A New Polyacetylene Compound from Atractylodes Rhizome

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A new polyacetylene compound (4), (6*E*,12*E*)-tetradecadiene-8,10-diyne-1,3-diol diacetate has been isolated along with (4*E*,6*E*,12*E*)-tetradecatriene-8,10-diyne-1,3-diol diacetate and atractylenolide I from Atractylodes Rhizome. The structure of 4 was determined on the basis of its spectral data and chemical reaction.

Keywords (6*E*,12*E*)-tetradecadiene-8,10-diyne-1,3-diol diacetate; (4*E*,6*E*,12*E*)-tetradecatriene-8,10-diyne-1,3-diol diacetate; (6*E*,12*E*)-tetradecadiene-8,10-diyne-1,3-diol; polyacetylene; *Atractylodes japonica*; Compositae; 2D-NMR

Atractylodes Rhizome described in the Japanese Pharmacopoeia is prepared from two kinds of plants, *Atractylodes japonica* KOIDZUMI *et* KITAMURA and *A. ovata* DE CANDOLLE. The crude drug prepared from the former plant is the Japanese product (和白朮), and the other is the Chinese product (唐白朮). Both products are used for the same clinical purposes, *i.e.*, as a stomachic, diuretic, and antisudorific in Japan.

The constituents of the crude drug have been studied, and the isolation of atractylon[1] and its derivatives,[2] a sesquiterpene[3] and diacetyl-atractylodiol (**2**)[4] have been reported.

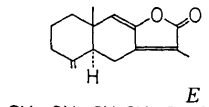
In this paper, we report on the isolation and structure determination of an acetylene compound (**4**) and identification of **3** and a furanosesquiterpenoid compound (**1**), from Japanese Atractylodes Rhizome.

Compounds **1**, **3** and **4** were isolated from the MeOH extracts of the crude drug by silica gel column chromatography and high performance liquid chromatography (HPLC).

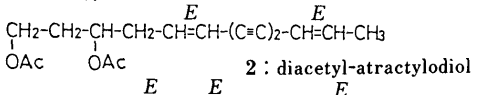
Compound **1** was identified as atractylenolide I by comparison of its melting point, proton nucler magnetic resonance (^{1}H-NMR), and infrared (IR) spectral data with those described in the literature.[5]

Compound **3** was identified as (4*E*, 6*E*, 12*E*)-tetradecatriene-8,10-diyne-1,3-diol diacetate by comparison of its spectral data with those described in the literature.[6] This is the first report on the isolation of **3** from this crude drug.

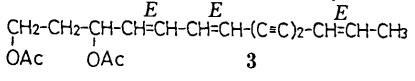
The new polyacetylene compound **4**, pale yellow oil, showed a molecular ion peak at *m/z* 302 ($C_{18}H_{22}O_4$) in its mass spectrum (MS). The IR spectrum of **4** showed acetylene bands at 2100 and 2190 cm^{-1}, ester bands at 1715, 1730 (sh) and 1200 cm^{-1}, and double bond bands at 1610 and 940 cm^{-1}. Its ultraviolet (UV) spectrum was very similar to that of compound **3** and diacetyl-atractylodiol (**2**)[4] (Chart 1). These spectral data suggested that **4** was a polyacetylene compound. The ^{1}H-NMR spectrum of **4** showed the presence of olefinic protons assignable to two *trans* double bonds at δ 5.56 (two overlapping d, J= 15.5 Hz, C_7-H and C_{12}-H), δ 6.25 (dt, J=15.5, J=6.9 Hz, C_6-H) and δ 6.31 (dq, J=15.5, J=6.9 Hz, C_{13}-H) and two acetyl groups at δ 2.04 and δ 2.05 (3H each, s). All ^{1}H-NMR signals were assigned by analysis of two dimentional nuclear magnetic resonance (2D-NMR). The carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of **4** showed eighteen signals; one methyl, four methylenes, one methine, four olefinic carbons, four acetylene carbons, and two acetyl groups. The ^{1}H- and ^{13}C-NMR



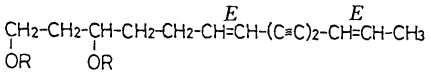
1 : atractylenolide I



2 : diacetyl-atractylodiol



3



4 : R=Ac
5 : R=H

Chart 1

TABLE I. ^{13}C-NMR Data for Compounds **4** and **5** [67.5 MHz in $CDCl_3$, δ (ppm)]

