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A HIGHLY STEREOSELECTIVE ROUTE TO 1-*C*-(2-HYDROXYARYL)-ALDITOL DERIVATIVES

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ABSTRACT

Arylation at C-1 of 2,3:4,5-di-*O*-isopropylidene-D-arabinose and 4-*O*-benzyl-2,3-*O*-isopropylidene-D-threose variously using titanium or magnesium salts of 4-*tert*-butylphenol, 2-naphthol, and 5-pentylresorcinol gave the epimeric 1-*C*-aryl-alditol derivatives. One of these derivatives, namely, 1-*C*-(3-*tert*-butyl-6-hydroxyphenyl)-2,3:4,5-di-*O*-isopropylidene-D-*gluco*-pentitol, forms a crystalline 1:3 inclusion compound with 4-*tert*-butylphenol, the structure of which, established by X-ray diffraction, shows that guest molecules are linked through hydrogen bonds to the hydrophilic cavity created by the helical chains of the hosts.

INTRODUCTION

The addition of organometallic reagents to a carbonyl group adjacent to a chiral sugar fragment has been used to produce a variety of vicinal polyol systems[1]. In this context, the addition of metal phenolates to 2,3-*O*-isopropylidene-D-glyceraldehyde gave 1-*C*-arylglycerol derivatives stereoselectively[2]. Variation of the metal counter-ion provided access to the *threo* or *erythro* series of derivatives.

We now report the application of this reaction to 2,3:4,5-di-*O*-isopropylidene-D-arabinose[3] (**4**) and 4-*O*-benzyl-2,3-*O*-isopropylidene-D-threose[4] (**5**).

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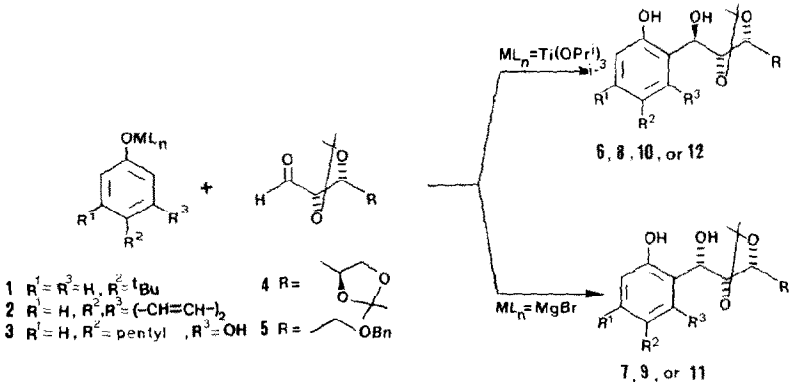
RESULTS AND DISCUSSION

Synthesis. — The reaction of **4** with the titanium compound prepared from $Ti(OPr^i)_4$ and 4-*tert*-butylphenol (**1**) under the conditions reported[2] to give *anti* addition products from **1** and 2,3-*O*-isopropylidene-D-glyceraldehyde gave the D-*manno*-pentitol **6** with 92% diastereoisomeric excess (d.e.) (Table I). Likewise, the D-*manno*-pentitol derivatives **10** (91% d.e.) and **12** (85% d.e.) were obtained by reacting **4** with the titanium derivatives of 2-naphthol (**2**) and 4-pentylresorcinol (**3**), respectively. The extension of this reaction, using the titanium salt of **1**, to **5** gave the D-*lyxo*-tetritol derivative **8** (93% d.e.).



Unlike the glyceraldehyde derivatives[2], reversal of the stereochemical outcome of the reaction proved to be difficult. In principle, this reversal could be achieved by a phenolate bearing a metal counter-ion which would be chelated between the aldehydo oxygen and the α-oxygen of **4** and **5**, thereby favouring 1,2-*syn* stereoselection[2,5].

