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Syntheses of Novel Glycosylidene-Spiro-Heterocycles Related to Hydantocidin

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Abstract

Reaction of 2,3,4,6-tetra-*O*-acetyl-1-bromo-1-deoxy-β-D-galactopyranosyl cyanide (**4**) with thiocyanate ions results in the formation of both anomers of per-*O*-acetylated 1-deoxy-1-thiocyanato-D-galactopyranosyl cyanides (**5a** and **5b**). The thiocyanate group in these products is resistant to isomerization into isothiocyanate even at elevated temperatures. The X-ray structure of **5a** is consistent with the operation of an *exo*-anomeric effect for the thiocyanate group. Compounds **5a** and **5b** react with hydrogen sulfide under mild conditions to yield galactopyranosylidene-spiro-thiazolidine (**8**) and -thiazoline (**9**, **12**, and **13**) derivatives.

Keywords: Carbohydrates; Thiazolidines; Thiazolines; Spiro compounds

1. Introduction

Glycosylidene-spiro-heterocycles have been the subject of increased attention during recent years following the discovery of (+)-hydantocidin **1**, a natural product with a unique spironucleoside structure and possessing potent herbicidal and plant growth regulatory activity [1,2]. Ensuing synthetic efforts were directed towards constructing analogous structures in order to test structure–activity relationships. Structural modifications introduced into either one of the 5-membered spiroanellated rings have generally resulted in a decrease in or even loss of herbicidal activity [3,4]. Of special interest are, however, those derivatives which contain a

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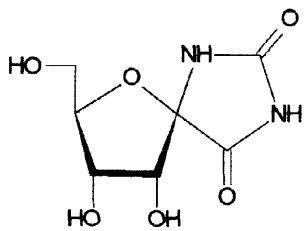
heterocycle spiroanellated to a *pyranose* rather than to a furanose ring. Their importance derives from the discovery that some representatives of this class of compounds are endowed with potent inhibitory activity toward glycosidases. Specifically, the D-glucopyranosylidene-spiro-hydantoin analogue (**2**) of hydantocidin was shown to be the most efficient inhibitor of muscle glycogen phosphorylase *b* known to date [5]. We have recently demonstrated that the thio-analogue **3** is also a potent inhibitor of glycogen phosphorylases *b* and *a* not only from muscle but of liver origin as well [6]. Some glucopyranosylidene-spiro-oxathiazoles, on the other hand, were found to be competitive inhibitors of sweet almond β-glucosidase [7].



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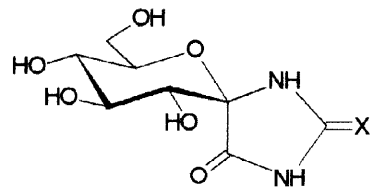


2 X = O
3 X = S

In view of obtaining and testing novel structures with potential glycosidase inhibitory activity [6,8,9] we have set out to investigate the preparation and reactivity of novel pyranose derivatives, bearing an SCN or NCS substituent at the quaternary anomeric centre, which can be expected to be suitable precursors for the construction of anomerically spiroanellated heterocycles (Figure 1).

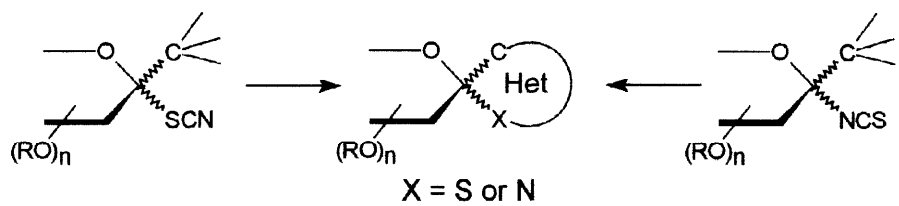


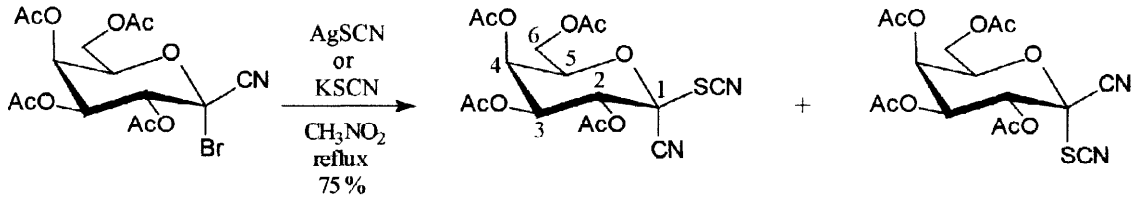
Figure 1

While glycosyl isothiocyanate derivatives are widely used as versatile intermediates for the synthesis of *N*-glycosylthiocarbamic acid derivatives [10,11], glycosylamino heterocycles [10,12], nucleoside analogues [13] or *N*-glycopeptides [14,15], sugar thiocyanates have found less frequent synthetic applications to date [16,17].

