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Hydrogen-bonding patterns in enaminones: (2*Z*)-1-(4-bromophenyl)-2-(pyrrolidin-2-ylidene)ethanone and its piperidin-2-ylidene and azepan-2-ylidene analogues

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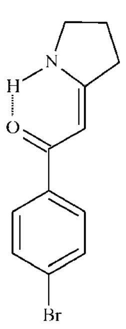
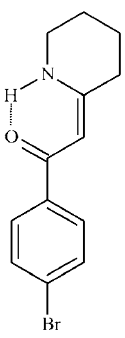
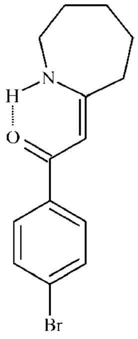
The title compounds, namely (2*Z*)-1-(4-bromophenyl)-2-(pyrrolidin-2-ylidene)ethanone, $C_{12}H_{12}BrNO$, (I), (2*Z*)-1-(4-bromophenyl)-2-(piperidin-2-ylidene)ethanone, $C_{13}H_{14}BrNO$, (II), and (2*Z*)-2-(azepan-2-ylidene)-1-(4-bromophenyl)ethanone, $C_{14}H_{16}BrNO$, (III), are characterized by bifurcated intra- and intermolecular hydrogen bonding between the secondary amine and carbonyl groups. The former establishes a six-membered hydrogen-bonded ring, while the latter leads to the formation of centrosymmetric dimers. Weak C—H···Br interactions link the individual molecules into chains that run along the [011], [101] and [101] directions in (I)–(III), respectively. Additional weak Br···O, C—H···π and C—H···O interactions further stabilize the crystal structures.

Comment

Enaminones (β-acylated enamines) are valuable intermediates for the synthesis of alkaloids and other nitrogen-containing heterocycles (Stanovnik & Svete, 2004; Cheng *et al.*, 2004; Negri *et al.*, 2004; Elliott *et al.*, 2006). These versatile systems play a pivotal role in our own research programme (Michael *et al.*, 1999). We have recently observed discrepancies in the reactivity of N-heterocyclic enaminones of different ring sizes (Michael *et al.*, 2001, 2002). The present investigation was undertaken in order to ascertain whether there might be underlying structural differences in the conjugated enaminone system as the size of the ring containing the N atom is varied. The three title compounds, (I)–(III), were selected as models to probe possible structural differences, in view of their ready preparation by the Eschenmoser sulfide contraction method (Roth *et al.*, 1971).


(I)


(II)


(III)

It was found that the bond lengths and angles for the conjugated and essentially planar enaminone core (N—

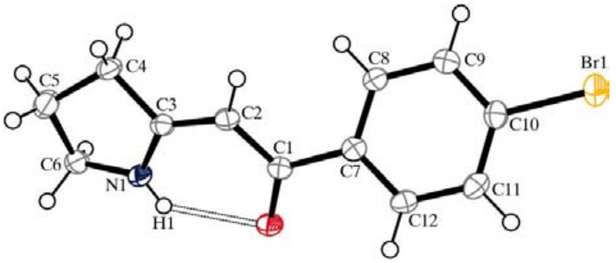


Figure 1
The molecular structure of (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The intramolecular hydrogen bond between atoms O1 and H1 is shown as a dotted bond.

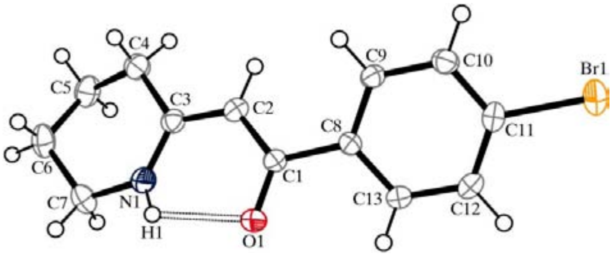


Figure 2
The molecular structure of (II), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The intramolecular hydrogen bond between atoms O1 and H1 is shown as a dotted bond.

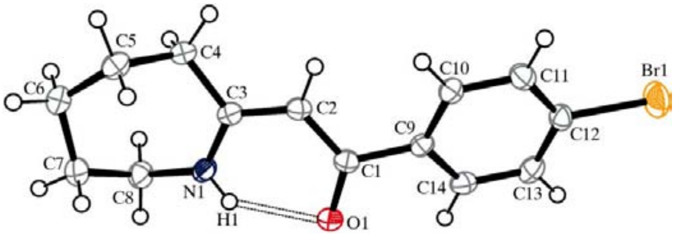


Figure 3
The molecular structure of (III), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The intramolecular hydrogen bond between atoms O1 and H1 is shown as a dotted bond.

