Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

3-[5-(4-Bromophenyl)-1*H*-pyrazol-3-ylamino]-5,5-dimethylcyclohex-2-en-1-one–(*Z*)-3-(4-bromophenyl)-3-chloroacrylonitrile (2/1): a stoichiometric cocrystal of a reaction product with one of its early precursors

Silvia Cruz,[a] Jairo Quiroga,[b] José M. de la Torre,[c] Justo Cobo,[c] John N. Low[d] and Christopher Glidewell[e]*

[a]Departamento de Química, Universidad de Nariño, Ciudad universitaria, Torobajo, AA 1175 Pasto, Colombia, [b]Grupo de Investigación de Compuestos Heterocíclicos, Departamento de Química, Universidad de Valle, AA 25360 Cali, Colombia, [c]Departamento de Química Inorgánica y Orgánica, Universidad de Jaén, 23071 Jaén, Spain, [d]Department of Chemistry, University of Aberdeen, Meston Walk, Old Aberdeen AB24 3UE, Scotland, and [e]School of Chemistry, University of St Andrews, Fife KY16 9ST, Scotland
Correspondence e-mail: cg@st-andrews.ac.uk

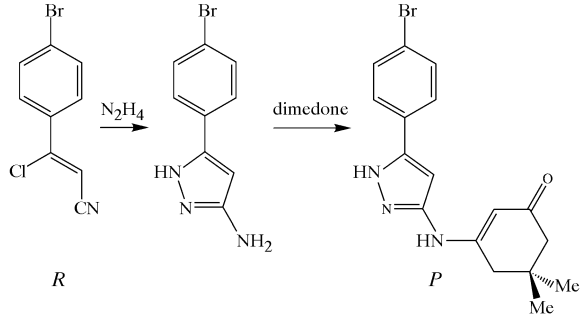
Received 8 August 2006
Accepted 23 August 2006
Online 12 September 2006

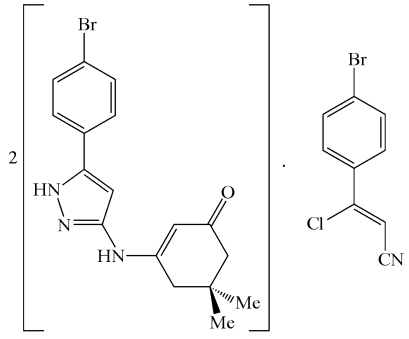
The title compound, $2C_{17}H_{18}BrN_3O\cdot C_9H_5BrClN$, was crystallized from the reaction between 5,5-dimethylcyclohexane-1,3-dione, triethyl orthoformate and 5-amino-3-(4-bromophenyl)pyrazole, which had itself been prepared from the reaction between (*Z*)-3-(4-bromophenyl)-3-chloroacrylonitrile and hydrazine. The compound is a stoichiometric 2:1 cocrystal of the reaction product 3-[5-(4-bromophenyl)-1*H*-pyrazol-3-ylamino]-5,5-dimethylcyclohex-2-en-1-one and the early reactant (*Z*)-3-(4-bromophenyl)-3-chloroacrylonitrile. The two independent molecules of cyclohex-2-en-1-one are linked by N—H···N and N—H···O hydrogen bonds into complex bilayers and the molecules of acrylonitrile are trapped within large cavities in the substructure formed by the cyclohex-2-en-1-one molecules.

Comment

We report here the molecular and supramolecular structure of the title compound, (I), which is a stoichiometric cocrystal of two molecules of 3-[3-(4-bromophenyl)-1*H*-pyrazol-5-ylamino]-5,5-dimethyl-2-cyclohexen-1-one, hereinafter designated *P* (for product) and one molecule of one of its upstream precursors, *viz*. (*Z*)-3-(4-bromophenyl)-3-chloroacrylonitrile, which had evidently been carried through the entire synthetic sequence and which is hereinafter designated *R* (for reactant).

