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.

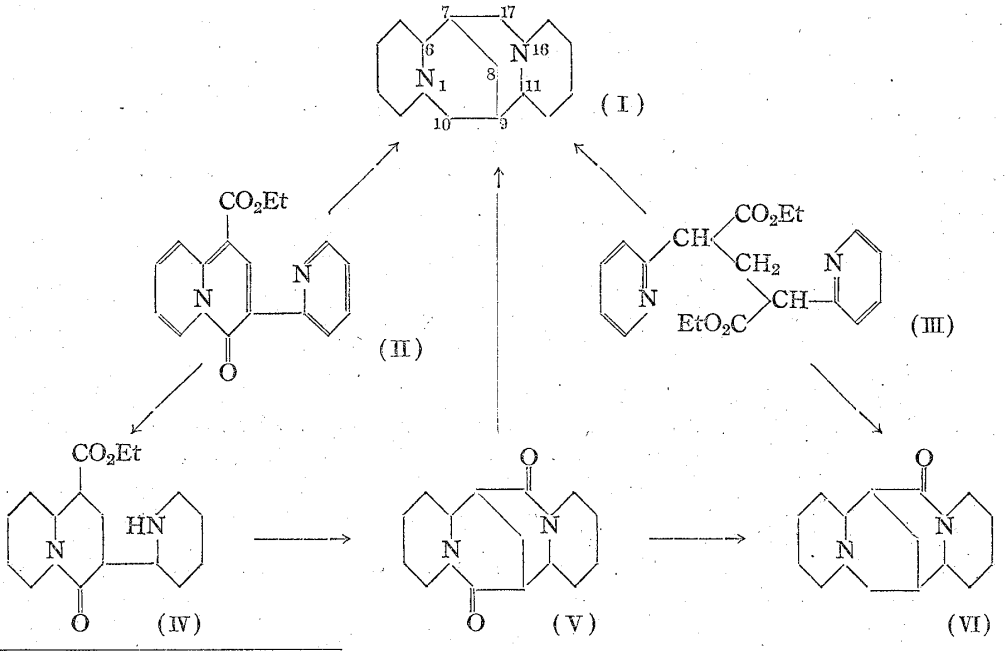
(Received May 20, 1954)

---

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).

Sorm and Keil[5,6] synthesized dioxosparteine by the same method as that of Galinovsky, and isolated two kinds of dioxosparteine by chromatography. One of the dioxosparteine, m.p. 172°, was reduced electrolytically to a base, $C_{15}H_{26}N_2$, which formed a dipicrate of m.p. 222°. The other dioxosparteine, m.p. 135°, after reduction yielded two dipicrates; m.p. 205° and m.p. 190°. It appears likely that the dipicrate, m.p. 222°, is that of *dl*–α–isosparteine and the dipicrate, m.p. 205°, is that of *dl*–sparteine.

In the present series of experiments, dioxosparteine was prepared according to the method of Galinovsky. (II) was catalytically reduced over platinum oxide in glacial acetic acid to 1–ethoxycarbonyl–3–(α–piperidyl)–4–oxoquinolizidine (IV), which was cyclized on being heated for 3 hrs. at 200° *in vacuo*. The product was chromatographed through alumina as a benzene solution and isolated into three isomeric dioxosparteines; (A) m.p. 135~137°, (B) m.p. 159~160°, and (C) m.p. 182~184°. The infrared spectra of these are shown in Fig. 1.

