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130. Yong-Yeng Lin,*1 Hiroshi Kakisawa,*2 Yoshio Shiobara, and Koji Nakanishi*1 : The Structure of Davallic Acid.*3

(*Department of Chemistry, Tohoku University*1 *and Department of Chemistry, Tokyo Kyoiku University*2)

The ethanol extract of the rhizome of a Chinese fern, *Davallia divaricata*, which is widely used as a diuretic and tonic in Taiwan, gave crystals having the molecular formula of $C_{30}H_{48}O_2$, m.p. 283°.

The present studies estabish its structure as I. It is a pentacyclic compound containing one carboxyl group and a trisubstituted double bond as revealed by spectroscopic and chemical properties of itself and derivatives. Namely, davallic acid has a strong absorption at 1700 cm^{-1} (KBr) due to the carboxylic acid function. Methylation led to methyl davallate (II) and acetylation gave the mixed anhydride (III). Reduction of the ester II with lithium aluminum hydride gave davallol (IV), which could be easily converted to the acetate (V), the tosylate (VI), and the aldehyde davallal (VII) (oxidation with chromic anhydride and pyridine).

The nature of the methyl groups was most clearly revealed by the 100 Mc. nuclear magnetic resonance spectrum of davallal (Fig. 1a) which showed five methyl singlets at 0.75, 0.77, 0.83, 0.94 and 1.00 p.p.m., and a triplet at 0.80, 0.86 and 0.92 p.p.m. with peak height ratios of ca. 1:2:1 that could be assigned either to an isopropyl group[1] or two secondary methyl groups. A single olefinic proton absorbed broadly at 5.36 p.p.m. (trisubstituted double bond, ν^{KBr} 820 cm^{-1}), while the aldehyde proton appeared at 10.00 p.p.m. as a singlet which shapened upon irradiating the region around 1.20 p.p.m., *i.e.*, $\Delta\omega = 880$ c.p.s. Evidently, the aldehyde proton is long-range coupled to methylene protons.[2] The hindered nature of the oxygen function was demonstrated by the fact that the nuclear magnetic resonance spectrum of the acetate (V) exhibited an AB type quartet at 3.9 and 4.2 p.p.m. (J=11 c.p.s.) assignable to the $-CH_2-$ of the acetoxymethylene group. This large differene in chemical shifts of the two protons can only be explained by a restricted rotation of the CH_2OAc group which greatly enhances the environmental nonequivalence of the two protons.[3] In conjunction with the singlet nature of the aldehydic proton in davallal (VII) it is evident that the oxygen-containing group is attached to a quaternary carbon atom.

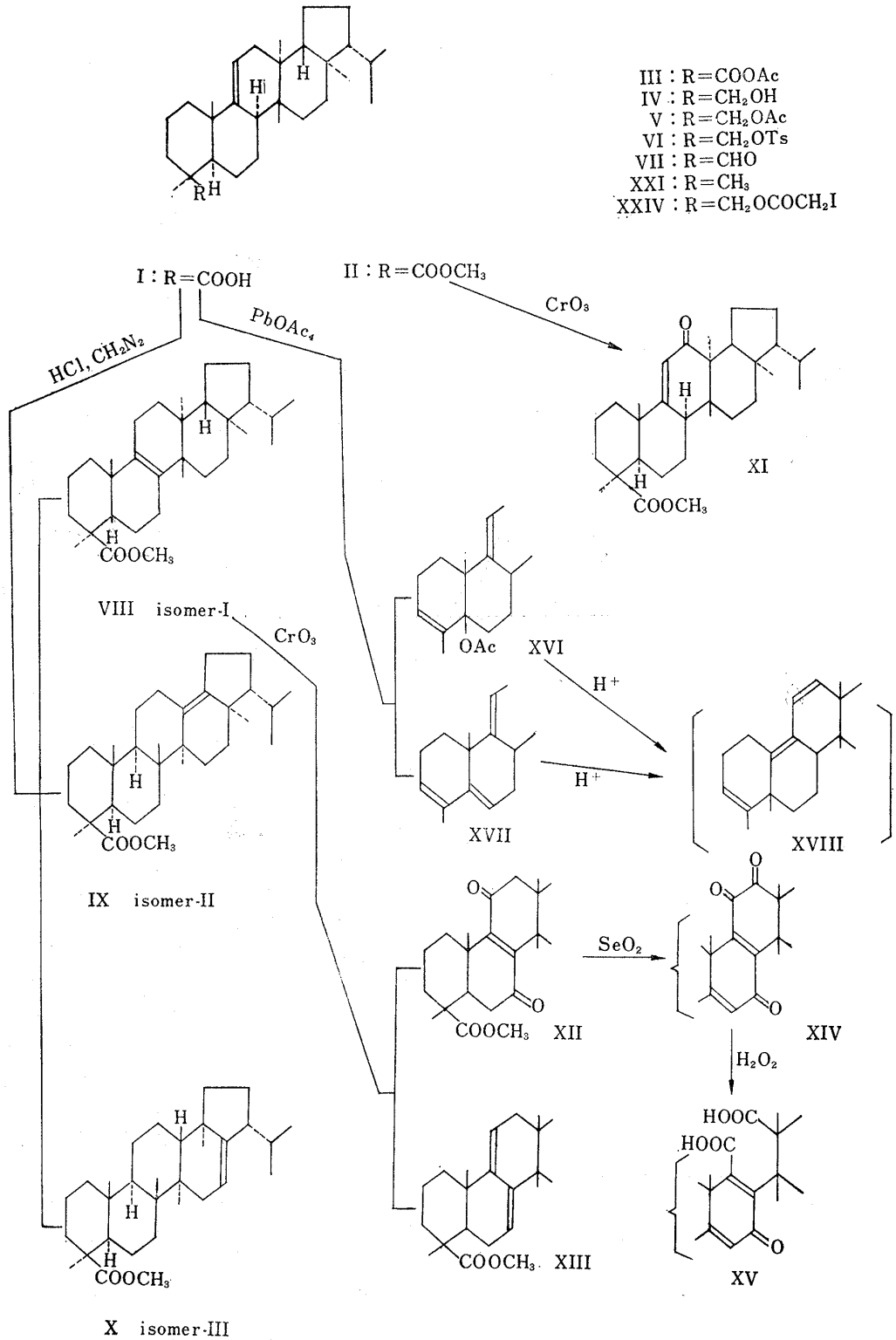
When davallic acid was refluxed in acetic acid/hydrochloric acid and the mixture of products methylated, isomerization occurred to give methyl isodavallate-I (VIII) and two other minor products, methyl isodavallate-II (IX) and -III (X). The nuclear magnetic resonance spectra of isomers-I and -II lacked olefinic protons, while that of isomers-III had a broad resonance at 5.20 p.p.m.

