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Simple Approach to *O*-Protected Deaminotunicaminyluracil[1]

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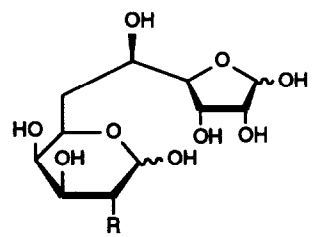
Abstract: A five-step synthesis of deaminotunicaminyluracil is presented. Coupling of the ylide, generated from the phosphonium salt **4**, with the aldehyde **5** afforded the undecose **6** in high yield. The key step in this synthesis was the hydroboration-oxidation reaction of the olefin **6**. For this purpose several hydroborating reagents were examined. The diborane-THF reagent led to the desired deaminotunicamine derivative **8**, as the predominant product. Condensation of undecose **8c** with 1,3-di-*O*-trimethylsilyluracil gave the title compound.

INTRODUCTION

In recent years a wide attention has been devoted to the synthesis of *C*-disaccharides[2], aimed at investigation of their role in glycobiology. Tunicamine **1a** being the undecose part of tunicamycins[3] can be consider as a *C*-disaccharide of an unusual structure. It consists of 6-deoxy-D-galactosamine, coupled through the C-6 atom with the C-5 atom of D-*allo*-pentofuranose. This eleven-carbon structure, together with the remarkable inhibitory effect of tunicamycins on the biosynthesis of polysaccharides and glycoproteins as well as their antitumour, antimicrobial and antifungal activities[3], becomes a major synthetic challenge.



1a: R=NH_2 (tunicamine)
1b: R=OH (deaminotunicamine)

Generally, two strategies leading to the synthesis of this undecose system have been reported. The first strategy is based on a semisynthetic approach involving either the elongation of D-ribose at the C-5 atom by cycloaddition with an appropriate diene[4], or the elongation of D-galactose at the C-6 atom by condensation with an appropriate 2-furan derivative[5].

The second strategy consists of direct junction of two readily available sugar units, so as to utilize fixed

chirality of both sugars for introduction of corresponding stereochemistry into the desired undecose. Consequently, the tactics require an efficient methodology for the construction of C-5—C-6 linkage, whereupon one hydroxy group of (*R*) configuration should be incorporated into the eleven-carbon molecule at C-5 in a stereoselective manner. With this goal in mind, Henry's nitroaldol condensation of two sugar units has been used to obtain a mixture of nitroproducts which after suitable transformation led to tunicamine[6]. According to a recently reported approach[7], tunicamine has been synthesized by temporary silicon-mediated reductive coupling of sugar aldehydes and sugar allylic alcohols[8].

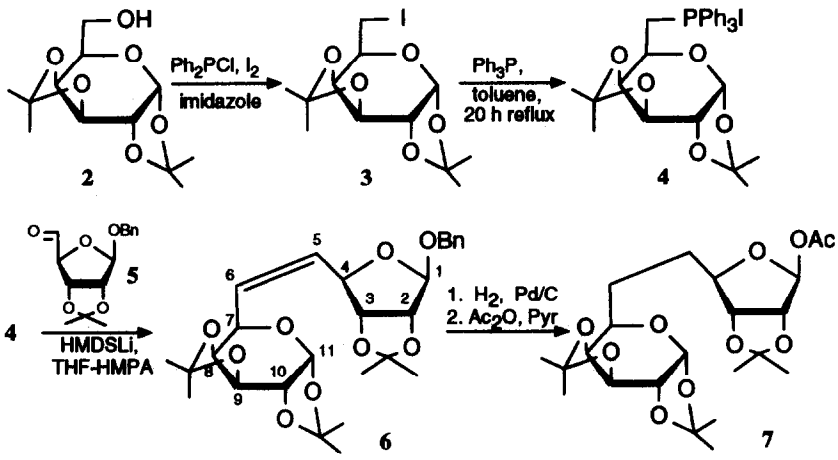
Surprisingly, the very attractive approach to tunicamine offered by the Wittig coupling reaction of the two sugar units "tail by tail", followed by hydration of the product, has not so far been examined.

The Wittig reaction was first applied by Secrist III *et al.*[9] in sugar chemistry for the generation of phosphonium ylides at the terminal carbon atom of furanoses and pyranoses has afforded the undecose analogue **6** as well as other unsaturated higher sugars. However, it has attracted very scant attention, perhaps due to the well-known[10] competing β-elimination process of the ylide derived from the phosphonium salt. So, Secrist's procedure when has been used for the synthesis of anamarine from D-glucose[11] afforded the Wittig condensation product in an only 35% yield. Therefore, modification of the Secrist procedure[9] for coupling of two sugar units was highly desirable.

