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Note

The synthesis and structure of the derivatives of 2-deoxy-2-hydroxyimino-D-*lyxo*-hexopyranosyl-L-cysteine and -thiophenol

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Abstract

3,4,6-Tri-*O*-acetyl-2-deoxy-2-hydroxyimino-β and -α-D-*lyxo*-hexopyranosides of thiophenol (**3**, **4**) and the methyl ester of *N*-benzoyl-L-cysteine have been synthesised by condensation of 3,4,6-tri-*O*-acetyl-2-deoxy-2-nitroso-α-D-galactopyranosyl chloride with thiophenol and the L-cysteine derivative, respectively. The conformation of the sugar residue and configuration of the anomeric centre as well as of the hydroxyimino group were established on the basis of the ^{1}H NMR (DQF–COSY, ROESY, TOCSY) spectrometric techniques and polarimetric data. Additionally, the structure of *S*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(*Z*)-hydroxyimino-β-D-*lyxo*-hexopyranosyl]-thiophenol (**3**) was supported by X-ray diffraction data. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Thioglycosides; L-Cysteine and thiophenol derivatives; 2-Deoxy-2-hydroxyimino sugars; Conformation and configuration; X-ray diffraction

1. Introduction

Thioglycopeptides, which are rather rarely found in nature, are conjugates of L-cysteine and D-glucose or D-galactose [1,2]. There is a relatively small number of literature reports concerned with the synthesis of these thioglycosides [3–7], despite the fact that they may play an important role in pharmacology because replacement of the anomeric oxygen of *O*-glycopeptides by sulfur will change the properties of the peptide–carbohydrate linkage [8]. On the other hand, *S*-alkyl and *S*-aryl glycosides are known as efficient donors of glycosyls for glycosidation reactions [9]. The phenylthioglycosides were successfully used both as donors and acceptors of glycosyls in a block synthesis of oligosaccharides [10].

Previously we have reported the synthesis of some thioglycosides of L-cysteine and thiophenol with the 2-deoxy-2-hydroxyimino-D-*arabino* structure of the sugar residue [11], which resulted in a variety of derivatives obtained by chemical modification at C-2 and C-3. In the present paper the same route was followed to prepare thioglycosides of L-cysteine and thiophenol with the 2-deoxy-2-hydroxyimino-D-*lyxo* structure.

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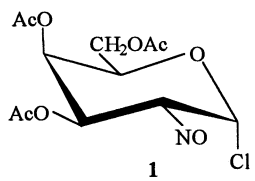
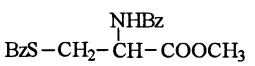
2. Results and discussion

The methyl ester of *N*,*S*-dibenzoyl-L-cysteine (**2**) was methanolyzed just before reaction with chloride **1**. Under these conditions only the benzoyl protection from the sulfur atom was removed [12]. The reaction of 3,4,6-tri-*O*-acetyl-2-deoxy-2-nitroso-α-D-galactopyranosyl chloride (**1**) with thiophenol gave *S*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(*Z*)-hydroxyimino-β- (**3**) and α-D-*lyxo*-hexopyranosyl]-thiophenol (**4**). Further, the reaction of **1** with *N*-benzoyl-L-cysteine methyl ester afforded the methyl ester of *N*-benzoyl-*S*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-hydroxyimino-α- (**5**) and -2-deoxy-2-(*Z*)-hydroxyimino-β-D-*lyxo*-hexopyranosyl]-L-cysteine (**6**). The glycosidation reaction was not stereospecific, affording both the α and β anomers (α:β ~ 2:1) with prevailing *Z* configuration of the hydroxyimino group. Oxime **5** had a *Z* configuration in chloroform and *E* in dimethyl sulfoxide.



1



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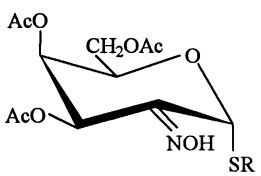
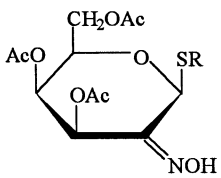


4, 5



3, 6

3, 4 R = Ph
5, 6 R = –CH2–CH–COOCH3
NHBz

The 2-hydroxyimino structure of compounds **3**–**6** was established on the basis of the ^{1}H NMR spectra, namely by the structure of the H-1 (s) and H-3 (d) signals, by intensity of the methyl signals corresponding to three *O*-acetyl groups, and by the presence of a hydroxyl proton signal (s) at low fields ($\delta \sim 10$–12). Further, the IR spectra of these compounds exhibited bands due to the OH (~ 3200 cm^{-1}) and C=N (~ 1650 cm^{-1}) vibrations.

The α configuration of the anomeric carbon atom was assigned for **4** and **5**, and the β configuration for **3** and **6**. These findings are supported by the $[\alpha]_D$ values, which are much lower for β anomers, and by analysis of ^{1}H NMR spectra. Thus, the H-1 signal of **4** and **5** (6.60 and 6.52, respectively) appears at higher δ values than that of the analogous proton of **3** and **6** (6.21 and 6.07, respectively) owing to the respective equatorial and axial orientation of H-1. The β configuration of **3** and **6** was also demonstrated by the investigation of the NOE effect in the ROESY 1D experiment, where irradiation of the H-1 proton caused the inversion of the H-5, H-4, H-3, and OH signals (Fig. 1), as expected for β anomers of this kind.

