organic compounds

N-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2-hydroxy-benzamide

Qing-Hua Wang,[a]* **Guo-Cong Guo,**[b] **Li-Zhen Cai,**[b] **Hong-Xu Guo,**[a] **Ming-Li Chen**[a] **and Wen Weng**[a]

[a]Department of Chemistry and Environmental Science, Zhangzhou Normal University, Zhangzhou 363000, People's Republic of China, and [b]State Key Laboratory of Structural Chemistry, Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences, Fuzhou 350002, People's Republic of China
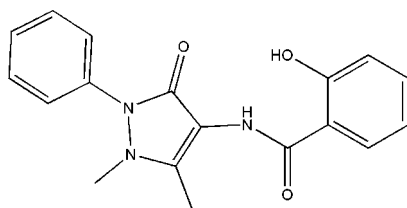Correspondence e-mail: wqh_1974@yahoo.com.cn

The title compound, $C_{18}H_{17}N_3O_3$, is a derivative of salicylic acid and is linked into dimers by intermolecular O—H···O hydrogen bonds. The amide unit [–CO–NH–] is not involved in any intermolecular hydrogen bonds. The salicylic phenyl ring forms a dihedral angle of 60.5 (9)° relate to the pyrazoline ring, while the diheral angle between the pyrazoline ring and the phenyl ring directly attached to it is 53.2 (6)°.

Related literature

For related literature, see: Bhatt & Topol (2003); Eikelboom *et al.* (2005); Hankey & Eikelboom (2004); Jain *et al.* (1999); Matsumoto *et al.* (1997); Mu *et al.* (2003); Tanaka *et al.* (2004); Urpí *et al.* (2003); Wen *et al.* (2006).

Experimental

Crystal data

$C_{18}H_{17}N_3O_3$	γ = 77.41 (3)°
M_r = 323.35	V = 815.8 (5) Å³
Triclinic, $P\bar{1}$	Z = 2
a = 8.081 (3) Å	Mo $K\alpha$ radiation
b = 8.833 (3) Å	μ = 0.09 mm⁻¹
c = 12.279 (4) Å	T = 292 (2) K
α = 80.37 (3)°	0.40 × 0.20 × 0.05 mm
β = 73.68 (2)°	

Data collection

RIGAKU AFC7 diffractometer	1652 reflections with $I > 2\sigma(I)$
Absorption correction: ψ scan (North *et al.*, 1968)	R_{int} = 0.046
T_{min} = 0.974, T_{max} = 0.999	3035 standard reflections every 6315 reflections intensity decay: 0.5%
3314 measured reflections	
3035 independent reflections	

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.059	222 parameters
$wR(F^2)$ = 0.172	H-atom parameters constrained
S = 1.04	$\Delta\rho_{max}$ = 0.25 e Å⁻³
3035 reflections	$\Delta\rho_{min}$ = −0.30 e Å⁻³

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

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1A···O3[i]	0.98	1.62	2.592 (4)	177
N1—H1B···O1	0.80	2.01	2.665 (4)	139
C3—H3A···O3[i]	0.93	2.56	3.230 (5)	130
C6—H6A···O2	0.93	2.43	2.764 (5)	101

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

Data collection: *WinAFC* (Rigaku, 2002); cell refinement: *WinAFC*; data reduction: *CrystalStructure* (Rigaku, 2002); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXL97*; software used to prepare material for publication: *SHELXL97*.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: RN2030).

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supplementary materials

N-(1,5-Dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)-2-hydroxybenzamide

Q.-H. Wang, G.-C. Guo, L.-Z. Cai, H.-X. Guo, M.-L. Chen and W. Weng

Comment

Aspirin is an important drug used to treat mild to moderate pain, and also to reduce fever or inflammation. It is sometimes used to treat or prevent heart attacks, strokes, and chest pain. Aspirin reduces the odds of serious atherothrombotic vascular events and death by about one quarter in a broad category of high risk patients. However, it still fails to prevent most serious vascular events in patients with symptomatic atherothrombosis. Recurrent vascular events in patients taking aspirin ("aspirin treatment failures") have many possible causes, and aspirin resistance has emerged as an additional contender (Bhatt & Topol, 2003; Hankey & Eikelboom, 2004; Eikelboom *et al.*, 2005). As part of our programme of synthesizing new derivatives of aspirin, the title compound, (I), was synthesized by the reaction between aspirin and 4-aminoantipyrine.

