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(2*S*,3*R*,4*R*,5*S*)-3,4,5-Trihydroxypipecolic acid dihydrate [(2*S*,3*R*,4*R*,5*S*)-3,4,5-trihydroxypiperidine-2-carboxylic acid dihydrate]

Kathrine V. Booth,[a]* Sarah F. Jenkinson,[a] David J. Watkin,[b] Hazel Sharp,[c] Paul Wyn Jones,[c] Robert J. Nash[c] and George W. J. Fleet[a]

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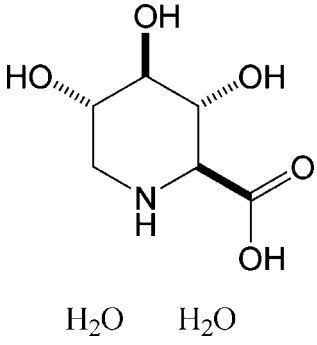
Key indicators: single-crystal X-ray study; T = 150 K; mean σ(C–C) = 0.003 Å; R factor = 0.038; wR factor = 0.097; data-to-parameter ratio = 9.6.

The relative configuration of the title compound, $C_6H_{11}NO_5\cdot 2H_2O$, was determined by X-ray crystallography; the absolute configuration was determined by the comparison of physical data with the literature [Fleet, Bashyal & Chow (1986). *Tetrahedron Lett.* **27**, 3205–3207; Fleet, Bashyal, Chow & Fellows (1987). *Tetrahedron*, **43**, 415–422; Bernotas & Ganem (1985). *Tetrahedron Lett.* **26**, 4981–4982]. The structure exists as an extensively hydrogen-bonded lattice, with each molecule acting as a donor and acceptor for seven hydrogen bonds.

Related literature

For related literature see: Manning *et al.* (1985); Kite (2003); Asano *et al.* (2000); Watson *et al.* (2001); Pereira *et al.* (1991); Bruce *et al.* (1992); Shilvock *et al.* (1996, 1998); Fleet *et al.* (1986, 1987); Bernotas & Ganem (1985); Nash *et al.* (1986); Görbitz (1999).



Experimental

Crystal data

$C_6H_{11}NO_5\cdot 2H_2O$
M_r = 213.19
Orthorhombic, $P2_12_12_1$
a = 6.4536 (2) Å
b = 6.7954 (2) Å
c = 20.7965 (8) Å
V = 912.03 (5) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.14 mm^{-1}
T = 150 K
0.60 × 0.20 × 0.05 mm

Data collection

Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.70, T_{max} = 0.99
4710 measured reflections
1232 independent reflections
1130 reflections with $I > 2\sigma(I)$
R_{int} = 0.028

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.097
S = 0.97
1216 reflections
127 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.51 e Å^{-3}
$\Delta\rho_{min}$ = −0.49 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O9—H8···O12^{i}	0.83	1.97	2.757 (2)	157
O7—H9···O14^{ii}	0.81	1.89	2.667 (2)	160
O8—H11···O12^{ii}	0.81	2.03	2.831 (2)	174
O13—H12···O11	0.81	2.03	2.821 (2)	166
O14—H54···O8^{iii}	0.83	1.96	2.791 (2)	172
O14—H15···O7^{iv}	0.84	1.96	2.796 (2)	174
O12—H14···O9^{v}	0.79	2.09	2.757 (2)	142

Symmetry codes: (i) $x+\frac{1}{2}, -y+\frac{3}{2}, -z$; (ii) $x+1, y, z$; (iii) $-x+1, y-\frac{1}{2}, -z+\frac{1}{2}$; (iv) $-x+1, y+\frac{1}{2}, -z+\frac{1}{2}$; (v) $x-\frac{1}{2}, -y+\frac{3}{2}, -z$.

