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CONSTITUENTS OF HIGH ALTITUDE HIMALAYAN HERBS, PART V.[1] A NEW DITERPENOID QUINONE FROM *SALVIA HIANS*

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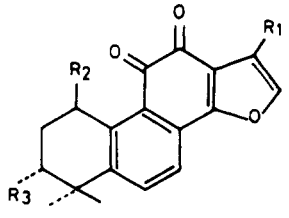
ABSTRACT.—A new red-colored ortho diterpenoid quinone, 3α,17-dihydroxytanshinone II [**2**], along with two known compounds tanshinone II [**1**] and β-sitosterol, has been isolated from the roots of the Himalayan herb *Salvia hians* and identified by uv, ir, ^{1}H-nmr, and mass spectral methods.

The roots of *Salvia hians* Royle ex Benth. (Labiatae), a native of the Kumaon Himalayan glaciers, are frequently used in folk medicine as a stimulant. Except for our earlier screening report (1), neither their folk medicinal use nor any of their chemical constituents have been reported in the literature. However, as a part of our program of investigating useful high altitude Himalayan herbs, we found the roots of *S. hians* to be rich in the colored diterpenoid quinone tanshinone II [**1**] and the new orthoquinoid diterpene 3α,17-dihydroxytanshinone II [**2**], along with β-sitosterol.

Two red and one white crystalline compounds were isolated from the roots of *S. hians*. The compounds were isolated and purified by cc, tlc, and hplc methods. The red-colored compound **1**, mp 198°, ms *m/z* 294 $[M]^+$, was identified as tanshinone II (2) on the basis of its uv, ir, ^{1}H-nmr, and mass spectral results.



1 R_1=Me, R_2=R_3=H
2 R_1=CH_2OH, R_2=H, R_3=OH
3 R_1=Me, R_2=H, R_3=OH
4 R_1=Me, R_2=OH, R_3=H

A red crystalline compound **2**, mp 209–210°, ms *m/z* 326 $[M]^+$, exhibited λ max (MeOH) 226, 250, 268, 350, and 450 nm. The ir spectrum was similar to that of compound **1**, but additional peaks at 3550 and 1050 cm^{-1} indicated the presence of hydroxyl groups. Its co-occurrence with tanshinone II [**1**] and its spectroscopic data all suggested that it was a doubly oxygenated analogue of **1** with composition $C_{19}H_{18}O_5$.

In the aromatic region of its ^{1}H-nmr spectra a one-proton singlet at δ 7.33 was observed and assigned to the furan proton at C-15. Two doublets were observed at δ 7.50 and 7.63 (each d, J = 8 Hz) attributable to ortho protons at C-6 and C-7. A six-proton gem dimethyl group appeared as two singlets at δ 1.31 and 1.35, but the non-α-substituted furan ring methyl group as observed in tanshinone II was absent. Instead, a two-proton methylene signal at δ 4.70 and a primary alcoholic OH at δ 3.77 were visible, indicating the presence of a CH_2OH group at C-16. The other hydroxyl group was observed at δ 3.69; both hydroxyl proton signals had disappeared on addition of D_2O. Methylene multiplets were observed at δ 3.32 and 2.27, and a double doublet at δ 3.96 (J = 8, 8 Hz) indicated the nature of the second hydroxyl group as α. However, the position of attachment of the second hydroxyl group in ring A was assigned by comparing the A-ring proton shift values with those of compounds **1**, **3**, and **4** (Table 1).

[1]For part IV of the series, see K.S. Khetwal, Binita Joshi, and R.S. Bisht, *Phytochemistry*, **29**, 1265 (1990).

TABLE 1. ^{1}H-nmr Chemical Shift Values of A-Ring Protons of Compounds **1–4**.

Chemical Shift	Compound			
	1[a]	**2**	**3**[b]	**4**[b]
H-1	3.21(2H)	3.32(2H)	3.30(2H)	4.98(1H)
H-2	1.73(2H)	2.27(2H)	1.94(2H)	2.04(2H)
H-3	1.73(2H)	3.46(1H)	3.74(1H)	2.04(2H)

[a]Reference Wel *et al.* (2).
[b]Reference Yong *et al.* (3) and Yong *et al.* (4).

