Synthesis of methyl 6-deoxy-4-*O*-(sodium sulfonato)-α-L-talopyranoside, its C-4 epimer and both isosteric [4-C-(potassium sulfonatomethyl)] derivatives

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Abstract

The 4-*O*-sulfuric esters of methyl 6-deoxy-α-L-talo- and -α-L-mannopyranoside were prepared. The first ester is a component of the glycopeptidolipid-type cell surface antigens of *M. avium*. The isosteric isomers (sugar-4-CH$_2$-SO$_3$Na) of both sulfate esters (sugar-4-O-SO$_3$Na) were synthesized using free radical addition reactions between sugar-exomethylene derivatives and either thioacetic acid or NaHSO$_3$. The addition products of thioacetic acid were converted into sugar-CH$_2$-sulfonic acids by oxidation with oxone. Characteristic ^{1}H- and ^{13}C-NMR data are given and discussed.

Keywords: Sugar sulfates, radical addition reaction, sugar-exomethylenes, radical addition of thioacetic acid or NaHSO$_3$, radical initiators: AIBN, *t*-butyl peroxybenzoate

Introduction

Most species of M*ycobacterium* are saprophytic species found in soil and some of them are serious human health threats.[1] Besides *Mycobacterium tuberculosis*[2] and *M. leprae*[3,4], the agents of human tuberculosis and leprosy, respectively, other 'atypical' or 'opportunistic' mycobacteria may also cause infections in humans.[5] Infections with the *M. avium* serocomplex are seen in up to 50% of the patients with AIDS in some areas of the world .[6-8]

Mycobacterial diseases are difficult to treat,[9] and this is directly related to the unusual complex structure of the cell-wall[9,10] of the organism. The cell-wall presents a formidable barrier[11] to the passage of antibiotics into the organism. The combination of different antibiotics can slowly destroy the integrity of the cell-wall and allow other antibiotics to pass into the organism more easily.
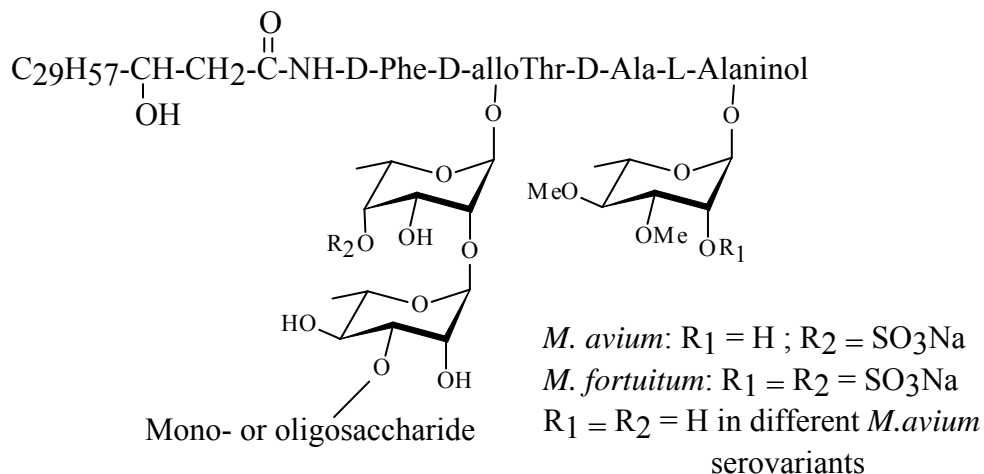
The mycobacterial cell-wall has five major components: [10,11]

i) the plasma membrane;

ii) peptidoglycan;

iii) the mycolyl-arabinogalactan (AG), both sugars are in furanosyl form in the polysaccharide;

iv) lipoarabinomannan (LAM) and lipomannan (LM) ;

v) glycolipids noncovalently bound to the large amount of mycolate esters. Because these glycolipids are on the outermost surface of the bacteria, these outer oligosaccharide haptens are responsible for the immunological properties of the bacteria. Thus, these haptens, after conjugation with suitable proteins, might aid the serodiagnosis of mycobacterial infections.[12,13]

These haptens, which are oligosaccharides, have very different, and very often exotic structures for the monosaccharide units. They are mainly deoxy sugars and contain many *O*-methyl substituents. Acyl groups also are present and pyruvic acid is common in acetalic form. These serospecific oligosaccharides glycosylate different "core" regions. Basically, these so-called extractable lipids, which contain the immunospecific oligosaccharides, can be classified into four groups:[12,13] glycopeptidolipids, lipooligosaccharides, phenolic glycolipids, and acylated trehalose derivatives.

The human pathogens *M. tuberculosis* and *M. avium* produce sulfated glycolipids and recently it was shown that the very conservative core region of glycopeptidolipids is also sulfated at position 4 of the 6-deoxy-L-talose of *M. avium*[14] and the 3,4-di-*O*-methyl-L-rhamnose at position 2 in the case of *M. fortuitum*.[15] It is worth mentioning that the 4-*O*-sulfated 6-deoxy-L-talose was isolated from an ethambutol-resistant *M. avium* strain cultured from a patient with AIDS.[14]

$$C_{29}H_{57}\text{-CH-CH}_2\text{-}\overset{\overset{O}{\|}}{C}\text{-NH-D-Phe-D-alloThr-D-Ala-L-Alaninol}$$

R_2O OH

MeO OMe OR_1

HO

Mono- or oligosaccharide

M. avium: $R_1 = H$; $R_2 = SO_3Na$

M. fortuitum: $R_1 = R_2 = SO_3Na$

$R_1 = R_2 = H$ in different *M. avium* serovariants

Figure 1

The biological role of sugar sulfate esters[16,17] and sugar C-sulfonic acids[18-20] cannot be overestimated. Sulfated sugars are common mediators of cell-cell and host-pathogen interactions.

