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p-Tolyl 2-*O*-benzyl-3,5-*O*-(di-*tert*-butylsilanediyl)-1-thio-α-D-arabinofuranoside

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Key indicators

Single-crystal X-ray study
T = 193 K
Mean σ(C–C) = 0.003 Å
R factor = 0.036
wR factor = 0.091
Data-to-parameter ratio = 18.5

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

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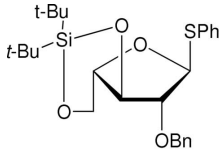
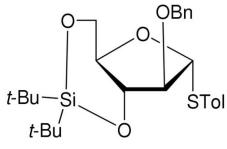
In the title compound, $C_{27}H_{38}O_4SSi$, the furanose ring adopts a nearly perfect E_4 envelope conformation, while the six-membered ring containing the Si atom exists in an approximate half-chair conformation. The conformation about the glycosidic linkage is that favored by the *exo*-anomeric effect.

Comment

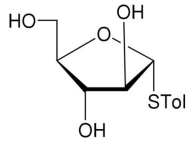
A recent paper by Zhu *et al.* (2006) reports an efficient and highly stereoselective synthesis of β-L-arabinofuranosides using a thioglycoside donor protected at O3 and O5 with a silyl acetal (I). Our group has a long-standing interest in the synthesis of D-arabinofuranosides from mycobacteria (Yin *et al.*, 2002; Yin & Lowary, 2001; Han *et al.*, 2003) and thus we prepared an analogous donor, (II), from the previously reported D-arabinofuranosyl thioglycoside, (III) (D'Souza *et al.*, 2000), in two steps *via* (IV) in 88% overall yield. The title compound, (II), was crystalline and an X-ray study was undertaken to confirm the structure of the molecule and also to make structural comparisons with computational work reported earlier on (I) (Zhu *et al.*, 2006).



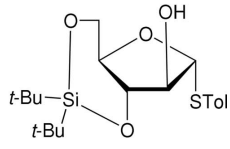
(I)



(II)



(III)



(IV)

The attachment of the silicon acetal to the monosaccharide results in the furanose ring being locked into a near-perfect E_4 conformation in which C4 is displaced below the plane formed by C1, C2, C3 and O4 (Fig. 1). The pseudorotational phase angle (*P*) of the furanose ring is 57.0° and the puckering amplitude (τ_m) is 43.1° (Altona & Sundaralingam, 1972). This conformation differs slightly from previous density functional theory calculations on (I), which suggested an envelope conformation with C3 displaced from the plane (Zhu *et al.*, 2006). The six-membered ring in (II) exists in a distorted half-chair conformation, in which Si, O3, O5, and C5 are approximately coplanar while C4 is displaced below, and C3 above, this plane. Here too there are slight differences from the computed structure of (I) in which the conformation of this ring was shown to be more chair-like (Zhu *et al.*, 2006). The conformation about the C1—S bond in (II) is that favored by the *exo*-anomeric effect (Lemieux & Koto, 1974), the C11—S—C1—C2 torsion angle being −164.11 (13)°. In the E_4 conformation adopted by the furanose ring, the thioglycoside

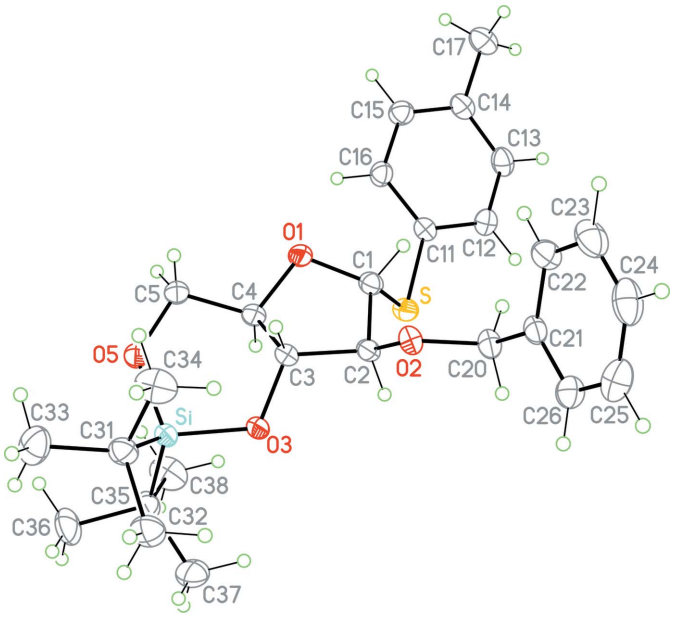


Figure 1
The molecular structure of (II). Displacement ellipsoids are drawn at the 30% probability level. H atoms are shown as arbitrarily small spheres.

unit is oriented pseudoaxially and the benzyloxy substitutent at C2 is pseudo-equatorially disposed.

