Tetrahedron Letters No.48, pp. 6069-6074, 1966. Pergamon Press Ltd.
Printed in Great Britain.

FERN CONSTITUENTS: ADIPEDATOL, FILICENAL AND OTHER TRITERPENOIDS ISOLATED FROM *ADIANTUM PEDATUM*

H. Ageta and K. Iwata

Shôwa College of Pharmacy, Setagaya, Tokyo

(Received 21 September 1966)

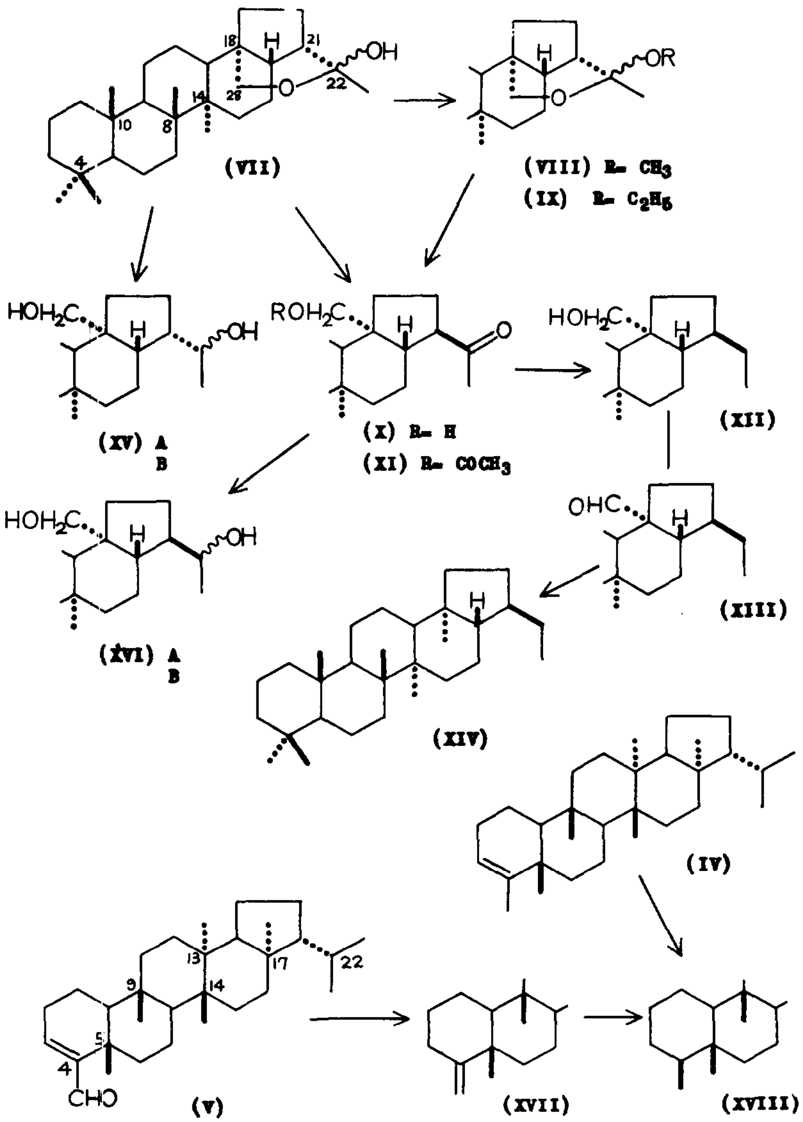
In previous communications[1)2)] we had reported the isolation and the structural studies on triterpenoids obtained from a japanese Maidenhair Fern, *Adiantum monochlamys* EATON. This communication is concerned with the isolation of seven triterpenoids from Northern Maidenhair Fern, *Adiantum pedatum* LINN. (Pteridaceae, "Kujaku-shida"), distributed in Japan, and the structural elucidations of two new compounds, adipedatol and filicenal.

