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

Anikó Tóthb, Judit Reményika, István Bajzaa, András Lipták*a,b

*aResearch Group for Carbohydrates of the Hungarian Academy of Sciences, and
bInstitute of Biochemistry, University of Debrecen, P.O.B. 55, Debrecen, H-4010 Hungary
E-mail : liptaka@tigris.klte.hu

Dedicated to Professor Gábor Bernáth on his 70th birthday
(received 10 Jan 03; accepted 03 Mar 03; published on the web 14 Mar 03)

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 1H and 13C NMR spectra of the synthesized methyl ethers, all of the L-mannopyranosyl derivatives and the mono- and disubstituted L-talopyranosyl analogues adopt a 1C4 conformation, but for each of the persubstituted talopyranosyl sugars the 4C1 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 mycobacteria1-3. Of the known cell-surface glycopeptidetype antigens, the serovariant 19 of M. avium possesses the most complicated structure4 with respect both to the sugar component, and the immunodeterminant pentasaccharide composition (Fig. 1.). The chemists4 who isolated and studied the structure
searched for the configuration of carbon C-4 of the branched-monomosaccharide 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). 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 1C4 (L) to 4C1 (L), no such change occurred in the case of 23, and the disaccharide also possessed the 1C4 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, benzylaion). 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-isopropyliden-3-C-methyl-α-L-talopyranoside (1), and -α-L-mannopyranoside (19) were methylated by means of the Brimacombe method 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-\(\alpha\)-L-talopyranoside (13) and methyl 6-deoxy-3-C-methyl-4-O-methyl-\(\alpha\)-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 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 benzylaion 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 (1). The sugar 36 was isolated earlier from a natural source, and following isolation and structural determination it was named nogalose.

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 constants the conformation of all of the prepared compounds can be studied. All of the 6-deoxy-3-C-methyl-$\alpha$-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-$\alpha$-L-talopyranoside: $\delta_H$, $\delta_C$ [ppm] and coupling constants [Hz]

| Compounds | Me 6-deoxy-3-C- | -2-OMe (13)$^a$ | -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)$^b$ | 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          |
| CH$_3$(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            | 7.0            | 6.7            | 6.7            |
| CH$_3$(6) | 17.3            | 16.9           | 16.98          | 16.87          | 17.0           | 16.67          | 16.82          | 14.92          | 15.98          |
| CH$_3$(3) | 1.25            | 1.3            | 1.26           | 1.28           | 1.27           | 1.27           | 1.22           | 1.29           | 1.38           |
| CH$_3$(3) | 23.3            | 22.28          | 18.33          | 22.36          | 18.65          | 23.73          | 18.63          | 18.43          | 20.37          |

$a$ In CD$_3$OD, $b$ In CCl$_3$D.

The situation in the case of the 6-deoxy-3-C-methyl-$\alpha$-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 tetruglycosyl alditol, 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-$\beta$-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-$\alpha$-L-mannopyranoside: $\delta_H$, $\delta_C$ [ppm] and coupling constants [Hz]

| Compounds | Me 6-deoxy-3-C-Me-\(\alpha\)-L-Manp (35)$^a$ | -2-OMe | -3-OMe | -4-OMe | 2,3-di-OMe | 2,4-di-OMe | 3,4-di-OMe | 2,3,4-tri-OMe (36)$^b$ | 2,6-di-OAc-3,4-di-OMe-$\beta$-D-Glcp-(1$\rightarrow$3)-(39)$^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        | 1.0        | 1.5             | 2.0                              |
| 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                            |
| CH$_3$(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                              |
| CH$_3$(6) | 18.40                                       | 18.51 | 14.99  | 18.48  | 17.95      | 18.01      | 17.90      | 18.03           | 18.50                            |
| CH$_3$(3) | 1.26                                        | 1.25  | 1.33   | 1.23   | 1.27       | 1.30       | 1.30       | 1.25            | 1.36                             |
| CH$_3$(3) | 19.18                                       | 19.11 | 18.46  | 19.54  | 14.50      | 18.54      | 14.37      | 14.99           | 15.80                            |

$^a$ In CD$_3$OD, $^b$ In CCl$_3$D.

**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,
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 Rf 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 (LiChrospherSi-60).

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

| Compounds | TLC (Rf)* | HPLC (Rt)** | HPLC (Rt)*** | TLC (Rf)* | Compounds |
|-----------|-----------|-------------|--------------|-----------|-----------|
| Me 6-deoxy-3-C-Me-α-L-Manp | | | | |
| -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.
** LiChrospherSi 60; Hexane/Ethyl acetate, 40:60.
*** LiChrospherSi 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 (Rf: 0.14), the following is the 2,3,4-tri-O-methyl glycoside (Rf: 0.16), and the most apolar is the 3,4-di-O-methyl derivative (Rf: 0.47). The Rf and...
R<sub>f</sub> 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<sub>f</sub> or the R<sub>t</sub> values, and no observable role of the order of the OH functions was experienced.

