# Prenylcoumarin Derivatives from the Leaves of An Indonesian Medicinal Plant *Murraya paniculata* (Rutaceae)

Takeshi KINOSHITA*,[a] and Kurnia FIRMAN[b]

*Faculty of Pharmaceutical Sciences, Teikyo University,[a] 1091–1 Suarashi, Sagamiko-machi, Kanagawa 199–01, Japan and Department of Pharmacy, Institut Teknologi Bandung,[b] Jalan Ganeca 10, Bandung 40132, Indonesia.*
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**A new prenylcoumarin was isolated from the leaves of *Murraya paniculata* (Rutaceae), and its structure was elucidated as 5,7-dimethoxy-8-[(*Z*)-3′-methylbutan-1′,3′-dienyl]coumarin on the basis of spectroscopic evidence. Five other coumarins were also obtained and identified with the known compounds coumurrayin, 5,7-dimethoxy-8-(3′-methyl-2′-oxobutyl)coumarin, toddalenone, toddasin and aurapten.**

**Key words** *Murraya paniculata*; Rutaceae; prenylcoumarin; 5,7-dimethoxy-8-[(*Z*)-3′-methylbutan-1′,3′-dienyl]coumarin; *cis*-dehydrocoumurrayin

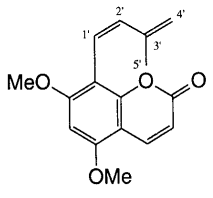
In recent papers[1] we reported the isolation of highly oxygenated flavonoids as major constituents of an Indonesian medicinal plant *Murraya paniculata* (L.) JACK (Rutaceae). Further investigation of the remaining minor fractions have shown the occurrence of several coumarins. The present paper deals with the isolation and characterization of coumarin derivatives, including one new compound, from the leaves of *M. paniculata* of Indonesian origin.

## Results and Discussion

The chloroform extract of the dried leaves of *M. paniculata* was repeatedly chromatographed on silica gel, Sephadex LH-20 and reversed-phase silica gel to afford compounds **1**—**6**. Compounds **1** and **2** were readily identified from physical and spectroscopic data as coumurrayin[2] and 5,7-dimethoxy-8-(3′-methyl-2′-oxobutyl)coumarin,[3] respectively, by comparison with those reported in the literature. Compounds **3** and **4** were identified as toddalenone[4] and toddasin,[5] respectively, by direct comparison with authentic samples. Toddalenone possesses a characteristic (*E*)-3-oxo-1-butenyl chain at C-8 of the 5,7-dimethoxycoumarin nucleus which is one carbon short of ordinary prenyl units. It was isolated from a rutaceous plant *Toddalia asiatica*[4] and is also known from *Murraya gleinei*.[6] Toddasin was an optically inactive dimeric coumarin derivative isolated from *T. asiatica*,[5] and this is the first report of isolation from plant sources other than the genus *Toddalia*. Compound **5** was characterized as 7-*O*-geranylcoumarin from spectroscopic data, and found to be identical to aurapten.[7] This coumarin derivative is known to occur widely in the genus *Citrus*,[7] and its presence in the genus *Murraya* was also confirmed by this study.

