Synthesis of the methyl ethers of methyl 6-deoxy-3-*C*-methyl-α-L-talopyranoside and -α-L-mannopyranoside. Examination of the conformation and chromatographic properties of the compounds

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Dedicated to Professor Gábor Bernáth on his 70th birthday

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Abstract

By synthesizing each of the methyl ethers of methyl 6-deoxy-3-*C*-methyl-α-L-talopyranoside (**17**) and -α-L-mannopyranoside (**35**), evidence was obtained that the 6-deoxy-3-*C*-methyl-2,4-di-*O*-methyl-α-L-mannopyranosyl unit is a building block of the pentasaccharide-containing antigen of the serovariant 19 of *M. avium*. Based on the ^{1}H and ^{13}C NMR spectra of the synthesized methyl ethers, all of the L-mannopyranosyl derivatives and the mono- and disubstituted L-talopyranosyl analogues adopt a $^{1}C_{4}$ conformation, but for each of the persubstituted talopyranosyl sugars the $^{4}C_{1}$ conformation is the most favoured. The TLC and HPLC mobilities of the mannopyranoside derivatives are dependent on the degree of substitution, however in the case of the talose sugars presumably the shape of the molecules, and the strong intramolecular hydrogen bondings are the factors determining the chromatographic behaviour.

Keywords: Methyl 6-deoxy-3-C-methyl-α-L-mannopyranoside, methyl 6-deoxy-3-C-methyl-α-L-talopyranoside, methyl ethers, conformation, chromatographic mobilities, H-bridges, *M. avium* antigens

Introduction

Two of the mycobacteria (*M. tuberculosis* and *M. leprae*) are specifically responsible for human pathogenic infections. On the contrary, the members of the serocomplex of *Mycobacterium avium* belong to the opportunistic human mycobacteria[1-3]. Of the known cell-surface glycopeptide (GLP)-type antigens, the serovariant 19 of *M. avium* possesses the most complicated structure[4] with respect both to the sugar component, and the immunodeterminant pentasaccharide composition (Fig. 1.). The chemists[4] who isolated and studied the structure

searched for the configuration of carbon C-4 of the branched-monosaccharide unit (i.e. 6-deoxy-3-*C*-methyl-2,4-di-*O*-methyl-L-manno- or talopyranose), which is the penultimate monosaccharide moiety. However, they could not determine this configuration unequivocally.

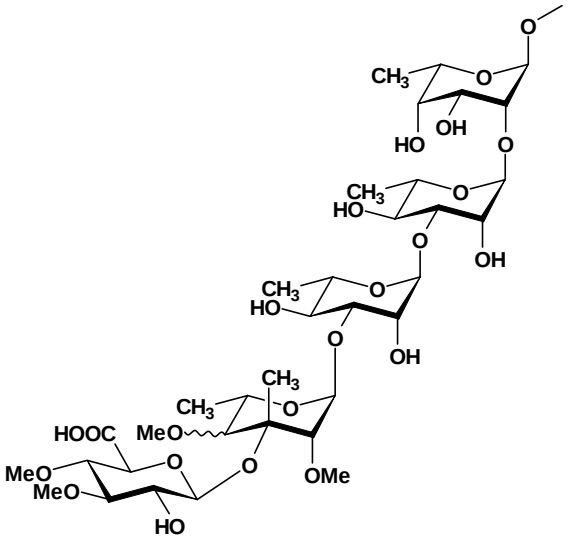


Figure 1

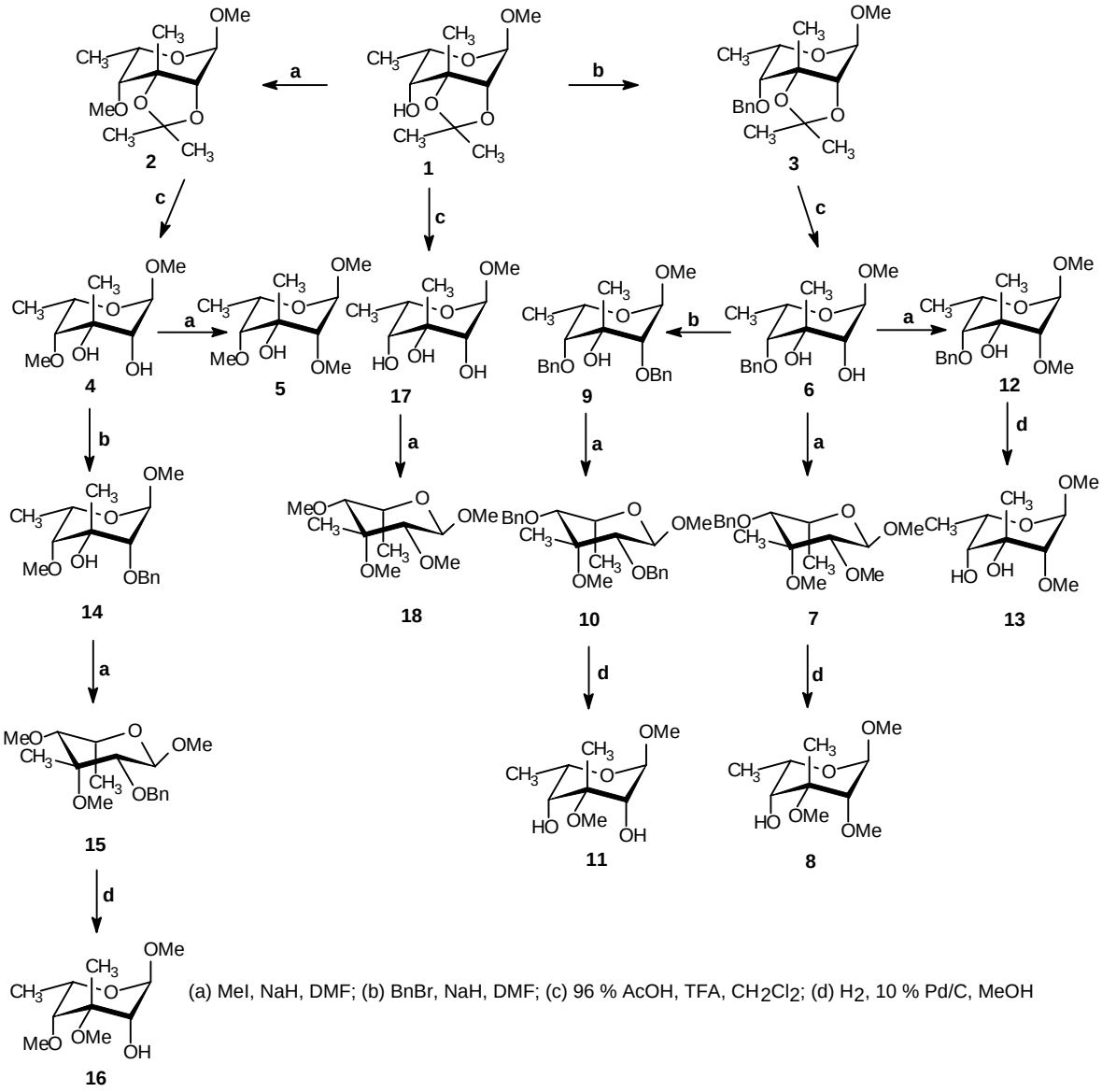
In order to synthesize the pentasaccharide, we prepared methyl 6-deoxy-3-*C*-methyl-4-*O*-methyl-α-L-manno- (**22**) and -talopyranoside (**4**), as well as methyl 6-deoxy-3-*C*-methyl-2,4-di-*O*-methyl-α-L-manno- (**23**) and -talopyranoside (**5**)[5]. In this way it was convincingly established that the sugar next to the last in the pentasaccharide has a *mannose*-configuration. Upon glycosylation of compounds **5** and **23** with 2,6-di-*O*-acetyl-3,4-di-*O*-methyl-D-glucopyranosyl trichloroacetimidate the conformation of the aglycone **5** changed from $^{1}C_{4}$ (L) to $^{4}C_{1}$ (L), no such change occurred in the case of **23**, and the disaccharide also possessed the $^{1}C_{4}$ conformation. We observed that the chromatographic behaviour (TLC, HPLC) of the similarly substituted manno- and talopyranose derivatives are rather different. For the discovery and explanation of these anomalies we decided to synthesize each of the methyl ethers of the two sugars, and also to study and compare their conformational and chromatographic properties.

