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Received 17 March 2005

Accepted 11 April 2005

Online 13 May 2005

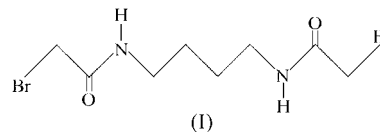
The title compound, C₈H₁₄Br₂N₂O₂, lies about an inversion centre and adopts a pleated conformation, with the C(O)—NH—CH₂—CH₂ and NH—CH₂—CH₂—CH₂ torsion angles of the butanediamine residue being -89.5 (6) and -62.1 (7)°, respectively. These data are useful in discerning the structure of polymers containing such a unit. A skew conformation is found for the Br—CH₂—C(O)—NH torsion angle [-124.2 (4)°]. The molecular packing is stabilized by strong hydrogen bonds between amide groups and also by weak CH₂⋯OC interactions. In this way, each molecule interacts with its six closest neighbours through eight hydrogen bonds.

Comment

The development of new biodegradable polymers currently receives much attention due to their increasing number of applications in different fields, such as medical technology. For instance, polyesters in general and glycolide derivatives in particular have been applied in surgical sutures and drug-delivery systems (Huang, 1985; Chu, 1997). Poly(ester amide)s have recently been considered due to their ability to establish intermolecular hydrogen bonds that improve mechanical properties. In this way, new materials with a sequential repeat unit made up of glycolic acid, a diamine and a dicarboxylic acid have been patented as bioabsorbable sutures (Barrows, 1985). We have recently demonstrated that these kinds of polymers can also be prepared by a condensation reaction between *N,N'*-bischloroacetyldiamines and dicarboxylate salts (Vera *et al.*, 2004), which results in both high yield and high molecular weight. The driving force of these polymerizations corresponds with the formation of metal halide salts (Epple & Kirschnick, 1997).

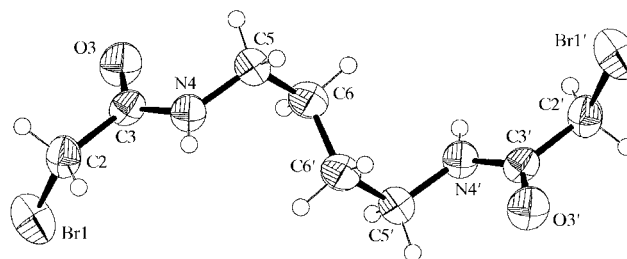
The title compound, (I), is also a suitable monomer for the preparation of a series of poly(ester amide)s which include glycolyl and butylenediamine residues. The study of its crystalline structure provides information on the arrangement of the reactive groups. In addition, the crystallographic model

compound resulting from this study is useful in discerning the structure of the related polymer fragment. Few crystallographic data on poly(ester amide)s are available. Results obtained with some polymers derived from α -amino acids indicate that structures with characteristic features of both polyesters and polyamides can be obtained (Paredes *et al.*, 1999).



The molecule of (I) is shown in Fig. 1 and principal torsion angles are given in Table 1. The amide group is planar within experimental error, with an r.m.s. deviation of 0.0360 Å for atoms C2, C3, O3, H4, N4 and C5 from the best plane passing through them. The molecules adopt a pleated conformation with an inversion symmetry centre (symmetry code: $1 - x, 1 - y, 1 - z$). The *tggtggt* sequence of torsion angles of the butane-diamide moiety was unexpected. An inspection of the Cambridge Structural Database (CSD, Version 5.26, November 2004, *ConQuest* Version 1.7; Allen, 2002; Bruno *et al.*, 2002) showed that the structures of only 30 molecules with this fragment have been solved to date, most of them corresponding to aromatic and cycloalkane derivatives or cyclic compounds. These are not entirely representative of conformational preferences, due to packing requirements associated with end rings or with geometric restrictions associated with the ring closure. Only five linear and aliphatic compounds are relevant to the structure reported here, namely 1,4-bis(propylaminomalonylamino)butane (CSD refcode QUJBE; Navarro *et al.*, 1995), butane-1,4-diylbis(acetamide) (ABAWOQ; Navarro *et al.*, 1998), *N,N'*-bis(glycylglycine)-1,4-diaminobutane bis(hydrogen chloride) (ACEHAS; Madhavaiah *et al.*, 2004), *N,N'*-bis(2-hydroxyiminopropionyl)-1,4-diaminobutane dihydrate (BIGFEC; Fritsky *et al.*, 1999) and butane-1,4-diylbis(formamide) (TOPPUJ; Chaney *et al.*, 1996).

