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Salvatrione: A Diterpene-monoterpene Conjugate from *Salvia bucharica*

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Abstract – *Salvia bucharica* belonging to the family Lamiaceae (Labiatae), afforded a novel terpenoid (**1**) named as salvatrione. The structure of **1** was elucidated through extensive 2-D NMR experiments and the biogenetic pathway of **1** has also been proposed. On biogenetic grounds, **1** may be considered to be a pseudo-triterpenoid as it is derived from the coupling of mono/ diterpenic units and not from squalene.

Key words – *Salvia bucharica*, Lamiaceae, salvatrione, pseudo-triterpenoid, characterization, 2D-NMR, biogenetic pathway.

Introduction

Salvia is the largest genus of the family Lamiaceae, previously called Labiatae (Chadha,1972). Chemical literature shows that the *Salvia* species are rich with diterpenoids (Hassan *et al.*, 1986). Recently, we have reported two new diterpenoids from *S. triloba* collected from Southern Palestine (Ali *et al.*, 2000) and pseudo-triterpenoids from *S. bucharica* (Ahmad *et al.*,1999; Ahmad *et al.*, 1999a). Some interesting biological activities have been reported for extractives of various species of the this genus. The diterpenoids of *S. officinalis* showed antiviral activity (Tada *et al.*, 1994). Many *Salvia* species have also shown cytostatic and antibacterial activities (Darias *et al.*, 1990; Ahmad *et al.*, 1994).

S. bucharica, locally called "sursuadah", is an aromatic plant found in Pakistan, Afghanistan and Central Asia (Ali *et al.*,1990). The plant is used traditionally for the treatment of liver disorders. In this communication, we describe the isolation and characterization of another new constituent named as salvatrione (**1**) from *Salvia bucharica*.

Experimental

General – Optical rotation was measured on a JASCO DIP-360 polarimeter. The IR and UV spectra were recorded on JASCO 320-A and Hitachi UV 3200 spectrophotometers, respectively. The EI- and HREI-MS were recorded on JMS HX 110 with a data system and on JMS-DA 500 mass spectrometers. The ^{1}H- and ^{13}C-NMR and HMBC spectra were taken in $CDCl_3$ with TMS as an internal standard on Bruker AM-500 NMR spectrometer.

Collection and identification – The plant material was collected from Baluchistan (Pakistan) in June, 1997, and identified by Dr. R. B. Tareen, Department of Botany, Baluchistan University, Quetta (Pakistan) where a voucher specimen (No. 354) of the plant material is deposited in the herbarium of the department.

Extraction and isolation – The air-dried (6 kg) and ground plant material was extracted with hexane (15L×3). After removing the solvent under reduced pressure, gummy residue thus obtained (92.71 g) was loaded on silica gel column and eluted with hexane-$CHCl_3$ with gradual increase in polarity. Salvatrione (1) was obtained from the fraction eluted from the column with 90% $CHCl_3$ in hexane and finally, purified as a gum (14.9 mg, 0.00024%) using $AgNO_3$-impregnated preparative TLC developed in $CHCl_3$- Me_2CO (9:1).

Salvatrione (1): $C_{30}H_{42}O_5$: $[\alpha]_D^{29}$ +86° (*c* 0.322, $CHCl_3$); IRν_{max} ($CHCl_3$)cm^{-1}: 3550 (OH), 1765, 1725, 1715 (C = O) and 1620 (C = C); UV (MeOH), λ_{max}, nm (logϵ): 255 (0.75), 229 br. (1.22) and 214

