Polyacetylene Compounds from Atractylodes Rhizome

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Two new polyacetylene compounds (4*E*,6*E*,12*E*)-1-acetoxy-3-isovaleryloxytetradeca-4,6,12-trien-8,10-diyn-14-ol (B), and (4*E*,6*E*,12*E*)-1-acetoxy-3-(2-methylbutyryloxy)tetradeca-4,6,12-trien-8,10-diyn-14-ol (C) have been isolated along with (4*E*,6*E*,12*E*)-1-acetoxy-3-senecioyloxytetradeca-4,6,12-trien-8,10-diyn-14-ol (A) from Atractylodes Rhizome (Karabyakujutu). The structures of these compounds were determined on the basis of their spectral data.

Keywords (4*E*,6*E*,12*E*)-1-acetoxy-3-senecioyloxytetradeca-4,6,12-trien-8,10-diyn-14-ol; (4*E*,6*E*,12*E*)-1-acetoxy-3-isovaleryloxytetradeca-4,6,12-trien-8,10-diyn-14-ol; (4*E*,6*E*,12*E*)-1-acetoxy-3-(2-methylbutyryloxy)tetradeca-4,6,12-trien-8,10-diyn-14-ol; Atractylodes Rhizome; Compositae; 2D-NMR

Atractylodes Rhizome is an important crude drug in Chinese traditional medicine and has been used as a stomachic, a diuretic, and an antisudorific. The Pharmacopoeia of Japan describes two kinds of original plants, *Atractylodes japonica* KOIDZUMI *et* KITAMURA and *A. ovata* DE CANDOLLE.[1] The crude drug prepared from the former plant is Wabyakujutu (WAB), and the other is Karabyakujutu (KAB). It is known that these crude drugs both contain atractylon and other terpenes as their major constituents.[2]

In our previous paper,[3] we reported the isolation and structural elucidation of polyacetylene compounds in WAB. In this paper, we describe the isolation and structure determination of two acetylene compounds B, C and identification of A from KAB.

The compound A $C_{21}H_{24}O_5$ (M^+ 356), a pale yellow oil, was presumed to be (4*E*,6*E*,12*E*)-1-acetoxy-3-senecioyloxytetradeca-4,6,12-trien-8,10-diyn-14-ol by comparison of its infrared (IR) and proton nuclear magnetic resonance (^{1}H-NMR) spectral data.[4] However, as the data of this compound does not seem to be complete, we wish to add to it. By the long range ^{1}H–carbon-13 nuclear magnetic resonance (^{13}C-NMR) correlation spectrum method, the structure of A was determined with respect to not only the position of the two substituent groups but also the assign of acetylene carbons. That is, the carbonyl carbon signals of the acetyl and senecioyl were observed to be correlated to the C_1-H and C_3-H signals. Four acetylene carbon signals were observed at 74.4, 76.8, 80.5 and 81.0 ppm. The signals of C_9 and C_{10} were observed further upfield than the signals of C_8 and C_{11}.[5] The olefinic proton signals at δ 5.70 (7-H) and δ 5.87 (12-H) were correlated with the carbon signal at 74.4 ppm, and (7-H) was also correlated with the carbon signal at 76.8 ppm (this carbon signal was observed in the solvent signals). Similarly, the olefinic proton signal at δ 6.66 (6-H) was correlated with the carbon signal at 80.5 ppm, and the methylen proton signal at δ 4.25 (14-H) was also slightly correlated with the carbon signal at 81.0 ppm (Fig. 2). From these spectral data, the carbon signals of compound A were assigned as shown in Table I.

The new polyacetylene compounds B and C showed the same molecular formula on the high-resolution mass (HR-MS) spectrum. These compounds also showed spectral data similar to those of compound A, except for the molecular ion peak at *m/z* 356 and the ultraviolet (UV) spectrum at 210 nm.

