Stereocontrolled Homologation of 1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose to 7-Deoxynonodialdose Epimers *via* Thiazole-Aldehyde Synthesis†

Alessandro Dondoni,*,[a] Sandra Ianelli,[b] Ladislav Kniezo,[a] Pedro Merino[a] and Mario Nardelli‡[b]

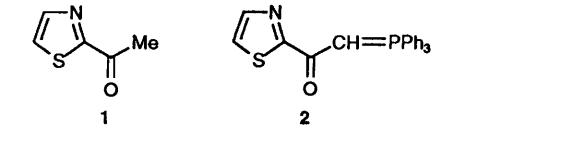
[a] *Dipartimento di Chimica, Laboratorio di Chimica Organica, Università degli Studi di Ferrara, Via L. Borsari 46, I-44100 Ferrara, Italy*

[b] *Istituto di Chimica Generale, Università degli Studi di Parma, Centro di Studio CNR per la Strutturistica Diffrattometrica, Viale delle Scienze 78, I-43100 Parma, Italy*

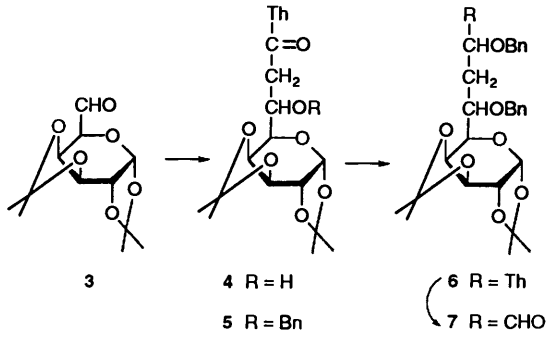
The three-carbon chain elongation of the title dialdose has been carried out by two approaches employing thiazole-based reagents: (i) aldol condensation with the lithium enolate of 2-acetylthiazole; (ii) olefination with triphenyl(thiazol-2-ylcarbonylmethylene)phosphorane and 1,4-addition of benzyl oxide anion to the resultant vinyl ketone. The stereoselective reduction of the resultant (*R*) and (*S*) β-hydroxy ketones, followed by protection of the hydroxy groups as benzyl ethers, afforded four compounds consisting of the galactopyranosyl ring substituted at C-5 with stereoisomeric 1,3-bis(benzyloxy)propyl units bearing the thiazol-2-yl ring at the terminus of the chain. The unmasking of the formyl group from the thiazolyl ring to give 7-deoxynonodialdoses was carried out in two cases. The unequivocal assignment of the structures of two intermediates isolated in each route was established by X-ray room-temperature crystal-structure analyses.

Recent reports from one of our laboratories have demonstrated application of the thiazole-aldehyde synthesis in carbohydrate chemistry.[1] Based on this reaction, various methods have been developed for the chain elongation of sugar-derived aldehydes R-CHO (R = polyalkoxy chain) to give homologues bearing one, two, or three more carbon atoms. For example, 2-acetylthiazole (2-ATT, **1**) and triphenyl(thiazol-2-ylcarbonylmethylene)phosphorane (2-TCMP, **2**) have been used as three-carbon-atom units in synthetic routes to higher 3-deoxyaldos-2-uloses and 2-ulosonic acids such as KDO,[2] KDN,[3] and their epimers at C-4. The reagent **1** acts *via* aldol condensation of its lithium enolate as a direct equivalent to pyruvaldehyde (route *A*), whereas phosphorane **2** affords, *via* Wittig olefination, an α,β-enone intermediate which then undergoes a Michael-type addition of an alkoxide anion (route *B*) (Scheme 1). These routes appeared to be complementary since they led to β-hydroxy and β-alkoxy ketones with opposite configurations at C-β.

We now report application of routes *A* and *B* to 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose **3** and show the stereoselective reduction of the resultant ketones **4** and **5** into four galactose derivates **6** bearing stereoisomeric 1,3-dialkoxy-3-(thiazol-2-yl)propyl units at C-5 (Scheme 2). The synthetic equivalence of compounds **6** to 7-deoxynonodialdoses **7** is demonstrated by the aldehyde unmasking from the thiazole ring. The side-chain elongation of the dialdose **3** is of considerable importance[4] since it provides an entry to biologically active higher sugars incorporating the 1,5-galactopyranosyl moiety.[5]



Scheme 1



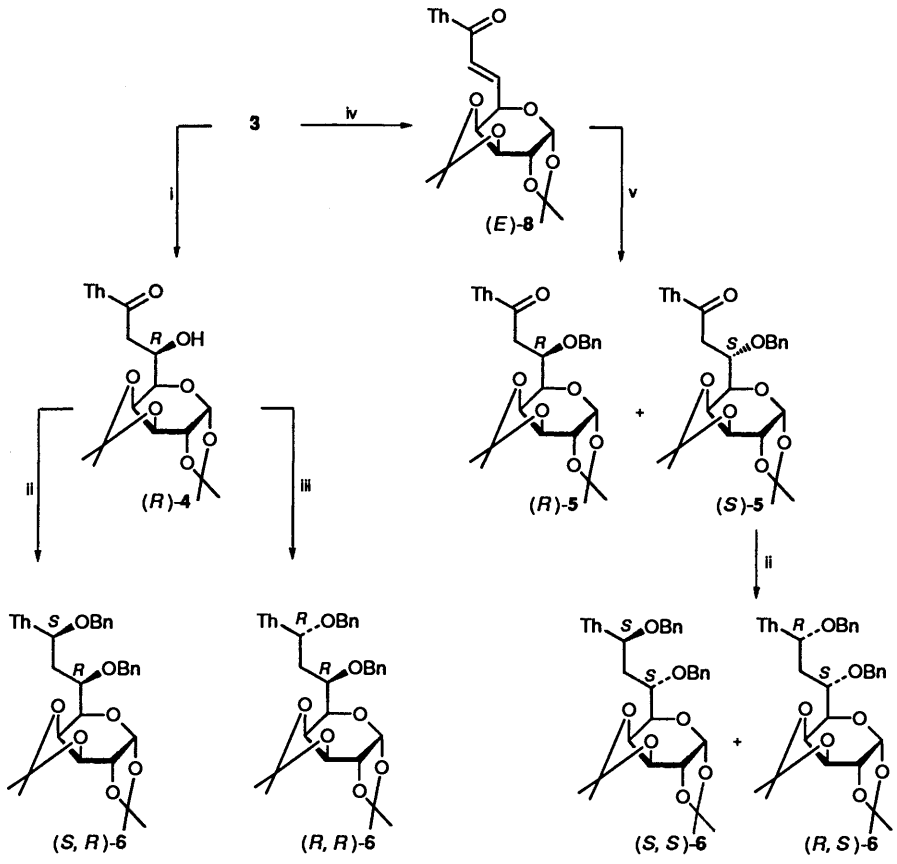
Scheme 2 (Th = thiazol-2-yl)

Results and Discussion

Homologation of the Dialdose **3**.—Following route *A*, the generation of the lithium enolate of 2-ATT **1** in the presence of dialdose **3** at −50 °C in tetrahydrofuran (THF) using lithium *tert*-butoxide, afforded exclusively the aldol (*R*)-**4** (ds ≥ 95%)[6] which was isolated in 58% yield (Scheme 3). The *R* configuration at the newly formed stereocentre in this compound was established by X-ray crystallography of the 1,3-diol derived from it (see below). On the other hand, following route *B*, the dialdose **3** was initially treated with the phosphorane **2** in refluxing chloroform to give the vinyl ketone (*E*)-**8** (85%) together with a small amount of the isomer (*Z*)-**8** (not shown). The *E* configuration of the main olefin (*E*)-**8** (coupling

† Thiazole-aldehyde synthesis: preparation of aldehydes from C-2-substituted thiazoles by thiazole-into-formyl conversion.

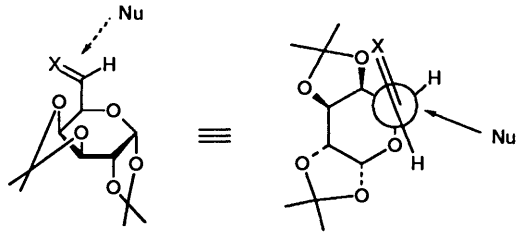
‡ Author to whom inquiries regarding the X-ray structure analysis should be addressed.



