Indium-Promoted Barbier-Type Allylations in Aqueous Media: New Access to 2-*C*- and 4-*C*-Branched Sugars

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Abstract: Indium-promoted Barbier-type allylations in aqueous media of 2-bromo-4-enopyranoside (**3**) and 4-bromo-2-enopyranosides (**2β**, **6α** and **6β**) provide a new access to different 2-*C*-branched sugars (**7**, **11**, **13**) and 4-*C*-branched sugar (**18**). Moreover, apart from the synthesis and characterization of these *C*-branched sugars, mechanistic aspects of these reactions are discussed.

Keywords: aqueous media; Barbier reaction; *C*-branched sugar; C-C coupling; indium

Introduction

During the last years, a number of metal-promoted coupling reactions in aqueous media has been developed.[1] Among them, indium-mediated organometallic reactions have elicited considerable interest.[2] In particular, the reaction of carbonyl compounds with allyl bromide and indium in water has been extensively examined because of its synthetic advantages. Indeed, indium is considered to be particularly effective because the reaction requires no activation and produces few side products.

In fact, water is now recognized as an attractive medium for many organic reactions but curiously, for the most part, recent sugar chemistry stays away from this development of organic synthesis in water.[3] Despite that, however, some papers report the coupling of unprotected sugars with malonate-derived nucleophiles such as barbituric derivatives,[4] Meldrum's acid[5] or pentane-2,4-dione,[6] or with Wittig-type reagents.[7] In the organometallic chemistry area, there also have been some examples of applications of the Barbier–Grignard reaction in aqueous medium to carbohydrate synthesis through the use of tin or indium. Generally, these metal-mediated allylations were applied to elongation of the carbon chain of carbohydrates, followed by conversions to higher carbon sugars after suitable derivatization.[8]

Recently, we reported a convenient protocol for the preparation of 2-*C*-branched sugars and *C*-disaccharides *via* indium-promoted Barbier-type allylations in aqueous media[9] starting from the α-anomer of **2**.

Because *C*-branched sugars are of current interest in carbohydrate chemistry,[10] we now describe an extension of this methodology to other bromoenopyranosides in order to obtain a wider range of *C*-branched sugars. In addition to the obvious applications in carbohydrate synthesis, especially a new access to C-4-branched sugars, our results contribute interesting stereochemical information about the indium allylation reactions.

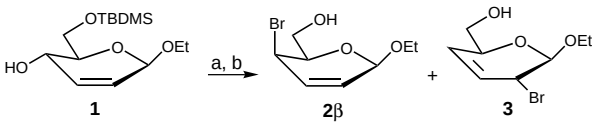
Results and Discussion

First, we started from the β-D-*erythro*-hex-2-enopyranoside **1**.[11] After inversion of the 4-hydroxy group under standard bromination conditions (triphenylphosphine, carbon tetrabromide) and then treatment with tetrabutylammoniun fluoride, we obtained in 77% overall yield the expected 4-bromo-2-enopyranoside **2β** and, surprisingly, the 2-bromo-4-enopyranoside **3** in a 1/1 ratio (Scheme 1).

Indeed, this $S_{N'}$ process leading to **3** was not observed when starting from the corresponding α-anomer of **2**. In this case, the same conditions led to the clean inversion at C-4.[9]

Then we tested the reactions with benzaldehyde under indium-promoted Barbier-type conditions. All the results are summarized in Table 1.

In the case of **2β**, the reaction, which took place in H_2O/EtOH (1:2) at 50 °C in 12 h, gave **7** in 45% yield as a unique stereoisomer as a result of complete regio- and



Scheme 1. (a) CBr_4, $(C_6H_5)_3P$, CH_2Cl_2; (b) $(C_4H_9)N^+F^-$, THF; (overall yield 77%, **2β/3** = 1/1).

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Table 1.

Entry	Reactants[a]	Products	Cond.[b]	Yield[c] [%]	Ratio[d]
1	**2b**	**7**	12; 50 °C	45	
2	**3**	**11, 13**	7; RT	60	**11/13** : 1/1
3	**6a**	**11, 18**	5; RT	70	**11/18** : 1/4.5
4	**6b**	**13**	1; RT	22	

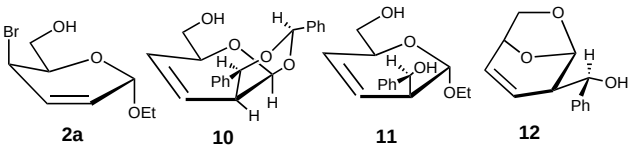
[a] C_6H_5CHO (3 equiv.), In (3 equiv.), solvent system: H_2O/EtOH (1/2).
[b] Conditions: reaction time (h); temperature (°C).
[c] Isolated yields.
[d] Diastereomeric ratio calculated by ^1H and ^{13}C NMR.

diastereoselectivities (Table 1, entry 1). The structure of **7** was deduced from spectral analysis. The ^1H NMR spectrum notably exhibits a doublet ($J_{1,2} = 2.9$ Hz) for the H-1 signal, indicating axial alkylation at C-2.[12] Furthermore, the presence of a 3,4-double bond was supported by the observation of allylic coupling between H-3 and H-5. These data indicate clearly that alkylation occurred at the γ position with a *syn* stereochemistry relative to the bromine atom. This implies the stereospecific formation of the allyl-indium intermediate with retention of stereochemistry followed by a six-membered cyclic transition state between the allyl-indium and the carbonyl compound.

For determining the configuration of the second new stereogenic center at the C-7 position, we tried to introduce a benzylidene group onto the C-1 and C-7 hydroxy groups as shown in Scheme 2.

However, under the usual conditions (benzaldehyde, zinc chloride), the 2-*C*-compound **7** did not give the expected benzylidene derivative **8** but only the unsaturated 2-*C*-anhydro-derivative **9** obtained in a poor yield (10%) after 12 h at 30 °C. In fact, these results suggest that the bulky phenyl substituent experiences severe steric interactions during the formation of the benzylidene ring.

With regard to these results and our previous report,[9] in which we have been able to prepare easily the benzylidene derivative **10** along with the anhydro derivative **12** from **11** without special problems, the configuration of the second new stereogenic center at the C-7 position of compounds **7** and **9** were deduced to be (*R*). Indeed, in these compounds **7** and **9**, the coupling constant $J_{2,7}$ were respectively 3.4 and 4.4 Hz instead of 7.3 and 6.8 Hz in the corresponding derivatives **11** and **12** in which we have unambiguously proved the *S* configuration at C-7.[9]



From a mechanistic point of view, the stereochemistry at C-7 can be explained by the formation of a six-membered cyclic transition state between the carbonyl compound and the allyl-indium sugar moiety in which the phenyl group is in axial position as depicted in Figure 1. Indeed, models showed clearly an unfavourable steric interaction between the phenyl substituent in the equatorial position and the β-ethoxy group. In the case of the α-anomer,[9] the reaction gave only one diastereoisomer which results from a similar transition state but where the phenyl group is in the equatorial position. Moreover, in the present case, the location of the phenyl group in the axial position could rationalize the moderate yield obtained in the allylation reaction (45%).

Then in a second attempt, the reaction was tried with the 2-bromo-4-enopyranoside **3** as depicted in Scheme 3.

