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Racemic 5-(4-chlorophenyl)-2-methoxyindeno[1′,2′:2,3]pyrido-[5,6-*d*]pyrimidine-4,6(3*H*,5*H*)-dione–dimethylformamide (1/1) and (5*RS*,5a*SR*,10b*SR*)-10b-hydroxy-2-methoxy-5-(4-methoxyphenyl)-5a,10b-dihydroindeno[1′,2′:2,3]pyrido[5,6-*d*]-pyrimidine-4,6(3*H*,5*H*)-dione–dimethylformamide (1/1): chains of rings generated by N—H···O and C—H···π(arene) hydrogen bonds

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5-(4-Chlorophenyl)-2-methoxyindeno[1′,2′:2,3]pyrido[5,6-*d*]-pyrimidine-4,6(3*H*,5*H*)-dione crystallizes as a 1:1 dimethylformamide solvate, $C_{21}H_{14}ClN_3O_3\cdot C_3H_7NO$. The heterocyclic molecules contain a planar fused-ring system and they are linked by paired N—H···O hydrogen bonds [H···O = 1.85 Å, N···O = 2.735 (4) Å and N—H···O = 179°] into centrosymmetric dimers, which are themselves linked into chains by a single C—H···π(arene) hydrogen bond. 10b-Hydroxy-2-methoxy-5-(4-methoxyphenyl)-5a,10b-dihydroindeno[1′,2′:2,3]-pyrido[5,6-*d*]pyrimidine-4,6(3*H*,5*H*)-dione also crystallizes as a 1:1 dimethylformamide solvate, $C_{22}H_{19}N_3O_5\cdot C_3H_7NO$. The heterocyclic molecules contain a sharply folded fused-ring system and they are linked by two independent N—H···O hydrogen bonds [H···O = 1.92 and 2.18 Å, N···O = 2.801 (2) and 3.051 (2) Å, and N—H···O = 175 and 173°] into chains of rings. In both compounds, the dimethylformamide molecules are pendent from the chains, linked *via* N—H···O and O—H···O hydrogen bonds, respectively.

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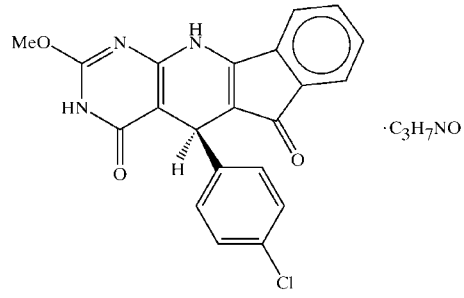
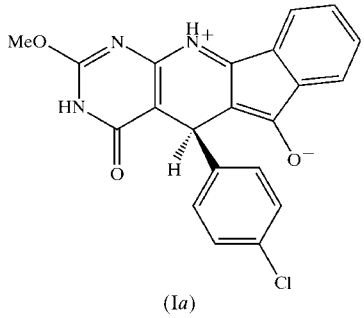
Comment

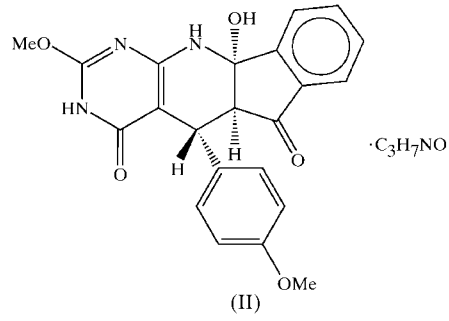
As part of our study of the synthesis of new fused heterocyclic systems of potential biological interest using multicomponent condensation reactions under environmentally friendly conditions, we report here on two indeno[1′,2′:2,3]pyrido[5,6-*d*]-pyrimidinediones obtained from reactions between 6-amino-pyrimidinone, aryl aldehydes and indandione activated by microwave radiation (Quiroga *et al.*, 2001). Both of these products form monosolvates, *viz*. (I) and (II), when crystallized from dimethylformamide solutions.



