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Palladium-catalyzed cross-coupling of aryl chlorides with O, N-chelate stabilized diarylborinates

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ABSTRACT

A series of O, N-chelated diarylborinates have been prepared and tested as arylboron counterpart alternative to oxygen-labile diarylborinic acids in palladium catalyzed Suzuki coupling of aryl chlorides. 3-Dimethylaminopropyl diarylborinates (**B-5a**), featuring a six-membered O, N-chelated boron ring that was confirmed by single crystal X-ray diffraction, displayed a delicately balanced stability and reactivity. Their cross-coupling with structurally various aryl chlorides could be effected as efficiently as that of the parent diarylborinic acids by using 0.1~1mol% $Pd(OAc)_2$/IPr/$P(OPh)_3$ as catalyst system, to provide the corresponding biaryls in good to excellent yields.

1. Introduction

Four-coordinate diarylborinates, in particular those bearing an intramolecular B-N coordinate bond, are much more stable than the corresponding three-coordinate ones [1]. In fact, the former, as stable derivatives of diarylborinic acids, has been increasingly found in pharmaceutical reagents [2] and advanced materials [3] while the later has been proposed as active intermediates in borinic acid catalyzed processes, e.g. aldol condensation [4], Mannich-type reaction [5] and amidation [6]. More recently, the parent five-membered O, N-chelated diarylborinate, 2-aminoethyl diphenylborinate (2-APB), has been identified as a universal blocker of transient receptor potential channels [7]. We have recently reported that diarylborinic acids could be used as a cost-effective aryl source in palladium and nickel catalyzed cross-coupling reactions with aryl (pseudo)halides [8], carboxylic acids [9] and amides [10]. However, the coordinatively unsaturated diarylborinic acids are sometimes oxygen-labile and prone to dehydration and protodeboronation, complicating their long-term storage, stoichiometry and applications as arylation reagents. Inspired by the great successes achieved by Burke et al. [11] in finely tuning the stability and reactivities of arylboronates via coordinative, electronic and steric properties of boron center, we anticipate that it should be possible to develop storage-stable and easy-to-handle diarylborinates to replace diarylborinic acids as arylation reagents in transition metal-catalyzed cross-couplings. Herein, we report palladium catalyzed cross-coupling of aryl chlorides, which are the least reactive but most practical aryl halides due to their low cost and wide availability, with a series of O, N-chelate stabilized diarylborinates, among them 3-dimethylaminopropyl diarylborinates performed as efficiently as diarylborinic acids.

2. Results and discussion

The cross-coupling of 4-acetylchlorobenzene (**Cl-1**) with 2-aminoethyl diphenylborinate (2-APB, **B-1**) was tested at first under the conditions that we had developed for *N*,*N*'-bis(2,6-diisopropylphenyl) imidazol-2-ylidene (IPr) palladium-catalyzed cross-coupling of aryl halides with free diarylborinic acids, 0.1mol % $Pd(OAc)_2$/IPr/$P(OPh)_3$ (1/1/2, mol/mol) in the presence of 2equiv. $K_3PO_4.3H_2O$ in *t*BuOH at 80 °C by using a slightly excess aryl source (B/Cl = 0.55 mol/mol, 1.1equiv. with respect to phenyl group) [8b]. The desired cross-coupling product, 4-acetylbiphenyl (**P-1**), was

