ANALYTICAL SCIENCES JUNE 2000, VOL. 16

Instrumental Achievements

Crystal Structure of 1-[2-[6-(4-Methoxyphenyl)-3(2*H*)-pyridazinone-2-yl]acetyl]-4-(2-pyridyl)piperazine

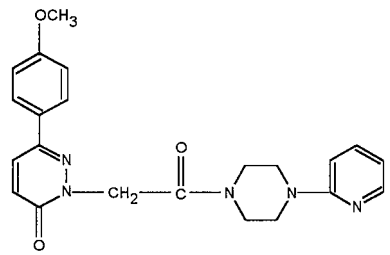
Şebnem Kandil İNGEÇ,*† Hüseyin SOYLU,* Engin KENDİ,**
Deniz S. DOĞRUER,* and M. Fethi ŞAHİN*****

**Gazi University, Gazi Education Faculty, Physics Department, 06500 Besevler, Ankara, Turkey*
***Hacettepe University, Department of Engineering Physics, 06532, Beytepe, Ankara, Turkey*
****Gazi University, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, 06330, Hipodrum, Ankara, Turkey*

(Received October 12, 1999; Accepted March 1, 2000)

Piperazine and its derivatives form an important class of organic compounds with pharmacological applications.[1] The title compound (Fig. 1) has analgesic activity. This compound was synthesized to evaluate for analgesic activity. First, 0.01 mol of [6-(4-methoxyphenyl)-3(2H)-pyridazinone-2-yl]acetic acid in 40 ml of dichloromethane at 0˚C (ice-bath) was treated with triethylamine (3 ml) and 0.01 mol of ethyl chloroformate. After stirring the reaction mixture at 0˚C for 15 min, 0.011 mol of 1-(2-pyridyl)piperazine was added to this solution. The final mixture was stirred at 0 – 25˚C for 24 h, evaporated to dryness, then treated with acetone. All of the solid materials were washed first with 1% NaOH and then with water, and then dried and crystallized from appropriate solvents. The structure was solved by direct methods by the use of SHELXS-97[4] and refined by full-matrix least-squares methods with anisotropic temperature factors for non-H atoms by using SHELXL-97.[5] Atoms H2, H3, H4, H7, H9, H13, H14, H18, H20 and H22 were located geometrically, the other H atoms were obtained by difference Fourier syntheses and refined isotropically. The ^{1}H-NMR spectra were recorded.

A perspective view of the title molecule, (I), showing the atom-numbering scheme is presented in Fig. 2. Table 1 gives the crystal and experimental data. The final coordinates and



(I)

Fig. 1 Chemical structure.

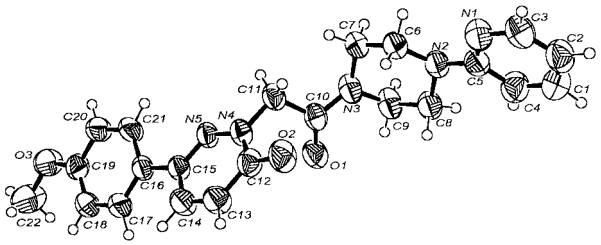


Fig. 2 Perspective view of the molecular structure of the title compound with the atom numbering scheme. The displacement ellipsoids are plotted at the 50% probability level.

† To whom correspondence should be addressed.

