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CONFERTDIOLIDE, A NOVEL SESQUITERPENOID LACTONE FROM *PARTHENIUM**

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Key Word Index—*Parthenium confertum* var. *lyratum*; Compositae; structure determination; photolysis; sesquiterpene.

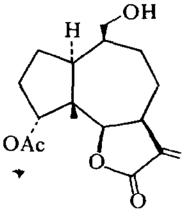
Abstract—Four sesquiterpene lactones were isolated from several populations of *Parthenium confertum* var. *lyratum* (Gray) collected in Sierra de Arteaga, southern Coahuila. Three of the compounds, hysterin, tetraneurin E and hymenin were previously isolated from other *Parthenium* species. The fourth constituent is the new cyclopropanoid sesquiterpene dilactone confertdiolide which represents a new structural type. The photolytic conversion of hymenin into confertdiolide confirmed its structure.

INTRODUCTION

In continuation of our search for sesquiterpene lactones in the *Parthenium confertum* complex we wish to report the results of our study of collections of *P. confertum* var. *lyratum* from southern Coahuila during the period 1974–1975. All samples yielded the known ambrosanolides hymenin (**3**) [1], tetraneurin E (**2**) [2], hysterin (**1**) [3], and the new sesquiterpene dilactone confertdiolide (**4**). Hymenin (**3**) was previously found in *P. confertum* [4] and *P. confertum* var. *microcephalum* [5], but not in *P. confertum* var. *lyratum*. The sesquiterpene lactone **3** has now been isolated from this variety and we consider it as the characteristic ambrosanolide of the *P. confertum* complex. This paper describes the isolation of **1–4** and presents evidence to support structure **4**.

RESULTS AND DISCUSSION

Confertdiolide (**4**) $C_{15}H_{18}O_4$, mp 156–158°; $[\alpha]_D^{22^\circ}$ -95.3° $CHCl_3$, is the first naturally occurring modified ambrosanolide which possesses a cyclopropane ring. It contains most of the structural features which characterize the pseudoguaianolides isolated from *Parthenium* species, such as an α,β-unsaturated γ-lactone ring closed to C-6, as indicated by the IR band at 1760 and the PMR doublet at 4.28 ppm ($J = 9$ Hz). The lactone is conjugated with an exocyclic methylene group, as shown by the typical low field doublets at 5.62 and 6.38 ppm (1H each, $J = 3.2$ Hz). In the PMR spectrum, the C-4 angular methyl group appeared as a singlet at 0.9 ppm and the C-10 methyl group at 1.2 ppm as a distorted doublet. In addition, **4** contains a saturated γ-lactone function, (IR band at 1780 cm^{-1}). The most important feature, which makes **4** different from the unknown ambrosanolides, is indicated in its PMR spectrum as an ABX system whose part X is a doublet of doublets centred at 1.49 (1H, $J_{AX} = 6$, $J_{BX} = 1.5$ Hz) and, which we attribute to the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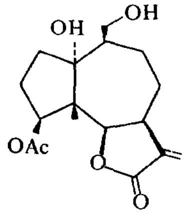
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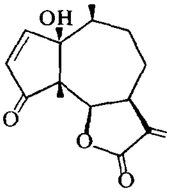
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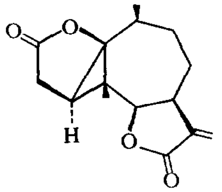
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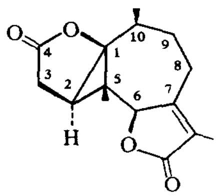
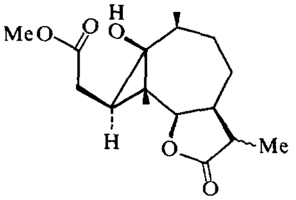


5 Isoconfertdiolide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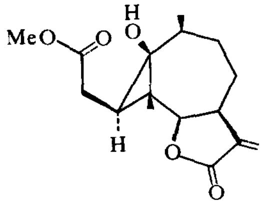
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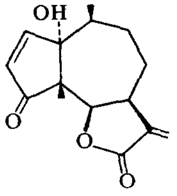
8 Parthenin

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only proton of a pentasubstituted cyclopropane ring. Proton X is coupled with an isolated vicinal methylene group, which appears as two doublets of doublets centred at 2.45 ppm (proton B) and 2.9 ppm (proton A), (J_{AB} = 19 Hz); the chemical shifts for these protons are in accord with a methylene group vicinal to the carbonyl group of a saturated γ-lactone as represented in **4**. Catalytic hydrogenation of **4** afforded an iso derivative, whose spectral data are in complete agreement with the proposed structure **5** (IR 1780, 1750, 1660); PMR 0.78 ppm (*s*, C_4-Me), 1.25 ppm (*d*, *J* = 7 Hz, C_{10}-Me); 4.43 ppm (*br* 1H, C-6) ABX. 2.95 ppm (*dd*, *J* = 6, 19 Hz, HA), 2.5 ppm (*d*, *d J* = 1.5, 19 Hz HB); 1.8 ppm (signal masked by methylene groups, HX).

