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# 2, 2-DIMETHYLCHROMENES FROM *EUPATORIUM ASCHEMBORNIANUM**

F. GÓMEZ, L. QUIJANO, J. S. CALDERÓN, A. PERALES and T. RÍOS

Instituto de Química, Universidad Nacional Autónoma de México, México 20, D.F., Mexico

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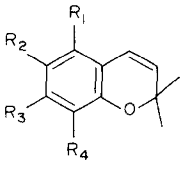
**Key Word Index**—*Eupatorium aschembornianum*; Compositae; Eupatorieae; chromenes; benzofuran derivative.

**Abstract**—Two new chromenes, eupatoriochromene B and C, and a new benzofuran derivative were isolated from the petrol-soluble fractions of the leaves and flowers of *Eupatorium aschembornianum.*

## INTRODUCTION

Several chromenes have been isolated from plants of the genera *Eupatorium* and *Ageratum*. Two of them (demethoxy-ageratochromene and ageratochromene) possess insect antijuvenile hormone activity in several orders [1]. As part of our chemical systematic study of plants of the tribe Eupatorieae, we previously investigated *Stevia monardaefolia* and isolated an isomer of ageratochromene (**1**) and demethoxy-ageratochromene (**3**) [2].

We now wish to report the isolation and structure elucidation of two new chromenes, which we have named eupatoriochromene B (**1**) and eupatoriochromene C (**2**), and a new benzofuran derivative (**8a**) from *Eupatorium aschembornianum* Schauer, besides the known demethoxy-ageratochromene (7-methoxy-2, 2-dimethylchromene) (**3**) [3], 5-hydroxy-6-acetyl-8-methoxy-2,2-dimethylchromene (**4**) [4], 5,8-dimethoxy-6-acetyl-2, 2-dimethylchromene (**5**) [5] and 2-isopropenyl 6-methoxy-2, 3-dihydrobenzofuran (**7**) [6].

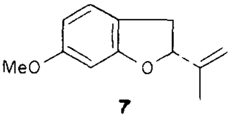


| | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|
| **1** | H | H | OMe | OMe |
| **2** | OMe | –CH(OH)Me | H | OMe |
| **3** | H | H | OMe | H |
| **4** | OH | Ac | H | OMe |
| **5** | OMe | Ac | H | OMe |
| **6** | OMe | –CH(OAc)Me | H | OMe |

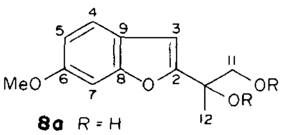
## RESULTS AND DISCUSSION

Eupatoriochromene B (**1**) is a colourless oil, $C_{13}H_{16}O_3$ ($M^+$ at $m/z$ 220). Its IR spectrum demonstrated the presence of a gem-dimethyl group (1378 and 1362 $cm^{-1}$) and a benzene ring (1610 and 1500 $cm^{-1}$). Its $^1H$ NMR spectrum was in accord with structure 1, showing sharp singlets at $\delta$ 1.46 (6H), 3.82 (3H) and 3.85 (3H), which corresponded to the 2, 2-dimethyl grouping of the chromene ring and two methoxyl groups. The protons at C-3 and C-4 appeared as a symmetrical AB pattern of doublets at $\delta$ 5.49 (1H, *d*, $J = 10$ Hz) and 6.26 (1H, *d*, $J = 10$ Hz), which were absent in the $^1H$ NMR spectrum of the dehydro derivative (**9**). The aromatic protons appeared as two doublets at $\delta$ 6.66 (1H, *d*, $J = 8$ Hz) and 6.39 (1H, *d*, $J = 8$ Hz) showing that the unoccupied positions on the ring were *ortho* to each other. Since the chemical shifts of H-3 and H-4 correspond to an unsubstituted chromene at C-5 [7], the methoxyl groups must be at C-7 and C-8. This assumption was confirmed by ozonolysis of **1** to afford the dialdehyde **10** whose $^1H$ NMR spectrum (Table 1) exhibited one doublet at $\delta$ 7.6, assigned to H-5, which shifted downfield due to the deshielding effect of the carbonyl group. Therefore H-5 must be *ortho* to the aromatic aldehyde.

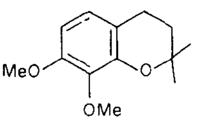
Eupatoriochromene C (**2**) is an oil, $C_{15}H_{20}O_4$ ($M^+$ at $m/z$ 264), which gave bands in the IR spectrum at