(I)



(I*a*)



(II)

The fused-ring system in (I) (Fig. 1) is essentially planar. Although the heterocyclic molecules are chiral, because of the stereogenic centre at atom C5, (I) crystallizes as a racemic mixture in space group $P2_1/c$; the reference molecule was selected as having an *R* configuration at atom C5. Compound (II) (Fig. 2) differs from (I) not only by having a different 4-substituent on the pendent aryl ring but also, more importantly, in having an additional H atom bonded to atom C5a and an OH group bonded to atom C10b. In contrast to the planar ring system in (I), the fused-ring system in (II) is folded sharply along the C5a—C10b bond. The dihedral angle between the planes through the two central rings is 74.9 (2)°. The heterocyclic component of (II) is chiral, with three

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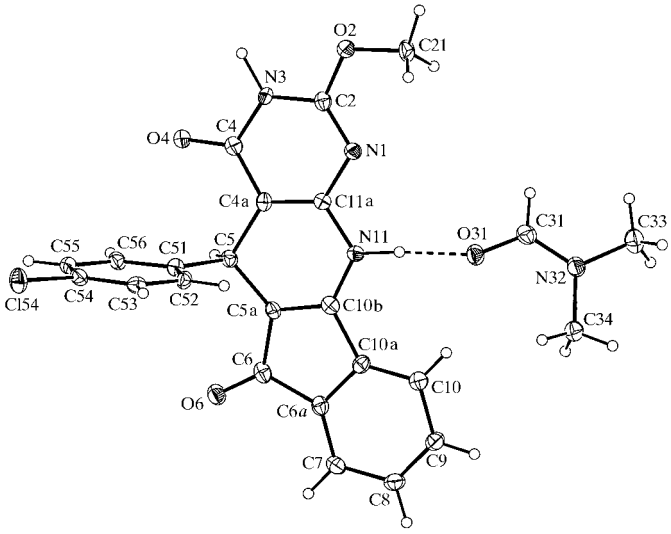


Figure 1
The independent molecular components in (I), showing the *R* enantiomorph of the heterocyclic component, together with the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

contiguous stereogenic centres at atoms C5, C5a and C10b. Compound (II) also crystallizes as a racemic mixture, this time in space group $P\overline{1}$. The reference molecule in (II) was again selected to have an *R* configuration at atom C5, and in this molecule, the configuration at both atom C5a and atom C10b is *S*. Hence the racemic mixture consists of molecules whose configurations are 5*R*,5a*S*,10b*S* and 5*S*,5a*R*,10b*R*. The additional H and OH substituents in (II) are thus attached to the same face of the fused-ring system as the aryl substituent at atom C5.

Within the heterocyclic component in (I), there are alternating C—C bond lengths in the fused benzenoid ring (C6a/C7–C10/C10a; Table 1). In addition, the N11—C11a and C5a—C6 distances are both significantly shorter than the analogous N1—C2 and C6—C6a bonds, respectively, while the C6—O6 distance is significantly longer in (I) than in (II) (Table 1). On the other hand, there is no evidence for any bond fixation in the fused benzenoid ring of (II), while all the bond distances in (II) that involve atoms C5a or C10b show the expected increases compared with the corresponding distances in (I). Taken together, the metrical data indicate both the polarization of the central conjugated amide unit in (I), which is not possible in (II), and some bond fixation in the fused benzenoid ring of (I). A number of canonical forms can be drawn to represent these two independent effects, of which (I*a*) (see scheme above) is typical. For (II), the unpolarized form, with a delocalized benzenoid ring in the fused system, is the appropriate representation. The dimethylformamide components show no unusual features.

In the asymmetric unit of (I), the two molecular components are linked by a nearly linear N—H···O hydrogen bond (Table 2). In addition, a second, rather short, N—H···O hydrogen bond generates a centrosymmetric four-molecule aggregate centred at $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$ (Fig. 3) and characterized by the graph-set descriptor $D_3^3(15)[R_2^2(8)]$ (Bernstein *et al.*, 1995). The $D[R]$ pattern occurs frequently in centrosymmetric

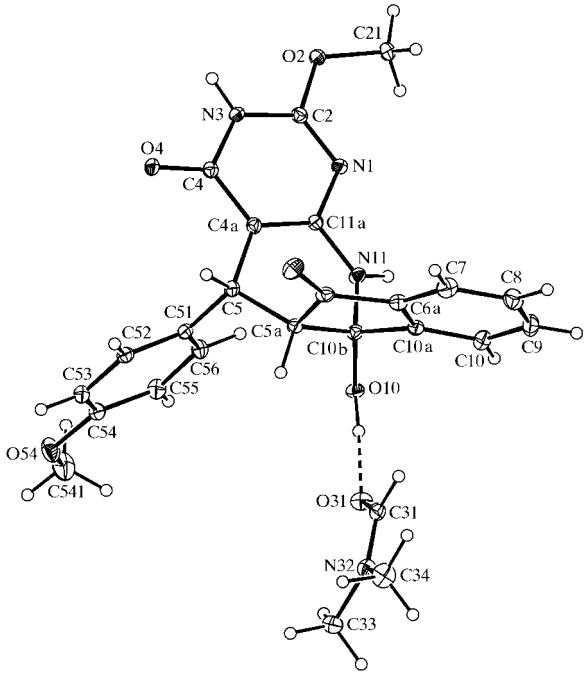


Figure 2
The independent molecular components in (II), showing the 5*R*,5a*S*,10b*S* enantiomorph of the heterocyclic component, together with the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

