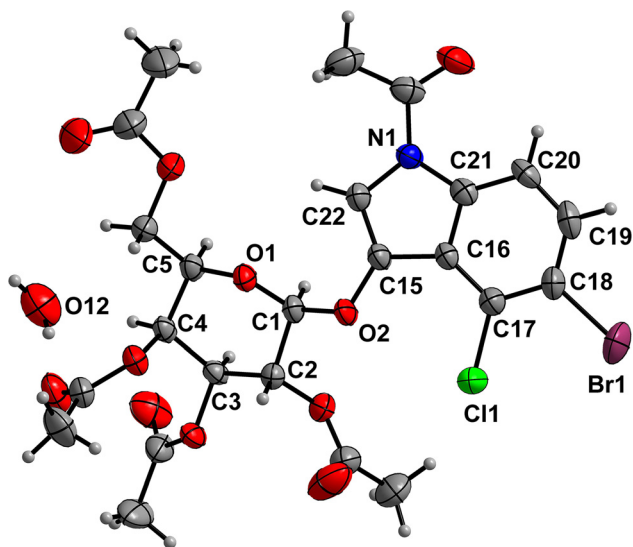


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Crystal structure of (2*R*,3*S*,4*S*,5*R*,6*S*)-2-(acetoxymethyl)-6-((1-acetyl-5-bromo-4-chloro-1*H*-indol-3-yl)oxy)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate hemihydrate C₂₄H₂₅BrClNO₁₁



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Abstract

C₂₄H₂₅BrClNO₁₁, monoclinic, *C*2 (no. 5), *a* = 28.914(5) Å, *b* = 7.9349(14) Å, *c* = 13.062(2) Å, β = 114.867(3)°, *V* = 2718.9(8) Å³, *Z* = 4, *R*_{gt}(*F*) = 0.0352, *wR*_{ref}(*F*²) = 0.0888, *T* = 296.15 K.

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The crystal 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.

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Table 1: Data collection and handling.

Crystal:	Block, clear light colourless
Size:	0.03 × 0.02 × 0.02 mm
Wavelength:	Mo Kα radiation (0.71073 Å)
μ:	1.67 mm ⁻¹
Diffractometer, scan mode:	Bruker APEX-II, φ and ω-scans
θ _{max} , completeness:	27.6°, >99%
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} , <i>R</i> _{int} :	8181, 5436, 0.018
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	<i>I</i> _{obs} > 2 σ(<i>I</i> _{obs}), 4033
<i>N</i> (<i>param</i>) _{refined} :	356
Programs:	Bruker programs [1], OLEX2 [2], SHELX [3], DIAMOND [4]

Source of materials

The title compound was synthesized by an improved Schmidt glycosylation [5]. To the solution of 5-bromo-4-chloro-3-indoxyl-1-acetate (2.88 g, 10 mmol) [6] and 2,3,4,6-tetra-*O*-acetyl-D-galactopyranosyl trichloroacetimidate (9.84 g, 20 mmol) [7] in anhydrous dichloromethane (100 mL), Et₃N (0.5 mL) was added firstly and followed by dropwise addition of BF₃ · Et₂O (5 mL) at −20 °C under argon atmosphere. The obtained mixture was stirred for 4 h until TLC showed the reaction was complete. After the reaction was quenched by saturated NaHCO₃ solution (10 mL), it was diluted with additional dichloromethane (100 mL). Then, the organic phase was washed with H₂O (50 mL) and saturated NaCl (50 mL). After dried with anhydrous Na₂SO₄ and filtered, the solvent was removed in vacuo. The obtained residue was purified by column chromatography to afford the title compound (2.80 g, 45.3%), which was further purified by recrystallization from ethanol. Crystals were obtained by slow evaporation from the ethanol solution at 268–270 K.

Experimental details

Hydrogen atoms were added using the AFIX options of the SHELX system. Their *U*_{iso} values were set to 1.2*U*_{eq} of all

