Methyl (3*SR*,4*RS*)-3-benzyl-4-hydroxy-2-oxo-pyrrolidine-3-carboxylate

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In the title compound, $C_{13}H_{15}NO_4$, the pyrrolidine ring exhibits an envelope conformation with two chiral centres. In the crystal structure, the molecules are linked by N—H···O, O—H···O and C—H···O intermolecular hydrogen bonds to form a three-dimensional network.

Comment

Kainic acid and its derivatives have received much attention in respect of imminohistochemical, neurochemical and behavioural studies in animal systems (Mikulecka *et al.*, 1999; Magnone *et al.*, 2000; Jousselin-Hosaja *et al.*, 2001). On the other hand, it is also a precursor in a multi-step synthesis of natural product components such as clausenamide, a liver protecting agent, obtained from the leaves of the plant *Clausena lansium* (Hartwig & Born, 1987). The title compound, (I) (Fig. 1), was obtained as reduced kainic acid in one of several steps in the synthesis of possible derivatives of clausenamide.

(I)
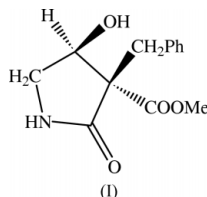
The pyrrolidine ring C1/C2/N1/C3/C4 has an envelope conformation, the C2/N1/C3/C4 moiety being almost planar; the C2—N1—C3—C4 torsion angle is −0.68 (14)°. The relative configurations of the chiral centres at atoms C1 and C4 are *R* and *S* (or *S* and *R*), respectively. The bond lengths and
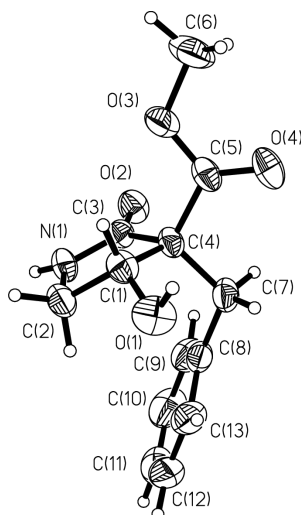

Figure 1
The molecular structure of the title compound, (I), with ellipsoids drawn at the 50% probability level.

angles (Table 1) are in agreement with literature values (Allen *et al.*, 1987). The benzyl C7/C8/C9/C10/C11/C12/C13 and ester O3/O4/C4/C5/C6 groups are both planar and make angles with the pyrrolidine ring of 77.75 (7) and 48.48 (6)°, respectively. The crystal packing is stablized by intermolecular hydrogen bonds, N1—H1A···O4^i, O1—H1B···O2^{ii} and C11—H11A···O2^{iii} (symmetry codes as in Table 2), forming a three-dimensional network (Fig. 2).

Experimental

The synthetic approach to the title compound, (I), began with condensation between readily available glycine methyl ester and methyl malonate potassium salt in equimolar amounts to give a diester in 92% yield. Dieckmann cyclization of this diester with sodium/methanol in toluene under reflux gave a β,β-diketoester, 2,4-dioxo-pyrrolidine-3-carboxylic acid methyl ester, in 91% yield. Alkylation of this β,β-diketoester was successfully carried out using benzyl bromide in the presence of tetrahydrofuran and tetrabutyl-ammonium fluoride (TBAF) to give 3-benzyl-2,4-dioxo-pyrrolidine-3-carboxylic acid methyl ester in 55% yield. Reduction of the alkyl-ated diketoester using NaBH$_4$/MeOH gave only one isomer of (I) in 65% yield. Crystals of (I), suitable for X-ray investigation, were obtained by slow evaporation of an ethyl acetate–petroleum ether solution.

Crystal data

C$_{13}$H$_{15}$NO$_4$	Mo $K\alpha$ radiation
$M_r = 249.26$	Cell parameters from 5914
Orthorhombic, $Pbca$	reflections
$a = 14.7891 (11)$ Å	$\theta = 2.6–27.5°$
$b = 10.8965 (8)$ Å	$\mu = 0.10$ mm^{-1}
$c = 15.4391 (11)$ Å	$T = 293 (2)$ K
$V = 2488.0 (3)$ Å^3	Slab, colourless
$Z = 8$	$0.48 \times 0.36 \times 0.14$ mm
$D_x = 1.331$ Mg m^{-3}	

Data collection

Bruker SMART APEX CCD area-detector	$R_{int} = 0.019$
	$\theta_{max} = 27.5°$
ω scans	$h = -19 \rightarrow 12$
15 920 measured reflections	$k = -14 \rightarrow 13$
2859 independent reflections	$l = -20 \rightarrow 19$
2429 reflections with $I > 2\sigma(I)$	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0755P)^2$
$R[F^2 > 2\sigma(F^2)] = 0.043$	$+ 0.3864P]$
$wR(F^2) = 0.128$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.06$	$(\Delta/\sigma)_{max} < 0.001$
2859 reflections	$\Delta\rho_{max} = 0.33$ e Å^{-3}
163 parameters	$\Delta\rho_{min} = -0.17$ e Å^{-3}
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

N1—C3	1.3313 (15)	C4—C5	1.5166 (15)
N1—C2	1.4448 (16)	C4—C7	1.5468 (16)
O1—C1	1.3988 (15)	C7—C8	1.5094 (17)
O2—C3	1.2266 (15)	C8—C13	1.3833 (19)
O3—C5	1.3210 (17)	C8—C9	1.3839 (19)
O3—C6	1.4535 (16)	C9—C10	1.381 (2)
O4—C5	1.1994 (15)	C10—C11	1.370 (3)
C3—C4	1.5307 (15)		
C3—N1—C2	115.41 (10)	C5—O3—C6	116.07 (12)
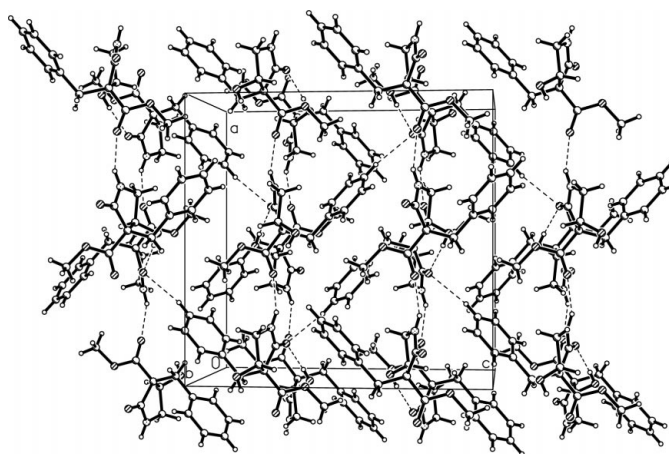
Figure 2
Packing diagram of (I), viewed down the *b* axis. The dashed lines denote the N—H···O, O—H···O and C—H···O hydrogen bonds.

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···O4^i	0.86	2.08	2.8847 (14)	157
O1—H1B···O2^{ii}	0.82	1.91	2.7309 (14)	176
C11—H11A···O2^{iii}	0.93	2.56	3.4747 (19)	169

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

After their location in a difference Fourier map, all H atoms were included in the refinement in geometrically calculated positions, and allowed to ride on the parent C, N or O atoms with C—H = 0.97 Å, N—H = 0.89 Å and O—H = 0.85 Å.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SAINT* (Siemens, 1996); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL, PARST* (Nardelli, 1995) and *PLATON* (Spek, 1990).

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