In this case (Table 1, entry 2), we obtained after 7 h at room temperature, in 65% total yield, a mixture in a 6/6/1 ratio of the C-2 axial product **11** that we previously obtained from **2α**,[9] the new C-2 equatorial adduct **13** and the known aldehyde **14**.[13]

In the ^1H NMR spectrum of **13**, the presence of a doublet at $\delta = 4.82$ for H-1 with a coupling constant $J_{1,2}$

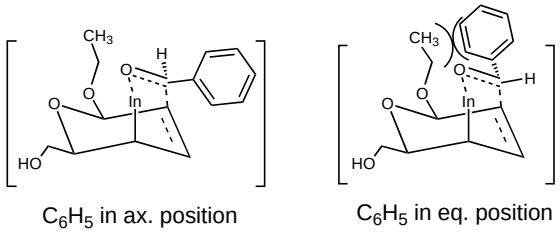
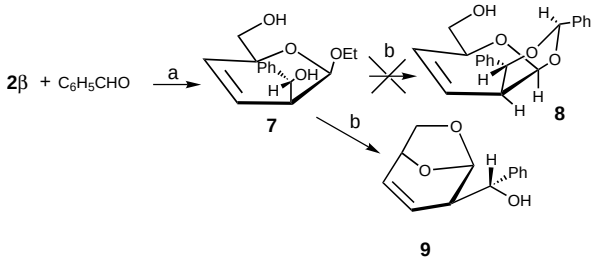
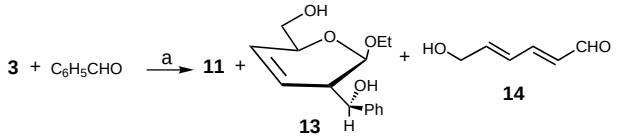


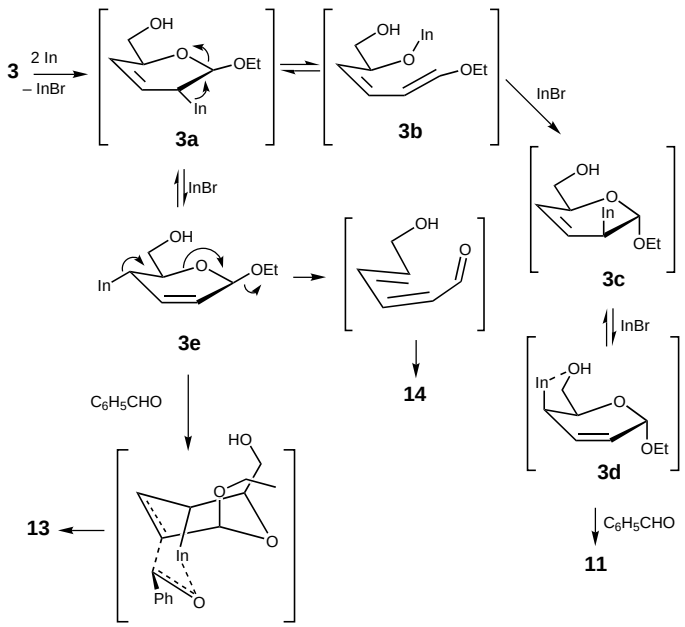
Figure 1.



Scheme 2. (a) In, EtOH/H_2O, 45%; (b) C_6H_5CHO, $ZnCl_2$, CH_2Cl_2, 10%.



Scheme 3. (a) In, EtOH/H_2O, 65%; **11/13/14** = 6/6/1.



Scheme 4.

= 5.9 Hz is in good agreement with a pseudo trans-diaxial antiperiplanar orientation of the C-1 and C-2 hydrogen atoms in a half-chair conformation.[12]

Generally, in these Barbier-type allylations, alkylation occurs at the γ position, with *syn* stereochemistry as a result of a cyclic six-membered chair transition state.[14] In this case, the formation of the expected C-4-branched sugar from **3**, which would require first the inversion of the pyranosidic ring, did not occur and the indium intermediate gave more readily a ring opening leading to **11**. With regard to the observed results, the formation of the two adducts **11**, **13** and the aldehyde **14** could be rationalized by the mechanism given in the Scheme 4.

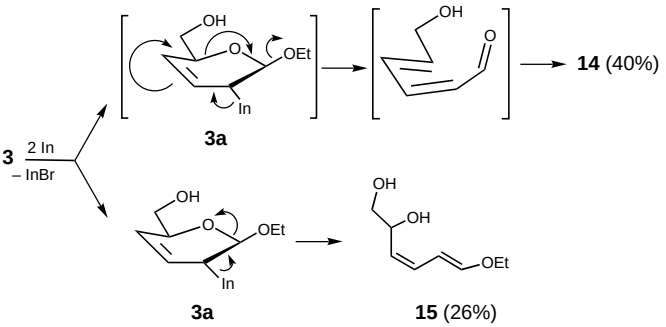
First, an allylindium(I) species **3a** is formed which could undergo a ring opening through β-elimination. In a second step, indium(I) bromide formed in the reaction could act as a Lewis acid and cause the cyclization of the enol ether derivative **3b** to give either **3a** or **3c**. These two intermediates result from an approach of the incoming oxygen atom *anti* relative to the electrophilic indium atom giving rise to compounds **3a** (1β,2α) and **3c** (1α,2β). Then, still in the presence of In(I)Br, species **3c** would be in equilibrium, *via* a stereospecific 1,3-allylindium migration, with its more favourable regioisomer **3d**, due to the chelation between the indium atom and the primary hydroxy group. Then, in the last step, *via* the usual six-membered cyclic transition state between the carbonyl compound and the allylindium sugar moiety **3d**, we would obtain the 2-*C*-axial adduct **11** already obtained in our previous work starting from **2α**. In **11**, C-7 which was assigned to be (*S*), implied a transition state with the phenyl group in equatorial position.

In the same manner, in the presence of InBr, the species **3a** exists in equilibrium, still through a stereospecific 1,3-allylindium migration, with its regioisomer **3e**. Then coupling with benzaldehyde would led to the 2-*C*-adduct **13**. In this last case, the formation of the six-membered chair transition state between aldehyde and the intermediate **3e** involves first inversion of the pyranosidic half-chair. In addition, we obtained in this reaction the aldehyde **14** which could come from the elimination of the ethoxy group in the intermediate **3e** followed by isomerization in acidic aqueous medium of the conjugate double bonds towards the more stable *trans-trans* isomer. So, from the intermediate **3e**, the two possibilities seem possible, either the coupling reaction or the elimination process whereas, in the case of **3a**, the coupling reaction leading to the 4-*C*-branched derivative did not occur, and we observed only the ring opening through β-elimination.

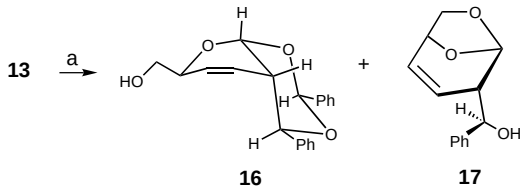
It is interesting to note that when the bromoenopyranoside **3** was treated with indium alone without any aldehyde (Scheme 5), we obtained two compounds, the previous aldehyde **14** and the enol-ether derivative **15**. Both compounds were shown to be relatively unstable and were obtained in moderate yields of 40% and 26%, respectively.

