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Weaker Lewis Acid, Better Catalytic Activity: Dual Mechanisms in Perfluoroarylborane-Catalyzed Allylstannation Reactions

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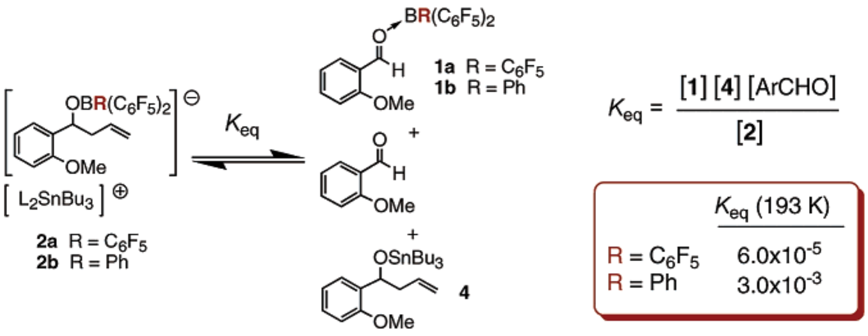
ABSTRACT



$PhB(C_6F_5)_2$ exhibits much higher activity as a Lewis acid catalyst for the allylstannation of aromatic aldehydes than the stronger Lewis acid $B(C_6F_5)_3$. This anomalous enhancement of catalytic activity for the weaker LA is shown to be partly due to decreased thermodynamic stability of ion pair 2b relative to 2a in the product-forming step of the reaction. A mechanistic path where the borane serves as the true LA catalyst is more important for the weakly Lewis acidic borane.

Lewis acids (LAs) enhance the rates of reactions involving carbonyl functions via coordination of an oxygen lone pair, which activates the C═O group toward attack by weak nucleophiles.[1] One of the precepts of LA catalysis is that, for isosteric LAs, greater LA strength translates into more effective activation of the C═O group and therefore higher rate enhancement.[2] Although this is likely the case on a fundamental level, complex mechanisms of operation can make this false on a practical level.[3]

Recently we reported the results of a detailed spectroscopic investigation on the mechanism of $B(C_6F_5)_3$-catalyzed allylstannation of *ortho* donor substituted aromatic aldehydes.[4] The picture that emerged showed that the majority of catalysis in this system is carried out by the stannylium cation in the ion pair **2a** depicted in Scheme 1. The borane is largely sequestered in the anion of this species once the reaction is initiated by allylstannation of substrate−borane adduct **1a**. Thus, in the presence of excess allylstannane, as would be

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(1) (a) *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed.; Wiley-VCH: Weinheim, 2000. (b) Shambayati, S.; Crowe, W. E.; Schrieber, S. L. *Angew. Chem., Int. Ed.* **1990**, *29*, 1053.

(2) Lewis acid strength has been shown to directly correlate with reactivity in LA-catalyzed reactions of carbonyls. (a) Ene reactions: Laszlo, P.; Teston-Henry, M. *Tetrahedron Lett.* **1991**, *32*, 3837. Laszlo, P.; Teston, M. *J. Am. Chem. Soc.* **1990**, *112*, 8750. (b) Aldol reactions: Kobayashi, S. *Eur. J. Org. Chem.* **1999**, 15 and references therein. (c) Classification of LAs on the basis of activity and selectivity: Kobayashi, S.; Tsuyoshi, B.; Nagayama, S. *Chem. Eur. J.* **2000**, *6*, 3491.

(3) (a) $La(OTf)_3$ and $Sm(OTf)_3$ were more effective than the stronger LA $Sc(OTf)_3$ (see ref 3b) in LA-catalyzed Baylis−Hillman reactions: Aggarwal, V. K.; Mereu, A.; Tarver, G. J.; McCague, R. *J. Org. Chem.* **1998**, *63*, 7183. (b) Fukuzumi, S.; Ohkubo, K. *J. Am. Chem. Soc.* **2002**, *124*, 10270.

(4) Blackwell, J. M.; Piers, W. E.; McDonald, R. *J. Am. Chem. Soc.* **2002**, *124*, 1295.

