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Two New Sesquiterpenes from *Atractylodes macrocehpala*

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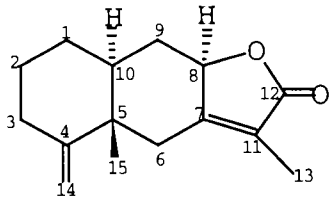
Abstract: Two new sesquiterpenes: beishulenolide A **1** and peroxiatractylenolide III **2** were isolated from *Atractylodes macrocephala* Koids (compositae).Their structures were elucidated on the basis of spectral evidence, especially 2D-NMR methods and chemical conversion.

Keywords: Beishulenolide A; peroxiatractylenolide III; *atractylodes macrocephala*; compositae.

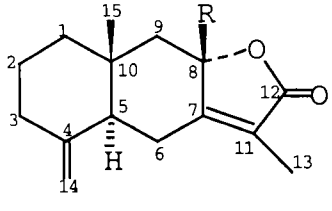
Atractylodes macrocephala Koidz (Compositae) is a perennial herb mainly distributed in the Zhejiang and Anhui Provinces of China. Its rhizome has been used as a traditional Chinese medicine from ancient times[1,2]. Two new sesquiterpenes, Beishulenolide A **1** and Peroxiatractylenolide III **2** have been isolated from a petroleum ether extract of this herb. Their structures were elucidated on the basis of spectral evidence, especially 2D-NMR methods and chemical conversion.

Compound **1** was isolated as colorless needles from ethyl acetate. HREIMS showed its peak at m/z = 232.1463 (M^+), in agreement to the molecular formula $C_{15}H_{20}O_2$ (calcd for $C_{15}H_{20}O_2$ m/z=232.1462). The IR spectrum (ν 1760 and 1680 cm^{-1}) in conjunction with the UV spectrum (λ_{max}^{MeOH} : 222 nm logε5.21) and a methyl signal at 1.79 in the ^{1}H-NMR spectrum indicates the presence of the typical-α-methylbutenolide moiety. H-15 high-field singlet at 0.69 and H-8 (5.08, triplet, J=8.68Hz) are the characteristics of eremophilanes [3,8,9]. The IR showed bands at 3065, 1640 and 895 cm^{-1}, which indicated a terminal olefinic bond in compound **1**. And the structure of terminal olefinic bond was also supported by ^{13}C- and ^{1}H-NMR data. The ^{13}C-DEPT spectra showed a quarternary

Figure 1. Structures of compounds 1–3



1. beishulenolide A



2. R=OOH, peroxiatractylenolide III
3. R=OH, atractylenolide III

carbon at 147.84 and a methylene carbon at 107.97. The ^{1}H-NMR spectrum showed a singlet at 4.62 ppm and another singlet at 4.87 ppm. All the two dimensional NMR experiments also supported the structure **1**. In the ^{1}H-^{13}C COSY spectra, C_1, C_2, C_3, C_6, C_8, C_9, C_{10}, C_{13}, C_{14}, C_{15} carbons were coupled to the protons resonated at δ (ppm): 1.62, 2.59, 1.99 and 2.37, 1.22, 5.02, 2.23 and 1.46, 1.47, 1.79, 4.62 and 4.87, 0.69. The ^{1}H- ^{1}H COSY spectra showed the connectivity of H-2 to both H-1 and H-3, H-9 to both H-8 and H-10, H-10 to H-1. Thus there are following two segments in compound **1**: $^1CH_2$-$^2CH_2$- $^3CH_2$ and ^{8}CH- $^9CH_2$- ^{10}CH. The COLOC spectra showed the connectivity of H-14, H-15 to C_4, C_5, C_6; H-13 to C_7, C_{11}, C_{12}; H-9 and H-6 to C_8. So the following segments could be determined in compound **1**: ^{5}C-$^{15}CH_3$, -^{7}C=^{11}C ($^{13}CH_3$) (^{12}C=O) and -$^6CH_2$-^{7}C-^{8}CH-$^9CH_2$-. The stereochmistry of **1** was assigned by comparison the spectral data of **1** with those similar known compounds[3,8,9]. From all these above evidence, we have determined compound **1** as beishulenolide A.