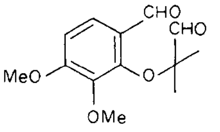
**7**



**8a** R = H
**8b** R = Ac



**9**



**10**

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Table 1. $^1H$ NMR data of compounds **1**, **2**, **6**, **8a**, **8b**, **9** and **10** (100 MHz, $CDCl_3$, TMS as int. standard)

| | **1** | **2** | **6** | **8a** | **8b** | **9** | **10** |
|---|---|---|---|---|---|---|---|
| H-3 | 5.49 *d* (10)* | 5.64 *d* (10) | 5.63 *d* (10) | 6.58 *s* | 6.57 *s* | 1.78 *t* (7) | 9.8 *s* |
| H-4 | 6.26 *d* (10) | 6.52 *d* (10) | 6.53 *d* (10) | 7.34 *d* (8) | 7.36 *d* (8) | 2.72 *t* (7) | 10.26 *s* |
| H-5 | 6.66 *d* (8) | | | 6.80 *dd* (8, 2) | 6.82 *dd* (8, 2) | 6.71 *d* (8) | 7.6 *d* (8) |
| H-6 | 6.39 *d* (8) | | | | | 6.41 *d* (8) | 6.76 *d* (8) |
| H-7 | | 6.85 *s* | 6.76 *s* | 6.95 *d* (2) | 6.97 *d* (2) | | |
| H-11 | | 5.14 *q* (6) | 6.16 *q* (6) | 3.66 *d* (11)<br>3.98 *d* (11) | 4.24 *d* (12)<br>4.48 *d* (12) | | |
| H-12 | | 1.47 *d* (6) | 1.51 *d* (6) | 1.58 *s* | 1.61 *s* | | |
| Gem-di Me | 1.46 *s* | 1.46 *s* | 1.46 *s* | | | 1.37 *s* | 1.36 *s* |
| OMe | 3.82 *s*<br>3.85 *s* | 3.72 *s*<br>3.84 *s* | 3.76 *s*<br>3.84 *s* | 3.82 *s* | 3.82 *s* | 3.81 *s*<br>3.81 *s* | 3.80 *s*<br>3.92 *s* |
| Ac | | | 2.06 *s* | | 2.04 *s* | | |

*Values in parentheses are coupling constants in Hz.

3410, 1380 and 1370 $cm^{-1}$ corresponding to a hydroxyl group and a gem-dimethyl group. Its $^1H$ NMR spectrum displayed sharp singlets at $\delta$ 1.46 (6H), 3.72 (3H), 3.84 (3H) assigned to the gem-dimethyl group and two methoxyl groups. It also gave rise to signals at $\delta$ 1.47 (3H, *d*, $J = 6$ Hz) and 5.14 (1H, *q*, $J = 6$ Hz) due to a 1-hydroxy–ethyl group. In the aromatic proton region only a singlet was found at $\delta$ 6.85, suggesting that the aromatic ring was trisubstituted. Acetylation of **2** with $Ac_2O$–pyridine gave the acetate **6**, which produced a new signal in the $^1H$ NMR spectrum (Table 1) at $\delta$ 2.06, corresponding to the acetyl group. Final confirmation of structure **2** was achieved by oxidation of eupatoriochromene C with pyridinium dichromate, which furnished the chromene **5**, whose IR and $^1H$ NMR data were identical to those of an authentic sample.

The third new compound isolated was the benzofuran derivative **8a**. It was obtained as an oil, $C_{12}H_{14}O_4$ ($M^+$ at *m/z* 222), which had IR absorptions at 3400, 1150 and 1050 $cm^{-1}$ indicating the presence of tertiary and primary hydroxyl groups. This was confirmed by acetylation with $Ac_2O$–pyridine to give the monoacetate **8b**. The $^1H$ NMR spectrum ($CDCl_3$) was in accord with structure **8a**. A one-proton singlet at $\delta$ 6.58 corresponded to H-3, as in methoxyeuparin [8]. Furthermore, the $^1H$ NMR spectrum exhibited signals at $\delta$ 7.34 (1H, *d*, $J = 8$ Hz), 6.80 (1H, *dd*, $J = 8$, 2 Hz) and 6.95 (*d*, $J = 2$ Hz) corresponding to H-4, H-5 and H-7, respectively. The resonance at $\delta$ 3.8 (2H, AB, $J = 11$ Hz) was assigned to the $-CH_2-OH$ group and a singlet at $\delta$ 1.58 (3H) to the tertiary methyl group. Based on all these facts we propose **8a** as the most likely structure for the benzofuran derivative.

## EXPERIMENTAL

Mps are uncorr. Known compounds were identified by comparison of the IR and $^1H$ NMR spectra. Elementary analyses were determined by Dr. F. Pascher, Germany.

*E. aschembornianum Sch.* was collected 5 km west of Topilejo D.F. on the México–Cuernavaca road in October 1978. A voucher specimen (Calderon-31) has been deposited at Herbario Nacional, UNAM (MEXU). Dried leaves and flowers (1.53 kg) of the plant were extracted first with petrol (36 g extract) and then with $CHCl_3$ (43 g extract). The petrol extract (36 g) was dissolved in $Me_2CO$, cooled, filtered and concd *in vacuo* to give 27 g extract, which was chromatographed on Si gel (1.35 kg) using petrol–$C_6H_6$ and $C_6H_6$–EtOAc. From the fractions eluted with petrol–$C_6H_6$ (3:1) (4 g), purification by prep. TLC gave 68 mg **3** and 57 mg **7**.

