

O2—C12—C11—C13 and the torsion angle C11—C7—C6—O1 at the lactone seven membered ring fusion bond are $-14.8(3)$ and $-30.1(1)^\circ$, respectively, and vary with those of 8β -angeloyloxymaximilianin [$-2.8(3)$ and $-13.1(2)^\circ$ respectively] (Watson & Zabel, 1982), bahia I [$-11.5(6)$ and $-18.5(3)^\circ$ respectively] (Herz, Govindan & Blount, 1980) and 7α -hydroxy-3-desoxyzaluzanin C [$-19.5(4)$, $-30.8(4)$, and $-6.8(4)$ and $-24.2(4)^\circ$ respectively]. Two independent molecules in the unit cell (Fronczek, Vargas & Fischer, 1984).

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Structure of 1-[(4-Acetamidophenyl)thio]-3-[4-(3-methylphenyl)piperazin-1-yl]propane Monohydrate

BY ALAIN CARPY AND JEAN-MICHEL LEGER

SDI 6315 CNRS, Faculté de Pharmacie, Université de Bordeaux II, 3, Place de la Victoire, 33076 Bordeaux CEDEX, France

AND JYOTI RAO AND ANIL K. SAXENA

Central Drug Research Institute, Chattar Manzil, PB No 173, Lucknow-226001, India

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Abstract. C₂₂H₂₉N₃OS.H₂O, $M_r = 401.57$, monoclinic, $P2_1/c$, $a = 6.511(1)$, $b = 14.914(3)$, $c = 22.550(4)$ Å, $\beta = 97.84(1)^\circ$, $V = 2169.1$ Å³, $Z = 4$, $D_x = 1.23$ g cm⁻³, $\lambda(\text{Cu } K\alpha) = 1.54178$ Å, $\mu = 14.59$ cm⁻¹, $F(000) = 864$, room temperature, $R = 0.058$ for 1270 observed reflections. This compound is a centrally active hypotensive agent. The molecule can be described by two planar moieties, *i.e.* the methylphenyl group and the [(4-acetamidophenyl)thio]propane group substituting a piperazine ring in a chair conformation. The overall conformation is *trans* extended.

Experimental. Colorless prism, dimensions $0.30 \times 0.20 \times 0.15$ mm. Density not measured. Unit-cell parameters and intensity data obtained from an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated Cu $K\alpha$ radiation in ω/θ scan mode

($0 < \theta < 65^\circ$). Cell dimensions refined by least-squares fitting of θ values of 22 reflections. No appreciable drop in intensity of a standard reflection (141) checked every 3600 s. 3690 independent reflections collected in $\pm h, k, l$, range $-11,0,0$ to $11,11,27$; 1270 observed reflections with $I > 3\sigma(I)$ used in subsequent calculations. Intensities corrected for Lorentz and polarization effects but not for absorption. Scattering factors for non-H atoms from *International Tables for X-ray Crystallography* (1974, Vol. IV, pp. 201–209) and for H from Stewart, Davidson & Simpson (1965). Structure solved with MULTAN80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980) and standard Fourier synthesis techniques. H atoms located by ΔF synthesis and refined. Block-diagonal-matrix least-squares refinement on F of observed reflections, $w = 1$ if $F_o < P$, $P = [F_o^2(\text{max.})/10]^2$, $w = (P/F_o)^2$ if $F_o > P$;

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Table 1. Atomic coordinates ($\times 10^4$) and equivalent isotropic temperature factors
$$U_{eq} = \frac{1}{3} \sum_i \sum_j \beta_{ij} a_i \cdot a_j$$

