of the solvent, the crude oil was dissolved in ethanol. The major and the minor products were separated by thin-layer chromatography on silica gel (R_F major 0.76, R_F minor 0.62). Crystals of the minor product suitable for X-ray analysis were grown from ethanol.

Crystal data

$C_{28}H_{25}NO_2$
$M_r = 407.49$
Monoclinic
$P2_1/n$
$a = 12.7246\,(15)$ Å
$b = 9.5273\,(17)$ Å
$c = 18.451\,(2)$ Å
$\beta = 93.098\,(12)°$
$V = 2233.5\,(6)$ Å^3
$Z = 4$
$D_x = 1.212$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 25 reflections
$\theta = 9.06$–$18.03°$
$\mu = 0.076$ mm^{-1}
$T = 296\,(1)$ K
Irregular
$0.30 \times 0.25 \times 0.25$ mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
ω scans
Absorption correction: none
3563 measured reflections
3409 independent reflections
1620 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.024$
$\theta_{\rm max} = 24.63°$
$h = -14 \rightarrow 0$
$k = -11 \rightarrow 0$
$l = -21 \rightarrow 21$
3 standard reflections
frequency: 120 min
intensity decay: 2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.050$
$wR(F^2) = 0.156$
$S = 0.995$
3409 reflections
280 parameters
H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0727P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max} = 0.196$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.162$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

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

O1—N	1.438 (3)	C2—C6	1.524 (4)
O1—C3	1.468 (3)	C3—C4	1.491 (4)
N—C23	1.430 (4)	C4—C5	1.326 (4)
N—C1	1.470 (4)	C5—C6	1.443 (4)
C1—C2	1.520 (4)	C6—C7	1.331 (4)
C2—C3	1.522 (4)	C7—C8	1.468 (4)
N—O1—C3	107.2 (2)	O1—C3—C4	114.0 (3)
C23—N—O1	111.8 (2)	O1—C3—C2	106.2 (2)
C23—N—C1	120.4 (2)	C4—C3—C2	104.5 (2)
O1—N—C1	102.4 (2)	C5—C4—C3	111.5 (3)
N—C1—C2	104.8 (2)	C4—C5—C6	112.3 (3)
N—C1—C15	106.8 (2)	C7—C6—C5	131.2 (3)
C2—C1—C15	112.9 (3)	C7—C6—C2	122.8 (3)
C1—C2—C3	102.5 (2)	C5—C6—C2	106.0 (3)
C1—C2—C6	115.0 (3)	C6—C7—C8	130.8 (3)
C3—C2—C6	105.2 (3)		

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1992). Cell refinement: *CAD*-4 *EXPRESS*. Data reduction: *PROCESS* in *MolEN* (Fair, 1990). Program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997*a*). Program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997*b*). Molecular graphics: *ORTEP*3 (Farrugia, 1997). Software used to prepare material for publication: *SHELXL*97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GS1028). Services for accessing these data are described at the back of the journal.

References

Enraf–Nonius (1992). *CAD*-4 *EXPRESS*. Version 5.1. Enraf–Nonius, Delft, The Netherlands.

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

Farrugia, L. J. (1997). *ORTEP*3. Version 1.02. University of Glasgow, Scotland.

Kubicki, M. M., Blacque, O., Djapa, F., Ciamala, K. & Vebrel, J. (1998). *Acta Cryst.* C**54**, 1027–1028.

Sheldrick, G. M. (1997*a*). *SHELXS*97. *Program for the Solution of Crystal Structures*. University of Göttingen, Germany.

Sheldrick, G. M. (1997*b*). *SHELXL*97. *Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.

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A flavone 1,4-dihydropyridine calcium antagonist

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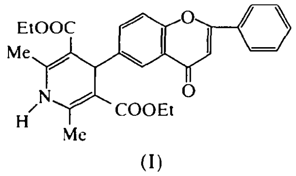
Abstract

In the title compound, diethyl 2,6-dimethyl-4-(2-phenyl-4-oxo-4*H*-1-benzopyran-6-yl)-1,4-dihydropyridine-3,5-dicarboxylate, $C_{28}H_{27}NO_6$, the 1,4-dihydropyridine ring exhibits a boat conformation. The benzopyran moiety of the flavone is nearly planar, and is approximately perpendicular to the 1,4-dihydropyridine ring [dihedral angle 87.1 (1)°]. The phenyl ring is twisted 10.7 (1)° from the plane of the benzopyran ring system.

