Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.015$
$wR(F^2) = 0.034$
$S = 1.127$
691 reflections
34 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0115P)^2 + 0.1774P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.23$ e Å^{-3}
$\Delta\rho_{\min} = -0.39$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)
Absolute structure: Flack (1983)
Flack parameter = 0.00 (5)

Table 1. *Selected geometric parameters (Å, °)*

I—C3	2.100 (5)	C1—C2	1.387 (4)
N—C1	1.337 (5)	C2—C3	1.386 (4)
N···I^{i}	2.988 (5)		
C1^{ii}—N—C1	115.2 (5)	C3—C2—C1	117.2 (4)
C1—N—I^{i}	122.4 (2)	C2—C3—C2^{ii}	119.8 (4)
N—C1—C2	125.3 (4)	C2—C3—I	120.1 (2)

Symmetry codes: (i) $x, y, 1 + z$; (ii) $-x, -y, z$.

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C1—H1···I^{i}	0.95	3.26	3.951 (4)	130.9
C1—H1···I^{ii}	0.95	3.51	4.165 (4)	127.9
C2—H2···N^{iii}	0.95	3.01	3.499 (4)	113.6

Symmetry codes: (i) $\frac{1}{4} + x, -\frac{1}{4} - y, \frac{3}{4} + z$; (ii) $\frac{1}{2} + x, y, \frac{1}{2} + z$; (iii) $\frac{1}{4} + x, -\frac{1}{4} - y, z - \frac{1}{4}$.

H atoms were included at calculated positions and refined using a riding model.

Data collection: *DIF*4 (Stoe & Cie, 1992*a*). Cell refinement: *DIF*4. Data reduction: *REDU*4 (Stoe & Cie, 1992*b*). Program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997). Molecular graphics: *XP* (Siemens, 1994*b*). Software used to prepare material for publication: *SHELXL*97.

We thank the Fonds der Chemischen Industrie for financial support and Mr A. Weinkauf for technical assistance.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1321). Services for accessing these data are described at the back of the journal.

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Acta Cryst. (1999). C**55**, 1310–1313

Colletoketol

ULRICH HÖLLER,[a] ANTHONY D. WRIGHT,[a]† GABRIELE M. KÖNIG[a]† AND PETER G. JONES[b]*

[a]*Institut für Pharmazeutische Biologie, Technische Universität Braunschweig, Mendelssohnstraße 1, 38106 Braunschweig, Germany, and* [b]*Institut für Anorganische und Analytische Chemie, Technische Universität Braunschweig, Postfach 3329, 38023 Braunschweig, Germany. E-mail: jones@xray36.anchem.nat.tu-bs.de*

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Abstract

The configuration of the title compound (6*R*,12*R*,14*R*)-(3*E*,9*E*)-12-hydroxy-6,14-dimethyl-1,7-dioxacyclotetradeca-3,9-diene-2,8,11-trione, $C_{14}H_{18}O_6$, at the two double bonds and three asymmetric centres has been confirmed. The α,β-unsaturated carbonyl functions depart significantly from planarity. The molecules are connected into layers parallel to the *xy* plane by one conventional and four C—H···O hydrogen bonds.

Comment

Research into new and biologically active natural products from marine sources also involves micro-organisms such as marine fungi. We recently isolated more than 1000 fungal strains from marine sponges and algae. One of the isolates was the obligate marine mitosporic fungus *Varicosporina ramulosa*, obtained from an unidentified alga of the genus *Cytoseira*, collected off Tenerife, Spain. Investigations of its culture extract yielded the five macrodiolides grahamimycin A$_1$, (1) (Ronald & Gurusiddaiah, 1980; Seidel & Seebach, 1982), colletoketol, (2) (MacMillan & Simpson, 1973), colletodiol, (3) (Grove *et al.*, 1966; MacMillan &

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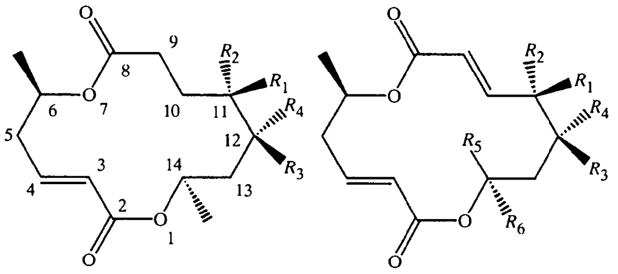
† Current address: Institute für Pharmazeutische Biologie der Universität Bonn, Nußallee 6, 53115 Bonn, Germany.

Simpson, 1973; Amstutz *et al.*, 1981), 9,10-dihydro-(6*R*,11*S*,12*S*,14*R*)-colletodiol, (4) (Ohta *et al.*, 1993) and 9,10-dihydro-(6*R*,11*R*,12*R*,14*R*)-colletodiol, (5), the last two being new fungal metabolites.



