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A general route to 4-*C*-branched sugars. Synthesis of methyl α-caryophylloside

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Abstract

The total synthesis of methyl 3,6-dideoxy-4-*C*-(D-*altro*-1,3,4,5 tetrahydroxyhexyl)-α-D-*xylo*-hexopyranoside, the methyl glycoside of the recently isolated 4-*C*-branched sugar caryophyllose, has been completed in a stereoselective and convergent manner. The synthesis of this dodecose relies on the diiodosamarium mediated coupling of two six-carbon fragments: a cyclic ketone and an acid chloride.

Keywords: 4-*C*-Branched monosaccharide; Diiodosamarium; Deoxy sugar

1. Introduction

Caryophyllose is a 4-*C*-branched sugar which was isolated in 1995 from the cell wall of a strain of *Pseudomonas caryophylli*, the causal agent of the bacterial wilt of carnation.[1] The complete structure of this dodecose has been elucidated early after[2] as 3,6,10-trideoxy-4-*C*-(D-*glycero*-1-hydroxyethyl)-D-*erythro*-D-*gulo*-decose (**1**) (Scheme 1) and it was later shown to occur in the cell wall as an homopolysaccharidic chain with (1→7)-α and -β linkages.[3,4] This compound belongs to the class of 4-*C*-branched sugars where are also found yersinioses A and B (Scheme 1) isolated from two different species of *Yersinia*,[5–7] and tridecose **3** found in an antigenic polysaccharide of *Mycobacterium gastri*.[8,9] In the course of our work on the full structural characterization of **3**, we have developed a synthetic approach to this class of products[10] which relies on the diiodosamarium-mediated coupling of a cyclic ketone **6** (Scheme 2) with an acid chloride, precursor of the side chain of the sugar. Following our preliminary communication on the implementation of this strategy for the first synthesis of methyl caryophylloside and yersiniosides,[11] we now describe our results for the preparation of methyl α-D-caryophylloside **2**.[†]

2. Results and discussion

The preparation of the coupling partners was straightforward as they could be easily made from commercially available materials. Cyclic ketone **6** was obtained in only four steps and 40% overall yield from methyl α-D-glucopyranoside via known methyl 3,6-dideoxy-α-D-*ribo*-hexopyranoside **4**.[13,14] Selective monosilylation of **4** with *tert*-butylchlorodimethylsilane (*t*-BDMSCl) and imidazole in DMF at −17 °C gave the C-4 alcohol **5** in 73% yield together with 19% of the bis-(silylated) product. Oxidation of **5** with pyri-

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[†] A second synthesis of caryophyllose has been published.[12]

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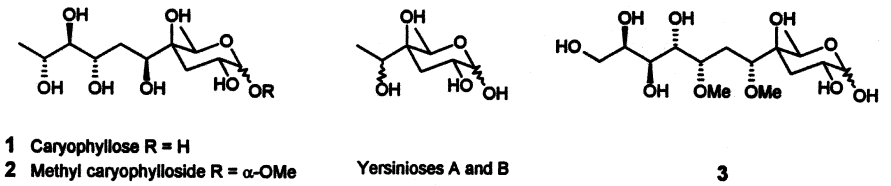
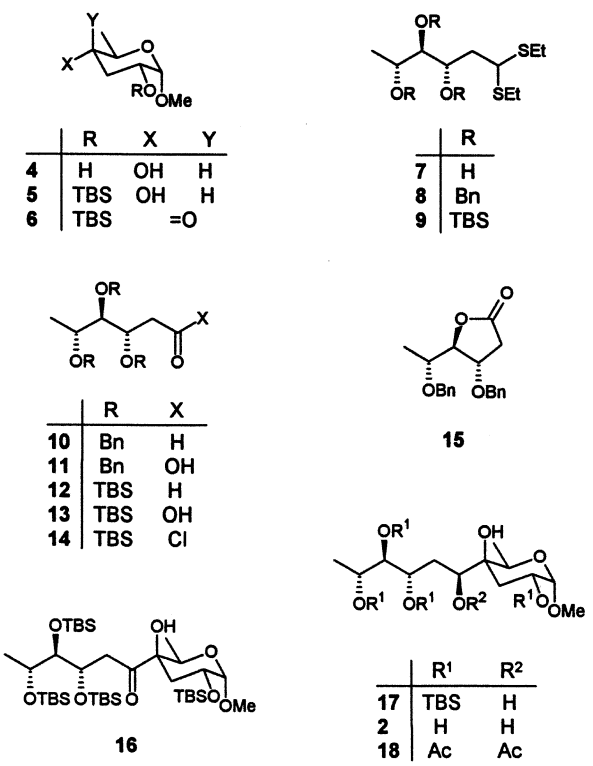


Scheme 1.

dinium chlorochromate in buffered dichloromethane[15] gave then ketone **6** in high yield (92%).

