridine.[24] The reaction was carried out in cyclohexane (20 mL) with 2,6-dichloropyridine (11 mmol, 1.63 g), $[Ir(OMe)(cod)]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBPin (19.8 mmol, 2.5 g). The reaction was stirred at 80 °C for 1 h. The crude product was purified as outlined in the general procedure to afford the pure product (2.65 g, 88%) as a white solid; mp 114−117 °C. Spectral data matched the reported data.

2,6-Dichloropyridene-4-*d*. The borylation step was carried out with 300 mg of 2,6-dichloropyridene (2 mmol) and 450 mg of HBpin (3.6 mmol, 1.8 equiv), 16.6 mg of (Ind)Ir(cod) (0.04 mmol, 2 mol %), and 6.0 mg of dmpe (0.04 mmol, 2 mol %) in 1 mL of heptane at 150 °C for 3.25 h. After removal of heptane by a gentle nitrogen flow, the crude borylation mixture was pumped down under high vacuum and charged with 0.5 mL of D_2O and 3 mL of THF. The deuteration step was then carried out at 150 °C for 60 min and worked up as described in the general procedure, after which the crude material was purified with a silica gel chromatography (CH_2Cl_2) to afford 273 mg of the deuterated compound (92%) as a white solid; 84−86 °C (86−88.5 °C for commercial nondeuterated compound). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 (t, $J_{H\text{-}D}$ = 1.1 Hz); ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.65; ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.6, 140.4 (t, $J_{C\text{-}D}$ = 25 Hz), 122.7; IR (neat): 3050, 2269, 1559, 1547, 1373, 1136, 986, 901, 739, 702 cm^{-1}; LRMS (EI): *m/e* 148 (M^+), 113. Anal. Calcd for $C_5H_2DNCl_2$: C, 40.31; N, 9.40. Found: C, 40.34; N, 8.80.

2,6-Dichloropyridine-4-*d* (Alternative Procedure). The deuteration was carried out in THF and D_2O as outlined in the general procedure with 4-Bpin-2,6-dichloropyridine (2 mmol, 496 mg) and $[Ir(OMe)(cod)]_2$ (2 mol %, 0.04 mmol, 26.4 mg). The reaction was heated at 80 °C for 2 h. When the reaction was complete, it was poured into water, and the product was extracted into Et_2O, dried over $MgSO_4$, and concentrated. The crude product was purified by sublimation (0.08 mmHg/45 °C) to afford the deuterated compound as a white solid (244 mg, 82%); mp 85−88 °C. ^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.36 (t. $J_{H\text{-}D}$ = 1.0 Hz, 2H); ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.61; ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.6 (t, $^3J_{C\text{-}D}$ = 1.71 Hz), 140.4 (t, $J_{C\text{-}D}$ = 25 Hz), 122.8; LRMS (EI): *m/z* 148 (M^+); HRMS (ESI+): *m/z* calculated for $[C_5H_3DCl_2N]^+$ 148.9783, found 148.9792. Percent D incorporation (based on quantitative ^{13}C NMR): 96.3%

Synthesis of 5-Bpin-3-chlorobenzotrifluoride. The reaction was carried out neat with 3-chlorobenzotrifluoride (11 mmol, 1.98 g), $[Ir(OMe)(cod)]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBPin (19.8 mmol, 2.5 g). The reaction was stirred at 80 °C for 1 h. The crude product was purified as outlined in the general procedure to afford the pure product (3.10 g, 92%) as a clear, colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, 2H, *J* = 8.2 Hz), 7.65 (s, 1H), 1.33 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.9, 136.9, 134.5, 131.7 (q, $^2J_{C-F}$ = 33 Hz), 129.4 (q, $^3J_{C-F}$ = 3.8 Hz), 127.9 (q, $^3J_{C-F}$ = 3.9 Hz), 123.4 (q, $^1J_{C-F}$ = 272 Hz), 84.6, 24.8; ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.1; FT-IR (KBr): 2982, 2933, 2873, 1611, 1367, 1296, 1172, 1140, 965, 887, 847, 823, 724, 706, 685 cm^{-1}; HRMS (ESI) *m/z* Calcd for $C_{13}H_{16}BClF_3O_3$ $[M + {}^{-}OH]^{-}$ 323.0836, found 323.0835.

3-Chlorobenzotrifluoride-5-*d*. The borylation step was carried out with 363 mg of 3-chlorobenzotrifluoride (2 mmol) and 450 mg of HBpin (3.6 mmol, 1.8 equiv), 16.7 mg of (Ind)Ir(cod) (0.04 mmol, 2 mol %), and 6.0 mg of dmpe (0.04 mmol, 2 mol %) in 2 mL of cyclohexane at 150 °C for 3 h. After removal of cyclohexane by a gentle nitrogen flow, the crude borylation mixture was pumped down under high vacuum and charged with 0.5 mL of D_2O and 3 mL of THF. The deuteration step was then carried out at 150 °C for 90 min and worked up as described in the general procedure, after which the crude material was purified with silica gel chromatography (pentane) to afford 244 mg of material containing 239 mg of the deuterated compound (66%) and 5 mg of pentane. Continuing evaporation afforded pure deuterated compound (some loss of product occurred) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60 (br, 1 H), 7.50−7.51 (br, 2 H); ^{2}H NMR (76.75 MHz, pentane): δ 7.45; ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.0, 132.3 (q, J_{C-F} = 34 Hz), 131.9, 129.9 (t, $J_{C\text{-}D}$ = 25 Hz), 125.7 (q, J_{C-F} = 4 Hz), 123.3 (q, J_{C-F} = 4 Hz), 123.3 (q, J_{C-F} = 272 Hz); IR (pentane solution film): 3087, 1576, 1426, 1310, 1175, 1134, 1103, 1161, 887, 708, 677 cm^{-1}; LRMS (EI): *m/e* 181 (M^+), 162, 146. HRMS (EI): *m/e* calcd for $[C_7H_3DClF_3 - Cl]^+$ 146.0328, found 146.0330.

3-Chlorobenzotrifluoride-5-*d* (Alternative Procedure). The deuteration was carried out in THF and D_2O as outlined in the general procedure with 5-Bpin-3-chlorobenzotrifluoride (2 mmol, 615 mg) and $[Ir(OMe)(cod)]_2$ (2 mol %, 0.04 mmol, 26.4 mg). The reaction was heated at 80 °C for 2 h. When the reaction was complete, it was poured into water and 1 M NaOH. The product was extracted into Et_2O, dried over $MgSO_4$, and concentrated. The crude product was purified by passing it through a short silica column ($CHCl_3$) to afford the deuterated compound as a clear oil (236 mg, 65%). THF (2.2 mg) and Et_2O were observed in the ^{13}C NMR and ^{1}H NMR spectra, respectively. But, owing to the volatility of the compound, it could not be removed, because of the risk of loss of the product. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (br s, 1H), 7.51 (d, *J* = 7.2 Hz, 2H); ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.42; ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.9 (t, $^3J_{C\text{-}D}$ = 1.7 Hz), 132.3 (dq, $^2J_{C-F}$ = 33 Hz, $^3J_{C\text{-}D}$ = 1.3 Hz), 131.9 (q, $^4J_{C-F}$ = 1.2 Hz), 129.9 (t, $^3J_{C\text{-}D}$ = 25 Hz), 125.7 (q, $^3J_{C-F}$ = 4 Hz), 123.33 (q, $^1J_{C-F}$ = 272.5 Hz), 123.32 (q, $^3J_{C-F}$ = 3.9 Hz); LRMS (EI): *m/z* 181 (M^+). Percent D incorporation (based on quantitative ^{13}C NMR): 98.1%

Synthesis of 5-Bpin-3-bromobenzonitrile.[44] The reaction was carried out neat with 3-bromobenzonitrile (11 mmol, 2.00 g), $[Ir(OMe)(cod)]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBPin (19.8 mmol, 2.5 g). The reaction was stirred at 50 °C for 2.5 h. The crude product was purified as outlined in the general procedure to afford the pure product (3.04 g, 90%) as a white solid; mp 83−86 °C. Spectral data matched the reported data.

