Aldehyde-Promoted Addition of 2-(Trimethylsilyl)thiazole to α,α′-Dialkoxy Ketones: A New Way to Branched-Chain Monosaccharides

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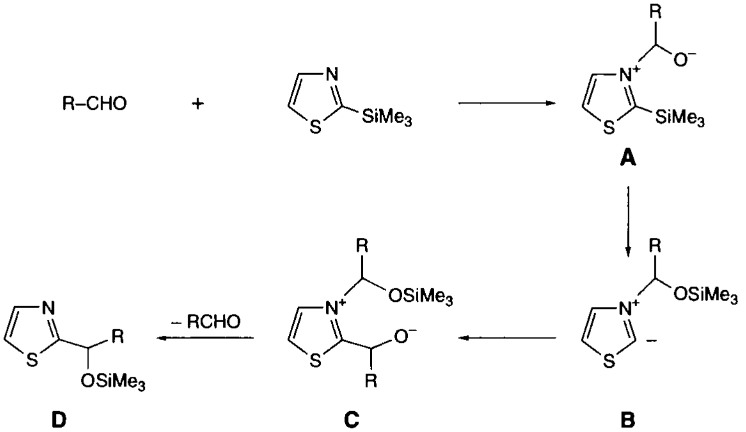
The reaction of 2-(trimethylsilyl)thiazole (2-TST) with several ketones was tested in the presence or absence of aldehydes. The keto aldehyde **5** (*Scheme 2*) was prepared from **1** *via* the hydroxy aldehyde **4** in 3 steps. It reacted with 2-TST to give, after desilylation and acetylation, the bis-thiazole **6**. The ketone **11**, obtained from **4** in 3 steps, reacted with 2-TST to give, after desilylation, **12**. The ketofuranose **17** (*Scheme 3*) reacted with 2-TST to yield exclusively the more stable D-*gluco* epimer **18**. The reaction of the ketone **11** (*Scheme 2*) with 2-TST was faster in the presence of 1 equiv. of the keto aldehyde **5**, suggesting that an aldehyde promotes the indirect and intermolecular addition of 2-TST to a ketone. We have studied the effect of several aldehydes on the rate of the reaction of the ketones **11** and **17** with 2-TST at different temperatures and at different concentrations of the ketones and of the aldehydes. Electrophilic aldehydes, and particularly 2-fluorobenzaldehyde (0.1 equiv.), promote the addition of 2-TST to electrophilic ketones.

Introduction. – 2-(Trimethylsilyl)thiazole (2-TST) is a formyl-anion equivalent that has been used mainly by *Dondoni* and coworkers for the homologation of aldehydes [1–6]. The proposed mechanism of homologation (*Scheme 1*) [7] postulates the addition of 2-TST to the formyl group, leading to a zwitterion intermediate **A**, followed by a C → O migration of the Me_3Si group to generate the ylide **B**, and the addition of **B** to a second molecule of the aldehyde, generating the zwitterion **C**[1]. Migration of the Me_3Si group and liberation of an equivalent of the aldehyde leads to the final product **D**.

Scheme 1



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[1] There is an obvious analogy between the reactivity of **B** and of the ylide derived from thiamine pyrophosphate [8–10].

The addition of 2-TST to aldehydes has been amply documented, while the addition to ketones appears to be restricted to trifluoromethyl ketones [11]. The above mechanism suggests that the reactivity of a ketone may be enhanced by introduction of a formyl group, as an ylide of type **B** obtained by addition of 2-TST to a formyl ketone might lead to an intramolecular formation of a C,C bond to the keto-carbonyl group. The nucleophilicity of an ylide of type **B** ought to be higher than the one of 2-TST, thus, an aldehyde (in catalytic amounts?) might also promote the indirect, intermolecular addition of 2-TST to a ketone. This would broaden the scope of 2-TST as a formyl-anion equivalent and open a new way to branched-chain monosaccharides.

We have examined these questions, on the one hand, by comparing the reactivity of the keto aldehyde **5** with the one of the related ketone **11** (*Scheme 2*) and, on the other hand, by comparing the reactivity of **11** and **17** (*Scheme 3*) in the presence or absence of added aldehydes. We report the results of our investigations.

Results and Discussion. – We prepared the keto aldehyde **5** *via* the hydroxy aldehyde **4** (*Scheme 2*), as the ring strain induced by the *trans*-annulated dioxolane ring shifts the position of the equilibrium between the hemiacetals and the corresponding hydroxy aldehyde in favour of the aldehyde, as shown for the 4-methoxybenzylidene analogue of **4** [12]. The hydroxy aldehyde **4** was obtained in two steps from allyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**1**) [13]. Benzylidenation according to *Li* and *Vasella* [14] led to a mixture of the (*S*)/(*R*)-diastereoisomers **2**/**3** (15:85; 74%), readily separated by FC. Deallylation of **3** gave the hydroxy aldehyde **4** (93%)[2].

The keto aldehyde **5** was obtained by oxidation of **4** with the *Dess-Martin* periodinane [15]. The crude product, obtained in 50–55% yield by addition of Et_2O and filtration, was homogeneous according to its ^1H-NMR spectrum in $CDCl_3$, but streaked on TLC, and could not be further purified by chromatography. This α,α′-dialkoxy ketone is expected to be highly electrophilic[3]). Treatment of crude **5** with 2-TST at 4°, followed by desilylation with Bu_4NF and acetylation, gave the (1*R*,5*R*)-1,5-bis-thiazole derivative **6** (27% from **5**). No diastereoisomers were observed. Small amounts (*ca.* 3%) of the monothiazole derivative **8** arising from incomplete oxidation of **4** were sometimes isolated. This monothiazole **8** was unambiguously prepared by treating **4** with 2-TST at 25°, followed by desilylation (→ **7**; 59%) and acetylation (98%). Attempts to prepare monothiazoles by treating **5** with less than 1 equiv. of 2-TST failed, and only lowered the yield of **6**.

The ketone **11** was obtained from the hydroxy aldehyde **4** in 47% overall yield by reduction with $NaBH_4$ (→ **9**), selective tritylation (→ **10**), and oxidation with periodinane. Similarly to **5**, the ketone **11** reacted slowly with 2-TST at 4°. At 25°, the reaction was complete after 48 h. Desilylation yielded 80% of the thiazolylglucitol **12**, that was acetylated in 79% yield to **13**.

We also tested the reactivity towards 2-TST in the case of the ketofuranose **17** [17] that should show a similarly enhanced electrophilicity as **5** and **11**, and, indeed, readily

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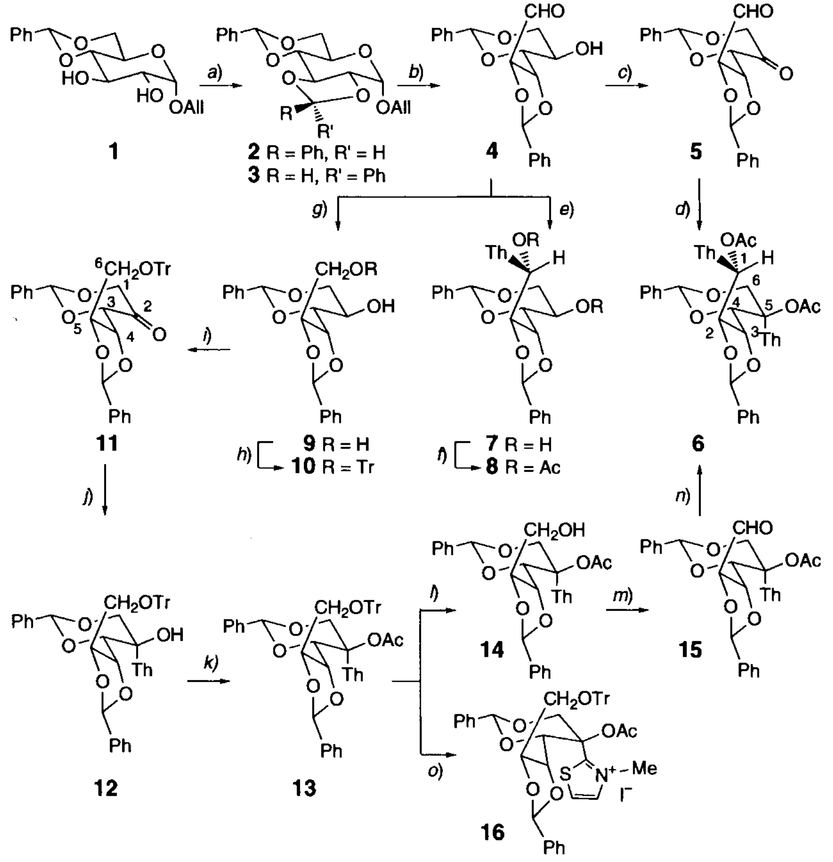
[2]) The ^1H-NMR spectrum of a solution of **4** in $CDCl_3$ kept at room temperature for several hours showed new signals, indicating the restricted stability of **4** under these conditions. Freshly prepared **4** was used for the synthesis of **5**.

[3]) Compare, *e.g.*, [16] and lit. cit. therein.