The low R<sub>f</sub> and R<sub>t</sub> 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<sub>f</sub> : 0.16; manno: R<sub>f</sub> : 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<sub>f</sub> : 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 <sup>4</sup>C<sub>1</sub> conformation, [R<sub>f</sub> : 0.40 (dichloromethane-acetone 95:5) and R<sub>f</sub> : 0.30 (hexane-ethyl acetate 7:3)] obtained by the methylation of the 4-O-benzyl ether 6 [R<sub>f</sub> : 0.37 (dichloromethane-acetone 95:5) and R<sub>f</sub> : 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<sup>11</sup>. 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<sub>3</sub> 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 CHCl₃. 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 ¹³C 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), CDCl₃ (77.00 ppm for ¹³C 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 1S (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 CH₂Cl₂, extracted with water, dried and concentrated to yield 3 (4.83 g, 82%) as a colourless syrup. Rf = 0.7 (hexane/ethyl acetate 7:3). C₁₈H₂₆O₅ (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 CH₂Cl₂ (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 CH₂Cl₂, 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. [α]D = -89.20 (c = 0.49 in CHCl₃). Rf = 0.3 (hexane/ethyl acetate 7:3). NMR data: δH (CDCl₃) 7.33 (m, 5H, Ph), 4.8 (d, 1H, J(1,2) = 1 Hz, H1), 4.75 (m, CH₂Ph), 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, CH₃(3)), 1.27 (d, 3H, J(5,6) = 6.5 Hz, CH₃(6)). δC (CDCl₃) 103.3 (C1), 84.9 (C4), 76.7 (CH₂Ph), 73.6 (C2), 69.58 (C3), 65.1 (C5), 55.2 (OCH₃), 22.5 (CH₃(3)), 17.1 (CH₃(6)). Anal. Calcd. for C₁₅H₂₂O₅ (282.34): C, 63.81; H, 7.85. Found: C, 63.75; H, 7.75.

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 CH₂Cl₂, extracted with water, dried and concentrated in vacuo. The resulting syrup
was purified on a column of silica gel (CH$_2$Cl$_2$/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$_2$Cl$_2$/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$_2$Ph), 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)). Anal. Calcd. for C$_7$H$_9$O$_3$: C, 66.43; H, 7.54. Found: C, 66.38; H, 7.45.

**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). $^1$H and $^{13}$C NMR data are collected in Table 1. Anal. Calcd. for C$_{13}$H$_{26}$O$_5$ (310.39): C, 65.78; H, 8.44. Found: C, 65.76; H, 8.39.