Bearing in mind previous conclusions concerning the influence of the 2-hydroxyimino group on the position of signals of adjacent protons [11,13], chemical shifts of H-1 and H-3 in **3** (δ 6.21 and 5.80, respectively), **4** (δ 6.60 and 5.72, respectively), $\mathbf{5}_Z$ (δ 6.52 and 5.72, respectively), $\mathbf{5}_E$ (δ 5.94 and 5.85, respectively) and **6** (6.07 and 5.80, respectively), as well as the ROESY 1D experiments for **3**–**6**, it has been established that the 2-hydroxyimino group has *Z* orientation in **3**, **4**, $\mathbf{5}_Z$ and **6** and *E* orientation in $\mathbf{5}_E$.

Whilst recording the ^{1}H NMR spectra in chloroform, compound **5** with *E* configuration of the hydroxyimino group underwent transformation to isomer *Z*. This transformation ($\mathbf{5}_E \rightarrow \mathbf{5}_Z$) did not take place in dimethyl sulfoxide. As we previously reported [11], the $\mathbf{5}_E \rightarrow \mathbf{5}_Z$ transformation is likely to be due to protonation of the nitrogen atom of the oxime group, which took place in chloroform. Since the reverse transformation ($\mathbf{5}_Z \rightarrow \mathbf{5}_E$) did not occur either in chloroform nor in dimethyl sulfoxide, we assumed that isomer $\mathbf{5}_Z$ is thermodynamically more stable than $\mathbf{5}_E$.

Although the absence of the two useful $J_{1,2}$ and $J_{2,3}$ proton coupling constants, as well as D-*lyxo* structure of **3**–**6**, prevent accurate conformational deduction from ^{1}H NMR data, we propose that (*Z*)-α-D-*lyxo* compounds (**4** and $\mathbf{5}_Z$) with $J_{3,4}$ 3.42 and

$J_{4,5} \sim 0$ Hz have $^4C_1$ conformation and (*E*)-α-D-*lyxo* ($\mathbf{5}_E$) with $J_{3,4}$ 3.91 and $J_{4,5}$ 1.46 Hz somewhat flattened $^4C_1$ chair form. The coupling constant $J_{4,5} \sim 1$ Hz in the case of D-galactosides is in agreement with $^4C_1$ conformation [14]. Deformation of the $^4C_1$ chair form in $\mathbf{5}_E$ is due to the unfavourable approach of the OH of oxime group at C-2 and the acetyl group at C-3. The examination of key coupling constants of **3** ($J_{3,4}$ 4.39, $J_{4,5}$ 4.88 Hz) and **6** ($J_{3,4}$ 3.42, $J_{4,5}$ 5.86 Hz), both β anomers with *Z* configuration of the hydroxyimino group, calls for a conformation other than $^4C_1$. This last form should be destabilised owing to the strong electrostatic repulsion of the nearly coplanar oriented dipoles of the C_1–SPh, C_2=N–OH and C_3–OAc bonds (Fig. 2). These unfavourable interactions may cause the adoption of any conformation other than $^4C_1$ [15,16]. Taking into account our diffractometric data for **3** and the fact that there is a difference ~ 0.4 ppm in the chemical shifts of the H-1 signals of α and β anomers, indicative of respective equatorial and axial orientation of the H-1, we assumed the $^{3,O}B$ conformation for **3** and **6** in solution (Fig. 2). This is in agreement with the ROESY 1D experiments for **3** and **6**. Interactions between H-1 and H-5, H-4, H-3, respectively, demonstrated in Fig. 1, were the strongest for H-1 and H-5, while being the weakest for H-1 and H-3, which is just possible in a $^{3,O}B$ conformation.

