Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Five 2-aryl-substituted tetrahydro-1,4-epoxy-1-benzazepines: isolated molecules and hydrogen-bonded chains and sheets

Sandra L. Gómez,[a] Alirio Palma,[a] Justo Cobo[b] and Christopher Glidewell[c]*

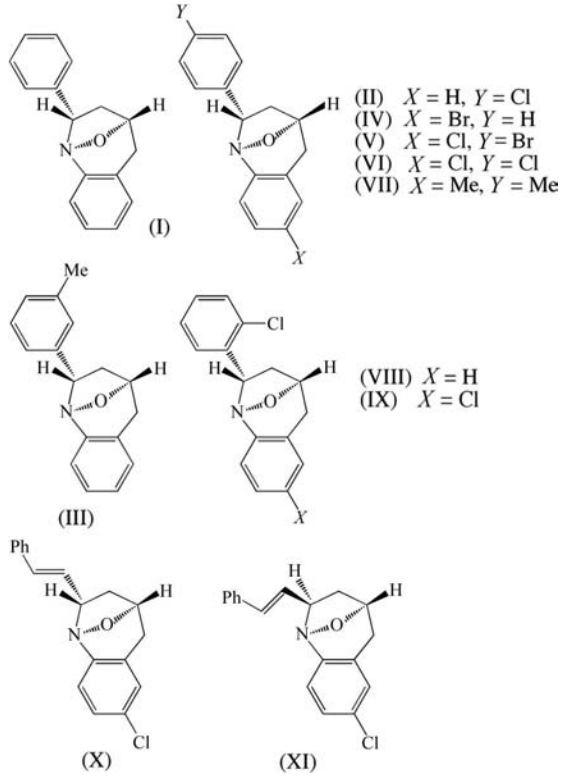
[a]Laboratorio de Síntesis Orgánica, Escuela de Química, Universidad Industrial de Santander, AA 678 Bucaramanga, Colombia, [b]Departamento de Química Inorgánica y Orgánica, Universidad de Jaén, 23071 Jaén, Spain, and [c]School of Chemistry, University of St Andrews, Fife KY16 9ST, Scotland
Correspondence e-mail: cg@st-andrews.ac.uk

Received 4 March 2010
Accepted 15 March 2010
Online 27 March 2010

(2*SR*,4*RS*)-2-*exo*-Phenyl-2,3,4,5-tetrahydro-1*H*-1,4-epoxy-1-benzazepine, $C_{16}H_{15}NO$, (I), (2*SR*,4*RS*)-2-*exo*-(4-chlorophenyl)-2,3,4,5-tetrahydro-1*H*-1,4-epoxy-1-benzazepine, $C_{16}H_{14}ClNO$, (II), and (2*SR*,4*RS*)-2-*exo*-(3-methylphenyl)-2,3,4,5-tetrahydro-1*H*-1,4-epoxy-1-benzazepine, $C_{17}H_{17}NO$, (III), all crystallize with $Z' = 2$, in the space groups *Cc*, $P2_1/n$ and $P2_1/c$, respectively. In each of (II) and (III), the conformations of the two independent molecules are significantly different. The molecules in (I) are linked by C—H···π(arene) hydrogen bonds to form two independent chains, each containing only one type of molecule. The molecules in (II) are linked into sheets by a combination of C—H···O, C—H···(N,O) and C—H···π(arene) hydrogen bonds, all of which link pairs of molecules related by inversion, while in (III), the molecules are linked into sheets by a combination of C—H···N, C—H···O and C—H···π(arene) hydrogen bonds. There are no direction-specific intermolecular interactions of any kind in the structure of (2*SR*,4*RS*)-7-bromo-2-*exo*-phenyl-2,3,4,5-tetrahydro-1*H*-1,4-epoxy-1-benzazepine, $C_{16}H_{14}BrNO$, (IV), but in the structure of (2*SR*,4*RS*)-2-*exo*-(4-bromophenyl)-7-chloro-2,3,4,5-tetrahydro-1*H*-1,4-epoxy-1-benzazepine, $C_{16}H_{13}BrClNO$, (V), a combination of one C—H···N hydrogen bond and one C—H···O hydrogen bond links the molecules into sheets of alternating centrosymmetric $R_2^2(14)$ and $R_6^6(22)$ rings. Comparisons are made with the structures of a number of related compounds.

Comment

We report here the structure of (2*SR*,4*RS*)-2-*exo*-phenyl-2,3,4,5-tetrahydro-1*H*-1,4-epoxy-1-benzazepine, (I) (Fig. 1), and the structures of four analogues, (II)–(V) (Figs. 2–5), each carrying no more than one substituent on each of the aryl rings. We compare these structures with those of several other analogues with similar substitution patterns, namely compounds (VI) and (IX) (Gómez *et al.*, 2008) and compounds (VII) and (VIII) (Gómez *et al.*, 2009) (see scheme). The work reported here is a continuation of a structural study of 2-substituted tetrahydro-1,4-epoxy-1-benzazepines (Acosta *et al.*, 2008, 2010*a*,*b*; Blanco *et al.*, 2008; Gómez *et al.*, 2008, 2009). These compounds are of potential importance in combating *Trypanosoma cruzi* and *Leishmania chagasi* parasites (Gómez Ayala *et al.*, 2006; Yépez *et al.*, 2006; Palma *et al.*, 2009). The compounds reported here exhibit some unexpected crystallization characteristics and no two of compounds (I)–(IX) show the same patterns of supramolecular aggregation. Compounds (I)–(V) were all prepared using the reaction of an appropriately substituted 2-allyl-*N*-benzylaniline with an excess of hydrogen peroxide solution in the presence of a catalytic quantity of sodium tungstate; the proposed mechanism involves oxidation of the starting amine to a nitrone intermediate, followed by a 1,3-dipolar cycloaddition step to give the products, which contain stereogenic centres at atoms C2 and C4 (Acosta *et al.*, 2008).



