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TERPENES AND FLAVONES OF *SALVIA CARDIOPHYLLA*

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Key Word Index—*Salvia cardiophylla*, Labiatae, diterpene, 2α-hydroxysugiol.

Abstract—The triterpenes, β-amyrin, ursolic and oleanolic acid, the flavones, 5-hydroxy-6,7,3′,4′-tetramethoxyflavone and 5,7-hyroxy-6,3′,4′-trimethoxyflavone and the diterpenes, cardiophyllidin, salviol and 2α-hydroxysugiol (reported for the first time) were isolated from the acetone extract of *Salvia cardiophylla*

As part of our research into species from the medicinal flora of Ibero-America [1–3] we have studied *Salvia cardiophylla* B, which is a herbaceous species found growing on the campus of the Universidad Nacional de Asunciòn, Paraguay. An earlier report [4] described a diterpene with a new *seco-ent*-neo-clerodanic skeleton isolated from this plant and given the name cardiophyllidin (**1**)

Compound **2** was isolated by chromatography, and crystallized in petrol–ethyl acetate, mp 269–271°. High resolution mass spectroscopy determined its formula as $C_{20}H_{28}O_3$. The IR spectrum showed absorption bands at 3670 and 3590 cm^{-1} (phenol and hydroxyl), 1720 (α,β-unsaturated carbonyl), together with aromatic signals In the ^1H NMR spectrum two aromatic protons were observed at δ7.90 and 6 74 The low chemical shift (δ7.90) indicated one to be the H-14 proton with a carbonyl group on C-7 while the other signal must be due to H-11. Two doublets of six protons at δ1 24 and 1 26 ($J = 7$ Hz) coupled with a benzylic heptet for a proton at δ3 18 indicated the presence of an isopropyl group on C-13 The most notable signal in the spectrum was a very broad multiplet centred at δ4 14 which, in an abietatriene diterpene structure, can only correspond to the geminal proton of a 2α-hydroxyl [5] The acetylation of compound **2** with acetic anhydride in pyridine led to the diacetate (**3**) which proved, in ^1H NMR spectrum, to have two acetate methyls, one upon an aromatic hydroxyl at δ2 38 and the other on an aliphatic hydroxyl at δ2.08 with the geminal proton at δ5 20 as a very broad multiplet

In order to establish the structure of this compound beyond doubt, salviol (**4**) was acetylated to give its diacetate (**5**) which was oxidized with chromium trioxide in glacial acetic acid [6] giving a product identical to **3**, which confirmed the structure of **2** as 2α-hydroxysugiol. The mass spectral (EIMS) fragmentation characteristics were in agreement with the proposed structure [7, 8].

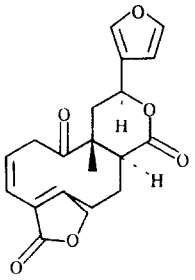
In the experimental section of this paper the high resolution H NMR data of the flavones 5-hydroxy-6,7,3′,4′-tetramethoxyflavone [9] and 5,7-dihydroxy-6,3′,4′-trimethoxyflavone [10] are also given as they have not been previously reported

EXPERIMENTAL

Mps uncorr Plant material was collected on the campus of the Universidad Nacional de Asuncion, Paraguay and a voucher specimen, Ferro 001, was deposited in the National Museum of Natural History, Smithsonian Institute, Washington DC

Extraction and isolation of the products The dried and finely powered aerial part (950 g) of *Salvia cardiophylla* Benth was extracted with Me_2CO (7 l) at room temp for one month After filtration, the solvent was evapd yielding a gum (107 g) which was subjected to dry CC over silica gel, yielding β-amyrin (200 mg), a mixture of ursolic and oleanolic acids (137 mg), salviol (**4**, 136 mg), 2α-hydroxysugiol (**2**, 120 mg), cardiophyllidin (**1**, 128 mg), 5-hydroxy-6,7,3′,4′-tetramethoxy-flavone (26 8 mg) and 5,7-dihydroxy-6,3′,4′-trimethoxyflavone (30 mg)

Compound **2** was crystallized from petrol–EtOAc mp 269–271°, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3670, 3590, 2950, 2920, 2860, 1720, 1660, 1600, 1460, 1370, 1280, 1260, 1240, ^1H NMR



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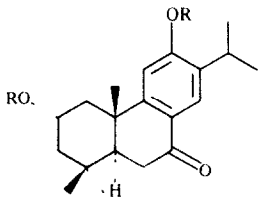

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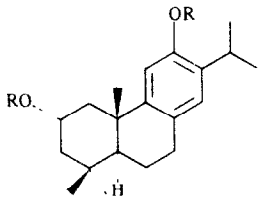
3 R = Ac



