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Journal of Organometallic Chemistry 567 (1998) 21–23

Journal of Organometallic Chemistry

Stereoselective synthesis of γ-aminoallyltins from vinyltin acetals

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Abstract

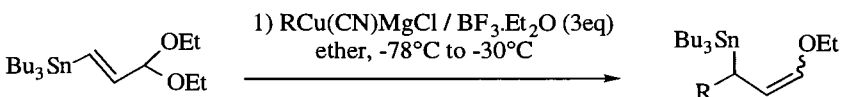
γ-Aminoallyltins were obtained by reacting $RCuCNMgCl/BF_3 \cdot Et_2O$ with aminoacetals derived from β-tributylstannylacrolein. The control of the stereochemistry of the double bond and of the absolute configuration of the newly created allylic carbon centre was proved possible. © 1998 Elsevier Science S.A. All rights reserved.

Keywords: γ-Aminoallyltins; Aminoacetals; β-Tributylstannylacrolein; Stereochemistry

1. Introduction

Functionalized allylmetals appear to be key reagents to achieve the stereoselective allylation of organic substrates [1] and in these series, special attention has been devoted to the addition of α-, γ-, δ- or ε-alkoxyallyltins on aldehydes which opens interesting possibilities to reach selectively polyoxygenated molecules [1,2]. In this type of reaction a stereospecific process involving a 6-membered cyclic transition state is observed when the reactions are performed thermally or under high pressure [1], while stereoselective reactions are observed when the allylations are achieved in the presence of boron trifluoride [1–3]. Furthermore, in this last case, it is possible to drive the reaction to the *syn* diastereoisomer [1] or to the *anti* diastereoisomer in function of the size of the substituent on the α-carbon related to tin [4].

Accordingly, we have developed a new approach to reach substituted γ-alkoxyallyltins from vinyltin acetals by reacting (*E*)-β-tributylstannylacrolein acetals with organocopper reagents in the presence of boron trifluoride etherate [5].



R = Me, Et, nBu, iPr, tBu, Me_3SiCH_2

Z/E = 80/20 to 100/0
(68-95%, isolated yield)

This approach has been proved efficient to obtain enantioenriched chiral allyltins starting from the corresponding acetals derived from chiral diols having a C_2 symmetry axis [5].

Due to the importance of compounds like amino sugars, we decided to attempt an extension of this strategy in order to obtain γ-aminoallyltins from *N*,*O*-acetals of β-tributylstannylacrolein. The appropriate precursors were obtained via transacetalisation of 1-tributylstannyl-3,3-diethoxyprop-1-ene **1** [6–8] with *N*-monoprotected aminoalcohols, the equilibrium being shifted by azeotropic distillation of ethanol.

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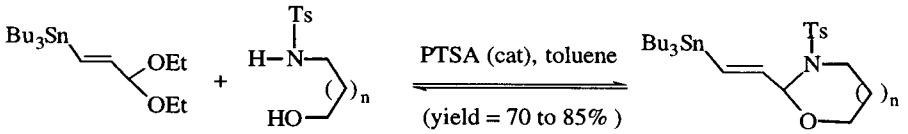
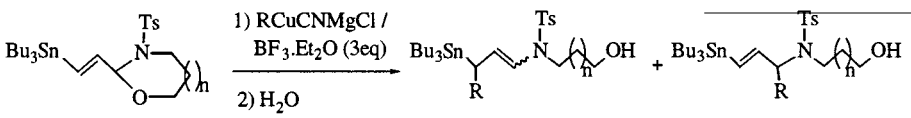
PII S0022-328X(98)00663-9



1 **2a** (n = 1), **2b** (n = 0)

in order to evaluate the different influences stemming from the nature of the aminoacetals (perhydroxazine **2a** or oxazolidine **2b**), the order of the cyanocuprates and the temperature (Table 1).

In both series, the desired S_N2' reaction was obtained at low temperature (compounds **3**–**7**), but competition with an S_N2 process was shown to be possible when increasing the temperature from -100 to -5°C (compounds **8**–**11**).



