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61. Ken'ichi Takeda, Tameto Okanishi, Hiroshi Ōsaka, Ariyoshi Shimaoka, and Norihide Maezono : Studies on the Steroidal Components of Domestic Plants. XXX.*1 Structure of Nogiragenin, a New Sapogenin isolated from *Metanarthecium luteo-viride* MAXIM.

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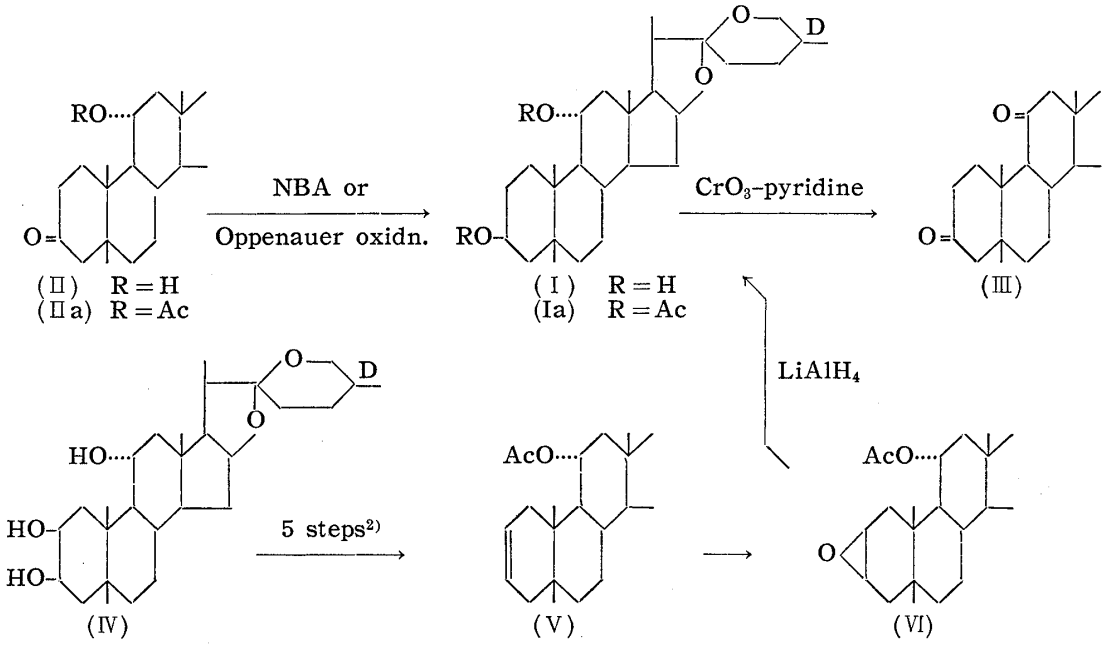
A new 11-oxygenated steroidal sapogenin was further isolated from *Metanarthecium luteo-viride* MAXIM. in addition to metagenin (IV).[1] This sapogenin, named nogiragenin, belongs to the 25D-series and is a dihydroxyspirostane. The origin of the name, nogiragenin, comes from the Japanese name for this plant, "Nogiran."

This new sapogenin was obtained from the benzene-chloroform (1:1) fraction before the metagenin fraction (chloroform-methanol) by chromatography on alumina (see experimental part). Nogiragenin (I) melts at 201°, $[\alpha]_D^{23}$ −70.6° (chloroform), and gives a diacetate (Ia), m.p. 209°. N-Bromoacetamide or the Oppenauer oxidation of this sapogenin afforded a monoketone derivative (II), m.p. 249°, $[\alpha]_D^{23}$ −66.3° (chloroform), and monoacetate (IIa), m.p. 214°, while chromium trioxide-pyridine oxidation of nogiragenin gave a diketone (III), m.p. 208°. These two monoketone and diketone derivatives are identical in all respects with the corresponding 11α-hydroxy-5β,25D-spirostan-3-one (II) and 3,11-dione (III), respectively. As the 11α-hydroxy-3-oxo- and 3,11-dioxo-spirostanes were already synthesized from hecogenin,[1,2] the position of each hydroxyl group in this sapogenin is deduced as C-3 and C-11, respectively.

Since the structure of metagenin is 2β,3β,11α-triol[1] (IV), the most probable structure of nogiragenin is considered to be 3β,11α-diol. From this assumption the synthesis of nogiragenin from metagenin was attempted by the following route.



*1 Part XXIX : Ann. Repts. Shionogi Research Lab., Vol. 10, 153 (1960).
*2 Imafuku, Amagasaki, Hyogo-ken (武田健一, 岡西為人, 大坂 弘, 島岡有昌, 前園憲英).
1) K. Takeda, K. Hamamoto : Tetrahedron Letters, No. 3, 1 (1960).
2) The detail of (1) : This Bulletin, **9**, 32 (1961).

