2-[(2-Oxopyrrolidin-1-yl)carbonylmethyl]-2,3-dihydro-1H-isoindole-1,3-dione: an antiamnesic agent

S. Thamotharan, V. Parthasarathi, P. Gupta, D. P. Jindal, P. Piplani and Anthony Linden
The title compound, C₁₄H₁₂N₂O₄, is a potential anti-amnesic agent. The pyrrolidinone ring has an envelope conformation. The dihedral angle between the N-substituted phthalimide moiety and the pyrrolidinone ring is 77.16 (5)°. In the solid state, symmetry-related molecules are linked by weak intermolecular C···H–O interactions, forming a continuous chain.

Comment

The conformations of molecules with anti-amnesic activity have attracted considerable interest (Amato et al., 1991), and the structure determination of the title compound, (I), was carried out to continue the investigation of a new class of anti-amnesic agents (Thamotharan, Parthasarathi, Malik et al., 2003; Thamotharan, Parthasarathi, Gupta et al., 2003).

Fig. 1 shows the molecular structure of (I) with the atom-numbering scheme. The geometric parameters of the N-substituted phthalimide moiety in (I) are almost the same as those in 2-(5-chloropyridin-2-yl)-2,3-dihydro-1H-isoindole-1,3-dione (Holband et al., 2001). The angles C₅–C₄–C₉ [117.2 (2)] and C₆–C₇–C₈ [117.4 (2)] are significantly smaller than the other angles in the benzene ring. Similar observations have been made in related structures (Christensen & Thom, 1971, and references therein). This angular distortion can be explained by the strain caused by fusion with the five-membered ring.

In (I), the five-membered pyrrolidinone ring exhibits an envelope conformation, with atom C₁₅ as the flap, a pseudo-rotation angle Δ = 270.3 (2)° and a maximum torsion angle ϕₘ = 30.7 (1)° for the atom sequence N₁₂–C₁₃–C₁₄–C₁₅–C₁₆ (Rao et al., 1981). The dihedral angle between the N-substituted phthalimide moiety and the pyrrolidinone ring is 77.16 (5)°. The planar central moiety, N₂–C₁₀–C₁₁–N₁₂, is oriented at angles of 7.62 (11) and 84.67 (10)° with respect to the pyrrolidinone and N-substituted phthalimide moieties, respectively.

In the crystal structure, atom C₁₅ acts as a donor for a weak intermolecular C···H–O interaction with carbonyl atom O₁ of an adjacent molecule. This interaction links the molecules into a chain, which runs parallel to the b axis and has a graph-set motif of C(9) (Bernstein et al., 1995). Atom C₁₆ has a weak intermolecular C···H–O interaction with carbonyl atom O₁₃.
of a different adjacent molecule. This interaction also links the molecules into a chain, which runs parallel to the b axis and has a graph-set motif of C(5) (Table 1) (Bernstein et al., 1995). A short intermolecular contact is observed, O3—C1 with a graph-set motif of C(2003). E Acta Cryst. C(1) 2.883 (3) Å [symmetry code: (i) x, y, z].

Experimental

A solution of (1,3-dioxo-1,3-dihydroisooindole-2-yl)acetyl chloride (1.0 g) in dichloromethane was stirred with pyrrolidinone. The dichloromethane was removed and crushed ice was added to the contents. The solid material obtained was filtered off and crystallized from methanol to afford crystals of (I) (yield 0.81 g, 66.5%; m.p. 473 K). A solution of (1,3-dioxo-1,3-dihydroisooindole-2-yl)acetyl chloride (1.0 g) in dichloromethane was stirred with pyrrolidinone. The dichloromethane was removed and crushed ice was added to the contents. The solid material obtained was filtered off and crystallized from methanol to afford crystals of (I) (yield 0.81 g, 66.5%; m.p. 473 K).

Crystal data

C14H12N2O4
Mr = 272.26
Orthorhombic, Pbcn
a = 10.7480 (2) Å
b = 8.3280 (1) Å
V = 2498.06 (7) Å³
Z = 8
Dx = 1.448 Mg m⁻³

Mo Kα radiation
Cell parameters from 2839 reflections
θ = 2.0°–26.0°
μ = 0.11 mm⁻¹
T = 160 (2) K
Plate, colourless
0.18 × 0.18 × 0.05 mm

Data collection

Nonius KappaCCD diffractometer
ω scans with κ offsets
Absorption correction: none
29914 measured reflections
2459 independent reflections
1620 reflections with I > 2σ(I)

Refinement

Refinement on F²
wR(F²) = 0.047
S = 1.03
2459 reflections
181 parameters
H-atom parameters constrained

Table 1

Hydrogen-bonding geometry (Å, °).

<table>
<thead>
<tr>
<th>D—H—A</th>
<th>D—H</th>
<th>H—A</th>
<th>D—A</th>
<th>D—H—A</th>
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<tr>
<td>C15—H152—O1i</td>
<td>0.99</td>
<td>2.44</td>
<td>3.426 (3)</td>
<td>175</td>
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<tr>
<td>C16—H162—O1ii</td>
<td>0.99</td>
<td>2.56</td>
<td>3.261 (3)</td>
<td>128</td>
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</table>

Symmetry codes: (i) 1∕2 − x, 1∕2 + y, 1∕2 − z; (ii) −x + 1∕2, 1∕2 + y, z.

All H atoms were placed in geometrically idealized positions (C—H = 0.95–0.99 Å) and constrained to ride on their parent atoms, with U(eq)(H) = 1.2Ueq(C).

Figure 1

View of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of arbitrary radii.

Data collection: COLLECT (Nonius, 2000); cell refinement: DENZO–SMN (Otwinski & Minor, 1997); data reduction: DENZO–SMN and SCALEPACK (Otwinski & Minor, 1997); program(s) used to solve structure: SIR92 (Altomare et al., 1994); program(s) used to refine structure: SHELXL97 (Sheldrick, 1997); molecular graphics: ORTEP-3 (Version 1.07; Farrugia, 1997); software used to prepare material for publication: SHELXL97 and PLATON (Spek, 2003).

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References