Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

2-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosylthio)-4-pyridin-4-yl-6,7,8,9-tetrahydro-5*H*-cyclohepta[*b*]pyridine-3-carbonitrile

Galal H. Elgemeie,[a] Mona M. Hussein[b] and Peter G. Jones[c]*

[a]Chemistry Department, Faculty of Science, Helwan University, Helwan, Cairo, Egypt, [b]Chemistry Department, Faculty of Science, Cairo University, Giza, Egypt, and [c]Institut für Anorganische und Analytische Chemie, Technische Universität Braunschweig, Postfach 3329, 38023 Braunschweig, Germany

Correspondence e-mail: jones@xray36.anchem.nat.tu-bs.de

Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.004 Å
R factor = 0.045
wR factor = 0.111
Data-to-parameter ratio = 18.6

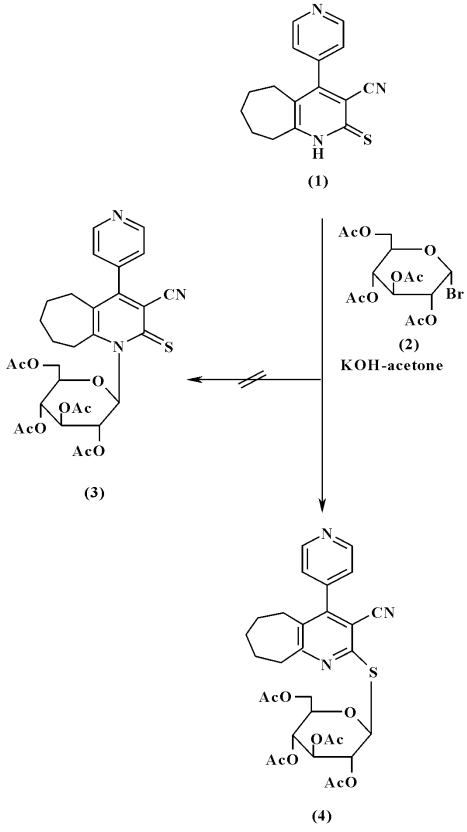
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

In the title compound, $C_{30}H_{33}N_3O_9S$, the glucoside moiety is attached to the pyridone *via* the S atom. The expected absolute configuration was confirmed. Dimensions at sulfur are S—C(pyridone) 1.780 (2), S—C(glucoside) 1.803 (2) Å, C—S—C 98.15 (11)°. There are three short H···O contacts (<2.5 Å) that determine the molecular packing.

Received 9 October 2002
Accepted 11 October 2002
Online 18 October 2002

Comment

There is increasing interest in the synthesis of nucleoside analogues and their incorporation into DNA sequences for the study of ligand–DNA and protein–DNA interactions. In recent reports, we described the preparation of various novel functionalized pyridinethione glycosides, which displayed antagonistic activity against human carcinoma cells and HIV (Attia & Elgemeie, 1995; Elgemeie *et al.*, 1997, 1998, 1999). In an earlier brief communication we had reported the use of dihydropyridinethione glycosides as P-glycoprotein (Pgp) substrates or inhibitors in the protein glycosylation process (Scala *et al.*, 1997). These common features encouraged us to develop a new straightforward synthesis of these compounds.



Here we describe a novel one-pot synthesis of the title pyridine thioglucoside (4) through reaction of a pyridine-2(1*H*)-

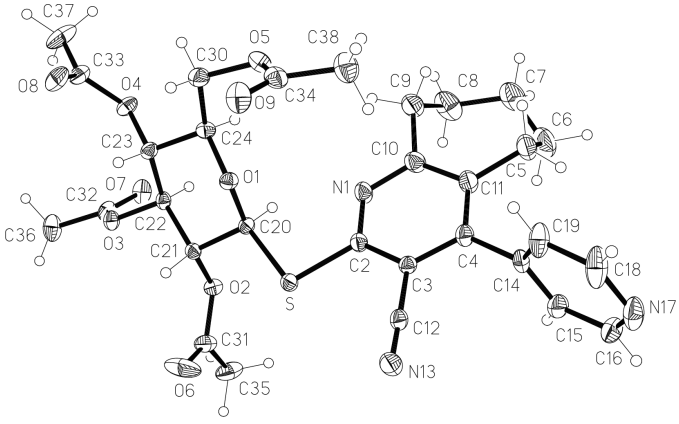


Figure 1
The molecule of compound (4) in the crystal. Ellipsoids are drawn at the 30% probability level. H-atom radii are arbitrary.

thione derivative (1) with 2,3,4,6-tetra–*O*-acetyl-α-D-glucopyranosyl bromide (2). However, this reaction could also give the pyridinethione *N*-glucoside regioisomer (3). Only one product was obtained; the spectra did not allow us to distinguish between (3) and (4). Here we report the X-ray structure analysis, which determines the product unambiguously to be the pyridine *S*-glucoside, (4).

The title compound, (4), is shown in Fig. 1. The absolute configuration was determined by anomalous dispersion effects and is consistent with the known configuration of the sugar. Bond lengths and angles (*e.g.* at sulfur; Table 1) may be regarded as normal. The sugar ring displays the usual chair conformation, with absolute torsion angles between 52.9 and 68.6°. The seven-membered ring adopts a conformation in which the atoms C5,C9,C10,C11 are approximately coplanar (mean deviation 0.02 Å), and the atoms C6,C7,C8 form a second plane parallel to the first [interplanar angle 1.0 (4)°]. The torsion angles around the S atom in the atom sequence C21,C20,S,C2,C3 are approximately antiperiplanar.

