

A three-dimensional hydrogen-bonded framework in (2*S**,4*R**)-7-fluoro-2-*exo*-[(*E*)-styryl]-2,3,4,5-tetrahydro-1*H*-1,4-epoxy-1-benzazepine

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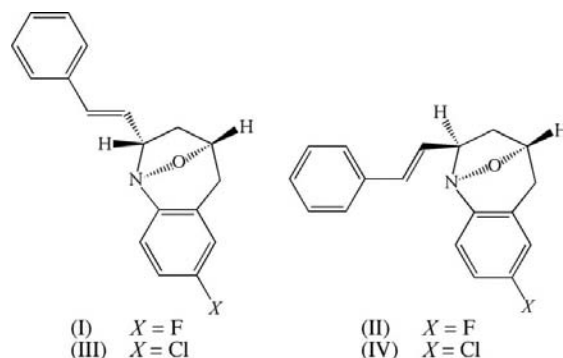
Molecules of the title compound, C₁₈H₁₆FNO, are linked into a three-dimensional framework structure by a combination of two C—H···O hydrogen bonds and three C—H···π(arene) hydrogen bonds. Comparisons are made with the (2*R*,4*R*) diastereoisomer and with the corresponding pair of diastereoisomeric 7-chloro analogues.

Comment

We report here the structure of the title compound, (I) (Fig. 1), and we compare its intermolecular hydrogen bonding with that in the (2*R*,4*R*) diastereoisomer, (II), and then we compare the diastereoisomeric pair, (I) and (II), with their 7-chloro analogues, (III) and (IV) (Acosta *et al.*, 2008). Both members of the diastereoisomeric pair, (I) and (II), crystallize as a single enantiomer in the space group *P*2₁. The absolute configurations could not be established and so for both compounds the configuration at C4 was arbitrarily set to be *R* for the crystals selected for data collection. By contrast, the 7-chloro analogues, (III) and (IV), both crystallize as racemic twins in the space groups *P*2₁ and *P*2₁2₁2₁, respectively (Acosta *et al.*, 2008). In view of the crystallization behaviour of (III) and (IV) and the absence from the synthetic procedure of any reagent capable of imparting enantioselective bias, it seems probable that all of these compounds, including (I), are in fact initially formed as racemic mixtures. On the other hand, if this is so, it is not at all easy to see why the 7-fluoro compounds (I) and (II) both crystallize as conglomerates, while their 7-chloro analogues (III) and (IV) both crystallize as racemic twins.

In the crystal structure of (I), there are two C—H···O hydrogen bonds (Table 1). The shorter of these, involving

atom C4 as the donor, links molecules related by the 2₁ screw axis along ($\frac{1}{2}$, y , $\frac{1}{2}$) into a *C*(3) chain (Bernstein *et al.*, 1995) running parallel to the [010] direction. This chain formation is augmented by the second, longer, hydrogen bond, which links molecules related by translation along [010] into a *C*(4) chain, while the combination of the two hydrogen bonds generates a chain of edge-fused *R*₃²(8) rings (Fig. 2).



In addition to the C—H···O hydrogen bonds there are also three C—H···π(arene) hydrogen bonds. All of these are fairly long, but they combine with the C—H···O hydrogen bonds to generate a three-dimensional hydrogen-bonded framework of considerable complexity. The formation of the framework can, however, be readily analysed in terms of two further one-dimensional substructures in addition to that formed by the two C—H···O hydrogen bonds. In the second and most complex substructure, atoms H4 and H6 in the molecule at (*x*, *y*, *z*) act as hydrogen-bond donors to, respectively, atom O14 in the molecule at ($1 - x$, $\frac{1}{2} + y$, $1 - z$) and the fused aryl ring in the molecule at ($2 - x$, $\frac{1}{2} + y$, $1 - z$). In addition, atom C8 at (*x*, *y*, *z*) acts as donor to the pendent C221–C226 aryl ring in

