organic compounds

Four 1-naphthyl-substituted tetrahydro-1,4-epoxy-1-benzazepines: hydrogen-bonded structures in one, two and three dimensions

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(2S*,4R*)-2-exo-(1-Naphthyl)-2,3,4,5-tetrahydro-1H-1,4-epoxy-1-benzazepine, $C_{20}H_{17}NO$, (I), crystallizes with $Z' = 2$ in the space group $P2_1$; the two independent molecules have the same absolute configuration, although this configuration is indeterminate. The molecules of each type are linked by a combination of C—H···O and C—H···π(arene) hydrogen bonds to form two independent sheets, each containing only one type of molecule. (2SR,4RS)-7-Methyl-2-exo-(1-naphthyl)-2,3,4,5-tetrahydro-1H-1,4-epoxy-1-benzazepine, $C_{21}H_{19}$-NO, (II), crystallizes as a true racemate in the space group $P2_1/c$, and a combination of C—H···N, C—H···O and C—H···π(arene) hydrogen bonds links the molecules into sheets, each containing equal numbers of the two enantiomorphs. (2S*,4R*)-2-exo-(1-Naphthyl)-7-trifluoromethyl-2,3,4,5-tetrahydro-1H-1,4-epoxy-1-benzazepine, $C_{21}H_{16}F_3NO_2$, (III), crystallizes as a single enantiomorph, as for (I), but now with $Z' = 1$ in the space group $P2_12_12_1$; again, the absolute configuration is indeterminate. A single C—H···π(arene) hydrogen bond links the molecules of (III) into simple chains. (2S,4R)-8-Chloro-9-methyl-2-exo-(1-naphthyl)-2,3,4,5-tetrahydro-1H-1,4-epoxy-1-benzazepine, $C_{21}H_{18}ClNO$, (IV), crystallizes as a single enantiomorph of well defined configuration, in the space group $P2_12_12_1$, where two independent C—H···π(arene) hydrogen bonds link the molecules into a single three-dimensional framework structure.

Comment

We report here the structures of four substituted 2-exo-(1-naphthyl)-2,3,4,5-tetrahydro-1H-1,4-epoxy-1-benzazepines, compounds (I)–(IV), carrying different simple substituents in the fused aryl ring (Figs. 1–4), and we compare these with the 7-chloro analogue compound, (V) (Gómez et al., 2008). The work reported here is a continuation of an extensive study of benzazepine derivatives of this general type, involving wide variations in both the aromatic moiety fused to the azepine ring and the substituent present at position 2 (Acosta et al., 2008, 2010a,b; Gómez et al., 2008, 2009, 2010; Blanco et al., 2008, 2009; Palma et al., 2009).
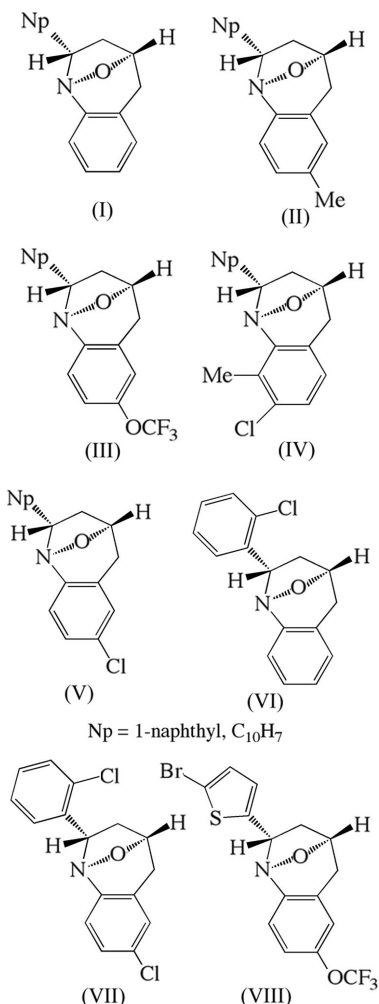
(I) (II) (III) (IV) (V) (VI)
Np = 1-naphthyl, $C_{10}H_7$
(VII) (VIII)

