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Masao Tomita : Studies on the Alkaloids of Magnoliaceous Plants. XIX.[1] The Structure of Magnolamine. (4).[2]

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Magnolamine was first described by Proskournina,[3] who isolated it from the leaves of Caucasian *Magnolia fuscata* and clarified it to belong to one of the biscoclaurine alkaloids. In an attempt to elucidate the structure of magnolamine, its tetramethyl ether was oxidized with potassium permanganate and a base of the corydaldine type and an acid (m.p. 280~281°, $C_{16}H_{14}O_7$; dimethyl ester, m.p. 130~131°), which she named magnolamic acid, were obtained. Magnolamic acid was next examined to determine the structure of the diphenyl ether portions of the molecule of magnolamine. A study of the alkali fusion products of magnolamic acid pointed to the structure of a dimethoxydiphenyl ether-dicarboxylic acid with both methoxyl groups on the same benzene ring. On this basis Proskournina proposed the structure (I) or (II) for the alkaloid.

This however proved to be incorrect when Tomita and Fujita[4] synthesized 2,3-dimethoxydiphenyl ether-5,4′-dicarboxylic acid (III) and 2,6-dimethoxydiphenyl ether-4,4′-dicarboxylic acid (IV) and compared them with the data of magnolamic acid and its dimethyl ester. On biogenetic considerations of the biscoclaurine alkaloids, Tomita, Fujita, and Nakamura[5] suggested that the formula (V) should be assigned to magnolamine and synthesized 3,4-dimethoxydiphenyl ether-6,4′-dicarboxylic acid (VI). Subsequently, Tomita and Kugo[2] also synthesized 2,3-dimethoxydiphenyl ether-6,4′-dicarboxylic acid (VII). Among these series of isomeric compounds synthesized, 3,4-dimethoxydiphenyl ether-6,4′-dicarboxylic acid (VI) and its dimethyl ester showed the same melting points as recorded for mognolamic acid and its dimethyl ester, which indicated that the most plausible formula[6] for magnolamine must be (V). At that time, however, it was impossible to communicate with Dr. Proskournina and confirm this by direct comparison with her sample.

Fortunately I was recently able, through the good offices of Prof. Dr. H. G. Boit of Humboldt University, Berlin, to obtain the samples of magnolamic acid and its dimethyl ester from Prof. Dr. N. F. Proskournina in Moscow and this enabled us to complete our studies. These materials and synthetic compounds showed no melting point depression on admixture (Table I) and their infrared spectra were identical. It follows, therefore, that magnolamic acid is 3,4-dimethoxydiphenyl ether-6,4′-dicarboxylic acid (VI) and hence magnolamine should be represented by formula (V).

As to the position of two phenolic hydroxyl groups in the benzene portions forming the tetrahydroisoquinoline rings of magnolamine, no confirmatory evidence has been brought forth as yet, but on biogenetic considerations of the biscoclaurine alkaloids

