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An orthorhombic polymorph of 10,11-dihydrocarbamazepine

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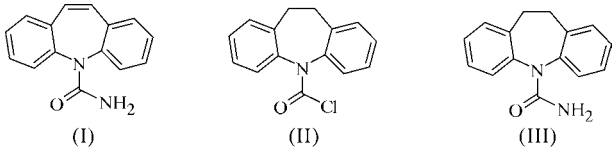
The title compound (systematic name: 10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine-5-carboxamide), $C_{15}H_{14}N_2O$, is shown to crystallize as an orthorhombic polymorph to complement the known monoclinic form. The molecular conformations of both forms are very similar, involving a bent conformation for the seven-membered azepine ring and an overall 'butterfly' shape. The molecules assemble into chains by way of N—H···O bonds and N—H···π interactions in both crystal modifications. The two polymorphs appear to form due to different van der Waals interactions between the layer-like sheets of molecules.

Comment

Carbamazepine, (I), is an anticonvulsant agent with many pharmaceutical and medicinal applications (Birkhimer *et al.*, 1985; Nagaraj *et al.*, 2005). Compound (I) is of considerable structural interest as it serves as a model compound for molecular-crystal polymorphism, with four crystalline forms known (Grzesiak *et al.*, 2003). It has been estimated (Henck *et al.*, 1997) that as many as one third of pharmaceutical solids may display crystal polymorphism which can have a dramatic effect on their physiological properties (Knapman, 2000).



The crystal structures of various derivatives of carbamazepine have been reported (Himes *et al.*, 1981; Lisgarten *et al.*, 1989; Hempel *et al.*, 2005; Nagaraj *et al.*, 2005; Johnston *et al.*, 2005). Recently, the crystal structure of 5-chlorocarbonyl-10,11-dihydro-5*H*-dibenz[*b*,*f*]azepine, (II), was published (Vijay *et al.*, 2005). The structure of the title compound, 10,11-dihydrocarbamazapine, (III), was reported by Bandoli *et al.* (1992) to be monoclinic, space group $P2_1/c$. We report here a second, orthorhombic (space group *Pbca*), modification of (III) (Table 1 and Fig. 1).

The geometric parameters for (III) fall within their expected ranges (Allen *et al.*, 1995). The dihedral angle between the best planes of the two benzene rings (C1–C6 and C9–C14) is 119.03 (4)°, compared with an equivalent value of 118.20 (12)° [calculated with *PLATON* (Spek, 2003)] in the monoclinic form of (III) (Bandoli *et al.*, 1992). The Bandoli paper cites this dihedral angle as 128°, perhaps as the result of a misprint. The central seven-membered azepine ring (C1/C6–C9/C14/N1) in (I) adopts the so-called bent transition state conformation (Hendrickson, 1967; Bocian & Strauss, 1977), intermediate between the boat and chair forms of a classical cycloheptane ring. In this conformation, five atoms (C1/C6–C8/N1) are almost coplanar [r.m.s. deviation from the best plane = 0.042 Å; maximum deviation = 0.050 (1) Å for atom C7], and atoms C9 and C14 are substantially displaced from the plane by 1.108 (2) and 1.149 (2) Å, respectively. This conformation, commonly seen in 10,11-dihydrocarbamazepines (Vijay *et al.*, 2005), has approximate C_s (mirror) symmetry, with the mirror plane passing through atom C6 and the mid-point of the C9—C14 bond, if atom N1 takes on the identity of a C atom for this analysis. The bond-angle sum of 359.7° about atom N1 in (III) indicates sp^2 hybridization for this atom and the N1/C15/O1/N2 grouping is statistically planar [r.m.s. deviation = 0.0004 Å; maximum deviation = 0.0008 (11) Å for atom C15]. Overall, this azepine conformation results in the molecule of (III) taking on a 'butterfly' shape, as previously described for related carbamazepine derivatives (Vijay *et al.*, 2005).

