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(*R*)-(−)-6-(4-Aminophenyl)-5-methyl-4,5-dihydropyridazin-3(2*H*)-one

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.046
wR factor = 0.128
Data-to-parameter ratio = 10.1

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

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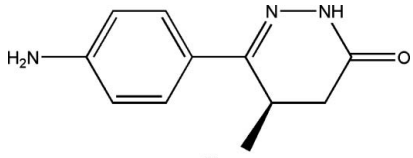
The title compound, $C_{11}H_{13}N_3O$, is a key intermediate in the synthesis of cardiotonic agents. The asymmetric unit consists of two molecules of the same enantiomer and the crystal packing is stabilized by intermolecular N—H···O hydrogen bonds.

Comment

The title compound, (I), is a key intermediate in the synthesis of cardiotonic agents that have long-acting effects on hypertensives and platelet aggregation (McEvoy & Allen, 1974; Seki *et al.*, 1998, Jiang & Sun, 1990, Dong *et al.*, 2005), such as amipizone (Thyes *et al.*, 1983) and levosimendan (Zhang *et al.*, 2004). However, the crystal structure has not been determined previously.



(I)

The asymmetric unit of the title compound consists of two molecules. Prout *et al.* (1994) have reported a racemic structure of almost the same molecule, but without the 5-methyl substituent. The title compound has a chiral C atom due to the introduction of the 5-methyl substituent in the pyridazine ring and the hydrogen-bonding patterns of the two compounds are also different. In addition to the antihypertensive activity, McEvoy & Allen (1974) have demonstrated compounds with the the 5-methyl substituent have a antihyhypertensive activity of longer duration than similar structures without a 5-methyl substituent.

Four intermolecular hydrogen bonds link the molecules into infinite chains (Table 1).

Experimental

Crude crystals of the title compound were synthesized according to the method of Owings *et al.* (1991). A solution of methyl 4-(4-aminophenyl)-3-methyl-4-oxobutyrate (11.2 g, 50.6 mmol) dissolved in methanol (90 ml) was treated with 860 ml of 1:9 *v*/*v* hydrazine–water, which was adjusted to pH 6.5 with glacial acetic acid. The above solution was heated at reflux for 1 h, cooled to room temperature, treated with 150 ml saturated aqueous sodium carbonate and extracted with 3 × 300 ml portions of ethyl acetate. The combined organic phases were washed with 100 ml saturated aqueous sodium carbonate, dried over magnesium sulfate and concentrated *in vacuo* to afford 9.28 g (90.5% yield) of the title compound. The crude

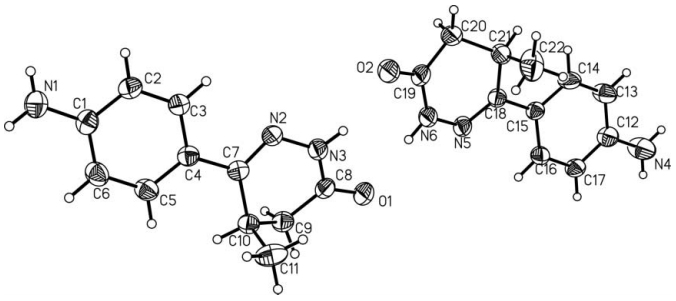


Figure 1
The asymmetric unit of the title compound, (I), showing the atom-labeling scheme and displacement ellipsoids drawn at the 30% probability level.

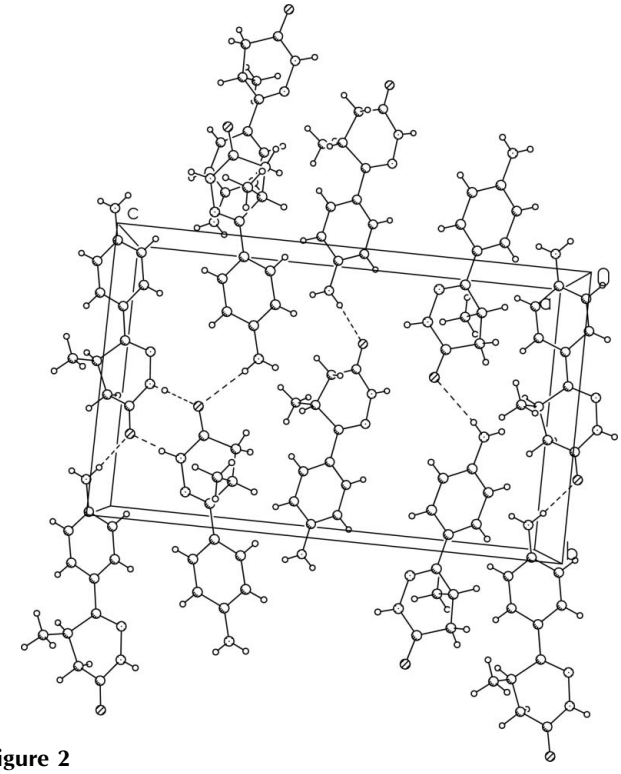


Figure 2
A packing diagram of the title compound, viewed along the *a* axis. Dashed lines represent N—H···O hydrogen bonds.

crystals were recrystallized by dissolving in ethyl acetate, boiling off solvent until the onset of turbidity, and cooling to obtain pure (I). The melting temperature of the product crystals was determined as 474 K, which agrees with the literature value of 474–476 K (Burpitt *et al.*, 1988) obtained by DSC (differential scanning calorimetry). Plate-like colorless single crystals of (I) suitable for X-ray diffraction were obtained by slow evaporation of an ethanol solution at room temperature.

Crystal data

$C_{11}H_{13}N_3O$
M_r = 203.24
Orthorhombic, $P2_12_12_1$
a = 9.765 (2) Å
b = 11.552 (2) Å
c = 18.796 (4) Å
V = 2120.3 (7) Å^3
Z = 8
D_x = 1.273 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 293 (2) K
Plate, colorless
0.51 × 0.16 × 0.06 mm

Data collection

Rigaku R-AXIS RAPID IP area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.942, T_{max} = 0.995
20514 measured reflections
2743 independent reflections
1914 reflections with $I > 2\sigma(I)$
R_{int} = 0.055
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.046
$wR(F^2)$ = 0.128
S = 1.04
2743 reflections
272 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0731P)^2 + 0.0063P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.18 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.0061 (18)

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

D—H···A	D—H	H···A	D···A	D—H···A
N4—H4B···O2^{i}	0.86	2.11	2.961 (4)	173
N6—H6B···O1^{ii}	0.86	2.02	2.883 (3)	177
N1—H1B···O1^{iii}	0.86	2.40	3.153 (4)	147
N3—H3B···O2^{iv}	0.86	2.15	2.921 (3)	149

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

All H atoms were placed in calculated positions and constrained to ride on their parent atoms, with C—H = 0.93–0.98 Å and U_{iso}(H) = 1.2U_{eq}(C), and N—H = 0.86 Å and U_{iso}(H) = 1.2U_{eq}(N).

Data collection: *RAPID-AUTO* (Rigaku, 2004); cell refinement: *RAPID-AUTO*; data reduction: *RAPID-AUTO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *SHELXTL*.

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