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Two closely related, and unexpected, quinolinone derivatives: a three-dimensional hydrogen-bonded framework structure and a hydrogen-bonded molecular ribbon of $R_2^2(18)$ and $R_4^4(24)$ rings

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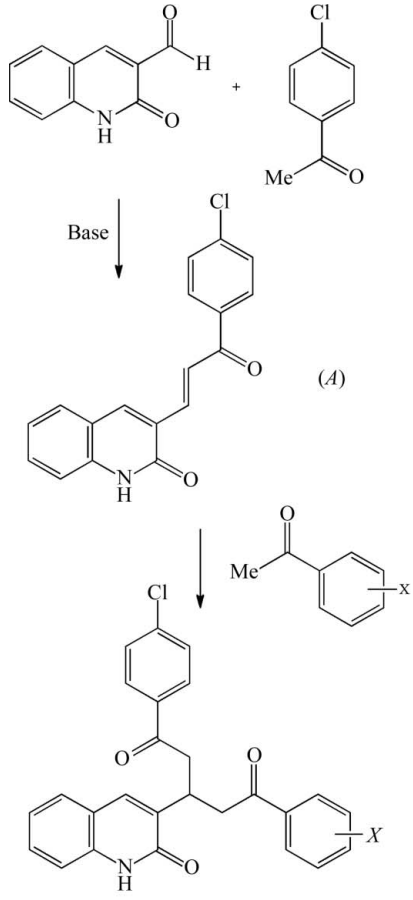
1,5-Bis(4-chlorophenyl)-3-(2-oxo-1,2-dihydroquinolin-3-yl)-pentane-1,5-dione, (I*a*), and 1,5-bis(2-chlorophenyl)-3-(2-oxo-1,2-dihydroquinolin-3-yl)pentane-1,5-dione, (I*b*), crystallize as an 84:16 mixture, $0.84C_{26}H_{19}Cl_2NO_3\cdot0.16C_{26}H_{19}Cl_2NO_3$, in the space group $I4_1/a$, where the molecules of the two isomers occupy very similar sites in the unit cell. A combination of one N—H···O hydrogen bond and one C—H···O hydrogen bond links the molecules, regardless of isomeric form, into a single three-dimensional framework structure. The molecules of (9*RS*,10*RS*)-8,9-bis(4-chlorobenzyl)-10-(2-oxo-1,2-dihydroquinolin-3-yl)-5,6,9,10-tetrahydrophenanthridine, $C_{36}H_{22}Cl_2N_2O_4$, (II), are linked by two hydrogen bonds, one each of the N—H···O and C—H···O types, into a molecular ribbon in which centrosymmetric rings of $R_2^2(18)$ and $R_4^4(24)$ types alternate. The hydrogen-bonded ribbons enclose channels, which contain highly disordered solvent molecules.

Comment

We report here the molecular and supramolecular structures of two closely related compounds, namely 1,5-bis(4-chlorophenyl)-3-(2-oxo-1,2-dihydroquinolin-3-yl)pentane-1,5-dione–1,5-bis(2-chlorophenyl)-3-(2-oxo-1,2-dihydroquinolin-3-yl)pentane-1,5-dione (84/16), (I) (Fig. 1), and (9*RS*,10*RS*)-8,9-bis(4-chlorobenzyl)-10-(2-oxo-1,2-dihydroquinolin-3-yl)-5,6,9,10-tetrahydrophenanthridine, (II) (Fig. 2), both of which were initially identified as unexpected by-products in the synthesis of a simple chalcone. As part of a synthetic programme focusing on novel quinolin-2-one derivatives having potential as antitumour agents (Abonía *et al.*, 2010), we have prepared a number of chalcones containing both quinolin-2-one and benzoyl units. In the preparation of the chalcone, (*A*) (see Scheme 1), by base-catalysed condensation between 2-oxoquinoline-3-carbaldehyde and 4-chloroacetophenone, compound (I) was also isolated, but in trace amounts, presumably resulting from a Michael-type addition reaction between chalcone (*A*) and further 4-chloroacetophenone. Subsequently, the reaction between chalcone (*A*) and an excess of 4-chloroacetophenone under basic conditions was, indeed, found to provide an acceptable yield of (I), which was found from the structural study to be, in fact, an 84:16 mixture of the two isomeric compounds (I*a*) and (I*b*) (see below). The origin of the 2-chloro substituent was eventually traced to one batch of commercial 4-chloroacetophenone, as used in the conversion of (*A*) to (I). Consistent with this, there