The six-carbon carboxylic acid, precursor of the caryophyllose side-chain was derived from commercially available 2,6-dideoxy-D-*ribo*-hexose (D-digitoxose) which is also easily prepared from methyl α-D-glucopyranoside.[16] Thus, treatment of 2,6-dideoxy-D-*ribo*-hexose with an excess of ethanethiol and concentrated hydrochloric acid[17] for 3 h at 0 °C gave the diethyl dithioacetal **7** in 81% yield. Perbenzylation with an excess of benzyl bromide and sodium hydride in DMF, followed by dithioacetal hydrolysis with mercuric oxide and mercuric chloride in aqueous acetone[18] gave the aldehyde **10** (69%). Finally, the carboxylic acid **11** was obtained in 92% yield from oxidation of **10** with Jones reagent[19].



Scheme 2.

However, all attempts to transform the acid **11** to the acid chloride were plagued by intramolecular nucleophilic attack of the C-4 oxygen atom and formation of considerable amounts of the 5-membered lactone **15**, arising from the nucleophilic attack of the C-4 oxygen atom on the activated carboxylic group. Such reactions are well documented in the literature.[20,21] In order to decrease the nucleophilicity of the C-4 oxygen atom, we introduced the more bulky *tert*-butyldimethylsilyl ether groups as protection for the hydroxyl functions of the acid side chain. Thus, dithioacetal **7** was treated with an excess of *tert*-butyldimethylsilyltriflate (TBDMSOTf) and pyridine in CH_2Cl_2 to give the trisilylated dithioacetal **9** in 90% yield. Unmasking of the aldehyde group was effected as above with $HgCl_2$ and HgO in aqueous acetone and **12** was obtained in excellent yield (93%). As the presence of acid-sensitive TBDMS ether groups in **12** precluded the use of Jones reagent for the conversion of **12** to acid **13**, this oxidation was carried out with buffered potassium permanganate in *tert*-butanol[22] affording the acid **13** in 83% yield. In this case, formation of the acid chloride **14** from **13** with oxalyl chloride and pyridine in tetrahydropyran (THP), and diiodosamarium-promoted coupling[23] of the crude acid chloride **14** (1.3 equiv) with ketone **6** (1 equiv) in THP proceeded smoothly. Expected products were isolated in 63% yield and in a 8:1 diastereoisomeric ratio.[10,11,24] Reduction of the major diastereomer **16** in chelating conditions[25] with sodium borohydride in methanol at 0 °C was very slow but the 1′*S* alcohol **17** was eventually obtained in 73% yield after 24 h at room temperature. Compared to our previous results on related compounds,[10,11] a slight decrease of the diastereoselectivity of the reduction was observed (1′*S*/1′*R*: 5:1) and this could be related

to the higher reaction temperature. Determination of the absolute configuration of the new C-1′ stereocenter was made according to the procedure used for the synthesis of **3**[10] and the result was fully consistent with reported examples by us and others.[12] Removal of all protecting groups was achieved in one step with dilute hydrochloric acid in aqueous THF and methyl α-D-caryophylloside **2** was isolated in 77% yield. Comparison with the natural product[1] and full characterization were done on the pentaacetylated derivative **18** obtained in 82% yield after acetylation with acetic anhydride in pyridine.

