Alkylboranes in the Suzuki−Miyaura Coupling: Stereochemical and Mechanistic Studies

Karl Matos and John A. Soderquist*

Department of Chemistry, University of Puerto Rico, Rio Piedras, Puerto Rico 00931-3346

Received September 10, 1997 (Revised Manuscript Received December 1, 1997)

Both *erythro* and *threo* isomers of *B*-(3,3-dimethyl-1,2-dideuterio-1-butyl)-9-BBN (**6**) were prepared from 3,3-dimethyl-1-butyne (**4**) through a hydroboration−deuteronolysis−hydroboration sequence employing first 9-BBN-H and then 9-BBN-D, or in reverse order, respectively. Employing the Whitesides protocol, the stereochemistry of B → Pd alkyl group transfer in the Suzuki−Miyaura coupling of **6** to PhBr has been found to occur with complete retention of configuration with respect to carbon. For the coupling process, the Lewis acidity of the boron plays an important role with *B*-alkyl-9-BBN (**10**) forming $[HO(R)\text{-}9\text{-}BBN]^{-1}$ (**12**) with the added base, in marked contrast to their *B*-alkyl-9-oxa-10-borabicyclo[3.3.2]decane counterparts (R-OBBD, **11**) which do not. This behavior parallels their coupling rates with the exclusive reaction of **10** over **11** in competitive experiments. Five five possible roles were demonstrated for the added base in the coupling: (1) the formation of **12**, (2) the hydrolysis of $Ph(Ph_3P)_2PdBr$ (**14**) to provide monomeric $Ph(Ph_3P)_2PdOH$ (**15**), (3) the complexation of $HOBR_2$ byproducts which can compete with **10** for base, (4) accelerated coupling rates for **11**, and (5) catalyst regeneration. Kinetic studies reveal that the couplings are zero-order in the borane but for **10** exhibit a first-order dependence on [PhBr] (i.e., oxidative addition), while for **11** exhibit a first-order dependence on $[OH^{-1}]$ (i.e., Pd(II)X hydrolysis). These data are interpreted in terms of attack of **14** by **12** to form a hydroxo μ_2-bridged intermediate **8(a)** [PhL_2 Pd ← (OH)BR(9-BBN)]. This provides the precursor to transmetalation through a four-centered transition state **9**. Because the analogous hydroxyborate complex is absent for **11**, **14** is hydrolyzed by OH^{-1} forming **15** in a slower process, with this ultimately reacting with **11** to form a related intermediate **8(b)** [PhL_2 Pd(OH) → BR(OBBD)] which also collapses to products through **9**.

The palladium-catalyzed coupling of organic halides or triflates with organoboranes under basic conditions (Suzuki−Miyaura coupling) provides a highly versatile method for the construction of new carbon−carbon bonds that tolerates many functional groups.[1] By analogy to related processes,[2] the coupling of organoboranes is believed to proceed through a catalytic cycle involving three basic steps: (1) the oxidative addition of the carbon electrophile to the zerovalent and coordinationally unsaturated PdL_2, where L is normally a phosphine ligand such as PPh_3, (2) the transmetalation of a nucleophilic carbon from boron to the $R'PdXL_2$, and (3) the rapid reductive elimination of the cross-coupling product with the regeneration of the PdL_2 catalyst (Figure 1).[1] It is the transmetalation step that differentiates one organometallic process from another. While tetraorganoorganoborate complexes ($[BR_4]^{-1}$) do undergo cross coupling,[1,3] the organoboranes (BR_3) themselves do not normally couple without added base, a feature of this coupling that is not fully understood.

The catalytic cycle illustrated in Figure 1 only superficially represents what is quite clearly a highly complex process. The introduction of both vinylic (alkynyl or aryl) and cyclopropyl groups can be accomplished through either of the combining partners, and the stereochemistry of the starting halide (or triflate) and borane is retained

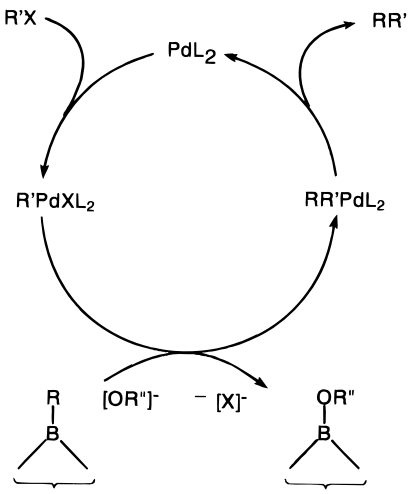


Figure 1. Suzuki−Miyaura catalytic cycle.

in the coupling products.[4] However, in alkyl group couplings, the specific combinations used in the couplings can be critical to the success of the process. For example, whereas primary alkyl groups can be efficiently coupled through the organoborane moiety, the coupling of alkyl iodides is plagued by competitive reduction and elimination processes.[5] Moreover, the coupling of secondary

(1) Miyaura, N.; Suzuki, A. *Chem. Rev. (Washington, D.C.)* **1995**, *95*, 2457.
(2) Farina, V.; Krishnamurthy, V.; Scott, W. J. In *Organic Reactions;* Paquette, L. A., Ed.; John Wiley & Sons: Inc.: New York, 1997; pp 1−652.
(3) Negishi, E. In *Aspects of Mechanism and Organometallic Chemistry;* Brewster, J. H., Ed.; Plenum Press: New York, 1978; p 285.
(4) (a) Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, *20*, 3437. (b) Hildebrand, J. P.; Marsden, S. P. *Synlett* **1996**, 893. (c) Wang, X.-Z.; Deng, M.-Z. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2663. (d) See also: Charette, A. B.; Giroux, A. *J. Org. Chem.* **1996**, *61*, 8718.
(5) Ishiyama, T.; Abe, S.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1992**, 691.

S0022-3263(97)01681-2 CCC: $15.00
Published on Web 01/22/1998

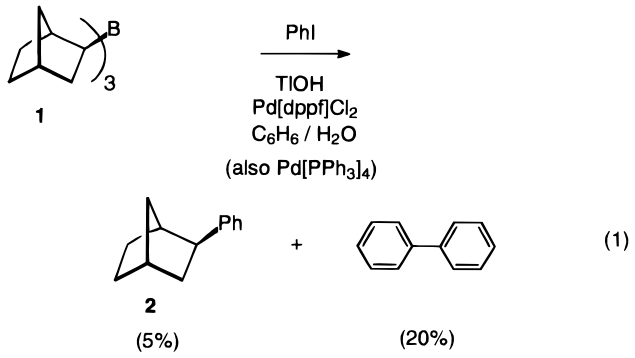
alkyl groups from organoboranes is, at best, only moderately successful.[6]

The type of organoborane employed must be also considered for the successful coupling of even simple primary alkylboranes. Either trialkylboranes (BR_3) or borinate esters (R_2BOR') are efficient coupling partners under the standard basic (NaOH) conditions.[1] However, more oxygenated derivatives (i.e., boronates ($RB(OR')_2$) require thallium bases (e.g., TlOH).[7,8] Thallium(I) is thought to remove halide as TlX, producing a PdOH species that accelerates the transmetalation of these weakly Lewis acidic boranes.[8] Because the successful coupling of alkylboranes appeared to us to be particularly sensitive to the specific conditions and substrates employed, we chose to examine this process under the standard conditions (i.e. $Pd(PPh_3)_4$, NaOH) to determine the following: (1) the stereochemistry of alkyl group transfer,[9] (2) the effect of alkyl versus alkoxy boron ligation on the rate of coupling, (3) the actual role of added base, and (4) the rate-limiting step in the catalytic process.

Results and Discussion

The Stereochemistry of Transmetalation. As the most straightforward approach to determining the stereochemistry of the B → Pd alkyl group transfer, we chose to examine the coupling of a stereodefined tri(*sec*-alkyl)-borane using $PdCl_2$ (dppf) catalyst,[6] conditions that were reported to provide optimal coupling. Trinorbornylborane (**1**, 97% exo) was prepared, and its cross-coupling with PhI was examined using TlOH as base in a C_6H_6/H_2O medium. After 12 h, only a 5% (GC) yield of the desired 2-phenylnorbornane (**2**, >97% exo)[10] together with the homocoupled product, biphenyl (20%), was obtained (eq 1). The use of $Pd(PPh_3)_4$ as the coupling catalyst gave identical results. This and other equally disappointing results with secondary alkylboranes[11] led us investigate primary alkylboranes whose couplings are more efficient.

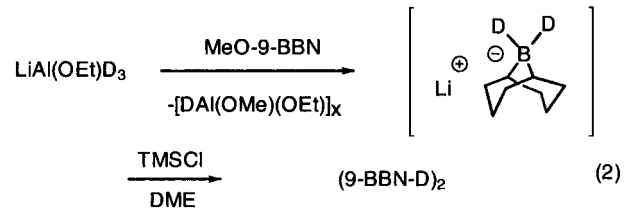
We found the Whitesides protocol[12] to be a particularly attractive approach to determine the stereochemistry of the transmetalation of primary alkylboranes. The method



(1)

takes advantage of preferential population of the *anti-periplanar* conformation for bulky 1,2-disubstituted ethanes. This results in characteristic *vicinal* proton coupling constants that, for their 1,2-dideuterio derivatives, are clearly observable in their ^{2}H-decoupled 500 MHz ^{1}H NMR spectra (cf. Scheme 1). Since both *erythro* and *threo* derivatives of *t*-BuCHDCHDPh (**3**) were known from Kabalka's studies on the stereochemistry of acyclic hydroboration,[12b] we selected these known systems as targets for the Suzuki−Miyaura process.