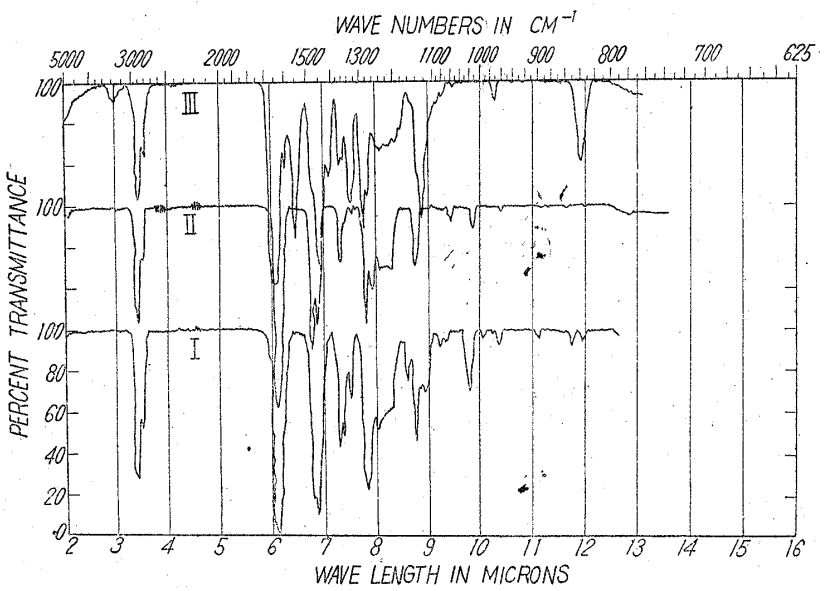


Fig. 1. Infrared Spectra of $C_{15}H_{22}O_2N_2$ in Chloroform
I: m.p. 137°, II: m.p. 160°, III: m.p. 184°

Marion and Leonard[7] discussed the stereochemistry of C_{15}–lupin alkaloids. Sparteine has three racemates according to whether the hydrogen atoms in C_6 and C_{11} are in *cis* or *trans* to the methylene bridge at C_8; (1) both *cis*, (2) *cis* and *trans*, and (3) both *trans*. Sparteine has a *cis–trans* configuration, and the α–isosparteine *cis–cis* configuration. The third racemate of both *trans* configuration, not yet found in nature, is called β–isosparteine. In the same manner dioxosparteine comes in three racemates.

The three kinds of dioxosparteine separated in the present experiments were reduced in 5% hydrochloric acid over platinum oxide to different products. (A) yielded a base, $C_{15}H_{24}N_2O$, m.p. 110°, from which *d*–tartrate was separated and this was identical to that of *l*–oxosparteine, the oxidation product of *l*–sparteine by $K_3Fe(CN)_6$. Since both sparteine and oxosparteine possess a *cis–trans* configuration, (A) also has a *cis–trans* configuration. (B) yielded a base, $C_{15}H_{26}N_2$, which formed a dipicrate melting at 219°. This must be the dipicrate of α–isosparteine, and (B) has a *cis–cis* configuration. (C) was not affected by the conditions in which (A) and (B) were reduced, but was reduced at 80~90° to a base, $C_{15}H_{26}N_2$, the dipicrate of which melted at 244~246°. This must be the isomeric

5) F. Sorm, B. Keil: Collection Czechoslov. Chem. Communs., **13**, 544 (1948).
6) *Ibid.*, **12**, 655 (1947).
7) L. Marion, N. J. Leonard: Can. J. Chem., **29**, 355 (1951).

racemate of sparteine, *dl*-β-isosparteine, and (C) has a *trans-trans* configuration. The infrared spectra of three kinds of dipicrate, *l*-sparteine dipicrate, and dipicrate of m.p. 219° and of m.p. 246°, are shown in Fig. 2.

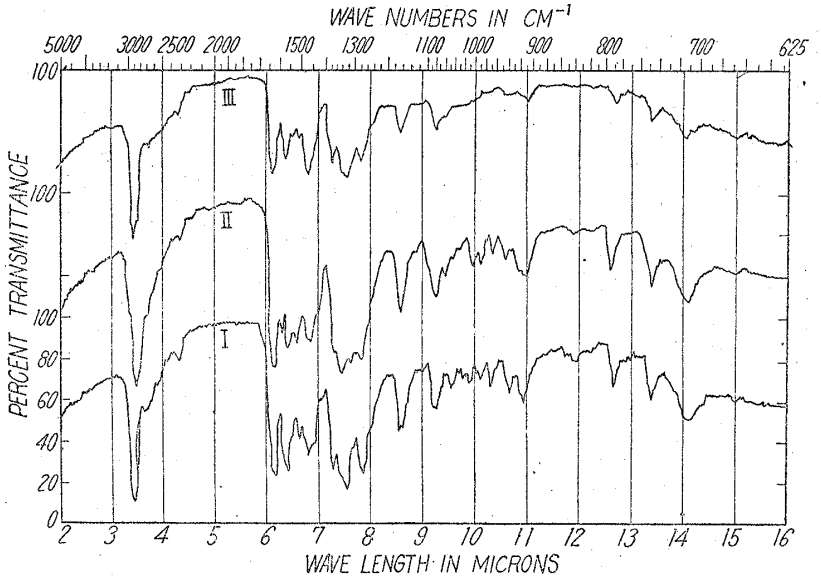


Fig. 2. Infrared Spectra of Dipicrate of $C_{15}H_{26}N_2$ in Nujol
I : *l*-Sparteine, II : α-Isosparteine, III : New Isomer

