3) *Agave salmiana* **Jacobi**—The leaves from the mature plant were cut longitudinally, dried, and rendered into a coarse ground product. One kg. of the coarse ground was treated as in the foregoing and 5 g. (0.5%) of crude crystals were obtained. These were submitted to chromatography and a small amount of wax-like substance was obtaind from the mixed solvent (i). The mixed solvent (ii) yielded 0.4 g. of crystals (XV), m.p. 260°, and 0.2 g. of crystals (XVI), m.p. 250∼254°; and the mixed solvent (iii), 0.1 g. of crystals (XVII), m.p. 255∼260°. Analytical results and mixed fusion indicated all three to be hecogenin, with (XVII) alone being slightly less pure. *Anal.* Calcd for $C_{27}H_{42}O_4$: C, 75.35; H, 9.77. Found: C, 74.95; H, 9.61.

Acetate: m.p. 250°. *Anal.* Calcd. for $C_{29}H_{44}O_5$: C, 73.72; H, 9.74. Found.: C, 94.13; H, 9.51.

Summary

Hecogenin (I) alone was obtained from the leaves of a medium mature plant of *Agave rigida* var. *sisalana* collected in August and December, but a small amount of crystals of m.p. 193° were also obtained besides (I) from the leaves of a young plant collected in June and September. The crystals showed no depression on admixture with tigogenin. The leaves from *Agave americana*, collected in March, also yielded a small amount of crystals of m.p. 230∼240° besides (I). The leaves of *Agave salmiana*, collected in August, also yielded (I) alone. These results did not agree with the reports of Marker, *et al.* that manogenin had been obtained from the same plants growing in the United States.

(Received April 20, 1954)

---

42. **Takuo Okuda**: Studies on the Components of *Coriaria japonica* A. Gray. XIII[1].

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

In the preceding paper of this series Kariyone and Sato[2] reported that a toxic component contained in fruits of *Coriaria japonica* along with coriamyrtin was identified as tutin, which had been extracted by Easterfield and Aston[3] from leaves of three species of *Coriaria* found in New Zealand, by mixed melting point and by a comparison of crystal forms and color tests.

Kinoshita[4] had also treated tutin of *C. japonica* and obtained acetyl, dihydro, and some other derivatives. Later Slater[5] noted that acetyltutin and dihydrotutin produced by him from tutin from New Zealand sources are markedly different in melting point from Kinoshita's derivatives, and on account of these results Slater pointed out that the identity of tutin from Japanese sources with tutin from New Zealand sources was not complete.

In the present study, the reasons for the discrepancy of melting points of derivatives were investigated by checking the experiments of Kinoshita and Slater. Identification and further observation on the structure of tutin were carried out by the aid of infrared absorption spectra. The presence of pseudotutin in *C. japonica* was also ascertained.

Slater described that the m.p. of the dihydro derivative produced on catalytic reduction

---

* Yoshida-konoe-cho, Sakyo-ku, Kyoto (奥田拓男).

[1] Part XII: J. Pharm. Soc. Japan, **73**, 930 (1953).

[2] T. Kariyone, T. Sato: *Ibid.*, **50**, 659 (1930).

[3] T. H. Easterfield, B. C. Aston: J. Chem. Soc., **79**, 120 (1901).

[4] K. Kinoshita: J. Chem. Soc. Japan, **51**, 99 (1930); *ibid.*, **52**, 171 (1931).

[5] S. N. Slater: J. Chem. Soc., **1943**, 50.

over palladium-charcoal catalyst as 190～192°, whereas the m.p. of dihydrotutin derived by Kinoshita had been recorded as 240°. The author discovered that the m.p. of Kinoshita's dihydrotutin had been described as 230° in the original paper, although it was described as 240° in the Chemical Abstracts⁶⁾. Kinoshita's dihydrotutin had been obtained over platinum and the description of the original is in agreement with our experiment. Moreover, in a subsequent paper of Slater⁷⁾, it was reported that tutin gave on hydrogenation two different dihydro derivatives, one α-dihydrotutin, m.p. 224～226°, derived from tutin in the presence of platinum catalyst, and the other β-dihydrotutin, m.p. 232～233°, obtained upon hydrogenation of tutin with a palladium-charcoal catalyst. Therefore it can be observed that the difference of m.p. between dihydrotutin obtained on hydrogenation with a platinum catalyst from Japanese tutin and α-dihydrotutin obtained by the same method from New Zealand tutin is 4°.

