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NEW HIGHLY OXIDIZED DITERPENE QUINONES FROM *Salvia fruticulosa* (LABIATAE)

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Abstract. The structures of fruticulins A and B, two highly oxidized diterpene quinones isolated from *Salvia fruticulosa*, were determined by spectroscopic methods, chemical transformations and X-ray crystallographic analysis of one of them. The free phenol derivative of fruticulin A was also isolated as a natural product.

Some years ago, the isolation and structural determination of icetexone, a rearranged abietane quinone isolated from *Salvia ballotaeflora* (Labiatae), was described.[1] *Salvia ballotaeflora* has been classified[2] in the Section *Tomentalle* of the Subgenus *Calosphace* of the *Labiatae* family. As a continuation of our systematic work on the phytochemistry of mexican Salvias,[3] we studied *Salvia fruticulosa* which also belongs to the Section *Tomentalle*.

Column chromatography over silica gel of the acetone extract of *S. fruticulosa* led to the isolation of fruticulins A and B and of the free phenol derivative of fruticulin A.

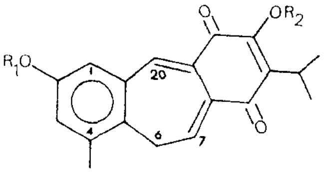
Fruticulin A, 1b, mp 190-193°C showed the molecular formula $C_{20}H_{20}O_4$ (m/z 324,$[M^+]$),which indicated a high degree of unsaturation. The IR and UV spectra[4] of 1b, were consistent with a highly conjugated quinonoid system. The ^1H NMR spectrum of 1b (Table 1) indicated the presence of an isopropyl group attached to the quinone ring. The presence (Table 1) of an aromatic methyl group, aromatic methoxy function and two aromatic protons in a *meta* relationship (two doublets, J=3 Hz) could only be explained if the A ring of fruticulin A is aromatic. A triplet observed at δ 6.95 (J=7 Hz) was assigned to H-7 and was shown to be coupled to the C_6 methylene (δ 3.1, J=7 Hz) by double resonance experiments. H-20 was observed as a sharp singlet at δ 8.10. The ^{13}C NMR spectrum of fruticulin A (Table 2) was consistent with the structure 1b proposed for it. The C_6 methylene was observed as a triplet at δ 28.42. Catalytic hydrogenation of 1b gave the dihydroderivative 2.

The structure 1b ascribed to fruticulin A is the first example of a diterpene quinone with an aromatic A ring and a seven-membered B ring. It can be biogenetically related to icetexone.[1] In order to corroborate the structure 1b proposed for fruticulin, the X-ray diffraction analysis of a single crystal of 1b was performed.

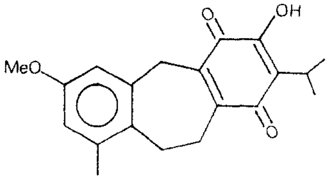
Crystals of fruticuline A are triclinic, space group P $\bar{1}$, with a=7.569 (3), b=9.271 (5), c=12,280 (6) Å, α=83.97 (4), β=77.68 (3), γ=81.05 (3)°, Z=2, Vc=829.3 (1), F(000)=344, Dcalc= 1.30 g cm^{-3}, λ(MoKα)=0.7107 Å, μ=0.84 cm^{-1} and T=293°K. The three dimensional data were measured on a Nicolet R3m four-circle diffractometer using ω-scan mode. A total of 2158 independent reflections were measured with $3<2\theta<45°$, of which 1810 were considered observed with $I>2.5\sigma(I)$. The structure was solved by combination of direct methods and partial structure expansion by an iterative E-Fourier procedure using SHELXTL programs.[5] The structure was refined by least-squares techniques, anisotropic refinement for all non-H atoms; H atoms riding on bonded C with fixed isotropic temperature factor, U=0.06 Å^2. The final discrepancies indices are R=0.045 and ωR=0.066. In the last cycle $(\Delta/\delta)_{max}$=0.060 and $\Delta\rho$ from -0.18 to +0.23eÅ^{-3}. Isotropic extinction parameter X=0.0046 and scattering factors from International Tables for X ray Crystallography (1974).[6] Figure 1 is a computer generated perspective drawing of the final X-ray model.[7]

Demethyl fruticuline A, 1a, was the most abundant diterpenoid product isolated from *S. fruticulosa* (0.01% dry weight). It showed mp 200-203°C and molecular formula $C_{19}H_{18}O_4$ (m/z 310, M$^+$). Acetylation of 1a (Ac$_2$O,AcONa r.t.) gave the diacetate 1c. Treatment of 1a with acetic anhydride and boron trifluoride etherate gave the hexaacetate 3. Its spectral data (IR,[8] ^{1}H and ^{13}C NMR, Tables 1 and 2) are in agreement with the structure 1c proposed.