TABLE I

DATA ON THE SYNTHESIS[a] AND PROPERTIES OF THE 1-*C*-ARYLALDITOL DERIVATIVES

Phenol[b]	*Aldehyde*	*Metal promoter*	*Product*	*Yield (%)*[c]	$[\alpha]_D^{20}$[d]	*D.e. (%)*[e]	*Configuration*
1	**4**	$Ti(OPr^i)_3^+$	**6**	65	−2.3	92	D-*manno*
1	**4**	$MgBr^+$	**7**	70	+8.4	90	D-*gluco*
1	**5**	$Ti(OPr^i)_3^+$	**8**	68	−20.0	93	D-*lyxo*
1	**5**	$MgBr^+$	**9**	63	+7.5	90	D-*xylo*
2	**4**	$Ti(OPr^i)_3^+$	**10**	78	−72.0	91	D-*manno*
2	**4**	$MgBr^+$	**11**	60	+1.8	89	D-*gluco*
3	**4**	$Ti(OPr^i)_3^+$	**12**	45	−14.0	85	D-*manno*

[a]Ti-based reactions: 10 mmol each of phenol and aldehyde; Mg-based reactions: phenol, 40 mmol; aldehyde, 10 mmol. [b]**1**, 4-*tert*-Butylphenol; **2**, 2-naphthol; **3**, 5-pentylresorcinol. [c]Isolated yield, based on aldehyde. [d]For solution in chloroform (*c* 0.5). [e]Diastereoisomeric excess determined by ^{1}H-n.m.r. spectroscopy.

In the reaction between **1** and **4**, however, recourse to the strongly chelating MgBr ion gave a nearly equimolecular mixture of the D-*manno*- (**6**) and D-*gluco*-pentitol (**7**) derivatives. The problem was solved by the use of an excess of bromomagnesium-phenolate (4:1 ArOMgBr–**4** molar ratio), which gave the D-*gluco*-pentitol derivative **7** with 90% d.e. from **1**. Likewise, the D-*gluco*-pentitol derivative **11** was obtained (89% d.e.) from **2** and **4**. By using a 4 molar excess of bromomagnesium salt of **1**, **5** gave the D-*xylo*-tetritol derivative **9** with a d.e. as high as 90%.

The above alditol derivatives were oils, and the major and minor diastereoisomers were isolated by chromatography on silica gel. When **7** was stored in the presence of an excess of 4-*tert*-butylphenol (**1**), colorless crystals were formed, which contained **7** and **1** in the ratio 1:3, and the result was repeatable. The D-*manno* isomer **6** did not form a crystalline adduct with **1**.

Addition of an excess of **1** to a 1:1 mixture of **6** and **7** gave crystals of the adduct of **1** and **7**, and **6** remained as an oil.

Configurational assignments. — The stereochemistry of the 1-*C*-arylalditol derivatives was established by X-ray and ^{1}H-n.m.r. studies, starting with an X-ray analysis of the adduct of **1** and **7**.

A perspective view of the host molecule is shown in Fig. 1. Since the configurations of C-8, C-9, and C-13 are *R*, it can be deduced that the configuration of C-7 is *S*.

There is a folding of the molecule and short intramolecular interactions of the oxygen atoms [O-1,2 2.84(1)Å, O-2,3 2.71(1)Å]. The torsion angles H–C-7–C-8–H and H–C-9–C-13–H are 171.5(1.0)° and 172.5(1.1)°, respectively.

As illustrated in Fig. 2, a short intermolecular hydrogen-bond [O-1 · · · O-2^i

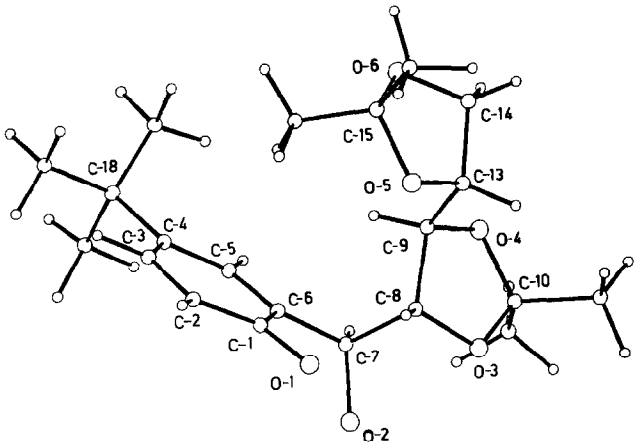


Fig. 1. Perspective view of the host molecule 1-*C*-(3-*tert*-butyl-6-hydroxyphenyl)-2,3:4,5-di-*O*-isopropylidene-D-*gluco*-pentitol (**7**); C-7,8,9,13,14 in the diagram correspond to C-1,2,3,4,5 in the pentitol moiety.