In our program, we wished to replace the sugar sulfate esters by sugar sulfonic acids and by sugar-methylene-sulfonic acids. Such investigations were accomplished in the case of sialyl

Lewis X[21,22] and *Helicobacter pylori* ligand analogs.[23] We developed new methods for the preparation of sugar sulfonic acids[24,25] and we supposed that sugar methylene-sulfonic acids, which are isosteric analogs of sugar sulfates, might be better replacements for sugar *O*-sulfates than sugar sulfonic acids.
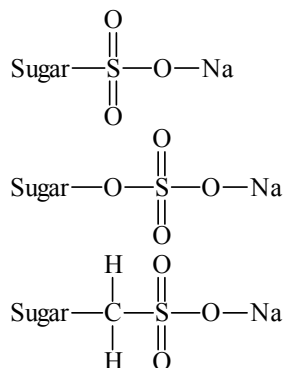

Figure 2

In this paper we wish to report on the syntheses of methyl 6-deoxy-4-*O*-sulfate-α-L-talopyranoside, its C-4-epimer derivative, methyl 4,6-dideoxy-4-*C*-methylene-sulfonic acid-α-L-talopyranoside, and methyl 4,6-dideoxy-4-*C*-(sodium methylene-sulfonic acid)-α-L-mannopyranoside.

Results and Discussion

The reagents most frequently employed for sulfation are complexes of sulfur trioxide with a tertiary amine (e.g. trimethylamine or pyridine) or an amide (formamide or dimethylformamide) in pyridine, dimethyl sulfoxide or *N,N*-dimethylformamide as the solvent. Other sulfation reagents that can be used are chlorosulfonic acid or piperidine-N-sulfonic acid in a polar, aprotic solvent.
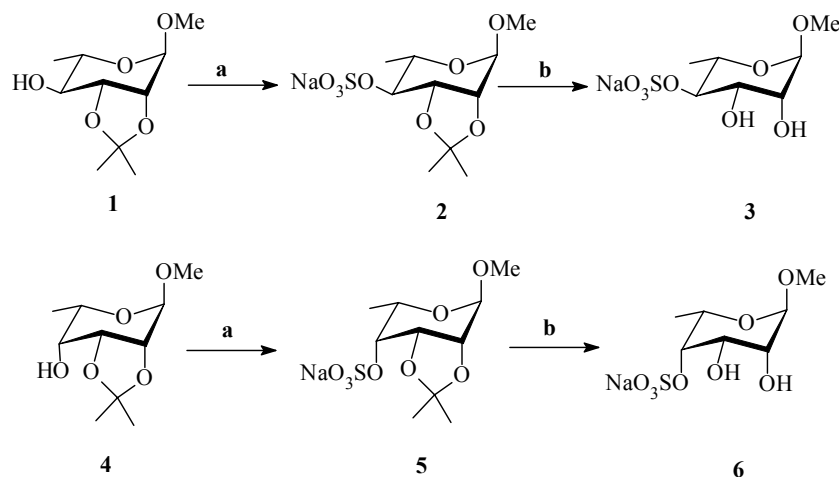
Scheme 1. a) 10 eq. SO$_3$˙py, DMF, 1h; NaHCO$_3$; 77% for **2**, 79% for **5**; b) 96% AcOH, 30 min., quant.

Methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**1**)[26] was treated with the SO₃·Pyridine complex in DMF for 1h at room temperature to give methyl 2,3-*O*-isopropylidene-4-*O*-(sodium sulfonato)-α-L-rhamnopyranoside (**2**) in 77% yield. Its ^{13}C-NMR spectrum showed the presence of a strong deshielding effect, which led to a downfield shift for C-4 of 6.9 ppm. In this case we could not detect any upfield shift in the adjacent carbon signals.[27] Hydrolysis of the isopropylidene group was achieved with acetic acid at room temperature for 30 min and the yield was quantitative. In the ^{13}C-NMR spectrum of methyl 4-*O*-(sodium sulfonato)-α-L-rhamnopyranoside (**3**), C-4 resonates at 81.1 ppm. This α-shift is 8.2 ppm. The ^{13}C-NMR data for methyl α-L-rhamnopyranoside and for compound **1** were published previously by Argentinean authors.[28]