*Eupatoriochromene B* (7, 8-*dimethoxy*-2, 2-*dimethylchromene*) (**1**). Chromatographic fractions eluted with petrol–$C_6H_6$ (1:1) (8 g), after purification by prep. TLC, afforded 123 mg **4**, mp 81–82° (lit. 88° [4]) and 203 mg **1**. Compound **1** was obtained as an oil; UV $\lambda_{max}^{EtOH}$ nm ($\epsilon$): 222 (16260), 273 sh (6080), 280 sh (5990); IR $\nu_{max}^{film}$ $cm^{-1}$: 1610, 1500, 1377, 1365; EIMS (probe) 70 eV, *m/z* (rel. int.): 220 $[M]^+$ (45), 215 $[M-Me]^+$ (100). (Found: C, 71.08; H, 7.55; O, 21.30. $C_{13}H_{16}O_3$ requires: C, 70.89; H, 7.52; O, 21.79%.)

*Eupatoriochromene C* (6-[1-*hydroxyethyl*]-5, 8-*dimethoxy*-2, 2-*dimethylchromene*) (**2**). Chromatographic fractions eluted with petrol–$C_6H_6$ (1:2) (10 g) and with $C_6H_6$–EtOAc (3:1) (3 g), after purification by prep. TLC, afforded 217 mg **5** [4] and 135 mg **2**, respectively. Compound **2** was obtained as an oil; UV $\lambda_{max}^{EtOH}$ nm ($\epsilon$): 225 (36 390), 271 sh (6360), 280 sh (5500), 318 (1440); IR $\nu_{max}^{film}$ $cm^{-1}$: 3410, 1645, 1380, 1370, 1125; EIMS (probe) 70 eV, *m/z* (rel. int.): 264 $[M]^+$ (25), 249 $[M-Me]^+$ (100). (Found: C, 67.50; H, 7.80; O, 24.30. $C_{15}H_{20}O_4$ requires: C, 68.16; H, 7.63; O, 24.21%.)

6-*Methoxy* 2-[1, 2-*dihydroxy*-2-*propyl*]*benzofuran* (**8a**). Chromatographic fractions of the $CHCl_3$ extract (18 g) eluted with $CHCl_3$–EtOAc (9:1) (1.5 g), after purification by prep. TLC, afforded 77 mg **8a**. Oil; IR $\nu_{max}^{film}$ $cm^{-1}$: 3400, 1630, 1500, 1150, 1050; EIMS (probe) 70 eV, *m/z* (rel. int.): 222 $[M]^+$ (14), 191 $[M-31]^+$ (78.5), 43 (100).

*Hydrogenation of* 7, 8-*dimethoxy*-2, 2-*dimethylchromene* (**1**). 80 mg **1** was hydrogenated ($PtO_2/H_2$) to give 60 mg of the dihydro derivative **9**. UV $\lambda_{max}^{EtOH}$ nm ($\epsilon$): 211 (19 730), 277 (2060); IR $\nu_{max}^{film}$ $cm^{-1}$: 1660, 1500, 1380, 1370; EIMS (probe) 70 eV, *m/z* (rel. int.): 222 $[M]^+$ (8), 207 $[M-Me]^+$ (10), 94 (100), 41 (95).

*Ozonolysis of* **1**. A soln of 100 mg **1** in $CH_2Cl_2$ (50 ml) was ozonized for 5 min. The ozonide was decomposed with $Me_2S$, the solvent removed and the residue pruified by prep. TLC giving 60 mg **10**. UV $\lambda_{max}^{EtOH}$ nm ($\epsilon$): 212 (12 850), 230 (12 350), 283 (10 400); IR $\nu_{max}^{film}$ $cm^{-1}$: 1730, 1675, 1590, 1500, 1380, 1370; EIMS (probe) 70 eV, *m/z* (rel. int.): 252 $[M]^+$ (4), 224 $[M-CO]^+$ (36.5), 223 $(M-CHO]^+$ (35), 181 $[M-71]^+$ (100).

*Acetylation of* **2**. Acetylation of **2** (50 mg) with $Ac_2O$–pyridine gave after prep. TLC the oily monoacetate **6**. UV $\lambda_{max}^{EtOH}$ nm ($\epsilon$): 227 (31 180), 274 (7010), 283 sh (5930), 320 (1720); IR $\nu_{max}^{film}$ $cm^{-1}$: 1735, 1650, 1600, 1500; EIMS (probe) 70 eV, *m/z* (rel. int.): 306 $[M]^+$ (13), 291 $[M-Me]^+$ (40), 43 (100).

6 - *Methoxy* - 2 - [1 - *acetoxy* - 2 - *hydroxy* - 2 - *propyl*]*benzofuran* (**8b**). A 30 mg sample of **8a** acetylated with $Ac_2O$–pyridine as usual, gave the acetate **8b** (28 mg). Oil, UV $\lambda_{max}^{EtOH}$ nm ($\epsilon$): 218 (7410), 246 (5950), 286 (3570); IR $\nu_{max}^{film}$ $cm^{-1}$: 3370, 1730, 1640, 1500, 1150; EIMS (probe) 70 eV *m/z* (rel. int.): 264 $[M]^+$ (96), 191 $[M-73]^+$ (92), 43 (100).

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