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Salvadiones-A and -B: Two Terpenoids Having Novel Carbon Skeleta from *Salvia bucharica*

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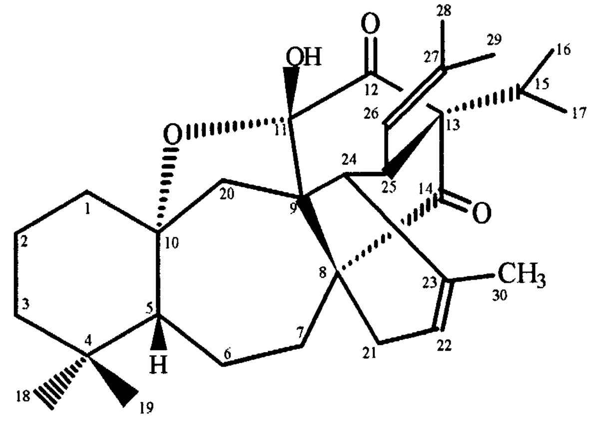
Two triterpenoids, salvadione-A (**1**) and salvadione-B (**2**), having novel carbon skeleta, were isolated from the hexane soluble fraction of *Salvia bucharica*. Their structures were determined through single-crystal X-ray diffraction analysis and are fully consistent with their NMR data.

The family Lamiaceae (Labiatae) is well-known because its members contain chemical constituents with antitumor activity.[1] *Salvia* is the largest genus of this family, having about 800 species found throughout the world.[2] *Salvia bucharica* is widely distributed from Afghanistan to Central Asia. In Pakistan it is found in the Baluchistan area where it is locally called "sursaudah".[3] The plant is used traditionally for the treatment of liver disorders and as a cooling medicine. Many members of this family have been studied for their essential oils.[4−6] Salvadiones-A and B were isolated from the hexane soluble part of *S. bucharica*.



Salvadione-A (1)

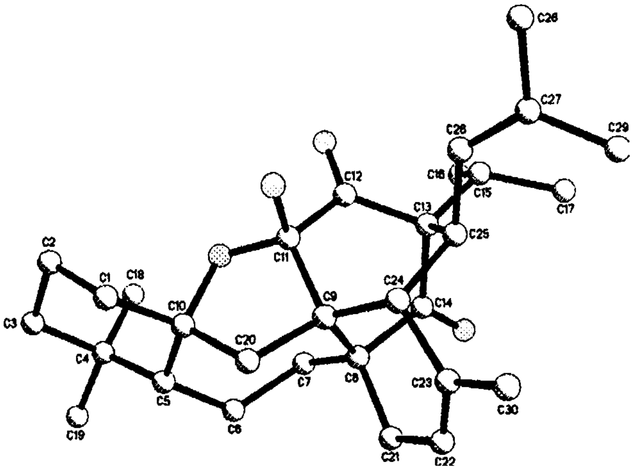


Figure 1. A computer-generated perspective drawing of the final X-ray model of Salvadione-A (**1**). Hydrogens are omitted for clarity.

Salvadione-A (**1**) has the molecular formula $C_{30}H_{42}O_4$ determined through HREIMS corresponding to the exact molecular mass *m/z* 466.3104 (calcd 466.3083) and showing 10 degrees of unsaturation. The IR spectrum ($CHCl_3$) showed absorption bands at 3600, 1760, 1710, 1610, 1600, and 1120 cm^{-1} due to the presence of hydroxyl, ketone, olefin, and ether functionalities, respectively. The ^{13}C NMR spectrum showed 30 carbon signals, which were resolved through a DEPT experiment into seven methyl, seven methylene, six methine, and 10 quaternary carbons. The two downfield olefin methine signals appeared at δ 119.1 (C-22) and 125.0 (C-26). The two ketone functions could be identified by the signals at δ 211.0 (C-12) and 203.3 (C-14), and the olefinic quaternary carbon signals appeared at δ 136.7 (C-23) and 131.7 (C-27). Forty one protons could be accounted through the DEPT experiment. The remaining proton was due to the hydroxyl function which was already confirmed through the IR spectrum. Two olefinic protons were identified by their signals at δ 5.25 (H-22) as a broad singlet and at δ 5.32 (H-26) as a doublet (J = 11.3 Hz) in the ^1H NMR spectrum. Among the methyls, the two secondary methyl signals appeared at δ 0.90 (H-16) and 1.05 (H-17) as doublets (J = 7.0 Hz). The most downfield methyl resonated at δ 1.68 (H-30) as a doublet (J = 1.7 Hz) due to coupling with a vinyl methyl (C-23). The remaining protons and carbon signals were assigned with the help of 2D-NMR spectroscopy, including HMBC, HMQC, and literature values.[7,8] The structure of **1** was determined

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(1) Fujita, E.; Node, M. *Prog. Chem. Org. Nat. Prod.* **1986**, *46*, 77.

