

Sheets built from C—H···O and C—H··· π (arene) hydrogen bonds in (2*RS*,6*SR*)-*N*-diphenylacetyl-2,6-diphenylpiperidin-4-one and (2*RS*,3*SR*,5*RS*,6*SR*)-3,5-dimethyl-*N*-phenylacetyl-2,6-diphenylpiperidin-4-one

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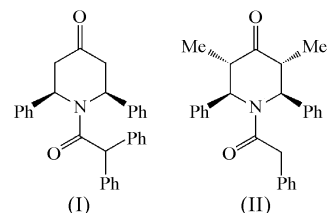
In (2*RS*,6*SR*)-*N*-diphenylacetyl-2,6-diphenylpiperidin-4-one, C₃₁H₂₇NO₂, (I), the piperidinone ring adopts an almost ideal twist-boat conformation, and the molecules are linked into sheets by a combination of one C—H···O hydrogen bond and one C—H··· π (arene) hydrogen bond. (2*RS*,3*SR*,5*RS*,6*SR*)-3,5-Dimethyl-2,6-diphenyl-*N*-phenylacetyl-piperidin-4-one, C₂₇H₂₇NO₂, (II), crystallizes with $Z' = 2$ in the space group $P\bar{1}$; the piperidinone rings adopt an almost ideal boat conformation in one of the molecules and a conformation between boat and twist-boat in the other. The molecules of (II) are linked into sheets by a combination of five C—H···O hydrogen bonds and one C—H··· π (arene) hydrogen bond.

Comment

Nitrogen heterocycles containing diphenylacetyl substituents exhibit antihypertensive activity (Wexler *et al.*, 1996). In order to study the activity of simple compounds containing phenylacetyl and diphenylacetyl substituents, the title compounds, (I) and (II), have been synthesized, and the conformations and supramolecular aggregation of these two compounds (Figs. 1 and 2) are reported here.

Within the piperidinone rings of compounds (I) and (II), the geometry at the carbonyl C atoms is planar and that at the N atoms is effectively planar, with a sum of the bond angles at N1 in (I) of 357.7 (2)°, and sums at N11 and N21 in (II) of 358.6 (3) and 359.3 (3)°, respectively. The ring-puckering parameters (Cremer & Pople, 1975) for this ring in compound

(I), $\theta = 95.6$ (2)° and $\varphi = 96.1$ (2)° for the atom sequence N1–C2–C3–C4–C5–C6, indicate a twist-boat conformation, for which the ideal parameters are $\theta = 90^\circ$ and $\varphi = (60n + 30)^\circ$. The phenyl substituents at C2 and C6 occupy equatorial and axial sites, respectively (Table 1), and in the selected reference molecule atoms C2 and C6 have *R* and *S* configurations, respectively. Hence, in the centrosymmetric space group $P2_1/n$, there are equal numbers of the 2*R*,6*S* and 2*S*,6*R* enantiomers.



Compound (II) (Fig. 2) crystallizes with $Z' = 2$. The molecules contain four stereogenic centres at $Cn2$, $Cn3$, $Cn5$ and $Cn6$ ($n = 1$ or 2) and the asymmetric unit was selected so that the two independent molecules have the same disposition of axial and equatorial substituents, namely axial at $Cn2$ and $Cn3$, and equatorial at $Cn5$ and $Cn6$ ($n = 1$ or 2) (Table 3). This choice of asymmetric unit, which leads to *R* configurations at C12, C15, C23 and C25, and *S* configurations at C13, C16, C22 and C24, provides a compact asymmetric unit in which the two independent molecules are linked by a pair of C—H···O hydrogen bonds.