Compounds (I)–(III) all crystallize as racemic mixtures of the (2*S*,4*R*) and (2*R*,4*S*) forms, each with $Z' = 2$ in the space groups *Cc*, $P2_1/n$ and $P2_1/c$, respectively. In each of these compounds it will be convenient to refer to the molecules containing atoms N11 and N21 (Figs. 1–3) as type 1 and type 2 molecules, respectively. The formation of racemic mixtures is to be expected as the synthetic procedure does not involve any reagent or solvent capable of imparting any enantiomeric bias to the product. The observation of $Z' = 2$ in the space group

Cc, as in (I), should always enjoin caution. Extensive scrutiny (Marsh, 1997, 2004, 2009) of the structures in this space group that have been deposited in the Cambridge Structural Database (Allen, 2002) has shown that over a long period the space-group assignments for some 10% of structures reported in space group *Cc* were, in fact, incorrect, although this proportion has been approximately halved for more recent depositions (Marsh, 2009). For (I), the ADDSYM routine in *PLATON* (Spek, 2009) gave no indication of any additional symmetry, a detailed comparison of the coordinates for corresponding pairs of atoms in the two independent molecules found no consistent relationships between them, and a projection of the structure down [010] showed no sign of any possible twofold rotation axis. We conclude that the space-group assignment for (I) is correct. Compound (IV) crystallizes with $Z' = 1$ in the space group $P2_12_12_1$, but as an inversion twin with twin fractions 0.497 (9) and 0.503 (9), rather than as a single enantiomer, so that this compound also appears to be a racemic mixture. Compound (V) crystallizes as a true racemic mixture with $Z' = 1$. In all cases, the reference molecules were selected as those having the (2*S*,4*R*) configuration.

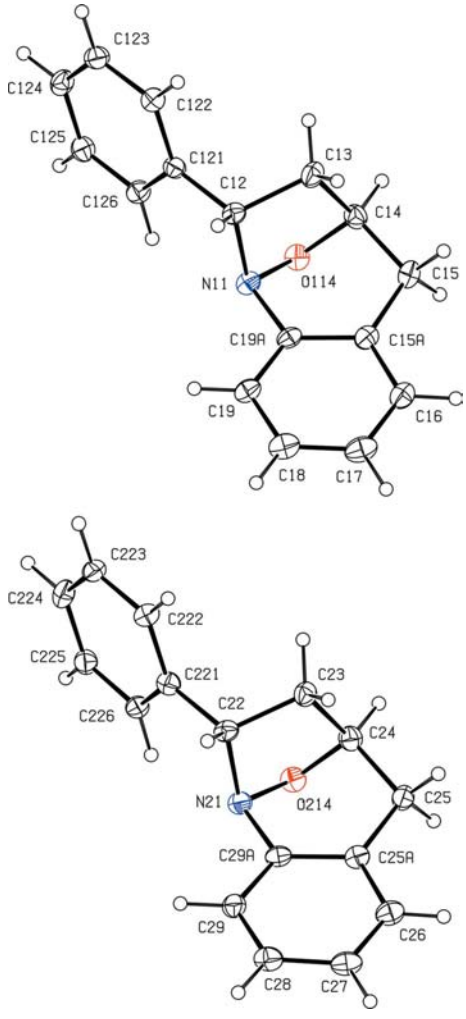


Figure 1
The two independent molecules of (I), showing the atom-labelling scheme: the type 1 molecule is at the top and the type 2 molecule is below. Displacement ellipsoids are drawn at the 30% probability level.

Compounds (VI) (Gómez *et al.*, 2008) and (VII) (Gómez *et al.*, 2009) crystallize as racemic mixtures of the (2*S*,4*R*) and (2*R*,4*S*) forms in the space groups $Pna2_1$ and $P2_1/n$, respectively. It was deduced that compound (VIII) (Gómez *et al.*, 2009), which is isomeric with (II), but which crystallizes with $Z' = 1$ in the space group $P2_1$ [*cf.* $Z' = 2$ in $P2_1/n$ for (II)], probably crystallizes as a conglomerate, while compound (IX), where $Z' = 1$ in the space group $P2_12_12_1$ (Gómez *et al.*, 2008), was refined as a single enantiomorph. However, the enantiomorph discriminating power (Flack & Bernardinelli, 2000) of the Flack (1983) *x* parameter [$x = 0.01$ (15)] was not high. Re-examination of the reflection data for (IX) has now permitted calculation of the Hooft *y* parameter [$y = -0.02$ (9)], which often provides more precise discrimination than *x* (Hooft *et al.*, 2008), confirming the correctness of the original refinement. There is thus no reason to suppose that any of compounds (I)–(IX) has been synthesized as other than a racemic mixture, but it is not at all clear, therefore, why (IV), (VIII) and (IX) all crystallize in space groups having neither reflection nor inversion operators. Compound (IV) is the only example in the series of 2-aryl derivatives (I)–(IX) that exhibits inversion twinning; on the other hand, the two diastereoisomeric 2-styryl compounds (X) and (XI) both crystallize as inversion twins, in the space groups $P2_1$ and $P2_12_12_1$, respectively (Acosta *et al.*, 2008).