Scheme 1

is no evidence for the presence of any 2-chloro substituent either in the other chlorinated aryl ring in (I) or in (II). As discussed below, the occurrence of the 2-chloro isomer, (I*b*), has a negligible effect on the supramolecular aggregation in (I). When chalcone (*A*) was crystallized from hot dimethylformamide solution, trace quantities of a second compound, (II), were also obtained, apparently resulting from a Diels–Alder type dimerization of (*A*), accompanied by the loss of two H atoms by aerial oxidation (see Scheme 2).

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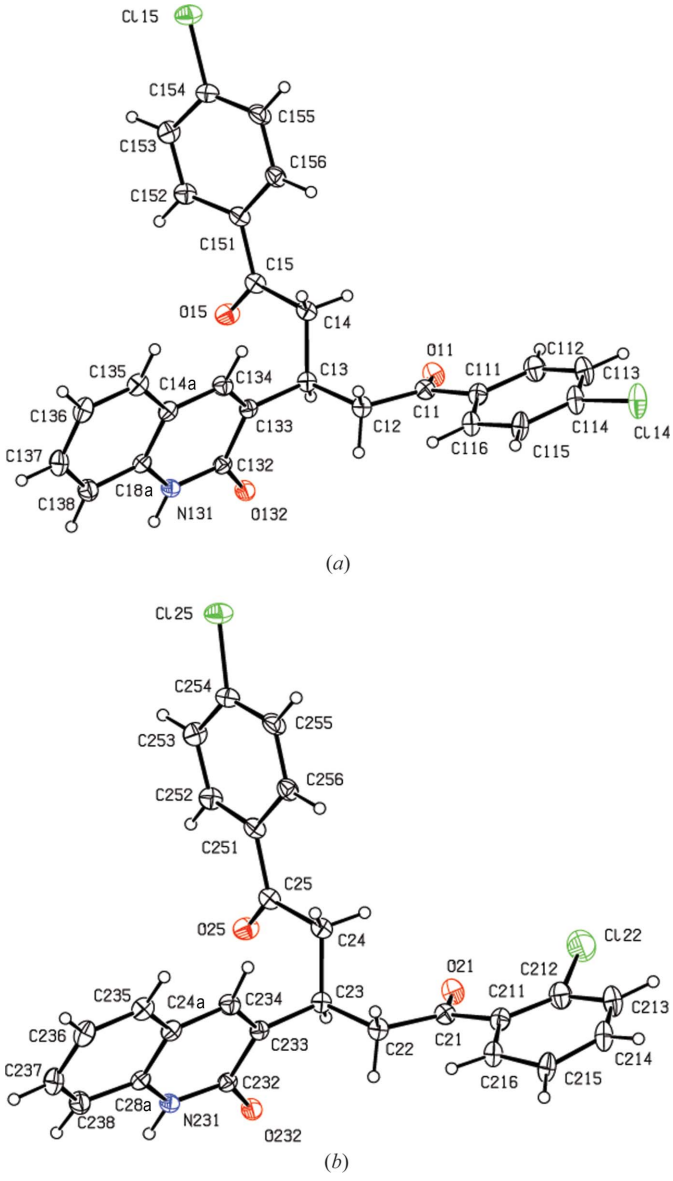
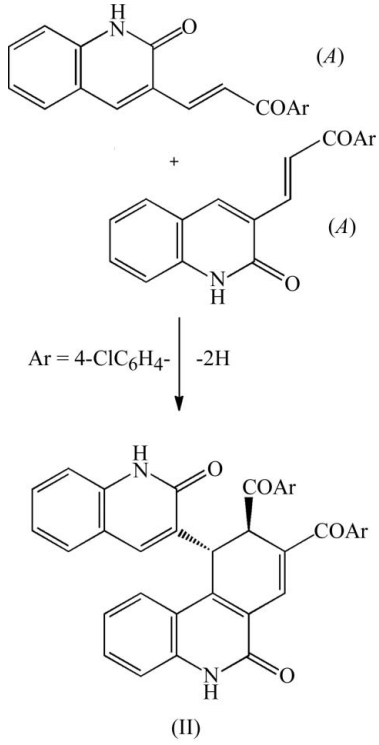


