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3-*epi*-Casuarine monohydrate

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Key indicators

Single-crystal X-ray study
T = 150 K
Mean *σ*(C–C) = 0.003 Å
Disorder in main residue
R factor = 0.047
wR factor = 0.072
Data-to-parameter ratio = 6.9

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

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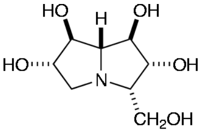
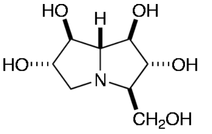
The title compound [systematic name: (1*R*,2*R*,3*S*,6*S*,7*S*,7a*R*)-3-hydroxymethyl-1,2,6,7-tetrahydroxypyrrolizidine monohydrate or (2*S*,3*R*,4*R*,5*R*,6*S*,7*S*)-2-hydroxymethyl-1-azabicyclo-[3.3.0]octan-3,4,6,7-tetraol monohydrate], $C_8H_{15}NO_5\cdot H_2O$, was formed in a synthetic sequence in which there were several ambiguities in the stereochemistry of the reactions. Its crystal structure was determined to resolve these ambiguities.

Comment

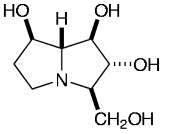
3-*epi*-Casuarine, (1), is a synthetic epimer of the natural product casuarine, (2) (Nash *et al.*, 1994), the most heavily oxygenated of the polyhydroxylated alkaloids which can be viewed as sugar mimics. Although the 6-*α*-D-glucoside of (2) is also a natural product (Wormald *et al.*, 1996), as yet no other diastereomers of casuarine have been isolated as natural products. In contrast, since the initial isolation of alexine (3) (without a hydroxyl group at C6) (Fellows *et al.*, 1988), a number of stereoisomers have been isolated (Asano *et al.*, 2000).



(1)



(2)



(3)

A combination of crystal structures and NMR studies have firmly established solid-state and solution conformations of a number of stereoisomers of alexine (Wormald *et al.*, 1998; Kato *et al.*, 2003), which may be used to rationalize their biological activity. Studies on the epimers of casuarine at

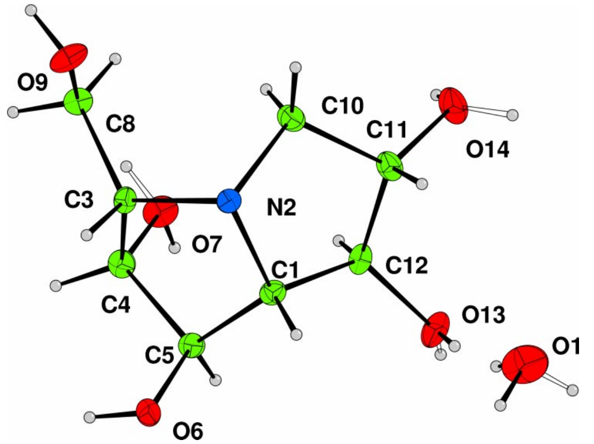


Figure 1
The asymmetric unit of (1), with displacement ellipsoids drawn at the 50% probability level. H-atom radii are arbitary. Unfilled O—H bonds indicate one of each pair of disordered H-atom positions.

