Carbamazepine trifluoroacetic acid solvate

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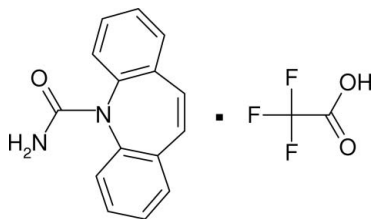Correspondence e-mail: alastair.florence@strath.ac.uk

Carbamazepine forms a 1:1 solvate with trifluoroacetic acid (systematic name: 5H-dibenzo[b,f]azepine-5-carboxamide trifluoroacetic acid solvate), $C_{15}H_{12}N_2O \cdot C_2HF_3O_2$. The compound crystallizes with one molecule of carbamazepine and one of trifluoroacetic acid in the asymmetric unit to form an $R_2^2(8)$ motif. The solvent molecule is disordered over two sites, with site-occupancy factors 0.53 (1) and 0.47 (1).

Related literature

For details on experimental methods used to obtain this form, see: Florence *et al.* (2003); Florence, Johnston, Fernandes *et al.* (2006). For related crystal structures of carbamazepine, see: Fleischman *et al.* (2003); Grzesiak *et al.* (2003); Florence, Johnston, Price *et al.* (2006); Florence, Leech *et al.* (2006). For other related literature, see: Etter (1990).

Experimental

Crystal data

$C_{15}H_{12}N_2O \cdot C_2HF_3O_2$	V = 1573.79 (7) Å^3
M_r = 350.29	Z = 4
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
a = 15.0142 (4) Å	μ = 0.13 mm^{-1}
b = 5.2871 (1) Å	T = 150 (2) K
c = 20.2489 (6) Å	$0.26 \times 0.12 \times 0.10$ mm
β = 101.735 (3)°	

Data collection

Oxford Diffraction Gemini diffractometer	T_{min} = 0.914, T_{max} = 1.000 (expected range = 0.902–0.987)
Absorption correction: multi-scan (*CrysAlis RED*; Oxford Diffraction, 2006)	14283 measured reflections
	3219 independent reflections
	2345 reflections with $I > 2\sigma(I)$
	R_{int} = 0.036

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.039	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2)$ = 0.102	
S = 1.09	$\Delta\rho_{max}$ = 0.18 e Å^{-3}
3219 reflections	$\Delta\rho_{min}$ = -0.20 e Å^{-3}
266 parameters	
31 restraints	

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

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N2—H11$\cdots$O3^i	0.88 (2)	2.30 (2)	2.966 (2)	134 (2)
N2—H12$\cdots$O3	0.90 (2)	2.01 (2)	2.889 (2)	166 (2)
O2—H13$\cdots$O1	0.90 (2)	1.54 (2)	2.4326 (18)	173 (2)

Symmetry code: (i) $-x + \frac{3}{2}, y + \frac{1}{2}, -z + \frac{3}{2}$.

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2006); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2006); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003) and *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *enCIFer* (Allen *et al.*, 2004) and *publCIF* (Westrip, 2007).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: LW2031).

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supplementary materials

Carbamazepine trifluoroacetic acid solvate

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Comment

The 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 been reported (Fleischman *et al.*, 2003, Florence, Johnston, Price *et al.*, 2006 and Florence, Leech *et al.*, 2006). This work forms part of a wider investigation that couples automated parallel crystallization (Florence, Johnston, Fernandes *et al.*, 2006) with crystal structure prediction methodology to investigate the basic science underlying solid-state diversity of the antiepileptic drug CBZ. The sample was identified as a novel form using multi-sample foil transmission X-ray powder diffraction analysis (Florence *et al.*, 2003). Subsequent manual recrystallization from a saturated trifluoroacetic acid solution (TFAA) by slow evaporation at 278 K yielded samples of the title compound suitable for single-crystal X-ray diffraction at 150 K (Fig. 1).