(2) Chadha, Y. R. *The Wealth of India*; Publications and Information Directorate; CSIR: New Delhi, 1972; p 327.

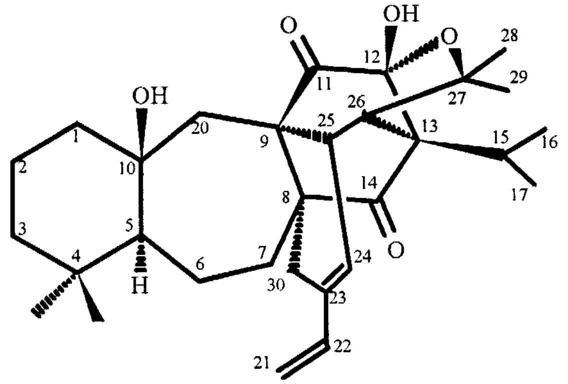
(3) Nasir, E.; Ali, S. I. *Flora of Pakistan*; Fakhri Printing Press: Karachi, 1986; Vol. 56, p 156.

(4) Chopra, R. N.; Nayar, S. L.; Chopra, I. C. *Glossary of Indian Medicinal Plants*; CSIR: New Delhi, 1956; p 189.

(5) Kirtikar, K. R.; Basu,. B. D. *Indian Medicinal Plants*; Indian Press: Allahabad, 1918; p 1031.

(6) Hasan, M.; Iqbal, R.; Ullah, I.; Haq, I. U.; *Islamabad J. Sci.* **1978**, *5*, 22. *Chem. Abstr.* **1980**, *93*, 230915 b.

10.1021/jo990024s CCC: $18.00



Salvadione-B (2)

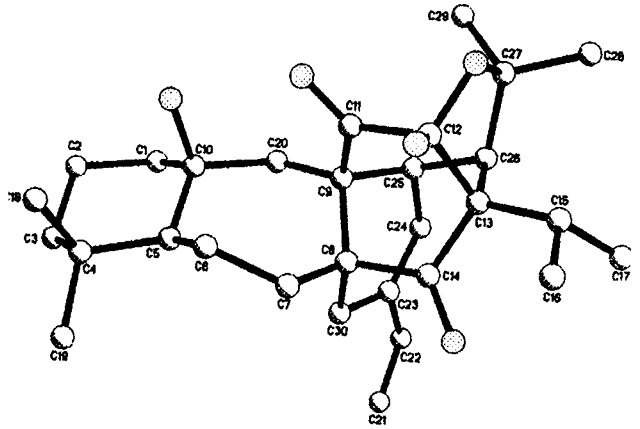


Figure 2. A computer-generated perspective drawing of the final X-ray model of Salvadione-B (**2**). Hydrogens are omitted for clarity.

by single-crystal X-ray diffraction analysis.[9] The X-ray structure of **1** (Figure 1, relative configuration) shows an ether linkage between C-10 and C-11, and thus the molecule contains five carbocycles.

Table 1. ^{1}H and ^{13}C NMR Assignments for 1 and 2[a]

