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10-(4-Chlorophenyl)-7-methyl-5,6-dihydrobenzo[*h*]pyrazolo[5,1-*b*]quinazoline and 2-(4-chlorophenyl)-5-methyl-6,7-dihydrobenzo[*h*]pyrazolo[1,5-*a*]quinazoline: isomeric molecules linked into hydrogen-bonded dimers or π-stacked chains

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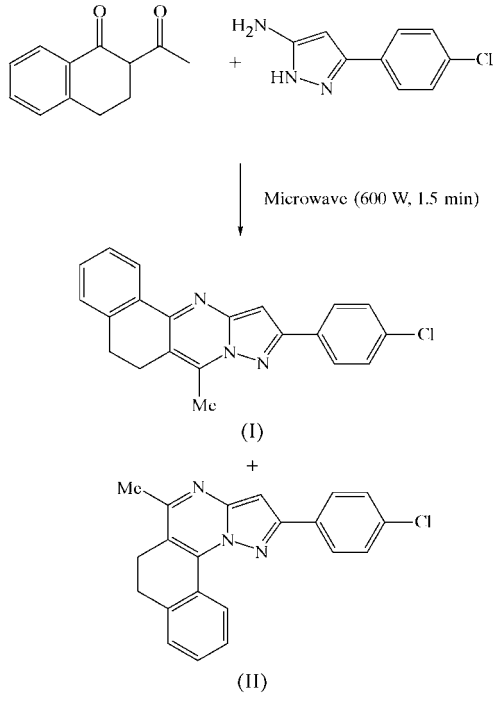
The isomeric title compounds 10-(4-chlorophenyl)-7-methyl-5,6-dihydrobenzo[*h*]pyrazolo[5,1-*b*]quinazoline, (I), and 2-(4-chlorophenyl)-5-methyl-6,7-dihydrobenzo[*h*]pyrazolo[1,5-*a*]-quinazoline, (II), both $C_{21}H_{16}ClN_3$, exhibit peripheral delocalization in the heteroaromatic portion of the fused ring system. The molecules of (I) are linked into centrosymmetric dimers by a single C—H···π(arene) hydrogen bond, and the molecules of (II), where $Z' = 2$, are linked by π–π stacking interactions into chains in which the two types of molecules alternate.

Comment

The quinazoline skeleton is an important pharmacophore which occurs frequently in medicinal chemistry literature (Fry *et al.*, 1994). In particular, pyrazolo[1,5-*c*]quinazolinones have been shown to be potent amino acid antagonists (McQuaid *et al.*, 1992), and anti-inflammatory, antiasthmatic and anti-allergenic agents and immunosuppressants (Casey *et al.*, 1980). Continuing our studies of the application of free-solvent cyclocondensation procedures under microwave irradiation, we have now prepared two benzo-fused pyrazolo[5,1-*b*]-quinazolines from a 5-aminopyrazole and 2-acetyl-1-tetralone, resulting in a regioisomeric mixture 10-(4-chlorophenyl)-7-methyl-5,6-dihydrobenzo[*h*]pyrazolo[5,1-*b*]quinazoline, (I), and 2-(4-chlorophenyl)-5-methyl-6,7-dihydrobenzo[*h*]pyrazolo[1,5-*a*]quinazoline, (II), in an approximate ratio of 1:4.

The isomeric compounds (I) and (II) both crystallize in space group $P\overline{1}$, but with Z' values of 1 and 2, respectively. Within the molecule of (I) (Fig. 1), the C10—C11 and C11—C12 bonds, which in the classically bond-localized form are double and single bonds, respectively, differ in length by only



ca 0.01 Å (Table 1). Similarly, the C12—N1 and N9—C10 bonds, which are formally double and single bonds, respectively, are nearly identical in length. At the same time, the N1a—C10 bond is much longer than the other formally single N—C bonds, N1a—C2 and N9—C10. Taken together, these observations indicate an important contribution to the overall molecular–electronic structure of the heterobicyclic portion of the molecule, of a fairly delocalized 10-π periphery with a rather weak cross-ring bond. A similar pattern of distances, leading to a similar conclusion, is apparent in each of the two independent molecules, 1 and 2, of compound (II) (Fig. 2 Table 3).

