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MINOR SESQUITERPENES OF FLOWERS OF *PARTHENIUM HYSTEROPHORUS*

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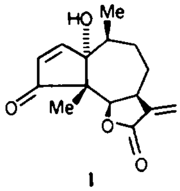
Key Word Index—*Parthenium hysterophorus*; Compositae; parthenin; coronopilin; new ambrosanolides; 2β-hydroxycoronopilin; 8β-hydroxycoronopilin; 11H,13-hydroxyparthenin.

Abstract—Three new ambrosanolides, 2β-hydroxycoronopilin, 8β-hydroxycoronopilin and 11-H,13-hydroxyparthenin, besides parthenin and coronopilin have been isolated and characterized from the defatted methanolic extract of flowers of *Parthenium hysterophorus*.

Over the years *Parthenium hysterophorus* L. (Compositae), a noxious weed, has invaded all parts of India [1]. Although the plant has some reputation as a folk medicine against certain afflictions, it is better known for its allergenic properties. The main constituents, parthenin [2, 3] and coronopilin [4], are associated with the toxicity of the plant and are reported to cause skin dermatitis. Much phytochemical work has appeared since the first structure elucidation of parthenin [3] and interest in its minor constituents is still unabated [5–8]. The methanolic extract of the flowers after careful examination on TLC showed the presence of a few minor and polar substances which seemed to be different from sesquiterpene lactones hitherto known from this plant. Therefore, a fresh attempt has been made to isolate these minor constituents of *P. hysterophorus* which may be responsible for its toxicity. The defatted methanol extract of the flowers after removal of most of the parthenin by crystallization was subjected to repeated column chromatography over silica gel which resulted in separation of coronopilin (**2**) and three new compounds which were assigned structures **3**–**5** on the basis of spectral data and chemical transformations.

The ^{1}H NMR spectrum of compound **4** displayed signals characteristic of an ambrosanolide, signals of two methyls were located at δ1.12 and 1.16 and those of the exocyclic methylene group of an α,β-unsaturated γ-lactone system were observed at 5.72 and 6.12, respectively. The IR spectrum showed a characteristic band for γ-lactone carbonyl at 1740 cm^{-1}. In comparison with the ^{1}H NMR spectrum of parthenin, the absence of signals due to the α,β-unsaturated cyclopentenone system was noted. Instead, an extra triplet at δ4.84 which shifted to 5.66 on acetylation indicated the presence of an extra hydroxyl, possibly at C-2 in ring A. The position of this hydroxyl was established at C-2 by preparing compound **4** from parthenin (**1**) (1:4 addition of H_2O) as described in the Experimental. The same compound was also prepared from parthenin, when adsorbed on basic alumina and kept for 25 days. The extent of conversion was about 10%. The configuration of the hydroxyl was determined to be β because of the ^{1}H NMR downfield placement of the C-2 proton which is caused by its close proximity to C-1 hydroxyl. Moreover, addition of $\bar{O}$H at C-2 is more facile from above the plane in the synthetic compound to form mostly the 2β-hydroxy isomer. In the ^{13}C NMR spectrum the C-2 carbon signal was located at δ68.8. That this compound was not an artifact was confirmed by the analysis of the crude extract which showed that it was present in the extract itself in very small quantities.

Another minor constituent was characterized as 8β-hydroxycoronopilin (**3**) on the basis of spectral studies. The molecular formula corresponded to $C_{15}H_{20}O_5$ which corresponded to hydroxycoronopilin. The ^{1}H NMR spectrum had in addition to signals which corresponded to most of the coronopilin signals, an extra multiplet at δ3.96. Location of this extra hydroxyl at C-8 and its stereochemistry were established by double irradiation experiments. Irradiation of the C-7 multiplet at δ3.36, collapsed the doublets for the C-6 and C-13 a and b protons to singlets and the δ3.96 multiplet to a triplet. Similarly irradiation of the multiplet at δ3.96 simplified the multiplet at δ3.36, thus confirming the presence of the hydroxyl at C-8. When the diffuse multiplet at δ2.10 was irradiated the δ3.96 multiplet changed into a doublet ($J = 4.5$ Hz). This low value of $J_{7,8}$ can be explained only when the C-8 hydroxyl is β-orientated. In the ^{13}C NMR spectrum the C-8 carbon was located downfield at δ81.0. The ^{13}C NMR data and mass spectrum fully agreed with the proposed structure as 8β-hydroxy coronopilin (**3**). The lack of sufficient material excluded the possibility of more chemical work.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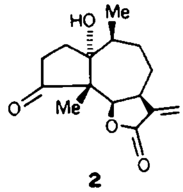
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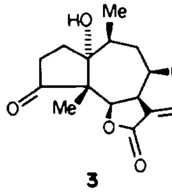
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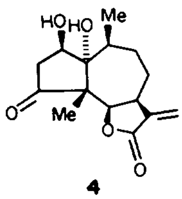
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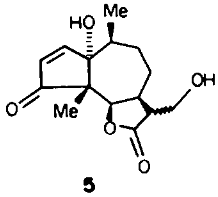
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The third new substance **5** mp 158°, $C_{15}H_{20}O_5$, showed all spectral signals corresponding to parthenin except for the exocyclic methylene indicating that this position is hydrogenated. A broad singlet at δ3.96, indicated a primary alcoholic methylene which showed a downfield displacement to δ4.23 as a doublet ($J = 6$ Hz) after acetylation. When **5** was treated with BF_3-etherate at room temperature, dehydration of the C-1 hydroxyl took place smoothly and a semi-solid was separated after chromatography. In the dehydration product the C-14 methyl singlet shifted to δ2.18 in the ^{1}H NMR spectrum. The signals for the C-2 and C-3 protons shifted to δ6.12 and 8.10, respectively. Most of the other signals showed only marginal shifts from their original positions. This observation established the presence of the primary alcoholic group at C-13. However its stereochemistry could not be finalised from the above data. The structure **5** is thus assigned as 11H, 13-hydroxyparthenin.

