Natural Product Sciences
23(3) : 208-212 (2017)
https://doi.org/10.20307/nps.2017.23.3.208

Sesquiterpenoids from the heartwood of *Juniperu s chinensis*

Hee Jin Jung[1], Byung-Sun Min[2], Hyun Ah Jung[3,*], and Jae Sue Choi[1,*]

[1]*Department of Food and Life Science, Pukyong National University, Busan 608-737, Republic of Korea*
[2]*College of Pharmacy, Catholic University of Daegu, Gyeongbuk 712-702, Republic of Korea*
[3]*Department of Food Science and Human Nutrition, Chonbuk National University, Jeonju 561-756, Republic of Korea*

Abstract – A new sesquiterpenoid, 11-hydroxy-valenc-1(10),3(4)-dien-2-one (**3**), two chemically synthesized but first isolate from nature, 3-oxocedran-8β-ol (**1**) and valenc-1(10),3(4),11(12)-trien-2-one (**2**) along with four known compounds, sugiol (**4**), (+)-nootkatone (**5**), 11-hydroxy-valenc-1(10)-en-2-one (**6**), and clovandiol (**7**), were isolated from the heartwood of *Juniperus chinensis*. All chemical structures were elucidated using extensive spectroscopic analysis including 1D and 2D NMR spectroscopy. Valenc-1(10),3(4),11(12)-trien-2-one (**2**) exhibited significant inhibitory activity against butyrylcholinesterase with an IC_{50} value of 68.45 µM.
Keywords – *Juniperus chinensis*, 3-Oxocedran-8β-ol, Valenc-1(10),3(4),11(12)-trien-2-one, 11-Hydroxy-valenc-1(10),3(4)-dien-2-one, Acetylcholinesterase, Butyrylcholinesterase

Introduction

The heartwood of *Juniperus chinensis* LINNE (Cupressaceae) has been used in the East Asian region as a traditional folk medicine for the treatment of colds, urinary tract infections, dysentery, hemorrhage, leucorrhea and rheumatic arthritis.[1,2] We previously reported the isolation of two new cholinesterases and β-site amyloid precursor protein cleaving enzyme 1 (BACE1) inhibitors, α-methyl artoflavanocoumarin and 5,7,4'-trihydroxy-2-styrylchromone, together with 20 known compounds, from *J. chinensis*.[3] As part of our continued work on *J. chinensis*, we report here the isolation of a new sesquiterpenoid, 11-hydroxy-valenc-1(10),3(4)-dien-2-one (**3**), two chemically synthesized but first isolate from nature, 3-oxocedran-8β-ol (**1**) and valenc-1(10),3(4),11(12)-trien-2-one (**2**) along with four known compounds, sugiol (**4**), (+)-nootkatone (**5**), 11-hydroxy-valenc-1(10)-en-2-one (**6**), and clovandiol (**7**). Herein, we describe the isolation, structure elucidation, and inhibitory activities of these compounds against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE).

*Author for correspondence
Jae Sue Choi, Department of Food and Life Science, Pukyong National University, Busan 608-737, Republic of Korea.
Tel: +82-51-629-5845; E-mail: choijs@pknu.ac.kr

Hyun Ah Jung, Department of Food Science and Human Nutrition, Chonbuk National University, Jeonju 561-756, Republic of Korea.
Tel: +82-63-270-4882; E-mail: jungha@jbnu.ac.kr

Experimental

General Experimental Procedures – Optical rotations were measured with a JASCO DIP-370 digital polarimeter. UV spectra were obtained with an Ultraspec 2100pro UV/Visible spectrophotometer. HR-ESI-MS and EI-MS were performed with a JEOL JMS-700 spectrometer (Tokyo, Japan). IR spectra (KBr) were recorded on a Perkin Elmer spectrum X spectrometer (Norwalk, CT, USA). NMR spectra were recorded in $CDCl_3$, CD_3OD, and DMSO-d_6 using a JEOL JNM ECP-600 spectrometer (Tokyo, Japan). Column chromatography was conducted using silica gel 60 (70 - 230 mesh, Merck, Darmstadt, Germany). TLC was performed on pre-coated Merck Kiesel gel 60 F_{254} plates (20 × 20 cm, 0.25 mm) and RP-18 F_{254s} plates (5 × 10 cm, Merck), and visualized by heating after spraying with 50% H_2SO_4.