Scheme 2

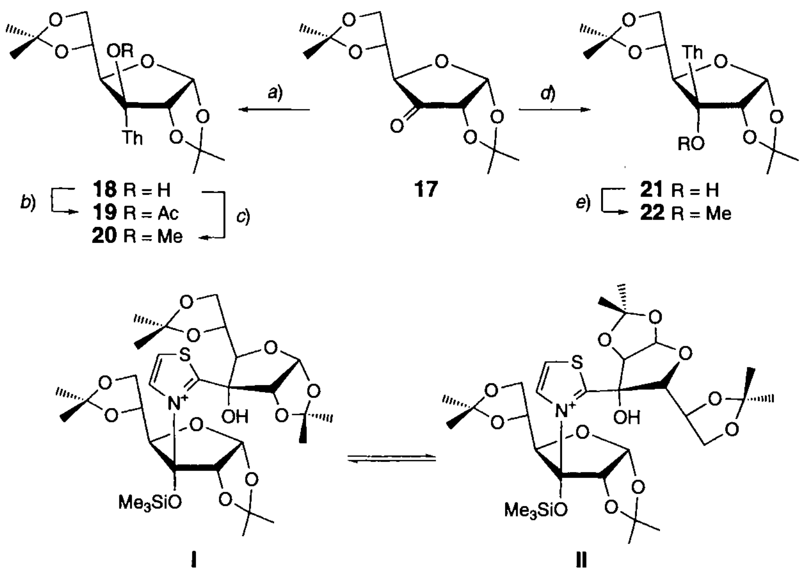


Th = thiazol-2-yl, Tr = Ph_3C

a) 3-Bromo-3-phenyldiazirine, KOH, DMSO, H_2O, 25°, 3 h; 74% (**2**/**3** 15:85). *b*) **3** KO^tBu, DMSO, 50°, 1 h; $HgCl_2$, HgO, acetone, H_2O, 25°, 30 min; 93%. *c*) *Dess-Martin* periodinane, CH_2Cl_2, 25°, 4 h; 53%. *d*) 2-(Trimethylsilyl)thiazole (2-TST), CH_2Cl_2, 0–4°, 12 h; Bu_4NF, THF, 25°, 2 h; Ac_2O, pyridine, 4-(dimethylamino)pyridine (DMAP), 25°, 12 h; 27%. *e*) 2-TST, CH_2Cl_2, 0–25°, 10 h; Bu_4NF, THF, 25°, 2 h; 59%. *f*) Ac_2O, pyridine, DMAP, 25°, 12 h; 98%, *g*) $NaBH_4$, EtOH, 0°, 1.5 h; 79%. *h*) Ph_3CCl, pyridine, DMAP, 100°, 24 h; 63%. *i*) *Dess-Martin* periodinane, CH_2Cl_2, 25°, 5 h; 94%). *j*) 2-TST, CH_2Cl_2, 25°, 48 h; Bu_4NF, THF, 25°, 2 h; 80%. *k*) Ac_2O, pyridine, DMAP, 25°, 12 h; 79%. *l*) $FeCl_3 \cdot 6\,H_2O$, CH_2Cl_2, 25°, 1 h; 58%. *m*) *Dess-Martin* periodinane, CH_2Cl_2, 25°, 2 h. *n*) 2-TST, CH_2Cl_2, 0–25°, 10 h; Bu_4NF, THF, 25°, 2 h; Ac_2O, pyridine, DMAP, 25°, 12 h; 48% from **14**. *o*) MeI, MeCN, 80°, 27 h; 69%.

forms a hydrate (*Scheme 3*). Treatment of **17** (obtained by coevaporating the mixture of **17** and its hydrate with toluene) with 2-TST at 80°, followed by desilylation yielded 60% of the D-*gluco*-configurated hydroxythiazole **18**, which was acetylated to **19** (81%) and etherified to **10** (19%). This is surprising in view of the usual *exo*-addition of nucleophiles to **17** [18] and related *cis*-bicyclo[3.3.0]octanones [19]. It may reflect equilibration of the diastereoisomeric intermediates **I** and **II**, corresponding to **C** in *Scheme 1*, and thus a slow O → O migration of the Me_3Si group. This explanation is consistent with the results of the equilibration of the adducts of $MeNO_2$ to **17** [20] and with the dependence on the reaction conditions of the diastereoselectivity of the addition of NaCN to **17** [21]. In keeping with this, addition of the lithium thiazolide, generated *in situ* from thiazole and BuLi [5], to **17** led only to the D-*allo* epimer **21**[4]) that was isolated in 48% yield.

Scheme 3



Th = thiazol-2-yl

a) 2-TST, THF, 80°, 36 h; Bu_4NF, THF, 25°, 2 h; 60%. *b*) Ac_2O, pyridine, DMAP, 25°, 65 h; 81%. *c*) KOH, MeI, DMSO, 25°, 2 h; 79%. *d*) BuLi, thiazole, CH_2Cl_2, –78°, 2 h; 48%. *e*) KOH, MeI, DMSO, 25°, 2 h; 98%.

The reaction of the ketone **11** with 1.1 equiv. of 2-TST at 4° was faster in the presence of 1 equiv. of the keto aldehyde **5** (12 h in the presence of **5** *vs.* 4 days in its absence) and gave rise to higher yields of **13** (78 *vs.* 63%). The bis-thiazole **6**, derived from **5**, was also isolated (24%). This observation suggests that in the reaction of **5** with 2-TST, the transfer of the thiazole moiety to the keto-carbonyl group may not be intra-, but intermolecular. For this reason, we studied the effect of several aldehydes on the rate of the reaction of the ketones **11** and **17** with 2-TST at different temperatures and at different concentrations of the ketones and of the aldehydes. Thus, **11** (0.06M in $CDCl_3$) was treated with 1.5 equiv. of 2-TST at 25°, in the presence of stoechiometric amounts or 0.1 equiv. of benzaldehyde, 4-nitrobenzaldehyde, and 2-methoxybenzaldehyde; the reactions were followed by ^{1}H-NMR, monitoring the phenylmethylene and H–C(1) signals of **11** and of the products (results in *Fig. 1,a*). All aldehydes, added in equivalent amounts, promoted the reaction. The effect was strongest for 4-nitrobenzaldehyde.

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[4]) As judged from the ^{1}H-NMR spectrum of the crude. Not surprisingly, attempts to equilibrate **21** failed (NaH in THF, ^{t}BuOH or KH in THF, or NaOMe n MeOH).

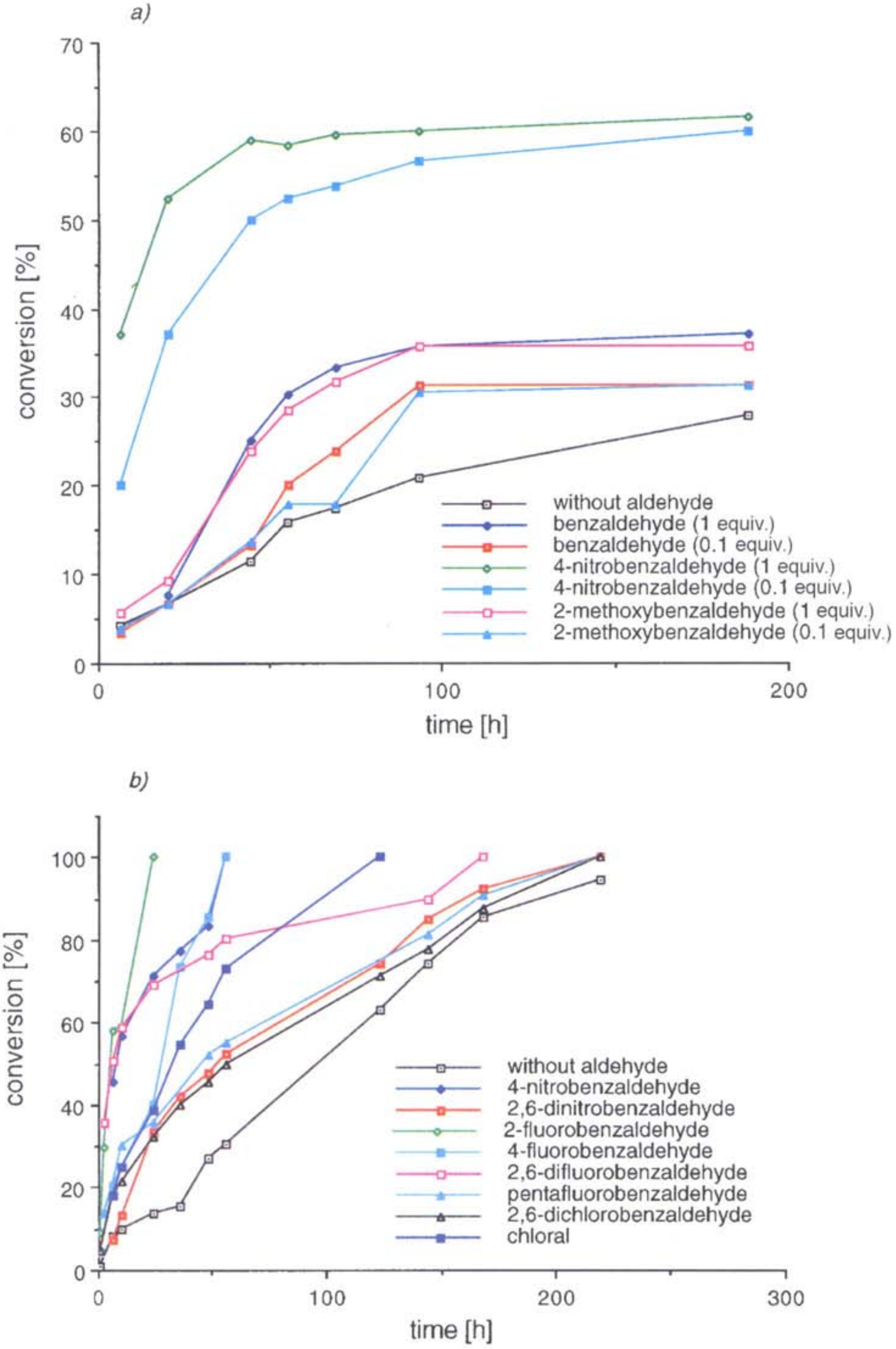

Fig. 1. *Effect of benzaldehydes on the reaction of* **11** *with 1.5 equiv. of 2-TST at 25°:* a) *1 or 0.1 equiv. of aldehyde and 0.06*M **11** *in* $CDCl_3$ *and* b) *0.1 equiv. of aldehyde and 0.3*M **11** *in* $CDCl_3$

Smaller amounts (0.1 equiv.) of benzaldehyde and 2-methoxybenzaldehyde had only a weak effect on the addition, while 0.1 equiv. of 4-nitrobenzaldehyde had almost the same effect as 1 equiv. Thus, the conversion of **11** (0.06M in $CDCl_3$) after 20 h amounted to 7% in the absence of 4-nitrobenzaldehyde; to 52% in the presence of 1 equiv. of 4-nitrobenzaldehyde, and to 37% in the presence of 0.1 equiv. of 4-nitrobenzaldehyde (*Fig. 1,a*). As the reaction was not complete even after 188 h, we increased the concentration of **11** to 0.3M, added 1.5 equiv. of 2-TST, and tested the effect of 0.1 equiv. of electron-poor aldehydes (4-nitrobenzaldehyde, 2,6-dinitrobenzaldehyde, 2-fluorobenzaldehyde, 4-fluorobenzaldehyde, 2,6-difluorobenzaldehyde, 2,3,4,5,6-pentafluorobenzaldehyde, 2,6-dichlorobenzaldehyde, and chloral; see *Fig. 1,b*). The best results were obtained with 2-fluorobenzaldehyde (100% conversion of **11** after 24 h *vs.* in 12% in the absence of an aldehyde). A decrease of the catalytic effect was observed with benzaldehydes substituted by more than one electron-withdrawing group (100% conversion after 24 h in the presence of 2-fluorobenzaldehyde *vs.* 69% in the presence of 2,6-difluorobenzaldehyde and 36% in the presence of 2,3,4,5,6-pentafluorobenzaldehyde).

An increase of the rate of the reaction of **17** (0.3M in C_6D_5Cl) with 1.5 equiv. of 2-TST in the presence of 0.1 equiv. of 2-fluorobenzaldehyde at 80° was also observed, the reaction being complete after 19 h *vs.* 41 h in the absence of an aldehyde (*Fig. 2,a*), and the overall yields of the product **19** obtained after acetylation of the crudes were 60 as compared to 50%. Under these conditions, the effect of the aldehyde on the rate of the reaction of 2-TST with **17** was particularly important during the first 5 h. This was more striking when the reactions were run at 25°; after 30 h, the conversion rates of **17** in the presence of fluorobenzaldehydes and in their absence became similar (*Fig. 2,b*)[5]).

