Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Ethyl *N*-[2-(hydroxyacetyl)phenyl]-carbamate, ethyl *N*-[2-(hydroxy-acetyl)-4-iodophenyl]carbamate and ethyl *N*-[2-(hydroxyacetyl)-4-methyl-phenyl]carbamate

Simon J. Garden,[a] Marilza B. Corrêa,[a] Angelo C. Pinto,[a] James L. Wardell,[a] John N. Low[b] and Christopher Glidewell[c]*

[a]Universidade Federal do Rio de Janeiro, Instituto de Química, Cidade Universitária, CT, Bloco A, Ilha do Fundão, Rio de Janeiro, RJ, CEP 21941-909, Brazil, [b]Department of Chemistry, University of Aberdeen, Meston Walk, Old Aberdeen AB24 3UE, Scotland, and [c]School of Chemistry, University of St Andrews, Fife KY16 9ST, Scotland
Correspondence e-mail: cg@st-andrews.ac.uk

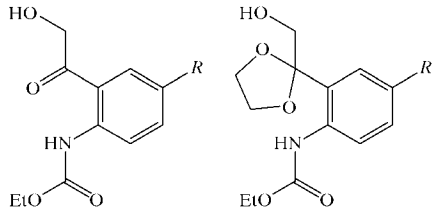
Received 20 February 2007
Accepted 21 February 2007
Online 17 March 2007

In ethyl *N*-[2-(hydroxyacetyl)phenyl]carbamate, $C_{11}H_{13}NO_4$, all of the non-H atoms lie on a mirror plane in the space group *Pnma*; the molecules are linked into simple chains by a single C—H···O hydrogen bond. The molecules of ethyl *N*-[2-(hydroxyacetyl)-4-iodophenyl]carbamate, $C_{11}H_{12}INO_4$, are linked into sheets by a combination of O—H···I and C—H···O hydrogen bonds and a dipolar I···O contact. Ethyl *N*-[2-(hydroxyacetyl)-4-methylphenyl]carbamate, $C_{12}H_{15}NO_4$, crystallizes with $Z' = 2$ in the space group $P\overline{1}$; pairs of molecules are weakly linked by an O—H···O hydrogen bond and these aggregates are linked into chains by two independent aromatic π–π stacking interactions.

Comment

We report here the structures of three related carbamate esters, ethyl *N*-[2-(hydroxyacetyl)phenyl]carbamate, (I), ethyl *N*-[2-(hydroxyacetyl)-4-iodophenyl]carbamate, (II), and ethyl *N*-[2-(hydroxyacetyl)-4-methylphenyl]carbamate, (III) (Figs. 1–3). These were prepared by simple deprotection of the ketal-protected analogues (IV)–(VI) (see scheme), whose synthesis from isatin precursors has recently been described (Garden *et al.*, 2003).

Compound (I) crystallizes with $Z' = 0.5$ in the space group *Pnma*, such that all the non-H atoms lie on a mirror plane, selected for the reference molecule as that at $y = \frac{3}{4}$. Compound (III) crystallizes with $Z' = 2$. Each of the independent molecules in compounds (II) and (III) adopts a conformation very similar to that in compound (I), as shown by the key torsion angles (Table 1 and Figs. 1–3). The corresponding torsion angles in compound (I) are all exactly 180° because of the internal mirror symmetry.



(I) R=H
(II) R=I
(III) R=Me
(IV) R=H
(V) R=I
(VI) R=Me

In each molecule, there are short intramolecular O—H···O and N—H···O contacts, both involving the carbonyl O atom (Tables 2–4). Regardless of whether these are regarded as genuine hydrogen bonds or as short dipolar contacts, they appear to have a decisive influence both on the molecular conformations and on the direction-specific intermolecular interactions. There are, for example, no intermolecular hydrogen bonds involving the N—H units in any of the compounds.

The molecules of compound (I) are linked by a single almost linear C—H···O hydrogen bond (Table 2). Aryl atom C3 in the molecule at (x, y, z) acts as hydrogen-bond donor to hydroxyl atom O22 in the molecule at ($-\frac{1}{2}+x, \frac{3}{2}-y, \frac{3}{2}-z$), so forming a $C(6)$ chain (Bernstein *et al.*, 1995) running parallel to the [100] direction and generated by the 2_1 screw axis along ($x, \frac{3}{4}, \frac{3}{4}$) (Fig. 4). Four chains of this type pass through each unit cell, but there are no direction-specific interactions between adjacent chains.