3-7 ; S_N2' **8-11** ; S_N2

2a (n = 1)

2b (n = 0)

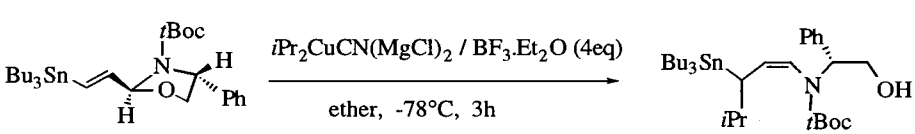
3, 8 (R = *n*Bu) ; **4, 9** (R = *i*Pr) ; **5, 10** (R = *t*Bu)

6 (R = *n*Bu) ; **7, 11** (R = *t*Bu)

While cyanocuprate order has minor influence both on the rate of the S_N2 side reaction and on the Z/E ratio for the S_N2' products, the temperature of the reaction can be of crucial importance both on the S_N2 contribution and on the isomeric distribution of S_N2' products (allyltins **3**–**7**). In practice, the S_N2 contribution is avoided at low temperature (-78 or -100°C) but the stereochemical course of the desired S_N2' reaction is strongly modified in the perhydroxazine series (**2a**) since reversed diastereoisomeric ratios were obtained at -100°C (high preference for the Z-isomer) and -5°C (high preference for the E-isomer). A similar result is not observed in the oxazolidine series (**2b**) where the preference for the Z-isomer was always high ($Z/E = 70/30$ to $100/0$).

Since products obtained in both series of reactions are likely to be obtained under kinetic control, it would mean that the *transoid* or *cisoid* conformation of the transition state is highly dependent on the temperature in the perhydroxazines series. Therefore, in order to obtain more information related to the reaction mechanism, chiral aminoacetals should be used in order to clarify this point.

Until now, we have just obtained a meaningful result from (*E*,*E*)-2-(*β*-tributylstannylvinyl)-oxazolidine **2c** derived from *N*-protected (*R*)-phenylglycinol.



2c **12** (Z/E = 100/0)

The allyltin **12** was obtained with the Z configuration ($^3J_{HH} = 8.2$ Hz) and probably as a single diastereoisomer since we have been unable to discriminate between the two possible diastereoisomers due to the benzylic and allylic asymmetric carbon atoms on the basis of ^{1}H-, ^{13}C- and ^{119}Sn-NMR spectra. Taking into account the optical rotation of **12** ($[\alpha]_D^{20} = -119.9°$), those for *N*-*t*-Boc derivative of phenylglycinol ($[\alpha]_D^{20} = -46°$) and the values of about $+120°$ observed for γ-alkoxyallyltins when the allylic carbon atom has the *S* configuration [2,5], it seems likely to assign the *R* configuration to the newly created allylic centre in **12** on the basis of the similarities in the polarisability of the bonds around the allylic carbon in the α-position related to tin.

Naturally, this last result, which might mean an *anti* S_N2' reaction on a *cisoid* conformation as already observed with organic analogues [10] and vinyltin acetals [5], must be confirmed and extended to other examples to allow a valuable discussion.

In spite of this, the above results demonstrate that γ-aminoallyltins are easily obtained from *N*-protected aminoacetals derived from β-tributylstannylacrolein. A possible control of the geometry of the double bond can be obtained in the perhydroxazine series and the use of the oxazolidine derived from (*R*) phenylglycinol allows access to the corresponding enantioenriched chiral γ-aminoallyltins.

Work is in progress in order to improve the understanding of the observed reactions and to evaluate the potential interest of this new class of functional allyltins reagents [11,12].

Table 1
Reaction of $R_nCuCN(MgCl)_n/BF_3 \cdot Et_2O$ with β-tributylstannylacrolein aminoacetals

Vinyltin reagent[a]	Experimental conditions[b] $R_nCuCN(MgCl)_n$	T (°C)	γ-Aminoallyltins[a,c] No. (Z/E)	S_N2'/S_N2	Overall yield[d]
2a	BuCuCNMgCl	−100	**3** (90/10)	100/0	(50)
2a	BuCuCNMgCl	−5	**3** (10/90)	90/10	(90) 70
2a	$iPr_2CuCN(MgCl)_2$	−110	**4** (75/25)	100/0	(>95)
2a	$iPr_2CuCN(MgCl)_2$	−5	**4** (20/80)	90/10	(>95) 86
2a	$t\text{-}Bu_2CuCN(MgCl)_2$	−100	**5** (70/30)	100/0	(>95) 85
2a	$t\text{-}Bu_2CuCN(MgCl)_2$	−10	**5** (20/80)	80/20	(>95) 80
2b	$Bu_2CuCN(MgCl)_2$	−78	**6** (90/10)	100/0	(>95) 75
2b	*i*PrCuCNMgCl	−78	**7** (80/20)	100/0	(>95) 80
2b	*i*PrCuCNMgCl	−5	**7** (100/0)	37/63	(80)
2b	$iPr_2CuCN(MgCl)_2$	−78	**7** (93/7)	95/5	(>95) 90
2b	$iPr_2CuCN(MgCl)_2$	−5	**7** (70/30)	75/25	(>95) 75

