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# (8*S*)-3-(2-Deoxy-3,5-di-*O*-*p*-toluoyl-α-D-*erythro*-pentofuranosyl)-3,6,7,8-tetrahydroimidazo[4,5-*d*][1,3]diazepin-8-ol

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**Key indicators**

Single-crystal X-ray study
*T* = 296 K
Mean σ(C–C) = 0.004 Å
*R* factor = 0.036
*wR* factor = 0.060
Data-to-parameter ratio = 8.9

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



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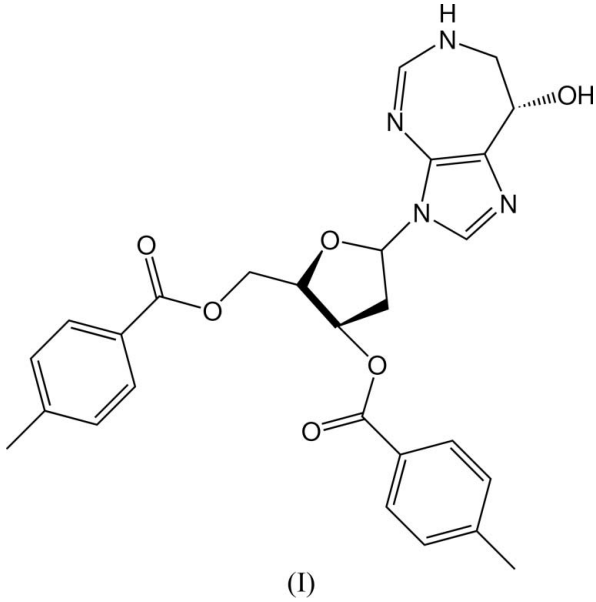
In the asymmetric unit of the title compound, $C_{27}H_{28}N_4O_6$, there are two independent molecules which have different conformations. The tetrahydrofuran and dihydrodiazepine rings adopt envelope conformations. The hydroxy, amino and carbonyl groups are all involved in hydrogen bonding.

## Comment

The title compound, (I), is an intermediate in the synthesis of pentostatin, which is an antimetabolite/antineoplastic agent, one of the newest chemotherapy drugs (Kasibhatla & Erion, 2000; Kasibhatla *et al.* 2001).




(I)

Compound (I) crystallizes with two independent molecules, *A* and *B*, in the asymmetric unit. These two molecules have different conformations (Fig. 1 and Table 1), and have different hydrogen-bonding characteristics (see below). In molecule *A*, the carbonyl group C12═O14 deviates from the least-squares plane of the C13–C18 aromatic ring, as shown by the O14—C12—C13—C14 torsion angle of 23.2 (5) Å. Iy contrast, in molecule *B*, the O34—C42—C43—C44 torsion angle is 2.5 (5)°, indicating coplanarity. In addition, there are significant differences in the relative orientations of the $C_6$-aromatic rings of the tolyl groups in molecules *A* and *B*, as seen by the dihedral angles between them of 30.33 (13) and 22.85 (13)°, respectively. Furthermore, in molecule *A*, the imidazole ring plane is almost parallel to the C21–C26 aromatic ring, forming a dihedral angle of 5.75 (14)°, but forming a dihedral angle of 29.76 (13)° with the second

