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Structural analysis of 6-*S*-(benzoxazol-2-yl)-6-deoxy 1,2:3,4-di-*O*-isopropylidene-6-thio-*α*-D-galactopyranose by means of X-ray diffraction, high resolution NMR spectroscopy, and molecular modelling[1]

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Abstract

The conformational behaviour of a representative azaheterocycle/thiosugar hybrid: 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-*α*-D-galactopyranose, **1**, has been characterised by X-ray crystallography, molecular modelling and NMR studies. The crystal of **1** ($C_{19}H_{23}NO_6S$) belongs to the monoclinic space group $P2_1$, with $a = 8.4330(4)$, $b = 10.287(3)$, $c = 11.417(4)$ Å, $\beta = 101.66(5)°$, $V = 970.0(5)$ Å^3, and $Z = 2$. The structure has been determined by X-ray diffraction at 299 K using an area detector. Least-squares refinement based on 2352 reflections yielded a final $wR2$ of 0.098, with $R1 = 0.040$ [for 2210 reflections with $F_o > 4\sigma(F_o)$]. The pyranose ring adopts a conformation between that of the screw-boat, $^{O}S_5$, and the twist-boat, $^{O}T_2$ forms. Proton NMR chemical shifts have been assigned by measurement of 1D and 2D spectra. The C-5–C-6 conformer populations in $CDCl_3$ solution have been estimated. In parallel, a

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[1] Data deposited with Cambridge Crystallographic Structural DataBase.

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conformational analysis using the crystal coordinates as the starting point has been made using the Tripos force field. The resulting potential energy surface indicates a high flexibility about the C-5–C-6 and C-6–S-6 bonds. The agreement between experimental and theoretical data is satisfactory and constitutes a validation of the conformational energy surface.

Keywords: Thiosugars; X-Ray diffraction; NMR; Molecular mechanics; Conformation

1. Introduction

As part of an ongoing program directed towards the use of thio-functionalised sugars in stereo-controlled synthesis, we have developed a new family of compounds which can be regarded as azaheterocycle/thiosugar hybrids [1]. These molecules display the unusual array of a saccharidic moiety connected through a sulfur atom to a nitrogen-containing heterocyclic system. A number of these hybrids have been shown to allow miscellaneous innovative methodological applications in saccharide chemistry [2–4] based upon a new reactivity concept we referred to as 'aza–thia-assistance' in a previous paper [5].

In the present work, the elucidation of the molecular and crystal structure of 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose (**1**) has been undertaken, through the use of X-ray diffraction. The extension to its conformational behaviour in solution has been performed via NMR spectroscopy in conjunction with molecular mechanics calculations.

2. Experimental

Nomenclature.—The sign and symbol of the torsion angles are those proposed by the Joint Commission on Biochemical Nomenclature [6]. A schematic representation of 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose is provided in Fig. 1, with the two torsion angles defined as:

ω = O-5–C-5–C-6–S-6
χ = C-5–C-6–S-6–C-21

The atomic labelling scheme is illustrated in Fig. 2.

Crystal structure determination.—Crystal data and summarised experimental procedures are collected in Table 1. A crystal suitable for X-ray structure determination was obtained from an ethanol solution. Data were collected using an Enraf–Nonius FAST area detector diffractometer and interpreted using MADNES [7]. Frames were integrated for 5 s over an angle of 0.16°. Unit cell dimensions and standard deviations were obtained using the INDEX and REFINE routines of MADNES with 87 reflections collected in four 10° ϕ scans separated by 90°. Reduced-cell calculations did not indicate higher lattice symmetry [8]. The 3975 reflections were obtained from a 190° ϕ rotation at $\chi = 0°$, and were corrected for Lorentz and polarisation effects. These were processed to give 2355 unique reflections ($R_{\text{int}} = 0.0327$) within a maximum θ of 27.5°,

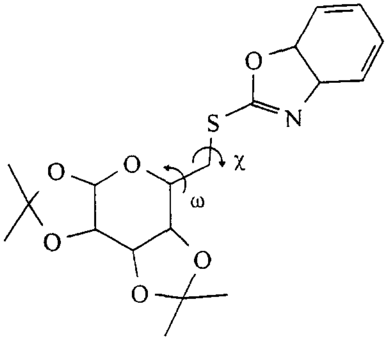

Fig. 1. Schematic representation of 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose with relevant torsion angles labelled.