When **4** was treated with $NaBH_4$ in MeOH, compound **6** was obtained in which the exocyclic methylene group was saturated and the second γ-lactone function was opened to give a methyl ester. The PMR spectrum of this compound confirmed structure **6**, since it showed the signal due to the methyl ester as a singlet at 3.72 ppm. Two doublets at 1.05 ppm and 1.25 ppm are indicative of the two secondary methyl groups at C-10 and C-11 respectively. The protons of the C-3 methylene group are coupled with the cylopropane proton, forming an ABX system with signals at 2.7 ppm (*d*, *d*, J_{AB} = 15 Hz, J_{AX} = 6 Hz) for HA, at 2.18 ppm (*d*, *d*, J_{AB} = 15 Hz) for HB and 0.83 ppm (*d*, *d*, J_{AX} = 6 Hz) for HX.

Confirmation of structure **4**, was achieved by its synthesis via photolytic conversion of hymenin (**3**). Agosta and Smith [6] have converted cyclopentenones via a cyclopropyl ketene rearrangement into methyl esters; this was successfully applied by Kagan *et al.* [7] to parthenin (**8**). As hymenin differs from parthenin only in the orientation of the OH group at C-1 we expected to obtain confertdiolide in a similar photolytic reaction. When hymenin was photolysed at 350 nm in AcOEt, it was converted to **4** in 50% yield. Therefore, the structure and stereochemistry of confertdiolide is as depicted in **4**.

When the photolytic reaction was carried out in MeOH, **4** and the methoxy derivative **7** were obtained in 3 : 1 ratio, thus indicating that the stereochemistry of hymenin is less favoured than that of parthenin, which did not afford any methoxy derivative [7].

EXPERIMENTAL

Mps are uncorr. IR spectra were recorded in $CHCl_3$ and UV in 95% EtOH unless otherwise stated. PMR spectra were performed in $CDCl_3$ using TMS as int. stand. and are given in δ scale. Analyses were determined by Dr. Pasher, Bonn, Germany.

Isolation of the lactones. Dried and ground material (796 g) of *Parthenium confertum* var. *lyratum* collected in October, 1974 in Sierra de Arteaga, Coahuila, was extracted with EtOH and worked up in the usual manner [8] leaving an oily residue (40.7 g), which was dissolved in C_6H_6 and chromatographed over Si gel. The fractions eluted with C_6H_6–AcOEt (4:1) were combined and crystallized from Me_2CO–isopropyl ether yielding **4** (224 mg) mp 155–157°; $[\alpha]_D^{22}$ −95.3° ($CHCl_3$), λ_{max} 212 nm, ε, 12 000, ν_{max} 1780 (γ lactone), 1760, 1650 cm^{-1} (Found. C, 68.82; H, 6.75; O, 24.35. $C_{15}H_{18}O_4$ requires C, 68.68, H, 6.92, O, 24.40%) From the fractions eluted with C_6H_6–AcOEt (3:2) there was obtained 1.095 g (**3**) mp 171–174° and 310 mg (**1**) mp 166–167°. The fractions eluted with C_6H_6–AcOEt (1:3) yielded 2.035 g **2**, mp 209–211° (from isopropyl ether).

Isoconfertdiolide (**5**). A soln of **4** (100 mg) in AcOEt was hydrogenated for 3 hr with Pd/C (15 mg). **5** crystallized from isopropyl ether with mp 153–155° (62 mg) ν_{max} 1775, 1750 and 1665 cm^{-1}, (Found C, 68.44, H, 6.71; O, 24.53. $C_{15}H_{18}O_4$ requires C, 68.68, H, 6.92; O, 24.40%)

Reduction of confertdiolide To a soln of (200 mg) in MeOH (50 ml) was added $NaBH_4$ (200 mg). The mixture was refluxed 7 hr, H_2O was added and AcOH to pH 7, the product was extracted with AcOEt and crystallized from isopropyl ether yielding 60 mg **6**, mp 126–127°, ν_{max} 3500, 1760 and 1630 cm^{-1} (Found; C, 64.83; H, 7.89; O, 26.76 $C_{16}H_{24}O_5$ requires. C, 64.84, H, 8.16; O, 27.00%).

Photolysis of hymenin. A soln of hymenin (250 mg) in AcOEt (250 ml) was irradiated at 350 nm (Rayonet Photochemical Reactor) at 20° in an Ar atmosphere. The reaction was followed by TLC. After 1.5 hr most of the starting material had disappeared. The solvent was removed *in vacuo*. The oily material obtained showed on TLC the presence of **4** and a small amount of starting material. The constituents of the reaction mixture were separated by prep TLC using AcOEt–hexane (1:1). The less polar product obtained was crystallized from Me_2CO–isopropyl ether and showed mp 150–155 (80 mg). It was identified as confertdiolide by standard methods. A soln of hymenin (250 mg) in MeOH (300 ml) was irradiated at 350 nm for 1.5 hr. The crude product obtained after removal of the solvent, showed in PMR the presence of **4** and a methyl ester. Prep TLC AcOEt–hexane (1:1) afforded a mixture of **4** and its methyl ester (**7**). On fractional crystallization **4** was obtained (100 mg; mp 140–150°). Prep TLC (AcOEt–hexane, 1:2) allowed the separation of (**7**) as an oily material (40 mg) ν_{max} 3450, 1750 (*br*) 905 cm^{-1}.

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