Synthesis of thiazole analogues of the immunosuppressive agent (1*R*,2*S*,3*R*)-2-acetyl-4(5)-(1,2,3,4-tetrahydroxybutyl)imidazole

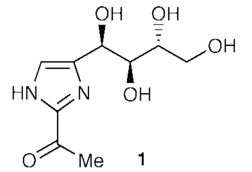
George R. Jeoffreys,[a] Alison T. Ung,[a] Stephen G. Pyne,*[a] Brian W. Skelton[b] and Allan H. White[b]

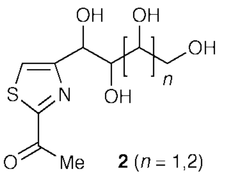
[a] *Department of Chemistry, University of Wollongong, Wollongong, NSW, 2522, Australia*
[b] *Department of Chemistry, University of Western Australia, Nedlands, WA, 6907, Australia*

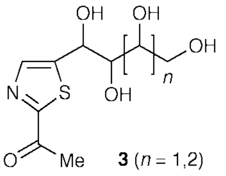
Received (in Cambridge) 7th May 1999, Accepted 23rd June 1999

The synthesis of four of the diastereoisomers of 2-acetyl-5-(1,2,3,4-tetrahydroxybutyl)thiazole and two of the diastereoisomers of 2-acetyl-5-(1,2,3,4,5-pentahydroxypentyl)thiazole and 2-acetyl-4-(1,2,3,4,5-pentahydroxypentyl)thiazole are reported. These syntheses involve the condensation of 5- or 4-metallated 2-(1,1-dimethoxyethyl)thiazoles with 2,3-*O*-isopropylidene-D-erythrono-1,4-lactone or 5-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-isopropylidene-D-ribonolactone followed by reductive ring-opening of the resulting lactols. The stereochemistries and structures of some key compounds have been determined by single crystal X-ray structural analysis.

As part of an ongoing medicinal chemistry project[1–6] we required the synthesis of the 4- and 5-thiazole analogues, **2** and **3** respectively, of the known immunosuppressive agent, (1*R*,2*S*,3*R*)-2-acetyl-4(or 5)-(1,2,3,4-tetrahydroxybutyl)imidazole (THI) **1**.[7–9] THI is a minor component of the common food additive Caramel Colour III. THI has been found to cause lymphopenia (depression of blood lymphocyte counts), without any apparent side-effects, in mice and rats that have been given THI in their drinking water.[7,8] Thus THI and its analogues have potential applications as an immunosuppressive agent in organ transplant biology or for preventing the onset of diabetes.[9]


1


2 ($n = 1,2$)


3 ($n = 1,2$)

Our general strategy for the synthesis of thiazole analogues of THI involves the condensation of 5- or 4-metallated 2-(1,1-dimethoxyethyl)thiazole with 2,3-*O*-isopropylidene-D-erythrono-1,4-lactone **6** or 5-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-isopropylidene-D-ribonolactone **21** followed by reductive ring-opening of the resulting lactols. The synthesis of four diastereoisomers of compound **2** ($n = 1$) has been reported as a communication.[5] We now report the details of this work and the synthesis of some pentahydroxypentyl analogues **2** ($n = 2$) and **3** ($n = 2$) and X-ray structures to support the stereochemical assignments made to the individual diastereoisomers.

Synthesis of 2-acetyl-5-(1,2,3,4-tetrahydroxybutyl)thiazoles

Commercially available 2-acetylthiazole **4** was converted to its dimethoxyketal **5** in 80% yield, using standard conditions. The 5-lithiothiazole derivative of **5** was generated at −78 °C and was then treated with 2,3-*O*-isopropylidene-D-erythrono-1,4-lactone **6** at the same temperature for 1.5 h. Quenching the reaction mixture at −78 °C, followed by column chromatography, gave the lactols **7a**,**b** in 62% yield as a 95:5 mixture of diastereoisomers, along with a small amount (7%) of the C-2 epimerized ketone **8** (Scheme 1). The amount of ketone **8** formed increased upon increasing the reaction temperature. For example, warming the reaction mixture to rt over 1 h, prior to quenching resulted in a 2:1 mixture of **7** and **8**, respectively. The stereochemistry of the ketone **8** will be discussed later in this paper.

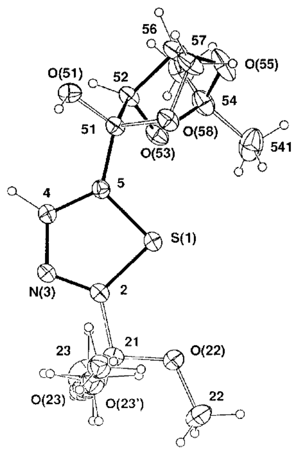
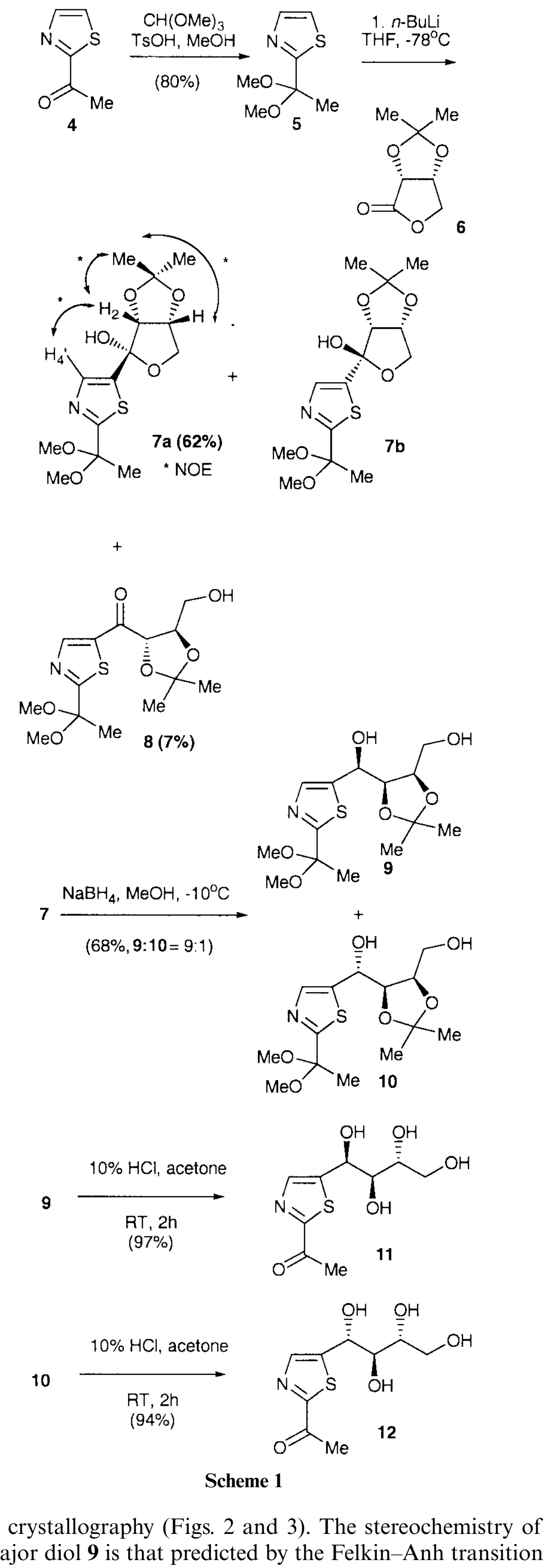


Fig. 1 Compound **7b**.

In solution ($CDCl_3$) the major lactol isomer was **7a** from NOESY experiments that showed significant cross-peaks between H4′ of the thiazole ring and H2 of the dihydrofuran ring (Scheme 1). Surprisingly, crystallization of this lactol mixture gave single crystals of lactol **7b**, as characterized by a single crystal X-ray study, which was expected to be thermodynamically less favoured than **7a** since the thiazole ring is *syn* to the sterically demanding 1,3-dioxolane ring. A projection of the structure of **7b** is shown in Fig. 1. It is possible that in the solid state intermolecular H-bonding favours formation of lactol **7b** over **7a**.

Reductive ring opening of **7** with sodium borohydride in methanol at −10 °C afforded a 9:1 mixture of the diols **9** and **10** that could be readily separated by column chromatography. The stereochemistry of these diols was also determined by



Scheme 1

X-ray crystallography (Figs. 2 and 3). The stereochemistry of the major diol **9** is that predicted by the Felkin–Anh transition model (**A**)[10–13] or the γ-chelated transition state model **B**,[14] in which hydride attack would be expected to occur from the convex face of the bicyclo[5.3.0]decane ring system in **B** (Fig. 4). Acid hydrolysis of the individual diastereoisomers **9** and **10** gave the tetrols **11** and **12**, respectively. Although, compound **11** had identical spectral properties to that obtained for **11** from our previous synthesis, the specific rotation of **11** from this work, $[\alpha]_D^{25}$ +18.3 (*c* 0.6, H_2O), was considerably higher than that obtained previously {$[\alpha]_D^{25}$ +7.7 (*c* 0.34, H_2O)} using a different synthetic route.[3]

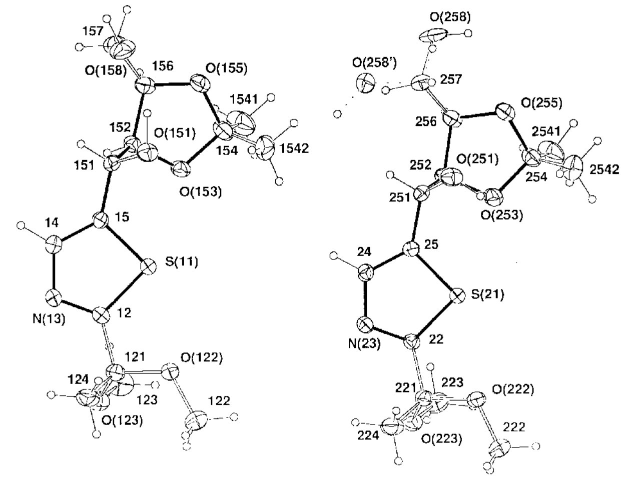


Fig. 2 Compound **9** (showing molecules **1** and **2**).

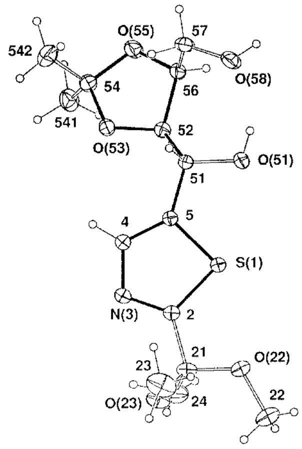


Fig. 3 Compound **10**.

