Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Methyl 1-(4-chlorobenzyl)-2-(4-methylpiperazin-1-yl)-1*H*-benzimidazole-5-carboxylate hemihydrate

Sabahat Özcan,[a]* Engin Kendi,[a] Meral Tunçbilek[b] and Hakan Göker[b]

[a]Department of Physics Engineering, Hacettepe University, Beytepe 06532, Ankara, Turkey, and [b]Department of Pharmaceutical Chemistry, Ankara University, Tandoğan 06100, Ankara, Turkey
Correspondence e-mail: sozcan@eti.cc.hun.edu.tr

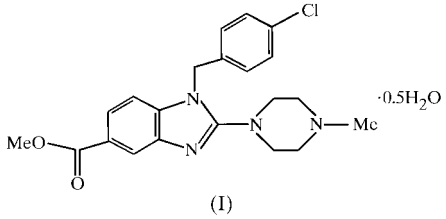
Received 7 July 1999
Accepted 5 January 2000

The title compound, $C_{21}H_{23}ClN_4O_2\cdot0.5H_2O$, contains two independent molecules in the asymmetric unit. In each molecule the piperazine ring adopts a chair conformation; the deviations of the piperazine N atoms from the best plane through the remaining four C atoms are −0.678 (3) and 0.662 (3) Å in molecule *A*, and 0.687 (3) and −0.700 (3) Å in molecule *B*. The molecules are linked by two hydrogen bonds of the O—H···N type involving the O atom of the water molecule of crystallization.

Comment

The benzimidazole nucleus is an essential part of many medicinally useful drugs. For example, omeprazole and lansoprazole are useful drugs in the treatment of peptic ulcers (Nishina *et al.*, 1996), pimobendan is a non-glucosidic cardiotonic drug (Güngör *et al.*, 1992), emedastine difumarate (KG-2413; Sakai *et al.*, 1989) and astemizole (Hismanal; Awouters *et al.*, 1983) were found to be useful for the treatment of allergic diseases, and enviroxime is an active drug against rhinoviruses (Victor *et al.*, 1997).

The present compound, (I), is also a benzimidazole and was prepared for its antimicrobial activity (Göker *et al.*, 1998). The structure of (I) was assigned by NMR, mass spectral and elemental analysis (Göker *et al.*, 1998). Considering the biological importance of substances containing the benzimidazole ring system, we describe in this paper the structure of compound (I).



(I)

The benzimidazole ring systems of the two molecules (*A* and *B*) are planar. The N1—C2 bond lengths [1.382 (4) and 1.390 (4) Å] are comparatively longer than the value reported for benzimidazole [1.346 (4) Å; Escande & Galigne, 1974]. The N1—C10 [1.455 (5) and 1.449 (5) Å] and N2—C2 [1.382 (5) and 1.379 (5) Å] bond lengths are normal for Csp^3—N and Csp^2—N bonds (Allen *et al.*, 1987). The phenyl ring at C10 is also planar and makes an angle of 101.19 (8)° for *A* and 79.42 (8)° for *B* with the plane through the complete benzimidazole ring system.

The Cl1 and Cl1′ atoms lie almost in the phenyl ring planes, with deviations of 0.016 (1) and 0.002 (1) Å from the phenyl planes, respectively.

The C—Cl bond length [Cl1—C14 1.744 (3) Å for *A* and 1.738 (3) Å for *B*] is within the normal range. In 1-benzyl-2-(2,6-dichloroanilinomethyl)-1*H*-benzimidazole, the C—Cl bond lengths are 1.739 (2) and 1.737 (2) Å (Kendi *et al.*, 1998).

The piperazine ring adopts a perfect chair conformation in *A* and *B* (Velmurugan *et al.*, 1994; Özbey *et al.*, 1998). Best planes through the four non-N atoms make dihedral angles of 42.22 (13)° in *A* and 32.81 (17)° in *B* with the benzimidazole ring systems. The methyl group at N4 of the piperazine ring is in the equatorial position (Allinger *et al.*, 1965).