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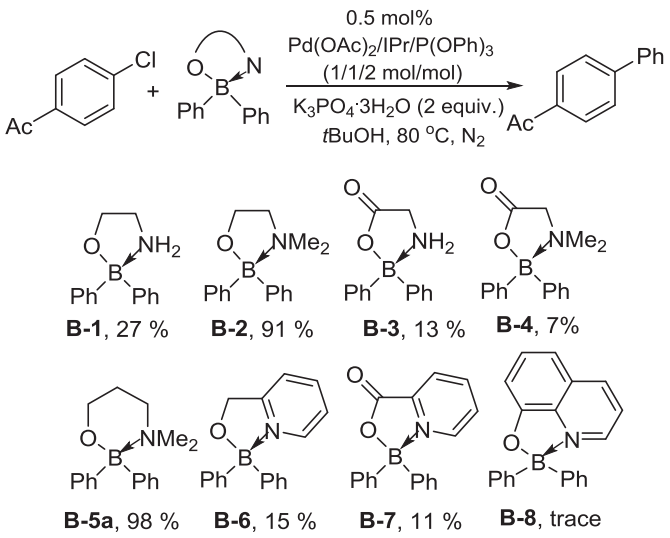
obtained in a low but promising yield (27%) (Scheme 1). Encouraged by the preliminary result, a couple of five/six-membered, O, N-chelate stabilized diarylborinates (**B-2**~**B-8**) [1b,12-15] were prepared by reaction of diarylborinic acids with representative N-containing alcohols or acids, e.g. dimethylaminoethanol, glycine, dimethyl glycine, pyridin-2-ylmethanol, picolinic acid, 3-(dimethylamino)propanol and quinolin-8-ol. Resonances at 4.45–11.92 ppm in ^{11}B NMR spectra of these diarylborinates are consistent with the O, N-chelated four-coordinate boron center [1b,2c]. The characteristic absorption of B-N (1350-1310cm-^{1}) in IR spectra also confirmed the formation of O, N-chelated four-coordinate boron center in these diarylborinates [16].

Reactivities of these diarylborinates in the model cross-coupling reaction were investigated. The biaryl product **P-1** could be obtained in 91% and 98% yields, respectively, with 2-dimethylaminoethyl diphenylborinate (**B-2**) and 3-dimethylaminopropyl diphenylborinate (**B-5a**) as the aryl source in the model reaction while the analogues **B-2**~**B4** and **B-6**~**B-8** performed poorly.

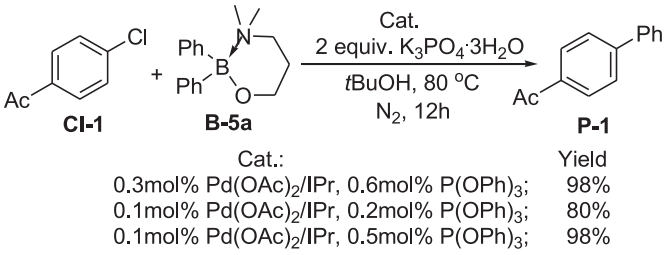
In fact, excellent yields for **P-1** could still be obtained when the catalyst loading was reduced to 0.3mol% or even 0.1mol% provided that $P(OPh)_3$ was increased to 5equiv. (0.5mol%) with respect to Pd/IPr (0.1mol%) (Scheme 2). The high reactivity of the six-membered O, N-chelated diphenylborinate (**B-5a**) may be attributed to the steric hindrance and/or the so-called through-bond interactions [1b].

Crystal structure of the most reactive diphenylborinate **B-5a** was determined and confirmed the presence of the six-membered N, O-chelate stabilized boron center (Fig. 1). The N→B coordinate bond distance is 1.7095(17)Å in **B-5a** is significantly longer than previously reported data for the related five/six-membered O, N-chelated diphenylborinates **B-1**, **B-2** and 3-aminopropyl diphenylborinate where the bond lengths range from 1.61 to 1.65 Å while the B-O (1.4542(16)Å) bond length is in the normal range from 1.35 to 1.48 Å [1b,17]. The B-C_{Ph} bond lengths (1.6425(18) and 1.6265(18) Å) are slightly longer than those in **B-1** (1.620 and 1.613 Å), **B-2** (1.627 and 1.614 Å) and 3-aminopropyl diphenylborinate (1.620 and 1.626 Å). The angles around the tetra-coordinated boron atom are between 102.9(9)° and 113.8(10)° closed to tetrahedral angle values.

Scope and limitation of the palladium-catalyzed cross-coupling of aryl chlorides with 3-dimethylaminopropyl diarylborinates have



Scheme 1. The coupling of 4-acetylchlorobenzene with O, N-chelate stabilized diarylborinates.