of which 2352 reflections were considered observed $[F_o^2 > -3\sigma(F_o^2)]$. An absorption/extinction correction was not applied. The structure was solved by automated Patterson methods (DIRDIF [9]) with refinement by full-matrix least-squares techniques (SHELXL-93 [10]). Anisotropic thermal parameters were used for all non-hydrogen atoms. All hydrogen atoms were included at calculated positions with an

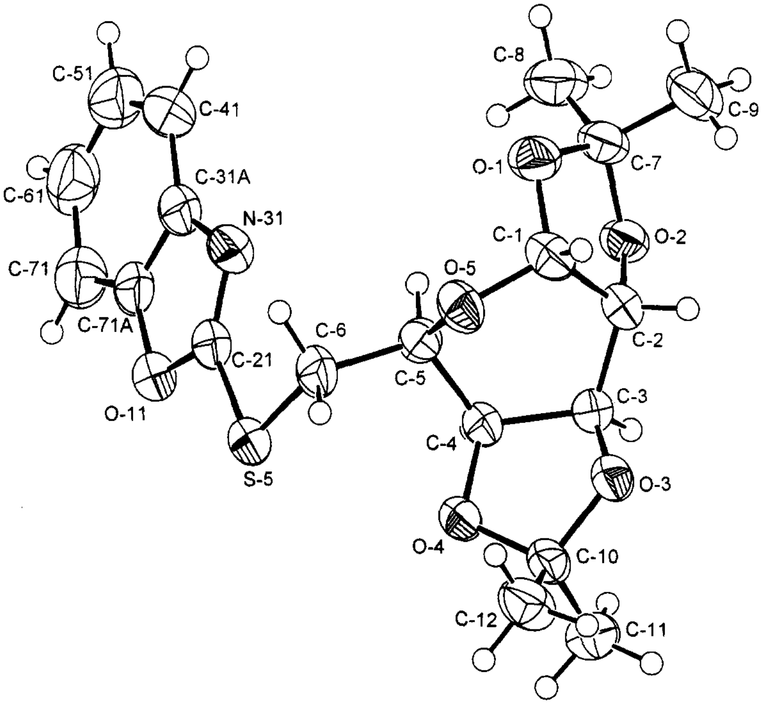

Fig. 2. ORTEP view of the 6-S-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose molecule with atom labels. Ellipsoids are drawn at the 50% probability level.

Table 1
Crystal data and data collection summary for 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose

Formula	$C_{19}H_{23}NO_6S$
Molecular weight	393.46
Crystal system	Monoclinic
Space group	$P2_1$
a (Å)	8.4330(4)
b (Å)	10.287(3)
c (Å)	11.417(4)
β (°)	101.66(5)
V (Å^3)	970.0(5)
D_{calc} (g cm^{-3})	1.347
Z	2
F(000)	416.0
μ (cm^{-1})	2.0
Crystal size (mm)	0.48 × 0.40 × 0.13
T (K)	299
θ range (°)	3.16–27.44
Wavelength (Mo K_α, monochromated) (Å)	0.71073
Crystal–detector distance (mm)	34.70(15)
Detector swing angle (°)	−35.01
Data set	−8:8, −8:16, −17:18
No. reflns collected	3975
No. unique reflns	2355
No. observed [$F_o^2 > -3\sigma(F_o^2)$] reflns	2352
No. refined parameters	271
R(int)	0.0327
Final R_1 [a]	0.0395 [for 2210 reflns with $F_o > 4\sigma(F_o)$]
Final wR_2 [b]	0.0976
Goodness of fit	1.064
Weighting scheme	$w^{-1} = \sigma^2(F_o^2)+(0.0465P)^2+0.21P$ [c]
Final $(\Delta/\sigma)_{mean}$, $(\Delta/\sigma)_{max}$.	0.000, 0.03
Min. residual density (e Å^{-3})	−0.14
Max. residual density (e Å^{-3})	0.17
Flack X parameter	−0.07(9)

[a] $R_1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$.
[b] $wR_2 = [\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{1/2}$.
[c] $P = (\mathrm{MAX}(F_o^2, 0)+2F_c^2)/3$.

isotropic displacement parameter dependent upon the equivalent isotropic displacement parameter of the carrier atom. The absolute configuration, established using the Flack parameter, concurred with that deduced from the chirality of the starting materials. Geometrical calculations and the ORTEP illustration were obtained with PLATON [11].