Compound B, a pale yellow oil and an unstable substance in the air, was observed to have a molecular ion peak at *m/z* 358 and a fragment ion peak at *m/z* 85 in the MS (the corresponding fragment ion peak was observed at *m/z* 83 in compound A). The molecular formula $C_{21}H_{26}O_5$ was confirmed by the HR-MS. The IR spectrum of B showed acetylene bands at 2200 and 2130 cm^{-1}. The ^{1}H-NMR spectrum of B showed olefinic protons assignable to three trans double bonds at δ 5.70 (d, J=15.5 Hz, C_7-H), 5.76 (dd, J=6.9, 15.2 Hz, C_4-H), 5.87 (d, J=16.9 Hz, C_{12}-H), 6.30 (dd, J=10.9, 15.2 Hz, C_5-H), 6.42 (dt, J=4.8, 16.0 Hz, C_{13}-H) and 6.66 (dd, J=10.9, 15.5 Hz, C_6-H) and the acetyl group at δ 2.04 (3H, s). Moreover, B showed methylene protons at δ 2.19 (d, J=6.4 Hz), a methine proton at δ 1.68 (m) and two methyl protons at δ 0.95 (d, J=6.6 Hz) instead of disappearance signals based on senecioyl substituent of A. From the comparison of the MS and ^{1}H-NMR spectral data of B with those of A, it was presumed that B had an isovaleryl substituent in its structure. The ^{13}C-NMR spectrum of B showed a carbonyl carbon at 172.2 ppm, a methylene carbon at 43.5 ppm, a methine carbon at 25.8 ppm and two methyl carbons at 22.4 ppm, respectively. These spectral data were also consistent with the data of the isovaleryl substituent.[6] Consequently, the compound B was elucidated to be (4*E*,6*E*,12*E*)-1-acetoxy-3-isovaleryloxytetradeca-4,6,12-trien-8,10-diyn-14-ol (Chart 1). The substituent position was determined by two dimentional nuclear magnetic resonance (2D-NMR) in the same manner as in the case of compound A.

The compound C, a pale yellow oil and an unstable substance in the air, was observed to have a molecular ion peak at *m/z* 358 and a fragment ion peak at *m/z* 85 in the MS. The molecular formula $C_{21}H_{26}O_5$ was confirmed by the HR-MS. The ^{1}H-NMR spectrum of C was also similar to that of compound B except for

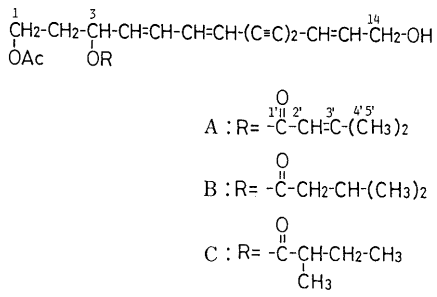

Chart 1

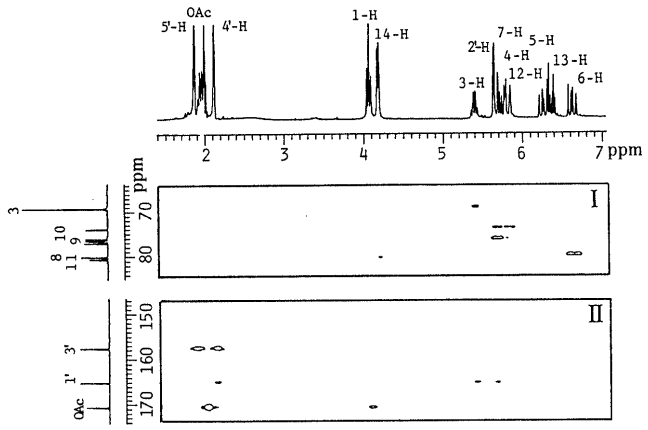

Fig. 1. The Long-Range ^{1}H–^{13}C Correlation Spectrum of A in the Upfield I and Downfield II

TABLE I. ^{13}C-NMR Data for Compounds A, B and C [67.5 MHz in $CDCl_3$ δ (ppm)]

