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LETTERS

Salvadiol: A Novel Triterpenoid from *Salvia bucharica*

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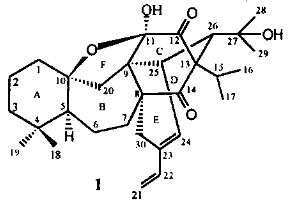
Abstract:: Salvadiol (**1**), a triterpene with a novel carbon skeleton has been isolated from the hexane soluble part of *Salvia bucharica* and characterized by single-crystal X-ray diffraction. The NMR data were rationalized on the basis of structure **1** determined by the X-ray technique. A biogenetic pathway for salvadiol is proposed.

Keywords:, Lamiaceae, *Salvia bucharica,* novel triterpenoid, X-ray diffraction, biogenesis.

Salvia bucharica M. pop., belongs to the family Lamiaceae, which has several members having chemical constituents with anti-tumor activity.[1] *Salvia* is the largest genus of this family with over 800 species found throughout the world.[2] Several species of the genus *Salvia* are used in folk medicines, for instance, *S. cavaleriei* is used for the treatment of dysentery, haemoptysis, boils and fall injuries.[3] *S. desoleria* for the treatment of menstrual, digestive and CNS diseases[4] and *S. bucharica* itself as a traditional medicine for the treatment of liver disorders. *S. bucharica* is a wild and aromatic shrub usually found in dry rocky places of east Afghanistan and southern parts of Pakistan.[5] From the hexane soluble part of *S. bucharica,* a novel triterpenoid has been isolated and characterized.



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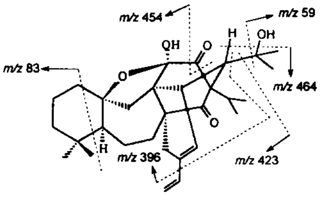

Figure 1. Possible mass fragmentations of salvadiol.

Salvadiol (**1**) $C_{30}H_{42}O_5$ was eluted with 30% ethyl acetate in hexane after repeated column chromatography from the hexane soluble part of *S. bucharica.* The HREI MS of **1** showed the M^+ at *m/z* 482.3036 in agreement with the molecular formula $C_{30}H_{42}O_5$ (calcd. *m/z* 482.3032) with ten degrees of

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unsaturation. The IR spectrum displayed strong absorption bands at 3450-3500, 1745 and 1710 cm^{-1} due to the hydroxyl and carbonyl functions. Weak IR absorptions at 1620, 1605 and 1120 cm^{-1} were due to the olefinic and ether functionalities. The various peaks (*m/z* 464, 454, 423, 396, 84 and 59) which appeared in the EI MS are described in Fig-1.

TABLE-1. NMR DATA of SALVADIOL (1).

C #	^{13}C δ	Mult.	^{1}H δ (mult., *J* in Hz)	C #	^{13}C δ	Mult.	^{1}H δ (mult., *J* in Hz)
1	41.1	CH_2	1.11 (m), 1.00 (m)	16	19.2	CH_3	1.15 (d, *J* = 6.8)
2	19.5	CH_2	1.30 (m), 1.13 (m)	17	20.0	CH_3	1.16 (d, *J* = 6.7)
3	41.4	CH_2	1.80 (m), 1.37 (m)	18	21.5	CH_3	0.85 (s)
4	36.0	C	-	19	32.6	CH_3	0.96 (s)
5	49.8	CH	1.25 (m)	20	42.4	CH_2	1.90 (d, *J* = 12.8); 1.84 (d, *J* =12.8)
6	21.0	CH_2	1.99 (m), 1.78 (m)	21	112.0	CH_2	5.21 (d, *J* = 17.5); 5.02 (d, *J* = 10.7)
7	32.4	CH_2	0.92 (m)	22	138.2	CH	6.34 (dd, *J* = 17.5, 10.7)
8	49.0	C	-	23	124.4	C	-
9	52.4	C	-	24	140.4	CH	5.94 (d, *J* = 6.7 Hz)
10	91.7	C	-	25	53.6	CH	3.39 (d, *J* = 9.0)
11	100.6	C	-	26	46.7	CH	not identified
12	209.9	C	-	27	74.8	C	-
13	70.7	C	-	28	29.8	CH_3	1.24 (s)
14	202.2	C	-	29	29.2	CH_3	1.23 (s)
15	24.8	CH	1.41 (m)	30	27.1	CH_2	2.70 (br. d, *J* =17.9), 2.47 (br.d, *J* =17.9)

