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Synthesis of Enantiomerically Pure C_2-Branched-2-Deoxy-Heptitols

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Abstract: *2,3; 4,5-Di-O-isopropylidene-al-L-(+)-arabinose* **1a** *reacts with di-l-menthylmalonate to give the hepturonates* **2a** *and* **3a** *in a manno-gluco 7.8.2.2 ratio. The C-2 branched 2-Deoxy-2-hydroxy-methyl-L-manno-heptitol* **6** *and 2-Deoxy-2-hydroxy-methyl-L-gluco-heptitol* **7** *were obtained by submitting* **2a** *and* **3a** *to routine procedures When the same reaction was performed with di-d-menthylmalonate a 3.5:6.5 mixture of* **2b** *and* **3b** *was obtained. A 8.2:1.8 anti-diastereoselectivity was also observed by reacting 2,3;4,5-O-tetraacetyl-al-D-(-)-arabinose* **1b** *with di-d-menthylmalonate. The absolute stereochemistry of the major hepturonate* **10** *obtained in this reaction was secured by a single crystal X-ray analysis.*

INTRODUCTION

The branched chain sugars have been extensively studied after their discovery as the glycosidic components of important antibiotics.[1] A useful approach for syntesize this class of compounds utilizes the addition of various branching reagents to a suitable carbonyl derivative of a sugar.[2]

In a preliminary communication[3] it was reported a simple stereoselective synthesis of optically active C_2-branched pentitols starting from 2,3-*O*-isopropylidene-D-(+)-glyceraldehyde and di-*d*- and *l*-menthyl malonate with different diastereoselectivity according to the matched and mismatched situations between both the asymmetric reagents.[4] These results prompted us to extend the method to common sugars, en route to homochiral higer rare monosaccarides synthesis.

Here is outlined a concise entry to C_2-branched-2-deoxy heptitols by using the addition of optically active malonates to protected L- or D-arabinose.

RESULTS AND DISCUSSION

***Synthesis of 2-Deoxy-2-hydroxymethyl-L-manno-heptitol* 6 *and 2-Deoxy-2-hydroxymethyl-gluco-heptitol* 7.** Compounds **6** and **7** were synthesized starting from di-*l*-menthyl malonate and 2,3;4,5-di-*O*-isopropylidene-*al*-L-(+)-arabinose **1a**[5] via the reaction steps depicted in Chart 1. Treatment of **1a** with di-*l*-menthyl malonate anion in THF in the presence of TMS-Cl resulted in a

stereoselective three carbon homologation affording *l*-menthyl(2-deoxy-2-carboxy-*l*-menthyl)-4,5; 6,7-di-*O*-isopropylidene-L-*manno*-hepturonate **2a** and the corresponding *l*-menthyl-L-*gluco*- diester **3a** (75%) in a 7.8 : 2.2 diastereomeric ratio. Compounds **2a** and **3a**, readily obtained in pure state by flash chromatography, were converted to the title dendro heptitols **6** and **7** and to the corresponding heptaacetates **8** and **9**, by routine procedures of reduction to **4** and **5**, deacetonation and acetylation (54% overall yield).

The above procedure performed with **1a** and di-*d*-menthyl malonate afforded the hepturonates **2b** and **3b** (76%) in near 3.5 : 6.5 ratio, which were converted to di-*O*-isopropylidene branched-heptitols **4** and **5** after chromatographic separation.

Moreover, the same protocol was applied to 2,3; 4,5-*O*-tetraacetyl-*al*-D-(-)-arabinose **1b**[6] and di-*d*-menthyl malonate obtaining the *d*-menthyl-(2-deoxy-2-carboxy-*d*-menthyl)-3-*O*-trimethylsilyl-4,5; 6,7-tetra-*O*-acetyl-D-*manno*-hepturonate **10** and *gluco*-diester **11** (64%) in 82:18 ratio. The major stereoisomer **10**, after chromatographic purification, was converted to the branched D-*manno*-heptaacetate **8'** (72% overall yield), as depicted in Chart 2. Also in this case, (even with a lower yield), the stereochemical course of the reaction is in conformity with the Felkin -Ahn rule[7] and in accordance with the prevalent anti-addition to the α-*O*-substituted aldehyde.[8]

It is noteworthy from these results that the cyclic or acyclic *O*-protection of the arabinose seems not to be relevant for the diastereoselectivity which appear rather to depend on the 'matched and mismatched cases' which happen between both the substrates used and the di-*d*- and *l*-menthyl malonate, in terms of double asymmetric induction.[4] In order to evaluate the true role played by the menthyl for the diastereoselectivity, the substrate **1a** was treated, with the same procedure, with diethyl malonate, selected as achiral reagent model. Surprisingly, in this case a complex mixture of products arising from a Knoevenagel-type condensation was obtained.