Compound **2** was isolated as colorless crystals. The HREIMS spectra showed peaks at m/z=265.1440 (M+H), in accordance with the molecular formula $C_{15}H_{20}O_4$ (Calcd for $C_{15}H_{20}O_4$ (M+H) m/z=265.1439). EIMS showed peaks at m/z = 248 (M+H-OH), m/z = 232 (M+H-OOH); The other peaks were very similar to those of atractylenolideIII [3-7]. The IR absorptions of compound **2** and atractylenolide III are almost the same. From the comparison of the ^{1}H- and ^{13}C-NMR data of compound **2** with those of atractylenolide III (especially the chemical shift value of C_8 in **2** was deshielded from 89.29 ppm in **3** to 103.84 ppm.), we could recognize a stronger electron withdrawing group than OH bonding to C_8 in compound **2**. From the above evidence, the stronger electron withdrawing group must be OOH. The presence of the hydroperoxide moiety was also supported by the fact that compound **2** gave a reddish-purple spot on thin-layer chromatography with N,N-dimethyl-p-phenylenediamine spray, which is a well-known detection reagent for peroxide[10]. Finally, the assignment was confirmed by reduction of **2** with triphenylphosphin (Ph_3P) to **3**. So **2** could be determined as peroxiatractylenolide III.

Compound **3** was identified as atractylenolide III by comparing their physical properities and their IR, UV, MS spectrascopic data with those reported. For the purpose of the assignments of the ^{1}H-NMR and ^{13}C-NMR spectra, ^{13}C-^{1}H Cosy, ^{1}H-^{1}H Cosy and Coloc data of Compound **1**, **2** and **3** were obtained, which allowed us to confirm the identity unambiguously.

Beishulenolide A **1**: Colourless needles (ethyl acetate), 78mg, $[\alpha]^{20}_D$ -24.5 (c, 0.4. EtOH), m.p. 110-112°C. HREIMS Calcd for $C_{15}H_{20}O_2$ (M) m/z (%)232.1462 found m/z = 232.1463 (23), 215 (M-OH, 17), 201 (7), 187 (7), 181 (8), 173 (6), 159 (10), 149 (33), 131 (56), 122 (13), 105 (19), 91 (38), 79 (45), 69 (100), 55 (87). IRν^{KBr}_{max} (cm^{-1}): 3065 (s), 1760 (s, $V_{C=O}$), 1680, 1640 (m,$V_{C=C}$), 1310 (s), 1100 (s), 895 (s). UV λ^{MeOH}_{max} nm (log) 222 (5.21). ^{1}HNMR (400MHz, $CDCl_3$, δ ppm, J Hz): H-1; 1.62, brs; H-2: 2.59, m; H-3α: 1.99, brd, J=12.36; H-3β:2.37, m; H-6: 1.22, s; H-8: 5.02, dd, J_1=J_2=8.68; H-9α: 2.23, dd, J_1=13.68, J_2=9.96; H-9β:1.46, dd, J_1=13.68, J_2=8.76; H-10: 1.47, brd, J=9.96; H-13: 1.79, s; H-14α: 4.62, s, H-14β: 4.87, s; H-15: 0.69, s. ^{13}CNMR (400MHz, $CDCl_3$,

δ ppm): C_1, 23.35, C_2, 24.61, C_3, 36.47, C_4, 147.84, C_5, 35.61, C_6, 29.67, C_7, 161.88, C_8, 77.99, C_9, 44.44, C_{10}, 42.83, C_{11}, 121.23, C_{12}, 175.78, C_{13}, 8.39, C_{14}, 107.97, C_{15}, 21.29.