4 R = H
5 R = Ac

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(200 MHz, $CDCl_3$) δ0 99 (3H, *s*), 1 03, (3H, *s*), 1 24 (3H, *d*, J = 7 Hz), 1.26 (3H, *d*, J = 7 Hz), 1.28 (3H, *s*), 1 85 (1H, *dd*, J = 15 Hz), 2.64 (3H, *m*), 3 18 (1H, *hept*, J = 7 Hz), 4 14 (1H, *m*), 6 21 (1H, *s*, OH), 6 74 (1H, *s*), 7.90 (1H, *s*), EIMS (direct inlet) 70 eV, *m/z* (rel int): 316 $[M]^+$ (71), 301 (6), 283 (100), 257 (17), 241 (31), 230 (17), 217 (15), 201 (26), 175 (30), 161 (72); HRMS calc. for $C_{20}H_{28}O_3$, 316 2036 Found, 316 2035

Preparation of 2α-Hydroxysugiol diacetate (**3**) 2α-hydroxysugiol (**2**) (8 mg) was dissolved in four drops of pyridine and 2 drops of Ac_2O were added After 2 hr at room temp work-up in the usual manner yielded compound **3** (6 5 mg after purification) as a gum ^{1}H NMR δ1 02 (3H, *s*), (1 10) (3H, s), 1.23 (3H, *d*, J = 7 Hz), 1 26 (3H, *d*, J = 7 Hz), 1.27 (3H, *s*), 2 09 (3H, *s*), 2.32 (3H, *s*), 3 01 (1H, *hept*, J = 7 Hz), 5 19 (1H, *m*), 6 98 (1H, *s*), 7 01 (1H, *s*) EIMS (direct inlet) 70 eV, *m/z* (rel int) 400 $[M]^+$ (3), 358 (18), 340 (2), 298 (9), 283 (18), 270 (3), 256 (3), 242 (6), 235 (4), 230 (5), 217 (17), 202 (12), 161 (10), 149 (12), 129 (10), 115 (12), 95 (24)

Oxidation of salviol diacetate (**5**) Compound **5** (15 mg) was added to a soln of CrO_3 (7 3 mg) in 1 5 ml glacial AcOH and left at 0° for 3 hr After usual work-up, 10 mg of a compound identical to 2α-hydroxysugiol diacetate (**3**) was obtained.

Identification of flavones 5-Hydroxy-6,7,3′,4′-tetramethoxyflavone was crystallized from MeOH mp 190–192°, IR-$\nu_{max}^{CHCl_3}$ cm^{-1}, 3660, 3000, 2930, 2840, 1700, 1650, 1600, 1580, 1510, 1480, 1450, 1430, 1350, 1320, 1290, 1170, 1140, 1120, 1020, 1010, UV λ_{max}^{EtOH} nm, 338, 275, 252, 240; ^{1}H NMR (200 MHz, $CDCl_3$): δ3 93 (3H, *s*), 3.97 (3H, *s*), 3.98 (3H, *s*), 3.99 (3H, *s*), 6 56 (1H, *s*), 6 59 (1H, *s*), 6 97 (1H, *d*, J = 8 5 Hz), 7 34 (1H, *d*, J = 2 Hz), 7.52 (1H, *dd*, J = 8 5 Hz, J = 2 Hz), 12 75, (1H, *s*), EIMS (direct inlet) 70 eV, *m/z* (rel. int.) 358 $[M]^+$ (11), 343 (12), 329 (3), 315 (4) 279 (5), 256 (2), 251 (2.5), 213 (3), 181 (3), 167 (17), 165 (3), 153 (6), 149 (74), HRMS calc for $C_{19}H_{18}O_7$, 358 1050 Found 358 1048.

5,7-Dihydroxy-6,3′,4′-trimethoxyflavone could not be crystallized by the methods used IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3530, 3000, 2940, 2840, 1700, 1650, 1600, 1585, 1510, 1490, 1450, 1435, 1360, 1325, 1170, 1120, 1035, 1020, 1009, 850 UV λ_{max}^{EtOH} nm: 340, 276, 241. ^{1}H NMR (200 MHz, $CDCl_3$) δ3 92 (3H, *s*), 3 97 (3H, *s*), 3 98 (3H, *s*), 5.81 (1H, *s*), 6.54 (1H, *s*), 6.58 (1H, *s*), 6.95 (1H, *d*, J = 8 5 Hz), 7 43 (1H, *dd*, J = 8 5 Hz, J = 2 Hz), 7 46 (1H, *d*, J = 2 Hz), 12.74 (1H, *s*) EIMS (direct inlet)70 eV, *m/z* (rel. int.) 344 $[M]^+$ (95), 343 (25), 330 (18), 329 (97), 327 (11), 315 (23), 301 (29), 298 (23), 286 (4), 284 (5), 269 (7), 230 (3), 215 (4), 181 (25), 165 (3), 153 (45), 149 (24), 134 (7) HRMS calc. for $C_{18}H_{16}O_7$, 344.0895 Found, 344 0876.

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