Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Carbamazepine furfural hemisolvate

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Key indicators

Single-crystal synchrotron study
T = 120 K
Mean σ(C–C) = 0.002 Å
R factor = 0.056
wR factor = 0.151
Data-to-parameter ratio = 19.2

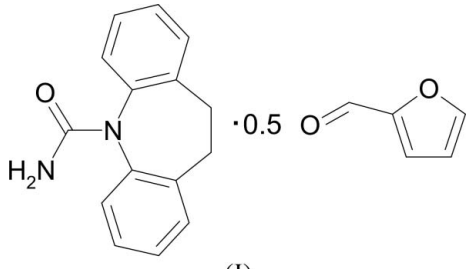
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 21 April 2005
Accepted 10 May 2005
Online 21 May 2005

In the title compound, $C_{15}H_{12}N_2O\cdot0.5C_5H_4O_2$, carbamazepine molecules retain the $R_2^2(8)$ N—H···O hydrogen-bonded dimer arrangement observed in the crystal structures of each of the four known anhydrous polymorphs. The furfural molecule is located between adjacent carbamazepine dimers and is hydrogen bonded to only one of the *anti*-oriented NH groups available on the dimer.

Comment

The antiepileptic compound carbamazepine (CBZ) is known to crystallize in at least four anhydrous polymorphic forms (Grzesiak *et al.*, 2003) and the crystal structures of several solvates and co-crystals have also been reported (Fleischman *et al.*, 2003). The title compound, (I), was produced during an automated parallel crystallization polymorph screen on CBZ. The sample was identified as a novel form using multisample X-ray powder diffraction analysis of all recrystallized samples (Florence *et al.*, 2003). Subsequent manual recrystallization from a saturated furfural solution by slow evaporation at 278 K yielded samples of the carbamazepine furfural hemisolvate suitable for synchrotron-based single-crystal X-ray analysis (Cernik *et al.*, 1997).



(I)

The asymmetric unit of (I) contains two molecules of CBZ and one of furfural (Fig. 1). Pairs of CBZ molecules are connected by two N—H···O hydrogen bonds (contacts 1 and 2, Fig. 2) to form the $R_2^2(8)$ dimer motif. This motif is observed in all of the known polymorphs and the majority of CBZ solvate crystal structures (Fleischman *et al.*, 2003). In all other CBZ solvate crystal structures, each of the NH donor groups is involved in hydrogen-bonding interactions; the *syn*-oriented NH group of CBZ forms the dimer motif and the *anti*-oriented NH donors connect to molecules of solvent. In (I), however, only one of the *anti*-oriented NH groups is utilized in a hydrogen bond between CBZ and solvent (contact 3, Fig. 2). The structure also contains four C—H···O interactions: contacts 4, 6 and 7 connect CBZ and furfural molecules, and contact 5 connects molecules of CBZ. The molecules pack

such that the polar groups (furfural and CBZ carboxamide moiety) and hydrophobic azepine rings are segregated into alternating polar and non-polar layers in the *ac* plane, which are stacked in the direction of the *b* axis.

Experimental

A single-crystal sample of the title compound was recrystallized from a furfural solution of carbamazepine (used as supplied from Sigma–Aldrich) by slow evaporation at 278 K.

Crystal data

$C_{15}H_{12}N_2O\cdot0.5C_5H_4O_2$
$M_r = 284.31$
Monoclinic, $P2_1/n$
$a = 5.1815\ (4)$ Å
$b = 26.0450\ (19)$ Å
$c = 20.5735\ (15)$ Å
$\beta = 91.302\ (2)^\circ$
$V = 2775.7\ (4)$ Å^3
$Z = 8$
$D_x = 1.361$ Mg m^{-3}
Synchrotron radiation, $\lambda = 0.6902$ Å
Cell parameters from 4821 reflections
$\theta = 2.5$–29.5°
$\mu = 0.11$ mm^{-1}
$T = 120\ (2)$ K
Plate, brown
$0.04 \times 0.04 \times 0.01$ mm

