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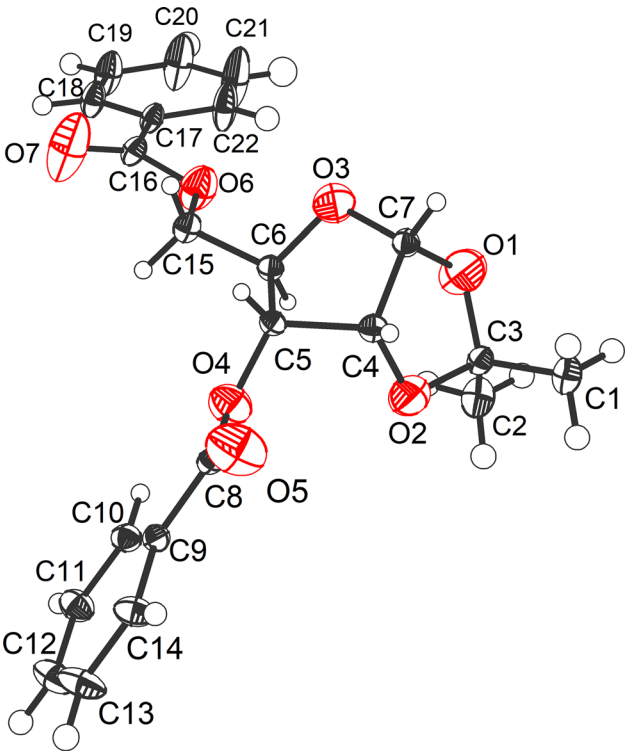
Crystal structure of 3,5–di-*O*-benzoyl-1,2-*O*-isopropylidene-α–D-ribose, $C_{22}H_{22}O_7$



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Abstract

$C_{22}H_{22}O_7$, orthorhombic, $C222_1$ (no. 20), a = 8.891(2) Å, b = 17.938(5) Å, c = 25.996(6) Å, V = 4146.0(18) Å^3, Z = 8, $R_{gt}(F)$ = 0.0461, $wR_{ref}(F^2)$ = 0.1189, T = 296 K.

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Table 1: Data collection and handling.

Crystal:	Block
Size:	0.30 × 0.28 × 0.22 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.10 mm^{-1}
Diffractometer, scan mode:	φ and ω
θ_{max}, completeness:	27.6°, >99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	16,702, 4539, 0.039
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 3164
$N(param)_{refined}$:	262
Programs:	CrysAlis^{PRO} [1], SHELX [2, 3], Diamond [4]

The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

1 Source of materials

The title compound was synthesized according to the previous reports [5–7]. 1,2-*O*-isopropylidene-α–D-ribose (1.9 g, 10.0 mmol) and triethylamine (6.9 mL, 50.0 mmol) were dissolved in anhydrous dichloromethane (30 mL). After it was cooled to 0 °C, benzoyl chloride (3.5 mL, 30.0 mmol) was added dropwise. After addition, the reaction mixture was stirred at room temperature for 3 h until TLC showed the reaction was finished. Then, the reaction was quenched with ice water. Another dichloromethane (30 mL) was added and the obtained reaction mixture was washed with 5 % aqueous HCl (30 mL × 2), water (30 mL × 2), and brine (30 mL × 2). After dried over anhydrous Na_2SO_4 and filtration, the solvent was evaporated under vacuum. The residue was purified to afford 3,5–di-*O*-benzoyl-1,2-*O*-isopropylidene-α–D-ribose (3.9 g, 98 %) by column chromatography, which was further recrystallized with ethanol. Crystals were acquired by slow evaporation from the solution at 268–270 K.

2 Experimental details

Fixed U_{iso} at 1.2 times for all C(H) groups, all C(H,H) groups and at 1.5 times for all C(H,H,H) groups; Ternary CH were refined with riding coordinates: C4(H4A), C5(H5A), C6(H6A), C7(H7A); Secondary CH_2 were refined with riding