The unknown compound **15** coming from ring opening in **3a**, exhibited ^{1}H NMR signals corresponding to conjugated 1*E*,3*Z*-diene ($J_{1,2}$ = 12.2 and $J_{3,4}$ = 11.0 Hz) with chemical shifts at δ = 6.60 (H-1), 5.78 (H-2), 6.03 (H-3) and 5.13 (H-4) for olefinic protons.[15] The H-4 showed a further coupling to an unshielded proton H-5 at δ = 4.60 (1H, d, *J* = 8.8 Hz).

Concerning the adduct **13**, formation of the benzylidene compound **16** onto the C-1 and C-7 hydroxy groups with concomitant elimination of the ethoxy group, showed that the configuration of new stereogenic center C-7 was (*R*) (Scheme 6).



Scheme 5.



Scheme 6. (a) C_6H_5CHO, $ZnCl_2$, CH_2Cl_2, **16** (15%), **17** (60%).

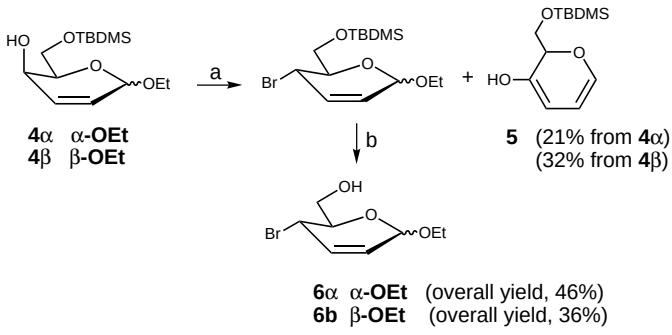
In this case, the bulky phenyl substituent at C-7 in **16** is ideally oriented away from the pyranosidic ring in an equatorial position. This is supported by the value of $J_{1,2} = 2.9$ Hz which indicates a *cis* relationship between the two six-membered cycles and the value $J_{2,7} = 10.7$ Hz which indicates a transdiaxial antiperiplanar orientation of the C-2 and C-7 hydrogen atoms. This *R* configuration of C-7 in **13** results from the more favourable equatorial position of the phenyl substituent in the transition state leading to **13**.

In this reaction and under these conditions, it is interesting to note the predominant formation of the 2-*C*-anhydro derivative **17** (60%).

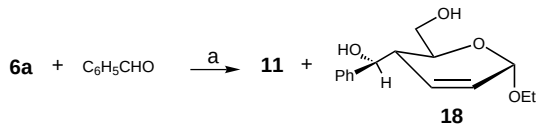
In the next part, allylation reactions were extended to 4-bromo-α-D-*erythro*-hex-2-enopyranoside **6α** and 4-bromo-β-D-*erythro*-hex-2-enopyranoside **6β**. The construction of the bromo derivative **6α** started from the known 2-enopyranoside **4α**[16] as depicted in Scheme 7.

It was obtained in 46% overall yield according to the same protocol used for the preparation of **2β** and **3**. However, in this reaction, we observed also the formation of the undesirable 3-hydroxy-(6-*tert*-butyldimethylsilyl)-2*H*-pyran **5** in 21% yield. Its formation could be explained by a deprotonation at C-4 of the phosphonium intermediate resulting in the elimination of the ethoxy group.

Then, we tested the allylation reaction with benzaldehyde under indium Barbier-type conditions (Table 1, entry 3). The reaction, conducted in a H_2O/EtOH (1:2) mixture at room temperature, afforded in 70% total yield the adduct **11** (that we previously obtained from **2α** and **3**), and a new compound **18** in a 1/4.5 ratio (Scheme 8).



Scheme 7. (a) CBr_4, $(C_6H_5)_3P$, CH_2Cl_2; (b) $(C_4H_9)N^+F^-$, THF.



Scheme 8. (a) In, EtOH/H_2O, 70%, **11/18** = 1/4.5.

The structure of **18** was deduced by ^{1}H NMR analysis. Particularly, the hydrogen atom H-4 was shielded compared with the 2-*C*-adducts **7**, **11** and **13**, indicating an alkylation at C-4. Moreover. the coupling constant $J_{4,5} = 8.0$ Hz indicates a *trans* diaxial orientation between the H-4 and H-5 hydrogen atoms.

With regard to all these results, it seems that, as previously, there would be an equilibrium between the allylindium(I) species **6a** and **6b** as shown in Figure 2.

In fact and in contrary to **3a**, the α-ethoxy-allylindium **6b** intermediate is stable to β-elimination and can lead to the 4-*C*-branched sugars after inversion of the half-chair sugar and formation of the six-membered cyclic transition state. This stability towards β-elimination could come from the anomeric effect which makes the intracyclic oxygen atom more positive and thus, reduces the possibility of elimination. To explain the formation of 4-*C*-adduct **18** instead of the expected C-2 branched sugar, mainly two factors could be invoked: first, the stabilization of anionic charge in C-2 position due to the neighbouring electrophilic anomeric center in the absence of a possible chelation with the hydroxy group at C-6 in *trans* position and, second, an unfavourable steric interaction between the α-ethoxy group and the phenyl substituent in equatorial C-2 position in the transition state leading to C-2-branched sugar. This is also strongly supported by the fact that the reaction with the β derivative **3e** which did not imply steric interactions in the transition state gave the corresponding C-2-branched sugar.

Concerning the adduct **11**, its formation should involve epimerization at C-4 or C-2, respectively, on the allylindium derivatives **6a** or **6b**. In order to determine the configuration of the new stereogenic center at the C-7 position, the 4-*C*-branched sugar **18** was elaborated to a mannose derivative as depicted in Scheme 9. Accordingly, *cis*-hydroxylation of **18** with osmium tetroxide

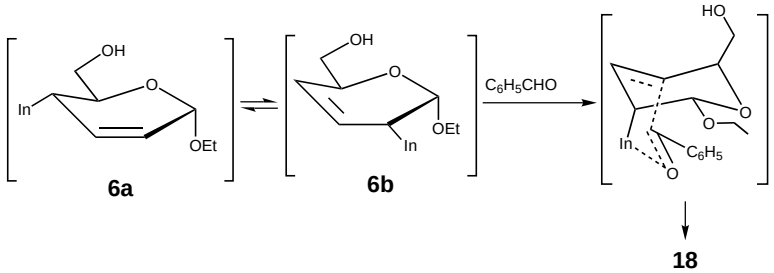
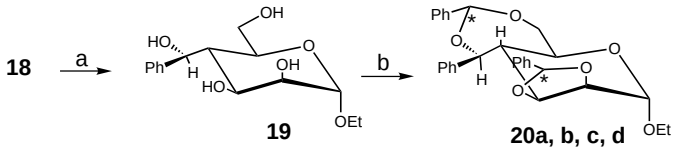


Figure 2.



Scheme 9. (a) OsO_4, NMO, CH_3COCH_3/H_2O, 87%; (b) $C_6H_5CH(OCH_3)_2$, CSA, CH_3CN, 71%.

gave with complete stereoselectivity the 4-*C*-mannose **19** in 87% yield. Then, treatment of the sugar **19** by benzaldehyde dimethyl acetal in the presence of catalytic camphorsulfonic acid led to a mixture of four diastereoisomers **20a – d** in 71% total yield.