Results and Discussion

Synthesis

The synthesis of the representatives of the two series was carried out in a similar way. The only exceptions were the selective alkylation reactions (methylation, benzylation). The required selective alkylations of the talopyranosides was achieved by sodium hydride-mediated reactions, whereas in the case of the mannopyranosides phase transfer-type catalysts were found most suitable. Methyl 6-deoxy-2,3-*O*-isopropylidene-3-*C*-methyl-α-L-talopyranoside (**1**)[5], and -α-L-mannopyranoside (**19**)[5] were methylated by means of the Brimacombe method[6] to obtain the

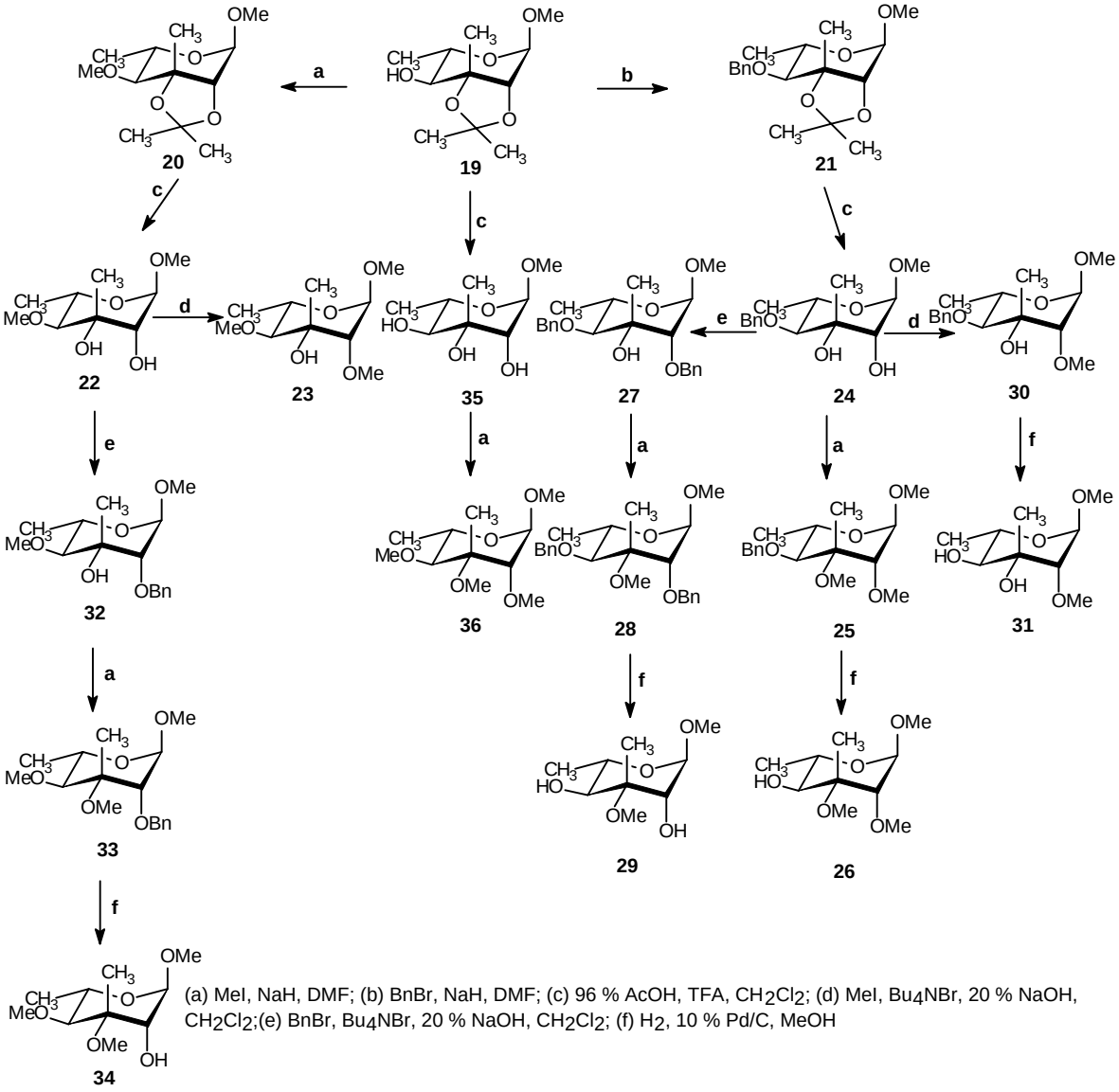
fully protected branched saccharides **2** and **20**, respectively. Benzylation of **1** and **19** was performed under similar conditions (NaH, BnBr/DMF) affording the 4-*O*-benzyl ethers **3** and **21**.



Scheme 1

Hydrolysis of the isopropylidene group of **3** and **21** with 60% acetic acid and a small quantity of trifluoroacetic acid in dichloromethane at room temperature furnished methyl 4-*O*-benzyl-6-deoxy-3-*C*-methyl-α-L-talopyranoside (**6**) and 4-*O*-benzyl-6-deoxy-3-*C*-methyl-α-L-mannopyranoside (**24**), respectively. Since both of these two sugars (i.e. **6** and **24**) contain a less reactive tertiary hydroxyl group (OH-3) besides the secondary OH-2, the selective methylation of the secondary hydroxyl group in both sugars was considered. However, the two sugars possessed rather different reactivities. Methylation of **6** gave 60% of **12**. At the same time, the

regioselectivity in the case of **24** was very low under similar conditions, and a complex product-mixture was obtained. Finally, under phase-transfer-conditions[7] methylation of **24** led to the isolation of **30** in 59% yield. Removal of the benzyl ether functions was accomplished by catalytic hydrogenation to afford methyl 6-deoxy-3-*C*-methyl-2-*O*-methyl-α-L-talopyranoside (**13**) and methyl 6-deoxy-3-*C*-methyl-4-*O*-methyl-α-L-mannopyranoside (**31**). The previous sugar (**13**) is the methyl glycoside of the naturally occurring saccharide vinelose[8,9].



Scheme 2

Regioselective benzylation of the sugars **6** and **24** at OH-2 resulted in a similar result as observed for the methylation: in the case of **6** benzylation was carried out in the presence of sodium hydride to give **9**, but this reaction for **24** proceeded only under phase transfer catalysis to yield **27**. The free OH-3 group of **9** and **27** was methylated in the presence of sodium hydride,

and the corresponding methyl ethers **10** and **28**, respectively, were obtained with 80% yield. Following hydrogenolysis of the benzyl groups, methyl 6-deoxy-3-*C*-methyl-3-*O*-methyl-α-L-talopyranoside (**11**) and methyl 6-deoxy-3-*C*-methyl-3-*O*-methyl-α-L-mannopyranoside (**29**) were isolated.

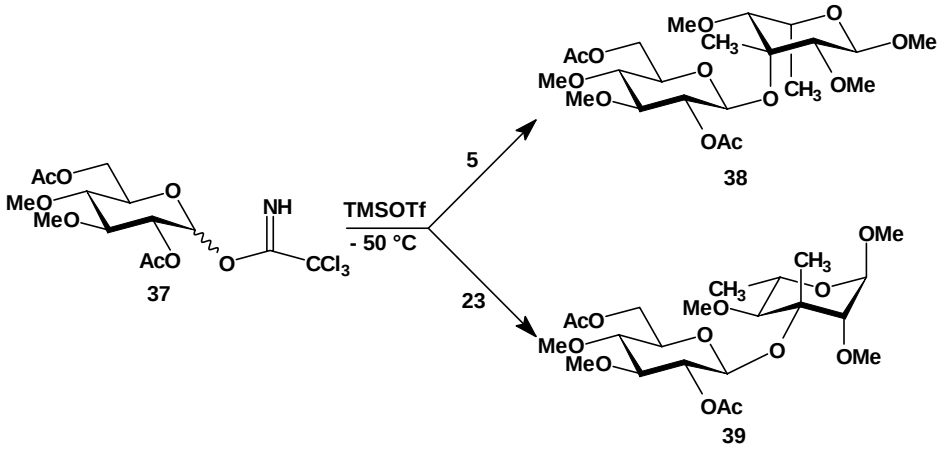
Preparation of methyl 6-deoxy-3-*C*-methyl-4-*O*-methyl-α-L-talopyranoside (**4**) and methyl 6-deoxy-3-*C*-methyl-3-*O*-methyl-α-L-mannopyranoside (**22**) from **2** and **20**, respectively, and selective methylation of these sugars at OH-2 furnishing methyl 6-deoxy-3-*C*-methyl-2,4-di-*O*-methyl-α-L-talopyranoside (**5**) and methyl 6-deoxy-3-*C*-methyl-2,4-di-*O*-methyl-α-L-mannopyranoside (**23**) was carried out[5] earlier.

Methyl 6-deoxy-3-*C*-methyl-2,3-di-*O*-methyl-α-L-talopyranoside (**8**) and the corresponding α-L-mannopyranoside (**26**) were prepared by the exhaustive methylation of the 4-*O*-benzyl derivatives **6** and **24**, followed by the hydrogenolysis of the resulting sugars **7** and **25**.

The synthesis of methyl 6-deoxy-3-*C*-methyl-3,4-di-*O*-methyl-α-L-talopyranoside (**16**), and of the -α-L-mannopyranoside (**34**) was done by means of the regioselective benzylation of **4** and **22**; compounds **4** and **22** were benzylated in the presence of NaH, and under phase transfer condition, respectively, to obtain the saccharides **14** and **32**. Methylation of the OH-3 groups led to **15** and **33**, which were debenzylated to obtain the final products **16** and **34**.

