perpendicular to the molecular axis. Estimates for libration corrections to be added to the apparent C(1)–C(2) and C(2)–N(3) bond lengths are +0·01 Å and +0·015 Å respectively.

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Structure of Carbamazepine: 5*H*-Dibenz[*b*,*f*]azepine-5-carboxamide

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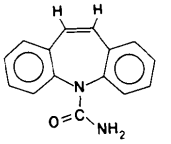
Abstract. $C_{15}H_{12}N_2O$, M_r = 236·27, monoclinic, $P2_1/n$, a = 7·537 (1), b = 11·156 (2), c = 13·912 (3) Å, β = 92·86 (2)°, Z = 4, D_m = 1·34 (2) (flotation), D_x = 1·343 Mg m^{-3}, μ(Mo $K\alpha$) = 0·080 mm^{-1}; R = 0·040 for 1751 observed reflections. In the tricyclic framework of carbamazepine, the central azepine ring has a boat conformation and the dihedral angle between the planar benzene moieties is 126·6°. Intermolecular hydrogen bonding between carboxamide groups forms centrosymmetric dimers. (CAS Reg. No. 298-46-4.)

Introduction. Carbamazepine (1) has clinical use because of its analgesic and anticonvulsant properties and is prescribed in the treatment of epilepsy and trigeminal neuralgia. X-ray structure determinations are used in pharmacological studies aimed at relating the molecular conformation of a given tricyclic drug to its physiological activity at the receptor site. In addition, accurate cell dimensions and molecular parameters are needed for (1) as it has been reported to exist in polymorphic forms (De Camp, Brannon & Maienthal, 1981). Here we report the results of a single-crystal X-ray analysis on carbamazepine obtained by recrystallization from absolute ethanol.



(1)

At the proof stage, it was discovered that this paper was being processed simultaneously with an independent structure determination of carbamazepine (Reboul, Cristau, Soyfer & Astier, 1981). As the coordinates of the latter structure can be transformed to ours ($x' = x - z$, $y' = -\frac{1}{2} + y$, $z' = \frac{1}{2} - z$), the compounds are the same and not polymorphic substances. A short comparison is given at the end of this paper.

* From a dissertation to be submitted to the Graduate School, The Catholic University of America, Washington, DC 20064, in partial fulfillment of the requirements for the PhD degree in chemistry.

Data were collected on a crystal of dimensions 0·25 × 0·27 × 0·30 mm using an automated four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation, λ = 0·71069 Å. Cell dimensions were determined by a least-squares refinement of the setting angles of 15 reflections with 2θ values ranging between 21 and 30°. The monoclinic symmetry was verified by reduction procedures (*International Tables for X-ray Crystallography*, 1969). Systematic extinctions observed on the diffractometer established the space group as $P2_1/n$ (No. 14). Integrated diffraction intensities were measured in the bisecting mode with $3° \leq 2\theta \leq 50°$. The peaks were scanned over a range of $2\theta(K\alpha_1)$ − 0·8° to $2\theta(K\alpha_2)$ + 1·0° using variable scan rates of 2·0 to 29·3° min^{-1} depending on the intensity of the preliminary count. Background counts were taken at each end of the scan with a ratio of total background time to scan time of 0·5. Four standard reflections which were measured periodically showed no apparent decrease in intensity during data collection. The estimated standard deviation in intensity, $\sigma(I)$, was calculated from $\sigma^2(I)$ = TC + 0·000506(TC)^2 where TC is the total observed counts and the constant was derived from a statistical analysis of the intensity distributions of the four standard reflections. The data were corrected for Lorentz and polarization effects. In view of the crystal size and linear absorption coefficient, no absorption correction was applied. Of the 2066 unique reflections measured, 1751 had $I \geq 3\sigma(I)$ and were subsequently used for structure determination and refinement.