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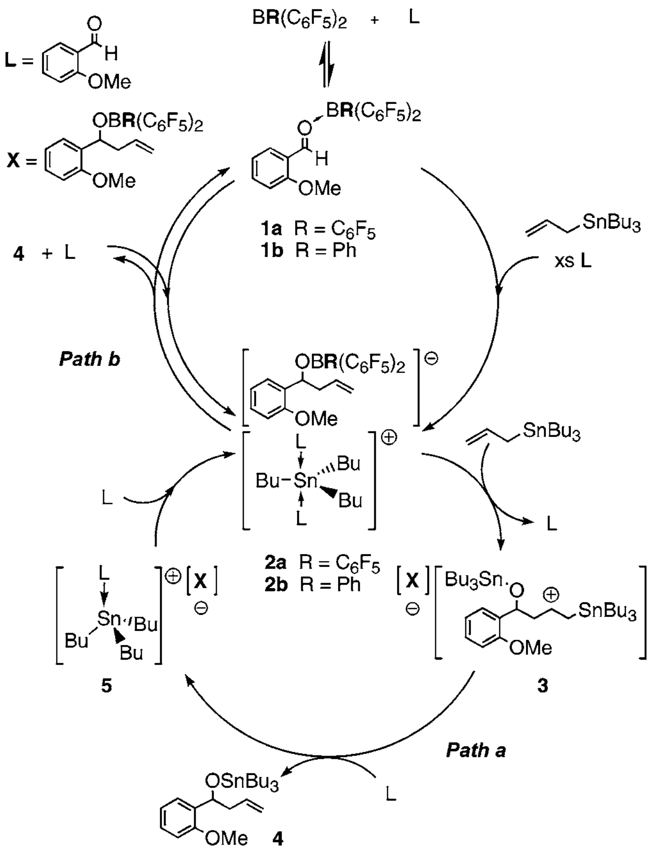
Scheme 1



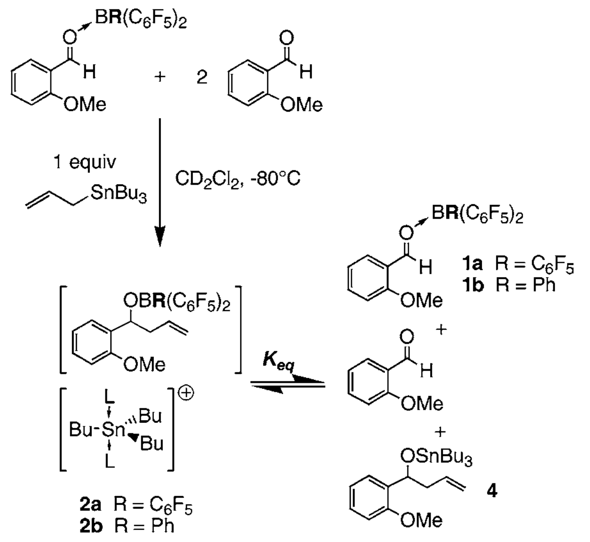
the case under catalytic conditions, **2a** undergoes allylation at −40 °C via aldehyde activation by the Lewis acidic stannylium cation giving ion pair **3** (path a, Scheme 1). *o*-Anisaldehyde substrate regenerates **2a** by displacement of stannyl ether product **4** and trapping of the monoligated intermediate **5**.

The traditionally expected product-forming path based on exclusive borane catalysis involves direct collapse of ion pair **2a** (path b). Previously, we observed that in the absence of excess allylSnBu$_3$ product formation from **2a** is slow at −40° but begins to occur upon warming from this temperature. Interestingly, in the presence of excess aldehyde substrate, formation of **4** via path b is significantly suppressed. Closer examination of this system reveals that this product-forming step is reversible and this equilibrium can be studied when allyl stannane reagent is absent.

Ion pair **2a** can be generated via the treatment of **1a** with 1 equiv of allylSnBu$_3$ in the presence of 2 equiv of *o*-anisaldehyde as shown in Scheme 2 (R = C_6F_5). At temperatures above −40 °C, onset of the "path b" equilibrium is observed; K_{eq} can also be approached from the right side of the equation by mixing stannyl ether **4** with *o*-anisaldehyde and **1a** in the appropriate ratio.

