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## 227. Masao Tomita,[*1] Tohru Kikuchi,[*1] Kiyoshi Bessho,[*1,*2] and Yasuo Inubushi[*3] : Studies on Pilocereine and Related Compounds.[*4] II.[*5] Cleavage of O-Methylisopilocereine by Metallic Potassium in Liquid Ammonia.[*6]

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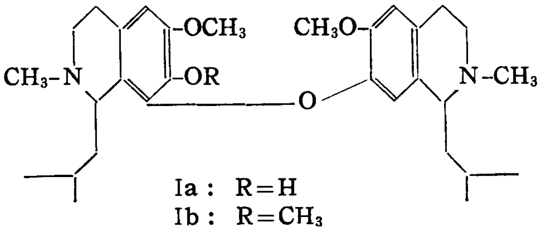
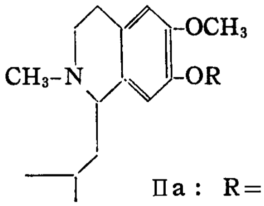
Pilocereine (m.p. 176~177°) is an optically inactive, kryptophenolic alkaloid isolated from *Lophocereus shottii* and some other species of cacti. Djerassi and his co-workers1) assigned the molecular formula $C_{30}H_{44}O_4N_2$ to it and concluded that it is a racemate represented by formula (Ia,) on the basis of elemental analysis, molecular weight determination and of the results of potassium-liq. ammonia cleavage reactions of its O-methyl and O-ethyl ethers.



Ia : R=H
Ib : R=$CH_3$



Ⅱa : R=H
Ⅱb : R=$CH_3$
Ⅱc : R=$C_2H_5$

In the course of their work, they attempted a sodium-liq. ammonia cleavage procedure on pilocereine itself. Results were unsatisfactory owing to incomplete reaction. However, replacement of sodium by potassium caused the cleavage of the diphenyl ether linkage to give the expected product (Ⅱa) (characterized as its O-methyl and O-ethyl ethers) and an unexpected product which gave a crystalline picrate, m.p. 235~337°. The latter was named "isopilocereine" because it was considered to have the same molecular formula $C_{30}H_{44}O_4N_2$ as pilocereine. When the reaction was carried out under more drastic conditions, one of the methoxyl groups of isopilocereine was cleaved yielding desmethylisopilocereine $C_{29}H_{42}O_4N_2$, m.p. 177.5~178°. Although conclusive results were

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[*4] A preliminary communication of this work (Part Ⅱ~Ⅶ) appeared in Tetrahedron Letters, No. 3, 127 (1963).
[*5] Part I. M. Tomita, K. Bessho : Yakugaku Zasshi, **79**, 1097 (1959).
[*6] Reported at the 3rd Symposium on the Chemistry of Natural Products (in Tokyo, 1958).
1) *a*) C. Djerassi, N. Frick, L.E. Geller : J. Am. Chem. Soc., **75**, 3632 (1953); *b*) C. Djerassi, S.K. Figdor, J.M. Bobbitt, F.X. Markley : *Ibid.*, **79**, 2203 (1957).

not obtained by a sequence of usual degradation procedures, including Hofmann degradation of the O-methyl ether of isopilocereine, it has been postulated that a reaction similar to a Smiles rearrangement (as shown in Chart 1) would probably have taken place in the course of this procedure, and that the structure of isopilocerine and desmethylisopilocereine might be shown as formulas (IIIa and IIIb), respectively.

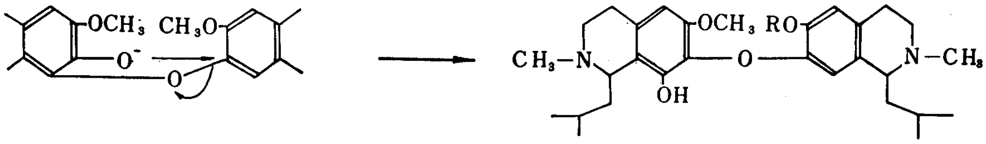
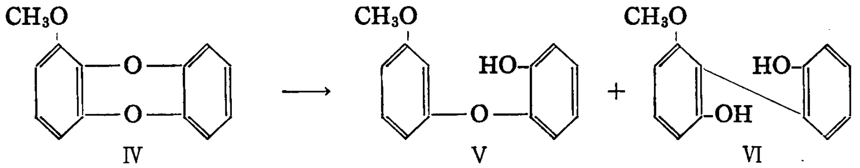


Chart 1.