The molecules of compound (II) are linked into sheets by the combined action of O—H···I and C—H···O hydrogen bonds (Table 3) and a two-centre dipolar I···O interaction. Hydroxyl atom O22 in the molecule at (x, y, z) acts as hydrogen-bond donor to atom I4 in the molecule at ($\frac{3}{2}-x, \frac{1}{2}+y, \frac{3}{2}-z$), so forming a $C(8)$ chain running parallel to the [010]

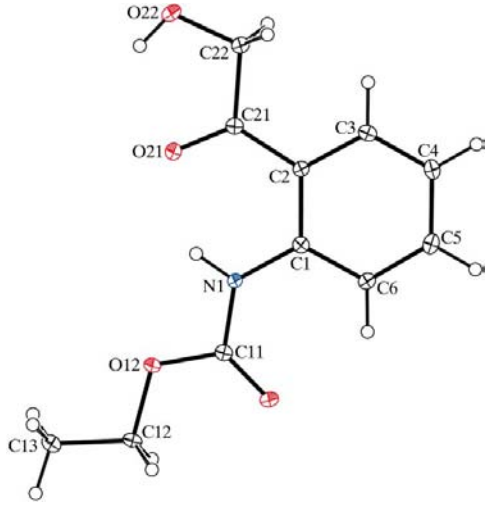


Figure 1
The molecule of compound (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

  DOI: 10.1107/S0108270107008682

direction and generated by the 2_1 screw axis along $(\frac{3}{4}, y, \frac{3}{4})$ (Fig. 5). At the same time, atom C22 at (x, y, z) acts as hydrogen-bond donor to carbonyl atom O21 in the molecule at $(-1 + x, y, z)$, so generating by translation a $C(4)$ chain running parallel to the [100] direction (Fig. 6), and the combination of [100] and [010] chains is sufficient to generate a sheet parallel to (001) (Fig. 7). This sheet is, in fact, reinforced by the dipolar interaction between atom I4 in the molecule at (x, y, z) and atom O22 in the molecule at $(\frac{1}{2} - x, -\frac{1}{2} + y, \frac{3}{2} - z)$, with $I\cdots O^{i}$ = 3.090 (3) Å and $C-I\cdots O^{i}$ = 175.6 (2)° [symmetry code: (i) $\frac{1}{2} - x, -\frac{1}{2} + y, \frac{3}{2} - z$]. Propagation of this interaction produces a $C(7)$ chain (Starbuck *et al.*, 1999) running parallel to the [010] direction and generated by the 2_1 screw axis along $(\frac{1}{4}, y, \frac{3}{4})$ (Fig. 7). In fact, of these three interactions, the combination of any two suffices to generate a sheet parallel to (001). Two sheets, related to one another by

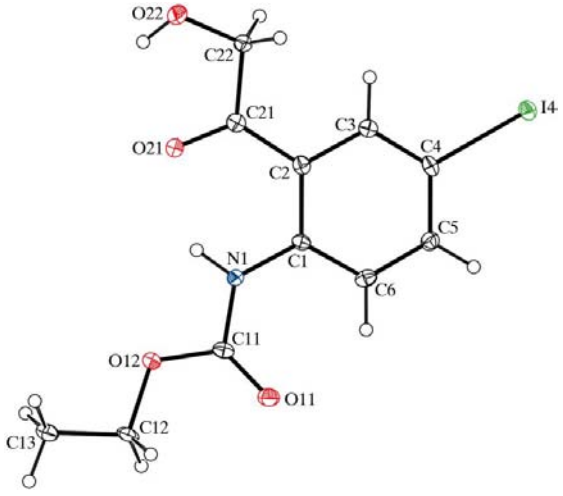


Figure 2
The molecule of compound (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

