

67. α -D-Glycosyl-Substituted α,α -D-Trehaloses with (1 $\rightarrow$ 4)-Linkage: Syntheses and NMR Investigations

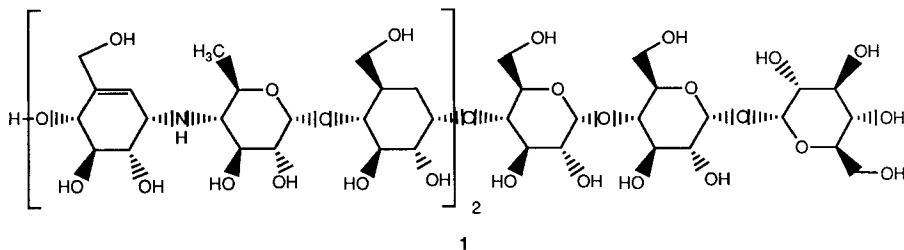
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Two symmetrical trehalose glycosyl 'acceptors' **4** and **6** were prepared and three of the unsymmetrical type, **8**, **10**, and **11**. Glucosylation of symmetrical 'acceptor' **4** gave a higher yield of trisaccharide (44%) than protective-group manipulation, namely *via* selective debenzylidenation **2** $\rightarrow$ **9** or monoacetylation **2** $\rightarrow$ **5** which proceeded in moderate yields (33–34%). A comparison of catalysts in the *cis*-glucosylation of trehalose 'acceptor' **10** with tetra-*O*-benzyl- β -D-glucopyranosyl fluoride **13** profiled triflic anhydride ((TF)₂O) as a new reactive promoter yielding 92% of trisaccharide **14**, deblocking gave the target saccharide α -D-glucopyranosyl-(1 $\rightarrow$ 4)- α,α -D-trehalose. ¹H-NMR spectra of most compounds were analyzed extensively. The use of the 1D TOCSY technique is advocated for its time efficiency, if needed supplemented by ROESY experiments.

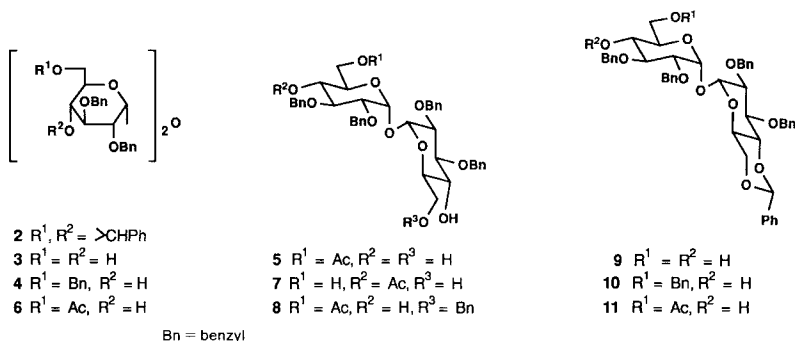
Introduction. – Trestatin A (**1**) is a pseudo-nonasaccharide obtained from strains of *Streptomyces dimorphogenes* which was developed as an α -amylase inhibitor [1] and which shows further interesting biological activities after sulfation [2]. For a synthesis of the 'right-hand' moiety of **1**, it seems adequate to use a trehalose building block because α,α -D-trehalose (= α -D-glucopyranosyl α -D-glucopyranoside) is a commercial starting



material. Thus, we studied the preparation of a number of suitably blocked glycosyl 'acceptors' and various glycosylation reactions with the aim to arrive at good yields of (1 $\rightarrow$ 4)-linked *cis*-glycosyl-trehaloses.

Results and Discussion. – 1. *Syntheses of Trehalose Glycosyl 'Acceptors'*. Trehalose is a molecule with approximate C₂ symmetry [3] in the solid state, and a similar conformation is observed in solution [4]. Consequently, selective formation of unsymmetrical derivatives of trehalose is likely to result in moderate yields. The simplest trehalose

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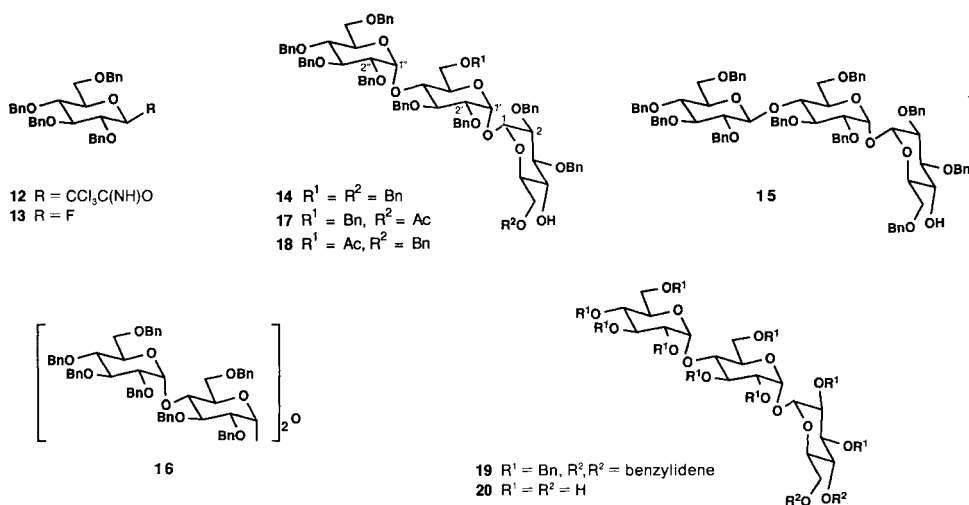
glycosyl 'acceptor' with an OH function free for glycosylation is of a symmetrical type. Such a compound is easily obtained from α,α -D-trehalose by benzylidenation [5] and benzylation [6] to give fully protected **2**, which, after removal of the 4,6-*O*-benzylidene groups with AcOH/H₂O, yields the known [6] **3**. Selective benzylation of the primary OH groups *via* a stannylated intermediate [7] in the presence of Bu₄NBr [8] afforded the symmetrical acceptor **4** in 83% yield. When the hydrolysis of dibenzylidene compound **2** with AcOH/H₂O was carried out for a prolonged period of time, a 33% yield of product **5**, monoacetylated at the primary position, could be obtained, along with tetrahydroxy compound **3** (26%), the diacetylated trehalose **6** [9] (10%), and secondary monoacetate **7** (4%). The diacetate **6** constitutes another symmetrical trehalose glycosyl 'acceptor'.

Selective benzylation [7] of the monoacetylated trehalose derivative **5** furnished the diol **8** (65%) along with hexabenzyl derivative **4** (16%), obviously obtained by deacetylation under the reaction conditions used and subsequent benzylation. Compound **8** is an interesting glycosyl 'acceptor' with two 4-OH groups in a different chemical environment. Generally, ester substitution leads to deactivation of neighbouring OH groups [10] [11]. An example of drastic deactivation of a 4-OH group by an ester in the 6-position was observed in glycosylations of lactose derivatives [12], although the substitution of the primary OH group of 2-acetamido-2-deoxy-D-glucopyranosides had no bearing on the reactivity of the neighbouring 4-OH group [10]. The difference in reactivity of acylated and alkylated sugars has been exploited for the modulation of reactivity of glycosyl 'donors' like pent-4-enyl glycosides [13] and thioglycosides [14] that were called 'armed' [13] when alkylated and 'disarmed' when acylated. In analogy, it was of interest to investigate, whether the substitution of the primary positions of D-trehalose would generate an 'armed' and a 'disarmed' glycosyl 'acceptor' in *one* molecule, *i.e.* in **8**.

Short-time treatment of dibenzylidene compound **2** with AcOH/H₂O led to re-isolation of starting material (52%), which could be recycled, and to a 34% yield of 2,2',3,3'-tetra-*O*-benzyl-4,6-*O*-benzylidene- α,α -D-trehalose (**9**). In a similar procedure, this compound had been prepared from **3** in 22–30% yield using AcCl/MeOH for debenzylidenation [15]. Selective benzylation [7] [8] of **9** furnished **10** in 86% yield, a trehalose glycosyl acceptor with only one 4-OH group available for glycosylation. A similar compound **11** could be obtained (79%) after benzylidenation of monoacetate **5** with dimethoxytoluene/TsOH in DMF [16].

2. Glycoside Syntheses. For the stereoselective synthesis of *cis*-glycosides, not only glycosyl chlorides and bromides in the classical *Königs-Knorr* reaction [17] have been

employed as glycosyl ‘donors’, but also glycosyl fluorides [18] and imidates [19], thioglycosides [20] [14], pentenyl glycosides [13] [21], and others. In our investigations, we have used 2,3,4,6-tetra-*O*-benzyl- β -D-glucopyranosyl trichloroacetimidate (**12**) [22] and fluoride (**13**) [18] as glycosyl ‘donors’, which are already known to give *cis*-glycosides also with glycosyl ‘acceptors’ of low reactivity [23] [18]. The solvent of choice in our glycosylations was Et₂O, which was shown repeatedly to favour the formation of *cis*-glycosides. Thus, reaction of trichloroacetimidate **12** with the symmetrical trehalose glycosyl ‘acceptor’ **4** using trimethylsilyl trifluoromethanesulfonate (trimethylsilyl triflate; Me₃SiOTf) as a strong catalyst [23] furnished a 32% yield of α -D-linked trisaccharide **14** along with β -D-linked trisaccharide **15** (0.4%) and a mixed fraction containing both compounds (6.5%, **14/15** $\approx$ 1:1); no tetrasaccharide was formed. The analogous reaction of fluoride **13** with **4** using TiF₄ [24] as catalyst gave a yield of 44% of α -D-linked trisaccharide **14** along with 23% of α -D-linked symmetrical tetrasaccharide **16**. A yield of *ca.* 40% of monosubstituted trehalose derivative in both cases is respectable and reflects the decreased reactivity of the second OH group after glycosylation of the first one.



Reaction of trichloroacetimidate **12** with trehalose diol **8** in the presence of Me₃SiOTf afforded 29% of trisaccharide **17** by glucosylation of the more reactive OH group and 5% of the regioisomer **18**. This 6:1 ratio of **17/18** reflects rather poor regioselectivity and suggests that more or different esters must be present to deactivate one site.

