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Crystal and molecular structure of (9aS,10S)-6-Oxo-6,7,8,9,9a,10-hexahydro-4H-thieno--[2,3-b]quinolizin-10-yl acetate

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Abstract: The title compound, $C_{13}H_{15}NO_3S$, is a chiral molecule with two stereogenic centres. Its absolute configuration was derrived from the synthesis and confirmed by structure determination. The expected stereochemistry of atoms C5 and C6 was confirmed to be *S*. The central N-heterocyclic rings are not planar and adopt a half-chair conformation. A calculation of least-squares planes showed that these rings are puckered in such a manner that the five atoms C1, C2, C3, C5 and N1 (second ring: N1, C6, C7, C10 and C11) are planar, while atoms C4 (C5) are displaced from these planes with the out-of-plane displacement of 0.582 (3) Å and 0,666 (2) Å in the second ring, respectively. Dihedral angle between the planes of the central N-heterocyclic rings is 40.0 (1)°. Crystal structure is stabilized by C—H···O hydrogen interactions.

Keywords: crystal structure, hydrogen interactions, quinolizine, single-crystal X-ray study

Introduction

Hydroquinolizine derivatives continue to atract the attention of organic and medicinal chemists because of their potential application as pharmaceutical drugs for the treatment of diabetes (Kubo et al., 2000). Benzoquinolizine derivatives are interesting as selective non-steroidal inhibitors of steroid 5α-reductase-1 (Guarna et al., 2001). Selective inhibition of 5α-reductase-1is currently investigated as a potential therapeutic tool for the treatment of dihydrotestosterone-related skin disorders, such as acne, alopecia, male baldness and hirsutism (Harris & Kozarich, 1997).

Hydroquinolizine derivatives also known as coumarin are important in a wide range of biological activities. This nucleus is the basis of various compounds possessing anticoagulant and antiinflammatory activities. Coumarin derivatives are known as bioactive compounds with weak toxic, anti-carcinogenic, anticoagulant and antibiotic activities. Also, coumarin shows special applications in the improvement of laser dye stability under Eximer-Laser pumping in the visible and UV regions (Antonov & Hohla, 1983).

Based on these facts and on our interest in developing a simple and efficient route for the synthesis of novel quinolizine derivatives, we report here the crystal structure of the title compound (Fig. 1), which crystallizes in the centrosymetric monoclinic space group $P2_1/n$ as racemic mixtures (SS, RR) with one crystallographically independent molecule in asymmetric unit.

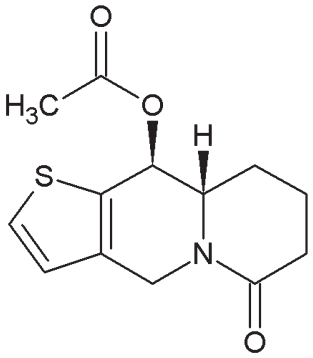

Fig. 1. Molecular structure of the title compound.

Experimental

The title compound (9aS,10S)-6-Oxo-6,7,8,9,9a,10-hexahydro-4H-thieno-[2,3-b]quinolizin-10-yl acetate was prepared according to a standard protocol described in literature (Šafář et al., 2016).

Geometry

All estimated standard deviations (esds) (except for the esd in the dihedral angle between two l.s. planes) were estimated using the full covariance matrix. The cell esds were taken into account individually in the

estimation of esds in distances, angles and torsion angles; correlations between esds in the cell parameters were only used when defined by crystal symmetry.

Refinement

Refinement of F^2 against all reflections. The weighted *R*-factor, *wR*, and the goodness of fit, S, are based on F^2, conventional *R*-factors, *R*, are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2s(F^2)$ was used only to calculate the *R*-factors(gt) etc. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on all data are even larger. All H atoms were positioned with idealized geometry using a constrained riding model with C—H distances in the range of 0.93–0.98 Å. The U_{iso}(H) values were set to 1.2 U_{eq}(C-aromatic) and 1.5 U_{eq}(C-methyl), respectively.

Data collection

Crystal data and conditions of data collection and refinement are reported in Tab. 1. CrysAlis CCD (Oxford Diffraction, 2009); cell refinement: CrysAlis RED (Oxford Diffraction, 2009); data reduction: CrysAlis RED (Oxford Diffraction, 2009); program(s) used to solve structure: SHELXS97 (Sheldrick, 2008); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: DIAMOND (Brandenburg, 2001); software used to prepare material for publication: enCIFer (Allen et al., 2004) and PLATON (Spek, 2009), WinGX (Farrugia, 1999).

