organic compounds

Imino Diels–Alder adducts. I. Two furo[3,2-c]quinoline diastereoisomers

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The structures of two diastereoisomers of 9-chloro-8-fluoro-4-phenyl-2,3,3a,4,5,9b-hexahydrofuro[3,2-c]quinoline, $C_{17}H_{15}ClFNO$, are very similar. The orientation of the furan ring, as a result of its fusion to the quinoline nucleus, constitutes the significant difference between the two structures. The dihedral angles between the furan and phenyl rings are 73.4 (1) and 63.8 (1)°.

Comment

Pyrano- and furoquinoline moieties have been extensively studied for a range of biological applications, such as psychotropic (Nesterova *et al.*, 1995), anti-allergic (Yamada *et al.*, 1992) and anti-inflammatory (Faber *et al.*, 1984) applications. Hence, efforts have been directed towards the synthesis of these compounds. We have recently synthesized and purified four diastereoisomers of disubstituted pyrano- and furoquinolines by the application of the imino Diels–Alder reaction using $ZrCl_4$ as a new catalyst (Mahesh *et al.*, 2004). These diastereoisomers differ according to the stereochemistry (*cis/trans*) of the ring-junction H atoms and the orientation (*endo/exo*) of the furan ring. The contrasting responses of the different isomers to bactericidal and bacteriolytic activity prompted us to carry out crystal structure determinations, with a view to understanding the structure–activity relationships. We present here the structures of two diastereoisomers of 9-chloro-8-fluoro-4-phenyl-2,3,3a,4,5,9b-hexahydrofuro[3,2-c]quinoline, denoted (I) (Fig. 1) and (II) (Fig. 2).

In all essential details, the structures of the two diastereoisomers are similar as far as bond distances and angles are concerned (Tables 1 and 3). The greatest differences are 0.018 Å in the bond distances (for C2—C1) and 3.3° in the angles (for O1—C5—C6). Atoms H7 and H8 have a *trans* arrangement in (I); the H7—C7—C8—H8 torsion angle of −176.9° is in accordance with a larger coupling constant (J = 10.8 Hz). In contrast, the other stereoisomer, (II), with a corresponding torsion angle of 55.3°, shows a coupling constant J = 5.2 Hz and is in a *cis* configuration.

The chloro- and fluoro-substituted benzene ring of the quinoline ring system is planar, with deviations of 0.047 (1) and −0.018 (1) Å for (I) and (II), respectively. The non-planar pyridine ring adopts a sofa conformation in both structures, with asymmetry parameters (Nardelli, 1983) of $\Delta C_S(C3)$ = 0.053 (1) and $\Delta C_2(C3-C9)$ = 0.069 (1) in (I), and $\Delta C_S(C3)$ = 0.057 (1) and $\Delta C_2(C4-C3)$ = 0.088 (1) in (II).
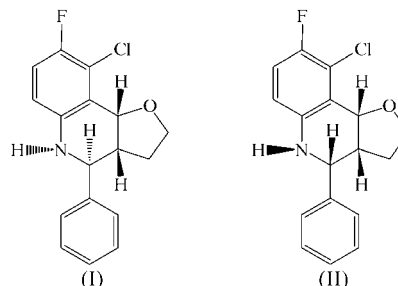
The most significant distinctive pattern in both structures is the perpendicular orientation of the furan ring (Fig. 3). This is oriented above the least-squares plane (N1/C9/C3/C4/C7) of the quinoline ring system in (I), with atom O1 displaced by 1.325 (2) Å, and below the plane in (II), with atom O1 displaced by −1.394 (2) Å. The C6—C7—C8—C12 torsion angle, between the furan and benzene rings, shows the role of ring fusion, with a value of −68.8 (2)° in (I) and 58.1 (2)° in (II).

The furan ring adopts a distorted envelope conformation in (I) [q_2 = 0.341 (2) Å and φ = 171.9 (5)°] and a twist conformation in (II) [q_2 = 0.345 (2) Å and φ = 92.3 (2)°] (Cremer & Pople, 1975).

