lactone (XI), methyl D-glucaro-(1→4)-lactonate (XII), ethyl D-glucaro-(1→4)-lactonate (XIII), L-gulonolactone (XIV) and D-mannuronolactone (XVI) were obtained from Chugai Pharmaceutical Co., Ltd.

Urine Samples——Samples of human urines were obtained from this laboratory. From rats (male Donryu rats, body weight: 300—350 g) and guinea pigs (male, body weight: 450—550 g) maintained on normal diets in metabolism cages 24-hour urine samples were collected without any preservative in the collecting vessels. Urines were stored at 0° if examined within 24 hr of collection, or otherwise stored at −20°.

Method of Administration——To man test compounds were administered orally with water. Freshly prepared aqueous solutions of I, II and III were given orally in 1 ml to rat and guinea pig using stomach tube or catheter. For intraperitoneal or intravenous injection I, II and III were dissolved in 0.9% saline just before use and given in 1 ml. IX was suspended in 5% *gummi arabicum* solution and the suspension was given orally or intraperitoneally in 1 ml.

Determination of D-Glucaric Acid (V)——Determination of V in urine was performed according to "Procedure I" of the method reported earlier.[1]

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Synthesis of Coumurrayin

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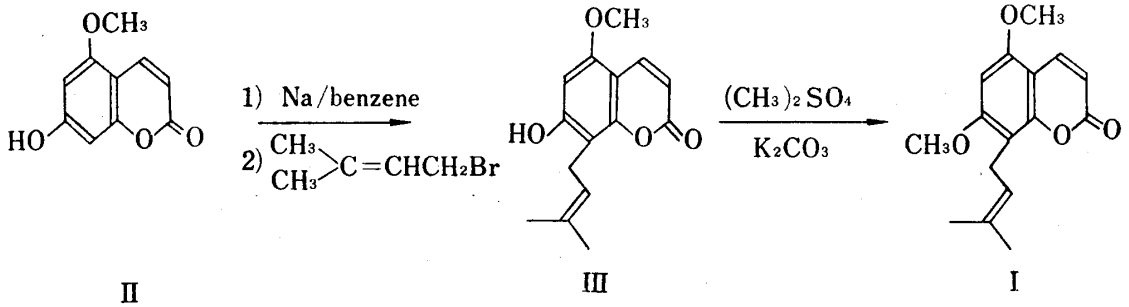
Recently, the structure of coumurrayin which was isolated from the ripe fruits of *Murraya paniculata* (L.) JACK (Rutaceae) has been elucidated as I by E. Ramstad, *et al.*[2] This paper deals with the synthesis of coumurrayin (I) from 7-hydroxy-5-methoxycoumarin (II).[3]



II III I

When sodium salt of II was treated with freshly distilled 1-bromo-3-methyl-2-butene in dry benzene under reflux, the 3-methyl-2-butenyl substituent was introduced to the expected C_8-position in II leading to 7-hydroxy-8-(3-methyl-2-butenyl)-5-methoxycoumarin (III). The structure of III was supported by the infrared (IR) absorption bands (in KBr) at 3360, 1690, 1600 and 1575 cm^{-1} and the nuclear magnetic resonance (NMR) spectrum of III taken in deuteropyridine, 1.67 (3H, broad singlet), 1.96 (3H, broad singlet), 3.80 (2H, broad doublet, J=7 cps) and 5.65 ppm (1H, broad triplet, J=7 cps), indicating the presence of a 3-methyl-

1) Location: *Yagotourayama, Tenpaku-cho, Showa-ku, Nagoya.*
2) E. Ramstad, W.C. Lin, T. Lin and W. Koo, *Tetrahedron Letters*, **1968**, 811.
3) T.R. Seshadri and M.S. Sood, *Indian J. Chem.*, 3, 354 (1965) [*C.A.*, **63**, 18009 (1965)].

2-butenyl group in III. Methylation of III with dimethyl sulfate in an alkaline medium gave the 5,7-dimethoxy derivative in good yield.

All physical properties of the product described in the experimental part were identical with those of natural coumurrayin (I) cited in the literature.[2]

Experimental[4]

