

2-(4-Chlorophenyl)-5-(4-nitrophenyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine-3,6-dicarbaldehyde: a chain of rings built from N—H···O and C—H···O hydrogen bonds

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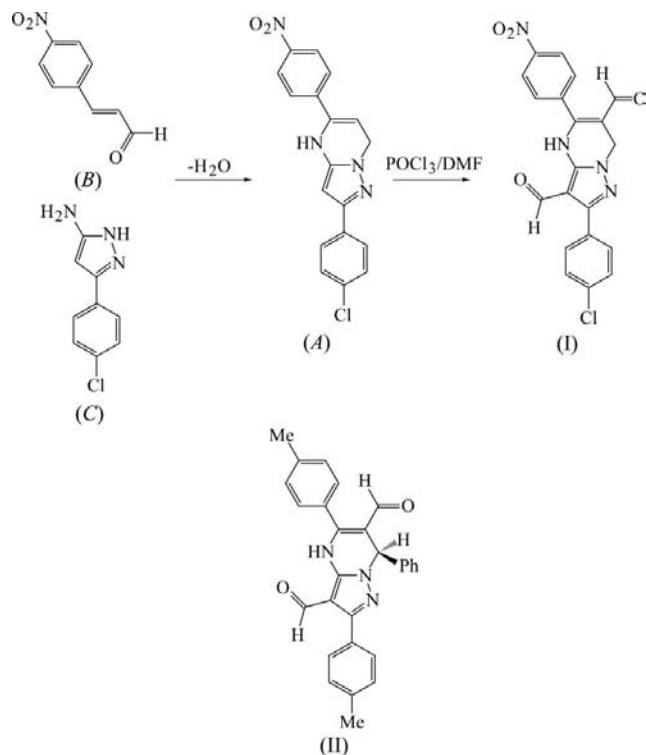
In the title compound, C₂₀H₁₃ClN₄O₄, the six-membered heterocyclic ring is planar and the molecular dimensions provide evidence for polarization of the molecular–electronic structure. Molecules are linked into a chain of rings by a combination of N—H···O and C—H···O hydrogen bonds, but the nitro group does not participate in the supramolecular aggregation. This study illustrates the marked influence of peripheral substituents on the pattern of hydrogen-bonded aggregation in compounds of this type.

Comment

As part of a continuing search for biologically active molecules containing fused pyrazole systems (Quiroga *et al.*, 2008), we have now prepared the title compound, (I), by use of the Vilsmeier–Haack reaction to effect double formylation of the precursor (A) (see the first scheme), itself formed by condensation of the simple reagents (B) and (C). Product (I) is of potential value as a precursor for modified or fused polycyclic pyrazolo[1,5-*a*]pyrimidine systems. We report here the structure of (I) and compare it with the closely related analogue, (II) (Low *et al.*, 2006). Both the molecular structure of (I) (Fig. 1) and its supramolecular aggregation show significant differences from those of compound (II), whose constitution differs from that of (I) not only in the nature of the 4-substituents in the aryl rings pendent from positions 2 and 5, but also in the presence of an additional unsubstituted phenyl ring at position 7.

Within the molecule of (I), the six-membered heterocyclic ring is effectively planar: the maximum deviation from the mean plane through the six ring atoms is 0.021 (3) Å for atom

C6. This contrasts with the corresponding ring in compound (II), which is significantly puckered into a nonplanar conformation intermediate between boat and screw-boat forms (Low *et al.*, 2006). The overall conformation of the molecule of (I) can thus be defined in terms of five torsion angles (Table 1) which show that, apart from the nitro group which makes a



dihedral angle of 9.4 (2)° with the adjacent aryl ring, the conformation of (I) is broadly similar to that of (II). In particular, the two independent carbaldehyde groups in (I) are both nearly coplanar with the heterocyclic ring system, with deviations from the mean ring plane of 0.236 (3) Å for atom O31 and 0.106 (2) Å for atom O61. While the short intramolecular N—H···O hydrogen bond to atom O31 (Table 2) may influence the orientation of one carbaldehyde group, there is no corresponding interaction which could influence the orientation of the carbaldehyde group bonded to atom C6. However, the intramolecular dimensions of (I) (Table 1)

