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Note

Synthesis of 3-*C*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-1-propene: a caveat☆

Christian Girard,* Marie-Laure Miramon, Tanguy de Solminihac, Jean Herscovici

Laboratoire de Chimie Bioorganique et de Biotechnologie Moléculaire et Cellulaire, UMR 7001 CNRS, Ecole Nationale Supérieure de Chimie de Paris, F-75005 Paris, France

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Abstract

During the preparation of 3-*C*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-1-propene, using a published Sakurai-type reaction on the parent methyl glycoside, some observations were made on the sensitivity to reaction conditions that were not previously reported. This Note presents the study of this allylation reaction followed by acetolysis, which ultimately led to the best conditions to obtain the *C*-glycoside, and on further transformations to yield the corresponding aldehydic and acidic derivatives.

Keywords: Silayl Lewis^x analogs; C-Glycosylic compound, synthesis; Sakurai allylation; Acetolysis

C-Glycosylic compounds, commonly referred to as *C*-glycosides, are the 1-deoxy analogues of natural products[1] and have shown high potencies in biological pathways involving sugars showing various activities.[2] For other purposes, *C*-glycosides have also been used as scaffolds to synthesize analogues of more complex sugars (oligosaccharides). As an example, *C*-glycosides of D-mannose were a key structure for the development of several sialyl Lewis^x (sLe^x) analogs with high affinity for human E-selectin.[3] During the course of our studies on interactions between sLe^x mimics and E-selectin, we needed to prepare model compounds that were already known for their activity in order to ascertain the required approaches and tests. We selected derivatives of *C*-mannose with a chemical differentiation between the C-6 position of the original sugar and its C-1 chain. The preparation of these derivatives involved a key intermediate; the 3-*C*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)propene (**4**).

The synthesis started with a classical benzylation of the commercially available methyl α-D-mannopyranoside (**1**) in moderate yield (Scheme 1).[4,5] A better procedure was the treatment of the sugar with sodium hydride (1.5 equiv per hydroxyl group), followed by benzylation with benzyl bromide (1.1 equiv per hydroxyl) in the presence of a catalytic amount of tetrabutylammonium iodide (0.1 equiv). A simplified workup procedure gave the desired methyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside (**2**) in an excellent yield (97%), even on a 20-g scale.

The following step implied the formation of the desired *C*-mannoside by a Sakurai-type general allylation reaction on the methyl glycoside **2** (Scheme 2).[6,7] Literature precedents reported that treatment of the methyl glycoside **2** with allyltrimethylsilane in acetonitrile in the presence of trimethylsilyl triflate gave access to the α-allylated *C*-mannoside **3** in 87% yield. When acetic anhydride was added before workup, an in situ

1 2

Scheme 1. Benzylation of methyl α-D-mannopyranoside (**1**).

☆ IUPAC name: 9-*O*-acetyl-4,8-anhydro-5,6,7-tri-*O*-benzyl-1,2,3-trideoxy-D-*glycero*-D-*galacto*-non-1-enitol.

* Corresponding author. Tel.: +33-1-44276722; fax: +33-1-53101292

E-mail address: cgirard@ext.jussieu.fr (C. Girard).

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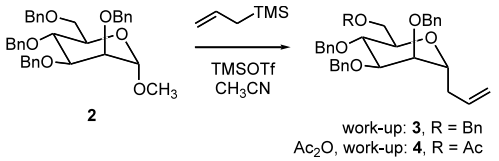


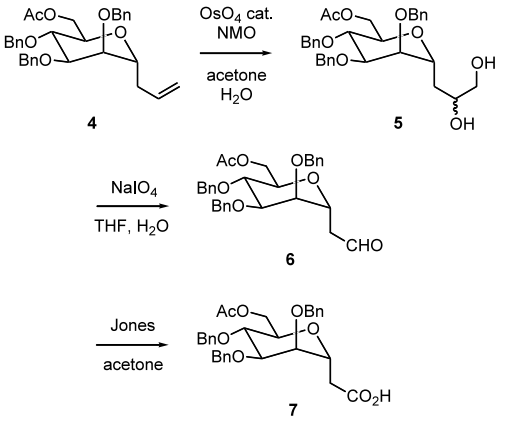
Scheme 2. Sakurai-type reaction on the methyl glycoside **2** to obtain the *C*-allyl mannosides **3** or **4**.

acetolysis took place to generate the 3-*C*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)propene (**4**) in 83% yield.[8,9]

However, in our hands this reaction was found to be quite delicate and sensitive. Our first attempt using the described procedure led to two products, having only a small R_f difference on silica gel. The two compounds were obtained in 76 and 22% isolated yields and identified as the desired 6′-*O*-acetyl derivative **4**, together with the 6′-*O*-benzyl analogue **3**.

