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Highly stereoselective synthesis of vicinal diols by stannous chloride-mediated addition of hydroxyallylic stannanes to aldehydes

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ABSTRACT

A new protocol for the synthesis of vicinal diols was accomplished by the reaction of unprotected α-hydroxymethylmetals, as hydroxymethyl anion equivalents, with aldehydes. The treatment of hydroxyallylic stannanes, which were prepared from α,β-unsaturated aldehydes and Bu_3SnLi in situ, with various aldehydes gave but-3-en-1,2-diols in the presence of $SnCl_2$. The stereochemistry of the diol and olefin moieties demonstrated *syn*- and *E*-selectivities, respectively. We propose the following reaction mechanism; transmetalation of a hydroxyallylic stannane with $SnCl_2$ gives a rearranged allylic tin(II) species that undergoes aldehyde addition via a cyclic transition state. The strict interaction between the unprotected hydroxy moiety and the tin(II) center accounts for the selectivity.

The synthesis of polyol compounds is important because of the numerous natural products that contain this structural motif.[1] In this regard, the stereoselective synthesis of vicinal diols has been studied intensively (Scheme 1). Among relevant stereoselective reactions, reductive coupling of carbonyls (pinacol coupling) does give vicinal diols,[2] but cross-/homo-selectivity and stereoselectivity are often difficult to be controlled. To overcome these limitations, alternative methodology has been developed. Although oxidation of olefins is a powerful method for the synthesis of vicinal diols (Scheme 1b),[3] oxidation of sites other than at the olefin moiety can interfere with the desired outcome. In this context, new regio- and stereoselective synthetic routes to 1,2-diols are still required. We hypothesized that the addition of a hydroxymethyl anion equivalent (hydroxymethyl metal species) to a carbonyl would accomplish the selective synthesis of vicinal diols because cross-selectivity is likely to occur and stereoselectivity can be controlled by metal-mediated carbonyl addition (Scheme 1c). To realize this reaction (c), the hydroxymethyl metal must be inert to acidic OH groups, yet possess suitable reactivity.

We chose an allylic stannyl compound **1a** (Scheme 2, M = *Sn*) as the hydroxymethyl anion equivalent because the Sn–C bond is usually inert to the hydroxy moiety, and it has the potential to react with carbonyl groups under certain conditions.[4] The reaction between the MOM-protected form of the allylic stannane **1a-MOM** with carbonyl groups reportedly is mediated by Lewis acids that are not compatible with free OH groups.[5,6] The unprotected allylic stannane **1** has not been used in organic syntheses, because the reaction conditions that are compatible with the free OH group are unknown. We previously reported the use of $SnCl_2$ for activation of allylic stannanes in a highly stereoselective carbonyl addition reaction. This system can be employed in the presence of OH groups.[7] Here, we report the highly stereoselective, $SnCl_2$-mediated addition of α-hydroxyallylic stannane to carbonyl groups.

The treatment of 2-butenal with Bu_3SnLi followed by aqueous quenching, extraction, and concentration gave the OH-substituted allylic stannane **1a** as a crude mixture. Its ^1H NMR spectrum is shown in Figure 1.

Purification of the crude product by distillation failed, giving a complicated mixture. Thus, the crude product, including **1a**, was evaporated for the removal of volatile compounds, followed immediately by treatment with benzaldehyde **2a** and $SnCl_2$. When **1a** was added to a mixture of **2a** and $SnCl_2$, the vicinal diol **3aa** was obtained in high yield and diastereoselectivity (Table 1, entry 1).[8] The stereochemistry of the product, bearing 1,2-*syn*-diol and *E*-olefin moieties, was unambiguously determined by X-ray analysis of compound **3aa–2**,[9] which was derived from **3aa**. Therefore, **3aa** was determined to also have the *syn*-*E*-form (Scheme 3). The solvents, dichloromethane, propionitrile, and THF, gave the product in high yields (entries 1–3), while DMSO did not give **3aa** (entry 4). Without additives, the reaction gave no desired product (entry 5). The use of typical Lewis acids that are often used for allylation by allylic stannanes,[10] such as $BF_3{\cdot}OEt_2$ or $TiCl_4$, gave no **3aa**, probably because the unprotected OH group caused decomposition of the Lewis acids (entries 6 and 7).

