Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Lamotriginium benzoate dimethylformamide solvate

Balasubramanian Sridhar* and Krishnan Ravikumar

Laboratory of X-ray Crystallography, Indian Institute of Chemical Technology, Hyderabad 500 007, India

Correspondence e-mail: sshiya@yahoo.com

Received 26 September 2005
Accepted 17 October 2005
Online 22 October 2005

Key indicators

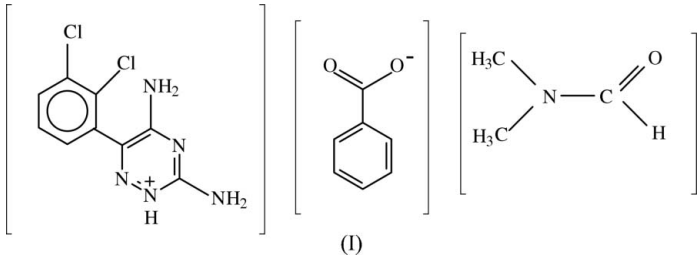
Single-crystal X-ray study
T = 273 K
Mean σ(C–C) = 0.006 Å
Disorder in solvent or counterion
R factor = 0.081
wR factor = 0.245
Data-to-parameter ratio = 12.1

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

Lamotriginium benzoate dimethylformamide solvate [systematic name: 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazin-2-ium benzoate dimethylformamide solvate], $C_9H_8Cl_2N_5^+\cdot C_7H_5O_2^-\cdot C_3H_7NO$, is protonated on the triazine ring. The dihedral angle between the dichlorobenzene and triazine rings is 89.6 (1)°. The dimethylformamide solvent molecule is disordered over two sites. N—H···O and N—H···N hydrogen bonding stabilizes the crystal structure.

Comment

Lamotrigine, phenytoin and carbamazepine are well known anticonvulsant compounds. They block sodium channels with striking voltage dependence (Liu *et al.*, 2003). These antiepileptic drugs have also been reported to have antimanic, antidepressant and mood-stabilizing effects (Berk, 1999). Lamotrigine may offer an alternative for the treatment of bipolar depression and was found to be effective against acute mania. However, the need for slow dosage adjustment and the risk of rash limit the overall clinical utility (Botts & Raskind, 1999). In continuation of the structural elucidation of drug molecules, the crystal structure determination of the title compound, (I) was undertaken and the results are presented here.



(I)

The crystal structure of lamotriginium benzoate dimethylformamide solvate, (I), and the atomic numbering scheme are given in Fig. 1. The asymmetric unit consists of one singly protonated lamotriginium cation, one benzoate anion and one dimethylformamide solvent molecule. Atoms O11, C32, C34 and C35 of the dimethylformamide solvent molecule are disordered over two sites with occupancies of 0.73 (1) and 0.27 (1). In all essential details, the molecular geometry (Table 1) is in good agreement with that of similar structures (Janes *et al.*, 1989; Potter *et al.*, 1999; Kubicki & Codding, 2001).

The expected proton transfer from benzoic acid to lamotrigine occurs at N2 of the triazine ring. Interestingly, only two lamotrigine structures with protonation on the triazine ring have been reported so far (Potter *et al.*, 1999; Janes *et al.*,

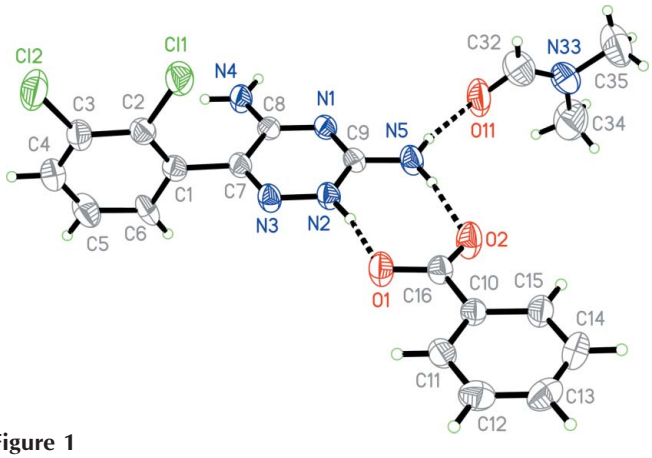


Figure 1
A view of (I), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. Hydrogen bonds are shown as dashed lines. The disordered atoms of the minor component (O11*A*, C32*A*, C34*A* and C35*A*) have been omitted for clarity.