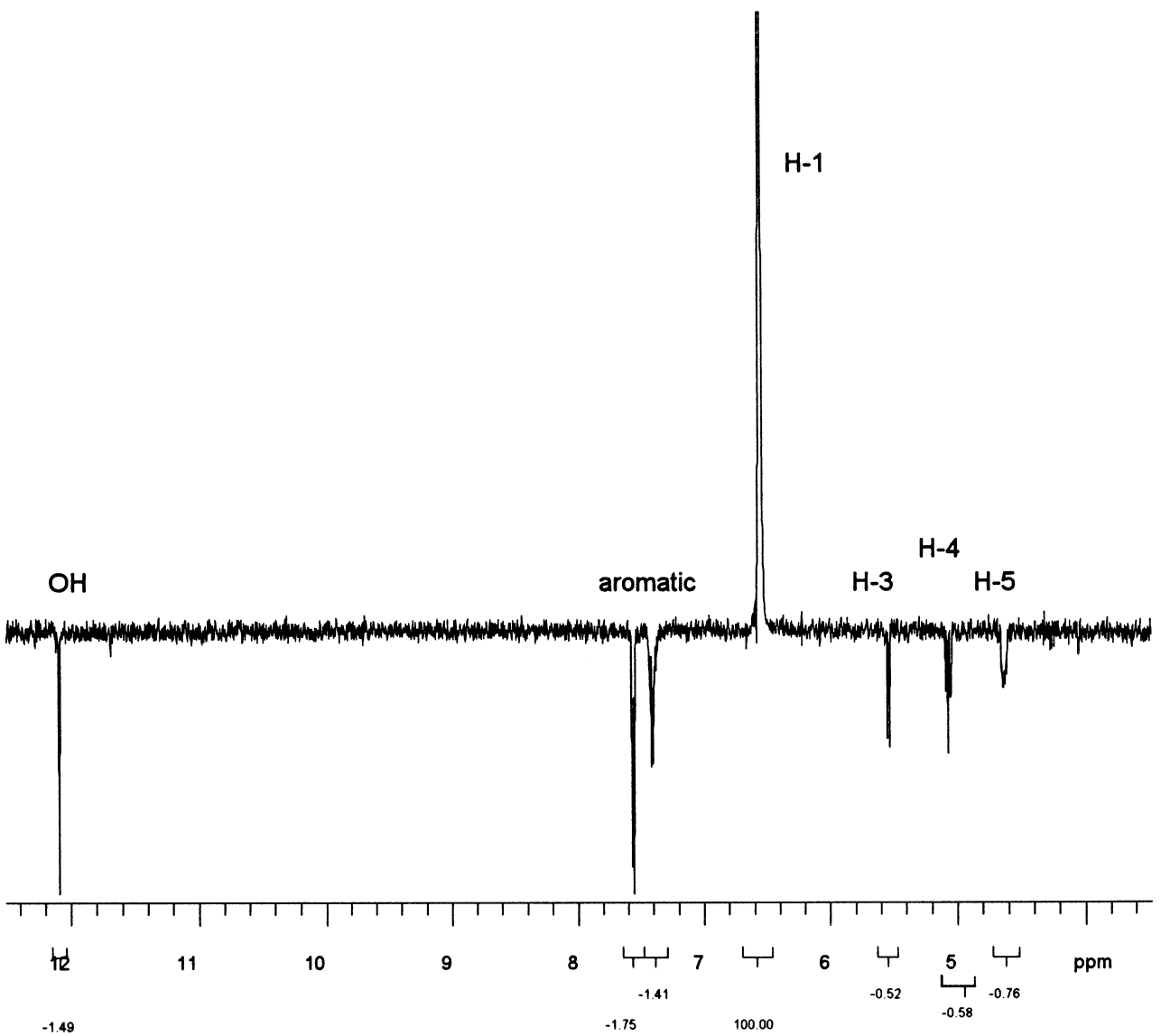


Fig. 1. ^{1}H NMR spectra of the ROESY 1D type of **3**.

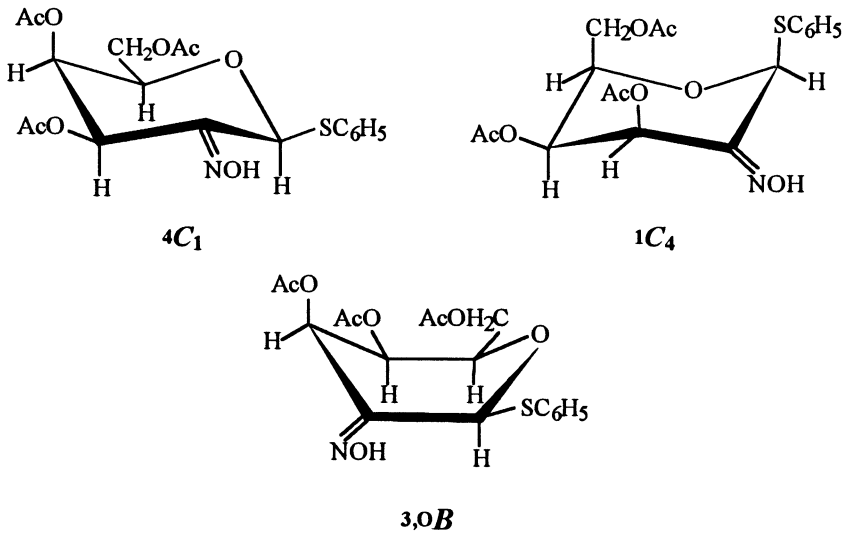


Fig. 2. Considered conformations for **3**.

Description of crystal structure.—In the crystal lattice, the compound shows two different conformations of the six-membered pyranose ring (Fig. 3). The first molecule adopts a $^{1}C_{4}$ chair conformation with three axial substituents (puckering parameters: $q = 0.486$ and $\phi = 68.82°$); the second molecule shows a flattened boat conformation $^{3,O}B$ with only one axial substituent (puckering parameters: $q = 0.687$ and $\phi = -11.6°$). Hydrogen-bonded molecules of the same conformation (O-2–H···O-8 $[x+1, y, z]$ and O-22–H···O-28 $[x-1, y-1, z]$) form layers of parallel lines perpendicular to the c axis with angles of 155.8 and 169.9° at the vertex hydrogen atoms, respectively. Crystallographic data, data collection and structure refinement are presented in Table 1. Non-hydrogen atom coordinates and equivalent isotropic temperature factors are presented in Table 2. Selected bond lengths, valence angles and torsion angles are given in Tables 3–5, respectively. The values of bond lengths and angles determined in this work agree well with the expected ones [17].