Scheme 3 *Reagents:* i, 2-ATT (**1**), Bu^{t}OLi; ii, DIBAL-H; iii, $Me_4\overset{+}{N}\ \overset{-}{B}H(OAc)_3$; iv, 2-TCMP (**2**); v, BnONa

constant of vinylic protons, J = 15.8 Hz) was expected on the basis of the stabilized nature of the phosphorus ylide **2** and the reaction conditions employed.[7] The Michael-type 1,4-addition of sodium benzyl oxide to (*E*)-**8** in THF at −50 °C was sufficiently diastereoselective to give rise to an 80:20 mixture of the epimers (*S*)-**5** and (*R*)-**5** which were individually isolated in 70 and 18% yield respectively. The X-ray structure determination of the major adduct (*S*)-**5** demonstrated the *S* configuration at C-6 (see below). Hence the aldol condensation route *A* and the olefination-alkoxylation route *B* appeared quite efficient for the stereoselective installation of *R* β-hydroxy- and *S* β-benzyloxypropanoyl moieties at C-5 of the galactopyranosyl ring starting from the dialdose **3**. A single transition-state model (Fig. 1) accounts for the above stereoselective nucleophilic additions to both the aldehyde **3** and the olefin (*E*)-**8**. Accordingly, attack of the nucleophile should take place on the face opposite to the plane of the pyranose ring of the aldehyde or alkene conformer as shown in Fig. 1. This model is reminiscent of the Cram open-chain model wherein the C=X double bond is flanked by the two least bulky groups attached to the adjacent centre.[8] Stereoselectivity according to a non-chelate model (in the Cram–Felkin sense) had been exhibited by the dialdose **3** in reactions with other nucleophiles[9] and in cycloaddition with dienes.[10] On the other hand, the work on the internal asymmetric induction in Michael-type addition of heteronucleophiles to alkene sugars is much more scanty.[3,11]

The β-hydroxy-directed diastereofacial reduction of the carbonyl group of (*R*)-**4** was then exploited to create a 1,3-diol unit with a new stereocentre in either configuration. The appropriate metal hydride reducing agent was easily chosen on the basis of previous work with this methodology.[12] Thus, the reduction of aldol (*R*)-**4** with diisobutylaluminium hydride DIBAL-H and tetramethylammonium triacetoxyborohydride [$Me_4NBH(OAc)_3$] produced (ds ≥ 95% in both cases) *syn*-



3 X = O ; (*E*)-**8**, X = CH·C(O)-Th

Fig. 1

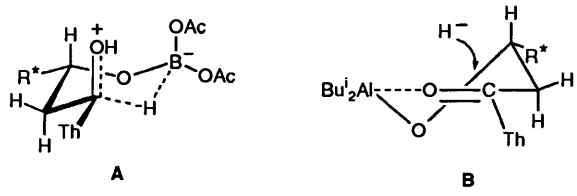


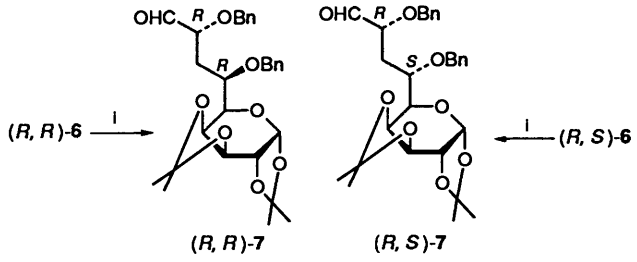
Fig. 2

and *anti*-1,3-diol epimers, respectively, which were isolated as the *O*-benzyl ethers (*S*,*R*)-**6** (90%) and (*R*,*R*)-**6** (96%). The structure of compound (*R*,*R*)-**6** was established by X-ray crystallography (see below). The *anti* 1,3-diol unit in this compound was expected on the basis of a stereochemical model,[12] suggesting that the reduction of (*R*)-**4** with the borohydride reducing agent[13] $Me_4NBH(OAc)_3$ should occur *via* intramolecular-hydride delivery in the chair-like chelate structure **A** involving an oxygen–boron bond (Fig. 2). On the other hand the *syn*-selectivity for the reduction of aldol (*R*)-**4** with DIBAL-H is consistent with an external hydride attack on the half-chair chelate structure **B** involving an oxygen–

aluminium bond.[14] It is worth mentioning that we have already exploited these hydroxy-directed stereocontrolled reductions of β-hydroxy ketones for the construction of 1,3-polyol chains.[15]

The β-benzyloxy group affected only rather weakly the asymmetric reduction of the carbonyl group of compound (*S*)-**5**. With either $LiAlH_4$ or DIBAL-H in the presence of lithium iodide (THF at −78 °C), the reaction was moderately selective (ds 76–78% by ^1H NMR spectroscopy) and gave rise to a mixture of *syn* and *anti* alcohols which were isolated as the *O*-benzyl ethers (*R*,*S*)-**6** (72%) and (*S*,*S*)-**6** (20%). The assignment of the configuration to the major isomer (*R*,*S*)-**6** was based on the assumption[16] that the reduction of (*S*)-**5** occurred with *syn* selectivity *via* an external hydride delivery on the less hindered face of the carbonyl conformer shown in Scheme 2. The stabilization of this conformer by β-chelation of the carbonyl and ether oxygens with lithium cation can be assumed. On the other hand, the reduction of (*R*)-**5** under the above conditions was essentially unselective, giving rise to a mixture of alcohols in 55:45 ratio. After benzylation, the NMR spectrum of the mixture superimposed on that of a mixture of bis ethers (*S*,*R*)-**6** and (*R*,*R*)-**6**. This correlation confirmed that the configuration of the newly formed stereocentre of the minor product obtained from the dialdose **3** *via* the Wittig–Michael route *B* is identical with that of the major product formed *via* the aldol condensation route *A*.

Having prepared four galactose derivatives bearing stereoisomeric thiazol-2-yl-1,3-dibenzyloxypropyl units at C-5, their equivalence to nonodialdoses was demonstrated by the formyl group unmasking of two of them. Thus, the application of the original one-pot thiazole-to-formyl deblocking protocol[17] to compounds (*R*,*R*)-**6** and (*R*,*S*)-**6** afforded the corresponding protected nonodialdoses (*R*,*R*)-**7** and (*R*,*S*)-**7** in good isolated yields (Scheme 4). It is worth pointing out that further chain



Scheme 4 *Reagents and conditions:* i, MeI, MeCN, reflux; then $NaBH_4$, MeOH, 0 °C; then $HgCl_2$, aq. MeCN, room temp.

elongation of these compounds is feasible by either process (*A* and *B*) or any other thiazole-based methodology.[1]

Crystal Structure of Ketone (*S*)-**5** *and Bis ether* (*R*,*R*)-**6**. Fig. 3 shows the ORTEP[18] drawings of the two molecules studied by X-ray diffraction, and Table 1 compares the most relevant structural parameters of these compounds. As shown in Scheme 3, both C(6) and C(4) in the side-chain of bis ether (*R*,*R*)-**6** have the *R* configuration, while the C(6) of (*S*)-**5** has the *S* configuration. In both compounds the galactopyranosyl moiety shows the *R* configuration at C(7), C(11) and C(13) and *S* at C(8) and C(10) according to the chirality of the common precursor D-galactose used in the syntheses. The absolute configuration of these stereocentres is in agreement with the Flack's index values (see Experimental section and Table 2).

The C(3)···C(7) carbon-atom chain is strictly planar in compound (*R*,*R*)-**6**, the maximum displacement from the least-squares plane being 0.010(5) Å for C(4). On the other hand, the same chain is deformed from planarity at the thiazole end in compound (*S*)-**5** as it appears that C(3) is 0.568(3) Å out of the least-squares plane through C(4), C(5), C(6) and C(7). This deformation is very likely to arise as a consequence of the π-conjugation between the heterocyclic ring and the carbonyl, as indicated by the small value [4.2(4)°] of the S–C(3)–C(4)–O(1) torsion angle. A value as large as 57.8(7)° is observed in compound (*R*,*R*)-**6** where conformational freedom exists about the C(3)–C(4) bond. In both cases the orientation of the thiazole ring places the sulfur on the same side of the carbonyl oxygen. The contact distance between these atoms is shorter when the ring is conjugated with the carbonyl [S···O(1) is 2.964(2) in (*S*)-**5** and 3.151(4) Å in (*R*,*R*)-**6**].