(1) R_1,R_2 = O; R_3,R_4 = O
(4) $R_1 = R_4$ = H; $R_2 = R_3$ = OH
(5) $R_1 = R_4$ = OH; $R_2 = R_3$ = H

(2) R_1,R_2 = O; $R_3 = R_5$ = H; R_4 = OH; R_6 = CH_3
(3) R_1 = OH; $R_2 = R_3 = R_5$ = H; R_4 = OH; R_6 = CH_3
(6) $R_1 = R_3 = R_4 = R_6$ = H; R_2 = OH; R_5 = CH_3

The structures of compounds (1), (3), (4) and (5) were elucidated mainly by NMR spectroscopy and degradation studies and by comparing their spectroscopic data and optical rotations with published values. Details of the structure elucidations and the spectroscopic data will be published elsewhere (Höller *et al.*, 1999). Compound (2) was found to have the same basic structure as both colletoketol and grahamimycin A on the basis of extensive one- and two-dimensional NMR studies. Whereas colletoketol possesses the 6*R*,12*R*,14*R* configuration (MacMillan & Simpson, 1973), the 6*R*,12*R*,14*S* configuration has been reported for grahamimycin A (Gurusiddaiah *et al.*, 1980). The possibility that colletoketol and grahamimycin A are identical also had to be considered (Gurusiddaiah & Ronald, 1981; Keck *et al.*, 1989). The ^{13}C NMR data for (2) were found to be in good agreement with values published for grahamimycin A, even though ^{1}H NMR data differed markedly. For colletoketol there appear to be no reported ^{13}C NMR data; other physical properties such as melting point and optical rotation proved in our investigations to be insufficient to determine unambiguously if (2) was identical with one of the two compounds in question. To resolve this issue a single-crystal X-ray-structure analysis of (2) was performed. The absolute configuration at C6 was determined to be *R* on the basis of alkaline hydroysis of (2), which yielded (−)-(5*R*)-hydroxy-(2*E*)-hexenoic acid as one of the main products (MacMillan & Simpson, 1973).

The structure of (2) (Fig. 1) is confirmed as the expected cyclotetradecadiene, with *E* configuration at both double bonds and *R* configuration at all three asymmetric centres. The torsion-angle sequence in the ring, starting at the O1—C2 bond and progressing to higher numbers, is $a_4g^+g^-g^+a_4g^-g^+g^-$, loosely regarding all values between 50 and 120° as '*gauche*' (see Table 1 for exact values). The α,β-unsaturated carbonyl systems of (2) show marked deviations from planarity; however, the groups O1, O21, C2, C3, C4, C5 and C11, O111, C10, C9, C8, O81 are both coplanar with a mean deviation of 0.1 Å. Otherwise, molecular dimensions are as expected.

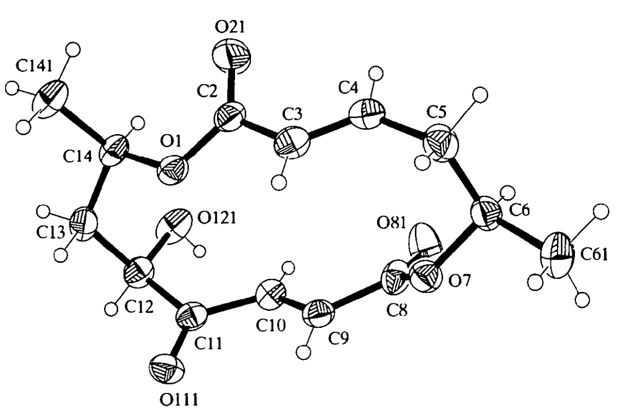


Fig. 1. View of the molecule of the title compound (2). Ellipsoids represent 50% probability levels. H atoms are of arbitrary radius.

In colletodiol, (3), the O atom at C11 is reduced to a hydroxyl function, the molecules being otherwise chemically identical (Amstutz *et al.*, 1981), but a closer spatial comparison is not possible because the coordinates of (3) are not available. A search for the ring system in the Cambridge Structural Database (version of October 1998; Allen & Kennard, 1993) revealed only one further example, namely a synthetic isomer of colletallol, (6) (Amigoni *et al.*, 1997), which was the goal of an enantioselective total synthesis. However, the ring conformation is markedly different from that of (2); converted to the numbering of (2) (Table 1), major torsion-angle differences are noted about several bonds, especially C4—C5 (−111°), C5—C6 (44°), C8—C9 (19°; pseudo-*E* rather than -*Z* about this bond with its partial double-bond character), C10—C11 (−113°), C12—C13 (142°) and C14—O1 (−80°). All values for the colletallol structure are calculated from coordinates extracted from the Cambridge Structural Database.

