ELSEVIER

Carbohydrate Research 262 (1994) 147–154

CARBOHYDRATE RESEARCH

Note

Stereochemical control in the formation of thiazolidines from O-protected reducing sugars

Anne Wadouachi [a], Daniel Beaupere [a,*], Raoul Uzan [a,*], Imane Stasik [a], David F. Ewing [b], Grahame Mackenzie [b]

[a] *Laboratoire de Chimie Organique, Université de Picardie Jules Verne, 33 Rue Saint-Leu, 80039 Amiens, France*

[b] *School of Chemistry, University of Hull, Hull HU6 7RX, United Kingdom*

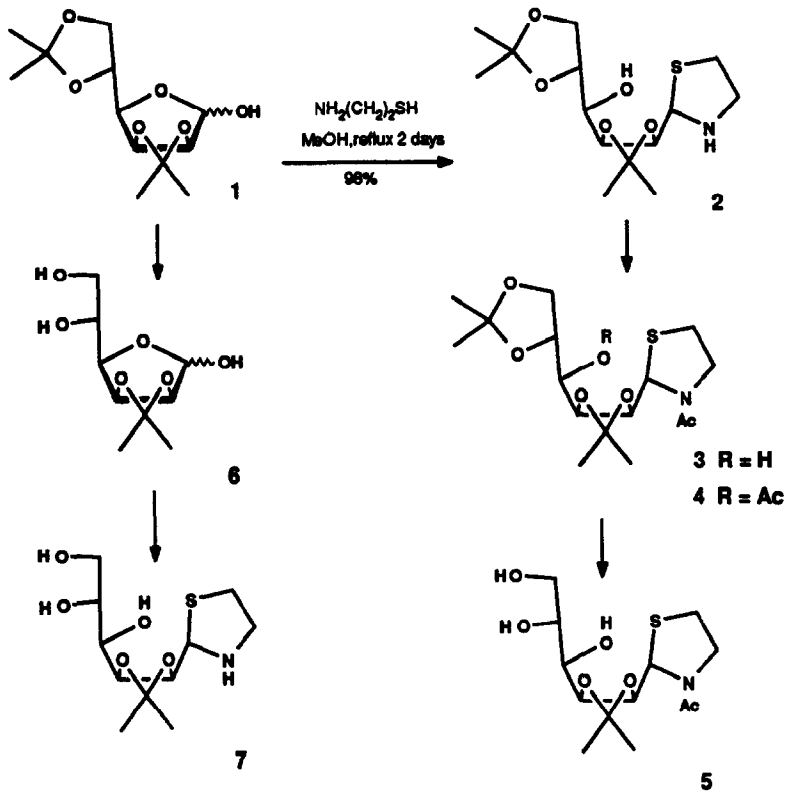
Received 17 January, 1994; accepted 24 March, 1994

Key words: 2-Polyhydroxyalkylthiazolidines; Thiazolidines; Stereoselectivity

The formation of thiazolidines from monosaccharides has been known for a long time. The major interest has centred on the condensation reaction between cysteine and reducing sugars without any O-protecting groups, leading to 2-(polyhydroxyalkyl)thiazolidine-4-carboxylic acids [1], and various biological properties have been reported [2]. The stereochemistry of the new chiral centre has been the subject of much investigation and the mutarotational behaviour established for a wide range of 2-(polyhydroxyalkyl)thiazolidine-4-carboxylic acids. These compounds were also fully characterised by ^{1}H and ^{13}C NMR spectroscopy [3]. The formation of thiazolidines from 2-aminoethanethiol is much less well studied and very few compounds of this type have been reported or adequately characterised. Early workers [4] reported some details for the derivatives from D-glucose, D-mannose, and D-galactose, and the arabinose derivative has been obtained as a 2(*R*), 2(*S*) epimeric mixture [5]. The condensation of 2-aminoethanethiol with O-protected aldoses is of interest since thiazolidine and related compounds have been widely investigated as radioprotective agents. Such compounds often have good activity and low toxicity [6]. It is particularly important to be able to vary the hydrophilicity and control the stereochemistry during the synthesis of these reagents. We now report a synthetic strategy which allows access to five variations in the pattern of the protecting groups in the thiazolidine derived from D-mannose

* Corresponding authors.