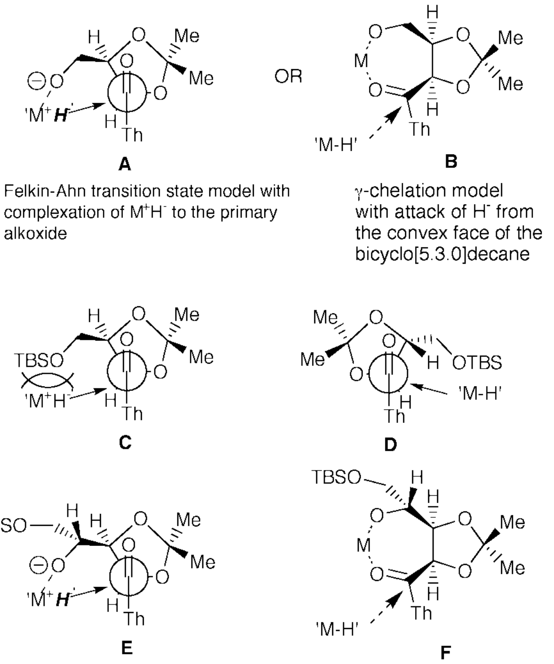
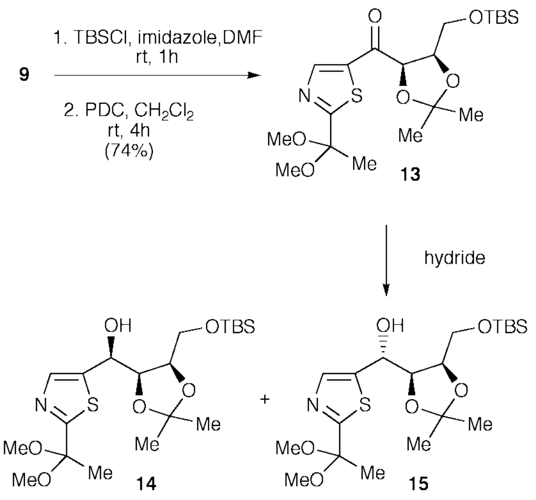


Fig. 4

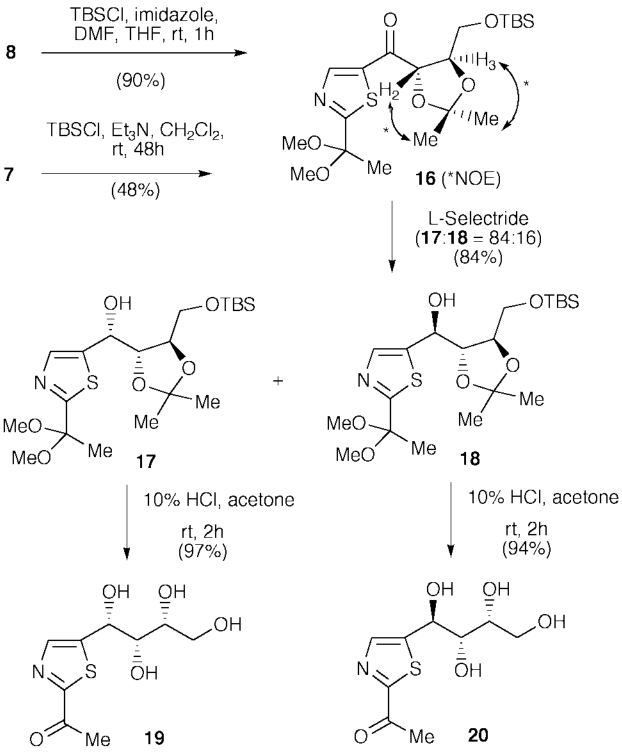
To examine the effect of the C4 hydroxy or alkoxy group on the reduction of the lactol **7**, and to test the likelihood of the transition states **A** and **B**, diol **9** was converted in two steps to the ketone **13** (Scheme 2). This ketone was different to the ketone **16** obtained from either the direct silylation of the



Reducing agent	dr (**14**:**15**)
DIBAL	37:63
NaBH$_4$	51:49
K-Selectride	50:50
L-Selectride	65:35

Scheme 2

hydroxy-ketone **8** with *tert*-butylchlorodimethylsilane (TBSCl)–imidazole or by a ring-opening–silylation–epimerization sequence on the lactol **7** using TBSCl and the stronger base triethylamine (Scheme 3). The latter reaction was very slow, the low yield of **16** (48%) obtained being due to the presence of unreacted starting material. NOESY experiments on **16** showed significant cross peaks between H2 and the β-Me of the dioxolane ring and between H3 and the α-Me of the dioxolane ring and thus revealed the *trans*-1,3-dioxolane structure.



Scheme 3

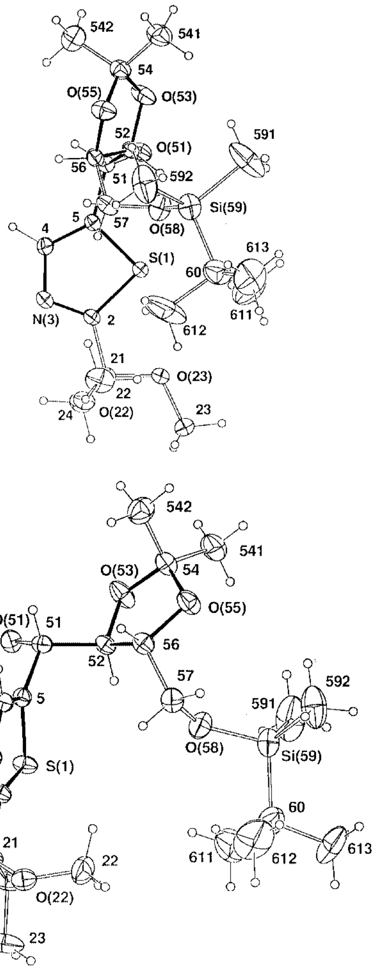


Fig. 5 Compound **17** (showing molecules **1** and **2**).

In contrast to **7**, the reduction of the keto group of the 4-*O*-silylated *cis*-1,3-dioxolane **13**, was poorly diastereoselective and gave nearly equal proportions of the diols **14** and **15** (Scheme 2). The structures of **14** and **15** were confirmed by their conversion to **9** and **10** respectively, by desilylation with tetrabutylammonium fluoride in THF. The poor diastereoselectivity in the reductions of **13** can be understood in terms of the transition state model **C** in which the OTBS group and the C2 methyl group on the 1,3-dioxolane ring, sterically hinder attack of hydride from the *Si* and *Re* faces of the carbonyl group, respectively. Thus, the free hydroxy group in transition state structures **A** and **B**, which can potentially coordinate the reducing agent, appears to be essential for obtaining a high degree of diastereoselectivity.

Reduction of the keto group of the 4-*O*-silylated *cis*-1,3-dioxolane **16** with a number of reducing agents (NaBH$_4$, DIBAL, Red-Al, K-Selectride and L-Selectride) gave mixtures of the diastereoisomeric alcohols **17** and **18**. The optimum diastereoselectivity was obtained (**17**:**18** = 84:16) when L-Selectride was employed at −78 °C. The stereochemistry assigned to **17** was unequivocally determined by an X-ray study (Fig. 5) and is that expected from the Felkin–Ahn transition state model **D**. Acid hydrolysis of the individual diastereoisomers **17** and **18** gave the tetrols **19** and **20**, respectively.

Synthesis of 2-acetyl-4-(1,2,3,4,5-pentahydroxypentyl)- and 2-acetyl-5-(1,2,3,4,5-pentahydroxypentyl)-thiazoles

The 5-lithiothiazole derivative of **5** was treated with 5-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-isopropylidene-D-ribonolactone **21**[15] at −78 °C for 1.5 h to give the lactol **22**, as a single isomer in 64% yield (Scheme 4). In contrast to the corresponding reaction of lithiated **5** with lactone **6**, no ring-opening ketone products were observed. X-Ray analysis of **22** showed it had the same relative stereochemistry as **7b** with respect to the thiazole and

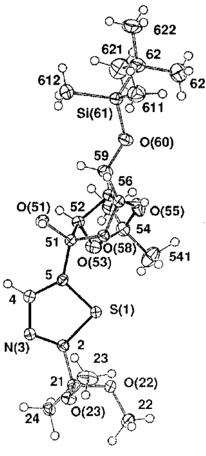


Fig. 6 Compound **22**.

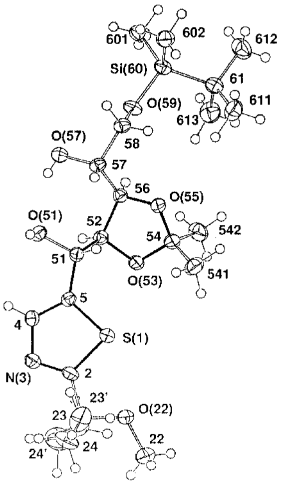


Fig. 7 Compound **24**.

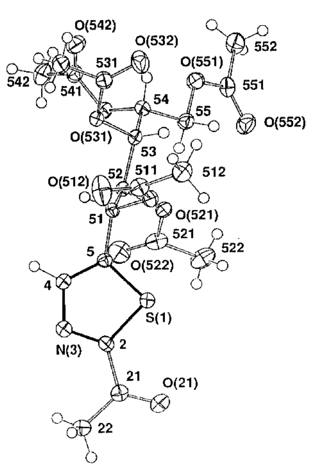
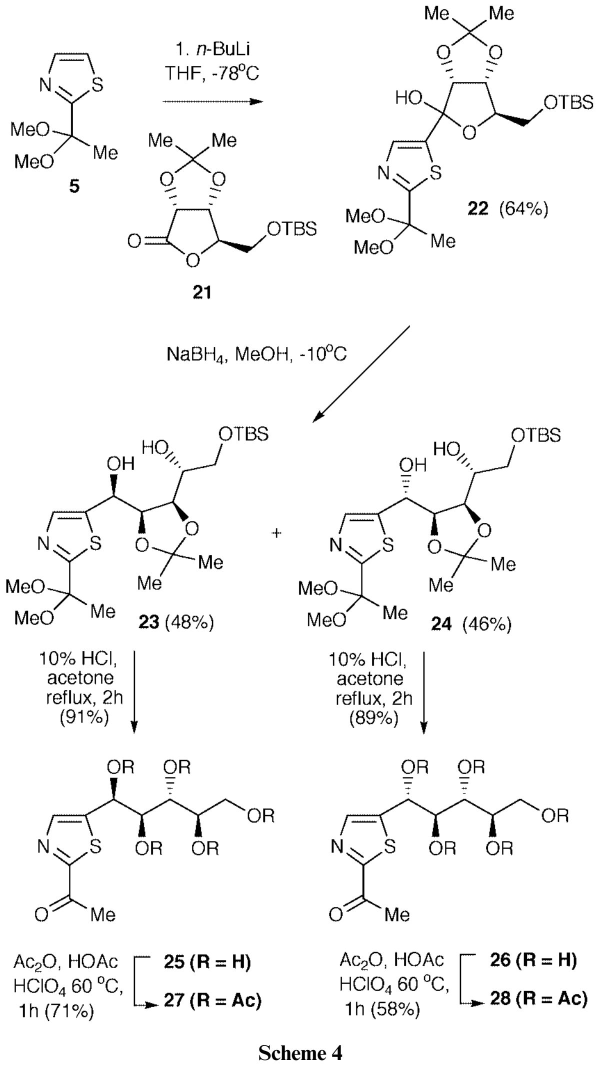


Fig. 8 Compound **27**.



Scheme 4

1,3-dioxolane rings (Fig. 6). Reduction of **22** with sodium borohydride in methanol at −10 °C afforded a mixture of the diols **23** and **24**. These could be isolated in diastereomerically pure form in 48% and 46% yields, respectively, by column chromatography. Attempts to reductively ring-open the lactol **22** with other reducing agents (*e.g.* DIBAL and L-Selectride) were unsuccessful and only starting lactol **22** was recovered. The poor diastereoselectivity in the reduction of **22** is in stark contrast to that found for the lactol **7** and is unexpected based on the transition state structures **A** and **B**. The corresponding transition state structures **E** and **F** for the reduction of ring-opened **22** do not appear to be made unfavourable by the extra $TBSOCH_2$ group which should occupy a pseudo-equatorial position. Acid hydrolysis of the individual diastereoisomers **23** and **24** gave the pentols **25** and **26**, respectively, in good yields, which were converted to their corresponding pentaacetates **27** and **28** respectively, under standard conditions.[4] The stereochemistry of **24** and **27** was confirmed by single crystal X-ray analysis (Figs. 7 and 8).

4-Bromo-2-(1,1-dimethoxyethyl)thiazole[6] underwent transmetallation at −78 °C and was then treated with the lactone **21** at −78 °C for 1.5 h (Scheme 5). Purification of the reaction mixture by column chromatography gave the desired lactol **29** (dr = 69:31) in 44% yield and surprisingly the isomeric 5-thiazole adduct **22** in 15% yield (Scheme 5). The latter compound must have arisen through formation of the more stable 5-lithiated thiazole derivative. Reduction of **29** with sodium borohydride in methanol at −10 °C afforded a 60:40 mixture of the diols **30** and **31**, respectively. Separation of this mixture by column chromatography gave diastereomerically pure **31** and **32** in 30% and 21% yields, respectively. The stereochemistry of **30** was secured by single crystal X-ray analysis (Fig. 9). Compounds **30** and **31** were converted to their pentols **32** and **33** respectively by acid hydrolysis. Small samples of these pentols were converted to their respective pentaacetates, **34** and **35**. The ^1H NMR analysis of the tetraacetate of THI (**1**) and its C1 epimer[4] and of the diastereomeric pairs **27** and **28** and **34** and **35** showed that H1, in compounds with the (1*R*)-stereochemistry (tetraacetate of **1**, **27** and **34**), comes further downfield of H1 in their respective isomers having the (1*S*)-stereochemistry. Furthermore, $J_{1,2}$ is generally smaller in the 1*R* diastereoisomer.

