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# Mechanistic insights into perfluoroaryl borane-catalyzed allylstannations: Toward asymmetric induction with chiral boranes*

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*Abstract*: The perfluoroaryl borane $B(C_6F_5)_3$ is an effective catalyst for a variety of organic transformations. In the hydrosilation of carbonyl functions, it activates the silane rather than the carbonyl substrate. In allylstannation reactions, two competing reaction pathways are observed, one involving tin cation catalysis, the other "true" borane catalysis. For $B(C_6F_5)_3$, the former mechanism dominates, while for the weaker Lewis acid $PhB(C_6F_5)_2$, the latter pathway is more prominent. Thus, chiral boranes of similar Lewis acid strength to $PhB(C_6F_5)_2$ have the potential to mediate asymmetric allylstannation of aldehyde substrates.

## INTRODUCTION

Although tris-pentafluorophenylborane, $B(C_6F_5)_3$ (Fig. 1), was first prepared over 40 years ago [1], it has only recently become widely available because of its efficacy as an olefin polymerization cocatalyst in single-site catalyst technology [2]. This rise to prominence has resulted in an assessment of its utility in other applications [3], particularly those pertaining to Lewis acid (LA) catalysis of organic transformations.

In comparison to the quintessential boron LA, $BF_3$, $B(C_6F_5)_3$ is relatively expensive ($15–80/g) but offers several advantages over $BF_3$. Most notably, $B(C_6F_5)_3$ is air- and moisture-stable; the B–C bonds are not prone to hydrolysis unless heated to high temperatures in the presence of water. Instead, a stable water adduct is formed (Fig. 1) which coordinates up to two further waters in a second sphere motif via hydrogen bonds [4]. The p$K_a$ of the mono aquo adduct has been measured at 8.4 in $CH_3CN$, indicating it is roughly as strong a Brønsted acid as HCl in that medium. Therefore, to avoid competing Brønsted acid-catalyzed pathways, $B(C_6F_5)_3$ should be dried before use, especially in mechanistic investigations such as those described below. This can be easily achieved by treating with a silane such as $Me_2SiCl(H)$, which effectively silates the water, followed by sublimation under high vacuum. This procedure results in pure, dry $B(C_6F_5)_3$, an ideal LA for carrying out detailed spectroscopic investigations. The LA strength of $B(C_6F_5)_3$ has been assessed at 0.68–0.77 on the Childs scale [5], which operates by measuring the perturbation in the $^1H$ chemical shift of the β-proton of coordinated crotonaldehyde (Fig. 1) from the free aldehyde. On this scale, $B(C_6F_5)_3$ is in between $BF_3$ and $BCl_3$ in terms of LA strength.

Several groups have utilized $B(C_6F_5)_3$ as an LA catalyst for organic reactions involving carbonyl or imine functions. For reactions such as the Mukaiyama aldol, the Diels–Alder reaction and various conjugate additions, the borane likely functions in a conventional manner, i.e., by coordinating the carbonyl function, activating it toward nucleophilic attack [6]. However, in the hydrosilation of carbonyl

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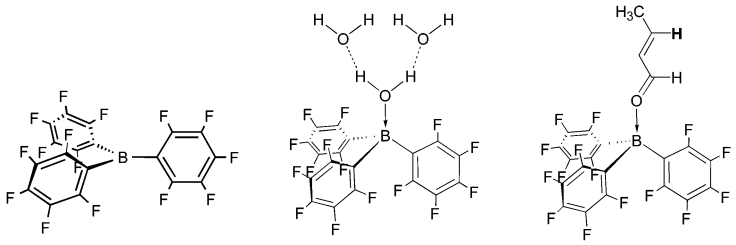
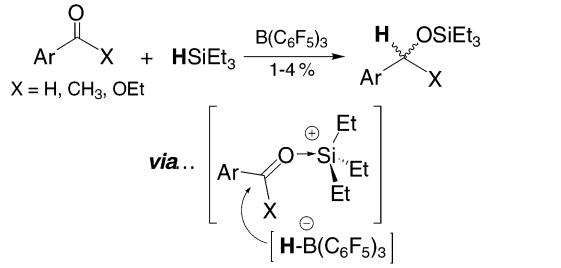


