

**Data collection**

Siemens SMART diffractometer with area detector  $\omega$  scans

Absorption correction: multi-scan (Blessing, 1995)

$T_{\min} = 0.946$ ,  $T_{\max} = 0.964$   
5329 measured reflections  
2979 independent reflections

2778 reflections with  $I > 2\sigma(I)$

$R_{\text{int}} = 0.036$

$\theta_{\max} = 27.49^\circ$

$h = -14 \rightarrow 13$

$k = -9 \rightarrow 8$

$l = 0 \rightarrow 14$

Intensity decay: none

**Refinement**

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.048$

$wR(F^2) = 0.126$

$S = 1.030$

2979 reflections

219 parameters

H atoms: see below

$w = 1/[\sigma^2(F_o^2) + (0.0904P)^2]$

where  $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.002$

$\Delta\rho_{\max} = 0.451 \text{ e } \text{\AA}^{-3}$

$\Delta\rho_{\min} = -0.292 \text{ e } \text{\AA}^{-3}$

Extinction correction: none

Scattering factors from

*International Tables for Crystallography* (Vol. C)

Absolute structure:

Flack (1983)

Flack parameter = 0.7 (10)

Table 1. Selected geometric parameters ( $\text{\AA}$ ,  $^\circ$ )

O1—C9	1.450 (2)	C8—C14	1.515 (3)
O1—C8	1.453 (2)	C9—C11	1.522 (3)
C7—C8	1.514 (3)	C9—C10	1.542 (2)
C8—C9	1.477 (3)		
O1—C8—C9	59.29 (12)	O1—C9—C8	59.54 (12)
O1—C8—C7	114.03 (16)	O1—C9—C11	111.76 (15)
C9—C8—C7	122.02 (16)	C8—C9—C11	120.44 (15)
O1—C8—C14	113.35 (15)	O1—C9—C10	114.43 (14)
C9—C8—C14	119.63 (17)	C8—C9—C10	120.40 (16)
C7—C8—C14	114.94 (17)	C11—C9—C10	115.96 (16)

Table 2. Hydrogen-bonding geometry ( $\text{\AA}$ ,  $^\circ$ )

D—H...A	D—H	H...A	D...A	D—H...A
O4—H4...O3 <sup>i</sup>	0.83	1.96	2.720 (2)	151.1

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

The data collection nominally covered a hemisphere of reciprocal space by a combination of three sets of exposures; each set had a different  $\varphi$  angle for the crystal and each exposure covered  $0.3^\circ$  in  $\omega$ . The crystal-to-detector distance was 4.94 cm. Crystal decay was monitored by repeating the initial frames at the end of data collection and analysing the duplicate reflections. H atoms were placed geometrically and refined with a riding model (including free rotation about C—C bonds for methyl groups) and with  $U_{\text{iso}}$  constrained to be 1.2 (1.5 for methyl groups) times  $U_{\text{eq}}$  of the carrier atom.

Data collection: SMART (Siemens 1994a). Cell refinement: SAINT (Siemens 1994a). Data reduction: SAINT. Program(s) used to solve structure: SHELXS97 (Sheldrick, 1990). Program(s) used to refine structure: SHELXL97 (Sheldrick, 1997). Molecular graphics: SHELXTL (Siemens 1994b). Software used to prepare material for publication: SHELXL97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: DA1020). 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.
- Blessing, R. H. (1995). *Acta Cryst. A* **51**, 33–38.
- Cambie, R. C., Denny, W. A., Hay, M. P., Mitchell, L. M., Rutledge, P. S. & Woodgate, P. D. (1998). *Aust. J. Chem.* In the press.
- Flack, H. D. (1983). *Acta Cryst. A* **39**, 876–881.
- Sheldrick, G. M. (1990). *Acta Cryst. A* **46**, 467–473.
- Sheldrick, G. M. (1997). *SHELXL97. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
- Siemens (1994a). SMART and SAINT. Area Detector Control and Integration Software. Siemens Analytical Instruments Inc., Madison, Wisconsin, USA.
- Siemens (1994b). SHELXTL. Siemens Analytical Instruments Inc., Madison, Wisconsin, USA.

