

Eight 7-benzyl-3-*tert*-butyl-1-phenyl-pyrazolo[3,4-*d*]oxazines, encompassing structures containing no intermolecular hydrogen bonds, and hydrogen-bonded structures in one, two or three dimensions

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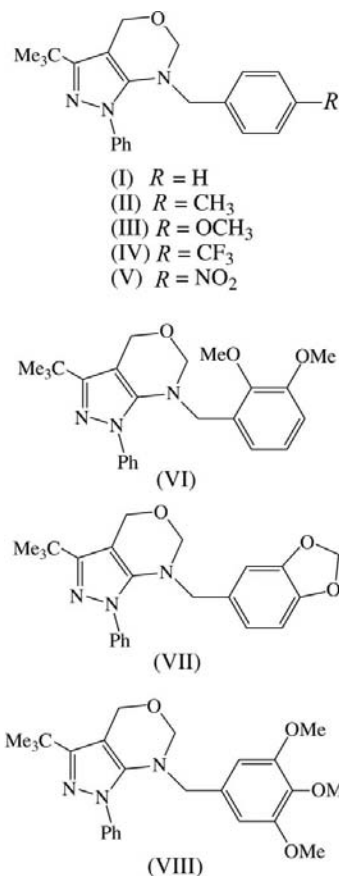
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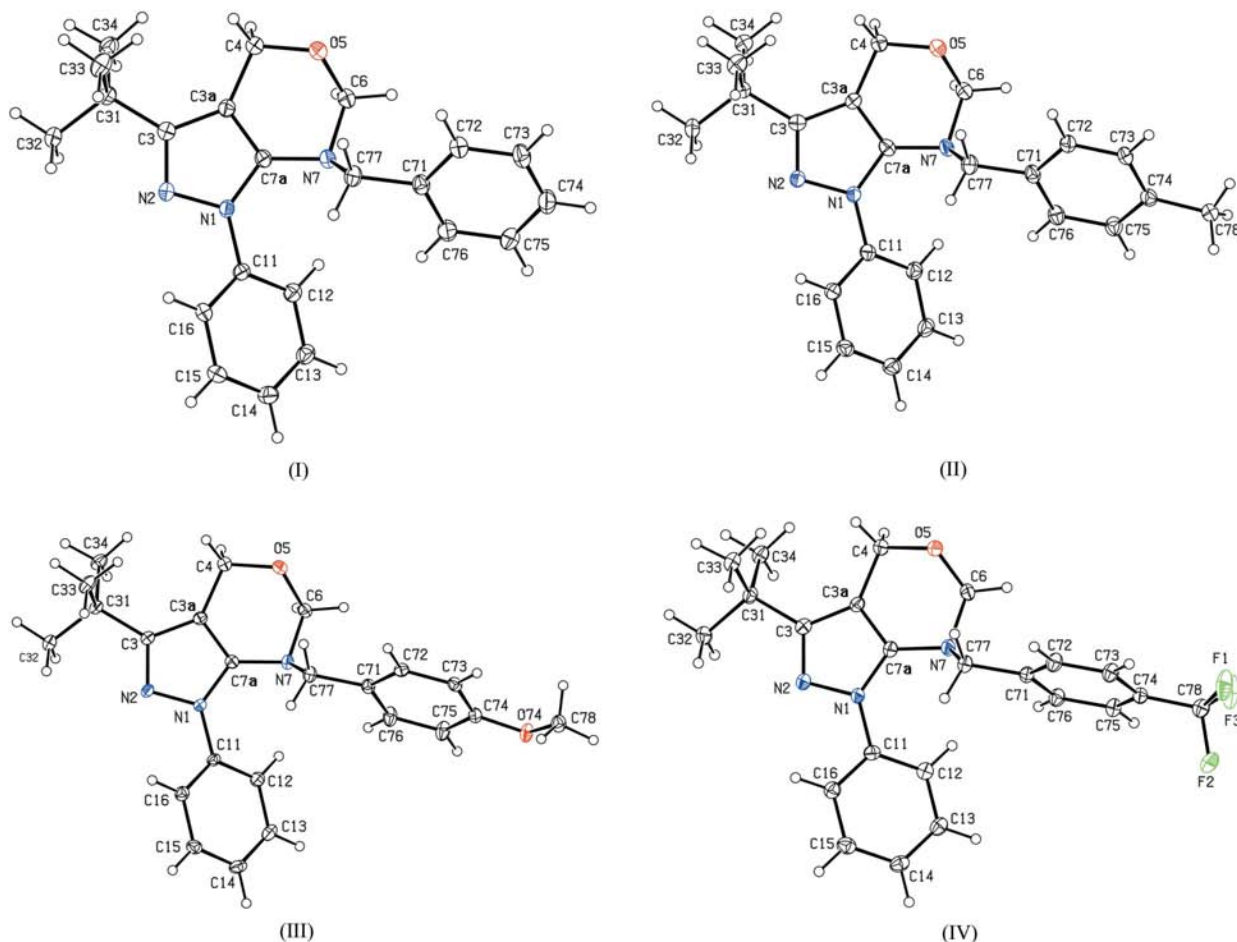
7-Benzyl-3-*tert*-butyl-1-phenyl-6,7-dihydro-1*H*,4*H*-pyrazolo[3,4-*d*][1,3]oxazine, C₂₂H₂₅N₃O, (I), and 3-*tert*-butyl-7-(4-methylbenzyl)-1-phenyl-6,7-dihydro-1*H*,4*H*-pyrazolo[3,4-*d*][1,3]oxazine, C₂₃H₂₇N₃O, (II), are isomorphous in the space group *P*₂₁, and molecules are linked into chains by C—H...O hydrogen bonds. In each of 3-*tert*-butyl-7-(4-methoxybenzyl)-1-phenyl-6,7-dihydro-1*H*,4*H*-pyrazolo[3,4-*d*][1,3]oxazine, C₂₃H₂₇N₃O₂, (III), which has cell dimensions rather similar to those of (I) and (II), also in *P*₂₁, and 3-*tert*-butyl-1-phenyl-7-[4-(trifluoromethyl)benzyl]-6,7-dihydro-1*H*,4*H*-pyrazolo[3,4-*d*][1,3]oxazine, C₂₃H₂₄F₃N₃O, (IV), there are no direction-specific interactions between the molecules. In 3-*tert*-butyl-7-(4-nitrobenzyl)-1-phenyl-6,7-dihydro-1*H*,4*H*-pyrazolo[3,4-*d*][1,3]oxazine, C₂₂H₂₄N₄O₃, (V), a combination of C—H...O and C—H...N hydrogen bonds links the molecules into complex sheets. There are no direction-specific interactions between the molecules of 3-*tert*-butyl-7-(2,3-dimethoxybenzyl)-1-phenyl-6,7-dihydro-1*H*,4*H*-pyrazolo[3,4-*d*][1,3]oxazine, C₂₄H₂₉N₃O₃, (VI), but a three-dimensional framework is formed in 3-*tert*-butyl-7-(3,4-methylenedioxybenzyl)-1-phenyl-6,7-dihydro-1*H*,4*H*-pyrazolo[3,4-*d*][1,3]oxazine, C₂₃H₂₅N₃O₃, (VII), by a combination of C—H...O, C—H...N and C—H... π (arene) hydrogen bonds, while a combination of C—H...O and C—H... π (arene) hydrogen bonds links the molecules of 3-*tert*-butyl-1-phenyl-7-(3,4,5-trimethoxybenzyl)-6,7-dihydro-1*H*,4*H*-pyrazolo[3,4-*d*][1,3]oxazine, C₂₅H₃₁N₃O₄, (VIII), into complex sheets. In each compound, the oxazine ring adopts a half-chair conformation, while the orientations of the pendent phenyl and *tert*-butyl substituents relative to the pyrazolo[3,4-*d*]oxazine unit are all very similar.