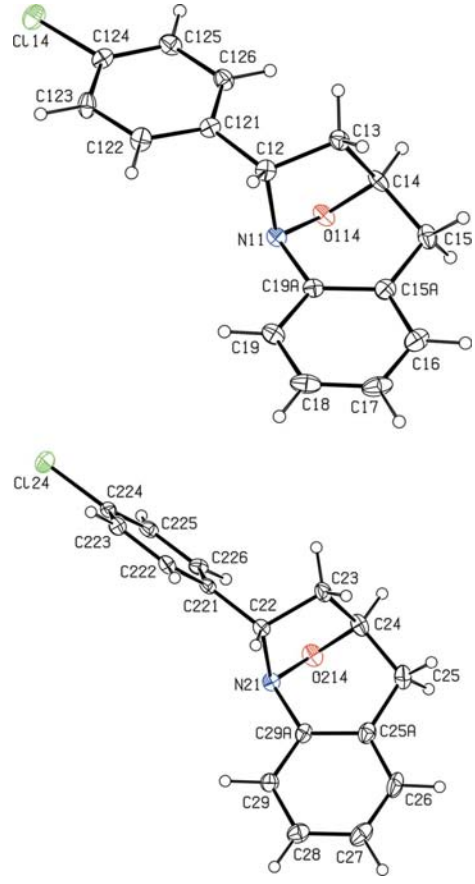


Figure 2
The two independent molecules of (II), showing the atom-labelling scheme: the type 1 molecule is at the top and the type 2 molecule is below. Displacement ellipsoids are drawn at the 30% probability level.

The ring-puckering parameters (Cremer & Pople, 1975), which define the conformation of the fused bicyclic system, in compounds (I)–(V) all have similar values (Table 1), showing that the shape of this ring system is largely unaffected by the nature of the substituents and the intermolecular interactions, and confirming that, in each of compounds (I)–(III), the two independent molecules in the selected asymmetric unit are indeed of the same hand. Considerably more variation is found in the orientation of the pendent aryl ring relative to the heterocyclic system, which is conveniently specified by the torsion angles Nx1—Cx2—Cx21—Cx22 (x = 1 and 2) in (I)–(III) or N1—C2—C21—C22 in (IV) and (V) (Table 1). While the two independent values for (I) are nearly the same (Fig. 1), they are very different in both (II) and (III) (Figs. 2 and 3). The ring orientation is similar for the type 2 molecules of (II) and (III), while the orientations in (IV) and (V) are similar to that in the type 1 molecule of (II).

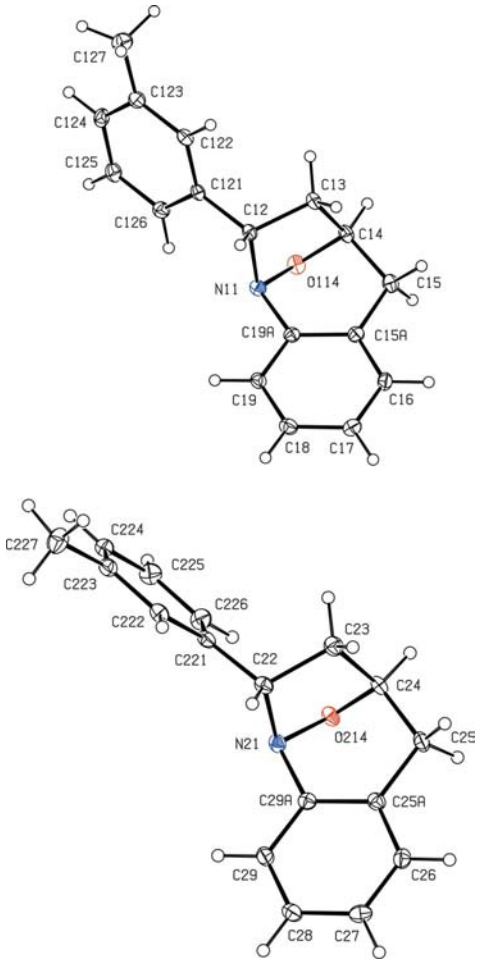


Figure 3
The two independent molecules of (III), showing the atom-labelling scheme: the type 1 molecule is at the top and the type 2 molecule is below. Displacement ellipsoids are drawn at the 30% probability level.

The supramolecular aggregation in (I)–(V) is based on various combinations of C—H···N, C—H···O and C—H···π(arene) hydrogen bonds, with no two structures exhibiting the same range of interactions. There are neither C—H···N nor C—H···O hydrogen bonds in the structure of (I). Instead the molecules are linked into two types of chain by two independent C—H···π(arene) hydrogen bonds (Table 2). One of these hydrogen bonds links type 1 molecules that are related by the C-centring operation into a chain running parallel to the [110] direction, while the second hydrogen bond similarly links type 2 molecules into another chain parallel to [110] but running in the opposite sense (Table 2 and Fig. 6). However, there are no direction-specific interactions between a type 1 molecule and any type 2 molecule. Eight chains, four of each type, pass through each unit cell, but there are no direction-specific interactions between the chains; thus, the hydrogen-bonded structure of (I) is one-dimensional.

The crystal structure of (II) contains two independent two-centre C—H···O hydrogen bonds, a three-centre C—H···(N,O) hydrogen bond and a C—H···π(arene) hydrogen bond, and the combination of these interactions links the molecules into a sheet of considerable complexity. However, the formation of the sheet is readily analysed using the substructure approach (Ferguson *et al.*, 1998*a*,*b*; Gregson *et al.*, 2000):

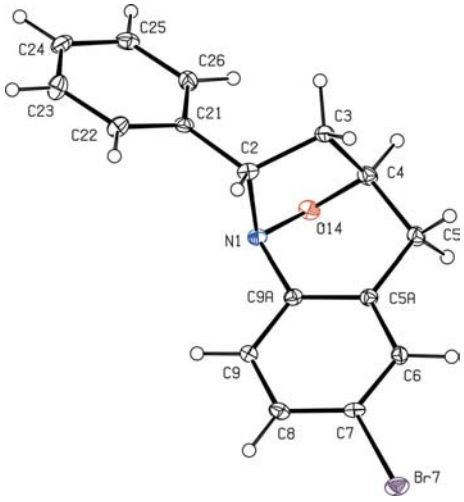


Figure 4
The molecular structure of (IV), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