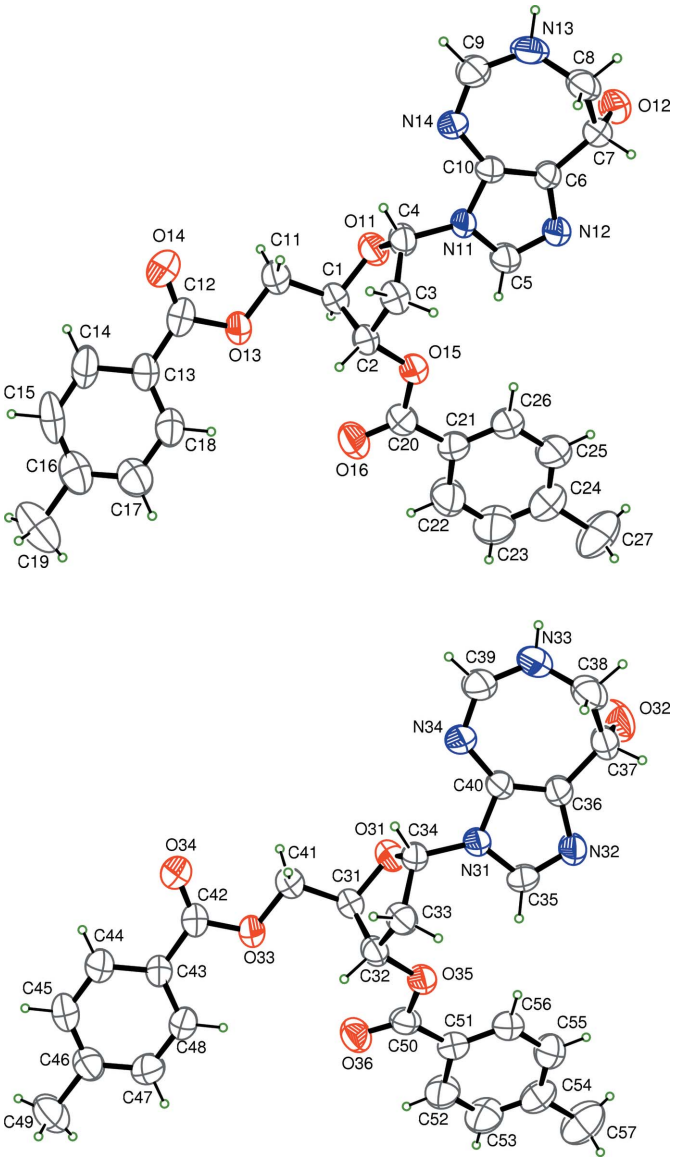



**Figure 1**
The molecular structures of the two indpendent molecules comprising the asymmetric unit of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

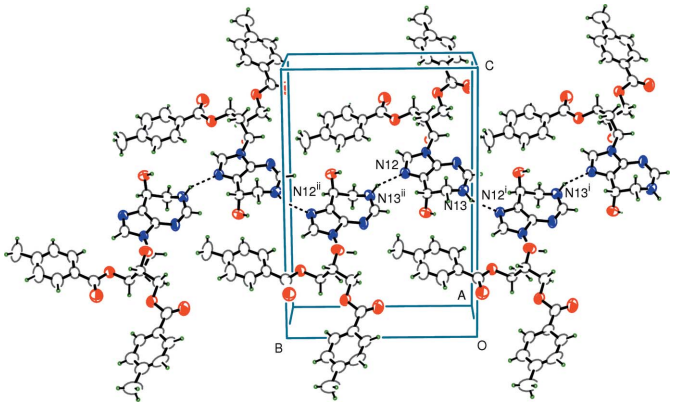



**Figure 2**
A packing diagram for (I). Dashed lines indicate hydrogen bonds. [Symmetry codes: (i) $1-x,-\frac{1}{2}+y,1-z$; (ii) $1-x,\frac{1}{2}+y,1-z$.]

aromatic ring containing C13–C18. In contrast, in molecule *B*, the imidazole ring is almost parallel to the C43–C48 aromatic ring [dihedral angle 7.57 (12)°] but forms a dihedral angle of 26.42 (13)° with the C51–C56 ring, *i.e.* opposite to what is observed for molecule *A*. In both independent molecules, the tetrahydrofuran and dihydrodiazepine rings adopt envelope conformations.

The hydroxy, amino and carbonyl groups are all involved in the hydrogen-bonding scheme, as detailed in Table 2. N—H···N hydrogen bonds link the molecules into a linear hydrogen-bonded ribbon motif along the *b*-axis direction and this chain is further stabilized by O—H···O interactions (Fig. 2).

## Experimental

To 3-(2-deoxy-3,5-di-*O*-*p*-toluoyl-α-D-*erythro*-pentafuranosyl)-6,7-dihydroimidazo[4,5-*d*][1,3]diazepin-8(3*H*)-one (5.0 g, 0.01 mol) dissolved in MeOH (150 ml) was added sodium borohydride (0.15 g, 0.004 mol). The solution was stirred at 298 K for 0.5 h, at the end of which time the excess reducing agent was decomposed by the addition of dry ice. High-performance liquid chromatography revealed a *ca* 1:1 mixture of (8*S*)-3-(2-deoxy-3,5-di-*O*-*p*-toluoyl-α-D-*erythro*-pentafuranosyl)-3,6,7,8-tetrahydroimidazo[4,5-*d*][1,3]diazepin-8-ol and (8*R*)-3-(2-deoxy-3,5-di-*O*-*p*-toluoyl-α-D-*erythro*-pentafuranosyl-3,6,7,8-tetrahydroimidazo[4,5-*d*][1,3]diazepin-8-ol. The above diastereoisomeric mixture was decolorized using active carbon and filtered. Evaporation of the filtrate left 4.2 g of a light-brown solid residue. This solid was dissolved in hot ethyl acetate (150 ml) and the solution was left to stand at 273 K for 3 d. The crystalline 8*S*-isomer was filtered off and washed with cold ethyl acetate. Recrystallization three times gave 99% analytically pure 8*S*-isomer (Baker & Putt, 1979; Showalter & Putt, 1981; Chan *et al.*, 1982). Compound (I) was recrystallized from an acetone solution yielding yellow crystals suitable for the X-ray diffraction study.

