

Imino Diels–Alder adducts. II. Two
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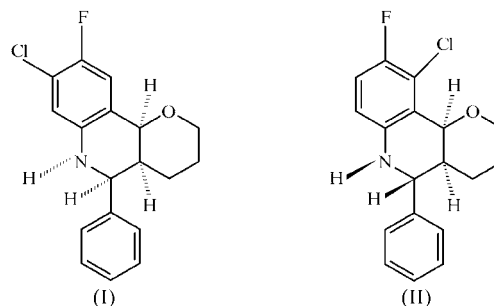
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8-Chloro-9-fluoro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline and 10-chloro-9-fluoro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2*H*-pyrano[3,2-*c*]quinoline, both C₁₈H₁₇ClFNO, are diastereoisomers, formed as the result of the imino Diels–Alder reactions of *N*-benzylideneanilines with 3,4-dihydro-2*H*-pyran. The crystal structures reveal the stereochemistry of the pyran ring, which is *endo*/*exo* to the quinoline ring system formed in the cycloaddition step. In both structures, the pyran ring adopts a chair conformation, while the nitrogen-containing heterocyclic ring prefers a half-chair conformation. The structures differ essentially in the relative orientation of the ring junction H atoms.

Comment

The pyranoquinoline moiety is commonly found in many alkaloids, *e.g.* findersine, oricine and verprisine, and derivatives of these alkaloids possess a significant range of biological activities, such as anti-allergic, psychotropic and anti-inflammatory (Yamada *et al.*, 1992; Faber *et al.*, 1984; Nesterova *et al.*, 1995). In addition, pyranoquinoline derivatives are used as potential pharmaceuticals (Mohamed, 1994). It is therefore not surprising that efforts are ongoing for the syntheses of these compounds by different methods (Ma *et al.*, 1999; C. J. Mahesh, 2004; M. Mahesh *et al.*, 2004). The Diels–Alder reaction catalysed by Lewis acids between *N*-benzylideneanilines and nucleophilic olefins is one of the powerful synthetic tools for constructing nitrogen-containing six-membered heterocyclic compounds. In this context, we have been examining a variety of conditions to achieve different product distributions. Recently, we described the synthesis and characterization of disubstituted pyrano- and furanoquinolines by application of the imino Diels–Alder reaction using ZrCl₄ as a potential green catalyst (M. Mahesh *et al.*, 2004). The individual diastereoisomers thus obtained differ according to the stereochemistry (*cis/trans*) of the ring junction H atoms and the orientation (*endo/exo*) of the pyran ring.

To elucidate the reaction stereochemistry and the molecular geometry of the structures, we have undertaken structural investigations of the title compounds, (I) and (II).



Both (I) and (II) crystallize in space group $P\bar{1}$, with two independent molecules in the asymmetric unit. The asymmetric unit of (I) was chosen to contain two molecules with *SSS* chirality (at the C5, C6, C10 and C5', C6', C10' atoms); the other half of the unit cell then contains pairs of molecules with *RRR* chirality. Similarly, in (II) the asymmetric unit was chosen to have two molecules of *RSS* chirality, and the other half of the unit cell has two molecules of *SRR* chirality. In both compounds, the geometries of the two independent molecules are very similar (Tables 1 and 3), the greatest differences being 0.008 [N1–C4 in (I)] and 0.030 Å [C16–C17 in (II)], and 1.8 [C4–N1–C5 in (I)] and 1.3° [C16–C17–C18 in (II)].

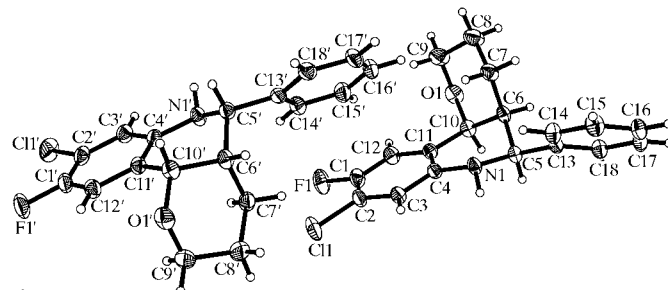


Figure 1
A view of the molecule of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

