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Application of Tri-*n*-butyltin Cuprate in Sugar Chemistry

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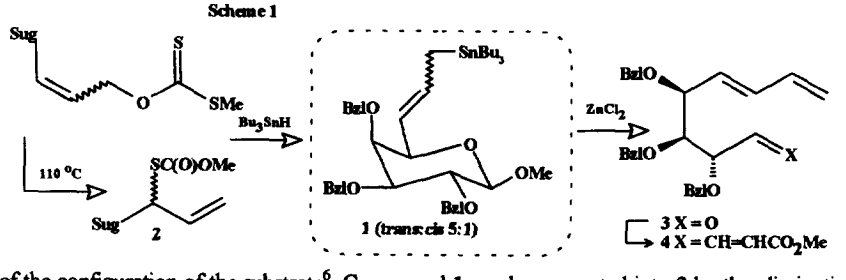
Abstract: *Reaction of sugar allyl bromides with tri-n-butyltin cuprate gives sugar allyltin derivatives with* ***retention*** *of the configuration of the double bond, what enables to prepare pure trans or cis olefins. Sugar aldehydes of the general formula Sug-CHO react also with 'Bu_3SnCu' to give α-tri-n-butyltin carbinols SugCH(OH)-$SnBu_3$. Reaction of "Bu_3SnCu" with α,β-unsaturated sugar aldehydes resulted in 1,4-addition and afforded products of the general formula Sug-CH-$SnBu_3$ -CH_2 CHO. Treatment of these compounds with zinc chloride affords open chain aldehydes with elimination of the tri-n-butyltin moiety.* Copyright © 1996 Elsevier Science Ltd

Organostannanes have found a wide application in organic synthesis[1]. One of the most interesting processes is the reaction of allyltin derivatives of general formula R-CH=CH-CH_2SnBu_3 with aldehydes what creates a new carbon-carbon bond. When Lewis acid is used as activator, the configuration of the product is always *syn*, regardless of the geometry (*cis* or *trans*) of starting olefin[2]; however without catalyst (at high temperature or under high pressure) ***E***-stannanes afford the *anti* products while ***Z***-stannanes *syn*[3]. Allyl tributyltin derivatives are also used for the creation of the new carbon-carbon bonds in radical reactions[4].

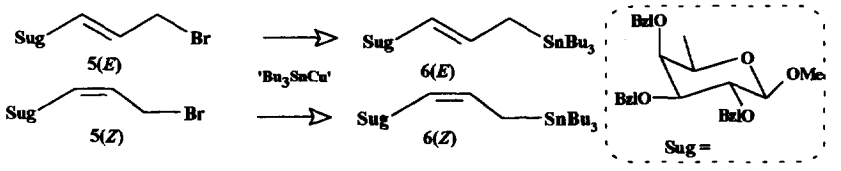
Althogh there are several methods for the preparation of allyltin derivatives most of them can not be applied in sugar chemistry[5]. We have found, that sugar allyltin derivatives (*e.g.* **1**) can be obtained only by reaction of allylic thiocarbonates (*e.g.* **2**) with Bu_3SnH as shown in Scheme 1; this reaction gives the *trans* derivatives (contaminated up to 20% with the *cis* isomer) ***regardless*** of the configuration of the substrate[6]. Compound **1** can be converted into **3** by the elimination of the Bu_3Sn- moiety in the presence of a mild Lewis acid and further into valuable synthon **4**[6].

Scheme 1



In this paper we would like to present an alternative method for the preparation of sugar allyltins which allows to prepare **stereoselectively** such *trans* as well as *cis* derivatives from sugar allylic bromides. For substitution of the bromine atom in allylic bromides with Bu_3Sn tributyltin lithium[7] is commonly used. However, reaction of sugar allylic bromides with Bu_3SnLi resulted only in decomposition of starting material. We applied, therefore, milder tin reagent: tri-*n*-butyltin cuprate[8] for this reaction and found that displacement of bromine atom in sugar allylic bromides proceeded smoothly and with **complete retention** of the configuration of the double bond. Representative example[9] is shown in Scheme 2.