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
Br1	0.01769 (2)	0.36828 (10)	0.38204 (4)	0.0875 (2)
Cl1	0.12887 (3)	0.37983 (18)	0.59233 (7)	0.0628 (3)
O1	0.32689 (7)	0.4137 (3)	0.68405 (16)	0.0341 (5)
O2	0.24105 (7)	0.4127 (3)	0.62902 (16)	0.0374 (6)
O3	0.25302 (8)	0.5958 (3)	0.82307 (18)	0.0392 (6)
O4	0.22933 (12)	0.3711 (5)	0.8930 (3)	0.0817 (9)
O5	0.35217 (8)	0.5777 (3)	0.99913 (17)	0.0384 (6)
O6	0.39719 (12)	0.8173 (4)	1.0401 (2)	0.0686 (9)
O7	0.40200 (7)	0.3654 (3)	0.91663 (15)	0.0362 (5)
O8	0.46503 (10)	0.4853 (4)	1.0655 (2)	0.0612 (8)
O9	0.40208 (8)	0.4274 (3)	0.59806 (19)	0.0515 (7)
O10	0.47939 (11)	0.3305 (7)	0.6380 (2)	0.0971 (14)
O11	0.19140 (11)	0.5443 (4)	0.1542 (2)	0.0677 (9)
O12	0.5000	0.8226 (7)	1.0000	0.0860 (15)
H12D ^a	0.4770	0.7781	1.0155	0.129*
H12E ^a	0.5126	0.7407	0.9783	0.129*
N1	0.21342 (9)	0.4861 (4)	0.3385 (2)	0.0365 (6)
C1	0.28626 (10)	0.5002 (5)	0.6922 (2)	0.0320 (7)
H1	0.2842	0.6155	0.6637	0.038*
C2	0.29389 (10)	0.5025 (4)	0.8146 (2)	0.0310 (7)
H2	0.2952	0.3875	0.8430	0.037*
C3	0.34318 (11)	0.5960 (4)	0.8831 (2)	0.0321 (7)
H3	0.3385	0.7157	0.8630	0.039*
C4	0.38792 (11)	0.5291 (4)	0.8633 (2)	0.0322 (8)
H4	0.4168	0.6067	0.8961	0.039*
C5	0.37367 (11)	0.5075 (4)	0.7381 (2)	0.0332 (7)
H5	0.3687	0.6194	0.7033	0.040*
C6	0.41433 (11)	0.4180 (5)	0.7169 (3)	0.0399 (9)
H6A	0.4471	0.4704	0.7601	0.048*
H6B	0.4162	0.3012	0.7401	0.048*
C7	0.22428 (14)	0.5163 (6)	0.8668 (3)	0.0495 (10)
C8	0.18588 (16)	0.6330 (6)	0.8774 (4)	0.0657 (12)
H8A	0.2027	0.7329	0.9171	0.098*
H8B	0.1693	0.5780	0.9183	0.098*
H8C	0.1610	0.6631	0.8035	0.098*
C9	0.38119 (13)	0.6990 (6)	1.0709 (3)	0.0459 (9)
C10	0.39033 (17)	0.6572 (7)	1.1884 (3)	0.0719 (14)
H10A	0.3583	0.6417	1.1927	0.108*
H10B	0.4087	0.7475	1.2375	0.108*
H10C	0.4099	0.5553	1.2111	0.108*
C11	0.44063 (11)	0.3632 (6)	1.0211 (3)	0.0415 (8)
C12	0.44785 (18)	0.1916 (6)	1.0709 (4)	0.0657 (12)
H12A	0.4154	0.1456	1.0597	0.099*
H12B	0.4694	0.1978	1.1502	0.099*
H12C	0.4635	0.1205	1.0349	0.099*
C13	0.43916 (14)	0.3766 (7)	0.5703 (3)	0.0629 (11)
C14	0.42313 (18)	0.3845 (11)	0.4459 (3)	0.107 (2)
H14A	0.3925	0.3201	0.4082	0.160*
H14B	0.4496	0.3388	0.4281	0.160*
H14C	0.4170	0.4996	0.4213	0.160*
C15	0.22233 (11)	0.4379 (4)	0.5140 (2)	0.0342 (8)
C16	0.16844 (11)	0.4370 (4)	0.4413 (2)	0.0306 (7)
C17	0.12481 (12)	0.4099 (5)	0.4576 (3)	0.0396 (8)
C18	0.07829 (11)	0.4096 (5)	0.3655 (3)	0.0438 (9)
C19	0.07509 (13)	0.4372 (5)	0.2580 (3)	0.0462 (10)

Table 2: (continued)

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
H19	0.0433	0.4344	0.1971	0.055*
C20	0.11701 (13)	0.4683 (4)	0.2387 (3)	0.0392 (8)
H20	0.1143	0.4891	0.1663	0.047*
C21	0.16437 (12)	0.4677 (4)	0.3319 (2)	0.0330 (7)
C22	0.24821 (12)	0.4667 (5)	0.4508 (3)	0.0385 (8)
H22	0.2835	0.4726	0.4777	0.046*
C23	0.22526 (14)	0.5214 (5)	0.2469 (3)	0.0446 (9)
C24	0.28000 (16)	0.5245 (7)	0.2712 (4)	0.0641 (12)
H24A	0.2964	0.6155	0.3220	0.096*
H24B	0.2837	0.5404	0.2022	0.096*
H24C	0.2955	0.4198	0.3052	0.096*

^aOccupancy: 0.5.

C(H) and C(H,H) groups. Their U_{iso} values were set to $1.5U_{\text{eq}}$ of all C(H,H,H) groups and O(H,H) groups. The absolute structure was established by the Flack parameter (0.033(7)).

Comment

The indoxyl glycosides are widely used as chromogenic substrates for detecting enzyme activities in histochemistry, biochemistry and bacteriology [8, 9]. Among them, 5-bromo-4-chloro-3-indoxyl- β -D-galactoside (X-gal) is applied as the reporter of gene *lac-z* derived from *E. coli*, which precipitate as greenish-blue 5,5'-dibromo-4,4'-dichloroindigo. Although X-gal is commercially available, it is very expensive. Since X-gal was first described by Horwitz in 1964 [10], its synthesis was seldom reported [11, 12]. During our large-scale employment X-gal in chromogenic culture media, an efficient synthetic process is needed. In addition, the crystal structures of indoxyl glycosides were not reported in the literature, which are important for understanding their interaction with corresponding glycosyl enzymes. During the development of its new synthetic process, the crystal structure of the title compound was obtained.

The asymmetric unit of the title structure contains one (*N*-acetyl-5-bromo-4-chloro-3-indoxyl)-2,3,4,6-tetra-*O*-acetyl- β -D-galactopyranoside and half a water molecule. The galactopyranoside derivate consists of *N*-acetyl-5-bromo-4-chloro-3-indoxyl and tetra-acetyl-protected galactopyranose that exhibit slightly distorted chair conformation. Bond lengths and angles are all 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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