	1		**2**	
C no.	^{13}C (m)	^{1}H (m, *J* in Hz)	^{13}C (m)	^{1}H (m, *J* in Hz)
1	40.5 (t)		46.1 (t)	
2	19.7 (t)		18.5 (t)	
3	41.3 (t)		43.4 (t)	
4	35.6 (s)		35.0 (s)	
5	50.7 (d)		49.1 (d)	
6	20.3 (t)		20.2 (t)	
7	31.6 (t)		32.4 (t)	
8	49.7 (s)		51.7 (s)	
9	50.9 (s)		53.7 (s)	
10	91.1 (s)		78.6 (s)	
11	99.7 (s)		219.1 (s)	
12	211.0 (s)		100.1 (s)	
13	71.3 (s)		61.3 (s)	
14	203.3 (s)		209.4 (s)	
15	22.4 (d)	2.16 (m)	26.2 (d)	2.4 (m)
16	16.8 (q)	0.90 (d, 7.0)	18.7 (q)	1.09 (d, 7.1)
17	18.7 (q)	1.05 (d, 7.0)	18.9 (q)	1.32 (d, 7.0)
18	32.5 (q)	0.83 (s)	32.0 (q)	0.82 (s)
19	21.7 (q)	0.93 (s)	21.2 (q)	0.89 (s)
20	42.1 (t)	1.96 (d, 14.0), 1.94 (d, 14.0)	42.1 (t)	
21	29.3 (t)	2.39 (br. m)	113.5 (t)	5.25 (d, 17.5), 5.08 (d, 10.7)
22	119.1 (t)	5.25 (br. s)	137.1 (d)	6.24 (dd, 17.5, 10.7)
23	136.7 (s)		136.3 (s)	
24	43.3 (d)	2.28 (d, 2.7)	126.7 (d)	5.46 (d, 5.6)
25	46.2 (d)	2.61 (dd, 11.3, 2.7)	55.3 (d)	
26	125.0 (d)	5.32 (d, 11.3)	40.5 (d)	2.50 (d, 5.5)
27	131.7 (s)		72.7 (s)	
28	18.5 (q)	1.65 (d, 1.35)	29.8 (q)	1.13 (s)
29	26.1 (q)	1.62 (d, 1.41)	28.6 (q)	1.42 (s)
30	26.4 (q)	1.68 (d, 1.69)	34.0 (t)	2.25 (d, 17.2), 2.83 (d, 17.2)

[a] NMR spectra were recorded in $CDCl_3$ at 300, 400 MHz (^{1}H) and at 75, 100 MHz (^{13}C), respectively.

Salvadione-B **(2)** was eluted from the same fraction and showed the exact molecular mass *m/z* 482.2975 in the HREIMS spectrum, corresponding to the molecular formula $C_{30}H_{42}O_5$ (calcd 482.3032) consistent with 10 degrees of unsaturation. The IR spectrum ($CHCl_3$) of **2** showed absorptions at 3550, 1705, 1600, 1585, 1250 cm^{-1} due to the hydroxyl, ketone, olefin, and ether functionalities, respectively. The ^{13}C NMR spectrum showed 30 carbon signals which were due, according to the DEPT spectrum to six methyl, eight methylene, six methine, and 10 quaternary carbons. In this way, 40 hydrogen atoms could be accounted and the remaining two must be due to the hydroxyl functions, which were confirmed through the IR spectrum. The ^{13}C NMR spectrum displayed two carbonyl signals at δ 219.0 (C-11) and 209.4 (C-14). A downfield quaternary carbon at δ 136.3 was assigned to the olefinic function (C-23). Similarly, two downfield methine signals appeared at δ 137.1 (C-22) and 126.7 (C-24) which were correlated to their respective protons in the ^{1}H NMR spectrum at δ 6.24 (dd, $J = 17.5$, 10.7 Hz) and 5.46 (d, $J = 5.6$ Hz) from an HMQC experiment. The most downfield methylene carbon resonated at δ 113.5 (C-21) which showed connectivity with the protons in the HMQC spectrum at δ 5.25 (d, $J = 17.5$ Hz) and 5.08 (d, $J = 10.7$ Hz). The two secondary methyls of the isopropyl unit exhibited resonances at δ 1.09 (d, $J = 7.1$ Hz) and 1.32 (d, $J = 7.0$ Hz), and the signals of the two tertiary methyls which were attached to the C-27 quaternary carbon were observed at δ 1.13 (H-28) and 1.42 (H-29) as singlets in the ^{1}H NMR spectrum. Their corresponding carbon signals appeared at δ 29.8 and 28.6 in the ^{13}C NMR spectrum, respectively. The remaining carbon and proton signals were assigned with the aid of an HMBC spectrum and the reported data of similar compounds.[7,8] The structure of **2** was ascertained through single-crystal X-ray diffraction analysis.[9] The X-ray structure of **2** (Figure 2, relative configuration) showed the presence of two tertiary hydroxyl functions; the remaining three oxygen atoms were involved in the two ketonic functions and an ether linkage. Therefore, compound **2** contains five carbocycles in the molecule.

