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# Methylfelbamate

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**Key indicators**

Single-crystal X-ray study
*T* = 294 K
Mean σ(C–C) = 0.006 Å
*R* factor = 0.045
*wR* factor = 0.111
Data-to-parameter ratio = 9.4

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



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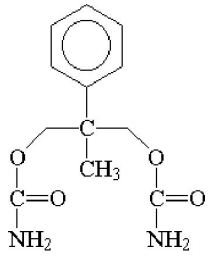
The crystal structure of 2-methyl-2-phenyl-1,3-propanediol dicarbamate (methylfelbamate), $C_{12}H_{16}N_2O_4$, contains two independent molecules in the asymmetric unit. The hydrogen-bonding scheme is three-dimensional and involves interactions of the type N—H···O, C—H···O and N—H···(π-arene). Stereochemical and molecular modelling investigations indicate that the mechanism for anti-epileptic action of the compound is probably different from those of other anticonvulsants.

## Comment

Methylfelbamate (MFBM), like felbamate, was shown many years ago to possess anticonvulsant activity (Ludwig *et al.*, 1969). However, unlike felbamate, no clinical investigations have been published to date. The initial data prompted us to look for possible structural and stereochemical correlations with structures of well known anti-epileptics, such as diphenylhydantoin (Camerman & Camerman, 1971) and diazepam (Camerman & Camerman, 1972). As in the case of felbamate, extensive work to correlate various structural features of MFBM responsible for biological action, such as electron-donating groups, hydrophobic regions and shape, with those of other anticonvulsants has been unsuccessful. This lack of obvious similarities between MFBM and other antiepileptics leads us to believe that the site and mechanism of action of MFBM (as for felbamate) must differ significantly from those of diphenylhydantoin or diazepam types of compounds.



MFBM

The structure of MFBM is presented in Fig. 1. Bond distances and angles are consistent with normal values. The two independent MFBM molecules have conformational differences which are mostly attributable to steric interactions, side-chain flexibility and crystal-packing forces. Unlike the conformation of felbamate (Hempel *et al.*, 2005), which is fully extended, the conformations of the carbamate arms of MFBM are partially lateral to the phenyl ring. Within each arm of the propanediol dicarbamate moiety, the conformation is constant

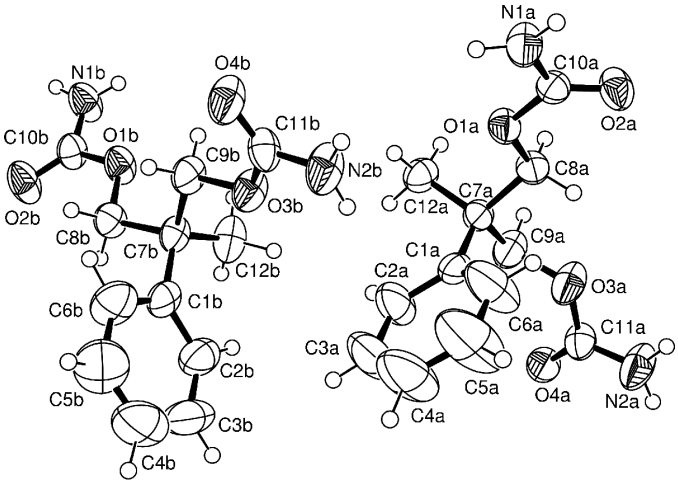



**Figure 1**
The two independent molecules of MFBM, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small circles of arbitrary radii.

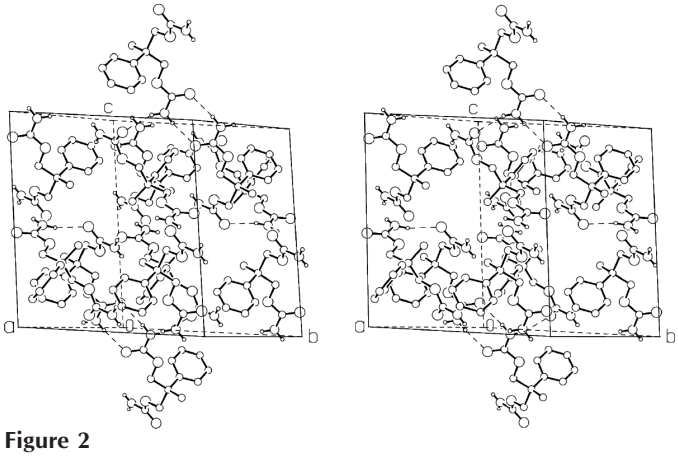



**Figure 2**
A stereoscopic view of the MFBM crystal packing. For clarity, only H atoms involved in the hydrogen bonding are shown. All the atoms are drawn as spheres of arbitrary radii. Dashed lines indicate N—H···O hydrogen bonds.

and the same as observed in felbamate. The torsion angles O2—C10—O1—C8 and O4—C11—O3—C9 in MFBM are −0.7 (4) and −0.2 (5)°, respectively, for molecule *A*, and −2.4 (4) and −1.1 (5)°, respectively, for molecule *B*.

