0.97). Sugar, Rf 0.22 (glucose 0.22).

Summary

Gracillin, a new diosgenin glycoside which was present together with dioscin in the water-insoluble saponins obtained from the rhizome of *Dioscorea gracillima* Miq., was proved to be composed of one mole each of diosgenin and of L-rhamnose and two of D-glucose. It afforded two prosapogenins C and A on partial hydrolysis, both of which were isolated and proved to be trillin (diosgenin monoglucoside) and glucosidoglucoside, respectively. Two possible formulae (I) and (II) were proposed for gracillin.

(Received January 12, 1956)

---

23. Morizo Ishidate and Masahisa Yoshida: The Cleavage of Camphor Ring. IV. 5-Dehydrosantenic Acid.

(*Pharmaceutical Institute, Medical Faculty, University of Tokyo**)

In the previous paper[1] it was shown that *d-trans*-7-hydroxy-π-apocamphor (7-hydroxy-α-santenone)(I) is hardly existent as such and converts spontaneously under ring cleavage between C_1 and C_7 to 1-methyl-4-acetylcyclohexan-2-one (II), whereas *d-trans*-7-hydroxy-π-apoborneol actually exists. Since the various hydroxycamphors, viz. 3-, 4-, 5-, and 6-hydroxycamphor, are all fairly stable compounds, the unstable character of (I) seemed to be due to the particular electronic property of C_7 atom caused by the strain of bicyclopentanone ring.

Now, in order to confirm this assumption and to compare with the monocyclic derivative, preparation of 5-hydroxy-π-apocamphoric acid (5-hydroxy-*d*-santenic acid) (VIII)** was attempted.

The starting meterial, 5-amino-α-santenic acid (VII), was synthesized by the following process. Isoketopinic acid (III) was oxidized with selenium dioxide to the quinone (IV). 7-Carbamyl-*trans*-π-apocamphoquinone (V) was further oxidized with hydrogen peroxide in alkaline medium to the corresponding dicarboxylic acid (VI), which was then subjected to Hofmann degradation to give 5-amino-α-santenic acid (VII), as its hydrochloride of m.p. 247°. If isoketopinoyl amide (IX) was treated with selenium dioxide in acetic anhydride, 7-cyano-π-apocamphoquinone (X) was mainly produced.

Diazotization of 5-amino-α-santenic acid (VII) resulted in a nitrogen-free dicarboxylic acid, $C_9H_{12}O_4$, m.p. 181°. The acid readily consumed hydrogen bromide and its infrared absorption spectrum (Fig. 1 A) proved to have no hydroxyl group, but to exhibit characteristic bands[2] at 6.06~6.10 and 11.00~11.24 μ (>C=CH_2). This indicates that the acid should have a structure of dehydrosantenic acid.

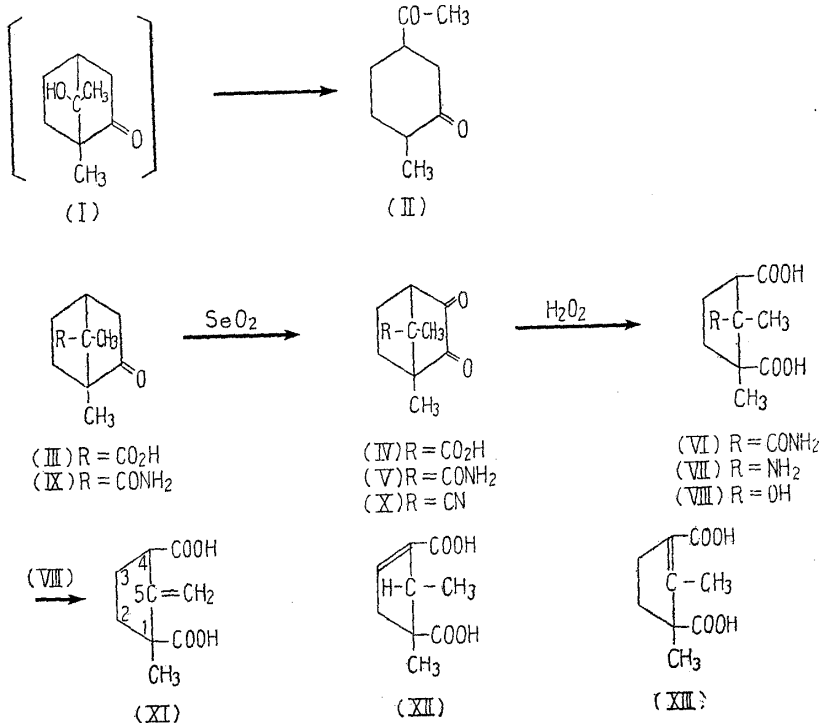
Among the possible dehydrosantenic acids, two optically inactive isomers, 3-

* Hongo, Tokyo (石館守三, 吉田正久).