| | x | y | z | $B_{eq}(\text{\AA}^2)$ |
|-------|------------|----------|----------|------------------------|
| C(1) | 8512 (10) | 3866 (5) | 3993 (3) | 5.1 (3) |
| C(2) | 6745 (10) | 3673 (5) | 3574 (3) | 5.2 (3) |
| C(3) | 6884 (10) | 3763 (5) | 2972 (3) | 4.9 (3) |
| C(4) | 8684 (9) | 4029 (4) | 2757 (3) | 4.1 (3) |
| C(5) | 10430 (10) | 4219 (5) | 3178 (3) | 5.1 (3) |
| C(6) | 10285 (10) | 4147 (5) | 3778 (3) | 5.5 (3) |
| N(7) | 8628 (8) | 4084 (4) | 2140 (2) | 4.6 (3) |
| C(8) | 10169 (10) | 4261 (4) | 1817 (3) | 5.1 (3) |
| O(9) | 11992 (7) | 4402 (3) | 2051 (2) | 5.8 (2) |
| C(10) | 9570 (11) | 4280 (5) | 1156 (3) | 5.8 (4) |
| S(11) | 8590 (3) | 3760 (2) | 4770 (1) | 7.5 (1) |
| C(12) | 5983 (10) | 3626 (5) | 4910 (3) | 5.5 (4) |
| C(13) | 6066 (12) | 3474 (6) | 5580 (3) | 6.4 (4) |
| C(14) | 3956 (11) | 3560 (5) | 5775 (3) | 5.8 (4) |
| N(15) | 3976 (8) | 3312 (4) | 6410 (2) | 4.7 (3) |
| C(16) | 5333 (11) | 3922 (5) | 6809 (3) | 5.8 (4) |
| C(17) | 5332 (10) | 3673 (5) | 7456 (3) | 5.6 (4) |
| N(18) | 3255 (8) | 3663 (4) | 7626 (2) | 5.1 (3) |
| C(19) | 1823 (11) | 3109 (5) | 7213 (3) | 6.0 (4) |
| C(20) | 1889 (11) | 3381 (5) | 6575 (3) | 6.0 (4) |
| C(21) | 3097 (11) | 3576 (5) | 8240 (3) | 5.1 (3) |
| C(22) | 4739 (11) | 3856 (5) | 8688 (3) | 5.7 (4) |
| C(23) | 4564 (12) | 3797 (6) | 9281 (3) | 6.7 (4) |
| C(24) | 2776 (14) | 3472 (5) | 9471 (4) | 7.2 (5) |
| C(25) | 1161 (15) | 3211 (6) | 9045 (4) | 7.9 (5) |
| C(26) | 1310 (13) | 3253 (5) | 8442 (4) | 7.0 (4) |
| C(27) | 6402 (14) | 4088 (7) | 9726 (4) | 9.4 (6) |
| O(28) | 4869 (7) | 3567 (3) | 1410 (2) | 5.6 (2) |

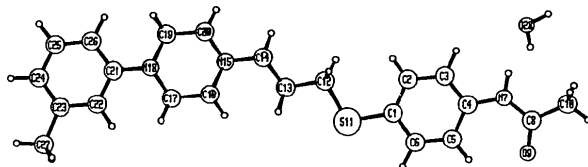


Fig. 1. Projection of the molecule showing the numbering of atoms.

anisotropic thermal parameters for non-H atoms and isotropic ones for H. Final $R = 0.058$, $wR = 0.072$, $S = 1.365$ (1270 reflections, 377 parameters). In final cycle, mean and max. Δ/σ 0.2 and 0.4. Residual electron density within $\pm 0.5 \text{ e \AA}^{-3}$. Calculations carried out on a Mini 6-92 CII Honeywell Bull computer. Unpublished programs from Laboratoire de Cristallographie, Université de Bordeaux I, F-33400 Talence.

A projection of the molecule is given in Fig. 1. Coordinates for non-H atoms are presented in Table 1.* Bond lengths and angles are summarized in Table 2. The molecule can be described by two flat areas: one containing the methylphenyl group and the other

