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COUMARINS FROM *AMYRIS BALSAMIFERA*

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Key Word Index—*Amyris balsamifera*; Rutaceae; coumarins; balsamiferone.

Abstract—Two new coumarins have been isolated from the aerial parts of *Amyris balsamifera*. On the basis of spectral and chemical data, these have been identified as (*R*)-(+)-6-(2′-hydroxy-3′-methyl-3′-butenyl)-7-methoxycoumarin and balsamiferone, 7-hydroxy-3,6-bis(3′-methyl-2′-butenyl)-coumarin.

INTRODUCTION

In the course of our studies [1] on the taxonomic significance of the constituents of Jamaican *Amyris*, we have examined another local species, *Amyris balsamifera*. This is the second of three Jamaican species which has been classified by some authors as belonging to the Burseraceae [2] and by others as Rutaceae [3]. *A. plumieri* has been implicated in chemotherapy [4] while the essential oil from *A. balsamifera* of Haiti is used commercially as a perfume fixative in soaps. This oil has been found to consist mainly of sesquiterpenes [5]. We now report the isolation and identification of two coumarins from the Jamaican variety of *A. balsamifera*, a finding which supports our earlier chemical evidence [1] for placing the Jamaican *Amyris* in Rutaceae.

RESULTS AND DISCUSSION

Benzene extraction of the dried, milled leaves and twigs followed by purification by column chromatography afforded coumarin (1) and balsamiferone (4).

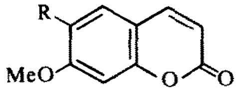
1, $C_{15}H_{16}O_4$, mp 112–113° showed a UV spectrum characteristic of a 7-oxycoumarin [6]. The NMR spectrum supported the 6-alkyl-7-oxy substituted coumarin [7] and the position of the hydroxy group on the side chain was established by oxidation to **2**. An additional carbonyl at 1678 cm^{-1} in the IR spectrum of **2**, enhancement of the absorption in the region of 223 nm [8] and a singlet and multiplet (2H each) at δ 3.91 and 5.98, respectively, in the NMR spectrum concurred. Correlation of **1** with (+)-2′,3′-dihydroxydihydrosuberosin (**3**) established the chirality of the 2′-carbons to be identical. Application of the benzoate rule [9, 10] established the configuration of this centre to be *R*.

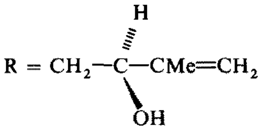
Balsamiferone (**4**) $C_{19}H_{22}O_3$, mp 135–137°, gave a reversible base shift of its UV maximum at 334 nm. The carbonyl band (1692 cm^{-1}) in its IR spectrum reflected the interaction of the phenolic group at C-7 [11]. In the NMR spectrum, three one-proton singlets at δ 6.93, 7.15 and 7.37 (H-8, H-5 and H-4, respectively) and typical signals at δ 1.67, 3.24 and 5.28 (overlapping signals for two dimethylallyl groups) supported the structure **4**.

The mass spectrum of balsamiferone (Scheme 1) concurred fully with the structure [12]. However the identical nature of the side chains mitigated against identifying a single fragmentation pathway. The enhanced stability of the ions **b′** and **c′**, due to the participation of the 7-hydroxy group, argues for their involvement, but the fragment **d** at *m/e* 255 favours the usual path [12]. Both processes may be simultaneous.

Acid treatment of balsamiferone gave the isomeric dihydropyran (**5**), mp 123–125°, with the carbonyl band of the coumarin now at 1709 cm^{-1}. The UV spectrum of **5** was unchanged in base while in its NMR spectrum signals for one of the dimethylallyl groups in **4** were replaced by a singlet (6H) at δ 1.38 and two mutually coupled triplets (2H each) at δ 1.86 and 2.81.