**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$_2$Cl$_2$, 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$_2$Ph), 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$_2$Ph), 65.1 (C5), 55.0 (OCH$_3$), 23.9 (CH$_3$(3)), 16.7 (CH$_3$(6)). Anal. Calcd. for C$_{22}$H$_{29}$O$_7$ (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$_2$Cl$_2$, 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$_2$Ph), 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$_2$Ph), 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 H₂ 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. [α]D = -93.35 (c = 0.37 in CHCl₃). Rf = 0.47 (hexane/ethyl acetate 1:1). ¹H and ¹³C NMR data are collected in Table 1. Anal. Calcd. for C₂₃H₃₈O₅ (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 CH₂Cl₂, 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. [α]D = -47.22 (c = 0.37 in CHCl₃). Rf = 0.26 (hexane/ethyl acetate 7:3). NMR data: δH (CDCl₃) 7.33 (m, 5H, Ph), 4.81 (d, 1H, J(1,2) = 1 Hz, H1), 4.72 (m, CH₂Ph), 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, OCH₃), 1.18 (d, 3H, J(5,6) = 6.5 Hz, CH₃(6)). Anal. Calcd. for C₁₆H₂₅O₅ (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 H₂ 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. [α]D = -57.69 (c = 0.26 in CHCl₃). Rf = 0.23 (hexane/ethyl acetate 1:1). ¹H and ¹³C NMR data are collected in Table 1. Anal. Calcd. for C₁₀H₁₃O₅ (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 4² (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 CH₂Cl₂, 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. [α]D = -29.10 (c = 0.35 in CHCl₃). Rf = 0.4 (hexane/ethyl acetate 7:3). NMR data: δH (CDCl₃) 7.32 (m, 5H, Ph), 4.68 (d, 1H, J(1,2) = 1 Hz, H1), 4.68 (m, CH₂Ph) 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, CH₃(3)), 1.34 (d, 3H, J(5,6) = 6.5 Hz, CH₃(6)). δC (CDCl₃) 99.7 (C1), 85.5 (C4), 79.7 (C2), 73.9 (C₃H₂Ph), 69.34 (C₃), 64.8 (C₅), 62.6, 54.9 (OCH₃), 23.9 (CH₃(3)), 16.6 (CH₃(6)). Anal. Calcd. for C₁₆H₂₅O₅ (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 CH₂Cl₂, 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: $\delta$H (CDCl$_3$) 7.32 (m, 5H, Ph), 4.84 (d, 1H, J(1,2) = 6.5 Hz, H1), 4.76 (m, CH$_2$Ph), 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)). 13C NMR data are collected in Table 1. Anal. Calcd. for C$_{10}$H$_{20}$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 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 13C 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 15 (1.3 g, 5.6 mmol) in dry DMF (5 ml) at 0 °C, the mixture was stirred for two hours at 50 °C. The mixture was diluted with CH$_2$Cl$_2$, 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 17 (250 mg, 94 %) as a colourless syrup. $[\alpha]_D = -93.96$ (c = 0.29 in CH$_2$OH). $R_f = 0.06$ (CH$_2$Cl$_2$/acetone 95:5). 1H and 13C NMR data are collected in Table 1. Anal. Calcd. for C$_5$H$_{16}$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$_2$Cl$_2$, 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 13C 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 18 (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$_2$Cl$_2$, 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$_2$Cl$_2$ (10 ml), acetic acid (10 ml, 60 %) and trifluoroacetic acid (1 ml) were added. The mixture was stirred for one hour at room temperature. The mixture was diluted...
with CH₂Cl₂, 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. [α]D = -82.62 (c = 0.59 in CHCl₃). Rf = 0.3 (hexane/ethyl acetate 7:3). NMR data: δH (CDCl₃) 7.3 (m, 5H,Ph), 4.59 (d, 1H, J(1,2) = 1.5 Hz, H1), 4.76 (m, 2H, CH₂Ph), 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, OCH₃), 1.31 (s, 3H, CH₃(3)), 1.23 (d, 3H, J(5,6) = 6 Hz, CH₃(6)). δC (CDCl₃) 103.2 (C1), 84.7 (C4), 76.5 (C2), 76.5 (C3), 74.79 (CH₂Ph), 67.6 (C5), 55.4 (OCH₃), 18.6 (CH₃(3)), 19.8 (CH₃(6)). Anal. Calcd. for C₁₅H₂₂O₅ (282.34): C, 63.81; H, 7.58. 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 CH₂Cl₂, 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. [α]D = -61.56 (c = 0.33 in CHCl₃). Rf = 0.4 (hexane/ethyl acetate 7:3). NMR data: δH (CDCl₃) 7.33 (m, 5H,Ph), 4.76 (d, 1H, J(1,2) = 2 Hz, H1), 4.76 (m, 2H, CH₂Ph), 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, OCH₃), 1.38 (s, 3H, CH₃(3)), 1.33 (d, 3H, J(5,6) = 6 Hz, CH₃(6)). ¹³C NMR (90 MHz, CDCl₃) δ = 98.1 (C1), 83.0 (C4), 80.8 (C2), 78.4 (C3), 75.3 (CH₂Ph), 66.3 (C5), 58.7, 54.9, 48.5 (OCH₃), 15.6 (CH₃(3)), 18.3 (CH₃(6)). Anal. Calcd. for C₁₇H₂₆O₅ (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 H₂ 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 (61 mg, 68 %) as a colourless syrup. [α]D = -38.16 (c = 0.28 in CHCl₃). Rf = 0.24 (hexane/ethyl acetate 1:1).