The permethylated glycosides **18** and **36** were prepared by the exhaustive methylation of methyl 6-deoxy-3-*C*-methyl-α-L-talopyranoside (**17**) and -α-L-mannopyranoside (**35**). The sugar **17** was obtained by the acid hydrolysis of methyl 6-deoxy-2,3-*O*-isopropylidene-3-*C*-methyl-α-L-talopyranoside[5] (**1**). The sugar **36** was isolated earlier from a natural source, and following isolation and structural determination it was named nogalose[8,10].

Both of the 2,4-di-*O*-methyl derivatives (**5** and **23**) were glycosylated with 2,6-di-*O*-acetyl-3,4-di-*O*-methyl-D-glucopyranosyl trichloroacetimidate (**37**). The conformational analysis of the resulting disaccharides **38** and **39** unequivocally proved that the structure of the saccharide unit next to the the last moiety in the pentasaccharide is 6-deoxy-3-*C*-methyl-2,4-di-*O*-methyl-L-mannopyranose.



Scheme 3

Conformational studies

Each representative of both of the synthesized carbohydrate series possesses two separated spin systems, and by the determination of the $^3J_{1,2}$ and $^3J_{4,5}$ coupling costants the conformation of all of the prepared compounds can be studied. All of the 6-deoxy-3-*C*-methyl-α-L-mannopyranoside derivatives adopt the $^1C_4$ conformation: $^3J_{1,2} \leq 2$ Hz and $^3J_{4,5} \geq 9$ Hz.

Table 1. ^{1}H and ^{13}C NMR data of the methyl ethers of methyl 6-deoxy-3-C-methyl-α-L-talopyranoside: δ_H, δ_C [ppm] and *coupling constants* [Hz]

Compounds	Me 6-deoxy-3-C-Me-α-L-Talp (**17**)[a]	-2-OMe (**13**)[b]	-3-OMe (**11**)[b]	-4-OMe (**4**)[b]	2,3-di-OMe (**8**)[b]	2,4-di-OMe (**5**)[b]	3,4-di-OMe (**16**)[b]	2,3,4-tri-OMe (**18**)[b]	2,6-di-OAc-3,4-di-OMe-β-D-Glcp-(1→3)- (**38**)[b]
H-1	4.7	4.75	4.80	4.72	4.73	4.71	4.73	4.70	4.69
	1.5	*1.5*	*1.0*	*1.0*	*1.0*	*1.0*	*1.0*	*4.5*	*4.1*
C-1	103.9	98.69	101.85	102.34	99.38	98.61	103.07	98.09	99.26
H-2	3.19	2.98	3.37	2.84	3.05	2.70	2.82	2.81	2.83
C-2	77.5	83.36	71.30	73.65	81.36	82.53	70.11	82.46	83.48
C-3	70.3	69.06	77.00	69.37	74.26	68.95	74.63	76.61	79.14
H-4	3.31	3.09	3.52	3.23	3.30	2.79	3.50	2.91	2.90
	1.5	*1.0*	*1.0*	*1.0*	*1.0*	*1.0*	*1.0*	*3.5*	*3.5*
C-4	74.8	76.69	73.62	87.11	72.95	85.76	85.52	83.52	83.89
H-5	3.96	3.94	3.90	3.90	3.77	3.85	3.86	4.03	4.04
C-5	66.7	65.16	64.77	65.01	65.73	68.95	64.98	67.08	67.57
C$\underline{H}_3$(6)	1.24	1.27	1.32	1.25	1.27	1.26	1.23	1.29	1.26
	6.0	*6.5*	*6.5*	*6.5*	*6.5*	*6.5*	*6.5*	*7.0*	*6.7*
$\underline{C}$H$_3$(6)	17.3	16.9	16.98	16.87	17.0	16.67	16.82	14.92	15.98
C$\underline{H}_3$(3)	1.25	1.3	1.26	1.28	1.27	1.27	1.22	1.29	1.38
$\underline{C}$H$_3$(3)	23.3	22.28	18.33	22.36	18.65	23.73	18.63	18.43	20.37

[a] In CD_3OD, [b] In CCl_3D.

The situation in the case of the 6-deoxy-3-*C*-methyl-α-L-talopyranosides is completely different: for the fully substituted glycosides (**7**, **10**, **15**, **18** and **38**) the $^4C_1$ conformation is predominant, as proved by the coupling constants ($^3J_{1,2} \approx$ 5-6 Hz and $^3J_{4,5} \approx$ 4-4.5 Hz). However, it has to be noted that all of the mono- and disubstituted talopyranoside derivatives exist exclusively in the $^1C_4$ conformation. We suppose that the steric hindrance is responsible for the change of the conformation and it appears only when each of the three OH groups is substituted.

The fact that in the anomeric proton signals in the ^{1}H NMR spectra of the tetraglycosyl alditol[4], isolated by the degradation of the antigen of the serovariant 19, three ca. 1 Hz and one 7.75 Hz coupling constants could be determined, and that this last coupling constant (7.75 Hz) was assigned to the 3,4-di-*O*-methyl-β-D-glucuronic acid moiety, proves that the building block next to the last one possesses L-*manno* (thus, not L-*talo*) configuration.

Table 2. ^{1}H and ^{13}C NMR data of the methyl ethers of methyl 6-deoxy-3-C-methyl-α-L-mannopyranoside: δ_H, δ_C [ppm] and *coupling constants* [Hz]

Compounds	Me 6-deoxy-3-C-Me-α-L-Manp (**35**)[a]	-2-OMe (**31**)[a]	-3-OMe (**29**)[a]	-4-OMe (**22**)[a]	2,3-di-OMe (**26**)[b]	2,4-di-OMe (**23**)[b]	3,4-di-OMe (**34**)[b]	2,3,4-tri-OMe (**36**)[b]	2,6-di-OAc-3,4-di-OMe-β-D-Glcp-(1→3)- (**39**)[b]
H-1	4.58	4.68	4.63	4.57	4.71	4.71	4.70	4.66	4.60
		1.5	*1.5*	*1.5*	*1.5*	*1.0*	*1.5*	*2.0*	*1.8*
C-1	103.28	100.19	103.14	103.22	98.32	97.78	100.44	97.94	99.05
H-2	3.47	3.06	3.74	3.40	3.27	3.08	3.70	3.23	3.21
C-2	76.39	86.32	75.51	76.39	80.34	86.20	71.29	80.73	83.70
C-3	73.58	73.80	78.18	74.52	77.05	73.25	78.32	77.96	80.76
H-4	3.39	3.31	3.48	3.04	3.50	2.90	3.02	3.02	3.17
	10	*10*	*10*	*9.5*	*9.5*	*10*	*9.5*	*9.5*	*9.6*
C-4	76.12	76.83	72.47	86.76	74.65	85.08	84.39	84.34	84.25
H-5	3.56	3.54	3.60	3.51	3.58	3.50	3.57	3.50	3.54
C-5	68.56	68.62	68.12	68.12	66.36	66.69	66.07	66.33	67.20
C$\underline{H}_3$(6)	1.26	1.23	1.31	1.25	1.27	1.29	1.29	1.25	1.28
	6.0	*6.0*	*6.0*	*6.0*	*6.0*	*6.0*	*6.0*	*6.0*	*6.2*
$\underline{C}$H$_3$(6)	18.40	18.51	14.99	18.48	17.95	18.01	17.90	18.03	18.50
C$\underline{H}_3$(3)	1.26	1.25	1.33	1.23	1.27	1.30	1.30	1.25	1.36
$\underline{C}$H$_3$(3)	19.18	19.11	18.46	19.54	14.50	18.54	14.37	14.99	15.80

[a] In CD_3OD, [b] In CCl_3D.

Chromatographic studies

In the case of carbohydrates carrying the same substituents, the chromatographic mobility is determined by the following structural features:

- the substitution degree/pattern,
- the steric position of the hydroxyl groups,
- the primary, secondary, or tertiary order/character of the OH groups,

- the shape of the molecule, and
- the role of the hydrogen-bonds.

In our studies the thin layer chromatographic and HPLC examination of the methyl ethers in the 6-deoxy-3-*C*-methyl-α-L-mannopyranosyl (**22**, **23**, **26**, **29**, **31**, **34** and **36**) and -α-L-talopyranosyl series (**4**, **5**, **8**, **11**, **13**, **16** and **18**), as well as of the disaccharides **38** and **39** was accomplished. In the case of the mannopyranoside derivatives the first three of the above molecular/structural features play a decisive role in the chromatographic behaviour. Considering the substitution degree/pattern , the mono-, di-, and trimethyl ethers can be readily and securely separated (compounds **22** and **26** possess identical R_f values). The *equatorial* OH groups are more polar (OH-4 > OH-3 > OH-2) than the *axial* ones, and the order: primary, secondary and tertiary leads to a decreasing polarity. A same behaviour, very similar to the TLC properties, was observed with the HPLC method (LiChros-pherSi-60).

