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A carbocyclic analogue of a protected β-D-2-deoxyribosylamine

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Key indicators

Single-crystal X-ray study
T = 213 K
Mean σ(C–C) = 0.003 Å
R factor = 0.031
wR factor = 0.083
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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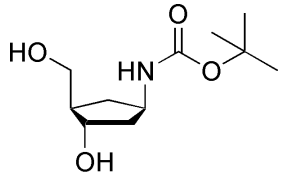
The title compound, *tert*-butyl *N*-[(1*R*,3*S*,4*R*)-3-hydroxy-4-(hydroxymethyl)cyclopentyl]carbamate, $C_{11}H_{21}NO_4$, is a very important intermediate for the enantioselective synthesis of carbocyclic analogues of 2′-deoxyribonucleotides. Its crystal structure proves that the relative substitution of the cyclopentane ring in this intermediate is the same as that in β-2-deoxyribosylamine.

Comment

Carbocyclic analogues of ribonucleotides exhibit an improved stability, because they do not contain the labile glycosidic linkage between the heterocycle and the sugar moiety. This feature makes them inhibitors of DNA glycosylases, due to the fact that they can recognize the functional groups of the analogue but are unable to cleave off the heterocycle (Chepanoske *et al.*, 1999). Furthermore, they are used in antiretroviral pharmaceuticals, such as Carbavir (Vince & Brownell, 1990) and 1592U89 (Daluge *et al.*, 1997). Here, the solid-state structure of a key intermediate, (I), of these carbocyclic nucleosides is discussed. Recently, it has also been used in the development of a stereochemically pure carbocyclic analogue of the common formamidopyrimidine of the guanosine (FaPydG) DNA lesion (Ober *et al.*, 2003).



(I)

The cyclopropane ring of the molecule of (I) exhibits a phase angle of pseudorotation (*P*) of 155.6° and an amplitude (ψ_m) of 41.2°. These values were calculated from the endocyclic torsion angles of the molecule (Altona & Sunderalingam, 1972). This result clearly indicates the presence of the south ^2E (C2′-*endo*), which is featured by the deoxyribose subunits of the nucleotides in a DNA strand with a B conformation. In B-DNA, the furanose moieties exhibit a phase angle of pseudorotation in the range 144–190° and an amplitude of 38.6±3° (Thibaudeau *et al.*, 1998). It is also found that the torsion angle χ around C5—C1—N1—C7 (as defined by Marklay *et al.*, 1998) in this intermediate is −105°, corresponding to an *anti* conformation.

The N- and O-bonded H atoms are involved in hydrogen bonds (see Table 2).

Experimental

The title compound was prepared from (1*R*)-(−)-2-azabicyclo[2.2.1]hept-5-en-3-one in several steps (Dominguez & Cullis, 1999). Single colourless orthorhombic crystals were obtained by evaporation of a saturated ethyl acetate solution for several days.

Crystal data

$C_{11}H_{21}NO_4$
M_r = 231.29
Orthorhombic, $P2_12_12_1$
a = 5.2765 (6) Å
b = 6.2163 (8) Å
c = 38.109 (4) Å
V = 1250.0 (3) Å^3
Z = 4
D_x = 1.229 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 9527 reflections
θ = 2.1–25.6°
μ = 0.09 mm^{-1}
T = 213 (2) K
Prism, colourless
0.35 × 0.20 × 0.18 mm

Data collection

Stoe IPDS-II diffractometer
ω scans
Absorption correction: none
8255 measured reflections
1430 independent reflections
1266 reflections with $I > 2\sigma(I)$
R_{int} = 0.051
θ_{max} = 25.6°
$h = -6 \rightarrow 6$
$k = -7 \rightarrow 7$
$l = -46 \rightarrow 46$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.083
S = 1.04
1430 reflections
160 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.061P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.12 e Å^{-3}
$\Delta\rho_{min}$ = −0.12 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.084 (8)

Table 1
Selected geometric parameters (Å, °).

C1—C2	1.518 (2)	C3—C4	1.538 (2)
C1—C5	1.530 (2)	C4—C5	1.544 (2)
C2—C3	1.521 (2)		
C2—C1—C5	103.39 (13)	C3—C4—C5	105.43 (13)
C1—C2—C3	103.54 (13)	C1—C5—C4	106.37 (13)
C2—C3—C4	104.75 (13)		
C7—N1—C1—C5	−105.46 (19)	O1—C3—C4—C5	−98.00 (15)
N1—C1—C2—C3	163.62 (15)	C2—C3—C4—C5	20.05 (18)
C5—C1—C2—C3	40.30 (17)	N1—C1—C5—C4	−151.99 (15)
C1—C2—C3—O1	77.14 (17)	C2—C1—C5—C4	−27.72 (18)
C1—C2—C3—C4	−37.60 (18)	C6—C4—C5—C1	127.70 (15)
O1—C3—C4—C6	141.17 (14)	C3—C4—C5—C1	4.76 (19)
C2—C3—C4—C6	−100.79 (17)		

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H10···O2^{i}	0.89 (2)	1.81 (2)	2.6790 (18)	166 (2)
O2—H11···O1^{ii}	0.95 (2)	1.76 (2)	2.6907 (18)	166.8 (19)
N1—H12···O3^{ii}	0.86 (2)	2.30 (3)	3.119 (2)	160 (2)

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

The reflections for the cell refinement were selected from the data set before the 'partials' were combined.The H atoms bonded to N and O atoms were refined independently with a common refined isotropic displacement parameter. The H atoms of the five-membered ring (and C6) were initially refined independently, but in the final stages of refinement they were included in the riding model approximation with refined C—H distances; these are in the range 0.95–1.00 Å. The isotropic displacement parameters were refined, but a common parameter was refined for both atoms of the methylene groups. The H atoms bonded to methyl C atoms were included in calculated positions with distances of 0.97 Å and subsequently included in the refinement in the riding model approximation with $U_{iso} = 1.5U_{eq}$(C). In the absence of anomalous dispersion effects, 911 Friedel pairs were merged, and the absolute configuration was assumed from the synthesis.

Data collection: *X-AREA* (Stoe & Cie, 2003); cell refinement: *X-AREA*; data reduction: *X-AREA*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *DIAMOND* (Brandenburg, 2001); software used to prepare material for publication: *SHELXL*97.

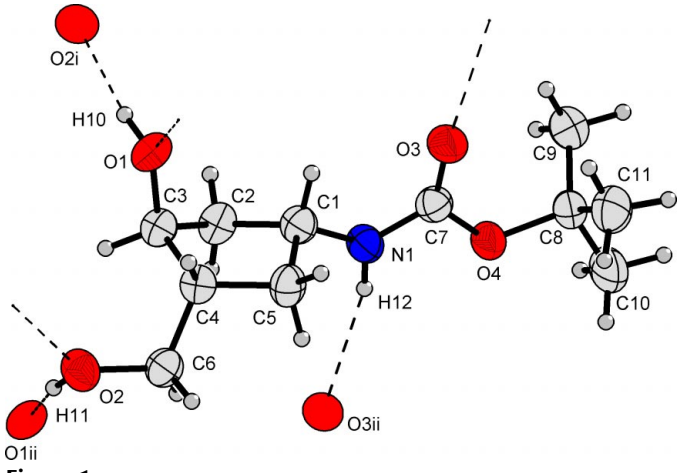


Figure 1
A view of (I), showing the hydrogen-bond interactions (dashed lines). Displacement ellipsoids are drawn at the 50% probability level. [Symmetry codes (i) and (ii) as in Table 2].

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