3. Conclusion

The diiodosamarium mediated coupling of an acid chloride and a ketone proved to be highly valuable for the short (only seven steps along the longest linear route) and convergent synthesis of the branched sugar caryophyllose. This methodology should find general use for the synthesis of other α-hydroxylated *C*-branched sugars.[26]

4. Experimental

General methods.—All reactions were performed under Ar in anhyd purified solvents. NMR spectra were recorded on Bruker DPX 250 or AMX 250 (operating at 250 MHz for ^{1}H and at 62.9 MHz for ^{13}C) spectrometers, chemical shifts are expressed in ppm, from Me_4Si for ^{1}H and ^{13}C spectra. Optical rotations were recorded at 20 °C on a Perkin–Elmer 241 polarimeter. IR spectra were recorded on a Perkin–Elmer 1600 series FTIR spectrometer. Mass spectra were obtained at the University of Orléans (France) with a Ribermag R10–10 spectrometer, products were chemically ionized with NH_3 (CI/NH_3). Elemental analysis were carried out at the Service Central de Microanalyse du CNRS at Vernaison or at the Laboratoire de Chimie de Coordination du CNRS at Toulouse (France).

Methyl 2-O-tert-*butyldimethylsilyl-3,6-dideoxy*-α-D-ribo-*hexopyranoside* (**5**).—A solution of methyl 3,6-dideoxy-α-D-*ribo*-hexopyranoside (1.09 g, 6.7 mmol) and imidazole (0.91 g, 13.4 mmol) in DMF (10 mL) was treated at −17 °C with *tert*-butylchlorodimethylsilane (1.01 g, 6.7 mmol). After 40 min, a further portion of *t*-BDMSCl (335 mg, 2.2 mmol) was added and the mixture was left for 1 h at −17 °C before quenching with a 5% $NaHCO_3$ solution. CH_2Cl_2 extraction and chromatography (3:1 petroleum ether–EtOAc) gave **5** as a colorless oil (1.37 g, 73%). $[\alpha]_D^{20}$ +80° (*c* 1.00, $CHCl_3$); IR (liquid film): ν 3441 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.48 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 3.78 (ddd, 1 H, $J_{2,3ax}$ 11.5, $J_{2,3eq}$ 5.0 Hz, H-2), 3.53 (dq, 1 H, $J_{5,4}$ 9.0, $J_{5,6}$ 6.0 Hz, H-5), 3.42 (s, 3 H, OCH_3), 3.28 (m, 1 H, $J_{4,3ax}$ 11.5, $J_{4,OH}$ 6.5, $J_{4,3eq}$ 4.5 Hz, H-4), 2.03 (ddd, 1 H, $J_{3eq,3ax}$ 11.5 Hz, H-3eq), 1.82 (m, 1 H, H-3ax), 1.47 (d, 1 H, OH), 1.25 (d, 3 H, H-6), 0.89 (s, 9 H, $C(CH_3)_3$), 0.08 (s, 6 H, $Si(CH_3)_2$); ^{13}C NMR ($CDCl_3$): δ 99.16 (C-1), 71.14 (C-4), 68.76 (C-5), 68.39 (C-2), 55.10 (OCH_3), 36.70 (C-3), 25.80 ($C(CH_3)_3$), 18.23 ($C(CH_3)_3$), 17.38 (C-6), −4.69 and −4.72 ($Si(CH_3)_2$); CIMS (NH_3): *m*/*z* 277 $[M+H]^+$. Anal. Calcd for $C_{13}H_{28}O_4Si$: C, 56.48; H, 10.21. Found: C, 56.14; H, 10.22.

Methyl 2-O-tert-*butyldimethylsilyl-3,6-dideoxy*-α-D-erythro-*hexopyranosid*-*4*-*ulose* (**6**).—A suspension of pyridinium chlorochromate (5.30 g, 24.6 mmol), NaOAc (2.02 g, 24.6 mmol) and 3 Å molecular sieves in CH_2Cl_2 (60 mL) was stirred for 30 min at rt before addition of a solution of **5** (1.94 g, 7.02 mmol) in CH_2Cl_2 (5 mL). After 30 min at rt, Et_2O was added, the mixture was filtered on Celite and the filtrate evaporated. Chromatography (7:1 heptane–EtOAc) gave ketone **6** as a colorless oil (1.78 g, 92%). $[\alpha]_D^{20}$ +98° (*c* 1.20, $CHCl_3$); IR (liquid film): ν 1728 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 4.70 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.14 (q, 1 H, $J_{5,6}$ 6.5 Hz, H-5), 4.11 (ddd, 1 H, $J_{2,3ax}$ 10.5, $J_{2,3eq}$ 5.5 Hz, H-2), 3.53 (s, 3 H, OCH_3), 2.75 (dd, 1 H, $J_{3ax,3eq}$ 15.5 Hz, H-3ax), 2.60 (dd, 1 H, H-3eq), 1.27 (d, 3 H, H-6), 0.89 (s, 9 H, $C(CH_3)_3$), 0.09 and 0.08 (2s, 2 × 3 H, $Si(CH_3)_2$); ^{13}C NMR ($CDCl_3$): δ 206.34 (C-4), 99.03 (C-1), 69.74 (C-5), 69.01 (C-2), 55.73 (OCH_3), 43.70 (C-3), 25.58 ($C(CH_3)_3$), 17.99 ($C(CH_3)_3$), 14.33 (C-6), −4.92 and −4.95 ($Si(CH_3)_2$); CIMS (NH_3):

