

Room-Temperature Direct β -Arylation of Thiophenes and Benzo[*b*]thiophenes and Kinetic Evidence for a Heck-type Pathway

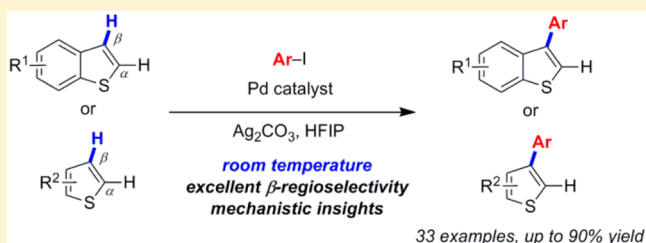
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Supporting Information

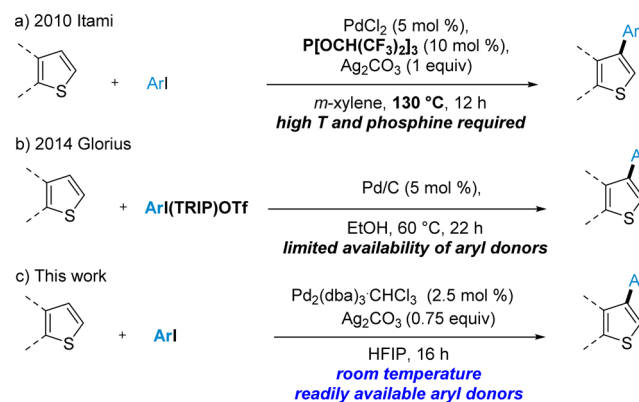
ABSTRACT: The first example of a regioselective β -arylation of benzo[*b*]thiophenes and thiophenes at room temperature with aryl iodides as coupling partners is reported. This methodology stands out for its operational simplicity: no prefunctionalization of either starting material is required, the reaction is insensitive to air and moisture, and it proceeds at room temperature. The mild conditions afford wide functional group tolerance, often with complete regioselectivity and high yields, resulting in a highly efficient catalytic system. Initial mechanistic studies, including ¹³C and ²H KIEs, suggest that this process occurs via a concerted carbo-palladation across the thiophene double bond, followed by a base-assisted anti-elimination.



1. INTRODUCTION

Heterobiaryl scaffolds are common motifs in pharmaceuticals, natural products, and organic electronic components. Methods for their efficient synthesis are of significant interest.¹ In recent years, direct C–H arylation of heteroarenes has emerged as an efficient approach to the synthesis of these heterobiaryls.² Major challenges in developing these methods involve the control of the regioselectivity of arylation^{2,3} and achieving mild reaction conditions,⁴ with most current methodologies requiring elevated temperatures, strong oxidants, and acids or bases. The direct arylation of thiophenes and benzo[*b*]thiophenes, which are widely present in biologically active molecules and organic electronic materials,⁵ is a rapidly growing area of research. Over the past few years, several methodologies allowing the direct arylation of thiophenes at the most acidic α position have been developed.⁶ Direct β -arylation of thiophenes has proven a more challenging task with only a handful of examples in the absence of directing groups reported.^{7,8} In 2010, Itami and co-workers reported a methodology for the selective β -arylation of thiophenes with iodoarenes (Scheme 1a), where a PdCl₂/P[OCH(CF₃)₂]₃ catalytic system was found essential for achieving high regioselectivity.^{7a} This report was followed by examples using aryl boronic acids,^{7b} aryltrimethyl silanes,^{7c} aryl chlorides,^{7d} and benzenesulfonyl chlorides^{7e} as aryl donors. However, all of these methods require high temperatures (80–150 °C), or require TFA as solvent, thus limiting functional group compatibility. Furthermore, some of these methods provide low yields with electron-deficient aryl donors, require a large excess of this coupling partner, and/or provide moderate C-3/C-2 regioselectivity. Recently, Glorius and co-workers reported a milder method that uses diaryliodonium salts (Scheme 1b, TRIP = 2,4,6-triisopropylphenyl) as coupling partners, allowing the selective

Scheme 1. Approaches to β -Regioselective Arylation of Thiophenes and Benzo[*b*]thiophenes



β -arylation to proceed at 60 °C.^{7f} However, a mild methodology employing more readily available coupling partners would be of significant utility. Herein, we report the first example of a methodology capable of performing β -arylation of thiophenes and benzo[*b*]thiophenes at room temperature. This method employs iodoarenes as coupling partners and proceeds in most cases with >99:1 regioselectivity. In addition, kinetic evidence implicating a Heck-type mechanistic pathway has been obtained for the first time.

