# Farnesyl Hydroxybenzoic Acid Derivatives from *Ferula kuhistanica*

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**Four new farnesyl hydroxybenzoic acid derivatives, kuhistanols E—H (1—4), were isolated from the roots of the Uzbekistan medicinal plant *Ferula kuhistanica*. The structures of the new compounds were elucidated based on spectroscopic and chemical evidence.**

**Key words** *Ferula kuhistanica*; Umbelliferae; prenylated benzoic acid; kuhistanols E—H

*Ferula kuhistanica* is used as a folk medicine for treating skin diseases and wounds in Uzbekistan. Plants of this genus have been shown to be a good source of biologically active compounds such as coumarins and sesquiterpene derivatives.[1)] During the course of our studies on the constituents of medicinal plants grown in Uzbekistan, we previously succeeded in the isolation and structural elucidation of seven new daucane esters (kuhistanicaols A—G),[2)] four new prenylated *p*-hydroxybenzoic acid derivatives (kuhistanols A—D), and 14 known compounds[3)] from the roots and stems of *F. kuhistanica*. In our continuing search for bioactive natural products, we isolated four new farnesyl *p*-hydroxybenzoic acid derivatives, kuhistanol E (**1**), F (**2**), G (**3**) and H (**4**), from methanol extracts of roots of *F. kuhistanica*. This paper describes the isolation and structural elucidation of these new compounds.

The methanol extracts of the air-dried roots of *F. kuhistanica* were partitioned between water and ethyl acetate. The ethyl acetate extracts were separated using repeated silica gel column chromatography, HPLC and gel permeation chromatography (GPC) to give compounds **1**—**4**.

Compound **1** was obtained as an amorphous powder. High-resolution electron impact-MS (HR-EI-MS) showed a molecular ion peak at *m/z* 358.2172 $[M]^+$, which, together with the $^1$H-NMR, $^{13}$C-NMR and distortionless enhancement by polarization transfer (DEPT) data, suggested a molecular formula of $C_{22}H_{30}O_4$. The $^1$H-NMR spectrum of **1** displayed the presence of a 1,3,4-trisubstituted benzene ring at $\delta_H$ 6.83 (1H, d, $J$=8.3 Hz, H-5), 7.84 (1H, dd, $J$=8.3, 2.1 Hz, H-6) and 7.87 (1H, d, $J$=2.1 Hz, H-2), a methine which connected with oxygen at $\delta_H$ 3.77 (1H, d, $J$=5.2 Hz), four methyls at $\delta_H$ 1.03, 1.05, 1.35 and 1.76 (each 3H, s), and a double-bond methine at $\delta_H$ 5.34 (1H, br t, $J$=7.0 Hz). Furthermore, the $^{13}$C-NMR spectrum (Table 1) of **1** displayed the presence of five methylenes, a tri-substituted double bond at $\delta_C$ 138.2 (s) and 121.8 (d), a methine at $\delta_C$ 55.2, two quaternary carbons at $\delta_C$ 45.4 and 87.5 and a carbonyl group at $\delta_C$ 171.7. Based on these findings, compound **1** was presumed to be a 3-substituted-4-hydroxybenzoic acid derivative with a sesquiterpene moiety, like kuhistanols A—D.[3)] The $^{13}$C-NMR spectral data of the sesquiterpene moiety (C-1′ to C-5′) in compound **1** were very similar to those of a kuhistanol A, and indicated the presence of the partial structure $-CH_2CH=CH(CH_3)CH_2CH_2-$. The remaining sesquiterpene moiety of compound **1** is estimated to be $C_9H_{15}O$, and was calculated to have two degrees of unsaturation. The remaining $^{13}$C-NMR data suggested the presence of two rings. In the $^1$H detected multiple bond connectivity (HMBC) spectrum of **1**, the methyl signals at $\delta_H$ 1.03 ($H_3$-15′) and 1.05 ($H_3$-12′), the methyl signal at $\delta_H$ 1.35 ($H_3$-14′), and the methine proton signal at $\delta_H$ 1.23 (H-6′) showed long-range correlations with the carbon signals at $\delta_C$ 55.2 (C-6′), 45.4 (C-11′) and 86.5 (C-10′), the carbon signals at $\delta_C$ 55.2 (C-6′), 87.5 (C-7′) and 39.0 (C-8′), and the carbon signals at $\delta_C$ 26.2 (C-5′), 87.5 (C-7′) and 45.4 (C-11′), respectively. Thus compound **1** was believed to contain a six-membered ring. The connection between C-7′ and C-10′ *via* an ether bond was confirmed by the HMBC spectrum. Thus, the methine proton signal at $\delta_H$ 3.77 (H-10′) showed long-range correlations with the carbon signals at $\delta_C$ 87.5 (C-7′). The $^{13}$C-NMR spectral data of the sesquiterpene moiety in **1** were also very similar to those of farnesiferol C[4)] (**6**), which is a farnesyl coumarin derivative, except for some methylene signals (**1**: $\delta_C$ 28.9, **6**: $\delta_C$ 65.0). The relative configurations of C-6′, C-7′ and C-10′ were determined to be 6′*S**, 7′*R** and 10′*S** based on the observed correlations of $\delta_H$ 1.05 ($H_3$-15) with $\delta_H$ 1.23 (H-6′) and 1.67 (Hb-9′) and correlations of $\delta_H$ 1.42 and 1.45 ($H_2$-5′) with $\delta_H$ 1.35 ($H_3$-14′) and 1.03 ($H_3$-12′) in the nuclear Overhauser enhancement spectroscopy (NOESY) spectrum of **1**. Thus, the structure of compound **1** was elucidated to be as shown.

