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Stereoselective Synthesis of Allyltins from Vinyltins: A New Route to Enantioenriched α-Substituted (γ-Alkoxyallyl)tins from Vinyltin Acetals

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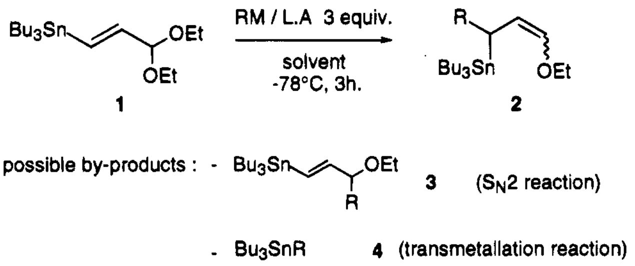
Summary: By using RCu(CN)MgX/BF$_3$·Et$_2$O, (γ-alkoxyallyl)tins are obtained *via* S_N2' substitution reaction of 3-(tributylstannyl)acrolein acetals with a high *Z* selectivity and a possible control of the stereochemistry at the newly created allylic carbon starting from a chiral acetal derived from 2(*R*),4(*R*)-(−)-pentanediol.

Scheme 1



During the last 15 years, functionalized allylmetals have been extensively used to achieve selective reactions,[1] and allyltin reagents have received special attention because of the ability of γ-substituted allyltins to add diastereoselectively to the enantiotopic faces of aldehydes.[1−3] Due to the importance of stereoselective synthesis of such oxygenated derivatives and the possibility for rearrangement of the allyltin unit, α- and γ-alkoxy- and (silyloxy)-substituted allyltins have emerged as valuable reagents.[4−8] Additional interest in these reagents stems from the fact that the reactions occur via a six-membered cyclic transition state when performed thermally or under high pressure to give *anti* derivatives,[1,5,7] and probably through an acyclic transition state in the presence of a Lewis acid to afford in general *syn* products.[1,8,9] To obtain the required α- or γ-oxygenated allyltins, several routes have been used. (α-Alkoxyallyl)tins have been obtained by the reaction of (α-chloro-α-alkoxymethyl)tributyltin with vinylmagnesium halides,[5] but this route is inefficient for obtaining enantiopure compounds. These can be obtained, however, from (α-hydroxyallyl)tins usually obtained by BINAL-H asymmetric reduction of the appropriate acyltins[6,10] or through separation of the diastereoisomeric mixture of the (−)-(menthyloxy)methoxy derivatives.[11] For racemic γ-oxygenated allyltins, preparations usually involve hydrostannation of methoxyallene,[4d] trapping of α-alkoxyallyl anions with triorganotin halides,[4c] S_N2' substitution of 2-ethoxy-3-alkenenitriles with stannyl anionoids,[12] and 1,4-addition of stannyl anionoids onto α,β-enals followed by quenching with a triorganosilyl reagent.[8] For the syntheses of enantiopure γ-oxygenated allyltins, the most efficient route would appear to be the stereospecific Lewis acid promoted rearrangement of the above α-oxygenated allyltins as reported by Marshall.[13]

In this paper, a more versatile procedure for the preparation of (γ-alkoxyallyl)tins is disclosed based on our recent method for enantioselectively obtaining (α-alkoxyalkyl)organotins from chiral α-stannyl acetals[14] and on usual behavior of allylic acetals for producing S_N2' products through reaction with soft nucleophiles in association with Lewis acids.[15] This new route starts from 1-(tributylstannyl)-3,3-diethoxyprop-1-ene (**1**) (Scheme 1), a product readily obtained with the pure *E* configuration.[16] The easy transmetalation of the Sn−C bond[17] in the vinyltin acetal **1** required that experimental conditions be carefully determined so as to produce the desired S_N2' reaction to give the (γ-ethoxyallyl)tins **2**.