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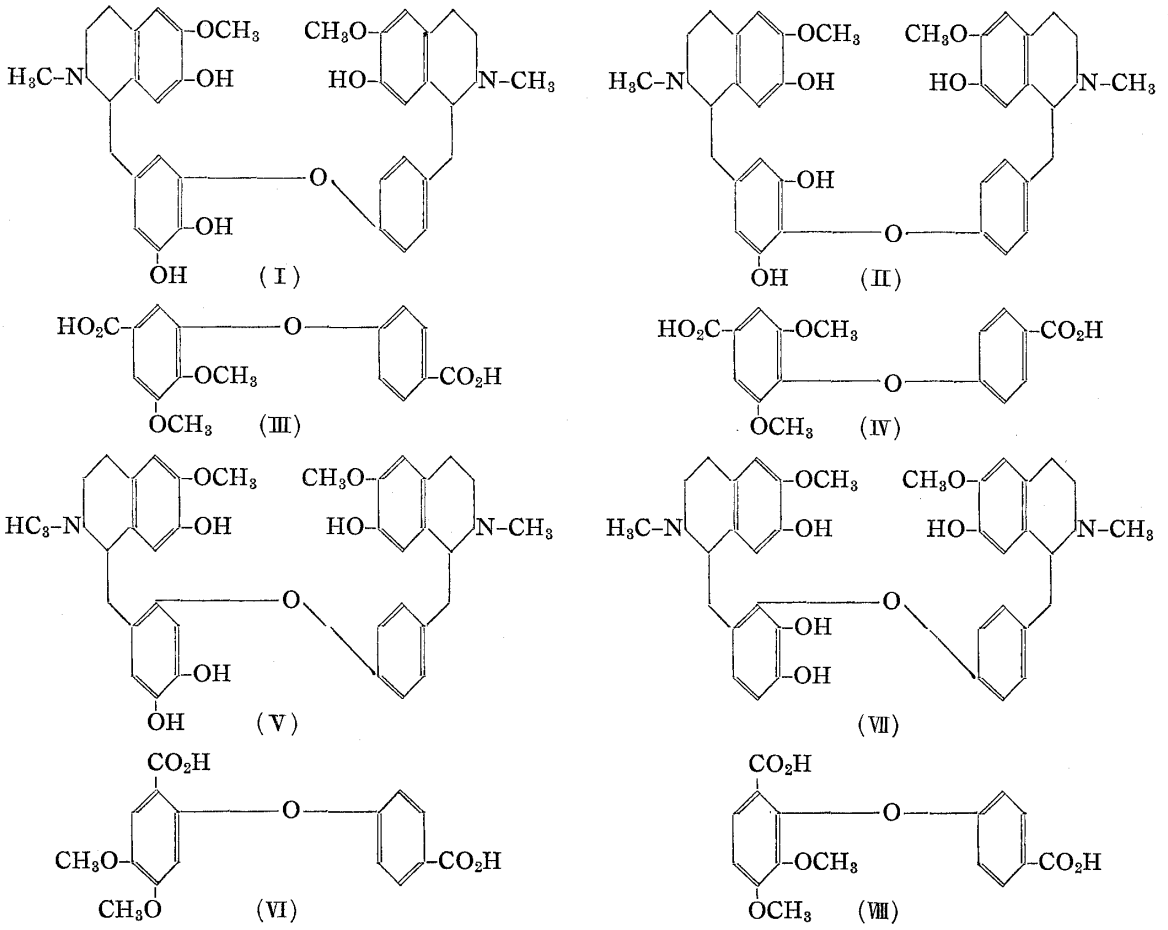

TABLE I.

	Recorded m.p.(°C)	Determined m.p.[a](°C)	Mixed m.p.[a]
Magnolamic acid[3]	280~281	280~283[b]	278~283
3,4-Dimethoxydiphenyl ether-6,4'-dicarboxylic acid (VI)[5]	285	285	
Dimethyl magnolamate[3]	130~131	131~132	131~134
Dimethyl ester[5] of (VI)	132.5~133	134(sint. at 131)	

a) m.p.s are uncorrected.

b) Proskournina's sample labeled m.p. 282~284°, but as determined by the author, it began to sinter at 270° and melted at 280~282° with effervescence.

it seems most probable to locate them in such positions as shown in formula (V).

I am indebted to Prof. Dr. N. F. Proskournina for the gift of samples for comparison in this work and to Prof. Dr. H. G. Boit of Humboldt University for his good offices in securing the sample on my behalf. I am also grateful to Messrs. Y. Matsui and M. Narisada of the Research Laboratory, Shionogi & Co., Ltd., for the infrared determinations.

Summary

The synthesized 3,4-dimethoxydiphenyl ether-6,4'-dicarboxylic acid (VI) and its dimethyl ester were compared directly with magnolamic acid and its dimethyl ester obtained by Proskournina and their identity was establisned. As a result it was confirmed that the most probable formula for magnolamine is (V).

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