Construction of All *O*-Alkoxy D-Tetrose and D-Pentose Stereoisomers from 2,3-*O*-Isopropylidene-D-glyceraldehyde Using 2-(Trimethylsilyl)thiazole as a Formyl Anion Equivalent

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Dedicated to Prof. H. Taniguchi (Kyushu Univ.) on the occasion of his 60th birthday.

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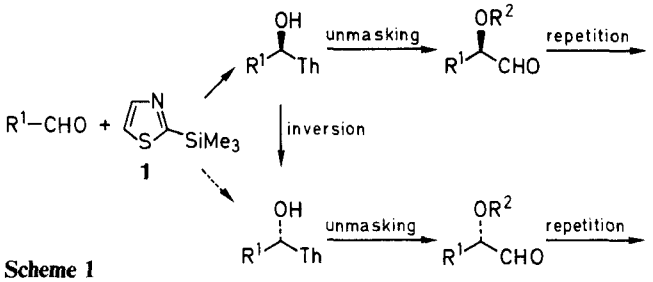
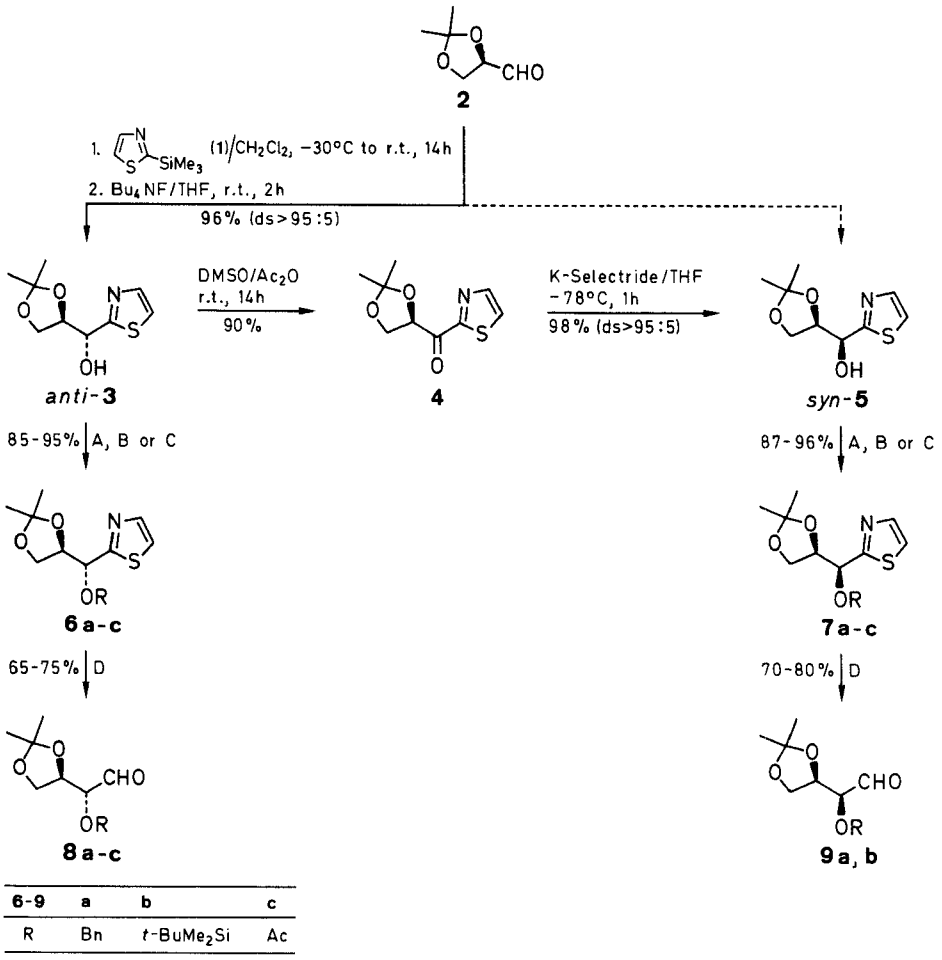
All D-tetroses and D-pentoses having differentially protected hydroxy groups are synthesized by an iterative one-carbon chain-elongation cycle commencing with the addition of 2-(trimethylsilyl)thiazole to 2,3-*O*-isopropylidene-D-glyceraldehyde. One half of the resulting secondary alcohol is epimerized by an oxidation–reduction sequence. The aldehydes are revealed from the two diastereomeric alcohols by thiazole-to-formyl conversion.

The search for new methodologies for the construction of chiral building blocks in high chemical yields and enantiomeric purity is a main topic in organic synthesis.[1] Either approach based on internal (substrate control) or external (reagent control)[2] asymmetric induction in carbon–carbon bond formation has its own validity that depends on several factors such as the availability of the starting material from natural sources (chiral pool)[3] and the extent of transmission of chirality in the former, the availability of asymmetric reagents and catalysts and their efficiency in the latter. In both cases the iterative use of a reaction sequence consisting of few key transformations appears of great relevance since it allows to construct in a stepwise fashion differentially protected polyfunctional chiral units. This approach offers several advantages over the methods employing natural products as advanced chiral educts[4] where selective functional group elaborations may require numerous protection–deprotection operations. Outstanding examples of iterative strategies are the homologations of aldehydes by olefination–epoxidation (Masamune–Sharpless)[2,5] and cyclocondensation (Danishefsky).[6] A variety of other methods have been also reported from different laboratories.[7] Our own method[8,9] consists of the substate control iterative one-carbon chain-elongation of aldehydes by addition of the formyl anion synthon using 2-(trimethylsilyl)thiazole (2-TST) **(1)** as its synthetic equivalent (Thiazole Route) (Scheme 1). Since the addition of **1** to chiral α,β-dialkoxy aldehydes occurs with *anti*-selectivity according to the Felkin–Ahn model,[10] a direct access to *syn*-diastereoisomers has been so far precluded. This limitation was overcome by inversion of the configuration of the hydroxy group in the *anti*-alcohol by an oxidation–reduction sequence.[11] Hence, this extended thiazole-mediated strategy should in principle provide access to all possible polyalkoxy higher homologues of a given chiral aldehyde. Having decided to investigate the scope and limit of this methodology, we report here the chain extention of 2,3-*O*-isopropylidene-D-glyceraldehyde **(2)** to all four- and five-carbon higher homologues having differentially protected hydroxy groups. Improved conditions are described for the hydroxy group inversion and it is demonstrated that the thiazole-to-formyl deblocking sequence is tolerant of a wide range of hydroxy protecting groups.



Scheme 1

The first cycle of the sequence was initiated by addition of 2-TST **(1)** to 2,3-*O*-isopropylidene-D-glyceraldehyde **(2)** as described[8] to afford, after in situ desilylation with tetrabutylammonium fluoride, the alcohol *anti*-**3** (ds 95%) in 96% isolated yield (Scheme 2). This reaction was performed on 0.05 mole scale of the aldehyde[12] **2** to obtain 10 g quantities of **3** without difficulty. On the other hand, the oxidation of similar quantities of **3** with potassium permanganate in the presence of the phase transfer agent tris[2-(2-methoxyethoxy)ethyl]amine (TDA-1)® according to our earlier procedure,[11] gave the ketone **4** in modest yield (30–35%). Therefore, this reaction was more conventiently carried out by Albright–Goldman oxidation[13] using acetic anhydride/dimethyl sulfoxide to give **4** in 90% yield after chromatography. The K-Selectride® (potassium tri-*sec*-butylborohydride) reduction of the ketone **4** afforded the inverted alcohol *syn*-**5** (ds 95%)[11] which was isolated in almost quantitative yield. The excellent yields of both reactions and the high level of diastereoselectivity of the latter as well as the execution of the entire sequence on a large scale confirmed the efficiency of this oxidation–reduction method for the epimerization of the α-hydroxyalkylthiazole *anti*-**3**. On the other hand, application of the Mitsunobu inverting esterification[14] to *anti*-**3** failed as reported for similar systems wherein an oxidation–reduction strategy had to be employed.[15,16] The alcohols *anti*-**3** and *syn*-**5** were protected as the *O*-benzyl, *O*-*tert*-butyldimethylsilyl, and *O*-acetyl derivatives **6a–c** and **7a–c**, respectively, from which the corresponding aldehydes **8a–c** (D-erythroses) and **9a,b** (D-threoses) were released by cleavage of the thiazole ring using our standard one-pot procedures[8,12] involving *N*-methylation (with methyl iodide), sodium borohydride-reduction, and mercury(II) chloride assisted hydrolysis. This result demonstrates that the unmasking sequence can be carried out in the presence of three hydroxy protecting groups very different in nature to give differentially protected polyhydroxy aldehydes. The use of the *O*-benzyl derivatives **8a** and **9a**, prepared from D-arabinose and dimethyl D-tartrate, respectively, for the synthesis of modified sugars of biological relevance has been recently described.[17,18]



