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A CHROMENE, AN ISOPRENYLATED METHYL HYDROXYBENZOATE AND A *C*-METHYL FLAVANONE FROM THE BARK OF *PIPER HOSTMANNIANUM*

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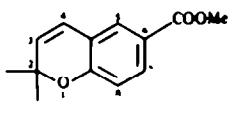
Key Word Index *Piper hostmannianum*; Piperaceae; methyl 2,2-dimethyl-2*H*-1-benzopyran-6-carboxylate; methyl 4-hydroxy-3-(2′-hydroxy-3′-methylbut-3′-enyl)-benzoate; flavanones; linalool.

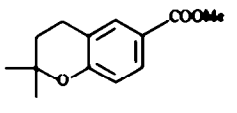
Abstract In addition to sitosterol, linalool, 5-hydroxy-7-methoxy-6,8-dimethylflavanone and 5,7-dihydroxyflavanone, two new natural products were isolated from *Piper hostmannianum* and characterized as methyl 2,2-dimethyl-2*H*-1-benzopyran-6-carboxylate and methyl 4-hydroxy-3-(2′-hydroxy-3′-methylbut-3′-enyl)-benzoate on the basis of spectroscopic data and chemical derivatization.

INTRODUCTION

The genus *Piper* is a source of several types of natural products, including among others alkaloids [1–7], lignans [8, 9], phenols [10–12], flavonoids [12, 13] and triterpenes [14]. The present work deals with the constituents of *P. hostmannianum*, a shrub of the Amazon region. Two new natural products, **1** and **3a**, linalool, sitosterol and two flavonoids were isolated from the stem bark. The flavanoids were characterized as 5-hydroxy-7-methoxy-6,8-dimethylflavanone (**4a**), previously isolated from *Unona lawii* (Annonaceae) [15] and 5,7-dihydroxyflavanone (pinocembrin, **4c**), known from several species [16]. The chromene (**1**) had been synthesized previously [17] but was not known as a natural product, although chromenes are widely distributed in nature [18].



1



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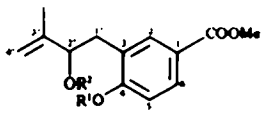
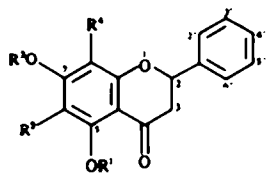


3a R¹ = R² = H
3b R¹ = R² = Ac



	R¹	R²	R³	R⁴
4a	H	Me	Me	Me
4b	Ac	Me	Me	Me
4c	H	H	H	H

* Based on part of the M.Sc. Thesis submitted by T.A.C. to Universidad Nacional de Colombia, Bogotá, Colombia (1986).

RESTULTS AND DISCUSSION

The new natural product **1** showed IR bands corresponding to an aromatic ring (1610, 1490 cm $^{-1}$) and an ester group (1720 cm $^{-1}$) while the UV spectrum showed three absorption maxima at 243, 290 and 322 nm (ε 16955, 2058 and 1332), suggesting the presence of a chromene skeleton [19]. The EI-MS showed the molecular ion at *m/z* 218 and the loss of 15 amu, which is characteristic of a 2,2-dimethyl-chromene [20]. The ^{1}H NMR spectrum was particularly informative since it revealed the presence of a trisubstituted benzene ring [δ6.82 (*d*, J = 7.5 Hz), 7.70 (*d*, J = 2.0 Hz) and 7.85 *dd*, J = 7.5 and 2.0 Hz)], the presence of a double bond (as an AB system at δ5.66 and 6.40 with J_{AB} = 9.0 Hz), a carboxymethyl singlet (δ3.87) and a geminal dimethyl group attached to an oxygen-bearing carbon (6H, *s*, δ1.45). The structure of **1** was further evident from its ^{13}C NMR spectrum (see Experimental), from comparison of its spectral data with those of a synthetic sample [17] and by catalytic hydrogenation which afforded compound **2**.

Compound **3a**, $C_{13}H_{16}O_4$ (M^+, *m/z* 236), $[\alpha]_D^{18}$ −6.7°, showed IR bands attributable to hydroxyl groups (3440 and 3160 cm $^{-1}$) an ester group (1685 cm $^{-1}$) and an aromatic ring (1608 cm $^{-1}$). Its ^{1}H NMR spectrum showed the presence of three aromatic protons: one *ortho*-coupled (δ6.94, *d*, J = 9.0 Hz), one *meta*-coupled (δ7.78, *d*, J = 3.0 Hz) and one *ortho–meta*-coupled (δ7.84, *dd*, J = 9.0 and 3.0 Hz). The side chain signals appeared as a vinylic methyl group (δ1.82), a terminal methylene group (δ4.90, 1H, *s* (*br*), H_{cis} and δ5.03, 1H, *s* (*br*), H_{trans}), two benzylic protons (δ2.82–3.05, *m*), a carbinolic proton (δ4.35–4.55, *m*) and a hydroxy group (δ2.68–2.82). The remaining signals were a carbomethoxyl singlet (δ3.90) and a phenolic hydroxyl (δ8.70–9.06). The latter signal and that of the aliphatic alcohol disappeared upon addition of D_2O.