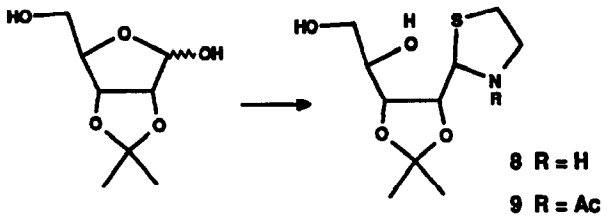
SSDI 0008-6215(94)00122-V



Scheme 1.

whilst maintaining excellent control of the stereospecificity of the new chiral centre.

Treatment of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**1**) [7] with 2-aminoethanethiol hydrochloride (neutralised with sodium methoxide — Method A) gave 2-(1,2:4,5-di-*O*-isopropylidene-D-*manno*-pentahydroxypentyl)thiazolidine (**2**) in quantitative yield. The presence of the isopropylidene group close to the anomeric centre in **1** gives rise to excellent stereocontrol and only one epimer was formed as judged by the ^{13}C NMR spectrum which consisted of a single set of lines. Regiospecific acetylation of **2** with one equivalent of acetic anhydride in pyridine gave the *N*-acetyl derivative (**3**), and with excess acetylating reagent the *O*,*N*-diacetyl derivative (**4**) was obtained (Scheme 1). Regioselective deprotection of **3** was achieved by the method of Iwata and Ohrui [8] to afford 3-acetyl-2-(1,2-*O*-isopropylidene-D-*manno*-pentahydroxypentyl)thiazolidine (**5**). No rearrangement of the the protecting group (to form the 2,3-acetal) occurred as judged by the similarity of the spectroscopic data with those for compounds **2** and **7**. The reactions leading to **3**, **4**, and **5** did not compromise the chiral integrity of the C-2 centre.



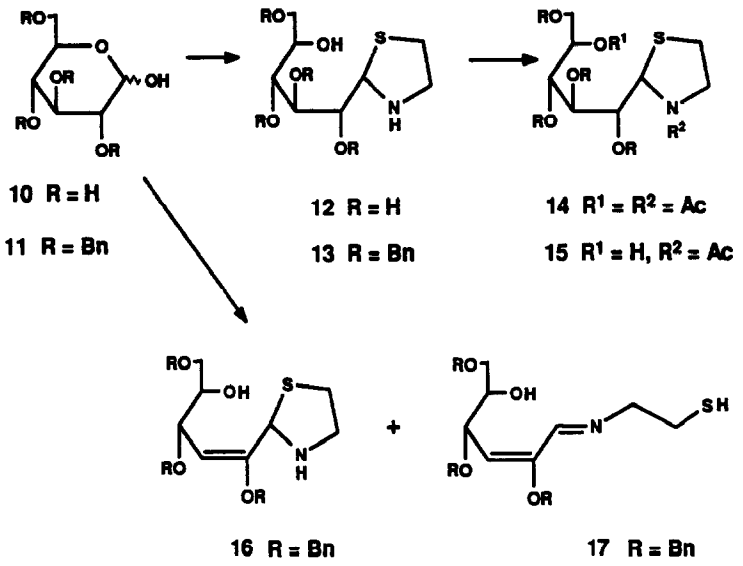
Scheme 2.

If compound **1** is first selectively deprotected to 2,3-*O*-isopropylidene-D-mannofuranose (**6**) and then converted into a thiazolidine by treatment with 2-aminoethanethiol hydrochloride (in the presence of triethylamine – Method B), 2-(1,2-*O*-isopropylidene-D-*manno*-pentahydroxypentyl)thiazolidine (**7**) is obtained quantitatively. As might be expected, the same level of stereocontrol is observed, only one epimer being formed. Thus five variations are accessible for the protection of the hydrophilic sites in 2-(D-*manno*-pentahydroxypentyl)thiazolidine, corresponding to blocking of anywhere between two and six sites.