Data collection: *COLLECT* (Nonius, 2001).; cell refinement: *DENZO*/*SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO*/*SCALEPACK*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *CAMERON* (Watkin *et al.*, 1996); software used to prepare material for publication: *CRYSTALS*.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: WN2187).

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supplementary materials

Acta Cryst. (2007). E**63**, o3783-o3784 [**doi:10.1107/S1600536807039281**]

(2*S*,3*R*,4*R*,5*S*)-3,4,5-Trihydroxypipecolic acid dihydrate [(2*S*,3*R*,4*R*,5*S*)-3,4,5-trihydroxypiperidine-2-carboxylic acid dihydrate]

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Comment

BR1 [(2*S*,3*R*,4*R*,5*S*)-3,4,5-trihydroxypipecolic acid] (**1**) previously obtained from seeds of *Baphia racemosa* (Manning *et al.*, 1985) and *Baphia parvaflora*, (Kite, 2003) has been isolated for the first time from seeds of the African medicinal tree *Baphia confusum*. BR1 (**1**) is the only trihydroxypipecolic acid that has been found in nature. Although there are over 100 naturally occurring pyrrolidines and piperidines, such as DNJ (**2**), (Asano *et al.*, 2000) which may be viewed as sugars mimics (Watson *et al.*, 2001), polyhydroxylated amino acids are relatively uncommon (Pereira *et al.*, 1991) though several other trihydroxypipecolic acids have been synthesized (Bruce *et al.*, 1992; Shilvock *et al.*, 1996; Shilvock *et al.*, 1998). This paper reports the determination by X-ray crystallographic analysis of the conformation and relative configuration of BR1. The absolute configuration is determined by comparison with the specific rotation of synthetic samples from D-glucuronolactone (Fleet *et al.*, 1986; Fleet *et al.*, 1987) and from D-glucose (Bernotas & Ganem, 1985).

The title compound (Fig. 2) crystallizes as its dihydrate. The crystal structure consists of hydrogen-bonded sheets lying approximately perpendicular to the *c* axis. O13 is embedded in the sheet and hydrogen bonded to adjacent molecules. O14 lies between the sheets and links them, acting as both a donor and an acceptor (Fig. 3).

Experimental

1 g of BR1 was isolated from the 50% aqueous ethanol extract of 2 kg of seeds of *Baphia confusum* (*Leguminosae*). The compound was isolated by binding it to Amberlite IR-120 (H^+ form, 2*L*) and after washing with copious water it was displaced with 2*M* NH_4OH. The bound material was concentrated by rotary evaporation and BR1 bound to Amberlite CG400 (OH^- form), washed well with water and displaced with 2*M* AcOH. After further concentration the oil was applied to an Amberlite CG-50 column (3.6 *x* 48 cm, NH_4^+ form) and eluted with distilled water. Analysis of fractions using GC—MS of the pretrimethylsilyl-derivative (Nash *et al.*, 1986) allowed fractions containing BR1 to be combined and these were then freeze-dried. Scanning the mass range 100–500 daltons on the GC—MS shows characteristic ions for BR1 at 217 (100%), 258 (50%), 348 (30%) and 375 (10%). BR1 was readily crystallized from 95% aq. EtOH by layering with acetone. m. p. 230–232 °C (dec), $[\alpha]_D^{18}$ +14.5 (c, 0.13 in water) [lit. (Fleet *et al.*, 1987): m.p. 228–232 °C, $[\alpha]_D^{20}$ +14.1 (0.3 in H_2O)]

Refinement

The relatively large ratio of minimum to maximum corrections applied in the multi-scan process (1:1.41) reflect changes in the illuminated volume of the crystal, which were kept to a minimum, and were taken into account (Görbitz, 1999) by the multi-scan inter-frame scaling (*DENZO*/*SCALEPACK*, Otwinowski & Minor, 1997).