NMR spectroscopy.—^{1}H spectra were recorded in $CDCl_3$ on a Bruker 400 MHz instrument operating in the Fourier-transform mode at 296 K. The ^{1}H chemical shifts were assigned from homonuclear correlation spectroscopy. The $^3J_{H-H}$ were extracted from a spectrum with a digital resolution of 0.12 Hz/pt. A set of linear equations was prepared with respect to the H-5–H-6a and H-5–H-6b coupling constants, calculated using a Karplus type equation [12] and the Haasnoot–Altona parameters [13], at the TG, GG, and GT conformations (where $\omega = 180, 60, -60°$, respectively):

$$P_{\mathrm{TG}} \times {}^{3}J_{\mathrm{H\text{-}5-H\text{-}6a(TG)}} + P_{\mathrm{GG}} \times {}^{3}J_{\mathrm{H\text{-}5-H\text{-}6a(GG)}} + P_{\mathrm{GT}} \times {}^{3}J_{\mathrm{H\text{-}5-H\text{-}6a(GT)}} = {}^{3}J_{\mathrm{H\text{-}5-H\text{-}6a(observed)}}$$

$$P_{\mathrm{TG}} \times {}^{3}J_{\mathrm{H\text{-}5-H\text{-}6b(TG)}} + P_{\mathrm{GG}} \times {}^{3}J_{\mathrm{H\text{-}5-H\text{-}6b(GG)}} + P_{\mathrm{GT}} \times {}^{3}J_{\mathrm{H\text{-}5-H\text{-}6b(GT)}} = {}^{3}J_{\mathrm{H\text{-}5-H\text{-}6b(observed)}}$$

$$P_{\mathrm{TG}} + P_{\mathrm{GG}} + P_{\mathrm{GT}} = 1$$

The C-5–C-6 conformer distribution was calculated by solution of these equations.

Molecular mechanics.—Molecular modelling was conducted using the Tripos force-field [14] under the SYBYL [15] software package. The Tripos force-field is a classic molecular mechanics method in which the potential energy is evaluated as a combination of various functions. This force-field has been the subject of a recent parameterisation capable of performing conformational analysis of carbohydrates [16]. The Grid Search procedure of SYBYL was used to compute the 'relaxed residue' potential energy surface over the whole angular range of ω and χ. The crystal coordinates were used as a starting point and the two torsion angles were incremented in steps of 10°. The dielectric constant was set to a value of 4, convergence was deemed to be reached at a gradient of 0.01, and an 8.0 Å cutoff was applied to non-bonded interactions.

3. Results and discussion

Molecular conformation in the solid state.—An ORTEP representation of 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose is shown in Fig. 2. The positional and isotropic thermal parameters for the non-hydrogen atoms are provided in Table 2. Bond lengths, bond angles, and selected torsion angles are listed in Tables 3–5, respectively. Within the pyranose system, the mean C–C bond length is 1.517 Å, while that for C–O is 1.424 Å. The absolute configuration at each pyranose carbon atom is found to be equivalent to that of α-D-galactopyranose. The 9-membered benzoxazol system is effectively planar with a maximum deviation of 0.017 Å from the mean plane and is oriented almost parallel (1.82(9)°) with the *c*-axis. The distinction between the ring angles C-31A–C-71A–C-71 (125.0(3)°) and C-61–C-71–C-71A (115.3(4)°) is often apparent in crystal structures that incorporate the benzoxazol system [17]. The TG C-5–C-6 conformation ($\omega = 192°$) can be considered normal for a monosaccharide having the *galacto* configuration. The pyranose ring exhibits puckering parameters [18]: *Q*: 0.617 Å, theta: 80.1°, and phi: 332.6°. This conformation lies between that of the screw-boat $^{O}S_{5}$ and the twist-boat $^{O}T_{2}$ forms and shows no deviation towards the boat $B_{2,5}$. These values show good agreement with the mean values of *Q*: 0.626 Å, theta: 79.2°, and phi: 324.4°; recently reported by Köll et al. [19]. The adopted conformation results in an axial aspect for the isopropylidene oxygens, equatorial for