The molecular structure of (I) with the atom labelling scheme is shown in Fig. 1. A s expected, the acetyl group of 2-acetylsalicylic acid residue has been eliminated through hydrolysis. The amide unit [–CO—NH–] is essentially coplanar with the salicylic phenyl ring [dihedral angle = 5.1 (5)°], similiar to other salicylic amide compounds (Matsumoto *et al.*, 1997; Mu *et al.*, 2003; Wen *et al.*, 2006). The salicylic phenyl ring forms a dihedral angle of 60.5 (9)° with the five-membered pyrazoline ring, while the dihedral angle between the pyrazoline ring and the phenyl ring directly attached to it is 53.2 (6)°. This observation was in agreement with other amide compounds containing the pyrazoline group (Jain *et al.*, 1999; Tanaka *et al.*, 2004)

The C7═O2 bond distance [1.226 (4) Å] and C7—N1 bond distance [1.356 (4) Å] are typical. It is noteworthy that as it is surrounded by bulky groups, the amide unit [–CO—NH–] did not make any intermolecular hydrogen bonds which is uncommon among amide compounds (Urpí *et al.*, 2003). The intramolecular N1—H1B···O1 and C6—H6A···O2 hydrogen bonds stabilize the molecular conformation. The intermolecular O1—H1A···O3 hydrogen bonds link the two molecules in the unit cell into dimers [Fig. 2 and Table 2], and the dimer is further stabilized by the weak C3—H3A···O3 hydrogen bonds. No other significant intermolecular distances could be detected among the dimers.

Experimental

30 mmol of aspirin and 3 ml of thionyl chloride were added to a 50 ml flask, then 2 drops of pyridine were added, then the mixture was heated at 70 C for 70 min. The excess thionyl chloride was removed under reduced pressure and the residue was dissolved in dichloromethane. The above solution was added dropwise to a solution of 30 mmol 4-aminoantipyrine in 10 ml of dichloromethane placed in an icebath. The mixture was stirred for 1 h, then 3 ml of triethylamine was added, and the mixture was again stirred for 3 h. The dichloromethane was removed by vacuum and 10 ml propanol was added, the solution was then treated with 10 ml of 6 *M* NaOH, the organic layer was acidified slowly with 6 *M* HCl until a large amount of yellow precipitate appeared. The precipitate was collected and washed with large amount of water. Single crystals of (I) were grown by slow evaporation in air of a mixed solution of dichloromethane/ethanol.

supplementary materials

Refinement

All methyl H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms (C—H = 0.96 Å and $U_{iso}(H) = 1.5U_{eq}(C)$), each group was allowed to rotate freely about its C—C bond. The hydroxyl and amide H atoms were positioned theoretically with the O—H and N—H bond distance refined. The other hydrogen atoms were located theoretically and refined on riding mode ($U_{iso}(H) = 1.2U_{eq}(C)$).
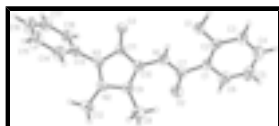
Figures

Fig. 1. View of the title compound, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of arbitrary size.
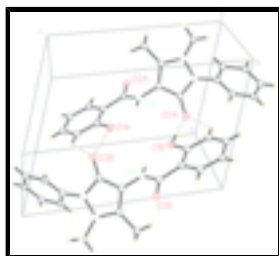
Fig. 2. A view of the hydrogen-bonded dimers in (I).

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Crystal data

$C_{18}H_{17}N_3O_3$	$Z = 2$
$M_r = 323.35$	$F_{000} = 340$
Triclinic, $P\bar{1}$	$D_x = 1.316$ Mg m^{-3}
Hall symbol: -P 1	Mo $K\alpha$ radiation $\lambda = 0.71073$ Å
$a = 8.081$ (3) Å	Cell parameters from 20 reflections
$b = 8.833$ (3) Å	$\theta = 12–30°$
$c = 12.279$ (4) Å	$\mu = 0.09$ mm^{-1}
$\alpha = 80.37$ (3)°	$T = 292$ (2) K
$\beta = 73.68$ (2)°	Plate, pale yellow
$\gamma = 77.41$ (3)°	$0.40 \times 0.20 \times 0.05$ mm
$V = 815.8$ (5) Å^3	