The molecules are linked in layers parallel to the *xy* plane by one conventional and four C—H···O hydrogen bonds (Table 2, Fig. 2). The keto O atom O111 acts as acceptor for three of these hydrogen bonds. In the colletallol isomer mentioned above (Amigoni *et al.*, 1997), inspection of the database coordinates reveals that the molecules are stacked parallel to the short *z* axis by a bifurcated hydrogen bond C2=O(···H—C3, ···H—C5), with short O111—H···O=C8 hydrogen bonds linking the stacks *via* a 2_1 operation.

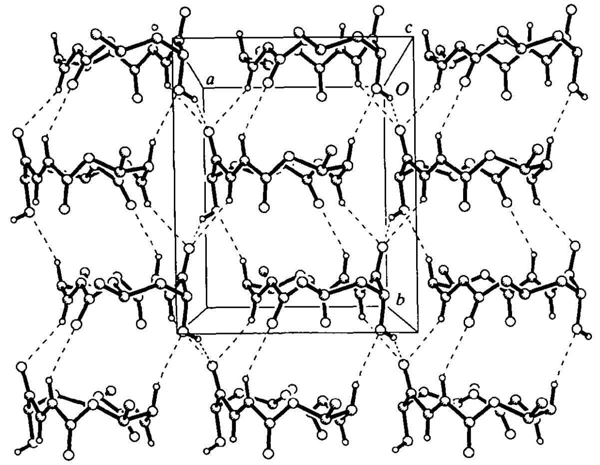


Fig. 2. Packing diagram of compound (2) with hydrogen bonds indicated by dashed lines. H atoms not involved in hydrogen bonds are omitted. Atoms are of arbitrary radius.

Experimental

Single crystals were grown from ethyl acetate.

Crystal data

$C_{14}H_{18}O_6$
$M_r = 282.28$
Orthorhombic
$P2_12_12_1$
$a = 7.765\,(1)$ Å
$b = 9.692\,(2)$ Å
$c = 18.855\,(3)$ Å
$V = 1419.0\,(4)$ Å^3
$Z = 4$
$D_x = 1.321$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 56 reflections
$\theta = 10$–$11.5°$
$\mu = 0.104$ mm^{-1}
$T = 143\,(2)$ K
Tablet
0.70 × 0.45 × 0.15 mm
Colourless

Data collection

Stoe Stadi-4 diffractometer
ω/θ scans
Absorption correction: none
3032 measured reflections
1892 independent reflections
1585 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.031$

$\theta_{\rm max} = 27.56°$
$h = -10 \rightarrow 4$
$k = 0 \rightarrow 12$
$l = 0 \rightarrow 24$
3 standard reflections
frequency: 60 min
intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.041$
$wR(F^2) = 0.103$
$S = 1.067$
1892 reflections
185 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0469P)^2 + 0.1913P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max} = 0.22$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.22$ e Å^{-3}
Extinction correction: *SHELXL*97 (Sheldrick, 1997)
Extinction coefficient: 0.029 (3)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Selected geometric parameters (Å, °)*

C3—C4	1.316 (3)	C9—C10	1.318 (3)
C8—C9	1.472 (3)	C10—C11	1.472 (3)
C14—O1—C2—C3	179.9 (2)	O7—C8—C9—C10	153.4 (2)
O1—C2—C3—C4	157.0 (2)	C8—C9—C10—C11	−166.6 (2)
C2—C3—C4—C5	−175.6 (2)	C9—C10—C11—C12	158.4 (2)
C3—C4—C5—C6	91.2 (3)	C10—C11—C12—C13	−111.1 (2)
C4—C5—C6—O7	−54.8 (3)	C11—C12—C13—C14	75.9 (3)
C5—C6—O7—C8	100.7 (2)	C2—O1—C14—C13	154.8 (2)
C6—O7—C8—C9	−154.2 (2)	C12—C13—C14—O1	−63.6 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C9—H9···O21$^{\rm i}$	0.95	2.48	3.306 (3)	145.6
C5—H5*A*···O121$^{\rm i}$	0.99	2.46	3.412 (3)	161.7
C4—H4···O111$^{\rm ii}$	0.95	2.50	3.375 (3)	153.3
O121—H121···O111$^{\rm iii}$	0.84	2.07	2.840 (2)	151.8
C10—H10···O111$^{\rm iii}$	0.95	2.59	3.389 (3)	142.6

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

H-atom treatment: hydroxy and methyl-H atoms as rigid groups (starting positions from difference syntheses, allowed to rotate but not tip), other H atoms riding. The absolute configuration could not be determined directly [the Flack (1983) parameter was indeterminate] and the Friedel opposites were therefore merged. However, the configuration at C6 was known from chemical degradation (see *Comment*).