The methylene protons of compound **2** (H_2-1) at δ 3.32 resemble very closely those of compounds **1** (δ 3.21) and **3** (δ 3.31), indicating the absence of any OH substitution at C-1. Further, had OH been substituted at C-1 it should have appeared downfield at around δ 4.98 as in the case of compound **4**. However, the appearance of the carbinyl proton of **2** at δ 3.96 corresponds with that of compound **3** (δ 3.74), confirming the attachment of the second hydroxyl group in ring A at C-3.

The white crystalline compound, mp 136–137°, ms *m/z* 414 $[M]^+$, was identified as β-sitosterol by comparing its physical and chemical properties with an authentic sample.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's are uncorrected. Uv spectra were recorded (MeOH) on a Hitachi model 220. Ir spectra (Perkin Elmer Model 298) were recorded as KBr discs. ^{1}H-nmr spectra (400 MHz) were recorded in $CDCl_3$ using TMS as an internal standard. Ms was determined in the ei mode at 70 eV by direct insertion on a Jeol JMS-300. Separation was carried out mainly by cc and tlc (Si gel G, 60–120 mesh Glaxo). Purity of the samples was checked by hplc using Water Associates 6000 A and M-45 pumps. Analytical, μ Bondapak C_{18} (4 mm × 30 cm), μ Bondapak C_8 (4 mm × 30 cm) steel columns or z-module cartridges were used at a constant solvent flow rate of 1.5 ml/mn. $CHCl_3$ (BDH/EM) and *n*-hexane (BDH/EM) were double-distilled before use.

PLANT MATERIAL.—The roots of the plant were collected from Pindari Glaciers of Kumaon Himalaya Uttar Pradesh at an altitude of 12,000 ft and identified in the Department of Botany, Kumaon University, Nainital, where the voucher specimen is stored.

EXTRACTION AND ISOLATION.—The roots (500 g) of the plant were shade-dried, powdered, and Soxhlet-extracted with 80% MeOH. The MeOH extract was concentrated under vacuum, and the residue was partitioned with $CHCl_3$-H_2O (1:1). The $CHCl_3$ extract was chromatographed on a Si gel G column (60–120 mesh, Glaxo) and eluted with a gradient of *n*-hexane, C_6H_6, and EtOAc. Elution with *n*-hexane–C_6H_6 (98:2) yielded tanshinone II [**1**], and elution with C_6H_6-EtOAc (99:1) yielded 3α,17-dihydroxytanshinone [**2**].

Tanshinone II [**1**].—Compound **1** (65 mg): red crystalline; mp 198°; uv λ max (MeOH) nm 224, 250, 268, 357, 460; ir (KBr) 3040, 1675, 1650, 1367, 1368, 835 cm^{-1}; ^{1}H nmr (400 MHz) ($CDCl_3$ with TMS as internal standard) δ 3.2 (2 m, H-1), 1.73 (m, 4H, H-2 and H-3), 1.30 (s, 3H, 4-Me), 1.34 (s, 3H, 4-Me), 7.54 and 7.65 (each d, J = 8.3 Hz, H-6 and H-7), 7.23 (s, 3H, 15-Me); eims *m/z* $[M]^+$ 294.

3α,17-Dihydroxytanshinone II [**2**].—Red colored crystals (15 mg): mp 209–210°; $C_{19}H_{18}O_5$; uv λ max (MeOH) nm 226, 250, 268, 350, 458; ir (KBr) 3550 (OH), 1675, 1650 (ortho quinoid), 1365, 1386 (gem dimethyl group), 3040, 835 (furan ring); ^{1}H nmr (400 MHz; ($CDCl_3$ with TMS as internal standard) δ 3.32 (2H, m, H-1), 2.27 (m, 2H, H-2), 3.96 (dd, 1H, H-3β, J = 8.24, 4.3 Hz), 1.31 (s, 3H, 4-Me), 1.35 (s, 3H, 4-Me), 7.5 and 7.63 (each 1H, d, J = 8.5 Hz, H-6 and H-7), 7.33 (s, H-15), 4.70 (s, 2H, CH_2); eims *m/z* $[M]^+$ 326.

β-*Sitosterol*.—White crystals (250 mg): mp 136–137°; eims *m/z* $[M]^+$ 414. Identified by comparison of ir and ^{1}H-nmr data, as well as co-chromatography with an authentic sample.

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