Hexane extraction of the dried leaves, followed by careful separation through chromatography over silica gel and alumina afforded four hydrocarbons, a conjugated aldehyde, a nor-triterpenoid ketone and a nor-triterpenoid hemiketal as shown in Table I, together with

Table I

compound		m.p.°C	yield %
isofernene (I)	$C_{30}H_{50}$	191-192	0.02
fernene (II)	$C_{30}H_{50}$	171-172	0.40
7-fernene (III)	$C_{30}H_{50}$	211-213	0.015
filicene (IV)	$C_{30}H_{50}$	224-226	0.015
filicenal (V)	$C_{30}H_{48}O$	ca. 272	0.04
adiantone (VI)	$C_{29}H_{48}O$	220-222	0.50
adipedatol (VII)	$C_{29}H_{48}O_2$	185-188	0.65

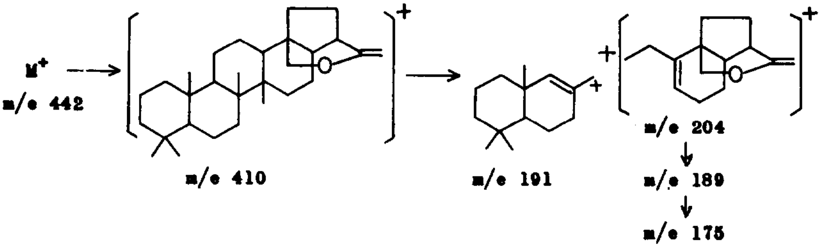
All m.p.s were measured by a Kopfler block and uncorrected. $[\alpha]_D$ were observed at 25°C, c=1.0 in $CHCl_3$ solutions. IR spectra were run using KBr disks.


OH
18
21
22
10
8
14
28
O
4
(VII)
OR
O
(VIII) R= CH3
(IX) R= C2H5
HOH2C
OH
(XV) A
B
ROH2C
O
(X) R= H
(XI) R= COCH3
HOH2C
(XII)
HOH2C
OH
(XVI) A
B
OHC
(XIII)
(XIV)
(IV)
9
13
14
17
22
5
4
CHO
(V)
(XVII)
(XVIII)

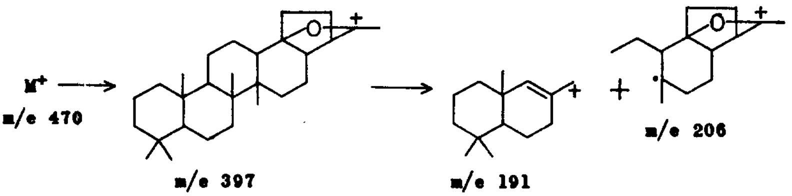
a small amount of sterols. The compounds (I), (II), (III), (IV) and (VI) were identified by direct comparison of m.p., IR, and VPC with those of authentic samples reported previously.[1)2)3)] Although the methanol extracts of the plant material gave a nor-triterpenoid ketal in a good yield (0.6%), the compound was proved to be identical with adipedatol methyl ether (VIII), which was supposed to be artificial.

Refluxing adipedatol (VII), $[\alpha]_D$ +88°, ν_{max} cm^{-1} 3400(OH), 1135, 1098, 1050(C-O), with methanol and ethanol, it readily changed into the methyl ether (VIII), $C_{30}H_{50}O_2$, m.p. 200-204°, $[\alpha]_D$ +107°, ν_{max} cm^{-1} 1132, 1098, 1040(C-O), and the ethyl ether (IX), $C_{31}H_{52}O_2$, m.p. 176-179°, $[\alpha]_D$ +103°, ν_{max} cm^{-1} 1150, 1108, 1036, respectively. The chemical shifts of the five methyl groups attached to C(4α), (4β), (10), (8) and (14) in the compounds (VII), (VIII) and (IX) were similar to those of hopane and derivatives (Table II).[2)4)] This fact suggested that adipedatol and its ethers have the same saturated hopane skelton having no oxygen function in ring A, B, C and D. The methyl signals at τ8.67 (VII), τ8.79 (VIII) and τ8.79 (IX) can be assigned to those at C(22) carrying oxygen functions, while the presence of $-OCH_3$ (VIII) and $-OC_2H_5$ (IX) was demonstrated by the signals at τ6.78, 3H singlet (VIII), and at τ6.45, 1H doublet (J=6.5 cps), 6.51, 1H doublet (J=6.5 cps) and τ8.77, 3H triplet (J=6.5 cps) (IX), respectively. These three compounds lacked the methyl signal at τ9.30-9.40, characteristic of that at C(18) in hopane and derivatives, whereas they had the tertiary methylene carrying a oxygen function, appearing as a pair of doublets (J=11 cps) at τ5.75, 6.85 (VII), τ6.04, 6.88 (VIII), and τ5.99, 6.89 (IX), respectively. This methylene can be assigned to that attached to C(18) on the basis of biogenetical aspects as well as the evidence for the carbon skelton of these compounds as described below. The chemical shifts of the methyl group at C(22) and one of the two protons of the methylene group at C(18) in adipedatol (VII) were considerably different from those in the ethers, (VIII) and (IX). This fact along with the chemical evidence for the hemiketal or the ketal structure at C(22) (see below) assumed the structure of adipedatol and its ethers as shown as in formula (VII), (VIII) and (IX).

