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CHEMO-, STEREO- AND REGIOSELECTIVE HYDROGENOLYSIS OF CARBOHYDRATE BENZYLIDENE ACETALS. SYNTHESIS OF BENZYL ETHERS OF BENZYL α-D-, METHYL β-D-MANNOPYRANOSIDES AND BENZYL α-D-RHAMNOPYRANOSIDE BY RING CLEAVAGE OF BENZYLIDENE DERIVATIVES WITH THE $LiAlH_4$-$AlCl_3$ REAGENT

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Abstract—Treatment of benzyl α-(**1**) and methyl β-D-mannopyranoside (**2**) with α,α-dimethoxytoluene gave the *exo* and *endo* isomers (**3**,**5** and **4**,**6**) of the dibenzylidene derivatives of **1** and **2**. Hydrogenolysis of the *exo* isomers (**3** and **5**) with a molar equivalent of AlH_2Cl gave the 3-O-benzyl-4,6-O-benzylidene derivatives (**7** and **21**), whereas the *endo* isomers (**4** and **6**) gave the 2-O-benzyl-4,6-O-benzylidene compounds (**8** and **22**). The 2-O-allyl ether **9** of **7**, the 3-O-allyl derivative (**10**) of **8** and compounds **21** and **22** were treated with an additional molar equivalent of AlH_2Cl at reflux and the products were the 4-O-benzyl-6-hydroxyl derivatives (**11**, **12**, **23** and **24**), whereas in the case of **22** the 6-O-benzyl-4-hydroxyl isomer (**25**) was also isolated. By deallylation of **11** and **12**, 3,4-(**13**) and 2,4-di-O-benzyl (**14**) ethers of **1** were prepared. Tosylation of **11** and **12**, and subsequent reduction of the products (**15** and **16**) made possible the preparation of the partially protected benzyl α-D-rhamnopyranoside derivatives (**17**–**20**). The structures of the compounds synthesized were characterized by ^1H and ^{13}C NMR spectroscopic investigation and by chemical methods.

The synthesis of complex oligosaccharides requires suitably protected aglycones. For the preparation of oligosaccharides containing D-mannose several derivatives of benzyl α-D-mannopyranoside have been prepared by phase-transfer catalysed alkylation[1] or dibuthylstannylidene-activated alkylation[1-5].

It has been shown that the reductive ring cleavage of benzylidene acetals with the $LiAlH_4$–$AlCl_3$ reagent is an alternative route to obtain partially protected sugar derivatives.[6] The dibenzylidene derivatives of mannopyranosides, in which two acetal rings with different ring-size are present and the dioxolane ring can exist in two stereoisomeric forms, are particularly attractive models to demonstrate the efficiency of this method.[7,8]

In this paper we wish to report the preparation and hydrogenolysis of both dibenzylidene isomers of benzyl α-D- and methyl β-D-mannopyranoside.

RESULTS AND DISCUSSION

Benzylidenation of benzyl α-D-mannopyranoside (**1**) with benzaldehyde in the presence of $ZnCl_2$ has been reported by two groups and only the *exo*-phenyl isomer (**3**) has been isolated.[7,9] At the same time the reaction of **1** with α,α-dimethoxytoluene in *N*,*N*-dimethylformamide in the presence of *p*-toluenesulfonic acid catalyst resulted in a 1:1 mixture (GLC and ^1H NMR) of the two di-O-benzylidene derivatives (**3** and **4**), possessing very different solubility in ethanol. **3** and **4** could be readily separated by simple fractional crystallization. The isomer with very low solubility proved to be the known *exo*-phenyl isomer, i.e. benzyl *exo*-2,3:4,6-di-O-benzylidene-α-D-mannopyranoside (**3**; $\delta_{acetal\,H}$: 6.22 and 5.56 ppm; $\delta_{acetal\,C}$: 103.0 and 102.0 ppm). To the second fraction the *endo*-phenyl configuration was assigned on the basis of ^1H and ^{13}C NMR investigation (**4**; $\delta_{acetal\,H}$: 5.93 and 5.48 ppm; $\delta_{acetal\,C}$: 103.9 and 101.6). The great difference between the solubility of the two isomers (**3** and **4**) explains the isolation of the *exo*-phenyl isomer (**3**), as exclusive product, in earlier studies. Under the reaction conditions of benzylidenation in the presence of $ZnCl_2$ compound **3** with extremely low solubility continously separated from the reaction medium, thereby favouring the equilibrium $\mathbf{1} \rightarrow \mathbf{3} \rightleftarrows \mathbf{4}$ to be shifted towards the formation of **3**.

To our knowledge the benzylidenation of methyl β-D-mannopyranoside (**2**) has not been studied as yet. Acetalation of compound **2** as described for **1** also resulted in both isomers (**5** and **6**), the ratio of which was found to be 28:72 (GLC). Compounds **5** and **6** showed different chromatographic mobility and could be separated by column chromatography. The configuration of the acetal carbon atom of the dioxolane ring in both crystalline isomers was assigned by ^1H NMR using the observation of Foster *et al.*[10] that the acetalic proton of dioxolane-type *endo*-benzylidene isomers resonates at higher field ($\delta_{acetal\,H}$: 5.92 and 5.52 ppm) than that of the *exo* phenyl isomers ($\delta_{acetal\,H}$: 6.29 and 5.60 ppm). This configuration determination is in good agreement with the ^{13}C NMR data which are also suitable to determine the configuration of dioxolane-type benzylidene acetals of carbohydrates.[11,12] The structure of compounds **5** and **6** was confirmed by ^{13}C NMR spectroscopic study; the assignment of the skeleton carbons was verified by selective heteronuclear decoupling $^{13}C\{^1H\}$ in the case of C-1, 2, 3 and C-4. These assignments were also verified by the measuring of $^1J_{C-H}$ coupling constants, their

values in the case of compound **6** are the following: $^1J_{C_1-H_1}$ 162 Hz; $^1J_{C_7-H_7}$ 99.3 Hz (dioxane) and $^1J_{C_8-H_8}$ 169.5 Hz (dioxolane). These values are in good agreement with the findings of Grindley and Gulasekharam[13] found in the case of simple dioxane and dioxolane derivatives, respectively. On the basis of these results the minor component was proved to be the *exo* phenyl isomer (**5**) and to the major product the *endo* phenyl structure (**6**) was assigned.

