Table 1. *Selected geometric parameters (Å, °)*

S—O2	1.439 (3)	C1—C5	1.575 (5)
S—O1	1.442 (3)	C2—C3	1.321 (5)
S—C10	1.777 (3)	C5—C9	1.522 (5)
S—C1	1.803 (3)	C5—C6	1.555 (5)
C1—C7	1.542 (4)	C6—C7	1.533 (5)
O2—S—O1	119.0 (2)	C7—C1—S	116.7 (2)
O2—S—C10	105.6 (2)	C5—C1—S	123.6 (2)
O1—S—C10	107.4 (2)	C9—C5—C4	113.5 (3)
O2—S—C1	105.7 (2)	C9—C5—C6	112.5 (3)
O1—S—C1	107.8 (2)	C4—C5—C6	114.8 (3)
C10—S—C1	111.28 (14)	C9—C5—C1	121.2 (3)
C2—C1—C7	114.9 (3)	C4—C5—C1	106.4 (3)
C2—C1—C5	103.0 (3)	C6—C5—C1	85.9 (3)
C7—C1—C5	90.5 (3)	C7—C6—C5	91.6 (3)
C2—C1—S	107.3 (2)	C6—C7—C1	87.9 (2)

H atoms were refined with fixed geometry, each riding on a carrier atom, with an isotropic displacement parameter 1.5 (for methyl H atoms) or 1.2 (for the other H atoms) times the value of the equivalent isotropic displacement parameter of the carrier atom.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *MolEN* (Fair, 1990). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *ZORTEP* (Zsolnai, 1995). Software used to prepare material for publication: *SHELXL93*.

This work has received partial support from FAPESP (Procs. 94/1213-5 and 94/2061-4), CNPq (Procs. 304204/84-6 and 300003/89-7), CAPES and FINEP.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1476). Services for accessing these data are described at the back of the journal.

References

Baughman, R. G. (1997). *Acta Cryst.* C**53**, 1928–1929.

Bolte, M. & Berger, B. (1996). *Acta Cryst.* C**52**, 1987–1989.

Chen, Y.-S., Khan, M., Rao, S. N., Krishnaiah, M. & Raju, K. V. N. (1996). *Acta Cryst.* C**52**, 1847–1849.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

Dickens, J. C. & Mori, K. (1989). *J. Chem. Ecol.* **15**, 517–528.

Enraf–Nonius (1989). *CAD-4 Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.

Fair, C. K. (1990). *MolEN. An Interactive Intelligent System for Crystal Structure Analysis*. Enraf–Nonius, Delft, The Netherlands.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Franke, W., Bartels, J., Krohn, S., Schultz, S., Baader, E., Tengo, J. & Schneider, D. (1989). *Pure Appl. Chem.* **61**, 539–542.

Monteiro, H. J. & Zukerman-Schpector, J. (1996). *Tetrahedron*, **52**, 3879–3888.

North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* A**24**, 351–359.

Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.

Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.

Tumlinson, J. H., Gueldner, R. C., Hardee, D. D., Thompson, A. C., Hedin, P. A. & Minyard, J. P. (1971). *J. Org. Chem.* **36**, 2616–2621.

Zsolnai, L. (1995). *ZORTEP. An Interactive Molecular Graphics Program*. University of Heidelberg, Germany.

Zukerman-Schpector, J. & Monteiro, H. (1996). *Acta Cryst.* C**52**, 1767–1770.

Zukerman-Schpector, J. & Monteiro, H. (1998). *Acta Cryst.* C**54**, 96–97.

Acta Cryst. (1998). C**54**, 1675–1677

The Antifungal Drug Clotrimazole

HYUN SONG AND HYUN-SO SHIN

Department of Chemical Engineering, Dongguk University, Seoul 100-715, Korea. E-mail: qsar@cakra.dongguk.ac.kr

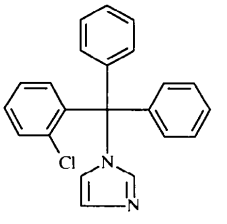
(Received 19 June 1997; accepted 5 May 1998)

Abstract

The structure of the title compound, 1-[(2-chlorophenyl)diphenylmethyl]-1*H*-imidazole, $C_{22}H_{17}ClN_2$, has been determined. The molecular conformation showed a weathercock-type structure and the three phenyl rings are almost perpendicular to the imidazole ring. The distances between the centres of the three phenyl rings and the centre of the imidazole ring are in the range 4.52–4.54 Å.