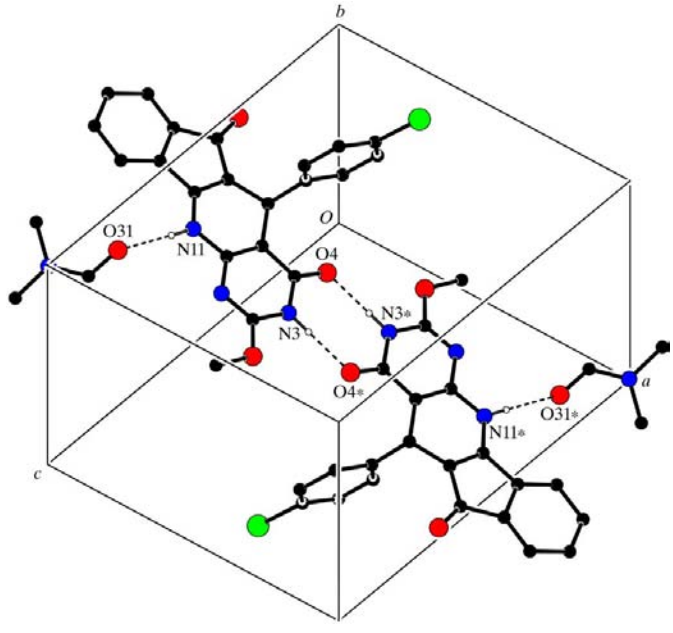


Figure 3
Part of the crystal structure of (I), showing the formation of a centrosymmetric four-molecule aggregate. For clarity, H atoms bonded to C atoms have been omitted. Atoms marked with an asterisk (*) are at the symmetry position $(1 - x, 1 - y, 1 - z)$.

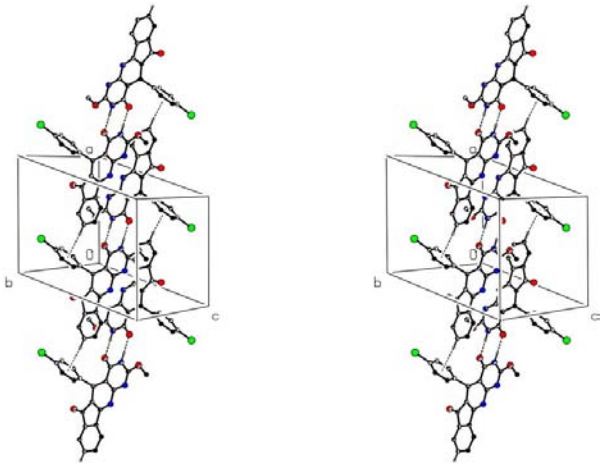


Figure 4
A stereoview of part of the crystal structure of (I), showing the formation of a [100] chain of rings built from N—H···O and C—H···π(arene) hydrogen bonds. For clarity, the dimethylformamide molecules have been omitted, as have all H atoms not involved in the motifs shown.

structures containing more than one molecule in the asymmetric unit (Bernstein *et al.*, 1995), for example, where centrosymmetric rings have a second pendent component (Patterson *et al.*, 1998). These centrosymmetric aggregates are linked into chains by a single short C—H···π(arene) hydrogen bond. Atom C8, part of the fused benzenoid ring in the molecule at (x, y, z), which itself lies in the aggregate centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$), acts as a hydrogen-bond donor to the corresponding benzenoid ring in the molecule at ($-1+x$, y, z), which forms part of the aggregate centred at ($-\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$). Propagation of the hydrogen bonds by translation and inversion then links centrosymmetric aggregates into a complex chain of rings running parallel to the [100] direction (Fig. 4). There are no direction-specific interactions between adjacent chains; in particular, aromatic π–π stacking interactions are absent from the structure of (I).

