Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

(3a*S*,5a*R*,10a*S*,11a*R*)-2,2-Dimethyl-3a,9,10,10a,11,11a-hexahydro-5a*H*-1,3-dioxolo[4,5:3′,4′]furo[2′,3′-*f*]-indolizin-8(4*H*)-one

Viktor Vrábel,[a]* Jozef Kožíšek,[b] Vratislav Langer,[c] Štefan Marchalín[d] and Mária Bobošíková[d]

[a]Department of Analytical Chemistry, Faculty of Chemical Technology, Slovak Technical University, Radlinského 9, SK-812 37 Bratislava, Slovak Republic, [b]Department of Physical Chemistry, Faculty of Chemical Technology, Slovak Technical University, Radlinského 9, SK-812 37 Bratislava, Slovak Republic, [c]Department of Environmental Inorganic Chemistry, Chalmers University of Technology, SE-41296 Göteborg, Sweden, and [d]Department of Organic Chemistry, Faculty of Chemical Technology, Slovak Technical University, Radlinského 9, SK-812 37 Bratislava, Slovak Republic

Correspondence e-mail: vrabel@cvt.stuba.sk

Key indicators

Single-crystal X-ray study
T = 183 K
Mean σ(C–C) = 0.003 Å
R factor = 0.035
wR factor = 0.082
Data-to-parameter ratio = 12.6

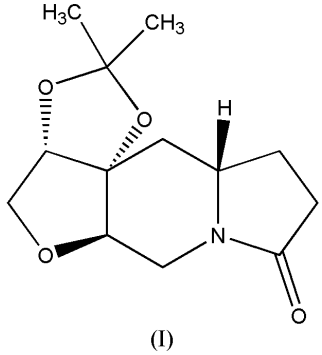
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 4 May 2004
Accepted 18 May 2004
Online 29 May 2004

In the crystal structure of the title compound, $C_{13}H_{19}NO_4$, there are two molecules in the asymmetric unit. The crystal which was used for collecting intensity data was twinned. The furoindolizine ring system adopts a fused envelope–chair–envelope conformation. The packing is stabilized by intermolecular C—H···O hydrogen bonds.

Comment

The synthesis of biologically active indolizine derivatives continues to attract the attention of organic chemists, because of their importance as pharmaceutical drugs, such as potential central nervous system depressants, calcium entry blockers, cardiovascular agents, spectral sensitizers and novel dyes (Gubin *et al.*, 1992; Poty *et al.*, 1994; Hema *et al.*, 2003). Several polyhydroxylated indolizines are interesting as inhibitors of glycosides (Hempel *et al.*, 1993; Brandi *et al.*, 1995). Indolizines have also been tested as antimycobacterial agents against mycobacterial tuberculosis (Gundersen *et al.*, 2003).



(I)

The structural investigation of the title compound, (I) (Fig. 1), has been undertaken as part of our study on the conformational changes caused by different substituents at positions on the furoindolizine ring system. Fig. 1 depicts the correct absolute configuration of the molecule as established by the synthesis of the compound. The asymmetric unit of (I) consists of two crystallographically independent molecules, *A* and *B*. The crystal structure was refined as a twin with orthorhombic pseudosymmetry, and the refined ratio of the two twin components is 0.578 (1):0.422 (1). The corresponding bond lengths and angles in the independent molecules (Fig. 1) agree with each other and are comparable to those in a related structure (Vrábel *et al.*, 2004).

The central six-membered ring is not planar and has a chair conformation (Cremer & Pople, 1975). It is puckered in such a manner that the four atoms C4, C5, C9 and C10 (C17, C18, C22 and C23 for molecule *B*) are coplanar to within 0.007 (2) Å [0.009 (2) Å for molecule *B*], while atoms N1 and

C3 (N2 and C16) are unequally displaced from this plane on opposite sides, with out-of-plane displacements of 0.582 (2) and −0.519 (2) Å, respectively [0.595 (2) and −0.525 (2) Å for molecule *B*]. The oxopyrrolidine ring has an envelope conformation, with atom C7 as the flap (C20 for molecule *B*). The deviations of atoms C7 and C20 from the mean plane of the remaining four atoms are 0.263 (3) and 0.260 (3) Å, respectively. There are three different types of intermolecular hydrogen bonds in the crystal structure. Atom C1 of molecule *A* is involved in weak intermolecular C—H···O interactions with atoms O6 and O7 of symmetry-related molecules *B*. Atoms C14 and C22 of molecule *B* act as donors for weak intermolecular C—H···O interactions with atom O2 of molecule *A*. A third type of intermolecular C—H···O interaction is between symmetry-related molecules *A*···*A*′ and *B*···*B*′ (Table 2).

