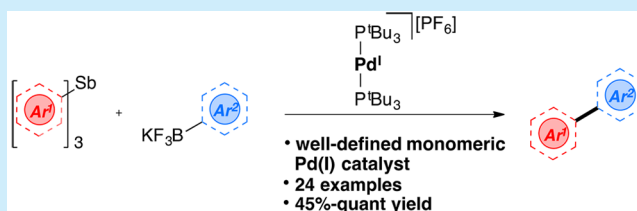




Oxidative Cross-Coupling of Boron and Antimony Nucleophiles via Palladium(I)

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ABSTRACT: The use of an isolatable, monomeric Pd(I) complex as a catalyst for the oxidative cross-coupling of aryl-antimony and aryl-boron nucleophiles is reported. This reaction tolerates a wide variety of substrates, with >20:1 selectivity for cross-coupled products. This strategy offers a new approach to achieving the selective cross-coupling of nucleophiles.



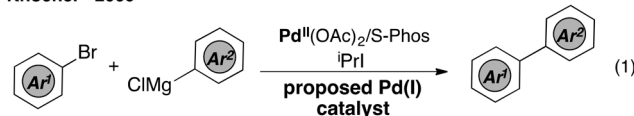
Transition-metal-catalyzed cross-coupling reactions are keystone transformations in contemporary organic chemistry.¹ Selectivity in these reactions has classically been achieved by exploiting the complementary metal-based reactivity of electrophilic and nucleophilic substrates. The electrophilic reagent is first oxidatively added to the metal catalyst, typically involving insertion into a carbon–halogen bond, before subsequent transmetalation with the nucleophilic coupling partner, enabling product formation through bond forming reductive elimination. While many successful coupling reactions exploit this sequence of events,² alternative strategies based on two nucleophiles or two electrophiles are comparatively underdeveloped.³ In recent years, coupling approaches involving single-electron redox events have emerged, with visible-light-promoted photoredox catalysis a particularly prominent example.⁴ Other single-electron transfer mediated processes proceed through internal redox mechanisms⁵ or use external oxidants.⁶ These alternative coupling approaches are made viable by transition-metal-based catalysts with accessible M(*n*)/M(*n* + 1) redox couples and, for this reason, have largely been associated with complexes of first row metals such as Ni,^{5,7} Cu,⁸ and Fe.⁹

Despite widespread use in cross-coupling reactions, the redox chemistry of palladium catalysts has largely been confined to the Pd(0)/Pd(II) couple. It has been speculated that Pd(I) intermediates are involved in radical atom transfer reactions¹⁰ and Kumada couplings (Scheme 1, eq 1).^{10,11} Dimeric Pd(I) phosphine complexes have shown catalytic application in trifluoromethylthiolation reactions (Scheme 1, eq 2).¹² They have also proven to be valuable sources of low-coordinate Pd(0), allowing effective catalysis of carbon–carbon bond forming reactions via a conventional Pd(0)/Pd(II) cycle.¹³

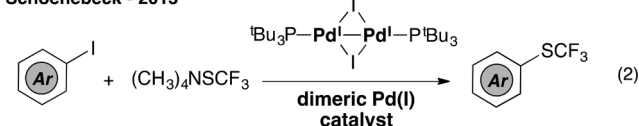
Recently, one of us demonstrated the facile one-electron oxidation of Pd(P^tBu₃)₂ (1) using ferrocenium hexafluorophosphate ([Fc][PF₆]) and subsequent isolation of [Pd(P^tBu₃)₂][PF₆] (2).¹⁴ This straightforward method for

Scheme 1. Reactions Promoted by Pd(I) Complexes

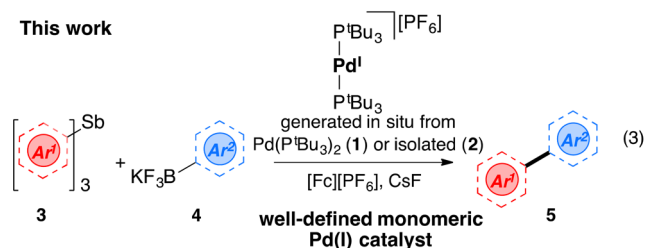
Knochel - 2009



Schoenebeck - 2015



This work



generation of monomeric palladium bis(phosphine) metal-radicals led us to speculate that the associated Pd(0)/Pd(I) redox couple could be exploited catalytically in single-electron transfer reactions. Herein, we report a highly selective oxidative coupling of organoboron- and organoantimony-based aryl nucleophiles mediated by commercially available 1 and [Fc][PF₆] or preformed 2 (Scheme 1, eq 3).