3-Bromobenzonitrile-5-*d*. The borylation step was carried out with 364 mg of 3-bromobenzonitrile (2 mmol) and 400 mg of HBpin (3.1 mmol, 1.55 equiv), 20.0 mg of $[Ir(OMe)(cod)]_2$ (0.03 mmol, 1.5 mol %), and 16.0 mg of dtbpy (0.06 mmol, 3 mol %) in 2 mL of heptane

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at room temperature for 6 h. After removal of heptane by a gentle nitrogen flow, the crude borylation mixture was pumped down under high vacuum and charged with 0.5 mL of D_2O and 3 mL of THF. The deuteration step was then carried out at 150 °C for 2 h and worked up as described in the general procedure, after which the crude material was purified with silica gel chromatography (CH_2Cl_2), followed by a sublimation at 45−50 °C under 0.1 mmHg to afford 257 mg of the deuterated compound (70%) as a white solid; mp 37−39 °C (38−40 °C for commercial nondeuterated compound). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (apparent t, J = 1.6 Hz, 1 H), 7.73 (br, 1 H), 7.59 (br, 1 H); ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.39; ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.0, 134.7, 130.5, 130.3 (t, $J_{C\text{-}D}$ = 25 Hz), 122.8, 117.2, 114.2; IR (neat): 3075, 2234, 1553, 1429, 1406, 1186, 909, 882, 785, 675 cm^{-1}; LRMS (EI): m/e 182 (M^+), 103. Anal. Calcd for C_7H_3DNBr: C, 45.94; N, 7.65. Found: C, 45.70; N, 7.53.

3-Bromobenzonitrile-5-*d* (Alternative Procedure). The deuteration was carried out in THF and D_2O as outlined in the general procedure with 5-Bpin-3-bromobenzonitrile (2 mmol, 616 mg) and $[Ir(OMe)(cod)]_2$ (2 mol %, 0.04 mmol, 26.4 mg). The reaction was heated at 80 °C for 2 h. When the reaction was complete, it was poured into water and 1 M NaOH. The product was extracted into CH_2Cl_2, dried over $MgSO_4$, and concentrated. The crude product was purified by sublimation (0.15 mmHg/50 °C) to afford the deuterated compound as a white solid (219 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (t, J = 1.8 Hz, 1H), 7.71 (br, 1H), 7.57 (br, 1H); ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.38; ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.0, 134.7, 130.6, 130.3 (t, $J_{C\text{-}D}$ = 25 Hz), 122.9 (t, $^3J_{C\text{-}D}$ = 1.5 Hz), 114.2 (t, $^3J_{C\text{-}D}$ = 1.4 Hz); LRMS (EI): m/z 182 (M^+); HRMS (EI): m/z calculated for $[C_7H_3DBrN]^+$ 181.9596, found 181.9590. Percent D incorporation (based on quantitative ^{13}C NMR): >98.1%.

Synthesis of 5-Bpin-3-chloro-*N*,*N*-dimethylaniline. The reaction was carried out neat with 3-chloro-*N*,*N*-dimethylaniline (11 mmol, 1.71 g), $[Ir(OMe)(cod)]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBPin (19.8 mmol, 2.5 g). The reaction was stirred at 80 °C for 16 h. The crude product was purified as outlined in the general procedure to afford the pure product (2.44 g, 79%) as a white solid; mp 128−131 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.12 (s, 1H), 7.02 (d, 1H, J = 2.49 Hz) 6.77 (t, 1H, J = 2.21 Hz), 2.97 (s, 6 H), 1.31 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.1, 134.8, 122.1, 116.5, 114.9, 83.9, 40.5, 24.9; ^{11}B NMR (160 MHz, $CDCl_3$): δ 30.52; FT-IR (KBr): 2974, 2926, 2809, 1601, 1562, 1432, 1372, 1325, 1304, 1152, 1110, 997, 964, 876, 847, 813, 703 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{14}H_{21}BClNO_2H$ $[M + H]^+$ 282.1435, found 282.1447.

3-Chloro-*N*,*N*-dimethylaniline-5-*d*. The borylation step was carried out with 312 mg of 3-chloro-*N*,*N*-dimethylaniline (2 mmol). The borylation step was carried out neat with 512 mg of HBpin (4 mmol, 2 equiv), 16.6 mg of (Ind)Ir(cod) (0.04 mmol, 2 mol %), and 6.0 mg of dmpe (0.04 mmol, 2 mol %) at 150 °C for 18 h. The crude borylation mixture was pumped down under high vacuum and charged with 0.5 mL of D_2O and 3 mL of DME. Ac_2O (102 mg, 1 mmol, 0.5 equiv) was also added at this time. The deuteration step was then carried out at 150 °C for 2 h followed by cooling to room temperature. It was basified with 5% NaOH to pH > 10 before being extracted with CH_2Cl_2. After drying and concentration, the crude material was purified with silica gel chromatography (pentane/CH_2Cl_2 3:1) to afford 292 mg of the deuterated compound (93%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.68 (br, 2 H), 6.58 (br, 1 H), 2.93 (s, 6 H); ^{2}H NMR (76.75 MHz, pentane): δ 7.14; ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.5, 134.9, 129.6 (t, $J_{C\text{-}D}$ = 24 Hz), 116.1, 112.2, 110.4, 40.3; IR (neat): 3085, 2892, 2807, 2272, 1593, 154, 1491, 1439, 1227, 1113, 986, 972, 675 cm^{-1}; LRMS (EI): m/e 155 ($[M - H]^+$). Anal. Calcd for C_8H_9DNCl: C, 61.35; N, 8.94. Found: C, 61.09; N, 8.86.

3-Chloro-*N*,*N*-dimethylaniline-5-*d* (Alternative Procedure). The deuteration was carried out in THF and D_2O as outlined in the general procedure with 5-Bpin-3-chloro-*N*,*N*-dimethylaniline (2 mmol, 563 mg) and $[Ir(OMe)(cod)]_2$ (2 mol %, 0.04 mmol, 26.4 mg). The reaction was heated at 80 °C for 4.5 h. When the reaction was complete, it was poured into water and 1 M NaOH. The product was extracted into Et_2O, dried over $MgSO_4$, and concentrated. The crude product was purified by Kugelrohr distillation (20 mmHg/120 °C) to afford the deuterated compound as a clear, colorless oil (231 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.67−6.65 (m, 2H), 6.56 (br s, 1H), 2.93 (s, 6 H); ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.14; ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.5, 134.9 (t, $^3J_{C\text{-}D}$ = 1.8 Hz), 129.7 (t, $J_{C\text{-}D}$ = 25 Hz), 116.0, 112.2, 110.4, 40.3; LRMS (EI): m/z $[M - H]^+$ 155; HRMS (ESI+): m/z calculated for $[M + H]^+$ $[C_8H_{10}DClN]^+$ 157.0643, found 157.0645. Percent D incorporation (based on quantitative ^{13}C NMR): 95.9%.

Synthesis of 5-Bpin-3-chloroanisole.[45] The reaction was carried out neat with 3-chloro-*N*,*N*-dimethylaniline (11 mmol, 1.56 g), $[Ir(OMe)(cod)]_2$ (1 mol %, 0.11 mmol, 73 mg), dtbpy (2 mol %, 0.22 mmol, 59 mg), and HBPin (19.8 mmol, 2.5 g). The reaction was stirred at 80 °C for 16 h. The crude product was purified as outlined in the general procedure to afford the pure product (2.24 g, 76%) as a clear, colorless oil. Spectral data matched the reported data.

3-Chloroanisole-5-*d*. The borylation step was carried out neat with 288 mg of 3-chloroanisole (2 mmol) and 400 mg of HBpin (3.1 mmol, 1.55 equiv), 16.6 mg of (Ind)Ir(cod) (0.04 mmol, 2 mol %), and 6.0 mg of dmpe (0.04 mmol, 2 mol %) at 150 °C for 12 h. The crude borylation mixture was pumped down under high vacuum and charged with 0.5 mL of D_2O and 3 mL of THF. The deuteration step was then carried out at 150 °C for 1 h and worked up as described in the general procedure, after which the crude material was purified with a silica gel chromatography (CH_2Cl_2), to afford 258 mg of the deuterated compound (90%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.91 (br, 1 H), 6.88 (t, J = 2.2 Hz, 1 H), 6.77 (br, 1 H), 3.78 (s, 3 H); ^{2}H NMR (76.75 MHz, pentane): δ 7.20; ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 134.9, 129.9 (t, $J_{C\text{-}D}$ = 24 Hz), 120.7, 114.3, 112.4, 55.3; IR (neat): 3083, 3007, 2963, 2940, 2834, 1593, 1574, 1458, 1258, 1237, 1044, 679 cm^{-1}; LRMS (EI): m/e 143 (M^+). Anal. Calcd for C_7H_6DClO: C, 58.55. Found: C, 58.61.