Compound **2** showed the same molecular formula as compound **1**. The $^1$H- and $^{13}$C-NMR spectral data of **2** revealed the same 3-substituted-4-hydroxybenzoic acid and farnesyl unit as those of **1**. The $^{13}$C-NMR spectral data of both compounds **2** and kuhistanol A[3)] were very similar except for C-4′–C-15′ (Table 1). The $^{13}$C-NMR spectrum of the farnesyl part of **2** showed the presence of four methyls, five methylenes, three methines ($\delta_C$ 37.1, 51.4, 123.5), two quaternary carbons ($\delta_C$ 44.7, 137.6), and one carbonyl carbon ($\delta_C$ 217.0). The $^1$H-NMR spectrum showed the presence of two doublet methyls ($\delta_H$ 0.89, 0.91, each 3H, d, $J$=6.7 Hz), and two singlet methyls ($\delta_H$ 0.57, 1.75, each 3H, s). From the $^1$H–$^1$H COSY and $^{13}$C–$^1$H COSY spectra of **2**, partial structures I, II, III, IV and V were determined (Fig. 2). In the HMBC spectrum of **2**, the correlations of $\delta_H$ 1.75 (H-13') with $\delta_C$ 33.8 (C-4') and 123.5 (C-2') indicated that partial structures I and IV were connected; the correlation of $\delta_H$ 0.57 (H-14′) with $\delta_C$ 37.1 (C-5′) and 51.4 (C-7′) indicated

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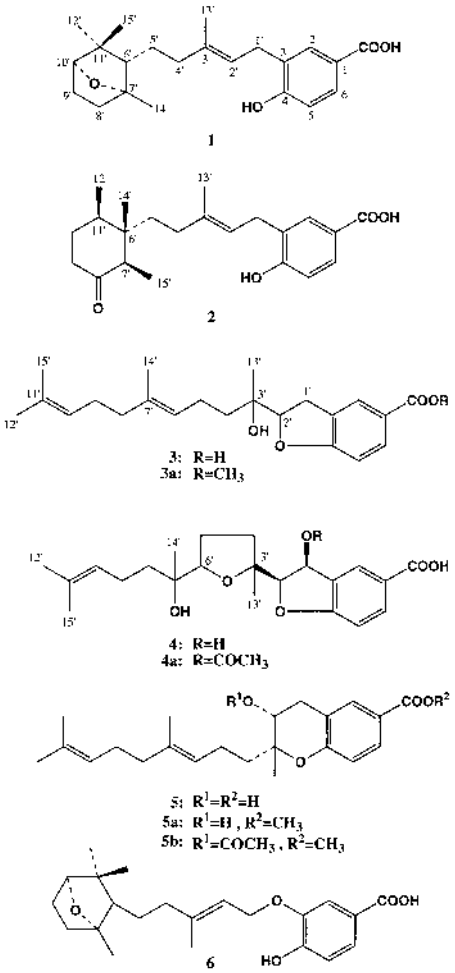