The piperidinone rings in the two independent molecules of (II) adopt somewhat different conformations. For the molecules denoted 1 and 2 (containing atoms N11 and N21, respectively), the ring-puckering parameters for the atom sequence $Nn1-Cn2-Cn3-Cn4-Cn5-Cn6$ are $\theta = 97.8$ (3)° and $\varphi = 252.7$ (3)° for $n = 1$, and $\theta = 93.8$ (2)° and $\varphi = 53.5$ (3)° for $n = 2$, indicating a boat conformation in molecule 2 (for which the idealized parameters are $\theta = 90^\circ$ and $\varphi = 60n^\circ$) and a conformation approximately midway between boat and twist-boat for molecule 1. Apart from this conformational differ-

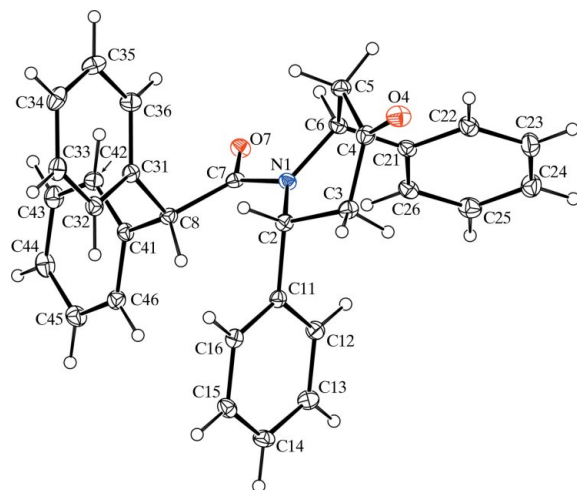


Figure 1

The 2*R*,6*S* enantiomer of compound (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.

ence, the two independent molecules in compound (II) are approximately enantiomorphous (Table 3).

The molecules of (I) are linked into sheets by two hydrogen bonds, one each of C—H···O and C—H··· π (arene) types (Table 2). The formation of the sheet is readily analysed in terms of the two simple substructural motifs formed by the individual hydrogen bonds. Piperidinone atom C6 in the molecule at (x, y, z) acts as hydrogen-bond donor to atom O7 in the molecule at $(1 - x, 1 - y, 1 - z)$, so forming a cyclic centrosymmetric $R_2^2(10)$ (Bernstein *et al.*, 1995) dimer centred at $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$ (Fig. 3). In the second motif, aryl atom C16 in the molecule at (x, y, z) acts as hydrogen-bond donor to aryl ring C41–C46 of the molecule at $(\frac{1}{2} - x, -\frac{1}{2} + y, \frac{3}{2} - z)$, so forming a chain running parallel to the [010] direction and generated by the 2_1 screw axis along $(\frac{1}{4}, y, \frac{3}{4})$ (Fig. 4). The linking of the

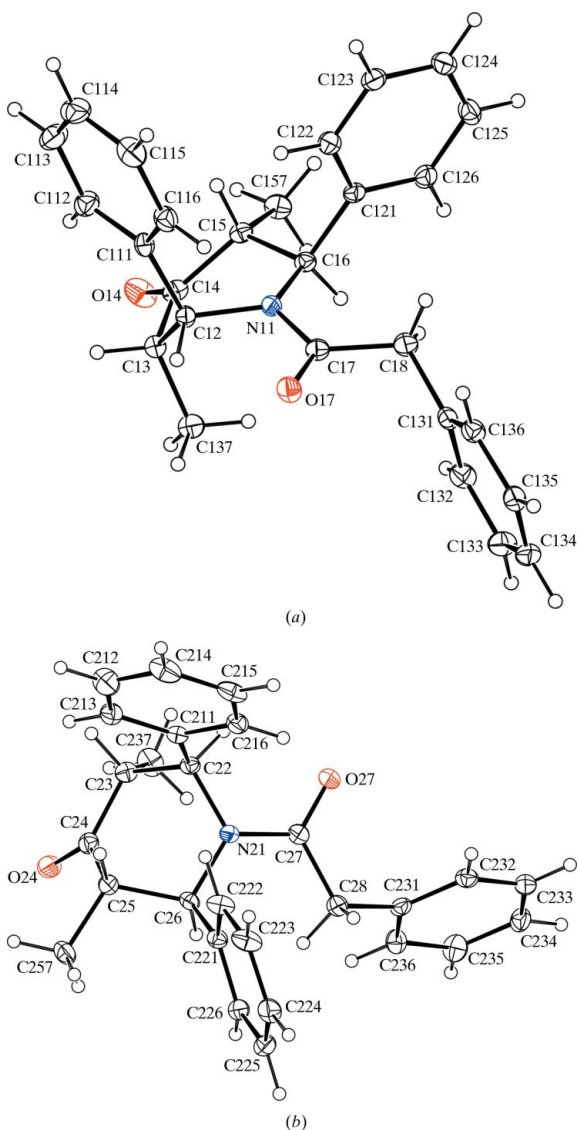


Figure 2

The two independent molecules in the selected asymmetric unit for compound (II), showing the atom-labelling scheme, *viz.* (a) the 2*R*,3*S*,5*R*,6*S* enantiomer of molecule 1 and (b) the 2*S*,3*R*,5*S*,6*R* enantiomer of molecule 2. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