The compound crystallizes in space group $P2_1/n$ with one molecule of CBZ and one molecule of TFAA in the asymmetric unit. The fluorine atoms in the solvent molecule are disordered over two sites, with site occupancy factors 0.53 (1) and 0.47 (1). In the crystal structure, each molecule is connected to a TFAA molecule by N–H⋯O and O–H⋯O hydrogen bonds (Table 1). Contacts 1 (*syn*-oriented) and 3 form the hydrogen-bonded $R_2^2(8)$ (Etter, 1990) hetero-dimer motif observed with other carboxylic acids (Fleischman *et al.*, 2003) (Fig. 2). CBZ also forms a second N–H⋯O contact (*anti*-oriented, contact 2) with an adjacent solvent molecule to form a chain of dimers running along the *b* axis.

Experimental

A single-crystal sample of the title compound was recrystallized from a saturated trifluoroacetic acid solution by isothermal solvent evaporation at room temperature.

Refinement

All non-hydrogen atoms were identified by direct methods and the positions of all the hydrogen atoms were obtained from the use of difference Fourier maps. In the final refinement, all hydrogen atoms were constrained to geometrically sensible positions with a riding model (*SHELX97*), except for H13, which was allowed to refine subject to a distance restraint and H11/H12 which were allowed to refine freely. The CF3 group exhibits significant disorder which was modelled as two distinct CF3 grounds with refined occupancy factors of about 53% and 47% respectively.
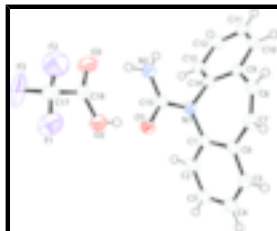
supplementary materials

Figures

Fig. 1. The asymmetric unit of CBZ-TFAA solvate showing 50% probablility displacement ellipsoids. Minor occupancy disordered atomic sites (trifluoroacetic acid) have been omitted for clarity.
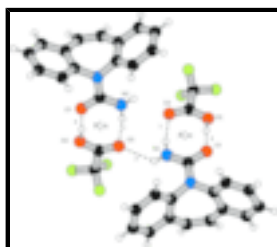

Fig. 2. Hydrogen bonded contacts in CBZ-TFAA showing the ajacent $R_2^2(8)$ hydrogen-bonded dimers connected by N–H···O contact (2, Table 1). Minor disorder components have been omitted for clarity.

5*H*-dibenzo[b,f]azepine-5-carboxamide trifluoroacetic acid solvate

Crystal data

$C_{15}H_{12}N_2O \cdot C_2HF_3O_2$	$F_{000} = 720$
$M_r = 350.29$	$D_x = 1.478$ Mg m^{-3}
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation $\lambda = 0.71073$ Å
Hall symbol: -P 2yn	Cell parameters from 5963 reflections
$a = 15.0142$ (4) Å	$\theta = 2.8$–28.6º
$b = 5.2871$ (1) Å	$\mu = 0.13$ mm^{-1}
$c = 20.2489$ (6) Å	$T = 150$ (2) K
$\beta = 101.735$ (3)º	Block, colourless
$V = 1573.79$ (7) Å^3	$0.26 \times 0.12 \times 0.10$ mm
$Z = 4$	

Data collection

Oxford Diffraction Gemini diffractometer	3219 independent reflections
Radiation source: Enhance (Mo) X-ray Source	2345 reflections with $I > 2\sigma(I)$
Monochromator: graphite	$R_{int} = 0.036$
$T = 150(2)$ K	$\theta_{max} = 26.4$º
φ and ω scans	$\theta_{min} = 2.8$º
Absorption correction: multi-scan (CrysAlis RED; Oxford Diffraction, 2006)	$h = -18 \rightarrow 18$
$T_{min} = 0.914$, $T_{max} = 1.000$	$k = -6 \rightarrow 6$
14283 measured reflections	$l = -25 \rightarrow 25$

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: difference Fourier map
$R[F^2 > 2\sigma(F^2)] = 0.039$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.102$	$w = 1/[\sigma^2(F_o^2) + (0.0497P)^2 + 0.1509P]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.09$	$(\Delta/\sigma)_{max} < 0.001$
3219 reflections	$\Delta\rho_{max} = 0.18$ e Å^{-3}
266 parameters	$\Delta\rho_{min} = -0.20$ e Å^{-3}
31 restraints	Extinction correction: none
Primary atom site location: structure-invariant direct methods	