Oxidation of methyl davallate (II) with chromic trioxide in acetic acid gave a ketone (XI), having spectroscopic properties suggestive of a transoid rather than a cisoid enone system : ν^{KBr} 1680 (strong) and 1605 (medium cm^{-1}), λ^{EtOH} 246 mμ (ε 9500), δ 5.32 p.p.m. On the other hand, oxidation of isomer-I (VIII) having the tetrasubstituted double bond

*1 Katahira, Sendai (林 栄 原, 塩原義雄, 中西香爾).
*2 Otsuka, Tokyo (柿沢 寛).
*3 Part of the present studies has been reported in a preliminary communication : K.Nakanishi, Y-Y. Lin, H. Kakisawa, H-Y. Hsu, H. C. Hsiu : Tetrahedron Letters, No.22, pp. 1451~1457, 1963.

1) J. M. Lehn, G. Ourisson : Bull. Soc. Chem. Fr., **1962**, 1137.
2) S. Sternhell : Rev. Pure and Appl. Chem. (Austr.), **14**, 15 (1964); C. A. Henrick, P. R. Jefferies : Austr. J. Chem., **17**, 915 (1964).
3) cf. K. Nakanishi, M. Ohashi, M. Tada, Y. Yamada : Tetrahedron, No. 5 (1965), footnote 14.

yielded an enedione (XII), ν^{KBr} 1680 (strong) and 1615 (weak) cm^{-1}, λ^{EtOH} 271 mμ (ε 7500), and a hetero-annular diene (XIII), λ^{EtOH} 233, 240 and 249 mμ (ε 2100, 2400, 1400). This diene, however, is a mixture as shown by the low ε values, the appearance of two methoxycarbonyl peaks in its nuclear magnetic resonance spectrum (3.62 and 3.66 p.p.m. intensity ratio ca. 1:2) and appearance of two peaks when submitted to vapor phase chromatography. Further oxidation of the enedione (XII) with selenium dioxide



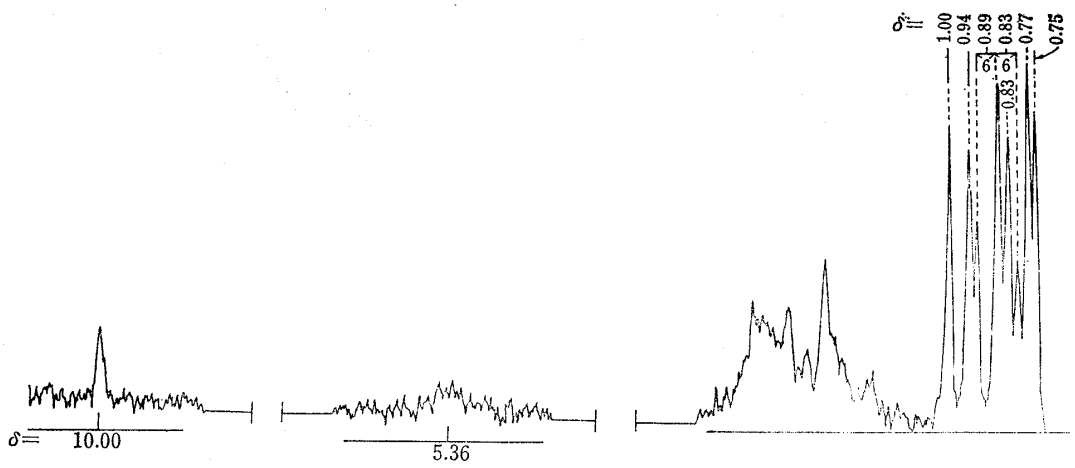


Fig. 1a. Nuclear Magnetic Resonance Spectrum of Davallal (Ⅶ), 100 Mc.

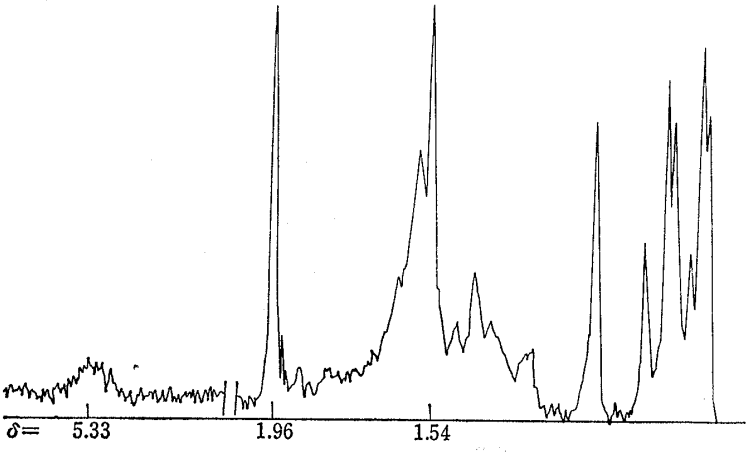


Fig. 1b. Nuclear Magnetic Resonance Spectrum of Acetoxynordiene (XVI), 100 Mc.