As expected, the thiazole ring is planar; π-conjugation with the carbonyl exerts some influence on the endocyclic bond distances not involving sulfur that become significantly longer, and on the exocyclic C(3)–C(4) bond that becomes shorter for compound (*S*)-**5**. Unfortunately, the degree of accuracy in the analysis of (*R*,*R*)-**6** is much lower than that of (*S*)-**5**, so these differences cannot be discussed in more depth, although the observed trend is quite well defined.

The conformation of the pyranose ring is a twist with two local pseudo-two-fold axes, one running along the mid-points of the C(7)–O(6) and C(10)–C(11) bonds and the other along the C(8)···C(19) direction. The puckering parameters[19] of the three rings of the sugar moiety, as set out in Table 3, are in acceptable good agreement for the two compounds.

All the benzyloxy substituents in both compounds show extended conformations with the C(ar)–CH_2 bond antiperiplanar with respect to the O–C (side-chain) bond. The conformation about the C(6)–C(7) bond is such as to have the O(7)–C(6) bond of the O(7)-benzyloxy substituent, antiperiplanar to O(6)–C(7) in (*R*,*R*)-**6** [O(6)–C(7)–C(6)–O(7) = 174.1(4)°], and synclinal [72.4(2)°] in (*S*)-**5**.

Experimental

M.p.s were taken using a Büchi 510 apparatus and are uncorrected. The ^1H and ^{13}C NMR spectra were recorded on a 300 MHz Gemini 300 Varian spectrometer unless otherwise stated. Chemical shifts are given in parts per million downfield from $SiMe_4$ as internal standard. *J* Values are given in Hz. IR spectra were recorded on a Perkin-Elmer Model 297 grating spectrometer. Elemental analyses were performed on a Model 1106 microanalyser (Carlo Erba). Optical rotations were measured at ~20 °C using a Perkin-Elmer Model 214 polarimeter, and are given in units of 10^{-1} deg cm^2 g^{-1}. TLC was carried on glass slides precoated with silica gel (Merck Kieselgel 60 F254), and preparative chromatography on columns of silica gel (Merck 70–230 mesh). All experiments were carried out with freshly distilled and dried solvents.

6,7-*Dideoxy*-1,2:3,4-*di*-O-*isopropylidene*-8-(*thiazol*-2-*yl*)-α-D-galacto-*oct*-6-*enodialdo*-1,5-*pyranose* (*E*)-**8**.—To a well stirred solution of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose[20] **3** (2.48 g, 9.6 mmol) in $CHCl_3$ (100 cm^3) was added triphenyl(thiazol-2-ylcarbonylmethylene)phosphorane[1,3] **2** (4 g, 10.3 mmol) and the reaction mixture was stirred for 24 h at 50 °C and then for an additional 60 h at room temperature. The solvent was evaporated off under reduced pressure and the residue was chromatographed (hexane–diethyl ether 4:1) to give the *alkenes* (*Z*)-**8** and (*E*)-**8**.

Z-**8**: (0.2 g, 6%), oil (Found: C, 55.5; H, 5.7; N, 3.6. $C_{17}H_{21}NO_6S$ requires C, 55.6; H, 5.8; N, 3.8%); $[\alpha]_D$ −129.7 (*c* 1.18, $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 1.32 (3 H, s), 1.34 (3 H, s), 1.49 (3 H, s) 1.57 (3 H, s), 4.37 (1 H, dd, *J* 2.4 and 5.1), 4.63 (1 H, dd, *J* 1.9 and 7.9), 4.70 (1 H, dd, *J* 2.4 and 7.9), 5.53 (1 H, ddd, *J*, 1.6, 1.9 and 7.1), 5.58 (1 H, d, *J* 5.1), 6.53 (1 H, dd, *J* 7.1 and 11.9), 7.49 (1 H, dd, *J* 1.6 and 11.9), 7.68 (1 H, d, *J* 3.0)

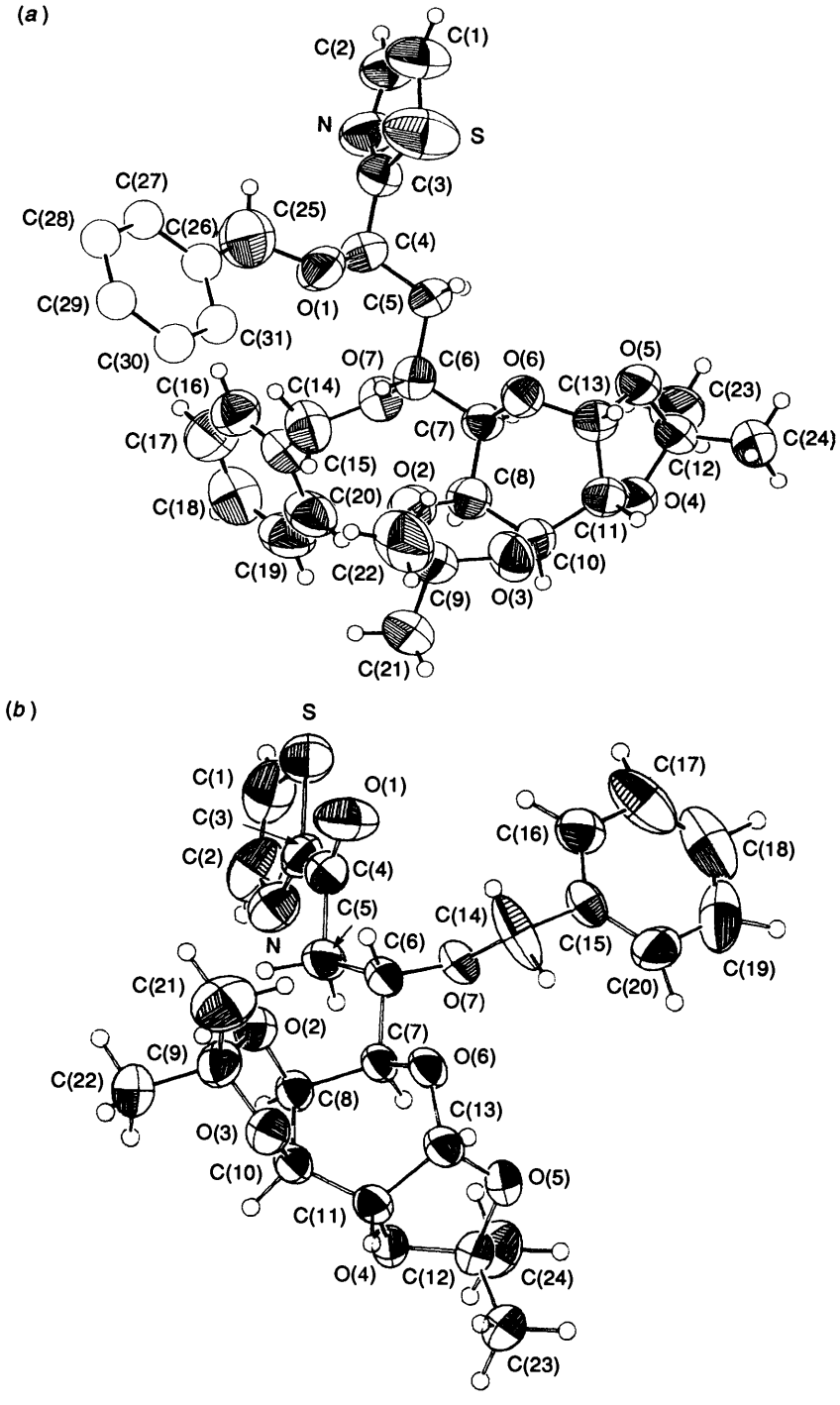


Fig. 3 ORTEP drawings of the molecules of compounds (*a*) (*R,R*)-**6** and (*b*) (*S*)-**5**, showing the atom labelling assumed for the crystal structure analysis. Ellipsoids at 50% probability level.

and 8.02 (1 H, d, *J* 3.0); δ_C(75.5 MHz; $CDCl_3$) 24.10, 24.78, 25.76, 25.82, 66.46, 70.24, 71.15, 73.17, 96.56, 109.11, 109.57, 122.32, 126.84, 145.27, 149.40, 168.82 and 182.96.

