Pergamon

Tetrahedron, Vol. 53, No. 31, pp. 10765-10774, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00676-5

Tri-*n*-Butyltin Cuprate as a Tool for the Preparation of Stannyl Derivatives of Carbohydrates[1]

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Abstract: *Reaction of tri-n-butyltin cuprate with sterically hindered allylbromides* ***10(E)*** *and* ***10(Z)*** *derived from D-galactose led exclusively to S_N2 products - allyl tributystannyl sugars* ***11(E)*** *and* ***11(Z)*** *in good yield and with retention of the configuration of the double bond. Reaction of 'Bu$_3$SnCu' with less sterically hindered allyl derivatives* ***5a*** *and* ***5b*** *(derived from D-glucose) gave a mixture of S_N2 and S_N2' products (****6*** *and* ***7*** *respectively). Treatment of methyl 2,3,4-tri-O-benzyl-6-O-mesyl-α-D-glucopyranoside (****13****) with 'Bu$_3$SnCu' afforded organotin* ***14****, which was further converted into an open-chain unsaturated aldehyde* ***15*** *(in the presence of zinc chloride). Reaction of 'Bu$_3$SnCu' with sugar aldehydes provided stannyl carbinols, while with α,β-unsaturated sugar aldehydes the 1,4-addition products are formed.* © 1997 Elsevier Science Ltd.

INTRODUCTION

Organostannanes are important intermediates in organic synthesis[2]. For example, vinyltin derivatives (RCH=CH-SnR$_3$) may-be used as vinyl anion equivalents; this methodology was applied by us for the preparation of higher carbon sugars with 12 and more carbon atoms in the chain[3] (Fig.1). One of the most useful organotin derivatives are allyltins which - on reaction with aldehydes - furnish homoallylic alcohols[4,5] (Fig.2). When this process is catalyzed by a Lewis acid, relative configuration of the newly created chiral centers is always *syn*, regardless of the geometry (*cis* or *trans*) of starting organometalic compound[4]. However, this configuration is strongly dependent on the geometry of the olefin when the reaction is performed without catalyst (*e.g.* at high

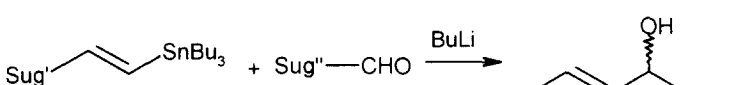


Fig.1

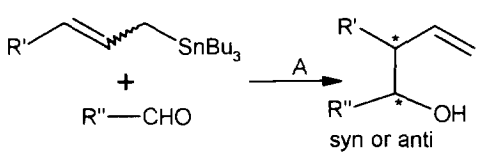


Fig. 2. A = Lewis acid, temperature or pressure

temperature or under high pressure); ***E***-stannanes afford the *anti* products while ***Z***-stannanes *syn*[5]. Allyl tributyltin derivatives are also used for creation of new carbon-carbon bonds in radical reactions[6]. The access to configurationally pure allyltins of desired geometry is, therefore, needed.

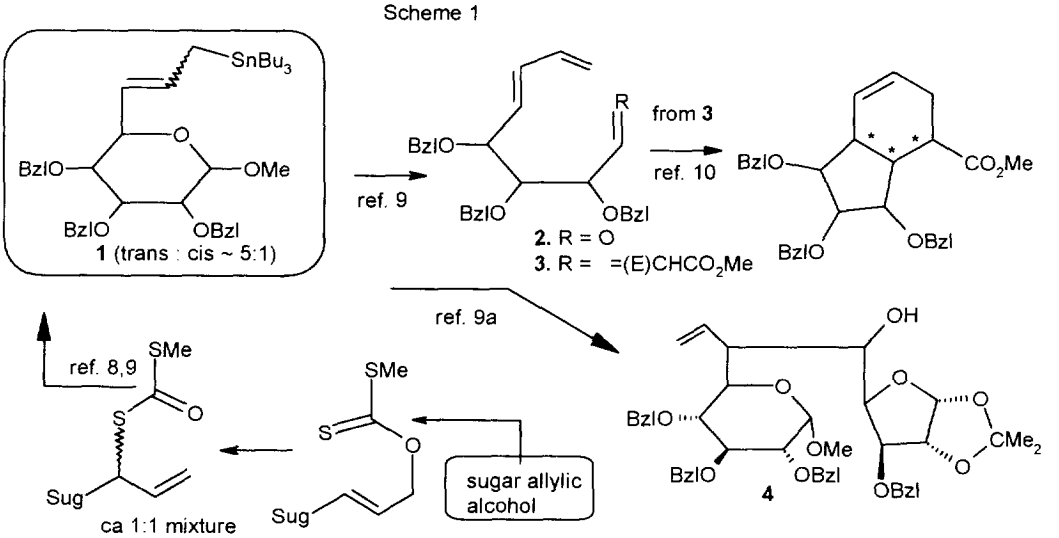
Although there are many methods for the preparation of allyltin derivatives[7], application of them in carbohydrate field is not easy. The best method involves conversion of allylic alcohols into xanthates followed by thermal rearrangement into thiocarbonates and subsequent reaction with tri-*n*-butyltin hydride[8] (Scheme 1).