Fig. 1

that I, III and V were connected and the correlation of $\delta_H$ 0.89 (H-12′) and 0.57 (H-14′) with $\delta_C$ 44.7 (C-6′) indicated that I and II were connected *via* C-6'. Correlations of $\delta_H$ 0.91 (H-15′) with $\delta_C$ 44.7 (C-6′) and 217.0 (C-8′), and those of $\delta_H$ 2.44 (H-9′) with $\delta_C$ 32.2 (C-10′) and 217.0 (C-8′) were observed. Based on results, the structure of the farnesyl part and the connection between C-1′ and C-3 were estimated to be as shown. In the NOESY spectrum, the proton signal at $\delta_H$ 0.57 (H-14′) was correlated with the proton signals at $\delta_H$ 0.91 (H-15′) and 1.60 ($H_{ax}$-10′), and the proton signal at $\delta_H$ 2.63 ($H_{ax}$-7′) was correlated with the proton signals at $\delta_H$ 2.08 ($H_{ax}$-11′) and 1.97 (H-4′). These results clearly showed that the relative configuration of **2** was 6′*S**, 7′*R**, 11′*R**.

Compound **3** had the same molecular formula $C_{22}H_{30}O_4$ as kuhistanol D (**5**).[3] The $^1$H- and $^{13}$C-NMR spectra of **3** showed the presence of four methyls, five methylenes, two trisubstituted double bonds, a 3,4-trisubstituted benzoic acid moiety, a methine and a quaternary carbon, both vicinal to an oxygen atom. The functional groups are the same as those observed in **5**. However, in the $^{13}$C-NMR spectra, the quaternary carbon atom vicinal to an oxygen atom resonated downfield ($\delta_C$ 90.4) compared to that ($\delta_C$ 67.9) in **5**, while $^1$H-NMR spectra, methine proton geminal to an oxygen atom resonated downfield ($\delta_H$ 4.75) compared to that ($\delta_H$ 3.87) in **5**. Methylation of **3** with $(CH_3)_3SiCHN_2$ gave a monomethyl derivative **3a** similar to the results in the methylation of **5**.

Table 1. $^{13}$C-NMR Spectral Data for Compounds **1**—**6**[a)]