Peroxiatractylenolide III **2**: Colourless neeles (ethyl acetate), 1213mg, $[\alpha]^{20}_D$ +249.0, (c, 0.4, EtOH), m.p. 191-192°C. HREIMS Calcd for $C_{15}H_{21}O_4$ (M+H) m/z (%) 265.1439 (15) found m/z=265.14398. 248 (M+H-OH, 40), 232 (M+H-OOH, 84), 220 (52), 215 (45), 203 (45), 191 (48), 175 (49), 159 (40), 147 (100), 133 (42), 121 (59), 105 (61), 91 (86), 79 (70), 67 (52), 55 (66). IRν^{KBr}_{max} (cm^{-1}): 3320 (vs, V_{O-H}), 3060 (w), 1740 (s,$V_{C=O}$), 1690, 1630 (m,$V_{C=C}$), 1320 (s), 1120 (s), 890 (s). UVλ^{EtOH}_{max} nm (log) 220 (4.68). ^{1}HNMR (400MHz, $CDCl_3$, δ ppm, J Hz): H-1α: 1.91, m, H-1β: 2.31, brd, J=11.28; H-2: 1.60, m; H-3α: 1.21, m, H-3β: 1.52, m; H-5: 1.79, brd, J=12.68; H-6α: 2.40, dd, J_1=13.04, J_2=1.08, H-6β: 2.58, dd, J_1=13.20, J_2=3.20; H-9α: 1.47, d, J=13.68, H-9β: 2.26, d, J=13.68; H-13: 1.74, s; H-14α: 4.55, s, H-14β: 4.81, s; H-15: 0.99, s. ^{13}CNMR (400MHz, $CDCl_3$, δ ppm): C_1, 36.08, C_2, 22.33, C_3, 41.33, C_4, 148.61, C_5, 51.73, C_6, 24.63, C_7, 161.22, C_8, 103.84, C_9, 51.20, C_{10}, 36.72, C_{11}, 121.87, C_{12}, 172.65, C_{13}, 8.07, C_{14}, 106.70, C_{15}, 16.54.

Reduction of **2** with triphenylphosphin to **3**: To a stirred solution of **2** (132 mg) in dichloromethane (15 ml), triphenylphosphin (Ph_3P, 2 eq., 262 mg) was added. The reaction mixture was stirred at room temperature for 2 hours. the solvent was evaporated, the residue was subjected to flash column (silica G, 2×20cm), eluted with petrol: ethyl acetate 4:1, 89.3 mg (yield 72.0%) and the purified product **3** was obtained.

Atractylenolide III **3**: Colourless needles (ethyl acetate), 86mg, $[\alpha]^{20}_D$ +28.4 (c, 0.4. EtOH), m.p. 196-197□. $C_{15}H_{20}O_3$, EIMS m/z (%) 231 (M-OH, 100), 215 (M-OH-CH_3, 37), 203 (28), 189 (42), 175 (37), 163 (52), 149 (29), 133 (37), 124 (35), 107 (49), 93 (59), 79 (49), 67 (40), 55 (46). IRν^{KBr}_{max} (cm^{-1}): 3470 (w), 3330 (s,V_{O-H}), 3070 (w), 1750 (s,$V_{C=O}$), 1660, 1630 (m, $V_{C=C}$), 1310 (s), 1100 (s), 890 (s). UVλ^{EtOH}_{max} nm (log): 220 (4.19). ^{1}HNMR (400MHz, $CDCl_3$, δ ppm, J Hz): H-1α: 1.70, brd, J=6.80, H-1β: 2.31, brd, J=12.52; H-2: 1.60, m; H-3α: 1.20, m, H-3β: 1.59, m; H-5: 1.89, m; H-6α: 2.71, d, J=12.88, H-6β: 2.77, d, J=14.36; H-9α: 1.37, d, J=14.56, H-9β: 2.60, dd, J_1=13.08, J_2=3.24; H-13: 1.68, s; H-14α: 4.60, s, H-14β: 4.81, s; H-15: 1.08, s. ^{13}CNMR (400MHz, $CDCl_3$, δ ppm): C_1, 35.85, C_2, 22.32, C_3, 42.11, C_4, 147.88, C_5, 52.84, C_6, 27.88, C_7, 164.46, C_8, 89.29, C_9, 49.71, C_{10}, 36.95, C_{11}, 124.39, C_{12}, 171.84, C_{13}, 8.40, C_{14}, 107.28, C_{15}, 17.15.

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