Experimental

The title compound was prepared by stereoselective dihydroxylation under the usual conditions. To a stirred solution of (4a*S*,9a*S*)-2,4,4a,5,6,7,9,9a-octahydrofuro[2,3-*f*]indolizin-7-one (100 mg, 0.56 mmol) in acetone and water (5 ml, 5:1) was added an aqueous solution of OsO_4 (0.3 ml, 4%) dropwise. *N*-Methylmorpholine *N*-oxide (0.2 g, 1.7 mmol) was then added. The reaction was monitored by thin-layer chromatography (TLC). The excess OsO_4 was decomposed by the addition of $Na_2S_2O_4$ (0.2 g, 1.1 mmol). After removal of the solvent and drying the residue, freshly distilled dichloromethane (5 ml), 2,2-dimethoxypropane (0.3 ml, 2.4 mmol) and *p*-toluenesulfonic acid (50 mg, 0.3 mmol) were added under an argon atmosphere, again with TLC monitoring. The organic phase was twice extracted with water and dried over $MgSO_4$. The product was purified by column chromatography (dichloromethane and acetone, 9:1) and crystallized from acetone in 50% yield as a sole diastereomer. Colorless block-shaped single crystals were prepared by recrystallization from an ethanol solution.

Crystal data

$C_{13}H_{19}NO_4$
M_r = 253.29
Monoclinic, $P2_1$
a = 5.9465 (1) Å
b = 17.7167 (3) Å
c = 11.8918 (2) Å
β = 90.037 (1)°
V = 1252.83 (4) Å^3
Z = 4
D_x = 1.343 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 6898 reflections
θ = 3.2–30.9°
μ = 0.10 mm^{-1}
T = 183 (2) K
Needle, colorless
0.85 × 0.10 × 0.08 mm

Data collection

Bruker SMART CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2002)
T_{min} = 0.920, T_{max} = 0.992
22580 measured reflections
4637 independent reflections
4190 reflections with $I > 2\sigma(I)$
R_{int} = 0.043
θ_{max} = 32.9°
$h = -9 \rightarrow 9$
$k = -27 \rightarrow 26$
$l = -17 \rightarrow 18$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.035
$wR(F^2)$ = 0.082
S = 1.04
4637 reflections
368 parameters
Only H-atom U's refined
$w = 1/[\sigma^2(F_o^2) + (0.0447P)^2 + 0.0464P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.21 e Å^{-3}
$\Delta\rho_{min}$ = −0.18 e Å^{-3}

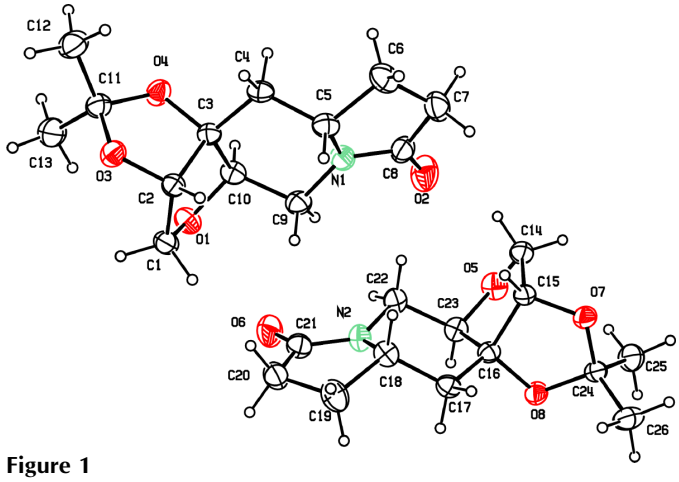


Figure 1
The asymmetric unit of (I), with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

Table 1
Selected geometric parameters (Å, °).