| C | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| 1 | 121.6 | 124.6 | 122.1 | 124.6 | 121.2 |
| 2 | 132.5 | 132.5 | 127.6 | 128.8 | 133.1 |
| 3 | 127.8 | 128.8 | 128.1 | 131.6 | 117.9 |
| 4 | 159.8 | 160.4 | 164.6 | 165.7 | 158.9 |
| 5 | 115.3 | 115.2 | 109.3 | 110.3 | 117.9 |
| 6 | 130.3 | 130.3 | 132.2 | 133.8 | 130.5 |
| 1′ | 28.9 | 29.1 | 29.9 | 73.7 | 31.9 |
| 2′ | 121.8 | 123.5 | 90.4 | 98.3 | 68.2 |
| 3′ | 138.2 | 137.6 | 73.9 | 84.7 | 80.9 |
| 4′ | 39.9 | 33.8 | 37.3 | 35.0 | 38.9 |
| 5′ | 26.2 | 37.1 | 22.2 | 27.2 | 22.5 |
| 6′ | 55.2 | 44.7 | 124.1 | 87.5 | 125.4 |
| 7′ | 87.5 | 51.4 | 136.2 | 73.6 | 136.3 |
| 8′ | 39.0 | 217.0 | 40.0 | 40.4 | 40.8 |
| 9′ | 25.9 | 42.4 | 26.9 | 22.8 | 27.7 |
| 10′ | 86.5 | 32.2 | 124.5 | 125.9 | 125.4 |
| 11′ | 45.4 | 37.1 | 131.8 | 131.9 | 132.1 |
| 12′ | 23.6 | 15.3 | 26.0 | 25.9 | 25.8 |
| 13′ | 16.3 | 16.4 | 23.2 | 23.7 | 19.0 |
| 14′ | 19.0 | 7.9 | 16.3 | 22.4 | 16.0 |
| 15′ | 26.2 | 15.6 | 18.0 | 17.7 | 17.7 |
| COOH | 171.7 | 172.5 | 171.9 | 169.8 | 170.0 |

*a*) Compounds **1** and **3** were measured in $CDCl_3$, compounds **2** and **4**—**6** were measured in $CD_3OD$.

However, while acetylation of **5a** gave mono-acetate **5b**, acetylation of **3a** did not yield the acetylated product. This fact indicated that compound **3** has a tertiary hydroxy group instead of the secondary alcohol observed in **5**. In the HMBC spectrum of **3**, the correlations of $\delta_H$ 3.16 and 3.27 ($H_2$-1′) with $\delta_C$ 128.1 (C-3), 164.6 (C-4), 90.4 (C-2′) and 73.9 (C-3′), and those of $\delta_H$ 1.32 (H-13′) with $\delta_C$ 37.3 (C-4′), 73.9 (C-3′) and 90.4 (C-2′) indicated the presence of a tetrahydrofuranobenzene ring and a hydroxyl group at C-3′ in compound **3**. In the NOESY spectrum, the stereochemistry of the double bond should be 6*E*, since correlations were observed between H-6′ and H-8′ and between H-14′ and H-5′. Based on these findings, the structure of compound **3** was elucidated to be as shown.

HR-EI-MS of **4** showed an $[M]^+$ ion peak at *m/z* 390.2040, which indicated a molecular formula of $C_{22}H_{30}O_6$. The $^1$H- and $^{13}$C-NMR spectral data of **4** showed the presence of a prenylated unit and an aromatic ring similar to those in compounds **1**–**3**. The $^1$H-NMR spectrum of **4** showed four singlet methyls and four methines at $\delta_H$ 5.34 (d, $J$=3.4 Hz), 4.95 (t, $J$=7.2 Hz), 3.65 (dd, $J$=8.9, 6.3 Hz) and 4.45 (d, $J$=3.4 Hz) for the prenylated unit. The $^{13}$C-NMR spectrum of the prenylated unit in **4** showed the presence of four methyls, four methylenes, four methines at $\delta_C$ 125.9, 98.3, 87.5, and 73.7, and three quaternary carbons at $\delta_C$ 131.9, 84.7, and 73.6. From the $^1$H–$^1$H COSY and $^{13}$C–$^1$H COSY spectra, the partial structures VI—X were obtained (Fig. 2). In the HMBC spectrum of **4**, the correlations of $\delta_H$ 1.00 ($H_3$-14′) with $\delta_C$ 40.4 (C-8′) and 87.5 (C-6′) indicated that of partial structures VI, VII and IX were connected, and; the correlation of $\delta_H$ 1.28 ($H_3$-13) with $\delta_C$ 35.0 (C-4′) and 98.3 (C-2′) indicated that partial structures VII, VIII and X were connected. These findings reveal the farnesyl carbon framework. The remaining problem in the structural elucidation of **4** was the position of the epoxy rings and the hydroxyl groups. The degree of unsaturation of **4** was eight, consisting of six for an