3. Experimental

General methods.—Melting points are uncorrected. Optical rotations were recorded using a Hilger–Watt polarimeter for solutions in $CHCl_3$. Thin-layer chromatography (TLC) was performed on E. Merck Kieselgel 60 F254 plates with: (A) 4:1:1 butanol–water–CH_3COOH; (B) 1:2 EtOAc–petroleum ether; (C) 2:3 EtOAc–petroleum ether; (D) 3:1

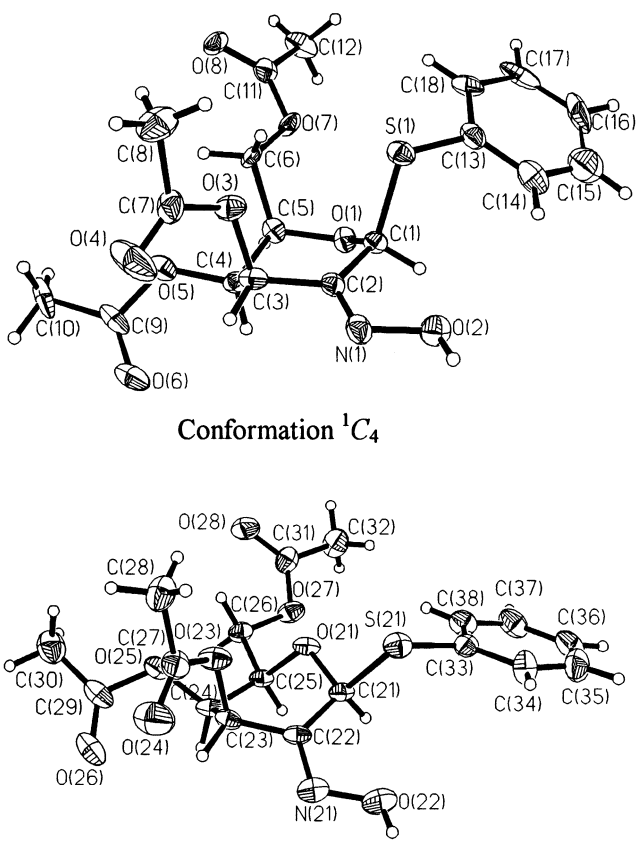


Fig. 3. Two independent molecules in the X-ray structure of **3**.

Table 1
Crystal data and summary of intensity and structure refinement

Compound	**3**
Colour/shape	colourless prisms
Empirical formula	$C_{18}H_{21}NO_8S$
Formula weight	411.42
$F(000)$	1296
Space group	$P3_2$
Cell constants	
a (Å)	10.786(2)
b (Å)	10.786(2)
c (Å)	30.559(6)
γ (°)	120
Cell volume (Å^3)	3078.9(10)
Formula units/unit cell	6
μ_{calc} (mm^{-1})	0.201
D_{calc} (g cm^{-3})	1.331
Crystal size (mm)	$0.3\times0.3\times0.6$
Diffractometer	Kuma KM4
Radiation	Mo K_α
Scan mode	$\theta/2\theta$
Scan width	$1.4+\mathrm{tg}\theta$
Standard reflections	331, 342, −224
Decay of standards	14%
Reflections collected	7264
Independent reflections	4579
Reflections observed ($F>2\sigma(I)$)	2197
2θ Range (°)	1.8–54
Ranges of h, k, l	$-13\rightarrow11$, $0\rightarrow13$, $0\rightarrow39$
No. of parameters varied	505
Function minimized	$\Sigma w(F_o^2-F_c^2)^2$
$w^{-1}=\sigma^2(F_o^2)+(axP)^2+bxP$ where $P=(\mathrm{Max}(F_o^2, 0)+2F_c^2)/3$	
a	0.0827
b	0.0000
Goodness-of-fit	1.000
R_1, wR_2 [$I>2\sigma(I)$]	0.0774, 0.1657
R_1, wR_2 (all reflections)	0.1593, 0.2057
$\Delta\rho_{max}$ (e Å^{-3})	0.32
$\Delta\rho_{min}$ (e Å^{-3})	−0.33

CCl_4–acetone; (E) 1:1 toluene–EtOAc. Column chromatography was performed on MN Kieselgel 60 (< 0.08 mm). The ^{1}H NMR spectra ($CDCl_3$ or Me_2SO, internal Me_4Si) were recorded with a Varian Unity Plus 500 (500 MHz) instrument. The IR spectra were recorded as Nujol mulls with a Bruker IFS 66 spectrophotometer. Field desorption mass spectra (FDMS) were recorded using a Varian Mat 711 mass spectrometer. Elemental analyses were conducted with a Carlo Erba EA1108 elemental analyser.

Table 2
Atomic coordinates ($\times10^4$) and equivalent isotropic displacement parameters (Å$^2\times10^3$) for **3** [a]

