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12-Methoxy-15-(1-pyrrolidino)podocarpa-8,11,13-triene-15-one

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Key indicators

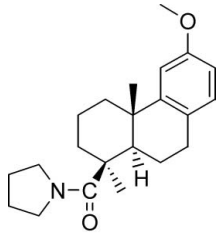
Single-crystal X-ray study
T = 93 K
Mean σ(C–C) = 0.002 Å
R factor = 0.035
wR factor = 0.091
Data-to-parameter ratio = 11.4

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

At 93 K, the five-membered pyrrolidine ring of the title compound [systematic name: 6-methoxy-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)(pyrrolidin-1-yl)methanone], $C_{22}H_{31}NO_2$, has an envelope geometry with one of the β C atoms at the flap position, displaced by 0.610 (3) Å from the plane defined by the other four atoms. There is a weak intermolecular C—H···O hydrogen bond involving the carbonyl O atom

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 in order to design new molecules that can modulate the lipoxygenase and cyclo-oxygenase pathways. The title pyrrolidinyl derivative, 12-methoxy-15-(1-pyrrolidino)podocarpa-8,11,13-triene-15-one, (I), was synthesized as one of a series of amide derivatives under investigation. In this paper, we present the X-ray crystallograpic analysis of (I) as a continuation of our previous studies (Bakare *et al.*, 2005.)



(I)

Selected bond distances and angles for (I) are listed in Table 1. The overall molecular geometry, with the atom-numbering scheme, is illustrated in Fig. 1. The geometric

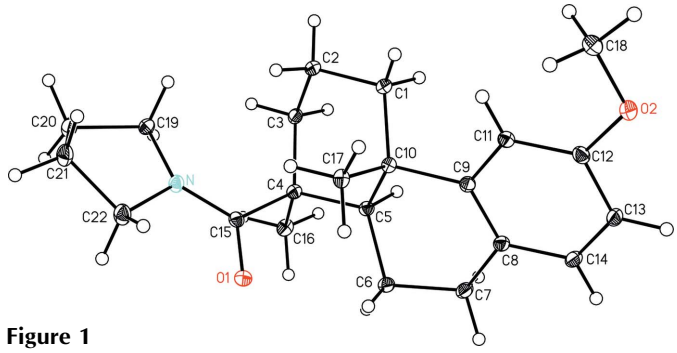


Figure 1
View of the molecular structure of (I), showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 20% probability level. H atoms are represented by circles of arbitrary size.

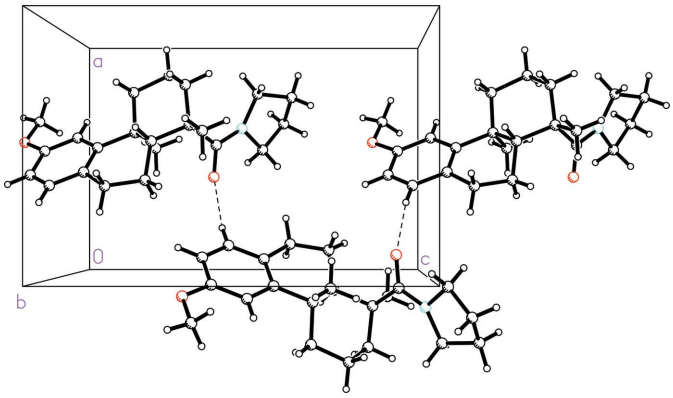


Figure 2
The molecular packing of (I), viewed along the *b* axis. Dashed lines indicate hydrogen bonds.

parameters of this derivative are similar to those observed previously (Bakare *et al.*, 2005). As previously reported (Couldwell *et al.*, 1985; Mondal *et al.*, 2003), ring *A* adopts the usual chair conformation, ring *B* is observed in the half-chair conformation and ring *C* is a planar aromatic ring. Since this compound was synthesized from natural podocarpic acid and the stereocenters were intact during the reactions, the stereochemistry of the compound is as shown. The heterocyclic pyrrrolidinyl ring, defined by atoms N/C19–C22, has an envelope geometry with atom C21 at the flap position, displaced by 0.610 (3) Å from the plane defined by atoms N/C19/C20/C22. There is a weak intermolecular C—H···O hydrogen bond between C14 and O1 (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 residue concentrated *in vacuo* to give a yellow oil (12-*O*-methylpodocarpoyl chloride, not analyzed). Dry benzene (5 ml) was added to the residue and the solvent removed again *in vacuo*. The acid chloride was added slowly to a stirred solution of pyrrolidine (in excess) in dry benzene (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 recrystallized from a solvent mixture of ethanol and distilled water (3:1 *v*/*v*) (m.p. 387–389 K). ^{1}H NMR ($CDCl_3$): δ 1.19 (3H, *s*), 1.32 (3H, *s*), 1.85 (2H, *bs*), 1.95 (2H, *bs*), 3.6. (4H, *bm*), 3.80 (3H, *s*), 6.65 (1H, *dd*), 6.80 (2H, *d*), 7.0 (1H, *dd*). EIMS: *m*/*s* 341 (M^+), 270, 228, 161.

