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Comment

Chlorojanerin, (I), was isolated from the ethanol extract of *Centaurea scoparia* Sieb. It belongs to the class of rare genuine chlorine-containing sesquiterpene lactones with a guaianolide skeleton, which bears the halogen at position C15, two hydroxy groups at positions C3 and C4, and two *exo*-methylene functions at C10 and C11, together with the 4-hydroxymethacryloyl moiety at C8. Members of the chlorine-containing natural compound family were frequently isolated from marine algae and fungi, but occasionally also identified in the Asteraceae as chlorinated sesquiterpene lactones (Engvild, 1986). Recently, the complete NMR data set, as well as the relative stereochemistry of chlorojanerin, has been reported (Youssef & Frahm, 1994), but no investigation of the absolute configuration has thus far been published. Chlorojanerin was first isolated from *Centaurea janeri* (Gonzalez, Bermejo, Gabrera, Galindo & Masanet, 1977) and its structure proposed on the basis of an incomplete set of ^1H NMR data. Neither the ^{13}C NMR data nor the relative stereochemistry of chlorojanerin were contained in this paper. The absolute configuration of chlorojanerin has been elucidated by means of X-ray diffraction analysis as (1*R*,3*S*,4*R*,5*S*,6*S*,7*R*,8*S*) and is presented here for the first time.

Acta Cryst. (1996). **C52**, 1791–1793

Absolute Configuration of Chlorojanerin,† a Chlorine-Containing Guaianolide from *Centaurea scoparia*

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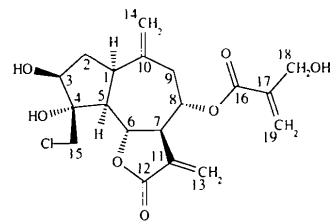
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(Received 23 October 1995; accepted 15 January 1996)

Abstract

The title guaianolide, chlorojanerin [(1*R*,3*S*,4*R*,5*S*,6*S*,7*R*,8*S*)-4-chloromethyl-3,4-dihydroxy-8-(4-hydroxymethacryloyl)-1*H*,5*H*,6*H*,7*H*-guaia-10(14),11(13)-dien-6,12-olide, C₁₉H₂₃ClO₇], was obtained from the ethanol extracts of the air-dried aerial flowering parts of the Egyptian plant *Centaurea scoparia* Sieb. Its absolute configuration has been elucidated by X-ray analysis, which confirms the structure as a chlorine-containing guaianolide with the 4-hydroxymethacryloyl function at the C8 position, as previously proposed on the basis of ^1H NMR and CD spectral evidence.

† IUPAC nomenclature: 9-chloromethyl-8,9-dihydroxy-3,6-bis(methylene)-2,3,3a,4,5,6,6a,7,8,9,9a,9b-dodecahydro-2-oxoazuleno[4,5-*b*]furan-4-yl 2-(hydroxymethyl)propenoate.



(I)

The dihedral angles H11—C1—C5—H51 (H1 α /H5 α) 42 (2), H51—C5—C6—H61 (H5 α /H6 β) -179 (2), H61—C6—C7—H71 (H6 β /H7 α) -140 (2) and H71—C7—C8—H81 (H7 α /H8 β) -173 (2) $^\circ$ (Table 3) give evidence of the *cis/anti/trans/trans*-junction of the five- and seven-membered rings, and the seven-membered and γ -lactone rings, as well as of the α -configuration of the ester moiety at position C8, together with the α orientation of the H atoms in positions 1, 3, 5 and 7, and the β orientation of the H atoms in positions 6 and 8 (Fig. 1). The hydroxy group in position 3 and the chloromethyl group in position 4 exist in a pseudo-equatorial, and the hydroxy group in position 4 and the ester moiety in position 8 in a pseudo-axial configuration, whereas the seven-membered ring assumes a distorted twist-chair-like conformation. The C6*S*/C7*R* *trans*-annulation of the γ -lactone ring is in agreement with the observed negative Cotton effect in the CD spectrum of chlorojanerin at 260 nm for the *n*- π^* transition of the α -methylene γ -lactone chromophore (Youssef & Frahm, 1996).