2. Results and discussion

1,1-Disubstituted glycosyl derivatives such as **4** [18] (Scheme 1) represent useful starting materials for the elaboration of heterocycles spiroanellated to the pyranoid ring [19,20]. With the aim of obtaining further derivatives suitable for heterocyclic ring closure we have studied the reactions of **4** with thiocyanate ions. Nucleophilic substitution of glycosyl halogenides with potassium thiocyanate yields glycosyl thiocyanates while with silver thiocyanate glycosyl isothiocyanates are formed [21] although exceptions to this rule [22] are also known.

Treatment of **4** with silver thiocyanate or potassium thiocyanate in nitromethane, acetone or acetonitrile solutions at reflux temperatures resulted in the formation of a mixture of two epimeric thiocyanates **5a** and **5b** (combined yield of 75%) which were separated by column chromatography. An equilibration experiment in nitromethane at 80 °C (bath temperature) in the presence of 2 equivalents of KSCN gave **5a** and **5b** in a 4 : 6 ratio indicating that **5a** is the kinetic product and **5b** is the thermodynamically more stable anomer. Formation of the corresponding isothiocyanates could not be observed under the conditions used. This may suggest that glycosylium ions are not formed in this reaction even in the presence of silver ions; this is in accordance with recent observations on reactions of compounds of type **4** with silver salts [8]. While **5a** can be formed by an S_N2 type substitution, formation of **5b** with retained configuration is less clearcut; mechanistic studies to explore this point are in progress.



4 **5a** **5b**

Scheme 1

Organic thiocyanates can be rearranged to the corresponding isothiocyanates by thermal isomerization [21,23].Compounds **5a** and **5b** however proved to be surprisingly stable even after prolonged (18 hours) heating at 130-140 °C in the melt, whereby only minor decomposition could be detected by TLC.

Both compounds display IR absorption bands (ν_{SCN}~2160-2170 cm^{-1}) and ^{13}C NMR chemical shift values (δ_C~105 ppm) characteristic for alkyl thiocyanates [16,24]. The anomeric configurations of the products were established from the values of $^3J_{CN,H\text{-}2}$ coupling constants [25] (see below). Single crystal X-ray study provided further confirmation of the structure of compound **5a** (Figure 2).

To the best of our knowledge there is no data in the literature on stereoelectronic effects involving thiocyanate groups. The X-ray structure of **5a** clearly shows a *gauche* arrangement of the ring oxygen and the SCN group along the C1-S bond (the corresponding dihedral angle, O1-C1-S1-C14 according to crystallographic numbering, is –72.2°). This may indicate operation of an *exo*-anomeric effect [26], facilitated by overlap of the n_S–$\sigma^*_{O1\text{-}C1}$ orbitals, in this structure.