The compounds reported here were all prepared using appropriate variations of the synthetic method described previously (Acosta et al., 2008), in which an N-substituted 2-allylaniline is oxidized with aqueous hydrogen peroxide solution in the presence of sodium tungstate as catalyst, yielding the fused tricyclic product in a one-pot process. Although the products all contain two stereogenic C atoms, there are no reagents employed in the synthetic procedure which are capable of inducing stereoselectivity or enantioselectivity in the final products. Despite this, only (II) crystallizes as a racemic mixture of (2S,4R) and (2R,4S) enantiomers, in the space group $P2_1/c$. In contrast, (IV) crystallizes as a single enantiomer in the space group $P2_12_12_1$, with the configuration (2S,4R) in the crystal selected for data collection, as shown by the values of the Flack x parameter (Flack, 1983) and the Hooft y parameter (Hooft et al., 2008) of 0.02 (7) and 0.01 (3), respectively. Compounds (I), where $Z' = 2$, and (III) crystallize in the Sohnke space groups $P2_1$ and $P2_12_12_1$,
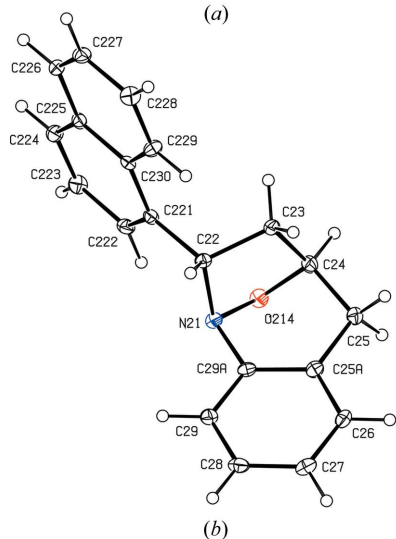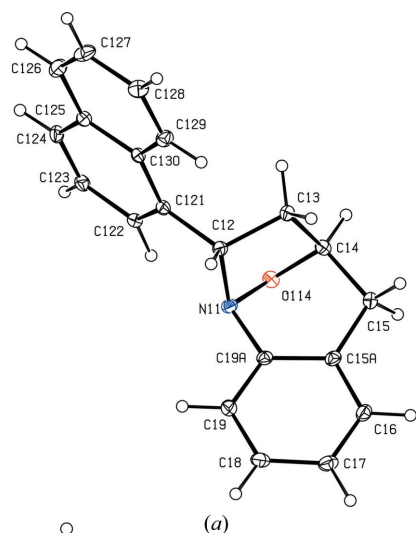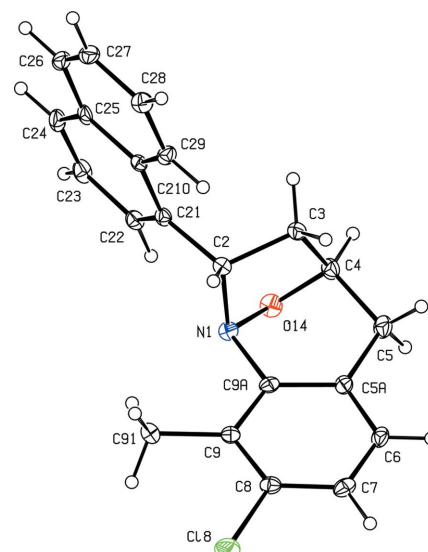
Figure 1
The two independent molecules of (I), showing the atom-labelling scheme. (a) A type 1 molecule and (b) a type 2 molecule, both shown as the (2S,4R) enantiomorph. Displacement ellipsoids are drawn at the 30% probability level.
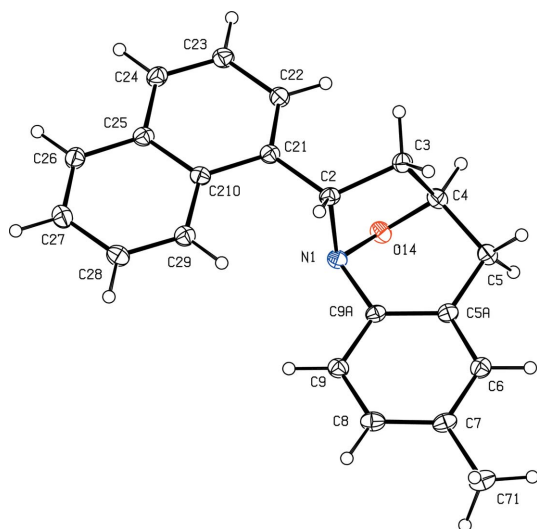
Figure 2
The (2S,4R) enantiomorph of (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.
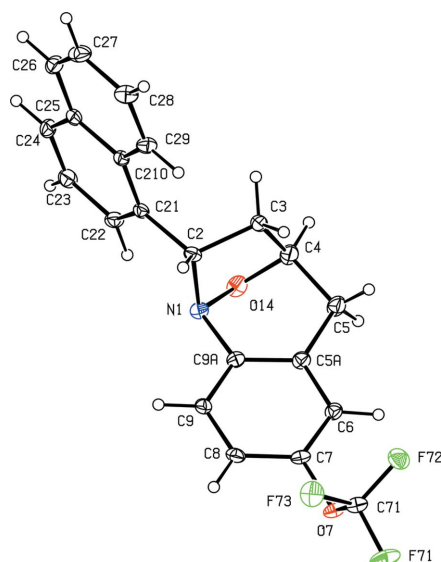
Figure 3
The molecular structure of (III), showing the atom-labelling scheme. The (2S,4R) enantiomorph is shown and the displacement ellipsoids are drawn at the 30% probability level.