Figure 1
The molecular structures of (*a*) the major isomer (I*a*) and (*b*) the minor isomer (I*b*) of (I), showing the atom-labelling schemes. Displacement ellipsoids are drawn at the 30% probability level.

Compound (I) contains geometric isomers (I*a*) and (I*b*) (Fig. 1) in an 84:16 ratio in the crystal selected for data collection. It is possible that this ratio may vary somewhat from one crystal to another and, in view of this and the absence of a simple small-integer ratio between the abundances of the two components, it may be better to regard (I) as a solid solution rather than as a cocrystal (Aitipamula *et al.*, 2012). Compound (I) crystallizes in the rather uncommon space group $I4_1/a$; in the February 2012 release of the Cambridge Structural Database (Allen, 2002), only 2086 entries out of a total of 603298, *ca* 0.35%, have the space group $I4_1/a$. In (I), the two isomeric forms occupy very similar positions within the unit cell (Fig. 3) and the similarity of the molecular conformations is confirmed by a comparison of the torsion angles (Table 1). Although the experimental uncertainties on the values for the minor isomer are fairly substantial, within that constraint the corresponding values for the two isomers are, in general, closely similar. In addition, the very different values (Table 1) of the two torsion angles C*x*1—C*x*2—C*x*3—C*x*4 and C*x*2—C*x*3—C*x*4—C*x*5 (where x = 1 or 2), which define the conformation of the molecular backbone in each isomer, show that the molecules of isomers (I*a*) and (I*b*) can have no internal symmetry. Both isomers are thus conformationally chiral, although the centrosymmetric space group accommodates equal numbers of the two conformational enantiomers. The close similarity between the conformations of (I*a*) and (I*b*) may be a straightforward consequence of the nature of the structure in which, at a minority of the molecular sites, a molecule of (I*b*) has simply replaced a molecule of (I*a*) and is thus constrained to adopt essentially the same overall molecular shape.



(II)

Scheme 2

In the molecule of (II) (Fig. 2), there are two stereogenic centres, at atoms C9 and C10, and the compound crystallizes as a true racemate with configuration (9*RS*,10*RS*). For the (9*R*,10*R*) enantiomer, ring C6a/C7/C8/C9/C10/C10a adopts a screw-boat conformation, with atoms C9 and C10 displaced on opposite sides of the mean plane of the ring by 0.220 (2) and 0.213 (2) Å, respectively. The ring-puckering parameters (Cremer & Pople, 1975) are Q = 0.342 (2) Å, θ = 61.9 (3)° and φ = 207.5 (4)°; for an idealized screw-boat form the ring-puckering angles are θ = 67.5° and φ =(60k + 30)°, where k represents an integer. The substituent atoms C97 and C103 (Fig. 2) both adopt axial positions on the screw-boat ring, presumably in order to minimize the steric interactions between the acyl substituent at C9 and the quinolinone substituent at C10.