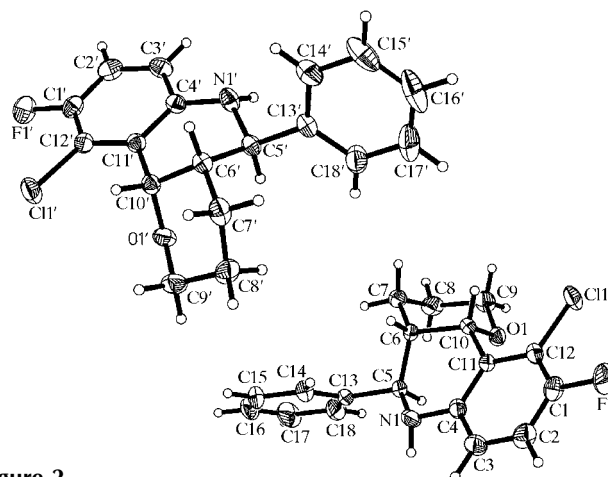


Figure 2
A view of the molecule of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

The geometric parameters of the two structures (Figs. 1 and 2) are not very different from the values found in the literature for other quinoline derivatives. More relevant differences between the structures are observed in the torsion angles as a result of both the different configuration at the C6 ring junction and the different packing of the crystals. One significant difference is the orientation of atoms H5 and H6. The H5—C5—C6—H6 torsion angles [-62.8 and -61.4° in (I)] indicate a *cis* arrangement and are in accordance with the coupling constant $J = 5.2$ Hz. Consequently, the structure of (II), with corresponding torsion angles of -173.5 and -173.8° , and a larger coupling constant, $J = 10.8$ Hz, has a *trans* configuration.

In both structures, the substituents on the quinoline ring system produce a considerable twist about the C5...C11 vector. The twist can be seen from the C5—C6—C10—C11 [48.5 (2) and 51.1 (2) $^\circ$ in (I), and -51.0 (3) and -51.0 (3) $^\circ$ in (II)] and C5—N1—C4—C11 [-21.7 (3) and -16.4 (3) $^\circ$ in (I), and 14.5 (4) and 13.5 (4) $^\circ$ in (II)] torsion angles. In addition, these values indicate the fusion strain exerted during ring formation in the Diels–Alder cycloaddition process.

It is interesting to note that in both structures the pyran ring is almost perpendicular to the quinoline ring system. In (I), atom O1 is displaced below the N1/C4/C11/C10 least-squares plane by 0.744 (2) Å in molecule 1 and above this plane by 0.694 (2) Å in molecule 2. Similarly, the corresponding displacements of atoms O1 in (II) are -1.335 (2) and -1.335 (2) Å. The relative configuration/orientation of the quinoline ring system and the pyran ring can be seen from the C5—C6—C10—O1 torsion angle [values of 175.4 (2) and 177.7 (2) $^\circ$ imply *trans* (*exo*) for (I), and 69.6 (3) and 69.7 (3) $^\circ$ imply *cis* (*endo*) for (II)].

The most appropriate puckering description for the pyridine ring is half-chair in both structures, with asymmetry parameters (Nardelli, 1983) $\Delta C_2(C4—C11)$ of 0.005 (1) and 0.043 (1) in (I), and 0.034 (1) and 0.038 (1) in (II). The conformation of the pyran ring in both structures is a chair, as expected, with atoms C6, C8, C9 and C10 defining the plane,

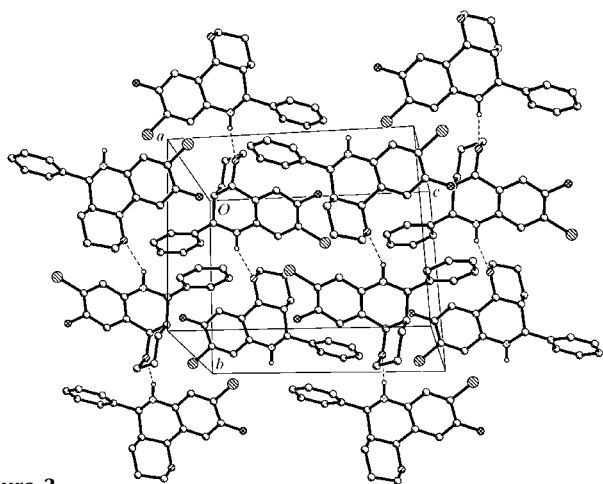


Figure 3
A packing diagram for (I), highlighting N—H...O intermolecular hydrogen bonds (dashed lines) forming molecular columns along the *a* axis. H atoms not involved in the interactions shown have been omitted for clarity.

