## DIENES, ENYNES AND STYRENES FROM MARKOVNIKOV VINYLBORANES VIA THE SUZUKI REACTION

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**Abstract.** The clean, efficient Pd-catalyzed cross coupling of vinyl, alkynyl and aryl bromides with Markovnikov vinylboranes gives 56-96% yields of the corresponding 1,3-dienes, 1-en-3-ynes and styrenes, with complete retention of configuration observed for the 1,3-dienes.

Until recently,<sup>2</sup> Markovnikov vinylboranes (*i.e.* **1**) were unavailable in the pure state and, as a consequence, these potentially versatile reagents have been largely excluded from the many synthetically useful conversions, which have been developed for vinylboranes.<sup>3</sup> Impressed with the versatility of the Suzuki protocol for the construction of new carboncarbon bonds,<sup>4</sup> we have found this approach to provide a highly useful entry to a variety of *C*-functionalized organosilanes.<sup>5</sup> In certain cases, it has proven to be synthetically advantageous to employ partially oxidized organoboranes such as *B*-alkyl-9-oxa-10-borabicyclo[3.3.2]decanes for these couplings because these air-stable reagents are easy to handle while also providing an efficient source of the *B*-alkyl moiety.<sup>5b,c</sup>

Internal vinylboranes also undergo vinyl group transfer under the Suzuki conditions, but few examples are known and none for compounds that correspond to the general type illustrated for 1 or  $2.^{5a.6}$  In this Letter, we report a very convenient route to  $\alpha$ -substituted styrenes, as well as to 2-substituted 1,3-dienes and 1-en-3-ynes *via* the Pd-catalyzed cross coupling of the appropriate aryl, alkenyl and alkynyl bromides with Markovnikov vinylboranes (1 or 2). Our results are presented in Table 1.<sup>7</sup>



Entry	Borane	R	$R^1$	t (h)	%Pd		Product Yield <sup>*</sup>		
							3	4	
1	1a	n-Pr	Ph	13	4	a	67 <sup>b</sup>	27°	
2	1b	n-Bu	Ph	14	8	b	66	25	
3	1b <sup>d</sup>	n-Bu	Ph	18	5	b	87	9	
4	2b	n-Bu	Ph	18	5	b	96	4	
5	1c	$CH_2TMS$	Ph	11	3	с	28	65	
6	<b>2</b> c	$\rm CH_2 TMS$	Ph	15	3	Cc	70	11	
7	$2c^{d}$	$CH_2TMS$	Ph	15	3	С	100	0	
8	1d	i-Pr	Ph	12	5	đ	(76)	<2	
9	1e	s-Bu	Ph	13	8	е	83	<2	
10	1f	i-Bu	Ph	12	7	f	83	3	
11	1f	<i>i</i> -Bu	t-CH=CH(n-Hx)	11	6	g	84(73)(>99%	E) <2	
12	<b>1f</b>	i-Bu	c-CH=CH( $n$ -Hx)	11	6	h	87(>99% <i>Z</i> )	<2	
13	1f	<i>i</i> -Bu	C≡C(n-Hx)	12	6	i	56	5	

Table 1. Styrenes, 1,3-Dienes, and 1-En-3-ynes from Markovnikov Vinylboranes.

<sup>a</sup> GC yield with internal hydrocarbon standard (isolated yield) (isomeric purity). <sup>b</sup> Includes  $\alpha$ -n-Pr- and  $\alpha$ -*i*-Pr-1-styrenes in a 94:6 ratio, respectively. <sup>c</sup> The possible isomeric product, isopropylbenzene was not formed in any detectable quantity. <sup>d</sup> 2 equiv of borane were used. <sup>c</sup> Unreacted PhBr (5%) was observed in this case.

Observable from the above results, is the fact that when  $R = 1^{\circ}$ , these alkyl groups compete with the 2-alkenyl group in the cross coupling process. To our knowledge this result is unprecented in the Suzuki reaction. For example, when tripropylborane is prepared from the hydroboration of propene, it consists of an 88:12 mixture of B(n-Pr)<sub>3</sub> and B(i- $Pr(n-Pr)_2$ , respectively.<sup>2</sup> Its treatment with  $\alpha$ -methoxyvinyllithium followed by chlorotrimethylsilane, produces an 88:6:6 mixture of the three possible isomers, 1a, 1a', and 1a", respectively.<sup>2</sup> The cross coupling of this mixture with bromobenzene gives both the  $\alpha$ -n-Pr (3a) and  $\alpha$ -i-Pr (3d) styrenes (67% total yield) in a 94:6 ratio, as well as npropylbenzene (27%), but not i-propylbenzene (Entry 1).



It is known that 1° groups are more readily transferred than are 2° groups.<sup>4b</sup> Thus, with R = i-Pr (1d), 3d was produced cleanly with no detectable quantity of *i*-propylbenzene coproduct (Entry 8). Similarly, 1e (R = s-Bu) selectively undergoes vinylic coupling with PhBr to provide 3e (83%) with no s-butylbenzene accompanying its formation (Entry 9). Consistent with a steric basis for this competetive alkyl group transfer, the  $\beta$ -branched 1° derivative, 1f (R = i-Bu) was found to give 3f (83%) together with a very minor amount of *i*-butylbenzene (3%) (Entry 10). With the appropriate alkenyl or alkynyl bromides, 1f provides the corresponding 1,3-dienes (3g,h) and 1-en-3-ynes (3i), the former in a completely stereoselective manner, with little 4 being formed (Entries 11-13).