3-Chloroanisole-5-*d* (Alternative Procedure). The deuteration was carried out in THF and D_2O as outlined in the general procedure with 5-Bpin-3-chloroanisole (5 mmol, 1.34 g), $[Ir(OMe)(cod)]_2$ (2 mol %, 0.1 mmol, 66.4 mg), and D_2O (1.25 mL). The reaction was heated at 80 °C for 3 h. When the reaction was complete, it was poured into water. The product was extracted into pentane, dried over $MgSO_4$, and concentrated. The crude product was purified by Kugelrohr distillation (25 mmHg/90 °C) to afford the deuterated compound as a clear, colorless oil (212 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.91 (br, 1H), 6.88 (t, J = 1.9 Hz, 1H), 6.77 (br, 1H), 3.78 (s, 3H); ^{2}H NMR (76.75 MHz, CH_2Cl_2): δ 7.20; ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 134.9 (t, $^3J_{C\text{-}D}$ = 1.8 Hz), 129.9 (t, $J_{C\text{-}D}$ = 25 Hz), 120.7, 114.3, 112.4, 55.4; LRMS (EI): m/z 143 (M^+); HRMS (EI): m/z calculated for $[C_7H_6DClO]^+$ 143.0248, found 143.0245. Percent D incorporation (based on quantitative ^{13}C NMR): 93.0%.

3-Bromo-5-iodophenyl Boronic Acid Pinacol Ester. The general procedure was applied to 566 mg of 1-bromo-3-iodobenzene (2.0 mmol). The borylation step was carried out with 510 mg of B_2pin_2 (2.0 mmol, 2.0 equiv of boron), 20.0 mg of $[Ir(OMe)(cod)]_2$ (0.03 mmol, 1.5 mol %), and 16.0 mg of dtbpy (0.06 mol, 3 mol %) in 4 mL of heptane in a dark environment at room temperature for 12 h. (Note: use of 2.0 equiv of high-quality HBpin could also be effective.) The reaction was carefully quenched by addition of EtOH and concentrated. The syrup was passed through a silica plug (CH_2Cl_2) to afford 700 mg of the borylated compound (86%) as a white solid; mp 88−92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 (brs, 1 H), 7.91 (t, J = 1.5 Hz, 1 H), 7.85 (brs, 1 H), 1.31 (s, 12 H); ^{11}B NMR (96 MHz, $CDCl_3$): δ 29.5; ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.0, 141.8, 136.6, 122.9, 94.6, 84.5, 24.8; IR (neat): 3058, 2980, 2930, 1537, 1429, 1399, 1372, 1337, 1269, 1167, 1142, 1113, 962, 862, 723, 698 cm^{-1}; LRMS (EI): m/e 408 (M^+), 393, 322, 309, 181, 133, 116, 101, 83, 58, 41. Anal. Calcd for $C_{12}H_{15}BrIBO_2$: C, 35.25; H, 3.70. Found: C, 35.39; H, 3.69.

1-Bromo-3-iodobenzene-5-*d*. In an air-free flask, 700 mg of 3-bromo-5-iodophenyl boronic acid pinacol ester (1.7 mmol) was charged with 55 mg of Crabtree's catalyst (0.068 mmol, 4 mol %) 0.5 mL of D_2O and 3 mL of DME. The deuteration was carried out at 150 °C for 4.5 h and worked up as described in the general procedure, after which the crude material was purified with silica gel chromatography (pentane), to afford 267 mg of the deuterated compound (55%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (t, J = 1.8 Hz, 1 H), 7.61 (br, 1 H), 7.45 (br, 1 H), a small peak at 6.95 (t, J = 8.0 Hz) was also present due to

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nondeuterated 5-position; ^{2}H NMR (76.75 MHz, pentane): δ 6.97; ^{13}C NMR (125 MHz, $CDCl_3$): δ 139.8, 136.0, 131.0 (t, $J_{C\text{-}D}$ = 25 Hz), 130.7, 123.1, 94.5; IR (neat): 3063, 1549, 1416, 1391, 1105, 864, 700, 673 cm^{-1}; LRMS (EI): m/e 283 (M^+), 156, 77. HRMS (EI) m/e calcd for $[C_7H_6DClO]^+$ 282.8604, found 282.8612.

Example of Calculating D% Incorporation. A GC-MS spectrum for the nondeuterated 1,2-dichlorobenzene was first recorded. The peak intensities for [M − H], M, and [M + H] were observed as such: 145 (M − H), 4.43%; 146 (M), 100%; 147 (M + H), 12.8%. Therefore, a ratio of [M − H]:M:[M + H] = 4.43:100:12.8 was obtained. We *assume* that this ratio also applies for 1,2-dichlorobenzene-d_1 (this assumption is true unless the M − H signal in the d_0 compound is due to the loss of the specific H that has been replaced by D). Thus, for 1,2-dichlorobenzene-d_1, we should expect a ratio of peak intensities for 146:147:148 to be also 4.43:100:12.8.

Next, a GC-MS spectrum of 1,2-dichlorobenzene (a mixture of d_0 and d_1 compounds) was recorded. The peak intensities were observed as such: 146 (M − H), 6.44%; 147 (M), 100%. If 1,2-dichlorobenzene is a mixture of x% d_0 compound and y% d_1 compound, then $x + y = 100$.

At the same time, consider that the peak 146 in the mass spectrum of 1,2-dichlorobenzene consists of two parts: the contributions from the d_0 and d_1 compounds, respectively. We assume that the peak intensities for [M − H]:M:[M + H] as 4.43:100:12.8 hold for both d_0 and d_1 compounds. Thus, for x% d_0 (M = 146), the contribution to the peak 146 (M) in the mass spectrum of 1,2-dichlorobenze is 100x, where the number 100 is the relative peak intensity for [M]. Likewise, for y% d_1 (M = 147), the contribution to the peak 146 (M − H) in the mass spectrum of 1,2-dichlorobenzene is 4.43y, where the number 4.43 is the relative peak intensity for [M − H]. Therefore, the intensity of 146 for 1,2-dichlorobenzene can be viewed as (100x + 4.43y). Similarly, the intensity of 147 for 1,2-dichlorobenzene can be viewed as (12.8x + 100y). Thus, the ratio of 146:147 can be rewritten as (100x + 4.43y)/(12.8x + 100y), which is 6.44:100 by experiment. So,

$$\frac{100x + 4.43y}{12.8x + 100y} = 0.0644$$

On the basis of these two equations, one can obtain the values of x = 2 and y = 98. Therefore, 1,2-dichlorobenzene is 98% d_1 compound.

Determination of Deuterium Incorporation by Quantitative ^{13}C NMR. The data were collected on an NMR spectrometer operating at 499.955 MHz. Each sample was prepared as 0.671 M in $CDCl_3$ (5.17 × 10^{-4} mol in 770 μL). In order to ensure that the ^{13}C experiments were quantitative, the longest T_1 was estimated using an inversion recovery experiment. The experiment was run using 1,2,3-trichlorobenzene-5-*d* with the delay set to give a null signal for the carbon with the longest T_1. The longest T_1 was 1.41 times that delay value. This gave an approximate T_1 of 41 s.

The percentage of deuterium incorporation was determined by quantitative ^{13}C NMR using an inverse gated experiment, in which decoupling is only on during acquisition. All experiments were run with 292 scans using a 3 min recycle delay (approximately 5 × T_1). Exponential multiplication with a line broadening factor of 0.5 Hz was used for all experiments. The number of scans used was such that a signal-to-noise ratio around the peak of interest was 100:1, and the digital resolution was set to give at least 5 points above the half height of the peak.

The percentage of deuterium incorporation was determined from the ^{13}C spectra by integration of the peaks corresponding to the C−D and the C−H impurity. Calculating the percentage from the integrals of the peaks of interest gave the percentage of deuterium incorporation.

Table 3, Entry 1. Synthesis of 2,7-Bis(Bpin)-3-methylindole. The general procedure for borylation was applied to 3-methylindole (393 mg, 3 mmol, 1 equiv), $[Ir(OMe)(cod)]_2$ (60 mg, 0.09 mmol, 6 mol % Ir), dtbpy (48 mg, 0.18 mmol, 6 mol %), and B_2pin_2 (838 mg, 3.30 mmol, 1.1 equiv) in cyclohexane at 60 °C for 18 h. Column chromatography (50% dichloromethane/hexanes, R_f 0.8) furnished the diborylated product as a pale yellow solid (902 mg, 79% yield, mp 122−124 °C). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.10 (s, 1 H), 7.76−7.70 (m, 2 H), 7.11 (dd, J = 7.8, 6.8 Hz, 1 H), 2.56 (s, 3 H), 1.41 (s, 12 H), 1.38 (s, 12 H); ^{13}C NMR {^{1}H} ($CDCl_3$, 125 MHz): δ 142.9, 131.2, 127.9, 124.2, 123.3, 118.4, 83.7, 83.5, 24.95, 24.88, 10.0; ^{11}B NMR ($CDCl_3$, 96 MHz): δ 29.4; FT-IR (neat) $\tilde{\nu}_{max}$: 3458, 2979, 2931, 1599, 1554, 1416, 1369, 1319, 1282, 1264, 1140, 1104, 841, 682 cm^{-1}; HRMS (ESI+): (m/z) calculated for $[M + H]^+$ $[C_{21}H_{32}B_2NO_4]^+$ 384.2517, found 384.2520.