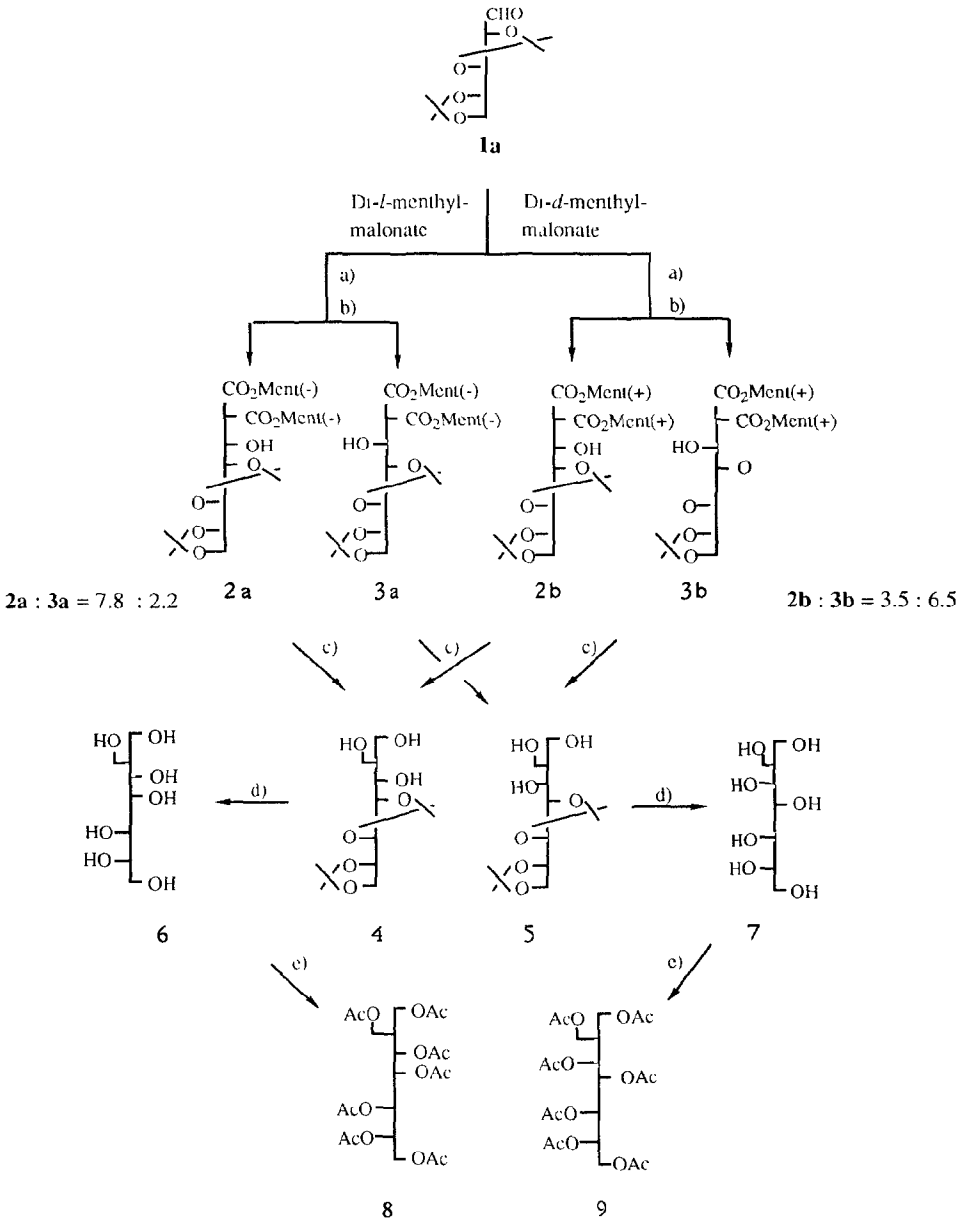
Assignment of the stereochemistry to the *gluco* and *manno* series of compounds, tentatively followed from its ^{1}H NMR spectra, was fully authenticated by an X-ray crystallographic study performed on the hepturonate **10** and its conversion to heptaacetate **8'**, whose enantiomeric relation with **8** was confirmed by the spectral data identical to those reported for the latter compound.

Description of the crystal structure of hepturonate 10. From Figure 1, which shows an ORTEP drawing of the molecule, it appears that the configurations at the chiral centres are as expected from the chiralities of the starting products and the stereochemical course of the reaction. The Newman projections of Figure 2 show the configurations and conformations about the bonds of the arabinose chain, giving the values of the torsion angles about them.

The particularly high values of U_{eq}'s and $r_{max.}/r_{min.}$ratios (anisotropy ratios) of some carbonyl oxygens and methyl carbons (see Table 1 and Figure 1) are indicative of dynamic or static disorder making the values of the distances and angles involving these atoms (Table 2) not accurate. Nevertheless the averaged values for the different kinds of bond distances and angles are satisfactory when compared with the corresponding values from the literature[9] given in square brackets: Si-C(sp^3) 1.854(5) [1857(18)], C=O 1.9043) [1.214(19)], O-C(sp^2) 1.331(6) [1.308(19)], O-C(sp^3) 1.457(7) [1.450(14)], C(sp^2)-C(sp^3) 1.512(6) [1.507(15)], C(sp^3)-C(sp^3) 1.519(2) [1530(15)] Å.

