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Stereoselective Synthesis of γ -Substituted (Z)-Allylic Boranes via Kinetically Controlled Hydroboration of Allenes with 10-TMS-9-borabicyclo[3.3.2]decane

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The hydroboration of allenes is a potentially useful but relatively undeveloped method for synthesis of allylic boranes.^{1–7} The hydroboration of monosubstituted allenes with di(isopinocampheyl)borane [(Ipc)₂BH] generally gives (*E*)-allylic boranes **4** with excellent selectivity.^{3,4,8} It is inferred, based on work of Wang who studied the hydroborations of 1-alkyl-1-trimethylsilyllallenes with 9-BBN and dicyclohexylborane,^{5,6} that the hydroboration of allenes **1** with (Ipc)₂BH proceeds via thermodynamically controlled isomerization^{4,9} of the kinetically formed (*Z*)-allylic borane **2** by way of the methallylborane isomer **3** (Figure 1).^{10,11,12} Thus, allene hydroboration has not proven generally useful⁸ for synthesis of the (*Z*)-allylic boranes **2** owing to the facile 1,3-isomerization of **2** that leads to **4** (Figure 1).^{4,9,13,14}

In connection with an ongoing research problem, we needed to develop a stereocontrolled synthesis of (*Z*)-allylic borane **2** [R = B(OR')₂] and explored the hydroboration of allene **1** [R = B(OR')₂] with (Ipc)₂BH. Because attempts to suppress the 1,3-allylic isomerization of **2** [R = B(OR')₂] by performing the hydroboration of **1** with (Ipc)₂BH even at -78 °C in the presence of transition metal catalysts¹⁵ were unsuccessful,¹⁶ we sought to identify a chiral dialkylborane that would hydroborate allenes **1** with high (*Z*)-stereoselectivity but without competitive 1,3-isomerization of the initially formed (*Z*)-allylic borane **2**. Based on the unusual thermal isomeric stability of (*E*)- and (*Z*)-crotyl-10-TMS-9-borabicyclo[3.3.2]decane reagents,^{17,18} we targeted the use of and report herein that 10-TMS-9-borabicyclo[3.3.2]decane **7**^{19,20} is highly effective as a reagent for kinetically controlled allene hydroboration leading to (*Z*)-allylic boranes **2**.¹⁰ *Importantly, of the Soderquist borane 7 has enabled us to synthesize several (Z)-allylboranes that are inaccessible by alternative synthetic methods.*¹

Non-racemic borane **7** [10-TMS-9-BBD-H] is easily prepared from pseudoephedrine complex **5** by using Soderquist's procedure (Scheme 1).^{19,20} Both enantiomers of **5** are commercially available but also are easily prepared in two steps from B-OMe-9-BBN.¹⁷ We found, however, that generation of **7** from **6** is best performed in the presence of the allene, owing to the instability of **7**.²¹

Conditions for the kinetically controlled allene hydroboration were optimized by using **8** as the substrate; stereoselectivity was assessed by subjecting the derived allylboranes to an allylboration-oxidation sequence³ with benzaldehyde (Table 1). A 1:1 mixture of *syn*-1,2-diol **11a** and the 1,2-*anti* diastereomer **12a** was obtained when the hydroboration of **8** was performed at 20 °C for 2 h (entry 1). Decreasing the hydroboration temperature from 20 °C to 0 °C led to a significant improvement in the reaction diastereoselectivity (87 : 13 favoring **11a**, entry 2).