Table 1
^{1}H NMR chemical shifts (δ), apparent multiplicities and coupling constants in Hz for compounds **7**, **9**, **10**, **12** and **13**

H	**7**	**9**	**10**	**12**	**13**
1	4.07 dd $J_{1,2a}$ 8.0 $J_{1,2b}$ 6.5	3.91 dd $J_{1,2a}$ 11.5 $J_{1,2b}$ 3.2	9.67 dd $J_{1,2a}$ 2.5 $J_{1,2b}$ 2.0	9.85 dd $J_{1,2a}$ 3.5 $J_{1,2b}$ 2.0	
2a	2.25 ddd $J_{2a,2b}$ 14.5 $J_{2a,3}$ 2.5	1.82 ddd $J_{2a,2b}$ 15.0 $J_{2a,3}$ 2.0	2.74 ddd $J_{2a,2b}$ 17.0 $J_{2a,3}$ 7.0	2.65 ddd $J_{2a,2b}$ 16.5 $J_{2a,3}$ 6.0	2.66–2.47 2.66–2.47 2.66–2.47
2b	2.04 ddd $J_{2b,3}$ 9.5	2.11 ddd $J_{2b,3}$ 9.5	2.54 ddd $J_{2b,3}$ 4.5	2.49 ddd $J_{2b,3}$ 4.5	2.66–2.47
3	4.01 ddd $J_{3,4}$ 6.5	4.15 m	4.21 ddd $J_{3,4}$ 4.0	4.40 m $J_{3,4}$ 3.0	4.35 m
4	3.45 dd $J_{4,5}$ 6.0	3.47 dd $J_{4,3}$ 1.5 $J_{4,5}$ 6.0	3.69 dd $J_{4,5}$ 6.0	3.55 dd $J_{4,5}$ 6.0	3.53 dd $J_{4,3}$ 3.0 $J_{4,5}$ 6.0
5	3.96 m	3.69 m	3.61 m	3.69 m	3.70 m
6	1.27 d $J_{6,5}$ 6.0	1.13 d $J_{6,5}$ 6.0	1.25 d $J_{6,5}$ 6.0	1.15 d $J_{6,5}$ 6.0	1.14 d $J_{6,5}$ 6.0
Other Signals	$2\times SCH_2$ 2.74, 2.62 $2\times SCH_2CH_3$ 1.26, 1.27 $3\times t$-BuSi 0.91–0.90 $6\times$ MeSi 0.14–0.08	$2\times SCH_2$ 2.76–2.49 $2\times SCH_2CH_3$ 1.25, 1.24	Ar 7.40–7.20 $6\times PhCH_2O$ 4.80–4.40	$3\times t$-BuSi 0.89 $6\times$ MeSi 0.14–0.05	$3\times t$-BuSi 0.90–0.87 $6\times$ MeSi 0.15–0.06

m/*z* 292 $[M + NH_4]^+$. No satisfactory analytical data could be obtained for this product.