The structure was solved by direct methods using *MULTAN* (Germain, Main & Woolfson, 1971) and was refined by full-matrix least-squares calculations. All H atoms were located in a difference Fourier map calculated at an intermediate stage of refinement. Anisotropic refinement of the non-hydrogen atoms with isotropic refinement of the H atoms resulted in a final $R(=\sum||F_o| - |F_c||/\sum|F_o|)$ of 0·040 and $R_w(=\sum w^{1/2}||F_o| - |F_c||/\sum w^{1/2}|F_o|)$ of 0·039. The function minimized was $\sum w(|F_o| - |F_c|)^2$ where $w = [\sigma(F_o)]^{-2}$. The average and maximum shift divided by error were 0·015 and 0·238, respectively. Analysis of the final difference Fourier map revealed no peak greater than 0·13 e Å^{-3}. The scattering factors used were those of Cromer & Mann (1968) for C, N, and O, and that of Stewart, Davidson & Simpson (1965) for H. All calculations (except *MULTAN*) were performed with the XRAY system (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976). Table 1 lists the final atomic parameters.*

Table 1. *Positional parameters and isotropic thermal parameters* (Å^2) *with estimated standard deviations in parentheses*

Equivalent isotropic temperature factors for the non-hydrogen atoms were calculated from $U_{eq} = \frac{1}{3}(U_{11} + U_{22} + U_{33})$.

	x	*y*	*z*	U_{eq}/U
C(1)	0·16994 (19)	0·32668 (13)	0·34962 (10)	0·0334 (8)
C(2)	0·01090 (22)	0·38562 (15)	0·33145 (13)	0·0420 (10)
C(3)	−0·02326 (25)	0·44459 (16)	0·24505 (14)	0·0479 (11)
C(4)	0·10271 (26)	0·44532 (16)	0·17676 (14)	0·0483 (11)
C(5)	0·26145 (25)	0·38678 (15)	0·19460 (12)	0·0444 (10)
C(6)	0·30031 (20)	0·32711 (14)	0·28150 (11)	0·0358 (9)
C(7)	0·47319 (23)	0·26905 (15)	0·29760 (13)	0·0441 (10)
C(8)	0·56837 (23)	0·25672 (15)	0·38023 (13)	0·0442 (10)
C(9)	0·52177 (21)	0·30109 (13)	0·47435 (12)	0·0376 (9)
C(10)	0·65596 (24)	0·33903 (15)	0·54086 (14)	0·0470 (11)
C(11)	0·61769 (27)	0·38598 (15)	0·62857 (14)	0·0507 (12)
C(12)	0·44418 (28)	0·39741 (16)	0·65297 (14)	0·0523 (12)
C(13)	0·30745 (27)	0·36109 (15)	0·58908 (12)	0·0454 (10)
C(14)	0·34668 (20)	0·31138 (14)	0·50150 (11)	0·0355 (9)
C(15)	0·11896 (19)	0·15949 (13)	0·45882 (11)	0·0332 (8)
N(1)	0·20460 (16)	0·26532 (11)	0·43921 (9)	0·0354 (7)
N(2)	0·17919 (21)	0·10045 (15)	0·53826 (11)	0·0472 (9)
O	−0·00559 (14)	0·12230 (9)	0·40655 (8)	0·0429 (7)
H(2)	−0·0750 (23)	0·3872 (14)	0·3792 (12)	0·048 (5)
H(3)	−0·1362 (24)	0·4868 (16)	0·2328 (13)	0·062 (6)
H(4)	0·0779 (22)	0·4858 (17)	0·1137 (14)	0·064 (6)
H(5)	0·3553 (22)	0·3867 (15)	0·1476 (12)	0·051 (5)
H(7)	0·5293 (22)	0·2451 (16)	0·2368 (13)	0·057 (5)
H(8)	0·6852 (23)	0·2256 (15)	0·3777 (12)	0·051 (5)
H(10)	0·7844 (24)	0·3302 (16)	0·5231 (12)	0·056 (5)
H(11)	0·7169 (23)	0·4114 (15)	0·6752 (13)	0·058 (5)
H(12)	0·4123 (23)	0·4294 (17)	0·7148 (14)	0·060 (6)
H(13)	0·1844 (25)	0·3666 (16)	0·6059 (12)	0·054 (5)
H(N21)	0·2716 (26)	0·1256 (16)	0·5728 (13)	0·055 (6)
H(N22)	0·1274 (22)	0·0323 (17)	0·5538 (13)	0·052 (5)

