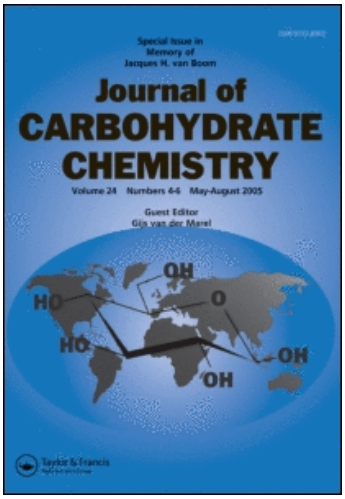


Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

2-Deoxy-2-*C*-(2,3-dideoxy-α-d-*erythro*-hexopyranosyl)-β-d-glucopyranoses: Reinvestigation of Synthesis, Use in Glycosylation, and Conformational Analyses by NMR

Hans Peter Wessel[a]; Gerhard Englert[a]
[a] Pharma Division, Preclinical Research, F. Hoffmann-La Roche Ltd, Basel, Switzerland

To cite this Article Wessel, Hans Peter and Englert, Gerhard(1995) '2-Deoxy-2-*C*-(2,3-dideoxy-α-d-*erythro*-hexopyranosyl)-β-d-glucopyranoses: Reinvestigation of Synthesis, Use in Glycosylation, and Conformational Analyses by NMR', Journal of Carbohydrate Chemistry, 14: 2, 179 — 196
To link to this Article: DOI: 10.1080/07328309508002062
URL: http://dx.doi.org/10.1080/07328309508002062

J. CARBOHYDRATE CHEMISTRY, 14(2), 179-196 (1995)

2-DEOXY-2-*C*-(2,3-DIDEOXY-α-D-*ERYTHRO*-HEXOPYRANOSYL)-β-D-GLUCOPYRANOSES: REINVESTIGATION OF SYNTHESIS, USE IN GLYCOSYLATION, AND CONFORMATIONAL ANALYSES BY NMR

Hans Peter Wessel* and Gerhard Englert

Pharma Division, Preclinical Research
F.Hoffmann-La Roche Ltd
CH-4002 Basel, Switzerland

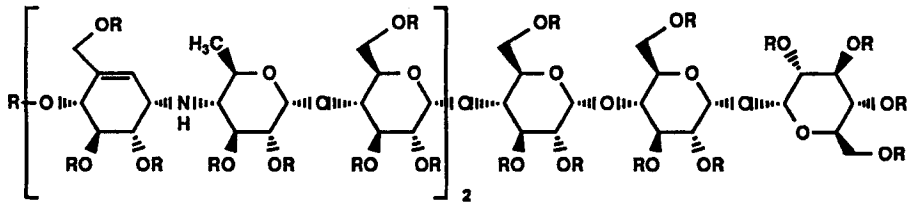
Received June 20, 1994 - Final Form October 5, 1994

ABSTRACT

Conformational investigations using 1D TOCSY and ROESY ^{1}H NMR experiments on 1,3,4,6-tetra-*O*-acetyl-2-*C*-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hexopyranosyl)-2-deoxy-β-D-glucopyranose (**8**) and related disaccharides showed that for steric reasons the C-linked hexopyranosyl ring occurs in the usually unfavoured $^1C_4$ conformation and reconfirmed the structure of 1,3,4,6-tetra-*O*-acetyl-2-*C*-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-2-deoxy-β-D-glucopyranose (**5**). Glycosylation of 2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl 2,3-di-*O*-benzyl-4,6-(*R*)-*O*-benzylidene-α-D-glucopyranoside (**13**) with acetate **8** using trimethylsilyl triflate as a catalyst afforded the α-D-linked tetrasaccharide **14**. A remarkable side product in this reaction was the unsaturated tetrasaccharide 2,3,6-tri-*O*-benzyl-4-*O*-[4,6-di-*O*-acetyl-2,3-dideoxy-2-*C*-(4,6-di-*O*-acetyl-2,3-dideoxy-β-D-*erythro*-hexopyranosyl)-α-D-*erythro*-hex-2-enopyranosyl]-α-D-glucopyranosyl 2,3-di-*O*-benzyl-4,6-(*R*)-*O*-benzylidene-α-D-glucopyranoside (**16**) where in the C-linked hexopyranosyl ring an isomerization to the β-anomer had taken place to allow for the favoured $^4C_1$ conformation. The tetrasaccharide **14** was deacetylated and hydrogenolyzed to form the fully deprotected tetrasaccharide **18**. The $^1C_4$ conformation of the C-glycosidic pyranose of this tetrasaccharide was maintained as shown by an in depth NMR analysis of its peracetate **19**.

INTRODUCTION

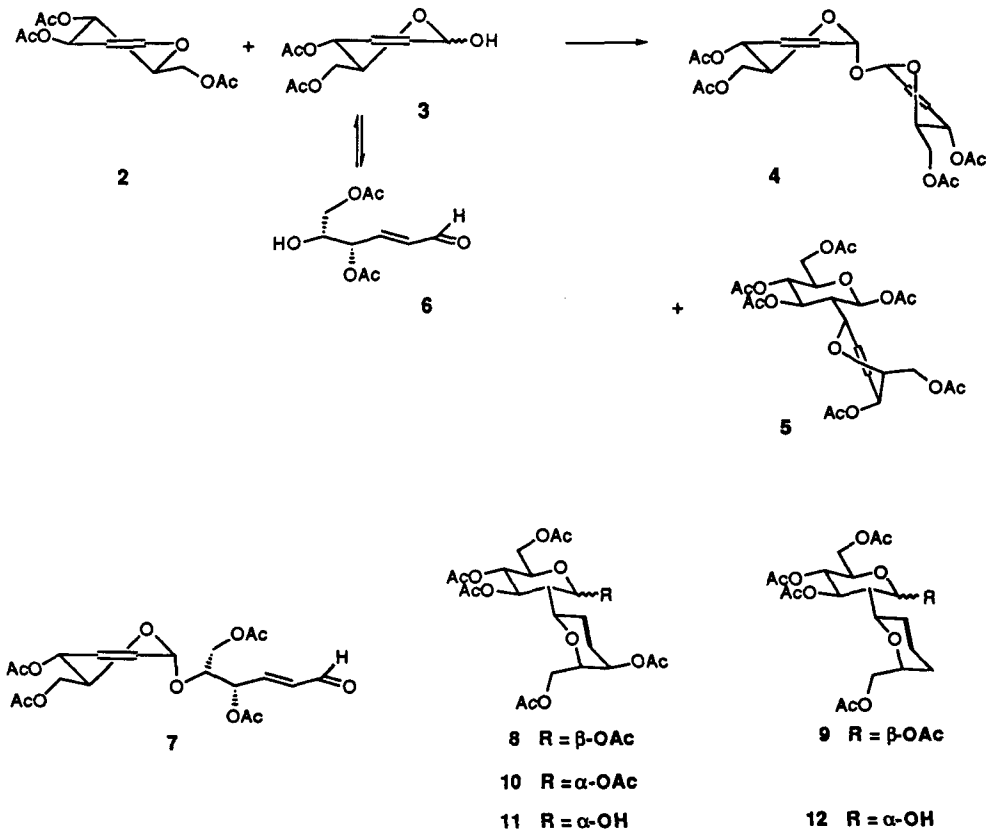
The pseudo-nonasaccharide derivative Trestatin A sulfate (**1**) had been identified[1] to be highly active in the inhibition of smooth muscle cell growth which is a pivotal process in the development of arteriosclerotic lesions.[2] Unlike the polysaccharide heparin, Trestatin A sulfate exhibited no antithrombin III mediated anticoagulant properties. To investigate the biological properties of even smaller compounds, Trestatin A tri-, tetra-, and pentasaccharide substructures have been prepared, namely 1→4-linked glucosyl,[3] maltosyl, and maltotriosyl[4] trehaloses. Substituting maltose by sophorose (2-*O*-β-D-glucopyranosyl-D-glucose), two isomeric sophorosyl trehalose tetrasaccharides were synthesized.[5] Here we describe the syntheses of 2-deoxy-2-*C*-glucosyl-glucose derivatives and their coupling to trehalose affording analogous trehalose tetrasaccharides together with conformational analyses of the compounds by NMR spectroscopy.



1 R = SO_3Na or H

RESULTS AND DISCUSSION

Tri-*O*-acetyl-D-glucal (**2**) and 4,6-di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enopyranose (**3**) had been described by Baer and Defaye and collaborators[6] to yield mainly 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**4**) and 1,3,4,6-tetra-*O*-acetyl-2-*C*- (4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl) -2-deoxy-β-D-glucopyranose (**5**) upon treatment with boron trifluoride etherate in benzene. We have reanalyzed that reaction substituting benzene with the less toxic toluene. Crystallization of the crude product furnished some *C*-glycoside **5** (3.5%). Chromatography revealed that disaccharide **4** was the main product (33% isolated yield), next the hitherto unknown 4,6-di-*O*-acetyl-



Scheme 1

5-*O*- (4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl) -*aldehydo*-2,3-dideoxy-D-*erythro*-*E*-hex-2-enose (7) was isolated as a syrup. Subsequent fractions contained β-acetate 5 along with its α-D-anomer which had very similar chromatographic properties and was difficult to purify by crystallization.