In this paper the reactions of a soft tin nucleophile ('Bu_3SnCu') with activated allyl derivatives of monosaccharides leading to sugar allyltins as well as their with sugar aldehydes will be presented.

RESULTS AND DISCUSSION

Recently we elaborated a convenient method[9] of the synthesis of sugar allyltins **1**, useful precursors of highly-oxidized chiral dienoaldehydes **2**, synthons for chiral carbocycles *via* intramolecular Diels-Alder

Scheme 1



cyclization reactions[10] (Scheme 1). Compound **1** can be used also as a starting material for the preparation of higher carbon sugars (*e.g.* a C-11 monosaccharide **4** shown in Scheme 1) by reaction with sugar aldehyde in the presence of a Lewis acid as was demonstrated by us some years ago[9a].

At least two problems are important in the preparation of allyltins: regio- and stereoselectivity. Method presented in Scheme 1 is fully regioselective, however it is not stereoselective; the *trans/cis* mixture of allyltins **1** (up to 5:1) is obtained ***regardless*** of the configuration of starting allylic alcohol[9b].

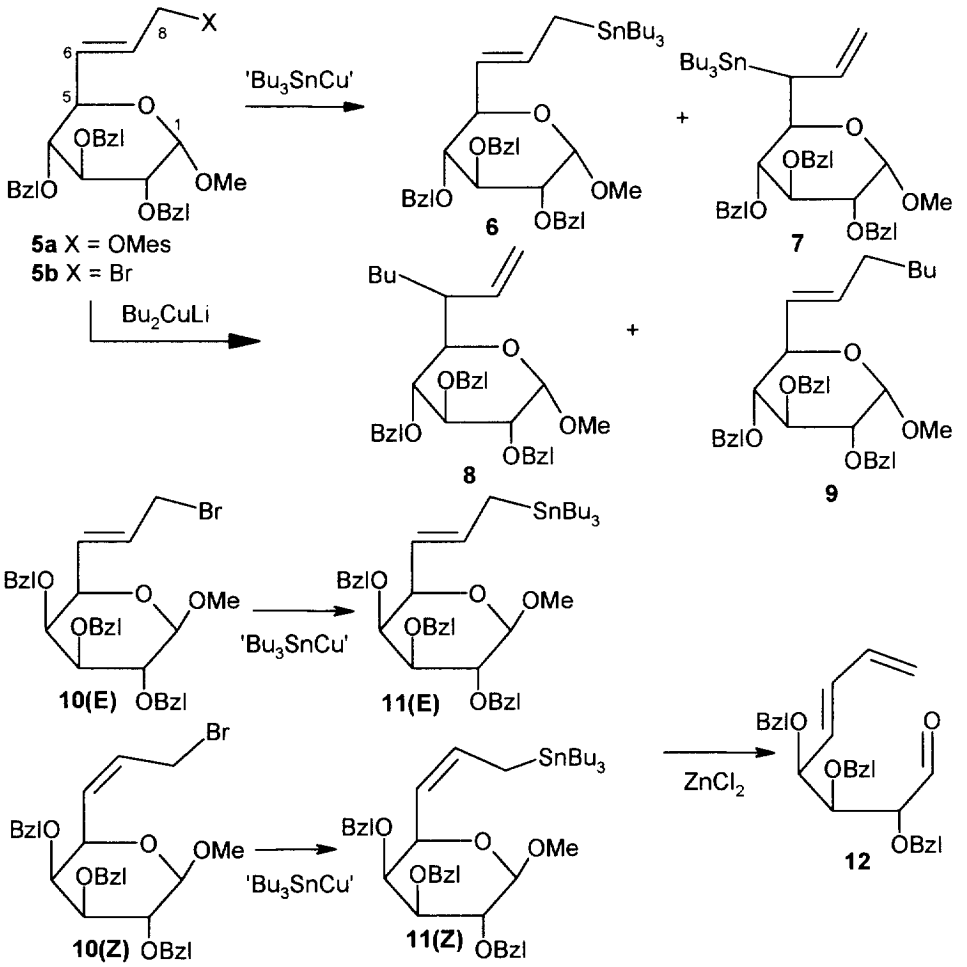
An alternative to reaction presented in Scheme 1 may-be a nucleophilic displacement of a tosylate or bromide in appropriate sugar derivatives with tin nucleophiles. Nucleophile can attack the allylic system according to either S_N2 or S_N2' mechanism, what depends on stereoelectronic and steric factors. Attack of a soft nucleophile according to an S_N2' mechanism (attack at the 'soft end') is preferred on sugar allylic mesylates, while for bromides the mixture of regioisomers can be obtained (the 'softness' of both ends is comparable). Indeed, we have found that a model reaction of mesylate **5a** Bu_2CuLi led exclusively to an S_N2'

product **8** (surprisingly, single stereoisomer), while the same process performed on bromide **5b** gave a mixture of regioisomers **8** and **9** (Scheme 2).

Application of this process for the preparation of sugar allyltins is presented in Scheme 2. Reaction of mesylate **5a** and bromide **5b** with commonly used tri-*n*-butyltin lithium[11] led only to decomposition of starting materials but, reaction with more soft nucleophile, tri-*n*-butyltin cuprate[12], found to be successful.