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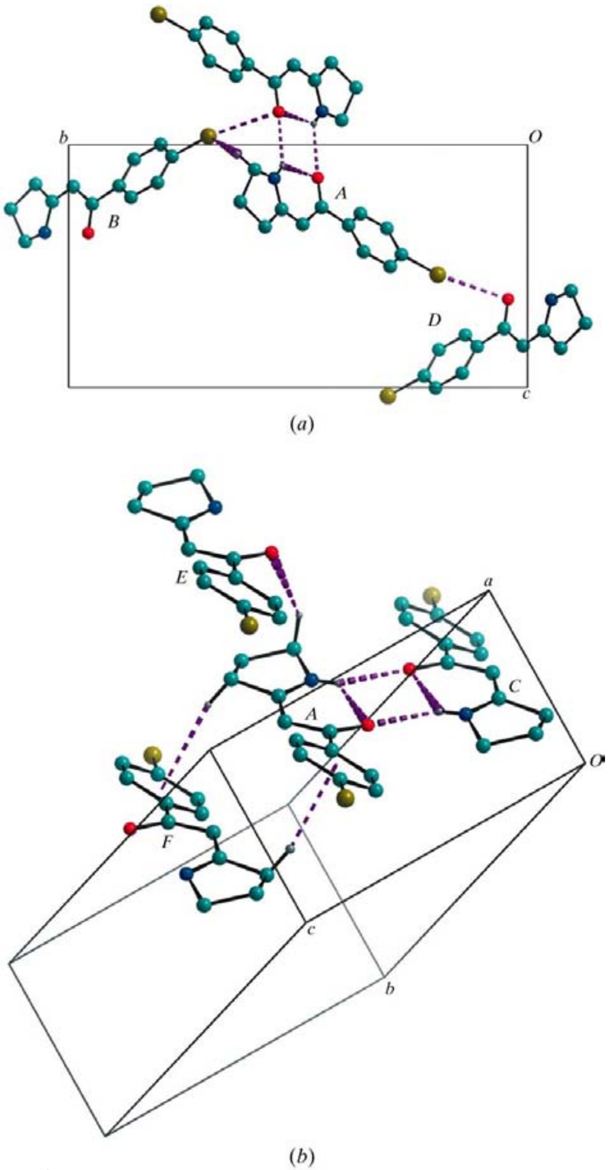
C=C—C=O) of the three compounds (Figs. 1–3) proved to be effectively the same and within the expected ranges (Allen *et al.*, 1987). More interesting, however, are their packing arrangements. Compounds (I)–(III) are characterized by bifurcated hydrogen bonds (one intramolecular and one intermolecular) between the secondary amine and carbonyl groups. The intramolecular N—H···O hydrogen bond between the donor atom N1 and the acceptor atom O1 can be described by the graph-set motif $S(6)$ (Etter *et al.*, 1990; Bernstein *et al.*, 1995). In compound (I), atom N1 also acts as an intermolecular hydrogen-bond donor *via* atom H1 to atom O1 at $(2 - x, 1 - y, -z)$. For compounds (II) and (III), the comparable intermolecular hydrogen bond is from atom N1 to atom O1 at $(2 - x, -y, 1 - z)$ and $(1 - x, 1 - y, 1 - z)$, respectively. This intermolecular hydrogen bonding leads to the formation of dimers described by the $R_2^2(12)$ graph-set motif.