By contrast, the bond lengths in the terminal carbocyclic rings of the fused ring system, ring C4a/C5–C8/C8a in (I) and rings C*n*1c/C*n*2–C*n*5/C*n*5a in (II), where $n = 1$ or 2 for the

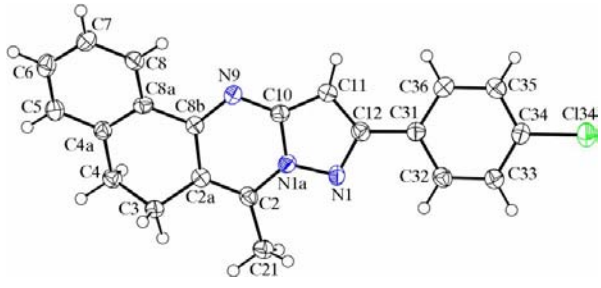


Figure 1
A view of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

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molecules of types 1 and 2 (Fig. 2), are consistent with typical aromatic delocalization. For the intervening non-planar rings, the ring-puckering parameters (Cremer & Pople, 1975) for the atom sequence C2a/C3/C4/C4a/C8a/C8b in (I), θ = 113.7 (4)° and φ = 268.4 (4)°, correspond to a conformation intermediate between the half-chair and screw-boat forms (Evans & Boeyens, 1989). For the atom sequences C*n*1b/C*n*1c/C*n*5a/C*n*6/C*n*7/C*n*7a in (II), the corresponding values are θ = 68.6 (4)° and φ = 205.6 (4)° for n = 1, and θ = 68.5 (4)° and φ = 206.6 (4)° for n = 2, corresponding very closely to the screw-boat conformation.

The molecules in (I) are linked into centrosymmetric dimers by means of a single C—H···π(arene) hydrogen bond (Table 2). Atom C3 in the molecule at (x, y, z) acts as hydrogen-bond donor, *via* the axial atom H3*A*, to the chlorinated ring (C31–C36) in the molecule at ($1-x$, $1-y$, $1-z$), so generating a dimer centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) (Fig. 3). There are no direction-specific interactions between these dimers.

In compound (II), the molecules are linked into chains by the concerted action of two independent π–π stacking interactions. The heterocyclic ring containing atom N19 in the type 1 molecule at (x, y, z) makes a dihedral angle of 1.5 (2)° with each of the chlorinated rings in the two type 2 molecules at (x, y, z) and ($1+x$, y, z). The interplanar spacings are both *ca* 3.47 Å, and the ring-centroid separations are 3.544 (2) Å within the asymmetric unit, and 3.546 (2) Å to the molecule at ($1+x$, y, z). These interactions are augmented by an entirely complementary pair of interactions between the ring containing atom N29 in the type 2 molecules at (x, y, z) and ($1+x$, y, z), and the chlorinated ring in the type 1 molecule at (x, y, z). Here, the dihedral angles between adjacent ring planes are both 7.2 (2)°, with interplanar spacings of *ca* 3.5 Å within the asymmetric unit and *ca* 3.47 Å to the adjacent unit. The respective ring-centroid separations are 3.589 (2) and 3.503 (2) Å. The effect of these interactions is to link the molecules into a chain running parallel to the [100] direction,

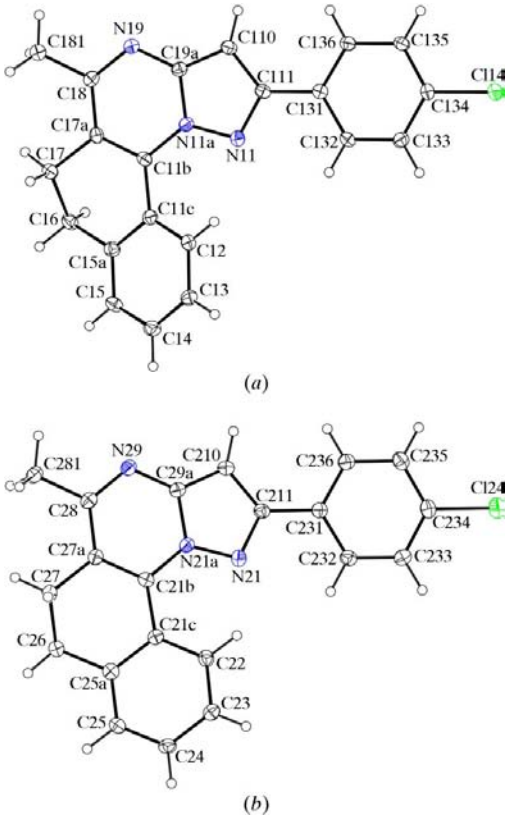

Figure 2
The two independent molecules of (II), showing the atom-labelling scheme in (*a*) a type 1 molecule and (*b*) a type 2 molecule. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