Tri-*n*-butyltin cuprate[12] is more sterically hindered than Bu_2CuLi and, therefore, the S_N2 reaction should be preferred. Indeed, treatment of the D-*gluco*-allyl mesylate **5a** with 'Bu_3SnCu'resulted in formation of the

Scheme 2



S_N2 product **6**, however, significant amounts of the rearranged S_N2'-regioisomer **7** were also obtained. The same results were obtained, unfortunately, with allyl bromide **5b** (Scheme 2).

The situation was changed when more sterically hindered sugar allylic bromide (derived from D-galactopyranose) was used; only the S_N2 product was formed. Moreover, this reaction proceeded also with

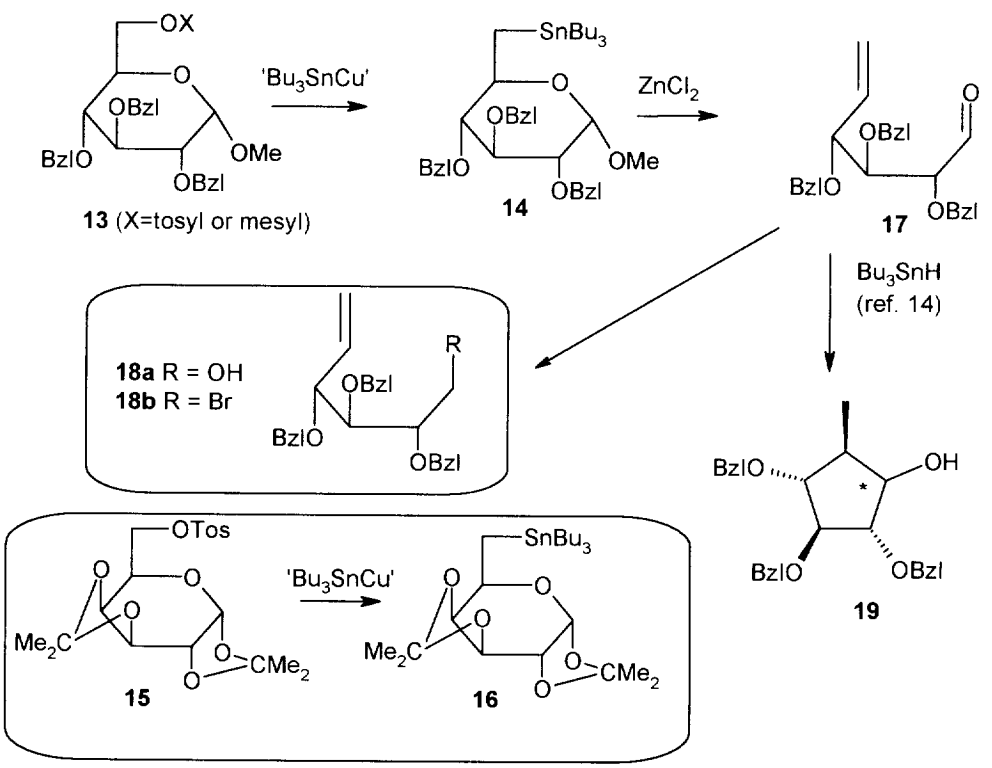
complete retention of the configuration of the olefin: from *trans*-allylic bromide **10(*E*)** *trans* allyltin **11(*E*)** was obtained, and from the *cis* **10(*Z*)** the *cis* organometallic species **11(*Z*)**.

Both compounds were converted into the same dieno-aldehyde **12** by treatment with zinc chloride in methylene chloride solution[9b].

Thus, reaction of tri-*n*-butyltin cuprate with sterically hindered sugar allylic bromides proceeded smoothly according to an S_N2 mechanism and with retention of the configuration of starting olefin. This method may be used as an alternative to that shown in Scheme 1.

The rearrangement-elimination reaction of sugar allyltins led to open-chain dienoaldehydes (Scheme 1); zinc chloride catalyzed process of 6-deoxy-6-(tri-*n*-butyltin)-sugars should produce chiral δ-unsaturated

Scheme 3



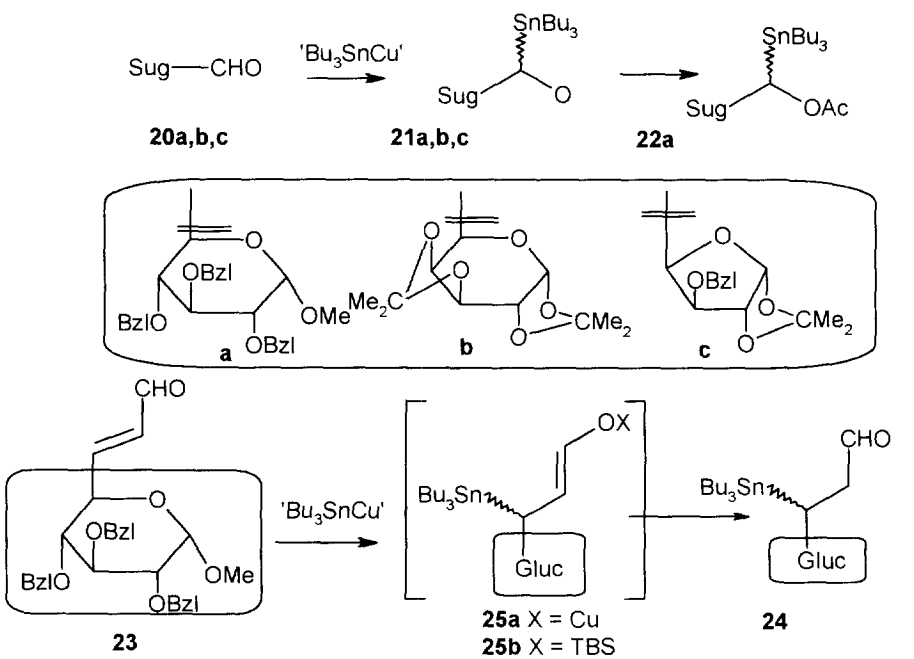
aldehydes that can be used for preparation of chiral cyclopentanes; the results are shown in Scheme 3.