Table 2
Final fractional coordinates and equivalent isotropic thermal parameters of the non-hydrogen atoms

Atom	x/a	y/b	z/c	U(eq) (Å^2)
S-6	0.89028(9)	−0.00501(8)	0.02194(5)	0.0500(2)
O-1	0.4726(3)	0.2225(3)	0.2860(2)	0.0557(9)
O-2	0.3015(2)	0.0665(2)	0.19740(15)	0.0460(6)
O-3	0.3035(3)	0.1810(2)	−0.1002(2)	0.0479(6)
O-4	0.5418(2)	0.0872(2)	−0.11387(14)	0.0455(6)
O-5	0.5793(3)	0.2481(2)	0.1164(2)	0.0458(6)
O-11	1.0387(3)	−0.1989(2)	0.1405(2)	0.0500(7)
N-31	0.9411(3)	−0.0600(3)	0.2617(2)	0.0486(9)
C-1	0.4381(4)	0.2556(3)	0.1627(2)	0.0469(10)
C-2	0.3047(4)	0.1602(3)	0.1062(2)	0.0438(10)
C-3	0.3358(3)	0.0910(3)	−0.0043(2)	0.0417(10)
C-4	0.5128(3)	0.0496(3)	0.0007(2)	0.0370(9)
C-5	0.6316(3)	0.1180(3)	0.1004(2)	0.0385(9)
C-6	0.7999(4)	0.1366(3)	0.0752(2)	0.0464(11)
C-7	0.3533(4)	0.1328(4)	0.3085(2)	0.0512(10)
C-8	0.4301(5)	0.0366(5)	0.4005(3)	0.0709(15)
C-9	0.2137(5)	0.2058(5)	0.3437(3)	0.0726(16)
C-10	0.3963(4)	0.1407(3)	−0.1850(2)	0.0445(10)
C-11	0.3077(5)	0.0371(4)	−0.2669(3)	0.0600(10)
C-12	0.4381(5)	0.2582(4)	−0.2500(3)	0.0602(12)
C-21	0.9575(3)	−0.0882(3)	0.1548(2)	0.0431(10)
C-31A	1.0202(4)	−0.1626(4)	0.3295(2)	0.0505(10)
C-41	1.0474(5)	−0.1902(5)	0.4518(3)	0.0677(13)
C-51	1.1279(5)	−0.3017(6)	0.4918(3)	0.0795(18)
C-61	1.1820(5)	−0.3873(5)	0.4133(4)	0.0788(16)
C-71	1.1588(5)	−0.3621(4)	0.2918(3)	0.0660(12)
C-71A	1.0787(4)	−0.2494(4)	0.2552(2)	0.0502(11)

$U_{eq} = 1/3$ of the trace of the orthogonalised U.

C-6, H-2 and H-3, while the remaining ring substituents, H-1 and H-4, assume a bisectional orientation. The isopropylidene ring O-1–C-1–C-2–O-2–C-7 has the puckering parameters Q: 0.314 Å and phi: 303.2° and can be represented as $^{O2}T_{C7}$. Parameters for the O-3–C-3–C-4–O-4–C-10 ring are Q: 0.309 Å and phi: 177.3°, leading to an E_{O3} description.

Conformation of the isolated molecule.—The relaxed ω–χ potential energy surface is shown in Fig. 3, with an outer limit set at 5 kcal mol^{-1} above the global minimum and iso-energy contours drawn at 1 kcal mol^{-1} increments. The nine energy minima revealed correspond to non-eclipsed conformations about the two torsion angles. The crystalline conformation, $\omega = 192°$, $\chi = 280°$, resides in one of these regions. The three low energy regions found with χ at approximately 180° are calculated to be more than 2 kcal mol^{-1} above the global energy minimum.