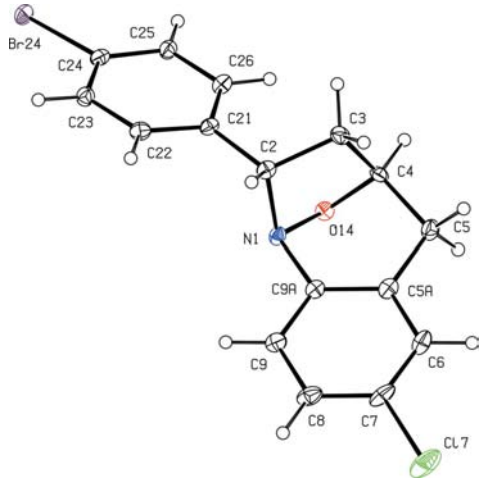


Figure 5
The molecular structure of (V), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

one substructure is built using the C—H···O and C—H···(N,O) hydrogen bonds, and the other is built using only the C—H···π(arene) hydrogen bond. In the first substructure, pairs of type 1 molecules related to one another by inversion are linked by pairs of symmetry-related C—H···O hydrogen bonds to form a series of $R_2^2(14)$ (Bernstein *et al.*, 1995) rings centred at $(n, \frac{1}{2} - n, \frac{1}{2})$, where n represents an integer. Pairs of type 2 molecules are similarly linked to form a second series of $R_2^2(14)$ rings centred at $(\frac{1}{2} - n, n, \frac{1}{2})$, where n again represents an integer. The two types of $R_2^2(14)$ dimer unit are linked by the three-centre C—H···(N,O) hydrogen bond, *via* an $R_1^2(3)$ ring motif, so forming a chain of rings running parallel to the $[1\bar{1}0]$ direction and containing three types of ring (Fig. 7). In the second substructure, pairs of molecules that are related by inversion and which lie in different $[1\bar{1}0]$ chains are linked by symmetry-related pairs of C—H···π(arene) hydrogen bonds (Fig. 8), and the effect of this motif is to link the chains along $[1\bar{1}0]$ into a complex sheet lying parallel to (001). Thus, the overall two-dimensional hydrogen-bonded structure of (II) can be envisaged as constructed from two substructures which are zero- and one-dimensional, respectively.

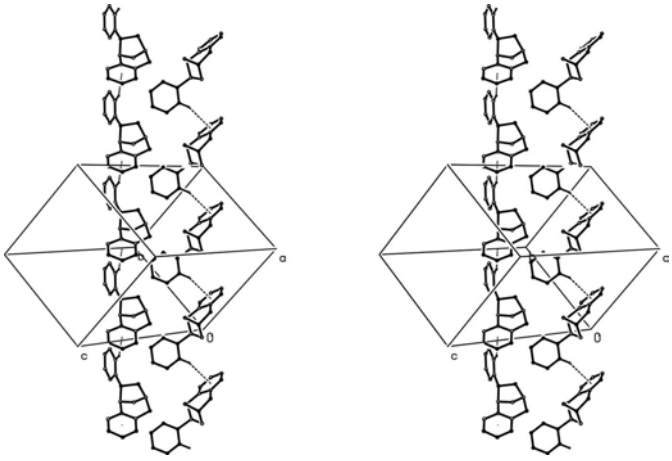


Figure 6
A stereoview of part of the crystal structure of (I), showing the formation *via* C—H···π interactions of two independent hydrogen-bonded chains along [110], each containing only one type of molecule. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

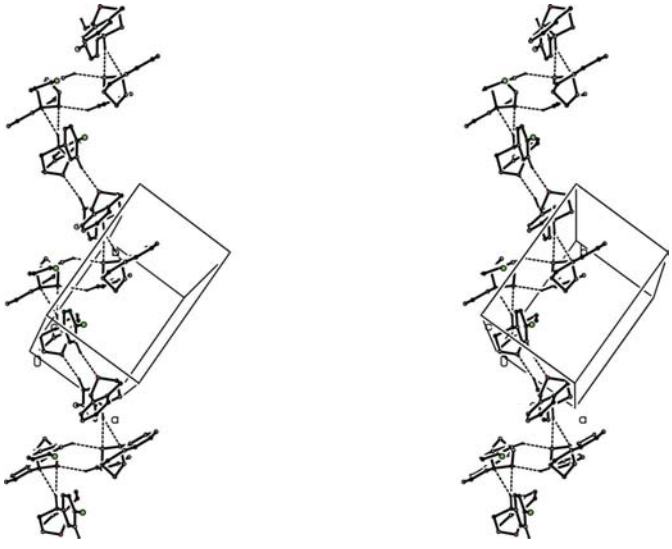


Figure 7
A stereoview of part of the crystal structure of (II), showing the formation of a hydrogen-bonded chain of rings along $[1\bar{1}0]$, and containing $R_1^2(3)$ rings and two types of $R_2^2(14)$ ring. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

The two independent molecules in the structure of (III) are linked within the selected asymmetric unit by an almost linear C—H···N hydrogen bond, weakly augmented by a C—H···π(arene) hydrogen bond (Table 2). The resulting bimolecular aggregates are linked into sheets by a combination of a C—H···O hydrogen bond and a second C—H···π(arene) hydrogen bond. Each of these interactions gives rise to a simple one-dimensional substructure, whose combination suffices to generate the sheet. In one substructure, type 1 molecules related by the *c*-glide plane at $y = 0.25$ are linked by a C—H···O hydrogen bond to form a $C(6)$ chain running parallel to the [001] direction, with type 2 molecules pendent from it. In the second substructure, bimolecular aggregates that are related by translation are linked by the C—H···π(arene) hydrogen bond having the C121–C126 ring as the acceptor to form a chain running parallel to [100]. The combination of the chains running parallel to [100] and [001] gives a sheet lying parallel to (010) (Fig. 9). Two sheets of this type pass through each unit cell, in the domains $0.0 < y < 0.5$ and $0.5 < y < 1.0$, respectively, but there are no direction-specific interactions between adjacent sheets.