Reaction of 'Bu$_3$SnCu' with methyl 2,3,4-tri-*O*-benzyl-6-*O*-mesyl-α-D-glucopyranoside (**13**) afforded organotin compound **14** in good yield. Similarly, 1,2:3,4-di-*O*-isopropylidene-6-*O*-tosyl-α-D-galactopyranose (**15**) afforded appropriate stannyl derivative **16**, although in lower yield. Such type of sugar organotins were obtained previously in rather low yield from sugar tosylates (or mesylates) by reaction with triphenyltin lithium[13]. Treatment of **14** with zinc chloride gave unsaturated aldehyde **17** which was used recently by us for the preparation of chiral cyclopentanes[14] (**19**). Alternatively, this aldehyde was reduced to an alcohol **18a** and further converted into bromide **18b**, useful synthon for studying of radical cyclization reactions.

Protected stannyl carbinols react with organohalides in the presence of CuCN what results in a clean substitution of Bu_3Sn- group with suitable nucleophile with retention of the configuration at the carbon atom[15]. Synthesis of sugar derived stannyl carbinols was initiated from sugar aldehydes (**20a,b,c**) and tri-*n*-butyltin cuprate; this reaction led smoothly to appropriate adducts **21** (Scheme 4). Usually the mixture of stereoisomers were obtained in a *ca* 5:1 ratio what can be easily determined by ^{119}Sn-NMR spectra. Two resonances at -31.8 (main isomer) and -33.2 ppm (minor product) could be observed in the spectrum of a crude mixture of **21a**[16]. Sugar-derived carbinols **21** are rather unstable under basic conditions (triethylamine, DMAP), and attempts to protect a free hydroxyl group with groups such as methoxymethyl (MOM), or benzyloxymethyl (BOM) failed; only protection as acetate (**22a**) was possible.

Addition of Bu_3SnLi to α,β-unsaturated aldehydes proceeds according to a 1,4-mechanism[17]; nevertheless there are examples that this reagent may add in a 1,2 mode[18]. Addition of 'Bu_3SnCu', much softer

Scheme 4



nucleophile, however, should proceed in a 1,4-mode[19]. We examined reaction of 'Bu_3SnCu' with methyl 2,3,4-tri-*O*-benzyl-6,7-dideoxy-oct-6(*E*)-eno-α-D-*gluco*-pyranosid-8-ulose (**23**) and found that only 1,4-addition product (**24**) was formed in good yield. Recently[20] compound **23** was used for preparation of alkoxy-allyltin derivative **25b**, *via* trapping of intermediate enolate **25a**. Such compounds are useful synthons for the preparation of higher carbon sugars, as was demonstrated recently by Marshall[20].

In conclusion, application of tri-*n*-butyltin cuprate in sugar chemistry allows to prepare various types of sugar-derived organotin products, useful intermediates in the synthesis of highly oxygenated chiral compounds.

Acknowledgment: This work was supported by a Grant **2P303 038 07** from the State Committee for Scientific Research, which is gratefully acknowledged.

Experimental

General methods: NMR spectra were recorded with a Bruker AM 500 spectrometer for solutions in $CDCl_3$ (internal Me_4Si). Most resonances were assigned by COSY (^1H-^1H and ^1H-^{13}C) correlations. Mass spectra [LSIMS (m-nitrobenzyl alcohol was used as a matrix to which sodium acetate was added) or EI] were recorded with a AMD-604 (AMD Intectra GmbH, Germany) mass spectrometer. All reactions with organometallics were performed under an argon atmosphere. Column chromatography was performed on silica gel (Merck, 70-230 mesh). Organic solutions were dried over anhydrous magnesium sulfate.

Sugar allylic mesylates or tosylates (**5a**, **13** and **15**) were prepared from appropriate alcohols: methyl 2,3,4-tri-*O*-benzyl-6,7-dideoxy-oct-6(E)-eno-α-D-*gluco*-pyranoside[9b], methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside and 1,2:3,4-di-O-isopropylidene-α-D-galactopyranose by reaction with 1.5 equiv. of mesyl (or tosyl) chloride, 2 equiv. of diisopropylethylamine and cat. amount of DMAP in methylene chloride at *ca* 5°C. Allylic bromides **5b**, **10(*E*)** and **10(*Z*)** were prepared by reaction of parent allylic alcohols[9b] by reaction with CBr_4/Ph_3P in C_6H_6 at room temperature[21]. Sugar aldehydes **20a,b** were prepared by a Swern oxidation[22] of parent alcohols, while aldehyde **20c** was obtained by periodic cleavage of 3-*O*-benzyl-monoacetonoglucose. Aldehyde **23** was obtained from methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranos-6-ulose and formylmethylene-triphenylphosphorane (Ph_3P=CH-CHO). The atoms were numbered according to sugar nomenclature (see Scheme 2).