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2sigma(F^2)$ is used only for calculating R-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	y	z	U_{iso}*/U_{eq}	Occ. (<1)
O1	0.61349 (8)	0.1916 (2)	0.88720 (6)	0.0347 (3)	
O2	0.73657 (9)	−0.1001 (3)	0.93120 (6)	0.0425 (4)	
N1	0.50894 (9)	0.3825 (3)	0.80755 (7)	0.0278 (3)	
C15	0.58756 (12)	0.2517 (3)	0.82554 (8)	0.0277 (4)	
N2	0.63435 (12)	0.1896 (3)	0.77939 (9)	0.0370 (4)	
C1	0.45500 (12)	0.4356 (3)	0.85706 (8)	0.0281 (4)	
C13	0.49565 (13)	0.6039 (3)	0.69997 (9)	0.0343 (4)	
H10	0.5419	0.7178	0.7206	0.041*	
C8	0.35742 (12)	0.0624 (3)	0.74805 (9)	0.0336 (4)	
H6	0.3343	−0.0869	0.7245	0.040*	
C3	0.43009 (13)	0.6803 (4)	0.95088 (9)	0.0367 (5)	
H2	0.4455	0.8194	0.9807	0.044*	
C9	0.39615 (12)	0.2490 (3)	0.70935 (9)	0.0294 (4)	
C7	0.35033 (12)	0.0752 (3)	0.81274 (9)	0.0330 (4)	
H5	0.3216	−0.0643	0.8294	0.040*	
O3	0.78814 (11)	−0.1266 (3)	0.83537 (7)	0.0581 (5)	
C2	0.47840 (12)	0.6364 (3)	0.90077 (9)	0.0321 (4)	

H1	0.5276	0.7439	0.8964	0.038*	
C10	0.36087 (12)	0.2735 (4)	0.63999 (9)	0.0348 (4)	
H7	0.3151	0.1593	0.6187	0.042*	
C6	0.38155 (11)	0.2784 (3)	0.86079 (8)	0.0292 (4)	
C5	0.33566 (12)	0.3238 (4)	0.91326 (9)	0.0353 (4)	
H4	0.2870	0.2156	0.9184	0.042*	
C16	0.78678 (13)	−0.1839 (4)	0.89305 (10)	0.0378 (5)	
C4	0.35940 (13)	0.5216 (4)	0.95756 (9)	0.0380 (5)	
H3	0.3271	0.5489	0.9927	0.046*	
C14	0.46605 (11)	0.4149 (3)	0.73755 (8)	0.0280 (4)	
C12	0.45728 (13)	0.6257 (4)	0.63196 (9)	0.0391 (5)	
H9	0.4768	0.7558	0.6058	0.047*	
C11	0.39068 (13)	0.4580 (4)	0.60228 (9)	0.0383 (5)	
H8	0.3654	0.4706	0.5554	0.046*	
C17	0.85526 (15)	−0.3839 (4)	0.92652 (11)	0.0485 (6)	
F1	0.8383 (4)	−0.4625 (10)	0.9861 (2)	0.0683 (15)	0.531 (10)
F2	0.8464 (4)	−0.5985 (7)	0.8905 (2)	0.0780 (18)	0.531 (10)
F3	0.9375 (2)	−0.3149 (10)	0.9393 (4)	0.078 (2)	0.531 (10)
F2A	0.9013 (5)	−0.4712 (16)	0.88091 (17)	0.093 (3)	0.469 (10)
F1A	0.8259 (5)	−0.5511 (14)	0.9580 (6)	0.125 (4)	0.469 (10)
F3A	0.9226 (4)	−0.2545 (11)	0.9669 (3)	0.089 (2)	0.469 (10)
H11	0.6226 (15)	0.257 (4)	0.7391 (12)	0.052 (7)*	
H12	0.6879 (16)	0.108 (4)	0.7928 (11)	0.055 (7)*	
H13	0.6928 (16)	0.008 (4)	0.9118 (12)	0.084 (8)*	