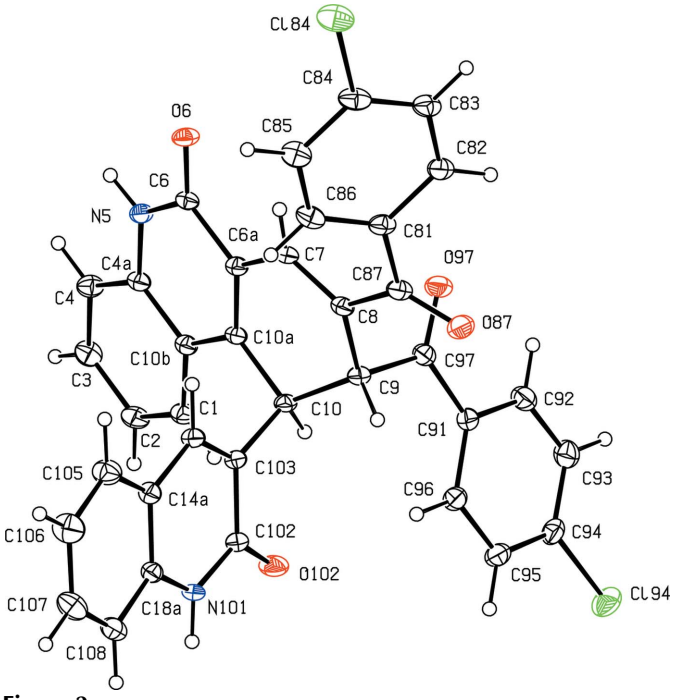


Figure 2
The molecular structure of the (9*R*,10*R*) enantiomer of (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

In the crystal structure of (I), the hydrogen bonds involving the two isomeric forms (I*a*) and (I*b*) are essentially the same (Table 2), as might be expected from the similarity of the two molecular conformations. Accordingly, it is necessary only to discuss the supramolecular aggregation of (I*a*). Two hydrogen bonds, one each of the N—H···O and C—H···O types, link the molecules of (I*a*) into a single three-dimensional framework, and it is convenient to analyse the formation of the framework in terms of two simple substructures (Ferguson *et al.*, 1998*a*,*b*; Gregson *et al.*, 2000), each involving just one type of hydrogen bond, and which are respectively one- and zero-dimensional.

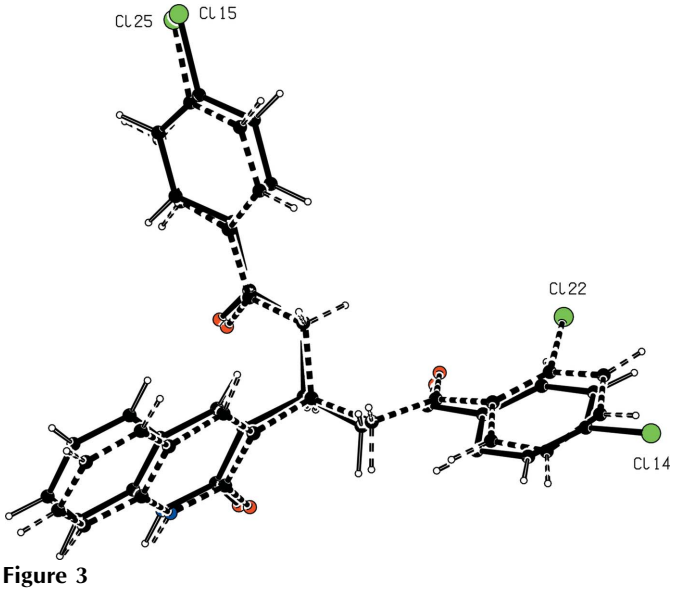


Figure 3
The major component, (I*a*) (solid lines), and the minor component, (I*b*) (dashed lines), of (I), showing the similarity in orientation and conformation of the two components.

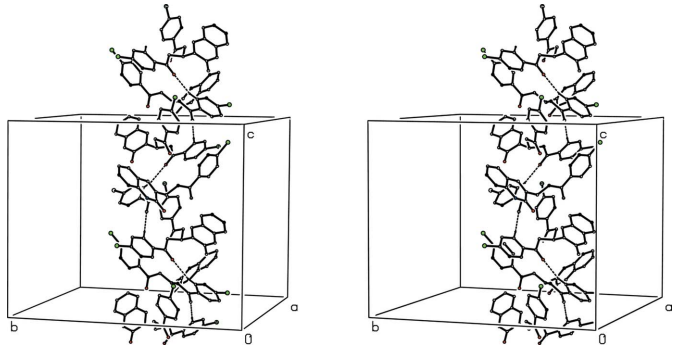


Figure 4
A stereoview of part of the crystal structure of (I), showing the formation of a hydrogen-bonded *C*(5) chain along $(\frac{3}{4}, \frac{1}{2}, z)$. For the sake of clarity, only the major isomer is included and H atoms not involved in the motif shown have been omitted.

