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PHENYLCOUMARINS FROM *OCHROCARPUS SIAMENSIS*

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Key Word Index—*Ochrocarpus siamensis*; Guttiferae; flowers; phenylcoumarins; acylcoumarins; synthesis.

Abstract—Two new phenylcoumarins, 6-butyryl-5-hydroxy-4-phenylseselin and 6-butyryl-5,7-dihydroxy-8-(3,3-dimethylallyl)-4-phenylcoumarin, were isolated from the flowers of *Ochrocarpus siamensis*.

The flowers of *Ochrocarpus siamensis* (Guttiferae), a tree widely distributed in northern Thailand, are used as a heart tonic in local medicine. It is interesting to note that most of the known 4-phenylcoumarins have been isolated from species of this plant family. We wish to report the isolation of two new phenylcoumarins and confirmation of their structures by synthesis.

Petrol extract of the flowers of *O. siamensis* yielded two phenolic crystalline compounds, **1**, $C_{24}H_{22}O_5$, and **2**, $C_{24}H_{24}O_5$. The IR spectrum of compound **1** showed an intense absorption at 1725 cm^{-1} (pyrone carbonyl). Its ^1H NMR spectrum showed the presence of a phenyl group (δ 7.40, 5H, *s*), a 2,2-dimethylchromene ring system (δ 5.65, 6.94, 2H, AB system J_{AB} = 10 Hz; δ 1.65, 6H, *s*) and a hydroxyl group (δ 14.73, 1H, *s*). Substitution at C-4 of the coumarin was apparent from the C-3 proton singlet at δ 6.01, and the nature of the substituent was deduced as a butyryl chain from the signals at δ 0.98 (3H, *t*, *J* = 7 Hz) 1.43–1.90 (2H, *m*) and 3.08 (2H, *t*, *J* = 7 Hz). The low field NMR resonance at δ 14.73 indicated hydrogen bonding, while the bathochromic shifts of the UV absorption maxima at 232, 282, 350 nm (log ε 4.60, 4.68, 3.97) to 250, 310, 433 nm in alkaline solution indicated a 6-acylcoumarin [1]. Thus the compound was assigned structure **1**. The angular fusion of the chromene ring was confirmed by acetylation which resulted in the appropriate NMR downfield shifts of $\Delta\delta$ 0.03 for H_α and 0.13 for H_β [2].

In the ^1H NMR spectrum of the second phenolic compound the signals which in compound **1** were due to the presence of the chromene ring were replaced by new signals due to the presence of a 3,3-dimethylallyl group and a second hydroxyl group. These findings suggested that the second coumarin had the structure **2** of the expected biogenetic precursor of **1**.

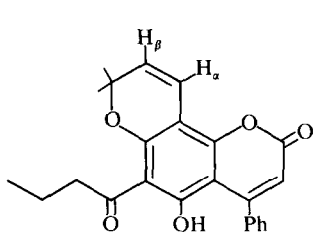
The structures of both coumarins **1** and **2** were subsequently proved by synthesis and interconversion as follows. Pechmann condensation of butyrylphloroglucinol with ethyl benzoyl acetate gave the intermediate **3**, which was easily separated from its 8-acyl isomer [3,4]. Alkylation of **3** with 2-methylbut-3-ene-2-ol [5,6] in dioxan in the presence of freshly distilled BF_3-etherate gave the desired coumarin **2**. Treatment of **3** with 3-methyl-2-butenal [7] in hot pyridine, on the other hand, afforded coumarin **1**. Finally, conversion of coumarin **2** to coumarin **1** was smoothly accomplished by using DDQ in benzene solution [8].

EXPERIMENTAL

IR: Nujol mull; UV: 95% EtOH; ^1H NMR: 60 MHz, $CDCl_3$ with TMS as int. standard; MS: probe 70 eV.

Extraction procedure. Ground, sun-dried flowers of *O. siamensis* (1 kg) were extracted with petrol (bp 40–60°) (5 l.) at room temp. for 5 days and the extract was filtered, concd, and chromatographed on a Si gel column.

Coumarin **1** (*6-butyryl-5-hydroxy-4-phenylseselin*). Fractions eluted with petrol–Et_2O (9:1) yielded, upon concn, yellow crystals which recrystallized from MeOH as yellow needles (480 mg), mp 138–139° EtOH–$FeCl_3$: deep green; IR ν_{max} cm^{-1}: 1725, 1630, 1600, 1575; UV λ_{max} nm (log ε): 232 (4.60), 282 (4.68), 350 (3.97); ^1H NMR: δ 0.98 (3H, *t*, *J* = 7 Hz), 1.43–1.90 (2H, *m*), 1.65 (6H, *s*), 3.98 (2H, *t*, *J* = 7 Hz), 5.65 and 6.94 (2H, AB system,



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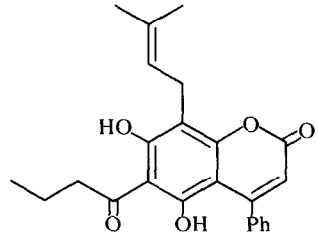

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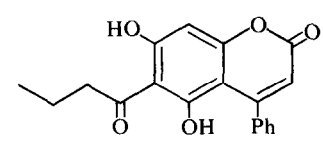

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J = 10 Hz), 6.01 (1H, *s*), 7.40 (5H, *s*), 14.73 (1H, *s*, removed with D_2O); MS *m/z* (rel. int.): 390 (M^+, 44), 375 (100), 357 (16), 347 (14).

