

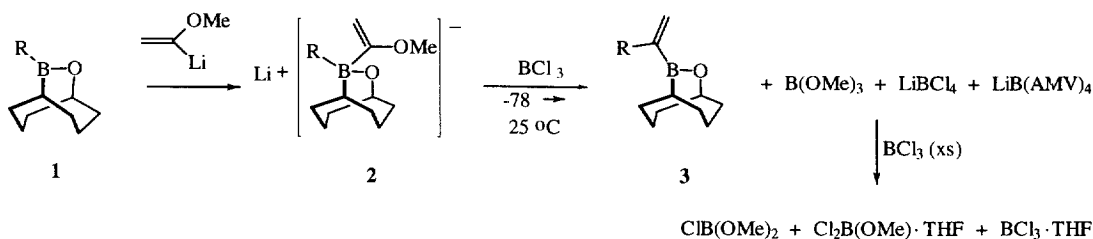
### MARKOVNIKOV VINYLBORINATES FROM 9-OXA-10-BORABICYCLO[3.3.2]DECANES

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**Abstract:** Alkylborinates **1** react with  $\alpha$ -methoxyvinyl lithium (LiAMV) to produce stable "ate" complexes, **2**, which undergo  $\text{BCl}_3$ -induced alkyl group migration providing new air-stable vinylborinates, **3**. These intermediates which are readily converted to either unsymmetrical 1,1-disubstituted alkenes (**7**) via the Suzuki-Miyaura coupling or, oxidatively, to methyl ketones, (**8**), one of which was converted to the antihistaminic drug, metron S, **10**. © 1997 Elsevier Science Ltd.

As synthetic intermediates, vinylboranes have proven value, undergoing a variety of useful functional group transformations and carbon-carbon bond-forming reactions.<sup>4</sup> Of the various choices available for such conversions, 9-borabicyclo[3.3.1]nonyl (9-BBN) derivatives or their oxidatively derived 9-oxa-10-borabicyclo[3.3.2]decyl (OBBD) counterparts provide superior stationary ligation for many of the known organoborane conversions. These bicyclic intermediates are thermally stable and selectively transfer the *B*-substituent avoiding the wastage of valuable groups as is encountered with symmetrical derivatives (*i.e.*  $\text{BR}_3$ ). Efficient routes to both *trans*-<sup>5</sup> and *cis*-<sup>6</sup> *B*-vinyl derivatives of these systems are now available, but not to their internal counterparts, (*i.e.*  $\text{R}_2\text{BCHR}=\text{CH}_2$ ). Markovnikov vinylboranes are prepared from trialkyl( $\alpha$ -methoxyvinyl)borate complexes ( $\text{Li}[\text{R}_3\text{B}-\text{CH}(\text{OMe})=\text{CH}]$ ) and chlorotrimethylsilane (TMSCl).<sup>7</sup> Unfortunately, the process is limited to the availability of  $\text{BR}_3$  (*e.g.*  $\text{R} = 1^\circ, 2^\circ$  but not  $3^\circ$ ) and can produce unwanted regioisomeric by-products derived from the organoborane. Moreover, two of these three *R* groups are wasted, or can also compete with the vinylic moiety to produce by-products in their subsequent transformations. Unfortunately, the process fails for 9-BBN derivatives which migrate one of the bridgehead C-B bonds rather than the *B*-alkyl group.<sup>7</sup> We wish to report the synthesis of isolable Markovnikov vinylborinates (**3**) from **1** which overcomes these earlier problems.

The facile conversion of *B*-alkyl derivatives of 9-BBN to **1** with trimethylamine *N*-oxide (TMANO) is both highly selective and efficient.<sup>8</sup> The resulting borinates resist further oxidation with



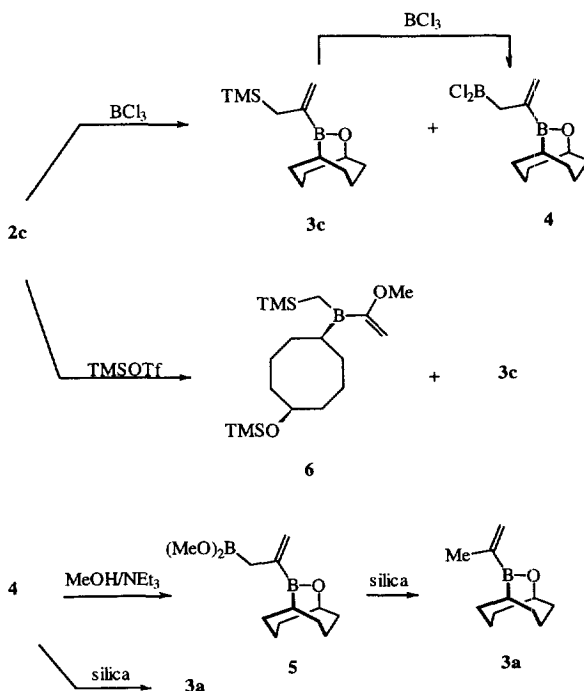
**Table 1.** Preparation of Markovnikov vinylborinates (**3**) from B-alkyl-OBBD derivatives (**1**).