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Supporting Information Available: Experimental procedures and spectroscopic data for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

The optimal balance between product yield and diastereoselectivity was obtained by performing the allene hydroboration at -10 °C for 5 h (75% yield, **11a:12a** = 91:9, entry 3). Reducing the reaction time resulted in lower yields due to incomplete hydroboration. On the other hand, increasing the reaction time to 12 h at -10 °C led to a reduced **11a:12a** ratio (entry 4), likely due to allylborane 1,3-isomerization under these conditions. Further reduction of the hydroboration temperature resulted in lower conversion, but with consistent 92 : 8 d.s., which presumably reflects the kinetic selectivity for hydroboration via the two, non-equivalent faces of allene **8** (entries 5-6).²²

By using the optimized conditions of entry 3 (Table 1), a variety of *syn*-diols were prepared with ≥ 90 : 10 d.s. in 71-77% yields and 95-96% e.e. from the allylboration of (*Z*)- γ -boryllallylborane **9** with other representative aldehydes (see SI). However, our main reason for developing the hydroboration of **8** with the Soderquist borane **7** was to use the derived (*Z*)- γ -boryllallylborane **9** in double allylboration reactions. As summarized in Scheme 2 (see also SI for the t.s.), a variety of (*Z*)-1,5-*anti*-diols **13** were obtained in 67-86% yield with ≥ 92 : 8 d.s. and in 94-96% e.e. 1,5-*anti*-Diols **13** are inaccessible by using our previously published, first generation double allylboration sequence.¹²

Additional examples of (*Z*)- γ -substituted allylboranes generated via allene hydroboration are provided in Table 2. Hydroboration of phenylallene (**14a**) with in situ generated borane **7** provided a solution of **15a** which was treated with aldehydes at -40 °C to give *syn*-homoallylic alcohols **16a** and **16b** with ≥ 93 :7 d.s. and 92-93% e.e. (entries 1, 2). In contrast, hydroboration of **14a** with (Ipc)₂BH provides the (*E*)-allylic borane, which in turn provides the *anti*-homoallylic alcohol epimer of **16**.⁴ Similarly, kinetically controlled hydroboration of phenyldimethylsilyllallene (**14b**) followed by treatment of the in situ generated (*Z*)- γ -silyllallylborane **15b** with representative aldehydes provided the *syn*- β -hydroxyallylsilanes **17a** and **17b** with 9 : 1 d.s. and 86-89% e.e. (entries 3, 4). We have previously documented the challenges associated with synthesis of (*Z*)- γ -silyllallylboranes, and the present route constitutes a significant improvement.²⁴ Tributylstannylallene (**14c**) also proved to be an excellent substrate for hydroboration with in situ generated **7** (entries 5,6). The resulting β -hydroxyallylstannanes **18a,b** are very sensitive to Peterson-type elimination during attempted chromatographic purification, or during attempts to functionalize the hydroxyl group. Therefore, the enantiomeric purity of **18** was assessed at the stage of 1,5-diol **20** following the BF₃-OEt₂ promoted reaction of predecessor borinate **19** with aldehydes at -78 °C (see SI). As with (*Z*)-allylborane **9**, **15c** readily isomerizes to the (*E*)- γ -stannylallylborane isomer at ambient temperature and therefore must be used immediately after the allene hydroboration step.

These examples provide clear evidence that the hydroboration of allenes **8** and **14a-c** with borane **7** provides (*Z*)- γ -substituted allylboranes **9** and **15a-c** as the kinetic product. All of the allylboration reactions summarized in Scheme 2 and Table 2 were performed under conditions that minimize allylborane isomerization and presumably reflect kinetic selectivity for hydroboration of the two diastereotopic faces of the allene substrates.²² Several additional experiments were performed with alkyl-substituted allenes **14d-14f** in order to probe the limits of the hydroboration selectivity. Whereas the hydroboration of *t*-butyl substituted **14d** proceeded with ≥ 99 :1 kinetic selectivity (Table 2 entry 7), selectivity dropped to ca. 78:22 for the hydroboration of cyclohexyl substituted **14e** (entry 8) and eroded to 60:40 with the less sterically demanding alkyl substituted allene **14f** (entry 9). The *syn:anti* selectivity in these cases is largely independent of hydroboration temperature (see SI), indicating that the modest to poor (*Z*)-selectivity with **14e** and **14f** is due to the ability of borane **7** to hydroborate the allenes *syn* to moderately sterically demanding alkyl groups.