The second derivative, of which Slater pointed out the difference of m.p., is acetyltutin. Kinoshita had obtained water-insoluble crystals, m.p. 240°, by heating tutin with acetic anhydride and pyridine. Analysis could not be carried out because of its poor yield. In a subsequent experiment Kinoshita had obtained another acetyl derivative, m.p. 183°, by heating tutin with acetic anhydride and sodium acetate. Slater's acetyltutin, m.p. 177°, had been derived in the same way in which Kinoshita had obtained his derivative of m.p. 240°. According to Slater the difference of m.p. between two acetyl derivatives produced by the same method by two authors is 63°. Kinoshita's first method was re-examined and two crystalline derivatives were actually produced by this reaction. One is slightly soluble in water and melts at 183～184° after recrystallization from 50% aqueous methanol. This can be presumed identical with Kinoshita's acetyltutin, m.p. 183°, obtained by his second method. The difference of m.p. therefore between this acetyltutin and Slater's acetyltutin is 6～7°. The other consists of colorless needles, m.p. 202～203°, insoluble in water like Kinoshita's derivative of m.p. 240°. The yield was very poor and further studies are yet to be carried out. A bromo derivative, $C_{15}H_{17}O_6Br$, was obtained from Japanese tutin. It melts at 258° and may be regarded identical with Slater's α-bromotutin, m.p. 256～257°.

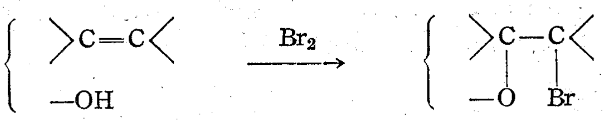
It was attempted to identify Japanese tutin with New Zealand tutin by a comparison of their infrared absorption spectra. This was made possible by the courtesy of Professor Slater, and it was found that their infrared spectra are completely identical. From the results of above experiments it may be concluded that the two tutins are quite identical and the difference of m.p. of their derivatives do not indicate any disagreement between the starting materials.

In the preceding paper of this series, the molecular formula of tutin was assigned as $C_{15}H_{18}O_6$ and it was presumed that tutin might be hydroxycoriamyrtin on account of the similarity of properties of tutin and coriamyrtin, $C_{15}H_{18}O_5$⁸⁾. Both tutin and coriamyrtin have one lactone and one double bond, their behaviors are anomalous in that they reduce Fehling's solution after hydrolysis with dilute mineral acid. On bromination they provide monobromo derivatives and give similar color by hydriodic acid or conc. sulfuric acid. Tutin is much more soluble in water and alcohol than coriamyrtin. In physiological actions they both show striking resemblance to picrotoxin. On bromination, coriamyrtin loses its double bond and hydroxyl group. These results can be observed in the infrared spectra of coriamyrtin and bromocoriamyrtin⁹⁾. The mechanism of this reaction may be explained by the hypothesis suggested by Robertson, *et al.*¹⁰⁾ on the bromination reaction

---

6) C. A., **26**, 5100 (1932).
7) S. N. Slater : J. Chem. Soc., **1943**, 143.
8) T. Kariyone, T. Sato : J. Pharm. Soc. Japan, **51**, 988 (1931).
9) T. Kariyone, T. Okuda : *Ibid.*, **73**, 930 (1953).
10) D. Mercer, A. Robertson : J. Chem. Soc., **1936**, 288.

of picrotoxinin, which is shown as follows:



