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trans-rac-2-Hexyl-1-oxo-3-(2-pyridyl)-1,2,3,4-tetrahydroisoquinoline-4-carboxylic acid

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Key indicators

Single-crystal X-ray study
T = 290 K
Mean σ(C–C) = 0.006 Å
R factor = 0.089
wR factor = 0.292
Data-to-parameter ratio = 16.0

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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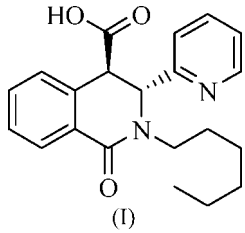
The title compound, $C_{21}H_{24}N_2O_3$, crystallizes as a racemic mixture of *R*,*R* and *S*,*S* enantiomers. The three-dimensional packing is stabilized by a system of hydrogen bonds and weak C—H···O interactions.

Comment

As a part of systematic studies of the reactions of homophthalic anhydrides with compounds containing C=O or C=N double bonds (Bogdanov & Palamareva, 2004; Kandinska *et al.*, 2006; Christov *et al.*, 2006), we have become interested in compounds with potential microbial activity. Thus, the title compound, (I), was synthesized while searching for new antibiotics containing an isoquinolinone core in their structure. The structure of (I) was determined by spectroscopic analysis (^{1}H NMR and IR) and microanalysis. In this paper, we report the X-ray crystal structure of (I).



(I)

In (I), the dihydroisoquinoline core is substituted with a carboxylic group in position 4, a 2-pyridinyl substituent in position 3 and an *n*-hexyl substituent in position 2. There is a *trans*-configuration of (I) with respect to the dihydroisoquinoline core conformation [according to IUPAC terminology (Moss, 1996)], with an antiperiplanar position of both substituents at atoms C8 and C9 [torsion angle C15—C8—C9—C10 = 163.4 (2)°]. The synthesis of (I) avoids any chiral compounds and hence (I) is a racemic mixture of *R*,*R* and *S*,*S* enantiomers. Fig. 1 shows the *R*,*R* isomer.

The structural parameters of (I) are analogous to those of similar compounds (Gzella *et al.*, 2002; Georgieva *et al.* 1994) and, as in the structure of 3-(2-furyl)-2-phenethyl-4-(pyrrolidin-1-ylcarbonyl)-3,4-dihydroisoquinolin-1(2*H*)-one (Petrova *et al.*, 2005), both aromatic rings are nearly planar and the pyridinone ring adopts a half-boat conformation, with atom C9 displaced 0.442 (5) Å out of the plane formed by the fused rings.

According to the Karplus equation (Karplus, 1963), the lower value of $^3J_{8,9}$ = 1.0 Hz in the ^{1}H NMR spectrum of (I) is in agreement with the synclinal position and the torsion angle of about 80° between the vicinal atoms H8 and H9. In (I), the H8—C8—C9—H9 torsion angle is 72°. This shows that the

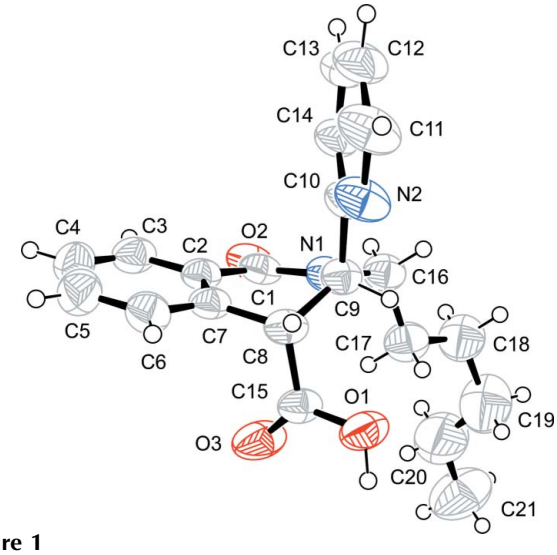


Figure 1
The molecular structure and atom-numbering scheme of (I), showing 50% probability displacement ellipsoids. H atoms are shown as small spheres of arbitrary radius.