Tab. 1. Experimental details.

Empirical formula	$C_{13}H_{15}NO_3S$
Formula weight	M_r = 265.32
Temperature	298(2) K
Wavelength	λ = 0.71073 Å, Mo K_α radiation,
Crystal system, space group	Monoclinic, $P2_1/n$
Unit cell dimensions	a = 8.2066 (3) Å
	b = 16.2865 (5) Å
	c = 10.2257 (4) Å
	β = 109.247 (4) °
Volume	V = 1290.34 (8) $Å^3$
Z, Calculated density	4, 1.366 Mg/m^3
Crystal size	0.25 × 0.30 × 0.35 mm
Reflections collected/unique	18976/2363; 1993 reflections with I > 2σ(I)
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2363/0/166
Goodness-of-fit on F^2	S = 1.09
Final R indices [I > 2σ(I)]	R1 = 0.040, wR2 = 0.118
Largest diff. peak and hole	0.30 and –0.26 e · A^{-3}
Monochromator	Graphite

Tab. 2. Selected geometric parameters: bond lengths [Å].

C1—N1	1.357 (2)	C8—C9	1.342 (3)
C1—C2	1.496 (3)	C9—C10	1.427 (3)
C2—C3	1.505 (4)	C1—O1	1.227 (3)
C3—C4	1.518 (3)	C6—O2	1.452 (2)
C4—C5	1.515 (3)	C12—O2	1.331 (2)
C5—C6	1.527 (2)	C10—C11	1.488 (3)
C5—N1	1.465 (2)	C12—O3	1.181 (3)
C6—C7	1.489 (2)	C12—C13	1.494 (3)
C7—S1	1.717 (2)	C11—N1	1.453 (2)
C8—S1	1.702 (3)	C7—C10	1.351 (3)

Tab. 3. Selected geometric parameters: bond angles [°].

N1—C1—O1	121.7 (2)	C8—C9—C10	112.9 (2)
O1—C1—C2	120.6 (2)	C10—C11—N1	110.4 (2)
N1—C1—C2	117.7 (2)	C9—C10—C11	126.2 (2)
C2—C3—C4	109.2 (2)	O2—C12—C13	111.7 (2)
C3—C4—C5	110.5 (2)	O2—C12—O3	122.8 (2)
C4—C5—C6	114.3 (2)	C7—C10—C9	112.0 (2)
C4—C5—N1	111.7 (1)	C7—C10—C11	126.2 (2)
C6—C5—N1	108.0 (1)	C5—C6—C7	109.3 (1)
C5—C6—O2	107.1 (1)	C1—N1—C11	119.2 (2)
C7—C6—O2	109.3 (1)	C1—N1—C5	126.3 (2)
C6—C7—S1	124.5 (1)	C11—N1—C5	114.5 (1)
C10—C7—S1	111.5 (1)	C6—C7—C10	124.0 (2)
O2—C12—O3	122.8 (2)	C6—O2—C12	119.0 (1)
C7—S1—C8	91.8 (1)	C7—O3—C12	107.4 (1)
C9—C8—S1	111.9 (2)		

Tab. 4. Hydrogen-bond geometry (Å, °).

D—H···A	D–H	H···A	D···A	D–H···A
C2—H2B···O3^{i}	0.97	2.40	3.291 (4)	151.7 (2)
C6—H6···O3	0.98	2.28	2.690 (3)	103.8 (1)
C11—H11B···O1	0.97	2.30	2.719 (3)	105.0 (1)

Symmetry codes: (i) –1/2 + x, 1/2 – y, –1/2 + z.

Results and Discussion

The absolute configuration is known from the synthesis and it was confirmed by the structure determination. The expected stereochemistry of atoms C5, C6 was confirmed to be S, S. Molecular geometry and the atom numbering scheme of the title compound are shown in Fig. 2. Crystal packing of the title compound is shown in Fig. 3 and geometric parameters are listed in Tab. 2 and Tab. 3.

Central N-heterocyclic rings are not planar and adopt a half-chair conformation with atoms C4 and C5 above the plane [0.582 (3) and 0.666 (2) Å, respectively] formed by the remaining five atoms N1, C1, C2, C3 and C5 (second ring: N1, C6, C7, C10 and C11), as confirmed by the ring-packering parameters (Cromer, Pople, 1975): Q = 0.493 (3) Å, θ = 128.1 (3)° and φ = 33.1 (4)° (Cremer-Pople puckering amplitude for second ring: Q = 0.500 (2) Å, θ = 50.1 (2)° and φ = 37.3 (3)°, respectively). Dihedral angle between the planes of the central N-heterocyclic rings is 40.0 (1)°. Atom N1 is sp^2-hybridized, as evidenced by the sum of the valence angles around it (360.0°). These data are consistent with the conjugation of the lone-pair electrons on N1 with an adjacent carbonyl, similar to the observed for amides.