Comment

In connection with our wider study of new synthetic routes to fused pyrazole derivatives having potential applications in fields such as drug precursors, pesticides and new materials (Elguero, 1984, 1996), we report here the structures of eight substituted pyrazolo[3,4-*d*]oxazines. These derivatives have been prepared following a synthetic sequence based on the condensation of a substituted 5-aminopyrazole with the appropriate aldehyde to provide (*E*)-3-*tert*-butyl-5-arylidene-amino-1-phenyl-1*H*-pyrazole derivatives, followed by reduction of these intermediates to the corresponding 5-aryl-methylamino-3-*tert*-butyl-1-phenyl-1*H*-pyrazoles (Castillo *et al.*, 2009), and finally reaction with formaldehyde under acid catalysis.



Thus, we now report the structures of 7-benzyl-3-*tert*-butyl-1-phenyl-6,7-dihydro-1*H*,4*H*-pyrazolo[3,4-*d*][1,3]oxazine, (I), and seven derivatives, (II)–(VIII) (see scheme and Figs. 1 and 2), bearing a range of simple substituents in the aromatic ring of the benzyl unit. Compounds (I) and (II) are isomorphous in the space group *P*₂₁. While compound (III) also crystallizes in *P*₂₁ with cell dimensions and atomic coordinates similar to those in (I) and (II), it cannot be regarded as either isomorphous or isostructural with (I) and (II). Thus, while the unit-cell vectors *a* and *b* both differ by less than 0.8% between compounds (I) and (II), the corresponding difference between (II) and (III) are both >2%; similarly, for the unit-cell vector *c*, the values for (I) and (II) differ by *ca* 1.3%, while those for (II) and (III) differ by *ca* 3.5%. Corresponding differences are

**Figure 1**

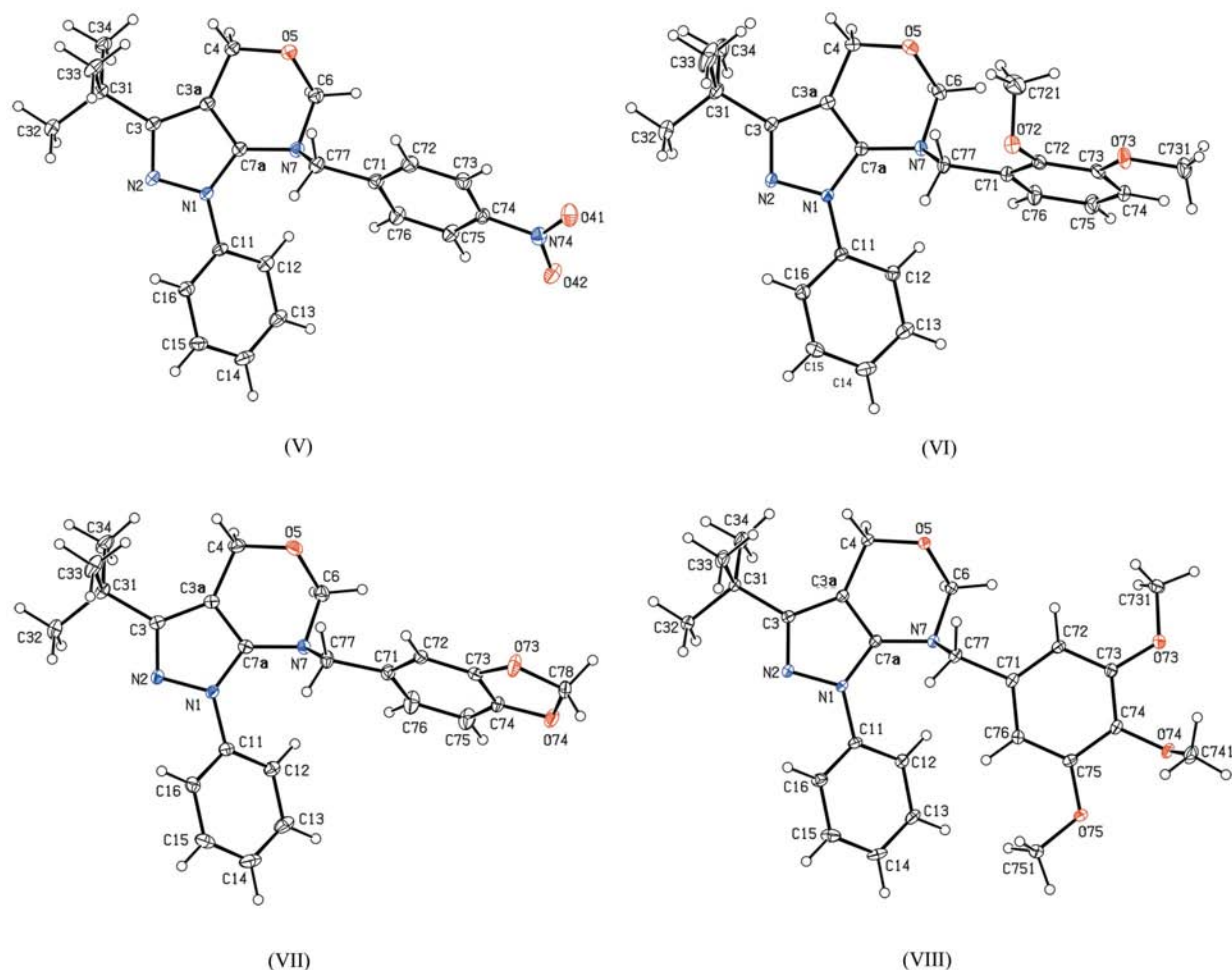
The molecular structures of compounds (I)–(IV), showing the atom-labelling schemes. Displacement ellipsoids are drawn at the 30% probability level.

also found for the cell angle β and the unit-cell volume. In addition, the intermolecular interactions in (III) differ significantly from those in (I) and (II) (see below). Compound (VI) also crystallizes in $P2_1$, but with cell dimensions significantly different from those in compounds (I)–(III).

