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Note

The role of sugar configuration in the acetolysis of 6-deoxyhexose methyl glycosides

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ABSTRACT

The acetolysis of several perbenzylated 6-deoxyhexose methyl glycosides under two mild conditions (10 equiv $ZnCl_2$ in 2:1 v/v Ac_2O–AcOH at 5 °C; 10:10:1 v/v/v Ac_2O–AcOH–TFA at 70 °C) was studied. We focused on the effect of sugar configuration on the competition between mechanisms with activation at exocyclic or endocyclic oxygen site. No effect was detected in acetolysis using the TFA protocol promoting an *exo*-activation mechanism, which affords 1-*O*-Ac-pyranosides regardless of sugar configuration. On the contrary, it has a primary role in determining the *endo*- versus *exo*-product distribution on $ZnCl_2$-promoted acetolysis.

Acetolysis is a widely used reaction in both synthetic and analytical carbohydrate chemistry, consisting in the cleavage of the glycosidic bond and the contemporary acetylation of the hydroxyl groups thus formed and/or present before the solvolysis. Acetolysis finds extensive application to the selective depolymerization of polysaccharides and provides useful information for their structural elucidation.[1] In synthetic carbohydrate chemistry, its main application is to convert alkyl or aryl glycosides of mono- and oligosaccharides into 1-O-acetylated derivatives, which are useful building blocks easily transformable into other derivatives.

Owing to the importance of acetolysis reaction in glycochemistry, several studies on the mechanism of this reaction exist in the literature.[2] The first step is the activation of endocyclic or exocyclic anomeric oxygen toward glycoside cleavage promoted by acetylium ion, which is formed from Ac_2O in acidic conditions. It has been shown that *endo*-activation proceeds more rapidly, nonetheless the distribution of acetolysis products is usually governed not by kinetic but by thermodynamic conditions, providing 1-*O*-Ac-pyranoside product **A** after acetic acid attack on the oxocarbenium ion (Scheme 1). On the contrary, the activation at the *endo*-site first affords acyclic acetyl methyl acetal **B**, which can be activated in turn by a second acetylium ion to give acyclic diacetyl acetal **D** and/or 1-*O*-Ac-furanoside derivative **E**. In acidic conditions, both **B** and **D** derivatives are in equilibrium with the aldehyde form, **C**. In the literature there are only a few scattered examples of acetolysis of common hexose glycosides affording predominantly *endo*-activation mechanism products.[2d,e,3] In the case of 6-deoxyhexoses, acetolysis with activation at *endo*-site should be more easily achieved because the lack of the electron-withdrawing oxygen atom at the 6-position enhances the nucleophilicity of the endocyclic oxygen. Indeed, some examples were reported on the acetolysis of 6-deoxyhexose glycosides affording **B**-, **C**-, **D**-, or **E**-like derivatives as the main products.[4]

We very recently developed two different protocols for the mild and selective acetolysis of 6-deoxyhexose methyl glycosides derivatized with armed protecting groups. The first protocol (10:10:1 v/v/v Ac_2O–AcOH–TFA at 70 °C)[5] allowed the conversion of disaccharide methyl glycosides composed of rhamnose and fucose into 1-*O*-acetyl pyranosides (**A**-like products) in good to excellent yield, without any significant competition of *endo*-activation mechanism.[6] On the contrary, the second protocol (10 equiv $ZnCl_2$ in 2:1 v/v Ac_2O–AcOH at 5 °C)[7] afforded in good yields 1-*O*-acetyl furanosides (**E**-like products) from rhamnose disaccharide methyl glycosides, as products of *endo*-activation mechanism.[8] In the present work we study the role of sugar configuration in driving the acetolysis of 6-deoxyhexose methyl glycosides preferentially to an *endo*- or *exo*-activated mechanism. For this reason, we first synthesized fully benzylated methyl glycosides of the most common natural deoxysugars (compounds **1**, **3**, **5**, **6**, **8**, **10** and **12**) through standard procedures. Then, these compounds were subjected to both protocols described above. Ac_2O–AcOH–TFA protocol furnished 1-*O*-Ac pyranosides in all studied cases in good to excellent yield (Table 1), confirming previously reported results on