2,6-Dideoxy-D-ribo-*hexose diethyl dithioacetal* (**7**).—2,6-Dideoxy-D-*ribo*-hexose (297 mg, 2.00 mmol) was suspended in ethanethiol (0.8 mL) at 0 °C. Concd HCl (0.35 mL of a 36% aq solution) was added and the reaction mixture was left at 0 °C for 3 h before neutralization with solid K_2CO_3 (340 mg, 2.46 mmol) and dilution with MeOH. The mixture was filtered, the precipitate washed twice with MeOH and the filtrate evaporated. The residue was taken up in CH_2Cl_2, the cloudy suspension was filtered, and the filtrate evaporated. Chromatography (10:1 CH_2Cl_2–MeOH) gave a clear oil (414 mg, 81%). $[\alpha]_D^{20}$ −24° (c 1.00, $CHCl_3$); ^{1}H NMR data see Table 1; ^{13}C NMR ($CDCl_3$): δ 76.89 (C-4); 71.94 (C-3); 69.20 (C-5); 48.41 (C-1); 38.61 (C-2); 24.27 and 23.89 (SCH_2CH_3); 18.65 (C-6); 14.35 (SCH_2CH_3). Anal. Calcd for $C_{10}H_{22}O_3S_2$: C, 47.21; H, 8.71. Found: C, 47.48; H, 8.74.

3,4,5 - Tri - O - tert - *butyldimethylsilyl* - *2,6-dideoxy*-D-ribo-*hexose diethyl dithioacetal* (**9**).—Compound **7** (100 mg, 0.39 mmol) was dissolved in CH_2Cl_2 (5 mL) and pyridine (0.48 mL) and treated at 0 °C with TMSOTf (0.41 mL, 1.75 mmol). After 24 h at rt, the mixture was hydrolyzed and extracted with CH_2Cl_2. Chromatography (10:1 petroleum ether–toluene) gave the product as a clear oil (211 mg, 90%). $[\alpha]_D^{20}$ −22° (c 1.14, $CHCl_3$); ^{1}H NMR data see Table 1; ^{13}C NMR ($CDCl_3$): δ 82.15 (C-4), 71.59 (C-3), 69.72 (C-5), 47.85 (C-1), 39.39 (C-2), 26.10, 26.05 ($C(CH_3)_3$), 24.28, 23.83 (SCH_2CH_3), 20.71 (C-6), 18.38, 18.13, 18.03 ($C(CH_3)_3$), 14.73, 14.17 (SCH_2CH_3), −3.50, −3.67, −4.15, −4.19, −4.66 (2) (CH_3Si). Anal. Calcd for $C_{28}H_{64}O_3S_2Si_3$: C, 56.31; H, 10.80. Found: C, 56.56; H, 10.91.

3,4,5 - Tri - O - *benzyl* - *2,6 - dideoxy* - D - ribo-*hexose* (**10**).—Compound **7** (414 mg, 1.63 mmol) was dissolved in DMF (12 mL) and treated at 0 °C with BnBr (1.16 mL, 9.8 mmol) and NaH (0.59 g of a 60% dispersion in mineral oil, 14.7 mmol, washed twice with petroleum ether). The reaction was left for 2 h at rt before treatment with MeOH. Dichloromethane extraction and chromatography (8:1 heptane–EtOAc) gave **8** as a clear oil (508 mg, 59%) $[\alpha]_D^{20}$ −12° (*c* 1.20, $CHCl_3$). This product was taken up in acetone (16 mL) and water (1.6 mL) and treated at rt with

$HgCl_2$ (575 mg, 1.21 mmol) and HgO (251 mg, 1.16 mmol). After 40 min, the reaction mixture was filtered on Celite and the filtrate evaporated. The residue was taken up in CH_2Cl_2 and washed with NH_4Cl solution. Chromatography (4:1 petroleum ether–EtOAc) gave **10** as a clear oil (281 mg, 69%). $[\alpha]_D^{20}$ −19° (*c* 1.00, $CHCl_3$); IR (liquid film): *v* 1723 cm^{-1}; ^1H NMR ($CDCl_3$) see Table 1; ^{13}C NMR ($CDCl_3$): δ 201.31 (C-1), 138.25, 138.21, 137.86, 128.39, 128.32, 128.09, 127.91, 127.83, 127.78, 127.66 (Ar), 81.96 (C-4), 75.01 (C-3), 74.48 (C-5), 73.95, 71.71, 70.73 (OCH_2Ph), 44.62 (C-2), 15.64 (C-6); Anal. Calcd for $C_{27}H_{30}O_4$: C, 77.48; H, 7.22. Found: C, 77.30; H, 6.86.