For the glucosylation of the benzylidenated trehalose derivative **10**, various reaction conditions have been investigated. With **12** as ‘donor’ and Me₃SiOTf as catalyst, a relatively low conversion into trisaccharide was observed in the case of a small excess of **12**; using a 9fold excess of **12**, however, 51% of trisaccharide **19** could be isolated. With 2 equiv. of fluoride **13** as ‘donor’ and Me₃SiOTf as a promoter [26], 45% of trisaccharide **19** were obtained. BF₃·Et₂O was not investigated as a catalyst; it seems to be a less strong catalyst judged by literature data [27] and, therefore, is not suitable for a relatively unreactive OH acceptor. *Mukaiyama*-reaction conditions using SnCl₂/AgOTf as catalyst

[28] furnished a 65 % yield of α -D-linked trisaccharide **19**, TiF_4 [24] gave a comparable yield of 68 %. The strength of the latter catalyst seems to have been underestimated due to use of solvents other than Et_2O in the reaction of fluorides with unreactive glycosyl acceptors. Finally, our new promoter [29] triflic anhydride Tf_2O led to a 92% isolated yield of trisaccharide **19**. In all these glycosylations, no β -D-linked saccharides could be isolated; the samples of **19** contained, however, up to 8% (judged by the integral of the benzylidene protons) of a second component, the structure of which could not be revealed.

Deprotection of **14** or **19** by standard hydrogenation gave α -D-glucopyranosyl-(1 $\rightarrow$ 4)- α , α -D-trehalose (**20**) in practically quantitative yield; deprotection of **17** provided the same trisaccharide **20** after deacetylation and hydrogenation. The structure of **20** was proven by NMR spectroscopy (see *Chapt. 3*). The optical rotation found ($[\alpha]_D^{20} = +176.4$) is well below the one reported [30] for the compound isolated from *Streptococcus lactis* ($[\alpha]_D = +207$), but in keeping with the data for the compound synthesized by an alternative route ($[\alpha]_D^{20} = 169$) [31]. For the compound prepared in low yield by glycosylation of α , α -D-trehalose using various glycohydrolases [32], no optical rotations are described.

3. *NMR Investigations.* In the course of this NMR investigation and in similar related studies, we have found the application of ^1H -correlated 2D (COSY), relayed 2D COSY, 2D total correlation spectroscopy (TOCSY, HOHAHA), and, where necessary, 2D double-quantum-coherence spectroscopy (DQC 2D; for a recent review of these techniques, see [33]) very useful for the assignment of the ^1H -NMR signals of carbohydrates. However, the total acquisition time needed to perform one or more of these techniques is, in practice, often prohibitive. Following the work of *Bax* and coworkers [34] [35], we rather prefer to apply instead of these 2D techniques a few selected 1D TOCSY experiments which can be performed normally in less than 1 h. Here it will be demonstrated that a set of three to four 1D TOCSY experiments per carbohydrate moiety is sufficient, in general, to obtain a complete ^1H -NMR subspectrum with high digital resolution and a complete assignment of all ^1H -signals of the selected moiety. Moreover, the linkage of the different moieties and hence the assignment of the obtained subspectra to the different carbohydrate rings can be very efficiently derived by a few selected 1D nuclear *Overhauser* effect (NOE) experiments [36].

The TOCSY experiment, which was originally introduced by *Braunschweiler* and *Ernst* [37] and later dubbed HOHAHA by *Bax* and coworkers, provides an excellent tool to obtain multiple-step coherence transfer in high-resolution ^1H -NMR spectroscopy. In the 1D variant, subspectra can be extracted from crowded overlapping regions corresponding, *e.g.*, to one set of coupled protons such as H-C(1) to H-C(6) of a carbohydrate moiety [35]. The only prerequisite is that at least one of these protons has a signal sufficiently separated from all the others. In carbohydrates of medium complexity, this is often valid for the anomeric protons.

For the 1D TOCSY experiments, we used essentially the procedure as proposed by *Bax et al.* [34] [35]. Firstly, a selected ^1H signal, *e.g.* of the anomeric proton, was inverted by a selective 180° pulse produced by a DANTE pulse train [38]. After a following unselective 90° pulse, an MLEV-17 mixing sequence followed, flanked by two trim pulses [39]. Then the difference FID was acquired with the selected 180° pulse on-resonance minus off-resonance. In order to improve the partly dispersive contributions to the line shapes, a *z*-filter with typically 10 delays between 6 μs and 50 ms was included into the pulse sequence before acquisition of the FID [35]. In order to achieve a full relay of magnetization between H-C(1) and H-C(6), a duration of the mixing time of 200 to 300 ms was found to be sufficient. Thus, if an assignment of the protons of the coupling network can be performed by consideration of chemical shifts and coupling constants, only one single 1D experiment per carbohydrate moiety is normally needed which can be experimentally performed in a few minutes. In all other cases, the full assignment of protons can be derived by a set of 3 to 4 experiments with increasing mixing times. It is assumed that the ^1H signals appear with increasing mixing time in the order of their position in the network. The validity of this procedure has been verified in our laboratory in numerous applications [36] and can often be readily proved by inspection of the distribution of

the intensities in the m 's revealing the relative position of the signals of coupling partners ('roof' effect in the case of medium or strong coupling). In other critical cases, a simple decoupling experiment can provide the needed information.

The subsequent assignment of the different subspectra to specific carbohydrate rings is, if needed, easily performed by a few selected NOE experiments. Since the normal (longitudinal) NOE has the undesirable property that its magnitude can be rather small or even vanishing at molecular masses between 600 and 1200 [40]. Here, its transverse variant ROESY (rotating-frame NOE spectroscopy [41], originally termed CAMELSPIN [42]) is the

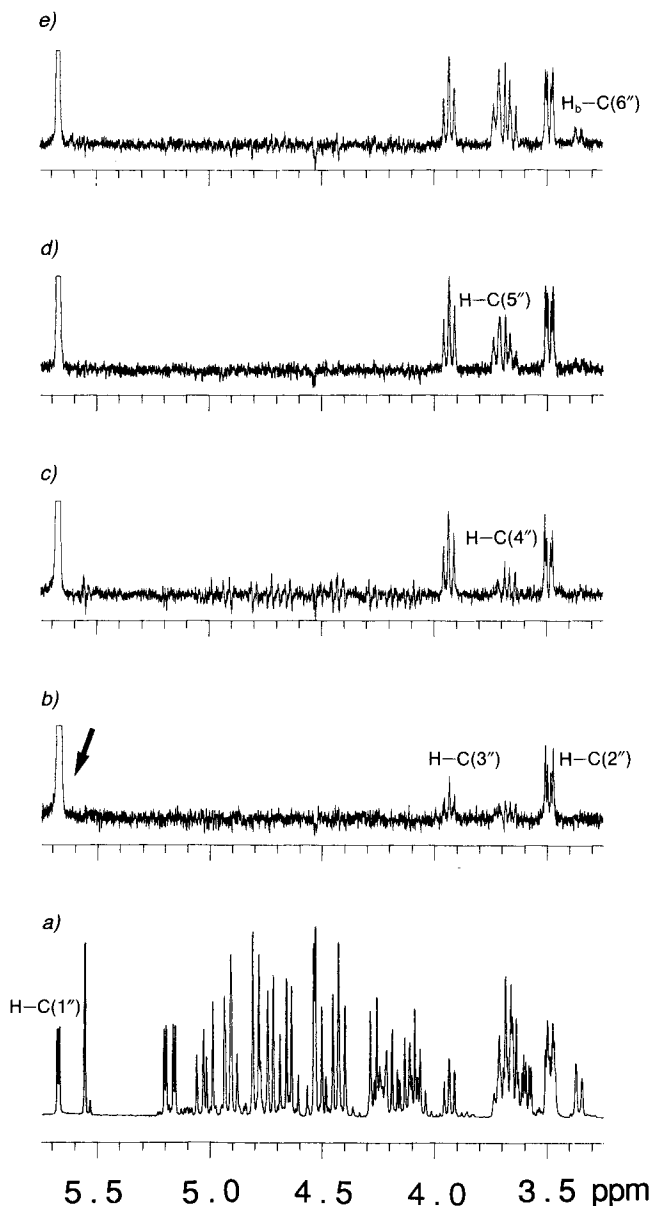


Fig. 1. a) 400-MHz ^1H -NMR partial spectrum (CDCl_3) of **19** (5.5 mg); b)–d) 1D TOCSY difference spectra with selective inversion of $\text{H}-\text{C}(1'')$ by a 180° DANTE pulse train ($2400 \cdot 2 \mu\text{s}$) and mixing times of 30, 60, 120, and 180 ms; 10 · 16 scans per experiment (ca. 20 min)

only remedy in this range of molecular masses. It has the known advantage that it yields a positive effect and is more intense here than the longitudinal NOE [40] [42].

In 1D ROESY, the experiment starts again with a 180° DANTE pulse inverting a selected proton signal. The mixing is provided by a train of 90° pulses separated by a delay according to the compensated ROESY protocol [43]. A difference FID is acquired with on- and off-resonance irradiation. This leads to a change of the intensity of the signals of other spatially proximate protons which is detected in the 1D ROESY difference spectrum.

As an example, our preferred strategy for the assignment of the ^1H signals of carbohydrates is demonstrated in Figs. 1–3. Figs. 1a, 2a, and 3a show the carbohydrate part of the ^1H -NMR at 400 MHz of **19** between 3.3 and 5.7 ppm containing the signals of 40 protons, including 9 AB - or A_2 -type spectra of the protective PhCH_2 groups.