Chemicals and Reagents – Electric-eel AChE (EC 3.1.1.7), horse-serum BChE (EC 3.1.1.8), acetylthiocholine iodide (ACh), butyrylthiocholine chloride (BCh), 5,5'-dithiobis-[2-nitrobenzoic acid] (DTNB), and berberine were purchased from Sigma-Aldrich Co. (St Louis, MO, USA). All of the solvents used for column chromatography were purchased from Merck, Fluka, or Sigma-Aldrich unless otherwise stated.

Plant Material – Heartwood parts of *J. chinensis* were purchased from Kyung-Dong medicinal market, Seoul, Korea in April 2012 and authenticated by Prof. B. W. Kim, Dong-Eui University, Busan, Korea. A voucher

specimen (No. 20120302) was deposited in the author's laboratory (Prof. J. S. Choi).

Extraction and Isolation – The dried heartwood (3.0 kg) of *J. chinensis* was extracted with 100% MeOH and concentrated to give a dark brown residue, which was partitioned as described previously to yield CH_2Cl_2 and EtOAc fractions, respectively.[3] The CH_2Cl_2 fraction (107 g) was subjected to chromatography on a silica gel column using CH_2Cl_2 : MeOH (100:1 → 1:1, gradient) as the eluent to yield 24 subfractions (CF1–CF24). Fraction CF5 (1.14 g) was subjected to chromatography on a silica gel column using *n*-hexane : EtOAc = 10:1 to yield compound **4** (10 mg). Fraction CF10 (2.8 g) was subjected to chromatography on a silica gel column using *n*-hexane: EtOAc = 9:1 to yield compound **1** (50 mg). The EtOAc fraction (147 g) was subjected to chromatography on a silica gel column and eluted with CH_2Cl_2 : MeOH (20:1 → 1:1, gradient) to yield 35 subfractions (EF01–EF35). Fraction EF6 (700 mg) was subjected to silica gel column chromatography using *n*-hexane : EtOAc = 15:1 → 1:1 to yield compound **5** (10 mg). Fraction EF7 (400 mg) was separated on a silica gel column using *n*-hexane : EtOAc = 8:1 to afford compound **2** (11 mg). Fraction EF10 (3 g) was chromatographed on a silica gel column and eluted with *n*-hexane : EtOAc=10:1 → 1:1 to obtain compound **6** (30 mg). Fraction EF14 (4 g) was subjected to chromatography on a silica gel column using *n*-hexane : EtOAc = 2:1 to yield compound **3** (15 mg). Fraction EF15 (2 g) was subjected to chromatography on a silica gel column using *n*-hexane : EtOAc = 2:1 to yield compound **7** (3.1 mg).

3-Oxocedran-8β-ol (1) – White amorphous powder, $[\alpha]_D^{25}$ –20.50° (c = 1.0, $CHCl_3$); UV (MeOH) λ_{max} (log ε): 227 (2.89) nm; IR (KBr) ν_{max}: 3390, 1710 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 2.44 (1H, ddd, J = 2, 11.9, 19.3 Hz, H-4α), 2.24 (1H, dd, J = 5.5, 19.3 Hz, H-4β), 2.17 (1H, ddd, J = 1.7, 5.5, 11.9 Hz, H-5β), 2.10 (1H, dq, J = 2, 7.3 Hz, H-2α), 2.08 (1H, m, H-9), 1.88 (1H, dt, J = 5.9, 12.82 Hz, H-10), 1.74 (1H, ddt, J = 1.3, 6, 13.3 Hz, H-9), 1.57 (1H, d, J = 5 Hz, H-7α), 1.48 (1H, m, H-10), 1.41 (3H, s, H-15), 1.39 (1H, dd, J = 5, 12.08 Hz, H-11α), 1.33 (1H, d, J = 12.08 Hz, H-11β), 1.30 (3H, s, H-13), 0.98 (3H, d, J = 7.3 Hz, H-12), 0.96 (3H, s, H-14). ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 219.91 (C-3), 74.21 (C-8), 58.19 (C-5), 52.63 (C-1), 52.34 (C-7), 48.40 (C-2), 44.10 (C-6), 37.71 (C-11), 35.84 (C-4), 35.17 (C-9), 34.40 (C-10), 30.11 (C-15), 30.04 (C-14), 27.79 (C-13), 8.91 (C-12); HR-ESI-MS m/z 259.1671 $[M + Na]^+$ (calcd for $C_{15}H_{24}O_2Na$, 259.1669).