Cat.:	Yield
0.3mol% $Pd(OAc)_2$/IPr, 0.6mol% $P(OPh)_3$;	98%
0.1mol% $Pd(OAc)_2$/IPr, 0.2mol% $P(OPh)_3$;	80%
0.1mol% $Pd(OAc)_2$/IPr, 0.5mol% $P(OPh)_3$;	98%

Scheme 2. The coupling of 4-acetylchlorobenzene with **B-5a.**

been explored (Table 1). Similar to the reaction of free diarylboronic acids, a large electronic effect was observed from aryl chlorides. For example, aryl chlorides bearing an electron-deficient benzene ring reacted smoothly with **B-5a** to give biaryl products in excellent yields (Entries 1–9).

However, reaction of electron-rich 4-(benzyloxy)phenyl chloride (**Cl-11**) with **B-5a** became rather sluggish under the model reaction conditions to offer biaryl **P-11** in just 11% yield although the high yields could be restored in the reaction of electron-rich aryl chlorides by using 1mol% catalyst loading under the otherwise identical conditions (Entries 10–19). Obviously, steric hindrance from a small ortho-substituent in these electron-deficient aryl chlorides could be overcome since the yields of biaryl products just slightly decreased compared with those with a substituent at para- or meta-positions. Compared with electron-deficient ones, steric hindrance of electron-rich aryl chlorides affected their coupling remarkably. For example, *o*-tolylchloride and *o*-methoxylphenyl chloride reacted to give biaryl products 2-methylbiphenyl (**P-13**, 72%) and 2-phenylanisole (**P-16**, 62%), in significantly lower yields than their para-isomers (Entries 12 and 15). The yield further decreased to 42% in the reaction of 2,6-dimethylphenyl chloride (Entry 13).

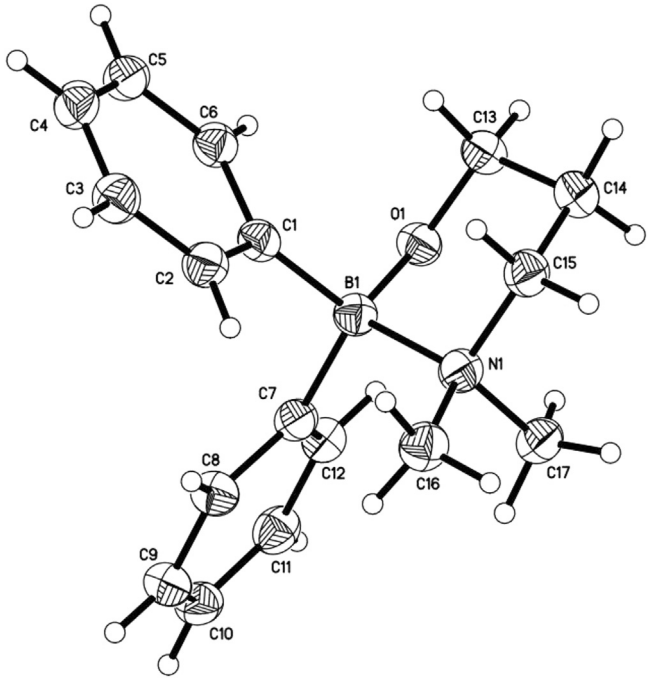


Fig. 1. An ORTEP view of the molecular structure of **B-5a**. B(1)-O(1) 1.4542(16)Å, B(1)-N(1) 1.7095(17)Å, B(1)-C(1) 1.6425(18)Å, B(1)-C(7) 1.6265(18)Å; O(1)-B(1)-C(7) 108.84(10)°, O(1)-B(1)-C(1) 112.19(10)°, C(7)-B(1)-C(1) 110.97(10)°, O(1)-B(1)-N(1) 102.86(9)°, C(7)-B(1)-N(1) 107.80(10)°, C(1)-B(1)-N(1) 113.76(10)°.