IIIa : R = $CH_3$
IIIb : R = H

On the other hand, it was already reported by Tomita and co-workers[2] that diphenyl ether derivatives with a phenolic hydroxyl group were not cleaved effectively by metallic sodium in liquid ammonia. Moreover, Inubushi, *et al.*[3] found that under usual conditions dibenzo-*p*-dioxin derivatives afforded considerable amounts of biphenyl derivatives, together with diphenyl ether derivatives which are normal cleavage products. Thus, for example, 1-methoxydibenzo-*p*-dioxin (IV) gave V and VI. These



IV V VI

Chart 2.

results led us to suppose that isopilocereine might be a biphenyl derivative produced by the same mechanism. Therefore, we reinvestigated the structures of isopilocereine and desmethylisopilocereine.[*7]

Treatment of pilocereine with potassium-liq. ammonia was carried out several times under various conditions and every time three products (IIa, isopilocereine, and desmethylisopilocereine) were obtained, but our results were slightly different from those reported by Djerassi, *et al.*; *i.e.*, on reaction at low temperature (−60°) a considerable amount of unchanged starting material was recovered suggesting that a comparatively high temperature and a long reaction time were required for completion of the reaction. After reaction at −34° (b.p. of liq. ammonia), a kryptophenolic base and a phenolic basic portion were separated from the reaction mixture according to the literature.[1b] The former afforded isopilocereine, which was identified as the dipicrate, m.p. 235°, while from the latter two bases were separated by countercurrent extraction from chloroform solution in pH 5.8 buffer solution. The aqueous phases afforded desmethylisopilocereine, m.p. 177~178°, and the chloroform phases gave IIa which was characterized as the oxalate (m.p. 213~214°, decomp.) and the picrate (m.p. 194~195°). Of these products, IIa is considered to be the same compound as lophocerine, one of the alkaloidal components of *L. shottii.*[4] Since lophocerine had not yet been characterized in a crystalline form, the synthesis of lophocerine (IIa) as shown in Chart 3 was

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[*7] The authors are indebted to Prof. C. Djerassi for kindly supplying pilocereine from which isopilocereine and desmethylisopilocereine were derived.

2) M. Tomita, Y. Inubushi, H. Niwa : Yakugaku Zasshi, **72**, 206, 220 (1952); M. Tomita, E. Fujita, T. Abe : *Ibid.*, **72**, 384 (1952).

3) Y. Inubushi, K. Nomura, E. Nishimura, M. Yamamoto : Yakugaku Zasshi, **78**, 1189 (1958); Y. Inubushi, K. Nomura : *Ibid.*, **79**, 838 (1959), **81**, 7 (1961), **82**, 696, 1341 (1962).

4) C. Djerassi, T. Nakano, J. M. Bobbitt : Tetrahedron, **2**, 58 (1958).

attempted[*8] and the compound was obtained as a crystalline picrate, m.p. 194~195°, oxalate, m.p. 213~214° (decomp.), and methiodide, m.p. 198~200°. Identification of the picrate and oxalate with those of the above-described bisected base (IIa) confirmed the structure of the latter.