In (II), the two independent molecular components (Fig. 2) are linked by a short O—H···O hydrogen bond (Table 3), and two N—H···O hydrogen bonds link the heterocyclic molecules into a chain of rings. In the shorter of the N—H···O hydrogen bonds, amide atom N3 in the molecule at (x, y, z) acts as a hydrogen-bond donor to amide atom O4 in the molecule at ($1-x$, $1-y$, $1-z$), so generating a centrosymmetric four-molecule $D_3^3(19)[R_2^2(8)]$ aggregate centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) (Fig. 5) and analogous to the corresponding aggregate formed by (I) (Fig. 3). In addition, atom N11 in the molecule at (x, y, z) acts as a donor in a longer hydrogen bond, to hydroxy atom O10 in the molecule at ($-x$, $-y$, $-z$), so forming a second $R_2^2(8)$ ring, this time centred at (0, 0, 0). The combination of the two ring motifs generates a chain of rings running parallel to the [111] direction (Fig. 6). Both C—H···π(arene) hydrogen bonds and aromatic π–π stacking interactions are absent from the structure of (II).

The constitutions of (I) and (II) and, in particular, the relative stereochemistry of (II) are of importance in the context of a general synthetic method for the preparation of fused pyridopyrimidinones by means of microwave heating in solvent-free systems (Quiroga *et al.*, 2001). Reaction of an aminopyrimidine with an aromatic aldehyde and benzoylacetonitrile (containing an activated methylene group) yielded firstly the hydrated intermediate (III) (see scheme below) followed, upon longer heating, by the loss of water to give (IV). However, the spectral techniques used for the identification of (III) and (IV) did not allow assignment of the relative stereochemistry of the three contiguous stereogenic centres. The syntheses of (I) and (II) are directly related to those of (IV) and (III), respectively, so that the relative stereochemistry in intermediate (III) can, with reasonable confidence, be assigned as being similar to that in (II). In any event, it is clear that the loss of water from intermediates of type (II) to form the new C=C double bond in the type-(I) products requires a *cis* elimination step.

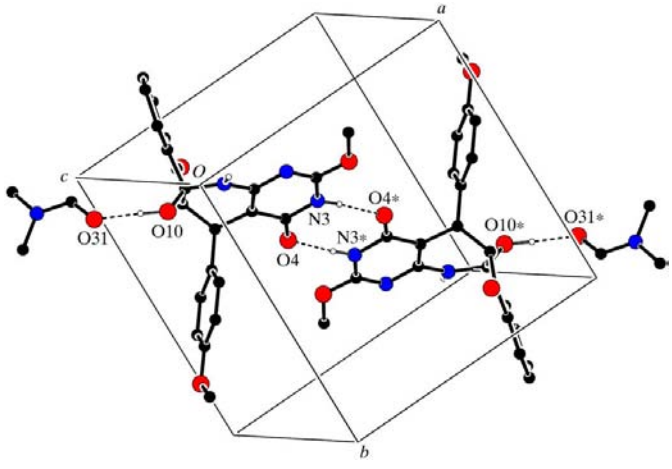


Figure 5
Part of the crystal structure of (II), showing the formation of a centrosymmetric four-molecule aggregate. For clarity, H atoms bonded to C atoms have been omitted. Atoms marked with an asterisk (*) are at the symmetry position ($1-x$, $1-y$, $1-z$).