In conclusion, we have developed a short, efficient and

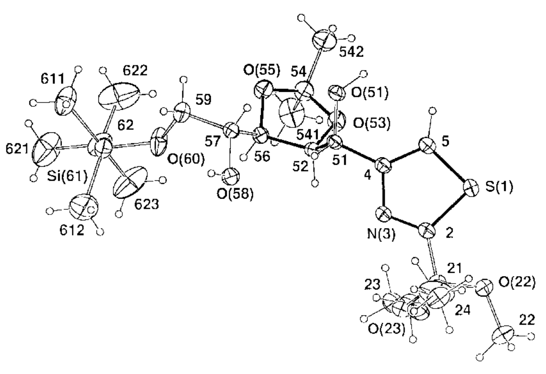
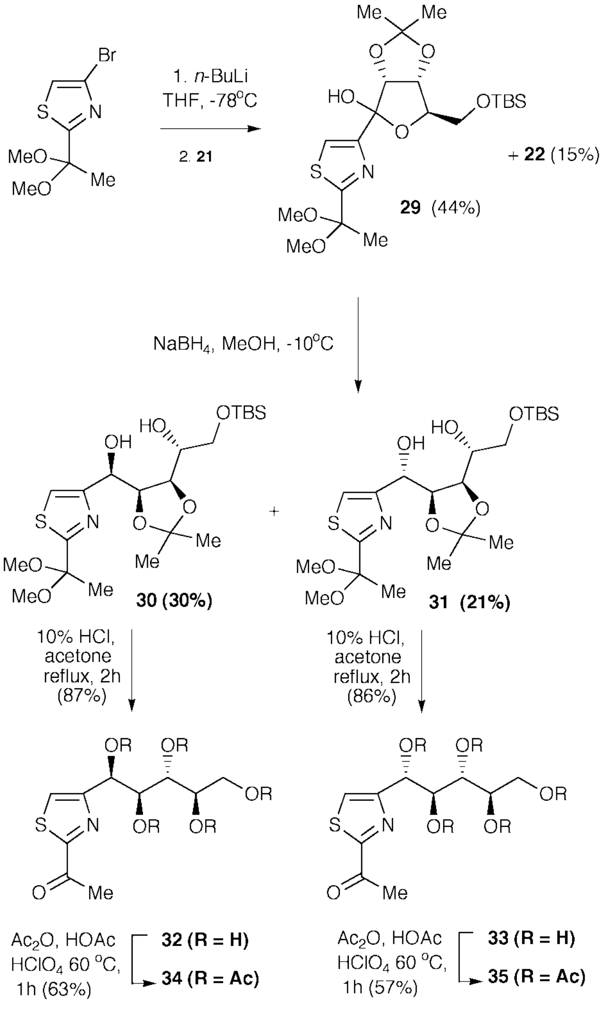


Fig. 9 Compound **30**.



Scheme 5

diastereoselective synthesis of the (1*S*,2*S*,3*R*)- and (1*R*,2*R*,3*R*)-5-thiazole analogues of the bioactive molecule THI from a common precursor, the lactol **3**. This methodology is complementary to the Sharpless asymmetric dihydroxylation method for the diastereoselective synthesis of the *syn*-1,2-diol moiety of THI and its analogues that have opposite stereochemistries at C-1 and C-2.[4,6] Extension of this methodology to prepare the pentahydroxypentyl 4-thiazole and 5-thiazole analogues was also efficient but the diastereoselectivity of the reductive ring-opening steps were poorly diastereoselective. Furthermore, this approach should be applicable to the diastereoselective synthesis of other polyhydroxylated bioactive molecules. Preliminary experiments on these analogues suggested that compound **11**, the 5-thiazole analogue of THI, had essentially the same activity *versus* concentration profile as THI in causing lymphopenia in mice, while the pentol **25** showed a slightly higher activity at the same concentration.

Experimental

General procedures were as described previously.[1,3,6] Unless otherwise indicated, all NMR spectra were recorded in CDCl$_3$ solution at 300 MHz (^{1}H NMR) or 77.5 MHz (^{13}C NMR). All melting points are uncorrected. 2-Acetyl thiazole and 2,3-*O*-isopropylidine-D-erythronolactone **2** were commercially available.

2-(1,1-Dimethoxyethyl)thiazole 5

To a solution of 2-acetylthiazole **4** (1 cm^3, 9.5 mmol) in dry methanol (30 cm^3) was added trimethyl orthoformate (11.16 cm^3, 95 mmol) and toluene-*p*-sulfonic acid (1.63 g). The mixture was heated under reflux for 24 h. After cooling the reaction mixture was poured into a separating funnel containing a saturated solution of sodium bicarbonate (60 cm^3). The aqueous layer was extracted with ether. The combined organic extracts were washed with 1 M sodium hydroxide (40 cm^3), a saturated aqueous solution of sodium chloride (40 cm^3) and dried over magnesium sulfate. The solvent was removed to give a dark yellow oil which was purified by column chromatography (25% ethyl acetate–hexane) to give **5** (1.31 g, 80%) as a yellow oil; δ_H 7.80 (d, 1H, *J* 3.2, 4-H), 7.30 (1H, d, *J* 3.2, 5-H), 3.23 (6H, s, 2 × OC*H*$_3$), 1.71 (3H, s, C*H*$_3$); δ_C 171.62 (C), 142.50 (CH), 119.55 (C), 100.70 (C), 49.01 (CH$_3$), 23.86 (CH$_3$); *m*/*z* (ES +ve) 173.6 (M + H, 50%).

2,3-*O*-Isopropylidene-1-[2-(1,1-dimethoxyethyl)thiazol-5-yl)]-α-D-furanose 7

To a cooled solution of the thiazole **5** (0.409 g, 2.37 mmol) in dry tetrahydrofuran (THF, 15 cm^3) at −78 °C was added dropwise a solution of *n*-butyllithium (1.63 cm^3, 2.61 mmol of a 1.6 M solution in *n*-hexane). The resulting mixture was left to stir at −78 °C for 40 min, then a solution of 2,3-*O*-isopropylidene-D-erythronolactone (0.410 g, 2.596 mmol) in dry THF (10 cm^3) was added slowly to the mixture and stirring was continued for 1.5 h. The reaction mixture was poured into a saturated solution of ammonium chloride (50 cm^3) and the aqueous layer was extracted with ethyl acetate (3 × 50 cm^3). The combined organic extracts were washed with a saturated solution of sodium chloride and dried over magnesium sulfate. The solvent was removed to give a thick yellow oil which was purified by column chromatography (30% ethyl acetate–hexane) to give **7** (0.487 g, 62%) as a white solid and **8** (0.054 g, 7%) as a colourless oil.

7: mp 114–115 °C; $[\alpha]_D^{28}$ −32.73 (*c* 2.3, CHCl$_3$) (Found: C, 50.65; H, 6.44; N, 4.16; S, 9.72. $C_{14}H_{21}O_6NS$ requires C, 50.74; H, 6.39; N, 4.23; S, 9.68%); δ_H 7.85 (1H, d, *J* 0.9, 4-H), 4.98 (1H, dd, *J* 3.9 and 5.7, 2′-H), 4.61 (1H, d, *J* 5.4, 3′-H), 4.16 (1H, dd, *J* 3.6 and 10.2, C*H*aHb), 4.08 (1H, d, *J* 10.5, CHa*H*b), 3.26 (3H, s, OC*H*$_3$), 3.22 (3H, s, OC*H*$_3$), 1.72 (3H, s, C*H*$_3$), 1.47 (3H, s, C*H*$_3$CCH$_3$), 1.29 (3H, s, CH$_3$CC*H*$_3$); δ_C 173.42 (C), 140.89 (CH), 138.50 (C), 112.84 (C), 104.62 (C), 100.86 (C), 85.81 (CH), 80.75 (CH), 71.04 (CH$_2$), 49.33 (OCH$_3$), 49.30 (OCH$_3$), 26.13 (CH$_3$), 24.72 (CH$_3$), 23.99 (CH$_3$); *m*/*z* (ES +ve) 332.1 (M + H, 100%), 300.5 (M − OCH$_3$, 100).

8: $[\alpha]_D^{28}$ 18.78 (*c* 1.4, CHCl$_3$); δ_H 8.73 (1H, s, 4-H), 4.77 (1H, d, *J* 7.2, 2′-H), 4.39 (1H, ddd, *J* 3.9, 3.9, 7.2 Hz, 3′-H), 3.98 (1H, ddd, *J* 3.0, 3.0 and 12.2, C*H*aHb), 3.74 (1H, ddd, *J* 3.6, 8.1 and 12.15, CHa*H*b), 3.26 (3H, s, OC*H*$_3$), 3.25 (3H, s, OC*H*$_3$), 1.72 (3H, s, C*H*$_3$), 1.54 (3H, s, C*H*$_3$CCH$_3$), 1.43 (3H, s, CH$_3$CC*H*$_3$); δ_C 191.82 (C), 179.82 (C), 149.99 (CH), 136.78 (C), 111.27 (C), 100.98 (C), 80.13 (CH), 78.62 (CH), 61.93 (CH$_2$), 49.54 (2 × OCH$_3$), 26.80 (CH$_3$), 26.03 (CH$_3$), 23.83 (CH$_3$); *m*/*z* (ES +ve) 331.8 (M + H, 20%), 300.4 (M − OCH$_3$).

2-(1,1-Dimethoxyethyl)-5-[(1*S*,2*R*,3*R*)- and (1*R*,2*R*,3*R*)-2,3-isopropylidenedioxy-1,4-dihydroxybutyl]thiazole 9 and 10

To the solution of the *α*-hemiacetal **7** (0.299 g, 0.88 mmol) in dry methanol (25 cm^3) at −10 °C was added portionwise solid sodium borohydride (0.37 g, 8.80 mmol). The reaction mixture was left to stir at −10 °C for 1.5 h. The solvent was removed and the residue was dissolved in water (30 cm^3) and the aqueous layer was extracted with ethyl acetate (3 × 50 cm^3). The combined organic extracts were dried over sodium sulfate. The solvent was removed under reduced pressure to give a clear oil that eventually solidified as a white solid. The white solid was purified by column chromatography (75% ethyl acetate–hexane) to give **9** (0.182 g, 62%) and **10** (0.018 g, 6%) as white solids.

9: $[\alpha]_D^{27}$ −18.21 (*c* 2.8, CHCl$_3$) (Found: C, 50.42; H, 6.99, N, 4.16; S, 9.68. $C_{14}H_{23}NO_6S$ requires C, 50.44; H, 6.95; N, 4.20; S, 9.62%); δ_H 7.76 (1H, d, *J* 0.6, 4-H), 5.13 (1H, dd, *J* 4.5 and 9.0, 1′-H), 4.38 (1H, dd, *J* 3.9 and 6.6, 2′-H), 4.29 (1H, ddd, *J* 6.9, 4.8 and 4.8, 3′-H), 3.81 (1H, ddd, *J* 0.9, 4.2 and 6.3, C*H*aHb), 3.81 (1H, d, *J* 2.1, CHa*H*b), 3.35 (1H, d, *J* 4.2, CH$_2$O*H*), 3.26 (3H, s, OC*H*$_3$), 3.24 (3H, s, OC*H*$_3$), 2.23 (1H, dd, *J* 5.1 and 5.1, C′(1)O*H*), 1.72 (3H, s, C*H*$_3$), 1.57 (3H, s, C*H*$_3$CCH$_3$), 1.43 (3H, s, CH$_3$CC*H*$_3$); δ_C 172.67 (C), 140.38 (CH), 139.59 (C), 108.88 (C), 100.92 (C), 79.86 (CH), 78.50 (CH), 66.15 (CH), 60.22 (CH$_2$), 49.38 (2 × OCH$_3$), 26.85 (CH$_3$), 24.96 (CH$_3$), 24.09 (CH$_3$); *m*/*z* (ES +ve) 333.7 (M + H, 70%), 302.00 (M − OCH$_3$, 100).