The initial reaction conditions (Entry 1, Table 1), using 2.1 equiv of allyltrimethylsilane and 0.5 equiv of trimetylsilyl triflate at 4 °C, gave **3**:**4** in a ratio of 3.5:1, in 98% yield. Adding more allyltrimethylsilane (2.7 equiv) at room temperature dropped the ratio of **3**:**4** to 1.8:1 (88% yield). When the reactions were conducted on larger scale (Entries 3 and 4), the ratios showed the same relation as a function of temperature. In these cases, the **3**:**4** ratios were 5.3:1 and 3.3:1, for 4 °C and room temperature, respectively (76 and 82% yields, respectively).

Acetolysis, selective to primary benzyl ethers, is usually successfully conducted by acetic anhydride in conjunction with strong protic or Lewis acids,[10] or iodine,[11] or with alkylating agents like trimethylsilyl triflate.[12] This is similar to the deprotection techniques of these ethers.[13–15] Based on the fact that acetylations or acetolysis can be performed with acetic anhydride in the presence of catalytic trimethylsilyl triflate (2 mol%),[16]



Scheme 3. Three-step sequence for the transformation of the *C*-allyl mannoside **4** into the acetic acid derivative **7**.

the presence of the catalyst was thus mandatory for the reaction to occur properly. If somehow the amount of catalyst is reduced, or if it is in part decomposed, this could reduce the efficiency of the acetolysis.

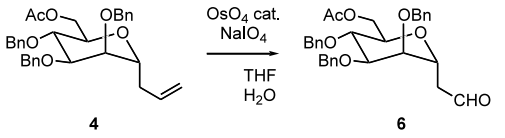
As a matter of fact, when we performed the allylation reaction at 4 °C, using twice the initial amount of trimethylsilyl triflate (Table 1, Entries 5 and 6), the desired 6′-*O*-acetyl derivative **4** was isolated as the sole product of the reaction in very good yields of 84–87% (up to a 100 mmol; 55.5-g scale).

In order to use the *C*-glycoside **4** as a scaffold for sialyl Lewis^x mimics, the C-1 allylic chain needed to be transformed to access aldehydic and acidic functionalities. For this purpose, we selected a very efficient approach that was already published.[8,9] In this article, the reactions were carried out on the 6′-*O*-hexadecyl ether analogue of **4**. This straightforward method was unfortunately quite sluggish with the 6′-*O*-acetyl derivative **4**, probably due to the nature of this acetate substituent, when compared to the ether one, and required purification at each step (Scheme 3).

Table 1
Results of the C-allylation of the methyl α-D-mannopyranoside **2** with allyltrimethylsilane in the presence of trimethylsilyl triflate, followed by acetolysis with acetic anhydride [a]

Entry	**2** (mmol)	AllylTMS (mmol (equiv))	TMSOTf (mmol (equiv))	**3** (%) [d]	**4** (%) [d]
1 [b]	1.3	2.7 (2.1)	0.6 (0.5)	22	76
2 [c]	1.8	4.8 (2.7)	0.9 (0.5)	31	57
3 [b]	10.5	29 (2.7)	5.3 (0.5)	12	64
4 [c]	18	48 (2.7)	9.1 (0.5)	19	63
5 [b]	38	80 (2.1)	42 (1.1)	0	84
6 [b]	100	271 (2.7)	122 (1.2)	0	87

[a] In CH_3CN at 0 °C: sequential dropwise addition of allyltrimethylsilane and TMSOTf, then 24 h reaction at the indicated temperature, before acetolysis (excess Ac_2O, 2 h) at 0 °C.
[b] Reaction at 4 °C.
[c] Reaction at room temperature.
[d] Isolated yields.



Scheme 4. Direct oxidation of the *C*-allyl mannoside **4** to the aldehyde **6** with osmium tetraoxide–sodium periodate.