Valenc-1(10), 3(4),11(12)-trien-2-one (2) – Colorless oil, $[\alpha]_D^{26}$ +109.10° (c = 1.0, MeOH); UV (MeOH) λ_{max} nm (log ε): 244 (4.74); IR (KBr) ν_{max}: 2830, 1625, 1490, 1020 cm^{-1}; ^{1}H-NMR (600 MHz, CD_3OD) δ : 6.09 (1H, d, J = 2.0 Hz, H-3), 6.08 (1H, d, J = 2.0 Hz, H-1), 4.76, 4.75 (each 1H, br s, H-12), 2.74 (1H, m, H-9β), 2.59 (1H, tt, J = 3.1, 12.8 Hz, H-7), 2.46 (1H, m, H-9α), 2.15 (1H, dd, J = 3.1, 12.8 Hz, H-6α), 2.09 (1H, d, J = 1.4 Hz, H-8β), 2.07 (3H, s, H-14), 1.74 (3H, s, H-13), 1.46 (3H, s, H-15), 1.35 (1H, dd, J = 3.1, 12.8 Hz, H-8α), 1.23 (1H, d, J = 12.8 Hz, H-6β). ^{13}C-NMR (125 MHz, CD_3OD) δ : 188.80 (C-2), 171.99 (C-10), 170.54 (C-4), 149.47 (C-11), 126.74 (C-3), 124.59 (C-1), 110.37 (C-12), 45.35 (C-5), 43.46 (C-6), 41.15 (C-7), 34.85 (C-8), 33.82 (C-9), 23.87 (C-15), 20.93 (C-13), 19.15 (C-14); HR-ESI-MS m/z 239.1421 $[M + Na]^+$ (calcd for $C_{15}H_{20}ONa$, 239.1406).

11-Hydroxy-valenc-1(10),3(4)-dien-2-one (3) – Colorless oil, $[\alpha]_D^{26}$ +118.50° (c = 1.0, MeOH); UV (MeOH) λ_{max} nm (log ε): 244 (4.78); IR (KBr) ν_{max}: 3320, 2830, 1625, 1490, 1020 cm^{-1}; ^{1}H-NMR (600 MHz, CD_3OD) δ : 6.08 (1H, d, J = 1.4 Hz, H-3), 6.06 (1H, d, J = 2.0 Hz, H-1), 2.66 (1H, m, H-9β), 2.45 (1H, m, H-9α), 2.27 (1H, dd, J = 2.8, 12.8 Hz, H-6α), 2.12 (1H, dd, J = 2.8, 12.8 Hz, H-8α), 2.07 (3H, s, H-14), 1.92 (1H, tt, J = 2.8, 12.8 Hz, H-7), 1.36 (3H, s, H-15), 1.20 (1H, d, J = 1.4 Hz, H-8β), 1.18 (3H, s, H-13), 1.13 (3H, s, H-12), 1.07 (1H, d, J = 12.8 Hz, H-6β). ^{13}C-NMR (125 MHz, CD_3OD) δ : 188.88 (C-2), 172.59 (C-10), 170.88 (C-4), 126.70 (C-3), 124.26 (C-1), 72.76 (C-11), 45.14 (C-5), 44.58 (C-7), 39.45 (C-6), 33.80 (C-9), 31.06 (C-8), 27.77 (C-13), 26.37 (C-12), 23.95 (C-15), 19.20 (C-14); HR-ESI-MS m/z 257.1522 $[M + Na]^+$ (calcd for $C_{15}H_{22}O_2Na$, 257.1512).