On the basis of the structure of these compounds, the C-7 configuration of the 4-*C*-branched sugar **18** was assigned to be (*S*) and was in agreement with the phenyl substituent in an equatorial position in the cyclic transition state. Indeed, in the four compounds **20a – d**, the H-4 hydrogen atom showed three large coupling constants of 9 – 10 Hz which implied the structure depicted in Scheme 9. The structures of the four compounds, which can be fully separated by flash chromatography, varied only in the configuration of the two quaternary carbon atoms of the two benzylidene groups.

Finally, in a last step, we examined the allylation reactions with **6β**. The synthesis of this compound started from the 2-enopyranoside **1** which was converted into its epimer **4β** by the Mitsunobu reaction (benzoic acid, DIAD, triphenylphosphine) and hydrolysis (sodium methoxide) in 54% overall yield following the method already described for **4α**.[15] Then, as previously, **4β** was transformed to its bromo derivative **6β** in 36% overall yield. Here, we also observed the formation of the undesired pyran **5** in 32% yield (Scheme 7).

Concerning the Barbier-type reaction (Table 1, entry 4), the allylation reaction, which took place in H_2O/EtOH at room temperature in 1 h, gave **13** in 22% yield as the unique *C*-branched sugar. In fact, in this reaction, the major product was the previous aldehyde **14**, isolated in 36% yield. The formation of the 2-*C*-branched sugar **13** and the aldehyde **14** could be rationalized as in the case of **3** via the formation of the allylindium species **3e** as depicted in Scheme 10.

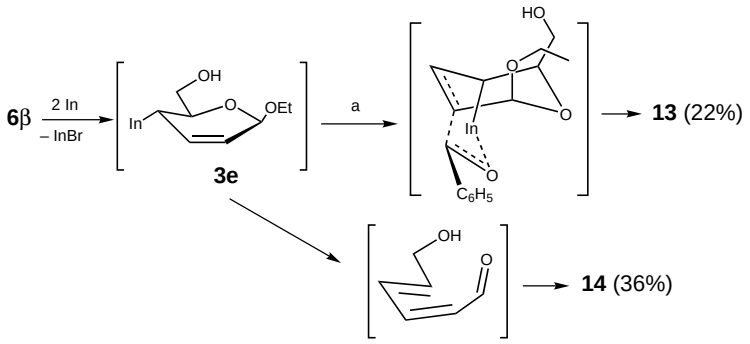
Conclusions

In conclusion, we have described that various bromoenopyranosides undergo indium Barbier-type allylations in aqueous media. These reactions gave a new access to C-branched sugars at C-2 and C-4. We have shown that the formation of allylindium is stereospecific with retention of configuration and that in the case of an axial bromine atom, we obtained γ-alkylation *syn* relative to the bromine atom through six-membered cyclic transition states. In the case of an equatorial bromine atom, after the stereospecific formation of allylindium, the coupling reactions which required energetic half-chair inversion allowed side reactions such as 1,3-allylindium migration (*syn* in stereochemistry) or inversion of configuration of the indium species notably through elimination-recombination. Overall, in this case, depending on 1,3-allylindium migration, α or γ selectivities could be observed.

Experimental Section

General Methods and Materials

All moisture-sensitive reactions were performed under argon using oven-dried glassware. If necessary, solvents were dried and distilled prior to use. Reactions were monitored on silica gel 60 F_{254}. Detection was performed using UV light, iodine and/or 5% sulfuric acid in ethanol, followed by heating. Flash chromatography were performed on silica gel 6 – 35 μm. ^1H and ^{13}C NMR spectra were recorded at room temperature with Bruker AC 200, 250 or AM 400 spectrometers. Chemical shifts are reported in δ vs. Me_4Si for ^1H NMR spectra (external reference for D_2O) and relative to the $CDCl_3$ resonance at 77.00 ppm for ^{13}C NMR spectra in $CDCl_3$ and relative to Me_4Si for ^{13}C NMR spectra in D_2O. Melting points were measured on a Reichert apparatus and were uncorrected. Optical rotations were measured on an Electronic Digital Jasco DIP-370 Polarimeter. Mass spectra were recorded in positive mode on a Finnigan MAT 95 S spectrometer using electrospray ionization. Elemental analyses were performed at the Service Central de Microanalyses du CNRS (Gif-sur-Yvette, France).



Scheme 10. (a) C_6H_5CHO, In, $EtOH/H_2O$.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3-dideoxy-β-D-*threo*-hex-2-enopyranoside (4β)

To a solution of the ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranoside **1** (1.4 g, 4.86 mmol), benzoic acid (1.78 g, 14.6 mmol), and $(C_6H_5)_3P$ (3.82 g, 14.6 mmol) in THF cooled to 0 °C was added diisopropyl azidodicarboxylate (DIAD) (3.6 mL, 14.6 mmol). The solution was stirred for 3 h at room temperature. Then the solution was diluted with diethyl ether and washed successively with a saturated aqueous solution of $NaHCO_3$ and brine. After being dried with $MgSO_4$, evaporation of the solvent gave the crude product which was partially purified by flash chromatography (petroleum ether/ethyl acetate, 9/1) to provide the crude benzoate. Then, the benzoate was dissolved in methanol (30 mL) and treated with a solution of sodium methoxide in methanol (0.03 M, 30 mL, 0.9 mmol) at room temperature overnight. The solution was diluted with diethyl ether and washed with a saturated aqueous solution of $NH_4^+Cl^-$. After extraction with diethyl ether, the solution was dried ($MgSO_4$) and concentrated. Flash chromatography of the residue (petroleum ether/ethyl acetate, 9/1) gave the *threo*-isomer **4β**; yield: 0.755 g (54%). Colourless oil; $[\alpha]_D$: –103° (CH_2Cl_2, *c* 1.7); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.09 (s, 6H, CH_3Si), 0.90 [s, 9H, $(CH_3)_3$], 1.25 (t, *J* = 7.1 Hz, 3H, CH_3), 2.05 (d, *J* = 9.8 Hz, 1H, OH), 3.44 – 3.70 (m, 2H, CH_2CH_3, H-5), 3.80 (dd, $J_{6a,5}$ = 5.9 Hz, $J_{6a,6b}$ = 10.2 Hz, 1H, 6a-H), 3.88 – 4.01 (m, 3H, CH_2CH_3, 6b-H, H-4), 5.06 (d, *J* = 1.5 Hz, 1H, H-1), 5.83 (d, $J_{2,3}$ = 10.3 Hz, 1H, H-2), 6.15 (ddd, *J* = 1.5 Hz, *J* = 4.9 Hz, 1H, H-3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = –5.6 (CH_3Si), –5.5 (CH_3Si), 15.1 (CH_3), 18.1 [$(CH_3)_3C$], 25.7 [$(CH_3)_3C$], 62.2, 62.5 (CH_2CH_3, C-6), 63.9, 75.6 (C-4, C-5), 97.5 (C-1), 130.6, 130.7 (C-2, C-3); anal.: calcd. for $C_{14}H_{28}O_4Si$ (288.46): C 58.29, H 9.78, Si 9.73; found: C 57.94, H 9.82, Si 9.90.