6-9	a	b	c
R	Bn	*t*-BuMe$_2$Si	Ac

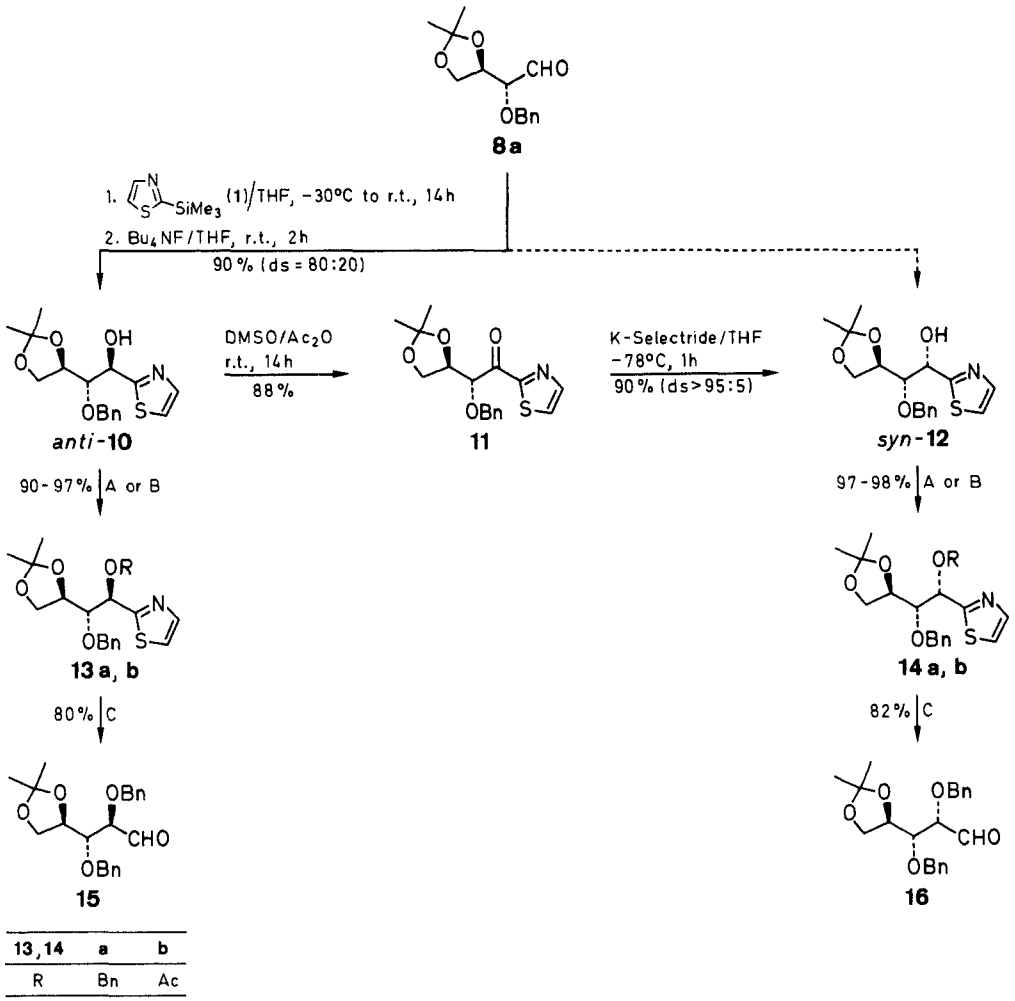
A: 1. NaH/THF, reflux, 20 min; 2. Bu_4NI/BnBr/THF, r.t., 14 h.
B: Ac_2O/Py/DMAP, r.t., 14 h.
C: *t*-$BuMe_2SiCl$/imidazole/DMF, 70 °C, 45 min.
D: 1. MeI/MeCN, reflux, 7–14 h; 2. $NaBH_4$/MeOH, r.t., 30 min; 3. $HgCl_2$/MeCN/H_2O, r.t., 20 min.

Scheme 2

Following the concept outlined in Scheme 1, the above sequence was repeated starting from the protected D-erythrose **8a** (Scheme 3). The formation of *anti*-**10** (Felkin product)[10] as the major stereoisomer from the addition of 2-TST (**1**) to **8a** has been already demonstrated by X-ray crystallography.[8] However, unlike the yield, the quoted diastereoselectivity (ds 95%) could not be duplicated as we now obtained *anti*-**10** and *syn*-**12** in a 80 : 20 ratio. This and other inconveniences were already pointed out for this reaction in our earlier reports.[8] On the other hand, the inverting oxidation–reduction sequence of *anti*-**10** to *syn*-**12** occurred with good yields (ca. 90%) and level of diastereoselectivity (ds ≥ 95%). After protection of the epimer alcohols *anti*-**10** and *syn*-**12** as the *O*-benzyl and *O*-acetyl derivatives **13a,b** and **14a,b**, the application of the thiazole-to-formyl deblocking sequence converted **13a** and **14a** into the tetralkoxy pentanal **15** (D-ribose) and **16** (D-arabinose). The optical rotations of these aldehydes compared quite well with the literature values.[19,20] Interesting enough, compound **15** has been used as a key intermediate for the synthesis of the pheromone *endo*-brevicomin[20] and **16** as the precursor to *C*-disaccharides.[21]

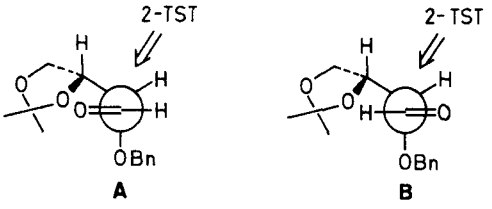
We next turned our attention toward the chain-extension of the D-threose derivative **9a** and quite surprisingly observed that the addition of 2-TST (**1**) occurred with *syn*-selectivity to give the alcohol *syn*-**17a** (ds 81%) as the major isomer (Scheme 4). The absolute configuration of this product was demonstrated by conversion via the *O*-benzyl derivative **20a** into the tetralkoxy pentanal **22** (D-xylose) by the standard formyl unmasking protocol and comparison of the latter with the product synthesized from natural D-xylose following literature procedures (Scheme 5). ^1H and ^{13}C NMR spectra of these aldehydes were superimposable. Unfortunately, since the compound obtained from the natural sugar showed on TLC some hardly removable impurities, very likely 1,2- and 1,3-*O*-isopropylidene regioisomers,[16] the optical rotations could not be compared.

The main product *syn*-**17a** indicates that the Felkin–Ahn[10] transition state model **A** (1,3-dioxolane ring inside)[24] does not apply to the addition of **1** to **9a** whereas model **B** (1,3-dioxolane ring outside)[24] would account for the observed selectivity. While we now suggest that in **A** a repulsive nonbonded interaction exists between oxygens



A: NaH/THF, reflux, 20 min; 2. Bu_4NI/BnBr/THF, r.t., 14 h.
B: Ac_2O/Py/DMAP, r.t., 14 h.
C: 1. MeI/MeCN, reflux, 7–14 h; 2. $NaBH_4$/MeOH, r.t., 30 min; 3. $HgCl_2$/MeCN/H_2O, r.t., 20 min.

Scheme 3



of the carbonyl and 1,3-dioxolane ring, studies aiming to substantiate this and other hypotheses which can explain the stereoselectivity of this reaction are underway.

With the aim to prepare the last remaining D-pentose having the *lyxo* configuration, the inverting protocol was applied to *syn*-**17a**. The first step using the Albright–Goldman oxidation method[13] provided the ketone **18a** in good isolated yield. On the other hand, the reduction of **18a** using various hydride releasing reagents,[25] eventually in the presence of chelating agents, turned out to be *syn*-selective to give the Felkin–Ahn–Houk alcohol *syn*-**17a** as major product or to be unselective to produce a mixture of *syn*-**17a** and *anti*-**19a** in ca. 1 : 1 ratio although in good overal yield (Table 6). These alcohols could be separated after conversion to their *O*-benzyl derivatives **20a** and **21**, respectively. Then the stereochemical assignment was made by transformation of **21** into the aldehyde **23** (D-lyxose) and comparison with the product prepared from natural D-lyxose by the sequence shown in Scheme 5. These aldehydes showed quite close specific rotations (Table 4) and their ^1H and ^{13}C NMR spectra were superimposable but different from those of **22** as well as of the product prepared from D-xylose.

