Cent. Eur. J. Chem. • 8(4) • 2010 • 725–731
DOI: 10.2478/s11532-010-0076-1

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Central European Journal of **Chemistry**

PXPd-catalyzed borylation of aniline derivatives

Invited Paper

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Received 09 January 2010; Accepted 24 February 2010

Abstract: Addition of pinacolborane ($HBO_2C_2Me_4$) to 2-iodoaniline can be catalyzed using a number of palladium complexes, including $[(t\text{-}Bu)_2PCl]_2PdCl_2$ (PXPd), to give the corresponding boronate ester 2-$H_2NC_6H_4(BO_2C_2Me_4)$ in excellent yields. The PXPd system could also be used in the catalyzed borylation of substituted anilines to give the corresponding aminoboronate esters in moderate to high yields.

Keywords: *Boron • Borylation • Catalysis • Cross-coupling • Palladium*

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1. Introduction

Compounds containing boronic acids ($RB(OH)_2$) or boronate esters ($RB(OR')_2$) have received considerable attention in catalyzed carbon-carbon bond formation reactions [1], solid-phase synthesis [2], macrocyclic chemistry [3], organometallic and organic synthesis [4], and as glucose sensors for diabetes therapy [5]. Interest in these compounds also arises from their potent biological activities [6]. Traditionally, arylboron compounds have been prepared by the transmetalation between aryllithium or –magnesium reagents and boron compounds that have good leaving groups such as alkoxy moieties [7]. In recent years, however, the use of palladium catalyzed borylations has proven to be a more convenient procedure for preparing arylboronate esters [8]. While reactive functional groups such as primary amines have proven problematic, elegant studies by Baudoin and co-workers [8b] have shown that 2-bromoaniline can be converted into the corresponding ortho boronate ester in good yields by addition of pinacolborane (HBpin, pin = $O_2C_2Me_4$) using a palladium catalyst system containing the monodentate phosphine ligand 2-(dicyclohexylphosphino)biphenyl (DCPB). Optimal yields for these reactions have been reported using dioxane as the solvent. Our interest in generating aminoboron compounds, along with the importance of these compounds in organic synthesis, prompted us to examine alternate routes to boronated aniline derivatives.

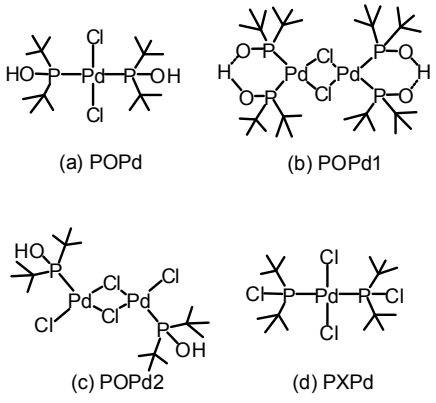

Figure 1. Structures of several palladium(II) complexes employed in this study.

2. Experimental Procedure

2.1. Materials and measurements

Reagents and solvents were purchased from Aldrich Chemicals. NMR spectra were recorded on a JEOL JNM-GSX270 FT spectrometer. ^{1}H-NMR chemical shifts are reported in parts per million (ppm) and are referenced to residual solvent protons in deuterated solvent at 270 MHz. ^{11}B-NMR

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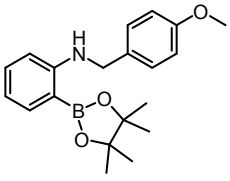
chemical shifts are reported in ppm and are referenced to BF_3·OEt_2 as an external standard at 87 MHz. ^{13}C-NMR chemical shifts are reported in ppm and are referenced to solvent carbon resonances at 68 MHz. ^{19}F-NMR spectra were recorded on a Varian Mercury Plus 200 NMR spectrometer and are reported in ppm and referenced to CF_3CO_2H as an external standard at 188 MHz. Multiplicities are reported as singlet (s), doublet (d), triplet (t), multiplet (m), overlapping (ov), and broad (br). Infrared spectra were obtained using a Mattson Genesis II FT-IR spectrometer and are reported in cm^{-1}. Melting points were measured uncorrected with a Mel-Temp apparatus. GC-MS analyses were conducted using a Varian Saturn 2000 GC/MS/MS coupled to a CP-3800 GC. The GC was equipped with the 1177 injection port connected to a SPB-1 (Supelco) fused silica column (30 m×0.25 mm i.d.×0.25 µm). The GC-MS spectrometer is controlled by the Saturn Workstation software, Version 5.51. Microanalyses for C, H, and N were carried out at Guelph Chemical Laboratories (Guelph, Ontario). Imines and the corresponding benzylamines were synthesized as reported previously [9].