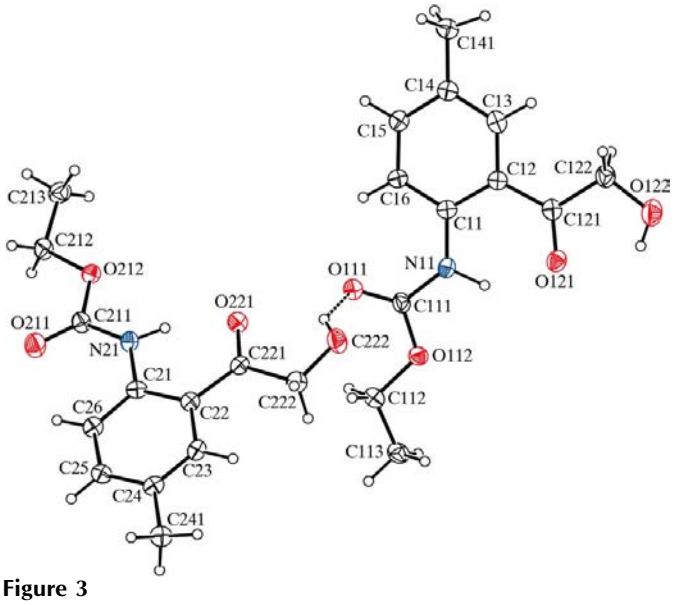


Figure 3
The two independent molecules of compound (III), showing the O—H···O hydrogen bond (dashed line) and the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

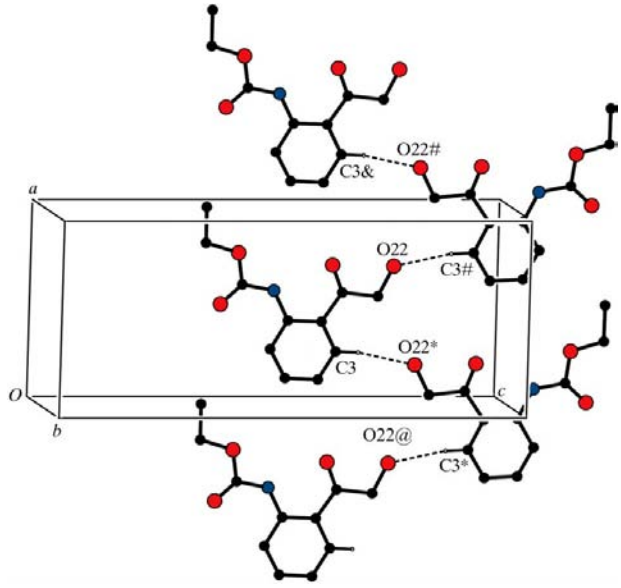


Figure 4
Part of the crystal structure of compound (I), showing the formation of a $C(6)$ chain of C—H···O hydrogen bonds (dashed lines) parallel to [100]. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*), hash (#), ampersand (&) or 'at' sign (@) are at the symmetry positions $(-\frac{1}{2} + x, \frac{3}{2} - y, \frac{3}{2} - z)$, $(\frac{1}{2} + x, \frac{3}{2} - y, \frac{3}{2} - z)$, $(1 + x, y, z)$ and $(-1 + x, y, z)$, respectively.