Perbenzoic acid oxidation of Δ^2-metagenin (V),[1] which was obtained from metagenin by the method of Djerassi[3b] as reported earlier,[1] afforded the 2β,3β-epoxide (VI), m.p. 224°, $[\alpha]_D^{22}$ −93.6°(chloroform). The configuration of the epoxide ring was assumed to be β, according to the report of Djerassi, *et al.*[3] Lithium aluminium hydride reduction of this β-epoxide gave the anticipated nogiragenin in a fair yield. Thus, the structure of nogiragenin is confirmed as 5β,25D-3β,11α-dihydroxyspirostane and therefore, metagenin is 2β-hydroxynogiragenin.

Experimental*3

Nogiragenin (5β,25D-Spirostane-3β,11α-diol) (I) and its Diacetate (Ia) from Plant Sources——Dried and powdered subterranean parts (15 kg.) of "Nogiran," which were collected in the neighborhood of the Rokuhara Farm in Iwate Prefecture in October, 1959, were treated in exactly the same manner as in the case of metagenin.[1] The residue (51 g.), obtained from 90% MeOH extract by acidic and alkaline saponification followed by $CHCl_3$ extraction, was chromatographed on alumina, the eluates with benzene-$CHCl_3$ (4:1-1:1) and $CHCl_3$ were collected, and purified from petr. ether-$CHCl_3$ (1:1), yielding 1.4 g. of crude crystals, m.p. 190~193°. The m.p. was raised by further recrystallization from Et_2O or $CHCl_3$ to 200~201°, $[\alpha]_D^{23}$ −70.6°(c=0.984). This is easily soluble in EtOH, Me_2CO, benzene, and $CHCl_3$, but hardly soluble in petr. ether. Liebermann and CCl_3·COOH tests are positive. IR ν_{max}^{Nujol} cm^{-1} : 876, 890, 918, 978; 890>918(25D); 3514(OH). *Anal.* Calcd. for $C_{27}H_{44}O_4$ (Nogiragenin, I) : C, 74.95; H, 10.25. Found : C, 74.72; H, 10,18.

The above diol (50 mg.) was acetylated wtih 1 cc. of Ac_2O on a water bath for 1 hr. and treated in the usual manner, yielding 31 mg. of nogiragenin diacetate (Ia), m.p. 208~209°, $[\alpha]_D^{23}$ −73.8°(c=0.968). IR ν_{max}^{Nujol} cm^{-1} : 860, 895, 924, 977; 895>924(25D); 1245, 1733(AcO). *Anal.* Calcd. for $C_{31}H_{48}O_6$: C, 72.06; H, 9.36. Found : C, 72.12; H, 9.49.

The eluate with $CHCl_3$-MeOH (4:1-1:1) furnished 2.05 g. of metagenin (IV), m.p. 270°, which were proved to be identical with the sample by a mixed m.p. and IR comparison.

11α-Hydroxy-5β,25D-spirostan-3-one(II)——a) Oxidation of Diol (I) with N-Bromoacetamide(NBA): To a solution of 100 mg. of nogiragenin (I) in 1.2 cc. of pyridine and 8 cc. of *tert*-BuOH a solution of 80 mg. of NBA in 2 cc. of water and 8 cc. of *tert*-BuOH was added and the mixture was left for 44 hr. at room temperature. The reaction mixture was treated with 40 cc. of 10% Na_2SO_3 solution and evaporated to dryness to leave a white crystalline product. Extraction with Et_2O-benzene (1:1) mixture followed by evaporation of the solvent yielded 95 mg. of crystalline powder, m.p. 240~242°, which was chromatographed on alumina. The eluates with benzene and benzene-Et_2O (1:1) furnished 82 mg. of needles, m.p. 247~249°, $[\alpha]_D^{23}$ −66.3°(c=1.042). IR ν_{max}^{Nujol} cm^{-1} : 1697(CO), 3556(OH). This showed no depression of mixed m.p. with the sample synthesized from hecogenin.[2] *Anal.* Calcd. for $C_{27}H_{42}O_4$: C, 75.31; H, 9.83. Found : C, 75.41; H, 9.92.

b) Oppenauer Oxidation from (I) : To a solution of 100 mg. of nogiragenin (I) in 2.5 cc. of toluene, 100 mg. of Al(iso-PrO)$_3$ in 1 cc. of cyclohexane and 0.4 cc. of toluene was added and the mixture was refluxed for 45 min. Extraction with Et_2O, followed by washing with 20 cc. of 5% HCl and water, and evaporation of Et_2O furnished 123 mg. of oily residue, which was recrystallized from Me_2CO-petr. ether to 66 mg. of the 3-ketone (II), m.p. 243~245°. Identification was established by admixture.

