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Catalytic asymmetric allylic transfer reaction: (4-trimethylsilylbut-2-ynyl)stannane as a new reagent leading to the enantioselective synthesis of dienyl alcohols

Chan-Mo Yu,*[a] Sook-Kyung Yoon,[ab] Seung-Joo Lee,[a] Jae-Young Lee[a] and Sung Soo Kim[b]

[a] *Department of Chemistry and Institute of Basic Science, Sungkyunkwan University, Suwon 440-746, Korea. E-mail: cmyu@chem.skku.ac.kr*

[b] *Division of Medicinal Chemistry, Korea Research Institute of Chemical Technology, Daejeon 305-600, Korea*

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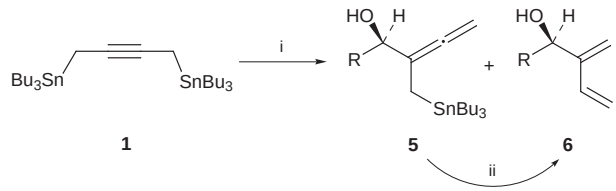
Catalytic enantioselective addition of (4-trimethylsilylbut-2-ynyl)tributylstannane to aldehydes provides trimethylsilylmethylallenyl alcohols in high enantioselectivity which can be converted with a second electrophile to the corresponding dienyl alcohols.

There is considerable interest in the development of catalytic process utilizing chiral Lewis acids to realize efficient and practical asymmetric syntheses.[1] In previous studies, we have demonstrated that the utilization of molecular synergetic reagents for catalytic asymmetric allylic transfer reactions resulted in not only a significant increase in the reaction rate but also a reduced dosage of chiral catalyst. Our approach involves the use of BINOL–Ti^{IV} complex as a chiral promoter along with Et_2BSPr^i or Me_3SiSPr^i as an accelerating synergetic reagent that has recently shown to provide highly enantioselective versions of allylic transfer reactions of achiral aldehydes such as allylation,[2] propargylation[3] and allenylation.[4] The efficiency of this protocol in terms of enantioselectivity and catalytic ability has encouraged us to apply the extension of this method to more versatile systems which would expand the scope and utility of allylic transfer reactions.[5] Described herein is an extension of the molecular accelerating strategy aimed at finding new reagents and realizing useful and practical ways to advance new levels of asymmetric synthesis. In this study we focus on the addition of a bifunctional reagent to an aldehyde and subsequent attack by a electrophile to form dienyl alcohols. The realization of an efficient method in this reaction should be valuable because many useful functional group transformations can be foreseen for chiral alcohols.[6] In the present research, the following observations were made: (i) (4-trimethylsilylbut-2-ynyl)stannane is effective as a new reagent; (ii) dramatic solvent effects are observed when using $PhCF_3$; (iii) the efficient chemical transformation of homoallenylsilane into dienyl alcohols.

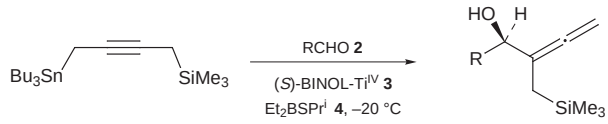
Our initial studies began with 1,4-bis(tributylstannyl)but-2-yne **1** as the allylic transfer reagent, which was prepared from the reaction of Bu_3SnLi (2 equiv.) with 1,4-dichlorobut-2-yne at −78 °C in THF.[7] The chiral catalyst, BINOL–Ti^{IV} complex **3**, was prepared by the reaction of (*S*)-BINOL (BINOL = 2,2′-dihydroxy-1,1′-binaphthol) and $Ti(OPr^i)_4$ (2:1) in the presence of 4 Å molecular sieves at 25 °C for 2 h.[8] Initial reactions of **1** and **2** in the presence of chiral catalyst **3** afforded none of the adduct **5** under various conditions. Fortunately, this lack of reactivity was overcome by introducing synergetic reagent Et_2BSPr^i **4**. Treatment of **1** with **2** (R = $PhCH_2CH_2$) and then **4** in the presence of **3** (10 mol%) at −20 °C for 20 h in CH_2Cl_2 afforded **5** along with undesired **6** in 58% combined yield in a ratio of 2:1 as judged by 500 MHz ^1H NMR analysis of the crude product (Scheme 1). Treatment of **5** with 10% HCl in THF cleanly gave dienyl alcohol **6** without loss of optical purity. Using heptanal as substrate under the same conditions, similar results were obtained but the formation of dienyl alcohol **6** still remained a problem. However, attempts at further conversion with benzaldehyde gave very poor results (< 10% conversion, at −20 °C for 36 h).