If the assumption that tutin is hydroxycoriamyrtin is correct, it would be expected, owing to the close analogy revealed so far in the chemistry of tutin and coriamyrtin, that one hydroxyl group of tutin should remain unchanged after bromination. This is supported by the following infrared absorption spectra. The main absorptions of infrared spectrum of tutin, as shown in Fig. 1,[11] as well as absorptions of lactone and double bond, are similar to the absorptions of coriamyrtin as deduced from the chemical evidence. In tutin, the absorption of hydroxyl group is wider than that in coriamyrtin, its peak being separated into two characteristic maxima at 2.82 μ and 2.87 μ. The double bond absorption (6.07 μ) observed in the spectrum of tutin is not present in that of bromotutin and this is in agreement with the relation of bromocoriamyrtin and coriamyrtin. However, the hydroxyl absorption is present in the spectrum of bromotutin, although its width is narrower than that of tutin and there is only one absorption maximum at 2.87 μ. It may be considered that the two peaks of the hydroxyl groups of tutin and the single peak of bromotutin are the result of one of the hydroxyl groups of tutin being lost on bromination similar to the hydroxyl group of coriamyrtin. Consequently the assumption that tutin is hydroxycoriamyrtin is endorsed by these infrared spectra. Concerning one hydroxyl group of tutin which is not split out on bromination, it may be considered to be primary or secondary hydroxyl group, because it is relatively easily acetylated.

In an earlier paper of this series it was reported that fruit juice of *C. japonica* contains coriamyrtin, tutin, and a crystalline substance, m.p. 184°[12]. In the present study it was found that these materials are also contained in the leaves and stems. From the crude crystals of coriamyrtin and viscous material attached to the crude crystals obtained from leaves and stems by the method described in the experimental section, small amount of tutin and colorless crystals, m.p. 184°, were separated by means of fractional crystallization. The analytical value of this corresponds to the composition of $C_{15}H_{18}O_6$, that is, with tutin. The specific rotation is $[\alpha]_D^{13.5}$: +14.7°. It is soluble in alcohol, water, ether, and chloroform, and sparingly soluble in benzene and petroleume ther. The infrared spectrum shows the presence of a hydroxyl, lactone groups, and a double bond and is identical for the most part with the absorption of tutin (Fig. 1). Remarkable differences are observed between 11 μ and 15 μ. A single peak of hydroxyl absorption is observed at 2.88 μ, which is not resolved as tutin. This substance gave a blood-red coloration with conc. sulfuric acid like tutin. On admixture with tutin, it began to melt at 184° and clarified near the m.p. of tutin. The author named this substance "pseudotutin". On bromination pseudotutin produced α-bromotutin.

It was found that pseudotutin is contained not only in leaves, stems, and fruit juice, but also in the seeds of *C. japonica*. From the seeds another crystalline substance, m.p. 259°, was isolated, investigation of which is in progress.

As described above, coriamyrtin, tutin, and pseudotutin are isolated from *C. japonica* indigenous to Japan. It had been reported that coriamyrtin was also extracted from *C. myrtifolia* of Europe[13] and tutin from New Zealand species of *Coriaria*. These are shown in Table I. It is interesting from the taxonomical points of view that these

---

11) Infrared spectra were determined by the Perkin-Elmer Model 12 C Single-Beam Recording Infrared Spectrophotometer.

12) T. Kariyone, T. Sato: J. Pharm. Soc. Japan, **50**, 106(1930).

13) M. J. Riban: Compt. rend., **63**, 476(1866).

substances whose skeletons are presumed to be identical[9] with the unique skeleton of picrotoxin are present in Coriaria species of Coriariaceae, while picrotoxin is contained in Anamirta and Cocculus species of Menispermaceae family.