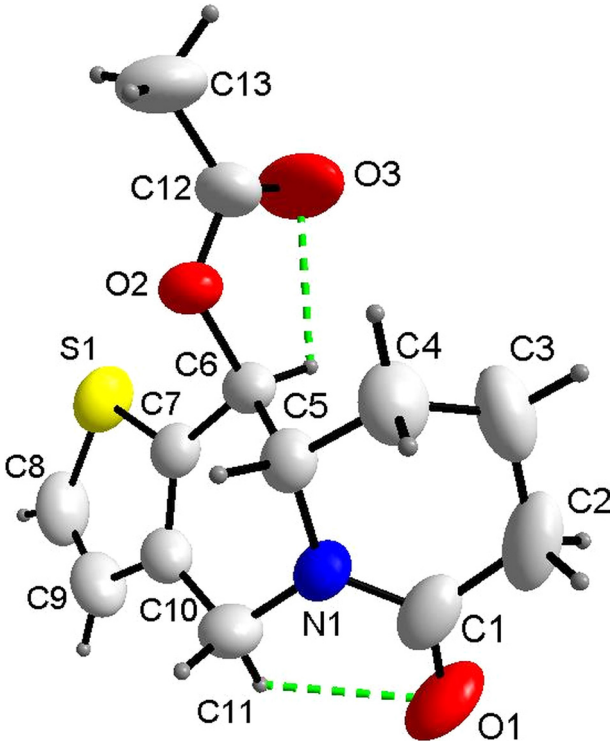

Fig. 2. Molecular structure of the title compound with the atom labelling scheme. Displacement ellipsoids are drawn at the 50 % probability level (Brandenburg, 2001). The intramolecular hydrogen interaction is shown as a dashed line.

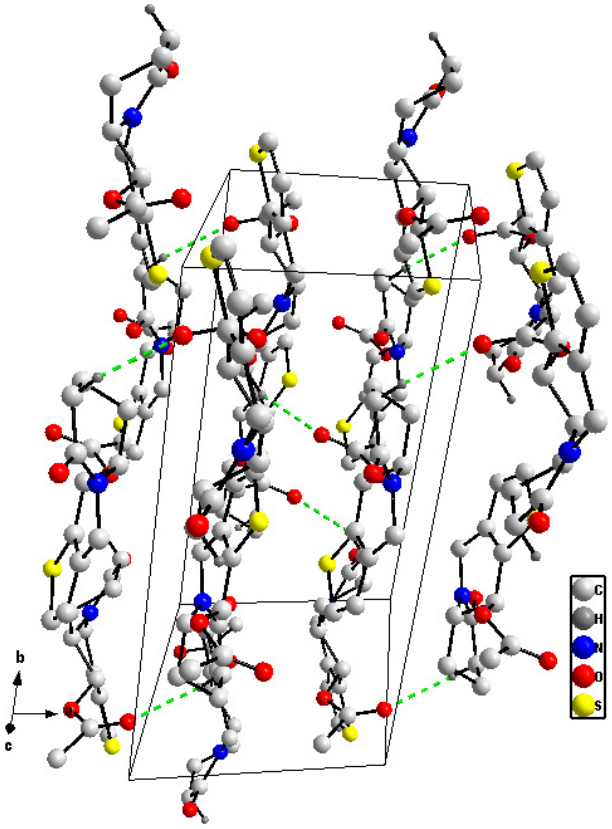

Fig. 3. Part of the crystal structure of the title compound, showing the formation of an intermolecular hydrogen interactions C(8) chain parallel to [100]. Green lines indicate hydrogen bonds. H atoms not involved in the motif have been omitted.

The crystal structure is stabilized by two intramolecular C6—H6···O3, C11—H11B···O1 and the intermolecular C2—H2B···O3 hydrogen interactions as H-atom donors, link the molecules into infinite C(8) (Bernstein et al., 1995) zigzag chains along the *a* axis (Figs. 2, 3 and Tab. 4). Bond length of the carbonyl group C1═O1 is 1.227 (3) Å which somewhat longer than typical carbonyl bonds. This may be due to atom O1 participating in intra- and intermolecular hydrogen interactions.

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