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2-*tert*-Butyl-5-methyl-7,8-dihydro-6*H*-cyclopenta[e]pyrazolo[1,5-*a*]pyrimidine: molecular stacks built from C—H···π(pyrazole) hydrogen bonds and π–π stacking interactions

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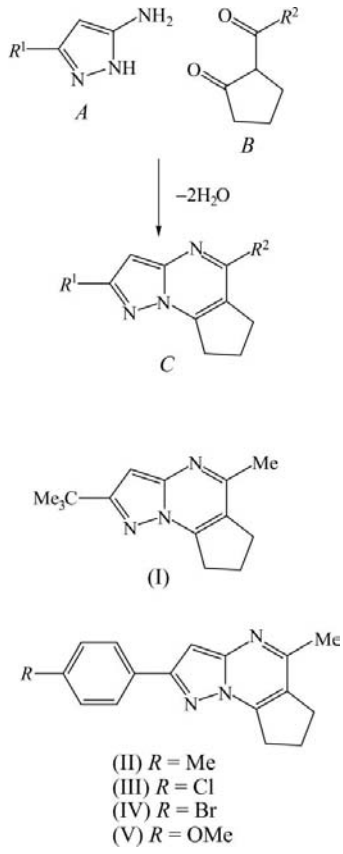
In the title compound, $C_{14}H_{19}N_3$, the bond distances within the heterocyclic portion of the molecule indicate incomplete π delocalization. The molecules are linked into stacks by a combination of two C—H···π(pyrazole) hydrogen bonds and two independent π–π stacking interactions between inversion-related pyrimidine rings. The significance of this study lies in its observation of significant differences in both molecular conformation and supramolecular aggregation between the title compound, an example of a 2-alkylpyrazolo[1,5-*a*]pyrimidine, and some analogous 2-arylpyrazolo[1,5-*a*]pyrimidines.

Comment

Pyrazolo[1,5-*a*]pyrimidines are purine analogues and their pharmacological activity (Novinson *et al.*, 1976; Senga *et al.*, 1981) has prompted interest in the development of efficient general procedures for their synthesis. One attractive route (Portilla *et al.*, 2005) to such compounds involves the condensation of a substituted 5-amino-1*H*-pyrazole (*A*) with a 2-acylcyclopentanone (*B*) to give the 2,5-disubstituted product (*C*). We report here the molecular and supramolecular structure of the title compound, (I) (Fig. 1), which was prepared using a simple fusion-induced condensation reaction between 5-amino-3-*tert*-butyl-1*H*-pyrazole and 2-acetylcyclopentanone under solvent-free conditions. We compare the structure of (I) with those of the aryl-substituted analogues (II)–(V) (see scheme), which were all prepared using similar condensation reactions under solvent-free conditions but induced by microwave irradiation (Portilla *et al.*, 2005).

In contrast to the conformations found for compounds (II)–(V), where the carbocyclic rings all adopt envelope conformations, the corresponding ring in (I) is effectively planar; the maximum deviation from the mean plane of the ring atoms in (I) is only 0.024 (3) Å, for atom C7. There is no obvious interpretation of this difference. While the tricyclic skeleton in (I) is effectively planar, the *tert*-butyl group is rotated by *ca* 10° from the conformation that corresponds to an approximate



mirror symmetry, as shown by the key torsion angles (Table 1). However, the pattern of the bond distances within the heterocyclic system in (I) (Table 1) shows a close similarity with those in (II)–(V), and, as before, this suggests a naphthalene-type arrangement of the ten π electrons in this system rather than full delocalization.