Experimental

Hydrogenation of 1-Ethoxycarbonyl-3-(α-pyridyl)-4-oxoquinolizine (II)—A solution of 10 g. of (II)[2] in 100 cc. glacial AcOH was shaken for 36 hrs. with 0.5 g. PtO_2 in H_2 at room temperature. The yellow fluorescent solution became colorless after absorption of 5500 cc. H_2 (theoretical amount for hydrogenation of seven double bonds, 5330 cc.). After the catalyst was filtered off, AcOH was removed on a water bath under reduced pressure and a brown oil remained.

Ring Closure to Dioxosparteine and its Separation by Chromatography—The above oil was heated *in vacuo* for 3 hrs. in a metal bath at 200°. The product was brownish gum (8.5 g.), which was dissolved in 100 cc. benzene and chromatographed on 400 g. alumina. Every 100 cc. of the effluent was fractionally collected. Fraction 1~21 yielded 1.15 g. of crystals (A); Fr. 22~40, 0.46 g. (B); Fr. 41~50 (developed with $CHCl_3$), 2.41 g. (C); Fr. 51~55 (developed with ether), 0; Fr. 56~60 (developed with ether containing 3% EtOH), 0.61 g. (D).

The recrystallization of crystals (A) from ether yielded colorless needles, m.p. 135~137°. *Anal.* Calcd. for $C_{15}H_{22}O_2N_2$: C, 68.7; H, 8.4; N, 10.70. Found : C, 68.97; H, 8.08; N, 10.98. *d*-Tartrate crystallized from MeOH, m.p. 174~175°. *Anal.* Calcd. for $C_{15}H_{22}O_2N_2 \cdot C_4H_6O_6$: C, 55.5; H, 6.79; N, 6.8. Found : C, 55.31; H, 6.63; N, 7.11. The recrystallization of the crystals (C) from EtOAc yielded colorless needles, m.p. 159~160°. *Anal.* Calcd. for $C_{15}H_{22}O_2N_2$: C, 68.7; H, 8.4; N, 10.70. Found : C, 68.27; H, 8.39; N, 10.62. *d*-Tartrate, m.p. 210~211°. *Anal.* Calcd. for $C_{15}H_{22}O_2N_2 \cdot C_4H_6O_6$: C, 55.5; H, 6.79; N, 6.8. Found : C, 55.53; H, 6.56; N, 7.12. The recrystallization of the crystals (D) from EtOAc–ether mixture yielded colorless small needles, m.p. 182~184°. *Anal.* Calcd. for $C_{15}H_{22}O_2N_2$: C, 68.7; H, 8.4; N, 10.70. Found : C, 68.33; H, 7.92; N, 10.77. *d*-Tartrate, m.p. 167~168°. *Anal.* Calcd. for $2C_{15}H_{22}O_2N_2 \cdot C_4H_6O_6$: N, 8.31. Found : N, 8.35. The crystals (B) was separated into two kinds of crystals, m.p. 135~137° and m.p. 160°, respectively identical with (A) and (C), by fractional recrystallization from ether and EtOAc.

Catalytic Hydrogenation of Dioxosparteine—i) The dioxosparteine, m.p. 135° (500 mg.), was hydrogenated in 5% HCl (20 cc.) over PtO_2 (300 mg.) at a room temperature. During 7 hrs., 176 cc. H_2 was absorbed (theoretical amount, 146 cc.). The catalyst was filtered off, the solution was made alkaline with 10% NaOH, and extracted with ether. The ethereal residue was recrystallized from petroleum ether and yielded colorless plates, m.p. 109~111°. Yield, 220 mg. *Anal.* Calcd. for $C_{15}H_{24}ON_2$ (Oxosparteine) : C, 72.6; H, 9.7; N, 11.29. Found : C, 73.21; H, 9.32; N, 11.39.