Having correlated the configurations of aldehydes **22** and **23** to those of D-xylose and D-lyxose, respectively, the unexpected *syn*-selectivity of the addition of 2-TST (**1**) to **9a** was sufficiently demonstrated. This diastereofacial bias was considerably increased by changing the benzyl protecting group with the bulkier *tert*-butyldimethylsilyl. Thus, the addition of **1** to the aldehyde **9b** afforded

Table 1. Addition of 2-TST (1) to Aldehydes

Product	Yield[a] (anti/syn)[b]	mp (°C)[c]	$[\alpha]_D^{20}$ (*c*, $CHCl_3$)	Molecular Formula[d]	^1H NMR ($CDCl_3$/TMS) (300 MHz) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) (75.5 MHz) δ
anti-**3**	96 (≥95 : 5)	114–116	+0.8 (0.79)	$C_9H_{13}NO_3S$ (215.3)	1.40 (s, 3H), 1.47 (s, 3H), 3.59 (br s, 1H, ex. D_2O), 4.00 (m, 2H), 4.45 (m, 1H), 5.07 (d, 1H, *J* = 5.1), 7.30 (d, 1H, *J* = 3.2), 7.73 (d, 1H, *J* = 3.2)	24.10, 25.55, 64.38, 70.75, 77.42, 109.39, 119.12, 141.84, 170.35
anti-**10**	90 (80 : 20)	105–107	+10.7 (0.22)	$C_{17}H_{21}NO_4S$ (335.4)	1.32 (s, 3H), 1.38 (s, 3H), 3.90 (dd, 1H, *J* = 8.5, 6.6), 4.00 (dd, 1H, *J* = 8.5, 6.4), 4.05 (dd, 1H, *J* = 5.3, 4.5), 4.20 (ddd, 1H, *J* = 6.6, 6.4, 5.3), 4.63 (d, 1H, *J* = 11.4), 4.71 (d, 1H, *J* = 11.4), 5.23 (d, 1H, *J* = 4.5), 7.35 (m, 6H), 7.78 (d, 1H, *J* = 3.2)[e]	25.35, 26.34, 66.10, 73.10, 74.57, 76.31, 82.27, 109.37, 119.80, 128.10, 128.19, 128.57, 138.45, 142.36, 171.24
syn-**17a**	92 (19 : 81)	oil	+27.3 (0.33)	$C_{17}H_{21}NO_4S$ (335.4)	1.41 (s, 3H), 1.48 (s, 3H), 3.91 (dd, 1H, *J* = 9.0, 7.5), 4.07 (dd, 1H, *J* = 9.0, 7.0), 4.12 (dd, 1H, *J* = 6.5, 2.0), 4.37 (d, 1H, *J* = 11.6), 4.41 (ddd, 1H, *J* = 7.5, 7.0, 6.5), 4.57 (d, 1H, *J* = 11.6), 5.02 (d, 1H, *J* = 2.0), 7.24 (m, 6H), 7.78 (d, 1H, *J* = 3.2)[e]	24.72, 25.53, 65.19, 71.66, 73.94, 76.52, 80.83, 109.13, 118.98, 127.35, 127.72, 127.86, 137.45, 142.05, 173.85

[a] Yield of isolated products.
[b] Determined by ^1H NMR.
[c] Solvent hexane/Et_2O.
[d] Satisfactory microanalyses obtained: C ±0.35, H ±0.15, N ±0.20.
[e] Solvent $CDCl_3/D_2O$.

Table 2. *O*-Benzyl Ethers

Entry[a]	Yield[b]	$[\alpha]_D^{20}$ (*c*, $CHCl_3$)	Molecular Formula[c]	^1H NMR ($CDCl_3$/TMS) (300 MHz) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) (75.5 Hz) δ
6a	95	+41.3 (0.95)	$C_{16}H_{19}NO_3S$ (305.4)	1.34 (s, 3H), 1.37 (s, 3H), 4.00 (m, 2H), 4.55 (m, 1H), 4.57 (d, 1H, *J* = 11.8), 4.68 (d, 1H, *J* = 11.8), 4.84 (d, 1H, *J* = 5.6), 7.31 (m, 6H), 7.84 (d, 1H, *J* = 3.2)	25.36, 26.50, 66.24, 72.80, 78.63, 79.09, 110.53, 120.59, 128.63, 128.77, 129.11, 138.00, 143.43, 170.49
7a	96	−48.9 (0.47)	$C_{16}H_{19}NO_3S$ (305.4)	1.36 (s, 3H), 1.38 (s, 3H), 4.06 (dd, 1H, *J* = 8.7, 6.5), 4.13 (dd, 1H, *J* = 8.7, 6.1), 4.58 (ddd, 1H, *J* = 6.9, 6.5, 6.1), 4.74 (d, 1H, *J* = 11.8), 4.91 (d, 1H, *J* = 11.8), 4.93 (d, 1H, *J* = 6.9), 7.48 (m, 6H), 7.96 (d, 1H, *J* = 3.1)	24.53, 25.46, 65.12, 71.43, 77.72, 79.22, 119.60, 109.65, 127.46, 127.68, 127.98, 137.07, 142.39, 169.22
13a	90	+75.0 (1.41)	$C_{24}H_{27}NO_4S$ (425.6)	1.28 (s, 3H), 1.31 (s, 3H), 3.88 (m, 2H), 4.08 (m, 2H), 4.54 (d, 1H, *J* = 11.9), 4.69 (d, 1H, *J* = 11.9), 4.73 (d, 1H, *J* = 11.6), 4.90 (d, 1H, *J* = 11.6), 5.10 (d, 1H, *J* = 2.6), 7.34 (m, 11H), 7.82 (d, 1H, *J* = 3.2)	24.40, 25.66, 65.32, 71.72, 73.93, 74.26, 79.31, 81.15, 108.51, 119.56, 127.28, 127.43, 127.47, 127.67, 127.91, 128.06, 137.23, 137.85, 142.17, 169.26
14a	97	−6.95 (1.87)	$C_{24}H_{27}NO_4S$ (425.6)	1.32 (s, 3H), 1.42 (s, 3H), 3.84 (dd, 1H, *J* = 8.0, 6.7), 4.00 (m, 2H), 4.22 (d, 1H, *J* = 11.5), 4.24 (m, 1H), 4.34 (d, 1H, *J* = 11.5), 4.55 (d, 1H, *J* = 11.5), 4.73 (d, 1H, *J* = 11.5), 5.03 (d, 1H, *J* = 3.1), 7.25 (m, 11H), 7.83 (d, 1H, *J* = 3.2)	24.52, 25.77, 65.73, 72.53, 74.44, 75.14, 78.99, 81.77, 108.37, 127.38, 127.67, 127.75, 127.80, 127.83, 127.92, 128.09, 137.04, 137.65, 142.44, 171.45
20a	96	−8.64 (0.59)	$C_{24}H_{27}NO_4S$ (425.6)	1.31 (s, 3H), 1.37 (s, 3H), 3.52 (m, 2H), 3.70 (dd, 1H, *J* = 6.6, 3.8), 4.25 (ddd, 1H, *J* = 7.0, 6.6, 6.5), 4.36 (d, 1H, *J* = 11.7), 4.54 (d, 1H, *J* = 11.5), 4.68 (d, 1H, *J* = 11.7), 4.70 (d, 1H, *J* = 11.5), 4.81 (d, 1H, *J* = 3.8), 7.30 (m, 11H), 7.78 (d, 1H, *J* = 3.2)	25.86, 26.88, 66.17, 72.83, 75.22, 76.47, 79.40, 82.45, 109.98, 120.89, 128.37, 129.01, 129.05, 129.14, 129.39, 129.52, 137.86, 139.07, 143.49, 171.28
21	90	−21.6 (0.80)	$C_{24}H_{27}NO_4S$ (425.55)	1.33 (s, 3H), 1.37 (s, 3H), 3.61 (dd, 1H, *J* = 8.5, 6.7), 3.90 (dd, 1H, *J* = 7.0, 5.4), 3.97 (dd, 1H, *J* = 8.5, 6.4), 4.22 (ddd, 1H, *J* = 7.7, 7.0, 6.4), 4.46 (d, 1H, *J* = 11.6), 4.53 (d, 1H, *J* = 11.4), 4.56 (d, 1H, *J* = 11.4), 4.68 (d, 1H, *J* = 11.6), 4.81 (d, 1H, *J* = 5.4), 7.30 (m, 10H), 7.36 (d, 1H, *J* = 3.2), 7.80 (d, 1H, *J* = 3.2)	25.40, 26.21, 66.22, 71.88, 74.42, 77.09, 79.12, 82.57, 109.04, 120.51, 127.73, 128.19, 128.27, 128.31, 128.40, 128.70, 137.55, 138.53, 142.73, 170.05

