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A MELAMPOLIDE AND AN EUDESMANOLIDE FROM *PERYMENIUM MENDEZII**

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Key Word Index—*Perymenium mendezii*; Compositae; Heliantheae; sesquiterpene lactones; melampolide; eudesmanolide.

Abstract—The aerial parts of *Perymenium mendezii* var. *verbesinioides*, afforded two new lactones, the eudesmanolide desacetyl-β-cyclotulipinolide and the melampolide perymeniolide, whose structures were elucidated by chemical and spectroscopic methods.

INTRODUCTION

The genus *Perymenium* belongs to the subtribe Verbisininae [1]. From this genus, only *P. ecuadoricum* has been analysed; this resulted in the isolation of several diterpenes with kaurene skeleton and the widely distributed pentaine [2]. We have now investigated the submontane perennial *P. mendezii*, which afforded the 8α-hydroxy-4,(15)-eudesmen-6α,12-olide (**1a**) and the melampolide (**2a**) which we have named perymeniolide.

RESULTS AND DISCUSSIONS

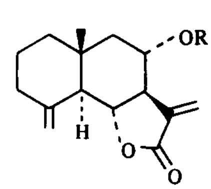
Lactone **1a** was isolated as a colourless gum, $C_{15}H_{20}O_3$ (EM). Its IR spectrum revealed the presence of a hydroxyl group, an α,β-unsaturated-γ-lactone ring system and double bonds (3450, 1765, 1670, 1650 cm^{-1}). The above mentioned and the analysis of the ^1H NMR spectrum allowed the assignments given in Table 1, which are in agreement with structure **1a**. On acetylation **1a** yielded the 8-acetyl derivative **1b** whose physical and spectral properties (Table 1), strongly support its identity with β-cyclo tulipinolide [3].

Table 1. ^1H NMR spectral data of compounds **1a** and **1b** (80 MHz, $CDCl_3$, TMS as int. standard)

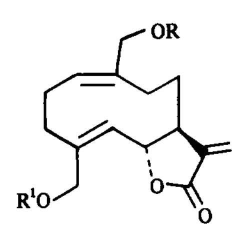
H	**1a**	**1b**
6	3.95 *t*	4.02 *t*
7	2.58 *tt*	2.81 *tt*
8	4.06 *ddd*	5.23 *ddd*
13a	6.1 *d*	6.1 *d*
13b	5.97 *d*	5.49 *d*
14	0.85 *s*	0.91 *s*
15a	4.9 *s (br)*	4.94 *s (br)*
15b	4.75 *s (br)*	4.8 *s (br)*
		2.08 *Ac*

J (Hz): Compound **1a**: 6,7 = 7,8 = 11; 7,13a = 3.5; 7,13b = 3; 8,9α = 11; 8,9β = 5; Compound **1b**: 6,7 = 7,8 = 12; 7,13a = 3.5; 7,13b = 3; 8,9α = 12; 8,9β = 5.

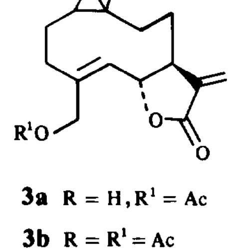
The second lactone, perymeniolide (**2a**), $[\alpha]_D + 241$ (*c* 0.153, $CHCl_3$), $C_{17}H_{22}O_5$ (mass spectrometry), was obtained as an oil. Its IR spectrum revealed the presence of a hydroxyl group (3460 cm^{-1}), a conjugated-γ-lactone ring system (1760 cm^{-1}), a saturated ester (1740 cm^{-1}) and double bonds (1662 cm^{-1}). Its ^1H NMR spectrum (Table 2) exhibited typical H-13 and H-13′ doublets at δ 6.16 and 5.44. The H-6 signal was located as a doublet of doublets at δ 4.46 (J = 10.5, 9.5 Hz) and it was coupled



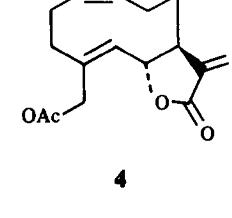
R
1a H
1b Ac



2a R = H, R^1 = Ac
2b R = R^1 = Ac
2c R = R^1 = H



3a R = H, R^1 = Ac
3b R = R^1 = Ac



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*Contribution No. 665 of the Instituto de Química, U.N.A.M.

