88. Masao Tomita, Yasuo Inubushi, and Mutsuo Kozuka: Studies on the Alkaloids of Menispermaceous Plants. CXI[1]. On the Structure of Biscoclaurine Alkaloids. (14)[2]. Synthesis of Trilobine-Type Alkaloid from Isotetrandrine. (1).

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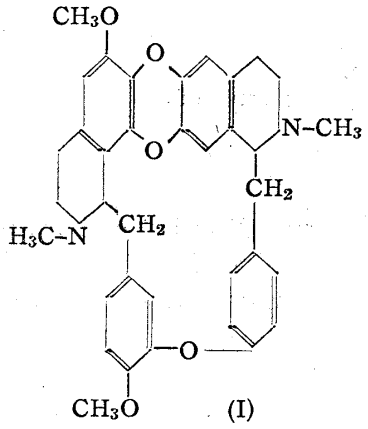
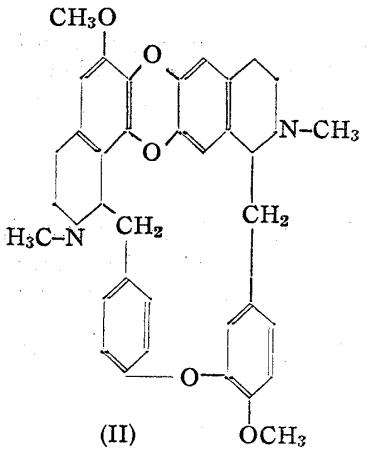
Trilobine and isotrilobine are the main bases[3] of *Cocculus trilobus* DC. (Japanese name "Ao-tsuzurafuji") and *Cocculus sarmentosus* Diels (Japanese name "Hohzan-tsuzurafuji"). Recently trilobine was also discovered from *Cocculus laurifolius* DC. (Japanese name "Kohshu-uyaku") by Tomita and Kusuda[4]. The structure of trilobine and isotrilobine was thoroughly studied by Kondo and Tomita[3], and subsequently by Tomita and Tani[3], as the result of which it was clarified that both belong to the biscoclaurine type of bases, and constitute a unique group possessing a diphenylene dioxide nucleus in their molecule. Thus, to date, the following two formulae, (I) and (II), have been proposed for their representation. This ambiguity implies that these bases are structurally isomeric with each other, and if one member of the pair is postulated to be trilobine, the other should correspond to isotrilobine, but it remains unsettled which of the structures (I) or (II) represents trilobine and which isotrilobine.



(I)



(II)

One of the authors, Tomita[3], discussed the processes by which a series of trilobine-isotrilobine bases may be produced in plants; according to his suggestions, the two molecules of the norcoclaurine-type base (III) may initially yield the oxyacanthine-berbamine type of base (IV) by dehydrogenation, from which by subsequent dehydration, the trilobine-isotrilobine type base (V) may form, or in this case, if (IV) undergoes dehydrogenation, the menisarine-type base (VI) may be formed. In the present series of experiments, attempts to derive a base of the trilobine-isotrilobine series from that of the oxyacanthine-berbamine were found successful and experimental evidence has been given for the above hypothesis. The results thereby obtained are described below.