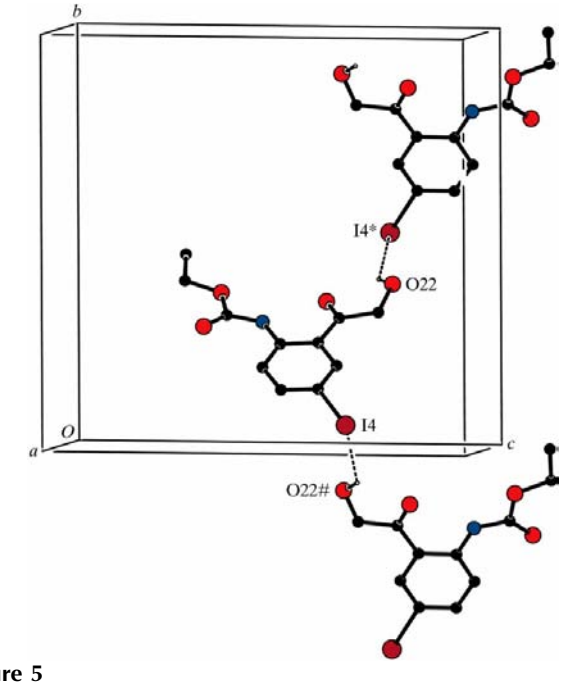


Figure 5
Part of the crystal structure of compound (II), showing the formation of a $C(8)$ chain of O—H···I hydrogen bonds (dashed lines) parallel to [010]. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) or hash (#) are at the symmetry positions $(\frac{3}{2} - x, \frac{1}{2} + y, \frac{3}{2} - z)$ and $(\frac{3}{2} - x, -\frac{1}{2} + y, \frac{3}{2} - z)$, respectively.

inversion, pass through each unit cell, but there are no direction-specific interactions between adjacent sheets.

The only intermolecular hydrogen bond in the structure of compound (III) is a rather weak O—H···O hydrogen bond within the selected asymmetric unit, and this is, in fact, the longer component of a very asymmetric three-centre O—H···(O_2) system (Table 4). Aside from this hydrogen bond, the supramolecular aggregation of compound (III) is determined by two independent aromatic π–π stacking interactions, each involving just one type of molecule. Rings C11–C16 at (x, y, z) and ($2-x$, $2-y$, $-z$) are strictly parallel, with an interplanar spacing of 3.342 (5) Å. The ring-centroid separation is 3.704 (5) Å, corresponding to a ring offset of 1.597 (5) Å. Similarly, rings C21–C26 at (x, y, z) and ($2-x$, $1-y$, $1-z$) are parallel, with an interplanar spacing of 3.313 (5) Å. Here, the ring-centroid separation is 3.687 (5) Å and the ring offset is 1.619 (5) Å. Propagation by inversion of these two stacking interactions then generates a chain running parallel to the [01$\bar{1}$] direction (Fig. 8).

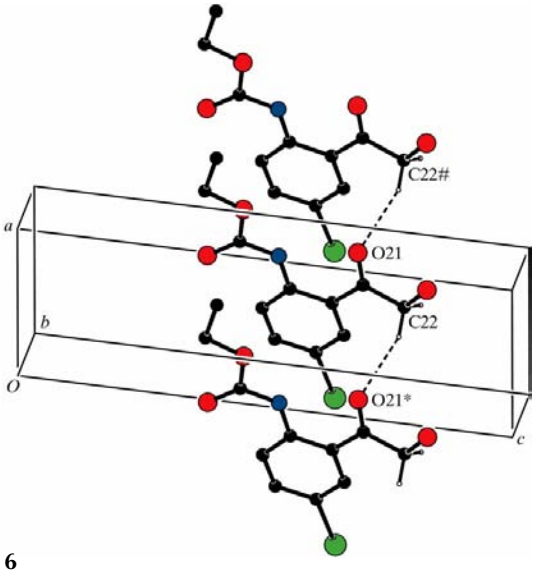


Figure 6
Part of the crystal structure of compound (II), showing the formation of a $C(4)$ chain of C—H···O hydrogen bonds parallel to [100]. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) or a hash (#) are at the symmetry positions ($-1+x$, y, z) and ($1+x$, y, z), respectively.

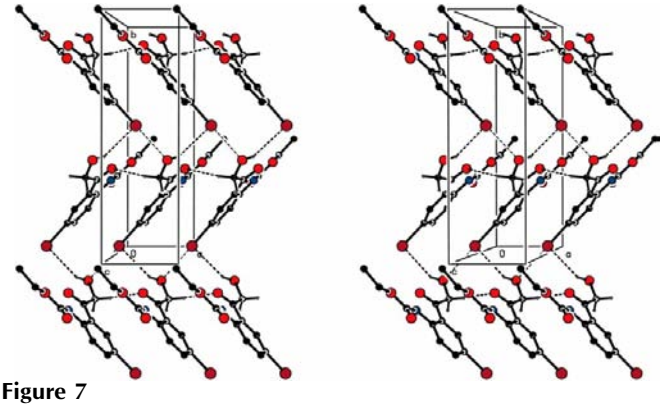


Figure 7
A stereoview of part of the crystal structure of compound (II), showing the formation of a sheet parallel to (001). For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

