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5-(1*H*-Indol-3-yl)-3-(4-methylphenyl)-4,5-dihydroisoxazoline

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Key indicators

Single-crystal X-ray study
T = 294 K
Mean σ(C–C) = 0.004 Å
R factor = 0.039
wR factor = 0.093
Data-to-parameter ratio = 9.0

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

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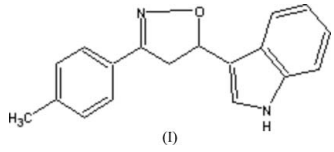
The title compound, $C_{18}H_{16}N_2O$, was synthesized by the cyclocondensation of 1-(1*H*-indol-3-yl)-3-(4-methylphenyl)-prop-1-en-3-one with hydroxylamine hydrochloride. The isoxazoline ring adopts an envelope conformation. Symmetry-related molecules are linked *via* N—H···O hydrogen bonds into a chain along the *a* axis.

Comment

Indole skeletons play an important role as intermediates for the design of many pharmacologically active compounds (Sundberg, 1996). Indole derivatives have been widely studied because of their biological activities, such as anti-inflammatory, antibacterial response *etc*. Isoxazole compounds demonstrate antiproliferative activity on tumor cells of different lineages and are able to induce erythroid differentiation and adipogenic conversion (Simoni *et al.*, 1991). Isoxazoline derivatives act as inhibitors of human leukocyte elastase (HLE) and cathepsin G (Cath G) (Groutas *et al.*, 1995). In view of these potential uses, we have recently focused our attention on the preparation of isoxazoline derivatives, using chalcone synthons (Darid *et al.*, 1998). The title compound, (I), was synthesized by the cyclocondensation of 1-(1*H*-indol-3-yl)-3-(4-methylphenyl)prop-1-en-3-one in the presence of hydroxylamine hydrochloride. An X-ray crystal structure determination of (I) was carried out to elucidate the structure, and the results are presented here.



(I)

In compound (I), the indole ring system is essentially planar (Fig. 1). The isoxazoline ring adopts an envelope conformation. Atom C9 deviates from the O1/N2/C10/C11 plane by 0.385 (4) Å. The N1/C1–C8 and C12–C17 planes form dihedral angles of 86.3 (1) and 14.8 (2)°, respectively, with the O1/N2/C10/C11 plane. Symmetry-related molecules are linked *via* N—H···O hydrogen bonds (Table 1) into a chain along the *a* axis.

Experimental

A mixture of *p*-methylacetophenone (4.64 g, 35 mmol) and indole-3-aldehyde (2.00 g, 14 mmol) in MeOH (50 ml) was stirred and then 60% aqueous KOH aqueous solution (17 ml) was added dropwise at 298 K. The mixture was stirred for 42 h at 323–333 K and then cooled to room temperature and poured into water. The resulting precipitate

was purified by preparative thin-layer chromatography (CH_2Cl_2/MeOH 18:1 as eluant) to give a yellow powder product, 1-(1*H*-indol-3-yl)-3-(4-methylphenyl)prop-1-en-3-one (0.593 g, m.p. 430–431 K, yield 16.5%). A mixture of 1-(1*H*-indol-3-yl)-3-(4-methylphenyl)-prop-1-en-3-one (0.25 g, 1 mmol) and hydroxylamine hydrochloride (0.17 g, 2.5 mmol) in EtOH (30 ml) was stirred, and NaOH (0.04 mg, 1 mmol) and water (8 drops) were added. The mixture was refluxed for 42 h and then cooled to 298 K. The mixture was filtered, the filtrate dried under pressure and the resulting solid was crystallized from EtOH to give a solid product (yield 54.3%). Single crystals of the title compound, suitable for X-ray diffraction study, were obtained by slow evaporation of a methanol solution (m.p. 440–442 K). ^{1}H NMR ($CDCl_3$, p.p.m.): 2.39 (*s*, 3H), 6.02 (*dd*, 1H, $_1J$ = 9.03 Hz, ^2J = 10.71 Hz), 3.52 (*dd*, 1H, ^1J = 10.86 Hz, ^2J = 16.56 Hz), 3.76 (*dd*, 1H, ^1J = 10.86 Hz, ^2J = 16.60 Hz), 7.09–7.64 (*m*, 9H), 8.15 (*br s*, 1H).

Crystal data

$C_{18}H_{16}N_2O$
M_r = 276.33
Orthorhombic, $P2_12_12_1$
a = 8.1881 (19) Å
b = 12.713 (3) Å
c = 14.239 (3) Å
V = 1482.3 (6) Å^3
Z = 4
D_x = 1.238 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1772 reflections
θ = 2.9–21.2°
μ = 0.08 mm^{-1}
T = 294 (2) K
Block, purple
0.30 × 0.24 × 0.12 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.968, T_{max} = 0.991
8368 measured reflections
1747 independent reflections
1120 reflections with $I > 2\sigma(I)$
R_{int} = 0.050
θ_{max} = 26.4°
$h = -9 \rightarrow 10$
$k = -12 \rightarrow 15$
$l = -17 \rightarrow 15$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.039
$wR(F^2)$ = 0.093
S = 1.02
1747 reflections
195 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0374P)^2 + 0.1511P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.11 e Å^{-3}
$\Delta\rho_{min}$ = −0.13 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···O1^{i}	0.82 (4)	2.13 (4)	2.937 (4)	170 (5)

Symmetry code: (i) $x - \frac{1}{2}, -y - \frac{1}{2}, -z + 1$.

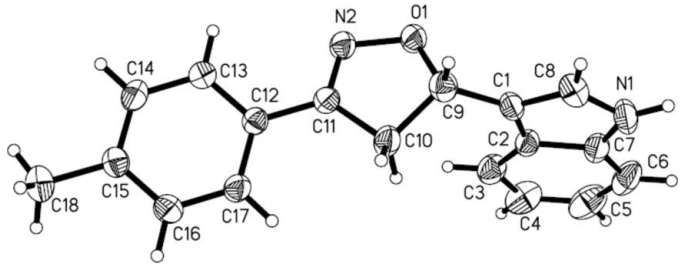


Figure 1
A view of (I), showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 30% probability level.

Atom H1*A* was located in a difference map and refined isotropically. The other H atoms were positioned geometrically (C—H = 0.93–0.97 Å) and constrained to ride on their parent atoms, with U_{iso}(H) values of 1.5U_{eq}(carrier atom) for methyl and 1.2U_{eq}(C) for the remaining H atoms. The methyl group was allowed to rotate freely about the C—C bond. In the absence of significant anomalous dispersion effects, Friedel pairs were merged before the final refinement.

Data collection: *SMART* (Bruker, 1997); cell refinement: *SAINT* (Bruker, 1997); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *SHELXTL*.

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