RESULTS AND DISCUSSION

In order to link the phosphonium salt **4** with the aldehyde **5** by Wittig reaction we modified the procedure as follows: 1) the phosphonium salt **4** was prepared from the iodide **3** by refluxing in toluene instead of

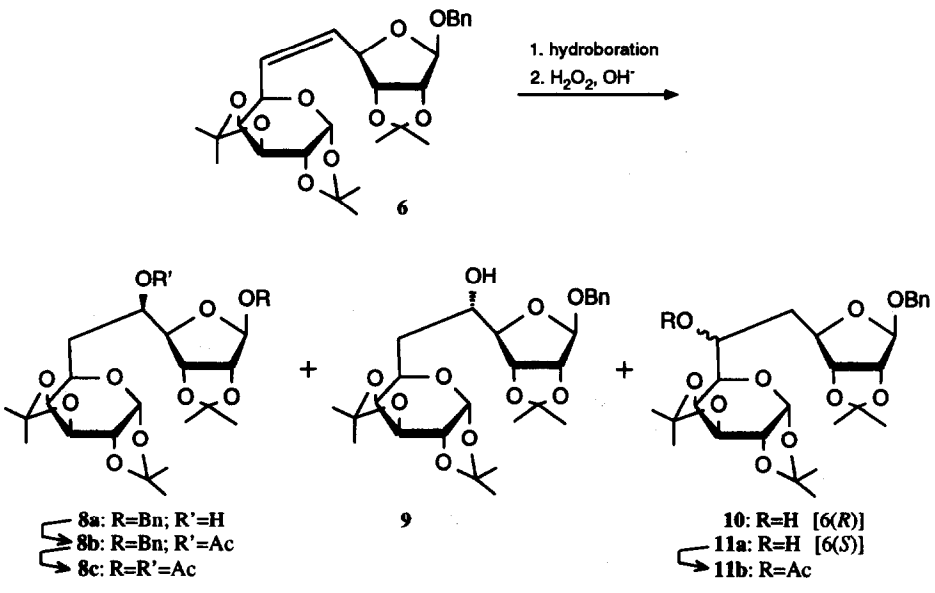
Scheme I



sulfolane[9] which allowed for direct isolation of **4** from the reaction mixture as a precipitate; 2) deprotonation of **4** was accomplished using the milder HMDSLi instead of BuLi; 3) the unstable ylide was generated in a mixture of the phosphonium salt **4** - aldehyde **5** in THF-HMPA, thus permitting the suppression of the β-elimination process. As a result, the condensation product **6** (Scheme I) was obtained in high yield, with complete stereoselectivity, forming C-5–C-6 *cis* linkage, as indicated by the coupling value $J_{5,6}$ 11.2 Hz. At atoms C-4 and C-7 of the undecose **6** the configuration of the appropriate chiral centers of the parent substrates **5** and **4** was preserved ($J_{4,3}$ < 0.5, $J_{8,7}$ 2.0 Hz). These data are in perfect agreement with those reported by Secrist[9] for the analogous undecose. The presence of the C-5–C-6 olefinic linkage in **6** makes it well suited to be functionalized in various ways. Thus, hydrogenation of **6** with Pd-C as a catalyst, followed by acetylation, afforded the corresponding 5,6-dideoxyundecose **7** (Scheme I) which, to our knowledge, is the first representative of such higher sugar.

Next, attention was turned to the hydroboration-oxidation reaction which should allow for direct introduction of one hydroxy group to the double bond of **6** (Scheme II). This reaction, to our knowledge, has never been examined in an analogous system.

Scheme II



Unlike the olefins that possess a stereodirecting allylic group capable of coordinating the approaching borane[12], or that have an evident allylic steric hindrance[13], the diastereoselection of the hydroboration of the unsubstituted *cis* olefin **6**, whose both vicinal centers seem to be equivalent, can hardly be predicted. So, in

order to find a system giving the highest stereocontrol, several hydroborating reagents *i.e.* 9-BBN, $ThBH_2$, $BH_3 \cdot Me_2S$, $BH_3 \cdot THF$ were examined. As shown in Table I, the olefin **6** failed to react with the large, sterically hindered 9-BBN reagent, even at elevated temperature. All other reagents reacted with **6** at low temperatures (-20 °C → +10 °C) to give, after oxidation with aqueous H_2O_2–NaOH, a mixture of three or four products, with one isomer predominating. The mixture was separated by chromatography to yield individual compounds in the form of alcohol or/and their *O*-acetyl derivatives.