Exploratory experiments indicate that the effect of the aldehydes on the addition of 2-TST may be restricted to highly electrophilic ketones. Thus, 2-TST did not add to 2-methoxyacetone and benzophenone, even in the presence of 2-fluorobenzaldehyde; while addition of 0.1 equiv. of 2-fluorobenzaldehyde to trifluoroacetophenone (0.3M in C_6D_5Cl) at 80° increased the rate of the known [11] addition of 2-TST: the conversion of trifluoroacetophenone after 65 h was enhanced from 18% in the absence of 2-fluorobenzaldehyde to 54% in its presence.

The configuration of the (*S*)- and (*R*)-isomers **2**/**3** was assigned by comparison of their ^{1}H- and ^{13}C-NMR data with the data of the corresponding 4,6-*O*-(4-methoxybenzylidene) derivatives [12]. The carbonyl group of the hydroxy aldehyde **4** gives rise to an IR absorption at 1702 cm^{-1} and to a ^{13}C-NMR *s* at 200.97 ppm. The ^{1}H-NMR spectrum shows the characteristic *d* of the formyl H at 9.89 ppm ($J(1,2) = 1.3$ Hz). HO–C(5) appears as a *d* at 3.13 ppm ($J(5,OH) = 5.4$ Hz). Oxidation of **4** to the keto aldehyde **5** is confirmed by the characteristic IR absorption for six-membered α-oxy ketones at 1740 and the formyl absorption at 1704 cm^{-1}. The bis-thiazole **6** and the monothiazole **8** are characterized by the typical ^{1}H-NMR *d* of the thiazole moiety (**6**: δ(SCH) = 7.29 and 7.38 ppm, δ(NCH) = 7.76 and 7.86 ppm; **8**: δ(SCH) = 7.39 ppm, δ(NCH) = 7.79 ppm). H_{eq}–C(6) of **6** is notably deshielded by the proximity of the C(5)-thiazolyl group (**6**: 5.30 ppm; **5**: 4.58 ppm; **8**: 4.58 ppm). The ketone **11** is characterized by a C=O ^{13}C-NMR resonance at 204.11 ppm and an IR band at 1740 cm^{-1}. The thiazole **12** is characterized by two ^{1}H-NMR *d* for the thiazole moiety at 7.40 and 7.69 ppm.

As shown by the similar values of $J(2,3)$ (5.0–6.0 Hz) and particularly of $J(3,4)$ (1.0–2.0 Hz), the acyclic derivatives **4**–**13** adopt a similar conformation in $CDCl_3$, characterized by a zig-zag arrangement of the C(2)–C(6) chain. To correlate the configuration of **6** and the one of **12**–**16**, the *gluco*-configurated aldehyde **15**,

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[5]) This is in keeping with the observation (by ^{1}H-NMR) that longer reaction times led to an irreversible reaction of the aldehyde with 2-TST. The products of this reaction were not isolated, but their characteristic ArC*H* signals were observed in the NMR spectra of the crude before and after desilylation.

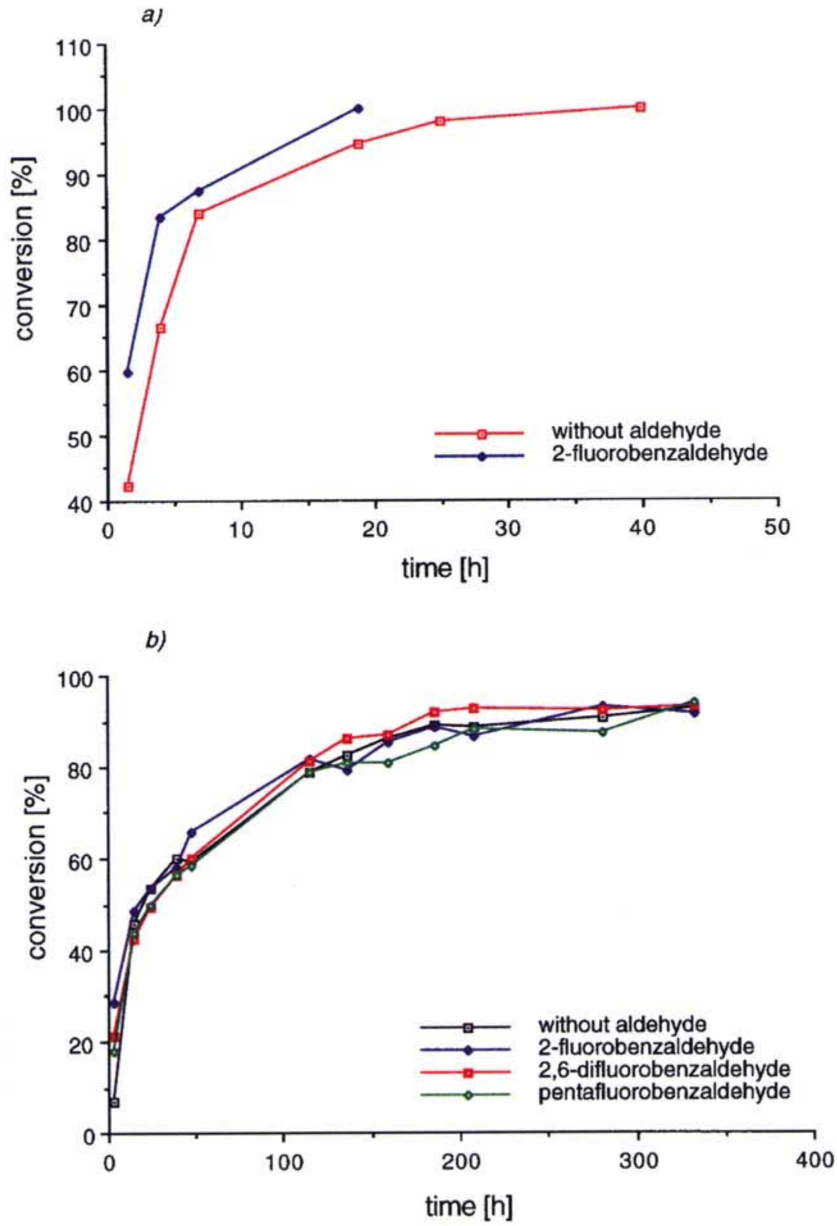

Fig. 2. *Effect of 0.1 equiv. of fluorobenzaldehydes on the reaction of* **17** *with 1.5 equiv. of 2-TST:* a) *0.3*M **17** *in C_6D_5Cl at 80° and* b) *0.3*M **17** *in $CDCl_3$ at 25°*

derived from **12** by acetylation (→ **13**), detritylation (→ **14**) and oxidation, was treated with 2-TST. The bis-thiazole obtained after desilylation and acetylation (48% from **14**) and the bis-thiazole **6** derived from **5** could not be distinguished from each other. Thus, the diastereoselectivity of the 2-TST addition to **5** and **15** is the same. A comparison of the CD spectra of the monothiazoles **8** and **13** with the CD spectrum of the bis-thiazole **6** (MeOH) shows a negative *Cotton* effect for **8** at 240 nm ($\Delta\varepsilon = -1.4$ cm$^2 \cdot$ mmol^{-1}), a positive *Cotton* effect for **13** ($\Delta\varepsilon = 5.8$ cm$^2 \cdot$ mmol^{-1}), and a positive *Cotton* effect of intermediate strength for **6** ($\Delta\varepsilon = 3.0$ cm$^2 \cdot$ mmol^{-1}). As the conformation of **6**, **8**, and **13** in MeOH must be very similar, as judged from the *J*(H,H) values in CD_3OD (*J*(2,3) ≈ 5.0–5.5 Hz, *J*(3,4) ≈ 1.0–1.5 Hz), this additivity of the *Cotton* effects of **8** and **13** in **6** further evidences that the C(1) configuration of **6** and **8** is the same, and confirms that **6** and **13** possess the same configuration at C(5). The C(1) configuration of **6**–**8** was assigned as (*R*) by analogy to the results of *Dondoni* and coworkers, who showed that 2-TST adds to α,β-dialkoxy aldehydes according to the *Felkin-Ahn* model [22]. The configuration at C(5) of **6** and **12**–**16** was established by measuring NOEs of the *N*-methylated salt **16**: a positive NOE between MeN and H–C(3) and the absence of a NOE between MeN and H–C(4) evidence the axial position of the thiazolyl group and thus the (5*R*)-configuration of **6** and **12**–**16**.

The configuration of the thiazolylfuranoses **18** and **21** was corroborated by NOEs for their respective methyl ethers **20** and **22**. In **20**, NOEs between MeO and both H–C(2) and H–C(5) and the absence of a NOE between MeO and H–C(4) evidence the *cis*-relation of MeO and H–C(2) and thus the D-*gluco*-configuration of **18**–**20**. In **22**, NOEs between MeO and both H–C(4) and H–C(2) and the absence of a NOE between MeO and H–C(5) confirm the *cis*-relation of OMe and H–C(4) and thus the D-*allo* configuration of **21** and **22**.

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Experimental Part

General. Solvents were distilled before use. Normal workup implies distribution of the crude product between CH_2Cl_2 and sat. aq. NH_4Cl soln. and ice, unless indicated otherwise, drying of the org. layer ($MgSO_4$), filtration, and evaporation of the filtrate. TLC: *Merck* silica gel *60F-254* plates; detection by heating with 'mostain' (400 ml of 10% H_2SO_4 soln., 20 g of $(NH_4)_6Mo_7O_{24} \cdot 6\,H_2O$, 0.4 g of $Ce(SO_4)_2$). Flash chromatography (FC): silica gel *Merck 60* (0.04–0.063 mm). UV Spectra (λ_{max} in nm (log ε)): 1-cm quartz cell. CD Spectra (λ_{max} in nm, $\Delta\varepsilon$ in cm$^2 \cdot$ mmol^{-1}): *Jasco-J-710* spectropolarimeter. IR Spectra: KBr or 3% $CHCl_3$ soln. ^{1}H-NMR (300 MHz, if not indicated otherwise) and ^{13}C-NMR (75 MHz, if not indicated otherwise): chemical shifts δ in ppm and coupling constants *J* in Hz. FAB- and CI-MS: 3-nitrobenzyl alcohol and NH_3, resp., as matrix, unless indicated otherwise.