2.2. Synthesis

Under an atmosphere of dinitrogen, a 1 mL toluene solution of pinacolborane (380 mg, 3.00 mmol) was added to a stirred 4 mL toluene solution of the appropriate iodoaniline (1.00 mmol), triethylamine (400 mg, 4.00 mmol), and PXPd (12 mg, 0.02 mmol). The mixture was heated at reflux for 2 h. Following the addition of a 5 mL saturated aqueous solution of NH_4Cl, the aqueous phase was extracted with three 10 mL portions of Et_2O and the organic phase dried over $MgSO_4$. Upon filtration and removal of solvent under vacuum, the resulting oil was dissolved in a minimum amount of hexanes and stored at 0°C. The resulting precipitate was collected by suction filtration.

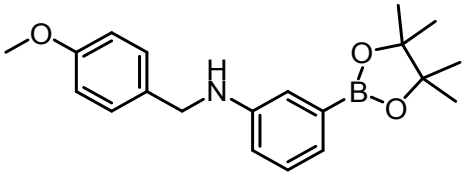
N-(4-Methoxybenzyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

Yield: 56% of a yellow oil. ^{1}H-NMR ($CDCl_3$) δ: 1.32 (s, 12H, pin), 3.80 (s, 3H, C*H*$_3$), 4.33 (d, *J* = 5.2 Hz, 2H, C*H*$_2$), 6.29 (br t, *J* = 5.2 Hz, 1H, N*H*), 6.52 (d, *J* = 8.2 Hz, 1H, Ar), 6.63 (t of d, *J* = 7.4, 0.8 Hz, 1H, Ar), 6.87 (d, *J* = 8.7 Hz, 2H, Ar), 7.24-7.31 (ov m, 3H, Ar), 7.65 (d of d, *J* = 7.4, 1.7 Hz, 1H, Ar). ^{11}B-NMR ($CDCl_3$) δ: 31(br). ^{13}C{^{1}H}-NMR ($CDCl_3$) δ: 25.0, 47.0, 55.4, 83.6, 109.9, 110 (br, *C*B), 114.0, 115.8, 128.2, 131.9, 133.2, 137.2, 154.5, 158.7. FT-IR (Nujol): 3404 (m, NH). Anal. Calcd. for $C_{20}H_{26}BNO_3$ (339.28): C, 70.80; H, 7.74 N, 4.13; Found: C, 71.15; H, 8.02; N, 3.97.



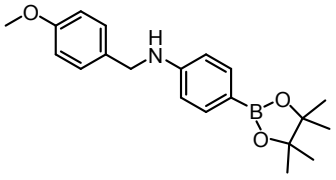
N-(4-Methoxybenzyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

Yield: 79%; mp 105°C. ^{1}H-NMR ($CDCl_3$) δ: 1.35 (s, 12H, pin), 3.80 (s, 3H, C*H*$_3$), 3.82 (br s, 1H, N*H*), 4.29 (br s, 2H, C*H*$_2$), 6.74 (m, 1H, Ar), 6.91 (d, *J* = 8.2 Hz, 2H, Ar), 7.13 (s, 1H, Ar), 7.16-7.22 (ov m, 2H, Ar), 7.31 (d, *J* = 8.2 Hz, 2H, Ar). ^{11}B-NMR ($CDCl_3$) δ: 30 (br). ^{13}C{^{1}H}-NMR ($CDCl_3$) δ: 24.8, 47.8, 55.3, 83.7, 114.0, 115.5, 119.2, 124.0, 128.7, 128.9, 130 (br, *C*B), 131.4, 147.6, 158.8. FT-IR (Nujol): 3398 (m, NH). Anal. Calcd. for $C_{20}H_{26}BNO_3$ (339.28): C, 70.80; H, 7.74 N, 4.13; Found: C, 71.22; H, 8.23; N, 4.02.