Despite the presence of two ring N atoms, N1 and N4, each carrying an in-plane lone pair of electrons potentially available for hydrogen-bond formation, there are, in fact, no C—H···N hydrogen bonds in the structure of (I). In this respect,

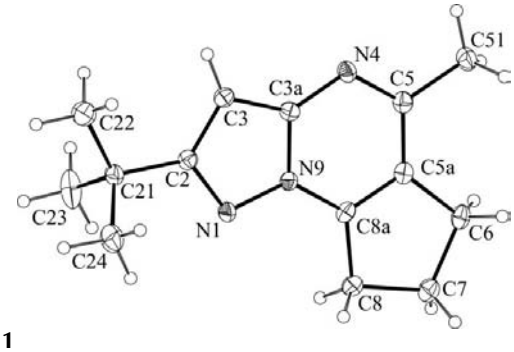


Figure 1
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

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(I) resembles compounds (II)–(IV), although a single C—H···N interaction is present in (V). The molecules of (I) are linked by a combination of C—H···π(pyrazone) hydrogen bonds (Table 2) and π–π stacking interactions. Atom C6 in the molecule at (x, y, z) acts as hydrogen-bond donor, *via* atoms H6*A* and H6*B*, respectively, to the pyrazole rings in the molecules at ($-x+1$, $-y+1$, $-z+1$) and ($-x+2$, $-y+1$, $-z+1$), respectively. Thus, the pyrazole ring accepts a C—H bond onto each face, such that the angle H6*A*···*Cg*1^{i}···H6*B*^{iii} [*Cg*1 represents the centroid of the pyrazole ring; symmetry codes: (i) $-x+1$, $-y+1$, $-z+1$; (iii) $x-1$, y, z] is 150°. In addition, the pyrimidine rings of the molecules at (x, y, z) and ($-x+1$, $-y+1$, z), which are strictly parallel because they are related by inversion, have an interplanar spacing of 3.422 (2) Å and a ring-centroid separation of 3.611 (2) Å, corresponding to a ring centroid offset of 1.152 (2) Å. Similarly, for the pyrimidine rings of the molecules at (x, y, z) and ($-x+2$, $-y+1$, $-z+1$), the interplanar separation is 3.443 (2) Å and the ring-centroid separation is 3.674 (2) Å, corresponding in this case to a ring-centroid offset of 1.282 (2) Å. The combined and cooperative effect of the C—H···π hydrogen bonds and the π–π stacking interaction is to link the molecules into a stack running parallel to the [100] direction, in which alternate molecules are related by inversion (Fig. 2).

In the isostructural compounds (II)–(IV) (Portilla *et al.*, 2005), the molecules are linked into chains by a single C—H···π(pyrazole) hydrogen bond, again involving atom C6 as the donor. In these hydrogen bonds, the H···A and D···A distances are all significantly greater than the corresponding distances in (I), while the organization of the molecules within the chains in (II)–(IV) effectively precludes the formation of a second C—H···π hydrogen bond, as found in (I). There is a single C—H···N hydrogen bond in (V), with one of the C—H bonds in the pendent aryl group providing the donor and the pyrimidine ring atom N4 as the acceptor. The resulting $C(7)$ (Bernstein *et al.*, 1995) chains are then linked into a sheet by means of a π–π stacking interaction between inversion-related heterocyclic rings. Compound (V) is thus the only member of this series so far observed to exhibit a C—H···N hydrogen bond, while (I) is the sole member in which the pyrazole ring acts as a double acceptor of hydrogen bonds.

Only in (V) does the substituent at atom C2 play any direct role in the hydrogen bonding. Nonetheless, the pattern of supramolecular aggregation in (I) is different from that in the isomorphous series (II)–(IV); likewise, the conformational difference between (I) and (II)–(V) involves the carbocyclic ring remote from the substituent at C2. Very subtle factors appear to connect the nature of the substituent at C2 with both the overall molecular conformation and the direction-specific intermolecular forces, making structure predictions extremely uncertain.