Initially, we prepared the *cis*-alkene **5** from the semireduction of *tert*-butylacetylene (**4**) with D_2 using Lindlar catalyst (63%). However, we observed minor amounts of regioisomeric HD adducts that ultimately interfere with the interpretation of the NMR data. This was especially true for *t*-BuCHDCH$_2$Ph, which we felt could be avoided through a wholly organoborane-based approach to **3**. Toward this end, we chose to first prepare $(9\text{-BBN-D})_2$ through the reduction of MeO-9-BBN with $LiAl(OEt)D_3$, which facilitates the separation of the 9-borata complex from the insoluble $[AlD(OMe)(OEt)]_x$ (eq 2).[13] Treatment the borohydride with TMSCl pro-



(2)

duces crystalline $(9\text{-BBN-D})_2$ (31%(from DME)), which contained ~10% 9-BBN-H that arose from protic impurities in the $LiAlD_4$ employed. The deuterioboration of 3,3-dimethyl-1-butyne (**4**, 100% excess, 0 °C) with this reagent followed by deuteronolysis with HOAc-d_4 gave the *cis*-1,2-dideuterated alkene **5** (60%) (Scheme 1). The product **5** contained **7** as the only observable isotopic impurity. The hydroboration of **5** with 9-BBN-H provides the *threo* borane **6*t*** (J_{H-H} = 4.8 Hz) in 92% yield. By simply reversing the 9-BBN-H/9-BBN-D order in this sequence, the intermediate *trans*-monodeutertioalkene **7** (63%) is smoothly converted to the *erythro* borane, **6*e*** (89%, J_{H-H} = 12.9 Hz). Coupling of **6*t*** with PhBr (NaOH, THF, 65 °C, 12 h) provides **3*t*** exclusively (85% from **5**, J = 4.8 Hz)[12b] while **6*e*** gives the erythro product **3*e*** (89%, >98% *erythro*, J = 12.5 Hz) (Figure 2). Originating from our $(9\text{-BBN-D})_2$, we observed minor amounts of *t*-BuCH$_2$-CHDPh (independently prepared from the hydroboration of **7** with 9-BBN-H) in both of the coupling products (i.e.,

(6) Miyaura, N.; Ishiyama, T.; Sasaki, H., Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314.

(7) (a) Sato, M.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1989**, 1405. (b) See also: Wright, S. W.; Hageman, D. L.; McClure, L. D. *J. Org. Chem.* **1994**, *59*, 6095.

(8) Armstrong, R. W.; Beau, J.-M.; Cheon, S. H.; Christ, W. J.; Fujioka, H.; Ham, W.-H.; Hawkins, L. D.; Jin, H.; Kang, S. H..; Kishi, Y.; Martinelli, M. J.; McWhorter, W. W., Jr.; Mizuno, M.; Nakata, M.; Stutz, A. E.; Talamas, F. X.; Taniguchi, M.; Tino, J. A.; Ueda, K.; Uenishi, J.-I.; White, J. B.; Yonaga, M. *J. Am. Chem. Soc.* **1989**, *111*, 7225.

(9) The stereochemical and competitive rate studies were presented at the 213th National Meeting of the American Chemical Society, San Francisco, CA, April, 1997; ORGN 582. Professor K. A. Woerpel later informed us of his similar approach and stereochemical conclusions. We thank him for this information. Ridgway, B. H.; Woerpel, K. A. *J. Org. Chem.* **1998**, *63*, 458−460.

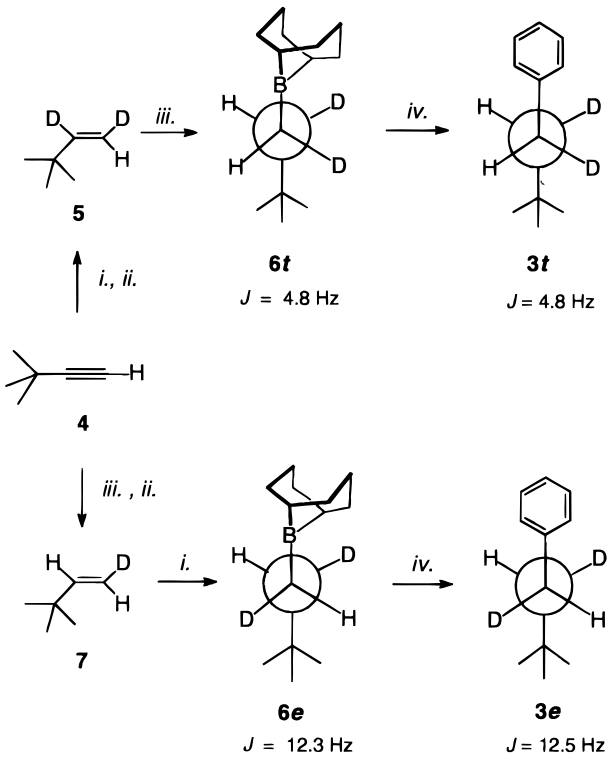
(10) (a) Carey, F. A.; Tremper, H. S. *J. Org. Chem.* **1969**, *34*, 4. (b) Schmerling, L. U. S. Patent 2480,267, 1949; *Chem. Abstr.* **1950**, *44*, 1136. (c) The use of benzene as the reaction solvent precluded its analysis as an expected reaction coproduct.[7]

(11) The reduction of PhBr to benzene was the only process observed with (*s*-Bu)$_3$B, (−)-*s*-BuB(OH)$_2$, and (±)-*s*-Bu-9-BBN under a variety of conditions and catalysts (unpublished studies with Dr. Anil M. Rane).

(12) (a) Whitesides, G. M.; Bock, P. L.; Boschetto, D. J.; Rasmussen, J. R.; Demers, J. M. *J. Am. Chem. Soc.* **1974**, *96*, 2814. (b) See also: Kabalka, G. W.; Newton, R. J., Jr.; Jacobus, J. *J. Org. Chem.* **1979**, *44*, 4185.

(13) Singaram, B.; Cole, T. E.; Brown, H. C. *Organometallics* **1984**, *3*, 1520.

Scheme 1[a]



[a] Key: (i) $(9\text{-BBN-D})_2$; (ii) CD_3COOD; (iii) $(9\text{-BBN-H}_2$; (iv) PhBr/$NaOH/Pd(PPh_3)_4$.

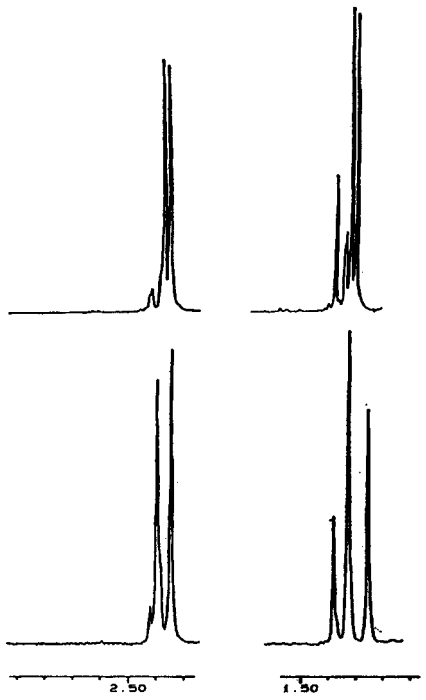
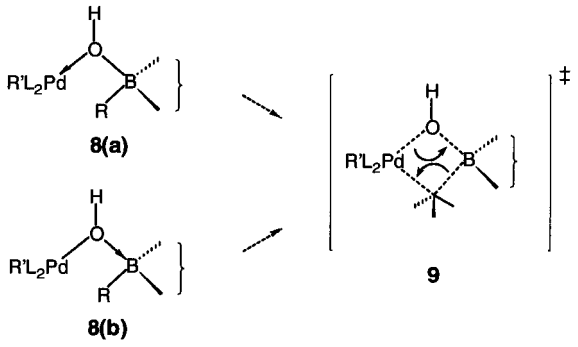


Figure 2. ^{2}H-decoupled 500 MHz ^{1}H NMR of the CHDPh (left) and CHD(*t*-Bu) (right) region for **3*t*** (above) and **3*e*** (below). Both contain $PhCHDCH_2$(*t*-Bu) whose signals are visible in the downfield portion of each set of doublets.

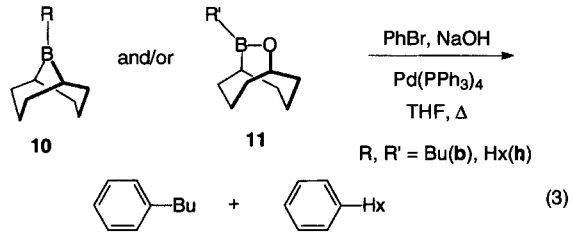
3). This impurity notwithstanding, the fact that even trace amounts of **3*e*** in **3*t*** would be observable in the CHD(*t*-Bu) region of its NMR spectrum (Figure 2) provides compelling evidence that the transmetalation of alkyl groups occurs with complete retention of configuration. The retention process suggested a four-centered

Scheme 2



hydroxo μ_2-bridged transition state model (**9**) (Scheme 2). This transition state could arise from the collapse of an intermediate, **8**, which could originate from either (a) the reaction of hydroxyborate (i.e., $(HOBR_3)^{-1}$) with Pd(II) (e.g., $R'L_2PdBr$) or (b) from the reaction of BR_3 with $R'L_2PdOH$. The collapse of **9** would be expected to facilitate this alkyl group transfer through an S_e2 (coord)[1] process. This model also suggested that either **8** or **9** should be more accessible for organoboranes that have a higher Lewis acidity. We submitted this hypothesis to test.