Molecular conformation in solution.—The chemical shift assignments provided in Table 6 were obtained by tracing the through-bond (scalar) coupling networks of the ^{1}H–^{1}H COSY NMR spectrum (Fig. 4). The measured pyranose $^3J_{H-H}$ couplings and those calculated for the crystalline conformation according to the equations of Altona et

Table 3
Bond lengths for 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose

Atoms	Distance (Å)	Atoms	Distance (Å)
S-6–C-6	1.806(3)	C-1–C-2	1.533(4)
S-6–C-21	1.734(3)	C-2–C-3	1.517(4)
O-1–C-1	1.420(3)	C-3–C-4	1.542(4)
O-1–C-7	1.426(5)	C-4–C-5	1.528(4)
O-2–C-2	1.423(3)	C-5–C-6	1.516(4)
O-2–C-7	1.429(3)	C-7–C-8	1.492(5)
O-3–C-3	1.418(3)	C-7–C-9	1.517(6)
O-3–C-10	1.424(4)	C-1–C-11	1.512(5)
O-4–C-4	1.432(3)	C-10–C-12	1.497(5)
O-4–C-10	1.437(4)	C-31A–C-41	1.398(4)
O-5–C-1	1.399(4)	C-31A–C-71A	1.389(5)
O-5–C-5	1.432(4)	C-41–C-51	1.364(7)
O-11–C-21	1.356(4)	C-51–C-61	1.397(7)
O-11–C-71A	1.386(3)	C-61–C-71	1.386(6)
N-31–C-21	1.289(3)	C-71–C-71A	1.364(6)
N-31–C-31A	1.396(5)		

Table 4
Bond angles for 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose

Atoms	Angle (°)	Atoms	Angle (°)
C-6–S-6–C-21	100.91(13)	O-1–C-7–C-8	109.5(3)
C-1–O-1–C-7	108.8(2)	O-1–C-7–C-9	109.9(3)
C-2–O-2–C-7	106.2(2)	O-2–C-7–C-8	108.6(3)
C-3–O-3–C-10	106.8(2)	O-2–C-7–C-9	110.9(3)
C-4–O-4–C-10	109.6(2)	C-8–C-7–C-9	113.0(3)
C-1–O-5–C-5	114.0(2)	O-3–C-10–O-4	104.54(19)
C-21–O-11–C-71A	103.5(2)	O-3–C-10–C-11	110.8(3)
C-21–N-31–C-31A	103.0(3)	O-3–C-10–C-12	108.6(3)
O-1–C-1–O-5	110.0(3)	O-4–C-10–C-11	109.8(3)
O-1–C-1–C-2	104.4(2)	O-4–C-10–C-12	109.2(3)
O-5–C-1–C-2	114.4(2)	C-11–C-10–C-12	113.5(2)
O-2–C-2–C-1	104.3(2)	S-6–C-21–O-11	113.14(18)
O-2–C-2–C-3	108.8(2)	S-6–C-21–N-31	129.7(3)
C-1–C-2–C-3	114.5(3)	O-11–C-21–N-31	117.2(3)
O-3–C-3–C-2	107.3(2)	N-31–C-31A–C-41	132.1(3)
O-3–C-3–C-4	104.0(2)	N-31–C-31A–C-71A	109.6(2)
C-2–C-3–C-4	115.3(2)	C-41–C-31A–C-71A	118.2(4)
O-4–C-4–C-3	103.6(2)	C-31A–C-41–C-51	118.4(4)
O-4–C-4–C-5	110.4(2)	C-41–C-51–C-61	121.4(4)
C-3–C-4–C-5	112.6(2)	C-51–C-61–C-71	121.7(4)
O-5–C-5–C-4	110.7(2)	C-61–C-71–C-71A	115.3(4)
O-5–C-5–C-6	103.3(2)	O-11–C-71A–C-31A	106.7(3)
C-4–C-5–C-6	114.5(2)	O-11–C-71A–C-71	128.2(3)
S-6–C-6–C-5	115.9(2)	C-31A–C-71A–C-71	125.0(3)
O-1–C-7–O-2	104.4(2)		

Table 5
Selected torsion angles for 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose

