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# MURRAYATIN, A COUMARIN FROM *MURRAYA EXOTICA*

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**Key Word Index**—*Murraya exotica*; Rutaceae; 7-methoxy-8-(2′-isovaleryloxy-3′-hydroxy-3′-methylbutyl) coumarin; murrayatin.

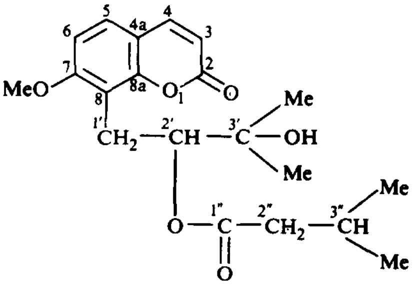
**Abstract**—The structure of murrayatin isolated from the leaves of *Murraya exotica* was established as 7-methoxy-8-(2′-isovaleryloxy-3′-hydroxy-3′-methylbutyl) coumarin from spectral analysis, chemical transformation and synthesis.

## INTRODUCTION

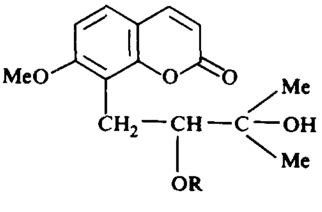
The plant *Murraya exotica* L. (Rutaceae) is known to yield several coumarins [1–6], carbazoles [7, 8] and flavonoids [9, 10]. Re-investigation of the leaves of this species has resulted in the isolation of a new coumarin, designated murrayatin. The present communication is concerned with the structural determination of murrayatin which is shown to be 7-methoxy-8-(2′-isovaleryloxy-3′-hydroxy-3′-methylbutyl) coumarin (1) from studies of spectra and chemical transformations, and which has been confirmed by partial synthesis from osthol epoxide.

## RESULTS AND DISCUSSION

The compound 1, $C_{20}H_{26}O_6$, $[M]^+$ 362, showed UV absorption maxima characteristic of a 7-oxygenated-8-substituted coumarin moiety [11, 12]. It did not produce any colouration with ferric chloride, indicating the absence of a phenolic OH function. The IR spectrum (KBr) exhibited strong absorption at 3425 (–OH), 1725–1700 (*br*, ester carbonyl and coumarinic carbonyl) and 1600, 1558, 1495 $cm^{-1}$ (aromatic nucleus). The 100 MHz $^1H$ NMR spectrum ($CDCl_3$) displayed the characteristic doublet pairs for C-3/C-4 and C-5/C-6 protons. The C-3 proton appeared as a doublet at $\delta$6.22 (1H, $J = 9.4$ Hz). The position of the doublet at $\delta$7.60 (1H, $J = 9.4$ Hz) for the C-4 proton clearly indicated the absence of any oxygen function at C-5 because such a function at C-5 would require this doublet to be shifted downfield by *ca* $\delta \geqslant 7.90$ [13]. The doublet at $\delta$7.07 (1H, $J = 8.6$ Hz) for the C-6 proton was not *meta*-coupled, indicating that C-8 must bear a carbon side chain. The proton at C-5 appeared as a doublet at $\delta$7.31 (1H, $J = 8.6$ Hz). The singlet at $\delta$3.93 for three protons was assigned to the OMe protons at the C-7 position. The appearance of a complex multiplet for two protons at $\delta$3.22 and a double doublet at $\delta$5.18 ($J_1 = 10.0$ and $J_2 = 2.80$ Hz) for one proton revealed the presence of a Ph–$C\underline{H}_2$–$C\underline{H}$– system in the molecule. Another complex multiplet at *ca* $\delta$1.98 accounted for four protons, of which one proton disappeared on deuteration. These four protons could be attributed to the presence of OH at C-3′, two protons at C-2″ and one proton at C-3″. The two singlets for three protons each at *ca* $\delta$1.32 and 1.36 were due to Me groups at C-3′. The downfield shifts of Me groups were due to their attachment to the OH bearing carbon. The two doublets (almost merged into a triplet) at $\delta$0.68 (3H, $J = 6$ Hz) and 0.72 (3H, $J = 6$ Hz) revealed the presence of a *gem*-di Me group at the C-3″ position. The presence of the *gem*-di Me group and the appearance of the complex signal for C-2″ and C-3″ protons indicated the presence of an isovaleryl residue attached through an oxygen linkage at C-2′. This attachment at C-2′ was supported by the fact that on alkaline hydrolysis, 1 yielded meranzin hydrate (2), identified by its conversion to meranzin hydrate acetate (3). Meranzin hydrate acetate (3) was characterized by direct comparison (co-TLC and co-IR) with an authentic sample [6]. On the basis of all the