2. RESULTS AND DISCUSSION

2.1. Reaction Optimization and Scope.

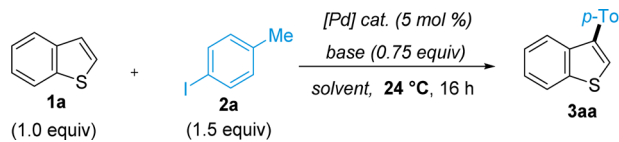
Research conducted in our group has previously highlighted the role of

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silver(I) carboxylate salts in enhancing the reactivity of a Pd/ArI system and enabling the direct arylation of indoles to proceed at room temperature.⁹ We used this catalytic system as our starting point for the investigation into the arylation of unsubstituted benzo[*b*]thiophene **1a** with 4-iodotoluene **2a** (Table 1, entry 1). Under these conditions, C-3 arylated adduct

Table 1. Optimization of Reaction Conditions^a



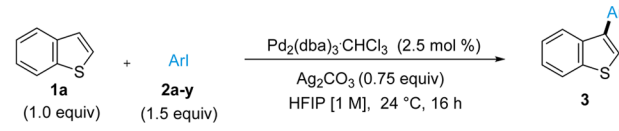
entry	base	[Pd] cat.	solvent	yield (%) ^a
1	<i>c</i> -C ₆ H ₁₁ CO ₂ Ag	Pd(OAc) ₂	H ₂ O	7
2	<i>p</i> -NO ₂ -C ₆ H ₄ CO ₂ Ag	Pd(OAc) ₂	H ₂ O	14
3	1-Ad-CO ₂ Ag	Pd(OAc) ₂	H ₂ O	11
4	<i>c</i> -C ₆ H ₁₁ CO ₂ Ag	Pd(OAc) ₂	TFE	15
5	Ag ₂ CO ₃	Pd(OAc) ₂	TFE	34
6	Ag ₂ CO ₃	Pd(OAc) ₂	HFIP	72
7	Ag ₂ CO ₃	Pd ₂ (dba) ₃ ·CHCl ₃	HFIP	92
8	K ₂ CO ₃	Pd ₂ (dba) ₃ ·CHCl ₃	HFIP	0
9	Ag ₂ CO ₃	none	HFIP	0

^aYields were calculated by ¹H NMR using an internal standard.

3aa was obtained as the major regioisomer, albeit with a yield of only 7%. Contrary to our experience with indoles, a screening of silver(I) carboxylates did not provide any improvement on the yield (entries 1–3 and Table S1). A solvent screening revealed that replacing H₂O with the more acidic 1,1,1-trifluoroethanol (TFE) and 1,1,1,3,3,3-hexafluoroisopropanol (HFIP)¹⁰ led to a marked increase in reactivity (Table 1, entries 4–6), with the latter solvent, in combination with Ag₂CO₃ as the base, affording **3aa** in 72% yield (Table 1, entry 6). However, significant amounts of the homocoupling product of benzo[*b*]thiophene **1a** were also observed. This undesired product could be formed upon reaction of **1a** with Pd(OAc)₂ while presumably forming the catalytically active Pd⁰ species. A change of precatalyst to Pd₂(dba)₃·CHCl₃ was effective at preventing homocoupling of **1a**, affording the desired C-3 arylated compound in 92% yield (Table 1, entry 7) with >99:1 C3:C2 regioselectivity without making use of any additional ligand. Control experiments further outlined the need for both Pd catalyst and Ag₂CO₃ (entries 8, 9).¹¹

Having optimized the process, we then investigated the scope of the reaction (Table 2). Iodobenzene and iodoarenes bearing *para* electron-donating groups reacted efficiently (**3aa**–**3ad**). Electron-withdrawing *para*-substituents also provided **3ae**–**3aj** in good to excellent yields. Remarkably, this method is completely compatible with benzylic alcohol (**3ad**) and aldehyde (**3ae**) functionalities, both sensitive to oxidation under harsher conditions, and with ketones (**3af**), which often require protection. Chloro- and bromo- substitution was also tolerated (**3ai** and **3aj**), albeit with somewhat reduced yields despite no obvious side products being observed.¹² Highly electron-withdrawing *para*-substituents, such as nitro and trifluoromethyl (**3ak** and **3al**), resulted in low reactivity. Gratifyingly, adding 5 mol % of tris(4-methoxyphenyl)phosphine to the catalytic system and raising the reaction temperature to 50 °C restored high yields for these less reactive iodoarenes, while maintaining high C3/C2 regioselectivity.