The one-dimensional substructure of (I) takes the form of a simple chain built using a C—H···O hydrogen bond having an aryl C—H unit as the donor. Aryl atom C156 in the molecule of (I*a*) at (*x*, *y*, *z*) acts as hydrogen-bond donor to acyl atom O15 in the molecule at $(y+\frac{1}{4}, -x+\frac{5}{4}, z+\frac{1}{4})$, while atom C156 at $(y+\frac{1}{4}, -x+\frac{5}{4}, z+\frac{1}{4})$ in turn acts as donor to atom O15 at $(-x+\frac{3}{2}, -y+1, z+\frac{1}{2})$, and so on, thereby forming a *C*(5) (Bernstein *et al.*, 1995) helical chain running parallel to the [001] direction and containing molecules related by the 4_3 screw axis along

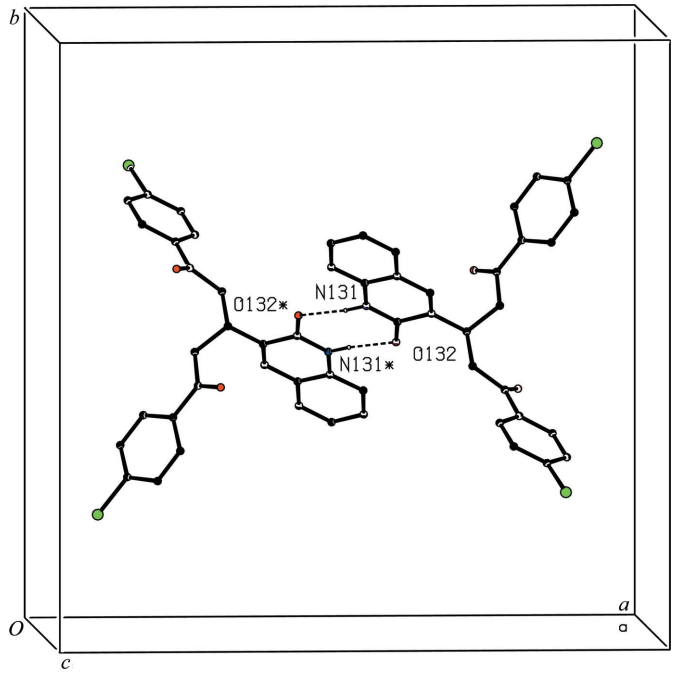


Figure 5
Part of the crystal structure of (I), showing the formation of a centrosymmetric $R_2^2(8)$ dimer. For the sake of clarity, only the major isomer is included and H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) are at the symmetry position $(-x+1, -y+1, -z+1)$.

$(\frac{3}{4}, \frac{1}{2}, z)$ (Fig. 4). There is also present a rather long C—H···O contact involving an aliphatic C—H unit; even if this were regarded as structurally significant, its role would be simply to reinforce the chain motif discussed above.

In the second, zero-dimensional, substructure, paired N—H···O hydrogen bonds link the molecules at (x, y, z) and $(-x + 1, -y + 1, -z + 1)$ into a centrosymmetric dimer characterized by an $R_2^2(8)$ motif (Fig. 5). The molecule at $(-x+1, -y+1, -z+1)$ is a component of the $C(5)$ chain built from molecules related by the 4_1 screw axis along $(\frac{1}{4}, \frac{1}{2}, z)$. Hence, the combination of these two motifs directly links the $C(5)$ chain along $(\frac{3}{4}, \frac{1}{2}, z)$ to the four analogous chains along $(\frac{1}{4}, \frac{1}{2}, z)$, $(\frac{5}{4}, \frac{1}{2}, z)$, $(\frac{3}{4}, 0, z)$ and $(\frac{3}{4}, 1, z)$, thus, in turn, linking all of the $C(5)$ chains into a continuous framework structure. Replacement, at any randomly selected molecular site, of a molecule of (I*a*) by a molecule of (I*b*) will have no significant influence on the supramolecular aggregation, as the direction-specific intermolecular interactions involving (I*a*) and (I*b*) are entirely equivalent (Table 2).