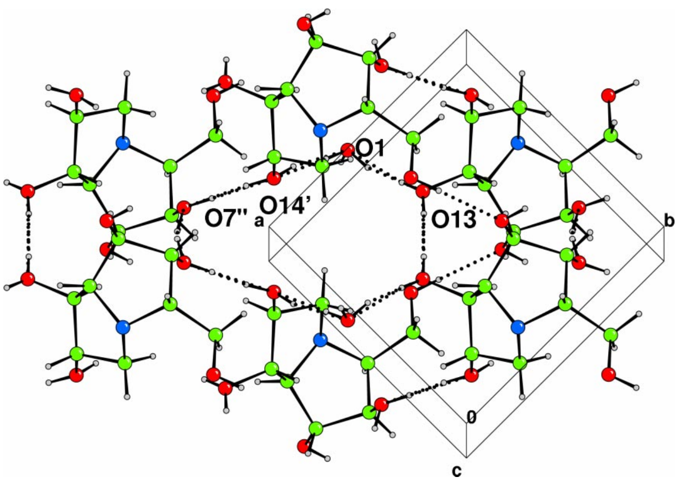


Figure 2
Partial packing diagram showing how the disorder in the hydrogen-bonded network results from the crystallographic twofold axis lying horizontally across the figure. The molecule containing atom O14′ is generated by the symmetry code $(2 - y, -x, \frac{1}{2} - z)$ and that containing atom O7″ by $(1 + x, 2 - y, z)$. Hydrogen bonds are shown as dotted lines.

present are scant (Bell *et al.*, 1997). Since coupling constants are notoriously unreliable in assigning the relative configuration at stereogenic centres in five-membered ring systems, a crystal structure was necessary to firmly establish the structure of the title compound, (1), and to allow comparison of the solution and solid-state conformation; this may allow the development of rationales for the glycosidase inhibition of casuarines.

Fig. 1 shows the asymmetric unit of (1). The open O—H bonds shown are to one of each pair of disordered H atoms. The crystal structure consists of a three-dimensional hydrogen-bonded network. Of particular interest is the hydrogen-bonded ring shown in Fig. 2. Because this ring straddles a twofold rotation axis, the hydrogen bonds in it are necessarily disordered and the H atoms have occupancy factors of exactly one-half.

Experimental

The title compound (Nash *et al.*, 2004) was recrystallized from 1,4-dioxane to give colourless prismatic crystals.

Crystal data

$C_8H_{15}NO_5 \cdot H_2O$
$M_r = 223.23$
Tetragonal, $P4_12_12$
$a = 7.6230$ (2) Å
$c = 33.8174$ (10) Å
$V = 1965.13$ (9) Å^3
$Z = 8$
$D_x = 1.509$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1241 reflections
$\theta = 5$–27°
$\mu = 0.13$ mm^{-1}
$T = 150$ K
Prism, colourless
0.40 × 0.20 × 0.20 mm

Data collection

Nonius KappaCCD diffractometer
ω scans
Absorption correction: multi-scan *DENZO/SCALEPACK* (Otwinowski & Minor, 1997)
$T_{min} = 0.96$, $T_{max} = 0.97$
9161 measured reflections
1372 independent reflections
1372 reflections with $I > -3\sigma(I)$
$R_{int} = 0.021$
$\theta_{max} = 27.5°$
$h = -9 \rightarrow 9$
$k = -6 \rightarrow 7$
$l = -42 \rightarrow 43$

Refinement

Refinement on F^2
$R[F^2>2\sigma(F^2)] = 0.047$
$wR(F^2) = 0.072$
$S = 1.01$
1372 reflections
199 parameters
H atoms: only coordinates refined
$w = 1/[\sigma^2(F) + (0.029P)^2 + 0.165P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.35$ e Å^{-3}
$\Delta\rho_{min} = -0.34$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

C1—C5	1.528 (3)	C5—O6	1.428 (2)
C1—C12	1.530 (3)	C8—O9	1.433 (2)
C1—N2	1.509 (2)	C10—C11	1.524 (3)
C3—C4	1.531 (3)	C10—N2	1.494 (2)
C3—C8	1.511 (3)	C11—C12	1.517 (3)
C3—N2	1.494 (3)	C11—O14	1.418 (2)
C4—C5	1.526 (3)	C12—O13	1.420 (2)
C4—O7	1.431 (2)		
C5—C1—C12	116.88 (16)	C3—C8—O9	109.04 (16)
C5—C1—N2	106.92 (15)	C11—C10—N2	103.10 (16)
C12—C1—N2	105.52 (15)	C10—C11—C12	101.71 (17)
C4—C3—C8	115.05 (17)	C10—C11—O14	112.16 (18)
C4—C3—N2	105.52 (15)	C12—C11—O14	114.32 (16)
C8—C3—N2	116.31 (16)	C1—C12—C11	102.10 (16)
C3—C4—C5	101.50 (16)	C1—C12—O13	113.73 (16)
C3—C4—O7	109.85 (17)	C11—C12—O13	114.58 (17)
C5—C4—O7	109.04 (15)	C1—N2—C3	106.05 (15)
C1—C5—C4	103.35 (16)	C1—N2—C10	107.10 (14)
C1—C5—O6	107.24 (16)	C3—N2—C10	117.00 (16)
C4—C5—O6	111.76 (15)		

H atoms were found in difference maps and refined with $U_{iso} = 0.02$ Å^2. In the absence of significant anomalous dispersion effects, Friedel pairs were averaged.

