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Nobusuke Kawano, Hiroshi Miura, and Eiko Matsuishi : The Partial Demethylation of Flavones. Ⅲ.*1 Preparation of Rhamnetin and 7-O-Methylmyricetin.

(*Faculty of Pharmaceutical Sciences, Nagasaki University**2)

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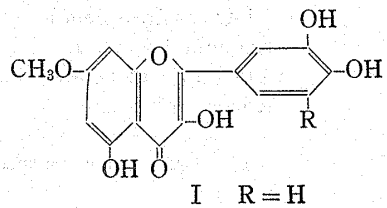
The synthesis of rhamnetin (I) has been reported by some workers.[1] However, none of them used the partial demethylation procedure of quercetin pentamethyl ether. We obtained rhamnetin from it and 7-O-methylmyricetin (Ⅱ)from myricetin hexamethyl ether by partial demethylation.



I R=H
Ⅱ R=OH

Reaction condition used was same with that in the case of the demethylation of apigenin trimethyl ether to genkwanin.[2] Rhamnetin was identified with a synthetic sample[1b] in itself and its acetate. When demethylated similarly myricetin hexamethyl ether[3] afforded a monomethyl ether of m.p. 267~268°. It was a new compound but should be 7-O-methylmyricetin (Ⅱ) because the observations reported by Simpson and Beton[4] and by this series of paper*1 showed that the 7-methoxyl group in flavones is fairly resistant to demethylation. The UV spectrum of this compound is in accord with the structure (Ⅱ) because this compoud as well as rhamnetin exhibits no bathochromic shift of the low-wavelength absorption band on addition of a little fused sodium acetate[5] as shown in Table I. The compound (Ⅱ)

Table I. Effect of Sodium Acetate on Low-Wavelength Absorption Band of UV Spectra

Compounds	λ_{max} (mμ)		$\Delta\lambda$
	EtOH	EtOH-NaOAc	
Quercetin	257	268	11
Rhamnetin	257	257	0
Myricetin	255	266	11
Mono-O-methylmyricetin	255	255	0

gives pentaacetate, m.p. 220~222° and pentaethyl ether, m.p. 133~134°. The NMR spectra of the pentaacetate and the related compounds also suggested that the monomethyl ether should be 7-O-methylmyricetin (Ⅱ) as shown in Table Ⅱ, in which the signals of rhamnetin tetraacetate are included.

*1 Part Ⅱ. This Bulletin, **15**, 232 (1967).
*2 4-23 Bunkyo-cho, Nagasaki (河野信助, 三浦博史, 松石英子).

1) *a*) R. Kuhn, I. Löw : Ber., **77**, 211 (1944). *b*) M. Shimizu, G. Ohta : Yakugaku Zasshi, **71**, 879 (1951). *c*) A. C. Jain, K. S. Pankajamani, T. R. Seshadri : J. Sci. Ind. Research (India), **12B**, 127 (1953).
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5) L. Jurd, R. M. Horowitz : J. Org. Chem., **22**, 1618 (1957).

Table II. NMR Signals (δ p.p.m.) of Methyl Protons[a)]

Compounds	Assigned position in flavone nucleus					
	7	5	3	3′	4′	5′
Hexa-O-methylmyricetin	3.79	3.97	4.06	3.88	3.88	3.88
Myricetin hexaacetate	(2.28)	(2.40)	(2.36)	(2.28)	(2.36)	(2.28)
Mono-O-methylmyricetin pentaacetate	3.76	(2.44)	(2.36)	(2.27)	(2.36)	(2.27)
Penta-O-methylquercetin	3.81	3.88	4.04	3.88	3.86	
Quercetin pentaactate	(2.24)	(2.41)	(2.28)	(2.28)	(2.28)	
Rhamnetin tetraacetate	3.76	(2.40)	(2.27)	(2.27)	(2.27)	
Tri-O-methylapigenin	3.82	3.82			3.72	
Apigenin triacetate	(2.27)	(2.48)			(2.24)	
Genkwanin diacetate	3.81	(2.51)			(2.26)	
Acacetin diacetate	(2.28)	(2.49)			3.74	

a) Figures in parentheses show the chemical shifts of acetyl protons.

Experimental*3

Rhamnetin (I)——A mixture of penta-O-methylquercetin (m.p. 145~146°, 0.5 g.), phenol (0.5 g.), Ac_2O (0.5 ml.), and hydroiodic acid (d=1.7, 7.5 ml.) was heated for 1 hr. in an oil bath at 120°, then poured into water (100 ml.) containing excess $NaHSO_3$ to give yellow substance which was filtered, washd with water and recrystallized from ethanol to afford yellow crystals (120 mg.), m.p. 280~282°. Further recrystallizations furnished minute yellow crystals, m.p. 286~286.5°, identical with synthetic[1b)] rhamnetin by admixture and IR spectrum. *Anal.* Calcd. for $C_{16}H_{12}O_7$: C, 60.76; H, 3.82. Found: C, 60.49; H, 3.88.

Tetraacetate——Above rhamnetin was acetylated with Ac_2O and pyridine to give almost colorless needles, m.p. and mixed m.p. 189~190°(lit.[1a)] 186~188°). *Anal.* Calcd. for $C_{24}H_{20}O_{11}$: C, 59.50; H, 4.16. Found: C, 59.49; H, 4.10.

7-O-Methylmyricetin (II)——Hexa-O-methylmyricetin[3)] (m.p. 152~153°, 0.5 g.) was demethylated as described above to give yellow crystals (260 mg.), m.p. 253~255°. Further recrystallizations from methanol afforded yellow prisms, m.p. 267~268°. *Anal.* Calcd. for $C_{16}H_{12}O_8$: C, 57.83; H, 3.64. Found: C, 57.64; H, 3.46.

Pentaacetate——Colorless needles, m.p. 220~222°. *Anal.* Calcd. for $C_{26}H_{22}O_{13}$: C, 57.58; H, 4.09. Found: C, 57.53; H, 3.96. NMR data are in the Table I.

Pentaethyl Ether——7-O-Methylmyricetin (m.p. 266~268°, 440 mg.) was ethylated with diethyl sulfate (5 ml.) and 30% KOH solution (ca. 8 ml.). Recrystallization of the crude product from ethanol gave cream-colored needles (130 mg.), m.p. 133~134°. *Anal.* Calcd. for $C_{26}H_{32}O_8$: C, 66.08; H, 6.83. Found: C, 66.17; H, 6.58.

*3 Melting Points were uncorrected. NMR spectra were determined on a Hitachi H-60 instrument with pyridine as solvent and tetramethylsilane as internal reference. UV spectra were measured by a Hitachi ESP-2 Recording Spectrophotometer.