Sugiol (4) – White amorphous powder, UV (MeOH) λ_{max} nm (log ε): 244 (4.24), 295 (3.56); IR (KBr) ν_{max}: 3362, 2921, 2850, 1644, 1377 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ : 10.26 (1H, s), 7.65 (1H, s, H-14), 6.78 (1H, s, H-11), 3.13 (1H, sept, J = 7 Hz, H-15), 1.16 (3H, d, J = 6.9 Hz, H-16), 1.14 (3H, s, H-20), 1.12 (3H, d, J = 6.9 Hz, H-17), 0.94 (3H, s, H-19), 0.88 (3H, s, H-18). ^{13}C-NMR (100 MHz, DMSO-d_6) δ : 196.47 (C-7), 160.08 (C-12), 155.79 (C-9), 132.46 (C-13), 124.94 (C-14), 122.50 (C-8), 109.29 (C-11), 49.04 (C-5), 40.80 (C-3), 40.13 (C-10), 37.42 (C-1), 35.47 (C-6), 32.83 (C-4), 32.26 (C-18). 26.00 (C-15), 23.01 (C-20), 22.34 (C-17), 22.17 (C-16), 21.10 (C-19), 18.44 (C-2); EI-MS (m/z, %): 300 (M^+, 71), 285 (M^+-CH_3, 100), 243 (26), 217 (27), 203 (23).

(+)-Nootkatone (5) – Colorless oil, $[\alpha]_D^{20}$ +195.5 (c = 0.1, $CHCl_3$); UV (MeOH) λ_{max} nm (log ε): 237 (3.23); IR (KBr) ν_{max}: 1672, 1620, 1415, 875 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD) δ : 5.66 (1H, s, H-1), 4.64, 4.61 (each 1H, br s, H-12), 2.52 (1H, m, H-9β), 2.31 (1H, tt, J = 2.8, 12.8 Hz, H-7), 2.30 (1H, m, H-9α), 2.26 (1H, d, J = 16.5 Hz,

H-3α), 2.09 (1H, d, J = 3.2, 16.5 Hz, H-3β), 1.94 (1H, dd, J = 2.8, 12.8 Hz, H-6α), 1.91 (1H, m, H-4), 1.85 (1H, d, J = 1.4 Hz, H-8β), 1.65 (3H, s, H-13), 1.27 (1H, dd, J = 2.8, 12.8 Hz, H-8α), 1.09 (1H, d, J = 12.8 Hz, H-6β), 1.07 (3H, s, H-15), 0.90 (3H, d, J = 6.8 Hz, H-14). ^{13}C-NMR (100 MHz, CD_3OD) δ : 202.40 (C-2), 174.42 (C-10), 150.47 (C-11), 125.00 (C-1), 109.66 (C-12), 45.37 (C-9), 42.80 (C-3), 41.84 (C-7), 41.51 (C-4), 40.75 (C-5), 34.09 (C-6), 32.98 (C-8), 21.00 (C-13), 17.14 (C-15), 15.15 (C-14).

11-Hydroxy-valenc-1(10)-en-2-one (6) – Colorless oil, $[\alpha]_D^{26.8}$ +112.50 (c = 0.1, $CHCl_3$); UV (MeOH) λ_{max} nm (log ε): 239 (4.12); IR (KBr) ν_{max}: 3020, 1620, 1380 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3OD) δ : 5.74 (1H, s, H-1), 2.54 (1H, m, H-9β), 2.40 (1H, m, H-9α), 2.34 (1H, d, J = 17.1 Hz, H-3α), 2.17 (1H, dd, J = 3.2, 17.1 Hz, H-3β), 2.13 (1H, dd, J = 3.2, 12.6 Hz, H-6α), 2.00 (1H, dd, J = 3.2, 12.6 Hz, H-8α), 1.98 (1H, m, H-4), 1.77 (1H, tt, J = 3.2, 12.6 Hz, H-7), 1.17 (3H, s, H-12), 1.19 (1H, d, J = 1.4 Hz, H-8β), 1.15 (3H, s, H-15), 1.13 (3H, s, H-13), 1.03 (1H, d, J = 12.6 Hz, H-6β), 1.00 (3H, s, J = 6.8 Hz, H-14). ^{13}C-NMR (100 MHz, CD_3OD) δ : 202.42 (C-2), 174.95 (C-10), 124.70 (C-1), 72.89 (C-11), 45.05 (C-7), 42.82 (C-3), 41.98 (C-4), 41.00 (C-6), 40.59 (C-5), 34.14 (C-9), 29.08 (C-8), 27.26 (C-12), 26.52 (C-13), 17.21 (C-15), 15.22 (C-14).