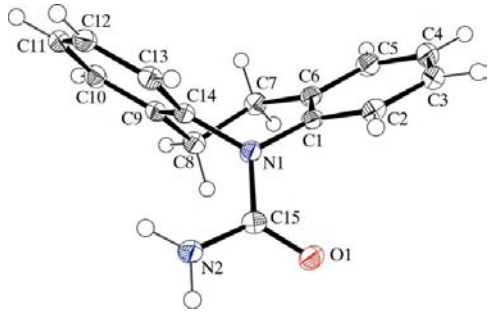


Figure 1
A view of (III), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitray radii.

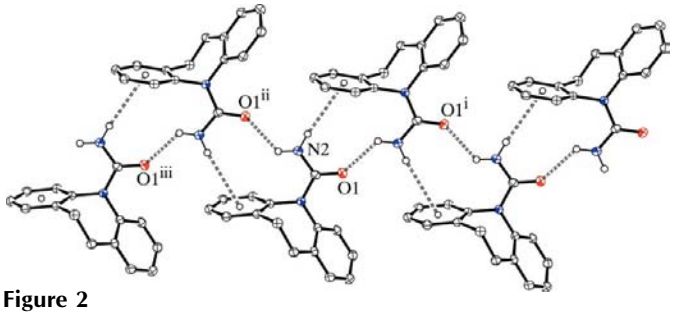


Figure 2
Detail of the structure of (III), showing a chain resulting from N—H···O and N—H···π interactions. All C-bound H atoms have been omitted for clarity. [Symmetry codes are as in Table 2; additionally: (iii) $x-1, y, z$.]

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The –NH_2 unit in (III) makes only one N—H···O hydrogen bond (Table 2). The H···O separation of 2.206 (18) Å suggests that it is a relatively weak interaction. This bond links the molecules into one-dimensional strings propagating in the *a* direction. The second H atom points towards the centroid of a nearby C9–C14 benzene ring (Fig. 2) and the resulting almost linear N—H···π interaction (Rodham *et al.*, 1993) thus appears to help to stabilize the [100] chains.

Any π–π stacking in (III) must be extremely weak, with the shortest aromatic ring centroid–centroid separation being 4.82 Å (Spek, 2003). A very similar situation occurs for the monoclinic polymorph (the shortest centroid–centroid separation is 4.78 Å). This contrasts strongly with the situation in (II), where no conventional hydrogen bonds are possible and π–π stacking dominates the crystal packing.

The monoclinic form of (III) shows a very similar molecular conformation to the title compound. It possesses the same extended chain structure (propagating in the [010] direction), consolidated by N—H···O and N—H···π interactions as in the orthorhombic form of (III). It differs in the arrangements of adjacent sheets of chains with respect to the monoclinic [001] and orthorhombic [001] directions. In the monoclinic phase, adjacent pseudo-sheets in the *c* direction all show the same orientation of the carbamoyl groupings (Fig. 3*a*). In the orthorhombic form (Fig. 3*b*), adjacent sheets of carbamoyl groupings alternate in a zigzag pattern. Inversion symmetry generates the adjacent [001] layer in the monoclinic phase and a glide operation performs the same task in the orthorhombic modification. No unusually short inter-sheet [001] intermolecular contacts were identified in either phase.

The fact that the density of 1.352 Mg m^{-3} of orthorhombic (III) reported here is significantly greater than that of the monoclinic form (1.301 Mg m^{-3}) suggests that the new form of (III) may be a more thermodynamically stable polymorph. Monoclinic (III) was recrystallized from ethanol, resulting in parallelepiped-shaped crystals. Thus, it seems likely (and typical) that the solvent plays an important role in determining the polymorph that results.