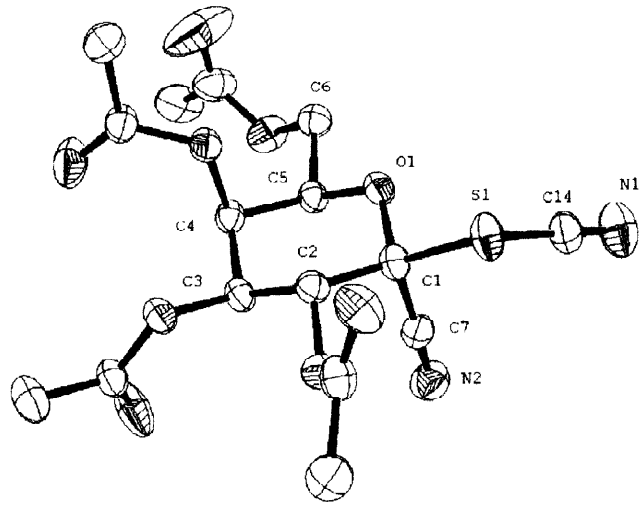
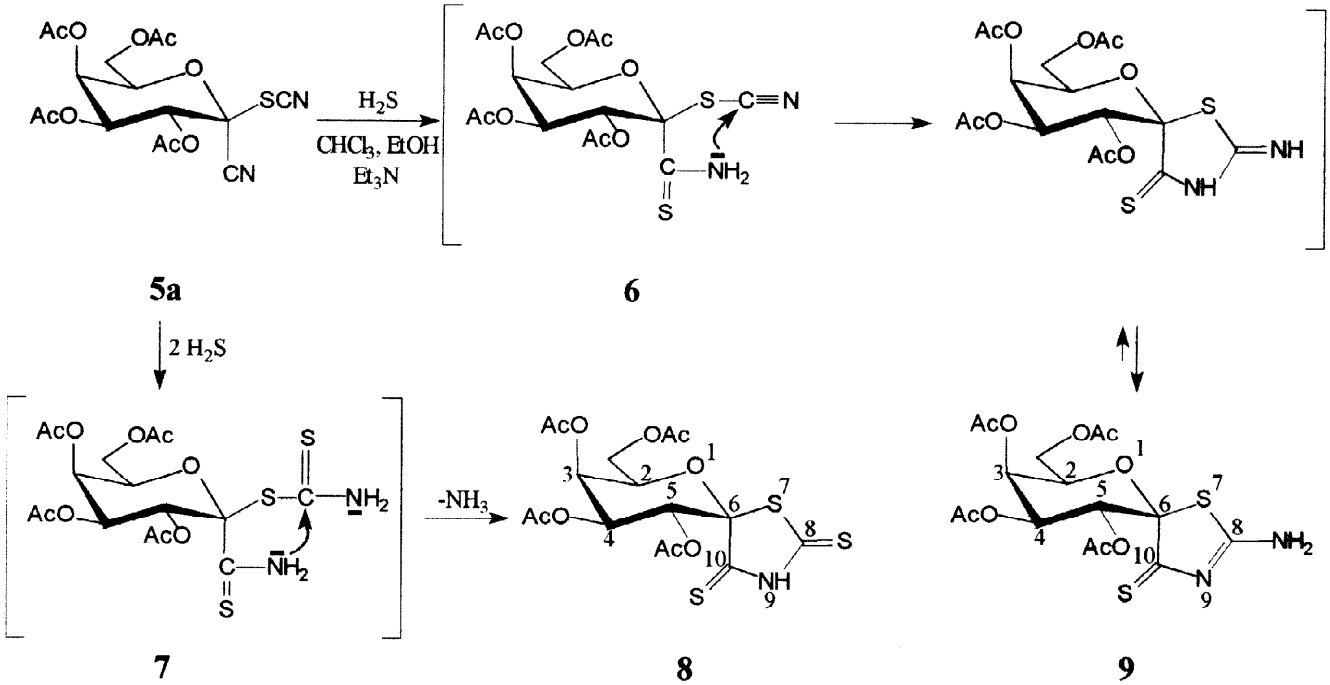


Figure 2

The reactivities of both functional groups attached to the anomeric carbon in **5a,b** make these compounds attractive targets for further transformations. We chose to study the addition reactions with hydrogen sulfide which can, in principle, occur either on the thiocyanato or the cyano groups or both [27]. Reaction of **5a** with hydrogen sulfide in ethanol/chloroform solution in the presence of triethylamine led to the formation of two major products **8** (58 %) and **9** (12 %) (Scheme 2). The formation of these compounds can be understood by assuming addition of one versus two moles of hydrogen sulfide to **5a** in the first step followed by subsequent cyclisation of the thioamide (**6**) and dithiocarbamic ester (**7**) intermediates in the second step.

When **5b** was allowed to react with hydrogen sulfide under similar conditions two products, **12** (46 %) and **13** (9 %), were isolated (Scheme 3); both proved to be isomeric aminothiazoline derivatives. The formation of these compounds requires addition of one equivalent of hydrogen sulfide to either the thiocyanato or the cyano group to give intermediates **10** and **11**, respectively. The cyclisations can be rationalized by nucleophilic attack of the dithiocarbamate/thioamide nitrogen to the positively polarized carbon atom of the CN or SCN moities to furnish **12** and **13**, respectively, after tautomerization of the primary cyclic products. In contrast to the reaction of **5a**, formation of a thiazolidine-dithione (cf. **8**) could not, however, be detected in measurable amounts in these reactions.



