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Carbohydrate Research 257 (1994) 127–135

CARBOHYDRATE RESEARCH

Note

1-Deoxy-1-isothiocyanato-D-fructose as intermediate in syntheses of 1,3-O(S),N-heterocycles

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(Received June 1st, 1993; accepted October 2nd, 1993)

An important problem in the chemistry of ketoses is the lack of selectivity due on one hand to the complexity of their tautomeric equilibria and on the other to their tendency to form tertiary oxocarbenium ions under acidic conditions. Thus, mixtures of open-chain, cyclic, and dehydration products are frequently obtained. To achieve an efficient control, study of the mechanism and identification of the transient intermediates for the different reactions involved becomes a crucial point. With this goal, and in the framework of a program concerning the synthesis of chiral heterocycles from carbohydrates, we have now re-examined the condensation reaction of 1-amino-1-deoxy-D-fructose with carbon disulfide. The mechanism of the reaction under different conditions is discussed. The key intermediate 1-deoxy-1-isothiocyanato-D-fructose has been unequivocally generated and used in the stereocontrolled synthesis of spiro and acyclic nucleosides.

The reaction of 1-amino-1-deoxy-D-fructose with CS_2 leads to the formation of azolidine-2-thione derivatives whose structures strongly depend on the reaction conditions (Scheme 1). In 1975, Jochims [1] reported the formation of a diastereomeric mixture of (5*R*)- and (5*S*)-5-hydroxy-5-(D-*arabino*-tetritol-1-yl)thiazolidine-2-thiones (**2**) by condensation of 1-amino-1-deoxy-D-fructose hydrochloride with CS_2 in the presence of an excess of Et_3N at 5°C. Recent work carried out in our laboratory [2] has shown that, starting from the corresponding acetate in the absence of base at 75°C, β-D-fructopyranosylspirooxazolidine-2-thione (**4**) is the main reaction product. These results can be explained by assuming the formation of different intermediates in each case. Thus, in the presence of Et_3N, the reaction probably proceeds via the dithiocarbamate **1**. Nucleophilic displacement on related

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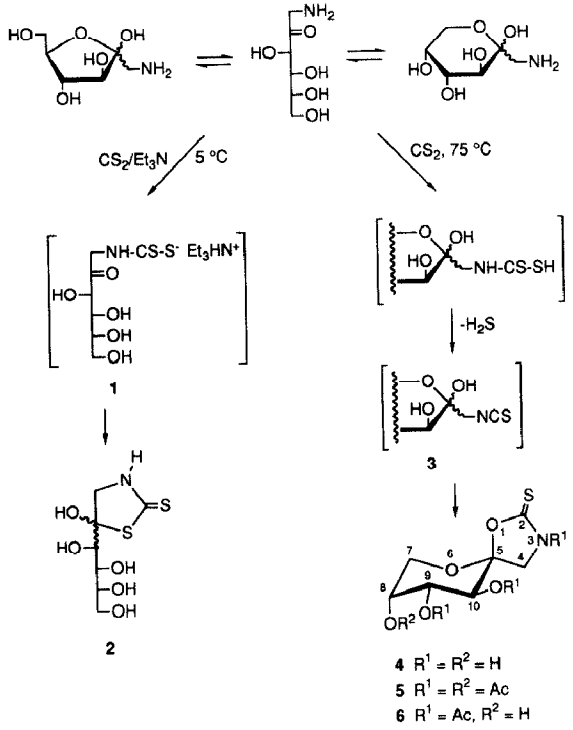
SSDI 0008-6215(93)E0391-D



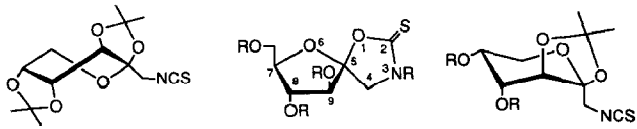
Scheme 1. Products formed by the action of carbon disulfide on 1-amino-1-deoxy-D-fructose.

salts by a β- or γ-located hydroxyl group is a classical method [3] for the preparation of 2-thioxotetrahydro-1,3-O,N-heterocycles. However, the latter reaction needs more strenuous conditions and prior derivatization is required in order to increase the yield of cyclic thiocarbamate [4]. Instead, under the milder conditions used in the experiment, **1** undergoes spontaneous cyclization involving the carbonyl group of fructose in its keto-form to give **2**.