Table 2. Direct C–H Arylation of Benzo[*b*]thiophene **1a** with Iodoarenes **2a–y**^a



3aa , 88% C3/C2 > 99:1	3ab , 88% C3/C2 > 99:1	3ac , 90% C3/C2 > 99:1	3ad , 86% C3/C2 > 99:1
3ae , 42% (96%) ^b C3/C2 = 97:3	3af , 88% C3/C2 = 98:2	3ag , 88% C3/C2 = 99:1	3ah , 89% C3/C2 > 99:1
3ai , 61% C3/C2 > 99:1	3aj , 35% C3/C2 = 99:1	3ak , 30% (89%) ^b C3/C2 = 97:3	3al , 10% (89%) ^b C3/C2 = 97:3
3am , 83% C3/C2 > 99:1	3an , 15% (72%) ^b C3/C2 = 91:9	3ao , 81% C3/C2 > 99:1	3ap , 56% (80%) ^c C3/C2 > 99:1
3aq , 88% C3/C2 > 99:1	3ar , 54% (80%) ^c C3/C2 = 99:1	3as , 18% (57%) ^d C3/C2 > 99:1	3at , 12% (63%) ^d C3/C2 > 99:1
3au , 48% (61%) ^b C3/C2 > 99:1	(S)-3av , 82% C3/C2 > 99:1 (ee > 99%)		
3aw , 0%	3ax , 84% C3/C2 > 99:1	3ay , 0%	

^aReactions carried out on a scale of 0.75 mmol of **1a**. Yields given are isolated. C3/C2 ratios were determined by GC–MS analysis of the crude reaction mixture. ^bPerformed at 50 °C and in the presence of 5 mol % of P(*p*-C₆H₄OMe)₃. ^cPerformed at 50 °C. ^dPerformed with 3 equiv of **1a**, 1 equiv of ArI, 0.5 equiv of Ag₂CO₃, and 5 mol % of P(*p*-C₆H₄OMe)₃ at 50 °C.

Both of these observations contrast with Itami's methodology,^{7a} where (1) electron-rich iodoarenes display lower reactivity and

(2) addition of an electron-rich phosphine ligand switches the regioselectivity to C2. The diverse features shown by our system suggest different mechanistic pathways (vide infra), and understanding these could lead to the development of new regioselective methodologies. *meta*-Substituted iodoarenes also showed good reactivity under our reaction conditions (**3am**–**3ao**). *ortho*-Substitution is tolerated, although a slightly higher temperature is required to achieve high yields (**3ap**–**3ar**). Heteroiodoarenes, such as 1- and 2-iodothiophene and *N*-tosyl-5-iodoindole, could also be successfully employed as coupling partners (**3as**–**3au**). Furthermore, we examined the applicability of our methodology toward the synthesis of non-natural amino acids, which could be further incorporated into peptides leading to isosteric molecules with potential biological properties.^{13,14} When we tested the coupling between benzo-*[b]*thiophene (**1a**) and (*S*)-*N*-Boc-4-iodo-phenylalanine (**2v**), the corresponding product was obtained in high yield. Furthermore, we were pleased to discover that no racemization took place with **3av** obtained in >99% enantiomeric excess.¹⁵ 4-Iodoaniline was not compatible with the reaction conditions (**3aw**), likely due to inactivation of the catalyst by coordination.¹⁶ Protecting the amine functional group to a less strongly coordinating acetamide gave the desired product in 84% yield (**3ax**). Similarly, no reactivity was observed with 4-iodobenzonitrile (**3ay**).