Comment

The 1,4-dihydropyridine-type (1,4-DHP) calcium antagonists (CAs), such as nifedipine and structurally related drugs, are known as a subset of a wider class of CAs, which are among the most commonly used drugs for patients with cardiovascular diseases (Hirakawa *et al.*, 1972; Nayler, 1988). In the search for new and better nifedipine analogues, the replacement of the 4-substituent with thioxanthen, benzophenone and fluorenone ring systems has been examined (Rampa *et al.*, 1991, 1992).

The aim of the present study was to establish the structural features of the title compound, (I), containing a 2-phenyl-4*H*-benzopyran-4-one moiety (flavone) that is already known to have a coronary dilatory effect (Itz & Pötzsch, 1963) and capillary resistance activity (Gabor, 1981), instead of the aryl substituent of nifedipine and related compounds. Studies involving this substituent have been reported previously (Kendi *et al.*, 1994; Kılcıgil *et al.*, 1998).



(I)

As in other dihydropyridine (DHP) structures, in (I), the DHP ring exhibits a boat conformation. The N1 and C4 atoms lie 0.116 (2) and 0.307 (2) Å, respectively, from the least-squares plane defined by the remaining four atoms of the DHP ring. The corresponding values in ethyl allyl 1,4-dihydro-2,6-dimethyl-4-[4-(4*H*-4-oxo-1-benzopyran-2-yl)phenyl]-3,5-pyridinedicarboxylate (Kendi *et al.*, 1994) are 0.130 and 0.276 Å, respectively, and in diallyl 1,4-dihydro-2,6-dimethyl-4-(2-phenyl-4*H*-1-benzopyran-4-oxo-6-yl)-3,5-pyridinedicarboxylate (Kılcıgil *et al.*, 1998), are 0.118 and 0.274 Å respectively. The puckering of the 1,4-DHP ring at N1 and C4, which is important for the biological activity of this class of compounds, is reflected in the torsion angles about the ring bonds to these atoms. For C6—C5—C4—C3 and C5—C4—C3—C2, the torsion angles in (I) are 23.8 (3) and −25.0 (3)°, respectively, compared with 17.9 and −22.0°, respectively, in nifedipine, and −21.8 and 22.5°, respectively, in diallyl–DHP. The torsion angles about the bonds to N1 in compound (I) are −12.5 (4) (C2—N1—C6—C5) and 11.3 (4)° (C6—N1—C2—C3); the corresponding angles are −11.3 and 7.4°, respectively, in nifedipine, and 12.4 and −11.9°, respectively, in diallyl–DHP. The torsion angles about the C4 ring bonds are greater than those for the N1 bonds, indicating that the puckering is greater at C4.

Structural studies on the nifedipine and nisoldipine series (Fossheim *et al.*, 1982, 1988) have shown that the most active compounds possess the smallest deviation from planarity in the DHP ring. The calcium antagonistic activity of (I) was also examined, using nifedipine as the reference compound, and preliminary biological findings have shown that this compound has comparable activity to that of nifedipine (Kılcıgil *et al.*, 1998).

The flavone molecule bound to C4 in (I) slightly deviates from planarity; the dihedral angle between the best planes of the benzopyran and phenyl rings, which are both planar as expected, is 10.7 (1)°. The benzopyran moiety is almost perpendicular to the DHP ring [dihedral angle 87.1 (1)°]. This is also shown by the torsion angles C3—C4—C6′—C5′ [−58.8 (2)°] and C5—C4—C6′—C5′ [65.0 (2)°], which should both be close to 60° if the aromatic ring bisects the 1,4-DHP