Acetylation of **3a** gave the diacetate **3b**, $C_{17}H_{20}O_6$, (M^+ 320), which lacked hydroxyl absorptions in the IR

spectrum but gave additional carbonyl bands at 1770 and 1740 cm^{-1}. The ^1H NMR spectrum of **3b** showed two acetate singlets at δ 2.00 and 2.40. The substituent at C-4 in **3a** had to be a hydroxyl group since H-5 suffered a downfield shift of 0.23 upon acetylation. Similarly, the substituent at C-2′ in **3a** was also a hydroxyl, since H-2′ was downfield shifted to δ 5.38 and one of the olefinic protons was diamagnetic shifted 0.13 ppm in the acetate **3b**. Irradiation of the H-2′ triplet in **3b** (δ_x = 5.38, $J_{AX} = J_{BX}$ = 7 Hz) collapsed the AB part of the ABX system (δ_A = 3.00, δ_B = 2.83, J_{AB} = 12 Hz) to an AB system, while irradiation at δ 2.90 changed the triplet (H-2′) to a singlet.

Further support for the structure of **3a** was provided by the MS which showed the base peak at *m/z* 166 due to the formation of the methyl 4-hydroxy, 3-methyl benzoate ion. It seems that compounds like **3a** are biogenetic uncyclized precursors of chromenes.

EXPERIMENTAL

Isolation of the constituents of Piper hostmannianum C.D.C. Stem bark was collected in the vicinity of Manaus, Amazonas, Brazil and identified by the botanist William Rodrigues. Voucher Herbarium INPA (Manaus) 64224. Dry powdered stem bark (1.9 kg) was percolated with C_6H_6 at room temp. The extract (13 g) was chromatographed on a silica gel (220 g) column, giving with petrol–$CHCl_3$ in the indicated proportions aliphatic esters (1.5 g, 1:0), sitosterol (1.3 g, 8:2), linalool (1.1 g, 8:2), **1** (0.07 g, 1:1) and **4a** (0.05 g, 1:1) and giving with $CHCl_3$–EtOAc in the indicated proportions **3a** (0.04 g, 8:2) and **4c** (0.01 g, 1:1). Spectral data and direct comparison with authentic samples established the identities of linalool and **4c**.

Methyl 2,2-dimethyl-2H-1-benzopyran-6-carboxylate (**1**). Oil. UV λ_{max}^{MeOH} nm (ε): 322, 290, 243 (1332, 2058, 16955); IR ν_{max}^{film} cm^{-1}: 3040, 2980, 2960, 2840, 2820, 1720, 1645, 1610, 1580, 1490, 1465, 1445, 1385, 1370, 1320, 1290, 1275, 1230, 1200, 1170, 1125, 1090, 990, 930, 910, 880, 850, 840, 760; ^1H NMR (90 MHz, $CDCl_3$): δ 1.45 (6H, *s*, C<u>H</u>$_3$-2), 3.87 (3H, *s*, COOC<u>H</u>$_3$-6), 5.66 (1H, *d*, *J* = 9.0 Hz, H-3), 6.40 (1H, *d*, *J* = 9.0 Hz, H-4), 6.82 (1H, *d*, *J* = 7.5 Hz, H-8), 7.70 (1H, *d*, *J* = 2.0 Hz, H-5), 7.85 (1H, *dd*, *J* = 7.5 and 2.0 Hz, H-7); ^{13}C NMR (25.2 MHz, $CDCl_3$): δ 77.23 (*s*, C-2), 121.53 (*d*, C-3), 127.88 (*d*, C-4), 130.88 (*d*, C-5)*, 122.37 (*s*, C-6), 130.81 (*d*, C-7)*, 115.97 (*d*, C-8), 156.94 (*s*, C-9), 120.48 (*s*, C-10), 166.57 (*s*, C-11), 51.71 (*q*, O<u>C</u>H$_3$-11), 28.27 (*q*, C-12 and C-13); EIMS 20 eV, *m/z* (rel. int.): 218 [M]$^+$ (24), 204 (12), 203 (100), 187 (4), 179 (6), 159 (4), 144 (7), 137 (12), 115 (5), 109 (5), 105 (5).