Extension of the above methodology to a pentose is demonstrated by the conversion of 2,3-*O*-isopropylidene-D-ribofuranose [9] into 2-(1,2-*O*-isopropylidene-D-*ribo*-tetrahydroxybutyl)thiazolidine (**8**) and regioselective acetylation of this compound to 3-acetyl-2-(1,2-*O*-isopropylidene-D-*ribo*-tetrahydroxybutyl)thiazolidine (**9**) (55%) (Scheme 2). In this case the stereocontrol exerted by the isopropylidene group was less effective and two epimers were obtained in the ratio 4:1.

For glucose, O-protection with isopropylidene groups is not a viable strategy. Condensation of D-glucose (**10**) with 2-aminoethanethiol hydrochloride (by Method A) without any O-protection gave the highly hydrophilic thiazolidine **12** (Scheme 3), but without any stereoselectivity. This hydrophilicity could only be modified to the extent of having protecting groups at all sites such as in **14** (by acetylation of **12**) or only at the N-site (by selective hydrolysis of **14** to give **15**). With the O-protected compound, 2,3,4,6-tetra-*O*-benzyl-D-glucose (**11**) as substrate, thiazolidine formation by Method B gave the expected product 2-(1,2,3,5-tetra-*O*-benzyl-D-*gluco*-pentahydroxypentyl)thiazolidine (**13**) in good yield, but as a mixture of epimers in the ratio 2:3. Evidently the benzyl protecting group does not exert the same stereocontrol in glucose as does the isopropylidene group in mannose.

The use of Method A with the protected glucose **11** led to unexpected results. Two products were formed, neither of which was **13**. This mixture was separated by chromatography on silica gel. The less polar compound (49%) appeared to be a pair of epimers on the basis of the ^{13}C NMR spectrum. The proton and carbon spectra suggested the presence of a thiazolidine ring and three benzyl groups, and this compound was identified as 2-(1,3,5-tri-*O*-benzyl-D-*erythro*-1,3,4,5-tetrahydroxypent-1-enyl)thiazolidine (**16**). Evidently elimination of the benzyloxy group has occurred at the C-3 position of 2,3,4,6-tetra-*O*-benzyl-D-glucose, a reaction which has been observed previously for this compound in presence of basic or nucleophilic reagents [10,11]. The more polar species (40%) was found to be the



Scheme 3.

acyclic precursor to **16**, that is the imine (**17**), formed as an *E,Z* mixture. This structure for compound **17** was confirmed by its cyclisation to **16**, in refluxing methanol.

1. Experimental

Melting points were determined with an Electrothermal 1A 9200 digital melting-point apparatus. Optical rotations were measured with a Dip-370 digital polarimeter. NMR spectra were recorded on a Bruker 300 WB spectrometer and chemical shifts are reported as δ values (ppm) relative to Me_4Si. TLC was performed on Silica Gel $60F_{254}$ (E. Merck) and zones were detected by UV lamp or by phosphomolybdic–H_2SO_4 or vanillin–H_2SO_4 reagents. Column chromatography was carried out on Silica Gel 60 (35–70 μm). 2-Aminoethanethiol hydrochloride was purchased from Aldrich.

*2-(1,2 : 4,5-Di-O-isopropylidene-*D-manno-*pentahydroxypentyl)thiazolidine* (**2**).—*Thiazolidine preparation: Method A.* Sodium methoxide (1.66 g, 30.7 mmol) was added to 2-aminoethanethiol hydrochloride (3.49 g, 30.7 mmol) in anhyd MeOH (30 mL) and the mixture stirred at room temperature for 30 min. Salts were removed by filtration, 2,3 : 4,5-di-*O*-isopropylidene-D-mannofuranose (4.0 g, 15.38 mmol) was added and the mixture refluxed for 2 days. The solvent was removed under reduced pressure and the crude gum chromatographed on silica gel (7 : 3, 6 : 4, and 1 : 1 hexane–EtOAc) to give **2** (4.8 g, 98%); mp 111–112°C; $[\alpha]_D^{20}$ – 24.7° (*c* 1.0, CH_2Cl_2); IR (KBr) ν_{max} 3288 (NH) cm^{-1}; ^1H NMR data ($CDCl_3$): δ 1.29 (s, 3 H, Me), 1.35 (s, 6 H, 2 × Me), 1.48 (s, 3 H, Me), 2.92–3.01 (m, 3 H, H-4a,4b,5a),