In each compound, the ring-puckering parameters (Cremer & Pople, 1975) show that the oxazine ring adopts an almost perfect half-chair conformation (Table 1): for this conformation, the idealized values of the puckering angles (calculated assuming equal bond distances throughout the ring) are $\theta = 129.2^\circ$ and $\varphi = (60n + 30)^\circ$, where n represents an integer. The rest of the skeletal conformation, defining the orientation of the pendent substituents relative to the pyrazolo[3,4-*d*]-oxazine unit, can be defined in terms of just four torsion angles (Table 1). These data show the following: (i) the aromatic ring (C11–C16) adopts a very similar orientation in every compound; (ii) the orientation of the *tert*-butyl group is always such that one atom, C32, is close to the plane of the pyrazole ring, but always displaced from it, with a maximum displacement of 0.413 (3) Å in compound (VII) and a minimum displacement of 0.186 (2) Å in compound (V), respectively; the orientation of the aromatic ring of the benzyl substituent shows by far the widest range, although with no obvious systematic variation. In compound (V), the dihedral angle between the nitro group and the adjacent aryl ring is $11.2 (2)^\circ$,

while the methoxy substituents exhibit different patterns of orientation in compounds (VI) and (VIII). In compound (VI), the methoxy atoms C721 and C731 are displaced from the plane of the ring (C71–C76) by 1.168 (4) and 0.009 (3) Å, respectively, while the displacements of atoms C731, C741 and C751 in compound (VIII) are 0.407 (2), 1.309 (2) and 0.262 (2) Å, respectively. In each compound, there is a short intramolecular C–H...N contact (Table 2) involving aryl atom C12 and ring atom N7; in every case, the C–H...N angle is narrow at 120° or less, suggesting that the interaction energy is likely to be small. This contact is probably adventitious, rather than a significant influence on the molecular conformation.

In each of compounds (I)–(VIII), the molecules have no internal symmetry and hence they are all chiral. While compounds (IV), (V), (VII) and (VIII) all crystallize as racemic mixtures of enantiomorphs, the crystals of compounds (I)–(III) and (VI) all contain a single enantiomorph. However, in the absence of significant resonant scattering, the enantiomorphs present in the crystals of compounds (I)–(III) and (VI) which had been selected for data collection cannot be identified. The synthesis of these compounds utilizes no reagents capable of imparting enantiomeric bias, and all are therefore expected to be formed as racemic mixtures, crystallizing as racemates for compounds (IV), (V), (VII) and

**Figure 2**

The molecular structures of compounds (V)–(VIII), showing the atom-labelling schemes. Displacement ellipsoids are drawn at the 30% probability level.

(VIII), and as conglomerates for compounds (I)–(III) and (VI).

Despite their close similarities in both constitution and conformation, compounds (I)–(VIII) nonetheless show some interesting variations in their supramolecular aggregation, which is dominated by C—H···O and C—H···N hydrogen bonds, along with a single C—H··· π (arene) hydrogen bond in each of compounds (II), (VII) and (VIII) (Table 2).

In both (I) and (II), molecules related by translation are linked into simple $C(9)$ (Bernstein *et al.*, 1995) chains running parallel to the [001] direction (Fig. 3). In addition, there is a rather long C—H··· π (arene) hydrogen bond in (II), the effect of which is to form a weak link between the chains along [001], so forming a sheet parallel to (010). No interaction of this kind can be identified in the structure of (I), so that while compounds (I) and (II) are isomorphous, they are not strictly isostructural (Acosta *et al.*, 2009). In contrast, there are no direction-specific intermolecular interactions in the structures of compounds (III), (IV) or (VI), despite the presence of additional potential hydrogen-bond acceptor atoms in compounds (III) and (VI) (Figs. 1 and 2).

The supramolecular aggregation in compound (V) is two-dimensional, in the form of deeply puckered sheets, and the formation of these sheets is readily analysed in terms of two

one-dimensional substructures. In the simpler of these two substructures, molecules related by the 2_1 screw axis along $(\frac{1}{2}, y, \frac{1}{4})$ are linked by a single C—H···O hydrogen bond (Table 2) into a simple $C(6)$ chain running parallel to the [010] direction (Fig. 4). In the second substructure, molecules related by the c -glide plane at $y = 0.75$ are linked by one C—H···N hydrogen bond and one C—H···O hydrogen bond to form a $C(6)C(8)[R_2^2(17)]$ chain of rings running parallel to the [001] direction (Fig. 5). The combination of these two chain motifs generates a sheet parallel to (100).

There are five independent hydrogen bonds in the structure of compound (VII), which together generate a three-dimensional framework structure, the formation of which can, however, be readily analysed in terms of three one-dimensional substructures, which involve, respectively, the three C—H···O hydrogen bonds, the C—H···N hydrogen bond and the C—H··· π (arene) hydrogen bond. In the first substructure (Fig. 6), pairs of molecules related by inversion are linked by two independent C—H···O hydrogen bonds to form a dimeric unit containing three edge-fused hydrogen-bonded rings, with a centrosymmetric $R_2^2(14)$ ring centred at $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$ flanked by two noncentrosymmetric but symmetry-related $R_2^2(7)$ rings. In addition, these units are linked by the third C—H···O hydrogen bond, forming a further $R_2^2(8)$ ring motif, this time