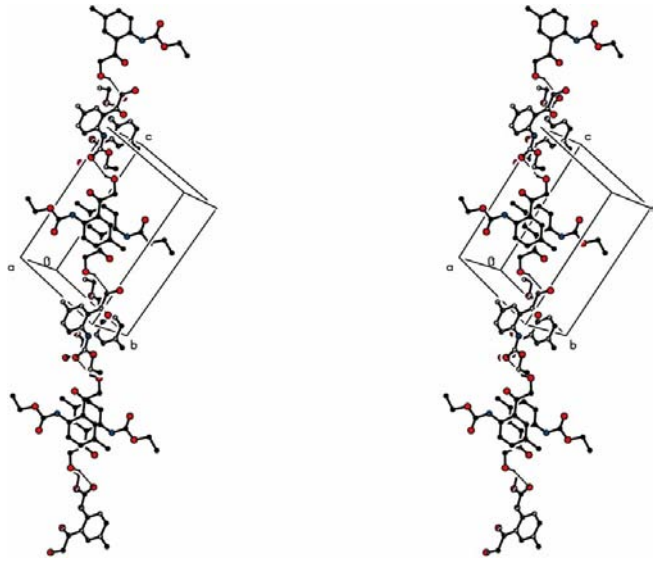


Figure 8
A stereoview of part of the crystal structure of compound (III), showing the formation of a π-stacked chain parallel to [01$\bar{1}$]. For the sake of clarity, H atoms not involved in the motif shown have been omitted.

Experimental

The ketal-protected derivatives (IV)–(VI) of compounds (I)–(III) were prepared from the corresponding isatins following the method described by Garden *et al.* (2003), and they were deprotected as follows. The protected carbamates (3.0 mmol) were dissolved or suspended in ethanol (10 ml). Aqueous hydrochloric acid (3 ml of a 3 *M* solution) was added and the mixtures were heated under reflux for 12 h, when thin-layer chromatography showed the complete consumption of the starting material. On cooling, the products partially crystallized from the reaction medium. Water (10 ml) was then added and, after complete precipitation, the products were isolated by filtration. The crude products were then recrystallized from ethanol to provide crystals suitable for single-crystal X-ray diffraction, in yields of 75–83%.

Analysis for compound (I): m.p. 388 K; ^{1}H NMR ($CDCl_3$): δ 10.85 (1H, *s*, NH), 8.54 (1H, *d*, J = 8.3 Hz, H6), 7.67 (1H, *d*, J = 8.3 Hz, H3), 7.60 (1H, *t*, J = 8.3 Hz, H5), 7.08 (1H, *t*, J = 8.3 Hz, H4), 4.88 (2H, *d*, J = 4.5 Hz, CH_2—OH), 4.25 (2H, *q*, J = 7.3 Hz, CH_2—CH_3), 3.52 (1H, *t*, J = 4.5 Hz, OH), 1.34 (3H, *t*, J = 7.3 Hz, CH_3); ^{13}C NMR ($CDCl_3$): δ 13.4 (CH_3), 60.3 and 64.4 (2 × CH_2), 116.8 and 140.6 (2 × quaternary C), 118.4, 120.5, 128.09 and 135.0 (4 × aromatic CH), 152.6 (C═O, carbamate), 199.9 (C═O, ketone); IR (KBr disk, ν, cm^{-1}): 3466, 3293, 2982, 2909, 1721, 1653, 1593, 1534, 1459, 1321, 1264, 1216, 1087, 1065, 1055, 973, 769.

Analysis for compound (II): m.p. 391 K; ^{1}H NMR ($CDCl_3$): δ 10.76 (1H, *s*, NH), 8.34 (1H, *d*, J = 9.0 Hz, H6), 7.90 (1H, *d*, J = 1.7 Hz, H3), 7.83 (1H, *dd*, J = 9.0 and 1.7 Hz, H5), 4.84 (2H, *s*, CH2—OH), 4.24 (2H, *q*, J = 7.1 Hz, CH_2—CH_3), 3.43 (1H, *br*, *s*, OH), 1.34 (3H, *t*, J = 7.1 Hz, CH_3); ^{13}C NMR ($CDCl_3$): δ 14.6 (CH_3), 61.9 and 65.8 (2 × CH_2), 83.7 (C—I), 120.1 and 141.5 (2 × quaternary C), 121.7, 137.7 and 144.6 (3 × aromatic CH), 153.6 (C═O, carbamate), 200.0 (C═O, ketone); IR (KBr disk, ν, cm^{-1}): 3480, 3277, 3113, 3000, 2903, 1727, 1645, 1573, 1510, 1389, 1304, 1220, 1059, 976, 836.

