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{2-[(1,5-Dimethyl-2-phenyl-3-oxo-2,3-dihydro-1*H*-pyrazol-4-ylimino)methyl]-phenoxy}acetic acid methanol hemisolvate

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.007 Å
R factor = 0.068
wR factor = 0.123
Data-to-parameter ratio = 14.8

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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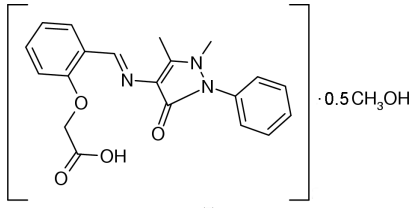
The title compound, $C_{20}H_{19}N_3O_4\cdot0.5CH_3OH$, has been synthesized and characterized by elemental analysis and single-crystal X-ray diffraction. The dihedral angles between the pyrazoline ring and the unsubstituted phenyl ring are different [80.9 (2) and 55.7 (2)°, respectively] in the two crystallographically independent molecules.

Comment

Antipyrine (2,3-dimethyl-1-phenyl-5-pyrazolone) and its derivatives exhibit a wide range of biological activities and applications (Ismail, 2000; Abd El Rehim *et al.*, 2001; Yadav *et al.*, 2003). Antipyrine shows minimal protein binding and is rapidly and completely absorbed from the gastrointestinal tract and extensively metabolized by the cytochrome P450 liver enzymes (Poulsen & Loft, 1988). Estimates of half-life and systemic clearance of antipyrine have been used for the *in vivo* assessment of hepatic drug oxidation in different species (Koning & Cantilena, 1994). Owing to its low pK_a value and its small degree of plasma protein binding, antipyrine is distributed in total body water. Schiff bases of salicyladehyde have demonstrated significant biological activity and new examples are being tested for their antitumor, antimicrobial, and antiviral activity (Tarafder *et al.*, 2002; Cukurovali *et al.*, 2002; Ali *et al.*, 2002). Recently, we have reported an antipyrine derivative (You *et al.*, 2003). As an extension of our work, a new antipyrine derivative, (I), is reported here.



(I)

The asymmetric unit of (I) consists of two independent molecules of the antipyrine derivative and one methanol molecule (Fig. 1). In both the independent molecules, the bond lengths and angles of the antipyrine moiety are in normal ranges, close to those observed in similar antipyrine Schiff bases (You *et al.*, 2003; Liang *et al.*, 2002). The dihedral angle between the N2/N3/C12/C10/C11 pyrazoline ring and the C15–C20 phenyl ring is 80.9 (2)° and that between the N5/N6/C31/C30/C32 pyrazoline ring and the C35–C40 phenyl ring is 55.7 (2)°. The torsion angles N3—N2—C15—C16, C11—N2—C15—C20, N6—N5—C35—C36 and C32—N5—C35—C40 are 76.6 (4), 85.1 (4), 135.7 (4) and 113.3 (4)°, respectively. Atom O4 deviates from the pyrazoline mean plane by

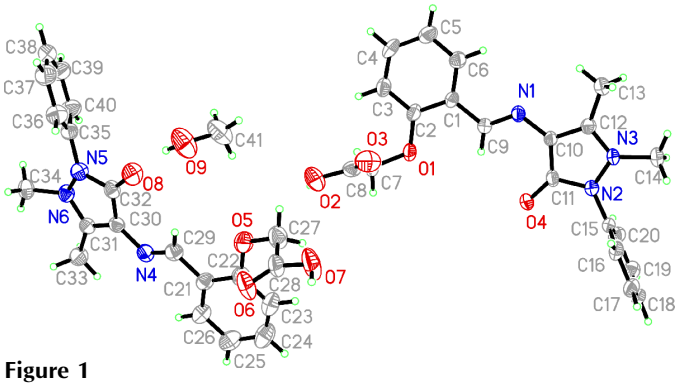


Figure 1
The asymmetric unit of the title compound, showing 30% probability displacement ellipsoids and the atom-numbering scheme.

0.075 (2) Å, whereas C13 and C14 deviate from it, on the other side, by 0.020 (3) and 0.144 (3) Å, respectively. Atom O8 deviates from the other pyrazoline mean plane by 0.062 (3) Å, whereas C33 and C34 deviate from it, on the opposite side, by 0.133 (3) and 0.492 (3) Å, respectively. Because of conjugation through the imino double bond, the pyrazoline and substituted phenyl ring in both molecules are nearly coplanar; the dihedral angle between the N2/N3/C12/C10/C11 pyrazoline ring and the C1–C6 phenyl ring is 19.2 (2)° (mean deviation from the combined mean plane is 0.152 Å) and that between N5/N6/C31/C30/C32 pyrazoline and the C21–C26 phenyl ring is 12.5 (2)° (mean deviation from the combined mean plane is 0.099 Å). This conformation is also facilitated by C9—H9*A*···O4 and C29—H29*A*···O8 intramolecular hydrogen bonds. As expected, both the molecules adopt *trans* configurations about the C29═N4 bond and C9═N1 bond.

The methanol molecule is linked to one of the independent molecule through an O—H···O hydrogen bond. The crystal structure is stabilized by O—H···O and C—H···O intermolecular hydrogen bonds (Table 1 and Fig. 2).