**Fig. 1** $B(C_6F_5)_3$, $B(C_6F_5)_3{\cdot}(3H_2O)$, and $B(C_6F_5)_3{\cdot}$(crotonaldehyde).

[7] or imine [8] functions, detailed mechanistic investigations revealed a nonconventional role for the LA which involved activation of the *silane* rather than the C=O or C=N bonds as the key to reaction turnover (eq. 1). Thus, although the borane forms stable and isolable adducts with several carbonyl [9] and imine [10] substrates, dissociation is required such that the borane can interact with the Si–H bond of the silane, rendering the silicon center subject to nucleophilic attack by the substrate. The resulting ion pair collapses via transfer of the hydridoborate hydrogen to the carbonyl or imine carbon, culminating the reductive process. We, and others, have applied this borane/silane catalytic system to the partial or complete silation of alcohols (eq. 2) [11], the hydrosilation of enones and silyl enol ethers [12], and the reduction of carboxylic acids [13] and phosphonic or phosphinic esters [14]. More sophisticated chemistry [15], such as the diastereoselective hydrosilation of ketones via chelation control in the silylium ion pair (eq. 3) [16], is being developed as these mechanistic ideas gain acceptance.



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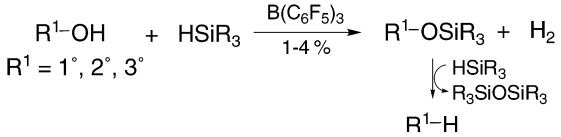

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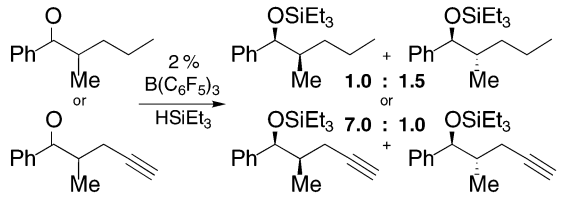


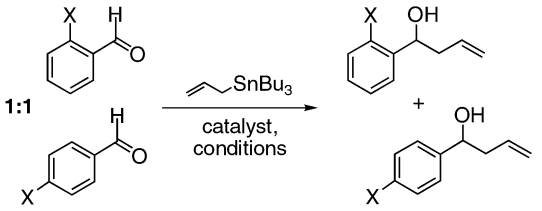
(3)

## ALLYLSTANNATION OF BENZALDEHYDES

With this backdrop in mind, we became interested in a report by Maruoka et al. detailing the chemoselective allylstannation of *ortho*-anisaldehyde in the presence of *para*-anisaldehyde as mediated by $B(C_6F_5)_3$ (Table 1, entry 1) [17]. The phenomenon appears to be quite general as long as an *ortho* substituent capable of electron pair donation is present (entries 2–4, no selectivity in entry 5) and does not depend greatly on the nature of the LA (entries 6 and 7). Taken together, these observations argue