Analysis for compound (III): m.p. 373–374 K; ^{1}H NMR ($CDCl_3$): δ 10.73 (1H, *s*, NH), 8.42 (1H, *d*, *J* = 8.0 Hz, H6), 7.44 (1H, *s*, H3), 7.42 (1H, *d*, *J* = 8.0 Hz, H5), 4.87 (2H, *s*, CH_2—OH), 4.25 (2H, *q*, *J* = 7.7 Hz, CH_2—CH_3), 3.52–3.58 (1H, *br s*, OH), 2.35 (3H, *s*, CH_3—Ar), 1.32 (3H, *t*, *J* = 7.7 Hz, CH_3—CH_2); ^{13}C NMR ($CDCl_3$): δ 14.7 and 20.8 (2 × CH_3), 61.5 and 65.6 (2 × CH_2), 118.1, 131.3 and 137.2 (3 × quaternary C), 119.7, 129.2 and 137.2 (3 × aromatic CH), 154.0 (C═O, carbamate), 201.1 (C═O, ketone); IR (KBr disk, ν, cm^{-1}): 3447, 3281, 3111, 2997, 2930, 1716, 1657, 1593, 1526, 1235, 1215, 1087, 1059, 987, 831.

Table 1
Selected torsion angles (°) for compounds (II) and (III).

	(II) *x* = nil	(III) *x* = 1	(III) *x* = 2
C*x*1—C*x*2—C*x*21—C*x*22	166.9 (4)	176.2 (4)	−176.9 (4)
C*x*2—C*x*21—C*x*22—O*x*22	−169.6 (4)	177.3 (4)	−177.0 (4)
C*x*2—C*x*1—N*x*1—C*x*11	−170.2 (4)	172.1 (4)	−177.9 (4)
C*x*1—N*x*1—C*x*11—O*x*12	−179.3 (4)	177.4 (4)	178.9 (4)
N*x*1—C*x*11—O*x*12—C*x*12	−176.8 (4)	−179.4 (4)	179.4 (4)
C*x*11—O*x*12—C*x*12—C*x*13	176.3 (4)	176.4 (4)	173.1 (4)

Compound (I)

Crystal data

$C_{11}H_{13}NO_4$
M_r = 223.22
Orthorhombic, *Pnma*
a = 8.2526 (6) Å
b = 6.5210 (2) Å
c = 19.7707 (2) Å
V = 1063.96 (8) Å^3
Z = 4
Mo *K*α radiation
μ = 0.11 mm^{-1}
T = 120 (2) K
0.22 × 0.15 × 0.07 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.969, T_{max} = 0.993
10184 measured reflections
1327 independent reflections
1105 reflections with $I > 2\sigma(I)$
R_{int} = 0.047

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.106
S = 1.03
1327 reflections
98 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O21	0.88	1.96	2.6780 (18)	137
O22—H22···O21	0.84	2.09	2.5880 (18)	118
C3—H3···O22^{i}	0.95	2.47	3.410 (2)	170

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

Compound (II)

Crystal data

$C_{11}H_{12}INO_4$
M_r = 349.12
Monoclinic, $P2_1/n$
a = 4.7535 (2) Å
b = 15.7179 (4) Å
c = 16.0700 (5) Å
β = 97.123 (2)°
V = 1191.40 (7) Å^3
Z = 4
Mo *K*α radiation
μ = 2.69 mm^{-1}
T = 120 (2) K
0.12 × 0.05 × 0.01 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.738, T_{max} = 0.974
14451 measured reflections
2721 independent reflections
2268 reflections with $I > 2\sigma(I)$
R_{int} = 0.055