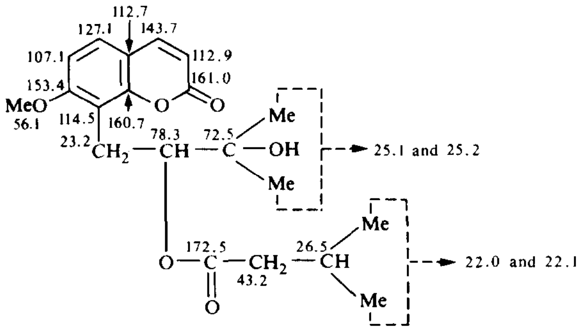


1

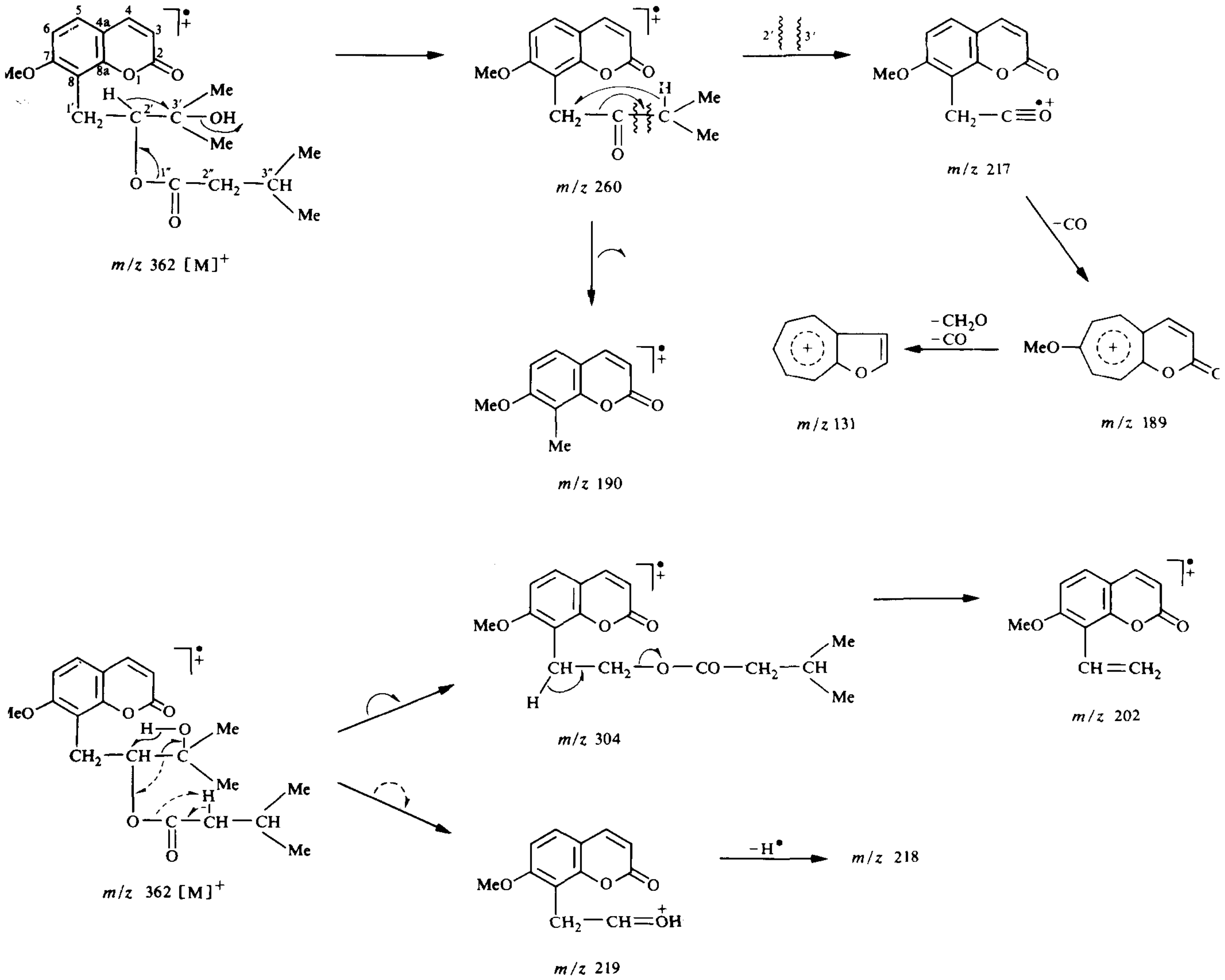


2 R = H

3 R = Ac



**1a**



Scheme 1. Mass spectral fragmentationof murrayatin (**1**).

evidence structure **1** was assigned to murrayatin.