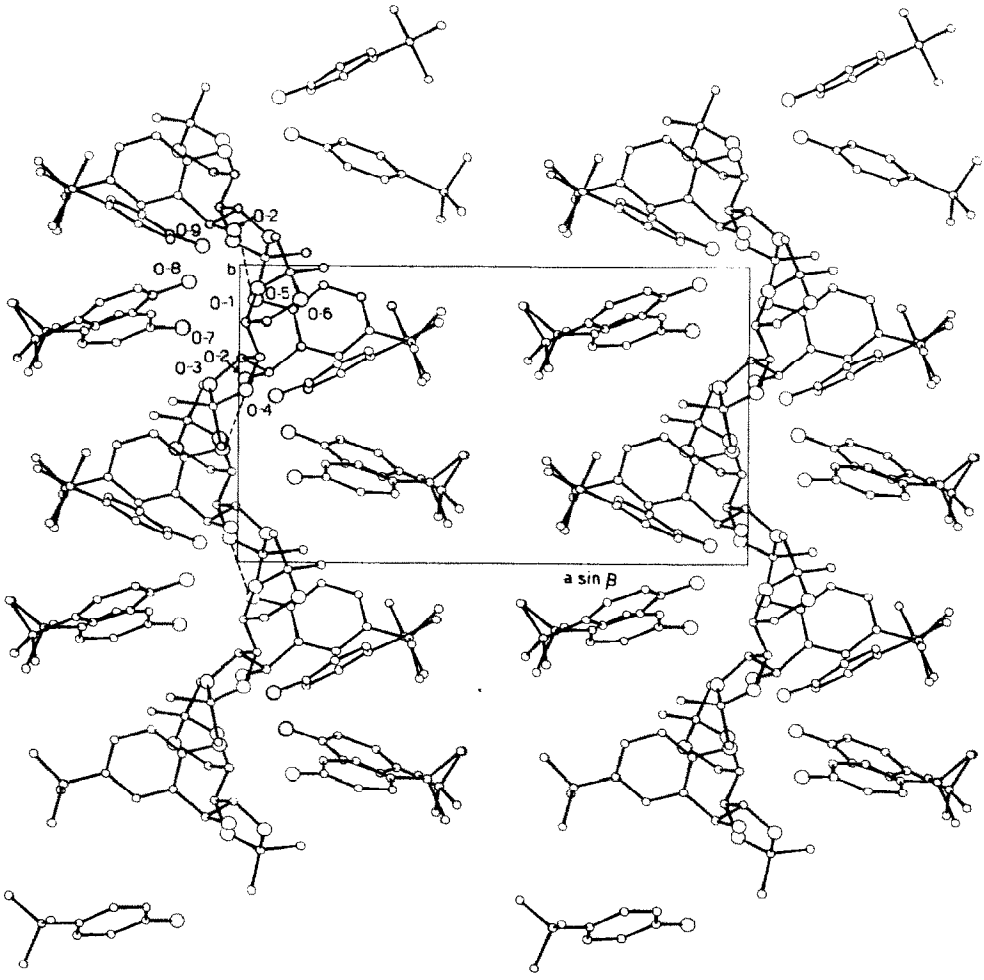


Fig. 2. Molecular packing projected along [001] for the 1:3 adduct of **7** and 4-*tert*-butylphenol. The disordered *tert*-butyl groups with the lowest occupancy factors have been omitted for clarity.

2.62(1)Å] joins the host molecules in right-handed helical (Δ) chains running along the screw axis at x = 0, z = ½. The guest molecules bring the phenolic oxygen into the interior of the hydrophilic cavity created by the helical chains of the hosts, forming hydrogen bonds [O-7 · · · O-1^{iii} 3.03(1)Å, O-7 · · · O-2^{iii} 3.13(1)Å (bifurcated); O-8 · · · O-4^{ii} 2.73(1)Å; O-9 · · · O-2^{i} 2.80(1)Å, O-9 · · · O-5 2.84(1)Å (bifurcated); i = $\bar{x}$ − 2, $\bar{y}$ + ½, $\bar{z}$ − 1; ii = $\bar{x}$ − 2, $\bar{y}$ + ½, $\bar{z}$; iii = $\bar{x}$ − 2, $\bar{y}$ − ½, $\bar{z}$ − 1]. Hence, the compound is an example of a binary co-ordinato-clathrate (aediculate-type)[6].