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

respectively, indicating the presence of only a single enantiomer in a given crystal, provided that inversion twinning is absent. However, in the absence of significant resonant scattering, the absolute stereochemistry of (I) and (III) remains unknown, although the relative stereochemistry at C2 and C4 is unambiguous.

The analogous compound, (V) (Gómez *et al.*, 2008), which differs from (II) only in the notional replacement of the 7-methyl substituent in (II) by a 7-chloro substituent in (V), is neither isomorphous nor isostructural with the racemic compound, (II). Instead, (V) crystallizes as a single enantiomorph in the space group $P2_12_12_1$, having the (2S,4R) configuration in the crystal selected for data collection, just as for (IV).

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These observations on (IV) and (V) prompted us to review briefly the crystallization characteristics of other compounds of this general type. Including the four compounds reported here, we have now determined the structures of 35 examples, and of these, 21 crystallize as genuine racemates in space groups containing reflection and/or inversion operators. A further five examples crystallize as inversion twins. In two of these, both in the space group $P2_12_12_1$, the twin fractions are equal to 0.5 within experimental uncertainty, indicating that these two compounds are also racemic, but in three other examples of inversion twins, all of them in the space group $P2_1$, one enantiomorph predominates in the crystals selected for data collection. However, in addition to (II) and (V), there are three other examples, namely compounds (VI) (Gómez *et al.*, 2009), (VII) (Gómez *et al.*, 2008) and (VIII) (Blanco *et al.*, 2008), which all crystallize as single enantiomorphs, in the space groups $P2_1$ for compounds (VI) and (VIII) and $P2_12_12_1$ for compound (VII), and which all have the (2*S*,4*R*) configuration in the crystals used for data collection. Finally, there are four examples, including (I) and (III) reported here, for which the absolute configuration could not be established because of insignificant resonant scattering. Hence, overall, we have 21 true racemates, five single enantiomers, five inversion twins and four structures where the configuration is indeterminate. To be sure, five examples crystallizing as single enantiomorphs from a total population of 35 compounds is only a small sample, but it is interesting that the absolute configuration was unambiguously established as (2*S*,4*R*) in each of these five examples.

The molecular conformations of (I), (II) and (IV) are fully defined by the shapes of the fused ring system and the orientation of the 2-(1-naphthyl)- substituent relative to the fused system. In (III), full definition of the conformation also requires specification of the orientation of the CF$_3$O– substituent. The shapes of the fused ring systems are conveniently defined in terms of the ring-puckering parameters (Cremer & Pople, 1975) for the fused five-and six-membered heterocyclic rings, which are compared in Table 1 with the corresponding values for the related compound, (V) (Gómez *et al.*, 2008). These parameters not only confirm that the reference molecules selected for (I)–(IV) all have the same absolute configuration, as do the two independent molecules in (I), but, when compared with those of the previously reported analogues, they show that the shape of the fused heterocyclic ring system is essentially invariant to the nature of the peripheral substituents. On the other hand, the naphthyl group appears to adopt one of two quite distinct orientations, with the naphthyl group in (II) having an orientation which is almost orthogonal to those in (I) and (III)–(V) (Table 1). In all of (I)–(V), one or other of the rings in the naphthyl substituent acts as an acceptor in C—H···π hydrogen bonds (see below), and these interactions may be influential in determining the orientation of this substituent. In (III), the dihedral angle between the C5a/C6–C9/C9a and C7/O7/C71 planes is 86.9 (2)°.

Just as (I)–(IV) all exhibit different crystallization characteristics, so too they all adopt different modes of supra-molecular aggregation, with hydrogen-bonded systems which are one-dimensional in (II), two-dimensional in (I) and (II), and three-dimensional in (IV). The dominant intermolecular interactions (Table 2) are of C—H···O and C—H···π(arene) types, with a single occurrence of a C—H···N hydrogen bond in (II). However, aromatic π–π stacking interactions are absent from the structures of (I)–(V). We have excluded from consideration as being structurally significant those C—H···π(arene) contacts having an H···*Cg* distance greater than 2.85 Å (*Cg* represents a ring centroid), a C···*Cg* distance greater than 3.70 Å or a C—H···*Cg* angle less than 130°. This last is consistent with a recent recommendation for inter-molecular hydrogen bonds, based on database analysis and intermolecular energy calculations (Wood *et al.*, 2009) for conventional hydrogen bonds of the general type D—H···A, where D represents C, N or O and A represents N or O.

