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Diacetyl-atractylodiol, a New Acetylenic Compound from *Atractylodes japonica* Koidzumi

In order to develop the chemical identification method of the two groups of Chinese crude drugs named "Bai-zhu" (Japanese: byaku-jutsu) and "Chang-zhu" (Japanese: sō-jutsu) and also in order to elucidate the biologically active principle of these drugs, we have first started with the chemical study on the rhizome of *Atractylodes japonica* (Compositae), which has been used as a substitute for "Bai-zhu"[1] and only 2-furaldehyde and acetaldehyde have been known as the constituents.[2] This communication deals with the structure elucidation of a new acetylenic compound named diacetyl-atractylodiol (Ia) in addition to the identification of atractylon (IIa).

On dry column chromatography using silica gel followed by ordinary silica gel column and thin-layer chromatography (TLC), the benzene extract of dry rhizome afforded a new acetylenic compound (Ia) in a 3.3% yield along with atractylon (IIa)[3] (*ca.* 25%, major) and its autoxidation derivatives (IIb and IIc) (minor).[3]

Diacetyl-atractylodiol (Ia), $[\alpha]_D$—4.8° ($CHCl_3$), infrared spectrum (IR) (CCl_4, cm^{-1}): 2195, 2125(w) (acetylene), 1745, 1240 (acetoxyl), 1620, 948 (double bond), is a quite unstable oily substance. The presence of an ene-diyne-ene chromophore[4] in Ia is revealed by its ultraviolet absorption maxima (λ_{max}^{EtOH} nm (log ε): 219 (4.53), 232 (4.54), 239 (4.54), 248 (4.42), 263 (4.07), 267 (sh) (4.00), 277 (4.27), 295 (4.45), 314 (4.38), 337 (3.54)), which are alike to those reported for aethusanol A[5] possessing the same chromophore. The proton magnetic resonance (PMR) spectrum[6] (CCl_4) of Ia shows the presence of an olefinic methyl (1.85, 3H, d.d, J=7 and 1.5, $C_{(13)}$-H_3), two acetoxyls (1.98, 6H, s), four olefinic protons (5.50, 2H, br.d, J=16, $C_{(6)}$-H, $C_{(11)}$-H, 6.22, 1H, d.t, J=7 and 16, $C_{(5)}$-H, and 6.22, 1H, d.q, J=7 & 16, $C_{(12)}$-H) and three protons attached to the acetoxyl-bearing carbons (4.00, 2H, t, J=7, $C_{(1)}$-H_2, & 4.87, 1H, qui, J=6, $C_{(3)}$-H), and the disposition of these functions was elucidated on the basis of the decoupling experiment as shown in Table I. Consequently, provided that diacetyl-atractylodiol is constituted with a thirteen-carbon chain, the structure (Ia) has become reasonable for it.

Catalytic hydrogenation of Ia over PtO_2 in EtOAc followed by KOH–H_2O–MeOH treatment furnished a saturated glycol (Ib), $C_{13}H_{28}O_2$,[7] mp 57—58°, $[\alpha]_D$—1.5° ($CHCl_3$), IR ($CHCl_3$): 3610, 3490 cm^{-1}, PMR ($CDCl_3$): 3.85 (2H, t, J=5, $C_{(1)}$-H_2), 3.85 (1H, qui, J=5, $C_{(3)}$-H), 2.82 (2H, br.s, exchangeble with D_2O), mass spectrum (m/e (%)): 75 (100), 57 (75-H_2O) (41). The base peak observed at m/e 75, which was derived through a typical α-cleavage of secondary alcohol,[8] substantiates the 1,3-diol structure for Ib. In addition, on treatment with CrO_3–H_2O–H_2SO_4 at 0° Ib furnished a 1-ol-3-keto derivative (Ic), $C_{13}H_{26}O_2$, IR (CCl_4): 3625, 3570, 1710 cm^{-1}, PMR (CCl_4): 2.32 (2H, t, J=7, $C_{(4)}$-H_2), 2.49 (2H, t, J=5, $C_{(2)}$-H_2), 3.66 (2H, t,

