Acta Cryst. (1991). C47, 458–459

Structure of a Potent Calcium Antagonist Benidipine Hydrochloride

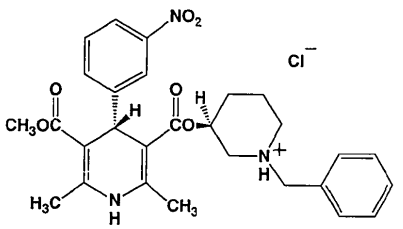
BY NORIAKI HIRAYAMA* AND ETSUYO SHIMIZU

Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd, 3-6-6 *Asahimachi, Machida, Tokyo* 194, *Japan*

(*Received* 11 *May* 1990; *accepted* 3 *July* 1990)

Abstract. 1,4-Dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic acid methyl 1-(phenylmethyl)-3-piperidinyl ester hydrochloride, $C_{28}H_{31}N_3O_7^+.Cl^-$, $M_r = 542{\cdot}03$, monoclinic, $P2_1/c$, $a = 11{\cdot}259\ (2)$, $b = 24{\cdot}764\ (1)$, $c = 10{\cdot}880\ (2)$ Å, $\beta = 111{\cdot}66\ (1)°$, $V = 2819{\cdot}3\ (9)$ Å^3, $Z = 4$, $D_x = 1{\cdot}84$ g cm^{-3}, λ(Cu $K\alpha$) = 1·54184 Å, $\mu = 16{\cdot}1$ cm^{-1}, $F(000) = 1172$, $T = 293$ K, $R = 0{\cdot}073$ for 4274 observed reflections with $I_o > 5\sigma(I_o)$. The 1,4-dihydropyridine ring takes a flat boat conformation with the C and N atoms deviating by 0·305 (3) and 0·125 (3) Å from the least-squares plane defined by the other four atoms in the ring. The dihedral angle between the plane and the least-squares plane of the nitrobenzene moiety is 89·2 (1)°. The nitro substituent points away from the 1,4-dihydropyridine ring. Both carbonyl groups are synperiplanar with respect to the ring double bond. The piperidine ring adopts a chair conformation.

Experimental. Crystal dimensions 0·4 × 0·3 × 0·2 mm. Enraf–Nonius CAD-4 diffractometer, graphite-monochromated Cu $K\alpha$ radiation. Intensities measured using $\omega/2\theta$-scan technique. Cell dimensions from setting angles of 23 independent reflections with $36 \le \theta \le 54°$. 6252 reflections surveyed in



the range $2 \le 2\theta \le 150°$; $-14 \le h \le 14$, $0 \le k \le 31$, $0 \le l \le 13$, 5285 reflections were unique ($R_{int} = 0{\cdot}026$), 4274 observed with $I_o > 5\sigma(I_o)$. Three reference reflections monitored periodically showed no significant variation in intensity. Absorption correction was not applied. Structure solved using *MULTAN*11/82 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982) and Fourier-map recycling. Refinement using *SDP-Plus* package (Frenz, 1985), full-matrix least-squares refinement on F, with non-H atoms having anisotropic temperature factors. Most of the H atoms were located from difference Fourier syntheses and the positions except those attached to methyl C atoms were refined. $w = 1/[\sigma^2(F_o) + (0{\cdot}02F_o)^2 + 1{\cdot}00]$, final $R = 0{\cdot}073$, $wR = 0{\cdot}084$, $S = 1{\cdot}474$, maximum shift/e.s.d. in the final least-squares cycle of 0·05, maximum peak in the final difference map 0·77 (8) e Å^{-3}. Secondary-extinction coefficient refined (final value of 1·80 ×

Table 1. *Positional parameters and equivalent isotropic thermal parameters with their e.s.d.'s*