### *Crystal data*

$C_{27}H_{28}N_4O_6$
$M_r = 504.54$
Monoclinic, $P2_1$
$a = 10.492\ (2)$ Å
$b = 12.849\ (3)$ Å
$c = 18.645\ (5)$ Å
$\beta = 97.949\ (10)°$
$V = 2489.5\ (10)$ Å$^3$
$Z = 4$
$D_x = 1.346$ Mg m$^{-3}$
Mo $K\alpha$ radiation
$\mu = 0.10$ mm$^{-1}$
$T = 296\ (1)$ K
Block, yellow
0.30 × 0.14 × 0.12 mm

### *Data collection*

Rigaku R-AXIS RAPID diffractometer
$\omega$ scans
Absorption correction: none
24329 measured reflections
5949 independent reflections
2974 reflections with $F^2 > 2\sigma(F^2)$
$R_{int} = 0.044$
$\theta_{max} = 27.5°$

### *Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.036$
$wR(F^2) = 0.060$
$S = 1.00$
5949 reflections
668 parameters
H-atom parameters constrained
$w = 1/[0.8800\sigma(F_o^2)]/(4F_o^2)$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.32$ e Å$^{-3}$
$\Delta\rho_{min} = -0.34$ e Å$^{-3}$
Extinction correction: Larson (1970), equation 22
Extinction coefficient: 198 (9)

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| O13—C11 | 1.437 (3) | N13—C9 | 1.344 (4) |
| O13—C12 | 1.354 (3) | N14—C9 | 1.274 (3) |
| O14—C12 | 1.193 (4) | N14—C10 | 1.382 (3) |
| O15—C20 | 1.341 (3) | N32—C36 | 1.378 (3) |
| O33—C41 | 1.455 (3) | N33—C39 | 1.339 (4) |
| O33—C42 | 1.335 (3) | N34—C39 | 1.292 (3) |
| O34—C42 | 1.208 (4) | N34—C40 | 1.368 (3) |
| O35—C50 | 1.356 (3) | C6—C7 | 1.486 (3) |
| N12—C6 | 1.392 (3) | C36—C37 | 1.505 (4) |
| | | | |
| C5—N11—C4—O11 | −68.0 (3) | O13—C12—C13—C18 | 24.0 (4) |
| C10—N11—C4—O11 | 116.9 (3) | O14—C12—C13—C14 | 23.2 (5) |
| C35—N31—C34—O31 | −85.1 (3) | O33—C42—C43—C48 | 3.0 (4) |
| C40—N31—C34—O31 | 91.9 (3) | O34—C42—C43—C44 | 2.5 (5) |

**Table 2**
Hydrogen-bond geometry (Å, °).

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O12—H121···O34$^{i}$ | 0.91 | 1.98 | 2.889 (3) | 173 |
| O32—H321···O16 | 0.91 | 2.23 | 3.013 (3) | 144 |
| N13—H130···N12$^{i}$ | 0.86 | 2.22 | 2.975 (3) | 146 |
| N33—H330···N32$^{ii}$ | 0.86 | 2.33 | 2.954 (3) | 130 |

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

O-bound H atoms were located from difference Fourier maps and included in the refinement based on the as-found O—H bond lengths (O—H = 0.91 Å), and with $U_{iso}$(H) = 1.2$U_{eq}$(parent atom). The N– and C-bound H atoms were included in the riding-model approximation, with N—H = 0.86 Å and C—H = 0.93–0.98 Å, and $U_{iso}$(H) = 1.2$U_{eq}$(parent atom). In the absence of significant anomalous scattering effects, 4005 Friedel pairs were averaged in the final refinement.

Data collection: *PROCESS-AUTO* (Rigaku, 1998); cell refinement: *PROCESS-AUTO*; data reduction: *CrystalStructure* (Rigaku/MSC, 2004); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *CrystalStructure*.

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