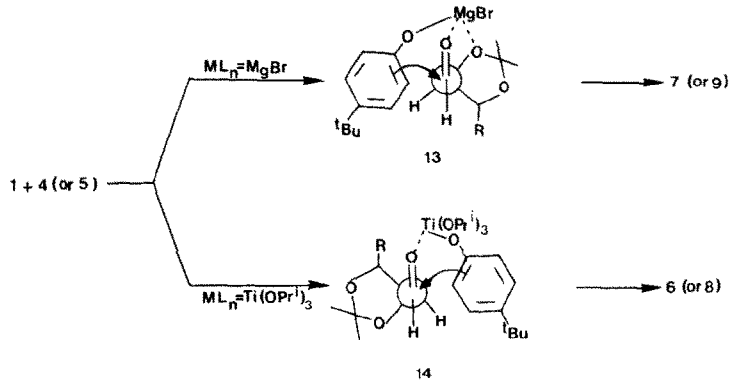
The disordered lipophilic methyl groups face those of the adjacent molecules derived from screw axes at x = ½ with van der Waals contacts.

Both five-membered rings [O-3–C-8–C-9–O-4–C-10 (2,3-*O*-isopropylidene group); O-5–C-15–O-6–C-14–C-13 (4,5-*O*-isopropylidene group)] show a twist conformation with the twist axis through C-10 and O-5, respectively [puckering parameters: q_2 = 0.17(1)Å, 0.33(1)Å; ϕ_2 = 58(4)°, −88(2)°; respectively][7]. The phenolic groups of the guest molecules are planar, whereas that of the host is significantly out of the mean benzene plane (−0.04Å)

In the ^{1}H-n.m.r. spectra, the signal for H-1 appeared as a doublet in the D-*manno* isomers [**6** δ 4.80 ($J_{1,2}$ 6.68 Hz); **10** δ 5.83 ($J_{1,2}$ 6.78 Hz); **12** δ 5.19 ($J_{1,2}$ 7.54 Hz)], whereas in D-*gluco* derivatives it appeared as an apparent triplet [**7** δ 4.87 ($J_{1,2}$ 4.52, $J_{1,OH}$ 5.27 Hz); **11** δ 5.84 ($J_{1,2}$ 4.14, $J_{1,OH}$ 3.77 Hz)][1,2]. In addition, for a given epimeric pair, the $J_{1,2}$ values for the 1,2-*anti* D-*manno* isomers are larger than those for the corresponding 1,2-*syn* D-*gluco* isomers.

In the tetritol series, the signal of H-1 appeared as a doublet in both the D-*lyxo* [**8** δ 4.93 ($J_{1,2}$ 5.27 Hz)] and D-*xylo* [**9** δ 4.83 ($J_{1,2}$ 7.54 Hz)] compounds in agreement with our previous results in the glycerol series, in which the $J_{1,2}$ value of 1,2-*syn* compounds was larger than that of 1,2-*anti* compounds[2].

Mechanistic considerations. — On the basis of previous studies[5,8], the reactions of organometallics with aldehydo carbons adjacent to a chiral alkoxy-substituted centre can be rationalized as follows. Where metal ions capable of bis-ligation with a given aldehydo reactant are involved, a double-chelate "Cram cyclic" transition-state model accounts for 1,2-*syn* preference[5]; otherwise, 1,2-*anti* selectivity occurs *via* a non-cyclic "Felkin–Anh" transition-state model[9]. The stereochemical results reported here accord with this rationale.



Depending upon the nature of the metal ion involved, molecular complexes **13** or **14** are formed. The proximity effects in such complexes[10] ensure activation of the reactants and regiospecific C-*ortho* carbon–carbon bond formation. With a highly oxygenophilic MgBr ion, 1,2-*syn* products preponderate, presumably *via* **13**, whereas the metal ion of reduced co-ordinating ability, Ti(OPr^i)$_3$, gave 1,2-*anti* products *via* **14**.