Table 3. Chromatographic properties (TLC, HPLC) of the synthesized methyl ethers

Compounds Me 6-deoxy-3-C-Me-α-L-Manp	TLC (R_f)*	HPLC (R_t)**		HPLC (R_t)***	TLC (R_f)*	Compounds Me 6-deoxy-3-C-Me-α-L-Talp
-2-OMe (**31**)	0.14	15.48		20.01	0.20	-2,4-di-OMe (**5**)
-3-OMe (**29**)	0.20	13.47		16.62	0.29	-2,3,4-tri-OMe (**18**)
-4-OMe (**22**)	0.24	9.58		12.29	0.22	-2-OMe (**13**)
-2,3-di-OMe (**26**)	0.24	12.59		10.76	0.28	-4-OMe (**4**)
-2,4-di-OMe (**23**)	0.44	6.55		10.05	0.13	-2,3-di-OMe (**8**)
-3,4-di-OMe (**34**)	0.48	5.23		9.13	0.47	-3-OMe (**11**)
-2,3,4-tri-OMe (**36**)	0.52	5.10		5.68	0.16	-3,4-di-OMe (**16**)
2,6-di-OAc-3,4-di-OMe-β-Glcp-D-(1→3)-(**39**)	0.36				0.23	2,6-di-OAc-3,4-di-OMe-β-D-Glcp-(1→3)-(**38**)

* Silica gel; Hexane/Ethyl acetate, 1:1.
** LiChros-pherSi 60; Hexane/Ethyl acetate, 40:60.
*** LiChros-pherSi 60; Hexane/Ethyl acetate, 50:50.

The chromatographic mobilities of the methyl ethers of 6-deoxy-3-*C*-methyl-α-L-talopyranosides are completely different as compared to those of the L-mannopyranosides. The most polar is the 2,4-di-*O*-methyl ether (R_f : 0.14), the following is the 2,3,4-tri-*O*-methyl glycoside (R_f : 0.16), and the most apolar is the 3,4-di-*O*-methyl derivative (R_f : 0.47). The R_f and

R_t values are summarized in Table 3. In the talopyranoside series the substitution degree does not influence the chromatographic properties. The steric position of the hydroxyl groups cannot be correlated either with the R_f or the R_t values, and no observable role of the order of the OH functions was experienced.

The low R_f and R_t values found for the tri-*O*-substituted talopyranosides is presumably in connection with the shape of the molecule. This assumption is substantiated, not only by the totally different mobilities of the two tri-*O*-methyl ethers (*talo*: R_f : 0.16; *manno*: R_f : 0.52), but also by the fact that despite the presence of the bulky *O*-3 substituent (2,6-di-*O*-acetyl-3,4-di-*O*-methyl-β-D-glucopyranosyl), the mobilities of the two disaccharides are rather different (R_f : 0.23 and 0.37). Another example is that the chromatographic mobilities of the 4-*O*-benzyl-2,3-di-*O*-methyl ether **7**, possessing $^4C_1$ conformation, [R_f : 0.40 (dichloromethane-acetone 95:5) and R_f : 0.30 (hexane-ethyl acetate 7:3)] obtained by the methylation of the 4-*O*-benzyl ether **6** [R_f : 0.37 (dichloromethane-acetone 95:5) and R_f : 0.30 (hexane ethyl acetate 7:3)] are practically the same, and independent of the methylation of the two free OH groups.

Upon chromatography there is a competition between the intramolecular H-bonds existing in the molecule, and those of the intermolecular H-bonds ensuring binding to the adsorbent and elution by the solvent. The role of the H-bonds influencing the chemical reactions of saccharides has been extensively studied[11]. By examining the above models, in this work we can only qualitatively analyse and consider that in the case of the talopyranoside derivatives, (i) the hydrogen bondings could be stronger, and (ii) there is a possibility for adopting various resonance-like boundary states. In such a process the presence of OH-3 in free or substituted form may be a determining factor.

In the case of the tri-*O*-substituted saccharide ethers no H-bondings are in operation, but due to the change of the conformation, the *equatorial* steric orientation of the OCH_3 groups may ensure a favourable fit to the surface of silicagel.

Conclusions

By the synthesis and the studies of the conformational properties of the title compounds, it was established that the penultimate monosaccharide unit in the pentasaccharide-type antigen of the serovariant 19 of *M. avium* is 6-deoxy-3-*C*-methyl-2,4-di-*O*-methyl-α-L-mannopyranose. For the explanation of the chromatographic mobilities of the prepared sugars, the number, the steric position, and order of the OH groups, as well as the role of the conformation of the pyranosyl skeleton, and of the hydrogen bondings were evaluated.

Experimental Section

General Procedures. Optical rotations were measured at room temperature with a Perkin-Elmer 241 automatic polarimeter in $CHCl_3$. TLC was performed on Kieselgel 60 F254 (Merck) with detection by charring with 50 % aqueous sulfuric acid. Column chromatography was performed on Silica gel 60 (Merck 63-200 mesh). For HPLC a Merck Hitachi liquid chromatograph equipped with a refractive index detector L-7490, programmable autosampler L-7250, pump L-7100, interface L-7000 was used. The samples were separated on a LiChrospher Si-60 (250*4 mm, 5 μm) by an isocratic system with n-hexane/ethyl acetate 50:50 or 40:60 eluent. The flowrate was 1 mL/min at 25 ˚C. Detection time was 20 minutes. The quality of the n-hexane and ethyl acetate were HPLC grade. Quantitative results are given on the basis of retention time. The ^1H (200, 360 and 500 MHz) and ^{13}C NMR (50.3, 90.54, 125.76 MHz) spectra were recorded with Bruker WP-200 SY, Bruker AM-360 and Bruker DRX-500 spectrometers. Internal references: TMS (0.00 ppm for 1H), $CDCl_3$ (77.00 ppm for ^{13}C for organic solutions). Elemental analyses were performed at the analytical laboratories in Debrecen. Abbreviations: Ac = acetyl, Bn = benzyl, Me = methyl.

Methyl 4-*O*-benzyl-6-deoxy-3-*C*-methyl-2,3-O-isopropylidene-α-L-talopyranoside (3). Sodium hydride (1.09 g) was added to a solution of **1**[5] (4.25 g, 18.3 mmol) in dry DMF (10 ml) at 0 °C, the mixture was stirred for 1 h, then benzyl bromide (6.5 ml) was added dropwise. After 1 h stirring at 0 °C, methanol (2 ml) was added, the mixture was concentrated *in vacuo*. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated to yield **3** (4.83 g, 82 %) as a colourless syrup. R_f = 0.7 (hexane/ethyl acetate 7:3). $C_{18}H_{26}O_5$ (322.40). The crude syrup was used for next step without purification.

Methyl 4-*O*-benzyl-6-deoxy-3-*C*-methyl-α-L-talopyranoside (6). To the solution of **3** (4.83 g, 14.98 mmol) in CH_2Cl_2 (10 ml), acetic acid (10 ml, 60 %) and triflouroacetic acid (2 ml) were added. The mixture was stirred for one hour at room temperature. The mixture was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The crude syrup was purified on a column of silica gel (hexane/ethyl acetate 7:3) to yield **6** (4.3 g, 96 %) as a colourless syrup. $[\alpha]_D$ = -89.20 (c = 0.49 in $CHCl_3$). R_f = 0.3 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.33 (m, 5H,Ph), 4.8 (d, 1H, *J*(1,2) = 1 Hz, H1), 4.75 (m, CH_2Ph), 3.97 (bm, 1H, H5), 3.3 (d, 1H, *J*(4,5) = 1 Hz, H4), 3.2 (d, 1H, H2), 3.37 (s, 3H, OCH3), 1.36 (s, 3H, CH_3(3)), 1.27 (d, 3H, *J*(5,6) = 6.5 Hz, CH_3(6)). δ_C ($CDCl_3$) 103.3 (C1), 84.9 (C4), 76.7 (CH_2Ph), 73.6 (C2), 69.58 (C3), 65.1 (C5), 55.2(OCH_3), 22.5 (CH_3(3)), 17.1 (CH_3(6)). Anal. Calcd. for $C_{15}H_{22}O_5$ (282.34): C, 63.81; H, 7.85. Found: C, 63.75; H, 7.76.

Methyl 4-*O*-benzyl-6-deoxy-3-*C*-methyl-2,3-di-O-methyl-α-L-talopyranoside (7). Sodium hydride (113 mg) was added to a solution of **6** (266 mg, 0.96 mmol) in dry DMF (5 ml) at 0 °C, the mixture was stirred for 1 h, then methyl iodide (351 μl) was added dropwise. After 1 h stirring at 0 °C, methanol (0.5 ml) was added, the mixture was concentrated. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup

was purified on a column of silica gel (CH_2Cl_2/acetone 95:5) to yield **7** (209 mg, 72 %) as a colourless syrup. $[\alpha]_D$ = -54.88 (c = 0.56 in $CHCl_3$). R_f = 0.4 (CH_2Cl_2/acetone 95:5). NMR data: δ_H ($CDCl_3$) 7.32 (m, 5H,Ph), 4.80(d, 1H, *J*(1,2) = 6 Hz, H1), 4.75 (m, CH_2Ph), 4.15 (bm, 1H, H5), 3.28 (d, 1H, *J*(4,5) = 5 Hz, H4), 2.79 (d, 1H, H2), 3.53, 3.46, 3.41 (3s, 9H, OCH_3), 1.35 (s, 3H, CH_3(3)), 1.38 (d, 3H, *J*(5,6) = 7 Hz, CH_3(6)). δ_C ($CDCl_3$) 98.0 (C1), 84.0 (C2), 80.9 (C4), 77.94 (C3), 73.5 (CH_2Ph), 68.5 (C5), 60.8, 56.1, 51.7 (OCH_3), 17.7 (CH_3(3)), 14.3 (CH_3(6)). Anal. Calcd. for $C_{17}H_{26}O_5$ (310.39): C, 65.78; H, 8.44. Found: C, 65.76; H, 8.39.