*Allyl (*S*)-2,3:(*R*)-4,6-Di-*O*-benzylidene-α-D-glucopyranoside* (**2**) *and Allyl (*R*)-2,3:(*R*)-4,6-Di-*O*-benzylidene-α-D-glucopyranoside* (**3**). At 25°, a vigorously stirred soln. of **1** [13] (8 g, 0.026 mol) and KOH (20.32 g, 0.363 mol) in DMSO/H_2O 86:14 (185 ml) was treated dropwise with a soln. of 3-bromo-3-phenyldiazirine (16.43 g, 0.084 mol) in hexane (110 ml). After 2 h, normal workup (AcOEt/H_2O) and FC (toluene/hexane/AcOEt 10:8:1) gave **2** (1.18 g, 11%) and **3** (6.5 g, 63%).

Data of **2**: White solid. R_f (Et_2O/hexane 2:1) 0.69. IR ($CHCl_3$): 3069*w*, 3008*m*, 2983*w*, 2933*m*, 2360*w*, 1956*w*, 1894*w*, 1812*w*, 1647*w*, 1608*w*, 1496*w*, 1455*m*, 1381*m*, 1312*w*, 1176*w*, 1109*s*, 1090*s*, 1056*s*, 1028*s*, 965*w*, 935*w*, 910*m*, 842*w*, 652*w*. ^{1}H-NMR ($CDCl_3$): 3.71 (*dd*, *J* = 3.1, 9.3, H–C(2)); 3.80–3.85 (*m*, H–C(5)); 3.90 (*t*, *J* = 10.3, H_{ax}–C(6)); 4.03 (*t*, *J* = 9.3, H–C(4)); 4.19 (*tdd*, *J* = 1.2, 6.2, 13.1, 1 allyl. H); 4.25–4.40 (*m*, 1 allyl. H, H_{eq}–C(6)); 4.41 (*t*, *J* = 9.6, H–C(3)); 5.27 (*qd*, *J* ≈ 1.2, 10.3, 1 olef. H); 5.33 (*d*, *J* = 3.1, H–C(1)); 5.38 (*qd*, *J* ≈ 1.2, 17.1, 1 olef. H); 5.64 (*s*, PhC*H*O–C(4)); 5.98 (*tdd*, *J* = 5.3, 10.6, 16.5, 1 olef. H); 6.19 (*s*, PhC*H*O–C(2)); 7.32–7.41 (*m*, 6 arom. H); 7.49–7.57 (*m*, 4 arom. H). ^{13}C-NMR ($CDCl_3$): 64.23 (*d*, C(5)); 68.76, 69.07 (2*t*, O*C*H_2CH=CH_2, C(6)); 75.72, 76.40 (2*d*, C(2), C(3)); 80.87 (*d*, C(4)); 97.01 (*d*, C(1)); 101.51 (*d*, Ph*C*HO–C(4)); 105.57 (*d*, Ph*C*HO–C(2)); 118.37 (*t*, CH=*C*H_2); 126.33–129.43 (several *d*); 133.35 (*d*, *C*H=CH_2); 136.94 (*s*); 137.93 (*s*). FAB-MS: 397 (100, $[M + 1]^+$).

Data of **3**: White solid. R_f (Et_2O/hexane 2:1) 0.64. IR ($CHCl_3$): 3070*w*, 3008*w*, 2930*m*, 2870*w*, 1957*w*, 1812*w*, 1648*w*, 1497*w*, 1457*m*, 1390*m*, 1360*w*, 1312*m*, 1174*s*, 1114*s*, 1087*s*, 1060*s*, 1028*s*, 962*m*, 925*w*, 842*w*, 652*w*, 622*w*. ^{1}H-NMR ($CDCl_3$): 3.75 (*dd*, *J* = 2.9, 9.1, H–C(2)); 3.80–3.84 (*m*, H–C(5)); 3.86 (*t*, *J* = 9.5, H_{ax}–C(6)); 3.94 (*t*, *J* = 9.1, H–C(4)); 4.19 (*tdd*, *J* = 1.2, 5.8, 13.3, 1 allyl. H); 4.29–4.39 (*m*, H_{eq}–C(6), H–C(3), 1 allyl. H); 5.25 (*qd*, *J* ≈ 1.6, 10.4, 1 olef. H); 5.38 (*d*, *J* = 2.9, H–C(1)); 5.39 (*qd*, *J* ≈ 1.7, 17.0, 1 olef. H); 5.62 (*s*, PhC*H*O–C(4)); 5.97 (*dddd*, *J* = 5.4, 6.6, 10.4, 17.0, 1 olef. H); 6.18 (*s*, PhC*H*O–C(2)); 7.32–7.41 (*m*, 6 arom. H); 7.49–7.57 (*m*, 4 arom. H). ^{13}C-NMR ($CDCl_3$): 63.79 (*d*, C(5)); 68.14, 68.36 (2*t*, O*C*H_2CH=CH_2, C(6)); 71.56, 77.86 (2*d*, C(2), C(3)); 80.81 (*d*, C(4)); 96.49 (*d*, C(1)); 100.87 (*d*, Ph*C*HO–C(4)); 104.94 (*d*, Ph*C*HO–C(2)); 116.87 (*t*, CH=*C*H_2); 125.60–128.68 (several *d*); 132.78 (*d*, *C*H=CH_2); 136.21 (*s*); 137.48 (*s*). FAB-MS: 397 (100, $[M + 1]^+$).

*(*R*)-2,3:(*R*)-4,6-Di-*O*-benzylidene-D-glucose* (**4**). A mixture of **3** (923 mg, 2.33 mmol) and KO^{t}Bu (575 mg, 5.12 mmol) in DMSO (21 ml) was stirred for 1 h at 50° and poured into ice. Normal workup (AcOEt/H_2O) gave

a crude, which was dissolved in acetone (24 ml) and H_2O (4 ml), and treated with HgO (492 mg, 2.27 mmol) and $HgCl_2$ (628 mg, 2.31 mmol). The mixture was stirred at 25° for 30 min, filtered through *Celite*, and evaporated. The residue was dissolved in CH_2Cl_2 and washed with 3M aq. KI. Evaporation gave **4** (772 mg, 93%). White foam. R_f (hexane/AcOEt 1:1) 0.17. IR ($CHCl_3$): 3423*m* (br.), 3068*w*, 3008*m*, 2931*w*, 2861*m*, 1734*m*, 1702*m*, 1599*w*, 1496*w*, 1458*s*, 1401*s*, 1312*s*, 1147*s*, 1089*s* (br.), 1027*s*, 977*s*, 915*m*, 874*w*. ^{1}H-NMR ($CDCl_3$): 3.13 (*d*, J = 5.4, exchange with CD_3OD, OH); 3.65 (*t*, J = 10.4, H_{ax}–C(6)); 3.74 (*dd*, J = 1.7, 9.1, H–C(4)); 4.18 (*ddd*, J = 5.4, 9.5, 10.4, H–C(5)); 4.30 (*dd*, J = 5.4, 10.8, H_{eq}–C(6)); 4.74–4.81 (*m*, H–C(2), H–C(3)); 5.51 (*s*, PhC*H*O–C(4)); 6.17 (*s*, PhC*H*O–C(2)); 7.20–7.60 (*m*, 10 arom. H); 9.89 (*d*, J = 1.3, H–C(1)). ^{13}C-NMR ($CDCl_3$): 61.67 (*d*, C(5)); 71.03 (*t*, C(6)); 75.89 (*d*, C(3)); 80.40 (*d*, C(2)); 82.08 (*d*, C(4)); 101.35 (*d*, Ph*C*HO–C(4)); 106.17 (*d*, Ph*C*HO–C(2)); 125.25–129.82 (several *d*); 136.33 (*s*); 137.35 (*s*); 200.97 (*d*, CHO).

*(*R*)-2,3:(*R*)-4,6-Di-*O*-benzylidene-*D-xylo*-hexos-5-ulose* (**5**). At 25°, a soln. of **4** (904 mg, 2.54 mmol) in CH_2Cl_2 (10 ml) was treated with *Dess-Martin* periodinane (3.23 g, 7.62 mmol). After 4 h, the mixture was diluted with Et_2O and filtered through *Celite*. Evaporation gave **5** (477 mg, 53%) which was used without further purification for the next step. Foam. R_f (AcOEt/hexane 6:4) 0.32. IR ($CHCl_3$): 3008*m*, 2936*m*, 2865*w*, 1740*m*, 1704*w*, 1615*s*, 1589*w*, 1519*s*, 1462*m*, 1397*m*, 1304*m*, 1251*s*, 1173*s*, 1145*s*, 1095*s*, 1035*s*, 980*w*, 909*m*, 863*w*, 833*s*. ^{1}H-NMR ($CDCl_3$): 4.45 (*d*, J = 8.1, H_{ax}–C(6)); 4.58 (*d*, J = 8.7, H_{eq}–C(6)); 4.63 (br. *s*, H–C(4)); 4.78 (*dd*, J = 1.9, 6.2, H–C(2)); 4.98 (*dd*, J = 1.9, 6.2, H–C(3)); 6.01 (*s*, PhC*H*O–C(4)); 6.23 (*s*, PhC*H*O–C(2)); 7.30–7.60 (*m*, 10 arom. H); 9.88 (*d*, J = 1.9, CHO).

