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Ni-Catalyzed Borylative Diene−Aldehyde Coupling: The Remarkable Effect of $P(SiMe_3)_3$

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Rapid construction of complex molecules with high regio- and stereoselectivity is a central objective in organic synthesis. In this regard, reactions that result in the formation of multiple new bonds and that establish multiple stereocenters are particularly valuable.[1] To address this topic, we recently initiated studies on the borylative coupling of unsaturated substrates.[2] In one manifestation of this strategy, we examined the Mori−Tamaru Ni-catalyzed coupling of aldehydes and dienes[3,4] but employed bis(pinacolato)diboron ($B_2(pin)_2$) as the reducing agent. In the presence of PCy_3 as an ancillary ligand for nickel, reaction product **3** (Scheme 1) is furnished as a single constitutional and stereoisomer. In accord with mechanistic studies by Ogoshi,[5] it is likely that this reaction occurs by a pathway involving oxidative cyclometalation to give **1**; subsequent transmetalation would furnish **2** and reductive elimination to connect C1 with the boryl ligand would release **3** from the catalyst. We considered that other ligands might alter the regioselectivity of the reductive elimination by connection of C3 and the boryl group and, thereby, furnish allylboronate **4** as the reaction product. The structural features of compound **4** − three contiguous stereocenters, an α-chiral allylboronate,[6] and a functional group pattern that maps onto polyketides − made this a compelling inquiry. In this report, we describe a remarkable turnover in regioselectivity of the borylative diene/aldehyde coupling when PCy_3 is replaced with $P(SiMe_3)_3$.

Initial exploratory studies focused on the nickel catalyzed reaction between 1 equiv each of 1,3-pentadiene, benzaldehyde, and $B_2(pin)_2$. While PCy_3 and $P(t\text{-}Bu)_3$ both promoted formation of terminal boronate **3** (analysis after oxidative workup with hydrogen peroxide), other alkyl and aryl phosphines, triaminophosphines, and simple phosphites were either ineffective or resulted in poor selectivity (Table 1). *However, when commercially available $P(SiMe_3)_3$ was employed, compound* **4** *was observed with excellent selectivity*.

In addition to compound **4**, byproducts comprising two aldehydes and one diene or two dienes and one aldehyde were also observed. Reasoning that reaction of **4** with unreacted aldehyde might compete with the catalytic process at later stages of reaction and deliver some of these byproducts, the concentrations of $B_2(pin)_2$ and pentadiene were increased. This strategy furnished optimal conditions for this three-component process. As depicted in Table 2, upon oxidation the borylative coupling reaction converts benzaldehyde and 1,3-pentadiene to the derived 1,3-diol with >20:1 diastereoselectivity.[7] Examination of other substrates revealed that, in general, the reaction is effective for aromatic and heteroaromatic aldehydes and generally delivers the 1,3-diol with excellent regio- and stereocontrol. To determine whether this transformation might apply to more common synthetic building blocks, the aliphatic aldehydes in entries 8−12 were also studied. These experiments suggest that the reaction can be effective with both linear and branched aliphatic aldehydes; additionally, a simple α-chiral aldehyde was found to react with Felkin selectivity thereby opening the possibility for asymmetric synthesis (entry 12).

Scheme 1

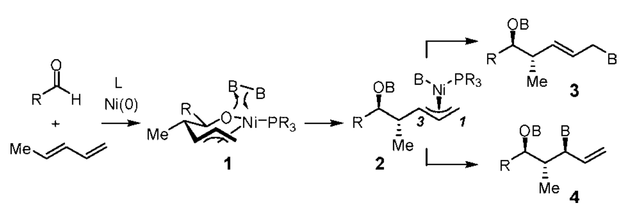
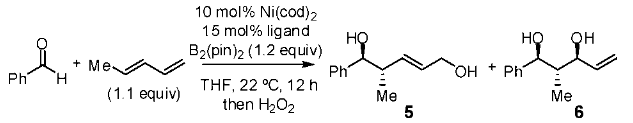


Table 1. Effect of Ligand On the Ni-Catalyzed Diborylative Coupling



entry	ligand	**5**:**6**	% yield[a]	d.r.[b]
1	none	>20:1	39	1:1
2	PCy_3	>20:1	69	>20:1
3	$P(t\text{-}Bu)_3$	>20:1	71	6:1
4	PPh_3	>20:1	63	5:1
5	$P(NMe_2)_3$	>20:1	16	>20:1
6	$P(OEt)_3$	>20:1	40	4:1
7	PEt_3	1:2	34	2:1
8	PMe_3	1:3	55	4:1
9	$P(SiMe_3)_3$	1:12	45	>20:1

[a] Isolated yield of major product. [b] d.r. of major product.