It was shown in several cases,[14–16] that the dioxolane rings are more reactive than the dioxane analogues and it was demonstrated that this finding is also valid for dibenzylidene mannopyranoside derivatives.[7,8] The cleavage of a dioxolane ring for carbohydrates requires only 5–10 min at room temperature, whereas a period of 1.5–2 h and reflux temperature (45°) is necessary to cleave the dioxane analogues rings. On the basis of these observations hydrogenolysis can be considered as a chemoselective process, the reagent (AlH_2Cl) being able to distinguish between the five- (dioxolane) and six-membered (dioxane) rings. At the same time the ring cleavage of the dioxolane skeleton is a stereoselective reaction; the place of attack of the reagent is determined by the steric position of the phenyl substituent.

The ring cleavage of **3** with one molar equivalent of the above reagent resulted in benzyl 3-O-benzyl-4, 6-O-benzylidene-α-D-mannopyranoside (**7**) and only traces of benzyl 2-O-benzyl-4, 6-O-benzylidene-α-D-mannopyranoside (**8**) was detected.[7] Otherwise, **7** and **8** can be easily differentiated by TLC: compound **8** has higher chromatographic mobility than that of **7**. Contrary to the above result the ring cleavage of **4** resulted in **8** as the only product. Compound **8** was synthesised with 22% yield by Swedish authors,[17] by direct benzylation of benzyl 4,6-O-benzylidene-α-D-mannopyranoside. Since the yield of preparation of benzyl 4, 6-O-benzylidene-α-D-mannopyranoside was also poor (36%) the overall yield of **8** was about 8%.

Both compounds **7** and **8** were conventionally allylated to obtain crystalline **9** and syrupy **10** in 84% and 70% yield, respectively. Hydrogenolysis of **9** at 45° resulted in high yield of benzyl 2-O-allyl-3, 4-di-O-benzyl-α-D-mannopyranoside (**11**). The cleavage of the 4,6-O-benzylidene ring of compound **10** proceeded with similar regioselectivity to give benzyl 3-O-allyl-2, 4-di-O-benzyl-α-D-mannopyranoside (**12**). **12** was prepared[1] recently using the following reaction sequence: benzyl 6-O-trityl-α-D-mannopyranoside → benzyl 3-O-allyl-6-O-trityl-α-D-mannopyranoside → benzyl 3-0-allyl-2, 4-di-0-benzyl-6-0-trityl-α-D-mannopyranoside → **12**.

Removal of the allyl groups from **11** and **12** using the Ogawa method[4] gave benzyl 3,4-[21](**13**) and benzyl 2,4-di-O-benzyl-α-D-mannopyranoside[3] (**14**), respectively.

Conventional tosylation of **11** and **12** resulted in compounds **15** and **16** with primary tosyloxy groups. Reduction of **15** and **16** with $LiAlH_4$ in ether-benzene (1:1) solution gave the corresponding fully protected α-D-rhamnopyranoside derivatives (**17** and **18**) with excellent yield.

On deallylation of compounds **17** and **18** in the presence of palladium-on-carbon benzyl 3,4-di-O-(**19**) and benzyl 2,4-di-O-di-O-benzyl-α-D-rhamnopyranoside (**20**) were obtained. The corresponding enantiomers have been prepared recently[20] and their physical and spectroscopic parameters are the same with that of **19** and **20**, except that $[\alpha]_D$ values are of the opposite sign.

Similar results were obtained with the hydrogenolysis of the dibenzylidene isomers of the β-anomers (**5** and **6**), and methyl 3-O-benzyl-4,6-O-benzylidene-β-D-mannopyranoside (**21**) was prepared from the *exo*-isomer (**5**), whereas the ring cleavage of the *endo*-isomer (**6**) resulted in methyl 2-O-benzyl-4,6-O-benzylidene-β-D-mannopyranoside (**22**). The synthesis of compounds **21** and **22** was published by Garegg;[18] methyl 4,6-O-benzylidene-β-D-mannopyranoside was benzylated with benzyl bromide in the presence of silver oxide in *N,N*-dimethylformamide. The 2-O-benzyl ether (**22**) was the major product and it was separated from **21** by fractional crystallization and column chromatography. Recently, Lee *et al.*[19] also synthesized compound **21**. Oxydation of methyl 3-O-benzyl-4,6-O-benzylidene-β-D-glucopyranoside yielded the corresponding ulose derivative, which was reduced to **21**.