There are several short H···O contacts that could be interpreted as hydrogen bonds. Ignoring those contacts involving the poorly resolved methyl H atoms, the three shortest have uncorrected lengths of *ca* 2.45 Å (Table 2) and lead to a three-dimensional packing.

Experimental

To a solution of the condensed pyridine-2(1*H*)-thione [(1); 2.81 g, (0.01 mol)] and potassium hydroxide [0.56 g, (0.01 mol) in distilled water (6 ml)] was added a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide [(2); 4.52 g, (0.011 mol)] in dry acetone (20 ml). The reaction mixture was stirred at room temperature for 2 h. The solvent was evaporated under reduced pressure at 303 K and the residue was washed with distilled water to remove the potassium bromide which had formed. The product was dried, and crystallized from ethanol in 80% yield to afford pale-yellow crystals (m.p. 456 K).

Crystal data

$C_{30}H_{33}N_3O_9S$
M_r = 611.65
Orthorhombic, $P2_12_12_1$
a = 8.0237 (14) Å
b = 10.2293 (14) Å
c = 38.636 (6) Å
V = 3171.1 (9) Å^3
Z = 4
D_x = 1.281 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 61 reflections
θ = 4.5–12.5°
μ = 0.16 mm^{-1}
T = 173 (2) K
Tablet, pale yellow
0.60 × 0.45 × 0.25 mm

Data collection

Siemens *P*4 diffractometer
ω scans
7824 measured reflections
7289 independent reflections
5529 reflections with $I > 2\sigma(I)$
R_{int} = 0.022
θ_{max} = 27.5°
$h = -10 \rightarrow 10$
$k = -13 \rightarrow 0$
$l = 0 \rightarrow 50$
3 standard reflections
every 247 reflections
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.045
$wR(F^2)$ = 0.111
S = 0.96
7289 reflections
392 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0643P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.018
$\Delta\rho_{max}$ = 0.43 e Å^{-3}
$\Delta\rho_{min}$ = −0.28 e Å^{-3}
Absolute structure: Flack (1983), 3142 Friedel pairs
Flack parameter = −0.09 (8)

Table 1
Selected geometric parameters (Å, °).

S—C2	1.780 (2)	N1—C2	1.327 (3)
S—C20	1.803 (2)	N1—C10	1.346 (3)
C2—S—C20	98.15 (11)	C2—N1—C10	119.1 (2)
C20—S—C2—C3	167.95 (19)	C20—C21—C22—C23	−52.9 (2)
C24—O1—C20—C21	−68.6 (2)	C21—C22—C23—C24	55.6 (2)
C2—S—C20—C21	160.43 (17)	C20—O1—C24—C23	67.5 (2)
O1—C20—C21—C22	58.3 (2)	C22—C23—C24—O1	−59.7 (2)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C37—H37*C*···O1^{i}	0.98	2.68	3.544 (3)	147
C24—H24···O6^{ii}	1.00	2.45	3.288 (3)	142
C19—H19···O7^{iii}	0.95	2.64	3.332 (3)	130
C38—H38*C*···O7^{iii}	0.98	2.67	3.379 (4)	129
C21—H21···O8^{iv}	1.00	2.47	3.364 (3)	149
C5—H5*A*···N13^{ii}	0.99	2.59	3.561 (4)	168
C35—H35*C*···N13^{v}	0.98	2.44	3.401 (4)	168
C15—H15···N17^{vi}	0.95	2.45	3.375 (4)	163

Symmetry codes: (i) $x-\frac{1}{2}, \frac{1}{2}-y, 2-z$; (ii) $x-1, y, z$; (iii) $x, 1+y, z$; (iv) $\frac{1}{2}+x, \frac{1}{2}-y, 2-z$; (v) $x, y-1, z$; (vi) $1-x, y-\frac{1}{2}, \frac{3}{2}-z$.

Methyl H atoms were located in difference syntheses, idealized (C—H 0.98 Å, H—C—H 109.5°) and refined on the basis of rigid groups allowed to rotate but not tip. However, the maxima were not very distinct and convergence was slow for those attached to C36. Other H atoms were included using a riding model with fixed C—H bond lengths (aromatic 0.95, methylene 0.99, methine 1.00 Å); U(H) values were fixed at $1.5U_{eq}$ of the parent atom for the methyl groups and $1.2U_{eq}$ for other H atoms.

Data collection: *XSCANS* (Fait, 1991); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *XP* (Siemens, 1994); software used to prepare material for publication: *SHELXL*97.

Financial support from the Fonds der Chemischen Industrie is gratefully acknowledged. We thank Mr A. Weinkauf for technical assistance.

References

Attia, A. M. & Elgemeie, G. E. H. (1995). *Carbohydr. Res.* **268**, 295–300.
Elgemeie, G. E. H., Attia, A. M. & Hussain, B. A. (1998). *Nucleosides Nucleotides*, **17**, 855–868.
Elgemeie, G. E. H., Attia, A. M. & Shehada, L. A. (1997). *Tetrahedron*, 53, 17441–17448.
Elgemeie, G. E. H., Mansour, O. A. & Metwally, N. H. (1999). *Nucleosides Nucleotides*, **18**, 113–123.
Fait, J. (1991). *Manuals to X-ray Program System*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Flack, H. D. (1983). *Acta Cryst*. A**39**, 876–881.
Scala, S., Akhmed, N., Rao, U. S., Paull, K., Lan, L., Dickstein, B., Lee, J., Elgemeie, G. E. H., Stein, W. D. & Bates, S. E. (1997). *Mol. Pharmacol.* **51**, 1024–1033.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.
Siemens (1994). *XP*. Version 5.03. Siemens Analytical X-ray Instruments, Madison, USA.