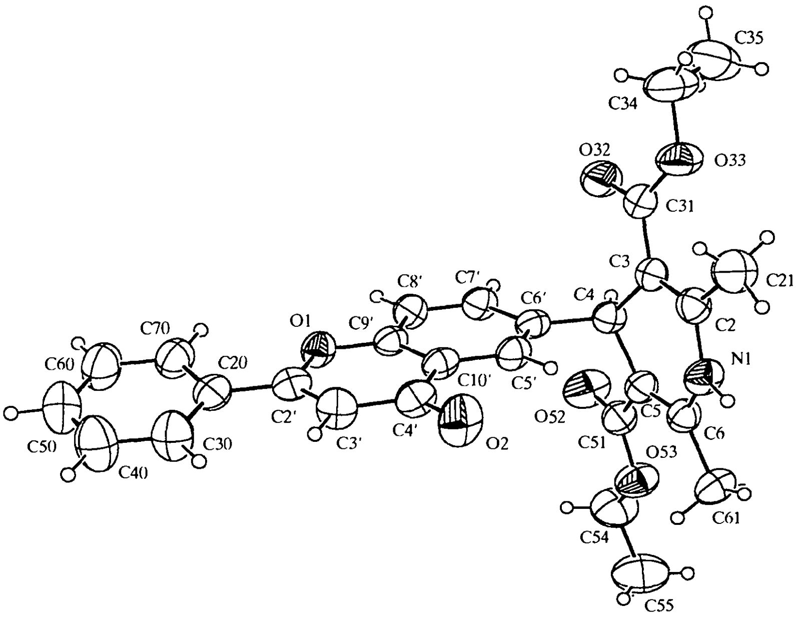


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of the title compound, showing the atom-numbering scheme. The displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small circles of arbitrary radii.

ring. These angles are 67.9 and −55.5°, respectively, for the diallyl derivative. The bond lengths and angles for the flavone moiety of the title compound are in good agreement, within experimental errors, with those observed in other flavone derivatives (Kendi *et al.*, 1994; Özbey *et al.*, 1997; Kılcıgil *et al.*, 1998).

In compound (I), the ester groups are twisted in the same direction, both being synperiplanar (*sp*,*sp*) to the ring double bonds. One ester is planar with the 1,4-DHP, with a C4—C3—C31—O32 torsion angle of −0.1 (4)°, while the second is slightly oriented out of the plane, with a C4—C5—C51—O52 torsion angle of 8.9 (4)°. Fossheim previously commented that the ester conformation observed in the crystal structure was probably a result of intermolecular hydrogen bonding and crystal-packing interactions (Fossheim, 1986). In the case of (I), the structure is also stabilized by inter- and intramolecular hydrogen bonds. Details of the hydrogen bonds are given in Table 2.

Experimental

The title compound was synthesized using the Hantzsch reaction (Hantzsch, 1882); details of the synthesis will be published elsewhere (Kılcıgil *et al.*, 1998).

Crystal data

$C_{28}H_{27}NO_6$
$M_r = 473.52$
Triclinic
$P\bar{1}$
$a = 9.9152\,(6)$ Å
$b = 11.0521\,(7)$ Å
$c = 13.7630\,(10)$ Å
$\alpha = 69.600\,(5)°$
$\beta = 73.969\,(6)°$
$\gamma = 65.035\,(5)°$
$V = 1266.7\,(2)$ Å^3
$Z = 2$
$D_x = 1.242$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71069$ Å
Cell parameters from 21 reflections
$\theta = 10.01–18.17°$
$\mu = 0.087$ mm^{-1}
$T = 295$ K
Prismatic
0.62 × 0.60 × 0.15 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical *via* ψ scans (*MolEN*; Fair, 1990)
$T_{\min} = 0.947$, $T_{\max} = 0.999$
5347 measured reflections
5125 independent reflections
3219 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.011$
$\theta_{\max} = 26.3°$
$h = 0 \rightarrow 12$
$k = -11 \rightarrow 13$
$l = -16 \rightarrow 17$
3 standard reflections
frequency: 120 min
intensity decay: 1.7%