All spectra were recorded in $CDCl_3$ (^{1}H: 300 MHz, ^{13}C: 125 MHz). Multiplicities were determined from DEPT spectra.

As compound **1** was obtained as a crystalline solid it was subjected to single crystal X-ray diffraction analysis.[6] Based on the X-ray structure (Fig. 2) various signals observed in ^{13}C and ^{1}H NMR spectra were assigned and are presented in (Table-1).

The carbon spectrum of **1** exhibited thirty signals which were resolved into six methyl, seven methylene, six methine and ten quaternary carbons through DEPT experiments. The two ketonic carbons appeared at δ 209.9 and 202.2 due to C-12 and C-14. Another downfield quaternary carbon at δ 124.4 was assigned to C-23. Three more oxygen-bearing quaternary carbons directly attached to the oxygen atoms in the molecule displayed their presence by the signals at δ 91.0, 100.6 and 74.8 and were ascribed to C-10, C-11 and C-27.

In the ^{1}H-NMR spectrum of **1**, four tertiary and two secondary methyls signals were present at δ 0.85, 0.96, 1.24, 1.23, 1.15 and 1.16. They were due to Me-18, Me-19, Me-28, Me-29, Me-16 and Me-17, respectively, which were correlated in the HMQC spectrum at δ 21.5, 32.6, 29.8, 29.2, 19.2 and 20.0. A downfield methylene signal which appeared in the carbon spectrum at δ 112.0 was due to the C-21 and its associated proton signals were observed as a pair of doublets at δ 5.02 (d, *J*=10.7 Hz, H-21a) and 5.21 (d, *J*=17.7 Hz, H-21b). The methine attached to this methylene (H-22) resonated at δ 6.34 (dd, *J*=17.5, 10.7 Hz) in the ^{1}H-NMR spectrum which was correlated to the signal at δ 138.2 in the HMQC spectrum. An endocyclic olefinic methine (H-24) signal appeared as a doublet at δ 5.94 (*J*=6.7 Hz) attached to a carbon resonating at δ 140.4. The signal due to H-25 appeared at δ 3.39 (d, *J*=9.0 Hz). The most upfield methine signal which appeared in the HMBC spectrum at δ 1.41 (m) was due to the isopropyl methine (H-15).The signals observed in the NMR spectra (^{1}H and ^{13}C) were correlated with the help of 2-D NMR techniques and are fully in agreement with the structure of **1** determined through X-ray crystallography. The crystal structure comprises of a novel triterpene skeleton consisting of a six complex fused ring system. Ring A has a chair conformation with axially oriented O-1 and C-18. Ring B has a twist-chair conformation with a *trans* ring junction to ring A and a *cis* junction to ring C. The tetrahydrofuranoid ring F has an envelope conformation. All bond lengths and angle are in accord with accepted values, while a resonance character involve between C (24) to C (21) was apparent from a shorter C-23/C-22 bond [1.471 (4) Å] and slightly longer C-21/C-22 and C-23/C-24 bonds [1.316 (4) and 1.334 (3) Å, respectively. As the molecule contains two ketonic and two olefinic functions which were also confirmed through NMR spectra, it was obvious that **1** contains five carbocycles in addition to an ether-bridge as shown in Fig-2.