atoms C7 being displaced by 0.626 (3) and -0.637 (2) Å in (I), and by 0.621 (3) and 0.622 (3) Å in (II), and atoms O1 being displaced by 0.592 (2) and 0.602 (2) Å in (I), and by -0.679 (2) and -0.670 (2) Å in (II). The phenyl ring substituted at atom C5 is rotated through the C5—C13 bond, the N1—C5—C13—C14 torsion angles being -21.8 (3) and -23.9 (3) $^\circ$ in (I), and 50.4 (4) and 53.6 (4) $^\circ$ in (II), perhaps to facilitate the *cis/trans* orientation of the H atoms at C5. The dihedral angles between the planes of the halogen-substituted benzene rings and the C5-phenyl rings are 44.5 (1) and 44.6 (1) $^\circ$ in (I), and 68.4 (1) and 71.0 (1) $^\circ$ in (II).

A striking feature is observed in the crystal packing of the two compounds. Interestingly, C—H...A contacts ($A = \text{Cl, F, O and N}$) are listed in Tables 2 and 4. In (I), the N atom of the quinoline ring system is involved in intermolecular hydrogen-bond formation with the O atom of the pyran ring in both molecules in the asymmetric unit (Fig. 3). Unusually, in (II), this conventional N—H...O hydrogen bond is not observed, even though good hydrogen-bonding functionalities are present. A similar feature has been noted in the structures of alloxan (Beyer *et al.*, 2001; Coombes *et al.*, 1997) and furoquinoline (Ravikumar *et al.*, 2004). This observation complements the views of Desiraju (2002): ‘hydrogen bonds are ubiquitous, directional and strong, and they do control the crystal packing rather effectively, but in the rarest of cases they can be absent. After all, any way to minimize the free energy of a crystal is a respectable way, and given that crystal structures are being determined in the numbers that they are, even axioms will be bypassed on occasion.’

Experimental

To a solution of the appropriate *N*-benzylideneaniline (5.5 mmol) in dichloromethane (5 ml) at room temperature were added ZrCl_4 (10 mol%) and 3-dihydropyran (5.5 mmol), and the mixture was stirred for 90 min. The completed reaction was quenched with water and the crude product was purified by column chromatography using 2% ethyl acetate and hexane, yielding the title compounds. Crystals suitable for X-ray study were obtained by recrystallization from a mixture of methanol and water (3:1) in each case.

Compound (I)

Crystal data

$\text{C}_{18}\text{H}_{17}\text{ClFNO}$
 $M_r = 317.78$
Triclinic, $P\bar{1}$
 $a = 10.5399$ (7) Å
 $b = 11.2005$ (7) Å
 $c = 13.4950$ (9) Å
 $\alpha = 82.597$ (1) $^\circ$
 $\beta = 83.890$ (1) $^\circ$
 $\gamma = 80.884$ (1) $^\circ$
 $V = 1553.85$ (18) Å³

$Z = 4$
 $D_x = 1.358$ Mg m⁻³
Mo $K\alpha$ radiation
Cell parameters from 4707 reflections
 $\theta = 2.4\text{--}26.2^\circ$
 $\mu = 0.26$ mm⁻¹
 $T = 273$ (2) K
Needle, colourless
 $0.19 \times 0.11 \times 0.09$ mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
 ω scans
15 105 measured reflections
5469 independent reflections
4629 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.026$
 $\theta_{\text{max}} = 25^\circ$
 $h = -12 \rightarrow 12$
 $k = -13 \rightarrow 13$
 $l = -16 \rightarrow 16$

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.053$
 $wR(F^2) = 0.129$
 $S = 1.09$
 5469 reflections
 397 parameters
 H-atom parameters constrained

$$w = 1/[\sigma^2(F_o^2) + (0.0541P)^2 + 0.6549P]$$

where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} = 0.001$
 $\Delta\rho_{\max} = 0.37 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.25 \text{ e } \text{\AA}^{-3}$

Table 1

Selected geometric parameters (\AA , $^\circ$) for (I).