When compound **21** was treated with $LiAlH_4$–$AlCl_3$ reagent at reflux temperature methyl 3,4-di-O-benzyl-β-D-mannopyranoside (**23**) was obtained. The presence of the bulky C_3-O-benzyl group near to the O-4 of the acetal ring hindered the attack of the reagent on this oxygen atom, and thus chloroalane formed complex at O-6 resulting in the bond fission at the primary carbon atom of the mannopyranoside skeleton. Being no such hindrance in the case of compound **22**, its hydrogenolysis afforded both isomeric benzyl ethers i.e. methyl 2,4-(**24**) and methyl 2,6-di-O-benzyl-β-D-mannopyranoside (**25**). The greater quantity of **24** as compared to **25** is in accordance with the proposed mechanism of the ring cleavage of the dioxane-type benzylidene derivatives of hexopyranosides.[22] The two isomers (**24** and **25**) were separated by column chromatography and their structure was confirmed by ^{13}C NMR spectroscopic examination. Since one of the benzyl groups is fixed in both compounds, the second one may only be placed either at position O-4 or O-6. In compound **24** the high field signal at 62.4 ppm can be assigned to C-6, so it is the 2,4-di-O-benzyl isomer. However, in compound **25** the signal at the highest field resonates at 69.9 ppm, unequivocally showing that the C_6-OH is protected.

Spectra of the benzyl ethers of α- and β-mannopyranosides show a very important remark; benzylation shifts (α-shift) +7–9 ppm, and these α-shifts are accompanied with a −2–3 ppm large upfield β-shifts at C-1 in the case of the α-anomers, but the value of these β-shifts is about 0.6 ppm downfield shift in the case of the β-anomers. Similar β-shift values were also found in the case of α- and β-L-rhamnopyranoside derivatives.

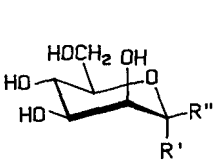
These structures were further substantiated by oxidation with periodic acid; compound **24** was stable under the used conditions whereas **25** could be cleaved by $NaIO_4$. In both cases the oxidation reaction was monitored by TLC.

EXPERIMENTAL

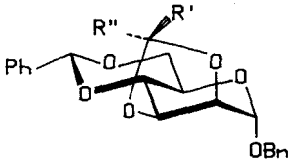
General. M.ps were determined on a Kofler apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. ^1H- and ^{13}C NMR spectra (for solution in $CDCl_3$) were taken at room temp. and at the frequency of 100.1 and 25.16 or 50.3 MHz with JEOL MH-100 and Varian XL-100-FT-15 or Bruker WP-200 SY spectrometers, using TMS or dioxan as an internal reference. TLC and column chromatography were performed on Kieselgel G (Merck) using the solvent system given in the parentheses.

Benzyl exo- (**3**) *and* endo-2,3:4,6-*di*-O-benzylidene-α-D-*mannopyranoside* (**4**)

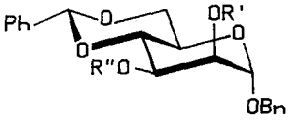
A mixture of **1** (2 g), α,α-dimethoxytoluene (4 g) and *p*-



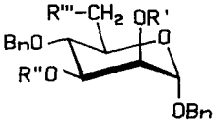
1 R'=OBn; R"=H
2 R'=H; R"=OCH_3



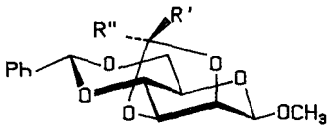
3 R'=Ph; R"=H
4 R'=H; R"=Ph



7 R'=H; R"=Bn
8 R'=Bn; R"=H
9 R'=All; R"=Bn
10 R'=Bn; R"=All

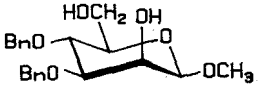


11 R'=All; R"=Bn; R'''=OH
12 R'=Bn; R"=All; R'''=OH
13 R'=H; R"=Bn; R'''=OH
14 R'=Bn; R"=H; R'''=OH
15 R'=All; R"=Bn; R'''=OTs
16 R'=Bn; R"=All; R'''=OTs
17 R'=All; R"=Bn; R'''=H
18 R'=Bn; R"=All; R'''=H
19 R'=H; R"=Bn; R'''=H
20 R'=Bn; R"=H; R'''=H

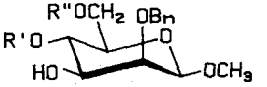


5 R'=Ph; R"=H
6 R'=H; R"=Ph

21 R'=H; R"=Bn
22 R'=Bn; R"=H



23



24 R'=Bn; R"=H
25 R'=H; R"=Bn

Table 1. ^{13}C NMR chemical shifts (ppm) and coupling constants (H_3)

Carbon \ Compound		2[a]	3	4	5	6	7	8	13	14	21	22	23	24	25
1		102.3	97.5	96.9	104.9	101.7	99.5	97.9	99.0	96.8	101.5	103.5	101.3	102.9	102.9
						162.0			169.9	167.0	158.0	157.0			
2		71.7	75.5	78.4	74.4	75.3	70.1	79.6[b]	68.6	78.6	69.8	78.6	71.7	78.0	77.6
3		74.5	77.6	74.1	76.9	76.6	75.9	68.8	80.0	72.1[b]	77.1	70.9	81.7	74.1	73.7
4		68.4	75.8	80.5	77.9	79.1	79.0	78.7[b]	74.1	76.5	78.5	79.4	75.8	76.7	70.6
5		77.6	60.8	60.6	65.4	65.3	63.7	63.9	72.3	71.7[b]	70.0	67.3	74.2	74.1	74.0
6		62.6	68.9	68.7	69.8	69.8	68.9	68.8	61.6	62.1	68.6	68.7	62.1	62.4	69.9
1-O-Benzyl	$-\underline{C}H_2-$		69.8	69.5			69.4	69.4	69.3	69.1					
	q		137.0	136.9			137.1	137.1	137.3	137.2					
1-O-Methyl	$-\underline{C}H_3$				56.8	56.7					56.9	57.2	57.1	57.2	57.1
2,3-O-Benzylidene	$-\underline{C}H=$		103.0	103.9	101.9	105.5									
						169.5									
	q		138.9	137.2	137.3	137.4									
4,6-O-Benzylidene	$-\underline{C}H=$		102.0	101.6	100.3	99.7	101.6	102.1			101.6	102.0			
						99.3									
	q		137.5	137.3	137.3	136.7	137.7	137.6			138.3	137.7			
2-O-Benzyl	$-\underline{C}H_2-$							73.8		73.1		75.5		75.0[b]	74.9
	q							137.8		138.6		138.6		138.5	138.7
3-O-Benzyl	$-\underline{C}H_2-$						73.1		75.1[b]		72.3		75.1[b]		
	q						138.1		138.6		137.8		133.5		
4-O-Benzyl	$-\underline{C}H_2-$								72.0[b]	74.7			75.4[b]	75.7[b]	
	q								138.2	137.9			133.3	138.5	
6-O-Benzyl	$-\underline{C}H_2-$														75.3
	q														138.3