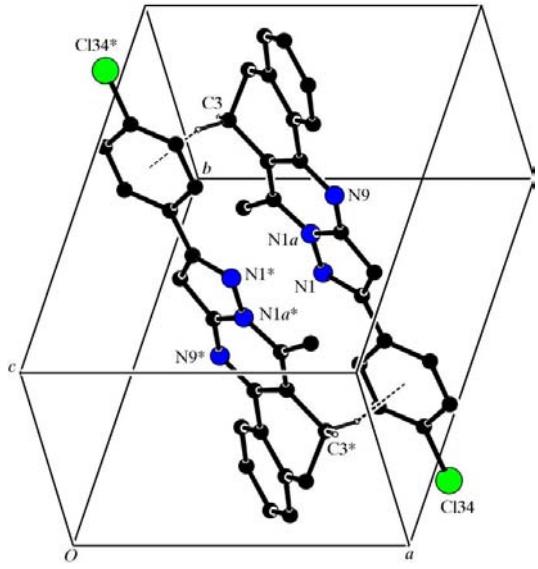

Figure 3
Part of the crystal structure of (I), showing the formation of a cyclic centrosymmetric dimer. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) are at the symmetry position ($1-x$, $1-y$, $1-z$).

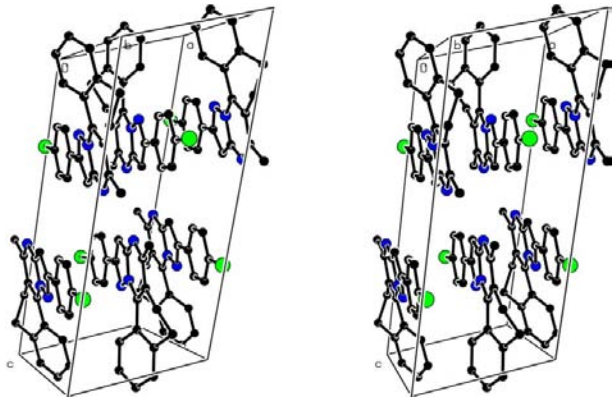

Figure 4
A stereoview of part of the crystal structure of (II), showing an antiparallel pair of π-stacked chains along [100]. For the sake of clarity, H atoms have been omitted.

in which molecules of the two types alternate. Two antiparallel chains of this type pass through each unit cell (Fig. 4), but there are no direction-specific interactions between adjacent chains.

Experimental

Equimolar quantities of 5-amino-3-(4-chlorophenyl)-1*H*-pyrazole (500 mg, 2.6 mmol) and 2-acetyl-1-tetralone (485 mg, 2.6 mmol) were placed in Pyrex open vessels and irradiated in a domestic microwave oven for 1.5 min at 600 W. The product mixture was extracted with ethanol. After the solvent had been removed, the products were separated by column chromatography on silica gel, using hexane–ethyl acetate (3:1 *v*/*v*) as eluant. Compound (I) was obtained as the first fraction (yield 18%, m.p. 449 K). MS (EI, 70 eV, %): 348/346 (8/35, *M*+1), 347/345 (39/100, M^+), 344 (28), 166 (11), 75 (8). Analysis found: C 72.9, H 4.6, N 12.2%; $C_{21}H_{16}ClN_3$ requires: C 72.9, H 4.7, N 12.2%. Yellow crystals of (I) suitable for single-crystal X-ray diffraction were obtained by direct evaporation of the chromatographic eluate. Compound (II) was obtained as the second fraction (yield 70%, m.p. 505 K). MS (EI, 70 eV, %): 348/346 (8/32, *M*+1), 347/345 (37/100, M^+), 344 (24), 166 (22), 75 (30). Analysis found: C 72.8, H 4.6, N 12.1%; $C_{21}H_{16}ClN_3$ requires: C 72.9, H 4.7, N 12.2%. Brown crystals of (II) suitable for single-crystal X-ray diffraction were obtained by direct evaporation of the chromatographic eluate.