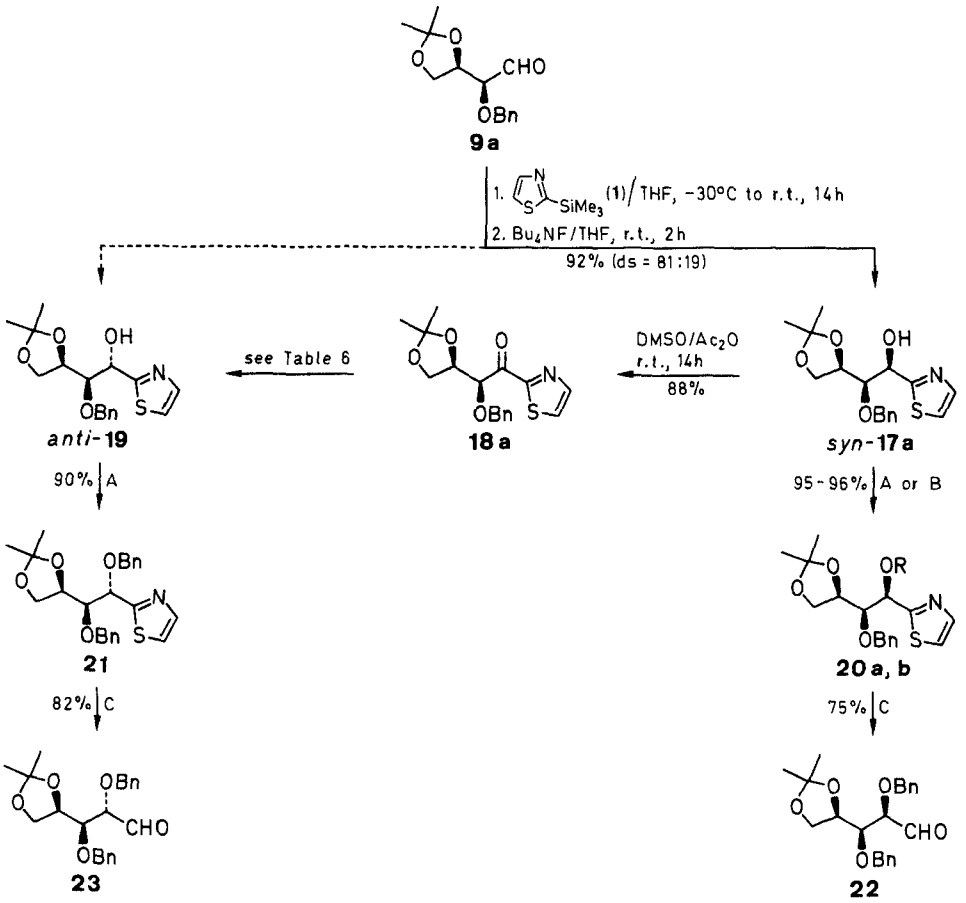
[a] All compounds are oils
[b] Yield of isolated products.
[c] Satisfactory microanalyses obtained: C ±0.40, H ±0.10, N ±0.22.

essentially one diastereoisomer (ds ≥ 95%), i.e. the bis-silylated 1,2-diol *syn*-**24** in 86% isolated yield (Scheme 6). The selective monodesilylation of *syn*-**24** by citric acid in methanol gave the alcohol **17b** which was readily oxidized to the ketone **18b** by the acetic anhydride/dimethyl sulfoxide reagent. As expected,[16] the reduction of this ketone having the carbonyl flanked by the bulky *O*-silyl group was highly selective giving rise to the

Table 3. Acetates

Entry[a]	Yield[b]	$[\alpha]_D^{20}$ (*c*, $CHCl_3$)	Molecular Formula[c]	IR (cm^{-1}) ν (C=O)[d]	^1H NMR ($CDCl_3$/TMS) (300 MHz) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) (75.5 MHz) δ
6c	95	+37.3 (2.20)	$C_{11}H_{15}NO_3S$ (241.3)	1750	1.38 (s, 6H), 2.20 (s, 3H), 4.07 (dd, 1H, *J* = 8.5, 6.2), 4.13 (dd, 1H, *J* = 8.5, 6.8), 4.71 (ddd, 1H, *J* = 6.8, 6.2, 4.5), 6.23 (d, 1H, *J* = 4.5), 7.38 (d, 1H, *J* = 3.2), 7.82 (d, 1H, *J* = 3.2)	19.89, 24.32, 25.39, 64.78, 71.24, 75.82, 109.72, 119.58, 142.59, 165.43, 169.44
7c	96	−32.4 (0.86)	$C_{11}H_{15}NO_3S$ (241.3)	1745	1.38 (s, 3H), 1.47 (s, 3H), 2.21 (s, 3H), 3.98 (dd, 1H, *J* = 9.2, 5.4), 4.06 (dd, 1H, *J* = 9.2, 6.5), 4.66 (ddd, 1H, *J* = 7.2, 6.5, 5.4), 6.26 (d, 1H, *J* = 7.2), 7.38 (d, 1H, *J* = 3.2), 7.80 (d, 1H, *J* = 3.2)	19.91, 24.41, 25.41, 65.33, 72.57, 76.54, 109.93, 119.54, 142.62, 165.67, 169.67
13b	97	+3.3 (0.81)	$C_{19}H_{23}NO_4S$ (361.5)	1750	1.32 (s, 3H), 1.38 (s, 3H), 2.18 (s, 3H), 3.89 (dd, 1H, *J* = 8.0, 5.1), 3.98 (dd, 1H, *J* = 8.0, 5.8), 4.80 (m, 2H), 4.65 (d, 1H, *J* = 10.9), 4.85 (d, 1H, *J* = 10.9), 6.52 (d, 1H, *J* = 2.7), 7.33 (m, 6H), 7.82 (d, 1H, *J* = 3.2)	21.44, 25.63, 26.79, 66.50, 73.94, 74.89, 75.52, 81.11, 110.01, 120.46, 128.77, 128.97, 129.27, 138.61, 143.61, 167.11, 170.31
14b	98	+44.3 (1.50)	$C_{19}H_{23}NO_4S$ (361.5)	1740	1.32 (s, 3H), 1.43 (s, 3H), 2.18 (s, 3H), 3.85 (dd, 1H, *J* = 8.2, 5.0), 3.95 (dd, 1H, *J* = 8.2, 5.6), 4.19 (m, 2H), 4.28 (d, 1H, *J* = 11.3), 4.40 (d, 1H, *J* = 11.3), 6.32 (d, 1H, *J* = 2.7), 7.30 (m, 2H), 7.58 (m, 3H), 7.68 (d, 1H, *J* = 3.2), 7.82 (d, 1H, *J* = 3.2)	19.90, 24.40, 25.74, 65.28, 72.45, 74.52, 74.90, 80.30, 108.77, 119.11, 127.56, 127.71, 128.03, 136.88, 142.64, 167.94, 169.50
20b	95	+25.9 (0.44)	$C_{19}H_{23}NO_4S$ (361.5)	1745	1.31 (s, 3H), 1.42 (s, 3H), 2.16 (s, 3H), 3.91 (dd, 1H, *J* = 8.5, 6.5), 3.96 (dd, 1H, *J* = 8.5, 6.3), 4.08 (dd, 1H, *J* = 6.4, 3.9), 4.15 (t, 1H, *J* = 6.4), 4.52 (d, 1H, *J* = 11.4), 4.62 (d, 1H, *J* = 11.4), 6.27 (d, 1H, *J* = 3.9), 7.16 (m, 2H), 7.25 (m, 3H), 7.33 (d, 1H, *J* = 3.2), 7.77 (d, 1H, *J* = 3.2)	19.81, 24.23, 25.37, 64.92, 71.94, 74.16, 75.21, 79.87, 109.11, 119.18, 127.28, 127.56, 127.86, 137.55, 142.41, 167.10, 169.46

[a] All compounds are oils.
[b] Isolated yields.
[c] Satisfactory microanalyses obtained: C ±0.27, H ±0.18, N ±0.24.
[d] Solvent: $CHCl_3$.



20	a	b
R	Bn	Ac

A: 1. NaH/THF, reflux, 20 min; 2. Bu_4NI/BnBr/THF, r.t., 14 h
B: Ac_2O/Py/DMAP, r.t., 14 h
C: 1. MeI/MeCN, reflux, 7–14 h; 2. $NaBH_4$/MeOH, r.t., 30 min; 3. $HgCl_2$/MeCN/H_2O, r.t. 20 min.