Crystal data

$C_{22}H_{31}NO_2$
M_r = 341.48
Orthorhombic, $P2_12_12_1$
a = 9.2758 (18) Å
b = 14.886 (3) Å
c = 13.785 (3) Å
V = 1903.5 (7) Å^3
Z = 4
D_x = 1.192 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5585 reflections
θ = 2.6–28.0°
μ = 0.08 mm^{-1}
T = 93 (2) K
Chunk, colorless
0.75 × 0.45 × 0.25 mm

Data collection

Bruker SMART 1K CCD area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.626, T_{max} = 1.000
14559 measured reflections
2585 independent reflections
2279 reflections with $I > 2\sigma(I)$
R_{int} = 0.053
θ_{max} = 28.1°
$h = -12 \rightarrow 11$
$k = -19 \rightarrow 19$
$l = -18 \rightarrow 18$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.091
S = 1.05
2585 reflections
226 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0484P)^2 + 0.2838P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.003
$\Delta\rho_{max}$ = 0.28 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C15	1.234 (2)	N—C22	1.477 (2)
O2—C12	1.374 (2)	C19—C20	1.531 (2)
O2—C18	1.423 (2)	C20—C21	1.519 (3)
N—C15	1.361 (2)	C21—C22	1.522 (3)
N—C19	1.477 (2)		
C15—N—C19	130.98 (15)	N—C15—C4	122.82 (15)
C15—N—C22	117.05 (15)	N—C19—C20	103.16 (14)
C19—N—C22	110.91 (14)	C21—C20—C19	103.84 (14)
O1—C15—N	118.53 (16)	C20—C21—C22	101.91 (15)
O1—C15—C4	118.65 (16)	N—C22—C21	103.34 (16)
C19—C20—C21—C22	−40.9 (2)	C20—C21—C22—N	36.00 (19)
C19—N—C22—C21	−18.3 (2)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
C14—H14A···O1^{i}	0.95	2.44	3.377 (2)	169

Symmetry code: (i) $-x+\frac{3}{2}, -y+2, z+\frac{1}{2}$.

All H atoms were initially located in a difference Fourier map. The methyl H atoms were then constrained to an ideal geometry, with C—H distances of 0.98 Å and U_{iso}(H) = 1.5U_{eq}(C), but each group was allowed to rotate freely about its C—C bond. All other H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, with C—H distances in the range 0.95–1.00 Å and U_{iso}(H) = 1.2U_{eq}(C). In the absence of significant anomalous scattering effects, Friedel pairs were averaged.

Data collection: *SMART-NT* (Bruker, 2001); cell refinement: *SAINT-NT* (Bruker, 2001; data reduction: *SAINT-NT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997*a*); molecular graphics: *SHELXTL* (Sheldrick, 1997*b*); software used to prepare material for publication: *SHELXTL*.

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References

Bakare, O., John, N., Butcher, R. J. & Zalkow, L. H. (2005). *Acta Cryst.* E**61**, o3791–o3793.

Bruker (2001). *SMART-NT* (Version 5.624) and *SAINT-NT* (Version 6.04). Bruker AXS Inc., Madison, Wisconsin, USA.
Couldwell, M. C., Smith R. A. J. & Simpson, J. (1985). *Acta Cryst.* C**41**, 983–985.
Mondal, S., Mukherjee, M., Roy, A. & Mukherjee, D. (2003). *Acta Cryst.* C**59**, o132–o134.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
Sheldrick, G. M. (1997*a*). *SHELXL97*. University of Göttingen, Germany.
Sheldrick, G. M. (1997*b*). *SHELXTL*. Bruker AXS Inc, Madison, Wisconsin, USA.