Summary

The structure of meteogenin, isolated from the rhizome of *Metanarthecium luteoviride* Maxim., was shown to be 1-methyl-19-nor-25D-spirosta-1,3,5(10)-trien-11α-ol (IIa). The relationship between luvigenin (I) and meteogenin (IIa) was established, and at the same time it was proved that the direction of the dienol-benzene rearrangement varied according to the presence of the double bond at C_6 or of the C_{11}-ketone.

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117. Kikuo Igarashi: Studies on the Steroidal Components of Domestic Plants. XXXVI.[1] Structure of Meteogenin. (2). On Meteogenone.

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As described in the preceding paper,[1] the structure of meteogenin, isolated from the rhizome of *Metanarthecium luteoviride* Maxim., was established as 1-methyl-19-nor-25D-spirosta-1,3,5(10)-trien-11α-ol (I). The interesting properties of meteogenone (II) are the subject of the present paper.

When meteogenone (II), obtained from meteogenin (I) by oxidation with chromium trioxide and pyridine,[1] was reduced with lithium aluminium hydride, a new hydroxy compound (IIIa), m.p. 185~187°, $[\alpha]_D^{17}$ +67.1°, and meteogenin were obtained in the ratio of 3:1. (IIIa) gave the acetate (IIIb), m.p. 184~186°, $[\alpha]_D^{17}$ +42.2°, afforded meteogenone by the oxidation with chromium trioxide and pyridine. These facts indicate that meteogenone (II) possesses the same skeleton as meteogenin (I) and that the new hydroxy compound is the 11β-hydroxy epimer of meteogenin (I), named epimeteogenin (IIIa).

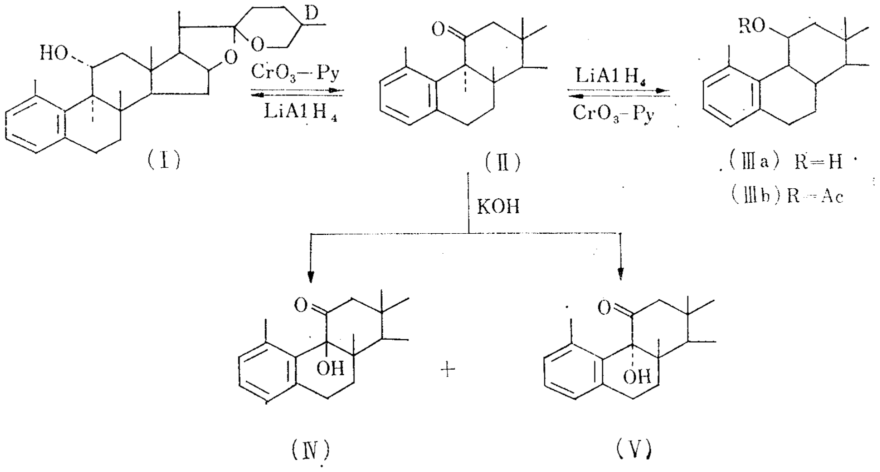

Chart 1.

[*1] Fukushima-ku, Osaka (五十嵐喜九男).

[1] Part XXXV. K. Igarashi: This Bulletin, **9**, 722 (1961).

In the field of stereochemistry, it is now known that in compounds such as meteogenone, having an aromatized ring A and C_{11}-ketone, the B/C *cis*-fused compound is of an order of stability similar to that of the *trans*-fused compound.[2,3] This situation is in marked contrast to that encountered in tne case of steroids with the normal saturated ring A, where the equilibrium is greatly in favour of the B/C *trans*-fused form.

From this point of view the isomerization of meteogenone (II) with alkali was attempted. When meteogenone was refluxed for 2 hours in 1% ethanolic potassium hydroxide solution, an isomer of the ketone was not obtained but two kinds of ketols were isolated in a good yield. The ketols were separated by fractional crystallization from acetone. The more soluble ketol (IV) showed m.p. 231~232°, $[\alpha]_D^{25}$ −75.2° and the less soluble ketol (V), m.p. 273~275°, $[\alpha]_D^{17}$ +165.7°. Neither ketol afforded the acetate even by refluxing with acetic anhydride and pyridine, and from this result the newly introduced hydroxyl groups were assumed to be tertiary. Based upon the structure of meteogenone the position of the hydroxyl groups is assumed to be C_9 and two ketols are considered to be the epimers at C_9.