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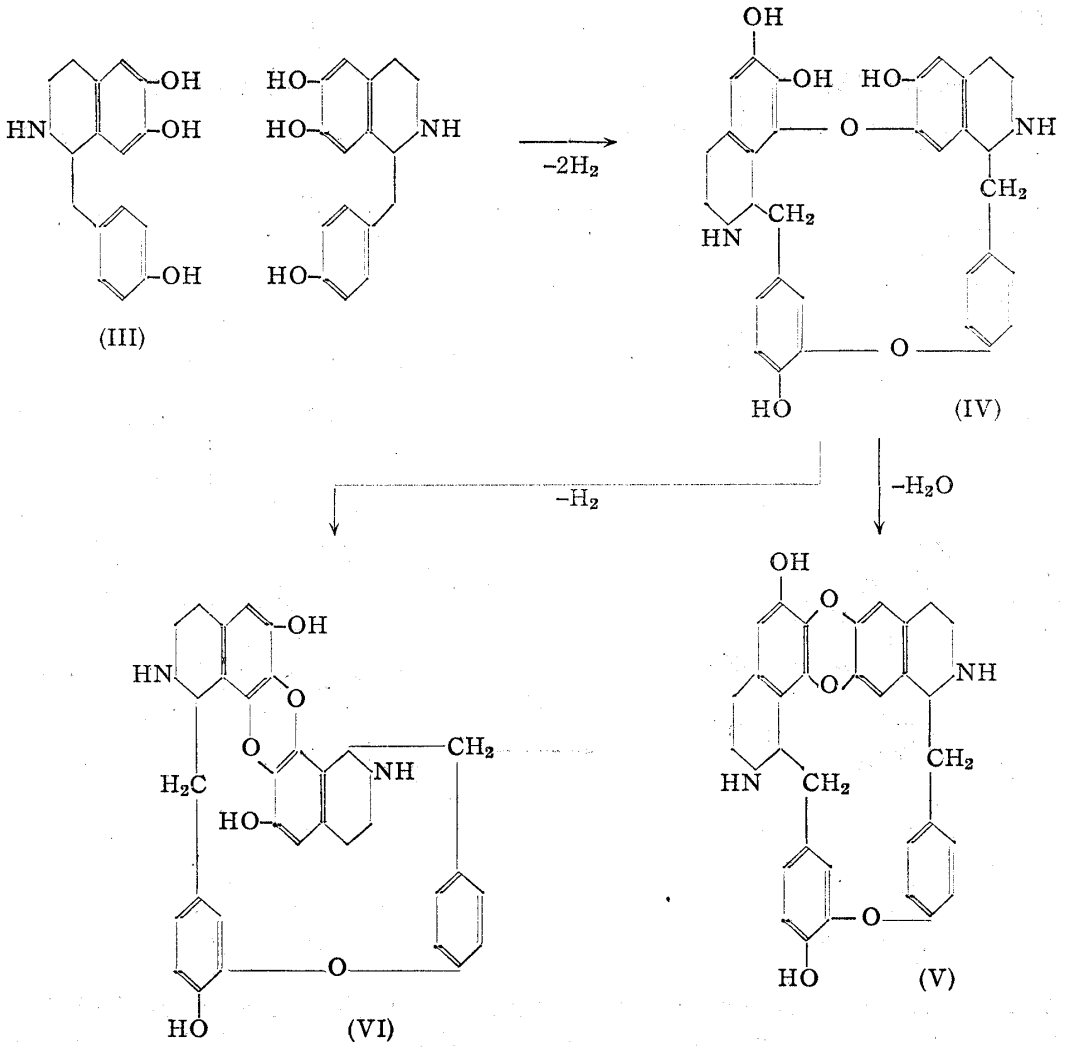
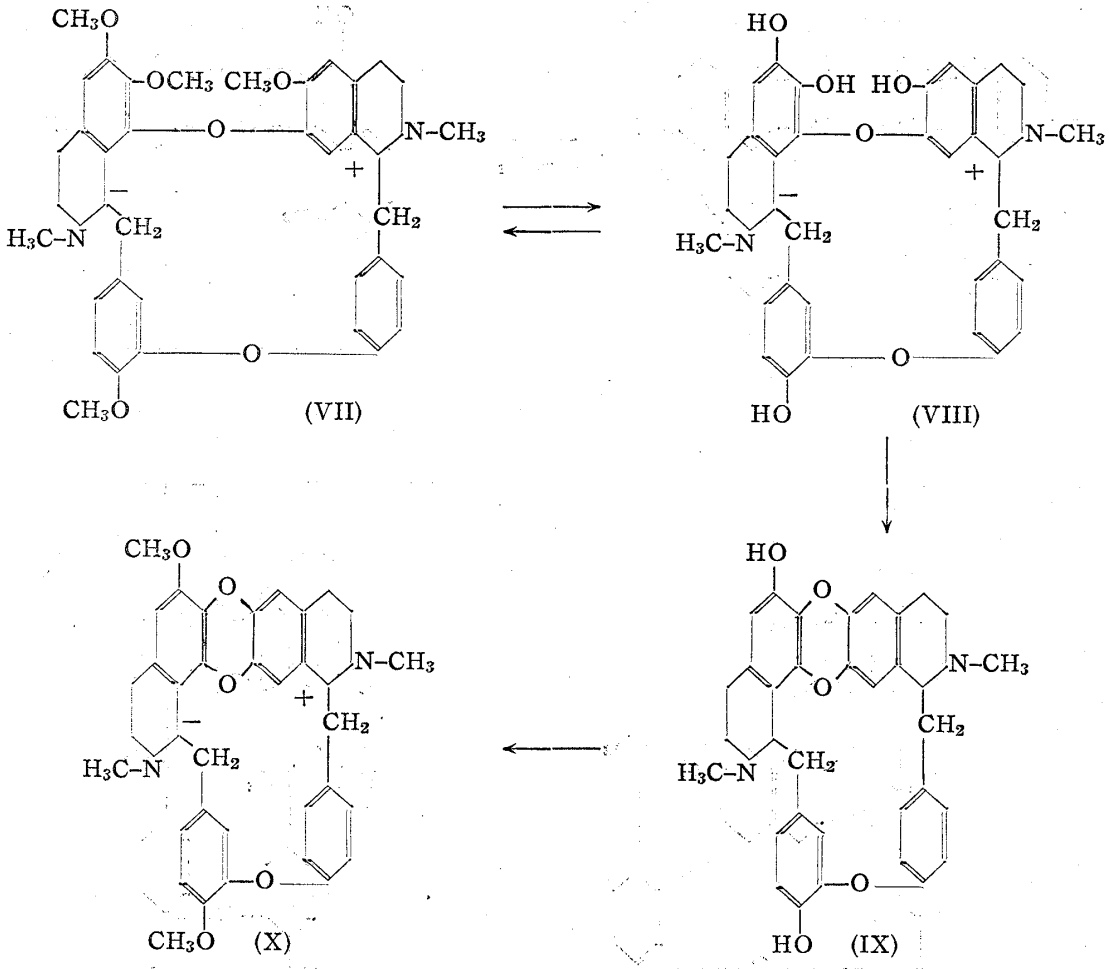
1) Part CX: F. Kusuda: This Bulletin, 1, 189(1953).
2) (13): M. Tomita, Y. Sasaki: This Bulletin, 1, 105(1953).
3) M. Tomita: Fortschr. Chem. org. Naturstoffe, 9, 175(1952).
4) M. Tomita, F. Kusuda: This Bulletin, 1, 1(1953).

