Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Molecular conformation and supramolecular aggregation in two fused pyrazoles: π-stacked $R_2^2(6)$ dimers in 2,8,8-trimethyl-6,7,8,9-tetrahydropyrazolo[2,3-*a*]quinazolin-6-one, and sheets of alternating $R_2^2(12)$ and $R_6^6(48)$ rings in 3-*tert*-butyl-4′,4′-dimethyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-spiro-1′-cyclohexane-2′,6′-dione

John N. Low,[a]‡ Justo Cobo,[b] Jaime Mera,[c] Jairo Quiroga[c] and Christopher Glidewell[d]*

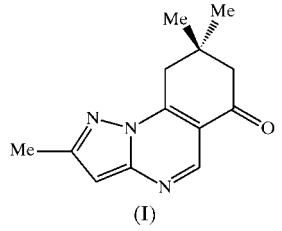
[a]Department of Chemistry, University of Aberdeen, Meston Walk, Old Aberdeen AB24 3UE, Scotland, [b]Departamento de Química Inorgánica y Orgánica, Universidad de Jaén, 23071 Jaén, Spain, [c]Grupo de Investigación de Compuestos Heterocíclicos, Departamento de Química, Universidad de Valle, AA 25360,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

Received 18 February 2004
Accepted 20 February 2004
Online 20 March 2004

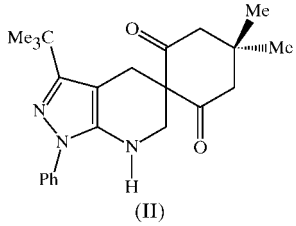
In 2,8,8-trimethyl-6,7,8,9-tetrahydropyrazolo[2,3-*a*]quinazolin-6-one, $C_{13}H_{15}N_3O$, (I), the heterobicyclic system is planar and exhibits peripheral ten π-electron delocalization. In 3-*tert*-butyl-4′,4′-dimethyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-spiro-1′-cyclohexane-2′,6′-dione, $C_{23}H_{25}N_3O_2$, (II), the pyrazole ring exhibits marked bond fixation, while the reduced pyridine ring adopts a half-chair conformation. Molecules of (I) are linked into centrosymmetric $R_2^2(6)$ dimers by a single C—H···N hydrogen bond [H···N = 2.50 Å, C···N = 3.3397 (17) Å and C—H···N = 148°], and these dimers are linked into chains by a single π–π stacking interaction. In (II), the combined action of one N—H···O hydrogen bond [H···O = 2.40 Å, N···O = 3.2248 (15) Å and N—H···O = 157°] and one C—H···O hydrogen bond [H···O = 2.48 Å, C···O = 3.407 (2) Å and C—H···O = 164°] links the molecules into sheets built from alternating centrosymmetric $R_2^2(12)$ and $R_6^6(48)$ rings; there is a weak C—H···N interaction [H···N = 2.60 Å, C···N = 3.5149 (18) Å and C—H···N = 154°] between molecules in adjacent sheets.

Comment

As part of a program aimed at the synthesis of fused pyrazolo derivatives (Quiroga *et al.*, 1999), we have been investigating three-component cyclocondensations induced by microwave irradiation. From the reactions between formaldehyde, 5,5-dimethylcyclohexane-1,3-dione (dimedone) and either 5-amino-3-methyl-1*H*-pyrazole or 5-amino-3-*tert*-butyl-1-phenylpyrazole (which differ primarily in terms of the absence or presence of the substituent at atom N1), we have isolated two very different products, whose molecular and supramolecular structures are presented here. Using 5-amino-3-methyl-1*H*-pyrazole, which has only an H atom at N1, we obtained 2,8,8-trimethyl-6,7,8,9-tetrahydropyrazolo[2,3-*a*]quinazolin-6-one, (I), while with the *N*-phenyl-substituted 5-amino-3-*tert*-butyl-1-phenylpyrazole, the product was 3-*tert*-butyl-4′,4′-dimethyl-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-spiro-1′-cyclohexane-2′,6′-dione, (II).