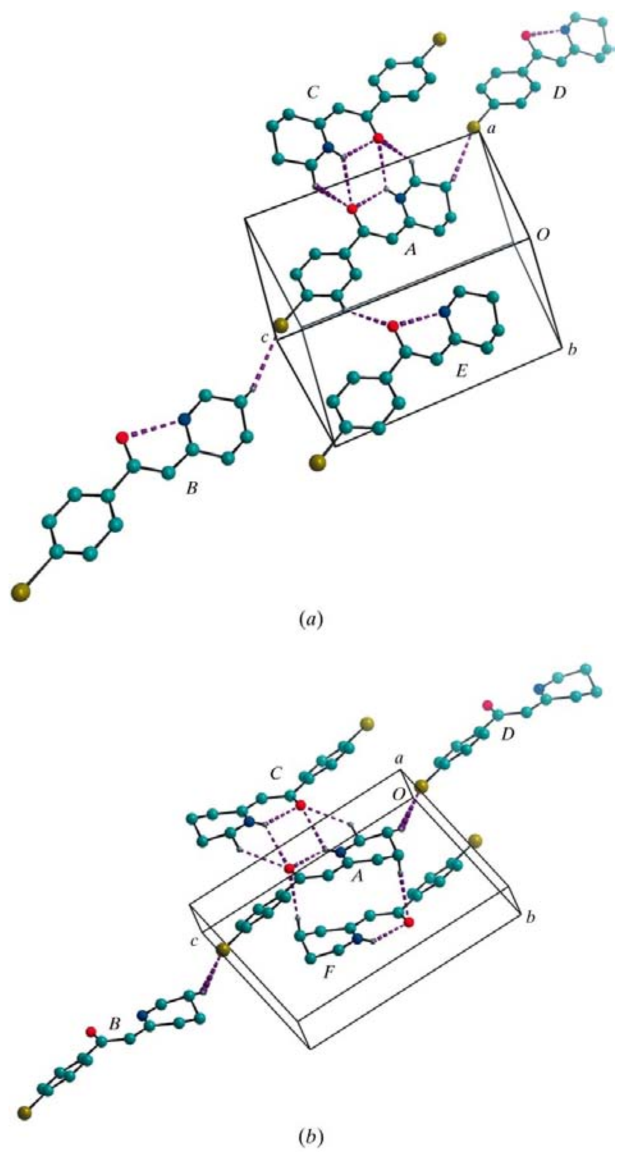
In the crystal structures of each compound, there is also a weak C—H···Br interaction (Figs. 4–6) that links the molecules together into chains along the [011], [101] and [101] directions in compounds (I), (II) and (III), respectively. The C—H···Br hydrogen-bond geometries (Tables 1–3) are



(*a*)

(*b*)

Figure 4
(*a*) Bifurcated N—H···O hydrogen bonding and weak C—H···Br and Br···O interactions in the structure of (I). (*b*) An alternative view of (I), showing the weak C—H···π and weak C—H···O interactions. In both views, molecules *A*, *B*, *C*, *D*, *E* and *F* are at the symmetry positions (x, y, z), $(\frac{3}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z)$, $(2 - x, 1 - y, -z)$, $(-\frac{1}{2} + x, \frac{1}{2} - y, \frac{1}{2} + z)$, $(1 + x, y, z)$ and $(2 - x, 1 - y, 1 - z)$, respectively.



(*a*)

(*b*)

Figure 5
(*a*) Part of the crystal structure of (II), showing the formation of hydrogen-bonded dimers by intermolecular N—H···O and C—H···O interactions. The molecules are linked together into chains along [101] by weak C—H···Br interactions. (*b*) An alternative view of (II), showing the formation of intramolecular $S(6)$, intermolecular $R_2^2(12)$ and intermolecular $R_2^2(14)$ rings built from N—H···O and weak C—H···O interactions. In both views, molecules *A*, *B*, *C*, *D*, *E* and *F* are at the symmetry positions (x, y, z), $(-1 + x, y, 1 + z)$, $(2 - x, -y, 1 - z)$, $(1 + x, y, -1 + z)$, $(-1 + x, y, z)$ and $(2 - x, 1 - y, 1 - z)$, respectively.

comparable with values reported in the literature (Ponnuswamy & Sony, 2006).

In addition to C—H$\cdots$Br interactions in compound (I), the chains of molecules extending along the [011] direction are further stabilized by Br$\cdots$O interactions [Br1$\cdots$O1^{i} = 3.161 (2) Å, C10—Br1$\cdots$O1^{i} = 165.39 (7)° and C1^{i}—O1$^{i}\cdots$Br1 = 98.2 (1)°; symmetry code: (i) $-\frac{1}{2}+x, \frac{1}{2}-y, \frac{1}{2}+z$] (Fig. 4). These values compare favourably with those obtained from a study of short O$\cdots$halogen interactions in biological molecules (Auffinger *et al.*, 2004). The crystal structure of (I) also contains a weak C—H$\cdots$*Cg* intermolecular interaction that extends along the [001] direction, where *Cg* is the centroid of the C7–C12 benzene ring. The pyrrolidine ring has an envelope conformation with atom C5 at the flap. The Cremer & Pople puckering parameters (Cremer & Pople, 1975) for this molecule are q_2 = 0.264 (2) Å and φ_2 = 113.8 (4)°.