Discussion. A view of the molecule with the atom labeling is presented in Fig. 1. Bond distances and angles are given in Table 2; selected dihedral angles are listed in Table 3.

The central azepine ring exists in a boat conformation relative to the C(1), C(6), C(9), C(14) plane (average deviation = 0·016 Å) with N(1), C(7), C(8) and N(2) lying −0·618 (2), −0·520 (2), −0·546 (2) and −2·395 (3) Å, respectively, from this plane. The distance of N(1) to the plane defined by its three substituents is 0·053 (1) Å, indicating that N(1) is much closer to sp^2 than to sp^3 hybridization. The atoms N(1), C(15), N(2), O define a plane (average deviation

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36110 (22 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

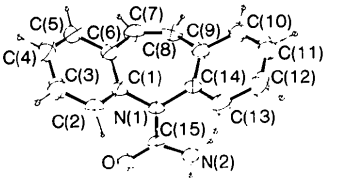


Fig. 1. Perspective view of the molecule showing the labeling scheme. Non-hydrogen atoms are represented by thermal ellipsoids drawn at the 50% level of probability (*ORTEP*, Johnson, 1965).

Table 2. *Bond distances* (Å) *and angles* (°) *with estimated standard deviations in parentheses*

C(1)–C(2)	1·380 (2)	C(9)–C(10)	1·402 (2)
C(1)–C(6)	1·399 (2)	C(9)–C(14)	1·395 (2)
C(1)–N(1)	1·434 (2)	C(10)–C(11)	1·372 (3)
C(2)–C(3)	1·383 (3)	C(10)–H(10)	1·02 (2)
C(2)–H(2)	0·95 (2)	C(11)–C(12)	1·373 (3)
C(3)–C(4)	1·376 (3)	C(11)–H(11)	1·01 (2)
C(3)–H(3)	0·98 (2)	C(12)–C(13)	1·387 (3)
C(4)–C(5)	1·375 (3)	C(12)–H(12)	0·97 (2)
C(4)–H(4)	1·00 (2)	C(13)–C(14)	1·384 (2)
C(5)–C(6)	1·398 (2)	C(13)–H(13)	0·97 (2)
C(5)–H(5)	0·99 (2)	C(14)–N(1)	1·438 (2)
C(6)–C(7)	1·462 (2)	C(15)–N(1)	1·379 (2)
C(7)–C(8)	1·331 (2)	C(15)–N(2)	1·346 (2)
C(7)–H(7)	1·00 (2)	C(15)–O	1·230 (2)
C(8)–C(9)	1·459 (2)	N(2)–H(N21)	0·87 (2)
C(8)–H(8)	0·95 (2)	N(2)–H(N22)	0·89 (2)