Butane-1,4-diylbis(acetamide) (Navarro *et al.*, 1998) was specifically investigated to gain insights into the structure of aliphatic polyamides. *Ab initio* quantum-mechanical calculations showed an energy minimum when the C(O)—NH—

**Figure 1**

A view of the molecule of (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. Primed atoms are at the symmetry position $(-x, 2 - y, -z)$.

$\text{CH}_2\text{—CH}_2$ (φ) and $\text{CH}_2\text{—CH}_2\text{—NH—C(O)}$ (φ') torsion angles tended to 90° and -90° , respectively, while the other main-chain torsion angles remained close to 180° . In contrast, the crystal structure showed a quasi-all-*trans* conformation and a packing which resembled the characteristic sheet structure of aliphatic polyamides. Only a slight deviation from 180° was observed for the φ and φ' torsion angles ($\pm 7.5^\circ$), which suggests the need to consider similar distortions in the structural modelling of polyamides. An all-*trans* conformation was also found in both *N,N'*-bis(2-hydroxyiminopropionyl)-1,4-diaminobutane dihydrate (Fritsky *et al.*, 1999) and butane-1,4-diylbis(formamide) (Chaney *et al.*, 1996); the latter compound, in addition to the characteristic hydrogen bonds between amide groups, has short contacts between the formyl H and the carbonyl O atoms.

Other structures have been postulated in polyamides when the specific chemical sequence (*i.e.* nylons derived from diamines and diacids with an odd number of C atoms) and the indicated conformation give rise to weak intermolecular interactions. Thus, a good hydrogen-bond geometry and an energetic stabilization can be attained by modifying the φ and φ' torsion angles towards skew conformations. This feature is clearly observed in 1,4-bis(propylaminomalonylamino)butane (Navarro *et al.*, 1995), a model compound for nylons derived from butanediamine and malonic acid. The φ and φ' torsion angles appear rather variable in aromatic derivatives. Thus,

values close to *trans* [173.4 and 169.5° for *p,p'*-dimethoxy-*N,N'*-tetramethylenedibenzamide (Brisson *et al.*, 1989) and *N,N'*-tetramethylenedibenzamide (Harkema *et al.*, 1980) derivatives, respectively], skew (120.0° for *p,p'*-dicyano-*N,N'*-tetramethylenedibenzamide; Brisson *et al.*, 1989) and *gauche* (79.8° for *p,p'*-di-*tert*-butyl-*N,N'*-tetramethylenedibenzamide; Brisson *et al.*, 1989) conformations have been experimentally observed. A pleated conformation with an unusual $\bar{t}st\bar{t}st$ sequence of torsion angles has been reported for only one linear and aliphatic compound, namely *N,N'*-bis(glycylglycine)-1,4-diaminobutane bis(hydrogen chloride) (Madhavaiah *et al.*, 2004).

The $\text{Br—CH}_2\text{—C(O)—NH}$ torsion angle of (I) has a skew [-124.2 (4°)] conformation that prevents an intramolecular electrostatic interaction between the Br atom and the H atom of the amide group. Intramolecular $\text{N—H}\cdots\text{Cl}$ hydrogen bonds have been reported for some related chloroacetamides (Urpí *et al.*, 2003; Rao & Mallikarjunan, 1973; Kalyanaraman *et al.*, 1978), a *cis* conformation being clearly stabilized in these cases. However, inspection of the CSD showed that this torsion angle is rather variable in bromoacetamide derivatives. Thus, only five compounds of a total of 17 bromoacetamide fragments have been reported to date. *Trans*, *gauche*, skew and *cis* conformations have been observed in one, five, seven and four fragments, respectively. In the last case, $\text{N—H}\cdots\text{Br}$ and $\text{N}\cdots\text{Br}$ distances close to 2.5 and 3.0 Å, respectively, were reported (Ozawa *et al.*, 1974; Yavorskii *et al.*, 1990; Amrhein *et al.*, 2002).

