Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.041$
$wR(F^2) = 0.077$
$S = 0.72$
2453 reflections
163 parameters
H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.0190F_o^2)^2]$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.19$ e Å^{-3}
$\Delta\rho_{min} = -0.15$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 2. *Selected geometric parameters (Å, °) for (II)*

O1—C8	1.448 (3)	O2—C10	1.441 (3)
O4—C14	1.442 (3)	O3—C12	1.430 (3)
C8—C9	1.515 (3)	O2—C7	1.409 (3)
C13—C14	1.512 (3)	O3—C11	1.419 (2)
C9—C10	1.505 (3)	O1—C7	1.416 (3)
C12—C13	1.506 (3)	O4—C11	1.411 (2)
O1—C8—C9	109.9 (2)	O3—C12—C13	110.1 (2)
C8—C9—C10	108.7 (2)	C12—C13—C14	108.3 (2)
C9—C10—O2	109.6 (2)	C13—C14—O4	110.2 (2)
C7—O2—C10	110.9 (2)	C14—O4—C11	110.7 (2)
O2—C7—O1	111.5 (2)	O4—C11—O3	111.2 (2)
C7—O1—C8	111.3 (2)	C11—O3—C12	111.2 (2)
C6—C1—C7—O1	−102.2 (3)	C10—O2—C7—O1	−61.5 (2)
C6—C1—C7—O2	19.1 (3)	O2—C7—O1—C8	60.1 (3)
C1—C2—C11—O3	−156.9 (2)	C11—O3—C12—C13	58.4 (3)
C1—C2—C11—O4	82.4 (3)	O3—C12—C13—C14	−54.7 (3)
C3—C2—C11—O3	25.7 (3)	C12—C13—C14—O4	54.5 (3)
C7—O1—C8—C9	−56.5 (3)	C13—C14—O4—C11	−58.0 (3)
O1—C8—C9—C10	54.2 (3)	C14—O4—C11—O3	60.9 (3)
C8—C9—C10—O2	−55.5 (3)	O4—C11—O3—C12	−61.4 (3)
C9—C10—O2—C7	59.4 (3)		

For both compounds, the crystal-to-detector distance was 5.023 cm. Data were collected in groups of 606, 435, and 230 frames at ϕ settings of 0, 90, and 180°, respectively. Each exposure covered −0.3° in ω for 30 s for compound (I) and 20 s for compound (II). Crystals of compound (I), immersed in Krytox oil, were cut to appropriate dimensions with a razor. H atoms were placed at calculated positions and refined with a riding model (methylene C—H = 0.99, methine C—H = 1.00 and aromatic C—H = 0.95 Å). The U_{iso} value for each H atom was set at 1.2 times the equivalent isotropic displacement value of the C atom to which it is attached.

For both compounds, data collection: *SMART* (Bruker, 1997); cell refinement: *SMART*; data reduction: *SAINT-Plus* (Bruker, 1997); program(s) used to solve structures: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structures: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL/PC* (Sheldrick, 1997); software used to prepare material for publication: *SHELXTL/PC*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1202). Services for accessing these data are described at the back of the journal.

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Absolute configuration of isocurcumenol†

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Abstract

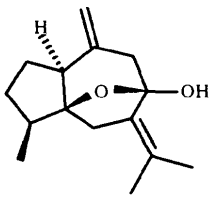
The absolute configuration of isocurcumenol, $C_{15}H_{22}O_2$ was determined as (3α,3aα,6α,8aβ). The C=C double bonds in the 5-isopropylidene and 8-methylene groups were confirmed. The molecules are arranged by intermolecular hydrogen bonds between the hydroxyl groups to form helices about 3_2 screw axes.