E-**8**: (3.0 g, 85%), m.p. 140–141 °C (Found: C, 55.5; H, 5.9; N, 4.0%); $[\alpha]_D$ −119.0 (*c* 0.63, $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 1.01 (3 H, s), 1.09 (3 H, s), 1.32 (3 H, s), 1.36 (3 H, s), 3.81 (1 H, dd, *J* 2.2 and 7.8), 4.13 (1 H, dd, *J* 2.4 and 4.9), 4.40 (1 H, dd, *J* 2.4 and 7.8), 4.54 (1 H, ddd, *J* 2.1, 2.2 and 3.9), 5.53 (1 H, d, *J* 4.9), 6.56 (1 H, d, *J* 3.0), 7.46 (1 H, d, *J* 3.0), 7.52 (1 H, dd, *J* 15.8 and 3.9) and 8.04 (1 H, dd, *J* 15.8 and 2.1); δ_C(75.5 MHz; $CDCl_3$) 23.91, 24.17, 25.55, 25.61, 68.13, 70.68, 71.15, 72.78, 96.71, 108.37, 109.58, 125.30, 125.94, 144.71, 145.11, 168.83 and 181.70.

6-O-*Benzyl*-7-*deoxy*-1,2:3,4-*di*-O-*isopropylidene*-8-(*thiazol*-2-*yl*)-β-L-glycero-D-galacto-*octodialdo*-1,5-*pyranose* (*S*)-**5** *and* α-D-glycero-*epimer* (*R*)-**5**.—To a well stirred suspension of NaH (0.38 g of a 60% dispersion in mineral oil, 9.5 mmol) in THF (15 cm^3) at room temperature was added anhydrous benzyl alcohol (1.08 g, 10 mmol). The mixture was refluxed for 30 min, then was cooled to −50 °C and a solution of enone (*E*)-**8** (0.95 g, 2.59 mmol) in THF (40 cm^3) was added at such a rate that the temperature inside the flask remained constant at −50 °C. After being stirred for 8 h at −50 °C, the reaction mixture was partitioned between saturated aq. NH_4Cl and diethyl ether. The organic layer was dried, and evaporated

Table 1 Comparison of selected bond distances (Å), bond angles (°) and torsion angles (°). Esds in parentheses

Compound	(*R*,*R*)-**6**	(*S*)-**5**	Compound	(*R*,*R*)-**6**	(*S*)-**5**
S–C(1)	1.692(12)	1.696(4)	S–C(3)	1.701(5)	1.707(3)
O(1)–C(4)	1.386(6)	1.211(3)	O(1)–C(25)	1.457(11)	
O(2)–C(8)	1.430(6)	1.423(3)	O(2)–C(9)	1.426(9)	1.425(3)
O(3)–C(9)	1.424(7)	1.422(3)	O(3)–C(10)	1.423(5)	1.417(3)
O(4)–C(11)	1.419(5)	1.424(3)	O(4)–C(12)	1.426(6)	1.428(3)
O(5)–C(12)	1.423(8)	1.438(3)	O(5)–C(13)	1.404(5)	1.410(3)
O(6)–C(7)	1.428(5)	1.442(3)	O(6)–C(13)	1.403(7)	1.399(3)
O(7)–C(6)	1.432(5)	1.429(3)	O(7)–C(14)	1.428(6)	1.406(3)
N–C(2)	1.343(13)	1.380(4)	N–C(3)	1.301(9)	1.294(4)
C(1)–C(2)	1.289(11)	1.340(6)	C(3)–C(4)	1.467(10)	1.463(4)
C(4)–C(5)	1.482(10)	1.509(4)	C(5)–C(6)	1.519(8)	1.516(3)
C(6)–C(7)	1.510(9)	1.515(3)	C(7)–C(8)	1.501(9)	1.526(3)
C(8)–C(10)	1.542(9)	1.534(3)	C(9)–C(21)	1.484(10)	1.492(4)
C(9)–C(22)	1.517(9)	1.514(4)	C(10)–C(11)	1.510(6)	1.504(3)
C(11)–C(13)	1.522(9)	1.529(3)	C(12)–C(23)	1.501(7)	1.506(4)
C(12)–C(24)	1.533(8)	1.511(4)	C(14)–C(15)	1.528(7)	1.491(4)
C(1)–S–C(3)	90.7(4)	89.4(2)	C(4)–O(1)–C(25)	112.4(4)	
C(8)–O(2)–C(9)	109.5(4)	108.6(2)	C(9)–O(3)–C(10)	108.2(3)	106.5(2)
C(11)–O(4)–C(12)	106.9(3)	107.2(2)	C(12)–O(5)–C(13)	110.0(3)	110.8(2)
C(7)–O(6)–C(13)	113.3(3)	114.7(2)	C(6)–O(7)–C(14)	114.6(4)	115.2(2)
C(2)–N–C(3)	111.2(6)	110.1(3)	S–C(1)–C(2)	108.8(7)	110.4(3)
N–C(2)–C(1)	117.6(10)	115.1(3)	S–C(3)–N	111.6(4)	114.9(2)
N–C(3)–C(4)	126.7(6)	124.3(2)	S–C(3)–C(4)	121.7(5)	120.7(2)
O(1)–C(4)–C(3)	111.0(4)	119.6(2)	C(3)–C(4)–C(5)	114.6(6)	117.8(2)
O(1)–C(4)–C(5)	105.9(4)	122.6(2)	C(4)–C(5)–C(6)	115.2(5)	112.2(2)
O(7)–C(6)–C(5)	110.2(4)	105.1(2)	C(5)–C(6)–C(7)	113.3(5)	112.4(2)
O(7)–C(6)–C(7)	106.1(4)	110.2(2)	O(6)–C(7)–C(6)	107.4(4)	106.9(2)
C(6)–C(7)–C(8)	114.4(5)	114.2(2)	O(6)–C(7)–C(8)	109.3(4)	109.0(2)
O(2)–C(8)–C(7)	109.3(4)	109.0(2)	C(7)–C(8)–C(10)	113.9(5)	112.9(2)
O(2)–C(8)–C(10)	104.2(4)	104.3(2)	O(2)–C(9)–O(3)	103.1(5)	104.8(2)
O(3)–C(9)–C(22)	109.3(4)	110.7(2)	O(3)–C(9)–C(21)	112.0(5)	110.2(2)
O(2)–C(9)–C(22)	107.2(5)	109.1(2)	O(2)–C(9)–C(21)	110.2(5)	108.7(2)
C(21)–C(9)–C(22)	114.3(7)	113.1(2)	O(3)–C(10)–C(8)	103.1(4)	104.5(2)
C(8)–C(10)–C(11)	114.2(4)	115.1(2)	O(3)–C(10)–C(11)	108.5(3)	109.3(2)
O(4)–C(11)–C(10)	106.7(3)	107.5(2)	C(10)–C(11)–C(13)	115.8(4)	114.2(2)
O(4)–C(11)–C(13)	104.3(4)	103.3(2)	O(4)–C(12)–O(5)	104.9(5)	104.2(2)
O(5)–C(12)–C(24)	109.0(4)	108.9(2)	O(5)–C(12)–C(23)	110.9(4)	110.3(2)
O(4)–C(12)–C(24)	110.5(4)	108.5(2)	O(4)–C(12)–C(23)	109.6(4)	111.3(2)
C(23)–C(12)–C(24)	111.8(4)	113.2(2)	O(6)–C(13)–C(11)	114.4(5)	114.6(2)
O(5)–C(13)–C(11)	104.8(4)	104.0(2)	O(5)–C(13)–O(6)	110.5(3)	111.3(2)
O(7)–C(14)–C(15)	106.2(4)	108.8(2)	C(14)–C(15)–C(20)	120.3(7)	121.9(3)
C(14)–C(15)–C(16)	121.6(6)	119.1(3)			
C(25)–O(1)–C(4)–C(3)	67.2(7)		C(4)–C(5)–C(6)–C(7)	−179.4(5)	177.4(2)
C(7)–O(6)–C(13)–O(5)	75.1(5)	79.5(2)	C(5)–C(6)–C(7)–C(8)	174.5(4)	−49.8(2)
C(13)–O(6)–C(7)–C(6)	−165.2(4)	−168.1(2)	C(6)–C(7)–C(8)–O(2)	−44.9(6)	−43.5(2)
C(14)–O(7)–C(6)–C(5)	−147.2(5)	147.0(2)	O(3)–C(10)–C(11)–O(4)	165.7(4)	169.9(2)
S–C(3)–C(4)–C(5)	−62.2(7)	−177.2(2)	C(8)–C(10)–C(11)–O(4)	−80.0(5)	−72.9(2)
C(3)–C(4)–C(5)–C(6)	−179.1(5)	153.1(2)			

under reduced pressure. Chromatography (silica gel; hexane–diethyl ether 4:1) afforded the β-*hydroxy ketones* (*R*)-**5** and (*S*)-**5**.

