100. New Synthetic Bromination Procedures for Use in Radiolabelling-Chemistry: Reaction of *C*-Metallated Derivatives of Carbohydrates with Bromide, in the Presence of Mild Oxidizing Agents[1])

by **Jean-Richard Neeser**[2]), **Laurance D. Hall** and **Julius A. Balatoni**

Chemistry Department, University of British Columbia, Vancouver, B.C., Canada V6T 1Y6

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Summary

In the presence of 2 mol-equiv. of AcONa, both triglycosylborane **1** and dicyclohexylglycosylborane **2** readily react with bromine chloride generated *in situ* from bromide and *N*-chlorosuccinimide (NCS) to give the bromo-sugar **3** (75 and 60%, resp.). The use of the BH_3-THF/bromide/NCS/2 AcONa procedure permits the rapid, face-specific synthesis of **6** (58% uptake of bromine) and face-selective synthesis of **8/9** (71% uptake of bromine), from vinyl ether derivatives **5** and **7**, respectively. The dicyclohexylborane/bromide/NCS/2 AcONa procedure leads to the fast and quantitative conversion of **11** to the bromosugar **12** (91%). Hydroboration-transmetallation sequences give access to *C*-mercuriated carbohydrates **13** (71%) and **14** (78%). The bis(glycosyl)mercury derivative **13** is spontaneously cleaved by reaction with one equivalent of bromide/chloramine-T/aqueous HCl-solution to give **3** (87%) and **14** (76%). Hydrostannylation of acetylenic sugar **15** gave the (*E*)-stannylvinyl derivative **16** as the major product. This latter precursor **16** is spontaneously cleaved by the bromide/chloramine-T/aqueous HCl-solution reagent to give the bromovinyl-sugar **17** (96%).

In recent years, the increasing interest in radiohalogen-containing radiopharmaceuticals [2] [3] for use in diagnostic nuclear medicine and positron emission tomography (PET) has led to the increased importance of the bromine radionuclides [2b]. The diversity of these isotopes (^{74}Br, ^{75}Br, ^{76}Br, ^{77}Br) as well as the greater strength of C,Br-bonds, as compared with C,I-bonds, are obviously responsible for this recent interest. Thus presently, organic synthetic methods for rapid bromination, compatible for example with the use of ^{75}Br (half-life 97 min), are being developed. It is well known that for most organometallic derivatives, the carbon/metal-bonds are cleaved rapidly by molecular bromine; on the other hand, cyclotron-produced bromine isotopes, like their iodine counterparts, are more readily obtained in the ionic form. This requires the use of mild oxidizing agents for the *in situ* generation of electrophilic bromine required for the cleavage of such organometallics.

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[1]) For preliminary reports, see [1].

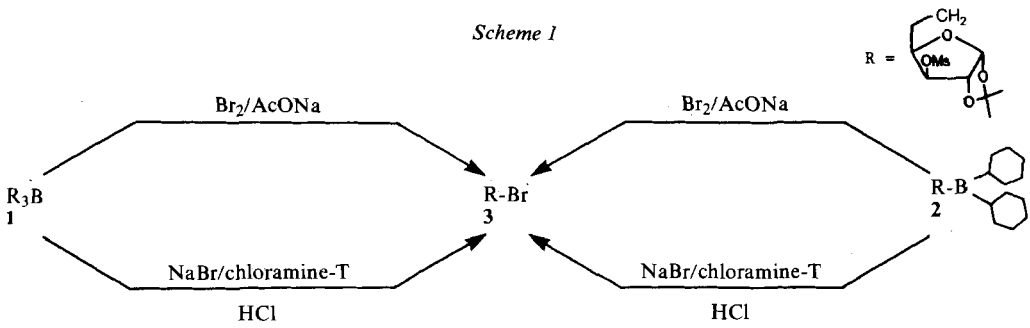
[2]) Present address: Research Department, Nestlé Products Technical Assistance Co. Ltd., CH-1000 Lausanne.

Kabalka et al. have already developed a method for the bromination of organoboranes by reaction with bromine chloride, generated *in situ* from bromide and chloramine-T (= *N*-chloro-*p*-toluenesulfonamide, sodium salt) in an acidic aqueous medium [4]; we have recently reported the results of the adaptation of this procedure to an unsaturated carbohydrate model [3]. We now report an extension of our earlier studies, which includes a new method for the fast brominating cleavage of organoboranes (which works in weakly basic medium), a new method for rapid conversion of bis(alkyl)mercury derivatives into alkylbromides, and a new procedure for the fast synthesis of a bromo-vinyl derivative from a stannyl-vinyl precursor.

The fact that methods for radiolabelling-chemistry have to be very mild, and compatible with a wide range of sensitive functional groups, together with the interest in the radiolabelled bromo-sugars themselves, have prompted us to carry on this study using carbohydrate substrates. This has also provided us with an opportunity to develop new synthetic routes to *C*-mercuriated sugars and to a stannyl-vinyl derivative of a carbohydrate.

