

15-(4-Chlorobenzylamino)-2-methoxypodocarpa-8,11,13-trien-15-one

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Key indicators

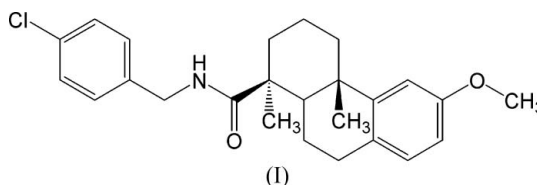
Single-crystal X-ray study
 $T = 93$ K
Mean $\sigma(\text{C}-\text{C}) = 0.003$ Å
 R factor = 0.034
 wR factor = 0.090
Data-to-parameter ratio = 12.9For details of how these key indicators were
automatically derived from the article, see
<http://journals.iucr.org/e>.

At 93 K, the benzylic C–N bond of the title compound [systematic name: *N*-(4-chlorobenzyl)-6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-1-carboxamide], $\text{C}_{25}\text{H}_{30}\text{ClNO}_2$, adopts almost perfect coplanarity with the amide carbonyl linkage, the dihedral angle between the C–N–C=O planes being only $2.5(3)^\circ$. There is weak intermolecular N–H···O hydrogen bonding between the two independent molecules comprising the asymmetric unit involving the carbonyl O atoms; this extends to link neighboring molecules into a chain.

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Comment

As part of our anti-inflammatory and anticancer discovery program, we are exploring the derivatization of the C-4 carboxyl group of podocarpic acid (Bakare *et al.*, 2005) in order to design new molecules that can modulate the lipoxigenase and cyclooxygenase pathways. Consequently, the title compound, (I), was synthesized as one of a series of amide derivatives under investigation; its structure is reported here.



The geometric conformation parameters of the three fused six-membered rings in each of the two independent molecules comprising the crystallographic asymmetric unit of (I) (Fig. 1 and Table 1) are similar to those observed previously (Bakare *et al.*, 2005; Couldwell *et al.*, 1985; Mondal *et al.*, 2003). In addition, the benzylic carbon-C19 to amide-N1 bond is almost coplanar with the amide carbonyl C15–O1 bond, with a dihedral angle of $2.5(3)^\circ$. This near coplanarity is probably due to partial double-bond character of the C15–N1 bond with bond lengths of 1.348 (2) and 1.350 (2) Å for the two independent molecules. The major difference between the independent molecules is evident from Fig. 1, which shows a significant twist about the C4–C15 bond. There are weak intermolecular N–H···O hydrogen bonds between N and O1 in adjacent molecules, resulting in the formation of chains along the *b* axis (Fig. 2 and Table 2).

Experimental

To sodium hydride (NaH, 100 mg, 4.16 mmol) was added a solution of 12-methoxypodocarpa-8,11,13-trien-15-oic acid (537 mg, 1.86 mmol) in dry benzene (13 ml). The resulting mixture was stirred for 30 min,

after which oxalyl chloride (2 ml) was slowly added and stirring continued for an additional 1 h. The reaction mixture was filtered and the filtrate concentrated *in vacuo* to give as a yellow oil, the acid chloride, 12-methoxypodocarpa-8,11,13-trienoyl chloride. Dry benzene (5 ml) was added to the residue and the solvent removed again *in vacuo*. The acid chloride, in benzene, was added slowly to a stirred solution of 4-chlorobenzylamine (in excess) in dry benzene (10 ml) at 273 K. The mixture was then allowed to warm to room temperature and stirred for 24 h before being filtered. The volatiles were removed *in vacuo* and the residue treated with hexane to give a white solid, which was purified by recrystallization from a solvent mixture of ethanol and distilled water (55%).

Crystal data

$C_{25}H_{30}ClNO_2$ $V = 1063.7 (2) \text{ \AA}^3$
 $M_r = 411.95$ $Z = 2$
 Triclinic, $P1$ $D_x = 1.286 \text{ Mg m}^{-3}$
 $a = 9.8466 (11) \text{ \AA}$ Mo $K\alpha$ radiation
 $b = 10.2147 (10) \text{ \AA}$ $\mu = 0.20 \text{ mm}^{-1}$
 $c = 10.8492 (12) \text{ \AA}$ $T = 93 (2) \text{ K}$
 $\alpha = 84.224 (2)^\circ$ Chunk, colorless
 $\beta = 80.232 (2)^\circ$ $0.44 \times 0.33 \times 0.23 \text{ mm}$
 $\gamma = 82.956 (2)^\circ$

Data collection

Bruker SMART 1K CCD 8349 measured reflections
 diffractometer 6817 independent reflections
 φ and ω scans 6495 reflections with $I > 2\sigma(I)$
 Absorption correction: multi-scan $R_{int} = 0.041$
 (SADABS; Sheldrick, 1996) $\theta_{max} = 28.2^\circ$
 $T_{min} = 0.878, T_{max} = 1$

Refinement

Refinement on F^2 $w = 1/[\sigma^2(F_o^2) + (0.0716P)^2]$
 $R[F^2 > 2\sigma(F^2)] = 0.034$ where $P = (F_o^2 + 2F_c^2)/3$
 $wR(F^2) = 0.090$ $(\Delta/\sigma)_{max} = 0.002$
 $S = 1.04$ $\Delta\rho_{max} = 0.37 \text{ e \AA}^{-3}$
 6817 reflections $\Delta\rho_{min} = -0.37 \text{ e \AA}^{-3}$
 529 parameters Absolute structure: Flack (1983),
 H-atom parameters constrained 1588 Friedel pairs
 Flack parameter: 0.04 (4)

Table 1

Selected geometric parameters ($\text{\AA}, ^\circ$).