Figs. 1b–e present the 1D TOCSY difference spectra obtained by inversion by a selective DANTE 180° pulse of the d at 5.67 ppm later to be assigned to the anomeric proton $\text{H}-\text{C}(1'')$. In Fig. 1b, obtained with a mixing time of 30 ms, only the signals of $\text{H}-\text{C}(2'')$ and, weaker in intensity, of $\text{H}-\text{C}(3'')$ are visible. With increasing mixing time (60 ms in Fig. 1c, 120 ms in Fig. 1d, and 180 ms in Fig. 1e), all further signals of protons

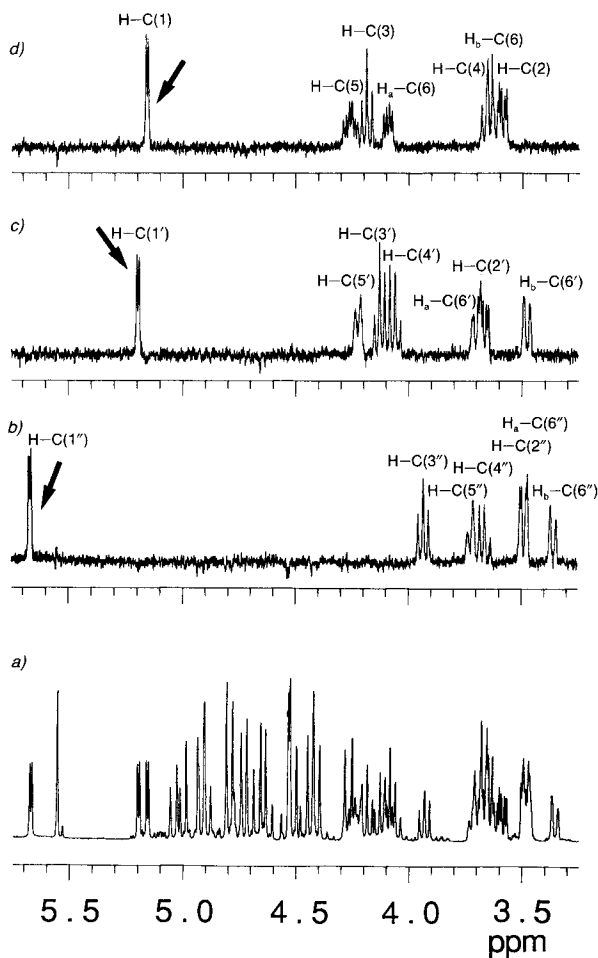


Fig. 2. 1D TOCSY difference spectra of **19** with selective inversion of all three anomeric protons at a mixing time of 360 ms.

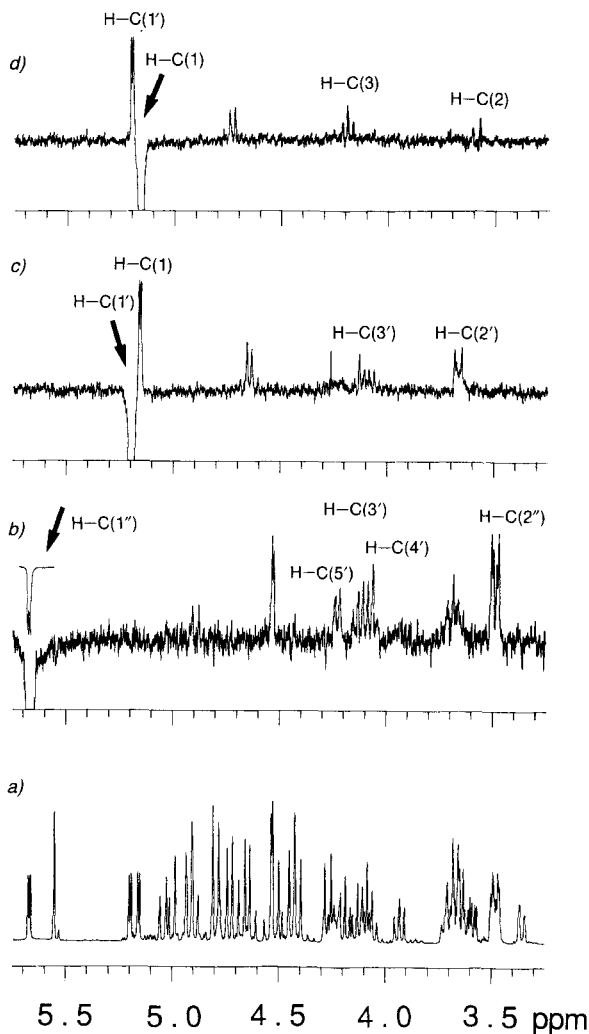


Fig. 3. 1D ROESY difference partial spectra of **19** obtained upon selective inversion of the anomeric protons with 0.6 s mixing time. Total measuring time ca. 20 min per experiment.

H-C(4''), H-C(5''), and H_b-C(6'') appear with increasing intensity in this order. The remaining signal of H_a-C(6'') is completely hidden by H-C(2'') as revealed by the intensity distribution of the signal of H_b-C(6'') more clearly seen in Fig. 2b. It is worth noting that the signals of H-C(2''), H-C(4''), and H-C(5'') are hardly detectable in Fig. 1a due to the strong spectral overcrowding. In contrast, the highly resolved subspectrum of this 1D TOCSY experiment allows the accurate determination of all chemical shifts and coupling constants. In view of the fact that only ca. 20 min were needed for each experiment, this technique is quite obviously very time-efficient.

Corresponding experiments were performed with the two other anomeric protons at 5.192 and 5.152 ppm, later to be assigned to H-C(1') and H-C(1), respectively. Fig. 2 displays the final subspectra of all three carbohydrate rings obtained with the longest mixing time of 360 ms used in these experiments. The assignments in Figs. 2b and 2c were

again possible by observing the sequence of appearance of the signals with increasing mixing time. *Figs. 2c* and *2d* clearly indicate that the selectivity of the DANTE sequence is indeed very satisfying since there are no disturbing effects visible upon irradiating either of the two closely spaced H–C(1') and H–C(1) signals which are only 16 Hz apart. Furthermore, it can be seen that at this mixing time, all signals have now approximately the same integral intensity, *i.e.* the magnetization of the anomeric protons has been uniformly distributed between all protons of the coupling network. It has been found that at long mixing times, often very small ROESY artifacts between spatially close protons are detectable in the TOCSY experiment. An example is seen in *Fig. 2c* where a very small negative signal is seen at the position of H–C(1).

After having obtained these subspectra, they had to be attributed to the different rings. An obvious starting point is the observation in *Fig. 2d* of a *ddd* at 4.226 ppm with two large ($J_{aa} \approx 10$ Hz) and one small coupling ($J_{ac} \approx 4.4$ Hz) which must be assigned to H–C(5). Thus, *Fig. 2d* represents the subspectrum of the first carbohydrate ring.

Figs. 3b–d present three 1D ROESY difference spectra of **19** obtained upon 180° inversion of the signals of the three anomeric protons. Since the signals of the irradiated protons were phased negatively, the signals of protons exhibiting a (positive) ROE appear as positive. In addition to some intra-ring ROE's a number of inter-ring ROE's are seen. The strongest inter-ring effects in *Fig. 3d* and *3c* are observed between the already assigned H–C(1') and its close neighbour H–C(1) proving that a 1–1' linkage is present. Hence, *Fig. 3c* must be attributed to the second ring. In *Fig. 3b*, strong inter-ring ROE's were detected between H–C(1'') and H–C(5'), H–C(3'), and H–C(4') pointing to a 1''–4' linkage. In all three carbohydrate moieties, intra-ring ROE's are mainly observable to the nearest neighbours such as H–C(2) and weakly to H–C(3) as well as to some methylene protons.

These examples of 1D TOCSY and ROESY spectra discussed so far convincingly demonstrate the power and efficiency of these techniques. According to our experience, the DANTE pulse train can be made sufficiently selective in most cases to avoid disturbing effects on neighbouring signals. This means that the excessive acquisition time of the corresponding 2D experiment can in many cases be avoided.

The structure of all new compounds was verified by their ¹H-NMR and, in part, by their ¹³C-NMR as is seen from the data given in the *Exper. Part*. Owing to their C₂ symmetry, the symmetrical trehalose derivatives **2–4** and **6** gave relatively simple (mono-)saccharide spectra which were readily assigned. More complicated spectra were observed for some of the unsymmetrical derivatives carrying similar but not identical substituents on the two pyranose rings. Thus, in a manner corresponding to that discussed above for **19**, the ¹H-NMR spectra of the benzylidenated glycosyl 'acceptor' **10** and of compound **5** and **16** were unambiguously assigned by use of 1D TOCSY, and in the latter case, additionally supported by 1D ROESY.

For a full assignment of **14**, a phase-sensitive DQF COSY, a relayed COSY, and a DQC 2D were carried out. A 2D COSY simplified the assignments of compounds **15**. Some 1D TOCSY experiments helped in the case of **20**.

The newly established α-D-linkages in **14** as well as in **16**, **17**, and **19** are evidenced by the shift of H–C(1'') ($\delta = 5.65$ – 5.66 , $J = 3.5$ – 3.6 Hz). In **18** with an acetate group at C(6'), the shift is slightly upfield ($\delta(\text{H–C}(1'')) = 5.53$). The structure of 4-acetate **7** was evident from the downfield shift of H–C(4) ($\delta = 4.88$) and the presence of one secondary

and two primary OH groups. It is interesting to note that the resonances of the 4-OH protons are significantly downfield shifted if an acetate is present in the neighbouring 6-position ($\delta(\text{OH}-\text{C}(4)) = 2.58\text{--}2.63$ for compounds **5**, **6**, **8**, and **11**); if the respective 6-position is benzylated or unsubstituted, the chemical shifts are at higher field ($\delta(\text{OH}-\text{C}(4)) = 2.45\text{--}2.39$ for **4**, **8**, **19**, and **14**; $\delta(\text{OH}-\text{C}(4)) = 2.45\text{--}2.48$ for **7** and **9**). This finding was used to assign the structures of **17** and **18** ($\delta(\text{OH}-\text{C}(4)) = 2.60$ in **17** with acetate at C(6), $\delta(\text{OH}-\text{C}(4)) = 2.36$ in **18** with benzyl at C(6)).

In three cases (**14**, **16**, and **19**), ^{13}C -NMR spectra were measured and here the assignments are based on ^{13}C -detected 2D H,C-COSY experiments. Both the one-bond and the multiple-bond versions were performed for this purpose.

The skillful technical assistance of Mr. A. Graf and Mr. R. Keller is gratefully acknowledged. We also wish to thank our colleagues from the Central Research Department for determination of physical and analytical data: Dr. W. Arnold (NMR), Dr. A. Dirscherl† (microanalyses), Dr. M. Grosjean (IR), Mr. W. Meister (MS), and Dr. W. Vetter (MS). Mrs R. Nachbur is thanked for typing the manuscript.

