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Hydrogen-bonded chains in 3-*tert*-butyl-5-[(4-methoxybenzyl)amino]-1-phenyl-1*H*-pyrazole and tetramolecular hydrogen-bonded aggregates in 5-[(benzotriazol-1-ylmethyl)(4-methoxybenzyl)amino]-3-*tert*-butyl-1-phenyl-1*H*-pyrazole

Rodrigo Abonía,[a] Emerson Rengifo,[a] Justo Cobo,[b] John N. Low[c] and Christopher Glidewell[d]*

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

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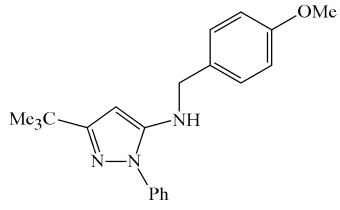
The molecules of 3-*tert*-butyl-5-[(4-methoxybenzyl)amino]-1-phenyl-1*H*-pyrazole, $C_{21}H_{25}N_3O$, are linked into simple *C*(9) chains by a single C—H···N hydrogen bond. 5-[(Benzotriazol-1-ylmethyl)(4-methoxybenzyl)amino]-3-*tert*-butyl-1-phenyl-1*H*-pyrazole, $C_{28}H_{30}N_6O$, crystallizes with $Z' = 2$ in the space group $P2_1/c$. The molecules are weakly linked into centrosymmetric tetramolecular aggregates by a combination of C—H···N and C—H···O hydrogen bonds.

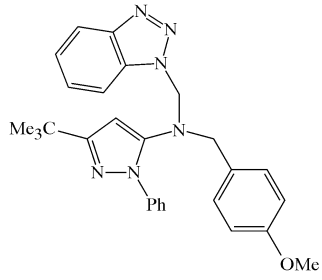
Comment

We are interested in the synthesis of compounds containing the pyrazolo[3,4-*b*]pyridine skeleton, which may have potential biological activity, and we have recently described the synthesis and structure of 3-methyl-1,4-diphenyl-1*H*-pyrazolo[3,4-*b*]pyridine, prepared by the reaction of 5-(3-phenyl-2-propynylidene)-2,2-dimethylcyclohexane-1,3-dione with 5-amino-3-methyl-1-phenylpyrazole (Low *et al.*, 2002). We report here the structures of two potential intermediates for the synthesis of fused pyrazolo ring systems *via* benzotriazole chemistry (Katritzky *et al.*, 1998), namely 3-*tert*-butyl-5-[(4-methoxybenzyl)amino]-1-phenyl-1*H*-pyrazole, (I), and 5-[(benzotriazol-1-ylmethyl)(4-methoxybenzyl)amino]-3-*tert*-butyl-1-phenyl-1*H*-pyrazole, (II) (Figs. 1 and 2).

Compound (I), whose molecules are chiral in the solid state, crystallizes in the enantiomeric pair of space groups $P4_12_12$ and $P4_32_12$; in the absence of racemic twinning, each crystal thus contains only one enantiomer. However, since the chirality is a consequence of the molecular conformation, it has no chemical significance, and it may be expected that the distribution of the crystalline product between the two space groups is essentially statistical. The coordination at amino atom N15 is markedly pyramidal and there is significant bond fixation within the pyrazole ring (Table 1), but the remaining bond distances are unremarkable.



(I)



(II)

Compound (II) crystallizes with $Z' = 2$ in the space group $P2_1/c$; the asymmetric unit (Fig. 2) was selected so that the two molecules within it are linked by C—H···O hydrogen bonds (Table 4) and in these circumstances the two molecules in the selected asymmetric unit are approximately, but not exactly, enantiomeric, as shown by the leading torsion angles (Table 3); the space-group symmetry ensures that the compound, as crystallized, is a true racemate. We denote the molecules containing atoms N15 and N45 as types 1 and 2, respectively. The intramolecular geometry is similar for the two molecules, albeit with some minor differences; in each molecule, the coordination at the central N atoms is distinctly pyramidal and there is significant bond fixation both within the pyrazole rings