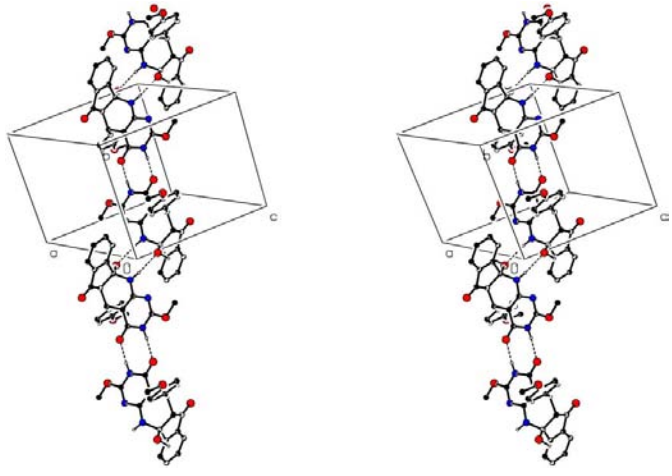
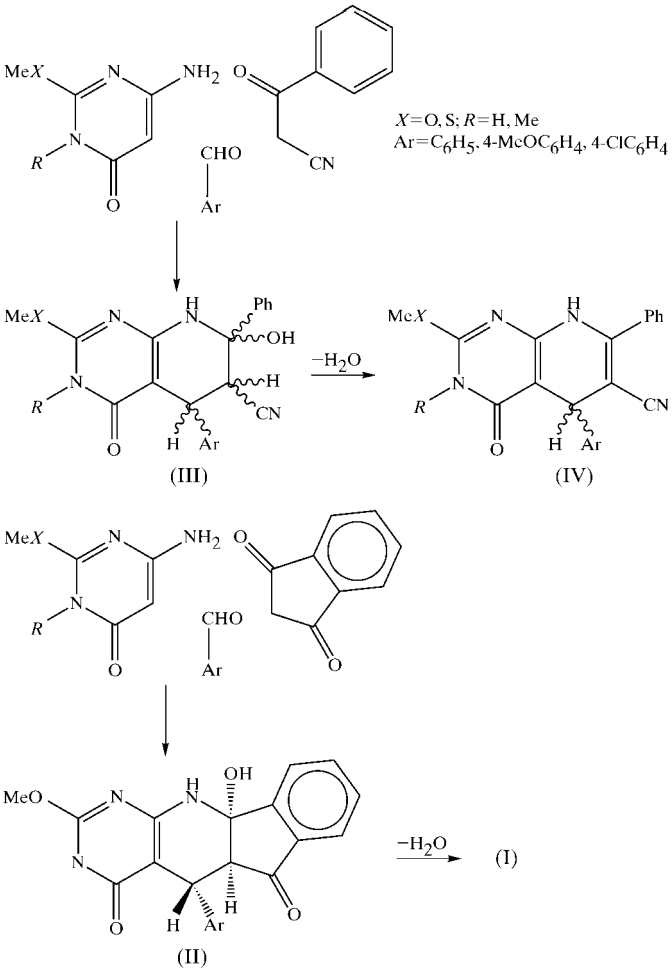


Figure 6
A stereoview of part of the crystal structure of (II), showing the formation of a chain of rings along [111]. For clarity, the dimethylformamide molecules have been omitted, as have all H atoms bonded to C atoms.



Experimental

For the synthesis of the heterocyclic component of (I), a homogeneous mixture containing equimolar amounts of 6-amino-2-methoxy-3*H*-4-pyrimidone, 4-chlorobenzaldehyde and indandione was placed in an open Pyrex glass vessel and irradiated in a domestic microwave oven for 5 min (at 600 W). The product of the reaction was recrystallized from absolute ethanol (yield 71%; m.p. 510 K). MS (EI) *m*/*z*: 393, 391 (M^+). For the synthesis of the heterocyclic component of (II), a similar mixture, but containing 4-methoxybenzaldehyde in place of 4-chlorobenzaldehyde, was irradiated in a domestic microwave oven for 45 s (at 600 W). The reaction product was filtered off, washed with ethanol and recrystallized from absolute ethanol (yield 76%; m.p. 455 K). Crystals of solvates (I) and (II) suitable for single-crystal X-ray diffraction were grown from dimethylformamide solutions.

Compound (I)

Crystal data

$C_{21}H_{14}ClN_3O_3\cdot C_3H_7NO$
M_r = 464.90
Monoclinic, $P2_1/c$
a = 10.6850 (6) Å
b = 17.6182 (12) Å
c = 12.3774 (8) Å
β = 108.523 (4)°
V = 2209.3 (2) Å^3
Z = 4
D_x = 1.398 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 4182 reflections
θ = 3.1–25.7°
μ = 0.21 mm^{-1}
T = 120 (2) K
Block, orange
0.08 × 0.04 × 0.02 mm

Data collection

Nonius KappaCCD diffractometer
φ scans, and ω scans with κ offsets
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995, 1997)
T_{min} = 0.977, T_{max} = 0.996
8314 measured reflections
4182 independent reflections
2135 reflections with $I > 2\sigma(I)$
R_{int} = 0.123
θ_{max} = 25.7°
$h = -13 \rightarrow 13$
$k = -21 \rightarrow 21$
$l = -15 \rightarrow 14$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.069
$wR(F^2)$ = 0.157
S = 0.96
4182 reflections
302 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0439P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.27 e Å^{-3}
$\Delta\rho_{min}$ = −0.29 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.0104 (12)

Table 1
Selected bond lengths (Å) for compounds (I) and (II).