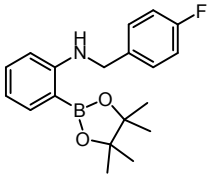
N-(4-Methoxybenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

Yield: 83%; mp 116-118°C. ^{1}H-NMR ($CDCl_3$) δ: 1.30 (s, 12H, pin), 3.80 (s, 3H, C*H*$_3$), 4.15 (br s, 1H, N*H*), 4.26 (br s, 2H, C*H*$_2$), 6.59 (d, *J* = 8.4 Hz, 2H, Ar), 6.86 (d, *J* = 8.4 Hz, 2H, Ar), 7.24 (d, *J* = 8.4 Hz, 2H, Ar), 7.62 (d, *J* = 8.4 Hz, 2H, Ar). ^{11}B-NMR ($CDCl_3$) δ: 32 (br). ^{13}C{^{1}H}-NMR ($CDCl_3$) δ: 24.9, 47.6, 55.4, 83.3, 112.3, 114.1, 129.0, 130 (br, *C*B), 130.8, 136.4, 150.3, 159.0. FT-IR (Nujol): 3373 (m, NH). Anal. Calcd. for $C_{20}H_{26}BNO_3$ (339.28): C, 70.80; H, 7.74; N, 4.13; Found: C, 70.31; H, 8.06; N, 4.16.



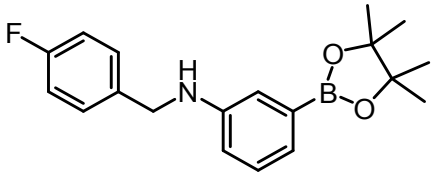
N-(4-Fluorobenzyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

Yield: 73%; mp 80-81°C. ^{1}H-NMR ($CDCl_3$) δ: 1.32 (s, 12H, pin), 4.36 (d, *J* = 5.7 Hz, 2H, C*H*$_2$), 6.31 (br t, *J* = 5.7 Hz, 1H, N*H*), 6.46 (d, *J* = 8.4 Hz, 1H, Ar), 6.63 (t, *J* = 6.7 Hz, 1H, Ar), 7.02 (m, 2H, Ar), 7.24 (t, *J* = 8.9 Hz, 1H, Ar), 7.32 (m, 2H, Ar), 7.65 (d of d, *J* = 7.4, 1.7 Hz, 1H, Ar). ^{11}B-NMR ($CDCl_3$) δ: 30 (br). ^{13}C{^{1}H}-NMR ($CDCl_3$) δ: 25.0, 46.9, 83.6, 109.9, 110 (br, *C*B), 115.4 (d, J_{CF} = 21 Hz), 116.0, 128.6 (d, J_{CF} = 8 Hz), 133.2, 135.6 (d, J_{CF} = 3 Hz), 137.2, 154.3, 161.9 (d, J_{CF} = 246 Hz, *C*F). ^{19}F{^{1}H}-NMR ($CDCl_3$) δ: -116.7. FT-IR (Nujol): 3415 (m, NH). Anal. Calcd. for $C_{19}H_{23}BFNO_2$ (327.24): C, 69.73; H, 7.10; N, 4.28; Found: C, 70.10; H, 6.86; N, 4.55.



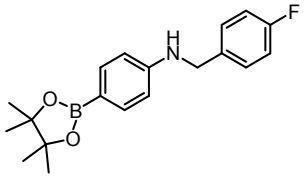
N-(4-Fluorobenzyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

Yield: 83%; mp 64-66°C. ^{1}H-NMR ($CDCl_3$) δ: 1.29 (s, 12H, pin), 3.94 (br s, 1H, N*H*), 4.30 (s, 2H, CH_2), 6.68 (m, 1H, Ar), 7.00 (m, 2H, Ar), 7.11-7.18 (ov m, 3H, Ar), 7.31 (m, 2H, Ar). ^{11}B-NMR δ: 31 (br). ^{13}C{^{1}H}-NMR δ: 25.0, 47.7, 83.8, 115.5 (d, J_{CF} = 21 Hz), 115.6, 119.4, 124.3, 128.9, 129.2 (d, J_{CF} = 8 Hz), 130 (br, *C*B), 135.3 (d, J_{CF} = 3 Hz), 147.5, 162.1 (d, J_{CF} = 245 Hz, *C*F). ^{19}F{^{1}H}-NMR δ: -114.6. FT-IR (Nujol): 3361 (m, NH). Anal. Calcd. for $C_{19}H_{23}BFNO_2$ (327.24): C, 69.73; H, 7.10; N, 4.28; Found: C, 69.43; H, 7.10; N, 4.50.