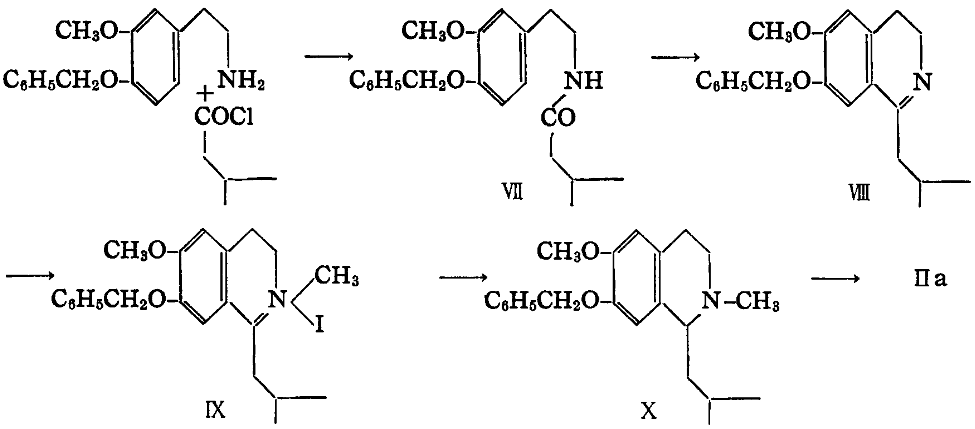

Chart 3.

The infrared spectrum of isopilocereine in chloroform solution showed distinct differences from that of pilocereine at regions near 3500, 1300, and 1050 $cm^{-1}$ (Fig. 1). Its ultraviolet spectrum showed a maximum at 285 mμ (log ε 3.85. Fig. 2) and was very similar to that of pilocereine. The lack of the K-band of biphenyl suggested that a diphenyl ether structure for isopilocereine would be more tenable than a biphenyl structure. However, Djerassi's tentative formula (IIIa), in which the *p*-position of the phenolic hydroxyl group has no substituent, seems inadequate because isopilocereine did not give a blue color with Gibbs reagent.[*9] Since the Hofmann degradation procedure had already been reported to be unsuccessful, as mentioned previously, our attention was again directed to the potassium-liq. ammonia procedure for O-methylisopilocereine as a means for elucidation of the structure.

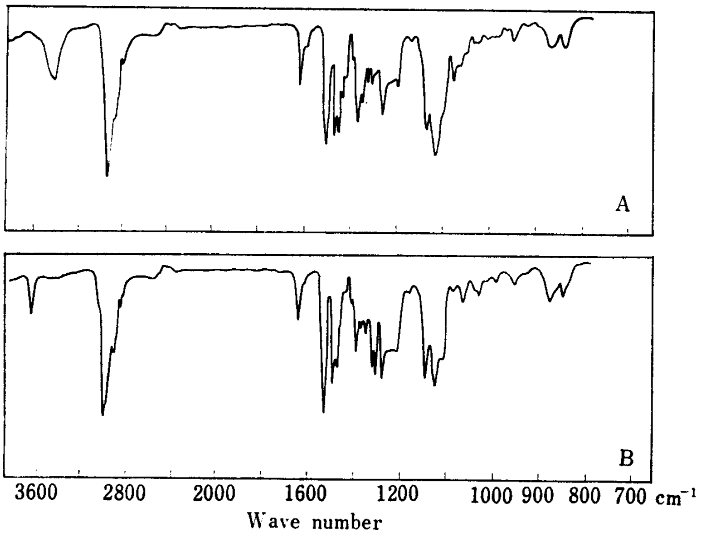

Fig. 1. Infrared Absorption Spectra (in $CHCl_3$)

A: Pilocereine
B: Isopilocereine

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[*8] The synthesis of lophocerine (IIa) was reported independently by J. M. Bobbitt and T. Chou (J. Org. Chem., **24**, 1106 (1959)) after our synthesis had been completed. Their results are quite in agreement with ours.

[*9] 2-Methyl-6,7-dimethoxy-1,2,3,4-tetrahydro-8-isoquinolinol (anhalidine) gives a deep blue color with Gibbs reagent.

