## organic compounds

Acta Crystallographica Section C Crystal Structure Communications ISSN 0108-2701

# $R_4^4(30)$ rectangular rings in 2,5-dioxopiperazine-1,4-diacetic acid

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Received 15 July 2003 Accepted 11 August 2003 Online 23 September 2003

Molecules of the title 2,5-dioxopiperazinedione derivative,  $C_8H_{10}N_2O_6$ , occupy centres of symmetry in the crystal structure. The six-membered ring has an almost planar conformation, with the substituent on nitrogen nearly perpendicular to the ring. The ideal geometry of the isolated molecule, as determined by *ab initio* HF–LCAO quantum-mechanical calculations, is slightly more puckered than that observed in the solid state. In the crystal structure, a strong hydrogen bond joins neighbouring molecules, thus forming a network of rectangular  $R_4^4(30)$  rings.

### Comment

The condensation of amino acids or their esters leads to 2,5piperazinediones, an important class of nitrogen-containing organic compounds. These cyclic compounds are found in nature as the result of protein degradation (Bray *et al.*, 1991; Steinberg & Lada, 1983) and are also described as antibiotics (Nakatsuka *et al.*, 1983), antitumorals (Arison & Beck, 1973) and models for protein studies (Benedetti *et al.*, 1976; Radding *et al.*, 1980). The dimerization of iminodiacetic acid or its esters leads naturally to *N*-substituted 2,5-piperazinediones, although the synthesis is generally a low-yield process (Jongkees, 1908; Dubsky & Granacher, 1917; Tapia-Benavides *et al.*, 1997). We have synthesized the title compound, (I), by the cyclization of iminodiacetic acid dimethyl ester in the presence of NiCl<sub>2</sub>.



The title *N*-substituted 2,5-piperazinedione molecule occupies a crystallographic centre of symmetry. The six-membered ring has an almost planar conformation (extremely flattened



Figure 1 An ORTEPII plot (Johnson, 1976) of (I). Displacement ellipsoids are drawn at the 50% probability level.

chair), with a weighted average torsion angle of  $7.63 (12)^{\circ}$  and puckering parameters (Cremer & Pople, 1975)  $Q, \theta$  and  $\varphi$  of 0.067 (2) Å, 7.5 (2)° and 0°, respectively (Fig. 1 and Table 1). The ideal geometry of the isolated molecule as determined by an ab initio HF-LCAO (Hartree-Fock linear combination of atomic orbitals) quantum-mechanical calculation using the GAMESS program (Schmidt *et al.*, 1993) and a 631(d,p) basis set, shows a slightly more puckered conformation, with an average torsion angle within the ring of 13.09°. N,N'-Dimethyldiketopiperazine (Groth, 1969) exhibits a ring conformation close to that of (I), with a weighted average torsion angle of 6.9 (4) $^{\circ}$ ; however, greater degrees of puckering have been found, for example, in 1,6-bis(methoxycarbonylmethyl)-2,5-piperazinedione, for which a weighted average torsion angle of 18.1 (2) $^{\circ}$  was reported (Tapia-Benavides *et al.*, 1997). Atoms O3 and C2 share the plane of the ring atoms, their deviations from the least-squares plane being 0.087 (4) and 0.086 (4) Å, respectively. The substituent on nitrogen is also planar and is almost perpendicular to the ring, the angle between the two least-squares planes being 89.55 (8)°. The C4-N1-C2-C1 and C3-N1-C2-C1 torsion angles are -84.4 (2) and 85.7 (3)°, respectively; the corresponding ideal values for the isolated molecule are -84.76 and  $81.04^{\circ}$ , and the corresponding torsion angles in 1,6-bis(methoxycarbonyl-



#### Figure 2

A view of the extended structure of (I), with hydrogen bonds shown as dashed lines. H atoms not participating in hydrogen bonding have been omitted for clarity.

methyl)-2,5-piperazinedione (Tapia-Benavides *et al.*, 1997) are -78.04 and  $84.94^{\circ}$ .

The large asymmetry in the two carboxy C–O distances [O1-C1 = 1.192 (3) Å and O2-C1 = 1.317 (3) Å] reflects the fact that the H atom is retained by the carboxy group. This H atom is involved in a strong  $O2-H2\cdots O3(x-1, -y-\frac{1}{2}, z-\frac{1}{2})$  hydrogen bond that links the molecules, with a donor-acceptor distance of 2.726 (3) Å and a  $D-H\cdots A$  angle of 166 (3)° (Table 2). Using graph-set analysis (Bernstein *et al.*, 1995) to describe patterns in the hydrogen-bond network, we find rectangular-shaped  $R_4^4(30)$  rings (Fig. 2).

### **Experimental**

Iminodiacetic acid was mixed with NiCl<sub>2</sub> in a solution of ethanol and water and heated at 333 K overnight. The solution was left to cool and evaporate slowly at room temperature; after a few months, small single crystals had grown (with a slight green superficial tint caused by impurities). Prior to data collection, Laue photographs of the crystal were taken in order to appraise its quality.

