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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: BK1168). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Absolute Configuration of 6-*O*-*p*-Bromobenzoylsalvileucolide Methyl Ester

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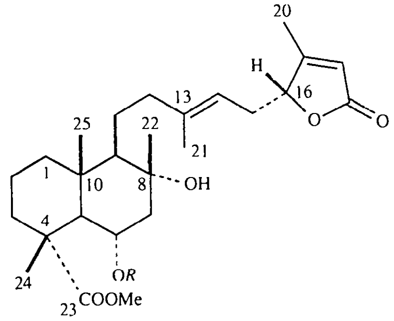
Abstract

The absolute configuration of the title compound, methyl 8-(4-bromobenzoyloxy)-5-[5-(2,5-dihydro-3-methyl-5-oxo-2-furanyl)-3-methyl-3-pentenyl]-6-hydroxy-1,4a,6-trimethyldecahydronaphthalene-1-carboxylate, $C_{33}H_{43}BrO_7$, a derivative of the sesterterpenoid salvileucolide methyl ester isolated from the aerial parts of two Iranian Salvia species, has been determined at 173 K. The compound belongs to the normal (10*R*) series and the configuration at C(16) is also *R*.

Comment

Salvileucolide methyl ester, (I), has been isolated as the major constituent from the aerial parts of *Salvia hypoleuca* (Rustaiyan, Niknejad, Nazarians, Jakupovic & Bohlmann, 1982) and *S. sahendica* (Matloubi Moghaddam, Zaynizadeh & Rüedi, 1995), both species being endemic to Iran. In the previous studies, the conformation of (I) was assigned by spectroscopic methods, especially by extensive ^1H and ^{13}C NMR experiments. The relative configuration at C(16) and the absolute configuration of the molecule, however, remained undetermined. Chemical transformation of (I) to an established reference compound (*e.g.* a suitable labdane derivative) and comparison of the chiroptical data would quite easily provide the absolute configuration of the skeleton. The determination of the stereochemistry at C(16) [*e.g.* by degradation of (I) to a 3-hydroxypentanoic acid derivative], however, is not expected to be unambiguously feasible without difficulties, probably due to racemization. This fact prompted us to undertake the X-ray analysis of the 6-O-*p*-bromobenzoyl ester, (II), where the Br atom greatly facilitates the direct determination of the absolute configuration. We now report the crystal structure of (II), which thereby establishes the structure of (I).



(I) *R* = H
(II) *R* = *p*-Br-benzoyl

The correct absolute configuration of (II), determined by refinement of the structure and the enantiopole parameter according to the method of Flack (1983), is depicted in Fig. 1. The compound has the 4*R*,6*S*,8*R*,9*R*,10*R*,13*E*,16*R* configuration. Therefore, as previously assumed (Rustaiyan *et al.*, 1982; Matloubi Moghaddam *et al.*, 1995), the natural product (I) belongs to the normal cyclic sesterterpenoid (10*R*) series and has an *R* configuration at C(16).

The bond lengths and angles generally have normal values. The two most significant exceptions are the values of 101.2 (4) and 130.3 (6)° for C(3)—C(4)—C(23) and C(18)—C(17)—C(20), respectively. These angles probably result from steric interactions between the two neighbouring ester groups in the first case and between the coplanar methyl group, C(20), and

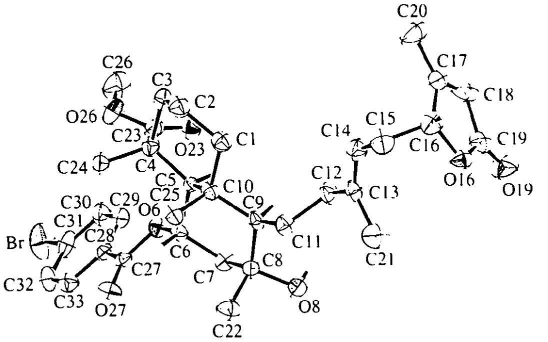


Fig. 1. View of the molecule of (II) showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. For clarity, only the H atoms at the chiral centres and that of the hydroxy group are included.