Atoms	Angle (°)	Atoms	Angle (°)
C-21–S-6–C-6–C-5	−79.7(2)	C-1–O-5–C-5–C-6	−168.7(2)
C-6–S-6–C-21–O-11	−177.2(2)	O-1–C-1–C-2–O-2	−11.8(3)
C-6–S-6–C-21–N-31	2.8(3)	O-5–C-1–C-2–C-3	−10.3(3)
C-7–O-1–C-1–C-2	−9.8(3)	O-2–C-2–C-3–O-3	167.5(2)
C-1–O-1–C-7–O-2	27.8(3)	C-1–C-2–C-3–C-4	39.1(3)
C-7–O-2–C-2–C-1	29.0(3)	O-3–C-3–C-4–O-4	−17.9(3)
C-2–O-2–C-7–O-1	−35.4(3)	C-2–C-3–C-4–C-5	−15.9(3)
C-10–O-3–C-3–C-4	32.2(3)	O-4–C-4–C-5–C-6	−35.8(3)
C-3–O-3–C-10–O-4	−34.0(3)	C-3–C-4–C-5–O-5	−34.7(3)
C-10–O-4–C-4–C-3	−2.5(3)	C-3–C-4–C-5–C-6	−151.0(2)
C-4–O-4–C-10–O-3	22.0(3)	O-5–C-5–C-6–S-6	−168.6(2)
C-5–O-5–C-1–C-2	−43.7(3)	C-4–C-5–C-6–S-6	−48.1(3)
C-1–O-5–C-5–C-4	68.2(3)		

al. [13] are compared in Table 7. These data suggest that the pyranose ring conformation observed in the crystal remains largely unaltered in solution. The measured $^3J_{\text{H-5–H-6ab}}$ represents the solution average orientation of these protons, and so may be considered as a 'virtual' conformation about the C-5–C-6 bond. The C-5–C-6 conformer populations were estimated at TG: 45%, GT: 41%, and GG: 14%, using limiting values calculated with the Haasnoot–Altona equation.

Crystal packing.—Geometric analysis of the crystal packing [11] indicated no unusual intermolecular close-contacts. The mode of molecular packing, was further explored by applying the atom-pair procedure of Kitaigorodsky [20] and partitioning the

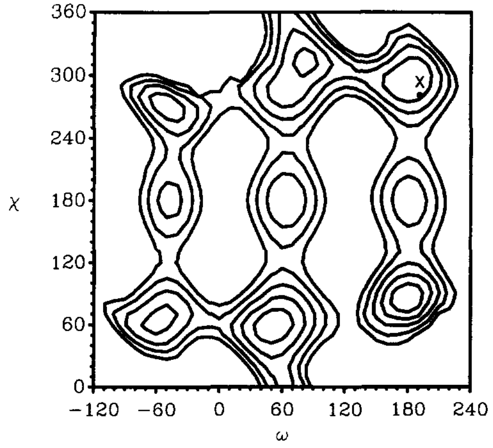

Fig. 3. Relaxed potential energy surface of 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose as a function of the ω and χ torsion angles. 1 kcal mol^{-1} iso-energy contours are included up to 5 kcal mol^{-1} above the minimum. The crystallographic conformation is labelled X.

Table 6
400 MHz ^{1}H NMR spectral assignment for 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose, measured in $CDCl_3$ at 296 K

Signal/δ (multiplicity)	Assignment
5.54 (d)	H-1
4.30 (dd)	H-2
4.63 (dd)	H-3
4.40 (dd)	H-4
4.34 (dd)	H-5
3.47 (dd)	H-6ab
1.27 (s), 1.34 (s), 1.36 (s), 1.46 (a)	H-8abc, H-9abc, H-11abc, H-12abc
7.22 (2dd)	H-51, H-61
7.40 (dd), 7.53 (dd)	H-41, H-71

Table 7
Measured and predicted ^{1}H–^{1}H coupling constants for 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose

Proton pair	Measured [a] ^3J (Hz)	Calculated [b] ^3J (Hz)
H-1,H-2	5.02	5.92
H-2,H-3	2.46	1.23
H-3,H-4	7.90	7.53
H-4,H-5	1.69	3.62
H-5,H-6a	6.92	6.07
H-5,H-6b	6.92	11.30

[a] $CDCl_3$, 400 MHz, 296 K.
[b] Crystallographic coordinates.