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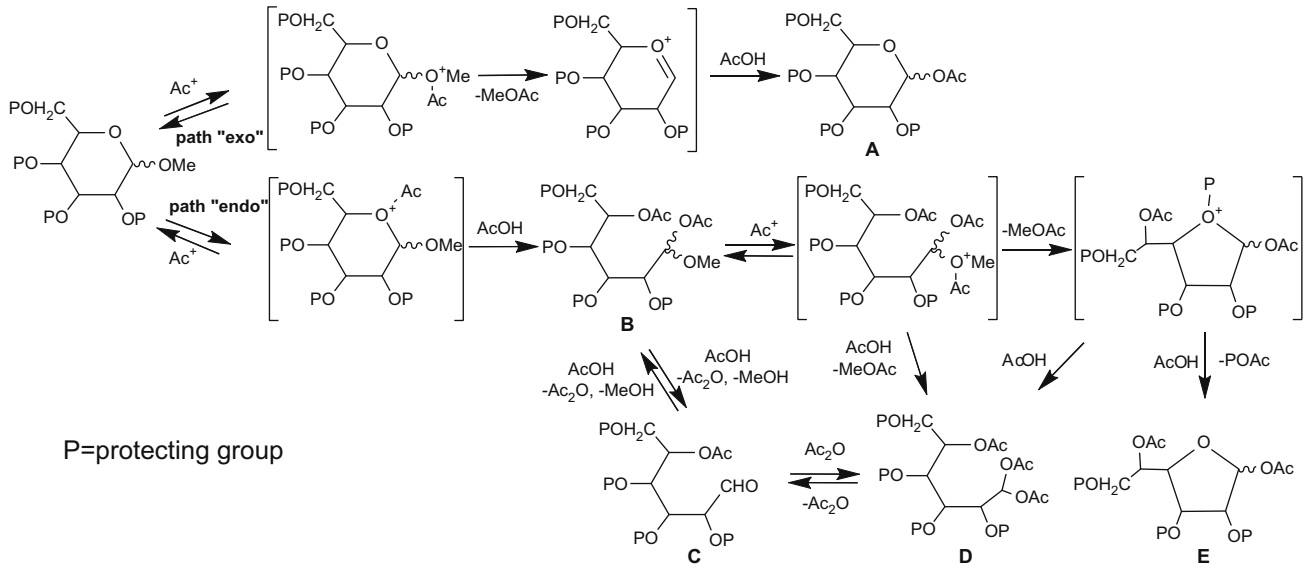


Scheme 1. *Endo*- versus *exo*-activation acetolysis mechanism.

rhamnose and fucose disaccharides.[6] Therefore, it seems that, in such conditions, acetolysis with activation at exocyclic oxygen is rather independent of sugar as well as anomeric configuration. On the contrary, acetolysis using the $ZnCl_2$ protocol afforded different compounds on the basis of the starting 6-deoxyhexose (Table 2). 6-Deoxy-mannose (rhamnose) methyl glycoside **1** gave 1-*O*-Ac furanoside **E**-like derivative **11** as the main product (62%) (entry 1). 6-Deoxy-talose (epifucose) glycoside **12** was acetolyzed using the $ZnCl_2$ protocol through an *endo*-activation mechanism, giving open-chain **B**- and **C**-like derivatives **13** and **14**, respectively (entry 2). Open-chain **C**- and **D**-like derivatives **15** and **16** were obtained from β-methyl 6-deoxy-glucoside (quinovoside) **3**, together with **E**-like furanoside **17**, whereas α-counterpart **5** afforded exclusively 1-*O*-Ac pyranoside **4**[9] (73%), as the product of an *exo*-activation mechanism (entries 3 and 4). A balanced competition between *exo*- and *endo*-mechanism can be hypothesized for 6-deoxy-altrose (altromethylose) glycoside **6**, which afforded an ~1:1 mixture between 1-*O*-Ac pyranoside **7** (50%) and **C**-like open-chain derivative **18** (42%) (entry 5). Finally, both α- and β-methyl fucoside gave exclusively 1-*O*-Ac pyranoside **9**[10] through the *exo*-activation mechanism (entries 6 and 7).

These results suggest that the role of configuration is crucial for driving the acetolysis using the $ZnCl_2$ protocol toward an *exo*- or *endo*-activation mechanism. The preference for a mechanism with activation at the endocyclic or exocyclic oxygen atom is strongly dictated by the anomeric configuration. The exocyclic oxygen is involved in the *exo*-anomeric effect in both anomers, whereas the endocyclic oxygen is involved in $n \rightarrow \sigma^*$ donation to the C_1–*O* bond only in the α-anomer.[2e] The overall effect is a general increased nucleophilicity of the endocyclic oxygen in the β-anomers, which explains the preference of β-quinovoside **3** to give *endo*-derived products with respect to α-counterpart **5**. In the β-fucoside case the main stereoelectronic effect is the strong through-space electron donation of the axially oriented *O*-4 substituent into the oxocarbenium ion formation, which highly enhances the first-order rate constant for the *exo*-activation involving *galacto*-configured alkyl glycosides with respect to *gluco*-configured counterparts;[2g] the result is that both fucoside anomers afford exclusively 1-*O*-Ac-pyranosides through an *exo*-activation mechanism. With the α-methyl glycosides, the role of configuration at *O*-2 seems to be very important too. Indeed, compounds having an axial *O*-2 such as rhamnoside **1** and epifucoside **12** afford products derived by an *endo*-activation, whereas α-methyl glycosides having an equatorial *O*-2 (quinovoside **5** and fucoside **8**) gave 1-*O*-Ac-pyranosides in high yields through an *exo*-activation mechanism. This could be ascribed to the antiperiplanar relationship of the C2–O2 and C1–O1 bonds, which enhances the electron-withdrawing effect of the axial *O*-2 on the *exo*-oxygen atom,[11] thus favoring an activation at the *endo*-site. With methyl 6-deoxy-α-altroside **6**, other stereoelectronic factors could countervail the *O*-2 axial effect, giving the simultaneous formation of products from both *exo*- and *endo*-mechanism. Interestingly, these results were very well replicated on disaccharide cases,[6,8] suggesting that a potential Zn(II)-sugar complexation[12] has a minor effect on the competition between *exo*- and *endo*-mechanism, because the geometry of such coordination should be highly dependent on saccharide structure. Regardless, a precise and detailed understanding of the role of 6-deoxysugar configuration on acetolysis reactions under kinetic control will surely need kinetics studies.

