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(2*S*,3*S*)-3-Hydroxy-1-(4-methoxybenzyl)-piperidine-2-carboxamide

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Key indicators

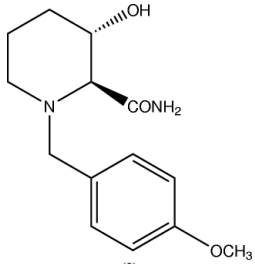
Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.005 Å
R factor = 0.044
wR factor = 0.124
Data-to-parameter ratio = 7.8

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

The title compound, $C_{14}H_{20}N_2O_3$, has been obtained as an unexpected product when attempting to prepare (2*S*,3*S*)-3-hydroxy-1-(4-methoxybenzyl)piperidine-2-carboxylic acid. The crystal structure involves intermolecular N—H···O and O—H···O hydrogen bonds.

Comment

(2*S*,3*S*)-3-Hydroxypiperidine-2-carboxylic acid (Mansour & Marc, 2001) is an interesting target molecule since it can be regarded as a conformationally constrained amino acid or a hydroxylated homoproline, with possible effects on physiological and pathological processes. In our studies on the total synthesis of this compound, we attempted to hydrolyse (2*R*,3*S*)-3-hydroxy-1-(4-methoxybenzyl)piperidine-2-carbonitrile to prepare (2*S*,3*S*)-3-hydroxy-1-(4-methoxybenzyl)-piperidine-2-carboxylic acid. During this experiment, the title compound, (I), was isolated unexpectedly.



(I)

The piperidine ring in (I) is in the chair conformation. The OH and amide groups are in *trans* diequatorial orientations. Bond lengths and angles in the piperidine ring (Table 1) are in agreement with values reported for a similar compound

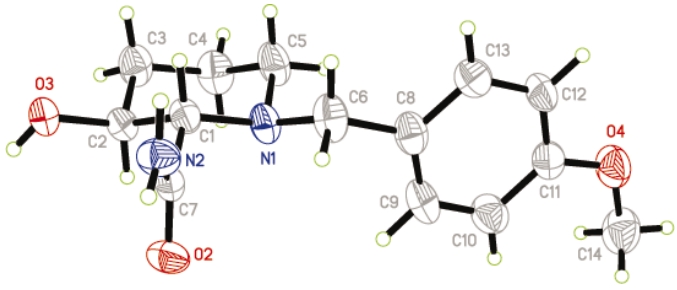


Figure 1
ORTEP-3 (Farrugia, 1997) plot of (I). Displacement ellipsoids are drawn at the 50% probability level. H atoms are drawn as spheres of arbitrary radii.

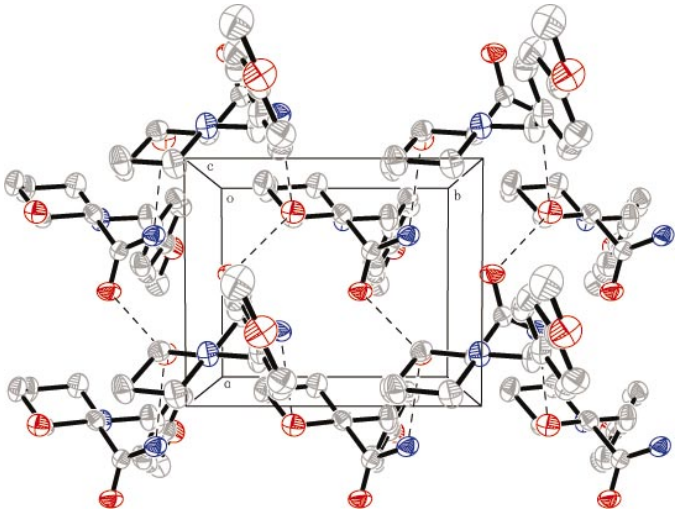


Figure 2
The molecular packing of (I), viewed along the *b* axis. Dashed lines indicate the hydrogen-bonding interactions.

(Battistini *et al.*, 1997). The crystal structure involves intermolecular N—H···O and O—H···O hydrogen bonds (Table 2).