Methyl 6-deoxy-3-*C*-methyl-2,3-di-*O*-methyl-α-L-talopyranoside (8). To the solution of **7** (130 mg, 0.42 mmol) in MeOH (10 ml), Pd/C (10 %, 10 mg) was added and the mixture was stirred for one hour under H_2 at room temperature. The mixture was filtered and concentrated. The crude syrup was purified on a column of silica gel (hexane/ethyl acetate 7:3) to yield **8** (90 mg, 97 %) as a colourless syrup. $[\alpha]_D$ = -80.11 (c = 0.26 in $CHCl_3$). R_f = 0.13 (hexane/ethyl acetate 1:1). ^1H and ^{13}C NMR data are collected in Table 1. Anal. Calcd. for $C_{10}H_{20}O_5$ (220.27): C, 66.43; H, 7.54. Found: C, 66.38; H, 7.45.

Methyl 2,4-di-*O*-benzyl-6-deoxy-3-*C*-methyl-α-L-talopyranoside (9). Sodium hydride (175 mg) was added to a solution of **6** (1.1 g, 4.99 mmol) in dry DMF (10 ml) at 0 °C, the mixture was stirred for 1 h, then benzyl bromide (1.39 ml) was added dropwise. After 1 h stirring at 0 °C, methanol (1 ml) was added, the mixture was concentrated *in vacuo*. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 8:2) to yield **9** (1.06 g, 57 %) as a colourless syrup. $[\alpha]_D$ = -30.63 (c = 0.21 in $CHCl_3$). R_f = 0.48 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.35 (m, 10H,Ph), 4.87 (d, 1H, *J*(1,2) = 1.5 Hz, H1), 4.74, 4.70 (m, CH_2Ph), 3.99 (bm, 1H, H5), 3.19 (d, 1H, *J*(4,5) = 2 Hz, H4), 3.12 (d, 1H, H2), 3.38 (s, 3H, OCH_3), 1.38(s, 3H, CH_3(3)), 1.33 (d, 3H, *J*(5,6) = 6.5 Hz, CH_3(6)). δ_C ($CDCl_3$) 99.3 (C1), 83.2 (C4), 80.3 (C2), 69.7 (C3), 75.9, 73.8 (CH_2Ph), 65.1 (C5), 55.0 (OCH_3), 23.9 (CH_3(3)), 16.7 (CH_3(6)). Anal. Calcd. for $C_{22}H_{28}O_5$ (372.46): C, 70.94; H, 7.58. Found: C, 70.96; H, 7.52.

Methyl 2,4-di-*O*-benzyl-6-deoxy-3-*C*-methyl-3-*O*-methyl-α-L-talopyranoside (10). Sodium hydride (43 mg) was added to a solution of **9** (359 mg, 0.96 mmol) in dry DMF (5 ml) at 0 °C, the mixture was stirred for 1 h, then methyl iodide (58 μl) was added dropwise. After 1 h stirring at 0 °C, methanol (0.5 ml) was added, the mixture was concentrated *in vacuo*. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 9:1) to yield **10** (306 mg, 81 %) as a colourless syrup. $[\alpha]_D$ = -37.49 (c = 0.89 in $CHCl_3$). R_f = 0.62 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.36 (m, 10H,Ph), 4.67 (d, 1H, *J*(1,2) = 6 Hz, H1), 4.77 (m, CH_2Ph), 4.22 (bm, 1H, H5), 3.32 (d, 1H, *J*(4,5) = 5.5 Hz, H4), 3.05 (d, 1H, H2), 3.54, 3.47 (2s, 6H, OCH_3), 1.3 (s, 3H, CH_3(3)), 1.49 (d, 3H, *J*(5,6) = 6.5 Hz, CH_3(6)). δ_C ($CDCl_3$) 98.2 (C1), 82.0 (C2), 81.0 (C4), 78.2 (C3), 74.4, 73.3 (CH_2Ph), 69.1 (C5), 56.3, 52.2 (OCH_3), 17.5 (CH_3(3)), 13.9 (CH_3(6)). Anal. Calcd. for $C_{23}H_{30}O_5$ (389.49): C, 71.48; H, 7.82. Found: C, 71.43; H, 7.85.

Methyl 6-deoxy-3-*C*-methyl-3-*O*-methyl-α-L-talopyranoside (11). To the solution of **10** (150 mg, 0.38 mmol) in MeOH (10 ml), Pd/C (10 %, 10 mg) was added and the mixture was stirred

for two hours under H_2 at room temperature. The mixture was filtered and concentrated. The crude syrup was purified on a column of silica gel (hexane : ethyl/acetate 7:3) to yield **11** (73 mg, 93 %) as a colourless syrup. $[\alpha]_D$ = -93.35 (c = 0.37 in $CHCl_3$). R_f = 0.47 (hexane/ethyl acetate 1:1). ^1H and ^{13}C NMR data are collected in Table 1. Anal. Calcd. for $C_9H_{18}O_5$ (206.24): C, 52.41; H, 8.80. Found: C, 52.36; H, 8.76.

Methyl 4-*O*-benzyl-6-deoxy-3-*C*-methyl-2-*O*-methyl-α-L-talopyranoside (12). Sodium hydride (79 mg) was added to a solution of **6** (500 mg, 1.79 mmol) in dry DMF (5 ml) at 0 °C, the mixture was stirred for 1 h, then methyl iodide (327.26 μl) was added dropwise. After 1 h stirring at 0 °C, methanol (1 ml) was added, the mixture was concentrated. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 7:3) to yield **12** (320 mg, 60 %) as a colourless syrup. $[\alpha]_D$ = -47.22 (c = 0.37 in $CHCl_3$). R_f = 0.26 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.33 (m, 5H,Ph), 4.81 (d, 1H, *J*(1,2) = 1 Hz, H1), 4.72 (m, CH_2Ph), 3.89 (bm, 1H, H5), 3.06 (d, 1H, *J*(4,5) = 1 Hz, H4), 2.85 (d, 1H, H2), 3.47, 3.36 (2s, 6H, OCH_3), 1.35 (s, 3H, CH_3(3)), 1.18 (d, 3H, *J*(5,6) = 6.5 Hz, CH_3(6)). Anal. Calcd. for $C_{16}H_{24}O_5$ (296.36): C, 64.84; H, 8.16. Found: C, 64.75; H, 8.11.

Methyl 6-deoxy-3-*C*-methyl-2-*O*-methyl-α-L-talopyranoside (13). To the solution of **12** (150 mg, 0.51 mmol) in MeOH (10 ml), Pd/C (10 %, 10 mg) was added and the mixture was stirred for one hour under H_2 at room temperature. The mixture was filtered and concentrated. The crude syrup was purified on a column of silica gel (hexane/ethyl acetate 7:3) to yield **13** (96 mg, 91 %) as a colourless syrup. $[\alpha]_D$ = -57.69 (c = 0.26 in $CHCl_3$). R_f = 0.23 (hexane/ethyl acetate 1:1). ^1H and ^{13}C NMR data are collected in Table 1. Anal. Calcd. for $C_9H_{18}O_5$ (206.24): C, 52.41; H, 8.80. Found: C, 52.39; H, 8.85.

Methyl 2-*O*-benzyl-6-deoxy-3-*C*-methyl-4-*O*-methyl-α-L-talopyranoside (14). Sodium hydride (266 mg) was added to a solution of methyl **4**[5] (1.215 g, 5.89 mmol) in dry DMF (5 ml) at 0 °C, the mixture was stirred for 1 h, then benzyl bromide (2.1 ml) was added dropwise. After 1 h stirring at 0 °C, methanol (1 ml) was added, the mixture was concentrated *in vacuo*. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 7:3) to yield **14** (1.34 g, 77 %) as a colourless syrup. $[\alpha]_D$ = -29.10 (c = 0.35 in $CHCl_3$). R_f = 0.4 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.32 (m, 5H,Ph), 4.67 (d, 1H, *J*(1,2) = 1 Hz, H1), 4.68 (m, CH_2Ph) 3.91 (bm, 1H, H5), 3.1 (d, 1H, *J*(4,5) = 1 Hz, H4), 2.77 (d, 1H, H2), 3.55, 3.27 (2s, 6H, OCH3), 1.3 (s, 3H, CH_3(3)), 1.34 (d, 3H, *J*(5,6) = 6.5 Hz, CH_3(6)). δ_C ($CDCl_3$) 99.7 (C1), 85.5 (C4), 79.7 (C2),73.9 (CH_2Ph), 69.34 (C3), 64.8 (C5), 62.6, 54.9 (OCH_3), 23.9 (CH_3(3)), 16.6 (CH_3(6)). Anal. Calcd. for $C_{16}H_{24}O_5$ (296.36): C, 64.84; H, 8.16. Found: C, 64.76; H, 8.11.