Refinement

Refinement on F
$R = 0.047$
$wR = 0.054$
$S = 1.05$
3219 reflections
316 parameters
H atoms: see below
Weight: $w = 0$ if $F^2 < 2\sigma F^2$, otherwise, $w = 1/[\sigma F^2 + (0.02F)^2 + 0.5]$

$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.20$ e Å^{-3}
$\Delta\rho_{\min} = -0.07$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

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

O1—C2′	1.360 (3)	C2—C3	1.358 (3)
O1—C9′	1.375 (3)	C2—C21	1.501 (3)
O2—C4′	1.240 (3)	C3—C4	1.519 (3)
O32—C31	1.207 (3)	C3—C31	1.465 (3)
O33—C31	1.346 (3)	C3′—C4′	1.438 (4)
O33—C34	1.443 (3)	C4′—C10′	1.457 (3)
O52—C51	1.210 (3)	C4—C5	1.523 (2)
O53—C51	1.341 (2)	C54—C55	1.486 (4)
O53—C54	1.447 (3)	C4—C6′	1.521 (4)
N1—C2	1.375 (2)	C5—C6	1.352 (3)
N1—C6	1.378 (2)	C5—C51	1.467 (3)
C2′—C3′	1.346 (3)	C6—C61	1.502 (3)
C2′—C20	1.471 (4)	C34—C35	1.468 (6)
C2′—O1—C9′	119.5 (2)	C2′—C20—C30	120.4 (2)
C31—O33—C34	116.9 (2)	O32—C31—C3	123.0 (2)
C51—O53—C54	115.8 (2)	C3—C4—C6′	111.5 (2)
C2—N1—C6	124.3 (2)	C5—C4—C6′	109.7 (2)
N1—C2—C3	118.9 (2)	C4—C5—C6	120.3 (2)
C3—C2—C21	128.0 (2)	C6—C5—C51	126.5 (2)
C2—C3—C4	120.1 (2)	N1—C6—C5	119.0 (2)
C2—C3—C31	125.9 (2)	C5—C6—C61	128.5 (2)
O2—C4′—C3′	122.8 (2)	C4—C6′—C5′	120.9 (2)
C3′—C4′—C10′	114.9 (2)	C5′—C6′—C7′	118.1 (2)
C3—C4—C5	111.3 (2)	O33—C34—C35	112.6 (2)
C8′—C9′—C10′	122.1 (3)	O52—C51—C5	123.1 (2)
C5′—C10′—C9′	117.9 (2)	O53—C54—C55	107.5 (2)
C6—N1—C2—C3	11.3 (4)	C2—C3—C4—C5	−25.0 (3)
C2—N1—C6—C5	−12.5 (4)	C3—C4—C5—C6	23.8 (3)
N1—C2—C3—C4	9.2 (4)	C4—C5—C6—N1	−6.7 (3)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C4—H4···O32	0.96	2.490	2.765 (3)	96.2
C4—H4···O52	0.96	2.437	2.757 (2)	99.0
C5′—H5′···O2	0.95	2.613	2.872 (3)	95.9
C70—H70···O1	0.95	2.334	2.685 (4)	101.2
C3′—H3′···O52$^{\rm i}$	0.95	2.542	3.420 (4)	153.4
C8′—H8′···O32$^{\rm ii}$	0.95	2.439	3.366 (3)	165.6
C34—H341···O1$^{\rm iii}$	0.95	2.782	3.509 (3)	133.9

Symmetry codes: (i) $x-1, y, z$; (ii) $1-x, 1-y, 1-z$; (iii) $x, 1+y, z$.

All non-H atoms were refined with anisotropic displacement parameters. H atoms were placed geometrically 0.95 Å from their parent atoms. For all H atoms, a riding model was used with $U_{\rm eq}({\rm H}) = 1.3U_{\rm eq}({\rm C})$.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1993). Data reduction: *MolEN* (Fair, 1990). Program(s) used to solve structure: *SIR* in *MolEN*. Program(s) used to refine structure: *LSFM* in *MolEN*. Molecular graphics: *MolEN* version of *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *MolEN* and *PARST* (Nardelli, 1995).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1166). Services for accessing these data are described at the back of the journal.