A NEW ROYLEANONE-TYPE DITERPENE FROM *SALVIA SESSEI*[1,2]

MANUEL JIMENEZ E.,* ENRIQUE PORTUGAL M., ALFONSO LIRA-ROCHA,
MANUEL SORIANO-GARCIA, and RUBEN A. TOSCANO

*Instituto de Química, Universidad Nacional Autónoma de México, Circuito Exterior,
Ciudad Universitaria, Coyoacán 04510, México, D.F.*

ABSTRACT.—A new royleanone-type diterpene quinone with a δ-lactone has been isolated from *Salvia sessei*. Its structure and relative configuration were determined by spectroscopic and chemical methods and by single crystal X-ray analysis.

To continue our studies (1) on the Labiatae family from Mexico, *Salvia sessei* Benth. was collected. This plant is a shrub 2 m in height, producing bright red flowers during the spring. From the Me_2CO extract of aerial parts a new royleanone-type diterpene was isolated; its structure was established as 7α-acetyl-12-hydroxyabieta-8,12-diene-11,14-dione-19,20-δ-lactone[3] [**1a**] on the basis of chemical, spectroscopic, and crystallographic data.

RESULTS AND DISCUSSION

Purification of the Me_2CO extract on charcoal gave the new diterpene that we call sessein [**1a**] as yellow crystals, mp 210° (yield 0.0073%). The molecular formula $C_{22}H_{26}O_7$ was obtained by elemental analysis and the molecular weight deduced from the mass spectrum. The mass spectrum did not exhibit a molecular ion peak but revealed the ion $[M - 60]^+$ (*m/z* 342) from the loss of an HOAc molecule (*m/z* 43, 100% for $[Ac]^+$). The ir spectrum showed hydroxyl and ester absorption bands. The absorption band at 1650 cm^{-1} showed the presence of *p*-benzoquinone moiety and at 1385 and 1375 cm^{-1}, an isopropyl group.

The absorption maxima in the uv spectrum at 270 and 407 nm supported the presence of a chromophore like that of royleanone [**2**] (2,3). The ^{1}H-nmr spectrum of **1a** did not show signals in the low-field region, so the quinone was substituted completely. The doublets at δ 1.18 and 1.23 (6H, *J* = 6 Hz) and the heptet at δ 3.15 (1H) were due to the protons of an isopropyl group. At δ 1.2 a singlet (3H) was attributed to a quaternary methyl group. The signal at δ 5.96 (dd, *J* = 1.5, 4 Hz) was assigned to H-7, which has a β-equatorial orientation and is the base proton of the acetate group (δ
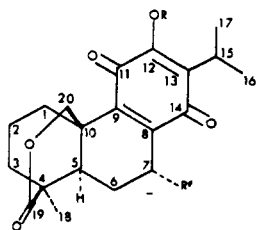
1a	R=H, R'=OAc
1b	R=Ac, R'=OAc
1c	R=H, R'=OH
1d	R=R'=H
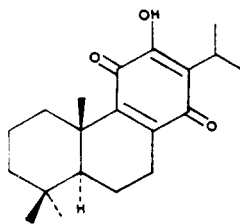
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[1]In memoriam: Dr. Jesús Romo Armería.

[2]Contribution No. 881 from Instituto de Química, UNAM.

[3]Systematic name: 2H-3,9b-propane-1H-naphtho[1,2-c]-pyran-2,6,9-trione-3,3a,4,5-tetrahydro-5-acetyl-8-hydroxy-3-methyl-7-(1-methylethyl)[9bS-*trans*-(3β,3aβ,5α,9bβ)].

2.05). Double resonance experiments and X-ray diffraction analysis supported this assignment. Two doublets for an AB system at δ 4.81 and 4.21 (2H, $J = 9$ Hz) were due to the C-20 methylene group of the δ-lactone. The B part of the system has an additional long-range interaction ($J = 1$ Hz). The irradiation of H-20's did not modify the C-18 methyl group signal, so the lactone closure is to C-20. The broad signal at δ 7.0 for the phenolic proton disappeared with D_2O. As additional chemical support, **1a** was acetylated to give **1b**. Basic hydrolysis of **1a** (K_2CO_3/MeOH) gave **1c**. The ir spectrum showed the presence of phenolic and secondary hydroxyl groups. Hydrogenolysis of **1a** (H_2, Pd/C) gave **1d**, which had lost the acetyl group. The reaction of **1a** with $NaBH_4$/MeOH gave **1d** as well. The ^1H-nmr signals of these products are listed in Table 1. The ^{13}C-nmr spectrum of **1a** supports the proposed structure (see Experimental). 1,2,5-Trimethyl-*p*-benzoquinone was used as a model in making these assignments (4). The relative stereochemistry of **1a** was confirmed by X-ray diffraction.