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.1626 (5)	0.0859 (2)	0.38010 (14)	0.0652 (10)
H1A	0.116402	0.043860	0.396622	0.098*
H1B	0.087305	0.114108	0.362154	0.098*
H1C	0.236943	0.068727	0.356095	0.098*
C2	0.3521 (5)	0.0935 (2)	0.45118 (17)	0.0773 (12)
H2A	0.306689	0.050838	0.467146	0.116*
H2B	0.432646	0.077580	0.429196	0.116*
H2C	0.390962	0.126199	0.477237	0.116*
C3	0.2360 (3)	0.13426 (15)	0.41978 (11)	0.0449 (7)
C4	0.2015 (3)	0.25657 (16)	0.39634 (10)	0.0412 (7)
H4A	0.155877	0.264618	0.362469	0.049*
C5	0.2739 (3)	0.32682 (15)	0.41806 (10)	0.0364 (6)
H5A	0.218325	0.370889	0.406401	0.044*
C6	0.2528 (3)	0.31661 (15)	0.47597 (10)	0.0389 (6)
H6A	0.324881	0.279962	0.489135	0.047*
C7	0.0852 (4)	0.23637 (16)	0.43776 (11)	0.0439 (7)
H7A	−0.017381	0.237567	0.423974	0.053*
C8	0.4671 (3)	0.35846 (15)	0.36009 (11)	0.0385 (7)
C9	0.6304 (3)	0.37551 (16)	0.35571 (11)	0.0412 (7)
C10	0.7246 (3)	0.37604 (16)	0.39792 (12)	0.0491 (8)
H10A	0.687503	0.363802	0.430283	0.059*
C11	0.8743 (4)	0.3948 (2)	0.39188 (16)	0.0634 (10)
H11A	0.937685	0.395709	0.420315	0.076*
C12	0.9296 (5)	0.4122 (2)	0.34423 (17)	0.0788 (13)
H12A	1.030490	0.424649	0.340360	0.095*
C13	0.8372 (5)	0.4113 (3)	0.30249 (17)	0.0803 (13)
H13A	0.875577	0.422604	0.270146	0.096*
C14	0.6865 (4)	0.3936 (2)	0.30784 (13)	0.0604 (9)
H14A	0.623356	0.394020	0.279316	0.073*
C15	0.2631 (4)	0.38726 (15)	0.50629 (10)	0.0456 (7)
H15A	0.358821	0.411607	0.500152	0.055*
H15B	0.182983	0.421154	0.496545	0.055*
C16	0.2560 (4)	0.42233 (16)	0.59383 (11)	0.0487 (7)
C17	0.2418 (4)	0.39580 (16)	0.64724 (11)	0.0499 (8)
C18	0.2857 (5)	0.44208 (19)	0.68670 (13)	0.0673 (11)
H18A	0.321579	0.489607	0.679348	0.081*
C19	0.2770 (7)	0.4187 (2)	0.73654 (13)	0.0937 (16)
H19A	0.310966	0.449345	0.762933	0.112*
C20	0.2182 (10)	0.3498 (2)	0.74772 (16)	0.137 (3)
H20A	0.209099	0.334167	0.781687	0.165*
C21	0.1737 (11)	0.3048 (3)	0.70877 (16)	0.163 (4)
H21A	0.134819	0.257896	0.716242	0.196*
C22	0.1848 (7)	0.3272 (2)	0.65851 (14)	0.1032 (19)
H22A	0.153551	0.295724	0.632184	0.124*
O1	0.1254 (3)	0.16429 (12)	0.45359 (9)	0.0612 (7)
O2	0.3056 (2)	0.19714 (11)	0.39654 (8)	0.0507 (6)
O3	0.1028 (2)	0.28716 (11)	0.47855 (7)	0.0469 (5)
O4	0.4308 (2)	0.33617 (10)	0.40787 (7)	0.0404 (5)
O5	0.3767 (3)	0.36370 (14)	0.32595 (8)	0.0577 (6)
O6	0.2492 (2)	0.36672 (10)	0.55980 (7)	0.0467 (5)
O7	0.2735 (4)	0.48615 (12)	0.58175 (9)	0.0806 (9)

coordinates: C15(H15A,H15B); Me were refined with riding coordinates: C1(H1A,H1B,H1C), C2(H2A,H2B,H2C); Aromatic/amide H were refined with riding coordinates: C10(H10A), C11(H11A), C12(H12A), C13(H13A), C14(H14A), C18(H18A), C19(H19A), C20(H20A), C21(H21A), C22(H22A).

3 Comment

Nucleosides, the basic building blocks of nucleic acids such as RNA and DNA, play crucial roles in many biological processes [8]. Modified nucleosides have demonstrated great therapeutic promise for antiviral and anticancer chemotherapies [9, 10]. Among them, sugar-modified nucleosides are a type of modified nucleoside with alterations to the ribose component at the 2′, 3′, or 5′ positions, affecting the conformation, stability, and reactivity of the nucleoside [11]. For instance, 2′-deoxy-2-fluoro-β–D-arabinoadenine (Fludarabine) is an FDA approved drug for the treatment of chronic lymphocytic leukemia (CLL) [12]. During our ongoing work to synthesize novel nucleoside analogues, 3,5-di-*O*-benzoyl-1,2-*O*-isopropylidene-α–D-ribose has been identified as a highly desirable key intermediate [13, 14]. Using this intermediate, we can synthesize a series of novel nucleosides and test them for antiviral activity. Recently, our group has developed an improved synthetic approach using tetra-*O*-acetyl-β–D-ribose as the starting material in three steps, with an overall yield of 86 %. The crystal structure of this intermediate has not been reported previously, which is crucial for analysing its conformation.

The title structure (see Figure) consists of a furanosy D-ribose with four OH groups protected by two benzoyl groups at O4 and O6 and a bridged isopropylidene at O1 and O2, where a large dihedral angle (116.1°) between O3–C7–C4–C5 and O1–C7–C4–O2 was observed. The orientation between C6–C15 bond and C7–O1 bond is a trans-form (that is, α-configuration). Summarily, the bond lengths and angles are in the expected ranges.

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Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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