3,4,5-Tri-O-tert-butyldimethylsilyl-2,6-dideoxy-D-ribo-*hexose* (**12**).—A solution of **9** (240 mg, 0.40 mmol) in acetone (7 mL) containing water (0.7 mL) was treated at rt with $HgCl_2$ (416 mg, 1.53 mmol) and HgO (105 mg, 0.48 mmol). After 3 h, the reaction mixture was treated as described above for the preparation of **10**. Chromatography (2:1 petroleum ether–toluene) gave the product as a clear oil (184 mg, 93%). $[\alpha]_D^{20}$ −6.5° (*c* 0.84, $CHCl_3$); IR (liquid film): *v* 1731 cm^{-1}; ^1H NMR data see Table 1; ^{13}C NMR ($CDCl_3$): δ 202.76 (C-1), 81.68 (C-4), 69.81 (C-3), 69.33 (C-5), 46.32 (C-2), 26.13, 26.09, 25.88 ($C(CH_3)_3$), 20.12 (C-6); 18.37, 18.09, 17.99 ($C(CH_3)_3$), −3.82, −4.22, −4.25, −4.49, −4.63, −4.72 (CH_3Si). Anal. Calcd for $C_{24}H_{54}O_4Si_3$: C, 58.71; H, 11.08. Found: C, 58.90; H, 10.94.

3,4,5-Tri-O-tert-butyldimethylsilyl-2,6-dideoxy-D-ribo-*hexuronic acid* (**13**).—Compound **12** (184 mg, 0.37 mmol) was dissolved in *t*-BuOH (3 mL), aq NaH_2PO_4 (1.7 mL of a 5% solution) was added and the mixture was treated at rt with $KMnO_4$ (1 mL of a 1 M solution, 1.0 mmol). After 2 h at rt, the reaction was quenched with satd $Na_2S_2O_3$ solution and diluted with CH_2Cl_2. Redissolution of the brown precipitate was effected by dropwise addition of a 3 M HCl solution before extraction with CH_2Cl_2. Chromatography (20:1 petroleum ether–EtOAc) gave **13** as a clear oil (158 mg, 83%). $[\alpha]_D^{20}$ −15.7° (*c* 1.59, $CHCl_3$); ^1H NMR data see Table 1; ^{13}C NMR ($CDCl_3$): δ 178.55 (C-1), 81.46 (C-4), 70.45 (C-3), 69.74 (C-5), 37.84 (C-2), 26.09, 25.92(2) ($C(CH_3)_3$), 20.13 (C-6), 18.34, 18.03, 17.99 ($C(CH_3)_3$), −4.06, −4.34, −4.40, −4.53, −4.67, −4.94 (CH_3Si). Anal. Calcd for $C_{24}H_{54}O_5Si_3$: C, 56.86; H, 10.74. Found: C, 57.27; H, 10.41.

*Methyl 2-O-tert-butyldimethylsilyl-3,6-dideoxy-4-C-(*D-ribo-*3,4,5-tri-O-tert-butyldimethylsilyl-3,4,5 trihydroxy-1-oxo-hexyl)*-D-xylo-*hexopyranoside* (**16**).—Compound **13** (143 mg, 0.28 mmol) was dissolved in THP (3 mL) and treated for 30 min at 0 °C with pyridine (0.1 mL) and $(COCl_2)_2$ (0.032 mL, 0.31 mmol). After warming to rt, the mixture was quickly filtered on oven-dried Celite, the filtrate was evaporated and dried under high vacuum for 30 min. The crude acid chloride **14** was then dissolved in THP (0.5 mL) and used immediately.

A suspension of diiodosamarium in THP was prepared from samarium powder (234 mg, 1.55 mmol) and 1,2-diiodoethane (292 mg, 1.04 mmol) in THP (6 mL). To this dark blue suspension, under Ar, were added at rt neat ketone **6** (59 mg, 0.22 mmol) and immediately after, the freshly prepared solution of acid chloride **14** in THP. After 10 min, the dark blue mixture was vigorously stirred under a stream of dry air until complete oxidation of the diiodosamarium occurred (greenish color) and then quenched with 5% NH_4Cl solution. The greenish yellow solid was filtrated on Celite and washed thoroughly with CH_2Cl_2. Work-up and chromatography (12:1 petroleum ether–EtOAc) gave **16** (105.3 mg, 63%, 8:1 mixture of diastereoisomers). Compound **16** was obtained in pure form after chromatography with 20:1 petroleum ether–EtOAc. $[\alpha]_D^{20}$ −3° (*c* 0.72, $CHCl_3$); ^1H NMR data see Table 2; ^{13}C NMR ($CDCl_3$): δ 209.18 (C-1′), 99.88 (C-1), 81.84 (C-4′), 81.11 (C-4), 69.99 (C-3′), 69.13 (C-5′), 66.09 (C-2), 64.74 (C-5), 55.48 (OCH_3), 39.98 (C-2′), 35.88 (C-3), 26.08, 26.06, 25.92, 25.76 ($C(CH_3)_3$), 20.67 (C-6′), 18.34, 18.13, 17.99 (2) ($C(CH_3)_3$), 14.09 (C-6), −3.83, −3.86, −4.46, −4.54, −4.58, −4.69 (2), −4.78 (CH_3Si). Anal. Calcd for $C_{37}H_{80}O_8Si_4$: C, 58.06; H, 10.54. Found: C, 57.80; H, 10.56.