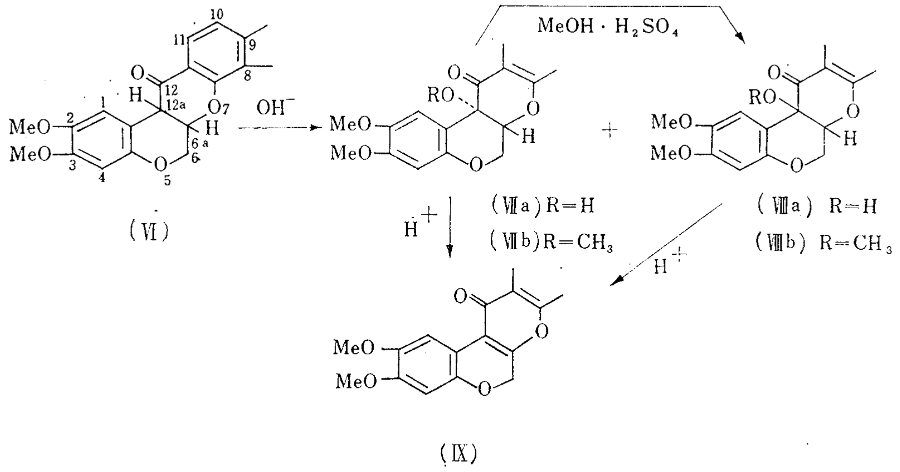

Chart 2.

On the other hand, a similar reaction can be seen in the case of the rotenone series (VI). Takei, *et al.*[4] and LaForge[5] reported that the compound of the rotenone series afforded two kinds of ketols, (VIIa) and (VIIIa), in alkaline solution by air-oxidation and that both ketols were dehydrated easily with acid to the same anhydro compound (IX). Recently, Crombie, *et al.*[3,6] reported that the newly introduced hydroxyl groups were at $C_{12\alpha}$ in (VI), the conformations of which were also proved from the infrared spectra, and

Table I.

	m.p.	$[\alpha]_D$	IR (cm^{-1})		UV mμ (log ε)
			max. (OH)	max. (Keton)	max.
(II)	177~178°	+180.5° (23°)		1721[a]	291 (1.57)
(IV)	231~232°	− 75.2° (25°)	3518	1706[b]	293 (1.91)
(V)	273~275°	+165.7° (17°)	3620	1722[b]	301 (1.90)

a) in CS_2 solution, 0.25 mm. cell
b) in CCl_4 solution, 20 mm. cell

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2) J. Elks, J.F. Oughton, L. Stephenson : Proc. Chem. Soc., **1959**, 6.
3) G. Büchi, J.S. Kaltenbronn, L. Crombic, P.J. Godin, D.A. Whiting : *Ibid.*, **1960**, 274.
4) S. Takei, S. Miyajima, M. Ono : Ber., **66**, 479 (1933).
5) F.B. La Forge, H.L. Haller : J. Am. Chem. Soc., **56**, 1620 (1934).
6) L. Crombie, P.J. Godin : Proc. Chem. Soc., **1960**, 276.

that the methyl ether of ketol (VIIIb) (B/C *trans*) was converted to the isomeric methyl ether of ketol (VIIIb) (B/C *cis*) by treatment with methanolic acid for a short period.

The physical constants of these ketols (IV) and (V) are shown in Table I. In the infrared spectra in diluted carbon tetrachloride solution, the hydroxyl group in the ketol (IV) is strongly intramolecularly bonded to the keto group but this is not the case in the ketol (V). In ultraviolet spectra the carbonyl band of the ketol (IV) did not exhibit a notable shift from that of the parent ketone (meteogenone), whereas that of the ketol (V) showed a marked shift toward longer wave length. From these results it seemed probable that the hydroxyl group of the ketol (IV) is equatorial and that of the ketol (V) is axial. Furthermore, the rotation values also supported this assumption.