$R_2^2(10)$ dimers by the C—H··· π (arene) hydrogen bond then generates the sheet.

Aryl atoms C16 in the molecules at (x, y, z) and $(1 - x, 1 - y, 1 - z)$, which form the $R_2^2(10)$ dimer centred at $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$, act as hydrogen-bond donors to rings C41–C46 in the molecules at $(\frac{1}{2} - x, -\frac{1}{2} + y, \frac{3}{2} - z)$ and $(\frac{1}{2} + x, \frac{3}{2} - y, -\frac{1}{2} + z)$, respectively, which are components of the dimers centred at $(0, 0, 1)$ and $(1, 1, 0)$. Similarly, rings C41–C46 at (x, y, z) and $(1 - x, 1 - y, 1 - z)$ accept hydrogen bonds from, respectively, aryl atoms C16 in the molecules at $(\frac{1}{2} - x, \frac{1}{2} + y, \frac{3}{2} - z)$

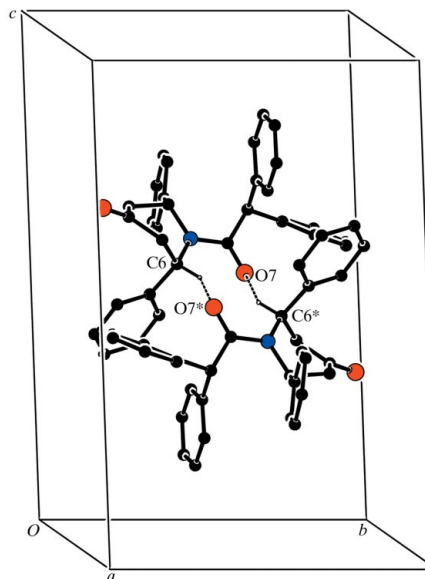


Figure 3

Part of the crystal structure of compound (I), showing the formation of a centrosymmetric $R_2^2(10)$ 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 $(1 - x, 1 - y, 1 - z)$.

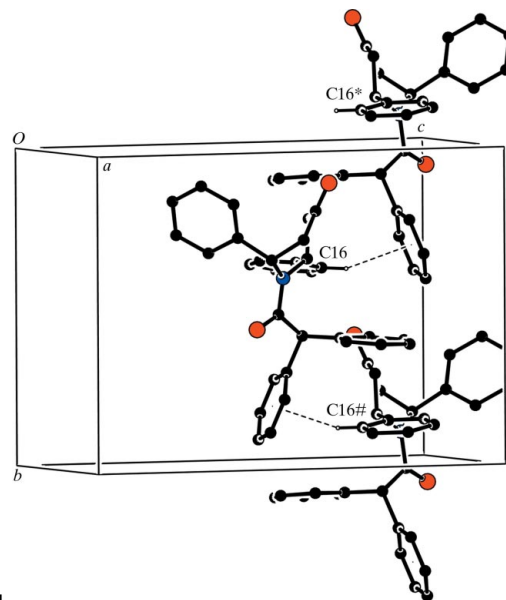


Figure 4

Part of the crystal structure of compound (I), showing the formation of a hydrogen-bonded chain along [010]. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) or a hash sign (#) are at the symmetry positions $(\frac{1}{2} - x, -\frac{1}{2} + y, \frac{3}{2} - z)$ and $(\frac{1}{2} - x, \frac{1}{2} + y, \frac{3}{2} - z)$, respectively.

and $(\frac{1}{2} + x, \frac{1}{2} - y, -\frac{1}{2} + z)$, which are themselves components of the dimers centred at $(0, 1, 1)$ and $(1, 0, 0)$. Propagation by the space group of this C—H... π (arene) hydrogen bond then links the $R_2^2(10)$ dimers to form a (101) sheet (Fig. 5).