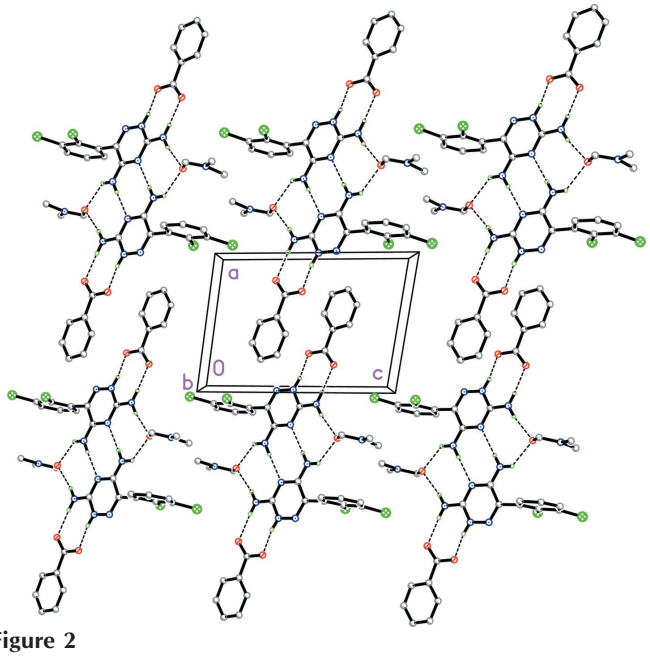


Figure 2
A packing diagram for (I), viewed down the *b* axis. Dashed lines indicate N—H···O and N—H···N hydrogen bonds. The disordered atoms of the minor component (O11*A*, C32*A*, C34*A* and C35*A*) and H atoms attached to C atoms have been omitted for clarity.

1989). The N1—C9 bond length [1.333 (5) Å] is slightly shorter than the value of 1.343 (3) Å for lamotrigine methanol solvate (Janes *et al.*, 1989) and 1.341 (3) Å for lamotrigine monohydrate (Kubicki & Codding, 2001). The corresponding value is 1.331 (3) Å for lamotriginium isethionate (Potter *et al.*, 1999).

The dihedral angle between the triazine and the dichlorophenyl ring is 89.6 (1)° and corresponding values are 66.08 (lamotriginium isethionate), 80.6 (9) (lamotrigine methanol solvate) and 76.42 (6)° (lamotrigine monohydrate).

In the benzoate anion, the carboxylate group is coplanar with the benzene ring, as shown by the dihedral angle of 6.3 (1)° between the two groups.

The benzoate ions form two hydrogen bonds to the lamotriginium cation, leading to the formation of a $R_2^2(8)$-type motif (Bernstein *et al.*, 1995). Two lamotriginium cations are linked by N—H···N hydrogen bonds to give inversion-generated dimers of an $R_2^2(8)$-type motif. It is interesting to note that the Cl atoms present in the structure are not involved in any interactions.

Experimental

Lamotrigine and benzoic acid were mixed in the stoichiometric ratio 1:1 and dissolved in aqueous dimethylformamide solvent (5 ml); crystals were obtained by slow evaporation.