The structure shows that the $COOCH_3$ group at C5 and the benzimidazole ring are almost coplanar with a torsion angle C4—C5—C51—O1 of 7.1 (5)° [173.5 (4)° in *B*]. The intramolecular distance C10—N2 of 2.968 (4) Å [3.033 (4) Å in *B*] is suggestive of a possible C—H···N interaction. Atom C10 is rotated towards the piperazine ring with a torsion angle C10—N1—C2—N3 of −162.7 (3)°, possibly to enable N2 to interact with the C10 proton to form an intramolecular hydrogen bond. This angle is 179.9 (4)° in 6-chloro-1-(phenylmethyl)-2-[*N*-(phenylmethyl)-*N*-(2,6-dichlorophenyl)]methyl-1*H*-benzimidazole (Tunçbilek *et al.*, 1997) and −179.6 (2)° in 1-benzyl-2-(2,6-dichloroanilinomethyl)-1*H*-benzimidazole (Kendi *et al.*, 1998).

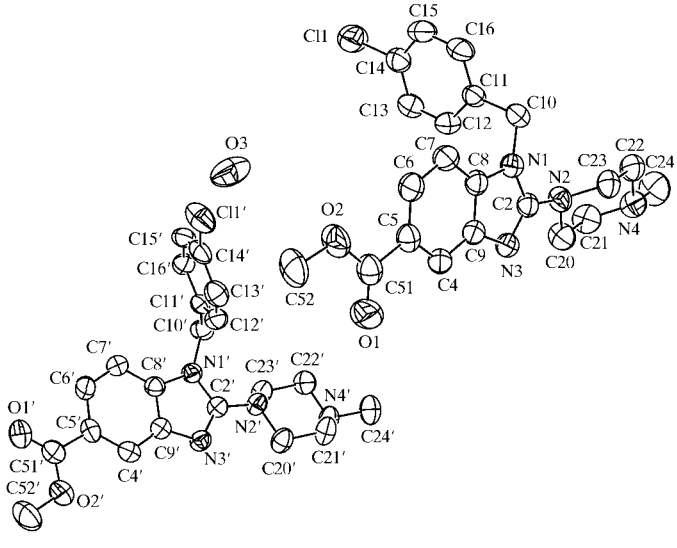


Figure 1
ORTEP (Johnson, 1965) drawing of the title compound showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

The molecules are linked by hydrogen bonds of the O—H···N type involving the O atom of the water molecule of crystallization. The O—N distances [2.873 (4) Å for *A* and 2.957 (4) Å for *B*] suggest that water acts as a hydrogen-bond donor to the piperazine ring. The H_2O(O3) molecule forms hydrogen bonds to both molecules in the asymmetric unit.

Experimental

The title compound was synthesized by the reaction of methyl 2-chloro-1-(*p*-chlorobenzyl)-1*H*-benzimidazole-5-carboxylate with *N*-methylpiperazine, and its structure was assigned by NMR, mass spectral and elemental analysis (Göker *et al.*, 1998).

Crystal data

$C_{21}H_{23}ClN_4O_2\cdot0.5H_2O$
M_r = 407.90
Triclinic, $P\overline{1}$
a = 11.227 (1) Å
b = 13.443 (1) Å
c = 15.835 (2) Å
α = 68.06 (1)°
β = 72.55 (1)°
γ = 76.30 (1)°
V = 2092.3 (3) Å^3
Z = 4
D_x = 1.295 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 11–18°
μ = 0.209 mm^{-1}
T = 295 K
Prismatic, yellow
0.40 × 0.40 × 0.40 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical ψ scans (North *et al.*, 1968)
T_{min} = 0.853, T_{max} = 0.922
8182 measured reflections
7754 independent reflections
5364 reflections with $I > 3\sigma(I)$
R_{int} = 0.015
θ_{max} = 25.7°
$h = -13 \rightarrow 0$
$k = -16 \rightarrow 15$
$l = -19 \rightarrow 18$
3 standard reflections
frequency: 120 min
intensity decay: 3.3%

Table 1
Selected geometric parameters (Å, °).