The structure of compound 7 was determined with the help of NMR, IR, and mass spectra. The presence of a free aldehyde was evident from the absorptions in the IR spectrum (2739 and 1699 cm^{-1}) and the aldehyde proton in the NMR spectrum (δ = 9.60 ppm). The expected α-D-linkage at the pseudoglucal was confirmed by a steady state NOE experiment: upon saturation of H-1' no clear NOE for H-5' was detected in the region of 4.3-4.1 ppm as would have been expected for a β-substituted pseudoglucal.

Instead, only a weak NOE was observed at a signal without any large coupling constant which cannot be H-5' since $J_{4',5'}$ = 9.5 Hz. It had been described by Fraser-Reid and Radatus[7] that pseudoglucal **3** in water/dioxane is in equilibrium with 4,6-di-*O*-acetyl-*aldehydo*-2,3-dideoxy-D-*erythro*-*E*-hex-2-enose (**6**) which could not be isolated but trapped as its acetate. It can be assumed that **6** was also present under our reaction conditions; thus, the formation of the *aldehydo* derivative **7** may be explained by an attack of the C-5 hydroxyl group of **6** at the double bond of glucal **2**.

The configuration and conformation of *C*-glycoside **5** had been determined by Ferrier and Prasad[8] in 1969. The quasi-axial orientation of H-1' had been deduced from ^{1}H NMR data, and the possibility of an allylic inversion at C-4' resulting in a β-D-*threo* configuration had been discarded based on chemical evidence and optical rotations. In the meantime it has become evident that the $J_{1,2}$ coupling constant is not a reliable predictor for the anomeric configuration of pseudoglycal *C*-glycopyranosides and, moreover, the Hudson isorotation rules[9] may be violated.[10] We have, therefore, thoroughly investigated by ^{1}H NMR spectroscopy the known[8] saturated *C*-glycoside **8**, obtained by hydrogenation of **5** in benzene in 89% yield together with the hydrogenolyzed product **9** (6.3%). As in previous cases[3-5] the assignment of the spectrum was essentially achieved by some 1D TOCSY experiments.

In a first set of experiments with **8** the doublet signal of H-1 showing one large diaxial coupling was inverted by a selective 180° pulse, provided by a DANTE pulse sequence. By a subsequent spin-locking MLEV-17 sequence magnetization was transferred from H-1 to its spin-coupled neighbours depending on the duration of the applied spin-locking period and the magnitude of the spin-couplings involved. In the difference spectrum with selective excitation on-resonance and off-resonance the signals of only those protons are observed (in addition to the excited one) that are attributed to the spin-coupled neighbours. Thus, with only 30 ms spin-locking duration, additional signals of the first two neighbours became visible, namely of H-2 at 2.05 ppm, appearing as a triplet of doublets with two large couplings ($J_{1,2}$ and $J_{2,3}$) and a small one ($J_{1',2}$), and of H-3 at 5.33 ppm observed as a triplet with two large couplings ($J_{2,3}$ and $J_{3,4}$). It is important to note that H-2 is hardly visible in the normal 1D spectrum due to the presence of the strong signals of the acetyl groups. In further experiments with increasing spin-locking duration (60, 120, and 240 ms) the signals of the remaining protons appeared

in the expected sequence, namely H-4, H-5 and H-6a,6b. It is noteworthy, that the transfer of magnetization between the two rings is relatively weak due to the small value of the coupling $J_{1',2} \approx 2$ Hz. Correspondingly, the signal of H-1' is only clearly detectable in the experiment with longest duration of the spin-locking. In a fully analogous set of 1D TOCSY experiments with excitation of H-1' the signals of the C-glycosidic pyranose ring were assigned, and the hidden signal of H-2'ax could be identified at 2.06 ppm. As a result it is concluded that protons H-1 to H-5 are all axially oriented and that the same is also true for H-1' in the second ring. In a 1D ROESY experiment, selective excitation of H-1 resulted, as expected, in strong ROEs at axial protons H-3 and H-5.

The crucial question whether the configuration is α-D-*erythro* or β-D-*threo* (i.e., whether H-5' is in equatorial or axial position) was answered by a 1D ROESY experiment. Upon selective inversion of the magnetization of H-1' no ROE was observed at H-5', however, strong effects were seen at H-6a', H-2'eq and H-3'ax. This proved that H-5' is oriented equatorially, and hence the configuration is α-D-*erythro* . In the same experiment inter-ring ROEs were observed at H-1, H-3, H-4, and possibly at H-2, the signal of which was partly obscured by some difference artefacts of the strong acetyl signals.

These results confirm the postulated[8] structure of C-glycoside **5**, as well as the rule by Casiraghi et al.[10] that for 2,3-unsaturated C-glucopyranosides a small vicinal coupling constant between H-5 and H-4 is diagnostic for an α-D-anomeric configuration (for **5** $J_{4',5'} \approx 1$ Hz). Furthermore, these data mean that the C-glycosidic pyranose ring of **8** is in the $^1C_4$ conformation with axial substituents at C-4' and C-5'. Molecular modelling calculations with compound **8** predict that the 'normal' $^4C_1$ conformation is disfavoured for steric reasons, the energy difference between both conformers was estimated to be 3 kcal/mol.[11] The presence of a reverse anomeric effect[8,12] favouring the equatorial position of the anomeric C-bonded substituent is therefore difficult to judge in this example. Also in the unsaturated glycoside **5**, the quasi-axial orientation of the C-4' acetate is likely to be determined by steric effects rather than the "allylic effect".[13]

The spectral characteristics of pentaacetate **9** are similar to those of hexaacetate **8**, especially, the $J_{1',2'ax}$ coupling constant is large (10.5 Hz). Since an anomerization in the course of the hydrogenolysis is not likely, this suggests the presence of a $^1C_4$ conformation with an axial substituent at C-5 of

the C-bonded pyranose ring. The slightly lower value of $J_{1',2'ax}$ compared to **8** may be explained by a higher flexibility of the pyranose ring due to the removal of one acetoxy group. These results indicate that the 4'-acetate does not play a major role in the conformational equilibrium of this pyranose ring and does not sterically interact with the reducing-end pyranose.

We also thoroughly investigated the α-D-anomeric acetate **10**, which could be obtained by hydrogenation of the crude α-D-anomeric analogue of C-glycoside **5**.[8] As before, the ^{1}H NMR assignments were supported by two sets of 1D TOCSY experiments starting from H-1 and from H-1'with spin-locks of 30, 60, 90, 120, 240, and 360 ms duration. A pulsed field z-gradient (PFG) 2D COSY provided further information on the sequence of coupled protons. A large coupling constant $J_{1',2'ax}$ = 8.5 Hz was found for **10**, which is, however, distinctly smaller than that of **8** ($J_{1',2'ax}$ = 11.8 Hz). Accordingly, small coupling constants (all in the range of 4 Hz) were measured for the equatorially oriented proton H-4' of **10**, which are in this case greater than those of **8** . Information on the spatial proximity of protons of compound **10** was derived from three 1D T-ROESY experiments (irradiation of H-1, H-2 and H-1'). As for **8**, the latter experiment did not clearly reveal any ROE between H-1' and H-5', possibly since the chemical shifts of these protons are relatively close (Δ = 0.11 ppm). However, a subsequent 2D T-ROESY experiment did not detect an ROE, either. From these results it can be concluded that the C-bonded pyranose of **10**, analogously to **8**, exists in a $^1C_4$ conformation, but seems to be under more conformational strain. Already simple molecular models of **10** suggest that the α-D-anomeric acetate imposes more steric hindrance than the β-D-anomer. It is interesting to note that excitation of H-1 resulted in ROEs to H-2, less pronounced to H-2'eq, and weakly to H-1', but also unexpectedly relatively strongly to H-5'. These effects are not fully accounted for by chair conformations of the C-bonded pyranose ring. However, a $^{3,O}B$ boat or related skew conformation would bring H-1 and H-5' close enough together to explain the observed ROE, and this conformation would be in accordance with a relatively large coupling constant $J_{2,1'}$ = 7.0 Hz as found for **10** .