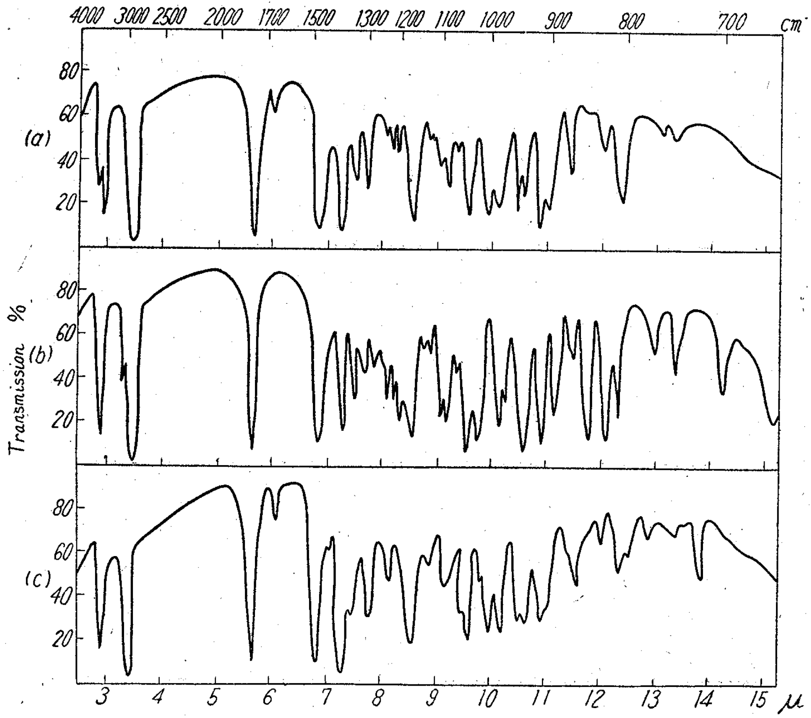


Fig. 1. Infrared Absorption Spectra in Nujol Suspension
(a) tutin (b) α-bromotutin (c) pseudotutin

TABLE I.

Plant / Component	*C. japonica* Japan	*C. myrtifolia* Europe	*C. thymifolia* *C. rustifolia* *C. angustissima* New Zealand
Coriamyrtin	leaves and stems fruit juice	stems	
Tutin	leaves and stems fruit juice, seeds		plants, seeds
Pseudotutin	leaves and stems fruit juice, seeds		

The author takes this opportunity to extend his deep gratitude to Professor Tatsuo Kariyone for his constant guidance and encouragement in the course of this work. Thanks are also due to Professor S. N. Slater of Victoria University College, New Zealand, who sent his precious sample of tutin for this work. The author's thanks are due to Mr. Takahiko Yuasa, the manager of the Osaka Factory of Sankyo Co. Ltd., who kindly facilitated our extraction operation, and to Messrs. K. Takaishi, T. Fujita, T. Miki, and S. Kitagawa for their cooperations in collection of plants and extraction of components. The author is indebted to Mr. Masao Yamaguchi of Osaka City University for taking the infrared spectra, and to Miss Hideko Iwata for microanalysis. A part of the expenses for this study were defrayed by the Grant in Aid for the Developmental Scientific Research provided by the Ministry of Education.

Experimental

Acetyltutin—A mixture of tutin (0.1 g.), acetic anhydride (0.5 cc.), and pyridine (0.2 cc.) was heated for 1.5 hrs. at 140°. The reaction mixture, diluted with water (2 cc.), deposited dark brown viscous material. The mother liquor separated from the precipitate was concentrated to dryness. The residue dissolved in boiling aq. EtOH, gradually separated colorless needles contaminated with viscous material. Recrystallization from aq. EtOH gave colorless needles, m.p. 183~184°. This product is soluble in MeOH and EtOH, slightly soluble in water.

The viscous material separated was extracted with successive quantities of water. The residue was taken up in boiling aq. EtOH, on cooling, colorless needles were deposited, recrystallized from aq. EtOH, m.p. 202~203°. This product, insoluble in water, soluble in MeOH and EtOH, gave depression of m.p. on admixture with the above product.

Bromotutin—To a hot aqueous solution of tutin (0.1 g.) an excess of bromine water was added. Somewhat concentrated liquor deposited white precipitate on cooling. Recrystallization from EtOH yielded colorless needles, m.p. 258°. Yield, 0.05 g. *Anal.* Calcd. for $C_{15}H_{17}O_6Br$: C, 48.28; H, 4.50. Found : C, 48.37; H, 4.44.

Dihydrotutin—A solution of tutin (0.1 g.) in AcOH (5 cc.) was shaken with platinum oxide in hydrogen. After 20 minutes the reduction was complete. Concentration of the filtered solution produced a white crystalline mass of dihydrotutin which was recrystallized from water to colorless needles, m.p. 230°. *Anal.* Calcd. for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found : C, 60.67; H, 6.64.