Reaction of methyl 2,3,4-tri-O-benzyl-6,7-dideoxy-8-mesyl-oct-6(E)-eno-α-D-gluco-pyranoside (5a) and methyl 2,3,4-tri-O-benzyl-8-bromo-6,7,8-trideoxy-oct-6(E)-eno-α-D-gluco-pyranoside (5b) with Bu_2CuLi. -To a cooled (-78°C) stirred suspension of CuCN (2.3 mM) in dry THF (5 mL) a solution of butyllithium in hexane (4.6 mM) was added and the mixture was stirred for 10 min. Mesylate **5a** or bromide **5b** (2 mM each in 3 mL of THF) were added by syringe during 10 min. The mixture was stirred for 30 min at -78°C and poured into vigorously stirred saturated ammonium chloride/ether (20:30 mL). After 30 min organic layer was separated, washed with water, dried and concentrated, and the products were purified by column chromatography (hexane - ethyl acetate, 95:5 to 7:1). Reaction of **5a** afforded exclusively the S_N2' product **8** in 85% yield; reaction of **5b** gave 45% of the S_N2 product **9** and 35% of **8**.

Methyl 2,3,4-tri-O-benzyl-6,7,8-trideoxy-6-butyl-oct-7-eno-α-D-gluco-1,5-pyranoside (8). ^1H NMR data δ: 5.70 (m, 1 H, H-7), 5.10 (dd, 1 H, $J_{8,8'}$ 2.2, $J_{7,8}$ 10.3 Hz, H-8), 4.96 (dd, 1 H, $J_{7,8'}$ 17.3 Hz, H-8'), 4.59 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 3.97 (dd, 1 H, $J_{2,3}$ 9.7, $J_{3,4}$ 9.0 Hz, H-3), 3.65(dd, 1 H, $J_{5,6}$ 1.6, $J_{4,5}$ 9.9 Hz, H-5), 3.45 (dd, 1 H, H-2), 3.40 (dd, 1 H, H-4), 3.37 (s, 3 H, OMe), 2.50 (m, 1 H, H-6), 1.55-1.20 (m, 6 H, CH_2 groups of *n*-butyl), 0.87 (t, 3 H, CH_3). ^{13}C NMR data δ:138.3 (C-7), 117.5 (C-8), 97.8 (C-1), 82.4, 80.3 and 79.3 (C-2,3,4), 72.8 (C-5), 55.0 (OCH_3), 43.8 (C-6), 31.8, 29.7, 22.6 and 14.0 (*n*-butyl).

Methyl 2,3,4-tri-O-benzyl-6,7,8-trideoxy-8-butyl-oct-6(E)-eno-α-D-gluco-1,5-pyranoside (9). ^1H NMR data (*inter alia*) δ: 5.85 (m, 1 H, H-7), 5.45 (dd, 1 H, $J_{6,7}$ 15.4, $J_{5,6}$ 7.5 Hz, H-6), 4.56 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.00 (dd, 1 H, $J_{2,3}$ 9.7, $J_{3,4}$ 9.0 Hz, H-3), 3.40 (dd, 1 H, H-2), 3.37 (s, 3 H, OMe), 3.25 (dd, 1 H, H-4), 2.05 (m, 2 H, H-8,8'), 1.55-1.20 (m, 6 H, CH_2 groups of *n*-butyl), 0.87 (t, 3 H, CH_3). HRMS, calc for $C_{34}H_{42}O_5Na$ ($M + Na^+$): 553.2924. Found: 553.2930.

General method of the reaction of tributyltin cuprate with sugar electrophiles.

1. Preparation of tributyltin cuprate. - To a cooled (to -78°C) and stirred suspension of CuCN (2.3 mM) in dry THF (5 mL) a solution of butyllithium in hexane (4.6 mM) was added and the mixture was stirred for 10 min. To a slightly yellow solution of resulting organocuprate, tri-*n*-butyltin hydride (neat, 4.6 mM) was added by a syringe at -78°C. After evolution of gas ceased the yellow mixture was stirred for 15 min at -78°C to yield a solution of crude tri-*n*-butyltin cuprate.

2. Reaction of 'Bu$_3$SnCu' with sugar electrophiles. - A solution of appropriate sugar electrophile (2 mM in 3 mL of dry THF) was added by a syringe to a solution of above prepared tributyltin cuprate in THF and the mixture was stirred at -78°C for 30 min for reactions with aldehydes or overnight at room temperature for reactions with bromides and mesylates. The mixture was diluted with ether (15 mL), aqueous saturated ammonium chloride (5 mL) was added and the mixture was stirred for 30 min at room temperature. Organic layer was separated, washed with water, dried and concentrated and a crude product was purified by chromatography (hexane - ethyl acetate, 95:5 to 6:1)

Reaction of mesylate ***5a*** *with Bu$_3$SnCu* according to a general procedure afforded 40% of known[9b] methyl 2,3,4-tri-*O*-benzyl-6,7,8-tri-deoxy-8-(tri-*n*-butylstannyl)-oct-6(*E*)-eno-α-D-*gluco*-1,5-pyranoside (**6**) and 35% of regioisomer **7** (single stereoisomer).