10: mp 83–84 °C; $[\alpha]_D^{25}$ −37.3 (*c* 1.16, CHCl$_3$) (Found: C, 50.44; H, 6.98; N, 4.24; S, 9.58. $C_{14}H_{23}NO_6S$ requires C, 50.44; H, 6.95; N, 4.20; S, 9.62%); δ_H 7.76 (1H, s, 4-H), 5.12 (1H, dd, *J* 3.6 and 9.0, 1′-H), 4.38 (1H, ddd, *J* 3.9, 5.4 and 7.2, 2′-H), 4.26 (1H, dd, *J* 5.4 and 8.7, 3′-H), 3.99 (1H, ddd, *J* 4.5, 7.2 and 11.6, C*H*aHb), 3.88 (1H, ddd, *J* 4.2, 6.9 and 11.1, CHa*H*b), 3.26 (3H, s, OC*H*$_3$), 3.25 (3H, s, OC*H*$_3$), 1.72 (3H, s, C*H*$_3$), 1.45 (3H, s, C*H*$_3$CCH$_3$), 1.35 (3H, s, CH$_3$CC*H*$_3$); δ_C 172.14 (C), 141.50 (C), 139.72 (CH), 108.83 (C), 100.91 (C), 80.28 (CH), 77.13 (CH), 66.67 (CH), 60.32 (CH$_2$), 49.39 (CH$_3$), 49.37 (CH$_3$), 27.90 (CH$_3$), 25.27 (CH$_3$), 24.18 (CH$_3$); *m*/*z* (ES +ve) 334.3 (M + H, 60%), 302.00 (M − OCH$_3$, 100).

(1′*S*,2′*R*,3′*R*)-2-Acetyl-5-(1,2,3,4-tetrahydroxybutyl)thiazole 11

Diol **9** (0.198 g, 0.594 mmol) was dissolved in acetone–water (17 cm^3, 1 : 1) and conc. hydrochloric acid (5 cm^3) was added dropwise to the solution. After stirring at room temperature for 2 h, acetone was removed under reduced pressure and the aqueous layer was washed with ether. Water was removed under high vacuum to give **11** as a dark yellow hygroscopic solid (0.164 g, 97.3%); $[\alpha]_D^{25}$ +18.3 (*c* 0.6, H$_2$O) [lit.,[3] $[\alpha]_D^{23}$ 7.7 (*c* 0.34, H$_2$O)]; δ_H (D$_2$O) 7.82 (1H, s, 4-H), 5.25 (1H, s, 1′-H), 3.69 (2H, m, 2′-H and 3′-H), 3.49 (2H, m, C*H*a*H*b), 2.51 (3H, s, C*H*$_3$); δ_C (D$_2$O) 192.71 (C), 165.04 (C), 149.01 (C), 140.04 (CH), 73.14 (CH), 70.32 (CH), 66.06 (CH), 62.41 (CH$_2$), 25.28 (CH$_3$); *m*/*z* (ES −ve) 282.3 (M + Cl$^-$, 100%) (Found: M + H, 248.059270. $C_9H_{14}NO_5S$ requires 248.059246).

(1′*R*,2′*R*,3′*R*)-2-Acetyl-5-(1,2,3,4-tetrahydroxybutyl)thiazole 12

To the solution of diol **10** (50 mg, 0.15 mmol) in acetone–water (4.4 cm^3, 1 : 1) was added dropwise conc. hydrochloric acid (0.22 cm^3). After stirring at room temperature for 2 h, acetone was removed under reduced pressure and the aqueous layer was washed with ether. Water was removed under high vacuum to give **12** as a dark yellow solid (40 mg, 94%); $[\alpha]_D^{25}$ −58.62 (*c* 1.45, H$_2$O); δ_H (D$_2$O) 7.81 (s, 1H, 4-H), 5.17 (1H, d, *J* 3.9, 1′-H), 3.76 (1H, dd, *J* 4.2 and 8.4, 2′-H), 3.54 (dd, 1H, *J* 2.7 and 11.7, 3′-H), 3.43 (1H, dd, *J* 5.7 and 11.7, C*H*aHb), 3.31 (1H, ddd, *J* 3.0, 6.0 and 8.1 CHa*H*b), 2.49 (3H, s, C*H*$_3$); δ_C (D$_2$O) 193.84 (C), 166.22 (C), 145.72 (C), 142.27 (CH), 72.78 (CH), 71.25 (CH), 67.72 (CH), 62.22 (CH$_2$), 25.28 (CH$_3$); *m*/*z* (ES +ve) 248.4 (M + 1, 100%) (Found: M + H, 248.059270. $C_9H_{14}NO_5S$ requires 248.059246).

2-(1,1-Dimethoxyethyl)-5-[(2*R*,3*R*)-4-*tert*-butyldimethylsilyloxy-1-oxo-2,3-isopropylidenedioxybutyl]thiazole 13

To the cold solution of diol **9** (0.518 g, 1.55 mmol) in dry tetrahydrofuran–dimethylformamide (3 : 1, 5 cm^3) at 0 °C was added *tert*-butylchlorodimethylsilane (0.24 g, 1.59 mmol) and imidazole (0.224 g, 3.294 mmol). The reaction mixture was left to stir at room temperature for 1 h then was diluted with dichloromethane–diethyl ether (2 : 1, 50 cm^3). The organic layer was washed with a solution of 1 M hydrochloric acid (50 cm^3), a saturated solution of sodium bicarbonate (50 cm^3), a saturated solution of sodium chloride (50 cm^3) and dried over magnesium sulfate. The solvent was removed under reduced pressure to give a pale yellow oil which was purified by flash-column chromatography to give a colourless oil (0.628 g, 90%). To a solution of this oil (0.628 g, 1.41 mmol) in dry dichloromethane (30 cm^3) was added pyridinium dichromate (1.66 g, 4.43 mmol) and 4 Å powdered molecular sieves (1 g). After stirring at room temperature for 18 h, the reaction mixture was filtered through a small pad of Celite and washed with dichloromethane (50 cm^3). The combined organic filtrates were washed with a cold solution of 1 M hydrochloric acid, a saturated solution of sodium bicarbonate and dried over magnesium sulfate. The solvent was removed to give a pale yellow oil which was purified by flash-column chromatography (45% ethyl acetate–hexane) to give **13** as a colourless oil (0.510 g, 82%); δ_H 8.62 (1H, s, 4-H), 5.00 (1H, d, *J* 7.8, 2′-H), 4.55 (1H, t, *J* 3.9, 3′-H), 3.71 (2H, d, *J* 3.9, C*H*$_2$), 3.25 (3H, s, OC*H*$_3$), 3.24 (3H, s, OC*H*$_3$), 1.68 (3H, s, C*H*$_3$), 1.64 (3H, s, C*H*$_3$CCH$_3$), 1.41 (3H, s, CH$_3$CC*H*$_3$), 0.68 (9H, s, C(C*H*$_3$)$_3$), −0.18 (3H, s, C*H*$_3$SiCH$_3$), −0.20 (3H, s, CH$_3$SiC*H*$_3$); δ_C 190.16 (C), 178.54 (C), 148.63 (CH), 137.96 (C), 110.26 (C), 101.02 (C), 79.94 (CH), 79.44 (CH), 61.24 (CH$_2$), 49.45 (OCH$_3$), 49.42 (OCH$_3$), 26.48 (CH$_3$), 25.63 (CH$_3$), 24.73 (CH$_3$), 24.01 (CH$_3$), 18.20 (C), −5.82 (CH$_3$), −6.01 (CH$_3$); MS *m*/*z* (ES +ve) 446.2 (M + H, 100%), 414.2 (M − OCH$_3$, 90) (Found: M + H, 446.203263. $C_{20}H_{36}NO_6SSi$ requires 446.203217).

2-(1,1-Dimethoxyethyl)-5-[(2*S*,3*R*)-4-*tert*-butyldimethylsilyloxy-1-oxo-2,3-isopropylidenedioxybutyl]thiazole 16

Method A. To a solution of ketone **8** (0.65 g, 0.196 mmol) in dry tetrahydrofuran–dimethylformamide (3 : 1, 6 cm^3) at 0 °C was added *tert*-butylchlorodimethylsilane (0.30 g) and imidazole (0.28 g). After stirring at room temperature for 1 h, the reaction mixture was diluted with dichloromethane–diethyl ether (2 : 1, 50 cm^3). The organic layer was washed with a solution of 1 M hydrochloric acid (50 cm^3). The acid layer was back-extracted with dichloromethane (50 cm^3). The combined organic extracts were washed with a saturated solution of sodium bicarbonate (50 cm^3), a saturated solution of sodium chloride and dried over magnesium sulfate. The solvent was removed under reduced pressure to give a pale yellow oil which was purified by flash-column chromatography (45% ethyl acetate–hexane) to give **16** as a colourless oil (0.786 g, 90%).

Method B. To the solution of lactol **7** (0.10 g, 0.3 mmol) in dry dichloromethane (10 cm^3) was added triethylamine (0.1 cm^3), 4-dimethylaminopyridine (1.5 mg) and *tert*-butylchlorodimethylsilane (70 mg). The reaction mixture was left to stir at room temperature over 2 days then was diluted with dichloromethane (20 cm^3). The organic layer was washed with a saturated solution of sodium chloride and dried over magnesium sulfate. The solvent was removed to give a dark yellow oil which was purified by flash-column chromatography (45% ethyl acetate–hexane) to give **16** (50 mg, 48%) as a colourless oil; δ_H 8.69 (1H, s, 4-H), 4.87 (1H, d, *J* 7.2, 2′-H), 4.32 (1H, ddd, *J* 3.6, 3.6 and 7.2, 3′-H), 3.93 (1H, dd, *J* 3.6 and 11.4, C*H*aHb), 3.81 (1H, dd, *J* 3.6 and 11.4, CHa*H*b), 3.26 (6H, s, 2 × OC*H*$_3$), 1.72 (3H, s, C*H*$_3$), 1.51 (3H, s, C*H*$_3$CCH$_3$), 1.45 (3H, s, CH$_3$CC*H*$_3$), 0.89 (9H, s, C(C*H*$_3$)$_3$), 0.80 (3H, s, C*H*$_3$SiCH$_3$), 0.75 (3H, s, CH$_3$SiC*H*$_3$); δ_C 191.60 (C), 179.50 (C), 149.50 (CH), 137.12 (C), 112.80 (C), 100.98 (C), 79.79 (CH), 79.32 (CH), 62.44 (CH$_2$), 49.54 (2 × OCH$_3$), 26.89 (CH$_3$), 26.30 (CH$_3$), 25.84 (CH$_3$), 23.89 (CH$_3$), 18.32 (C), −5.32 (CH$_3$), −5.47 (CH$_3$); *m*/*z* (ES +ve) 446.0 (M + H, 30%), 414 (100) (Found: M + H, 446.203263. $C_{20}H_{36}NO_6SSi$ requires 446.203217).

General procedure for the reduction of ketones 13 and 16

A. With NaBH$_4$. To the stirred solution of the ketone **13** or **16** (0.86 mg, 0.20 mmol) in dry methanol (10 cm^3) at −78 °C was added portionwise solid sodium borohydride (76 mg, 2.0 mmol). After stirring for 6 h, methanol was removed under reduced pressure and the residue was taken up in water (20 cm^3) and the aqueous layer was extracted with ethyl acetate (20 cm^3 × 3). The combined organic extracts were dried over magnesium sulfate and the solvent was removed under reduced pressure to give a colourless oil. Purification by column chromatography (50% ethyl acetate–hexane) gave a mixture of the diastereoisomeric alcohols. The two alcohols were separated by preparative TLC (75% ethyl acetate–hexane).

B. With DIBAL. To the stirred solution of the ketone **13** or **16** (43 mg, 0.10 mmol) in dry toluene (2 cm^3) at −78 °C was added dropwise a solution of diisobutylaluminium hydride (0.2 mmol). After standing at −78 °C for 24 h, the reaction mixture was quenched with dry methanol (2 cm^3) then diluted with a saturated solution of ammonium chloride (5 cm^3). The aqueous layer was extracted with ethyl acetate (10 cm^3 × 3) and worked up in similar manner to that described in **A**.