7-Hydroxy-5-methoxycoumarin (II)——This compound was prepared by the slightly modified method of Seshadri, *et al.*[3] The cyclization was carried out in the presence of a small amount of iodine; a mixture of 2,4-dihydroxy-6-methoxybenzaldehyde (4 g), NaOAc (6 g) and Ac_2O (13.2 g) containing iodine (80 mg) was heated initially at 120° for 2 hr, and then at 180—185° for additional 4 hr. After treating the reaction mixture with a small amount of H_2O to decompose excess Ac_2O, the separated crystalline product was taken up in ether. The ether solution was washed several times with dil. $NaHCO_3$ then H_2O, and dried over Na_2SO_4. Removal of the solvent left a crystalline solid which was chromatographed on silicagel (Mallinckrodt, 100 mesh) and eluted with $CHCl_3$ to give a white solid. Recrystallization from AcOEt afforded colorless needles of 7-acetoxy-5-methoxycoumarin (2.5 g), mp 132—135°. Mass *m/e*: 234 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1775, 1750, 1615, 1575, 1195, 1105 and 850. NMR (in $CDCl_3$) ppm: 2.33 (3H, s), 3.93 (3H, s), 6.29 (1H, d, $J=9.5$ cps), 6.52 (1H, d, $J=2$ cps), 6.73 (1H, d, $J=2$ cps) and 8.03 (1H, d, $J=9.5$ cps). *Anal.* Calcd. for $C_{12}H_{10}O_5$: C, 61.54; H, 4.30. Found: C, 61.50; H, 4.34. The 7-acetoxy derivative (2 g) thus obtained was added to a solution of ethanolic H_2SO_4 (prepared from EtOH (67 ml), H_2O (33 ml) and conc. H_2SO_4 (5.2 ml)) and the resulting reaction mixture was heated under reflux for about 1 hr. After cooling, the separated crystals were collected by filtration. The filtrate was neutralized with $NaHCO_3$ and evaporated to dryness under reduced pressure. The residue was extracted with hot AcOEt, dried over Na_2SO_4 and evaporated to give the second crop of crystals which was combined with the first crop of the crystals obtained above. Recrystallization from MeOH afforded colorless needles of II (1.384 g), mp 244—245°. Mass *m/e*: 192 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 3230, 1690, 1600, 1245, 1165 and 830. NMR (in DMSO) ppm: 3.87 (3H, s), 6.08 (1H, d, $J=9.5$ cps), 6.33 (2H, broad s) and 7.93 (1H, d, $J=9.5$ cps). *Anal.* Calcd. for $C_{10}H_8O_4$: C, 62.50; H, 4.20. Found: C, 62.68; H, 4.13.

7-Hydroxy-8-(3-methyl-2-butenyl)-5-methoxycoumarin (III)——To a solution of Na (96 mg) in abs. EtOH (16 ml) was added 7-hydroxy-5-methoxycoumarin (II) (800 mg), and the resulting solution was evaporated to dryness under reduced pressure. The residual yellow crystals were suspended in dry benzene and evaporated again to remove a trace of H_2O completely. The residue was again suspended in dry benzene (50 ml), to which was added dropwise 1-bromo-3-methyl-2-butene (745 mg) under cooling. The reaction temperature was gradually rised to 50° and kept for 1 hr with stirring. The mixture was then refluxed for additional 3 hr. After cooling, the deposited precipitate was collected by filtration and washed with THF. The washings and the reaction filtrate were combined and evaporated to dryness under reduced pressure. The residual crystalline solid was chromatographed on silicagel (Wako-gel, C-100), eluted with $CHCl_3$ and recrystallized from MeOH to give colorless needles (85 mg), mp 196—197°. Mass *m/e*: 260 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3360, 1690, 1600, 1575, 1310, 1250, 1130 and 820. NMR (in C_5D_5N) ppm: 1.67 (3H, broad s), 1.96 (3H, broad s), 3.68 (3H, s), 3.80 (2H, broad d, $J=7$ cps), 5.65 (1H, broad t, $J=7$ cps), 6.20 (1H, d, $J=9.5$ cps), 6.55 (1H, s) and 7.97 (1H, d, $J=9.5$ cps). *Anal.* Calcd. for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20. Found: C, 68.95; H, 6.14.

Coumurrayin {5,7-dimethoxy-8-(3-methyl-2-butenyl)coumarin} (I)——A mixture of III (80 mg), Me_2SO_4 (47 mg) and K_2CO_3 (85 mg) in dry acetone (2 ml) was refluxed for 3 hr with stirring. After cool, the mixture was acidified with AcOH and evaporated to dryness under reduced pressure. To the residue was added a small amount of dil. NaOH to make the solution slightly basic, and extracted with CH_2Cl_2. The extract was washed with H_2O and dried over Na_2SO_4. Evaporation of the solvent gave a crystalline solid which was recrystallized from MeOH to afford colorless needles (69 mg), mp 156—157°. Mass *m/e*: 274 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1713, 1609, 1502, 1450, 1430, 1329, 1252, 1228, 1163, 1129, 1118, 814 and 645.[5] NMR (in $CDCl_3$) ppm: 1.66 (3H, broad s), 1.82 (3H, broad s), 3.45 (2H, broad d, $J=7$ cps), 3.94 (6H, s), 5.23 (1H, broad t, $J=7$ cps), 6.12 (1H, d, $J=9.5$ cps), 6.33 (1H, s) and 7.97 (1H, d, $J=9.5$ cps). *Anal.* Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 69.84; H, 6.56.

4) All melting points are uncorrected. The spectra were recorded on the following instruments: IR, Nihon-Bunko IR-E; Mass, Hitachi RMU-6-E; NMR, Varian A-60 using TMS as an internal standard (TMS=0 ppm).

5) This spectrum was recorded on a Nihon-Bunko IR-G.