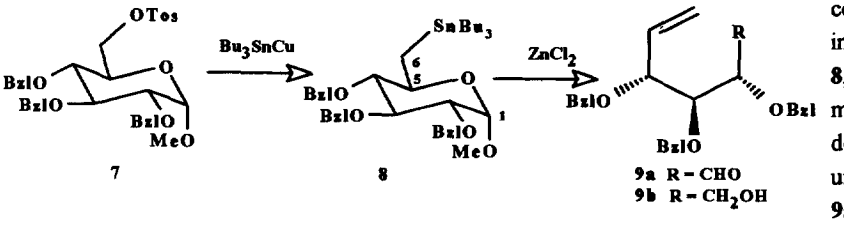
Scheme 2



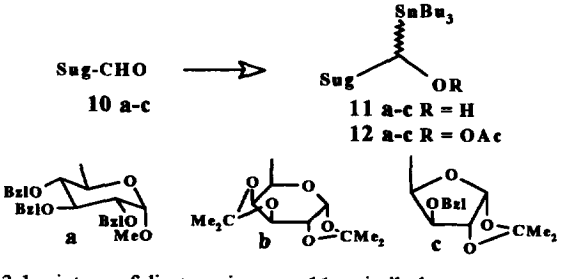
Treatment of methyl 2,3,4-tri-*O*-benzyl-8-bromo-6,7,8-tri-deo-xy-β-D-*galacto*-oct-6-eno-pyranose[10] (**5*E*** or **5*Z***) with 'Bu3SnCu' gives appropriate allyl tri-butyltin-derivatives with the **same configuration** of the double bond[11] (**6*E*** and **6*Z*** respectively). Reaction of both isomers **6(*E*)** and **6(*Z*)** with zinc chloride resulted in the opening of the sugar ring with the elimination of tri-butylstannyl moiety (*cf.* Scheme 1) and afforded **the same** dienoaldehyde **3** having the *trans* configuration of the olefinic system[11].

Reaction of Ph_3SnLi with sugar tosylates is known to afford triphenylstannyl sugars ($Sug\text{-}CH_2SnPh_3$) in low, however, yield[12]. This type of compounds can serve as precursors of the open chain aldehydes *via* a rearrangement-elimination reaction.

Application of tributyltin cuprate to less reactive sugar derivatives is presented below. Tosylate **7** was converted smoothly into stannylated sugar **8**, which - upon treatment with zinc chloride rearranged to the unsaturated aldehyde **9a**[13]; the method presented here is convenient for the preparation of highly oxygenated open-chain sugar aldehydes with terminal double bond; 'Bu3SnCu' is superior to tributyltin lithium, since the latter with sugar tosylates gives low yields of the stannylated compounds.



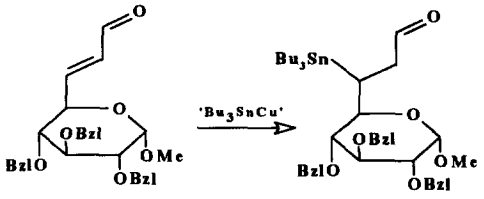
Reaction of Bu_3SnLi with aldehydes followed by protection of the resulting hydroxyl group leads to α-alkoxy (acyloxy) organostannanes. Treatment of these compounds with organohalides in the presence of CuCN results in a clean substitution of Bu_3Sn- group with suitable electrophile with retention of the configuration at the carbon atom[14]



We have examined, therefore, the possibility of the synthesis of such sugar-derived derivatives. Reaction of aldehydes **10a-c** with Bu_3SnLi was unsuccessful due to decomposition of the starting uloses. However, application of softer nucleophile 'Bu3SnCu' led to appropriate stannyl-carbinols in good yield. For example, addition of 'Bu3SnCu' to the *gluco*-aldehyde **10a** gave a *ca* 3:1 mixture of diastereoisomers **11a**; similarly were prepared carbinols **11b** and **11c**.

These compounds are very sensitive towards bases and can be protected in high yields only as acetates **12a-c** (Ac_2O, Et_3N, DMAP in CH_2Cl_2)[15]

We examined also the reaction of tin nucleophiles with α,β-unsaturated sugar aldehydes. Although for 1,4-addition to such systems tributyltin lithium[7] is commonly used[16a,b], there are some examples that this reagent can add in a 1,2-mode[16c].