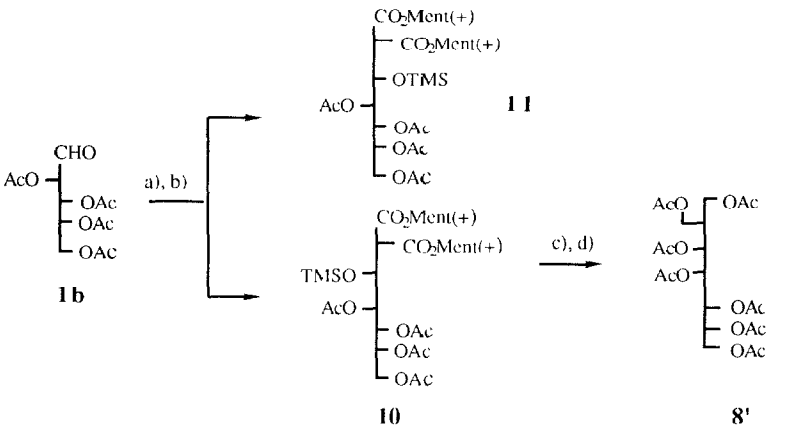
The planes of the acetoxy groups show a tendency of being perpendicular to the arabinose backbone, the dihedral angles they form with the plane through the C3-C4-C5-C6-C7 chain (which is practically planar

Chart 1



a): LDA, Dimenthylmalonate, TMSCl (2 mol equiv., to malonate) in THF, -80°C, 1 h;
b): Arabinose **1a** (2 mol equiv., to malonate), -80°C, 3 h (81.5%);
c): $LiAlH_4$ (5 mol equiv, to **2** and **3**), in Et_2O, rfx, 2 h (75%); d): CF_3COOH/H_2O 2:1 v/v, 24 h (83.4%); e): Ac_2O, Py, DMAP, 12 h (64% and 67%).

Chart 2



a): LDA, Di-*d*-menthylmalonate, TMSCl (2 mol equiv., to malonate) in THF, -80° C, 1h;
b): Arabinose **1b** (2 mol equiv., to malonate), -80°C, 3h (64%);
c): $LiAlH_4$ (5 mol equiv. to **10**) in Et_2O, rfx, 2 h; d): Ac_2O, Py, DMAP, r. t., 12 h.

with displacements less than 0.03 Å) being: 85.2(1)° for O41,C41,O42, 76.5(1) for O61,C61,O62,C62, 73.0(2)° for O71,C71,C72.

The two *d*-menthyl substituents show no significant differences in their structure and conformation (see Table 2). The cyclohexane rings in them have a chair conformation with total puckering amplitudes[10]: Q_T=0.574(3) Å for C11,.. C16 ring and Q_T=0.560(3) Å for C21, ...C26 ring (Δ/σ=1.94). Their orientation with respect to the O-C(O)-C plane is determined by intramolecular steric hindrance; the dihedral angles between the mean plane through the cyclohexane ring and the O-C(O)-C plane are: 107.4(1)° for C11,...C16 system, and 99.5(1)° for C21,...C26; that between the C2,C1,O1,O13 and C2,C8,O2,O23 planes is 79.9(1)°, i.e. there is a tendency for these planes to be mutually perpendicular.

The orientation of the trimethylsiloxy substituent is determined by intramolecular steric hindrance, the conformation about the C3-O3 bond being defined by the C2-C3-O3-Si = -132.2(2)° torsion angle and that about the Si-O3 bond is approximately eclipsed: C3-O3-Si-C32 = 10.6(3)°.

The molecules are packed in the crystal by van der Waals interactions.

CONCLUSIONS

Chiral C-branched derivatives of sugars are valuable synthetic intermediates for the synthesis of complex glycosidic structures. The simple preparation of C_2-branched-2-deoxy-*manno*- and *gluco*-heptitols **6** and **7** here reported show the advantage that the starting materials are readily obtainable in optically pure form from the "chiral pool". Although not excellent,[4] the stereoselectivity of this double asymmetric synthesis is still useful, considering the easy purification of the major diester obtained. Moreover it is noteworthy that the method provides the C_2-branched sugar derivatives **4** and **5** in which the C-3 and C-4 functionalities are suitably differentiated for their use as intermediates in other synthetic purposes. Extension of this chemistry to the synthesis of parent and homologous polyols in enantiomerically pure form will be reported in due course.

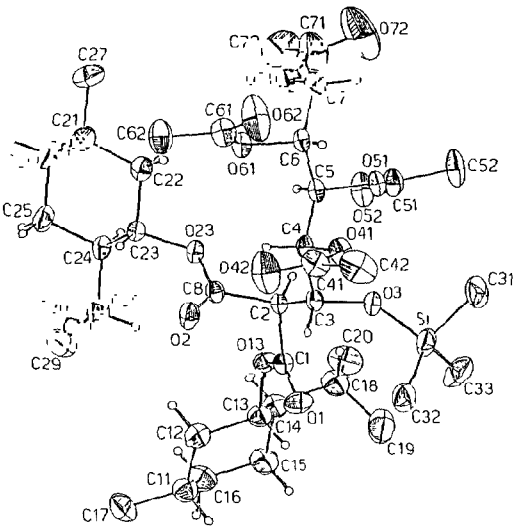


Figure 1. ORTEP drawing of the hepturonate **10** molecule. The methyl hydrogens have been omitted for clarity. Ellipsoid 50%.