Scheme 4

Table 4. Aldehydes

Entry[a]	Yield[b]	$[\alpha]_D^{20}$ (*c*, $CHCl_3$)	Molecular Formula[c]	IR (cm^{-1}) ν (C=O)[d]	^1H NMR ($CDCl_3$/TMS) (300 MHz) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) (75.5 MHz) δ
8a	70	+29.5 (1.70)	$C_{14}H_{18}O_4$ (250.3)	1730	1.33 (s, 3H), 1.42 (s, 3H), 3.80 (dd, 1H, *J* = 5.8, 1.8), 3.92 (dd, 1H, *J* = 8.5, 5.3), 4.06 (dd, 1H, *J* = 8.5, 6.3), 4.34 (ddd, 1H, *J* = 6.3, 5.8, 5.3), 4.59 (d, 1H, *J* = 11.8), 4.72 (d, 1H, *J* = 11.8), 7.35 (m, 5H), 9.70 (d, 1H, *J* = 1.8)	25.14, 26.50, 66.51, 73.70, 75.37, 83.53, 110.62, 128.80, 128.87, 129.20, 138.12, 202.20
8b	65	−1.5 (0.79)	$C_{13}H_{26}O_4Si$ (274.4)	1720	0.11 (s, 3H), 0.12 (s, 3H), 0.92 (s, 9H), 1.34 (s, 3H), 1.43 (s, 3H), 3.93 (dd, 1H, *J* = 8.5, 5.9), 4.03 (dd, 1H, *J* = 8.5, 6.2), 4.06 (dd, 1H, *J* = 6.1, 1.6), 4.25 (q, 1H, *J* = 6.0), 9.68 (d, 1H, *J* = 1.6)	−5.41, −4.99, 17.90, 24.96, 25.44, 26.30, 65.82, 75.88, 78.04, 110.12, 202.15
8c	75	+45.2 (0.61)	$C_9H_{14}O_5$ (202.2)	1745, 1720	1.34 (s, 3H), 1.43 (s, 3H), 2.17 (s, 3H), 3.96 (dd, 1H, *J* = 8.8, 5.4), 4.11 (dd, 1H, *J* = 8.8, 6.4), 4.40 (ddd, 1H, *J* = 6.4, 6.0, 5.4), 5.04 (dd, 1H, *J* = 6.0, 0.6), 9.63 (d, 1H, *J* = 0.6)	20.09, 24.79, 26.13, 66.07, 74.24, 78.03, 110.86, 170.36, 197.07
9a	80	−14.6 (0.37)	$C_{14}H_{18}O_4$ (250.3)	1720	1.37 (s, 3H), 1.45 (s, 3H), 3.87 (dd, 1H, *J* = 5.4, 1.6), 3.97 (dd, 1H, *J* = 8.9, 5.7), 4.07 (dd, 1H, *J* = 8.9, 6.5), 4.39 (ddd, 1H, *J* = 6.5, 5.7, 5.4), 4.67 (d, 1H, *J* = 12.0), 4.81 (d, 1H, *J* = 12.0), 7.40 (m, 5H), 9.76 (d, 1H, *J* = 1.6)	25.38, 26.42, 65.85, 73.93, 75.94, 83.60, 110.60, 128.98, 129.07, 129.45, 138.02, 203.06
9b	70	+187.1 (0.65)	$C_{13}H_{26}O_4Si$ (274.4)	1720	0.06 (s, 3H), 0.08 (s, 3H), 0.92 (s, 9H), 1.31 (s, 3H), 1.39 (s, 3H), 3.92 (dd, 1H, *J* = 8.8, 6.1), 4.02 (dd, 1H, *J* = 4.8, 1.3), 4.04 (dd, 1H, *J* = 8.8, 6.7), 4.29 (ddd, 1H, *J* = 6.7, 6.1, 4.8), 9.67 (d, 1H, *J* = 1.3)	−5.57, −5.26, 17.86, 24.81, 25.37, 25.73, 65.04, 76.40, 77.80, 109.91, 202.78
15	80	+45.1 (1.20)[e]	$C_{22}H_{26}O_5$ (370.5)	1730	1.32 (s, 3H), 1.34 (s, 3H), 3.73 (dd, 1H, *J* = 8.5, 2.0), 3.88 (dd, 1H, *J* = 8.8, 4.2), 4.09 (dd, 1H, *J* = 8.8, 6.3), 4.14 (dd, 1H, *J* = 2.0, 1.2), 4.38 (ddd, 1H, *J* = 8.5, 6.3, 4.2), 4.50 (d, 1H, *J* = 11.6), 4.62 (d, 1H, *J* = 11.6), 4.72 (d, 1H, *J* = 12.2), 4.83 (d, 1H, *J* = 12.2), 7.33 (m, 10H), 9.73 (d, 1H, *J* = 1.2)	24.19, 25.37, 66.25, 72.10, 72.60, 73.03, 81.63, 81.91, 108.94, 127.59, 127.63, 127.68, 127.72, 128.11, 128.17, 136.87, 137.08, 202.49
16	82	−7.2 (1.00)[f]	$C_{22}H_{26}O_5$ (370.5)	1730	1.33 (s, 3H), 1.42 (s, 3H), 3.94 (dd, 1H, *J* = 8.5, 6.1), 3.98 (dd, 1H, *J* = 6.7, 2.8), 4.06 (dd, 1H, *J* = 2.8, 1.3), 4.09 (dd, 1H, *J* = 8.5, 6.0), 4.30 (ddd, 1H, *J* = 6.7, 6.1, 6.0), 4.58 (m, 2H), 4.68 (d, 1H, *J* = 11.2), 4.78 (d, 1H, *J* = 11.2), 7.40 (m, 10H), 9.78 (d, 1H, *J* = 1.3)	25.59, 26.94, 57.66, 67.27, 74.35, 75.05, 80.62, 84.79, 109.82, 128.86, 128.94, 129.04, 129.19, 129.35, 129.47, 138.12, 138.30, 204.39
22	75	+13.7 (0.60)	$C_{22}H_{26}O_5$ (370.5)	1725	1.35 (s, 3H), 1.43 (s, 3H), 3.68 (dd, 1H, *J* = 8.4, 7.0), 3.76 (dd, 1H, *J* = 5.8, 4.1), 3.81 (dd, 1H, *J* = 8.4, 6.6), 3.87 (dd, 1H, *J* = 4.1, 1.2), 4.42 (ddd, 1H, *J* = 7.0, 6.6, 5.8), 4.50 (d, 1H, *J* = 12.0), 4.67 (d, 1H, *J* = 11.7), 4.74 (d, 1H, *J* = 11.7), 4.81 (d, 1H, *J* = 12.0), 7.35 (m, 10H), 9.74 (d, 1H, *J* = 1.2)	24.85, 25.41, 61.85, 72.59, 73.04, 75.32, 78.69, 81.67, 109.30, 127.56, 127.71, 127.85, 128.03, 128.21, 128.26, 136.30, 137.20, 201.93
23	82	−7.2 (0.50)[g]	$C_{22}H_{26}O_5$ (370.5)	1725	1.34 (s, 3H), 1.39 (s, 3H), 3.82 (m, 2H), 3.93 (dd, 1H, *J* = 4.3, 1.7), 3.98 (dd, 1H, *J* = 8.3, 6.5), 4.29 (m, 1H), 4.53 (d, 1H, *J* = 11.9), 4.69 (d, 1H, *J* = 11.9), 4.70 (d, 1H, *J* = 11.6), 4.71 (d, 1H, *J* = 11.6), 7.34 (m, 10H), 9.69 (d, 1H, *J* = 1.7)	25.33, 26.10, 65.99, 73.01, 73.68, 76.74, 80.02, 83.85, 109.67, 128.14, 128.33, 128.37, 128.46, 128.67, 128.86, 137.34, 138.08, 201.79

[a] All compounds are oils.
[b] Isolated yields.
[c] Satisfactory microanalyses obtained: C ± 0.35, H ± 0.15.
[d] Solvent ($CHCl_3$).
[e] Lit. (Ref. 20) +46.3 (0.72, MeOH)
[f] Lit. (Ref. 19) +6.0 (1.46) for the antipode.
[g] −8.1 (0.51) when prepared from D-lyxose.

monosilylated diol **17b** and its regioisomer **25** in different ratio depending on the reducing agent and solvent employed. Desilylation of these compounds and bis-benzylation of the resulting diol gave a product identical in all respect to **20a** of Scheme 4.