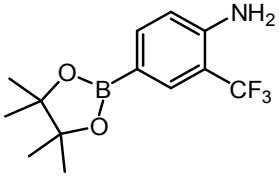
N-(4-Fluorobenzyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

Yield: 85%; mp 137-138°C. ^{1}H-NMR ($CDCl_3$) δ: 1.28 (s, 12H, pin), 4.22 (br t, *J* = 5.5 Hz, N*H*), 4.32 (d, *J* = 5.5 Hz, 2H, CH_2), 6.58 (d, *J* = 8.4 Hz, 2H, Ar), 7.00 (m, 2H, Ar), 7.28 (m, 2H, Ar), 7.62 (d, *J* = 8.4 Hz, 2H, Ar). ^{11}B-NMR δ: 30 (br). ^{13}C{^{1}H}-NMR δ: 24.9, 47.1, 83.3, 112.0, 115.5 (d, J_{CF} = 21 Hz), 129.0 (d, J_{CF} = 8 Hz), 130 (br, *C*B), 134.8 (d, J_{CF} = 3 Hz), 136.5, 150.4, 162.2 (d, J_{CF} = 246 Hz, *C*F). ^{19}F{^{1}H}-NMR δ: -115.9. FT-IR (Nujol): 3363 (m, NH). Anal. Calcd. for $C_{19}H_{23}BFNO_2$ (327.24): C, 69.73; H, 7.10; N, 4.28; Found: C, 69.30; H, 7.05; N, 4.46.



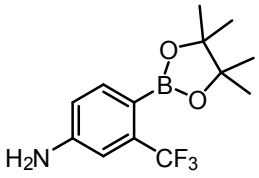
2-(Trifluoromethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzeneamine

Yield: 43%; mp 72-74°C. ^{1}H-NMR ($CDCl_3$): δ 1.32 (s, 12H, pin), 4.35 (br s, 2H, NH_2), 6.70 (d, *J* = 8.2 Hz, 1H, Ar), 7.71 (d, *J* = 8.2 Hz, 1H, Ar), 7.89 (s, 1H, Ar). ^{11}B-NMR ($CDCl_3$): δ 30 (br). ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 25.0, 83.9, 113.3 (q, J_{CF} = 30 Hz), 115.5 (br, *C*B), 116.3, 125.3 (q, J_{CF} = 272 Hz, *C*F_3), 133.9 (q, J_{CF} = 5 Hz), 139.5, 147.1 (q, J_{CF} = 2 Hz). ^{19}F{^{1}H}-NMR ($CDCl_3$): δ -62.9. FT-IR: 3240 (m, NH), 3367 (m, NH), 3494 (m, NH). Anal. Calcd. for $C_{13}H_{17}NO_2BF_3$ (287.12): C, 54.38; H, 5.98; N, 4.88; Found: C, 54.22; H, 6.20; N, 4.87.



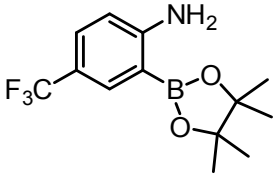
3-(Trifluoromethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzeneamine

Yield: 20%; mp 102-103°C. ^{1}H-NMR ($CDCl_3$): δ 1.33 (s, 12H, pin), 3.94 (br s, 2H, NH_2), 6.75 (dd, *J* = 8.0, 2.2 Hz, 1H, Ar), 6.94 (d, *J* = 2.2 Hz, 1H, Ar), 7.59 (d, *J* = 8.0 Hz, 1H, Ar). ^{11}B-NMR ($CDCl_3$): δ 30 (br). ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 25.1, 83.9, 112.0 (q, J_{CF} = 5 Hz), 116.3 (br, *C*B), 116.4, 124.3 (q, J_{CF} = 272, *C*F_3), 135.8 (q, J_{CF} = 32 Hz), 137.4, 148.3. ^{19}F{^{1}H}-NMR ($CDCl_3$): δ -60.5. FT-IR (Nujol): 3242 (m, NH), 3375 (m, NH), 3483 (m, NH). Anal. Calcd. for $C_{13}H_{17}NO_2BF_3$ (287.12): C, 54.38; H, 5.98; N, 4.88; Found: C, 54.83; H, 5.53; N, 4.39.



