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Note

Synthesis of (5*S*,8*R*,9*R*,10*S*)-8,9,10-trihydroxy-2-thioxo-1,6-dioxa-3-azaspiro[4.5]decane from 1-amino-1-deoxy-D-*arabino*-hexulose

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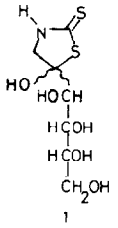
The reaction of 1-amino-1-deoxy-D-*arabino*-hexulose with carbon disulphide at 5° yields[1] 5-hydroxy-5-(D-*arabino*-tetritol-1-yl)thiazolidine-2-thione (**1**), whereas 3-alkyl analogues (**2**), with the D-*arabino*, D-*lyxo*, D-*ribo*, and D-*threo* configurations, are prepared[2,3] from *N*-alkyl-D-glycopyranosylamines and carbon disulphide. Little attention has been directed to the syntheses of analogous spiro-nucleoside derivatives. The furanosylspiro-oxazolidine-2-thione (**3**) was obtained[4,5] by reaction of D-fructose and thiocyanic acid. The spiro structure **4** was proposed[6] for the product of reaction of 1-amino-1-deoxy-D-*arabino*-hexulose with phenyl isothiocyanate, although the compound was not isolated, and we have described[7] the preparation of (2*R*,3*R*,4*S*,5*S*)-3,4-dihydroxy-2-hydroxymethyl-8-methyl-6-phenyl-7- thioxo-1-oxa-6,8-diazaspiro[4.4]-nonane (**5**) and the 5*R* isomer from 1-deoxy-1-methylamino-D-*lyxo*-hexulose and phenyl isothiocyanate.



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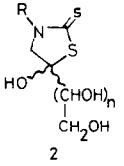

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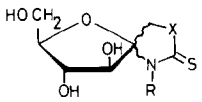
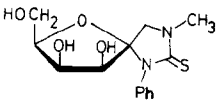


3 X=O, R=H
4 X=NH, R=Ph



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We now report that the reaction of 1-amino-1-deoxy-D-*arabino*-hexulose acetate with carbon disulphide at 75° gave (49%) (5*S*,8*R*,9*R*,10*S*)-8,9,10-trihydroxy-2-thioxo-1,6-dioxa-3-azaspiro[4.5]decane (**6**), $[\alpha]_D$ −200° (*cf.* +18° for **1**), λ_{max} 243 nm (close to that for tetrahydro-oxazole-2-thiones[8] and different from that for thiazoli-

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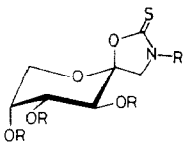
dine-2-thiones[3]); the high resolution mass spectrum showed the exact atomic composition for the molecular ion. The ^{1}H-n.m.r. spectrum (see Experimental) indicated the presence of one NH and three OH groups, which confirmed the pyranoid structure. The i.r. absorptions[9] at 1537 (δ_{NH}) and 1174 cm^{-1} ($\nu_{C=S}$) and the ^{13}C-n.m.r. data confirmed the oxazole structure. The spiro carbon (C-5) resonated at 112.5 p.p.m., and was more deshielded than the similar carbon of **2**[3] (88–90 p.p.m.), consistent with bonding to two oxygen atoms.

Conventional treatment of **6** with acetic anhydride–pyridine at room temperature or with acetic anhydride and zinc chloride at 150° yielded the tetra-acetate **7**. The ^{1}H-n.m.r. data ($J_{9,10}$ 10.3; $J_{7,8}$, $J_{7',8}$, and $J_{8,9}$ 1.3–2.9 Hz) are consistent with a major $^1C_4$(D) conformation in solution in chloroform. The $J_{7,7'}$ value (13.7 Hz) accords with an axial acetoxyl group[10] on C-8.

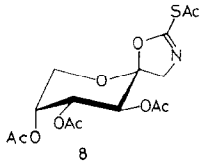
The thioacetyl structure (**8**) for **7** was ruled out by the i.r. (1160 cm^{-1}) and ^{13}C-n.m.r. (182.8 p.p.m.) data which are characteristic of the C=S group (*cf.* ~194 p.p.m. for C=O[11]). The ^{1}H-singlet at 2.81 p.p.m. is assigned to the NAc, because its chemical shift is similar to that of NAc groups of related 2-thioxoheterocycles[12,13] (*cf.* 235 p.p.m. for the acetylthio group[14]). This chemical shift is indicative[13] of the conformation **9**, where the methyl group is deshielded by the nearby C=S bond.

The *S* configuration for C-5 in **7** has been demonstrated by X-ray diffraction[15].

A possible mechanism for the synthesis of **6** from fructosamine and carbon disulphide at 75° involves the formation of the thiocarbamate **10** and the isothiocyanate **11**. This mechanism is related with that proposed[16] for the reaction of aminoalcohols and carbon disulphide.