Table I

HYDROBORATION CONDITIONS	PROPORTION OF ISOMERS (8+9+10+11=100%)			
	8 (5*R*)	**9** (5*S*)	**10** (6*R*)	**11** (6*S*)
$ThBH_2$, THF, -20° → 10 °C	33	0	22	45
$ThBH_2$, hexane, -20° → 10 °C	34	0	24	42
$BH_3 \cdot Me_2S$, THF, -5° → 10 °C	44	14	18	24
$BH_3 \cdot Me_2S$, THF, -20° → 10 °C	48	12	20	20
$BH_3 \cdot THF$, -20° → 10°C	47	9	22	22
$BH_3 \cdot THF$ (>10eq.), -20°→ 10°C	58	7	19	16
9-BBN, -5° → 40°C	0	0	0	0

The configuration of all compounds was elucidated on the basis of ^1H NMR spectra. Thus, the H-5 and H-6 protons of the two 5-OH epimers showed coupling constants $J_{5,6a}$ 2.6; $J_{5,6b}$ 9.9 Hz for **8** (R), being in full accord with the literature data[5], and $J_{5,6a}$ 6.3; $J_{5,6b}$ 8.3 Hz for **9** (S), whereas the coupling constants of the epimeric pair of 6-OH regioisomers were as follows: $J_{5a,6}$ 2.3; $J_{5b,6}$ 9.4 Hz for **10** (R), and $J_{5a,6}$ 5.5; $J_{5b,6}$ 7.0 Hz for **11** (S). These data, supported by X-ray analysis of **8c** (5R) and **10** (6R) regioisomers[14], allowed us to establish unambiguously the structure of all hydroboration-oxidation products.

The reaction mixture was contaminated by a low (~2%) amount of benzyl 5-*C*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*pyranos-6-yl)-2,3-*O*-isopropylidene-5-keto-α-D-*ribo*furanoside which was isolated and described.

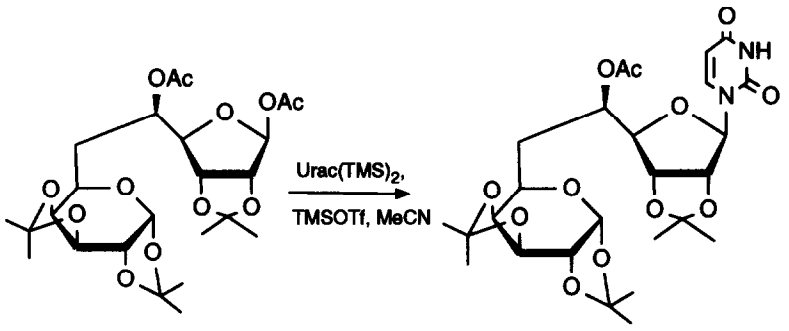
As shown in Table I, the stereochemical outcome of the hydroboration reaction was strongly dependent on the reagent employed and only slightly dependent on the reaction conditions. Thus, the reaction of **6** with

the sterically hindered $ThBH_2$ afforded the 6-OH regioisomer **11** as the main product, whereas the reaction with the sterically undemanding diborane led to the desired 5-OH regioisomer **8**; the "new" hydroxy group is in both cases located at the same face of the molecule. Diastereoface-selective addition to the substrate **6** (the ratio of sum **8+11**:**9+10** = 3.5:1 for $ThBH_2$ and 2:1 for BH_3·THF) seems to be consistent with hydroboration *via* the Kishi-Houk[13,15] model involving the addition of the borane to the less hindered face of the olefinic linkage.

The hydroboration of **6** by diborane, leading to deaminotunicamine **8**, is less stereoselective than that of $ThBH_2$, possibly on steric grounds. On the other hand, the additional stereocenters present in **6** impose a considerable steric bias on double bond addition. This bias manifests itself by preferable formation of the 5-OH regioisomer **8** upon application of diborane. In contrast, the use of thexylborane gives predominantly the 6-OH regioisomer **11**. The preponderating hydration of **6** at C-6 upon use of the $ThBH_2$ reagent is difficult to explain. However, when assuming steric demand of this reagent, the addition of boron at the C-6 atom of the double bond may be directed by initial coordination of boron to the acetal oxygens[16] in a suitably rigid conformation (due to 3,4-*O*-isopropylidene[5]) of the galactopyranose unit. Evidently, more experimental data for the estimation of these results are needed.

Condensation of **8c** with 1,3-di-*O*-trimethylsilyluracil (Scheme III) was accomplished in 56% yield, leading to the title compound **12**.

Scheme III



8c **12**

Although the stereoselectivity of the hydroboration step is *ca.* 3:2 in favour of the desired product **8**, the synthesis of the title compound in five steps from diacetonogalactose **2** is still attractive. Moreover, the method enables the simple preparation of modified analogues as it was demonstrated by the synthesis of dideoxyundecose **7** and isomer **11** 6(S).

EXPERIMENTAL

General methods. - Optical rotations were determined with a JASCO DIP-360 digital polarimeter. ^{1}H NMR spectra were recorded on BRUKER AM-500 (500 MHz) or on VARIAN AC-200 (200 MHz) spectrometers with Me_4Si as internal standard. High resolution mass spectra (HR-MS) were measured with AMD-604 mass spectrometer. IR spectra were recorded on Perkin-Elmer 1640 FT - IR spectrometer. Melting points were measured on Kofler hot stage and are uncorrected. Reactions were monitored by TLC on silica gel 60 F_{234} plates (Merck), and preparative chromatography was performed on silica gel G (Merck 230-400 mesh). Solvent composition was quoted as *v/v*. Proportions of the stereoisomers described in Table I were determined on Shimadzu C-R4A Chromatopac with UV spectrometric detector (wavelength 254 nm) using ET 250/8/4 Nucleosil® 100-7 analytical column (eluant hexane-ethyl acetate, 4:1).