General Procedure for the Bromination Reaction

To a solution of the ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxyhex-2-enopyranoside **1**, **4α** or **4β** (1 mmol) in CH_2Cl_2 (5 mL) maintained under argon at –78 °C, were added $(C_6H_5)_3P$ (1.5 mmol) and CBr_4 (1.1 mmol). The suspension was stirred at 0 °C until the reaction was complete then quenched with a saturated aqueous solution of $NaHCO_3$ and extracted with CH_2Cl_2. The organic phase was dried ($MgSO_4$) then concentrated. Flash chromatography of the crude residue gave the intermediate ethyl 6-*O*-(*tert*-butyldimethylsilyl)-bromodideoxyhexenopyranoside and the 6-*O*-(*tert*-butyldimethylsilyl)-2*H*-pyran-3-ol **5** (in the case of **4α** and **4β**). Then the ethyl 6-*O*-(*tert*-butyldimethylsilyl)-bromodideoxyhexenopyranoside was dissolved in THF (5 mL) and treated at 0 °C with a solution of $NBu_4^+F^-$ (1 M in THF, 1.1 mmol). The mixture was stirred at room temperature for 3 h, then quenched with water and extracted with Et_2O. The organic phase was washed several times with saturated aqueous NH_4Cl solution, dried ($MgSO_4$) then concentrated. Flash chromatography of the residue (petroleum ether/ethyl acetate, 3/1 to 1/1) gave the corresponding bromo-enopyranosides **2β**, **3**, **6α** and **6β**.

Ethyl 4-Bromo-2,3,4-trideoxy-β-D-*threo*-hex-2-enopyranoside (2β): Yield: 38%; white crystals; mp 51 – 53 °C; $[\alpha]_D$: –249° (CH_2Cl_2, *c* 1.1); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.1 Hz, 3H, CH_3), 2.76 (br s, 1H, OH), 3.62 – 3.96 (m, 5H, CH_2CH_3, H-5, 6a-H, 6b-H), 4.51 – 4.54 (m, 1H, H-4), 5.37 (m, 1H, H-1), 5.75 (dd, $J_{2,1}$ = 1.0 Hz, $J_{2,3}$ = 9.8 Hz, 1H, H-2), 6.22 (ddd, $J_{3,1}$ = 1.5 Hz, $J_{3,4}$ = 5.4 Hz, 1H, H-3); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.2 (CH_3), 44.6 (C-4), 63.3, 65.0 (CH_2CH_3, C-6), 73.9 (C-5), 97.5 (C-1), 129.8, 130.4 (C-2, C-3); MS (EI high resolution): *m/z* calcd. for $C_8H_{13}O_3BrNa$: 258.994587; found: 258.99465.

Ethyl 2-Bromo-2,3,4-trideoxy-β-D-*erythro*-hex-3-enopyranoside (3): Yield: 39%; white solid; mp 47 – 48 °C; $[\alpha]_D$: –341° (CH_2Cl_2, *c* 1.2); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.1 Hz, 3H, CH_3), 2.40 – 2.50 (br s, 1 H, OH), 3.61 – 3.70 (m, 2H, CH_2CH_3, 6a-H), 3.75 (dd, $J_{6b,5}$ = 3.4 Hz, $J_{6b,6a}$ = 11.7 Hz, 1H, 6b-H), 3.91 – 4.03 (m, 1H, CH_2CH_3), 4.45 – 4.53 (m, 2H, H-2, H-5), 4.87 (d, $J_{1,2}$ = 5.4 Hz, 1H, H-1), 5.75 (td, *J* = 1.5 Hz, $J_{3,4}$ = 10.3 Hz, 1H, H-3), 6.02 (td, *J* = 2.5 Hz, 1H, H-4); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.0 (CH_3), 45.0 (C-2), 64.8, 65.4 (CH_2CH_3, C-6), 74.7 (C-5), 101.5 (C-1), 127.6, 128.5 (C-3, C-4); MS (EI): *m/z* = 259.0 ($M + Na^+$); anal.: calcd. for $C_8H_{13}O_3Br$ (237.09): C 40.53, H 5.53, O 20.24; found: C 40.29, H 5.51, O 20.07.

Ethyl 4-Bromo-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside (6α): Yield: 46%; colourless oil; $[\alpha]_D$: 166° (CH_2Cl_2, *c* 1.1); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.1 Hz, 3H, CH_3), 2.32 (br s, 1H, OH), 3.49 – 3.62 (m, 1H, CH_2CH_3), 3.76 – 3.98 (m, 3H, CH_2CH_3, 6a-H, 6b-H), 4.07 – 4.14 (td, $J_{5,6}$ = 2.5 Hz, $J_{5,4}$ = 9.8 Hz, 1H, H-5), 4.63 – 4.69 (m, 1H, H-4), 5.03 (br s, 1H, H-1), 5.76 (ddd, *J* = 1.9 Hz, *J* = 2.9 Hz, $J_{2,3}$ = 10.2 Hz, 1H, H-2), 6.12 (d, 1H, H-3); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.2 (CH_3), 41.5 (C-4), 62.2, 64.2 (CH_2CH_3, C-6), 71.9 (C-5), 94.0 (C-1), 127.0, 131.4 (C-2, C-3); MS (EI high resolution): *m/z* calcd. for $C_8H_{13}O_3BrNa$: 258.994587; found: 258.99468.

Ethyl 4-Bromo-2,3,4-trideoxy-β-D-*erythro*-hex-2-enopyranoside (6β): Yield: 36%; colourless oil; $[\alpha]_D$: 46° (CH_2Cl_2, *c* 1.4); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.1 Hz, 3H, CH_3), 2.47 (br s, 1H, OH), 3.57 – 3.69 (m, 1H, CH_2CH_3), 3.78 – 4.01 (m, 3H, CH_2CH_3, 6a-H, 6b-H), 4.07 – 4.12 (m, 1H, H-5), 4.65 – 4.70 (m, 1H, H-4), 5.27 (br s, 1H, H-1), 5.77 (td, *J* = 1.7 Hz, $J_{2,3}$ = 9.8 Hz, 1H, H-2), 6.16 (ddd, *J* = 1.7 Hz, *J* = 3.4 Hz, 1H, H-3); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.1 CH_3), 41.9 (C-4), 63.1, 64.1 (CH_2CH_3, C-6), 78.5 (C-5), 95.4 (C-1), 128.3, 130.5 (C-2, C-3); MS (EI high resolution): *m/z* calcd. for C8H13O3BrNa: 258.994587; found: 258.99458.

6-*O*-(*tert*-butyldimethylsilyl)-2*H*-pyran-3-ol (5): Colourless oil; $[\alpha]_D$: 20° (CH_2Cl_2, *c* 0.9); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.06 (s, 3H, $SiCH_3$), 0.07 (s, 3H, $SiCH_3$), 0.90 [s, 9H, $SiC(CH_3)_3$], 2.89 (br s, 1H, OH), 3.79 – 3.88 (m, 2H, 6a-H, 6b-H), 4.75 (dd, $J_{5,6a}$ = 4.9 Hz, $J_{5,6b}$ = 6.3 Hz, 1H, H-5), 6.30 – 6.35 (m, 2H, H-2, H-3), 7.37 (m, 1H, H-1); ^{13}C NMR (63 MHz, $CDCl_3$): δ = –5.5 [$Si(CH_3)_2$], 18.2 [$(CH_3)_3C$], 25.8 [$(CH_3)_3C$], 65.6 (C-6), 68.3 (C-5), 107.0, 110.2, 142.0 (C-1, C-2, C-3), 153.6 (C-4); MS (EI high resolution): *m/z* calcd. for $C_{12}H_{22}O_3SiNa$: 265.123593; found: 265.12364.