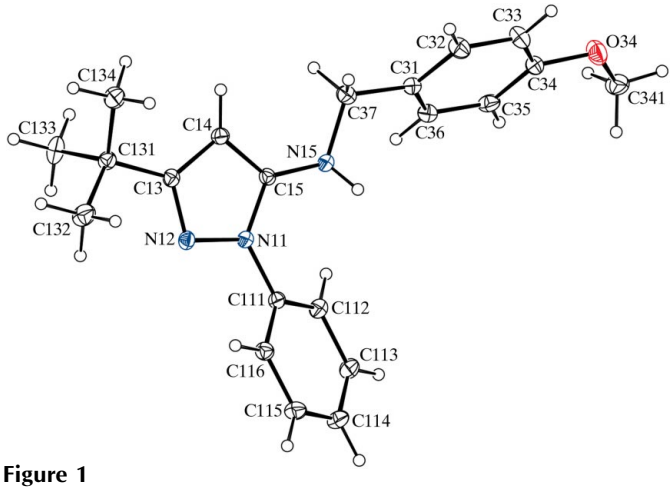


Figure 1
A molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

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and within the benzotriazole units (Table 3), where the bond fixation in the carbocyclic rings is reminiscent of that in naphthalene.

In both compounds, the C atoms of the methoxy substituents are almost coplanar with the adjacent aryl rings; the angles at the O atoms are both well above the normal value at ethereal O atoms, and the exocyclic C—C—O angles at C34 and C64 show the usual differences of *ca* 10°.

The molecules of compound (I) are linked by a single C—H···N hydrogen bond (Table 2) into simple *C*(9) (Bernstein *et al.*, 1995) chains generated by translation (Fig. 3). Eight chains of this type pass through each unit cell, but there are no direction-specific interactions between the chains. In particular, there are no potential acceptors within hydrogen-bonding range of amino atom N15, and C—H···π(arene) hydrogen bonds and aromatic π–π stacking interactions are both absent from the structure of (I).

Within the selected asymmetric unit of compound (II), there are two intermolecular C—H···O contacts (Table 4),

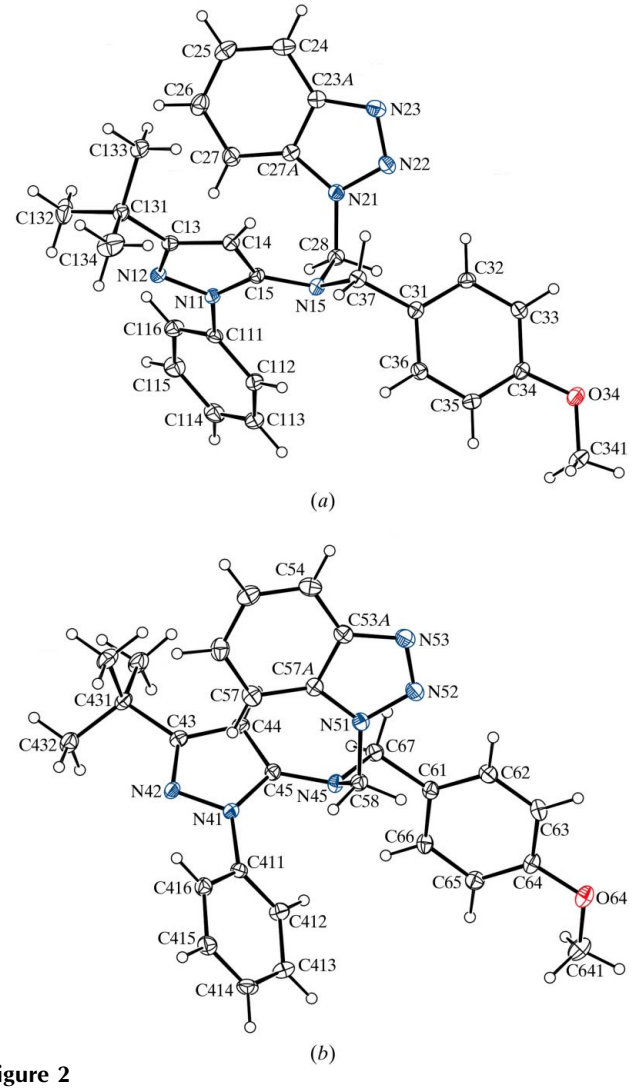

Figure 2
The two independent molecules of (II), showing the atom-labelling schemes for (*a*) a type 1 molecule and (*b*) a type 2 molecule. Displacement ellipsoids are drawn at the 30% probability level.