Data collection

RIGAKU AFC7 diffractometer	$R_{int} = 0.046$
Radiation source: fine-focus sealed tube	$\theta_{max} = 25.5°$
Monochromator: graphite	$\theta_{min} = 1.7°$
$T = 292(2)$ K	$h = -2 \rightarrow 9$

ω scans	$k = -10 \rightarrow 10$
Absorption correction: ψ scan (North *et al.*, 1968)	$l = -14 \rightarrow 14$
$T_{min} = 0.974$, $T_{max} = 0.999$	3035 standard reflections
3314 measured reflections	every 6315 reflections
3035 independent reflections	intensity decay: ?
1652 reflections with $I > 2\sigma(I)$	

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.059$	H-atom parameters constrained
$wR(F^2) = 0.172$	$w = 1/[\sigma^2(F_o^2) + (0.0763P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.04$	$(\Delta/\sigma)_{max} < 0.001$
3035 reflections	$\Delta\rho_{max} = 0.25$ e Å^{-3}
222 parameters	$\Delta\rho_{min} = -0.30$ e Å^{-3}
Primary atom site location: structure-invariant direct methods	Extinction correction: none

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit S are based on F^2, conventional *R*-factors *R* are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($Å^2$)

	x	y	z	U_{iso}*/U_{eq}
O1	0.4576 (3)	0.8879 (3)	0.6450 (2)	0.0449 (7)
H1A	0.505	0.958	0.677	0.067*
O2	0.2766 (4)	0.5236 (3)	0.5621 (2)	0.0509 (7)
O3	0.4224 (3)	0.9187 (3)	0.27299 (19)	0.0360 (6)
N1	0.3037 (4)	0.7766 (3)	0.5176 (2)	0.0364 (7)
H1B	0.3440	0.845	0.5304	0.044*
N2	−0.0060 (4)	0.8561 (3)	0.3461 (2)	0.0385 (7)
N3	0.1437 (4)	0.8972 (3)	0.2665 (2)	0.0343 (7)
C1	0.4237 (4)	0.6208 (4)	0.6708 (3)	0.0319 (8)
C2	0.4799 (4)	0.7415 (4)	0.7031 (3)	0.0335 (8)
C3	0.5601 (5)	0.7145 (4)	0.7929 (3)	0.0427 (9)