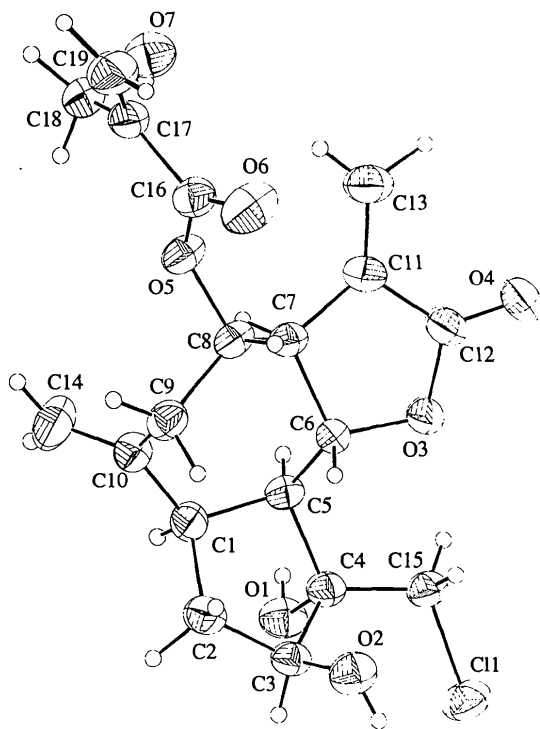


Fig. 1. Projection of chlorojanerin shown with 50% probability displacement ellipsoids for the non-H atoms.

Comparison of the X-ray diffraction and ¹H NMR data for chlorojanerin shows conformational differences between the crystal structure and that in solution. The dihedral angles between C—H bonds in the five-membered ring obtained from X-ray diffraction data differ from the values calculated from the corresponding vicinal coupling constants (³J) derived from the Karplus equation. The calculated dihedral angles within the seven-membered ring (Table 3) are in agreement with those derived from measured ³J values (estimated error for the NMR determination is ±10°), which indicates the similarity of the seven-membered ring conformations in both crystal and solution. Greater deviations, found for the dihedral angles H11—C1—C2—H21 (H1α/H2α), H21—C2—C3—H31 (H2α/H3α) and H22—C2—C3—H31 (H2β/H3α), could be due to the increased flexibility of the five-membered ring in solution. Three intermolecular hydrogen bonds were found involving hydroxy groups: O1—H1...O4ⁱ, O7—H3...O6ⁱⁱⁱ and O2—H2...O7ⁱⁱ (see Table 2).

Experimental

Chlorojanerin was isolated in 0.03% yield estimated for dry weight from the ethanol extract of the Egyptian plant *Centaurea scoparia* Sieb. by homogenization and solvent extraction followed by column chromatography of the crude extract on silica gel (Youssef & Frahm, 1994). Colourless

prisms were prepared by slow evaporation from a methanol solution [m.p. 451–453 K; [α]_D²⁵ +73.0° (c = 5.2, MeOH)].

Crystal data

C₁₉H₂₃O₇
M_r = 398.84
 Monoclinic
*P*2₁
a = 8.193 (5) Å
b = 10.546 (6) Å
c = 11.092 (6) Å
 β = 103.21 (4)°
V = 933.027 Å³
Z = 2
D_x = 1.420 Mg m⁻³
D_m not measured

Mo *K*α radiation
 λ = 0.71073 Å
 Cell parameters from 25 reflections
 θ = 3–16.5°
 μ = 0.24 mm⁻¹
T = 293 K
 Prism
 0.40 × 0.35 × 0.30 mm
 Colourless

Data collection

Syntex R3 four-circle diffractometer
 θ scans
 Absorption correction: none
 7467 measured reflections
 4275 independent reflections
 4026 observed reflections
 [*F* > 1.5σ(*F*)]