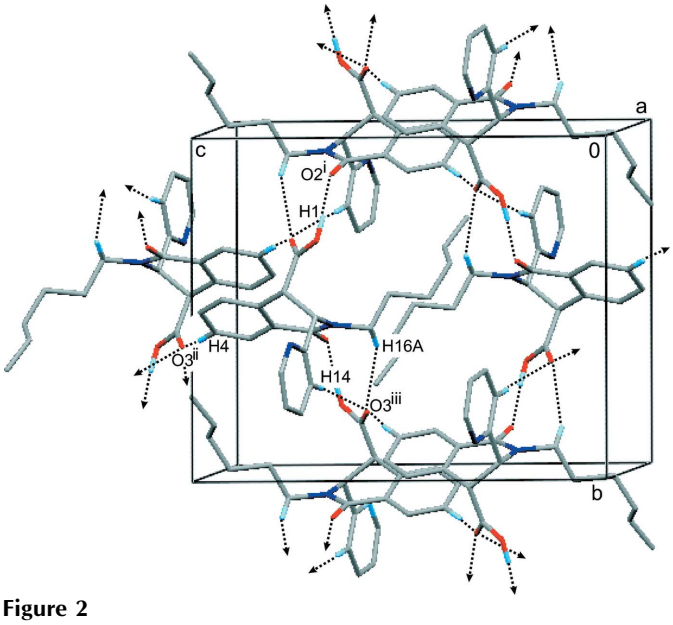


Figure 2
The molecular packing in (I). Hydrogen bonds and weak C—H···O interactions are represented by dotted lines. All H atoms, except those involved in hydrogen bonds and C—-H···O interactions, have been omitted.

observed conformation is identical both in the crystal structure and in solution, in contrast with a previously published conformationally flexible isochromanone (Bogdanov *et al.*, 2004), which possesses different conformations in the solid state and in solution.

Molecules of (I) are linked through O1—H1···O1^{i} hydrogen bonds (symmetry codes as in Table 1) between the hydroxyl O atom of the COOH group and the dihydroisoquinoline O atom (Table 1), forming one-dimensional chains along the *b* axis. These chains are additionally stabilized by weak C14—H14···O3^{iii} and C16—H16*A*···O3^{iii} interactions. Weak C4—H4···O4^{ii} interactions are responsible for the formation of centrosymmetric dimer units, producing pseudo-layers parallel to (10$\bar{1}$).

Experimental

Compound (I) was synthesized by the well known reaction between homophthalic anhydride and an imine (Haimova *et al.*, 1977). A solution of *N*-[1-(pyridine-2-yl)-methylidene]-*N*-hexylamine (6.0 g, 0.032 mol) in dry 1,2-dichloroethane (30 ml) was added dropwise to a hot and stirred suspension of homophthalic anhydride (5.12 g, 0.032 mol) in dry 1,2-dichloroethane (20 ml). The reaction mixture was boiled at 356 K and stirred for 1 h. After working up the reaction mixture, compound (I) crystallized as colourless needles from ethyl acetate (yield 8.29 g, 75%; m.p. 388–390 K). Analysis, calculated for $C_{21}H_{24}N_2O_3$: C 71.57, H 6.86%; found: C 71.25, H 7.24%. The product was characterized by ^{1}H NMR and IR spectra. Single crystals were obtained by slow evaporation of a solution of (I) in a chloroform–ethyl acetate mixture (3:1) at room temperature.

The ^{1}H NMR spectrum of (I) was obtained on a Bruker Advance DRX-250 spectrometer at 250.13 MHz in DMSO-d_6 at 293 K with tetramethylsilane as internal standard. ^{1}H NMR (250 MHz, DMSO-d_6, p.p.m.): 0.81–0.92 (3H, *m*, –CH$_3$), 1.18–1.35 (6H, *m*, –CH$_2$–), 1.45–1.63 (2H, *m*, –CH$_2$–), 2.73–2.84 (1H, *m*, –CH$_2$–), 4.03–4.15 (1H, *m*, –CH$_2$–), 4.41 (1H, *d*, *J* = 1.0 Hz, H8), 5.33 (1H, *d*, *J* = 1.0 Hz, H9), 7.01 (1H, *dd*, *J* = 7.9 Hz, Ph-H), 7.17–7.21 (2H, *m*, Ph-H), 7.30–7.39 (2H, *m*, Pyr-H), 7.66 (1H, *dt*, *J* = 1.8 and 7.8 Hz, Ph-H), 7.87 (1H, *dd*, *J* = 2.3 and 6.8 Hz, Ph-H), 8.48 (1H, *dm*, *J* = 4.8 Hz, Pyr-H).