In the absence of base, the formation of transient 1-deoxy-1-isothiocyanato-D-fructose (**3**) as a key intermediate was postulated [2]. Intramolecular cyclization involving the anomeric hydroxyl group of the β-D-fructopyranose tautomer would then afford the oxazolidine derivative **4**, as reported for simpler β-hydroxyalkyl isothiocyanates [5,6]. This approach has been recently used in the synthesis of pseudo-*C*-nucleosides from 6-deoxy-6-isothiocyanatoaldoses [7,8].

In support of the above hypothesis, when the formation of an isothiocyanate intermediate is prevented by the presence of an alkyl substituent on the nitrogen atom, only thiazolidine-2-thiones with acyclic substituents are formed [9]. In order to obtain definitive evidence for this mechanism, we have now unequivocally generated the unprotected intermediate **3** from 1-deoxy-2,3 : 4,5-di-*O*-isopropylidene-1-isothiocyanato-β-D-fructopyranose (**7**) by treatment with 90% CF_3CO_2H–H_2O, and identified the reaction products. Compound **7** was prepared from 1-amino-1-deoxy-2,3 : 4,5-di-*O*-isopropylidene-β-D-fructopyranose hydrochloride

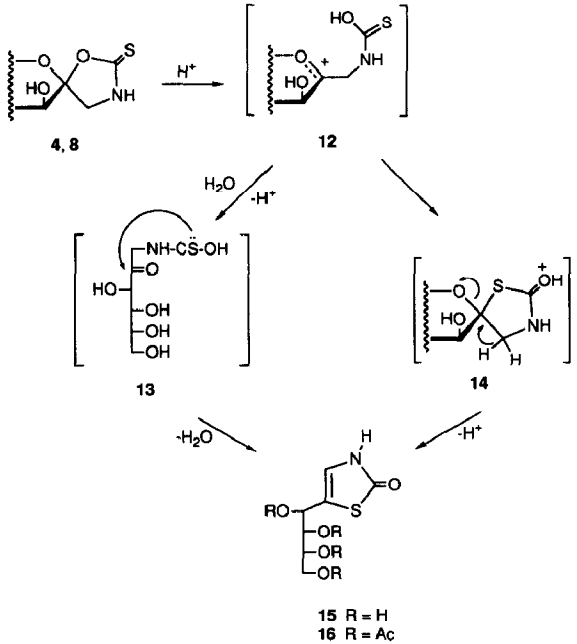
[10] by reaction with thiophosgene, following the method previously reported for the synthesis of glycosyl isothiocyanates [11,12] and 6-deoxy-6-isothiocyanatoaldoses [7,8].



7 8 R = H 9 R = Ac 10 R = H 11 R = Ac

The outcome of the reaction was found to be highly dependent on reaction and workup conditions. Under optimized conditions (see Experimental), compound **4** was almost the sole reaction product, together with a small proportion of its β-D-fructofuranosyl analogue **8**, thus strongly supporting the reaction pathway discussed above.

When the reaction was conducted at lower temperatures, significant amounts of unreacted **7** as well as the product of partial deprotection **10** were present in the reaction mixture. No products bearing a single isopropylidene group at O-4,5 were detected, thus excluding an effect of the protecting group on the formation of the major pyranosyl derivative. This result accords with the order of stability reported for both isopropylidene groups of 2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose, using an acidic resin as deprotection reagent [13], but differs from that observed in



4, 8 12 13 14 15 R = H 16 R = Ac

Scheme 2.

the formation of diketose dianhydrides from isopropylidene derivatives with HF-based reagents [14].

It has been recently reported [15,16] that, in reactions involving the anomeric position of fructose derivatives in the cyclic form, the composition of the product mixture depends largely on the initial pyranose–furanose ratio. A marked tendency to retain the original ring size has been observed, and this effect may explain the high selectivity towards the pyranosyl derivative **4** observed in this reaction as compared, for instance, with Fischer glycosidation of 1-amino-1-deoxy-D-fructose derivatives [17]. The preference for the β-anomeric configuration agrees with the order of thermodynamic stability found for methyl fructosides [18] as well as spiro derivatives of fructose [15,19,20].