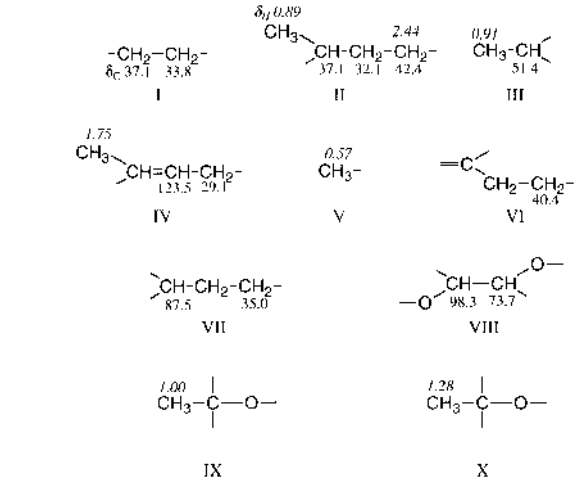

Fig. 2

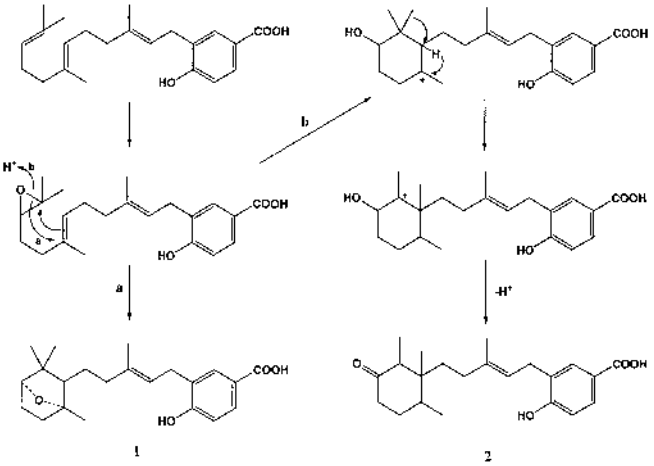

Fig. 3. Possible Biosynthetic Pathway for Compounds **1** and **2**

aromatic ring, a carboxylic acid and a double bond. The remaining two degrees of unsaturation suggested the presence of two more rings. The acetylation of **4** gave mono-acetate **4a**, which revealed that the proton at $\delta_H$ 5.34 (H-1′) in **4** was shifted downfield to $\delta_H$ 6.43 in **4a**. This indicated the presence of one secondary hydroxyl group at C-1′ and the lack of a phenolic hydroxyl group in compound **4**. In the HMBC spectrum, the correlation of $\delta_H$ 4.45 (H-2′) with $\delta_C$ 165.7 (C-4) indicated that C-4 and C-2′ were connected *via* oxygen. The remaining ring was estimated to be between C-3′ and C-6′ or C-3′ and C-7′ *via* oxygen. The latter possibility was ruled out because there is one secondary hydroxyl group in compound **4**, and the chemical shifts of $\delta_C$ 87.5 and 84.7 are in good agreement with a five-membered, rather than a six-membered ether ring. The relative configuration of H-1′ and H-2′ was determined to be *cis* from the coupling constant of 3.4 Hz.[5] Based on these findings, the structure of **4** was elucidated as shown.

A possible biosynthetic pathway for **1** and **2** is shown in Fig. 3.

## Experimental

**General Experimental Procedures** NMR (400 MHz for $^1$H-NMR, 100 MHz for $^{13}$C-NMR) spectra were measured on a Bruker ARX 400 NMR spectrometer with tetramethylsilane as an internal standard and mass spectra were measured on a JEOL JSMD-300 instrument; column chromatography: Silica gel 60 (Merck), Sephadex LH-20 (Pharmacia); HPLC: GPC (Shodex H-2001, 2002, $CHCl_3$), silica gel (Merck, LiChrosorb Si60), ODS (Merck LiChrosorb RP18). IR spectra were recorded on a Perkin-Elmer 1720 FT-IR spectrometer, UV spectra on a Shimadzu UV2100 UV-VIS recording spectrophotometer. Optical rotations were measured with JASCO DIP-370 digital polarimeter.