Data collection: *COLLECT* (Nonius, 1997); cell refinement: *DENZO/SCALEPACK*; data reduction: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); structure solution: *SIR*92 (Altomare *et al.*, 1994); structure refinement: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *CAMERON* (Watkin *et al.*, 1996).

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(1*R*,2*R*,3*S*,6S,7*S*,7aR)-3-Hydroxymethyl-1,2,6,7- tetrahydroxypyrrolizidine monohydrate or (2*S*,3*R*,4*R*,5*R*,6*S*,7S)-2-Hydroxymethyl- 1-azabicyclo[3.3.0]-octan-3,4,6,7-tetraol monohydrate

Crystal data

$C_8H_{15}NO_5 \cdot H_2O$
M_r = 223.23
Tetragonal, $P4_12_12$
a = 7.6230 (2) Å
c = 33.8174 (10) Å
V = 1965.13 (9) Å^3
Z = 8
F(000) = 960
D_x = 1.509 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 1241 reflections
θ = 5–27°
μ = 0.13 mm^{-1}
T = 150 K
Prism, colourless
0.40 × 0.20 × 0.20 mm

Data collection

Nonius KappaCCD diffractometer
Graphite monochromator
ω scans
Absorption correction: multi-scan DENZO/SCALEPACK (Otwinowski & Minor, 1997)
T_{min} = 0.96, T_{max} = 0.97
9161 measured reflections
1372 independent reflections
1372 reflections with $I > -3\sigma(I)$
R_{int} = 0.021
θ_{max} = 27.5°, θ_{min} = 5.2°
$h = -9 \rightarrow 9$
$k = -6 \rightarrow 7$
$l = -42 \rightarrow 43$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.072
S = 1.01
1372 reflections
199 parameters
48 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: difference Fourier map
Only H-atom coordinates refined
$w = 1/[\sigma^2(F) + (0.029P)^2 + 0.165P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$(\Delta/\sigma)_{max}$ = 0.000220
$\Delta\rho_{max}$ = 0.35 e Å^{-3}
$\Delta\rho_{min}$ = −0.34 e Å^{-3}

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

	x	y	z	U_{iso}*/U_{eq}	Occ. (<1)
C1	0.5890 (3)	0.6822 (3)	0.32134 (5)	0.0133	
C3	0.4333 (3)	0.9335 (3)	0.34563 (5)	0.0126	
C4	0.3029 (3)	0.8110 (3)	0.32505 (5)	0.0147	