The molecules of compound (II) are linked into complex sheets by means of five independent C—H...O hydrogen bonds and one C—H... π (arene) hydrogen bond (Table 4),

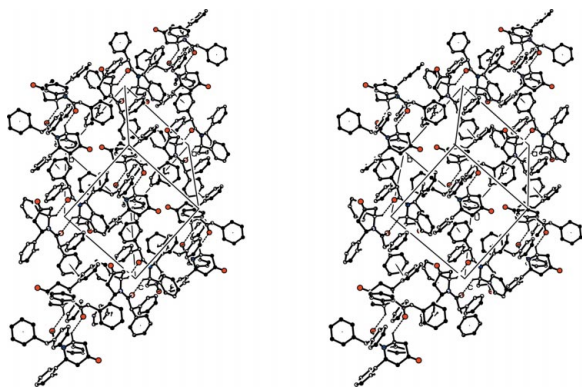


Figure 5
A stereoview of part of the crystal structure of compound (I), showing the formation of a hydrogen-bonded (101) sheet. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

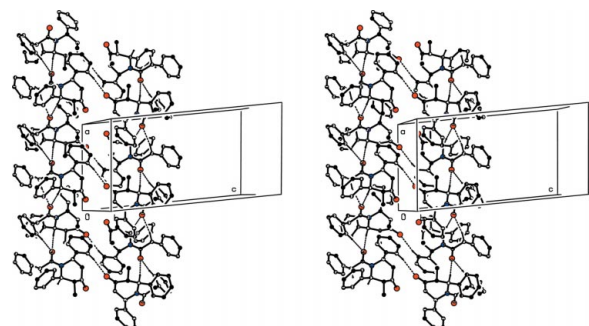


Figure 6
A stereoview of part of the crystal structure of compound (II), showing the formation of a hydrogen-bonded ribbon along [100]. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

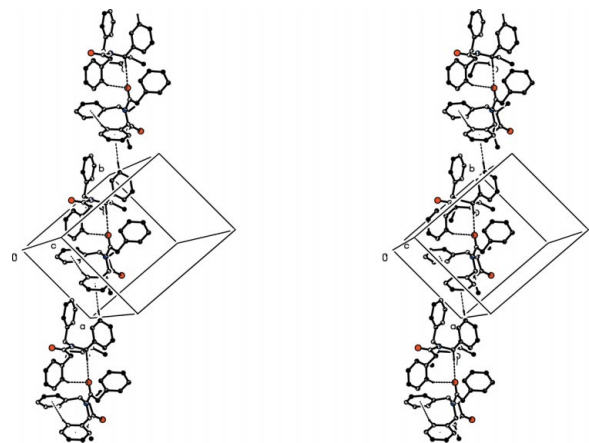


Figure 7
A stereoview of part of the crystal structure of compound (II), showing the formation of a hydrogen-bonded chain along $[110]$. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

but the formation of the sheet is readily described in terms of simpler substructural motifs. Within the asymmetric unit, atoms C16 and C132 in molecule 1 both act as hydrogen-bond donors to atom O27 in molecule 2, so forming an $R_2^2(9)$ (Bernstein *et al.*, 1995) ring. Similarly, atoms C26 and C28 in the type 2 molecule at (x, y, z) both act as hydrogen-bond donors to atom O17 in the type 1 molecule at $(1 + x, y, z)$, so forming a second ring motif, this time of $R_2^2(7)$ type. Propagation by translation of these hydrogen bonds then generates a chain of rings running parallel to the [100] direction (Fig. 5). Antiparallel pairs of such chains are linked by the final C—H...O hydrogen bond; atom C212 in the type 1 molecule at (x, y, z) acts as hydrogen-bond donor to atom O14 in the type 1 molecule at $(1 - x, 1 - y, -z)$. The linking of pairs of chains thus produces a complex [100] ribbon, in which $R_4^4(24)$ rings centred at $(n + \frac{1}{2}, \frac{1}{2}, 0)$ ($n = \text{zero or integer}$) alternate with $R_4^4(28)$ rings centred at $(n, \frac{1}{2}, 0)$ ($n = \text{zero or integer}$) in the central portion, flanked on either side by antiparallel sets of alternating $R_2^2(7)$ and $R_2^2(9)$ rings (Fig. 6).