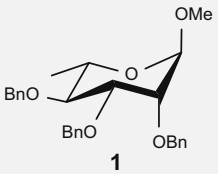
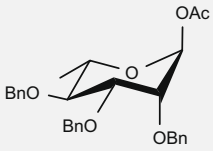
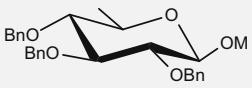
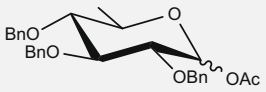
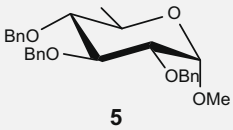
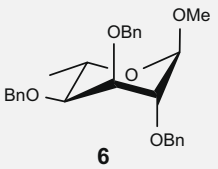
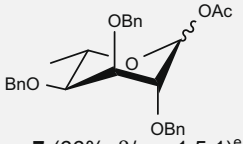
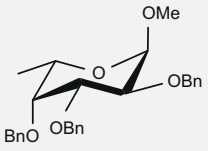
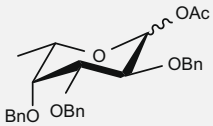
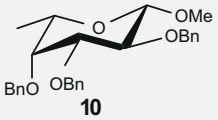
To summarize, this work demonstrated that the 6-deoxyhexose configuration has no effect in acetolysis under Ac_2O–AcOH–TFA reaction conditions, which promote an *exo*-activation mechanism affording 1-*O*-Ac-pyranosides. On the contrary, 6-deoxyhexose configuration has a primary role in determining the *endo*- versus *exo*-activation product distribution on $ZnCl_2$-promoted acetolysis.

1. Experimental

1.1. General methods

^1H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 (^1H: 400 MHz, ^{13}C: 100 MHz) instrument in $CDCl_3$ ($CHCl_3$ as an internal standard, ^1H: $CHCl_3$ at δ 7.26; ^{13}C: $CDCl_3$ at δ 77.0). Assignment of proton chemical shifts was based on 1D HOHAHA experiments. Positive MALDI-MS spectra were recorded on an Applied Biosystem Voyager DE-PRO MALDI-TOF mass spectrometer in the positive mode: compounds were dissolved in CH_3CN at a concentration of 1 mg/mL, and 1 μL of these solutions was mixed with 1 μL of a 20 mg/mL solution of 2,5-dihydroxybenzoic acid in 7:3 CH_3CN–0.1 M trifluoroacetic acid. Optical rotations were measured on a JASCO P-1010 polarimeter. Elemental analyses were performed on a Carlo Erba 1108 instrument. Analytical thin layer

Table 1
Acetolysis on 6-deoxyhexose methyl glycosides with 10:10:1 v/v/v Ac_2O–AcOH–TFA at 70 °C (see Section 2 for details)

Entry[a]	Methyl glycoside	Time (h)	Products[b]
1[6b]	 **1**	21	 **2** (61%;62[c])
2	 **3**	46	 **4**[9] (59%, α/β = 3.5:1)[d]
3	 **5**	19	**4**[9] (72%, α/β = 3:1)[d]
4	 **6**	21	 **7** (66%, β/α = 1.5:1)[e]
5	 **8**	24	 **9**[10] (99%, α/β = 4:1)[d]
6	 **10**	24	**9**[10] (83%, α/β = 3:1)[d]

[a] Reaction conducted on 0.1 mmol scale, unless otherwise specified.
[b] Isolated yield.
[c] Yield on 1 mmol scale.
[d] Anomeric ratio measured by ^1H NMR.
[e] Anomeric ratio measured by isolation of the two anomers.

chromatography (TLC) was performed on aluminum plates precoated with Merck Silica Gel 60 F_{254} as the adsorbent. The plates were developed with 10% H_2SO_4 ethanolic solution and then heated to 130 °C. Column chromatography was performed on Merck Kieselgel 60 (63–200 mesh).

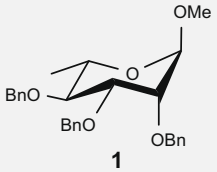
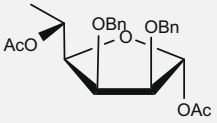
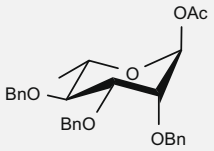
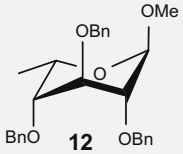
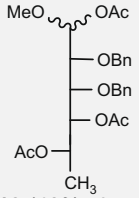
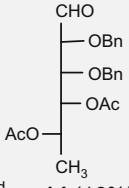
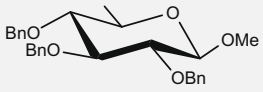
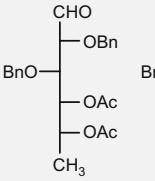
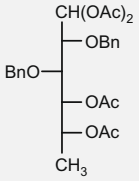
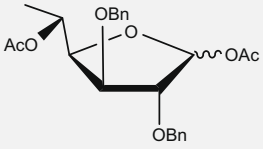
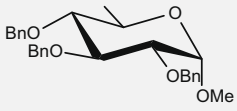
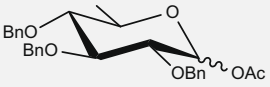
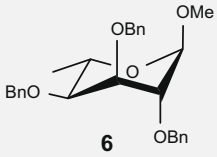
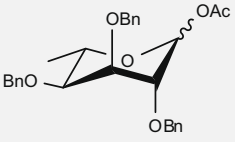
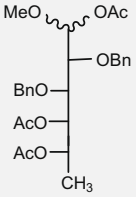
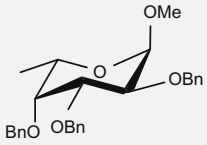
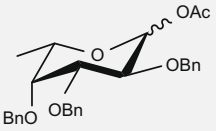
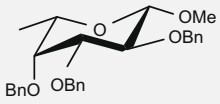
1.2. General procedure for acetolysis using TFA[6b]