6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-(triphenylphosphonio)-α-D-*galacto*pyranose Iodide (4). A solution of **3**[17] (3.2 g, 8.6 mmol) and PPh_3 (11.3 g, 43.0 mmol) in 30 mL of toluene was heated under argon atmosphere at 110 °C for 20 h. The precipitated product was filtered and washed with toluene, affording 5.6 g (89%) of **4**; mp 255-257 °C (lit.[9] 251-253 °C); $[\alpha]_D^{20}$ -22.2° (*c* 1.4, chloroform) [lit.[9] $[\alpha]_D^{25}$ -24.8° (*c* 2.8, chloroform)]; ^{1}H NMR (200 MHz): δ 1.06, 1.16, 1.37, 1.49 (4 s, 4 × 3 H, 2 iPr); 3.70 (dt, 1 H, H-6a); 4.19 (dd, 1 H, H-2); 4.35 (m, 1 H, H-5); 4.62 (bd, 1 H, H-3); 4.74 (bd, 1 H, H-4); 4.95 (dt, 1 H, H-6b); 5.21 (d, 1 H, H-1); 7.57-7.94 (m, 15 H, arom.); $J_{1,2}$ 5.1, $J_{2,3}$ 2.3, $J_{3,4}$ 6.5, $J_{6a,5}$ 10.9, $J_{6a,6b}$ 15.6, $J_{6a,P}$ 10.9, $J_{6b,P}$ 15.3 Hz.

Benzyl 2,3-*O*-isopropylidene-β-D-*ribo*-pentodialdo-1,4-furanoside (5). - Simply prepared from D-ribose on the following way: to 14.4 g (96 mmol) of D-ribose in acetone (150 mL) was added 0.5 mL conc. H_2SO_4. The mixture was stirred for 2 h at room temperature. After addition of benzyl alcohol (30 mL) and benzene (50 mL) the mixture was evaporated *in vacuo*. The residue containing BnOH was stirred for additional 3 h. Sulfuric acid was neutralized with triethylamine, the mixture diluted with $CHCl_3$ (100 mL) and consequently washed with water, aq. HCl (0.1 N), water, aq. $NaHCO_3$, water, and dried over $MgSO_4$. Chloroform was evaporated under reduced pressure, and benzyl alcohol was distilled off under high *vacuo*. The residue was dissolved in Et_2O and left for crystallization giving fine needles of *benzyl 2,3-*O*-isopropylidene*-β-D-ribo*furanoside* (11.2 g, 42% yield); mp 102-104 °C (lit.[18] 104-105 °C); $[\alpha]_D^{20}$ -75.8° (*c* 1.8, chloroform); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.32, 1.48 (2 s, 2 × 3 H, iPr); 3.55-3.78 (m, 2 H, H-5a, H-5b); 4.44 (t, 1 H, H-4); 4.57 and 4.77 (ABq, 2 H, OCH_2Ph, *J* 11.7 Hz); 4.66 and 4.86 (2 d, 2 H, H-2, H-3); 5.18 (s, 1 H, H-1); 7.30-7.36 (m, 5 H, arom.); $J_{2,3}$ 6.0, $J_{4,5a} = J_{4,5b}$ 3.0 Hz.

The Swern oxidation of this compound leading to **5** was performed as follows: to a solution of oxalyl chloride (1.5 mL, 17.5 mmol) in CH_2Cl_2 (50 mL) was dropwise added DMSO (2.5 mL, 35 mmol) in CH_2Cl_2 (10 mL) at -78 °C. After the bubbling was subsided, *benzyl 2,3-*O*-isopropylidene*-β-D-ribo*furanoside* (3 g, 10.7 mmol) in 10 mL CH_2Cl_2 was added. The mixture was warmed up to -10 °C and triethylamine (10 mL)

was added. After 15 min the reaction was diluted with $CHCl_3$ and washed with aq. HCl (0.1 N), H_2O, aq. $NaHCO_3$, H_2O, and dried over $MgSO_4$. Evaporation of the solvent and filtration through silica gel (hexane-ethyl acetate, 3:1) afforded 2.7 g of **5**. The crude aldehyde, thus obtained was used for the Wittig reaction.