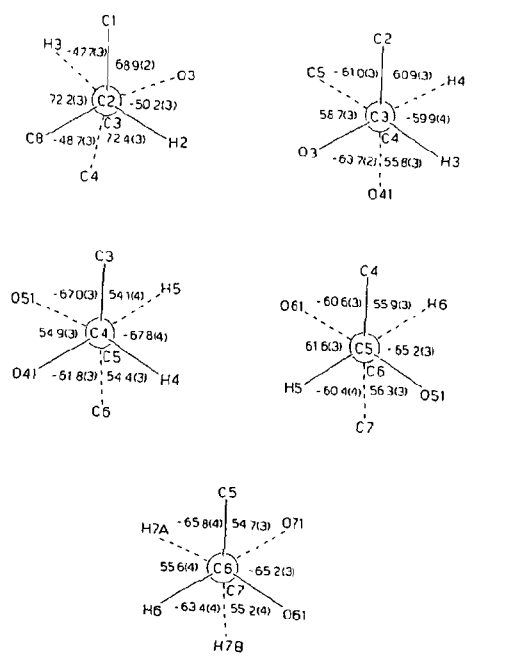


Figure 2. Newman projections about bonds of the molecular backbone.

Table 1. Fractional atomic co-ordinates ($\times 10^4$), equivalent isotropic displacement parameters ($A^2 \times 10^4$) (one third trace of the diagonalized matrix), and ratios between max. and min. principal axes of the displacement ellipsoids for **10**. E.s.d.'s in parentheses

Atom	X/a	Y/b	Z/c	Ueq	Rmax/Rmin
S1	2022.5(3)	3997.5(6)	5683.0(7)	894(3)	2.74
O1	586.7(8)	4210.8(14)	6663.4(15)	916(9)	2.47
O13	-64.3(7)	3302.0(11)	5973.6(13)	685(7)	1.88
O2	-126.0(7)	5559.0(13)	4920.1(16)	847(8)	2.66
O23	-367.1(6)	4436.5(10)	3883.3(13)	599(6)	1.99
O3	1454.2(6)	4030.7(12)	4962.2(13)	663(6)	2.24
O41	1672.8(7)	5654.2(11)	3886.5(15)	741(7)	2.54
O42	1239(1)	6967(2)	4092(3)	1449(15)	4.15
O51	1604.1(6)	4033.2(11)	2833.1(13)	626(6)	2.29
O52	1037.3(8)	2825.9(12)	3029.3(19)	970(9)	3.19
O61	693.3(6)	5799.3(11)	1918.1(14)	686(6)	1.90
O62	1236(1)	6903(2)	1379(3)	1640(17)	6.49
O71	709.5(8)	4090.7(14)	936.8(15)	873(8)	1.48
O72	1220(2)	3056(3)	235(4)	2696(30)	6.79
C1	347(1)	3925(2)	5947(2)	596(9)	1.28
C2	450.0(8)	4225.3(15)	4876.3(18)	519(8)	1.60
C3	1032.6(9)	4704.6(16)	4808.2(20)	569(9)	1.80
C4	1125.4(9)	5192.6(16)	3822.3(21)	588(9)	2.08
C5	1121.3(9)	4634.6(16)	2873.2(20)	561(9)	2.23
C6	1179(1)	5198(2)	1932(2)	617(9)	1.80
C7	1204(1)	4671(2)	990(2)	784(12)	1.43
C8	-47(1)	4828(2)	4570(2)	561(9)	1.61
C11	-1085(1)	3242(2)	8178(2)	882(13)	1.41
C12	-795(1)	3517(2)	7211(2)	812(12)	1.52
C13	-269(1)	2997(2)	6961(2)	698(10)	1.82
C14	-402(1)	1999(2)	6876(2)	776(11)	1.84
C15	-685(2)	1696(2)	7858(3)	988(14)	2.24
C16	-1216(2)	2243(2)	8097(3)	1009(15)	1.96
C17	-1629(1)	3791(3)	8389(3)	1190(16)	2.09
C18	108(2)	1415(2)	6555(3)	985(14)	2.41
C19	578(2)	1373(3)	7346(3)	1421(21)	2.15
C20	-79(2)	485(2)	6230(3)	1391(20)	2.61
C21	-1242(1)	5311(3)	1743(2)	964(15)	1.95
C22	-754(1)	4889(2)	2329(2)	785(12)	1.44
C23	-851(1)	4931(2)	3434(2)	605(9)	1.76
C24	-1407(1)	4489(2)	3754(2)	675(10)	1.92
C25	-1900(1)	4904(2)	3160(3)	926(14)	2.78
C26	-1800(1)	4863(3)	2050(3)	1091(17)	2.83
C27	-1144(2)	5282(4)	627(3)	1662(25)	3.66
C28	-1507(1)	4487(2)	4877(3)	874(13)	2.31
C29	-1640(2)	5415(3)	5315(3)	1257(18)	2.03
C30	-1976(1)	3815(3)	5162(3)	1196(16)	2.91
C31	2660(1)	4020(3)	4851(3)	1386(19)	5.08
C32	2032(1)	4952(2)	6576(3)	1217(17)	3.29
C33	1989(2)	2903(3)	6327(3)	1470(21)	3.32
C41	1669(2)	6548(2)	4017(3)	908(14)	3.03
C42	2266(2)	6915(2)	4088(3)	1320(18)	4.87
CS1	1499(1)	3146(2)	2896(3)	768(12)	2.25
C52	2046(1)	2616(2)	2738(3)	1152(16)	4.64
C61	783(2)	6643(2)	1610(3)	888(13)	2.43
C62	239(1)	7174(2)	1603(3)	1171(17)	3.21
C71	763(2)	3321(3)	497(4)	1440(23)	3.37
C72	225(2)	2797(3)	465(4)	1673(26)	3.50