Similar treatment of methyl 6-deoxy-2,3-O-isopropylidene-α-L-talopyranoside (**4**)[29] with the SO₃·Pyridine complex resulted in methyl 6-deoxy-2,3-O-isopropylidene-4-O-(sodium sulfonato)-α-L-talopyranoside (**5**). Comparing the ^{13}C-NMR spectra of compounds **5** and **4**,[30] a very large downfield shift of 13.5 ppm was observed at C-4 and there was a considerable upfield shift (6.9 ppm) at C-3.
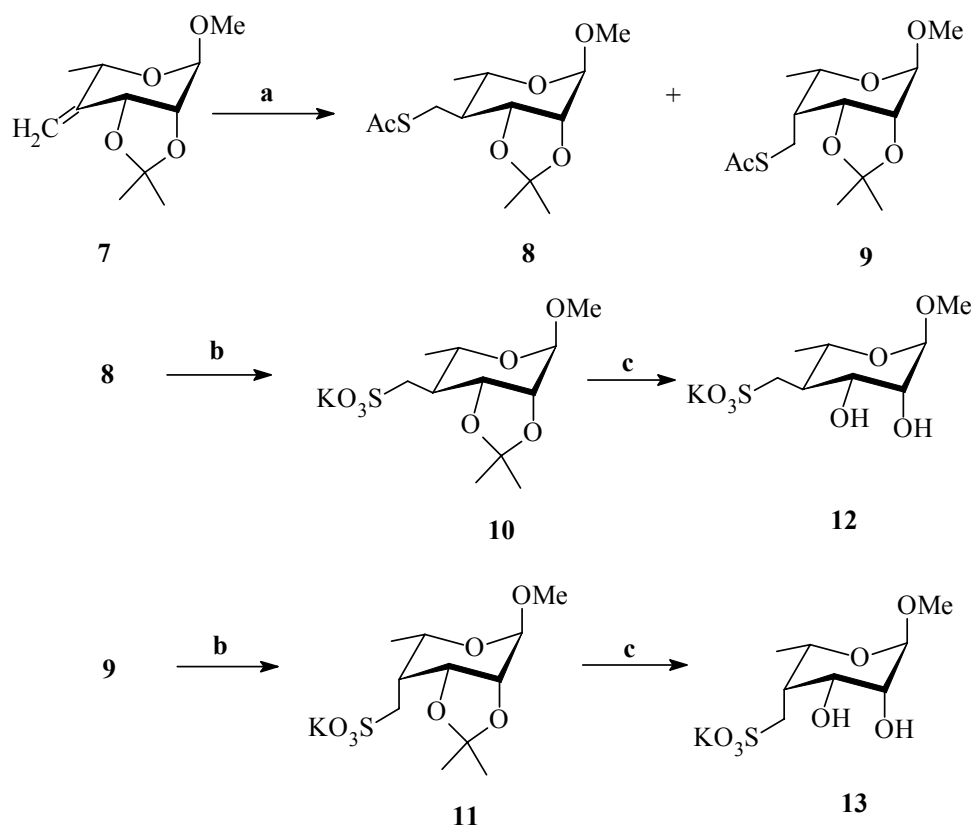
Scheme 2. a) 5 eq. AcSH, AIBN, toluene, 80°C, 8h, 22% **8**:**9**=1:1; b) 2.5 eq. oxone, 20 eq. KOAc, AcOH, 54% for **10**, 69% for **11**; c) 96% AcOH, 60°C, 1h, quant.

Precise prediction of ^{13}C chemical shifts is rather difficult, as various factors, such as conformational distortions and steric crowding of the substituents may influence the molecular environment of the individual carbon atoms. Hydrolysis of the isopropylidene acetal resulted in the target compound **6** with quantitative yield. The ^{13}C chemical shifts are in the normal region, the value for C-4 is 80.1 ppm, and the α-shift is 7.3 ppm. The ^{13}C-NMR spectrum of methyl 6-deoxy-α-L-talopyranoside was measured in CDCl$_3$.[31]

For the preparation of the 4-deoxy-4-*C*-(sodium sulfonatomethyl) derivatives **10** and **12** of methyl α-L-rhamnopyranoside or methyl 6-deoxy-α-L-talopyranoside, methyl 4,6-dideoxy-2,3-*O*-isopropylidene-4-*C*-methylene-α-L-*lyxo*-hexopyranoside[32] (**7**) was used. The synthesis of the latter from methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyran-4-uloside[29] using Tebbe's reagent[33] was accomplished according to the van Boom methodology.[34]

The well-known photoaddition reaction of cysteamine to allyl[35] groups, which leads to the corresponding amino-thioethers, was applied for the synthesis of a pentavalent glycocluster.[36] A similar radical photoaddition catalysed by AIBN also was reported with perbenzylated exocyclic glycals in benzene solution using freshly distilled thioacetic acid at reflux temperature; only the ß-*C*-glycoside (1-*S*-acetyl-2,6-anhydro-1-deoxy-3,4,5,7-tetra-*O*-benzyl-D-*glycero*-D-*gulo*-heptitol) was formed in 82% yield. To the best of our knowledge, radical addition reactions with uloso-sugars have not been published previously.

The AIBN or ABCN catalysed free radical addition reaction between compound **7** and thioacetic acid in toluene resulted in a 1:1 mixture of methyl 4,6-dideoxy-2,3-*O*-isopropylidene-4-*C*-(acetylthiomethyl)-α-L-mannopyranoside (**8**) and -α-L-talopyranoside (**9**). The yield was very low (22%) even at high temperature (80ºC) and after a long reaction time (8h). The C-4 epimers could be separated, and their chirality also could be determined by measuring the values of the $^3J_{H4,H5}$ coupling constants (10.1 Hz for **8** and 6.9 Hz for **9**). The COSY and HETCOR ^{1}H- and ^{13}C-NMR spectra and Mw measurements for compounds **8** and **9** using ESI-TOF verified the postulated structures. Some very characteristic ^{13}C-NMR data are worthy of mention: the C-4 resonance of the *manno*-isomer (**8**) is at 44.1 ppm, whereas, in the case of the *talo*-isomer (**9**), it is at higher field (36.4 ppm). The CH$_2$-groups in each compound resonate nearly at the same fields (27.6 and 27.8 ppm).