In the crystal structure of (IV), there are no direction-specific intermolecular interactions of any kind: there are no hydrogen bonds or aromatic π–π stacking interactions.

A combination of C—H···N and C—H···O hydrogen bonds, one of each type (Table 2), links the molecules of (V) into a sheet of centrosymmetric rings. Pairs of symmetry-related C—H···O hydrogen bonds link the molecules at

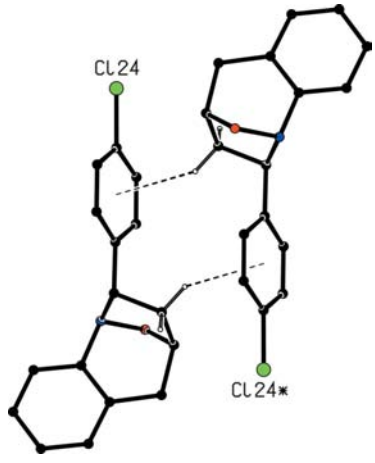


Figure 8
Part of the crystal structure of (II), showing a pair of symmetry-related C—H···π(arene) hydrogen bonds which link the chains along $[1\bar{1}0]$ into a sheet parallel to (001). For the sake of clarity, the unit-cell outline and H atoms bonded to C atoms not involved in the motif shown have been omitted. The atom marked with an asterisk (*) is at the symmetry position $(-x, -y, 1 - z)$.

(x, y, z) and ($1 - x$, $1 - y$, $1 - z$) into a centrosymmetric $R_2^2(14)$ dimer unit centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$), and this substructural unit can conveniently be regarded as the key building block in the formation of the sheet. The C—H···N hydrogen bond directly links the reference dimer at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) to four other dimers of this type, centred, respectively, at ($\frac{1}{2}$, 0, 0), ($\frac{1}{2}$, 0, 1), ($\frac{1}{2}$, 1, 0) and ($\frac{1}{2}$, 1, 1), so generating a sheet parallel to (100) and containing $R_2^2(14)$ and $R_6^6(22)$ rings, with both types centrosymmetric, alternating in a chessboard fashion (Fig. 10). If the dimer units are regarded as the nodes of the resulting two-dimensional net, then this net is of the (4,4) type. The crystal structure of (V) also contains a fairly short Br···Cl contact involving molecules related by the *c*-glide plane at $y = \frac{3}{4}$ [Br···Cl^{x} = 3.4875 (12) Å, C—Br···Cl^{x} = 142.74 (10)° and Br···Cl^{x}—C^{x} = 144.98 (14)°; symmetry code: (x) $1 + x$, $\frac{3}{2} - y$, $\frac{1}{2} + z$]. The Br···Cl^{x} distance is somewhat shorter than the sum of the van der Waals radii (3.61 Å; Bondi, 1964). If this interaction is attractive (Ramasubbu *et al.*, 1986), then it links molecules into a chain parallel to the [201] direction and thereby links the hydrogen-bonded sheets into a continuous three-dimensional framework structure.

Thus, no two of compounds (I)–(V) show the same patterns of supramolecular aggregation, and no two structures exhibit the same range of intermolecular hydrogen bonds. In this connection, it is therefore of interest briefly to compare the structures of (I)–(V) with those of the close analogues (VI)–(IX) (Gómez *et al.*, 2008, 2009) (see scheme).

In the structure of (VI) (Gómez *et al.*, 2008), a combination of C—H···N and C—H···O hydrogen bonds, one of each type, links molecules related by a 2_1 screw axis in the space group $Pna2_1$ into a chain of edge-fused $R_3^3(12)$ rings, in a motif entirely different from any of those found in the rest of this series. By contrast, in the structure of (VII) (Gómez *et al.*, 2009), which might reasonably have been expected to be rather similar to that of (VI), or even to be isostructural with (VI), pairs of molecules are linked into centrosymmetric dimer units by pairs of symmetry-related C—H···π(arene) hydrogen bonds [*cf.* the dimer formation in (V) using C—H···O hydrogen bonds], and these dimer units in (VII) are linked into sheets by a C—H···N hydrogen bond, so forming a (4,4)-type net, as in (V). The hydrogen-bonded structures of (VIII) (Gómez *et al.*, 2009) and (IX) (Gómez *et al.*, 2008) are both three-dimensional; in (VIII), the hydrogen-bonded framework is built from one C—H···O hydrogen bond and three independent C—H···π(arene) hydrogen bonds, while that in (IX) is built from one C—H···O hydrogen bond and two independent C—H···π(arene) hydrogen bonds. These two compounds are the only ones in this series where the hydrogen-bonded structures are three dimensional.