Clovandiol (7) – White needle, ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 3.80 (1H, dd, J = 5.9, 10.2 Hz, H-10), 3.33 (1H, br s, H-2), 2.00 (1H, m, H-4α), 1.97 (1H, m, H-3β), 1.71 (1H, m, H-11α), 1.64 (1H, m, H-4β), 1.62 (1H, m, H-3α), 1.56 (1H, d, J = 12.6 Hz, H-9α), 1.52 (1H, m, H-11β), 1.44 (1H, m, H-6), 1.41 (1H, m, H-8α), 1.37 (1H, m, H-7α), 1.28 (1H, m, H-7β), 1.09 (1H, m, H-8β), 1.04 (3H, s, H-14), 0.97 (3H, s, H-13), 0.92 (1H, J = 13.0 Hz, H-9β), 0.86 (3H, s, H-15). ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 80.90 (C-10), 75.11 (C-2), 50.47 (C-6), 47.54 (C-11), 44.21 (C-5), 37.14 (C-12), 35.54 (C-9), 34.72 (C-1), 31.44 (C-14), 33.13 (C-8), 28.33 (C-13), 26.35 (C-4), 26.01 (C-3), 25.42 (C-15), 20.66 (C-7).

Cholinesterase Inhibition Assay – The cholinesterase inhibitory activities of the isolated compounds were evaluated using the spectrophotometric method developed by Ellman with minor modifications.[4] Briefly, reaction mixtures containing 140 μL of sodium phosphate buffer (pH 8.0), 20 μL of test sample solution (test concentration up to 200 μM), and 20 μL of either AChE or BChE solution were mixed and incubated for 15 min at room temperature. All of the tested samples and the positive control (berberine) were dissolved in 10% analytical-grade DMSO. Reactions were initiated by adding 10 μL of DTNB and 10 μL of either ACh or BCh. The hydrolysis of ACh or BCh was monitored by tracking the formation of the yellow 5-thio-2-nitrobenzoate anion at 412 nm for 15 min, resulting from the reaction of DTNB with thiocholine released by the enzyme. Each reaction was performed in triplicate, and results were measured in 96-well microplates using a microplate spectrophotometer (Molecular Devices, Sunnyvale, CA, USA).

Result and Discussion

The MeOH extract of *J. chinensis* heartwood was suspended in distilled water (H_2O) and successively partitioned with dichloromethane (CH_2Cl_2), ethyl acetate (EtOAc), and *n*-butanol (*n*-BuOH) to yield CH_2Cl_2, EtOAc, *n*-BuOH fractions, and H_2O residue, respectively. Repeated column chromatography of the CH_2Cl_2 and EtOAc fractions led to the isolation of a new sesquiterpenoid, 11-hydroxy-valenc-1(10),3(4)-dien-2-one (**3**), two chemically synthesized but first isolate from nature, 3-oxocedran-8β-ol (**1**)[5-7] and valenc-1(10),3(4),11(12)-trien-2-one (**2**)[8-10] together with four known compounds, sugiol (**4**),[11,12] (+)-nootkatone (**5**),[13] 11-hydroxy-valenc-1(10)-en-2-one (**6**),[13,14] and clovandiol (**7**)[15] (Fig. 1).

Compound **1** was obtained as a white amorphous powder. The molecular formula was established as $C_{15}H_{24}O_2$ based on NMR and a quasi-molecular ion peak at *m/z* 259.1671 $[M + Na]^+$ (calcd *m/z* 259.1669 for $C_{15}H_{24}O_2Na$) with HR-ESI-MS. The ^{1}H- and ^{13}C-NMR spectra of **1** were similar to those of cedrol, which has previously been isolated from *J. chinensis*, except for the presence of a ketone group (δ_C 219.91) at C-3 in **1**. The mass spectrum of **1**, which had a molecular ion peak 14 mass units higher than that of cedrol, further indicated the presence of a ketone group at the C-3 position in **1**. The position of the ketone group was confirmed by HMBC experiments. The HMBC correlations between δ 2.10 (H-2) / δ 2.44 (H-4) / δ 2.17 (H-5) / δ 0.98 (H-12) and δ 219.91 (C-3) confirmed that **1** was 3-oxocedran-8β-ol (3-oxocedrol). Although **1** was previously obtained from biotransformation of cedrol by *Cephalosporium aphidicola* and *Curvularia lunata*,[5-7] this is the first reported isolation of **1** from nature.