(*Z*)-1-(Benzyl 2,3-*O*-isopropylidene-β-D-*ribo*-tetrafuranosid-4-yl)-2-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-pentopyranos-5-yl)ethylene (6). - A solution of phosphonium salt **4** (1.00 g, 1.58 mmol) and aldehyde **5** (0.66 g, 2.37 mmol) in 24 mL THF-HMPA (5:1) under argon atmosphere was cooled to -70 °C while lithium bis(trimethylsilyl)amide (1.6 mL, 1 M solution in hexane) was added. The solution was warmed up to -10 °C within 1 h and quenched with saturated aq. NH_4Cl. The mixture was stirred at room temperature for 1 h, then extracted with diethyl ether. Combined ether extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure to give a syrup, which was subjected to chromatography on silica gel. Elution with hexane-ethyl acetate (4:1) gave 576 mg (70%) of **6** as a colorless syrup, $[\alpha]_D^{20}$ -63.0° (*c* 1.5, chloroform); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.29, 1.33, 1.35, 1.46, 1.47, 1.59 (6 s, 6 × 3 H, 3 iPr); 4.33 (dd, 1 H, H-10); 4.34 (dd, 1 H, H-8); 4.40 and 4.70 (ABq, 2 H, OC*H*$_2$Ph, *J* 11.6 Hz); 4.63 (dd, 1 H, H-9); 4.68-4.73 (m, 3 H, H-7, H-3, H-2); 4.97 (dd, 1 H, H-4); 5.15 (s, 1 H, H-1); 5.57 (d, 1 H, H-11); 5.72-5.79 (m, 2 H, H-6, H-5); 7.27-7.35 (m, 5 H, arom.); ^{1}H NMR (500 MHz, C_6D_6): δ 1.14, 1.47, 1.36, 1.48, 1.51, 1.55 (6 s, 6 × 3 H, 3 iPr); 4.16 (dd, 1 H, H-8); 4.18 (dd, 1 H, H-10); 4.26 and 4.72 (ABq, 2 H, OC*H*$_2$Ph, *J* 11.6 Hz); 4.50 (dd, 1 H, H-9); 4.53 (bd, 1 H, H-3); 4.64 (d, 1 H, H-2); 4.93 (~d, 1 H, H-7); 5.32 (s, 1 H, H-1); 5.35 (~d, 1 H, H-4); 5.55 (1 H, d, H-11); 5.79 (ddd, 1 H, H-5); 6.02 (ddd, 1 H, H-6); $J_{2,3}$ 5.9, $J_{4,3}$ < 0.5, $J_{5,4}$ 9.1, $J_{5,6}$ 11.2, $J_{5,7}$ 1.3, $J_{6,4}$ 1.4, $J_{6,7}$ 7.9, $J_{8,7}$ 2.0, $J_{8,9}$ 7.9, $J_{9,10}$ 2.4, $J_{10,11}$ 5.1 Hz. HR-MS/EI: $C_{26}H_{33}O_9$ $(M\text{-}CH_3)^+$. Calc.: 489.2125. Found: 489.2125.

1-*O*-Acetyl-5-deoxy-5-*C*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*pyranos-6-yl)-2,3-*O*-isopropylidene-β-D-*ribo*-pentofuranose (7). - To a solution of **6** (60 mg, 0.119 mmol) in EtOH (96%, 10 mL) Pd-C catalyst (10%, 30 mg) was added and the mixture was stirred under hydrogen for 24 h. The mixture was filtered through Celite and co-evaporated with toluene *in vacuo* to dryness. The residue was acetylated in Ac_2O-Py for 2 h. Excess of acetic anhydride and pyridine were co-evaporated with toluene *in vacuo*. The crude product was filtered through silica gel using hexane - ethyl acetate (3:1) as eluant, to give **7** as a colorless syrup (49 mg, 90%), $[\alpha]_D^{20}$ -61.4° (*c* 1.0, chloroform); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.31, 1.32, 1.34, 1.43, 1.47, 1.51 (6 s, 6 × 3 H, 3 iPr); 1.51-1.88 (m, 4 H, H-5a, H-5b, H-6a, H-6b); 2.04 (s, 3 H, OAc); 3.75 (ddd, 1 H, H-7); 4.10 (dd, 1 H, H-8); 4.28 (dd, 1 H, H-10); 4.35 (dd, 1 H, H-4); 4.57 (dd, 1 H, H-9), 4.59 (d, 1 H, H-3); 4.71 (d, 1 H, H-2); 5.51 (d, 1 H, H-11); 6.16 (s, 1 H, H-1); $J_{2,3}$ 5.9, $J_{4,5a}$ 10.8, $J_{4,5b}$ 5.2, $J_{7,6a}$ 3.5, $J_{7,6b}$ 9.8, $J_{8,7}$ 1.8, $J_{8,9}$ 7.9, $J_{9,10}$ 2.3, $J_{10,11}$ 5.1 Hz. HR-MS/EI: $C_{21}H_{31}O_{10}$ $(M\text{-}CH_3)^+$. Calc.: 443.1917. Found: 443.1921.