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54429 (26 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Bond distances (\AA) and angles ($^\circ$)

| | | | |
|-------------------|------------|-------------------|------------|
| C(1)—C(2) | 1.415 (9) | N(15)—C(16) | 1.483 (8) |
| C(1)—C(6) | 1.376 (9) | N(15)—C(20) | 1.461 (8) |
| C(1)—S(11) | 1.753 (7) | C(16)—C(17) | 1.506 (10) |
| C(2)—C(3) | 1.379 (9) | C(17)—N(18) | 1.456 (9) |
| C(3)—C(4) | 1.387 (8) | N(18)—C(19) | 1.477 (9) |
| C(4)—C(5) | 1.407 (8) | N(18)—C(21) | 1.407 (8) |
| C(4)—N(7) | 1.389 (7) | C(19)—C(20) | 1.501 (10) |
| C(5)—C(6) | 1.375 (9) | C(21)—C(22) | 1.403 (9) |
| N(7)—C(8) | 1.343 (8) | C(21)—C(26) | 1.393 (10) |
| C(8)—O(9) | 1.250 (8) | C(22)—C(23) | 1.405 (10) |
| C(8)—C(10) | 1.489 (9) | C(23)—C(24) | 1.383 (11) |
| S(11)—C(12) | 1.780 (7) | C(23)—C(27) | 1.516 (12) |
| C(12)—C(13) | 1.520 (10) | C(24)—C(25) | 1.381 (12) |
| C(13)—C(14) | 1.503 (10) | C(25)—C(26) | 1.376 (12) |
| C(14)—N(15) | 1.478 (8) | | |
| | | | |
| C(2)—C(1)—C(6) | 118.1 (6) | C(14)—N(15)—C(20) | 110.1 (5) |
| C(2)—C(1)—S(11) | 124.0 (5) | C(16)—N(15)—C(20) | 107.5 (5) |
| C(6)—C(1)—S(11) | 117.9 (5) | N(15)—C(16)—C(17) | 110.9 (5) |
| C(1)—C(2)—C(3) | 118.7 (6) | C(16)—C(17)—N(18) | 112.5 (5) |
| C(2)—C(3)—C(4) | 123.0 (6) | C(17)—N(18)—C(19) | 111.6 (5) |
| C(3)—C(4)—C(5) | 117.7 (5) | C(17)—N(18)—C(21) | 117.1 (5) |
| C(3)—C(4)—N(7) | 117.3 (5) | C(19)—N(18)—C(21) | 116.4 (5) |
| C(5)—C(4)—N(7) | 124.9 (5) | N(18)—C(19)—C(20) | 110.9 (6) |
| C(4)—C(5)—C(6) | 119.4 (6) | N(15)—C(20)—C(19) | 112.0 (6) |
| C(1)—C(6)—C(5) | 123.0 (6) | N(18)—C(21)—C(22) | 119.9 (6) |
| C(4)—N(7)—C(8) | 129.4 (5) | N(18)—C(21)—C(26) | 122.0 (6) |
| N(7)—C(8)—O(9) | 122.7 (6) | C(22)—C(21)—C(26) | 118.0 (6) |
| N(7)—C(8)—C(10) | 115.7 (5) | C(21)—C(22)—C(23) | 120.2 (6) |
| O(9)—C(8)—C(10) | 121.6 (6) | C(22)—C(23)—C(24) | 120.7 (7) |
| C(1)—S(11)—C(12) | 106.8 (3) | C(22)—C(23)—C(27) | 118.1 (7) |
| S(11)—C(12)—C(13) | 106.7 (5) | C(24)—C(23)—C(27) | 121.2 (7) |
| C(12)—C(13)—C(14) | 111.6 (6) | C(23)—C(24)—C(25) | 118.5 (7) |
| C(13)—C(14)—N(15) | 112.0 (5) | C(24)—C(25)—C(26) | 121.7 (8) |
| C(14)—N(15)—C(16) | 111.1 (5) | C(21)—C(26)—C(25) | 120.9 (7) |

containing the (4-acetamidophenyl)thio group. These areas are linked together *via* the piperazine ring in the chair conformation and the *trans*-extended propane group. The torsion angles defining the conformation of the chain are: C(6)—C(1)—S(11)—C(12) = 168 (1), C(1)—S(11)—C(12)—C(13) = 176 (1), S(11)—C(12)—C(13)—C(14) = 167 (1), C(12)—C(13)—C(14)—N(15) = 173 (1) and C(13)—C(14)—N(15)—C(20) = -178 (1) $^\circ$. N(15) is sp^3 hybridized (average valence angles 109.6 $^\circ$). Owing to the 3-methylphenyl substituent the hybridization state of N(18) exhibits an sp^2 character (average valence angles 115.1 $^\circ$), the axial lone pair being able to participate in resonance with the phenyl ring [N(18)—C(21) = 1.407 (8) \AA]. The possibility for resonance is also evidenced by the position of the phenyl ring *vs* the mean plane of the piperazine chair [dihedral angle 13 (1) $^\circ$]. The angle between the mean plane of the piperazine and that of the chain is 23 (1) $^\circ$.