In summary, a methodology has been displayed that employing thiazole as a source of the formyl group enables to extend the chain of the readily available 2,3-*O*-isopropylidene-D-glyceraldehyde (**2**) to give all tetrose and pentose epimers. The method is rather practical and efficient since all reactions occur with good chemical yields and high levels of internal asymmetric induction with one exception only. It has been also shown that the hydroxy groups in the resulting polyhydroxy aldehydes can be differentiated by using different protecting groups, i.e., benzyl, silyl, acetyl. This feature is a prerequisite for selective synthetic elaborations which is not readily met by preparative procedures employing natural products. The method described has shown an unexpected stereochemical outcome that offers the oportunity for future studies on the mechanism and stereochemistry of the addition of 2-TST (**1**) to chiral polyalkoxy aldehydes. A challenging goal is also the

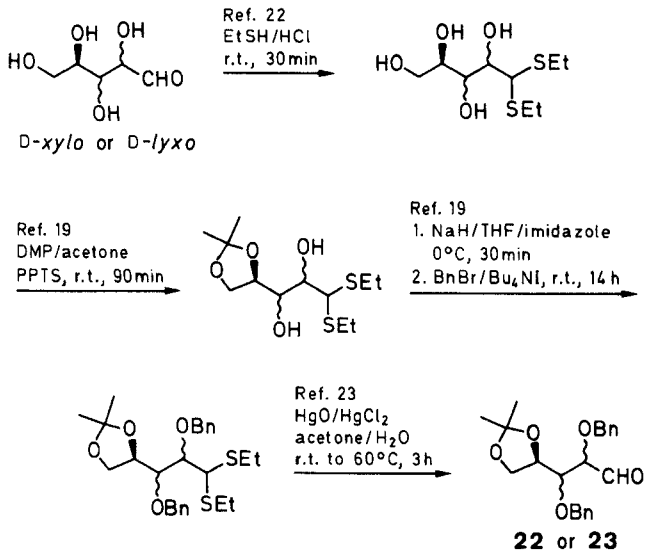
Table 5. Thiazolyl Ketones

Entry	Yield[b]	mp (°C)[b]	$[\alpha]_D^{20}$ (*c*, $CHCl_3$)	Molecular Formula[c]	IR (cm^{-1}) ν (C=O)[d]	^1H NMR ($CDCl_3$/TMS) (300 MHz) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) (75.5 MHz) δ
4	90	70–72	+39.3 (0.56)	$C_9H_{11}NO_3S$ (213.3)	1710	1.50 (s, 3H), 1.55 (s, 3H), 4.18 (dd, 1H, *J* = 8.6, 5.6), 4.59 (dd, 1H, *J* = 8.6, 8.0), 5.62 (dd, 1H, *J* = 8.0, 5.6), 7.75 (d, 1H, *J* = 3.1), 8.05 (d, 1H, *J* = 3.1)	25.65, 25.96, 67.50, 78.37, 111.96, 127.07, 145.78, 165.60, 109.39
11	88	oil[e]	+13.9 (0.31)	$C_{17}H_{19}NO_4S$ (333.4)	1715	1.28 (s, 3H), 1.36 (s, 3H), 4.10 (m, 2H), 4.63 (d, 1H, *J* = 11.7), 4.65 (m, 1H), 4.71 (d, 1H, *J* = 11.7), 5.19 (d, 1H, *J* = 6.8), 7.30 (m, 5H), 7.73 (d, 1H, *J* = 3.2), 8.06 (d, 1H, *J* = 3.2)	24.27, 25.40, 65.75, 72.66, 75.48, 79.79, 109.40, 126.31, 127.61, 127.83, 127.95, 136.72, 144.67, 165.57, 191.54
18a	88	100–102	−22.9 (0.35)	$C_{17}H_{19}NO_4S$ (333.4)	1715	1.31 (s, 3H), 1.32 (s, 3H), 4.05 (m, 2H), 4.55 (d, 1H, *J* = 12.0), 4.76 (m, 1H), 4.83 (d, 1H, *J* = 12.0), 5.25 (d, 1H, *J* = 5.0), 7.30 (m, 5H), 7.72 (d, 1H, *J* = 3.0), 8.04 (d, 1H, *J* = 3.0)	25.81, 26.57, 66.21, 73.94, 77.03, 81.10, 111.04, 127.71, 129.05, 129.30, 129.49, 138.57, 146.12, 167.25, 191.85

[a] Yield of isolated products.
[b] Solvent: hexane/Et_2O.
[c] Satisfactory microanalyses obtained: C ±0.38, H ±0.13, N ±0.18.
[d] Solvent: $CHCl_3$.
[e] Solidifies in freezer.

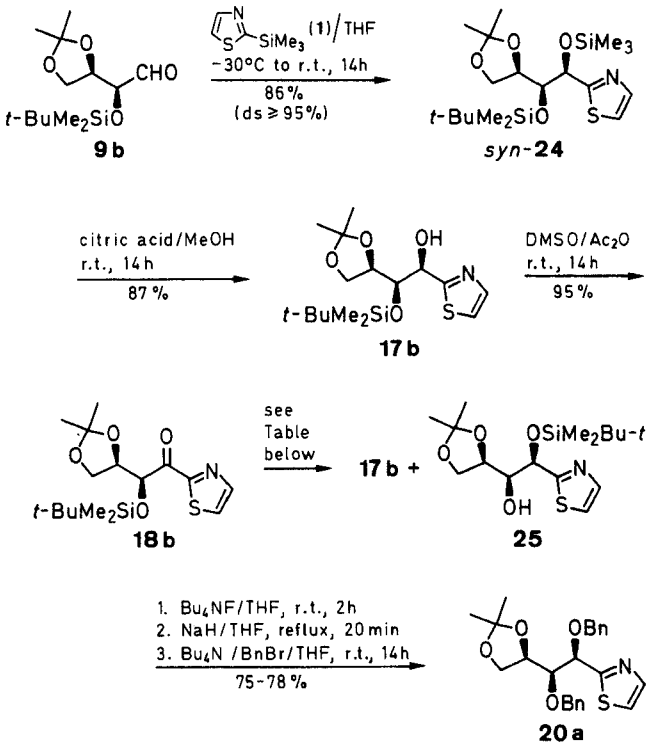
Table 6. Reduction of Ketone **18a**

Reagent	Conditions	**19/17a** Ratio	Yield (%)
K-Selectride	THF/−78°C	< 5 : 95	96
L-Selectride	THF/−78°C	< 5 : 95	95
$NaBH_4$	MeOH/−70°C	20 : 80	90
Red-Al	toluene/0°C	< 5 : 95	87
$Zn(BH_4)_2$	Et_2O/−50°C	< 5 : 95	90
DIBAL-H	THF/−78°C	41 : 59	92
DIBAL-H	Et_2O/−78°C	40 : 60	91
DIBAL-H/$ZnCl_2$	THF/−78°C	21 : 79	86
DIBAL-H/LiI	THF/−78°C	40 : 60	88
LiAl(±-BuO)$_3$H	THF/−78°C	30 : 70	94
LiAl(±-BuO)$_3$H/LiI	THF/−78°C	18 : 82	90
$LiAlH_4$	THF/−78°C	25 : 75	96
$LiAlH_4$	Et_2O/−78°C	44 : 56	100



Scheme 5

iterative repetition of the strategy for the preparation of more extended polyhydroxylated carbon chains.



Reagent	Conditions	**17b/25** Ratio	Yield (%)
K-Selectride (2 mol)	THF/−78°C	40 : 60	90
DIBAL-H (2 mol)	THF/−78°C	23 : 77	87
$NaBH_4$ (2 mol)	MeOH/−70°C	43 : 57	95
$NaBH_4$ (5 mol)	MeOH/−70°C	9 : 91	98

Scheme 6

Melting points were determined on a Büchi SMP-20 apparatus and are uncorrected. IR spectra were obtained on a Perkin-Elmer Model 297 grating spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a 300 MHz Varian Gemini-300 spectrometer using TMS as internal standard. Optical rotations were measured at ca. 20°C using a Perkin-Elmer Model 214 polarimeter. Elemental anyleses were performed on a 1106 Microanalizer (Carlo Erba). Thin layer

chromatography (TLC) used glass-slides precoated with silica gel (Merck Kiesel gel 60 F_{254}), preparative chromatography columns of silica gel (Merck 70–230 mesh) and flash chromatography columns of silica gel (Merck 230–400 mesh). All experiments were carried out under N_2 atmosphere and with freshly distilled and dried solvents. 2-(Trimethylsilyl)thiazole **(1)** was prepared from 2-bromothiazole as described.[12,26] (*R*)-2,3-*O*-Isopropylideneglyceraldehyde **(2)** was synthesized from D-mannitol by oxidation with sodium periodate.[27]

Addition of 2-(Trimethylsilyl)thiazole (1) to Aldehydes; General Procedure:
To a stirred solution of aldehyde (5 mmol) in CH_2Cl_2 or THF (25 mL) at 30 °C, the reagent **1** (1.17 g, 7.5 mmol) in the same solvent (1.5 mL) was slowly added. Stirring was continued for 14 hours at r.t. The solvent was removed in vacuum, the residue dissolved in THF (40 mL) and then Bu_4NF 1 M solution in THF (7.5 mL, 7.5 mmol) was added. After 2 h stirring, the solvent was distilled in vacuo and the residue dissolved in CH_2Cl_2 (40 mL). The solution was washed with H_2O (2 × 20 mL) and the separated organic phase was dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue chromatographed through a short column (silica gel, Et_2O/hexane 3 : 2) to isolate the major adduct (Table 1).

***O*-Benzylation; General Procedure:**
To a solution of the alcohol (4 mmol) in anhydr. THF (50 mL), a 60% suspension of NaH (4.25 mmol) in mineral oil was added at r.t. The mixture was refluxed for 20 min and then Bu_4NI (148 mg, 0.4 mmol) and benzyl bromide (727 mg, 4.25 mmol) were successively added at r.t. The solution was stirred for 14 h, the solvent distilled in vacuum and the residue treated with sat. aq $NaHCO_3$ (40 mL) and extracted with CH_2Cl_2 (2 × 25 mL). The organic phase was dried (Na_2SO_4), the solvent removed under reduced pressure and the residue chromatographed through a short column (silica gel, hexane/Et_2O 3 : 2) to give the pure *O*-benzyl ether (Table 2).