[a] Chemical shifts for 2 are taken from ref. 23. [b] Assignments may be reversed.

toluene-sulfonic acid monohydrate (0.04 g) in N,N-dimethylformamide (15 ml) was stirred for 3 h at 75° in a 50-ml flask attached to a water aspirator and fitted with an air condenser. The reaction mixture was diluted with chloroform (150 ml), washed with aqueous sodium hydrogen carbonate (3 × 20 ml) and water (5 × 50 ml). The dried soln was evaporated to give crystalline residue. The crude product was suspended in 10 ml of cold ethanol and filtered to give a 1:1 mixture (^{1}H NMR) of **3** and **4** (2.60 g). This mixture was recrystallized from hot ethanol (185 ml) to give **3** (1.22 g) and repeated crystallization from 240 ml of ethanol yielded pure **3** (1.18 g; 35.8%), m.p. 188°, $[\alpha]_D$ + 35° (c 1.20, chloroform); lit[7] m.p. 188–189°, $[\alpha]_D$ + 34° (c 1.0, chloroform). ^{1}H NMR δ6.22 (s, 1 H, dioxolane Ph–CH=), 5.56 (s, 1 H, dioxane Ph–CH=), 5.12 (s, 1 H, H-1). Calc. for $C_{27}H_{26}O_6$: C, 72.63; H, 5.87. Found: C, 72.68; H, 5.92%. The mother liquor of the first crystallization of **3** was evaporated to 25 ml. The crystalline product (1.0 g) was recrystallized from 15 ml of ethanol to give pure **4** (0.92 g; 27.9%), m.p. 106–107°, $[\alpha]_D$ − 8.5° (c1.02, chloroform). ^{1}H NMR: δ5.93 (s, 1 H, dioxolane Ph–CH=), 5.48 (s, 1 H, dioxane Ph–CH=), 5.25 (s, 1 H, H-1). Calc. for $C_{27}H_{26}O_6$: C, 72.63; H, 5.87. Found: C, 72.54; H, 5.81%.

Methyl exo- (**5**) *and* endo-2,3:4,6-*di*-O-benzylidene-β-D-*mannopyranoside* (**6**)

A mixture of methyl β-D-mannopyranoside (**2**; 2 g), α,α-dimethoxytoluene (6.32 g), N,N-dimethylformamide (10 ml) and *p*-toluenesulfonic acid (100 mg) was stirred in vacuo at 50° for 2 h. Two products were detected on TLC; R_f 0.58 and 0.51 (chloroform) in a ratio of 1:3. The reaction mixture was diluted with dichloromethane (100 ml), washed with aqueous sodium hydrogen carbonate (2 × 20 ml) and water (3 × 20 ml). The organic layer was dried (Na_2SO_4) and evaporated. The syrupy residue was steam distilled and the residue was extracted with dichloromethane (3 × 50 ml). The organic phase was washed with water, dried and concentrated to yield a mixture of crystalline products (3.22 g), containing two components in a ratio of 28.4:71.6 (GLC).

These two compounds were separated by column chromatography (chloroform). The product eluted first (R_f 0.58) was crystalline **5** (0.78 g; 20.5%); it was recrystallized from ethanol (30 ml) to obtain 0.54 g (14.2%), m.p. 204–205°, $[\alpha]_D$ − 98° (c 0.78, chloroform). ^{1}H NMR δ7.62–7.10 (m, 10 H, aromatic protons), 6.29 (s, 1 H, dioxolane Ph–CH=), 5.60 (s, 1 H, dioxane Ph–CH=), 4.76 (d, 1 H, H-1, $J_{1,2}$ = 2.7 Hz), 4.56 (dd, H-3, $J_{2,3}$ = 6.2 Hz, $J_{3,4}$ = 7.2 Hz), 4.38 (dd, H-6e, $J_{5,6e}$ = 4.8 Hz, $J_{6a,6e}$ = 10.2 Hz), 4.36 (dd, H-2), 4.19 (dd, H-4, $J_{4,5}$ = 11.2 Hz), 3.78 (dd, H-6a, $J_{5,6a}$ = 9.6 Hz), 3.61–3.30 (m, 4 H, OCH_3 and H-5). Calc. for $C_{21}H_{22}O_6$: C, 68.10; H, 5.99. Found: C, 67.42; H, 5.92%.