Data collection

Bruker SMART APEX2 CCD diffractometer
Fine-slice ω scans
Absorption correction: none
28844 measured reflections
8144 independent reflections
5329 reflections with $I > 2\sigma(I)$
$R_{int} = 0.053$
$\theta_{max} = 29.5^\circ$
$h = -7 \rightarrow 7$
$k = -37 \rightarrow 35$
$l = -29 \rightarrow 28$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.057$
$wR(F^2) = 0.151$
$S = 1.01$
8144 reflections
424 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0702P)^2 + 0.8667P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.30$ e Å^{-3}
$\Delta\rho_{min} = -0.25$ e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N2—H1N···O1A^{i}	0.91 (2)	1.91 (2)	2.817 (2)	175 (2)
N2A—H3N···O1^{ii}	0.93 (2)	1.95 (2)	2.876 (2)	175 (2)
N2A—H4N···O3	0.89 (2)	2.13 (2)	2.961 (2)	156 (2)
C3A—H3A···O3^{i}	0.95	2.45	3.250 (2)	142
C13—H13···O1^{ii}	0.95	2.55	3.449 (2)	159
C16—H16···O1A^{iii}	0.95	2.48	3.108 (2)	124
C18—H18···O1	0.95	2.56	3.283 (2)	133

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

The H atoms of the six- and five-membered rings of carbamazepine and furfural were positioned geometrically at distances of 0.95 Å (CH) from the parent C atoms; a riding model was used during the refinement process. The U_{iso}(H) values were constrained to be 1.2 times U_{eq} of the carrier atom. The remaining H atoms were located in a difference synthesis and were refined isotropically [C—H = 0.95 (2)–1.01 (2) Å and N—H = 0.85 (3)–0.93 (2) Å].

Data collection: *APEX2* (Bruker, 2004); cell refinement: *SAINT* (Bruker, 2004); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL*97.

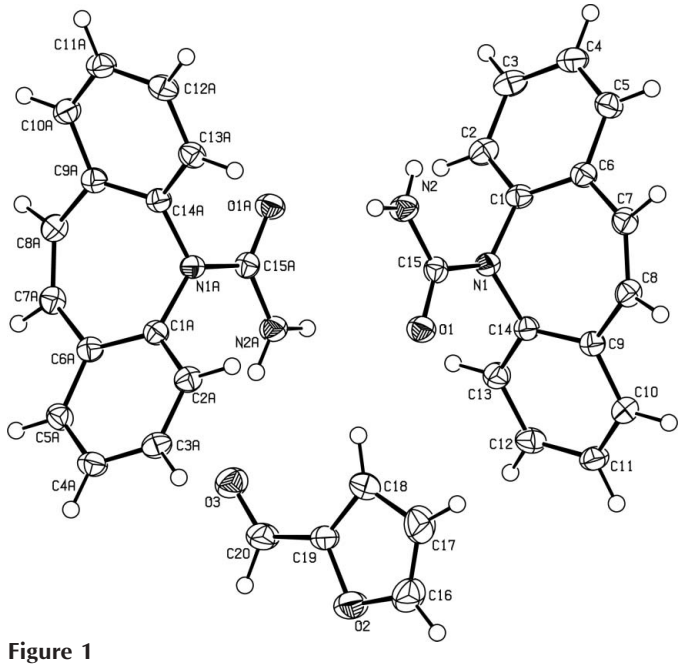


Figure 1
View of the asymmetric unit of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

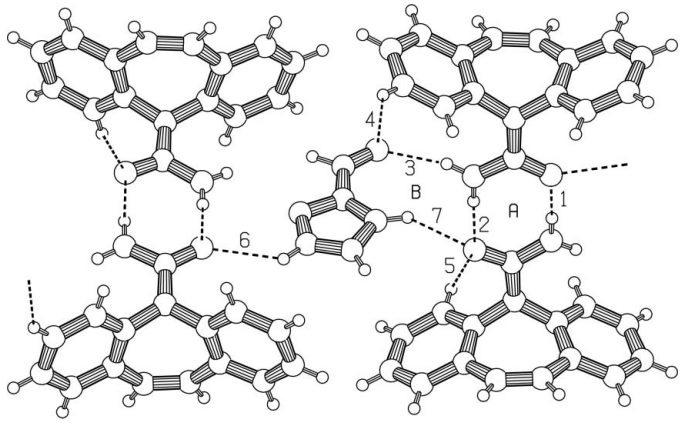


Figure 2
A packing diagram of (I). Dashed lines indicate hydrogen bonds, which produce the two ring motifs, *viz*. *A* [the $R_2^2(8)$ CBZ dimer] and *B* [an $R_3^2(9)$ motif linking one solvent molecule to the dimer].

We thank the Basic Technology programme of the UK Research Councils for funding this work under the project Control and Prediction of the Organic Solid State (URL: www.cposs.org.uk). Thanks are also due to Professor W. Clegg and the EPSRC National Crystallography Service for data collection.

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