The process can be also applied to the regioselective C-4 arylation of C-2 and C-3 substituted thiophenes (Table 3). In

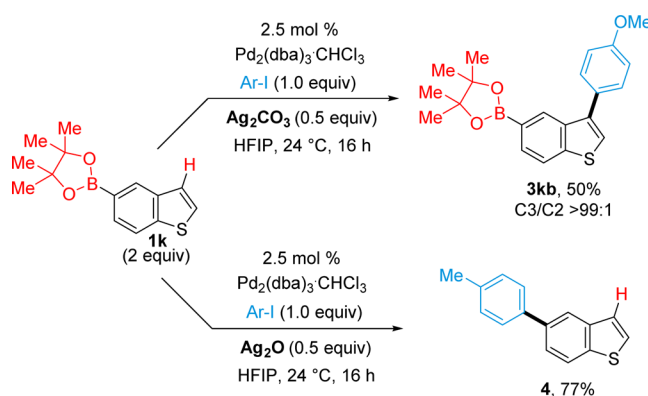
Table 3. Direct C–H Arylation of Thiophenes 1b–1j with Iodoarene 2a^a

^aReactions carried out on a scale of 0.75 mmol of **1**. Yields given are isolated. Regioselectivity was determined by GC–MS of the crude reaction mixture. ^bReaction performed at 50 °C.

most examples, nearly complete regioselectivity was observed, with >99:1 of C-4 arylation versus all other regioisomers. Moderately electron-withdrawing and -donating substituents were found compatible with the reaction, but lower yields or decomposition were observed with stronger electron-donating or -withdrawing substituents. The reaction conditions tolerate free alcohols (**3ia**) and a SiMe₃ substituent (**3ja**).

To further explore the compatibility of our room-temperature conditions with sensitive functional groups, we tested a substrate containing a boronic ester substitution (Scheme 2). Remarkably, good yield and chemo- and regioselectivity toward the C-3 arylation product **3kb** were obtained under our

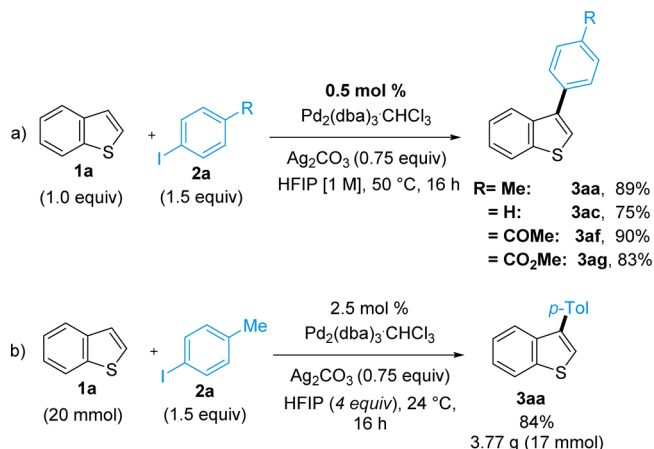
Scheme 2. Chemoselectivity toward C–H Activation in the Presence of Boronic Esters



standard conditions. Conversely, a simple change of base from Ag₂CO₃ to Ag₂O effected a complete switch in chemo-selectivity, providing the Suzuki coupling adduct **4** in 77% yield.

The reaction setup is highly practical as the reagents can be weighed under air and the reaction is neither air- nor moisture-sensitive. We also explored whether further tailoring of the reaction would accommodate particular practical needs between concentration, catalyst loading, and temperature of reaction. For example, in the reaction of **1a** with **2a**, the catalyst loading could be reduced to only 0.5 mol %, affording **3aa** in 89% when reacting at 50 °C instead of room temperature (Scheme 3a). These conditions were applied to a selection of

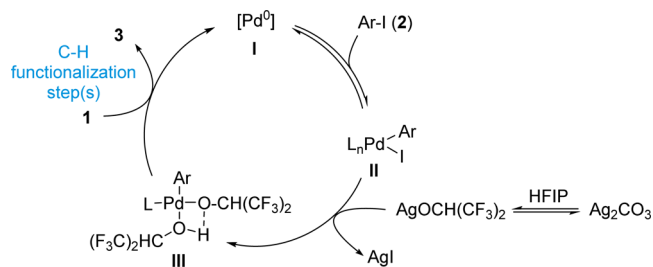
Scheme 3. Reactions at Low Catalyst Loading and 20 mmol Scale-Up



substrates, which gave the corresponding arylated compounds in good to high yields (75%–90%). To our knowledge, this is the lowest palladium catalyst loading reported for a C-3 arylation of (benzo)thiophenes. Furthermore, the amount of HFIP solvent can be significantly reduced to only 4 equiv, while maintaining the same high yields of **3aa** (86%, see Table S6). Finally, the reaction is amenable to scaling up: the arylation of **1a** with **2a** using only 4 equiv of HFIP could be directly run at a 20 mmol of **1a** scale without any modifications, to afford 3.77 g (84%) of pure isolated adduct **3aa** (Scheme 3b).