Hydroboration of *(Z)-1-(benzyl 2,3-O-isopropylidene-β-D-ribo-tetrafuranosid-4-yl)-2-(1,2:3,4-di-O-isopropylidene-α-D-galacto-pentopyranos-5-yl)ethylene* (6). - To a solution of **6** (505 mg, 1 mmol) in dry THF (20 mL) was added dropwise BH_3·THF (1.2 M in THF, 12 mmol) at -20 °C under argon atmosphere.

The mixture was allowed to warm up to 10 °C within 0.5 h. Excess of diborane was decomposed by the addition of MeOH. The resulting mixture was treated with aq. NaOH (3 mL, 25% solution) and H_2O_2 (3 mL, 40% aq. solution) at room temperature. After 2 h the mixture was neutralized with aq. NH_4Cl, extracted with diethyl ether, dried ($MgSO_4$) and concentrated *in vacuo* to a syrup. Chromatography (hexane - ethyl acetate, 2:1) on silica gel gave four fractions in the ratio *ca.* 1:4:29:9.

Benzyl 5-*C*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*pyranos-6-yl)-2,3-*O*-isopropylidene-5-keto-α-D-*ribo*-furanoside. - Eluted as the first fraction (8.4 mg, 2%), syrup, $[\alpha]_D^{20}$ -86.8° (*c* 0.3, chloroform); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.31, 1.32, 1.32, 1.44, 1.46, 1.57 (6 s, 6 × 3 H, 3 iPr); 2.92 (dd, 1 H, H-6a); 2.99 (dd, 1 H, H-6b); 4.20 (dd, 1 H, H-8); 4.29 (dd, 1 H, H-10); 4.37 (m, 1 H, H-7); 4.53 and 4.80 (ABq, 2 H, OCH_2Ph, *J* 12.1 Hz); 4.57 (d, 1 H, H-2); 4.61 (dd, 1 H, H-9); 4.63 (bs, 1 H, H-4); 5.18 (s, 1 H, H-1); 5.29 (dd, 1 H, H-3); 5.45 (d, 1 H, H-11); 7.25-7.40 (m, 5 H, arom.); $J_{2,3}$ 5.9, $J_{3,4}$ 0.9, $J_{6a,6b}$ 17.2, $J_{6a,7}$ 6.2, $J_{6b,7}$ 7.6, $J_{8,7}$ 2.0, $J_{8,9}$ 7.9, $J_{9,10}$ 2.5, $J_{10,11}$ 5.1 Hz. IR (film) 1721 cm^{-1} (C=O). HR-MS/EI: $C_{26}H_{33}O_{10}$ $(M\text{-}CH_3)^+$. Calc.: 505.2074. Found: 505.2075.

Benzyl 5-*O*-acetyl-5-*C*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*pyranos-6-yl)-2,3-*O*-isopropylidene-α-L-*talo*-pentofuranoside (9). - Eluted as the second fraction, syrup (36 mg, 7%), $[\alpha]_D^{20}$ -85.5° (*c* 1.0, chloroform); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.31, 1.32, 1.35, 1.46, 1.46, 1.50 (6 s, 6 × 3 H, 3 iPr); 1.72 (dt, 1 H, H-6a); 2.03 (m, 1 H, H-6b); 3.30 (broad signal, 1 H, OH); 3.78-3.84 (m, 1 H, H-5); 3.97 (ddd, 1 H, H-7); 4.19 (dd, 1 H, H-8); 4.30 (dd, 1 H, H-10); 4.50 (d, 1 H, H-4); 4.55 and 4.79 (ABq, 2 H, OCH_2Ph, *J* 11.6 Hz); 4.60 (dd, 1 H, H-9); 4.66 (d, 1 H, H-3); 4.86 (d, 1 H, H-2); 5.17 (s, 1 H, H-1); 5.51 (d, 1 H, H-11); 7.28-7.37 (m, 5 H, arom.); $J_{2,3}$ 6.0, $J_{4,5}$ 2.9, $J_{6a,5}$ 6.3, $J_{6a,6b}$ 13.8, $J_{6a,7}$ 6.3, $J_{6b,5}$=$J_{6b,7}$ 8.3, $J_{8,7}$ 1.8, $J_{8,9}$ 7.9, $J_{9,10}$ 2.4, $J_{10,11}$ 5.1 Hz. HR-MS/EI: $C_{26}H_{35}O_{10}$ $(M\text{-}CH_3)^+$. Calc.: 507.2230. Found: 507.2228.