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0331 (7)	0.0466 (8)	0.0232 (7)	0.0093 (6)	0.0028 (5)	0.0017 (6)
O2	0.0423 (8)	0.0537 (9)	0.0320 (7)	0.0178 (7)	0.0083 (6)	0.0050 (6)
N1	0.0255 (7)	0.0352 (8)	0.0212 (8)	0.0000 (6)	0.0015 (6)	0.0017 (6)
C15	0.0262 (9)	0.0312 (9)	0.0244 (9)	−0.0030 (7)	0.0022 (7)	−0.0009 (8)
N2	0.0327 (9)	0.0523 (10)	0.0259 (9)	0.0084 (8)	0.0056 (7)	0.0033 (8)
C1	0.0277 (9)	0.0325 (10)	0.0220 (9)	0.0067 (7)	0.0003 (7)	0.0047 (7)
C13	0.0376 (10)	0.0366 (10)	0.0278 (10)	−0.0031 (8)	0.0048 (8)	−0.0002 (8)
C8	0.0329 (10)	0.0301 (10)	0.0358 (11)	−0.0015 (8)	0.0021 (8)	−0.0022 (8)
C3	0.0438 (11)	0.0375 (11)	0.0254 (10)	0.0082 (9)	−0.0008 (8)	−0.0006 (8)
C9	0.0286 (9)	0.0305 (9)	0.0277 (10)	0.0023 (7)	0.0026 (7)	−0.0004 (7)
C7	0.0295 (9)	0.0322 (10)	0.0359 (11)	−0.0018 (8)	0.0031 (8)	0.0056 (8)
O3	0.0580 (10)	0.0832 (11)	0.0354 (9)	0.0306 (9)	0.0153 (7)	0.0042 (8)
C2	0.0353 (10)	0.0326 (10)	0.0257 (9)	0.0014 (8)	0.0002 (8)	0.0048 (8)
C10	0.0296 (9)	0.0432 (11)	0.0291 (10)	0.0000 (8)	−0.0002 (8)	−0.0039 (9)
C6	0.0265 (9)	0.0314 (10)	0.0277 (9)	0.0046 (7)	0.0010 (7)	0.0059 (8)
C5	0.0270 (9)	0.0470 (11)	0.0309 (10)	0.0034 (8)	0.0037 (8)	0.0080 (9)
C16	0.0353 (10)	0.0465 (12)	0.0309 (11)	0.0059 (9)	0.0050 (8)	−0.0051 (9)
C4	0.0353 (10)	0.0512 (12)	0.0263 (10)	0.0138 (9)	0.0033 (8)	0.0043 (9)
C14	0.0270 (9)	0.0331 (10)	0.0231 (9)	0.0031 (7)	0.0032 (7)	−0.0002 (7)
C12	0.0444 (11)	0.0426 (11)	0.0310 (10)	0.0024 (9)	0.0092 (9)	0.0084 (9)

C11	0.0387 (11)	0.0496 (12)	0.0245 (10)	0.0067 (9)	0.0013 (8)	0.0016 (9)
C17	0.0459 (13)	0.0552 (14)	0.0436 (13)	0.0144 (11)	0.0071 (11)	−0.0038 (12)
F1	0.078 (3)	0.068 (3)	0.062 (2)	0.043 (2)	0.0242 (17)	0.0320 (19)
F2	0.090 (3)	0.051 (2)	0.090 (3)	0.022 (2)	0.009 (2)	−0.0199 (18)
F3	0.0276 (16)	0.068 (3)	0.137 (6)	0.0041 (16)	0.015 (2)	0.043 (3)
F2A	0.104 (5)	0.119 (5)	0.057 (2)	0.082 (5)	0.016 (2)	−0.002 (3)
F1A	0.083 (4)	0.061 (4)	0.252 (11)	0.030 (3)	0.082 (6)	0.076 (6)
F3A	0.062 (3)	0.134 (4)	0.061 (3)	0.048 (3)	−0.015 (2)	−0.011 (2)

Geometric parameters (Å, °)