Reaction of mesylate ***5b*** (HRMS, calc for $C_{30}H_{33}O_5BrNa$: 575.1424. Found: 575.1409) with Bu_3SnCu afforded 50% of **6** and 25% of **7** (single stereoisomer).

Methyl 2,3,4-tri-O-benzyl-6,7,8-tri-deoxy-6-(tri-n-butylstannyl)-oct-7eno-α-D-gluco-1,5-pyranoside (7). ^{1}H NMR data δ: 6.00 (m, 1 H, H-7), 4.80 (m, 2 H, H-8,8'), 4.59 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 3.94 (t, 1 H, $J_{2,3}$ $J_{3,4}$ 9.4 Hz, H-3), 3.81(dd, 1 H, $J_{5,6}$ 1.6, $J_{4,5}$ 9.5 Hz, H-5), 3.48 (dd, 1 H, H-2), 3.46 (dd, 1 H, H-4), 3.41 (s, 3 H, OMe), 2.76 (dd 1 H, $J_{6,7}$ = 11.2 H-6), 1.65-0.8 (3 *n*-butyl groups). ^{13}C NMR data δ:138.1 (C-7), 111.0 (C-8), 98.9 (C-1), 81.8, 80.5 and 80.4 (C-2,3,4), 72.8 (C-5), 56.4 (OCH_3), 34.3 (C-6), 29.1, 27.4, 13.7 and 9.4 (3 *n*-butyl groups). HRMS: calc for $C_{42}H_{60}O_5{}^{120}SnNa$ (M + Na$^+$): 787.3360. Found: 787.3351.

Methyl 2,3,4-tri-O-benzyl-6,7,8-tri-deoxy-8-(tri-n-butylstannyl)-oct-6(E)-eno-α-D-galacto-1,5-pyranoside [11(E)] was obtained in 75% yield from bromide **10(*E*)** according to a general procedure and its spectral data were identical to those reported previously[9b].

Methyl 2,3,4-tri-O-benzyl-6,7,8-tri-deoxy-8-(tri-n-butylstannyl)-oct-6(Z)-eno-α-D-galacto-1,5-pyranoside [11(Z)]. Obtained in 70% yield from bromide **10(*Z*)** according to a general procedure. ^{1}H-NMR data δ: 5.71 (m, 1 H, H-7), 5.41 (dd, 1 H, $J_{5,6}$ 8.0, $J_{6,7}$ 9.8 Hz, H-6), 4.29 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.08 (d, 1 H, $J_{4,5}$ < 1 Hz, H-5), 3.86 (dd, 1 H, $J_{2,3}$ 9.8 Hz,H-2), 3.68 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 3.55 (s, 3 H, OMe), 3.54 (dd, 1 H, H-3), 1.75 - 1.59 (m 2 H, H-8,8'); ^{13}C NMR data 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 (OCH_3), 11.4 (C-8). HRMS (EI): calc for $C_{38}H_{51}O_5{}^{120}Sn$ (M - Bu): 707.2758. Found: 707.2748.

Conversion of ***11(E)*** *and* ***11(Z)*** *into dienoaldehyde* ***12.*** To a solution of a stannyl compound [**11(*E*)** and/or **11(*Z*)**, *ca* 0.5 mM] in methylene chloride (15 mL) a solution (2.2M in CH_2Cl_2) of $ZnCl_2/Et_2O$ complex (0.5 mL) was added and the mixture was stirred at room temperature until tlc (hexane - ethyl acetate, 5:1) showed disappearance of the starting material and formation of a new, more polar product (*ca.* 2 h). The

mixture was diluted with ether (50 mL), water (20 mL) was added, organic phase was separated, washed with 0.5M H_2SO_4 and water, dried and concentrated and the product was purified by column chromatography (hexane - ethyl acetate, 7:1 to 4:1); the same dieno-aldehyde **12**[9b] with the *E*-configuration at the C5-C6 double bond was isolated from **11*(E)*** (85%) and **11*(Z)*** (80%).

Methyl 2,3,4-tri-O-benzyl-6-deoxy-6-(tri-n-butylstannyl)-α-D-gluco-1,5-pyranoside ***(14)***. Obtained from **13** [from tosylate in 75% yield (calculated on consumed tosylate), from mesylate 70% overall]. ^{1}H NMR data δ: 4.49 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 3.93 (dd, 1 H, $J_{2,3}$ 9.6, $J_{3,4}$ 9.2 Hz, H-3), 3.81(dt, 1 H, $J_{5,6}$ 4.1, $J_{5,6'}$ 9.2 $J_{4,5}$ 9.2 Hz, H-5), 3.50 (dd, 1 H, H-2), 3.06 (dd, 1 H, H-4), 3.37 (s, 3 H, OMe), 1.6 (m, both H-6), 1.5-0.8 (3 *n*-butyl groups). ^{13}C NMR data δ: 99.1 (C-1), 85.8, 81.8 and 80.4 (C-2,3,4), 75.7 (C-5), 55.7 (OCH_3), 17.5 (C-6), 29.1, 27.4, 13.7 and 9.7 (3 *n*-butyl groups).