Methyl 2-*O*-benzyl-6-deoxy-3-*C*-methyl-3,4-di-*O*-methyl-α-L-talopyranoside (15). Sodium hydride (45 mg) was added to a solution of **14** (300 mg, 1.01 mmol) in dry DMF (5 ml) at 0 °C, the mixture was stirred for 1 h, then methyl iodide (189 μl) was added dropwise. After 1 h stirring at 0 °C, methanol (0.5 ml) was added, the mixture was concentrated. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup

was purified on a column of silica gel (hexane/ethyl acetate 7:3) to yield **15** (270 mg, 86 %) as a colourless syrup. $[\alpha]_D$ = -23.65 (c = 0.31 in $CHCl_3$). R_f = 0.44 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.32 (m, 5H,Ph), 4.84 (d, 1H, *J*(1,2) = 6,5 Hz, H1), 4.76 (m, CH_2Ph), 4.24 (bm, 1H, H5), 3.05 (d, 1H, *J*(4,5) =5 Hz, H4), 3.02 (d, 1H, H2), 3.5, 3.42, 3.39 (3s, 9H, OCH_3), 1.29 (s, 3H, CH_3(3)), 1.42 (d, 3H, *J*(5,6) = 7 Hz, CH_3(6)). δ_C ($CDCl_3$) 98.5 (C1), 83.5 (C4), 81.9 (C2), 74.4 (CH_2Ph), 78.0 (C3), 68.6 (C5), 59.6, 56.2, 52.1 (OCH_3), 17.5 (CH_3(3)), 13.9 (CH_3(6)). Anal. Calcd. for $C_{17}H_{26}O_5$ (310.39): C, 65.78; H, 8.44. Found: C, 65.77; H, 8.49.

Methyl 6-deoxy-3-*C*-methyl-3,4-di-*O*-methyl-α-L-talopyranoside (16). To the solution of **15** (200 mg, 0.64 mmol) in MeOH (10 ml), Pd/C (10 mg, 10 %) was added and the mixture was stirred for one hour under H_2 at room temperature. The mixture was filtered and concentrated. The crude syrup was purified on a column of silica gel (hexane/ethyl acetate 7:3) to yield **16** (113 mg, 80 %) as a colourless syrup. $[\alpha]_D$ = -85.52 (c = 0.28 in $CHCl_3$). R_f = 0.16 (hexane/ethyl acetate 1:1). ^1H and ^{13}C NMR data are collected in Table 1. Anal. Calcd. for $C_{10}H_{20}O_5$ (220.27): C, 54.53; H, 9.15. Found: C, 54.55; H, 9.06.

Methyl 6-deoxy-3-*C*-methyl-α-L-talopyranoside (17). To the solution of **1**[5] (320 mg, 1.38 mmol) in CH_2Cl_2 (10 ml), acetic acid (5 ml, 60 %) and triflouroacetic acid (1 ml) were added. The mixture was stirred for two hours at 50 °C. The mixture was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The crude syrup was purified on a column of silica gel (CH_2Cl_2/acetone 8:2) to yield **17** (250 mg, 94 %) as a colourless syrup. $[\alpha]_D$ = -93.96 (c = 0.29 in CH_3OH). R_f = 0.06 (CH_2Cl_2/acetone 95:5). ^1H and ^{13}C NMR data are collected in Table 1. Anal. Calcd. for $C_8H_{16}O_5$ (192.21): C, 49.99; H, 8.39. Found: C, 49.91; H, 8.41.

Methyl 6-deoxy-3-*C*-methyl-2,3,4-tri-*O*-methyl-α-L-talopyranoside (18). Sodium hydride (180 mg) was added to a solution of **17** (190 mg, 0.99 mmol) in dry DMF (5 ml) at 0 °C, the mixture was stirred for 1 h, then methyl iodide (562.5 μl) was added dropwise. After 1 h stirring at 0 °C, methanol (1 ml) was added, the mixture was concentrated. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 1:1) to yield **18** (150 mg, 65 %) as a colourless syrup. $[\alpha]_D$ = -58.05 (c = 0.97 in $CHCl_3$). R_f = 0.29 (hexane/ethyl acetate 1:1). ^1H and ^{13}C NMR data are collected in Table 1. Anal. Calcd. for $C_{11}H_{22}O_5$ (234.29): C, 56.39; H, 9.46. Found: C, 56.36; H, 9.49.

Methyl 4-*O*-benzyl-6-deoxy-2,3-*O*-isopropylidene-3-C-methyl-α-L-mannopyranoside (21). Sodium hydride (338 mg) was added to a solution of **19**[5] (1.3 g, 5.6 mmol) in dry DMF (20 ml) at 0 °C, the mixture was stirred for 1 h, then benzyl bromide (2 ml) was added dropwise. After 1 h stirring at 0 °C, methanol (2 ml) was added, the mixture was concentrated *in vacuo*. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated to yield **21** (1.5 g, 83 %) as a colourless syrup. R_f = 0.76 (hexane/ethyl acetate 7:3). $C_{18}H_{26}O_5$ (322.40). The crude syrup was used for next step without purification.

Methyl 4-*O*-benzyl-6-deoxy-3-*C*-methyl-α-L-mannopyranoside (24). To the solution of **21** (1.5 g, 4.65 mmol) in CH_2Cl_2 (10 ml), acetic acid (10 ml, 60 %) and triflouroacetic acid (1 ml) were added. The mixture was stirred for one hour at room temperature. The mixture was diluted

with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The crude syrup was purified on a column of silica gel (hexane/ethyl acetate 7:3) to yield **24** (1.07 g, 82.6 %) as a colourless syrup. $[\alpha]_D$ = -82.62 (c = 0.59 in $CHCl_3$). R_f = 0.3 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.3 (m, 5H,Ph), 4.59 (d, 1H, *J*(1,2) = 1.5 Hz, H1), 4.76 (m, 2H, CH_2Ph), 3.59 (bm, 1H, H5), 3.35 (d, 1H, *J*(4,5) = 9.5 Hz, H4), 3.45 (d, 1H, H2), 3.31 (s, 3H, OCH_3), 1.31 (s, 3H, CH_3(3)), 1.23 (d, 3H, *J*(5,6) = 6 Hz, CH_3(6)). δ_C ($CDCl_3$) 103.2 (C1), 84.7 (C4), 76.5 (C2), 76.5 (C3), 74.79 (CH_2Ph), 67.6 (C5), 55.4 (OCH_3), 18.6 (CH_3(3)), 19.8 (CH_3(6)). Anal. Calcd. for $C_{15}H_{22}O_5$ (282.34): C, 63.81; H, 7.85. Found: C, 63.85; H, 7.82.

Methyl 4-*O*-benzyl-6-deoxy-3-*C*-methyl-2,3-di-*O*-methyl-α-L-mannopyranoside (25). Sodium hydride (91 mg) was added to a solution of **24** (214 mg, 0.77 mmol) in dry DMF (5 ml) at 0 °C, the mixture was stirred for 1 h, then methyl iodide (282 μl) was added dropwise. After 1 h stirring at 0 °C, methanol (0.5 ml) was added, the mixture was concentrated. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 7:3) to yield **25** (152 mg, 64 %) as a colourless syrup. $[\alpha]_D$ = -61.56 (c = 0.33 in $CHCl_3$). R_f = 0.4 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.33 (m, 5H,Ph), 4.76 (d, 1H, *J*(1,2) = 2 Hz, H1), 4.76 (m, 2H, CH_2Ph), 3.68 (bm, 1H, H5), 3.4 (d, 1H, *J*(4,5) = 9.5 Hz, H4), 3.34 (d, 1H, H2), 3.52, 3.38, 3.3 (3s, 9H, OCH_3), 1.38 (s, 3H, CH_3(3)), 1.33 (d, 3H, *J*(5,6) = 6 Hz, CH_3(6)). ^{13}C NMR (90 MHz, $CDCl_3$) δ = 98.1 (C1), 83.0 (C4), 80.8 (C2), 78.4 (C3), 75.3 (CH_2Ph), 66.3 (C5), 58.7, 54.9, 48.5 (OCH_3), 15.6 (CH_3(3)), 18.3 (CH_3(6)). Anal. Calcd. for $C_{17}H_{26}O_5$ (310.39): C, 65.78; H, 8.44. Found: C, 65.75; H, 8.39.