In summary, kinetically controlled hydroboration of monosubstituted allenes **8** and **14a-d** with the readily accessible Soderquist borane **7** constitutes a convenient, selective (≥ 9 : 1) and

preparatively useful method for synthesis of (Z)- γ -(substituted)allylboranes **9** and **15a-d**. These reagents, which undergo allylboration of aldehydes with typically 89-96% e.e., are representative of (Z)-allylic boranes that are inaccessible, or accessible only with great difficulty,²⁴ by alternative methods. This work also defines the opportunities for selective, kinetic hydroboration of monosubstituted allenes. Applications of this methodology in natural products synthesis are currently under investigation and will be reported in due course.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
Synthesis of (*E*)-Allylic Boranes via Allene Hydroboration

Scheme 1.
Synthesis of Borane 7

Scheme 2.
Enantioselective Synthesis of (Z)-1,5-Diols **13**

Table 1

Optimization of the hydroboration of **8** using borane, **7**

entry	hydroboration conditions		% yield ^a	d.s. 11a:12a ^b
	temperature (°C)	time (h)		
1	20	2	66	51:49
2	0	2	69	87:13
3	-10	5	75 (95 % e.e.) ^c	91:9
4	-10	12	63	84:16
5	-20	12	66	92:8
6	-30	12	36	92:8

^a Isolated yields of **11a-12a**.^b Diastereomer ratios were determined by ¹H NMR analysis.^c Determined by Mosher ester analysis.²³

Table 2

Kinetic Controlled Hydroboration-Allylboration of Allenes **14**

	<p>14a, R₁ = Ph 14b, R₁ = SiMe₂Ph 14c, R₁ = SnBu₃ 14d, R₁ = <i>t</i>-Bu 14e, R₁ = <i>o</i>-C₆H₁₁ 14f, R₁ = <i>n</i>-C₈H₁₇</p>			<p>16, R₁ = Ph 17, R₁ = SiMe₂Ph 18, R₁ = SnBu₃ 21, R₁ = <i>t</i>-Bu 22, R₁ = <i>o</i>-C₆H₁₁ 23, R₁ = <i>n</i>-C₈H₁₇</p>		
	<p>19, R = 10-TMS-9-BBD</p>		<p>20a, R₂ = Ph, R₃ = Ph(CH₂)₂ 20b, R₂ = Ph(CH₂)₂, R₃ = Ph</p>			
entry	R ₁	R ₂	product	% yield ^d	syn:anti ^b	% e.e. ^c
1 ^{d,f,h}	Ph	Ph	16a	74	94:6	93
2 ^{d,f,h}	Ph	Ph(CH ₂) ₂	16b	60	93:7	92
3 ^{d,f,i}	SiMe ₂ Ph	Ph	17a	79	90:10	86
4 ^{d,f,i}	SiMe ₂ Ph	Ph(CH ₂) ₂	17b	71	90:10	89
5 ^{e,g,h}	SnBu ₃	Ph	18a	>66 ^j	88:12	93 ^k
6 ^{e,g,h}	SnBu ₃	Ph(CH ₂) ₂	18b	>67 ^j	91:9	94 ^l
7 ^{m,f,h}	<i>t</i> -Bu	Ph	21	70	99:1	93
8 ^{m,g,h}	<i>o</i> -C ₆ H ₁₁	Ph	22	86 ⁿ	78:22	98
9 ^{m,g,h}	<i>n</i> -C ₈ H ₁₇	Ph	23	81 ⁿ	60:40	98

^a Isolated yields of the indicated product, unless noted otherwise.

^b Diastereomer ratios for **16-18** and **21-23** were determined by ¹H NMR analysis of crude reaction mixtures.

^c Determined by the Mosher method.²³

^d Hydroboration: 0°C/12h.

- ^e Hydroboration: -10°C/5h.
^f Allylboration: -40°C/12h.
^g Allylboration: -78°C/4h.
^h Work-up: ethanolamine.
ⁱ Work-up: pH 7 buffer (KH₂PO₄/NaOH).
^j Isolated yield of **20** from **14c**.
^k % e.e. of **20a**.
^l % e.e. of **20b**.
^m Hydroboration: 0°C/2-6h.
ⁿ Combined yield, *syn-anti* mixture.