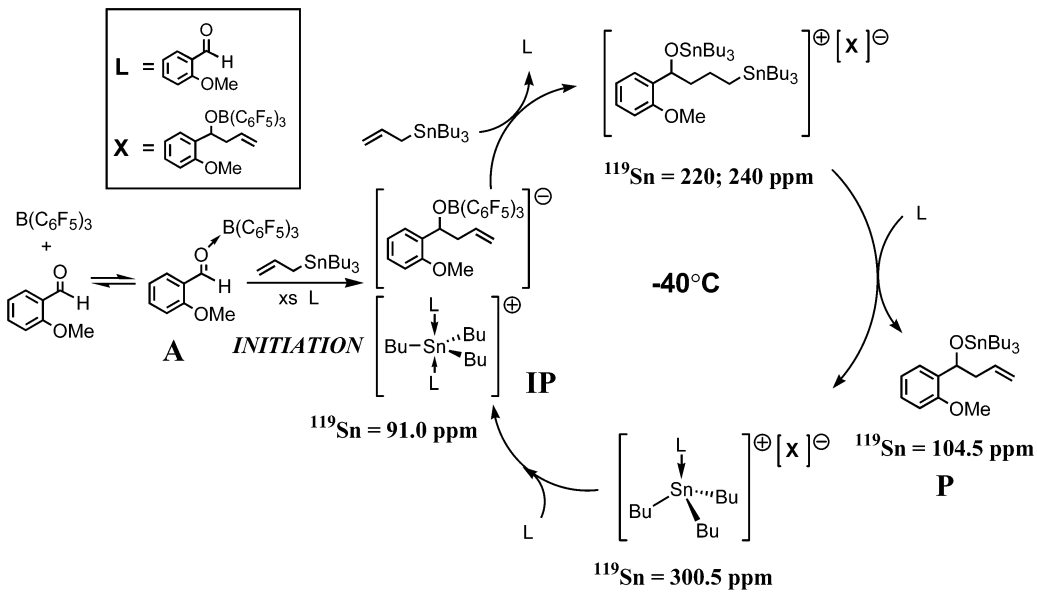
against a chelation-based explanation for the selectivity, which was initially proposed by Maruoka and coworkers [18]. For this reason, we embarked on a detailed spectroscopic and mechanistic investigation of this chemistry; the results of these studies are summarized in Scheme 1 [19].

**Table 1** *Ortho*:*para* selectivity in the catalytic allylstannation of benzaldehydes[a].




| Entry | Catalyst | X | Ratio (*ortho*:*para*) |
|---|---|---|---|
| 1 | $B(C_6F_5)_3$ | OMe | >20:1 |
| 2 | $B(C_6F_5)_3$ | F | 5:1 |
| 3 | $B(C_6F_5)_3$ | Cl | 3:1 |
| 4 | $B(C_6F_5)_3$ | OTBS | 18:1 |
| 5 | $B(C_6F_5)_3$ | Me | 1.1:1 |
| 6 | $[Bu_3Sn]^+[B(C_6F_5)_4]^-$ | OMe | 12.5:1 |
| 7[b] | $BF_3{\cdot}OEt_2$ | OMe | 7:1 |

[a]Conditions: toluene, –40 °C, 2.5 mol % catalyst.
[b]Reaction performed in $CH_2Cl_2$ at –78 °C.



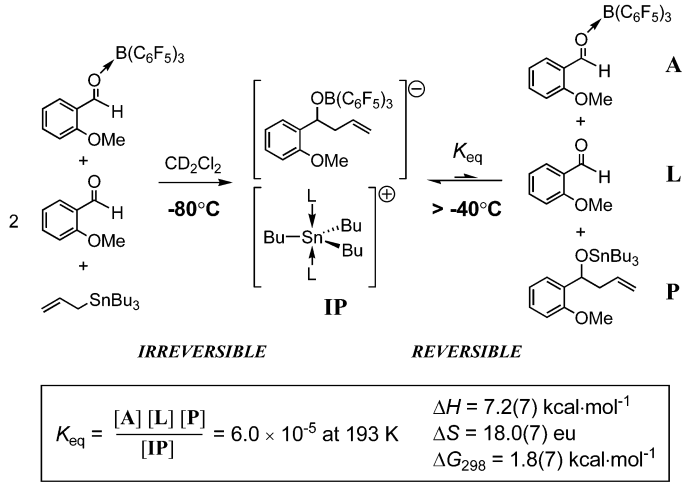

**Scheme 1**

In contrast to the hydrosilation chemistry, the borane/aldehyde adduct is attacked by the more nucleophilic organotin reagent in an irreversible C–C bond-forming reaction to form an ion pair (IP) consisting of a tributylstannylium ion solvated by two substrate molecules and an alkoxyborate counteranion. This ion pair is quite stable at low temperatures (–78 °C) where turnover of the reaction is very

slow. As the reaction mixture is warmed to temperatures of about –40 °C, product formation begins via an $[R_3Sn]^+$-catalyzed mechanism as indicated in the Scheme. Thus, the $B(C_6F_5)_3$ functions here mainly as an initiator, while the majority of the catalysis is mediated by the tin cation generated upon initial attack of allyltributyltin on the borane-activated substrate.