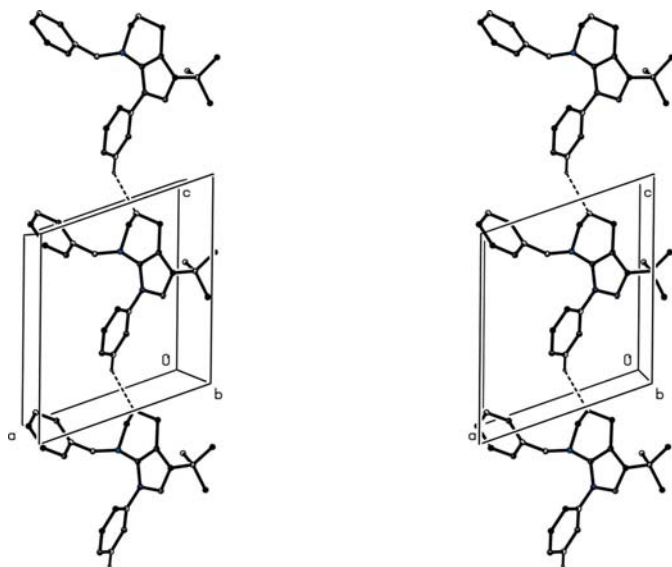


Figure 3
A stereoview of part of the crystal structure of compound (I), showing the formation of a hydrogen-bonded $C(9)$ chain along $[001]$. For the sake of clarity, H atoms not involved in the motif shown have been omitted. An entirely similar chain is formed by compound (II).

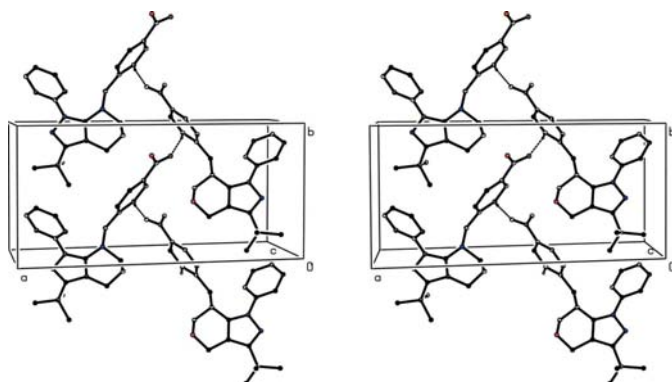


Figure 4
A stereoview of part of the crystal structure of compound (V), showing the formation of a hydrogen-bonded $C(6)$ chain along $[010]$. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

centrosymmetric and centred at $(0, 1, \frac{1}{2})$. Propagation by inversion of these hydrogen bonds then generates a ribbon running parallel to the $[1\bar{1}0]$ direction, in which $R_2^2(8)$ rings centred at $(n, 1 - n, \frac{1}{2})$ alternate with $R_2^2(14)$ rings centred at $(\frac{1}{2} + n, \frac{1}{2} - n, \frac{1}{2})$, where n represents an integer (Fig. 6). A symmetry-related chain runs in the $[110]$ direction.

In the second substructure in (VII), a single $C-H \cdots N$ hydrogen bond links molecules related by the c -glide plane at $y = 0.75$ into a simple $C(11)$ chain running parallel to the $[201]$ direction (Fig. 7). Finally, a rather weak $C-H \cdots \pi(\text{arene})$ hydrogen bond links molecules related by translation into a chain running along $[100]$. The combination of the one-dimensional substructures parallel to $[100]$, $[110]$, $[1\bar{1}0]$ and $[201]$ is sufficient to link the molecules into a single three-dimensional framework.

Although the hydrogen-bonded supramolecular structure of compound (VIII) is only two-dimensional, as opposed to the three-dimensional structure found in compound (VII), it

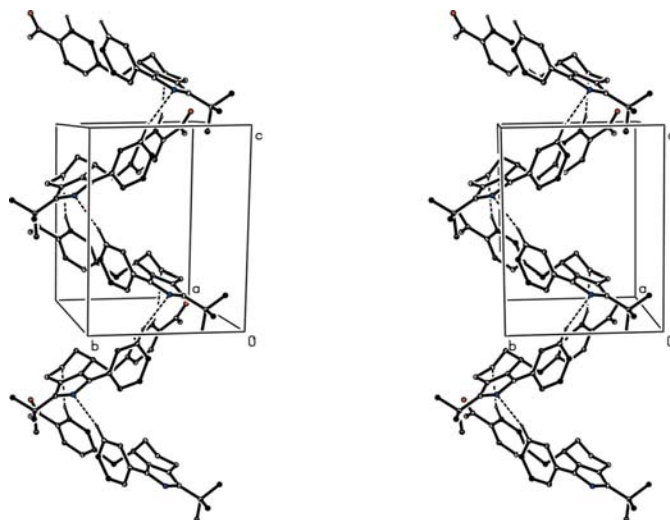


Figure 5
A stereoview of part of the crystal structure of compound (V), showing the formation of a hydrogen-bonded $C(6)C(8)[R_2^2(17)]$ chain of rings along $[001]$. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