*1,5-Di-*O*-acetyl-(*R*)-2,3:(*R*)-4,6-di-*O*-benzylidene-1,5-di-*C*-(thiazol-2-yl)-D-glucitol* (**6**). At 0°, a soln. of **5** (478 mg, 1.34 mmol) in CH_2Cl_2 (15 ml) was treated with 2-TST (425 µl, 2.68 mmol) and stirred at 4° for 12 h. After evaporation and drying *i.v.*, a soln. of the residue in THF (17 ml) was treated with 1M Bu_4NF soln. in THF (3.5 ml) and stirred for 2 h. After evaporation and normal workup, a soln. of the residue in pyridine (7 ml) and Ac_2O (7 ml) was treated with DMAP (50 mg, 0.41 mmol) and stirred for 12 h at 25°. Evaporation and FC (Et_2O/hexane 8:2) gave **6** (220 mg, 27%). Oil. R_f (Et_2O/hexane 7:3) 0.24. UV (MeOH): 218 (3.5), 244 (3.7). CD (MeOH): 240 (3.0). IR ($CHCl_3$): 3123*w*, 3092*w*, 3069*w*, 3007*s*, 2928*w*, 2866*m*, 1748*s*, 1664*w*, 1612*w*, 1498*m*, 1457*m*, 1402*m*, 1370*s*, 1310*m*, 1248*s*, 1152*s*, 1087*s*, 1056*s*, 1027*s*, 908*s*. ^{1}H-NMR ($CDCl_3$): 2.02 (*s*, Ac); 2.16 (*s*, Ac); 4.02 (*d*, J = 1.2, H–C(4)); 4.08 (*d*, J = 11.2, H_{ax}–C(6)); 4.84 (*dd*, J = 1.2, 5.0, H–C(3)); 4.98 (*dd*, J = 4.7, 5.0, H–C(2)); 5.30 (*d*, J = 11.2, H_{eq}–C(6)); 5.75 (*s*, 2 PhC*H*); 6.42 (*d*, J = 4.7, H–C(1)); 7.04–7.08 (*m*, 2 arom. H); 7.20–7.24 (*m*, 3 arom. H); 7.29 (*d*, J = 3.4, irrad. at 7.76 → *s*, SCH); 7.38 (*d*, J = 3.1, irrad. at 7.86 → *s*, SCH); 7.40–7.44 (*m*, 3 arom. H); 7.60–7.64 (*m*, 2 arom. H); 7.76 (*d*, J = 3.1, irrad. at 7.29 → *s*, NCH); 7.86 (*d*, J = 3.1, irrad. at 7.38 → *s*, NCH). ^{1}H-NMR (CD_3OD): 2.01 (*s*, Ac); 2.13 (*s*, Ac); 4.11 (br. *s*, H–C(4)); 4.15 (*d*, J = 11.2, H_{ax}–C(6)); 4.83–4.85 (*m*, H–C(3)); 4.91 (*dd*, J = 4.4, 5.0, H–C(2)); 5.15 (*d*, J = 11.2, H_{eq}–C(6)); 5.65 (*s*, PhC*H*O–C(4)); 5.87 (*s*, PhC*H*O–C(2)); 6.42 (*d*, J = 4.0, H–C(1)); 7.00–7.04 (*m*, 2 arom. H); 7.20–7.25 (*m*, 3 arom. H); 7.41–7.45 (*m*, 2 arom. H, SCH); 7.49 (*d*, J = 3.4, SCH); 7.63–7.69 (*m*, 3 arom. H, NCH); 7.88 (*d*, J = 3.4, NCH). ^{13}C-NMR ($CDCl_3$): 20.55 (*q*, Me); 21.25 (*q*, Me); 71.71 (*d*, C(1)); 73.55 (*t*, C(6)); 73.99, 78.89 (2*d*, C(2), C(3)); 75.46 (*s*, C(5)); 83.71 (*d*, C(4)); 103.6 (*d*, Ph*C*HO–C(4)); 105.38 (*d*, Ph*C*HO–C(2)); 120.03 (*d*, SCH); 120.13 (*d*, SCH); 125.99–129.58 (several *d*); 136.81 (*s*); 137.31 (*s*); 140.93 (*d*, NCH); 143.07 (*d*, NCH); 164.60 (*s*, C=O); 165.93 (*s*, C=O); 169.08 (*s*, C=N); 169.67 (*s*, C=N). FAB-MS: 609 (100, $[M + 1]^+$).

*(*R*)-(*R*)-2,3:(*R*)-4,6-Di-*O*-benzylidene-1-*C*-(thiazol-2-yl)-D-glucitol* (**7**). At 0°, a soln. of **4** (990 mg, 2.78 mmol) in CH_2Cl_2 (10 ml) was treated with 2-(trimethylsilyl)-1,3-thiazole (2-TST; 661 µl, 4.17 mmol), warmed to 25°, and stirred for 10 h. After evaporation and drying *i.v.*, the soln. of the residue in THF (17 ml) was treated with 1M Bu_4NF soln. in THF (5 ml) and stirred for 2 h. Evaporation, normal workup, and FC (hexane/AcOEt 1:1) gave **7** (706 mg, 59%). White foam. R_f (hexane/AcOEt 1:1) 0.25. IR ($CHCl_3$): 3583*m* (br.), 3394*m* (br.), 3070*w*, 3007*w*, 2962*m*, 2933*m*, 2861*m*, 1631*w*, 1498*m*, 1458*s*, 1400*s*, 1311*w*, 1294*w*, 1260*s*, 1145*s*, 1089*s*, 1071*s*, 1027*s*, 982*w*, 915*m*. ^{1}H-NMR ($CDCl_3$): 3.11 (br. *s*, exchange with CD_3OD, OH); 3.42 (*dd*, J = 2.8, 9.3, H–C(4)); 3.55 (*t*, J = 10.6, H_{ax}–C(6)); 3.75 (br. *s*, exchange with CD_3OD, OH); 3.96–4.01 (*m*, addn. of CD_3OD → *ddd*, J = 5.3, 9.6, 10.0, H–C(5)); 4.23 (*dd*, J = 5.3, 10.9, H_{eq}–C(6)); 4.75 (*dd*, J = 2.8, 5.0, H–C(3)); 4.98 (*t*, J = 5.0, H–C(2)); 5.28 (*d*, J = 4.7, H–C(1)); 5.43 (*s*, PhC*H*O–C(4)); 6.10 (*s*, PhC*H*O–C(2)); 7.36–7.40 (*m*, 6 arom. H); 7.39 (*d*, J = 3.1, irrad. at 7.79 → *s*, SCH); 7.40–7.50 (*m*, 4 arom. H); 7.79 (*d*, J = 3.1, irrad. at 7.39 → *s*, NCH). ^{13}C-NMR ($CDCl_3$): 61.57 (*d*, C(5)); 70.80 (*t*, *C*(6)); 71.74 (*d*, C(1)); 75.59 (*d*, C(3)); 78.89 (*d*, C(2)); 82.40 (*d*, C(4)); 101.14 (*d*, Ph*C*HO–C(4)); 105.29 (*d*, Ph*C*HO–C(2)); 120.00 (*d*, SCH); 126.13–129.66 (several *d*); 136.74 (*s*); 137.65 (*s*); 142.15 (*d*, NCH); 170.91 (*s*, C=N). FAB-MS: 442 (100, $[M + 1]^+$).

*(*R*)-1,5-Di-*O*-acetyl-(*R*)-2,3:(*R*)-4,6-di-*O*-benzylidene-1-*C*-(thiazol-2-yl)-D-glucitol* (**8**). A soln. of **7** (167 mg, 0.37 mmol) in pyridine (3 ml) and Ac_2O (3 ml) was treated with 4-(dimethylamino)pyridine (DMAP; 10 mg, 0.09 mmol) and stirred for 12 h at 25°. Evaporation and FC (Et_2O/hexane 7:3) gave **8** (195 mg, 98%).

White foam. R_f (Et_2O/hexane 7:3) 0.5. UV (MeOH): 218 (3.6), 243 (3.7). CD (MeOH): 240 (−1.4). IR ($CHCl_3$): 3094*w*, 3070*w*, 3008*m*, 2958*w*, 2929*w*, 2861*m*, 1743*s*, 1499*m*, 1458*m*, 1402*w*, 1372*s*, 1311*w*, 1248*s*, 1148*s*, 1090*s*, 1027*s*, 982*m*, 914*m*. ^{1}H-NMR ($CDCl_3$): 2.07 (*s*, Ac); 2.17 (*s*, Ac); 3.59 (*t*, $J \approx 10.3$, H_{ax}−C(6)); 3.84 (br. *d*, $J = 9.6$, H−C(4)); 4.58 (*dd*, $J = 5.3, 10.6$, H_{eq}−C(6)); 4.67 (*dd*, $J = 1.2, 5.0$, H−C(3)); 5.15 (*dd*, $J = 4.0, 5.0$, H−C(2)); 5.20 (*ddd*, $J = 5.3, 9.0, 10.0$, H−C(5)); 5.58 (*s*, PhC*HO*−C(4)); 6.15 (*s*, PhC*HO*−C(2)); 6.42 (*d*, $J = 4.0$, H−C(1)); 7.35–7.40 (*m*, 8 arom. H, SCH); 7.42–7.50 (*m*, 2 arom. H); 7.82 (*d*, $J = 3.1$, NCH). ^{1}H-NMR (CD_3OD): 2.06 (*s*, Ac); 2.10 (*s*, Ac); 3.65 (*t*, $J = 10.3$, H_{ax}−C(6)); 3.84 (*dd*, $J = 1.5, 9.6$, H−C(4)); 4.41 (*dd*, $J = 5.3, 10.6$, H_{eq}−C(6)); 4.65 (*dd*, $J = 1.5, 5.3$, H−C(3)); 5.00 (*dd*, $J = 4.0, 5.3$, H−C(2)); 5.12 (*ddd*, $J = 5.3, 10.0$, H−C(5)); 5.58 (*s*, PhC*HO*−C(4)); 6.01 (*s*, PhC*HO*−C(2)); 6.39 (*d*, $J = 4.0$, H−C(1)); 7.25–7.40 (*m*, 8 arom. H); 7.45–7.55 (*m*, 2 arom. H); 7.63 (*d*, $J = 3.1$, SCH); 7.85 (*d*, $J = 3.1$, NCH). ^{13}C-NMR ($CDCl_3$): 20.87 (*q*, Me); 20.91 (*q*, Me); 63.75 (*d*, C(5)); 67.84 (*t*, C(6)); 71.87 (*d*, C(1)); 74.98 (*d*, C(3)); 77.27 (*d*, C(2)); 79.78 (*d*, C(4)); 101.72 (*d*, Ph*C*HO−C(4)); 105.84 (*d*, Ph*C*HO−C(2)); 120.28 (*d*, SCH); 126.18–129.45 (several *d*); 136.94 (*s*); 137.26 (*s*); 143.01 (*d*, NCH); 165.35 (*s*, C=O); 169.62, 169.78 (2*s*, C=O, C=N). FAB-MS: 526 (100, $[M + 1]^+$).

*(*R*)-2,3:(*R*)-4,6-Di-O-benzylidene-*D*-glucitol* (**9**). At 0°, a soln. of **4** (770 mg, 2.16 mmol) in EtOH (22 ml) was treated with $NaBH_4$ (163 mg, 4.32 mmol). After 1.5 h at 0°, the soln. was diluted with phosphate buffer (10 ml; prepared by the addn. of aq. NaOH soln. to a soln. of 10 g of $NaH_2PO_4 \cdot 2\,H_2O$ in 100 ml of H_2O until pH *ca.* 6) until pH 5–6 and extracted with Et_2O. Evaporation and FC (AcOEt/hexane 6:4) gave **9** (611 mg, 79%). Oil. R_f (AcOEt/hexane 7:3) 0.53. IR ($CHCl_3$): 3588*w*, 3419*m* (br.), 3070*w*, 3008*m*, 2930*m*, 2860*m*, 1956*w*, 1812*w*, 1560*w*, 1496*w*, 1458*s*, 1400*s*, 1312*w*, 1148*s*, 1090*s*, 1072*s*, 1026*s*, 976*s*, 917*m*, 893*w*, 861*w*, 644*w*. ^{1}H-NMR (CD_3OD): 3.62 (*t*, $J = 10.4$, H_{ax}−C(6)); 3.75 (*dd*, $J = 1.2, 9.1$, H−C(4)); 3.79–3.81 (*m*, 2 H−C(1)); 4.00 (*ddd*, $J = 5.4, 9.1, 10.4$, H−C(5)); 4.26 (*dd*, $J = 5.4, 10.4$, H_{eq}−C(6)); 4.47–4.50 (*m*, H−C(2), H−C(3)); 5.58 (*s*, PhC*HO*−C(4)); 5.95 (*s*, PhC*HO*−C(2)); 7.30–7.54 (*m*, 10 arom. H). ^{13}C-NMR (CD_3OD): 62.90 (*d*, C(5)); 63.91 (*t*, C(1)); 72.64 (*t*, C(6)); 77.54 (*d*, C(3)); 79.19 (*d*, C(2)); 83.66 (*d*, C(4)); 102.80 (*d*, Ph*C*HO−C(4)); 106.70 (*d*, Ph*C*HO−C(2)); 127.58–130.72 (several *d*); 139.42 (*s*); 139.86 (*s*). FAB-MS: 359 (18, $[M + 1]^+$), 179 (16), 105 (100).