The H atoms were all located in a difference map, but those attached to carbon atoms were repositioned geometrically. The H atoms were initially refined with soft restraints on the bond lengths and angles to regularize their geometry (C—H

in the range 0.93–0.98, N—H to 0.86, O—H = 0.82 Å) and U_{iso}(H) (in the range 1.2–1.5 times U_{eq} of the parent atom), after which the positions were refined with riding constraints.

Figures

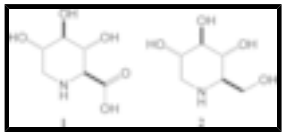

Fig. 1. The title compound (**1**) and related compound DNJ (**2**).

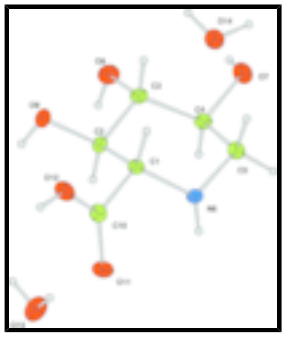

Fig. 2. The title compound with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radius.

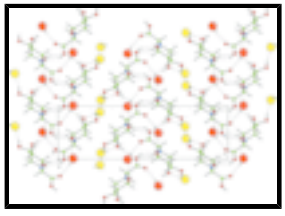

Fig. 3. Packing diagram viewed perpendicular to the plane of the hydrogen bonded (dashed lines) sheets. O13, coloured red, is embedded within the sheet. O14, coloured yellow, links the sheets together. O13 and O14 are drawn with a radius of 0.5 Å.

(2*S*,3*R*,4*R*,5*S*)-3,4,5-Trihydroxypiperidine-2-\ carboxylic acid dihydrate

Crystal data

$C_6H_{11}N_1O_5·2H_2O$	F_{000} = 456
M_r = 213.19	D_x = 1.553 Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Mo $K\alpha$ radiation λ = 0.71073 Å
Hall symbol:	Cell parameters from 1088 reflections
a = 6.4536 (2) Å	θ = 5–27°
b = 6.7954 (2) Å	μ = 0.14 mm^{-1}
c = 20.7965 (8) Å	T = 150 K
V = 912.03 (5) Å^3	Lath, colourless
Z = 4	0.60 × 0.20 × 0.05 mm

Data collection

Nonius KappaCCD diffractometer	1130 reflections with $I > 2\sigma(I)$
Monochromator: graphite	R_{int} = 0.028
T = 150 K	θ_{max} = 27.5°

ω scans	θ_{min} = 5.3º
Absorption correction: multi-scan (DENZO/SCALEPACK; Otwinowski & Minor, 1997)	h = −8→8
T_{min} = 0.70, T_{max} = 0.99	k = −8→8
4710 measured reflections	l = −26→26
1232 independent reflections	

Refinement

Refinement on F^2	H-atom parameters constrained
Least-squares matrix: full	Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.04P)^2 + 0.79P]$, where $P = [\max(F_o^2,0) + 2F_c^2]/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.038	$(\Delta/\sigma)_{max}$ = 0.0001
$wR(F^2)$ = 0.097	$\Delta\rho_{max}$ = 0.51 e Å^{-3}
S = 0.97	$\Delta\rho_{min}$ = −0.49 e Å^{-3}
1216 reflections	Extinction correction: None
127 parameters	
Primary atom site location: structure-invariant direct methods	
Hydrogen site location: inferred from neighbouring sites	