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## Intermediates in the Synthesis of (+)-Grandisol. III.† (1*S*,5*R*)-2,5-Dimethyl-1-(phenylsulfonyl)bicyclo[3.2.0]hept-2-ene

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**Abstract**

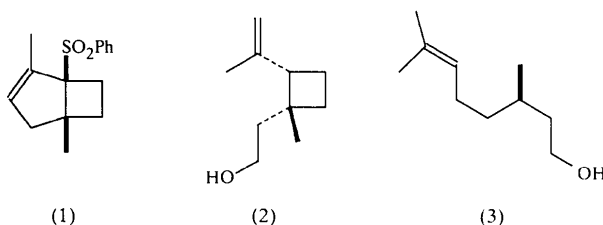
In the title compound,  $\text{C}_{15}\text{H}_{18}\text{O}_2\text{S}$ , the cyclopentene ring is in an envelope conformation and the cyclobutane ring is puckered. The phenylsulfonyl and the junction methyl groups are *cis* with respect to each other.

**Comment**

The terpene (+)-*cis*-2-isopropenyl-1-methylcyclobutane-ethanol, (2), *i.e.* (+)-grandisol (Tumlinson *et al.*, 1971), is the principal component in the aggregation pheromone produced by the male cotton boll weevil, *Anthonomus grandis* Boheman (Franke *et al.*, 1989), which is a serious pest in Brazilian cotton fields. The potential use of this terpene in traps for monitoring crop infestation in integrated pest management makes it a target for synthetic organic chemists, especially the

† Part II: Zukerman-Schpector & Monteiro (1998).

more active (+)-enantiomer (Dickens & Mori, 1989). As the success of a synthetic route aimed at the synthesis of (+)-grandisol, starting with the readily available (+)-citronellol, (3), depends on the generation of intermediates with the correct functionality and stereochemistry, the unambiguous determination of their stereostructures is required. We report here the crystal structure determination of another intermediate, (1).



A view of the molecule showing the atom-numbering scheme is presented in Fig. 1. The S atom is tetrahedrally bonded to two C and two O atoms, with tetrahedral angles ranging from 105.6(2) to 111.28(14)°, except for O=S=O which is 119.0(2)°. The S=O and the S—C(aromatic) distances, and the O=S=O angle are in good agreement, within experimental error, with the averages of 12 S=O (1.432 Å) and six S—C distances (1.766 Å), and six O=S=O angles (118.5°) reported previously (Zukerman-Schpector & Monteiro, 1996, 1998; Baughman, 1997; Bolte & Berger, 1996; Chen *et al.*, 1996). The phenylsulfonyl and junction methyl groups are *cis* with respect to each other, the rings being, therefore, *cis*-fused. The absolute structure was indicated by the Flack (1983) parameter, which refined to 0.01(3). Cremer & Pople (1975) puckering parameters show that the five-membered ring is in an envelope conformation [ $q_2 = 0.147(4)$  Å and  $\phi_2 = 145(2)^\circ$ ]. The four-membered ring is puckered [dihedral angle between C1/C7/C5 and C5/C6/C7 of 22.1(5)°] and makes a dihedral angle of 67.7(2)° with the best least-squares plane through the five-membered ring. The phenyl ring makes dihedral angles of 131.8(2) and 96.3(2)° with the five- and four-membered rings, respectively.

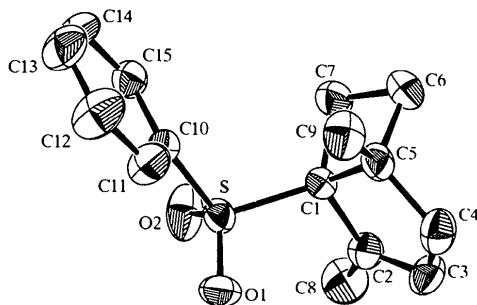


Fig. 1. The molecular structure of (1) showing 50% probability displacement ellipsoids.