Compound **2** was obtained as a colorless oil. The molecular formula was determined as $C_{15}H_{20}O$ based on NMR and a quasi-molecular ion peak at *m/z* 239.1421 $[M + Na]^+$ (calcd *m/z* 239.1406 for $C_{15}H_{20}ONa$) with HR-ESI-MS. The ^{1}H-NMR spectrum of **2** revealed the presence of a tertiary methyl singlet signal at δ 1.46 (3H, s), an isopropenyl group at δ 4.76, 4.75 (each 1H, br s, H-

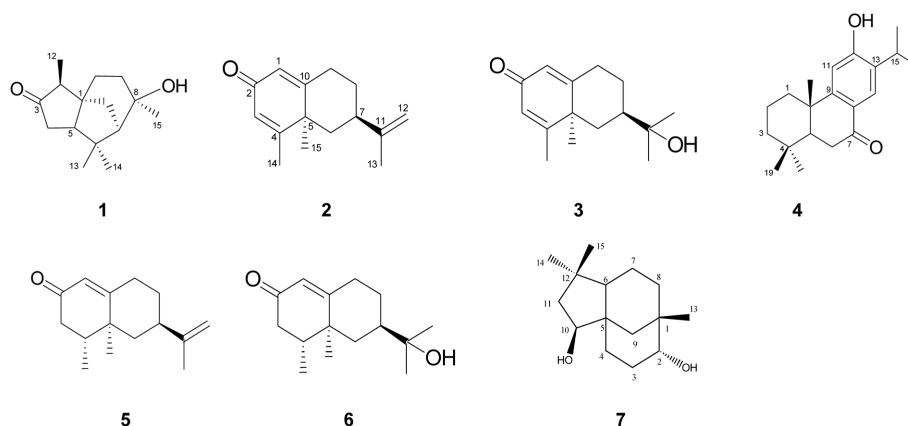

Fig. 1. Chemical structures of isolated compounds **1** - **7**.

12) and δ 1.74 (3H, s, H-13), two olefinic doublet signals at δ 6.08 (1H, d, J = 2.0 Hz, H-1) and 6.09 (1H, d, J = 2.0 Hz, H-3), and a methyl singlet at δ 2.07 (3H, s), suggesting that **2** was a valencene-type sesquiterpenoid.[13,16] This observation was further supported by ^{13}C-NMR, which, when coupled with the distortionless enhancement by polarization transfer (DEPT) spectra, showed 15 carbon signals including one α, β-unsaturated carbonyl carbon (δ_C 188.80), two olefinic quaternary carbons (δ_C 170.54 & 171.99), and two olefinic methine carbons (δ_C 124.59 & 126.74). The ^{1}H- and ^{13}C-NMR spectra of **2** were analogous to those of (+)-nootkatone (**5**),[13] except for the presence of a double bond at C-3 and C-4 in **2**. This assumption was further supported by an HMBC correlation between the methine proton at δ 6.09 (H-3) and methyl carbon at δ 19.15 (C-14). In addition, the relative configuration of C-7 in **2** could be deduced from the J values of H-7 (δ_H 2.59, J = 3.1, 12.8 Hz), which indicated a β-orientation of the isopropenyl group compared with 1α-hydroxyeudesma-5,11-dien-2-one (δ_H 2.07, J = 3.7, 13.0 Hz).[18] Therefore, the structure of **2** was determined to be valenc-1(10),3(4),11(12)-trien-2-one (3,4-dehydro-nootkatone). Although there was a previous report on the chemical synthesis of racemic 3, 4-dehydro-nootkatone through dehydrogenation of 4-epi-nootkatone with 2,3-dichloro-5,6-dicyanobenzoquinone,[8-10] this is the first reported isolation of **2** from nature.

Compound **3** was obtained as a colorless oil. The molecular formula was established as $C_{15}H_{22}O_2$ based on NMR and a quasi-molecular ion peak at m/z 257.1522 [M + Na]$^+$ (calcd m/z 257.1512 for $C_{15}H_{22}O_2Na$) with HR-ESI-MS. The ^{1}H- and ^{13}C-NMR spectra of **3** were similar to those of **2**, except that the isopropenyl group at C-7 in **2** was replaced with a hydroxyisopropyl group in **3**.[17] This assignment was further supported by HMBC correlation between the methine proton at δ 1.92 (H-7) and the hydroxylated quaternary carbon at δ 72.76 (C-11). The relative configuration at C-7 was determined to be identical to **2** on the basis of J values of H-7 (δ_H 1.92, J = 2.8, 12.8 Hz). Accordingly, the structure of **3** was identified as 11-hydroxy-valenc-1(10),3(4)-dien-2-one.