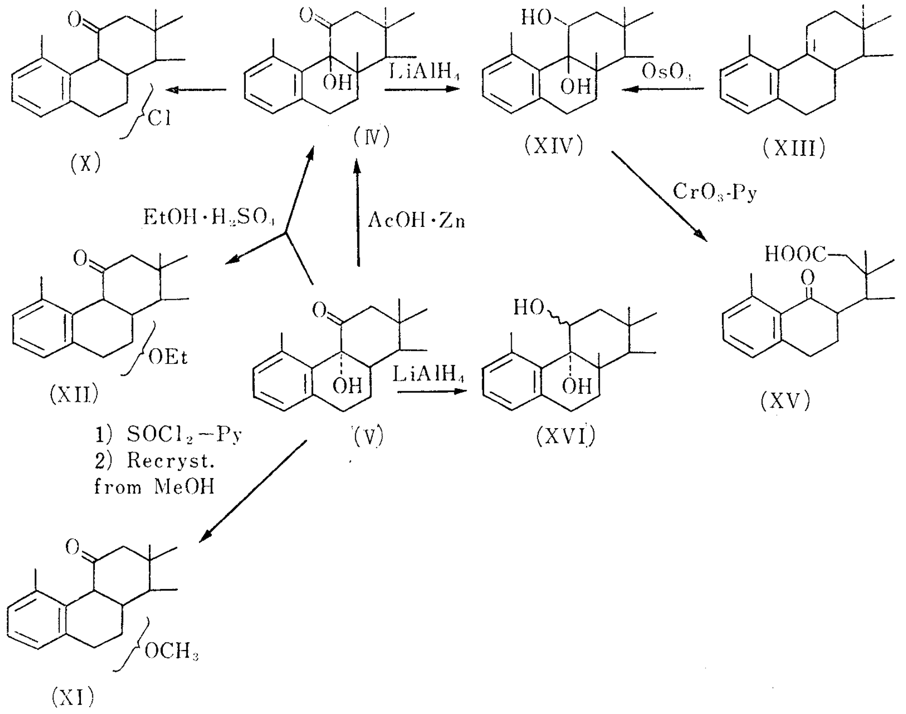

Chart 3.

Next, dehydration reaction of ketols, (IV) and (V), was attempted, but contrary to expectation the anhydro derivatives could not be obtained. Both ketols were recovered unchanged on treatment with phosphoryl chloride and pyridine at room temperature overnight. When treated with thionyl chloride and pyridine, ketol (IV) afforded a chloroketone (X), m.p. 214~215° (decomp.), $[\alpha]_D^{18}$ +42.3°, whereas ketol (V) gave a compound $C_{28}H_{38}O_4$, m.p. 204~206°, $[\alpha]_D^{17}$ +197.5°, after repeated recrystallization of the chlorine containing reaction product from methanol. The infrared spectrum showed that this is a methoxyketone (XI), and the initially produced chloroketone showed to have been converted to the methyl ether during recrystallization from methanol. Throughout these experiments the anhydro derivative was not isolated. When (X) was refluxed with silver nitrate in pyridine only a colored resin was obtained. The chloroketone (X) and the methoxyketone (XI) could not be examined further because of the small quantities.

The dehydration of the ketols, (IV) and (V), with 10% ethanolic sulfuric acid was effected under similar conditions used in the rotenone series. Ketol (IV) was refluxed for 3 hours in 10% ethanolic sulfuric acid but only the starting material was recovered. Ketol (V) was treated in a similar manner and the product was chromatographed, whereby (XII), m.p. 147~149°, was obtained in 20% yield. This was assumed to be an ethoxyketone (XII) from the analytical values as well as from the infrared spectrum, but no further examination was made. In addition another product, m.p. 231~232°, was obtained in 50% yield, which was shown to be identical with the ketol (IV) by mixed melting point determination and by direct comparison of each infrared spectrum.