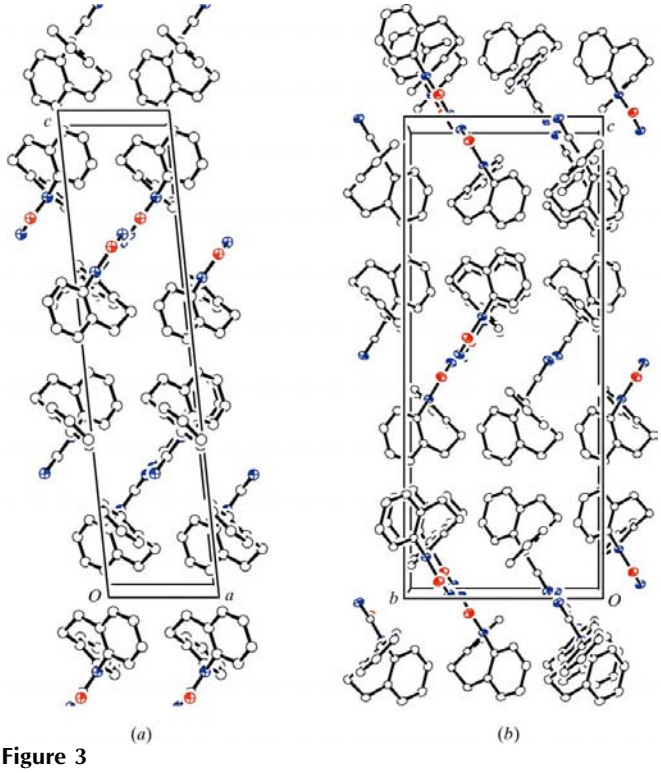

Figure 3
(*a*) Unit-cell packing in the monoclinic form of (III), viewed approximately down [100]. Displacement ellipsoids are drawn at the 50% probability level and all H atoms have been omitted for clarity. (*b*) Unit-cell packing in the orthorhombic form of (III), viewed approximately down [010]. Displacement ellipsoids are drawn at the 30% probability level and all H atoms have been omitted for clarity [redrawn from Bandoli *et al.* (1992)].

Experimental

The sample of (III) was kindly supplied by Jubilant Organosys, Nanjangud, India. The compound was recrystallized from acetonitrile (m.p. 473 K).

Crystal data

$C_{15}H_{14}N_2O$
M_r = 238.28
Orthorhombic, *Pbca*
a = 9.0592 (4) Å
b = 10.3156 (5) Å
c = 25.0534 (12) Å
V = 2341.27 (19) Å^3
Z = 8
D_x = 1.352 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 3022 reflections
θ = 2.9–27.5°
μ = 0.09 mm^{-1}
T = 120 (2) K
Block, colourless
0.28 × 0.24 × 0.18 mm

Data collection

Nonius KappaCCD area-detector diffractometer
ω and φ scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2003)
T_{min} = 0.976, T_{max} = 0.987
16158 measured reflections
2680 independent reflections
2289 reflections with $I > 2\sigma(I)$
R_{int} = 0.042
θ_{max} = 27.6°
h = −11 → 8
k = −13 → 12
l = −32 → 32

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.042
$wR(F^2)$ = 0.108
S = 1.09
2680 reflections
169 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0384P)^2 + 1.5004P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

Table 1
Selected torsion angles (°).

N1—C1—C6—C7	−4.2 (2)	C8—C9—C14—N1	−2.76 (17)
C1—C6—C7—C8	−4.4 (2)	C6—C1—N1—C14	−52.01 (17)
C6—C7—C8—C9	62.06 (16)	C9—C14—N1—C1	73.18 (16)
C7—C8—C9—C14	−70.51 (15)		

Table 2
Hydrogen-bond geometry (Å, °).

*Cg*1 is the centroid of the C9–C14 ring at (−0.3474, 0.3861, 0.3981).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H1···*Cg*1^{i}	0.887 (18)	2.86	3.75	173
N2—H2···O1^{ii}	0.915 (18)	2.206 (18)	2.8970 (16)	131.7 (14)

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

The N-bound H atoms were located in a difference map and their positions were freely refined. The C-bound H atoms were positioned geometrically, with C—H distances in the range 0.95–0.99 Å, and refined as riding. The constraint $U_{iso}(H) = 1.2U_{eq}$(carrier) was applied in all cases.

Data collection: *COLLECT* (Nonius, 1998); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997), *SCALEPACK* and *SORTAV* (Blessing, 1995); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG3005). Services for accessing these data are described at the back of the journal.

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