The supramolecular aggregation in (II) also involves a combination of N—H···O and C—H···O hydrogen bonds (Table 2), but here the resulting hydrogen-bonded structure is only one-dimensional. Acting in isolation, the N—H···O hydrogen bond links molecules of (II) related by translation into a $C(9)$ chain running parallel to the [100] direction, while the C—H···O hydrogen bond, acting alone, links inversion-related pairs of molecules to form an $R_2^2(18)$ motif. In combination, the two hydrogen bonds generate a molecular ribbon parallel to [100], in which centrosymmetric rings centred at $(n, \frac{1}{2}, 0)$ alternate with centrosymmetric $R_4^4(24)$ rings centred at $(n + \frac{1}{2}, \frac{1}{2}, 0)$, where n represents an integer in each case (Fig. 6). The only other direction-specific intermolecular contact in the structure of (II) (Table 2) has a fairly long H···O distance and, more significantly, a small C—H···O angle, and for this reason alone (*cf.* Wood *et al.*, 2009) it is not regarded as structurally significant. Even if this contact were significant, it would not affect the overall supramolecular aggregation, since its action would simply be a reinforcement of the chain generated by the N—H···O hydrogen bond. The stacking of the hydrogen-bonded ribbons is such as to enclose substantial cavities. Although *PLATON* (Spek, 2009) indicates the presence of two such spaces, centred close to the origin and to $(\frac{1}{2}, 0, \frac{1}{2})$, this space, in fact, takes the form of a single continuous channel parallel to [100] (Fig. 7). This space appears to contain disordered solvent molecules, but no chemically sensible model could be developed to account for the associated peaks in the difference map (see *Refinement*). It is possible that the solvent species within the channels are mobile (Farrell *et al.*, 2002).

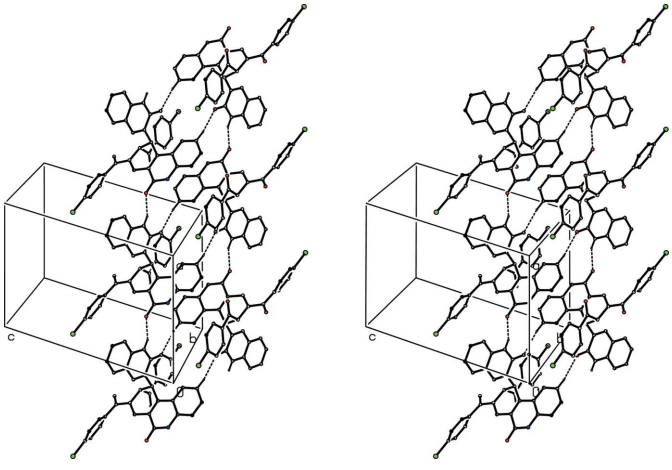


Figure 6
A stereoview of part of the crystal structure of (II), showing the formation of a hydrogen-bonded ribbon along [100] consisting of alternating $R_2^2(18)$ and $R_4^4(24)$ rings. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

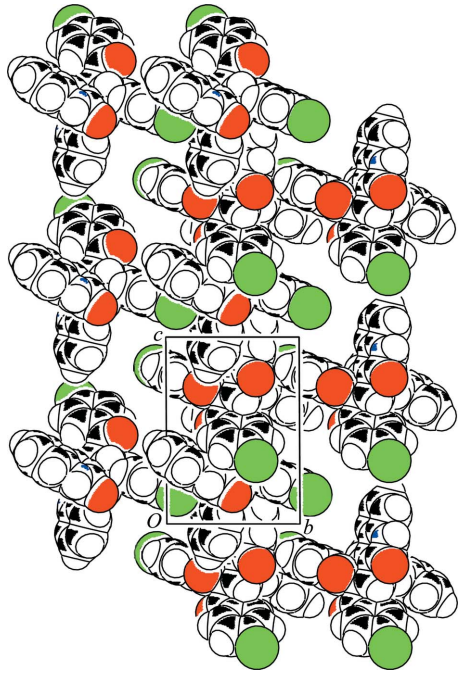


Figure 7
A space-filling view, approximately along [100], of part of the crystal structure of (II), showing the channels between the hydrogen-bonded ribbons.