Experimental Part

General. Solvents and reagents were obtained from Fluka (puriss. p.a.). Evaporation: Büchi rotary evaporator, at $30\text{--}40^\circ/\text{in vacuo}$. TLC: precoated silica gel 60 F-254 plates (Merck), detection by UV light (254 nm) and spraying with a 10% soln. of conc. H_2SO_4 in MeOH followed by heating. Column chromatography (CC): silica gel 60 (Merck, 0.063–0.200 mm). MPLC (medium-pressure liquid chromatography): Lobar columns, Lichroprep Si 60 (40–63 μm , Merck) at 2–5 bar (Labomatic MD 80/100 pump). M.p. (uncorrected): Büchi-510 apparatus. $[\alpha]_D^{25}$: Perkin-Elmer-241 polarimeter, 1-dm cell. IR (cm^{-1}): Nicolet-7199-FT-IR spectrophotometer. MS: EI: MS 9 with SS 200 data system (Finnigan MAT); CI: MAT 90 (Finnigan MAT); FAB: MS 902 with DS 2050 (VG) data system. NMR: AC-250-, AM-400-, or AM-500-Bruker FT spectrometers at ca. 23° in CDCl_3 , $(\text{D}_6)\text{DMSO}$, or D_2O ; internal TMS or 3-(trimethylsilyl)(D₄) propionate as reference. The 400-MHz instrument was used for all 2D and the 1D TOCSY and ROESY experiments. The latter were done in the 'reverse' mode using the decoupler as the source of ^1H excitation. The DANTE pulse train consisted of 650 or 2400 short pulses of 2 μs duration, separated by a delay of 70 μs at a power level of 18 H or 19 H (high-power mode). In the ROESY experiments, a duty cycle of 0.08 was chosen. For further details, we refer to [44]. Standard Bruker software and microprograms were applied for all other experiments. Typical experimental parameters were as follows: a) Double-quantum filtered phase-sensitive COSY of **14**: acquisition $500 \cdot 4$ K in F_1 and F_2 , zero-filling to 2 K in F_1 , spectral width 3268 Hz in both directions, acquisition times 153 and 630 ms, shifted sine-bell filters ($\pi/8$), digital resolution 3.2 and 1.6 Hz/pt, relaxation delay 0.65 s, 80 scans per experiment, ca. 16 h measuring time. b) Relayed COSY of **14**: same as a), with a mixing delay of 31 ms. c) DQC-2D of **14**: acquisition $489 \cdot 4$ K, zero-filling to 2 K in F_1 , spectral width 7426 and 3623 Hz in F_1 and F_2 , acquisition time 135 and 565 ms, sine-bell filters, digital resolution 3.54 and 1.77 Hz/pt, relaxation delay 1 s, 65 h measuring time. d) One-bond H,C-COSY experiment of **19**: acquisition $350 \cdot 4$ K, zero-filling in F_1 to 1 K, spectral width 16667 and 4000 Hz, acquisition time 87.5 and 123 ms, sine-bell filters, 8.1 and 3.9 Hz digital resolution, 1 s relaxation delay, 96 scans and 2 dummy scans per experiment, ca. 12 h total measuring time. e) Long-range correlation of **19**: Same conditions as in d), except 192 scans per experiment, 1.2 s relaxation delay, mixing delay 62.5 ms, ca. 25 h total acquisition time.

2,3-Di-O-benzyl-4,6-O-benzylidene- α -D-glucopyranosyl 2,3-Di-O-benzyl-4,6-O-benzylidene- α -D-glucopyranoside (2). Starting with 4,6:4',6'-di-O-benzylidene- α , α -D-trehalose [5], **2** was prepared following [6]. The crude product was crystallized by addition of glacial AcOH. Colourless crystals. M.p. $140.3\text{--}141.3^\circ$. $[\alpha]_D^{20} = +57.4$ ($c = 0.5$, dioxane). IR (KBr): 1605w, 1491w, 1089s, 985s. ^1H -NMR (400 MHz, CDCl_3): 7.51–7.49 (m, 2 arom. H); 7.40–7.25 (m, 13 arom. H); 5.55 (s, PhCH); 5.11 (d, $J(1,2) = 3.8$, H–C(1)); 4.95, 4.84 (2d, $J = 11.2$, PhCH₂); 4.83, 4.72 (2d, $J = 12.0$, PhCH₂); 4.27 (ddd $\approx$ dt, $J(5,6\text{eq}) = 4.5$, $J(5,6\text{ax}) \approx 10$, $J(4,5) \approx 10$, H–C(5)); 4.13 (dd $\approx$ t, H–C(3)); 4.12 (dd, $J(6\text{eq},6\text{ax}) = 10.2$, H_{eq}–C(6)); 3.66, 3.63 (2dd $\approx$ t, H–C(4), H_{ax}–C(6)); 3.61 (dd, $J(2,3) = 9.3$, H–C(2)). EI-MS: 787 (0.5, $[M - \text{Bn}]^+$), 431 (2, monosaccharide anomeric ene), 447 (1, $[M - 431]^+$), 341 (2, $[431 - \text{Bn} + \text{H}]^+$), 91 (100, Bn⁺).

2,3,6-Tri-O-benzyl- α -D-glucopyranosyl 2,3,6-Tri-O-benzyl- α -D-glucopyranoside (4). To a suspension of tetra-benzyl compound **3** (13.4 g, 19.1 mmol) in toluene (1.07 l) was added dibutyltin oxide (29.3 ml, 57.2 mmol). The mixture was heated under reflux in a *Dean-Stark* apparatus continuously removing H_2O . After 4 h, benzyl bromide (11.3 ml, 95.1 mmol) and Bu_4NBr (2.1 g, 5.76 mmol) were added to the clear soln. at 80° . Two more additions of benzyl bromide (22.6 ml, 190.2 mmol each) and Bu_4NBr (4.2 g, 11.5 mmol each) were made after 17 and another 23 h. After a total of 57 h, the mixture was cooled, poured on ice/aq. $NaHCO_3$ soln., and extracted with CH_2Cl_2 . The dried crude product was chromatographed (AcOEt/hexane 1:3) and the product fraction crystallized from AcOEt/hexane: pure **4** (11.2 g, 66.5%). Another crystallization of the mother liquor furnished more colourless crystals of **4** (2.73 g, 16.3%). M.p. $99-100^\circ$. $[\alpha]_D^{20} = +115.2$ ($c = 0.5$, dioxane). IR (KBr): 3477m, 1602w, 1492m, 1097s, 1057s, 1003s, 735s, 698s. 1H -NMR (250 MHz, $CDCl_3$): 7.37–7.26 (m, 15 arom. H); 5.24 (d, $J(1,2) = 3.5$, H–C(1)); 5.01, 4.79 (2d, $J = 11.5$, $PhCH_2$); 4.71, 4.63 (2d, $J = 11.8$, $PhCH_2$); 4.51, 4.43 (2d, $J = 12.0$, $PhCH_2$); 4.12 (ddd, $J(5,6a) = 5.0$, H–C(5)); 3.88 (dd $\approx t$, $J(3,4) = 8.8$, H–C(3)); 3.68 (ddd, $J(4,5) = 10.0$, $J(4,4-OH) = 2.8$, OH–C(4)); 3.57 (dd, $J(2,3) = 9.9$, H–C(2)); 3.52 (dd, H_a –C(6)); 3.46 (dd, $J(5,6b) = 3.4$, $J(6a,6b) = 10.2$, H_b –C(6)); 2.37 (d, OH–C(4)). FAB-MS: 433 (2, monosaccharide anomeric ene), 91 (100, Bn^+).

2',3'-Di-O-benzyl- α -D-glucopyranosyl 6-O-Acetyl-2,3-di-O-benzyl- α -D-glucopyranoside (5), 6'-O-Acetyl-2',3'-di-O-benzyl- α -D-glucopyranosyl 6-O-Acetyl-2,3-di-O-benzyl- α -D-glucopyranoside (6), and 2',3'-Di-O-benzyl- α -D-glucopyranosyl 4-O-Acetyl-2,3-di-O-benzyl- α -D-glucopyranoside (7). A mixture of **2** (118 g, 77.1 mmol) and 80% aq. AcOH was heated for 9 h at 80° , left for 65 h at r.t., and evaporated (bath temp. 60°). The residue was taken up in CH_2Cl_2 and Et_2O , and slightly impure crystals of **3** (15.5 g) were removed by filtration. The mother liquor was evaporated and chromatographed (acetone/hexane 1:2 $\rightarrow$ 1:1). The first major fraction furnished slightly yellow crystals of **6**, which were recrystallized from acetone/hexane to give pure **6** (6.29 g, 10.4%) [9]. The main fraction gave slightly yellow crystals of **5** (20.95 g) which were recrystallized from acetone/hexane to give pure **5** (13.4 g, 23.3%), a second crystallization gave another 5.54 g (9.7%) of pure **5**. The next fraction consisted of impure crystals of **3** (7.1 g) which were recrystallized together with the crystals obtained first to yield pure **3** (14.3 g, 26.3%). The mother liquor was chromatographed (acetone/hexane 1:1) to afford pure **7** (1.96 g, 3.4%) which has a slightly higher R_f value than **3** in the eluent used.

5: Colourless crystals. M.p. 133° . $[\alpha]_D^{20} = +156$ ($c = 0.5$, dioxane). IR (KBr): 3472s (br.), 1750s, 1605m, 1498m, 1242s, 1100s, 1047s, 736s, 697s. 1H -NMR (400 MHz, $CDCl_3$): 7.41–7.27 (m, 20 arom. H); 5.191 (d, $J(1',2') = 3.5$, H–C(1')); 5.189 (d, $J(1,2) = 3.5$, H–C(1)); 5.03, 4.78 (2d, $J = 11.4$, $PhCH_2$); 5.01, 4.83 (2d, $J = 11.1$, $PhCH_2$); 4.71 (s, $PhCH_2$); 4.31 (dd, $J(5,6a) = 3.7$, $J(6a,6b) = 12.4$, H_a –C(6)); 4.14 (ddd, $J(4,5) = 10.0$, $J(5,6b) = 2.3$, H–C(5)); 4.02 (ddd, $J(4',5') = 9.7$, $J(5',6'b) \approx 3.5$, H–C(5')); 3.91 (dd, H_b –C(6)); 3.89 (dd $\approx t$, H–C(3)); 3.88 (dd $\approx t$, $J(3',4') = 9.4$, H–C(3')); 3.65 (ddd, $J(5',6'a) = 4$, $J(6'a,6'b) = 12.5$, H_a –C(6')); 3.61 (ddd, H_b –C(6')); 3.60 (ddd $\approx dt$, H–C(4')); 3.553 (dd, $J(2,3) = 9.3$, H–C(2)); 3.545 (dd, $J(2',3') = 9.5$, H–C(2')); 3.46 (ddd, $J(3,4) = 9.2$, H–C(4)); 2.62 (d, $J(4,4-OH) = 3.4$, OH–C(4)); 2.37 (d, $J(4',4'-OH) = 3.0$, OH–C(4')); 2.04 (s, AcO); 1.65 (t, $J(6',6'-OH) = 6.1$, OH–C(6')). CI-MS: 385 (10, acetylated monosaccharid ene). Anal. calc. for $C_{42}H_{48}O_{12}$ (744.83): C 67.72, H 6.50; found: C 67.71, H 6.54.

