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Two-Carbon Homologation of Aldehydes. Synthesis of *trans*-α, β-Unsaturated Aldehydes

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Abstract: 2-tri-*n*-Butylstannylvinyl ethers are useful synthetic equivalents of acetaldehyde in 2-carbon homologation reactions. When reacted with aldehydes in the presence of $BF_3{\cdot}OEt_2$ the corresponding *trans*- α, β-unsaturated aldehydes are obtained in high yield.

The transformation of aldehydes to their α, β-unsaturated analogs with a two-carbon chain extension is a very useful reaction. The latter functionality is widely present in natural products including insect antifeedants and pheromones.[1]

A simple approach for the synthesis of α, β-unsaturated aldehydes is the aldol condensation between an aldehyde and a carbonyl compound. Nevertheless, this strategy is often not useful due to competing self condensation of the aldehyde.[2] A solution to this problem is the use of a Schiff base.[3] Other methods involve the use of Wittig condensations,[4] or the reaction of 2-(cyclohexylimino)ethylphosphonate with aldehydes.[5] In the latter method, double bond isomerization has been reported during hydrolysis. Reaction of *cis*-2-ethoxyvinyllithium with aldehydes has also been used as a synthetic approach.[6]

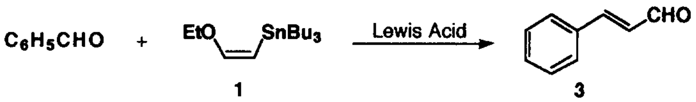
In this paper we report that *cis*- or *trans*- 2-tri-*n* -butylstannylvinyl ethers, can be used as acetaldehyde equivalents in the synthesis of *trans*-α, β-unsaturated aldehydes. We have developed the method as a "one-pot" process.

Initial reactions of *cis*-tributylstannylvinyl ethyl ether **1**,[7] with benzaldehyde at -78 or 0 °C gave no reaction (Table 1, entry 1). The reaction was conducted at -78 °C, using several Lewis acids with the best yields being obtained with Et_2AlCl and boron trifluoride etherate (Table 1, entries 6 and 7). These reactions proceeded stereospecifically to yield *trans* -cinnamaldehyde, **3**, as the only detectable product.

Reaction of the *trans*- isomer[8] (**2**) with benzaldehyde, under the same conditions used for the *cis* isomer **1**, gave only *trans* -cinnamaldehyde, **3**.

To determine if this process could be applied to other aldehydes, the reaction of **1** with different substrates was performed (Table 2). In all the reactions conducted, the *trans*-isomer of the α, β-unsaturated aldehydic product was obtained. No products were obtained when the reaction was performed with aliphatic or aromatic ketones (Table 2, entries 6, 7), thus this reaction is highly chemoselective. No reaction was observed with saturated aldehydes.

Table 1. Use of Different Lewis Acids in the Homologation of Benzaldehyde



1 **3**

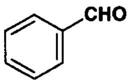
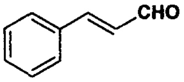
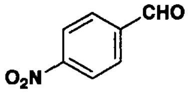
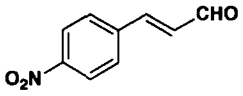
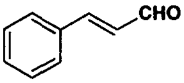
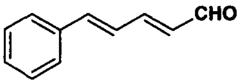
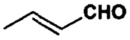
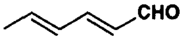
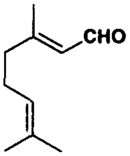
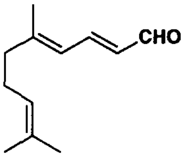
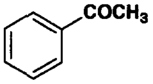
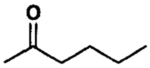
Entry	Lewis Acid	% yield of **3**[a]
1	none	0
2	LiBr	0
3	$TiCl_4^b$	0
4	$Ti(i\text{-}PrO)_4$	0
5	$ZnCl_2$	10
6	Et_2AlCl	60
7	$BF_3 \cdot OEt_2$	91

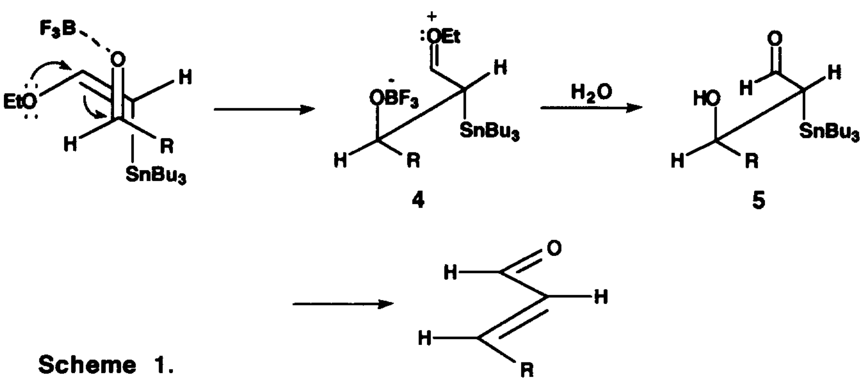
[a] Calculated by G.C. analysis, based on the amount of benzaldehyde consumed.
[b] In this case the vinylstannyl compound, 1, was decomposed by the catalyst.

A possible mechanism for this transformation involves nucleophilic attack of the π electrons of **1** (or **2**) on a Lewis acid activated carbonyl group to form adduct **4** (Scheme 1). Hydrolysis of this intermediate would generate the corresponding β-hydroxy tributylstannane, **5**, whose *trans*-deoxystannylation would yield the *trans*-α, β-unsaturated aldehyde. It is known that deoxystannylations are facile in β-hydroxy trialkylstannyl alkanes and occur in a *trans* manner.[9]

This method represents a procedure for the homologation reaction of aldehydes into α, β-unsaturated aldehydes with a two carbon-chain extension. The stereoselectivity as well as the chemoselectivity obtained makes it very attractive for stereoselective transformations of aldehydes in the presence of other carbonyl groups, such as ketones or saturated aldehydes without protection-deprotection procedures.

Table 2. Synthesis of *trans*- α, β- Unsaturated Aldehydes

Entry	Starting Material	Product	Isolated Yield (%)
1			86
2			35
3			63
4			78
5			73
6		N.R.	—
7		N.R.	—



Scheme 1.

Typical Procedure:

To a cold (-78 °C) dichloromethane solution (6 mL) of benzaldehyde (0.20 mL, 2 mmol) was added *via* syringe $BF_3\cdot OEt_2$ (0.25 mL, 2 mmol). A solution of 2-*cis* -(or *trans*-) tri-*n*-butylstannylvinyl ethyl ether (0.724 g, 2 mmol) in dichloromethane (3mL) was added dropwise and the resulting mixture stirred at -78 °C for 1 h. After quenching (MeOH:H_2O, 1:1) at -78 °C the solution was allowed to warm to rt. The organic layer was washed with water and dried ($MgSO_4$). The product was purified by column chromatography.

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