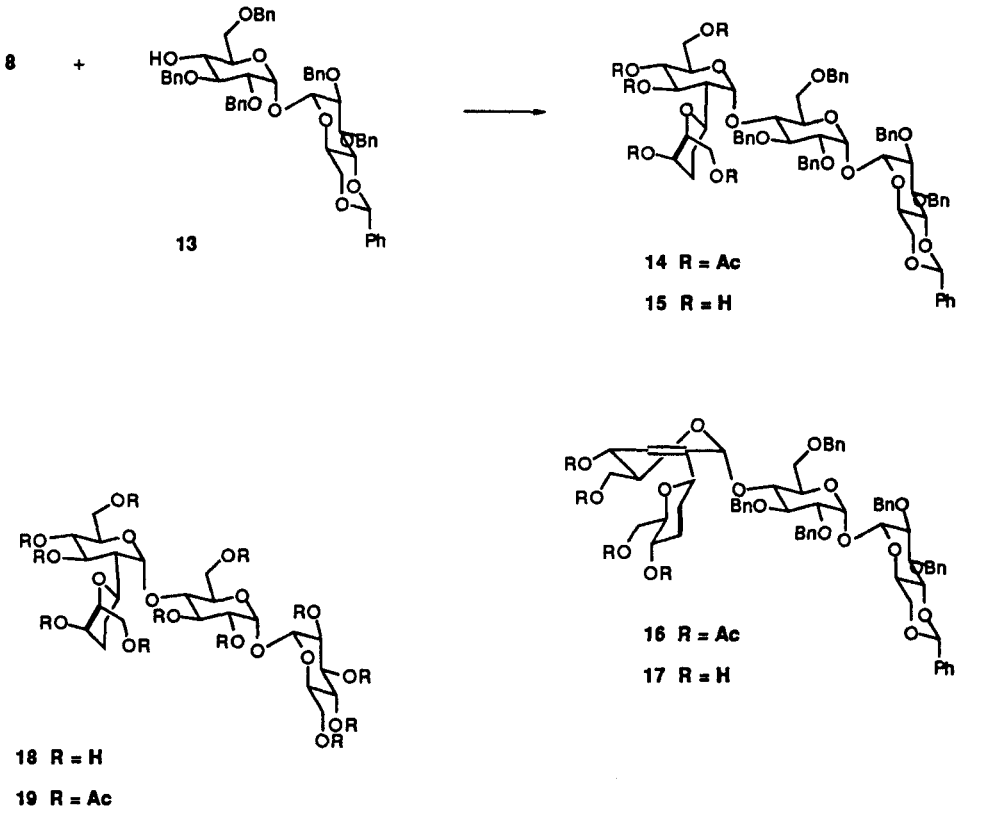
To prepare a glycosyl donor for Koenigs-Knorr glycosidations, **8** and **9**, respectively, were treated with hydrogen bromide/acetic acid in dichloromethane at low temperature. From the reaction with **8** a fraction was isolated which gave a mass spectrum of a bromide (*m/z* 524/526 for [M + NH_4 - AcOH]$^+$) but the compound decomposed under NMR conditions. The main

products isolated in brominations of **8** and **9** were the hemiacetals **11** and **12**. For **11**, the $J_{1',2'ax}$ coupling constant is large again. It seems that the removal of the α-D-anomeric acetate leads to a relief of steric constraints, so that in the C-glycosidic pyranose the $^1C_4$ chair conformation can largely prevail.

Esters are also known to be suitable leaving groups in the presence of Lewis acids.[14] With trimethylsilyl trifluromethylsulfonate (TMS triflate) as promoter β-D-anomeric esters were reactive enough to glycosylate secondary hydroxyl groups[15] so that disaccharide acetate **8** was investigated as a glycosyl donor. Reaction of **8** with the well-established[3,4,16] trehalose glycosyl acceptor 2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl 2,3-di-*O*-benzyl-4,6-(*R*)-*O*-benzylidene-α-D-glucopyranoside (**13**) afforded mainly tetrasaccharide **14** in slightly impure form. It was, therefore, purified and characterized as compound **15** after deacetylation. As a by-product in the glycosylation reaction the unsaturated tetrasaccharide **16** was isolated in 12% yield.

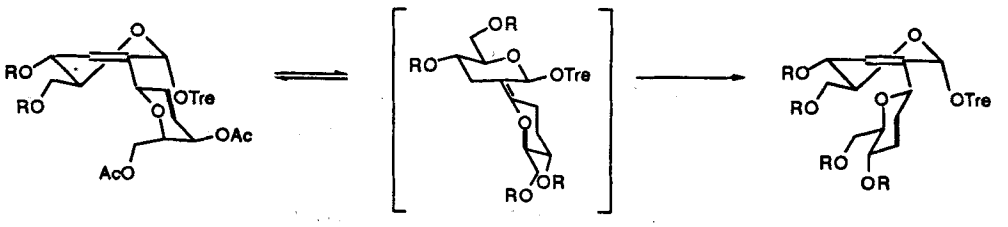
The ^1H NMR spectrum of **15** in DMSO-d_6 indicated the α-D-linkage of the newly formed glycosidic bond (H-1'' at 5.63 ppm, $J_{1'',2''}$ = 2.9 Hz). The spectrum could not be completely assigned although some 1D TOCSY experiments (selective inversion of H-1'', H-1, H-1' and of H-2''), a PFG 2D COSY, and a 2D T-ROESY experiment were performed to disentangle the in parts strongly overlapping spectrum. In addition, some of the signals were obscured by the water signal near 3.33 ppm. The hydroxyl protons were partly identified upon addition of some D_2O. Unfortunately, this shifted the remaining H_2O signal downfield to about 3.6 ppm hiding several signals in this crowded region. Thus, protons H-1 through H-6a,b, H-1' through H-6'a,b, H-1'' through H-4'', and H-1''' through H-4''' and most of the OH signals were identified. H-4''' was located near 3.4 ppm and seemed not to exhibit any large couplings as evidenced from corresponding cross peaks in the 2D spectra. This is in accordance with the expected $^1C_4$ conformation. Definite proof for this conformation is given below after further transformation of the compound.

Usually, anomeric esters with participating neighbouring groups have been employed in glycosylation reactions to guarantee the stereochemical course of the reaction. We found exclusive formation of α-D-glycoside in the presence of a non-participating *C*-glycoside at C-2. This complete stereoselectivity without a directing substituent is remarkable although some α/β-selectivity had been been observed in the presence of a strong catalyst such as TMS triflate.[17]



Scheme 2

The unsaturated nature of tetrasaccharide **16** was obvious from the molecular ion in the mass spectrum as well as the pronounced down-field shift and the multiplicity of H-3'' in the ^{1}H NMR spectrum. Moreover, in the ^{13}C spectrum, C-2'' and C-3'' were assigned at 139.93 and 122.50 ppm, respectively. The complete interpretation of the ^{1}H spectrum was possible with the help of 1D TOCSY experiments. In particular, a large coupling constant $J_{4'',5''}$ = 9.7 Hz indicated the presence of a $^{O}H_5$ half-chair conformation for the hex-2-enopyranosyl ring. Assignments in the trehalose moiety of the tetrasaccharide were made after excitations of H-1/H-1' and H-5'. The stereochemistry of the newly formed glycosidic bond was determined in a 2D T-ROESY experiment which showed strong cross peaks between H-1'' and H-4', but not with H-5'', thus demonstrating the quasi-equatorial position of H-1''. The large coupling constants $J_{4''',5'''}$ = 10.0 Hz and $J_{1''',2'''ax}$ = 10 Hz were indicative of a β-D-linked 2,3-dideoxy-D-*erythro*-hexopyranosyl ring in the normal $^4C_1$ conformation.



Scheme 3

Similar results were found for compound **17** which was obtained by deacetylation of **16** and also was thoroughly investigated using 1D TOCSY and T-ROESY experiments. Unexpectedly, a change of configuration at C-1''' had occurred in **16** and **17** with respect to **8** (and **14** and **15**). As described above, the α-D-linked 2,3-dideoxy-D-*erythro*-hexopyranosyl ring is forced into an energetically unfavoured $^1C_4$ conformation. It should, therefore, have a tendency to isomerize to the β-D-configuration which can occur in the more stable $^4C_1$ conformation. No saturated analogue of tetrasaccharide **15** with inverted configuration could be isolated. It is thus suggested that the isomerization had happened during or after the elimination of acetic acid as depicted in Scheme 3.

Finally, tetrasaccharide **15** was hydrogenolyzed in the presence of palladium-on-carbon to furnish the completely deblocked tetrasaccharide **18**, the *C*-linked analogue to the sophorosyl trehalose described earlier.[5] To facilitate the spectroscopic characterization, **18** was converted to its peracetate **19** by standard acetylation.