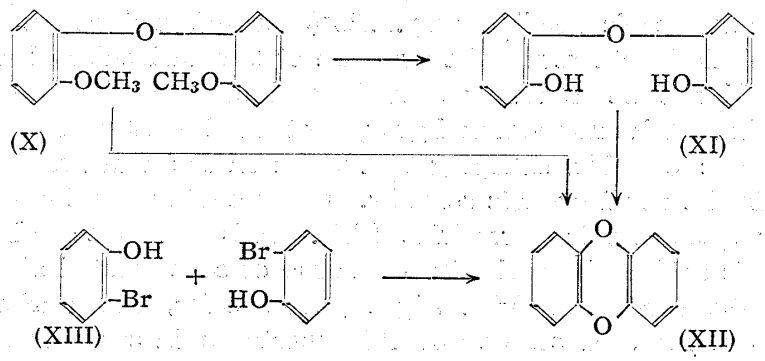


Some time ago, Kondo and Yano[5] reported that tetrandrine (VII)[6], when allowed to react with hydrobromic acid, yielded demethyltetrandrine, a phenolic base formed by the demethylation of its four methoxyl groups. In the present experiment the same reaction as above was applied to isotetrandrine. Isotetrandrine (VII), when heated with hydrobromic acid (d=1.78) at 100° for 3 hrs., or when heated with hydrobromic acid and glacial acetic acid in a sealed tube at 100° for 40 minutes, furnished demethylisotetrandrine (VIII). This substance forms microscopic needles, m. p. 230°(decomp.) and shows $[\alpha]_D^5$: +299.1° in pyridine. The analytical data reveal the presence of two molecules of water of crystallization, which could not be readily removed, and correspond to the composition of $C_{34}H_{34}O_6N_2.2H_2O$. It contains no methoxyl group by the Zeisel estimation and gives a green coloration with ferric chloride, changing to a violet on the addition of alkali. It is very sparingly soluble in the usual organic solvents. On methylation with diazomethane, this substance (VIII) regenerates isotetrandrine (VII). This substance (VIII) is dissolved in concentrated sulfuric acid, and on addition of a drop of concentrated nitric acid or a piece of potassium nitrate, produces only a slight yellow color, which after standing for a long time, changes to blue. A solution of this substance in concentrated sulfuric acid is

5) H. Kondo, K. Yano: J. Pharm. Soc. Japan, 49, 315(1929); *ibid.*, 50, 224(1930); *ibid.*, 52, 827 (1932); Ann., 497, 90(1932).
6) In formula (VII), the two centers of asymmetry in isoterandrine, are (−, +), whereas those in tetrandrine are (+, +). [cf. M. Tomita, E. Fujita: J. Pharm. Soc. Japan, 71, 1039(1951)].



allowed to stand for a while or warmed a little, after which concentrated nitric acid or potassium nitrate is added, when a blue color immediately results. This reaction indicates the presence of a diphenylene dioxide nucleus. In general, a group of the biscoclaurine type of bases, possessing the diphenylene dioxide nucleus, including the series of trilobine-isotrilobine, menisarine, etc., and their derivatives, give a positive test for this reaction.[7] Accordingly, in this case, it seems probable that by the action of concentrated sulfuric acid, demethylisotetrandrine (VIII) undergoes dehydration, followed by cyclization of a diphenylene dioxide nucleus, and the base of (IX) type may have been formed.



On the other hand, the following are known as the general method of synthesizing diphenylene dioxide derivatives. The first method by which, as described by Ullmann

7) M. Tomita: J. Pharm. Soc. Japan, 52, 889(1932); *ibid.*, 54, 893(1934).

and Stein[8], 2,2′-dimethoxydiphenyl ether (X) is allowed to react with hydrobromic acid, and by demethylation and subsequent cyclization, led directly to (XII). The second by which cyclization of 2,2′-dihydroxydiphenyl ether (XI) is effected by dehydration by means of hydrobromic acid; and the third, as employed by Tomita[9], of synthesizing diphenylene dioxide (XII) by condensation of the potassium salt of *o*-halophenol (XIII) in the presence of copper powder.

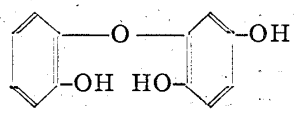
The present experiment was carried out under somewhat more powerful condition of demethylation than that referred to above. When demethylisotetrandrine (VIII) was heated with hydrobromic acid (d=1.78) in a sealed tube at 130° for 3 hrs., it yielded short pillar-shaped crystals, showing m. p. 290° (decomp.). This substance is a phenolic base with $[\alpha]_D^6$: +61.4° (pyridine), and gives no color reaction with ferric chloride. The analytical values correspond to the composition of $C_{34}H_{32}O_5N_2$, which is in perfect agreement with that of anhydro-demethylisotetrandrine (IX). Addition of concentrated nitric acid or a piece of potassium nitrate to a solution of this base in concentrated sulfuric acid gives a blue coloration. This color reaction resembles that for diphenylene dioxide seen among the trilobine-isotrilobine series, and (IX) base shows the same color reactions as trilobine or isotrilobine. On the other hand, isotetrandrine (VII), when allowed to react with hydrobromic acid under a more powerful condition of the above demethylation, also arrived at anhydro-demethylisotetrandrine (IX) in one step.