(*R*)-**5**: (0.086 g, 18%), oil (Found: C, 60.7; H, 6.3; N, 3.1. $C_{24}H_{29}NO_7S$ requires C, 60.6; H, 6.15; N, 2.95%); $[\alpha]_D$ −27.9 (*c* 0.38, $CHCl_3$); δ_H(300 MHz; C_6D_6) 1.28 (3 H, s), 1.35 (3 H, s), 1.45 (3 H, s) 1.52 (3 H, s), 3.47 (1 H, dd, *J* 7.8 and 17.0), 3.64 (1 H, dd, *J* 3.7 and 17.0), 3.82 (1 H, dd, *J* 1.7 and 9.0), 4.26 (1 H, dd, *J* 2.4 and 5.0), 4.41 (1 H, ddd, *J* 3.7, 7.8 and 9.0), 4.45 (1 H, dd, *J* 1.7 and 8.0), 4.59 (1 H, dd, *J* 2.4 and 8.0), 4.66 (1 H, d, *J* 10.9), 4.67 (1 H, d, *J* 10.9), 5.48 (1 H, d, *J* 5.0), 7.18–7.28 (5 H, m), 7.63 (1 H, d, *J* 3.2) and 7.98 (1 H, d, *J* 3.2); δ_C(75.5 MHz; C_6D_6) 24.18, 24.70, 25.79, 25.85, 41.42, 69.13, 70.48, 70.84, 70.95, 73.55, 74.30, 96.56, 108.82, 109.28, 126.22, 127.84, 128.36, 128.54, 138.91, 145.07, 168.19 and 193.07

(*S*)-**5**: (0.86 g, 70%), m.p. 120–121 °C (Found: C, 60.4; H, 6.4; N, 2.9%); $[\alpha]_D$ −87.5 (*c* 0.72, $CHCl_3$); δ_H(300 MHz; C_6D_6) 1.32 (3 H, s), 1.36 (3 H, s), 1.48 (3 H, s), 1.54 (3 H, s), 3.47 (1 H, dd, *J* 3.4 and 16.8), 3.70 (1 H, dd, *J* 9.3 and 16.8), 4.06 (1 H, dd, *J* 1.8 and 7.4), 4.34 (1 H, dd, *J* 2.4 and 5.1), 4.38 (1 H, dd, *J* 1.8 and 8.0), 4.44 (1 H, ddd, *J* 3.4, 7.4 and 9.3), 4.63 (1 H, dd, *J* 2.4 and 8.0), 4.69 (1 H, d, *J* 11), 4.89 (1 H, d, *J* 11), 5.62 (1 H, d, *J* 5.1), 7.18–7.43 (5 H, m), 7.66 (1 H, d, *J* 3.2) and 7.99 (1 H, d, *J* 3.2); δ_C (75.5 MHz; C_6D_6) 24.12, 24.76, 25.74, 25.81, 40.23, 69.24, 70.57, 70.93, 71.15, 73.97, 75.67, 96.58, 108.86, 109.63, 126.22, 127.56, 128.30, 128.36, 139.37, 145.01, 168.10 and 192.38.

(6*S*,8*S*)-6,8-*Di*-O-*benzyl*-7-*deoxy*-1,2:3,4-*di*-O-*isopropylidene*-8-(*thiazol*-2-*yl*)-D-threo-α-D-galacto-*octopyranose* (*S*,*S*)-**6** *and Epimer* (*R*,*S*)-**6**.—A well stirred solution of compound (*S*)-**5** (0.2 g, 0.42 mmol) and LiI (0.064 g, 0.46 mmol) in anhydrous diethyl ether (15 cm^3) was cooled to −78 °C and DIBAL-H (1 cm^3 of a 1.5 mol dm^{-3} solution in toluene, 1.5 mmol) was added. After the mixture had been stirred for 1 h at −78 °C, ethyl acetate (2 cm^3) was added and the reaction mixture was partitioned between saturated aq. sodium hydrogen carbonate and diethyl ether. The organic layer was dried over sodium sulfate and the solvent was evaporated under reduced pressure. The residue (0.2 g) was shown by ^1H

Table 2 Experimental data for the X-ray analyses

Compound	(*R*,*R*)-**6**	(*S*)-**5**
Formula	$C_{31}H_{37}NO_7S$	$C_{24}H_{29}NO_7S$
M	566.7	475.6
Space group	$P3_12_1$	$P2_12_12_1$
a/Å	10.310(5)	22.453(3)
b/Å	10.310(5)	12.151(1)
c/Å	52.101(10)	9.220(1)
V/Å^3	4796(3)	2515.5(5)
Z	6	4
D_x/Mg m^{-3}	1.177	1.256
Reflections for lattice parameters: number	27	30
θ range/°	13/27	20/38
F(000)	1806	1008
T/K	292(2)	292(2)
Crystal size/mm	0.13 × 0.37 × 0.77	0.34 × 0.39 × 0.44
μ/mm^{-1}	1.223	1.502
Scan speed/deg min^{-1}	3–12	3–12
Scan width/°	1.2 + 0.35 tan θ	1.2 + 0.35 tan θ
θ-range for intensity collection/°	4.9/70.1	3.9/70.2
h-range	10/12	−27/27
k-range	−12/0	0/14
l-range	−63/10	−7/11
Standard reflection	−3 23 3	2 3 5
Intensity variation	none	none
No. of measured reflections	9745	5307
No. of unique reflections	6102	4783
R(int)	0.0573	0.0141
No. of reflections used in the refinement[a] (*N*)	6074	4778
No. of reflections omitted ($\Delta/\sigma > 5$)	28	5
No. of reflections with $I > 2\sigma(I)$	2074	3040
No. of refined parameters (*P*)	329	307
Extinction parameter (SHELXL),[b] *q*	0.0065(8)	0.0066(2)
Max. LS shift to esd ratio	−0.044	−0.001
Min/max height in final $\Delta\rho$ map e Å^{-3}	−0.17/0.26	−0.13/0.14
$wR2 = [\Sigma w(\Delta F^2)^2/\Sigma w(F_o^2)^2]^{1/2}$	0.1424	0.0790
*wR*2 for all data	0.2336	0.0892
$S2 = [\Sigma w(\Delta F^2)^2/(N - P)]^{1/2}$	1.104	0.977
$R1 = \Sigma\|\Delta F\|/\Sigma\|F_o\|$ for $I > 2\sigma(I)$	0.0621	0.0364
*R*1 for all data	0.1779	0.0671
Flack *x* parameter	0.00(5)	−0.02(2)
g ($w = 1/[\sigma^2(F_o^2) + (gP)^2]$ where $P = (F_o^2 + 2F_c^2)/3$)	0.0871	0.0363

[a] Refinement on F^2 for all reflections except those flagged for possible systematic errors. The observed threshold $I > 2\sigma(I)$ is used only for calculating *R*(obs), *etc.* given here for comparison with refinements on *F*. [b] $F_c^* = kF_c[1 + 0.001\ F_c^2\lambda^3/\sin(2\theta)]^{-1/4}$.

Table 3 Puckering parameters for the sugar moieties

	(*R*,*R*)-**6**	(*S*)-**5**
Ring O(6), C(7), C(8), C(10), C(11), C(3)		
q_2	0.607(4) Å	0.625(2) Å
q_3	−0.132(4) Å	0.101(2) Å
Q_T	0.622(4) Å	0.633(2) Å
φ	−149.0(4)°	−145.8(2)°
θ	102.3(4)°	99.2(2)°
conformation	half chair	half chair
Ring C(9), O(2), C(8), C(10), O(3)		
q	0.306(5) Å	0.305(2) Å
φ	161.8(9)°	−163.2(4)°
conformation	half chair	half chair
Ring C(12), O(4), C(11), C(13), O(5)		
q	0.282(4) Å	0.300(2) Å
φ	29.4(8)°	9.0(4)°
conformation	envelope–half chair	half chair–envelope

NMR spectroscopy to be a mixture of two diastereoisomers in a 78:22 ratio. This material was dissolved in dimethylformamide (6 cm^3), cooled to 0 °C and NaH (50 mg of a 60% dispersion in mineral oil, 1.25 mmol) was added. After 20 min at 0 °C the (stirred) reaction mixture was treated with benzyl bromide (0.09 g, 0.53 mmol) and was stirred at room temperature for another 12 h. The reaction mixture was poured into water (30 cm^3) and extracted with diethyl ether. The organic layer was dried over sodium sulfate, and evaporated under reduced pressure. Chromatography (silica gel; hexane–diethyl ether 7:3) afforded *compounds* (*S*,*S*)-**6** and (*R*,*S*)-**6**.