Related literature. The two substructures 1-[4-(4-acetamidophenyl)thio]propyl and (3-methylphenyl)-piperazine have been identified as potential hypotensive pharmacophores (Rao, Saxena, Saxena, Singh, Kar & Srimal, 1987; Murti, Bhandari, Ram, Prabhakar, Saxena, Jain, Gulati, Srimal, Dhawan, Nityanand & Anand, 1989). This assump-

tion received validation as central-hypotensive activity was observed for 4-[3-aryl(thio/sulfonyl)propyl] piperazines/piperidines (Rao, Srimal, Audry, Carpy & Saxena, 1991). The title compound is the most promising one of the series. Its molecular structure is comparable with that of 1-(3-methylphenyl)-4-(2- β -quinolylethyl)piperazine (centhaquin) (Carpy & Saxena, 1991).

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Structure and Absolute Configuration of (3*S*)-[(1*S*,2*R*,4*S*)-2-Acetoxy-4-methyl-1-cyclohexyl]-2,2-dichloro-3-methylcyclobutanone

BY J. ZUKERMAN-SCHPECTOR AND E. E. CASTELLANO

Instituto de Física Química de São Carlos, Universidade de São Paulo, Caixa Postal 369, 13560 São Carlos – SP, Brazil

AND TIMOTHY J. BROCKSOM AND LUCIMAR A. MOREIRA

Departamento de Química, Universidade Federal de São Carlos, Caixa Postal 676, 13560 São Carlos – SP, Brazil

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Abstract. C₁₄H₂₀Cl₂O₃, $M_r = 307.22$, orthorhombic, $P2_12_12_1$, $a = 7.0329$ (7), $b = 9.983$ (2), $c = 22.644$ (6) Å, $V = 1589.8$ (9) Å³, $Z = 4$, $D_x = 1.284$ g cm⁻³, $\lambda(\text{Mo } K\alpha) = 0.71073$ Å, $\mu = 4.1$ cm⁻¹, $F(000) = 648$, $T = 298$ K, $R = 0.0412$ for 1533 observed reflections. The cyclobutanone ring is puckered with a dihedral angle between C(1)—C(2)—C(4) and C(2)—C(3)—C(4) of 22.0 (8)°. The carbonyl O atom is displaced from the C(1)—C(2)—C(4) plane to the *endo* side by 0.109 (5) Å. The absolute configuration of the molecule was ascertained both by chemical means and by a comparison of the R_g values for the determined structure and its inverse.

Experimental. Crystals of the title compound were obtained from ethyl acetate at 277 K. The data collection and refinement parameters are summarized in Table 1.

The structure was solved using standard direct methods and difference Fourier techniques. In the final cycles of full-matrix least-squares refinement all non-H atoms were treated anisotropically. H atoms included, as fixed contributors, at positions found

from a difference synthesis, all with a common isotropic temperature factor that refined to $U = 0.108$ (4) Å². Data were corrected for Lp and absorption, max. and min. transmission factors 1.88, 0.76 (Walker & Stuart, 1983). Scattering factors for non-H atoms were taken from Cromer & Mann (1968) with corrections for anomalous dispersion from Cromer & Liberman (1970), for H atoms scattering factors were taken from Stewart, Davidson & Simpson (1965). Programs used: *SHELX76* (Sheldrick, 1976) and *ORTEP* (Johnson, 1965). Most of the calculations were performed on a VAX 6420 computer of the Instituto de Física e Química de São Carlos.

Atomic coordinates are listed in Table 2,* bond lengths and bond angles are listed in Table 3. Fig. 1 is a projection of the molecule showing the atom labeling.

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54419 (13 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.