In (I), each of the two independent molecules forms a hydrogen-bonded sheet. These two sheets are similar in overall architecture but different in detail, although there are no significant direction-specific interactions between adjacent sheets. Molecules of type 1, containing atom N11 (Fig. 1*a*), are linked by a combination of one C—H···O hydrogen bond and one C—H···π(arene) hydrogen bond, having atoms C14 and C18 as the donors, into a sheet lying parallel to (001) in the domain $-0.3 < z < 0.3$ and containing the 2_1 screw axes at $z = 0$ (Fig. 5). Molecules of type 2, containing atom N21, are also linked into sheets, but now by means of three hydrogen bonds, one of C—H···O type and two of C—H···π(arene) type having atoms C24, C26 and C28 as the donors. This sheet also lies parallel to (001), in the domain $0.2 < z < 0.8$, and it contains the 2_1 screw axes at $z = \frac{1}{2}$ (Fig. 6). The corresponding pairs of intermolecular interactions involving atoms C14 and C24 on the one hand, and atoms C18 and C28 on the other, both have recognisably similar sets of dimensions, although with differences which are sufficient to preclude the possibility of any additional crystallographic symmetry. However, the corresponding pair of contacts involving atoms C16 and C26 has very different dimensions, such that while the contact
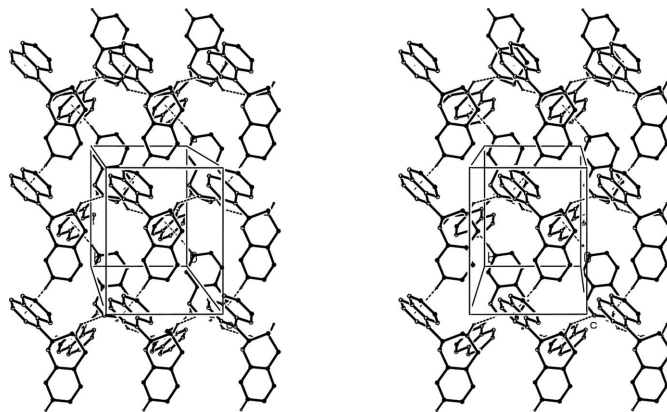

Figure 5
A stereoview of part of the crystal structure of (I), showing the formation of a hydrogen-bonded sheet parallel to (001) and containing only type 1 molecules. All molecules are shown in the (2*S*,4*R*) configuration and H atoms not involved in the motifs shown have been omitted.
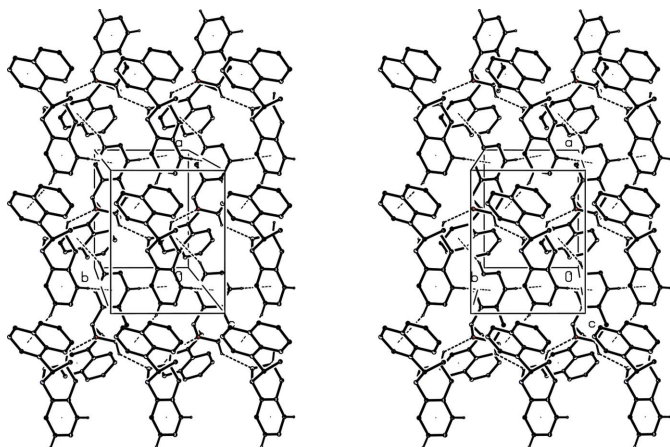
Figure 6
A stereoview of part of the crystal structure of (I), showing the formation of a hydrogen-bonded sheet parallel to (001) and containing only type 2 molecules. All molecules are shown in the (2S,4R) configuration and H atoms not involved in the motifs shown have been omitted.
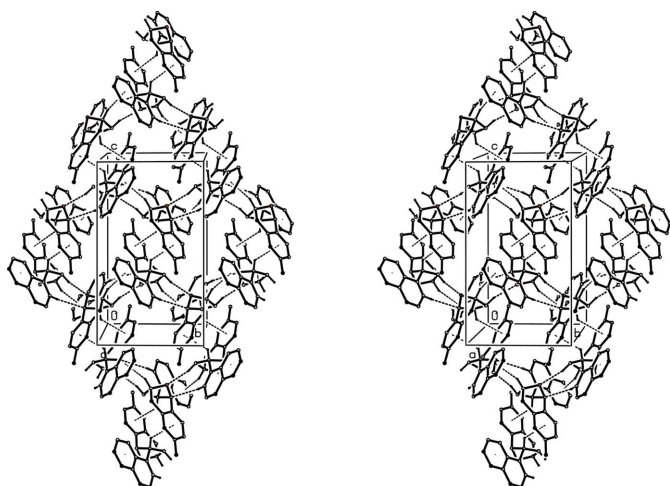

Figure 7
A stereoview of part of the crystal structure of (II), showing the formation of a hydrogen-bonded sheet parallel to (100). H atoms not involved in the motifs shown have been omitted.

involving C26 must be regarded as a structurally significant hydrogen bond, that involving C16, by contrast, is probably no more than an adventitious short contact.