(I)



(II)

The presence or otherwise of a substituent at atom N1 in the precursor pyrazole appears to determine which two nucleophilic atoms participate in the cyclocondensation. Ring atom N1 and amine atom N5 are involved in the formation of (I), while ring atom C3 along with atom N5 are involved in the formation of (II). In the formation of (II), two molecules of formaldehyde give a double Mannich-type reaction between the activated methylene group in the dimedone component and the two nucleophilic residues of the pyrazole ring, resulting in an interesting spiro-pyrazolopyridine derivative.

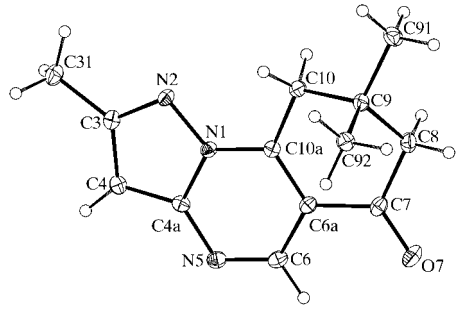


Figure 1
The molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

‡ Postal address: Department of Electrical Engineering and Physics, University of Dundee, Dundee DD1 4HN, Scotland.

 DOI: 10.1107/S0108270104004159

In (I) (Fig. 1), the two fused heterocyclic rings (N1/N2/C3/C4/C4a/N5/C6/C6a/C10a) are completely planar, with the bond angles at each of atoms N1, C3, C4a, C6a and C10a independently summing to 360.0° within experimental uncertainty. For the carbocyclic ring (C6a/C7–C10/C10a), the ring-puckering parameters (Cremer & Pople, 1975) for the atom sequence C6a—C7···C10—C10a [θ = 54.3 (2)° and φ = 163.8 (2)°] indicate an envelope conformation (Evans & Boeyens, 1989), consistent with the enforced coplanarity of atoms C6a, C7, C10a and C10. This ring thus exhibits a pseudo-mirror plane passing through atoms C6a, C9, C91 and C92 (Fig. 1).

The bond lengths in the fused heterocyclic rings in (I) show some unusual values (Table 1). Thus, for example, the formally single C4a—N5 and C10a—N1 bonds are only slightly longer than the formally double C3═N2 bond, although each of these single bonds is significantly shorter than the formally single C4a—N1 bond. Similarly, the lengths of the C3—C4 and C4═C4a bonds, formally single and double bonds, respectively, differ by less than 0.03 Å. These observations, together with the planarity at atom N1, suggest that this heterocyclic system exhibits a degree of naphthalene-type delocalization, involving a peripheral system of ten π electrons with only modest participation by the cross-ring bond (Glidewell & Lloyd, 1984).

The conformation of (II) (Fig. 2) is more complex than that of (I). Although the pyrazole ring in (I) is planar, with the bond angles at each of atoms N1, C3, C3a and C7a summing independently to 360.0° within experimental uncertainty, the six-membered heterocyclic ring is not planar, in contrast to the heterocyclic ring in (I), and includes a markedly non-planar N atom (N7). For the atom sequence N7—C6—C5—C4—C3a—C7a, the ring-puckering parameters [θ = 130.7 (2)° and φ = 269.7 (2)°] indicate a half-chair conformation. As expected, the spiro-fused carbocyclic C5/C51–C55 ring adopts a nearly perfect chair conformation [θ = 5.6 (2)°; this angle is zero for the ideal chair conformation]. Finally, the dihedral angle between the pendent phenyl ring and the pyrazole ring is 11.8 (2)°, while the orientation of the *tert*-butyl group is such that atom C34 is nearly coplanar with the pyrazole ring (Table 3). The bond lengths in the heterocyclic portion of the molecule (Table 3) are consistent with complete bond fixation in the pyrazole ring according to the classical representation shown in the scheme above. The remaining geometric parameters show no unusual values.