The compound was obtained from the reaction between 5-amino-3-(4-bromophenyl)pyrazole, 5,5-dimethylcyclohexane-1,3-dione (dimedone) and triethyl orthoformate, which, it had been hoped, would yield a pyrazolo[3,4-*b*]quinoline derivative. The pyrazole component of this reaction had itself been prepared using the reaction of (*Z*)-3-(4-bromophenyl)-3-chloroacrylonitrile (component *R*) and hydrazine (see scheme), and evidently the excess of component *R* had been carried right through the synthesis, leading to the isolation of the cocrystal, compound (I).





(I)

For the sake of convenience, we shall refer to the molecules containing N11, N21 and N31 (Fig. 1) as types 1–3, respectively. The cocrystal thus contains two molecules, those of types 1 and 2, of the expected product *P*, along with one molecule, that of type 3, of the precursor compound *R*. Although the atomic displacement parameters of molecule 3 are generally higher than those of molecules 1 and 2, refinement of the site occupancy for component *R* confirmed that the occupancy is unity and that the composition of the cocrystal is stoichiometrically 2:1. While the two independent molecules of component *P* are linked into bilayers by a combination of N—H···N and N—H···O hydrogen bonds, there are no direction-specific intermolecular interactions involving the molecules of component *R*. Hence, this component is, in effect, captive within the supramolecular structure generated by component *P*, in the manner of a clathrate, and the molecule of *R* thus has somewhat greater freedom of movement than the molecules of *P*.

The non-aromatic carbocyclic rings in the type 1 and 2 molecules both adopt envelope conformations, folded across the vectors C134···C136 and C234···C236. The ring-puckering parameters (Cremer & Pople, 1975) for the atom sequences C131–C136 and C231–C236 are θ = 52.2 (4)° and φ = 234.7 (5)° for the type 1 molecule, and θ = 128.5 (4)° and φ = 48.3 (5)° for the type 2 molecule, so that the two molecules of *P* in the selected asymmetric unit are nearly enantiomeric.

  DOI: 10.1107/S0108270106033968

However, this choice has no significance, as the space group accommodates equal numbers of both enantiomers of the type 1 and 2 molecules. For an idealized envelope conformation, the ring-puckering parameters are 54.7° (or 125.3° for the enantiomorphic ring) and $\varphi = (60k)°$ (where k = zero or integer). The dihedral angle between the planes of the aryl and pyrazole rings is 19.0 (2)° in the type 1 molecule and 18.4 (2)° in the type 2 molecule, and the corresponding torsion angles (Table 1) indicate the near-enantiomeric relationship of the two reference molecules. The type 3 molecule is nearly planar, as shown by the leading torsion angles. The bond distances and interbond angles present no unusual features.

The molecules of component *P* are linked into bilayers by three N—H···O hydrogen bonds and one N—H···N hydrogen bond (Table 2), and the formation of the bilayer is readily analysed, firstly in terms of the formation of single sheets by the three N—H···O hydrogen bonds only, and then of the pairwise linking of these sheets by the N—H···N hydrogen bond. Within the selected asymmetric unit, the two independent molecules of component *P* are linked by an N—H···O hydrogen bond. In addition, atom N11 in the type 1 molecule at (x, y, z) acts as hydrogen-bond donor to atom O13 in the type 1 molecule at $(\frac{1}{2} + x, \frac{1}{2} + y, z)$, so generating by translation a *C*(9) (Bernstein *et al.*, 1995) chain of type 1 molecules running parallel to the [110] direction. Similarly, atom N21 in the type 2 molecule at (x, y, z) acts as hydrogen-bond donor to atom O23 in the type 2 molecule at $(-\frac{1}{2} + x, \frac{1}{2} + y, z)$, so generating by translation a second *C*(9) chain, this time built from type 2 molecules and running parallel to the $[\bar{1}10]$ direction. The combination of the [110] and $[\bar{1}10]$ chains, linked by the N—H···O hydrogen bond within the asymmetric unit, generates a sheet of $R_8^8(44)$ rings parallel to (001) (Fig. 2).