Carbon	A	B	C	Carbon	A	B	C
1	60.4	60.3	60.3	12	108.6	108.9	108.9
2	33.3	33.3	33.4	13	145.7	145.5	145.5
3	69.6	70.3	70.3	14	62.4	62.7	62.7
4	134.8	134.4	134.5	CH_3	20.8	20.9	20.9
5	130.9	131.5	131.5	O=C–O	171.1	171.0	171.0
6	143.4	143.3	143.4	R			
7	111.1	111.5	111.5	1′	165.6	172.2	175.8
8	80.5	80.5	80.5	2′	115.5	43.5	41.2
9	76.8	77.3	77.3	3′	158.0	25.8	26.7
10	74.4	74.6	74.6	4′	20.2	22.4	11.6
11	81.0	81.1	81.0	5′	27.4	22.4	16.6

the signals of the substituent. The ^{1}H-NMR spectrum of compound C showed two methyl protons at δ 0.89 (3H, t, J=7.3 Hz) and at δ 1.15 (3H, d, J=6.9 Hz). The ^{13}C-NMR spectrum of C showed a carbonyl carbon at 175.8 ppm, a methylene carbon at 26.7 ppm, a methine carbon at 41.2 ppm and two methyl carbons at 11.6 and 16.6 ppm, respectively. These spectral data were consistent with the data of the methylbutyryl substituent.[7] Therefore, compound C was determined to be (4*E*,6*E*,12*E*)-1-acetoxy-3-(2-methylbutyryloxy)tetradeca-4,6,12-trien-8,10-diyn-14-ol.

Experimental

Apparatus The UV spectra were recorded with a Shimadzu UV-3000 spectrometer and IR spectra were taken with a JASCO FT/IR-7000 spectrometer. The ^{1}H- and ^{13}C-NMR spectra were taken with a JEOL JNM-GX270 spectrometer with tetramethylsilane as an internal standard. MS were taken with a Hitachi M-2000. Preparative high performance liquid chromatography (HPLC) was performed by using a Waters M-600 system, and a Waters 490 detector with an Inertsil ODS column (Gasukurokogyo Inc., 26 mm i.d. × 25 cm). Silica gel 60 (Merck, 0.063—0.200 mm) was used for column chromatography.

Isolation Procedure The dried powder of KAB (3 kg) (commercially obtained from Mikuni Co., Ltd. 1988) was extracted 3 times with *n*-hexane (9 l) at room temperature. The solution was concentrated, and the extract (69.6 g) was chromatographed on silica gel and eluted with a mixture of *n*-hexane and AcOEt. A mixture of compounds A, B and C was obtained from the fraction eluted with *n*-hexane–AcOEt (1 : 1). These compounds were purified by preparative HPLC (solvent, MeOH : H_2O = 65 : 35; flow rate 13 ml/min; monitor wavelength at 350 nm) to give A (700 mg), B (30 mg) and C (30 mg).

(4*E*,6*E*,12*E*)-1-Acetoxy-3-senecioyloxytetradeca-4,6,12-trien-8,10-diyn-14-ol (A) A pale yellow oil. UV λ_{max}^{MeOH} nm (log ε): 337 (4.4), 315 (4.6), 296 (4.4), 279 (4.2), 266 (4.5), 250 (4.5), 214 (4.5). IR ν (neat) cm^{-1}: 3460 (OH), 2200, 2130 (C≡C), 1740, 1228 (CH_3CO_2), 1651, 986 (CH=CH-CH=CH). ^{1}H-NMR ($CDCl_3$) δ: 1.91 (3H, d, J=1.3 Hz, $C_{5'}$-H), 1.98 (2H, m, C_2-H), 2.04 (3H, s, OAc), 2.16 (3H, d, J=1.3 Hz, $C_{4'}$-H), 4.11 (2H, t, J=6.3 Hz, C_1-H), 4.25 (2H, br d, J=4.8 Hz, C_{14}-H), 5.43 (1H, dt, J=6.5 Hz, C_3-H), 5.68 (1H, m, $C_{2'}$-H), 5.70 (1H, d, J=15.5 Hz, C_7-H), 5.77 (1H, dd, J=6.5, 15.2 Hz, C_4-H), 5.87 (1H, d, J=16.9 Hz, C_{12}-H), 6.30 (1H, dd, J=10.9, 15.2 Hz, C_5-H), 6.41 (1H, dt, J=4.8, 15.8 Hz, C_{13}-H), 6.66 (1H, dd, J=10.9, 15.5 Hz, C_6-H). MS *m/z*: 356 (M^+), 296 ($M-CH_3CO_2H$), 273 ($M-C_5H_7O$), 83 (C_5H_7O).