[a] Compounds **2**–**11** have been characterized on the basis of their physicochemical data.
[b] Typical experimental procedure for **7**: in a Schlenk reactor containing **2b** (100 mg) in dry degased ether (5 ml) were added 0.055 mmol of $BF_3 \cdot Et_2O$ (three equivalents) at −78°C before addition (cannula transfer), at the desired temperature, of a solution obtained by addition at −50°C of the Grignard reagent (1.11 mmol, six equivalents) to a stirred suspension of dry copper cyanide (47 mg, three equivalents) in ether (5 ml) over 30 min. The obtained mixture is allowed to react at the desired temperature until complete disappearance of **2b** (TLC monitoring). After hydrolysis at −78°C and usual treatments, compound **7** was purified by flash chromatography [9].
[c] The assignment of the Z or E configuration for **3**–**7** and **12** is done on the basis of ^1H, ^{13}C and ^{119}Sn-NMR spectra, the main argument being the value of the coupling constant $^3J_{HH}$ across the double bond ($^3J_{HH}$ ca. 7.5–8 Hz in the Z-isomer while $^3J_{HH}$ ca. 13.5–14 Hz in the E-isomer).
[d] Values in brackets are conversion rates (NMR evaluation) while underlined values are isolated yields.

Acknowledgements

The authors are grateful to Chemetall, Schering and Rhône-Poulenc Societies for gifts of organometallic starting materials and to MESR and AGISMED for financial support.

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[9] γ-Aminoallyltins **3**–**7** can be purified on silica gel using hexane/ether (80/20) or hexane/ethyl acetate/triethylamine (83/15/2) as eluent. Meaningful NMR signals for ***7Z*** and for its isomers ***7E*** and ***11E*** (obtained when the reaction was performed at higher temperature): ***7Z***: ^1H-NMR δ (ppm): 2.73 (H_α, dd, $^3J_{1H} = 13.3$, $^3J_{1H} = 8.7$, superimposed with N–CH, $^2J_{SnH} = 53$); 5.67 (H_β, dd, $^3J_{1H} = 13.3$, $^3J_{1H} = 7.5$, $^3J_{SnH} = 22$); 5.03 (H_γ, d, $^3J_{1H} = 7.5$,$^4J_{SnH} = 16.5$); ^{13}C-NMR δ (ppm): $C_\alpha = 38.1$ ($^1J_{SnC} = 267/278$); $C_\beta = 140.1$ ($^2J_{SnC} = 35.5$); $C_\gamma = 119.7$ ($^3J_{SnC} = 49$); ^{119}Sn-NMR δ (ppm): −13.1. ***7E***: ^1H-NMR δ (ppm): 2.01 (H_α, dd, $^3J_{1H} = 6.9$, $^3J_{1H} = 11.4$); 5.16 (H_β, dd, $^3J_{1H} = 13.6$, $^3J_{1H} = 11.7$, $^3J_{SnH} = 22$); 6.17 (H_γ, d, $^3J_{1H} = 13.6$, $^4J_{SnH} = 18$); ^{13}C-NMR δ (ppm): $C_\alpha = 39$; $C_\beta = 120.8$; $C_\gamma = 121.5$; ^{119}Sn-NMR δ (ppm): −16.4. **11**: ^1H-NMR δ (ppm): 5.87 (H_α, d, $^3J_{1H} = 19$, $^2J_{SnH} = 73$); 5.59 (H_β, dd, $^3J_{1H} = 19$, $^3J_{1H} = 7$, $^3J_{SnH} = 63$); 3.86 (H_γ, dd, superimposed with CH_2–O); ^{119}Sn-NMR δ (ppm): –44.3.
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