Extraction and Isolation of Tutin and Pseudotutin from Leaves and Stems of *Coriaria japonica*

A) **Extraction of Mixed Crystals**—The cut and air-dried leaves (or stems) of *C. japonica* (1 kg.) were extracted three times with 7 L. of boiling 40% aq. MeOH. The extracts were combined and concentrated at first under atmospheric pressure then under a reduced pressure to 3 L. 80 g. of aluminum acetate was added to the extract under constant agitation and heating on water bath. The precipitate was filtered off, the filtrate concentrated to 1 L., and after cooling extracted three times with 300 cc. each. of $CHCl_3$. $CHCl_3$ layer was dried over $CaCl_2$, removal of $CHCl_3$ yielded the crude crystals covered by dark green viscous material. The viscous material was washed out with EtOH, yielding colorless crystals. Yield, approx. 0.5 g. from leaves, and 0.25 g. from stems.

B) **Separation of Tutin**—Procedure (A) was repeated and the crude crystals obtained were combined and recrystallized from EtOH, yielding coriamyrtin. The mother liquor separated from coriamyrtin was concentrated. The deposited crystalline mass, m.p. approx. 180°, was recrystallized from water. The mother liquor was concentrated four times successively and the deposited crystals were removed each time. The last deposited crude crystals, m.p. 180~190°, were recrystallized from water to colorless pillars, m.p. 212°. When mixed with tutin, m.p. 213°, obtained from the seeds of the same plants, no melting point depression was observed. *Anal.* Calcd. for $C_{15}H_{18}O_6$: C, 61.21; H, 6.17. Found : C, 61.11; H, 6.07.

C) **Separation of Pseudotutin**—In procedure (B) the filtered mother liquor of the crude crystals, m.p. 180~190°, was concentrated and allowed to stand, depositing colorless pillars, and was recrystallized from water, m.p. 184°. This product was also purified by sublimation (150°/5 mm. Hg). *Anal.* Calcd. for $C_{15}H_{18}O_6$: C, 61.21; H, 6.17. Found : C, 61.53; H, 6.14.

The ethanol solution of the dark green viscous material washed off from the crude mixed crystals in procedure (A) was concentrated, and was extracted three times with boiling water for two hrs. each, using fifteen times its volume of water. The combined infusion was shaken with one-tenth volume of benzene. The benzene layer, after concentration, yielded coriamyrtin. The water layer was concentrated to a dark brown viscous material and allowed to stand for three weeks. The granular crystals which separated out were dissolved in hot water, decolorized by charcoal and concentrated five times successively. Each time the deposited crystalline mass was removed and the last deposited crystals, m.p. approx. 178°, were recrystallized from water to pillars, m.p. 184°. When mixed with the previously obtained pseudotutin no melting point depression was observed. On admixture with tutin, it began to melt at 184° and clarified near 213°.

Extraction of Pseudotutin from Seeds of *Coriaria japonica*—The finely powdered seeds (1 kg.) of *C. japonica* were immersed in benzene for 24 hrs. After removing the benzene solution, the residue was boiled three times with 2 L. of 30% aq. EtOH each for 3 hrs. The concentrated infusion was extracted with ether for 24 hrs. The ether extract was dried over calcium chloride. On distillation a light brown crystalline mass was obtained. This was dissolved in hot water and decolorized with charcoal. On cooling, small amount of white crystals were deposited. Recrystallized from EtOH, m.p. 259° (decomp.). The mother liquor, after concentration, deposited tutin, which was filtered off. The filtrate was somewhat concentrated and allowed to stand. Light brown granular crystals were separated. Recrystallized from water to colorless pillars, m.p. 184°. The infrared spectrum was identical with pseudotutin obtained from leaves and stems. *Anal.* Calcd. for $C_{15}H_{18}O_6$: C, 61.21; H, 6.17. Found : C, 61.45; H, 6.34.

Bromination of Pseudotutin—Pseudotutin (0.1 g.) was dissolved in boiling water, and bromine water was added in excess. The material which separated was filtered off and recrystallized from EtOH, m.p. 258°. When mixed with α-bromotutin, no melting point depression was observed. *Anal.* Calcd. for $C_{15}H_{17}O_6Br$: C, 48.28; H, 4.50. Found: C, 48.35; H, 4.62.

Summary

1) Melting points of the derivatives of tutin were reëxamined and identification of

tutin by infrared spectra was carried out to solve the questions raised by Slater on the previous report of this series which identified Japanese tutin with New Zealand tutin.

