

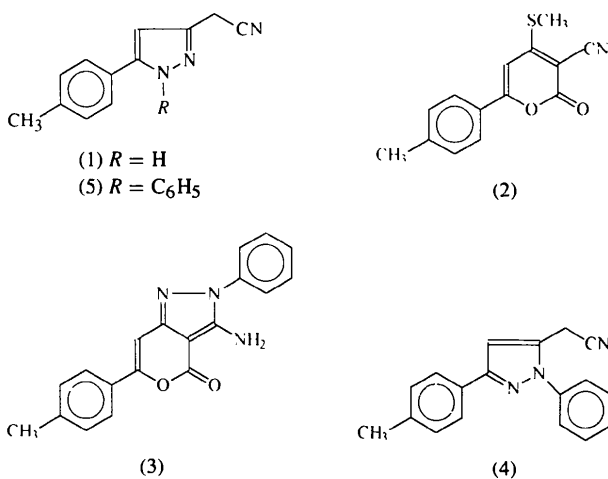
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5-Cyanomethyl-3-(4-methylphenyl)-1-phenylpyrazole

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Abstract

The title nitrile, 3-(4-methylphenyl)-1-phenylpyrazole-5-acetonitrile, C₁₈H₁₅N₃, is one of the products obtained from the reaction of 3-cyano-6-(4-methylphenyl)-4-methylthio-2-oxo-2H-pyran with phenylhydrazine. The asymmetric unit contains two almost identical molecules differing only in the orientations of the phenyl and methylphenyl groups with respect to the planar pyrazole nucleus.

Comment

Owing to the widespread applications of pyrazole derivatives in medicinal, agricultural and synthetic chemistry (Kurowski, Dunky & Geddawi, 1986; Rosiere & Grossman, 1951; Seki, Watanabe & Suga, 1988; Chauhan, Singh & Chatterjee, 1993), we have synthesized a large number of novel compounds containing the pyrazole nucleus. One of our compounds, (1), showed significant anti-invasive activity against solid tumours. In order to establish the structure–activity relationship, several analogues of (1), including the title compound, (4), have been synthesized.

The reaction of 3-cyano-6-(4-methylphenyl)-4-methylthio-2-oxo-2H-pyran, (2), with phenylhydrazine produced two *N*-phenylpyrazoles. One of these was unequivocally identified as (3) from a detailed analysis of its spectral data. However, the position of the phenyl ring in the second compound remained unclear; that is, the compound was either (4) or (5). This X-ray investigation was undertaken to remove this ambiguity.

The asymmetric unit contains two molecules of (4), one of which is illustrated in Fig. 1. The corresponding bond lengths for these two molecules are the same within experimental error and in each case the pyrazole nucleus is flat. The main difference between these molecules is in the orientation of the peripheral aromatic groups relative to the plane of the pyrazole nucleus. In the first molecule the phenyl and methylphenyl groups are inclined at angles of 59.5 (1) and 15.7 (2)°, respectively, relative to the plane of the pyrazole ring; the corresponding values for the second molecule are 51.8 (1) and 17.1 (2)°. All of the bond lengths and angles are unexceptional; specifically the cyanide group is essentially linear with an average C—C—N angle of 179.3 (5)°. There are no unusual intermolecular interactions.

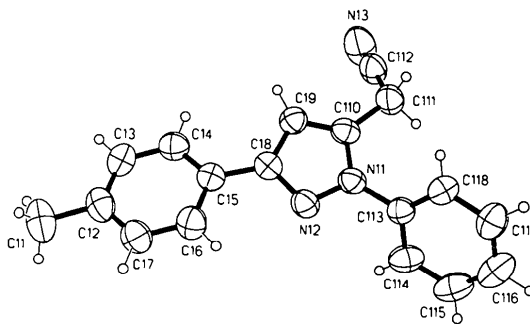


Fig. 1. View of one molecule showing the atomic numbering. Displacement ellipsoids are drawn at the 30% probability level. The second molecule has an analogous numbering scheme.