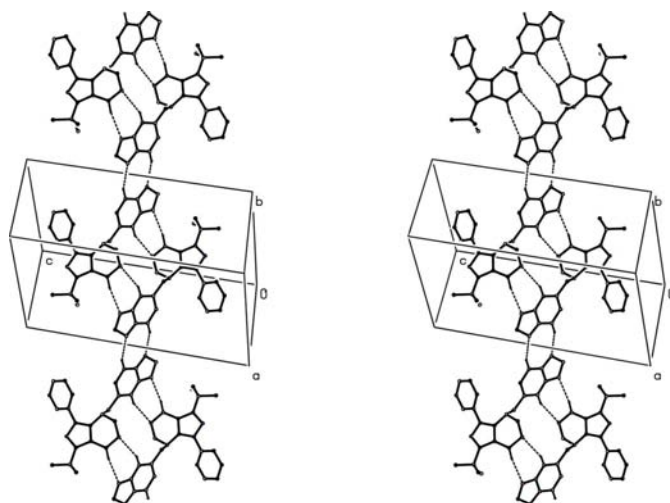
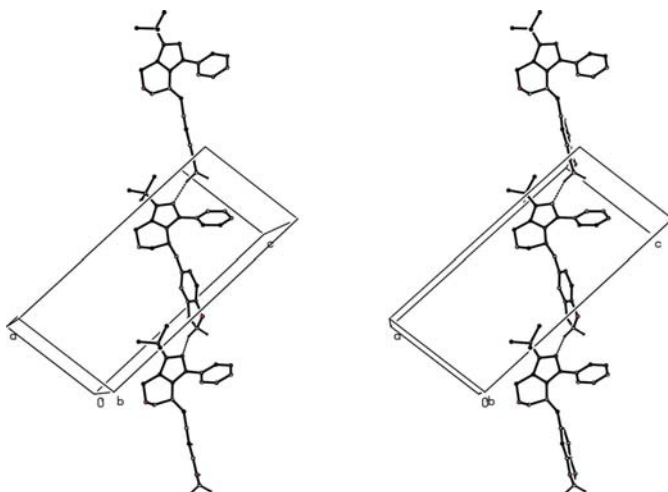
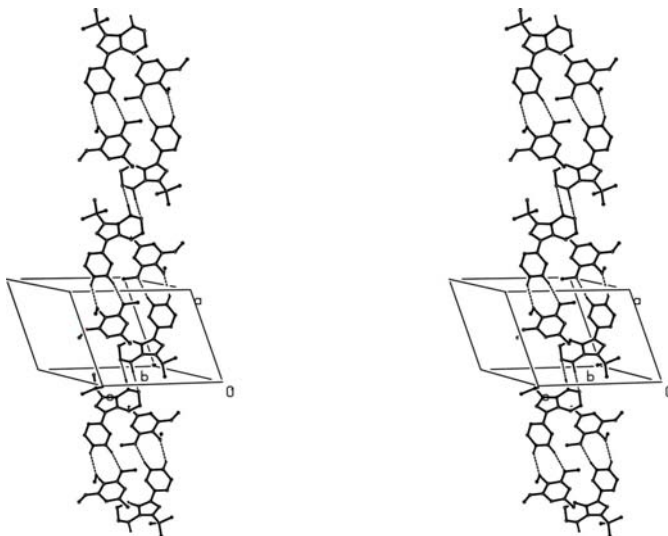


Figure 6
A stereoview of part of the crystal structure of compound (VII), showing the formation of a hydrogen-bonded ribbon running along $[110]$, and containing three types of ring. For the sake of clarity, H atoms not involved in the motif shown have been omitted. A symmetry-related chain runs parallel to the $[110]$ direction.

shares with compound (VII) the formation of a ribbon containing three types of ring (two of them centrosymmetric, built from three independent $C-H \cdots O$ hydrogen bonds), even though the details of the ribbon construction for the two compounds are different (Table 2). Pairs of molecules related by inversion are again linked by two $C-H \cdots O$ hydrogen bonds to form a dimer containing three edge-fused rings, but now with a centrosymmetric $R_2^2(24)$ ring flanked by two non-centrosymmetric $R_2^2(8)$ rings (Fig. 8). The third $C-H \cdots O$ hydrogen bond here generates a centrosymmetric $R_2^2(6)$ ring, and the combination of the these motifs generates a ribbon running parallel to the $[2\bar{1}0]$ direction, with $R_2^2(6)$ rings centred at $(2n, \frac{1}{2} - n, \frac{1}{2})$, alternating with $R_2^2(24)$ rings centred at $(-1 + 2n, 1 - n, \frac{1}{2})$, where n represents an integer (Fig. 8).

**Figure 7**

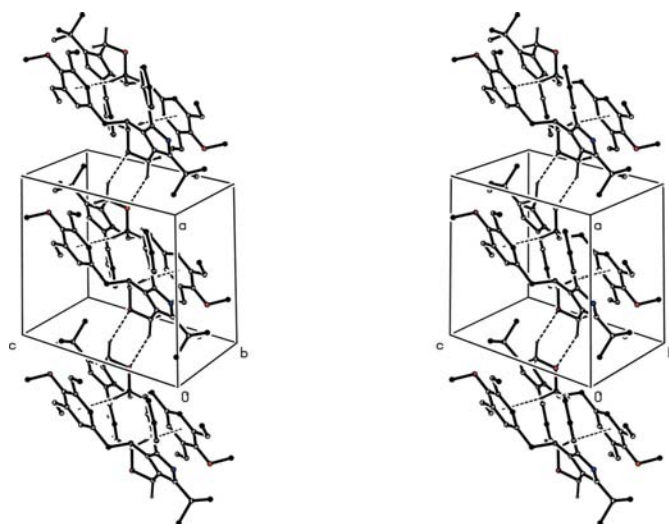
A stereoview of part of the crystal structure of compound (VII), showing the formation of a simple hydrogen-bonded $C(11)$ chain along $[201]$. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

**Figure 8**

A stereoview of part of the crystal structure of compound (VIII), showing the formation of a hydrogen-bonded ribbon running along $[2\bar{1}0]$, and containing three types of ring. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

In the second substructure of compound (VIII), a combination of $C-H \cdots O$ and $C-H \cdots \pi(\text{arene})$ hydrogen bonds generates a chain of edge-fused rings parallel to the $[100]$ direction, where centrosymmetric $R_2^2(6)$ rings centred at $(n, \frac{1}{2}, \frac{1}{2})$, where n represents an integer, formed by paired $C-H \cdots O$ hydrogen bonds alternate with centrosymmetric rings at $(\frac{1}{2} + n, \frac{1}{2}, \frac{1}{2})$ formed by paired $C-H \cdots \pi(\text{arene})$ hydrogen bonds (Fig. 9). The combination of the chains along $[100]$ and the ribbons along $[2\bar{1}0]$ generates a sheet parallel to (001) .

The structures reported here illustrate the subtle and often unpredictable interplay between intra- and intermolecular forces, particularly the interplay between intermolecular hydrogen bonding and molecular conformation, manifested here in the orientation of the aryl ring in the benzyl unit (Table 1). Thus, in compounds (III), (IV) and (VI), where

**Figure 9**

A stereoview of part of the crystal structure of compound (VIII), showing the formation of a hydrogen-bonded chain of rings running along $[100]$. For the sake of clarity, H atoms bonded to C atoms not involved in the motif shown have been omitted.

there are no intermolecular hydrogen bonds, the conformations adopted by the benzyl unit are very similar. Similarly, in the isomorphous pair of compounds (I) and (II), where the chain-forming $C-H \cdots O$ hydrogen bond does not involve the benzyl unit, the overall conformations are very similar; the $C-H \cdots \pi(\text{arene})$ unit in compound (II), which is to be regarded on geometric grounds as weak, appears to have little influence on the molecular conformation. The structures of compounds (VII) and (VIII) both contain a number of hydrogen bonds which involve the benzyl unit, providing both donors and acceptors in compound (VII) but only acceptors in compound (VIII). While this gives rise to a distinct benzyl ring orientation in compound (VIII), the conformation of compound (VII) is not significantly different from those of compounds (III) and (IV), where there are no direction-specific interactions of any kind between the molecules.