C(2)–C(1)–C(6)	120·50 (14)	C(10)–C(9)–C(14)	117·22 (15)
C(2)–C(1)–N(1)	120·37 (14)	C(9)–C(10)–C(11)	121·71 (17)
C(6)–C(1)–N(1)	119·13 (13)	C(10)–C(11)–C(12)	120·03 (18)
C(1)–C(2)–C(3)	120·55 (16)	C(11)–C(12)–C(13)	120·04 (18)
C(2)–C(3)–C(4)	119·86 (17)	C(12)–C(13)–C(14)	119·77 (18)
C(3)–C(4)–C(5)	119·79 (17)	C(9)–C(14)–C(13)	121·18 (15)
C(4)–C(5)–C(6)	121·67 (17)	C(9)–C(14)–N(1)	119·55 (14)
C(1)–C(6)–C(5)	117·62 (14)	C(13)–C(14)–N(1)	119·22 (14)
C(1)–C(6)–C(7)	123·05 (14)	N(1)–C(15)–N(2)	116·06 (13)
C(5)–C(6)–C(7)	119·33 (15)	N(1)–C(15)–O	121·50 (14)
C(6)–C(7)–C(8)	127·99 (17)	N(2)–C(15)–O	122·44 (14)
C(7)–C(8)–C(9)	126·61 (16)	C(1)–N(1)–C(14)	116·80 (12)
C(8)–C(9)–C(10)	119·79 (15)	C(1)–N(1)–C(15)	120·90 (12)
C(8)–C(9)–C(14)	122·96 (14)	C(14)–N(1)–C(15)	121·88 (12)

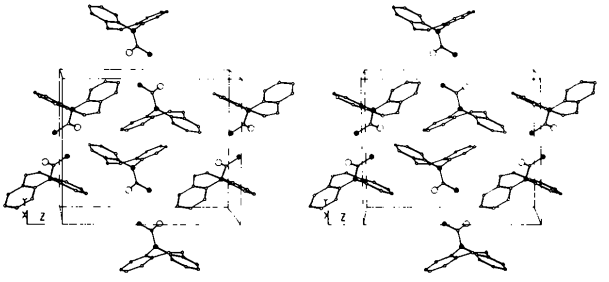


Fig. 2. Stereoscopic view of the packing. The molecules are hydrogen-bonded between carboxamide groups, forming centrosymmetric dimers.

= 0·0008 Å) which makes an angle of 6·0° with that defined by C(1), C(14), C(15). In (1), the bond distances and angles and the conformation of the azepine ring are in general agreement with the corresponding values reported for 2-morpholinomethyl-5*H*-dibenz[*b*,*f*]azepine (Carpy, Gadret, Goursolle, Leger & Lehuede, 1979), 1-(*p*-bromobenzenesulfonyl)-1*H*-azepine (Paul, Johnson, Paquette, Barrett & Haluska, 1968), and 1-(phenoxycarbonyl)-1*H*-azepine (Lindner & von Gross, 1972).

The two benzene moieties defined by C(1),...C(6) and C(9),...C(14) are planar (average deviation = 0·003 and 0·006 Å, respectively) and form a 126·6° dihedral angle. These same planes make angles of 27·9 and 27·5° with the plane defined by C(1), C(6), C(9) and C(14). The centers of the two benzene moieties lie 4·84 Å apart, with N(2) 4·98 and 3·60 Å from the centers of the rings defined by C(1),...C(6) and C(9),...C(14), respectively. Two additional parameters useful in describing the conformation of the tricyclic moiety in (1) are the skew distance and the twist angle. The skew distance of 0·655 Å is defined as the difference between the non-bonded distances C(6)···C(9) [3·102 (2) Å] and C(1)···C(14) [2·447 (2) Å] while the twist angle of −2·8° was calculated by averaging the values of the two dihedral angles C(1)–C(6)···C(9)–C(14) [−2·5 (1)°] and C(6)–C(1)···C(14)–C(9) [−3·2 (1)°]. These slight distortions from the ideal mirror symmetry in the tricyclic moiety (Reboul, Cristau, Soyfer & Estienne, 1980) may be attributed to the presence of the carboxamide group and to the molecular packing.