Comment

Isocurcumenol is a sesquiterpene found in *Curcuma sp.* (Zingiberaceae). It was isolated from *Curcuma zedoaria* Roscoe (Hikino *et al.*, 1969; Shiobara, Asakawa *et al.*, 1985), but was also found in *Curcuma kwangsiensis* S. G. Lee & C. F. Liang (Chen *et al.*, 1983), *Curcuma heyneana* Valeton & van Zijp (Firman, Kinoshita, Itai & Sankawa, 1988; Firman, Kinoshita & Sankawa, 1988), *Curcuma aeruginosa* Roxburgh (Zhang *et al.*, 1986; Zwaving & Bos, 1992), *Curcuma cochinchinensis* Gagnepain (Dung *et al.*, 1996), *Curcuma harmandii* Gagnepain (Dung *et al.*, 1997) and *Curcuma phaeocaulis* Valeton (Hou *et al.*, 1997). Crystals which deposited from zedoary oil were first reported by Haensel

† CAS Registry Number [24063-71-6]; CAS name: 3*S*-(3α,3aα,6α,8aβ)-octahydro-3-methyl-8-methylene-5-(1-methylethylidene)-6*H*-3a,6-epoxyazulen-6-ol. IUPAC name: (3α,3aα,6α,8aβ)-5-isopropylidene-3-methyl-8-methylene-3a,6-epoxyperhydroazulen-6-ol.

(1899*a*,*b*). Soon after this, elemental analysis (found: C 76.3, H 9.8, O 13.9%), melting point (415.5 K) and specific rotation [(+)- in alcoholic solution] were reported (Haensel, 1900). Hikino *et al.* (1966) suggested these crystals to be curcumol, although the reported specific rotation of curcumol is opposite to Haensel's report. We obtained a 100-year-old sample of crystals of the title compound, (I), deposited from zedoary oil. The structure determination shows these crystals to be isocurcumenol.



(I)

Accurate molecular dimensions for (I) were obtained from a measurement at 135 K using a CCD area detector with Mo $K\alpha$ radiation. The absolute configuration was determined from a second measurement performed with Cu $K\alpha$ radiation at room temperature (294 K) on an Enraf–Nonius CAD-4 diffractometer. The Flack x parameter (Flack, 1983) refined to $x = -0.03(13)$ in space group $P3_2$. Thus, the enantiomorphous space group $P3_1$ can be rejected at the 7.8σ significance level. The absolute configuration at the chiral centres is similar to those observed in the related compounds curcumol (Inayama *et al.*, 1984), curcumenol and oxycurcumenol (Firman, Kinoshita, Itai & Sankawa, 1988; Shiobara, Iwata *et al.*, 1985).

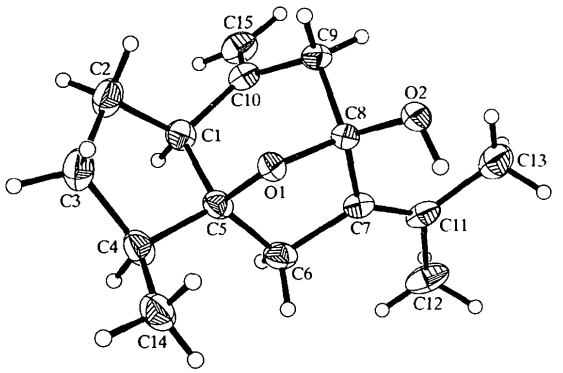


Fig. 1. The structure of (I) at 135 K, with 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms are drawn as spheres of an arbitrary radius.

The C7—C11 and the C10—C15 bonds correspond to double bonds. The five-membered ring labelled C1–C5 has a C5-*endo* envelope conformation, with C5 about 0.61 Å out of the plane through C1, C2, C3 and C4. The shortest intramolecular contact distance is 2.43 (1) Å between O2 and H13*B*. This distance approaches the van der Waals contact distance of 2.4 Å between O and H. There are no other short intramolecular contacts. The molecules are arranged by intermolecular hydrogen bonds between the hydroxyl groups to form infinite threefold helices running in the crystallographic c direction. There are no other significant intermolecular contacts.

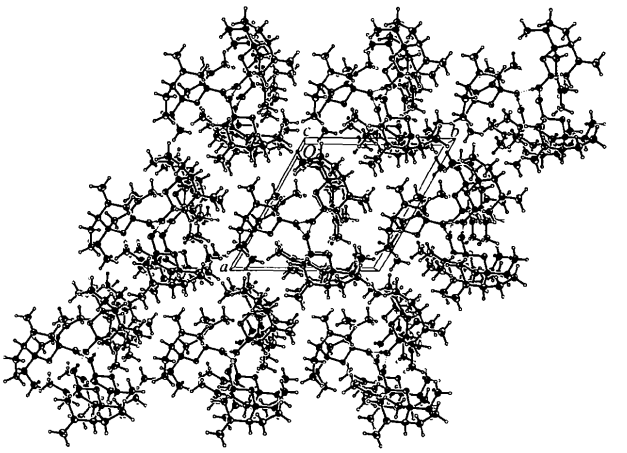


Fig. 2. The crystal packing of (I) at 135 K viewed along the c axis.