Experimental

3-Cyano-6-(4-methylphenyl)-4-methylthio-2-oxo-2*H*-pyran (2) (2.57 g, 0.01 mol) was suspended in methanol (50 ml) and phenylhydrazine (1.9 ml, 0.02 mol) was added. The reaction mixture was refluxed for 30 min, cooled and crushed ice was then added. The white solid that precipitated was purified by column chromatography on silica gel using petrol-ethyl acetate (9:1) as eluant; white crystals of (4) were obtained (1.23 g, 45%), m.p. 391 K.

Crystal data

$C_{18}H_{15}N_3$	Mo $K\alpha$ radiation
$M_r = 273.33$	$\lambda = 0.71073 \text{ \AA}$
Monoclinic	Cell parameters from 30 reflections
$P2_1/c$	$\theta = 9-10^\circ$
$a = 30.061 (14) \text{ \AA}$	$\mu = 0.073 \text{ mm}^{-1}$
$b = 7.218 (4) \text{ \AA}$	$T = 293 (2) \text{ K}$
$c = 14.283 (8) \text{ \AA}$	Block
$\beta = 103.26 (4)^\circ$	$0.49 \times 0.34 \times 0.19 \text{ mm}$
$V = 3016.5 (28) \text{ \AA}^3$	White
$Z = 8$	
$D_x = 1.204 \text{ Mg m}^{-3}$	

Data collection

Siemens <i>P3R3</i> diffractometer	$\theta_{\max} = 22.55^\circ$
$\omega-2\theta$ scans	$h = -32 \rightarrow 31$
Absorption correction:	$k = -7 \rightarrow 1$
none	$l = 0 \rightarrow 15$
4924 measured reflections	3 standard reflections
3948 independent reflections	monitored every 200 reflections
2530 observed reflections	intensity decay: none
$[I > 2\sigma(I)]$	
$R_{\text{int}} = 0.0486$	

Refinement

Refinement on F^2	$\Delta\rho_{\max} = 0.184 \text{ e \AA}^{-3}$
$R[F^2 > 2\sigma(F^2)] = 0.0614$	$\Delta\rho_{\min} = -0.171 \text{ e \AA}^{-3}$
$wR(F^2) = 0.1940$	Extinction correction:
$S = 1.035$	<i>SHELXL93</i> (Sheldrick, 1993)
3923 reflections	Extinction coefficient:
382 parameters	0.0057 (8)
H atoms riding	Atomic scattering factors
$w = 1/[\sigma^2(F_o^2) + (0.0682P)^2 + 1.4282P]$	from <i>International Tables for Crystallography</i> (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)
where $P = (F_o^2 + 2F_c^2)/3$	
$(\Delta/\sigma)_{\max} = -0.478$	

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (\AA^2)

$$U_{\text{eq}} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$$

	x	y	z	U_{eq}
N11	0.13424 (9)	0.3707 (4)	0.4400 (2)	0.0499 (8)
N12	0.14533 (10)	0.2307 (4)	0.5037 (2)	0.0524 (8)
N13	-0.00090 (15)	0.3809 (6)	0.2029 (3)	0.1035 (15)
N21	0.36526 (10)	0.6432 (4)	0.8125 (2)	0.0529 (8)
N22	0.35529 (10)	0.7881 (5)	0.8643 (2)	0.0581 (8)
N23	0.50153 (15)	0.6167 (6)	0.7088 (3)	0.0998 (14)
C11	0.1091 (2)	-0.5376 (6)	0.7171 (3)	0.0895 (15)