The aggregation in (II) is determined by a combination of C—H$\cdots$N, C—H$\cdots$O and C—H$\cdots\pi$(arene) hydrogen bonds which link molecules related by the 2_1 screw axis along ($\frac{1}{2}$, y, $\frac{3}{4}$) into a complex chain running parallel to the [010] direction (Fig. 7). Chains of this type are linked *via* a centrosymmetric motif containing inversion-related pairs of a second, weaker, C—H$\cdots\pi$(arene) hydrogen bond, so forming a sheet parallel to (100) (Fig. 7).

The hydrogen-bonded structure of (III) is very simple, as a single C—H$\cdots\pi$(arene) hydrogen bond links molecules related by the 2_1 screw axis along ($\frac{1}{4}$, $\frac{1}{2}$, z) into simple chains parallel to [001] (Fig. 8). There are no direction-specific interactions between adjacent chains so that, unlike the hydrogen-bonded structures of (I) and (II), that of (III) is only one-dimensional.
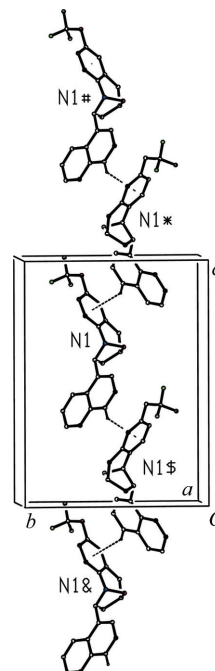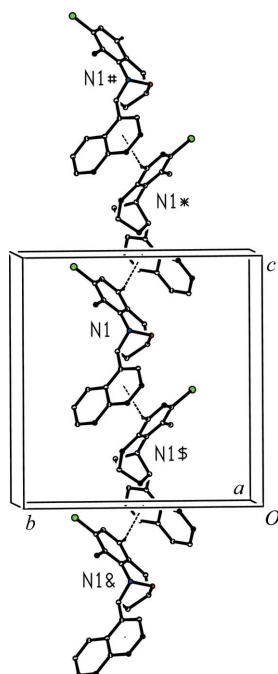

Figure 8
Part of the crystal structure of (III), showing the formation of a hydrogen-bonded chain parallel to [001]. H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*), a hash symbol (#), a dollar sign ($) or an ampersand (&) are at the symmetry positions ($\frac{1}{2} - x$, $1 - y$, $\frac{1}{2} + z$), (x, y, $1 + z$), ($\frac{1}{2} - x$, $1 - y$, $-\frac{1}{2} + z$) and (x, y, $-1 + z$), respectively.

In the crystal structure of (IV), just two independent C—H$\cdots\pi$(arene) hydrogen bonds link the molecules into a continuous three-dimensional framework structure. It is convenient to analyse the formation of this structure in terms of the actions of the individual hydrogen bonds, firstly when each is acting alone and then when they act in combination. Acting alone, the hydrogen bond having atom C6 as the donor links molecules related by the 2_1 screw axis along ($\frac{3}{4}$, $\frac{1}{2}$, z) into a chain running parallel to [001] (Fig. 9), and that having atom C27 as the donor links molecules related by the 2_1 screw axis along (x, $\frac{3}{4}$, $\frac{1}{2}$) into a second chain, this time running parallel to [100] (Fig. 10). Finally, the combination of these two hydrogen bonds, acting alternately, generates a chain running parallel to the [010] direction (Fig. 11). The combination of these distinct chain motifs parallel to [100], [010] and [001] suffices to generate a continuous three-dimensional structure.

Although different donor atoms and acceptor rings are involved in the hydrogen bonding in (III) and (IV), nevertheless the overall architectures of the chains parallel to [001] in these two compounds are strikingly similar, as shown in Figs. 8 and 9, which also illustrate the rather different values of the cell-vector ratio c/b in (III) and (IV).