<b>1</b>	R	<b>2</b> : $^{11}\text{B}$ -NMR ( $\delta$ ppm) <sup>a</sup>	Yield of <b>3</b> (%) <sup>b</sup>
<b>a</b>	Me	-3.3	57
<b>b</b>	<i>n</i> -Hx	-2.9	87 (73) <sup>c</sup>
<b>c</b>	TMSCH <sub>2</sub>	-2.9	81 <sup>d</sup>
<b>d</b>	TMSCH <sub>2</sub> CH <sub>2</sub>	-2.0	83
<b>e</b>	<i>c</i> -Hx	-2.0	83
<b>f</b>	<i>t</i> -Bu	-1.2	90

<sup>a</sup> Recorded at 300 MHz (THF/C<sub>6</sub>H<sub>12</sub>) using C<sub>6</sub>D<sub>6</sub> as an internal lock (BF<sub>3</sub>·OEt<sub>2</sub>  $\delta$  0.00). <sup>b</sup> Isolated yields. <sup>c</sup> Yield with TMSOTf. <sup>d</sup> Yield employing 1.0 equiv of BCl<sub>3</sub>.

this reagent and are also remarkably stable toward further oxidation in the open air. This suggested that the OBBD ring system might provide effective spectator ligation for the **2**–**3** conversion. Reaction of **1** with LiAMV (1.64 equiv) leads to the quantitative formation of a stable "ate" complex **2**. Unfortunately, **2** fails to react with TMSCl even at reflux temperature. However, smooth alkyl group transfer is observed with boron trichloride (BCl<sub>3</sub>, 1.3 equiv) to produce the corresponding Markovnikov vinylborinates **3** (Table 1).<sup>9</sup>

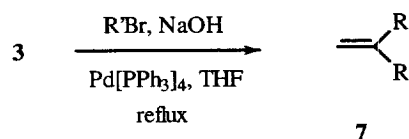
The borate complexes **2** show a regular  $\beta$ -effect in their  $^{11}\text{B}$  NMR chemical shifts, the magnitude of which is attenuated but in the same direction as is common in  $^{13}\text{C}$  NMR spectroscopy. The isolation of **3** is greatly facilitated by the fact that these compounds are remarkably air stable and are easily purified by column chromatography (SiO<sub>2</sub>). Trimethyl borate (B(OMe)<sub>3</sub>,  $^{11}\text{B}$  NMR  $\delta$  14.6) and lithium tetrachloroborate (LiBCl<sub>4</sub>,  $^{11}\text{B}$  NMR  $\delta$  15.1) are also produced in this process. While 1 equiv of BCl<sub>3</sub> induces these migrations, additional BCl<sub>3</sub> (30 mol% excess) is employed to remove the unreacted LiAMV reagent from the reaction medium, forming lithium tetrakis( $\alpha$ -methoxyvinyl)borate ( $^{11}\text{B}$  NMR  $\delta$  -1.0). Any remaining BCl<sub>3</sub> equilibrates with B(OMe)<sub>3</sub> forming chloromethoxyboranes (BCl(OMe)<sub>2</sub> ( $\delta$  20.0), BCl<sub>2</sub>(OMe)·THF ( $\delta$  5.6), BCl<sub>3</sub>·THF ( $\delta$  7.0)).



Unlike the other vinylborinates, we found that **3c**, which contains the allylsilane functionality, is very sensitive to the amount of  $\text{BCl}_3$  used. After treatment of **2c** with  $\text{BCl}_3$  (1.3 equiv) and purification of the product mixture by column chromatography, both the desired **3c** and **3a** are isolated in a ca. 3:1 ratio (NMR). The vinylborane, **3a**, is evidently formed through the electrophilic conversion of the allylsilane to an allyldichloroborane **4** (identified as its dimethoxy derivative, **5**) with  $\text{BCl}_3$  which undergoes hydrolysis on silica.<sup>10</sup> Fortunately, this second process can be avoided through the use of 1 equiv of  $\text{BCl}_3$  and pure **3c** was isolated in good yield (Table 1).