A comparison of the ^{13}C NMR spectra of all the compounds is presented in Table 1.

EXPERIMENTAL

All mmps are uncorr.

The defatted MeOH extract of (88 g) *Parthenium hysterophorus* flowers (1 kg, collected locally) after crystallizing most of the parthenin (38 g) was run on a silica gel (BDH) column and eluted with C_6H_6, EtOAc and MeOH in increasing proportions. This provided four sesquiterpene lactones in pure form (**2-5**) besides parthenin (**1**), sitosterol and its glucoside.

Compound **2**. Colourless crystalline compound (2 g) mp 176–178° $[\alpha]_D^{25}$ $-28.5°$ (MeOH) analysed for $C_{15}H_{18}O_4$. (Found C 71.11, H 7.07 requires C 68.68, H. 6.91%). Identified as (−)-coronopilin on comparison with an authentic sample of (−)-coronopilin (lit [9] mp 177–178°).

Compound **3**. Colourless crystalline compound (0.065 g) mp 165–167° $[\alpha]_D^{30}$ $-26.66°$ (MeOH) analysed for $C_{15}H_{20}O_5$. (Found C 65.14, H 7.50 requires C 64.27, H 7.10%). IR ν_{max}^{KBr} cm^{-1}: 3370, 1740, 1700, 1650, 1470, 1390, 1340, 1270, 1095 and 970 ^{1}H NMR (CD_3CN): δ1.20 (3H, *s*, C-5Me), 1.26 (3H, *d*, $J = 7$ Hz, C-10Me), 2.0–2.9 (7H, *m*, C-2,3,9 and 10 protons), 3.36 (1H, *m*, C-7H), 3.96 (1H, *br s*, CHOH), 4.76 (1H, *d*, $J = 7.6$ Hz, C-6H), 5.72 (1H, *d*, $J = 2.5$ Hz, C-13H_a) and 6.16 (1H, *d*, $J = 2.5$ Hz, C-13H_b). MS *m/z* (rel. int.): 280 $[M]^+$ (8), 262 (22), 244 (27), 217 (10), 215 (14), 201 (12), 192 (16), 190 (70), 163 (10), 150 (7), 155 (2), 123 (13), 111 (11), 95 (13) and 41 (100).

Table 1. ^{13}C NMR spectra of compounds **1–5**

C	**1** ($CDCl_3$)	**2** ($CDCl_3$)	**3** (Acetone-d_6)	**4** (CD_3OD)	**5** ($CDCl_3$)
1	83.4	84.8	86.0	86.0	83.8
2	162.8	31.8	33.4	68.8	162.0
3	130.8	32.5	29.0	41.8	130.8
4	209.8	213.0	208.0	218.0	207.5
5	58.2	59.0	59.6	62.7	57.6
6	78.5	80.0	82.5	81.8	78.8
7	43.8	44.5	46.0	46.5	41.8
8	27.6	27.4	81.0	28.8	25.4
9	29.2	30.0	29.0	31.5	28.4
10	39.8	42.2	42.8	38.4	38.4
11	140.1	135.8	145.0	143.0	45.8
12	170.4	165.8	172.0	173.0	170.0
13	120.2	116.5	123.0	122.5	61.4
14	16.7	14.2	15.8	15.0	17.0
15	17.4	16.8	16.6	17.0	19.0