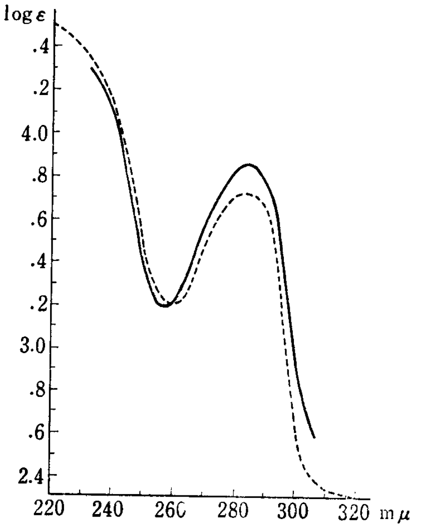
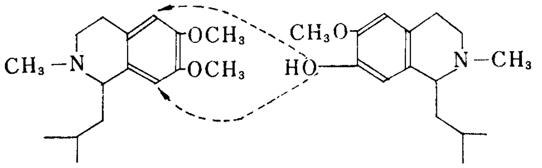


Fig. 2. Ultraviolet Absorption Spectra (in EtOH)

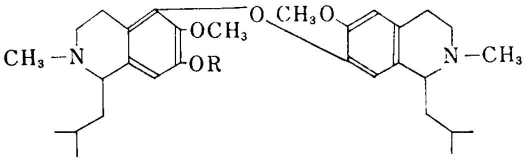
——— Isopilocereine
------ Pilocereine[1a)]

Methylation of isopilocereine was effected by treatment with diazomethane and O-methylisopilocereine was obtained in a crystalline state, m.p. 91~92°. The infrared spectra of this O-methyl ether in chloroform solution and in a potassium bromide disk also differed slightly from those of O-methylpilocereine. When treated with metallic potassium in liquid ammonia in the usual manner, O-methylisopilocereine afforded IIa and IIb quantitatively as bisected bases; both were characterized as crystalline picrates. Thus it was confirmed that O-methylisopilocereine has a diphenyl ether type structure and is represented by either formula (Ib or XIb). Consequently the structure of isopilocereine should be Ia or XIa.*[10]

If the structure of isopilocereine is represented by formula (Ia) which is that assigned to pilocereine, they should be stereoisomers. However, another racemic alkaloid piloceredine $C_{30}H_{44}O_4N_2$, m.p. 165~166°, had also been isolated from *L. shottii* by Djerassi, *et al.*, who concluded that this conpound is the diastereomer of pilocereine and is represented by the same formula (Ia). Furthermore it was reported that the infrared spectrum of piloceredine was identical with that of pilocereine when measured in chloroform solution, although distinct differences were noticed in Nujol mull. Formula (Ia) includes two asymmetric carbons and at most two racemic diastereomers are possible. Thus if pilocereine and piloceredine are taken for diastereomers of Ia, it is untenable to give the same formula to isopilocereine. Therefore, it was deduced that isopilocereine and O-methylisopilocereine should have structures (XIa) and (XIb), respectively.



IIb IIa



XIa : R=H
XIb : R=$CH_3$

## Experimental*[11]

**Cleavage of Pilocereine by Potassium in Liquid Ammonia**——Potassium metal (2.3 g.) was dissolved in 800 ml. of liq. $NH_3$ at −34°(boiling point). To this blue-colored solution was added dropwise a solution of 1.5 g. of pilocereine in 50 ml. of benzene-$Et_2O$ mixture (1:9) with stirring. After 6 hr. of continuous stirring, the excess of potassium was destroyed with anhyd. $NH_4Cl$ which was added cautiously until the blue color had disappeared. The reaction mixture was allowed to stand overnight to evaporate the solvent, and the residue was partitioned between $Et_2O$ and 3% NaOH. The $Et_2O$ phase was evaporated to leave 0.80 g. of a non-phenolic, basic oil, whereas 0.75 g. of phenolic, basic fraction was obtained from the alkaline aqueous phase.

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*[10] Since there is no color with Gibbs reagent the structures with phenolic hydroxyl groups at 6-positions of their tetrahydroisoquinoline nuclei are excluded (cf. H. Inoue, Y. Kanaya, Y. Murata : This Bulletin, **7**, 573 (1959)).

*[11] All melting points are uncorrected.