Table 2. ^{1}H NMR spectra of perymeniolide and derivatives (80 MHz, $CDCl_3$, TMS as int. standard)

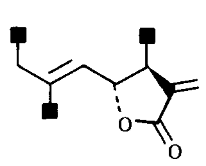
H	2a	2b	2c	3a	3b	4
1	5.45†	5.5†	5.45†	3.0 *dd*	2.9 *dd*	6.47 *t* (*br*)
				9, 3.5	10, 3.5	8
5	5.28 *d* (*br*)	5.28 *d*	5.2 *d*	5.43 *d*	5.47 *d*	5.24 *d*
	10.5	10	12.5	10	10.5	11.5
6	4.66 *dd*	4.64 *dd*	4.83 *dd*	4.62 *t*	4.68 *t*	4.63 *t*
	10.5, 9.5	10, 9	12.5, 11	10	10.5	11.5
13a	6.16 *d*	6.15 *d*	6.16 *d*	6.18 *d*	6.2 *d*	6.13 *d*
	3.5	3.5	3.5	3.5	3.5	3.5
13b	5.44 *d*	5.43 *d*	5.44 *d*	5.44 *d*	5.43 *d*	5.45 *d*
	3	3	3	3	3	3
14a	4.17 *d*	4.61 *d*		3.92 *d* (*br*)	4.43 *d*	
	10	12.5	4.1*	11	12	9.42 *d*
14b	3.92 *d*	4.37 *d*		3.48 *d* (*br*)	3.92 *d*	2
	10	12.5		3	12	
15a			4.5 *d*		4.82 *d*	
	4.75*	4.72*	13	4.73*†	13	4.75*†
15b			4.18 *d*		4.63 *d*	
			13		13	
OCOMe	2.1	2.06		2.06	2.1, 2.08	2.1

*Intensity two protons, centre of an AB system.
†Superimposed signal.

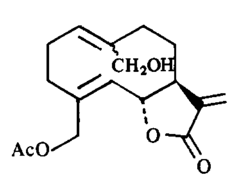
with a broad doublet at δ 5.28 (J = 10.5 Hz) which was attributed to H-5. The values of $J_{5,6}$ and $J_{6,7}$ allowed us to propose the partial structure A with a *trans*-4,5-double bond.

Furthermore, the ^{1}H NMR spectrum showed at δ 5.45 a partially superimposed signal due to the vinylic proton H-1 and two AB systems. The first one was centred at δ 4.08 (3.92, *d*, 10 Hz and 4.17, *d*, 10 Hz) and was assigned to the C-14 methylene which has a hydroxyl group bonded to it. This assignment was made because when perymeniolide was treated with MCPBA it afforded the monoepoxide **3a** whose NMR spectrum showed the signals for the C-14 methylene shifted to higher field (δ 3.92 and 3.48). The signal for H-1 was also shifted in the same way and appeared as a doublet of doublets at δ 3.0. The presence of a hydroxyl group was demonstrated by acetylation of **2a** which yielded the diacetate **2b**, the ^{1}H NMR spectrum of which showed a downfield displacement of H-14 and H-14′ (δ 4.61 and 4.37) and a new singlet at δ 2.01 (3H). The diacetyl derivative **3b** was obtained by acetylation of **3a**. In **3b**, the C-14 protons were paramagnetically shifted (δ 4.43 and 3.92).

The other AB system (δ 4.75, *s*, 2H) supported an acetoxy group and it was ascribed to a C-15 methylene. Alkaline saponification of **2a** afforded the diol **2c**, the ^{1}H NMR spectrum of which showed the signals for the C-15 protons displaced to higher field (δ 4.18 and 4.5). This fact permitted the expansion of structure **A** to that of structure **B**.



A



B

The stereochemistry of the 1(10)-double bond was established by oxidation of **1a** to the α,β-unsaturated aldehyde (**4**). In this compound, the signal for the aldehydic proton appeared at δ 9.42 as a doublet (J = 2 Hz). This displacement is characteristic for *cis*-conjugated aldehydes in those melampolides with that functionality [4]. Furthermore, a very similar compound has been described recently as a component of *Dicoma tomentosa* [5]. The identity between this compound and **4** was confirmed by comparison of the ^{1}H NMR and IR spectra.