On mild acetylation with acetic anhydride, (IX) afforded an acetylated derivative which has a basic property. This substance crystallizes in the form of pillars, m. p. 210, $[\alpha]_D^{24}$: +118.6° (chloroform). The analytical figures represnt the compositon of the diacetate.

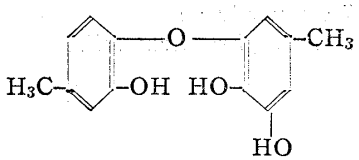
Methylation of anhydro-demethylisotetrandrine (IX) with diazomethane gives rise to O-methyl-anhydro-demethylisotetrandine (X), which crystallized in the form of rhombic pillars and melted at 272~274°, $[\alpha]_D^{24}$: +66.8° (chloroform). From the analytical results, it has the composition of $C_{36}H_{36}O_5N_2$, and contains two methoxyls. This substance produces a blue coloration with sulfuric-nitric acid. By oxidation with potassium permanganate, (X) yielded 2-methoxydiphenyl ether-5,4′-dicarboxylic acid.

From the above experimental results, it follows that since the two centers of asymmetry in isotetrandrine are (−, +), O-methyl-anhydro-demethylisotetrandrine (X) obtained from isotetrandrine (VII) is not identical with trilobine or isotrilobine itself, and hence must presumably be a new isomeride of the latter bases.

Prior to this, when one of the authors, Tomita[10], carried out the same mode of cyclization with hydrobromic acid on diphenyl ether derivatives possessing phenolic hydroxyl group such as 2,5,2′-trihydroxydiphenyl ether (XIV) or 2,3,2′-trihydroxy-5,4′-dimethyldiphenyl ether (XV) following the Ullmann method, he experienced that the reaction did not proceed smoothly, only a small amount of product showing the diphenylene dioxide reaction being obtained, or all the products became resinous.



(XIV)



(XV)

Contrary to this, as we have found this time, the similar reaction on demethylisotetrandrine proceeded very satisfactorily, and the yield of the cyclization to diphenylene

8) F. Ullmann, A. Stein: Ber., 39, 624 (1906).
9) M. Tomita: J. Pharm. Soc. Japan, 52, 429(1932).
10) M. Tomita: *Ibid.*, 56, 814(1936).

dioxide was good. This reason may be accounted for by the fact that the portion of the structure of (XV) type in the two isoquinoline residues of demethylisotetrandrine (VIII) molecule is fixed at the position which is liable to undergo dehydration. Fig. 1 and Fig. 2 are the molecular models of demethylisotetrandrine (VIII) and anhydro-demethylisotetrandrine (IX) which illustrate that the positions of the two hydroxyl groups in demethylisotetrandrine (VIII) are so close to each other that they readily form the diphenylene dioxide nucleus by undergoing dehydration.

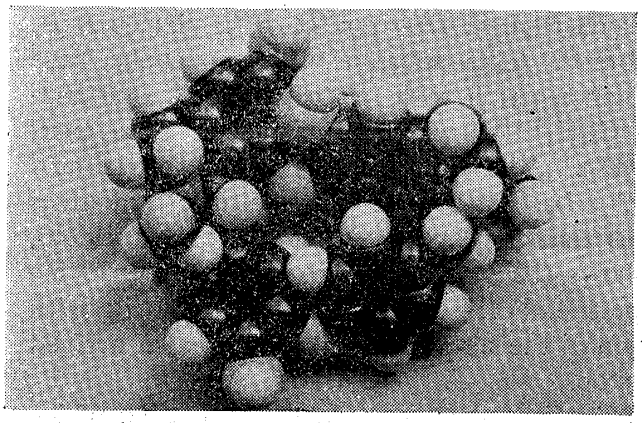


Fig. 1.
Demethylisotetrandrine (VIII)

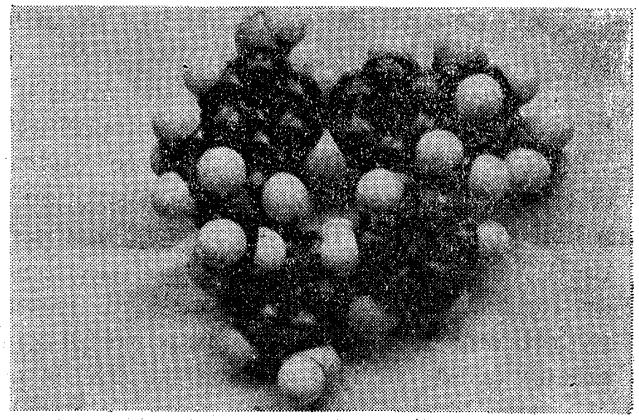


Fig. 2.
Anhydro-demethylisotetrandrine (IX)

In this reaction, addition of red phosphorus to hydrobromic acid showed no variation in the yield.

The ultraviolet absorption spectra of several kinds of above derivatives, derived from isotetrandrine, are shown in Figs. 3 and 4.