The conformation of the isocurcumenol molecule is very similar to the conformation observed for curcumol (Inayama *et al.*, 1984; Harimaya *et al.*, 1991). The only difference between the molecules is the C7—C11 bond, which is a single bond in curcumol and a double bond in isocurcumenol. Both structures have isomorphous crystal structures. The low value ($\pi = 0.0079$) of the unit cell similarity index defined by Kálmán *et al.* (1993) shows both crystal structures to be very similar. The conformation of the title compound is also rather similar to the conformation previously found for isocurcumol (Hakim *et al.*, 1993). In the latter case, C9—C10 is a double bond and C7—C11 and C10—C15 are single bonds.

Experimental

A sample of the title compound was obtained from the collection of the monastic school in Ettal (Bavaria, Germany). The label on the brown bottle read: 'Crystals deposited from zedoary oil, recrystallized from petrol ether; date: 22nd August, 1899; melting point: 144°C'. Spectroscopic data were in agreement with those reported for isocurcumenol (Firman, Kinoshita, Itai & Sankawa, 1988; Hikino *et al.*, 1969; Hou *et al.*, 1997). Crystals suitable for the diffraction experiments were obtained by slow evaporation of a solution of (I) in ethyl acetate at 277 K. Our determination of the melting point gave 415–416 K.

Compound (I) at 135 K

Crystal data

$C_{15}H_{22}O_2$
M_r = 234.33
Trigonal
$P3_2$
a = 12.0864 (15) Å
c = 7.9291 (11) Å
V = 1003.1 (2) Å^3
Z = 3
D_x = 1.164 Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 242 reflections
θ = 3–23°
μ = 0.075 mm^{-1}
T = 135 (2) K
Prism
0.55 × 0.50 × 0.50 mm
Colourless

Data collection

Siemens SMART CCD area-detector diffractometer
ω scans
Absorption correction: none
18 520 measured reflections
4093 independent reflections
3820 reflections with $I > 2\sigma(I)$

R_{int} = 0.053
θ_{max} = 31.7°
$h = -17 \rightarrow 15$
$k = -16 \rightarrow 17$
$l = -11 \rightarrow 10$
367 standard reflections
frequency: 540 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.034
$wR(F^2)$ = 0.095
S = 1.193
4093 reflections
243 parameters
H atoms refined isotropically
$w = 1/[\sigma^2(F_o^2) + (0.06P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.003
$\Delta\rho_{max}$ = 0.262 e Å^{-3}
$\Delta\rho_{min}$ = −0.184 e Å^{-3}

Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.023 (5)
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = 0.1 (6)

Table 1. *Hydrogen-bonding geometry (Å, °) for (I) at 135 K*

D—H···A	D—H	H···A	D···A	D—H···A
O2—H02···O2^{i}	0.86 (1)	2.10 (2)	2.960 (1)	176 (1)

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

Compound (I) at 294 K

Crystal data

$C_{15}H_{22}O_2$
M_r = 234.33
Trigonal
$P3_2$
a = 12.157 (3) Å
c = 8.050 (2) Å
V = 1030.3 (4) Å^3
Z = 3
D_x = 1.133 Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
λ = 1.54180 Å
Cell parameters from 25 reflections
θ = 16–38°
μ = 0.574 mm^{-1}
T = 294 (2) K
Prism
0.55 × 0.55 × 0.30 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
ω scans
Absorption correction: empirical *via* ψ scans (*MolEN*; Fair, 1990)
T_{min} = 0.770, T_{max} = 0.842
7333 measured reflections
2304 independent reflections
2279 reflections with $I > 2\sigma(I)$