Tetrasaccharide **19** was fully analyzed by NMR spectroscopy. Most signals could be assigned from the 1D TOCSY spectra. With the help of a COSY spectrum, only one 1D TOCSY experiment per pyranose ring was necessary. The COSY spectrum indicated the shift of H-5; the shifts of H-6b, H-2''', and H-3''' were taken from the hetero-COSY spectrum. H-1''' is seen to be axially oriented, whereas H-4''' and H-5''' are in equatorial position. The *C*-linked pyranose is thus α-D-linked and exists in the $^1C_4$ conformation.

EXPERIMENTAL

General Procedures. Solvents and reagents were bought from Fluka. Evaporation: *in vacuo*, conducted with Büchi rotary evaporator. TLC: precoated silica gel 60F-254 plates (Merck), detection by UV light (254 nm) and

spraying with a 10% solution of concentrated sulfuric acid in methanol followed by heating. Melting points were determined with a Büchi Model 510 capillary apparatus and are uncorrected. Specific rotations: Perkin-Elmer Polarimeter 241, measured at 20 °C. IR: Nicolet 7199 FT-IR spectrophotometer. MS: MS 902 (FAB) with data system DS 2050 (VG), VG 7070 F (CI) with data system SS 300, and MS 9 updated with Finnigan ZAB console, data system SS 200, VG Altrichem (EI: 70eV). ^{1}H NMR: Bruker AC 250 (250 MHz), AM-400 (400 MHz) with Aspect 3000, ARX-400 (400 MHz) with ASPECT 1 station and z-gradient accessory kit with 10 Amps power amplifier for pulsed field z-gradient (PFG) experiments, AMX2-600 (600 MHz) with ASPECT 1 station; chemical shifts in ppm relative to tetramethylsilane or sodium 2,2,3,3-tetradeutero-3-(trimethylsilyl)-propionate as internal standard; standard Bruker pulse programs were applied except for the 1D TOCSY, 1D ROESY with 'chopped' 90° spin-lock, and 1D and 2D T-ROESY[18] with ($180°_x$ - $180°_{-x}$)n spin-lock of 0.6 s duration (n=2400); selective excitation was achieved by a sequence of DANTE pulses; all experimental details were essentially as described before.[3,19]

4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl 4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (4), 1,3,4,6-Tetra-*O*-acetyl-2-*C*-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-2-deoxy-β-D-glucopyranose (5), and 4,6-Di-*O*-acetyl-5-*O*-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-*aldehydo*-2,3-dideoxy-D-*erythro*-*E*-hex-2-enose (7). Glucal **2** (80.0 g, 0.29 mol) was reacted with pure **3** (75.4 g, 0.327 mol, prepared from 90.0 g of **2** and purified by filtration through silica gel) in the presence of BF_3 etherate (20 mL) according to ref. 6, but employing toluene as solvent. From the crude product mixture pure **5** (5.5 g, 3.5%) was obtained by crystallisation from ethyl acetate/hexane. The filtrate was chromatographed on silica gel (ethyl acetate/hexane 1:3 → 1:1). Six fractions were collected, the first consisting of pure **4** (37.6 g, 33%). The second fraction (6.58 g) consisted of slightly impure **4**. After a mixed fraction, fraction four consisted of **7** (14.1 g, 11%). Crystallizations of fraction five (23.7 g), containing some **7** and mainly **5** and its α-anomeric isomer, furnished **5** (5.64 g, containing ca. 10% α-anomer) and crystals of mainly α-anomer of **5** (1.78 g). Fraction six consisted of a mixture of **5** and its α-D-anomeric acetate.

4: Colourless crystals from ethyl acetate/hexane, mp 73.9-74.4 °C (ref. 6: mp 68-69 °C, 69-70 °C, or 73.5-74 °C depending on the mode of crystallization;

ref. 20: mp 68-72 °C); ^{1}H NMR data ($CDCl_3$, 250 MHz) were in accordance with ref. 6.

5: Colourless crystals from ethyl acetate/hexane, mp 205-206 °C (ref. 6: mp 206 °C); ^{1}H NMR ($CDCl_3$, 250 MHz; H,H-COSY) δ 6.02 (dd, $J_{2',3'}$ = 10.8 Hz, $J_{1',2'}$ = 1.8 Hz, $J_{2',4'}$ < 0.5 Hz, H-2'), 5.92 (d, $J_{1,2}$ = 9.0 Hz, H-1), 5.88 (dddd, $J_{1',3'}$ = 2.5 Hz, $J_{3',4'}$ = 5.8 Hz, $J_{3',5'}$ = 0.8 Hz, strong cross-peak in H,H-COSY, H-3'), 5.45 (dd, $J_{2,3}$ = 11.0 Hz, $J_{3,4}$ = 9.0 Hz, H-3), 5.01 (dd ~ t, $J_{4,5}$ = 10.8 Hz, H-4), 4.78 (ddd ~ br d, $J_{4',5'}$ ≈ 1 Hz, $J_{1',4'}$ ≈ 1 Hz, H-4'), 4.50 (dd, $J_{5',6a'}$ = 9.9 Hz, $J_{6a',6b'}$ = 12.0 Hz, H-6a'), 4.35 ($J_{5,6a}$ = 4.2 Hz, $J_{6a,6b}$ 12.8 = Hz, H-6a), 4.33 (ddd ~ d, H-1'), 4.20 (ddd ~ dd, $J_{5',6b'}$ = 3.5 Hz, H-5'), 4.05 (dd, $J_{5,6b}$ = 2.1 Hz, H-6b), 3.80 (ddd, H-5), 3.79 (dd, H-6b'), 2.21 (ddd, $J_{1',2}$ = 1.5 Hz, H-2), 2.09 (s, 6H, OAc), 2.08, 2.07 (2s, OAc), 2.02 (s, 6H, OAc).

7: Syrup, $[\alpha]_D$ +66.5° (*c* 0.2, dioxane); IR (film) 2739 (CHO), 1742 (br, C=O ester), 1699 (C=O aldehyde), 1290, 1098 (ester); MS (CI) *m/z* 460 (100%, $[M + NH_4]^+$); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 9.60 (d, $J_{1,2}$ = 7.6 Hz, H-1), 6.79 (dd, $J_{2,3}$ = 16.0 Hz, $J_{3,4}$ = 5.0 Hz, H-3), 6.29 (ddd, $J_{2,4}$ = 1.6 Hz, H-2), 5.95 (ddd ~ br d, $J_{2',3'}$ = 10.0 Hz, $J_{1',2'}$ ≈ 1.5 Hz, H-2'), 5.80 (m_c, H-3'), 4.79 (ddd, $J_{4,5}$ = 8.4 Hz, H-4), 5.32 (ddd, $J_{4,5}$ = 9.5 Hz, $J_{3,4}$ = 3.5 Hz, $J_{2,4}$ = 1.5 Hz, H-4'), 5.23 (dd ~ br d, H-1'), 4.30 - 4.09 (m, 6H, H-5, H-5', H-6, H-6'), 2.15, 2.11, 2.10, 2.09 (4s, OAc).

Anal. Calcd for $C_{20}H_{26}O_{11}$: C, 54.30; H, 5.92. Found: C, 54.56; H, 5.97.

1,3,4,6-Tetra-*O*-acetyl-2 - *C* - (4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hexopyranosyl)-2-deoxy-β-D-glucopyranose (8): Colourless crystals, mp 102 °C (ref. 8: mp 95-96 °C); ^{1}H NMR ($CDCl_3$, 400 MHz; 1D TOCSY, 1D ROESY) δ 5.98 (d, $J_{1,2}$ = 8.4 Hz, H-1), 5.33 (dd, $J_{2,3}$ = 10.3 Hz, H-3), 5.02 (dd ~ t, $J_{3,4}$ = 9.0 Hz, H-4), 4.75 (br s, H-4'), 4.32 (dd, $J_{6a,6b}$ = 12.4 Hz, H-6a), 4.30 (dd, $J_{5',6a'}$ = 7.0 Hz, $J_{6a',6b'}$ = 11.0 Hz, H-6a'), 4.07 (dd, H-6b; ddd ~ br t, H-5'), 4.02 (dd, $J_{5',6b'}$ = 5.5 Hz, H-6b'), 3.80 (ddd, $J_{4,5}$ = 9.9 Hz, $J_{5,6a}$ = 4.9 Hz, $J_{5,6b}$ = 2.2 Hz, H-5), 3.67 (ddd ~ br d, $J_{1',2'ax}$ = 11.8 Hz, $J_{1',2'eq}$ ≈ 2.5 Hz, $J_{1',2}$ ≈ 2 Hz, H-1'), 2.18, 2.11, 2.074, 2.067, 2.03, 2.02 (6s, OAc), 2.06 (~ dddd, H-2'ax), 2.05 (ddd ~ dt, H-2), 1.90 (dddd ~ dq, $J_{3'eq,3'ax}$ = 14.5 Hz, H-3'eq), 1.79 (m_c, $J_{2'ax,3'ax}$ = 13.0 Hz, $J_{3'ax,4'}$ ≈ 3.5 Hz, H-3'ax), 1.36 (dddd ~ dq, $J_{2'eq,2'ax}$ = 13.5 Hz, $J_{2'eq,3'ax}$ ≈ 3.5 Hz, $J_{2'eq,3'eq}$ ≈ 3 Hz, H-2'eq); ^{13}C NMR ($CDCl_3$, 100 MHz; ^{1}H-detected one-bond ^{1}H,^{13}C 2D COSY) δ 170.99, 170.69, 170.25, 169.98, 169.94, 168.26 (6 C=O), 91.64 (C-1), 73.59 (C-5'), 72.16 (C-5), 70.61 (C-3), 69.28 (C-4), 66.70 (C-1', C-4'), 62.04 (C-6), 60.74 (C-6'), 48.06 (C-2), 24.42 (C-3'), 23.51 (C-2'), 21.28, 21.08, 20.83, 20.76 (4 Ac), 20.70 (2 Ac).