The dihydroxylation during 16 h of **4** with a catalytic amount of osmium tetraoxide in the presence of *N*-methylmorpholine *N*-oxide gave the corresponding diol **5** (only 44% yield). The periodate oxidation of the 1,2-diol **5** to the aldehyde **6** (2 h, 98%), followed by Jones oxidation to the carboxylic acid **7** (73%), proceeded, however, more efficiently. The global yield for the three steps was only of 31%, with the limiting step being the osmium dihydroxylation procedure.

In order to improve the process, we decided to try the one-pot transformation of the alkene **4** to the corresponding aldehyde **6**. The first attempt was to use potassium permanganate on alumina, to get rid of the toxic osmium tetraoxide procedure.[17] However, the alkene **4** was found to be quite unreactive, even after prolonged reaction times. The other selected method was to use a mixture of catalytic osmium tetraoxide and excess sodium periodate, the latter being the co-oxidant for the osmium, as well as the reagent to cleave the diol to the aldehyde in situ (Scheme 4).[18]

This procedure was found to be very efficient and fast when compared to the previous two-step approach (Table 2). The alkene **4** was directly transformed in fair yields (60–70%) into the aldehyde **6** in 3–16 h depending on the scale. The 15-h reaction time on the large scale was selected to ensure a complete transformation, since the reaction mixture became quite difficult to stir because of the thick precipitate that formed.

When compared to the three-step procedure, the one-pot oxidation of the alkene **4** is much better. For a shorter (or same) time than the dihydroxylation process, the direct passage to the aldehyde **6** is possible. In terms of yields, the one-pot procedure gave 60–70% yield in aldehyde **6**, while the two steps only afforded 43%. The aldehyde **6** was finally oxidized to 2-*C*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)acetic acid (**7**) by Jones reagent (73%). The overall yield to obtain the acid (**7**) from the mannopyranosyl alkene **4**, is thus of 51% instead of 31% for the previously described three-step method.

In this Note, we present our work on the preparation of the important basic structure for sLe^x mimics: the 2-*C*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)acetic acid (**7**). For this purpose, we found the best conditions for the initial benzylation reaction of the starting material. A study of a Sakurai-type allylation reaction on our substrate, followed by acetolysis, showed that this transformation can be very sensitive. Having found the conditions that worked in our hands, we finally undertook the final transformation stages. Due to the sensitivity of our derivative, the usual three-step transformation of the alkene **4** to the acid **7** was not suitable. A one-pot oxidation using the osmium tetraoxide–sodium periodate system gave fast and convenient access to the important aldehyde **6**, which was then easily transformed in carboxylic acid **7** by Jones' reagent.

1. Experimental

General methods.—All reagents and chromatographic solvents were purchased and used without purification. *N*,*N*-Dimethylformamide (DMF) and acetonitrile were dried on CaH_2 and kept over molecular sieves under nitrogen. Acetone and tetrahydrofuran (THF) were distilled to remove stabilizants and/or impurities prior to use. Flash chromatographs were performed on SDS 60 A C.C 35–70-μm silica gel. Thin-layer chromatography (TLC) was developed on E. Merck Silica Gel 60 F_{254} coated plastic plates and visualized under UV or by spraying 5% H_2SO_4 in EtOH. Polarimetric measurements ($[\alpha]_D$) were recorded at 20 °C in distilled dichloromethane on a JASCO P-1010 polarimeter at 589 nm (sodium lamp). Infrared spectroscopy (FTIR) was performed on a single-beam Nicolet 205 Fourier-transform spectrophotometer as films on NaCl, and absorptions are reported in cm^{-1}.

Table 2
Direct oxidation of the alkene **4** to the aldehyde **6** using the osmium tetraoxide–sodium periodate system [a]

Entry	**4** (mmol (g))	OsO_4 (mmol (equiv))	$NaIO_4$ (mmol (equiv))	Time (h)	**6** (%) [b]
1	4.2 (2.2)	0.042 (0.01)	21.2 (5)	3	70
2	8.9 (4.6)	0.09 (0.01)	44.5 (5)	6	57
3	6.7 (3.5)	0.07 (0.01)	34 (5)	15	57
4	29 (15)	0.29 (0.01)	143 (5)	16	62
5	30.5 (16)	0.31 (0.01)	152 (5)	15	57

[a] In 1:1 THF–water.
[b] Isolated yields.