H3A	0.5964	0.7959	0.8138	0.051*
C4	0.5857 (6)	0.5671 (5)	0.8509 (3)	0.0534 (11)
H4A	0.6400	0.5491	0.9105	0.064*
C5	0.5308 (6)	0.4454 (5)	0.8207 (3)	0.0538 (11)
H5A	0.5471	0.3460	0.8601	0.065*
C6	0.4521 (5)	0.4735 (4)	0.7320 (3)	0.0451 (10)
H6A	0.4163	0.3913	0.7118	0.054*
C7	0.3312 (4)	0.6347 (4)	0.5786 (3)	0.0340 (8)
C8	−0.0865 (5)	0.7305 (5)	0.5453 (3)	0.0514 (10)
H8A	−0.0464	0.7222	0.6129	0.077*
H8B	−0.0970	0.6290	0.5328	0.077*
H8C	−0.1987	0.7983	0.5544	0.077*
C9	0.0415 (4)	0.7958 (4)	0.4454 (3)	0.0357 (8)
C10	0.2097 (4)	0.8112 (4)	0.4337 (3)	0.0330 (8)
C11	0.2777 (4)	0.8774 (4)	0.3207 (3)	0.0298 (8)
C12	−0.1205 (5)	0.7886 (5)	0.3012 (4)	0.0573 (12)
H12A	−0.2250	0.7753	0.3601	0.086*
H12B	−0.0603	0.6891	0.2765	0.086*
H12C	−0.1512	0.8573	0.2378	0.086*
C13	0.1241 (5)	1.0148 (4)	0.1731 (3)	0.0364 (9)
C14	−0.0168 (5)	1.1366 (4)	0.1865 (3)	0.0473 (10)
H14A	−0.1029	1.1401	0.2551	0.057*
C15	−0.0294 (6)	1.2534 (5)	0.0975 (4)	0.0619 (12)
H15A	−0.1244	1.3356	0.1062	0.074*
C16	0.0973 (6)	1.2488 (5)	−0.0035 (3)	0.0592 (12)
H16A	0.0889	1.3284	−0.0628	0.071*
C17	0.2373 (5)	1.1263 (5)	−0.0174 (3)	0.0533 (11)
H17A	0.3235	1.1235	−0.0860	0.064*
C18	0.2498 (5)	1.0077 (5)	0.0704 (3)	0.0448 (9)
H18A	0.3423	0.9234	0.0603	0.054*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0595 (17)	0.0373 (14)	0.0491 (15)	−0.0200 (13)	−0.0298 (13)	0.0060 (12)
O2	0.0665 (19)	0.0377 (15)	0.0614 (18)	−0.0179 (13)	−0.0309 (15)	−0.0050 (13)
O3	0.0328 (14)	0.0405 (14)	0.0377 (13)	−0.0137 (11)	−0.0085 (11)	−0.0041 (11)
N1	0.0454 (18)	0.0354 (16)	0.0347 (16)	−0.0147 (14)	−0.0166 (14)	−0.0007 (13)
N2	0.0326 (17)	0.0479 (18)	0.0386 (17)	−0.0179 (14)	−0.0097 (14)	0.0004 (14)
N3	0.0313 (16)	0.0413 (17)	0.0322 (16)	−0.0132 (14)	−0.0092 (13)	0.0015 (13)
C1	0.0309 (19)	0.0331 (19)	0.0286 (18)	−0.0025 (15)	−0.0037 (15)	−0.0057 (15)
C2	0.0325 (19)	0.0336 (19)	0.0327 (19)	−0.0090 (16)	−0.0051 (16)	−0.0004 (15)
C3	0.054 (2)	0.045 (2)	0.034 (2)	−0.0176 (19)	−0.0163 (18)	0.0001 (17)
C4	0.069 (3)	0.057 (3)	0.042 (2)	−0.014 (2)	−0.029 (2)	0.005 (2)
C5	0.080 (3)	0.037 (2)	0.043 (2)	−0.002 (2)	−0.024 (2)	0.0053 (18)
C6	0.056 (2)	0.033 (2)	0.046 (2)	−0.0074 (18)	−0.012 (2)	−0.0038 (17)
C7	0.0314 (19)	0.036 (2)	0.0354 (19)	−0.0077 (16)	−0.0079 (16)	−0.0055 (16)
C8	0.042 (2)	0.064 (3)	0.046 (2)	−0.019 (2)	−0.0070 (19)	0.004 (2)

C9	0.036 (2)	0.039 (2)	0.0319 (19)	−0.0121 (17)	−0.0067 (16)	−0.0011 (16)
C10	0.036 (2)	0.0337 (19)	0.0314 (19)	−0.0096 (16)	−0.0091 (16)	−0.0034 (15)
C11	0.035 (2)	0.0280 (18)	0.0305 (18)	−0.0092 (15)	−0.0095 (16)	−0.0064 (14)
C12	0.054 (3)	0.069 (3)	0.063 (3)	−0.030 (2)	−0.026 (2)	−0.001 (2)
C13	0.038 (2)	0.044 (2)	0.0323 (19)	−0.0102 (18)	−0.0134 (17)	−0.0049 (16)
C14	0.046 (2)	0.052 (2)	0.038 (2)	−0.005 (2)	−0.0045 (18)	−0.0041 (19)
C15	0.064 (3)	0.054 (3)	0.053 (3)	0.009 (2)	−0.013 (2)	0.004 (2)
C16	0.071 (3)	0.061 (3)	0.040 (2)	−0.009 (3)	−0.018 (2)	0.011 (2)
C17	0.053 (3)	0.069 (3)	0.034 (2)	−0.012 (2)	−0.0085 (19)	0.002 (2)
C18	0.040 (2)	0.058 (2)	0.032 (2)	−0.0015 (19)	−0.0067 (17)	−0.0056 (18)

Geometric parameters (Å, °)