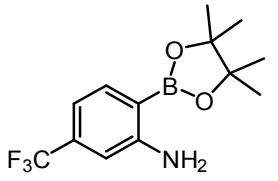
4-(Trifluoromethyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

Yield: 71%; mp 117-118°C. ^{1}H-NMR ($CDCl_3$): δ 1.35 (s, 12H, pin), 5.07 (br s, 2H, NH_2), 6.59 (d, *J* = 8.6 Hz, 1H, Ar), 7.41 (dd, *J* = 8.6, 2.4 Hz, 1H, Ar), 7.86 (d, *J* = 2.4 Hz, 1H, Ar). ^{11}B-NMR ($CDCl_3$): δ 30 (br). ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 25.4, 84.1, 110.3 (br, *C*B), 114.2, 118.6 (q, J_{CF} = 33 Hz), 125.1 (q, J_{CF} = 271 Hz, *C*F_3), 129.6 (q, J_{CF} = 3 Hz), 134.3 (q, J_{CF} = 4 Hz), 156.2. ^{19}F{^{1}H}-NMR ($CDCl_3$): δ -61.5. FT-IR (Nujol): 3376 (m, NH), 3474 (m, NH). Anal. Calcd. for $C_{13}H_{17}NO_2BF_3$ (287.12): C, 54.38; H, 5.98; N, 4.88; Found: C, 54.41; H, 6.10; N, 4.85.



5-(Trifluoromethyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

Yield: 69%; mp 64-65°C. ^{1}H-NMR ($CDCl_3$): δ 1.35 (s, 12H, pin), 4.93 (br, 2H, NH_2), 6.80 (s, 1H, Ar), 6.87 (d, *J* = 7.8 Hz, 1H, Ar), 7.70 (d, *J* = 7.8 Hz, 1H, Ar). ^{11}B-NMR ($CDCl_3$): δ 30 (br). ^{13}C{^{1}H}-NMR ($CDCl_3$): δ 25.0, 84.2, 111.1 (q, J_{CF} = 4 Hz), 112.2 (br, *C*B), 113.1 (q, J_{CF} = 4 Hz), 124.3 (q, J_{CF} = 273 Hz, *C*F_3), 134.5 (q, J_{CF} = 32 Hz), 137.7, 153.9. ^{19}F{^{1}H}-NMR ($CDCl_3$): δ -64.0. FT-IR (Nujol): 3398 (m, NH), 3460 (m, NH), 3504 (m, NH). Anal. Calcd. for $C_{13}H_{17}NO_2BF_3$ (287.12): C, 54.38; H, 5.98; N, 4.88; Found: C, 54.49; H, 5.99; N, 4.89.



2.3. X-ray crystallography

Crystals of 2-APBpin suitable for an X-ray diffraction study were grown from a saturated hexane solution at 5°C. Single crystals were coated with Paratone-N oil, mounted using a glass fibre and frozen in the cold stream of the goniometer. A hemisphere of data were collected on a Bruker AXS P4/SMART 1000 diffractometer using ω and θ scans with a scan width of 0.3° and exposure time of 10 s. The detector distance was 5 cm. The data were reduced [10a] and corrected for absorption [10b]. The structures were solved by direct methods and refined by full-matrix least squares on F^2 [10c]. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were found in Fourier difference maps and refined isotropically.