EXPERIMENTAL

General. — Reagents and solvents were purified and dried using standard methods. ^{1}H-N.m.r. spectra were recorded with a Bruker AM-270 spectrometer on solutions in $CDCl_3$ (internal Me_4Si).

Elemental analyses were performed at the Istituto di Chimica Farmaceutica dell'Università degli Studi di Parma. I.r. spectra were recorded with a Perkin–Elmer 298 spectrophotometer as films on NaCl discs. Optical rotations were measured with an Autopol III polarimeter and a 1-dm tube.

The X-ray analysis was done on a Siemens AED three-circle diffractometer under the control of a General Automation Jumbo 220 Computer. Calculations were carried out partly on a Cray X-MP/12 computer of the Centro di Calcolo Elettronico Interuniversitario dell'Italia Nord-Orientale (Bologna) and partly on a Gould SEL 32/77 computer of the Centro di Studio per la Strutturistica Diffrattometrica del C.N.R. (Parma).

Silica gel (Merck 7734, 70–230 mesh) was used for column chromatography. All reactions were performed in oven-dried glassware under a positive pressure of nitrogen.

Phenols **1–3** were commercial products. 2,3:4,5-Di-*O*-isopropylidene-D-arabinose[3] and 4-*O*-benzyl-2,3-*O*-isopropylidene-D-threose[4] (**5**) were prepared according to the methods reported.

Reactions of isopropoxytitanium phenolates with **4** *and* **5**. — To a solution of titanium tetra-isopropoxide (2.84 g, 10 mmol) in toluene (50 mL) was added the appropriate phenol (**1–3**, 10 mmol). The 2-propanol was distilled off and, after cooling to 0°, a solution of **4** or **5** (10 mmol) in toluene (20 mL) was added with stirring. The solution was kept for 20 h at 0–2°, then quenched with saturated aqueous ammonium chloride, and extracted with CH_2Cl_2 (3 × 50 mL), and the combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The oily residue was subjected to column chromatography (hexane–acetone mixtures). The following compounds were prepared in this manner. The yields and $[\alpha]_D$ values are recorded in Table I.

1-*C*-(3-*tert*-Butyl-6-hydroxyphenyl)-2,3:4,5-di-*O*-isopropylidene-D-*manno*-pentitol (**6** from **4** and **1**). ^{1}H-N.m.r. data: δ 7.91 (s, 1 H, OH), 7.22 (dd, 1 H, $J_{4',5'}$ 8.30, $J_{2',4'}$ 2.30 Hz, H-4'), 7.14 (d, 1 H, $J_{2',4'}$ 2.30 Hz, H-2'), 6.83 (d, 1 H, $J_{4',5'}$ 8.30 Hz, H-5'), 4.87 (d, 1 H, $J_{1,2}$ 6.78 Hz, H-1), 4.27 (s, 1 H, OH), 4.20 (dd, 1 H, $J_{5a,5b}$ 8.29, $J_{4,5a}$ 6.03 Hz, H-5a), 4.15 (dd, 1 H, $J_{2,3}$ 8.29, $J_{1,2}$ 6.78 Hz, H-2), 4.10 (ddd, 1 H, $J_{3,4}$ 8.29, $J_{4,5a}$ 6.03, $J_{4,5b}$ 5.27 Hz, H-4), 3.98 (dd, 1 H, $J_{5a,5b}$ 8.29, $J_{4,5b}$ 5.27 Hz, H-5b), 3.78 (t, 1 H, $J_{2,3}$ 8.29 Hz, H-3), 1.50, 1.40, 1.37, and 1.34 (4 s, each 3 H, 2 Me_2C), 1.28 (s, 9 H, Me_3C); ν_{max} 3360, 3020, 1375, 1230, 1070, and 760 cm^{-1}.

Anal. Calc. for $C_{21}H_{32}O_6$: C, 66.30; H, 8.48. Found: C, 66.12; H, 8.52.