***O*-Silylation; General Procedure:**
To a solution of alcohol (3 mmol) in DMF (2 mL), imidazole (408 mg, 6 mmol) and *t*-$BuMe_2SiCl$ (940 mg, 4.2 mmol) were added. The solution was stirred at 70 °C for 45 min, cooled to r.t., poured into H_2O (100 mL) and extracted with Et_2O (2 × 40 mL). The organic phase was dried (Na_2SO_4), the solvent evaporated and the residue chromatographed through a short column to give the pure *O*-silyl ether (silica gel, hexane/Et_2O 9 : 1).

(1R,2R)-1-O-tert-Butyldimethylsilyl-2,3-O-isopropylidene-1-(2-thiazolyl)-1,2,3-propanetriol **(6b)**: Yield: 85%; oil; $[\alpha]_D^{20}$ + 30.4° (*c* = 1.45, $CHCl_3$).

$C_{15}H_{27}NO_3SSi$	calc.	C 54.67	H 8.26	N 4.25
(329.5)	found	54.48	8.40	4.18

^1H NMR ($CDCl_3$): δ = 0.08 (s, 3 H), 0.13 (s, 3 H), 0.90 (s, 9 H), 1.32 (s, 3 H), 1.41 (s, 3 H), 3.81 (dd, 1 H, *J* = 8.1, 6.6 Hz), 3.98 (dd, 1 H, *J* = 8.1, 6.8), 3.45 (ddd, 1 H, *J* = 6.8, 6.6, 4.2 Hz), 5.17 (d, 1 H, *J* = 4.2 Hz), 7.27 (d, 1 H, *J* = 3.2 Hz), 7.73 (d, 1 H, *J* = 3.2 Hz).

^{13}C NMR ($CDCl_3$): δ = −5.41, −5.21, 18.10, 24.98, 25.47 (3C), 26.15, 64.54, 72.47, 79.37, 109.89, 119.36, 142.98, 173.49.

(1S,2R)-1-O-tert-Butyldimethylsilyl-2,3-O-isopropylidene-1-(2-thiazolyl)-1,2,3-propanetriol **(7b)**: Yield: 87%, oil; $[\alpha]_D^{20}$ −43.3° (*c* = 0.97, $CHCl_3$).

$C_{15}H_{27}NO_3SSi$	calc.	C 54.67	H 8.26	N 4.25
(329.5)	found	54.75	8.32	4.36

^1H NMR ($CDCl_3$): δ = 0.01 (s, 3 H), 0.10 (s, 3 H), 0.89 (s, 9 H), 1.30 (s, 3 H), 1.36 (s, 3 H), 3.90 (dd, 1 H, *J* = 8.8, 6.8 Hz), 4.07 (dd, 1 H, *J* = 8.8, 6.6 Hz), 4.18 (q, 1 H, *J* = 6.7 Hz), 4.98 (d, 1 H, *J* = 6.7 Hz), 7.27 (d, 1 H, *J* = 3.2 Hz), 7.68 (1 H, *J* = 3.2 Hz).

^{13}C NMR ($CDCl_3$: δ = −5.50, −5.15, 17.94, 25.15, 25.44 (3C), 26.09, 65.70, 74.89, 79.54, 108,89, 119.54, 142.68, 173.07.

***O*-Acetylation; General Procedure:**
To a solution of alcohol (1 mmol) in pyridine (2 mL) and Ac_2O (1.5 mL) a catalytic amount of DMAP was added. The solution was stirred for 14 h at r.t. The solvent was removed under reduced pressure and the residue treated with sat. aq $NaHCO_2$ (40 mL) and extracted with Et_2O (2 × 30 mL). The organic phase was dried (Na_2SO_4), the solvent evaporated and the residue chromatographed through a short column to give the pure acetate (silica gel, Et_2O/hexane 1 : 1) (Table 3).

Formyl Deblocking; General Procedure:
The thiazole derivative (3.5 mmol) was treated with MeI (4.97 g, 35 mmol) in MeCN (30 mL). The solution was refluxed until total disappearance of the starting material (7–14 h, TLC monitoring). The solvent was removed under reduced pressure and Et_2O was added to precipitate the thiazolium salt which was filtered and washed with the same solvent.

The salt was dissolved in MeOH (30 mL), and $NaBH_4$ (266 mg, 7 mmol) was added portionwise at r.t. The mixture was stirred for 30 min. The solvent was partially removed under reduced pressure and the residue treated with brine (30 mL) and extracted with CH_2Cl_2 (2 × 20 mL). The separated organic phase was dried (Na_2SO_4) and the solvent removed in vacuum to yield the thiazolidine.

The crude thiazolidine was dissolved in MeCN (10 mL) and added to a solution of $HgCl_2$ (949 mg, 3.5 mmol) in MeCN/H_2O (4 : 1, 40 mL) at r.t. The mixture was stirred for 20 min, filtered through Celite, the filtrate concentrated in vacuum and the residue dissolved in CH_2Cl_2 (50 mL) and washed with 1 M aq KI (2 × 25 mL). The organic phase was dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude aldehyde was purified by column chromatography (silica gel, hexane/Et_2O 3 : 2) (Table 4).

Oxidation; General Procedure:
To a solution of alcohol (2 mmol) in DMSO (9 mL), Ac_2O (4 mL) was slowly added at r.t. The solution was stirred for 14 h and then poured into sat. aq. $NaHCO_3$ (100 mL). Stirring was continued for 30 min at r.t. The mixture was extracted with Et_2O (50 mL), and the organic phase was washed with H_2O (2 × 20 mL), and then dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue chromatographed through a short column (silica gel, hexane/Et_2O, 3 : 2) to give the pure ketone (Table 5).

Reduction with K-Selectride®; General Procedure:
To a solution of the ketone (1 mmol) in dry THF (50 mL) at −78 °C, 1 M solution of K-selectride® (2 mL, 2 mmol) was slowly added. The solution was stirred at −78 °C for 1 h and quenched with H_2O (4 mL). The solvent was removed under reduced pressure and the residue treated with brine (50 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The organic phase was dried (Na_2SO_4), the solvent evaporated and the residue chromatographed through a short column (silica gel, Et_2O/hexane, 3 : 2) to isolate the main alcohol.

*(1S,2R)-2,3-O-Isopropylidene-1-(2-thiazolyl)-1,2,3-propanetriol syn-***(5)**: Yield: 98%; ds ≥ 95%; oil; $[\alpha]_D^{20}$ −7.9 °C (*c* = 0.66, $CHCl_3$).

$C_9H_{13}NO_3S$	calc.	C 50.22	H 6.09	N 6.51
(215.3)	found	50.30	5.75	6.42

^1H NMR ($CDCl_3$): δ = 1.38 (s, 3 H), 1.46 (s, 3 H), 3.29 (d, 1 H, *J* = 4.9 Hz, ex. D_2O), 4.09 (m, 2 H), 4.43 (dd, 1 H, *J* = 12.2, 6.2 Hz), 4.92 (dd, 1 H, *J* = 5.7, 4.9 Hz), 7.38 (d, 1 H, *J* = 3.2 Hz), 7.80 (d, 1 H, *J* = 3.2 Hz).

^{13}C NMR ($CDCl_3$): δ = 25.45, 26.91, 66.66, 73.48, 79.17, 110.87, 120.25, 143.51, 172.09.

*(1S,2R,3R)-2-O-Benzyl-3,4-O-isopropylidene-1-(2-thiazolyl)-1,2,3,4-butanetetraol syn-***(12)**: Yield: 90% ; ds ≥ 95%; oil; $[\alpha]_D^{20}$ + 19.5° (*c* = 1.81, $CHCl_3$).

$C_{17}H_{21}NO_4S$	calc.	C 60.87	H 6.31	N 4.18
(335.4)	found	61.10	6.26	4.04

^1H NMR ($CDCl_3$): δ = 1.38 (s, 3 H), 1.47 (s, 3 H), 3.54 (d, 1 H, *J* = 8.7 Hz, ex. D_2O), 3.86 (dd, 1 H, *J* = 8.5, 6.0 Hz), 4.08 (dd, 1 H, *J* = 8.5, 6.2 Hz), 4.19 (dd, 1 H, *J* = 6.8, 2.1 Hz), 4.26 (d, 1 H, *J* = 11.2 Hz), 4.28, (m, 1 H), 4.44 (d, 1 H, *J* = 11.2 Hz), 5.19 (dd, 1 H, *J* = 8.7, 2.0 Hz), 7.30 (m, 6 H), 7.82 (d, 1 H, *J* = 3.2 Hz).