Competitive Rate Studies for Trialkylboranes *versus* Alkylborinates. Both *B*-alkyl-9-BBN derivatives (**10**) and the corresponding 9-oxa-10-borabicyclo[3.3.2]-decanes (OBBD, **11**), unlike alkylboronates ($RB(OR')_2$), provide effective coupling partners under the standard conditions ($Pd(PPh_3)_4$, NaOH, THF, reflux). We felt that a direct comparison of their relative coupling rates would be informative because the 9-BBN derivatives are much more Lewis acidic than are their OBBD counterparts. The remarkably robust borinate derivatives (**11**) were readily prepared through the selective oxidation of **10** with anhydrous trimethylamine *N*-oxide (TMANO) for both the *n*-butyl (**b**) and *n*-hexyl (**h**) series.[14] All combinations of these boranes, **10b**, **10h**, **11b**, and **11h**, were submitted in pairs to the coupling conditions employing 1.0 equiv of each borane with 0.80 equiv of PhBr and 2.0 equiv of base (eq 3). The results of these competitive



studies are summarized in Table 1. It can be noted that, as expected, little difference is observed in Bu versus Hx couplings (cf. Table 1, entries 1 and 4). However, when **10**/**11** pairs are compared (Tables 1, entries 3 and 4), *only the 9-BBN derivatives (**10**) undergo coupling.* This remarkable and previously unknown feature of the Suzuki–Miyaura reaction clearly has potential synthetic importance for selective couplings.[15] To better under-

(14) (a) Soderquist, J. A.; Najafi, M. R. *J. Org. Chem.* **1986**, *51*, 1330. (b) Soderquist, J. A.; Santiago, B. *Tetrahedron Lett.* **1990**, *31*, 5541.

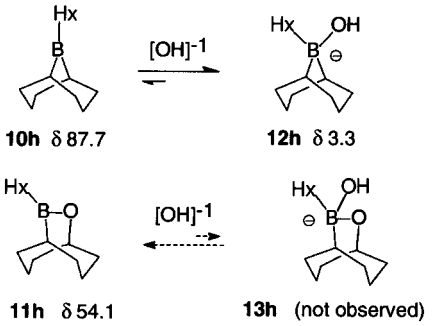
(15) Selective couplings employing the electrophilic partner have demonstrated value. See: (a) Roush, W. R.; Moriarty, K. J.; Brown, B. B. *Tetrahedron Lett.* **1990**, *31*, 6509. (b) Rivera, I.; Colberg, J. C.; Soderquist, J. A. *Tetrahedron Lett.* **1992**, *33*, 6915.

Table 1. Competitive Couplings for 10 vs 11

				Yield[b]	
entry[a]	**10**	**11**	time (h)	PhBu	PhHx
1	**b,h**		1	40	48
2	**h**	**b**	12	0	86
3	**b**	**h**	12	84	0
4		**b,h**	12	44	49

[a] All reactions were carried out employing a 1:1 ratio of boranes. [b] GC yields are based on PhBr (0.8 equiv).

Scheme 3



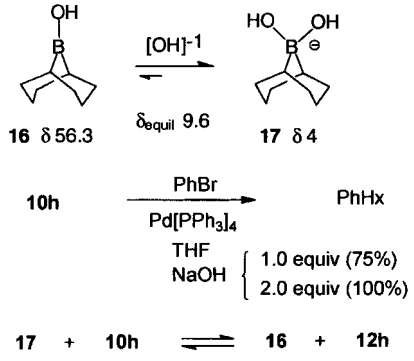
stand this selectivity, we chose to carefully examine the role played by the added base on the process.

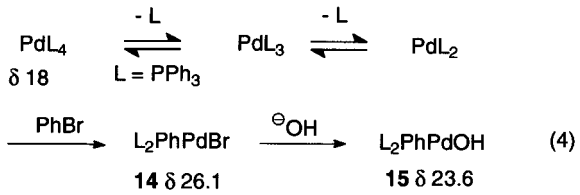
The Role of Base in the Coupling Process. Since Frankland's discovery of triethylborane in 1859,[16] organoboranes have been known to strongly interact with base. However, because alkoxy versus alkyl substitution as well as structural effects in the borane can affect this complexation,[17] we chose to examine this behavior for 9-BBN versus OBBD derivatives to clearly understand this phenomenon in our systems.

Employing ^{11}B NMR, we found that Hx-9-BBN (**10h**) (1.0 M in THF) exhibits its characteristic trialkylborane absorbance at δ 87.7 (Scheme 3). Upon the addition of 1.0 equiv of NaOH(aq) (4.0 M), the system becomes biphasic, and this broadened absorbance shifts upfield to δ 12.0. A second equivalent of base further shifts this value to δ 6.0 and a third to δ 3.3 where this now sharp peak is essentially unaffected by additional base.[17c] These data clearly indicate a **10h/12h** equilibrium wherein the borane is mainly present as its hydroxyborate complex (**12h**) and, were the system homogeneous, a calculated $K_{eq} \sim 10^2$.[17b] By contrast, the ^{11}B NMR of its OBBD counterpart, **11h** (δ 54.1), remains unchanged with added NaOH, indicating that no significant hydroxyborinate complex (**13h**) is formed under basic conditions. This hydroxide ion complexation behavior parallels the selectivity observed for alkyl versus alkoxy boron ligation in their coupling rates, in that more hydroxide complexation produces a faster coupling process.

We turned our attention to the palladium component and to the extensive information that is available on the oxidative addition step[18] to identify the possible intermediates that could lead to **9**. We confirmed,[18a] through ^{31}P NMR analysis, that the ligand-labile Pd(PPh_3)$_4$ (broad singlet, δ 18.0 (1:1 THF, C_6D_6); 14.6 (C_6D_6))[19] reacts cleanly with PhBr (1:1) at 67 °C to produce a 1:2 ratio of *trans*-BrPdPh(PPh_3)$_2$ (**14**, δ 26.1 (sharp singlet, THF)) and PPh_3 (δ −3.2, broad) (eq 4). Under mock catalytic

Scheme 4





conditions at 27 °C in THF (Pd(PPh_3)$_4$/PhBr = 1:49), the initial reaction rate is pseudo-first-order (-d [Pd(PPh_3)$_4$]/dt = k_{obs} [Pd[PPh_3]$_4$], $k_{obs} = 2.3 \times 10^{-5}$ s^{-1} = k[PhBr]; k = 1.3×10^{-5} M^{-1} s^{-1}). This demonstrates that the oxidative addition step in the catalytic cycle can occur at room temperature.

To the **14**/PPh_3 mixture in THF we added 2.0 equiv of NaOH(aq) (4.0 M) and observed that **14** is partially hydrolyzed, giving the monomeric HOPdPh(PPh_3)$_2$ (**15**, δ 23.6 (~33% of **14**, 2 h))[20] probably through an addition−elimination process characteristic of Pd(II) substitutions.[21] We observed no dimeric species,[22] undoubtedly, a consequence of the excess PPh_3 present in the mixture and the use of the polar solvent.[20] Also, the amount of triphenylphosphine oxide (TPPO, δ 27.0) in the mixture increases significantly after the base addition, a consequence of Pd(II) → Pd(0) reduction.[20] Heating this mixture at reflux temperature hastens the **14** → **15** conversion, which reaches ~90% after 2 h. These data demonstrate that the added base can hydrolyze Pd(II) halides producing monomeric hydroxypalladium(II) species (e.g., **15**) under these conditions.

To evaluate a possible third role for the added base, we examined the coupling process to determine the stoichiometry of the reaction with respect to base. The catalytic reaction (PhBr, **10h** (0.8:1), Pd(PPh_3)$_4$ (3 mol %), THF, 65 °C, 8 h, $C_{10}H_{22}$ (internal GC standard)) was conducted with 1.0 and 2.0 equiv of NaOH/Hx-9-BBN producing PhHx in 75% and 100% yields, respectively (Scheme 4). To better understand this 1:2 **10h**/OH^{-1}

(16) (a) Frankland, E.; Duppa, B. F. *Proc. R. Soc. (London)* **1859**, *10*, 568. (b) Frankland, E. *Ann.* **1862**, *124*, 138.

(17) (a) Soderquist, J. A. In *Encyclopedia of Inorganic Chemistry*,; King, R. B., Ed.; J. Wiley & Sons: Ltd.: London, 1994; pp 401−432. (b) Brown, H. C.; Soderquist, J. A. *J. Org. Chem.* **1980**, *45*, 846. (c) Other bases (2.0 equiv) that are effective in the coupling also behave similarly with *B*-Bu-9-BBN, regardless of their steric bulk (i.e., LiOH (δ 4.1), LiOMe (δ 3.9), LiO-*t*-Bu (δ 2.2), LiOSi(Pr-*i*)$_3$ (δ −2.2).

(18) (a) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585. (b) Hegedus, L. S. In *Organometallics in Organic Synthesis*; Schlosser, M., Ed.; Wiley: New York, 1994; p 383.

(19) Mann, B. E.; Musco, A. *J. Chem. Soc., Dalton Trans.* **1975**, 1673.

(20) Grushin, V. V.; Alper, H. *Organometallics* **1996**, *15*, 5242.

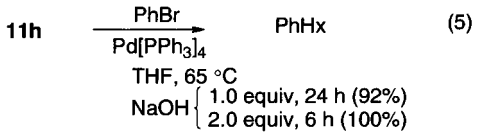
(21) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; pp 241−244.