The use of longer reaction times or higher temperatures during workup resulted in the opening of the spiro compounds **4** and **8** and subsequent rearrangement to give the 4-thiazoline-2-one derivative **15**. We had previously observed [21] that 6,5-cyclic thiocarbamates of aldoses undergo CS → CO transformation by treatment with aqueous acid without opening of the heterocyclic ring, to give the corresponding oxazolidinones. In this case, the rather stable ion **12** must be readily formed, leading to the acyclic *C*-nucleoside **15** via either the keto-tautomer **13** or the spirothiazolidinone **14** (Scheme 2).

Chromatographic separations and structural assignments for **4**, **8**, **10**, and **15** were performed after conventional acetylation of the crude reaction mixtures (→ **5**, **9**, **11**, **16**). A partially protected derivative of **4** having the less reactive axial HO-8 free (**6**) was also isolated.

Comparison of the spectroscopic data for **5** and **6** allowed unequivocal assignment of their ^{1}H and ^{13}C NMR spectra. Some of the previous assignments [2] made for **5** on the basis of Eu(fod)$_3$ correlations must be corrected (see Experimental). The structure of **6** was confirmed by the strong shielding effect observed for H-8 and the deshielding effect [22] (~ 2 ppm) for the β-carbons C-7 and C-9 in ^{1}H and ^{13}C NMR spectroscopy, respectively, as compared with the peracetylated derivative **5**.

The furanoid structure of compound **9** was evident from the ^{1}H and ^{13}C NMR data. The β configuration was established on the basis of the $J_{8,9}$ value. It has been claimed [23,24] that this value falls within the ranges 1.4–2.4 Hz (mean 2.0 Hz) or 5.5–9.7 Hz (mean 7.1 Hz) for α- or β-D-fructofuranose derivatives, respectively. The experimental value (6.7 Hz) agrees with the assigned structure. Furthermore, the values of $J_{7,8}$ and $J_{8,9}$ accord with data reported [25] for homologous coupling constants of spirodioxanyl-β-D-fructofuranosides, suggesting that the furanoid ring adopts a conformation close to E_4(D), with C-8 out of the plane of the other ring atoms. Although the ^{13}C chemical shift for the anomeric C-5 atom (108.3 ppm) is higher than that expected for a β-D-fructofuranosyl derivative (~ 104.7 ppm), the deviation is analogous to that observed for its β-D-fructopyranosyl counterpart **5**, whose anomeric configuration has been unequivocally established by X-ray spectroscopy [26]. The presence of the thiocarbamate bridge was confirmed by ^{13}C NMR ($\delta_{C=S}$ 182.5) and UV spectroscopy ($\pi \rightarrow \pi^*$ transition). The ^{1}H and ^{13}C chemical shifts for the NCO*CH*$_3$ group are indicative of a parallel

disposition between the methyl and the thiocarbonyl groups, as reported for related *N*-acetyloxazolidine-2-thiones [2,7,8].

Compounds **7** and **11** showed the characteristic IR absorption (~ 2100 cm^{-1}) and ^{13}C signal (~ 134 ppm) for the NCS group. The EI-mass spectra showed weak molecular peaks and the losses of $CH_2NCS\cdot$ and CH_3NCS as the main primary fragmentations. This fragmentation pattern agrees with that observed for 6-deoxy-6-isothiocyanatoaldoses [7,8] and probably reflects the higher stability of primary deoxyisothiocyanato sugars as compared to glycosyl isothiocyanates, for which no molecular peak is observed, and the losses of $NCS\cdot$ and HNCS are much favoured [27]. Both ^1H and ^{13}C NMR data for **7** and **11** accord with reported data for 2,3:4,5-di- and 2,3-*O*-isopropylidene derivatives of D-fructose, respectively [13,28].