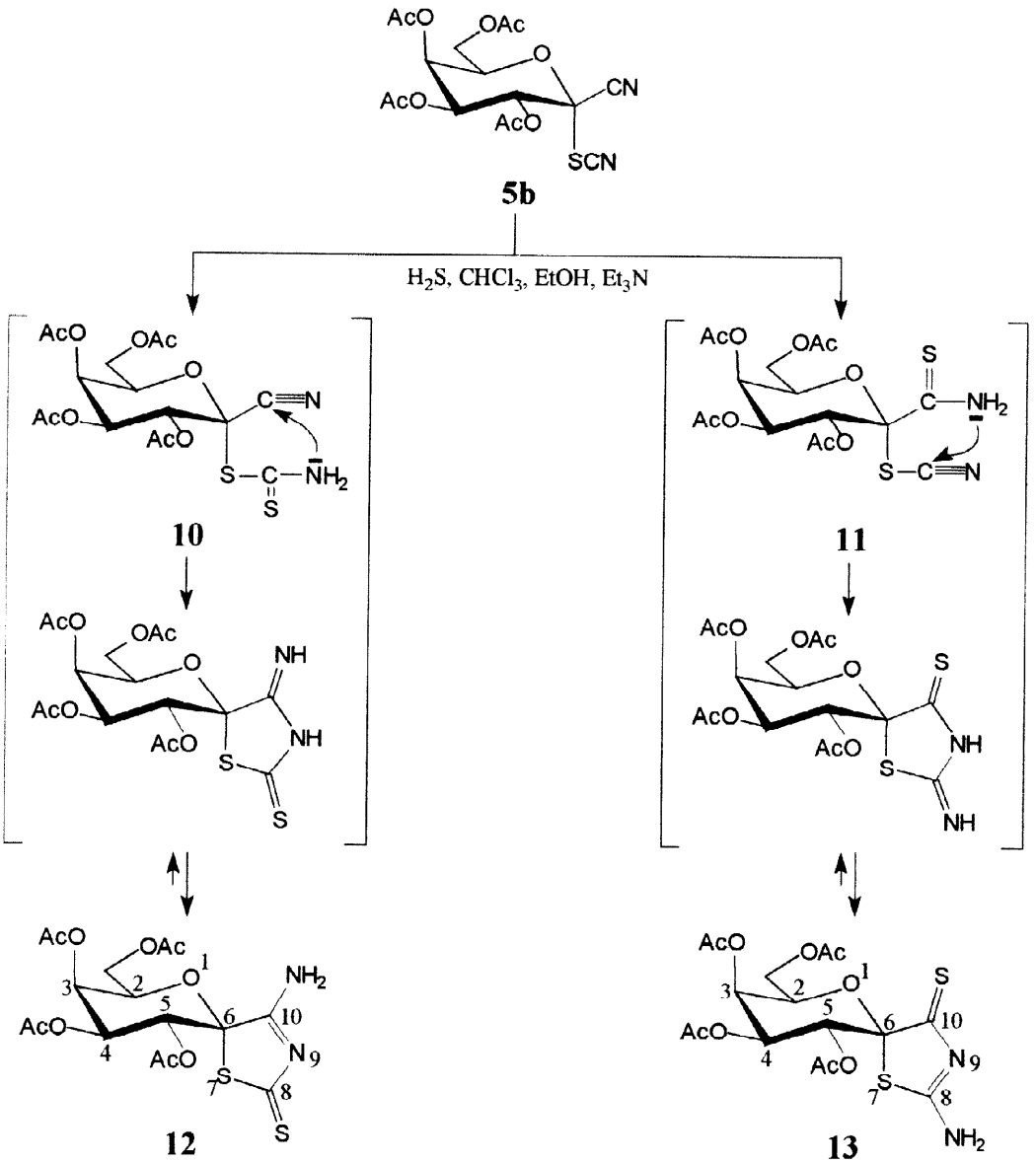
Scheme 2

Table 1
Selected ^{13}C and ^{15}N chemical shifts [ppm]

Compound	δ_{CN} [a]	δ_{SCN} [a]	$\delta_{C\text{-}1}$ [a]	$\delta_{C\text{-}6}$ [a]	$\delta_{C\text{-}8}$ [a]	$\delta_{C\text{-}10}$ [a]	δ_{NH2} [b]	$\delta_{N\text{-}9}$ [b]
5a	111.4	104.9	82.9	-	-	-	-	-
5b	113.6	104.8	84.8	-	-	-	-	-
8	-	-	-	99.6	196.5	201.2	-	210.3[a]
9	-	-	-	105.9	179.8	216.4	119.6	270.7
12	-	-	-	104.3	211.3	178.4	117.2	264.6
13	-	-	-	110.9	180.8	215.4	118.6	266.1

Measured in [a]$CDCl_3$ solution; [b]DMSO-d_6 solution.