(22) (a) Grushin, V. V.; Alper, H. *Organometallics* **1993**, *12*, 1890. (b) Amatore, C.; Jutand, A.; Medeiros, M. J. *New J. Chem.* **1996**, *20*, 1143.

stoichiometry, we carried out the hydrolysis of [9-BBN-H]$_2$ in THF (25 °C, 3 h) with 1.0 equiv of NaOH(aq). By ^{11}B NMR, the intermediate HO-9-BBN (**16** δ 56.3) or O(9-BBN)$_2$ (δ 57.5) at δ 54.5 was observed to ultimately produce mainly its hydroxy complex, [(HO)$_2$-9-BBN]$^{-1}$ (**17** ^{11}B NMR δ 9.6) which, when fully formed, exhibits a signal at δ 4 (Scheme 4).[23] This mixture was further examined by ^{11}B NMR. First, with a second equiv of NaOH, this peak shifts upfield slightly to δ 6.8, indicating that, as for Hx-9-BBN, hydroxide complexation is nearly complete at equilibrium. Second, the addition of Hx-9-BBN (**10h**, 1.0 equiv) to **17** (1:1 **16**/NaOH) results in an overlapping set of two peaks, one centered at δ 31.6 and the other sharper peak at δ 13.4, suggesting that both **10h** and **16** together with their hydroxy complexes, **12h** and **17**, are all in equilibrium on approximately the NMR time scale. Thus, this high affinity of **16** for base differs markedly from that of the OBBD derivative **11h** despite their both being borinate derivatives (i.e., R$_2$BOR′).[24]

The 1:2 **10h**/OH^{-1} coupling mixture was examined after its completion by ^{11}B NMR, revealing a broadened signal at δ 8.5 indicating that, under these optimal conditions, the formation of **17** is essentially complete. The same dark mixture (Pd(0) ppt) was also examined by ^{31}P NMR, which revealed TPPO (δ 31.4) and a broadened and upfield-shifted signal at δ 15.9 indicating that the Pd(PPh$_3$)$_4$ that remains is in the presence of an excess of PPh$_3$. Moreover, we also examined the ^{31}P NMR chemical shift of TPPO, which proved to be highly dependent on the species present in the mixture. Values in the δ 31−32 range were observed for TPPO in the presence of **17** or other hydroxyborate complexes (e.g. **12**) while with Pd(0), PPh$_3$, or Hx-9-BBN without base, this signal can be found in the δ 25−28 range.[25]

With 1.0 equiv of NaOH, the R-OBBD (**11**) coupling is more effective than with its 9-BBN counterpart (92%, 24 h), but its coupling is much faster with 2.0 equiv of base (100%, 6 h) (eq 5). The byproduct, *B*-HO-OBBD (δ 37), does not complex OH^{-1} significantly. Thus, the added base can accelerate the coupling for OBBD derivatives although they exhibit little or no tendency to form hydroxyborate complexes.



A fifth role for the added base was also examined. The catalyst, Pd(PPh$_3$)$_4$, is well-known to be both light- and air-sensitive.[18b] The quality of commercial material varies considerably and normally contains TPPO (^{31}P NMR δ ~25). However, despite this variability, most samples function effectively under the standard coupling conditions (PhBr (0.8−1.0 equiv), borane (1.0 equiv), base (2.0 equiv), Pd cat. (2−3mol %), THF, reflux, 6−12 h). The cross-coupling products and [(HO)$_2$-9-BBN]$^{-1}$ (^{11}B−NMR δ 8.5) are produced efficiently. Moreover, ^{31}P NMR reveals that TPPO (δ 31.3 (shifted downfield by [(HO)$_2$-9-BBN]$^{-1}$)) and Pd(PPh$_3$)$_4$ (δ 16, br) are present as the soluble phosphorus species. By contrast, when this process is carried out for 9-BBN derivatives (**10**) at room temperature (Figures 3-5), we noted that, after an initial smooth conversion, the mixtures darken and essentially stop at ca. 60% conversion (2−3 h), regardless of the base stoichiometry employed. After 8 h, when these mixtures are heated (65 °C), the 1:2 **10b**/NaOH reaction resumes immediately, ultimately producing BuPh (92%, 26 h) (Figure 3), whereas with a 1:1 stoichiometry, no immediate further conversion is observed (Figure 5).

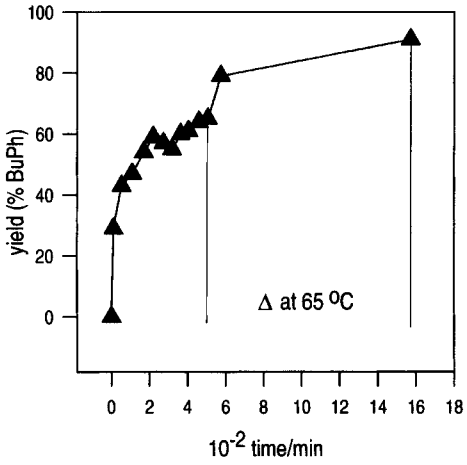


Figure 3. Yield of BuPh vs time for the coupling of PhBr and **10b** with NaOH (2.0 equiv), 8 h (27 °C), then 18 h (65 °C).

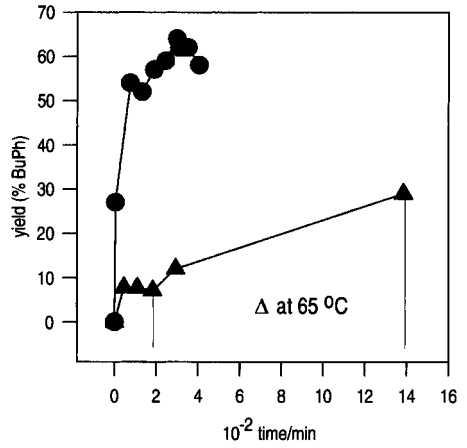


Figure 4. Yield of BuPh vs time for the coupling of PhBr and **10b** with NaOH (2.0 equiv): ●, 27 °C; ▲, Pd[PPh$_3$]$_4$/PhBr/NaOH (2.0 equiv) was heated at 65 °C for 2 h, **10b** was added at 27 °C (t = 0). After 3 h, the mixture was heated at 65 °C.

We felt that the catalyst was being consumed through either the formation of metallic Pd, catalyst poisoning, or possibly the formation of Pd(II) species which are not reduced to Pd(0) at ambient temperatures. The reduction of Pd(II) intermediates at elevated temperatures with PPh$_3$ under basic conditions is a well-documented process.[22] This process appeared to explain the catalyst regeneration, because at ~60% conversion the 1:2 stoichiometry provides more than enough base to complex both the boron reactants and products, leaving free OH^{-1} to facilitate the Pd(II) reduction with the oxidative

(23) (a) Köster, R.; Seidel, G.; Bläster, D.; Boese, R. *Z. Naturforsh.* **1994**. *49b*, 370. (b) Köster, R.; Seidel, G. *Chem. Ber.* **1992**. *125*, 1351.

(24) This result was somewhat surprising because our previous related comparisons with trimethylamine base had revealed similar complexation behavior for MeO-9-BBN versus Me-OBBD.[17b] We attribute this difference to the fact that with small ligands in 9-BBN complexes such as **17**, the steric consequences of each of these ligands being in an axial position with respect to one ring of the bicyclic system, are minimal. MMX calculations also suggest a relief of ring strain with the boron rehybridization to sp^3, an effect not found for OBBD systems.

(25) For related observations, see: Mehta, P.; Zeldin, M. *Inorg. Chim. Acta* **1977**, *22*, L33.

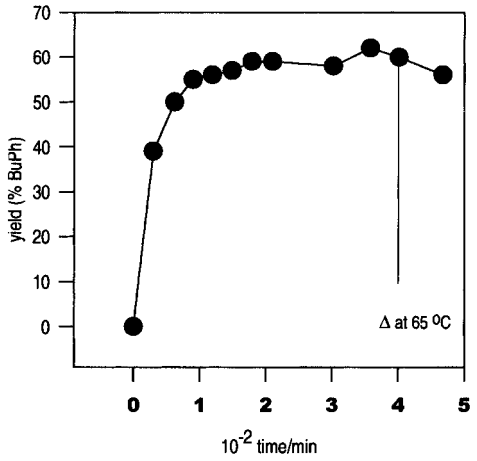
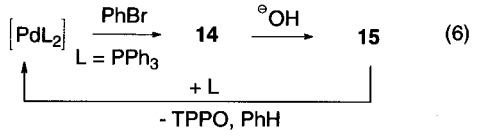


Figure 5. Yield of BuPh vs time for the coupling of PhBr and **10b** with NaOH (1.0 equiv) at 27 °C for 6.7 h and then heating at 65 °C.

formation of TPPO. This contrasts to the 1:1 reaction where, at ~60% conversion, the base is essentially wholly complexed to boron, as either $[HO(Bu)\text{-}9\text{-}BBN]^{-1}$ (**12b**) or $[(HO)_2\text{-}9\text{-}BBN]^{-1}$ (**17**). Insufficient base is present to reduce the spent Pd(II) back to Pd(0), and the coupling does not resume with heating. To test this explanation, we chose to carry out several additional experiments.

To gain support for the Pd(II) reduction, we left out the borane and heated PhBr and NaOH (1:2) with 2.2 mol % $Pd(PPh_3)_4$ in THF for 3 h (Figure 4). This produces variable amounts of PPh_3 (δ −2.7 (30−60%)), TPPO (δ 27.0 (15−32%), $BrPdPh(PPh_3)_2$ (δ 26.0 (10−22%), and $HOPdPh(PPh_3)_2$ (δ 23.5 (15−19%)) depending upon the quality of the catalyst used. However, by GCMS, we also observed small amounts of C_6H_6 being produced during this period. This suggested that the decomposition of $HOPdPh(PPh_3)_2$ or other Pd(II) species in the presence of PPh_3 occurs under these conditions. This can be rationalized through the formation of $[Pd(PPh_3)_2]$ (and TPPO) through $HPdPh(PPh_3)_2$ followed by reductive elimination PhH, ultimately leading back to $BrPdPh(PPh_3)_2$ through the oxidative addition of PhBr (eq 6).[26] By contrast, with the 1:1 PhBr/NaOH stoichiometry, heating produces PPh_3 (30%), TPPO (35%), and $BrPdPh(PPh_3)_2$ (**14**, 26%) together with, as expected, less of its hydrolysis product, $HOPdPh(PPh_3)_2$ (**15**, 9%).