The non-phenolic base was converted into the picrate and recrystallized from $Me_2CO$ to give 0.60 g. of yellow plates, m.p. 235°(decomp.). This was identified with an authentic sample of isopilocereine dipicrate by mixed melting point and IR comparison. *Anal.* Calcd. for $C_{30}H_{44}O_4N_2 \cdot 2C_6H_3O_7N_3$ : C, 52.82; H, 5.28; 2-$CH_3O$, 6.51. Found : C, 53.10, 52.86; H, 5.67, 5.52; $CH_3O$, 6.67, 6.87.

The phenolic, basic fraction showed two spots on PPC[12] (Rf. 0.70, 0.56) and also two fixed zones on MPC[12] (pH 5.8～5.6, 5.2～5.0). A half portion of the crude base (0.40 g.) was partitioned by countercurrent extraction using nine separatory funnels each of which contained 20 ml. of $CHCl_3$ and 25 ml. of pH 5.8 buffer solution. The $CHCl_3$ phases thus obtained (Fract. 1～9) showed a single spot (Rf. 0.70) on PPC; they were combined and evaporated to yield 0.16 g. of an oily base, to which an ethanolic solution of oxalic acid (½ mole equivalent) was added. Gradually a crystalline precipitate separated. Recrystallizations from EtOH gave 0.15 g. of colorless pillars, m.p. 213～214°(decomp.), which are easily soluble in EtOH when the excess of oxalic acid exists. This oxalate was identified as 1-isobutyl-2-methyl-6-methoxy-1,2,3,4-tetrahydro-7-isoquinolinol (lophocerine) (Ⅱa) oxalate by mixed melting point and IR comparison (in Nujol) with the synthetic sample (described later). *Anal.* Calcd. for $C_{15}H_{23}O_2N \cdot \frac{1}{2}(COOH)_2$ : C, 65.28; H, 8.22; $CH_3O$, 10.54. Found : C, 64.74, 64.76; H, 8.25, 8.26; $CH_3O$, 10.69.

The free base regenerated from the above oxalate was converted into picrate and recrystallized from EtOH as yellow rhombic crystals, m.p. 194～195°. Identification with the picrate of synthetic lophocerine (Ⅱa) was accomplished by mixed melting point and IR comparison (in Nujol). *Anal.* Calcd. for $C_{15}H_{23}O_2N \cdot C_6H_3O_7N_3$ : C, 52.71; H, 5.48; $CH_3O$, 6.49. Found : C, 52.54, 52.68; H, 5.60, 5.61; $CH_3O$, 7.27.

Of the buffer solution layers, Fract. 14～18 showed a single spot (Rf. 0.56) on PPC. They were combined and evaporated to a syrup which crystallized on trituration with EtOH. Recrystallization from EtOH yielded 0.15 g. of colorless cubes, m.p. 176～177°, which showed melting point depression on admixture with pilocereine. Identification of this compound with desmethylisopilocereine was achieved by IR comparison. *Anal.* Calcd. for $C_{29}H_{42}O_4N_2$ : C, 72.16; H, 8.77. Found : C, 71.92, 72.08; H, 8.59, 8.69.

The other half portion (0.40 g.) of the crude bisected, phenolic base crystallized on seeding with desmethylisopilocereine. Recrystallization from EtOH yielded 0.18 g. of desmethylisopilocereine, m.p. 176°. The mother liquor, when treated with 1/2 mole equivalent of oxalic acid, gave 0.15 g. of lophocerine (Ⅱa) oxalate, m.p. 213～214°(decomp.).

**O-Methylisopilocereine**——The oily free base liberated from 0.42 g. of isopilocereine dipicrate was methylated with diazomethane in $Et_2O$ at room temperature. After two weeks the solvent was evaporated and the residue was dissolved in dil. HCl and washed with $Et_2O$. Basification of this acidic solution with NaOH and extraction with $Et_2O$ furnished 0.20 g. of an oily substance, which crystallized gradually and showed m.p. 85～92°. This was chromatographed on $Al_2O_3$[13] (0.7 × 5 cm.) with benzene and recrystallized from hexane to give colorless needles, m.p. 91～92°. *Anal.* Calcd. for $C_{31}H_{46}O_4N_2$: C, 72.90; H, 9.08. Found : C, 72.82; H, 8.76.