**Plant Material** The roots of *Ferula kuhistanica* were collected in July 1997 from Uzbekistan. Herbarium specimens (98C008) are deposited in the herbarium of Institute of Botany, Academy of Sciences, Uzbekistan and the Graduate School of Pharmaceutical Sciences, Kyoto University.

**Extraction and Isolation** The roots of *F. kuhistanica* (2.25 kg) were crushed and extracted with MeOH at 60 °C for 6 h three times. The MeOH extracts were concentrated *in vacuo* to give a residue, which was partitioned between EtOAc and $H_2O$. The EtOAc layer was concentrated *in vacuo* to give a residue (247 g), which was chromatographed over silica gel. The column was eluted with solvents to increase polarity (hexane–EtOAc; $CHCl_3$–MeOH) to give 21 frs. Fraction 11 (7.6 g) was then applied to a silica gel column with $CHCl_3$–MeOH as eluent to give 17 frs. (11.1—11.17). Fraction 11.10 (783 mg) was loaded on to Sephadex LH-20 column and the column was eluted with MeOH to give 7 frs. (11.10.1—11.10.7). Fraction 11.10.3 (584 mg) was subjected to HPLC (ODS, MeOH : $H_2O$=9 : 1) to give **1** (110 mg). Fraction 11.10.4 (80 mg) was subjected to HPLC (ODS, MeOH : $H_2O$=7 : 3) to give **2** (8 mg). Fraction 11.8 (1 g) was loaded on to Sephadex LH-20 column eluted with MeOH to give 5 frs. (11.8.1—11.8.5). Fraction 11.8.3 (600 mg) was subjected repeated HPLC [(1) GPC, MeOH, (2) $SiO_2$, hexane–EtOAc=1 : 1, (3) ODS, MeOH : $H_2O$=7 : 3) and further purified by preparative TLC (hexane : EtOAc=1 : 3) to give **3** (5.2 mg). Fraction 14 (9.0 g) was applied to silica gel column with $CHCl_3$–MeOH as eluent to give 14 frs. (14.1—14.14). Fraction 14.9 (920 mg) was loaded on to Sephadex LH-20 column and the column was eluted with MeOH to give 6 frs. (14.9.1—14.9.6). Fraction 14.9.4 (578 mg) was subjected to repeated HPLC [(1) ODS, MeOH : $H_2O$=8 : 2, (2) ODS, MeOH : $H_2O$=7 : 3, (3) $SiO_2$, hexane : EtOAc=1 : 5] to give **4** (10 mg).

Kuhistanol E (**1**): $[\alpha]_D^{25}$ +4.4° (*c* 1.0, MeOH); IR (KBr) cm$^{-1}$: 3420, 2970, 1683, 1279, 1123, 758. UV $\lambda_{max}$ (MeOH) nm (log $\varepsilon$): 258 (4.1), 211 (4.2). $^1$H-NMR ($CDCl_3$) $\delta_H$: 1.03 (3H, s, H-15′), 1.05 (3H, s, H-12′), 1.23 (1H, dd, *J*=6.6, 8.3 Hz, H-6′), 1.35 (3H, s, H-14′), 1.42 (1H, m, H-5′), 1.45 (1H, m, H-5′), 1.47 (1H, m, H-8′), 1.50 (1H, m, H-8′), 1.67 (1H, m, H-9′), 1.76 (3H, s, H-13′H), 1.91 (1H, m, H-9′), 3.39 (2H, d, *J*=7.0 Hz, H-1′), 3.77 (1H, d, *J*=5.2 Hz, H-10′), 5.34 (1H, br t, *J*=7.0 Hz, H-2′), 6.83 (1H, d, *J*=8.3 Hz, H-5), 7.84 (1H, dd, *J*=2.1, 8.3 Hz, H-6), 7.87 (1H, d, *J*=2.1 Hz, H-2); $^{13}$C-NMR ($CDCl_3$): Table 1; HR-EI-MS *m/z*: 358.2172 [M]$^+$ (Calcd for $C_{22}H_{30}O_4$: 358.2144). EI-MS *m/z* (rel. int.): 43 (100), 69 (45), 109 (37), 135 (45), 151 (67), 153 (66), 189 (32), 204 (25), 340 (23), 358 (15).