Since the catalyst regeneration could also occur through the known reduction of Pd(II) with organoboranes,[26] we added Hx-9-BBN (1.0 equiv) to the above 1:2 mixture at room temperature, which results in an immediate precipitation of Pd(0). ^{31}P NMR also reveals a broad signal (δ 23) attributable to $Pd(PPh_3)_4$, plus TPPO (δ 34.0). We also confirmed, through ^{11}B NMR analysis, that the boranes are mainly present as their hydroxyborates (δ 14.9 and 6.3). The coupling process prepared in this way does proceed, but at a much reduced rate compared to the standard conditions (cf. Figure 4), consistent with the loss of catalyst (i.e., Pd(0)) through its precipitation from solution. The behavior observed with the 1:1 PhBr/NaOH mixture differs significantly in that the addition of Hx-9-BBN produces a much slower Pd(0) precipitation and less hydroxyborate formation (^{11}B NMR δ 31(br, major), 11.2, 3.2). Moreover, no $BrPdPh(PPh_3)_2$ or $HOPdPh(PPh_3)_2$ remains after the borane addition. Importantly, no soluble Pd(0) species is formed. Only TPPO (δ 32.6) and an unknown phosphorus species at δ 24.2 (sharp) in the ^{31}P NMR spectrum of the reaction mixture are present. These results allow us to conclude that neither $BrPdPh(PPh_3)_2$ nor $HOPdPh(PPh_3)_2$ can be responsible for the cessation of the room-temperature cross-coupling. The boranes would convert these to Pd(0), at least with the 1:1:2 PhBr, **10**, NaOH stoichiometry. Although we were unable to identify the precise Pd species that is used in the catalyst regeneration, it is clear that base plays an instrumental role in the process.

Thus, we have found five possible roles for the base in the Suzuki−Miyaura coupling: (1) the formation of hydroxyborate complexes (e.g., **12**), (2) the hydrolysis of Pd(II)X intermediates to monomeric Pd(II)OH species, (3) the complexation of $HOBR_2$ byproducts that can compete for base with the trialkylborane reagents used for the coupling, (4) accelerated coupling rates for OBBD derivatives, and (5) catalyst regeneration.

Kinetic Studies. It has been previously noted that the slow step in the catalytic cycle can change with the halide used in the electrophilic partner.[27] The above studies had suggested to us that this phenomenon could also be seen with changes in the organoborane employed for the coupling.[28] Having observed considerable variation in the quality of the $Pd(PPh_3)_4$ (which invariably contains TPPO) obtained from various commercial sources, we conducted all of the kinetic studies described below with the same catalyst to avoid introducing an unwanted variable. Kinetic studies were conducted under dilute conditions (~0.2 M) at constant reaction volumes for the coupling of PhBr with the 9-BBN derivative, **10b**, and NaOH(aq) in THF ($Pd(PPh_3)_4$, 2.2 mol %)) at 27 °C monitoring the production of BuPh (GC, PhEt as an internal standard) with time. Initial rates (~60% conversion) with 1.0 and 2.0 equiv of PhBr and also of $[HO(Bu)\text{-}9\text{-}BBN]^{-1}$ (**12b**) revealed that the reaction rate is independent of the concentration of **12b** (Figure 7), but is first-order in [PhBr]: $d[PhBu]/dt = k_{obs}[PhBr]$, $k_{obs} = (1.1 \pm 0.5) \times 10^{-4}\ s^{-1}$ (Figure 6). Therefore, it is the oxidative addition step in the catalytic cycle that is rate-limiting for the coupling of *B*-alkyl-9-BBN derivatives (**10**) with PhBr.

It was difficult to understand the remarkable 9-BBN/OBBD selectivity as arising from a process that occurs after the rate-limiting step. As a consequence, we turned our attention to the kinetics of the Bu-OBBD (**11b**) coupling to determine its slow step. As anticipated, the coupling was much slower than that for **10**, leading us to conduct the study at 65 °C. Not surprisingly, the reaction proved to be zero-order in [PhBr] (Figure 8). However, since we had observed no association of OH^{-1} with **11b**, we examined each separately and found the rate to be independent of [**11b**] but first-order in base: $d[PhBu]/dt = k_{obs}[OH^{-1}]$, $k_{obs}(65\ °C) = (1.45 \pm 0.1) \times 10^{-5}$

(26) Suzuki, A. *Pure Appl. Chem.* **1991**, *63*, 419.

(27) Smith, G. B.; Dezeny, G. C.; Hughes, D. L.; King, A. O.; Verhoeven, T. R. *J. Org. Chem.* **1994**, *59*, 8151.

(28) We had previously found selectivities that were affected by the partial oxidation of the organoboranes: Rivera, I.; Soderquist, J. A. *Tetrahedron Lett.* **1991**, *32*, 2311.

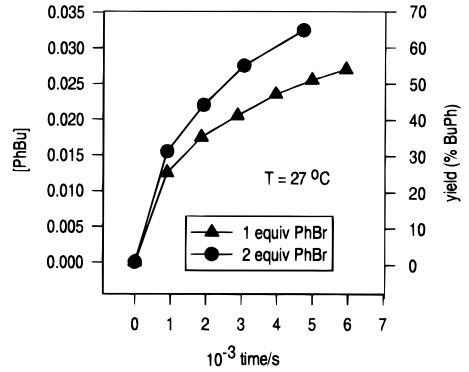


Figure 6. Yield of BuPh vs time for the coupling of PhBr and **12b** at 27 °C at constant reaction volume: ●, 1.0 equiv of PhBr; ▲, 2.0 equiv of PhBr.

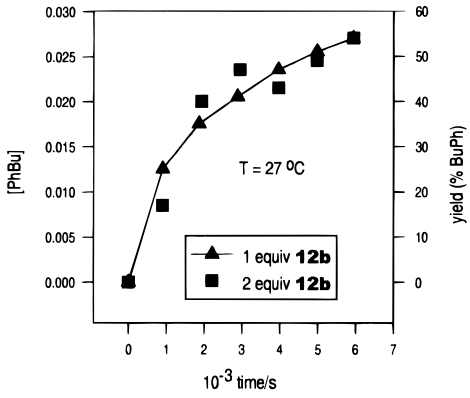


Figure 7. Yield of BuPh vs time for the coupling of PhBr and **12b** at 27 °C at constant reaction volume: ●, 1.0 equiv of **12b**; ▲, 2.0 equiv of **12b**.

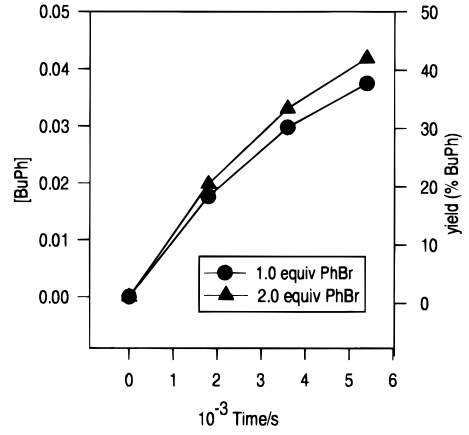


Figure 8. Yield of BuPh vs time for the coupling of PhBr and **11b**/NaOH (1:1) at 65 °C at constant reaction volume: ●, 1.0 equiv of PhBr; ▲, 2.0 equiv of PhBr.

s^{-1} (Figures 9 and 10). The hydrolysis of $BrPdPh(PPh_3)_2$ (**14**) is rate-determining for the coupling of *B*-alkyl-OBBD derivatives (**11**) with PhBr. It is interesting that, while the reaction rates for 9-BBN and OBBD derivatives are strikingly different, neither has the boron component in the slow step of the coupling.

Conclusions

In summary, the Suzuki–Miyaura catalytic cycle consists of a series of sequential reactions whose rates vary with the individual reacting species.[27,28] Our results

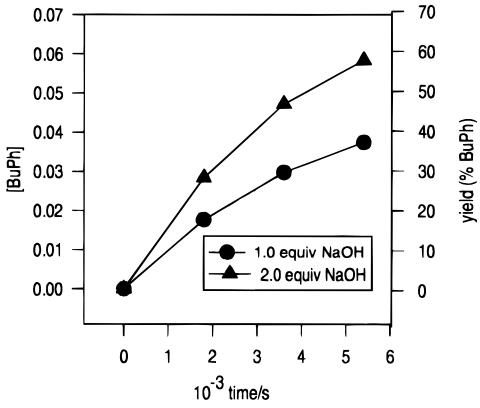


Figure 9. Yield of BuPh vs time for the coupling of **11b** and PhBr (1:1) at 65 °C at constant reaction volume: ●, 1.0 equiv of NaOH; ▲, 2.0 equiv of NaOH.

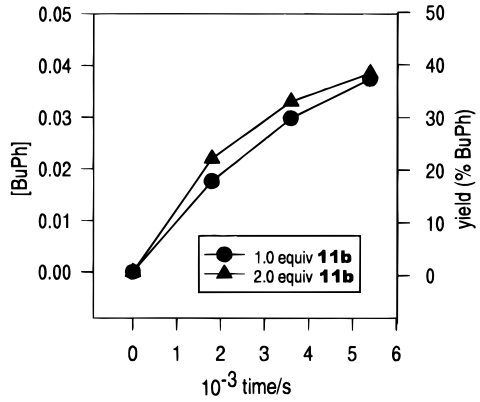


Figure 10. Yield of BuPh vs time for the coupling of **11b** and PhBr/NaOH (1:1) at 65 °C at constant reaction volume: ●, 1.0 equiv of **11b**; ▲, 2.0 equiv of **11b**.

suggest that the actual cycle is much more complex than has been previously pictured,[1] particularly when the base is included. The new features are illustrated in Figure 11. Our results indicate that the formation of $BrPdPh(PPh_3)_2$ (**14**) at 27 °C is rate-limiting for R-9-BBN derivatives (**10**). These organoboranes are present principally as their hydroxyborate complexes, **12**. The reaction of **12** with **14** is rapid, probably displacing bromide forming a hydroxo μ_2-bridged intermediate **8a** that facilitates the alkyl B → Pd transmetalation with retention of configuration through a four-centered transition state (**9**). This intermediate would also be expected to be of lower energy than that of a related species derived from more oxygenated organoboranes such as **11** due to the greater Lewis acidity of **10**. The resulting $PhPdR(PPh_3)_2$ rapidly gives PhR and regenerates $Pd(PPh_3)_2$. The boron byproduct, **16**, can effectively compete with **10** for base, so that the optimal **10**/OH^{-1} stoichiometry is 1:2, which ensures that **12** will be present to continue the cycle once $BrPdPh(PPh_3)_2$ (**14**) is regenerated. At room temperature, in a slower process, $HOPdPh(PPh_3)_2$ (**15**) is also continuously produced from **14** under these basic conditions. Reacting with **10**, this minor pathway through **8b** can also contribute to the coupling process.