Nuclear magnetic resonance (NMR) was recorded on a Brucker Avance DRX 300 spectrometer in $CDCl_3$ with Me_4Si (0.1%) as the internal standard. It was completed by correlation (COSY, HETCOR) and differential (DEPT) spectroscopy and chemical shift differentiation of *C*-glycosides.[7b,7c]Chemical shifts (δ) are reported in parts per million (ppm) relative to TMS (0 ppm) and coupling constants (J) in hertz. Mass spectrometry (Finnigan SSQ 7000, chemical ionization, NH_3) and microanalyses were done by Aventis Pharma Analytical Services (Vitry-sur-Seine, France).

Preparation of methyl 2,3,4,6-tetra-O-*benzyl*-α-D-*mannopyranoside* (**2**).—Methyl α-D-mannopyranoside (**1**, 20 g, 103 mmol) was added portionwise over 30 min to a suspension of washed (hexanes, three times) NaH (41.2 g of a 60% in mineral oil; 24.7 g NaH, 618 mmol, 6 equiv) in DMF (750 mL) at 0 °C under nitrogen. The mixture was stirred at rt for 2 h. TBAI (3.8 g, 10.3 mmol, 0.1 mol%) was added to the thick mixture, followed by dropwise addition of BnBr (79.3 g, ~55 mL, 464 mmol, 4.5 equiv) over 45 min. The reaction was stirred for 18 h, after which the mixture was limpid. The volatiles were then evaporated in vacuo to dryness. The isolated solid was triturated with Et_2O (3×250 mL). The combined organic extracts were washed with water (250 mL) and brine (250 mL) before being dried ($MgSO_4$) and evaporated under vacuum. The benzylated sugar **2** was isolated as an oil (55.4 g, 97%): $[\alpha]_D$ $+23.4 \pm 0.6°$ (*c* 1, CH_2Cl_2), lit.[10a] $+28.0°$ (*c* 1, $CHCl_3$), lit.[5] $+29.2°$ (*c* 1.59, $CHCl_3$); R_f 0.26 (4:1 heptane–AcOEt); IR (film, NaCl): ν 3068, 3032 (νCH-Ar), 2909 (νCH-alkyl), 1603, 1600 (νC=C Ar), 1496, 1455, 1358 (δCH-alkyl) and 1086 (νC–O–C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.29 (m, 20 H, H-Ar), 4.93 (d, 1 H, J_{gem} 10.8 Hz, CH_2Ph), 4.83 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.68 (m, 6 H, CH_2Ph), 4.55 (d, 1 H, J_{gem} 10.8 Hz, CH_2Ph), 4.03 (pt, 1 H, $J_{3,4/4,5}$ 9.0 Hz, H-4), 3.93 (dd, 1 H, $J_{2,3}$ 3.0, $J_{3,4}$ 9.0 Hz, H-3), 3.84 (dd, 1 H, $J_{1,2}$ 1.9, $J_{2,3}$ 2.8 Hz, H-2), 3.79 (m, 3 H, H-5,6) and 3.37 (s, 3 H, CH_3O-1) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.6 (C^{IV}-Ar), 128.4 (C-Ar), 127.7 (C-Ar), 99.1 (C-1), 80.3 (C-3), 75.1 (C-4, CH_2Ph), 74.8 (C-2), 73.5 (CH_2Ph), 72.7 (CH_2Ph), 72.2 (CH_2Ph), 71.8 (C-5), 69.5 (C-6) and 54.8 (CH_3O-1) ppm; CIMS: m/z 572 ($[M + NH_4]^+$). Anal. Calcd for $C_{35}H_{38}O_6$: C, 75.79; H, 6.91. Found: C, 75.77; H, 7.14.