3.51 (m, 2 H, H-3',5b), 3.95–4.10 (m, 3 H, H-4',5'a,5'b), 4.40, 4.47 (m, 2 H, $J_{1',2'}$ 7.9 Hz, H-1',2'), 4.65 (d, 1 H, $J_{1',2}$ 1.9 Hz, H-2); ^{13}C NMR data ($CDCl_3$): δ 24.2, 25.2, 26.1, 26.8 (4 × Me), 35.1 (C-4), 51.7 (C-5), 67.3 (C-5'), 67.5 (C-2), 70.3 (C-3'), 75.7 (C-4'), 77.5 (C-1', C-2'), 108.5 and 109.1 (2 × OCO). Anal. Calcd for $C_{14}H_{25}NO_5S$: C, 52.66; H, 7.83; N, 4.38; S, 10.03. Found: C, 52.54; H, 7.87; N, 4.27; S, 9.90.

*3-Acetyl-2-(1,2 : 4,5-di-*O*-isopropylidene-*D*-manno-pentahydroxypentyl)thiazolidine* (**3**) *and 3-acetyl-2-(3-*O*-acetyl-1,2 : 4,5-di-*O*-isopropylidene-*D*-manno-pentahydroxypentyl)thiazolidine* (**4**).—A solution of **2** (2.45 g, 7.68 mmol) and Ac_2O (0.87 mL, 9.21 mmol, 1.2 equiv) in pyridine (20 mL) was stirred at room temperature for 12 h. The solvent was removed and the residue chromatographed on silica gel (1:1 hexane–EtOAc), to give **3** (2.17 g, 78%); mp 156–157°C; $[\alpha]_D^{20}$ −95.1° (*c* 0.4, CH_2Cl_2); IR (KBr) ν_{max} 1637 (NCO) cm^{-1}; ^{1}H NMR data ($CDCl_3$): δ 1.28 (s, 6 H, 2 × Me), 1.36, 1.41 (2 s, each 3 H, Me), 2.15 (s, 3 H, Ac), 2.87–3.06 (m, 2 H, H-4a,4b), 3.31 (m, 1 H, H-5a), 3.53 (dd, 1 H, $J_{2',3'}$ 7.4, $J_{3',4'}$ 9.3 Hz, H-3'), 3.99 (m, 3 H, H-4',5'a,5'b), 4.25 (dd, 1 H, $J_{1',2'}$ 7.3 Hz, H-1'), 4.35 (d, 1 H, H-2'), 4.52 (m, 1 H, H-5b), 5.6 (d, 1 H, $J_{1',2}$ 9.9 Hz, H-2); ^{13}C NMR data ($CDCl_3$): δ 22.7 (*Me*CO), 24.1, 25.3, 26.3, 26.9 (4 × Me), 29.3 (C-4), 45.7 (C-5), 61.1 (C-2), 66.5 (C-5'), 70.2 (C-3'), 74.8 (C-2'), 76.2 (C-4'), 78.6 (C-1'), 109.1 (OCO), 169.5 (C = O). Anal. Calcd for $C_{16}H_{27}NO_6S$ (361.45): C, 53.18; H, 7.47; N, 3.87; S, 8.86. Found: C, 53.12; H, 7.51; N, 3.70; S, 8.65.

A similar reaction with an excess of Ac_2O gave **4** as a gum (80%); $[\alpha]_D^{20}$ +80.3° (*c* 1.0, CH_2Cl_2); IR (KBr) ν_{max} 1738 (OCO), 1638 (NCO) cm^{-1}; ^{1}H NMR data ($CDCl_3$): δ 1.26, 1.28, 1.32, 1.54, (4 s, each 3 H, Me), 2.03, 2.08 (2 s, each 3 H, Ac), 2.85, 3.16 (m, 2 H, H-4a,4b), 3.71 (m, 2 H, H-5a,5b), 3.84 (t, 1 H, H-5'a), 3.95 (dd, 1 H, $J_{5'a,5'b}$ 7.8 Hz, H-5'b), 4.18 (q, 1 H, $J_{4',5'a}$ 8.3, $J_{4',5'b}$ 6.5 Hz, H-4'), 4.33 (dd, 1 H, $J_{2',3'}$ 3.8 Hz, H-2'), 4.52 (dd, 1 H, $J_{1',2'}$ 7.0 Hz, H-1'), 5.27 (d, 1 H, $J_{1',2}$ 1.5 Hz, H-2), 5.46 (dd, 1 H, $J_{3',4'}$ 4.7 Hz, H-3'); ^{13}C NMR data ($CDCl_3$): δ 20.1, 22.2 (2 × *Me*CO), 24.0, 24.3, 24.4, 25.2 (4 × Me), 29.9 (C-4), 49.4 (C-5), 61.6 (C-2), 64.7 (C-5'), 68.2 (C-3'), 74.7 (C-4'), 74.9 (C-2'), 77.9 (C-1'), 107.7, 108.2 (2 × OCO), 167.8, 168.9 (2 × C = O).