The IR and UV data for the acyclic derivative **16** agreed with reported data for 4-thiazoline-2-ones, discarding an isomeric oxazolinethione structure [29,30]. A ^{13}C signal at δ 167.3 (NHCOS) and an EIMS peak at m/z 372 ($M^+ - OH\cdot$) additionally support the presence of the amide moiety [31,32]. The negative value of the optical rotation is in agreement [9,33] with the *S*-configuration of C-1′, while the vicinal coupling constants observed in the ^1H NMR spectrum are indicative of the existence of a complex conformational equilibrium for the tetraacetoxybutyl substituent in $CDCl_3$ solutions.

1. Experimental

General methods.—Melting points were determined with a Gallenkamp apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 polarimeter, using 1-cm cells. UV spectra were recorded with a Philips PU 8710 spectrophotometer. IR spectra were recorded with a Bomen Michelson MB-120 FTIR spectrophotometer. ^1H (300 and 500 MHz) and ^{13}C NMR spectra (75.5 and 125.7 MHz) were recorded with Bruker 300 and 500 AMX spectrometers for solutions in $CDCl_3$. Tetramethylsilane was used as internal standard. Assignments of ^1H signals were confirmed by COSY experiments. Gated decoupling spectra were used to assist in carbon signal assignments. EI-mass spectra were obtained with a Kratos MS-80 RFA instrument under the following conditions: ionizing energy, 35 eV; ionizing current, 100 μA; accelerating voltage, 4 kV; resolution, 1000 (10% valley definition). TLC was performed on Silica Gel 30 F_{254} (E. Merck) plates with visualization by UV light and by charring with 10% H_2SO_4, and column chromatography was carried out with Silica Gel 60 (E. Merck, 70–230 mesh).

*1-Deoxy-2,3 : 4,5-di-*O*-isopropylidene-1-isothiocyanato-β-*D*-fructopyranose* (**7**).—To a heterogeneous mixture of 1-amino-1-deoxy-2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose hydrochloride [10] (1.2 g, 4.06 mmol) in $CHCl_3$ (20 mL), water (20 mL), and $CaCO_3$ (1.23 g, 12.3 mmol) was added $CSCl_2$ (0.72 g, 0.48 mL, 6.09 mmol). The mixture was vigorously stirred for 1.5 h and then filtered. The organic layer was separated, washed with water, dried ($MgSO_4$), and concentrated. The crude product was chromatographed (4:1 petroleum ether–EtOAc), giving **7** (1.05

g, 88%) as an oil; $[\alpha]_D^{20}$ – 65.8° (*c* 1.1, $CHCl_3$); ν_{max}^{film} 2118 (NCS), 1383 and 1381 cm^{-1} (*gem*-dimethyl); ^1H NMR (500 MHz): δ 4.63 (dd, 1 H, $J_{3,4}$ 2.7, $J_{4,5}$ 7.9 Hz, H-4), 4.31 (d, 1 H, H-3), 4.24 (ddd, 1 H, $J_{5,6a}$ 1.8, $J_{5,6b}$ 0.8 Hz, H-5), 3.93 (d, 1 H $J_{1a,1b}$ 14.4 Hz, H-1a), 3.90 (dd, 1 H, $J_{6a,6b}$ 13.0 Hz, H-6a), 3.77 (dd, 1 H, H-6b), 3.75 (d, 1 H, H-1b), 1.56, 1.47, 1.46, and 1.35 (4 s, each 3 H, 4 Me); ^{13}C NMR (125.7 MHz), δ 132.2 (NCS), 109.3 108.8 (2*C*Me_2), 100.6 (C-2), 70.3 (2 C, C-3,5), 69.7 (C-4), 61.4 (C-6), 49.8 (C-1), 26.3, 25.6, 25.1 and 23.7 (4 Me); EIMS: *m/z* 301 (1%, M^+), 286 (70, $M^+ - Me^·$), 229 (100, $M^+ - CH_2NCS^·$), 228 (5, $M^+ - CH_3NCS$), 226 (5, 286 – AcOH), 171 (64, 229 – Me_2CO). Anal. Calcd for $C_{13}H_{19}NO_5S$: C, 51.81; H, 6.36; N, 4.65; S, 10.64, Found: C, 51.84; H, 6.13; N, 4.62; S, 10.85.