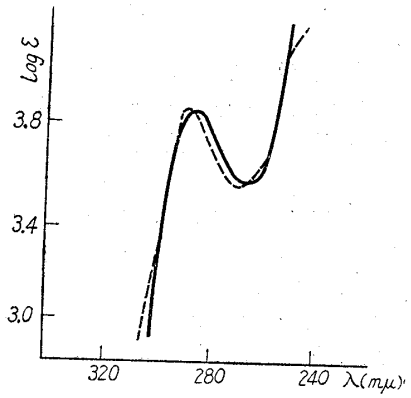


Fig. 3.
——·—— Isotetrandrine
- - - - - - - - Demethylisotetrandrine

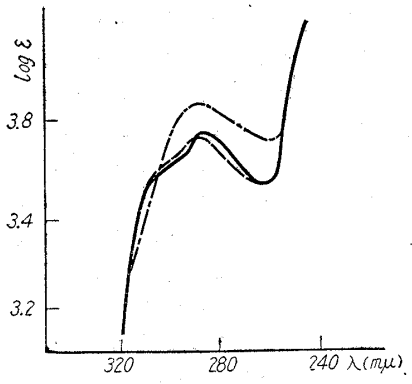


Fig. 4.
———— O-Methyl-anhydrodemethylisotetrandrine
— — — Trilobine or Isotrilobine
——·—— Anhydro-demethylisotetrandrine

As shown in Fig. 3, isotetrandrine (VII) (λ_{max} 282 mμ, log ε=3.85; λ_{min} 260 mμ, log ε=3.45) and demethylisotetrandrine (VIII) (λ_{max} 284 mμ, log ε=3.85; λ_{min} 260 mμ, log ε=3.48) have the same type of absorption curves, which are in exact accordance with those of the oxyacanthine-berbamine type of bases. Fig. 4 shows the absorption curves of anhydro-demethylisotetrandrine (IX) (λ_{max} 293 mμ, log ε=3.86; λ_{min} 260 mμ, log ε=3.67) and O-methyl-anhydro-demethylisotetrandrine (X) (λ_{max} 287 mμ, log ε=3.74; λ_{min} 261 mμ, log ε=3.49), which differ to some degree from those of the oxyacanthine-berbamine series in

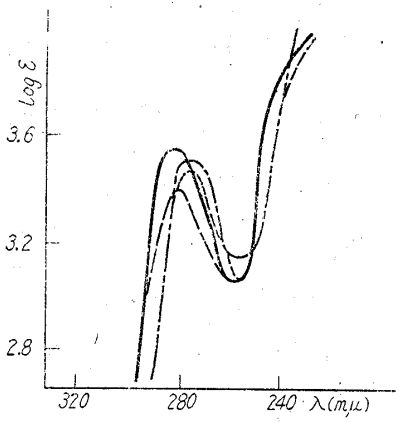


Fig. 5.
———— 2-Methoxy-5,4′-dimethyldiphenyl ether
——·—— 2,2′,3′-Trimethoxydiphenyl ether
— — — 2,2′3′-Trimethoxy-5,4′-dimethyldiphenyl ether
- - - - - - - - 2-Methoxydiphenyl ether

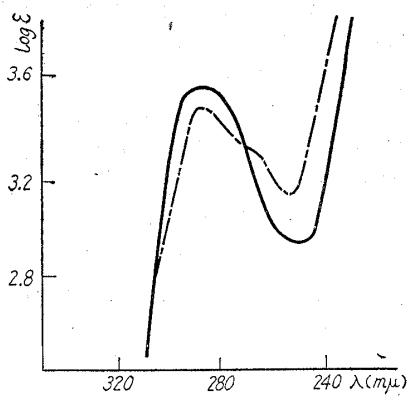


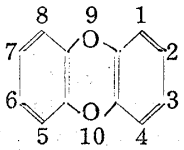
Fig. 6.
———— Diphenylene dioxide
——·—— 1-Methoxydiphenylene dioxide

that the maximum of absorption has shifted to a somewhat longer wave length range and has a broad absorption band. The above characteristics agree reasonably well with those of trilobine (I) or (II) (λ_{max} 287 mμ, log ε=3.73; λ_{min} 261 mμ, log ε=3.50) or demethyltrilobine or demethylisotrilobine[11]. Fig. 5 represents the absorption spectra of several kinds of methoxydiphenyl ether, including 2-methoxydiphenyl ether (λ_{max} 272 mμ, log ε=3.50; λ_{min} 250 mμ, log ε=3.00), 2-methoxy-5,4′-dimethyldiphenyl ether (λ_{max} 278 mμ, log ε=3.60; λ_{min} 252mμ, log ε=3.00), 2,2′,3′-trimethoxydiphenyl ether (λ_{max} 273 mμ, log ε=3.55; λ_{min} 250 mμ, log ε=3.10), and 2,2′,3′-trimethoxy-5,4′-dimethyldiphenyl ether (λ_{max} 275 mμ, log ε=3.45; λ_{min} 252 mμ, log ε=3.00), and Fig. 6, those of diphenylene dioxide (λ_{max} 290 mμ, log ε=3.60; λ_{min} 250 mμ, log ε=2.90) and 1-methoxydiphenylene dioxide (λ_{max} 290 mμ, log ε=3.50; λ_{min} 255 mμ, log ε=3.10).[12] As is apparent from Figs. 5 and 6, when the absorption spectra of methoxydiphenyl ether and methoxydiphenylene dioxide, which are respectively regarded as the fundamental skeletons constituting the molecular structures of the oxyacanthine-berbamine and trilobine-isotrilobine series, are compared, the maximum of absorption in the latter has shifted to a longer wave length range, and has a wide absorption band. This difference corresponds to that in absorption curves between the oxyacanthine-berbamine and trilobine-isotrilobine type of bases, and it may be attributable to the presence of a diphenylene dioxide nucleus.