The formation of dienyl alcohol **6** from **5** was attributed to the acidic reaction media (Pr^iOH with Ti^{IV} species).† We speculated that the limited scope of the reaction and the side reaction with **1** can be solved by introducing the relatively less bulky and more stable silyl substituent instead of the stannyl group at C-4 on **1**. The new reagent **7**, a crucial compound in the present research, was prepared from propargyltrimethylsilane by the following sequences. Lithiation of propargylsilane with BuLi in THF (−78 °C, 1 h) followed by addition of paraformaldehyde (−78 to −20 °C, 2 h) gave (4-hydroxybut-2-ynyl)silane in 74% yield after distillation.[9] Treatment of (4-hydroxybut-2-ynyl)silane with BuLi at −78 °C for 1 h in THF followed by reaction with TsCl at −78 °C for 1 h and then −20 °C for 2 h gave the corresponding tosylate which used in the next reaction without isolation. Subsequent treatment of the tosylate with Bu_3SnLi at −78 °C for 2 h afforded **7**. Final purification of **7** was effected by distillation (75–82% yield, bp 121–122 °C at 0.4 mmHg).‡ Initial experiments on the allylic transfer reaction of **7** with various aldehydes promoted by **3** along with **4** under similar conditions (−20 °C for 18–24 h in CH_2Cl_2) afforded encouraging but marginal results. Although no or trace amounts (> 30:1) of dienyl alcohols **6** were produced during the reaction, the product yields for **8** ranged from 39 to 72% with 83–92% ee, as indicated in Table 1. After exploring numerous sets of conditions, we were delighted to find that the use of α,α,α-trifluorotoluene ($PhCF_3$) as solvent led to the best results in terms of chemical yields and enantioselectivities.[10] Under optimal conditions, the allylic transfer reaction was carried out according to the following procedure: The red–brown mixture of (*S*)-BINOL–Ti^{IV} complex (10 mol%) was cooled to −20 °C, and **2** (R = $PhCH_2CH_2$) was added. To this mixture was added dropwise **7** (1.2 equiv.) in $PhCF_3$ followed by **4** (1.2 equiv.) in $PhCF_3$ using a gas-tight syringe *via* a syringe pump over 1 h along the wall of the flask while keeping the temperature below −20 °C. After 18 h at −20 °C, the mixture was quenched by the addition of a saturated aqueous $NaHCO_3$. After work up, chromatography on Et_3N treated silica gel gave **8** (R = $PhCH_2CH_2$) in 78% yield with 97% ee. Additional experiments with various aldehydes were carried out and representative



Scheme 1 *Reagents and conditions*: i, RCHO **2**, (*S*)-BINOL–Ti^{IV} **3** (10 mol%), Et_2BSPr^i **4**, −20 °C, 20 h, CH_2Cl_2 [R = $PhCH_2CH_2$, 58% (68:32), 91% ee; R = C_6H_{13}, 55% (57:43), 88% ee]; ii, 10% aq. HCl, 0 °C, 2 h, THF.