2) The inference that tutin is hydroxycoriamyrtin was endorsed by infrared spectra.

3) Tutin was isolated from mixed crystals extracted from leaves and stems of *Coriaria japonica.*

4) Pseudotutin, was newly extracted from plants and it was found that it is identical with the crystalline component of fruit juice, m.p. 184°. Its properties were investigated.

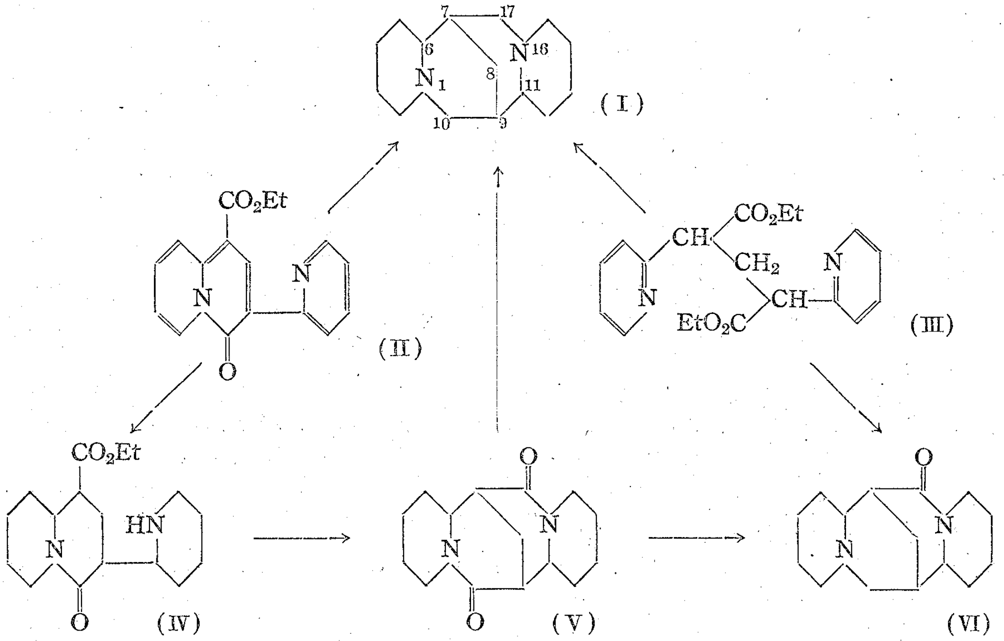
(Received May 20, 1954)

---

43. **Kyosuke Tsuda* and Yoshinobu Satoh**** : Synthesis of Lupin Alkaloids. I. Synthesis of a New Isomer of Sparteine.

(Pharmaceutical Institute, Medical Faculty, University of Kyushu, and Takamine Research Laboratory, Sankyo Co., Ltd.**)*

The total synthesis of *dl*-sparteine (I) was reported in 1950 by Leonard and Beyler[1]. They found that 1-ethoxycarbonyl-3-(α-pyridyl)-4-oxoquinolizine (II) and diethyl 2,4-di-(α-pyridyl)-glutarate (III), both of which Clemo, *et al.*[2,3] used as the intermediate in their synthesis of oxosparteine (VI), could be converted to *dl*-sparteine and *dl*-α-isosparteine in one step by their hydrogenation in dioxane solution over copper chromite catalyst at 250° and at 350°, atmospheric pressure. Galinovsky and Kainz[4] found that on catalytic reduction followed by cyclization, (II) was converted to dioxosparteine (V), and this is readily reduced to oxosparteine (VI). From (III), by the same method, Clemo, *et al.*[3] gained dioxosparteine, m.p. 113°.



---

* Hakata, Fukuoka (津田恭介). ** Nishi-Shinagawa, Shinagawa-ku, Tokyo (佐藤義信).

1) N. J. Leonard, R. E. Beyler : J. Am. Chem. Soc., **72**, 1316 (1950).
2) G. R. Clemo, W. McG. Morgan, R. Laper : J. Chem. Soc., **1936**, 1025.
3) G. R. Clemo, R. Raper, W. S. Short : *Ibid.*, **1949**, 663.
4) F. Galinovsky, G. Kainz : Monatsh., **77**, 137 (1949).