1,3,4,6-Tetra-*O*-acetyl-2 - *C* - (6-*O*-acetyl-2,3,4-trideoxy-α-D-*erythro*-hexopyranosyl)-2-deoxy-β-D-glucopyranose (9). Colourless crystals, mp 123 °C (ref. 8: mp 118-9 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.95 (d, $J_{1,2}$ = 7.8 Hz, H-1), 5.31 (dd ~ t, $J_{2,3}$ = 9.7 Hz, H-3), 5.03 (dd ~ t, $J_{3,4}$ = 9.2 Hz, H-4), 4.33 (dd, $J_{5',6a'}$ = 6.0 Hz, H-6a'), 4.31 (dd, H-6a), 4.10 (dddd, H-5'), 4.06 (dd, $J_{6a,6b}$ = 12.5 Hz, H-6b), 3.95 (dd, $J_{5',6b'}$ = 5.0 Hz, $J_{6a',6b'}$ = 12.0 Hz, H-6b'), 3.81 (ddd, $J_{4,5}$ = 9.8 Hz, $J_{5,6a}$ = 5.0 Hz, $J_{5,6b}$ = 2.2 Hz, H-6b), 3.65 (br d, $J_{1',2'ax}$ = 10.5 Hz, H-1'), 2.16, 2.11, 2.07, 2.03, 2.01 (5s, OAc), 2.03 (m, H-2), 1.69 - 1.56 (6H, H-2',3',4').

1,3,4,6-Tetra-*O*-acetyl- 2 -*C* - (4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hexopyranosyl)-2-deoxy-α-D-glucopyranose (10): Colourless crystals, mp 180 °C (ref. 8: mp 177-8 °C); ^{1}H NMR ($CDCl_3$, 400 MHz; 1D TOCSY, 1D T-ROESY, z-PFG H,H 2D COSY) δ 6.43 (d, $J_{1,2}$ = 3.3 Hz, H-1), 5.49 (dd, $J_{2,3}$ = 11.2 Hz, $J_{3,4}$ = 9.2 Hz, H-3), 5.05 (dd ~ t, $J_{4,5}$ ≈10 Hz, H-4), 4.72 (ddd ~ q, $J_{3'ax,4'}$ + $J_{3'eq,4'}$ ≈ 8 Hz, H-4'), 4.32 (dd, $J_{5,6a}$ = 3.8 Hz, H-6a), 4.13 (dd, $J_{5',6a'}$ = 7.0 Hz, $J_{6a',6b'}$ = 11.5 Hz, H-6a'), 4.08 (dd, $J_{5',6b'}$ = 4.5 Hz, H-6b'), 4.06 (ddd ~ br t, H-5), 4.03 (dd, $J_{5,6b}$ = 2.4 Hz, H-6b), 3.93 (ddd ~ dt, $J_{4',5'}$ ≈ 4.0 Hz), 3.82 (ddd, $J_{1',2'ax}$ = 8.5 Hz, $J_{1',2'eq}$ = 3.5 Hz, H-1'), 2.40 (ddd, $J_{2,1'}$ = 7.0 Hz, H-2), 2.14, 2.10, 2.09, 2.08, 2.029, 2.028 (6s, OAc), 1.89 - 1.82 (2H, H-3'), 1.76 (dddd, $J_{2'ax,3'eq}$ = 5.0 Hz, H-2'ax), 1.49 (m, H-2'eq); ^{13}C NMR ($CDCl_3$, 100 MHz; ^{1}H-detected one-bond and long-range ^{1}H,^{13}C 2D COSY) δ 170.93, 170.64 (2C, C=O), 170.21 (2C, C=O), 169.89, 168.44 (2C, C=O), 90.91 (C-1), 73.14 (C-5'), 69.70 (C-4), 69.56 (C-3), 69.31 (C-5), 68.85 (C-1'), 67.10 (C-4'), 61.93 (c-6), 61.73 (C-6'), 45.64 (C-2), 24.28 (C-3'), 24.03 (C-2'), 21.08, 21.00, 20.92 (3C, Ac), 20.72 (2C, Ac), 20.65 (Ac).

3,4,6-Tri-*O*-acetyl-2 - *C*- (4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hexopyranosyl)-2-deoxy-α-D-glucopyranose (11). A solution of **8** (490 mg, 0.9 mmol) in dry dichloromethane (1 mL) was treated with HBr/acetic acid (3 mL). After 3 h at 0 °C the reaction mixture was poured into ice/water and extracted with dichloromethane. The organic solution was washed with ice/bicarbonate solution and water, dried over magnesium sulfate, concentrated, and the residue chromatographed over silica gel (ethyl acetate/hexane 2:1) to give **11** as mainly α-anomer. Colourless syrup, MS (CI) *m/z* 522 (100%, $[M + NH_4]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.56 (dd, $J_{2,3}$ = 11.8 Hz, $J_{3,4}$ = 9.0 Hz, H-3), 5.55 (dd ~ br d, $J_{1,2}$ ≈ 3.5 Hz, H-1), 5.00 (dd ~ t, $J_{4,5}$ = 10.9 Hz, H-4), 4.81 (ddd ~ br s, ΣJ ≈ 7 Hz, H-4'), 4.52 (d, $J_{1,1\text{-OH}}$ = 1.8 Hz, 1-OH), 4.37 (dd, $J_{5,6a}$ = 4.5 Hz, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.34 (dd, $J_{5',6a'}$ = 8.0 Hz, H-6a), 4.32 (ddd, H-5), 4.17 (ddd ~ br t, $J_{4',5'}$ ≈ 1.5 Hz, H-5'), 4.06 (dd, $J_{5,6b}$ = 1.8 Hz, $J_{6a,6b}$ = 12.0 Hz, H-6b), 4.02 (dd, $J_{5',6b'}$ = 5.0 Hz, $J_{6a',6b'}$ = 12.0 Hz, H-6b'), 3.94 (ddd ~ dt, $J_{1',2'ax}$ = 11.5 Hz,

$J_{1',2'eq} + J_{1',2}$ = 5.5 Hz, H-1'), 2.113, 2.110, 2.08, 2.03, 2.02 (5s, OAc), 2.08 - 1.80 (m, 3H), 1.50 (m_c, 1H).

Anal. Calcd for $C_{22}H_{32}O_{13}$: C, 52.38; H, 6.39. Found: C, 52.22; H, 6.45.

3,4,6 - Tri - *O* - acetyl - 2-*C* - (6 -*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hexopyranosyl)-2-deoxy-α-D-glucopyranose (12). A solution of **9** (100 mg, 0.2 mmol) in dry dichloromethane (0.2 mL) was treated with HBr/acetic acid (0.6 mL). After 0.5 h at 0 °C the reaction mixture was worked up as described for **11**. Chromatography using ethyl acetate/hexane 1:1 as eluent furnished **12** (27 mg, 30%) as a syrup, MS (FAB) *m/z* 464 (100%, $[M + NH_4]^+$), 404 (70%, $[M + NH_4 - AcOH]^+$); ^1H NMR ($CDCl_3$, 400 MHz) δ 5.54 (dd, $J_{2,3}$ = 11.3 Hz, H-3), 5.51 (d, $J_{1,2} \approx 3.2$ Hz, H-1), 4.72 (br s, OH-1), 3.39 (dd, $J_{5',6'a}$ = 8.7 Hz, H-6a'), 3.37 (dd, H-6a), 4.32 (ddd, $J_{4,5}$ = 10.0 Hz, $J_{5,6a}$ = 4.0 Hz, H-5), 4.24 (dddd, $J_{4'eq,5'} + J_{4'ax,5'} \approx 8$ Hz, H-5'), 4.06 (dd, $J_{6a,6b}$ = 12.0 Hz, H-6b), 3.94 (dd, $J_{5',6b'}$ = 4.0 Hz, $J_{6a',6b'}$ = 12.0 Hz, H-6b'), 3.89 (ddd ~ dt, $J_{1',2'ax}$ = 10.0 Hz, $J_{2,1'} \approx 3$ Hz, H-1'), 2.11, 2.09 (2s, OAc), 2.05 (ddd ~ dt, H-2), 2.02 (s, 6H, OAc), 1.85 - 1.55 (m, 6H, H-2',3',4').