1) Parts I and II; M. Yoshida: This Bulletin, **3**, 215, 219(1955); Part III, M. Ishidate, M. Yoshida: *Ibid.*, **4**, 43(1956).

** *trans*-π-Apocamphor and *trans*-π-apocamphoric acid would be synonymous with α-santenone and α-santenic acid, respectively.

2) D. Barnard, *et al.*: J. Chem. Soc., **1950**, 915; L. Ruzicka, *et al.*: Helv. Chim. Acta, **32**, 2125 (1949).



dehydro- (XII), m.p. 170°,[3] and 4-dehydro-santenic acid (XIII), m.p. 198°,[4] are known. It has been shown that the catalytic reduction of the former and the reduction of the hydrobromide of the latter gave the same *dl*-santenic acid.

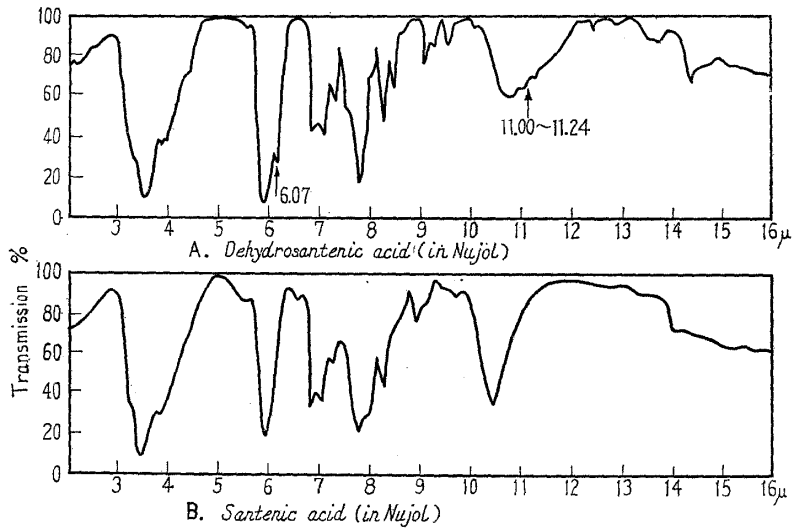


Fig. 1.

Infrared Spectra

The newly obtained dehydrosantenic acid was found highly resistant to the usual catalytic hydrogenation, even with Raney nickel catalyst at high pressure. On ozonolysis of the acid, formaldehyde was determined, but the expected ketone or keto-carboxyl compound could not be isolated, probably due to the unstability of the product, such as β-ketocarboxylic acid. Although the above result is short of definite evidence, it is highly probable that the acid of m.p. 181° possesses a structure of 5,6-dehydrosantenic acid (XI).

3) T. Enkvist : J. prakt. Chem., [2], **137**, 261(1933).
4) G. Komppa : Ber., **65**, 1708(1933).

Experimental

d-trans-π-**Carboxy-π-apocamphoquinone** (**IV**)[5]—A mixture of isoketopinic acid (III)(50 g.) and SeO_2 (50 g.) in 100 cc. of AcOH was refluxed for 20 hrs. The reaction mixture, after being separated from Se was concentrated. The yellow crystals obtained were dissolved in benzene and subjected to chromatography on alumina column. The column was eluted with acetone, the acetone solution was evaporated, and the solid so obtained was recrystallized from dil. EtOH to yellow prisms, m.p. 238~240°(reported[4] m.p. 230°). *Anal.* Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.53; H, 6.34.

d-trans-π-**Carbamyl-π-apocamphoquinone** (**V**)—To 50 g. of (IV) was added 100 cc. of $SOCl_2$ and heated for 3 hrs. Excess $SOCl_2$ was evaporated, the residue was dissolved in ether. The ether solution, after being washed with cold water and $NaHCO_3$ solution, was evaporated. The solid obtained was recrystallized from ether to yellow prisms, m.p. 139~140°, indentified as *d-π*-apocamphoquinone-7-carboxylic chloride. *Anal.* Calcd. for $C_{10}H_{11}O_3Cl$: C, 56.30; H, 5.20. Found: C, 55.94; H, 5.19. The chloride was dissolved in ether and treated with NH_4OH solution. The separated solid so obtained (17 g.), yellow prisms, m.p. 223~225°; $[\alpha]_D^{21°}$: +12.37°(in EtOH, c=3.2). *Anal.* Calcd. for $C_{10}H_{11}O_3N$: C, 60.08; H, 6.56; N, 7.18. Found: C, 60.51; H, 6.98; N, 7.24.