TABLE 1. ^1H-nmr Data of **1a–1d** (δ from TMS in $CDCl_3$, 80 MHz).[a]

Proton	Compound			
	1a	**1b**	**1c**	**1d**
H-7[b]	5.96 dd	5.95 dd	4.76 dd	
	(4, 1.5)	(4, 1.5)	(4, 1.5)	
H-15	3.15 heptet	3.11 heptet	3.15 heptet	3.15 heptet
	(6)	(6)	(6)	(6)
Me-16	1.23 d	1.21 d	1.21 d	1.20 d
	(7)	(7)	(7)	(7)
Me-17	1.18 d	1.21 d	1.23 d	1.21 d
	(7)	(7)	(7)	(7)
Me-18	1.20 s	1.25 s	1.3 s	1.28 s
H-20	4.81 d	4.9 d	4.81 d	4.83 d
(pro-*R*)	(9)	(9)	(9)	(9)
H-20[c]	4.21 dd	4.23 dd	4.21 dd	4.31 dd
(pro-*S*)	(9, 1.5)	(9, 105.)	(9, 1.5)	(9, 1.5)
12-OH	7.00 br s		7.1 br s	7.05 br s
7-OAc	2.05 s	2.08 s		
12-OAc		2.35 s		

[a]The coupling constants are in parentheses.
[b]$J_{6\alpha,7\beta}$ and $J_{6\beta,7\beta}$.
[c]J_{gem} and $J_{1\alpha,20}$.

The molecular structure is illustrated in Figure 1, and the coordinates are listed in Table 2.[4] Table 3 lists the bond lengths and angles. The cyclohexane ring exhibits a chair conformation. The average bond length and angle for the chair structure are 1.537(4) Å and 110.8(3)°, respectively, which agree with values obtained for cyclohexane (5). The average value of the torsion angle is 55.9(3)°. The methyl substituent at C-4 is equatorial. The cyclohexene ring adopts a half-chair conformation. The fusion to the cyclohexane ring is *trans* with torsion angles of 46.5(3) and −64.3(3)°, respectively. The angle between the plane of the cyclohexene ring and the acetate group at C-7 is 86.7(5)°. The δ-lactone ring can best be described as having a distorted chair conformation. The 1,4-benzoquinone ring shows normal geometry
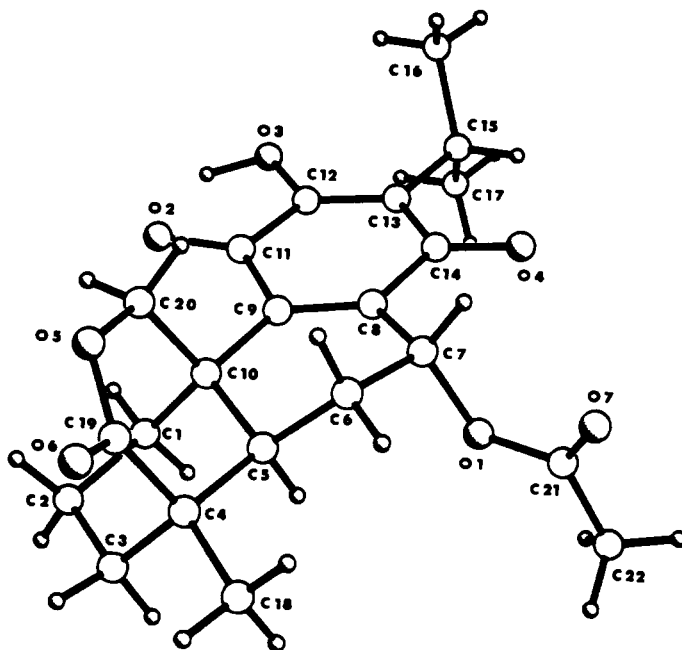
FIGURE 1. Molecular structure of sessein [**1a**].