*3-Acetyl-2-(1,2-*O*-isopropylidene-*D*-manno-pentahydroxypentyl)thiazolidine* (**5**).—Compound **3** (4.52 g, 12.52 mmol) was treated with copper(II) chloride dihydrate (10.69 g, 62.7 mmol, 5 equiv) in EtOH (110 mL). The mixture was stirred at room temperature for 17 h, then $NaHCO_3$ (11.0 g, 131 mmol) was added. After 40 min, water (23 mL) was added and 2 h later a further 91 mL was added. The mixture was then filtered and concentrated and the residue purified by chromatography on silica gel (EtOAc, 8:1 EtOAc–MeOH with 1% Et_3N) to give **5** as a gum (2.61 g, 65%); $[\alpha]_D^{20}$ −84.8° (*c* 0.8, MeOH); ^{1}H NMR data ($CDCl_3$): δ 1.34, 1.49 (2 s, each 3 H, Me), 2.23 (s, 3 H, Ac), 3.17, 3.21 (m, 2 H, H-4a,4b), 3.47 (m, 1 H, H-5a), 3.65 (m, 3 H, H-3',4',5'a), 3.81 (d, 1 H, $J_{5'a,5'b}$ 9.5 Hz, H-5'b), 4.38 (m, 2 H, H-1',5b), 4.56 (d, 1 H, $J_{1',2'}$ 7.3 Hz, H-2'), 5.84 (d, 1 H, $J_{1',2}$ 9.5 Hz, H-2); ^{13}C NMR data ($CDCl_3$): δ 23.0 (*Me*CO), 24.6, 26.4 (2 × Me), 29.3 (C-4), 47.0 (C-5), 62.4 (C-2), 64.6 (C-5'), 71.0 (C-4'), 72.9 (C-3'), 76.0 (C-2'), 79.5 (C-1'), 109.8 (OCO), 172.2 (C = O). Anal. Calcd for $C_{13}H_{23}NO_6S$ (321.38): C, 48.59; H, 7.16; N, 4.36; S, 9.96. Found: C, 48.62; H, 7.20; N, 4.28; S, 9.98.

2,3-O-Isopropylidene-D-mannofuranose (**6**).—Compound **1** was selectively deprotected by the method described above for **3** to give **6** (61%); mp 74–75°C; $[\alpha]_D^{20}$ +11.3° (*c* 1.02, MeOH): ^{1}H NMR data (MeOD): δ 1.33, 1.43 (2 s, each 3 H, Me), 3.59 (dd, 1 H, $J_{6a,6b}$ 11.7 Hz, H-6a), 3.78 (dd, 1 H, $J_{5,6b}$ 2.3 Hz, H-6b), 3.88 (dd, 1 H, $J_{5,6a}$ 6.0 Hz, H-5), 4.03 (dd, 1 H, $J_{4,5}$ 8.9 Hz, H-4), 4.50 (dd, 1 H, $J_{2,3}$ 5.8 Hz, H-2), 4.87 (dd, 1 H, $J_{3,4}$ 3.5 Hz, H-3), 5.24 (s, 1 H, H-1); ^{13}C NMR data (MeOH): δ 25.0, 26.4 (2 × Me), 65.2 (C-6), 70.7 (C-5), 80.3 (C-4), 81.2 (C-3), 86.7 (C-2), 102.2 (C-1), 113.6 (OCO).