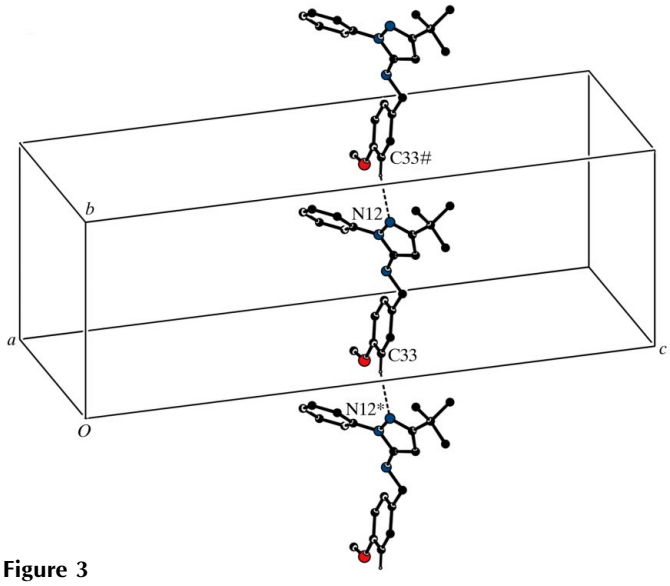

Figure 3
Part of the crystal structure of (I), showing the formation of a hydrogen-bonded *C*(9) chain along [010]. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with as asterisk (*) or a hash (#) are at the symmetry positions (x, $-1+y$, z) and (x, $1+y$, z), respectively.

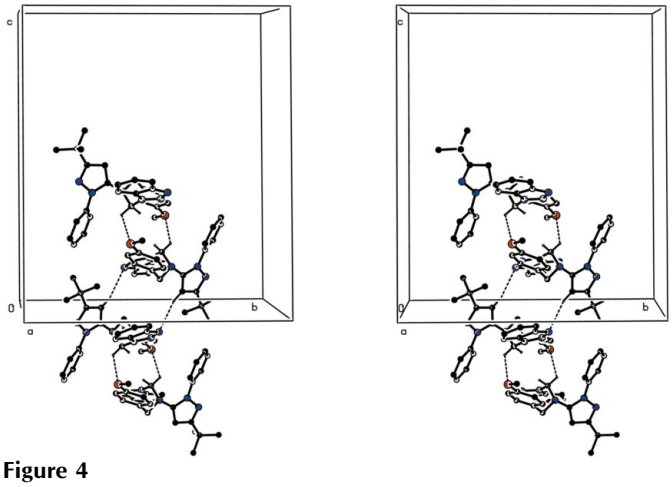

Figure 4
A stereoview of part of the crystal structure of (II), showing the formation of a centrosymmetric tetramolecular aggregate. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

one of which is certainly too long and weak to be regarded as a hydrogen bond; there are no other interactions linking these molecules, which form an approximately centrosymmetric pair centred close to ($\frac{1}{4}$, $\frac{1}{2}$, $\frac{1}{4}$). In addition, pairs of type 1 molecules are linked by paired C—H···N hydrogen bonds into centrosymmetric $R_2^2(16)$ dimers centred at (0, $\frac{1}{2}$, 0), so forming a tetramolecular aggregate with the two type 1 molecules in the centre and the type 2 molecules at the periphery (Fig. 4), but there are no direction-specific interactions between these aggregates.