Anal. Calcd for $C_{20}H_{30}O_{11}$: C, 53.81; H, 6.77. Found: C, 53.69; H, 6.81.

2,3,6-Tri-*O*-benzyl-4-*O*-[4,6-di-*O*-acetyl-2,3-dideoxy-2-*C*-(4,6-di-*O*-acetyl-2,3-dideoxy-β-D-*erythro*-hexopyranosyl)-α-D -*erythro*- hex -2-enopyranosyl] -α - D-glucopyranosyl 2,3-Di-*O*-benzyl-4,6-(*R*)-*O*-benzylidene-α-D-glucopyranoside (16). A solution of well-dried glycosyl donor **8** (1.638 g, 3.0 mmol) and glycosyl acceptor **13** (2.643 g, 3.0 mmol) in absolute dichloromethane (9 mL) was stirred for 1 h at room temperature in the presence of molecular sieves. A solution of trimethylsilyl triflate (180 mL) in absolute dichloromethane (1 mL) was added dropwise at -20 °C. The reaction mixture was stirred for 1 h at -20 °C and then was allowed to reach room temperature. After 1 h at ambient temperature the solution was poured into ice/bicarbonate solution and extracted with ethyl acetate. The organic phases were washed with water, dried over sodium sulfate, and concentrated. The residue was chromatographed on silica gel using toluene/ethyl acetate as eluent to recover unchanged **13** (480 mg, 18%). Then, pure unsaturated tetrasaccharide **16** (480 mg, 12%) was obtained, followed by an impure fraction (1.81 g, ca. 44%) consisting mainly of tetrasaccharide **14**.

16: $[\alpha]_D$ +80.0° (*c* 0.2, dioxane); MS (FAB) *m/z* 1307 (100%, $[M + H]^+$), 1329.7 (80%, $[M + Na]^+$); ^1H NMR ($CDCl_3$, 400 MHz; 1D TOCSY; 1D and 2D T-ROESY) δ 7.51 - 7.49 (m, 2H, aromat), 7.40 - 7.38 (m, 5H, aromat), 7.33 - 7.21 (m, 23H, aromat), 5.87 (~ br s, $J_{3'',4''} \approx 2.5$ Hz, H-3''), 5.57 (s, -CHPh), 5.48 (br s,

$J_{1'',3''} \approx 1.5$ Hz, H-1''), 5.29 (d, $J_{1,2} = 3.9$ Hz, H-1; dd ~ br d, $J_{4'',5''} = 9.7$ Hz, H-4''), 5.28, 4.66 (2 d, J = 12.3 Hz, 3'-OCH_2Ph), 5.26 (d, $J_{1',2'} \approx 4$ Hz, H-1'), 4.98, 4.87 (2 d, J = 11.5 Hz, 3-OCH_2Ph), 4.82, 4.78 (2 d, J = 12.0 Hz, 2-OCH_2Ph), 4.67, 4.54 (2 d, J = 11.5 Hz, 2'-OCH_2Ph), 4.55, 4.46 (2 d, J = 12.2 Hz, 6'-OCH_2Ph), 4.55 (ddd ~ dt, $J_{3'''eq,4'''} = 4.5$ Hz, $J_{3'''ax,4'''} \approx 11$ Hz, H-4'''), 4.27 (ddd, $J_{5',6a'} = 2.5$ Hz, $J_{5',6b'} = 5.5$ Hz, H-5'), 4.21 (ddd ~ dt, $J_{5,6a} = 4.4$ Hz, H-5), 4.18 (dd ~ t, $J_{3,4} = 8.8$ Hz, H-3), 4.15 (dd, H-6a'''), 4.13 (dd, $J_{6a,6b} = 9.8$ Hz, H-6a), 4.11 (dd ~ t, $J_{3',4'} \approx 8.6$ Hz, H-3'), 4.10 (dd, H-6b'''), 4.06 (dd, $J_{5'',6a''} = 4.0$ Hz, $J_{6a'',6b''} = 12.0$ Hz, H-6a''), 3.90 (dd, H-6b''), 3.88 (dd ~ t, $J_{4',5'} = 9.8$ Hz, H-4'), 3.87 (dd ~ br d, $J_{1''',2'''ax} \approx 10$ Hz, H-1'''), 3.73 (ddd, $J_{5'',6b''} = 2.4$ Hz, H-5''), 3.69 (dd ~ t, $J_{5,6b} \approx 10$ Hz, H-6b), 3.68 (dd, $J_{2',3'} = 9.6$ Hz, H-2'), 3.67 (dd ~ t, $J_{4,5} \approx 10$ Hz, H-4), 3.63 (dd, $J_{2,3} = 9.6$ Hz, H-2), 3.58 (dd, H-6a'), 3.55 (dd, $J_{6a',6b'}$ 10.0 Hz, H-6b'), 3.47 (ddd, $J_{4''',5'''} = 10.0$ Hz, $J_{5''',6a'''} = 4.5$ Hz, $J_{5''',6b'''} = 2.5$ Hz, H-5'''), 2.12, 2.02, 2.00, 1.96 (4s, 12H, OAc), 1.81 (dddd, $J_{3'''eq,3'''ax} = 13.5$ Hz, H-3'''eq), 1.45 (dddd ~ br ddd, $J_{2'''eq,3'''eq} = 1.5$ Hz, $J_{2'''eq,3'''ax} = 3.5$ Hz, H-2'''eq), 1.18 (dddd ~ ddt, H-3'''ax), 1.10 (dddd ~ ddt, $J_{2'''ax,3'''eq} = 3.5$ Hz, $J_{2'''ax,3'''ax} \approx 13$ Hz, $J_{2'''ax,2'''eq} \approx 13$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz; one-bond and long-range $^1H,^{13}C$ 2D COSY) δ 171.01, 170.65, 170.18, 169.91, (4C, C=O), 139.93 (C-2''), 138.82, 138.54, 138.09, 138.05, 137.48, 137.14 (6C, aromat), ca. 128.9-125.63 (aromat), 122.50 (C-3''), 101.20 (C-8), 94.58 (C-1''), 94.30 (C-1), 92.80 (C-1'), 82.34 (C-4), 80.84 (C-3'), 79.60 (C-2'), 78.53 (C-3), 78.45 (C-2), 77.34 (C-5'''), 75.11 (2C, C-1''', 3-OCH_2Ph), 73.65 (C-4), 73.40 (6'-OCH_2Ph), 73.16 (2-OCH_2Ph), 72.97 (3'-OCH_2Ph), 72.77 (2'-OCH_2Ph), 70.38 (C-5'), 69.40 (C-6'), 69.00 (C-6), 67.58 (C-4'''), 66.91 (C-5''), 65.12 (C-4'''), 63.31 (C-6'''), 62.94 (C-5), 62.41 (C-6''), 30.67 (C-2'''), 29.04 (C-3'''), 22.69, 21.11, 21.04, 20.81 (4C, Ac).

Anal. Calcd for $C_{74}H_{82}O_{21}$: C, 67.98; H, 6.32. Found: C, 67.67; H, 6.35.

2,3,6-Tri-*O*-benzyl-4-*O*-[2-deoxy-2-*C*-(2,3-dideoxy-α-D-*erythro*-hexopyranosyl)-α-D-glucopyranosyl]-α-D-glucopyranosyl 2,3-Di-*O*-benzyl-4,6-(*R*)-*O*-benzylidene-α-D-glucopyranoside (15). A part of the slightly impure tetrasaccharide **14** fraction (1.40 g, ~1.02 mmol) was dissolved in methanol (10 mL) and stirred in the presence of a catalytic amount of anhydrous sodium carbonate for 16 h. Then the solution was neutralized with IR 120 (H^+) ion exchange resin and filtered. The filtrate was taken to dryness and chromatographed on silica gel using ethyl acetate/methanol/water 98. : 1 : 0.5 as eluent to furnish 15 (1.005 g, 85%) as a colourless syrup, $[\alpha]_D$ +124.0° (*c* 0.2, dioxane); MS (FAB) *m/z* 1157.5 (10%, $[M + H]^+$), 1179.4 (40%, $[M + Na]^+$, 1195.3 (50%, $[M + K]^+$); ^1H NMR ($CDCl_3$, 400 and 600 MHz; 1D TOCSY, 2D