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

	x	y	z	U_{iso}*/U_{eq}
C1	0.2706 (4)	0.4469 (3)	0.09371 (10)	0.0125
C2	0.4597 (4)	0.5852 (3)	0.09037 (11)	0.0135
C3	0.5846 (4)	0.5616 (3)	0.15241 (10)	0.0140
C4	0.6474 (4)	0.3472 (3)	0.16360 (10)	0.0145
C5	0.4652 (4)	0.2059 (4)	0.15918 (10)	0.0162
N6	0.3496 (3)	0.2409 (3)	0.09815 (9)	0.0138
O7	0.7297 (3)	0.3209 (3)	0.22635 (8)	0.0201
O8	0.7650 (3)	0.6819 (3)	0.15172 (8)	0.0203
O9	0.3908 (3)	0.7817 (2)	0.08402 (8)	0.0188
C10	0.1319 (4)	0.4703 (3)	0.03465 (11)	0.0145
O11	0.1734 (3)	0.3657 (2)	−0.01336 (8)	0.0182
O12	−0.0094 (3)	0.5953 (3)	0.03846 (8)	0.0197
O13	0.5093 (3)	0.4875 (3)	−0.09049 (9)	0.0245
O14	0.1139 (3)	0.4431 (3)	0.25178 (8)	0.0219
H53	0.1888	0.4763	0.1325	0.0144*
H21	0.5494	0.5483	0.0542	0.0152*
H31	0.4980	0.6064	0.1881	0.0164*
H41	0.7446	0.3060	0.1304	0.0185*
H51	0.3738	0.2288	0.1943	0.0194*
H52	0.5136	0.0728	0.1598	0.0200*
H8	0.4482	0.7978	0.0488	0.0298*

H9	0.8379	0.3808	0.2289	0.0308*
H11	0.8225	0.6618	0.1179	0.0318*
H12	0.4020	0.4671	−0.0716	0.0382*
H13	0.5566	0.5959	−0.0797	0.0377*
H54	0.1524	0.3750	0.2828	0.0338*
H15	0.1530	0.5584	0.2601	0.0337*
H2	0.3560	0.1726	0.0693	0.0227*
H14	−0.0891	0.6336	0.0122	0.0341*

Atomic displacement parameters (Å^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0129 (11)	0.0128 (10)	0.0117 (9)	0.0014 (9)	−0.0002 (9)	−0.0008 (9)
C2	0.0157 (11)	0.0108 (10)	0.0139 (9)	0.0004 (9)	0.0010 (9)	0.0003 (9)
C3	0.0150 (11)	0.0135 (10)	0.0137 (9)	−0.0042 (9)	−0.0011 (9)	−0.0019 (9)
C4	0.0147 (11)	0.0157 (10)	0.0131 (10)	−0.0001 (10)	−0.0022 (8)	−0.0015 (8)
C5	0.0186 (11)	0.0153 (11)	0.0148 (10)	−0.0016 (10)	−0.0031 (9)	0.0008 (8)
N6	0.0176 (9)	0.0122 (9)	0.0115 (8)	0.0011 (8)	−0.0013 (8)	−0.0020 (7)
O7	0.0190 (9)	0.0225 (9)	0.0189 (8)	−0.0048 (8)	−0.0075 (7)	0.0031 (7)
O8	0.0191 (9)	0.0206 (9)	0.0210 (8)	−0.0092 (8)	0.0005 (7)	−0.0019 (7)
O9	0.0272 (10)	0.0112 (7)	0.0179 (7)	0.0014 (8)	0.0001 (8)	0.0014 (6)
C10	0.0133 (11)	0.0153 (10)	0.0150 (10)	−0.0031 (10)	0.0005 (9)	0.0012 (8)
O11	0.0183 (8)	0.0215 (8)	0.0147 (7)	0.0005 (8)	−0.0015 (6)	−0.0036 (7)
O12	0.0195 (9)	0.0240 (9)	0.0157 (7)	0.0072 (8)	−0.0020 (7)	0.0011 (7)
O13	0.0186 (9)	0.0196 (8)	0.0353 (10)	0.0016 (8)	0.0032 (8)	−0.0010 (8)
O14	0.0265 (10)	0.0202 (8)	0.0189 (8)	−0.0019 (9)	−0.0046 (7)	0.0010 (7)

Geometric parameters (Å, °)