Similar mechanistic pathways have been implicated in LA-catalyzed allylsilation reactions [20], but have not generally been thought to be important for the more nucleophilic allyl tin reagents. The dominance of a tin cation-catalyzed pathway has obvious implications for the potential efficacy of chiral perfluorarylborane catalysts for asymmetric induction in this reaction and suggests that "turning on" a pathway involving true borane catalysis will be a key challenge in the deployment of such catalysts.

Such a borane-catalyzed pathway would necessitate direct collapse of the IP formed upon C–C bond formation to product via transfer of the alkoxy group from boron to tin. This would regenerate the adduct A for further reaction with allyltin reagent. It is possible to isolate and study this product-forming step upon generation of the ion pair in the absence of excess allyltin reagent by mixing the aldehyde, borane, and tin reagents in a 3:1:1 ratio as shown in Scheme 2. When this reaction is performed at –80 °C in $CD_2Cl_2$, the IP is generated smoothly and, upon warming, an equilibrium is established in which product P is generated along with the $B(C_6F_5)_3$/*ortho*-anisaldehyde adduct A and free aldehyde L. The equilibrium constant can be evaluated at various temperatures by determining the concentrations of the various components by $^1H$ and $^{19}F$ NMR spectroscopy [21].




$$K_{eq} = \frac{[\mathbf{A}]\,[\mathbf{L}]\,[\mathbf{P}]}{[\mathbf{IP}]} = 6.0 \times 10^{-5} \text{ at } 193 \text{ K}$$

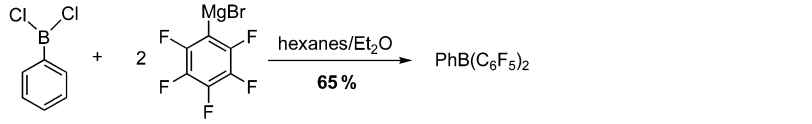
$\Delta H = 7.2(7)$ kcal·mol$^{-1}$
$\Delta S = 18.0(7)$ eu
$\Delta G_{298} = 1.8(7)$ kcal·mol$^{-1}$

**Scheme 2**

This experiment allows for a rare glimpse into the thermodynamic factors affecting the product-forming step of an LA-catalyzed reaction. As shown in the Scheme, this equilibrium, in the product-forming direction, is enthalpically disfavored, but entropically favored. Although there are obviously ill-defined kinetic factors that come into play, we reasoned that if one could make the equilibrium more enthalpically favorable, one might render this pathway more important for product formation than the tin-catalyzed pathway described above in Scheme 1. Since the stability of the IP is likely related to the strong B–O bond formed in the irreversible allylation step, it is possible that a slightly *weaker* LA might lead to a thermodynamically less stable IP, and favor the right-hand side of the equilibrium.

Our choice for this weaker LA was the phenyl-bis-pentafluorophenyl derivative $PhB(C_6F_5)_2$. This compound is best prepared from $PhBCl_2$ and freshly prepared $C_6F_5MgBr$, generated from $C_6F_5Br$ and $^i$PrMgBr as shown in eq. 4 [22]. The use of fresh pentafluorophenyl Grignard reagent is key to obtaining good yields of $PhB(C_6F_5)_2$, which can be purified by sublimation. Unlike $B(C_6F_5)_3$, this borane is

highly water-sensitive, producing the borinic acid $HOB(C_6F_5)_2$ in the presence of water. As determined using the Child's method, $PhB(C_6F_5)_2$ is clearly a weaker LA than the fully fluorinated $B(C_6F_5)_3$ (Table 2). Its Child's acidity of 0.54 renders it about the same as $SnCl_4$ or $Et_2AlCl$, so it is still a relatively strong LA by virtue of the two remaining $C_6F_5$ groups on the boron. However, in a competition experiment for benzaldehyde, $B(C_6F_5)_3$ wins decisively (eq. 5); no trace of the $PhB(C_6F_5)_2$/benzaldehyde adduct is observed, and the equilibrium is effectively shifted completely to the right-hand side of eq. 5 in this experiment.

