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2-Phenyl-7,8-dihydro-6*H*-cyclopenta[e]-pyrazolo[1,5-*a*]pyrimidine

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Key indicators

Single-crystal X-ray study
T = 143 K
Mean σ(C–C) = 0.004 Å
R factor = 0.054
wR factor = 0.146
Data-to-parameter ratio = 12.5

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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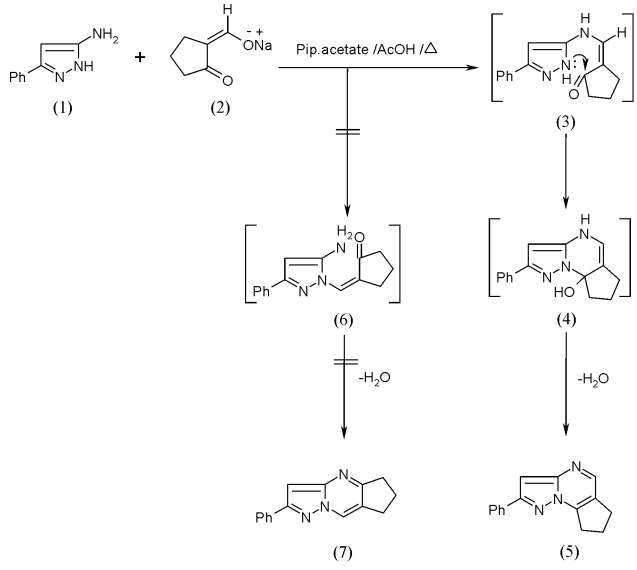
The title compound, $C_{15}H_{13}N_3$, was distinguished from its linear tricyclic isomer by X-ray structure analysis. Bond lengths and angles [*e.g.* N—N 1.355 (3) Å] are normal. The molecules are associated by C—H···N hydrogen bonds to form ribbons.

Comment

Structural changes of the natural purines have led to several potent antagonists in biological systems. Of special interest are the anti-tumour agents 6-mercaptopurine and 6-thioguanine. The synthesis of the pyrazolo[1,5-*a*]pyrimidine ring system was undertaken to provide new isomers of various biologically active purines, in the hope that new anti-tumour agents might be discovered. Additionally, it was felt that a study of such compounds would be worthwhile fundamental research.



As part of our programme for the development of new, simple and efficient procedures for the synthesis of purine analogues and other antimetabolites (Elgemeie *et al.*, 1997, 1998, 1999), we have recently reported various successful approaches for the synthesis of pyrazolopyrimidines. Such purine analogues could have interesting and useful properties as antimetabolites in biochemical reactions of purines (Elgemeie *et al.*, 1994). We report here a novel one-pot synthesis of a cyclopentane ring-fused pyrazolo[1,5-*a*]pyrimidine by reaction of the sodium salt of 2-(hydroxymethylene)-1-cyclopentanone (2) with 5-amino-3-phenylpyrazole (1) in the presence of piperidine acetate/acetic acid (see Scheme). The adduct thus formed has two possible structures, (5) or (7). Initial nucleophilic attack by the exocyclic amino group at the formyl group, followed by cyclization and elimination of

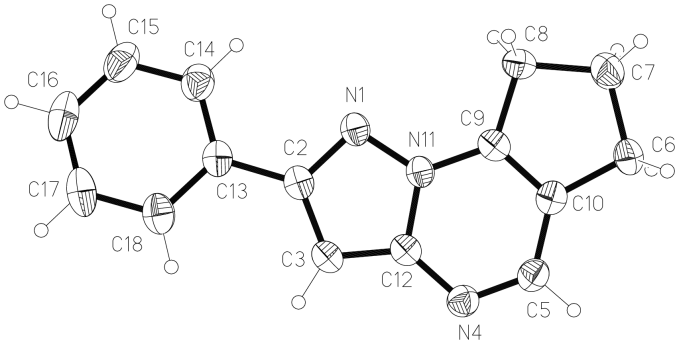


Figure 1
The molecule of compound (5) in the crystal. Ellipsoids are drawn at the 50% probability level. H atom radii are arbitrary.

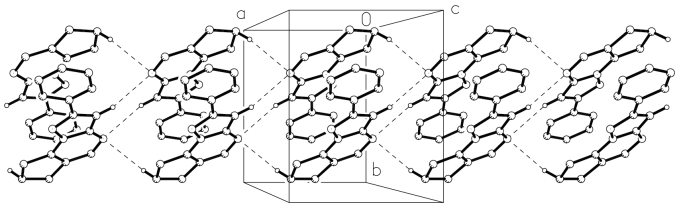


Figure 2
Packing diagram of the title compound, showing hydrogen bonds (dashed lines). H atoms not involved in H bonds are omitted.

water, would give the non-linear tricyclic compound (5); alternatively, attack of the endocyclic ring nitrogen at the formyl group followed by cyclization leads to compound (7). Only one product was obtained; its spectra (*e.g.* ^{1}H-NMR with two signals at δ 7.00 and 8.45 p.p.m. for pyrazole and pyrimidine protons) did not allow us to distinguish between (5) and (7).