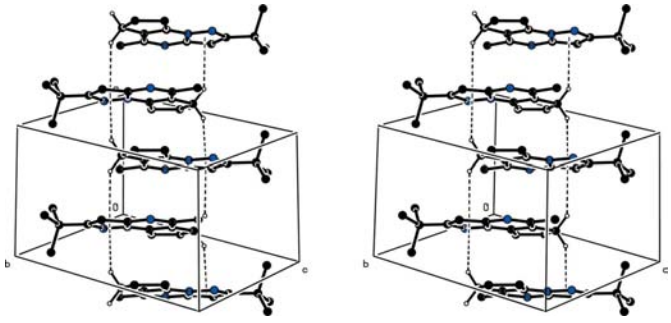

Figure 2
A stereoview of part of the crystal structure of (I), showing the formation of a stack of molecules along [100] built from a combination of C—H···π(pyrazole) hydrogen bonds and π–π stacking interactions. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

Experimental

Equimolar quantities (2 mmol of each component) of 5-amino-3-*tert*-butyl-1*H*-pyrazole and 2-acetylcyclopentanone were mixed thoroughly at room temperature. The mixture was heated in an oil bath at 393 K for 1.5 min. It was then stirred and allowed to cool to room temperature, at which point it solidified. The solid material was extracted with ethanol; after removal of this solvent, the product, (I), was recrystallized from dimethylformamide to give yellow crystals suitable for single-crystal X-ray diffraction (yield 93%, m.p. 459–461 K). MS (70 eV) m/z (%): 229 (64, M^+), 214 (100), 187 (87), 106 (19), 53 (20), 41 (527), 39 (40).

Crystal data

$C_{14}H_{19}N_3$
M_r = 229.32
Triclinic, $P\overline{1}$
a = 6.8665 (6) Å
b = 9.4084 (14) Å
c = 11.147 (2) Å
α = 91.611 (14)°
β = 107.728 (14)°
γ = 111.097 (12)°
V = 632.22 (18) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.07 mm^{-1}
T = 120 (2) K
0.38 × 0.37 × 0.25 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.966, T_{max} = 0.982
15695 measured reflections
2898 independent reflections
1804 reflections with $I > 2\sigma(I)$
R_{int} = 0.049

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.062
$wR(F^2)$ = 0.180
S = 1.11
2898 reflections
158 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.29 e Å^{-3}
$\Delta\rho_{min}$ = −0.29 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.353 (3)	C5—C5a	1.409 (3)
C2—C3	1.397 (3)	C8a—N9	1.354 (3)
C3—C3a	1.387 (3)	N9—N1	1.356 (3)
C3a—N4	1.355 (3)	C3a—N9	1.389 (3)
N4—C5	1.329 (3)	C5a—C8a	1.360 (3)
N1—C2—C21—C22	170.4 (2)	C3—C2—C21—C22	−10.1 (4)
N1—C2—C21—C23	−69.1 (3)	C3—C2—C21—C23	110.4 (3)
N1—C2—C21—C24	49.8 (3)	C3—C2—C21—C24	−130.7 (3)

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

*Cg*1 is the centroid of the pyrazole ring (atoms N1/C2/C3/C3a/N9).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C6—H6*A*···*Cg*1^{i}	0.99	2.76	3.602 (3)	144
C6—H6*B*···*Cg*1^{ii}	0.99	2.70	3.581 (3)	148

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

Crystals of (I) are triclinic; the space group $P\overline{1}$ was selected and confirmed by the structure analysis. All H atoms were located in difference maps and then treated as riding atoms in geometrically idealized positions, with C—H distances of 0.95 (pyrazole), 0.98 (CH_3) or 0.99 Å (CH_2), and with $U_{iso}(H) = kU_{eq}(C)$, where $k = 1.5$ for the methyl groups and $k = 1.2$ for all other H atoms. The ADDSYM routine in *PLATON* (Spek, 2003) suggested a possible revision of the space group to *C*2/*m* with $Z' = \frac{1}{2}$, but in the revised unit cell, angles α and γ deviated from 90° by more than 0.3° in each case; moreover, the orientation of the *tert*-butyl group relative to the adjacent ring, as indicated by the leading torsion angles (Table 1), suffices to rule out the possibility of any internal mirror symmetry for the molecule of (I).

Data collection: *COLLECT* (Hooft, 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: SK3259). Services for accessing these data are described at the back of the journal.

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