Experimental

p-Tolyl 3,5-*O*-(di-*t*-butylsilanediyl)-1-thio-α-D-arabinofuranoside (IV). To a solution of (III) (3.00 g, 11.7 mmol) in CH_2Cl_2 (92 ml) and DMF (19 ml) at 273 K was added 2,6-lutidine (5.50 ml, 47.2 mmol) and di-*t*-butylsilyl bis(trifluoromethanesulfonate) (3.93 ml, 10.8 mmol). The reaction mixture was stirred for 4.5 h, after which it was concentrated *in vacuo*, diluted with EtOAc and washed successively with water and brine. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a residue that was purified by flash column chromatography (hexanes, 10:1 hexanes/EtOAc) to afford (IV) as a white, amorphous solid (yield 3.17 g, 93%). Data for (IV): R_F 0.49 (5:1 hexanes/EtOAc); $[\alpha]_D$ +155.6 (c 0.7, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (*d*, 2H, J = 8.1 Hz, ArH), 7.13 (*d*, 2H, J = 8.4 Hz, ArH), 5.25 (*d*, 1H, J = 5.9 Hz, H-1), 4.31–4.34 (*dd*, 1H, J = 4.6, 4.6 Hz, H-5), 4.12–4.15 (*m*, 1H, H-2), 3.98–4.02 (*m*, 1H, H-3), 3.92–3.96 (*m*, 1H, H-5′), 3.88–3.91 (*m*, 1H, H-4), 2.33 (*s*, 3H, $ArCH_3$), 2.57 (*d*, 1H, J = 3.2 Hz, OH), 1.06 [*s*, 9H, $C(CH_3)_3$], 0.98 [*s*, 9H, $C(CH_3)_3$]; HRMS (ESI) *m*/*z* calculated for $C_{20}H_{32}O_4SSi$ + Na: 419.1683, found: 419.1680. Analysis calculated for $C_{20}H_{32}O_4SSi$: C 60.57, H 8.13, S 8.08%; found: C 60.09, H 8.06, S 7.66%.

p-Tolyl 2-*O*-benzyl-3,5-*O*-(di-*t*-butylsilanediyl)-1-thio-α-D-arabinofuranoside (II). Benzyl bromide (1.66 ml, 14.0 mmol) and NaH (0.36 g, 15.1 mmol) were added to a solution of (IV) (1.50 g, 3.78 mmol) in dry THF (28 ml) and the reaction mixture was stirred for 9.5 h at 273 K. The reaction was quenched by the addition of CH_3OH and the reaction mixture was concentrated *in vacuo*. The residue was diluted with CH_2Cl_2 and washed sequentially with a solution of 1 *N* HCl, a saturated solution of $NaHCO_3$, water and brine. The organic phase was dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was then purified by flash column chromatography (hexanes, 15:1 hexanes/EtOAc) to give the product as a white, amorphous solid (yield 1.75 g, 95%), which was recrystallized from hexanes–EtOAc (m.p. 349–351 K). Data for (II): R_F 0.77 (5:1 hexanes/EtOAc); $[\alpha]_D$ +157.2 (c 0.8, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41–7.43 (*m*, 2H, ArH), 7.31–7.39 (*m*, 5H, ArH), 7.09–7.10 (*m*, 2H, ArH), 5.36 (*d*, 1H, J = 5.4 Hz, H-1), 4.80 (ABq, 2H, J = 12.0 Hz, $PhCH_2$), 4.32–4.34 (*m*, 1H, H-5), 4.13–4.15 (*m*, 1H, H-3), 3.97–3.98 (*m*, 1H, H-2), 3.95–3.96 (*m*, 1H, H-5′), 3.89–3.92 (*m*, 1H, H-4), 2.33 (*s*, 3H, $ArCH_3$), 1.08 [*s*, 9H, $C(CH_3)_3$], 0.99 [*s*, 9H, $C(CH_3)_3$]; HRMS (ESI) *m*/*z* calculated for $C_{27}H_{38}O_4SSi$ + Na: 509.2153, found: 509.2152. Analysis calculated for $C_{27}H_{38}O_4SSi$: C 66.62, H 7.87, S 6.59%; found: C 66.82, H 7.89, S 6.10%.

Crystal data

$C_{27}H_{38}O_4SSi$
M_r = 486.72
Monoclinic, $P2_1$
a = 14.2256 (15) Å
b = 6.4531 (7) Å
c = 15.0426 (16) Å
β = 101.8651 (14)°
V = 1351.4 (2) Å^3
Z = 2
D_x = 1.196 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.19 mm^{-1}
T = 193 (2) K
Prism, colorless
0.52 × 0.41 × 0.15 mm

Data collection

Bruker SMART 1000 CCD PLATFORM area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2003)
T_{min} = 0.809, T_{max} = 0.972
9410 measured reflections
5524 independent reflections
4875 reflections with $I > 2\sigma(I)$
R_{int} = 0.019
θ_{max} = 26.4°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.036
$wR(F^2)$ = 0.091
S = 1.04
5524 reflections
299 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0466P)^2 + 0.1539P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}
Absolute structure: Flack (1983), 2491 Friedel pairs
Flack parameter: 0.00 (6)

H atoms were placed in idealized positions (C—H = 0.95–1.00 Å) and refined as riding with U_{iso}(H) = 1.2U_{eq}(C).

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2003); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 2003); software used to prepare material for publication: *SHELXTL*.

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