J|A|C|S COMMUNICATIONS

Published on Web 09/23/2009

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)$_2$BH] generally gives (*E*)-allylic boranes **4** with excellent selectivity.[3,4,8] It is inferred, based on work by Wang who studied the hydroborations of 1-alkyl-1-trimethylsilylallenes with 9-BBN and dicyclohexylborane,[5,6] that the hydroboration of allenes **1** with (Ipc)$_2$BH proceeds via thermodynamically controlled isomerization[4,9] of the kinetically formed (*Z*)-allylic borane **2** by way of the methallylborane isomer **3** (Figure 1).[10−12] Thus, allene hydroboration has not proven useful[8] for synthesis of **2** owing to the facile 1,3-isomerization of **2** leading to **4** (Figure 1).[4,9,13,14]

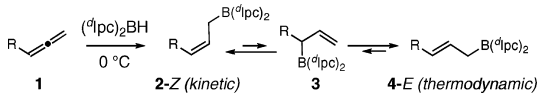
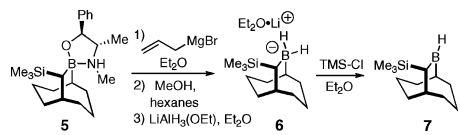


Figure 1. Synthesis of (*E*)-allylic boranes via allene hydroboration.

In connection with an ongoing research problem, we needed to develop a stereocontrolled synthesis of **2** [R = B(OR′)$_2$] and explored the hydroboration of **1** [R = B(OR′)$_2$] with (Ipc)$_2$BH. Because attempts to suppress the 1,3-allylic isomerization of **2** [R = B(OR′)$_2$] by performing the hydroboration of **1** with (Ipc)$_2$BH even at −78 °C in the presence of transition metal catalysts[15] 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 **2**.[10] Importantly, the Soderquist borane **7** has enabled us to synthesize several (*Z*)-allylboranes that are inaccessible by alternative synthetic methods.[1]

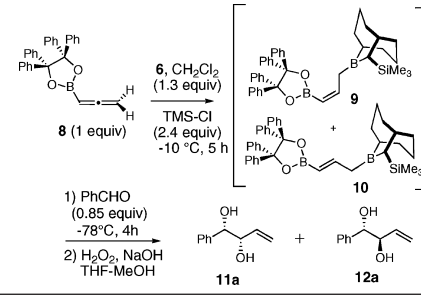
Nonracemic borane **7** [10-TMS-9-BBD-H] is easily prepared from pseudoephedrine complex **5** by using Soderquist's procedure (Scheme 1).[19,20] Both enantiomers of **5** are commercially available but also are easily prepared in two steps from B-OMe-9-BBN.[17] We found, however, that generation of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

Scheme 1. Synthesis of Borane **7**



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 sequence[3] 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 to 0 °C led to a significant improvement in the reaction diastereoselectivity (87:13 favoring **11a**, entry 2). 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. Yet, 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, nonequivalent faces of allene **8** (entries 5,6).[22]

Table 1. Optimization of the Hydroboration of **8** Using Borane **7**



	hydroboration conditions			
entry	temp (°C)	time (h)	% yield[a]	d.s. **11a:12a**[b]
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

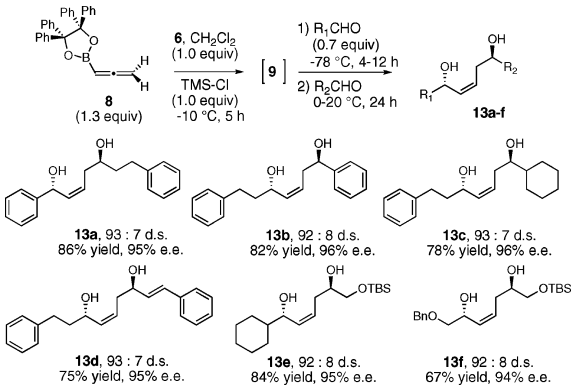
[a] Isolated yields of **11a**−**12a**. [b] Diastereomer ratios were determined by ^{1}H NMR analysis. [c] Determined by Mosher ester analysis.[23]

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 allylborations of (*Z*)-γ-borylallylborane **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 **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 **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)$_2$BH provides the (*E*)-allylic borane, which in turn provides the *anti*-homoallylic alcohol epimer of **16**.[4] Similarly,

10.1021/ja905494c CCC: $40.75

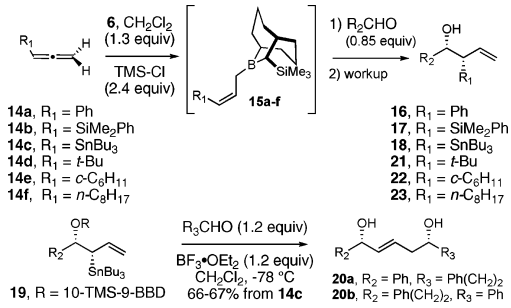
Scheme 2. Enantioselective Synthesis of (*Z*)-1,5-Diols **13**



kinetically controlled hydroboration of phenyldimethylsilylallene (**14b**) followed by treatment of the in situ generated (*Z*)-γ-silylallylborane **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-silylallylboranes, 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 BF_3−OEt_2 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

Table 2. Kinetic Controlled Hydroboration−Allylboration of Allenes **14**



entry	R_1	R_2	product	% yield[a]	*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]	$SiMe_2Ph$	Ph	**17a**	79	90:10	86
4[d,f,i]	$SiMe_2Ph$	$Ph(CH_2)_2$	**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]	*t*-Bu	Ph	**21**	70	99:1	93
8[m,g,h]	*c*-C_6H_{11}	Ph	**22**	86[n]	78:22	98
9[m,g,h]	*n*-C_8H_{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/12 h. [e] Hydroboration: −10 °C/5 h. [f] Allylboration: −40 °C/12 h. [g] Allylboration: −78 °C/4 h. [h] Workup: ethanolamine. [i] Workup: pH 7 buffer (KH_2PO_4/NaOH). [j] Isolated yield of **20** from **14c**. [k] % e.e. of **20a**. [l] % e.e. of **20b**. [m] Hydroboration: 0 °C/2−6 h. [n] Combined yield, *syn*/*anti* mixture.

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** to probe the limits of the hydroboration selectivity. Whereas the hydroboration of *tert*-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 **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 allylborations 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.

Acknowledgment. This work was supported by the NIH (GM038436 and GM026782) and a fellowship to J.K. from the Ministère des Affaires Etrangères et Européennes (France).

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.

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JA905494C