O1—C10	1.426 (3)	O1'—C10'	1.429 (3)
O1—C9	1.432 (3)	O1'—C9'	1.437 (3)
N1—C4	1.386 (3)	N1'—C4'	1.378 (3)
N1—C5	1.460 (3)	N1'—C5'	1.458 (3)
C16—C17	1.371 (4)	C16'—C17'	1.372 (4)
C10—O1—C9	113.90 (17)	C10'—O1'—C9'	113.55 (17)
C4—N1—C5	118.23 (17)	C4'—N1'—C5'	120.02 (18)
C14—C13—C5	123.45 (19)	C14'—C13'—C5'	123.02 (19)
C16—C17—C18	120.1 (2)	C16'—C17'—C18'	120.1 (2)

Table 2

Hydrogen-bond geometry (\AA , $^\circ$) for (I).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N1'—H1A'···O1 ⁱ	0.90	2.55	3.016 (2)	113
N1—H1A···O1 ⁱⁱⁱ	0.90	2.41	3.034 (2)	127
C7—H72···N1	0.97	2.56	2.942 (3)	103
C7'—H72'···N1'	0.97	2.60	2.965 (3)	102
C3—H3···O1 ⁱⁱⁱ	0.93	2.60	3.368 (3)	140
C3'—H3'···O1 ⁱ	0.93	2.57	3.322 (3)	138
C10—H10···F1 ⁱⁱⁱ	0.98	2.55	3.523 (3)	174

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

Compound (II)

Crystal data

$C_{18}H_{17}ClFNO$
 $M_r = 317.78$
 Triclinic, $P\bar{1}$
 $a = 8.3032 (8) \text{ \AA}$
 $b = 10.5190 (11) \text{ \AA}$
 $c = 18.1165 (18) \text{ \AA}$
 $\alpha = 104.234 (2)^\circ$
 $\beta = 92.309 (2)^\circ$
 $\gamma = 91.783 (2)^\circ$
 $V = 1531.1 (3) \text{ \AA}^3$
 $Z = 4$
 $D_x = 1.379 \text{ Mg m}^{-3}$
 Mo $K\alpha$ radiation
 Cell parameters from 5061 reflections
 $\theta = 2.8\text{--}26.4^\circ$
 $\mu = 0.26 \text{ mm}^{-1}$
 $T = 273 (2) \text{ K}$
 Needle, pale yellow
 $0.18 \times 0.10 \times 0.07 \text{ mm}$

Data collection

Bruker SMART APEX CCD area-detector diffractometer
 ω scans
 14 616 measured reflections
 5373 independent reflections
 4502 reflections with $I > 2\sigma(I)$

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.067$
 $wR(F^2) = 0.166$
 $S = 1.16$
 5373 reflections
 397 parameters
 H-atom parameters constrained

$$w = 1/[\sigma^2(F_o^2) + (0.0703P)^2 + 1.0004P]$$

where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} < 0.001$
 $\Delta\rho_{\max} = 0.33 \text{ e } \text{\AA}^{-3}$
 $\Delta\rho_{\min} = -0.26 \text{ e } \text{\AA}^{-3}$

Table 3

Selected interatomic distances (\AA) for (II).

O1—C10	1.430 (3)	O1'—C10'	1.428 (3)
O1—C9	1.436 (4)	O1'—C9'	1.433 (4)
N1—C4	1.392 (4)	N1'—C4'	1.391 (4)
N1—C5	1.459 (4)	N1'—C5'	1.461 (4)
C16—C17	1.374 (7)	C16'—C17'	1.344 (7)

Table 4

Hydrogen-bond geometry (\AA , $^\circ$) for (II).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
C10—H10···C11	0.98	2.71	3.061 (3)	102
C10'—H10'···C11'	0.98	2.70	3.065 (3)	103

H atoms were positioned geometrically and were treated as riding on their parent C atoms, with C—H distances of 0.93 (aromatic), 0.98 (CH) and 0.97 \AA (CH₂), N—H distances of 0.90 \AA , and $U_{\text{iso}}(\text{H})$ values of $1.2U_{\text{eq}}(\text{C}, \text{N})$. The data coverage is 100% of all independent reflections to $2\theta = 50^\circ$ (a d -spacing of 0.841 \AA); close examination revealed that missing reflections [12 and 20 reflections for (I) and (II), respectively] lie only in high-angle ($2\theta > 45^\circ$) regions.

For both compounds, data collection: SMART (Bruker, 2001); cell refinement: SAINT (Bruker, 2001); data reduction: SAINT; structure solution: SHELXS97 (Sheldrick, 1997); structure refinement: SHELXL97 (Sheldrick, 1997); molecular graphics: SHELXTL/PC (Sheldrick, 1990); software used to prepare material for publication: SHELXL97 and PARST (Nardelli, 1995).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1815). Services for accessing these data are described at the back of the journal.

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