

**123. Hiroshi Mitsuhashi and Yuzuru Shimizu :** Studies on the Constituents of Asclepiadaceae Plants. III.<sup>1)</sup> The Structure of Cynanchogenin.\*<sup>2</sup>(2).

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Cynanchogenin ( $C_{28}H_{42}O_6$ ) from the root of *Cynanchum caudatum* MAX. (Asclepiadaceae), which is present as a form of glycoside containing D-cymarose<sup>3)</sup> and gives deacylcynanchogenin,  $C_{21}H_{32}O_5$ , and 3,4-dimethyl-2-pentenoic acid on alkaline hydrolysis,<sup>1)</sup> was submitted to selenium-dehydrogenation to clarify the carbon skeleton.

The reaction mixture of 1.8g. of cynanchogenin heated with 4g. of selenium in  $N_2$ -atmosphere at  $310^\circ$  for 24 hours was extracted exhaustively with ether and subsequent usual treatment gave 220 mg. of neutral portion and 6 mg. of phenolic portion. The neutral portion was chromatographed over neutral alumina to give two crystalline products. One of them (A), which shows very similar ultraviolet spectrum to that of benzo[a]fluorene,<sup>3)</sup> was rechromatographed over neutral alumina. The colorless plates, m.p.  $140\sim 147^\circ$ , eluted with hexane-benzene were recrystallized from methanol-acetone to fine plates, m.p.  $146\sim 150^\circ$ . This substance had quite the same ultraviolet spectrum as the hydrocarbon first gained by the dehydrogenation of veratramine and jervine by Jacobs, *et al.*,<sup>4)</sup> and the melting point also confirmed it.\*<sup>3</sup>

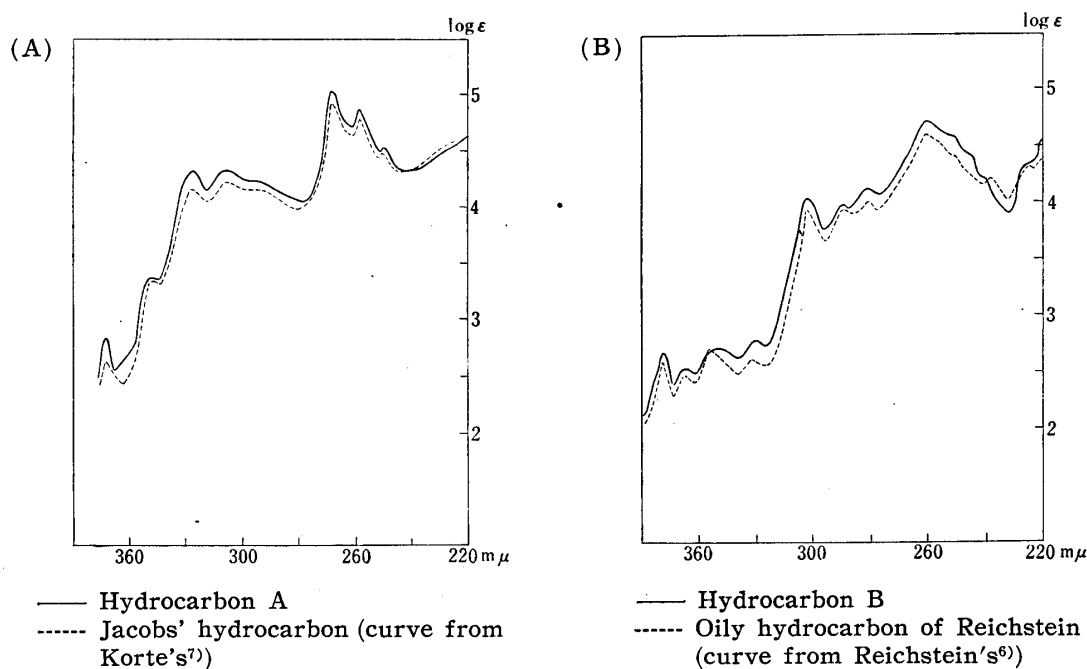


Fig. 1.

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\*<sup>2</sup> This work was reported at the 4th Hokkaido Local Meeting of the Pharmaceutical Society of Japan, September 26, 1959, and printed as a communication in this Bulletin, **6**, 749(1959).

\*<sup>3</sup> The melting point of Jacobs' hydrocarbon was given as a broad range (maximum  $155^\circ$ ).

1) Part II : This Bulletin, **8**, 318(1960).

2) Part I : *Ibid.*, **8**, 313(1960).

3) R. A. Friedel, M. Orchin : "Ultra-violet Spectra of Aromatic Compounds" (1951). John Wiley & Sons, New York.

4) W. A. Jacobs, C. C. Craig, G. LaVin : J. Biol. Chem., **141**, 51(1941); W. A. Jacobs, Y. Sato : *Ibid.*, **181**, 55(1949).