2.2. Mechanistic Considerations. **2.2.1. Mechanistic Outline.** A plausible mechanistic pathway involving a Pd^{0/II} catalytic cycle is outlined in Scheme 4. The cycle would start by oxidative addition of Ar–I **2** to Pd(0) (**1**) to form PdArI species

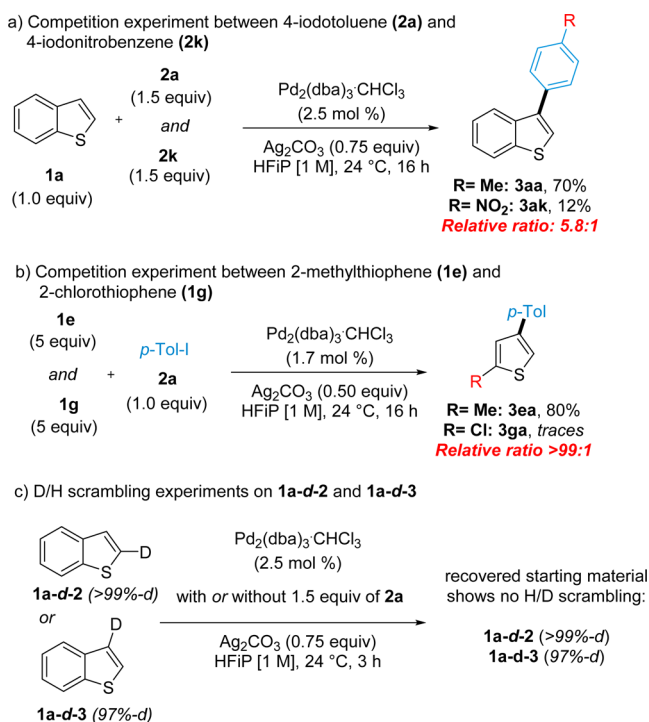
Scheme 4. Plausible Reaction Mechanism



II. HFIP is a mildly acidic solvent (pK_a 9.3), which would react with Ag_2CO_3 in an acid–base equilibrium forming $AgOCH(CF_3)_2$, which can then transmetallate with II to form Pd alkoxide III. These species may be further stabilized by H-bonding with another molecule of HFIP.¹⁷ Pd-species III would then undergo the C–H arylation step or steps (vide infra) on the benzo[*b*]thiophene substrate 1.

A competition experiment between 4-iodotoluene (2a) and 4-iodonitrobenzene (2k) was carried out, resulting in a relative reactivity of 5.8:1 (Scheme 5a).¹⁸ If the oxidative addition was

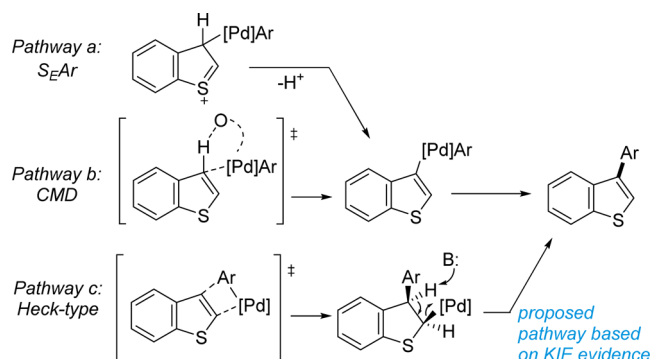
Scheme 5. Competition and Deuteration Experiments



irreversible, coupling with the electron-poor iodoarene (albeit in low yield) would be the expected major product.¹⁹ Instead, the result obtained suggests that oxidative addition is reversible and occurs before the rate-limiting step, consistent with our mechanistic proposal in Scheme 4. Alternatively, a $Pd^{II/IV}$ pathway has also been proposed to explain a C–H arylation mediated by $Pd(OAc)_2$ and $AgOAc$ displaying a similar reactivity trend.²⁰