3. Results and Discussion

Recently, Li [11] demonstrated that air-stable Pd/phosphinous acid complexes $[(t\text{-Bu})_2P(OH)]_2PdCl_2$ (abbreviated POPd, Fig. 1a) and $\{[(t\text{-Bu})_2PO\cdots H\cdots OP(t\text{-Bu})_2]PdCl\}_2$ (abbreviated POPd1, Fig. 1b) are efficient catalysts for the Suzuki-Miyaura cross coupling of aryl chlorides. These compounds have also shown recent utility as catalysts in a number of reactions [12] including the NaOH-promoted cross-coupling of arylsiloxanes with aryl chlorides and bromides in water [12a]. We have found that reactions of commercially-available 2-iodoaniline with HBpin using these catalyst systems, without additional phosphine ligands, also gave good yields of the boron-containing aniline derivative 2-(4,4,5,5-tetramethyl-[1,3,2]-dioxaborolan-2-yl)phenylamine (2-APBpin) (Table 1, entries 4 & 6, respectively) [8b,d]. As seen in the seminal work by Baudoin and co-workers [8b], optimal yields were achieved using 3 equivalents of HBpin and 4 equivalents of triethylamine as the base. The synthesis of aminoboron derivatives is of singular interest, as these compounds are remarkably potent enzyme inhibitors [6j] and many have been investigated extensively for their application in boron neutron capture therapy [6c]. The formation of 2-APBpin in these catalyzed borylations was confirmed by melting point, multinuclear NMR spectroscopy and GC-MS data. The structural analysis of this aminoboron compound was carried out by an X-ray diffraction study (Fig. 2) and crystallographic data presented in Table 2. The B–O bond distances of 1.3690(16) and 1.3705(16) Å are typical for those observed in other Bpin structures where the boron is three coordinate [13]. The molecule showed no appreciable intra- or intermolecular interaction between the Lewis acidic boron atom and the basic amine group. Such interactions may be responsible for observed antimicrobial properties in related diaminoboron compounds [6f].

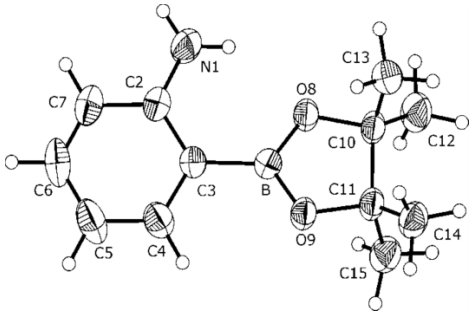
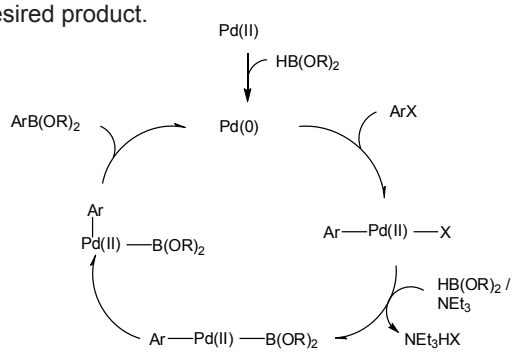


Figure 2. The molecular structure of 2-APBpin with displacement ellipsoids shown at 30% probability level. Selected bond distances (Å) and angles (°): B-O(8) 1.3690(16), B-O(9) 1.3705(16), B-C(3) 1.5467(18), N(1)-C(2) 1.3622(18), B-N(1) 2.974(2); O(8)-B-O(9) 112.76(11), O(8)-B-C(3) 123.99(11), O(9)-B-C(3) 123.22(11).

These borylation reactions are believed to proceed *via* initial reduction of the palladium(II) salt, by the borane, to an active palladium(0) species [1]. Once reduced, oxidative addition of the aryl halide followed by transmetallation of the borane with the Pd-X moiety gives a palladium boryl (Pd-$B(OR)_2$) intermediate, which must isomerize before reductive elimination can give the desired aryl boronate ester product (Scheme 1). It has also been postulated that once the palladium(0) species is present, oxidative addition of the dialkoxyborane species occurs first to give a reactive palladium hydrido boryl intermediate. This transient species can rapidly go through a transmetallation of the aryl halide, followed by isomerization and reductive elimination to give the desired product.



Scheme 1. A plausible catalytic cycle for the borylation of aryl halides.