The reaction pathway implies the necessity of dihydroxylation of the double bond of (1); thus, this was attempted with osmium tetroxide and potassium permanganate, but the reactions were very sluggish and preparatively useless. It was then postulated that this was due to the hindered nature of the substrate. The result of this crystal structure determination shows that this could be the reason, because the conformation of this intermediate is different to the conformations of all other previously determined structures, as can be seen in the values of the C10—S—C1—C5 torsion angle: 178.02(14)° in (1*S*,2*R*,3*S*,5*R*)-2,5-dimethyl-1-(phenylsulfonyl)bicyclo[3.2.0]heptane-2,3-diol (Zukerman-Schpector & Monteiro, 1996), 164.0(3)° in (1*S*,5*S*)-5-methyl-1-(phenylsulfonyl)bicyclo[3.2.0]heptan-2-one (Zukerman-Schpector & Monteiro, 1998) and 54.1(3)° in this work.

## Experimental

The synthesis of the title compound has been described by Monteiro & Zukerman-Schpector (1996). Crystals were obtained by slow evaporation from EtOH at 269 K.

### Crystal data

C<sub>15</sub>H<sub>18</sub>O<sub>2</sub>S  
*M<sub>r</sub>* = 262.366  
 Orthorhombic  
*P*2<sub>1</sub>2<sub>1</sub>  
*a* = 7.6013(6) Å  
*b* = 11.771(1) Å  
*c* = 14.896(2) Å  
*V* = 1332.8(2) Å<sup>3</sup>  
*Z* = 4  
*D<sub>x</sub>* = 1.3075 Mg m<sup>-3</sup>  
*D<sub>m</sub>* not measured

Mo *K*α radiation  
 $\lambda$  = 0.71073 Å  
 Cell parameters from 25 reflections  
 $\theta$  = 9.24–18.16°  
 $\mu$  = 0.234 mm<sup>-1</sup>  
*T* = 293 K  
 Prismatic  
 0.30 × 0.15 × 0.10 mm  
 Colourless

### Data collection

Enraf–Nonius CAD-4 diffractometer  
 $\omega/2\theta$  scans  
 Absorption correction:  $\psi$  scan (North *et al.*, 1968)  
 $T_{\min} = 0.955$ ,  $T_{\max} = 0.999$   
 1361 measured reflections  
 1361 independent reflections

1076 reflections with  $F^2 > 2\sigma(F^2)$   
 $\theta_{\max} = 25^\circ$   
 $h = -9 \rightarrow 0$   
 $k = 0 \rightarrow 13$   
 $l = -17 \rightarrow 0$   
 3 standard reflections  
 frequency: 30 min  
 intensity decay: 1.1%

### Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.034$   
 $wR(F^2) = 0.080$   
 $S = 1.100$   
 1361 reflections  
 165 parameters  
 H atoms: see below  
 $w = 1/[\sigma^2(F_o^2) + (0.044P)^2 + 0.2293P]$   
 where  $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.001$   
 $\Delta\rho_{\max} = 0.189 \text{ e } \text{Å}^{-3}$   
 $\Delta\rho_{\min} = -0.243 \text{ e } \text{Å}^{-3}$   
 Extinction correction: none  
 Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. Selected geometric parameters ( $\text{\AA}$ ,  $^\circ$ )

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*.

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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.* **C53**, 1928–1929.  
 Bolte, M. & Berger, B. (1996). *Acta Cryst.* **C52**, 1987–1989.  
 Chen, Y.-S., Khan, M., Rao, S. N., Krishnaiah, M. & Raju, K. V. N. (1996). *Acta Cryst.* **C52**, 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.* **A39**, 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.* **A24**, 351–359.  
 Sheldrick, G. M. (1990). *Acta Cryst.* **A46**, 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.* **C52**, 1767–1770.  
 Zukerman-Schpector, J. & Monteiro, H. (1998). *Acta Cryst.* **C54**, 96–97.

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## The Antifungal Drug Clotrimazole

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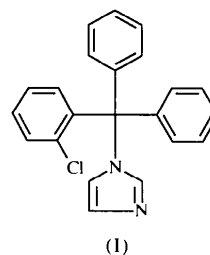
(Received 19 June 1997; accepted 5 May 1998)

## 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).



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