2.2.2. Studies on the C–H Functionalization Pathway. The C–H functionalization steps could proceed through: (a) an electrophilic aromatic substitution (S_EAr) pathway; (b) a concerted metalation-deprotonation (CMD); or (c) a Heck-type process (Scheme 6).^{2b,f} Pathway a involves an electrophilic

Scheme 6. Possible Mechanistic Pathways for the C–C Bond Formation Step



attack by $Ar-Pd^{II}$ at C-3 of benzo[*b*]thiophene followed by deprotonation and reductive elimination. This pathway is inconsistent with the regioselectivity of arylation observed for thiophenes, given that these are most nucleophilic in the α , not β position. For pathway b, an unusual C–H activation at the less acidic position needs to be invoked to explain the β -regioselectivity of the process. Pathway c, on the other hand, involves a carbo-palladation followed by an *anti*- β -hydride elimination or a more likely base-assisted E2 elimination. Calculations by Fu have shown that a base-assisted E2-type elimination may indeed be a viable process in certain cases.^{21a} Itami and Studer have also reported calculations that favor the hypothesis of a carbo-palladation pathway on the C-3 arylation of thiophenes with arylboronic acids.^{20b}

With the aim of obtaining experimental evidence supporting one of these mechanistic pathways for the C–C bond-forming step, we set out a competition experiment between 2-methyl- (1e) and 2-chloro-thiophene (1g) showing that the more electron-rich 1e reacts exclusively (>99:1, Scheme 5b). This suggests that the C–H activation step does not proceed via a concerted metalation-deprotonation (pathway b), where the electron-poor 1g should react faster, or that the C–H activation step is not rate-determining.²² Furthermore, a CMD process would be expected to occur at the most acidic α -position in the thiophene, rather than the observed β -arylation.²³ To test whether a reversible CMD process might be in operation in our system, H/D scrambling experiments were attempted by subjecting benzo[*b*]thiophene 1a-d-3 and 1a-d-2 to the reaction conditions in the presence and in the absence of ArI : in all cases recovered starting material 1 showed no D/H scrambling (Scheme 5c), suggesting that a non-rate-determining reversible CMD process is also unlikely.

With the aim of obtaining supporting evidence for a Heck-type pathway, we set out to determine the $^{13}C/^{12}C$ and D/H KIEs for the process. Kinetic isotope effect (KIE) measurements have proven to be invaluable tools to assess mechanistic hypotheses in a wide variety of transition metal-catalyzed reactions.²⁴ Within the C–H functionalization arena, 2H KIEs are often measured and can provide information on the nature of the C–H activation event. On the other hand, despite their potential for providing new and complementary information, ^{13}C KIEs are rarely determined. This is likely due to the difficulty in preparing ^{13}C isotopically labeled substrates. Over the last two decades, Singleton and co-workers have demonstrated that ^{13}C natural abundance in substrates can be used to determine intermolecular competitive ^{13}C KIEs by quantitative ^{13}C NMR.^{25,26} During the course of a reaction, the

starting material will become more enriched in ^{13}C at those positions with a positive $^{13}\text{C}/^{12}\text{C}$ kinetic isotopic effect; therefore, an increase in the ratio of $^{13}\text{C}/^{12}\text{C}$ between the recovered starting material and the original starting material will result. This ratio (R/R_0) is directly related to the fractional conversion of reagents (F) and the KIEs by eqs 1 and 2.^{25,27}

$$R/R_0 = (1 - F)^{(1/\text{KIE})-1} \quad (1)$$

$$\text{KIE} = \frac{\log(1 - F)}{\log[(1 - F)R/R_0]} \quad (2)$$

Importantly, the experimental KIEs on benzo[*b*]thiophene will reflect the first irreversible step between the catalyst and benzo[*b*]thiophene, regardless of what is the rate-determining step in the overall process.²⁸ Therefore, this is an ideal technique to directly probe the nature of the C–H arylation step. Following this procedure, we carried out two independent experiments, which allowed the simultaneous measurement of ^{13}C KIE at C-2, C-3, and C-4. These experiments indicated the presence of a significant primary ^{13}C KIE at both C-3 and C-2 positions of benzo[*b*]thiophene: KIEs of 1.042 ± 0.006 and 1.044 ± 0.005 were obtained for C-3 position, while KIEs of 1.015 ± 0.006 and 1.014 ± 0.005 were determined for C-2 (Figure 1a, values in black). These KIEs are consistent with a Heck process (see discussion below).