9-O-*Acetyl*-*4,8*-*anhydro*-*5,6,7*-*tri*-O-*benzyl*-*1,2,3*-*trideoxy*-D-glycero-D-galacto-*non*-*1*-*enitol* (*3*-C-(*6*-O-*acetyl*-*2,3,4*-*tri*-O-*benzyl*-α-D-*mannopyranosyl*)*propene*, **4**).—To solution of sugar **2** (55.5 g, 100 mmol) in acetonitrile (200 mL) at 0 °C under nitrogen, allyltrimethylsilane (30.8 g, ~42.9 mL, 270 mmol, 2.7 equiv) was added, followed after 15 min by dropwise addition of TMSOTf (27 g, ~22 mL, 121 mmol, 1.2 equiv) over 30 min. The reaction was stirred at the same temperature for 24 h. The resulting orange mixture was kept at 0 °C, and excess Ac_2O (145 mL, ~1.5 mol) was carefully added dropwise (exothermic reaction!), followed by 2 h stirring. The mixture was then poured into CH_2Cl_2 (1 L) and stirred vigorously with satd aq $NaHCO_3$ (1.5 L) for 1 h (important CO_2 evolution!). The phases were separated, and the organic layer was washed with water (500 mL) and brine (500 mL), and then it was dried ($MgSO_4$) and evaporated under reduced pressure. The red–brown oily residue was purified by flash chromatography on silica gel (4:1 heptane–AcOEt) to afford the *C*-glycoside **4** as an oil (42.4 g, 87%): $[\alpha]_D$ $+3.9 \pm 0.2°$ (*c* 1, CH_2Cl_2); R_f 0.30 (4:1 heptane–AcOEt); IR (film, NaCl): ν 3063, 3027 (νCH-Ar), 2909 (νCH-alkyl), 1737 (νC=O ester), 1605 (νC=C alkene), 1603, 1600 (νC=C Ar), 1496, 1454, 1368 (δCH-alkyl), 1235 (νC–O ester) and 1091 (νC–O–C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.34 (m, 15 H, H-Ar), 5.74 (m, 1 H, H-2), 5.04 (m, 2 H, H-1_{cis},1_{trans}), 4.77 (d, 1 H, J_{gem} 11.4 Hz, CH_2Ph), 4.59 (m, 5 H, CH_2Ph), 4.41 (dd, 1 H, $J_{5',6'a}$ 5.9, $J_{6'a,6'b}$ 11.7 Hz, H-6′a), 4.26 (dd, 1 H, $J_{5',6'b}$ 2.6, $J_{6'a,6'b}$ 11.7 Hz, H-6′b), 4.10 (dt, 1 H, $J_{1',2'/1',3a}$ 1.8, $J_{1',3b}$ 6.3 Hz, H-1′), 3.80 (ls, 3 H, H-3′,4′,5′), 3.65 (dd, 1 H, $J_{1',2'}$ 2.2, $J_{2',3'}$ 4.4 Hz, H-2′), 2.33 (m, 2 H, H-3a,3b) and 2.07 (s, 3 H, OCOCH_3-6′) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.9 (OC=OCH_3-6′), 138.2 (C^{IV}-Ar), 134.1 (C-2), 128.5 (C-Ar), 128.0 (C-Ar), 117.3 (C-1), 77.1 (C-3′), 75.3 (C-2′), 75.0 (C-4′), 74.0 (CH_2Ph), 72.4 (C-1′,5′, CH_2Ph), 71.7 (CH_2Ph), 63.3 (C-6′), 34.5 (C-3) and 20.9 (OCOCH_3-6′) ppm; CIMS: m/z 534 ($[M + NH_4]^+$). Anal. Calcd for $C_{32}H_{36}O_6$: C, 74.39; H, 7.02. Found: C, 74.05; H, 7.55.

If the reaction was conducted with less TMSOTf, two products could be detected by TLC in 7:4 heptane–AcOEt that were identified as the 6-*O*-acetyl derivative **4** (R_f 0.40) and the 6-*O*-benzyl **3** one (R_f 0.55).