The packing in (I) is characterized by the establishment of strong intermolecular hydrogen bonds between amide groups along a single direction (Fig. 2). In this way, each molecule interacts with its four closest neighbours *via* *c*-glide-plane operations. The hydrogen bonds are essentially linear and have normal geometry (Table 2). In addition, weak intermolecular $\text{CH}_2\cdots\text{OC}$ hydrogen bonds (Fig. 2 and Table 2) link inversion-related molecules. This kind of $\text{CH}_2\cdots\text{OC}$ interaction has also been found in related ester compounds (Urpí *et al.*, 2004; Martínez-Palau *et al.*, 2005). The quasi-perpendicular orientation between the pleated tetramethylene segment and the terminal bromoacetamide fragments should be emphasized. The molecular conformation and packing clearly differ from those of related butane-1,4-diylbis(halogenoacetate) compounds (Urpí *et al.*, 2004; Martínez-Palau *et al.*, 2005), where strong hydrogen-bond interactions cannot be established.

Experimental

In a round-bottomed flask provided with a magnetic stirrer, butane-1,4-diamine (0.05 mol) and sodium hydroxide (0.1 mol) were dissolved in water (50 ml). Bromoacetyl bromide (0.10 mol) was dissolved in ethyl ether (20 ml) and added dropwise. The resulting two-phase mixture was stirred for 1 h in an ice-cooled bath. Drops of a 1 M NaOH solution were also added in order to keep the pH close to 10–11 and to neutralize the hydrobromic acid produced during the reaction. The white solid which precipitated was filtered off, washed copiously with water and ethyl ether, and then recrystallized from ethanol to give colourless crystals of (I) (yield 85%; m.p. 408 K).

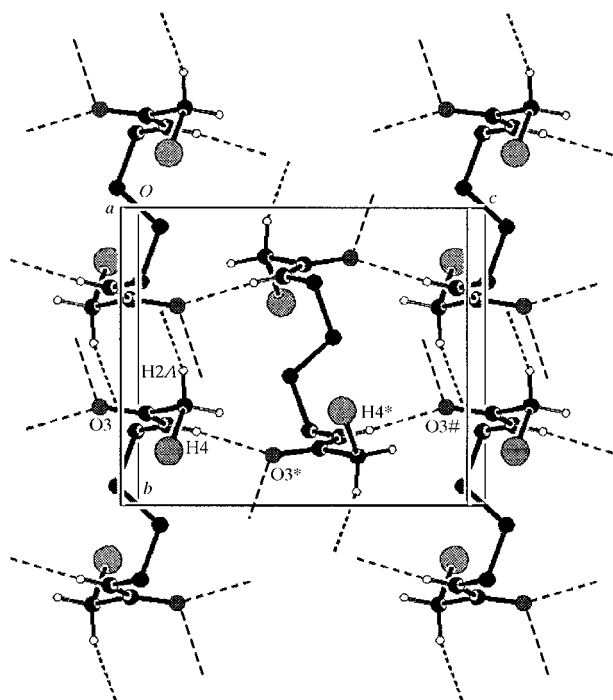


Figure 2

The crystalline packing of (I). A view along the crystallographic *a* axis has been selected in order to show both the conformation of the tetramethylene segment and the network of hydrogen-bond interactions (dashed lines). Atoms marked with an asterisk (*) or a hash (#) are at the symmetry positions $(x, \frac{3}{2} - y, z + \frac{1}{2})$ and $(x, y, 1 + z)$, respectively. Atom H2A forms a hydrogen bond with atom O3 at $(1 - x, 1 - y, -z)$; this has been omitted for clarity.