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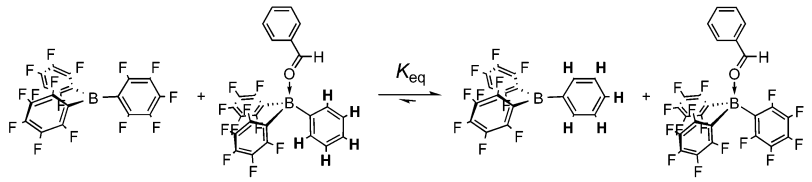


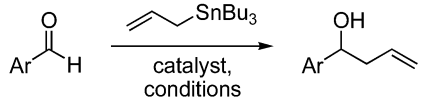

(5)

**Table 2** Relative Lewis acid strengths.

| Lewis acid | Child's acidity |
|---|---|
| $B(C_6F_5)_3$ | 0.68 ± 0.03 |
| $Et_2AlCl$ | 0.59 ± 0.03 |
| $PhB(C_6F_5)_2$ | 0.54 ± 0.03 |
| $SnCl_4$ | 0.52 ± 0.04 |

Despite being a demonstrably weaker LA than $B(C_6F_5)_3$, the phenyl-substituted borane is a superior allylation catalyst for allylation of benzaldehyde substrates (Table 3). For example, at temperatures where tin cation catalysis is known to be slow, the $PhB(C_6F_5)_2$-catalyzed reaction is finished while the $B(C_6F_5)_3$-mediated reaction is only 21 % completed in the same time (entries 1 and 2). The same trends apply for benzaldehyde (entries 3–6) and *para*-substituted derivatives (entries 7–10), although for very electrophilic substrates such as *p*-$NO_2$-benzaldehyde the difference in activity is less pronounced.

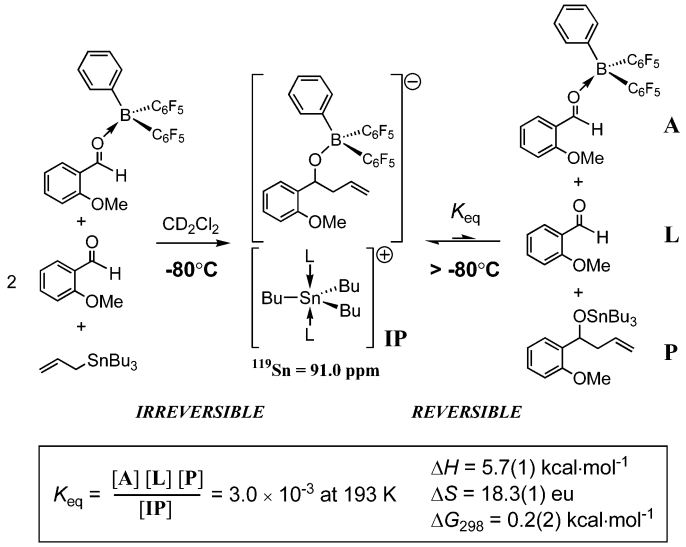
**Table 3** Lewis acid-catalyzed allylstannation of benzaldehydes[a].




| Entry | Catalyst | Ar | T (°C) | Time (min) | Convn. (%)[b] |
|---|---|---|---|---|---|
| 1 | $B(C_6F_5)_3$ | *o*-MeO-$C_6H_4$ | –44 | 75 | 21 |
| 2 | $PhB(C_6F_5)_2$ | *o*-MeO-$C_6H_4$ | –44 | 75 | 100 |
| 3 | $B(C_6F_5)_3$ | $C_6H_5$ | –44 | 60 | 95 |
| 4 | $PhB(C_6F_5)_2$ | $C_6H_5$ | –44 | 40 | 100 |
| 5 | $B(C_6F_5)_3$ | $C_6H_5$ | –78 | 600 | 62 |
| 6 | $PhB(C_6F_5)_2$ | $C_6H_5$ | –78 | 600 | 96 |
| 7 | $B(C_6F_5)_3$ | *p*-Cl-$C_6H_4$ | –78 | 300 | 38 |
| 8 | $PhB(C_6F_5)_2$ | *p*-Cl-$C_6H_4$ | –78 | 300 | 100 |
| 9 | $B(C_6F_5)_3$ | *p*-$NO_2$-$C_6H_4$ | –78 | 70 | 95 |
| 10 | $PhB(C_6F_5)_2$ | *p*-$NO_2$-$C_6H_4$ | –78 | 70 | 100 |