O1—C15	1.2704 (19)	C9—C10	1.403 (2)
O2—C16	1.264 (2)	C7—C6	1.461 (2)
O2—H13	0.900 (19)	C7—H5	0.9500
N1—C15	1.353 (2)	O3—C16	1.211 (2)
N1—C1	1.439 (2)	C2—H1	0.9500
N1—C14	1.443 (2)	C10—C11	1.369 (3)
C15—N2	1.320 (2)	C10—H7	0.9500
N2—H11	0.88 (2)	C6—C5	1.400 (3)
N2—H12	0.90 (2)	C5—C4	1.377 (3)
C1—C2	1.381 (2)	C5—H4	0.9500
C1—C6	1.395 (2)	C16—C17	1.533 (3)
C13—C14	1.383 (2)	C4—H3	0.9500
C13—C12	1.385 (3)	C12—C11	1.379 (3)
C13—H10	0.9500	C12—H9	0.9500
C8—C7	1.337 (2)	C11—H8	0.9500
C8—C9	1.453 (3)	C17—F1A	1.223 (5)
C8—H6	0.9500	C17—F3	1.263 (4)
C3—C4	1.381 (3)	C17—F2	1.340 (3)
C3—C2	1.382 (3)	C17—F2A	1.343 (4)
C3—H2	0.9500	C17—F1	1.348 (4)
C9—C14	1.398 (2)	C17—F3A	1.350 (5)
C16—O2—H13	115.4 (14)	C1—C6—C5	117.10 (16)
C15—N1—C1	119.75 (13)	C1—C6—C7	123.50 (16)
C15—N1—C14	121.05 (14)	C5—C6—C7	119.39 (17)
C1—N1—C14	117.35 (13)	C4—C5—C6	121.51 (18)
O1—C15—N2	122.21 (16)	C4—C5—H4	119.2
O1—C15—N1	117.95 (15)	C6—C5—H4	119.2
N2—C15—N1	119.84 (16)	O3—C16—O2	129.10 (18)
C15—N2—H11	121.6 (14)	O3—C16—C17	117.23 (18)
C15—N2—H12	118.4 (14)	O2—C16—C17	113.66 (17)
H11—N2—H12	118 (2)	C5—C4—C3	120.00 (18)
C2—C1—C6	121.60 (17)	C5—C4—H3	120.0
C2—C1—N1	119.38 (16)	C3—C4—H3	120.0
C6—C1—N1	118.99 (15)	C13—C14—C9	121.82 (16)
C14—C13—C12	119.48 (17)	C13—C14—N1	119.83 (15)
C14—C13—H10	120.3	C9—C14—N1	118.34 (15)
C12—C13—H10	120.3	C11—C12—C13	119.85 (18)
C7—C8—C9	127.90 (17)	C11—C12—H9	120.1

C7—C8—H6	116.0	C13—C12—H9	120.1
C9—C8—H6	116.0	C10—C11—C12	120.34 (17)
C4—C3—C2	119.91 (18)	C10—C11—H8	119.8
C4—C3—H2	120.0	C12—C11—H8	119.8
C2—C3—H2	120.0	F3—C17—F2	110.0 (3)
C14—C9—C10	116.76 (16)	F1A—C17—F2A	113.6 (4)
C14—C9—C8	123.75 (16)	F3—C17—F1	105.0 (4)
C10—C9—C8	119.46 (16)	F2—C17—F1	102.1 (3)
C8—C7—C6	127.64 (17)	F1A—C17—F3A	110.8 (5)
C8—C7—H5	116.2	F2A—C17—F3A	99.5 (3)
C6—C7—H5	116.2	F1A—C17—C16	116.6 (4)
C1—C2—C3	119.78 (18)	F3—C17—C16	115.6 (3)
C1—C2—H1	120.1	F2—C17—C16	111.1 (2)
C3—C2—H1	120.1	F2A—C17—C16	109.0 (2)
C11—C10—C9	121.66 (17)	F1—C17—C16	112.1 (3)
C11—C10—H7	119.2	F3A—C17—C16	105.7 (3)
C9—C10—H7	119.2		

Hydrogen-bond geometry (Å, °)

D—H···A	D—H	H···A	D···A	D—H···A
N2—H11···O3[i]	0.88 (2)	2.30 (2)	2.966 (2)	134 (2)
N2—H12···O3	0.90 (2)	2.01 (2)	2.889 (2)	166 (2)
O2—H13···O1	0.90 (2)	1.54 (2)	2.4326 (18)	173 (2)

Symmetry codes: (i) −x+3/2, y+1/2, −z+3/2.

Fig. 1

Fig. 2