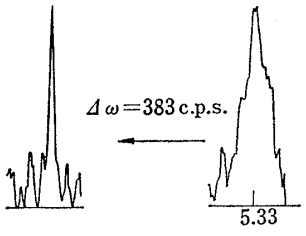


Fig. 1c. Decoupled Trace of Acetoxynordiene (XVI)

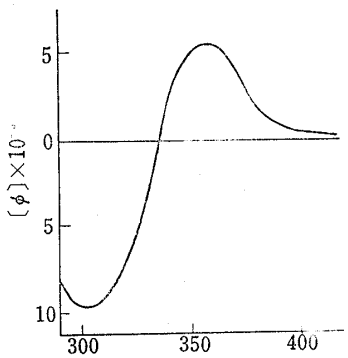


Fig. 2. Optical Rotatory Dispersion Curve of Enone (Ⅺ)

furnished a dienetrione (XIV), λ^{EtOH} 215 and 283 mμ (ε 7500 and 7900), having an α-diketone grouping as indicated by its conversion to a secodicarboxylic acid (XV) upon cleavage with alkaline peroxide. These series of transformations are well known in the field of tetracyclicterpenoids[4] and establishes that the double bond in isomer-I is located at C_8. This evidence together with the formations of an enone (Ⅺ) and diene (ⅩⅢ) enables one to place the trisubstituted double bond in the starting compound either at C_9-C_{11} or C_7.

A choice in favor of the C_9-C_{11} location of the double bond was made on grounds of the ultraviolet absorption of the nortriene (XVⅡ) and mass spectroscopy (described below). Thus, decarboxylation of davallic acid with lead tetraacetate (refluxed for 20

4) G. Ourisson, P. Crabbé, O. R. Rodig : "Tetracyclic Triterpenes," 58 (1964), Hermann, Paris.

hours in benzene under a stream of nitrogen) followed by alumina chromatography yielded two products, an acetoxynordiene (XVI) and a nortriene (XVII). The nuclear magnetic resonance spectrum of the acetoxy nor-compound (XVI) (Fig. 1b) indicated that the acetoxyl group (ν^{KBr} 1740 cm^{-1}) was attached to a quaternary carbon atom. Moreover, irradiation of the olefin methyl at 1.54 p.p.m. caused the ill-defined olefin proton at 5.33 p.p.m. (two-proton intensity) to become a sharp singlet (Fig. 1c); this establishes presence of the grouping -HC=C(Me)-. As shown in Fig. 1c, the decoupled trace appears as one sharp signal in spite of the fact that it is composed of two olefin protons. Presumably, when the olefin methyl protons are irradiated, the allylic methylenes at C_2 and C_{12} in structure (XVI) also become saturated under conditions employed for the double resonance ($\Delta\omega$=383 c.p.s., *i.e.*, irradiation centered around 1.50 p.p.m.), and furthermore, chemical shifts of the two olefin protons are accidentally coincident. The trisubstituted double bond originally present in davallic acid probably occupies the same position in this acetoxy nor-compound because treatment of methyl davallate (II) with lead tetraacetate under identical conditions resulted in recovery of starting material. Structure (XVII) for the triene is based on its spectroscopic properties. Namely, the ultraviolet absorption of the triene (XVII) has the fine structure characteristic of hetero-annular dienes, λ^{EtOH} 234, 241 and 249 mμ (ε 9700, 10700 and 7300), and the nuclear magnetic resonance spectrum has a broad peak of three-proton intensity around 5.36 p.p.m. and an olefin methyl signal at 1.54 p.p.m. When the two nor-compounds (XVI) and (XVII) were treated with hydrogen chloride in chloroform, they both afforded a small amount of another compound; because of its minute quantity this product has not been investigated further but ultraviolet maxima at 239, 246 and 254 mμ, namely bathochromic shifts of 5 mμ as compared to the triene (XVII), enables one to tentatively assign structure (XVIII) to this isonortriene (based on structure (I) deduced below for davallic acid).

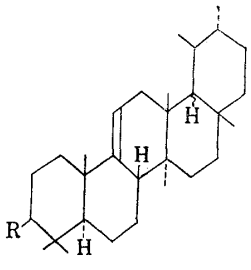
As described above, acid rearrangement of davallic acid gives the Δ^8 isomer (VIII) as the main product, which in turn suggests the double bond to be located either at C_9-C_{11} or C_7-C_8 in the original compound. The fragmentation patterns resulting from electron bombardment (Table I, described below) and the ultraviolet maximum of the triene (XVII) centered at 241 mμ, which excludes the possibility of a conjugated triene formation, are in accord with a C_9-C_{11} location for the unsaturation. This is also corroborated by the fact that the enone (XI) was unreactive towards bromine; if the double bond were at C_7-C_8, the 7-en-6-one system would be brominated at C_5, provided that C_5 is unsubstituted by a methyl group.

It has been mentioned above that chromic acid oxidation of methyl isodavallate-I yielded the transoid diene (XIII) having its ultraviolet absorption centered at 240 mμ. This maximum at 240 mμ is typical for the 7,9(11)-dienes having 13α,14β-methyl groups such as those derived from multiflorenol,[5] bauerenol,[6] arundoin[7] and the euphane group of tetracyclic triterpenes,[8]; in contrast the 7,9(11)-diene system of 13β,14α-methyl compounds such as those derived from lanosterol[8] and arborene (XIX)[9] absorb at 236, 243 and 252 mμ. The optical rotatory dispersion (ORD) curve of the 13α,14β-methyl enone (XI) exhibited a positive Cotton effect as shown in Fig. 2, which is opposite to that of the 13β,14α-methyl arboren-12-one.[9] The significance of the sign of the R-band Cotton effect, however, cannot be fully interpreted because it has been

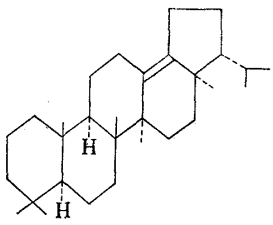
5) P. Sengupta and H. N. Khastgir : Tetrahedron, **19**, 123 (1963).
6) F. N. Lahey, M. V. Leeding : Proc. Chem. Soc. (London), **1958**, 342.
7) G. Eglinton, R. J. Hamilton, M. Martin-Smith, S. J. Smith, G. Subramanian : Tetrahedron Letters, **1964**, 2323.
8) Ref. 4, p. 188.
9) H. Vorbrüggen, S. C. Pakrashi, C. Djerassi : Ann. **668**, 57 (1963).