[a]Conditions: $CH_2Cl_2$, 0.1 M in ArCHO, 0.5 mmol ArCHO, 0.55 mmol allyl$SnBu_3$, 5.0 mol % catalyst.
[b]Conversion of ArCHO by GC after quenching reaction aliquot in $H_2O$.

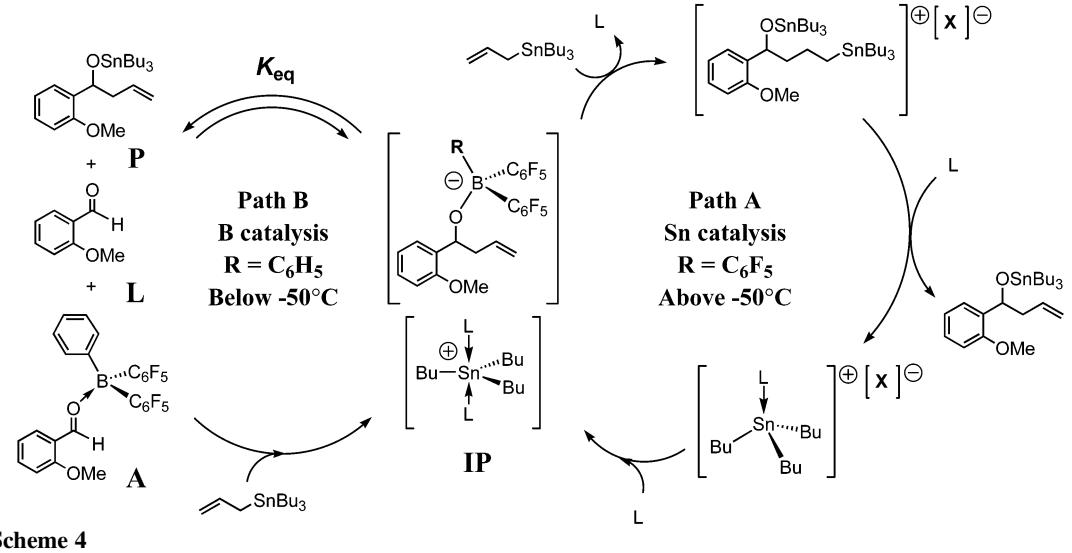
This observation is an unusual one since it is a largely accepted tenet of LA catalysis that stronger LAs should result in enhanced rates of reaction, and not decreased activity. At least part of the explanation for this phenomenon lies in the effect of substituting a phenyl group for a pentafluorophenyl group on the equilibrium described above in Scheme 2. A similar experiment using $PhB(C_6F_5)_2$ instead of $B(C_6F_5)_3$ allows for study of the analogous equilibrium in this case (Scheme 3). Already in the formation of the IP, it is apparent that the right-hand side of the equilibrium is more favored in this case, since signals for A, L, and P are immediately detectable at –80 °C in this experiment where they were not apparent until a warmer temperature regime in the equilibrium of Scheme 2 [23]. Van't Hoff analysis of this equilibrium gives a similar value for $\Delta S$ as expected, but $\Delta H$ is almost 2 kcal $mol^{-1}$ less than that determined for the $B(C_6F_5)_3$ equilibrium. Again, kinetic factors must also be important for the observed higher rate of catalysis using $PhB(C_6F_5)_2$, but clearly there is a positive effect on the thermo-




**Scheme 3**

dynamics of the product-forming step in the reaction when using the weaker LA. Whereas the stronger LA $B(C_6F_5)_3$ is "leveled" to the strength of $[Bu_3Sn(L)]^+$, $PhB(C_6F_5)_2$ provides a closer match to the tin cation in terms of LA strength, allowing for more facile transfer of the alkoxy group from boron to tin and turnover via a "true" borane-catalyzed pathway.