Fruticuline B, showed mp 173-174°C and molecular formula $C_{19}H_{18}O_4$ (m/z 310, M$^+$). Its IR, UV[9] and ^{1}H NMR spectra, (Table 1) are consistent with the phenanthrene quinone structure 4 proposed for it. This *bis nor*-diterpene quinone could be biogenetically derived from fruticuline A, 1b, therefore it can be considered of an abietanoid origin.



1a $R_1=R_2=H$
1b $R_1=Me, R_2=H$
1c $R_1=R_2=Ac$



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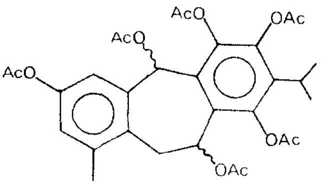

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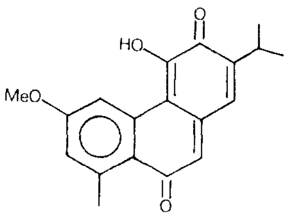

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TABLE 1. ^{1}H NMR SPECTRAL DATA OF DITERPENOID CONSTITUENTS OF *S. fruticulosa* AND DERIVATIVES

	1a	1b	1c	2	*3	4
H-1	6.81 d (3)	6.97 d (3)	7.1 br s§	6.6 br s§	7.15 d (3)	7.1 br s§
H-3	6.75 d (3)	6.82 d (3)	7.1 br s§	6.6 br s§	6.9 d (3)	7.1 br s§
H-6	3.1 d (7)	3.1 d (7)	3.15 d (8)	2.95 m	3.5 dd (15,6) 3.95 dd (15,1)	
H-7	6.92 t (7)	6.95 t (7)	6.92 t (8)	2.9 m	6.55 dd (6,1)	8.4 s
H-14	- -	- -	- -	- -	- -	8.6 s
H-20	8.0 s	8.10 s	8.1 s	3.95 t (2)	7.5 br s	- -
3H-18	2.35 s	2.35 s	2.45 s	2.32 s	2.0 br s	2.7 s
-OH ring C	7.65 s	7.60 s	- -	7.15 s	- -	7.5 s
-OH ring A	5.4 bs	- -	- -	- -	- -	- -
i-propyl	3.35 spt(7)	3.35 spt(7)	3.5 spt(7)	3.12 spt(7)	3.1 spt(7)	3.45 spt(7)
group	1.25 d (7)	1.25 d (7)	1.25 d (7)	1.20 d (7)	1.25 d (7)	1.35 d (7)
-O Me	- -	3.8 s	- -	3.75 s	- -	3.95 s
-OCOMe	- -	- -	2.4 s 2.3 s	- -	1.45 -2.2**	- -

Run at 80 MHz using $CDCl_3$ as solvent unless otherwise stated, and TMS as internal standard. Coupling constants in Hz are in parenthesis. Chemical shifts are in δ values.
* Run as C_6D_6 solution at 70°C. ** Six methyl signals. § Overlapped signals.