(*S*,*S*)-**6**: (0.048 g, 20%), oil (Found: C, 65.2; H, 6.6; N, 2.6.

$C_{31}H_{37}NO_7S$ requires C, 65.5; H, 6.7; N, 2.6%); $[\alpha]_D$ −36.4 (*c* 0.45, $CHCl_3$); δ_H(300 MHz; C_6D_6) 1.28 (3 H, s), 1.31 (3 H, s), 1.45 (3 H, s), 1.50 (3 H, s), 2.05 (1 H, ddd, *J* 2.8, 10.9 and 14.1), 2.28 (1 H, ddd, *J* 2.7, 10.3 and 14.1), 3.87 (1 H, dd, *J* 1.8 and 7.6), 4.08 (1 H, ddd, *J* 2.7, 7.6 and 10.9), 4.21 (1 H, dd, *J* 1.8 and 7.9), 4.28 (1 H, dd, *J* 2.4 and 5.0), 4.29 (1 H, d, *J* 11.4), 4.39 (1 H, d, *J* 11.1), 4.53 (1 H, dd, *J* 2.4 and 7.9), 4.55 (1 H, d, *J* 11.4), 4.91 (1 H, d, *J* 11.1), 5.08 (1 H, dd, *J* 2.8 and 10.3), 5.59 (1 H, d, *J* 5.0), 7.19–7.37 (1 H, m) and 7.73 (1 H, d, *J* 3.2); δ_C(75.5 MHz; C_6D_6) 24.16, 24.76, 25.76, 25.81, 38.53, 70.60, 70.89, 71.14, 71.49, 72.07, 73.38, 75.06, 75.71, 96.62, 108.80, 109.57, 119.32, 127.56, 127.95, 128.19, 128.31, 128.47, 128.61, 138.36, 139.64, 142.88 and 174.66.

(*R*,*S*)-**6**: (0.172 g, 72%), oil (Found: C, 65.6; H, 6.6; N, 2.5%); $[\alpha]_D$ −38.8 (*c* 0.85, $CHCl_3$); δ_H(300 MHz; C_6D_6) 1.30 (3 H, s), 1.34 (3 H, s), 1.37 (3 H, s), 1.50 (3 H, s), 2.35 (2 H, m), 3.69 (1 H, m), 4.00 (1 H, dd, *J* 1.9 and 7.6), 4.30 (1 H, dd, *J* 2.4 and 5.0), 4.34 (1 H, d, *J* 11.0), 4.38 (1 H, dd, *J* 1.9 and 8.0), 4.53 (2 H, s), 4.57 (1 H, dd, *J* 2.4 and 8.0), 4.58 (1 H, d, *J* 11.0), 5.19 (1 H, dd, *J* 6.9 and 7.2), 5.59 (1 H, d, *J* 5.0), 7.23–7.48 (11 H, m) and 7.80 (1 H, d, *J* 3.2); δ_C(75.5 MHz; C_6D_6) 24.17, 24.72, 25.66, 25.80, 38.50, 65.76, 70.50, 70.88, 71.17, 71.60, 71.96, 73.44, 76.12, 96.50, 108.71, 109.31, 119.59, 127.53, 127.94, 128.21, 128.32, 128.42, 128.63, 138.13, 139.62, 142.68 and 174.00.

6,8-*Di*-O-*benzyl*-1,2:3,4-*di*-O-*isopropylidene*-β-L-erythro-D-galacto-*nonodialdo*-1,5-*pyranose* (*R*,*S*)-**7**.—A solution of the thiazole derivative (*R*,*S*)-**6** (0.15 g, 0.26 mmol) in freshly distilled acetonitrile (5 cm^3) was treated with methyl iodide (2.2 g, 15.5 mmol) and the reaction mixture was refluxed under nitrogen for 24 h. The solvent was evaporated under reduced pressure, and the residue was dissolved in methanol (10 cm^3) and treated with $NaBH_4$ (50 mg, 1.3 mmol). After the mixture had been stirred for 15 min at room temperature it was evaporated under reduced pressure and the residue was partitioned between CH_2Cl_2 and saturated aq. sodium hydrogen carbonate. The organic layer was separated, dried over sodium sulfate, and the solvent was distilled under reduced pressure. The residue was dissolved in acetonitrile (2 cm^3) and then treated with a solution of $HgCl_2$ (90 mg, 0.33 mmol) in a 4:1 mixture of acetonitrile–water (3 cm^3). After being stirred for 15 min at room temperature the mixture was distilled to dryness under reduced pressure, the residue was treated with aq. potassium iodide (10 cm^3), and the mixture was extracted with chloroform (3 × 10 cm^3). The organic layers were combined, dried over sodium sulfate, and evaporated under reduced pressure. Chromatography (silica gel; hexane–diethyl ether 3:2) yielded the *aldehyde* (*R*,*S*)-**7** (0.11 g, 82%) as an oil (Found: C, 67.9; H, 7.2. $C_{29}H_{36}O_8$ requires C, 68.2; H, 7.1%); $[\alpha]_D$ −51.6 (*c* 0.79, $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 1.24 (3 H, s), 1.26 (3 H, s), 1.37 (3 H, s), 1.42 (3 H, s), 1.94–2.05 (1 H, m), 2.18–2.29 (1 H, m), 3.81–3.95 (3 H, m), 4.19–4.26 (2 H, m), 4.45 (1 H, d, *J* 10.8), 4.51 (1 H, m), 4.57 (2 H, m), 4.79 (1 H, d, *J* 10.8), 5.51 (1 H, d, *J* 5.1), 7.14–7.35 (10 H, m) and 9.45 (1 H, d, *J* 0.9); δ_C(75.5 MHz; $CDCl_3$) 24.23, 24.71, 25.76, 25.84, 32.04, 70.47, 70.87, 71.30, 71.84, 72.12, 73.40, 74.82, 80.32, 96.48, 108.82, 109.50, 127.66, 127.90, 128.19, 128.46, 128.69, 128.76, 138.68, 139.19 and 203.05.

7-*Deoxy*-1,2:3,4-*di*-O-*isopropylidene*-8-(*thiazol*-2-*yl*)-α-D-glycero-D-galacto-*octodialdo*-1,5-*pyranose* (*R*)-**4**.—To a well stirred solution of *tert*-butyl alcohol (0.74 g, 10 mmol) in anhydrous THF (15 cm^3) was added, drop by drop, butyllithium (10.24 mmol, 6.4 cm^3 of a 1.6 mol dm^{-3} solution in hexane) at room temperature. The mixture was stirred for 30 min, before being cooled to −50 °C, and a solution of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose[20] **3** (2.58 g, 10 mmol) and 2-acetylthiazole **1** (1.3 g, 10.24 mmol) in anhydrous THF (40 cm^3) was added drop by drop. After 2 h at −50 °C, the mixture was treated with saturated aq. NH_4Cl (40 cm^3), stirred for 10 min, and then allowed to warm to room temperature. Water (20 cm^3) was added, and the two liquid layers were separated. The aqueous layer was extracted with diethyl ether (4 × 25 cm^3). The combined organic layers were dried over sodium sulfate, and the solvent was evaporated under reduced pressure. Chromatography (silica gel; hexane–diethyl ether 1:1) yielded the *aldol adduct* (*R*)-**4** (2.23 g, 58%, ds > 95%) as an oil (Found: C, 52.9; H, 6.2; N, 3.9. $C_{17}H_{23}NO_7S$ requires C, 53.0; H, 6.0; N, 3.6%); $[\alpha]_D$ −60.5 (*c* 0.39, $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 1.27 (3 H, s), 1.35 (3 H, s), 1.44 (3 H, s), 1.49 (3 H, s), 3.35 (1 H, dd, *J* 8.7 and 17.4), 3.55 (1 H, d, *J* 5.6), 3.62 (1 H, dd, *J* 2.7 and 17.4), 3.73 (1 H, dd, *J* 1.9 and 8.7), 4.30 (1 H, dd, *J* 2.4 and 5.1), 4.40 (1 H, dddd, *J* 2.7, 5.2, 8.7 and 8.7), 4.51 (1 H, dd, *J* 1.9 and 8.0), 4.63 (1 H, dd, *J* 2.4 and 8.0), 5.51 (1 H, d, *J* 5.1), 7.69 (1 H, d, *J* 3.2) and 8.01 (1 H, d, *J* 3.2); δ_C(75.5 MHz; $CDCl_3$) 24.17, 24.66, 25.70, 25.76, 42.63, 66.68, 69.39, 70.56, 70.74, 73.62, 96.58, 108.83, 109.56, 126.61, 145.18, 167.54 and 194.34.