4,8-*Anhydro*-*5,6,7*-*tri*-O-*benzyl*-*1,2,3*-*trideoxy*-D-glycero-D-galacto-*non*-*1*-*enitol* (*3*-C-(*2,3,4,6*-*tetra*-O-*benzyl*-α-D-*mannopyranosyl*)-*1*-*propene*, **3**).—$[\alpha]_D$ $+5.2 \pm 0.5°$ (*c* 1, CH_2Cl_2), $+5.35 \pm 0.06°$ (*c* 7.2, CH_2Cl_2), lit.[6] $-3.0°$ (*c* 7, $CHCl_3$); R_f 0.30 (4:1 heptane–AcOEt); IR (film, NaCl): ν 3063, 3029 (νCH-Ar), 2907 (νCH-alkyl), 1641 (νC=C alkene), 1604, 1586 (νC=C Ar), 1496, 1454, 1362 (δCH-alkyl) and 1095 (νC–O–C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.33 (m, 20 H, H-Ar), 5.78 (m, 1 H, H-2), 5.04 (m, 2 H, H-1_{cis},1_{trans}), 4.74 (d, 1 H, J_{gem} 11.4 Hz, CH_2Ph), 4.58 (m, 7 H, CH_2Ph), 4.08 (m, 1 H, H-1′), 3.82 (m, 4 H, H-3′,4′,5′,6′a), 3.74 (dd, 1 H, $J_{5',6'b}$ 3.1, $J_{6'a,6'b}$ 10.1 Hz, H-6′b), 3.65 (dd, 1 H, $J_{1',2'}$ 3.1, $J_{2',3'}$ 4.6 Hz, H-2′) and 2.36 (m, 2 H, H-3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.5 (C^{IV}-Ar), 134.5 (C-2), 128.4 (C-Ar), 128.1 (C-Ar), 127.8 (C-Ar), 117.3 (C-1), 77.0 (C-3′), 75.3 (C-2′), 75.1 (C-4′), 73.9 (C-5′, CH_2Ph), 73.4 (CH_2Ph), 72.4 (C-1′), 72.2 (CH_2Ph), 71.7 (CH_2Ph), 69.3 (C-6′) and 34.8 (C-3) ppm; CIMS m/z 582 ($[M + NH_4]^+$). Anal. Calcd for $C_{37}H_{40}O_5$: C, 78.69; H, 7.14. Found: C, 78.43; H, 7.58.

8-O-*Acetyl-3,7-anhydro-4,5,6-tri*-O-*benzyl-2-deoxy*-D-glycero-D-galacto-*octose (2*-C-*(6*-O-*acetyl-2,3,4-tri*-O-*benzyl-α*-D-*mannopyranosyl)acetaldehyde*, **6**).—According to Xie et al.,[18] the 6-*O*-acetyl alkene derivative **4** (15 g, 29 mmol) in 1:1 THF–water (550 mL) was treated with $NaIO_4$ (30.5 g, 143 mmol, 5 equiv) and OsO_4 (2.5% wt. solution in *t*-BuOH, 3.6 mL, ~74 mg OsO_4, 0.29 mmol) at rt, in a flask equipped with a rubber septum. The mixture was left stirring overnight (16 h) in order to insure a complete tranformation. The mixture was then diluted with water to solubilize the thick, white precipitate and extracted with CH_2Cl_2 (3 × 350 mL). The combined organic extracts were washed with brine (350 mL), dried ($MgSO_4$) and evaporated in vacuo. The crude oil was purified by flash chromatography on silica (4:1 to 3:1 heptane–AcOEt) to give the aldehyde **6** as an oil (9.3 g, 62%): $[\alpha]_D$ +37.2 ± 0.4° (*c* 1, CH_2Cl_2); R_f 0.23 (7:4 heptane–AcOEt); IR (film, NaCl): *ν* 3066, 3027 (*ν*CH-Ar), 2907 (*ν*CH-alkyl), 2868, 2736 (*ν*CH-aldehyde), 1731 (*ν*C=O ester/aldehyde), 1603, 1600 (*ν*C=C Ar), 1496, 1455, 1363 (*δ*CH-alkyl), 1230 (*ν*C–O ester) and 1091 (*ν*C–O–C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 9.70 (ls, 1 H, H-1), 7.34 (m, 15 H, H-Ar), 4.68 (dd, 1 H, $J_{5',6'a}$ 8.2, $J_{6'a,6'b}$ 11.5 Hz, H-6′a), 4.58 (m, 1 H, H-1′), 4.49 (m, 6 H, CH_2Ph), 4.07 (dd, 1 H, $J_{5',6'b}$ 3.8, $J_{6'a,6'b}$ 11.5 Hz, H-6′b), 3.98 (m, 1 H, H-5′), 3.80 (dd, 1 H, *J* 3.0, *J* 4.7 Hz, H-3′), 3.61 (m, 2 H, H-2′,4′), 2.71 (ddd, 1 H, $J_{1,2a}$ 1.6, $J_{1',2a}$ 5.7, $J_{2a,2b}$ 16.2, H-2a), 2.55 (ddd, 1 H, $J_{1,2b}$ 2.9, $J_{1',2b}$ 8.4, $J_{2a,2b}$ 16.4, H-2b) and 2.06 (s, 3 H, OCOCH_3-6′) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 200.7 (C-1), 170.9 (O*C*=*O*CH_3-6′), 137.8 (C^{IV}-Ar), 128.6 (C-Ar), 128.1 (C-Ar), 75.9 (C-2′), 74.7 (C-4′), 73.6 (C-3′,5′), 73.0 (CH_2Ph), 72.6 (CH_2Ph), 71.6 (CH_2Ph), 65.8 (C-1′), 62.0 (C-6′), 45.6 (C-2) and 20.9 (OCOCH_3-6′) ppm; CIMS: *m*/*z* 536 ($[M + NH_4]^+$). Anal. Calcd for $C_{31}H_{34}O_7$: C, 71.80; H, 6.61. Found: C, 71.59; H, 6.36.