The X-ray analysis, presented here, establishes the structure (5) in the solid state (Fig. 1). This implies that, under acidic conditions, protonation of the ring nitrogen (the most nucleophilic centre) directs reaction to the exocyclic amino function, which will initially attack the unhindered formyl group of (2).

Molecular dimensions, *e.g.* the N1—N11 bond length of 1.355 (3) Å, (Table 1) are normal. The tricyclic ring system is planar (r.m.s. deviation 0.025 Å) and makes an interplanar angle of 11.9 (1)° with the phenyl group.

The molecules are associated into ribbons, parallel to the *a* axis, by a bifurcated system consisting of two weak hydrogen bonds of the form C—H···N4 (Fig. 2, Table 2). Additionally, the contact C7—H7*B*···*Cg* (*Cg* is the centre of gravity of the phenyl ring), with H···*Cg* 2.86 Å and an angle of 140°, may be significant.

Experimental

A solution of 5-amino-3-phenylpyrazole [(1); 1.47 g, 0.01 mol], the sodium salt of 2-(hydroxymethylene)-1-cyclopentanone [(2); 3.4 g, 0.01 mol] and piperidine acetate (1 ml; prepared from 4.2 ml glacial acetic acid, 10 ml water and 7.2 ml piperidine) was refluxed in water (50 ml) for 10 min. Acetic acid (1.5 ml) was added to the hot solution and reflux was continued for 3 h. The reaction mixture was allowed to cool to room temperature. The precipitate was collected by filtration and crystallized from ethanol in 80% yield (m.p. 448 K).

Crystal data

$C_{15}H_{13}N_3$
M_r = 235.28
Monoclinic, $P2_1/n$
a = 7.006 (3) Å
b = 8.702 (3) Å
c = 19.115 (4) Å
β = 99.36 (3)°
V = 1149.9 (7) Å^3
Z = 4
D_x = 1.359 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 46 reflections
θ = 10–11.5°
μ = 0.08 mm^{-1}
T = 143 (2) K
Prism, colourless
0.60 × 0.25 × 0.15 mm

Data collection

Stoe Stadi-4 diffractometer
ω/θ scans
Absorption correction: none
2717 measured reflections
2032 independent reflections
1483 reflections with $I > 2\sigma(I)$
R_{int} = 0.031
θ_{max} = 25.0°
$h = -8 \rightarrow 0$
$k = -10 \rightarrow 2$
$l = -22 \rightarrow 22$
3 standard reflections
frequency: 60 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.054
$wR(F^2)$ = 0.146
S = 1.04
2032 reflections
163 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.063P)^2 + 0.6661P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

N1—C2	1.354 (3)	N4—C12	1.354 (3)
N1—N11	1.355 (3)	C5—C10	1.397 (4)
C2—C3	1.395 (3)	C9—C10	1.363 (3)
C3—C12	1.378 (3)	C9—N11	1.365 (3)
N4—C5	1.313 (3)	N11—C12	1.397 (3)
C2—N1—N11	103.29 (19)	C9—C10—C5	119.7 (2)
N1—C2—C3	112.6 (2)	N1—N11—C9	126.8 (2)
C3—C2—C13	127.5 (2)	N1—N11—C12	113.05 (19)
C12—C3—C2	106.0 (2)	C9—N11—C12	120.1 (2)
C5—N4—C12	117.4 (2)	N4—C12—C3	133.2 (2)
N4—C5—C10	123.2 (2)	N4—C12—N11	121.7 (2)
C10—C9—N11	117.8 (2)	C3—C12—N11	105.1 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C3—H3···N4^{i}	0.95	2.62	3.548 (3)	165
C7—H7*A*···N4^{ii}	0.99	2.69	3.464 (4)	135

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

H atoms were included using a riding model, with fixed C—H bond lengths (aromatic 0.95, methylene 0.99 Å); U(H) values were fixed at $1.2U_{eq}$ of the parent atom.

Data collection: *DIF*4 (Stoe, 1992); cell refinement: *DIF*4; data reduction: *REDU*4 (Stoe, 1992); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *XP* (Siemens, 1994); software used to prepare material for publication: *SHELXL*97.

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