The infrared absorption spectrum of O-methyl-anhydro-demethylisotetrandrine (X) also gave the same type as that of trilobine or isotrilobine, and there was found a detectable difference between the oxyacanthine-berbamine and trilobine-isotrilobine series. A detailed report will be published in the succeeding paper.

From the foregoing experiments, attempts to derive the base of a trilobine-isotrilobine type from isotetrandrine, one of the bases of oxyacanthine-berbamine series, have been

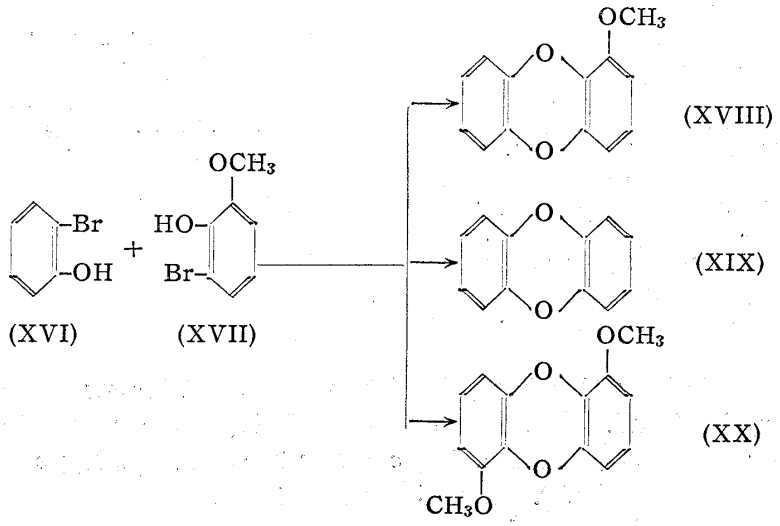
11) H. Kondo, E. Ochiai: J. Pharm. Soc. Japan, 49, 425(1929).
12) Nomenclature of diphenylene dioxide derivatives used is as follows;



[Beilsteins Handbuch der org. Chemie, 4 Aufl. Bd. XIX (1934); M. Tomita: J. Pharm. Soc. Japan, 58, 1060(1935)].

found successful, and an experimental evidence has been obtained for the view that in plant body, trilobine-isotrilobine type of bases may be formed by the dehydration of oxyacanthine-berbamine type of bases.

1-Methoxydiphenylene dioxide (XVIII), used for the measurement of the ultraviolet absorption spectrum, is a new compound that has not hitherto been described in litetrature. Its synthesis was effected by the condensation of the potassium salt of bromoguaiacol (XVII) with potassium salt of *o*-bromophenol (XVI), following the method[13] of synthesizing usual diphenylene dioxide derivatives, and a mixture of three kinds ((XVIII), (XIX) and (XX)) of diphenylene dioxide derivatives so obtained was separated by chromatography.



The authors wish to express their thanks to Mr. M. Akasu of Kaken Chemical Drug Co. Ltd., for the donation of isotetrandrine, and to the Ministry of Education for a Grant from the Scientific Research Fund.

Experimental[14]

(1) Demethylisotetrandrine (VIII)—(i) Using hydrobromic acid: A solution of 1 g. of isotetrandrine in 20 cc. of hydrobromic acid (d=1.78) was heated at 100° for 3 hrs. After the completion of the reaction the mixture was poured into 30 cc. of water, when the white hydrobromide precipitated. This was collected and dissolved in a small amount of methanol. The solution was then made alkaline with ammonia, and heated, depositing microscopic needles. The crude crystals were suspended in methanol and redissolved by addition of aqueous hydrobromic acid. Subsequently the solution was made alkaline with ammonia, and the base was purified by liberation, m.p. 230° (decomp.); yield, 0.8 g. This substance is very sparingly soluble in nearly all organic solvents such as ether, chloroform, benzene, alcohol, and acetone. A solution of this substance in concentrated sulfuric acid gives a yellow color on addition of a piece of potassium nitrate, which on standing for a while, changes to a greenish blue. After this is dissolved and kept standing for a while, a piece of potassium nitrate is added, when a greenish blue color immediately results. It gives a green color with ferric chloride, changing to violet on addition of alkali. No methoxyl group was found. $[\alpha]_D^5$: +299.1° (in pyridine, l=0.3 dm., c=0.79). *Anal.* Calcd. for $C_{34}H_{34}O_6N_2.2H_2O$: C, 67.75; H, 6.36; N, 4.65. Found: C, 67.39; H, 6.17; N, 4.70.

(ii) Using glacial acetic acid saturated with hydrobromic acid: To 1 g. of isotetrandrine was added 8 cc. of glacial acetic acid saturated with hydrobromic acid at 0°, and the mixture was heated in a sealed tube at 100° for 30 minutes. The content was poured into 50 cc. of water, and made alkaline with ammonia, and the depositing precipitate was collected by filtration. A suspension of the precipitate in a small portion of methanol was redissolved by the addition of aqueous hydrobromic acid, and made alkaline with ammonia. On warming, microscopic needles, m.p. 230° (decomp.), appeared. Yield, 0.6 g.