We examined other Lewis acids such as  $\text{BF}_3 \cdot \text{EE}$  which also produces a **3c/3a** mixture from **2c**. Trimethylsilyl triflate (TMSOTf) reacted with **2b** even at  $-78^\circ\text{C}$  to provide **3b** in good yield (73%). However, when TMSOTf was added to **2c** at  $-78^\circ\text{C}$ , **3c** was produced in low yield (30%) with the cyclooctylvinylborane **6** being the major product (70%). By adding the TMSOTf dropwise, the ratio of **3c/6** increased to 66:34 and to essentially 100:0 when this slow addition was repeated with a precooled ( $-78^\circ\text{C}$ ) THF solution of TMSOTf (ca. 1 M). MMX calculations suggest that  $\beta$ -branching of the B-alkyl group in **2** restricts access to the methoxy group by the Lewis acid. With a localized exotherm, ring-opening can occur through a competitive attack on the ring O atom, a process which is irreversible for silylation, but may be reversible for the  $\text{BCl}_3$  process.

These vinylboranes **3** undergo Suzuki-Miyaura cross coupling reaction with vinyl and aryl bromides producing dienes and styrenes **7** cleanly (Table 2),<sup>11</sup> free of competitive alkyl-group migration, in contrast to our earlier procedure which employed internal vinylboranes containing the dialkylboryl moiety.<sup>12</sup>

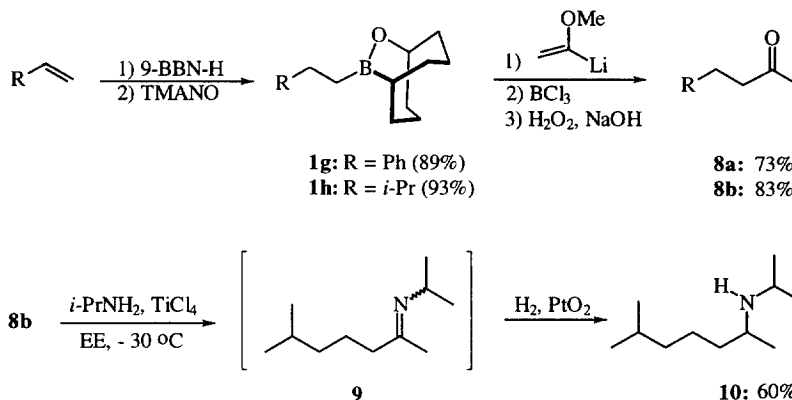


**Table 2.** Dienes and Styrenes **7** from **3** through Suzuki-Miyaura Coupling.

<b>3</b> (R)	R'	<b>7</b>	Yield <sup>a</sup>
<b>f</b> (t-Bu)	$\text{CH}_2=\text{CPh}$	<b>a</b>	80
<b>f</b> (t-Bu)	<i>cis</i> - $\text{CH}=\text{CHBu}$	<b>b</b>	59
<b>c</b> (n-Hx)	<i>trans</i> - $\text{CH}=\text{CHMe}$	<b>c</b>	63
<b>d</b> (TMSCH <sub>2</sub> CH <sub>2</sub> )	<i>p</i> -anisyl	<b>d</b>	68

<sup>a</sup> Isolated yields of analytically pure material.

Methyl ketones **8** are easily prepared through the oxidation of **3**, the overall process representing the regioselective hydroacetylation of alkenes. As an example, we prepared **8b** (one-pot procedure) and converted it, through the Evans method,<sup>14</sup> to imine **9** which was hydrogenated over Adams catalyst to provide the antihistaminic drug metron S, **10**,<sup>13</sup> in 46% overall yield from 3-methyl-1-butene. This approach to **8** appears to be very general and highly useful.