O1—C2	1.369 (4)	C6—H6A	0.9300
O1—H1A	0.9823	C8—C9	1.489 (5)
O2—C7	1.226 (4)	C8—H8A	0.9600
O3—C11	1.254 (4)	C8—H8B	0.9600
N1—C7	1.356 (4)	C8—H8C	0.9600
N1—C10	1.403 (4)	C9—C10	1.360 (5)
N1—H1B	0.8034	C10—C11	1.417 (4)
N2—C9	1.370 (4)	C12—H12A	0.9600
N2—N3	1.399 (4)	C12—H12B	0.9600
N2—C12	1.467 (4)	C12—H12C	0.9600
N3—C11	1.389 (4)	C13—C14	1.379 (5)
N3—C13	1.432 (4)	C13—C18	1.381 (5)
C1—C6	1.396 (5)	C14—C15	1.382 (5)
C1—C2	1.398 (5)	C14—H14A	0.9300
C1—C7	1.499 (5)	C15—C16	1.368 (6)
C2—C3	1.392 (5)	C15—H15A	0.9300
C3—C4	1.379 (5)	C16—C17	1.378 (6)
C3—H3A	0.9300	C16—H16A	0.9300
C4—C5	1.386 (5)	C17—C18	1.381 (5)
C4—H4A	0.9300	C17—H17A	0.9300
C5—C6	1.372 (5)	C18—H18A	0.9300
C5—H5A	0.9300		
C2—O1—H1A	109.5	H8A—C8—H8C	109.5
C7—N1—C10	124.3 (3)	H8B—C8—H8C	109.5
C7—N1—H1B	117.9	C10—C9—N2	109.4 (3)
C10—N1—H1B	117.9	C10—C9—C8	130.3 (3)
C9—N2—N3	107.0 (3)	N2—C9—C8	120.3 (3)
C9—N2—C12	123.2 (3)	C9—C10—N1	127.8 (3)
N3—N2—C12	115.9 (3)	C9—C10—C11	108.7 (3)
C11—N3—N2	109.0 (2)	N1—C10—C11	123.4 (3)
C11—N3—C13	123.4 (3)	O3—C11—N3	123.1 (3)
N2—N3—C13	119.3 (3)	O3—C11—C10	131.3 (3)
C6—C1—C2	117.2 (3)	N3—C11—C10	105.5 (3)
C6—C1—C7	116.5 (3)	N2—C12—H12A	109.5
C2—C1—C7	126.3 (3)	N2—C12—H12B	109.5
O1—C2—C3	119.5 (3)	H12A—C12—H12B	109.5

O1—C2—C1	119.7 (3)	N2—C12—H12C	109.5
C3—C2—C1	120.8 (3)	H12A—C12—H12C	109.5
C4—C3—C2	120.0 (3)	H12B—C12—H12C	109.5
C4—C3—H3A	120.0	C14—C13—C18	120.1 (3)
C2—C3—H3A	120.0	C14—C13—N3	120.3 (3)
C3—C4—C5	120.3 (4)	C18—C13—N3	119.5 (3)
C3—C4—H4A	119.8	C13—C14—C15	119.7 (4)
C5—C4—H4A	119.8	C13—C14—H14A	120.2
C6—C5—C4	119.1 (4)	C15—C14—H14A	120.2
C6—C5—H5A	120.4	C16—C15—C14	120.3 (4)
C4—C5—H5A	120.4	C16—C15—H15A	119.9
C5—C6—C1	122.6 (4)	C14—C15—H15A	119.9
C5—C6—H6A	118.7	C15—C16—C17	120.1 (4)
C1—C6—H6A	118.7	C15—C16—H16A	120.0
O2—C7—N1	121.4 (3)	C17—C16—H16A	120.0
O2—C7—C1	121.2 (3)	C16—C17—C18	120.1 (4)
N1—C7—C1	117.3 (3)	C16—C17—H17A	119.9
C9—C8—H8A	109.5	C18—C17—H17A	119.9
C9—C8—H8B	109.5	C13—C18—C17	119.7 (4)
H8A—C8—H8B	109.5	C13—C18—H18A	120.2
C9—C8—H8C	109.5	C17—C18—H18A	120.2

Hydrogen-bond geometry (Å, °)

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1A···O3^{i}	0.98	1.62	2.592 (4)	177
N1—H1B···O1	0.80	2.01	2.665 (4)	139
C3—H3A···O3^{i}	0.93	2.56	3.230 (5)	130
C6—H6A···O2	0.93	2.43	2.764 (5)	101

Symmetry codes: (i) $-x+1$, $-y+2$, $-z+1$.

Fig. 1

Fig. 2