6: No physical data in [9]. Colourless crystals. M.p. 160° . $[\alpha]_D^{20} = +138.4$ ($c = 0.5$, dioxane). IR (KBr): 3463m, 1729s, 1603w, 1498w, 1244s, 1120s, 1027s, 752m, 700m. 1H -NMR (250 MHz, $CDCl_3$): 7.42–7.25 (m, 10 arom. H); 5.19 (d, $J(1,2) = 3.3$, H–C(1)); 5.00, 4.84 (2d, $J = 11.0$, $PhCH_2$); 4.74, 4.69 (2d, $J = 12.0$, $PhCH_2$); 4.32 (dd, $J(5,6a) = 3.2$, $J(6a,6b) = 12.5$, H_a –C(6)); 4.15 (ddd $\approx$ br. d, $J(4,5) \approx 10$, H–C(5)); 3.90 (dd, $J(5,6b) = 1.5$, H_b –C(6)); 3.89 (dd $\approx t$, H–C(3)); 3.55 (dd, $J(2,3) = 9.8$, H–C(2)); 3.45 (ddd $\approx dt$, $J(4,5) \approx 10$, $J(4,4-OH) = 3.5$, H–C(4)); 2.63 (d, OH–C(4)); 2.04 (s, AcO). CI-MS: 385 (15, monosaccharide anomeric ene). Anal. calc. for $C_{44}H_{50}O_{13}$ (786.87): C 67.16, H 6.41; found: C 67.11, H 6.53.

7: Syrup. $[\alpha]_D^{20} = +96.8$ ($c = 0.5$, dioxane). IR (film): 3454s (br.), 1742s, 1600w, 1107s, 1045s, 737s, 698s. 1H -NMR (250 MHz, $CDCl_3$): 7.39–7.29 (m, 20 arom. H); 5.20, 5.18 (2d, $J(1,2) = 3.6$, H–C(1), H–C(1')); 5.05, 4.83 (2d, $J = 11.3$, $PhCH_2$); 4.92, 4.73, 4.72, 4.715, 4.67, 4.66 (6d, 3 $PhCH_2$); 4.88 (dd $\approx t$, H–C(4)); 4.06–4.00 (m, 2 H); 3.94–3.69 (m, 2H); 3.68–3.61 (m, H–C(4'), 2 H–C(6')); 3.61, 3.56 (2dd, $J = 9.5$, H–C(2), H–C(2')); 3.40 (ddd, H_a –C(6)); 3.21 (ddd, H_b –C(6)); 2.48 (d, OH–C(4')); 2.48 (dd, CH_2OH); 1.99 (s, AcO); 1.76 (dd $\approx t$, CH_2OH). Anal. calc. for $C_{42}H_{48}O_{12}$ (771.27) + 3.5% AcOEt: C 67.28, H 6.59; found: C 67.57, H 6.64.

6'-O-Acetyl-2',3'-di-O-benzyl- α -D-glucopyranosyl 2,3,6-Tri-O-benzyl- α -D-glucopyranoside (8). To a suspension of **5** (5.6 g, 7.5 mmol) in toluene (450 ml) was added dibutyltin oxide (5.8 ml, 11.3 mmol). The mixture was heated under reflux in a *Dean-Stark* apparatus continuously removing H_2O , and the volume was reduced to 200 ml. After 4 h, benzyl bromide (9 ml, 74.8 mmol) and Bu_4NBr (1.66 g, 4.48 mmol) were added to the soln. at 80° . Another addition of the same amounts of benzyl bromide and Bu_4NBr was made after 40 h. The starting material had reacted completely 6 h later, and the mixture was cooled, poured onto ice/ $NaHCO_3$ soln., and extracted with CH_2Cl_2 . The dried crude product was chromatographed (AcOEt/hexane 1:3) to give **4** (0.98 g, 16%), followed by

pure **8** (4.06 g, 65%) as a syrup. $[\alpha]_D^{20} = +125.8$ ($c = 0.5$, dioxane). IR (film): 3440m (br.), 1741s, 1604w, 1492m, 1241s, 1096s, 1003s, 736s, 698s. $^1\text{H-NMR}$ (250 MHz, CDCl_3): 7.38–7.25 (m, 25 arom. H); 5.21 (d, $J(1,2) = 3.1$, H–C(1), H–C(1')); 5.02, 4.82 (2d, $J = 11.5$, PhCH_2); 5.00, 4.80 (2d, $J = 11.2$, PhCH_2); 4.71, 4.64 (2d, $J = 12.0$, PhCH_2); 4.70 (s, PhCH_2); 4.51, 4.44 (2d, $J = 12.0$, PhCH_2); 4.31 (dd, $J(5',6'a) = 4.0$, $J(6'a,6'b) = 12.4$, $\text{H}_a\text{--C}(6')$); 4.18–4.09 (m, H–C(5), H–C(5')); 3.89 (dd, $J(5',6'b) = 2.0$, $\text{H}_b\text{--C}(6')$); 3.88 (dd $\approx t$, H–C(3), H–C(3')); 3.68 (ddd $\approx dt$, H–C(4)); 3.58, 3.52 (2dd, $J(2,3) = J(2',3') = 9.8$, H–C(2), H–C(2')); 3.52 (dd, $\text{H}_a\text{--C}(6)$); 3.47 (dd, $\text{H}_b\text{--C}(6)$); 3.44 (ddd $\approx dt$, H–C(4')); 2.61 (d, $J(4',4'\text{-OH}) = 3.4$, OH–C(4')); 2.39 (d, $J(4,4\text{-OH}) = 2.8$, OH–C(4)); 2.03 (s, AcO). EI-MS and FAB-MS: no M^+ . Anal. calc. for $\text{C}_{49}\text{H}_{54}\text{O}_{12}$ (834.96): C 70.49, H 6.50; found: C 70.29, H 6.72.

2',3'-Di-O-benzyl- α -D-glucopyranosyl 2,3-Di-O-benzyl-4,6-O-benzylidene- α -D-glucopyranoside (**9**). To a soln. of **2** (207.8 g, 236.4 mmol) in AcOH (840 ml) was added H_2O (4.6 ml, 862 mmol) dropwise at 70°. After 80 min, the mixture was poured into a soln. of NaOH (529 g, 572 mmol) in cold H_2O (4 l), and the product was extracted with CH_2Cl_2 , dried (MgSO_4), and evaporated. CC (AcOEt/hexane 1:1→2:1) furnished slightly impure starting material **2** (110.9 g, 52%), followed by pure **9** [15] (63.57 g, 34%), which was used in the next reaction without crystallization. Further elution afforded fully debenzylidenated derivative **3** (12.3 g, 6.5%). **9**: $[\alpha]_D^{20} = +104$ ($c = 0.2$, dioxane); [15]: $[\alpha]_D^{20} = +82$ ($c = 1$, CHCl_3). $^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.52–7.50 (m, 2 arom. H); 7.40–7.27 (m, 23 arom. H); 5.56 (s, PhCH); 5.15, 5.14 (2d, H–C(1), H–C(1')); 5.01, 4.76 (2d, $J = 11.4$, PhCH_2); 4.97, 4.86 (2d, $J = 11.2$, PhCH_2); 4.80, 4.70 (2d, $J = 11.9$, PhCH_2); 4.25 (ddd $\approx dt$, $J(4,5) = 4.8$, H–C(5)); 4.13 (dd $\approx t$, $J(3,4) = 9.2$, H–C(3)); 4.11 (dd, $J(5,6\text{eq}) = 4.7$, $J(6\text{eq},6\text{ax}) = 9.2$, $\text{H}_{\text{eq}}\text{--C}(6)$); 4.01 (ddd $\approx dt$, $J(4',5') = 9.9$, H–C(5')); 3.88 (dd $\approx t$, $J(3',4') \approx 9.5$, H–C(3')); 3.67 (dd $\approx t$, $\text{H}_{\text{ax}}\text{--C}(6)$); 3.65 (dd $\approx t$, H–C(4)); 3.63–3.55 (m, H–C(4'), 2 H–C(6')); 3.61 (dd, $J(1,2) \approx 3.5$, $J(2,3) \approx 9.5$, H–C(2)); 3.53 (dd, $J(1',2') = 3.7$, $J(2',3') = 9.5$, H–C(2')); 2.45 (d, $J(4,\text{OH}) = 3.1$, OH–C(4')); 1.74 (t, OH–C(6')).

2',3',6'-Tri-O-benzyl- α -D-glucopyranosyl 2,3-Di-O-benzyl-4,6-O-benzylidene- α -D-glucopyranoside (**10**). To a soln. of **9** (28.52 g, 36.1 mmol) in toluene (2.2 l) was added bistrityltin oxide and heated under reflux in a Dean-Stark apparatus for 4 h continuously removing H_2O . The volume was reduced to ca. 800 ml. Bu_4NBr (3.84 g, 11.9 mmol) and benzyl bromide (42.8 ml, 360 mmol) were added to the soln. at 80°. After 16 h at 100°, the mixture was cooled, poured onto ice/ NaHCO_3 soln., and extracted with CH_2Cl_2 . The crude product was chromatographed (acetone/hexane 1:2 (containing 1% Et_3N)). Product fractions were pooled and crystallized from acetone/hexane to give pure **10** (23.34 g, 73.5%). The mother liquor was evaporated and rechromatographed (same solvent). Crystallization of product fractions gave more colourless crystals of pure **10** (4.13 g, 13%). M.p. 122°. $[\alpha]_D^{20} = +95.6$ ($c = 0.5$, dioxane). $^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.52–7.49 (m, 2 arom. H); 7.41–7.22 (m, 28 arom. H); 5.55 (s, PhCH); 5.18 (d, H–C(1')); 5.17 (d, H–C(1)); 5.01, 4.79 (2d, $J = 11.2$, PhCH_2); 4.96, 4.85 (2d, $J = 11.6$, PhCH_2); 4.76, 4.70 (2d, $J = 11.0$, PhCH_2); 4.71 (s, PhCH_2); 4.52, 4.45 (2d, $J = 12.0$, PhCH_2); 4.26 (ddd $\approx dt$, $J(5,6a) = 4.8$, $J(5,6b) \approx 10$, H–C(5)); 4.12 (dd $\approx t$, $J(3,4) \approx 9.3$, H–C(3)); 4.12 (ddd $\approx dt$, H–C(5')); 4.11 (dd, $J(6a,6b) = 10.2$, $\text{H}_a\text{--C}(6)$); 3.87 (dd $\approx t$, $J(3',4') \approx 8.9$, H–C(3')); 3.68 (ddd $\approx dt$, $J(4',5') \approx 9.8$, H–C(4')); 3.66, 3.64 (2dd $\approx t$, $\text{H}_b\text{--C}(6)$, H–C(4)); 3.599 (dd, $J(1,2) = 3.8$, $J(2,3) = 9.3$, H–C(2)); 3.596 (dd, $J(1',2') = 3.6$, $J(2',3') = 9.6$, H–C(2')); 3.51 (dd, $J(5',6') = 3.9$, $J(6'a,6'b) = 10.5$, $\text{H}_a\text{--C}(6')$); 3.46 (dd, $J(5',6'b) = 3.3$, $\text{H}_b\text{--C}(6')$); 2.30 (d, $J(4',4'\text{-OH}) = 2.8$, OH–C(4')). Anal. calc. for $\text{C}_{54}\text{H}_{56}\text{O}_{11}$ (881.03): C 73.62, H 6.41; found: C 73.66, H 6.44.

