An Acetylene and a Monoterpene Glycoside from *Adenocaulon himalaicum*

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Abstract: **The methanolic extract of the aerial parts of *Adenocaulon himalaicum* (Asteraceae) has yielded a new acetylene, 1-*O*-feruloyl-tetradeca-4*E*,6*E*,12*E*-triene-8,10-diyne (1), a new monoterpene glycoside, 9-hydroxylinaloyl-3-*O*-(4-*O*-coumaroyl)-β-D-glucopyranoside (2), and eight known compounds. Their structures were established by chemical and spectroscopic methods.**

Adenocaulon himalaicum Edgew (Asteraceae), a perennial herb, is distributed mainly in southeast Asia, and its aerial parts have been used to treat abscesses, hemorrhage, and inflammation in Korean folk medicine (1), (2). On reviewing the literature of *Adenocaulon* species, only caffeic acid derivatives have been isolated from *A. adhaerescens* (3). Because there have been no previous studies on *A. himalaicum*, a chemical investigation of the methanolic extract of this plant was undertaken and led to the isolation of two new (**1**, **2**) and eight known compounds (**3 – 10**).

Five known compounds, phytol (**3**) (4), parasorboside (**7**) (5), prunasin (**8**) (6), (*Z*)-3-hexenyl β-D-glucopyranoside (**9**) (7) and 9-hydroxylinaloyl glucoside (**10**) (8) were characterized by comparing their physical and spectroscopic data with those reported in the literature. Three known monoglycerides, 1-*O*-(9*Z*,12*Z*,15*Z*-octadecatrienoyl)glycerol (**4**), 1-*O*-hexadecanoylglycerol (**5**), and 1-*O*-(9*Z*,12*Z*-octadecadienoyl)glycerol (**6**), were identified by ^{1}H-NMR and GC-MS analysis (9).

Compound **1** was obtained as a pale yellow oil and its molecular formula was determined to be $C_{24}H_{24}O_4$ by HREIMS (*m/z* 376.1688, M^+). Its IR spectrum displayed absorption bands at 2200, 2120 and 1703 cm^{-1}, indicating the presence of acetylene and ester groups. The UV spectrum of **1** suggested the presence of a diene-diyne moiety (10). The ^{1}H- and ^{13}C-NMR spectra exhibited the presence of the *trans*-feruloyl moiety (11). The remaining ^{1}H- and ^{13}C-NMR signals of **1** were very similar to those of tetradeca-4*E*,6*E*,12*E*-triene-8,10-diyn-1-ol reported in the literature (10), (12), except for the downfield shift of H-1 (δ 3.62 to δ 4.20). In the HMBC spectrum, long-range correlation was observed between the feruloyl carbonyl carbon C-9′ (δ 168.0) and the H-1 proton (δ 4.20) (Fig. **1**). Therefore, the structure of **1** was determined as 1-*O*-feruloyl-tetradeca-4*E*,6*E*,12*E*-trien-8,10-diyne.

Compound **2** was obtained as colorless gum with a molecular formula of $C_{25}H_{34}O_9$ by HRFABMS (*m/z* 501.2110, $[M + Na]^+$).

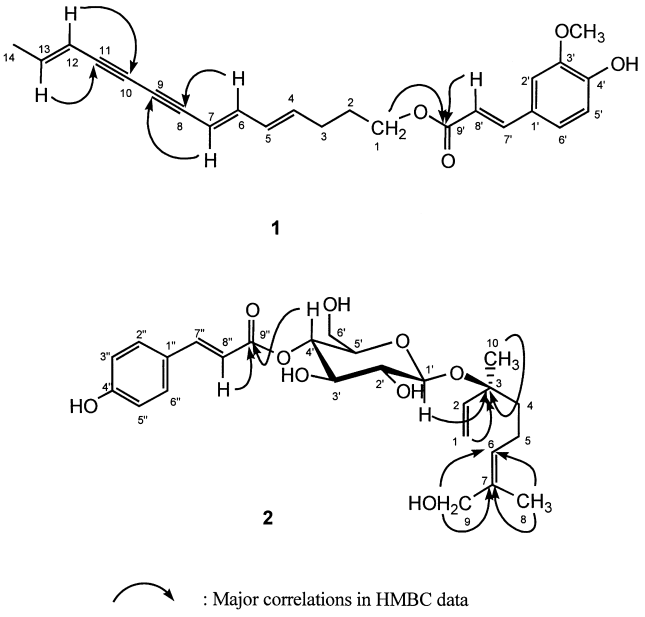

Fig. 1 Structures of compounds **1** and **2**.