Four such sheets pass through each unit cell, lying in the domains $-0.05 < z < 0.29$, $0.21 < z < 0.55$, $0.45 < z < 0.79$ and $0.71 < z < 1.05$. Pairs of these sheets, related by twofold rotation axes, are linked by paired N—H···N hydrogen bonds involving type 2 molecules only. Atom N23 in the type 2 molecule at (x, y, z), which lies in the domain $0.45 < z < 0.79$, acts as hydrogen-bond donor to atom N22 in the type 2 molecule at $(1 - x, y, \frac{3}{2} - z)$, which lies in the domain $0.71 < z < 1.05$. The resulting $R_2^2(8)$ motif (Fig. 3), generated by the twofold rotation axis along $(\frac{1}{2}, y, \frac{3}{4})$, thus links pairs of (001) sheets to form bilayers. Two bilayers pass through each unit cell, in the domains $0.45 < z < 1.05$ and $-0.05 < z < 0.55$, generated by the twofold rotation axes at $z = \frac{3}{4}$ and $z = \frac{1}{4}$, respectively, but there are no direction-specific interactions between the bilayers.

The bilayers built from the molecules of types 1 and 2 occupy *ca* 71% of the total unit-cell volume, as indicated by the VOID calculation in *PLATON* (Spek, 2003), equivalent to *ca* 377 Å^3 per molecule of component *P*, leaving *ca* 319 Å^3 per molecule of component *R*. Thus, for the molecules of

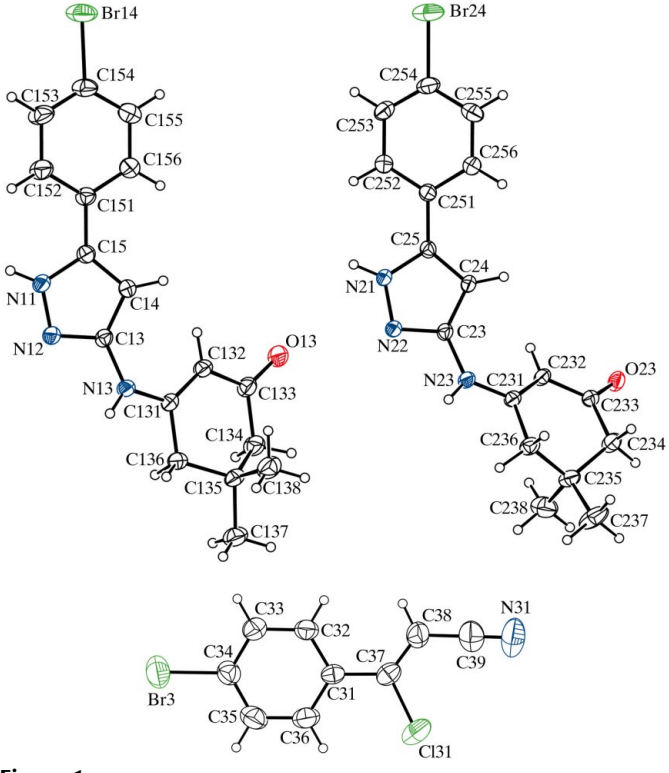


Figure 1
The three independent molecules in compound (I), showing the atom-labelling scheme, *viz*. (*a*) the type 1 molecule of component *P*, (*b*) the type 2 molecule of component *P* and (*c*) the molecule of component *R*. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