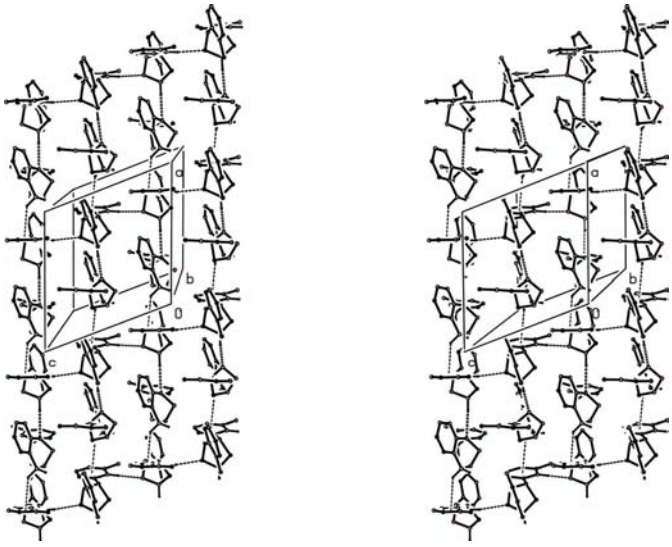


Figure 9
A stereoview of part of the crystal structure of (III), showing the formation of a hydrogen-bonded sheet parallel to (010) and built from C—H···N, C—H···O and C—H···π(arene) hydrogen bonds. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

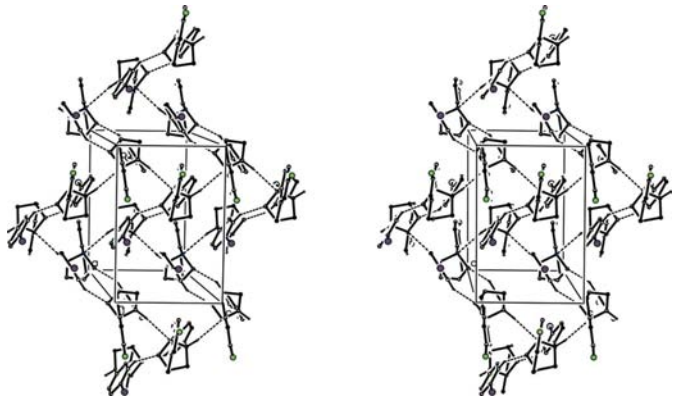


Figure 10
A stereoview of part of the crystal structure of (V), showing the formation of a hydrogen-bonded sheet parallel to (100) containing $R_2^2(14)$ and $R_6^6(22)$ rings. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

Experimental

For the preparation of compounds (I)–(V), sodium tungstate dihydrate (5–10 mol%), followed by 30% aqueous hydrogen peroxide solution (0.30 mol, added dropwise), were added to a stirred solution of the appropriately substituted 2-allyl-*N*-benzylaniline (0.10 mol) in methanol (30 ml). The resulting mixtures were then stirred at ambient temperature for periods ranging from 48 to 72 h. Each mixture was filtered and the solvent removed under reduced pressure. Toluene (40 ml) was added to the organic residues and the resulting solution was heated to *ca* 333 K for periods ranging from 6 to 8 h. After cooling of each solution to ambient temperature, the solvent was removed under reduced pressure and the crude product was purified by chromatography on silica gel using heptane–ethyl acetate (compositions ranged from 60:1 to 40:1 *v*/*v*) as eluant. Crystallization from heptane gave colourless crystals suitable for single-crystal X-ray diffraction. For (I) (yield 61%, m.p. 361–362 K), MS (70 eV) *m*/*z* (%): 237 (M^+, 40), 220 (24), 208 (7), 194 (14), 130 (7), 104 (100), 91 (25), 77 (31). For (II) (yield 63%, m.p. 331–333 K), MS (70 eV) *m*/*z* (%): 271 [M^+ (^{35}Cl), 21], 254 (13), 242 (3), 228 (3), 130 (5), 104 (100), 91 (14), 77 (25). For (III) (yield 67%, m.p. 352–353 K), MS (70 eV) *m*/*z* (%): 251 (M^+, 55), 234 (36), 222 (10),

208 (12), 130 (8), 104 (100), 91 (33), 77 (22). For (IV) (yield 63%, m.p. 356–358 K), MS (70 eV) *m*/*z* (%): 315 [M^+ (^{79}Br), 31], 298 (11), 286 (6), 208 (11), 184 (100), 132 (40), 104 (54), 77 (80). For (V) (yield 76%, m.p. 417–419 K), MS (70 eV) *m*/*z* (%): 349 [M^+ (^{79}Br, ^{35}Cl), 20], 334 (10), 182 (13), 152 (13), 139 (100), 102 (23), 89 (30), 77 (30).

Compound (I)

Crystal data

$C_{16}H_{15}NO$
M_r = 237.29
Monoclinic, *Cc*
a = 10.7475 (7) Å
b = 10.7842 (12) Å
c = 20.5812 (19) Å
β = 91.688 (7)°
V = 2384.4 (4) Å^3
Z = 8
Mo *K*α radiation
μ = 0.08 mm^{-1}
T = 120 K
0.51 × 0.33 × 0.18 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.952, T_{max} = 0.985
15795 measured reflections
2214 independent reflections
1595 reflections with $I > 2\sigma(I)$
R_{int} = 0.072

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.046
$wR(F^2)$ = 0.123
S = 1.08
2214 reflections
325 parameters
2 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.24 e Å^{-3}

Compound (II)

Crystal data

$C_{16}H_{14}ClNO$
M_r = 271.73
Monoclinic, $P2_1/n$
a = 8.2405 (14) Å
b = 11.5432 (16) Å
c = 27.442 (2) Å
β = 101.030 (13)°
V = 2562.1 (6) Å^3
Z = 8
Mo *K*α radiation
μ = 0.29 mm^{-1}
T = 120 K
0.46 × 0.26 × 0.10 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.889, T_{max} = 0.972
33797 measured reflections
4745 independent reflections
2978 reflections with $I > 2\sigma(I)$
R_{int} = 0.079

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.050
$wR(F^2)$ = 0.108
S = 1.05
4745 reflections
343 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}

Compound (III)