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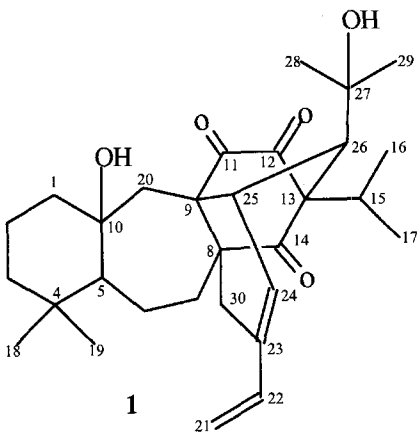
br. (1.15); HREI-MS: *m/z* 482.3028; EI-MS: see Fig.1a; ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 2.19 (1H, m, H-15), 0.97 (3H, d, J = 6.9 Hz, H-16), 1.39 (3H, d, J = 6.8 Hz, H-17), 0.86 (3H, s, H-18), 1.04 (3H, s, H-19), 5.21(1H, dd, J = 17.4,1.30 Hz, H-21A), 5.03 (1H, dd, J = 10.7,1.30 Hz, H-21B), 6.30 (1H, dd, J = 17.4, 10.7Hz, H-22), 5.55 (1H, d, J = 4.5Hz, H-24), 3.12 (1H, dd, J = 4.5, 4.2Hz, H-25), 2.98(1H, d, J = 4.2 Hz, H-26), 1.35 (3H, s, H-28), 1.44 (3H, s, H-29), 2.52 (1H, d, J-16.8Hz, H-30A) and 2.36 (1H, d, J = 16.8 Hz, H-30B); ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 42.0 (C-1), 19.8 (C-2), 41.9 (C-3), 35.9 (C-4), 50.7 (C-5), 20.5 (C-6), 32.2 (C-7), 51.3 (C-8), 53.3 (C-9), 93.2 (C-10), 206.4 (C-11), 193.5 (C-12), 63.4 (C-13), 209.7 (C-14), 29.4 (C-15), 18.2 (C-16), 18.4 (C-17), 32.4 (C-18), 21.8 (C-19), 41.6 (C-20), 113.5 (C-21), 137.7 (C-22), 138.5 (C-23), 127.1 (C-24), 52.8 (C-25), 41.3 (C-26), 73.0 (C-27), 28.3 (C-28), 27.5 (C-29) and 42.0 (C-30); HMBC: see Fig. 1b.

Selective ^{1}H-^{1}H homonuclear decoupling experiments:

Irradiation of δ 5.21(dd, H-21A)→δ 5.03 (dd, H-21B)→d (J = 10.7 Hz), δ 6.30 (dd, H-22)→d (J = 10.7 Hz); Irradiation of δ 6.30 (dd, H-22)→δ 5.03 (dd, H-21B)→d (J = 1.3 Hz), δ 5.21(dd, H-21A)→ d (J = 1.3 Hz); Irradiation of δ 3.12 (dd, H-25)→δ 5.55 (d, H-24)→s, δ 2.98 (d, H-26)→s

Results and Discussion

The hexane soluble part of *Salvia bucharica* yielded a novel terpenoid as a gum named as salvatrione (**1**). The EI-MS of **1** indicated the molecular mass 482 Daltons which was reconfirmed by FDMS. The molecular formula of **1** was determined through



1

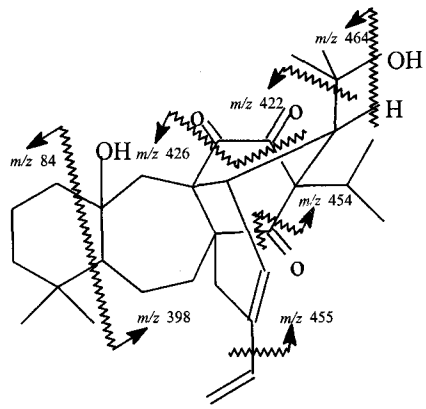


Fig. 1a. Possible MS fragmentation pattern of **1**.

HRMS as $C_{30}H_{42}O_5$ (calcd. *m/z* 482.3032, observed *m/z* 482.3028) showing ten degrees of unsaturation. The various peaks appeared in the EI-MS are explained in Fig. 1a. The UV spectrum displayed a shoulder at 255 nm and intense absorptions at 229, 214 nm. The IR spectrum of the same compound showed five significant absorption bands at 3550, 1765, 1725, 1715 and 1620 cm^{-1} revealing the presence of hydroxyl, ketonic and olefinic functionalities in the molecule.

The ^{1}H-NMR spectrum of **1** showed the signals at δ 6.30 (dd, J = 17.4, 10.7 Hz), 5.21 (br.d, J = 17.4 Hz) and 5.03 (d, J = 10.7 Hz) due to vinyl moiety. Another downfield signal at δ 5.55 as a doublet (J = 4.5 Hz) attested for H-24. The same spectrum displayed four singlets having three protons integration each at δ 1.44, 1.35, 0.86 and 1.04, assigned to four tertiary methyls (H-29, H-28, H-18 and H-19). The signals at δ 0.97 (H-16) and 1.39 (H-17) appeared as doublets having coupling constants 6.9 and 6.8 Hz, respectively, due to the isopropyl moiety.