Oxidation of compound **8** with oxone[38] resulted in the methylene-sulfonic acid potassium salt (**10**). Analogous treatment of compound **9** gave the *talo*-isomer **11**. The carbon NMR spectra for both isomers (**10** and **11**) showed the same C-4 chemical shift values and the differences which were observed for the C-4 epimers of the thioacetates **8** and **9**.

Hydrolysis of the isopropylidene group in compound **10** using acetic acid resulted in a quantitative yield of **12**, and similarly compound **11** yielded **13**. Interestingly, the chemical shift values of the epimeric C-4's are nearly the same (42.3 and 41.9 ppm), but a considerable difference was observed for the CH$_2$-group-values (51.5 and 47.0 ppm).
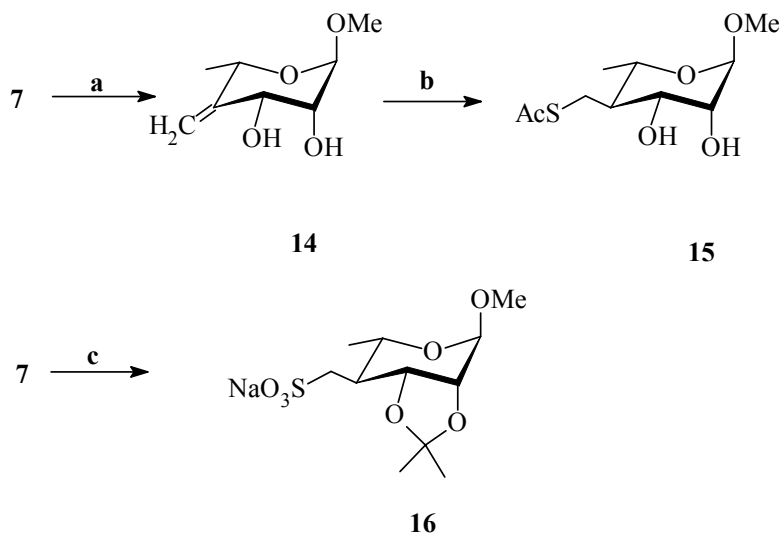
Scheme 3. a) CF$_3$COOH, H$_2$O, DCM, 1h, 73%; b) 5 eq. AcSH, AIBN, toluene, 80°C, 8h, 17%; *t*-butyl peroxybenzoate, NaHSO$_3$, EtOH-H$_2$O, reflux, 56%.

It was mentioned earlier that the thioacetic acid addition to the perbenzylated exocyclic glycal resulted only in the *equatorial* methylene-thioacetate derivative. To clear up the role of the isopropylidene acetal in compound **7**, we hydrolysed the isopropylidene group and the resulting methyl 4,6-dideoxy-4-*C*-exomethylene-α-L-*lyxo*-hexopyranoside (**14**) was treated with thioacetic acid in the presence of AIBN catalyst. Surprisingly, only one isomer was formed and it proved to be methyl 4,6-dideoxy-4-*C*-(acetylthiomethyl)-α-L-mannopyranoside (**15**) which is the *equatorial* isomer. Unfortunately, the yield was again very low (17%) and it could not be increased. It seems very propable that the uloso-glycosides also react in a radical addition reaction, and the photoaddition leads mainly to the *equatorial* product. The flexible conformation of the unsaturated compound is an important prediction. This assumption was also supplied by the fact that hydrogensulfite addition catalysed by *tert*-butyl peroxybenzoic acid resulted exclusively in compound **16**. This observation is in a good accordance with earlier results where the authors [39-41] allowed methyl 6-deoxy-α- and ß-D-*xylo*-hex-5-enopyranoside, methyl 6-deoxy-ß- and -α-L-*arabino*-hex-5-enopyranoside and methyl 6-deoxy-α-D-*lyxo*-hex-5-enopyranoside to react with hydrogen sulfite in aqueous solution. The main or exclusive products were the D-sugars in which the 6-sulfonate moieties were in an *equatorial* position.

In conclusion, we have demonstrated that the isosteric analogs of compounds **3** and **6**, which are sugar-*O*-sulfates, could be obtained from sugar exomethylene derivatives by radical addition reactions using either thioacetic acid or sodium hydrogen sulfite.

Experimental Section

General Procedures. Optical rotations were measured at room temperarure with a Perkin-Elmer 241 automatic polarimeter in $CHCl_3$, MeOH and H_2O. 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). The ^{1}H (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 ^{1}H for organic solutions), $CDCl_3$ (77.00 ppm for ^{13}C), MeOH-d_4 (49.05 ppm for ^{13}C) and DSS (0.00 ppm for ^{1}H for aqueous solutions). MALDI-TOF MS analyses of the compounds were performed in the positive-ion mode using a Bruker Biflex MALDI-TOF mass spectrometer equipped with delayed-ion extraction. Desorption/ionization of the sample molecules was effected with a 337 nm nitrogen laser. The spectrum was performed in 2,5-dihydroxybenzoic acid (DHB) matrix by mixing 0.5 μl of the matrix solution with 0.5 μl of the sample on the target and it was allowed to dry at room temperature. Identification of the compounds was done on the basis of the mass of the $[M+Na]^+$ peak. ESI-MS analyses of the compounds were performed in the negative-ion mode using Bruker BIOTOF II. Elemental analyses were performed at the analytical laboratories of the University of Debrecen.