As for felbamate, molecular modelling calculations (*INSIGHT*; Biosym Technologies, 1989) indicated a 30.0 kcal mol$^{-1}$ (1 kcal mol$^{-1}$ = 4.184 kJ mol$^{-1}$) higher energy for rotation about the O1—C10 bond.

The molecules of MFBM in the crystal structure form a three-dimensional N—H···O hydrogen-bonded network and, in contrast with felbamate, there are no distinct hydrophobic and hydrophilic regions. A contribution to the crystal packing from non-standard weak hydrogen bonds of the types C—H···O and N—H···($\pi$-arene) (Steiner, 1997) is also observed (Table 1). The outer atoms in each phenyl ring have high anisotropic displacement parameters. There are no intermolecular approaches to the ring atoms of less than 3.5 Å (2.8 Å for H); this loose crystal packing may result in minor disorder in the positions of the outer ring atoms.

## Experimental

Crystals of methylfelbamate (Wallace Laboratories) suitable for X-ray crystal structure analysis were obtained by slow crystallization from methanol–water mixture (10:1). The crystals were colourless transparent needles.

*Crystal data*

$C_{12}H_{16}N_2O_4$
$M_r$ = 252.27
Triclinic, $P\overline{1}$
$a$ = 9.984 (2) Å
$b$ = 12.040 (3) Å
$c$ = 14.360 (4) Å
$\alpha$ = 96.74 (2)°
$\beta$ = 95.82 (2)°
$\gamma$ = 126.51 (3)°
$V$ = 1345.8 (8) Å$^3$
$Z$ = 4
$D_x$ = 1.245 Mg m$^{-3}$
Cu $K\alpha$ radiation
Cell parameters from 16 reflections
$\theta$ = 22–50°
$\mu$ = 0.79 mm$^{-1}$
$T$ = 294 (2) K
Needle, colourless
0.5 × 0.2 × 0.2 mm

*Data collection*

Picker FACS-1 four-circle diffractometer
$\omega/2\theta$ scans
3626 measured reflections
3385 independent reflections
2591 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.017
$\theta_{max}$ = 55.0°
$h = 0 \rightarrow 10$
$k = -12 \rightarrow 10$
$l = -15 \rightarrow 15$
3 standard reflections
every 100 reflections
intensity decay: 0.3%

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.045
$wR(F^2)$ = 0.111
$S$ = 1.02
3385 reflections
362 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0304P)^2 + 0.4196P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.14 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.13 e Å$^{-3}$
Extinction correction: *SHELXL97* (Sheldrick, 1997)
Extinction coefficient: 0.0068 (5)

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

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N1$A$—H101···O2$A^{i}$ | 0.86 (3) | 2.09 (3) | 2.946 (3) | 176 (3) |
| N1$B$—H201···O4$A^{ii}$ | 0.83 (3) | 2.26 (3) | 3.079 (3) | 170 (3) |
| N1$A$—H102···O4$B^{iii}$ | 0.82 (3) | 2.25 (3) | 3.012 (4) | 154 (3) |
| N1$B$—H202···O2$B^{iv}$ | 0.87 (3) | 2.10 (3) | 2.954 (3) | 167 (3) |
| N2$A$—H104···O4$A^{v}$ | 0.86 (4) | 2.09 (4) | 2.936 (4) | 169 (3) |
| N2$B$—H203···O4$B^{iii}$ | 0.83 (3) | 2.10 (3) | 2.914 (4) | 166 (3) |
| C6$B$—H6$B$···O2$A^{vi}$ | 0.93 | 2.52 | 3.414 (4) | 162 |
| C8$A$—H8$A$1···O2$B^{vii}$ | 0.97 | 2.50 | 3.431 (3) | 160 |
| N2$B$—H204···$Cg1^{viii}$ | 0.86 (4) | 2.80 (4) | 3.640 (4) | 166 (4) |
| N2$A$—H103···$Cg2^{vii}$ | 0.90 (4) | 2.72 (5) | 3.619 (4) | 169 (4) |

Symmetry codes: (i) $-x, -y+2, -z$; (ii) $x-1, y-1, z$; (iii) $-x, -y+1, -z$; (iv) $-x, -y, -z+1$; (v) $-x+2, -y+3, -z+1$; (vi) $x, y-1, z$; (vii) $x, y+1, z$; (viii) $x, y, z$. $Cg1$ is the centroid of the C1$A$–C6$A$ ring and $Cg2$ is the centroid of the C1$B$–C6$B$ ring.

H atoms bonded to C atoms were placed in calculated positions [C—H = 0.93–0.96 Å] and included in the refinement in the riding-model approximation. One overall isotropic displacement parameter was refined for phenyl-ring H atoms and another for methyl and methylene H atoms. The amino H atoms were refined independently with isotropic displacement parameters; the final N—H distances range from 0.82 (3) to 0.90 (4) Å.

Data collection: *Picker Operating Manual* (Picker, 1967); cell refinement: *Picker Operating Manual*; data reduction: *Picker Operating Manual*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97*

(Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

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