Table 2. Bond distances (Å) and angles (°) of hepturonate **10**. E s d 's in parentheses.

Si-03	1.642(2)			C4 -041-C41	118.1(2)	C5-051-C51	117 6(2)
Si-C31	1.859(3)	Si-C32	1.856(4)	C6 -061-C61	117 5(2)	C7-071-C71	118 3(3)
Si-C33	1.843(4)			01-Cl-013	124.4(3)	02-C8-023	125 8(3)
Ol-Cl	1.190(3)	02-C8	1.197(3)	013-Cl -C2	110.1(2)	023-C8-C2	111 1(2)
013-C1	1.334(3)	023-C8	1 321(3)	01 -Cl -C2	125.5(2)	02 -C8-C2	123 1(2)
013-C13	1.477(3)	023-C23	1.476(3)	Cl -C2 -C8	107.8(2)	Cl -C2-C3	109 4(2)
03-C3	1.420(3)			C3 -C2 -C8	112.7(2)		
042-C41	1 186(5)	052-C51	1.192(3)	03 -C3 -C2	106.1(2)	03-C3-C4	111 3(2)
062-C61	1.170(5)	072-C71	1.191(7)	C2 -C3 -C4	113 4(2)	C3-C4-C5	117 8(2)
041-C41	1.339(4)	051-C51	1.344(3)	C4-C5-C6	113.2(2)	C5-C6-C7	114.7(2)
061-C61	1.337(4)	071 -C71	1 293(5)	041-C4 -C3	107.4(2)	051-C5-C4	111 4(2)
041-C4	1.453(3)	051-C5	1 440(3)	061-C6-C5	106 3(2)	071-C7-C6	109 1(2)
061-C6	1.445(3)	071-C7	1 442(4)	041-C4-C5	108 2(2)	051-C5-C6	104.0(2)
C41-C42	1.500(5)	C51-C52	1 515(4)	061-C6 -C7	110.2(2)		
C61-C62	1.495(5)	C71-C72	1.478(7)	C16-Cl l-C17	111 4(3)	C26-C21-C27	112 6(3)
Cl-C2	1.522(4)	C2-C8	1 522(3)	C12-Cl l-C17	111 3(3)	C22-C21-C27	112.6(3)
C2-C3	1.538(3)			C12-Cl l-C16	108 6(3)	C22-C21-C26	108.8(3)
C3-C4	1.523(4)	C4-C5	1 518(4)	Cl l-C12-C13	112.9(3)	C21-C22-C23	112.3(3)
C5-C6	1.520(4)	C6-C7	1.487(4)	013-C13-C12	107 3(2)	023-C23-C22	105 5(2)
Cll-C12	1 528(4)	C21-C22	1 520(4)	013-C13-C14	107 4(2)	023-C23-C24	108 9(2)
Cll-C16	1.519(5)	C21-C26	1.518(5)	C12-C13-C14	112 2(2)	C22-C23-C24	113.0(2)
Cll-C17	1.536(5)	C21-C27	1.515(5)	C13-C14-C18	114 5(3)	C23-C24-C28	114.4(2)
C12-C13	1 514(4)	C22-C23	1 499(4)	C13-C14-CIS	108 0(2)	C23-C24-C25	108 8(2)
C13-C14	1.520(4)	C23-C24	1 517(3)	C15-C14-C18	114 0(3)	C25-C24-C28	113.5(2)
C14-C15	1.540(5)	C24-C25	1.531(4)	C14-C15-C16	112 0(3)	C24-C25-C26	112 3(2)
C14-C18	1.535(5)	C24-C28	1 .522(4)	Cll-C16-C15	112 0(3)	C21-C26-C25	112 5(3)
C15-C16	1.516(5)	C25-C26	1.507(5)	C14-C18-C20	111 9(3)	C24-C28-C30	111 0(3)
C18-C19	1 527(6)	C28-C29	1.531(5)	C14-C18-C19	112 6(3)	C24-C28-C29	114 1(3)
C18-C20	1 513(5)	C28-C30	1 530(5)	CI9-C18-C20	111.8(3)	C29-C28-C30	110 4(3)
C32-Si-C33	112 0(2)	C3-Si-C33	109 3(2)	041-C41-042	122 5(3)	051-C51-052	124.5(3)
C31-Si-C32	111.3(2)			061-C61-062	122 2(3)	071-C71-072	120 9(4)
03 -Si-C33	105.5(1)	03-Si-C32	1115(1)	041-C41-C42	111 3(3)	051-C51-C52	110.3(2)
03-Si-C31	107.1(1)			061-C61-C62	111 3(3)	071-C71-C72	113.4(4)
Si-03 -C3	131 9(2)			042-C41-C42	126 2(3)	052-C51-C52	125.2(3)
Cl-013-C13	118 0(2)	C8-023 C23	119.9(2)	062-C61-C62	126 5(3)	072-C71-C72	125.3(4)