the H atom on C(17) in the latter case. The two cyclohexane rings form a slightly distorted double-chair conformation as shown by the ring torsion angles and the puckering parameter θ (Cremer & Pople, 1975), which is 9.9 (5) and 11.1 (5)° for the rings containing C(1) and C(6), respectively (an ideal chair has θ = 0°). Except for the methyl group at C(10), the heaviest substituents on the cyclohexane rings always occupy equatorial positions. The five-membered ring is planar, with a maximum deviation from the least-squares plane of 0.013 (5) Å. The bond lengths within the ring show that the O(16)—C(19) and C(18)—C(19) bonds have acquired some π-bond character.

An intermolecular hydrogen bond between the hydroxy group and the carbonyl O atom of the *p*-bromobenzoate group links the molecules into infinite one-dimensional chains which run parallel to the crystallographic *a* axis.

Experimental

The extraction and isolation of (I) was performed as described by Matloubi Moghaddam, Zaynizadeh & Rüedi (1995). For (II), a solution of (I) (13 mg, 0.029 mmol) and *p*-bromobenzoyl chloride (40 mg, 0.18 mmol) in pyridine (1 ml) was stirred overnight at 343 K. Column chromatography (silica gel, hexane–acetone 9:1 to 6:1) of the crude reaction product afforded (II) (18.5 mg, 100%). Recrystallization from hexane–Et_2O followed by hexane–acetone solution (diffusion method) yielded crystals which were suitable for X-ray analysis, m.p. 331–332 K (uncorrected); $[\alpha]_D$ +39.6° (EtOH, *c* 0.58); IR ν_{max} (cm^{-1}, $CHCl_3$): 2952 (CH), 1760 (sh), 1742, 1717 (γ-lactone, CO_2Me and CO_2-*p*-Br-phenyl), 1646 (C═C), 1273 (C—O); ^1H NMR (300 MHz, $CDCl_3$): δ 0.98 (*s*, 3H, H-25, *i.e.* H atoms at position 25), 1.16 (*s*, 3H, H-22), 1.27 (*s*, 3H, H-24), 1.68 (*s*, 3H, H-21), 2.08 (*s*, 3H, H-20), 2.18 (*dd*, 1H, J = 3.9, 12.2 Hz, H-7α), 2.32 (*dt*, 1H, J $\simeq$7, 15 Hz, H-15′), 2.47 (*d*, 1H, J = 11.6 Hz, H-5), 2.73 (*ddd*, 1H, J = 4.5, 7.5, 15 Hz, H-15), 3.39 (*s*, 3H, OMe), 4.91 (*t*, 1H, J = 5 Hz, H-16), 5.07 (*t*, 1H, J = 7.3 Hz, H-14), 5.24 (*dt*, 1H, J = 3.9, 11.4 Hz, H-6), 5.93 (*brs*, 1H, H-18), 7.57 and 7.80 (each *d*, each 2H, J = 8.5 Hz, *p*-Br-phenyl H); ^{13}C NMR (300 MHz, $CDCl_3$): δ 13.0 [C(20)], 16.2 [C(24)], 16.4 and 16.5 [C(21) and C(25)], 17.2 [C(2)], 23.1 [C(11)], 25.1 [C(22)], 30.2 [C(15)], 38.4 [C(3)], 38.5 [C(10)], 38.9 [C(1)], 42.6 [C(12)], 44.6 [C(4)], 49.7 [C(7)], 51.8 (OMe), 52.7 [C(5)], 60.0 [C(9)], 70.2 [C(6)], 73.3 [C(8)], 84.3 [C(16)], 116.4 [C(14)], 117.6 [C(18)], 128.2 and 129.3 (quaternary phenyl C), 131.3 and 131.6 (tertiary phenyl C), 141.0 [C(13)], 165.4 [C(27)], 168.2 [C(17)], 173.4 [C(19)], 179.3 [C(23)]; CIMS (NH_3) *m/z* (relative intensity): 650, 648 $[M + NH_4]^+$ (23), 632, 630 $[M]^+$ (1), 448 $[M - p\text{-Br-benzoyl}, (I)]^+$ (2), 431 (30), 430 $[M - p\text{-Br-benzoyl} - H_2O]^+$ (100).