Table 3, Entry 1. Deborylation of 2,7-Bis(Bpin)-3-methylindole.[33] Deborylation of this substrate was particularly sensitive to the quality of the MeOH used. 3-Methyl-2,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (0.5 mmol, 191.5 mg) was weighed in air into a 10 mL microscale round-bottom flask equipped with a stir bar. A 1.0 mL aliquot of freshly collected dry dichloromethane was withdrawn from the still head with an oven-dried needle and syringe. The dichloromethane was added into the flask while stirring open to air, and the starting material was completely dissolved. Anhydrous, high purity grade methanol was added into the reaction flask while stirring and open to air. $[Ir(OMe)(cod)]_2$ (5 mg, 1.5 mol %) was weighed on weigh paper in air and added to the flask as a solid. A reflux condenser was fitted with an argon inlet and attached to the flask. The flask was heated under positive pressure of argon in a 60 °C oil bath for 45 min. The reaction was light yellow and homogeneous. As the reaction stirred in the oil bath, the color darkened to brown. The reaction was concentrated to a dark brown oil by rotary evaporation, and crude NMR was taken.

The crude NMR indicated 80% of the desired monodeborylation product, 3-methyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole, 10% diborylated starting material, and 10% unborylated 3-methylindole were present. Column chromatography (10% ethyl acetate/hexanes, R_f 0.40−0.45) furnished the product as a white solid (116 mg, 68% yield, mp = 71−72 °C). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.93 (s, 1H), 7.69 (dd, J = 7.8, 1.0 Hz, 1 H), 7.63 (dd, J = 7.1, 1.0 Hz, 1 H), 7.11 (dd, J = 7.8, 7.1 Hz, 1 H), 7.00 (m, 1 H), 2.33 (d, J = 1.2 Hz, 3 H), 1.38 (s, 12 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 141.4, 129.1, 127.2, 122.3, 121.5, 118.5, 111.0, 83.7, 25.0, 9.6; ^{11}B NMR ($CDCl_3$, 96 MHz) δ 31.6; FT-IR (neat) $\tilde{\nu}_{max}$: 3463, 2977, 2926, 2864, 1607, 1593, 1491, 1437, 1372, 1325, 1291, 1204, 1136, 1105, 1047, 966, 849, 752, 683 cm^{-1}; HRMS (ESI+): (m/z) calculated for $[C_{15}H_{21}BNO_2]^+$ 258.1665, found 258.1668.

Table 3, Entry 2. Synthesis of 2,7-Bis(Bpin)-4-cyanoindole.[46] The general procedure for borylation was applied to 4-cyanoindole (142 mg, 1 mmol, 1 equiv), $[Ir(OMe)(cod)]_2$ (10 mg, 0.015 mmol, 3 mol % Ir), dtbpy (8 mg, 0.03 mmol, 3 mol %), and B_2pin_2 (318 mg, 1.25 mmol, 1.25 equiv) in hexane at 60 °C for 16 h. The crude reaction mixture was passed through a plug of silica gel eluting with CH_2Cl_2 to afford the diborylated product as an off white solid (366 mg, 93% yield, mp 158−160 °C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.50 (s, 1 H), 7.67 (d, J = 7.3 Hz, 1 H), 7.42 (d, J = 7.3 Hz, 1 H), 7.29 (d, J = 2.0 Hz, 1 H), 1.40 (s, 12 H), 1.37 (s, 12 H); ^{13}C NMR {^{1}H} ($CDCl_3$, 125 MHz): δ 142.6, 129.9, 128.1, 124.4, 118.4, 112.0, 106.4, 85.5, 84.5, 24.9, 24.8; ^{11}B NMR ($CDCl_3$, 96 MHz): δ 29.8; FT-IR (neat) $\tilde{\nu}_{max}$: 3445, 2980, 2936, 2218, 1545, 1373, 1332, 1296, 1142, 972, 852, 775, 704, 680 cm^{-1}; HRMS (EI +): (m/z) calculated for $[M + H]^+$ $[C_{21}H_{28}B_2N_2O_4]^+$ 394.2235, found 394.2234.

Table 3, Entry 2. Deborylation of 2,7-Bis(Bpin)-4-cyanoindole.[33] The general procedure for deborylation was applied to the diborylated compound (197 mg, 0.50 mmol, 1 equiv) and $[Ir(OMe)(cod)]_2$ (5 mg, 0.0075 mmol, 3 mol % Ir) at 55 °C for 1 h. A silica plug was run with CH_2Cl_2, and the product was isolated as a pale yellow solid (114 mg, 85% yield, mp 146−148 °C). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.44 (s, 1H), 7.63 (d, J = 7.3 Hz, 1 H), 7.45 (d, J = 7.3 Hz, 1 H), 7.41 (dd, J = 3.2, 2.4 Hz, 1 H), 6.74 (dd, J = 3.2, 2.4 Hz, 1 H), 1.39 (s, 12 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 140.6, 128.3, 128.1, 126.8, 124.2, 118.7, 105.7, 101.1, 84.5, 24.9; ^{11}B NMR ($CDCl_3$, 96 MHz) δ 31.2; FT-IR (neat) $\tilde{\nu}_{max}$: 3389, 2980, 2228, 1603, 1508, 1401, 1373, 1337, 1310, 1207, 1142, 1109, 1080, 968, 887, 851, 822, 741, 681 cm^{-1}; HRMS (ESI +): (m/z) calculated for $[C_{15}H_{18}BN_2O_2]^+$ 269.1461, found 269.1462.

Table 3, Entry 3. Synthesis of 2,7-Bis(Bpin)-5-bromoindole. The general procedure for borylation was applied to 5-bromoindole (392 mg, 2 mmol, 1 equiv), $[Ir(OMe)(cod)]_2$ (40 mg, 0.06 mmol, 6 mol % Ir), dtbpy (32 mg, 0.12 mmol, 6 mol %), and B_2pin_2 (635 mg, 2.50 mmol, 1.25 equiv) in cyclohexane at 60 °C for 15 h. The crude reaction

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mixture was passed through a plug of silica gel eluting with CH_2Cl_2. The volatiles were removed to afford the diborylated product as an off-white solid (838 mg, 94% yield, mp 138−140 °C). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.30 (s, 1 H), 7.87 (d, J = 2.2 Hz, 1 H), 7.75 (d, J = 2.0 Hz, 1 H), 7.02 (d, J = 2.0 Hz, 1 H), 1.39 (s, 12 H), 1.36 (s, 12 H); ^{13}C NMR {^{1}H} ($CDCl_3$, 125 MHz): δ 141.6, 133.3, 129.2, 127.1, 113.0, 112.9, 84.21, 84.20, 24.9, 24.8; ^{11}B NMR ($CDCl_3$, 96 MHz): δ 29.3; FT-IR (neat) $\tilde{\nu}_{max}$: 3449, 2980, 2923, 1590, 1546, 1417, 1361, 1317, 1299, 1258, 1142, 970, 872, 852, 734, 701 cm^{-1}; HRMS (ESI+): (m/z) calculated for $[M + H]^+$ $[C_{20}H_{29}B_2BrNO_4]^+$ 448.1466, found 448.1472.

Table 3, Entry 3. Deborylation of 2,7-Bis(Bpin)-5-bromoindole.[33] The general procedure for deborylation was applied to the diborylated compound (224 mg, 0.50 mmol, 1 equiv) and $[Ir(OMe)(cod)]_2$ (5 mg, 0.0075 mmol, 3 mol % Ir) at 55 °C for 1 h 45 min. Column chromatography (50% dichloromethane/hexanes, R_f 0.7) furnished the desired product as an off-white solid (134 mg, 83% yield, mp 130−132 °C). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.19 (s, 1H), 7.85 (d, J = 1.7 Hz, 1 H), 7.71 (d, J = 1.9 Hz, 1 H), 7.25−7.23 (m, 1 H), 6.47−6.46 (m, 1 H), 1.38 (s, 12 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 139.5, 131.4, 128.8, 126.4, 125.3, 112.9, 101.6, 84.2, 24.9; ^{11}B NMR ($CDCl_3$, 96 MHz) δ 30.9; FT-IR (neat) $\tilde{\nu}_{max}$: 3447, 2978, 1599, 1507, 1454, 1420, 1391, 1368, 1327, 1310, 1294, 1273, 1181, 1167, 1142, 978, 864, 847, 731, 689, 677 cm^{-1}; HRMS (ESI+): (m/z) calculated for $[C_{14}H_{18}BBrNO_2]^+$ 322.0614, found 322.0617.