6'-O-Acetyl-2',3'-di-O-benzyl- α -D-glucopyranosyl 2,3-Di-O-benzyl-4,6-O-benzylidene- α -D-glucopyranoside (**11**). A soln. of **5** (1.0 g, 1.34 mmol) in DMF (2 ml) and dimethoxytoluene (0.4 ml, 2.6 mmol) was kept in a rotary evaporator under slightly reduced pressure at 30° in the presence of a catalytic amount of TsOH. After 6 h, the same amounts of reagents were added, and the reaction was continued in the same way. After another 6 h, the same amounts of reagents were added, and the reaction was continued for 20 h. Then the mixture was poured onto ice/aq. NaHCO_3 soln. and extracted with Et_2O 3 times. The org. soln. was washed with H_2O , dried (MgSO_4), and evaporated. CC (acetone/hexane 1:4) gave pure **11** (880 mg, 79%). Colourless syrup. $[\alpha]_D^{20} = +105.4$ ($c = 0.5$, dioxane). IR (film): 3425w (br.), 1738s, 1605w, 1493m, 1091s, 1025s, 745s, 698s. $^1\text{H-NMR}$ (250 MHz, CDCl_3): 7.55–7.49 (m, 2 arom. H); 7.43–7.23 (m, 23 arom. H); 5.56 (s, PhCH); 5.16, 5.15 (2d, H–C(1), H–C(1')); 4.99, 4.98, 4.86, 4.83, 4.82, 4.70 (6d, 3 PhCH_2); 4.72 (s, PhCH_2); 4.29 (dd, $J(5',6'a) = 3.5$, $J(6'a,6'b) = 12.0$, $\text{H}_a\text{--C}(6')$); 4.27 (ddd $\approx dt$, $J(5,6a) = 5.0$, H–C(5)); 4.17–4.08 (m, $\text{H}_a\text{--C}(6)$, H–C(5')); 4.13 (dd $\approx t$, H–C(3)); 3.90 (dd, $J(5,6'b) = 2.1$, $J(6'a,6'b) = 12.0$, $\text{H}_b\text{--C}(6')$); 3.88 (dd $\approx t$, $J(3',4') \approx 9.1$, H–C(3')); 3.67 (dd $\approx t$, H–C(4)); 3.65 (dd $\approx t$, $\text{H}_b\text{--C}(6)$); 3.62 (dd, $J(1,2) = 3.8$, $J(2,3) = 9.5$, H–C(2)); 3.54 (dd, $J(1',2') = 3.8$, $J(2',3') = 9.9$, H–C(2')); 3.44 (ddd $\approx dt$, $J(4',5') \approx 10$, $J(4',4'\text{-OH}) = 3.5$, H–C(4')); 2.58 (d, OH–C(4')); 2.05 (s, AcO).

O-(2'',3'',4'',6''-Tetra-O-benzyl- α -D-glucopyranosyl)-(1''→4')-(2',3',6'-tri-O-benzyl- α -D-glucopyranosyl) 2,3,6-Tri-O-benzyl- α -D-glucopyranoside (**14**) and O-(2'',3'',4'',6''-Tetra-O-benzyl- β -D-glucopyranosyl)-(1''→4')-(2',3',6'-tri-O-benzyl- α -D-glucopyranosyl) 2,3,6-Tri-O-benzyl- α -D-glucopyranoside (**15**). To a soln. of **4** (2.0 g, 2.26 mmol) and imidate **12** (2.17 g, 3.17 mmol) in abs. Et_2O (74 ml) was added a soln. of Me_3SiOTf in Et_2O (2.64 ml

of 73 μl /10 ml Et_2O) at -20° . The soln. was allowed to warm up to r.t. After 2 h, the soln. was cooled to -20° , and a soln. of **12** (1.086 g, 1.59 mmol) in dry Et_2O (7 ml) and MeSiOTf (1.32 ml of Et_2O soln. (see above)) were added. The soln. was allowed to reach r.t. again. After 3.5 h, NaHCO_3 (2.0 g) was added and stirred for 5 min. The mixture was then poured onto dil. NaHCO_3 soln. and extracted with Et_2O . The org. phases were washed with H_2O , dried (Na_2SO_4), and evaporated. The crude material was chromatographed (toluene/acetone 24:1), and product fractions were rechromatographed (toluene/acetone 19:1) to give pure **14** (1.008 g, 32%) followed by pure **15** (14 mg, 0.4%) with an intermediate fraction containing both products (207 mg, 6.5%; **14**/**15** $\approx$ 1:1).

14: Colourless syrup. $[\alpha]_D^{20} = +101.5$ ($c = 0.2$, dioxane). $^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.38–7.15 (m , 50 arom. H); 5.66 (d , $J(1'',2'') = 3.6$, $\text{H-C}(1'')$); 5.24 (d , $J(1',2') = 3.6$, $\text{H-C}(1')$); 5.21 (d , $J(1,2) = 3.5$, $\text{H-C}(1)$); 5.08, 4.84 (2*d*, $J = 11.2$, PhCH_2); 5.03, 4.90 (2*d*, $J = 12.0$, PhCH_2); 4.90, 4.78 (2*d*, PhCH_2); 4.78, 4.40 (2*d*, PhCH_2); 4.68, 4.62 (2*d*, $J = 12.0$, PhCH_2); 4.62, 4.56 (2*d*, $J = 12.0$, PhCH_2); 4.55, 4.505 (2*d*, $J = 12.0$, PhCH_2); 4.51, 4.27 (2*d*, $J = 12.2$, PhCH_2); 4.495, 4.46, 4.425, 4.405 (4*d*, 2 PhCH_2); 4.20 (*ddd*, $\approx dt$, $\text{H-C}(5')$); 4.12 (*dd*, $\approx t$, $J(3',4') = 9.5$, $\text{H-C}(3')$); 4.10 (*ddd*, $\approx dt$, $J(5,6a) \approx 3.5$, $\text{H-C}(5)$); 4.05 (*dd*, $\text{H-C}(4')$); 3.935 (*dd*, $J(2'',3'') = 9$, $J(3'',4'') = 10$, $\text{H-C}(3'')$); 3.928 (*dd*, $\approx t$, $J(3,4) = 9.7$, $\text{H-C}(3)$); 3.72 (*ddd*, $\approx dt$, $\text{H-C}(5'')$); 3.69 (*dd*, $\text{H}_a\text{-C}(6')$); 3.67 (*ddd*, $\approx dt$, $\text{H-C}(4)$); 3.66 (*dd*, $\approx t$, $\text{H-C}(4'')$); 3.64 (*dd*, $J(2',3') = 9.4$, $\text{H-C}(2')$); 3.56 (*dd*, $J(2,3) = 9.8$, $\text{H-C}(2)$); (*dd*, $\text{H}_a\text{-C}(6)$); 3.49 (*dd*, $J(5'',6'a) = 3.6$, $\text{H}_a\text{-C}(6'')$); 3.48 (*dd*, $\text{H-C}(2'')$); 3.47 (*dd*, $\text{H}_b\text{-C}(6')$); 3.35 (*dd*, $J(5'',6'b) = 1.5$, $J(6'a,6'b) = 11.0$, $\text{H}_b\text{-C}(6'')$); 2.36 (d , $J(4,4\text{-OH}) = 3.0$, $\text{OH-C}(4)$). Anal. calc. for $\text{C}_{88}\text{H}_{92}\text{O}_{16}$ (1405.688): C 75.19, H 6.60; found: C 74.88, H 6.54.

15: Colourless syrup. $[\alpha]_D^{20} = +80.0$ ($c = 0.2$, dioxane). $^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.34–7.08 (m , 50 arom. H); 5.16 (d , $\text{H-C}(1'')$); 5.15 (d , $\text{H-C}(1)$); 5.12, 4.98, 4.85, 4.81 (4*d*, 4H, PhCH_2); 4.79 (d , PhCH_2); 4.77, 4.76, 4.69, 4.67, 4.61, 4.60, 4.57 (*d*, 7 H, PhCH_2); 4.54 (d , 2 H, PhCH_2); 4.49 (d , 1 H, PhCH_2); 4.41 (d , 2 H, PhCH_2); 4.41 (d , $\text{H-C}(1'')$); 4.38, 4.34 (2*d*, 2 H, PhCH_2); 4.20 (*ddd*, $\approx \text{br. } d$, $J(4',5') = 10$, $\text{H-C}(5')$); 4.10 (*ddd*, $J(4,5) = 9.8$, $\text{H-C}(5)$); 4.03 (*dd*, $\approx t$, $\text{H-C}(4'')$); 3.94 (*dd*, $\approx t$, $\text{H-C}(3')$); 3.88 (*dd*, $\approx t$, $\text{H-C}(3)$); 3.83 (*dd*, $J(5',6'a) = 3$, $J(6'a,6'b) = 11.0$, $\text{H}_a\text{-C}(6')$); 3.70 (*dd*, $J(5'',6'a) = 1.4$, $J(6'a,6'b) = 11$, $\text{H}_a\text{-C}(6'')$); 3.66 (*dd*, $\approx t$, $\text{H-C}(4)$); 3.60 (*dd*, $\approx t$, $J(3'',4'') = 8.9$, $\text{H-C}(4'')$); 3.52 (*dd*, $\text{H-C}(2)$); 3.51–3.46 (m , $\text{H-C}(3)$, $\text{H}_a\text{-C}(6)$, $\text{H}_b\text{-C}(6')$, $\text{H}_b\text{-C}(6'')$); 3.48 (*dd*, $\approx t$, $\text{H-C}(3'')$); 3.50 (*dd*, $\text{H-C}(2'')$); 3.40 (*dd*, $J(5,6b) = 3.4$, $J(6a,6b) = 10.5$, $\text{H}_b\text{-C}(6)$); 3.38 (*dd*, $\approx t$, $\text{H-C}(2'')$); 3.30 (*ddd*, $J(5'',6'b) = 4.5$, $J(4'',5'') = 10.0$, $\text{H-C}(5'')$); 2.29 (*br. s.*, $\text{OH-C}(4)$).