Comment

The title compound, (I) (common names Clotrimazole, Lotromin, Mycelex-G and Canesten), is a member of antifungal imidazole derivatives with broad-spectrum activity against tinea infections and candidiasis (Hoogerheide & Wyka, 1982). It is generally believed that antifungal activity of imidazoles results from the disorganization of the fungal cytoplasmic membrane, which is a consequence of inactivation of P-450 by binding between the N atom of the imidazole ring and the haem site (Hansch *et al.*, 1990).



(I)

Recently, the mechanism of antifungal agents has been clarified by X-ray analysis studies on inhibitors bound to P-450 (Poulous, Finzel *et al.*, 1985, 1987; Poulous & Howard, 1987). Crystal structures of antifungal imidazoles have also been reported (Peeters *et al.*, 1979; Freer *et al.*, 1986; Shin *et al.*, 1987).

As part of our studies on the structure–activity relationship of its imidazole agents, the crystal structure of (I) has been determined. The title compound was purchased from SIGMA chemicals.

The overall molecular conformation of the title compound may be described as a weathercock type which

has the three phenyl rings as the fan. The three phenyl rings are almost perpendicular to the C7—N20 bond axis of the imidazole ring. The dihedral angles between the three phenyl rings (*A*, *B* and *C*) and the imidazole ring are 126.8 (3), 78.5 (3) and 107.5 (2)°, respectively. Each of the four ring systems in the molecule is almost planar, the maximum deviation of 0.010 (2) Å is at the C14 and C15 atoms of phenyl ring *C*. In the imidazole ring the C21=N22 and C23=C24 bond lengths are 1.315 (3) and 1.346 (3) Å, respectively. These values are much shorter (0.032 Å about C23—C24) than those of pure imidazole (1.378 Å; McMullan *et al.*, 1979). In the three phenyl rings, the C=C bond lengths range from 1.365 (4) to 1.400 (3) Å and the average distance is 1.381 Å. These values are in good agreement with those in miconazole (Peeters *et al.*, 1979), econazole (Freer *et al.*, 1986), econazole nitrate (Suh *et al.*, 1990) and sulconazole nitrate (Shin *et al.*, 1997).

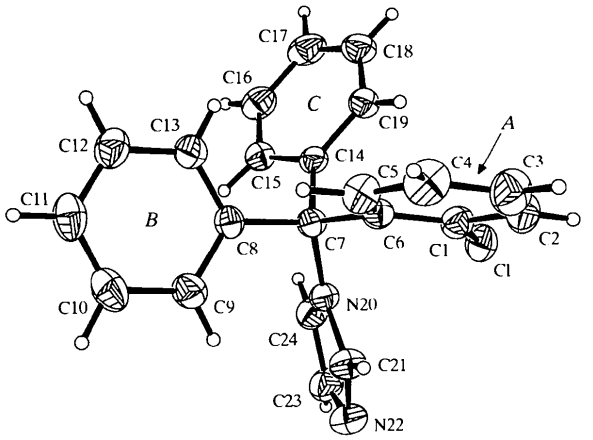


Fig. 1. Molecular structure showing 40% probability displacement ellipsoids.

To obtain information for use in structure–activity studies of antifungal imidazoles, the distances (l_1, l_2 and l_3) between the centre of the imidazole ring and the centres of the three aromatic rings (*A*, *B* and *C*) were calculated. The distances l_1, l_2 and l_3 are 4.52, 4.54 and 4.52 Å, respectively. The corresponding distance l_1 in the antifungal imidazoles such as miconazole, econazole and sulconazole nitrate are within the range 4.52–4.97 Å (except for econazole nitrate, 5.70 Å).

The dihedral angles between the aromatic ring *A*, which is halogen substituted, and the imidazole ring are in the range 95.2–126.8° (except for econazole nitrate, 10.6°).

The result of conformational analysis may be used as a basis for the definition of structural parameters necessary for the range of activity of this class of compounds.

Experimental

Crystals of (I) were grown from chloroform solution by slow evaporation at room temperature.