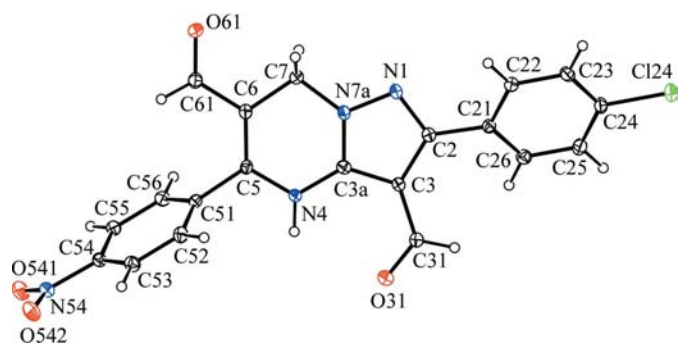
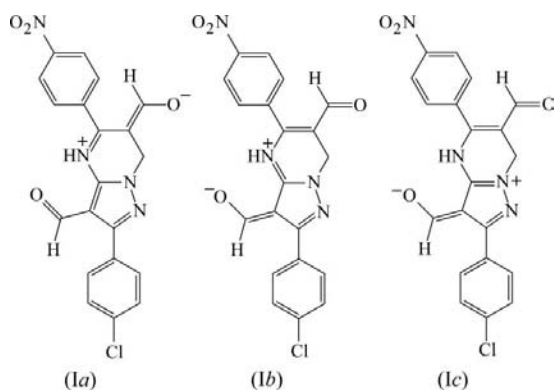


Figure 1

The molecular structure of compound (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

provide some evidence for the polarization of its molecular structure, such that the potential for electronic delocalization is optimized when the carbaldehyde groups are coplanar with the heterocyclic system, and this may thus be the dominant factor controlling the orientation of the carbaldehyde groups. Firstly, the C31—O31 and C61—O61 bonds are both long for their type (mean literature value = 1.192 Å; Allen *et al.*, 1987), while the C3—C31 and C6—C61 bonds are both short (mean literature value = 1.464 Å). Secondly, the C5—C6 bond is long for its type (mean literature value = 1.331 Å), and the C3a—N4 and N4—C5 bonds have almost identical lengths. These observations, taken all together, indicate that polarized forms such as (Ia)–(Ic) (see the second scheme) are contributors to the overall molecular–electronic structure. The molecular dimensions of compound (II) were not discussed in the original report (Low *et al.*, 2006), but re-examination of the structure of (II) shows that it exhibits exactly the same pattern of intramolecular distances as found here for (I), pointing to a similar interpretation of the carbaldehyde conformations.



The intramolecular hydrogen bond mentioned earlier forms an $S(6)$ motif (Bernstein *et al.*, 1995) and it is, in fact, the longer and weaker component of an asymmetric three-centre $N-H \cdots (O)_2$ system (Table 2), in which the shorter component links the molecules at (x, y, z) and $(\frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z)$, which are related by the 2_1 screw axis along $(\frac{1}{4}, y, \frac{1}{4})$. Propagation of this hydrogen bond forms a $C(6)$ chain running parallel to the [010] direction (Fig. 2). This [010] chain is reinforced by a $C-H \cdots O$ hydrogen bond which forms a $C(9)$

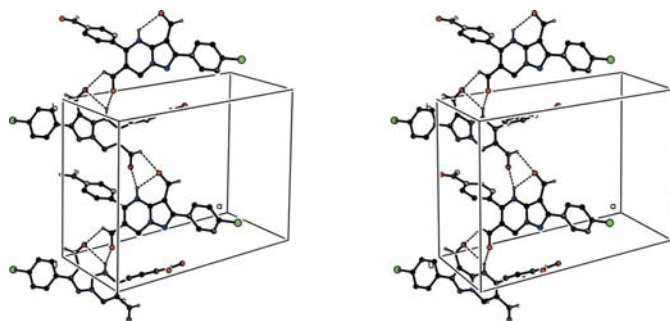


Figure 2
A stereoview of part of the crystal structure of compound (I), showing the formation of a hydrogen-bonded chain of rings. For the sake of clarity, H atoms bonded to ring C atoms have been omitted.