¹H NMR (DMSO): δ 8.21 (*t*, 2H, NH), 3.77 (*s*, 4H, BrCH₂CO), 3.01 (*m*, 4H, NHCH₂), 1.35 (*m*, 4H, NHCH₂CH₂); ¹³C NMR (DMSO): δ 166.02 (CO), 38.83 (NHCH₂), 29.72 (BrCH₂CO), 26.38 (NHCH₂CH₂).

Crystal data

C₈H₁₄Br₂N₂O₂ $D_x = 1.842 \text{ Mg m}^{-3}$
 $M_r = 330.01$ Mo $K\alpha$ radiation
 Monoclinic, $P2_1/c$ Cell parameters from 25 reflections
 $a = 8.7065 (18) \text{ \AA}$ $\theta = 12\text{--}21^\circ$
 $b = 7.7518 (13) \text{ \AA}$ $\mu = 6.79 \text{ mm}^{-1}$
 $c = 9.333 (4) \text{ \AA}$ $T = 293 (2) \text{ K}$
 $\beta = 109.15 (2)^\circ$ Plate, colourless
 $V = 595.1 (3) \text{ \AA}^3$ $0.4 \times 0.2 \times 0.04 \text{ mm}$
 $Z = 2$

Data collection

Enraf–Nonius CAD-4 diffractometer $R_{\text{int}} = 0.029$
 $\omega/2\theta$ scans $\theta_{\text{max}} = 30.0^\circ$
 Absorption correction: Gaussian $h = -12 \rightarrow 11$
 (PLATON; Spek, 2003) $k = 0 \rightarrow 10$
 $T_{\text{min}} = 0.228, T_{\text{max}} = 0.761$ $l = 0 \rightarrow 13$
 1816 measured reflections 1 standard reflection
 1729 independent reflections frequency: 120 min
 837 reflections with $I > 2\sigma(I)$ intensity decay: none

Refinement

Refinement on F^2 H atoms treated by a mixture of independent and constrained refinement
 $R[F^2 > 2\sigma(F^2)] = 0.060$
 $wR(F^2) = 0.159$ $w = 1/[\sigma^2(F_o^2) + (0.0771P)^2]$
 $S = 1.02$ where $P = (F_o^2 + 2F_c^2)/3$
 1729 reflections $(\Delta/\sigma)_{\text{max}} < 0.001$
 72 parameters $\Delta\rho_{\text{max}} = 0.85 \text{ e \AA}^{-3}$
 $\Delta\rho_{\text{min}} = -0.54 \text{ e \AA}^{-3}$

Table 1

Selected torsion angles ($^\circ$).

C5–N4–C3–O3	0.5 (8)	Br1–C2–C3–N4	–124.2 (4)
C5–N4–C3–C2	–176.6 (5)	C3–N4–C5–C6	–89.5 (6)
Br1–C2–C3–O3	58.7 (6)	N4–C5–C6–C6 ⁱ	–62.1 (7)

Symmetry code: (i) $-x, 2 - y, -z$.

Table 2

Hydrogen-bond geometry ($\text{\AA}, ^\circ$).

$D\text{--}H\cdots A$	$D\text{--}H$	$H\cdots A$	$D\cdots A$	$D\text{--}H\cdots A$
N4–H4 ⁱⁱⁱ ⋯O3 ⁱⁱ	0.78 (5)	2.07 (5)	2.853 (6)	173 (5)
C2–H2A ⁱⁱⁱ ⋯O3 ⁱⁱⁱ	0.97	2.49	3.367 (6)	150

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

The amide H atoms, which are involved in hydrogen bonds, were located in difference Fourier maps and refined isotropically. The remaining H atoms were placed in calculated positions, with C–H = 0.97 Å, and refined isotropically riding on their attached C atoms. The displacement parameters of the two H atoms of each CH₂ group were refined as free variables.

Data collection: CAD-4 Software (Kiers, 1994); cell refinement: CAD-4 Software; data reduction: WinGX-PC (Version 1.64.05; 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.

