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(*E*)-2-Boryl-1,3-butadiene Derivatives of the 10-TMS-9-BBDs: Highly Selective Reagents for the Asymmetric Synthesis of *anti*-1,2-Disubstituted 3,4-Pentadien-1-ols

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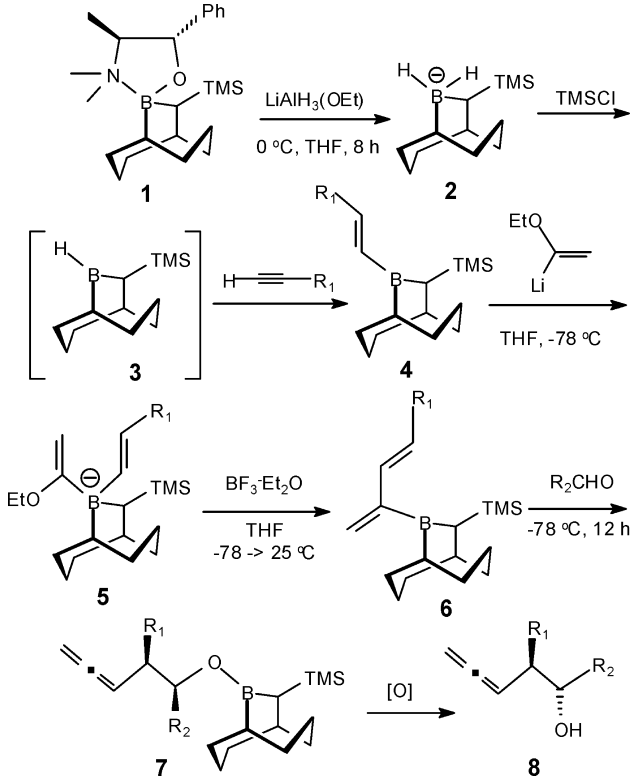
Because of the immense synthetic importance of asymmetric allylation and related conversions, these processes continue to evolve within both the stoichiometric and catalytic arenas. One developing area can be found in the use of unsaturated organoboranes to provide γ-substituted allenyl or allylboranes stereoselectively through carbenoid insertion processes.[1] These reagents expand the scope of "crotylation" by introducing a wide variety of groups into the β-stereogenic position of the resulting homopropargylic or homoallylic alcohols. Robust spectator ligation is essential to effectively orchestrate each step of the process with complete stereocontrol. We chose to push the limits of the remarkable 10-TMS-9-borabicyclo [3.3.2] decanes (10-TMS-9-BBDs)[1a,b,2] to selectively direct sequential organoborane conversions en route to nonracemic *trans*-2-boryl-1,3-dienes (**6**). We envisaged **6** as a new type of asymmetric allylborating agent to provide β-substituted nonracemic chiral homoallenic carbinols **8**. Our reaction sequence is shown in Scheme 1.

Scheme 1



First reported by Negishi, 2-boryl-1,3-butadienes are known to undergo oxidation and protonolysis to give the expected dienes and α,β-unsaturated ketones, repectively.[3] These boranes can also be employed in Diels−Alder cycloadditions,[4] and related reagents do add to aldehydes with allylic transposition.[5] Isolable as pure, stable compounds, **6** appeared to us to have the ideal properties for developing highly selective new reagents for this unusual type of asymmetric allylboration. The versatility inherent in the above protocol for variations in both R_1 and R_2 makes this route to nonracemic allene-containing alcohols **8** very attractive.