Hydroboration-bromination. – Our earlier studies showed [3] that both glycosylborane derivatives **1** and **2** react more readily to the bromo-sugar **3** with molecular bromine/methanolic sodium acetate than with bromide/chloramine-T/aqueous HCl-solution (see *Scheme 1*). The available data in organoborane chemistry [5a]

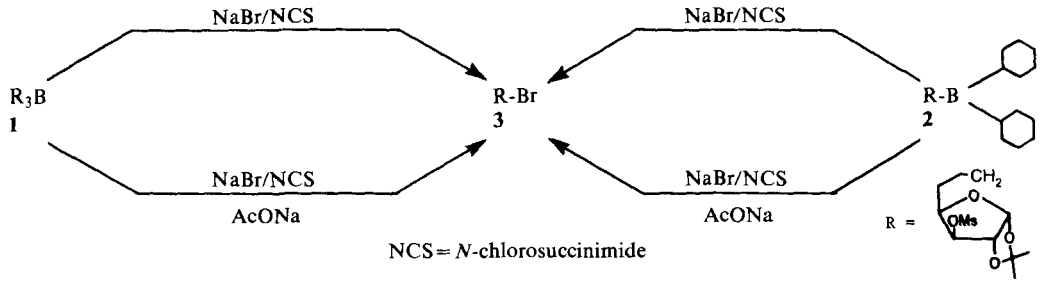
Scheme 1



suggest that for ionic halogenating cleavages, activation of the substrate in an electron-rich organoborane-'ate' complex, gives the best results. In this regard, the fact that *in situ* oxidation of bromide with chloramine-T requires the presence of HCl obviously rules out any possibility of activating the organoborane with a weak base in such a reaction. Many other reagents have been used to oxidize bromide, such as *N*-chlorotetrafluorosuccinimide [6], *N*-chlorosuccinimide [7], organic hypohalites [8], acetic acid/hydrogen peroxide [9]; among these one of the most convenient and extensively used is *N*-chlorosuccinimide (NCS) [10]. Thus, a desire to explore other methods for generating BrCl *in situ* for the ionic brominating cleavage of organoboranes and which are compatible with a weakly basic medium, led to an investigation of the use of NCS for this purpose.

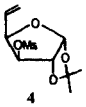
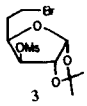
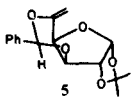
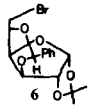
Starting with the unsaturated carbohydrate model **4** (5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methanesulfonyl-α-D-*xylo*-hex-5-enofuranose), we have investigated the reaction of both the triglycosylborane **1** and the dicyclohexylglycosyl-

Scheme 2



borane **2** with one equivalent of Br^-/NCS, either without activation of **1** (**2**) or in the presence of two equivalents of methanolic sodium acetate (see *Scheme 2*). If the results obtained with the Br^-/NCS procedure are similar to those obtained previously [3] using chloramine-T/HCl as an oxidizing agent, the results obtained with the Br^-/NCS/2 AcONa procedure require some comments. After activation with acetate, either **1** or **2** readily react with one equivalent of BrCl prepared *in situ* from Br^- and NCS; furthermore, in both cases, the chromatogram of the reaction mixture revealed a cleaner electrophilic cleavage than those previously obtained with the *Kabalka* procedure. Surprisingly, after workup and column chromatography, the isolated yield for the conversion of **1** into bromo-sugar **3** using our procedure was similar (75%), but not better than previously obtained.

Table 1. *Bromination of organoboranes derivative of unsaturated carbohydrates*

Substrate	Product	Hydroborating Agent	Brominating Agent	Halogenation Time (min)	% Isolated Yield[a])
 4	 3	BH_3/THF	NaBr/2 chloramine-T/HCl	15	75 (25)[b])
			NaBr/NCS		75 (25)
			NaBr/NCS/2 AcONa		75 (25)
			NaBr/2 chloramine-T/HCl		36 (36)[b])[c])
			NaBr/NCS		42 (42)[c])
			NaBr/NCS/2 AcONa		60 (60)
 5	 6	BH_3/THF	NaBr/NCS/2 AcONa	15	58 (19)
 7	 8 +  9	BH_3/THF	NaBr/NCS/2 AcONa	15	71 (24)
 11	 12		NaBr/NCS/2 AcONa	15	91 (91)

[a]) Isolated yields based on the brominating agent. The numbers in parentheses refer to isolated yields based on starting unsaturated carbohydrates.

[b]) Results of [3].

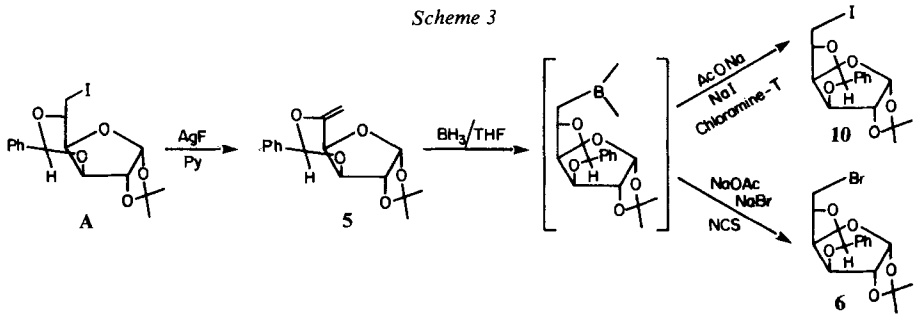
[c]) The product **3** isolated from these procedures is mixed with an unidentified carbohydrate-containing by-product.