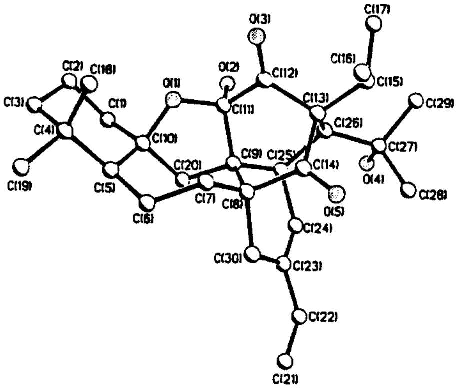
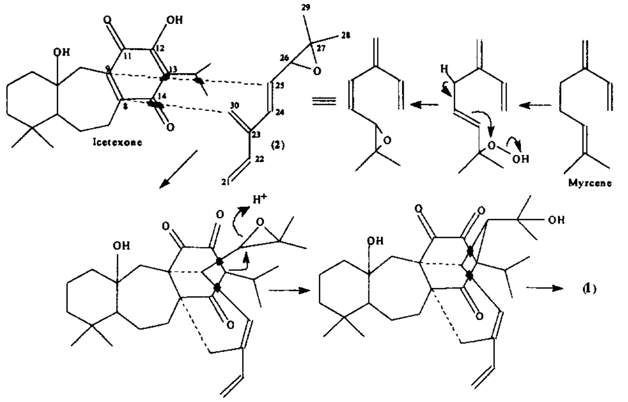


Fig. 2. X-ray structure of **1**.

Compound **1** has a novel carbon skeleton and named salvadiol which is supposed to be derived from icetexone precursor through the addition of **2** which could be formed by autoxidation of myrcene. The coupling of both the units can be rationalized in terms of a Diels-Alder type reaction as shown in Scheme-1. The numbering in **1** is given on biogenetic grounds.



Scheme-1: A proposed biogenetic pathway to salvadiol

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[6]. **1**: white needles (MeOH-C_6H_{14}), m.p. 207-209°C; $[\alpha]_D^{27}$ 87° (*c* 0.322, $CHCl_3$); UV λ_{max} nm (log ∈) (MeOH): 230 (3.89); EI MS *m/z* (rel. int.): 482 $[M]^+$(5.6), 464 [M^+-H_2O] (18.2), 454 [M^+-CO] (19), 436 [M^+-H_2O-C_2H_4] (85), 423 [M^+-C_3H_7O] (29), 396 [M^+-C_3H_7O- C_2H_4] (92); Crystal data for **1**: $C_{30}H_{42}O_5$, Base peak = 482.64amu, Orthorombic, space group $P2_12_12_1$, **a** = 11.521 (2)A, **b** = 14.8230 (10) and **c** = 5.611 (2) A°, V = 2666.0 (6) A^3 (CuK_α λ = 1.54178 A°), Z = 4, $D_{calc.}$ = 1.202 Mg/m^3, F (000) = 1048, μ (Cu-Kα) = 0.637 mm^{-1}. Crystal size (mm) 0.30 × 0.25 × 0.35. X-ray diffraction data were collected at 293 (2) K° in the range = 3.5° to 135° ($-1 \leq h \leq 11$; $-1 \leq k \leq 15$; $-16 \leq l \leq 16$) on a Nicolet Single-crystal X-ray diffractometer (P_4. System, Bruker). Structure was solved by direct method with program SHELXTL (version 5) and refined by Full-matrix least-squares on F^2. Anistropic thermal parameters were refined for all the non-hydrogen atoms. All the hydrogen atoms were located in the difference Fourier map The positional and isotropic thermal parameters of the hydroxyl H-atom were refined. Riding models were used to place the rest of the H-atoms in their idealized position. In the final least-squares refinment cycles on F^2, the model converged at R_2 = 4.6%, wR_2 = 12.69% and GOF = 1.051 for the 3921 reflection with [I > σ (1)] and 326 parameters. In the final difference Fourier synthesis, the electron density fluctuated in the range of 0.206 to -0.266 e$Å^3$. Atomic coordinates, bond lengths and angles and thermal parameters will be deposited at the Cambridge Crystallographic Data Centre (CCDC).