Experimental

A mixture of the corresponding 5-arylmethylamino-3-*tert*-butyl-1-phenyl-1*H*-pyrazole (0.29 mmol), ethanol (0.5 ml), acetic acid (0.5 ml) and formaldehyde (0.9 mmol, as an aqueous solution) was heated at 328 K for 10–16 h. After each reaction was complete, the solvent was reduced to one-third of the initial volume, and the resulting solid was collected by filtration and washed with cold ethanol. The products thus obtained were crystallized from ethanol except for (I) which was crystallized from hexane, to give colourless crystals suitable for single-crystal X-ray diffraction. For (I): yield 81%, m.p. 405–406 K; MS (70 eV) m/z (%) = 347 (100) [M^+], 316 (11), 302 (12), 256 (29), 228 (9), 91 (16), 77 (9) [Ph]; analysis found: C 75.8, H 7.5, N 12.3%; $C_{22}H_{25}N_3O$ requires C 76.0, H 7.3, N 12.1%. For (II): yield 86%, m.p. 403–404 K; MS (70 eV) m/z (%) = 361 (51) [M^+], 256 (16), 105 (100) [C_8H_9]; analysis found: C 76.2, H 7.5, N 11.5%; $C_{23}H_{27}N_3O$ requires C 76.4, H 7.5, N 11.6%. For (III): yield 83%, m.p. 436–437 K; MS (70 eV) m/z (%) = 377 (10) [M^+], 121 (100) [C_8H_9O]; analysis found: C 72.9, H 7.1, N 10.9%; $C_{23}H_{27}N_3O_2$ requires C 73.2, H 7.2, N 11.1%. For (IV): yield 87%,

m.p. 425–426 K; MS (70 eV) m/z (%) = 415 (100) [M^+], 370 (24), 170 (31), 159 (24) [$C_8H_6F_3$]; analysis found: C 66.6, H 5.9, N 9.9%; $C_{23}H_{24}F_3N_3O$ requires C 66.5, H 5.8, N 10.1%. For (V): yield 79%, m.p. 408–409 K; MS (70 eV) m/z (%) = 392 (100) [M^+], 256 (41), 228 (24), 170 (25); analysis found: C 67.1, H 6.3, N 14.1%; $C_{22}H_{24}N_4O_3$ requires C 67.3, H 6.2, N 14.3%. For (VI): yield 83%, m.p. 385–386 K; MS (70 eV) m/z (%) = 407 (34) [M^+], 151 (100) [$C_9H_{11}O_2$], 136 (81), 91 (21), 77 (10) [Ph]; analysis found: C 70.5, H 7.3, N 10.2%; $C_{24}H_{29}N_3O_3$ requires C 70.7, H 7.2, N 10.3%. For (VII): yield 88%, m.p. 436–437 K; MS (70 eV) m/z (%) = 391 (11) [M^+], 135 (100) [$C_8H_7O_2$]; analysis found: C 70.8, H 6.4, N 10.9%; $C_{23}H_{25}N_3O_3$ requires C 70.6, H 6.4, N 10.7%. For (VIII): yield 79%, m.p. 439–440 K; MS (70 eV) m/z (%) = 437 (5) [M^+], 181 (100) [$C_{10}H_{13}O_3$]; analysis found: C 68.5, H 7.1, N 9.3%; $C_{25}H_{31}N_3O_4$ requires C 68.6, H 7.1, N 9.6%.

Compound (I)

Crystal data

$C_{22}H_{25}N_3O$ $V = 951.11$ (18) Å³
 $M_r = 347.45$ $Z = 2$
 Monoclinic, $P2_1$ Mo $K\alpha$ radiation
 $a = 8.8930$ (10) Å $\mu = 0.08$ mm^{−1}
 $b = 11.1321$ (12) Å $T = 120$ K
 $c = 10.2078$ (9) Å $0.41 \times 0.25 \times 0.22$ mm
 $\beta = 109.749$ (7)°

Data collection

Bruker–Nonius KappaCCD 15738 measured reflections
 diffractometer 2303 independent reflections
 Absorption correction: multi-scan 1768 reflections with $I > 2\sigma(I)$
 (SADABS; Sheldrick, 2003) $R_{int} = 0.057$
 $T_{min} = 0.885$, $T_{max} = 0.975$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.043$ 1 restraint
 $wR(F^2) = 0.103$ H-atom parameters constrained
 $S = 1.10$ $\Delta\rho_{max} = 0.20$ e Å^{−3}
 2303 reflections $\Delta\rho_{min} = -0.26$ e Å^{−3}
 239 parameters

Compound (II)

Crystal data

$C_{23}H_{27}N_3O$ $V = 964.22$ (15) Å³
 $M_r = 361.48$ $Z = 2$
 Monoclinic, $P2_1$ Mo $K\alpha$ radiation
 $a = 8.9500$ (7) Å $\mu = 0.08$ mm^{−1}
 $b = 11.2146$ (10) Å $T = 120$ K
 $c = 10.0768$ (9) Å $0.32 \times 0.22 \times 0.15$ mm
 $\beta = 107.572$ (5)°

Data collection

Bruker–Nonius KappaCCD 15494 measured reflections
 diffractometer 2323 independent reflections
 Absorption correction: multi-scan 1443 reflections with $I > 2\sigma(I)$
 (SADABS; Sheldrick, 2003) $R_{int} = 0.096$
 $T_{min} = 0.957$, $T_{max} = 0.989$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.052$ 1 restraint
 $wR(F^2) = 0.149$ H-atom parameters constrained
 $S = 1.07$ $\Delta\rho_{max} = 0.27$ e Å^{−3}
 2323 reflections $\Delta\rho_{min} = -0.30$ e Å^{−3}
 249 parameters

Compound (III)

Crystal data

$C_{23}H_{27}N_3O_2$ $V = 1000.93$ (4) Å³
 $M_r = 377.48$ $Z = 2$
 Monoclinic, $P2_1$ Mo $K\alpha$ radiation
 $a = 9.1888$ (2) Å $\mu = 0.08$ mm^{−1}
 $b = 11.4499$ (3) Å $T = 120$ K
 $c = 9.7210$ (2) Å $0.15 \times 0.12 \times 0.05$ mm
 $\beta = 101.857$ (1)°