Mindful of results already obtained with related organic substrates,[15] we examined the reaction of **1** with organocopper or organocuprate reagents in the presence of boron trifluoride etherate under various conditions (solvent, copper salt, main metal...). The results are summarized in Table 1.

From these preliminary experiments, it is clear, albeit somewhat difficult to rationalize, that the desired compound **2** is obtained most efficiently and with a high preference for the *Z* isomer by using an organocopper or a lower order organocuprate reagent in ether. The nature of the copper salt (CuI or CuCN), as well as the nature of the main metal salt (LiX or MgX$_2$), has only a

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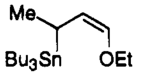
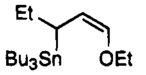
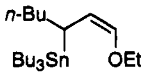
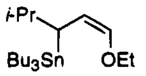
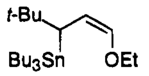
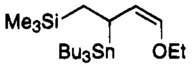
Table 1. Reaction of RM/CuX/BF_3·Et_2O with 1-(Tributylstannyl)-3,3-diethoxyprop-1-ene[a]

entry	RM	CuX	RM/CuX	solvent	yield (%)	**2** (*Z*/*E*)	**3**	**4**[b]
1	MeLi·LiBr	CuI	1	ether	76	99.5 (92/8)	0	0.5
2	MeLi·LiBr	CuCN	1	ether	81	84 (81/19)	12	4
3	MeLi·LiBr	CuBr·Me_2S	1	ether	50	0	0	100
4	EtMgBr	CuI	1	ether	79	95 (94/6)	1.5	3.5
5	MeLi·LiBr	CuCN	1	THF	25	100 (89/11)	0	0
6	MeLi	CuI	2	ether	71	63 (24/76)	29	8
7	MeLi·LiBr	CuI	2	ether	55	84 (66/34)	10.5	5.5

[a] All of these reactions were conducted in ether at −78 °C over 3 h using 3 equiv of organometallic reagent and 3 equiv of boron trifluoride etherate for 1 equiv of vinyltin acetal **1**. [b] Due to the use of an excess of organometallic reagent, transmetallation reaction may occur from compound **1** and/or **2**.

Table 2. Synthesis of (*Z*)-α-Substituted (γ-Ethoxyallyl)tins 2a–f from 1

entry	organometallic precursor	(γ-ethoxyallyl)tin	no.	yield (*Z*/*E*) (%)
1	MeLi		**2a**	81 (80/20)
2	EtMgBr		**2b**	75 (94/6)
3	*n*-BuMgBr		**2c**	68 (96/4)
4	*i*-PrMgCl		**2d**	85 (98/2)
5	*t*-BuMgCl		**2e**	70(98/2)
6	Me_3SiCH_2MgCl		**2f**	95 (100/0)

minor influence, but the use of THF as solvent dramatically decreases the yield of **2**. Furthermore, while the copper bromide–dimethyl sulfide complex favors the transmetalation reaction (formation of **4**), dimethyl cuprate affords a mixture that contains the transmetalation product **4**, the S_N2 substitution product **3**, and the S_N2' substitution products **2*E*** and **2*Z*** (diastereoisomeric ratio highly depending on experimental conditions).

From these observations, it was decided to perform subsequent reactions, in general, with Grignard reagents and copper cyanide to generate the reactive species. All reactions were conducted in ether at −78 °C over 3 h with 3 equiv of the organometallic-boron trifluoride complex for 1 equiv of the vinyltin acetal **1**.

The obtained results (*cf.* Table 2) demonstrate that vinyltin acetal **1** can be efficiently converted into numerous (γ-alkoxyallyl)tins with high *Z* selectivity. In every case, the S_N2' reaction is the main or nearly exclusive pathway and the preference for the *Z* isomer is always high (80–100%). Among the products, compound **2f** is of particular interest, a bimetallic species that is able to undergo two successive allyl-type reactions: the first one as an allyltin, the second one as an allylsilane.

