(*Z*)-1,2,3,4-Tetraboryl-2-butene: A Reagent for Stereoselective One-pot Triple Aldehyde Addition

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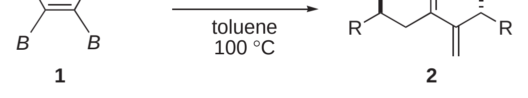
(*Z*)-1,2,3,4-Tetraboryl-2-butene reacted with three molecules of 2,3-dialkylidene-1,5-alkanediol as a single stereoisomer. Preparation and triple addition of the butene can be effected in a single operation.

Dimetalated compounds have emerged as versatile reagents for an efficient construction of complex molecules,[1,2] because the compounds, in principle, allow us to perform multiple carbon–carbon and carbon–heteroatom bond formations in one-pot and can also act as precursors of polyfunctional organometallic reagents.[3] In view that allylmetal compounds are extremely useful reagents for carbon–carbon bond formation with excellent regio- and stereocontrol,[4] γ-metalated allylmetals constitute an especially attractive class of dimetalated reagents for stereoselective domino and sequential reactions.[5,6] Indeed, Flamme and Roush demonstrated γ-borylated allylic boranes to react two molecules of aldehydes in one-pot, providing both *syn*- and *anti*-1,5-alkanediols with high enantioselectivities, respectively.[5c] Further appropriate installation of metals into γ-metalated allylmetals are quite intriguing not only to maximize the potential of the allylmetals as reagents for domino reactions but also to shed a light on a new synthetic methodology utilizing polymetalated compounds, if such reagents can be easily prepared and handled as well as perform multiple carbon–carbon bond formation with high regio- and stereocontrol in all steps. We recently reported facile and stereoselective synthesis of (*Z*)-1,2,3,4-tetrakis(pinacolato)boryl-2-butene (**1**), involving Pt-catalyzed 1,4-diborylation of 2,3-diboryl-1,3-butadiene (**3**) with bis(pinacolato)diboron (**4**).[7] We envisioned that the tetraborylated reagent **1** could perform multiple aldehyde addition because **1** can be regarded as double hybrid of the γ-borylated allylic boranes. We report herein that **1** undergoes triple aldehyde addition in one-pot, affording 2,3-dialkylidene-1,5-alkanediols **2** in good yields as a single stereoisomer (eq 1). In addition, one-pot preparation–triple addition of **1** is also demonstrated.



(1)

1 **2**

B: pinacolatoboryl *single stereoisomer !*

A toluene solution of **1** and 4 equiv. of benzaldehyde was heated at 100 °C for 14 h, giving rise to **2a** (R = Ph) in 86% yield as a single stereoisomer which turned out to be a 1:3 adduct (See Supporting Information). When the same reaction was carried out in toluene at 80 °C or in 1,2-dichloromethane or 1,4-dioxane at 100 °C resulted in decrease of the isolated yields (30–71%) of **2a**, respectively.

Representative examples of this stereoselective triple aldehyde addition are summarized in Table 1. Various kinds of aromatic aldehydes were applicable to the reaction in good yields (Entries 1–7), while the addition to such aliphatic aldehydes as 3-phenylpropanal and propanal also proceeded in good yields (Entries 8 and 9). Benzyloxyacetaldehyde was found to react smoothly at 80 °C (Entry 10). Noteworthy is that all products **2b**–**2k** were isolated as a single stereoisomer, indicating that each step of the whole transformation proceeded in a highly stereoselective manner (for mechanism, see vide infra). As a consequence, we succeeded one-pot conversion of four C–B bonds into two C–C bonds and a C=C bond with perfect 1,5-remote and olefinic stereocontrol.[8]