Experimental

(2*R*,3*S*)-3-Hydroxy-1-(4-methoxybenzyl)piperidine-2-carbonitrile (100 mg, 0.41 mmol) was dissolved in a 12 *N* aqueous HCl solution (25 ml). The mixture was stirred at 333 K for 2 d, neutralized with Na_2CO_3 and extracted with ethyl acetate. Flash chromatographic purification on silica gel (ethyl acetate/petroleum ether 30:1) yielded the pure product (63 mg). Suitable crystals were obtained by recrystallization from a mixture of ethyl acetate and petroleum ether (m.p. 432–433 K).

Crystal data

$C_{14}H_{20}N_2O_3$
M_r = 264.32
Monoclinic, $P2_1$
a = 6.0743 (13) Å
b = 7.2436 (16) Å
c = 15.916 (3) Å
β = 95.334 (4)°
V = 697.3 (3) Å^3
Z = 2
D_x = 1.259 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4825 reflections
θ = 2.6–28.6°
μ = 0.09 mm^{-1}
T = 293 (2) K
Plate, colorless
0.23 × 0.15 × 0.09 mm

Data collection

Bruker SMART APEX CCD diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2001)
T_{min} = 0.980, T_{max} = 0.992
6682 measured reflections
1335 independent reflections
1331 reflections with $I > 2\sigma(I)$
R_{int} = 0.020
θ_{max} = 25.0°
$h = -7 \rightarrow 7$
$k = -8 \rightarrow 8$
$l = -18 \rightarrow 18$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.124
S = 1.09
1335 reflections
172 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0647P)^2 + 0.3487P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.006
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

C1—N1	1.454 (4)	C7—O2	1.214 (4)
C1—C7	1.508 (4)	C7—N2	1.315 (4)
C1—C2	1.520 (5)	C8—C9	1.362 (6)
C2—O3	1.413 (4)	C8—C13	1.374 (5)
C2—C3	1.493 (5)	C9—C10	1.361 (5)
C3—C4	1.500 (5)	C10—C11	1.374 (5)
C4—C5	1.504 (6)	C11—O4	1.345 (4)
C5—N1	1.448 (5)	C11—C12	1.369 (5)
C6—N1	1.444 (5)	C12—C13	1.360 (5)
C6—C8	1.500 (5)	C14—O4	1.406 (5)
N1—C1—C7	110.8 (3)	C9—C8—C6	120.7 (3)
N1—C1—C2	110.1 (3)	C13—C8—C6	121.8 (3)
C7—C1—C2	108.6 (3)	C10—C9—C8	122.2 (3)
O3—C2—C3	112.1 (3)	C9—C10—C11	119.8 (4)
O3—C2—C1	106.5 (3)	O4—C11—C12	116.0 (3)
C3—C2—C1	110.9 (3)	O4—C11—C10	125.2 (3)
C2—C3—C4	109.5 (3)	C12—C11—C10	118.7 (3)
C3—C4—C5	109.7 (3)	C13—C12—C11	120.5 (3)
N1—C5—C4	111.5 (3)	C12—C13—C8	121.3 (3)
N1—C6—C8	112.5 (3)	C11—O4—C14	118.0 (3)
O2—C7—N2	123.3 (3)	C6—N1—C5	110.3 (3)
O2—C7—C1	121.1 (3)	C6—N1—C1	111.2 (3)
N2—C7—C1	115.6 (3)	C5—N1—C1	109.8 (3)
C9—C8—C13	117.4 (3)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2*B*···O2^{i}	0.86	2.24	3.027 (4)	153
N2—H2*C*···O3^{ii}	0.86	2.05	2.864 (4)	158
O3—H3*C*···O2^{iii}	0.82	1.87	2.686 (3)	180

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

The H atoms were positioned geometrically (C—H = 0.93, 0.98, 0.97 or 0.96 Å for aromatic, tertiary, methylene or methyl H atoms, respectively; O—H = 0.82 Å and N—H = 0.86 Å) and were included in the refinement in the riding-model approximation. U_{iso}(H) values were set equal to xU_{eq} of the carrier atom, where x = 1.5 for methyl and x = 1.2 for all other H atoms. In the absence of significant anomalous scattering effects, Friedel pairs were merged; the absolute configuration was assumed from the synthesis.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97.

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