11α-Acetoxy-5β,25D-spirostan-3-one (IIa)——The above 11α-ol (II) (62 mg.) was left to stand with 0.5 cc. of Ac_2O and 1 cc. of pyridine overnight and treated in the usual manner. The crude product (60 mg.) was chromatographed on alumina and the eluate with petr. ether-benzene (1:1) yielded 52 mg. of crystals, m.p. 208~209°, which were recrystallized from $CHCl_3$-hexane to needles, m.p. 211~214°, $[\alpha]_D^{20}$ −63.8°(c=0.528). IR ν_{max}^{Nujol} cm^{-1} : 1244, 1725(C=O and AcO). This showed no depression of mixed m.p. with the sample synthesized from hecogenin.[2] *Anal.* Calcd. for $C_{29}H_{44}O_5$: C, 73.69; H, 9.36. Found : C, 73.91; H, 9.33.

5β,25D-Spirostane-3,11-dione (III)——To a solution of 200 mg. of nogiragenin (I) in 4 cc. of pyridine, 200 mg. of CrO_3 in 2 cc. of pyridine was added and left for 24 hr. at room temperature. The precipitate formed by dilution with water was collectd, washed with water, and dissolved in a mixture of $CHCl_3$-Et_2O (1:1). The organic solvent layer was washed with 10% H_2SO_4, 5% NaOH, and water, and evaporated to leave 167 mg. of crude crystals, m.p. 199~207°. This product was chromato-

*3 All melting points are uncorrected. Rotations were measured in $CHCl_3$ solution.

3) *a*) C. Djerassi, J. Fishman, J. A. Moore : Chem. & Ind. (London), **1954**, 1320; *b*) C. Djerassi, J. Fishman : J. Am. Chem. Soc., **77**, 4291 (1955).

graphed on alumina and the eluate with benzene-Et_2O (1:9) yielded 133 mg. of crystals, m.p. 207~208° (from $CHCl_3$-petr. ether). IR ν_{max}^{Nujol} cm^{-1} : 1710 (C=O). Identification with the sample from hecogenin was established by admixture and IR spectral comparison. *Anal.* Calcd. for $C_{27}H_{40}O_4$: C, 75.66; H, 9.41. Found : C, 75.32; H, 9.49.

2β,3β-Epoxy-5β,25D-spirostan-11α-ol Acetate (VI)——To a solution of 500 mg. of 5β,25D-spirost-2-en-11α-ol acetate[2] (V) in 50 cc. of $CHCl_3$, 10 cc. of $CHCl_3$, solution of perbenzoic acid (46.7 mg./cc.) was added, cooling with ice, and left for 24 hr. at room temperature. The reaction mixture was poured into 200 cc. of Et_2O and the Et_2O layer was washed successively with 5% NaI, 5% $Na_2S_2O_3$, 5% $NaHCO_3$, and water. Evaporation of the solvent furnished 551 mg. of crude crystals, which were recrystallized from $CHCl_3$-petr. ether to needles, m.p. 222~224°, $[\alpha]_D^{22}$ −93.6° (c=0.993). IR ν_{max}^{Nujol} cm^{-1}: 1246, 1725 (AcO), 815 (epoxide). *Anal.* Calcd. for $C_{29}H_{44}O_5$: C, 73.69; H, 9.38. Found : C, 73.55; H, 9.28.

$LiAlH_4$ Reduction of 2β,3β-Epoxy-5β,25D-spirostan-11α-ol Acetate (VI)——A solution of 300 mg. of the above epoxide (VI) in 30 cc. of Et_2O was refluxed with 300 mg. of $LiAlH_4$ for 4 hr. The reaction mixture was treated with 10% Na_2SO_4 solution, acidified with 10% H_2SO_4, and extracted with Et_2O. The Et_2O layer was washed, dried, and evaporated to yield 304 mg. of crude crystals, which were purified from $CHCl_3$-hexane to the diol (I), m.p. 200~201°. This showed no depression with nogiragenin.

The above diol was refluxed with Ac_2O to give the diacetate, m.p. 208~209°, which proved to be identical with nogiragenin diacetate by mixed m.p. and IR comparison.

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Summary

A new 11-oxygenated sapogenin, nogiragenin, was isolated from *Metanarthecium luteoviride* Maxim. and the structure 5β,25D-spirostane-3β,11α-diol was assigned to it by its synthesis from metagenin via 2β,3β-epoxide.

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