Table 8
Intermolecular packing interactions

Symmetry descriptor	Close contacts	E (kcal mol^{-1})
$\mathrm{II}+a-b$	187	−15.9
$\mathrm{II}+a$	187	−15.9
$\mathrm{I}-a$	83	−8.6
$\mathrm{I}+a$	83	−8.6
$\mathrm{II}+2a-b$	54	−5.8
$\mathrm{II}+2a$	54	−5.8
$\mathrm{II}+2a-b+c$	55	−4.0
$\mathrm{II}+2a+c$	55	−4.0
$\mathrm{II}+a-b+c$	26	−2.1
$\mathrm{II}+a+c$	26	−2.1
$\mathrm{I}-c$	28	−1.7
$\mathrm{I}+c$	28	−1.7

$\mathrm{I}=x,\ y,\ z$; $\mathrm{II}=-x,\ \frac{1}{2}+y,\ -z$.

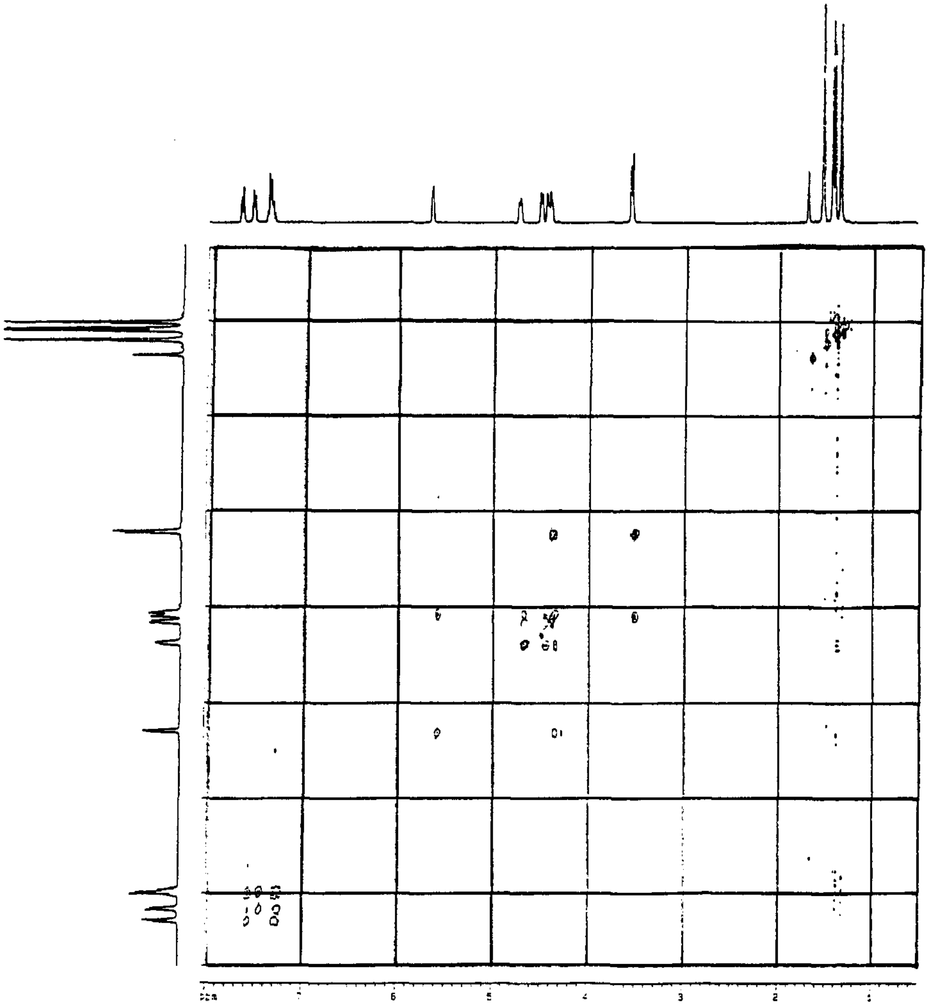

Fig. 4. The ^1H and ^1H–^1H COSY spectrum of 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose in $CDCl_3$ at 400 MHz.