The structures of the new heterocyclic derivatives have been unequivocally established by NMR spectroscopy. ^{13}C NMR spectra indicated the presence of one (in **9**, **12** and **13**) versus two (in **8**) thiocarbonyl groups at characteristic chemical shifts around or above 200 ppm (Table 1). Coupled $^{15}N/^{1}H$ HSQC versus HMBC spectra were instrumental (Table 2) in assessing the number and the nature of nitrogen atoms in these systems. In order to determine the hybridization states of the nitrogens in the spirobicyclic products we used phase sensitive gradient $^{15}N/^{1}H$ HSQC experiment with multiplicity editing [28]. The presence of one NH_2 group and one sp^2-hybridized tertiary nitrogen with characteristic chemical shift values [29] were unambiguously identified in **9**, **12** and **13**, whereas, a single downfield shifted secondary nitrogen was only detected in **8** [30] (Table 1).



Scheme 3

Table 2
Long-range $^{13}C/^{1}H$ and $^{15}N/^{1}H$ HMBC correlations

Compound	C-6	C-8	C-10	N-9
8	H-9	H-9	H-9	-
9	-		NH_{2a}	NH_{2a}
12	$NH_{2a,b}$	NH_{2a}	NH_{2a}	NH_{2a}
13	-		NH_{2a}	NH_{2a}

Table 3.
Three-bond $^{13}C/^{1}H$ couplings (Hz)

Compound	$^{3}J_{CN/H-2}$	$^{3}J_{C-10/H-5}$
5a	7.7	-
5b	3.5	-
8	-	6.7
9	-	5.2
12	-	~2
13	-	2.9

The presence of one NH_2 group and one sp^2-hybridized tertiary nitrogen with characteristic chemical shift values [29] were unambiguously identified in **9**, **12** and **13**, whereas, a single downfield shifted secondary nitrogen was only detected in **8** [30] (Table 1).

The connectivities in the heterorings were, on the other hand, determined in a straightforward way from long-range $^{13}C/^{1}H$ and $^{15}N/^{1}H$ HMBC correlations (Table 2). It should be noted that the crucial HMBC cross-peaks between C-6, C-8, C-10 and the NH proton in **8** could only be detected at low temperature (269 K) because of excessive line broadening of the respective ^{1}H NMR resonance (H-9) at room temperature.

Vicinal proton-proton coupling constants (see Experimental) were consistent with the $^{4}C_1$ conformation of the pyranose rings in the starting materials (**5a,b**) and all isolated products (**8**, **9**, **12** and **13**). Hence, the configurations of the anomeric carbons in **5a,b** and those of the spiro-carbons (C-6) in **8**, **9**, **12** and **13** could be defined as shown in the respective formulas by measuring the $^{3}J_{CH}$ values as shown in Table 3.

It is of note that δ-values for H-4*ax* and H-2*ax* are shifted downfield in the isomers in which the C=S carbon is in axial position (**8** and **9**) and the opposite holds for H-5 chemical shift in **13** where the position of C=S is equatorial; this is in complete accordance with the empirical chemical shift rule formulated by us previously for similar spirobicyclic compounds [19].

Several tautomeric forms are conceivable for the aminothiazolines **9**, **12** and **13**; NMR spectroscopic data (^{1}H, ^{13}C, ^{15}N) are, however, only compatible with the overwhelming predominance of the aminothiazolinethione structures indicated (Schemes 2 and 3). These forms are stabilized by the conjugation of the thiocarbonyl double bond with the endo double bond in the thiazoline ring.

3. Conclusion

Both anomers of acetylated 1-deoxy-1-thiocyanato-D-galactopyranosyl cyanides were prepared representing the first examples of glycosyl thiocyanates with a quaternary anomeric centre. Heterocyclization of these compounds was effected by reacting with hydrogen sulfide to give galactopyranosylidene-spiro-thiazoline and -thiazolidine derivatives. The structure of each new compound was unequivocally proven by NMR spectroscopy and X-ray crystallography. The operation of an *exo*-anomeric effect in **5a** represents, for the first time, a stereoelectronic effect involving the SCN group.