shown in the oleanane series (13β,14α-methyl) that the sign is positive when the C_{18}-H is β but is negative when the C_{18}-H is α.[9]

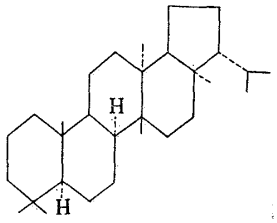
Since the mass spectra of arborene (XIX), davallic acid derivatives (Table I), and fernene (XXI)[10] were all characterized by a characteristic base peak at M-167, the Wolff-Kishner reduction of davallal (Ⅶ) was carried out at Stanford University[11] in connection with structural studies of these closely related substances, and it was found that the hydrocarbon (XXI) derived from davallal was identical with fernene (m.p., VPC, IR).[11] The exact nature of ring E in arborinol (XX) still remains to be established,[9] but fernene was subsequently converted[10] to hopene-Ⅱ (XXⅡ)[12] by being refluxed for 20 hours in acetic acid/hydrochloric acid. This correlation established that fernene and davallic acid both had the unique rearranged hopane skeleton. Davallic acid had already been shown to have the 9(11)-ene structure (*vide supra*), and moreover, results of the lead tetraacetate decarboxylation and mass fragmentations (*vide infra*) could only be accounted for by placing the oxygen function of davallic acid at C_4. Structures of fernene and davallic acid were thus elucidated simultaneously.*[3,10]



XIX : R=H_2
XX : R=α-H,β-OH



XXII



XXIII

TABLE I. Cracking Pattern of Davallic Acid Derivatives

	R	M^+	M-15	M-R	M-(R+15+H)	a	b (M-167)	c
Ⅱ or Ⅷ	COOMe	454 (20)	439 (70)	395 (5)	379 (5)	301 (15)	**287**	275 (10)
Ⅳ	CH_2OH	426 (15)	411 (50)	395 (2)	—	273 (15)	**259**	247 (15)
Ⅶ	CHO	424 (10)	409 (40)	395 (25)	379 (5)	271 (15)	**257**	245 (15)
XXI	CH_3	410 (15)	395 (60)		379 (10)	257 (25)	**243**	231 (20)

Intensities relative to base peak at M-167(b) are enclosed in parentheses.

The typical fragmentations of davallic acid derivatives are summarized in Table I (see also Figs. 3a and 3b). They are characterized by a strong M-15 peak due to loss of the C_{17}-methyl group[13] and a base peak at M-167. Evidently, the cation of largest abundance retains the oxygen function because the change in base peaks for compounds (Ⅱ, Ⅳ, Ⅶ, Ⅷ and XXI) parallels the change in the nature of the oxygen function. The m/e (M-167) peak, as already mentioned, constitutes the base peak of arborene that carries a 9(11)-double bond and has been assigned[9,14] to the cleavage indicated in Figs.

10) H. Ageta, K. Iwata, S. Natori : Tetrahedron Letters, **1963**, 1447.
11) D. Vorbrüggen : private communication (1963).
12) G. V. Baddeley, T. G. Halsall, E. R. H. Jones : J. Chem. Soc., **1961**, 3891.
13) C. Djerassi, H. Budzikiewicz and J. M. Wilson : Tetrahedron Letters, **1962**, 263.
14) H. Budzikiewicz, J. M. Wilson, C. Djerassi : J. Am. Chem. Soc., **85**, 3688 (1963); H. Budzikiewicz, C. Djerassi, D. H. Williams : "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. 2, 130 (1964). Holden-Day, San Francisco.

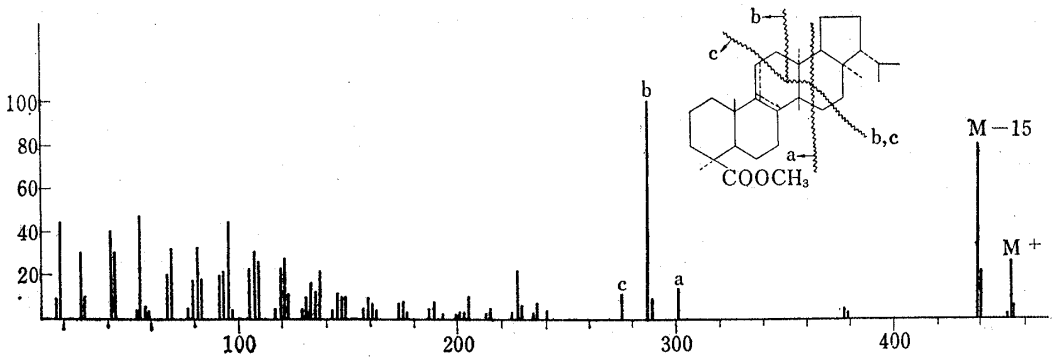


Fig. 3a. Mass Spectrum of Me-(iso)davallate II (or VIII)

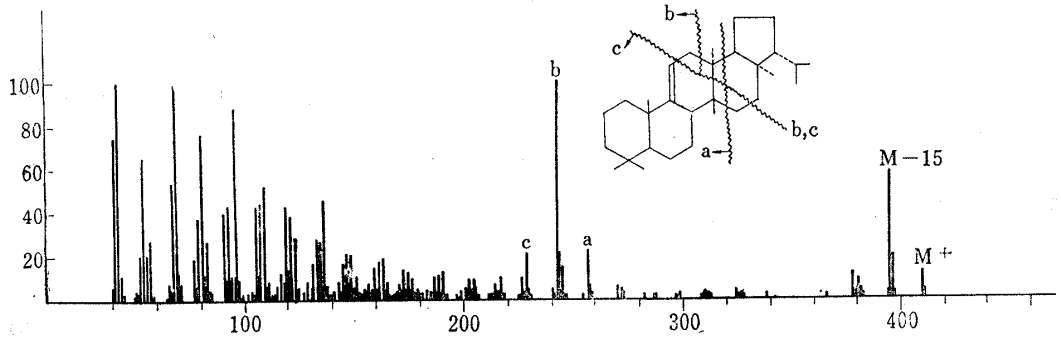


Fig. 3b. Mass Spectrum of Fernene (XXI)

3a and 3b; arundoin,[7] another 9(11)-ene triterpenoid, is also characterized by this intensive M-167 peak.