R_{int} = 0.033
θ_{max} = 69.94°
$h = -14 \rightarrow 14$
$k = -14 \rightarrow 14$
$l = -7 \rightarrow 9$
3 standard reflections
frequency: 94 min
intensity decay: 7.8%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.027
$wR(F^2)$ = 0.088
S = 1.546
2304 reflections
243 parameters
H atoms refined isotropically
$w = 1/[\sigma^2(F_o^2) + (0.05P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.006
$\Delta\rho_{max}$ = 0.119 e Å^{-3}
$\Delta\rho_{min}$ = −0.087 e Å^{-3}

Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.036 (3)
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = −0.03 (13)

Data collection: *SMART* (Siemens, 1995) for (I) at 135 K; *CAD*-4 *Software* (Enraf–Nonius, 1989) for (I) at 294 K. Cell refinement: *SMART* for (I) at 135 K; *CAD*-4 *Software* for (I) at 294 K. Data reduction: *SAINT* (Siemens, 1995) for (I) at 135 K; *MolEN* (Fair, 1990) for (I) at 294 K. For both compounds, program(s) used to solve structures: *SHELXS*96 (Sheldrick, 1990); program(s) used to refine structures: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *XP* in *SHELXTL* (Sheldrick, 1996); software used to prepare material for publication: *SHELXL*97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: KA1324). Services for accessing these data are described at the back of the journal.

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Acta Cryst. (1999). C**55**, 1598–1599

The absolute configuration of an intermediate cyclic sulfoximine in the asymmetric synthesis of transition-state analog inhibitors of γ-glutamylcysteine synthetase

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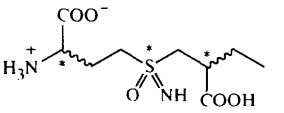
Abstract

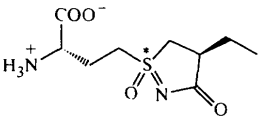
The crystal structure of a cyclic sulfoximine, 2-amino-4-(4-ethyl-1,3-dioxo-4,5-dihydro-1,2-thiazol-1-yl)butanoic acid, $C_9H_{16}N_2O_4S$, was determined to ascertain its stereochemistry. The absolute configuration of the chiral S atom was *S* on the basis of the (*S*)-α-carbon derived from the synthetic precursor, L-homocysteine.

Comment

We demonstrated that sulfoximine derivative (1), a rationally designed transition-state analog, served as



(1)



(2)

an extremely potent mechanism-based inactivator of γ-glutamylcysteine synthetase (γ-GCS, EC 6.3.2.2) (Katoh *et al.*, 1996). This compound, however, was composed of eight possible stereoisomers with respect to two chiral C and one chiral S atom. The inhibition of γ-GCS was reported to be highly dependent on the absolute configuration of the chiral S atom for buthionine sulfoximine, a well known inhibitor of γ-GCS (Campbell *et al.*, 1991). The chirality of the sulfoximine S atom was also important in the inhibition of glutamine synthetase, a mechanistically related synthetase, by methionine sulfoximine (Christensen *et al.*, 1969; Manning *et al.*, 1969; Neidle & Rogers, 1970; Meister, 1992). The establishment of the absolute configuration at the sulfoximine S atom not only helps us understand the detailed three-dimensional structure as an essential element for transition-state mimicry, but also provides evidence for the way in which the mechanism-based enzyme inactivation occurs. In the course of our stereoselective synthesis of sulfoximine (1), we separated two diastereomeric cyclic sulfoximines with respect to the chiral S atom, as a key intermediate (Tokutake *et al.*, 1998). We therefore determined the stereochemistry of one of the diastereomers, (2), by X-ray diffraction analysis to elucidate the relationship between the chirality of the S atom and the enzyme inhibitory activity of sulfoximine (1).

Because of the insolubility of cyclic sulfoximine (2) in water, crystals of (2) were obtained from a mixture of 0.5 *N* HCl–EtOH. The elemental analyses and X-ray diffraction analysis, however, showed that the crystals obtained were not of the HCl salt of sulfoximine (2), but of a zwitterionic amino acid. The molecular structure of cyclic sulfoximine (2) is shown in Fig. 1. The results confirmed clearly that the absolute configuration of the chiral S atom was *S*, based on the known chirality of the α-carbon (C2). The torsion angles in the five-membered ring are in the range 3.9 (2)–14.1 (3)°, indicating that the five-membered ring adopts a planar and not a half-chair

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