The mass spectrum of the methyl ether (VIII), m/e M^+ 442(2), M^+-CH_3OH 410(39), 204(30), 191(100), 189(18) and 175(23), supported the above assumption, being assigned to the fragments as shown as follows.



By refluxing with 10% ethanolic KOH for 40 hrs.. adipedatol (VII) afforded the keto alcohol (X), $C_{29}H_{48}O_2$, m.p. 285-287°, $[\alpha]_D$ +6°, ν_{max} cm^{-1} 3480, 1038(-OH), 1689(C=O). The same compound was also obtained from adipedatol methyl ether (VIII) by treatment with 5% H_2SO_4-AcOH-benzene at a room temperature. The NMR spectrum of (X) clearly showed the presence of the methyl ketone (τ7.86) and the hydroxymethylene attached to C(18)(τ6.11, 6.44, a pair of doublets, J=12 cps). Since the compound (X) has been obtained by alkali or acid treatment, it should have the more stable configuration at C(21),[5] i.e. 28-hydroxy-21αH-30-nor-hopan-22-one. Treatment of (X) with acetic anhydride-pyridine gave the acetate (XI), $C_{31}H_{50}O_3$, m.p. 191-193°, $[\alpha]_D$ -7°, ν_{max} cm^{-1} 1710(C=O), 1737, 1250($OCOCH_3$), a pair of doublets at τ5.74, 5.99 (J=13 cps). The mass spectrum showed the molecular peak at m/e 470(7), M^+-CH_2OCOCH_3 at m/e 397(75) besides the fragments at m/e 206 (47), 205(43) and 191(100).



Wolff-Kishner reduction of the keto alcohol (X) afforded 21αH-30-nor-hopan-28-ol (XII), $C_{29}H_{50}O$, m.p. 171-172°, $[\alpha]_D$ -4°, ν_{max} cm^{-1} 3940, 1034(-OH), in which the ethyl group was demonstrated by a triplet of the methyl signal at τ9.15 (J=6.5 cps). Chromic acid-pyridine oxidation of (XII) gave the aldehyde (XIII), $C_{29}H_{48}O$, m.p.

Table II Chemical shifts of the methyl groups (τ-value)
(Varian A-60, CCl_4 or $CDCl_3$ solution)

compound	methyl groups attached to C( )				
	4α,4β,10	8	14	18*	22
(VII)	9.16,9.19,9.20	9.03	9.03	5.75d,6.85d(J=11 cps)	8.67
(VIII)	9.15,9.19,9.19	9.03	9.04	6.04d,6.88d(11)	8.79
(IX)	9.16,9.19,9.20	9.03	9.06	5.99d,6.89d(11)	8.77
(X)	9.15,9.19,9.20	9.00	9.00	6.11d,6.44d(12)	7.86
(XI)	9.16,9.19,9.21	9.02	9.02	5.74d,5.99d(13)	7.86
(XII)	9.15,9.18,9.19	9.01	8.97	6.11d,6.52d(12)	9.15t(6.5)
(XIV)	9.15,9.18,9.20	9.03	9.05	9.35	9.15t(6.5)
(XV) A	9.15,9.18,9.18	9.02	8.91	6.09d,6.42d(11)	8.86d(6.5)
(XV) A**	9.12,9.17,9.17	8.96	8.75	5.81d,6.06d(12)	8.70d(6.5)
(XV) B**	9.12,9.17,9.17	8.95	8.86	5.83d,6.12d(12)	8.67d(6.5)

* 2H signals of the methylene group except for (XIV)
** observed in a deutero-pyridine solution

162-163°, ν_{max} 2700, 1714(CHO), Wolff-Kishner reduction of which afforded the saturated hydrocarbon (XIV), $C_{29}H_{50}$, m.p. 185-187°. This hydrocarbon was proved to be identical with 21αH-30-nor-hopane (isoadiantane)[6] derived from isoadiantone and it was confirmed that adipedatol has the carbon skelton of 30-nor-hopane.