Methyl glycoside (100 μmol) was dissolved in Ac_2O (1.5 mL) and treated with AcOH (1.5 mL) and TFA (150 μL). The solution was stirred at 70 °C in a round-bottomed flask closed with a glass stopper. The reaction was stopped by cooling to rt when TLC (3:1 petroleum ether–EtOAc or 7:1 pentane–EtOAc or 9:1 toluene–EtOAc) showed full or almost complete disappearance of the starting material (see Table 1). It is worth noting that a small amount (≤10%) of unreacted starting material could be still detected in some cases; nonetheless, longer reaction times were detrimental for the yield, as the products could react further by debenzylation. The mixture was then diluted with CH_2Cl_2 (25 mL) and washed successively with water (25 mL) and 1 M $NaHCO_3$ (25 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated to give a residue that was subjected to flash chromatography.

1.3. General procedure for acetolysis using $ZnCl_2$

Methyl glycoside (100 μmol) was dissolved in a 2:1 v/v Ac_2O/AcOH mixture (1.5 mL), cooled to 5 °C, and then treated with freshly fused $ZnCl_2$ (1.0 mmol). The reaction was worked up as indicated for TFA protocol.

Table 2
Acetolysis on 6-deoxyhexose methyl glycosides with 10 equiv $ZnCl_2$ in 2:1 v/v Ac_2O–AcOH at 5 °C (see Section 2 for details)

Entry[a]	Methyl glycoside	Time (h)	Products[b]
1	 **1**	21	 **11** (63%; 62%[c])  **2**[13] (22%; 25%[c])
2	 **12**	48	 **13** (48%, dr = 1.5:1)[d]  **14** (16%)
3	 **3**	46	 **15** (25%)  **16** (23%)  **17** (24%; α/β = 2.5:1)[e]
4	 **5**	19	 **4**[9] (73%, α/β = 4.5:1)[e]
5	 **6**	21	 **7** (50%, β/α = 1.7:1)[f]  **18** (42%, dr = 1.2:1)[d]
6	 **8**	24	 **9**[10] (98%, α/β = 4:1)[e]
7		24	**9**[10] (72%, α/β = 5:1)[e]

[a] Reaction conducted on 0.1 mmol scale, unless otherwise specified.
[b] Isolated yield.
[c] Yield on 1 mmol scale.
[d] Diastereoisomeric ratio measured by ^{1}H NMR.
[e] Anomeric ratio measured by ^{1}H NMR.
[f] Anomeric ratio measured by isolation of the two anomers.

1.4. 1-*O*-Acetyl-2,3,4-tri-*O*-benzyl-6-deoxy-α-L-altropyranose (7α)

$[\alpha]_D$ +4 (*c* 0.9; CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.25 (m, 15H, H-Ar), 5.99 (br s, 1H, H-1), 4.66 (d, 1H, J_{gem} = 12.1 Hz, OC*H*HPh), 4.52–4.45 (m, 5H, 5 OC*H*HPh), 4.35–4.31 (dq, 1H, $J_{5,4}$ = 9.2 Hz, $J_{5,6}$ = 6.5 Hz, H-5), 3.78–3.75 (m, 2H, H-2, H-3), 3.50 (dd, 1H, $J_{4,5}$ = 9.2 Hz, $J_{4,3}$ = 2.8 Hz, H-4), 2.02 (s, 3H, C*H*$_3$CO), 1.29 (d, 3H, $J_{6,5}$ = 6.3 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9 (CO), 138.1, 138.0, 137.6 (3C$_{ipso}$–Bn), 128.6–127.7 (C-Ar), 92.3 (C-1), 73.7, 72.7, 72.6, 72.1, 71.5, 66.1, 65.9 (C-2, C-3, C-4, C-5, 3OC*H*$_2$Ph), 21.1 (C*H*$_3$CO), 17.8 (C-6). MALDI TOF-MS: calcd for $C_{29}H_{32}O_6$ (*m/z*), 476.22; found, 499.05 $[M+Na]^+$; Anal. Calcd for $C_{29}H_{32}O_6$: C, 73.09; H, 6.77. Found: C, 73.30; H, 6.62.