2-(1,2-O-Isopropylidene-D-manno-pentahydroxypentyl)thiazolidine (**7**).—*Thiazolidine preparation: Method B.* A mixture of compound **6** (2.3 g, 10.45 mmol), 2-aminoethanethiol (1.78 g, 15.68 mmol, 1.5 equiv), and Et_3N (2.2 mL, 1.5 equiv) was stirred in MeOH (50 mL) at 65°C overnight under Ar. Then the mixture was concentrated and the residue purified by chromatography on silica gel (8:1, 6:1, and 4:1 EtOAc–MeOH) to afford **7** as a gum (100%); $[\alpha]_D^{20}$ −51.8° (*c* 1.0, MeOH); ^{13}C NMR data ($CDCl_3$): δ 25.3, 26.4 (2 × Me), 34.6 (C-4), 49.5 (C-5), 63.1 (C-2), 64.5 (C-5′), 71.3 (C-4′), 72.7 (C-3′), 79.5 (C-1′), 76.5 (C-2′), 109.3 (OCO).

2-(1,2-O-Isopropylidene-D-ribo-tetrahydroxybutyl)thiazolidine (**8**) *and 3-acetyl-2-(1,2-O-isopropylidene-D-ribo-tetrahydroxybutyl)thiazolidine* (**9**).—2,3-*O*-Isopropylidene-D-ribofuranose [9] was converted into a thiazolidine by Method A or B. The crude material was acetylated directly by the procedure described for **2**, but using a reaction time of 4.5 h, to give **9** as a gum (55%); $[\alpha]_D^{20}$ +15.7° (*c* 1.09, MeOH); IR (KBr) ν_{max} 1638 (NCO) cm^{-1}; ^{1}H NMR data ($CDCl_3$): major epimer, δ 1.46, 1.68 (2 s, each 3 H, Me), 2.26 (s, 3 H, Ac), 3.06, 3.32, (m, 2 H, H-4a,4b), 3.59 (dd, 1 H, $J_{3',4'}$ 5.2 Hz, H-4′), 3.76 (dd, 1 H, $J_{3',4'b}$ 2.3, $J_{4',4'b}$ 12.1 Hz, H-4′b), 3.97 (m, 3 H, H-3′,5a,5b), 4.40 (dd, 1 H, $J_{2',3'}$ 9.85 Hz, H-2′), 4.89 (d, 1 H, $J_{1',2'}$ 7.2 Hz, H-1′), 5.70 (s, 1 H, H-2); minor epimer, δ 1.48, 1.72 (2 s, each 3 H, Me), 2.28 (s, 3 H, Ac), 5.60 (s, 1 H, H-2); ^{13}C NMR data ($CDCl_3$): major epimer, δ 25.6 (*Me*CO), 27.0, 27.8 (2 × Me), 33.7 (C-4), 53.6 (C-5), 64.6 (C-2), 66.7 (C-4′), 72.0 (C-3′), 78.1 (C-2′), 80.9 (C-1′), 112.9 (OCO), 174.7 (CO); minor epimer, δ 24.6 (*Me*CO), 32.7 (C-4), 51.6 (C-5), 65.5 (C-2), 83.4 (C-1′), 113.6 (OCO), 174.4 (CO).