Compound **6** was obtained as colorless needles of mp 114—116 °C. Its molecular formula $C_{16}H_{16}O_4$ was confirmed by elementary analysis and mass spectrometry. The ultraviolet (UV) spectrum [$\lambda_{max}$ 262, 278 sh and 319 nm] readily indicated the 5,7-dimethoxy-8-substituted coumarin skeleton for compound **6**. The $^1$H-nuclear magnetic resonance ($^1$H-NMR) spectrum revealed the presence of a set of two doublets [$\delta$ 6.14 (1H, d, $J$= 9.6 Hz) and 7.98 (1H, d, $J$=9.6 Hz)] and a singlet proton at $\delta$ 6.31 in the aromatic region along with two methoxyls at $\delta$ 3.91 and 3.95, which is attributable to the 5,7-dimethoxycoumarin skeleton. The remaining $^1$H-NMR signals at $\delta$ 1.61 (3H, s), 4.83 (1H, m), 4.85 (1H, br s), 6.15 (1H, d, $J$=12.1 Hz) and 6.39 (1H, dd, $J$=12.1, 0.7 Hz) were readily assigned to allyl methyl, *exo*-methylene and olefinic protons respectively. The presence of a long-range coupling between a proton signal at $\delta$ 6.39 and *exo*-methylene proton at $\delta$ 4.85 was confirmed by an irradiation experiment. Hence the remaining $C_5H_7$ side chain of the molecule at the 8-position was elucidated as $-CH=CH-C(CH_3)=CH_2$ (3-methylbutan-1,3-dienyl) from the above spectral evidence. The $^{13}$C-NMR signals at $\delta$ 20.7 ($CH_3$), 116.7 ($=CH_2$), 117.1 (CH), 136.6 (CH) and 142.6 ($=C<$) were also supportive of this partial structure. The magnitude (12.1 Hz) of a coupling constant between olefinic protons suggested that the olefin is in *Z*-form. Thus the structure of compound **6** was assigned as 5,7-dimethoxy-8-[(*Z*)-3′-methylbutan-1′,3′-dienyl]-coumarin (*cis*-dehydrocoumurrayin) (**6**). The isomeric coumarin derivative gleinadiene (*trans*-dehydrocoumurrayin) was isolated from *M. gleinei*.[6] Interestingly, the $^1$H-NMR signals for the side chain protons of gleinadiene appeared in much lower field than those of compound **6**. This may be explained as follows: there is a disruption of conjugation between the *cis*-dienyl group and the coumarin skeleton due to the steric hindrance while the *trans*-dienyl side chain co-occurs on the same plane as the coumarin skeleton.

The first author previously pointed out the possible occurrence of several chemical races in *M. paniculata*, and instated Formosan and Indonesian races.[8] The Formosan race[9] can be clearly distinguished from the Indonesian race by the absence of 5,7-dimethoxy-8-prenylcoumarins




(**6**)

* To whom correspondence should be addressed.

that are principal constituents of the latter.[8] The present study on the leaves of the Indonesian race has revealed the presence of characteristic 5,7-dimethoxycoumarin derivatives such as toddalenone, toddasin and 5,7-dimethoxy-8-[(*Z*)-3′-methylbutan-1′,3′-dienyl]coumarin, and thus the instatement of the Indonesian chemical race was further substantiated.

## Experimental

All melting points were measured on a Yanagimoto melting point apparatus and are uncorrected. Spectral data were obtained using the following apparatus: proton and carbon-13 nuclear magnetic resonance ($^1$H- and $^{13}$C-NMR) spectra with JEOL JNM GSX-400 (1H, 400 MHz; $^{13}$C, 100 MHz) spectrometer with tetramethylsilane (TMS) as internal standard; mass spectra (MS) with a JEOL SX-102A mass spectrometer; infrared (IR) spectra with a JASCO FT/IR-8000 infrared spectrometer; ultraviolet (UV) spectra with a Shimadzu UV-240 spectrometer. Column chromatography was carried out with the following materials: Wakogel C-200 or Merck Kieselgel 60 (eluted with benzene–acetone or hexane–ethyl acetate), Sephadex LH-20 (Pharmacia, eluted with MeOH–$CHCl_3$) and RP-8 reversed-phase silica gel (Merck, eluted with MeOH–$H_2O$). Thin-layer chromatography (TLC) was conducted on a 0.25 mm precoated silica gel plate ($60GF_{254}$, Merck), and spots were detected by inspection under short (254 nm) or long (360 nm) wavelength UV lights, or by the colors developed with 10% $H_2SO_4$ spraying followed by heating on a hot plate.

**Plant Material** The leaves of *Murraya paniculata* were collected in 1984 through 1985 near Sukabumi, Java, Indonesia. A voucher specimen was on deposit at the Herbarium of the University of Tokyo. Another lot of samples was also collected near Bandung, Java, Indonesia, by the second author (K. F.). Since microchemical analysis of both samples by TLC showed the same chemical spectrum, chemical work was undertaken with the plant materials collected in Sukabumi.