The easy transacetalization reaction of **1** with chiral diols having a C_2 symmetry axis[18] suggested that it might be possible to prepare enantioenriched (γ-alkoxyallyl)tins **6a–c** from vinyltin acetal **5** (Scheme 2).

(γ-Alkoxyallyl)tins **6a–c** can in fact be obtained by this way with a high preference for the *Z* isomer (*cf.* Table 3). The observed diastereoisomeric excesses for the *Z* and *E* isomers have been determined and found to be 28–78% for the *Z* isomer while a single product has been found (within the limits of the NMR measurement) for the *E* isomer in **6c**.

Scheme 2

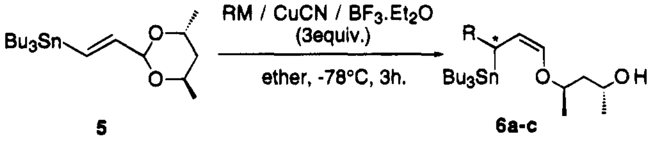


Table 3. Synthesis of Chiral (γ-Alkoxyallyl)tins 6a–c from 5

entry	organometallic precursor	no.	yield (%)	*E* (de)	*Z* (de)
1	*n*-BuMgCl	**6a**	61	6 (nd)	94 (78)
2	*i*-PrMgCl	**6b**	65	6 (nd)	94 (68)
3	*t*-BuMgCl	**6c**	80	25 (>98)	75 (28)

Taking into account Marshall's reports, the absolute configuration of the newly created center has been assigned in the major isomer in the case of **6a** which exhibits an $[\alpha]_D$ value of +117°, strongly suggesting an *S*-configuration for the allylic carbon atom on the basis of the observed values for similar (γ-alkoxyallyl)tins (with R = Bu and OMOM or OBOM as alkoxy group on the vinylic carbon, the reported $[\alpha]_D$ values are +119° and +116°, respectively, for 95% ee of *S*-enantiomer[13]). Reaction of **5** with lithium dibutylcuprate produced a side product **6d** (R = H) that gave an $[\alpha]_D$ value of only −3.2°. From this, it is reasonable to assume that the major contribution to the optical rotation of (*Z*)-**6a** is due to the asymmetric allylic carbon atom.

The observed stereochemistry can be explained by analogy with results previously obtained with organic acetals,[15] but to understand some discrepancies in the diastereoisomeric ratios for **2** and **6** much more detailed studies are required. The nature of the main group salt and size of the entering alkyl group seem to have a great influence.[19]

This reaction is presently being studied with the goal of improving the stereoselectivities and understanding the mechanism. In addition, other γ-alkoxyallyltins having even greater potential in selective organic synthesis are currently under evaluation.

Typical Procedure for the Preparation of 2a–f and 6a–c. In a Schlenk tube, a solution of organolithium or organomagnesium reagent (2.2 mmol) was added dropwise at −30 °C to a stirred copper cyanide (1.19 g, 2.2 mmol) suspension in anhydrous ether until obtention of a homogeneous solution. This last was

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(18) Transacetalization reaction of **1** with 2(*R*),4(*R*)-(−)-pentanediol was performed in refluxing cyclohexane using a catalytic amount of *p*-toluenesulfonic acid (yield = 83%).

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cooled at −78 °C before addition of boron trifluoride etherate (0.26 mL, 2.2 mmol, syringe method), further stirring for 20 min, and subsequent addition of vinyltin acetal **1** or **5** (0.7 mmol in 2 mL of ether). The reaction mixture was stirred over 3 h and allowed to warm up to −50 °C for hydrolysis (aqueous $NaHCO_3$ solution). After ether extraction (3 × 20 mL) and usual treatments, the crude products were chromatographied on silica gel to afford compounds **2a**−**f** or **6a**−**c**.

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Supplementary Material Available: Tabulated ^1H NMR, ^{13}C NMR, MS, and IR data for compounds **2b**−**f** and **6a**−**c.** ^1H NMR spectra for all new compounds (13 pages). This material is contained in libraries on microfiche, immediatly follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.