Coumarin **2** (*6-butyryl-5,7-dihydroxy-8-(3,3-dimethylallyl)-4-phenylcoumarin*). Fractions eluted with petrol–Et_2O (4:1) after concn deposited yellow needle-shaped crystals which after recrystallizations from petrol–C_6H_6 gave pale yellow needles (700 mg), mp 116–117°. EtOH–$FeCl_3$: brownish-green; IR ν_{max} cm^{-1}: 3340, 1700, 1620, 1580; UV λ_{max} nm: (log ε) 235 (4.11), 280 (4.21), 335 (3.71); ^1H NMR: δ 0.93 (3H, *t*, J = 7 Hz), 1.38–1.95 (2H, *m*), 1.76 (3H, *d*, J = 0.5 Hz), 1.90 (3H, *d*, J = 0.5 Hz), 2.98 (2H, *t*, J = 7 Hz), 3.57 (2H, *d*, J = 7.5 Hz), 5.31 (1H, *t*(*br*), J = 7.5 Hz), 5.96 (1H, *s*), 7.52 (5H, *s*), 9.72 (1H, *s*), 11.15 (1H, *s*, signals at 9.72 and 11.15 removed with D_2O); MS *m/z*: 392 (M^+, 90), 377 (16), 349 (66), 337 (100).

Synthesis of coumarin **3** (*6-butyryl-5,7-dihydroxy-4-phenylcoumarin*) [3, 4]. To a mixture of butyrylphloroglucinol (1 g) and ethyl benzoyl acetate (1 g) in glacial HOAc (15 ml) was added conc. H_2SO_4 (0.6 ml). The resulting yellow soln was kept at room temp. for 3 days when crystals separated (0.51 g) and were recrystallized from MeOH to give pale yellow needles, mp 228–229°. EtOH–$FeCl_3$: brownish green; IR ν_{max} cm^{-1}: 3225, 1675, 1605; ^1H NMR (DMSO): δ 0.88 (3H, *t*, J = 7 Hz), 1.58 (2H, *m*), 3.05 (2H, *t*, J = 7 Hz), 5.82 (1H, *s*), 6.39 (1H, *s*), 7.38 (5H, *s*).

Synthesis of coumarin **1** (*6-butyryl-5-hydroxy-4-phenylseselin* [7]. To a soln of **3** (100 mg) in dry pyridine (15 ml) at room temp. was added 3-methyl-2-butenal (52 mg) and the reaction temp. raised and kept at 110° for 10 hr. Removal of pyridine under red. pres. yielded a solid which was dissolved in $CHCl_3$ (30 ml), washed with H_2O (2 × 50 ml) and dried (Na_2SO_4). Removal of the solvent gave the coumarin **1** (96 mg) which recrystallized as yellow needles from MeOH. (Found: C, 73.75; H, 5.71%; requires: C, 73.85; H, 5.64%).

Synthesis of coumarin **2** (*6-butyryl-5,7-dihydroxy-8-(3,3-dimethylallyl)-4-phenylcoumarin*) [5, 6]. To a stirred soln of **3** (150 mg) in dry dioxan (10 ml) was added freshly distilled BF_3–etherate (0.5 ml) followed by 2-methyl-3-buten-2-ol (0.05 ml) and the resulting soln stirred at 50° for 90 min. Excess Et_2O was added and the ethereal soln washed well with H_2O and dried (Na_2SO_4). Upon concn the unreacted coumarin **3** crystallized out. The remaining mother liquor was subjected to prep. TLC with C_6H_6–EtOAc (5:1). In this manner **2** was obtained and recrystallized from petrol–C_6H_6 (22 mg). (Found: C, 73.20; H, 6.23%; requires: C, 73.47; H, 6.12%).

Conversion of coumarin **1** *to coumarin* **2** *by oxidative cyclisation with DDQ* [8]. To a soln of **1** (25 mg) in dry C_6H_6 (3 ml) was added DDQ (15 mg). The orange soln was stirred overnight at room temp., then filtered to remove the residue, which was washed thoroughly with C_6H_6. The C_6H_6 filtrates were combined, and chromatographed on a Si gel column from which **2** (19 mg) was eluted with EtOAc–C_6H_6 (1:49).

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