O1—C10	1.426 (3)	O5—C23	1.428 (3)
O1—C1	1.454 (3)	O5—C14	1.445 (3)
O3—C11	1.433 (3)	O7—C24	1.433 (3)
O4—C11	1.432 (3)	O8—C24	1.444 (2)
N1—C8	1.355 (3)	N2—C21	1.358 (3)
N1—C9	1.442 (3)	N2—C22	1.458 (3)
N1—C5	1.461 (3)	N2—C18	1.460 (3)
C10—O1—C1	106.96 (16)	C23—O5—C14	106.61 (16)
C2—O3—C11	109.00 (15)	C15—O7—C24	109.21 (15)
C8—N1—C9	125.3 (2)	C21—N2—C22	124.6 (2)
C9—N1—C5	118.15 (17)	C22—N2—C18	117.96 (16)
C10—C3—C2	103.40 (16)	C23—C16—C15	102.99 (16)
O2—C8—N1	125.2 (2)	O6—C21—N2	124.6 (2)
C11—O4—C3—C10	119.34 (19)	C24—O8—C16—C23	120.00 (17)
O3—C2—C3—C4	96.71 (19)	O7—C15—C16—C17	96.3 (2)
C3—C4—C5—N1	47.9 (2)	C16—C17—C18—N2	48.7 (2)
N1—C5—C6—C7	−19.7 (3)	N2—C18—C19—C20	−23.6 (3)
N1—C9—C10—O1	−162.63 (17)	N2—C22—C23—O5	−163.21 (17)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C1—H1*A*···O6^{i}	0.99	2.53	3.358 (3)	141
C1—H1*B*···O7^{ii}	0.99	2.47	3.359 (3)	150
C6—H6*B*···O2^{i}	0.99	2.58	3.476 (4)	150
C14—H14*A*···O2	0.99	2.50	3.324 (3)	141
C14—H14*B*···O3^{iii}	0.99	2.46	3.383 (3)	156
C22—H22*A*···O2	0.99	2.58	3.527 (3)	160
C26—H26*B*···O4^{iv}	0.98	2.54	3.498 (3)	166

Symmetry codes: (i) $x-1, y, z$; (ii) $x, y, 1+z$; (iii) $1+x, y, z-1$; (iv) $2-x, \frac{1}{2}+y, 1-z$.

H atoms were positioned geometrically and treated as riding atoms (C—H = 0.95–0.99 Å), with refined individual U_{iso} values. The absolute configuration could not be reliably determined for this compound using Mo radiation, and has been assigned on the basis of the synthesis; Friedel pairs were merged.

Data collection: *SMART* (Siemens, 1995); cell refinement: *SAINT* (Siemens, 1995); data reduction: *SAINT*; program(s) used to solve

structure: *SHELXTL* (Bruker, 2001); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*97.

This work was supported by the Grant Agency of the Slovak Republic (grants 1/9249/02 and 1/9255/02).

References

Brandi, A., Cicchi, S., Cordero, F. M., Frignoli, R., Goti, A., Picasso, S. & Vogel, P. (1995). *J. Org. Chem.* **60**, 6806–6812.
Bruker (2001). *SHELXTL*. Version 6.10. Bruker AXS Inc., Madison, Wisconsin, USA.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1362.
Gubin, J., Lucchetti, J., Mahaux, J., Nisato, D., Rosseels, G., Clinet, M., Polster, P. & Chatelain, P. (1992). *J. Med. Chem.* **35**, 981–988.
Gundersen, L. L., Negussie, A. H., Rise, F. & Ostby, O. B. (2003). *Arch. Pharm.* **336**, 191–195.
Hema, R., Porthasarathi, K., Nallu, M. & Linden, A. (2003). *Acta Cryst.* C**59**, o703–o705.
Hempel, A., Camerman, N., Mastropaolo, D. & Camerman, A. (1993). *J. Med. Chem.* **36**, 4082–4086.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Poty, C., Gibon, V., Evrard, G., Norberg, B., Vercauteren, D. P., Gubin, J., Chatelain, P. & Durant, F. (1994). *Eur. J. Med. Chem.* **29**, 911–923.
Sheldrick, G. M. (2002). *SADABS*. Version 2.03. University of Göttingen, Germany.
Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.
Siemens (1995). *SMART* and *SAINT*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Vrábel, V., Kožíšek, J., Langer, V. & Marchalín, Š. (2004). *Acta Cryst.* E**60**, o932–o933.