As alluded to in the introduction, general structure **4** possesses an α-chiral allylic boronate, a motif that often engages in highly selective carbonyl allylation reactions. To probe the capacity for structures such as **4** to participate in stereoselective allylations, benzaldehyde and 1,3-pentadiene were subjected to borylative coupling and, after 12 h, isobutyraldehyde was added to the reaction mixture. This single-pot reaction sequence delivered 1,6-diol **9** (Scheme 2) in good yield, as a single regioisomer, and with excellent levels of 1,5-stereoinduction (>20:1 d.r.) and olefin stereocontrol. Considering the olefin configuration in the reaction product, it appears plausible that boronate **7** reacts with isobutyraldehyde by way of transition structure **8** with the α-substituent occupying a pseudoequatorial position.[8]

$P(SiMe_3)_3$ is a relatively unknown ligand in transition metal catalysis,[9] and the reversal in regioselectivity when it is used in place of PCy_3 or $P(t\text{-}Bu)_3$ deserves comment. Data in Table 1 reveal that smaller ligands may favor formation of **4** (entries 7 and 8 versus entries 2 and 3), which might suggest that $P(SiMe_3)_3$ simply serves as a precursor to PH_3 (reaction with adventitious moisture).[10] However, *in situ* ^{31}P NMR analysis of reactions in the presence of $P(SiMe_3)_3$ shows that most of the ligand remains unmodified ($^{31}P\ \delta = -251.4$ ppm) over the course of the catalytic reaction.[11] The fact that the cone angle of $P(SiMe_3)_3$ is similar to that of $P(t\text{-}Bu)_3$ (178° versus 182°)[12] suggests that the difference in regioselectivity observed with these ligands may arise from electronic rather than steric differences. While the ^{13}C NMR

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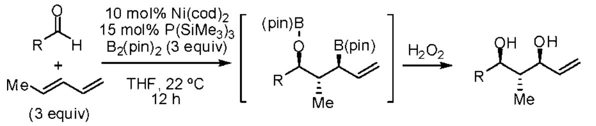
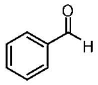
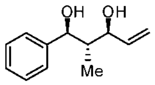
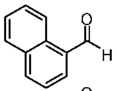
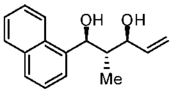
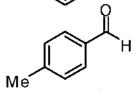
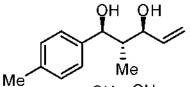
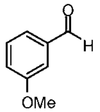
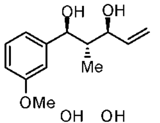
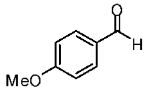
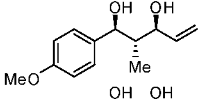
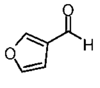
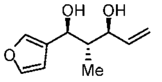
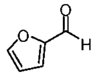
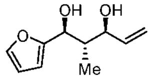
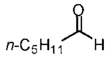
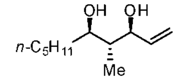
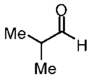
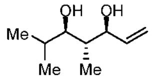
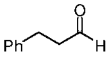
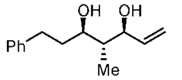
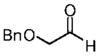
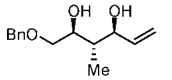
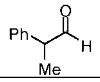
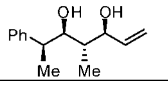
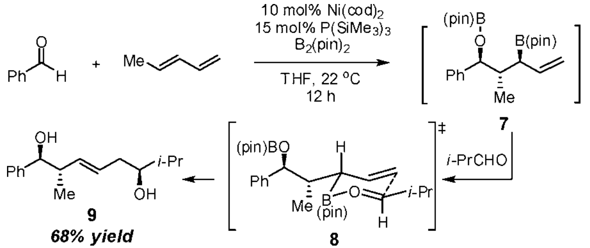
Table 2. Ni(cod)$_2$/P(SiMe$_3$)$_3$-Catalyzed Diborylative Coupling



entry	aldehyde	product	d.r.[a]	% yield[b]
1			>20:1	67
2			>20:1	73
3			>20:1	64
4			>20:1	57
5			>20:1	57
6			>20:1	55
7			>20:1	54
8			>20:1	58[c]
9			>20:1	50[c]
10			>20:1	45[c]
11			>20:1	37[c]
12			6:1[d]	49[c]

[a] Determined by ^{1}H NMR analysis of unpurified reaction mixture. [b] Isolated yield of purified material. Value is an average of two experiments. [c] Run with 1.1 equiv of diene and 1.2 equiv of B$_2$(pin)$_2$. [d] Ratio refers to Felkin/anti Felkin selectivity. Reaction for 24 h.

Scheme 2



chemical shift[13] and IR analysis (A$_1$ CO stretching frequency) of (Me$_3$Si)$_3$PNi(CO)$_3$ suggest that P(SiMe$_3$)$_3$ and trialkylphosphines are electronically similar ligands, analyses by both Bartik[14] and Helm[15] indicate that P(SiMe$_3$)$_3$ can act as an electron acceptor. Thus a tentative hypothesis is that the large cone angle of P(SiMe$_3$)$_3$, combined with an ability to act as an electron acceptor, may facilitate reductive elimination of **4** from **2**, prior to allyl isomerization required for formation of **3**.[16]

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Supporting Information Available: Characterization and procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) Consistent with this hypothesis, the borylative coupling reaction with tris(2,4-di-*tert*-butylphenyl) phosphite as the ligand (cone angle = 215°;Crous, R.; Datt, M.; Foster, D.; Bennie, L.; Steenkamp, C.; Huyser, J.; Kirsten, L.; Steyl, G.; Roodt, A. *Dalton Trans.* **2005**, 1108) also furnishes **4** selectively, albeit in an inferior yield relative to P(SiMe$_3$)$_3$.

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