*R*_{int} = 0.0412
 θ_{max} = 27.5°
h = -10 → 10
k = -13 → 13
l = -14 → 14
 3 standard reflections monitored every 200 reflections
 intensity decay: none

Refinement

Refinement on *F*
R = 0.0354
wR = 0.0366
S = 2.34
 4026 reflections
 338 parameters
 All H-atom parameters refined
w = 1/[σ²(*F*) + 0.0003*F*²]
 (Δ/σ)_{max} = 0.01
 Δρ_{max} = 0.41 e Å⁻³
 Δρ_{min} = -0.32 e Å⁻³

Extinction correction: Larson (1970)
 Extinction coefficient: 583 (23)
 Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, Table 2.3.1)
 Absolute configuration: Flack (1983) parameter = -0.01 (5)

Table 1. Fractional atomic coordinates and equivalent isotropic displacement parameters (Å²)

$$U_{eq} = (1/3)\sum_i\sum_j U_{ij}a_i^*a_j^*a_i \cdot a_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{eq}
C11	0.95129 (7)	0.2081 (3)	0.81748 (5)	0.0523
O1	0.9264 (2)	0.3701 (3)	0.5916 (1)	0.0405
O2	1.1501 (2)	0.0766 (3)	0.6154 (2)	0.0450
O3	0.6598 (2)	0.0351 (3)	0.4630 (1)	0.0419
O4	0.4233 (2)	-0.0736 (3)	0.4359 (2)	0.0664
O5	0.6930 (2)	0.0420 (3)	0.0450 (1)	0.0398
O6	0.6875 (3)	-0.1668 (3)	0.0061 (2)	0.0630
O7	0.3525 (2)	0.1073 (3)	-0.1437 (2)	0.0538
C1	0.9672 (3)	0.2648 (3)	0.3630 (2)	0.0349
C2	1.1352 (3)	0.2194 (4)	0.4450 (2)	0.0431
C3	1.1099 (2)	0.2027 (3)	0.5760 (2)	0.0335
C4	0.9249 (2)	0.2365 (3)	0.5689 (2)	0.0319
C5	0.8332 (2)	0.2162 (3)	0.4310 (2)	0.0308
C6	0.7757 (2)	0.0830 (3)	0.3909 (2)	0.0307
C7	0.6767 (2)	0.0779 (3)	0.2543 (2)	0.0323
C8	0.7858 (3)	0.0252 (3)	0.1721 (2)	0.0348

C9	0.9517 (3)	0.0955 (3)	0.1889 (2)	0.0382
C10	0.9463 (2)	0.2326 (3)	0.2264 (2)	0.0372
C11	0.5217 (3)	0.0053 (3)	0.2597 (2)	0.0389
C12	0.5239 (3)	-0.0181 (3)	0.3910 (2)	0.0432
C13	0.3931 (3)	-0.0314 (4)	0.1717 (3)	0.0559
C14	0.9289 (4)	0.3240 (4)	0.1434 (2)	0.0592
C15	0.8465 (3)	0.1684 (3)	0.6614 (2)	0.0387
C16	0.6591 (3)	-0.0594 (3)	-0.0284 (2)	0.0385
C17	0.5835 (3)	-0.0219 (3)	-0.1582 (2)	0.0410
C18	0.5079 (3)	0.1068 (4)	-0.1825 (2)	0.0495
C19	0.5887 (4)	-0.1051 (4)	-0.2466 (2)	0.0600

Table 2. Selected geometric parameters (\AA , $^\circ$)