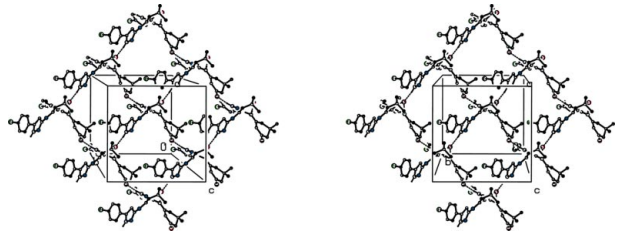


Figure 2
A stereoview of part of the crystal structure of compound (I), showing the formation of a hydrogen-bonded sheet parallel to (001) built from the type 1 and 2 molecules only. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

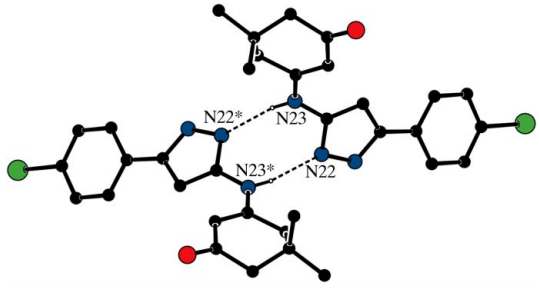


Figure 3
Part of the crystal structure of compound (I), showing the $R_2^2(8)$ motif, built from type 2 molecules only, which links the (001) sheets into bilayers. For the sake of clarity, the unit-cell outline and H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) are at the symmetry position $(1 - x, y, \frac{3}{2} - z)$.

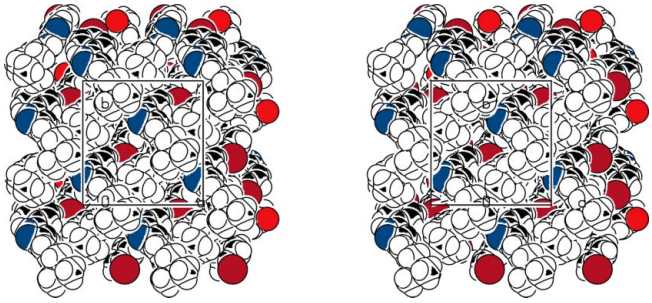


Figure 4
A space-filling stereoview of part of the crystal structure of compound (I), showing only the type 1 and 2 molecules in the domain $\frac{1}{4} < z < \frac{3}{4}$ and the resulting cavities.

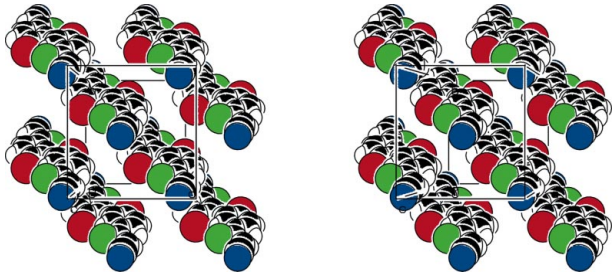


Figure 5
A space-filling stereoview of part of the crystal structure of compound (I), showing the pairwise arrangement of the type 3 molecules in the domain $\frac{1}{4} < z < \frac{3}{4}$.

component *P*, the mean volume per non-H atom is *ca* 17.1 Å^3, satisfactorily close to the average value of 18 Å^3 proposed by Kempster & Lipson (1972) for light-atom structures, while the mean volume available per non-H atom for component *R* is *ca* 26.6 Å^3, some 50% higher. The use of element-specific atomic volumes (Hofmann, 2002) leads to estimated volumes for the molecules of components *P* and *R* of 406.7 and 210.5 Å^3, respectively, which differ from the available volumes estimated by *PLATON* by *ca* 8 and −34%, respectively. The substantial molecular volume available to the molecules for component *R*, coupled with the absence of any direction-specific intermolecular forces involving the molecules of *R*, may account for the apparently large atomic displacement parameter values for component *R*.

The 29% of the cell volume not occupied by the bilayers forms four large centrosymmetric cavities per unit cell, centred at ($\pm\frac{1}{4}$, $\pm\frac{1}{4}$, 0) and ($\pm\frac{1}{4}$, $\mp\frac{1}{4}$, $\frac{1}{2}$) (Fig. 4), each of which accommodates two molecules of component *R* related to one another by inversion (Fig. 5).