Its IR spectrum displayed absorption bands at 3334 and 1690 cm^{-1}, indicating the presence of hydroxy and ester groups. The ^{1}H- and ^{13}C-NMR spectra for **2** indicated the presence of a *trans*-coumaroyl group (13). The remaining signals in ^{1}H- and ^{13}C-NMR spectra were very similar to those of 9-hydroxylinaloyl glucoside (**10**) (8). In the HMBC spectrum, long-range connectivities were observed between the coumaroyl ester carbon C-9″ (δ 167.9) and the H-4′ proton (δ 4.85), and C-3 (δ 80.8) and the H-1′ (δ 4.41), respectively (Fig. **1**). The alkaline hydrolysis of **2** afforded 9-hydroxylinaloyl glucoside and its ^{1}H-NMR and $[\alpha]_D$ data were in agreement with those of **10** (8). Based on these evidences, the structure of **2** was determined as 9-hydroxylinaloyl-3-*O*-(4-*O*-coumaroyl)-β-D-glucopyranoside.

Materials and Methods

Mps: uncorr. NMR: in $CDCl_3$ or CD_3OD, Bruker AMX 500 and Varian UNITY INOVA 500. IR: in CCl_4, Nicolet model 205 FT-IR spectrophotometer. MS: VG70-VSEQ mass spectrometer. GC-MS: Hewlett-Packard 6890 GC (column: HP-5SM)/Hewlett-Packard 5973 MSD system. CC: silica gel (Merck, 230 – 400 mesh). TLC: Merck precoated silica gel F_{254} plates and RP-18 F_{254s} plates. LPLC: Merck Lichroprep Lobar®-A Si 60 & Lobar®-A RP-18 (240 × 10 mm).

A. himalaicum was collected in Chuck-Ryung Mt., Kyungi-Do, Korea in September 1997. A voucher specimen (SKK-97-010) is deposited in the College of Pharmacy at SungKyunKwan University.

The dried and chopped aerial parts of *A. himalaicum* (4.4 kg) were extracted with MeOH (10 L) three times at room temperature. The resultant MeOH extract (180 g) was suspended in H_2O and then successively partitioned to give CH_2Cl_2 (35 g), EtOAc (13 g) and *n*-BuOH (13 g) soluble fractions. The CH_2Cl_2 extract (35 g) was chromatographed on silica gel (350 g) using

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gradient solvent system of hexane : EtOAc [5 : 1 (2.5 L), 2 : 1 (1.5 L) and 1 : 1 (1.5 L)], hexane : EtOAc : MeOH (10 : 10 : 1 and 5 : 5 : 1, each 1.5 L), and EtOAc : MeOH (20 : 1, 5 : 1 and 1 : 1, each 1.5 L) to give eight main fractions [M1 (2.5 L) and M2 – M8 (each 1.5 L)]. Fr. M3 (8 g) was chromatographed on silica gel (350 g) eluted with CH_2Cl_2 : MeOH (60 : 1) to give three fractions [M31 (2 L), M32 (1 L) and M33 (2 L)]. Fr. M31 (700 mg) was rechromatographed on silica gel (70 g) eluted with hexane : EtOAc (5 : 1) to give two subfractions [M311 (70 ml) and M312 (200 ml)], and Fr. M311 (200 mg) was purified with silica gel Lobar®-A column (CH_2Cl_2) to yield **1** (10 mg) and **3** (150 mg). Fr. M5 (5.2 g) was chromatographed on silica gel (200 g; hexane : EtOAc : MeOH, 2 : 5 : 0.5) to give four subfractions [M51 and M52 (each 240 ml), M53 (320 ml, M54 (600 ml)]. Fr. M51 (1.1 g) was rechromatographed on silica gel (100 g; CH_2Cl_2 : MeOH, 20 : 1) to give two subfractions [M511 (150 ml) and M512 (500 ml)], and Fr. M511 (150 mg) was purified with C-18 RP column (50 g, 80% MeOH) to afford **4** (100 mg). Fr. M52 (2.0 g) was rechromatographed on silica gel (180 g; CH_2Cl_2 : MeOH, 20 : 1) to give two subfractions [M521 (280 ml) and M522 (1 L)], and Fr. M521 (200 mg) was chromatographed on Sephadex LH-20 (50 g, CH_2Cl_2 : MeOH, 1 : 1) to give two subfractions [M5211 (60 ml) and M5212 (100 ml)], Fr. M5211 (50 mg) and Fr. M5212 (120 mg) was further purified with RP-18 Lobar®-A column (80% MeOH) to afford **5** (11 mg) and **6** (10 mg), respectively. Fr. M7 (3.0 g) was chromatographed on silica gel (200 g; CH_2Cl_2 : MeOH : H_2O, 50 : 10 : 1) to give two subfractions (M71 and M72, each 1 L). Fr. M72 (500 mg) was further subjected to Sephadex LH-20 (50 g, CH_2Cl_2 : MeOH, 1 : 1) column chromatography and purified with silica gel Lobar®-A column (EtOAc : MeOH : H_2O, 50 : 10 : 1) to afford **7** (10 mg).