Second compound eluted **6** had R_f 0.51 (2.02 g; 53.0%). Recrystallization from ethanol (80 ml) gave 1.74 (45.7%), m.p. 199–200°, $[\alpha]_D$ − 139° (c 1.52, chloroform). ^{1}H NMR: δ7.70–7.10 (m, 10 H, aromatic protons), 5.92 (s, 1 H, dioxolane Ph–CH=), 5.54 (s, 1 H, dioxane Ph–CH=), 4.82 (d, 1 H, H-1, $J_{1,2}$ = 2.7 Hz), 4.45 (dd, H-3, $J_{2,3}$ = 6.6 Hz, $J_{3,4}$ = 6.6 Hz), 4.38 (dd, H-6e, $J_{5,6e}$ = 5.1 Hz, $J_{6a,6e}$ = 9.3 Hz), 4.34 (dd, H-2), 4.22 (dd, H-4, $J_{4,5}$ = 9.2 Hz), 3.74 (dd, H-6a, $J_{5,6a}$ = 9.3 Hz), 3.61–3.37 (m, 4 H, OCH_3 and H-5). Calc. for $C_{21}H_{22}O_6$: C, 68.10; H, 5.99. Found: C, 68.23; H, 6.08%.

Benzyl 3-*O*-*benzyl*-4,6-*O*-*benzylidene*-α-D-*mannopyranoside* (**7**)

To a soln of **3** (3.0 g) in 1:1 ether–dichloromethane (60 ml) 0.3 g of $LiAlH_4$ was added and the solution was cooled to room temp. To the cold soln $AlCl_3$ (1.0 g) in ether (10 ml) was added and the mixture was stirred for 15 min. The excess of $LiAlH_4$ was decomposed with ethyl acetate (2 ml), and $Al(OH)_3$ was precipitated by addition of water (5 ml). After dilution with ether (40 ml) the organic layer was separated and the residue washed with a little ether. The organic phase was washed with water (2 × 30 ml), dried and concentrated to yield **7** (2.45 g; 81.3%), m.p. 89° (from 15 ml of ethanol), $[\alpha]_D$ +56° (c1.3, chloroform); lit[7] m.p. 88–89°, $[\alpha]_D$ + 55.4° (c0.5, chloroform). R_f 0.70 (19:1 benzene-methanol). ^{1}H NMR δ5.51 (s, 1 H, Ph–CH=), 4.84 (s, 1 H, H-1), 4.67 and 4.50 (2 q, 4 H, 2 Ph–CH_2–), 2.52 (b, 1 H, OH). Calc. for $C_{27}H_{28}O_6$: C, 72.30; H, 6.29. Found: C, 72.18; H, 6.31%.

Benzyl 2-*O*-*benzyl*-4, 6-*O*-*benzylidene*-α-D-mannopyranoside (**8**)

Compound **4** (1.50 g) in 1:1 ether–dichloromethane (30 ml) was treated with 0.15 g of $LiAlH_4$ and 0.5 g of $AlCl_3$ as described for **7**. After work-up of the reaction mixture 1.29 g (85.6%) of **8** was obtained, m.p. 98–100° (from ethanol), $[\alpha]_D$ + 42° (c0.72, chloroform); lit[17] m.p. 97–98°, $[\alpha]_D$ + 40° (c0.2, chloroform). R_f 0.75 (19:1 benzene–methanol).

^{1}H NMR data: δ5.50 (s, 1 H, Ph–CH=), 4.88 (s, 1 H, H-1), 4.78–4.30 (m, 4 H, 2 Ph–C_2–), 2.50 (b, 1 H, OH). Calc. for $C_{27}H_{28}O_6$: C, 72.30; H, 6.29. Found: C, 71.94; H, 6.04%.

Benzyl 2-*O*-*allyl*-3-*O*-*benzyl*-4,6-*O*-*benzylidene*-α-D-*mannopyranoside* (**9**)

A mixture of **7** (5 g), N,N-dimethylformamide (80 ml) and NaH (0.78 g) was stirred for 1 h. Allyl bromide (2.8 ml) was added and stirring was continued for 16 h. The excess of NaH was decomposed with methanol (8 ml) and the mixture was diluted with dichloromethane (200 ml). The solution was washed with water (5 × 100 ml), dried and concentrated. Three recrystallization of the solid residue from 15–15 ml of ethanol yielded **9** (4.58 g; 84.2%), m.p. 107°, $[\alpha]_D$ + 72.48° (c1.20, chloroform), R_f 0.65 (4:1 n-hexane–ethyl acetate). ^{1}H NMR: δ5.94 (m, 1 H, –CH=), 5.66 (s, 1 H, Ph–CH=), 5.25 (m, 2 H, $=CH_2$), 4.89 (s, 1 H, H-1), 4.77 and 4.65 (2 q, 4 H, 2 Ph–CH_2–). Calc. for $C_{30}H_{32}O_6$: C, 73.75; H, 6.60. Found: C, 73.82; H, 6.64%.

Benzyl 3-*O*-*allyl*-2-*O*-*benzyl*-4,6-*benzylidene*-α-D-*mannopyranoside* (**10**)

A mixture of **8** (2.18 g), N,N-dimethylformamide (10 ml) and powdered KOH (1.16 g) was stirred with allyl bromide (0.65 ml) for 2 h at room temp. The reaction mixture was diluted with dichloromethane (100 ml) and filtered. The organic soln was washed with water (3 × 50 ml), dried and evaporated. The crude product was purified on a Kieselgel G column (120 g) using 4:1 light petroleum – ethyl acetate as eluant. The pure syrupy **10** (1.65 g; 69.9%) had $[\alpha]_D$ + 72° (c0.68, chloroform), R_f 0.8 (4:1 n-hexane—ethyl acetate). ^{1}H NMR δ5.80 (m, 1 H, –CH=), 5.58 (s, 1 H, Ph–CH=), 5.18 (m, 2 H, $=CH_2$), 4.84 (s, 1 H, H-1), 4.72 and 4.64 (2 q, 4 H, 2 Ph–CH_2). Calc. for $C_{30}H_{32}O_6$: C, 73.75; H, 6.60. Found: C, 73.65, H, 6.66%.