Crystal data

$C_{8}H_{10}N_{2}O_{6}$ $M_{r} = 230.18$ Monoclinic, $P_{2_{1}}/c$ $a = 5.5322 (6) \text{ Å}$ $b = 9.1505 (13) \text{ Å}$ $c = 9.8235 (8) \text{ Å}$ $\beta = 108.189 (7)^{\circ}$ $V = 472.44 (9) \text{ Å}^{3}$ $Z = 2$	$D_x = 1.618 \text{ Mg m}^{-3}$ Mo K $\alpha$ radiation Cell parameters from 14 reflections $\theta = 7.7-13.6^{\circ}$ $\mu = 0.14 \text{ mm}^{-1}$ T = 293 (2)  K Plate, colourless $0.27 \times 0.23 \times 0.09 \text{ mm}$
Data collection	
Enraf-Nonius CAD-4 diffractometer $\omega$ -2 $\theta$ scans 2943 measured reflections 872 independent reflections 604 reflections with $I > 2\sigma(I)$ $R_{int} = 0.045$	$\theta_{\max} = 25.5^{\circ}$ $h = -6 \rightarrow 6$ $k = -11 \rightarrow 11$ $l = -11 \rightarrow 11$ 3 standard reflections frequency: 180 min intensity decay: 3%
Refinement	
Refinement on $F^2$ $R[F^2 > 2\sigma(F^2)] = 0.042$ $wR(F^2) = 0.117$ S = 1.05 872 reflections 76 parameters H atoms treated by a mixture of independent and constrained refinement	$w = 1/[\sigma^{2}(F_{o}^{2}) + (0.0482P)^{2} + 0.2592P]$ where $P = (F_{o}^{2} + 2F_{c}^{2})/3$ $(\Delta/\sigma)_{max} < 0.001$ $\Delta\rho_{max} = 0.31 \text{ e} \text{ Å}^{-3} - \Delta\rho_{min} = -0.26 \text{ e} \text{ Å}^{-3}$

The position of the carboxy H atom was determined from a difference Fourier map and refined freely, with the  $U_{iso}$  value constrained to  $1.5U_{eq}(O)$ . The remaining H atoms were constrained to an ideal geometry and were allowed for as riding on their parent atoms. Examination of the crystal structure with *PLATON* (Spek, 2003) showed that there are no solvent-accessible voids in the crystal lattice.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *HELENA* (Spek, 1997); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997);

#### Table 1

Selected geometric parameters (Å, °).

O1-C1	1.192 (3)	N1-C3	1.329 (3)
O2-C1	1.317 (3)	N1-C2	1.455 (3)
O3-C3	1.236 (3)		
$C_{3}-N_{1}-C_{4}$	124.31 (18)	01 - C1 - O2	124.1 (2)
C2-N1-C4	115.65 (17)	N1-C2-C1	110.26 (18)
$C_{3}-N_{1}-C_{2}-C_{1}$	85.7 (3)	$C_2 - N_1 - C_3 - O_3$	4.8 (3)
O1-C1-C2-N1	-5.0(4)	C4-N1-C3-O3	174.0 (2)
O2-C1-C2-N1	176.95 (19)		

## Table 2

Hydrogen-bonding geometry (Å, °).

 $D-H\cdots A$  D-H  $H\cdots A$   $D\cdots A$   $D-H\cdots A$ 
 $O2-H2\cdots O3^i$  0.89 (4)
 1.85 (4)
 2.726 (3)
 166 (3)

Symmetry code: (i)  $x - 1, -\frac{1}{2} - y, z - \frac{1}{2}$ .

program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*97.

Financial assistance from Fundação para a Ciência e a Tecnologia (Sapiens POCTI/QUI/42536) and Chymiotechnon, Portugal, is acknowledged.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FA1026). Services for accessing these data are described at the back of the journal.

### References

Arison, B. H. & Beck, J. L. (1973). Tetrahedron, 29, 2743–2746.

- Benedetti, E., Marsh, R. E. & Goodman, M. (1976). J. Am. Chem. Soc. 98, 6676–6684.
- Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). Angew. Chem. Int. Ed. Engl. 34, 1555–1573.
- Bray, A. M., Maeji, N. J., Campbell, R. A. & Geysen, H. M. (1991). J. Org. Chem. 56, 6659–6671.
- Cremer, D. & Pople, J. A. (1975). J. Am. Chem. Soc. 97, 1354-1358.
- Dubsky, J. V. & Granacher, C. (1917). Chem. Ber. 50, 1962–1969.
- Enraf–Nonius (1989). *CAD-4 Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.
- Groth, P. (1969). Acta Chem. Scand. 23, 3155.
- Johnson, C. K. (1976). ORTEPII. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
- Jongkees, W. J. A. (1908). Recl Trav. Chim. 27, 287-326.
- Nakatsuka, S., Yamada, K., Yoshida, K., Asano, O., Murakami, Y. & Goto, T. (1983). Tetrahedron Lett. 24, 5627–5630.
- Radding, W., Donzel, B., Ueyama, N. & Goodman, M. (1980). J. Am. Chem. Soc. 102, 5999–6005.
- Schmidt, M. W., Baldridge, K. K., Boatz, J. A., Elbert, S. T., Gordon, M. S., Jensen, J. J., Koseki, S., Matsunaga, N., Nguyen, K. A., Su, S., Windus, T. L., Dupuis, M. & Montgomery, J. A. (1993). J. Comput. Chem. 14, 1347–1363.
- Sheldrick, G. M. (1997). SHELXS97 and SHELXL97. University of Göttingen, Germany.
- Spek, A. L. (1997). HELENA. University of Utrecht, The Netherlands.
- Spek, A. L. (2003). J. Appl. Cryst. 36, 7-13.
- Steinberg, S. M. & Lada, J. L. (1983). J. Org. Chem. 48, 2295-2298.
- Tapia-Benavides, A. R., Tlahuext, H. & Contreras, R. (1997). *Heterocycles*, 45, 1679–1686.