(6*R*,8*S*)-6,8-*Di*-O-*benzyl*-7-*deoxy*-1,2:3,4-*di*-O-*isopropylidene*-8-(*thiazol*-2-*yl*)-α-D-erythro-D-galacto-*octopyranose* (*S*,*R*)-**6**.—The method described above for the reduction of compound (*S*)-**5**, but without LiI, was applied to compound (*R*)-**4** (100 mg, 0.26 mmol) to give, after column chromatography (silica gel; hexane–diethyl ether 7:3) pure *title compound* (*S*,*R*)-**6** (0.132 g, 90%, ds > 95%) as an oil (Found: C, 65.3; H, 6.4; N, 2.3. $C_{31}H_{37}NO_7S$ requires C, 65.5; H, 6.7; N, 2.6%); $[\alpha]_D$ − 63.6 (*c* 0.81, $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 1.28 (3 H, s), 1.32 (3 H, s), 1.40 (3 H, s), 1.47 (3 H, s), 2.28 (1 H, dt, *J* 6.7 and 14.4), 2.40 (1 H, ddd, *J* 4.4, 7.2 and 14.4), 3.70–3.83 (2 H, m), 4.24 (1 H, dd, *J* 2.3 and 5.0), 4.41 (1 H, dd, *J* 1.8 and 8.0), 4.50–4.70 (5 H, m), 5.09 (1 H, t, *J* 7.0), 5.47 (1 H, d, *J* 5.0), 7.20–7.38 (11 H, m) and 7.74 (1 H, d, *J* 3.0); δ_C(75.5 MHz; $CDCl_3$) 24.12, 24.62, 25.69, 25.72, 40.28, 66.80, 70.02, 70.52, 70.81, 71.56, 72.79, 74.15, 76.75, 96.54, 108.66, 109.02, 119.48, 127.71, 127.87, 128.32, 128.46, 128.64, 128.83, 138.32, 139.07, 142.63 and 174.43.

(6*R*,8*R*)-6,8-*Di*-O-*benzyl*-7-*deoxy*-1,2:3,4-*di*-O-*isopropylidene*-8-(*thiazol*-2-*yl*)-β-L-threo-D-galacto-*octopyranose* (*R*,*R*)-**6**.—To a solution of tetramethylammonium triacetoxyborohydride (1.7 g, 6.4 mmol) in acetonitrile (4 cm^3) was added anhydrous acetic acid (4 cm^3). The mixture was stirred at room temperature for 30 min, then cooled to −40 °C and a solution of compound (*R*)-**4** (0.35 g, 0.91 mmol) was added. The reaction mixture was stirred at −40 °C for 24 h, then aq. 1 mol dm^{-3} sodium potassium tartrate (5 cm^3) was added. The reaction mixture was allowed to warm to room temperature and partitioned between ethyl acetate and saturated aq. sodium hydrogen carbonate. The organic layer was dried over sodium sulfate and evaporated under reduced pressure to give the crude diol (0.33 g, 94%) which, according to ^1H NMR spectroscopy, was at least 95% diastereomerically pure. Benzylation as described above afforded, after column chromatography (silica gel; hexane–diethyl ether 7:3) pure *bis ether* (*R*,*R*)-**6** (0.41 g, 96%, ds > 95%), m.p. 118–120 °C (Found: C, 65.3; H, 6.6; N, 2.3%) $[\alpha]_D$ +0.58 (*c* 1.55, $CHCl_3$); $[\alpha]_D$ +6.35 (*c* 1.15, MeOH); δ_H(300 MHz; $CDCl_3$) 1.24 (3 H, s), 1.32 (3 H, s), 1.41 (3 H, s), 1.45 (3 H, s), 1.90 (1 H, ddd, *J* 2.9, 10.1 and 14.6), 2.44 (1 H, ddd, *J* 2.5, 10.6 and 14.6), 3.58 (1 H, dd, *J* 1.5 and 9.1), 4.0 (1 H, ddd, *J* 2.5, 9.1 and 10.1), 4.22 (1 H, dd, *J* 1.8 and 4.5), 4.26–4.35 (2 H, m), 4.38 (1 H, dd, *J* 1.5 and 7.2), 4.51–4.65 (3 H, m), 5.06 (1 H, dd, *J* 2.9 and 10.6), 5.49 (1 H, d, *J* 5.1), 7.18–7.36 (11 H, m) and 7.69 (1 H, d, *J* 3.2); δ_C(75.5 MHz; $CDCl_3$) 24.14, 24.61, 25.77, 25.81, 42.15, 68.88, 69.90, 70.53, 70.85, 71.20, 73.57, 73.86, 75.95, 96.62, 108.57, 109.16, 119.54, 127.78, 127.98, 128.11, 128.38, 128.60, 128.79, 138.19, 139.18, 142.61 and 174.89.

6,8-*Di*-O-*benzyl*-7-*deoxy*-1,2:3,4-*di*-O-*isopropylidene*-β-L-threo-D-galacto-*nonodialdo*-1,5-*pyranose* (*R*,*R*)-**7**.—The method described above for the conversion of compound (*R*,*S*)-**6** into the nonodialdose (*R*, *S*)-**7** was applied to compound (*R*,*R*)-**6** (170 mg, 0.3 mmol) to give, after column chromatography (silica gel; hexane–diethyl ether 2:3), the *aldehyde* (*R*,*R*)-**7** (110 mg, 72%) as an oil (Found: C, 68.3; H, 6.9. $C_{29}H_{36}O_8$ requires C, 68.2; H, 7.1%); $[\alpha]_D$ −0.4 (*c* 1.02, $CHCl_3$); δ_H(300 MHz; $CDCl_3$) 1.28 (3 H, s), 1.33 (3 H, s), 1.45 (3 H, s), 1.47 (3 H, s), 1.81 (1 H, ddd, *J* 4.0, 9.3 and 14.7), 2.22 (1 H, ddd, *J* 2.2, 9.4 and 14.7), 3.66 (1 H, dd, *J* 1.6 and 8.8), 3.88 (1 H, dt, *J* 2.9 and 8.8), 4.01 (1 H, ddd, *J* 2.2, 4.0 and 9.5), 4.26 (1 H, dd, *J* 2.2 and 5.0), 4.40 (1 H, m), 4.35 (1 H, d, *J* 11.6), 4.41 (1 H, d, *J* 11.8), 4.59 (1 H, m), 4.61 (1 H, d, *J* 11.8), 4.64 (1 H, d, *J* 11.6), 5.50 (1 H, d, *J* 5.0), 7.20–7.40 (10 H, m) and 9.61 (1 H, d, *J* 2.2); δ_C(75.5 MHz; $CDCl_3$) 24.06, 24.56, 25.73, 25.80, 33.01, 69.57, 70.48, 70.79, 71.10, 72.14, 73.22, 73.75, 80.73, 96.56, 108.60, 109.19, 127.88, 127.93, 128.27, 128.38, 128.63, 128.70, 137.84, 138.77 and 203.54.

Reduction of Compound (R)-**5**.—The reduction of compound (*R*)-**5** (0.12 g) as described above for diastereoisomer (*S*)-**5** afforded a 55:45 mixture (^{1}H NMR) of diastereoisomeric alcohols (0.12 g). Benzylation as described above gave a 56:44 mixture of dibenzyl derivatives whose ^{1}H NMR spectrum was superposable on those bis ethers (*S*,*R*)-**6** and (*R*,*R*)-**6**.