To the solution of *dl*-oxosparteine (200 mg.) in 1.5 cc. MeOH was added a solution of *d*-tartaric acid (121 mg.) in 2 cc. MeOH. The mixture was cooled in an ice box, and the tartrate crystallized out. Recrystallization from MeOH yielded colorless small needles, m.p. 236° (decomp.). This substance showed no depression of the melting point when fused with the *d*-tartrate of the oxidation product of

natural *l*-sparteine. *Anal.* Calcd. for $C_{19}H_{30}O_7N_2$ (Oxosparteine tartrate) : N, 7.03. Found : N, 6.85.

ii) Dioxosparteine, m.p. 160°, was reduced in 5% HCl solution at a room temperature over PtO_2 as in the foregoing. The product was derived to the dipicrate, m.p. 219° (from EtOH–dioxane). *Anal.* Calcd. for $C_{15}H_{26}N_2 \cdot 2C_6H_3O_7N_3$ (α-Isosparteine dipicrate) : C, 46.82; H, 4.66; N, 16.28. Found : C, 46.58; H, 4.74; N, 15.85.

iii) Dioxosparteine, m.p. 184°, was reduced in 5% HCl solution at 80~90° over PtO_2 as before. The product formed a dipicrate, m.p. 244~246° (from EtOH). *Anal.* Calcd. for $C_{15}H_{26}N_2 \cdot 2C_6H_3O_7N_3$: C, 46.82; H, 4.66; N, 16.28. Found : C, 46.52; H, 5.26; N, 15.87.

Summary

Dioxosparteine, obtained from 1-ethoxycarbonyl-3-(α-pyridyl)-4-oxoquinolizine, was chromatographically separated into three isomers : (A) m.p. 135~137°, (B) m.p. 159~160°, and (C) m.p. 182~184°. They were respectively reduced to oxosparteine, α-isosparteine, and a new isomer of sparteine.

(Received May 26, 1954)

---

44. Shigehiko Sugasawa and Takashi Tatsuno : Oxidation of N-(β-3′,4′-Methylenedioxyphenethyl)-3-ethylpyridinium Salt and the Constitution of the Resultant Pyridone.

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

The course of the oxidation of 3-substituted pyridinium salts (I) is governed only by the nature of R′, whereas R seems to have hardly any influence. The results hitherto obtained in our laboratories are as follows :

When R′ is carboxyl[1], N-methylpyrrolidyl-2[2], phenyl[3], or α-ethylenedioxyethyl[3], pyridone-6 (III) type of derivatives are the main, if not the sole, products, while N-methyl-3-ethylpyridinium salt gave only N-methyl-3-ethylpyridone-2 in a good yield[4]. In these cases, the constitution of pyridones were proved by chemical method, but in some cases this method of confirmation is not always an easy task to do.

One of us (T. T.) proposed to make use of the dipole moment data in such cases to deduce the constitution and his attempts along this line have achieved substantial results. The present paper adds another successful example of his method of deduction.

When N-β-3′,4′-methylenedioxyphenethyl-3-ethylpyridinium bromide was subjected to alkaline ferricyanide oxidation, there was obtained a single pyridone derivative in a good yield. By measuring the dipole moment of this pyridone Tatsuno attributed N-(β-3′,4′-methylenedioxyphenethyl)-3-ethylpyridone-2 (IIb) to this substance, which was proved to be correct by an independent synthesis.

Ethyl α-carbethoxy-γ-cyanobutyrate (IV)[5] was prepared from acrylonitrile and diethyl malonate and this was then reduced to furnish ethyl 2-ketonipecotate (V), followed by ethylation (VI). After hydrolysis the latter was subjected to decarboxylation, yielding (VII), N-potassio derivative of which was then condensed with β-3,4-methylenedioxyphe-

* Hongo, Tokyo (菅沢重彦, 辰野 高).

1) Sugasawa, Sakurai, Okayama : Ber., **74**, 537 (1941).
2) Sugasawa, Tatsuno : J. Pharm. Soc. Japan, **72**, 248 (1952).
3) Sugasawa, Kirisawa : Unpublished.
4) Sugasawa, Ban : J. Pharm. Soc. Japan, **72**, 1336 (1952).
5) Koelsch : J. Am. Chem. Soc., **65**, 2460 (1943).