Compound **4**. Amorphous powder (0.35 g), $[\alpha]_D^{38}$ $-12.5°$ (MeOH), analysed for $C_{15}H_{20}O_5$. (Found C 66.0, H 7.38 requires C 64.27, H 7.19%). IR ν_{max}^{KBr} cm^{-1}; 3400, 3360, 1740, 1720, 1645, 1445, 1390, 1240, 1160 and 1070. ^{1}H NMR (CD_3OD): δ1.12 (3H, *s*, C-5Me), 1.16 (3H, *d*, $J = 7$ Hz, C-10Me), 1.60–2.4 (6H, *m*, C-3H_a, C-8, 9 and 10 protons), 2.80 (1H, *dd*, $J = 8.5$ and 19 Hz, C-3H_b), 3.40 (1H, *m*, C-7H), 4.84 (1H, *t*, $J = 7.5$ Hz, C-2H), 5.00 (1H, *d*, $J = 7.5$ Hz, C-6H), 5.72 (1H, *d*, $J = 2.5$ Hz, C-13H_a) and 6.12 (1H, *d*, $J = 2.5$ Hz, C-13H_b). MS *m/z* (rel. int): 280 $[M]^+$ (25), 264 (84), 204 (85), 191 (80), 142 (97), 135 (50), 107 (100), 95 (95), 56 (95) and 43 (80).

Acetylation of **4** with Ac_2O–pyridine afforded a semi-solid analysed for $C_{17}H_{22}O_6$. (Found C 64.39, H 6.99 requires C 63.34, H 6.87%). ^{1}H NMR ($CDCl_3$): δ1.12 (3H, *s*, C-5Me), 1.16 (3H, *d*, $J = 7$ Hz, C-10Me), 2.10 (3H, *s*, C-2, OCOMe), 3.00 (1H, *dd*, $J = 8.5$ and 18 Hz, C-3H_b), 3.40 (1H, *m*, C-7H), 5.00 (1H, *d*, $J = 7.5$ Hz, C-6H), 5.66 (1H, *t*, $J = 7.5$ Hz, C-2H), 5.62 (1H, *d*, $J = 2.5$ Hz, C-13H_a) and 6.26 (1H, *d*, $J = 2.5$ Hz, C-13H_b).

Conversion of parthenin to 2β-hydroxy parthenin. Parthenin (**1**) (200 mg) was taken in aq. $KHCO_3$ and heated on a steam bath for 20 hr. The aq. mix. was extracted with EtOAc, the solvent removed *in vacuo* to give a crude reaction product which after CC on silica gel yielded 80 mg of **2** (identified by co-TLC and spectroscopy).

Coumpound **5**. Colourless crystalline compound (0.095 g), mp 157 − 9°, $[\alpha]_D^{28}$ $+20.0°$ (MeOH) analysed for $C_{15}H_{20}O_5$. (Found C 64.98, H 7.49 requires C 64.27, H 7.19%). IR ν_{max}^{KBr} cm^{-1}: 3420, 2900, 1742, 1700, 1482, 1390, 1340, 1320, 1270, 1180, 1095, 1035, 1010 and 980. ^{1}H NMR ($CDCl_3$): δ1.27 (3H, *d*, $J = 7.0$ Hz, C-10Me), 1.30 (3H, *s*, C-5Me), 3.00 (1H, *m*, C-7H), 3.96 (2H, *brs*, C-13 CH_2OH), 5.00 (1H, *d*, $J = 7.5$ Hz, C-6H), 6.12 (1H, *d*, $J = 6$ Hz, C-3H) and 7.6 (1H, *d*, $J = 6$ Hz, C-2H). MS *m/z* (rel. int.): 280 $[M]^+$, (9) 262 (52), 249 (17), 235 (21), 216 (52), 192 (40), 162 (49), 152 (70), 144 (60), 135 (50), 124 (90) and 112 (100). Acetylation with Ac_2O–pyridine afforded a semi-solid analysed for $C_{17}H_{22}O_6$. (Found C 64.44, H 7.22 requires C 63.34, H 6.87%). ^{1}H NMR (CCl_4): δ1.17 (3H, *d*, $J = 7$ Hz, C-10Me), 1.23 (3H, *s*, C-5Me), 2.06 (3H, *s*, C-13, CH_2OCOMe), 2.80 (1H, *m*, C-7H), 4.23 (2H, *d*, $J = 6$ Hz, CH_2OAc), 4.86 (1H, *d*, $J = 7.5$ Hz, C-6H), 6.03 (1H, *d*, $J = 6$ Hz, C-3H) and 7.43 (1H, *d*, $J = 6$ Hz, C-2H).