The fact that in such a reaction only one of the three groups on boron reacts, prompted us to use dicyclohexylborane as a hydroborating reagent since this would increase the efficiency of the bromination reaction with respect to the unsaturated starting material **4**. This approach resulted in the conversion of **2** into **3**, using the new Br^-/NCS/2 AcONa procedure, and the isolation of pure **3** in 60% yield (based on **4**). This result suggests that this latter procedure is more selective for the preferential cleavage of the primary alkyl carbohydrate-containing group, than is the Br^-/chloramine-T/HCl. Our results are summarized in *Table 1*.

Vinyl-ether derivatives such as **5** and **7** are well-known to undergo hydrogenation reaction to give the two products arising from attack at the two possible faces of the double bond; one product is always favored because of the difference in steric hindrance between the *exo*- and *endo*-faces of the bicyclic system [11]. As a part of the investigation of the bromination method presently developed, we have studied the stereochemistry of this hydroboration-bromination sequence as applied to **5** and **7**. It was found that, whereas **5** gives access to only one bromo-sugar (**6**, isolated in 58% yield) with complete face-specificity, **7** leads to a mixture of both possible products (**8** and **9**, 59:41 by ^{1}H-NMR., 71% isolated yield). In each case, the favored product is the expected one, arising from attack on the *exo*-face of either **5** or **7**. The configuration at C(5) of **6**, **8** and **9** was easily proven on the basis of their ^{1}H-NMR. spectra as follows. The fact that **5** was prepared from the 6-iodo-*α*-D-*gluco* derivative **A** (see *Exper. Part*), together with the fact that the analogous 'hydroboration-iodination' sequence [3] can be applied to **5** (see *Scheme 3*), gave us the opportunity to synthesize the iodo-sugar **10** *via* organoborane technology, and then to compare the ^{1}H-NMR. spectra of **A**, **6** and **10**. This comparison led to the unambiguous assignment of the *β*-L-*ido* configuration for both **6** and **10**. The mixture of **8** and **9** presents a nicely dispersed ^{1}H-NMR. spectrum, wich permitted us to assign the structures of the major (**8**) and minor (**9**) products.

In addition to the fact that use of dicyclohexylborane as a hydroborating agent increases the yield with respect to the unsaturated starting material, this latter procedure opens the door to the utilization of 'hydroxy-free' carbohydrate derivatives as starting materials. For such reactions, the hydroboration requires one additional equivalent of dicyclohexylborane for each hydroxy group present in the starting molecule; this causes the spontaneous conversion of the alcohol function to its borinic ester. To demonstrate this new synthetic possibility, we have investigated the reaction of **11** with 2.2 equivalents of dicyclohexylborane, followed by

Scheme 3

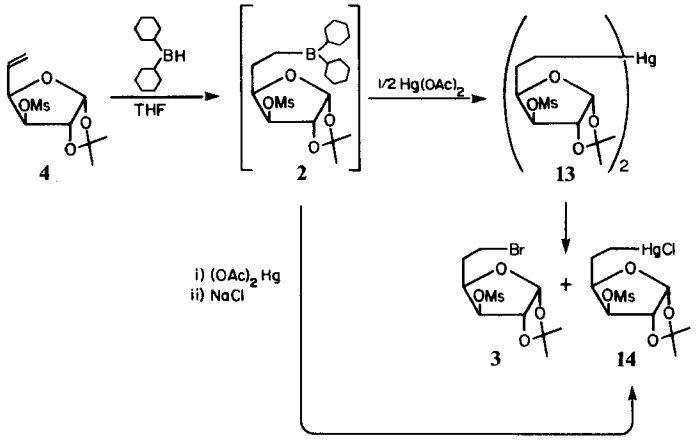


bromination of the intermediate using the Br^-/NCS/2 AcONa procedure (s. *Table 1*). This reaction sequence led to the bromo-sugar **12** in very high yield (91%); this could be the result of intramolecular activation of the mixed organoborane by the alcohol group (regenerated by the added methanolic CH_3COONa-solution) to form a 6-membered-ring intermediate which has a favorable geometry for the incoming electrophilic reagent. In the context of radiolabelling-carbohydrate chemistry, this result could be very important, because the possibility of labelling sugars which have unprotected hydroxy groups clearly reduces the number of deblocking steps, which have to follow the labelling step.