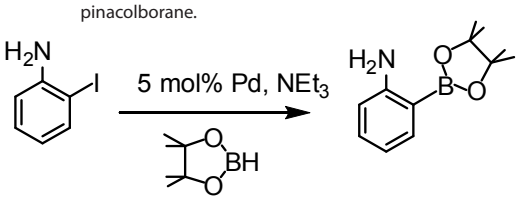
While yields are moderate for reactions using the palladium-phosphinous acid complexes, excess HBpin is required to facilitate this reaction. This is presumably due to HBpin reacting with the polar P-OH groups. Indeed, we have found that stoichiometric addition of HBpin to these compounds led to extensive degradation of the borane to give H_2 and pinBOBpin [14]. Further work is needed, however, to elucidate the fate of the palladium complexes in these reactions. As deleterious reaction

of the HBpin with the phosphinous acid groups led to degradation of the borane and catalyst, we decided to examine the analogous reactions using the structurally related phosphine chloride complexes. Remarkably, we found that reactions using $[(t\text{-Bu})_2PCl]_2PdCl_2$ (abbreviated PXPd, Fig. 1d) gave near quantitative conversion of 2-iodoaniline to 2-APBpin (entries 1 & 2) without significant decomposition of either the catalyst or the dialkoxyborane. Reactions run in toluene gave slightly greater yields than those reactions run in dioxane. Unfortunately, significantly lower yields of the desired product were obtained in reactions run in THF (entry 9) or those using the dimeric complex $\{[(t\text{-Bu})_2PCl]PdCl\}_2$ (abbreviated PxPd2, entry 3). Interestingly, reactions with the bulky DCPB/$Pd(OAc)_2$ system (entry 7), also gave low yields and attempts to use a phosphine free catalyst system ($Pd(OAc)_2$) afforded none of the desired products (entry 10). Not surprisingly, attempts to catalyze this reaction using other metal complexes, such as $Ni(OAc)_2$ and $RhCl(PPh_3)_3$, proved unsuccessful (entries 11 & 12, respectively).

Encouraged by these results, we then decided to investigate the borylation of other iodoaniline derivatives (Table 3). Reactions using 3 equivalents of HBpin and the PXPd precatalyst in toluene gave good to excellent yields of the desired boronate ester compounds. Reactions of bulky ortho iodoanilines (entries 4 & 7) gave lower yields than their meta and para counterparts presumably due to the increased steric bulk in these systems. Substitution on the benzyl group did not have a significant effect on yields. While similar yields were obtained with the analogous bromides, we did not observe any significant product formation for reactions with the corresponding chlorides. Benzylamines containing boron groups have been examined recently for potential antifungal properties [9].

We then examined the borylation of commercially-available aniline derivatives containing electron-withdrawing trifluoromethyl groups. The generation of the corresponding boronate ester compounds has been of recent interest in the preparation of MRI probes [15], electroactive luminophores [16], and in the preparation of pharmaceutically relevant dihydroquinolones [17]. As shown in Scheme 2, yields of isolated product are moderate if the bromide is ortho to the amine group, where the position of the CF_3 has little effect. Yields are much lower, however, if the bromide group is para to the amine where the lowest yield was found in the case where the CF_3 is ortho to the leaving group. Attempts to improve yields using other metal complexes proved unsuccessful.

Table 1. Metal catalyzed borylation of 2-iodoaniline with pinacolborane.



Entry	Catalyst	Solvent	Yield[a,b]
1	PXPd	toluene	>95
2	PXPd	dioxane	95
3	PXPd2	dioxane	75
4	POPd	dioxane	75
5	$Pd(OAc)_2 + 4PPh_3$	dioxane	75
6	POPd1	dioxane	65
7	$Pd(OAc)_2$ + 4DCPB	dioxane	30
8	POPd2	dioxane	30
9	PXPd	THF	10
10	$Pd(OAc)_2$	dioxane	0
11	$Ni(OAc)_2$	dioxane	0
12	$RhCl(PPh_3)_3$	dioxane	0

[a] Yields of products as determined by GC-MS and analysis of integrated ^{1}H-NMR spectra.

[b] Products are characterized by spectral analysis (^{1}H- and ^{11}B-NMR and GC-MS) and compared with authentic sample.

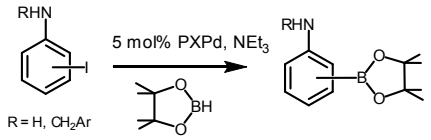
Table 2. Crystallographic data collection parameters for 2-APBpin.