The packing for (1) is shown in Fig. 2. Intermolecular hydrogen bonding between carboxamide groups forms centrosymmetric dimers with N(2)–H(N22) = 0·89 (2), H(N22)···O = 2·04 (2) Å and N(2)–H(N22)···O = 178 (2)°. Similar hydrogen bonding has been observed in (10*RS*,5*RS*,9*SR*)-10β-ethyl-5,6,7,8,9,10-hexahydro-5α,9α-methanobenzocyclooctene-10α-carboxamide (Kojić-Prodić, Ružić-Toroš & Golič, 1980) and in cyclopentadecanone phenylsemicarbazone (van den Hoek, Oonk & Kroon, 1979).

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Note added in proof: A comparison of this structure determination with the one of Reboul *et al.* (1981) is of interest because the precision of the two experiments is about the same and the two determinations were carried out using different instruments and wavelengths. The molecular parameters are in very close agreement with each other. The bond distances and angles in the carbamazepine molecule determined in the two experiments agree to within an average of 1·5 and 1·2 e.s.d.'s, respectively. Likewise, the molecular conformation is

Table 3. *Selected dihedral angles* (°) *with estimated standard deviations in parentheses*

N(1)–C(1)–C(6)–C(7)	−0·9 (2)	C(9)–C(14)–N(1)–C(1)	−68·5 (2)	C(1)–N(1)–C(15)–N(2)	170·7 (1)
C(1)–C(6)–C(7)–C(8)	−32·9 (3)	C(9)–C(14)–N(1)–C(15)	104·2 (2)	C(14)–N(1)–C(15)–O	178·0 (1)
C(6)–C(7)–C(8)–C(9)	−1·2 (3)	C(14)–N(1)–C(1)–C(6)	64·2 (2)	C(14)–N(1)–C(15)–N(2)	−1·6 (2)
C(7)–C(8)–C(9)–C(14)	31·3 (3)	C(15)–N(1)–C(1)–C(6)	−108·5 (2)	C(1)–C(6)···C(9)–C(14)	−2·5 (1)
C(8)–C(9)–C(14)–N(1)	6·7 (2)	C(1)–N(1)–C(15)–O	−9·6 (2)	C(6)–C(1)···C(14)–C(9)	−3·2 (1)

found to be the same in both studies, as revealed by comparing least-squares-plane analyses and dihedral angles. With the exception of the angle C(1)–N(1)–C(15)–N(2), all dihedral angles are in excellent agreement (an average difference of 1·5 e.s.d.'s). Finally, the distance between the N and O atoms in the N–H···O hydrogen bond is identical in both structures.

The authors in addition wish to recognize the work of Chang, Yang, Yoo, Wang, Pletcher & Sax (1981) on the crystal structure determination of carbamazepine acetone solvate.

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The Structure of the Orthorhombic Form of Tolbutamide (1-*n*-Butyl-3-*p*-toluenesulphonylurea)

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Abstract. $C_{12}H_{18}N_2O_3S$ (form *A*), orthorhombic, $Pna2_1$, a = 20·223 (11), b = 7·831 (9), c = 9·090 (10) Å, Z = 4, λ(Mo $K\alpha$) = 0·7107 Å, D_x = 1·246, D_m (flotation) = 1·251 Mg m^{-3}. R = 0·048 for 988 reflections. The four molecules in the unit cell occur in hydrogen-bonded pairs.

Introduction. Many drugs exist in two or more polymorphic forms, and in some cases such polymorphs have been shown to have different levels of bio-availability, *e.g.* cortisone acetate (Macek, 1954). On the other hand, the polymorphs of acetylhexamide show no such differences (Muller & Lagas, 1979). The current elucidation of the crystal structure of tolbutamide was undertaken to study the differences between the polymorphs of this compound which might lead to one or other type of behaviour. Two polymorphs of tolbutamide are known (Simmons, Ranz, Gyanchandani & Picotte, 1972; Leary, Ross & Thomas, 1981), and the orthorhombic form, designated as form *A* by Simmons, is the form normally used in pharmaceutical preparations. This material was first synthesized by Makhnenko & Sysoeva (1959) and crystallizes as plates on the addition of *n*-hexane to a

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