C12	0.10702 (15)	-0.3565 (6)	0.6633 (3)	0.0604 (11)
C13	0.06945 (14)	-0.3061 (6)	0.5934 (3)	0.0645 (11)
C14	0.06786 (13)	-0.1429 (5)	0.5427 (3)	0.0565 (10)
C15	0.10487 (11)	-0.0216 (5)	0.5608 (2)	0.0485 (9)
C16	0.14242 (13)	-0.0704 (5)	0.6331 (3)	0.0583 (10)
C17	0.14337 (14)	-0.2338 (6)	0.6827 (3)	0.0625 (11)
C18	0.10576 (12)	0.1434 (5)	0.5023 (2)	0.0465 (9)
C19	0.06988 (12)	0.2305 (5)	0.4368 (2)	0.0509 (9)
C110	0.08885 (12)	0.3735 (5)	0.3986 (2)	0.0506 (9)
C111	0.06871 (12)	0.5140 (5)	0.3237 (3)	0.0630 (11)
C112	0.02988 (15)	0.4401 (6)	0.2559 (3)	0.0659 (11)
C113	0.16927 (11)	0.4959 (5)	0.4269 (2)	0.0459 (9)
C114	0.20692 (13)	0.4297 (6)	0.3977 (3)	0.0654 (11)
C115	0.24080 (14)	0.5545 (8)	0.3890 (3)	0.0765 (13)
C116	0.23778 (15)	0.7370 (8)	0.4110 (3)	0.0773 (13)
C117	0.20025 (14)	0.7995 (6)	0.4391 (3)	0.0678 (12)
C118	0.16555 (12)	0.6794 (5)	0.4466 (3)	0.0560 (10)
C21	0.3959 (2)	1.5539 (7)	1.1101 (3)	0.101 (2)
C22	0.3965 (2)	1.3740 (6)	1.0580 (3)	0.0687 (12)
C23	0.36009 (15)	1.2526 (7)	1.0438 (3)	0.0718 (12)
C24	0.36057 (13)	1.0874 (6)	0.9968 (3)	0.0636 (11)
C25	0.39729 (12)	1.0374 (5)	0.9587 (2)	0.0510 (9)
C26	0.43414 (14)	1.1573 (6)	0.9740 (3)	0.0617 (11)
C27	0.43370 (15)	1.3224 (6)	1.0230 (3)	0.0692 (12)
C28	0.39579 (12)	0.8713 (5)	0.9006 (2)	0.0510 (9)
C29	0.43082 (12)	0.7777 (5)	0.8703 (2)	0.0531 (10)
C210	0.41085 (15)	0.6350 (5)	0.8151 (2)	0.0505 (9)
C211	0.43012 (12)	0.4922 (6)	0.7594 (3)	0.0635 (11)
C212	0.47009 (15)	0.5621 (6)	0.7303 (3)	0.0662 (11)
C213	0.32915 (12)	0.5263 (6)	0.7639 (2)	0.0506 (9)
C214	0.29095 (13)	0.6053 (6)	0.7057 (3)	0.0703 (12)
C215	0.25560 (15)	0.4919 (9)	0.6609 (3)	0.090 (2)
C216	0.2583 (2)	0.3064 (9)	0.6723 (4)	0.091 (2)
C217	0.2964 (2)	0.2278 (7)	0.7305 (3)	0.0845 (14)
C218	0.33191 (14)	0.3408 (6)	0.7771 (3)	0.0670 (11)

Table 2. Selected geometric parameters (\AA , $^\circ$)

N11—N12	1.350 (4)	C15—C18	1.459 (5)
N11—C110	1.357 (4)	C18—C19	1.404 (5)
N11—C113	1.432 (4)	C19—C110	1.353 (5)
N12—C18	1.342 (4)	C110—C111	1.497 (5)
N13—C112	1.135 (5)	C111—C112	1.438 (6)
N21—N22	1.354 (4)	C25—C28	1.453 (5)
N21—C210	1.364 (4)	C28—C29	1.401 (5)
N21—C213	1.424 (4)	C29—C210	1.351 (5)
N22—C28	1.349 (4)	C210—C211	1.498 (5)
N23—C212	1.129 (5)	C211—C212	1.449 (6)
N12—N11—C110	111.9 (3)	C19—C110—N11	106.7 (3)
N12—N11—C113	119.0 (3)	C19—C110—C111	131.8 (3)
C110—N11—C113	129.1 (3)	N11—C110—C111	121.5 (3)
C18—N12—N11	105.1 (3)	N13—C112—C111	179.4 (5)
N22—N21—C210	111.4 (3)	N22—C28—C29	110.1 (3)
N22—N21—C213	119.0 (3)	N22—C28—C25	119.6 (3)
C210—N21—C213	129.5 (3)	C29—C28—C25	130.3 (3)
C28—N22—N21	105.1 (3)	C210—C29—C28	106.4 (3)
N12—C18—C19	110.0 (3)	C29—C210—N21	107.0 (3)
N12—C18—C15	120.5 (3)	C29—C210—C211	131.3 (3)
C19—C18—C15	129.4 (3)	N21—C210—C211	121.6 (3)
C110—C19—C18	106.3 (3)	N23—C212—C211	179.1 (5)

The phenyl rings were restrained to be flat with twofold rotational symmetry. H atoms were added at calculated positions and refined using a riding model. Anisotropic displacement parameters were used for all non-H atoms; each H atom was given an isotropic displacement parameter equal to 1.2 (1.5 for methyl H atoms) times the equivalent isotropic displacement parameter of the C atom to which it is attached.