13) M. Tomita, T. Tani: J. Pharm. Soc. Japan, **62**, 476(1942).

14) All melting points are uncorrected. The authors wish to express their gratitude to Mr. K. Hozumi, Mr. K. Imaeda, and Miss H. Iwata in the Microanalytical Laboratory of the Pharmaceutical Institute, University of Kyoto, for carrying out the micronalyses reported herein.

(iii) Action of diazomethane on demethylisotetrandrine: 0.5 g. of demethylisotetrandrine was dissolved by warming in 30 cc. of tetrahydrofuran, and an ether solution of diazomethane prepared from nitrosomethylurea was added. The mixture was allowed to stand for 3 days. This manipulation was repeated once more by treating with an additional amount of an ether solution of diazomethane. The reaction mixture was filtered and the filtrate was freed from the solvent. The residue was chromatographed in benzene on alumina, and the first eluate recrystallized from ether-acetone, yielding 0.3 g. of the crystals, m.p. 178~180°, undepressed by admixture with isotetrandine, m.p. 181~182°.

(2) Anhydro-demethylisotetrandrine (IX)—(i) Starting with demethylisotetrandrine: A solution of 0.5 g of demethylisotetrandrine in 5 g. of hydrobromic acid (d=1.78) was heated in a sealed tube at 130~135° for 3 hrs. After the reaction was complete, the content was poured into a small amount of water and the hydrobromide deposited. This was dissolved in a small amount of methanol and rendered alkaline by the addition of ammonia. On gently warming, 0.4 g. of needles, m.p. 290°, crystallized out. They dissolve in concentrated sulfuric acid and on addition of a piece of potassium nitrate give a blue coloration. $[\alpha]_D^6$: +61.4° (in pyridine, l=0.3 dm., c=0.54). *Anal.* Calcd. for $C_{34}H_{32}O_5N_2$: C, 74.45; H, 5.83; N, 5.10. Found: C, 74.57; H, 6.00; N, 5.03.

(ii) Starting with isotetrandrine: A mixture of 1.5 g. of isotetrandrine and 50 cc. of hydrobromic acid (d=1.78) was heated in a sealed tube at 100° for 3 hrs. The reaction mixture was poured into 100 cc. of water and the depositing hydrobromide was collected by filtration. This was dissolved in a small portion of methanol, made weakly alkaline by the addition of ammonia, and warmed. Then, the first crop of 0.6 g. of demethylisotetrandrine (VIII) crystallizing in needles, m.p. 230° (decomp.), deposited. The mother liquor filtered from the above crystals was treated with an additional amount of ammonia, and warmed gently. The second crop of 0.25 g. of anhydro-demethylisotetrandrine (IX) crystallizing in short pillars, m.p. 290° (decomp.), was obtained. They give a blue coloration with sulfuric-nitric acids.

(iii) Anhydro-demethylisotetrandrine acetate: A mixture of 0.2 g. of anhydro-demethylisotetrandrine and 2 cc. of acetic anhydride was warmed on a water bath at 60° for 40 minutes. Then the reaction mixture was neutralized with potassium carbonate and extracted with chloroform. The extract was dried over anhydrous sodium sulfate, and the solvent removed. Recrystallization of the residue from methanol yielded needles, m.p. 210°; yield, 0.1 g. $[\alpha]_D^{24}$: +118.6° (in chloroform, l=0.3 dm., c=0.25). *Anal.* Calcd. for $C_{38}H_{36}O_7N_2 \cdot H_2O$: C, 70.2; H, 5.8. Found: C, 69.57; H, 5.63.

(3) O-Methyl-anhydro-demethylisotetrandrine (X)—1 g. of anhydro-demethylisotetrandrine (IX) was dissolved by warming in 30 cc. of tetrahydrofuran and mixed with an ether solution of diazomethane evolved from 3 g. of nitrosomethylurea. The mixture was allowed to stand for 3 days, and subsequently after treatment with an additional amount of an ether solution of diazomethane, for a further 3 days. The reaction mixture was filtered once, and the filtrate was freed from the solvent. The residue was dissolved in benzene and purified by chromatography on alumina. The first eluate afforded a slightly yellowish oily product, which on addition of ethanol crystallized in the form of rhombic pillars. Yield, 0.4 g. Recrystallized from acetone it showed m.p. 272~274°. This compound gives a blue coloration with sulfuric-nitric acids. $[\alpha]_D^{24}$: +66.8° (in chloroform, l=0.3 dm., c=0.59). *Anal.* Calcd. for $C_{36}H_{36}O_5N_2$: C, 74.96; H, 6.30; OCH_3, 10.76. Found: C, 74.76; H, 6.55; OCH_3, 10.41.

(4) Oxidation of O-Methyl-anhydro-demethylisotetrandrine (X) by potassium permanganate—A solution of 0.2 g. of (X) in a small amount of dilute sulfuric acid was neutralized with aqueous potassium carbonate, then aqueous potassium permanganate was added dropwise with vigorous stirring at room temperature, until the permanganate color disappeared. Manganese dioxide was filtered off and washed throughly with dilute alkali solution. The filtrate and the washings were combined and concentrated to a small volume. The solution was then acidified with hydrochloric acid, and extracted with ether. The ether extract was freed from the solvent and the residue was recrystallized from alcohol to m.p. 310°, undepressed by admixture with 2-methoxydiphenyl ether-5,4'-dicarboxylic acid.