The one-dimensional supramolecular structure of (I) is readily analysed in terms of a single C—H···N hydrogen bond (Table 2) and a single aromatic π–π stacking interaction. Atom C6 in the molecule at (x, y, z) acts as a hydrogen-bond donor to atom N5 in the molecule at ($1-x$, $1-y$, $1-z$), thereby forming a centrosymmetric dimer centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) and characterized by an $R_2^2(6)$ motif (Bernstein *et al.*, 1995; Fig. 3). The six-membered heterocyclic rings (N1/C4a/N5/C6/C6a/C10a) in the molecules at (x, y, z) and ($-x$, $1-y$, $1-z$)

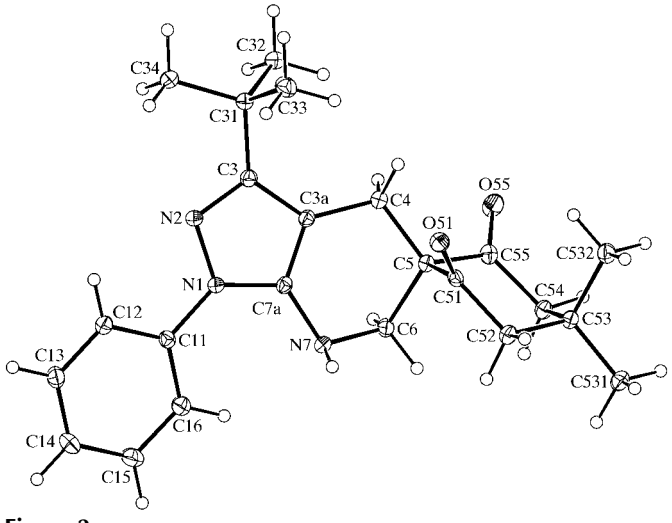


Figure 2
The molecule of (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

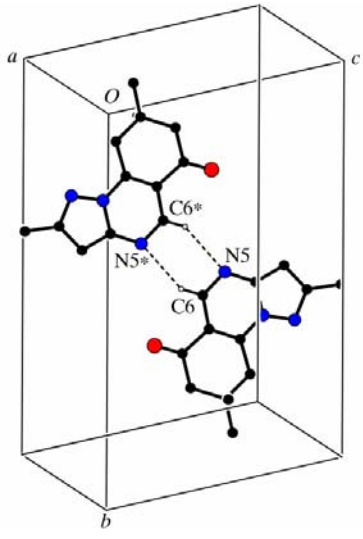


Figure 3
Part of the crystal structure of (I), showing the formation of an $R_2^2(6)$ dimer. For clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) are at the symmetry position ($1-x$, $1-y$, $1-z$).

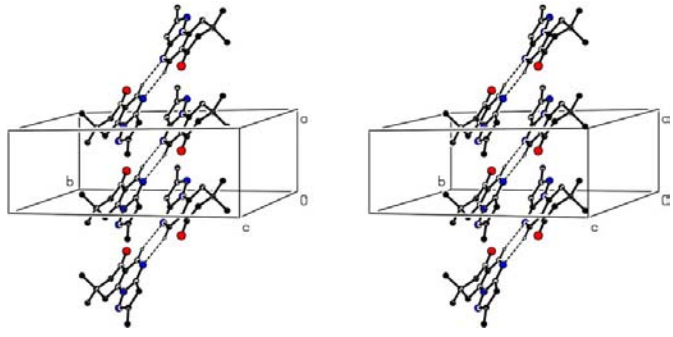


Figure 4
A stereoview of part of the crystal structure of (I), showing the formation of a π-stacked chain of $R_2^2(6)$ dimers. For clarity, H atoms not involved in the motif shown have been omitted.

are parallel, with an interplanar spacing of 3.293 (2) Å. The ring-centroid separation is 3.557 (2) Å, corresponding to a centroid offset of 1.345 (2) Å. The effect of the π–π stacking interaction is to link adjacent $R_2^2(6)$ dimers into a chain running parallel to the [100] direction (Fig. 4). Two chains of this type pass through each unit cell but there are no direction-specific interactions between adjacent chains.