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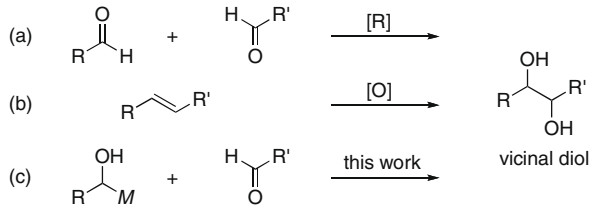
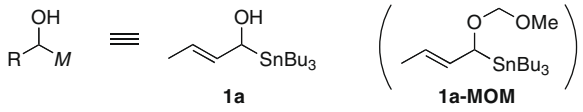
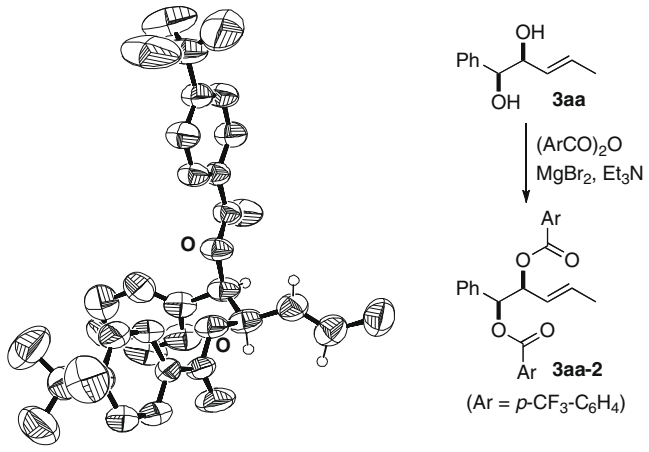


Scheme 1. Synthetic protocols of vicinal diols.



Scheme 2. Hydroxylallylic stannane **1a** as a hydroxymethyl anion equivalent.



Scheme 3. Ortep drawing of **3aa–2**. Some hydrogens are omitted for clarity.

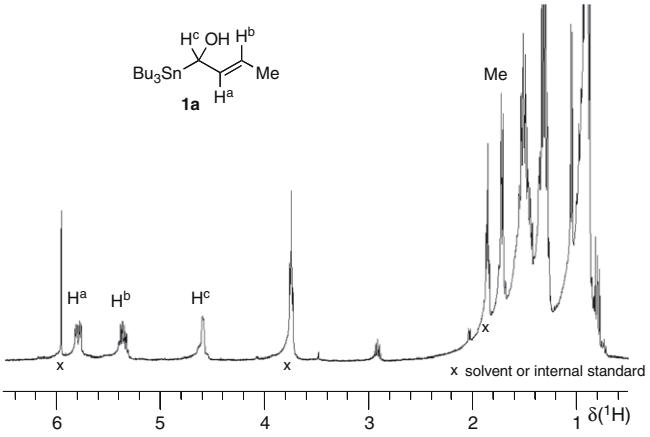
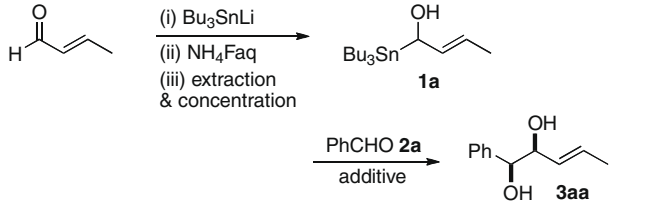


Figure 1. ^{1}H NMR spectrum of in situ-generated hydroxylallylic stannane **1a**.