Catalytic hydrogenation of **1**. To a soln of **1** (69 mg) in MeOH (15 ml) was added 10% Pd-C (120 mg) and the mixture was stirred in an atmosphere of H_2 for 1 hr. The catalyst was filtered off and the filtrate on evaporation gave **2** (55 mg). Colourless crystals, mp 83°. IR ν_{max}^{KBr} cm^{-1}: 3020, 2970, 2940, 1710, 1610, 1580, 1495, 1440, 1420, 1380, 1365, 1350, 1335, 1320, 1290, 1260, 1240, 1220, 1190, 1175, 1165, 1115, 1100, 1025, 975, 945, 935, 920, 875, 765; ^1H NMR (60 MHz, $CDCl_3$): δ 1.28 (6H, *s*, CH_3-2), 1.70 (2H, *t*, *J* = 7.0 Hz, 2H-3), 2.70 (2H, *t*, *J* = 7.0 Hz, 2H-4), 3.80 (3H, *s*, COOC<u>H</u>$_3$-6), 6.70 (1H, *d*, *J* = 10.0 Hz, H-8), 7.60–7.90 (2H, *m*, H-5 and H-7); EIMS 70 eV, *m/z* (rel. int.): 220 [M]$^+$ (46), 205 (15), 189 (13), 185 (100), 173 (13), 166 (12), 161 (23), 145 (8), 144 (7), 133 (13), 105 (27).

Methyl 4-hydroxy-3-(2′-hydroxy-3′-methylbut-3′-enyl)-benzoate (**3a**). Colourless crystals, mp 120°. $[\alpha]_D^{18}$ −6.7 ($CHCl_3$; *c* 0.006). UV λ_{max}^{MeOH} nm (ε): 262, 224 (13688, 14632); $\lambda_{max}^{MeOH + MeONa}$ nm (ε): 303, 230 (18762, 10384); $\lambda_{max}^{MeOH + MeONa + HCl}$ nm (ε): 262, 224 (13806, 14160); IR ν_{max}^{KBr} cm^{-1}: 3440, 3160, 3022, 3000, 2960, 2930, 1685, 1608, 1455, 1432, 1380, 1340, 1305, 1290, 1195, 1170, 1120, 1062, 1032, 1000, 895, 832, 770; ^1H NMR (90 MHz, $CDCl_3$): δ 1.82 (3H, *s*, C<u>H</u>$_3$-3′), 2.68–2.82 (1H, *m*, O<u>H</u>-2′), 2.82–3.05 (2H, *m*, 2H-1′), 3.90 (3H, *s*, COOC<u>H</u>$_3$-1), 4.35–4.55 (1H, *m*, H-2′), 4.90 (1H *s* (*br*), H_{cis}-4′), 5.03 (1H, *s* (*br*), H_{trans}-4′), 6.94 (1H, *d*, *J* = 9.0 Hz, H-5), 7.78 (1H, *d*, *J* = 3.0 Hz, H-2), 7.84 (1H, *dd*, *J* = 9.0 and 3.0 Hz, H-6), 8.70–9.06 (1H, *s* (*br*), O<u>H</u>-4); EIMS 30 eV, *m/z* (rel. int.): 236 [M]$^+$ (5), 218 (4), 205 (6), 187 (5), 167 (8), 166 (100), 165 (22), 159 (8), 158 (6), 151 (18), 144 (7), 135 (19), 134 (29), 107 (45), 71 (16).

Methyl 4-acetoxy-3-(2′-acetoxy-3′-methylbut-3′)-enyl-benzoate (**3b**). (Ac_2O, C_5H_5N, 48 hr room temp.). Oil IR ν_{max}^{film} cm^{-1}: 3080, 3020, 2955, 2920, 2850, 1770, 1740, 1725, 1660, 1618, 1500, 1450, 1380, 1300, 1280, 1250, 1220, 1200, 1180, 1130, 1030, 920, 770; ^1H NMR (80 MHz, $CDCl_3$): δ 1.80 (3H, *s*, C<u>H</u>$_3$-3′), 2.00 (3H, *s*, COOC<u>H</u>$_3$-2′), 2.40 (3H, *s*, COOC<u>H</u>$_3$-4), 2.83 and 3.00 (AB of ABX, 2H, J_{AB} = 12, J_{AX} = 7, J_{BX} = 7, 2H-1′), 3.90 (3H, *s*, COOC<u>H</u>$_3$-1), 4.90 (2H, *s* (*br*), H-4′), 5.38 (1H, *t*, *J* = 7, H-2′), 7.20 (1H, *d*, *J* = 8.5 Hz, H-5), 7.99 (2H, *m*, H-6 and H-2); EIMS 70 eV, *m/z* (rel. int.): 320 [M]$^+$ (11), 289 (7), 278 (19), 260 (28), 236 (3), 218 (75), 205 (3), 208 (58), 203 (43), 190 (46), 187 (14), 166 (84), 159 (50), 151 (4), 135 (6), 134 (14), 107 (12), 43 (100).

