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THE SYNTHESIS OF dl-N-METHYLDIHYDROMENISARINE

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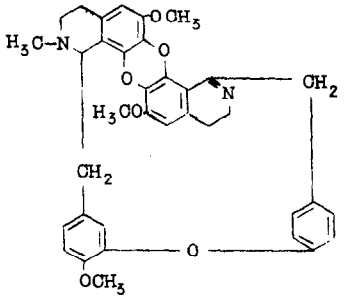
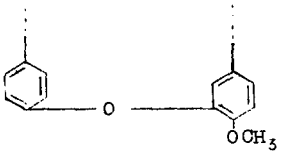
MENISARINE is one of the alkaloids present in Formosan Cocculus sarmentosus Diels (Menispermaceae), and one of the authors, Tomita[1] proposed by degradation reactions structure (Ia) or (Ib) for this alkaloid.



Ia



Ib

This paper presents a synthetic proof for the above proposed structure.

2,7-Bis-(2-aminoethyl)-4,9-dimethoxydibenzo-p-dioxin (II),[2] prepared previously, was allowed to condense with 6-methoxy-diphenylether-3,4'-diacetic acid (III)[3] by a high dilution method[4] to yield the bis-acetamide (IV).

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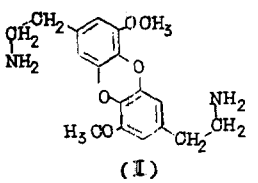
[1] M. Tomita, J. Pharm. Soc. Japan 55, 637 (1935); M. Tomita and C. Tani, Ibid. 62, 468 (1942).

[2] S. Ueda, J. Pharm. Soc. Japan 82, 714 (1962).

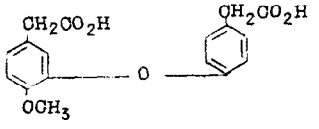
[3] H. Kondo and S. Uyeo, J. Pharm. Soc. Japan 53, 557 (1933).

[4] H. Stetter and J. Marx, Liebigs Ann. 607, 59 (1957); H. Taniyama and B. Yasui, J. Pharm. Soc. Japan 81, 1216 (1961).

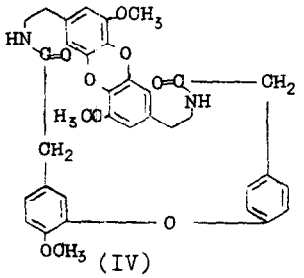
The compound (IV) was then subjected to the Bischler-Napieralski reaction, and the isoquinoline derivative thus obtained was led to the N-methyl-1,2,3,4-tetrahydroisoquinoline derivative (V) by reduction with sodium borohydride, followed by the N-methylation of the resulting tetrahydroderivative with formic acid and formaldehyde. The compound (V) was obtained at m.p. 180-183°, and gave identical infra-red spectra (in chloroform) with N-methyldihydromenisarine derived by the N-methylation of dihydromenisarine.[1]



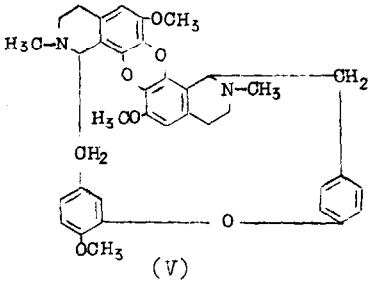
(I)



(III)



(IV)



(V)

Furthermore, the synthetic dl-N-methyldihydromenisarine (V), after conversion into the methosulphate, was submitted to the Hofmann degradation, and the methine base was obtained, whose infra-red (in chloroform) and ultra-violet spectra (in EtOH) were superimposable with those of natural N-methyldihydromenisarinemethylmethine.[1]*

Thus, it has been confirmed synthetically that menisarine has structure (Ia) or (Ib).

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* This compound is optically inactive.