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Ethyl 3-(10-chloroanthracenyl)-5-(1-phenyl-2-hydroxyethenyl)isoxazole-4-carboxylate: an enol produced by Dess–Martin oxidation

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Key indicators

Single-crystal X-ray study
T = 87 K
Mean σ(C–C) = 0.002 Å
R factor = 0.035
wR factor = 0.095
Data-to-parameter ratio = 12.7

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

The title compound, $C_{28}H_{20}ClNO_4$, is a very stable enol produced by a Dess–Martin oxidation, not the expected ketone. The enol form is stabilized by intramolecular hydrogen bonding and the molecules associate into dimers *via* weak C—H···N hydrogen bonding.

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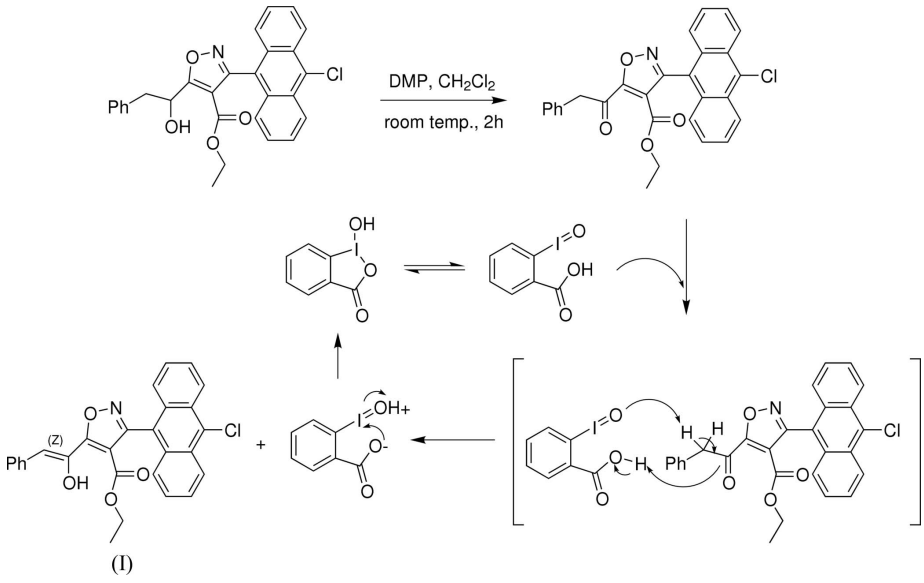
Comment

During our pursuit of a structure–activity relationship study of a series of anticancer agents, (Verner *et al.*, 1990; Zhou *et al.*, 1997), the title compound, (I), was produced by a Dess–Martin oxidation (Dess & Martin, 1983, 1991) {see Nicolaou *et al.* (2002, and references therein) for general reviews on applications of Dess–Martin periodinane [DMP, 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one] and related hypervalent iodine reagents} and its structure was characterized (Fig. 1).



(I)

The mechanism of enol formation is proposed in the scheme. DMP was prepared by complete oxidation of 2-iodobenzoic acid, followed by acetylation of 2-iodoxybenzoic acid (IBX). However, if the oxidation of iodobenzoic acid is incomplete, an intermediate, iodosobenzoic acid, will be produced, which can tautomerize between an open and a closed form (Moss *et al.*, 1998). It is possible that the presence of an open form of iodosobenzoic acid facilitates the deprotonation of an α-hydrogen and protonation of the ketone. After esterification, iodosobenzoic acid will be regenerated through its closed form. No reaction was observed when IBX was used as the only catalyst in the oxidation reaction of

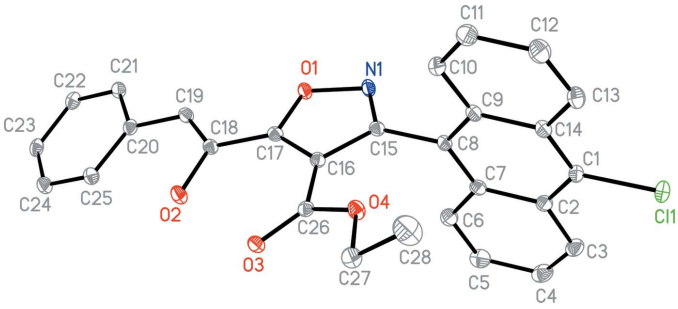


Figure 1
Molecular structure of (I), showing 30% probability displacement ellipsoids. H atoms have been omitted for clarity.

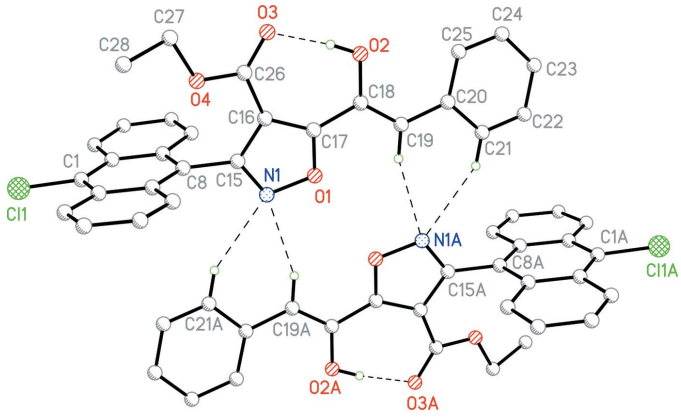


Figure 2
Illustration of hydrogen bonding (dashed lines) in (I). Only the H atoms involved in these interactions are shown.

phenethyl alcohol, nor was an enol formed when IBX was reacted with a ketone.