The occurrence of these coumarins in *A. balsamifera* parallels the discovery of dehydrogeijerin (**6**) and hopeyhopin (**7**) as metabolites of *A. madrensis* [13] and



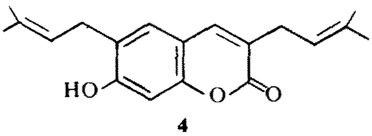
1 

$R = CH_2\text{—}\underset{OH}{\overset{H}{C}}\text{—}CMe{=}CH_2$

2 R = $CH_2COCMe{=}CH_2$
3 R = $CH_2CHOHCOHMe_2$
6 R = $COCH{=}CMe_2$

7 

$R = \overset{O}{COCH\text{—}CMe_2}$



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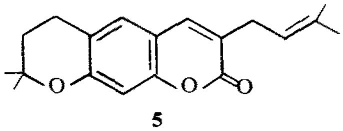

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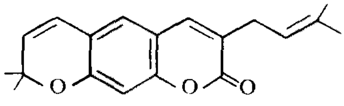

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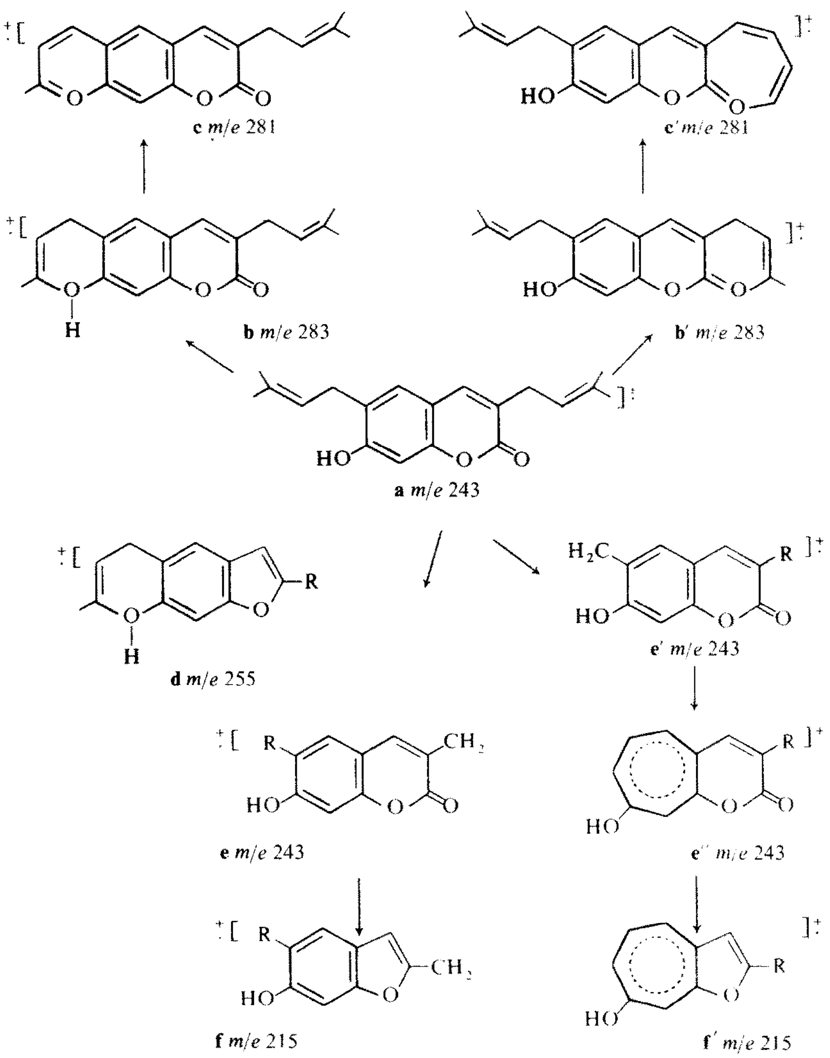

Scheme 1. (R = dimethylallyl).

3-(3′, 3′-dimethyl)allylxanthyletin (**8**) of *A. simplicifolia* [14]. Before submitting this article it was observed that the constitution of our coumarin (**1**) seemed identical to tamarin [15]. However, the NMR spectrum of the ketone corresponding to **2** differed especially in the critical values of the olefinic methylene signals. We have confirmed our assignments to be correct.