Hydroboration-mercuration-bromination. – An important strategic objective for the development of methods suitable for labelling in nuclear medicine is to have precursors which are stable and can be stored for a long time and used directly for bromination reactions. In this regard, organoborane solutions are less than ideal. Conversely, organomercurials are well known to be stable, easily handled compounds; furthermore, it has long been known that C, Hg-bonds are cleaved rapidly by halogens (I_2, Br_2 and Cl_2) [12]. In such reactions, dialkylmercurials (R_2Hg) are more reactive than *C*-chloromercuriated alkyl derivatives (RHgCl) [12]. *Bühler & Brown* have already reported that mixed organoboranes, obtained by hydroboration of terminal olefins with dicyclohexylborane, readily react with 0.5 equivalent of mercury diacetate yielding bis(primary alkyl)mercury derivatives [13]. In addition, conversion of alkenes into bromoalkanes *via* a *'one-pot'* hydroboration-transmetallation-bromination sequence has been reported, using Br_2 as the brominating reagent [14].

Prompted by these reports, we first investigated the reaction of **2** with 0.5 equivalent of $(AcO)_2Hg$, which led to the isolation of pure **13** (71%) after 1.5 h of reaction at 25°. The product **13** was easily characterized, and is stable to storage. When exposed to one equivalent of Br^-/chloramine-T/aqueous HCl-solution, **13** was spontaneously cleaved by BrCl to yield in 3 min the chloromercuriated product **14** as a precipitate (76%), and the expected bromo-sugar **3** (87% isolated yield). An independent synthesis of **14** by application of a known procedure [15]

Scheme 4

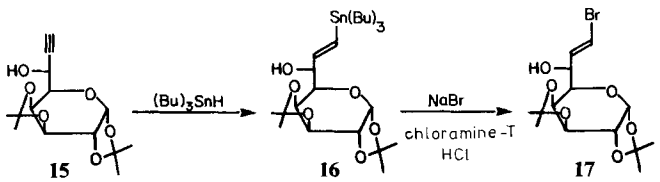


involved the reaction of **2** with one equivalent of $(AcO)_2Hg$ (0.5 h, 25°), followed by addition of NaCl and filtration (78% isolated yield). It was found that both the samples of **14** (from **2** and **13**) were identical (see *Scheme 4*). Investigation of the Br^-/NCS procedure for the synthesis of **3** from **13** has not led to as clean and rapid reaction as the one cited above. This observation suggests that, if the Br^-/NCS/2 AcONa method for generating BrCl *in situ* is preferable for cleavage of organoboranes, the Br^-/chloramine-T/aqueous HCl-solution method, is undoubtably better for rapid and clean cleavage of organomercurials by BrCl. Since bis-(glycosyl)mercury compounds can now be obtained by methoxy-mercuration of enolic sugar derivatives [16] this obviously extends the scope of the above bromination procedure.

Hydrostannylation-bromination. – In the context of medical studies, the *in vivo* stability of the labelled compounds is one of the main requirements. In this regard the most stable C,Hal-bond that a pharmaceutical can contain involves an sp^2-hybridized C-atom. This explains in part the increasing interest in synthesis of [^{18}F]fluoroaryl, [^{125}I]iodovinyl and [^{82}Br]bromovinyl derivatives of steroids [17–20]. In these latter examples, organoborane [18], organotin [19] and organomercurial [20] technologies have been successfully used in fast reactions with [^{125}I]ICl and -I^-/chloramine-T [18], [^{125}I]I_2 [19] and [^{82}Br]Br_2 [20] reagents. Recently, fast bromination of aryltin derivatives has been reported, using the [^{82}Br]Br^-/chloramine-T/HCl procedure, for the preferential cleavage of aryl,Sn-bond, when mixed tributylaryltin derivatives were used as precursors [21].

Prompted by this report, we have investigated the feasibility and stereochemical course of this procedure for the rapid synthesis of bromovinyl derivatives. For this purpose, the preparation of the precursor **16** from the acetylenic sugar **15** [22a] was carried out by reaction with five equivalents of tributyltinhydride in refluxing dioxane (101.5°, overnight). In the mixture of three products the (*E*)-vinyl-stannyl derivative **16** predominated and was purified by column chromatography. Anticipating the possible reaction of **17** with the BrCl reagent, **16** was reacted with 0.9 equivalent of Br^-/chloramine-T/aqueous HCl-solution giving in less than 3 min in a clean, specific cleavage of the C(sp^2),Sn-bond (see *Scheme 5*) the (*E*)-bromo-

Scheme 5



vinyl derivative **17**. After usual workup and column chromatography, **17** was isolated in pure form in 96% yield (with respect to the brominating reagent).

This procedure could have many useful extensions including the possible fast synthesis of (*E*)-5-(2-bromovinyl)-2′-deoxyuridine derivatives which are claimed to be useful in treatment of herpes [22b].

Conclusion. – The high speed of the reported reactions, along with the high yield of the halogenated products and the ease of workup and purification, all appear to justify further studies of *C*-metallated sugars as precursors for radiolabelling.