TOCSY (70 ms spin-lock), 2D ROESY) δ 7.41 - 7.22 (m, 30H, aromat), 5.71 (s, 1H, CHPh), 5.63 (d, $J_{1'',2''}$ = 2.9 Hz, H-1''), 5.33 (d, $J_{1,2}$ = 3.4 Hz, H-1), 5.27 (d, $J_{1',2'}$ = 3.2 Hz, H-1'), 4.88 (d, 4''-OH), 4.87, 4.72 (2d, 2H, CH_2Ph), 4.84, 4.79 (2d, 2H, J_{gem} = 11.5 Hz, CH_2Ph), 4.72, 4.67 (2d, 2H, J_{gem} = 10.8 Hz, CH_2Ph), 4.69, 4.62 (2d, 2H, J_{gem} = 10.8 Hz, CH_2Ph), 4.54 (d, $J_{3'',3''\text{-OH}}$ = 5.5 Hz, 3''-OH), 4.46, 4.38 (2d, 2H, J_{gem} = 12.0 Hz, CH_2Ph), 4.41 (d, $J_{4''',4'''\text{-OH}}$ = 4.4 Hz, 4'''-OH), 4.30 (dd ~ t, ΣJ = 11.8 Hz, 6''-OH), 4.21 (dd, $J_{6a,6b}$ = 10.0 Hz, $J_{5,6a}$ = 4.7 Hz, H-6a), 4.13 (dd ~ t, ΣJ ≈ 11 Hz, 6'''-OH), 4.09 (dd ~ t, $J_{3',4'}$ ≈ 9.0 Hz, H-3'), 4.06 (ddd ~ dt, H-5), 3.99 (dd ~ t, $J_{3,4}$ = 9.0 Hz, H-3), 3.83 (dd ~ t, $J_{4',5'}$ ≈ 9.2 Hz, H-4'), 3.79 (dd ~ t, $J_{5,6b}$ = 10.4 Hz, H-6b), 3.76 (dd ~ t, $J_{4,5}$ ≈ 9.8 Hz, H-4), 3.70 (dd, $J_{2,3}$ = 9.5 Hz, H-2), 3.60 (dd, $J_{2',3'}$ = 10.0 Hz, H-2'), 3.56 (ddd, H-1'''), 3.55 (H-5'), 3.46 (ddd ~ dt, $J_{2'',3''}$ + $J_{3'',4''}$ ≈ 20 Hz, H-3''), 3.46 (H-6a''), 3.43 (H-4'''), 3.40 (H-6b''), 3.34 (ddd ~ dt, $J_{4'',5''}$ ≈ 10 Hz, detectable after addition of a trace of D_2O, H-5''), 3.17 (ddd ~ dt, $J_{4'',5''}$ + $J_{3'',4''}$ ≈ 18 Hz, $J_{4'',4''\text{-OH}}$ = 5.0 Hz, H-4''), 1.84 - 1.72, 1.51 - 1.45 (2m, 2H each, H-2''', H-3'''), 1.62 (ddd ~ dt, $J_{2'',3''}$ + $J_{2'',1'''}$ = 19.8 Hz, H-2'').

Anal.Calcd for $C_{66}H_{76}O_{18}$: C, 68.50; H, 6.62. Found: C, 68.37; H, 6.65.

2,3,6-Tri-*O*-benzyl-4-*O*-[2,3-dideoxy-2-*C*-(2,3-dideoxy-β-D-*erythro*-hexopyranosyl)-α-D-*erythro*-hex-2-enopyranosyl]-α-D-glucopyranosyl 2,3-Di-*O*-benzyl-4,6-(*R*)-*O*-benzylidene-α-D-glucopyranoside (17). A solution of **16** (335 mg, 0.256 mmol) in methanol (3 mL) was stirred in the presence of a catalytic amount of anhydrous sodium carbonate for 16 h. Then the solution was neutralized with IR 120 (H^+) ion exchange resin and filtered. The filtrate was taken to dryness and chromatographed on silica gel using ethyl acetate/methanol/water 88.5 : 1 : 0.5 as eluent to furnish **17** (270 mg, 92%) as a colourless syrup, $[\alpha]_D$ +84.5° (*c* 0.2, dioxane); MS (FAB) *m/z* 1161.3 (70%, $[M + Na]^+$, 1177.3 (40%, $[M + K]^+$); ^1H NMR (DMSO-d_6 + trace of D_2O, 400 MHz; 1D TOCSY; 1D ROESY) δ 7.41 - 7.15 (m 30H, aromat), 5.87 (~ br s, $J_{3'',4''}$ ≤ 2 Hz, H-3''), 5.68 (s, 1H, -CHPh), 5.46 (s, $J_{1'',3''}$ ≤ 2 Hz, H-1''), 5.36 (d, $J_{1',2'}$ = 3.3 Hz, H-1'), 5.30 (d, $J_{1,2}$ = 3.6 Hz, H-1), 5.10, 4.66 (2 d, 2H, J = 12.0 Hz, 3'-CH_2Ph), 4.78 (s, 2H, 3-CH_2Ph), 4.75, 4.73 (2 d, 2H, J = 12.0 Hz, 2-CH_2Ph), 4.71,4.57 (2 d, 2H, J = 11.8 Hz, 2'-CH_2Ph), 4.46, 4.42 (2 d, 2H, J = 11.2 Hz, 6'-CH_2Ph), 4.12 (2H, dd ~ br d, $J_{6a,6b}$ = 10.0 Hz, H-6a; ddd ~ br d, H-5'), 4.00 (ddd ~ br t, $J_{4,5}$ = 10 Hz, H-5), 3.97 (dd ~ t, $J_{3',4'}$ = 9 Hz, H-3'), 3.92 (dd ~ br d, H-4''), 3.91 (dd ~ t, $J_{2,3}$ ≈ 9 Hz, H-3), 3.87 (dd ~ t, $J_{4',5'}$ = 10 Hz, H-4'), 3.76 (dd ~ t, $J_{5,6a}$ ≤ 1.5 Hz, $J_{5,6b}$ ≈ 10 Hz, H-6b), 3.75 (dd ~ t, $J_{3,4}$ ≈ 9 Hz, H-4), 3.72 (2H, dd, $J_{2',3'}$ = 9 Hz; dd ~ br d, $J_{1''',2'''ax}$ = 11 Hz, H-1'''), 3.69 (dd ~ br d, $J_{5',6a'}$ ≤ 2 Hz, H-6a'), 3.65 (dd, $J_{5'',6a''}$ = 2.0 Hz, H-6a''), 3.63 (dd, H-2), 3.57 (2H, dd ~ br d, $J_{5',6b'}$ ≤ 2.5 Hz,

H-6b'; dd ~ br d, H-6a''), 3.49 (dd, $J_{6a'',6b''}$ = 12.0 Hz, $J_{5'',6b''}$ = 4.0 Hz, H-6b''), 3.42 (dd, $J_{5''',6b'''}$ = 6.0 Hz, $J_{6a''',6b'''}$ = 12.0 Hz, H-6b'''), 3.36 (ddd, $J_{4'',5''}$ = 9.8 Hz, $J_{5'',6a''}$ = 1.8 Hz, H-5''), 3.15 (ddd ~ dt, $J_{3'''ax,4'''}$ = 10.0 Hz, $J_{3'''eq,4'''}$ = 5.0 Hz, H-4'''), 3.06 (ddd, $J_{4''',5'''}$ = 9.0 Hz, H-5'''), 1.60 (m, 1H, H-3'''eq), 1.35 (m, 1H, H-2'''eq), 1.20 (m, 1H, H-3'''ax), 1.05 (m, 1H, H-2'''ax); ^{13}C NMR (DMSO-d_6 + trace of D_2O, 100 MHz; ^1H-detected one-bond and long-range $^1H,^{13}C$ 2D COSY) δ 138.54, 138.39, 138.16, 137.87, 137.52, 137.44, 137.02 (7C, 6C aromat and C-2''), 128.81 -125.92 (aromat), ca. 127 (C-3''), 100.15 (C-8), 92.96 (C-1''), 92.67 (C-1), 91.19 (C-1'), 83.06 (C-5'''), 80.85 (C-3'), 80.68 (C-4), 79.36 (C-2'), 78.02 (C-2), 77.28 (C-3), 75.28 (C-1'''), 73.49 (CH_2Ph), 72.48 (CH_2Ph), 72.35 (2C, C-5'', CH_2Ph), 71.95 (2C, 2 CH_2Ph), 71.27 (C-4'), 70.08 (C-5'), 69.67 (C-6'), 67.83 (C-6), 65.04 (C-4'''), 62.74 (C-5), 61.66 (C-4''), 61.35 (C 6'''), 60.07 (C-6''), 32.44 (C-3'''), 30.93 (C-2''').

Anal. Calcd for $C_{66}H_{30}O_{17}$: C, 69.58; H, 6.55. Found: C, 69.16; H, 6.83.