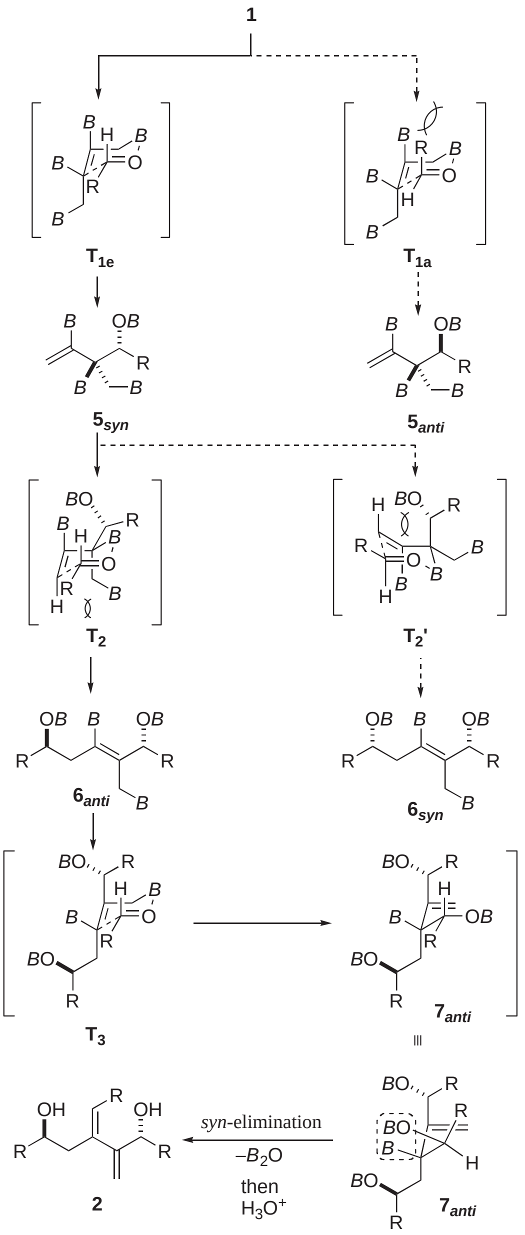
Table 1. Stereoselective triple aldehyde addition of **1** leading to **2**

Entry	R	Product	Yield/%[a]
1	2-Naphthyl	**2b**	63
2	4-C_6H_5-C_6H_4	**2c**	86
3	4-CF_3-C_6H_4	**2d**	63
4	4-MeO-C_6H_4	**2e**	80
5	3-MeO-C_6H_4	**2f**	69
6	2-MeO-C_6H_4	**2g**	82
7	3,5-$(MeO)_2$-C_6H_3	**2h**	57
8	$C_6H_5(CH_2)_2$	**2i**	83
9	C_2H_5	**2j**	71
10[b]	$PhCH_2OCH_2$	**2k**	73

[a]Isolated yield. [b]The reaction proceeded at 80 °C.

The stereochemical outcome is reasonably explained by assuming 6-membered cyclic transition states which is well accepted for allylation of allylic borane reagents (Scheme 1).[4] Reagent **1** would react with RCHO via $\mathbf{T_{1e}}$ in which substituent R adapted an equatorial position in favor of $\mathbf{T_{1a}}$ with axial-positioned R, giving rise to $\mathbf{5}_{syn}$. The second allylation with $\mathbf{5}_{syn}$ would proceed via $\mathbf{T_2}$ over $\mathbf{T_2}'$ to produce $\mathbf{6}_{anti}$, because 1,3-diaxial repulsion between H and CH(O*B*)R was much severe than those between H and CH_2*B*. Third RCHO would be allylated with $\mathbf{6}_{anti}$ via $\mathbf{T_3}$ to generate $\mathbf{7}_{anti}$ which should cause β-elimination of the remaining boryl and boroxy groups in a syn-fashion to give **2** in preference to the fourth addition due probably to the steric hindrance around the boryl group. Even when one equiv. of RCHO was employed, neither 1:1 nor 1:2 adduct was detected during the reaction, indicating that the first addition was considered to be a rate-determining step of the sequence.

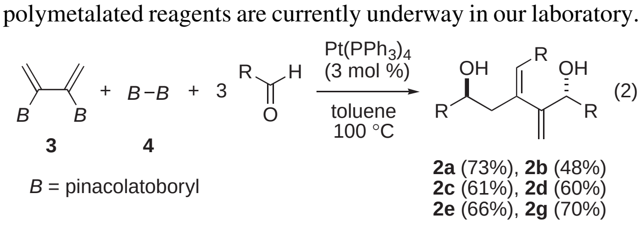
Furthermore, the triple addition can be performed in conjunction with the preparation of **1** (eq 2). Thus, a solution of **3** (1.0 equiv.), **4** (1.4 equiv.), RCHO (3.5 equiv.), and $Pt(PPh_3)_4$ (3 mol %) in toluene was heated at 100 °C for 11–17 h, affording **2a**–**2e**, and **2g** as a single stereoisomer, respectively, in acceptable yields at once.[7b] In other words, sequential stereoselective formation of two carbon–boron bonds and three carbon–carbon



Scheme 1. Plausible mechanism for the stereoselective triple aldehyde addition [B = pinacolatoboryl].

bonds is possible in a single operation.

In summary, we have demonstrated that the first triple aldehyde addition of the tetraborylated 2-butene takes place under excellent stereocontrol. The present results illustrate high potential of a novel synthetic methodology that utilizes tetrametalated compounds. Further studies on preparation and reactions of polymetalated reagents are currently underway in our laboratory.



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