Carbon	4	5[a]	Carbon	4	5[a]
1	60.6	60.9	10	73.2[c]	74.4[c]
2	33.1	41.3	11	80.0[b]	81.4
3	70.4	69.9	12	109.9	111.6
4	33.1	38.1	13	143.5	145.3
5	29.1	31.2	14	18.9	19.9
6	146.6	149.9	CH_3	21.1	—
7	109.5	110.6		20.9	—
8	79.3[b]	81.4	O=C–O	170.9	—
9	72.4[c]	74.1[c]		170.6	—

a) In CD_3OD. *b*, *c*) Assignments with the same number may be interchanged in each column. The signals due to the acetylene carbons were assigned by comparison with the ^{13}C-NMR data of 2,4-hexadiyne.[7]

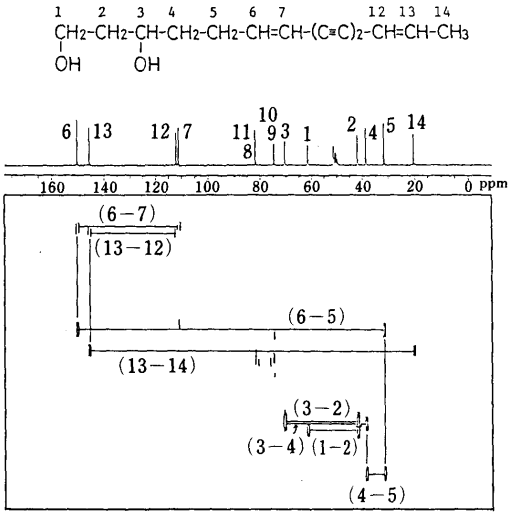


Fig. 1. 2-D INADEQUATE ^{13}C Spectrum of **5** in CD_3OD

spectra and the molecular formula suggested that compound **4** was a linear chain carbon compound. The C–C connectivity was determined from the inadequate ^{13}C-NMR spectrum (Fig. 1) of **5**, which was obtained by hydrolysis of **4**.

From these spectral data, the structure of **4** was elucidated to be (6*E*,12*E*)-tetradecadiene-8,10-diyne-1,3-diol diacetate (**4**).

Experimental

The melting points were measured on a Yanaco melting point apparatus and are uncorrected. The UV spectra were recorded with a Shimadzu UV-3000 spectrometer and IR spectra were taken with a JASCO A-102 spectrometer. The ^1H and ^{13}C-NMR spectra were taken with a JEOL JNM-GX270 spectrometer with tetramethylsilane as an internal standard. MS were taken with a Shimadzu-LKB 9000B. HPLC was performed with a Waters M-600 system (column: Kusano RP-18, 20 μm, 300 × 25 mm i.d.). Silica gel 60 (Merck, 0.063—0.200 mm was used for column chromatography.

Isolation Procedure The dried powder of Japanese Atractylodes Rhizome (1 kg) (commercially obtained at Sapporo in 1986) was extracted 3 times with refluxing MeOH (total 6 l). The MeOH solution was concentrated and the extract (140 g) was partitioned 3 times between water (1 l) and AcOEt (1 l) to give 75 g of AcOEt extract. The AcOEt extract was further treated with petroleum ether at room temperature to give soluble (60.5 g) and insoluble (14.5 g) portions. The soluble portion was chromatographed on silica gel and eluted with a mixture of *n*-hexane and AcOEt.

Compound **1** (500 mg) was obtained from the fraction eluted with *n*-hexane–AcOEt (4 : 1). A mixutre of **3** and **4** was obtained from the fraction eluted with *n*-hexane–AcOEt (3 : 2). Compounds **3** and **4** were purified by HPLC (MeCN : MeOH : H_2O = 65 : 20 : 15; flow rate, 5 ml/min; monitor wavelength, 270 nm) to give **3**, (150 mg) and **4** (200 mg).

Atractylenolide I (1) mp 109.5—110.5 °C, colorless needles from MeOH–H_2O. UV λ_{max}^{hexane} nm (log ε): 274 (4.19). IR ν_{max}^{KBr} cm^{-1}: 1750 (C=O), 1640 (C=C), 1006 (C–O–C), 880 (C=CH). ^1H-NMR (CCl_4) δ: 0.92 (3H, s, CH_3), 1.85 (3H, s, CH_3), 4.59 and 4.86 (1H, each, br s, C=CH_2), 5.45 (1H, s, C=CH).