The EtOAc extract (13 g) was chromatographed on Sephadex LH-20 (70 g) using EtOAc : MeOH (1 : 1) to give three main fractions [E1 (600 ml), E2 (160 ml) and E3 (320 ml)]. Fr. E2 (3.6 g) was chromatographed on silica gel (200 g) eluting with CH_2Cl_2 : MeOH : H_2O (35 : 10 : 1) to give three subfractions (E21 – E23, each 200 ml). Fr. E21 (700 mg) was rechromatographed on silica gel (50 g) eluted with CH_2Cl_2 : MeOH : H_2O (35 : 10 : 1) to give two subfractions [E211 (60 ml) and E212 (300 ml)], and Fr. E211 (50 mg) was further purified with RP-18 Lobar®-A column (50% MeOH) to yield **2** (10 mg). Fr. E23 (1.5 g) was chromatographed on silica gel (70 g; CH_2Cl_2 : MeOH : H_2O, 60 : 3 : 0.5) to give **8** (40 mg). The BuOH extract (13 g) was chromatographed (200 g) on silica gel using EtOAc : MeOH : H_2O (12 : 3 : 0.6) to give six main fractions [B1 – B3 (each 800 ml) and B4 – B6 (each 1.5 L)]. Fr. B1 (1 g) was chromatographed on Sephadex LH-20 (50 g, MeOH) to give two subfractions [B11 (50 ml) and B12 (100 ml)], and Fr. B12 (300 mg) was purified with silica gel (70 g, EtOAc : MeOH : H_2O, 50 : 10 : 1) column chromatography to give **9** (20 mg). Fr. B2 (2.1 g) was chromatographed on Sephadex LH-20 (MeOH) to give two fractions [B21 (50 ml) and B22 (200 ml)]. Fr. B21 (600 mg) was rechromatographed on silica gel (70 g) eluted with CH_2Cl_2 : MeOH : H_2O (12 : 3 : 0.4) to give two subfractions [B211 (80 ml) and B212 (120 ml)], and Fr. B211 (30 mg) was further purified with RP-18 Lobar®-A column (30% MeOH) to afford **10** (20 mg).

1-O-Feruloyltetradeca-4E,6E,12E-triene-8,10-diyne (**1**): yellow oil; UV: λ_{max}^{EtOH} nm (log ε) = 336 (4.51), 316 (4.58), 297 (4.45), 267 (4.33), 248 (4.46), 214 (4.36); IR: ν_{max}^{neat} cm^{-1} ν = 3020, 2965, 2940, 2200 (w), 2120 (w), 1703, 1635, 1602, 1514, 1431, 1264, 1215, 1173, 1033; EIMS: *m/z* (rel. int.) = 376 (M^+, 12), 332 (3), 252 (3), 199 (8), 182 (22), 177 (100), 167 (28); HREIMS: $C_{24}H_{24}O_4$ found: 376.1688 calcd.: 376.1675; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.79 – 1.83 (5H, m, H_2-2, H_3-14), 2.26 (2H, br.q, J = 7.0 Hz, H_2-3), 3.93 (3H, s, OCH_3), 4.20 (2H, t, J = 6.5 Hz, H_2-1), 5.57 (1H, d, J = 15.5 Hz, H-7), 5.58 (1H, dt, J = 16.0, 1.0 Hz, H-12), 5.87 (1H, s, OH), 5.87 (1H, dt, J = 15.0, 7 Hz, H-4), 6.15 (1H, dd, J = 15.0, 11.0 Hz, H-5), 6.28 (1H, d, J = 16.0 Hz, H-8′), 6.31 (1H, dq, J = 16.0, 7.0 Hz, H-13), 6.67 (1H, dd, J = 15.5, 11.0 Hz, H-6), 6.92 (1H, d, J = 8.0 Hz, H-6′), 7.03 (1H, d, J = 1.5 Hz, H-2′), 7.08 (1H, dd, J = 8.0, 1.5 Hz, H-5′), 7.60 (1H, d, J = 16.0 Hz, H-7′); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 19.7 (q, C-14), 28.8 (t, C-2), 30.1 (t, C-3), 56.7 (q, OCH_3), 64.4 (t, C-1), 73.2 (s, C-9), 76.8 (s, C-10), 81.1 (s, C-8), 82.1 (s, C-11), 109.0 (d, H-7), 110.0 (d, H-2′), 110.7 (d, H-12), 115.4 (d, C-6′), 116.1 (d, C-8′), 123.8 (d, C-5′), 127.7 (s, C-1′), 131.0 (d, C-5), 138.6 (d, C-4), 144.2 (d, C-13), 145.3 (d, C-6), 145.6 (d, C-7′), 147.5 (s, C-3′), 148.7 (s, c-4′), 168.0 (s, C-9′).