General Procedure for Reaction of Bromoenopyranoside with Benzaldehyde

To a solution of bromo-enopyranoside **2β**, **3**, **6α** or **6β** in H_2O/EtOH (1/2) were added indium powder (3 equiv.) and benzaldehyde (3 equiv.). The suspension was stirred until the reaction was complete, as judged by consumption of the bromoenopyranoside (see Table 1). The reaction was then quenched with a saturated aqueous $NaHCO_3$ solution, filtered and concentrat-

ed. Flash chromatography of the residue (petroleum ether/ethyl acetate, 4/1 to 1/3) gave the corresponding 2-*C*- and 4-*C*-branched sugars **7**, **11**, **13** and **18**.

Ethyl 2-*C*-[(*R*)-1-Phenyl-1-hydroxymethyl]-3,4-dideoxy-β-D-*threo*-hex-3-enopyranoside (7): Yield: 45%; colourless oil; $[\alpha]_D$: 40° (CH_2Cl_2, *c* 1.0); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.1 Hz, 3H, CH_3), 2.58 – 2.63 (m, 1H, H-2), 3.49 – 3.70 (m, 2H, CH_2CH_3, 6a-H), 3.79 (dd, $J_{6b,5}$ = 2.9 Hz, $J_{6b,6a}$ = 11.7 Hz, 1H, 6b-H), 3.94 – 4.10 (m, 1H, CH_2CH_3), 4.41 – 4.43 (m, 1H, H-5), 4.86 (d, $J_{7,2}$ = 3.4 Hz, 1H, H-7), 5.23 (d, $J_{1,2}$ = 2.9 Hz, 1H, H-1), 5.64 (ddd, *J* = 2.4 Hz, *J* = 4.4 Hz, $J_{3,4}$ = 10.2 Hz, 1H, H-3), 5.79 (td, *J* = 1.7 Hz, 1H, H-4), 7.22 – 7.36 (m, 5H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.1 (CH_3), 45.1 (C-2), 64.7, 65.0 (CH_2CH_3, C-6), 71.1, 75.2 (C-5, C-7), 99.4 (C-1), 124.4, 126.0, 127.1, 127.8, 128.1 (C_6H_5, C-3, C-4), 142.1 (C_6H_5); MS (EI): *m/z* = 287.1 ($M + Na^+$); anal.: calcd. for $C_{15}H_{20}O_4$ (264.32): C 68.16, H 7.63, O 24.21; found: C 67.66, H 7.78, O 24.18.

Ethyl 2-*C*-[(*R*)-1-Phenyl-1-hydroxymethyl]-3,4-dideoxy-β-D-*erythro*-hex-3-enopyranoside (13): Yield: 30%; white solid; $[\alpha]_D$: –87° (CH_2Cl_2, *c* 1.0); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.1 Hz, 3H, CH_3), 2.36 (m, 1H, OH), 2.60 – 2.67 (m, 1H, H-2), 3.55 – 3.77 (m, 3H, CH_2CH_3, 6a-H, 6b-H), 3.99 – 4.12 (m, 1H, CH_2CH_3), 4.34 – 4.39 (m, 1H, H-5), 4.56 (d, $J_{7,2}$ = 8.8 Hz, 1H, H-7), 4.82 (d, $J_{1,2}$ = 5.9 Hz, 1H, H-1), 5.29 (td, *J* = 2.7 Hz, $J_{3,4}$ = 10.2 Hz, 1H, H-3), 5.61 (td, *J* = 2.0 Hz, 1H, H-4), 7.30 – 7.38 (m, 5H, C_6H_5); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.0 (CH_3), 46.6 (C-2), 64.6, 64.9 (CH_2CH_3, C-6), 74.8, 75.2 (C-5, C-7), 100.8 (C-1), 125.4, 126.9, 127.1, 127.9, 128.3 (C_6H_5, C-3, C-4), 141.2 (C_6H_5); MS (EI): *m/z* = 287.2 ($M + Na^+$); anal.: calcd. for $C_{15}H_{20}O_4$ (264.32): C 68.16, H 7.63, O 24.21; found: C 67.72, H 7.62, O 24.17.

Ethyl 4-*C*-[(*S*)-1-Phenyl-1-hydroxymethyl]-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (18): Yield: 57%; colourless oil; $[\alpha]_D$: 16° (CH_2Cl_2, *c* 1.0); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.1 Hz, 3H, CH_3), 2.71 – 2.79 (br t, $J_{4,5}$ = 8.0 Hz, 1H, H-4), 3.47 – 3.59 (m, 1H, CH_2CH_3), 3.77 – 4.00 (m, 4H, CH_2CH_3, H-5, 6a-H, 6b-H), 4.55 (d, $J_{7,4}$ = 8.8 Hz, 1H, H-7), 4.97 (br s, 1H, H-1), 5.44 (d, $J_{2,3}$ = 10.2 Hz, 1H, H-2), 5.76 (td, *J* = 2.7 Hz, 1H, H-3), 7.29 – 7.41 (m, 5H, C_6H_5); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.3 (CH_3), 43.2 (C-4), 63.6, 65.4 (CH_2CH_3, C-6), 71.1, 75.9 (C-5, C-7), 93.6 (C-1), 126.8, 126.9, 128.3, 128.7, 129.8 (C_6H_5, C-2, C-3), 142.1 (C_6H_5); MS (EI): *m/z* = 287.1 ($M + Na^+$); anal.: calcd. for $C_{15}H_{20}O_4$ (264.32): C 68.16, H 7.63, O 24.21; found: C 67.81, H 7.64, O 24.54.

(2*E*,4*E*)-6-Hydroxyhexanedienal (14) and (2*E*,4*Z*)-5,6-dihydroxy-1-ethoxyhexane (15)

To a stirred solution of 2-bromo-4-enopyranoside **3** (100 mg, 0.421 mmol) in H_2O (2 mL) was added indium powder (145 mg, 1.26 mmol). After 1 h at room temperature, the reaction was quenched with a saturated aqueous $NaHCO_3$ solution, filtered and concentrated. Flash chromatography of the residue (petroleum ether/ethyl acetate, 3/1 to 1/1) gave the aldehyde **14** (yield: 19 mg, 40%) and then **15** (yield: 17 mg, 26%).