O-(2,3,4,6-Tetra-O-benzyl- α -D-glucopyranosyl)-(1 $\rightarrow$ 4)-(2,3,6-tri-O-benzyl- α -D-glucopyranosyl) O-(2,3,4,6-Tetra-O-benzyl- α -D-glucopyranosyl)-(1 $\rightarrow$ 4)-2,3,6-tri-O-benzyl- α -D-glucopyranoside (**16**). To a soln. of well-dried **4** (500 mg, 566 mmol) and β -D-fluoride **13** (619 mg, 1.14 mmol) in abs. Et_2O (5 ml) was added TiF_4 (35 mg, 285 μmol) at 0° in the presence of 4 Å molecular sieves (*ca.* 1 g). After stirring for 18 h at r.t., the mixture was filtered over a small amount of silica gel, evaporated, and subjected to MPCL (toluene/AcOEt 19:1). The main fraction consisted of pure **14** (355 mg, 44.6%). The preceding fraction was rechromatographed (MPLC, toluene/AcOEt 39:1) to give pure **16** (240 mg, 22%) as a colourless syrup. $[\alpha]_D^{20} = +93.0$ ($c = 0.2$, dioxane). IR (film): 1605w, 1498m, 1101s. $^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.30–7.25 (m , 23 arom. H); 7.15–7.08 (m , 12 arom. H); 5.66 (d , $J(1',2') = 3.5$, $\text{H-C}(1')$); 5.23 (d , $J(1,2) = 3.8$, $\text{H-C}(1)$); 5.14, 4.96 (2*d*, $J = 11.8$, PhCH_2); 4.91, 4.792 (2*d*, $J = 10.9$, PhCH_2); 4.788, 4.41 (2*d*, $J = 11.0$, PhCH_2); 4.62, 4.54 (2*d*, $J = 12.2$, PhCH_2); 4.56, 4.49 (2*d*, $J = 12.1$, PhCH_2); 4.51, 4.26 (2*d*, $J = 12.2$, PhCH_2); 4.45, 4.38 (2*d*, $J = 12.2$, PhCH_2); 4.18 (*ddd*, $\approx \text{br. } d$, $\text{H-C}(5)$); 4.17 (*dd*, $\approx t$, $\text{H-C}(3)$); 4.05 (*dd*, $\approx t$, $\text{H-C}(4)$); 3.93 (*dd*, $J(3',4') = 9.0$, $\text{H-C}(3')$); 3.72 (*ddd*, $J(4',5') = 10$, $J(5',6'a) \approx 2.5$, $\text{H-C}(5')$); 3.68 (*dd*, $J(5,6a) = 3.5$, $J(6a,6b) = 11.2$, $\text{H}_a\text{-C}(6)$); 3.65 (*dd*, $\approx t$, $\text{H-C}(4'')$); 3.64 (*dd*, $J(2,3) = 9.6$, $\text{H-C}(2)$); 3.48 (*dd*, $\text{H}_a\text{-C}(6')$); 3.48 (*dd*, $J(2',3') \approx 10$, $\text{H-C}(2')$); 3.45 (*dd*, $J(5,6b) \approx 1.5$, $\text{H}_b\text{-C}(6)$); 3.35 (*dd*, $J(5',6'b) = 1.5$, $J(6'a,6'b) = 10.7$, $\text{H}_b\text{-C}(6'')$). $^{13}\text{C-NMR}$ (100.62 MHz, CDCl_3): 139.15 (q); 138.83 (q); 138.51 (q); 138.15 (q); 138.02 (q); 137.92 (q , 2C); 97.35 (d , C(1')); 94.02 (d , C(1)); 81.86 (d , C(3')); 81.52 (d , C(3)); 79.43 (d , C(2')); 79.18 (d , C(2)); 77.64 (d , C(4')); 75.48 (t , PhCH_2); 74.93 (t , PhCH_2); 74.28 (t , PhCH_2); 73.44 (t , PhCH_2); 73.40 (d , C(4)); 73.11 (t , PhCH_2); 72.88 (t , PhCH_2); 72.60 (t , PhCH_2); 70.88 (d , C(5')); 70.47 (d , C(5)); 68.53 (t , C(6)); 68.17 (t , C(6')). Anal. calc. for $\text{C}_{122}\text{H}_{126}\text{O}_{21}$ (1928.329): C 75.99, H 6.59; found: C 75.79, H 6.85.

O-(2'',3'',4'',6''-Tetra-O-benzyl- α -D-glucopyranosyl)-(1'' $\rightarrow$ 4'')-2',3',6'-tri-O-benzyl- α -D-glucopyranosyl 6-O-Acetyl-2,3-di-O-benzyl- α -D-glucopyranoside (**17**) and O-(2'',3'',4'',6''-Tetra-O-benzyl- α -D-glucopyranosyl)-(1'' $\rightarrow$ 4'')-(6'-O-acetyl-2',3'-di-O-benzyl- α -D-glucopyranosyl) 2,3,6-Tri-O-benzyl- α -D-glucopyranose (**18**). To a soln. of well dried **8** (500 mg, 599 mmol) and **12**, (581 mg, 848 mmol) in dry Et_2O (15 ml) was added MeSiOTf (0.63 ml of 7.3 μl of Me_3SiOTf in 1.0 ml of Et_2O) at -20° . The mixture was slowly warmed up to $+5^\circ$, poured onto ice/aq. NaHCO_3 soln. after 40 min, and extracted with Et_2O . The Et_2O soln. was washed with H_2O , dried (Na_2SO_4), and evaporated. The crude product was chromatographed (toluene/AcOEt 9:1) to give **18** (40 mg, 5%) and **17** (230 mg, 29%) as a colourless syrup together with an intermediate fraction containing both compounds (90 mg, 11%; **17**/**18** $\approx$ 1:1).

17: IR (film) 1741s, 1603w, 1496m, 1210m, 1096s, 1008s, 737s, 698s. $^1\text{H-NMR}$ (400 MHz CDCl_3): 5.65 (*d*, $J(1'',2'') = 3.5$, $\text{H-C}(1'')$); 5.22, 5.19 (*2d*, $J = 3.7$ and 3.5 , $\text{H-C}(1)$ and $\text{H-C}(1')$, resp.); 2.60 (*d*, $J(4\text{-OH}) = 3.5$, $\text{OH-C}(4)$); 2.02 (*s*, AcO). The compound was further characterized after deprotection.

18: $[\alpha]_D^{20} = +99.2$ ($c = 0.25$, dioxane). IR (film): 3440m (br.), 1743s, 1604w, 1496m, 1216s, 1098s, 1004s, 736s, 698s. $^1\text{H-NMR}$ (400 MHz, CDCl_3): 5.53 (*d*, $J(1'',2'') = 3.6$, $\text{H-C}(1'')$); 5.20 (*2d*, $J = 3.5$, $\text{H-C}(1)$, $\text{H-C}(1')$); 2.36 (*d*, $J(4,4\text{-OH}) = 2.8$, $\text{OH-C}(4)$); 1.94 (*s*, AcO).

O-(2'',3'',4'',6''-Tetra-*O*-benzyl- α -D-glucopyranosyl)-(1'' $\rightarrow$ 4')-(2',3',6'-tri-*O*-benzyl- α -D-glucopyranosyl) 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene- α -D-glucopyranoside (**19**).

a) To a soln. of **10** (500 mg, 0.57 mmol) and **12** (3.51 g, 5.13 mmol) in dry Et_2O (60 ml) was added Me_3SiOTf (0.63 ml of a soln. containing 7.3 $\mu\text{l/l}$ ml Et_2O) at -20° . After 4 h, the same amount of catalyst was added. The soln. was warmed up to r.t., and NaHCO_3 was added. After 5 min, the mixture was poured onto aq. NaHCO_3 soln. and extracted with Et_2O . The Et_2O soln. was washed with H_2O twice and evaporated. The residue was chromatographed (AcOEt /hexane 1:3). The product fractions were rechromatographed (AcOEt /hexane 1:4) to give **19** (400 mg, 51%).

b) To a soln. of **10** (450 mg, 0.51 mmol) and **13** (533 mg, 1.02 mmol) in dry Et_2O (30 ml) was added MeSiOTf (1.85 ml of a soln. containing 100 μl /5 ml Et_2O) at -5° in the presence of molecular sieves (*ca.* 1 g). The mixture was allowed to reach r.t., after 2 h of stirring it was poured onto ice/aq. NaHCO_3 soln. and extracted with Et_2O . The org. soln. was washed with H_2O twice, dried (Na_2SO_4), and evaporated. CC (AcOEt /hexane 1:4) furnished **19** (320 mg, 45%).

c) To a suspension of **10** (500 mg, 0.57 mmol), AgOTf (172 mg, 0.67 mmol), and SnCl_2 (127 mg, 0.67 mmol) in dry Et_2O (2.5 ml) was added dropwise a soln. of **13** (619 mg, 1.14 mmol) in dry Et_2O (5 ml) at 5° . After 2 h at r.t., the mixture was filtered over a pad of *Speedex*, poured onto ice/aq. NaHCO_3 soln., and extracted with Et_2O . The org. soln. was washed with H_2O twice, dried (Na_2SO_4), and evaporated. CC (AcOEt /hexane 1:4) furnished **19** (520 mg, 65%).