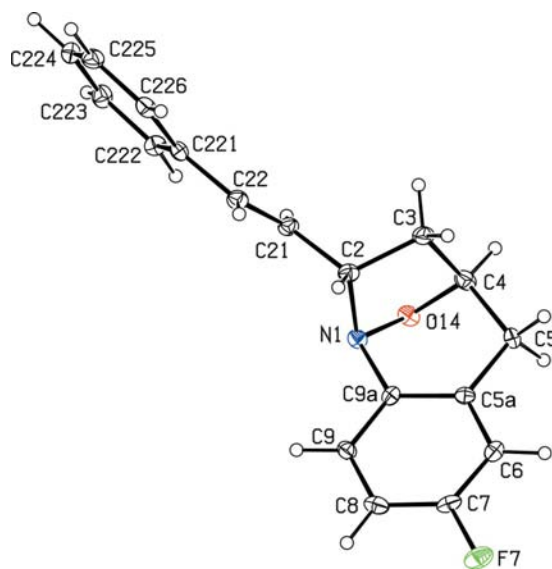
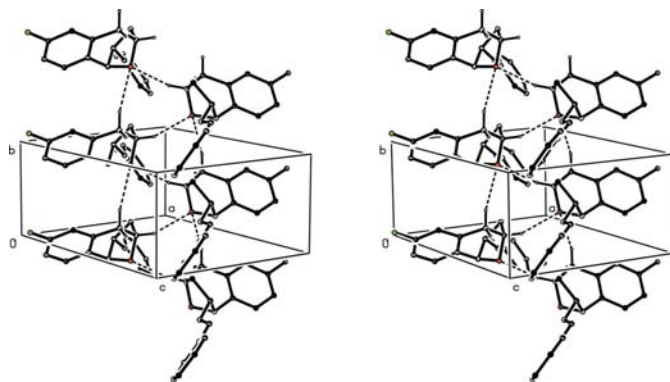


Figure 1

The molecular structure of the (2*S*,4*R*) enantiomer of (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.

**Figure 2**

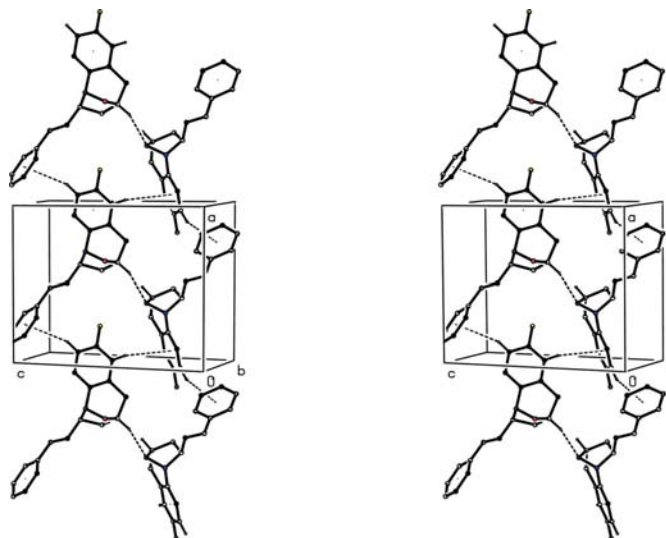
A stereoview of part of the crystal structure of (I), showing the formation of a $C(3)C(4)[R_3^2(8)]$ chain of rings along [010] built from two independent $C-H\cdots O$ hydrogen bonds. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

the molecule at $(1+x, y, z)$. The combination of these three hydrogen bonds then generates a chain of edge-fused rings running parallel to the [100] direction and containing two distinct types of hydrogen-bonded ring (Fig. 3). For the final substructure, atoms C4 and C22 in the molecule at (x, y, z) act as hydrogen-bond donors to, respectively, atom O14 in the molecule at $(1-x, \frac{1}{2}+y, 1-z)$ and the pendent aryl ring in the molecule at $(1-x, \frac{1}{2}+y, 2-z)$, so forming a chain running parallel to the [001] direction and built from alternating $C-H\cdots O$ and $C-H\cdots\pi(\text{arene})$ hydrogen bonds and in which alternate molecules act as double donors of hydrogen bonds and as double acceptors (Fig. 4). The combination of this simple chain along [001] with the chains of rings along [100] and [010] suffices to generate a continuous three-dimensional structure.