Table 3, Entry 4: Deborylation of 2,7-Bis(Bpin)-Boc-L-tryptophan Methyl Ester.[21] The general procedure for deborylation was applied to the diborylated compound (150 mg, 0.26 mmol, 1 equiv) and $[Ir(OMe)(cod)]_2$ (2.6 mg, 0.0039 mmol, 3 mol % Ir) at rt for 2 h. Column chromatography (20% ethyl acetate/hexanes, R_f 0.4) furnished the product as a white solid (67 mg, 58% yield, mp 177−179 °C). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.12 (s, 1 H), 7.66 (d, J = 8.1 Hz, 1 H), 7.63 (d, J = 7.1 Hz, 1 H), 7.11 (dd, J = 7.8, 7.1 Hz, 1 H), 7.04 (s, 1 H), 5.05 (d, J = 7.8 Hz, 1 H), 4.63−4.61 (m, 1 H), 3.66 (s, 3 H), 3.29 (d, J = 4.9 Hz, 2 H), 1.41 (s, 9 H), 1.37 (s, 12 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.7, 155.2, 141.3, 129.5, 126.6, 122.7, 122.3, 119.1, 109.6, 83.8, 79.7, 54.2, 52.2, 28.3, 27.9, 24.9; ^{11}B NMR ($CDCl_3$, 96 MHz) δ 30.6; FT-IR (neat) $\tilde{\nu}_{max}$: 3453, 2981, 2919, 2853, 2252, 1742, 1708, 1599, 1492, 1437, 1373, 1331, 1167, 1135, 799, 735 cm^{-1}; $[\alpha]^{20}_D$ + 39.3 (c 1.0, $CHCl_3$); HRMS (ESI+): (m/z) calculated for $[C_{23}H_{34}BN_2O_6]^+$ 445.2510, found 445.2519.

Table 3, Entry 5: Deborylation of *N*-Boc-3,5-bis(Bpin)-7-azaindole. The general procedure for deborylation was applied to the diborylated compound (235 mg, 0.50 mmol, 1 equiv) and $[Ir(OMe)(cod)]_2$ (5 mg, 0.0075 mmol, 3 mol % Ir) at 55 °C for 4 h. Column chromatography (10% ether/dichloromethane, R_f 0.4) furnished the product as a white solid (84 mg, 49% yield, mp 95−98 °C). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.82 (d, J = 1.5 Hz, 1 H), 8.26 (d, J = 1.7 Hz, 1 H), 7.58 (d, J = 4.2 Hz, 1 H), 6.46 (d, J = 4.2 Hz, 1 H), 1.64 (s, 9 H), 1.33 (s, 12 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 151.3, 149.9, 147.8, 135.9, 126.4, 122.4, 104.7, 84.0, 83.9, 28.1, 24.8; ^{11}B NMR ($CDCl_3$, 96 MHz) δ 31.2; FT-IR (neat) $\tilde{\nu}_{max}$: 2980, 2935, 1759, 1733, 1606, 1562, 1535, 1478, 1358, 1319, 1251, 1150, 1102, 1028, 968, 856, 770, 734, 685 cm^{-1}; HRMS (ESI+): (m/z) calculated for $[C_{18}H_{26}BN_2O_4]^+$ 345.1986, found 345.1985.

Table 3, Entry 6: One-Pot Synthesis of 2-Cyano-3-Bpin-thiophene.[47] The general procedure for one-pot diborylation/deborylation was applied to 2-cyanothiophene (93 μL, 109 mg, 1.00 mmol, 1.00 equiv). The diborylation step was carried out with HBPin (363 μL, 320 mg, 2.50 mmol, 2.50 equiv) for 4 h. The deborylation step was carried out for 5.5 h. Column chromatography (20% ethyl acetate/hexanes, R_f 0.6) furnished the product as a pale yellow solid (178 mg, 75% yield, mp 64−66 °C). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.53 (d, J = 4.9 Hz, 1 H), 7.37 (d, J = 4.9 Hz, 1 H), 1.34 (s, 12 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 133.3, 131.5, 118.0, 114.3, 84.7, 24.8; ^{11}B NMR ($CDCl_3$, 96 MHz) δ 28.8; FT-IR (neat) $\tilde{\nu}_{max}$: 2980, 2939, 2220, 1520, 1402, 1381, 1373, 1314, 1271, 1140, 986, 908, 853, 841, 752, 691 cm^{-1}; HRMS (ESI +): (m/z) calculated for $[M + H]^+$ $[C_{11}H_{15}BNO_2S]^+$ 236.0917, found 236.0923.

Table 3, Entry 7: One-Pot Synthesis of 2-Bromo-3-Bpin-thiophene. The general procedure for one-pot diborylation/deborylation was applied to 2-bromothiophene (194 μL, 326 mg, 2.00 mmol, 1.00 equiv). The diborylation step was carried out with HBPin (870 μL, 768 mg, 6.00 mmol, 3.00 equiv) for 22 h. The deborylation step was carried out for 10 h. A silica plug with CH_2Cl_2 afforded the product as a pale yellow solid (460 mg, 80% yield, mp 48−50 °C). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.17 (d, J = 5.4 Hz, 1 H), 7.12 (d, J = 5.4 Hz, 1 H), 1.32 (s, 12 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 133.3, 126.2, 122.5, 83.8, 24.8; ^{11}B NMR ($CDCl_3$, 96 MHz) δ 29.5; FT-IR (neat) $\tilde{\nu}_{max}$: 3104, 2978, 2930, 1524, 1428, 1415, 1388, 1366, 1306, 1272, 1140, 965, 896, 853, 675 cm^{-1}; HRMS (APCI+): (m/z) calculated for $[C_{10}H_{15}BBrO_2S]^+$ 289.0069, found 289.0065.

Table 3, Entry 8: One-Pot Synthesis of 2-Methyl-3-Bpin-thiophene.[48] The general procedure for one-pot diborylation/deborylation was applied to 2-methylthiophene (194 μL, 196 mg, 2.00 mmol, 1.00 equiv). The diborylation step was carried out with HBPin (870 μL, 768 mg, 6.00 mmol, 3.00 equiv) for 48 h. The deborylation step was carried out for 5 h. Column chromatography (50% dichloromethane/hexanes, R_f 0.5) furnished the product as a colorless oil (325 mg, 72% yield). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.20 (d, J = 5.1 Hz, 1 H), 7.02 (d, J = 5.1 Hz, 1 H), 2.69 (s, 3 H), 1.31 (s, 12 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.5, 133.1, 121.9, 83.1, 24.9, 15.6; ^{11}B NMR ($CDCl_3$, 96 MHz) δ 29.8; FT-IR (neat) $\tilde{\nu}_{max}$: 2978, 2926, 1536, 1435, 1414, 1389, 1372, 1314, 1302, 1273, 1215, 1165, 1146, 1086, 1024, 963, 870, 679 cm^{-1}; HRMS (ESI+): (m/z) calculated for [M + H]+ $[C_{11}H_{18}BO_2S]^+$ 225.1121, found 225.1118.

Table 3, Entry 9: Synthesis of 3,5-Bis(Bpin)-2-chlorothiophene. The general procedure for borylation was applied to 2-chlorothiophene (3.9 mL, 5 g, 42 mmol, 1 equiv), $[Ir(OMe)(cod)]_2$ (560 mg, 0.84 mmol, 4 mol % Ir), dtbpy (452 mg, 1.68 mmol, 4 mol %), and HBPin (18.4 mL, 16.2 g, 126 mmol, 3.00 equiv) in pentane at rt for 60 h. The crude reaction mixture was passed through a plug of silica gel eluting with CH_2Cl_2 to afford the diborylated product as a white solid (14.8 g, 95% yield, mp 129−131 °C). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.72 (s, 1 H), 1.30 (s, 12 H), 1.29 (s, 12 H); ^{13}C NMR {^{1}H} ($CDCl_3$, 125 MHz): δ 146.3, 143.6, 84.2, 83.8, 24.8, 24.7; ^{11}B NMR ($CDCl_3$, 96 MHz): δ 29.0; FT-IR (neat) $\tilde{\nu}_{max}$: 2976, 2928, 1539, 1456, 1371, 1340, 1309, 1140, 1042, 964, 851, 665 cm^{-1}; Anal. Calcd for $C_{16}H_{25}B_2ClO_4S$: C, 51.87; H, 6.80; Found: C, 51.69; H, 7.00.

Table 3, Entry 9: Deborylation of 3,5-Bis(Bpin)-2-chlorothiophene. The general procedure for deborylation was applied to the diborylated compound (185 mg, 0.50 mmol, 1 equiv) and $[Ir(OMe)(cod)]_2$ (5 mg, 0.0075 mmol, 3 mol % Ir) at 55 °C for 0.5 h. The crude reaction mixture was passed through a plug of silica gel eluting with CH_2Cl_2 to afford the product as an off-white solid (73 mg, 60% yield, mp 27−29 °C). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.13 (d, J = 5.6 Hz, 1 H), 7.03 (d, J = 5.6 Hz, 1 H), 1.32 (s, 12 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 140.1, 132.4, 123.3, 83.8, 24.8; ^{11}B NMR ($CDCl_3$, 96 MHz) δ 28.5; FT-IR (neat) $\tilde{\nu}_{max}$: 2980, 2939, 1528, 1431, 1420, 1391, 1372, 1310, 1273, 1213, 1167, 1142, 1088, 1024, 966, 899, 855, 833, 745, 675 cm^{-1}; HRMS (APCI+): (m/z) calculated for $[C_{10}H_{15}BClO_2S]^+$ 245.0574, found 245.0578.