Reactions of 7 *in aq 90% CF_3CO_2H.*—(*a*) A solution of 7 (0.6 g, 1.99 mmol) in aq 90% CF_3CO_2H (5 mL) was kept at 20°C under reduced pressure (15 mmHg) until distillation of acetone ceased (~ 15 min). The solvent was then removed under vacuum (0.1 mmHg) at the same temperature, and the resulting syrupy residue was acetylated (1.1 Ac_2O–pyridine, 6 mL, overnight). The acetylation product, which contained a main component (TLC), was subjected to column chromatography (1 : 1 petroleum ether–EtOAc) to give successively:

(*5S,8R,9R,10S*)-*8,9,10-Triacetoxy-3-acetyl-2-thioxo-1,6-dioxa-3-azaspiro[4.5]decane* (**5**; 0.47 g, 61%); R_f 0.72; mp 119–120°C; $[\alpha]_D^{20}$ – 220° (*c* 1, $CHCl_3$); lit [2] mp 120–122°C, $[\alpha]_D^{20}$ – 220° (*c* 1 $CHCl_3$); ^1H NMR (300 MHz); δ 5.50 (d, 1 H, $J_{9,10}$ 10.2 Hz, H-10), 5.40 (m, 1 H, H-8), 5.38 (dd, 1 H, $J_{8,9}$ 4.0 Hz, H-9), 4.23 (dd, 1 H, $J_{7a,7b}$ 13.4, $J_{7a,8}$ 1.2 Hz, H-7a), 4.10 (d, 1 H, $J_{4a,4b}$ 13.0 Hz, H-4a), 3.94 (d, 1 H, H-4b), 3.89 (dd, 1 H, $J_{7b,8}$ 1.7 Hz, H-7b), 2.77 (s, 3 H, NAc), 2.14, 2.07, and 1.97 (3 s, each 3 H, 3 OAc); ^{13}C NMR (75.5 MHz); δ 182.8 (C=S), 170.7 (C=O amide), 169.8, 169.7, 169.4 (3 C=O ester), 104.6 (C-5), 67.9 (2 C, C-8,9), 66.6 (C-10), 63.8 (C-7), 53.9 (C-4), 25.8 (NCO*C*H_3), 20.7, 20.4, and 20.3 (3OCO*C*H_3), and:

(*5S,7R,8R,9S*)-*8,9-Diacetoxy-7-acetoxymethyl-3-acetyl-2-thioxo-1,6-dioxa-3-azaspiro[4.4]nonane* (**9**; 0.085 g, 11%); R_f 0.57; syrup; $[\alpha]_D^{20}$ – 55° (*c* 1, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 267 nm (ε_{mM} 15.2); ν_{max}^{film} 1750 (C=O ester), 1709 (C=O amide), 1223 cm^{-1} (C–O–C and C=S); ^1H NMR (500 MHz): δ 5.53 (dd, 1 H, $J_{7,8}$ 5.6, $J_{8,9}$ 6.7 Hz, H-8), 5.46 (d, 1 H, H-9), 4.57 (dd, 1 H, $^2J_{Ha,Hb}$ 12.3, $^3J_{7,Ha}$ 3.7 Hz, CH_2OAc), 4.35 (td, 1 H, $^3J_{7,Hb}$ 6.0 Hz, H-7), 4.32 (d, 1 H, $J_{4a,4b}$ 12.8 Hz, H-4a), 4.22 (d, 1 H, H-4b), 4.15 (dd, 1 H, CH_2OAc), 2.80 (s, 3 H, NAc), 2.19, 2.15, and 2.10 (3 s, each 3 H, 3 OAc); ^{13}C NMR (125.7 MHz), δ 182.5 (C=S), 170.6 (C=O amide), 170.4, 170.1, 169.8 (3 C=O ester), 108.3 (C-5), 80.5 (C-7), 76.9 (C-9), 74.3 (C-8), 62.8 (*C*H_2OAc), 53.1 (C-4), 25.9 (NCO*C*H_3), 20.7, 20.5, and 20.3 (3 OCO*C*H_3); EIMS: *m/z* 389 (2%, M^+). Anal. Calcd for $C_{15}H_{19}NO_9S$: C, 46.27; H, 4.92; N, 3.60; S, 8.23, Found: C, 46.07; H, 4.95; N, 3.38; S, 8.14.