Experimental

For the synthesis of compound (I), sodium borohydride (4.5 mmol) was added in small portions over a period of 2 h to a solution of 3-*tert*-

butyl-5-[(4-methoxybenzylidene)amino]-1-phenylpyrazole (1.50 mmol) in methanol (30 ml). After the addition had been completed, the reaction mixture was heated under reflux for 3 h. The mixture was then cooled to ambient temperature and water (20 ml) was added; the mixture was neutralized with 5% aqueous hydrochloric acid (5 ml) and then extracted with ethyl acetate (3 × 10 ml). The combined extracts were dried with sodium sulfate and the organic solvent was then removed under reduced pressure, giving compound (I) as a pale-yellow solid (yield 98%, m.p. 372 K). MS (70 eV) *m*/*e* (%): 335 (13), 121 (100); IR (cm^{-1}): 3319 (NH), 1245, 1033 (OCH_3). Crystals suitable for single-crystal X-ray diffraction were grown by slow evaporation of a solution in ethyl acetate–hexane (1:2 *v*/*v*). For the synthesis of compound (II), a mixture of compound (I) (0.06 mmol) and 1-(hydroxymethyl)benzotriazole (0.06 mmol) in ethanol (5 ml) was heated under reflux for 1 h. After cooling the mixture to ambient temperature, a colourless precipitate was formed, which was collected by filtration and washed with ethanol to give compound (II) (yield 65%, m.p. 435 K). MS (70 eV) *m*/*e* (%): 466 (3), 347 (3), 227 (43), 121 (100), 77 (22). Crystals suitable for single-crystal X-ray diffraction were grown by slow evaporation of a solution in ethanol.

Compound (I)

Crystal data

$C_{21}H_{25}N_3O$
M_r = 335.44
Tetragonal, $P4_32_12$
a = 10.9665 (14) Å
c = 30.796 (6) Å
V = 3703.7 (10) Å^3
Z = 8
D_x = 1.203 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.08 mm^{-1}
T = 120 (2) K
Block, pale-yellow
0.52 × 0.28 × 0.08 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.940, T_{max} = 0.994
77731 measured reflections
2521 independent reflections
1840 reflections with $I > 2\sigma(I)$
R_{int} = 0.096
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.052
$wR(F^2)$ = 0.120
S = 1.05
2521 reflections
230 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0508P)^2 + 1.6749P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}

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

N11—N12	1.380 (3)	C14—C15	1.383 (4)
N12—C13	1.331 (3)	C15—N11	1.371 (3)
C13—C14	1.414 (4)		
C33—C34—O34	115.3 (3)	C34—O34—C341	118.4 (3)
C35—C34—O34	124.1 (3)		
C33—C34—O34—C341	174.1 (3)		

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

D—H···A	D—H	H···A	D···A	D—H···A
C33—H33···N12^{i}	0.95	2.47	3.398 (4)	166

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

Compound (II)

Crystal data

$C_{28}H_{30}N_6O$
M_r = 466.58
Monoclinic, $P2_1/c$
a = 12.5184 (2) Å
b = 18.5142 (5) Å
c = 21.7580 (5) Å
β = 96.0730 (15)°
V = 5014.5 (2) Å^3
Z = 8
D_x = 1.236 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.08 mm^{-1}
T = 120 (2) K
Needle, colourless
0.28 × 0.16 × 0.08 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.966, T_{max} = 0.994
55879 measured reflections
11492 independent reflections
7071 reflections with $I > 2\sigma(I)$
R_{int} = 0.077
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.059
$wR(F^2)$ = 0.113
S = 1.03
11492 reflections
639 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0458P)^2 + 0.5141P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.19 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}

