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A Convenient Synthesis of Protected and Free Homoallylic Alcohols: Catalytic Use of Dibutyltin Dichloride in the Allylation of Aldehydes With Allyltributyltin

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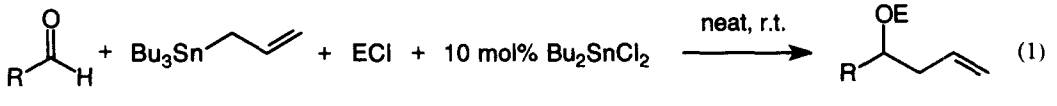
Abstract: A new procedure for the allylation of aldehydes with allyltributyltin in the presence of 10 mol% dibutyltin dichloride and either an acid chloride or trimethylsilyl chloride has been developed. Homoallylic esters, carbonates, trimethylsilyl ethers, and alcohols were obtained in up to 99% yield.

The addition reaction of allylic tin reagents with aldehydes in the presence of promoters or catalysts is a useful method for the synthesis of homoallylic alcohols.[1,2] Despite much work in this field, few *catalytic* allylation systems have been described.[3,4] We became interested in this problem as part of an ongoing program to develop useful, catalytic, enantioselective reactions based on diorganotin dihalides.[5] In connection with these efforts, we have found that dibutyltin dichloride functioned as an effective catalyst for the allylation of aldehydes with allyltributyltin in the presence of an acid chloride or trimethylsilyl chloride (eq 1).

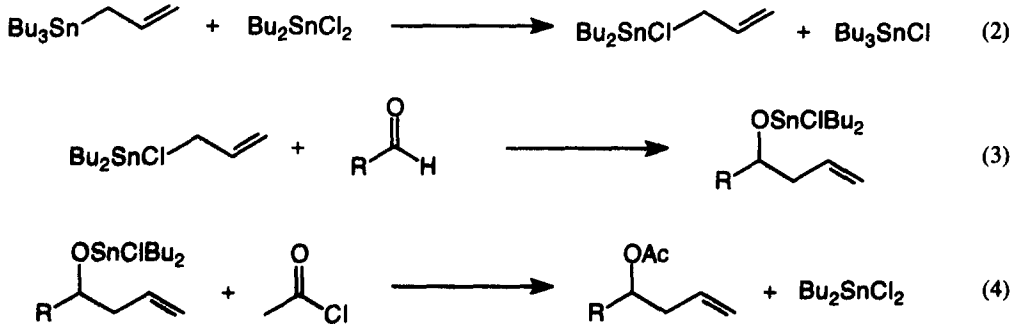


(1)

Our work on this catalytic allylation was inspired by three known reactions, which if operating in sequence would establish a catalytic cycle.[6] First, dibutyltin dichloride and allyltributyltin undergo a rapid redistribution reaction at room temperature, yielding tributyltin chloride and allyldibutyltin chloride (eq 2).[7] Second, allyldibutyltin chloride reacts with aldehydes and ketones to give homoallylic chlorodibutyltin alkoxides (eq 3). Third, homoallylic acetates and dibutyltin dichloride are obtained by treating the homoallylic tin alkoxide adduct with acetyl chloride (eq 4).[8,9] The first two reactions have been utilized in the allylation of aldehydes using dibutyltin dichloride as a stoichiometric promotor;[10] the third reaction suggested to us the possibility of a catalytic allylation (Figure 1). A previous report implied that such a catalytic allylation would proceed effectively only in the presence of coordinating additives.[3e] In light of eqs 2-4, we believed that such additives were unnecessary and would ultimately complicate the development of an enantioselective system.

We indeed found that treatment of aldehydes with allyltributyltin, a catalytic amount of dibutyltin dichloride, and either an acid chloride or trimethylsilyl chloride neat at room temperature followed by aqueous

KF workup[11] afforded *O*-protected homoallylic alcohols (eq 1, Table 1).[12, 13] Reactions with benzaldehyde employing benzoyl chloride, acetyl chloride, benzyl chloroformate, and methyl chloroformate provided the corresponding esters (entries 2-5), and trimethylsilyl chloride gave the trimethylsilyl ether (entry 1).[14] Methyl carbonates were obtained from a variety of aldehydes (entries 5-10); free alcohols were obtained from the crude carbonates after a hydrolytic KOH / methanol workup.[15] With 2-octanone and methyl chloroformate, we detected less than 5% product after 3 hours at room temperature.



This new allylation procedure enjoys some advantages compared to known methods. Protected homoallylic alcohols are available in a single step. Because no solvent is used for the reaction itself, large-scale applications should be facilitated. Finally, reaction times are generally short and catalyst loadings are moderate.

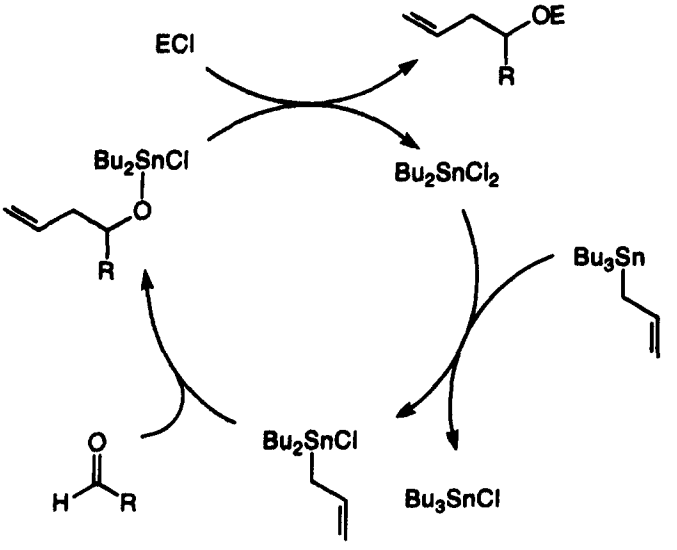


Figure 1. Plausible catalytic cycle for the allylation of aldehydes with allyltributyltin using dibutyltin dichloride in the presence of an acid halide (E=COMe, COPh, CO_2Me, CO_2Bn) or trimethylsilyl chloride (E=Me_3Si).