In addition to a C—H... π (arene) interaction within the type 2 molecule, a second such interaction links the molecules into chains; atom C123 in the type 1 molecule at (x, y, z) acts as hydrogen-bond donor to the C211–C216 ring in the type 2 molecule at $(-1 + x, 1 + y, z)$. In combination with the two C—H...O hydrogen bonds within the asymmetric unit, this C—H... π (arene) hydrogen bond generates by translation a chain running parallel to the $[\bar{1}10]$ direction (Fig. 7). The combination of the [100] and $[\bar{1}10]$ chains then generates a complex (001) sheet. There are no direction-specific interactions between adjacent sheets.

Experimental

Samples of the title compounds were prepared by acylation of piperidinones in the presence of triethylamine as proton acceptor, using anhydrous benzene as the solvent. For (I), 2,6-diphenylpiperidin-4-one was acylated with diphenylacetyl chloride, and for (II), 3,5-dimethyl-2,6-diphenylpiperidin-4-one was acylated with phenylacetyl chloride. In each case, the acyl chloride (5 mmol) was added dropwise over a period of 1 h to a solution of the piperidinone (2.5 mmol) in benzene (50 ml) containing triethylamine (1.4 ml) held between 273 and 278 K. These mixtures were heated under reflux for 8–10 h, until the reactions were complete (as shown by thin-layer chromatography); the mixtures were then cooled and washed with 10% aqueous sodium hydrogen carbonate solution. Removal of the solvent then yielded the products. Crystals suitable for single-crystal X-ray diffraction were grown by slow evaporation of solutions in ethanol. For (I), yield 69% and m.p. 456–458 K; for (II), yield 61% and m.p. 431–433 K.

Compound (I)

Crystal data

$C_{31}H_{27}NO_2$	$Z = 4$
$M_r = 445.54$	$D_x = 1.278 \text{ Mg m}^{-3}$
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation
$a = 11.2499 (2) \text{ \AA}$	$\mu = 0.08 \text{ mm}^{-1}$
$b = 11.8622 (3) \text{ \AA}$	$T = 120 (2) \text{ K}$
$c = 18.2320 (5) \text{ \AA}$	Block, colourless
$\beta = 107.8750 (15)^\circ$	$0.16 \times 0.10 \times 0.02 \text{ mm}$
$V = 2315.59 (10) \text{ \AA}^3$	

Data collection

Nonius KappaCCD area-detector diffractometer	27266 measured reflections
φ and ω scans	5309 independent reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)	4069 reflections with $I > 2\sigma(I)$
$T_{\min} = 0.975$, $T_{\max} = 0.998$	$R_{\text{int}} = 0.051$
	$\theta_{\text{max}} = 27.6^\circ$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0437P)^2 + 0.8526P]$
$R[F^2 > 2\sigma(F^2)] = 0.045$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.113$	$(\Delta/\sigma)_{\text{max}} = 0.001$
$S = 1.03$	$\Delta\rho_{\text{max}} = 0.22 \text{ e } \text{\AA}^{-3}$
5309 reflections	$\Delta\rho_{\text{min}} = -0.25 \text{ e } \text{\AA}^{-3}$
307 parameters	
H-atom parameters constrained	

Table 1

Selected torsion angles ($^\circ$) for (I).

C6—N1—C2—C11	−136.22 (12)	C2—N1—C6—C21	88.59 (14)
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Table 2

Hydrogen-bond geometry (\AA , $^\circ$) for (I).

Cg is the centroid of the C41–C46 ring.

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
C6—H6 \cdots O7 ⁱ	1.00	2.35	3.120 (2)	133
C16—H16 \cdots Cg ⁱⁱ	0.95	2.71	3.505 (2)	142

Symmetry codes: (i) $-x + 1, -y + 1, -z + 1$; (ii) $-x + \frac{1}{2}, y - \frac{1}{2}, -z + \frac{3}{2}$.