TABLE 2.   Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Temperature Factors ($\mathring{A}^2 \times 10^3$) for **1a**.

Atom	x	y	z	U_{eq} [a]
O-1	7675(3)	4019(1)	10094(1)	53(1)*
O-2	4062(3)	6389(1)	8187(1)	56(1)*
O-3	1972(3)	7011(1)	9233(1)	55(1)*
O-4	3927(4)	4553(2)	10570(1)	75(1)*
O-5	6618(3)	4058(2)	7159(1)	74(1)*
O-6	8691(4)	3063(2)	6895(1)	80(1)*
O-7	7493(4)	2596(2)	10417(1)	84(1)*
C-1	8038(5)	5832(2)	8044(2)	54(1)*
C-2	9383(5)	5613(2)	7439(2)	62(1)*
C-3	10535(4)	4804(2)	7607(2)	56(1)*
C-4	9439(4)	3989(2)	7887(1)	46(1)*
C-5	8216(4)	4288(2)	8517(2)	43(1)*
C-6	7175(4)	3536(2)	8883(2)	51(1)*
C-7	6261(4)	3875(2)	9557(2)	49(1)*
C-8	5308(4)	4756(2)	9452(1)	45(1)*
C-9	5515(4)	5242(2)	8856(1)	42(1)*
C-10	6872(4)	5015(2)	8267(1)	42(1)*
C-11	4225(4)	6008(2)	8757(1)	42(1)*
C-12	3015(4)	6289(2)	9357(2)	45(1)*
C-13	2891(4)	5833(2)	9973(2)	46(1)*
C-14	4006(4)	5029(2)	10040(1)	50(1)*
C-15	1597(5)	6082(2)	10571(2)	53(1)*
C-16	−429(5)	6063(2)	10328(2)	62(1)*
C-17	2076(5)	6971(2)	10907(2)	71(1)*
C-18	10816(5)	3270(2)	8100(2)	67(1)*
C-19	8245(4)	3661(2)	7286(2)	56(1)*
C-20	5719(4)	4658(3)	7642(2)	56(1)*
C-21	8142(5)	3320(2)	10497(2)	58(1)*
C-22	9595(6)	3581(3)	11024(2)	84(2)*

[a]$*U_{eq} = (U_{11} \times U_{22} \times U_{33})^{1/3}$.

TABLE 3.   Bond Lengths (Å) and Angles (°) for Sessein [1a].

Bond lengths		Bond lengths	
O-1–C-7	1.454(4)	O-1–C-21	1.348(4)
O-2–C-11	1.222(3)	O-3–C-12	1.343(3)
O-4–C-14	1.238(4)	O-5–C-19	1.340(4)
O-5–C-28	1.437(4)	O-6–C-19	1.286(4)
O-7–C-21	1.196(4)	C-1–C-2	1.532(5)
C-1–C-10	1.549(4)	C-2–C-3	1.589(5)
C-3–C-4	1.552(4)	C-4–C-5	1.545(4)
C-4–C-18	1.523(4)	C-4–C-19	1.586(4)
C-5–C-6	1.524(4)	C-5–C-10	1.537(4)
C-6–C-7	1.517(4)	C-7–C-8	1.588(4)
C-8–C-9	1.348(4)	C-3–C-14	1.588(4)
C-9–C-10	1.517(4)	C-9–C-11	1.495(4)
C-10–C-20	1.537(4)	C-11–C-12	1.488(4)
C-12–C-13	1.358(4)	C-13–C-14	1.459(4)
C-13–C-15	1.509(4)	C-15–C-16	1.533(5)
C-15–C-17	1.528(5)	C-21–C-22	1.496(5)