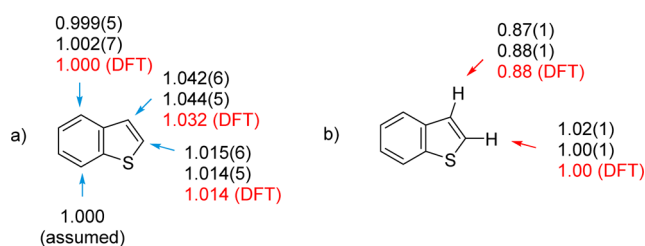


Figure 1. Determination of KIEs. Values in black correspond to the experimentally determined ^{13}C (a) and ^2H (b) intermolecular KIEs (two repeats). Figures in brackets correspond to the standard deviation in the last digit as determined from six measurements. Values in red correspond to the DFT predicted KIEs for the proposed olefin insertion step (Scheme 6, pathway c).

Because of the low sensitivity of ^2H NMR, measuring ^2H KIEs using the same analytical technique is generally very time-consuming or results in too large an error. To overcome this problem, we carried out a modification on Singleton's procedure: we partially deuterated the benzo[*b*]thiophene starting material at C-2 and C-3 (ca. 1% each) and used an internal standard.²⁹ This allowed for an extremely accurate measurement of the ^2H KIEs. Two independent experiments (Figure 1b, black) showed an inverse KIE at C-3 (0.87 ± 0.01 , 0.88 ± 0.01) and no KIE at C-2 (1.02 ± 0.01 , 1.00 ± 0.01). The presence of an inverse kinetic isotope effect is consistent with a change in the hybridization at the carbon atom during the rate-determining step from sp^2 to sp^3 . These values contrast with the positive ^2H KIEs measured by Glorius and co-workers (1.5 for C3 and 1.2 for C2) where a heterogeneous catalytic process is proposed.^{7f}

Taken together, the ^{13}C and ^2H KIE values are consistent with a carbopalladation step onto the C2–C3 double bond of the benzo[*b*]thiophene (Scheme 6c). On the other hand, these values are inconsistent with both the CMD and the electrophilic-metalation pathways (Scheme 6a and b), where

a significant ^{13}C KIE should be only be observed at C-3 (not at C-2). Furthermore, a large primary ^2H KIE would be expected at C-3 for the CMD process.³⁰ For a rate-limiting carbopalladation step, it would be expected that ^{13}C KIEs would be observed for both C-2 and C-3 carbon atoms along with inverse ^2H KIEs at both positions. Here, we observed both ^{13}C KIEs and an inverse KIE at the C-3 proton of benzo[*b*]thiophene. However, no ^2H KIE at C-2 was observed. Computational experiments (vide infra) revealed that, in this specific case, a ^2H KIE would not be expected at C-2.

To further probe the mechanism of the reaction, DFT modeling of a plausible carbopalladation step between benzo[*b*]thiophene and the likely active intermediate Pd[Ph-(OCH(CF₃)₂) (HOCH(CF₃)₂)] (III, Scheme 4) was performed (Figure 2). The calculation in the gas phase showed

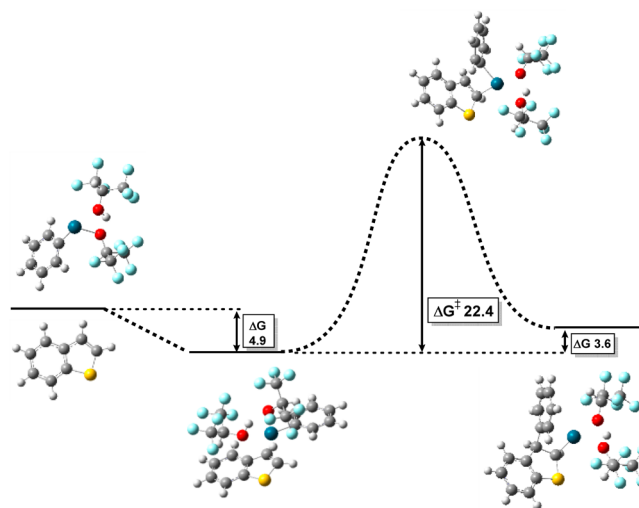


Figure 2. Computational studies for a plausible carbopalladation step of the Heck-type pathway in the gas phase. Structures and energies calculated by DFT (B3LYP/LanL2Dz for Pd, 6-31G(d) for other atoms). Gibbs free energies (G) are in kcal mol⁻¹.