The mass spectra of methyl davallate (II) and methyl isodavallate-I (VIII) were superimposable, thus indicating a shift of the 9(11)-double bond to 8, 9 (or *vice versa*) had occurred.

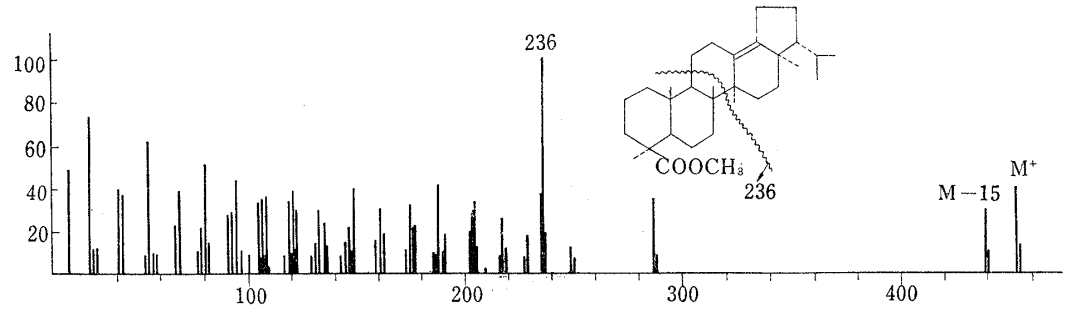


Fig. 4a. Mass Spectrum of Methyl Isodavallate-II (IX)

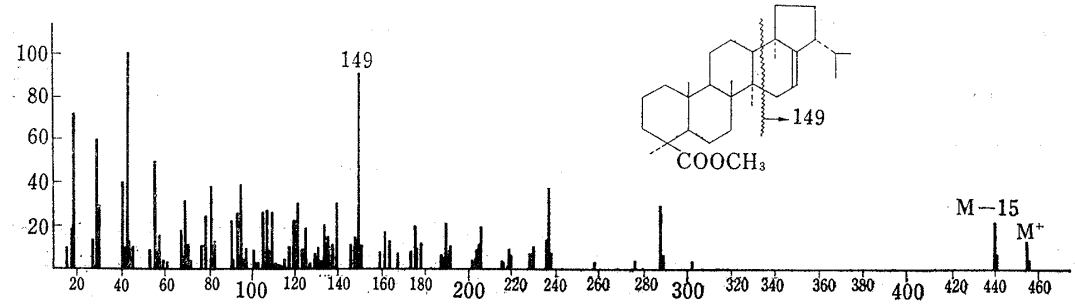


Fig. 4b. Mass Spectrum of Methyl Isodavallate-III (X)

Formation of isomer-II (IX) is similar to the euphenol-isoeuphenol rearrangement. The base peak at m/e 236 (*i.e.*, M-218) in the mass spectrum of this isomer is assigned to the cleavage shown in Fig. 4a. The m/e 236 peak presumably arises from a rearrangement of the double bond to C_{12} upon bombardment followed by allylic cleavage; the fragment containing rings D and E are seen at m/e 218.

Because only a small amount of isomer-III (X) was available, no chemical studies could be carried out. However, the broad nuclear magnetic resonance peak at 5.20 p.p.m., and especially the mass spectrum (Fig. 4b) indicated the double bond had migrated to the 16,17-position with concomitant 1,2-shifts of the angular hydrogens and methyl groups (retro-Diels-Alder cleavage).[14]

These transformations of davallic acid into isomers-I, -II and -III necessitate 8α/14β/13α/18β/17α configurations at ring junctures as shown in structures (I) and (Ia) (Fig. 5). Ring B is fixed in a boat conformation and this accounts for the facile rearrangement of davallic acid to the C_8-ene isomer having a half-chair ring B. The carboxyl group is assigned a β-axial configuration in view of the pK_{MCS} of isodavallic acid-I (VIII) at 8.60*[4] (calcd. for a- and e-COOH, respectively, 8.41 and 7.91),[15] the doublet[16] at 1147 and 1160 cm^{-1} in the infrared spectrum (CCl_4) of methyl davallate, and the chemical shift of the $-CH_2OAc$ quartet centered at δ^{CCl_4} 4.05[17] in the nuclear magnetic resonance spectrum of davallyl acetate (V).

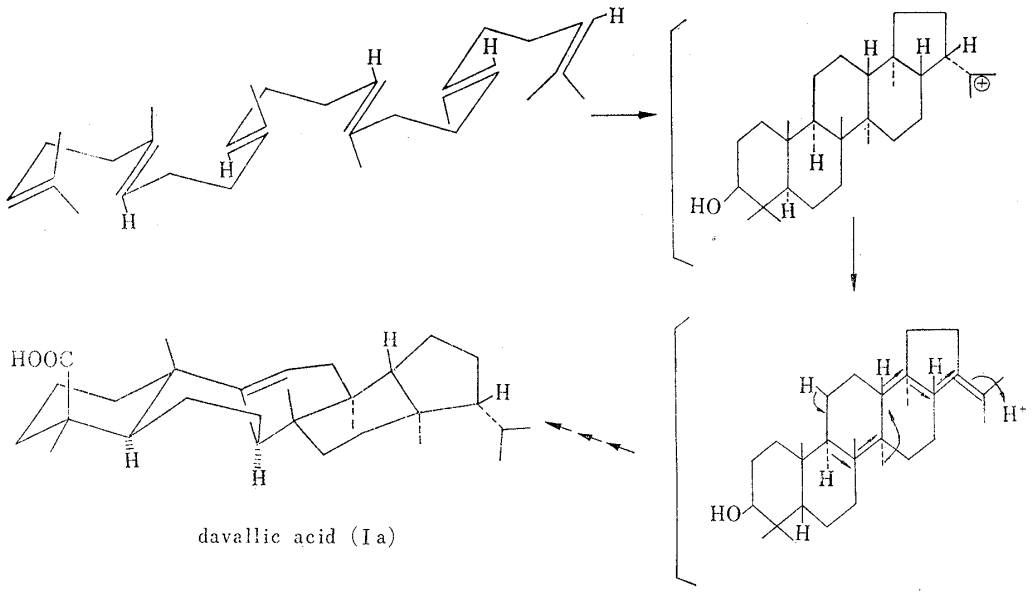


Fig. 5.