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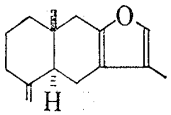
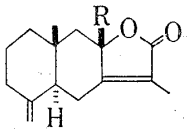
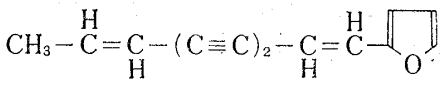
6) δ Values at 90 MHz, J and $W_{h/2}$ values in Hz. Abbreviations: br.d.: broad doublet, d.d.: doublet of doublet, d.q.: doublet of quartet, d.t.: doublet of triplet, m.: multiplet, q.: quartet, qui.: quintet, s.: singlet, t.: triplet.
7) The compounds described with the chemical formulae gave the satisfactory analytical values.
8) R.A. Friedel, J.L. Shultz and A.G. Sharkey, Jr., *Analytical Chem.*, **28**, 926 (1956).



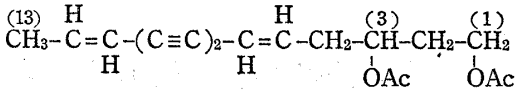
IIa : atractylon



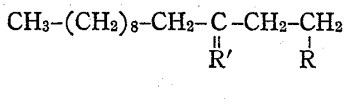
IIb : R=H
IIc : R=OH



III : atractylodin



Ia: diacetyl-atractylodiol



	R′	R
Ib :	H, OH	OH
Ic :	O	OH
Id :	H, OH	OTs
Ie :	H, OH	H
If :	O	H

TABLE I. The Decoupling Experiment of Diacetyl-atractylodiol (Ia)
(δ values at 90 MHz in CCl_4, J values in Hz)

Decoupled protons	Irradiated at 1.85 ($C_{(13)}$-H_3, $C_{(2)}$-H_2, $C_{(4)}$-H_2)	Irradiated at 5.50 ($C_{(6)}$-H, $C_{(11)}$-H)	Irradiated at 6.22 ($C_{(5)}$-H, $C_{(12)}$-H)
$C_{(1)}$-H_2 (t, J=7)	br.s.		
$C_{(3)}$-H (qui, J=6)	br.s.[a]		
$C_{(5)}$-H (d.t, J=7 & 16)	br.d. (J=16)	deformed	
$C_{(6)}$-H (br.d, J=16)	d. (J=16)		[b]
$C_{(11)}$-H (br.d, J=16)	d. (J=16)		[b]
$C_{(12)}$-H (d.q, J=7 & 16)	br.d. (J=16)	deformed	
$C_{(13)}$-H_3 (d.d, J=7 & 1.5)		d. (J=7)	br.s.

a) Due to simultaneous irradiation on $C_{(2)}$-H_2 and $C_{(4)}$-H_2.
b) Unobserved due to disturbance caused by irradiation beat.

J=5, $C_{(1)}$-H_2). The double resonance experiment of Ic disclosed that the active methylene protons on $C_{(2)}$ coupled with the protons on $C_{(1)}$ bearing a primary hydroxyl. The accumulated evidence mentioned above indicates the presence of the 1,3-glycol moiety in Ib and therefore the 1,3-diacetate moiety in Ia.

On treatment with *p*-TsCl in dry pyridine Ib yielded a monotosylate (Id), IR (CCl_4): 3620, 3550, 1597, 1466, 1338, 1175, 1155, 660 cm^{-1}, PMR (CCl_4): 3.63 (1H, m, $W_{h/2}$=18, $C_{(3)}$-H), 3.9—4.4 (2H, m, $C_{(1)}$-H_2), in which only the primary hydroxyl was tosylated. Reduction of Id with $LiAlH_4$ in dry ether at reflux gave in a good yield a 3-ol derivative (Ie), $[\alpha]_D$—0.9°, IR (CCl_4): 3620 cm^{-1}, PMR (CCl_4): 0.89 (3H, deformed t, $C_{(13)}$-H_3), 0.90 (3H, t, J=6.5, $C_{(1)}$-H_3), 3.40 (1H, br.s, $W_{h/2}$=14, $C_{(3)}$-H). A monoketone (If), mp 27—28°, IR (CCl_4): 1723 cm^{-1}, PMR (CCl_4): 0.87 (3H, deformed t, $C_{(13)}$-H_3), 0.98 (3H, t, J=6.5, $C_{(1)}$-H_3), 2.29 (2H, t, J=6, $C_{(4)}$-H_2), 2.32 (2H, q, J=6.5, $C_{(2)}$-H_2), prepared from Ie under the same oxidation conditions as for Ib was found to be identical with tridecan-3-one in all respects (mp, mixed mp, TLC, gas-liquid chromatography (GLC) (PEGS, 3% SE-30), IR, PMR).