¹H and ¹³C NMR data are collected in Table 2. Anal. Calcd. for C₁₀H₁₆O₅ (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).** Bu₄NBr (64 mg) was added to a solution of 24 (380 mg, 1.72 mmol) in CH₂Cl₂ (30 ml) and aqueous 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 CH₂Cl₂, 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. [α]D = -20.48 (c = 0.48 in CHCl₃). Rf = 0.44 (hexane/ethyl acetate 7:3). NMR data: δH (CDCl₃) 7.36 (m, 10H,Ph), 4.78 (d, 1H, J(1,2) = 1.5 Hz, H1), 4.80, 4.70 (m, 2H, CH₂Ph), 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, OCH₃), 1.42 (s, 3H, CH₃(3)), 1.36 (d, 3H, J(5,6) = 6 Hz, CH₃(6)). δC (CDCl₃) 98.4 (C1), 84.3 (C4), 83.3 (C2), 73.4 (C3), 75.2, 73.4 (CH₂Ph), 66.5 (C5), 54.8 (OCH₃), 18.2 (CH₃(3)), 19.0 (CH₃(6)). Anal. Calcd. for C₂₁H₂₈O₅ (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 CH₂Cl₂, 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. [α]D = -24.78 (c = 0.55 in CHCl₃). Rf = 0.54 (hexane/ethyl acetate 7:3). NMR data: δH (CDCl₃) 7.38 (m, 10H, Ph), 4.77 (d, 1H, J(1,2) = 2 Hz, H1), 4.78, 4.72 (m, CH₂Ph), 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, OCH₃), 1.4 (s, 3H, CH₃(3)), 1.37 (d, 3H, J(5,6) = 6 Hz, CH₃(6)). δC (CDCl₃) 99.1 (C1), 82.9 (C4), 78.6 (C2), 78.6 (C3), 75.1, 72.8 (CH₂Ph), 66.6 (C5), 54.9, 48.9 (OCH₃), 15.6 (CH₃(3)), 18.4 (CH₃(6)). Anal. Calcd. for C₂₃H₃₀O₅ (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 H₂ 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. [α]D = -72.89 (c = 0.57 in CH₃OH). Rf = 0.20 (hexane/ethyl acetate 1:1). ¹H and ¹³C NMR data are collected in Table 2. Anal. Calcd. for C₁₉H₁₈O₅ (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). Bu₄NBr (34 mg) was added to a solution of 24 (207 mg, 0.74 mmol) in CH₂Cl₂ (17 ml) and aqueous 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 CH₂Cl₂, 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. [α]D = -79.27 (c = 0.59 in CHCl₃). Rf = 0.44 (hexane/ethyl acetate 7:3). NMR data: δH (CDCl₃) 7.33 (m, 5H, Ph), 4.81 (d, 1H, J(1,2) = 1 Hz, H1), 4.72 (m, 2H, CH₂Ph), 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, OCH₃), 1.35 (s, 3H, CH₃(3)), 1.18 (d, 3H, J(5,6) = 6.5 Hz, CH₃(6)). δC (CDCl₃) 97.6 (C1), 85.0 (C4), 75.1 (CH₂Ph), 84.0 (C2), 73.4 (C3), 66.4 (C5), 59.0, 54.8 (OCH₃), 18.1 (CH₃(3)), 18.9 (CH₃(6)). Anal. Calcd. for C₁₆H₂₄O₅ (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 H₂ 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. [α]D = -44.18 (c = 0.30 in CH₃OH). Rf = 0.14 (hexane/ethyl acetate 1:1). ¹H and ¹³C NMR data are collected in Table 2. Anal. Calcd. for C₁₀H₁₈O₅ (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). Bu₄NBr (22 mg) was added to a solution of methyl 22⁵ (108 mg, 0.52 mmol) in CH₂Cl₂ (10 ml) and aqueous 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 CH₂Cl₂, 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. [α]D = -15.41 (c = 0.10 in CHCl₃). R₇ = 0.51 (hexane/ethyl acetate 1:1). NMR data: δH (CDCl₃) 7.24 (m, 5H, Ph), 4.56 (d, 1H, J(1,2) = 1 Hz, H1), 4.52 (m, 2H, CH₂Ph) 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, OCH₃), 1.18 (s, 3H, CH₃(3)), 1.18 (d, 3H, J(5,Me(6)) = 6 Hz, CH₃(6)). δC (CDCl₃) 98.7 (C1), 86.1 (C4), 83.0 (C2), 73.4 (CH₂Ph), 73.4 (C3), 66.7 (C5), 61.4, 54.9 (OCH₃), 17.9 (CH₃(3)), 18.5 (CH₃(6)). Anal. Calcd. for C₁₈H₂₄O₅ (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 CH₂Cl₂, 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. [α]D = -26.00 (c = 0.21 in CHCl₃). R₇ = 0.62 (hexane/ethyl acetate 7:3). NMR data: δH (CDCl₃) 7.33 (m, 5H, Ph), 4.72 (d, 1H, J(1,2) = 2 Hz, H1), 4.68 (m, 2H, CH₂Ph), 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, OCH₃), 1.3 (s, 3H, CH₃(3)), 1.33 (d, 3H, J(5,6) = 6 Hz, CH₃(6)). δC (CDCl₃) 99.0 (C1), 84.4 (C4), 78.6 (C2), 72.7 (CH₂Ph), 78.1 (C3), 66.6 (C5), 61.1, 54.8, 48.9 (OCH₃), 15.2 (CH₃(3)), 18.2 (CH₃(6)). Anal. Calcd. for C₁₇H₂₁O₅ (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 H₂ 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. [α]D = -112.12 (c = 0.21 in CHCl₃). R₇ = 0.48 (hexane/ethyl acetate 1:1). ¹H and ¹³C NMR data are collected in Table 2. Anal. Calcd. for C₁₀H₂₀O₅ (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 35⁵ (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 CH₂Cl₂, 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. [α]D = -54.74 (c = 0.46 in CHCl₃). R₇ = 0.52 (hexane/ethyl acetate 1:1). ¹H and ¹³C NMR data are collected in Table 2. Anal. Calcd. for C₁₁H₂₂O₅ (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 CH2Cl2 (5 ml) TMSOTf (129 µl, 0.67 mmol) was added at -50 °C. After 20 min. stirring at -50 °C, Et3N (100 µl) was added, the mixture was diluted with CH2Cl2 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. [α]D = +53.9 (c = 0.82 in CHCl3). Rf = 0.23 (hexane/ethyl acetate 1:1). NMR data:

δH (CDCl3) 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, OCH3), 2.06, 2.04 (2s, 6H, Ac.CH3), 1.38 (s, 3H, CH3(3)), 1.26 (d, 3H, J(5,6) = 6.8 Hz, CH3(6)).

δC (CDCl3) 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, 55.2 (OCH3), 21.2, 20.8, 20.4 (Ac.CH3), 16.0 (CH3(3)).

Anal. Calcd. for C22H38O12 (494.54): C, 53.43; H, 7.74. Found: C, 53.38; H, 7.69.

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 CH2Cl2 (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. Et3N (100 µl) was added, the mixture was diluted with CH2Cl2, extracted with water, dried and concentrated in vacuo. The resulting syrup was purified on a column of silica gel (CH2Cl2 : acetone 95 : 5) to yield 4 (165 mg, 42 %) as a colourless syrup. [α]D = -25.45 (c = 0.3 in CHCl3). Rf = 0.36 (hexane/ethyl acetate 1:1). NMR data:

δH (CDCl3) 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, OCH3), 2.8, 2.6 (2s, 6H, Ac.CH3), 1.36 (s, 3H, CH3(3)), 1.28 (d, 3H, J(5,6) = 6.2 Hz, CH3(6)).

δC (CDCl3) 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, 21.2, 21.0 (Ac.CH3), 18.5 (CH3(6)), 15.8 (CH3(3)).

Anal. Calcd. for C22H38O12 (494.54): C, 53.43; H, 7.74. Found: C, 53.38; H, 7.69.

Acknowledgments

This research was supported by grant of the Hungarian Academy of Sciences (AK P2000-162 2,4).
References

1. Lipták, A.; Borbás, A.; Bajza, I. Med. Res. Rev. 1994, 14, 307.
2. Aspinall, G.O.; Chatterjee, D.; Brennan, P.J. Adv. Carbohydr. Chem. Biochem. 1995, 51, 169.
3. Lowary, T.L. In Glycoscience: Chemistry and Chemical Biology: Fraser-Reid, B.; Tatsuta, K.; Thiem, J. (Eds.), Springer 2001, p. 2005.
4. Chatterjee, D.; Bozic, C.; Aspinall, G.O.; Brennan, P.J. J. Biol. Chem. 1988, 263, 4092.
5. Gyergyói, K.; Tóth, A.; Bajza, I.; Lipták, A. Synlett 1998, 127.
6. Brimacombe, J.S. In Meth. Carbohydr. Chem.: Whistler, R.L.; BeMiller, J.N. (Eds.), Acad. Press 1972, Vol VI, p. 376.
7. Roy, R. In Handbook of Phase Transfer Catalysis: Sasson, Y.; Neumann, R. (Eds.), Blackie Academic and Professional 1997, p. 244.
8. Wiley, P.F., MacKellar, F.A.; Caron, E.L.; Kelly, R.B. Tetrahedron Lett. 1968, 663.
9. Brimacombe, J.S.; Mahmood, S.; Rollins, A.J. J. Chem. Soc. Perkin I 1975, 1292.
10. Wiley, P.F.; Duchamp, D.J.; Hsiung, V.; Chidester, C.G. J. Org. Chem. 1971, 36, 2670.
11. Vasella, A. In Glycosylidene Carbenes: Hecht, S.M. Bioorganic Chemistry: Carbohydrates (Eds.), Oxford Univ. Press 1999, p. 56.