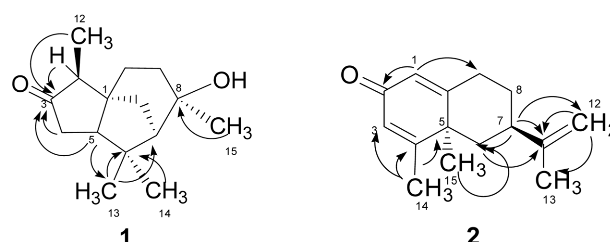

Fig. 2. Key HMBC correlations of compounds **1** and **2**.

Only compound **2** exhibited significant BChE inhibitory activity with an IC_{50} value of 68.45 μM. This was compared to the positive control berberine, which had a BChE inhibitory activity with an IC_{50} value of 18.75 μM. None of the other isolated compounds showed inhibitory activity against AChE and BChE up to 200 μM. From these results, it can be concluded that the BChE inhibitory activity of compound **2** might be explained by presence of 11-12 ene moiety and two double bonds at C-1-10 and C-3-4 as well as a ketone group at C-2, which significantly enhanced activity.

Acknowledgments

This work was supported by a Research Grant from Pukyong National University (2017 Year).

References

(1) Corner, E. J. H. Wayside Trees of Malaya; Malayan Nature Society: Malaysia, **1988**, pp 396-446.

(2) But, P. P. H.; Kimura, T.; Gue, J. X.; Sung, C. K. International Collation of Traditional and Folk Medicine; World Scientific Publishing Co., Ltd.: Singapore, **1997**, pp 16-17.
(3) Jung, H. J.; Jung, H. A.; Min, B. S.; Choi, J. S. *Chem. Pharm. Bull*. **2015**, *63*, 955-960.
(4) Ellman, G. L.; Courtney, K. D.; Andres, V. Jr.; Feather-stone, R. M. *Biochem. Pharmacol*. **1961**, *7*, 88-95.
(5) Hanson, J. R.; Nasir, H. *Phytochemistry* **1993**, *33*, 835-837.
(6) Gand, E.; Hanson, J. R.; Nasir, H. *Phytochemistry* **1995**, *39*, 1081-1084.
(7) Collins, D. O.; Reese, P. B. *Phytochemistry* **2001**, *56*, 417-421.
(8) Caine, D.; Chu, C. Y. *Tetrahedron Lett*. **1974**, *15*, 703-706.
(9) Caine, D.; Chu, C. Y.; Graham, S. L. *J. Org. Chem*. **1980**, *45*, 3790-3797.
(10) Pesaro, M.; Bozzato, G.; Schudel, P. *Chem. Commun (London).* **1968**, *19*, 1152-1154.
(11) Kuo, Y. H.; Wu, T. R.; Cheng, M. C.; Wang, Y. *Chem. Pharm. Bull*. **1990**, *38*, 3195-3201.
(12) Chang, C. I.; Chen, W. C.; Shao, Y. Y.; Yeh, C. R.; Yang, N. S.; Chiang, W.; Kuo, Y. H. *Nat. Prod. Res*. **2008**, *22*, 1158-1162.
(13) Savona, G.; Piozzi, F.; De La Torre, M. C.; Servettaz, O. Rodríguez, B. *Phytochemistry* **1987**, *26*, 571-572.
(14) Xu, J.; Su, J.; Li, Y.; Tan, N. *Chem. Nat. Compd*. **2013**, *49*, 457-461.
(15) Zhang, C.; Zhou, A.; Zhang, M. *China Journal of Chinese Materia Medica* **2009**, *34*, 994-998.
(16) Furusawa, M.; Hashimoto, T.; Noma, Y.; Asakawa, Y. *Chem. Pharm. Bull*. **2005**, *53*, 1513-1514.
(17) Naf, F.; Decorzant, R.; Thommen, W. *Helv. Chim. Acta* **1982**, *65*, 2212-2223.
(18) Wittayalai, S.; Mahidol, C.; Prachyawarakorn, V.; Prawat, H.; Ruchirawat, S. *Phytochemistry* **2014**, *99*, 121-126.

Received April 5, 2017
Revised June 9, 2017
Accepted June 10, 2017