Crystal data

$C_{33}H_{43}BrO_7$
M_r = 631.60
Orthorhombic
$P2_12_12_1$
a = 10.433 (2) Å
b = 33.313 (1) Å
c = 9.000 (4) Å
V = 3128 (1) Å^3
Z = 4
D_x = 1.341 Mg m^{-3}

Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 25 reflections
θ = 18.0–20.0°
μ = 1.364 mm^{-1}
T = 173 (1) K
Plate
0.48 × 0.38 × 0.14 mm
Colourless

Data collection

Rigaku AFC-5*R* diffractometer
ω scans
Absorption correction: empirical *via* ψ scan (North, Phillips & Mathews, 1968)
T_{min} = 0.760, T_{max} = 1.000
9448 measured reflections
7179 independent reflections
3771 observed reflections [$I > 2\sigma(I)$]

R_{int} = 0.042
θ_{max} = 27.5°
$h = 0 \rightarrow 13$
$k = -1 \rightarrow 43$
$l = -1 \rightarrow 11$
3 standard reflections monitored every 150 reflections
intensity decay: insignificant

Refinement

Refinement on F
R = 0.0511
wR = 0.0360
S = 1.458
3771 reflections
374 parameters
H atoms: see text
$w = 1/[\sigma^2(F_o) + (0.005F_o)^2]$
$(\Delta/\sigma)_{max}$ = 0.0004
$\Delta\rho_{max}$ = 0.64 e Å^{-3}
$\Delta\rho_{min}$ = −0.49 e Å^{-3}

Extinction correction: none
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)
Absolute configuration: Flack (1983) parameter = −0.02 (1)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
Br	0.23165 (5)	0.00655 (1)	0.74750 (9)	0.0717 (2)
O(6)	0.3963 (3)	0.18547 (9)	1.0625 (4)	0.029 (1)
O(8)	0.3150 (4)	0.3272 (1)	1.0133 (5)	0.040 (1)