1.5. 1-*O*-Acetyl-2,3,4-tri-*O*-benzyl-6-deoxy-β-L-altropyranose (7β)

$[\alpha]_D$ −4.2 (*c* 1.6; CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.22 (m, 15H, H-Ar), 6.02 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1), 4.63 (d, 1H, J_{gem} = 12.4 Hz, OC*H*HPh), 4.56 (d, 1H, J_{gem} = 12.1 Hz, OC*H*HPh), 4.50 (d, 1H, J_{gem} = 12.4 Hz, OC*H*HPh), 4.49 (d, 1H, J_{gem} = 12.1 Hz, OC*H*HPh), 4.45 (d, 1H, J_{gem} = 11.8 Hz, OC*H*HPh), 4.42 (d, 1H, J_{gem} = 11.8 Hz, OC*H*HPh), 4.09 (dq, 1H, $J_{5,4}$ = 9.0 Hz, $J_{5,6}$ = 6.3 Hz, H-5), 3.74 (dd, 1H, $J_{3,2}$ = 4.3 Hz, $J_{3,4}$ = 2.9 Hz, H-3), 3.65 (dd, 1H, $J_{2,3}$ = 4.4 Hz, $J_{2,1}$ = 1,5 Hz, H-2), 3.49 (dd, 1H, $J_{4,5}$ = 9.0 Hz, $J_{4,3}$ = 2.9 Hz, H-4), 2.10 (s, 3H, C*H*$_3$CO), 1.31 (d, 3H, $J_{6,5}$ = 6.3 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1 (CO), 138.0–137.9 (3C$_{ipso}$–Bn), 128.5–127.8 (C-Ar), 91.8 (C-1), 77.7, 74.6, 73.5, 72.9, 72.8, 72.0, 70.4 (C-2, C-3, C-4, C-5, 3OC*H*$_2$Ph), 21.1 (C*H*$_3$CO), 18.1 (C-6); MALDI TOF-MS: calcd for $C_{29}H_{32}O_6$ (*m/z*), 476.22; found, 499.06 $[M+Na]^+$; Anal. Calcd for $C_{29}H_{32}O_6$: C, 73.09; H, 6.77. Found: C, 72.95; H, 6.56.

1.6. 1,5-Di-*O*-acetyl-2,3-di-*O*-benzyl-α-L-rhamnofuranose (11)

$[\alpha]_D$ −11.8 (*c* 1.6; CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.30 (m, 10H, H-Ar), 6.29 (d, 1H, $J_{1,2}$ = 2.3 Hz, H-1), 5.27 (quintet, 1H, $J_{5,6}$ = $J_{5,4}$ = 6.0 Hz, H-5), 4.71 (d, 1H, J_{gem} = 1.6 Hz, OC*H*HPh), 4.68 (d, 1H, J_{gem} = 11.6 Hz, OC*H*HPh), 4.63 (d, 1H, J_{gem} = 11.6 Hz, OC*H*HPh), 4.50 (d, 1H, J_{gem} = 11.6 Hz, OC*H*HPh), 4.23 (m, 2H, H-3, H-4), 4.02 (dd, 1H, $J_{2,3}$ = 4.4 Hz, $J_{2,1}$ = 2.3 Hz, H-2), 2.07, 1.92 (2s, 6H, 2C*H*$_3$CO), 1.32 (d, 3H, $J_{6,5}$ = 6.4 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 169.8 (2CO), 137.7, 137.4 (2C$_{ipso}$–Bn), 128.5–127.5 (C-Ar), 99.3 (C-1), 81.7, 81.6, 76.8, 73.2, 72.6, 69.2 (C-2, C-3, C-4, C-5, 2OC*H*$_2$Ph), 21.2 (2C*H*$_3$CO), 16.1 (C-6); MALDI TOF-MS: calcd for $C_{24}H_{28}O_7$ (*m/z*), 428.18; found, 450.99 $[M+Na]^+$; Anal. Calcd for $C_{24}H_{28}O_7$: C, 67.28; H, 6.59. Found: C, 67.46; H, 6.50.

1.7. 1,4,5-Tri-*O*-acetyl-2,3-di-*O*-benzyl-6-deoxy-1-*O*-methyl-L-talose acetal (13)