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.039
$wR(F^2)$ = 0.077
S = 1.16
2721 reflections
156 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.75 e Å^{-3}
$\Delta\rho_{min}$ = −0.60 e Å^{-3}

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O21	0.88	1.94	2.655 (4)	137
O22—H22···O21	0.84	2.14	2.607 (4)	115
O22—H22···I4^{i}	0.84	2.98	3.578 (3)	130
C22—H22*A*···O21^{ii}	0.99	2.50	3.439 (6)	157

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

Compound (III)

Crystal data

$C_{12}H_{15}NO_4$
M_r = 237.25
Triclinic, $P\overline{1}$
a = 7.085 (7) Å
b = 10.711 (11) Å
c = 15.587 (16) Å
α = 87.916 (11)°
β = 80.861 (13)°
γ = 89.664 (11)°
V = 1167 (2) Å^3
Z = 4
Synchrotron radiation (Clegg, 2000)
λ = 0.7848 Å
μ = 0.10 mm^{-1}
T = 120 (2) K
0.20 × 0.01 × 0.01 mm

Data collection

Bruker SMART APEXII CCD area-detector diffractometer
5906 measured reflections
3115 independent reflections
2117 reflections with $I > 2\sigma(I)$
R_{int} = 0.039
θ_{max} = 25.5°

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.084
$wR(F^2)$ = 0.245
S = 1.02
3115 reflections
314 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.52 e Å^{-3}
$\Delta\rho_{min}$ = −0.31 e Å^{-3}

Table 4
Hydrogen-bond geometry (Å, °) for (III).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N11—H11···O121	1.00	1.86	2.660 (5)	135
N21—H21···O221	0.93	1.84	2.653 (5)	144
O122—H122···O121	0.84	2.07	2.578 (5)	118
O222—H222···O221	0.84	2.09	2.579 (5)	116
O222—H222···O111	0.84	2.57	3.216 (7)	135

For compound (I), the systematic absences permitted $Pna2_1$ and *Pnma* (= *Pnam*) as possible space groups; *Pnma* was selected and confirmed by the subsequent structure analysis. For compound (II), the space group $P2_1/n$ was uniquely assigned from the systematic absences. Crystals of compound (III) are triclinic; space group $P\overline{1}$ was selected and confirmed by the subsequent structure analysis. This compound was refined as a non-merohedral twin (twin fraction = 0.16). All H atoms were located in difference maps and then treated as riding atoms, with C—H = 0.95 (aromatic), 0.98 (CH_3) or 0.99 Å (CH_2), N—H = 0.88–1.00 Å and O—H = 0.84 Å, and with U_{iso}(H) =

kU_{eq}(carrier), where k = 1.5 for the hydroxyl and methyl groups, and 1.2 for all other H atoms.

Data collection: *COLLECT* (Nonius, 1999) for (I) and (II); *APEX2* (Bruker, 2003) for (III). Cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT* for (I) and (II); *SAINT* (Bruker, 2001) for (III). Data reduction: *DENZO* and *COLLECT* for (I) and (II); *SAINT* for (III). For all compounds, 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).

X-ray data for (I) and (II) were collected at the University of Southampton, England; the authors thank the staff at Southampton for their help and advice. Synchrotron data for (III) were collected at the EPSRC National Crystallography Service, Daresbury; the authors thank Professor W. Clegg and his staff for their help and advice. JLW thanks CNPq and FAPERJ for financial support. SJG and ACP thank CNPq for financial support, and CAPES for a grant for MBC.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3102). 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.
Bruker (2001). *SAINT*. Version 6.02. Bruker AXS Inc., Madison, Wisconsin, USA.
Bruker (2003). *APEX2*. Bruker AXS Inc., Madison, Wisconsin, USA.
Clegg, W. (2000). *J. Chem. Soc. Dalton Trans.* pp. 3223–3232.
Ferguson, G. (1999). *PRPKAPPA*. University of Guelph, Canada.
Garden, S. J., Corrêa, M. B. & Pinto, A. C. (2003). *Tetrahedron Lett.* **44**, 7617–7621.
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.
Starbuck, J., Norman, N. C. & Orpen, A. G. (1999). *New J. Chem.* **23**, 969–972.