Adipedatol was treated with Lithium in ethyl amine to give two isomeric diols, diol (XV) A, $C_{29}H_{50}O_2$, m.p. 227-230°, $[\alpha]_D$ +28°, ν_{max} cm^{-1} 3200, 1052, 1028(-OH), and diol (XV) B, $C_{29}H_{50}O_2$, m.p. 250, 264-267°, $[\alpha]_D$ +52°, ν_{max} cm^{-1} 3300, 1036(-OH). On the other hand, $LiAlH_4$ reduction of the keto alcohol (X) gave also two isomeric diols, diol (XVI) A, $C_{29}H_{50}O_2$, m.p. 240-241°, $[\alpha]_D$ +16°, ν_{max} cm^{-1} 3325, 1089, 1033(-OH), and diol (XVI) B, ν_{max} cm^{-1} 3250, 1075, 1035(-OH). Although the same 18,22-diol structure in these four diols were suggested by their NMR spectra, they were different one another. The diols (XVI) have the 21αH-configuration as described above, and therefore the diols (XV) should have the original 21βH-configuration. The diols A and B must be isomeric at C(22) both in (XV) and (XVI). The absolute configuration of these diols at C(22) as well as the stereochemistry at C(22) in adipedatol and its ethers will be presented in a separate paper.

The presence of a conjugated aldehyde group in the second new compound, filicenal (V), $[\alpha]_D$ +74° (c=0.5), was demonstrated by its IR, ν_{max} cm^{-1} 2720, 1682, 1630, as well as by its UV, λ_{max}^{EtOH} $m\mu$ 234 (ε 13.000).[7] The chemical shifts observed in a deutero-pyridine solution, τ 9.05, 9.05, 9.05, 9.28, 9.08 doublet (J=7.5 cps) and 9.16 doublet (J=7.5 cps), of the six methyl groups attached to C(9), (14), (13), (17), (22) and (22), respectively, were similar to those of filicene (IV). The remaining methyl signal at τ 8.49 can be assigned to that at C(5), which is subject to the very strong deshielding effect of the double bond and the carbonyl. A vinyl proton was observed at τ 3.03 as a multiplet.

Wolff-Kishner reduction of filicenal (V) afforded a hydrocarbon, filic-4(23)-ene (XVII), m.p. 206-209°, ν_{max} cm^{-1} 3080, 1635, 890 (exocyclic methylene). As the movement of the double bond during this reaction is well-known,[7] it has been concluded under biogenetical consideration that the aldehyde group should be at C(4) in filicenal, i.e. filic-3-en-23-al (V). Catalytic hydrogenation of the hydrocarbon (XVII) established its carbon skelton by giving a saturated hydrocarbon, m.p. 212-215°, which was proved to be identical with filicane (XVIII) derived from filicene previously.[1]

It is very interesting to know that adipedatol and filicenal are the first examples of the natural triterpenoids having the hemiketal and the conjugated aldehyde groups, respectively.

Acknowledgements. Thanks are due to Center of Microanalysis, Kyoto University; Central Research Laboratories, Sankyo Co., for elemental analyses, mass spectrometries, and NMR measurements.

References.

1) H.Ageta, K.Iwata, S.Natori: Tetrahedron Letters, 1964, 3413

2) H.Ageta, K.Iwata, Y.Arai, Y.Tsuda, K.Isobe, S.Fukushima: ibid., 1966, in press

3) G.Berti, F.Bottari, A.Marsili, J.-M.Lehn, P.Witz, G.Ourisson: ibid., 1963, 1283

4) S.Huneck, J.-M.Lehn: Bull.Chim.Soc.France, 1963, 1702

5) G.V.Baddeley, T.G.Halsall, E.R.H.Jones: J.Chem.Soc., 1961, 3891

6) G.Berti, F.Bottari, A.Marsili, L.Mazzanti: Il Farmaco, 18, 424 (1963)

7) G.Lardelli, Hs.K.Krüsi, O.Jeger, L.Ruzicka: Helv.Chim.Acta., 31, 1815 (1948)