**Cleavage of O-Methylisopilocereine with Potassium in Liquid Ammonia**——O-Methylisopilocereine (0.8 g.) was allowed to react with 0.80 g. of K in liq. $NH_3$ at $-60 \sim -50°$ for 5 hr. Then $NH_4Cl$ was added to discharge the blue color of the reaction mixture and the solvent was allowed to evaporate on standing overnight. Separation of the residue in the usual manner afforded 0.36 g. of a non-phenolic base and 0.38 g. of a phenolic base. Treatment of the former with picric acid and recrystallization from $Me_2CO$-EtOH furnished 0.62 g. of yellow plates, m.p. 184～185°. This was identified with an authentic sample of 1-isobutyl-2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (O-methyllophocerine) (Ⅱb) picrate by mixed melting point and IR comparison (in Nujol). *Anal.* Calcd. for $C_{16}H_{25}O_2N \cdot C_6H_3O_7N_3$ : C, 53.65; H, 5.73; 2$CH_3O$, 12.60. Found : C, 53.69, 53.97; H, 5.70, 5.80; $CH_3O$, 12.81.

The free base regenerated from the mother liquor was further examined by PPC, but any other base could not be detected.

The phenolic, basic fraction afforded on treatment with picric acid in EtOH solution 0.58 g. of yellow, rhombic crystals, m.p. 194～195°. Identity of this compound with lophocerine (Ⅱa) picrate was

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[12] Following abbreviations are used in these papers (Part Ⅱ～Ⅷ).

PPC : Paper chromatography, BuOH-AcOH-$H_2O$ (63:10:27), ascending method.

MPC : Multi-buffered paper chromatography, McIlvaine buffers (double strength), $CHCl_3$, ascending method.

PEP : Paper electrophoresis, 5*M* AcOH, 50 v/cm.

Toyo filter paper No. 50 was used for these experiments.

TLC : Thin layer chromatography, Aluminium Oxide G according to Stahl (Merck), $CHCl_3$.

Spots of the bases were detected with Dragendorff reagent.

[13] Unless noted otherwise, Aluminium Oxide according to Brockmann (Merck) was used.

established by mixed melting point and IR comparison (in Nujol) with a synthetic specimen. *Anal.* Calcd. for $C_{15}H_{23}O_2N \cdot C_6H_3O_7N_3$ : C, 52.71; H, 5.48; $CH_3O$, 6.49. Found : C, 52.54, 52.87; H, 5.63, 5.71; $CH_3O$, 7.09.

The free base liberated from the mother liquor was examined by PPC, but no other base could be detected.

**Synthesis of 1-Isobutyl-2-methyl-6-methoxy-1,2,3,4-tetrahydro-7-isoquinolinol (Lophocerine) (IIa).** i) **N-(3-Methoxy-4-benzyloxyphenethyl)isovaleramide (VII)**——To a mixture of 20% aqueous solution of $K_2CO_3$ (5 ml.) and an ethereal solution (200 ml.) of 3-methoxy-4-benzyloxyphenethylamine regenerated from 2.0 g. of the oxalate was added dropwise a dry ethereal solution of 1.6 g. of isovaleryl chloride with stirring. The mixture was further stirred at room temperature for 1.5 hr., then the $Et_2O$ layer was separated from the aqueous layer, washed with 2% NaOH, 2% HCl, and then with $H_2O$. After drying over anhyd. $K_2CO_3$ and concentration of the solution, 1.45 g. of amide (Ⅶ) was obtained as colorless needles, m.p. 112~114°(73%). Two recrystallizations from $CHCl_3$-$Et_2O$ provided an analytical sample, m.p. 114.5~115°. *Anal.* Calcd. for $C_{21}H_{27}O_3N$ : C, 73.87; H, 7.97. Found : C, 73.97; H, 7.68.

