

Morpholine-2,5-dione

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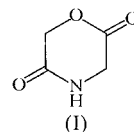
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In the title compound, C₄H₅NO₃, the morpholine ring adopts a boat conformation that is distorted towards twist-boat, the boat ends being the two Csp³ atoms of the ring. The molecular packing is stabilized by the establishment of strong intermolecular NH...OC hydrogen bonds, which give rise to centrosymmetric dimers, and a network of weak CH₂...OC hydrogen bonds, where each dimer interacts with eight neighbouring morpholinedione rings.

Comment

Recently, there has been much interest in developing biodegradable polymers since they have a wide range of applications in the biomedical field (Huang, 1985). Most of these materials belong to the family of aliphatic polyesters, and they are mainly obtained by ring-opening polymerization of lactones such as glycolide and lactide. Poly(ester amides) also constitute a group with potential applications in the above field because of their ability to establish strong intermolecular hydrogen-bond interactions between the amide groups (Montané *et al.*, 2002). These hydrogen bonds may enhance mechanical and thermal properties, while degradability may be ensured by the presence of labile ester groups. Poly-peptides belong to the family of poly(ester amides) and have an additional feature of interest because they are usually composed of metabolizable α -amino acid and α -hydroxy acid units. These polymers can be synthesized by ring-opening polymerization reactions of morpholine-2,5-dione derivatives (In't Veld *et al.*, 1990). Furthermore, copolymerization of these rings with lactones such as caprolactone (In't Veld *et al.*, 1992) or glycolide (In't Veld *et al.*, 1994), in order to obtain products exhibiting a wide range of properties, has been assayed with promising results. Despite the growing interest in this class of polymers, data on structures of starting monomers are limited to a few publications. Thus, only the crystal structures of substituted morpholine-2,5-diones, such as (3*R*,6*S*)-3-benzyl-6-isopropylmorpholine-2,5-dione (Bolte & Egert, 1994), 3-benzyl-3-hydroxy-6-methylamino-6-(2-methylpropyl)-

morpholine-2,5-dione (Iijima *et al.*, 1992) and (\pm)-6-benzyl-3,3-dimethylmorpholine-2,5-dione (Linden *et al.*, 2001), have been reported. In the present work, we study the structure of unsubstituted morpholine-2,5-dione, (I). It is worth noting that this ring has a chemical constitution that is intermediate between that of the cyclic dipeptide of glycine (piperazine-2,5-dione) and the glycolide ring.



The molecule of (I) is shown in Fig. 1, and selected torsion angles are given in Table 1. The ester and amide groups are almost planar, with r.m.s. deviations of 0.002 Å for atoms C3, C2, O2 and O1, and 0.046 Å for atoms C6, C5, O5, N4 and C3, from the mean planes passing through these atoms. The cyclic molecule has an irregular skew-boat conformation in which the two indicated planar groups occur. The boat ends are the two Csp³ atoms, which have deviations of 0.322 (1) (atom C3) and 0.359 (2) Å (atom C6) from the base of the boat defined by the other four ring atoms. The twist of the ring results from the slight non-planarity of the base atoms, which is indicated by the deviations of the C3–N4–C5–C6 and C6–O1–C2–C3 torsion angles from 0° (Table 1). The puckering parameters (Cremer & Pople, 1975) are $Q = 0.404$ (1) Å, $\theta = 87.9$ (2)° and $\varphi = 313.1$ (2)°, which indicate a conformation midway between boat (ideal values of $\theta = 90^\circ$ and $\varphi = 60k^\circ$, where k is an integer) and twist-boat [$\theta = 90^\circ$ and $\varphi = (60k + 30)^\circ$]. Equivalent ring-puckering parameters were found for (\pm)-6-benzyl-3,3-dimethylmorpholine-2,5-dione [$Q = 0.463$ (2) Å, $\theta = 92.4$ (2)° and $\varphi = 133.4$ (2)°] and (3*R*,6*S*)-3-benzyl-6-isopropylmorpholine-2,5-dione [$Q = 0.494$ (2) Å, $\theta = 93.1$ (2)° and $\varphi = 129.3$ (2)°] (Linden *et al.*, 2001), whereas an almost completely flat boat was found for the only other substituted morpholine ring compound studied so far (Iijima *et al.*, 1992). This is the only studied compound that has substituted groups on both Csp³ atoms.

In (I), the NH group forms an intermolecular hydrogen bond with the amide O atom of an adjacent molecule (Table 2 and Fig. 2). This acceptor molecule then donates back to the first molecule, thereby linking pairs of molecules into centrosymmetric dimers whose interactions can be described by the graph-set motif $R_2^2(8)$ (Bernstein *et al.*, 1995). These interactions were found in the previously studied morpholinediones and explained in detail for (\pm)-6-benzyl-3,3-dimethylmorpholine-2,5-dione (Linden *et al.*, 2001).

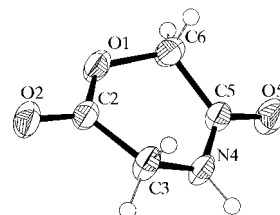


Figure 1

The molecular structure of (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

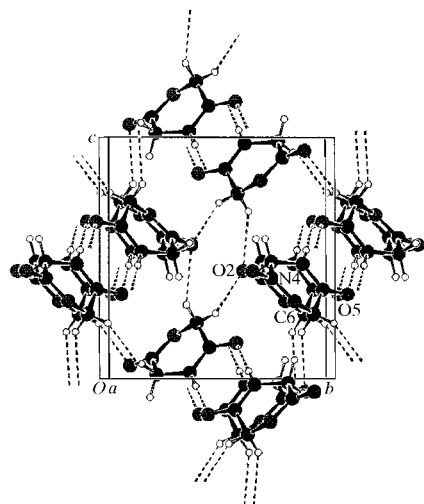


Figure 2
The molecular packing of (I). The dashed lines indicate hydrogen bonds.