The broad-band spectrum of **1** showed thirty carbon signals which were resolved through DEPT experiments into six methyl, eight methylene, six methine by difference, and ten quaternary carbons. Out of six, four tertiary methyls appeared at δ 32.4 (C-18), 21.8 (C-19), 28.3 (C-28) and 27.5 (C-29). The methyls due to isopropyl unit appeared at δ 18.4 (C-17) and 18.2 (C-16). The downfield methylene resonated at δ 113.5 was attested for C = CH_2 (C-21). Similarly, a downfield methine signal at δ 127.1 was assigned to C-24. The three ketonic carbonyls due to C-11, C-12 and C-14 resonated at δ 206.4, 193.5 and 209.7, respectively, which were also confirmed by

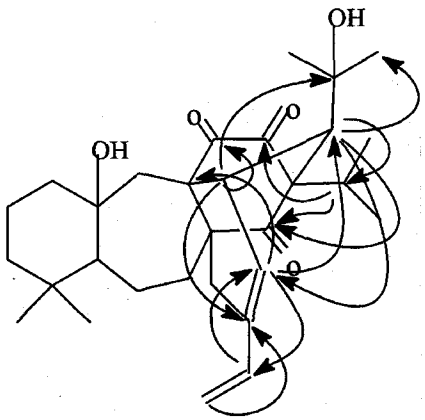
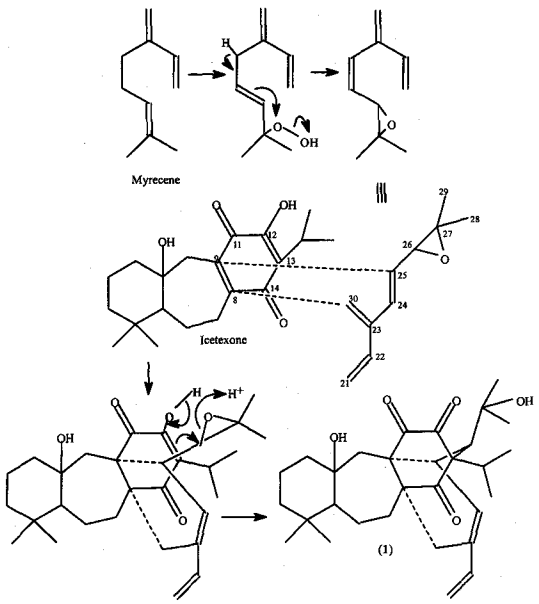


Fig. 1b. Selective HMBC connectivities in **1**.

IR spectrum. Another downfield signal at δ 138.5 was ascribed to olefinic quaternary carbon (C-23).

The various proton-proton, proton-carbon and carbon-carbon connectivities were determined with the aid of HMBC (Fig. 1b), HMQC and decoupling experiments. Out of ten degrees of unsaturation in the molecule, five could be explained by three ketonic and two olefinic functions and the rest of five due to the carbocycles.

On the basis of spectral information, comparative studies with salvadiol, a novel terpenoid isolated by us from the same source having the same skeleton (Ahmad, 1999) and on biogenetic grounds (scheme-1)



Scheme 1. A proposed biogenetic pathway to salvatrione (**1**).

the structure of salvatrione is assigned as **1**.

The stereochemistry of various centers could not be determined. It is proposed that the monoterpeneic unit (myrcene) couples after auto-oxidation with diterpenic unit (ice-texone) and this coupling may proceeds via Diels-Alder type reaction. The carbon numbering in **1** is also given on the basis of biogenetic grounds. It must be clarified here that although **1** contains thirty carbons, it cannot be classified under triterpenoid as it is not derived from squalene. However, on biogenatic grounds the term diterpene-monoterpene conjugate may be used. It is to clarify here that the possibility **1** may be an artifact of salvadiol was ruled out when salvadiol did not give **1** on treatment with trifluroacetic acid.

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