Methyl 2,3-O-isopropylidene-4-O-(sodium sulfonato)-α-L-rhamnopyranoside (2). A solution of **1** (1.0 g, 4.58 mmol) in DMF (30 mL) was treated with the SO_3·Py complex (7.3 g, 46.0 mmol) for 1 h at rt, then cold saturated $NaHCO_3$ solution was added in excess (pH > 7). The resulting mixture was concentrated in *vacuo*. Then, MeOH (100 ml) was added and after stirring for 20 min., the insolubles were removed by filtration. The filtrate was concentrated under reduced pressure and then purified on a column of silica gel (DCM-MeOH 9:1) to give (1.13 g, 3.53 mmol) of **2** (77 %). $[\alpha]_D$ = -21.5 (c=0.29 in MeOH). R_f = 0.51 (DCM-MeOH 8:2).
NMR data: δ_H (CD$_3$OD) 4.79 (s, 1H, H1), 4.23 (t, 1H, $J(3,4)$ = 3.3 Hz, H3), 4.15 (dd, 1H, $J(4,5)$ = 4.9 Hz, H4), 4.11 (dd, 1H, $J(2,3)$ = 2.9 Hz, H2), 3.69 (m, 1H, $J(5,6)$ = 3.2 Hz, H5), 3.38 (s, 3H, OMe), 1.54 and 1.35 (2s, 6H, CMe$_2$), 1.36 (d, 3H, CH$_3$(6)). δ_C (CD$_3$OD) 110.5 (**C**Me$_2$), 99.5 (C1), 81.1 (C4), 78.1 (C3), 77.1 (C2), 65.8 (C5), 55.2 (OMe), 28.0 and 26.5 (C**Me$_2$**), 18.2 (C6). Exact mass Calcd.: 320.05. Found: 320.31.

Methyl 4-O-(sodium sulfonato)-α-L-rhamnopyranoside (3). A solution of **2** (50 mg, 0.156 mmol) in acetic acid (96 %) (3.0 mL) was stirred for 30 min. at rt, then the mixture was concentrated in *vacuo* to give **3** (quant). $[\alpha]_D$ = -79.1 (c=0.18 in MeOH). R_f = 0.45 (DCM-MeOH 75:25).
NMR data: δ_H (CD$_3$OD) 4.60 (s, 1H, H1), 4.26 (t, 1H, $J(4,5)$ = 4.7 Hz, $J(3,4)$ = 4.4 Hz, H4), 3.85 (m, 2H, H2, H3), 3.66 (m, 1H, $J(5,6)$ = 3.0 Hz, H5), 3.38 (s, 3H, OMe), 1.35 (d, 3H, CH$_3$(6)). δ_C (CD$_3$OD) 102.1 (C1), 81.1 (C4), 71.8 (C2), 71.7 (C3), 67.6 (C5), 55.3 (OMe), 17.9 (C6). Anal. Calcd. for C$_7$H$_{13}$O$_8$SNa (280.23): C, 30.00; H, 4.68. Found: C, 30.01; H, 4.63.

Methyl 6-deoxy-2,3-O-isopropylidene-4-O-(sodium sulfonato)-α-L-talopyranoside (5). A solution of **4** (1.0 g, 4.58 mmol) in DMF (30 mL) was treated with the SO_3·Py complex (7.3 g, 46.0 mmol) for 1 h at rt, then cold saturated $NaHCO_3$ solution was added in excess (pH > 7). The resulting mixture was concentrated in *vacuo*. Then, MeOH (100 ml) was added and, after stirring for 20 min., the insolubles were removed by filtration. The filtrate was concentrated under reduced pressure and then purified on a column of silica gel (DCM-MeOH 9:1) to give (1.16 g, 3.62 mmol) of **5** (79 %). $[\alpha]_D$ = -59.6 (c=0.36 in MeOH). R_f = 0.41 (DCM-MeOH 8:2).

NMR data: δ_H (CD_3OD) 4.73 (dd, 1H, $J(4,5)$ = 2.5 Hz, H4), 4.61 (d, 1H, $J(1,2)$ = 1.0 Hz, H1), 4.57 (dd, 1H, $J(3,4)$ = 1.9 Hz, H3), 4.09 (dd, 1H, $J(2,3)$ = 3.3 Hz, H2), 4.18 (m, 1H, H5), 3.42 (s, 3H, OMe), 1.55 and 1.34 (2s, 6H, C**Me**$_2$), 1.41 (d, 3H, $J(5,6)$ = 3.3 Hz, $CH_3(6)$). δ_C (CD_3OD) 111.6 (**C**Me$_2$), 100.3 (C1), 76.4 (C2), 74.3 (C3), 72.4 (C4), 67.3 (C5), 56.0 (OMe), 26.7 and 25.5 (C**Me$_2$**), 17.4 (C6). Exact mass Calcd.: 320.05. Found: 320.32.

Methyl 6-deoxy-4-O-(sodium sulfonato)-α-L-talopyranoside (6). A solution of **5** (50 mg, 0.156 mmol) in acetic acid (96 %) (3.0 mL) was stirred for 30 min. at rt, then the mixture was concentrated in *vacuo* to give **6** (quant). $[\alpha]_D$ = -66.6 (c=0.15 in H_2O). R_f = 0.45 (DCM-MeOH 75:25).