For the less Lewis acidic OBBD derivatives (**11**), the **8b** pathway dominates. In contrast to their 9-BBN counterparts, the hydroxyborate complexes (**13**) of these borinates are too energetic to permit them to enter the cycle. In this case, it is the formation of $HOPdPh(PPh_3)_2$ (**15**) from **14** that is rate-limiting. The reaction of **15** with

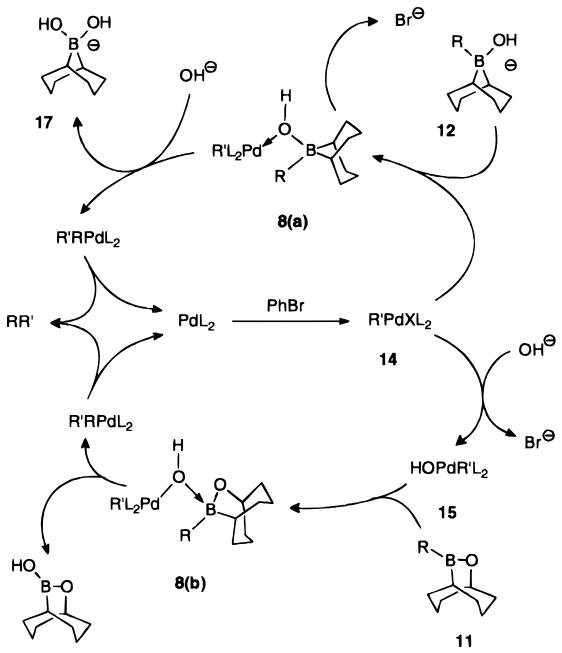


Figure 11. Modified Suzuki−Miyaura catalytic cycle illustrating the roles played by added base.

11 provides an alternative way to reach the key hydroxo μ_2-bridged species (**8b**). Collapse of this intermediate as for the 9-BBN couplings produces the desired coupling. We hasten to add that the key differences in these 9-BBN and OBBD processes appear to center around the delivery of hydroxide to the $BrPdPh(PPh_3)_2$. In the former instance, the borane (**10**) solvates hydroxide in the form of the hydroxyborate (**11**). This would be expected to greatly facilitate the bromide substitution leading directly to **8a**. This undergoes rapid transmetalation with subsequent reductive elimination. By contrast, the OBBD derivatives **11** cannot perform this task because of the instability of their hydroxyborate complexes (i.e., **13**). Therefore, the major form of the hydroxide is $[OH^{-1}]_{aq}$ and its reaction with $BrPdPh(PPh_3)_2$ requires higher temperatures to be effective in the catalytic cycle. We conclude that this substitution process is clearly slower than the formation of $BrPdPh(PPh_3)_2$ in the oxidative addition step (eq 6). However, it is faster than the hydroxyborate process (**8a**) because OBBD derivatives fail to significantly complex hydroxide ion. Palladium delivers the hydroxide to the free borane species in the form of **15** in a rapid process compared to its formation. In both the 9-BBN and OBBD processes, the Pd(II) reacts rapidly with the major boron-containing species present in solution. We cannot rule out that this is a function of the mixed solvent system employed or that other bases or boranes may behave differently.[29] The energetics of the individual steps in this catalytic process are obviously very dependent upon the specific reagents and conditions employed.

Experimental Section

General Methods. All experiments were carried out in predried glassware (1 h, 150 °C) under a nitrogen atmosphere. Standard handling techniques for air-sensitive compounds were employed throughout this study.[30] NMR spectra were recorded in either $CDCl_3$ or C_6D_6 as indicated: ^1H(either 500 or 300 MHz), ^{13}C (75 MHz); ^{11}B (96.5 MHz); ^{31}P (121.5 MHz). GC/MS (70 eV) and GC kinetic and analytical data were obtained with 30 m × 0.23 mm. i. d. 20% SE-30 vitreous silica open tubular columns. Columns were silylated (MSTFA) prior to analytical runs.

Reaction of Iodobenzene with 1. To a solution of PhI (0.20 g, 1.0 mmol) in C_6H_6 (5 mL) and $Pd(dppf)Cl_2$ (0.025 g, 0.03 mmol) in C_6H_6 (2.3 mL) was added **1**[30] (0.324 g, 1.1 mmol) followed by addition of TlOH (7.3 mL of 0.45 M, 3.3 mmol). The reaction mixture was held at reflux temperature for 12 h. GC analysis of the reaction mixture using dodecane (0.17 g, 1.0 mmol) as an internal standard showed the formation of isomerically pure *exo*-2-phenylnorbornane (**2**, 5%) along with biphenyl (20%). Both species were independently prepared and identified by MS and ^1H NMR to corroborate their identity. The use of $Pd[PPh_3]_4$ as the catalyst in the cross-coupling reaction gave identical results.

9-Borabicyclo[3.3.1]nonane-*D*. To a solution of $LiAlD_4$ in EE (50 mL of 1.0 M, 50.0 mmol) was added ethyl acetate (2.2 g, 25.0 mmol) dropwise. The resulting solution was cooled to 0 °C, and *B*-methoxy-9-borabicyclo[3.3.1]nonane was added dropwise. After the addition, the reaction mixture was well mixed and centrifuged. The clear supernatant solution was transferred via double-ended needle to a second vial. The solid dialkoxyalane was washed with EE (2 × 25 mL), and the washings were combined with the supernatant. TMSCl (5.4 g, 50.0 mmol) was added dropwise, and the resulting mixture was centrifuged and the supernatant transferred to another flask. The solid LiCl was washed with EE (2 × 25 mL), and the washings were combined with the supernatant solution. The solvent was removed under reduced pressure, and the solid residue was recrystallized from monoglyme (100 mL) to give 1.88 g of $(9\text{-BBN-D})_2$ (31%): ^1H NMR (300 MHz, C_6D_6) δ 1.53 (m, 2 H), 1.65 (m, 2 H), 1.87 (m, 7 H); ^{13}C NMR (75 MHz, C_6D_6) δ 20.0, 23.8, 33.2; ^{11}B NMR (96 MHz, C_6D_6) δ 27.7; HRMS (EI) *m*/*z* calcd for $C_{18}H_{28}BD_2$ (M^+) 246.2659, found 246.2661. Crystallographic data: $C_{18}H_{28}BD_2$, $M = 246$; monoclinic (space group *C*2/*m* (#12)); $a = 14.5215$ Å, $b = 15.4645$ Å, $c = 6.8799$ Å; $V = 1543.1771$ Å; D_{calc} 1.050 g/cm^3; $Z = 2$.

threo*-1,2-Dideuterio-3,3-dimethyl-1-phenylbutane (3*t*). Method A.** A solution of PhBr (0.71 g, 4.5 mmol) and $Pd[PPh_3]_4$ (0.10 g, 0.087 mmol) in THF (5.0 mL) was added to a mixture of **6*t (1.04 g, 5.0 mmol), NaOH (3.3 mL, 3 M), and THF (5.0 mL). After the reaction mixture was heated for 12 h, pentane (50 mL) was added. The organic phase was washed with water (20 × 100 mL) and filtered through alumina. Concentration followed by distillation gave 0.39 g of **3*t*** (52%, 44 °C at 15 Torr): ^1H NMR (500 MHz, ^2H decoupled, C_6D_6 (see Figure 2)) δ 0.90 (s, 9 H), 1.40 (d, $J = 4.8$ Hz, 1 H), 2.44 (d, $J = 4.8$ Hz, 1 H), 7.10 (m, 3 H), 7.18 (m, 2 H); ^{13} C NMR (75 MHz, C_6D_6) 29.3, 30.4, 31.2 (t, $J_{C-^2H} = 19.3$ Hz), 46.2 (t, $J_{C-^2H} = 19.3$ Hz), 125.8, 128.0, 128.0, 143.6; MS *m*/*z* 164 (M^+, 44), 108 (34), 92 (100), 55 (33); HRMS (EI) *m*/*z* calcd for $C_{12}H_{16}D_2$ (M) 164.1534, found 164.1533. **Method B.** To a solution of 9-BBN-H (1.21 g, 9.9 mmol) in THF (10 mL) was added **5** (0.86 g, 9.9 mmol). The reaction mixture was stirred for 2 h, and NaOH (3.3 mL, 3 M) and THF (5.0 mL) were added. A solution of PhBr (1.10 g, 7.0 mmol) and $Pd[PPh_3]_4$ (0.20 g, 0.17 mmol) in THF (5.0 mL) was added to the mixture. After the solution was heated for 12 h, pentane (50 mL) was added. The organic phase was washed with water (20 × 100 mL) and filtered through alumina. Concentration gave 0.98 g (85%) of **3*t***.

erythro*-1,2-Dideuterio-3,3-dimethyl-1-phenylbutane (3*e*).** A solution of PhBr (0.79 g, 5.0 mmol) and $Pd(PPh_3)_4$ (0.10 g, 0.087 mmol) in THF (5.0 mL) was added to a mixture of **6*e (1.10 g, 5.3 mmol), NaOH solution in water (1.8 mL, 3 M), and THF (5.0 mL). After the reaction mixture was heated for 12 h, pentane (50 mL) was added. The organic phase was washed with water (20 × 100 mL) and filtered through alumina. Concentration followed by distillation gave 0.73 g of **3*e*** (89%,

(29) For example, we observed that the "ate" complex from **6*e*** and *t*-$BuCH_2Li$ couples to give a 60: 40 mixture of **3*e*/3*t*** together with an equal amount of *t*-$BuCH_2Ph$.