The reason why the ketols, (IV) and (V), were resistant to the dehydration reactions is not clear. A similar phenomenon that the ketol (V) (B/C *trans*) was converted to the ketol (IV) (B/C *cis*) was also encountered in the case of the methyl ethers of rotenone series.

In the tertiary hydroxyl elimination of α-ketol (IV) with zinc and acetic acid,[7] the unchanged starting material was recovered, while in the case of the ketol (V) the ketol (IV) was obtained in 40% yield. In both cases the expected ketone was not isolated. These isomerisations are also related to the stability of the B/C *cis* juncture in the ketol (IV).

In order to confirm synthetically the position of the hydroxyl groups of the ketols, (IV) and (V), the following experiments were carried out. Anhydrometeogenin (XIII) prepared from meteogenin as described in the preceding paper,[1] was oxidized with osmium tetroxide and the product was chromatogrphed on alumina to give a diol (XIV), showing a double melting point at 117° and 187~189°, $[\alpha]^{19}_{D}$ $-145.5°$, in 50% yield. The diol (XIV) was oxidized with chromium trioxide and pyridine but only a small amount of a compound, m.p. 150~156°, was obtained. This could not be purified further because of the small quantity, but from the infrared spectrum this seemed to be a keto-acid (XV). Oxidation of the ketol (IV) with chromium trioxide and pyridine was also unsuccessful and only the starting material was recovered.

When the ketol (IV) was reduced with lithium aluminium hydride, a diol, double m.p. 117°/186~189°, $[\alpha]^{13}_{D}$$-150.1°$, was obtained as the sole product in a good yield. This diol was shown to be identical with the authentic sample of the diol (XIV) by mixed melting point and by direct comparison of each infrared spectrum. From this experiment, the hydroxyl group of the ketol (IV) was confirmed to be located at C_9 and the configuration of the diol (XIV) was also proved to be $9\beta,11\beta$-diol. It is an interesting fact that osmium tetroxide attacked the double bond of (XIII) from the β-side of the molecule but the reason has not yet been made clear. Based upon the above findings the hydroxyl group of the ketol (V) at C_9 is unambiguous.

When the ketol (V) was reduced with lithium aluminium hydride, a diol (XVI), m.p. 245~247°, $[\alpha]^{13}_{D}$ $+52.7°$, was obtained as a main product. The configuration of this diol was assumed to be $9\alpha,11\beta$-diol[8] but no further examination was made. Thus, meteogenone (II) did not afford C_9-epimeteogenone with alkali.

On the other hand, Stephenson, *et al.*[2] found that 1-methyl-3,17α,21-trihydroxy-19-norpregna-1,3,5(10)-triene-11,20-dione 3,17α,21-triacetate (XVIIa) afforded the 11-enol acetate (XVIII), and when (XVIII) was saponified and reacetylated, the C_9-epi-11-ketone (XIX) was obtained as a major product together with a small amount of (XVIIb). According to

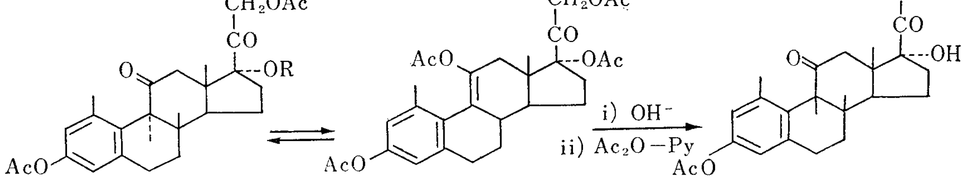

Chart 2

(XVIIa) R=Ac
(XVIIb) R=H

(XVIII)

(XIX)

Chart 4.

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[7] R. S. Rosenfeld: J. Am. Chem. Soc., **79**, 5540 (1957).
[8] R. Littell, S. Bernstein: *Ibid.*, **78**, 985 (1956).

their reports, the enol acetylation of meteogenone was attempted. However, the expected enol acetate was not isolated because the cleavage of ring F of meteogenone proceeded faster than the enol acetylation of the ketone.