5-Hydroxy-7-methoxy-6,8-dimethylflavanone (**4a**). Yellow crystals, mp 146–147°. $[\alpha]_D^{18}$ + 100.5° ($CHCl_3$; *c* 0.010). UV λ_{max}^{MeOH} nm (ε): 358, 286 (3278, 14155); $\lambda_{max}^{MeOH + MeONa}$ nm (ε): 360, 288 (2831, 13410); $\lambda_{max}^{MeOH + AlCl_3}$ nm (ε): 358, 314 sh, 287 (2235, 5066, 13112); $\lambda_{max}^{MeOH + AlCl_3 + HCl}$ nm (ε): 358, 314, 287 (2086, 4470, 11324); IR ν_{max}^{KBr} cm^{-1}: 3075, 3045, 2978, 2950, 2860, 1635, 1598, 1525, 1500, 1455, 1425, 1375, 1360, 1312, 1295, 1205, 1170, 1135, 1110, 1035, 1005, 970, 950, 910, 818; ^1H NMR (90 MHz, $CDCl_3$): δ 2.12 (6H, *s*, C<u>H</u>$_3$-6 and C<u>H</u>$_3$-8), 2.85 (1H, *dd*, *J* = 16.5 and 4.5 Hz, H_e-3), 3.03 (1H, *dd*, *J* = 12.0 and 16.5 Hz, H_a-3), 3.77 (3H, *s*, O*CH*$_3$-7), 5.40 (1H, *dd*, *J* = 12.0 and 4.5 Hz, H-2), 7.50 (5H, *s* (*br*), H-2′, 6′), 12.10 (1H, *s*, O<u>H</u>-5); ^{13}C NMR (25.2 MHz, $CDCl_3$): δ 79.40 (*d*, C-2), 43.32 (*t*, C-3), 197.32 (*s*, C-4), 159.11 (*s*, C-5), 109.90 (*s*, C-6), 8.10 (*q*, <u>C</u>H$_3$-6), 165.18 (*s*, <u>C</u>-7), 59.62 (*q*, *CH*$_3$O-7), 104.70 (*s*, C-8), 8.66 (*q*, <u>C</u>H$_3$-8), 157.54 (*s*, C-9), 98.90 (*s*, C-10), 138.24 (*s*, C-1′), 124.53 (*d*, C-2′ and C-6′), 128.39 (*d*, C-3′ C-4′ and C-5′); EIMS 70 eV (rel. int.): 298 [M]$^+$ (100), 297 (16), 221 (28), 194 (64), 166 (77), 151 (9), 137 (18), 123 (16), 104 (13), 77 (25).

5-Acetoxy-7-methoxy-6,8-dimethylflavanone (**4b**). Oil. IR ν_{max}^{film} cm^{-1}: 3018, 2920, 2850, 1770, 1690, 1615, 1500, 1450, 1405, 1370, 1350, 1300, 1275, 1215, 1160, 1105, 1030, 1005, 970, 950, 850, 750; ^1H NMR (80 MHz, $CDCl_3$): δ 2.01 (3H, *s*, C<u>H</u>$_3$-6) 2.18 (3H, *s*, C<u>H</u>$_3$-8), 2.38 (3H, *s*, COOC<u>H</u>$_3$), 2.77 (1H, *dd*, *J* = 16.5 and 4.5 Hz, H_e-3), 3.00 (1H, *dd*, *J* = 12.0 and 16.5 Hz, H_a-3), 3.70 (3H, *s*, OC<u>H</u>$_3$-7), 5.38 (1H, *dd*, $J_{a,a}$ 12.0 Hz and $J_{a,e}$ = 4.5 Hz, H-2), 7.44 (5H, *s*, H-2′, 6′); EIMS 70 eV (rel. int.): 340 [M]$^+$ (8), 299 (47), 298 (100), 297 (34), 221 (40), 194 (100), 193 (13), 166 (73), 165 (15), 123 (10), 104 (21), 91 (5), 77 (13).

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