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Regulation of equilibria in the catalytic asymmetric allylic transfer reaction: unusual 1,2-carbonyl addition of 3-trimethylsilyl-2-propenylstannane†

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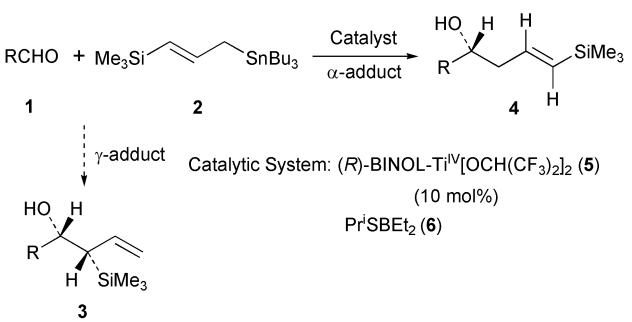
Catalytic enantioselective addition of 3-trimethylsilyl-2-propenylstannane to aldehydes promoted by BINOL–Ti(IV) catalyst along with synergistic reagent provides unusual 1,2-adducts with high levels of enantioselectivity.

During the course of our research program aimed at finding new reagents and realizing useful and practical ways to expand the scope of allylic transfer reactions, we became quite interested in the utilization of 3-trimethylsilyl-2-propenyltributylstannane **2** as a bifunctional allylating reagent. The background to this current study was the discovery that the sequential catalytic allylic transfer reaction of 2-trimethylsilylmethyl-2-propenyltributylstannane with two carbonyl functionalities resulted in the formation of a variety of tetrahydropyrans with high levels of enantio- and diastereoselectivity.[1] The availability of efficient synthetic methods for achieving absolute stereoselectivity *via* a catalytic process in the production of enantiomerically pure compounds is of considerable current interest in the field of synthetic chemistry.[2] In this regard, allylic transfer reactions provide excellent stereoselective routes for converting aldehydes into the corresponding alcohols.[3] In the light of widespread advances in catalytic methods for the synthesis of chiral substances, the allylic transfer reactions of carbonyl functionalities using a chiral Lewis acid catalyst led to significant developments in the area of asymmetric synthesis.[4] In previous studies, we have disclosed that the utilization of synergistic reagents for catalytic asymmetric reactions resulted in a significantly increased catalytic ability as a consequence of expediting regeneration of chiral catalyst to provide highly catalytic versions of enantioselective allylic transfer reactions of achiral aldehydes such as allylation,[5] propargylation,[6] allenylation,[7] and dienylation.[8] It was envisaged that the realization of an efficient catalytic method for the synthesis of **3** from **2** by the usual S_E2' pathway could be valuable because product **3** can serve as a precursor for the synthesis of dihydropyrans.[9] However, we have observed that the catalytic reaction did not proceed through the S_E2' reaction pathway to form **3**. We report herein our discovery of the exclusive formation of **4** with high levels of regio- and enantioselectivity (Scheme 1).



Scheme 1 General pathways for the allylic transfer reaction of allylstannane **2**.

† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/cc/b3/b304356h/

The first study for preliminary experiments focused on the feasibility of **2** for catalytic asymmetric allylic transfer with achiral aldehydes promoted by a chiral Lewis acid catalyst. Initial attempts at the addition of **2** to heptanal indicated that the conversion into the corresponding alcohol could not be realized with a variety of chiral Lewis acids including BINOL–Ti^{IV} complex. We subsequently observed that synergistic reagents could also be employed for this purpose.[5–8] After surveying various conditions, several key points emerged: 1) initial experiments on the allylic transfer reaction of **2** with heptanal promoted by (*R*)-BINOL–Ti(IV) (a 2 : 1 mixture of BINOL and $Ti(OPr^i)_4$, 20 mol%) along with Et_2BSPr^i at −20 °C for 24 h in CH_2Cl_2 afforded encouraging but only marginal results—although the reaction proceeded, products were formed as an isomeric mixture and in low chemical yield; 2) BINOL–Ti(IV)$[OCH(CF_3)_2]_2$ (**5**),[1] which was previously utilized for sequential allylic transfer reactions, in the presence of 4 Å molecular sieves proved to be the most efficient catalyst; 3) the utilization of Et_2BSPr^i (**6**) as a synergistic reagent proved to be essential for the catalytic process; 4) the reaction performed at −20 °C in $PhCF_3$ always gave the best results in terms of chemical yields and enantioselectivities; 5) the catalytic process produced the 1,2-carbonyl addition adduct **4** as a single regioisomer (*E*)-vinylsilane as judged by analysis of 500 MHz ^{1}H NMR. This high regio- and stereoselectivity in the formation of **4** from **2** is not common; structurally similar crotylstannane is usually converted into 2-methylallyl alcohol by reaction with aldehyde mediated by a Lewis acid catalyst in the absence of equilibrating reagents such as $BuSnCl_3$.[10]

Under optimal conditions, the catalytic allylic transfer reaction was conducted by dropwise addition of Et_2BSPr^i (**6**, 1.2 equiv.) in $PhCF_3$ at −20 °C to the mixture of **1** (R = nC_6H_{13}, 1 equiv.) and **2** in the presence of (*R*)-BINOL–Ti(IV)$[OCH(CF_3)_2]_2$ (**5**, 10 mol%) in $PhCF_3$. After 18 h at −20 °C, the reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$. Usual workup and silica gel chromatography afforded **4a** (89% isolated yield, 96% ee). The reliability of the catalytic reaction was further examined with several aldehydes as listed in Table 1.

Although the exact mechanistic aspects of this transformation have not been rigorously elucidated, the following pathway

Table 1 Allylic transfer reaction of **2** with achiral aldehydes[a]

Entry	RCHO	**4**	*t*/h	Yield (%)[b]	ee (%)[c]
1	nC_6H_{13}	**a**	18	89	96
2	$PhCH_2CH_2$	**b**	18	74	93
3	Ph	**c**	18	83	91
4	4-Br-Ph	**d**	18	81	93
5	$BuCO(CH_2)_3$	**e**	24	84	91
6	PhC≡C	**f**	24	71	88
7	PhCH=CH	**g**	36	47	83

[a] Reaction was run at −20 °C in $PhCF_3$ with 10 mol% of **6**. [b] Yields refer to isolated and purified yield. [c] Enantiomeric excesses were determined by preparation of (+)-MTPA ester derivatives, analysis by 500 MHz ^{1}H NMR (all entries), and by HPLC using a chiral column (Chiracel OD-H, 1–2% Pr^iOH in hexane, entries 2, 3, 4, 6).

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could be a probable regio- and stereochemical route on the basis of product formation. In general, allylic transfer of **2** to aldehydes catalyzed by a Lewis acid catalyst might lead mainly to **3** *via* an S_E2' process. However, the sterically bulky trimethylsilyl substituent on **2** would not allow appropriate orientation between reagent and substrate–catalyst complex, depicted as **A** in Fig. 1, to produce **3**. Therefore the formation of **4** could be explained if the reaction produced products from the equilibrium of **2** to **5** and **6** under the reaction conditions. Since antiperiplanar attack would lead to the particular product **4** or **7** *via* stereochemical models **B** or **C**, the major reaction pathway could be dependent on the stability in the transition state under kinetic control such as orientations and steric factors without a necessary link to stabilities of product and tin reagents. Thus, we believe that the origin of the regiochemical and *trans* geometry outcomes for this transformation might be a subtle geometrical preference for orientation in the transition states offered by this catalytic system. The stereochemical course of this catalytic process is likely to be due to a geometrical preference of **B** compared with **C** for a minimum allylic strain with existing substituents in Fig. 1. Thus, this allylic transfer reaction led to the formation of **4** with high levels of stereoselectivity through the stereochemical model **B**.

The products **4** are readily amenable to further conversion into useful synthetic intermediates by functional group transformations of vinylsilane[11] as demonstrated in Scheme 2.