The hydrogen-bonded dimers in compound (II) are further reinforced by a weak C—H$\cdots$O interaction between atom H7*A* and atom O1 at $(2-x, -y, 1-z)$, producing a motif described by the graph set $R_2^2(12)$. A second set of C—H$\cdots$O interactions, occurring between atom H5 and atom O1 at $(2-x, 1-y, 1-z)$, gives rise to another set of intermolecular bonded dimers described by the $R_2^2(14)$ graph set (Fig. 5). In this structure, the piperidine ring adopts a half-chair conformation [puckering amplitude Q_T = 0.483 (3) Å, θ = 136.7 (4)° and φ = 26.9 (5)°].

In addition to the N—H$\cdots$O and C—H$\cdots$Br interactions discussed earlier, the structure of (III) also contains C—H$\cdots$O^{i} and C—H$\cdots$*Cg*^{i} interactions [*Cg* is the centroid of the C9–C14 ring; symmetry code: (i) $1-x, -\frac{1}{2}+y, \frac{3}{2}-z$] that link molecules together into chains along the [011] direction (Fig. 6). In this structure, the seven-membered ring has a total puckering amplitude *Q* of 0.7524 (17) Å.

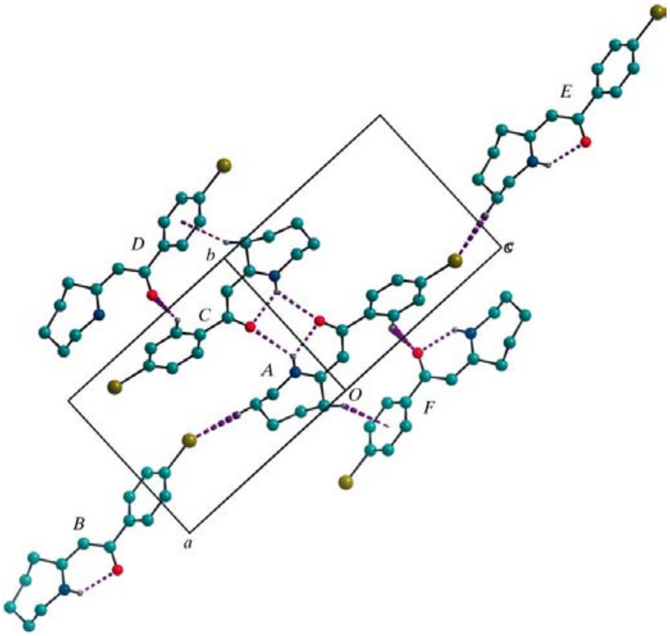


Figure 6
Part of the crystal structure of (III), showing the intra- and intermolecular N—H$\cdots$O hydrogen-bonding pattern. Chains of molecules are linked together along the [101] direction by weak C—H$\cdots$Br interactions, and along the [011] direction by weak C—H$\cdots\pi$ and weak C—H$\cdots$O interactions. Molecules *A*, *B*, *C*, *D*, *E* and *F* are at the symmetry positions (x, y, z), $(1+x, \frac{1}{2}-y, -\frac{1}{2}+z)$, $(1-x, 1-y, 1-z)$, $(x, \frac{3}{2}-y, -\frac{1}{2}+z)$, $(-1+x, \frac{1}{2}-y, \frac{1}{2}+z)$ and $(1-x, -\frac{1}{2}+y, \frac{3}{2}-z)$, respectively.

Experimental

The syntheses of compounds (I)–(III) were adapted from the procedure described by Roth *et al.* (1971) for the preparation of (I). 4-Bromophenacyl bromide (1.05 equivalents) was added to a solution of the appropriate thiolactam [pyrrolidine-2-thione, piperidine-2-thione or azepane-2-thione; 1.0 equivalent; *cf.* Curphey (2002)] in $CHCl_3$ (5 ml per mmol). After 30 min at room temperature, the solvent was removed on a rotary evaporator. The resulting mixture was kept at room temperature for 48 h to ensure that the reaction went to completion. The resulting solid was partitioned between CH_2Cl_2 and aqueous saturated K_2CO_3 solution. The organic phase was separated off and the aqueous phase was extracted with a further portion of CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and evaporated to yield the crude S-alkylated intermediate. This was dissolved in dry $CHCl_3$ (10 ml per mmol) to which triphenylphosphine (2 equivalents) was added. The solution was heated under reflux for 24 h, after which the solvent was evaporated. The crude enaminone product was purified by chromatography on silica gel with dichloromethane as eluant, followed by ethyl acetate–hexane (2:3), to afford the desired products, (I)–(III).