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

N11—N12	1.3795 (17)	N41—N42	1.3838 (18)
N12—C13	1.3290 (19)	N42—C43	1.3315 (19)
C13—C14	1.408 (2)	C43—C44	1.409 (2)
C14—C15	1.372 (2)	C44—C45	1.371 (2)
C15—N11	1.369 (2)	C45—N41	1.367 (2)
N21—N22	1.3655 (18)	N51—N52	1.3629 (19)
N22—N23	1.3039 (18)	N52—N53	1.3093 (18)
N23—C23*A*	1.380 (2)	N53—C53*A*	1.382 (2)
C23*A*—C24	1.398 (2)	C53*A*—C54	1.404 (2)
C24—C25	1.364 (2)	C54—C55	1.372 (3)
C25—C26	1.403 (3)	C55—C56	1.406 (2)
C26—C27	1.378 (2)	C56—C57	1.372 (2)
C27—C27*A*	1.398 (2)	C57—C57*A*	1.395 (2)
C27*A*—N21	1.3712 (19)	C57*A*—N51	1.3705 (19)
C23*A*—C27*A*	1.389 (2)	C53*A*—C57*A*	1.390 (2)
C15—N15—C28	112.94 (12)	C45—N45—C58	115.37 (12)
C15—N15—C37	113.97 (12)	C45—N45—C67	115.34 (13)
C28—N15—C37	114.00 (13)	C58—N45—C67	114.52 (13)
C33—C34—O34	115.70 (15)	C63—C64—O64	115.66 (16)
C35—C34—O34	124.44 (14)	C65—C64—O64	124.11 (15)
C34—O34—C341	116.83 (13)	C64—O64—C641	116.64 (14)
N12—N11—C111—C112	−143.20 (15)	N42—N41—C411—C412	132.59 (15)
N12—C13—C131—C132	−13.3 (2)	N42—C43—C431—C432	−35.5 (2)
N11—C15—N15—C28	65.91 (18)	N41—C45—N45—C58	−63.80 (19)
C15—N15—C28—N21	65.98 (17)	C45—N45—C58—N51	−70.54 (18)
N15—C28—N21—N22	91.31 (17)	N45—C58—N51—N52	−103.19 (17)
N11—C15—N15—C37	−161.90 (13)	N41—C45—N45—C67	159.09 (13)
C15—N15—C37—C31	160.59 (13)	C45—N45—C67—C61	−149.29 (14)
N15—C37—C31—C32	101.72 (18)	N45—C67—C61—C62	−107.87 (17)

For compound (I), the systematic absences permitted $P4_12_12$ and $P4_32_12$ as possible space groups. In the absence of significant resonant scattering, it was not possible to distinguish between these enantiomeric space groups for the crystal selected for data collection; $P4_32_12$ was selected, although this choice has no chemical significance, and the Friedel equivalent reflections were merged. For compound (II), the space group $P2_1/c$ was uniquely assigned from the systematic

Table 4
Hydrogen-bond geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
C14—H14···N23^{i}	0.95	2.61	3.531 (2)	162
C28—H28A···O64	0.99	2.55	3.273 (3)	129
C58—H58A···O34	0.99	2.64	3.252 (3)	120

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

absences; 16 low-angle reflections were partially obscured by the beam stop and hence these reflections were omitted from the refinement. All H atoms were located in difference maps; H atoms bonded to C atoms were then treated as riding atoms in geometrically idealized positions, 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) = kU_{eq}(C), where k is 1.5 for the methyl groups and 1.2 for all other H atoms bonded to C atoms. The H atom bonded to N15 in compound (I) was allowed to ride at the position deduced from the difference maps, giving an N—H distance of 0.88 Å [U_{iso}(H) = 1.2U_{eq}(N)].

For (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, 1997). For (II), data collection: *COLLECT* (Hooft, 1999); cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *OSCAIL* (McArdle, 2003) and *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *OSCAIL* and *SHELXL97*. For both compounds, molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PRPKAPPA* (Ferguson, 1999).

X-ray data for compound (I) were collected at 'Servicios Técnicos de Investigación' of the Universidad de Jaén, Spain, and for compound (II) at the EPSRC National Crystallography Service, University of Southampton, England. JC thanks the Consejería de Innovación, Ciencia y Empresa (Junta de Andalucía, Spain) and the Universidad de Jaén for financial support. RA and ER thank COLCIENCIAS and UNIVALLE (Universidad del Valle, Colombia) for financial support and RA thanks AUIP for supporting a research trip.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: LN3029). Services for accessing these data are described at the back of the journal.

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