Table 3, Entry 10: Synthesis of 2,5-Bis(Bpin)-3-cyanothiophene.[49] The general procedure for borylation was applied to 3-cyanothiophene (4.16 mL, 5 g, 46 mmol, 1 equiv), $[Ir(OMe)(cod)]_2$ (455 mg, 0.69 mmol, 3 mol % Ir), dtbpy (369 mg, 1.38 mmol, 3 mol %), and HBPin (16.6 mL, 14.7 g, 115 mmol, 2.50 equiv) in pentane at rt for 1.5 h. The crude reaction mixture was passed through a plug of silica gel eluting with CH_2Cl_2 to afford the diborylated product as a white solid (16.2 g, 98% yield, mp 138−140 °C). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.80 (s, 1 H), 1.34 (s, 12 H), 1.31 (s, 12 H); ^{13}C NMR {^{1}H} ($CDCl_3$, 125 MHz): δ 140.3, 118.8, 115.2, 85.1, 84.8, 24.7; ^{11}B NMR ($CDCl_3$, 96 MHz): δ 28.8; FT-IR (neat) $\tilde{\nu}_{max}$: 2980, 2936, 2230, 1525, 1373, 1269, 1138, 1055, 962, 850, 667 cm^{-1}; HRMS (FAB+): (m/z) calculated for $C_{17}H_{26}B_2NO_4S$: 362.1768, found 362.1778.

Table 3, Entry 10: Deborylation of 2,5-Bis(Bpin)-3-cyanothiophene.[16] The general procedure for deborylation was applied to the diborylated compound (361 mg, 1.00 mmol, 1 equiv) and $[Ir(OMe)(cod)]_2$ (10 mg, 0.015 mmol, 3 mol % Ir) at 55 °C for 5 h. The crude reaction mixture was passed through a plug of silica gel eluting with CH_2Cl_2. The volatiles were removed to afford the plug

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product. The plug product was washed with cold hexanes to furnish the product as a white solid (137 mg, 58% yield, mp 90−92 °C). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.13 (d, J = 1.2 Hz, 1 H), 7.75 (d, J = 1.2 Hz, 1 H), 1.32 (s, 12 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 141.0, 138.2, 114.9, 111.8, 84.8, 24.7; ^{11}B NMR ($CDCl_3$, 96 MHz) δ 28.1; FT-IR (neat) $\tilde{\nu}_{max}$: 3100, 2979, 2931, 2227, 1542, 1437, 1386, 1355, 1303, 1264, 1138, 1025, 960, 880, 849, 661; cm^{-1}; HRMS (ESI+): (m/z) calculated for $[M + H]^+$ $[C_{11}H_{15}BNO_2S]^+$ 236.0917, found 236.0921.

Monoborylation of Clopidogrel (2). The general procedure for borylation was applied to clopidogrel (161 mg, 0.50 mmol, 1 equiv), $[Ir(OMe)(cod)]_2$ (5 mg, 0.0075 mmol, 3 mol % Ir), dtbpy (4 mg, 0.015 mmol, 3 mol %), and HBPin (109 mL, 96 mg, 0.75 mmol, 1.50 equiv) in methyl *tert*-butyl ether at rt for 1 h 15 min. Column chromatography (5% ether/dichloromethane, R_f 0.6) furnished the product **2** as a sticky yellow precipitate (126 mg, 56% yield). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.66−7.64 (m, 1 H), 7.39−7.37 (m, 1 H), 7.28−7.22 (m, 2 H), 7.20 (s, 1 H), 4.89 (s, 1 H), 3.74 (d, J = 14.2 Hz, 1 H), 3.70 (s, 3 H), 3.63 (d, J = 14.2 Hz, 1 H), 2.89−2.85 (m, 4 H), 1.29 (s, 12 H); ^{13}C NMR {^{1}H} ($CDCl_3$, 125 MHz): δ 171.3, 141.2, 135.6, 135.0, 134.7, 133.9, 129.9, 129.8, 129.4, 127.1, 83.9, 67.7, 52.1, 50.5, 47.9, 25.9, 24.7; ^{11}B NMR ($CDCl_3$, 96 MHz): δ 28.9; FT-IR (neat) $\tilde{\nu}_{max}$: 2978, 2950, 1752, 1478, 1378, 1333, 1267, 1214, 1167, 1143, 1037, 1014, 997, 853, 755, 732 cm^{-1}; $[\alpha]^{20}_D$ +28.0 (c 1.0, $CHCl_3$); HRMS (ESI+): (m/z) calculated for $[C_{22}H_{28}BClNO_4S]^+$ 448.1521, found 448.1523.

Deuterodeborylation of Monoborylated Clopidogrel.[50] The general procedure for deborylation was applied to compound **2** (112 mg, 0.25 mmol, 1 equiv) and $[Ir(OMe)(cod)]_2$ (5 mg, 0.0075 mmol, 6 mol % Ir) in 1.25 mL of $CD_3OD/CDCl_3$ (2:1) at 55 °C for 2 h 30 min. Column chromatography (5% ether/dichloromethane, R_f 0.7) furnished the product as a thick pale yellow oil (65 mg, 81% yield, 92% D-incorporation). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.69−7.66 (m, 1 H), 7.40−7.37 (m, 1 H), 7.28−7.23 (m, 2 H), 6.65 (s, 1 H), 4.89 (s, 1 H), 3.74 (d, J = 14.2 Hz, 1 H), 3.70 (s, 3 H), 3.61 (d, J = 14.4 Hz, 1 H), 2.89−2.85 (m, 4 H); ^{13}C NMR {^{1}H} ($CDCl_3$, 125 MHz): δ 171.3, 134.6, 133.8, 133.2, 133.1, 129.9, 129.7, 129.4, 127.1, 125.0, 67.8, 52.1, 50.6, 48.2, 25.6, 25.5; FT-IR (neat) $\tilde{\nu}_{max}$: 2949, 2921, 2846, 2815, 1741, 1470, 1434, 1260, 1227, 1200, 1166, 1029, 755 cm^{-1}; $[\alpha]^{20}_D$ +42.2 (c 0.7, $CHCl_3$); HRMS (ESI+): (m/z) calculated for $[C_{16}{}^1H_{16}{}^2H\ ClNO_2S]^+$ 323.0731, found 323.0734.

Diborylation of Clopidogrel. The general procedure for borylation was applied to clopidogrel (322 mg, 1.00 mmol, 1 equiv), $[Ir(OMe)(cod)]_2$ (20 mg, 0.03 mmol, 6 mol % Ir), dtbpy (16 mg, 0.06 mmol, 6 mol %), and HBPin (435 mL, 384 mg, 3.00 mmol, 3.00 equiv) in methyl *tert*-butyl ether at rt for 30 h. Column chromatography (15% ether/dichloromethane, R_f 0.4) furnished the product as a pale yellow solid in a 1:1 mixture of **3a** and **3b** (441 mg, 77% yield, mp 72−80 °C). ^{1}H NMR ($CDCl_3$, 500 MHz): **3a** δ 7.99 (d, J = 1.5 Hz, 1 H), 7.69−7.64 (m, 1 H), 7.37 (d, J = 7.8 Hz, 1 H), 7.21 (s, 1 H), 4.92 (s, 1 H), 3.74 (d, J = 14.2 Hz, 1 H), 3.70 (s, 3 H), 3.63 (d, J = 14.2 Hz, 1 H), 2.88−2.84 (m, 4 H), 1.30 (s, 12 H), 1.29 (s, 12 H); **3b** δ 7.81 (s, 1 H), 7.69−7.64 (m, 2 H), 7.19 (s, 1 H), 4.90 (s, 1 H), 3.76 (d, J = 14.2 Hz, 1 H), 3.68 (s, 3 H), 3.61 (d, J = 14.2 Hz, 1 H), 2.88−2.84 (m, 4 H), 1.32 (s, 12 H), 1.29 (s, 12 H); ^{13}C NMR {^{1}H} ($CDCl_3$, 125 MHz): **3a** δ 171.3, 141.3, 137.9, 136.2, 135.7, 135.1, 133.1, 129.2, 84.0, 83.8, 67.6, 52.1, 50.5, 47.7, 24.86, 24.85, 24.83, 24.7; **3b** δ 171.1, 141.2, 135.8, 135.6, 134.9, 134.5, 133.1, 129.3, 84.2, 83.9, 67.8, 52.1, 50.6, 47.9, 25.9, 24.82, 24.79, 24.7; ^{11}B NMR ($CDCl_3$, 96 MHz): δ 28.6; FT-IR (neat) $\tilde{\nu}_{max}$: 2979, 2931, 1744, 1479, 1382, 1357, 1327, 1271, 1166, 1144, 1107, 1014, 855, 733 cm^{-1}; $[\alpha]^{20}_D$ +31.3 (c 1.0, $CHCl_3$); HRMS (ESI+): (m/z) calculated for $[C_{28}H_{39}B_2ClNO_6S]^+$ 574.2373, found 574.2381.