Table 1 Allylic transfer reactions of **7** with achiral aldehydes[ab]



7 **8**

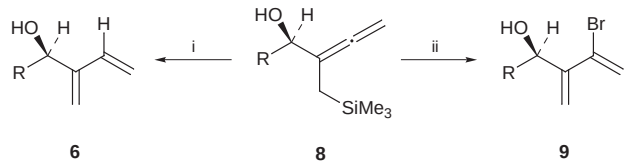
Entry	R	Solvent	*t*/h	Yield (%)[c]	Ee (%)[d]
1	$PhCH_2CH_2$	CH_2Cl_2	18	62	92
2	$PhCH_2CH_2$	$PhCF_3$	18	78	97
3	C_6H_{13}	CH_2Cl_2	18	60	90
4	C_6H_{13}	$PhCF_3$	18	83	97
5	Ph	CH_2Cl_2	24	39	84
6	Ph	$PhCF_3$	24	54	91
7	$Me_3SiC{\equiv}C$	CH_2Cl_2	24	50	83
8	$Me_3SiC{\equiv}C$	$PhCF_3$	24	62	88

[a] All reactions were carried out at −20 °C in indicated solvent. [b] BINOL:Ti(OPr^i)$_4$ = 2:1 (10 mol%). [c] Yields refer to isolated and purified products. [d] Ees were determined by preparation of (+)-MTPA ester derivatives, analysis by 500 MHz ^{1}H NMR spectroscopy, and comparison with corresponding diastereomers which were prepared from (*R*)-BINOL-Ti^{IV}.

results are summarised in Table 1. It is noteworthy that the formation of bis-allylated diol was not detected. Also, reduced dosage of chiral catalyst **3** (5 mol%) resulted in diminished chemical yield and longer reaction time (**2**, R = $PhCH_2CH_2$, −20 °C, 36 h, 34%).

The absolute configuration of the predominating enantiomer of the adducts **8** was unambiguously established after conversion to **6** by comparison of their specific rotations with that of known alcohols.[11] The absolute sense of the asymmetric induction parallels previous observations on catalytic allylations that employed the (*S*)-BINOL–Ti^{IV} catalyst.[2–4]

The adducts **8** are readily amenable to further conversion with electrophiles to give the useful synthetic intermediates, dienyl alcohols, with retention of enantiopurity, as described in Scheme 2. For example, the alcohol **6** was obtained from the reaction of **8** (R = $PhCH_2CH_2$) with acidic media in 78% isolated yield (a 4:1 mixture of aqueous HF and HCl at 0 °C in THF). Treatment of **8** (R = $PhCH_2CH_2$) with bromine (1.1 equiv.) in the presence of pyridine (5 equiv.) in CH_2Cl_2 at −78 °C for 1 h afforded **9** along with the corresponding silyl ether (less than 10%) which was readily desilylated with Bu_4NF in THF (over all 71% yield).



6 **8** **9**

Scheme 2 *Reagents and conditions*: i, aq. HF/HCl (4:1), 0 °C, THF (R = $PhCH_2CH_2$, 78%; R = C_6H_{13}, 81%; R = Ph, 68%); ii, Br_2 (1.1 equiv.), pyridine (5 equiv.), −78 °C, 1 h, CH_2Cl_2, then TBAF, THF (R = $PhCH_2CH_2$, 71%; R = C_6H_{13}, 74%).

In summary, this paper describes a new bifunctional reagent for the catalytic asymmetric allylic transfer reaction in a very general and efficient way which promises to be widely applicable. We believe that the products can serve as synthetic intermediates for the synthesis of chiral substances by selective functional group transformations.

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Notes and references

† Removal of Pr^{i}OH under reduced pressure after formation of catalyst resulted in significantly diminished chemical yields. Also, according to the results of control experiments under identical conditions except for the use of aldehyde, we did not observe formation of any buta-2,3-dienylstannane from **1**.

‡ Compound **7** was prepared in quantity, purified by distillation, and is stable to storage, whereas compound **1** could not be distilled and is somewhat unstable to storage at −20 °C over more than a week.

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