1-*C*-(2-Hydroxynaphthyl)-2,3:4,5-di-*O*-isopropylidene-D-*manno*-pentitol (**10** from **4** and **2**). ^{1}H-N.m.r. data: δ 9.24 (s, 1 H, OH), 7.88 (d, 1 H, $J_{3',4'}$ 8.50 Hz, H-4'), 7.73 (d, 1 H, $J_{5',6'}$ 8.50 Hz, H-5'), 7.71 (d, 1 H, $J_{7',8'}$ 8.50 Hz, H-8'), 7.40 (t,

1 H, $J_{5',6'}$ 8.50 Hz, H-6'), 7.30 (t, 1 H, $J_{6',7'}$ 8.50 Hz, H-7'), 7.13 (d, 1 H, $J_{3',4'}$ 8.50 Hz, H-3'), 5.83 (d, 1 H, $J_{1,2}$ 6.78 Hz, H-1), 4.67 (s, 1 H, OH), 4.42 (t, 1 H, $J_{2,3}$ 7.10 Hz, H-2), 4.18 (m, 1 H, H-5a), 4.07 (m, 1 H, H-5b), 3.96 (m, 1 H, H-4), 3.88 (m, 1 H, H-3), 1.43, 1.39, 1.36, and 1.26 (4 s, each 3 H, 2 Me_2C); ν_{max} 3290, 2900, 1600, 1370, 1215, 1060, 840, and 740 cm^{-1}.

Anal. Calc. for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.20; H, 7.25.

1-*C*-(2,6-Dihydroxy-4-pentylphenyl)-2,3:4,5-di-*O*-isopropylidene-D-*manno*-pentitol (**12** from **4** and **3**). ^{1}H-N.m.r. data: δ 7.45 (s, 2 H, OH), 6.25 (s, 2 H, H-3' and H-5'), 5.19 (d, 1 H, $J_{1,2}$ 7.54 Hz, H-1), 4.80 (bs, 1 H, OH), 4.10 (m, 2 H, H-2 and H-5a), 3.94 (m, 2 H, H-4 and H-5b), 3.73 (m, 1 H, H-3), 2.40 (m, 2 H, CH_2-α), 1.30 (m, 6 H, CH_2), 1.33, 1.30, 1.28, and 1.26 (4 s, each 3 H, 2 Me_2C), 0.81 (t, 3 H, Me-ω); ν_{max} 3360, 2915, 1630, 1590, 1455, 1370, 1220, 1070, 910, 850, and 730 cm^{-1}.

Anal. Calc. for $C_{22}H_{34}O_7$: C, 64.37; H, 8.35. Found: C, 64.30; H, 8.28.

4-*O*-Benzyl-1-*C*-(3-*tert*-butyl-6-hydroxyphenyl)-2,3-*O*-isopropylidene-D-*lyxo*-tetritol (**8** from **5** and **1**). ^{1}H-N.m.r. data: δ 7.86 (s, 1 H, OH), 7.30 (m, 5 H, Ph), 7.09 (dd, 1 H, $J_{3',4'}$ 8.30, $J_{2',4'}$ 2.30 Hz, H-4'), 6.98 (d, 1 H, $J_{2',4'}$ 2.30 Hz, H-2'), 6.69 (d, 1 H, $J_{4',5'}$ 8.30 Hz, H-5'), 4.93 (d, 1 H, $J_{1,2}$ 5.27 Hz, H-1), 4.38 (s, 2 H, CH_2Ph), 4.13 (m, 1 H, H-3), 4.06 (dd, 1 H, $J_{1,2}$ 5.27, $J_{2,3}$ 6.78 Hz, H-2), 3.73 (s, 1 H, OH), 3.26 (m, 2 H, H-4a and H-4b), 1.34 and 1.32 (2 s, each 3 H, 2 Me_2C), 1.17 (s, 9 H, Me_3C); ν_{max} 3360, 2930, 1500, 1375, 1220, 1080, and 760 cm^{-1}.

Anal. Calc. for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82. Found: C, 71.29; H, 7.61.