4. Experimental

Melting points were measured in open capillary tubes or on a Kofler hot-stage and are uncorrected. Optical rotations were determined with a Perkin-Elmer 241 polarimeter at room temperature. IR spectra were recorded with a Perkin-Elmer 16 PC FT-IR instrument. NMR spectra were recorded with Bruker WP 200 SY (200/50 MHz for $^{1}H/^{13}C$) or Avance DRX 500 (500/125/50 MHz for $^{1}H/^{13}C/^{15}N$) spectrometers. Chemical shifts are referenced to Me_4Si (^{1}H), to the residual solvent signals (^{13}C) or to NH_4Cl as external standard (^{15}N). The $^{13}C/^{1}H$ and $^{15}N/^{1}H$ correlations through one-bond as well as long-range couplings were obtained from sensitivity enhanced [31] gradient HSQC [32] and gradient HMBC [33] experiments, respectively. The HSQC and HMBC experiments have been carried out at 500 MHz (^{1}H). Typical time domain data matrices for the heterocorrelated measurements were of 2K × 512 data points in size. Fast-atom bombardment (FAB) mass spectra were obtained using a VG-7070MS mass spectrometer. TLC was performed on DC-Alurolle, Kieselgel 60 F_{254} (Merck), and the spots were visualised by gentle heating. For column chromatography Kieselgel 60 (Merck, particle size 0.063-0.200 mm) was used. Organic solutions were dried over anhydrous $MgSO_4$ and concentrated in vacuo at 40-50 °C (bath temperature). Nitromethane was distilled from P_4O_{10} directly in the reaction flask. Other solvents were of commercial analytical grade quality and have been used without further purification. H_2S was obtained by reacting ferrous sulphide with 6M hydrochloric acid in a Kipp apparatus and the gas was transferred through towers filled with glass wool and calcium chloride granulates before being bubbled into the reaction mixtures. AgSCN was prepared as described in [34] and dried in a vacuum dessiccator over P_4O_{10}.

Preparation of 2,3,4,6-tetra-*O*-acetyl-1-deoxy-1-thiocyanato-D-galactopyranosyl cyanides 5a,b: To a solution of **4** [10] (1 g, 2.28 mmol) in 25 ml dry CH_3NO_2 were added molecular sieves (4 Å) and either dry KSCN (2 equivalents) or freshly prepared dry AgSCN (4 equivalents). The reaction mixtures were stirred and heated with an oil bath at 100 °C until the starting material disappeared (TLC, 3-5 h for KSCN or ~26 h for AgSCN). After filtration the solvent was evaporated and the residue separated by column chromatography using ethyl acetate–hexane (1:2) as eluent. The two anomers **5a** and **5b** were obtained in a ~6:4 ratio and the total isolated yield was 0.69g (75%). Both anomers were separately recrystallised from ethanol.
5a: colourless crystals; mp 124-126 °C; $[\alpha]_D$ +89 (c 1.53, $CHCl_3$); ν_{SCN}=2172 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 5.54 (1H, dd, *J*=3.2, <1 Hz, H-4), 5.43 (1H, d, *J*=10.3 Hz, H-2), 5.26 (1H, dd, *J*=10.3, 3.2 Hz, H-3), 4.45 (1H, ddd, *J*=6.7, 6.0, <1 Hz, H-5), 4.27-4.16 (2H, two d, *J*=11.6 Hz, H-6,6'); ^{13}C-NMR ($CDCl_3$): δ 111.4 (CN, $^{3}J_{H\text{-}2,CN}$=7.7 Hz), 104.9 (SCN), 82.9 (C-1), 75.5, 69.3, 67.8, 66.0 (C-2 to C-5), 60.4 (C-6). Anal. found: C, 46.67; H, 4.48; N, 6.70; S, 7.79. Calcd. for $C_{16}H_{18}N_2O_9S$ (414.39): C, 46.38; H, 4.38; N, 6.76; S, 7.74.