The third fraction eluted (285 mg), being a mixture of **8a** and **11a**, was acetylated by the use of Ac_2O-Py-DMAP. Separation by chromatography (hexane - ethyl acetate, 3:1) gave (in order of elution):

Benzyl 5-*O*-acetyl-5-*C*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*pyranos-6-yl)-2,3-*O*-isopropylidene-β-D-*allo*-pentofuranoside (8b). - 244 mg (43% yield from **6**); crystallized from ethanol, mp 112-114 °C; $[\alpha]_D^{20}$ -112.6° (*c* 1.1, chloroform); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.30, 1.33, 1.38, 1.46, 1.46, 1.56 (6 s, 6 × 3 H, 3 iPr); 1.69 (ddd, 1 H, H-6a); 1.98 (s, 3 H, OAc); 2.32 (ddd, 1 H, H-6b); 3.77 (dt, 1 H, H-7); 4.07 (dd, 1 H, H-8); 4.17 (dd, 1 H, H-4); 4.26 (dd, 1 H, H-10); 4.41 and 4.77 (ABq, 2 H, OCH_2Ph, *J* 12.0 Hz); 4.57 (dd, 1 H, H-9); 4.66 (d, 1 H, H-2); 4.79 (dd, 1 H, H-3); 5.12 (s, 1 H, H-1); 5.35 (ddd, 1 H, H-5); 5.44 (d, 1 H, H-11); 7.27-7.40 (m, 5 H, arom.); $J_{2,3}$ 6.0, $J_{3,4}$ 1.0, $J_{4,5}$ 7.6, $J_{5,6a}$ 9.9, $J_{5,6b}$ 2.6, $J_{6a,6b}$ 13.2, $J_{6a,7}$ 2.6, $J_{6b,7}$ 10.6, $J_{8,7}$ 1.9, $J_{8,9}$ 7.9, $J_{9,10}$ 2.4, $J_{10,11}$ 5.2 Hz. HR-MS/EI: $C_{28}H_{37}O_{11}$ $(M\text{-}CH_3)^+$. Calc.: 549.2336. Found: 549.2329.

Benzyl 5-*C*-(6-*O*-acetyl-1,2:3,4-di-*O*-isopropylidene-L-*glycero*-α-D-*galacto*pyranos-6-yl)-5-deoxy--2,3-*O*-isopropylidene-α-D-*ribo*furanoside (11b). - Isolated as a syrup (79 mg, 15%); $[\alpha]_D^{20}$ -86.4° (*c* 1.0, chloroform); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.26, 1.31, 1.33, 1.44, 1.46, 1.53 (6 s, 6 × 3 H, 3 iPr); 1.94-2.03

(m, 1 H, H-5a); 2.07 (s, 3 H, OAc); 1.94-2.03 (m, 1 H, H-5b); 3.90 (dd, 1 H, H-7); 4.23 (dd, 1 H, H-8); 4.29 (dd, 1 H, H-10); 4.38 (dd, 1 H, H-4); 4.48 and 4.79 (AB, 2 H, OCH_2Ph, *J* 11.8 Hz); 4.52 (dd, 1 H, H-9); 4.62 (dd, 1 H, H-3); 4.71 (d, 1 H, H-2); 5.15 (s, 1 H, H-1); 5.39 (m, 1 H, H-6); 5.55 (d, 1 H, H-11); 7.28-7.35 (m, 5 H, arom.); $J_{2,3}$ 6.0, $J_{3,4}$ 0.8, $J_{4,5ab}$ 6.6 and 8.5, $J_{6,5ab}$ 5.5 and 7.0, $J_{6,7}$ 6.5, $J_{7,8}$ 1.6, $J_{8,9}$ 7.9, $J_{9,10}$ 2.3, $J_{10,11}$ 5.1 Hz. HR-MS/EI: $C_{28}H_{37}O_{11}$ $(M\text{-}CH_3)^+$. Calc.: 549.2336. Found: 549.2334.

Benzyl 5-*C*-(6-*O*-acetyl-1,2:3,4-di-*O*-isopropylidene-D-*glycero*-α-D-*galacto*pyranos-6-yl)-5-deoxy-2,3-*O*-isopropylidene-α-D-*ribo*furanoside (10). - Eluted as the fourth fraction, crystals (from ethanol) (72 mg, 13%), mp 157 °C; $[\alpha]_D^{20}$ -58.5° (*c* 1.0, chloroform); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.31, 1.31, 1.35, 1.41, 1.47, 1.49 (6 s, 6 × 3 H, 3 iPr); 1.67-1.74 (m, 1 H, H-5a); 2.15-2.23 (m, 1 H, H-5b); 2.55 (broad signal, 1 H, OH); 3.60 (dd, 1 H, H-7); 4.12 (m, 1 H, H-6); 4.30 (dd, 1 H, H-10); 4.43 and 4.75 (ABq, 2 H, OCH_2Ph, *J* 11.8 Hz); 4.46 (dd, 1 H, H-8); 4.58 (ddd, 1 H, H-4); 4.62 (dd, 1 H, H-9); 4.68 (dd, 1 H, H-3); 4.71 (d, 1 H, H-2); 5.16 (s, 1 H, H-1); 5.43 (d, 1 H, H-11); 7.29-7.33 (m, 5 H, arom.); $J_{2,3}$ 6.0, $J_{3,4}$ 0.8, $J_{4,5a}$ 4.0, $J_{4,5b}$ 11.0, $J_{5a,5b}$ 13.6, $J_{5a,6}$ 9.4, $J_{5b,6}$ 2.3, $J_{7,6}$ 8.5, $J_{7,8}$ 2.0, $J_{8,9}$ 7.9, $J_{9,10}$ 2.5, $J_{10,11}$ 5.1 Hz. HR-MS/EI: $C_{26}H_{35}O_{10}$ $(M\text{-}CH_3)^+$. Calc.: 507.2230. Found: 507.2228.