The two-dimensional supramolecular aggregation in (II) involves two hydrogen bonds, one each of the N—H···O and C—H···O types; there is also a long and rather weak C—H···N contact, which may just be significant (Table 4). However, C—H···π(arene) hydrogen bonds and aromatic π–π stacking interactions are absent from the structure of (II). Atom N7 in the molecule at (x, y, z) acts as a hydrogen-bond donor to carbonyl atom O51 in the molecule at ($1-x$, $1-y$, $1-z$), so forming a centrosymmetric $R_2^2(12)$ dimer centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) (Fig. 5). Dimers of this type are linked into sheets by the C—H···O hydrogen bond.

Aryl atom C15 in the molecule at (x, y, z) acts as a hydrogen-bond donor to the second carbonyl O atom, O55, in the molecule at ($-1+x$, $\frac{1}{2}-y$, $-\frac{1}{2}+z$), while atom C15 at ($-1+x$, $\frac{1}{2}-y$, $-\frac{1}{2}+z$) in turn acts as a donor to atom O55 at ($-2+x$, y, $-1+z$). In this manner, a $C(11)$ chain is formed, running parallel to the [201] direction and generated by the c-glide plane at $y=\frac{1}{4}$ (Fig. 6). In the reference [201] chain, the molecules at (x, y, z) and ($-1+x$, $\frac{1}{2}-y$, $-\frac{1}{2}+z$) form $R_2^2(12)$ dimers with the molecules at ($1-x$, $1-y$, $1-z$) and ($-x$, $-\frac{1}{2}+y$, $\frac{1}{2}-z$), respectively. These latter two molecules lie in [20$\bar{1}$] chains generated by the c-glide planes at $y=\frac{3}{4}$ and $y=-\frac{1}{4}$, respectively. Hence, propagation by the space group of these two hydrogen-bond motifs generates a (20$\bar{1}$) sheet built from $R_2^2(12)$ and $R_6^6(48)$ rings, both of which are centrosymmetric and alternating in a chessboard fashion (Fig. 7). The resulting net is of (6,3)-type if the isolated molecules of (II) are regarded as the nodes of the net and of (4,4)-type if the $R_2^2(12)$ dimers are taken as the nodes (Batten & Robson, 1998).

Finally, there is a weak C—H···N interaction (Table 4), in which atom C54 at (x, y, z) acts as a hydrogen-bond donor, *via*

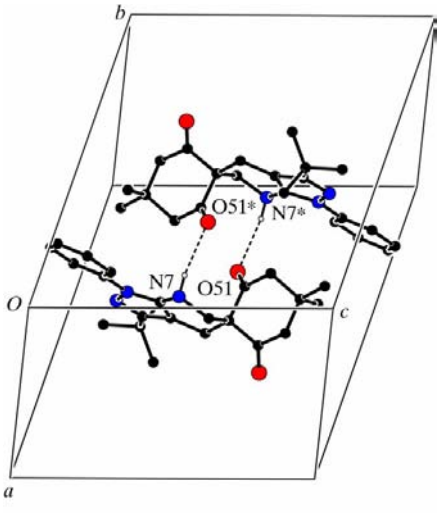


Figure 5
Part of the crystal structure of (II), showing the formation of an $R_2^2(12)$ dimer. For clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) are at the symmetry position ($1-x$, $1-y$, $1-z$).