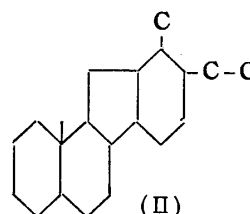
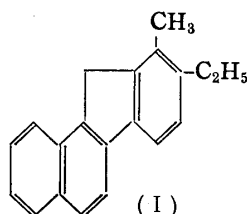
The structure of Jacobs' hydrocarbon had remained unknown, but was recently proved to be 7-ethyl-8-methylbenzo[*a*]fluorene (I) by synthesis.<sup>5)</sup>

The other crystal (B), which seems to be a mixture, gave very similar ultraviolet spectrum to that of oily hydrocarbon obtained from desisovaleryldrevogenin-A,  $C_{22}H_{36}O_6$ , which also gave Jacobs' hydrocarbon as the main dehydrogenation product and was assumed to have a hydrogenated benzo[*a*]fluorene skeleton.<sup>6)</sup>

Since angular methyl group is usually removed by dehydrogenation, the C-21 skeleton of deacylcynanchogenin seems to be c-nor-D-homopregnane (II), which might be formed by the bonding of C-12 to C-14 on ring closure. As a series of c-nor-D-homo-steroids exists in steroidal alkaloids, such a skeleton can also be expected in pregnane series.

Asclepiadaceae plants yield a series of ester glycosides containing 2-deoxymethyl-pentose. Reichstein, *et al.* assigned benzofluorene skeleton to drevogenin-A from *Dregea volubilis*<sup>6)</sup> and Korte, *et al.* also obtained Jacobs' hydrocarbon from condurangin from *Marsdenia condurango*.<sup>7,8)</sup>

In 1940, Cornforth, *et al.* isolated sarcostine,  $C_{21}H_{34}O_6$ , from *Sarcostemma australe*<sup>9)</sup> and gave normal steroid skeleton to it,<sup>10)</sup> but recently Reichstein, *et al.* suggested it has c-nor-D-homopregnane skeleton.<sup>10-12)</sup>



#### Experimental\*4

**Dehydrogenation of Cynanchogenin**—1.8 g. of cynanchogenin was well mixed with Se metal in a tube replaced with  $N_2$ -atmosphere, with a capillary terminal. The tube was heated at  $280\sim 290^\circ$  for 4 hr. and then at  $310^\circ$  for 20 hr. in a metal bath. After cool, the reaction mixture was powdered and extracted with ten 20-cc. portions of  $Et_2O$ . The  $Et_2O$  layer with fluorescence was washed with 40 cc. each of 10% HCl, 10% KOH, and water successively. After drying over  $Na_2SO_4$ , evaporation gave 220 mg. of oily residue, which showed very strong green fluorescence. The KOH extract gave 6 mg. of phenolic fraction, besides acid substance (3,4-dimethyl-2-pentenoic acid). Thorough examination was not made on the phenolic portion.

TABLE I. Adsorption Alumina Chromatography of the Neutral Portion

Fract. No.	Solvent	Eluate	
1~8	Hexane	trace	oil
9	Benzene:hexane (1:9)	trace	white crystals
10	Benzene:hexane (1:1)	ca. 4 mg.	white crystals
11	"	8 mg.	yellow oil + crystals
12	"	20 mg.	oil + crystals
13	"	10 mg.	oil + crystals
14~16	"	not weighed	yellow oil
17~22	Benzene	"	

each fraction 10 cc.

\*4 All m.p.s were measured on Kofler block.

5) L. Keller, Ch. Tamm, T. Reichstein: *Helv. Chim. Acta*, **41**, 1633(1958).

6) R. E. Winkler, T. Reichstein: *Ibid.*, **38**, 721(1954).

7) F. Korte, J. Rippahn: *Ann.*, **621**, 1527(1959).

8) F. Korte: *Chem. Ber.*, **88**, 1527(1955); F. Korte, H. Weitkamp: *Ibid.*, **89**, 2669(1953).

9) J. W. Cornforth, J. C. Earl: *J. Chem. Soc.*, **1939**, 737.

10) *Idem*: *Ibid.*, **1940**, 1443.

11) J. M. Nascimento, H. Jaeger, Ch. Tamm, T. Reichstein: *Helv. Chim. Acta*, **42**, 661(1959).

12) J. W. Cornforth: *Chem. & Ind. (London)*, **1959**, 602.

**Chromatography of the Neutral Portion**—220 mg. of the neutral portion was chromatographed over 12 g. of alumina (neutral, activated at 200° for 2 hr.) to give the results shown in Table I.

The crystals from fraction No. 10 have unsharp m.p. near 100° and white-blue fluorescence under ultraviolet ray. Recrystallization was attempted to purify them but in vain.

Fraction No. 12 gave 15 mg. of crystals, m.p. 100~120°(unsharp), from MeOH, which was rechromatographed over 2.5 g. of neutral alumina (detected by fluorescence under UV). The results are given in Table II.

TABLE II. Rechromatography of Fraction 12

Fract. No.	Solvent	Eluate
1	Benzene-hexane 5:95	trace white crystals
2	"	ca. 1 mg. white crystals
3	"	" "
4	"	ca. 0.7 mg. yellow crystals
5	"	" "
6	"	ca. 0.5 mg. yellow crystals
7	"	ca. 8 mg. yellow crystals

each fraction 10 cc.

Fraction Nos. 2 and 3 washed twice with MeOH showed m.p. 140~147° and was recrystallized from MeOH-Me<sub>2</sub>CO several times to give fine colorless plates, m.p. 146~150°. UV  $\lambda_{\text{max}}^{\text{cyclohexane}}$  m $\mu$  (log  $\epsilon$ ) : 249.5 (4.50), 258 (4.85), 268 (5.02), 304 (4.33), 317 (4.32), 332 (3.37), 348 (2.88).

### Summary

Cynanchogenin was dehydrogenated with selenium and two crystalline hydrocarbons were separated. As one of them seems to be Jacobs' hydrocarbon, the carbon skeleton of cynanchogenin was supposed to be c-nor-D-homopregnane.

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