C1—C2	1.542 (3)	C5—H51	0.952
C1—N6	1.493 (3)	C5—H52	0.957
C1—C10	1.528 (3)	N6—H2	0.760
C1—H53	0.985	O7—H9	0.810
C2—C3	1.530 (3)	O8—H11	0.807
C2—O9	1.414 (3)	O9—H8	0.828
C2—H21	0.982	C10—O11	1.255 (3)
C3—C4	1.530 (3)	C10—O12	1.248 (3)
C3—O8	1.423 (3)	O12—H14	0.794
C3—H31	0.978	O13—H12	0.807
C4—C5	1.521 (3)	O13—H13	0.829
C4—O7	1.420 (3)	O14—H54	0.832
C4—H41	0.974	O14—H15	0.841
C5—N6	1.491 (3)		
C2—C1—N6	107.68 (18)	C3—C4—H41	109.7
C2—C1—C10	111.34 (18)	C5—C4—H41	105.9
N6—C1—C10	110.34 (18)	O7—C4—H41	112.0
C2—C1—H53	109.7	C4—C5—N6	109.73 (18)
N6—C1—H53	108.8	C4—C5—H51	109.3

C10—C1—H53	108.9	N6—C5—H51	108.5
C1—C2—C3	108.35 (18)	C4—C5—H52	110.0
C1—C2—O9	109.31 (19)	N6—C5—H52	109.0
C3—C2—O9	110.11 (18)	H51—C5—H52	110.2
C1—C2—H21	110.2	C1—N6—C5	111.90 (17)
C3—C2—H21	108.0	C1—N6—H2	122.8
O9—C2—H21	110.8	C5—N6—H2	123.2
C2—C3—C4	111.59 (18)	C4—O7—H9	108.6
C2—C3—O8	111.22 (18)	C3—O8—H11	106.7
C4—C3—O8	109.39 (19)	C2—O9—H8	93.8
C2—C3—H31	107.9	C1—C10—O11	117.1 (2)
C4—C3—H31	109.4	C1—C10—O12	116.59 (19)
O8—C3—H31	107.2	O11—C10—O12	126.3 (2)
C3—C4—C5	112.76 (19)	C10—O12—H14	130.8
C3—C4—O7	111.00 (18)	H12—O13—H13	109.7
C5—C4—O7	105.40 (18)	H54—O14—H15	105.6

Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
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Fig. 1