In (V) (Gómez *et al.*, 2008), a combination of one C—H$\cdots$O and two C—H$\cdots\pi$(arene) hydrogen bonds links the molecules into a continuous three-dimensional structure which is significantly different from that formed by (IV). Whereas the three-dimensional structure of (IV) is best analysed in terms of three separate one-dimensional substructures, in the hydrogen-bonded structure of (V) two
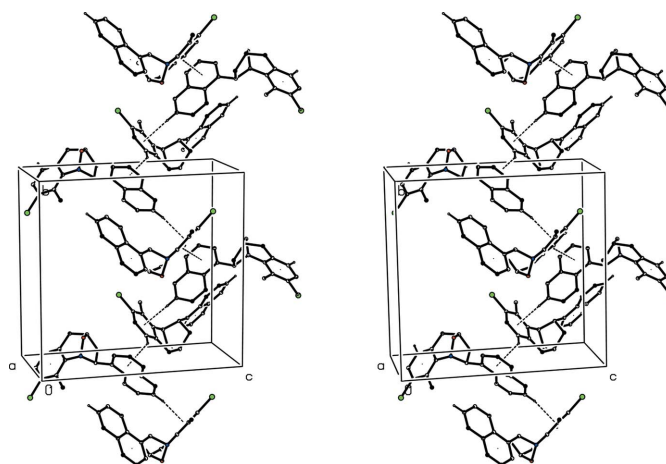
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Figure 9
Part of the crystal structure of (IV), showing the formation of a hydrogen-bonded chain parallel to [001] and containing only one type of hydrogen bond. H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*), a hash symbol (#), a dollar sign ($) or an ampersand (&) are at the symmetry positions $(\frac{3}{2} - x, 1 - y, \frac{1}{2} + z)$, $(x, y, 1 + z)$, $(\frac{3}{2} - x, 1 - y, -\frac{1}{2} + z)$ and $(x, y, -1 + z)$, respectively.
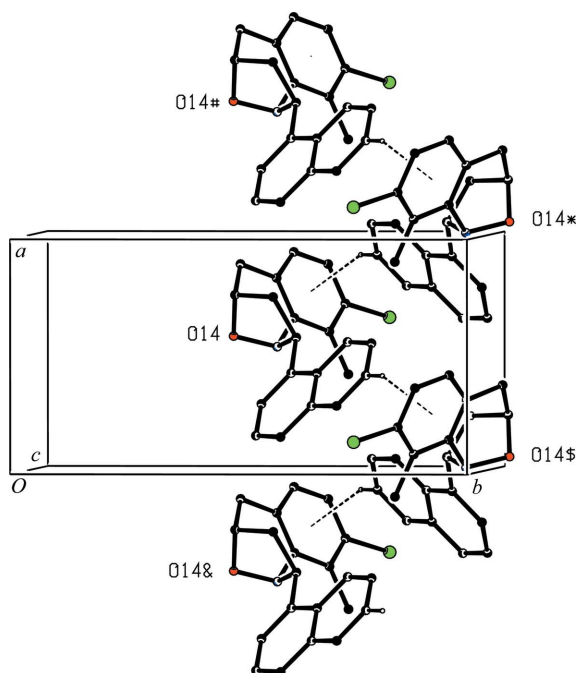
Figure 10
Part of the crystal structure of (IV), showing the formation of a hydrogen-bonded chain parallel to [100] and containing only one type of hydrogen bond. H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*), a hash symbol (#), a dollar sign ($) or an ampersand (&) are at the symmetry positions $(\frac{1}{2} + x, \frac{3}{2} - y, 1 - z)$, $(1 + x, y, z)$, $(-\frac{1}{2} + x, \frac{3}{2} - y, 1 - z)$ and $(-1 + x, y, z)$, respectively.

substructures can be identified. The C—H$\cdots$O hydrogen bond in (V) forms a one-dimensional substructure, while the two

Figure 11
A stereoview of part of the crystal structure of (IV), showing the formation of a hydrogen-bonded chain parallel to [010] and containing two types of hydrogen bond. H atoms not involved in the motifs shown have been omitted.

C—H$\cdots\pi$(arene) hydrogen bonds form a two-dimensional substructure.