(4*E*,6*E*,12*E*)-1-Acetoxy-3-isovaleryloxytetradeca-4,6,12-trien-8,10-diyn-14-ol (B) A pale yellow oil. UV λ_{max}^{MeOH} nm (log ε): 337 (4.4), 315 (4.5), 296 (4.4), 279 (4.2), 266 (4.4), 250 (4.4), 210 (4.3). IR ν (neat) cm^{-1}: 3462 (OH), 2200, 2132 (C≡C), 1740, 1243 (CH_3CO_2), 986 (CH=CH-CH=CH). ^{1}H-NMR ($CDCl_3$) δ: 0.95 (6H, d, J=6.6 Hz, $C_{4'5'}$-H), 1.68 (1H, m, $C_{3'}$-H), 1.97 (2H, m, C_2-H), 2.04 (3H, s, OAc), 2.19 (2H, d, J=6.4 Hz, $C_{2'}$-H), 4.10 (2H, td, J=2.4, 6.8 Hz, C_1-H), 4.26 (2H, br d, J=4.8 Hz, C_{14}-H), 5.42 (1H, dt, J=6.9 Hz, C_3-H), 5.70 (1H, d, J=15.5 Hz, C_7-H), 5.76 (1H, dd, J=15.2, 6.9 Hz, C_4-H), 5.87 (1H, d, J=16.9 Hz, C_{12}-H), 6.30 (1H, dd, J=10.9, 15.2 Hz, C_5-H), 6.42 (1H, dt, J=4.8, 16.0 Hz, C_{13}-H), 6.66 (1H, dd, J=10.9, 15.5 Hz, C_6-H). MS *m/z*: 358 (M^+), 298 ($M-CH_3CO_2H$), 273 ($M-C_5H_9O$), 85 (C_5H_9O). HR-MS *m/z*: M^+ Calcd for $C_{21}H_{26}O_5$ 358.1779. Found *m/z*: 358.1703.

(4*E*,6*E*,12*E*)-1-Acetoxy-3-(2-methylbutyryloxy)tetradeca-4,6,12-trien-8,10-diyn-14-ol (C) A pale yellow oil. UV λ_{max}^{MeOH} nm (log ε): 337 (4.4), 315 (4.5), 296 (4.4), 279 (4.2), 266 (4.4), 250 (4.5), 210 (4.3). IR ν (neat) cm^{-1}: 3462 (OH), 2364, 2200 (C≡C), 1740, 1245 (CH_3CO_2), 1187, 986 (CH=CH-CH=CH). ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J=7.3 Hz, $C_{4'}$-H), 1.15 (3H, d, J=6.9 Hz, $C_{5'}$-H), 1.47 (2H, m, $C_{3'}$-H), 1.97 (2H, m, C_2-H), 2.04 (3H, s, OAc), 2.36 (1H, m, $C_{2'}$-H), 4.09 (2H, td, J=2.6, 6.4 Hz, C_1-H), 4.26 (2H, br d, J=4.8 Hz, C_{14}-H), 5.42 (1H, dt, J=6.9 Hz, C_3-H), 5.70 (1H, d, J=15.5 Hz, C_7-H), 5.76 (1H, dd, J=15.2, 6.9 Hz, C_4-H), 5.87 (1H, d, J=15.9 Hz, C_{12}-H), 6.30 (1H, dd, J=10.9, 15.2 Hz, C_5-H), 6.42 (1H, dt, J=4.8, 15.9 Hz, C_{13}-H), 6.66 (1H, dd, J=10.9, 15.5 Hz, C_6-H). MS *m/z*: 358 (M^+), 298 ($M-CH_3CO_2H$), 273 ($M-C_5H_9O$), 85 (C_5H_9O). HR-MS *m/z*: M^+ Calcd for $C_{21}H_{26}O_5$ 358.1779. Found *m/z*: 358.1871.

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