6 R=H
7 R=Ac



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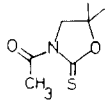

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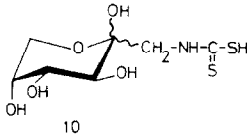

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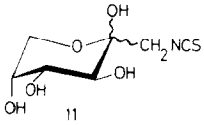

11

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were measured at 5461 Å, using a 1-cm cell. I.r. spectra were recorded for KBr discs. ^{1}H-N.m.r. sprectra were obtained at 200 MHz. Assignments were confirmed by decoupling experiments and H/D exchange. ^{13}C-N.m.r. spectra were recorded at 50.3 MHz for solutions in $CDCl_3$ and $(CD_3)_2SO$. Proton-decoupled APT[17] spectra were obtained in order to assist in signal assignments. The e.i.-mass spectrum was obtained at

70 eV, with an ion-source temperature of 200°; accelerating voltage, 4 kV; resolution 10.000 (10% valley definition). The elemental composition of the molecular ion was determined by a peak-matching method relative to PFK.

(5S,8R, 9R,10S)-8,9,10-Trihydroxy-2-thioxo-1,6-dioxa-3-azaspiro[4.5]decane (**6**). — A mixture of 1-amino-1-deoxy-D-*arabino*-hexulose acetate[18] (2 g, 5.0 mmol), carbon disulphide (2 mL, 33.2 mmol), and methanol (75 mL) was stirred at 75° until the amino sugar disappeared (t.l.c.; dichloromethane–methanol, 5 : 1). The mixture was cooled to room temperature, filtered, and concentrated. Recrystallization of the product (1.34 g, 71%) from methanol gave **6** (0.92 g, 49%), m.p. 157–158°, $[\alpha]_D^{22}$ −200° (*c* 1, pyridine); λ_{max}^{MeOH} 243 (ε_{mM} 18.0); ν_{max} 3400 (OH), 3200 (NH), 2950, 2920, 2900 (CH), 1537 (NH), and 1174 cm^{-1} (C=S). ^{1}H-N.m.r. data [$(CD_3)_2SO$]: δ 10.20 (bs, 1 H, NH), 5.75 (d, 1 H, $J_{H,OH}$ 3.8 Hz, OH), 5.10 (d, 1 H, $J_{H,OH}$ 1.8 Hz, OH), 5.00 (d, 1 H, $J_{H,OH}$ 1.1 Hz, OH), 4.10–3.40 (m, 7 H, H-4,4′,7,7′,8,9,10) (the signals at δ 10.20, 5.75, 5.10, and 5.00 disappeared on addition of D_2O); ^{13}C, δ 187.2 (C-2), 112.5 (C-5), 71.1 (C-8), 70.0 (2 C, C-9,10), 67.2 (C-7), and 51.9 (C-4). Mass spectrum: *m/z* 221.03630 (M^+; calc. for $C_7H_{11}NO_5S$: 221.03579).

(5S,8R,9R,10S)-8,9,10-Triacetoxy-3-acetyl-1,6-dioxa-3-azaspiro [4.5]decane (**7**). — Conventional treatment of **6** (1.0 g, 4.5 mmol) with pyridine (5 mL) and acetic anhydride (5 mL, 53.0 mmol) gave **7** (1.12 g, 67%). After recrystallization from ethanol, the product (0.86 g, 51%) had m.p. 120–122°, $[\alpha]_D^{22}$ −220° (*c* 1, chloroform); λ_{max}^{MeOH} 265 (ε_{mM} 14.0); ν_{max} 2980, 2963, 2958, 2930 (CH), 1750 (CO, ester), 1700 (CO, amide), 1240, 1080 (C-O), and 1160 cm^{-1} (C=S). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.60 (d, 1 H, $J_{8,9}$ 2.9 Hz, H-9), 5.58 (d, 1 H, $J_{9,10}$ 10.3 Hz, H-10), 5.54 (m, 1 H. H-8), 4.33 (dd, 1 H, $J_{7,7'}$ 13.7, $J_{7,8}$ 1.3 Hz, H-7), 4.13 (d, 1 H, $J_{4,4'}$ 14.2 Hz, H-4), 3.98 (dd, 1 H, $J_{7',8}$ 2.1 Hz, H-7′), 3.94 (d, 1 H, H-4′), 2.81 (s, 3 H, NAc), 2.18, 2.11, and 2.01 (3 s, 9 H, 3 OAc); ^{13}C, δ 182.8 (C-2), 171.1, 167.8, 167.5, 167.3 (4 C=O), 104.4 (C-5), 69.2 (2 C, C-9,10), 68.3 (C-8), 63.6 (C-7), 53.8 (C-4), 26.0 ($NCOCH_3$), 20.4, 20.2, and 19.7 (3 $OCOCH_3$).

Anal. Calc. for $C_{15}H_{19}NO_9S$: C, 46.27; H, 4.92; N, 3.60; S, 8.24. Found: C, 46.27; H, 5.01; N, 3.71; S, 8.70.

Compound **7** (49%) was also obtained when the acetylation reaction was performed at 150° (30 min) in the presence of zinc chloride.

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