chain, and the combination of all these hydrogen bonds generates an $S(6)C(6)C(9)[R_2^2(5)]$ chain of rings (Fig. 2). In this chain, the $R_2^2(5)$ motif actually contains three hydrogen bonds, but atoms H4 and O31 act, respectively, as a double donor and a double acceptor. Four chains of this type pass through each unit cell, but there are no direction-specific interactions between the chains.

It is interesting to note that, despite the large excess in (I) of potential hydrogen-bond donors in the form of aromatic C—H bonds over potential hydrogen-bond acceptors, the O atoms of the nitro group play no part in the hydrogen bonding. Nor are there any dipolar nitro–nitro interactions (Garden *et al.*, 2006; Glidewell *et al.*, 2006), analogous to the well documented dipolar carbonyl–carbonyl interactions (Allen *et al.*, 1998).

The action of the hydrogen bonds in (I) differs from that in (II) (Low *et al.*, 2006). While (II) also contains an asymmetric $N-H \cdots (O)_2$ system, the shorter component generates a centrosymmetric dimer containing an $R_2^2(12)$ motif, rather than a $C(6)$ chain as in (I). There are two $C-H \cdots O$ hydrogen bonds in the structure of (II), which link the $R_2^2(12)$ dimers into sheets, but both of these donor atoms are components of the unsubstituted phenyl ring, which is absent from the constitution of (I). Hence, the supramolecular aggregation in compounds of this type is very markedly influenced by the nature of the peripheral substituents.

Experimental

A mixture of 5-amino-3-(4-chlorophenyl)-1*H*-pyrazole, (C) (1.9 mmol), and 1-(4-nitrophenyl)propenone, (B) (1.9 mmol), in dimethylformamide (1 ml) was heated under reflux for 20 min to afford the intermediate 2-(4-chlorophenyl)-5-(4-nitrophenyl)-4,7-dihydropyrazolo[1,5-*a*]pyrimidine, (A). The reaction mixture was cooled to ambient temperature and the intermediate was collected by filtration, washed with ethanol and dried, and then purified by chromatography on alumina using chloroform as the eluent. Phosphoryl chloride (2.1 mmol) was then added dropwise to a suspension of the pyrazolopyrimidine intermediate (1.0 mmol) in dimethylformamide (2 ml) at 273 K. When the addition was complete, the reaction mixture was stirred vigorously for 0.5 h at ambient temperature. The resulting solid product, (I), was collected by filtration, dried and recrystallized from dimethylformamide to give yellow crystals suitable for single-crystal X-ray diffraction (yield 65%, m.p. 555–557 K). MS (m/z , %): 410/408 (35/100, M^+), 407 (53), 361 (51), 350 (70), 102 (31), 75 (42), 40 (82).

Crystal data

$C_{20}H_{13}ClN_4O_4$	$V = 3486.7$ (17) Å ³
$M_r = 408.79$	$Z = 8$
Monoclinic, $C2/c$	Mo $K\alpha$ radiation
$a = 23.943$ (5) Å	$\mu = 0.26$ mm ⁻¹
$b = 13.445$ (2) Å	$T = 120$ (2) K
$c = 12.336$ (5) Å	$0.46 \times 0.36 \times 0.24$ mm
$\beta = 118.594$ (10)°	

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer	40202 measured reflections
Absorption correction: multi-scan (SADABS; Shelldrick, 2003)	4002 independent reflections
$T_{\min} = 0.891$, $T_{\max} = 0.941$	2520 reflections with $I > 2\sigma(I)$
	$R_{\text{int}} = 0.066$