C5	0.3967 (3)	0.6348 (3)	0.32832 (5)	0.0134	
C8	0.3964 (3)	1.1270 (3)	0.34060 (5)	0.0147	
C10	0.6936 (3)	0.9642 (3)	0.29892 (5)	0.0159	
C11	0.7902 (3)	0.8174 (3)	0.27746 (5)	0.0153	
C12	0.6562 (3)	0.6704 (3)	0.27879 (5)	0.0144	
N2	0.6108 (2)	0.8718 (2)	0.33311 (4)	0.0123	
O1	1.0215 (3)	0.4208 (2)	0.30776 (4)	0.0344	
O6	0.38422 (19)	0.56342 (18)	0.36727 (4)	0.0166	
O7	0.2878 (2)	0.8576 (2)	0.28420 (4)	0.0193	
O9	0.5046 (2)	1.2241 (2)	0.36747 (4)	0.0208	
O13	0.7232 (2)	0.5026 (2)	0.26855 (4)	0.0224	
O14	0.8418 (2)	0.8671 (2)	0.23878 (4)	0.0223	
H11	0.664 (2)	0.607 (2)	0.3385 (4)	0.0200*	
H31	0.423 (2)	0.909 (2)	0.3747 (4)	0.0200*	
H41	0.188 (2)	0.813 (2)	0.3375 (4)	0.0200*	
H51	0.352 (2)	0.550 (2)	0.3088 (4)	0.0200*	
H61	0.296 (2)	0.592 (3)	0.3792 (6)	0.0200*	
H71	0.243 (5)	0.779 (4)	0.2713 (9)	0.0200*	0.5000
H72	0.241 (6)	0.952 (4)	0.2811 (13)	0.0200*	0.5000
H81	0.272 (2)	1.145 (2)	0.3473 (5)	0.0200*	
H82	0.417 (2)	1.166 (2)	0.3136 (4)	0.0200*	
H91	0.468 (3)	1.328 (2)	0.3688 (6)	0.0200*	
H101	0.775 (2)	1.056 (2)	0.3078 (5)	0.0200*	
H102	0.604 (2)	1.017 (2)	0.2816 (5)	0.0200*	
H111	0.895 (2)	0.779 (2)	0.2922 (4)	0.0200*	
H121	0.562 (2)	0.702 (2)	0.2606 (5)	0.0200*	
H131	0.800 (4)	0.473 (6)	0.2828 (11)	0.0200*	0.5000
H132	0.663 (5)	0.447 (5)	0.2536 (11)	0.0200*	0.5000
H141	0.761 (4)	0.885 (6)	0.2234 (10)	0.0200*	0.5000
H142	0.930 (7)	0.815 (6)	0.2300 (12)	0.0200*	0.5000
H1001	0.926 (3)	0.426 (7)	0.2982 (13)	0.0200*	0.5000
H1002	1.010 (3)	0.375 (3)	0.3294 (5)	0.0200*	
H1003	1.053 (6)	0.343 (5)	0.2936 (11)	0.0200*	0.5000

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0161 (11)	0.0120 (11)	0.0116 (8)	0.0011 (9)	−0.0005 (8)	0.0002 (8)
C3	0.0128 (11)	0.0135 (11)	0.0114 (8)	0.0018 (9)	0.0009 (8)	−0.0009 (8)
C4	0.0159 (11)	0.0163 (11)	0.0118 (8)	0.0004 (9)	−0.0007 (9)	0.0000 (8)
C5	0.0164 (11)	0.0124 (11)	0.0114 (9)	−0.0010 (9)	0.0006 (8)	−0.0008 (8)
C8	0.0158 (11)	0.0145 (11)	0.0137 (8)	−0.0005 (9)	−0.0025 (9)	−0.0004 (8)
C10	0.0165 (11)	0.0163 (12)	0.0150 (9)	−0.0017 (9)	0.0021 (9)	0.0015 (8)
C11	0.0152 (11)	0.0196 (12)	0.0112 (9)	0.0005 (9)	0.0013 (8)	0.0024 (9)
C12	0.0134 (11)	0.0165 (11)	0.0132 (9)	0.0039 (9)	−0.0004 (8)	−0.0023 (8)
N2	0.0128 (9)	0.0114 (9)	0.0127 (7)	0.0003 (8)	0.0004 (7)	0.0000 (7)
O1	0.0557 (13)	0.0293 (11)	0.0182 (8)	0.0015 (10)	−0.0030 (9)	0.0012 (7)
O6	0.0176 (8)	0.0165 (8)	0.0158 (7)	0.0029 (7)	0.0053 (6)	0.0030 (6)

O7	0.0231 (9)	0.0196 (9)	0.0153 (7)	0.0012 (8)	−0.0061 (7)	0.0009 (7)
O9	0.0291 (10)	0.0113 (8)	0.0219 (7)	0.0017 (7)	−0.0074 (7)	−0.0043 (7)
O13	0.0246 (10)	0.0187 (9)	0.0240 (8)	0.0048 (8)	0.0022 (7)	−0.0084 (7)
O14	0.0229 (9)	0.0303 (10)	0.0136 (7)	0.0024 (8)	0.0049 (7)	0.0030 (7)