NMR data: δ_H (D_2O) 4.73 (d, 1H, $J(1,2)$ = 1.5 Hz, H1), 4.51 (dd, 1H, $J(4,5)$ = 1.0 Hz, H4), 4.05 (m, 1H, H5), 3.92 (t, 1H, $J(3,4)$ = 3.5 Hz, H3), 3.67 (dd, 1H, $J(2,3)$ = 3.5 Hz, H2), 3.37 (s, 3H, OMe), 1.31 (d, 3H, $J(5,6)$ = 6.5 Hz, $CH_3(6)$). δ_C (D_2O) 102.9 (C1), 80.1 (C4), 69.2 (C2), 66.4 (C5), 66.2 (C3), 55.8 (OMe), 17.1 (C6). Anal. Calcd. for $C_7H_{13}O_8SNa$ (280.23): C, 30.00; H, 4.68. Found: C, 29.95; H, 4.65.

Methyl 4-deoxy-2,3-O-isopropylidene-4-C-(acetylthiomethyl)-α-L-rhamnopyranoside (8) and methyl 4,6-dideoxy-2,3-O-isopropylidene-4-C-(acetylthiomethyl)-α-L-talopyranoside (9). To a solution of **7** (1.00 g, 4.67 mmol) in toluene (50 mL) was added thioacetic acid (1.67 ml, 23.4 mmol) and AIBN (112 mg, 0.460 mmol). The solution was stirred at 80 ^{o}C for 4 h. The solvent was removed in *vacuo* and the crude product was then purified on a column of silica gel (DCM- EtOAc 99:1) to give (150 mg, 0.52 mmol) of **8** (11 %) **and** (150 mg, 0.52 mmol) of **9** (11 %).

8. $[\alpha]_D$ = -21.8 (c=0.46 in $CHCl_3$). R_f = 0.41 (DCM-EtOAc 97:3).

NMR data: δ_H ($CDCl_3$) 4.83 (s, 1H, H1), 3.95 (m, 2H, H2, H3), 3.54 (m, 1H, $J(4,5)$ = 10.1 Hz, H5), 3.34 (s, 3H, OMe), 3.20 (dd, 1H, $^3J(4,A)$ = 4.0, $^2J(A,B)$ = 13.8, CH_{2A}), 2.98 (dd, 1H, $^3J(4,B)$ = 5.0, CH_{2B}), 2.30 (s, 3H, SAc), 1.75 (m, 1H, H4), 1.45 and 1.30 (2s, 6H, C**Me**$_2$), 1.20 (d, 3H, $J(5,6)$ = 6.1 Hz, $CH_3(6)$). δ_C ($CDCl_3$) 108.9 (**C**Me$_2$), 98.1 (C1), 74.1, 73.6 (skeleton C), 64.5 (C5), 54.8 (OMe), 44.1 (C4), 30.6 (SAc), 28.1 and 26.2 (C**Me$_2$**), 27.6 (CH_2), 18.6 (C6). Anal. Calcd. for $C_{13}H_{22}O_5S$ (290.38): C, 53.77; H, 7.64. Found: C, 53.71; H, 7.60.

9. $[\alpha]_D$ = -46.6 (c=0.45 in $CHCl_3$). R_f = 0.33 (DCM-EtOAc 97:3).

NMR data: δ_H ($CDCl_3$) 4.53 (d, 1H, $J(1,2)$ = 2.5 Hz, H1), 4.40 (dd, 1H, $J(3,4)$ = 3.2 Hz H3), 4.08 (m, 1H, $J(4,5)$ = 6.9 Hz, H5), 3.92 (dd, 1H, $J(2,3)$ = 7.0 Hz, H2), 3.38 (s, 3H, OMe), 3.05 (dd, 1H, $^3J(4,A)$ = 7.0, $^2J(A,B)$ = 13.5, CH_{2A}), 2.92 (dd, 1H, $^3J(4,B)$ = 8.5, CH_{2B}), 2.33 (m, 1H, H4), 2.31 (s, 3H, SAc), 1.46 and 1.28 (2s, 6H, C**Me**$_2$), 1.32 (d, 3H, $J(5,6)$ = 6.7 Hz, $CH_3(6)$). δ_C

(CDCl$_3$) 109.5 (**C**Me$_2$), 98.8 (C1), 74.7, 73.1 (skeleton C), 67.9 (C5), 55.8 (OMe), 36.4 (C4), 30.7 (SAc), 27.8 (CH$_2$), 26.8 and 24.8 (C**Me$_2$**), 17.5 (C6). Anal. Calcd. for C$_{13}$H$_{22}$O$_5$S (290.38): C, 53.77; H, 7.64. Found: C, 53.69; H, 7.55.

Methyl 4-deoxy-2,3-O-isopropylidene-4-C-(potassium sulfonatomethyl)-α-L-rhamnopyranoside (10). To a stirred solution of **8** (50 mg, 0.172 mmol) in glacial acetic acid (3 mL) were added potassium acetate (338 mg, 3.44 mmol) and OXONE (2KHSO$_5$, KHSO$_4$, K$_2$SO$_4$) (264 mg, 0.43 mmol). After 16 h at room temperature, the mixture was diluted with cold water (3 mL), and cold saturated NaHCO$_3$ solution was added in excess (pH > 7). The resulting mixture was concentrated in *vacuo*. Then, MeOH (10 ml) was added and, after stirring for 20 min., the insolubles were removed by filtration. The filtrate was concentrated under reduced pressure and then purified on a column of silica gel (DCM-MeOH 9:1) to give (31 mg, 0.093 mmol) of **10** (54 %). [α]$_D$ = -57.8 (c=0.37 in MeOH). R$_f$ = 0.65 (DCM-MeOH 75:25).
NMR data: δ_H (CD$_3$OD) 4.79 (s, 1H, H1), 4.75 (dd, 1H, J(3,4) = 9.0 Hz H3), 4.08 (m, 1H, J(4,5) = 9.3 Hz, H5), 3.97 (d, 1H, J(2,3) = 5.3 Hz, H2), 3.36 (s, 3H, OMe), 3.15 (dd, 1H, ^3J(4,A) = 4.3, ^2J(A,B) = 14.7, CH$_{2A}$), 3.03 (dd, 1H, ^3J(4,B) = 4.4, CH$_{2B}$), 1.92 (m, 1H, H4), 1.47 and 1.32 (2s, 6H, CMe$_2$), 1.34 (d, 3H, J(5,6) = 6.3 Hz, CH$_3$(6)). δ_C (CDCl$_3$) 110.0 (C**Me$_2$**), 99.9 (C1), 75.2, 75.0 (skeleton C), 66.7 (C5), 55.3 (OMe), 50.6 (CH$_2$), 43.7 (C4), 28.5 and 26.7 (C**Me$_2$**), 20.0 (C6). Anal. Calcd. for C$_{11}$H$_{19}$O$_7$SK (334.43): C, 39.51; H, 5.73. Found: C, 39.50; H, 5.65.