8-O-*Acetyl-3,7-anhydro-4,5,6-tri*-O-*benzyl-2-deoxy*-D-glycero-D-galacto-*octonic acid (2*-C-*(6*-O-*acetyl-2,3,4-tri*-O-*benzyl-α*-D-*mannopyranosyl)acetic acid*, **7**).—Based on Ref. 8, the aldehyde **6** (23.8 g, 46 mmol) and Celite (22 g) were added to acetone (200 mL). The suspension was cooled to 0 °C, and Jones' reagent (22 mL)[19] was then added dropwise to the reaction mixture at a rate similar to a titration (the red color of Jones faded quickly on contact of the aldehyde solution). At the end of the addition, the mixture stayed red (with greenish colored Celite) due to excess of reagent, and was stirred at 0 °C for 2 h. Isopropyl alcohol (25 mL) was added to quench the excess of oxidant, the mixture was filtered through a pad of Celite, and the solids were washed with acetone (2 × 75 mL). The filtrate was the poured into AcOEt (1 L) and stirred vigorously with 1 N HCl (1 L) for 15 min. The phases were separated, and the organic extract was washed with brine (250 mL), dried ($MgSO_4$) and evaporated under vacuum. The resulting oil was flash chromatographed on silica (1:3:0.01 heptane–AcOEt–AcOH) to afford the acid **7** as a colorless oil (18.0 g, 73%): $[\alpha]_D$ +18.8 ± 0.4° (*c* 1, CH_2Cl_2); R_f 0.20 (7:4 heptane–AcOEt); IR (film, NaCl): *ν* 3043 (large, *ν*CO_2H) 3086, 3064, 3027 (*ν*CH-Ar), 2925, 2868 (*ν*CH-alkyl), 1736 (*ν*C=O ester), 1714 (*ν*C=O acid), 1496, 1450, 1373 (*δ*CH-alkyl), 1240 (*ν*C–O ester) and 1112 (*ν*C–O–C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 7.30 (m, 15 H, H-Ar), 4.52 (m, 8 H, H-1′,6′a,CH_2Ph), 4.18 (dd, 1 H, $J_{5',6'b}$ 3.7, $J_{6'a,6'b}$ 11.9 Hz, H-6′b), 4.00 (m, 1 H, H-5′), 3.80 (dd, 1 H, *J* 2.9, *J* 5.3 Hz, H-3′), 3.65 (m, 2 H, H-2′,4′), 2.76 (dd, 1 H, $J_{1',2a}$ 4.6, $J_{2a,2b}$ 15.8, H-2a), 2.55 (dd, 1 H, $J_{1',2b}$ 8.5, $J_{2a,2b}$ 15.7, H-2b) and 2.04 (s, 3 H, OCOCH_3-6′) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): *δ* 175.3 (C-1), 170.4 (O*C*=*O*CH_3-6′), 137.8 (C^{IV}-Ar), 128.6 (C-Ar), 128.0 (C-Ar), 75.5 (C-2′), 74.7 (C-4′), 74.4 (C-5′), 73.6 (C-3′), 72.9 (CH_2Ph), 71.6 (CH_2Ph), 67.6 (C-1′), 62.2 (C-6′), 36.4 (C-2) and 20.6 (OCOCH_3-6′) ppm; CIMS: *m*/*z* 552 ($[M + NH_4]^+$). Anal. Calcd for $C_{31}H_{34}O_8$: C, 69.65; H, 6.41. Found: C, 69.35; H, 6.00.

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