	x	y	z	U_{eq}
S-1	1912(3)	6464(3)	3208(1)	59(1)
N-1	5375(9)	8688(8)	3615(3)	62(2)
O-1	1872(6)	7009(6)	4094(2)	53(2)
O-2	5340(7)	7416(8)	3550(2)	70(2)
O-3	3384(7)	10036(7)	3388(2)	65(2)
O-4	4992(14)	12335(10)	3388(4)	163(6)
O-5	2869(6)	10757(6)	4238(2)	61(2)
O-6	5021(9)	12126(9)	4521(3)	92(2)
O-7	−723(6)	6902(6)	3930(2)	58(2)
O-8	−1910(6)	7892(7)	3632(2)	63(2)
C-1	2787(7)	7069(8)	3750(2)	44(2)
C-2	4135(9)	8494(9)	3703(3)	49(2)
C-3	4060(9)	9809(9)	3772(3)	54(2)
C-4	3159(8)	9585(8)	4179(3)	49(2)
C-5	1683(8)	8216(8)	4158(3)	50(2)
C-6	607(8)	8264(8)	3852(3)	48(2)
C-7	4009(13)	11358(11)	3225(4)	73(3)
C-8	3273(17)	11370(17)	2796(4)	105(5)
C-9	3887(12)	12003(10)	4422(3)	72(3)
C-10	3436(15)	13069(10)	4470(4)	100(4)
C-11	−1900(10)	6875(10)	3817(3)	61(3)
C-12	−3207(9)	5526(11)	3919(4)	79(3)
C-13	873(10)	4593(9)	3302(3)	64(3)
C-14	1592(13)	3851(12)	3367(4)	90(4)
C-15	790(2)	2390(17)	3453(6)	125(6)
C-16	−700(2)	1678(13)	3453(5)	131(7)
C-17	−1390(11)	2453(13)	3391(4)	97(5)
C-18	−601(9)	3912(10)	3313(3)	66(3)
S-21	2697(3)	7376(3)	1383(1)	69(1)
N-21	1921(10)	4660(9)	2093(3)	78(3)
O-21	4710(6)	8380(6)	1989(2)	55(2)
O-22	775(9)	4877(9)	2042(3)	101(3)
O-23	5225(8)	6092(7)	1715(2)	73(2)
O-24	4757(13)	3833(11)	1701(4)	130(4)
O-25	6857(7)	7364(7)	2404(2)	68(2)
O-26	6609(12)	5558(10)	2822(3)	106(3)
O-27	6357(7)	10836(7)	2448(3)	75(2)
O-28	8541(9)	12145(8)	2189(3)	90(2)
C-21	3248(9)	7266(8)	1943(3)	55(2)
C-22	3110(9)	5844(8)	2039(3)	55(2)
C-23	4440(9)	5835(8)	2131(3)	56(2)
C-24	5384(10)	6968(9)	2459(3)	61(3)
C-25	5263(9)	8291(8)	2417(3)	51(2)
C-26	6646(9)	9653(8)	2476(3)	60(2)
C-27	5320(13)	5005(13)	1550(3)	75(3)
C-28	6170(13)	5374(15)	1124(3)	90(4)
C-29	7375(14)	6593(12)	2611(4)	80(4)
C-30	8912(15)	7237(16)	2549(5)	104(4)
C-31	7425(12)	12069(11)	2314(4)	74(3)
C-32	7089(13)	13211(12)	2280(5)	97(4)
C-33	1883(10)	8437(10)	1460(3)	61(2)
C-34	503(13)	7899(14)	1304(4)	90(4)
C-35	−122(14)	8739(15)	1348(5)	109(5)
C-36	558(15)	10068(15)	1553(4)	95(4)
C-37	1937(14)	10596(12)	1696(4)	90(4)
C-38	2597(12)	9795(10)	1648(4)	74(3)

[a] U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

Table 3
Selected bond lengths (Å) for **3**

Conformation $^1C_4$		Conformation $^{3,O}B$	
S-1–C-1	1.856(8)	S-21–C-21	1.835(8)
N-1–C-2	1.276(10)	N-21–C-22	1.291(10)
N-1–O-2	1.368(9)	N-21–O-22	1.376(11)
O-1–C-1	1.421(9)	0-21–C-21	1.433(9)
O-1–C-5	1.428(9)	0-21–C-25	1.460(9)
O-3–C-3	1.465(9)	0-23–C-23	1.474(10)
O-5–C-4	1.457(10)	0-25–C-24	1.435(10)
C-1–C-2	1.504(10)	C-21–C-22	1.494(11)
C-2–C-3	1.475(11)	C-22–C-23	1.466(12)
C-3–C-4	1.523(11)	C-23–C-24	1.515(11)
C-4–C-5	1.539(10)	C-24–C-25	1.503(11)
C-5–C-6	1.512(10)	C-25–C-26	1.491(10)

Table 4
Selected valence angles (°) for **3**

Conformation $^1C_4$		Conformation $^{3,O}B$	
C-2–N-1–O-2	111.4(8)	C-22–N-21–O-22	110.5(9)
C-1–O-1–C-5	118.2(6)	C-21–O-21–C-25	110.4(6)
O-1–C-1–C-2	114.3(6)	O-21–C-21–C-22	110.1(7)
O-1–C-1–S-1	115.1(5)	O-21–C-21–S-21	107.1(5)
C-2–C-1–S-1	109.6(5)	C-22–C-21–S-21	112.4(6)
N-1–C-2–C-3	115.4(8)	N-21–C-22–C-23	117.4(8)
N-1–C-2–C-1	125.9(8)	N-21–C-22–C-21	125.5(9)
C-3–C-2–C-1	118.7(7)	C-23–C-22–C-21	116.7(7)
O-3–C-3–C-2	108.6(7)	O-23–C-23–C-22	107.9(7)
O-3–C-3–C-4	110.5(7)	O-23–C-23–C-24	107.9(7)
C-2–C-3–C-4	107.5(7)	C-22–C-23–C-24	112.7(7)
O-5–C-4–C-3	111.1(6)	O-25–C-24–C-23	111.1(7)
O-5–C-4–C-5	105.6(6)	O-25–C-24–C-25	108.4(7)
C-3–C-4–C-5	112.9(7)	C-23–C-24–C-25	111.5(7)
O-1–C-5–C-6	114.0(7)	O-21–C-25–C-26	106.6(6)
O-1–C-5–C-4	109.2(6)	O-21–C-25–C-24	111.8(6)
C-6–C-5–C-4	115.9(7)	C-26–C-25–C-24	114.0(7)

X-ray diffraction experiment.—X-ray measurements were carried out on a KUMA KM-4 four-circle diffractometer. The structures were solved by direct methods with the SHELXS program [18] and refined employing the full-matrix least-squares method implemented in the SHELXL program [19]. Anisotropic displacement coefficients were applied to all non-hydrogen atoms. All hydrogen atoms were refined in idealised positions with isotropic temperature factors 1.2 times the equivalent isotropic temperature factor of the adjacent C or O atom. The atomic scattering factors were taken from the International Tables for X-ray Crystallography (1993). Molecular illustrations were drawn using the ORTEP program [20].