*(*R*)-2,3:(*R*)-4,6-Di-O-benzylidene-1-O-trityl-*D*-glucitol* (**10**). A soln. of **9** (548 mg, 1.53 mmol) and Ph_3CCl (639 mg, 2.29 mmol) in pyridine (3.3 ml) was treated with DMAP (9.35 mg, 0.08 mmol), stirred for 12 h at 100°, and poured into ice. Normal workup (AcOEt/H_2O) and FC (hexane/AcOEt 8:2) gave **10** (582 mg, 63%). White foam. R_f (hexane/AcOEt 7:3) 0.37. IR ($CHCl_3$): 3566*w* (br.), 3088*w*, 3066*w*, 3008*m*, 2927*s*, 2856*m*, 1958*w*, 1894*w*, 1813*w*, 1597*w*, 1491*s*, 1459*m*, 1449*s*, 1394*m*, 1312*w*, 1293*w*, 1177*w*, 1151*m*, 1088*s*, 1028*s*, 1002*w*, 978*s*, 909*s*, 868*w*, 646*w*, 632*m*. ^{1}H-NMR ($CDCl_3$): 2.52 (*d*, $J = 5.0$, exchange with CD_3OD, OH); 3.39 (*dd*, $J = 5.0, 10.0$, H−C(1)); 3.56–3.62 (*m*, H'−C(1), H−C(4), H_{ax}−C(6)); 4.07–4.22 (*m*, H_{eq}−C(6), H−C(5)); 4.48 (*dd*, $J = 1.6, 6.2$, H−C(3)); 4.67 (*q*, $J \approx 5.5$, H−C(2)); 5.49 (*s*, PhC*H*−C(4)); 6.07 (*s*, PhC*HO*−C(2)); 7.20–7.54 (*m*, 25 arom. H). ^{13}C-NMR ($CDCl_3$): 61.78 (*d*, C(5)); 64.85 (*t*, C(1)); 71.01 (*t*, C(6)); 75.96, 76.26 (2*d*, C(2), C(3)); 81.58 (*d*, C(4)); 86.98 (*s*, Ph_3C); 101.28 (*d*, Ph*C*HO−C(4)); 105.26 (*d*, Ph*C*HO−C(2)); 126.13–129.59 (several *d*); 137.29 (*s*); 137.63 (*s*); 143.81 (*s*, 3 arom. C). FAB-MS: 601 (9, $[M + 1]^+$), 600 (26), 599 (43), 243 (100, Ph_3C^+).

*(*R*)-1,3:(*R*)-4,5-Di-O-benzylidene-6-O-trityl-*L-xylo*-hex-2-ulose* (**11**). At 25°, a soln. of **10** (488 mg, 0.813 mmol) in CH_2Cl_2 (3.8 ml) was treated with *Dess-Martin* periodinane (517 mg, 1.22 mmol). After 5 h, the mixture was diluted with Et_2O and filtered through *Celite*. Evaporation and FC (hexane/AcOEt 8:2) gave **11** (459 mg, 94%). White foam. R_f (hexane/AcOEt 7:3) 0.6. IR ($CHCl_3$): 3586*w*, 3467*w*, 3088*w*, 3065*m*, 3007*s*, 2875*m*, 1957*w*, 1900*w*, 1815*w*, 1740*s*, 1598*m*, 1491*m*, 1459*s*, 1449*s*, 1389*s*, 1312*w*, 1292*w*, 1149*s*, 1090*s*, 1027*s*, 1002*w*, 978*s*, 909*s*. ^{1}H-NMR ($CDCl_3$): 3.39 (*dd*, $J = 5.6, 9.6$, H−C(6)); 3.63 (*dd*, $J = 5.3, 9.6$, H'−C(6)); 4.50–4.65 (*m*, 2 H−C(1), H−C(3), H−C(5)); 4.73 (*dd*, $J = 1.6, 6.5$, H−C(4)); 6.00 (*s*, PhC*HO*−C(1)); 6.19 (*s*, PhC*HO*−C(4)); 7.20–7.65 (*m*, 25 arom. H). ^{13}C-NMR ($CDCl_3$): 64.51 (*t*, C(6)); 72.79 (*t*, C(1)); 75.85, 77.95 (2*d*, C(4), C(5)); 83.15 (*d*, C(3)); 87.08 (*s*, Ph_3C); 99.31 (*d*, Ph*C*HO−C(1)); 105.62 (*d*, Ph*C*HO−C(4)); 126.21–129.56 (several *d*); 136.95 (*s*); 137.02 (*s*); 143.70 (*s*, 3 arom. C); 204.11 (*s*, C(2)). FAB-MS: 597 (3, $[M + 1]^+$), 243 (100, Ph_3C^+).

*(*R*)-2,3:(*R*)-4,6-Di-O-benzylidene-5-C-(thiazol-2-yl)-1-O-trityl-*D*-glucitol* (**12**). At 0°, a soln. of **11** (168 mg, 0.28 mmol) in CH_2Cl_2 (1 ml) was treated with 2-TST (89 µl, 0.56 mmol), warmed to 25°, and stirred for 48 h. After evaporation and drying *i.v.*, the soln. of the residue in THF (3.5 ml) was treated with 1M Bu_4NF soln. in THF (700 µl) and stirred for 2 h. Evaporation, normal workup, and FC (hexane/AcOEt 8:2) gave **12** (154 mg, 80%). White foam. R_f (hexane/AcOEt 7:3) 0.36. IR ($CHCl_3$): 3434*m*, 3066*m*, 3007*s*, 2964*w*, 2926*w*, 2864*m*, 1493*s*, 1449*s*, 1385*s*, 1314*w*, 1297*w*, 1261*s*, 1143*w*, 1090*s*, 1027*s*, 978*m*, 900*w*. ^{1}H-NMR ($CDCl_3$): 3.22 (*dd*, $J = 5.6, 9.3$, H−C(1)); 3.51 (*dd*, $J = 6.2, 9.6$, H'−C(1)); 4.06 (br. *s*, H−C(4), 2 H−C(6)); 4.39 (*dd*, $J = 1.2, 5.9$, H−C(3)); 4.52 (*dd*, $J = 5.6, 5.9$, H−C(2)); 5.77 (*s*, PhC*HO*−C(4)); 5.79 (*s*, PhC*HO*−C(2)); 7.20–7.50 (*m*, 25 arom. H, SCH); 7.69 (*d*, $J = 3.1$, NCH). ^{13}C-NMR ($CDCl_3$): 65.12 (*t*, C(1)); 69.25 (*t*, C(6)); 75.11 (*s*, C(5)); 75.11, 76.77 (2*d*, C(2),

C(3)); 84.47 (*d*, C(4)); 86.98 (*s*, Ph_3*C*); 102.71 (*d*, Ph*C*HO–C(4)); 104.36 (*d*, Ph*C*HO–C(2)); 121.46 (*d*, SCH); 126.16–129.4 (several *d*); 137.11 (*s*); 139.25 (*s*); 143.83 (*d*, NCH); 169.50 (*s*, C=N). FAB-MS: 684 (38, $[M + 1]^+$), 243 (100).

5-O-Acetyl-(R)-2,3:(R)-4,6-di-O-benzylidene-5-C-(thiazol-2-yl)-1-O-trityl-D-glucitol (**13**). A soln. of **12** (154 mg, 0.225 mmol) in pyridine (3.5 ml) and Ac_2O (3.5 ml) was treated with DMAP (6 mg, 0.05 mmol) and stirred for 12 h at 25°. Evaporation and FC (hexane/AcOEt 8:2) gave **13** (128 mg, 79%). White foam. R_f (hexane/AcOEt 7:3) 0.73. UV (MeOH): 218 (4.3). CD (MeOH): 240 (5.8). IR ($CHCl_3$): 3007*m*, 2966*s*, 2877*m*, 1740*s*, 1585*m*, 1460*m*, 1429*w*, 1382*m*, 1288*w*, 1261*s*, 1143*m*, 1092*s*, 1016*s*, 909*s*. ^{1}H-NMR ($CDCl_3$): 2.13 (*s*, Ac); 3.15 (*dd*, $J = 7.2, 9.0$, H–C(1)); 3.62 (*dd*, $J = 6.3, 9.0$, H'–C(1)); 4.14 (*d*, $J = 11.2$, H_{ax}–C(6)); 4.29 (*d*, $J = 1.6$, H–C(4)); 4.40 (*td*, $J = 5.9, 7.2$, H–C(2)); 4.58 (*dd*, $J = 1.5, 5.9$, H–C(3)); 5.40 (*d*, $J = 11.2$, H_{eq}–C(6)); 5.69 (*s*, PhC*H*O–C(4)); 5.82 (*s*, PhC*H*O–C(2)); 7.10–7.14 (*m*, 2 arom. H); 7.20–7.50 (*m*, 21 arom. H, SCH); 7.62–7.66 (*m*, 2 arom. H); 7.70 (*d*, $J = 3.1$, NCH). ^{1}H-NMR (CD_3OD): 2.05 (*s*, Ac); 3.29–3.34 (*m*, H–C(1)); 3.50 (*dd*, $J = 5.3, 9.6$, H'–C(1)); 4.20 (*d*, $J = 11.5$, H_{ax}–C(6)); 4.31 (*d*, $J = 1.2$, H–C(4)); 4.35 (*q*, $J \approx 5.9$, H–C(2)); 4.58 (*dd*, $J = 1.5, 5.9$, H–C(3)); 5.20 (*d*, $J = 11.2$, H_{eq}–C(6)); 5.60 (*s*, PhC*H*O–C(4)); 5.88 (*s*, PhC*H*O–C(2)); 7.05–7.15 (*m*, 2 arom. H); 7.20–7.50 (*m*, 21 arom. H, SCH); 7.61 (*d*, $J = 3.4$, NCH). ^{13}C-NMR ($CDCl_3$): 21.30 (*q*, Me); 65.14 (*t*, C(1)); 73.72 (*t*, C(6)); 75.59 (*s*, C(5)); 75.93, 77.14 (2*d*, C(2), C(3)); 83.11 (*d*, C(4)); 87.16 (*s*, Ph_3*C*); 102.97 (*d*, Ph*C*HO–C(4)); 104.41 (*d*, Ph*C*HO–C(2)); 120.13 (*d*, SCH); 126.18–129.55 (several *d*); 136.97 (*s*); 137.29 (*s*); 140.95 (*s*, 3 arom. C); 143.85 (*d*, NCH); 164.60 (*s*, C=O); 169.36 (*s*, C=N). FAB-MS: 726 (60, $[M + 1]^+$), 725 (51), 724 (100), 243 (83).