ii) **1-Isobutyl-6-methoxy-7-benzyloxy-3,4-dihydroisoquinoline (VIII)**——A solution of 1.4 g. of the amide (Ⅶ) in 6 ml. of dry toluene was gently refluxed with 6 ml. of $POCl_3$ for 2.5 hr. The solvent and the excess of $POCl_3$ were distilled off under reduced pressure, and the residue, after washing three times with petr. ether, was dissolved in dil. HCl. The acidic solution was washed with $Et_2O$, basified with NaOH, and extracted with $Et_2O$. The $Et_2O$ solution was dried over anhyd. $K_2CO_3$ and evaporated to yield a yellowish syrup (1.31 g.). Treatment with an ethanolic solution of oxalic acid and recrystallization from MeOH-EtOH gave 1.47 g. (87%) of dihydroisoquinoline (Ⅷ) oxalate as colorless needles, m.p. 174.5~175° (decomp.). *Anal.* Calcd. for $C_{21}H_{25}O_2N \cdot (COOH)_2$ : C, 66.81; H, 6.58. Found : C, 67.02; H, 6.39.

iii) **1-Isobutyl-6-methoxy-7-benzyloxy-3,4-dihydroisoquinoline Methiodide (IX)**——Dihydroisoquinoline compound (Ⅷ) regenerated from 0.70 g. of the oxalate was dissolved in MeOH and refluxed with excess MeI for 4 hr. to yield 0.73 g. (93%) of yellow plates of the methiodide (Ⅸ), m.p. 214~215° (decomp.). Recrystallization from $Me_2CO$ gave an analytical sample. *Anal.* Calcd. for $C_{22}H_{28}O_2NI$: C, 56.77; H, 6.06. Found : C, 56.76; H, 5.98.

iv) **1-Isobutyl-2-methyl-6-methoxy-7-benzyloxy-1,2,3,4-tetrahydroisoquinoline (O-Benzyllophocerine) (X)**——A solution of 1.40 g. of the methiodide (Ⅸ) in 300 ml. of MeOH was treated with 1.5 g. of $NaBH_4$. After evaporation of the solvent under reduced pressure and usual acid-alkali treatment, the oily product was dissolved in 4 ml. of 5% HCl. Colorless needles of X·hydrochloride were collected by suction and recrystallized from $CHCl_3$-$Et_2O$ to yield 1.04 g. (90%) of granular crystals, m.p. 213~214°. *Anal.* Calcd. for $C_{22}H_{29}O_2N \cdot HCl \cdot \frac{1}{2}H_2O$ : C, 68.64; H, 7.59. Found : C, 68.86, 68.67; H, 7.95, 7.79.

v) **1-Isobutyl-2-methyl-6-methoxy-1,2,3,4-tetrahydro-7-isoquinolinol (Lophocerine) (IIa)**——O-Benzyllophocerine (X) hydrochloride (100 mg.) was dissolved in 3 ml. of 20% HCl and heated for 1 hr. in a boiling water bath. The reaction mixture was washed with $Et_2O$, basified with NaOH, and washed again with $Et_2O$ to remove the starting material. After addition of excess $NH_4Cl$ to this alkaline solution, the phenolic base was extracted with $Et_2O$, and the $Et_2O$ extract was dried over anhyd. $K_2CO_3$ and evaporated. The residue (60 mg.) was treated with 1/2 mole equivalent of oxalic acid in EtOH. The crystalline oxalate thus obtained was recrystallized from EtOH to give 50 mg. of colorless prisms, m.p. 213~214°(decomp.), which were identified with the oxalate of the bisected, phenolic base (Ⅱa) derived from pilocereine by mixed melting point and IR comparison (in Nujol). *Anal.* Calcd. for $C_{15}H_{23}O_2N \cdot \frac{1}{2}(COOH)_2$ : C, 65.28; H, 8.22. Found : C, 65.02; H, 8.16.