Methyl 4-deoxy-4-C-(potassium sulfonatomethyl)-α-L-rhamnopyranoside (12). A solution of **10** (20 mg, 0.0598 mmol) in acetic acid (96 %) (1.5 mL) was stirred at 60 ^{o}C for 1 h, then the mixture was concentrated in *vacuo* to give **12** (quant). [α]$_D$ = -67.6 (c=0.31 in MeOH). R$_f$ = 0.35 (DCM-MeOH 7:3).
NMR data: δ_H (CD$_3$OD) 4.63 (d, 1H, J(1,2) = 1.5 Hz, H1), 3.94 (dd, 1H, J(3,4) = 10.9 Hz, H3), 3.81 (m, 1H, J(4,5) = 10.4 Hz, H5), 3.72 (dd, 1H, J(2,3) = 3.2 Hz, H2), 3.33 (s, 3H, OMe), 3.00 (d, 2H, CH$_{2A}$, CH$_{2B}$), 2.16 (m, 1H, H4), 1.33 (d, 3H, J(5,6) = 6.2 Hz, CH$_3$(6)). δ_C (CD$_3$OD) 102.7 (C1), 70.9 (C3), 70.5 (C2), 68.7 (C5), 55.2 (OMe), 51.5 (CH$_2$), 42.3 (C4) 19.4 (C6). Exact mass Calcd.: 294.018. Found: 294.093.

Methyl 4,6-dideoxy-2,3-O-isopropylidene-4-C-(potassium sulfonatomethyl)-α-L-talopyranoside (11). To a stirred solution of **9** (50 mg, 0.172 mmol) in glacial acetic acid (3 mL) were added potassium acetate (338 mg, 3.44 mmol) and OXONE (2KHSO$_5$, KHSO$_4$, K$_2$SO$_4$) (264 mg, 0.43 mmol). After 16 h at room temperature, the mixture was diluted with cold water (3 mL), and cold saturated NaHCO$_3$ solution was added in excess (pH > 7). The resulting mixture was concentrated in *vacuo*. Then, MeOH (10 ml) was added and, after stirring for 20 min., the insolubles were removed by filtration. The filtrate was concentrated under reduced pressure and then purified on a column of silica gel (DCM-MeOH 9:1) to give (40 mg, 0.120 mmol) of **11** (69 %). [α]$_D$ = -60.6 (c=0.16 in MeOH). R$_f$ = 0.55 (DCM-MeOH 75:25).
NMR data: δ_H (CD$_3$OD) 4.67 (dd, 1H, J(3,4) = 2.5 Hz, H3), 4.52 (d, 1H, J(1,2) = 3.2 Hz, H1), 4.27 (m, 1H, J(4,5) = 6.7 Hz, H5), 3.92 (dd, 1H, J(2,3) = 7.0 Hz, H2), 3.42 (s, 3H, OMe), 2.95 (m, 3H, H4, CH$_{2A}$, CH$_{2B}$), 1.47 and 1.30 (2s, 6H, CMe$_2$), 1.39 (d, 3H, J(5,6) = 6.5 Hz, CH$_3$(6)).

δ_C (CD$_3$OD) 110.8 (**C**Me$_2$), 100.2 (C1), 76.4, 75.7 (skeleton C), 70.3 (C5), 56.5 (OMe), 51.7 (CH$_2$), 34.6 (C4), 27.6 and 25.3 (C**Me$_2$**), 17.8 (C6). Anal. Calcd. for C$_{11}$H$_{19}$O$_7$SK (334.43): C, 39.51; H, 5.73. Found: C, 39.44; H, 5.64.

Methyl 4,6-dideoxy-4-C-(potassium sulfonatomethyl)-α-L-talopyranoside (13). A solution of **11** (20 mg, 0.0598 mmol) in acetic acid (96 %) (1.5 mL) was stirred at 60 ^{o}C for 1 h, then the mixture was concentrated in *vacuo* to give **13** (quant). [α]$_D$ = -53.5 (c=0.16 in MeOH). R$_f$ = 0.35 (DCM-MeOH 7:3).