Experimental[*2]

Reduction of Meteogenone (II) with $LiAlH_4$——A solution of 500 mg. of meteogenone, m.p. 177~178°, dissolved in 5 cc. of dehyd. tetrahydrofuran and 10 cc. of dehyd. Et_2O was added under ice-cooling and with stirring to a suspension of 250 mg. of $LiAlH_4$ in 30 cc. of dehyd. Et_2O. The mixture was stirred at room temperature for 30 min., refluxed gently for 1.5 hr. and cooled with ice. After decomposition of excess $LiAlH_4$ by adding 5 cc. of AcOEt, 10 cc. of H_2O was added and the produced precipitate was dissolved by adding dil. HCl. The solution was extracted with $CHCl_3$ and the $CHCl_3$ solutian was washed with H_2O, dried and evaporated. The residue was chromatographed on 15 g. of Al_2O_3. The product (358 mg.) eluted with petr. ether-benzene (6:4~4:6) was crystallized from MeOH to give 253 mg. of rods, m.p. 170~180°. Recrystallization from the same solvent gave the pure sample (IIIa), m.p. 185~187°, $[\alpha]_D^{17}$ +67.1°±2.5° (c=1.065). *Anal.* Calcd. for $C_{27}H_{38}O_3$: C, 78.98; H, 9.33. Found: C, 79.09; H, 9.42. IR $\lambda_{max}^{CS_2}$ cm^{-1} : 3610 (OH), 3080 (╒), 772, 740 (benzene). UV λ_{max} mμ (log ε) : 205.5 (4.34), 217 (shoulder), 267 (2.41), 272 (2.31).

(IIIa) was refluxed with Ac_2O and pyridine for 3 hr. and the product was crystallized from MeOH to give the acetate (IIIb) as plates, m.p. 184~186°, $[\alpha]_D^{17}$ +42.2°±2° (c=1.028). *Anal.* Calcd. for $C_{29}H_{40}O_4$: C, 76.95; H, 8.91. Found : C, 76.93; H, 8.85. IR $\lambda_{max}^{CS_2}$ cm^{-1} : 1738 (acetate), 771, 750 (benzene).

Then the product (126 mg.) eluted with petr. ether-benzene (3:7~1:9), benzene and benzene-Et_2O (9:1) was crystallized from MeOH to give 78 mg. of prisms, m.p. 150~154°. Recrystallization from the same solvent gave the pure sample, m.p. 157~158°, which was shown to be identical with the authentic sample of meteogenin (I) by mixed melting point determination and by direct comparison of each infrared spectrum. The acetate was also identical with meteogenin acetate.

Conversion of Epimeteogenin (IIIa) to Meteogenone (II)——Epimeteogenin (IIIa) was oxidized with CrO_3 and pyridine overnight at room temperature in the usual manner and the product was crystallized from MeOH to give prisms, m.p. 177~178°, which were identical with the authentic sample of meteogenone by mixed melting point determination and by direct comparison of each infrared spectrum.

Alkaline Oxygenation of Meteogenone (II)——A solution of 600 mg. of meteogenone dissolved in 60 cc. of dehyd. EtOH containing 600 mg. of KOH was refluxed for 2 hr. After cooling, dry-ice was saturated, the solution was poured into H_2O and the product was extracted with $CHCl_3$. The $CHCl_3$ solution was washed with H_2O, dried, and evaporated. The residue was crystallized from MeOH to give 492 mg. of crystals, m.p. 221~240°. They were treated with ca. 20 cc. of hot Me_2CO, acetone-insoluble crystals were collected and the filtrate was concentrated until crystallization began. After crystallization was complete, crystals were collected and combined with acetone-insoluble crystals and recrystallized from CH_2Cl_2-Me_2CO to yield 122 mg. of prisms (V), m.p. 273~275°, $[\alpha]_D^{17}$ +165.7°±2° (c=1.111). *Anal.* Calcd. for $C_{27}H_{36}O_4$: C, 76.38; H, 8.55. Found : C, 76.56; H, 8.80. IR λ_{max}^{Nujol} cm^{-1} : 3560 (OH), 1724 (ketone). $\lambda_{max}^{CCl_4}$ (in 20 mm. cell) cm^{-1} : 3620 (OH), 1722 (ketone). UV λ_{max} mμ (log ε) : 269 (2.62), 277 (2.59), 301 (1.91).