Compound (II)

Crystal data

$C_{27}H_{27}NO_2$	$V = 2130.23 (17) \text{\AA}^3$
$M_r = 397.50$	$Z = 4$
Triclinic, $P\bar{1}$	$D_x = 1.239 \text{ Mg m}^{-3}$
$a = 9.9503 (4) \text{\AA}$	Mo $K\alpha$ radiation
$b = 11.8623 (6) \text{\AA}$	$\mu = 0.08 \text{ mm}^{-1}$
$c = 18.5654 (8) \text{\AA}$	$T = 120 (2) \text{ K}$
$\alpha = 77.920 (2)^\circ$	Plate, colourless
$\beta = 84.699 (3)^\circ$	$0.24 \times 0.14 \times 0.03 \text{ mm}$
$\gamma = 85.731 (2)^\circ$	

Data collection

Nonius KappaCCD area-detector diffractometer	39607 measured reflections
φ and ω scans	9842 independent reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)	6200 reflections with $I > 2\sigma(I)$
$T_{\min} = 0.971$, $T_{\max} = 0.998$	$R_{\text{int}} = 0.094$
	$\theta_{\text{max}} = 27.8^\circ$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.1421P)^2 + 1.0691P]$
$R[F^2 > 2\sigma(F^2)] = 0.088$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.262$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$S = 1.03$	$\Delta\rho_{\text{max}} = 0.37 \text{ e } \text{\AA}^{-3}$
9842 reflections	$\Delta\rho_{\text{min}} = -0.33 \text{ e } \text{\AA}^{-3}$
546 parameters	
H-atom parameters constrained	

For compound (I), the space group $P2_1/n$ was uniquely assigned from the systematic absences. Crystals of compound (II) are triclinic; the space group $P\bar{1}$ was selected and confirmed by the analysis. All H

Table 3

Selected torsion angles ($^\circ$) for (II).

C16—N11—C12—C111	−81.2 (3)	C26—N21—C22—C211	79.8 (3)
N11—C12—C13—C137	61.7 (4)	N21—C22—C23—C237	−81.1 (3)
C12—N11—C16—C121	123.0 (3)	C22—N21—C26—C221	−119.8 (3)
N11—C16—C15—C157	−165.7 (3)	N21—C26—C25—C257	172.3 (3)

Table 4

Hydrogen-bond geometry (\AA , $^\circ$) for (II).

Cg1 is the centroid of the C211–C216 ring and Cg2 is the centroid of the C221–C226 ring.

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
C16—H16 \cdots O27	1.00	2.34	3.342 (4)	174
C132—H132 \cdots O27	0.95	2.59	3.482 (4)	156
C26—H26 \cdots O17 ⁱ	1.00	2.35	3.343 (4)	172
C28—H28B \cdots O17 ⁱ	0.99	2.48	3.398 (4)	153
C212—H212 \cdots O14 ⁱⁱ	0.95	2.41	3.339 (5)	164
C222—H222 \cdots Cg1	0.95	2.97	3.902 (4)	169
C123—H123 \cdots Cg2 ⁱⁱⁱ	0.95	2.92	3.849 (4)	166

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

atoms were located in difference maps and then treated as riding, with C—H distances of 0.95 (aromatic), 0.99 (CH₂) or 1.00 \AA (aliphatic CH), and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$.

For both compounds, data collection: COLLECT (Nonius, 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 (Sheldrick, 1997); molecular graphics: PLATON (Spek, 2003); software used to prepare material for publication: SHELXL97 and PRPKAPPA (Ferguson, 1999).

The 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.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG3009). Services for accessing these data are described at the back of the journal.

References

- Bernstein, J., Davis, R. E., Shimon, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
- Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
- Ferguson, G. (1999). *PRPKAPPA*. University of Guelph, Canada.
- McArdle, P. (2003). *OSCAIL for Windows*. Version 10. Crystallography Centre, Chemistry Department, NUI Galway, Ireland.
- Nonius (1999). *COLLECT*. 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.
- Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
- Sheldrick, G. M. (2003). *SADABS*. Version 2.10. University of Göttingen, Germany.
- Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
- Wexler, R. R., Greenlee, W. J., Irvin, J. D., Goldberg, M. R., Prendergast, K., Smith, R. D. & Timmermans, P. B. M. W. M. (1996). *J. Med. Chem.* **39**, 625–656.