$B_{eq} = (4/3)\Sigma_i\Sigma_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq} (Å^2)
Cl	0·0147 (1)	0·72597 (5)	0·4664 (1)	5·70 (3)
O(1)	1·0356 (2)	0·5156 (1)	0·7608 (3)	5·38 (7)
O(2)	0·8606 (2)	0·53606 (9)	0·8031 (2)	3·70 (5)
O(3)	0·4166 (2)	0·4017 (1)	0·4165 (2)	4·37 (6)
O(4)	0·4632 (2)	0·4483 (1)	0·6042 (2)	4·44 (6)
O(5)	0·6458 (4)	0·4476 (2)	1·1981 (3)	10·5 (1)
O(6)	0·6463 (3)	0·5179 (1)	1·0856 (3)	6·57 (8)
N(1)	0·8221 (3)	0·3829 (1)	0·5381 (3)	3·94 (7)
N(2)	0·6602 (4)	0·4697 (2)	1·1045 (3)	6·00 (9)
N(3)	0·8079 (2)	0·6538 (1)	0·7393 (3)	3·53 (6)
C(1)	0·7146 (3)	0·4525 (1)	0·6745 (3)	3·04 (7)
C(2)	0·8491 (3)	0·4593 (1)	0·6750 (3)	3·27 (7)
C(3)	0·8993 (3)	0·4232 (1)	0·6141 (4)	3·74 (8)
C(4)	0·6910 (3)	0·3831 (1)	0·4997 (3)	3·47 (7)
C(5)	0·6347 (3)	0·4180 (1)	0·5561 (3)	3·07 (7)
C(6)	0·7196 (3)	0·4279 (1)	0·8049 (3)	3·16 (7)
C(7)	0·6859 (3)	0·4585 (1)	0·8930 (3)	3·69 (8)
C(8)	0·6938 (3)	0·4361 (2)	1·0123 (4)	4·22 (8)
C(9)	0·7327 (3)	0·3834 (2)	1·0459 (4)	4·38 (9)
C(10)	0·7636 (3)	0·3530 (2)	0·9576 (4)	4·26 (8)
C(11)	0·7578 (3)	0·3746 (1)	0·8375 (3)	3·70 (8)
C(12)	1·0329 (3)	0·4215 (2)	0·6154 (5)	5·4 (1)
C(13)	0·9271 (3)	0·5049 (1)	0·7480 (3)	3·59 (7)
C(14)	0·6267 (4)	0·3422 (2)	0·3937 (4)	4·45 (9)
C(15)	0·4968 (3)	0·4212 (1)	0·5161 (3)	3·33 (7)
C(16)	0·3309 (3)	0·4506 (2)	0·5869 (4)	4·62 (9)
C(17)	0·9315 (3)	0·5800 (1)	0·8873 (4)	3·96 (8)
C(18)	0·9363 (3)	0·6277 (1)	0·8043 (4)	4·03 (8)
C(19)	0·7505 (3)	0·6686 (2)	0·8391 (4)	4·09 (8)
C(20)	0·7383 (4)	0·6190 (2)	0·9144 (4)	4·40 (9)
C(21)	0·8666 (4)	0·5921 (2)	0·9826 (4)	4·54 (9)
C(22)	0·8248 (3)	0·7019 (2)	0·6603 (4)	4·55 (9)
C(23)	0·7006 (3)	0·7289 (2)	0·5819 (4)	4·29 (8)
C(24)	0·6609 (4)	0·7736 (2)	0·6299 (4)	5·4 (1)
C(25)	0·5446 (5)	0·7980 (2)	0·5590 (5)	6·5 (1)
C(26)	0·4697 (4)	0·7768 (2)	0·4376 (5)	6·4 (1)
C(27)	0·5082 (4)	0·7340 (2)	0·3870 (4)	6·1 (1)
C(28)	0·6258 (4)	0·7093 (2)	0·4576 (4)	5·2 (1)
O(*w*)	0·1660 (4)	0·7403 (2)	0·7748 (4)	10·0 (1)

* To whom correspondence should be addressed.

0108-2701/91/020458-02$03.00

Table 2. *Selected bond lengths* (Å) *and angles* (°)

O(1)—C(13)	1·207 (4)	N(3)—C(22)	1·521 (5)
O(2)—C(13)	1·359 (5)	C(1)—C(2)	1·522 (5)
O(2)—C(17)	1·457 (4)	C(1)—C(5)	1·531 (5)
O(5)—N(2)	1·218 (6)	C(2)—C(3)	1·354 (5)
O(6)—N(2)	1·212 (5)	C(2)—C(13)	1·470 (4)
N(1)—C(3)	1·379 (4)	C(4)—C(5)	1·346 (5)
N(1)—C(4)	1·378 (8)	C(17)—C(18)	1·500 (5)
N(2)—C(8)	1·455 (6)	C(17)—C(21)	1·503 (7)
N(3)—C(18)	1·500 (4)	C(19)—C(20)	1·510 (6)
N(3)—C(19)	1·500 (6)	C(20)—C(21)	1·514 (5)