Table 1. Synthesis of protected and free homoallylic alcohols.

entry	R	ECl	time (h)	yield (%)[a] OE	yield (%)[a] OH
1[b]	Ph	Me_3SiCl	4	76	-
2	Ph	PhCOCl[c]	2	89	-
3	Ph	MeCOCl[c]	2	86	-
4	Ph	BnOCOCl	4	85	-
5	Ph	MeOCOCl	3	89	99
6	*t*-Bu[d]	MeOCOCl	58	48[e]	-[f]
7	*c*-C_6H_{11}	MeOCOCl	3	87	83
8	*n*-C_7H_{15}	MeOCOCl	3	83	84
9	(E)-PhCH=CH	MeOCOCl	3	92[g]	98[g]
10	Ph(Me)CH[h]	MeOCOCl	5	73[i]	76[i]

a) Isolated yields are reported. All compounds displayed satisfactory NMR (^1H and ^{13}C) and mass spectral data. For reaction conditions, see notes 12 and 15. b) Limiting allyltributyltin (0.95 eq) was used. c) Limiting acid chloride (0.95 eq) was used. d) The aldehyde was treated as in note 8 of reference 5. e) A *ca.* 20% yield of the corresponding alcohol was also obtained. f) The volatility of the alcohol prevented a reliable yield determination. g) The 1,2-addition product was isolated. h) The aldehyde was distilled before use. i) A 2:1 ratio of diastereoisomers (determined by ^1H NMR) was obtained.

In summary, we have developed a simple procedure for the allylation of aldehydes with allyltributyltin using dibutyltin dichloride as a catalyst. Either protected or unprotected homoallylic alcohols are available in good yields by employing the appropriate reaction and workup conditions. Efforts directed toward the development of an enantioselective version of this new catalytic system are in progress.

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11. The tributyltin fluoride produced in the workup is an air-stable white solid which is insoluble in water and many organic solvents (it is partially soluble in THF, methanol and ethanol). For a review of tributyltin fluoride, see: Schumann, H.; Schumann I. In *Gmelin Handbuch der Anorganischen Chemie. Zinn-Organische Verbindung*; Bitterer, H., Ed.; Springer-Verlag: Berlin, 1978; Part 5, p 24. In a typical run with benzaldehyde and methyl chloroformate, 83% crude tributyltin fluoride was recovered. It may thus be feasible to *recycle* the toxic tributyltin-containing byproducts. We observed, however, that some hydrolysis of esters occurred during the workup (tlc). No attempt to quantify this hydrolysis was generally made. We have also used NH_4F as the fluoride ion source. This reagent caused lower yields compared to KF for some substrates.
12. **General Experimental Procedure (Esters and Ethers):** Allyltributyltin (1.6 mmol, 1.1 eq.) was added to dibutyltin dichloride (0.15 mmol, 0.1 eq.) under a nitrogen atmosphere. The homogeneous mixture was stirred for 2 minutes after which the aldehyde (1.5 mmol, 1.0 eq.) was added followed by trimethylsilyl chloride or the acid chloride (1.7 mmol, 1.1 eq.) after another 2 minutes. The homogeneous liquid was stirred for the indicated time. The resulting crude product was treated sequentially with ether (15 mL), water (5 mL), and KF (4.9 mmol, 3.2 eq) with vigorous stirring for 2 minutes. After filtration of the white precipitate (Bu_3SnF), the organic phase was washed with water (5 mL) and brine (5 mL) and dried over $MgSO_4$. Evaporation of the solvent followed by flash chromatography (3:1 Skelly B / CH_2Cl_2) or elution through a short plug of Florisil® with Skelly B (silyl ethers) afforded the pure alcohol derivatives as colorless oils.
13. Less than 5% conversion was observed for all reactions in the absence of dibutyltin dichloride under otherwise identical conditions, except in the case of benzaldehyde/acetyl chloride (entry 3, *ca.* 10% uncatalyzed conversion). Treatment of benzaldehyde with allyltributyltin and 10 mol% Bu_2SnCl_2 in the absence of trapping reagent produced the homoallylic tin alkoxide in approximately 20% yield after 18 h based on ^1H NMR spectroscopy of the crude reaction mixture. The exchange reaction in eq 5 may not be favorable under these conditions.

(5)

14. The following electrophiles provided no protected product in the case of benzaldehyde: methyl iodide; methanesulfonyl chloride; and *t*-butyldimethylsilyl chloride. Chloromethyl methyl ether gave complex mixures in the presence and absence of catalyst. The use of trimethylsilyl chloride with cinnamaldehyde and cyclohexanecarboxaldehyde gave product mixtures.
15. **General Experimental Procedure (Alcohols):** The procedure for esters and ethers was followed (note 12). After being treated with brine, the organic phase was evaporated. The residue was treated sequentially with methanol (3 mL), KOH (0.5 g), and water (0.2 mL) with vigorous stirring for 5-60 minutes at room temperature. The reaction was diluted with ether (10 mL) and brine (4 mL). Solids were removed by filtration through a pad of celite. The aqueous phase was extracted twice with ether (5 mL) and the combined organic fractions were dried over $MgSO_4$. Evaporation of solvent (residual water was usually present, but no attempt was made to remove it) followed by chromatography of the residue (5:1 Skelly B / EtOAc) yielded the alcohol products as colorless oils.

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