1,5-Di-*O*-acetyl-5-*C*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*pyranos-6-yl)-2,3-*O*-isopropylidene-β-D-*allo*-pentofuranose (8c). - Hydrogenation of **8b** (80 mg, 0.142 mmol) in EtOH (10 mL) was carried out as described for the conversion of **6** → **7**, yielded **8c** (61 mg, 83%); mp 194-195 °C (crystallization from diethyl ether); $[\alpha]_D^{20}$ -69.1° (*c* 1.0, chloroform); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.30, 1.31, 1.32, 1.42, 1.46, 1.47 (6 s, 6 × 3 H, 3 iPr); 1.57-1.63 (m, 1 H, H-6a); 2.07, 2.10 (2 s, 2 × 3 H, 2 OAc); 2.19 (ddd, 1 H, H-6b); 3.73 (dt, 1 H, H-7); 4.04 (dd, 1 H, H-8); 4.16 (bd, 1 H, H-4); 4.28 (dd, 1 H, H-10); 4.57 (dd, 1 H, H-9); 4.70 (d, 1 H, H-2); 4.75 (bd, 1 H, H-3); 5.20 (ddd, 1 H, H-5); 5.47 (d, 1 H, H-11); 6.17 (s, 1 H, H-1); $J_{2,3}$ 5.9, $J_{3,4}$ < 0.5, $J_{5,4}$ 9.0, $J_{5,6a}$ 10.2, $J_{5,6b}$ 2.6, $J_{6a,7}$ 2.1, $J_{6b,6a}$ 15.1, $J_{6b,7}$ 10.9, $J_{8,7}$ 2.0, $J_{8,9}$ 7.8, $J_{9,10}$ 2.3, $J_{10,11}$ 5.2 Hz. HR-MS/EI: $C_{23}H_{33}O_{12}$ $(M\text{-}CH_3)^+$. Calc.: 501.1972. Found: 501.1973.

1-[5-*O*-Acetyl-5-*C*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*pyranos-6-yl)-2,3-*O*-isopropylidene-β-D-*allo*-pentofuranoside]uracil (12). - A mixture of uracil (22 mg, 0.205 mmol) and hexamethylenedisilane (3 mL) was stirred at 130 °C under argon. After 3 h of heating, anhydrous toluene (10 mL) was added and the reaction was concentrated *in vacuo*. The residue, dissolved in dry MeCN (5 mL), was treated with a solution of the substrate **8c** (50 mg, 0.097 mmol in 1 mL of MeCN), then TMSOTf (36 µL, 0.198 mmol) in MeCN (1 mL) was slowly added at -20 °C under argon. After 1 h the temperature was raised to 40 °C, and heating was continued for 2 h. The mixture was concentrated under reduced pressure. Chromatography (hexane - ethyl acetate, 2:1) of the residue, afforded **12** (31 mg, 56%) as an amorphous powder; $[\alpha]_D^{20}$ -58.7° (*c* 1.0, chloroform); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.32, 1.32, 1.34, 1.43, 1.46, 1.51 (6 s, 6 × 3 H, 3 iPr); 1.72 (ddd, 1 H, H-6a); 2.03-2.08 (m, 1 H, H-6b); 3.89 (dt, 1 H, H-7); 4.08 (dd, 1 H, H-8); 4.29 (dd, 1 H, H-10); 4.47 (bd, 1 H, H-4); 4.59 (dd, 1 H, H-9); 4.83 (dd, 1 H, H-3); 4.90 (dd, 1 H, H-2); 5.17 (dt, 1 H, H-5); 5.51 (dd, 1 H, H-11); 5.70 (dd, 1 H, H-5'); 6.06 (d, 1 H, H-1); 7.46 (d, 1 H, H-6');

8.51 (broad signal, 1 H, NH); $J_{1,2}$ 4.3; $J_{2,3}$ 5.9; $J_{3,4}$ 1.0; $J_{4,5}$ 4.5; $J_{5,6a}$ 7.5; $J_{5,6b}$ 4.7; $J_{6a,6b}$ 14.8; $J_{6a,7}$ 2.3; $J_{7,6b}$ 10.4; $J_{8,7}$ 1.9; $J_{8,9}$ 7.8; $J_{9,10}$ 2.2; $J_{10,11}$ 5.1; $J_{5',6'}$ 8.2 Hz. HR-MS/EI: $C_{25}H_{33}N_2O_{12}$ $(M\text{-}CH_3)^+$. Calc.: 553.2033. Found: 553.2035.

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