To avoid any isomeric impurities and to obtain a clearer picture of the competetive nature of this reaction, pure tri-*n*-butylborane was prepared from a Grignard method,<sup>8</sup> and converted to **1b** ( $\mathbf{R} = n$ -Bu). Indeed, both **3b** (66%) and *n*-butylbenzene (**4b**) (25%) were observed from its cross coupling to PhBr (Entry 2). With a 100% excess of **1b**, the yield of **3b** increased to 87% while **4b** was reduced to 9% (Entry 3). However, with the oxidation of **1b** employing trimethylamine *N*-oxide (TMANO) (1 equiv) in CHICl<sub>3</sub> at 0°C to **2b**,<sup>9</sup> the cross coupling (1:1) with PhBr gave **3b** (96%) with only 4% of **4b** (Entry 4).

The problem of competitive alkyl group transfer became far more serious when 1c (R =  $CH_2TMS$ ) was examined with PhBr in this coupling process. Our previous studies had revealed that the trimethylsilylmethyl group was efficiently transferred to a variety of substrates,<sup>5b</sup> and this proved to be the case for 1c which gave TMSCH<sub>2</sub>Ph (4c) as the major reaction product (65%) (Entry 5). However, with the oxidation of 1c to give 2c (ca. 80% chemical purity), the yield of the desired 3c increased dramatically from 28% to 70% (Entry 6). With a 100% excess of the reagent, the conversion to 3c was quantitative (Entry 7).

While the precise nature of this Pd-catalyzed cross coupling process is unknown, the extensive studies of Negishi<sup>10</sup> indicate that the transmetallation (M/Pd exchange) is the slow step in the reaction with vinylmetallic reagents, including boron reagents.<sup>4b</sup> We suggest that the group transfer is carbanionic in nature<sup>11</sup> and that steric factors can play an important role. For **1**, its conversion to [(HO)B(C(R):CH<sub>2</sub>)R<sub>2</sub>]<sup>-</sup> under the reaction conditions, is indicated from <sup>11</sup>B NMR data where the signal for **1b** ( $\delta$  76 ppm) disappears with its exothermic reaction with aqueous NaOH to produce a major broad absorbance at  $\delta$  0 ppm. Apparently, either **3** or **4** can result from the reaction of [(HO)B(C(R)=CH<sub>2</sub>)R<sub>2</sub>]<sup>-</sup> with Pd(II) species of the general type, R<sup>1</sup>PdXL<sub>2</sub> (L = PPh<sub>3</sub>). Normally, vinylic group transfer is favored, but in the

case of  $R = CH_2TMS$ , the alkyl group transfer dominates and **4c** is the principal product. After this process occurs, the  $[(HO)_2BR_2]^-$  or  $[(HO)_2BR(C(R)=CH_2)]^-$  by-products, could also participate in the catalytic cycle to provide alternative sources of R or  $C(R)=CH_2$  groups. We observed that **4b** increased relative to **3b** as the reaction nears completion. This, together with the increase in the yield of **3b** employing an excess of **1b**, suggest that this latter process is occurring in our systems.

GC analysis of the reaction mixtures derived from 2c revealed its rapid hydrolysis to produce TMSCH<sub>2</sub>OH. From the above, it is reasonable to assume that  $[(HO)_2BR(C(R)=CH_2)]^$ is the principal boron species derived from 2. It was fortunate that with an excess of 2c, the formation of 4c could be completely suppressed, because the further oxidation of 2cwith TMANO failed to provide  $(TMSCH_2O)_2BC(CH_2TMS)=CH_2$  efficiently.<sup>9c</sup> Differences exist between the transfer of alkyl vs. alkenyl groups in this reaction. For example, whereas alkaneboronic esters apparently do not provide an efficient source of alkyl groups, alkeneboronic esters or acids efficiently transfer vinyl groups.<sup>4,6,10,12</sup> Conversely, whereas tetraalkylborates effectively transfer 1° alkyl groups, the transfer of vinyl groups from vinyl(trialkyl))borates is very inefficient.<sup>4b,10</sup> We suggest that when B-C bonds are replaced by B-O bonds in these reacting borate complexes, vinyl over alkyl group transfer becomes progressively more favorable. This, coupled with statistical factors, can account for the significant increase in the yield of **3** over **4** employing **2** vs. **1** in this reaction.

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7. The preparation of 3g is representative: A mixture of NaOH (0.72 g, 18 mmol), water (3 mL) and THF (3 mL) and **1f** (0.888 g, 4.3 mmol) was added to a solution of *E*-1-bromo-1-octene (0.723 g, 3.79 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (0.25 g, 0.22 mmol) in THF (5 mL). After heating at reflux for 11 h, separation and extraction of the aqueous layer with pentane (3 x 20 mL) followed by concentration of the organic material at reduced pressure gave a residue which was filtered through neutral alumina with pentane. Distillation at 0.2 Torr afforded 0.54 g (73%) of **3g** (bp 73-4°C). For GC analysis, a measured quantity of *n*-alkane was added and the product yield was determined from the corrected peak areas.

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