X-Ray Crystallography.—The relevant data for the crystal-structure analyses are summarized in Table 2. The lattice parameters were determined using Cu-Kα_1 radiation (λ = 1.540 562 0 Å) and refined by a least-squares procedure[21] using the Nelson and Riley[22] extrapolation function. The integrated intensities were measured on a Siemens-AED diffractometer with Cu-Kα mean radiation, using the θ–2θ scan mode and a modified version[23] of the Lehmann and Larsen[24] peak-profile analysis procedure. All reflections were corrected for Lorentz and polarization effects; no correction for absorption was considered.

The structure of compound (*S*)-**5** was solved by the direct methods of SHELXS-86,[25] while attempts to solve the structure of compound (*R*,*R*)-**6** by means of the commonly used direct-method programs failed. This structure was solved by using the new version of program SIR (SIR92)[26] which succeeded in giving a partially refined structure (*R* = 0.11) excepting the C(26)···C(31) phenyl ring which, afterwards, turned out to be highly disordered.

Both structures were refined by full-matrix least-squares on *F* using SHELX-76,[27] and on F^2 using SHELXL-92[28] programs. The two types of refinement gave final results not significantly different so all the data of Table 2 and the structural parameters of Table 1 as well as those discussed in the text are from the F^2 refinements. The hydrogen atoms were located in calculated positions riding on the attached carbon atoms, and the disordered phenyl of compound (*R*,*R*)-**6** was treated as a rigid body with calculated geometry and high isotropic displacement parameters. This disorder, giving intensity data of poor quality, is responsible for the difficulties encountered in solving the structure of compound (*R*, *R*)-**6** and the relatively low accuracy of the results obtained from its refinement. No attempt was made to define the disorder, this probably being a rotational one about the C(25)–C(26) bond.

The absolute configurations were assigned on the basis of Flack's[29] index and on the known chirality of the galactose ring.

All calculations were carried out on the ENCORE-91 and POWERNODE-6040 computers of the 'Centro di Studio per la Strutturistica Diffrattometrica del C.N.R. (Parma)'. In addition to the above programs, PARST[30] was used for the calculations concerning the geometrical aspects of the crystal structures.

Atomic scattering factors and anomalous-scattering coefficients were taken from the International Tables for X-Ray Crystallography.[31] The final atomic coordinates, fractional coordinates for all atoms, bond lengths, bond angles, and torsional angles have been deposited at the Cambridge Crystallographic Data Centre.*

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* See 'Instructions for Authors', *J. Chem. Soc., Perkins Trans. 1*, 1994, issue 1.

References

1 A. Dondoni, *Carbohydrate Synthesis via Thiazoles*, in *Modern Synthetic Methods*, ed. R. Scheffold, Verlag Helvetica Chimica Acta, Basel, 1992, p. 377; *Bull. Soc. Chim. Belg.*, 1992, **101**, 433.
2 A. Dondoni and P. Merino, *J. Org. Chem.*, 1991, **56**, 5294; A. Dondoni, P. Merino and J. Orduna, *Tetrahedron Lett.*, 1991, **32**, 3247.
3 A. Dondoni, A. Marra and P. Merino, *J. Am. Chem. Soc.*, 1994, **116**, in the press.
4 A. M. Sepulchre, A. Gateau-Olesker, G. Lukacs, G. Vass, S. D. Gero and W. Voelter, *Tetrahedron Lett.*, 1972, 3945; P. Coutrot, C. Grison, M. Tabyaoui, S. Czernecki and J.-M. Valéry, *J. Chem. Soc., Chem. Commun.*, 1988, 1515; S. Czernecki and J.-M. Valéry, *J. Carbohydr. Chem.*, 1988, **7**, 151; A. Dondoni, G. Fantin, M. Fogagnolo and P. Merino, *J. Carbohydr. Chem.*, 1990, **9**, 735; Ph. Maillard, C. Huel and M. Momenteau, *Tetrahedron Lett.*, 1992, **33**, 8081.
5 S. J. Danishefsky and M. P. DeNinno, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 15; J. S. Brimacombe, in *Studies in Natural Product Chemistry*, ed. A.-ur Rahman, Elsevier, Amsterdam, 1989, vol. 4, part C, p. 157.
6 For the convenient use of % diastereoselectivity (ds) instead of % diastereoisomeric excess (de), see: S. Thaisrivongs and D. Seebach, *J. Am. Chem. Soc.*, 1983, **105**, 7407.
7 B. E. Maryanoff and A. B. Reitz, *Chem. Rev.*, 1989, **89**, 863.
8 For reviews on the so-called Cram's Rule see: E. L. Eliel, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, New York, 1983, vol. 2, part A, p. 125; J. Mulzer, H.-J. Altenbach, M. Braun, K. Krohn and H.-U. Reissig. *Organic Synthesis Highlights*, VCH Verlagsgesellschaft, Weinheim, 1991, p. 3.
9 S. J. Danishefsky, W. H. Pearson, D. F. Harvey, C. J. Maring and J. P. Springer, *J. Am. Chem. Soc.*, 1985, **107**, 1256; S. J. Danishefsky, M. P. DeNinno, G. B. Phillips, R. E. Zelle and P. A. Lartey, *Tetrahedron*, 1986, **42**, 2809; A. Dondoni, G. Fantin, M. Fogagnolo and A. Medici, *Tetrahedron*, 1987, **43**, 3533; A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici and P. Pedrini, *J. Org. Chem.*, 1989, **54**, 693.
10 S. J. Danishefsky, C. J. Maring, M. R. Barbachyn and B. E. Segmuller, *J. Org. Chem.*, 1984, **49**, 4564.
11 A. Dondoni, A. Boscarato and A. Marra, *Synlett*, 1993, 256.
12 For recent articles with leading references on the reduction of β-hydroxy ketones to either *syn* or *anti* 1,3-diols see: D. A. Evans, K. T. Chapman and E. M. Carreira, *J. Am. Chem. Soc.*, 1988, **110**, 3560; D. A. Evans and A. H. Hoveyda, *J. Org. Chem.*, 1990, **55**, 5190; D. A. Evans, J. A. Gauchet-Prunet, E. M. Carreira and A. B. Charette, *J. Org. Chem.*, 1991, **56**, 741.
13 For a review of the uses of acyloxyborohydrides in synthesis see: G. W. Gribble and C. F. Nutaitis, *Org. Prep. Proced. Int.*, 1985, **17**, 317.
14 S. Kiyooka, H. Kuroda and Y. Shimasaki, *Tetrahedron Lett.*, 1986, **27**, 3009.

15 A. Dondoni and P. Merino, *Synthesis*, 1993, 903.
16 Y. Mori, M. Kuhara, A. Takeuchi and M. Suzuki, *Tetrahedron Lett.*, 1988, **29**, 5419.
17 For an improved procedure see: A. Dondoni, A. Marra and D. Perrone, *J. Org. Chem.*, 1993, **58**, 275.
18 C. K. Johnson, ORTEP, Report ORNL-3794, Oak Ridge National Laboratory, Tennessee, 1965.
19 D. Cremer and J. A. Pople, *J. Am. Chem. Soc.*, 1975, **97**, 1354.
20 R. F. Butterworth and S. Hanessian, *Synthesis*, 1971, 70.
21 M. Nardelli and A. Mangia, *Ann. Chim. (Rome)*, 1984, **74**, 163.
22 J. B. Nelson and D. P. Riley, *Proc. Phys. Soc. London*, 1945, **57**, 160, 477.
23 D. Belletti, F. Ugozzoli, A. Cantoni and G. Pasquinelli, Internal Report, March 1, 1979, Centro di Studio per la Strutturistica Diffrattometrica del C.N.R., Parma, Italy, 1979.
24 M. S. Lehmann and F. K. Larsen, *Acta Crystallogr., Sect. A*, 1974, **30**, 580.
25 G. M. Sheldrick, SHELXS-86, Program for Crystal Structure Solution, University of Göttingen, Germany, 1986.
26 G. Giacovazzo, private communication.
27 G. M. Sheldrick SHELXL-76, Program for Crystal Structure Determination, University of Göttingen, Germany, 1976.
28 G. M. Sheldrick, SHELXS-92, Program for Crystal Structure Refinement, University of Cambridge, England, 1992.
29 H. D. Flack, *Acta Crystallogr., Sect. A*, 1983, **39**, 876.
30 M. Nardelli, *Comput. Chem.*, 1983, **7**, 95.
31 *International Tables for X-ray Crystallography*, Kynoch Press (Present Distributor Kluver Academic Publishers, Dordrecht), 1974, vol. 4, pp. 99 and 149.

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