Table 1. 2-Butadienylboration of Aldehydes with the 10-TMS-9-BBDs

6	R^1	R_2	**8**	yield[a]	dr[b]	ee[c]	abs. config.[d]
a*R*	Me[e]	Ph	**a**	75	>99:1	99	1*R*,2*R*
a*S*	Me[e]	Ph	**a**	75	>99:1	99	1*S*,2*S*
b*R*	n-C_5H_{11}	Ph	**b**	74	>99:1	98	1*R*,2*R*
c*R*	Ph	Pr	**c**	65	>99:1	99	1*S*,2*S*
b*R*	n-C_5H_{11}	Pr	**d**	73	>99:1	98	1*S*,2*R*
b*S*	n-C_5H_{11}	p-$MeOC_6H_4$	**e**	72	>99:1	99	1*S*,2*S*
b*R*	n-C_5H_{11}	p-$MeOC_6H_4$	**e**	66	>99:1	99	1*R*,2*R*
b*R*	n-C_5H_{11}	o-ClC_6H_4	**f**	56	>99:1	99	1*R*,2*R*
d*S*	$(CH_2)_4Cl$	Ph	**g**	78	>99:1	99	1*S*,2*S*
e*S*	c-Pr	Ph	**h**	75	>99:1	99	1*S*,2*S*

[a] Isolated yields of analytically pure material. [b] No signals attributable to the *syn* alcohols were observed by NMR for **8** where 1% would be observable. [c] Product ee was determined by ^{31}P NMR of the Alexakis esters of **8**. [d] The absolute configuration of **8d** was determined by its conversion to **12** whose optical rotation is known.[10] The 1,2 notation refers to the stereogenic centers in **8** where the alcohol carbon is C-1. [e] (1*R*,2*R*)-**8a** (*cf.* [α] = +96.5 (*c* 1.2, CH_2Cl_2, ≥99% ee) vs (1*S*,2*S*)-(**8a**) [α] = −96.8 (*c* 1.2, CH_2Cl_2, ≥99% ee)).

Recently,[2g,h] we reported the hydroboration of representative alkene types with **3** generating the reagent from the air-stable crystalline **1** with $LiAlH_3(OEt)$ followed by TMSCl.[6] With the alkyne present, its *in situ* hydroboration with **3** gives **4** which can be isolated in ≥96% yield by simple filtration and concentration. Unlike 9-BBN-H, **3** undergoes only the monohydroboration of 1-alkynes to provide **4** cleanly.[7]

The **4**→**6** conversion benefits from the fact that **5** is formed as a single isomer (^{11}B NMR δ −15) having the geometry shown in Scheme 1 based upon confirming NOESY data and calculations supporting the *cis* relationship of the alkenyl and TMS groups (see Supporting Information). This permits both access to the ethoxy group by the BF_3 and its *anti* conformation relative to the alkenyl group which undergoes B→C migration. In contrast to 9-BBN systems, the BBD ring resists migrations of this type resulting in the exclusive formation of **6**.[8] After the reaction is complete, the addition of $(i\text{-Pr})_2NEt$ forms BF_3 adducts which precipitate, facilitating the isolation of **6**. The *trans* stereochemistry of **4** is preserved in **6** ($^3J_{H-H}$ = 16−17 Hz).

The conversion of **1**→**6**, while a complex multistep sequence, is operationally quite simple producing **6** as stable reagents for a new type of asymmetric allylboration process. The addition of representative aldehydes to **6** at −78 °C results in a smooth allylboration in ≤12 h as evidenced by the disappearance of the ^{11}B NMR signal for **6** at δ 82[9] with the concomitant formation of **7** at δ 55. After an oxidative

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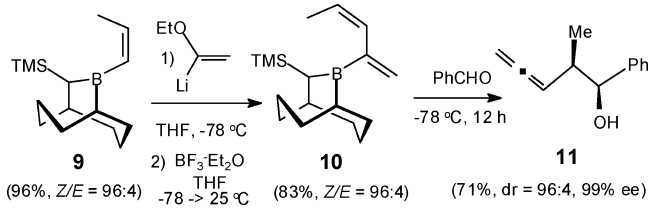
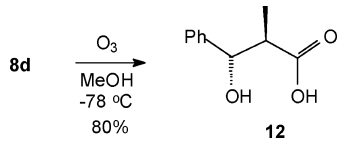
Figure 1. Pretransition state complex **14** with Spartan 06-generated space-filling model.