O2A—C12A	1.378 (3)	O2B—C12B	1.375 (2)
O2A—C18A	1.413 (3)	O2B—C18B	1.430 (2)
O1A—C15A	1.233 (2)	O1B—C15B	1.232 (2)
N1A—C15A	1.348 (2)	N1B—C15B	1.350 (2)
N1A—C19A	1.462 (3)	N1B—C19B	1.460 (2)
C4A—C15A	1.545 (3)	C4B—C15B	1.541 (2)
C4A—C16A	1.544 (3)	C4B—C16B	1.546 (3)
C4A—C5A	1.565 (2)	C4B—C5B	1.566 (2)
C12A—O2A—C18A	117.61 (19)	C12B—O2B—C18B	116.89 (14)
C15A—N1A—C19A	120.34 (15)	C15B—N1B—C19B	122.46 (15)
C5A—C4A—C15A	117.98 (15)	C5B—C4B—C15B	113.92 (14)
C5A—C4A—C16A	109.55 (15)	C5B—C4B—C16B	109.45 (14)
O2A—C12A—C11A	115.13 (19)	O2B—C12B—C13B	124.18 (17)
O2A—C12A—C13A	124.42 (19)	O2B—C12B—C11B	115.91 (16)
O1A—C15A—N1A	120.03 (17)	O1B—C15B—N1B	120.97 (16)
O1A—C15A—C4A	121.72 (15)	O1B—C15B—C4B	120.05 (16)
N1A—C15A—C4A	118.14 (15)	N1B—C15B—C4B	118.83 (15)
N1A—C19A—C20A	113.14 (16)	N1B—C19B—C20B	111.61 (15)
C19A—N1A—C15A—O1A	2.5 (3)	C19B—N1B—C15B—O1B	-1.2 (3)

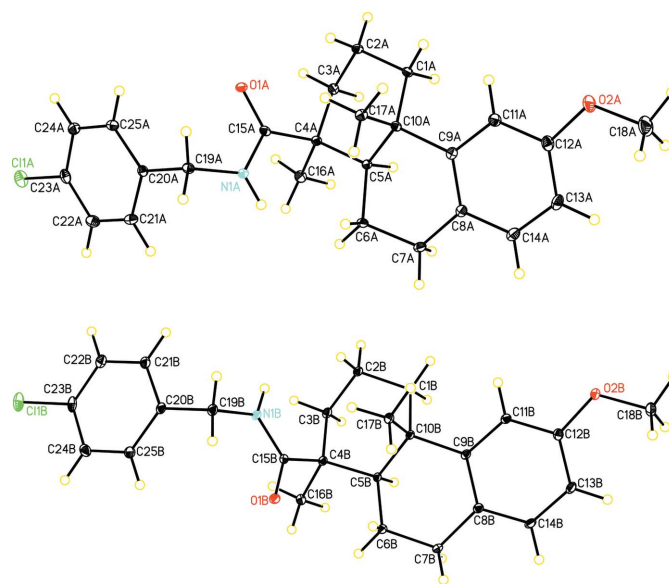


Figure 1 View of the two independent molecules of (I) in the asymmetric unit, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level.

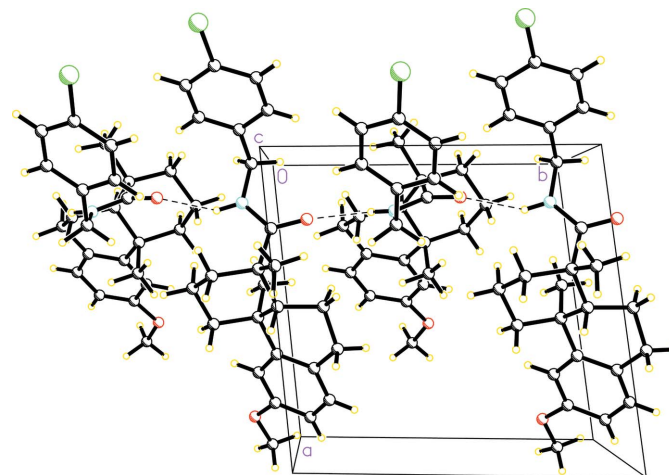


Figure 2

The molecular packing of (I), viewed approximately down the c axis, showing the $N-H \cdots O$ hydrogen-bonding interactions (dashed lines) in the b -axis direction.

Table 2

Hydrogen-bond geometry ($\text{\AA}, ^\circ$).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
$N1A-H1AC \cdots O1B$	0.88	2.19	2.9154 (19)	140
$N1B-H1BC \cdots O1A^i$	0.88	2.23	2.9802 (19)	143

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

The methyl H atoms were constrained to an ideal geometry, with $C-H = 0.98 \text{ \AA}$ and $U_{iso}(H) = 1.5U_{eq}(C)$, but each group was allowed to rotate freely about its $C-C$ bond. The position of the amine-H atoms were constrained to an ideal geometry, with $N-H = 0.88 \text{ \AA}$

and $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{N})$. All other H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, with C–H = 0.95–1.00 Å and $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINTPlus* (Bruker, 1999); data reduction: *SAINTPlus*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1999); software used to prepare material for publication: *SHELXTL*.

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