5b: colorless small needles: mp 101-102 °C; $[\alpha]_D$ +226 (c 1.05, $CHCl_3$); ν_{SCN}=2164 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 5.88 (1H, d, *J*=10.3 Hz, H-2), 5.56 (1H, dd, *J*=3.2, 1.1 Hz, H-4), 5.16 (1H, dd, *J*=10.3, 3.2 Hz, H-3), 4.54 (1H, ddd, *J*=7.7, 4.7, 1.1 Hz, H-5), 4.31 (1H, dd, *J*=11.9, 4.7 Hz, H-6), 4.19 (1H, dd, *J*=11.9, 7.7 Hz, H-6'); ^{13}C-NMR ($CDCl_3$): δ 113.6 (CN, $^3J_{H\text{-}2,CN}$=3.5 Hz), 104.8 (SCN), 84.8 (C-1), 72.5, 67.8, 67.5, 66.1 (C-2 to C-5), 60.6 (C-6). Anal. found: C, 46.70; H, 4.49; N, 6.81; S, 7.85. Calcd. for $C_{16}H_{18}N_2O_9S$ (414.39): C, 46.38; H, 4.38; N, 6.76; S, 7.74.

Addition of hydrogen sulfide to 5a: 0.1 g (~ 0.24 mmol) of **5a** was dissolved in 2 ml $CHCl_3$ and 4 ml EtOH was added. H_2S was bubbled through the reaction mixture to saturation at room temperature (45-50 min). Et_3N was then added (the ratio of **5a**/Et_3N was 12:13) and the introduction of H_2S continued for another 45 min. The solvents were evaporated and the residue was separated by column chromatography using ethyl acetate–hexane (1:1) as eluent.

(2*R*,3*S*,4*S*,5*R*,6*R*)-3,4,5-triacetoxy-2-acetoxymethyl-1-oxa-7-thia-9-aza-spiro[4,5]decane-8,10-dithione 8: Isolated yield: 65 mg (58%); orange-yellow syrup; $[\alpha]_D$ -87 (c 1.42, $CHCl_3$); ^{1}H-NMR ($CDCl_3$): δ 10.36 (1H, bs, NH), 6.29 (1H, dd, *J*=10.6, 3.3 Hz, H-4), 5.73 (1H, d, *J*=10.6 Hz, H-5), 5.57 (1H, dd, *J*=3.3, 1.4 Hz, H-3), 5.43 (1H, ddd, *J*=6.6, 6.4, 1.4 Hz, H-2), 4.16 (1H, dd, *J*=11.3, 6.6 Hz, CH_2), 4.10 (1H, dd, *J*=11.3, 6.4 Hz, CH_2); ^{13}C-NMR ($CDCl_3$): δ 201.2 (C-10, $^3J_{H\text{-}5,C\text{-}10}$=6.7 Hz), 196.5 (C-8), 99.6 (C-6), 71.1 (C-2), 67.9 (C-5), 67.3 (C-4), 67.2 (C-3), 61.4 (CH_2); ^{15}N-NMR ($CDCl_3$): δ 210.3 (N-9). High resolution MS: Calcd. for $C_{16}H_{19}NO_9S_3$ $[M+H]^+$ 466.0300. Found 466.0304, Δ (mmu) 0.14.

(2*R*,3*S*,4*S*,5*R*,6*R*)-3,4,5-triacetoxy-2-acetoxymethyl-8-amino-1-oxa-7-thia-9-aza-spiro[4,5]dec-8-ene-10-thione 9: Isolated yield: 13 mg (12%); brownish–orange amorphous powder; $[\alpha]_D$ +118 (c 0.44, $CHCl_3$); ^{1}H-NMR (DMSO-d_6): δ10.06 (1H, bs, NH_2), 9.86 (1H, bs, NH_2), 6.54 (1H, dd, *J*=10.6, 3.4 Hz, H-4), 5.79 (1H, ddd, *J*=6.8, 5.6, 1.3 Hz, H-2), 5.71 (1H, d, *J*=10.6 Hz, H-5), 5.46 (1H, dd, *J*=3.4, 1.3 Hz, H-3), 4.07 (1H, dd, *J*=11.4, 5.6 Hz, CH_2), 3.98 (1H, dd, *J*=11.4, 6.8 Hz, CH_2); ^{13}C-NMR ($CDCl_3$): δ 216.4 (C-10, $^3J_{H\text{-}5,C\text{-}10}$=5.2 Hz), 179.8 (C-8), 105.9 (C-6), 70.0, 67.5, 67.5, 67.3 (C-2 to C-5), 61.7 (CH_2); ^{15}N-NMR (DMSO-d_6): δ 119.6 (NH_2), 270.7 (N-9). High resolution MS: Calcd. for $C_{16}H_{20}N_2O_9S_2$ $[M+H]^+$ 449.0689. Found 449.0689, Δ (mmu) 0.13.