4-*O*-[2-Deoxy-2-*C*-(2,3-dideoxy-α-D-*erythro*-hexopyranosyl)-α-D-glucopyranosyl]-α-D-glucopyranosyl α-D-glucopyranoside (18). A solution of **15** (264 mg, 0.23 mmol) in ethanol/water 3:2 (10 mL) was hydrogenated in the presence of palladium-on-carbon (100 mg) for 16 h at room temperature. Filtration over Speedex and evaporation of solvents gave **18** quantitatively (141 mg) as a colourless syrup, $[\alpha]_D$ +169.5° (*c* 0.2, water); MS (FAB) *m/z* 641 (1%, $[M + Na]^+$, 657 (0.2%, $[M + K]^+$); ^1H NMR (D_2O, 400 MHz) δ 5.69 (d, $J_{1'',2''}$ = 3.2 Hz, H-1''), 5.19, 5.18 (2d, 2H, $J_{1,2} \approx J_{1',2'} \approx$ 3.6 Hz, H-1, H-1'), 4.19 (ddd, 1H), 4.14 (dd, 1H), 3.93 (ddd, 1H), 3.88 (m, 1H), 3.86 - 3.62 (m, 16H), 2.27 - 2.18 (m, 2H), 1.92 (m_c, 1H), 1.86 - 1.68 (m, 2H).

Anal. Calcd for $C_{24}H_{42}O_{18}$: C, 46.60; H, 6.84. Found: C, 45.70; H, 6.86.

4-*O*-[3,4,6-Tri-*O*-acetyl-2-*C*-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hexopyranosyl)-2-deoxy-α-D-glucopyranosyl]-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranoside (19). A solution of **18** (10 mg, 16 μmol) in pyridine (0.2 mL) and acetic anhydride (0.1 mL) was left for 48 h, then evaporated, taken up in toluene and filtered through a pad of silica gel. The filtrate was concentrated and lyophilized from dioxane to give **19** (16 mg) as a colourless solid, $[\alpha]_D$ +120° (*c* 0.15, dioxane); MS (FAB) *m/z* 1146.1 (70%, $[M + Na]^+$, 1162.4 (40%, $[M + K]^+$); ^1H NMR ($CDCl_3$, 400 MHz; 1D TOCSY, COSY; 1D ROESY) δ 5.54 (dd, $J_{3',4'}$ = 7.6 Hz, H-3'), 5.46 (dd ~ t, $J_{3,4}$ = 9.4 Hz, H-3), 5.36 (d, $J_{1'',2''}$ = 3.4 Hz, H-1''), 5.30 (dd, $J_{3'',4''}$ = 9.1 Hz, H-3''), 5.29 (d, $J_{1,2}$ = 4.0 Hz, H-1), 5.22 (d, $J_{1',2'}$ = 3.9 Hz, H-1'), 5.05 (dd ~ t, $J_{4,5}$ = 9.1 Hz, H-4), 5.04 (dd, $J_{2,3} \approx$ 10.1 Hz, H-2), 4.99 (dd, $J_{2',3'}$ = 9.5 Hz, H-2'), 4.98 (dd ~ t, $J_{4'',5''} \approx$ 10.6

Hz, H-4''), 4.76 (ddd~ q, ΣJ = 11.0 Hz, H-4'''), 4.39 (dd, $J_{6a',6b'}$ = 12.0 Hz, $J_{5',6a'}$ = 3.1 Hz, H-6a'), 4.38 (dd, $J_{5''',6a'''}$ = 7.5 Hz, H-6a'''), 4.29 (dd, $J_{6a'',6b''}$ = 12.0 Hz, $J_{5'',6a''}$ = 4.0 Hz, H-6a''), 4.25 (dd, $J_{5',6b'}$ = 5.1 Hz, H-6b'), 4.21 (dd, $J_{6a,6b}$ = 13.0 Hz, $J_{5,6a}$ = 5.8 Hz, H-6a), 4.14 (dd, $J_{6a''',6b'''}$ = 11.5 Hz, $J_{5''',6b'''}$ = 4.5 Hz, H-6b'''), 4.05 (ddd, H-5), 4.04 (dd, H-6b), 4.02 (dd, $J_{4',5'}$ = 9.6 Hz, H-4'), 4.00 (dd, $J_{5'',6b''}$ = 2.0 Hz, H-6b''), 3.97 (ddd, H-5'), 3.94 (ddd, H-5''), 3.91 (ddd, H-5'''), 3.80 (ddd ~ dt, $J_{1''',2a'''}$ + $J_{1''',2e'''}$ = 12.7 Hz, H-1'''), 2.30 (ddd, $J_{2'',3''}$ = 11.5 Hz, $J_{2'',1'''}$ = 5.1 Hz, H-2''), 2.111, 2.105, 2.102, 2.098 (6H), 2.087, 2.070, 2.067, 2.052, 2.014 (9H) (12 Ac), 1.96 - 1.84 (m, 2H, H-3'''), 1.70 - 1.59 (m, 2H, H-2'''); ^{13}C NMR ($CDCl_3$, 100 MHz; ^1H-detected one-bond and long-range $^1H,^{13}C$ 2D COSY) δ 170.57 (3C, CO), 170.42, 170.22, 170.09, 169.97, 169.80, 169.77, 169.66, 169.62, 169.56 (9 CO), 97.64 (C-1''), 91.83 (C-1), 91.48 (C-1'), 73.80 (C-5'''), 72.32 (2C, C-3', C-4'), 70.17 (C-2'), 69.95 (C-2), 69.87 (C-4'', C-3), 69.57 (C-1'''), 69.05 (C-5'), 68.94 (C-3''), 68.76 (C-5''), 68.45 (C-4), 68.25 (C-5), 67.25 (C-4'''), 62.97 (C-6'), 62.14 (C-6''), 61.82 (C-6), 61.26 (C-6'''), 47.17 (C-2''), 24.06 (C-3'''), 23.24 (C-2'''), 21.20, 21.14, 21.05, 20.90, 20.72, 20.68, 20.66 (7 CH_3), 20.62 (3C, CH_3), 20.54, 20.49 (2 CH_3).

Anal. Calcd for $C_{48}H_{66}O_{30}$: C, 51.34; H, 5.92. Found: C, 51.16; H, 5.95.

ACKNOWLEDGEMENTS

We thank Mr. R. Keller for expert technical assistance and the following colleagues for the determination of physical data: Dr. W. Arnold (NMR), Dr. A. Dirscherl† (MA), and Mr. W. Meister (MS).

REFERENCES AND NOTES

1. H. P. Wessel, M. Hosang, T. B. Tschopp and B.-J. Weimann, *Carbohydr. Res.*, **204**, 131 (1990).
2. R. Ross and J. Glomset, *Science* , **180**, 1332 (1973).
3. H. P. Wessel, G. Englert and P. Stangier, *Helv. Chim. Acta*, **74**, 682 (1991).
4. H. P. Wessel, B. Mayer and G. Englert, *Carbohydr. Res.*, **242**, 141 (1993).
5. H. P. Wessel and G. Englert, *J. Carbohydr. Chem.*, accepted for publication.
6. H. H. Baer, L. Siemsen, J. Defaye and K. Burak, *Carbohydr. Res.*, **134**, 49 (1984).
7. B. Fraser-Reid and B. Radatus, *J. Am. Chem. Soc.*, **92**, 5288 (1970).
8. R. J. Ferrier and N. Prasad, *J. Chem. Soc. (C)* , 581 (1969).
9. C. S. Hudson, *Adv. Carbohydr. Chem.* **3**, 1 (1948).
10. G. Casiraghi, M. Cornia, L. Colombo, G. Rassu, G. Gasparri Fava, M. Ferrari Belicchi and L. Zetta, *Tetrahedron Lett.*, **29**, 5549 (1988).

11. Collaboration with Dr. K. Gubernator, Dept. New Technologies, Roche Basel.
12. R. U. Lemieux and A. R. Morgan, *Can. J. Chem.*, **43**, 2205 (1965).
13. R. J. Ferrier and G. H. Sankey, *J. Chem. Soc. (C)*, 2346 (1966).
14. R. R. Schmidt, *Angew. Chem.*, **98**, 213 (1986).
15. H. Paulsen and M. Paal, *Carbohydr. Res.*, **135**, 53 (1984).
16. H. P. Wessel, *Tetrahedron Lett.*, 31, 6863 (1990).
17. T. Mukaiyama, S. Kobayashi and S. Shoda, *Chem. Lett.*, 907 (1984).
18. T.-L. Hwang and A. J. Shaka, *J. Am. Chem. Soc.*, **114**, 3157 (1992).
19. G. Englert, T. Aakermann and S. Liaaen-Jensen, *Magn. Reson. Chem.*, **31**, 910 (1993).
20. I. Lundt and C. Pedersen, *Acta Chem. Scand.*, **20**, 1369 (1966).