Experimental

For the synthesis of (I), a solution of chalcone (*A*) (100 mg, 0.32 mmol) and 4-chloroacetophenone (61 mg, 0.40 mmol, 1.25 equivalents) in a mixture of 95% aqueous ethanol (5 ml) and 20% aqueous sodium hydroxide solution (2 drops) was heated under reflux for 7 h; after this time, the chalcone had been completely consumed, as indicated by thin-layer chromatography. The mixture was cooled to ambient temperature and water (2 ml) was added. The resulting solid, (I), was collected by filtration and washed with water (2 × 0.5 ml). Colourless crystals suitable for single-crystal X-ray diffraction were grown by slow evaporation, at ambient temperature and in air, from a solution in ethanol (yield 72%, m.p. 484 K). Analysis found: C 67.0, H 4.3, N 2.9%; $C_{26}H_{19}Cl_2NO_3$ requires: C 67.3, H 4.1, N 3.0%.

Compound (II) was isolated in trace quantities as pale-yellow crystals as a by-product during the crystallization of colourless chalcone (*A*) from a solution in hot dimethylformamide (m.p. 519 K). Analysis found: C 69.9, H 3.7, N 4.4%; $C_{36}H_{22}Cl_2N_2O_4$ requires: C 70.0, H 3.6, N 4.5%.

Table 1
Selected torsion angles (°) for isomers (I*a*) and (I*b*).

(I*a*)		(I*b*)	
C112—C111—C11—C12	−167.9 (5)	C212—C211—C21—C22	−168 (4)
C111—C11—C12—C13	160.3 (4)	C211—C21—C22—C23	160 (3)
C11—C12—C13—C14	−62.6 (4)	C21—C22—C23—C24	−65 (3)
C12—C13—C14—C15	176.9 (6)	C22—C23—C24—C25	175 (3)
C13—C14—C15—C151	164.6 (9)	C23—C24—C25—C251	166 (4)
C14—C15—C151—C152	−168.8 (9)	C24—C25—C251—C252	175 (6)
C11—C12—C13—C133	174.8 (4)	C21—C22—C23—C233	172 (2)
C12—C13—C133—C132	−95.5 (5)	C22—C23—C233—C232	−105 (3)

Table 2
Hydrogen bonds and short intramolecular contacts (Å, °) for (I) and (II).

Compound	*D*—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
(I*a*)	N131—H131···O132^{i}	0.88	1.96	2.840 (7)	175
	C156—H156···O15^{ii}	0.95	2.46	3.386 (12)	165
	C12—H12*A*···O11^{ii}	0.99	2.56	3.451 (5)	149
(I*b*)	N231—H231···O232^{i}	0.88	2.20	3.07 (5)	168
	C256—H256···O25^{ii}	0.95	2.46	3.41 (7)	176
	C22—H22*A*···O21^{ii}	0.99	2.58	3.42 (3)	142
(II)	N101—H101···O6^{iii}	0.88	2.02	2.850 (2)	156
	C2—H2···O102^{iv}	0.95	2.42	3.345 (3)	163
	C108—H108···O6^{iii}	0.95	2.57	3.291 (3)	133

Symmetry codes: (i) $-x+1, -y+1, -z+1$; (ii) $y+\frac{1}{4}, -x+\frac{5}{4}, z+\frac{1}{4}$; (iii) $x+1, y, z$; (iv) $-x+2, -y+1, -z$.