^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.26 (m, 10H′ + 10H″, H-Ar), 5.98 (d, 1H′, $J_{1,2}$ = 6.8 Hz, H-1′), 5.89 (d, 1H″, $J_{1,2}$ = 4.2 Hz, H-1″), 5.31 (dq, 1H′, $J_{5,6}$ = 6.5 Hz, $J_{5,4}$ = 2.8 Hz, H-5′), 5.27 (m, 2H″, H-4″, H-5″), 5.23 (dd, 1H′, $J_{4,3}$ = 8.3 Hz, $J_{4,5}$ = 2.8 Hz, H-4′), 4.81 (d, 1H″, J_{gem} = 11.5 Hz, OC*H*HPh″), 4.74 (d, 1H′, J_{gem} = 11.9 Hz, OC*H*HPh′), 4.72 (d, 1H″, J_{gem} = 11.5 Hz, OC*H*HPh″), 4.68 (d, 1H′, J_{gem} = 11.9 Hz, OC*H*HPh′), 4.62 (d, 1H′, J_{gem} = 10.7 Hz, OC*H*HPh′), 4.55 (s, 2H″, OC*H*$_2$Ph″), 4.40 (d, 1H′, J_{gem} = 10.7 Hz, OC*H*HPh′), 3.84 (dd, 1H′, $J_{3,4}$ = 8.3 Hz, $J_{3,2}$ = 2.2 Hz, H-3′), 3.76 (m, 2H″, H-2″, H-3″), 3.73 (dd, 1H′, $J_{2,1}$ = 6.8 Hz, $J_{2,3}$ = 2.2 Hz, H-2′), 3.43 (s, 3H′ + 3H″, 2OCH_3), 2.12 (s, 3H′, CH_3CO′), 2.09 (s, 3H″, CH_3CO″), 2.07 (s, 3H″, CH_3CO″), 2.03 (s, 3H′, CH_3CO′), 1.97 (s, 3H′, CH_3CO′), 1.93 (s, 3H″, CH_3CO″), 1.16 (d, 3H′, $J_{6,5}$ = 6.5 Hz, H-6′), 1.13 (d, 3H″, $J_{6,5}$ = 6.1 Hz, H-6″); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.9 (CO′), 170.3 (CO″), 170.0 (CO′), 169.8 (2CO″), 169.7 (CO′), 137.9 (C$_{ipso}$–Bn′), 137.8 (C$_{ipso}$–Bn″), 137.3 (C$_{ipso}$–Bn′), 137.2 (C$_{ipso}$–Bn″), 128.5–127.5 (C-Ar), 98.1 (C-1″), 97.8 (C-1′), 78.7, 76.8, 74.0, 73.1, 72.8, 69.1 (C-2′, C-3′, C-4′, C-5′, 2OCH_2Ph′), 78.3, 76.6, 74.3, 73.4, 72.6, 69.2 (C-2″, C-3″, C-4″, C-5″, 2OCH_2Ph″), 57.9 (OCH_3''), 57.3 (OCH_3'), 21.1–21.0 (2CO$_C$H$_3'$, 2COCH_3''), 20.9 (COCH_3'), 20.8 (COCH_3''), 17.0 (C-6″), 16.8 (C-6′); MALDI TOF-MS: calcd for $C_{27}H_{34}O_9$ (*m/z*), 502.22; found, 525.02 $[M+Na]^+$; Anal. Calcd for $C_{27}H_{34}O_9$: C, 64.53; H, 6.82. Found: C, 64.49; H, 6.85.

1.8. 4,5-Di-*O*-acetyl-2,3-di-*O*-benzyl-6-deoxy-L-talose (14)

^1H NMR (400 MHz, $CDCl_3$): δ 9.57 (s, 1H, H-1), 7.34–7.26 (m, 10H, H-Ar), 5.33–5.29 (m, 2H, H-5, H-4), 4.73 (d, 1H, J_{gem} = 10.0 Hz, OC*H*HPh), 4.70 (d, 1H, J_{gem} = 10.0 Hz, OC*H*HPh), 4.51 (d, 1H, J_{gem} = 11.1 Hz, OC*H*HPh), 4.42 (d, 1H, J_{gem} = 11.1 Hz, OC*H*HPh), 4.05 (d, 1H, $J_{2,3}$ = 2.2 Hz, H-2), 3.97 (dd, 1H, $J_{3,4}$ = 8.2 Hz, $J_{3,2}$ = 2.2 Hz, H-3), 2.05 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 1.17 (d, 3H, $J_{6,5}$ = 6.4 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.7 (C-1), 170.9, 169.4 (2CO), 137.9, 137.3 (2C$_{ipso}$–Bn), 128.4–127.6 (C-Ar), 81.3, 78.5, 73.2, 72.6, 72.1, 68.4 (C-2, C-3, C-4, C-5, 2OCH_2Ph), 20.9, 20.7 (2COCH_3), 16.7 (C-6); MALDI TOF-MS: calcd for $C_{24}H_{28}O_7$ (*m/z*), 428.18; found, 451.00 $[M+Na]^+$; Anal. Calcd for $C_{24}H_{28}O_7$: C, 67.28; H, 6.59. Found: C, 67.46; H, 6.48.

1.9. 4,5-Di-*O*-acetyl-2,3-di-*O*-benzyl-D-quinovose (15)

$[\alpha]_D$ +10 (*c* 0.4; CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 9.73 (s, 1H, CHO), 7.36–7.23 (m, 10H, H-Ar), 5.35 (dd, 1H, $J_{4,5}$ = 6.4 Hz, $J_{4,3}$ = 3.0 Hz, H-4), 5.10 (quintet, 1H, $J_{5,4}$ = $J_{5,6}$ 6.4 Hz, H-5), 4.77 (d, 1H, J_{gem} = 12.0 Hz, OC*H*HPh), 4.57 (s, 2H, OC*H*$_2$Ph), 4.52 (d, 1H, J_{gem} = 12.0 Hz, OC*H*HPh), 3.92 (m, 2H, H-2, H-3), 2.02 (s, 3H, CH_3CO), 1.97 (s, 3H, CH_3CO), 1.19 (d, 3H, $J_{6,5}$ = 6.4 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.1 (CHO), 169.9, 169.7 (2CO), 136.9, 136.8 (2C$_{ipso}$–Bn), 128.6–128.0 (C-Ar), 80.6, 77.5, 74.1, 73.2, 72.1, 68.6 (C-2, C-3, C-4, C-5, 2OCH_2Ph), 21.2, 20.8 (2CH_3CO), 15.8 (C-6); MALDI TOF-MS: calcd for $C_{24}H_{28}O_7$ (*m/z*), 428.18; found, 451.01 $[M+Na]^+$; Anal. Calcd for $C_{24}H_{28}O_7$: C, 67.28; H, 6.59. Found: C, 67.09; H, 6.49.