Geometric parameters (Å, º)

C1—C5	1.528 (3)	C10—H101	0.983 (15)
C1—C12	1.530 (3)	C10—H102	0.985 (15)
C1—N2	1.509 (2)	C11—C12	1.517 (3)
C1—H11	0.993 (15)	C11—O14	1.418 (2)
C3—C4	1.531 (3)	C11—H111	0.986 (15)
C3—C8	1.511 (3)	C12—O13	1.420 (2)
C3—N2	1.494 (3)	C12—H121	0.974 (14)
C3—H31	1.003 (14)	O1—H1001	0.800 (18)
C4—C5	1.526 (3)	O1—H1002	0.815 (15)
C4—O7	1.431 (2)	O1—H1003	0.801 (18)
C4—H41	0.975 (15)	O6—H61	0.814 (15)
C5—O6	1.428 (2)	O7—H71	0.814 (18)
C5—H51	0.985 (15)	O7—H72	0.812 (19)
C8—O9	1.433 (2)	O9—H91	0.838 (15)
C8—H81	0.985 (15)	O13—H131	0.791 (18)
C8—H82	0.973 (14)	O13—H132	0.804 (17)
C10—C11	1.524 (3)	O14—H141	0.816 (18)
C10—N2	1.494 (2)	O14—H142	0.83 (5)
C5—C1—C12	116.88 (16)	C11—C10—H102	110.5 (10)
C5—C1—N2	106.92 (15)	N2—C10—H102	111.0 (10)
C12—C1—N2	105.52 (15)	H101—C10—H102	109.1 (12)
C5—C1—H11	109.0 (10)	C10—C11—C12	101.71 (17)
C12—C1—H11	108.8 (9)	C10—C11—O14	112.16 (18)
N2—C1—H11	109.5 (10)	C12—C11—O14	114.32 (16)
C4—C3—C8	115.05 (17)	C10—C11—H111	111.7 (10)
C4—C3—N2	105.52 (15)	C12—C11—H111	108.2 (10)
C8—C3—N2	116.31 (16)	O14—C11—H111	108.6 (9)
C4—C3—H31	106.5 (10)	C1—C12—C11	102.10 (16)
C8—C3—H31	105.9 (10)	C1—C12—O13	113.73 (16)
N2—C3—H31	107.0 (10)	C11—C12—O13	114.58 (17)
C3—C4—C5	101.50 (16)	C1—C12—H121	109.5 (10)
C3—C4—O7	109.85 (17)	C11—C12—H121	106.9 (10)
C5—C4—O7	109.04 (15)	O13—C12—H121	109.6 (10)
C3—C4—H41	112.1 (10)	C1—N2—C3	106.05 (15)
C5—C4—H41	114.1 (10)	C1—N2—C10	107.10 (14)
O7—C4—H41	109.9 (9)	C3—N2—C10	117.00 (16)
C1—C5—C4	103.35 (16)	H1001—O1—H1002	107 (4)
C1—C5—O6	107.24 (16)	H1001—O1—H1003	94 (5)
C4—C5—O6	111.76 (15)	H1002—O1—H1003	104 (4)
C1—C5—H51	112.6 (10)	C5—O6—H61	114.2 (15)

C4—C5—H51	111.5 (10)	C4—O7—H71	112 (3)
O6—C5—H51	110.2 (9)	C4—O7—H72	112 (3)
C3—C8—O9	109.04 (16)	H71—O7—H72	113 (4)
C3—C8—H81	106.8 (10)	C8—O9—H91	109.2 (14)
O9—C8—H81	109.6 (10)	C12—O13—H131	112 (3)
C3—C8—H82	111.9 (10)	C12—O13—H132	115 (3)
O9—C8—H82	110.1 (10)	H131—O13—H132	131 (5)
H81—C8—H82	109.3 (12)	C11—O14—H141	115 (3)
C11—C10—N2	103.10 (16)	C11—O14—H142	115 (3)
C11—C10—H101	111.5 (10)	H141—O14—H142	117 (4)
N2—C10—H101	111.5 (9)		