Methyl 6-deoxy-3-*C*-methyl-2,3-di-*O*-methyl-α-L-mannopyranoside (26). To the solution of **25** (128 mg, 0.41 mmol) in MeOH (10 ml), Pd/C (10 %, 10 mg) was added and the mixture was stirred for one hours under H_2 at room temperature. The mixture was filtered and concentrated. The crude syrup was purified on a column of silica gel (hexane/ethyl acetate 7:3) to yield **26** (61mg, 68 %) as a colourless syrup. $[\alpha]_D$ = -38.16 (c = 0.28 in $CHCl_3$). R_f = 0.24 (hexane/ethyl acetate 1:1).^{1}H and ^{13}C NMR data are collected in Table 2. Anal. Calcd. for $C_{10}H_{20}O_5$ (220.27): C, 54.53; H, 9.15. Found: C, 54.56; H, 9.12.

Methyl 2,4-di-*O*-benzyl-6-deoxy-3-*C*-methyl-α-L-mannopyranoside (27). Bu_4NBr (64 mg) was added to a solution of **24** (380 mg, 1.72 mmol) in CH_2Cl_2 (30 ml) and aqeous 20 % NaOH (9.65 ml) at 0 °C, then benzyl bromide (1.8 ml) was added dropwise, the mixture was stirred for one day. The mixture was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 8:2) to yield **27** (320 mg, 50 %) as a colourless syrup. $[\alpha]_D$ = -20.48 (c = 0.48 in $CHCl_3$). R_f = 0.44 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.36 (m, 10H,Ph), 4.78 (d, 1H, *J*(1,2) = 1.5 Hz, H1), 4.80, 4.70 (m, 2H, CH_2Ph), 3.68 (bm, 1H, H5), 3.3 (d, 1H, *J*(4,5) = 9.5 Hz, H4), 3.34 (d, 1H, H2), 3.38 (s, 3H, OCH_3), 1.42 (s, 3H, CH_3(3)), 1.36 (d, 3H, *J*(5,6) = 6 Hz, CH_3(6)). δ_C ($CDCl_3$) 98.4 (C1), 84.3 (C4), 83.3 (C2), 73.4 (C3), 75.2, 73.4 (CH_2Ph), 66.5 (C5), 54.8 (OCH_3), 18.2 (CH_3(3)), 19.0 (CH_3(6)). Anal. Calcd. for $C_{22}H_{28}O_5$ (372.46): C, 70.94; H, 7.58. Found: C, 70.91; H, 7.56.

Methyl 2,4-di-*O*-benzyl-6-deoxy-3-*C*-methyl-3-*O*-methyl-α-L-mannopyranoside (28). Sodium hydride (37 mg) was added to a solution of **27** (306 mg, 0.82 mmol) in dry DMF (5 ml) at 0 °C, the mixture was stirred for 1 h, then methyl iodide (50 μl) was added dropwise. After 1 h stirring at 0 °C, methanol (0.5 ml) was added, the mixture was concentrated *in vacuo*. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 9:1) to yield **28** (251 mg, 78.6 %) as a colourless syrup. $[\alpha]_D$ = -24.78 (c = 0.55 in $CHCl_3$). R_f = 0.54 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.38 (m, 10H,Ph), 4.77 (d, 1H, *J*(1,2) = 2 Hz, H1), 4.78, 4.72 (m, CH_2Ph), 3.72 (bm, 1H, H5), 3.52 (d, 1H, *J*(4,5) = 9.5 Hz, H4), 3.58 (d, 1H, H2), 3.37, 3.26 (2s, 6H, OCH_3), 1.4 (s, 3H, CH_3(3)), 1.37 (d, 3H, *J*(5,6) = 6 Hz, CH_3(6)). δ_C ($CDCl_3$) 99.1 (C1), 82.9 (C4), 78.6 (C2), 78.6 (C3), 75.1, 72.8 (CH_2Ph), 66.6 (C5), 54.9, 48.9 (OCH_3), 15.6 (CH_3(3)), 18.4 (CH_3(6)). Anal. Calcd. for $C_{23}H_{30}O_5$ (389.49): C, 71.48; H, 7.82. Found: C, 71.42; H, 7.85.

Methyl 6-deoxy-3-*C*-methyl-3-*O*-methyl-α-L-mannopyranoside (29). To the solution of **28** (200 mg, 0.51 mmol) in MeOH (10 ml), Pd/C (10 %, 10 mg) was added and the mixture was stirred for two hours under H_2 at room temperature. The mixture was filtered and concentrated. The crude syrup was purified on a column of silica gel (hexane/ethyl acetate 1:1) to yield **29** (95 mg, 91.7 %) as a colourless syrup. $[\alpha]_D$ = -72.89 (c = 0.57 in CH_3OH). R_f = 0.20 (hexane/ethyl acetate 1:1). ^1H and ^{13}C NMR data are collected in Table 2. Anal. Calcd. for $C_9H_{18}O_5$ (206.24): C, 52.41; H, 8.80. Found: C, 52.37; H, 8.77.

Methyl 4-*O*-benzyl-6-deoxy-3-*C*-methyl-2-*O*-methyl-α-L-mannopyranoside (30). Bu_4NBr (34 mg) was added to a solution of **24** (207 mg, 0.74 mmol) in CH_2Cl_2 (17 ml) and aqeous 20 % NaOH (5 ml) at 0 °C, then methyl iodide (1.7 ml) was added dropwise, the mixture was stirred for three days. The mixture was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 8:2) to yield **30** (130 mg, 59 %) as a colourless syrup. $[\alpha]_D$ = -79.27 (c = 0.59 in $CHCl_3$). R_f = 0.44 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.33 (m, 5H,Ph), 4.81 (d, 1H, *J*(1,2) = 1 Hz, H1), 4.72 (m, 2H, CH_2Ph), 3.89 (bm, 1H, H5), 3.06 (d, 1H, *J*(4,5) = 1 Hz, H4), 2.85 (d, 1H, H2), 3.47, 3.36 (2s, 6H, OCH_3), 1.35 (s, 3H, CH_3(3)), 1.18 (d, 3H, *J*(5,6) = 6.5 Hz, CH_3(6)). δ_C ($CDCl_3$) 97.6 (C1), 85.0 (C4), 75.1 (CH_2Ph), 84.0 (C2), 73.4 (C3), 66.4 (C5), 59.0, 54.8 (OCH_3), 18.1 (CH_3(3)), 18.9 (CH_3(6)). Anal. Calcd. for $C_{16}H_{24}O_5$ (296.36): C, 64.84; H, 8.16. Found: C, 64.79; H, 8.12.

Methyl 6-deoxy-3-*C*-methyl-2-*O*-methyl-α-L-mannopyranoside (31). To the solution of **30** (130 mg, 0.44 mmol) in MeOH (10 ml), Pd/C (10 %, 10 mg) was added and the mixture was stirred for one hour under H_2 at room temperature. The mixture was filtered and concentrated. The crude syrup was purified on a column of silica gel (hexane : ethyl acetate 1:1) to yield **31** (76 mg, 83.7 %) as a colourless syrup. $[\alpha]_D$ = -44.18 (c = 0.30 in CH_3OH). R_f = 0.14 (hexane/ethyl acetate 1:1). ^1H and ^{13}C NMR data are collected in Table 2. Anal. Calcd. for $C_9H_{18}O_5$ (206.24): C, 52.41; H, 8.80. Found: C, 52.45; H, 8.76.

Methyl 2-*O*-benzyl-6-deoxy-3-*C*-methyl-4-*O*-methyl-α-L-mannopyranoside (32). Bu_4NBr (22 mg) was added to a solution of methyl **22**[5] (108 mg, 0.52 mmol) in CH_2Cl_2 (10 ml) and aqeous 20 % NaOH (3.3 ml) at 0 °C, then benzyl bromide (622 μl) was added dropwise, the mixture was stirred for one day. The mixture was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 8:2) to yield **32** (135 mg, 87 %) as a colourless syrup. $[\alpha]_D$ = -15.41 (c = 0.10 in $CHCl_3$). R_f = 0.51 (hexane/ethyl acetate 1:1). NMR data: δ_H ($CDCl_3$) 7.24 (m, 5H,Ph), 4.56 (d, 1H, *J*(1,2) = 1 Hz, H1), 4.52 (m, 2H, CH_2Ph) 3.43 (bm, 1H, H5), 2.86 (d, 1H, *J*(4,5) = 9.5 Hz, H4), 3.22 (d, 1H, H2), 3.43, 3.2 (2s, 6H, OCH_3), 1.18 (s, 3H, CH_3(3)), 1.18 (d, 3H, *J*(5,Me(6)) = 6 Hz, CH_3(6)). δ_C ($CDCl_3$) 98.7 (C1), 86.1 (C4), 83.0 (C2), 73.4 (CH_2Ph), 73.4 (C3), 66.7 (C5), 61.4, 54.9 (OCH_3), 17.9 (CH_3(3)), 18.5 (CH_3(6)). Anal. Calcd. for $C_{16}H_{24}O_5$ (296.36): C, 64.84; H, 8.16. Found: C, 64.81; H, 8.18.