A picrate was prepared from a 50 mg. portion of the oxalate and recrystallized from EtOH to give 60 mg. of yellow, rhombic crystals, m.p. 194~195°. Identification of this compound with the bisected, phenolic base (Ⅱa) picrate was accomplished by mixed melting point and IR comparison (in Nujol). *Anal.* Calcd. for $C_{15}H_{23}O_2N \cdot C_6H_3O_7N_3$ : C, 52.71; H, 5.48. Found : C, 52.95; H, 5.59.

Another 50 mg. of the oxalate was converted into the methiodide by the usual method and recrystallized from $Me_2CO$-MeOH to give 70 mg. of colorless needles, m.p. 198~200°. *Anal.* Calcd. for $C_{16}H_{26}O_2NI$ : C, 49.11; H, 6.70. Found : C, 49.18; H, 6.79.

When X·hydrochloride (190 mg.) was hydrogenated in MeOH in the presence of Pd-C for 30 min., the reaction product gave 170 mg. of lophocerine (Ⅱa) picrate, m.p. 194~195°.

vi) **O-Methyllophocerine (IIb)**——The free base regenerated from 700 mg. of the synthetic lophocerine oxalate was left with an ethereal solution of excess diazomethane for a week at room temperature. Treatment of the reaction mixture in the usual manner afforded 550 mg. of a non-phenolic base.

A picrate was prepared from a 200 mg. portion of this base and recrystallized from $Me_2CO$-EtOH to give 300 mg. of yellow plates, m.p. 184~185°, which were identified as 1-isobutyl-2-methyl-6,7-

dimethoxy-1,2,3,4-tetrahydroisoquinoline (Ⅱb) picrate[5] by mixed melting point and IR comparison (in Nujol). *Anal.* Calcd. for $C_{16}H_{25}O_2N \cdot C_6H_3O_7N_3$ : C, 53.65; H, 5.73. Found : C, 53.74; H, 6.01.

Another 200 mg. portion of the free base was converted into the oxalate in EtOH and recrystallized from MeOH-EtOH-$Et_2O$ yielding 180 mg. of colorless plates, m.p. 136~137°(decomp.). *Anal.* Calcd. for $C_{16}H_{25}O_2N \cdot (COOH)_2$ : C, 61.17; H, 7.70. Found : C, 61.02; H, 7.49.

The free base liberated from 50 mg. of the oxalate was refluxed with MeI (2 ml.) and MeOH (2 ml.) for 4 hr. The solvent and the reagent were distilled off and the residue was treated with $Me_2CO$ to give a crystalline methiodide. Recrystallization from hexane-$Me_2CO$ affoded 60 mg. of colorless plates, m.p. 196~198°. *Anal.* Calcd. for $C_{17}H_{28}O_2NI$ : C, 50.37; H, 6.96. Found : C, 50.09; H, 6.93. The melting point depressed to 175~180° on admixture with lophocerine (Ⅱa) methiodide.

**vii) O-Ethyllophocerine (IIc)**——Synthetic lophocerine (Ⅱa) regenerated from 50 mg. of the oxalate was treated with an ethereal solution of diazoethane. After standing at room temperature for 3 days, usual treatment of the reaction mixture gave 40 mg. of a non-phenolic base. The picrate was recrystallized from $Me_2CO$-EtOH as yellow plates, m.p. 149~150°, 70 mg. (rec.[6] m.p. 151.5~152.5°). *Anal.* Calcd. for $C_{17}H_{27}O_2N \cdot C_6H_3O_7N_3$ : C, 54.54; H, 5.97. Found : C, 54.32; H, 6.27.

## Summary

Potassium-liq. ammonia cleavage of O-methylisopilocereine yielded Ⅱa and Ⅱb as bisected bases. This suggested that the structure of isopilocereine is either Ia or XIa, although the previous assignment of Ia to pilocereine and piloceredine by Djerassi, *et al.* excluded structure (Ia).

The synthesis of lophocerine (Ⅱa) is also reported.

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[6] C. Djerassi, F. X. Markley, R. Ehrlich : J. Org. Chem., **21**, 975 (1956).