Crystal data

$C_{17}H_{17}NO$
M_r = 251.32
Monoclinic, $P2_1/c$
a = 10.9966 (17) Å
b = 23.691 (10) Å
c = 10.6323 (8) Å
β = 111.661 (8)°
V = 2574.3 (12) Å^3
Z = 8
Mo *K*α radiation
μ = 0.08 mm^{-1}
T = 120 K
0.48 × 0.30 × 0.14 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.965, T_{max} = 0.989
30931 measured reflections
4790 independent reflections
3352 reflections with $I > 2\sigma(I)$
R_{int} = 0.075

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.114
S = 1.07
4790 reflections
345 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.31 e Å^{-3}

Compound (IV)

Crystal data

$C_{16}H_{14}BrNO$
M_r = 316.19
Orthorhombic, $P2_12_12_1$
a = 5.5214 (3) Å
b = 10.2982 (12) Å
c = 22.900 (3) Å
V = 1302.1 (2) Å^3
Z = 4
Mo *K*α radiation
μ = 3.15 mm^{-1}
T = 120 K
0.22 × 0.20 × 0.18 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.471, T_{max} = 0.568
14968 measured reflections
2989 independent reflections
2587 reflections with $I > 2\sigma(I)$
R_{int} = 0.051

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.032
$wR(F^2)$ = 0.064
S = 1.07
2989 reflections
173 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.51 e Å^{-3}
$\Delta\rho_{min}$ = −0.50 e Å^{-3}
Absolute structure: Flack (1983), 1228 Bijvoet pairs
Flack parameter: 0.497 (9)

Compound (V)

Crystal data

$C_{16}H_{13}BrClNO$
M_r = 350.63
Monoclinic, $P2_1/c$
a = 15.3626 (16) Å
b = 11.5436 (13) Å
c = 7.8832 (13) Å
β = 96.080 (11)°
V = 1390.1 (3) Å^3
Z = 4
Mo *K*α radiation
μ = 3.14 mm^{-1}
T = 120 K
0.32 × 0.32 × 0.24 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.406, T_{max} = 0.470
19930 measured reflections
3181 independent reflections
2267 reflections with $I > 2\sigma(I)$
R_{int} = 0.072

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.095
S = 1.06
3181 reflections
181 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.86 e Å^{-3}
$\Delta\rho_{min}$ = −0.56 e Å^{-3}

Table 1
Selected geometric parameters (Å, °) for compounds (I)–(V).

Ring-puckering parameters†‡						
		Five-membered ring		Six-membered ring		
Compound	x	Q_2	φ_2	Q	θ	φ
(I)	1	0.460 (4)	200.8 (5)	0.631 (4)	55.8 (4)	344.3 (5)
(I)	2	0.458 (4)	201.3 (6)	0.637 (4)	54.7 (4)	342.0 (5)
(II)	1	0.452 (2)	201.6 (3)	0.628 (2)	51.5 (3)	341.3 (3)
(II)	2	0.427 (3)	189.6 (4)	0.641 (3)	54.1 (3)	348.0 (3)
(III)	1	0.458 (2)	197.7 (3)	0.625 (2)	51.7 (2)	342.8 (3)
(III)	2	0.435 (2)	182.9 (3)	0.613 (2)	52.6 (2)	353.5 (3)
(IV)	–	0.435 (3)	189.9 (4)	0.605 (3)	49.5 (3)	347.6 (4)
(V)	–	0.453 (3)	200.1 (4)	0.630 (3)	52.7 (3)	343.8 (4)

Torsion angles N*x*1—C*x*2—C*x*21—C*x*22‡		
Compound	x	Angle
(I)	1	179.6 (4)
(I)	2	177.4 (4)
(II)	1	85.2 (3)
(II)	2	136.8 (2)
(III)	1	−178.32 (19)
(III)	2	139.9 (2)
(IV)	–	105.1 (3)
(V)	–	97.3 (3)

† Ring-puckering parameters for the five- and six-membered rings refer to the atom sequences O*x*14—N*x*1—C*x*2—C*x*3—C*x*4 and O*x*14—N*x*1—C*x*9*A*—C*x*5*A*—C*x*5—C*x*4, respectively. ‡ x = 1 or 2 for (I)–(III), and x is nul for (IV) and (V).

All H atoms were located in difference maps and then treated as riding atoms in geometrically idealized positions, with C—H distances of 0.95 (aromatic), 0.98 (CH_3), 0.99 (CH_2) or 1.00 Å (aliphatic CH) and with $U_{iso}(H) = kU_{eq}(C)$, where k = 1.5 for the methyl groups in (III), which were permitted to rotate but not to tilt, and 1.2 for all other H atoms. In this series, the reference molecules were all selected as those having the (2*S*,4*R*) configuration. Although each of the hydrogen bonds in (II) links a pair of molecules of the opposite hand, the selection of an asymmetric unit containing two molecules of the same hand, to be consistent with all the other compounds, was judged to be the more preferable choice. In the absence of significant resonant scattering in (I), the Friedel-equivalent reflections were merged prior to the final refinements; hence the correct orientation of the structure of (I) relative to the polar-axis directions could not be established. A careful search for possible additional symmetry in (I) revealed none and, indeed, attempts to solve the structure of (I) in the space group *C*2/*c* did not lead to any readily interpretable solutions. The refinement for (IV) was handled as an inversion twin in the space group $P2_12_12_1$, leading to twin fractions of 0.497 (9) and 0.503 (9), so that, within the experimental uncertainty, the crystal selected for data collection appears to contain a true racemic mixture.

For all compounds, data collection: *COLLECT* (Hooft, 1999); cell refinement: *DIRAX*/*LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003). Program(s) used to solve structure: *SIR2004* (Burla *et al.*, 2005) for (I), (II) and (IV); *SHELXS97* (Sheldrick, 2008) for (III) and (V). For all 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*.