Benzyl 2-*O*-*allyl*-3, 4-*di*-*O*-*benzyl*-α-D-*mannopyranoside* (**11**)

A soln of **9** (3 g) in ether (60 ml) and dichloromethane (100 ml) was treated with $LiAlH_4$ (1 g) and $AlCl_3$ (3 g) in ether (40 ml) for 1.5 h at reflux temp. The crude syrupy product (2.96 g) was purified on a Kieselgel G column (150 g) using 7:3 n-hexane – ethyl acetate as the eluant. Yield: 2.68 g (88.9%), $[\alpha]_D$ + 38° (c1.8, chloroform), R_f 0.22 (n-hexane—ethyl acetate 7:3). ^{1}H NMR data: δ5.80 (m, 1 H, –CH=), 5.08 (m, 2 H, $=CH_2$), 4.93 (s, 1 H, H-1), 4.96–4.35 (m, 6 H, 3 Ph–CH_2–), 2.42 (b, 1 H, OH), Calc. for $C_{30}H_{34}O_6$: C, 73.44; H, 6.98. Found: C, 73.56; H, 7.01%.

Benzyl 3-*O*-*allyl*-2, 4-*di*-*O*-*benzyl*-α-D-*mannopyranoside* (**12**).

To a soln of **10** (1.57 g) in 1:1 ether–dichloromethane (80 ml) 0.52 g of $LiAlH_4$ was added with stirring and the mixture was slowly heated to the boiling point. To the hot soln $AlCl_3$ (1.57 g) in ether (20 ml) was added and boiling was continued for additional 1.5 h. After usual work-up, the solid residue was recrystallized from a mixture of c-hexane (3 ml) and n-hexane (20 ml) to give **12** (1.12 g; 71%), m.p. 60°, $[\alpha]_D$ + 71° (c1.69, chloroform); lit[1] m.p. 57–58°, $[\alpha]_D$ + 59° (c1.1, chloroform). R_f 0.34 (n-hexane–ethylacetate 7:3). Calc. for $C_{30}H_{34}O_6$: C, 73.44; H, 6.98. Found: C, 73.52; H, 7.03%.

Benzyl 3,4-*di*-*O*-*benzyl*-α-D-*mannopyranoside* (**13**)

Compound **11** (0.2 g) and 10% palladium-on-carbon catalyst (0.1 g) were suspended in 2:1:1 ethanol–acetic acid–water (30 ml) mixture and boiled for 30 h. The reaction mixture was then filtered, the filtrate evaporated and the residue was purified on a Kieselgel G column (15 g) using 9:1 chloroform–acetone as the eluant. The syrupy **13** (154 mg; 83.9%) had $[\alpha]_D$ + 44°(c0.9, chloroform); lit[21] syrup, $[\alpha]_D$ + 55° (c1, chloroform). R_f 0.18 (9:1 chloroform–acetone). ^{1}H NMR: δ4.88 (s, 1 H, H-1), 4.57 (s, 2 OH), 5.00–4.10 (m, 6H, 2Ph–CH_2–). Calc. for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 71.82; H, 6.82%.

Benzyl 2,4-*di*-*O*-*benzyl*-α-D-*mannopyranoside* (**14**)

Compound **12** (1.2 g) was treated with palladium-on-carbon (0.5 g) in 2:1:1 ethanol–ethyl acetate–water (100 ml) for 24 h. After work-up, the solid residue was recrystallized from ethanol (15 ml) to give **14** (0.87 g; 78.9%), m.p. 86°, $[\alpha]_D + 50°$ (c1.12, chloroform); lit[3] m.p. 85–86°, $[\alpha]_D + 51°$ (c0.2, chloroform). R_f 0.45 (9:1 chloroform–acetone). ^{1}H NMR δ4.88 (s, 1 H, H-1), 5.00–4.30 (m, 6 H, 3 Ph–C<u>H</u>$_2$–), 2.40 (b, 2 H, 2 O<u>H</u>). Calc. for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 72.03, H, 6.80%.

Benzyl 2-*O*-*allyl*-3,4-*di*-*O*-*benzyl*-6-*O*-(*p*-*toluenesulfonyl*)-α-D-*mannopyranoside* (**15**)

A soln of **11** (1.44 g) in pyridine (20 ml) was chilled in ice and then was treated with toluene p-sulphonyl chloride (0.86 g). The mixture was kept for 1 h in ice-water, then for 48 h at room temp. After pouring into 100 g of ice-water the solid was filtered off and washed with 3 × 50 ml of ice-water. The crude product was recrystallized from 30 ml of hexane to obtain **15** (1.52 g; 80.4%), m.p. 57–58°, $[\alpha]_D + 49°$ (c 1.49, chloroform), R_f 0.64 (7:3 n-hexane–ethyl acetate). ^{1}H NMR: δ5.90 (m, 1 H, –C<u>H</u>=), 5.20 (m, 2H, =C<u>H</u>$_2$), 4.82 (q, 2 H, Ph–C<u>H</u>$_2$–), 4.66 (s, 2 H, Ph–C<u>H</u>$_2$–), 4.56 (s, 1 H, H-1), 4.52 (q, 2 H, Ph–C<u>H</u>$_2$–), 2.37 (s, 3 H, CC<u>H</u>$_3$). Calc. for $C_{37}H_{40}O_8S$: C, 68.92; H, 6.25; S, 4.97. Found: C, 69.10; H, 6.31; S, 5.10%.