d-π-**Carbamyl-π-apocamphoric Acid** (**VI**)—To a solution of 10 g. of (V) in 100 cc. of 6% NaOH, 100 cc. of 5% H_2O_2 was added dropwise, forming a colorless solution. The solution was acidified with dil. H_2SO_4 and extracted with ether. The combined ether extracts was washed, dried, and evaporated to 7 g. of colorless crystals. Recrystallization from dil. EtOH gave a white plate crystals of m.p. 193~194° and $[\alpha]_D^{21}$: +8.3°(in EtOH, c=3.0). *Anal.* Calcd. for $C_{10}H_{15}O_5N$: C, 52.39; H, 6.60; N, 6.11. Found: C, 52.15; H, 6.42; N, 6.39.

d-**5-Amino-α-santenic Acid Hydrochloride** (**VII**)—To a solution of 11.2 g. of (VI) in 80 cc. of 10% NaOH was added NaOBr solution (prepared from 2.5 cc. of Br_2 and 70 cc. of 10% NaOH) under cooling, then heated at 70° for 0.5 hr. The reaction mixture was acidified with conc. HCl, and concentrated *in vacuo*. The separated crystalline residue was extracted with dehyd. EtOH. EtOH extract gave on addition of ether white needles, m.p. 246~247°, $[\alpha]_D^{21}$: +23.5°(in EtOH, c=3.0). *Anal.* Calcd. for $C_9H_{18}O_5NCl$: C, 42.27; H, 7.10; N, 5.48. Found: C, 42.17; H, 7.12, N, 5.58.

7-Cyano-*trans***-π-apocamphoquinone** (**X**)—A solution of 150 g. of isoketopinoyl amide in 300 cc. of Ac_2O was heated with 200 g. of SeO_2 at 140~150° for 8 hrs. The reaction mixture was worked up as described above for (IV). There were obtained yellow prisms, m.p. 200°(yield, 56 g.), $[\alpha]_D^{20}$: +46.4°(in EtOH, c=4.3), which were identified as (X). *Anal.* Calcd. for $C_{10}H_{11}O_2N$: C, 67.91; H, 6.26; N, 8.19. Found: C, 67.80; H, 6.30; N, 7.91,

The same compound was prepared from 7-cyano-*trans*-π-apocamphor [m.p. 181~182°; $[\alpha]_D^{20}$: +17.7°(in EtOH, c=3.2). *Anal.* Calcd. for $C_{10}H_{13}ON$: C, 73.59; H, 8.03. Found: C, 73.66; H, 8.05] and SeO_2.

5-Cyano-α-santenic Acid—Fifty grams of 7-cyano-*trans*-π-apocamphoquinone (X) was oxidized with H_2O_2 as described for (VI). The acid was obtained, after recrystallization from EtOH to colorless prisms, m.p. 205~206°; $[\alpha]_D^{16}$: +40.8°(in MeOH, c=6.5). *Anal.* Calcd. for $C_{10}H_{13}O$: C, 56.84; H, 6.20. Found: C, 56.49; H, 6.83.

5-Cyanosantenic Anhydride—Obtained from the above acid by treatment with AcCl. Colorless prisms (from petr. ether), m.p. 215°; $[\alpha]_D^{10.7}$: −6.81°(in EtOH, c=3.7). *Anal.* Calcd. for $C_{10}H_{11}O_3N$: C, 62.16; H, 5.74. Found: C, 62.51; H, 5.94.

5-Dehydrosantenic Acid (**XI**)—To a solution of 5 g. of 5-amino-α-santenic acid hydrochloride (VII) in 30 cc. of 5% HCl was added slowly 4.5 g. $NaNO_2$ under cooling. The reaction mixture was extracted with ether. The ether extract was dried and evaporated to dryness to yield 5 g. of syrup which crystallized on standing in a cool place. Recrystallization from dil. EtOH gave colorless plates, m.p. 180~181°; $[\alpha]_D^{21}$: +117°(in EtOH, c=1.7). *Anal.* Calcd. for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 59.08; H, 6.48. 0.090 g. consumed 9.33 cc. of 0.1*N* NaOH (Calcd. 9.76 cc.). This compound is insoluble in water and soluble in organic solvents. It gives negative Legal and $FeCl_3$ reaction, but it spontaneously decolorizes Br_2 in AcOH solution.