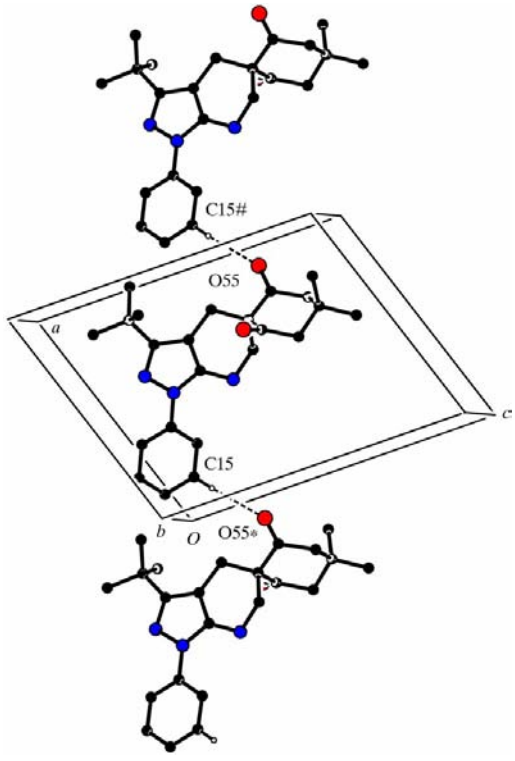


Figure 6
Part of the crystal structure of (II), showing the formation of a $C(11)$ chain along [201]. For clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) or a hash (#) are at the symmetry positions ($-1+x$, $\frac{1}{2}-y$, $-\frac{1}{2}+z$) and ($1+x$, $\frac{1}{2}-y$, $\frac{1}{2}+z$), respectively.

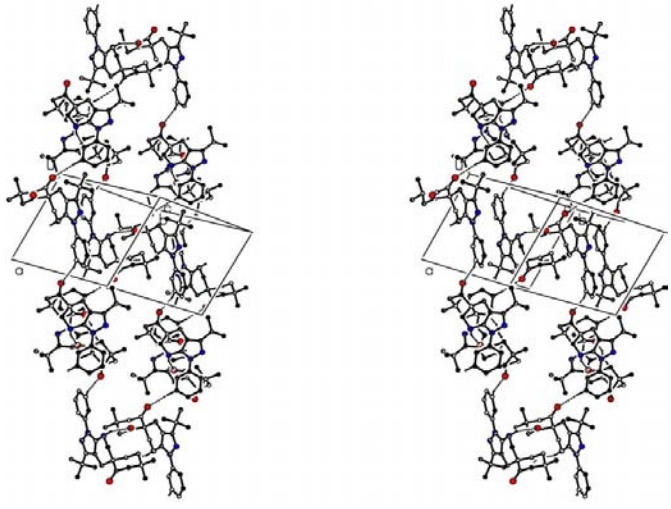


Figure 7
A stereoview of part of the crystal structure of (II), showing the formation of a (20$\bar{1}$) sheet of alternating $R_2^2(12)$ and $R_6^6(48)$ rings.

H54*B*, to ring atom N1 in the molecule at $(x, \frac{1}{2}-y, \frac{1}{2}+z)$. The coplanarity of atom N1 means that it is unlikely to be very basic, and hence it is likely to be a poor hydrogen-bond acceptor; accordingly, the H···N and C···N distances in this interaction are significantly longer than those in the C—H···N hydrogen bond of (I) (Table 2). On the other hand, if this

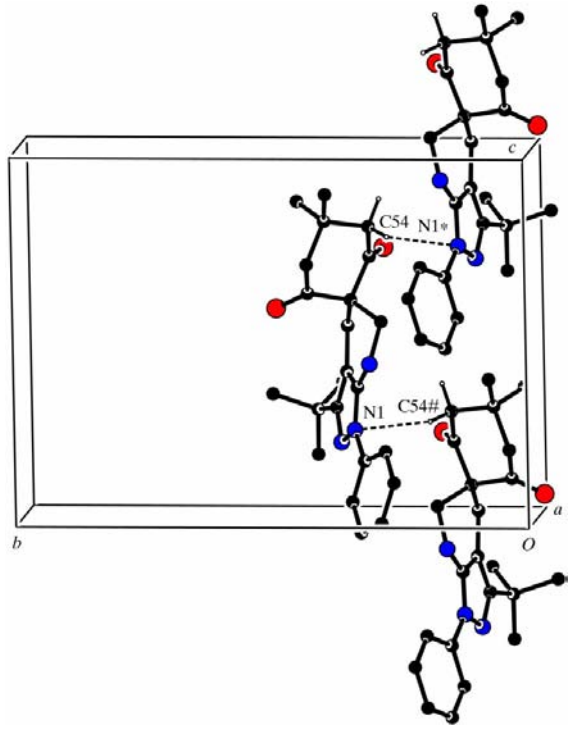


Figure 8
Part of the crystal structure of (II), showing the formation of a $C(8)$ chain along [001]. For clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) or a hash (#) are at the symmetry positions $(x, \frac{1}{2}-y, \frac{1}{2}+z)$ and $(x, \frac{1}{2}-y, -\frac{1}{2}+z)$, respectively.