Accordingly, the structure (Ia) has been established for diacetyl-atractylodiol. As for the absolute configuration at $C_{(3)}$ in Ia, the further work is in progress. Diacetyl-atractylodiol (Ia) showed a weak inhibitory effect against some *Eumycetes*,[9] which seems to be an observation of interest in view of the usage of the plant material.

9) The authors are grateful to Dr. S. Noguchi of the Res. Lab. of Takeda Chem. Ind. for a biological assay.

While atractylodin (III), a furanoid acetylenic compound initially isolated from a Manchurian *Atractylodes* species,[10] has been found in several crude drugs belonging to "Chang-zhu",[11] diacetyl-atractylodiol (Ia) is an only acetylenic compound elucidated in one of the crude drugs grouped in "Bai-zhu". It is worth to mention here that the elucidation of the occurrence of these two distinct acetylenic compounds in two different groups of crude drugs "Bai-zhu" and "Chang-zhu" is in good accord with a botanical diagnosis for the original plants of two groups.

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Synthesis of (±)-Desmethyldecaline

Desmethyldecaline,[1] an alkaloid from *Decodon verticillatus* (L.) ELL. (Lythraceae), was assigned the structure (I) based on the evidence that it was converted to decaline (II)[1–3] by methylation of the hydroxyl group and on the biogenetic consideration, however, the position of hydroxyl group at C-4″ or C-5″ has not yet been determined chemically. We tried to synthesize I in order to establish the structure of desmethyldecaline.

Benzylation of the *trans*-quinolizidin-2-one (III)[2] with benzyl chloride gave in 83% yield the benzyl ether (IV) [*m/e*: 445, 443 (M^+, 1: 1), $\nu_{max}^{CHCl_3}$ cm^{-1}: 2790, 2760 (Bohlmann bands), 1718 (C=O)], which was reduced with the Henbest catalyst [$IrCl_4$–HCl–$(CH_3O)_3P$–iso-PrOH][4] to afford the axial alcohol (V) and the equatorial alcohol (VI) in the ratio of 11: 1 in 84% yield. The both alcohols (V and VI) were acetylated with acetic anhydride in pyridine to give the acetyl derivative (VII) [*m/e*: 447, 445 (M^+, 1: 1), δ: 5.00 (1H, m, W_H=7 Hz, CHOAc)] and the epimeric acetyl derivative (VIII) [*m/e*: 447, 445 (M^+, 1: 1), δ: 4.76 (1H, t–t, J=11; 4.5 Hz, CHOAc)], respectively.

The Ullmann condensation of VII with methyl 4-hydroxyhydrocinnamate[5] afforded the biphenyl ether (IX) [*m/e*: 587 (M^+), $\nu_{max}^{CHCl_3}$ cm^{-1}: 2800, 2770, 2740 (Bohlmann bands), 1728 (C=O)], which was hydrolyzed to furnish the hydroxy acid (X) [*m/e*: 531 (M^+)]. Heating of X with *p*-toluenesulfonic acid in benzene effected lactonization and debenzylation, providing the lactone (I) [mp 259—261°, *m/e*: 423 (M^+), $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550 (OH), 2800, 2730 (Bohlmann bands), 1720 (C=O), δ: 5.20 (1H, br-s, OH), 4.86 (1H, m, W_H=7 Hz, CHOCO), 3.91 (3H, s, OCH_3)] in 37% yield, which was treated with diazomethane to afford (±)-decaline (II).[2]

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