Crystal data

$C_{21}H_{24}N_2O_3$
M_r = 352.42
Monoclinic, $P2_1/n$
a = 9.8917 (4) Å
b = 12.9205 (9) Å
c = 15.5882 (9) Å
β = 103.216 (6)°
V = 1939.5 (2) Å^3
Z = 4
Mo *K*α radiation
μ = 0.08 mm^{-1}
T = 290 (2) K
0.5 × 0.25 × 0.1 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
Absorption correction: none
3907 measured reflections
3770 independent reflections
2371 reflections with $I > 2\sigma(I)$
R_{int} = 0.035
3 standard reflections
every 200 reflections
intensity decay: −1%

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.089
$wR(F^2)$ = 0.292
S = 1.04
3770 reflections
236 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.40 e Å^{-3}
$\Delta\rho_{min}$ = −0.31 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O2^{i}	0.95	1.68	2.619 (2)	168
C4—H4···O3^{ii}	0.93	2.69	3.529 (3)	151
C14—H14···O3^{iii}	0.93	2.53	3.411 (3)	157
C16—H16*A*···O3^{iii}	0.97	2.54	3.271 (3)	132

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

In all our crystallization attempts, crystals of (I) grew as platelets. The crystal selected gave diffraction data which produced a crystal structure of lower than normal precision. The C19—C20 bond is

shorter than normal [1.376 (8) Å], but we attribute this to possible slight disorder of the C atoms in question. This disorder has not been modelled.

H atoms were placed in idealized positions, with $O-H_{hydroxy}$ = 0.95, $C-H_{aromatic}$ = 0.93, $C-H_{methylene}$ = 0.97, $C-H_{methine}$ = 0.98 and $C-H_{methyl}$ = 0.96 Å, and constrained to ride on their parent atoms, with $U_{iso}(H) = 1.2U_{eq}(C)$ or $1.5U_{eq}(O,C_{methyl})$.

Data collection: *CAD-4 EXPRESS* (Enraf–Nonius, 1994); cell refinement: *CAD-4 EXPRESS*; data reduction: *XCAD4* (Harms & Wocadlo, 1995); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997) and *Mercury* (Version 1.4; Macrae *et al.*, 2006); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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References

Bogdanov, M. G. & Palamareva, M. D. (2004). *Tetrahedron*, **60**, 2525–2530.
Bogdanov, M. G., Todorov, I. S., Manolova, P. G., Cheshmedzhieva, D. V. & Palamareva, M. D. (2004). *Tetrahedron Lett.* **45**, 8383–8386.
Christov, P. P., Kozekov, I. D. & Palamareva, M. D. (2006). *J. Heterocycl. Chem.* **43**, 1015–1019.
Enraf–Nonius (1994). *CAD-4 EXPRESS*. Version 5.1/1.2. Enraf–Nonius, Delft, The Netherlands.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Georgieva, A., Stanoeva, E., Karamfilova, K., Spassov, S., Angelova, O., Haimova, M., De Kimpe, N. & Boelens, M. (1994). *Tetrahedron*, **50**, 9399–9410.
Gzella, A., Brózda, D., Koroniak, Ł. & Rozwadowska, M. D. (2002). *Acta Cryst.* C**58**, o503–o506.
Haimova, M. A., Mollov, N. M., Ivanova, S. C., Dimitrova, A. I. & Ognyanov, V. I. (1977). *Tetrahedron*, **33**, 331–336.
Harms, K. & Wocadlo, S. (1995). *XCAD4*. University of Marburg, Germany.
Kandinska, M. I., Kozekov, I. D. & Palamareva, M. D. (2006). *Molecules*, **11**, 403–414.
Karplus, M. (1963). *J. Am. Chem. Soc.* **85**, 2870–2871.
Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl. Cryst.* **39**, 453–457.
Moss, G. P. (1996). *Pure Appl. Chem.* **68**, 2193–2222.
Petrova, R., Shivachev, B., Kosev, K., Stoyanova, M. & Angelova, S. (2005). *Acta Cryst.* E**61**, o2248–o2250.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.