interaction is indeed significant, its presence generates a $C(8)$ chain running parallel to the [001] direction (Fig. 8), which serves to link adjacent $(20\bar{1})$ sheets into a three-dimensional array.

Experimental

For the synthesis of (I), a mixture of 5-amino-3-methyl-1*H*-pyrazole (1.16 mmol), dimedone (1.16 mmol) and formaldehyde (1.20 mmol) was placed in an open Pyrex glass vessel and irradiated in a domestic microwave oven for 2 min (at 600 W). The resulting solid was washed with ethanol, dried and recrystallized from ethanol (m.p. 398 K, yield 54%). The mass spectrum (EI, 70 eV) shows the following peaks: *m*/*z* (%) 229 (83, M^+), 173 (100), 145 (20), 77 (19), 51 (22), 39 (22). For the synthesis of (II), a mixture of 5-amino-3-*tert*-butyl-1-phenylpyrazole (1.1 mmol), dimedone (1.1 mmol) and formaldehyde (4.0 mmol) was placed in an open Pyrex glass vessel and irradiated in a domestic microwave oven for 3 min (at 600 W). The product of the reaction was recrystallized from absolute ethanol (m.p. 487 K, yield 58%). The mass spectrum (EI, 70 eV) shows the following peaks: *m*/*z* (%) 379 (60, M^+), 295 (50), 294 (100), 77 (31), 57 (25), 55 (27), 41 (43).

Compound (I)

Crystal data

$C_{13}H_{15}N_3O$
$M_r = 229.28$
Monoclinic, $P2_1/n$
$a = 5.9856\ (3)$ Å
$b = 18.1464\ (9)$ Å
$c = 10.7139\ (4)$ Å
$\beta = 98.457\ (3)^\circ$
$V = 1151.06\ (9)$ Å^3
$Z = 4$
$D_x = 1.323$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2592 reflections
$\theta = 3.0$–27.5°
$\mu = 0.09$ mm^{-1}
$T = 120\ (2)$ K
Block, yellow
0.36 × 0.30 × 0.20 mm

Data collection

Nonius KappaCCD diffractometer
φ scans, and ω scans with κ offsets
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995, 1997)
$T_{min} = 0.931$, $T_{max} = 0.983$
12 603 measured reflections
2592 independent reflections
2068 reflections with $I > 2\sigma(I)$
$R_{int} = 0.060$
$\theta_{max} = 27.5^\circ$
$h = -7 \rightarrow 7$
$k = -23 \rightarrow 23$
$l = -13 \rightarrow 13$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.043$
$wR(F^2) = 0.114$
$S = 1.04$
2592 reflections
157 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0624P)^2 + 0.2121P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.34$ e Å^{-3}

Table 1
Selected interatomic distances (Å) for (I).

N1—N2	1.3646 (14)	C4a—N5	1.3581 (13)
N2—C3	1.3398 (16)	N5—C6	1.3120 (17)
C3—C4	1.3997 (15)	C6—C6a	1.4203 (18)
C4—C4a	1.3733 (11)	C6a—C10a	1.3730 (18)
C4a—N1	1.3996 (12)	C10a—N1	1.3556 (16)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C6—H6···N5^{i}	0.95	2.50	3.3397 (17)	148

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

Compound (II)