Crystal data

$C_9H_8N_5Cl_2^+\cdot C_7H_5O_2^-\cdot C_3H_7NO$
M_r = 451.31
Triclinic, $P\overline{1}$
a = 8.9585 (13) Å
b = 10.5522 (15) Å
c = 12.3183 (18) Å
α = 79.442 (2)°
β = 78.703 (2)°
γ = 71.864 (2)°
V = 1075.8 (3) Å^3
Z = 2
D_x = 1.393 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2930 reflections
θ = 2.4–23.5°
μ = 0.34 mm^{-1}
T = 273 (2) K
Block, colorless
0.19 × 0.11 × 0.09 mm

Data collection

Bruker SMART CCD area detector diffractometer
ω scans
Absorption correction: none
10413 measured reflections
3788 independent reflections
2817 reflections with $I > 2\sigma(I)$
R_{int} = 0.021
θ_{max} = 25.0°
$h = -10 \rightarrow 10$
$k = -12 \rightarrow 12$
$l = -14 \rightarrow 14$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.081
$wR(F^2)$ = 0.245
S = 1.05
3788 reflections
312 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1386P)^2 + 0.6793P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 1.05 e Å^{-3}
$\Delta\rho_{min}$ = −0.51 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

Cl1—C2	1.709 (4)	N2—C9	1.345 (4)
Cl2—C3	1.721 (5)	N5—C9	1.323 (5)
N1—C8	1.330 (4)	O1—C16	1.282 (4)
N1—C9	1.333 (5)	O2—C16	1.225 (4)
N2—N3	1.340 (4)		
O2—C16—C10	120.2 (3)	O1—C16—C10	115.7 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
N5—H5*B*···O2	0.86	1.93	2.785 (4)	172
N5—H5*A*···O11	0.86	2.10	2.952 (6)	171
N4—H4*B*···O11*A*^{i}	0.86	2.26	2.957 (13)	139
N4—H4*B*···O11^{i}	0.86	2.14	2.806 (6)	134
N4—H4*A*···N1^{i}	0.86	2.12	2.976 (4)	173
N2—H2···O1	0.86	1.72	2.572 (4)	169

Symmetry code: (i) $-x+1, -y+1, -z+1$.

The site-occupation factors of the dimethylformamide solvent molecule were refined to 0.73 (1) and 0.27 (1). A number of restraints were imposed on this molecule, as follows: C32═O11 = 1.25 (1) Å, C32—N33 = 1.35(1 Å), N33—C34 = N33—C35 = 1.45 (1) Å. H atoms were positioned geometrically and treated as riding atoms, with C—H distances in the range 0.93–0.96 Å and with U_{iso}(H) values of $1.5U_{eq}$(C) for methyl H and $1.2U_{eq}$(C,N) for other H atoms. The methyl groups were allowed to rotate but not to tip. An unassigned maximum (positive) residual density was observed 0.93 Å from atom H4.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL*/*PC* (Sheldrick, 1990); software used to prepare material for publication: *SHELXL97*.

The authors thank Dr J. S. Yadav, Director of IICT, for his kind encouragement and support.

References

Berk, M. (1999). *Eur. Neuropsychopharmacol.* **4**, S119–S123.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Botts, S. R. & Raskind, J. (1999). *Am. J. Health Syst. Pharm.* **56**, 1939–1944.
Bruker (2001). *SAINT* (Version 6.28a) and *SMART* (Version 5.625). Bruker AXS Inc., Madison, Wisconsin, USA.
Janes, R. W., Lisgarten, J. N. & Palmer, R. A. (1989). *Acta Cryst.* C**45**, 129–132.
Kubicki, M. & Codding, P. W. (2001). *J. Mol. Struct.* **570**, 53–60.
Liu, G., Yarov-Yarovoy, V., Nobbs, M., Clare, J. J., Scheuer, T. & Catterall, W. A. (2003). *Neuropharmacology*, **44**, 413–422.
Potter, B., Palmer, R. A., Withnall, R., Leach, M. J. & Chowdhry, B. Z. (1999). *J. Chem. Crystallogr.* **29**, 701–706.
Sheldrick, G. M. (1990). *SHELXTL*/*PC*. Bruker AXS Inc., Madison, Wisconsin, USA.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.