Table 1
Generation of hydroxyallylic stannane **1a** and its reaction with benzaldehyde **2a** in the presence of additives[a]



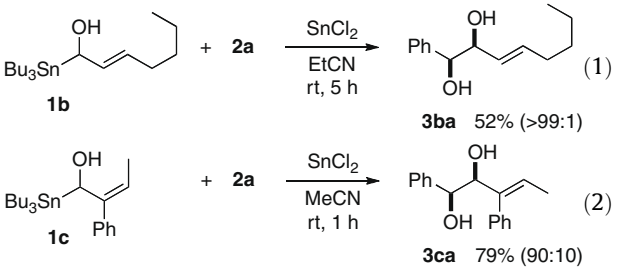
Entry	Additive	Solvent	Conditions	Yield (%)	*syn:anti*
1	$SnCl_2$	CH_2Cl_2	rt, 5 h	84	>99:1
2	$SnCl_2$	EtCN	rt, 5 h	83	>99:1
3	$SnCl_2$	THF	rt, 5 h	84	>99:1
4	$SnCl_2$	DMSO	rt, 5 h	0	—
5	—	CH_2Cl_2	rt, 5 h	0	—
6	$BF_3{\cdot}OEt_2$	CH_2Cl_2	−78 °C, 3 h	0	—
7	$TiCl_4$	CH_2Cl_2	−78 °C, 3 h	12	—

[a] The reaction was carried out using α-hydroxyallylic stannane **1a** (1.0 mmol), benzaldehyde **2a** (1.0 mmol), and additive (1.0 mmol) in solvent (2 mL).

We explored the generality of this method by using various types of aldehydes **2** in the reaction; the results are shown in Table 2. The aromatic aldehydes **2a–c** with either electron-donating or -withdrawing groups gave the products in high yield and in a stereoselective manner (entries 1–3). The α,β-unsaturated aldehyde **2d** also afforded the diol **3ad** (entry 4). Use of the aliphatic aldehydes **2e** and **2f** also resulted in highly stereoselective diol synthesis (entries 5 and 6). The aldehyde **2g** with an olefinic moiety afforded the corresponding product **3ag** without any change in the double bond (entry 7).

The product derived from the aliphatic aldehyde was also characterized based on X-ray analysis of its derivative **3ae–2**.[11] The ORTEP drawing is shown in Scheme 4. The vicinal OH groups were in the *syn*-form, as was observed for the aromatic system.

The hydroxyallylic stannane **1b**, which was prepared from 2-heptenal with a longer carbon chain, gave the product **3ba** upon reaction with benzaldehyde **2a** (Eq. 1).[8] The phenyl-substituted enal (2-phenyl-2-butenal)[12] generated the corresponding stannane **1c** with a *Z*-olefin moiety, which reacted with **2a** to give the diol **3ca** in high yield.[8,13] In both cases, the stereochemistry of the product demonstrated the *syn*- and *E*-form, independent of the olefinic geometry of the starting reagents.



Scheme 5 illustrates a plausible mechanism that accounts for the stereoselectivity of the reaction. Transmetalation of hydroxyallylic stannane **1** with $SnCl_2$ in an S_E2' manner gives the allylic tin(II) species **4**, in the *Z*-form due to the strong interaction between the unprotected OH moiety and the tin(II) center. The addition of species **4** to the carbonyl compound gives the vicinal diol **3** in the *syn*-form via a cyclic transition state[14] **5**. Formation of the *E*-geometry (i.e., cis orientation of R^1 relative to R^2) is ascribed to the equatorial position of R^1 in **5**. Unfortunately, direct observation of intermediate **4** was impossible because of the short lifetime of the compound. In fact, premixing of **1a** with $SnCl_2$ for 5 min followed by the addition of benzaldehyde **2a** gave only Bu_3SnCl without formation of the desired product **3aa**. It is interesting that the MOM-protected stannane **1a-MOM** had lower product yield and selectivity compared with the unprotected stannane **1a** (Eq. 3). This result confirms the efficiency of the unprotected hydroxyallylic nucleophile.