	(I)	(II)
N1—C2	1.299 (5)	1.302 (2)
C2—N3	1.353 (5)	1.351 (2)
N3—C4	1.392 (5)	1.396 (2)
C4—C4a	1.420 (5)	1.416 (3)
C4a—C11a	1.378 (5)	1.383 (3)
C11a—N1	1.379 (5)	1.373 (2)
C4a—C5	1.537 (5)	1.509 (3)
C5—C5a	1.502 (5)	1.544 (3)
C11a—N11	1.380 (5)	1.358 (2)
N11—C10b	1.345 (5)	1.454 (2)
C5a—C10b	1.361 (5)	1.558 (3)
C5a—C6	1.469 (6)	1.529 (3)
C6—C6a	1.512 (6)	1.471 (3)
C6a—C7	1.383 (6)	1.400 (3)
C7—C8	1.400 (6)	1.379 (3)
C8—C9	1.383 (5)	1.394 (3)
C9—C10	1.404 (6)	1.397 (3)
C10—C10a	1.374 (5)	1.389 (3)
C10a—C10b	1.486 (6)	1.526 (3)

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

*Cg*1 is the centroid of the C51–C56 ring.

D—H···A	D—H	H···A	D···A	D—H···A
N3—H3···O4^{i}	0.88	1.85	2.735 (4)	179
N11—H11···O31	0.88	1.98	2.857 (4)	172
C8—H8···*Cg*1^{ii}	0.95	2.63	3.561 (5)	167

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

Compound (II)

Crystal data

$C_{22}H_{19}N_3O_5\cdot C_3H_7NO$
M_r = 478.50
Triclinic, $P\overline{1}$
a = 10.4172 (2) Å
b = 10.8540 (3) Å
c = 11.6112 (3) Å
α = 94.2692 (12)°
β = 116.0676 (12)°
γ = 94.4530 (13)°
V = 1167.08 (5) Å^3
Z = 2
D_x = 1.362 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5297 reflections
θ = 2.9–27.6°
μ = 0.10 mm^{-1}
T = 120 (2) K
Block, yellow
0.20 × 0.10 × 0.04 mm

Data collection

Nonius KappaCCD diffractometer
φ scans, and ω scans with κ offsets
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995, 1997)
T_{min} = 0.974, T_{max} = 0.996
5297 measured reflections
5297 independent reflections
3719 reflections with $I > 2\sigma(I)$
R_{int} = 0.073
θ_{max} = 27.6°
$h = -13 \rightarrow 13$
$k = -14 \rightarrow 13$
$l = -15 \rightarrow 15$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.055
$wR(F^2)$ = 0.148
S = 1.04
5297 reflections
326 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0589P)^2 + 0.5313P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.37 e Å^{-3}

Table 3
Hydrogen-bonding geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
O10—H10*B*···O31	0.99	1.67	2.661 (2)	177
N3—H3···O4^{i}	0.88	1.92	2.801 (2)	175
N11—H11···O10^{iii}	0.88	2.18	3.051 (2)	173

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

For (I), space group $P2_1/c$ was uniquely assigned from the systematic absences. Crystals of (II) are triclinic, and space group $P\overline{1}$ was assigned and confirmed by the successful structure analysis. All H atoms were located from difference maps and subsequently treated as riding atoms [C—H = 0.95 (aromatic), 0.98 (methyl) or 1.00 Å (aliphatic), N—H = 0.88 Å and O—H = 0.99 Å], being allowed to ride at the distances deduced from the difference maps. The long O—H distance in (II) may be influenced by the short O···O distance in the associated hydrogen bond (Table 3). Examination of the refined structure of (II) using *PLATON* (Spek, 2003) showed the presence of small voids centred at approximately $(\frac{1}{2}, 0, \frac{1}{2})$ and at symmetry-related positions, each having a volume of ∼43 Å^3. However, these voids contain negligible electron density.

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: *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. JC thanks the Ministerio de Educación, Cultura y Deportes (Programa de Cooperación con Iberoamérica, AECI) of Spain. CC and JQ thank COLCIENCIAS and the Universidad de Valle for financial support.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1698). Services for accessing these data are described at the back of the journal.

References

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.
Ferguson, G. (1999). *PRPKAPPA*. University of Guelph, Canada.
McArdle, P. (2003). *OSCAIL*. Version 10 for Windows. 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.
Patterson, I. L. J., Glidewell, C. & Ferguson, G. (1998). *Acta Cryst.* C**54**, 1970–1974.
Quiroga, J., Cisneros, C., Insuasty, B., Abonía, R., Nogueras, M. & Sánchez, A. (2001). *Tetrahedron Lett.* **42**, 5625–5627.
Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.