While exploring the reactivity of 2, we noted that 2 equiv of this complex promoted the selective two-electron oxidative coupling of SbPh₃ and aryl trifluoroborate salt 4a to deliver

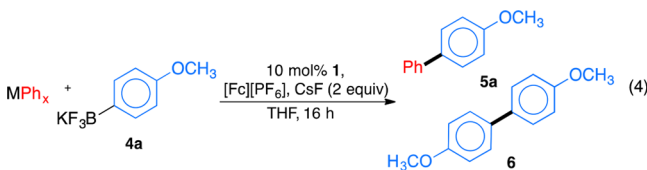
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biaryl **5a** in 78% yield. We looked to develop a catalytic version of this coupling by examining the use of **1**, with $[\text{Fc}][\text{PF}_6]$ as the stoichiometric oxidant to generate **2** *in situ*, with the addition of CsF (Table 1). Pleasingly, this reaction gave extremely high

Table 1. Oxidative Coupling of Aryl Nucleophiles



entry	MPh _x	t, °C	ratio Ph/4a/ oxidant	variation	yield 5a, % ^a (ratio 5a:6) ^b
1	SbPh ₃	rt	3:1:2	—	67 (>20:1)
2	SbPh ₃	60	1:2:3	—	86 (>20:1)
3	SbPh ₃	60	1:2:3	2 as cat.	84 (>20:1)
4	SbPh ₃	60	1:2:3	no Pd cat.	<5
5	SbPh ₃	60	1:2:0	no oxidant	<5
6	SbPh ₃	60	1:2:1 ^c	O ₂ oxidant	<5
7	SbPh ₃	60	1:2:3	AgBF ₄ oxidant	54
8	SbPh ₃	60	1:2:3	Selectfluor oxidant	70
9	SbPh ₃	60	1:2:3	no CsF	8 ^d
10	BPh ₃	rt	3:1:2	—	31 (2:1)
11	SnPh ₄	rt	4:1:2	—	nd ^e (1:4.5)
12	PbPh ₄	rt	4:1:2	—	44 (11:1)
13	BiPh ₃	rt	3:1:2	—	54 (4:1)

^aIsolated yield. ^bDetermined by ¹H NMR analysis of crude mixture. ^cPerformed under 1 atm of O₂. ^dSignificant polymerization of solvent observed. ^eNot determined.

selectivity for the cross-coupling, delivering biaryl **5a** in 67% yield (Table 1, entry 1). Using 0.33 equiv of the antimony reagent (1 equiv with respect to the phenyl group), all three aryl groups could be transferred at 60 °C, using a 2:3 ratio of **4a**/ $[\text{Fc}][\text{PF}_6]$ to give an 86% yield of **5a** (entry 2).

Replacing catalyst **1** with the preformed Pd(I) salt **2** had little effect on yield, while the reaction failed in the absence of a palladium catalyst (Table 1, entries 3 and 4). The electron-rich Pd(PCy₃)₂ complex was also a successful catalyst, while Pd(PPh₃)₄ and Pd₂dba₃ gave reduced yields of 44% and 40%. The addition of excess Hg(0) to the reaction mixture did not affect the yield, suggesting that the reaction is not catalyzed by heterogeneous palladium. Moreover, monitoring the conversion of the reaction over time did not show any evidence of an induction period (see Supporting Information (SI)).

The reaction did not proceed in the absence of the oxidant, while O₂ as the oxidant gave only a trace amount of product (Table 1, entries 5, 6). A screen of alternative oxidants (see SI) identified AgBF₄ and Selectfluor as viable reagents, consistent with a pathway involving single-electron oxidation of palladium (Table 1, entries 7, 8).^{15a,b} Low conversion was observed in the absence of CsF, along with the formation of a THF-derived polymer.