Crystal data

$C_{22}H_{17}ClN_2$
M_r = 344.83
Triclinic
$P\bar{1}$
a = 8.7590 (5) Å
b = 10.5540 (12) Å
c = 10.6064 (14) Å
α = 114.116 (14)°
β = 96.957 (7)°
γ = 97.535 (7)°
V = 870.5 (2) Å^3
Z = 2
D_x = 1.316 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 25 reflections
θ = 4.5–14.5°
μ = 0.225 mm^{-1}
T = 293 (2) K
Prism
0.42 × 0.25 × 0.21 mm
Colourless

Data collection

CAD-4 diffractometer
ω–2θ scans
Absorption correction: none
3177 measured reflections
2967 independent reflections
2345 reflections with $I > 2\sigma(I)$
R_{int} = 0.010

θ_{max} = 25°
$h = 0 \rightarrow 9$
$k = -11 \rightarrow 11$
$l = -11 \rightarrow 11$
3 standard reflections
every 200 reflections
frequency: 60 min
intensity decay: <2%

Refinement

Refinement on F^2
$R(F)$ = 0.037
$wR(F^2)$ = 0.086
S = 1.06
2967 reflections
294 parameters
All H-atom parameters refined

$w = 1/[\sigma^2(F_o)^2 + (0.04P)^2 + 0.3261P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

Cl—C1	1.743 (2)	C10—C11	1.370 (3)
C1—C2	1.381 (3)	C11—C12	1.367 (3)
C1—C6	1.400 (3)	C12—C13	1.376 (3)
C2—C3	1.375 (3)	C14—C19	1.379 (3)
C3—C4	1.373 (4)	C14—C15	1.395 (3)
C4—C5	1.386 (3)	C15—C16	1.374 (3)
C5—C6	1.390 (3)	C16—C17	1.382 (3)
C6—C7	1.551 (3)	C17—C18	1.365 (4)
C7—N20	1.498 (2)	C18—C19	1.379 (3)
C7—C14	1.541 (2)	N20—C21	1.356 (3)
C7—C8	1.551 (2)	N20—C24	1.371 (3)
C8—C9	1.384 (3)	C21—N22	1.315 (3)
C8—C13	1.386 (3)	N22—C23	1.372 (3)
C9—C10	1.389 (3)	C23—C24	1.346 (3)
C2—C1—C6	121.9 (2)	C11—C10—C9	120.3 (2)
C2—C1—Cl	116.0 (2)	C12—C11—C10	119.2 (2)
C6—C1—Cl	122.1 (2)	C11—C12—C13	120.8 (2)
C3—C2—C1	120.0 (2)	C12—C13—C8	121.2 (2)
C4—C3—C2	119.7 (2)	C19—C14—C15	117.1 (2)
C3—C4—C5	120.1 (2)	C19—C14—C7	122.8 (2)
C4—C5—C6	121.9 (2)	C15—C14—C7	119.7 (2)

C5—C6—C1	116.5 (2)	C16—C15—C14	121.3 (2)
C5—C6—C7	120.8 (2)	C15—C16—C17	120.7 (2)
C1—C6—C7	122.7 (2)	C18—C17—C16	118.3 (2)
N20—C7—C14	111.17 (14)	C17—C18—C19	121.2 (2)
N20—C7—C6	106.75 (14)	C14—C19—C18	121.4 (2)
C14—C7—C6	111.50 (15)	C21—N20—C24	106.0 (2)
N20—C7—C8	108.76 (14)	C21—N20—C7	124.7 (2)
C14—C7—C8	107.43 (15)	C24—N20—C7	129.2 (2)
C6—C7—C8	111.24 (15)	N22 C21—N20	112.5 (2)
C9—C8—C13	117.4 (2)	C21—N22—C23	104.2 (2)
C9—C8—C7	122.5 (2)	C24—C23—N22	111.1 (2)
C13—C8—C7	120.2 (2)	C23—C24—N20	106.1 (2)
C8—C9—C10	121.2 (2)		

The space group $P\bar{1}$ was determined from non-systematic absences. Intensity data were corrected for Lorentz and polarization effects. The crystal structure was solved by direct methods using *SHELXS*86 (Sheldrick, 1985) and refined by full-matrix least-squares methods using *SHELXL*93 (Sheldrick, 1993) with anisotropic displacement parameters for all non-H atoms. All H atoms were located from difference Fourier maps and were refined isotropically in the final cycles. There were no significant features in the final difference Fourier map. Refinement of the H atoms led to C—H distances in the range 0.88 (3)–1.02 (2) Å. U values vary from 0.038 (6) to 0.078 (8) with a mean of 0.057 (8) Å^2. All geometrical calculations were performed using *GEOM*. All computations were performed using IBM PCs.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *CAD*-4 *Software*. Data reduction: *Xtal*3.2 (Hall *et al.*, 1992). Program(s) used to solve structure: *SHELXS*86. Program(s) used to refine structure: *SHELXL*93. Molecular graphics: *ORTEX* (McArdle, 1995). Software used to prepare material for publication: *SHELXL*93.

The authors are grateful to Professor S. I. Cho, University of Seoul City, for data collection.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: BK1362). Services for accessing these data are described at the back of the journal.