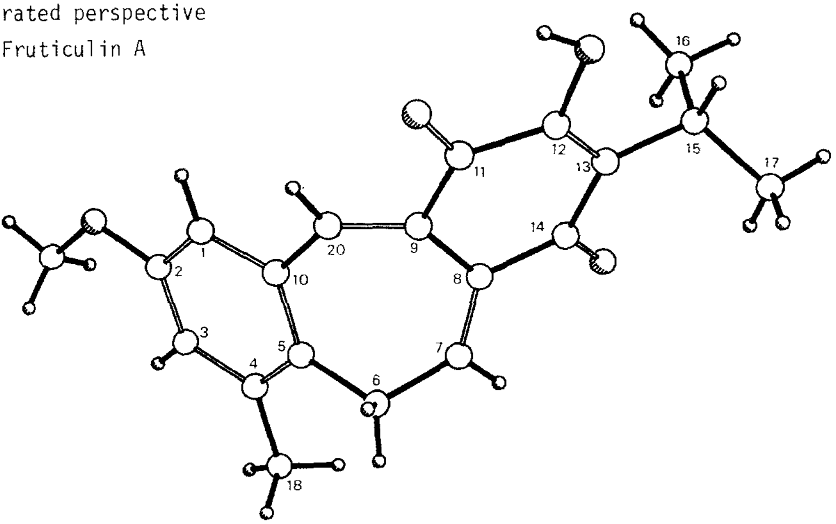
TABLE 2. ^{13}C NMR SPECTRAL DATA OF COMPOUNDS 1b, 2 AND 3.§

	1b	2	3
C_1	112.25 (d)	112.27 (d)	122.12 (d)
C_2	157.58 (s)	157.79 (s)	148.82 (s)
C_3	121.55 (d)	114.8 (d)	124.10 (d)
C_4	136.14 (s)	139.97 (s)	138.69 (s)
C_5	129.7 (s)	136.65 (s)	132.66 (s)
C_6	28.42 (t)	28.73 (t)	29.0 (t)
C_7	140.80 (d)	28.73 (t)	66.74 (d)
C_8	133.27 (s)*	130.9 (s)	128.64*(s)
C_9	132.18 (s)*	130.9 (s)	129.65*(s)
C_{10}	135.78 (s)	146.07 (s)	137.41 (s)
C_{11}	183.23 (s)	183.76 (s)	140.68 (s)
C_{12}	154.7 (s)	150.10 (s)	142.80 (s)
C_{13}	127.14 (s)	125.54 (s)	135.93 (s)
C_{14}	183.95 (s)	187.43 (s)	147.29 (s)
C_{15}	25.2 (d)	24.4 (d)	27.39 (d)
C_{16}	19.62 (q)	19.94 (q)	Ψ
C_{17}	19.62 (q)	19.94 (q)	Ψ
C_{18}	20.14 (q)	20.04 (q)	19.66 (q)
C_{20}	133.81 (d)	27.34 (t)	69.83 (d)
-OMe	55.39 (q)	55.21 (q)	

$\S$ Run at 20 MHz using $CDCl_3$ as solvent and TMS as internal standard. SFORD multiplicities are in parenthesis. *Values in any vertical column may be interchanged. Ψ Overlapped with six methyl signals ($OCOCH_3$) between 19.66 and 20.97 ppm. Six carbonyl signals are observed between 167.3 and 170.46 ($O\underline{C}OCH_3$).

Figure 1

Computer-generated perspective drawing of Fruticulin A



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1. Watson, W., Taira, Z., Domínguez, X., González, H., Gutiérrez, M., Aragón, R., Tetrahedron Letters 29, 2501 (1976).
2. Epling, C., Repert. Spec. Nov. Beih., 110: 1-383 (1939).
3. Esquivel, B., Cárdenas, J., Ramamoorthy, T. P., Rodríguez-Hahn, L., Phytochemistry in press and references there cited.
4. IR (CHCl$_3$) ν_{max} cm^{-1}: 3672, 3371, 1657, 1603, 1555, 1467, 1440, 1394, 1300, 1275, 1178. UV λ_{max}^{MeoH} nm (ε): 215 (32000), 250 (10000), 278 (11500), 325 (16500), 420 (4200).
5. Sheldrick, G. M. (1981). SHELXTL, revision 3. An Integrated System for Solving, Refining and Displaying Crystal Structures for Diffraction Data, Univ. of Göttingen, Federal Republic of Germany.
6. International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham, Kynoch Press.
7. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre.
8. mp. 258-260°C; IR(CHCl$_3$) ν_{max} cm^{-1}: 1774, 1729, 1600, 1430, 1371, 1237, 1190, 1018.
9. IR (CHCl$_3$) ν_{max} cm^{-1}: 3386, 1657, 1614, 1501, 1469, 1406, 1385, 1266, 1053. UV λ_{max}^{MeOH} nm (ε): 210 (27500), 230 (43000), 300 (37000), 340 (17000), 400 (4300).

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