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.329 (3)	C7—N7a	1.445 (3)
C2—C3	1.423 (4)	N7a—N1	1.371 (3)
C3—C3a	1.401 (4)	C3a—N7a	1.337 (3)
C3a—N4	1.377 (3)	C3—C31	1.432 (4)
N4—C5	1.374 (3)	C31—O31	1.222 (3)
C5—C6	1.356 (4)	C6—C61	1.442 (4)
C6—C7	1.507 (4)	C61—O61	1.223 (3)
N1—C2—C21—C22	35.0 (4)	N4—C5—C51—C52	68.2 (3)
C2—C3—C31—O31	−171.9 (3)	C53—C54—N54—O541	−172.4 (2)
C5—C6—C61—O61	−179.5 (3)		

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

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
N4—H4...O31	0.88	2.52	3.011 (3)	116
N4—H4...O61 ⁱ	0.88	2.00	2.853 (3)	163
C61—H61...O31 ⁱⁱ	0.95	2.47	3.043 (3)	118

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

$R[F^2 > 2\sigma(F^2)] = 0.051$	262 parameters
$wR(F^2) = 0.139$	H-atom parameters constrained
$S = 1.08$	$\Delta\rho_{\max} = 0.36 \text{ e } \text{Å}^{-3}$
4002 reflections	$\Delta\rho_{\min} = -0.43 \text{ e } \text{Å}^{-3}$

The systematic absences permitted *C2/c* and *Cc* as possible space groups; *C2/c* was selected and confirmed by the subsequent structure analysis. All H atoms were located in difference maps and then treated as riding atoms, with C—H = 0.99 (CH₂) or 0.95 Å (all other H atoms) and N—H = 0.88 Å, and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{parent})$.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *DIRAX/LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003); program(s) used to solve structure: *SIR2004* (Burla *et al.*, 2005); program(s) used to refine structure: *OSCAIL* (McArdle, 2003) and *SHELXL97* (Sheldrick, 2008); molecular

graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PRPKAPPA* (Ferguson, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3236). Services for accessing these data are described at the back of the journal.

References

- Allen, F. H., Baalham, C. A., Lommerse, J. P. M. & Raithby, P. R. (1998). *Acta Cryst.* **B54**, 320–329.
- Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
- Bernstein, J., Davis, R. E., Shimon, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
- Burla, M. C., Caliandro, R., Camalli, M., Carrozzini, B., Cascarano, G. L., De Caro, L., Giacovazzo, C., Polidori, G. & Spagna, R. (2005). *J. Appl. Cryst.* **38**, 381–388.
- Duisenberg, A. J. M., Hooft, R. W. W., Schreurs, A. M. M. & Kroon, J. (2000). *J. Appl. Cryst.* **33**, 893–898.
- Duisenberg, A. J. M., Kroon-Batenburg, L. M. J. & Schreurs, A. M. M. (2003). *J. Appl. Cryst.* **36**, 220–229.
- Ferguson, G. (1999). *PRPKAPPA*. University of Guelph, Canada.
- Garden, S. J., Wardell, J. L., Low, J. N., Skakle, J. M. S. & Glidewell, C. (2006). *Acta Cryst.* **E62**, o3762–o3764.
- Glidewell, C., Low, J. N., Skakle, J. M. S. & Wardell, J. L. (2006). *Acta Cryst.* **C62**, o1–o4.
- Low, J. N., Cobo, J., Trilleras, J. & Glidewell, C. (2006). *Acta Cryst.* **E62**, o4930–o4932.
- McArdle, P. (2003). *OSCAIL for Windows*. Version 10. Crystallography Centre, Chemistry Department, NUI Galway, Ireland.
- Nonius (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.
- Quiroga, J., Trilleras, J., Insuasty, B., Abonía, R., Noguera, M. & Cobo, J. (2008). *Tetrahedron Lett.* **49**, 2689–2691.
- Sheldrick, G. M. (2003). *SADABS*. Version 2.10. University of Göttingen, Germany.
- Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.
- Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.