Kuhistanol F (**2**): $[\alpha]_D^{25}$ +4.7° (*c* 0.7, MeOH); IR (KBr) cm$^{-1}$: 3444, 2938, 2363, 1702, 1613, 1261, 1089; UV $\lambda_{max}$ (MeOH) nm (log $\varepsilon$): 257 (4.0), 207 (4.2); $^1$H-NMR ($CD_3OD$) $\delta_H$: 0.57 (3H, s, H-14′), 0.89, 0.91 (each 3H, d, *J*=6.7 Hz, 12′-$H_3$, $H_3$-14′), 1.42 (1H, m, Ha-5′), 1.50 (1H, m, Hb-5′), 1.60 (1H, m, H-10′), 1.75 (3H, s, H-13′), 1.88 (1H, m, Hb-10′), 1.97 (1H, ddd, *J*=4.6, 12.5, 12.5 Hz, Ha-4′), 2.08 (1H, m, H-11′), 2.11 (1H, m, Hb-4′), 2.23 (1H, dd, *J*=3.5, 13.7 Hz, Ha-9′), 2.44 (1H, ddd, *J*=7.3, 13.7, 13.7 Hz, Hb-9′), 2.63 (1H, q, *J*=6.7, H-7′), 3.30 (2H, t, *J*=7.1 Hz, H-1′), 5.39 (1H, t, *J*=7.1 Hz, H-2′), 6.76 (1H, d, *J*=8.2 Hz, H-5), 7.69 (1H, br d, *J*=8.2 Hz, H-6), 7.76 (1H, br s, H-2). $^{13}$C-NMR ($CD_3OD$): Table 1; HR-EI-MS *m/z*: 357.2065 [M−H]$^+$ (Calcd for $C_{22}H_{29}O_4$: 357.2066). EIMS *m/z* (rel. int.): 55 (52), 69 (36), 107 (16), 139 (100), 151 (49), 189 (38), 340 (13), 358 (5).

Kuhistanol G (**3**): $[\alpha]_D^{25}$ 0° (*c* 0.8, MeOH); IR (KBr) cm$^{-1}$: 3424, 2931, 2363, 1686, 1612, 1450, 1249, 1117. UV $\lambda_{max}$ (MeOH) nm (log $\varepsilon$): 291 (3.7), 263 (4.1), 208 (4.3). $^1$H-NMR ($CDCl_3$) $\delta_H$: 1.32 (3H, s, H-13′), 1.43 (1H, m, Ha-4′), 1.47 (1H, m, Hb-4′), 1.59 (3H, s, H-15′), 1.63 (3H, s, H-14′), 1.67 (3H, s, H-12′), 1.91 (2H, t, *J*=7.8 Hz, H-8′), 2.00 (2H, m, $H_2$-9′), 2.05 (2H, m, $H_2$-5′), 3.16 (1H, dd, *J*=9.5, 15.9 Hz, Ha-1′), 3.27 (1H, dd, *J*=8.6, 15.9 Hz, Hb-1′), 4.75 (1H, dd, t, *J*=8.6, 9.5 Hz, H-2′), 5.08 (1H, t, *J*=6.7 Hz, H-10′), 5.14 (1H, t, *J*=6.9 Hz, H-6′), 6.81 (1H, d, *J*=8.4 Hz, H-5), 7.91 (1H, s, H-2), 7.93 (1H, d, *J*=8.4 Hz, H-6); $^{13}$C-NMR ($CDCl_3$): Table 1. HR-FAB-MS *m/z*: 381.2034 [M+Na]$^+$ (Calcd for $C_{22}H_{30}O_4Na$: 381.2042). EI-MS *m/z* (rel. int.): 69 (100), 109 (47), 136 (15), 151 (61), 207 (39), 297 (32), 315 (28), 358 (10).