*Dimeric 3,4,6-tri-*O*-acetyl-2-deoxy-2-nitroso-α-*D*-galactopyranosyl chloride* (**1**).—Prepared according to the literature procedure [21]; mp 128–130 °C, lit. 128–131 °C; $[\alpha]_D^{20}$ + 134° (*c* 0.5), lit. $[\alpha]_D^{23}$ + 128° (*c* 2.2).

N,S-*Dibenzoyl-*L*-cysteine methyl ester* (**2**).—To a mixture of L-cysteine (2 g, 16.5 mmol) and 1 M NaOH (50 mL, 50 mmol), cooled to 0 °C, benzoyl chloride (4 mL) was added with vigorous stirring, while the temperature of the mixture was kept between 0 and 5 °C. The mixture was stirred for 30 min at room temperature (rt). Neutralization of the aqueous solution (~ 0 °C) with 36% HCl caused *N,S*-dibenzoyl-L-cysteine to separate. The precipitate was filtered off, washed with cold water and dried. Recrystallisation from $CHCl_3$ afforded pure *N,S*-dibenzoyl-L-cysteine (50%); mp 173–175 °C; $[\alpha]_D^{20}$ − 131° (*c* 0.49); R_f 0.84 (solvent A) (the structure was confirmed by the ^{1}H NMR and IR data). Then a solution of *N,S*-dibenzoyl-L-cysteine (2.5 g, 7.6 mmol) in CH_3OH saturated with HCI (40 mL) was kept for 2 h in a refrigerator. The precipitate was filtered off, washed and dried to yield **2** (78%); mp 140–141 °C, lit. 140–141 °C [12]; $[\alpha]_D^{20}$ + 53° (*c* 0.48), lit. $[\alpha]_D^{25}$ + 55.5° (*c* 2) [12].

S-*[3,4,6-Tri-*O*-acetyl-2-deoxy-2-(Z)-hydroxyimino-β-* (**3**) *and* -α-D-lyxo-*hexopyranosyl]-thiophenol* (**4**).—A solution of **1** (0.675 g, 2 mmol) and thiophenol (0.41 mL, 4 mmol) in DMF (20 mL) was stirred for 3 h at ~ 20 °C until the starting chloride **1** disappeared (TLC, solvent B). Then the mixture was diluted with $CHCl_3$ (100 mL), washed with satd $NaHCO_3$ solution (5 × 15 mL), water (5 × 15 mL), and dried (Na_2SO_4). Concentration under diminished pressure gave a syrup, which was chromatographed (solvent C) to afford first **3** (17%); mp 150–152 °C ($CHCl_3$–*n*-heptane); $[\alpha]_D^{20}$ − 137° (*c* 0.48); R_f 0.37 (solvent C); IR: *ν* 3220 (OH), 1752 (ester CO), 1590 (C=N), 1226 (O–C) cm^{-1}; ^{1}H NMR (DMSO): *δ* 1.98, 2.09, 2.10 (3 s, 9 H, 3 AcO), 4.32 (dd, 1 H, $J_{5,6'}$ 4.89 Hz, H-6′), 4.40 (m, 1 H, $J_{5,6}$ 8.54 Hz, H-5), 4.70 (dd, 1 H, $J_{6,6'}$ 11.48 Hz, H-6), 5.38 (t, 1 H, $J_{4,5}$ 4.88 Hz, H-4), 5.80 (d, 1 H, $J_{3,4}$ 4.39 Hz, H-3), 6.21 (s,

1 H, H-1), 7.40, 7.55 (2 m, 5 H, aromatic), 12.13 (s, 1 H, OH); FDMS: m/z 411 (M^+). Anal. Calcd for $C_{18}H_{21}NO_8S$: C, 52.54; H, 5.15; N, 3.40; S, 7.79. Found: C, 52.32; H, 5.19; N, 3.42; S, 7.60.

Eluted second was **4** (39%, syrup); $[\alpha]_D^{20}$ + 146° (*c* 0.51); R_f 0.29 (solvent C); IR: *v* 3200 (OH), 1745 (ester CO), 1650 (C=N), 1230 (O–C) cm^{-1}; ^1H NMR (DMSO): δ 1.97, 2.03, 2.10 (3 s, 9 H, 3 AcO), 4.05 (d, 2 H, $J_{5,6}$ 6.35 Hz, 2 H-6), 4.85 (t, 1 H, H-5), 5.51 (d, 1 H, $J_{4,5} \sim 0$ Hz, H-4), 5.72 (d, 1 H, $J_{3,4}$ 3.42 Hz, H-3), 6.60 (s, 1 H, H-1), 7.40, 7.55 (2 m, 5 H, aromatic), 11.88 (s, 1 H, OH); FDMS: m/z 411 (M^+). Anal. Calcd for $C_{18}H_{21}NO_8S$: C, 52.54; H, 5.15; N, 3.40; S, 7.79. Found: C, 52. 14; H, 5.41; N, 3.04; S, 7.42.