5-O-Acetyl-(R)-2,3:(R)-4,6-di-O-benzylidene-5-C-(thiazol-2-yl)-D-glucitol (**14**). At 25°, a soln. of **13** (200 mg, 0.276 mmol) in CH_2Cl_2 (10 ml) was treated with $FeCl_3 \cdot 6\,H_2O$ (194 mg, 0.717 mmol) and stirred for 1 h. Normal workup and FC (hexane/AcOEt 1:1) gave **14** (77 mg, 58%). White foam. R_f (hexane/AcOEt 1:1) 0.18. IR ($CHCl_3$): 3278*m* (br.), 3070*w*, 3008*m*, 1750*s*, 1497*m*, 1458*m*, 1401*w*, 1371*s*, 1309*m*, 1248*s*, 1152*w*, 1132*w*, 1091*s*, 1056*s*, 1027*s*, 948*w*, 917*w*, 894*w*. ^{1}H-NMR ($CDCl_3$): 2.22 (*s*, Ac); 3.67 (*t*, $J = 6.5$, exchange with CD_3OD, OH); 3.80–3.88 (*m*, addn. of $CD_3OD \rightarrow$ *d*, $J = 5.0$, 2 H–C(1)); 4.12 (*d*, $J = 10.6$, H_{ax}–C(6)); 4.24 (*d*, $J = 5.3$, H–C(4)); 4.36 (*t*, $J = 5.3$, H–C(3)); 4.63 (*q*, $J \approx 5.3$, H–C(2)); 5.38 (*d*, $J = 10.9$, H_{eq}–C(6)); 5.79 (*s*, PhC*H*O–C(4)); 5.82 (*s*, PhC*H*O–C(2)); 7.26–7.40 (*m*, 8 arom. H); 7.36 (*d*, $J = 3.1$, SCH); 7.59–7.61 (*m*, 2 arom. H): 7.78 (*d*, $J = 3.1$, NCH). ^{13}C-NMR ($CDCl_3$): 21.38 (*q*, Me); 63.73 (*t*, C(1)); 73.08 (*t*, C(6)); 75.51 (*s*, C(5)); 76.69, 79.31 (2*d*, C(2), C(3)); 81.56 (*d*, C(4)); 102.95 (*d*, Ph*C*HO–C(4)); 103.53 (*d*, Ph*C*HO–C(2)); 120.73 (*d*, SCH); 126.44–129.51 (several *d*); 136.63 (*s*); 136.97 (*s*); 140.79 (*d*, NCH); 165.31, 169.12 (2*s*, C=N, C=O). FAB-MS: 484 (100, $[M + 1]^+$).

Transformation of **14** *into* **6**. At 25°, a soln. of **14** (70 mg, 0.1449 mmol) in CH_2Cl_2 (1.3 ml) was treated with *Dess-Martin* periodinane (123 mg, 0.2899 mmol). After 2 h, the mixture was diluted with Et_2O and filtered through *Celite*. After evaporation, the crude aldehyde **15** (59 mg) was dissolved in CH_2Cl_2 (550 µl), treated at 0° with 2-TST (35 µl; 0.2182 mmol), warmed to 25°, and stirred for 14 h. After evaporation and drying *i.v.*, a soln. of the residue in THF (2 ml) was treated with 1M Bu_4NF soln. in THF (100 µl) and stirred for 2 h. After evaporation and normal workup, a soln. of the residue in pyridine (2 ml) and Ac_2O (2 ml) was treated with DMAP (10 mg, 0.09 mmol) and stirred for 12 h at 25°. Evaporation and FC (Et_2O/hexane 7:3) gave **6** (42.2 mg, 48%).

5-O-Acetyl-(R)-2,3:(R)-4,6-di-O-benzylidene-5-C-(3-methylthiazolium-2-yl)-1-O-trityl-D-glucitol Iodide (*= 2-(5-O-Acetyl-(R)-2,3:(R)-4,6-di-O-benzylidene-1-O-trityl-D-glucitol-5-C-yl)-3-methylthiazolium Iodide*; **16**). A soln. of **13** (128 mg, 01.76 mmol) in MeCN (2 ml) was treated with MeI (2 ml, 0.182 mol) and stirred at 80° for 27 h. Evaporation, addition of Et_2O, and filtration of the precipitate gave **16** (106 mg, 69%). Yellow solid. R_f (AcOEt/MeOH 9:1) 0.32. IR ($CHCl_3$): 3064*w*, 3008*w*, 2950*m*, 2434*w*, 2367*w*, 1962*w*, 1775*m*, 1749*w*, 1599*w*, 1561*w*, 1492*m*, 1450*m*, 1402*w*, 1371*m*, 1310*w*, 1262*m*, 1152*m*, 1090*s*, 1023*s*, 978*w*, 918*w*, 900*w*, 861*w*, 818*w*, 632*w*. ^{1}H-NMR ($CDCl_3$): 2.31 (*s*, Ac); 3.54–3.66 (*m*, 2 H–C(1)); 4.15 (*s*, MeN); 4.32 (*d*, $J = 11.2$, H_{ax}–C(6)); 4.42 (*q*, $J \approx 5.5$, H–C(2)); 4.56 (br. *s*, H–C(4)); 4.78 (*d*, $J = 5.9$, H–C(3)); 5.15 (*d*, $J = 11.5$, H_{eq}–C(6)); 5.53 (*s*, PhC*H*O–C(2)); 5.99 (*s*, PhC*H*O–C(4)); 7.19–7.63 (*m*, 25 arom. H); 8.10 (*d*, $J = 3.7$, SCH); 8.14 (*d*, $J = 3.7$, NCH). ^{13}C-NMR ($CDCl_3$): 21.19 (*q*, *Me*CO); 42.96 (*q*, MeN); 64.17 (*t*, C(1)); 73.41 (*t*, C(6)); 74.83 (*s*, C(5)); 74.93, 76.30 (2*d*, C(2), C(3)); 82.01 (*d*, C(4)); 87.53 (*s*, Ph_3*C*); 103.21 (*d*, Ph*C*HO–C(4)); 105.55 (*d*, Ph*C*HO–C(2)); 125.32 (*d*, SCH); 126.00–130.13 (several *d*); 135.03 (*s*); 135.74 (*s*); 139.95 (*d*, NCH); 143.54 (*s*, 3 arom. C); 168.78 (2*s*, C=N, C=O).

1,2:5,6-Di-O-isopropylidene-3-C-(thiazol-2-yl)-α-D-glucofuranose (**18**). At 25°, a soln. of **17** [17] (210 mg, 0.81 mmol) in THF (3 ml) was treated with 2-TST (257 µl, 1.62 mmol) and heated at 80° for 36 h. After evaporation and drying *i.v.*, a soln. of the residue in THF (5 ml) was treated with 1M Bu_4NF soln. in THF (1.5 ml) and stirred for 2 h. Evaporation followed by normal workup and FC (hexane/AcOEt 1:1) gave **18** (167 mg, 60%). White solid. R_f (hexane/AcOEt 7:3) 0.2. IR ($CHCl_3$): 3443*m* (br.), 3123*w*, 3092*w*, 2991*s*, 2938*m*, 2891*m*, 1495*m*, 1455*m*, 1384*s*, 1374*s*, 1320*w*, 1307*w*, 1248*s*, 1164*s*, 1108*m*, 1074*s*, 1017*s*, 868*s*, 844*s*. ^{1}H-NMR (CDCl$_3$): 1.13 (*s*, Me); 1.22 (*s*, Me); 1.34 (*s*, Me); 1.64 (*s*, Me); 4.04 (*dd*, J = 5.3, 9.0, H–C(6)); 4.09 (*dd*, J = 6.5, 9.0, H'–C(6)); 4.33 (*q*, $J \approx$ 5.9, H–C(5)); 4.42 (*d*, J = 3.4, H–C(2)); 4.46 (*d*, J = 5.9, H–C(4)); 5.05 (*s*, exchange with CD$_3$OD, OH); 6.08 (*d*, J = 3.4, H–C(1)); 7.44 (*d*, J = 3.4, irrad. at 7.79 → *s*, SCH); 7.79 (*d*, J = 3.4, irrad. at 7.44 → *s*, NCH). ^{13}C-NMR (CDCl$_3$): 24.87 (*q*, Me); 25.86 (*q*, Me); 26.56 (*q*, Me); 26.96 (*q*, Me); 66.61 (*t*, C(6)); 73.47 (*d*, C(5)); 82.47 (*s*, C(3)); 84.89, 86.59 (2*d*, C(2), C(4)); 105.54 (*d*, C(1)); 109.19 (*s*, Me$_2$*C*); 113.35 (*s*, Me$_2$*C*); 121.60 (*d*, SCH); 141.00 (*d*, NCH); 167.26 (*s*, C=N). FAB-MS: 344 (100, $[M+1]^+$), 286 (62), 228 (32).

3-O-Acetyl-1,2:5,6-di-O-isopropylidene-3-C-(thiazol-2-yl)-α-D-glucofuranose (**19**). A soln. of **18** (167 mg, 0.49 mmol) in pyridine (2 ml) and Ac$_2$O (2 ml) was treated with DMAP (10 mg, 0.09 mmol) and stirred for 65 h at 25°. Evaporation and FC (hexane/AcOEt 8:2) gave **19** (152 mg, 81%). White solid. UV (MeOH): 219 (3.4), 245 (3.7). CD (MeOH): 245 (–1.6). R_f (hexane/AcOEt 7:3) 0.42. IR (CHCl$_3$): 2992*s*, 2938*w*, 2902*w*, 1755*s*, 1492*w*, 1456*w*, 1384*w*, 1374*s*, 1314*w*, 1248*s*, 1165*s*, 1113*w*, 1073*s*, 1055*s*, 1020*s*, 948*w*, 930*w*, 909*m*, 871*m*. ^{1}H-NMR (CDCl$_3$): 1.28 (*s*, Me); 1.30 (*s*, Me); 1.38 (*s*, Me); 1.62 (*s*, Me); 2.14 (*s*, Ac); 4.12 (*dd*, J = 6.5, 8.4, H–C(6)); 4.22 (*dd*, J = 5.6, 8.4, H'–C(6)); 4.53 (*d*, J = 3.1, H–C(4)); 4.60 (*ddd*, J = 3.1, 5.9, 6.5, H–C(5)); 5.19 (*d*, J = 3.7, irrad. at 6.00 → *s*, H–C(2)); 6.00 (*d*, J = 3.7, irrad. at 5.19 → *s*, H–C(1)); 7.34 (*d*, J = 3.1, irrad. at 7.75 → *s*, SCH); 7.75 (*d*, J = 3.4, irrad. at 7.34 → *s*, NCH). ^{13}C-NMR (CDCl$_3$): 21.54 (*q*, *Me*CO); 25.20 (*q*, Me); 25.96 (*q*, Me); 26.49 (*q*, 2 Me); 64.95 (*t*, C(6)); 72.60 (*d*, C(5)); 82.10, 84.23 (2*d*, C(2), C(4)); 87.61 (*s*, C(3)); 105.04 (*d*, C(1)); 108.50 (*s*, Me$_2$*C*); 113.64 (*s*, Me$_2$*C*); 120.91 (*d*, SCH); 141.57 (*d*, NCH); 161.69 (*s*, C=N); 169.41 (*s*, C=O). FAB-MS: 386 (100, $[M+1]^+$).