d) To a soln. of **10** (500 mg, 0.57 mmol) and **13** (619 mg, 1.14 mmol) in dry Et_2O (5 ml) was added TiF_4 (35 mg, 0.285 mmol) at 0° in the presence of 4 Å molecular sieves (*ca.* 1 g). The mixture was stirred for 16 h at r.t., filtered over a layer of silica gel, and evaporated. MPLC (AcOEt /hexane 1:4) furnished **19** (540 mg, 68%).

e) To a soln. of **10** (881 mg, 1.0 mmol) and **13** (1085 mg, 2.0 mmol) in dry Et_2O (40 ml) was added a soln. of TiF_2O (181 μl , 1 mmol) in dry Et_2O (5 ml) at -20° in the presence of 4-Å molecular sieves. The mixture was stirred for 3 h at r.t., poured onto ice/aq. NaHCO_3 soln., and extracted with Et_2O . The org. soln. was washed with H_2O twice, dried (Na_2SO_4), and evaporated. MPLC (AcOEt /hexane 1:5) gave **19** (1.295 g, 92%). Colourless syrup. $[\alpha]_D^{20} = +80.8$ ($c = 0.5$, dioxane). $^1\text{H-NMR}$ (400 MHz, CDCl_3): 7.51–7.49 (*m*, 2 arom. H); 7.43–7.39 (*m*, 4 arom. H); 7.33–7.08 (44 arom. H); 5.66 (*d*, $J(1'',2'') = 3.6$, $\text{H-C}(1'')$); 5.55 (*s*, PhCH); 5.19 (*d*, $J(1',2') = 3.8$, $\text{H-C}(1')$); 5.15 (*d*, $J(1,2) = 3.8$, $\text{H-C}(1)$); 5.04, 4.89 (*2d*, $J = 12.2$, PhCH_2); 4.99, 4.91 (*2d*, PhCH_2); 4.915, 4.79 (*2d*, $J = 11$, PhCH_2); 4.79, 4.40 (*2d*, $J = 11.0$, PhCH_2); 4.75, 4.695 (*2d*, $J = 12.5$ PhCH_2); 4.67, 4.615 (*2d*, $J = 11.5$, PhCH_2); 4.55, 4.51 (*2d*, $J = 12.2$, PhCH_2); 4.51, 4.26 (*2d*, $J = 12.0$, PhCH_2); 4.46, 4.41 (*2d*, $J = 12.0$, PhCH_2); 4.26 (*ddd* $\approx$ *dt*, $\text{H-C}(5)$); 4.23 (*ddd* $\approx$ *dt*, $\text{H-C}(5')$); 4.18 (*dd* $\approx$ *t*, $J(3',4') = 9.1$, $\text{H-C}(3)$); 4.13 (*dd* $\approx$ *t*, $J(3',4') \approx 9.5$, $\text{H-C}(3')$); 4.09 (*dd*, $J(5,6a) = 4.0$, $J(6a,6b) = 10.5$, $\text{H}_a\text{-C}(6)$); 4.06 (*dd* $\approx$ *t*, $\text{H-C}(4')$); 3.93 (*dd*, $J(3'',4'') = 9.6$, $\text{H-C}(3'')$); 3.72 (*ddd* $\approx$ *dt*, $\text{H-C}(5'')$); 3.70 (*dd*, $\text{H}_a\text{-C}(6'')$); 3.66 (*dd*, $J(2',3') = 9.8$, $\text{H-C}(2')$); 3.63 (*dd* $\approx$ *t*, $\text{H-C}(4)$); 3.65 (*dd*, $J(5,6b) \approx 9.5$, $\text{H}_b\text{-C}(6)$, and *dd* $\approx$ *t*, $J(4'',5'') = 9.7$, $\text{H-C}(4'')$); 3.58 (*dd*, $J(2,3) = 9.8$, $\text{H-C}(2)$); 3.49 (*dd*, $J(5'',6'a) = 3.3$, $\text{H}_a\text{-C}(6'')$); 3.48 (*dd*, $J(2'',3'') = 8.9$, $\text{H-C}(2'')$); 3.35 (*dd*, $J(5'',6'b) = 1.5$, $J(6'a,6'b) = 10.5$, $\text{H}_b\text{-C}(6'')$). $^{13}\text{C-NMR}$ (100.62 MHz, CDCl_3): 139.1 (*q*); 138.9 (*q*, 2C); 138.6 (*q*); 138.2 (*q*, 2C); 138.1 (*q*); 138.0 (*q*); 137.8 (*q*); 137.6 (*q*); 128.9–126.1 (*ca.* 20 *d* arom. C); 101.2 (*d*, PhCH); 97.3 (*d*, $\text{C}(1'')$); 95.3 (*d*, $\text{C}(1)$); 94.1 (*d*, $\text{C}(1')$); 82.5 (*d*, $\text{C}(4)$); 81.9 (*d*, $\text{C}(3'')$); 81.6 (*d*, $\text{C}(3')$); 79.5 (*d*, 2C, $\text{C}(2')$, $\text{C}(2'')$); 78.7 (*d*, $\text{C}(3)$); 78.6 (*d*, $\text{C}(2)$); 77.7 (*d*, $\text{C}(4'')$); 75.5, 75.3, 74.9, 74.3, 73.5 (*5t*, 5 PhCH_2); 73.4 (*d*, $\text{C}(4')$); 73.3 (*t*, PhCH_2); 73.1 (*t*, 2C, 2 PhCH_2); 72.9 (*t*, PhCH_2); 70.9 (*d*, $\text{C}(5'')$); 70.6 (*d*, $\text{C}(5')$); 69.0 (*t*, $\text{C}(6)$); 68.6 (*t*, $\text{C}(6')$); 68.2 (*t*, $\text{C}(6'')$); 62.9 (*d*, $\text{C}(5)$).

O-(α -D-Glucopyranosyl)-(1'' $\rightarrow$ 4')- α -D-glucopyranosyl α -D-Glucopyranoside (**20**).

a) A soln. of **19** (200 mg, 0.14 mmol) in AcOEt (2 ml) and EtOH (2 ml) was hydrogenated at r.t. in the presence of 5% Pd/C (20 mg). After 18 h, the mixture was filtered over a pad of *Speedex*, evaporated, and again submitted to hydrogenation in $\text{H}_2\text{O}/\text{EtOH}$ 4:1 for 48 h in the presence of the same amount of catalyst. Filtration and chromatography over *LH 20*[®] ($\text{H}_2\text{O}/\text{MeOH}$ 1:1) gave pure **20** (67 mg, 93%).

b) A soln. of **14** (390 mg, 0.66 mmol) in AcOEt (2 ml) and MeOH (20 ml) was hydrogenated at r.t. in the presence of 5% Pd/C (200 mg). After 6.5 h, the mixture was filtered, the residue carefully washed with AcOEt , MeOH , and H_2O ; the soln. evaporated, and the material hydrogenated in MeOH (40 ml) and H_2O (5 ml) using 10% Pd/C (500 mg) as catalyst. After 18 h, the mixture was filtered over a pad of *Speedex*, and the residue washed with H_2O . Evaporation gave pure **20** (330 mg, 99%).

c) To a soln. of **17** (215 mg, 0.158 mmol) in MeOH (5ml) and AcOEt (2.5 ml) was added anh. Na_2CO_3 (25 mg) and stirred at r.t. After 2 h, the suspension was filtered over a pad of *Speedex* and evaporated. MPLC ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ 3:1) furnished O-2'',3'',4'',6''-tetra- O-benzyl- α -D-glucopyranosyl)-(1'' $\rightarrow$ 4'')-(2',3',6'-tri-O-benzyl- α -D-glucopyranosyl) 2,3-di-O-benzyl- α -D-glucopyranoside (184 mg, 88%) as a colourless syrup. $[\alpha]_{\text{D}}^{20} = +100.4$ ($c = 0.5$, dioxane). $^1\text{H-NMR}$ (400 MHz, CDCl_3): 5.65 (d , $J(1'',2'') = 3.5$, H-C(1'')); 5.22, 5.20 ($2d$, $J = 3.7$ and 3.5 , H-C(1') and H-C(2), resp.); 2.32 (br. s, OH-C(4)); 1.58 (br. s, OH-C(6)).

Part of this deacetylated compound (100 mg, 0.076 mmol) was hydrogenated as described under *b*) to give pure **20** (37 mg, 97%), identical to the material obtained before.

20: Colourless foam. $[\alpha]_{\text{D}}^{20} = +176.4$ ($c = 0.5$, H_2O ; [30]: $[\alpha]_{\text{D}}^{20} = +207 \pm 4.5$ ($c = 0.778$, $c = 0.383$, H_2O); [31]: $[\alpha]_{\text{D}}^{20} = +169$ ($c = 0.4$, H_2O)). $^1\text{H-NMR}$ (500 MHz, D_2O): 5.43 (d , $J(1'',2'') = 3.9$, H-C(1'')); 5.20 (d , H-C(1')); 5.19 (d , H-C(1)); 4.12 ($dd \approx t$, $J(3',4') \approx 8.9$, H-C(3')); 3.95 (ddd , $J(4',5') = 9.9$, $J(5',6'a) = 2.0$, $J(5',6'b) = 4.5$, H-C(5')); 3.88 (dd , $\text{H}_a\text{-C}(6')$); 3.88–3.73 (m , H-C(5''), 2 H-C(6'')); 3.85 ($dd \approx t$, $J(3,4) \approx 9$, H-C(3)); 3.84 (ddd , H-C(5)); 3.83 (dd , $\text{H}_b\text{-C}(6'')$); 3.80–3.72 (m , 2 H-C(6)); 3.70 ($2dd \approx t$, $J(3'',4'') \approx 10$, H-C(3''), H-C(4'')); 3.69 (dd , $J(2',3') \approx 10$, H-C(2'')); 3.65 (dd , $J(1,2) = 3.9$, $J(2,3) = 10.0$, H-C(2)); 3.59 (dd , $J(2'',3'') = 10.0$, H-C(2'')); 3.43 ($dd \approx t$, $J(4,5) \approx 10$, H-C(4)); 3.42 ($dd \approx t$, $J(4'',5'') \approx 9$, H-C(4'')). FAB-MS: 527 (1, $[M + \text{Na}]^+$). Anal. calc. for $\text{C}_{18}\text{H}_{32}\text{O}_{16}$ (504.44): C 42.86, H 6.39; found: C 42.35, H 6.27.

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