15: Colourless oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.1 Hz, 3H, CH_3), 3.52 (dd, $J_{6a,5}$ = 7.8 Hz, $J_{6a,6b}$ = 11.2 Hz, 1H, 6a-H), 3.62 (dd, $J_{6b,5}$ = 3.9 Hz, 1H, 6b-H), 3.84 (q, 1H, CH_2CH_3), 4.60 (td, 1H, H-5), 5.13 (dd, $J_{4,5}$ = 8.8 Hz, $J_{4,3}$ = 11.0 Hz, 1H, H-4), 5.78 (t, 1H, H-2), 6.04 (t, 1H, H-3), 6.60 (d, $J_{1,2}$ = 12.2 Hz, 1H, H-1); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.7 (CH_3), 65.8, 66.3 (CH_2CH_3, C-6), 69.1 (C-5), 101.8, 123.1, 129.1 (C-2, C-3, C-4), 152.8 (C-1); MS (EI): *m/z* = 181.0 ($M + Na^+$).

1,6-Anhydro-2-*C*-[(*R*)-1-phenyl-1-hydroxymethyl]-3,4-dideoxy-β-D-*threo*-hex-3-enopyranoside (9)

To a solution of **7** (85 mg, 0.322 mmol) in CH_2Cl_2 (3 mL) under argon, were added zinc chloride (53 mg, 0.386 mmol) and benzaldehyde (327 μL, 3.22 mmol). The suspension was stirred at 30 °C overnight, then quenched with a saturated aqueous solution of $NaHCO_3$ and extracted with CH_2Cl_2. The organic phase was washed several times with a saturated aqueous $NH_4^+Cl^-$ solution, dried ($MgSO_4$) then concentrated. Flash chromatography of the residue (petroleum ether/ethyl acetate, 10/1 to 1/1) gave **9**; yield: 7 mg (10%); colourless oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.88 – 2.91 (m, 1H, H-2), 3.74 – 3.79 (m, 1H, 6a-H), 4.03 (d, $J_{6b,6a}$ = 6.3 Hz, 1H, 6b-H), 4.69 (t, *J* = 4.1 Hz, 1H, H-5), 4.94 (d, $J_{7,2}$ = 4.4 Hz, 1H, H-7), 5.58 (t, *J* = 2.2 Hz, 1H, H-1), 5.66 (td, *J* = 2.2 Hz, $J_{3,4}$ = 10.0 Hz, 1H, H-3), 6.12 (ddd, *J* = 2.0 Hz, *J* = 4.4 Hz, 1H, H-4), 7.28 – 7.42 (m, 5H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 50.0 (C-2), 71.4, 72.5 (C-5, C-7), 72.8 (C-6), 103.3 (C-1), 124.9, 126.0, 127.5, 128.4, 129.7 (C_6H_5, C-3, C-4), 141.7 (C_6H_5); MS (EI high resolution): *m/z* calcd. for $C_{13}H_{14}O_3Na$: 241.084064; found: 241.08400.

1,7-*O*-Benzylidene-2-*C*-[(*R*)-1-phenyl-1-hydroxymethyl]-3,4-dideoxy-α-D-*erythro*-hex-3-enopyranoside (16) and 1,6-Anhydro-2-*C*-[(*R*)-1-phenyl-1-hydroxymethyl]-3,4-dideoxy-α-D-*erythro*-hex-3-enopyranoside (17)

To a solution of **13** (54 mg, 0.204 mmol) in CH_2Cl_2 (2 mL) under argon, were added zinc chloride (33 mg, 0.245 mmol) and benzaldehyde (103 μL, 1.02 mmol). The suspension was stirred at room temperature overnight, then quenched with a saturated aqueous solution of $NaHCO_3$ and extracted with CH_2Cl_2. The organic phase was washed several times with a saturated aqueous $NH_4^+Cl^-$ solution, dried ($MgSO_4$) then concentrated. Flash chromatography of the residue (petroleum ether/ethyl acetate, 10/1 to 1/1) gave first **17** (yield: 27 mg, 60%) then **16** (yield: 10 mg, 15%).**16:** White solid; $[\alpha]_D$: –64° (CH_2Cl_2, *c* 0.8); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.26 – 2.29 (br s, 1H, OH), 2.62 – 2.70 (m, 1H, H-2), 3.61 – 3.69 (m, 1H, 6a-H,), 3.79 (dd, *J* = 8.5 Hz, *J* = 12.0 Hz, 1H, 6b-H), 4.72 – 4.76 (m, 1H, H-5), 4.94 (d, $J_{7,2}$ = 10.2 Hz, 1H, H-7), 5.46 (ddd, *J* = 2.4 Hz, *J* = 6.3 Hz, $J_{3,4}$ = 10.3 Hz, 1H, H-3), 5.51 (d, $J_{1,2}$ = 2.9 Hz, 1H, H-1), 5.77 (dd, $J_{4,5}$ = 2.9 Hz, 1H, H-4), 6.33 (s, 1H, CH), 7.32 – 7.46 and 7.58 – 7.62 (m, 10H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 40.9 (C-2), 63.6 (C-6), 77.1, 80.3 (C-5, C-7), 91.0, 95.3 (C-1, CH), 125.7, 126.5, 127.1, 128.5, 129.0 (C_6H_5, C-3, C-4), 137.7, 138.9 (C_6H_5); MS (EI high resolution): *m/z* calcd. for $C_{20}H_{20}O_4Na$: 347.125929; found: 347.12603.

17: Colourless oil; $[\alpha]_D$: –69° (CH_2Cl_2, *c* 0.9); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.35 – 2.42 (m, 1H, H-2), 2.47 (br s, 1H, OH), 3.73 (dd, $J_{6a,5}$ = 4.1 Hz, $J_{6a,6b}$ = 6.3 Hz, 1H, 6a-H), 3.92 (d, 1H, 6b-H), 4.68 (m, 2H, H-5, H-7), 5.24 (ddd, *J* = 1.9 Hz, *J* = 3.9 Hz, $J_{3,4}$ = 9.8 Hz, 1H, H-3), 5.79 (br s, 1H, H-1), 6.10 (ddd, *J* = 2.0 Hz, *J* = 4.4 Hz, 1H, H-4), 7.28 – 7.40 (m, 5H, C_6H_5);

^{13}C NMR (63 MHz, $CDCl_3$): δ = 49.5 (C-2), 71.1, 74.2 (C-5, C-7), 72.4 (C-6), 100.7 (C-1), 125.7, 126.2, 127.8, 128.5, 130.3 (C_6H_5, C-3, C-4), 142.2 (C_6H_5); MS (EI): *m/z* = 241.1 ($M + Na^+$); anal.: calcd. for $C_{13}H_{14}O_3$ (218.25): C 71.54, H 6.47, O 21.99; found: C 71.67, H 6.54, O 22.19.