**Extraction and Isolation** The dried leaves (1 kg) of *M. paniculata* were extracted two times with $CHCl_3$ (4 l) at room temperature, and the combined extracts were evaporated to dryness under reduced pressure to yield a greenish viscous syrup (98.9 g). The whole extract was dissolved in acetone (*ca.* 500 ml) and adsorbed on silica gel (100 g). The adsorbed material was transferred to a silica gel column (column size 10 × 28 cm) packed in hexane. The column was eluted with the following solvent system: hexane (4.5 l), hexane–AcOEt 10:1 (3 l), 5:1 (2 l), 4:1 (2 l), 3:2 (3 l), 1:1 (3 l) and acetone (3 l). Fractions of 500 ml each were collected and combined into twelve fractions (Fr. I—XII) on the basis of their TLC patterns. Fraction II (4.58 g) was subjected to silica gel column chromatography on elution with benzene–acetone (B-A). Fractions eluted with benzene were combined and rechromatographed over Sephadex LH-20 and RP-8 reversed-phase silica gel to give aurapten (**5**) (200 mg), mp 62—63 °C (lit.[7] 62—63 °C). Fraction IV (0.45 g) was purified by RP-8 silica gel column chromatography to furnish coumurrayin (**1**) (30 mg), mp 156—157 °C (lit.[2] 158—158.5 °C). Fraction V (1.72 g) was chromatographed over silica gel on elution with B-A increasing the amount of acetone stepwise. Separation of fractions eluted with 1—2% B-A afforded 5,7-dimethoxy-8-[(*Z*)-3′-methylbutan-1′,3′-dienyl]coumarin (**6**) (130 mg). Fraction VIII (3.71 g) was subjected to Sephadex LH-20 followed by RP-8 silica gel column chromatography to give 5,7-dimethoxy-8-(3-methyl-2-oxobutyl)coumarin (**2**) (140 mg), mp 131—132 °C (lit.[3] 129—130 °C). Fraction XII was chromatographed over silica gel (column size 6.5 × 18.5 cm) on elution with the stepwise gradient solvent system of B-A. Fractions of 400 ml each were collected. Fractions eluted with 9% B-A, on crystallization from acetone, afforded 460 mg of toddasin (**4**), mp 242—243 °C (lit.[5] 246—249 °C). Fractions eluted with 16% B-A yielded toddalenone (**3**) (30 mg), mp 239—240 °C (lit.[4] 246—249 °C).

**5,7-Dimethoxy-8-[(*Z*)-3′-methylbutan-1′,3′-dienyl]coumarin (6)** Colorless needles from MeOH–$H_2O$, mp 114—116 °C. IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3000, 1715, 1595, 1437, 1335, 1223, 1123, 1101, 820. UV $\lambda_{max}^{MeOH}$ nm (log $\varepsilon$): 262 (4.13), 278 sh (4.09), 319 (4.17). $^1$H-NMR ($CDCl_3$) $\delta$: 1.61 (3H, s, 5′-$CH_3$), 3.91 (3H, s, 5-$OCH_3$), 3.95 (3H, s, 7-$OCH_3$), 4.83 (1H, m, 4′-H), 4.85 (1H, br s, 4′-H), 6.14 (1H, d, $J$=9.6 Hz, 3-H), 6.15 (1H, d, $J$=12.1 Hz, 2′-H), 6.31 (1H, s, 6-H), 6.39 (1H, dd, $J$=12.1, 0.7 Hz, 1′-H), 7.98 (1H, d, $J$=9.6 Hz, 4-H). $^{13}$C-NMR ($CDCl_3$) $\delta$: 20.7 (5′-C), 55.9 (5-$OCH_3$), 56.0 (7-$OCH_3$), 90.1 (6-C), 103.6 (10-C), 108.1 (8-C), 111.1 (3-C), 116.7 (4′-C), 117.1 (1′-C), 136.6 (2′-C), 138.6 (4-C), 142.6 (3′-C), 152.9 (9-C), 156.2 (5-C), 160.4 (7-C), 161.3 (2-C). EI-MS *m/z* (rel. int.): 272 ($M^+$, 92), 241 (53), 213 (29), 149 (100). HR-MS: Calcd for $C_{16}H_{16}O_4$: 272.1049. Found: 272.1061. *Anal.* Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.77; H, 5.94.

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