13 14 (two diastereoisomers)

Addition of Bu_3SnLi to 2,3,4-tri-*O*-benzyl-6,7-dideoxy-6(*E*)-eno-α-D-*gluco*-octapyranos-8-ulose (**13**) caused only decomposition of the starting aldehyde, however, appli-cation of tri-*n*-butyltin cuprate resulted in clean formation of tin adducts **14**[17]. Surprisingly, no stereodifferentiation was observed since a *ca* 1:1 mixture of diastereoisomeric **14** was obtained.

The work on application of tin derivatives of simple monosaccharides in the synthesis of highly functionalized chiral compounds is in progress.

In conclusion: tri-*n*-bytultin cuprate reacts readily with *a.* sugar allylic bromides to give allyltin derivatives with **retention** of the configuration of the double bond, *b.* sugar tosylates (to terminal stannylated derivatives), *c.* sugar aldehydes (to α-tri-*n*-bytultin carbinols), and *d.* α,β-unsaturated sugar aldehydes (to form 1,4-adducts). This reagent is superior to Bu_3SnLi at least in sugar chemistry, since tributyltin lithium caused mainly decomposition of sugar derivatives. Such sugar-derived tin compounds can undergo the β-elimination process in the presence of Lewis acids (zinc chloride) what opens a convenient route to highly functionalized chiral unsaturated aldehydes.

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8. Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Reuter, D. C. *Tetrahedron Lett.*, **1989**, *30*, 2065; although we depicted this reagent as 'Bu_3SnCu' the nature of this species is much more complicated and its structure *according* to Lipshutz should be written as $Bu(Bu_3Sn)Cu(CN)Li_2$.

9. *Typical experimental procedure*: to a suspension of CuCN (2.3 mmol) in abs. THF (5 mL) a solution of BuLi (4.6 mmol) in hexane was added by syringe and the mixture was stirred at -78 °C under an argon atmosphere for 10 min. Bu_3SnH (4.6 mmol) was added and stirring was continued for another 10 min at -78 °C. A solution of suitable sugar electrophile (2 mmol in 3 mL of THF of: allyl bromide *cis* or *trans*, aldehyde, or α,β-unsaturated aldehyde) was added, the mixture was stirred for 5 min at -78 °C and partitioned between ether\5% NH_4Cl, the organic phase was separated and the product was isolated by column chromatography (hexane - ethyl acetate, 6:1). Rection with sugar tosylate was carried out for 16 h at room temp.

10. Prepared by bromination (CBr_4\Ph_3P) of parent *cis* and *trans* allylic alcohols[6].

11. Compound **6(*E*)** was identical with that prepared previously[6]; **6(*Z*)**: ^{1}H-NMR δ: 5.71 (~q, $J_{6,7}$ = **9.8**, $J_{7,8}$ = $J_{7,8'}$ = ~9 Hz, H-7), 5.41 (H-6), 4.29 (d, $J_{1,2}$ = 7.6 Hz, H-1), 4.08 ($J_{5,6}$ = 8.0 Hz, H-1), 3.83 (dd, $J_{2,3}$ = 9.8 Hz, H-2), 3.68 ($J_{4,5}$ ~ 1.0 Hz, H-4), 3.54 ($J_{3,4}$ = 3.0 Hz, H-3), 3.55 (s, OMe), 1.75 - 1.59 (CH_2SnBu_3); ^{13}C-NMR δ: 132.0 (C-7), 120.4 (C-6), 105.0 (C-1), 82.3 (C-3), 79.4 (C-2), 76.8 (C-4), 70.6 (C-5), 57.0 (OMe), 11.4 (C-8). All signals in the ^{1}H- and ^{13}C-NMR spectra were assigned by appropriate 2D experiments. Mass spectrum (EI): 707.2748 [(M^+ - C_4H_9) calcd. for $C_{38}H_{51}O_5\,^{120}Sn$, 707,2758]. For dienoaldehyde **3** obtained from **6(*E*)**, the *trans* configuration was assigned[6]; the same product was obtained by reaction of **6(*Z*)** with $ZnCl_2$.