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Experimental Part

General. – NMR. spectra were run at 270 MHz using a home-built, pulse *Fourier* transform NMR. spectrometer. All chemical shifts are reported in ppm downfield from Me_4Si, coupling constants J in Hz. The mass spectra (*m/z*) were recorded at low resolution on a *Varian MAT Atlas CH4-B* or on a *AEI MS-50* mass spectrometer. The specific optical rotation ($[\alpha]_D$) values were obtained with a *Perkin-Elmer 241 MC* polarimeter.

Starting unsaturated carbohydrate derivatives were prepared as follows: **4** as previously reported [3]; **7** according to the published procedure [23]; in the same way, **5** was obtained in good yield by the action of AgF in pyridine on the 6-deoxy-6-iodo-glucofuranose derivative **A** [24]; **11** [25] was prepared in two steps from a stock of 3-*O*-acetyl-1,2-*O*-isopropylidene-5,6-di-*O*-methanesulfonyl-α-D-glucofuranose; **15** was obtained according to the published procedure [22a] and cleanly separated of its L-*glycero* epimer by column chromatography on silica gel with CH_2Cl_2/hexane/Et_2O 6:2:1. Before use, **4**, **5** and **11** were purified by recrystallization from CH_3OH, and **7** by sublimation.

Hydroborations. – Hydroborations were carried out as previously reported [3]. The *BH_3/THF-procedure* was used for the synthesis of 1 mmol of **1** from 792 mg of **4**, for 0.7 mmol of triglycosylborane derivative from 609 mg of **5**; and for 1 mmol of triglycosylborane derivative from 726 mg of **7**. The *dicyclohexylborane procedure* was used for the synthesis of 2 mmol of **2** from 528 mg of **4** , of 24 mmol of **2** from 6.34 g of **4**, and of 2 mmol of dicyclohexyl(glycosyl)borane derivative from 366 mg of **11**; the latter synthesis requires 4.4 mmol of dicyclohexylborane and slow addition of the solution of **11** in THF to avoid strong evolution of H_2.

Brominations of organoboranes. – *Bromide/*N*-chlorosuccinimide (NCS) procedure: Bromination of one group on boron from 1 mmol of* **1** *{or 2 mmol of* **2***}*. To the organoborane solution in THF, 1M aq. NaBr (1 ml {or 2 ml}) was added. The mixture was cooled to 0° and shielded from light. A 0.2M solution of NCS in THF/CH_3OH 1:1 (5 ml {or 10 ml}) was added and the mixture stirred 15 min at 0°. After pouring into 20 ml of H_2O, the mixture was extracted with 4 times 10 ml of Et_2O; the combined Et_2O layers were washed with 2 times 10 ml of H_2O and dried over anh. $MgSO_4$. Column chromatography on silica gel with Et_2O/hexane 2:1 yielded 260 mg (75%) of pure **3** {or 290 mg (42%) of **3** mixed with an unidentified carbohydrate-containing by-product}, which was identical to an authentic sample [3].

Methanolic sodium acetate/bromide/NCS procedure: Bromination of one group on boron from 1 mmol of **1** *{or 2 mmol of* **2***}*. To the organoborane solution in THF, 1M methanolic AcONa (2 ml {or 4 ml}), followed by 1 ml {or 2 ml} of 1M methanolic NaBr were added. The mixture was treated as above and yielded 260 mg (75%) {or 415 mg (60%)} of pure **3**.

*Preparation of 3,5-*O*-benzylidene-6-bromo-6-deoxy-1,2-*O*-isopropylidene-β-*L*-idofuranose* (**6**). The above methanolic AcONa/NaBr/NCS procedure was used for the bromination of 0.7 mmol of the triglycosylborane derivative of **5**. After the usual workup, column chromatography on silica gel with Et_2O/hexane 1:2 yielded 150 mg (58%) of pure **6**, m.p. 131–134°, $[\alpha]_D^{22} = -20.73°$ ($c = 0.5$, $CHCl_3$). – ^{1}H-NMR. ($CDCl_3$): 1.34 and 1.53 (2 *s*, each 3 H, CMe_2); 3.60 (*d*×*d*, $J(5,6) = 6.9$, $J_{gem} = 10.3$, 1 H, one H–C(6)); 3.68 (*d*×*d*, $J(5,6) = 6.6$, 1 H, the other H–C(6)); 4.24 (*t*×*d*, $J(4,5) = 1.6$, 1 H, H–C(5)); 4.28 (*t*, 1 H, H–C(4)); 4.44 (*d*, $J(3,4) = 1.7$, 1 H, H–C(3)); 4.65 (*d*, $J(1,2) = 3.5$, 1 H, H–C(2)); 5.51 (*s*, 1 H, PhC*H*); 6.01 (*d*, 1 H, H–C(1)); 7.35–7.51 (*m*, 5 H, *Ph*CH). – MS.: 129 (31), 113 (55), 107 (27), 105 (63), 100 (100), 85 (27), 77 (24), 43 (90), 42 (27), 41 (29), 32 (57).