C. With Red-Al. To the stirred solution of the ketone **13** or **16** (43 mg, 0.10 mmol) in dry toluene (2 cm^3) at 0 °C was added a solution of Red-Al (0.50 mmol, 0.16 cm^3 of 3.3 M solution in toluene). The reaction mixture was left to stir at 0 °C for 20 min then at room temperature for 10 min. The reaction was quenched with a saturated solution of sodium chloride (1 cm^3) and the resultant mixture was extracted with ethyl acetate (10 cm^3 × 3) and worked up in similar manner to that described in **A**.

D. With L- or K-Selectride. To the stirred solution of the ketone **13** or **16** (43 mg, 0.10 mmol) in dry tetrahydrofuran (4 cm^3) at −78 °C was added a solution of L- or K-Selectride (0.30 mmol, 0.3 cm^3 of 1 M solution in tetrahydrofuran). After stirring at −78 °C for 2 h, the reaction mixture was quenched with a solution of 10% sodium hydroxide (4 cm^3) and 30% hydrogen peroxide (2 cm^3). The reaction was stirred at room temperature for 2 h and was then diluted with a saturated solution of sodium chloride (2 cm^3). The mixture was extracted with ethyl acetate then worked up in similar manner to that described in **A**.

2-(1,1-Dimethoxyethyl)-5-[(1S,2R,3R)-2,3-isopropylidenedioxy-1-hydroxy-4-(tert-butyldimethylsilyloxy)butyl]thiazole **14**. Mp 48–49 °C (Found: C, 53.76; H, 8.44; N, 2.97; S, 7.13. $C_{20}H_{37}NO_6SSi$ requires C, 53.66; H, 8.33; N, 3.13; S, 7.16%); δ_H 7.72 (1H, s, 4-H), 5.19 (1H, dd, *J* 2.7 and 4.5, 1′-H), 4.31 (1H, dd, *J* 2.7 and 6.6, 2′-H), 4.24 (1H, ddd, *J* 3.3, 5.7 and 5.7, 3′-H), 3.97 (1H, dd, *J* 6.3 and 11.4, C*H*aHb), 3.82 (1H, dd, *J* 3.6 and 11.1, CHa*H*b), 3.70 (1H, d, *J* 5.1, C(1)O*H*), 3.26 (3H, s, OC*H*$_3$), 3.24 (3H, s, OC*H*$_3$), 1.70 (s, 3H, C*H*$_3$), 1.57 (3H, s, C*H*$_3$CCH$_3$), 1.39 (3H, s, CH$_3$CC*H*$_3$), 0.90 (9H, s, C(C*H*$_3$)$_3$), 0.11 (3H, s, C*H*$_3$SiCH$_3$), 0.10 (3H, s, CH$_3$SiC*H*$_3$); δ_C 172.20 (C), 140.20 (CH), 140.01 (C), 108.80 (C), 101.04 (C), 79.99 (CH), 77.05 (CH), 66.36 (CH), 61.28 (CH$_2$), 49.42 (CH$_3$), 49.35 (CH$_3$), 26.74 (CH$_3$), 25.81 (CH$_3$), 24.94 (CH$_3$), 24.17 (CH$_3$), 18.27 (C), −5.50 (CH$_3$), −5.53 (CH$_3$); *m*/*z* (ES +ve) 448.2 (M + H, 85%), 416.2 (M − OCH$_3$, 100).

2-(1,1-Dimethoxyethyl)-5-[(1R,2R,3R)-2,3-isopropylidenedioxy-1-hydroxy-4-(tert-butyldimethylsilyloxy)butyl]thiazole **15**. Oil; $[\alpha]^{26}_{D}$ −25.08 (*c* 3.05, CH$_2$Cl$_2$); δ_H 7.79 (1H, d, *J* 0.6, 4-H), 5.08 (1H, ddd, *J* 0.6, 3.3 and 9.0, 1′-H), 4.80 (1H, d, *J* 3.3, 2′-H), 4.35–4.25 (2H, m, 3′-H and O*H*), 3.91 (1H, dd, *J* 9.6 and 10.8, C*H*aHb), 3.71 (1H, dd, *J* 3.3 and 10.5, CHa*H*b), 3.26 (3H, s, OC*H*$_3$), 3.24 (3H, s, OC*H*$_3$), 1.71 (3H, s, C*H*$_3$), 1.40 (3H, s, C*H*$_3$CCH$_3$), 1.31 (3H, s, CH$_3$CC*H*$_3$), 0.92 (9H, s, C(C*H*$_3$)$_3$), 0.15 (3H, s, C*H*$_3$SiCH$_3$), 0.14 (3H, s, CH$_3$SiC*H*$_3$); δ_C 171.29 (C), 140.16 (C), 140.04 (CH), 108.84 (C), 100.99 (C), 80.99 (CH$_2$), 76.99 (CH), 66.66 (CH), 61.72 (CH$_2$), 49.32 (CH$_3$), 49.26 (CH$_3$), 27.91 (CH$_3$), 25.67 (CH$_3$), 25.20 (CH$_3$), 24.08 (CH$_3$), 18.10 (C), −5.67 (CH$_3$), −5.69 (CH$_3$); *m*/*z* (ES +ve) 448.2 (M + H, 90%), 416.2 (M − OCH$_3$, 100) (Found: M + H, 448.218914. $C_{20}H_{38}NO_6SSi$ requires 448.218865).

2-(1,1-Dimethoxyethyl)-5-[(1R,2S,3R)-2,3-isopropylidenedioxy-1-hydroxy-4-(tert-butyldimethylsilyloxy)butyl]thiazole **17**. Mp 79–80 °C; $[\alpha]^{22}_{D}$ −6.26 (*c* 1.95, CH$_2$Cl$_2$) (Found: C, 53.90; H, 8.68; N, 3.13; S, 7.32. $C_{20}H_{37}NO_6SSi$ requires C, 53.66; H, 8.33; N, 3.13; S, 7.16%); δ_H 7.74 (1H, d, *J* 0.6, 4-H), 5.05 (1H, ddd, *J* 0.6, 4.5 and 7.8, 1′-H), 4.20 (1H, dd, *J* 4.5 and 7.8, 2′-H), 3.92 (1H, ddd, *J* 4.2, 6.6 and 7.8, 3′-H), 3.61 (1H, dd, *J* 4.5 and 6.3, C*H*aHb), 3.49 (1H, d, *J* 7.8, CHa*H*b), 3.26 (3H, s, OC*H*$_3$), 3.24 (3H, s, OC*H*$_3$), 1.71 (3H, s, C*H*$_3$), 1.58 (3H, s, C*H*$_3$CCH$_3$), 1.42 (3H, s, CH$_3$CC*H*$_3$), 0.89 (9H, s, C(C*H*$_3$)$_3$), 0.06 (3H, s, C*H*$_3$SiCH$_3$), 0.056 (3H, s, CH$_3$SiC*H*$_3$); δ_C 172.20 (C), 140.35 (CH), 139.35 (C), 109.86 (C), 100.92 (C), 81.61 (CH), 77.21 (CH), 67.96 (CH), 63.46 (CH$_2$), 49.35 (CH$_3$), 49.32 (CH$_3$), 27.03 (CH$_3$), 27.05 (CH$_3$), 25.79 (CH$_3$), 24.05 (CH$_3$), 18.34 (CH$_3$), −5.59 (CH$_3$), −5.60 (CH$_3$); *m*/*z* (ES +ve) 448.0 (M + H, 100%), 416.0 (M − OCH$_3$, 70).

2-(1,1-Dimethoxyethyl)-5-[(1S,2S,3R)-2,3-isopropylidenedioxy-1-hydroxy-4-(tert-butyldimethylsilyloxy)butyl]thiazole **18**. Oil; $[\alpha]^{23}_{D}$ +6.63 (*c* 2.35, CH$_2$Cl$_2$); δ_H 7.74 (1H, s, 4-H), 4.96 (1H, d, *J* 4.5, 1′-H), 4.07 (1H, br s, 2H′), 3.97 (1H, dd, *J* 1.8 and 5.4, 3H′), 3.78 (1H, dd, *J* 3.3 and 10.2, C*H*aHb), 3.65–3.60 (1H, m, CHa*H*b), 3.25 (3H, s, OC*H*$_3$), 3.23 (3H, s, OC*H*$_3$), 1.71 (3H, s, C*H*$_3$), 1.41 (3H, s, C*H*$_3$CCH$_3$), 1.36 (3H, s, CH$_3$CC*H*$_3$), 0.91 (9H, s, C(C*H*$_3$)$_3$), 0.10 (3H, s, C*H*$_3$SiCH$_3$), 0.09 (3H, s, CH$_3$SiC*H*$_3$); δ_C 171.54 (C), 139.80 (CH), 139.34 (C), 109.44 (C), 100.83 (C), 82.29 (CH), 78.96 (CH), 69.06 (CH), 63.75 (CH$_2$), 49.18 (CH$_3$), 49.14 (CH$_3$), 26.72 (CH$_3$), 26.69 (CH$_3$), 25.67 (CH$_3$), 23.95 (CH$_3$), 18.12 (C), −5.69 (CH$_3$), −5.74 (CH$_3$); *m*/*z* (ES +ve) 448.0 (M + H, 100%), 416.0 (M − OCH$_3$, 40) (Found: M + H, 448.218914. $C_{20}H_{38}NO_6NSSi$ requires 448.218865).

(1′*R*,2′*S*,3′*R*)-2-Acetyl-5-(1,2,3,4-tetrahydroxybutyl)thiazole 19

To a stirred solution of **17** (0.20 g, 0.44 mmol) in ethanol (4.5 cm^3) was added a solution of 10% hydrochloric acid (2.2 cm^3). The reaction was left to stir at room temperature for 2 h. Ethanol was removed under reduced pressure and the aqueous layer was washed with diethyl ether. Water was removed under high vacuum to give **19** as a dark yellow hydroscopic solid (0.116 g, 93%) that was judged to be > 95% purity from ^{1}H NMR analysis; $[\alpha]^{22}_{D}$ −28.5 (*c* 1.35, H$_2$O); δ_H (D$_2$O) 7.84 (1H, s, 4H), 5.07 (1H, d, *J* 5.4 , 1′-H), 3.61 (1H, dd, *J* 3.0 and 5.1, 2′-H), 3.63–3.64 (3H, m, 3′-H and C*H*$_2$), 2.49 (3H, s, C*H*$_3$); δ_C(D$_2$O) 193.29 (C), 165.85 (C), 148.39 (C), 141.46 (CH$_2$), 73.59 (CH), 71.02 (CH), 67.87 (CH), 62.10 (CH$_2$), 25.28 (CH$_3$); *m*/*z* (ES +ve) 247.8 (M + H, 90%) (Found: M + H, 248.059270. $C_9H_{14}NO_5S$ requires 248.059246).

(1′*S*,2′*S*,3′*R*)-2-Acetyl-5-(1,2,3,4-tetrahydroxybutyl)thiazole 20

The title compound was prepared from **18** (41 mg, 0.09 mmol) in a similar manner to that described above for the synthesis of **19**. Compound **20** was obtained as a dark yellow hydroscopic solid (24 mg, 94%); $[\alpha]_D^{23}$ 18.30 (*c* 1.2, H_2O); δ_H (D_2O) 7.82 (s, 1H, 4-H), 4.92 (1H, d, *J* 7.8, 1′-H), 3.76 (1H, br m, 2′-H), 3.56 (1H, br d, *J* 8.1, 3′-H), 3.48 (2H, m, CH_2OH), 2.49 (3H, s, CH_3); δ_C (D_2O) 191.80 (C), 164.81 (C), 148.53 (C), 139.79 (CH), 72.63 (CH), 69.35 (CH), 66.66 (CH), 62.13 (CH_2), 25.28 (CH_3); *m/z* (ES +ve) 247.8 (M + H, 70%) (Found: M + H, 248.059270. $C_9H_{14}NO_5S$ requires 248.059246).