O3—C6	1.464 (2)	C5—C6	1.516 (3)	
O3—C12	1.336 (2)	C6—C7	1.548 (3)	
C1—C2	1.542 (3)	C7—C8	1.520 (3)	
C1—C5	1.554 (3)	C7—C11	1.496 (3)	
C1—C10	1.524 (3)	C8—C9	1.522 (3)	
C2—C3	1.524 (3)	C9—C10	1.508 (3)	
C3—C4	1.541 (3)	C11—C12	1.474 (3)	
C4—C5	1.557 (2)			
C12—O3—C6	112.0 (2)	C7—C6—O3	105.2 (1)	
C5—C1—C2	104.2 (2)	C7—C6—C5	112.2 (2)	
C10—C1—C2	113.6 (2)	C8—C7—C6	110.6 (2)	
C10—C1—C5	118.5 (2)	C11—C7—C6	103.7 (2)	
C3—C2—C1	107.5 (2)	C11—C7—C8	117.3 (2)	
C4—C3—C2	105.7 (2)	C9—C8—C7	112.3 (2)	
C5—C4—C3	105.4 (1)	C10—C9—C8	114.8 (2)	
C4—C5—C1	101.3 (1)	C9—C10—C1	119.0 (2)	
C6—C5—C1	111.7 (2)	C12—C11—C7	107.9 (2)	
C6—C5—C4	117.6 (2)	C11—C12—O3	109.9 (2)	
C5—C6—O3	110.9 (2)	C4—C15—C11	111.1 (1)	
D—H...A		D...A		D—H...A
O1—H1...O4 ⁱ		2.873 (3)		149 (3)
O2—H2...O7 ⁱⁱ		2.823 (3)		164 (3)
O7—H3...O6 ⁱⁱⁱ		2.888 (4)		177 (3)

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

Table 3. Conformation of chlorojanerin found in the crystal (X-ray) and in solution (^1H NMR) defined by the interproton dihedral angle $\varphi(\text{H}_i, \text{H}_j)$

H_i, H_j	$\varphi(\text{H}_i, \text{H}_j)$ (X-ray)	$^3J(\text{H}_i, \text{H}_j)$ (Hz)	$\varphi(\text{H}_i, \text{H}_j)$ (^1H NMR)*
H1 α /H2 α	-36 (2)	11.3	15
H1 α /H2 β	-154 (2)	7.5	145
H1 α /H5 α	42 (2)	8.5	40
H2 α /H3 α	8 (2)	6.1	30
H2 β /H3 α	123 (2)	0.0	90
H5 α /H6 β	-179 (2)	11.0	170
H6 β /H7 α	-140 (2)	9.0	135
H7 α /H8 β	-173 (2)	9.5	160
H8 β /H9 β	-35 (2)	5.0	40
H8 β /H9 α	82 (2)	1.5	80

* The sign of the interproton dihedral angle cannot be determined due to the periodicity of the Karplus relationship.

The structure was solved by direct methods. All H atoms were refined isotropically, with non-H atoms being refined anisotropically.

Data collection: Syntex R3 software. Cell refinement: Syntex R3 software. Data reduction: CRYSTALS (Watkin, Carruthers & Betteridge, 1985). Program(s) used to solve structure: SIR92 (Altomare *et al.*, 1994). Program(s) used to refine structure: CRYSTALS. Molecular graphics: CRYSTAN88 (Burzlaff & Rothammel, 1988). Software used to prepare material for publication: CRYSTALS and local software.

Financial support from BASF Aktiengesellschaft, Ludwigshafen, and Fonds der Chemischen Industrie are gratefully acknowledged. We also wish to thank Mr V. Brecht for carefully measuring the NMR spectra.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: CF1061). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Acta Cryst. (1996). **C52**, 1793–1795

(Bromodifluoromethyl)diphenylphosphine Sulfide

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(Received 14 March 1996; accepted 1 April 1996)

Abstract

The P—S bond in $\text{C}_{13}\text{H}_{10}\text{BrF}_2\text{PS}$ is somewhat shorter [1.9348 (11) \AA] and the P—CF₂Br bond longer [1.884 (3) \AA] than standard values, which may reasonably be attributed to the halogen substituents. The conformation about the P—CF₂Br bond is *gauche*.

Comment

Surprisingly few compounds containing the moiety $\text{Ph}_2\text{P}(=\text{S})\text{R}$ have been subjected to structure determi-