N-*Benzoyl*-S-*[3,4,6-tri*-O-*acetyl-2-deoxy-2-hydroxyimino*-α- (**5**) *and* β-D-lyxo-*hexopyranosyl]*-L-*cysteine methyl ester* (**6**).—To a suspension of **2** (1.03 g, 3 mmol) in abs MeOH (24 mL), 0.5 M methanolic CH_3ONa (6 mL) was added in an atmosphere of hydrogen with stirring at ~20 °C [12]. The ester dissolved completely during 5 min, and then the mixture was neutralised with AcOH and concentrated. The crude residue was dissolved in DMF (10 mL) and added to the solution of **1** (0.545 g, 1.61 mmol) in DMF (10 mL). The resulting solution was stirred at ~20 °C until the starting chloride **1** disappeared (3 h, TLC, solvent D). Then the mixture was diluted with chloroform (100 mL), washed with satd $NaHCO_3$ solution (5 × 15 mL), water (5 × 15 mL), and dried (Na_2SO_4). Concentration under diminished pressure gave a syrup, which was chromatographed (solvent E) to yield first **5** (37%); mp 152–154 °C ($CHCl_3$–*n*-heptane); $[\alpha]_D^{20}$ + 98° (*c* 0.46); R_f 0.32 (solvent E); IR 3350 (OH), 1747 (ester CO), 1650 (amide I), 1536 (amide II), 1225 (O–C) cm^{-1}; ^1H NMR: $\mathbf{5}_Z$ ($CDCl_3$): δ 1.96, 2.10, 2.17 (3 s, 9 H, 3 AcO), 3.34, 3.51 (2 dd, 2 H, Cys–H_β), 3.84 (s, 3 H, CO_2Me), 4.06 (dd, 1 H, $J_{6,6'}$ 11.23 Hz, H-6), 4.23 (dd, 1 H, $J_{5,6'}$ 5.37 Hz, H-6′), 4.68 (t, 1 H, $J_{5,6}$ 7.33 Hz, H-5), 5.33 (m, 1 H, Cys–H_α), 5.51 (d, 1 H, $J_{4,5} \sim 0$ Hz, H-4), 5.72 (d, 1 H, $J_{3,4}$ 3.42 Hz, H-3), 6.52 (s, 1 H, H-1), 7.88 (d, 1H, $J_{NH,\ CH}$ 7.57 Hz, Cys–NH); $\mathbf{5}_E$ (DMSO): δ 1.95, 2.00, 2.08 (3 s, 9 H, 3 AcO), 3.19 (m, 2

Table 5
Selected torsion angles (°) for **3**

Conformation $^1C_4$		Conformation $^{3,O}B$	
C-5–O-1–C-1–C-2	40.8(10)	C-25–O-21–C-21–C-22	−53.0(9)
C-5–O-1–C-1–S-1	−87.3(7)	C-25–O-21–C-21–S-21	−175.6(5)
O-2–N-1–C-2–C-3	−179.1(7)	O-22–N-21–C-22–C-23	173.3(8)
O-2–N-1–C-2–C-1	2.0(12)	O-22–N-21–C-22–C-21	1.0(13)
S-1–C-1–C-2–N-1	−88.4(9)	S-21–C-21–C-22–N-21	−72.0(11)
O-1–C-1–C-2–C-3	−38.1(10)	O-21–C-21–C-22–C-23	−3.7(10)
S-1–C-1–C-2–C-3	92.8(7)	S-21–C-21–C-22–C-23	115.6(7)
N-1–C-2–C-3–O-3	105.8(8)	N-21–C-22–C-23–O-23	114.3(9)
C-1–C-2–C-3–O-3	−75.2(9)	C-21–C-22–C-23–O-23	−72.6(9)
C-1–C-2–C-3–C-4	44.4(9)	C-21–C-22–C-23–C-24	48.0(10)
O-3–C-3–C-4–O-5	−54.1(9)	O-23–C-23–C-24–O-25	−34.9(10)
C-2–C-3–C-4–O-5	−172.4(6)	C-22–C-23–C-24–O-25	−154.7(7)
C-2–C-3–C-4–C-5	−53.9(9)	C-22–C-23–C-24–C-25	−33.7(10)
O-3–C-3–C-4–C-5	64.4(9)	O-23–C-23–C-24–C-25	86.1(9)
C-1–O-1–C-5–C-6	81.2(9)	C-21–O-21–C-25–C-26	−167.5(7)
C-1–O-1–C-5–C-4	−50.4(9)	C-21–O-21–C-25–C-24	67.3(9)
O-5–C-4–C-5–O-1	179.2(6)	O-25–C-24–C-25–O-21	102.1(8)
C-3–C-4–C-5–O-1	57.5(9)	C-23–C-24–C-25–O-21	−20.4(10)
O-5–C-4–C-5–C-6	48.7(9)	O-25–C-24–C-25–C-26	−18.9(10)
C-3–C-4–C-5–C-6	−73.0(9)	C-23–C-24–C-25–C-26	−141.4(8)
H-3–C-3–C-4–H-4	−52.6	H-23–C-23–C-24–H-24	−35.4
H-4–C-4–C-5–H-5	49.4	H-24–C-24–C-25–H-25	−21.1
H-5–C-5–C-6–H-6A	−177.5	H-25–C-25–C-26–H-26A	−177.3
H-5–C-5–C-6–H-6B	61.3	H-25–C-25–C-26–H-26B	63.2