For example, the (*Z*)-bromovinylic alcohol **8** was obtained by the treatment of **4b** with bromine followed by Bu_4NF in 79% yield.[12] The absolute configuration of the predominating enantiomer of the adducts **4** was unambiguously established, after conversion of **8** into **9** under the reduction conditions described in Scheme 2, by comparison of their specific rotations with those of known alcohols.[4] Dihydropyran-2-ylacetate **10** was obtained from **8** using the following two-step sequence in 61% yield: 1) synthesis of β-alkoxyacrylate from **8** with ethyl propiolate in the presence of 4-methylmorpholine; 2) radical cyclisation of β-alkoxyacrylate with a stannyl radical source.[13] Synthesis of the 5,6-dihydropyran-2-one **11** was accomplished by carbonylative cyclization of **8** with $Ni(CO)_2(PPh_3)_2$ in the presence of Et_3N under reflux for 30 min in $PhCF_3$ in 83% yield.[14]

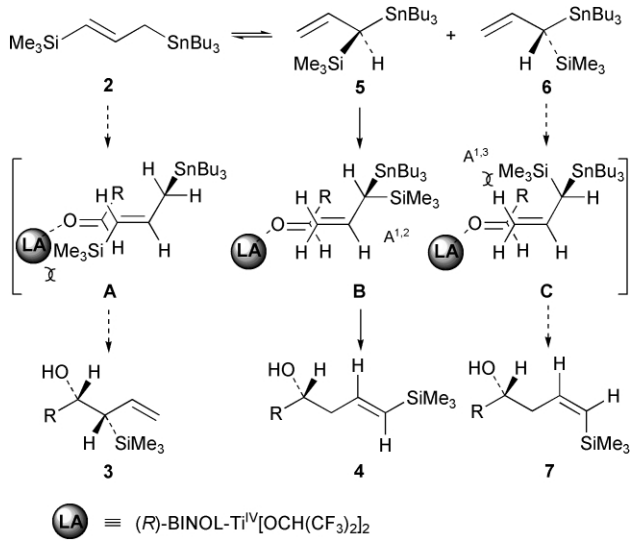
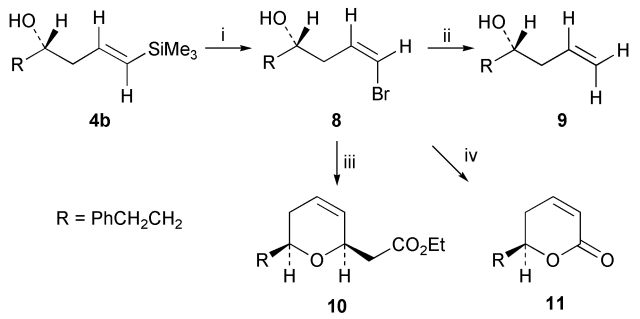


Fig. 1 Plausible stereochemical pathway for the formation of **4** from the equilibrium of **2** to **5** and **6**.



Scheme 2 *Reagents and conditions*: i. Br_2, −78 °C, CH_2Cl_2, then Bu_4NF, THF, 79%; ii. AIBN(cat.), Bu_3SnH, reflux, benzene, 63%; iii. ethyl propiolate, 4-methylmorpholine, 23 °C, and then AIBN(cat.), Bu_3SnH, reflux, benzene, 61%; iv. $Ni(CO)_2(PPh_3)_2$, Et_3N, reflux, 30 min, $PhCF_3$, 83%.

In summary, this communication describes a new and efficient catalytic asymmetric allylic transfer reaction of **2** with achiral aldehydes in the production of unusual 1,2-carbonyl addition product **4** with high levels of regio- and enantioselectivity, which promises to be widely applicable. We believe this observation could be a useful example of α-addition through the equilibrium of reagents regulated by an external chiral Lewis acid catalyst based on the Curtin–Hammett principle. We believe that the products can serve as synthetic intermediates for useful substances.

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