Data collection

Bruker–Nonius KappaCCD 12855 measured reflections
 diffractometer 2411 independent reflections
 Absorption correction: multi-scan 2237 reflections with $I > 2\sigma(I)$
 (SADABS; Sheldrick, 2003) $R_{int} = 0.036$
 $T_{min} = 0.980$, $T_{max} = 0.996$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.038$ 1 restraint
 $wR(F^2) = 0.085$ H-atom parameters constrained
 $S = 1.19$ $\Delta\rho_{max} = 0.17$ e Å^{−3}
 2411 reflections $\Delta\rho_{min} = -0.20$ e Å^{−3}
 257 parameters

Compound (IV)

Crystal data

$C_{23}H_{24}F_3N_3O$ $\gamma = 67.162$ (9)°
 $M_r = 415.45$ $V = 1000.6$ (2) Å³
 Triclinic, $P\bar{1}$ $Z = 2$
 $a = 9.0277$ (11) Å Mo $K\alpha$ radiation
 $b = 9.8597$ (12) Å $\mu = 0.11$ mm^{−1}
 $c = 12.6835$ (18) Å $T = 120$ K
 $\alpha = 85.531$ (11)° $0.27 \times 0.17 \times 0.14$ mm
 $\beta = 74.180$ (11)°

Data collection

Bruker–Nonius KappaCCD 24473 measured reflections
 diffractometer 4601 independent reflections
 Absorption correction: multi-scan 2336 reflections with $I > 2\sigma(I)$
 (SADABS; Sheldrick, 2003) $R_{int} = 0.099$
 $T_{min} = 0.922$, $T_{max} = 0.986$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.061$ 274 parameters
 $wR(F^2) = 0.183$ H-atom parameters constrained
 $S = 1.04$ $\Delta\rho_{max} = 0.33$ e Å^{−3}
 4601 reflections $\Delta\rho_{min} = -0.37$ e Å^{−3}

Compound (V)

Crystal data

$C_{22}H_{24}N_4O_3$ $V = 1930.3$ (3) Å³
 $M_r = 392.45$ $Z = 4$
 Monoclinic, $P2_1/c$ Mo $K\alpha$ radiation
 $a = 19.164$ (2) Å $\mu = 0.09$ mm^{−1}
 $b = 8.7781$ (7) Å $T = 120$ K
 $c = 11.7188$ (12) Å $0.33 \times 0.22 \times 0.18$ mm
 $\beta = 101.717$ (10)°

Data collection

Bruker–Nonius KappaCCD 27769 measured reflections
 diffractometer 4417 independent reflections
 Absorption correction: multi-scan 2821 reflections with $I > 2\sigma(I)$
 (SADABS; Sheldrick, 2003) $R_{int} = 0.066$
 $T_{min} = 0.917$, $T_{max} = 0.984$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.050$
 $wR(F^2) = 0.116$
 $S = 1.09$
 4417 reflections

265 parameters
 H-atom parameters constrained
 $\Delta\rho_{\max} = 0.24 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.29 \text{ e } \text{\AA}^{-3}$

Compound (VI)

Crystal data

$\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}_3$
 $M_r = 407.50$
 Monoclinic, $P2_1$
 $a = 8.8268 (10) \text{ \AA}$
 $b = 11.6521 (10) \text{ \AA}$
 $c = 10.3831 (7) \text{ \AA}$
 $\beta = 93.747 (9)^\circ$
 $V = 1065.63 (17) \text{ \AA}^3$
 $Z = 2$
 Mo $K\alpha$ radiation
 $\mu = 0.09 \text{ mm}^{-1}$
 $T = 120 \text{ K}$
 $0.25 \times 0.20 \times 0.19 \text{ mm}$

Data collection

Bruker–Nonius KappaCCD
 diffractometer
 Absorption correction: multi-scan
 (SADABS; Sheldrick, 2003)
 $T_{\min} = 0.972$, $T_{\max} = 0.984$

17934 measured reflections
 2560 independent reflections
 2132 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.049$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.044$
 $wR(F^2) = 0.112$
 $S = 1.13$
 2560 reflections
 276 parameters

1 restraint
 H-atom parameters constrained
 $\Delta\rho_{\max} = 0.32 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.27 \text{ e } \text{\AA}^{-3}$

Compound (VII)

Crystal data

$\text{C}_{23}\text{H}_{25}\text{N}_3\text{O}_3$
 $M_r = 391.46$
 Monoclinic, $P2_1/c$
 $a = 9.1164 (14) \text{ \AA}$
 $b = 11.3303 (18) \text{ \AA}$
 $c = 19.694 (2) \text{ \AA}$
 $\beta = 99.775 (13)^\circ$
 $V = 2004.7 (5) \text{ \AA}^3$
 $Z = 4$
 Mo $K\alpha$ radiation
 $\mu = 0.09 \text{ mm}^{-1}$
 $T = 120 \text{ K}$
 $0.38 \times 0.12 \times 0.08 \text{ mm}$

Data collection

Bruker–Nonius KappaCCD
 diffractometer
 Absorption correction: multi-scan
 (SADABS; Sheldrick, 2003)
 $T_{\min} = 0.977$, $T_{\max} = 0.993$

28641 measured reflections
 4592 independent reflections
 2768 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.098$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.069$
 $wR(F^2) = 0.165$
 $S = 1.16$
 4592 reflections

265 parameters
 H-atom parameters constrained
 $\Delta\rho_{\max} = 0.32 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.49 \text{ e } \text{\AA}^{-3}$

Compound (VIII)

Crystal data

$\text{C}_{25}\text{H}_{31}\text{N}_3\text{O}_4$
 $M_r = 437.53$
 Triclinic, $P\bar{1}$
 $a = 9.8189 (10) \text{ \AA}$
 $b = 10.0499 (8) \text{ \AA}$
 $c = 12.8130 (14) \text{ \AA}$
 $\alpha = 68.710 (9)^\circ$
 $\beta = 72.537 (8)^\circ$
 $\gamma = 70.982 (8)^\circ$
 $V = 1089.8 (2) \text{ \AA}^3$
 $Z = 2$
 Mo $K\alpha$ radiation
 $\mu = 0.09 \text{ mm}^{-1}$
 $T = 120 \text{ K}$
 $0.36 \times 0.25 \times 0.15 \text{ mm}$

Table 1

Conformational parameters (\AA , $^\circ$) for compounds (I)–(VIII).