Angles		Angles	
C-7–O-1–C-21	116.9(2)	C-19–O-5–C20	124.3(2)
C-2–C-1–C-10	112.0(2)	C-1–C-2–C-3	111.6(3)
C-2–C-3–C-4	115.3(2)	C-3–C-4–C-5	108.7(2)
C-3–C-4–C-18	108.5(2)	C-5–C-4–C-18	112.3(2)
C-3–C-4–C-19	107.3(2)	C-5–C-4–C-19	110.1(2)
C-18–C-4–C-19	109.8(3)	C-4–C-5–C-6	114.3(2)
C-4–C-5–C10	109.5(2)	C-6–C-5–C-10	110.8(2)
C-5–C-6–C-7	110.8(2)	O-1–C-7–C-6	109.0(2)
O-1–C-7–C-8	106.3(2)	C-6–C-7–C-8	112.7(2)
C-7–C-8–C-9	122.4(2)	C-7–C-8–C-14	115.4(2)
C-9–C-8–C-14	122.1(2)	C-8–C-9–C-10	123.8(2)
C-8–C-9–C-11	116.9(2)	C-10–C-9–C-11	119.1(2)
C-1–C-10–C-5	107.7(2)	C-1–C-10–C-9	111.7(2)
C-5–C-10–C-9	110.2(2)	C-1–C-10–C-20	111.4(2)
C-5–C-10–C-20	109.1(2)	C-9–C-10–C-20	106.6(2)
O-2–C-11–C-9	122.1(2)	O-2–C-11–C-12	118.4(2)
C-9–C-11–C-12	119.5(2)	O-3–C-12–C-11	115.4(2)
O-3–C-12–C-13	121.5(3)	C-11–C-12–C-13	123.0(3)
C-12–C-13–C-14	117.3(3)	C-12–C-13–C-15	123.7(3)
C-14–C-13–C-15	119.0(2)	O-4–C-14–C-8	117.6(3)
O-4–C-14–C-13	121.8(3)	C-8–C-14–C-13	120.5(2)
C-13–C-15–C-16	111.4(2)	C-13–C-15–C-17	112.8(3)
C-16–C-15–C-17	111.0(3)	O-5–C-19–O-6	117.3(3)
O-5–C-19–C-4	119.4(3)	O-6–C-19–C-4	123.3(3)
O-5–C-20–C-10	117.3(3)	O-1–C-21–O-7	123.2(3)
O-1–C-21–C-22	110.1(3)	O-7–C-21–C-22	126.7(3)

[a]Estimated standard deviations are given in parentheses.

(6,7), with average distances and angles of C-C 1.488(4), C=C 1.349(4), C=O 1.226(4) Å; C-C-C 120.0(2), C=C-C 119.8(3), and O=C-C 120.0(3)°.

Thus, it is established that **1a** is a diterpene of the royleanone type with a δ-lactone and is related to constituents of other *Salvia* species (8).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—All melting points were determined on a Fischer-Johns apparatus and are uncorrected. The uv spectra were recorded with a Perkin-Elmer 552 spectrophotometer and the ir spectra with Perkin-Elmer 283 and 681 spectrophotometers. The ^{1}H- and ^{13}C-nmr spectra were

recorded with a Varian FT-80A spectrometer. Mass spectra were measured with a Hewlett-Packard 5985 spectrometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter.

PLANT MATERIAL.—Aerial parts of *S. sessei* were collected on the México-Cuernavaca (km 40) Highway in June. The plant was identified by Dr. T.P. Ramamoorthy, Departamento de Botánica, Instituto de Biología, UNAM, México, and a voucher specimen was deposited in the MEXU Herbarium, Instituto de Biología, UNAM, México.

ISOLATION OF **1a**.—Dried leaves were extracted with Me_2CO. Evaporation of the solvent under reduced pressure gave a dark residue (49 g). A portion of the residue (5 g) was treated with charcoal. A yellow solid was obtained and was purified by repeated crystallization from Et_2O. This procedure afforded **1a** (750 mg) as yellow crystals, mp 208–210°, $[\alpha]^{25}D +89°$ ($c = 2$, $CHCl_3$); uv (MeOH) λ max nm (log ϵ) 208 (4.13), 270 (4.04), 407 (2.98); ir ($CHCl_3$, cm^{-1}) 3410, 1735, 1650, 1620, 1385, 1375; ^{13}C nmr (20.1 MHz, $CDCl_3$) 25.94 (C-1), 20.92 (C-2), 35.54 (C-3), 42.03 (C-4), 24.41 (C-5), 40.28 (C-6), 62.31 (C-7), 126.01 (C-8), 140.47 (C-9), 37.79 (C-10), 184.67 (C-11), 151.23 (C-12), 143.89 (C-13), 183.60 (C-14), 42.77 (C-15), 19.66 (C-16),* 19.89 (C-17),* 20.92 (C-18),* 174.58 (C-19), 73.51 (C-20). [*Interchangeable.]

