by distillation was recrystallized from combined acetone and ether to colorless needles, m.p. 137–138° (0.02 g.). The melting point showed no depression when this substance was fused with 3-ethoxy-4-methoxy-6-ethylbenzoic acid, m.p. 137.5–138°, derived from coclaurine.

Summary

From the bark of *Magnolia obovata*, Thunb., belonging to the *Magnoliaceae*, a new alkaloid, named magnocurarine, was isolated, and its chemical structure has been determined as *N*-methylcoclaurine methyl hydroxide (II).

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318. Masao Tomita, Eiichi Fujita and Toshio Nakamura: Studies on the Alkaloids of Magnoliaceous Plants. II.

Structure of Magnolamine, an Alkaloid of *Magnolia fuscata*. (2)

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Proskurnina¹⁾ proposed an empirical formula $C_{36}H_{40}N_2O_7 = C_{32}H_{24}O(OH)_4(OCH_3)_2(NCH_3)_2$ for magnolamine, an alkaloid of Caucasian *Magnolia fuscata*, and by oxidation of its tetramethyl ether, obtained 1-keto-6,7-dimethoxy-*N*-methyl-tetrahydroisoquinoline and magnolamic acid, m.p. 280–281°, $C_{16}H_{14}O_7$ (dimethyl ester, m.p. 131–132°). Then he offered formula (I) or (II) for magnolamine on account of the oxidation process of its tetraethyl ether, and of obtaining 4-hydroxybenzoic acid by alkali fusion of magnolamic acid.

If formula (I) or (II) Proskurnina assumed is right, magnolamic acid should be 2,3-dimethoxydiphenyl ether-5,4'-dicarboxylic acid (III) or 2,6-dimethoxydiphenyl ether-4,4'-dicarboxylic acid (IV). On the other hand, however, we clarified that the data of (III), (IV) and their dimethyl esters we had prepared, were completely different from the ones of magnolamic acid. Due to the above result we pointed out in a former

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1) N. F. Proskurnina: J. Gen. Chem. U.S.S.R., **16**, 129 (1946); C. A. **41**, 460 (1947).

report²⁾ that both constitutional formulae (I) and (II) were not appropriate for magnolamine.

Magnolamine belongs to the dauricine type of biscoclaurine alkaloids and is not O₆-base of ordinary dauricine type, but O₇-base. An extra oxygen atom in magnolamine persists as a phenolic hydroxyl group on benzene nucleus forming diphenyl ether. Also, as a consequence of alkali fusion of magnolamic acid 4-hydroxybenzoic acid is grasped, so that two methoxyl groups in magnolamic acid must exist on the same benzene nucleus.

On the basis of above experimental results by Proskurnina and our knowledge obtained, and also when we surmise the mechanism of formation of magnolamine in plants, considering the process of biogenesis that biscoclaurine alkaloid is produced from coclaurine as the original substance, following matter can be considered. Namely, when we assume the structure of magnolamine as composed of one component coclaurine (V), and the other hydroxycoclaurine (VI), formula (VII) or (VIII) can be gained.

In other words, according to whether the diphenyl ether linkage is present in the 6-position of hydroxycoclaurine molecule (VI) or in the 2-position, (VII) or (VIII) is derived as a constitutional formula of magnolamine.

Yet we know the following experimental fact. In the instance of 1-methyl-3,4-dihydroxybenzene, etc., substitution reaction is prone to take place ordinarily in the 6-position rather than in the 2-position.

From this idea, formula (VII) is surmised to be rational for the structure of magnolamine. Therefore, if magnolamine has the structure (VII), magnolamic acid must be 3,4-dimethoxydiphenyl ether-6,4'-dicarboxylic acid (XI, R=H).

2) M. Tomita, E. Fujita: This Journal, **70**, 411 (1950); C. A. **45**, 2492 (1951).

From the foregoing view-point, we synthesized the dimethyl ester (XI, R=CH₃) from methyl 6-bromoveratrate (IX) and methyl 4-hydroxybenzoate (X) by Ullmann's reaction. By saponification of this substance the free acid (XI, R=H) is obtained. As we expected, the data of the acid obtained are identical with those of magnolamic acid as shown in the following table.

	Acid	Methyl ester
Magnolamic acid	C ₁₆ H ₁₄ O ₇ m.p. 280-281°	C ₁₈ H ₁₈ O ₇ m.p. 131-132°
C ₁₆ H ₁₄ O ₇ m.p. 285°	C ₁₈ H ₁₈ O ₇ m.p. 132.5-133°

From the experimental results obtained and from the view-point of biogenesis regarding biscoclaurine alkaloids, it is considered to be most rational that the structure of magnolamine should be represented by formula (VII).

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Experimental

Methyl 3,4-dimethoxydiphenyl ether-6,4'-dicarboxylate (XI, R=CH₃)—0.3 g. of metallic potassium is dissolved in 8 cc. of anhydrous methanol, and methanol solution of 1.1 g. of methyl *p*-hydroxybenzoate is added, and the solvent is removed under diminished pressure to dryness. Then 2 g. of methyl 6-bromoveratrate, 0.1 g. of Natur Kupfer C and 0.1 g. of anhydrous copper acetate are added, mixed well, and the mixture is heated in an oil bath at 200° for 5 hrs. The reaction mixture is repeatedly extracted with warm ether, and crystals deposit on standing of the ethereal extract. These crystals are separated, dissolved in methanol, and, after decoloration with charcoal, recrystallized from methanol, and 0.96 g. of colorless prismatic crystals, m.p. 132.5-133°, are obtained. *Anal.* Calcd. for C₁₈H₁₈O₇: C, 62.42; H, 5.24. Found: C, 62.23, 62.51; H, 5.38, 4.80.

3,4-Dimethoxydiphenyl ether-6,4'-dicarboxylic acid (XI, R=H)—Dimethyl ester is heated with *N*-alcoholic potassium hydroxide solution in a water bath for 2 hrs. and hydrolysis is carried out. The solvent is removed, the residue dissolved in water, and by acidification with hydrochloric acid, precipitate deposits. This is extracted with ether, the solvent is removed after drying of the ethereal extract with anhydrous sodium sulfate, and the residue is recrystallized from acetone, to colorless minute crystals, m.p. 285°. This acid melts at 288° in vacuo. *Anal.* Calcd. for C₁₆H₁₄O₇: C, 60.38; H, 4.43. Found: C, 59.91, 60.40; H, 4.60, 4.50.

Summary

The authors synthesized 3,4-dimethoxydiphenyl ether-6,4'-dicarboxylic acid (XI, R=H), m.p. 285°, and its dimethyl ester (XI, R=CH₃), m.p. 132.5-133°, from methyl 6-bromoveratrate (IX) and methyl 4-hydroxybenzoate (X) by Ullmann's reaction. The data of these substances were found to be quite identical with those of magnolamic acid, m.p. 280-281°, and its dimethyl ester, m.p. 131-132°. According to these experimental results and from the view-point of the biogenesis of biscoclaurine alkaloids, the presumption of formula (VII) for magnolamine seems to be most rational.

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