EXPERIMENTAL

Mps are uncorr. UV spectra are for EtOH solns. IR spectra were determined in $CHCl_3$. The 60 MHz NMR spectra were recorded in $CDCl_3$ solns on a Jeol JNM PMX-60 spectrometer with TMS (δ 0.00) as internal standard. Plant material was collected and identified by G. Proctor, Travelling Officer, The Herbarium, Institute of Jamaica.

Extraction and isolation. Dried, milled leaves and twigs (317 g) were percolated with cold C_6H_6 until the eluate was pale yellow. Evapn of the solvent yielded a gum (21.9 g) of which a portion (20 g) was chromatographed on Al_2O_3(600 g). Fractions eluted with C_6H_6 and 20% EtOAc in C_6H_6 were rechromatographed and further purified by PLC to yield coumarin (**1**) (1.079 g). Balsamiferone (**4**) (359 mg) was obtained after PLC of fractions taken with 40% EtOAc in C_6H_6.

Coumarin (**1**). Recrystallization from EtOAc–hexane gave colourless needles, mp 112–113°. (Found: C, 69.20; H, 6.22. $C_{15}H_{16}O_4$ requires: C, 69.21; H, 6.20%). $[\alpha]_D^{25}$ + 27.3 (*c* 1.285, $CHCl_3$). UV λ_{max} nm (log ε): 225.3 (3.98), 245 sh (3.55), 254 sh (3.52), 300 sh (3.85), 330.5 (4.12). IR ν cm^{-1}: 3378, 2882, 1709, 1616, 1563, 1379, 1126, 1007, 893, 819. ^1H NMR (60 MHz): δ 1.82 (3H, *s*, C-3′ Me), 2.37 (1H, *bs*, exchanged with D_2O, O-H), 2.58 (1H, *dd*, *J* = 14, 8 Hz, C-1′), 3.03 (1H, *dd*, *J* = 14, 5 Hz, C-1′), 4.30 (1H, *dd*, *J* = 8, 5 Hz, C-2′), 3.87 (3H, *s*, OMe), 4.80, 4.88 (each 1H, *m*, $W_{\frac{1}{2}}$ = 5 Hz, C-4′ methylene), 6.13 (1H, *d*, *J* = 9 Hz, C-3), 6.70 (1H, *s*, C-8), 7.23 (1H, *s*, C-5), 7.58 (1H, *d*, *J* = 9 Hz, C-4).

The ketone (**2**). **1** (50 mg) dissolved in Me_2CO (4 ml) was treated with Jones' reagent in the usual manner. After work-up and PLC, the ketone (**2**) was recrystallized from Me_2CO–petrol as plates, mp 117–118°. (Found: C, 69.92; H, 5.28; O, 24.72. $C_{15}H_{14}O_4$ requires: C, 69.75: H, 5.46: O, 24.78%). UV λ_{max} nm (log ε): 222.5 (4.46), 255.5 sh (4.06), 285 sh (4.12), 327 (4.18). IR ν cm^{-1}: 2858, 1725, 1678, 1621, 1563, 1381, 1130. ^1H NMR (60 MHz): δ 1.92 (3H, *s*, C-3′ Me), 3.81 (3H, *s*, OMe), 3.98 (2H, *s*, C-1'), 5.78, 6.04 (each 1H, *m*, C-4' methylene), 6.16 (1H, *d*, $J = 10$ Hz, C-3), 6.73 (1H, *s*, C-8), 7.12 (1H, *s*, C-5), 7.50 (1H, *d*, $J = 10$ Hz, C-4).