Experimental

Salicylaldehyde, chloroacetic acid and 4-aminoantipyrine were available commercially and were used without further purification. A mixture of salicylaldehyde (0.10 mol, 12.2 g), chloroacetic acid (0.10 mol, 9.4 g) and sodium hydroxide (0.21 mol, 8.4 g) in distilled water (50 ml) was heated at 353 K for 1 h, with stirring. The mixture was steam-distilled to remove the excess salicylaldehyde. An appropriate amount (0.11 mol, 9.9 ml) of concentrated hydrochloric acid (37%) was added to the stirred solution. The resulting yellow solid, (2-formylphenoxy)acetic acid, was filtered off and washed three times with EtOH–H_2O (1:1 *v*/*v*), and dried in a vacuum desiccator using P_4O_{10} (yield 82.7%). Analysis found: C 59.98, H 4.49, N 35.54%; calculated for $C_9H_8O_4$: C 60.00, H 4.48, N 35.52%. This intermediate (1.0 mmol, 180.2 mg) and 4-aminoantipyrine (1.0 mmol, 203.4 mg) were dissolved in methanol (20 ml). The mixture was stirred for 30 min at room temperature to give copious amounts of a brown solid. This was isolated, washed three times with methanol and then dissolved in methanol (70 ml). After keeping the resulting solution in air for 5 d, yellow block-shaped crystals of (I) were formed at the bottom of the vessel by slow evaporation of the solvent (yield 69.3%). Analysis found: C 64.38, H 5.60, N 11.11%; calculated for $C_{41}H_{42}N_6O_9$: C 64.56, H 5.55, N 11.02%.

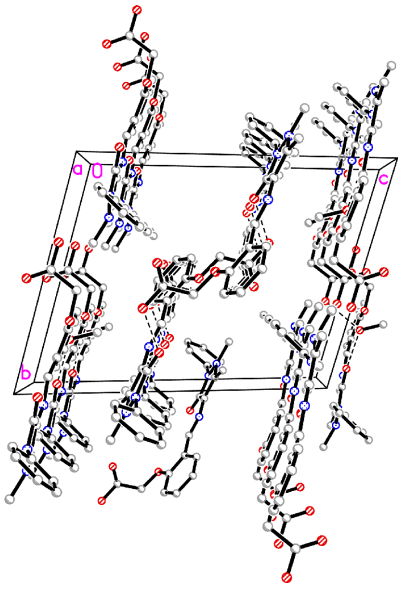


Figure 2
The packing of the title compound, viewed along the *a* axis.

Crystal data

$C_{20}H_{19}N_3O_4·0.5CH_4O$
M_r = 381.41
Triclinic, $P\overline{1}$
a = 11.264 (2) Å
b = 12.324 (3) Å
c = 16.137 (3) Å
α = 98.05 (3)°
β = 110.25 (3)°
γ = 107.55 (3)°
V = 1927.6 (7) Å^3
Z = 4
D_x = 1.314 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3180 reflections
θ = 2.8–23.1°
μ = 0.09 mm^{-1}
T = 293 (2) K
Block, yellow
0.31 × 0.22 × 0.13 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.971, T_{max} = 0.988
8968 measured reflections
7577 independent reflections
2902 reflections with $I > 2\sigma(I)$
R_{int} = 0.035
θ_{max} = 26.5°
h = −12 → 13
k = −15 → 15
l = −20 → 14

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.068
$wR(F^2)$ = 0.123
S = 0.89
7577 reflections
513 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0273P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.18 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O9—H9*B*···O8	0.90 (3)	1.69 (4)	2.567 (5)	165 (4)
O7—H7*C*···O9^{i}	0.82	1.76	2.574 (5)	176
O2—H2*A*···O4^{ii}	0.82	1.75	2.564 (4)	171
C7—H7*A*···O1^{ii}	0.97	2.43	3.314 (6)	151
C9—H9*A*···O4	0.93	2.37	3.051 (5)	130
C29—H29*A*···O8	0.93	2.42	3.077 (6)	128
C33—H33*B*···O6^{iii}	0.96	2.51	3.340 (4)	145
C34—H34*A*···O6^{iii}	0.96	2.36	3.189 (5)	144

Symmetry codes: (i) 1 − *x*, 1 − *y*, 2 − *z*; (ii) 1 − *x*, 1 − *y*, 1 − *z*; (iii) 1 − *x*, −*y*, 2 − *z*.

All H atoms, except H9*B*, were placed in geometrically idealized positions and constrained to ride on their parent atoms, with C—H and O—H distances of 0.93–0.97 and 0.82 Å, respectively, and with U_{iso}(H) = 1.2 or 1.5U_{eq}(C) and 1.5U_{eq}(O). Atom H9*B* was refined isotropically, giving an O—H distance of 0.90 (3) Å. The ratio of observed to unique reflections is low (38%), probably due to the poor diffraction quality of the crystal.

Data collection: *SMART* (Siemens, 1996); cell refinement: *SMART*; data reduction: *SAINT* (Siemens, 1996); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997*a*); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997*a*); molecular graphics: *SHELXTL* (Sheldrick, 1997*b*); software used to prepare material for publication: *SHELXTL*.

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