The molecular packing of (I) is also characterized by the establishment of weak hydrogen-bond interactions between CH_2 and CO groups (Table 2). In this way, the ester carbonyl group of a morpholinedione ring forms a bifurcated hydrogen bond with the glycolidyl H atoms of two neighbouring rings. Furthermore, each glycolidyl H atom of the former ring interacts with the carbonyl ester group of a different neighbouring molecule. Note that similar and short $\text{H}\cdots\text{O}$ distances are found (2.48 and 2.40 Å). These interactions were not reported for the previously studied morpholine-2,5-diones, which comprise mono- or disubstituted glycolidyl units. However, weak $\text{C}\cdots\text{H}\cdots\text{O}$ intermolecular hydrogen bonds playing a decisive role in the crystal organization were also found in the related glycolide ring (Belen'kaya *et al.*, 1997) and indeed in the lactide ring (van Hummel *et al.*, 1982; Belen'kaya *et al.*, 1997), the $\text{H}\cdots\text{O}$ distances being within the 2.33–2.44 Å range.

Experimental

Compound (I) was synthesized by the cyclization reaction of the *N*-chloroacetyl glycine sodium salt performed under the conditions reported previously (In't Veld *et al.*, 1994). The reaction was carried out under vacuum, using Celite and Sb_2O_3 as adsorbent and catalyst, respectively. The temperature of the reaction was maintained at 423 K for 2 h and then at 488 K for 4 h. A yellow solid sublimed and was recrystallized from acetonitrile to give colourless prismatic crystals (yield 32%, m.p. 466 K). ^1H NMR (DMSO): δ 8.34 (*b*, 1H, NH), 4.65 (*s*, 2H, OCH_2), 4.00 (*d*, 2H, NHCH_2). ^{13}C NMR (DMSO): δ 166.84 (CONH), 165.84 (COO), 67.89 (COOCH_2), 42.73 ($\text{CONH}\text{-CH}_2$). IR (KBr, ν , cm^{-1}): 2932 (CH_2), 1748 ($\text{C}=\text{O}$, ester), 1694 (amide I), 1436 (amide II), 1265 ($\text{C}-\text{O}-\text{C}$).

Crystal data

$\text{C}_4\text{H}_5\text{NO}_3$
 $M_r = 115.09$
Monoclinic, $P2_1/n$
 $a = 5.379$ (5) Å
 $b = 9.218$ (2) Å
 $c = 9.794$ (2) Å
 $\beta = 92.28$ (4)°
 $V = 485.2$ (5) Å³
 $Z = 4$

$D_x = 1.575$ Mg m⁻³
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
 $\theta = 10\text{--}22^\circ$
 $\mu = 0.14$ mm⁻¹
 $T = 293$ (2) K
Needle, colourless
0.60 × 0.14 × 0.10 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
 ω scans
1471 measured reflections
1406 independent reflections
1139 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.012$

$\theta_{\text{max}} = 30.0^\circ$
 $h = -7 \rightarrow 7$
 $k = 0 \rightarrow 12$
 $l = 0 \rightarrow 13$
1 standard reflection
frequency: 120 min
intensity decay: none

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.044$
 $wR(F^2) = 0.130$
 $S = 1.05$
1406 reflections
79 parameters
H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0732P)^2 + 0.1054P]$
where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\text{max}} < 0.001$
 $\Delta\rho_{\text{max}} = 0.30$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.25$ e Å⁻³

Table 1

Selected torsion angles (°).

| | | | |
|-------------|-------------|-------------|-------------|
| C6–O1–C2–C3 | –11.27 (18) | O1–C2–C3–N4 | –22.40 (18) |
| C3–N4–C5–C6 | –8.71 (19) | C2–O1–C6–C5 | 36.48 (19) |
| C5–N4–C3–C2 | 33.13 (19) | N4–C5–C6–O1 | –26.12 (19) |

Table 2

Hydrogen-bond geometry (Å, °).

| $D\cdots H\cdots A$ | $D\text{--}H$ | $H\cdots A$ | $D\cdots A$ | $D\text{--}H\cdots A$ |
|-----------------------------------|---------------|-------------|-------------|-----------------------|
| N4–H4 \cdots O5 ⁱ | 0.88 (2) | 2.01 (2) | 2.888 (2) | 177 (2) |
| C6–H61 \cdots O2 ⁱⁱ | 0.97 | 2.48 | 3.301 (2) | 142 |
| C6–H62 \cdots O2 ⁱⁱⁱ | 0.97 | 2.40 | 3.297 (2) | 153 |

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

The amide H atom was located in a difference Fourier map and refined isotropically. The remaining H atoms were placed in calculated positions, with $\text{C}\text{--}\text{H}$ distances of 0.97 Å, and treated as riding on their attached C atoms. The U_{iso} parameters of the two H atoms of each CH_2 group were refined as free variables.

Data collection: *CAD-4 Software* (Kiers, 1994); cell refinement: *CAD-4 Software*; data reduction: *WinGX-PC* (Farrugia, 1999); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *WinGX-PC*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: OB3002). Services for accessing these data are described at the back of the journal.

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