Addition of hydrogen sulfide to 5b: 0.1 g (~0.24 mmol) of **5b** was dissolved in 2 ml $CHCl_3$ and 4 ml EtOH was added. H_2S was bubbled through the reaction mixture to saturation at room temperature (30-35 min). Et_3N was then added (the ratio of **5b**/Et_3N was 1:1) and the introduction of H_2S continued for another 30 min. The solvents were evaporated and the residue was separated by column chromatography using ethyl acetate–hexane (2:1) as eluent.

(2*R*,3*S*,4*S*,5*R*,6*R*)-3,4,5-triacetoxy-2-acetoxymethyl-10-amino-1-oxa-7-thia-9-aza-spiro[4,5]dec-9-ene-8-thione 12: Isolated yield: 50 mg (46%); pale yellow amorphous powder; $[\alpha]_D$ +103 (c 1.06, $CHCl_3$); ^{1}H-NMR (DMSO-d_6): δ 10.01 (1H, bs, NH_2), 9.75 (1H, bs, NH_2), 5.67 (1H, d, *J*=10.5 Hz, H-5), 5.37 (1H, dd, *J*=3.5, 1.2 Hz, H-3), 5.07 (1H, dd, *J*=10.5, 3.5 Hz, H-4), 4.28 (1H, ddd, *J*=7.0, 5.1, 1.2 Hz, H-2), 4.10 (1H, dd, *J*=11.6, 5.1 Hz, CH_2), 4.06 (1H, dd, *J*=11.6, 7.0 Hz, CH_2); ^{13}C-NMR ($CDCl_3$): δ 211.3 (C-8), 178.4 (C-10, $^3J_{H\text{-}5,C\text{-}10}$~2 Hz), 104.3 (C-6), 76.3 (C-2), 70.1 (C-4), 68.1 (C-5), 67.0 (C-3), 61.0 (CH_2); ^{15}N-NMR (DMSO-d_6): δ 117.2 (NH_2), 264.6 (N-9). High resolution MS: Calcd. for $C_{16}H_{20}N_2O_9S_2$ $[M+H]^+$ 449.0689. Found 449.0689, Δ (mmu) 0.11.

(2*R*,3*S*,4*S*,5*R*,6*S*)-3,4,5-triacetoxy-2-acetoxymethyl-8-amino-1-oxa-7-thia-9-aza-spiro[4,5]dec-9-ene-10-thione 13: Isolated yield: ~10 mg (9%); yellow syrup; ^{1}H-NMR (DMSO-d_6): δ 9.94 (1H, bs, NH_2), 9.87 (1H, bs, NH_2), 5.93 (1H, d, *J*=10.7 Hz, H-5), 5.41 (1H, dd, *J*=3.5, ~1 Hz, H-3), 5.15 (1H, dd, *J*=10.7, 3.5 Hz, H-4), 4.38 (1H, ddd, *J*=6.8, 5.4, ~1 Hz, H-2), 4.15-3.96 (2H, m, CH_2); ^{13}C-NMR ($CDCl_3$): δ 215.4 (C-10, $^3J_{H\text{-}5,C\text{-}10}$=2.9 Hz), 180.8 (C-8), 110.9 (C-6), 75.5, 71.6, 69.6, 66.9 (C-2 to C-5), 61.2 (CH_2); ^{15}N-NMR (DMSO-d_6): δ 118.6 (NH_2), 266.1 (N-9). High resolution MS: Calcd. for $C_{16}H_{20}N_2O_9S_2$ $[M+H]^+$ 449.0689. Found 449.0689, Δ (mmu) 0.06.

X-Ray crystallography of 5a: Colourless block crystals (0.35 x 0.2 x 0.15 mm) of $C_{16}H_{18}N_2O_9S$, grown from ethanol, M=414.38, monoclinic, a = 9.288(2) Å, b = 7.654(1) Å, c = 14.478(1) Å, β = 101.39°, V = 1009 Å^3, Z = 2, space group: P21, ρcalc= 1.364 g.cm^{-3}. Data were collected at 293(1) K, Enraf Nonius MACH3 diffractometer, Mo Kα radiation λ = 0.71073 Å, ω-2θ motion, θ_{max} = 25°, 1905 reflections of which 1763 were unique with I > 2σ(I), decay: 2%. The structure was solved using the SIR-92 software [35] and refined on F^2 using SHELX-97 [36] program, publication material was prepared with the WINGX-97 suite [37] , R(F) = 0.0349 and wR(F2) = 0.0989 for 1905 reflections, 269 parameters, Flack-parameter [38] : 0.1(1).

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6. References

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