Compound **5** (50 mg) was stirred in dry Et_2O in the presence of a few drops of BF_3–etherate. After 1 hr, the mixture was poured into cold H_2O and extracted with Et_2O and chromatographed on silica gel to give the dehydrated product (15 mg), a semi-solid which analysed for $C_{15}H_{18}O_4$. UV λ_{max}^{MeOH} nm: 295. ^{1}H NMR ($CDCl_3$): δ1.28 (3H, s, C-5Me), 2.10 (3H, s, C-10Me), 4.12 (2H, *d*, $J = 6$ Hz, $-CH_2OH$), 3.28 (1H, *m*, C-7H), 480 (1H, *d*, $J = 7.5$ Hz, C-6H), 6.12 (1H, *d*, $J = 6$ Hz, C-3H) and 8.10 (1H, *d*, $J = 6$ Hz, C-2H).

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A LABDANE DITERPENOID AND STEROL FROM *LAGERSTROEMIA LANCASTERI*

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Key Word Index—*Lagerstroemia lancasteri*; Lythraceae; labdane diterpenoid; sterol; lagerstronolide; stigmast-4-ene-3β,6α-diol.

Abstract—A new labdane diterpenoid, lagerstronolide, having a β-substituted γ-butyrolactone moiety, and stigmast-4-ene-3β,6α-diol were isolated together with sitosterol glucoside from *Lagerstroemia lancasteri*. The structures of the new compounds were determined by means of spectral and chemical analysis. This is the first report of labdane diterpenoid in the Lythraceae family.

INTRODUCTION

Earlier work on the leaves and twigs of *Lagerstroemia lancasteri* afforded six triterpenoids and sitosterol [1]. Further investigation of this plant led to the isolation of a new diterpenoid named lagestronolide (**1**) and a 3,6-dihydroxysterol (**2**) and the known sitosterol glucoside in addition to the previously reported compounds [1].

RESULTS AND DISCUSSION

Lagerstronolide (**1**), mp 162°, $C_{22}H_{32}O_4$ (M^+ at m/z 360.2301) $[\alpha]_D$ $-7.3°$, gave a positive Legal test indicating the presence of an α,β-unsaturated γ-lactone moiety [2]. Its UV spectrum showed a maximum at 213 nm (ε10000) and its IR spectrum showed bands at 1785, 1765 (β-substituted γ-acetoxybutenolide [3]) 1645 and 885 cm^{-1} (exo-cyclic methelene group [4]). The ^{1}H NMR spectrum (100 MHz) of compound **1** which showed singlets at δ0.78 (3H), 0.80 (3H), and 1.00 (3H) for three tertiary methyl groups and two broad singlets at δ4.63 and 5.10 respectively are in accordance with the structure **1** having an exocyclic methelene group located at C-8 [4]. The absolute configuration of **1** was not certain but a labdane was more likely, as the optical rotation was opposite in sign to that of a similar *ent*-labdane derivative [3]. The methylene and methine protons appeared as multiplets in the region δ1.2–1.65 and 1.85–2.40, respectively. The presence of a β-substituted γ-acetoxybutenolide moiety was also demonstrated by the proton signals ascribed to the olefinic and oxygen bearing methine proton at δ6.81 and 5.91 (*s*, 1H each) [3] and the acetoxy methyl group appeared as a singlet at δ2.16. The presence of ion peaks at m/z 360, 300, 285 and 109 [3] in the mass spectrum of lagerstronolide confirmed its structure as **1**.

Compound **2** was isolated from the $CHCl_3$–MeOH (19:1) eluant as colourless needles, mp 220° (M^+ at m/z 430). Its IR spectrum showed the presence of hydroxyl groups (3300 cm^{-1}) and the ^{1}H NMR spectrum showed the olefinic proton at δ5.50 (1H, *br s*, $W_{1/2} = 3$ Hz) and the carbinol methine protons appeared at 4.18 (H-3, *m*, $W_{1/2} = 13$ Hz) and 4.10 (H-6, *t*, $J = 7$ Hz), respectively. Compound **2** on oxidation with CrO_3–AcOH [5] followed by *in situ* reduction with Zn dust [6] afforded the known compound 5α-stigmastane-3,6-dione (**3**), mp 199° (M^+ at m/z 428) [7]. The hydroxyl group at C-6 has been assigned as equatorial (α) from the *J*-value (7 Hz) of the H-6 signal. The hydroxyl group at C-3 is β and equatorially oriented on the basis of biogenetic consideration. The structure of **2** was also supported by its mass spectral fragmentations (see experimental). Thus the structure of compound **2** was established to be stigmast-4-ene-3β,6α-diol. The structure of sitosterol glucoside was elucidated by its hydrolysis to sitosterol and glucose.