$C_{16}H_{19}BrO_5$ Calc. C 51.77 H 5.16 Br 21.52% Found C 52.02 H 5.22 Br 21.56%

*Preparation of 6-bromo-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose* (**8**) *and 6-bromo-6-deoxy-1,2:3,4-di-*O*-isopropylidene-β-*L*-altropyranose* (**9**). The above methanolic AcONa/NaBr/NCS procedure was followed for the bromination of 1 mmol of the triglycosylborane derivative of **7**. The usual workup and column chromatography on silica gel with Et_2O/hexane 1:3 yielded 230 mg (71%) of **8**/**9** (59:41, by ^{1}H-NMR.), syrup. – ^{1}H-NMR. ($CDCl_3$): 1.27–1.47 (5 *s*, 12 H, 2 CMe_2); **8** (59%): 3.35 ($d\times d$, $J(5,6)=6.9$, $J_{gem}=10.1$, 1 H, one H–C(6)); 3.45 ($d\times d$, $J(5,6)=7.0$, 1 H, the other H–C(6)); 3.91 ($t\times d$, $J(4,5)=1.6$, 1 H, H–C(5)); 4.26 ($d\times d$, $J(1,2)=5.0$, $J(2,3)=2.4$, 1 H, H–C(2)); 4.31 ($d\times d$, $J(3,4)=7.8$, 1 H, H–C(4)); 4.57 ($d\times d$, 1 H, H–C(3)); 5.47 (*d*, 1 H, H–C(1)); **9** (41%): 3.32 ($d\times d\times d$, 1 H, H–C(5)); 3.42 ($d\times d$, $J(5,6)=6$, 1 H, one H–C(6)); 3.60 ($d\times d$, $J(5,6)=2.4$, $J_{gem}=10.9$, 1 H, the other H–C(6)); 4.05 ($d\times d$, $J(4,5)=9.3$, $J(3,4)=5.4$, 1 H, H–C(4)); 4.18 (*d*, 1 H, H–C(2)); 4.49 (*d*, 1 H, H–C(3)); 5.24 (*d*, $J(1,2)=2.3$, 1 H, H–C(1)). – MS.: 309 and 307 (each 16, M^+-Me), 113 (9), 100 (17), 85 (19), 81 (12), 71 (9), 59 (28), 57 (9), 43 (100), 41 (13), 32 (40).

$C_{12}H_{19}BrO_5$ Calc. C 44.60 H 5.93 Br 24.72% Found C 44.89 H 6.02 Br 24.66%

*Preparation of 6-bromo-5,6-dideoxy-1,2-*O*-isopropylidene-α-*D*-xylo-hexofuranose* (**12**). The above methanolic AcONa/NaBr/NCS procedure was followed for the bromination of 2 mmol of the dicyclohexyl(glycosyl)borane derivative of **11**. The usual workup and column chromatography on silica gel with Et_2O/hexane 1:1 yielded 480 mg (91%) of pure **12**, m.p. 98–100°, $[\alpha]_D^{23}=-1.03°$ ($c=1$, $CHCl_3$). – ^{1}H-NMR. ($CDCl_3$): 1.32 and 1.52 (2 *s*, each 3 H, CMe_2); 1.98 (br. *s*, 1 H, HO); 2.10–2.20 (*m*, 1 H, one H–C(5)); 2.26–2.39 (*m*, 1 H, the other H–C(5)); 3.47–3.62 (*m*, 2 H, 2 H–C(6)); 4.16 (*d*, $J(3,4)=2.5$, 1 H, H–C(3)); 4.32 ($d\times d\times d$, $J(4,5)=5.3$ and 7.9, 1 H, H–C(4)); 4.52 (*d*, $J(1,2)=3.7$, 1 H, H–C(2)); 5.90 (*d*, 1 H, H–C(1)). – MS.: 253 and 251 (each 13, M^+-Me), 71 (11), 59 (100), 57 (10), 55 (11), 43 (59), 41 (14), 32 (11), 29 (11), 28 (60).

$C_9H_{15}BrO_4$ Calc. C 40.47 H 5.66 Br 29.91% Found C 40.45 H 5.69 Br 29.79%

Iodination of organoboranes. – *Preparation of 3,5-*O*-benzylidene-6-deoxy-6-iodo-1,2-*O*-isopropylidene-β-*L*-idofuranose* (**10**). The procedure given in [26] was followed for the iodination of 0.7 mmol of the triglycosylborane derivative of **5**. The usual workup [3] and column chromatography on silica gel with Et_2O/hexane 1:2 yielded 210 mg (72%) of pure **10**, m.p. 157–159°, $[\alpha]_D^{22}=-36.77°$ ($c=1$, $CHCl_3$). – ^{1}H-NMR. ($CDCl_3$): 1.34 and 1.53 (2 *s*, each 3 H, CMe_2); 3.42 ($d\times d$, $J(5,6)=7.4$, $J_{gem}=10.2$, 1 H, one H–C(6)); 3.49 ($d\times d$, $J(5,6)=6.9$, 1 H, the other H–C(6)); 4.18 ($t\times d$, $J(4,5)=1.6$, 1 H, H–C(5)); 4.32 (*t*, 1 H, H–C(4)); 4.42 (*d*, $J(3,4)=1.8$, 1 H, H–C(3)); 4.65 (*d*, $J(1,2)=3.6$, 1 H, H–C(2)); 5.49 (*s*, 1 H, PhC*H*); 6.00 (*d*, 1 H, H–C(1)); 7.35–7.51 (*m*, 5 H, *Ph*CH). – MS.: 418 (19, M^+), 129 (27), 113 (73), 107 (19), 105 (54), 100 (100), 85 (19), 59 (23), 43 (92), 41 (23), 32 (96).