9-Hydroxylinaloyl-3-O-(4-O-coumaroyl)-β-D-glucopyranoside (**2**): colourless gum; $[\alpha]_D^{20}$: – 17.39° (CH_3OH; *c* 0.14); UV: λ_{max}^{EtOH} nm (log ε) = 313 (2.79), 228 (2.58), 204 (2.66); IR: ν_{max}^{neat} cm^{-1} ν = 3334, 1690, 1603, 1168; FABMS: *m/z* (rel. int.) = 501 (24), 147 (100); HRFABMS: $C_{25}H_{34}O_9Na$ found: 501.2110 calcd.: 501.2101; ^{1}H-NMR (500 MHz, CD_3OD): δ = 1.37 (3H, s, H_3-10). 1.66 (3H, s, H_3-8), 1.70 (3H, br.q, J = 6.0 Hz, H_2-4), 2.16 (2H, m, H_2-5), 3.30 (1H, dd, J = 9.0, 8.0 Hz, H-2′), 3.41 (1H, m, H-5′), 3.51 (1H, dd, J = 12.0, 5.5 Hz, H-6′), 3.59 (1H, dd, J = 12.0, 2.5 Hz, H-6′), 3.62 (1H, t, J = 9.0 Hz, H-3′), 3.92 (2H, s, H_2-9), 4.41 (1H, d, J = 8.0 Hz, H-1′), 4.85 (1H, t, J = 10.0 Hz, H-4′), 5.19 (1H, dd, J = 11.0, 1.0 Hz, H-1_{cis}), 5.23 (1H, dd, J = 16.5, 1.0 Hz, H-1_{trans}), 5.42 (1H, br.t, J = 6.5 Hz, H-6), 6.13 (1H, dd, J = 16.5, 11.0 Hz, H-2), 6.37 (1H, d, J = 15.5 Hz, H-8″), 6.82 (2H, d, J = 8.5 Hz, H-3″, 5″), 7.48 (2H, d, J = 8.5 Hz, H-2″, 6″), 7.67 (1H, d, J = 15.5 Hz, H-7″); ^{13}C-NMR (125 MHz, CD_3OD): δ = 13.1 (q, C-8), 22.6 (t, C-5), 22.9 (q, C-10), 40.6 (t, C-4), 61.9 (t, C-6′), 68.3 (t, C-9), 72.0 (d, C-4′), 74.5 (d, C-2′*), 75.2 (d, C-5′*), 75.3 (d, C-3′*), 80.8 (s, C-3), 98.6 (d, C-1′), 114.2 (d, C-8″), 114.4 (t, C-1), 116.2 (d, C-3″, C-5″), 126.3 (d, C-6), 126.4 (s, C-1″), 130.6 (d, C-2″, C-6″), 135.1 (s, C-7), 143.7 (d, C-2), 146.5 (d, C-7″), 160.7 (s, C-4″), 167.9 (s, C-9″); (* interchangeable each other).

Alkaline hydrolysis of **2** (3): 2 mg of **2** were dissolved in 1 ml of MeOH and NaOMe (28 mg) was added. After stirring the mixture for 5 h at R.T., the solution was neutralized with 2N HCl to pH 7, and then concentrated in vacuo. The resulting residue was purified by silica gel (1 g) column chromatography ($CHCl_3$: MeOH : H_2O, 40 : 10 : 1) to afford **10** (1 mg).

Phytol (**3**): colorless oil, $[\alpha]_D^{20}$: – 1.0 (MeOH; *c* 1.4).

Parasorboside (**7**): colorless gum, $[\alpha]_D^{20}$: + 1.0 (MeOH; *c* 0.1).

Prunasin (**8**): white powder, m.p. 140 °C, $[\alpha]_D^{20}$: – 51.8 (MeOH; *c* 0.5).

(Z)-*3-Hexenyl β-D-glucopyranoside* (**9**): colorless gum, $[\alpha]_D^{20}$: – 33.2 (MeOH; *c* 0.16).

9-Hydroxylinaloyl glucoside (**10**): colorless gum, $[\alpha]_D^{20}$: + 12.5 (MeOH; *c* 0.08).

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