(*b*) Compound 7 (0.591) g, 1.96 mmol) was dissolved in aq 90% CF_3CO_2H (5mL) at – 10°C under stirring, and the resulting solution was kept at 0°C for 1 h. The solvent was removed at < 20°C under reduced pressure (0.1 mmHg) and the resulting syrupy residue was acetylated as described above. The acetylation product, which contained at least three components (TLC, 1 : 1 petroleum ether–EtOAc), was subjected to column chromatography using a 4 : 1 → 1 : 1 petroleum ether–EtOAc gradient as eluent, to give, first, unreacted 7 (0.10 g, 17%) and then:

4,5-Di-O-acetyl-1-deoxy-2,3-O-isopropylidene-1-isothiocyanato-β-D-fructopyranose (**11**; 0.12 g, 18%), isolated as an oil which crystallized on standing; mp 107–109°C; $[\alpha]_D^{20}$ − 19.0° (*c* 0.7, $CHCl_3$); ν_{max}^{KBr} 2104 (NCS), 1753 (C=O), 1371 (*gem*-dimethyl), 1236 cm^{-1} (C–O–C); ^1H NMR (300 MHz): δ 5.56 (t, 1 H, $J_{3,4}$ 4.0, $J_{4,5}$ 4.0 Hz, H-4), 5.21 (td, 1 H, $J_{5,6a}$ 4.0, $J_{5,6b}$ 7.2 Hz, H-5), 4.15 (d, 1 H, H-3), 3.94 (dd, 1 H, $J_{6a,6b}$ 12.2 Hz, H-6a), 3.86 (d, 1 H, $J_{1a,1b}$ 14.5 Hz, H-1a), 3.77 (d, 1 H, H-1b), 3.71 (dd, 1 H, H-6b), 2.13, 2.02 (2 s, each 3 H, 2Ac), 1.54 and 1.40 (2 s, each 3 H, CMe_2); ^{13}C NMR (75.5 MHz), δ 169.5 (2 C=O), 134.2 (NCS), 111.5 (CMe_2), 101.3 (C-2), 74.2 (C-3), 66.4 (C-4), 64.4 (C-5), 61.8 (C-6), 47.5 (C-1), 27.4, 26.3 (CMe_2), and 20.6 (2 C, 2 $COCH_3$); EIMS: *m/z* 345 (2%, M^+), 273 (85, $M^+ - CH_2NCS^{\cdot}$), 272 (5, $M^+ - CH_3NCS$). Anal. Calcd for $C_{14}H_{19}NO_7S$: C, 48.69; H, 5.55; N, 4.06; S, 9.28. Found: C, 48.64; H, 5.30; N, 4.11; S, 9.12.

Further elution provided, successively, **5** (0.18 g, 24%), **9** (0.038 g, 5%), and finally:

(5S,8R,9R,10S)-9,10-Diacetoxy-3-acetyl-8-hydroxy-2-thioxo-1,6-dioxa-3-azaspiro-[4.5]decane (**6**; 0.020 g, 3%) as a syrup; $[\alpha]_D^{20}$ − 114° (*c* 0.8, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 268 nm (ε_{mM} 19.7); ν_{max}^{film} 3440 (OH), 1748 (C=O ester), 1713 (C=O amide), 1229 cm^{-1} (C–O–C and C=S); ^1H NMR (300 MHz), δ 5.65 (d, 1 H, $J_{9,10}$ 10.3 Hz, H-10), 5.42 (dd, 1 H, $J_{8,9}$ 2.9 Hz, H-9), 4.29 (m, 1 H, H-8), 4.26 (dd, 1 H, $J_{7a,7b}$ 12.6, $J_{7a,8}$ 1.2 Hz, H-7a), 4.18 (d, 1 H, $J_{4a,4b}$ 12.9 Hz, H-4a), 4.03 (dd, 1 H, $J_{7b,8}$ 1.7 Hz, H-7b), 4.00 (d, 1 H, H-4b), 2.84 (s, 3 H, NAc), 2.14, and 2.13 (2 s, each 3 H, 2 OAc); ^{13}C NMR (75.5 MHz), δ 183.0 (C=S), 170.8 (C=O amide), 169.8 169.4 (2 C=O ester), 104.9 (C-5), 70.6 (C-9), 67.2 (C-8), 66.8 (C-10), 65.5 (C-7), 53.9 (C-4), 25.9 ($NCOCH_3$), 20.6 and 20.4 (3 $OCOCH_3$); EIMS: *m/z* 347 (1%, M^+), 332 (46, $M^+ - Me$), 329 (1, $M^+ - H_2O$), 302 (23, $M^+ - Ac^{\cdot}$), 287 (55, $M^+ - AcOH$), 272 (50, 332 − AcOH). Anal. Calcd for $C_{13}H_{17}NO_8S$: C, 44.95; H, 4.93; N, 4.03; S, 9.23. Found: C, 44.59; H, 4.70; N, 3.95; S, 8.85.