(5) 1-Methoxydiphenylene dioxide (XVIII)—4.7 g. of *o*-bromophenol and 5.5 g. of *o*-bromoguaiacol was added to a solution of 2.1 g. of metallic sodium in methanol and the methanol distilled off under a reduced pressure. To the residue was added 0.7 g. of copper powder and 0.7 g. of anhydrous copper acetate, and the mixture was heated in an oil bath at 190~200° for 3.5 hrs. The reaction mixture was extracted with ether, the ether extract washed with 3% aqueous sodium hydroxide, and after drying with anhydrous potassium carbonate, the ether was removed, yielding 1.2 g. of the residue. This was dissolved in 20 cc. of benzene and passed through a columm of alumina (1×15 cm.) and the chromatogram developed with benzene. The benzene eluate was sectioned into 25 fractions, each consisting of 2 cc. Fractions 1~5 gave no product. Fractions 6~9 yielded crystals of m.p. 77~119°, and fractions 10~16, m.p. 118~127°, and fractions 17~25, m.p.

155～188°. The crystals obtained from fractions 6～9 were crystallized from petroleum ether and melted at 116～119°, either alone or in admixture with diphenylene dioxide (XIX). The crystals from fractions 10～16, when recrystallized from methanol, showed m.p. 127～128°, identical with 1-methoxydiphenylene dioxide (XVIII). Yield, 0.25 g. *Anal.* Calcd. for $C_{13}H_{10}O_3$: C, 72.89; H, 4.67; OCH_3, 14.48. Found: C, 72.56; H, 4.82; OCH_3, 15.06. The crystals from fractions 17～25 showed m.p. 193.5～195.5 after recrystallization from ether, identical with 1,5-dimethoxydiphenylene dioxide (XX). Yield, 0.05 g.

Summary

Attempts to derive O-methyl-anhydro-demethylisotetrandrine (X), which possesses a diphenylene dioxide nucleus, belonging to the trilobine-isotrilobine series, from isotetrandrine (VII), one of the bases of the oxyacanthine-berbamine type, were found successful. It has thus been clarified that this substance is a new isomeride of trilobine or isotrilobine, (I) or (II).

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89. Masao Tomita, Yasuo Inubushi, and Mutsuo Kozuka: Studies on the Alkaloids of Menispermaceous Plants. CXII. On the Structure of Biscoclaurine Alkaloids. (15). Synthesis of Trilobine-Type Alkaloid from Isotetrandrine. (2). Hofmann Degradation.

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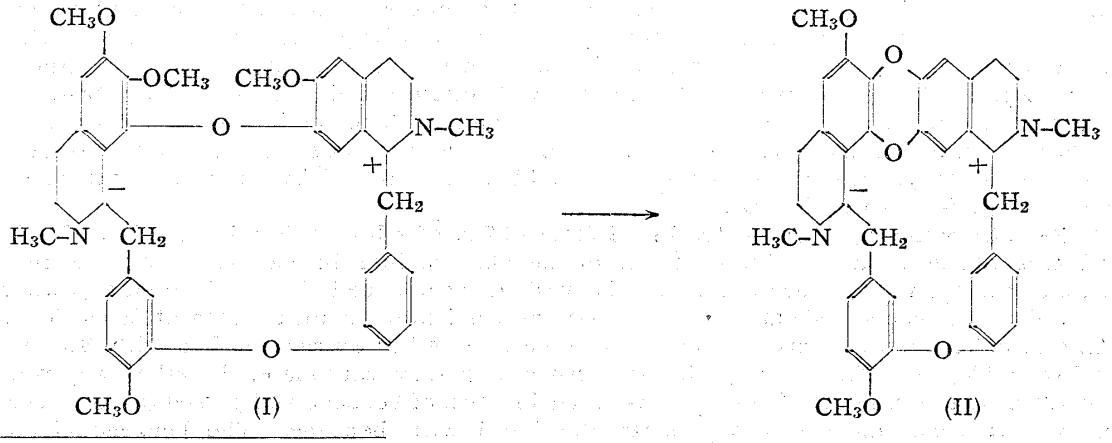
In the previous report[1] of this series, it was shown that O-methyl-anhydro-demethyl-isotetrandrine (II) was successfully derived from isotetrandrine (I) and that this substance (II) might be one of the isomers of trilobine ($[\alpha]_D^9$: +302.8° in chloroform) or isotrilobine ($[\alpha]_D^8$: +314.8° in chloroform), (III) or (IV), considering the steric configurations (−, +) of the two asymmetric centers in the molecule of isotetrandrine ($[\alpha]_D$: +146° in chloroform). It is natural, therefore, that this new base (II) cannot be compared directly with trilobine or isotrilobine but if this base (II) can be led to the optically inactive methine base with the elimination of its asymmetric centers by submitting to the first stage of Hofmann degradation, it seems possible to establish the structure of trilobine or isotrilobine (III or IV) by comparison with its corresponding inactive methine base derived from trilobine or isotrilobine. From such a point of view, the authors carried out the Hofmann degradation on O-methyl-anhydro-demethylisotetrandrine (II).



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1) M. Tomita, Y. Inubushi, M. Kozuka: Part CXI. This Bulletin, 1, 360(1953).