The above Me_2CO filtrate was concentrated and cooled at 0°, whereby 202 mg. of needles, m.p. 215~222°, were obtained. Recrystallization from MeOH gave the pure sample (IV), m.p. 231~232°, $[\alpha]_D^{25}$ −75.2°±3° (c=0.565). *Anal.* Calcd. for $C_{27}H_{36}O_4$: C, 76.38; H, 8.55. Found : C, 76.66; H, 8.75. IR λ_{max}^{Nujol} cm^{-1} : 3514 (OH), 1700 (ketone). $\lambda_{max}^{CCl_4}$ (in 20 mm. cell) cm^{-1} : 3518 (OH), 1706 (ketone). UV λ_{max} mμ (log ε) : 269 (2.69), 277 (2.70), 293 (1.93).

Both ketols were refluxed with Ac_2O and pyridine for 2 hr. but only the starting materials were recovered.

Attempts of Dehydration of Ketols, (IV) and (V)

a) With $POCl_3$ and Pyridine——i) To a solution of 30 mg. of ketol (IV) in 3 cc. of pyridine, 0.3 cc. of $POCl_3$ was added dropwise with stirring and under ice-cooling. The solution was allowed to stand at room temperature overnight and poured into ice-water, and the product was extracted with $CHCl_3$. The $CHCl_3$ solution was washed with H_2O, dil. HCl, H_2O, dil. $NaHCO_3$ and H_2O successively, dried and evaporated. Only the starting material was recovered.

[*2] All melting points were measured with the H. Bock, Monoscop IV (Frankfurt/M) and are uncorrected. Infrared spectra were measured with the Nihon Bunko Infrared Spectrophotometer, Model DS-301. Ultraviolet spectra were measured with the Hitachi Recording Ultraviolet Spectrophotometer EPS-2 in 95% EtOH. Rotations were measured with the Rudolf Photoelectric Polarimeter, Model 200 in $CHCl_3$.

ii) Ketol (V) was treated similarly, but only the starting material was recovered.

b) With $SOCl_2$ and Pyridine——i) To a solution of 50 mg. of ketol (IV) in 2 cc. of pyridine, 0.1 cc. of $SOCl_2$ was added dropwise under ice-cooling and with stirring, and the solution was allowed to stand at room temperature for 1 hr. After treating in the usual manner recrystallization of the product from MeOH gave 20 mg. of needles (X), m.p. 214～215°(decomp.), $[\alpha]_D^{18}$ $+42.3°\pm4°(c=0.587)$. *Anal.* Calcd. for $C_{27}H_{35}O_3Cl$: C, 73.20; H, 7.96; Cl, 8.00. Found : C, 72.93, H, 8.26: Cl, 8.18. IR λ_{max}^{Nujol} cm^{-1} : 1722 (ketone), 1598, 1586 (benzene).

The infrared and ultraviolet spectra showed that the residue did not contain any α,β-unsaturated ketone.

To a solution of 20 mg. of chloroketone (X) in 1 cc. of pyridine, 70 mg. of $AgNO_3$ was added and the mixture was refluxed for 3 hr. on an oil bath. After cooling the mixture was poured into H_2O and the product was extracted with AcOEt. The AcOEt solution was washed with H_2O, dil. HCl and H_2O successively, dried and evaporated. The residue was purified by chromatography but only a colored resin was obtained.

ii) 30 mg. of ketol (V) was treated as above. Repeated recrystallization of the product from MeOH gave chlorine free crystals (10 mg.) (XI) as plates, m.p. 204～206°, $[\alpha]_D^{17}$ $+197.5°\pm2°(c=1.162)$. *Anal.* Calcd. for $C_{28}H_{38}O_4$: C, 76.67; H, 8.73; OCH_3, 7.08. Found : C, 76.63; H, 8.96; OCH_3, 7.20. IR λ_{max}^{Nujol} cm^{-1} : 1722 (ketone), 1589 (benzene).