The structure of davallic acid has recently been confirmed by X-ray crystallographic studies carried out on the iodoacetate of davallol (XXIV).[18]

Davallic acid*[3] with the unique C_4-carboxyl group and fernene[10] belong biogenetically to the rearranged hopane group of triterpenes (Fig. 5), and the name fernane has been proposed*[3,10] for the corresponding saturated hydrocarbon (XXIII). It is interesting that

*[4] Davallic acid itself was not soluble enough for pK measurements.

15) C. P. Pascual, W. Simon : Helv. Chim. Acta, **47**, 683 (1964).

16) Equatorial and axial COOMe groups of terpenes can be differentiated by their IR absorptions at 1245 and 1155 cm^{-1} (sometimes doublet), respectively : S. Bory, M. Fetizon : Bull. Soc. Chim. Fr., **1964**, 570.

17) A. Gandemer, M. J. Polonsky, E. Wenkert : *Ibid.*, **1964**, 407.

18) Private communication from Dr. E. N. Maslen, University of Western Australia, Perth.

triterpenoids with skeletons of a more advanced rearrangement state have since been isolated from ferns and characterized, *e.g.*, adianene (5,6-ene),[19] filicene (3,4-ene),[19] adiantoxide (3,4-epoxide).[20]

Experimental

The NMR spectra were measured with Varian A-60 and HR-100 models using tetramethylsilane as internal reference. Measurements with the latter instrument were kindly carried out by Dr. N. S. Bhacca, Varian Associates. The mass spectra were measured with CEC 21-1030 (Stanford University) and Hitachi RMU-6D instruments. The ORD curves were taken with a self-recording JASCO ORD/UV-5 spectropolarimeter.

Extraction——Rhizomes of the Chinese fern (2 kg.), *Davallia divaricata Blume* ("kutzuipo" in Chinese; "takasagoshinobu" in Japanese) collected in the middle and southern parts of Formosa were extracted by refluxing in ethyl alcohol (17 L.) for 2 hr., each extraction being repeated thrice. The combined extracts were allowed to stand overnight, the deposited wax removed, and the filtrate was concentrated *in vacuo* to about 1.5 L. The solution was again allowed to stand overnight, and the deposited material was recrystallized from acetone to give davallic acid (30 mg.), m.p. 283°; ν_{max}^{KBr} 1700 cm^{-1}; $[\alpha]_D$ +94.2°. *Anal.* Calcd. for $C_{30}H_{48}O_2$: C, 81.76; H, 10.98. Found: C, 82.11; H, 10.49.

Methyl Davallate (II)——An ethereal solution of davallic acid (200 mg.) was treated with an excess of ethereal diazomethane and the mixture was allowed to stand overnight. Removal of the solvent and recrystallization from acetone-benzene gave needles, m.p. 231~232°; ν_{max}^{KBr} 1740 cm^{-1}; λ_{max}^{EtOH} 207 mμ (ε 5100). *Anal.* Calcd. for $C_{31}H_{50}O_2$: C, 81.88; H, 11.08. Found: C, 82.45; H, 11.23.

Acetic Davallic Anhydride (III)——Davallic acid (300 mg.) in pyridine (2 ml.) and acetic anhydride (1 ml.) was refluxed for 15 min. After cooling the solution was poured into water, and the precipitate was recrystallized from acetic anhydride to give III, m.p. 226° (decomp.); ν_{max}^{KBr} cm^{-1}: 1815, 1740. *Anal.* Calcd. for $C_{32}H_{50}O_3$: C, 79.62; H, 10.44. Found: C, 79.89; H, 10.44.

Davallol (IV)——The ester (II, 300 mg.) in absolute ether (10 ml.) was refluxed with 10 ml. of ethereal lithium aluminum hydride solution for 2 hr. About 2 ml. of acetone was added to the mixture, the precipitated aluminum hydroxide was dissolved by addition of 10% sulfuric acid, and the mixture was extracted with ether. The ether solution was washed with sodium bicarbonate solution and water, dried, the solvent was removed, and the residue was recrystallized from ethanol to afford IV (250 mg.), m.p. 169~170°; $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300, 1030. *Anal.* Calcd. fof $C_{30}H_{50}O$: C, 84.44; H, 11.81. Found: C, 84.25; H, 12.03.

Davallyl Acetate (V)——Davallol (100 mg.) was dissolved in a 1:1 mixture of pyridine-acetyl anhydride (2 ml.). The mixture was refluxed for 2 hr., poured into water, and the white solid was recrystallized from ethanol to give the acetate, m.p. 191°; $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750, 1250, 1045. *Anal.* Calcd. for $C_{32}H_{52}O_2$: C, 81.99; H, 11.18. Found: C, 81.96; H, 11.20.

Davallyl Tosylate (VI)——Davallol (240 mg.) and *p*-toluenesulfonyl chloride (200 mg.) in a 1:1 mixture of benzene-pyridine (4 ml.) was refluxed for 5 hr. The reaction mixture was extracted with ether, and washed with dilute H_2SO_4, NaOH, and water. Recrystallization from acetone gave VI, m.p. 196~197°. Yield, 85%. *Anal.* Calcd. for $C_{37}H_{56}O_3S$: C, 76.50; H, 9.71. Found: C, 76.30; H, 9.56.