Methylation of **3**: A solution of **3** (2.0 mg) was treated with $(CH_3)_3SiCHN_2$, for 5 h at room temperature to give **3a** (1.5 mg). $^1$H-NMR ($CD_3OD$) $\delta_H$: 1.31, 1.59, 1.62, 1.67 (each 3H, s), 3.15 (1H, dd, *J*=9.4, 15.8 Hz), 3.25 (1H, dd, *J*=8.4, 15.8 Hz), 3.87 (3H, s, $OCH_3$), 4.73 (1H, t, *J*=9.1

Hz), 5.08 (1H, t, $J$=6.7 Hz, 10′-H), 5.14 (1H, t, $J$=6.9 Hz, 6′-H), 6.78 (1H, d, $J$=8.8 Hz), 7.85 (1H, s), 7.86 (1H, d, $J$=8.8 Hz).

Kuhistanol H (**4**): $[\alpha]_D^{25}$ 0° (*c* 0.6, MeOH); IR (KBr) $cm^{-1}$: 3391, 2973, 2931, 1687, 1319, 1265, 1124, 998; UV $\lambda_{max}$ (MeOH) nm (log $\varepsilon$): 290 (3.5), 259 (4.1), 210 (4.2); $^1$H-NMR ($CD_3OD$) $\delta_H$: 1.00 (3H, s, H-14′), 1.23 (1H, m, Ha-8′), 1.28 (3H, s, H-13′), 1.33 (1H, m, Hb-8′), 1.51 (3H, s, H-12′), 1.63 (3H, s, H-15′), 1.77 (1H, ddd, $J$=4.0, 9.0, 12.0 Hz Ha-4′), 1.79 (2H, m, H-9′), 1.92 (1H, m, Ha-5′), 1.94 (1H, m, Hb-5′), 2.33 (1H, ddd, $J$=9.0, 9.9, 12.0 Hz, Hb-4′), 3.65 (1H, dd, $J$=6.3, 8.9 Hz, H-6′), 4.45 (1H, d, $J$=3.7 Hz, H-2′), 4.95 (1H, br t, $J$=7.2 Hz, H-10′), 5.34 (1H, d, $J$=3.7 Hz, H-1′), 6.86 (1H, d, $J$=8.5 Hz, H-5), 7.95 (1H, dd, $J$=1.7, 8.5 Hz, H-6), 8.04 (1H, s, H-2). $^{13}$C-NMR ($CD_3OD$): Table 1. HR-EI-MS *m/z*: 390.2040 $[M]^+$ (Calcd for $C_{22}H_{30}O_6$: 390.2042). EI-MS *m/z* (ret. int.): 43 (100), 55 (50), 69 (82), 85 (62), 97 (43), 109 (61), 127 (29), 135 (41), 151 (11), 165 (37), 179 (6), 189 (63), 202 (58), 211 (36), 290 (54), 372 (55), 390 (2).

Acetylation of **4**: **4** (2.0 mg) was subjected to acetylation with $Ac_2O$–pyridine for 3 h at room temperature to give **4a** (1.2 mg). $^1$H-NMR ($CD_3OD$) $\delta_H$: 0.94, 1.28, 1.51, 1.62 (each 3H, s), 2.08 (3H, s, OAc), 3.55 (1H, dd, $J$=6.3, 8.9 Hz), 4.66 (1H, d, $J$=2.5 Hz), 4.91 (1H, br t, $J$=7.1 Hz), 6.43 (1H, d, $J$=2.5 Hz, 1′-H), 6.90 (1H, d, $J$=8.5 Hz), 7.98 (1H, d, $J$=8.5 Hz), 8.03 (1H, s).

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