Crystal data

$C_{23}H_{29}N_3O_2$
$M_r = 379.49$
Monoclinic, $P2_1/c$
$a = 10.0469\ (2)$ Å
$b = 16.4547\ (4)$ Å
$c = 12.7983\ (2)$ Å
$\beta = 108.4950\ (12)^\circ$
$V = 2006.52\ (7)$ Å^3
$Z = 4$
$D_x = 1.256$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4595 reflections
$\theta = 3.0$–27.5°
$\mu = 0.08$ mm^{-1}
$T = 120\ (2)$ K
Plate, colourless
0.20 × 0.10 × 0.03 mm

Data collection

Nonius KappaCCD diffractometer
φ scans, and ω scans with κ offsets
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995, 1997)
$T_{min} = 0.927$, $T_{max} = 0.994$
27 838 measured reflections
4595 independent reflections
3298 reflections with $I > 2\sigma(I)$
$R_{int} = 0.051$
$\theta_{max} = 27.5^\circ$
$h = -12 \rightarrow 13$
$k = -21 \rightarrow 21$
$l = -16 \rightarrow 16$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0749P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.042$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.124$	$\Delta\rho_{max} = 0.26$ e Å^{-3}
$S = 1.03$	$\Delta\rho_{min} = -0.34$ e Å^{-3}
4595 reflections	
258 parameters	
H-atom parameters constrained	

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

N1—N2	1.3784 (15)	C3a—C7a	1.3628 (19)
N2—C3	1.3318 (17)	C7a—N1	1.3739 (16)
C3—C3a	1.4210 (17)		
N2—C3—C31—C32	−135.69 (13)	N2—C3—C31—C34	−14.90 (18)
N2—C3—C31—C33	103.95 (14)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N7—H7···O51^{i}	0.88	2.40	3.2248 (15)	157
C15—H15···O55^{ii}	0.95	2.48	3.407 (2)	164
C54—H54*B*···N1^{iii}	0.99	2.60	3.5149 (18)	154

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

For (I) and (II), space groups $P2_1/n$ and $P2_1/c$, respectively, were uniquely assigned from the systematic absences. All H atoms were located from difference maps and subsequently treated as riding atoms, with C—H distances of 0.95 (aromatic and heteroaromatic CH groups), 0.98 (CH_3) and 0.99 Å (CH_2), and N—H distances of 0.88 Å.

For both compounds, data collection: *KappaCCD Server Software* (Nonius, 1997); cell refinement: *DENZO–SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO–SMN*; program(s) used to solve structure: *OSCAIL* (McArdle, 2003) and *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *OSCAIL* [for (I) only] and *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL*97 and *PRPKAPPA* (Ferguson, 1999).

X-ray data were collected at the EPSRC X-ray Crystallographic Service, University of Southampton, England; the authors thank the staff for all their help and advice. JNL thanks NCR Self-Service, Dundee, for grants that have provided computing facilities for this work. JQ and JM thank COLCIENCIAS and Universidad del Valle, and JC thanks Consejería de Educación y Ciencia (Junta de Andalucía, Spain) for financial support.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1707). Services for accessing these data are described at the back of the journal.

References

Batten, S. R. & Robson, R. (1998). *Angew. Chem. Int. Ed.* **37**, 1460–1494.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Blessing, R. H. (1995). *Acta Cryst.* A**51**, 33–37.
Blessing, R. H. (1997). *J. Appl. Cryst.* **30**, 421–426.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Evans, D. G. & Boeyens, J. C. A. (1989). *Acta Cryst.* B**45**, 581–590.
Ferguson, G. (1999). *PRPKAPPA*. University of Guelph, Canada.
Glidewell, C. & Lloyd, D. M. G. (1984). *Tetrahedron*, **40**, 4455–4472.
McArdle, P. (2003). *OSCAIL for Windows*. Version 10. Crystallography Centre, Chemistry Department, NUI Galway, Ireland.
Nonius (1997). *KappaCCD Server Software*. Windows 3.11 Version. Nonius BV, Delft, The Netherlands.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Quiroga, J., Insuasty, B., Hormaza, A., Gamenara, D., Domínguez, L. & Saldaña, J. (1999). *J. Heterocycl. Chem.* **36**, 11–13.
Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.