These detailed spectroscopic and mechanistic studies have thus delineated two competing mechanistic pathways for turnover in the catalytic allylstannation of benzaldehyde substrates (Scheme 4). Path A is a tin cation-mediated pathway, in which the borane is effectively sequestered in the counteranion of the stannylium species responsible for the majority of the catalysis. This pathway dominates in the $B(C_6F_5)_3$-initiated reactions, since reaction turnover is not generally observed until the medium is warmed to temperatures where it is known that tin cations are effective catalysts for this reaction. Path B, however, is a pathway where genuine borane catalysis takes place, and its relative importance is governed to some extent by the thermodynamic characteristics of the equilibria discussed above. Thermodynamic destabilization of the IP appears to favor product formation via alkoxide transfer from boron to tin, "turning on" catalysis by Path B. This is indicated by the macroscopic observation that $PhB(C_6F_5)_2$ catalyzes the allylation of *ortho*-anisaldehyde at very low temperatures—conditions under which tin cation catalysis is nullified and catalysis by $B(C_6F_5)_3$ is very slow.



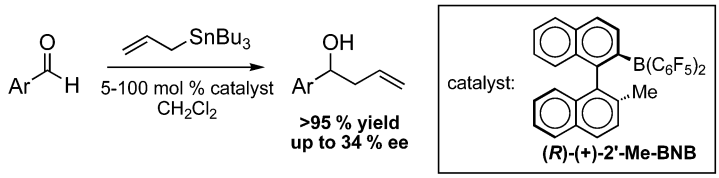

**Scheme 4**

These observations are critical for the goal of using chiral perfluoroaryl boranes for effecting these allylations in an enantioselective way. Catalysis by Path A has little hope of influencing the C–C bond-forming step beyond the first turnover—the initiation step. However, Path B brings the chiral borane into play in each turnover and thus provides hope that a chiral borane will exert sufficient asymmetric influence for high enantioselectivity.

Preliminary results toward this goal suggest that this is the case. We have prepared the chiral borane shown in eq. 6, which incorporates a binaphthyl group as the chiral element [24]. This material can be prepared in five steps from enantiopure (*R*)-2,2′-dibromo-1,1′-binaphthyl in an overall yield of 56 % ($[\alpha]_D$ = + 448). Assessment of the diastereopurity of (–)-diethyltartrate derivatives of two intermediates in the synthesis indicates that the 2′-Me-BNB has >99 % enantiopurity.

(*R*)-(+)-2′-Me-BNB is an effective catalyst for the allylstannation of benzaldehydes (eq. 6), giving high yields of the allylic alcohol products upon work-up. Furthermore, while observed ee's are modest, the fact that any enantioselection is observed at all is indicative that some measure of Path B

borane catalysis is operative. We are currently modifying the structure of the chiral borane to optimize its performance in this and other reactions. These results will be reported in detail in due course.




(6)

## CONCLUSIONS

In conclusion, we have performed detailed mechanistic studies on the perfluoroarylborane-initiated or -mediated allylstannation of aromatic aldehydes. The studies illustrate the complexity of these reactions and underscore that subtle changes in catalyst or substrate structure can strongly influence the mechanistic pathway taken for reaction turnover. Two competing pathways in this particular reaction have been identified, and some of the thermodynamic factors influencing the choice between them have been delineated. We have used this knowledge in the development of chiral perfluoroaryl boranes and observed slim, but definite enantioselection in the allylation of benzaldehyde and *ortho*-anisaldehyde. These preliminary results are encouraging, and the information we have concerning the structures of the borane/substrate adducts and the mechanisms of the reactions offer strong suggestions for the direction of further development.

## ACKNOWLEDGMENTS

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23. The components of the equilibrium of Scheme 3 that are different than those of Scheme 2, i.e., IP and A, were prepared separately and their NMR spectroscopic signatures matched those observed in the equilibrium experiments.
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