Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

2′-Hydroxy-3′-(morpholin-4-yl-methyl)-4′,6′-dimethoxy-2-chloro-chalcone

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Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.004 Å
R factor = 0.043
wR factor = 0.088
Data-to-parameter ratio = 14.4

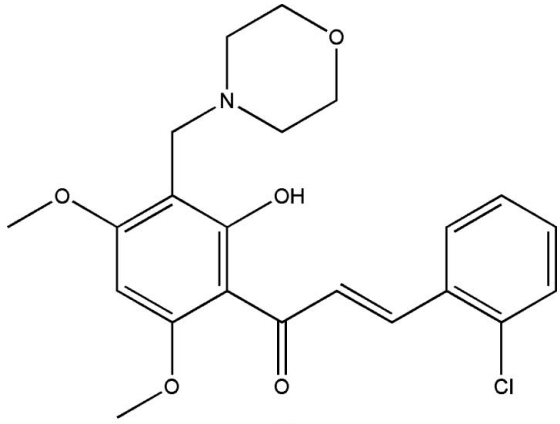
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 5 September 2005
Accepted 19 September 2005
Online 21 September 2005

In the title compound, $C_{22}H_{24}ClNO_5$, the carbonyl group is in an *s-cis* configuration with respect to the olefinic double bond. In the crystal structure, there are weak π-stacking interactions but there are no significant intermolecular hydrogen bonds.

Comment

Chalcones possess anti-inflammatory, antimalarial and anti-fertility activities, and are also reported as having antitumor activity (De Vincenzo *et al.*, 1995; Pettit *et al.*, 2001; Kumar *et al.*, 2003). With this in mind, a series of chalcones have been synthesized in our lab and have been evaluated for antitumor activity *in vitro* against various human tumor cell lines. Among them, the title compound has a broad antitumor spectrum and low micromolar IC50 ranging from 4.8 to 22.7 μmol l^{-1} against six human tumor cell lines. In order to obtain detailed information on its molecular conformation in the solid state, an X-ray structure determination of the title compound, (I), has been carried out.



(I)

The title molecule is illustrated in Fig. 1. The configuration of the carbonyl group with respect to the olefinic double bond is *s-cis*, which is the same as in two related structures (Ravishankar *et al.*, 2003; Moorthi *et al.*, 2005). The *trans* arrangement of the H atoms in the —CH═CH— group is consistent with the solution-phase ^{1}H NMR studies (*J* = 15.6 Hz; Li & Su, 1994). The atoms in the unsaturated ketone group are essentially coplanar in accordance with the π-electron conjugation. The exocyclic angles around C10 deviate from the normal trigonal value of 120°, with a larger C11—C10—C9 angle of 125.4 (3)° and a smaller C15—C10—C9 angle of 118.6 (3)°. This may be the result of the intramolecular O—H···O hydrogen bond (Table 1). In the crystal structure, the only significant intermolecular interactions

present are weak π stacking, where the central aromatic ring (C10–C15) and the *p*-chlorobezene ring (C1–C6), from pairs of molecules related by centers of symmetry, are separated by a centroid–centroid distance of 3.660 (2) Å and a perpendicular distance of 3.49 Å (Fig. 2).

Experimental

The title compound was obtained from phloroglucinol *via* the Hoesch reaction (Gulati *et al.*, 1943), etherification (Juntend & Junte, 1988), Aldol condensation (Bu *et al.*, 1997) and the Mannich reaction (Wilds *et al.*, 1963). A crystal suitable for crystallographic study was obtained by slow crystallization from acetone at room temperature.

Crystal data

$C_{22}H_{24}ClNO_5$
M_r = 417.89
Monoclinic, $C2/c$
a = 13.408 (2) Å
b = 10.517 (2) Å
c = 29.505 (6) Å
β = 92.90 (2)°
V = 4154.9 (13) Å^3
Z = 8
D_x = 1.336 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 28 reflections
θ = 2.9–14.8°
μ = 0.22 mm^{-1}
T = 296 (2) K
Plate, yellow
0.60 × 0.50 × 0.12 mm

Data collection

Siemens *P*4 diffractometer
ω scans
Absorption correction: ψ scan (*SHELXTL*; Bruker, 1997)
T_{min} = 0.874, T_{max} = 0.974
4451 measured reflections
3872 independent reflections
1515 reflections with $I > 2\sigma(I)$
R_{int} = 0.033
θ_{max} = 25.5°
$h = 0 \rightarrow 16$
$k = 0 \rightarrow 12$
$l = -35 \rightarrow 35$
3 standard reflections
every 97 reflections
intensity decay: 3.3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.088
S = 0.81
3872 reflections
269 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0262P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.17 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.00184 (12)

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

D—H···A	D—H	H···A	D···A	D—H···A
O5—H0···O2	0.90 (3)	1.62 (3)	2.452 (3)	152 (3)

All H atoms were positioned geometrically and allowed to ride on their attached atoms, with O—H, C—H(CH), C—H(CH_2) and C—H(CH_3) distances of 0.90, 0.93, 0.97 and 0.96 Å, respectively. The isotropic displacement parameters of the H atoms were fixed at $1.7U_{eq}$(O) or $1.2U_{eq}$(C). The small ratio of observed to unique reflections (39%) limits the reliability of the structure.

Data collection: *XSCANS* (Bruker, 1997); cell refinement: *XSCANS*; data reduction: *SHELXTL* (Bruker, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXTL*.

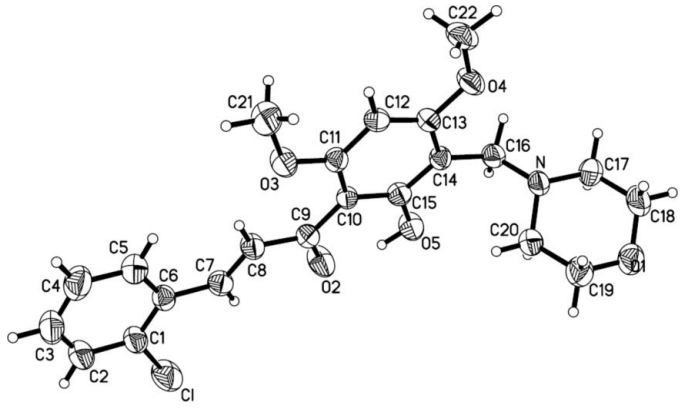


Figure 1
View of (I), showing the atom-labeling scheme and displacement ellipsoids at the 40% probability level.

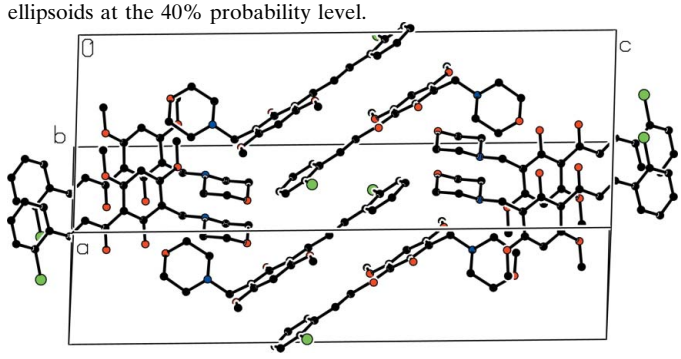


Figure 2
Packing diagram (*PLATON*; Spek, 2003) of (I), showing the weak π-stacking interactions in the center of the unit cell. H atoms have been omitted.

X-ray data were collected at Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences.

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