Experimental

For the preparation of (I)–(IV), 30% aqueous hydrogen peroxide solution (0.30 mol) was added dropwise to sodium tungstate dihydrate (7 mol%), and this mixture was then added to a stirred solution of the appropriately substituted 2-allyl-*N*-(1-naphthylmethyl)aniline (0.10 mol) in methanol (20 ml). The resulting mixtures were then stirred at ambient temperature for 72 h. Each mixture was filtered and the solvent removed under reduced pressure. Toluene (25 ml) was added to the organic residue and the resulting solution was heated at 333 K for periods ranging from 6 to 24 h. After cooling 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 as eluent (compositions ranged from 40:1 to 15:1 v/v). Crystallization from heptane gave colourless crystals of (I)–(IV) suitable for single-crystal X-ray diffraction. Analysis for (I): m.p. 402–403 K, yield 67%; MS (70 eV) m/z (%): 287 (M^+, 61), 270 (38), 258 (18), 244 (22), 154 (100), 153 (80), 127 (18), 105 (38), 104 (55). Analysis for (II): m.p. 463–464 K, yield 65%; MS (70 eV) m/z (%): 301 (M^+, 56), 284 (25), 272 (16), 258 (16), 154 (60), 153 (64), 127 (16), 119 (81), 118 (100). Analysis for (III): m.p. 397–398 K, yield 70%; MS (70 eV) m/z (%): 371 (M^+, 24), 354 (14), 342 (7), 328 (7), 189 (33), 188 (51), 154 (100), 153 (70), 127 (14). Analysis for (IV): m.p. 453–454 K, yield 63%; MS (70 eV) m/z (%): 335 (M^+, ^{35}Cl, 13), 318 (7), 306 (3), 292 (3), 154 (100), 153 (64), 152 (25), 127 (11).

Compound (I)

Crystal data

$C_{20}H_{17}NO$	$V = 1457.7$ (9) Å^3
$M_r = 287.35$	$Z = 4$
Monoclinic, $P2_1$	Mo $K\alpha$ radiation
$a = 8.974$ (4) Å	$\mu = 0.08$ mm^{-1}
$b = 7.1817$ (8) Å	$T = 120$ K
$c = 22.718$ (9) Å	$0.38 \times 0.21 \times 0.14$ mm
$\beta = 95.39$ (3)°	

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.961$, $T_{max} = 0.989$

20821 measured reflections
3589 independent reflections
3064 reflections with $I > 2\sigma(I)$
$R_{int} = 0.051$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.046$
$wR(F^2) = 0.099$
$S = 1.14$
3589 reflections
397 parameters

1 restraint
H-atom parameters constrained
$\Delta\rho_{max} = 0.23$ e Å^{-3}
$\Delta\rho_{min} = -0.28$ e Å^{-3}

Table 1
Selected conformational parameters for (I)–(V).

Puckering parameters for five-membered rings are defined for the atom sequence Ox14−Nx1−Cx2−Cx3−Cx4, and those for six-membered rings are defined by the atom sequence Ox14−Nx1−Cx9a−Cx5a−Cx5−Cx4.

Ring-puckering parameters (Å, °)

| | Five-membered ring | | Six-membered ring | | |
	Q_2	φ_2	Q	θ	φ
(I), molecule 1	0.449 (3)	194.0 (4)	0.632 (2)	56.1 (3)	347.7 (3)
(I), molecule 2	0.438 (3)	197.0 (4)	0.622 (3)	52.5 (3)	344.5 (3)
(II)	0.449 (2)	199.1 (3)	0.615 (2)	51.4 (2)	346.1 (3)
(III)	0.449 (2)	200.9 (3)	0.643 (2)	55.1 (3)	343.6 (3)
(IV)	0.434 (2)	199.9 (3)	0.628 (2)	52.4 (2)	341.0 (3)
(V)	0.440 (3)	188.7 (4)	0.630 (3)	54.7 (3)	347.5 (4)

Torsion angles (°) Nx1−Cx2−Cx21−Cx22

(I)	$x = 1$	−9.4 (3)
(I)	$x = 2$	−10.9 (4)
(II)	$x =$ nul	−99.7 (3)
(III)	$x =$ nul	−10.7 (3)
(IV)	$x =$ nul	−19.3 (3)
(V)†	$x =$ nul	−5.9 (4)

† Data for (V) are taken from Gómez *et al.* (2008).

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

Cg1 represents the centroid of the C15a/C16–C19/C19a ring, Cg2 that of the C25a/C26–C29/C29a ring, Cg3 that of the C121–C125/C130 ring, Cg4 that of the C221–C225/C230 ring, Cg5 that of the C5a/C6–C9/C9a ring, Cg6 that of the C25–C210 ring and Cg7 that of the C21–C25/C210 ring.