3-Acetyl-2-(1,2,3,4,5-penta-O-acetyl-D-gluco-pentahydroxypentyl)thiazolidine (**14**). —D-Glucose (20.0 g) was converted into a thiazolidine by Method A using 0.5 equiv of 2-aminoethanethiol and a reaction time of 15 h at room temperature. The precipitated product, 2-(D-*gluco*-pentahydroxypentyl)thiazolidine (**12**), was taken up in pyridine (100 mL) and Ac_2O (35 mL) added dropwise at 5–10°C. After stirring for 48 h at room temperature, the pyridine was removed under reduced pressure and the residue extracted with CH_2Cl_2. This extract was washed (water), dried (Na_2SO_4), concentrated, and chromatographed on silica gel (6:1, 1:1, and 1:2 hexane–EtOAc) to give **14** (19.4 g, 78%); mp 94–95°C; $[\alpha]_D^{20}$ −20.4° (*c* 1.0, CH_2Cl_2); IR (KBr) ν_{max} 1738 (OCO), 1638 (NCO) cm^{-1}; ^{1}H NMR data ($CDCl_3$): δ 1.82–1.85 (m, 15 H, 5 × Ac), 2.02 (s, 3 H, Ac), 2.97 (m, 2 H, H-4a,4b), 3.54 (m, 2 H, H-5a,5b), 3.84 (dd, 1 H, $J_{4',5'a}$ 5.3 Hz, H-5′a), 4.01 (dd, 1 H, $J_{5'a,5'b}$ 12.5 Hz, H-5′b), 4.86 (m, 1 H, $J_{3',4'}$ 2.9 Hz, H-4′), 5.09 (dd, 1 H, $J_{2',3'}$ 8.1 Hz, H-3′), 5.21 (dd, 1 H, H-2′), 5.22 (d, 1 H, $J_{1',2}$ 8.1 Hz, H-2), 5.39 (dd, 1 H, $J_{1',2'}$ 3.2 Hz, H-1′); ^{13}C NMR data ($CDCl_3$): δ 20.3, 20.4, 20.5, 22.7 (6 × *Me*CO), 30.9 (C-4), 50.1 (C-5),

61.5 (C-5'), 61.6 (C-2), 67.8 (C-3'), 68.0 (C-4'), 70.0 (C-2'), 71.7 (C-1'), 168.8–170.3 (C = O).

*3-Acetyl-2-(*D-gluco-*pentahydroxypentyl)thiazolidine* (**15**).—Compound **14** (4.55 g, 10.14 mmol) and NaOMe (55 mg, 0.1 equiv) were stirred in anhyd MeOH (20 mL) until the reaction was complete (33 min, monitored by TLC, 15:1:4 MeCN–AcOH–water). The mixture was neutralised with Amberlyst 15-WET resin and filtered. The filtrate was concentrated and chromatographed on silica gel (5:1 EtOAc–MeOH) to give **15** (2.3 g, 81%); mp 126–127°C; $[\alpha]_D^{20}$ −58.3° (*c* 1.0, MeOH); IR (KBr) ν_{max} 1624 (NCO) cm^{-1}; ^1H NMR data (D_2O): major epimer, δ 2.16 (s, 3 H, Me), 3.05 (m, 1 H, H-4a), 3.23 (m, 1 H, H-4b), 3.52–3.84 (m, 6 H, H-5a,2',3',4',5'a,5'b), 3.97 (m, 1 H, H-5b), 4.10 (dd, 1 H, $J_{1',2'}$ 5.8 Hz, H-1'), 5.40 (d, 1 H, $J_{1',2}$ 4.1 Hz, H-2); ^{13}C NMR data (D_2O): major epimer, δ 25.4 (*Me*CO), 32.9 (C-4), 53.9 (C-5), 65.7 (C-5'), 66.8 (C-2), 73.6, 74.0, 75.7, 77.7 (C-1',2',3',4'), 175.2 (C = O); minor epimer, δ 24.4 (*Me*CO), 31.9 (C-4), 51.7 (C-5), 67.7 (C-2), 174.8 (C = O). Anal. Calcd for $C_{10}H_{19}NO_6S$ (281.32): C, 42.70; H, 6.76; N, 4.98; S, 11.38. Found: C, 42.77; H, 6.74; N, 4.89; S, 11.42.

*2-(1,2,3,5-Tetra-*O*-benzyl-*D*-gluco-pentahydroxypentyl)thiazolidine* (**13**).—2,3,4,6-Tetra-*O*-benzyl-D-glucose (1.18 g, 2.2 mmol) was converted into a thiazolidine by Method B, using 2-aminoethanethiol hydrochloride (0.50 g, 4.4 mmol) and Et_3N (0.615 mL, 2 equiv) and worked up in the usual way to give **13** as a gum (0.84 g, 64%); $[\alpha]_D^{20}$ +24.3° (*c* 0.3, CH_2Cl_2); ^{13}C NMR data ($CDCl_3$): major epimer, δ 38.9 (C-4), 44.7 (C-5), 68.9 (C-2), 69.1 (C-5'), 73.1, 73.5, 75.0, 75.6 (CH_2Ph), 80.2, 82.5, 86.0, 91.0 (C-1',2',3',4'), 127.6–128.4 (Ph), 132.2–138.8 (C-*ipso*); minor epimer, δ 39.1 (C-4), 45.3 (C-5).