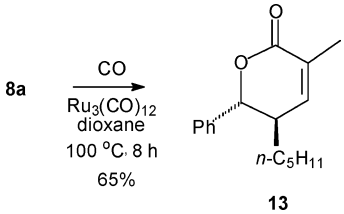
workup (30% H_2O_2, 3 M NaOH), silica gel chromatography provides the homoallenic carbinols **8** in 54−74% yield as essentially single compounds (Table 1).



Employing the Grignard reagent derived from *cis*-1-bromopropene, we prepared the *cis*-vinylboranes **9** (10*S*, 10*R*, and (±)-**9**, 96%, *Z*/*E* = 96:4). These were converted to the *cis*-dienes **10** ($^3J_{H-H}$ = 10 Hz) which add smoothly to PhCHO to give the *syn*-alcohols **11** (71%, dr = 96:4, 99% ee). This provided us with comparative data for the diastereomeric composition of **8a** whose NMR signals were well resolved from those of **11**. From (±)-**3**, racemic alcohols (±)-**8** were prepared and converted to the corresponding Alexakis esters for analysis by ^{31}P NMR. Under conditions where ≤1% of the isomeric esters was observable, the enantiomeric purity of **8** was determined to be 98−99% ee. Under these conditions and by both ^{1}H and ^{13}C NMR of **8**, no evidence could be found for the formation of *syn* diastereomeric products. This is expected due to the pure *trans* geometry of **6**.



While the absolute stereochemistry of **8** was predictable based upon a wide range of related asymmetric conversions with the 10-TMS-9-BBD systems, we chose to convert **8d** to the known (2*R*,3*S*)-β-hydroxy acid **12** (80%) through ozonolysis to confirm our assignments.[10] As is apparent from this result, the **6**→**8**→**12** conversion provides a potentially very versatile route to *anti*-α-substituted β-hydroxy acids of high optical purities.



To further demonstrate useful conversions of **8**, the α,β-unsaturated δ-lactone **13** was prepared from **8a** through a Takahashi Ru-catalyzed cyclocarbonylation.[11] Through this conversion, it is now possible to prepare this important class of biologically active natural products in optically pure form with *anti*-4,5-disubstitution.[12]

As illustrated in Figure 1, the most stable *B*-chiral pretransition state aldehyde−**6** (i.e., **14**) complex positions the aldehyde *cis* to the TMS group in an *anti* aldehyde−**6** adduct which is down with respect to the BBD ring. A steric-based preference for a chairlike transition state with these geometrical features was recently supported by calculations at the B3LYP/6-31G* level for allylboration with the BBD reagents.[13]

In summary, this work reports the efficient stepwise construction of optically pure 2-boryl-1,3-butadienes **6**. As a new type of asymmetric allylborating agent, **6** provides an extremely selective protocol for the preparation of *anti*-1,2-disubstituted 3,4-pentadien-1-ols **8** as essentially single diastereomers in enantiomerically pure form. The conversion of **8** to substituted β-hydroxy acids **12** through ozonolysis and to nonracemic δ-lactones **13** through Ru-catalyzed cyclocarbonylation was demonstrated.

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Supporting Information Available: Experimental procedures, analytical data, and selected spectra for **1**−**13**, **15**, and derivatives. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) The 2-boryl-1,3-butadienes **6** exhibit significantly downfield ^{11}B NMR signals (δ 80−82) compared to their vinylic precursors **4** (δ 72−74) suggesting that boron's −K effect is essentially absent in **6** (see: Soderquist, J. A.; Santiago, B. *Tetrahedron Lett.* **1990**, *31*, 5113. This contrasts with 1-(10′-TMS-9′-BBD)-3-methyl-1,3-butadiene **15** (δ 72) where the −K effect is uninhibited (see Supporting Information).

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