Monodeborylation of Diborylated Clopidogrel. The general procedure for deborylation was applied to the diborylated compounds (144 mg, 0.25 mmol, 1 equiv) and $[Ir(OMe)(cod)]_2$ (5 mg, 0.0075 mmol, 6 mol % Ir) at 55 °C for 5 h. Column chromatography (15% ether/dichloromethane, R_f 0.6) furnished the product as a sticky yellow precipitate in a 1:1 mixture of **4a** and **4b** (89 mg, 80% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): **4a** δ 8.03 (d, J = 1.5 Hz, 1 H), 7.66 (dd, J = 7.8, 1.5 Hz, 1 H), 7.38 (d, J = 8.1 Hz, 1 H), 7.04 (d, J = 5.1 Hz, 1 H), 6.66 (d, J = 5.1 Hz, 1 H), 4.91 (s, 1 H), 3.80−3.72 (m, 1 H), 3.71 (s, 3 H), 3.66−3.58 (m, 1 H), 2.88−2.85 (m, 4 H), 1.30 (s, 12 H); **4b** δ 7.82 (s, 1 H), 7.68−7.64 (m, 2 H), 7.03 (d, J = 5.1 Hz, 1 H), 6.64 (d, J = 5.1 Hz, 1 H), 4.90 (s, 1 H), 3.80−3.72 (m, 1 H), 3.69 (s, 3 H), 3.66−3.58 (m, 1 H), 2.88−2.85 (m, 4 H), 1.32 (s, 12 H); ^{13}C NMR {^{1}H} ($CDCl_3$, 125 MHz): **4a** δ 171.3, 137.9, 136.2, 135.6, 133.4, 133.3, 133.1, 129.2, 125.3, 122.6, 84.0, 67.7, 52.1, 50.7, 48.0, 24.87, 24.85; **4b** δ 171.1, 136.5, 135.8, 134.5, 133.25, 133.21, 133.17, 129.4, 125.2, 122.7, 84.2, 67.9, 52.1, 50.7, 48.3, 24.83, 24.79; ^{11}B NMR ($CDCl_3$, 96 MHz): δ 29.9; FT-IR (neat) $\tilde{\nu}_{max}$: 2985, 2950, 2930, 1744, 1604, 1435, 1386, 1357, 1331, 1204, 1167, 1145, 964, 858, 736, 703, 681 cm^{-1}; $[\alpha]^{20}_D$ +67.0 (c 0.7, $CHCl_3$); HRMS (ESI+): (m/z) calculated for $[C_{22}H_{28}BClNO_4S]^+$ 448.1521, found 448.1525.

Protodeborylation of 5-Bpin-3-chloro-*N*,*N*-dimethylaniline Using CsF.[8] Using the reaction conditions reported by Aggarwal and co-workers, 5-Bpin-3-chloro-*N*,*N*-dimethylaniline (1 mmol, 281 mg), CsF (1.5 mmol, 228 mg), and water (1.1 mmol, 20 mL) were combined in dry 1,4-dioxane (10 mL) in an air-free flask under N_2. The reaction was sealed and stirred at 45 °C for 48 h. The reaction was monitored by GC/MS. No reaction was observed, and the starting material was left unchanged.

Protodeborylation of 5-Bpin-3-chloro-*N*,*N*-dimethylaniline Using TBAF.[8] Using the reaction conditions reported by Aggarwal and co-workers, two reactions were set up using 5-Bpin-3-chloro-*N*,*N*-dimethylaniline (0.25 mmol, 70 mg), TBAF·3H_2O (0.375 mmol, 118 mg), and either pentane (2.5 mL) or toluene (2.5 mL) as the solvent in an air-free flask under N_2. The reactions stirred at 45 °C for 24 h. GC/FID showed trace conversion for the reaction in toluene, but no reaction for the one in pentane. The temperature was then increased to 60 °C, and the reaction was stirred an additional 24 h. GC/FID and GC/MS showed no change.

Base-Promoted Protodeborylation of 4-Bpin-2,6-dichloropyridine.[9] Using the reaction conditions reported by Perrin and co-workers, 4-Bpin-2,6-dichloropyridine (0.1 mmol, 27.4 mg) was dissolved in THF (5 mL). A basic solution of KOH (200 mM, 5 mL) was added, and the reaction was stirred at room temperature for 24 h. The reaction was monitored by GC/FID, but no reaction was observed. The starting material was left unchanged.

Protodeborylation of 2,7-Bis(Bpin)-3-methylindole Using Trifluoroacetic Acid (No Catalyst).[21] Under a N_2 atmosphere, a 10 mL Schlenk flask was charged with 2,7-bis(Bpin)-3-methylindole (0.297 mmol, 113.8 mg). Dry dichloromethane (2 mL) was added via syringe, and the solution was cooled in an ice bath to 0 °C. Trifluoroacetic acid (3 mL) was added dropwise to the cooled solution. Upon completion of the trifluoroacetic acid addition, the reaction was stirred at 0 °C for a further 10 min. Then, the ice bath was removed, and the reaction was allowed to stir at room temperature. After 3 h, the reaction was diluted with dichloromethane (50 mL) and washed with saturated sodium bicarbonate solution (50 mL). The organic layer was dried over $MgSO_4$, and the solution was concentrated. ^{1}H NMR was acquired for the resulting orange/brown oil. At least four products were observed in the spectrum. They are proposed to be 3-methylindole, 7-Bpin-3-methylindole, 2-Bpin-3-methylindole, and 2,7-bis(Bpin)-3-methylindole. However, there are an additional four species with apparent NH peaks that could not be identified.

Protodeborylation of 4-Bpin-2,6-dichloropyridine Using Trifluoroacetic Acid (No Catalyst).[21] Under a N_2 atmosphere, a 10 mL Schlenk flask was charged with 4-Bpin-2,6-dichloropyridine (0.297 mmol, 82.5 mg). It was dissolved in dry dichloromethane and cooled in an ice bath to 0 °C. Trifluoroacetic acid was added via syringe slowly over a few minutes. Once all of the TFA had been added, the reaction was allowed to stir an additional 10 min at 0 °C. Then, the ice bath was removed and the reaction was allowed to come to room temperature. It was monitored by ^{1}H NMR for 18 h, but no reaction was observed. The starting material was left unchanged.

One-Pot Borylation/Deborylation of 3-Methylindole Using Acetic Acid (No Palladium).[21] Under a N_2 atmosphere in a glovebox, an air-free flask was charged with 3-methylindole (1.53 mmol, 201 mg), $[Ir(OMe)cod]_2$ (2.5 mol %, 38.3 μmol, 25.4 mg), and 4,4′-di-*tert*-butylbipyridine (5 mol %, 76.6 μmol, 25.4 mg). They were dissolved in THF (11 mL), and the HBpin (7.66 mmol, 0.970 g) was added in a single portion. The flask was sealed and brought out of the glovebox. It was

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heated at 60 °C for 9 h. Then, the reaction was cooled to room temperature, and the volatiles were removed under reduced pressure. The red/brown residue was then dissolved in acetic acid (4.0 mL), and the reaction was stirred at 30 °C. After 11 h, the reaction was determined to be complete, so it was filtered through Celite using ethyl acetate (150 mL), and the filtrate was washed with saturated sodium bicarbonate solution (200 mL). The organic layer was then dried over $MgSO_4$ and concentrated. The resulting residue was purified by column chromatography (10% EtOAc/90% Hexanes) to afford the 7-Bpin-3-methylindole as a white solid (0.800 mmol, 205.8 mg, 52.3%)

Protodeborylation of 2,7-Bis(Bpin)-3-methylindole Using Pd/AcOH.[21] Under a N_2 atmosphere, a 10 mL Schlenk flask was charged with 2,7-bis(Bpin)-3-methylindole (1 mmol, 383 mg) and $Pd(OAc)_2$ (5 mol %, 0.05 mmol, 11.2 mg). The flask was sealed, and acetic acid (2.6 mL) was added via syringe. The reaction was stirred at 30 °C. After 8 h the reaction was filtered through Celite using ethyl acetate (100 mL), and then it was washed with saturated sodium bicarbonate (150 mL). The organic layer was dried over $MgSO_4$ and concentrated to afford a dark brown oil. ^{1}H NMR showed that there was a second product resulting from the reaction. However, not all of the peaks from this product could be resolved from the deborylation product. Attempts to separate the 7-Bpin-3-methylindole product from the unknown product by column chromatography were unsuccessful. When the amount of palladium was increased to 20 mol %, the amount of the unknown that was observed doubled. An LC/MS (ES+) acquired of this mixture of products showed two masses. The first mass was m/z 257.976 $[M + H]^+$ for the 7-Bpin-3-methylindole. The second mass was m/z 513.064 $[M + H]^+$ for the unknown, which we propose is a coupling product between two of the 2,7-bis(Bpin)-3-methylindoles catalyzed by the palladium in the reaction (shown below).