1.10. 1,1,4,5-Tetra-*O*-acetyl-2,3-di-*O*-benzyl-D-quinovose acetal (16)

$[\alpha]_D$ +19 (*c* 0.5; CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.28 (m, 10H, H-Ar), 6.97 (d, 1H, $J_{1,2}$ = 3.2 Hz, H-1), 5.24 (d, 1H, $J_{4,5}$ = 5.9 Hz, $J_{4,3}$ = 3.2 Hz, H-4), 5.16 (quintet, 1H, $J_{5,4}$ = $J_{5,6}$ = 6.2 Hz, H-5), 4.78 (d, 1H, J_{gem} = 10.9 Hz, OC*H*HPh), 4.74 (d, 1H, J_{gem} = 11.6 Hz, OC*H*HPh), 4.71 (d, 1H, J_{gem} = 11.6 Hz, OC*H*HPh, 4.52 (d, 1H, J_{gem} = 10.9 Hz, OC*H*HPh), 3.81 (m, 2H, H-2, H-3), 2.09 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3CO), 2.03 (s, 3H, CH_3CO), 1.97 (s, 3H, CH_3CO), 1.21 (d, 3H, $J_{6,5}$ = 6.2 Hz, H-6); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 170.0, 168.7, 168.5 (4 CO), 137.7, 137.5 (2C$_{ipso}$–Bn), 128.6–127.8 (C-Ar), 88.1 (C-1), 78.0, 76.1, 74.7, 74.1, 73.3, 69.2 (C-2, C-3, C-4, C-5, 2OCH_2Ph), 21.1, 20.9, 20.8, 20.7 (4CH_3CO), 15.8 (C-6); MALDI TOF-MS: calcd for $C_{28}H_{34}O_{10}$ (*m/z*), 530.22, found, 552.89 $[M+Na]^+$; Anal. Calcd for $C_{28}H_{34}O_{10}$: C, 63.39; H, 6.46. Found: C, 63.11; H, 6.24.

1.11. 1,5-Di-*O*-acetyl-2,3-di-*O*-benzyl-D-quinovofuranose (17)

^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.24 (m, 10H$_\alpha$ + 10H$_\beta$, H-Ar), 6.35 (d, 1H$_\alpha$, $J_{1,2}$ = 4.2 Hz, H-1$_\alpha$), 6.16 (br s, 1H$_\beta$, H-1$_\beta$), 5.24 (dq, 1H$_\beta$, $J_{5,6}$ = 7.4 Hz, $J_{5,6}$ = 6.3 Hz, H-5$_\beta$), 5.18 (dq, 1H$_\alpha$, $J_{5,6}$ = 6.2 Hz, $J_{5,4}$ = 4.5 Hz, H-5$_\alpha$), 4.64 (m, 2H$_\alpha$ + 1H$_\beta$, 2OC*H*HPh$_\alpha$ + OC*H*HPh$_\beta$), 4.58 (d, 1H$_\alpha$, J_{gem} = 12.0 Hz, OC*H*HPh$_\alpha$), 4.55 (d, 1H$_\beta$, J_{gem} = 12.0 Hz, OC*H*HPh$_\beta$), 4.50 (d, 1H$_\alpha$, J_{gem} = 11.5 OC*H*HPh$_\alpha$), 4.48 (d, 1H$_\beta$, J_{gem} = 12.0 Hz, OC*H*HPh$_\beta$), 4.41 (d, 1H$_\beta$, J_{gem} = 12.0 Hz, OC*H*HPh$_\beta$), 4.36 (dd, 1H$_\alpha$, $J_{4,3}$ = 5.8 Hz, $J_{4,5}$ = 4.5 Hz, H-4$_\alpha$), 4.29 (dd, 1H$_\beta$, $J_{4,5}$ = 7.4 Hz, $J_{4,3}$ = 5.0 Hz, H-4$_\beta$), 4.12 (m, 2H$_\alpha$, H-2$_\alpha$, H-3$_\alpha$), 4.04 (br s, 1H$_\beta$, H-2$_\beta$), 4.03 (dd, 1H$_\beta$, $J_{3,4}$ = 5.0 Hz, $J_{3,2}$ = 1.3 Hz, H-3$_\beta$), 2.09 (s,