ACETYLATION OF **1a**.—Compound **1a** (200 mg) was dissolved in pyridine (1 ml) and Ac_2O (1 ml). The reaction mixture was warmed on a steam bath for 1 h. The oily reaction product, after the usual workup, was purified by crystallization from EtOAc/hexane to afford **1b**, mp 194–197°, eims *m/z* (rel. int.) $[M - 42]^+$ 402 (3), $[M - 60]^+$ 384 (37); ir ($CHCl_3$, cm^{-1}) 1775, 1740, 1670, 1620, 1385, 1375.

BASIC HYDROLYSIS OF **1a**.—To a solution of **1a** (200 mg) in MeOH was added a K_2CO_3 solution (200 mg MeOH/H_2O). The yellow solution became deep violet. The reaction mixture was refluxed 1 h and concentrated. The residue was extracted with EtOAc. The organic phase was washed with 5% HCl followed by H_2O, dried over Na_2SO_4, and evaporated. The product reaction was crystallized from hexane to afford **1c** (140 mg), mp 114–116°; eims *m/z* (rel. int.) $[M]^+$ 360 (55.7), $[M - 18]^+$ 342 (65). Acetylation of **1c** afforded **1b**.

HYDROGENOLYSIS OF **1a**.—A solution of **1a** (100 mg) in EtOAc was treated with H_2 (Pd/C 5%) for 3 h. The reaction mixture was filtered and evaporated to give an oily product that was purified by preparative tlc on silica (hexane-EtOAc, 4:6) to afford **1d** (30 mg), which was crystallized from EtOAc, mp 175°; ir ($CHCl_3$, cm^{-1}) 3400, 1730, 1640, 1615.

REDUCTION OF **1a** WITH $NaBH_4$.—To a solution of **1a** (100 mg) in THF (5 ml, freshly distilled from $LiAlH_4$) was added $NaBH_4$ (100 mg). After 15 min, the reaction mixture was poured into H_2O, acidified with HCl, and extracted with EtOAc several times. The combined extracts were washed with H_2O, dried over Na_2SO_4, and evaporated. Compound **1d** crystallized from the oily residue.

X-RAY STRUCTURE DETERMINATION OF SESSEIN [**1a**].—Crystals of sessein ($C_{22}H_{26}O_7$, M_r 402.45) prepared by slow evaporation from Et_2O are orthorhombic, space group $P2_12_12_1$ with a = 7.225(2), b = 15.059(3), c = 18.803(3) Å, V = 2045.8(6) Å^3, and d_{calc} = 1.306 g/cm^3 for Z = 4. Graphite monochromatized CuKα radiation (λ = 1.5418 Å) was used to measure the intensity of the 1632 independent reflections for $2\theta < 115°$, of which 491 were observed $[I > 2.5\sigma(I)]$, on a crystal of $0.20 \times 0.20 \times 0.24$ nm with the aid of Nicolet R3m diffractometer, index range h 0↦7, k 0↦16, l 0↦20, ω-scan mode, variable scan speed, scan width 1.0° (θ), two standard reflections monitored every 50 measurements. No intensity decay was observed during the experiment. Intensities were corrected for Lorentz and polarization effects, but absorption was ignored. The crystal structure was solved by direct methods using SHELXTL (9), using 161|F| > 1.6, and refined by least-squares. In the final refinement, anisotropic thermal factors were used for the non-H atoms, and fixed isotropic temperature factors U = 0.06 Å^2 for the atoms riding on the bonded C atoms (C-H direction along bisector of C-C-C angle, C-H distance = 0.96 Å). The final discrepancy indexes were R = 0.036 and ωR = 0.055 for the 1491 observed reflections. In the last cycle (Δ/σ) max = 0.094; residual electron density was within -0.156 to 0.139 eÅ^{-3}, and the isotropic extinction parameter was X = 0.0054. Scattering factors were from International Tables for X-ray Crystallography (10). All computations were performed on a Nova 4S computer, and plots were drawn on a Tektronix plotter with the SHELXTL system of programs.

ACKNOWLEDGMENTS

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