Benzyl 3-*O*-*allyl*-2,4-*di*-*O*-*benzyl*-6-*O*-(*p*-*toluenesulfonyl*)-α-D-*mannopyranoside* (**16**)

Compound **12** (0.8 g) was tosylated with p-toluenesulfonyl chloride (0.37 g) in pyridine (15 ml) as described for **15**. The crude product (0.91 g) was purified on a Kieselgel G column (30 g) with 7:3 light petroleum–ethyl acetate as the eluant to give crystalline **16** (0.7 g; 66.6%), m.p. 56–60°, $[\alpha]_D + 102°$ (c0.79, chloroform), R_f 0.80 (7:3 n-hexane–ethyl acetate). ^{1}H NMR: δ5.80 (m, 1 H, –C<u>H</u>=), 5.18 (m, 2 H, =C<u>H</u>$_2$), 4.90–4.50 (3 q, 6 H, 3 Ph–CH$_2$–), 4.41 (s, 1 H, H-1), 2.32 (s, 3 H, CC<u>H</u>$_3$). Calc. for $C_{37}H_{40}O_8S$: C, 68.92; H, 6.25; S, 4.97. Found: C, 69.10; H, 6.30; S, 5.02%.

Benzyl 2-*O*-*allyl*-3,4-*di*-*O*-*benzyl*-α-D-*rhamnopyranoside* (**17**)

A soln of **15** (0.97 g) in a 1:1 mixture (30 ml) of dry benzene and dry ether was allowed to react, at reflux temp., with 300 mg of $LiAlH_4$. The conversion was complete within 30 min and the presence of only one product could be detected. After cooling, the excess of the reagent was decomposed with 2 ml of ethyl acetate and $Al(OH)_3$ was precipitated by the addition of water (15 ml). The organic layer was decanted and the residue washed with 2 × 10 ml of ether. The combined organic layer was extracted with water (3 × 20 ml), dried and concentrated to give syrupy **17** (0.61 g; 86%), $[\alpha]_D + 55°$ (c1.3, chloroform), R_f0.65 (7:3 n-hexane—ethyl acetate). ^{1}H NMR data: δ5.84 (m, 1 H, –C<u>H</u>=), 5.08 (m, 2 H, =CH$_2$), 4.82 (s, 1 H, H-1), 4.90–4.30 (m, 6 H, 3 Ph–C<u>H</u>$_2$–), 1.32 (d, 3 H, H-6, $J_{5,6}$ = 6.3 Hz). Calc. for $C_{30}H_{34}O_5$: C, 75.92; H, 7.22. Found: C, 76.04; H, 7.26%.

Benzyl 3-*O*-*allyl*-2,4-*di*-*O*-*benzyl*-α-D-*rhamnopyranoside* (**18**)

A soln of **16** (0.48 g) in a 1:1 mixture (15 ml) of benzene and ether was reduced with $LiAlH_4$ (150 mg) as described for **17**. The syrupy residue was purified on a Kieselgel G column (25 g) with 3:1 n-hexane–ethyl acetate as the eluant to give **18** (320 mg; 90.6%), $[\alpha]_D + 58°$ (c0.97, chloroform), R_f0.69 (7:3 n-hexane—ethyl acetate). ^{1}H NMR: δ5.85 (m, 1 H, –C<u>H</u>=), 5.20 (m, 2 H, =C<u>H</u>$_2$), 4.66 (s, 1 H, H-1), 5.00–4.25 (m, 6 H, 3 Ph–C<u>H</u>$_2$–), 1.30 (d, 3 H, H-6, $J_{5,6}$ = 6.3 Hz). Calc. for $C_{30}H_{34}O_5$: C, 75.92; H, 7.22. Found: C, 75.86; H, 7.20%.

Benzyl 3,4-*di*-*O*-*benzyl*-α-D-*rhamnopyranoside* (**19**)

Compound **17** (0.56 g) was treated with palladium-on-carbon catalyst (0.2 g) in a 2:1:1 mixture of ethanol—acetic acid—water (40 ml) for 34 h as described for **13**. The crude product was purified on a Kieselgel G column (25 g) with 9:1 benzene–methanol as the eluant to give syrupy **19** (0.41 g; 80%), $[\alpha]_D + 60°$ (c1.25, chloroform); lit[20] data for the L-isomer: syrup, $[\alpha]_D - 58°$ (c0.6, chloroform). R_f0.52 (19:1 benzene–methanol). Calc. for $C_{27}H_{30}O_5$: C, 74.63; H, 6.96. Found: C, 74.79; H, 6.88%.

Benzyl 2,4-*di*-*O*-*benzyl*-α-D-*rhamnopyranoside* (**20**)

Compound **18** (0.95 g) was deallylated with palladium-on-carbon (0.3 g) in a 2:1:1 mixture of ethanol—acetic acid—water 60 ml for 36 h as given for **13**. The crude product was chromatographed on a Kieselgel G column (30 g) with 19:1 benzene–methanol to give syrupy **20** (0.72 g; 82.2%), $[\alpha]_D + 43°$ (c1.62, chloroform); lit[20] data for the L-isomer: syrup, $[\alpha]_D - 42°$ (c0.64, chloroform). R_f0.64 (19:1 benzene–methanol). Calc. for $C_{27}H_{30}O_5$: C, 74.63; H, 6.96. Found: C, 74.83; H, 7.01%.