2-(1,1-Dimethoxyethyl)-5-[5-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-isopropylidene-D-ribofuranosyl]thiazole 22

A solution of *n*-butyllithium (3.54 cm^3, 1.4 M in hexanes, 4.95 mmol) was added with stirring to a cooled (−78 °C) solution of the thiazole **5** (570 mg, 3.3 mmol) in dry tetrahydrofuran (10 cm^3). After stirring for 40 min, a solution of the D-ribonolactone derivative **21** (995 mg, 3.3 mmol) in dry tetrahydrofuran (10 cm^3) was added dropwise and stirring at −78 °C was continued for 90 min. The reaction was quenched by pouring into saturated ammonium chloride solution (50 cm^3) and was extracted with dichloromethane (3 × 50 cm^3). The combined organic extracts were washed with saturated sodium chloride solution and dried over magnesium sulfate, before concentrating *in vacuo* to yield a yellow-brown crystalline compound (1.892 g, 121%) which was recrystallized from 20% ethyl acetate–hexane to yield a white crystalline solid (1.001 g, 64%), mp 147–149 °C (Found: C, 52.98; H, 7.89; N, 2.84. $C_{21}H_{37}NO_7SSi$ requires C, 53.03; H, 7.84; N, 2.94%); δ_H 7.90 (1H, s, 4-H), 5.65 (1H, s, OH), 4.90 (1H, dd, *J* 1.5, 5.65, 2′-H), 4.59 (1H, d, *J* 5.65, 3′-H), 4.42 (1H, br s, 4′-H), 3.84 (2H, m, OCH_2), 3.24 (3H, s, OCH_3), 3.22 (3H, s, OCH_3), 1.75 (3H, s, CH_3), 1.50 (3H, s, CH_3), 1.25 (3H, s, CH_3), 0.98 (9H, s, *tert*-butyl), 0.19 (3H, s, $SiCH_3$), 0.18 (3H, s, $SiCH_3$); δ_C (75.6 MHz; $CDCl_3$) 172.6 (C), 141.76 (CH), 137.41 (C), 113.13 (C), 105.21 (C), 101.05 (C), 88.32 (CH), 86.23 (CH), 81.86 (CH), 64.58 (CH_2), 49.42 (CH_3), 49.37 (CH_3), 26.55 (CH_3), 25.80 (CH_3), 25.07 (CH_3), 24.19 (CH_3), 18.31 (C), −5.63 (CH_3), −5.66 (CH_3); *m/z* (ES +ve) 476.2138 (M + H; $C_{21}H_{38}NO_7SSi$ requires 476.2138), 444 (100%).

2-(1,1-Dimethoxyethyl)-5-(1,4-dihydroxy-2,3-isopropylidenedioxy-5-*tert*-butyldimethylsilyloxypentyl)thiazole 23 and 24

Sodium borohydride (596 mg, 15.7 mmol) was added to a stirred solution of the lactol **22** (1 g, 2.1 mmol) in dry methanol (50 cm^3) at 0 °C over a period of 1 h. The reaction was left for 3 h at 0 °C before quenching with saturated ammonium chloride solution (50 cm^3). Extraction with dichloromethane (3 × 50 cm^3) yielded an organic fraction which was washed with saturated sodium chloride solution and dried over magnesium sulfate before concentrating *in vacuo*. The crystalline crude product (961 mg, 96%) was purified by column chromatography using silica gel (1 : 1 ethyl acetate–hexane) to yield **23** (461 mg, 48%) as a fine powdery solid and **24** (442 mg, 46%) as a crystalline solid.

23: mp 150–153 °C; δ_H 7.69 (1H, s, 4-H), 5.39 (1H, dd, *J* 1.77, 7.47, 1′-H), 4.35 (1H, dd, *J* 2.08, 6.23, 2′-H), 4.11 (1H, dd, *J* 6.23, 9.34, 3′-H), 4.03 (1H, m, 4′-H), 3.79 (1H, dd, *J* 3.14, 10.10, 5′-Ha), 3.65 (1H, dd, *J* 4.91, 10.10, 5′-Hb), 3.27 (1H, d, *J* 7.47, 1′-OH), 3.22 (6H, 2s, OCH_3), 2.9 (1H, d, *J* 5.65, 4′-OH), 1.68 (3H, s, CH_3), 1.5 (3H, s, CH_3), 1.32 (3H, s, CH_3), 0.9 (9H, s, *tert*-butyl), 0.09 (6H, s, $2CH_3$); δ_C 172.03 (C), 140.86 (C), 140.12 (CH), 108.906 (C), 100.98 (C), 79.61 (CH), 76.19 (CH), 69.285 (CH), 65.99 (CH), 64.24 (CH_2), 49.36 (CH_3), 49.34 (CH_3), 26.72 (CH_3), 25.78 (CH_3), 24.61 (CH_3), 24.12 (CH_3), 18.24 (C), −5.42 (CH_3), −5.54 (CH_3); *m/z* (ES +ve) 478.2294 (M + H, $C_{21}H_{40}NO_7SSi$ requires 478.2294), 446 (100).

24: mp 88–89 °C; δ_H 7.78 (1H, d, *J* 0.7, 4-H), 5.13 (1H, dd, *J* 3.04, 9.14, 1′-H), 4.91 (1H, d, *J* 3.04, 1′-OH), 4.27 (1H, dd, *J* 5.33, 9.45, 2′-H), 4.13 (1H, dd, *J* 5.33, 9.45, 3′-H), 3.91 (1H, m, 5′-Ha), 3.87 (1H, m, *J* 3.3, 4′-H), 3.66 (1H, dd, *J* 8.11, 10.81, 5′-Hb), 3.39 (1H, d, *J* 3.3, 4′-OH), 3.24 (6H, 2s, OCH_3), 1.71 (3H, s, CH_3), 1.38 (3H, s, CH_3), 1.28 (3H, s, CH_3), 0.91 (9H, s, *tert*-butyl), 0.096 (6H, s, $2CH_3$); δ_C 171.39 (CH), 140.36 (CH), 140.21 (CH), 109.13 (CH), 101.02 (CH), 81.08 (CH), 77.131 (CH), 69.31 (CH), 66.52 (CH), 64.14 (CH_2), 49.42 (CH_3), 49.35 (CH_3), 28.01 (CH_3), 25.82 (CH_3), 25.35 (CH_3), 24.15 (CH_3), 18.27 (C), −5.40 (CH_3), −5.46 (CH_3); *m/z* (ES +ve) 478.2294 (M + H, $C_{21}H_{40}NO_7SSi$ requires 478.2294), 446 (100).

2-Acetyl-5-[(1*R*,2*R*,3*R*,4*R*,5)-pentahydroxypentyl]thiazole 25

Compound **23** (200 mg, 0.42 mmol) was refluxed in a 50 : 50 mixture of acetone and 10% hydrochloric acid solution for 2 h. Upon completion, the acetone was removed *in vacuo* and the remaining aqueous solution was washed with diethyl ether. The water was removed *in vacuo*, leaving the crude product as a dark yellow oil (106 mg, 91%). ^1H NMR analysis showed this product to be >95% pure. δ_H (D_2O) 7.77 (1H, s, 4-H), 5.22 (1H, s, 1′-H), 3.73 (1H, dd, *J* 3.3, 7.2), 3.67 (1H, dd, *J* 4.4, 8.4), 3.56 (2H, m), 3.45 (1H, dd, *J* 7.5, 12); δ_C (D_2O) 212.1 (C), 183.9 (C), 167.4 (C), 159.3, 92.3 (CH), 90.9 (CH), 89.5 (CH), 85 (CH), 80.1 (CH_2), 43.8 (CH_3); *m/z* (ES +ve) 300 (M + Na, 100%), 278 (M + H, 100%), 260 (M + H − H_2O, 35%).

2-Acetyl-5-[(1*S*,2*R*,3*R*,4*R*,5)-pentahydroxypentyl]thiazole 26

Compound **24** (200 mg, 0.42 mmol) was hydrolysed as described above for the preparation of compound **25** from **23**. The product was obtained as a dark yellow oil (103 mg, 89%). ^1H NMR analysis showed this product to be >95% pure. δ_H (D_2O) 7.77 (1H, s, 4-H), 5.1 (1H, d, *J* 3.93, 1′-H), 3.78 (1H, dd, *J* 4.05, 8.10), 3.61 (1H, m), 3.51 (1H, dd, *J* 2.47, 11.92), 3.37 (1H, dd, *J* 7.42, 11.92), 3.14 (1H, dd, *J* 4.50, 8.10); δ_C (D_2O) 212.1 (C), 184.7 (C), 164.4 (C), 160.6 (C), 91.7 (CH), 90.7 (CH), 90.1 (CH), 86.3 (CH), 80.1 (CH_2), 43.8 (CH_3); *m/z* (ES +ve) 300 (M + Na, 20%), 278 (M + H, 60%), 260 (M + H − H_2O, 3%).

2-Acetyl-5-[(1*R*,2*R*,3*R*,4*R*,5)-pentaacetylpentyl]thiazole 27

To a stirred solution of acetic anhydride (3 cm^3) and glacial acetic acid (5 cm^3) was added a sample of **25** (100 mg, 0.36 mmol). A perchloric acid–acetic anhydride catalyst (1 g of 70% hydrochloric acid in 2.3 g acetic anhydride) was added (4 drops) and the mixture was stirred at 60 °C for 1 h before being poured into ice–water (20 cm^3). After extraction with ethyl acetate (3 × 20 cm^3) the combined organic extracts were dried over magnesium sulfate and concentrated *in vacuo*. The product was purified by semi-prep. TLC on silica plates (eluent 50% ethyl acetate–hexane) to yield a pale yellow oil (110 mg, 63%); δ_H 7.94 (1H, s, 4-H), 6.40 (1H, d, *J* 3.69, 1′-H), 5.44 (1H, dd, *J* 3.69, 7.60, 2′-H), 5.33 (1H, dd, *J* 3.96, 7.60, 3′-H), 5.22 (1H, m, *J* 3.3, 11.02, 4′-H), 4.33 (1H, dd, *J* 3.3, 12.08, 5′-Ha), 4.17 (1H, dd, *J* 7.66, 12.08, 5′-Hb), 2.68 (3H, s, CH_3), 2.16 (3H, s, Ac), 2.10 (3H, s, Ac), 2.094 (3H, s, Ac), 2.090 (3H, s, Ac), 2.04 (3H, s, Ac); *m/z* (CI +ve) 488.1226 (M + H, $C_{20}H_{26}NO_{11}S$ requires 488.1226) 428 (65%), 386 (77).

2-Acetyl-5-[(1*S*,2*R*,3*R*,4*R*,5)-pentaacetylpentyl]thiazole 28

The title compound was prepared from **26** (100 mg, 0.36 mmol) as described above for the synthesis of **27** from **25**. The product was purified by semi-prep. TLC on silica plates (eluent 50% ethyl acetate–hexane) to yield a pale yellow oil (101 mg, 58%); δ_H 7.9 (1H, s, 4-H), 6.25 (1H, d, *J* 4.63, 1′-H), 5.57 (1H, dd, *J* 4.63, 6.24, 2′-H), 5.24 (1H, m, 3.26, 6.65, 4′-H), 5.18 (1H, dd, *J* 5.15, 6.24, 3′-H), 4.30 (1H, dd, *J* 3.26, 12.18, 5′-Ha), 4.1 (1H, dd, *J* 6.65, 12.18, 5′-Hb), 2.69 (3H, s, CH_3), 2.16 (3H, s, Ac), 2.09 (3H, s, Ac), 2.07 (3H, s, Ac), 2.03 (3H, s, Ac), 2.01 (3H, s, Ac); *m/z* (CI +ve) 488.1226 (M + H, $C_{20}H_{26}NO_{11}S$ requires 488.1226), 428 (65%), 386 (37).

2-(1,1-Dimethoxyethyl)-4-[5-*O*-(*tert*-butyldimethylsilyl)-2,3-*O*-isopropylidene-D-ribofuranosyl]thiazole 29

4-Bromo-2-(1,1-dimethoxyethyl)thiazole[6] (520 mg, 2.06 mmol) was dissolved in anhydrous diethyl ether (10 cm^3) and cooled to −78 °C before addition of *n*-butyllithium (2.2 cm^3, 1.4 M solution in hexanes, 3.1 mmol). After stirring at −78 °C for 30 min, a solution of the D-ribonolactone derivative **21** (623 mg, 2.06 mmol) in dry diethyl ether (5 cm^3) was added dropwise. The reaction was left stirring at −78 °C for 90 min, before pouring into saturated ammonium chloride solution (15 cm^3) and extracting the aqueous layer with dichloromethane (3 × 25 cm^3). The combined organic layers were washed with saturated sodium chloride solution before drying over magnesium sulfate and concentrating *in vacuo* to yield a yellow oil (1083 mg, 110%). Purification on a silica gel column (eluent 30% ethyl acetate–hexane) gave two major products. The title compound was isolated (433 mg, 44%) and ^{1}H NMR analysis showed this to be a 69:31 mixture of isomers which was used as such for the following reaction. Also isolated was the addition product in the C5 thiazole position as a crystalline solid (142 mg, 14.5%).