For compound (I), yield 66%; m.p. 443–446 K [literature m.p. 446–447 K (Roth *et al.*, 1971)]. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si): δ 2.00–2.10 (2H, *m*, 5-H), 2.74 (2H, *m*, 4-H), 3.66 (2H, *m*, 6-H), 5.75 (1H, *s*, 2-H), 7.52 and 7.74 (4H, 2 × *m*, 8-H, 9-H, 11-H, 12-H), 10.28 (1H, *s*, NH); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si): δ 186.4 (C=O), 170.0 (C3), 138.9 (C7), 131.3 and 128.7 (C8, C9, C11, C12), 125.1 (C10), 85.9 (C2), 47.9 (C6), 33.0 (C4), 21.3 (C5).

For compound (II), yield 55%; m.p. 388–390 K. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si): δ 1.76–1.88 (4H, *m*, 5-H and 6-H), 2.50 (2H, *t*, 4-H), 3.40 (2H, *t*, 7-H), 5.51 (1H, *s*, 2-H), 7.50 and 7.71 (4H, 2 × *d*, *J* = 8.2 Hz, 9-H, 10-H, 12-H, 13-H), 11.70 (1H, *s*, NH); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si): δ 185.9 (C=O), 166.6 (C3), 139.9 (C8), 131.6 and 128.8 (C9, C10, C12, C13), 125.0 (C11), 90.5 (C2), 41.6 (C7), 29.3 (C4), 22.5 and 19.6 (C5, C6). HRMS (EI), found: 281.0216; $C_{13}H_{14}{}^{81}BrNO$ requires: 281.0238.

For compound (III), yield 76%; m.p. 418–421 K. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si): δ 1.68–1.77 (6H, *m*, 5-H, 6-H, and 7-H), 2.44 (2H, *m*, 4-H), 3.43 (2H, *d*, 8-H), 5.61 (1H, *s*, 2-H), 7.51 and 7.73 (4H, 2 × *m*, 10-H, 11-H, 13-H, and 14-H), 11.54 (1H, *s*, NH); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si): δ 186.6 (C=O), 171.8 (C3), 139.4 (C9), 128.5 and 131.3 (C10, C11, C13, C14), 124.9 (C12), 90.8 (C2), 44.5 (C8), 35.4, 30.6, 29.2 and 25.7 (C4, C5, C6, C7). HRMS (EI), found: 295.0402; $C_{14}H_{16}{}^{81}BrNO$ requires: 295.0395.

Compound (I)

Crystal data

$C_{12}H_{12}BrNO$
M_r = 266.14
Monoclinic, $P2_1/n$
a = 5.6636 (3) Å
b = 18.9255 (9) Å
c = 10.0500 (5) Å
β = 94.1360 (10)°

V = 1074.42 (9) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 3.80 mm^{-1}
T = 173 (2) K
0.37 × 0.30 × 0.20 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
Absorption correction: multi-scan [*SADABS* in *SAINT-NT* (Bruker, 2005); ratio of minimum to maximum apparent transmission = 0.688943; for $T_{\min}$ below, $T_{\min} = T_{\max} \times$ min-to-max ratio]
$T_{\min} = 0.334$, $T_{\max} = 0.517$ (expected range = 0.302–0.468)
9815 measured reflections
2595 independent reflections
2307 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.020$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.024$
$wR(F^2) = 0.068$
$S = 1.06$
2595 reflections
140 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\max} = 0.52$ e Å^{-3}
$\Delta\rho_{\min} = -0.60$ e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °) for (I).

Cg is the centroid of the C7–C12 benzene ring.

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1—H1$\cdots$O1	0.79 (2)	2.25 (2)	2.798 (2)	128 (2)
N1—H1$\cdots$O1$^{\rm i}$	0.79 (2)	2.30 (2)	2.9124 (19)	136 (2)
C6—H6$B\cdots$O1$^{\rm ii}$	0.99	2.72	3.524 (3)	139
C4—H4$B\cdots Cg^{\rm iii}$	0.99	2.71	3.679 (2)	166
C6—H6$A\cdots$Br1$^{\rm iv}$	0.99	2.97	3.701 (2)	132

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

Compound (II)