Ring-puckering parameters			
	Q	θ	φ
(I)	0.496 (3)	128.3 (3)	146.7 (4)
(II)	0.491 (4)	128.8 (5)	143.9 (7)
(III)	0.501 (2)	128.6 (2)	146.1 (3)
(IV)	0.499 (3)	127.6 (3)	150.1 (4)
(V)	0.475 (2)	132.3 (2)	145.3 (3)
(VI)	0.498 (3)	127.7 (3)	151.3 (4)
(VII)	0.488 (3)	130.1 (4)	149.6 (4)
(VIII)	0.498 (2)	128.6 (2)	148.1 (2)

Selected torsion angles

	A	B	C	D
(I)	145.5 (2)	−14.8 (4)	−67.5 (3)	117.1 (3)
(II)	143.5 (4)	−13.7 (5)	−69.2 (5)	122.1 (4)
(III)	142.89 (19)	−19.9 (3)	−71.6 (2)	143.1 (2)
(IV)	150.6 (2)	−11.1 (4)	−70.9 (3)	147.0 (3)
(V)	140.79 (17)	−11.8 (2)	−75.3 (2)	138.65 (18)
(VI)	151.1 (2)	−11.7 (4)	−68.5 (3)	148.5 (3)
(VII)	142.7 (2)	−21.5 (3)	−71.8 (3)	146.8 (2)
(VIII)	142.14 (15)	−19.1 (2)	−83.53 (16)	84.69 (18)

Notes: puckering parameters are calculated for the atom sequence O5–C4–C3a–C7a–N7–C6. Torsion angles: $A = \text{N2–N1–C11–C12}$; $B = \text{N2–C3–C31–C32}$; $C = \text{C6–N7–C77–C71}$; $D = \text{N7–C77–C71–C72}$.

Table 2

Hydrogen bonds and short intramolecular contacts (\AA , $^\circ$) for compounds (I)–(VIII).

Cg1 represents the centroid of the C71–C76 ring.

Compound	$D\cdots H\cdots A$	$D\cdots H$	$H\cdots A$	$D\cdots A$	$D\cdots H\cdots A$
(I)	C12–H12 \cdots N7	0.95	2.55	3.079 (4)	115
	C15–H15 \cdots O5 ⁱ	0.95	2.42	3.210 (3)	140
	C12–H12 \cdots N7	0.95	2.60	3.103 (5)	113
	C15–H15 \cdots O5 ⁱ	0.95	2.61	3.258 (5)	126
	C4–H41 \cdots Cg1 ⁱⁱ	0.99	2.96	3.872 (5)	154
(II)	C12–H12 \cdots N7	0.95	2.62	3.108 (3)	113
	C12–H12 \cdots N7	0.95	2.48	3.040 (4)	118
	C12–H12 \cdots N7	0.95	2.55	3.062 (3)	114
	C13–H13 \cdots N2 ⁱⁱⁱ	0.95	2.55	3.399 (2)	148
	C72–H72 \cdots O41 ^{iv}	0.95	2.37	3.293 (3)	163
(III)	C75–H75 \cdots O5 ⁱⁱⁱ	0.95	2.50	3.409 (2)	161
	C12–H12 \cdots N7	0.95	2.45	3.043 (4)	120
	C77–H77 \cdots O72	0.99	2.40	2.776 (4)	102
	C12–H12 \cdots N7	0.95	2.55	3.078 (3)	115
	C4–H42 \cdots O73 ^v	0.99	2.41	3.381 (4)	167
(IV)	C72–H72 \cdots O5 ^v	0.95	2.52	3.413 (3)	156
	C75–H75 \cdots O74 ^{vi}	0.95	2.55	3.456 (4)	160
	C78–H78 \cdots N2 ^{vii}	0.99	2.48	3.338 (4)	145
	C4–H41 \cdots Cg1 ^{viii}	0.99	2.91	3.799 (3)	150
	C12–H12 \cdots N7	0.95	2.53	3.071 (2)	116
(V)	C4–H42 \cdots O5 ^{ix}	0.99	2.47	3.354 (2)	148
	C13–H13 \cdots O75 ^x	0.95	2.57	3.466 (2)	157
	C14–H14 \cdots O74 ^x	0.95	2.46	3.247 (2)	140
	C6–H62 \cdots Cg1 ^v	0.99	2.76	3.737 (2)	167
	C12–H12 \cdots N7	0.95	2.53	3.071 (2)	116

Symmetry codes: (i) $x, y, -1 + z$; (ii) $-1 + x, y, z$; (iii) $x, \frac{3}{2} - y, \frac{1}{2} + z$; (iv) $1 - x, -\frac{1}{2} + y, \frac{1}{2} - z$; (v) $1 - x, 1 - y, 1 - z$; (vi) $-x, 2 - y, 1 - z$; (vii) $-1 + x, \frac{3}{2} - y, -\frac{1}{2} + z$; (viii) $1 + x, y, z$; (ix) $-x, 1 - y, 1 - z$; (x) $2 - x, -y, 1 - z$.

Data collection

Bruker–Nonius KappaCCD
 diffractometer
 Absorption correction: multi-scan
 (SADABS; Sheldrick, 2003)
 $T_{\min} = 0.958$, $T_{\max} = 0.987$
 30046 measured reflections
 4970 independent reflections
 3754 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.050$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.047$	295 parameters
$wR(F^2) = 0.120$	H-atom parameters constrained
$S = 1.07$	$\Delta\rho_{\max} = 0.24 \text{ e } \text{\AA}^{-3}$
4970 reflections	$\Delta\rho_{\min} = -0.32 \text{ e } \text{\AA}^{-3}$

All H atoms were located in difference maps and then treated as riding atoms in geometrically idealized positions, with C—H = 0.95 (aromatic), 0.98 (CH₃) or 0.99 Å (CH₂) and $U_{\text{iso}}(\text{H}) = kU_{\text{eq}}(\text{C})$, where $k = 1.5$ for methyl groups and 1.2 for all other H atoms. The methyl groups were permitted to rotate about the adjacent C—X (X = C or O) bonds but not to tilt. In the absence of significant resonant scattering, the Flack x parameters (Flack, 1983) for compounds (I)–(III) and (VI) were indeterminate; accordingly, the Friedel-equivalent reflections were merged, and for these compounds it is not possible to establish the absolute configurations of the molecules in the crystals which were selected for data collection. For all compounds, the reference molecules were selected to have the same absolute configuration (see Figs. 1 and 2).

For all compounds, 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: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PLATON*.

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