interactions among the molecules surrounding the reference molecule. In addition to the simple practice of counting intermolecular contacts within 1.5 times the sum of the atomic van der Waals radii, the interactions were also estimated using a 6-exp potential in conjunction with the coefficients recently derived by Fillipini and Gavezzotti [21]. The twelve strongest molecule–molecule interactions resulting from this analysis are provided in Table 8, and both methods of calculation clearly demonstrate the packing anisotropy of this structure. By far the strongest pair of interactions is that generating the screw axis of the space group, where the molecular strings so created have a molecule–molecule packing interaction some 2 times greater than the next strongest interaction. This linear string of closely-packed molecules is highlighted in Fig. 5. Association of

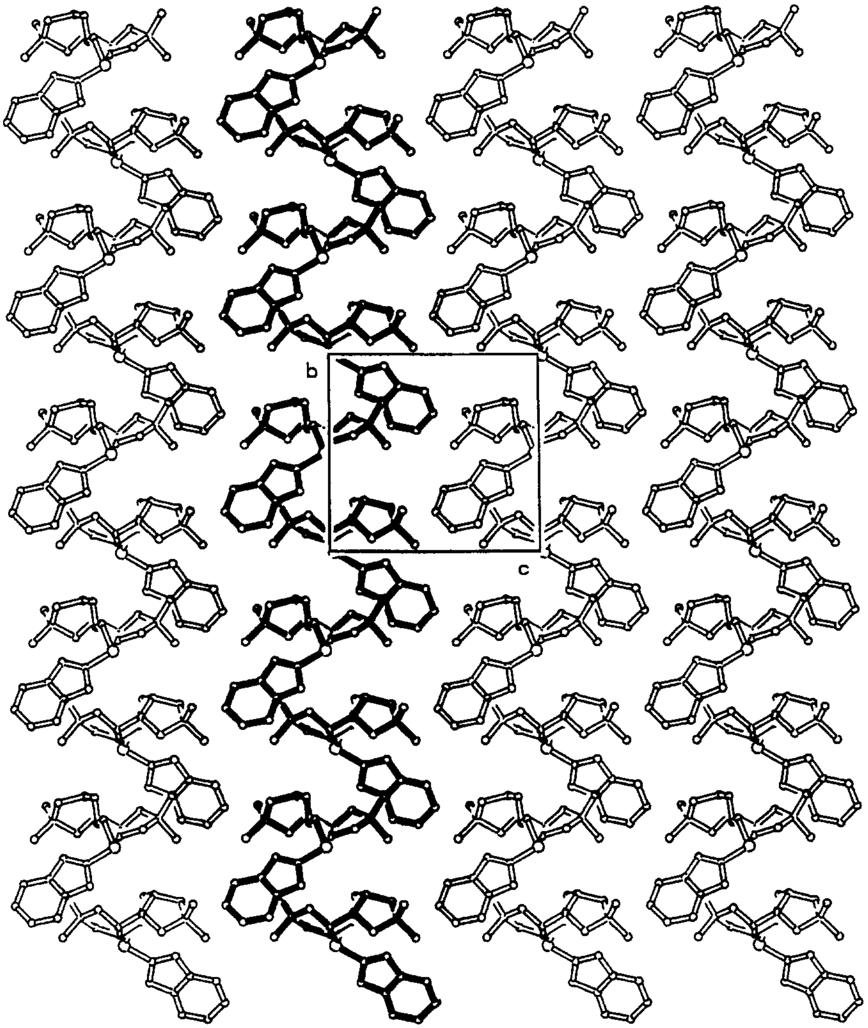

Fig. 5. Packing diagram for 6-*S*-(benzoxazol-2-yl)-6-deoxy-1,2:3,4-di-*O*-isopropylidene-6-thio-α-D-galactopyranose viewed parallel to the *a*-axis and with hydrogen atoms omitted for clarity. The linear chain resulting from the strongest molecule–molecule interaction pairs is highlighted.

these molecular strings gives rise to the *a*-axis translation, and accounts for the next two strongest interaction pairs. The fourth strongest and subsequent interaction pairs provided in the table arise from molecular propagation in the third dimension.

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