Crystal Structure and Absolute Configuration of Pendulone

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The complete structure of the title compound, C₁₇H₁₆O₆, isolated from the roots of *Oxytropis falcata* Bunge, was confirmed unambiguously by a single-crystal X-ray analysis. The absolute configuration was established by circular dichroism (CD). The bond distances and angles are within the expected ranges. The quinone ring is linked to the chroman ring by C(3) at an equatorial position. The crystal structure is also stabilized by intermolecular hydrogen bonds.

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There are more than 20 species of *Oxytropis* distributed in different regions of China. Most of the *Oxytropis* species are highly poisonous to livestock. For sheep and cattle, lengthy exposure will result in chronic intoxication with such symptoms as emaciation, acyesis, abortus, still birth or abnormalities, and may even cause death. To establish biomedical applications of the poisonous species, a careful phytochemistry investigation of the roots of *Oxytropis falcata* Bunge collected in China in 2006, was carried out by our group.

The air-dried roots of *O. falcata* (0.5 kg) were extracted three times (each for 7 days) successively with EtOH at room temperature. The resultant extract was concentrated under reduced pressure to yield a residue (90 g), which was suspended in water and fractionated by successive partitioning with petroleum ether (60 – 90°C), EtOAc and 1-BuOH. The EtOAc fraction (10 g) was subjected to repeated column chromatography. The title compound (20 mg), as one of the components, was isolated. The NMR and MS spectroscopy analysis of this compound disclosed its isoflavanquinone skeleton and pattern of substitution, which was determined to be 7-hydroxy-3',4'-dimethoxyisoflavanquinone, the first report of isoflavanquinone from this genus, previously identified as pendulone.¹ However, the absolute configuration remained unknown. The CD spectrum of pendulone, correlated with that of (3*R*)-Astragaluquinone,² exhibited a positive cotton effect in the 270 – 300 nm region. Thus, pendulone was defined unambiguously by its 3*R* absolute stereochemistry.

Leishmaniasis is endemic in tropical regions, currently

prevalent throughout the world, and in at least 88 countries.³ In a previous investigation, pendulone exhibited remarkable *in vitro* antileishmanial activity with an IC₅₀ value of 0.07 µg/ml.⁴ The interesting biological activity of the title compound has stimulated efforts toward a detailed X-ray analysis to disclose its inherent three-dimensional structure, and has provided scientists with tools to understand the biological mechanisms of action and to develop animal models for human diseases.

Red crystals suitable for an X-ray structural analysis were obtained by slowly evaporating from a petroleum ether-acetone solution at room temperature. The crystal and experiment data are given in Table 1. The structure was solved by direct methods and refined with anisotropic temperature factors for non-H atoms. All H atoms, except for that of the hydroxyl group, which was found from difference Fourier maps, were calculated geometrically. The atomic parameters of the non-hydrogen

Table 1 Crystal and experiment data

CCDC No. 676279
Formula: C ₁₇ H ₁₆ O ₆
Formula weight: 316.30
Crystal system: Orthorhombic
Space group: <i>P</i> 2 ₁ 2 ₁ 2 ₁ <i>Z</i> = 4
<i>a</i> = 7.2614(10) Å
<i>b</i> = 13.1656(18) Å
<i>c</i> = 15.635(2) Å
<i>V</i> = 1494.8(4) Å ³
Calculated density: 1.406 Mg/m ³
Temperature = 294(2) K
Absorption coefficient: 0.107 mm ⁻¹
<i>F</i> (0 0 0) = 664
Crystal size = 0.26 × 0.20 × 0.18 mm
θ range for data collection: 2.02 to 27.35°
Data/restraints/parameters: 3343/0/212
Goodness-of-fit on <i>F</i> ² : 1.042
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]: <i>R</i> 1 = 0.0394, <i>wR</i> = 0.0923
Extinction coefficient = 0.0055(13)
Largest diff. peak and hole: 0.125 and -0.127 e.Å ⁻³
Refinement method: Full-matrix least-squares on <i>F</i> ²

Fig. 1 Chemical structure of pendulone.

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Table 2 Atomic coordinates and equivalent isotropic displacement parameters