1,2:3,4-Di-O-isopropylidene-6-deoxy-6-(tri-n-butylstannyl)-α-D-galacto-1,5-pyranose ***(16)***. Obtained from tosylate **15** in 35 % yield (65% calculated on consumed **15**). ^{1}H NMR data (*inter alia*) δ: 5.50 (d, 1 H, $J_{1,2}$ 5.2 Hz, H-1), 4.57 (dd, 1 H, $J_{2,3}$ 2.3, $J_{3,4}$ 7.9 Hz, H-3), 4.25 (dd, 1 H, H-2), 4.03 (dd, 1 H, $J_{4,5}$ 1.8 Hz, H-4), 3.91 (m, 1 H, H-5), 1.6 (m, both H-6), 1.5-0.8 (3 *n*-butyl groups). ^{13}C NMR data δ: 96.7 (C-1), 74.4 (C-4), 71.5 (C-3), 70.4 (C-2), 66.8 (C-5). HRMS (EI): calc for $C_{20}H_{37}O_5{}^{120}Sn$ (M - Bu): 477.16734. Found: 4778.16629.

Methyl 2,3,4-tri-O-benzyl-6-(tri-n-butylstannyl)-α-D-gluco-1,5-pyranoside ***(21a)***. Obtained from aldehyde **20a** in 75 % yield as a mixture (*ca* 5:1 ^{119}Sn NMR estimation[16]) of stereoisomers. ^{1}H NMR data (*inter alia*) for the *main stereoisomer* δ: 4.57 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.21 (m, 1 H, H-6), 4.00 (dd, 1 H, $J_{2,3}$ 9.6, $J_{3,4}$ 9.3 Hz, H-3), 3.78 (t, 1 H, $J_{4,5}$ 9.3 Hz, H-4), 3.61 (dd, 1 H, $J_{4,5}$ 9.4 Hz, $J_{5,6}$ 1.1, H-5), 3.48 (dd, 1 H, H-2), 3.39 (s, 3 H, OMe); ^{13}C NMR data δ: 98.9 (C-1), 82.0 (C-3), 80.1 (C-2), 75.9 (C-4), 75.6 (C-5), 65.8 (C-6), 56.3 (OCH_3).

1,2:3,4-Di-O-isopropylidene-6-(tri-n-butylstannyl)-α-D-galacto-1,5-pyranose ***(21b)***. Obtained from aldehyde **20b** in 65 % yield as a ca 5:1 mixture. ^{1}H NMR data (*inter alia*) for the *main stereoisomer* δ: 5.60 (d, 1 H, $J_{1,2}$ 5.1 Hz, H-1), 4.58 (dd, 1 H, $J_{2,3}$ 2.3, $J_{3,4}$ 9.2 Hz, H-3), 4.31 (dd, 1 H, H-2), 4.19 (m, 1 H, H-5), 4.17 (dd, 1 H, $J_{4,5}$ 1.8 Hz, H-4), 1.5-0.8 (3 *n*-butyl groups). ^{13}C NMR data δ: 96.7 (C-1), 72.7 (C-4), 71.8 (C-6), 71.3 (C-3), 70.7 (C-2), 67.4 (C-5).

3-O-Benzyl-1,2-O-isopropylidene-5-(tri-n-butylstannyl)-α-D-gluco-1,4-furanose ***(21c)***. Obtained from aldehyde **20c** in 70% yield as a *ca* 3:1 mixture. ^{1}H NMR data (*inter alia*) *main stereoisomer* δ: 6.00 (d, $J_{1,2}$ 4.0 Hz, H-1), 4.40 (dd, $J_{4,5}$ 3.9, $J_{5,OH}$ 1.7 Hz, H-5), 4.32 (t, $J_{3,4}$ 3.9 H-4), 4.04 (d, H-3), 3.09 (d, OH), 1.6-0.8 (3 *n*-butyl groups); *minor stereoisomer* δ: 5.94 (d, $J_{1,2}$ 4.0 Hz, H-1), 4.04 (d, $J_{3,4}$ 3.6 Hz H-3), 1.6-0.8 (3 *n*-butyl groups).

Methyl 6-O-acetyl-2,3,4-tri-O-benzyl-6-(tri-n-butylstannyl)-α-D-gluco-1,5-pyranoside ***(22a)*** was obtained by acetylation of **21a** with Ac_2O/di-isopropylethylamine/DMAP in methylene chloride solution at room temperature for 30 min. Purification by column chromatography (hexane - ethyl acetate, 95:5 to 7:1) afforded 70% of **21a**. ^{1}H NMR data (*inter alia*) δ: 5.32 (d, 1 H, $J_{5,6}$ 1.6 Hz, H-6), 4.66 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.01 (dd, 1 H, $J_{2,3}$ 9.6, $J_{3,4}$ 9.3 Hz, H-3), 3.78 (~t, 1 H, $J_{4,5}$ 9.5 Hz, H-5), 3.45 (dd, 1 H, H-5), 3.45 (s, 3 H, OMe); 3.44 (dd, 1 H, H-2), 2.03 (s, 3 H, OAc). ^{13}C NMR data (*inter alia*) δ: 170.6 (OAc), 99.1 (C-1), 81.9 (C-3), 80.1 (C-2), 77.1 (C-4), 73.9 (C-5), 68.6 (C-6), 57.0 (OCH_3),