C(13)—O(2)—C(17)	116·1 (3)	N(1)—C(4)—C(5)	119·7 (3)
C(3)—N(1)—C(4)	123·2 (3)	C(1)—C(5)—C(4)	120·9 (3)
O(5)—N(2)—O(6)	122·4 (4)	O(1)—C(13)—O(2)	121·6 (4)
O(5)—N(2)—C(8)	117·9 (4)	O(1)—C(13)—C(2)	127·6 (4)
O(6)—N(2)—C(8)	119·7 (4)	O(2)—C(13)—C(2)	111·0 (3)
C(18)—N(3)—C(.9)	111·2 (3)	O(2)—C(17)—C(18)	110·1 (3)
C(18)—N(3)—C(22)	107·6 (3)	O(2)—C(17)—C(21)	106·8 (3)
C(19)—N(3)—C(22)	113·2 (3)	C(18)—C(17)—C(21)	113·2 (3)
C(2)—C(1)—C(5)	109·8 (3)	N(3)—C(18)—C(17)	112·4 (4)
C(1)—C(2)—C(3)	121·4 (3)	N(3)—C(19)—C(20)	110·1 (3)
C(1)—C(2)—C(13)	118·8 (4)	C(19)—C(20)—C(21)	111·2 (3)
C(3)—C(2)—C(13)	119·9 (4)	C(17)—C(21)—C)(20)	111·6 (3)
N(1)—C(3)—C(2)	119·1 (3)		

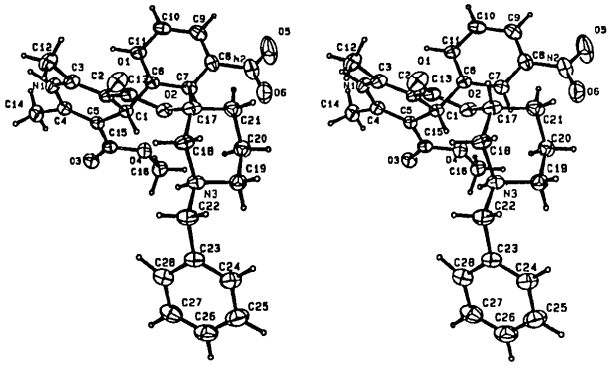


Fig. 1. An *ORTEP*II drawing (Johnson, 1976) of the molecule with the numbering system. The thermal ellipsoids are depicted at the 30% level.

10^{-6}). Scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV). Final fractional coordinates and equivalent B values are listed in Table 1. Bond distances and angles are listed in Table 2.* Fig. 1 shows a stereoview of the molecule with the atomic numbering.

Related literature. The title compound is a newly developed dihydropyridine-type calcium antagonist and shows potent and long lasting antihypertensive, as well as anti-anginal, effects. The synthesis, pharmacological activities and pharmacokinetic studies are discussed in detail in a special issue of *Arzneimittel Forschung/Drug Research* (1988) on benidipine hydrochloride.

* 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 53396 (17 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Arzneimittel Forschung/Drug Research (1988). Vol. 38, pp. 1662–1763. (Special issue on a new calcium antagonist, benidipine hydrochloride.)

FRENZ, B. A. (1985). *Enraf–Nonius SDP-Plus Structure Determination Package*. Version 3.0. Enraf–Nonius, Delft, The Netherlands.

JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1982). *MULTAN*11/82. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

Acta Cryst. (1991). C**47**, 459–461

Structure of the Flavone Hymenoxin

BY WILLIAM H. WATSON* AND RAM P. KASHYAP

Department of Chemistry, Texas Christian University, Fort Worth, Texas 76129, *USA*

FENG GAO† AND TOM J. MABRY

Department of Botany, The University of Texas, Austin, Texas 78713, *USA*

(*Received* 8 *May* 1990; *accepted* 2 *July* 1990)

Abstract. 2-(3,4-Dimethoxyphenyl)-5,7-dihydroxy-6,8-dimethoxy-4*H*-chromen-4-one, $C_{19}H_{18}O_8$, M_r = 374·38, monoclinic, $P2_1/n$, a = 9·026 (4), b = 15·054 (6), c = 12·829 (6) Å, β = 100·98 (4)°, V = 1711 (1) Å^3, Z = 4, D_x = 1·450 g cm^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, μ = 1·07 cm^{-1}, F(000) = 784, T = 295 K, R = 0·0778 for 2280 independent reflections. The nearly planar AB ring system (0·04 Å r.m.s.d.), O(1)

* Author to whom correspondence should be addressed.

† Currently: Department of Chemistry and Cancer Research Institute, Arizona State University, Tempe, Arizona, USA.

0108-2701/91/020459-03$03.00