This research was supported through the CICYT grant MAT2003/01004 and FEDER funds.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1832). Services for accessing these data are described at the back of the journal.

References

Allen, F. H. (2002). *Acta Cryst.* **B58**, 380–388.
 Amrhein, P., Shivanyuk, A., Johnson, D. W. & Rebek, J. (2002). *J. Am. Chem. Soc.* **124**, 10349–10358.
 Barrows, T. H. (1985). US Patent No. 4 529 792.
 Brisson, J., Gagne, J. & Brisse, F. (1989). *Can. J. Chem.* **67**, 840–849.
 Bruno, I. J., Cole, J. C., Edgington, P. R., Kessler, M., Macrae, C. F., McCabe, P., Pearson, J. & Taylor, R. (2002). *Acta Cryst.* **B58**, 389–397.
 Chaney, J. D., Goss, C. R., Folting, K., Santarsiero, B. D. & Hollingsworth, M. D. (1996). *J. Am. Chem. Soc.* **118**, 9432–9433.
 Chu, C. C. (1997). *Wound Closure Biomaterials and Devices*, edited by C. C. Chu, J. A. von Fraunhofer & H. P. Greisler, ch. 5, pp. 65–106. Boca Raton: CRC Press.
 Epple, M. & Kirschnick, H. (1997). *Chem. Ber. Recl.* **130**, 291–294.
 Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
 Fritsky, I. O., Karaczyn, A., Kozłowski, H., Glowiak, T. & Prisyazhnaya, E. V. (1999). *Z. Naturforsch. Teil B*, **54**, 456–460.
 Harkema, S., van Hummel, G. J. & Gaymans, R. J. (1980). *Acta Cryst.* **B36**, 3182–3184.
 Huang, S. J. (1985). *Encyclopedia of Polymer Science and Engineering*, Vol. 2, edited by H. F. Mark, N. M. Bikales, C. G. Overberger & G. Menges, pp. 230–232. New York: Wiley–Interscience.
 Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
 Kalyanaraman, B., Kispert, L. D. & Atwood, J. L. (1978). *J. Cryst. Mol. Struct.* **8**, 175–181.
 Kiers, C. (1994). *CAD-4 Software*. UNIX Version. Enraf–Nonius, Delft, The Netherlands.
 Madhavaiah, C., Parvez, M. & Verma, S. (2004). *Bioorg. Med. Chem.* **12**, 5973–5982.
 Martínez-Palau, M., Puiggali, J., Solans, X. & Urpí, L. (2005). *Acta Cryst.* **E61**, o1028–o1031.
 Navarro, E., Alemán, C. & Puiggali, J. (1998). *Macromolecules*, **31**, 408–416.
 Navarro, E., Puiggali, J. & Subirana, J. A. (1995). *Macromol. Chem. Phys.* **196**, 2361–2370.
 Ozawa, T., Iitaka, Y., Hirobe, M. & Okamoto, T. (1974). *Chem. Pharm. Bull.* **22**, 2069–2074.
 Paredes, N., Casas, M. T., Puiggali, J. & Lotz, B. (1999). *J. Polym. Sci. Polym. Phys. Ed.* **37**, 2521–2533.
 Rao, S. T. & Mallikarjunan, M. (1973). *Cryst. Struct. Commun.* **2**, 257–260.
 Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
 Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
 Urpí, L., Jiménez, K., Solans, X., Rodríguez-Galán, A. & Puiggali, J. (2003). *Acta Cryst.* **C59**, o24–o25.
 Urpí, L., Martínez-Palau, M., Font-Bardia, M. & Puiggali, J. (2004). *Acta Cryst.* **C60**, o847–o849.
 Vera, M., Rodríguez-Galán, A. & Puiggali, J. (2004). *Macromol. Rapid Commun.* **25**, 812–817.
 Yavorskii, A. S., Pavlovskii, V. I., Andronati, S. A., Dvorkin, A. A., Gifeisman, T. & Simonov, Y. A. (1990). *Zh. Obshch. Khim. (Russian J. Gen. Chem.)*, **60**, 354–360. (In Russian.)