3H$_\alpha$, CH$_3$CO$_\alpha$), 2.04 (s, 3H$_\beta$, CH$_3$CO$_\beta$), 1.97 (s, 3H$_\alpha$, CH$_3$CO$_\alpha$), 1.91 (s, 3H$_\beta$, CH$_3$CO$_\beta$), 1.34 (d, 3H$_\beta$, $J_{6,5}$ = 6.2 Hz, H-6$_\beta$), 1.30 (d, 3H$_\alpha$, $J_{6,5}$ = 6.2 Hz, H-6$_\alpha$); ^{13}C NMR (100 MHz, CDCl$_3$): δ 170.1, 169.9 (2CO$_\alpha$), 170.1, 169.8 (2CO$_\beta$), 137.6, 137.2 (2C$_{ipso}$–Bn$_\alpha$), 137.4, 137.1 (2C$_{ipso}$–Bn$_\beta$), 128.5–127.5 (C-Ar), 100.2 (C-1$_\beta$), 94.4 (C-1$_\alpha$), 84.5, 84.2, 80.5, 72.1, 72.0, 68.6 (C-2$_\beta$, C-3$_\beta$, C-4$_\beta$, C-5$_\beta$, 2OCH$_2$Ph$_\beta$), 83.2, 80.0, 77.0, 73.3, 72.6, 69.0 (C-2$_\alpha$, C-3$_\alpha$, C-4$_\alpha$, C-5$_\alpha$, 2OCH$_2$Ph$_\alpha$), 21.2–21.1 (2CH$_3$CO$_\alpha$ + 2CH$_3$CO$_\beta$), 17.2 (C-6$_\beta$), 15.8 (C-6$_\alpha$); MALDI TOF-MS: calcd for $C_{24}H_{28}O_7$ (*m/z*), 428.18; found, 451.39 [M+Na]$^+$; Anal. Calcd for $C_{24}H_{28}O_7$: C, 67.28; H, 6.59. Found: C, 66.99; H, 6.38.

1.12. 1,4,5-Tri-*O*-acetyl-2,3-di-*O*-benzyl-1-*O*-methyl-6-deoxy-L-altrose acetal (18)

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.36–7.26 (m, 10H′ + 10H″, H-Ar), 6.00 (d, 1H′, $J_{1,2}$ = 6.3 Hz, H-1′), 5.94 (d, 1H″, $J_{1,2}$ = 4.1 Hz, H-1″), 5.47 (dd, 1H′, $J_{4,3}$ = 6.2 Hz, $J_{4,5}$ = 3.9 Hz, H-4′), 5.39 (dd, 1H″, $J_{4,3}$ = 5.3 Hz, $J_{4,5}$ = 4.0 Hz, H-4″), 5.28 (dq, 1H′, $J_{6,5}$ = 6.5 Hz, $J_{5,4}$ = 3.9 Hz, H-5′), 5.25 (dq, 1H″, $J_{6,5}$ = 6.5 Hz, $J_{5,4}$ = 4.0 Hz, H-5″), 4.74 (d, 1H′, J_{gem} = 11.5 Hz, OC*H*HPh′), 4.72 (d, 1H″, J_{gem} = 11.2 Hz, OC*H*HPh″), 4.70 (d, 1H″, J_{gem} = 11.2 Hz, OC*H*HPh″), 4.69 (d, 1H′, J_{gem} = 11.5 Hz, OC*H*HPh′), 4.67 (d, 1H″, J_{gem} = 11.2 Hz, OC*H*HPh″), 4.66 (s, 2H′, OCH_2Ph′), 4.64 (d, 1H″, J_{gem} = 11.2 Hz, OC*H*HPh″), 3.88 (dd, 1H′, $J_{3,4}$ = 6.2 Hz, $J_{3,2}$ = 3.8 Hz, H-3′), 3.80 (t, 1H″, $J_{3,2}$ = $J_{3,4}$ = 5.3 Hz, H-3″), 3.67 (dd, 1H″, $J_{2,3}$ = 5.3 Hz, $J_{2,1}$ = 4.2 Hz, H-2″), 3.63 (dd, 1H′, $J_{2,1}$ = 6.3 Hz, $J_{2,3}$ = 3.8 Hz, H-2′), 3.50 (s, 3H″, OCH$_3''$), 3.37 (s, 3H′, OC*H*$_3'$), 2.06 (s, 3H′, C*H*$_3$CO′), 2.05 (s, 3H″, C*H*$_3$CO″), 2.03 (s, 3H″, C*H*$_3$CO″), 1.99 (s, 6H′, 2C*H*$_3$CO′), 1.98 (s, 3H″, C*H*$_3$CO″), 1.26 (d, 3H′ + 3H″, $J_{6,5}$ = 6.5 Hz, H-6′, H-6″); ^{13}C NMR (100 MHz, CDCl$_3$): δ 170.8 (CO′), 170.5 (CO″), 170.1 (CO′), 170.0 (CO′), 169.8 (2CO″), 138.1 (C$_{ipso}$–Bn′), 138.0 (2C$_{ipso}$–Bn″), 137.9 (C$_{ipso}$–Bn′), 128.8–127.5 (C-Ar), 97.6 (C-1′, C-1″), 79.5, 77.3, 74.9, 73.3, 72.4, 69.5 (C-2′, C-3′, C-4′, C-5′, 2OCH$_2$Ph′), 78.9, 77.7, 74.8, 73.9, 73.0, 72.2 (C-2″, C-3″, C-4″, C-5″, 2OCH$_2$Ph″), 57.9 (OCH$_3''$), 57.2 (OCH$_3'$), 21.1–20.9 (3COCH$_3'$, 3COCH$_3''$), 15.3 (C-6″), 15.2 (C-6′); MALDI TOF-MS: calcd for $C_{27}H_{34}O_9$ (*m/z*), 502.22; found, 524.96 [M+Na]$^+$; Anal. Calcd for $C_{27}H_{34}O_9$: C, 64.53; H, 6.82. Found: C, 64.75; H, 6.80.

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