Data collection: Siemens *P3R3* system. Cell refinement: Siemens *P3R3* system. Data reduction: *SHELXTL-Plus* (Sheldrick, 1991). Program(s) used to solve structure: *SHELXTL-Plus*. Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: CF1012). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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3-[3-(4-Bromophenyl)-1-phenylpyrazol-5-yl]-2H-1-benzopyran-2-one

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Abstract

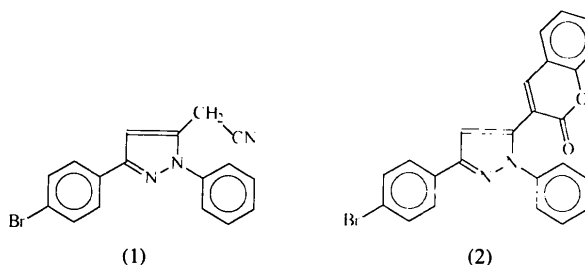
In the title compound, C₂₄H₁₅BrN₂O₂, the angles formed by the planes of the bromophenyl, phenyl and coumarin groups with the plane of the pyrazole nucleus are 19.3, 38.8 and 65.6°, respectively. The absolute structure has been determined.

Comment

Many compounds containing the pyrazole nucleus are used as drugs, insecticides and pesticides (Weily & Wiley, 1964; Taki, Meki, Fujimoto, Umeda & Imahase, 1992). Consequently, we have synthesized several diphenyl-substituted pyrazolylacetonitriles [*e.g.* compound (1)] and have established that such compounds have strong anti-invasive activity against solid tumours. The presence of a reactive methylene group in these pyrazole derivatives can be used in various ways to syn-

thesize compounds containing the pyrazole moiety and with the potential for biological activity.

In this investigation, salicylaldehyde was condensed with the pyrazole (1) to produce the coumarin derivative (2). The point of attachment of the coumarin group to the pyrazole nucleus was confirmed using ¹H NMR and mass spectrometry. The aim of this X-ray investigation was to obtain further structural information regarding the orientations of the groups attached to the pyrazole nucleus.



The molecular structure, as determined in this investigation, is illustrated in Fig. 1. The pyrazole nucleus is flat within experimental error, and the planar peripheral phenyl and bromophenyl groups are inclined with respect to the pyrazole plane at angles of 38.8 (6) and 19.3 (7)°, respectively. The coumarin unit is not exactly flat, but the least-squares plane through the ring atoms, with r.m.s. deviation 0.023 Å, is inclined at an angle of 65.6 (4)° to the plane of the pyrazole nucleus.

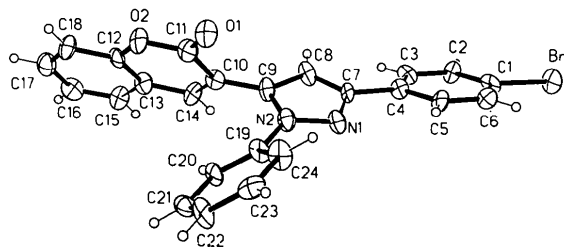


Fig. 1. View of the molecule showing the atomic numbering. Displacement ellipsoids are drawn at the 30% probability level.

The propeller-like orientations of the peripheral groups give a chiral molecule. The observed value of the absolute structure parameter (Flack, 1983) is $-0.02(3)$. This is within one e.s.d. of zero and its e.s.d. is also relatively small; thus it provides strong evidence that the absolute structure has been assigned correctly. All bond lengths and angles are unexceptional. The generally low precision associated with the determination is due to poor crystal quality.

Experimental

Salicylaldehyde (0.13 ml, 0.0012 mol) was added to a solution of (1) (0.34 g, 0.001 mol) in ethanol (20 ml). After the