O(16)	0.2476 (3)	0.48466 (8)	1.6209 (3)	0.037 (1)
O(19)	0.0492 (4)	0.4778 (1)	1.5292 (4)	0.058 (2)
O(23)	0.2467 (3)	0.17074 (9)	1.3412 (4)	0.044 (1)
O(26)	0.3964 (3)	0.12412 (9)	1.3787 (4)	0.047 (1)
O(27)	0.5532 (3)	0.18148 (9)	0.8895 (4)	0.035 (1)
C(1)	0.4830 (4)	0.2758 (1)	1.4900 (6)	0.033 (2)
C(2)	0.5384 (5)	0.2404 (2)	1.5783 (6)	0.040 (2)
C(3)	0.4704 (5)	0.2014 (2)	1.5366 (6)	0.037 (2)
C(4)	0.4701 (5)	0.1919 (1)	1.3672 (5)	0.029 (2)
C(5)	0.4331 (4)	0.2298 (1)	1.2769 (5)	0.021 (1)
C(6)	0.4451 (4)	0.2250 (1)	1.1098 (5)	0.026 (2)
C(7)	0.3691 (4)	0.2571 (1)	1.0288 (5)	0.029 (2)
C(8)	0.4100 (5)	0.2998 (1)	1.0691 (6)	0.030 (2)
C(9)	0.4188 (4)	0.3041 (1)	1.2404 (6)	0.028 (1)
C(10)	0.4959 (4)	0.2705 (1)	1.3208 (5)	0.026 (2)
C(11)	0.4532 (4)	0.3475 (1)	1.2883 (6)	0.034 (2)
C(12)	0.3530 (5)	0.3663 (1)	1.3925 (6)	0.038 (2)
C(13)	0.3923 (5)	0.4058 (1)	1.4603 (6)	0.032 (2)
C(14)	0.4050 (5)	0.4095 (1)	1.6056 (6)	0.042 (2)
C(15)	0.4379 (5)	0.4471 (2)	1.6895 (6)	0.050 (2)
C(16)	0.3196 (5)	0.4696 (1)	1.7465 (7)	0.042 (2)
C(17)	0.2236 (6)	0.4445 (1)	1.8303 (6)	0.041 (2)
C(18)	0.1151 (5)	0.4449 (1)	1.7585 (7)	0.049 (2)
C(19)	0.1251 (6)	0.4696 (2)	1.6243 (7)	0.042 (2)
C(20)	0.2602 (7)	0.4236 (1)	1.9695 (6)	0.068 (3)
C(21)	0.4093 (6)	0.4395 (1)	1.3514 (6)	0.057 (2)
C(22)	0.5292 (5)	0.3116 (2)	0.9796 (6)	0.042 (2)
C(23)	0.3578 (5)	0.1615 (1)	1.3566 (6)	0.035 (2)
C(24)	0.5994 (5)	0.1732 (1)	1.3230 (5)	0.038 (2)
C(25)	0.6417 (4)	0.2732 (1)	1.2846 (5)	0.032 (2)
C(26)	0.2915 (6)	0.0956 (2)	1.3998 (7)	0.063 (2)
C(27)	0.4601 (5)	0.1672 (1)	0.9503 (5)	0.026 (2)
C(28)	0.4026 (4)	0.1278 (1)	0.9091 (5)	0.026 (2)
C(29)	0.2942 (5)	0.1126 (1)	0.9766 (6)	0.035 (2)
C(30)	0.2437 (5)	0.0761 (1)	0.9305 (6)	0.041 (2)
C(31)	0.3028 (5)	0.0555 (1)	0.8175 (6)	0.042 (2)
C(32)	0.4125 (4)	0.0694 (1)	0.7502 (7)	0.042 (2)
C(33)	0.4614 (4)	0.1062 (1)	0.7967 (6)	0.036 (2)