Experimental

A solution of 5-amino-3-(4-bromophenyl)pyrazole [1.0 mmol, itself prepared from the reaction of (*Z*)-3-(4-bromophenyl)-3-chloroacrylonitrile with excess hydrazine; see scheme in *Comment*], 5,5-dimethylcyclohexane-1,3-dione (dimedone; 1.0 mmol) and triethyl orthoformate (1.0 mmol) in ethanol (20 ml) was heated under reflux for 10 h. The reaction mixture was cooled to ambient temperature and crystals of the title compound, (I), were collected by filtration.

Crystal data

$2C_{17}H_{18}BrN_3O\cdot C_9H_5BrClN$
M_r = 963.01
Monoclinic, *C*2/*c*
a = 13.4390 (4) Å
b = 13.8680 (4) Å
c = 46.1620 (15) Å
β = 93.050 (2)°
V = 8591.1 (5) Å^3
Z = 8
D_x = 1.489 Mg m^{-3}
Mo *Kα* radiation
μ = 2.92 mm^{-1}
T = 293 (2) K
Block, colourless
0.44 × 0.26 × 0.20 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.338, T_{max} = 0.557
49869 measured reflections
9729 independent reflections
5997 reflections with $I > 2\sigma(I)$
R_{int} = 0.037
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.051
$wR(F^2)$ = 0.136
S = 1.03
9729 reflections
505 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0539P)^2 + 16.273P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.002
$\Delta\rho_{max}$ = 0.62 e Å^{-3}
$\Delta\rho_{min}$ = −0.73 e Å^{-3}

Table 1
Selected torsion angles (°).

N11—C15—C151—C152	17.8 (5)	C32—C31—C37—C38	−6.1 (6)
N21—C25—C251—C252	−16.9 (5)	C31—C37—C38—C39	177.1 (4)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N11—H11···O13^{i}	0.86	1.96	2.801 (3)	166
N13—H13···O23	0.86	2.02	2.880 (3)	177
N21—H21···O23^{ii}	0.86	1.96	2.798 (3)	164
N23—H23···N22^{iii}	0.86	2.16	3.009 (3)	169

Symmetry codes: (i) $x+\frac{1}{2}, y+\frac{1}{2}, z$; (ii) $x-\frac{1}{2}, y+\frac{1}{2}, z$; (iii) $-x+1, y, -z+\frac{3}{2}$.

The systematic absences permitted *C*2/*c* and *Cc* as possible space groups; *C*2/*c* was selected and confirmed by the successful structure analysis. All H atoms were located in difference maps and then treated as riding atoms, with distances C—H = 0.93 (aromatic and alkenic), 0.96 (CH_3) or 0.97 Å (CH_2) and N—H = 0.86 Å, and with U_{iso}(H) = kU_{eq}(C,N), where *k* = 1.5 for the methyl groups and 1.2 for all other H atoms.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *SIR2004* (Burla *et al.*, 2005); program(s) used to refine structure: *OSCAIL* (McArdle, 2003) and *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PRPKAPPA* (Ferguson, 1999).

X-ray data were collected at the EPSRC National Crystallography Service, University of Southampton, England; the authors thank the staff for all their help and advice. JC and JMT thank the Consejería de Innovación, Ciencia y Empresa (Junta de Andalucía, Spain) and the Universidad de Jaén for financial support. JMT also thanks Universidad de Jaén for a

scholarship grant supporting a short stay at the EPSRC National Crystallography Service, University of Southampton. JQ and SC thank COLCIENCIAS, UNIVALLE (Universidad del Valle, Colombia) and UDENAR (Universidad de Nariño, Colombia) for financial support.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FA3037). Services for accessing these data are described at the back of the journal.

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