(*c*) Compound 7 (0.3 g, 1 mmol) was treated with aq 90% CF_3CO_2H (3 mL) at 20°C as described in (*a*). Removal of the solvent was then effected at 40°C under reduced pressure (15 mmHg). Water (3 × 15 mL) was added and evaporated at the same temperature, and the final syrupy residue was dried over P_2O_5 and acetylated. The acetylation product, which contained a main component (TLC), was chromatographed (3:1 CCl_4–acetone) to give:

5-(Tetra-O-acetyl-D-arabino-tetritol-1-yl)-4-thiazoline-2-one (**16**; 0.25 g, 65%); R_f 0.3; mp 148–150°C (from $CHCl_3$–Et_2O); $[\alpha]_D^{20}$ − 6° (*c* 1.2, $CHCl_3$); $\lambda_{max}^{CHCl_3}$ 244 nm (ε_{mM} 11.5); ν_{max}^{KBr} 3335 (NH), 1750 (C=O ester), 1684 (NHCO), 1219 cm^{-1} (C–O–C); ^1H NMR (500 MHz): δ 7.53 (d, 1 H, $J_{4,NH}$ 10.8 Hz, NH), 6.96 (d, 1 H, H-4), 5.53 (d, 1 H, $J_{1',2'}$ 5.3 Hz, H-1'), 5.47 (t, 1 H, $J_{2',3'}$ 5.3 Hz, H-2'), 5.18 (m, 1 H, H-3'), 4.28 (dd, 1 H, $J_{3',4'a}$ 3.4, $J_{4'a,4'b}$ 12.2 Hz, H-4'a), 4.14 (dd, 1 H, $J_{3',4'b}$ 5.9 Hz, H-4'b), 2.09, 2.07, 2.06, and 2.03 (4 s, each 3 H, 4 Ac); ^{13}C NMR (75.5 MHz), δ 170.4, 169.7 169.5, 168.2 (4 C=O ester), 167.3 (C-2), 126.8 (C-5), 115.9 (C-4), 69.5, 69.3, 68.6 (C-1', 2', 3'), 61.4 (C-4'), 20.6, 20.5 (2 C), and 20.4 (4 Me); EIMS: *m/z* 389 (47%, M^+), 372 (2, $M^+ - OH^{\cdot}$), 329 (25, $M^+ - AcOH$), 269 (10, $M^+ - 2$ AcOH), 209 (40, $M^+ - 3$ AcOH), 100 (90, cation 4-thiazoline-2-one-5-yl), 60 (100,

AcOH). Anal. Calcd for $C_{15}H_{19}NO_9S$: C, 46.27; H, 5.13; N, 3.75. Found: C, 46.04; H, 5.38; N, 3.57.

Compound **16** was also prepared from pure **5** (0.2 g, 0.5 mmol) by Zemplén deacylation, treatment of the crude unprotected derivative [2] **4** with aq 90% CF_3CO_2H (2 mL), and reacetylation of the reaction mixture as described above. Column chromatography of the resulting product yielded **16** (0.134 g, 67%).

2. Acknowledgments

The authors thank the Dirección General de Investigación Científica y Técnica for financial support (grant number PB91-0617), the Junta de Andalucía for the award of a scholarship (to J.L.J.B.), and the Ministerio de Educatión y Ciencia of Spain for a postdoctoral fellowship (to J.M.G.F.).

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