Catalytic Reduction of (**XI**)—Hydrogenation of (XI) with PtO_2, 10% Pd-C, or Raney-Ni as a catalyst failed, only to give the unchanged material.

Hydrogenation with Raney Ni at high pressure (150 atm.) in MeOH or aq. NaOH solution of (XI) gave a syrup which could not be purified further.

Ozonolysis—A solution of 0.92 g. of (XI) in 40 cc. $CHCl_3$:AcOEt (1:1) was treated with O_3 at −10°. The reaction mixture was then evaporated to remove the solvent and treated with water, and HCHO thereby produced was identified by chromotoropic acid test. The mother liquor was treated with semicarbazide but no ketone derivatives were found.

5) M. Ishidate, H. Kawahata, K. Nakasawa: J. Pharm. Soc. Japan, **62**, 11(1942).

Infrared Absorption Spectra—The infrared spectra of 5-dehydro-α-santenic acid and santenic acid are given in Fig. 1, A and B (Perkin-Elmer Model 21 double-beam). From Fig. 1 A, it seems most likely that the bands at 6.07 and 11.00~11.24 μ indicate the presence of $>C=C<^{H}_{H}$ and a band corresponding to hydroxyl group (2.77 or 3.03~3.15 μ) is not observed.

Summary

d-5-Amino-α-santenic acid was prepared from *d*-isoketopinic acid as the starting material. The diazotization of this produced a dehydrosantenic acid, the dehydration product of the expected 5-hydroxy-α-santenic acid. The structure of the unsaturated acid was assumed as 5-dehydrosantenic acid.

(Received January 12, 1956)

24. Shoji Shibata, Takao Murakami, Isao Kitagawa, and Teruo Kishi : Metabolic Products of Fungi. VIII.* Rugulosin. (1). The Structure of Dianhydrorugulosin and Its Relation to the Structure of Iridoskyrin.

(*Pharmaceutical Institute, Medical Faculty, University of Tokyo***)

In the previous paper,[1] we reported that radicalisin,[2] $C_{30}H_{22}O_{10}$, a yellow pigment isolated from the laboratory cultures of *Endothia parasitica*(Murr.) Anderson et Anderson and *E. fluens* Shear et Stevens (syn. *E. radicalis* Fr.), is identical with rugulosin which was isolated by Raistrick and his co-workers[3] from the cultures of *Penicillium rugulosum* Thom and *P. wortamanni* Klöcker grown on a Czapek-Dox solution.

The general properties of rugulosin and its derivatives were described in the papers by Raistrick[3] and by the present writers,[1,2] though the conclusive evidences for the chemical structure have not yet been elucidated. One of the noticeable reactions of rugulosin is the dehydration reaction that involves conversion of rugulosin, which is not an anthraquinone itself, into a compound having anthraquinone properties.

Breen, Dacre, Raistrick, and Smith[3] showed that on heating in conc. H_2SO_4, rugulosin, $C_{30}H_{22}O_{10}$, was converted into a compound m.p. 325°, with a molecular formula $C_{30}H_{18}O_8$, which was named aurantio-rugulosin and was suggested to be a homolog of iridoskyrin,[4] with two hydroxyls less. Iridoskyrin was derived from rubroskyrin[4] by an analogous reaction.

We have also obtained a dehydrated product of rugulosin, m.p. 321°, orange red crystals having a molecular formula $C_{30}H_{18}O_8$, in 60% yield by boiling in 95% formic acid or in 10% yield by boiling either in 55% H_2SO_4 or in glacial acetic acid. It was named dianhydrorugulosin and would be identical with aurantio-rugulosin though there are some discrepancies in the melting points of its derivatives.

* Part VII : This Bulletin, **3**, 286(1955).

** Hongo, Tokyo (柴田承二, 村上孝夫, 北川 勲, 貴志光雄).

1) S. Shibata, T. Murakami, O. Tanaka, G. Chihara, M. Sumimoto : This Bulletin, **3**, 274(1955).
2) S. Shibata, O. Tanaka, G. Chihara, H. Mitsuhashi : *Ibid.*, **1**, 302(1953).
3) J. Breen, J. C. Dacre, H. Raistrick, G. Smith : Biochem. J. (London), **60**, 618(1955).
4) B. H. Howard, H. Raistrick : *Ibid.*, **57**, 212(1954).