EXPERIMENTAL SECTION

2,3;4,5-di-*O*-isopropylidene-*al*-L-(+)-arabinose 1a. This material was prepared from commercial L-(+)-arabinose according to literature protocols.[5]

2,3;4,5-*O*-tetraacetyl-*al*-D-(+)-arabinose 1b. This material was prepared starting from commercial 1,2-*O*-isopropylidene-D-mannitol, via its 3,4; 5,6-*O*-tetraacetylation, followed by deacetonation and glycol cleavage.[6]

Di-*d*- and *l*-menthyl malonates were prepared from commercial *d*-menthol, *l*-menthol and malonic acid according to literature protocols.[11]

***l*-Menthyl-(2-deoxy-2-carboxy-*l*-menthyl)-4,5;6,7-di-*O*-isopropylidene-L-*manno*- and L-*gluco*-hepturonates 2a and 3a**. Di-*l*-menthylmalonate (1.5 g, 3 9 mmol) was dissolved in dry THF (15 ml) under argon, and to the solution, cooled to -80° C, LDA (1.03 g, 9 7 mmol) and TMS-Cl (1.0 ml, 7.8 mmol) were added; after 1 h stirring, 2,3:4,5-di-*O*-isopropylidene-*al*-L-(+)-arabinose **1a** (1 79 g, 7.8 mmol), dissolved in 5 ml THF and cooled at the same temperature, was added via cannula over 5 min, and the mixture was allowed to stirr for 3 h. A saturated aqueous NH_4Cl solution was added at -80° C and, after the ambient temperature was reached, the THF layer was sepatated and the aqueous solution extracted with EtOAc (2x20 ml). The organic layers were collected, washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The

residue was flash-chromatographed on silica (80:20 hexane/ethyl acetate) to afford 1.8 g (81.5%) of **2a** and **3a** as a mixture of isomers in a 7.8:2.2 diastereomeric ratio (^{1}HNMR). A further chromatographic separation allowed the stereoisomers to be obtained in a pure state: **2a**, glass: $[\alpha]_D$ -62 (*c* 0.28, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ: 4.85-4.68 (2H, m); 4.26 (1H,m); 4.21-3.86 (5H, m); 3.74-3.78 (5H, m); 2.07-2.02 (2H, m); 2.0-1.92 (2H, m); 1.74-1.65(4H, m), 1.54-1.28 (2H,m); 1.45, 1.39, 1.33, 1.30 (4s, each 3H); 1.08-0.68 (26H m); **3a**, glass: $[\alpha]_D$ -41 (*c* 0.64, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ: 4.84-4.61 (2H, m); 4.45 (1H, dd, J = 6.1, 2.1); 4.20-3.92 (5H,m); 3.63 (1H, d, J = 6.1); 3.32 (1H, d, J = 8.1); 2.08-1.93 (4H, m); 1.74-1.65 (4H, m); 1.45, 1.39, 1.34, 1.31 (4S, each 3H); 1.54-1.28 (2H, m); 1.09-0.70 (26H, s).

***d*-Menthyl-(2-deoxy-2-carboxy-*d*-menthyl)-4,5;6,7-di-*O*-isopropylidene-L-*manno*- and L-*gluco*-hepturonates 2b and 3b.** Compounds **2b** and **3b** were prepared with the same procedure starting from di-*d*-menthyl malonate (2.29 g, 5.9 mmol), LDA (1.57 g, 14.7 mmol), TMS-Cl (1.5 ml, 11.9 mmol) and **1a** (2.75 g, 11.9 mmol) in 81% yield (2.9 g) and a 3.5 : 6.5 diasteromeric ratio **2b**, glass: $[\alpha]_D$ +49 (*c* 4.8, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ: 4.80-4.73 (2H, m); 4;31(1H, dq, J = 5.1, 2.4); 4.14-4.03 (2H, m); 4.02-3.93 (3H, m); 3.76 (1H, d, J = 5.7), 3.69 (1H, d, J = 5.5); 2.07-2.02 (4H, m); 1.74-1.64 (4H, m); 1.52-1.20 (2H, m), 1.44, 1.37, 1.35,1.34 (4s, each 3H); 1.16-0.72 (26H, m); **3b**, glass: $[\alpha]_D$ +58 (*c* 2.1, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ: 4.77 (1H, t, J = 8.4); 4.76 (1H, t, J = 8.4), 4.41 (1H, dt, J = 6.6, 1.8); 4.14-3.90 (5H, m); 3.72 (2H, d, J = 7.2); 2.07-1.83 (4H, m); 1.74-1.64 (4H, m); 1.42, 1.38 (2s, each 3H); 1.34 (6H, s); 1.51-1.26 (2H, m); 1.12-0.76 (26H, m).