H, Cys–H_β), 3.67 (s, 3 H, CO_2Me), 4.07 (d, 2 H, 2 H-6), 4.63 (t, 1 H, $J_{5,6}$ 6.35 Hz, H-5), 4.71 (m, 1 H, Cys–H_α), 5.35 (dd, 1 H, $J_{4,5}$ 1.46 Hz, H-4), 5.85 (d, 1 H, $J_{3,4}$ 3.91 Hz, H-3), 5.94 (s, 1 H, H-1), 8.92 (d, 1 H, $J_{NH,\,CH}$ 7.82 Hz, Cys–NH), 11.30 (s, 1 H, OH); FDMS: m/z 540 (M^+). Anal. Calcd for $C_{23}H_{28}N_2O_{11}S$: C, 51.10; H, 5.22; N, 5.18; S, 5.93. Found: C, 50.80; H, 5.22; N, 5.03; S, 5.82.

Eluted second were **5** and **6** (25%, syrup, **5**:**6** ~ 1:2). The comparison of ^{1}H NMR spectra and optical rotations of **5** and a mixture of **5** and **6**, respectively, made it possible to estimate for **6** $[\alpha]_D^{20}$ +29°; R_f 0.28 (solvent E); ^{1}H NMR (TOCSY, DMSO): $\delta \sim 2.10$ (3 s, 9 H, 3 AcO), 3.44 (t, 2 H, Cys–H_β), 4.33 (m, 1 H, $J_{5,6}$ 7.81 Hz, H-5), 4.45 (dd, 1 H, $J_{5,6'}$ 5.86 Hz, H-6′), 4.49 (dd, 1 H, $J_{4,5}$ 5.86 Hz, H-4), 4.73 (dd, 1 H, $J_{6,6'}$ 11.72 Hz, H-6), 5.22 (d, 1 H, Cys–H_α), 5.80 (d, 1 H, $J_{3,4}$ 3.42 Hz, H-3), 6.07 (s, 1 H, H-1), 7.34 (d, 1 H, $J_{NH,\,CH}$ 7.82 Hz, Cys–NH); FDMS: m/z 540 (M^+).

4. Supplementary material

Full crystallographic details, excluding structure features, have been deposited with the Cambridge Crystallographic Data Centre. These data may be obtained, on request, from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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References

[1] (a) R.G. Spiro, *Adv. Protein Chem.*, 27 (1973) 349–467. (b) J. Montreuil, *Adv. Carbohydr. Chem. Biochem.*, 37 (1980) 157–223.
[2] (a) C.J. Lote, J.B. Weiss, *FEBS Lett.*, 16 (1971) 81–85. (b) J.B. Weiss, C.J. Lote, H. Bobiński, *Nature–New Biology*, 234 (1971) 25–26.
[3] M.L.P. Monsigny, D. Delay, M. Vaculik, *Carbohydr. Res.*, 59 (1977) 589–593.
[4] E. Baran, S. Drabarek, *Polish J. Chem.*, 52 (1978) 941–946.
[5] M. Elofsson, B. Walse, J. Kihlberg, *Tetrahedron Lett.*, 32 (1991) 7613–7616.
[6] M. Gerz, H. Matter, H. Kessler, *Angew. Chem., Int. Ed. Engl.*, 32 (1993) 269–271.
[7] G. Hummel, O. Hindsgaul, *Angew. Chem., Int. Ed. Engl.*, 38 (1999) 1782–1784.
[8] L.A. Marcaurelle, C.R. Bertozzi, *Chem. Eur. J.*, 5 (1999) 1384–1390.
[9] P.J. Garegg, *Adv. Carbohydr. Chem. Biochem.*, 52 (1997) 179–205.
[10] H. Paulsen, *Angew. Chem., Int. Ed. Engl.*, 34 (1995) 1432–1434.
[11] B. Liberek, R. Frankowski, Z. Smiatacz, *Polish J. Chem.*, 73 (1999) 1153–1161.
[12] L. Zervas, I. Photaki, N. Ghelis, *J. Am. Chem. Soc.*, 85 (1963) 1337–1341.
[13] R.U. Lemieux, R.A. Earl, K. James, T.L. Nagabhushan, *Can. J. Chem.*, 51 (1973) 19–26.
[14] G. Rubinstenn, J. Esnault, J-M. Mallet, P. Sinay, *Tetrahedron: Asymmetry*, 8 (1997) 1327–1336.
[15] Z. Ciunik, R. Walczyna, Z. Smiatacz, *J. Carbohydr. Chem.*, 13 (1994) 193–205.
[16] Z. Smiatacz, I. Chrzczanowicz, H. Myszka, P. Dokurno, *J. Carbohydr. Chem.*, 14 (1995) 723–735.
[17] F.H. Allen, O. Kennard, D.G. Watson, L. Brammer, A.G. Orpen, R.J. Taylor, *J. Chem. Soc., Perkin Trans. 2*, S1 (1987).
[18] G.M. Sheldrick, SHELXS, *Acta Crystallogr., Sect. A* 46 (1990) 467–473.
[19] G.M. Sheldrick, SHELXL, Program for the Refinement of Crystal Structures, University of Göttingen, Germany 1997.
[20] C.K. Johnson, ORTEP, Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, TN, USA, 1976.
[21] R.U. Lemieux, T.L. Nagabhushan, I.K. O'Neill, *Can. J. Chem.*, 46 (1968) 413–418.