CCDC deposit no.	241954
Chemical formula	$C_{12}H_{18}BNO_2$
Formula mass	219.08
Crystal system	monoclinic
Space group	P2(1)/c
a (Å)	10.0970(13)
b (Å)	9.9124(13)
c (Å)	13.2168(18)
β (°)	109.795(2)
V (Å^3)	1244.6(3)
Z	4
D_{calcd} (mg m^{-3})	1.169
Crystal dimensions (mm^3)	0.40×0.225×0.20
T (K)	198(1)
Radiation	MoKα (λ = 0.71073)
μ (mm^{-1})	0.077
Total reflections collected	8345
Total unique reflections	2799
No. of variables	217
R_{int}	0.0256
θ (°)	2.14 to 27.49
Largest diff peak & hole (e Å^{-3})	0.209 and -0.168
GoF on F^2	1.073
R_1[a] [I>2σ(I)]	0.0404
wR_2[b] (all data)	0.1111

[a] $R_1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$.

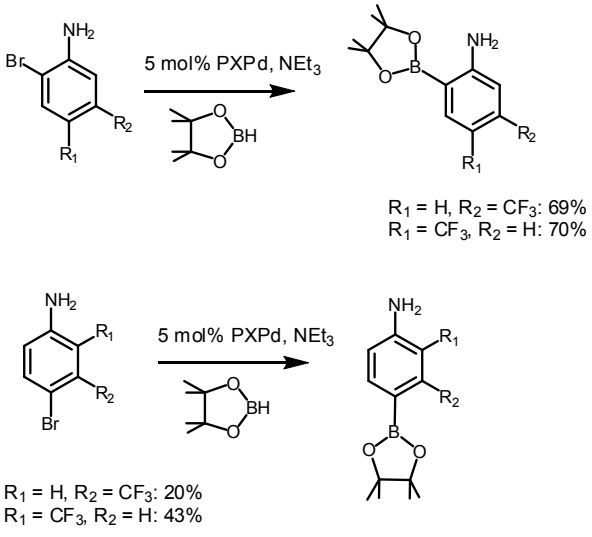
[b] $wR_2 = (\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[wF_o^4])^{1/2}$, where $w = 1/[\sigma^2(F_o^2) + (0.0498 * P)^2 + (0.1942 * P)]$ where $P = (\max(F_o^2, 0) + 2 * F_c^2)/3$.

Table 3. PXPd catalyzed borylation of substituted iodoanilines.



Entry	R	I	Yield[a]
1	H	ortho	>95
2	H	meta	95
3	H	para	83
4	4-MeOC$_6$H$_4$CH$_2$	ortho	56
5	4-MeOC$_6$H$_4$CH$_2$	meta	79
6	4-MeOC$_6$H$_4$CH$_2$	para	83
7	4-FC$_6$H$_4$CH$_2$	ortho	73
8	4-FC$_6$H$_4$CH$_2$	meta	83
9	4-FC$_6$H$_4$CH$_2$	para	85

[a] Reactions were conducted in toluene and products were characterized by ^{1}H-, ^{11}B-, ^{13}C-, and ^{19}F-NMR spectroscopy, FT-IR, and elemental analysis.



Scheme 2. Borylation of aniline derivatives containing trifluoromethyl groups.

4. Conclusions

In summary, we have shown that PXPd can be used to effectively catalyze the borylation of various aniline derivatives with excess pinacolborane to give the corresponding boron containing aniline derivatives. Although other Pd/phosphinous acid complexes could be used to catalyze this transformation, reactions with PXPd gave the best yields and less decomposition of the starting borane. No additional phosphine is needed to facilitate these reactions. Future work in this area will be to examine the analogous reactions using diboron sources in an effort to improve atom economy, the results of which will be published in due course.

Acknowledgements

The authors thank the Natural Science and Engineering Research Council of Canada (SAW), the Canada Research Chairs Program/Canadian Foundation for Innovation/Atlantic Innovation Foundation and Mount Allison University for financial support. We also thank Dr. George Li (CombiPhos Catalysts, Inc.) for the most generous gift of palladium catalysts and anonymous reviewers for helpful comments.

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