$C_{16}H_{19}IO_5$ Calc. C 45.95 H 4.58 I 30.34% Found C 46.14 H 4.54 I 30.19%

Mercuration of organoboranes. – *Preparation of bis(5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methanesulfonyl-α-*D*-xylo-hexofuranos-6-yl)mercury* (**13**). The hydroboration was carried out using the dicyclohexylborane procedure for the synthesis of 24 mmol of **2**. In this case, the reaction flask was previously equipped with a side flask attached by a short length of large-diameter flexible rubber tubing [5b]; in this side flask was placed 3.84 g (12 mmol) of $(AcO)_2Hg$. After the synthesis of **2** was completed, the $(AcO)_2Hg$ was added (still in inert atmosphere) from the attached side flask and stirring continued for 1.5 h at 25°. The mixture was poured into pentane (300 ml) at 0°, the syrupy precipitate decanted, washed with pentane (100 ml), dissolved in THF (50 ml) and filtered off through 20 g of silica gel. The silica gel was washed with THF (100 ml), and the combined THF-filtrates were concentrated and dried overnight to yield 6.24 g (71%) of pure **13**, m.p. 69–72°, $[\alpha]_D^{22}=-34.49°$ ($c=0.8$, $CHCl_3$). – ^{1}H-NMR. ($CDCl_3$): 0.86–1.24 (*m*, 2 H, 2 H–C(6)); 1.32 and 1.51 (2 *s*, each 3 H, CMe_2); 1.99–2.26 (*m*, 2 H, 2 H–C(5)); 3.08 (*s*, 3 H, SO_2CH_3); 4.15 ($d\times d\times d$, $J(3,4)=2.5$, $J(4,5)=5.5$ and 8.0, 1 H, H–C(4)); 4.77 (*d*, $J(1,2)=4.0$, 1 H, H–C(2)); 4.97 (*d*, 1 H, H–C(3)); 5.95 (*d*, 1 H, H–C(1)). – MS.: 265 (24), 207 (71), 155 (45), 113 (32), 111 (100), 83 (58), 69 (28), 59 (44), 57 (60), 55 (28), 43 (74), 28 (65).

$C_{20}H_{34}HgO_{12}S_2$ Calc. C 32.85 H 4.69% Found C 33.15 H 4.76%

*Preparation of (5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methanesulfonyl-α-*D*-xylo-hexofuranos-6-yl)-mercury chloride* (**14**). The hydroboration was carried out using the same equipment as above (see preparation of **13**) for the synthesis of 2 mmol of **2**. In the side flask was placed 640 mg (2 mmol) of

$(AcO)_2Hg$. The addition of $(AcO)_2Hg$ was followed by stirring at 25° for 0.5 h. The mixture was poured into 10 ml of cold H_2O and 1M aq. NaCl (2.5 ml) was added dropwise at 0°. The mixture was filtered, and the precipitate was washed with cold H_2O (10 ml) and cold Et_2O (10 ml) and dried overnight to yield 782 mg (78%) of pure **14**, m.p. 174–175°. – ^{1}H-NMR. ($(CD_3)_2SO$): 1.27 and 1.43 (2 *s*, each 3 H, CMe_2); 1.61–1.70 (*m*, 2 H, 2 H–C(6)); 1.94–2.02 (*m*, 2 H, 2 H–C(5)); 3.30 (*s*, 3 H, SO_2Me); 4.09 (*t*×*d*, *J*(3,4) = 2.5, *J*(4,5) = 6.5, 1 H, H–C(4)); 4.76 (*d*, *J*(1,2) = 3.9, 1 H, H–C(2)); 5.00 (*d*, 1 H, H–C(3)); 5.92 (*d*, 1 H, H–C(1)).

$C_{10}H_{17}ClHgO_6S$ Calc. C 23.96 H 3.42% Found C 23.72 H 3.40%

Our preliminary report [1a] includes the exper. details of the procedure of *bromination of organomercurial*, used for the conversion of **13** into **3** and **14**.