Table 2
Hydrogen-bond parameters (Å, °) for (I)–(III) and (V).

*Cg*1, *Cg*2, *Cg*3 and *Cg*4 represent the centroids of rings C15*A*/C16–C19/C19*A*, C25*A*/C26–C29/C29*A*, C221–C226 and C121–C126, respectively.

Compound	D—H···A	D—H	H···A	D···A	D—H···A
(I)	C122—H122···*Cg*1^{i}	0.95	2.58	3.469 (5)	156
	*C*222—H222···*Cg*2^{ii}	0.95	2.71	3.610 (5)	158
(II)	C22—H22···O114^{iii}	1.00	2.37	3.357 (3)	168
	C22—H22···N11^{iii}	1.00	2.56	3.442 (3)	147
	C125—H125···O114^{iii}	0.95	2.38	3.248 (3)	152
	C225—H225···O214^{iv}	0.95	2.50	3.428 (3)	164
	C23—H23*B*···*Cg*3^{v}	0.99	2.78	3.596 (3)	140
(III)	C14—H14···N21	1.00	2.58	3.559 (3)	165
	C122—H122···O114^{vi}	0.95	2.49	3.413 (3)	163
	C15—H15*A*···*Cg*3	0.99	2.76	3.495 (3)	132
	C25—H25*B*···*Cg*4^{vii}	0.99	2.79	3.586 (3)	138
(V)	C2—H2···N1^{viii}	1.00	2.56	3.535 (4)	164
	C25—H25···O14^{ix}	0.95	2.40	3.290 (4)	155

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

The authors thank Centro de Instrumentación Científico-Técnica of the Universidad de Jaén and the staff for data collection. AP and SLG thank COLCIENCIAS for financial support (grant No. 1102-408-20563). JC thanks the Consejería de Innovación, Ciencia y Empresa (Junta de Andalucía, Spain), the Universidad de Jaén (project reference UJA_07_16_33) and Ministerio de Ciencia e Innovación (project reference SAF2008-04685-C02-02) for financial support.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FA3218). Services for accessing these data are described at the back of the journal.

References

Acosta, L. M., Bahsas, A., Palma, A., Cobo, J., Low, J. N. & Glidewell, C. (2008). *Acta Cryst.* C**64**, o514–o518.
Acosta, L. M., Palma, A., Bahsas, A., Cobo, J. & Glidewell, C. (2010*a*). *Acta Cryst.* C**66**, o206–o208.
Acosta, L. M., Palma, A., Bahsas, A., Cobo, J. & Glidewell, C. (2010*b*). *Acta Cryst.* C**66**, o209–o214.
Allen, F. H. (2002). *Acta Cryst.* B**58**, 380–388.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Blanco, M. C., Raysth, W., Palma, A., Cobo, J., Low, J. N. & Glidewell, C. (2008). *Acta Cryst.* C**64**, o524–o528.
Bondi, A. (1964). *J. Phys. Chem.* **68**, 441–451.
Burla, M. C., Caliandro, R., Camalli, M., Carrozzini, B., Cascarano, G. L., De Caro, L., Giacovazzo, C., Polidori, G. & Spagna, R. (2005). *J. Appl. Cryst.* **38**, 381–388.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Duisenberg, A. J. M., Hooft, R. W. W., Schreurs, A. M. M. & Kroon, J. (2000). *J. Appl. Cryst.* **33**, 893–898.
Duisenberg, A. J. M., Kroon-Batenburg, L. M. J. & Schreurs, A. M. M. (2003). *J. Appl. Cryst.* **36**, 220–229.
Ferguson, G., Glidewell, C., Gregson, R. M. & Meehan, P. R. (1998*a*). *Acta Cryst.* B**54**, 129–138.
Ferguson, G., Glidewell, C., Gregson, R. M. & Meehan, P. R. (1998*b*). *Acta Cryst.* B**54**, 139–150.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Flack, H. D. & Bernardinelli, G. (2000). *J. Appl. Cryst.* **33**, 1143–1148.
Gómez, S. L., Raysth, W., Palma, A., Cobo, J., Low, J. N. & Glidewell, C. (2008). *Acta Cryst.* C**64**, o519–o523.
Gómez, S. L., Sanabria, C. M., Palma, A., Bahsas, A., Cobo, J. & Glidewell, C. (2009). *Acta Cryst.* C**65**, o465–o469.
Gómez Ayala, S. L., Stashenko, E., Palma, A., Bahsas, A. & Amaro-Luis, J. M. (2006). *Synlett*, pp. 2275–2277.
Gregson, R. M., Glidewell, C., Ferguson, G. & Lough, A. J. (2000). *Acta Cryst.* B**56**, 39–57.
Hooft, R. W. W. (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.
Hooft, R. W. W., Straver, L. H. & Spek, A. L. (2008). *J. Appl. Cryst.* **41**, 96–103.
Marsh, R. E. (1997). *Acta Cryst.* B**53**, 317–322.
Marsh, R. E. (2004). *Acta Cryst.* B**60**, 252–253.
Marsh, R. E. (2009). *Acta Cryst.* B**65**, 782–783.
Palma, A., Yépez, A. E., Leal, S. M., Coronado, C. A. & Escobar, P. (2009). *Bioorg. Med. Chem. Lett.* **19**, 2360–2363.
Ramasubbu, N., Parthrasarthy, R. & Murray-Rust, P. (1986). *J. Am. Chem. Soc.* **108**, 4308–4314.
Sheldrick, G. M. (2003). *SADABS*. Version 2.10. University of Göttingen, Germany.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.
Yépez, A. E., Palma, A., Stashenko, E., Bahsas, A. & Amaro-Luis, J. M. (2006). *Tetrahedron Lett.* **47**, 5825–5828.