Application of the benzoate rule. **1** (65 mg) was benzoylated in Py (1 ml) and PhCOCl (0.2 ml) in the dark. After work-up and PLC the benzoate was obtained as an oil which resisted all efforts at crystallization. ^{1}H NMR (60 MHz): δ 1.69 (3H, *s*, C-3' $\underline{\text{Me}}$), 3.1 (2H, *m*, C-1'), 3.81 (3H, *s*, O-CH_3), 4.87 (2H, *m*, C-4' methylene), 6.11 (1H, *d*, $J = 9.5$ Hz, C-3), 6.64 (1H, *s*, C-8), 7.14 (1H, *s*, C-5), 7.57 (1H, *d*, $J = 9.5$ Hz, C-4), 7.2–7.5 and 7.8–7.9 (3H and 2H respectively, multiplets, benzoate). The direction and magnitude of the specific rotation, $[\alpha]_D^{25} + 77.7$ (*c* 2.86, $CHCl_3$) of this benzoate with respect to **1**, $[\alpha]_D^{25} + 27.3$, indicate the *R*-configuration of the 2'-carbon.

2',3'-Dihydroxydihydrosuberosin (**3**). **1** (47 mg) dissolved in dioxan (5 ml) was refluxed with 10% aq. oxalic acid (8 ml) for 48 hr. Work-up and PLC followed by recrystallization from EtOAc–hexane gave plates, mp 133–135°. $[\alpha]_D^{25} + 49.2°$ (*c* 0.315, $CHCl_3$). This compound was identical in all respects to an authentic sample of (+)-2', 3'-dihydroxydihydrosuberosin (**3**).

Balsamiferone (**4**). The solid from PLC was recrystallized from Me_2CO–petrol as pale yellow needles, mp 135–137°. (Found: M^+ 298.1558; $C_{19}H_{22}O_3$ requires: 298.1569). UV λ_{max} (log ε): 219 (4.16), 250 sh (3.64), 258 sh (3.56), 334 (4.23) shifting in base to 237 (4.00), 273 sh (3.52), 305 sh (3.42), 367.5 (4.35). IR ν cm^{-1}: 3165, 2874, 1692, 1618, 1585, 1381, 1130. ^{1}H NMR (90 MHz): δ 1.64, 1.73, 1.82 (12H, each *bs*, 2 × $\underline{Me}_2C{=}$), 3.20, 3.32 (each 2H, *d*, $J = 8$ Hz, 2 × $C\underline{H}_2$—CH=), 5.28 (2H, *bt*, $J = 8$ Hz, 2 × CH_2—C$\underline{H}$=), 6.45 (1H, *s*, OH), 7.15 (1H, *s*, C-5), 6.93 (1H, *s*, C-8), 7.37 (1H, *s*, C-4). MS *m/e* (rel. int.): 298 (16%, M^+), 283 (8), 281 (7), 244 (16), 243 (100), 215 (11), 201 (8), 199 (11), 115 (17).

The dihydropyran (**5**). A soln of balsamiferone (**4**) (80 mg) in dioxan (7 ml) was treated with conc H_2SO_4 (4 drops) and refluxed for 3.5 hr. Work-up and PLC furnished the dihydropyran (**5**), recrystallized from Me_2CO–petrol as plates, mp 123–125°. (Found: M^+ 293.1572; $C_{19}H_{22}O_3$ requires: 298.1569). UV λ_{max} nm (log ε): 221 (4.12), 250 sh (3.72), 261.5 sh (3.76), 332 (4.24), unchanged in acid or base. IR ν cm^{-1}: 1709, 1623, 1568, 1493, 1143. ^{1}H NMR (60 MHz): δ 1.38 (6H, *s*, $\underline{Me}_2$C—O), 1.86 (2H, *t*, $J = 7$ Hz, $C\underline{H}_2$—C—O), 2.81 (2H, *t*, $J = 7$ Hz, CH_2—$C\underline{H}_2$—Ar), 3.19 (2H, *d*, $J = 7.5$ Hz, $C\underline{H}_2$—CH=), 5.29 (1H, *bm*, —CH_2—C$\underline{H}$=), 6.66 (1H, *s*, C-8), 7.06 (1H, *s*, C-5), 7.26 (1H, *s*, C-4).

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