Atom	x	y	z	U(eq)
C(2)	11031(3)	4823(1)	1582(2)	55(1)
C(3)	8994(3)	4986(1)	1429(1)	41(1)
C(4)	8377(3)	4271(1)	716(1)	52(1)
C(5)	8377(3)	2373(1)	460(1)	51(1)
C(6)	8997(3)	1403(1)	609(1)	49(1)
C(7)	10406(3)	1250(1)	1185(1)	43(1)
C(8)	11192(3)	2069(1)	1600(1)	45(1)
C(9)	10552(3)	3042(1)	1433(1)	40(1)
C(10)	9121(3)	3217(1)	869(1)	41(1)
C(1')	8504(3)	6074(1)	1245(1)	41(1)
C(2')	6555(3)	6374(1)	1418(1)	44(1)
C(3')	6000(2)	7453(1)	1334(1)	44(1)
C(4')	7222(3)	8153(1)	1068(1)	43(1)
C(5')	9121(3)	7841(1)	835(1)	46(1)
C(6')	9657(3)	6776(1)	942(1)	47(1)
C(7')	3531(3)	7601(2)	2322(2)	76(1)
C(8')	5596(4)	9676(2)	1458(2)	72(1)
O(1)	11389(2)	3813(1)	1885(1)	58(1)
O(2)	11100(2)	307(1)	1371(1)	59(1)
O(3)	5415(2)	5737(1)	1622(1)	64(1)
O(4)	4193(2)	7676(1)	1456(1)	59(1)
O(5)	6957(2)	9157(1)	960(1)	58(1)
O(6)	10229(2)	8470(1)	572(1)	61(1)

$U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

atoms are listed in Table 2. Selected bond lengths, bond angles and torsion angles are given in Table 3.

In addition, as shown in Fig. 2, a distorted half-chair conformation of the dihydropyran ring can be observed from the deviations of the atoms O(1), C(2), C(3) and C(4) from the best least-squares plane through the benzene ring and from the torsion angle of the bond O(1)–C(2)–C(3)–C(4), $-63.8(2)^\circ$. The quinone ring is linked to the chroman ring by C(3) in an equatorial position.

The packing of the molecules is stabilized by a system of hydrogen bonds, which generates a catenulate framework that is much different from the helical arrangement along the c axis of its homologue Claussequinone.⁵ The molecules are linked head to tail by the only intermolecular hydrogen bond of $2.7945(19)\text{\AA}$ between O(2) of the hydroxyl group of one and O(6) of the carbonyl group of another. The O(2)–H and O(6)–H distance are 0.8200 and $2.0300\text{\AA}$, respectively, and the angle formed is 154.00° . There are two intramolecular C–H...O interactions [C7'...O3, $3.016(3)$, $2.823(3)$. H7'1...O3, H8'1...O4, 2.4500 , $2.3800\text{\AA}$ and C7'–H7'1...O3, C8'–H8'1...O4, 118.00 , 108.00°].

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Table 3 Selected bond lengths ($\text{\AA}$), bond angles ($^\circ$) and torsion angles ($^\circ$)

C(2)–O(1)	1.436(2)	C(2')–O(3)	1.222(2)
C(2)–C(3)	1.514(3)	C(3')–O(4)	1.358(2)
C(3)–C(1')	1.503(2)	C(4')–O(5)	1.346(2)
C(3)–C(4)	1.527(2)	C(5')–O(6)	1.225(2)
C(4)–C(10)	1.508(3)	C(7')–O(4)	1.441(3)
C(7)–O(2)	1.370(2)	C(8')–O(5)	1.431(2)
C(9)–O(1)	1.378(2)		
O(1)–C(2)–C(3)	111.15(15)	C(2')–C(1')–C(3)	116.21(16)
C(1')–C(3)–C(2)	113.37(16)	C(4')–C(3')–O(4)	122.16(18)
C(1')–C(3)–C(4)	112.23(15)	O(4)–C(3')–C(2')	117.24(17)
C(2)–C(3)–C(4)	108.32(17)	C(3')–C(4')–O(5)	128.15(18)
C(10)–C(4)–C(3)	110.30(15)	O(5)–C(4')–C(5')	111.93(17)
O(2)–C(7)–C(6)	122.97(17)	O(6)–C(5')–C(4')	120.36(17)
O(2)–C(7)–C(8)	117.08(17)	C(9)–O(1)–C(2)	115.67(14)
O(1)–C(9)–C(8)	115.84(15)	C(3')–O(4)–C(7')	116.11(17)
C(6')–C(1')–C(3)	125.42(17)	C(4')–O(5)–C(8')	119.89(17)
O(1)–C(2)–C(3)–C(1')	170.93(15)	C(4)–C(3)–C(1')–C(2')	79.6(2)
O(1)–C(2)–C(3)–C(4)	$-63.8(2)$	C(3)–C(1')–C(2')–O(3)	$-6.4(3)$
C(1')–C(3)–C(4)–C(10)	172.27(16)	C(3)–C(1')–C(2')–C(3')	174.12(16)
C(2)–C(3)–C(4)–C(10)	46.4(2)	C(3)–C(1')–C(6')–C(5')	$-175.52(17)$
C(2)–C(3)–C(1')–C(6')	23.0(3)	C(10)–C(9)–O(1)–C(2)	$-15.4(2)$
C(4)–C(3)–C(1')–C(6')	$-100.2(2)$	C(8)–C(9)–O(1)–C(2)	166.67(16)
C(2)–C(3)–C(1')–C(2')	$-157.24(17)$	C(3)–C(2)–O(1)–C(9)	47.9(2)

Fig. 2 Molecular structure of pendulone along with the labeling atoms. Displacement ellipsoids are drawn at the 30% probability level.

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