Compound (I)

Crystal data

$C_{21}H_{16}ClN_3$
M_r = 345.82
Triclinic, $P\overline{1}$
a = 9.2382 (8) Å
b = 10.3054 (8) Å
c = 10.3184 (9) Å
α = 62.720 (4)°
β = 83.098 (4)°
γ = 70.531 (5)°
V = 822.54 (12) Å^3
Z = 2
D_x = 1.396 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3763 reflections
θ = 3.3–27.6°
μ = 0.24 mm^{-1}
T = 120 (2) K
Plate, yellow
0.34 × 0.19 × 0.08 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.914, T_{max} = 0.981
17 454 measured reflections
3763 independent reflections
2156 reflections with $I > 2\sigma(I)$
R_{int} = 0.094
θ_{max} = 27.6°
$h = -11 \rightarrow 11$
$k = -13 \rightarrow 12$
$l = -13 \rightarrow 13$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.065
$wR(F^2)$ = 0.153
S = 0.96
3763 reflections
229 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0709P)^2 + 0.3108P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.30 e Å^{-3}
$\Delta\rho_{min}$ = −0.30 e Å^{-3}

Table 1
Selected geometric parameters (Å) for (I).

N1—N1a	1.357 (3)	N9—C10	1.351 (3)
N1a—C2	1.365 (3)	C10—C11	1.381 (4)
C2—C2a	1.365 (4)	C11—C12	1.393 (4)
C2a—C8b	1.442 (4)	C12—N1	1.345 (3)
C8b—N9	1.319 (3)	N1a—C10	1.394 (3)

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

*Cg*1 is the centroid of the C31–C36 ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C3—H3*A*···*Cg*1^{i}	0.99	2.92	3.815 (3)	150

Symmetry code: (i) $1-x, 1-y, 1-z$.

Compound (II)

Crystal data

$C_{21}H_{16}ClN_3$
M_r = 345.82
Triclinic, $P\overline{1}$
a = 7.0098 (3) Å
b = 15.0306 (7) Å
c = 17.0060 (8) Å
α = 111.492 (2)°
β = 101.406 (3)°
γ = 97.981 (3)°
V = 1589.81 (13) Å^3
Z = 4
D_x = 1.445 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 7321 reflections
θ = 3.0–27.6°
μ = 0.25 mm^{-1}
T = 120 (2) K
Needle, pale brown
0.14 × 0.04 × 0.03 mm

Data collection

Nonius KappaCCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.949, T_{max} = 0.993
35 785 measured reflections
7321 independent reflections
4073 reflections with $I > 2\sigma(I)$
R_{int} = 0.113
θ_{max} = 27.6°
$h = -8 \rightarrow 9$
$k = -19 \rightarrow 19$
$l = -22 \rightarrow 22$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.061
$wR(F^2)$ = 0.152
S = 1.03
7321 reflections
453 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0614P)^2 + 0.1965P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.30 e Å^{-3}
$\Delta\rho_{min}$ = −0.37 e Å^{-3}

Table 3
Selected geometric parameters (Å) for (II).

N11—N11a	1.359 (3)	N21—N21a	1.355 (3)
N11a—C11b	1.381 (3)	N21a—C21b	1.378 (3)
C11b—C17a	1.378 (4)	C21b—C27a	1.381 (4)
C17a—C18	1.419 (4)	C27a—C28	1.422 (4)
C18—N19	1.321 (3)	C28—N29	1.316 (3)
N19—C19a	1.351 (3)	N29—C29a	1.350 (3)
C19a—C110	1.379 (4)	C29a—C210	1.377 (4)
C110—C111	1.398 (4)	C210—C211	1.390 (4)
C111—N11	1.348 (3)	C211—N21	1.348 (3)
N11a—C19a	1.393 (3)	N21a—C29a	1.403 (3)

Crystals of compounds (I) and (II) are triclinic. For each, the space group $P\overline{1}$ was selected and confirmed by the structure analysis. All H atoms were located from difference maps and subsequently treated as riding atoms, with C—H distances of 0.95 (aromatic and heteroaromatic), 0.98 (CH_3) or 0.99 Å (CH_2), and with $U_{iso}(H) = 1.2U_{eq}(C)$, or $1.5U_{eq}(C)$ for the methyl groups.

For both compounds, data collection: *COLLECT* (Nonius, 1998); cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s)

used to solve structure: *OSCAIL* (McArdle, 2003) and *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *OSCAIL* and *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL*97 and *PRPKAPPA* (Ferguson, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1742). Services for accessing these data are described at the back of the journal.

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