Ethyl 4-*C*-[(*S*)-1-Phenyl-1-hydroxymethyl]-α-D-mannopyranoside (19)

To a solution of **18** (75 mg, 0.284 mmol) in acetone/water (8/1, 2 mL) were added 4-methylmorpholine *N*-oxide monohydrate (77 mg, 0.568 mmol) and osmium tetroxide (0.1 M/*t*-BuOH, 284 μL, 0.1 equiv.). The reaction mixture was stirred overnight at room temperature then diluted with AcOEt and washed several times with a saturated aqueous Na_2SO_3 solution. The organic phase was dried ($MgSO_4$) then concentrated. Flash chromatography of the residue (petroleum ether/ethyl acetate, 1/1 to 0/1) gave the triol **19**; yield: 74 mg (87%); white solid; mp 43 – 45 °C; $[\alpha]_D$: 56° (CH_2Cl_2, *c* 1.3); ^{1}H NMR (250 MHz, CD_3OD): δ = 1.09 (t, *J* = 7.1 Hz, 3H, CH_3), 2.35 (td, $J_{4,7}$ = 2.4 Hz, $J_{4,5} = J_{4,3}$ = 10.2 Hz, 1H, H-4), 3.31 – 3.42 (m, 2H, 6a-H, CH_2CH_3), 3.56 (dd, $J_{6b,5}$ = 2.2 Hz, $J_{6b,6a}$ = 12.0 Hz, 1H, 6b-H), 3.64 – 3.74 (m, 3H, CH_2CH_3, H-2, H-5), 4.02 (dd, $J_{3,2}$ = 2.9 Hz, 1H, H-3), 4.72 (d, $J_{1,2}$ = 1.9 Hz, 1H, H-1), 5.18 (d, 1H, H-7), 7.20 – 7.44 (m, 5H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.6 (CH_3), 42.3 (C-4), 62.6 (CH_2CH_3, C-6), 67.0, 68.8, 69.5, 73.4 (C-2, C-3, C-5, C-7), 99.0 (C-1), 126.5, 127.8, 128.3, 140.1 (C_6H_5); anal.: calcd. for $C_{15}H_{22}O_6$ (298.27): C 60.39, H 7.43, O 32.18; found: C 59.89, H 7.47, O 32.74.

Ethyl 2,3-*O*-Benzylidene, 6,7-*O*-benzylidene-4-C-[(*S*)-1-Phenyl-1-hydroxymethyl]-α-D-mannopyranosides (20a, b,c, d).

To a solution of **19** (60 mg, 0.201 mmol) in CH_3CN (2 mL) at 0 °C under argon, were added benzaldehyde dimethyl acetal (181 μL, 1.20 mmol) and *dl*-10-camphorsulfonic acid (5 mg, 0.02 mmol). The suspension was stirred at room temperature during four hours, then quenched with a saturated aqueous solution of $NaHCO_3$ and extracted with CH_2Cl_2. The organic phase was washed several times with a saturated aqueous $NH_4^+Cl^-$ solution, dried ($MgSO_4$) then concentrated. Flash chromatography of the residue (petroleum ether/ethyl acetate, 9.5/0.5 to 9/1) gave the four diastereoisomers in the following order: **20a**, **20b**, **20c** and **20d**.**20a, b,c, d**: Yield: 68 mg (71%); colourless oil; MS (EI): *m/z* = 497.2 ($M + Na^+$); anal.: calcd. for $C_{29}H_{30}O_6$ (474.55): C 73.40, H 6.37, O 20.23; found: C 72.83, H 6.65, O 20.08.

20a: 10%; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.0 Hz, 3H, CH_3), 2.38 (q, $J_{4,3} = J_{4,5} = J_{4,7}$ = 10.1 Hz, 1H, H-4), 3.46 – 3.58 (m, 1H, CH_2CH_3), 3.72 – 3.88 (m, 3H, H-2, H-5, CH_2CH_3), 4.11 – 4.19 (m, 3H, H-3, 6a-H, 6b-H), 4.48 (d, 1H, H-7), 5.14 (s, 1H, H-1), 5.79 (s, 1H, CH), 5.97 (s, 1H, CH), 7.05 – 7.08 and 7.22 – 7.35 (m, 18H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.0 (CH_3), 47.0 (C-4), 63.3, 67.5 (CH_2CH_3, C-6), 67.8, 73.8, 74.3, 74.5 (C-2, C-3, C-5, C-7), 97.9, 99.7, 101.0 (C-1, 2 CH), 125.5, 126.5, 127.2, 127.7, 128.1, 128.3, 128.6, 138.5, 140.7 (C_6H_5).

20b: 14%; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3H, CH_3), 2.22 (q, $J_{4,3} = J_{4,5} = J_{4,7}$ = 9.9 Hz, 1H, H-4), 3.49 – 3.61 (m, 1H, CH_2CH_3), 3.73 – 3.87 (m, 2H, H-5, CH_2CH_3), 3.95 (d, $J_{2,3}$ = 5.9 Hz, 1H, H-2), 4.03 (dd, 1H, H-3), 4.11 (m, 2H, 6a-H, 6b-H), 4.40 (d, 1H, H-7), 5.22 (s, 1H, H-1), 5.60 (s, 1H, CH), 5.90 (s, 1H, CH), 7.01 – 7.38 (m, 18H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.0 (CH_3), 50.3 (C-4), 63.2, 67.6 (CH_2CH_3, C-6), 68.0, 72.7, 73.9, 76.2 (C-2, C-3, C-5, C-7), 97.8, 99.6, 103.0 (C-1, 2 CH), 126.4, 127.5, 127.7, 127.9, 128.0, 128.2, 128.6, 137.3, 138.6, 139.9 (C_6H_5).

20c: 18%; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.1 Hz, 3H, CH_3), 2.30 (q, $J_{4,3} = J_{4,5} = J_{4,7}$ = 9.9 Hz, 1H, H-4), 3.44 – 3.59 (m, 1H, CH_2CH_3), 3.67 – 3.95 (m, 5H, H-2, H-5, 6a-H, 6b-H, CH_2CH_3), 4.29 (dd, $J_{3,2}$ = 4.9 Hz, 1H, H-3), 4.71 (d, 1H, H-7), 5.12 (s, 1H, H-1), 5.74 (s, 1H, CH), 5.91 (s, 1H, CH), 7.03 – 7.08 and 7.19 – 7.42 (m, 18H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.0 (CH_3), 47.9 (C-4), 62.9, 63.2 (CH_2CH_3, C-6), 67.9, 74.2, 79.2 (C-2, C-3, C-5, C-7), 97.9, 99.2, 101.0 (C-1, 2 CH), 125.5, 126.3, 126.9, 127.9, 128.1, 128.4, 128.6, 138.5, 138.9, 140.8 (C_6H_5).

20d: 29%; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.1 Hz, 3H, CH_3), 2.10 (q, $J_{4,3} = J_{4,5} = J_{4,7}$ = 9.8 Hz, 1H, H-4), 3.48 – 3.60 (m, 1H, CH_2CH_3), 3.70 (dd, *J* = 2.4 Hz, *J* = 10.3 Hz, 1H, 6a-H), 3.77 – 3.95 (m, 3H, H-5, 6b-H, CH_2CH_3), 3.99 (d, $J_{2,3}$ = 5.9 Hz, 1H, H-2), 4.20 (dd, 1H, H-3), 4.62 (d, 1H, H-7), 5.18 (s, 1H, H-1), 5.61 (s, 1H, CH), 5.85 (s, 1H, CH), 7.15 – 7.48 (m, 18H, C_6H_5); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.0 (CH_3), 51.3 (C-4), 63.1, 63.2 (CH_2CH_3, C-6), 68.1, 72.5, 76.2, 79.4 (C-2, C-3, C-5, C-7), 97.8, 99.2, 103.0 (C-1, 2 CH), 126.3, 127.5, 127.7, 127.9, 128.1, 128.4, 128.7, 137.3, 138.9, 140.3 (C_6H_5).

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