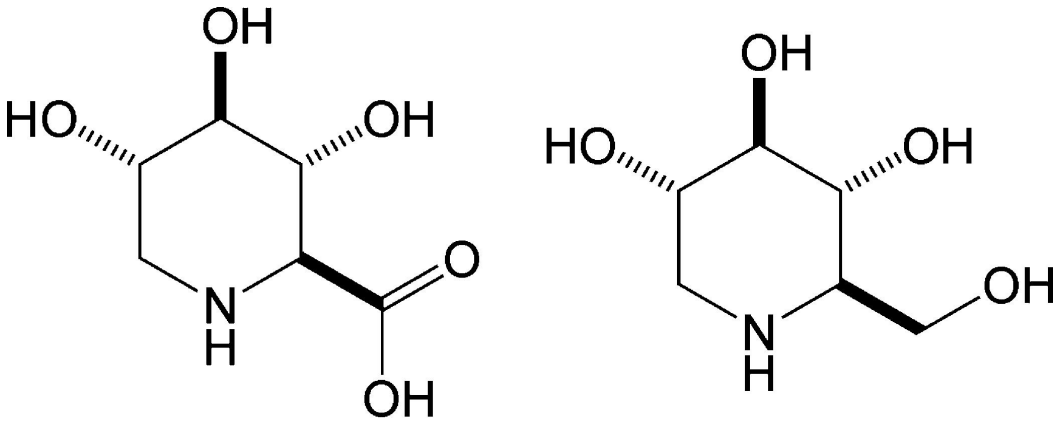

Fig. 2

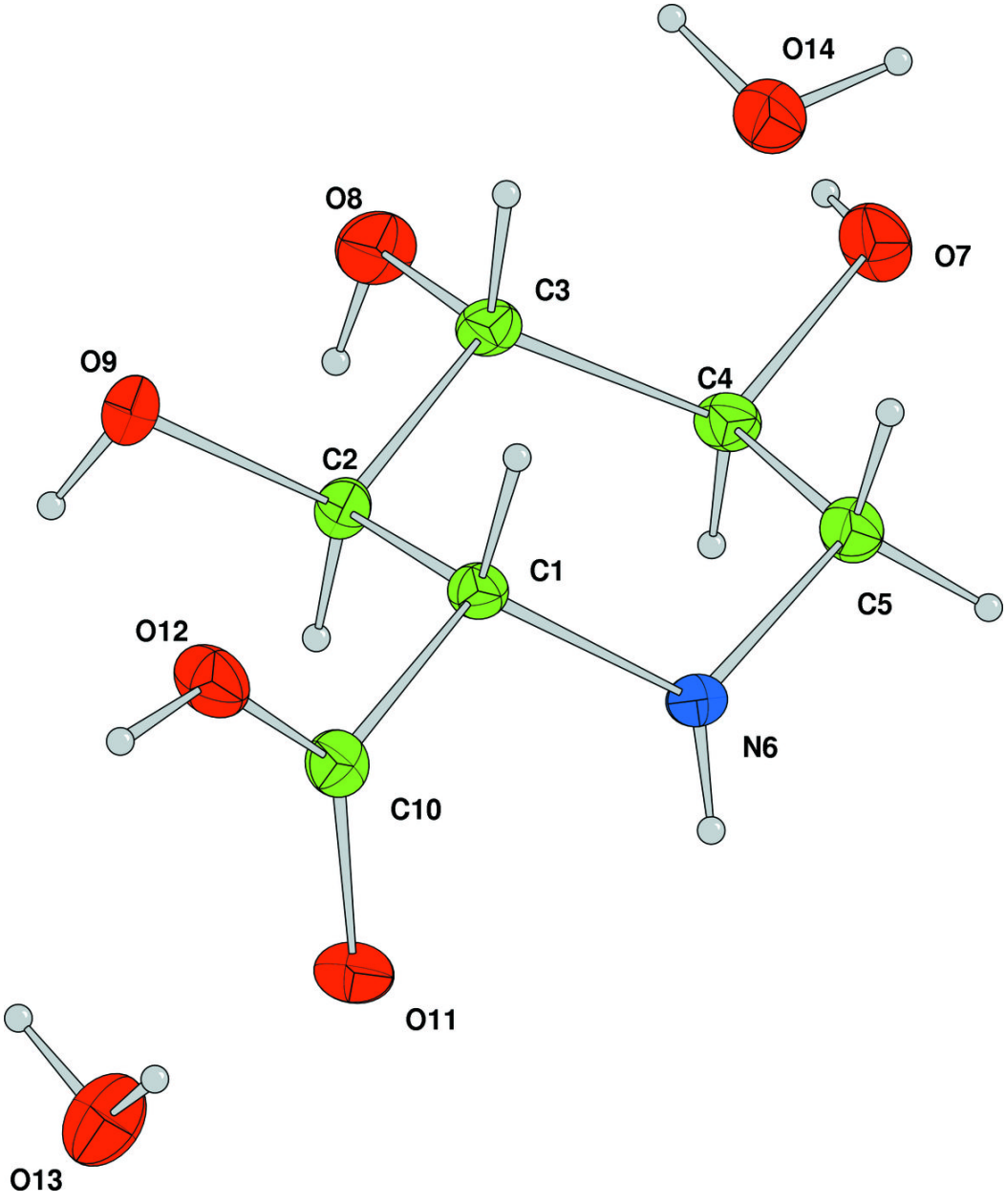

Fig. 3