(30) Brown, H. C. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975.

44 °C at 15 Torr): ^{1}H NMR (500 MHz, ^{2}H decoupled, C_6D_6 (see Figure 2)) δ 0.90 (s, 9 H), 1.40 (d, J = 12.9 Hz, 1 H), 2.44 (d, J = 12.9 Hz, 1 H) 7.10 (m, 3 H), 7.18 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) 29.3, 30.4, 31.2 (t, J_{C-^2H} = 19.3 Hz), 46.2 (t, J_{C-^2H} = 19.3 Hz), 125.8, 128.0, 128.0, 143.6; MS *m*/*z* 164 (M, 44), 108 (34), 92 (100), 55 (33); HRMS (EI) *m*/*z* calcd for $C_{12}H_{16}D_2$ (M) 164.1534, found 164.1533.

***cis*-1,2-Dideuterio-3,3-dimethyl-1-butene (5). Method A.** A mixture of **4** (4.91 g, 60.0 mmol), Lindlar catalyst (0.30 g), and quinoline (3.0 mL) was connected to a low-pressure hydrogenation apparatus and submitted to freeze−pump−thaw (3×). The apparatus was evacuated and deuterium gas was admitted to a pressure slightly above 1 atm. Stirring was started, and rapid absorption was observed. After approximately 1.1 equiv of D_2 were consumed, the reaction was stopped. Trap-to-trap distillation gave 3.55 g (69%) of **5**: ^{1}H NMR (500 MHz, ^{2}H-decoupled, C_6D_6) δ 0.95 (s, 9 H), 4.90 (s, 1 H); ^{13}C NMR (75 MHz, C_6D_6) δ 29.3, 33.5 108.8 (t, J_{C-^2H} = 24.0 Hz), 149.2 (t, J_{C-^2H} = 24.0 Hz); MS *m*/*z* (relative intensity) 86 (M^+, 12), 71 (100), 55 (18); HRMS (EI) *m*/*z* calcd for $C_6H_{10}D_2$ (M^+) 86.1065, found 86.1067. **Method B.** To a flask surmounted with a cold-trap condenser were added 9-BBN-D (3.90 g, 31.7 mmol) and THF (65 mL). This solution was cooled to 0 °C, and **4** (5.3 g, 65 mmol) was added. The reaction mixture was stirred for 18 h and allowed to warm to room temperature. The solvent was removed under vacuum and the resulting residue was cooled to 0 °C. Acetic acid-d_4 (2.03 g, 31.7 mmol) was added dropwise. A subsequent trap-to-trap distillation gave 1.63 g (60%) of **5**.

threo*-9-(1,2-Dideuterio-3,3-dimethyl-1-butyl)-9-borabicyclo[3.3.1]nonane (6*t*).** To a solution of 9-borabicyclo-[3.3.1]nonane (1.83 g, 15.0 mmol) in THF (20.0 mL) at 25 °C was added **5** (1.51 g, 17.5 mmol). After 2 h, the solvent was removed under vacuum. Distillation gave 2.86 g of **6*t (92%, 88 °C at 0.2 Torr): ^{1}H NMR (500 MHz, ^{2}H decoupled C_6D_6) δ 0.93 (s, 9 H), 1.21 (m, 2 H), 1.29 (d, J = 4.8 Hz, 1 H), 1.42 (d, J = 4.8 Hz, 1 H), 1.69 (m, 4 H), 1.77 (m, 2 H), 1.85 (m, 6 H); ^{13}C NMR (75 MHz, C_6D_6) δ 22.0, 23.7, 29.3, 31.7, 33.6, 34.2, 38.1; ^{11}B NMR (96 MHz, C_6D_6) δ 88.1; MS *m*/*z* (relative intensity) 208 (M, 34), 121 (42), 93 (49), 65 (63), 57 (100); HRMS (EI) *m*/*z* calcd for $C_{14}H_{25}BD_2$ (M) 208.2331, found 208.2334.

erythro*-9-(1,2-Dideuterio-3,3-dimethyl-1-butyl)-9-borabicyclo[3.3.1]nonane (6*e*).** To a solution of 9-borabicyclo-[3.3.1]nonane-*D* (1.83 g, 15.0 mmol) in THF (20.0 mL) at 25 °C in a round-bottomed flask was added **7**. After 2 h, the solvent was removed under vacuum. Distillation gave 2.85 g of **6*e (91%, bp 74 °C at 0.05 Torr): ^{1}H NMR (500 MHz, ^{2}H decoupled, C_6D_6) δ 0.93 (s, 9 H), 1.21 (m, 2 H), 1.29 (d, J = 12.3 Hz, 1 H), 1.42 (d, J = 12.3 Hz, 1 H), 1.69 (m, 4 H), 1.77 (m, 2 H), 1.85 (m, 6 H); ^{13}C NMR (75.0 MHZ, C_6D_6) δ 23.0, 23.6, 31.0, 33.5; ^{11}B NMR (96 MHz, C_6D_6) δ 88.0; MS *m*/*z* (relative intensity) 208 (M^+, 34), 121 (42), 93 (49), 65 (63), 57 (100); HRMS (EI) *m*/*z* calcd for $C_{14}H_{25}BD_2$ (M^+) 208.2331, found 208.2334.

***trans*-1-Deuterio-3,3-dimethyl-1-butene (7).** To a flask surmounted with a cold trap condenser was added *trans*-9-(3,3-dimethyl-1-butenyl)-9-borabicyclo[3.3.1]nonane (10.33 g, 50.6 mmol). Acetic acid-*d* (3.24 g, 50.6 mmol) was added dropwise at 0 °C. A subsequent trap-to-trap distillation gave 3.09 g of **7** (73%): ^{1}H NMR (500 MHz, ^{2}H decoupled, C_6D_6) δ 0.95 (s, 9 H), 4.85 (d, J = 17.4 Hz, 1 H), 5.73 (d, J = 17.4 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6) δ 29.2, 33.7, 109.0 (t, J_{C-2H} = 23.9 Hz), 149.6; HRMS (EI) *m*/*z* calcd for $C_6H_{11}D$ (M) 85.1002, found 85.1005.

Competitive reactions (Table 1). A solution of PhBr (0.13 g, 0.8 mmol) and $Pd(PPh_3)_4$ (0.025 g, 0.022 mmol) in THF (2.0 mL) was added to a mixture of *B*-alkyl-9-BBN (**10**, 1.0 mmol) and/or *B*-alkyl-10-oxa-9-borabicyclo[3.3.2]decanes **11**, (1.0 mmol), NaOH solution in water (0.67 mL, 3 M), and THF (5.0 mL). The reaction mixture was heated for 12 h. GC analysis of the reaction mixtures was performed using tetradecane (0.20 g, 1.0 mmol) as an internal standard. These results are summarized in Table 1. All species were identified by mass spectral analysis comparing each to authentic samples.

14 from $Pd(PPh_3)_4$. The 1:1 stoichiometric reaction of PhBr with $Pd(PPh_3)_4$ is described in the text. For the mock-catalytic reaction: To an NMR tube containing $Pd(PPh_3)_4$ (0.030 g (99% pure), 0.026 mmol) in THF (0.6 mL) was added PhBr (0.188 g, 1.2 mmol (the total volume of the resultant mixture is 0.80 mL; the initial concentration of $Pd(PPh_3)_4$ ([$Pd(PPh_3)_4$]$_0$ = 0.032 M; [PhBr]$_0$ = 1.5 M)). An initial ^{31}P NMR (121.5 MHZ, THF) spectrum was taken indicating the presence of $Pd(PPh_3)_4$ (δ 18). Spectra were recorded at different times where the area of the peaks corresponding to $Pd(PPh_3)_4$ (δ 18) and **14** (δ 26.1) were measured; time (s) [% **14**]: 900 [2.5], 1800 [4.7], 2700 [6.7], 3600 [8.3], 5400 [11.2], 7200 [16.3]. Since PhBr under these conditions is present in a 46-fold excess, pseudo-first-order conditions were assumed. A first-order treatment of these data gives: time (s) [ln[$Pd(PPh_3)_4$]]; 900 [−3.47], 1800 [−3.49], 2700 [−3.51], 3600 [−3.53], 5400 [−3.56], 7200 [−3.62]. From these data, k_{obs} = 2.3 × 10^{-5} s^{-1} and $k = k_{obs}$/[PhBr] = 1.3 × 10^{-5} M^{-1} s^{-1}.

Hydrolysis of 14. To a solution of $Pd(PPh_3)_4$ (0.025 g, 0.022 mmol) in THF (2.0 mL ((δ 19.3, 86%) and TPPO (δ 25.0, 14%)) was added PhBr (0.157 g, 1.00 mmol). The mixture was heated at reflux for 1 h (^{31}P NMR **14** δ 26.1 and PPh_3 δ −3.2 (1:2)). NaOH (0.49 mL of 4.1 M, 2.0 mmol) was added, noting the formation of **15** (δ 23.6, 2 h (∼33% of **14**)). The mixture was heated, producing **15** (94%, 2 h). In another experiment, the reaction mixture was partitioned between distilled H_2O (4 mL) and hexane (25 mL). The aqueous phase was separated and washed with hexane (10 mL). To the aqueous phase was added $AgNO_3$ (1.6 mL of 0.5 M, 0.8 mmol) where AgBr was observed to form, indicating the presence of NaBr.