^{13}C NMR ($CDCl_3$): δ = 24.48, 25.89, 65.90, 70.91, 74.13, 74.85, 80.99, 108.93, 118.96, 127.71, 127.79 (2C), 128.11 (2C), 137.24, 142.51, 174.09

Reduction of (2*S*,3*R*)-2-Benzyloxy-3,4-isopropylidenedioxy-1-(2-thiazolyl)-1-butanone (18a) with $LiAlH_4$:
To a suspension of $LiAlH_4$ (114 mg, 3 mmol) in Et_2O (20 mL) at −78 °C, a solution of ketone **18a** (1.0 g, 3 mmol) in Et_2O (20 mL) was slowly added. The solution was stirred for 2 h at −78 °C and then EtOAc was carefully added until no reaction was observed. H_2O was then added to form a precipitate which was filtered. The filtrate was dried (Na_2SO_4) and the solvent evaporated at reduced pressure to yield a mixture (1.0 g, 100 %) of the *anti*-**19** and *syn*-**17a** in 44 : 56 ratio (measured by 300 MHz ^1H NMR). This crude material was *O*-benzylated as detailed above. Flash chromatography (silica gel, hexane/Et_2O, 4 : 1) of the crude material (1.15 g, 90 %) afforded pure **21** (0.45 g) and **20a** (0.6 g) (Table 3).

Addition of 2-(Trimethylsilyl)thiazole (1) to the Aldehyde 9b:
To a stirred solution of **9b** (1.37 g, 5 mmol) in THF (25 mL) at −30 °C, the reagent **1** (1.17 g, 7.5 mmol) in the same solvent (15 mL) was slowly added. Stirring was continued for 14 h at r.t. The solvent was distilled and the residue chromatographed through a short column (silica gel, hexane/Et_2O, 9 : 1) to give **24** as an oil. Yield: 1.85 g (86 %); ds ≥ 95 %; oil; $[\alpha]_D^{20}$ + 15.° (*c* = 0.64, $CHCl_3$).

$C_{19}H_{37}NO_4SSi_2$	calc.	C 52.86	H 8.64	N 3.24
(431.7)	found	53.02	8.55	3.30

^1H NMR ($CDCl_3$): δ = −0.09 (s, 3 H), 0.04 (s, 3 H), 0.07 (s, 9 H), 0.83 (s, 9 H), 1.28 (s, 3 H), 1.37 (s, 3 H), 3.72 (m, 1 H), 3.95 (m, 3 H), 4.95 (d, 1 H, *J* = 3.0 Hz), 7.27 (d, 1 H, *J* = 3.2 Hz), 7.73 (d, 1 H, *J* = 3.2 Hz).

^{13}C NMR ($CDCl_3$): δ = −5.20, −4.77, −0.53 (3 C), 17.99, 25.18, 25.61 (3 C), 26.28, 65.92, 74.39, 77.42 (2 C), 108.48, 119.20, 142.70, 172.66.

The bis-silylated compound *syn*-**24** was dissolved in 5 % methanolic citric acid (30 mL) and the solution stirred for 14 h at r.t. The solution was poured into sat. aq $NaHCO_3$ (100 mL) and extracted with Et_2 (3 × 30 mL). The organic phase was dried (Na_2SO_4), the solvent distilled under reduced pressure and the residue chromatographied (silica gel, hexane/Et_2O, 4 : 1) to give pure (1*R*,2*S*,3*R*)-2-*tert*-butyldimethylsilyl-3,4-*O*-isopropylidene-1-(2-thiazolyl)-1,2,3,4-butanetetrol (**17b**): Yield: 1.34 g (87 %, 75 % from **9b**); oil: $[\alpha]_D^{20}$ + 2.7° (*c* = 0.56, $CHCl_3$).

$C_{16}H_{29}NO_4SSi$	calc.	C 53.45	H 8.13	N 3.90
(359.6)	found	53.37	7.96	4.02

^1H NMR ($CDCl_3$): δ = −0.31 (s, 3 H), 0.06 (s, 3 H), 0.75 (s, 9 H), 1.37 (s, 3 H), 1.44 (s, 3 H), 3.76 (d, 1 H, *J* = 8.7 Hz ex D_2O), 3.94 (dd, 1 H, *J* = 8.3, 8.0 Hz), 4.08 (dd, 1 H, *J* = 8.3, 6.4 Hz), 4.23 (ddd, 1 H, *J* = 8.0, 7.0, 6.4 Hz), 4.42 (dd, 1 H, *J* = 7.0, 3.1 Hz), 4.84 (dd, 1 H), *J* = 8.7, 1.3 Hz), 7.26 (d, 1 H, *J* = 3.2 Hz), 7.77 (d, 1 H, *J* = 3.2 Hz).

^{13}C NMR ($CDCl_3$): δ = −6.00, −4.97, 17.76, 25.13, 25.42 (3 C), 26.27, 65.72, 71.95, 75.88, 76.11, 109.65, 119.39, 143.10, 175.09.

(2*S*,3*R*)-2-*tert*-Butyldimethylsilyloxy-3,4-isopropylidenedioxy-1-(2-thiazolyl)-1-butanone (18b):
The alcohol **17b** (852 g, 2.37 mmol) was oxidized with DMSO/Ac_2O as detailed above. Column chromatography (silica gel, hexane/Et_2O, 9 : 1) gave 805 mg (95 %) of **18b** as an oil; $[\alpha]_D^{20}$ −11° (*c* = 0.73, $CHCl_3$).

$C_{16}H_{27}NO_4SSi$	calc.	C 53.75	H 7.61	N 3.92
(357.5)	found	53.58	7.80	4.04

IR ($CHCl_3$): $\nu = 1720\ cm^{-1}$

^1H NMR ($CDCl_3$): δ = 0.03 (s, 3 H), 0.05 (s, 3 H), 0.89 (s, 9 H), 1.24 (s, 3 H), 1.25 (s, 3 H), 4.04 (dd, 1 H, *J* = 8.4, 6.7 Hz), 4.08 (dd, 1 H, *J* = 8.4, 6.0 Hz), 4.71 (ddd, 1 H, *J* = 6.7, 6.0, 3.9 Hz), 5.44 (d, 1 H, *J* = 3.9 Hz), 7.69 (d, 1 H, *J* = 3.1 Hz), 7.98 (d, 1 H, *J* = 3.1 Hz).

^{13}C NMR ($CDCl_3$): δ = −5.61, −5.16, 18.03, 25.09, 25.47, 25.66, 65.28, 74.81, 77.22, 110.19, 126.62, 145.14, 166.17, 191.48.

Reduction of Ketone 18b with $NaBH_4$:
To a solution of **18b** (0.5 g, 1.4 mmol) in MeOH (20 mL) at −70 °C, $NaBH_4$ (266 mg, 7 mmol) was slowly added. The solution was stirred for 1 h at −78 °C and slowly warmed to r.t. The solvent was distilled at reduced pressure and the residue partitioned between brine (30 mL) and Et_2O (30 mL). The separated organic phase was dried (Na_2SO_4) and the solvent distilled in vacuo to yield a 91 : 9 mixture (ratio determined by 300 MHz, ^1H NMR) of **25** and **17b** (490 mg, 98 %). Flash chromatography (silica gel, hexane/Et_2O, 3 : 2) afforded pure **25** (425 mg); oil; $[\alpha]_D^{20}$ +16.1° (*c* = 0.92, $CHCl_3$).

$C_{16}H_{29}NO_4SSi$	calc.	C 53.45	H 8.13	N 3.90
(359.6)	found	53.60	8.01	3.74

^1H NMR ($CDCl_3$): δ = 0.03 (s, 3 H), 0.14 (s, 3 H), 0.95 (s, 9 H), 1.28 (s, 3 H), 1.36 (s, 3 H), 3.80 (m, 2 H), 3.98 (m, 3 H), 5.13 (d, 1 H, *J* = 4.6 Hz), 7.31 (d, 1 H, *J* = 3.2 Hz), 7.73 (d, 1 H, *J* = 3.2 Hz).

^{13}C NMR ($CDCl_3$): δ = −5.51, −5.45, 17.78, 25.31, 25.43 (3 C), 25.98, 66.34, 73.85, 74.57, 75.55, 109.38, 119.22, 142.78, 174.00.

Desilylation and Bisbenzylation of Alcohols 17b and 25:
A solution of **17b** or **25** (360 mg, 1 mmol) in THF (10 mL) was treated at r.t. with 1 M solution of Bu_4NF in THF (1 mL, 1 mmol). The solution was stirred for 2 h. The solvent was distilled and the residue dissolved in EtOAc (10 mL). The solution was washed with H_2O (3 × 20 mL), dried (Na_2SO_4) and the solvent distilled under reduced pressure. The crude material was benzylated as detailed above using two equivalents of NaH and benzyl bromide. The yield of **20a** was 75 % from **17b** and 78 % from **25**.

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