2-Deoxy-2-hydroxy-methyl-4,5;6,7-di-*O*-isopropylidene-L-*manno*- and L-*gluco*-heptitols 4 and 5. The diester **2a** (402 mg, 0.67 mmol) was dissolved in anhydrous THF (10 ml) in the presence of $LiAlH_4$ (64 mg, 1.17 mmol) and the mixture refluxed for 2 h under argon, then cautiously quenched with water, extracted with EtOAc (3X10 ml) and dried over $MgSO_4$. Evaporation of the organic layers and flash chromatograpy over silica gel (90 : 10 ethyl acetate / methanol) afforded 184 mg (75%) of the protected 2-deoxy-heptitol **4**, as a glass: $[\alpha]_D$ -4 (*c* 0.46, $CHCl_3$), ^{1}HNMR (300 MHz, $CDCl_3$) δ: 4.20 (1H, dd, 8.1, 2.04); 4.17-3.85 (6H, m); 3.77-3.71 (2H, m); 3.0 (3H, bs); 1.45 (6H, s); 1.36 (6H, s). When the same reduction was performed on **3a**, compound **5** was obtained in the same yield as a glass: $[\alpha]_D$ -7.8 (*c* 0.98, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ: 4.16-4.04 (3H, m), 3.98-3.83 (6H, m); 2.72 (3H, bs); 1.89 (1H, sext, J = 5.1); 1.42, 1.41, 1.39, 1.38 (4s, each 3H). In parallel, diesters **2b** and **3b**, submitted to the above reductive procedure, afforded heptitols **4** and **5** in near the same yield, with physical and spectral characteristics identical to those reported in the preceding preparation.

2-Deoxy-2-hydroxy-methyl-L-*manno*-heptitol 6. A solution of **4** (184 mg) in CF_3COOH (3 ml) and water (1.5 ml) was stirred at room temperature for 24 h, then evaporated in vacuo to give 111 mg (83.4%) of **6** as a glass: ^{1}HNMR (300 MHz, CD_3OD) δ: 4.79 (7H, s); 3.82-3.49 (10H, m); 1.95 (1H, bs).

2-Deoxy-2-hydroxy-methyl-L-*gluco*-heptitol 7 Prepared by deacetonation of compound **5** as above, glass: ^{1}HNMR (300 MHz, CD_3OD) δ: 4.41 (7H, s); 3.92 (1H, m); 3.85-3.48 (9H, m).

2-Deoxy-2-hydroxy-methyl-L-*manno*-heptitol heptaacetate 8. To a solution of **6** (111 mg), in dry pyridine (5 ml), Ac_2O (5 ml) and a catalytic amount of DMAP were added under argon. The mixture was stirred for 12 h at room temperature, quenched with water, extracted with CH_2Cl_2 (3X5 ml), and dried over $MgSO_4$. Concentration of the solution gave compound **8** (168 mg, 64%) as a glass: $[\alpha]_D$ -29 (*c* 0.42, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ: 5.45 (1H, dd, J = 3, 2.1, C-4); 5.42 (1H, m, C-5); 5.22 (1H, dd, J = 8.1, 3.9, C-3); 5.07 (1H, m,C-6), 4.27-4.04 (1H, m); 2.28 (1H, dsext, J = 4.8, 3.9, C-2); 2.11, 2.10, 2.09, 2.08, 2.07, 2.06, 2.04 (7s, each 3H). Anal. Calcd. for $C_{22}H_{32}O_{14}$: C, 50.76; H, 6.19. Found: C, 50.51; H, 6.38.

2-Deoxy-2-hydroxy-methyl-L-*gluco*-heptitol heptaacetate 9. Prepared as compound **8** by acetylation of heptitol **7** (67% yield), glass: $[\alpha]_D$ -23 (*c* 0.28, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ: 5.55 (1H, dd, J = 8.7, 2.7, C-4); 5.51 (1H, dd, J = 7.8, 3.3, C-5); 5.26 (1H, dd, J = 8.4, 2.4, C-3); 5.10 (1H, m, C-6); 4.29-4.19 (4H, m); 3.97-3.95 (2H, m); 2.46 (1H, bs), 2.17, 2.14, 2.09, 2.08, 2.07, 2.06, 2.04 (7s, each 3H). Anal. Calcd for $C_{22}H_{32}O_{14}$: C, 50.76; H, 6.19. Found: C, 50.88; H, 6.06.