Cl1—C14	1.744 (3)	Cl1′—C14′	1.738 (3)
O1—C51	1.188 (5)	O1′—C51′	1.192 (5)
O2—C51	1.343 (4)	O2′—C51′	1.317 (5)
N1—C2	1.382 (4)	N1′—C2′	1.390 (4)
N1—C10	1.455 (5)	N1′—C10′	1.449 (5)
N2—C2	1.382 (5)	N2′—C2′	1.379 (5)
N3—C2	1.304 (5)	N3′—C2′	1.309 (5)
N4—C24	1.466 (7)	N4′—C24′	1.468 (6)
C5—C51	1.488 (7)	C5′—C51′	1.496 (7)
C51—O2—C52	116.1 (3)	C51′—O2′—C52′	115.0 (3)
C20—N2—C23	110.8 (3)	C2′—N2′—C20′	114.1 (3)
C21—N4—C22	109.7 (3)	C22′—N4′—C21′	108.0 (3)
N1—C2—N3	114.0 (3)	N1′—C2′—N3′	113.7 (3)
O1—C51—O2	123.4 (4)	O1′—C51′—O2′	123.2 (5)
C20—N2—C23—C22	59.7 (4)	C23′—N2′—C20′—C21′	57.7 (4)
C22—N4—C21—C20	−58.2 (4)	C21′—N4′—C22′—C23′	−61.3 (4)
C4—C5—C51—O1	7.1 (5)	C4′—C5′—C51′—O2′	−4.0 (5)
N1—C10—C11—C12	−38.6 (5)	N1′—C10′—C11′—C16′	−139.7 (3)
C12—C13—C14—Cl1	179.5 (3)	C16′—C15′—C14′—Cl1′	−179.1 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
O3—H31···N4^{i}	0.95	2.69	2.957 (4)	97
O3—H32···N4^{ii}	0.95	2.25	2.873 (4)	123

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

Refinement

Refinement on F
R = 0.053
wR = 0.068
S = 1.24
5364 reflections
514 parameters
H-atoms constrained
$w = 1/[\sigma F^2 + (0.02F)^2 + 1]$
$(\Delta/\sigma)_{max}$ = 0.010
$\Delta\rho_{max}$ = 0.35 e Å^{-3}
$\Delta\rho_{min}$ = −0.10 e Å^{-3}

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1993); cell refinement: *CAD*-4 *EXPRESS*; data reduction: *MolEN* (Fair, 1990); program(s) used to solve structure: *MolEN*; program(s) used to refine structure: *MolEN*; molecular graphics: *MolEN*. Hydrogen bonds were calculated with *PARST* (Nardelli, 1995).

The authors acknowledge the purchase of the CAD-4 diffractometer under grant DPT/TBAG1 of the Scientific and Technical Research Council of Turkey.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1230). Services for accessing these data are described at the back of the journal.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans.* 2, pp. S1–19.
Allinger, N. L., Carpenter, J. G. D. & Karkowski, F. M. (1965). *J. Am. Chem. Soc.* **87**, 1232–1236.
Awouters, F. H. L., Niemegeers, C. J. E. & Janssen, P. A. J. (1983). *Arzneim. Forsch.* (*Drug Res.*), **33**, 381–388.
Enraf–Nonius (1993). *CAD*-4 *EXPRESS*. Version 1.1. Enraf–Nonius, Delft, The Netherlands.
Escande, A. & Galigne, J. G. (1974). *Acta Cryst.* B**30**, 1647–1648.
Fair, C. K. (1990). *MolEN*. Enraf–Nonius, Delft, The Netherlands.
Göker, H., Tunçbilek, M., Ayhan, G. & Altanlar, N. (1998). *Farmaco*, **53**, 415–420.
Güngör, T., Foquet, A., Teulon, J. M., Provost, D., Cazes, M. & Cloarec, A. (1992). *J. Med. Chem.* **35**, 4455–4463.
Johnson, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
Kendi, E., Özbey, S., Tunçbilek, M. & Göker, H. (1998). *Acta Cryst.* C**54**, 854–856.
Nardelli, M. (1995). *J. Appl. Cryst.* **28**, 659.
Nishina, K., Mikawa, N., Takao, Y., Shiga, M. & Obara, H. (1996). *Anesth. Analg.* **82**, 832–836.
North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351–359.
Özbey, S., Kendi, E., Göker, H. & Tunçbilek, M. (1998). *J. Chem. Crystallogr.* **28**, 461–464.
Sakai, T., Hamada, T., Awata, N. & Watanabe, J. (1989). *J. Pharm. Dyn.* **12**, 530–536.
Tunçbilek, M., Göker, H., Ertan, R., Eryiğit, R., Kendi, E. & Altanlar, N. (1997). *Arch. Pharm.* **330**, 372–376.
Velmurugan, D., Govindasamy, L., Subramanian, E., Rajendran, T. M. & Kandaswamy, M. (1994). *Acta Cryst.* C**50**, 931–933.
Victor, F., Loncharich, J. T., Tang, J. & Spitzer, W. A. (1997). *J. Med. Chem.* **40**, 3478–3483.