29 (Minor isomer): δ_H 7.47 (1H, s, 5-H), 5.26 (1H, s, OH), 4.98 (1H, d, *J* 6.82, 2′-H), 4.85 (1H, dd, *J* 3.24, 6.82, 3′-H), 4.27 (1H, ddd, *J* 3.24, 4.16, 5.17, 4′-H), 3.77 (1H, dd, *J* 5.17, 10.97, 5′-Hb), 3.71 (1H, dd, *J* 4.16, 10.97, 5′-Ha), 3.23 (3H, s, OCH_3), 3.18 (3H, s, OCH_3), 1.68 (3H, s, CH_3), 1.62 (3H, s, CH_3), 1.39 (3H, s, CH_3), 0.83 (9H, s,*tert*-butyl), 0.01 (3H, s, $SiCH_3$), −0.01 (3H, s, $SiCH_3$).

29 (Major isomer): δ_H 7.46 (1H, s, 5-H), 4.86 (1H, dd, *J* 1.33, 5.78, 3′-H), 4.75 (1H, d, *J* 5.78, 2′-H), 4.53 (1H, s, OH), 4.38 (1H, ddd, *J* 1.33, 3.51, 4.65, 4′-H), 3.86 (1H, dd, *J* 4.65, 10.82, 5′-Hb), 3.79 (1H, dd, *J* 3.51, 10.82, 5′-Ha), 3.21 (3H, s, OCH_3), 3.18 (3H, s, OCH_3), 1.72 (3H, s, CH_3), 1.34 (3H, s, CH_3), 1.24 (3H, s, CH_3), 0.91 (9H, s, *tert*-butyl), 0.11 (3H, s, $SiCH_3$), 0.10 (3H, s, $SiCH_3$).

2-(1,1-Dimethoxyethyl)-4-(1,4-dihydroxy-2,3-isopropylidenedioxy-5-*tert*-butyldimethylsiloxypentyl)thiazole 30 and 31

Sodium borohydride (32 mg, 0.85 mmol) was added to a cooled, stirred solution of the lactol **29** (269 mg, 0.56 mmol) in dry methanol (5 cm^3) over a period of 1 h. The solution was stirred for 3 h, then quenched with saturated ammonium chloride solution and extracted with dichloromethane. The combined organic fractions were washed with saturated sodium chloride solution and dried over magnesium sulfate. Concentration *in vacuo* yielded the crude product as a mixture of isomers, in a 41:59 ratio (**31**:**30**) with an overall yield of 65%. Purification on a silica column (eluent 25% ethyl acetate–hexane) gave **30** as an orange oil (81 mg, 30%) and **31** as a white crystalline solid (56 mg, 21%).

30: δ_H 7.26 (1H, s, 4-H), 5.07 (1H, dd, *J* 4.07, 9.2, 1′-H), 4.69 (1H, d, *J* 4.07, 1′-OH), 4.53 (1H, dd, *J* 5.19, 9.2, 2′-H), 4.21 (1H, dd, *J* 5.19, 9.51, 3′-H), 3.98 (1H, m, 4′-H), 3.92 (1H, dd, *J* 2.88, 10.01, 5′-Ha), 3.73 (1H, dd, *J* 6.25, 10.01, 5′-Hb), 3.68 (1H, d, *J* 3.64, C(5)OH), 3.25 (6H, 2s, $2(OCH_3)$), 1.71 (3H, s, CH_3), 1.36 (3H, s, CH_3), 1.26 (3H, s, CH_3), 0.9 (9H, s, *tert*-butyl), 0.09 (6H, s, $2CH_3$); δ_C 171.28 (C), 156.23 (C), 116.78 (CH), 108.65 (C), 100.91 (C), 79.91 (CH), 77.06 (CH), 69.48 (CH), 68.08 (CH), 64.44 (CH_2), 49.33 (CH_3), 27.99 (CH_3), 25.86 (CH_3), 25.42 (CH_3), 24.2 (CH_3), 18.325 (C), −5.38 (CH_3); *m*/*z* (ES +ve) 478.2294 (M + H, $C_{21}H_{40}NO_7SSi$ requires 478.2294).

31: δ_H 7.31 (1H, s, 4-H), 5.33 (1H, dd, *J* 2.7, 6.5, 1′-H), 4.67 (1H, dd, *J* 2.9, 5.9, 2′-H), 4.14 (1H, dd, *J* 5.93, 9.38, 3′-H), 4.08 (1H, m, 4′-H), 3.85 (1H, dd, *J* 3.1, 10.15, 5′-Ha), 3.71 (1H, dd, *J* 5.1, 10.15, 5′-Hb), 3.41 (1H, d, *J* 6.7, 1′-OH), 3.21 (6H, 2s, $2(OCH_3)$), 3.20 (1H, d, *J* 5.4, 4′-OH), 1.69 (3H, s, CH_3), 1.45 (3H, s, CH_3), 1.29 (3H, s, CH_3), 0.88 (9H, s, *tert*-butyl), 0.07 (6H, s, $2CH_3$); δ_C 171.63 (C), 157.72 (C), 115.64 (CH), 108.32 (C), 100.89 (C), 78.92 (CH), 76.39 (CH), 69.24 (CH), 64.38 (CH_2), 49.40 (CH_3), 49.36 (CH_3), 27.26 (CH_3), 25.86 (CH_3), 24.89 (CH_3), 24.31 (CH_3), 18.31 (C), −5.37 (CH_3), −5.44 (CH_3); *m*/*z* (CI +ve) 478.2294 (M + H, $C_{21}H_{40}NO_7SSi$ requires 478.2294).

2-Acetyl-4-[(1*R*,2*R*,3*R*,4*R*,5)-pentahydroxypentyl]thiazole 32

Compound **30** (97 mg, 0.203 mmol) was refluxed in a 50:50 mixture (10 cm^3) of acetone and 10% hydrochloric acid solution for 2 h. Upon completion, the acetone was removed *in vacuo* and the remaining aqueous solution washed with diethyl ether. The water was removed *in vacuo*, leaving the crude product as a dark yellow oil (49 mg, 87%). ^{1}H NMR analysis showed this product to be >95% pure. δ_H (D_2O) 7.27 (1H, s, 4-H), 5.05 (1H, d, 1′-H), 3.4–3.95 (5H, series of m, 2′-H to 6′-H), 2.53 (3H, s, CH_3); *m*/*z* (ES +ve) 300 (M + Na, 100%), 278 (M + H, 22%), 260 (M + H − H_2O, 21%).

2-Acetyl-4-[(1*S*,2*R*,3*R*,4*R*,5)-pentahydroxypentyl]thiazole 33

Compound **31** (60 mg, 0.125 mmol) was treated as described above for the preparation of **32** from **30** to yield the title compound as a dark yellow oil (30 mg, 86%). ^{1}H NMR analysis showed this compound to be >95% pure. δ_H (D_2O) 7.74 (1H, s, 4′-H), 5.08 (1H, d, *J* 2.29, 1′-H), 3.87 (1H, dd, *J* 2.32, 7.78, 2′-H), 3.80–3.67 (2H, m, 3′-H, 4′-H), 3.65 (1H, dd, *J* 2.84, 11.86, 5′-Ha), 3.52 (1H, dd, *J* 7.02, 11.86, 5′-Hb), 2.54 (3H, s, CH_3); *m*/*z* (ES +ve) 278 (M + H, 25%), 260 (M + H − H_2O, 98%).

2-Acetyl-4-[(1*R*,2*R*,3*R*,4*R*,5)-pentaacetylpentyl]thiazole 34

To a stirred solution of acetic anhydride (3 cm^3) and glacial acetic acid (5 cm^3) was added a sample of **32** (10 mg, 0.036 mmol). A perchloric acid–acetic anhydride catalyst (1 g of 70% $HClO_4$ in 2.3 g acetic anhydride) was added (4 drops) and the mixture was stirred at 60 °C for 1 h before being poured into ice–water (20 cm^3). After extraction with ethyl acetate (3 × 20 cm^3) the combined organic extracts were dried over magnesium sulfate and concentrated *in vacuo*. The product was purified by semi-prep. TLC on silica gel plates (eluent 50% ethyl acetate–hexane) to yield a finely crystalline product (11 mg, 63%). δ_H 7.53 (1H, s, 4-H), 6.24 (1H, d, *J* 4.06, 1′-H), 5.70 (1H, dd, *J* 4.06, 7.69, 2′-H), 5.35 (1H, dd, *J* 3.7, 7.69, 3′-H), 5.21 (1H, m, *J* 3.35, 7.43, 11.00, 4′-H), 4.37 (1H, dd, *J* 3.35, 12.07, 5′-Ha), 4.15 (1H, dd, *J* 7.43, 12.07, 5′-Hb), 2.68 (3H, s, CH_3), 2.15 (3H, s, Ac), 2.094 (3H, s, Ac), 2.073 (3H, s, Ac), 2.058 (3H, s, Ac), 2.029 (3H, s, Ac); *m*/*z* (CI +ve) 488.122658 (M + H, $C_{20}H_{26}NO_{11}S$ requires 488.122658).

2-Acetyl-4-[(1*S*,2*R*,3*R*,4*R*,5)-pentaacetylpentyl]thiazole 35

Compound **33** (30 mg, 0.108 mmol) was treated as described above for the preparation of **34** from **32** to yield a finely crystalline product (30 mg, 57%). δ_H 7.59 (1H, s, 4-H), 6.18 (1H, d, *J* 5.51, 1′-H), 5.75 (1H, dd, *J* 5.51, 5.87, 2′-H), 5.40 (1H, dd, *J* 4.34, 5.87, 3′-H), 5.29 (1H, m, *J* 3.03, 7.10, 4′-H), 4.35 (1H, dd, *J* 3.03, 12.10, 5′-Ha), 4.07 (1H, dd, *J* 7.10, 12.10, 5′-Hb), 2.63 (3H, s, CH_3), 2.18 (3H, s, Ac), 2.049 (3H, s, Ac), 2.009 (3H, s, Ac), 2.001 (3H, s, Ac), 1.978 (3H, s, Ac); *m*/*z* (CI+) 488.122658 (M + H, $C_{20}H_{26}NO_{11}S$ requires 488.122658).

Structure determinations†

Diffraction data were acquired in a number of modes, at the specified temperature, all instruments equipped with monochromatic Mo-Kα radiation, $\lambda = 0.710_7$ Å. Using a single counter instrument in $2\theta/\theta$ scan mode, N unique reflections were measured within the specified $2\theta_{max}$ limit, N_o with $I > 3\sigma(I)$ being considered 'observed', gaussian absorption corrections

---

† CCDC reference number 207/345.

being applied. Data were also measured using a Bruker AXS CCD instrument ($2\theta_{max}$ = 58°), $N_{tot(al)}$ reflections within a full sphere being merged to N unique, R_{int} as specified after 'empirical'/multiscan absorption correction within the proprietary/preprocessing software SMART/SAINT; the 'observed' criterion, where applicable, was $F > 4\sigma(F)$. Anisotropic thermal parameter forms were refined in a full matrix context for non-hydrogen atoms, $(x, y, z, U_{iso})_H$ being constrained at estimated values. Conventional residuals R, R_w (statistical weights) on $|F|$ are quoted at convergence. Neutral atom complex scattering factors were employed within the Xtal 3.4 program system.[16] Pertinent results are given in the Figures and below; individual variations in procedure/difficulties/idiosyncrasies are cited as 'variata'. Molecular projections as shown in Figs. 1–9 are projected normal to the common heterocyclic ring, which, together with the second common ring and linkages, is shown with solid bonds; additional projections are offered to clarify the appendages where appropriate. A common *ad hoc* crystallographic numbering is shown, carbon atoms denoted by number only. Non-hydrogen atoms are shown with 20 (room-temperature) or 50% (low temperature) probability displacement ellipsoids. Bond lengths and angles are generally as expected throughout the array and are not addressed further, the interest lying in the isomeric and conformational variation discussed in the text above and shown in the Figures.