Compound	$D−H\cdots A$	$D−H$	$H\cdots A$	$D\cdots A$	$D−H\cdots A$
(I)	C14−H14$\cdots$O114^i	1.00	2.58	3.411 (4)	140
	C24−H24$\cdots$O214^{ii}	1.00	2.48	3.263 (4)	135
	C16−H16$\cdots Cg$1^{iii}	0.95	2.96	3.736 (3)	139
	C26−H26$\cdots Cg$2^{iv}	0.95	2.61	3.550 (3)	170
	C18−H18$\cdots Cg$3^{v}	0.95	2.61	3.553 (3)	170
	C28−H28$\cdots Cg$4^{vi}	0.95	2.72	3.634 (4)	163
(II)	C3−H3$A\cdots$O14^{vii}	0.99	2.59	3.552 (3)	164
	C22−H22$\cdots$N1^{vii}	0.95	2.54	3.316 (3)	139
	C2−H2$\cdots Cg$5^{viii}	1.00	2.81	3.558 (3)	132
	C4−H4$\cdots Cg$6^{vii}	1.00	2.71	3.626 (3)	153
(III)	C24−H24$\cdots Cg$5^{ix}	0.95	2.74	3.539 (3)	143
(IV)	C6−H6$\cdots Cg$7^{x}	0.95	2.75	3.522 (2)	139
	C27−H27$\cdots Cg$5^{xi}	0.95	2.57	3.432 (3)	151

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

Compound (II)

Crystal data

$C_{21}H_{19}NO$
$M_r = 301.37$
Monoclinic, $P2_1/c$
$a = 10.7760$ (13) Å
$b = 8.9612$ (11) Å
$c = 15.4241$ (15) Å
$\beta = 96.799$ (10)°

$V = 1479.0$ (3) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.08$ mm^{-1}
$T = 120$ K
$0.30 \times 0.28 \times 0.24$ mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.965$, $T_{max} = 0.980$

19719 measured reflections
2744 independent reflections
1737 reflections with $I > 2\sigma(I)$
$R_{int} = 0.067$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.059$
$wR(F^2) = 0.167$
$S = 1.09$
2744 reflections

209 parameters
H-atom parameters constrained
$\Delta\rho_{max} = 0.30$ e Å^{-3}
$\Delta\rho_{min} = -0.31$ e Å^{-3}

Compound (III)

Crystal data

$C_{21}H_{16}F_3NO_2$
$M_r = 371.35$
Orthorhombic, $P2_12_12_1$
$a = 7.2209$ (5) Å
$b = 13.140$ (2) Å
$c = 17.559$ (2) Å

$V = 1666.0$ (3) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.12$ mm^{-1}
$T = 120$ K
$0.21 \times 0.20 \times 0.14$ mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.957$, $T_{max} = 0.984$

20342 measured reflections
2193 independent reflections
1899 reflections with $I > 2\sigma(I)$
$R_{int} = 0.038$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.086$
$S = 1.18$
2193 reflections

244 parameters
H-atom parameters constrained
$\Delta\rho_{max} = 0.18$ e Å^{-3}
$\Delta\rho_{min} = -0.25$ e Å^{-3}

Compound (IV)

Crystal data

$C_{21}H_{18}ClNO$
$M_r = 335.81$
Orthorhombic, $P2_12_12_1$
$a = 7.4394$ (7) Å
$b = 14.498$ (3) Å
$c = 15.136$ (3) Å

$V = 1632.5$ (5) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.24$ mm^{-1}
$T = 120$ K
$0.24 \times 0.17 \times 0.16$ mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.935$, $T_{max} = 0.963$

16529 measured reflections
3731 independent reflections
3028 reflections with $I > 2\sigma(I)$
$R_{int} = 0.046$

organic compounds

All H atoms were located in difference maps and then treated as riding atoms in geometrically idealized positions, with C—H = 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, which were permitted to rotate but not to tilt, and 1.2 for all other H atoms. Compound (IV) crystallized as a single enantiomorph in the space group $P2_12_12_1$ and, for the crystal selected for data collection, the (2S,4R) configuration was established by means of the Flack x parameter (Flack, 1983) of 0.02 (7) and the Hooft y parameter (Hooft *et al.*, 2008) of 0.01 (3), calculated for 1581 Bijvoet pairs (99% coverage). Compound (II) crystallized as a racemic mixture in the centrosymmetric space group $P2_1/c$ and the reference molecule was selected as one having the (2S,4R) configuration, to be consistent with (IV). In the absence of significant resonant scattering for (I) and (III), Friedel-equivalent reflections were merged prior to the final refinements, and again the reference molecules were specified as having the (2S,4R) configuration. The two independent molecules of (I) have the same configuration.

For all compounds, data collection: *COLLECT* (Nonius, 1999); cell refinement: *DIRAX/LSQ* (Duisenberg *et al.*, 2000); data reduction: *EVALCCD* (Duisenberg *et al.*, 2003); program(s) used to solve structure: *SIR2004* (Burla *et al.*, 2005); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PLATON*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG3246). Services for accessing these data are described at the back of the journal.

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