Methyl 2-O-tert-*butyldimethylsilyl-3,6-dideoxy-4*-C-*(*D-altro-*3,4,5-tri*-O-tert-*butyldimethylsilyl-1,3,4,5-tetrahydroxyhexyl)*-D-xylo-*hexopyranoside* (**17**).—Compound **16** (38.1 mg, 0.05 mmol) was treated at rt with an excess of $NaBH_4$ in MeOH (2 mL) for 24 h. Work-up and chromatography (10:1 petroleum ether–EtOAc) gave starting compound **16** (4.0 mg, 10%), the 1′*R* isomer of **17** (6.0 mg, 15%) and **17** (27.8 mg, 73%). $[\alpha]_D^{20}$ +11.8° (*c* 2.27, $CHCl_3$); ^1H NMR data see Table 2; ^{13}C NMR ($CDCl_3$): δ 99.49 (C-1), 81.66 (C-4′), 74.55 (C-4), 71.74, 71.46 (C-1′, C-3′), 69.42 (C-5′), 67.05 (C-2), 65.82 (C-5), 55.22 (O*C*H_3), 33.94 (C-2′), 33.11 (C-3), 26.18, 26.00, 25.97, 25.87 (C(*C*H_3)$_3$), 19.71 (C-6′), 18.39, 18.28, 18.05 (*C*(CH$_3$)$_3$), 13.85 (C-6), −4.06, −4.16, −4.28 (2), −4.47, −4.58, −4.61, −4.67 (*C*H_3Si). Anal. Calcd for $C_{37}H_{82}O_8Si_4$: C, 57.91; H, 10.77. Found: C, 57.98; H, 11.11.

Methyl 2-O-*acetyl-3,6-dideoxy-4*-C-*(*D-altro-*1,3,4,5-tetra*-O-*acetyl-1,3,4,5 tetrahydroxyhexyl)*-D-xylo-*hexopyranoside* (**18**).—Compound **17** (26 mg, 0.034 mmol) was dissolved in MeOH (1 mL) and treated with HCl (50 μL of a 6 M aq solution) for 3 h at rt. The reaction mixture was neutralized with a basic resin, filtrated and the filtrate evaporated. Chromatography (6:1 CH_2Cl_2–

Table 2
^1H NMR chemical shifts (δ), apparent multiplicities and coupling constants in Hz for compounds **16**, **17**, **2** and **18**