Crystal data

$C_{13}H_{14}BrNO$
$M_r = 280.16$
Triclinic, $P\overline{1}$
$a = 6.9303$ (2) Å
$b = 7.6280$ (2) Å
$c = 12.1060$ (3) Å
$\alpha = 99.844$ (2)°
$\beta = 99.5450$ (10)°
$\gamma = 102.189$ (2)°
$V = 602.64$ (3) Å^3
$Z = 2$
Mo $K\alpha$ radiation
$\mu = 3.39$ mm^{-1}
$T = 173$ (2) K
0.49 × 0.19 × 0.17 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
Absorption correction: integration [face-indexed using *XPREP* in *SAINT-NT* (Bruker, 2005)]
$T_{\min} = 0.380$, $T_{\max} = 0.593$
7739 measured reflections
2903 independent reflections
2387 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.033$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.027$
$wR(F^2) = 0.107$
$S = 1.14$
2903 reflections
149 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\max} = 0.52$ e Å^{-3}
$\Delta\rho_{\min} = -0.36$ e Å^{-3}

Table 2
Hydrogen-bond and weak intermolecular interaction geometry (Å, °) for (II).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1—H1$\cdots$O1	0.82 (4)	2.17 (4)	2.656 (3)	118 (3)
N1—H1$\cdots$O1$^{\rm i}$	0.82 (4)	2.55 (4)	3.168 (3)	133 (3)
C5—H5$B\cdots$O1$^{\rm ii}$	0.99	2.63	3.609 (3)	172
C7—H7$A\cdots$O1$^{\rm i}$	0.99	2.58	3.297 (4)	129
C10—H10$\cdots$O1$^{\rm iii}$	0.95	2.40	3.194 (3)	141
C6—H6$A\cdots$Br1$^{\rm iv}$	0.99	3.05	3.894 (3)	144

Symmetry codes: (i) $-x+2, -y, -z+1$; (ii) $-x+2, -y+1, -z+1$; (iii) $x-1, y, z$; (iv) $x+1, y, z-1$.

Compound (III)

Crystal data

$C_{14}H_{16}BrNO$
$M_r = 294.19$
Monoclinic, $P2_1/c$
$a = 12.2867$ (3) Å
$b = 8.2416$ (2) Å
$c = 12.9404$ (4) Å
$\beta = 100.702$ (2)°
$V = 1287.58$ (6) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 3.18$ mm^{-1}
$T = 173$ (2) K
0.49 × 0.44 × 0.15 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
Absorption correction: integration [face-indexed using *XPREP* in *SAINT-NT* (Bruker, 2005)]
$T_{\min} = 0.305$, $T_{\max} = 0.647$
9654 measured reflections
3103 independent reflections
2401 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.043$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.025$
$wR(F^2) = 0.065$
$S = 1.02$
3103 reflections
158 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\max} = 0.45$ e Å^{-3}
$\Delta\rho_{\min} = -0.41$ e Å^{-3}

Table 3
Hydrogen-bond and weak intermolecular interaction geometry (Å, °) for (III).

Cg is the centroid of the C9–C14 benzene ring.

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1—H1$\cdots$O1	0.811 (19)	2.057 (19)	2.6841 (18)	134.0 (17)
N1—H1$\cdots$O1$^{\rm i}$	0.811 (19)	2.467 (19)	3.0757 (17)	132.7 (17)
C10—H10$\cdots$O1$^{\rm ii}$	0.95	2.59	3.439 (2)	149
C4—H4$B\cdots Cg^{\rm ii}$	0.99	2.67	3.5996 (17)	157
C7—H7$A\cdots$Br1$^{\rm iii}$	0.99	2.95	3.6838 (18)	131

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

For all three title compounds, with the exception of atoms H1, all H atoms were positioned geometrically and allowed to ride on their parent atoms, with C—H bond lengths of 0.95 (aromatic), 0.99 (CH_2) or 0.98 Å (CH_3). Isotropic displacement parameters for these atoms were set equal to 1.2 (aromatic and CH_2) or 1.5 (CH_3) times $U_{\rm eq}$ of the parent atom. Atoms H1 were found in difference Fourier maps and refined freely.

For all three compounds, data collection: *APEX2* (Bruker, 2005); cell refinement: *APEX2*; data reduction: *SAINT-NT* (Bruker, 2005); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997) and *DIAMOND* (Brandenburg, 1999); software used to prepare material for publication: *WinGX* (Farrugia, 1999) and *PLATON* (Spek, 2003).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: AV3112). Services for accessing these data are described at the back of the journal.

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