References

Enraf–Nonius (1989). *CAD*-4 *Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.

Freer, A. A., Pearson, A. & Salole, E. G. (1986). *Acta Cryst.* C**42**, 1350–1352.

Hall, S. R., Flack, H. D. & Stewart, J. M. (1992). Editors. *Xtal*3.2 *Reference Manual*. Universities of Western Australia, Australia, Geneva, Switzerland, and Maryland, USA.

Hansch, C., Sammes, P. G. & Taylor, J. B. (1990). *Comprehensive Medicinal Chemistry*, Vol. 2, pp. 134–142. Oxford: Pergamon Press.

Hoogerheide, J. H. & Wyka, B. E. (1982). *Analytical Profiles of Drug Substances*, Vol. 11, edited by K. Florey, pp. 225–255. New York: Academic Press.

McArdle, P. (1995). *ORTEX. Molecular Graphic Program.* University of Galway, Ireland.

McMullan, R. K., Epstein, J., Ruble, J. R. & Craven, B. M. (1979). *Acta Cryst.* B**35**, 688–691.

Peeters, O. M., Blaton, N. M. & De Ranter, C. J. (1979). *J. Bull. Soc. Chem. Belg.* **88**, 265–272.

Poulous, T. L., Finzel, B. C., Gunsalus, I. C., Wagner, G. C. & Kraut, J. (1985). *J. Biol. Chem.* **260**(30), 16122–16130.

Poulous, T. L., Finzel, B. C. & Howard, A. J. (1987). *J. Mol. Biol.* **195**, 687–700.

Poulous, T. L. & Howard, A. J. (1987). *Biochemistry*, **26**, 8165–8174.

Sheldrick, G. M. (1985). *SHELXS*86. *Program for the Solution of Crystal Structures*. University of Göttingen, Germany.

Sheldrick, G. M. (1993). *SHELXL*93. *Program for Crystal Structure Refinement*. University of Göttingen, Germany.

Shin, H. S., Song, H., Cho, S. I. & Park, K. I. (1997). *Bull. Kor. Chem. Soc.* **18**(1), 14–18.

Shin, W. (1978). GEOM. *Program for Molecular Geometry Calculations*. University of Seoul National, Korea.

Suh, I. W., Cho, S. I. & Park, K. I. (1990). *Kor. J. Cryst.* **1**, 14–18.

Acta Cryst. (1998). C**54**, 1677–1679

(4*S*,5*R*,2′*R*)-3,4-Dimethyl-1-[2′-(1-naphthyl)-2′-phenylacetyl]-5-phenylimidazolidin-2-one

RICARDO BAGGIO,[a] GUILLERMO LOTZ,[b] SARA PALACIOS[b] AND RAÚL A. MARIEZCURRENA[c]

[a]*Departamento de Física, Comisión Nacional de Energía Atómica, Buenos Aires, Argentina,* [b]*CEQUIMAP, Facultad de Ciencias Qímicas, Universidad Nacional de Córdoba, Córdoba, Argentina, and* [c]*Laboratorio de Cristalografía y Química del Estado Sólido, Facultad de Química, Universidad de la República, Montevideo, Uruguay. E-mail: baggio@cnea.edu.ar*

(*Received 7 April 1998; accepted 5 May 1998*)

Abstract

The title compound, (4*S*,5*R*)-3,4-dimethyl-1-[(2*R*)-2-(1-naphthyl)-2-phenylacetyl]-5-phenylimidazolidin-2-one, $C_{29}H_{26}N_2O_2$, has two different aryl groups at the α-carbon which confer a stereogenic character on the site. The geometry of the molecule is stabilized by an intramolecular hydrogen bond linking the acetamide and imidazolidine groups, which gives a planar character to the core.

Comment

Acetamides have been reported as herbicides, especially those with an α-chloro substituent (Couderchet *et al.*, 1986). We have been studying the families of α-aryl- and α,α-diarylacetamides and both have shown interesting growth-inhibitor properties against *Avena sativa* and *Cyperus rotundus* (Palacios *et al.*, 1995). The diaryl family has a stereogenic center when the aryl groups are different. In order to synthesize enantiomerically pure α,α-(1-naphthyl)phenylacetamide, we have recently prepared the imidazolidin-2-one derivative (Lotz *et al.*, 1994). The reaction described (see *Experimental*) provides two epimeric species, *viz.* (4*S*,5*R*,2′*S*)-, (1), and (4*S*,5*R*,2′*R*)-3,4-dimethyl-1-[2′-(1-naphthyl)-2′-phenyl-