Hydrostannylation. – *Preparation of* (E)*-7,8-dideoxy-1,2:3,4-di*-O*-isopropylidene-8*-C*-tributylstannyl*-D-glycero-*α*-D-galacto-*oct-7-enopyranose* (**16**). A solution of **15** [22a] (390 mg, 1.37 mmol) in 1,4-dioxane (3 ml) was prepared under N_2. Tributyltinhydride (2.20 g, 7.56 mmol; 2 ml) was added and the mixture boiled under reflux (101.5°) overnight under N_2. At this time, the TLC. showed the total conversion of **15** into a mixture of 3 new products, in which the compound of highest polarity (**16**) was strongly dominant. After removing the solvent under reduced pressure, the crude mixture was chromatographed on a column silica gel with CH_2Cl_2/hexane/Et_2O 6:6:1. A first fraction (390 mg) still contained the 3 products, whereas the second fraction (330 mg) was pure **16**. Rechromatography of the first fraction gave additional 80 mg of pure **16** (52%, overall isolated yield), syrup, $[\alpha]_D^{23} = -36.08°$ (*c* = 1, $CHCl_3$). – ^{1}H-NMR. ($CDCl_3$): 0.77–1.54 (3 *m*, 39 H, 2 CMe_2 and 3 Bu); 2.81 (*d*, *J*(6,OH) = 7.0, 1 H, HO); 3.68 (*d*×*d*, *J*(4,5) = 1.7, *J*(5,6) = 6.5, 1 H, H–C(5)); 4.32 (*d*×*d*, *J*(1,2) = 5.0, *J*(2,3) = 2.3, 1 H, H–C(2)); 4.34 (*m*, 1 H, H–C(6)); 4.45 (*d*×*d*, *J*(3,4) = 8.0, 1 H, H–C(4)); 4.61 (*d*×*d*, 1 H, H–C(3)); 5.59 (*d*, 1 H, H–C(1)); 6.17 (*d*×*d*, *J*(6,7) = 4.4, *J*(7,8) = 19.2, 1 H, H–C(7)); 6.38 (*d*×*d*, *J*(6,8) = 1.4, 1 H, H–C(8)). – MS. (peaks below *m/z* 60 have not been considered): 519, 518, 517, 516, 515, 514 (25, 100, 43, 78, 32 and 42); 463, 462, 461, 460, 459, 458 (2, 11, 5, 12, 5 and 7); 387, 386, 385, 384, 383, 382 (2, 9, 3, 8, 3 and 5); 290, 289, 288, 287, 286, 285 (7, 27, 8, 18, 5 and 10); 252, 251, 250, 249, 248, 247 (11, 25, 10, 13, 2 and 8); 234, 233, 232, 231, 230, 229 (5, 21, 6, 16, 7 and 14); 178, 177, 176, 175, 174, 173 (8, 38, 13, 29, 9 and 15); 171 (17), 100 (26), 71 (41).

$C_{26}H_{48}O_6Sn$ Calc. C 54.28, H 8.41% Found C 54.21 H 8.52%

Bromination of *16*. – *Preparation of* (E)*-8*-C*-bromo-7,8-dideoxy-1,2:3,4-di*-O*-isopropylidene*-D-glycero-*α*-D-galacto-*oct-7-enopyranose* (**17**). To a solution of 325 mg of **16** (0.56 mmol) in THF (2.5 ml), 0.5 mmol of NaBr in H_2O (1 ml) was added. The mixture was cooled to 0° and shielded from light. Chloramine-T (282 mg, 1 mmol) in 1.5 ml of THF/H_2O 1:1 was added in 1 portion, and then 1.5 ml of 10% aq. HCl-solution, which had been saturated with NaCl, was added to the mixture. After 3 min of stirring at 0°, the mixture was poured into an aq. AcONa-solution (1M, 10 ml), extracted with Et_2O (3 times 5 ml), washed with H_2O (2 times 5 ml) and concentrated under reduced pressure. Column chromatography on silica gel with CH_2Cl_2/hexane/Et_2O 6:2:1 yielded 175 mg (96%) of pure **17**, m.p. 81–82°, $[\alpha]_D^{25} = -66.46°$ (*c* = 1.1, $CHCl_3$). – ^{1}H-NMR. ($CDCl_3$): 1.34, 1.36, 1.48 and 1.52 (4 *s*, each 3 H, 2 CMe_2); 2.85 (br. *s*, 1 H, HO); 3.67 (*d*×*d*, *J*(4,5) = 1.2, *J*(5,6) = 6.7, 1 H, H–C(5)); 4.34 (*d*×*d*, *J*(2,3) = 2.1, *J*(1,2) = 5.0, 1 H, H–C(2)); 4.35 (*m*, 1 H, H–C(6)); 4.44 (*d*×*d*, *J*(3,4) = 7.9, 1 H, H–C(4)); 4.64 (*d*×*d*, 1 H, H–C(3)); 5.57 (*d*, 1 H, H–C(1)); 6.38 (*d*×*d*, *J*(6,7) = 5.2, *J*(7,8) = 13.8, 1 H, H–C(7)); 6.50 (*d*×*d*, *J*(6,8) = 0.8, 1 H, H–C(8)). – MS.: 230 (15), 229 (20), 171 (28), 113 (15), 100 (34), 85 (22), 71 (100), 59 (43), 43 (85), 32 (20), 28 (89).

$C_{14}H_{21}BrO_6$ Calc. C 46.04 H 5.80 Br 21.88% Found C 46.21 H 5.85 Br 21.73%

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