Attempted formation of **13** from 2,3,4,6-tetra-*O*-benzyl-D-glucose (2.37 g, 4.4 mmol) by Method A gave, after work up, a mixture of two species, R_f 0.18 and 0.26 (TLC, 6:4 hexane–EtOAc). This mixture was chromatographed (silica gel, 6:4, 1:1, and 1:2 hexane–EtOAc, then EtOAc) to give a first component, 2-(1,3,5-tri-*O*-benzyl-2-deoxy-D-*gluco*-1,3,4,5-tetrahydroxypent-1-enyl)thiazolidine (**16**); ^{13}C NMR data ($CDCl_3$): epimeric mixture (ca. 1:1), δ 36.4 (C-4), 53.1 (C-5), 66.7, 66.8 (C-2), 69.4, 69.6, 70.3, 73.3 (CH_2Ph), 70.9, 71.1 (C-5'), 72.5, 72.8, 74.7, 76.0 (C-3',4'), 98.8, 99.6 (C-2'), 127.5–128.5 (Ph), 136.5–138.5 (C-*ipso*), 154.6, 154.7 (C-1').

A second component was the imine (**17**); ^{13}C NMR data ($CDCl_3$): epimeric mixture (ca. 1:1), δ 35.6, 36.4 (CH_2S), 52.5, 52.7 (CH_2N), 69.4, 69.6, 70.0, 70.9, 73.4, 74.9 (CH_2Ph), 71.2 (C-6), 72.2, 72.8, 73.9, 74.7, 76.1 (C-4,5), 109.5, 110.1 (C-1), 127.5–128.3 (C-*ipso*), 156.5, 157.1 (C-2).

References

[1] R. Bognár, L. Somogyi, and Z. Györgydeák, *Leibigs Ann. Chem.*, 738 (1970) 68–78; J.C. Roberts, R.T. Nagasawa, R.T. Zerta, R.F. Fricke, and D.J.W. Goon, *J. Med. Chem.*, 30 (1987) 1891–1896.

[2] T. Gajda, L. Nagy, N. Rozlosnik, L. Korecz, and K. Burger, *J. Chem. Soc., Dalton Trans.*, (1992) 475–479.

[3] J. Radomski and A. Temeriusz, *Carbohydr. Res.*, 187 (1989) 223–237.
[4] W.A. Bonner and W. Meyer zu Reckendorf, *Chem. Ber.*, 94 (1961) 225–228.
[5] A.H. Siriwardena, A. Chiaroni, C. Riche, and D.S. Grierson, *J. Org. Chem.*, 57 (1992) 5661–5666.
[6] J. Satgé, A. Cazes, M. Bouchaut, M. Fatome, H. Sentenac-Roumanou, and C. Lion, *Eur. J. Med. Chem.–Chim. Ther.*, 17 (1982) 433–436; M. Fatome, H. Sentenac-Roumanou, C. Lion, J. Satgé, and G. Rima, *Eur. J. Med. Chem.*, 23 (1988) 257–266; Y. Robbe, J.-P. Fernandez, G. Subra, J.-P. Chapat, H. Sentenac-Roumanou, and M. Fatome, *ibid.*, 23 (1988) 155–164.
[7] O.T. Schmidt, *Methods Carbohydr. Chem.*, 2 (1963) 319; I. Régnault, G.L. Ronco, and P. Villa, *Brevet Générale Sucrière*, No. 8915995 (1989).
[8] M. Iwata and H. Ohrui, *Bull. Chem. Soc. Jpn.*, 54 (1981) 2837–2838.
[9] P.A. Levene and E.T. Stiller, *J. Biol. Chem.*, 102 (1933) 187–201.
[10] L. Dheilly, C. Fréchou, D. Beaupère, R. Uzan, and G. Demailly, *Carbohydr. Res.*, 224 (1992) 301–306.
[11] F. Nicotra, F. Ronchetti, G. Russo, and L. Toma, *Tetrahedron Lett.*, 25 (1984) 5697–5700.