Methyl 2-*O*-benzyl-6-deoxy-3-*C*-methyl-3,4-di-*O*-methyl-α-L-mannopyranoside (33). Sodium hydride (18 mg) was added to a solution of **32** (120 mg, 0.404 mmol) in dry DMF (5 ml) at 0 °C, the mixture was stirred for 1 h, then methyl iodide (76 μl) was added dropwise. After 1 h stirring at 0 °C, methanol (0.5 ml) was added, the mixture was concentrated. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 9:1) to yield **33** (93 mg, 74 %) as a colourless syrup. $[\alpha]_D$ = -26.00 (c = 0.21 in $CHCl_3$). R_f = 0.62 (hexane/ethyl acetate 7:3). NMR data: δ_H ($CDCl_3$) 7.33 (m, 5H,Ph), 4.72 (d, 1H, *J*(1,2) = 2 Hz, H1), 4.68 (m, 2H, CH_2Ph), 3.61 (bm, 1H, H5), 3.18 (d, 1H, *J*(4,5) =9.5 Hz, H4), 3.05 (d, 1H, H2), 3.5, 3.34, 3.22 (3s, 9H, OCH_3), 1.3 (s, 3H, CH_3(3)), 1.33 (d, 3H, *J*(5,6) = 6 Hz, CH_3(6)). δ_C ($CDCl_3$) 99.0 (C1), 84.4 (C4), 78.6 (C2), 72.7 (CH_2Ph), 78.1 (C3), 66.6 (C5), 61.1, 54.8, 48.9 (OCH_3), 15.2 (CH_3(3)), 18.2 (CH_3(6)). Anal. Calcd. for $C_{17}H_{26}O_5$ (310.39): C, 65.78; H, 8.84. Found: C, 65.77; H, 8.80.

Methyl 6-deoxy-3-*C*-methyl-3,4-di-*O*-methyl-α-L-mannopyranoside (34). To the solution of **33** (83 mg, 0.27 mmol) in MeOH (10 ml), Pd/C (10 %, 10 mg) was added and the mixture was stirred for one hour under H_2 at room temperature. The mixture was filtered and concentrated. The crude syrup was purified on a column of silica gel (hexane/ethyl acetate 7 : 3) to yield **34** (55 mg, 92 %) as a colourless syrup. $[\alpha]_D$ = -112.12 (c = 0.21 in $CHCl_3$). R_f = 0.48 (hexane/ethyl acetate 1:1). ^1H and ^{13}C NMR data are collected in Table 2. Anal. Calcd. for $C_{10}H_{20}O_5$ (278.3): C, 54.53; H, 9.15. Found: C, 54.55; H, 9.19.

Methyl 6-deoxy-3-*C*-methyl-2,3,4-tri-*O*-methyl-α-L-mannopyranoside (36). Sodium hydride (189 mg) was added to a solution of methyl **35**[5] (200 mg, 1.04 mmol) in dry DMF (5 ml) at 0 °C, the mixture was stirred for 1 h, then methyl iodide (592 μl) was added dropwise. After 1 h stirring at 0 °C, methanol (1 ml) was added, the mixture was concentrated. The residue was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (hexane/ethyl acetate 9 : 1) to yield **36** (153 mg, 66 %) as a colourless syrup. $[\alpha]_D$ = -54.74 (c = 0.46 in $CHCl_3$). R_f = 0.52 (hexane/ethyl acetate 1:1). ^1H and ^{13}C NMR data are collected in Table 2. Anal. Calcd. for $C_{11}H_{22}O_5$ (234.29): C, 56.39; H, 9.46. Found: C, 56.42; H, 9.51.

Methyl 6-deoxy-3-*C*-methyl-2,4-di-*O*-methyl-3-*O*-(2,6-di-*O*-acetyl-3,4-di-*O*-methyl-β-D-glucopyranosyl)-α-L-talopyranoside (38). To the solution of the donor **37** (1035 mg, 2.37 mmol) and acceptor **5** (347 mg, 1.58 mmol) in dry CH_2Cl_2 (5 ml) TMSOTf (129 μl, 0.67 mmol) was added at -50 °C. After 20 min. stirring at -50 °C, Et_3N (100 μl) was added, the mixture was diluted with CH_2Cl_2 and after extractive work-up the crude syrup was purified on a short column of silica (hexane/ethyl acetate 1:1) to yield pure **38** (265 mg, 34 %) both as colourless syrups. $[\alpha]_D$ = +53.9 (c = 0.82 in $CHCl_3$). R_f = 0.23 (hexane/ethyl acetate 1:1). NMR data: δ_H ($CDCl_3$) 4.91 (dd, 1H, *J*(2',3') = 9.2 Hz, H2'), 4.75 (d, 1H, *J*(1',2') = 7.8 Hz, H1'), 4.69 (d, 1H, *J*(1,2) = 4.1 Hz, H1), 4.33 (dd, 1H, *J*(5',6'a) = 2.3, *J*(6'a,6'b) = 11.7 Hz, H6'a), 4.18 (dd, 1H, *J*(5',6'b) = 6.5, H6'b), 4.04 (bm, 1H, H5), 3.40 (ddd, 1H, H5'), 3.29 (t, 1H, *J*(3',4') = 8.8 Hz, H3'), 3.19 (dd, 1H, *J*(4',5') = 9.8 Hz, H4'), 2.90 (d, 1H, *J*(4,5) = 3.5 Hz, H4), 2.83 (d, 1H, H2), 3.49, 3.41, 3.40, 3.35 (4s, 15H, OCH_3), 2.06, 2.04 (2s, 6H, Ac.CH_3), 1.38 (s, 3H, CH_3(3)), 1.26 (d, 3H, *J*(5,6) = 6.8 Hz, CH_3(6)). δ_C ($CDCl_3$) 170.6, 169.4 (Ac.C=O), 99.3 (C1), 95.8 (C1'), 85.4 (C3'), 83.9 (C4), 83.5 (C2), 80.1 (C4'), 79.2 (C3), 73.3 (C2'), 73.1 (C5'), 67.6 (C5), 63.7 (C6'), 60.4, 61.0, 59.9, 55.8 (OCH_3), 21.2, 20.8, (Ac.CH_3), 20.4 (CH_3(3)), 16.0 (CH_3(6)). Anal. Calcd. for $C_{22}H_{38}O_{12}$ (494.54): C, 53.43; H, 7.74. Found: C, 53.41; H, 7.72.

Methyl 6-deoxy-3-*C*-methyl-2,4-di-*O*-methyl-3-*O*-(2,6-di-*O*-acetyl-3,4-di-*O*-methyl-β-D-glucopyranosyl)-α-L-mannopyranoside (39). The solution of the donor **37** (560 mg, 1.38 mmol) and acceptor **23** (180 mg, 0.8 mmol) in dry CH_2Cl_2 (4 ml) was cooled to -50 °C, then TMSOTf (78 μl, 0.41 mmol) was added dropwise and the mixture was stirred for 30 min. Et_3N (100 μl) was added, the mixture was diluted with CH_2Cl_2, extracted with water, dried and concentrated *in vacuo*. The resulting syrup was purified on a column of silica gel (CH_2Cl_2 : acetone 95 : 5) to yield **4** (165 mg, 42 %) as a colourless syrup.$[\alpha]_D$ = -25.45 (c = 0.3 in $CHCl_3$). R_f = 0.36 (hexane/ethyl acetate 1:1). NMR data: δ_H ($CDCl_3$) 4.98 (dd, 1H, *J*(2',3') = 9.6 Hz, H2'), 4.75 (d, 1H, *J*(1',2') = 8 Hz, H1'), 4.6 (d, 1H, *J*(1,2) = 1.8 Hz, H1), 4.37 (dd, 1H, *J*(5',6'a) = 2.1, *J*(6'a,6'b) = 11.8 Hz, H6'a), 4.22 (dd, 1H, *J*(5',6'b) = 6.1, H6'b), 3.54 (bm, 1H, H5), 3.42 (ddd, 1H, H5'), 3.31 (dd, 1H, *J*(3',4') = 8.9 Hz, H3'), 3.21 (d, 1H, H2), 3.20 (dd, 1H, *J*(4',5') = 9.8 Hz, H4'), 3.17 (d, 1H, *J*(4,5) = 9.6 Hz, H4), 3.32, 3.4, 3.41, 3.5 (4s, 15H,OCH_3), 2.8, 2.6 (2s, 6H, Ac.CH_3), 1.36 (s, 3H, CH_3(3)), 1.28 (d, 3H, *J*(5,6) = 6.2 Hz, CH_3(6)). δ_C ($CDCl_3$) 170.6, 169.2 (Ac.C=O), 99.0 (C1), 95.5 (C1'), 85.4 (C3'), 84,2 (C4), 83.7 (C2), 80.6 (C3), 79.8 (C4'), 73.3 (C5'), 73.1 (C2'), 67.2 (C5), 63.4 (C6'), 61.4, 60.7, 59.3, 55.2, (OCH_3), 21.2, 21.0 (Ac.CH_3), 18.5 (CH_3(6)), 15.8 (CH_3(3)). Anal. Calcd. for $C_{22}H_{38}O_{12}$ (494.54): C, 53.43; H, 7.74. Found: C, 53.38; H, 7.69.

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