The enol form is stabilized by the formation of a strong intramolecular hydrogen bond (Table 1) with an O···O distance of 2.6193 (14) Å. The anthracenyl group is almost perpendicular to the isoxazole plane [85.51 (4)°], which is similar to analogous anthracenyl isoxazole structures in the Cambridge Structural Database (CSD; Version 5.27; Allen, 2002), *viz.* ethyl 3-(10′-chloro-9′-anthracenyl)-5-methyl-4-isoxazolecarboxylate (74.3°; Han *et al.*, 2003; CSD refcode EZENEC), ethyl 3-(10′-chloro-9′-anthracenyl)-5-(2-phenylethyl)-4-isoxazolecarboxylate (78.5°; Han *et al.*, 2002, and references therein; CSD refcode MUQMOA), and ethyl 3-(9-anthryl)-5-methyl-4-isoxazolecarboxylate (80.7°; Mosher *et al.*, 1996; CSD refcode TEKJIC). Unlike previous anthracenyl isoxazoles, the orientation in compound (I) allows the molecule to form weakly associated dimers *via* non-classical hydrogen bonds (Table 1) between the pendant phenyl ring and the isoxazole N atom (Fig. 2). This synthon has been reported in the isoxazole *N*-(2,6-dimethylphenyl)-5-methylisoxazole-3-carboxamide (Jaulmes *et al.* 1993; CSD refcode HABRUX) forming a three-dimensional network with phenyl C···N distances of *ca* 3.7 Å.

Experimental

Ethyl 3-(10-chloroanthracenyl)-5-(1-hydroxy-2-phenethyl)-isoxazole-4-carboxylate (100 mg, 0.21 mmol) was added to a stirred solution of DMP (135 mg, 0.32 mmol, 1.5 equivalents) in CH_2Cl_2 (15 ml). After 2 h, the solution was diluted with diethyl ether (50 ml) and poured into saturated aqueous $NaHCO_3$ (50 ml) containing $Na_2S_2O_4$ (12.5 g). The mixture was stirred for 10 min. After diethyl ether (50 ml) was added, the layers were separated. The ether layer was extracted with saturated aqueous $NaHCO_3$ (50 ml) and water (50 ml), and dried over Na_2SO_4. Filtration and removal of the ether by rotary evaporation was followed by recrystallization hexane–ethyl acetate (3:1) produced compound (I) as pale-yellow prisms in 98% yield (m.p. 465.5–466.0 K). ^{1}H NMR ($CDCl_3$, p.p.m.): δ 0.053 (*t*, *J* = 7.2 Hz, 3H), 3.67 (*q*, *J* = 7.2 Hz, 2H), 6.83 (*d*, *J* = 1.5 Hz, 1H), 7.30 (*m*, 1H), 7.45 (*m*, 2H), 7.55 (*m*, 2H), 7.66 (*m*, 4H), 7.98 (*d*, *J* = 8.7 Hz, 2H), 8.63 (*d*, *J* = 8.7 Hz, 2H), 10.99 (*d*, *J* = 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, p.p.m.): δ 12.12, 62.25, 110.00, 112.75, 122.02, 125.11, 125.57, 126.83, 126.91, 127.81, 128.30, 128.48, 130.11, 131.12, 131.25, 135.04, 139.68, 160.78, 165.14, 171.68; EI–MS: 469.17 (M^+), 350.10, 277.05, 237.05, 91.05. The desired ketone product can be obtained from the same procedure; however, the yield of ketone is variable. Fractional recrystallization using hexanes–EtOAc (3:1) resulted in a good separation of the ketone and enol mixture.

Crystal data

$C_{28}H_{20}ClNO_4$
M_r = 469.90
Monoclinic, $P2_1/n$
a = 10.6621 (12) Å
b = 15.5874 (17) Å
c = 13.2180 (15) Å
β = 92.069 (2)°
V = 2195.3 (4) Å^3
Z = 4
D_x = 1.422 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 7425 reflections
θ = 2.3–30.0°
μ = 0.21 mm^{-1}
T = 87 (2) K
Parellelepiped, pale yellow
0.44 × 0.41 × 0.19 mm

Data collection

Bruker/Siemens SMART APEX diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Bruker, 2001)
T_{min} = 0.913, T_{max} = 0.961
32656 measured reflections
3975 independent reflections
3724 reflections with $I > 2\sigma(I)$
R_{int} = 0.021
θ_{max} = 25.3°
h = −12 → 12
k = −18 → 18
l = −15 → 15

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.095
S = 1.05
3975 reflections
312 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0505P)^2 + 1.2473P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.29 e Å^{-3}
$\Delta\rho_{min}$ = −0.44 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
C19—H19···N1^{i}	0.95	2.68	3.5669 (19)	156
C21—H21···N1^{i}	0.95	2.60	3.4849 (19)	155
O2—H2A···O3	0.86 (2)	1.77 (2)	2.6193 (14)	173 (2)

Symmetry code: (i) $-x+1, -y+1, -z+1$.

Atom H2*A* was located and refined freely. All other H atoms were positioned geometrically and refined using a riding model, with U_{iso}(H) constrained to be $1.2U_{eq}$ of the carrier atom and C—H = 0.95–0.99 Å.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT-Plus* (Bruker, 2001); data reduction: *SAINT-Plus*; program(s) used to solve structure: *XS* in *SHELXTL* (Bruker, 2001); program(s) used to refine structure: *XL* in *SHELXTL*; molecular graphics: *XP* in *SHELXTL*; software used to prepare material for publication: *XCIF* in *SHELXTL*.

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