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### References and Notes

1. Graduate student supported by the NIH-MBRS program (SO6-GM08122).
2. Graduate student supported by U.S. Department of Education Graduate Fellowship (P200A902093).
3. Graduate student supported by Patricia Robert Harris Graduate Fellowship (P094B0116-94).
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9. Representative procedure for **3f**: Into a centrifuge tube containing Sn(AMV)<sub>4</sub> (0.835 g, 2.41 mmol) in pentane (5 mL) at 0 °C, was added LiBu (3.90 mL (2.11 M), 8.23 mmol) dropwise with constant stirring. After 30 min, the reaction mixture was warmed to 25 °C over 30 min. The mixture was centrifuged, and the LiAMV was washed with C<sub>5</sub>H<sub>12</sub> (3 X 5 mL) and fresh C<sub>5</sub>H<sub>12</sub> (5 mL) and THF (5 mL) were added. At -78 °C, **1f** (0.967 g, 4.98 mmol) was added and subsequently warmed to 25 °C over 1 h to ensure complete formation of **2f** (<sup>11</sup>B-NMR δ -1.2). The reaction mixture was cooled to -78 °C and BCl<sub>3</sub> in hexanes (7.6 mL of 1 M), 7.6 mmol) was slowly added and the mixture was warmed to 25 °C. After 1 h, C<sub>5</sub>H<sub>12</sub> (10 mL) was added to ensure the complete precipitation of Li salts and the mixture was centrifuged, the supernatant was decanted and the solid was washed with pentane (5 mL). The combined solution was concentrated and filtered through silica gel (C<sub>5</sub>H<sub>12</sub>) to give 0.967 g (90%, bp 55 °C, 0.25 Torr) of pure **3f**. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ 1.13 (s, 9H), 1.46 - 1.53 (m, 4H), 1.61-1.71 (m, 4H), 1.82 - 1.90 (m, 5H), 4.63 (s, 1H), 5.39 (s, 1H), 5.53 (s, 1H); <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>) δ 22.2, 25.5, 26.3, 31.8, 73.0 (OBBD ring), 30.3 ((CH<sub>3</sub>)<sub>3</sub>C), 35.8 ((CH<sub>3</sub>)<sub>3</sub>C), 120.8 (C-1), 163.2 (C-2); <sup>11</sup>B-NMR (96 MHz, CDCl<sub>3</sub>) δ 46.5; IR (neat) 1600 cm<sup>-1</sup>; MS *m/z* (rel. abundance) 220 (M<sup>+</sup>, 28), 110 (36), 95 (22), 82 (54), 67 (100), 55 (30); HRMS (EI): exact mass calc for C<sub>14</sub>H<sub>25</sub>BO requires 220.1998, found 220.1998.
10. The formation of the **4** was supported by treating **2c** with 2 equiv of BCl<sub>3</sub>. After 1h, MeOH(xs) and NEt<sub>3</sub> (xs) was added. <sup>11</sup>B-NMR analysis in C<sub>6</sub>D<sub>6</sub> indicated the formation of **5** (δ 28.2 ((MeO)<sub>2</sub>B), 44.1 (OBBD ring). TMSOMe was detected as the other product by GC-MS (*m/z* (rel. abundance): 104 (3), 89(24), 73(14), 57(100)). The reaction mixture was filtered through silica (C<sub>5</sub>H<sub>12</sub>), concentrated and analyzed by MS and NMR confirming the formation of **3a**.
11. Representative procedure for **7a**: A mixture of **3f** (0.705 g, 3.20 mmol) and aqueous NaOH (3.2 mL of 3 M, 9.6 mmol) in THF (2.5 mL) was added to Pd[PPh<sub>3</sub>]<sub>4</sub> (0.100 g, 0.087 mmol) and α-bromostyrene (0.533 g, 2.91 mmol) in THF (4 mL). The reaction mixture was heated to reflux temperature overnight (followed by GC). After cooling to 25 °C, C<sub>5</sub>H<sub>12</sub> (20mL) was added and the organic phase was washed with water (10 x 25 mL), filtered through alumina and concentrated to give 0.435 g (80%, bp 60 °C, 0.25 Torr) of **7a**. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): δ 1.11 (s, 9H), 5.08 (d, *J* = 1.5 Hz, 1H), 5.14 (d, *J* = 1.8 Hz, 1H), 5.35 (d, *J* = 1.5 Hz, 1H), 5.47 (d, *J* = 1.8 Hz, 1H), 7.32 - 7.42 (m, 3H), 7.53 - 7.56 (m, 2H), <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>) δ 30.7 ((CH<sub>3</sub>)<sub>3</sub>C), 35.9 ((CH<sub>3</sub>)<sub>3</sub>C), 126.6, 127.3, 128.0, 141.3 (*o*, *p*, *m*, *i* of phenyl ring), 112.6 (C-1), 114.7 (C-4), 151.4 (C-3), 158.7 (C-2). IR (neat): 1600, 1570 cm<sup>-1</sup>. MS: *m/z* (rel. intensity) 186 (M<sup>+</sup>, 19), 171 (17), 156 (10), 143 (64), 129 (100), 115 (41), 91 (16), 77 (29), 57 (13), 51 (13).
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