The phenyl substituent at C8 is rotated through the C8—C12 bond by −134.6 (2)° in (I) and 32.8 (2)° in (II), perhaps to facilitate the *cis/trans* orientation of the H atoms at C8. A non-bonded interaction between atoms H17 and H8 of 2.36 Å is observed in (II), while this distance is 3.58 Å in (I).
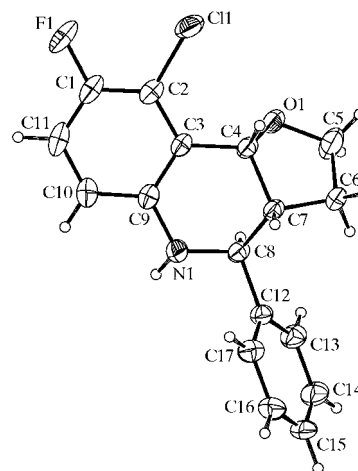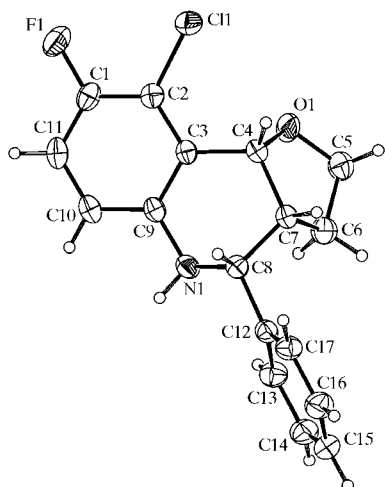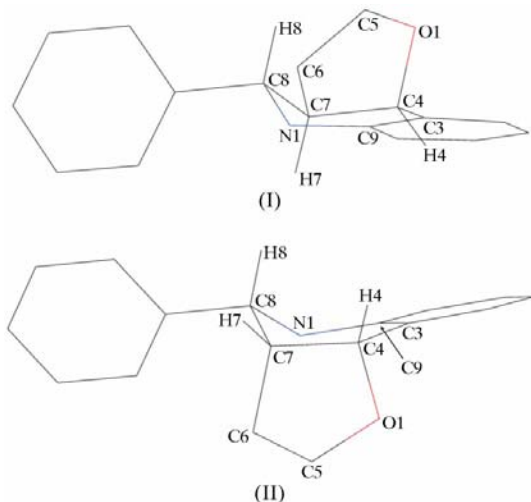

Figure 1
A view of the molecule of (I), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. The molecule shown is the inverse of the molecule in the asymmetric unit.

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Figure 2
A view of the molecule of (II), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

Figure 3
The orientational difference in the furan ring between the structures of (I) and (II) visualized through the least-squares plane fitting atoms N1/C9/C3/C4/C7.

The crystal structure is stabilized by a C—H···F intermolecular interaction in (I) (Table 2), whereas no such interaction is observed in (II). Furthermore, symmetry-related molecules are interlinked by weak C—H···π interactions in both compounds. In (I), atom H11 is 2.87 Å from the centroid of the phenyl substituent (C12–C17) at symmetry position ($\frac{1}{2} + x$, $\frac{1}{2} + y$, z), with an angle of 159° and a C11···centroid distance of 3.752 (3) Å. Similarly in (II), atom H11 is 2.86 Å from the centroid of the phenyl substituent at symmetry position ($2 - x$, $1 - y$, $1 - z$), with an angle of 133° and a C11···centroid distance of 3.561 (2) Å.

Experimental

To a solution of N-benzylidene-3-chloro-4-fluoroaniline (5.5 mmol) in dichloromethane (5 ml) at room temperature were added 2,3-dihydrofuran (5.5 mmol) and $ZrCl_4$ (10 mol%), and the resulting

solution was stirred for 90 min. The reaction was quenched with water and the crude product was purified by column chromatography using an ethyl acetate–hexane mixture as eluant to yield the title compound. Crystals for X-ray study were obtained by recystallization from a mixture of methanol and water (3:1).

