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8-Chloro-10,11-dihydro-4-aza-5*H*-dibenzo[*a*,*d*]-cyclohepten-5-one

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.003 Å
R factor = 0.041
wR factor = 0.142
Data-to-parameter ratio = 12.1

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

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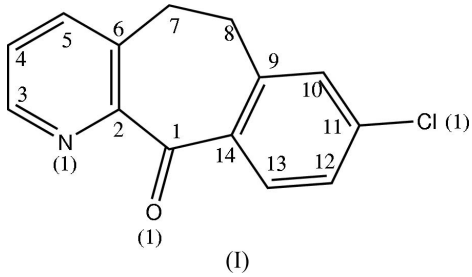
The title compound, $C_{14}H_{10}ClNO$, is the key intermediate in the synthesis of the antihistaminic drug loratadine. The molecule contains a tricyclic fused-ring system composed of a benzene ring, a pyridine ring and a central non-planar seven-membered ring.

Comment

The title compound, (I), is the key intermediate in the synthesis of loratadine and descarboethoxyloratadine (DCL), which is the major active metabolite of loratadine. It is well known that loratadine, a long-acting tricyclic antihistamine with selective peripheral histamine H_1-receptor antagonistic activity, is a prodrug that is metabolized to an active metabolite, decarboethoxyloratadine (DCL), to a large extent by the hepatic cytochrome P450 CYP3A4 system – a major isozyme in the human liver known for metabolizing a large variety of xenobiotics and endogenous biochemicals (Haria *et al.*, 1994). As part of a search to find a better industrial synthesis for the title compound, we are optimizing the reaction conditions. Its structure was elucidated by spectroscopic methods and is now confirmed by this single-crystal X-ray diffraction analysis.



(I)

Compound (I) was obtained as colorless monoclinic block-shaped crystals. A view of molecule (I) is shown in Fig. 1 and

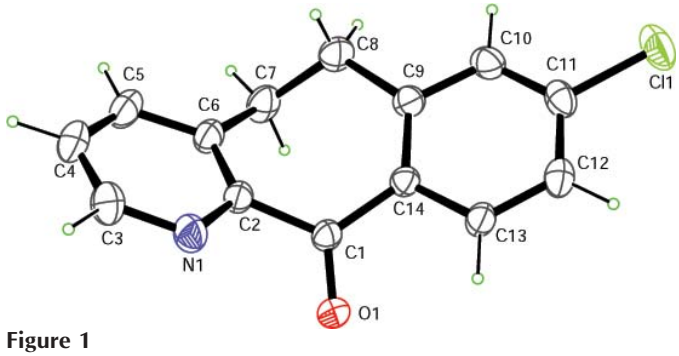


Figure 1
A view of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

selected dimensions are given in Table 1. The molecule contains a tricyclic fused-ring system composed of a benzene ring, a pyridine ring and a central non-planar seven-membered ring, whose conformation, *viz*. twist–boat, very closely resembles that of two (symmetry-equivalent) seven-membered rings found in a similar ring system in 7,8,15,16-tetrahydrodibenzo[*d*,*d*′]benzo[1,2-*a*;4,5-*a*′]dicycloheptene-5,13-dione (Briant *et al.*, 1988).

Experimental

3-[2-(3-Chlorophenyl)ethyl]pyridine-2-carboxylic acid (2.62 g, 0.01 mol) was suspended in thionyl chloride (4 ml) and stirred at room temperature for 10 min, then refluxed for 1.5 h. A brown viscous oil was obtained by removal of the excess thionyl chloride, and carbon disulfide (45 ml) was added. After the mixture was brought into one phase by stirring at room temperature, $AlCl_3$ (2.6 g, 0.02 mol) was added and the mixture was stirred for another 16 h. The product was hydrolyzed by the addition of dilute hydrochloric acid and the aqueous phase was extracted with chloroform three times, The combined extracts were washed with water, dried with $MgSO_4$, filtered and concentrated to afford 2.2010 g of the pure title compound, (I). Crystals suitable for X-ray structure analysis were obtained by slow evaporation of a methanol solution at room temperature.

Crystal data

$C_{14}H_{10}ClNO$
M_r = 243.69
Monoclinic, $P2_1/n$
a = 6.8221 (3) Å
b = 23.023 (1) Å
c = 7.6719 (3) Å
β = 107.176 (2)°
V = 1151.2 (1) Å^3
Z = 4
D_x = 1.406 Mg m^{-3}
Mo Kα radiation
Cell parameters from 7263 reflections
θ = 2.9–27.4°
μ = 0.31 mm^{-1}
T = 293 (1) K
Block, colorless
0.52 × 0.50 × 0.40 mm

Data collection

Rigaku R-AXIS RAPID diffractometer
ω scans
Absorption correction: multi-scan (*ABSCOR*; Higashi,1995)
T_{min} = 0.770, T_{max} = 0.883
8508 measured reflections
2554 independent reflections
1871 reflections with $F^2 > 2\sigma(F^2)$
R_{int} = 0.025
θ_{max} = 27.5°
$h = -8 \rightarrow 7$
$k = -29 \rightarrow 29$
$l = -9 \rightarrow 9$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.041
$wR(F^2)$ = 0.142
S = 1.00
1871 reflections
155 parameters
H-atom parameters constrained
$w = 1/[0.004F_o^2 + \sigma(F_o^2)]/(4F_o^2)$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.26 e Å^{-3}
Extinction correction: Larson (1970), equation 22
Extinction coefficient: 2.5 (6) × 10^2

Table 1
Selected geometric parameters (Å, °).

Cl1—C11	1.739 (2)	C7—C8	1.514 (3)
O1—C1	1.215 (2)	C8—C9	1.514 (3)
C1—C2	1.512 (2)		
C1—C14—C9	126.7 (2)	C8—C9—C14	125.7 (2)
C3—N1—C2—C1	−177.9 (2)	C6—C7—C8—C9	73.6 (2)
C2—C6—C7—C8	−66.0 (2)	C7—C8—C9—C14	−24.1 (3)

After their location in a difference map, all H atoms were positioned geometrically (C—H = 0.97–0.98 Å) and allowed to ride on their attached atoms, with $U_{iso}(H) = 1.2U_{eq}(C)$.

Data collection: *RAPID-AUTO* (Rigaku/MSC, 2004); cell refinement: *RAPID-AUTO*; data reduction: *CrystalStructure* (Rigaku/MSC, 2004); program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *WinGX* (Farrugia, 1999); software used to prepare material for publication: *CrystalStructure*.

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