the initial formation of an exergonic C2,C3-olefin π -complex ($\Delta G = -4.9$ kcal/mol). The subsequent carbopalladation step afforded a free energy barrier of 22.4 kcal/mol, which is consistent with a room-temperature process.^{31,32} Furthermore, on the basis of these calculated structures, ISOEFF was used to predict the ^{13}C and ^2H KIEs corresponding to this step.^{33,34} The predicted values are strikingly close to the experimentally observed ones (Figure 1a and b, values in red), highlighting the usefulness of combined ^{13}C and ^2H KIE studies to distinguish between the proposed mechanistic pathways. Conversely, DFT modeling of a plausible CMD pathway^{21a,23} in the gas phase (see the Supporting Information) leads to a higher free energy barrier of 24.7 kcal/mol and a predicted H/D KIE of 5.2 at C3.³⁵

3. CONCLUSION

In summary, we have described the first catalytic system capable of β -arylation of benzo[*b*]thiophenes and thiophenes at room temperature. This system delivers very high regioselectivities, presents broad functional group tolerance, and can be carried out in an open flask and in the absence of phosphine ligands (with the exception of highly electron-poor iodoarenes). Preliminary mechanistic studies have provided the first experimental kinetic evidence supporting a Heck-type reaction

pathway in C–H arylations of heteroarenes. Further investigations on the mechanism are ongoing in our laboratories and will be reported in due course.

4. EXPERIMENTAL SECTION

General Procedure. Pd₂(dba)₃·CHCl₃ (19.5 mg, 2.5 mol %), Ag₂CO₃ (155 mg, 0.56 mmol, 0.75 equiv), aryl iodide **2** (1.12 mmol, 1.5 equiv), and (benzo)thiophene **1** (0.75 mmol, 1.0 equiv) were stirred in hexafluoro-2-propanol (0.75 mL) at 24 °C for 16 h. After this time, the resultant mixture was diluted with EtOAc (5 mL) and filtered through a plug of silica. The silica plug was flushed with EtOAc (30 mL), and the filtrate was evaporated to dryness under reduced pressure. Purification via automated column chromatography afforded the desired arylated (benzo)thiophenes **3**.

Representative Example. 3-(*p*-Tolyl)benzo[*b*]thiophene (**3aa**; 20 mmol Scale Reaction: *Scheme 3b*). Benzo[*b*]thiophene **1a** (2.74 g, 20 mmol, 1.0 equiv), 4-iodotoluene **2a** (6.67 g, 30 mmol, 1.5 equiv), Ag₂CO₃ (4.1 g, 15 mmol, 0.75 equiv), and Pd₂(dba)₃·CHCl₃ (518 mg, 0.5 mmol, 2.5 mol %) were stirred in 8.4 mL of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) at 24 °C for 16 h. After this time, the resultant mixture was diluted with EtOAc (15 mL) and filtered through a plug of silica. The silica plug was flushed with EtOAc (50 mL), and the filtrate was evaporated to dryness under reduced pressure. Product **3aa** was then isolated by column chromatography (hexane) as a colorless oil in 84% yield (3.77 g, 17 mmol). *R*_f (hexane): 0.48. ¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.02–7.97 (m, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.47–7.44 (m, 2H), 7.42 (s, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 2.50 (s, 3H). ¹³C NMR (101 MHz, CDCl₃): δ (ppm) 140.9, 138.2, 138.2, 137.4, 133.3, 129.6, 128.7, 124.5, 124.4, 123.1, 123.1, 123.0, 21.2. HRMS: calcd for C₁₅H₁₂S, 225.0660 (M + H⁺); found, 225.0730.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b12242.

Experimental procedures and characterization data (PDF)

X-ray data for compound **3ak** (CIF)

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Notes

The authors declare no competing financial interest.

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