The residue gave positive Beilstein's test but the infrared and ultraviolet spectra showed that it did not contain the unsaturated ketone.

c) With 10% EtOH-H_2SO_4——i) A solution of 30 mg. of ketol (IV) in 5 cc. of 10% EtOH-H_2SO_4 was refluxed for 3 hr., but only the starting material was recovered.

ii) 50 mg. of ketol (V) was treated as above and the product was chromatographed on 2 g. of Al_2O_3. The product eluted with petr. ether-benzene (6:4) was crystallized from 70% EtOH to give 7 mg. of needles (XII), m.p. 147～149.°. *Anal.* Calcd. for $C_{29}H_{40}O_4$: C, 76.95; H, 8.91. Found : C, 76.68; H, 8.91. IR λ_{max}^{Nujol} 1713 cm^{-1}(ketone). Then the product eluted with petr. ether-benzene and benzene-ether (9:1～8:2) was crystallized from MeOH to give 18 mg. of needles, m.p. 231～232°, which were identical with the authentic sample of ketol (IV) by mixed melting point determination and by comparison of each infrared spectrum.

Reaction of Ketols, (IV) and (V) with Zn-AcOH——i) To a solution of 46 mg. of ketol (IV) in 25 cc. of glacial AcOH 2.8 g. of Zn dust was added and the mixture was refluxed. After 10 hr. a further of 2.2 g. Zn dust was added and the mixture was refluxed for a further 14 hr. Zn was removed and the filtrate was evaporated *in vacuo* to dryness. Only the starting material was recovered.

ii) 65 mg. of ketol (V) was treated as above. Recrystallization of the product from MeOH gave 20 mg. of needles, m.p. 230～232°, which were identical with ketol (IV). The mother liquor was chromatographed on Al_2O_3. The product (27 mg.) eluted with petr. ether-benzene (5:5～1:9) and benzene was crystallized from acetone, whereupon 7 mg. of ketol (IV) and 5 mg. of the starting material were obtained.

OsO_4 Oxidation of Anhydrometeogenin (XIII)——To a solution of 132 mg. of anhydrometeogenin (XIII) (amorphous), dissolved in 5 cc. of dehyd. benzene and 0.2 cc. of pyridine, 130 mg. of OsO_4 was added and the solution was allowed to stand at room temperature for 96 hr. The precipitated osmate was dissolved by addition of 20 cc. of dry. dioxane and the solution was saturated with H_2S in order to decompose the osmate. The produced precipitate was removed and the filtrate was evaporated *in vacuo* to dryness. The residue was dissolved in hot MeOH and the MeOH solution was treated with Norit and evaporated. The residue was chromatographed on 4 g. of neutral Al_2O_3. The product eluted with benzene and benzene-Et_2O (9:1～6:4) was crystallized from petr. ether to give 63 mg. of plates, m.p. 105～117°. When this crude substance was recrystallized from MeOH the pure (XIV) showed double melting point, 117°/187～189°, $[\alpha]_D^{12}$ $-143.0°\pm2°(c=1.044)$. *Anal.* Calcd. for $C_{27}H_{38}O_4$: C, 76.02; H, 8.98. Found : C, 76.15; H, 9.08. IR λ_{max}^{Nujol} cm^{-1} : 3522, 3290 (OH), 1594, 1581 (benzene).

Oxidation of Diol (XIV) with CrO_3-Pyridine——A solution of 19 mg. of diol (XIV) in 0.2 cc. of pyridine was added under ice-cooling and with stirring to a mixture of 1 cc. of pyridine and 10 mg. of CrO_3, and the mixture was allowed to stand at room temperature overnight. After treating in the usual manner the product was chromatographed on 1 g. of Al_2O_3. The product (7 mg.) eluted with petr. ether-benzene, benzene and benzene-$CHCl_3$ was not crystallized. The product (5 mg.) eluted with $CHCl_3$-AcOH (9:1) was crystallized from MeOH to give 2 mg. of plates, m.p. 150～156°. This could not be purified further. IR λ_{max}^{Nujol} cm^{-1} : 3300～2600 (COOH), 1705 (COOH), 1680, 1630, 1595 (aromatic ketone).