The proposed structure **1** for the new coumarin was further supported by its $^{13}C$ NMR spectrum and also its mass spectral fragmentation pattern. The chemical shifts for the $^{13}C$ NMR spectrum were assigned (in **1a**) and the interpretations were in conformity with those having similar structural patterns [14]. The origin of some of the ion species arising from the mass fragmentation of **1** is shown in Scheme 1.

**1** was subsequently synthesized in poor yield from osthol epoxide and isovaleric acid and was found to be identical with the natural product (co-TLC and co-IR).

## EXPERIMENTAL

Plant material was collected locally and identified by Dr. S. R. Das, Survey Officer, Regional Research Institute (Ay.), Calcutta 700009. A voucher specimen has been deposited at the Department of Pure Chemistry, Calcutta University. Mps are uncorr. The UV spectrum was recorded in 95% aldehyde-free EtOH. $^1H$ NMR (100 MHz) and $^{13}C$ NMR (50 MHz) spectra were recorded with TMS as an int. standard in $CDCl_3$. The MS were recorded at 25 eV. Specific optical rotations were measured in $CHCl_3$. Deactivated $Al_2O_3$ (basic Brockmann) and 5% argentine Si gel G (BDH, 60–120 mesh) for column chromatography and Si gel G (Merck) for TLC were used. Samples were routinely dried over $P_2O_5$ for 24 hr.

*Isolation of murrayatin* (**1**). Air-dried, powdered leaves of *M. exotica* (8 kg) were exhaustively extracted with petrol in a Soxhlet for 24 hr. After removal of solvent, the crude extract was chromatographed over deactivated $Al_2O_3$. $C_6H_6$ and $C_6H_6$–$CHCl_3$ (1:3) eluates on rechromatography over 5% argentine Si gel afforded **1**, eluted with $C_6H_6$–EtOAc (9:1). It was purified by crystallization from petrol–$Me_2CO$ (4:1). (Found: C, 66.46, H, 7.03; $C_{20}H_{26}O_6$ requires: C, 66.30, H, 7.18%); mp 108–110°; yield: 0.0025%; $R_f$ 0.32 ($C_6H_6$–EtOAc, 3:7); $[\alpha]_D^{22}$ $+104.7°$ ($CHCl_3$; *c* 0.97); UV $\lambda_{max}^{EtOH}$ nm: 323, 258, 248 (log $\varepsilon$: 4.14, 3.58, 3.54); MS *m/z* (rel. int.): 362 $[M]^+$ (6), 304 (12), 261 (19.5), 260 (100), 245 (9), 220 (14), 219 (88), 218 (25), 217 (67), 202 (32), 190 (40), 189 (23) and 131 (9).

*Alkaline hydrolysis of* **1** *and acetylation of hydrolysed product* (**2**). Murrayatin (**1**, 80 mg) in MeOH (1 ml) was mixed with MeOH–KOH (7.5 ml, 3.3%) and the mixture refluxed for 1 hr. After usual work-up, meranzin hydrate (**2**, 50 mg) was crystallized from petrol (40–60°), mp 123–124°, $[\alpha]_D^{22}$ $-24.07°$ ($CHCl_3$; *c* 1.08). It was acetylated with pyridine–$Ac_2O$ followed by heating at 100° for 1 hr. On keeping overnight, the acetylated product was isolated following the usual procedure. The crude product was filtered through a bed of Si gel and eluted with $C_6H_6$–EtOAc (4:1) to afford a solid residue. This was purified by crystallization from petrol–$Me_2CO$ (7:3) to furnish meranzin hydrate acetate (**3**, 55 mg), mp 139–140°, characterized by direct comparison (co-TLC and co-IR) with an authentic sample.

*Synthesis of murrayatin* (**1**). In dry $C_6H_6$ (5 ml), osthol epoxide (100 mg) was dissolved and to it was added freshly distilled isovaleric acid (0.5 ml). The mixture was refluxed for 32 hr. The reaction mixture was diluted with $C_6H_6$ (100 ml) and washed successively with 2% $NaHCO_3$ (3 × 20 ml) and $H_2O$. The organic layer was dried ($Na_2SO_4$) and the solvent distilled off. The residue was purified by prep. TLC ($C_6H_6$–EtOAc, 4:1) to afford crude murrayatin (15 mg) and osthol epoxide (70 mg). The crude murrayatin was crystallized from petrol–$Me_2CO$ (4:1), mp 106°. It showed a single spot on TLC. A further increase in mp was not observed.

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