Reaction of Davallyl Tosylate (VI) with Sodium Iodide——The tosylate (180 mg.) and 160 mg. of freshly molten sodium iodide in 5 ml. of dry acetone (6 ml.) were placed in a sealed tube, and the tube was heated overnight on an oil bath at 160°. The reaction mixture was extracted with ether, then washed with sodium bisulfite solution. Removal of the solvent gave a brown oil, which upon recrystallization from acetone gave crystals identical with the starting material.

Davallal (VII)——Davallol (240 mg.) in anhydrous pyridine (5 ml.) was added to a chromic acid-pyridine complex solution, which was prepared by adding 0.6 g. of chromic anhydride to 10 ml. of pyridine at 15~20° with stirring. The mixture was allowed to stand overnight, then poured into water and extracted with ether. Recrystallization from acetone gave 150 mg. of VII, m.p. 149°; ν_{max}^{KBr} cm^{-1}: 2710, 1725; M^+ (molecular peak), 424.

Isomerization of Davallic Acid with Acid——Davallic acid (1 g.) was dissolved in 50 ml. of boiling acetic acid, and after adding concentrated hydrochloric acid until saturation, the mixture was refluxed for 14 hr. Concentration of the reaction mixture yielded isodavallic acid-I, which was then methylated with ethereal diazomethane in the usual manner. Recrystallization of the product from ethyl acetate gave methyl isodavallate-I (VIII, 800 mg.), m.p. 230°, ν_{max}^{KBr} 1740 cm^{-1}, λ_{max}^{EtOH} 207 mμ (ε 5500). *Anal.* Calcd. for $C_{31}H_{50}O_2$: C, 81.88; H, 11.08. Found: C, 81.84; H, 11.09. Concentration of the mother liquor gave crystals which were recrystallized from ethyl acetate and then from acetone-chloroform to afford methyl

19) H. Ageta, K. Iwata, S. Natori: Tetrahedron Letters, **1964**, 3413.
20) G. Berti, F. Bottari, A. Marsilli: *Ibid.*, **1964**, 1.

isodavallate-II (IX), m.p. 215°, ν_{max}^{KBr} 1740 cm^{-1}, M^+ (molecular peak) 454. Further concentration of the mother liquor and several recrystallizations from ethanol yielded methyl isodavallate-III (X), m.p. 165°, ν_{max}^{KBr} 1740 cm^{-1}, M^+ (molecular peak) 454. The yields of isomers -II anp-III were extremely poor and in several cases none of the third isomer could be isolated.

Enone (XI)——Methyl davallate (170 mg.) in 10 ml. of boiling acetic acid was treated dropwise with 150 mg. of chromic anhydride in 5 ml. of glacial acetic acid from the top of the condenser. The oxidant was rapidly consumed to give a green solution. After addition of the oxidant had been completed, the mixture was poured into boiling water with vigorous stirring, and the white solid was recrystallized from methanol when the enone (XI) was obtained, m.p. 252°; ν_{max}^{KBr} cm^{-1}: 1740, 1680, 1605; λ_{max}^{EtOH} 246 mμ (ε9500). *Anal.* Calcd. for $C_{31}H_{48}O_3$: C, 79.43; H, 10.32. Found: C, 81.56; H, 10.47.

Enedione (XII) and Diene (XIII)——Methylisodavallate-I (900 mg.) was dissolved in glacial acetic acid and a solution of chromic acid (400 mg.) in 5 ml. of acetic acid was added dropwise from the top of the condenser. The mixture was refluxed for a further 20 min., and then worked up in the usual manner. Recrystallization from methanol gave crude crystals, which were chromatographed on alumina, and eluted successively with ether, benzene, chloroform, and ethyl acetate. The fraction eluted with ether was taken to dryness and the residue was recrystallized from methanol-chloroform to afford the *trans*-diene (XIII), 300 mg., m.p. 207~208°; ν_{max}^{KBr} 1740 cm^{-1}; λ_{max}^{EtOH} mμ (ε): 233 (2100), 240 (2400), 249 (1400) (the low ε-value is due to a contaminant as indicated by VPC). The benzene, chloroform and ethyl acetate fractions gave a mixture of the diene and pale yellow crystals, which upon recrystallizattion from methanol gave the endione (XII), 100 mg., yellow needles, m.p. 211°, ν_{max}^{KBr} cm^{-1}: 1740, 1680, 1615; λ_{max}^{EtOH} 271 mμ (ε 7500). Formation of the diene (XIII) seems to be favored by the presence of slight amount of impurities contained in the acetic acid. Usage of pure acetic acid, which when boiled with chromic acid consumed none of the oxidant, gave the enedione (XII) as the sole product. Yield 38%. *Anal.* Calcd. for $C_{31}H_{46}O_4$ (XII): C, 77.13; H, 9.61. Found: C, 77.15; H, 9.34.

Oxidation of the Enedione (XII) with Selenium Dioxide——The enedione (XII) (220 mg.) in a 1:1 mixture of acetic acid-acetic anhydride (20 ml.) was refluxed with selenium dioxide (250 mg.) for 3.5 hr. The precipitate was filtered and the filtrate was poured into water to give an orange solid. The small amount of red selenium remaining in the solid was removed by boiling in methanol with freshly precipitated silver. Recrystallization from methanol gave the dienetrione (XIV, 120 mg.), m.p. 231°; ν_{max}^{KBr} cm^{-1}: 1740, 1700, 1660, 1620; λ_{max}^{EtOH} mμ (ε): 215 (7500), 283 (7800). *Anal.* Calcd. for $C_{31}H_{42}O_5$: C, 75.27; H, 8.56. Found: C, 75.92; H, 8.74.