The equilibrium constant (eq 1) can be evaluated at various temperatures by using ^{1}H and ^{19}F NMR spectroscopy to determine the concentrations of the components. A van't Hoff plot for this equilibrium is shown in Figure 1 (open circles),

Scheme 2



giving a value of 18.0(7) eu for ΔS and 7.21(6) kcal mol^{-1} for ΔH.

$$K_{eq} = \frac{[\mathbf{1}][\mathbf{4}][\mathrm{ArCHO}]}{[\mathbf{2}]} \qquad (1)$$

Although the conditions of this experiment do not mimic those of the catalytic reaction directly, this equilibrium represents the product-forming step in a borane-catalyzed mechanism and offers a rare opportunity to assess the thermodynamic factors affecting this process. The thermodynamic data suggest that the product-forming step in path b is largely entropically driven and is enthalpically disfavored perhaps as a result of the fact that the high Lewis acidity of $B(C_6F_5)_3$ stabilizes the ion pair **2a** via a strong B−O bond. A weaker Lewis acid might be expected to make path b more enthalpically favorable. Indeed, the partially fluorinated LA $PhB(C_6F_5)_2$,[5] which is a weaker LA than its fully fluorinated

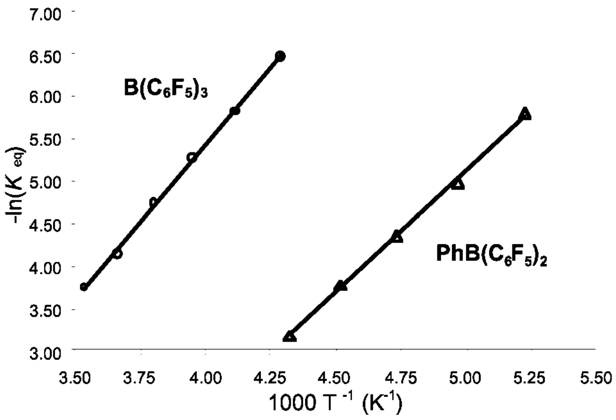
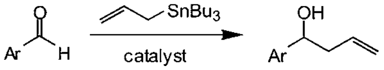


Figure 1. van't Hoff plots of −ln(K_{eq}) versus 1000 T^{-1} for the equilibria in Scheme 2: (○) $B(C_6F_5)_3$, (Δ) $PhB(C_6F_5)_2$.

Table 1. Lewis Acid Catalyzed Allylstannation of Benzaldehyde[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 loading. [b] Conversion of ArCHO by GC after quenching reaction aliquot into H_2O.

counterpart,[6] is a significantly more active allylation catalyst than $B(C_6F_5)_3$ toward o-anisaldehyde (Table 1, entries 1 and 2).

To probe the origin of this unusual observation, the thermoynamic data for the equilibrium involving ion pair **2b** was acquired in a fashion analogous to that described above for **2a** (Scheme 2). As with the $B(C_6F_5)_3$-promoted reaction, all of the allyl$SnBu_3$ was rapidly and irreversibly consumed in a C−C bond forming reaction with borane-activated aldehyde. Equilibrium was reached after ∼5 h at −80 °C. The only signals in the ^{119}Sn NMR spectrum of the equilibrium mixture are of stannyl ether **4** at 110 ppm and a signal identical to that reported for the *bis*-aldehyde ligated tributyltin cation $[(o\text{-anisaldehyde})_2SnBu_3]^+$ at 92 ppm.[4] The ^{19}F NMR spectrum indicates the presence of only two fluorine-containing species; the borane−aldehyde adduct **1b** and a second set of signals due to the alkoxy borate species **2b**.[7] Finally, van't Hoff analysis of this equilibrium (Figure 1, open triangles) yields a ΔS value of 18.3(1) eu and a ΔH of 5.70(5) kcal mol^{-1}. Not surprisingly, the ΔS values for these two equilibria are quite similar, but the $\Delta\Delta H$ of 1.51(5) kcal mol^{-1} indicates that the ion pair **2b** is less enthalpically stable than the fully fluorinated alkoxyborate **2a**. The least-squares analysis of the van't Hoff plots allows estimation of K_{eq} values at one temperature for direct comparison of the two boranes. At 193 K, K_{eq} values are estimated to be 3.0×10^{-3} for $PhB(C_6F_5)_2$ and 6.0×10^{-5} for $B(C_6F_5)_3$.

The higher activity observed for the weaker LA extends to other aromatic aldehyde substrates (Table 1). Benzaldehyde itself is a more active substrate, but at both −44 and −78 °C $PhB(C_6F_5)_2$ is a more effective catalyst than $B(C_6F_5)_3$.[8] The same trend exists for p-chlorobenzaldehyde, while the difference is less pronounced for the highly activated substrate p-nitrobenzaldehyde at −78 °C. This latter observation is likely a reflection of the effect of the *para* substituent on the thermodynamic stability of the ion pairs **2** and suggests that the balance between path a or b is also affected by the nature of the substrate.