***d*-Menthyl-(2-deoxy-2-carboxy-*d*-menthyl)-3-*O*-trimethylsilyl-4,5;6,7-*O*-tetra-acetyl-D-*manno*- and D-*gluco*-hepturonates 10 and 11.** The products were obtained as the preceding hepturonates starting from 2,3; 4,5-*O*-tetraacetyl-*al*-D-(-)-arabinose **1b** (500 mg, 1.57 mmol), di-*d*-menthyl malonate (300 mg, 0.78 mmol), LDA (200 mg, 1.95 mmol), TMS-Cl (0 2 ml, 1.57 mmol) in anhydrous THF (8 ml) (352 mg, 64% yield) and a 8.2:1.8 diastereomeric ratio (^{1}H NMR). Chromatography on silica gel (80:20 hexane/ethyl acetate) allowed to obtain the pure isomers **10** as a white solid, and **11** as a glass. The solid D-*manno*-hepturonate **10** was crystallized from hexane; colorless crystals; mp 125-126° C; $[\alpha]_D$ +64 (*c* 0.31, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ: 5.64 1H, dd, J = 8.7, 1.5); 5.22 (1H, dd, J = 5.8, 1.5); 4.75 (1H, dt, J = 8.7, 3.8); 4.66 (1H, dt, J = 8.7, 3.8); 4.49 (1H, dt, J = 8.7, 3.8); 4.24-4.14 (2H, m); 3.71 (1H, d, J = 8.7); 2.09, 2.06, 2.04, 2.03 (4s, each 3H); 2.07-1 83 (4H, m); 1.16-1.04 (4H, m); 1.02-0.76 (20H, m). Compound **11**: $[\alpha]_D$ +49 (*c* 0.92, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ: 5.52 (1H, dd, 7.8, 3.9); 5.36 (1H, t, J = 6.9); 5.17 (1H, m); 4.81-4.71 (2H, m); 4.26-4.12 (3H, m), 3.49 (1H, d, J = 7.2); 2.08, 2.07, 2.06, 2.04 (4s, each 3H); 2.08-1.90 (4H, m); 1.76-1.64 (4H, m); 1.06-0.75 (20H, m).

2-Deoxy-2-hydroxy-methyl-D-*manno*-heptitol heptaacetate 8'. Was obtained in pure form: $[\alpha]_D$ +29 (*c* 0.61, $CHCl_3$), by treatment of **10** with $LiAlH_4$, acetylation of the crude reduction product performed as above, and flash chromatography over silica gel (98:2 hexane/ethyl acetate). Spectral characteristics of compound **8'** were identical to those reported for **8**.

Structure Determination. *Crystal data*: $C_{39}H_{66}O_{13}Si$, M = 771.03, orthorhombic, space group $P2_12_12_1$, a = 23.317(7), b = 14.863(5), c = 13 381(4) Å, V = 4637(2) Å^3, Z = 4, D_c = 1.104 gcm^{-3}, μ = 0.878 mm^{-1} (Cu-Kα_1, λ = 1.540562 Å) Data were collected at room temperature on a Siemens AED single-crystal diffractometer using the nickel-filtered Cu-Kα radiation and the $\theta/2\theta$ scan mode. 9608 reflections with θ in the range 3-70° were measured, 8383 of them were independent and 8379 were used in the refinement, 4 having Δ/σ>6 being omitted. The integrated intensities were obtained by a modified version[12] of the Lehmann & Larsen[13] peak-profile analysis procedure. All reflections were corrected for Lorentz and polarisation effects, but not for absorption.

The structure was determined by direct methods with use of SHELXS86[14] program and refined by anisotropic full matrix least-squares on F^2, using SHELXL92.[15] The hydrogen atoms were put at the calculated positions riding on the attached carbons. In the last cycles of refinement a weighting scheme $w = 1/[\sigma^2(F_o^2)+0.0557\ g^2]$ with $g=[\max(F_o^2,0)+2F_c^2]/3$ was used. Final $wR2=[\sum w(\Delta F^2)^2/\Delta w(F_o^2)^2]^{1/2}$ values were 0.0936 for 8379 data and 0.0954 for all 8383 data. The $R1=\sum|\Delta F|/\sum|F_o|$ values are 0.0368 for 4038 $F_o>4\sigma F_o$ and 0.0881 for all 8383 data.

The absolute configuration was determined by the Flack's x parameter.[16]

The analysis of the anisotropic atomic displacements, carried out in terms of LST rigid body model according to Schomaker & Trueblood[17] and Trueblood[18] using the THMV program[19], gave a quite high value of the residual index $R_{WU} = [\sum(w\Delta U)^2/\sum(wU_o)^2]^{1/2}$ = 0.256, [$\Delta U=Ui_j$(obs.)-U_{ij}(calc.)], indicative that internal motions (or static disorder) are relevant (see description of the structure). Indeed a little improvement to R_{WU} = 0.194 is obtained if internal motions according to Dunitz & White[20] are considered.

The atomic scattering factors and the anomalous-scattering coefficients are from International Tables for X-ray Crystallography.[21] The final atomic co-ordinates for non-H atoms are given in Table 1. Throughout the paper the averaged values are means weighted according to the reciprocals of the variances and the corresponding e.s.d.'s are the largest of the values of the "external" and "internal" standard deviations.[22]

The calculations were carried out on the ENCORE-GOULD-POWERNODE 6040 and ENCORE 91 computers of the 'Centro di Studio per la Strutturistica Diffrattometrica del C.N.R.(Parma)'. In addition to the quoted programs, LQPARM[23], PARST[24] and ORTEP[25] have been used, the first for refinement of lattice parameters, the second for geometrical calculations, the last for molecular drawing.

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom co-ordinates and anisotropic displacement parameters.[26]

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26. Tables of H atom co-ordinates, displacement parameters and torsion angles are available from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield road, Cambridge CB2 IEW Any request should be accompanied by the full literature citation for this paper.