Table 1 Crystal and experimental data

Formula: $C_{22}H_{23}N_5O_3$	
Formula weight = 405.45	
Crystal system: triclinic	
Space group: *P*-1	$Z = 2$
$a = 9.475(1)$Å	$\alpha = 75.92(2)^\circ$
$b = 10.389(3)$Å	$\beta = 68.57(1)^\circ$
$c = 11.267(2)$Å	$\gamma = 87.25(2)^\circ$
$V = 1000.3(4)$Å^3	
$D_x = 1.346$ g/cm^3	
μ (Cu K$_\alpha$) = 0.754 mm^{-1}	
$T = 295$ K	
Color: white	
F(0 0 0) = 428	
Crystal size = 0.18 × 0.36 × 0.40 mm	
Radiation = 1.5418 Å (Cu K$_\alpha$)	
$\theta_{max} = 74.23^\circ$	
$R = 0.0591$	
$wR = 0.1506$	
No. of reflections used = 2992	
No. of parameters = 309	
Goodness-of-fit = 1.137	
$(\Delta/\sigma)_{max} = 0.03$	
$(\Delta\rho)_{max} = 0.31$ eÅ^{-3}	
$(\Delta\rho)_{min} = -0.22$ eÅ^{-3}	
Measurements: Enraf-Nonius CAD-4 diffractometer	
Refinement: full matrix least-squares (SHELXL-97)	
Program system: CAD-4 EXPRESS software	
Structure determination: SHELXS-97	
Treatment of hydrogen atoms: mixed	

Table 2 Final coordinates and equivalent anisotropic thermal parameters for non-hydrogen atoms

Atom	*x*	*y*	*z*	U_{eq}/Å^2
C1	0.6855(6)	0.9409(6)	-0.2226(5)	0.095(1)
C2	0.7519(5)	1.0645(5)	-0.2579(4)	0.085(1)
C3	0.7960(5)	1.1014(4)	-0.1689(4)	0.079(1)
C4	0.6657(5)	0.8573(4)	-0.1023(4)	0.082(1)
C5	0.7123(4)	0.8996(3)	-0.0161(3)	0.0629(8)
C6	0.7200(4)	0.8800(4)	0.2001(3)	0.0682(9)
C7	0.7173(4)	0.7803(4)	0.3227(3)	0.0688(9)
C8	0.5743(5)	0.7147(4)	0.1606(4)	0.0710(9)
C9	0.5696(5)	0.6225(4)	0.2873(3)	0.075(1)
C10	0.4605(4)	0.6970(3)	0.4902(3)	0.0598(8)
C11	0.4869(4)	0.7752(4)	0.5803(3)	0.0614(8)
C12	0.2393(4)	0.8687(3)	0.6562(3)	0.0630(8)
C13	0.0970(4)	0.8589(4)	0.7640(4)	0.0699(9)
C14	0.0750(4)	0.7756(4)	0.8809(3)	0.0674(9)
C15	0.1947(3)	0.6940(3)	0.8994(3)	0.0542(7)
C16	0.1790(4)	0.6042(3)	1.0282(3)	0.0551(7)
C17	0.0392(4)	0.5595(4)	1.1241(3)	0.0654(8)
C18	0.0258(4)	0.4749(4)	1.2453(3)	0.072(1)
C19	0.1544(4)	0.4351(4)	1.2703(3)	0.0673(9)
C20	0.2964(4)	0.4790(4)	1.1764(3)	0.0707(9)
C21	0.3073(4)	0.5632(4)	1.0570(3)	0.0664(9)
C22	0.0175(6)	0.2931(7)	1.4792(5)	0.129(3)
N1	0.7782(4)	1.0217(3)	-0.0495(3)	0.0771(9)
N2	0.6989(3)	0.8155(3)	0.1047(3)	0.0642(7)
N3	0.5791(4)	0.6965(3)	0.3791(3)	0.0699(8)
N4	0.3441(3)	0.7829(3)	0.6860(2)	0.0585(7)
N5	0.3248(3)	0.6965(3)	0.8032(2)	0.0554(6)
O1	0.3420(3)	0.6343(3)	0.5236(2)	0.0778(8)
O2	0.2722(3)	0.9448(3)	0.5468(2)	0.0793(8)
O3	0.1565(3)	0.3510(4)	1.3837(3)	0.091(1)

$U_{eq} = (1/3)\,\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* (\boldsymbol{a}_i \cdot \boldsymbol{a}_j)$.