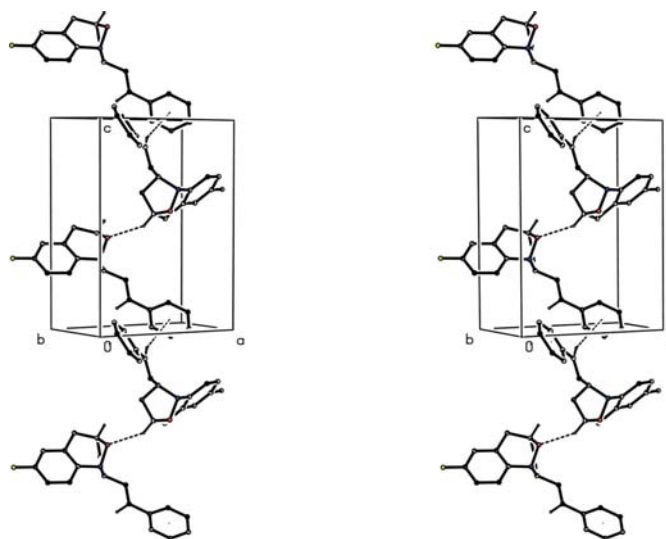
The complexity of the hydrogen bonding in (I) is in sharp contrast with the simplicity observed in the structure of its diastereoisomer, (II), where just a single $C-H\cdots O$ hydrogen bond links molecules related by translation into simple $C(4)$ chains (Acosta *et al.*, 2008). In addition, $C-H\cdots\pi(\text{arene})$ interactions are absent from the structure of (II). Moreover, the chains in (II) run parallel to the [100] direction in the space group $P2_1$, whereas in (I), also in the space group $P2_1$, the $C(4)$ motif is generated by translation along the [010] direction.

The hydrogen-bonded structures of the diastereoisomeric pair (III) and (IV) are also sharply different (Acosta *et al.*, 2008). In (III), a combination of $C-H\cdots O$ and $C-H\cdots N$ hydrogen bonds links the molecules into a chain of $R_3^2(9)$ rings, similar to that in (I), but $C-H\cdots\pi(\text{arene})$ hydrogen bonds are absent from the structure of (III). In (IV), which unlike (I)–(III) crystallizes in the space group $P2_12_12_1$, the molecules are linked into complex chains by a combination of a two-centre $C-H\cdots N$ hydrogen bond and a three-centre $C-H\cdots(O,N)$ hydrogen bond, but again $C-H\cdots\pi(\text{arene})$ hydrogen bonds are absent from this structure.

Compounds (I) and (III) have similar unit-cell dimensions, except for the unit-cell vector a , where the value in (III) exceeds that in (I) by ca 0.53 Å, or some 5.2%. In contrast, the b and c values in (I) and (III) each differ by less than 1%, and

**Figure 3**

A stereoview of part of the crystal structure of (I), showing the formation of a chain of edge-fused rings along [100] built from two independent $C-H\cdots\pi(\text{arene})$ hydrogen bonds and one $C-H\cdots O$ hydrogen bond. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

**Figure 4**

A stereoview of part of the crystal structure of (I), showing the formation of a chain along [001] built from alternating $C-H\cdots\pi(\text{arene})$ and $C-H\cdots O$ hydrogen bonds. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

the β angles also differ by less than 1° . Thus, the difference of ca 5.3% in the unit-cell volumes is almost entirely accounted for by the difference in the a repeat vectors. Thus, compounds (I) and (III) are approximately isomorphous but they are not isostructural, firstly because (III) crystallizes as a racemic twin while (I) does not, and secondly because there are no $C-H\cdots\pi(\text{arene})$ hydrogen bonds in the structure of (III). In addition to the different values of the a repeat vector, a detailed comparison of the atomic coordinates for (I) and (III) shows some significant differences, particularly for the C and

H atoms involved in the C—H... π (arene) hydrogen bonds in (I).

The bond distances and angles in (I) present no unusual values. The ring-puckering angles (Cremer & Pople, 1975) indicate that both of the heterocyclic rings adopt conformations intermediate between envelope and half-chair forms.