H	**16** [a]	**17** [a]	**2** [b]	**18** [c]
1	4.59 d	4.52 d	4.68 d	4.93 d
	$J_{1,2}$ 3.5	$J_{1,2}$ 3.5	$J_{1,2}$ 3.5	$J_{1,2}$ 3.5
2	4.13 ddd	4.04 ddd	4.05 m	5.15 ddd
	$J_{2,3a}$ 11.5	$J_{2,3a}$ 11.5	$J_{2,3a}$ 12.0	$J_{2,3a}$ 12.5
	$J_{2,3e}$ 4.5	$J_{2,3e}$ 4.5	$J_{2,3e}$ 5.0	$J_{2,3e}$ 5.0
3eq	1.50 dd	1.58 dd	1.89–1.74	2.05 dd
	$J_{3e,3a}$ 12.0	$J_{3e,3a}$ 12.0		$J_{3e,3a}$ 12.0
3ax	2.39 m	1.98 m	2.03 m	2.39 m
			$J_{3a,3e}$ 12.0	
5	4.18 q	4.09 q	4.24 q	4.00 q
	$J_{5,6}$ 6.5	$J_{5,6}$ 6.5	$J_{5,6}$ 6.5	$J_{5,6}$ 6.5
6	0.92 d	1.16 d	1.24 d	1.34 d
1′		3.70 m	3.82 dd	5.35 dd
	$J_{1',2'a}$ 1.5	$J_{1',2'a}$ 7.0	$J_{1',2'a}$ 11.0	
	$J_{1',OH}$ 3.0	$J_{1',2'b}$ 5.0	$J_{1',2'b}$ 2.5	
	$J_{1',2'b}$ 10.5			
2′a	3.12 dd	1.90 ddd	1.89–1.74	2.09 ddd
	$J_{2'a,2'b}$ 17.5	$J_{2'a,2'b}$ 14.5	1.89–1.74	$J_{2'a,2'b}$ 14.5
	$J_{2'a,3'}$ 8.5	$J_{2'a,3'}$ 6.5	1.89–1.74	$J_{2'a,3'}$ 2.5
2′b	2.38 dd	1.56 m	1.89–1.74	2.48 ddd
	$J_{2'b,3}$ 2.5	$J_{2'b,3}$ 4.0		$J_{2'b,3}$ 11.5
3′	4.58 m	4.05 m	3.89 m	5.37 ddd
	$J_{3',4'}$ 2.0	$J_{3',4'}$ 3.5		$J_{3',4'}$ 3.5
4′	3.48 dd	3.61 dd	3.49 dd	5.53 dd
	$J_{4',5'}$ 6.0	$J_{4',5'}$ 6.0	$J_{4',5'}$ 6.0	$J_{4',5'}$ 6.0
5′	3.60 m	3.85 m	3.94 m	5.28 m
	$J_{5',6'}$ 6.0	$J_{5',6'}$ 6.0	$J_{5',6'}$ 6.0	$J_{5',6'}$ 6.0
6′	1.15 d	1.13 d	1.31 d	1.19d
Other signals	OH s 4.02	OH (C-1′) d 2.88	OMe s 3.49	OMe s 3.05
	OMe s 3.46	OH (C-4) s 2.10		OAc 5s 1.88
	4 × *t*-BuSi 0.94,	OMe s 3.40		1.75, 1.74,
	0.90, 0.87, 0.83	4 × *t*-BuSi 0.90, 0.89		1.72, 1.70
	8 × MeSi 0.19–0.03	8 × MeSi 0.16–0.07		

[a] In $CDCl_3$.
[b] In CD_3OD.
[c] In C_6D_6.

MeOH) gave methyl α-D-caryophylloside **2** (8.1 mg, 77%). $[\alpha]_D^{20}$ + 56° (*c* 0.81, MeOH); ^{1}H NMR data see Table 2; ^{13}C NMR (CD_3OD): δ 100.55 (C-1), 79.67 (C-4′), 75.93 (C-4), 71.64 (C-1′), 70.47 (C-3′), 69.62 (C-5′), 67.99 (C-5), 66.50 (C-2), 55.81 (OCH_3), 34.14 (C-3), 32.72 (C-2′), 18.91 (C-6′), 13.75 (C-6). **2** (8.1 mg, 0.026 mmol) was dissolved in pyridine (1 mL) and acetylated with Ac_2O (0.5 mL) at 80 °C for 30 min to give pentaacetate **18** (11.2 mg, 82%) after chromatography (1:1 petroleum ether–EtOAc). $[\alpha]_D^{20}$ + 49° (*c* 0.88, $CHCl_3$); ^{1}H NMR data see Table 2; ^{13}C NMR ($CDCl_3$): δ 170.43, 170.39, 170.07, 169.93 (*C*O), 96.21 (C-1), 74.15 (C-4), 73.59, 70.03, 68.23, 67.70, 67.51, 66.06 (C-5), 55.38 (OCH_3), 29.63 (C-2′), 27.44 (C-3), 21.08, 21.03, 20.89, 20.85, 20.79 (CH_3CO), 16.26 (C-6′), 13.31 (C-6). Anal. Calcd for $C_{23}H_{36}O_{13}$: C, 53.07; H, 6.97. Found: C, 53.31; H, 6.87.

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