(4*E*, 6*E*,12*E*)-Tetradecatriene-8,10-diyne-1,3-diol Diacetate (3) A pale yellow oil. $[\alpha]_D$ +0.4° (*c* = 1.0, MeOH). UV λ_{max}^{MeOH} nm (log ε): 337 (4.36), 315 (4.51), 296 (4.38), 279 (4.16), 266 (4.37), 249 (4.41), 214 (4.27). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2190, 2100 (C≡C), 1725, 1220 (CH_3CO_2), 1610, 980 (CH=CH–CH=CH). ^1H-NMR ($CDCl_3$) δ: 1.83 (3H, dd, *J* = 1.7, 6.9 Hz, C_{14}-H), 1.98 (2H, dq, *J* = 2.0, 6.6 Hz, C_2-H), 2.04 and 2.07 (3H each, s, OAc), 4.09 (2H, m, C_1-H), 5.40 (1H, q, *J* = 6.6 Hz, C_3-H), 5.53—5.62 (1H, m, C_{12}-H), 5.70 (1H, d, *J* = 15.5 Hz, C_7-H), 5.75 (1H, dd, *J* = 6.6, 15.5 Hz, C_4-H), 6.29 (1H, dq, *J* = 15.5, 6.9 Hz, C_{13}-H), 6.35 (1H, dd, *J* = 10.3, 15.5 Hz, C_5-H), 6.64 (1H, dd, *J* = 15.5, 10.3 Hz, C_6-H). MS *m/z*: 300 (M^+), 240 ($M^+ - CH_3CO_2H$), 197 (240 − CH_3CO).

(6*E*,12*E*)-Tetradecadiene-8,10-diyne-1,3-diol Diacetate (4) A pale yellow oil. $[\alpha]_D$ 0° (*c* = 1.17, MeOH). UV λ_{max}^{MeOH} nm (log ε): 313 (4.29), 293 (4.37), 277 (4.20), 262 (3.95), 248 (4.34), 238 (4.49), 232 (4.50), 219 (4.48). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2100, 2190 (C≡C), 1200, 1610, 1715 and 1730 (sh) (CH_3CO_2). ^1H-NMR ($CDCl_3$) δ: 1.69 (2H, dt, *J* = 5.4, 7.3 Hz, C_4-H), 1.82 (3H, dd, *J* = 1.7, 6.9 Hz, C_{14}-H), 1.88 (2H, dt, *J* = 5.4, 6.4 Hz, C_2-H), 2.04 and 2.05 (3H each, s, OAc), 2.18 (2H, dt, *J* = 6.9, 7.3 Hz, C_5-H), 4.08 (2H, t, *J* = 6.4 Hz, C_1-H), 4.99 (1H, q, *J* = 5.4 Hz, C_3-H), 5.56 (2H, d, *J* = 15.5 Hz, C_7-H and C_{12}-H), 6.25 (1H, dt, *J* = 6.9, 15.5 Hz, C_6-H), 6.31 (1H, dq, *J* = 15.5, 6.9 Hz, C_{13}-H). MS *m/z*: 302 (M^+), 242 ($M^+ - CH_3CO_2H$), 199 (242 − CH_3CO). High-resolution MS: *m/z* 302.1530 (M^+): Calcd 302.1518.

Hydrolysis of 4 A solution of **4** (20 mg) in 3% KOH–MeOH (7 ml) was heated at 60 °C for 10 min. After cooling, the solution was neutralized with 1 N HCl, and MeOH was removed under reduced pressure. The resulting mixture was extracted with Et_2O. The organic layer was dried over anhydrous Na_2SO_4 and **5** was obtained as a pale yellow amorphous powder (9.3 mg). $[\alpha]_D$ +0.73° (*c* = 1.1, MeOH). UV λ_{max}^{MeOH} nm (log ε): 313 (4.29), 293 (4.37), 277 (4.23), 262 (3.95), 248 (4.35), 238 (4.51), 231 (4.53), 218 (4.50). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 1295 (OH), 2100, 2190 (C≡C). ^1H-NMR (CD_3OD) δ: 1.48—1.58 (2H, m, C_4-H), 1.65 (2H, q, *J* = 5.9 Hz, C_2-H), 1.81 (3H, dd, *J* = 6.9, 1.7 Hz, C_{14}-H), 2.14—2.38 (2H, m, C_5-H), 3.67 (3H, m, C_1-H and C_3-H), 5.60 (1H, d, *J* = 15.5 Hz, C_{12}-H), 5.61 (1H, d, *J* = 15.5 Hz, C_7-H), 6.29 (1H, dq, *J* = 15.5, 6.9 Hz, C_{13}-H), 6.34 (1H, dt, *J* = 15.5, 6.9 Hz, C_6-H). MS *m/z*: 218 (M^+).

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