Methyl 3-*O*-*benzyl*-4, 6-*O*-*benzylidene*-β-D-*mannopyranoside* (**21**)

To a soln of **5** (0.5 g) in 1:1 dichloromethane-ether (40 ml) 52 mg of $LiAlH_4$ and a solution of $AlCl_3$ (200 mg) in ether (10 ml) were added. The mixture was stirred at room temp. for 90 min. After working up in the usual manner the crystalline product (490 mg; 97.4%) was shown by TLC (19:1 dichloromethane–acetone to consist of a major (R_f0.51) and a minor component (R_f0.62) in a ratio of 95:5. It was recrystallized three times from ethanol (5 ml) to yield 250 mg (49.7%) of **21**. M.p. 119–120°, $[\alpha]_D - 31°$ (c0.93, chloroform); lit[18] m.p. 119.5–120°, $[\alpha]_D - 32°$ (c0.8, chloroform). ^{1}H NMR: δ5.55 (s, 1 H, Ph–C<u>H</u>=), 4.77 (q, 2 H, Ph–C<u>H</u>$_2$–), 4.29 (d, 1 H, H-1, $J_{1,2}$ = 1.5 Hz), 2.70 (s, 1 H, O<u>H</u>). Calc. for $C_{21}H_{24}O_6$: C, 67.73; H, 6.50. Found: C, 67.21; H, 6.42%.,

Methyl 2-*O*-*benzyl*-4,6-*O*-*benzylidene*-β-D-*mannopyranoside* (**22**)

Compound **6** was hydrogenolyzed as described above for **5**. After 6 min no starting material was present and three spots could be observed on TLC: R_f 0.62, 0.40 and 0.21. GLC examination of this mixture showed the ratio of the products to be 80.6:14.2:5.2. The reaction mixture was worked up in the usual manner to yield 480 mg of crude syrupy **22**. Crystallization from ethanol (10 ml) gave pure **22**: 320 mg (63.6%), m.p. 150–152°, $[\alpha]_D - 128°$ (c0.79, chloroform); lit[18] m.p. 153.5–154°, $[\alpha]_D - 131°$ (c0.2, chloroform). R_f0.62 (19:1 dichloromethane–acetone). ^{1}H NMR: δ5.49 (s, 1 H, Ph–C<u>H</u>=), 5.18–3.10 (m, 9 H, Ph–C<u>H</u>$_2$– and skeleton protons), 2.64 (b, 1 H, O<u>H</u>). Calc. for $C_{21}H_{24}O_6$: C, 67.73; H, 6.50. Found: C, 67.42, H, 6.41%.

Methyl 3, 4-*di*-*O*-*benzyl*-β-D-*mannopyranoside* (**23**)

A mixture of **21** (100 mg), $LiAlH_4$ (10 mg) and $AlCl_3$ (34 mg) was boiled in 1:1 ether-dichloromethane (10 ml) for 2 h. After working up syrupy **23** (84 mg; 83.5%) was obtained as single product, $[\alpha]_D - 27.9°$ (c0.39, chloroform), R_f 0.45 (19:1 dichloromethane–methanol). ^{1}H NMR: δ4.99–4.50 (m, 4 H, 2 Ph–C<u>H</u>$_2$–), 4.32 (d, 1 H, H-1, $J_{1,2}$ = 0.9 Hz), 3.49 (s, 3 H, OC<u>H</u>$_3$), 2.63 (b, 2 H, 2 O<u>H</u>). Calc. for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.82; H, 7.11%.

Methyl 2,4-(**24**) *and* 2,6-*di*-*O*-*benzyl*-β-D-*mannopyranoside* (**25**)

Compound **22** (0.2 g) was reacted with $LiAlH_4$ (20 mg) and $AlCl_3$ (70 mg) in 1:1 ether-dichloromethane (20 ml) at reflux temp. for 30 min. TLC showed the presence of two products in 3:1 ratio, which were identical with the by-products detected in the hydrogenolysis mixture of **6**. After usual working up the products were isolated by column chromatography (19:1 dichloromethane–acetone). First fraction crystalline **24** (104 mg; 51.5%) was recrystallized from ethyl acetate—light petroleum, m.p. 56–58°, $[\alpha]_D - 87°$ (c0.8, chloroform), R_f0.40 (19:1 dichloromethane–acetone). ^{1}H NMR: δ4.81 and 4.68 (2 q, 4 H, 2 Ph–C<u>H</u>$_2$–), 4.38 (d, 1 H, H-1, $J_{1,2}$ = 1.0 Hz), 3.52 (s, 3 H, OC<u>H</u>$_3$), 2.46 (b, 2 H, 2 O<u>H</u>). Calc. for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.22; H, 7.11%.

Second fraction was crystalline: **25** (36 mg; 17.8%) and was recrystallized from ethyl acetate—light petroleum, m.p. 99–101°, $[\alpha]_D - 110°$ (c0.37, chloroform), R_f0.21 (19:1 dichloromethane–acetone). ^{1}H NMR data: δ5.13–4.28 (m, 4 H, 2 Ph–C<u>H</u>$_2$–), 4.34 (d, 1 H, H-1, $J_{1,2}$ = 1.0 Hz), 3.49 (s, 3H, OC<u>H</u>$_3$), 3.02 (b, 1 H, O<u>H</u>), 2.54 (b, 1 H, O<u>H</u>). Calc. for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.34; H, 7.07%.

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