Data collection: *DIF*4 (Stoe & Cie, 1992*a*). Cell refinement: *DIF*4. Data reduction: *REDU*4 (Stoe & Cie, 1992*b*). Program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997). Molecular graphics: *XP* (Siemens, 1994). Software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1328). Services for accessing these data are described at the back of the journal.

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X-ray investigations of benzopyran derivatives substituted at position 3

Agnieszka J. Rybarczyk,[a] Tomasz A. Olszak,[a] Magdalena Małecka[a] and Jolanta Nawrot-Modranka[b]

[a]*Department of Crystallography, University of Łódź, Pomorska 149/153, PL-90236 Łódź, Poland, and* [b]*Institute of Inorganic Chemistry, Medical University, Muszyńskiego 1, PL-90236 Łódź, Poland. E-mail: arybarcz@krysia.uni.lodz.pl*

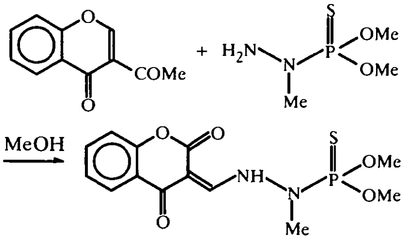
(*Received 20 January 1999; accepted 30 March 1999*)

Abstract

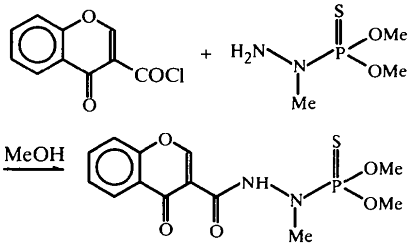
The structures of two isomeric compounds, (*E*)-3-{[2-(dimethoxythiophosphoryl)-2-methylhydrazino]methylidene}-3,4-dihydro-2*H*-1-benzopyran-2,4-dione, $C_{13}H_{15}N_2O_5PS$, and 3-{[2-(dimethoxythiophosphoryl)-2-methylhydrazino]carbonyl}-3,4-dihydro-4*H*-1-benzopyran-4-one, $C_{13}H_{15}N_2O_5PS$, have been determined from X-ray data and compared. The benzopyran moieties of both molecules are planar. Extra six-membered rings are formed by N—H···O hydrogen bonds. The geometry around the P atoms is tetrahedral, slightly deformed to trigonal pyramidal.

Comment

This paper opens X-ray studies on a group of benzopyran derivatives substituted with phosphorohydrazide at position 3. These compounds are expected to exhibit anticancer activity (Nawrot-Modranka & Graczyk, 1999). Investigations of (*E*)-3-{[2-(dimethoxythiophosphoryl)-2-methylhydrazino]methylidene}-3,4-dihydro-4*H*-1-benzopyran-4-one, (I), were undertaken to determine its tautomeric form in the crystal state, since H^1 NMR spectroscopy did not give conclusive information about its structure. Its isomer, 3-{[2-(dimethoxythiophosphoryl)-2-methylhydrazino]carbonyl}-3,4-dihydro-2*H*-1-benzopyran-2,4-dione, (II), was also studied. The study of (I) and (II) was carried out in order to obtain structural information about the conformation of the rings and the environment around the P atom in both molecules.



(I)



(II)

The title compounds differ from each other only in the position of the carbonyl O atom [O621 in (I) and O51 in (II)]. Their conformations are nearly the same.

The fused benzene and pyran rings are flat and almost coplanar. Both molecules are found with the amino NH group taking part in intramolecular hydrogen bonds, forming planar six-membered rings in both compounds; the maximum deviation from the best plane (Nardelli, 1996) is 0.020 (2) Å for (I) and 0.010 (1) Å for (II).

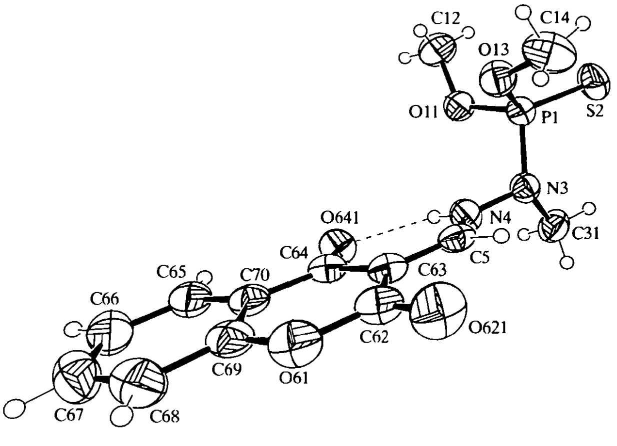


Fig. 1. *ORTEX* (McArdle, 1995) drawing of compound (I), showing the atomic numbering scheme and the intramolecular hydrogen bond. Displacement ellipsoids are shown at the 40% probability level and H atoms are shown as spheres of arbitrary radii.