1,2:5,6-Di-O-isopropylidene-3-O-methyl-3-C-(thiazol-2-yl)-α-D-glucofuranose (**20**). A soln. of **18** (27 mg, 0.079 mmol) and KOH (17 mg, 0.304 mmol) in DMSO (160 µl) was stirred for 5 min, treated with MeI (20 µl, 0.16 mmol), and stirred for 2 h. Normal workup (CH$_2$Cl$_2$/H$_2$O) and FC (hexane/AcOEt 7:3) gave **20** (22 mg, 79%). White solid. UV (MeOH): 245 (3.7). CD (MeOH): 255 (–0.4). R_f (hexane/AcOEt 7:3) 0.35. IR (CHCl$_3$): 2991*s*, 2939*w*, 2837*w*, 1490*m*, 1456*m*, 1383*s*, 1374*s*, 1314*w*, 1270*w*, 1248*s*, 1164*s*, 1119*w*, 1080*s*, 1058*w*, 1020*s*, 946*w*, 870*s*. ^{1}H-NMR (CDCl$_3$): 1.31 (*s*, Me); 1.35 (*s*, Me); 1.38 (*s*, Me); 1.56 (*s*, Me); 3.38 (*s*, MeO); 4.10 (*dd*, J = 6.8, 8.7, H–C(6)); 4.13 (*dd*, J = 5.9, 8.4, H'–C(6)); 4.56 (*d*, J = 4.4, H–C(4)); 4.60 (*dt*, J = 4.4, 6.2, H–C(5)); 4.87 (*d*, J = 3.7, H–C(2)); 6.01 (*d*, J = 3.7, H–C(1)); 7.40 (*d*, J = 3.1, SCH); 7.90 (*d*, J = 3.1, NCH). ^{13}C-NMR (CDCl$_3$): 25.13 (*q*, Me); 26.07 (*q*, Me); 26.69 (*q*, Me); 26.95 (*q*, Me); 53.27 (*q*, MeO); 66.03 (*t*, C(6)); 73.00 (*d*, C(5)); 82.22, 84.96 (2*d*, C(2), C(4)); 87.24 (*s*, C(3)); 105.08 (*d*, C(1)); 108.58 (*s*, Me$_2$*C*); 113.29 (*s*, Me$_2$*C*); 120.73 (*d*, SCH); 142.31 (*d*, NCH); 163.50 (*s*, C=N). FAB-MS: 358 (97, $[M+1]^+$), 300 (37), 168 (100), 154 (62).

1,2:5,6-Di-O-isopropylidene-3-C-(thiazol-2-yl)-α-D-allofuranose (**21**). At –78°, a mixture of 1.6M BuLi in hexane/CH$_2$Cl$_2$ 5:7 (1 ml) was treated with a soln. of thiazole (55 µl, 0.0773 mmol) in CH$_2$Cl$_2$ (667 µl), stirred for 30 min, treated with a soln. of **17** (67 mg, 0.258 mmol) in CH$_2$Cl$_2$ (667 µl), and stirred for 2 h at –78°. Normal workup and FC (hexane/AcOEt 8:2) gave **21** (43 mg, 48%). White solid. R_f (hexane/AcOEt 1:1) 0.69. IR (CHCl$_3$): 3544*m* (br.), 3123*w*, 3090*w*, 2993*s*, 2938*w*, 2886*w*, 1500*m*, 1455*m*, 1384*s*, 1375*s*, 1315*w*, 1251*s*, 1163*s*, 1129*m*, 1096*w*, 1073*s*, 1058*s*, 1013*s*, 930*w*, 891*w*, 873*m*, 844*m*. ^{1}H-NMR (CDCl$_3$): 1.22 (*s*, Me); 1.40 (*s*, Me); 1.43 (*s*, Me); 1.66 (*s*, Me); 3.58 (*dd*, J = 5.6, 7.8, H–C(6)); 3.62 (*s*, exchange with CD$_3$OD, OH); 3.71–3.80 (*m*, H–C(5), H'–C(6)); 4.18 (*d*, J = 6.8, H–C(4)); 4.63 (*d*, J = 3.7, H–C(2)); 6.15 (*d*, J = 3.7, H–C(1)); 7.38 (*d*, J = 3.1, SCH); 7.80 (*d*, J = 3.1, NCH). ^{13}C-NMR (CDCl$_3$): 25.10 (*q*, Me); 26.54 (*q*, 2 Me); 26.77 (*q*, Me); 66.53 (*t*, C(6)); 73.59 (*d*, C(5)); 82.34 (*s*, C(3)); 82.65, 83.79 (2*d*, C(2), C(4)); 105.39 (*d*, C(1)); 109.44 (*s*, Me$_2$*C*); 113.48 (*s*, Me$_2$*C*); 119.77 (*d*, SCH); 143.04 (*d*, NCH); 170.56 (*s*, C=N).

1,2:5,6-Di-O-isopropylidene-3-O-methyl-3-C-(thiazol-2-yl)-α-D-allofuranose (**22**). A soln. of **21** (85 mg, 0.248 mmol) and KOH (53 mg, 0.946 mmol) in DMSO (600 µl) was stirred for 5 min, treated with MeI (74 µl, 1.188 mmol), and stirred for 3 h. Normal workup and FC (hexane/AcOEt 8:2) gave **22** (87 mg, 98%). White solid. UV (MeOH): 244 (3.6). CD (MeOH): 248 (4.8). R_f (hexane/AcOEt 1:1) 0.81. IR (CHCl$_3$): 2992*s*, 2929*w*, 2903*w*, 2838*w*, 1495*m*, 1455*m*, 1384*s*, 1374*s*, 1308*w*, 1261*s*, 1163*s*, 1127*w*, 1076*s*, 1022*s*, 968*m*, 928*w*, 874*s*, 850*w*, 818*w*. ^{1}H-NMR (CDCl$_3$): 1.25 (*s*, Me); 1.41 (*s*, 2 Me); 1.64 (*s*, Me); 3.42 (*dd*, J = 6.2, 8.4, H–C(6)); 3.49 (*s*, MeO); 3.52 (*dd*, J = 5.9, 8.4, H'–C(6)); 3.64 (*q*, $J \approx$ 6.2, H–C(5)); 4.38 (*d*, J = 5.9, H–C(4)); 4.92 (*d*, J = 3.7, H–C(2)); 6.12 (*d*, J = 3.4, H–C(1)); 7.45 (*d*, J = 3.4, SCH); 7.77 (*d*, J = 3.1, NCH). ^{13}C-NMR (CDCl$_3$): 25.20 (*q*, Me); 26.40 (*q*, Me); 26.61 (*q*, Me); 27.04 (*q*, Me); 54.59 (*q*, MeO); 66.03 (*t*, C(6)); 73.67 (*d*, C(5)); 82.10, 82.40 (2*d*, C(2), C(4)); 88.05 (*s*, C(3)); 105.44 (*d*,C(1)); 109.29 (*s*, Me$_2$*C*); 113.16 (*s*, Me$_2$*C*); 120.70 (*d*, SCH); 142.92 (*d*, NCH); 169.04 (*s*, C=N). FAB-MS: 358 (67, $[M+1]^+$), 342 (71), 300 (100).

REFERENCES

[1] A. Dondoni, *Pure Appl. Chem.* **1990**, *62*, 643.
[2] A. Dondoni, 'Carbohydrate Synthesis *via* Thiazoles', in 'Modern Synthetic Methods', Ed. R. Scheffold, Verlag Helvetica Chimica Acta, Basel, 1992, p. 377.
[3] A. Dondoni, L. Colombo, 'New Formyl Anion and Cation Equivalents', in 'Advances in the Use of Synthons in Organic Chemistry', Ed. A. Dondoni, Jai Press Inc., London, 1993, Vol. 1, p. 1.
[4] A. Dondoni, 'Advances in the Use of Synthons in Organic Chemistry', Jai Press Inc., London, 1995, Vol. 2.
[5] A. Dondoni, A. Marra, 'Thiazole-Based One-Carbon Extension of Carbohydrate Derivatives', in 'Preparative Carbohydrate Chemistry', Ed. S. Hanessian, 1997, p. 173.
[6] N. K. Khare, R. K. Sood, G. O. Aspinall, *Can. J. Chem.* **1994**, *72*, 237.
[7] A. Dondoni, Y. D. Wu, J. K. Lee, K. N. Houk, *J. Org. Chem.* **1996**, *61*, 1922.
[8] R. Kluger, *Pure Appl. Chem.* **1997**, *69*, 1957.
[9] R. Breslow, R. Kim, *Tetrahedron Lett.* **1994**, *35*, 699.
[10] H. Stetter, H. Kuhlmann, *Org. Synth.* **1983**, *62*, 170.
[11] A. Dondoni, *Synthesis* **1995**, 654.
[12] C. Waldraff, Dissertation, Universität Zürich, 1995.
[13] D. M. Hall, *Carbohydr. Res.* **1980**, *86*, 158.
[14] C. Li, A. Vasella, *Helv. Chim. Acta* **1993**, *76*, 211.
[15] D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155.
[16] H. J. Carlsen, S. Karsten, T. Ulven, A. Kari, *Acta Chem. Scand.* ***1996***, *50*, 185.
[17] D. C. Lankin, S. T. Nugent, S. N. Rao, *Carbohydr. Res.* **1993**, *244*, 49.
[18] J. Yoshimura, *Adv. Carbohydr. Chem. Biochem.* **1984**, *42*, 78.
[19] H. C. Brown, W. J. Hammar, J. H. Kawakami, I. Rothberg, D. L. Vander Jagt, *J. Am. Chem. Soc.* **1967**, *89*, 6381.
[20] K. Sato, J. Yoshimura, C. Shin, *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1191.
[21] A. Rosenthal, B. L. Cliff, *Can. J. Chem.* **1976**, *54*, 543.
[22] A. Dondoni, J. Orduna, P. Merino, *Synthesis* **1992**, 201.

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