Oxidation of Ketol (IV) with CrO_3-Pyridine——Ketol (IV) was oxidized with CrO_3-pyridine as above but only the starting material was recovered.

Reduction of Ketol (IV) with $LiAlH_4$——To a suspension of 30 mg. of $LiAlH_4$ in 5 cc. of dehyd. Et_2O, was added dropwise under ice-cooling and with stirring a solution of 45 mg. of ketol (IV) in 5 cc. of dehyd. tetrahydrofuran, and the mixture was refluxed gently for 3 hr. After working up in the usual manner recrystallization of the product from MeOH yielded 36 mg. of plates, double m.p. 117°/186~189°, $[\alpha]_D^{13}$ $-150.1° \pm 2°$ (c=1.583), which were identical with the authentic sample of the diol (XIV) by mixed melting point determination and by direct comparison of each infrared spectrum.

When ketol (IV) was refluxed in MeOH with $NaBH_4$ for 5 hr., reduction did not proceed and only the starting material was recovered.

Reduction of Ketol (V) with $LiAlH_4$——37 mg. of ketol (V) was reduced with $LiAlH_4$ as above. Recrystallization of the product from MeOH gave 18 mg. of diol (XVI) as prisms, m.p. 245~247°, $[\alpha]_D^{13}$ $+52.7° \pm 2°$ (c=1.294). *Anal.* Calcd. for $C_{27}H_{38}O_4$: C, 76.02; H, 8.98. Found: C, 75.88; H, 9.13. IR λ_{max}^{Nujol} cm^{-1}: 3588 (OH), 1597, 1590 (benzene). The second crop (8 mg.), m.p. 229~240° also gave identical infrared spectrum with the diol (XVI).

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Summary

When meteogenone (II) was refluxed in diluted alkaline solution, two kinds of ketols, (IV) and (V), in place of C_9-epimeteogenone were obtained in a good yield. The newly introduced hydroxyl groups were synthetically confirmed to be located at C_9 and the conformations of those groups were also established from the infrared and ultraviolet spectra as well as from the rotation values.

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118. Kyosuke Tsuda, Toshinobu Asai, Yoshihiro Sato, Tokuji Tanaka und Hiroko Hasegawa: Untersuchungen auf dem Gebiet der mikrobiologischen Umsetzung. XI.[1] Hydroxylierung von Progesteron in der 7α-, 7β-, 14α-, 15α- oder 15β-Stellung durch *Helminthosporium sativum*.

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In einer früheren Mitteilung[2] berichteten wir über die Hydroxylierung in 15α-Stellung von Reichsteins Substanz S durch *Helminthosporium sativum* PAMMEL, KING et BAKKE. Inzwischen wurden die Studien über die Umsetzung von Progesteron mit diesen Mikroben fortgeführt. Im folgenden seien die Ergebnisse kurz zusammengefasst.

Bei der Inkubation von Progesteron (Pregn-4-en-3,20-dion) (I) mit *H. sativum* isolierten wir mittels der mit Silikagel durchgeführten Chromatographie zwei Monohydroxy- und drei Dihydroxy-Derivate des Progesterons. Das Monohydroxy-progesteron vom Schmp. 228~230° und das vom Schmp. 202~204.5° waren mit dem bekannten 15α-Hydroxy-(II),[3,4]

[*1] Yayoi-cho, Bunkyo-ku, Tokio (津田恭介, 朝井勇宣, 佐藤良博, 田中篤治, 長谷川弘子).

1) X. Mitt. K. Tsuda, T. Asai, Y. Sato, T. Tanaka, T. Matsuhisa, H. Hasegawa: Dieses Bulletin, **8**, 626 (1960).

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