NMR data: δ_H (CD$_3$OD) 4.65 (d, 1H, J(1,2) = 3.1 Hz, H1), 4.14 (m, 1H, J(4,5) = 3.4 Hz, H5), 4.03 (t, 1H, J(3,4) = 4.1 Hz, J(2,3) = 4.1 Hz, H3), 3.56 (m, 2H, CH$_{2A}$, H2), 3.38 (s, 3H, OMe), 3.00 (dd, 1H, ^3J(4,A) = 6.2, ^3J(4,B) = 4.4, CH$_{2B}$), 2.39 (m, 1H, H4), 1.33 (d, 3H, J(5,6) = 6.7 Hz, CH$_3$(6)). δ_C (CD$_3$OD) 102.4 (C1), 71.5 (C2), 70.2 (C3), 68.6 (C5), 55.6 (OMe), 47.0 (CH$_2$), 41.9 (C4), 18.1 (C6). Exact mass Calcd.: 294.018. Found: 294.098.

Methyl 4,6-dideoxy-4-C-methylene-α-L-*lyxo*-hexopyranoside (14). To a stirred solution of **7** (900 mg, 4.20 mmol) in 90 mL of CH$_2$Cl$_2$, 9 mL of trifluoroacetic acid and one drop of water were added. After 1 h, the mixture was washed with saturated NaHCO$_3$ solution (15 ml) and H$_2$O (15 ml), dried and evaporated to give (534 mg, 3.06 mmol) of **14** (73 %). [α]$_D$ = -132.8 (c=0.88 in MeOH). R$_f$ = 0.46 (DCM-acetone 8:2).

NMR data: δ_H (CD$_3$OD) 5.22 and 5.06 (2H, CH$_2$) 4.61 (d, 1H, H1), 4.37 (d, 1H, H3), 4.26 (q, 1H, H5), 3.75 (dd, 1H, H2), 3.39 (s, 3H, OMe), 1.35 (d, 3H, CH$_3$(6)). δ_C (CD$_3$OD) 149.0 (C$_q$), 108.1 (CH$_2$=), 103.1 (C1), 73.3, 70.3, 67.1 (skeleton C), 55.6 (OMe), 17.4 (C6). Anal. Calcd. for C$_8$H$_{14}$O$_4$ (174.20): C, 55.16; H, 8.10. Found: C, 55.10; H, 8.03.

Methyl 4,6-dideoxy-4-C-(acetylthiomethyl)-α-L-mannopyranoside (15). To a solution of **14** (500 mg, 2.87 mmol) in toluene (20 ml) was added thioacetic acid (1.03 ml, 14.35 mmol) and AIBN (50 mg, 0.205 mmol). The solution was stirred at 80 ^{o}C for 4 h. The solvent was removed in *vacuo* and the crude product was then purified on a column of silica gel (DCM-MeOH 97:3) to give (122 mg, 0.488 mmol) of **15** (17 %). [α]$_D$ = -48.5 (c=1.11 in MeOH). R$_f$ = 0.55 (DCM:MeOH 92:8). NMR data: δ_H (CD$_3$OD) 4.56 (s, 1H, H1), 3.68-3.58 (m, 3H, H2, H3, H5), 3.32 (s, 3H, OMe), 3.28 (dd, 1H, ^3J(4,A) = 3.9, ^2J(A,B) = 14.0, CH$_{2A}$), 3.15 (dd, 1H, ^3J(4,B) = 3.5, CH$_{2B}$), 2.33 (s, 3H, SAc), 1.94 (m, 1H, H4), 1.23 (d, 3H, J(5,6) = 6.3 Hz, CH$_3$(6)). δ_C (CD$_3$OD) 103.1 (C1), 70.8, 68.8, 68.0 (skeleton C), 55.3 (OMe), 44.3 (C4), 30.7 (SAc), 27.7 (CH$_2$), 19.4 (C6).

Anal. Calcd. for C$_{10}$H$_{18}$O$_5$S (250.31): C, 47.98; H, 7.25. Found: C, 47.90; H, 7.20.

Methyl 4-deoxy-2,3-O-isopropylidene-4-C-(sodium sulfonatomethyl)-α-L-rhamnopyranoside (16). A solution of **7** (113 mg, 0.527 mmol) in 70 % EtOH (40 ml) was treated with NaHSO$_3$ (520 mg) and *tert*-butyl peroxybenzoate (48 μl) and then the mixture was heated under reflux for 4 h. After cooling, removal of the solvent from the reaction mixture furnished a residue that was purified by silica gel column chromatography (DCM-MeOH 9:1) to give (94 mg, 0.295 mmol) **16** (56 %). [α]$_D$ = -60.3 (c=0.85 in MeOH). R$_f$ = 0.35 (DCM-MeOH 7:3).

NMR data: δ_H (CD$_3$OD) 4.63 (d, 1H, J(1,2) = 1.5 Hz, H1), 3.94 (dd, 1H, J(3,4) = 10.9 Hz, H3), 3.81 (m, 1H, J(4,5) = 10.4 Hz, H5), 3.72 (dd, 1H, J(2,3) = 3.2 Hz, H2), 3.33 (s, 3H, OMe), 3.00

(d, 2H, CH$_{2A}$, CH$_{2B}$), 2.16 (m, 1H, H4), 1.33 (d, 3H, J(5,6) = 6.2 Hz, CH$_3$(6)). δ$_C$ (CD$_3$OD) 102.7 (C1), 70.9 (C3), 70.5 (C2), 68.7 (C5), 55.2 (OMe), 51.5 (CH$_2$), 42.3 (C4) 19.4 (C6). Anal. Calcd. for C$_{11}$H$_{19}$O$_7$SNa (318.32): C, 41.51; H, 6.02. Found: C, 41.47; H, 5.97.

Acknowledgements

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