Methyl 2,3,4-tri-O-benzyl-6,7-dideoxy-6-(tri-n-butylstannyl)-α-D-gluco-oct-1,5-pyranosid-8-ulose

(24). Reaction of **23** with Bu_3SnCu gave two stereoisomers which were separated by column chromatography (hexane - ethyl acetate, 95:5 to 8:1). *First isomer* (35% yield) ^1H NMR data δ: 9.54 (dd, 1 H, $J_{7,8}$ 2.6 and 1.2 Hz, H-8), 4.53 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 3.97 (dd, 1 H, $J_{2,3}$ 9.8, $J_{3,4}$ 8.8 Hz, H-3), 3.89 (dd, 1 H, $J_{4,5}$ 9.4, $J_{5,6}$ 2.0 Hz, H-5), 3.42 (dd, 1 H, H-2), 3.40 (s, 3 H, OMe); 3.37 (dd, 1 H, H-4), 2.55 and 2.43 (m, 2 H, H-7,7'), 2.05 (m, 1 H, H-6). ^{13}C NMR data (*inter alia*) δ: 202.7 (C-8), 98.7 (C-1), 82.1 (C-3), 80.4 (C-4), 78.1 (C-2), 74.5 (C-5), 56.7 (OCH_3), 42.2 (C-6), 18.8 (C-7). *Second isomer* (30% yield) ^1H NMR data δ: 9.64 (dd, 1 H, $J_{7,8}$ 2.3 and 2.0 Hz, H-8), 4.44 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 3.94 (dd, 1 H, $J_{2,3}$ 9.7, $J_{3,4}$ 8.8 Hz, H-3), 3.70 (dd, 1 H, $J_{4,5}$ 9.7, $J_{5,6}$ 1.7 Hz, H-5), 3.47 (dd, 1 H, H-2), 3.33 (s, 3 H, OMe); 3.13 (dd, 1 H, H-4), 2.61 and 2.12 (m, 2 H, H-7,7'), 1.62 (m, 1 H, H-6). ^{13}C NMR data (*inter alia*) δ: 202.7 (C-8), 97.6 (C-1), 82.0 (C-3), 81.9 (C-4), 80.0 (C-2), 74.0 (C-5), 55.1 (OCH_3), 46.5 (C-6), 23.2 (C-7).

*Synthesis of 2,3,4-tri-O-benzyl-1-bromo-1,5,6-tri-deoxy-D-xylo-5-en-hexitol (**18b**).*

To a solution organotin **14** (430 mg, 0.59 mM) in methylene chloride (15 mL) a solution (2.2M in CH_2Cl_2) of $ZnCl_2/Et_2O$ complex (0.5 mL) was added and the mixture was stirred at room temperature until tlc (hexane - ethyl acetate, 5:1) showed disappearance of the starting material and formation of a new, more polar product (*ca.* 2 h). The mixture was diluted with ether (50 mL), water (20 mL) was added, organic phase was separated, washed with 0.5M H_2SO_4 and water, dried and concentrated. Column chromatography (hexane - ethyl acetate, 7:1 to 4:1) gave aldehyde **17** (210 mg, 0.50 mM, 85%) which was reduced with sodium borohydride in methanol/THF affording 2,3,4-tri-*O*-benzyl-5,6-di-deoxy-D-*xylo*-5-en-hexitol (**18a**, quant) . ^1H NMR data δ: 5.88 (ddd, 1 H, $J_{4,5}$ 7.4, $J_{5,6t}$ 17.3, $J_{5,6c}$ 10.9 Hz, H-5), 5.30 (m, 2 H, H-6,6'), 4.10 (dd, 1 H, $J_{3,4}$ 4.6 Hz, H-4), 3.66 (m, 2 H, H-2,3), 3.71 (m, 1 H, H-1) and 3.55 (m, 1 H, H-1'). ^{13}C NMR data δ: 135.1 (C-5), 118.8 (C-6), 74.7, 72.8 and 70.7 (C-2,3,4), 61.5 (C-1).

A solution of the above alcohol **18a** (201 mg, 0.48 mM), triphenylphosphine (188 mg, 0.72 mM) and tetrabromomethane (240 mg, 0.72 mM) in dry benzene (15 mL) was stirred overnight at room temperature. Hexane (15 mL) was added, the precipitated triphenylphosphine oxide was filtered off and the filtrate was evaporated to dryness. Bromide **18b** (365 mg, 0.42 mM, 87%) was isolated by column chromatography (hexane - ethyl acetate, 9:1 to 5:1). ^1H NMR data δ: 5.81 (ddd, 1 H, $J_{4,5}$ 7.6, $J_{5,6t}$ 17.3, $J_{5,6c}$ 10.4 Hz, H-5), 5.28 (m, 2 H, H-6,6'), 4.10 (m, 1 H, H-4), 3.78 (m, 2 H, H-2,3), 3.53 (m, 1 H, H-1) and 3.34 (m, 1 H, H-1'). HRMS calc for $C_{27}H_{29}O_3BrNa$ ($M + Na^+$): 503.1198. Found: 503.1122.

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(*Received in UK* 16 *May* 1997; *accepted* 5 *June* 1997)