Compound (I)

Crystal data

$C_{17}H_{15}ClFNO$	Mo $K\alpha$ radiation
$M_r = 303.75$	Cell parameters from 448
Monoclinic, $C2/c$	reflections
$a = 17.0056 (17)$ Å	$\theta = 2.2–27.5°$
$b = 10.7527 (11)$ Å	$\mu = 0.28$ mm^{-1}
$c = 15.7079 (16)$ Å	$T = 293 (2)$ K
$\beta = 99.367 (2)°$	Needle, yellow
$V = 2834.0 (5)$ Å^3	$0.20 \times 0.15 \times 0.11$ mm
$Z = 8$	
$D_x = 1.424$ Mg m^{-3}	

Data collection

Bruker SMART APEX CCD area-detector diffractometer	$R_{int} = 0.025$
	$\theta_{max} = 28.0°$
ω scans	$h = -22 \rightarrow 21$
8450 measured reflections	$k = -14 \rightarrow 13$
3079 independent reflections	$l = -18 \rightarrow 20$
2244 reflections with $I > 2\sigma(I)$	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0731P)^2$
$R[F^2 > 2\sigma(F^2)] = 0.053$	$+ 1.4718P]$
$wR(F^2) = 0.147$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 1.03$	$(\Delta/\sigma)_{max} < 0.001$
3079 reflections	$\Delta\rho_{max} = 0.30$ e Å^{-3}
190 parameters	$\Delta\rho_{min} = -0.19$ e Å^{-3}
H-atom parameters constrained	

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

C1—C2	1.363 (3)	C4—C7	1.531 (3)
O1—C5—C6	109.1 (2)		
C6—C7—C8—C12	−68.8 (2)		

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

D—H···A	D—H	H···A	D···A	D—H···A
C6—H6B···F1^i	0.97	2.47	3.108 (2)	123
C17—H17···F1^{ii}	0.93	2.55	3.460 (3)	167

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

Compound (II)

Crystal data

$C_{17}H_{15}ClFNO$	$D_x = 1.427$ Mg m^{-3}
$M_r = 303.75$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 6613
$a = 8.1796 (6)$ Å	reflections
$b = 17.9041 (12)$ Å	$\theta = 2.3–27.8°$
$c = 9.6562 (7)$ Å	$\mu = 0.28$ mm^{-1}
$\beta = 91.0170 (10)°$	$T = 293 (2)$ K
$V = 1413.91 (17)$ Å^3	Needle, colourless
$Z = 4$	$0.18 \times 0.15 \times 0.13$ mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
ω scans
16 081 measured reflections
3334 independent reflections
2940 reflections with $I > 2\sigma(I)$

$R_{int} = 0.020$
$\theta_{max} = 28.0°$
$h = -10 \rightarrow 10$
$k = -23 \rightarrow 23$
$l = -12 \rightarrow 12$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.050$
$wR(F^2) = 0.136$
$S = 1.08$
3334 reflections
190 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0746P)^2 + 0.326P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.34$ e Å^{-3}
$\Delta\rho_{min} = -0.19$ e Å^{-3}

Table 3
Selected geometric parameters (Å, °) for (II).

C1—C2	1.381 (2)	C4—C7	1.546 (2)
O1—C5—C6	105.8 (2)		
C6—C7—C8—C12	58.1 (2)		

All H atoms were positioned geometrically and treated as riding on their parent atoms, with aromatic C—H = 0.93 Å, methylene C—H = 0.98 Å, ethylene C—H = 0.97 Å and N—H = 0.90 Å, and with $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl and $1.2U_{eq}(C,N)$ for other H atoms.

For both isomers, data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1995).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1768). Services for accessing these data are described at the back of the journal.

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