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

O(16)—C(16)	1.447 (6)	C(8)—C(9)	1.551 (7)
O(16)—C(19)	1.373 (6)	C(9)—C(10)	1.557 (6)
O(19)—C(19)	1.198 (6)	C(9)—C(11)	1.550 (5)
C(1)—C(2)	1.535 (6)	C(11)—C(12)	1.537 (6)
C(1)—C(10)	1.539 (7)	C(12)—C(13)	1.509 (6)
C(2)—C(3)	1.527 (7)	C(13)—C(14)	1.320 (7)
C(3)—C(4)	1.557 (7)	C(14)—C(15)	1.503 (6)
C(4)—C(5)	1.549 (6)	C(15)—C(16)	1.532 (6)
C(5)—C(6)	1.517 (6)	C(16)—C(17)	1.507 (7)
C(5)—C(10)	1.558 (6)	C(17)—C(18)	1.303 (7)
C(6)—C(7)	1.518 (6)	C(18)—C(19)	1.466 (7)
C(7)—C(8)	1.528 (6)	C(27)—C(28)	1.492 (6)
C(6)—O(6)—C(27)	116.5 (4)	C(1)—C(10)—C(5)	108.3 (4)
C(2)—C(1)—C(10)	113.1 (4)	C(1)—C(10)—C(9)	109.4 (4)
C(1)—C(2)—C(3)	110.6 (4)	C(5)—C(10)—C(9)	106.9 (3)
C(2)—C(3)—C(4)	114.4 (4)	C(9)—C(11)—C(12)	113.0 (4)
C(3)—C(4)—C(5)	110.5 (4)	C(11)—C(12)—C(13)	114.7 (4)
C(3)—C(4)—C(23)	101.2 (4)	C(12)—C(13)—C(14)	120.6 (5)
C(4)—C(5)—C(6)	114.5 (4)	C(13)—C(14)—C(15)	126.7 (5)
C(4)—C(5)—C(10)	118.1 (4)	C(14)—C(15)—C(16)	113.1 (4)
C(6)—C(5)—C(10)	107.9 (4)	O(16)—C(16)—C(17)	103.7 (4)
C(5)—C(6)—C(7)	111.1 (4)	C(16)—C(17)—C(18)	108.9 (5)
C(6)—C(7)—C(8)	113.3 (4)	C(18)—C(17)—C(20)	130.3 (6)
C(7)—C(8)—C(9)	109.8 (4)	C(17)—C(18)—C(19)	110.6 (5)
C(8)—C(9)—C(10)	115.2 (4)	O(16)—C(19)—C(18)	106.8 (5)
C(1)—C(2)—C(3)—C(4)	54.3 (6)	C(5)—C(6)—C(7)—C(8)	58.2 (5)
C(1)—C(10)—C(5)—C(4)	−48.8 (5)	C(5)—C(10)—C(9)—C(8)	−56.2 (5)
C(2)—C(1)—C(10)—C(5)	54.9 (5)	C(6)—C(5)—C(10)—C(9)	61.7 (4)
C(2)—C(3)—C(4)—C(5)	−46.0 (6)	C(6)—C(7)—C(8)—C(9)	−48.1 (5)
C(3)—C(2)—C(1)—C(10)	−59.5 (5)	C(7)—C(6)—C(5)—C(10)	−64.5 (4)
C(3)—C(4)—C(5)—C(10)	44.5 (5)	C(7)—C(8)—C(9)—C(10)	48.9 (5)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O(8)—H(8)···O(27$^{\rm i}$)	0.71 (4)	2.25 (4)	2.883 (5)	150 (5)

Symmetry code: (i) $x - \frac{1}{2}, \frac{1}{2} - y, 2 - z$.

The data collection was extended to include the measurement of the intensities of the Friedel opposites of all reflections within the listed *hkl* range. Friedel pairs were not averaged during the data reduction so that the effects of anomalous dispersion could be used for the determination of the absolute configuration. Azimuthal scans of three reflections were used for an empirical absorption correction (North, Phillips & Mathews, 1968). The hydroxy H atom was located in a difference electron density map and was refined isotropically. All other H atoms were fixed at ideal positions [d(C—H) = 0.95 Å] with fixed isotropic displacement parameters of $1.2U_{\rm eq}$ of the parent C atom. The largest peaks of residual electron density (< 0.64 e Å^{-3}) were close to the Br atom. Elsewhere the largest peak was 0.34 e Å^{-3}. For the determination of the absolute configuration, the *CRYSTALS* program system (Watkin, Carruthers & Betteridge, 1985) was used to refine the final atomic coordinates together with the enantiopole parameter (Flack, 1983). The refined value of the enantiopole parameter was −0.02 (1), thus confirming that the atomic coordinates represented the correct enantiomorph.

MSC/AFC Diffractometer Control Software (Molecular Structure Corporation, 1991) was used for data collection and cell determination, and *TEXSAN* software (Molecular Structure Corporation, 1989) was used for data reduction, structure refinement and the preparation of publication material. The structure was solved using *SHELXS*86 Patterson methods (Sheldrick, 1990) and the Fourier expansion routine of *DIRDIF*92 (Beurskens *et al.*, 1992). Molecular graphics were produced using *ORTEP*II (Johnson, 1976).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates, torsion angles and complete geometry have been deposited with the IUCr (Reference: KA1151). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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