Stoichiometric data. A solution of PhBr (0.13 g, 0.8 mmol) and $Pd(PPh_3)_4$ (0.025 g, 0.022 mmol) in THF (2.0 mL) was added to a mixture of **10h** or **11h** (1.0 mmol) and NaOH-(aq) (1.0 or 2.0 equiv) and THF (5.0 mL). Decane (0.14 g, 1.0 mmol) was used as an internal standard in the reactions. The reaction mixture was heated at reflux, and GC analyses of aliquots of the reaction mixtures were taken initially every 20 min and monitored until no further increase in PhHx was detectable. Yields were calculated using predetermined correction factors versus standard, and these and the reaction times are given in the text.

Kinetic Data for the PhBr, 10b, NaOH Coupling (1:1:2) at Ambient Temperature Followed by Heating. A mixture of PhBr (0.16 g, 1.0 mmol) and $Pd(PPh_3)_4$ (0.025 g, 0.022 mmol) in THF (2.0 mL) was added to a mixture of **10b** (0.18 g, 1.0 mmol), HxPh (G C standard, 0.16 g, 1.0 mmol), and aqueous NaOH (0.56 mL of 3.6 M, 2.0 mmol) in THF (2.0 mL). The mixture was stirred at 27 °C, and aliquots were periodically withdrawn and analyzed by GC. t_0 = 0.0, t_1 = 10, t_2 = 53, t_3 = 109, t_4 = 170, t_5 = 219, t_6 = 272, t_7 = 318, t_8 = 363, t_9 = 404, t_{10} = 460, t_{11} = 506 min to give 0.0 (t_0), 0.29 (t_1), 0.43 (t_2), 0.47 (t_3), 0.54 (t_4), 0.59 (t_5), 0.57 (t_6), 0.55 (t_7), 0.60 (t_8), 0.61 (t_9), 0.64 (t_{10}), and 0.65 (t_{11}) mmol of PhBu product, respectively. Subsequently, the reaction was heated at 65 °C, and aliquots were periodically withdrawn and analyzed by GC. t_{12} = 575, t_{13} = 1572 min to give 0.79 (t_{12}) and 0.91 (t_{13}) mmol of PhBu product. C.F. (PhBu vs PhHx) = 1.1. These data are plotted in Figures 3 and 4. **1:1:2** A mixture of PhBr (0.16 g, 1.0 mmol) and $Pd(PPh_3)_4$ (0.025 g, 0.022 mmol) in THF (2.0 mL) was added to HxPh (GCstandard, 0.16 g, 1.0 mmol) and aqueous NaOH (0.56 mL of 3.6 M, 2.0 mmol) in THF (2.0 mL). The mixture was heated at 65 °C for 2 h. **10b** was added, and the reaction mixture was stirred at 27 °C. Aliquots were periodically withdrawn and analyzed by GC. t_0 = 0.0, t_1 = 45, t_2 = 109, t_3 = 183 min to give 0.0 (t_0), 0.078 (t_1), 0.077 (t_2), and 0.071 (t_3) of PhBu product, respectively. Subsequently, the reaction was heated at reflux, and aliquots were periodically withdrawn and analyzed by GC. t_4 = 293, t_5 = 1384 to give 0.12 (t_4), 0.29 (t_5) of PhBu product, respectively. These data are plotted in Figure 4. **1:1:1.** A mixture of PhBr in THF (1.0 mL of 1.0 M, 1.0 mmol) and $Pd(PPh_3)_4$ (0.025 g, 0.022 mmol) in THF (1.0 mL) was added to a mixture of **10b** in THF (2.08 mL of 0.48 M, 1.0 mmol), HxPh (G. C. standard, 0.16 g, 1.0 mmol), and aqueous NaOH (0.24 mL of 4.2 M, 1.0 mmol) in THF (3.0 mL). The mixture was

stirred at 27 °C, and aliquots were periodically withdrawn and analyzed by GC. $t_0 = 0.0$, $t_1 = 30$, $t_2 = 62$, $t_3 = 90$, $t_4 = 119$, $t_5 = 149$, $t_6 = 179$, $t_7 = 210$, $t_8 = 302$, $t_9 = 358$, $t_{10} = 401$ min to give 0.0 (t_0), 0.39 (t_1), 0.50 (t_2), 0.55 (t_3), 0.56 (t_4), 0.57 (t_5), 0.59 (t_6), 0.59 (t_7), 0.58 (t_8), 0.62 (t_9), and 0.60 (t_{10}) mmol of PhBu product, respectively. Subsequently, the reaction was refluxed and an aliquot was withdrawn and analyzed by GC. $t_{11} = 467$ min to give 0.56 (t_{11}) mmol of PhBu product. These data are plotted in Figure 5.

Kinetic Data. All kinetic runs were conducted using the same batch sample of catalyst. Runs were checked for reproducibility with the 1:1:1 stoichiometries for **10b** and **11b**, as well as for the runs where a rate dependence was observed. The relative peak areas for PhBu versus an internal standard were determined, and using a predetermined correction factor, product yields were calculated and plotted versus time in Figures 6−10. The first-order treatment (ln [PhBu] versus time of the data gave the cited k_{obs} values, which are given in the text. **PhBr, 10b, NaOH Coupling (1:1:1) at 27 °C.** An equimolar mixture of PhBr and PhEt (GC standard) in THF (5.0 mL of 0.2 M, 1.0 mmol each) was added to an equimolar mixture of **10b** and NaOH (from 4.2 M aqueous solution) in THF (5.0 mL of 0.2 M, 1.0 mmol each). A solution of $Pd\{PPh_3\}_4$ (0.025 g, 0.022 mmol) in THF (1.0 mL) was added, and the total volume of the mixture was brought to 20.0 mL with THF. The mixture was stirred at 27 °C, and aliquots were periodically withdrawn and analyzed by GC. $t_0 = 0.0$, $t_1 = 15$, $t_2 = 31$, $t_3 = 48$, $t_4 = 66$, $t_5 = 83$, $t_6 = 99$ min to give 0.0 (t_0), 0.25 (t_1), 0.35 (t_2), 0.41 (t_3), 0.47 (t_4), 0.51 (t_5), and 0.54 (t_6) mmol of PhBu product, respectively. These data are plotted in Figures 6 and 7. **1:2:2.** An equimolar mixture of PhBr and PhEt (GC standard) in THF (5.0 mL of 0.2 M, 1.0 mmol each) was added to an equimolar mixture of **10b** and NaOH (from 4.2 M aqueous solution) in THF (10.0 mL of 0.2 M, 2.0 mmol each). A solution of $Pd(PPh_3)_4$ (0.025 g, 0.022 mmol) in THF (1.0 mL) was added, and the total volume of the mixture was brought to 20.0 mL with THF. The mixture was stirred at 27 °C, and aliquots were periodically withdrawn and analyzed by GC. $t_0 = 0.0$, $t_1 = 15$, $t_2 = 32$, $t_3 = 49$, $t_4 = 66$, $t_5 = 83$, $t_6 = 99$ min to give 0.0 (t_0), 0.17 (t_1), 0.40 (t_2), 0.47 (t_3), 0.43 (t_4), 0.49 (t_5), and 0.54 (t_6) mmol of PhBu product, respectively. These data are plotted in Figure 7. **2:1:1**. $t_0 = 0.0$, $t_1 = 15$, $t_2 = 32$, $t_3 = 51$, $t_4 = 79$ min to give 0.0 (t_0), 0.31 (t_1), 0.44 (t_2), 0.55 (t_3), and 0.65 (t_4) mmol of PhBu product, respectively. These data are plotted in Figure 6. **PhBr, 11b, NaOH Coupling (1:1:1) at 65 °C.** A mixture of PhBr in THF (1.0 mL of 1.0 M, 1.0 mmol) and PhHx in THF (GC standard, 2.0 mL of 0.5 M, 1.0 mmol) was added to a mixture of **11b** in THF (1.75 mL of 0.57 M, 1.0 mmol) and aqueous NaOH (0.24 mL of 4.2 M, 1.0 mmol). A solution of $Pd(PPh_3)_4$ in THF (2.0 mL of 0.011 M, 0.022 mmol) was added, and the total volume of the mixture was brought to 10.0 mL with THF. The mixture was refluxed and stirred at 65 °C, and aliquots were periodically withdrawn and analyzed by GC. $t_0 = 0.0$, $t_1 = 30$, $t_2 = 60$, $t_3 = 90$ min to give 0.0 (t_0), 0.16 (t_1), 0.27 (t_2), and 0.34 (t_3) mmol of PhBu product, respectively. These data are plotted in Figures 8−10. **2:1:1.** $t_0 = 0.0$, $t_1 = 30$, $t_2 = 60$, $t_3 = 90$ min to give 0.0 (t_0), 0.18 (t_1), 0.30 (t_2), and 0.38 (t_3) mmol of PhBu product, respectively. These data are plotted in Figure 8. **1:1:2.** $t_0 = 0.0$, $t_1 = 30$, $t_2 = 60$, $t_3 = 90$ min to give 0.0 (t_0), 0.26 (t_1), 0.43 (t_2), and 0.53 (t_3) mmol of PhBu product, respectively. These data are plotted in Figure 9. **1:2:1.** $t_0 = 0.0$, $t_1 = 30$, $t_2 = 60$, $t_3 = 90$ min to give 0.0 (t_0), 0.20 (t_1), 0.30 (t_2), and 0.35 (t_3) mmol of PhBu product, respectively. These data are plotted in Figure 10.

Acknowledgment. The support of the NSF-EPSCoR (USR-9452893) and NIH-MBRS program (SO6-GM08122) is gratefully acknowledged. Helpful discussions with Professor L. S. Hegedus on palladium substitutions are very much appreciated. We also thank Dr. Anil M. Rane and Jorge Ramos for carrying out several experiments and Jose R. Martinez for obtaining the 500 MHz NMR spectra.

JO971681S