We also examined the use of nonantimony-based aryl transfer reagents, to determine if this oxidative coupling strategy could be applied more generally to other pairs of nucleophiles. Coupling of **4a** with triphenylborane gave a 2:1 mixture of the cross-coupled product **5a** and the dimer **6** along with biphenyl. Tetraphenyltin gave predominantly **6**, while tetraphenyllead and triphenylbismuth showed useful selectivity toward the cross-coupled biaryl (Table 1, entries 10–13). Gratifyingly, of the five coupling partners tested, four were viable, highlighting the orthogonal reactivity enabled by this approach.

With the optimized reaction conditions established, we next set about applying this coupling to a number of aryl-borate and antimony compounds (Figure 1). All triaryl-antimony reagents were synthesized in one step from commercially available SbCl₃ and were bench stable. While triarylantimony reagents have seen limited use as nucleophiles in organic synthesis,^{15c} they offer improved stability compared with organometallic reagents based on Mg or Zn, and when all three aryl groups are utilized, better atom economy than most B- or Sn-based reagents. Care should

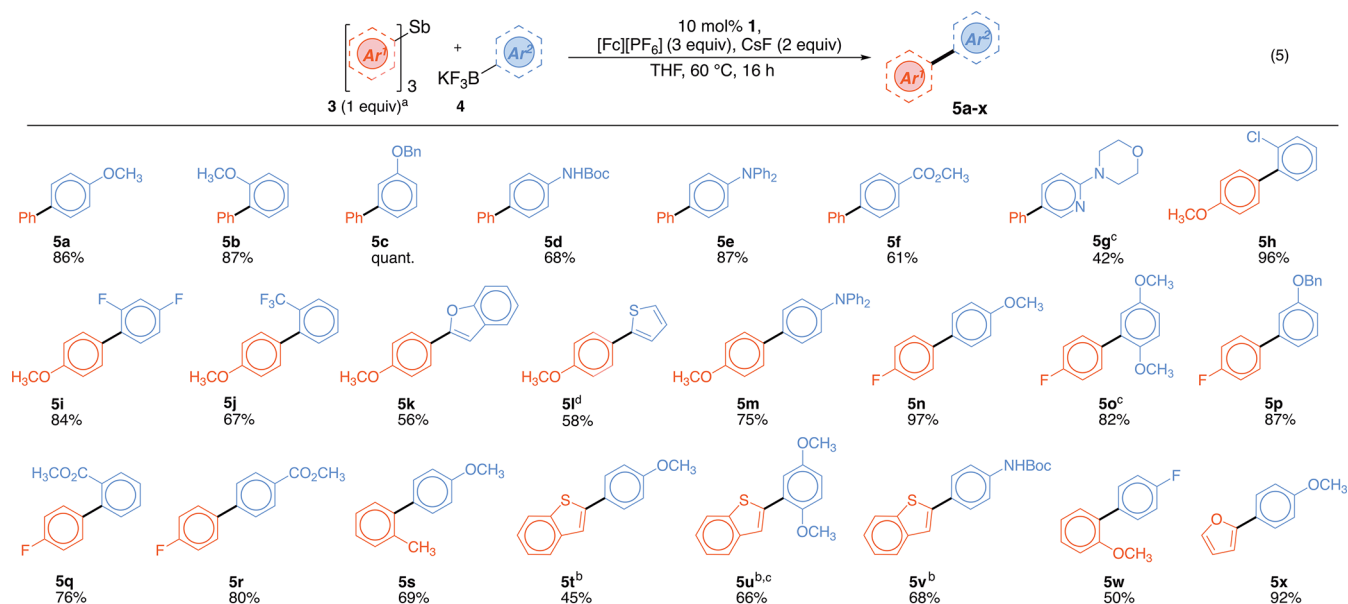


Figure 1. Scope of the boron/antimony coupling.

nucleophiles. This strategy offers a new approach for achieving selectivity in palladium catalyzed cross-coupling reactions and demonstrates that single-electron redox events at palladium can be harnessed for new catalytic organic transformations.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: [10.1021/acs.orglett.8b01989](https://doi.org/10.1021/acs.orglett.8b01989).

Full experimental data, including synthetic procedures, characterization data, and NMR spectra (PDF)

Accession Codes

CCDC 1839868 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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(17) As deduced in a recent copper catalyzed oxidative coupling reaction. See ref **8**.

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