Crystal/refinement data

7b. $C_{14}H_{21}NO_6S$, M = 331.4. Single-counter instrument, *T ca.* 295 K. Orthorhombic, space group $P2_12_12_1$ (D_2^4, No. 19), a = 23.949(6), b = 11.294(2), c = 6.166(1) Å, V = 1668 Å^3. D_c (Z = 4) = 1.32_0 g cm^{-3}; $F(000)$ = 704. μ_{Mo} = 2.2 cm^{-1}; specimen: 0.38 × 0.36 × 0.15 mm; 'T'$_{min, max}$ = 0.94, 0.95. $2\theta_{max}$ = 50°; N_{tot} (hemisphere) = 6203, N = 1726 (R_{int} = 0.028), N_o = 1431; R = 0.039, R_w = 0.042; n_v = 217, $|\Delta\rho_{max}|$ = 0.21 e Å^{-3}.

Variata. At C(21), one of the pendant methyl groups was disordered with the methoxy group; site occupancies of both were set at 0.5 after trial refinement (C, O isotropic thermal parameter forms). The (OH(51)) hydroxy hydrogen atom was observed in difference maps, and appears to be hydrogen-bonded to N(3) of an adjacent molecule. (O,H···N ($\frac{1}{2} - x$, $1 - y$, $z - \frac{1}{2}$) 2.828(4), $1._9$ Å). Chirality was assigned from the chemistry.

9. $C_{14}H_{23}NO_6S$, M = 333.4. Single-counter instrument, *T ca.* 295 K. Monoclinic, space group $P2_1$ (C_2^2, No. 4), a = 6.644(1), b = 18.553(3), c = 13.507(2) Å, β = 97.31(1)°, V = 1651 Å^3. D_c (Z = 4) = 1.34_1 g cm^{-3}; $F(000)$ = 712. μ_{Mo} = 2.2 cm^{-1}; specimen: 0.68 × 0.23 × 0.70 mm; 'T'$_{min, max}$ = 0.91, 0.95. $2\theta_{max}$ = 50°; N_{tot} (hemisphere) = 4248, N = 2289 (R_{int} = 0.019); R = 0.044, R_w = 0.079 (refinement on F^2 (all data)); n_v = 406, $|\Delta\rho_{max}|$ = 0.34 e Å^{-3}.

Variata. All hydrogen atoms were observed in difference maps; hydroxy OH(258) was disordered over a pair of sites, occupancy set at 0.5 each after trial refinement. Chirality was assigned from the chemistry. In molecule 1, OH(151) is intramolecularly hydrogen-bonded to O(158) (O,H···O 2.712(5), $1._8$ Å); other putative hydrogen-bonds are weaker with distances between the parent atoms greater than 2.8 Å.

10. $C_{14}H_{23}NO_6S$, M = 333.4. Single-counter instrument, *T ca.* 295 K. Tetragonal, space group $P4_1$ (C_4^2, No. 76), a = 9.330(3), c = 19.648(8) Å, V = 1710 Å^3. D_c (Z = 4) = 1.29_5 g cm^{-3}; $F(000)$ = 712. μ_{Mo} = 2.2 cm^{-1}; specimen: 0.43 × 0.37 × 0.40 mm; 'T'$_{min, max}$ = 0.92, 0.94. $2\theta_{max}$ = 48°; N_{tot} = 4966, N = 1378 (R_{int} = 0.042) (refinement on F^2 (all data)); R = 0.038, R_w = 0.059; n_v = 291, $|\Delta\rho_{max}|$ = 0.17 e Å^{-3}.

Variata. $(x, y, z, U_{iso})_H$ were refined throughout; chirality was assigned from the chemistry. OH(51) is intramolecularly hydrogen-bonded to O(58) (O,H···O 2.719(6), 1.96(5) Å), with OH(58) intermolecularly hydrogen-bonded to N(3) of an adjoining molecule (O,H···N ($x - 1$, y, z) 2.840(5), 2.09(7) Å).

17. $C_{20}H_{36}NO_6SSi$, M = 446.7. Single-counter instrument, *T ca.* 295 K. Orthorhombic, space group $P2_12_12_1$, a = 30.699(5), b = 10.843(1), c = 7.615(2) Å, V = 2535 Å^3. D_c (Z = 4) = 1.17_1 g cm^{-3}; $F(000)$ = 964. μ_{Mo} = 2.1 cm^{-1}; specimen: 0.70 × 0.40 × 0.85 mm; 'T'$_{min, max}$ = 0.91, 0.95. $2\theta_{max}$ = 50°; N_{tot} = 8012, N = 2565 (R_{int} = 0.025), N_o = 2007; R = 0.056, R_w = 0.072; n_v = 263, $|\Delta\rho_{max}|$ = 0.73 e Å^{-3}.

Variata. Chirality was assigned from the chemistry. The hydroxy hydrogen atom was not located.

22. $C_{21}H_{37}NO_7SSi$, M = 475.7. Area-detector instrument, *T ca.* 153 K. Orthorhombic, space group $P2_12_12_1$, a = 6.9634(5), b = 10.0227(8), c = 36.608(3) Å, V = 2555 Å^3. D_c (Z = 4) = 1.23_6 g cm^{-3}; $F(000)$ = 1024. μ_{Mo} = 2.1 cm^{-1}; specimen: 0.70 × 0.22 × 0.11 mm; 'T'$_{min, max}$ = 0.83, 0.97. N_{tot} = 27955, N = 3759 (R_{int} = 0.024), N_o = 3677; R = 0.038, R_w = 0.074.

Variata. $(x, y, z, U_{iso})_H$ were refined. Friedel data were preserved distinct, the absolute structure parameter x_{abs} refining to −0.02(18). Hydroxyl OH(51) is hydrogen-bonded to N(3) of an adjacent molecule ($\frac{1}{2} + x$, $1\frac{1}{2} - y$, $\bar{z}$) (O,H···N 2.817(6), 2.13(8) Å).

24. $C_{21}H_{39}NO_7SSi$, M = 477.7. Area-detector instrument, *T ca.* 153 K. Orthorhombic, space group $P2_12_12_1$, a = 5.8742(4), b = 16.675(1), c = 26.302(2) Å, V = 2576 Å^3. D_c (Z = 4) = 1.23_2 g cm^{-3}; $F(000)$ = 1032. μ_{Mo} = 2.1 cm^{-1}; specimen: 0.40 × 0.10 × 0.10 mm; 'T'$_{min, max}$ = 0.68, 0.96. N_{tot} = 28121, N = 3737 (R_{int} = 0.041), N_o = 3120; R = 0.040, R_w = 0.026; n_v = 452, $|\Delta\rho_{max}|$ = 0.39 e Å^{-3}.

Variata. Methyl 24 was disordered (site occupancies set at 0.5 after trial refinement) with one of the associated methoxy groups. (x, y, z, U_{iso}) were refined for all fully weighted hydrogen atoms. O(51,57) are in close proximity (O···O 2.800(3) Å), with the OH(57) hydrogen hydrogen-bonded to O(51) (H···O 2.14(3) Å). OH(51) is hydrogen-bonded to N(3) of an adjacent molecule (OH···N ($\frac{1}{2} + x$, $\frac{1}{2} - y$, $2 - z$) 2.792(4), 2.00(3) Å).

27. $C_{20}H_{25}NO_{11}S$, M = 487.5. Area-detector instrument, *T ca.* 153 K. Monoclinic, space group $P2_1$, a = 9.820(1), b = 8.170(1), c = 14.692(2) Å, β = 99.986(2)°, V = 1161 Å^3. D_c (Z = 2) = 1.39_4 g cm^{-3}; $F(000)$ = 512. μ_{Mo} = 2.0 cm^{-1}; specimen: 0.60 × 0.13 × 0.10 mm; 'T'$_{min, max}$ = 0.77, 0.96. N_{tot} = 13077, N = 3123 (R_{int} = 0.027), N_o = 2610; R = 0.040, R_w = 0.041; n_v 399, $|\Delta\rho_{max}|$ = 0.33 e Å^{-3}.

Variata. $(x, y, z, U_{iso})_H$ (all H) were refined.

30·H$_2$O. $C_{21}H_{41}NO_8SSi$, M = 495.7. Area-detector instrument, *T ca.* 300 K. Orthorhombic, space group $P2_12_12_1$, a = 7.3320(6), b = 15.956(1), c = 24.333(2) Å, V = 2847 Å^3. D_c (Z = 4) = 1.15_6 g cm^{-3}; $F(000)$ = 1072. μ_{Mo} = 2.0 cm^{-1}; specimen: 0.55 × 0.45 × 0.40 mm; 'T'$_{min, max}$ = 0.76, 0.94. N_{tot} = 20618, N = 3235 (R_{int} = 0.021), N_o = 2341; R = 0.043, R_w = 0.041; n_v = 319, $|\Delta\rho_{max}|$ = 0.25 e Å^{-3}.

Variata. Methyl 24/methoxy 23 were modelled as disordered between both sets of sites, occupancies 0.42(2) and complement. Hydroxylic atoms were located in difference maps. Friedel data were preserved distinct with the absolute structure parameter x_{abs} refining to 0.02(15). Hydroxy OH(51) is hydrogen-bonded to the water molecule (O,H···O ($x - 1$, y, z) 2.703(4), 1.8 Å) while hydroxy O(58) is hydrogen-bonded to O(51) of an adjoining molecule (O,H···O ($\frac{1}{2} + x$, $1\frac{1}{2} - y$, $1 - z$) 2.707(4), 1.8 Å). One of the water molecule hydrogen atoms is hydrogen-bonded to the nitrogen atom (O,H(b)···N 2.928(5), 2.0 Å).

Acknowledgements

We thank Johnson and Johnson Research Pty. Limited (Sydney) for supporting this project and the Australian Research Council for an APA(I) scholarship to GRJ.

References

1 M. D. Cliff and S. G. Pyne, *J. Org. Chem.*, 1995, **60**, 2378.
2 M. D. Cliff and S. G. Pyne, *Tetrahedron Lett.*, 1995, **36**, 5969.
3 A. T. Ung, S. G. Pyne, B. W. Skelton and A. H. White, *Tetrahedron*, 1996, **52**, 14069.
4 M. D. Cliff and S. G. Pyne, *J. Org. Chem.*, 1997, **62**, 1023.
5 S. G. Pyne and A. T. Ung, *Synlett*, 1998, 280.
6 A. T. Ung and S. G. Pyne, *Tetrahedron*: *Asymmetry*, 1998, **9**, 1395.
7 A. Iscaro, I. R. Mackay and C. O'Brien, *Immunol. Cell. Biol.*, 1988, **66**, 395.
8 S. J. P. Golin and J. A. Phillips, *Clin. Exp. Immunol.*, 1991, **85**, 335.
9 T. E. Mandel, M. Koulmanda and I. R. Mackay, *Clin. Exp. Immunol.*, 1992, **88**, 414.
10 M. Cherest, H. Felkin and N. Prudent, *Tetrahedron Lett.*, 1968, 2199.
11 N. T. Anh, *Top. Curr. Chem.*, 1980, **88**, 145.
12 H. Chikashita, T. Nikaya, H. Uemura and K. Itoh, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 2121.
13 For the reductions of related thiazolyl ketones see: (*a*) A. Dondoni, D. Perrone, *Synthesis*, 1993, 1162; (*b*) A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici and P. Pedrini, *J. Org. Chem.*, 1989, **54**, 693; (*c*) A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici and P. Pedrini, *J. Org. Chem.*, 1989, **54**, 702.
14 S. Jiang, G. Singh and R. H. Wightman, *Chem. Lett.*, 1996, 67.
15 P. D. Kane and J. Mann, *J. Chem. Soc.*, *Perkin Trans. 1*, 1984, 657.
16 *The Xtal 3.4 User's Manual*, eds. S. R. Hall, G. S. D. King and J. M. Stewart, University of Western Australia, Lamb, Perth, 1995.

Paper 9/03675J