Table 3 Selected bond distances (Å), angles (˚) and torsion angles (˚)

C3	N1	1.353(5)		C5	N1	1.347(5)	
C5	N2	1.392(4)		C6	N2	1.471(5)	
C6	C7	1.504(5)		C7	N3	1.453(5)	
C8	N2	1.464(5)		C8	C9	1.500(5)	
C9	N3	1.459(5)		C10	O1	1.212(4)	
C10	N3	1.343(4)		C10	C11	1.536(5)	
C11	N4	1.454(4)		C12	N4	1.381(5)	
C12	C13	1.435(5)		C13	C14	1.338(5)	
C14	C15	1.429(5)		C15	N5	1.306(4)	
C15	C16	1.482(4)		C16	C17	1.381(4)	
C18	C19	1.371(5)		C19	O3	1.368(4)	
C22	O3	1.407(5)		N4	N5	1.359(3)	
C2	C1	C4	121.1(4)	C3	C2	C1	117.1(4)
N2	C6	C7	111.8(3)	C7	N3	C9	110.9(3)
O1	C10	C11	120.6(3)	N4	C11	C10	109.5(3)
O2	C12	C13	126.2(3)	C14	C13	C12	121.3(3)
C17	C16	C21	117.5(3)	C16	C17	C18	121.7(3)
C15	N5	N4	117.5(3)	C19	C18	C17	119.4(3)
C5	N1	C3	118.7(4)	C19	O3	C22	118.1(3)
N3	C10	C11	N4	171.9(3)	O2	C12	C13	C14	-177.5(4)
N5	C15	C16	C17	-158.9(3)	C17	C18	C19	O3	-178.8(4)
O3	C19	C20	C21	179.1(4)	N2	C5	N1	C3	177.6(3)
N1	C5	N2	C8	154.0(3)	N1	C5	N2	C6	16.1(4)
C4	C5	N2	C8	-28.9(5)	C7	C6	N2	C5	-174.9(3)
O1	C10	N3	C7	171.6(3)	C11	C10	N3	C7	-12.8(5)
O1	C10	N3	C9	2.5(5)	C11	C10	N3	C9	178.2(3)
O2	C12	N4	N5	178.1(3)	C10	C11	N4	N5	101.1(3)
C18	C19	O3	C22	4.6(7)	C20	C19	O3	C22	-174.6(5)

equivalent thermal parameters for non-hydrogen atoms are given in Table 2; selected bond distances and angles are given in Table 3. The bond lengths and angles are comparable to those observed in related compounds.[1-3] Piperazine is a non-planar six-membered ring containing four C and two N atoms. The piperazine ring adopts a chair conformation with the N2 and N3 atoms deviating by 0.270(3) and –0.161(3)Å, respectively, on opposite sides of the least-squares plane through C6, C7, C8 and C9.

The pyridazine, phenyl and pyridyl rings are planar within the experimental error. The piperazine ring makes dihedral angles of 11.6(3)˚, 79.0(1)˚ and 57.2(1)˚ with the pyridyl, pyridazine and phenyl rings, respectively. The methoxy group are almost coplanar with the aromatic rings, as shown by a torsion angle of –174.6(5)˚ for C20–C19–O3–C22. The dihedral angle between this plane and the plane defined by N1–C1–C2–C3–C4–C5 is 63.4(1)˚. The dihedral angle between the pyridazine ring and methoxyphenyl group is 21.9(2)˚.

Acknowledgements

The authors wish to acknowledge the purchase of a CAD4 diffractometer under Grant DPT/TBAG1 of the Scientific and Technical Research Council of Turkey.

References

1. S. B. Majumder, M. Mukherjee, G. K. Patra, D. Datta, and M. Helliwel, *Acta Crystallogr*., **1999**, *C55*, 668.
2. G. Mairesse, J. C. Boiven, D. J. Thomas, J. P. Bonte, and D. Lesieur, *Acta Crystallogr*., **1987**, *C43*, 2128.
3. D. P. Elder, I. A. Selby, R. O. Gould, and P. Taylor, *Acta Crystallogr*., **1992**, *C48*, 871.
4. G. M. Sheldrick, SHELXS-97. Program for the Solution of Crystal Structures, **1997**, Univ. of Göttingen, Germany.
5. G. M. Sheldrick, SHELXL-97. Program for the Refinement of Crystal Structures, **1997**, Univ. of Göttingen, Germany.