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13. Compound **8** was obtained in 75% yield (calcd. on consumed tosylate), ^{1}H-NMR δ: 44.49 (d, $J_{1,2}$ = 3.5 Hz, H-1), 4.06 (dt, $J_{4,5}$ = $J_{5,6}$ = 9.2, $J_{5,6'}$ = 4.1 Hz, H-5), 3.93 (dd, $J_{2,3}$ = 9.6, $J_{3,4}$ = 9.2 Hz, H-3), 3.50 (s, OMe), 3.06 (t, H-4), 1.60 (m, CH_2SnR_3); aldehyde **9a** ^{1}H-NMR δ: 9.70. Reduction of **9a** with $NaBH_4$ afforded alcohol **9b** ^{1}H-NMR δ: 5.88 (ddd, $J_{4,5}$ = 7.4, $J_{5,6}$ = 10.9, $J_{5,6'}$ = 17.3 Hz, H-5), 5.32 and 5.30 (H-6,6'), 4.38 (dd, $J_{3,4}$ = 4.6 Hz), 3.70 and 3.55 (AB, J = 11.7 Hz, CH_2OH); ^{13}C-NMR δ: 135.1 (C-5), 118.8 (C-6), 81.7, 80.4, 79.5, 61.5 (C-1).

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15. Main diastereoisomer **11a** (signals of sugar part cited only): ^{1}H-NMR δ: 4.57 (d, $J_{1,2}$ = 3.6 Hz, H-1), 4.21 (dd, $J_{6,OH}$ = 9.9, $J_{5,6}$ = 1.1 Hz, H-6), 4.00 (dd, $J_{2,3}$ =9.6, $J_{3,4}$ = 9.3 Hz, H-3), 3.78 (t, $J_{4,5}$ = 9.4 HZ, H-4), 3.61 (dd, H-5), 3.48 (dd, H-2), 3.39 (s, OMe); ^{13}C-NMR δ: 99.1 (C-1), 82.0 (C-3), 80.1 (C-2), 75.9 (C-4), 75.6 (C-5), 65.8 (C-6), 56.3 (OMe). Acetylation gave **12a**; OAc signal δ: 2.03 (^{1}H-NMR) and 170.6 (^{13}C-NMR).

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17. Adduct **16**: first diastereoisomer: ^{1}H-NMR δ: 9.54 (dd, $J_{7,8}$ = 2.6, $J_{7',8}$ = 1.2 Hz, **CHO**), 4.53 (d, $J_{1,2}$ = 3.6 Hz, H-1), 3.97 (dd, $J_{2,3}$ = 9.8, $J_{3,4}$ = 8.8 Hz H-3), 3.89 (dd, $J_{5,6}$ = 2.0, $J_{4,5}$ = 9.4 Hz H-5), 3.42 (dd, H-2), 3.40 (s, OMe), 3.37 (dd, H-4), 2.55 (m, $J_{7,7'}$ = 17.7, $J_{6,7}$ = 5.1 Hz, H-7), 2.43 (m, H-7'), 2.06 (m, **CH**-$SnBu_3$); ^{13}C-NMR δ: 202.7 (**CHO**), 98.7 (C-1), 82.1 (C-2), 80.4 (C-3), 78.1 (C-4), 56.7 (OMe), 42.2 (C-6), 18.8 (C-7); second diastereoisomer: ^{1}H-NMR δ: 9.64 (~t, $J_{7,8}$ = 2.3, $J_{7',8}$ = 2.0 Hz, **CHO**), 4.44 (d, $J_{1,2}$ = 3.5 Hz, H-1), 3.94 (dd, $J_{2,3}$ = 9.7, $J_{3,4}$ = 8.8 Hz H-3), 3.70 (dd, $J_{5,6}$ = 1.7, $J_{4,5}$ = 9.7 Hz H-5), 3.47 (dd, H-2), 3.33 (s, OMe), 3.13 (dd, H-4), 2.61- 2.12 (m, CH_2SnBu_3), 1.63 (m, **CH**-$SnBu_3$); ^{13}C-NMR δ: 202.7 (**CHO**), 97.6 (C-1), 82.0 (C-3), 81.9 (C-4), 74.0 (C-5), 55.1 (OMe), 46.5 (C-6), 23.2 (C-7).

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