Reactions of bromomagnesium-phenolates with **4** *and* **5**. — To a solution of ethylmagnesium bromide prepared *in situ* from ethyl bromide (4.32 g, 40 mmol) and magnesium turnings (0.96 g) in ether (150 mL) was added a solution of the phenol (**1** or **2**, 40 mmol) in ether (150 mL) dropwise with stirring at room temperature. The ether was removed under vacuum with gentle warming, and anhydrous CH_2Cl_2 (100 mL) was added. After cooling at 0°, a solution of **4** or **5** (10 mmol) in CH_2Cl_2 (50 mL) was added dropwise with stirring, and the mixture was stored for 20 h at 0–2°. The reaction was quenched with an excess of aqueous ammonium chloride and extracted with CH_2Cl_2 (3 × 50 mL). The combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The oily residue was subjected to column chromatography (hexane–acetone mixtures). The following compounds were prepared in this manner; the yields and $[\alpha]_D$ values are recorded in Table I.

1-*C*-(3-*tert*-Butyl-6-hydroxyphenyl)-2,3:4,5-di-*O*-isopropylidene-D-*gluco*-pentitol (**7** from **4** and **1**). ^{1}H-N.m.r. data: δ 7.83 (s, 1 H, OH), 7.17 (dd, 1 H, $J_{4',5'}$ 8.30, $J_{2',4'}$ 2.30 Hz, H-4'), 7.05 (d, 1 H, $J_{2',4'}$ 2.30 Hz, H-2'), 6.78 (d, 1 H, $J_{4',5'}$ 8.30 Hz, H-5'), 4.87 (t, 1 H, $J_{1,OH}$ 5.27, $J_{1,2}$ 4.52 Hz, H-1), 4.24 (dd, 1 H, $J_{2,3}$ 6.40, $J_{1,2}$ 4.52 Hz, H-2), 3.97 (dd, 1 H, $J_{5a,5b}$ 8.29, $J_{4,5a}$ 6.03 Hz, H-5a), 3.93 (dd, 1 H, $J_{2,3}$ 6.40, $J_{3,4}$ 6.00 Hz, H-3), 3.85 (m, 1 H, H-4), 3.74 (dd, 1 H, $J_{5a,5b}$ 8.29, $J_{4,5b}$ 5.27 Hz, H-5b), 3.28 (d, 1 H, $J_{1,OH}$ 5.27 Hz, OH), 1.36, 1.35, 1.27, and 1.24 (4 s, each 3 H, 2 Me_2C), 1.21 (s, 9 H, Me_3C); ν_{max} 3400, 2990, 1735, 1500, 1375, 1220, 1070, 760 cm^{-1}.

Anal. Calc. for $C_{21}H_{32}O_6$: C, 66.30; H, 8.48. Found: C, 66.15; H, 8.41.

1-*C*-(2-Hydroxynaphthyl)-2,3:4,5-di-*O*-isopropylidene-D-*gluco*-pentitol (**11** from **4** and **2**). ^{1}H-N.m.r. data: δ 8.64 (s, 1 H, OH), 7.85 (d, 1 H, $J_{3',4'}$ 8.50 Hz, H-4'), 7.76 (d, 1 H, $J_{4',5'}$ 8.50 Hz, H-5'), 7.71 (d, 1 H, $J_{7',8'}$ 8.50 Hz), 7.46 (t, 1 H, $J_{5',6'}$ 8.50 Hz, H-6'), 7.31 (t, 1 H, $J_{6',7'}$ 8.50 Hz, H-7'), 7.14 (d, 1 H, $J_{3',4'}$ 8.50 Hz, H-3'), 5.84 (t, 1 H, $J_{1,2}$ 4.14, $J_{1,OH}$ 3.77 Hz, H-1), 4.40 (dd, 1 H, $J_{2,3}$ 6.40, $J_{1,2}$ 4.14 Hz, H-2), 4.15 (t, 1 H, $J_{3,4}$ 7.00, $J_{2,3}$ 6.40 Hz, H-3), 4.00 (m, 2 H, H-4 and H-5a), 3.83 (dd, 1 H, $J_{5a,5b}$ 8.29, $J_{4,5b}$ 4.52 Hz, H-5b), 3.13 (d, 1 H, $J_{1,OH}$ 3.77 Hz, OH), 1.57, 1.40, 1.29, and 1.17 (4 s, each 3 H, 2 Me_2C); ν_{max} 3310, 2900, 1600, 1360, 1215, 1060, 840, and 740 cm^{-1}.

Anal. Calc. for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.48; H, 7.12.