Thus, although $B(C_6F_5)_3$ is clearly a stronger LA than $PhB(C_6F_5)_2$,[6] this leads not to higher activity as an allylation catalyst but rather to greater thermodynamic stability of the product of the first C−C bond forming step in the reaction, **2a**. The ion pair **2b**, on the other hand, does not fall into as deep a well and the equilibrium is more biased toward product **4** and **1b**, which in the presence of excess allyltin reagent is rapidly allylated, shunting the reaction toward path b. However, while the data for the equilibria of Scheme 2 provide a partial explanation for the observed higher activity for the weaker Lewis acid $PhB(C_6F_5)_2$, clearly there are ill-defined kinetic factors contributing to the higher rate of transfer of the alkoxy group from boron to tin in **2b** as opposed to **2a**. Possibly, the substitution of one C_6F_5 group for a less electron-withdrawing C_6H_5 renders the alkoxy group significantly more nucleophilic in the phenyl-substituted borate anion, lowering the barrier to product-forming transfer to tin. Given that the intimate mechanisms of these equilibria likely involve multiple steps, the factors affecting the observed rates are complex.

In summary, unlike $B(C_6F_5)_3$, the weaker LA $PhB(C_6F_5)_2$ likely functions as a true LA catalyst for the allylstannation reaction and is in practical terms much more effective than either $B(C_6F_5)_3$ or $[Bu_3Sn(L)]^+$. In effect, $B(C_6F_5)_3$ is partially buffered to the strength of $[Bu_3Sn(L)]^+$, and as previously determined,[4] a significant portion of the catalysis occurs via path a for this borane. $PhB(C_6F_5)_2$ is strong enough to promote allylation but weak enough to more effectively transfer the OR group to tin to complete the reaction via path b. This concept can only be extended so far, however; the substantially weaker LA BPh_3 (Child's Lewis acidity = 0.06) is not an active catalyst for the allylstannation of benzaldehyde at or below −44 °C, so a threshold borane Lewis acidity is required in order to initiate this reaction.[9]

The ability to "turn on" path b via modification of Lewis acidity has significant implications for development of this chemistry, since chiral boranes can be expected to be effective for asymmetric allylation procedures by this mech-

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(5) Deck, P. A.; Beswick, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 1772.

(6) (a) $PhB(C_6F_5)_2$ exhibits a Child's Lewis acidity[6b] (0.54) lower than that of $B(C_6F_5)_3$ (0.68). In addition to significantly weaker Child's Lewis acidity, in a competition experiment between $B(C_6F_5)_3$ (1 equiv) and $PhB(C_6F_5)_2$ (1 equiv) for PhCHO (0.9 equiv) in CD_2Cl_2, only the $B(C_6F_5)_3$−PhCHO adduct **1a** was observed by ^{19}F NMR, confirming the higher Lewis acidity of $B(C_6F_5)_3$ for PhCHO (see Supporting Information). (b) Childs, R. F.; Mulholland, D. L.; Nixon, A. *Can. J. Chem.* **1982**, *60*, 801.

(7) The spectroscopic signature of the alkoxyborate anion in **2b** was identical to that of its $[NBu_4]^+$ salt, generated separately (see Supporting Information for details).

(8) (a) At the same temperatures and times, use of separately prepared[8b] stannylinium cation $[Bu_3Sn]^+[B(C_6F_5)_4]^-$ as a catalyst gives conversions of 40% at −44°C and 9% at −78°C. (b) Lambert, J. B.; Kuhlmann, B. *J. Chem. Soc., Chem. Commun.* **1992**, 931.

(9) (a) Unfortunately, the final member of this family of boranes, namely, $Ph_2B(C_6F_5)$ is prone to redistribution,[9b] such that small amounts of $PhB(C_6F_5)_2$ are always present, skewing comparisons between the two. (b) Bradley, D. C.; Harding, I. S., Keefe, A. D.; Motevalli, M.; Zheng, D. H. *J. Chem. Soc., Dalton Trans.* **1996**, 3931.

anism but not via the tin-catalyzed path a. We are pursuing the synthesis of chiral perfluroaryl boranes and further examining the effects of solvent and temperature on the equilibria described herein to inform our design of new LAs.

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Supporting Information Available: Full experimental and characterizational details and K_{eq} data. This material is available free of charge via the Internet at http://pubs.acs.org.

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