Compound (I)

Crystal data

$0.84C_{26}H_{19}Cl_2NO_3{\cdot}0.16C_{26}H_{19}Cl_2NO_3$
M_r = 464.32
Tetragonal, $I4_1/a$
a = 22.268 (4) Å
c = 18.398 (5) Å
V = 9123 (4) Å^3
Z = 16
Mo $K\alpha$ radiation
μ = 0.31 mm^{-1}
T = 120 K
0.34 × 0.34 × 0.26 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.902, T_{max} = 0.923
32275 measured reflections
5197 independent reflections
3789 reflections with $I > 2\sigma(I)$
R_{int} = 0.047

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.054
$wR(F^2)$ = 0.159
S = 1.09
5197 reflections
392 parameters
85 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.45 e Å^{-3}
$\Delta\rho_{min}$ = −0.33 e Å^{-3}

Compound (II)

Crystal data

$C_{36}H_{22}Cl_2N_2O_4$
M_r = 617.46
Triclinic, $P\overline{1}$
a = 10.6771 (19) Å
b = 11.5208 (15) Å
c = 15.7275 (13) Å
α = 83.956 (11)°
β = 72.795 (13)°
γ = 68.204 (14)°
V = 1715.9 (5) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 0.23 mm^{-1}
T = 120 K
0.34 × 0.31 × 0.18 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.932, T_{max} = 0.960
7841 measured reflections
7841 independent reflections
5593 reflections with $I > 2\sigma(I)$

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.051
$wR(F^2)$ = 0.161
S = 1.12
7841 reflections
397 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.34 e Å^{-3}
$\Delta\rho_{min}$ = −0.48 e Å^{-3}

For (I), the space group $I4_1/a$ was uniquely assigned from the systematic absences and the cell setting having the origin at a centre of inversion was employed. From an early stage in the refinement of (I) it was apparent that the Cl substituent on one of the aryl rings was distributed over two positions, corresponding to the presence of the two geometric isomers, *viz.* (I*a*) and (I*b*) (Fig. 1), the molecules of which occupy very similar positions in the unit cell. This disorder was handled by restraining the bonded distances and the one-angle nonbonded distances in the minor isomer, (I*b*), with the exception of those involving atom Cl22, to be equal to the corresponding distances in the major isomer, (I*a*), subject to s.u. values of 0.005 and 0.01 Å, respectively. The C114—Cl14 and C212—Cl22 bond lengths were restrained to a common value of 1.74 (2) Å. In addition, the values of the anisotropic displacement parameter (ADP) components for the pairs of the corresponding atoms in the two isomers which occupy essentially the same physical space in different unit cells were constrained to be equal. Subject to these conditions, the refinement of (I) converged smoothly to give occupancy factors for the major and minor isomers of 0.840 (2) and 0.160 (2), respectively, in the crystal selected for data collection. Examination of the refined structure of (I) using *PLATON* (Spek, 2009) revealed the presence of a number of small voids at the special positions of $\overline{4}$ symmetry, each of volume *ca* 34 Å^3, too small to accommodate even the smallest of solvent molecules.

For (II), the reference molecule was selected as one having the *R* configuration at atoms C9 and C10. Conventional refinement converged at R = 0.162 for 7841 unique data, of which 5685 were labelled observed, from a total of 43906 measured reflections having R_{int} = 0.0413. Examination of this structure using *PLATON* (Spek, 2009) identified apparent void space around the origin (volume *ca* 284 Å^3) and around $(\frac{1}{2}, 0, \frac{1}{2})$ (volume *ca* 126 Å^3). In addition, the difference map contained a number of substantial peaks, but it proved impossible to develop from these any sensible model for any plausible solvent species. It is possible both that more than one solvent species is present and that the solvent molecules are disordered over a number of sites, or even mobile. Accordingly, the data were subjected to the SQUEEZE procedure in *PLATON*, which indicated a total of *ca* 60 additional electrons per unit cell, and the refinement was then continued using the modified data set.

All H atoms in (I*a*) and (II) were located in difference maps, while those in (I*b*) were added in calculated positions. Subsequently, all H atoms were treated as riding in geometrically idealized positions, with C—H = 0.95 (aromatic), 0.99 (CH_2) or 1.00 Å (aliphatic CH) and N—H = 0.88 Å, and with U_{iso}(H) = 1.2U_{eq}(C,N).

For both compounds, data collection: *COLLECT* (Nonius, 1999); cell refinement: *DIRAX*/*LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003). Program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008) for (I); *SIR2004* (Burla *et al.*, 2005) for (II). For both compounds, 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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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG3252). Services for accessing these data are described at the back of the journal.

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