Protodeborylation of 2,7-Bis(Bpin)-3-methylindole Using Ir/AcOH.[21] Under a N_2 atmosphere, a 10 mL Schlenk flask was charged with 2,7-bis(Bpin)-3-methylindole (0.297 mmol, 113.8 mg) and $[Ir(OMe)cod]_2$ (2.5 mol %, 7.5 μmol, 5 mg). The flask was sealed, and acetic acid (776 μL) was added via syringe. The reaction was stirred at 30 °C for 8 h. ^{1}H NMR of the reaction mixture showed that the deborylation reaction was approximately 75% complete.

Protodeborylation of 5-Bpin-3-chloro-*N*,*N*-dimethylaniline Using Pd/AcOH.[21] Under a N_2 atmosphere, a 10 mL Schlenk flask was charged with 5-Bpin-3-chloro-*N*,*N*-dimethylaniline (0.5 mmol, 140.8 mg) and $Pd(OAc)_2$ (5 mol %, 0.025 mmol, 5.6 mg). Acetic acid (1.3 mL) was added via syringe, and the reaction was allowed to stir at 30 °C for 25 h. The reaction was monitored by ^{1}H NMR and GC-FID by removing an aliquot from the reaction, diluting it with ethyl acetate, and washing with a saturated sodium bicarbonate solution. The organic layer was separated and concentrated. ^{1}H NMR and GC-FID were acquired of the residue. The spectrum showed 5% deborylation of the starting material and 5% of the homocoupled biaryl product.

Protodeborylation of 2,5-Bis(Bpin)-3-cyanothiophene Using Pd/AcOH.[21] Under a N_2 atmosphere a 10 mL Schlenk flask was charged with 2,5-bis(Bpin)-3-cyanothiophene (0.5 mmol, 140.8 mg) and $Pd(OAc)_2$ (5 mol %, 0.025 mmol, 5.6 mg). Acetic acid (1.3 mL) was added via syringe, and the reaction was allowed to stir at 30 °C for 25 h. The reaction was monitored by ^{1}H NMR by removing an aliquot from the reaction and diluting it with $CDCl_3$ to aquire the spectrum directly. 22% deborylation was observed over 25 h. However, the reaction was not exclusively selective. ^{1}H NMR integrals showed approximately 14% for the 5-borylated product and 8% for the 2-borylated product.

Protodeborylation of 3,5-Bis(Bpin)-2-cyanothiophene Using Pd/AcOH.[21] Under a N_2 atmosphere a 10 mL Schlenk flask was charged with 3,5-bis(Bpin)-2-cyanothiophene (0.5 mmol, 180.5 mg) and $Pd(OAc)_2$ (5 mol %, 0.025 mmol, 5.6 mg). Acetic acid (1.3 mL) was added via syringe, and the reaction was allowed to stir at 30 °C for 23 h. The reaction was monitored by ^{1}H NMR by removing an aliquot from the reaction and diluting it with $CDCl_3$ to aquire the spectrum directly. 11% deborylation was observed over 23 h.

Protodeborylation of 3,5-Bis(Bpin)-2-methylthiophene Using Pd/AcOH.[21] Under a N_2 atmosphere a 10 mL Schlenk flask was charged with 3,5-bis(Bpin)-2-methylthiophene (0.5 mmol, 175 mg) and $Pd(OAc)_2$ (5 mol %, 0.025 mmol, 5.6 mg). Acetic acid (1.3 mL) was added via syringe, and the reaction was allowed to stir at 30 °C for 23 h. The reaction was monitored by ^{1}H NMR by removing an aliquot from the reaction and diluting it with $CDCl_3$ to acquire the spectrum directly. 59% deborylation was observed over 23 h.

Protodeborylation of 5-Bpin-3-chloro-*N*,*N*-dimethylaniline Using Pd/AcOH (Elevated Temperature).[21] Under a N_2 atmosphere a 10 mL Schlenk flask was charged with 5-Bpin-3-chloro-*N*,*N*-dimethylaniline (0.5 mmol, 140.8 mg) and $Pd(OAc)_2$ (4 mol %, 0.02 mmol, 4.5 mg). Acetic acid (1.3 mL) was added via syringe, and the reaction was allowed to stir at 80 °C for 4.5 h. The reaction was cooled and filtered through Celite with ethyl acetate (50 mL). Then, it was washed with saturated $NaHCO_3$ (50 mL) and dried with $MgSO_4$. The solvent was removed under reduced pressure, and ^{1}H NMR was acquired for the crude reaction material. 3% deborylation of the starting material was observed along with 4% of the homocoupled biaryl product.

Protodeborylation of 5-Bpin-3-chloro-*N*,*N*-dimethylaniline Using Palladium and THF/H_2O. Under a N_2 atmosphere a 10 mL Schlenk flask was charged with 5-Bpin-3-chloro-*N*,*N*-dimethylaniline (0.25 mmol, 70 mg) and $Pd(OAc)_2$ (4 mol %, 0.01 mmol, 2.2 mg) in THF (750 μL). Degassed DI water (125 μL) was added via syringe, and the reaction was allowed to stir at 80 °C for 4.5 h. GC-FID was acquired of the reaction, and it showed <1% deborylation of the starting material and 1% of the homocoupled biaryl product.

Protodeborylation of 2,7-Bis(Bpin)-3-methylindole Using Palladium and CH_2Cl_2/MeOH. Under a N_2 atmosphere a 10 mL Schlenk flask was charged with 2,7-bis(Bpin)-3-methylindole (0.25 mmol, 95.7 mg) and $Pd(OAc)_2$ (3 mol %, 0.0075 mmol, 1.7 mg) in dichloromethane (0.5 mL). Dry, degassed methanol (1.0 mL) was added, and the reaction was stirred at 60 °C. It was monitored for 3 h. After 50 min 17% deborylation to the 7-Bpin-3-methylindole was observed along with 3% to the 3-methylindole, but no further reaction was evident.

Protodeborylation of 2,5-Bis(Bpin)-3-cyanothiophene Using Palladium and CH_2Cl_2/MeOH. Under a N_2 atmosphere a 10 mL Schlenk flask was charged with 2,5-bis(Bpin)-3-cyanothiophene (0.25 mmol, 90.5 mg) and $Pd(OAc)_2$ (3 mol %, 0.0075 mmol, 1.7 mg) in CH_2Cl_2 (0.5 mL). Dry, degassed methanol (1.0 mL) was added via syringe, and the reaction was allowed to stir at 55 °C for 5 h. At that time, 42% deborylation to the 5-Bpin-3-cyanothiophene was observed along with 7% to the 2-Bpin-3-cyanothiophene.

Protodeborylation of 3,5-Bis(Bpin)-2-cyanothiophene Using Palladium and CH_2Cl_2/MeOH. Under a N_2 atmosphere a 10 mL Schlenk flask was charged with 3,5-bis(Bpin)-2-cyanothiophene (0.5 mmol, 180.5 mg) and $Pd(OAc)_2$ (3 mol %, 0.015 mmol, 3.4 mg) in CH_2Cl_2 (0.8 mL). Dry, degassed methanol (1.7 mL) was added via syringe, and the reaction was allowed to stir at 55 °C for 5.5 h. At that time, 15% deborylation to 3-Bpin-2-cyanothiophene was observed.

Protodeborylation of 3,5-Bis(Bpin)-2-methylthiophene using Palladium and CH_2Cl_2/MeOH. Under a N_2 atmosphere a 10 mL Schlenk flask was charged with 3,5-bis(Bpin)-2-methylthiophene (0.5 mmol, 175 mg) and $Pd(OAc)_2$ (3 mol %, 0.015 mmol, 3.4 mg) in CH_2Cl_2 (0.8 mL). Dry, degassed methanol (1.7 mL) was added via syringe, and the reaction was allowed to stir at 55 °C for 5 h. At that time, 39% deborylation to 3-Bpin-3-methylthiophene was observed.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01588.

NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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