4-*O*-Benzyl-1-*C*-(3-*tert*-butyl-6-hydroxyphenyl)-2,3-*O*-isopropylidene-D-*xylo*-tetritol (**9** from **5** and **1**). ^{1}H-N.m.r. data: δ 7.64 (s, 1 H, OH), 7.30 (m, 5 H, Ph), 7.22 (dd, 1 H, $J_{4',5'}$ 8.30, $J_{2',4'}$ 2.30 Hz, H-4'), 7.03 (d, 1 H, $J_{2',4'}$ 2.30 Hz, H-2'), 6.82 (d, 1 H, $J_{4',5'}$ 8.30 Hz, H-5'), 4.83 (d, 1 H, $J_{1,2}$ 7.54 Hz, H-1), 4.38 (s, 2 H, CH_2-Ph), 4.18 (dd, 1 H, $J_{1,2}$ 7.54, $J_{2,3}$ 6.81 Hz, H-2), 4.11 (dd, 1 H, $J_{3,4b}$ 6.03, $J_{3,4a}$ 3.77 Hz, H-3), 3.34 (bs, 1 H, OH), 3.23 (dd, 1 H, $J_{4a,4b}$ 10.55, $J_{3,4a}$ 6.03 Hz, H-4a), 3.07 (dd, 1 H, $J_{4a,4b}$ 10.55, $J_{3,4b}$ 3.77 Hz, H-4b), 1.45 (s, 6 H, 2 Me_2C), 1.26 (s, 9 H, Me_3C); ν_{max} 3360, 2920, 1375, 1240, 1080, and 740 cm^{-1}.

Anal. Calc. for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82. Found: C, 71.24; H, 7.78.

4-tert-Butylphenol–7 clathrate. — To a solution of **7** (100 mg, 0.26 mmol) in ether (10 mL) was added 4-*tert*-butylphenol (**1**; 200 mg, 1.3 mmol), and the solution was slowly concentrated in a stream of nitrogen. The oily residue was stored at 21–22° until colorless crystals separated (usually 2–5 days). The crystals (135 mg, 71% based on **7**) were collected, washed with a few drops of cold hexane, and had m.p. 77–78°.

Anal. Calc. for $C_{51}H_{74}O_9$: C, 73.70; H, 8.97. Found: C, 73.64; H, 9.06.

*Crystallography**. — Crystal data for the 4-*tert*-butylphenol–**7** clathrate: M_r = 831.1; monoclinic space group $P2_1$ (from systematic absences and structural analysis); cell dimensions, a = 18.038(3)Å, b = 10.626(2)Å, c = 13.559(2)Å, β = 101.99(2)°; V = 2542.2(8)Å^3; Z = 2; CuK_α λ = 1.54178 Å, μ = 5.49 cm^{-1}; D_c = 1.086 g.cm^{-3}; 3569 reflections measured, 3057 with $I > 2\,\sigma(I)$ used in refinement of 444 parameters; $(\Delta\rho)_{max}$ = 0.29, $(\Delta\rho)_{min}$ = −0.28; max 2θ = 140°.

A selected crystal (0.22 × 0.13 × 0.29 mm^3) was sealed, and the intensity data were collected at room temperature in the ω–2θ step-scanning mode, using Ni-filtered CuK_α radiation. No correction for absorption was applied. The structure was solved by direct methods, using the SHELX-86 program[11], and refined by full-matrix least-squares to R = 0.106 and R_w = 0.121 (observed reflections only) using the SHELX-76 program[12].

*Lists of bonds lengths and angles, final atomic co-ordinates, and thermal parameters with their estimated standard deviations have been deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/404/*Carbohydr. Res.*, 186 (1989) 207–215.

The aromatic hydrogen atoms and H-7, H-8, and H-13 (bonded to the chiral carbon atoms) were located from a difference Fourier synthesis. All other protons, except the phenolic protons, were generated geometrically.

The *tert*-butyl groups of the guest molecules are disordered on three positions with a strong correlation between partial occupancies and high thermal motion, and so they have not been refined. Anisotropic thermal parameters were used for all non-hydrogen atoms except those of the *tert*-butyl groups. Scattering factors for C, H, and O were taken from ref. 13.

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