Oxidation of the Dienetrione (XIV) with Hydrogen Peroxide——The dienetrione (XIV, 150 mg.) in dioxane (8 ml.) was treated with 3 ml. of 10% potassium hydroxide solution, and the mixture was kept at 60° on a water bath. To this there was added 1.5 ml. of a 30% hydrogen peroxide solution. After 15 min. the color of the solution began to fade, and became almost colorless in 30 min. An additional 1 ml. of hydrogen peroxide was added, the mixture was refluxed for another 30 min. and was then poured into water. The water solution was extracted with ether, and the ether layer was washed with 5% aqueous potassium hydroxide solution. The alkaline solutions were combined, acidified with hydrochloric acid, and the acid solution was extracted with ether and treated as usual to give 80 mg. of a white solid. The solid, after recrystallization from benzene-ethyl acetate gave the secodicarboxylic acid (XV), m.p. 230°; ν_{max}^{KBr} cm^{-1}: 1740, 1700, 1690, 1630; λ_{max}^{EtOH} 252 mμ (ε 8800). *Anal.* Calcd. for $C_{31}H_{44}O_7$: C, 70.43; H, 8.39. Found: C, 70.87; H, 7.89.

Acetoxynordiene (XVI) and Nortriene (XVII)——A mixture of davallic acid (700 mg.) and lead tetraacetate (3 g.) in 200 ml. of dry benzene was refluxed for 14 hr. under nitrogen. The reaction mixture was poured into an aqueous ferrous sulfate solution, extracted with ether, and the ether layer was washed successively with water, sodium carbonate and water. After removal of the solvent under reduced pressure an oil was obtained, which was chromatographed on alumina, and eluted with hexane. The first and second fractions (30 ml. each), after recrystallization from acetone, gave the nortriene (XVII), m.p. 187°, 95.5 mg., λ_{max}^{EtOH} mμ (ε): 234 (9700), 241 (10700), 249 (7300). *Anal.* Calcd. for $C_{29}H_{44}$: C, 88.70; H, 11.30. Found: C, 88.29; H, 11.34. Fractions No. 3 to No. 8, after recrystallization from ethanol, gave the acetoxynordiene (XVI), m.p. 207~208°, 46.2 mg., ν_{max}^{KBr} 1740 cm^{-1}, λ_{max}^{EtOH} end absorption. *Anal.* Calcd. for $C_{31}H_{48}O_2$: C, 82.24; H, 10.69. Found: C, 81.97; H, 11.12.

Treatment of the Acetoxynordiene (XVI) and the Nortriene (XVII) with Dry Hydrogen Chloride——The diene (XVI) and triene (XVII) (50 mg. each), respectively, were dissolved in chloroform and dry hydrogen chloride was bubbled into the solutions for 30 min. at room temperature. The solvent was evaporated and the residue was recrystallized from ethanol when a minute amount of a product exhibiting the same IR and UV absorptions was obtained from both starting materials, m.p. 176°, λ_{max}^{EtOH} mμ (ε): 239 (2500), 246 (2600), 254 (1700).

Davallyl iodoacetate (XXIV)——Davallol (100 mg.) dissolved in a mixture of 20 ml. of benzene and 0.5 ml. of chloroacetyl chloride (prepared by heating monochloroacetic acid with benzoyl chloride) was refluxed for 5 hr. After addition of water to the reaction mixture, it was extracted with ether, and the ether extract was worked up as usual. Recrystallization from ethanol gave davallyl chloroacetate, plates, m.p.

164~166°. The chloroacetate (70 mg.) and finely divided potassium iodide (1 g.) were refluxed for 4 hr. in 20 ml. of acetone. Recrystallization of the product from ethanol gave davallyl iodoacetate, needles, m.p. 175~176° (50 mg.). *Anal.* Calcd. for $C_{32}H_{51}O_2I$: C, 64.63; H, 8.65. Found: C, 64.37; H, 8.69.

Bromination of the Enone (XI)——To a boiling solution of 30 mg. of the $\alpha\beta$-unsaturated ketone (XI) in 2 ml. of glacial acetic acid was added 2 drops of bromine in 1 ml. of acetic acid. No absorption of bromine occurred. The starting material was recovered after refluxing the mixture for 2 hr, and allowing it to stand overnight.

The mass spectra were measured at Stanford University and some at Hitachi Co., Naka Laboratories. The authors are grateful to Professor C. Djerassi and Dr. H. Vorbrüggen for discussions and identification of davallene. The studies were carried out in close contact with the studies of fernene,[10] and we acknowledge this close cooperation.

Summary

The structure of davallic acid has been established as shown by I on the basis of chemical reactions and various physico-chemical data. The structure has received support from independent studies.

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131. Hideo Seki, Kenji Koga,*1 Hisayuki Matsuo,*1,*2 Sadao Ohki,*3 Ichiro Matsuo,*4 and Shun-ichi Yamada*1: Studies on Optically Active Amino Acids. V*5. Synthesis of Optically Active α-Aminoalcohols by the Reduction of α-Amino Acid Esters with Sodium Borohydride.

(*Faculty of Pharmaceutical Sciences, University of Tokyo,*1 *Tokyo College of Pharmacy*3 *and Medical School, Self Defence Force*4)

It is generally accepted that sodium borohydride, a useful reducing agent for aldehydes and ketones, does not reduce carboxylic esters and orthoesters. This facts were shown by many instances in the literatures reported by Brown,[1] Chaikin[2], and other many researchers.[3] However, there are some "abnormal" cases[4~7] in which reduction of ester groups to the corresponding primary alcohols has been observed, especially in the field of sugar chemistry. Wolfrom, *et al.*[5] reported that sugar esters and lactones were reduced by sodium borohydride and other instances[6] were given in this region.

*1 Hongo, Tokyo, Japan (関 英男, 古賀憲司, 松尾寿之, 山田俊一).
*2 Present address: Rikagaku kenkyusho, the Institute of the Physical and Chemical Research, Komagome, Bunkyo-ku, Tokyo.
*3 Uenosakuragi-cho, Taito-ku, Tokyo (大木貞雄).
*4 Ikeshiri-cho, Setagaya-ku, Tokyo (松尾市郎).
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