Experimental

To a stirred solution of 2-allyl-*N*-cinnamyl-4-fluoroaniline (0.10 mol) in methanol (40 ml) was added sodium tungstate dihydrate, Na₂WO₄·2H₂O (5 mol%), followed by 30% aqueous hydrogen peroxide solution (0.30 mol). The resulting mixture was then stirred at ambient temperature for 8 h, filtered, and the solvent removed under reduced pressure. Toluene (50 ml) was added to the solid residue and the resulting solution was heated under reflux for 6 h. After cooling the solution to ambient temperature, the solvent was removed under reduced pressure and the crude product was purified by chromatography on silica using heptane–ethyl acetate as eluant (composition gradient 90:1 to 10:1 *v/v*). Crystallization from heptane gave colourless crystals of the title compound, (I), suitable for single-crystal X-ray diffraction (yield 52%, m.p. 423–424 K). MS (70 eV) *m/z* (%): 281 (*M*⁺, 67), 264 (33), 251 (21), 148 (41), 122 (100), 96 (33).

Crystal data

C ₁₈ H ₁₆ FNO	<i>V</i> = 691.1 (7) Å ³
<i>M_r</i> = 281.32	<i>Z</i> = 2
Monoclinic, <i>P</i> 2 ₁	Mo <i>K</i> α radiation
<i>a</i> = 10.052 (4) Å	μ = 0.09 mm ⁻¹
<i>b</i> = 5.299 (4) Å	<i>T</i> = 120 K
<i>c</i> = 12.976 (8) Å	0.36 × 0.08 × 0.06 mm
β = 91.10 (4)°	

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer	9381 measured reflections
Absorption correction: multi-scan (SADABS; Sheldrick, 2003)	1432 independent reflections
<i>T</i> _{min} = 0.956, <i>T</i> _{max} = 0.995	1112 reflections with <i>I</i> > 2σ(<i>I</i>)
	<i>R</i> _{int} = 0.081

Refinement

<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)] = 0.049	1 restraint
<i>wR</i> (<i>F</i> ²) = 0.107	H-atom parameters constrained
<i>S</i> = 1.12	$\Delta\rho_{\max}$ = 0.23 e Å ⁻³
1432 reflections	$\Delta\rho_{\min}$ = -0.24 e Å ⁻³
190 parameters	

All H atoms were located in difference maps and then treated as riding atoms in geometrically idealized positions, with C—H = 0.95 (aromatic), 0.99 (CH₂) or 1.00 Å (aliphatic CH) and with *U*_{iso}(H) = 1.2*U*_{eq}(C). The *y* coordinate for atom N1 was set to have precisely the same value as for the corresponding atom in compound (III) in order to ease comparison of the two sets of atomic coordinates. In the absence of significant resonant scattering, the Flack *x* parameter (Flack, 1983) was indeterminate (Flack & Bernardinelli, 2000), likewise the Hooft *y* parameter (Hooft *et al.*, 2008). Accordingly, the Friedel-equivalent reflections were merged prior to the final refinement. The configuration at atom C4 in the reference molecule of (I) was set to be *R*, for consistency both with compounds (II)–(IV) (Acosta *et al.*, 2008), and with several related compounds (Blanco *et al.*, 2008; Gómez *et al.*, 2008, 2009) crystallizing as single enantiomorphs, where the configurations at C4 were deduced on the basis of the Flack *x* and the Hooft *y* parameters to be *R* in every case; on this

Table 1

Hydrogen-bond geometry (Å, °).

Cg1 represents the centroid of the C5a/C6–C9/C9a ring and Cg2 represents the centroid of the C221–C226 ring.

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
C4—H4...O14 ⁱ	1.00	2.39	3.278 (5)	148
C5—H5B...O14 ⁱⁱ	0.99	2.57	3.504 (6)	157
C6—H6...Cg1 ⁱⁱⁱ	0.95	2.98	3.815 (5)	147
C8—H8...Cg2 ^{iv}	0.95	2.97	3.860 (5)	158
C22—H22...Cg2 ^v	0.95	3.00	3.896 (5)	158

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

basis the configuration for atom C2 in the reference molecule of (I) is *S*.

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.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG3231). Services for accessing these data are described at the back of the journal.

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