Salvadiones-A and -B, having the novel carbon skeleta, are presumably derived from an icetexone-type precursor[10] through the addition of geranylpyrophosphate. The carbon skeleta in salvadiones-A and -B are numbered on biogenetic grounds.

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[7] Parvez, A.; Choudhary, M. I.; Akhter, F.; Noorwala, M.; Mohammad, F. V.; Hasan, N. M.; Zamir, T.; Ahmad, V. U. *J. Org. Chem.* **1992**, *57*, 4339.

[8] Ahmad, V. U.; Parvez, A.; Hasan, N. M. *Tetrahedron Lett.* **1993**, *34*, 5337.

[9] The crystals of **1** were orthorhombic whereas those of **2** were trigonal. Other X-ray diffraction data have been deposited with the editor.

[10] Watson, W. H.; Taira, Z.; Dominguez, X. A.; Gonzales, H.; Guiterrez, M.; Aragon, R. *Tetrahedron Lett.* **1976**, *29*, 2501.

Experimental Section

Collection, Extraction, and Isolation Procedures. *Salvia bucharica* M. Pop. (whole part) was collected from Quetta, Baluchistan, Pakistan, in June, 1997, and was identified by one of us (R.B.T.). A voucher specimen (No. 354) of the plant has been deposited in the herbarium of the Botany Department, University of Baluchistan, Quetta. The plant material (dried, 6.0 kg) was chopped into small pieces and soaked in hexane (5 L × 3), for a period of 10 days each. The combined hexane extract was concentrated by means of evaporation at low pressure to give a gum (92.71 g) which was subjected to vacuum liquid chromatography using hexane and hexane−chloroform mixtures of increasing polarity up to 100% chloroform and then methanol. The fraction eluted with 35% chloroform in hexane was subjected to flash chromatography (silica gel 230−400). The fraction obtained with 30% chloroform in hexane from flash chromatography was further purified by preparative layer chromatography (silica gel F_{254}) using hexane and ethyl acetate (6:4) as a mobile phase. Two bands were scratched out. The upper band yielded **1** as a white powder which was finally washed with methanol to give needles (22.0 mg, 0.0004%). The lower band yielded **2** as light yellow crystals which were similarly washed with methanol to give colorless sharp crystals (20.0 mg, 0.0003%). The NMR data of **1** and **2** are given in Table 1.

Salvadione-A (1): $C_{30}H_{42}O_4$; $[\alpha]^{25}_D$ +37.92° ($CHCl_3$, *c* 0.371); mp 197−198 °C; IR ν_{max} ($CHCl_3$) cm^{-1}: 3600 (OH), 1760, 1710 (C=O), 1610, 1600 (C=O); EIMS *m/z* 466 (29) $[M]^+$, 451 (3), 438 (19) $[M - CO]^+$, 423 (6) $[M - C_3H_7]^+$, 395(19), 382 (100), 354 (82), 311 (8), 241 (21), 231 (29), 123 (51), 69 (63); HREIMS *m/z* 466.3104 (M^+, $C_{30}H_{42}O_4$), 438.3098 $(M - CO)^+$, 423.2715 $(M - C_3H_7)^+$; NMR: see Table 1.

Salvadione-B (2): $C_{30}H_{42}O_5$; $[\alpha]^{25}_D$ +27.93° ($CHCl_3$, *c* 0.368); mp 190−191 °C; IR ν_{max} ($CHCl_3$) cm^{-1}: 3550 (OH), 1705 (C=O), 1600, 1585 (C=O); UV (MeOH), λ_{max} nm (log ϵ): 260 sh (3.45), 236 sh (4.09), 222 br (4.21); EIMS *m/z* 482 (15) $[M]^+$, 464 (6) $[M - H_2O]^+$, 439 (11) $[M - C_3H_7]^+$, 436 (100), 421 (12), 406 (22), 300 (55), 202 (13), 155 (45), 69 (41); HREIMS *m/z* 482.2975 (M^+, $C_{30}H_{42}O_5$), 464.2877 $(M - H_2O)^+$, 439.2684 $(M - C_3H_7)^+$; NMR: see Table 1.

Supporting Information Available: The ^{1}H and ^{13}C NMR and X-ray crystallographic data, for salvadiones-**A** and -**B**. This material is available free of charge via the Internet at http://pubs.acs.org.

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