EXPERIMENTAL

Extraction of P. mendezii. Aerial parts of *P. mendezii* DC. var. *verbinioides* (DC.) Fay (1.1 kg) collected in Cuernavaca, Morelos State, México (voucher on deposit in Herbarium of Universidad Nacional Autónoma de México. MEXU-311688), were extracted with $CHCl_3$. The crude gum (69.2 g) was percolated through a tonsil [6] column using as eluents hexane, $CHCl_3$ and EtOAc (2 l. each), which gave 8.8, 31.1 and 26.1 g of residue, respectively. The EtOAc fraction was decolourized with activated charcoal and chromatographed over silica gel ($CHCl_3$–Me_2CO). Fractions eluted with $CHCl_3$–Me_2CO (97:3) gave 38 mg **1a**. Colourless liquid; IR ν_{max}^{film} cm^{-1}: 3450, 1765, 1670, 1650. (Calc. for $C_{15}H_{20}O_3$: MW 248. Found MW (MS) 248.) Other significant peaks in the MS were at m/z: 253 $[M - Me]^+$, 230 $[M - H_2O]^+$, 215 $[M - Me - H_2O]^+$. Fractions eluted with $CHCl_3$–Me_2CO (9:1) gave 1.37 g **2a**. Colourless gum; UV λ_{max}^{EtOH} 212 nm (ε 11 700); $[\alpha]_D$ +241 (c 0.153, $CHCl_3$); IR ν_{max}^{film} cm^{-1}: 3460, 1760, 1740, 1662. (Calc. for $C_{17}H_{22}O_5$: MW 306. Found MW (CIMS) 306.) Other peaks in the CIMS were at m/z (rel. int.): 288 $[M - H_2O]^+$, 246 $[M - AcOH]^+$, 228 $[M - AcOH - H_2O]^+$.

Acetylation of **1a**. Pyridine–Ac_2O (1:1, 1 ml) was added to 10.4 mg **1a**. After 1 hr the mixture was worked up as usual to give 8.3 mg **1b**. Mp 135–136° (EtOAc–hexane); IR ν_{max}^{film} cm^{-1}: 1772, 1740, 1670, 1645. (Calc. for $C_{17}H_{22}O_4$: MW 290. Found MW (MS) 290.) Other significant peaks in the MS were at m/z (rel. int.):

275 $[M - Me]^+$, 230 $[M - AcOH]^+$, 43 (100).

Epoxidation of **2a**. MCPBA (98.6 mg) was added to a soln of **1a** (100 mg) in $CHCl_3$ (10 ml). The mixture was refluxed by 3 hr and percolated through a tonsil column with 50 ml of $CHCl_3$ to give unreacted MCPBA. The second eluate (EtOAc, 50 ml) gave, after crystallization from Me_2CO–hexane, 32.4 mg **3a**. Mp 107–109°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3570, 1760, 1735, 1665. (Calc. for $C_{17}H_{22}O_6$: MW 322. Found MW (CIMS) 322.) Other significant peaks in the EIMS were at m/z 291 $[M - MeO]^+$, 262 $[M - AcOH]^+$, 249 $[M - C_2H_2O - MeO]^+$, 244 $[M - AcOH - H_2O]^+$, 231 $[M - AcOH - MeO]^+$, 213 $[M - AcOH - MeO - H_2O]^+$, 81 (92), 79 (100), 43 (78).

Acetylation of **2a**. Ac_2O (1 ml) was added to a soln of **2a** (100 mg) in pyridine (1 ml). After 10 min, H_2O was added and the mixture worked up as usual to give 55 mg **2b**. Colourless oil; IR ν_{max}^{film} cm^{-1}: 1763, 1735, 1664. (Calc. for $C_{19}H_{24}O_6$: MW 348. Found MW (CIMS) 348.) Other prominent peaks in the MS were at m/z: 306 $[M - C_2H_2O]^+$, 289 $[M - AcO]^+$, 247 $[M - AcO - C_2H_2O]^+$, 229 $[M - AcO - AcOH]^+$ (100), 81 (14.8) 79 (9.8), 43 (11).

Acetylation of **3a**. Ac_2O (1 ml) was added to a soln of **3a** (130.8 mg) in pyridine (1 ml). After 30 min, H_2O was added and the mixture worked up as usual. Crystallization from $CHCl_3$–hexane gave 87.3 mg **3b**, mp 163–164°; IR $\nu_{max}^{CHCl_3}$ cm^1: 1760, 1738, 1665. (Calc. for $C_{19}H_{24}O_7$: MW 364. Found MW (MS) 364.) Other characteristic peaks in the MS were at m/z (rel. int.): 322 $[M - C_2H_2O]^+$, 304 $[M - AcOH]^+$, 291 $[M - C_2H_2O - MeO]^+$, 262 $[M - AcOH - C_2H_2O]^+$, 231 $[M - AcOH - C_2H_2O - MeO]^+$, 226 $[M - 2AcOH - H_2O]^+$, 216 $[M - 2AcOH - CO]^+$, 81 (25), 79 (33.5), 43 (100).

Hydrolysis of **2a**. A soln of 106 mg **2a** in 5 ml MeOH was stirred with 245 mg $KHCO_3$ for 15 hr. The mixture was diluted with 50 ml $CHCl_3$ and percolated through a silica gel column. After evaporation of $CHCl_3$ 60.5 mg of a mixture of two components (TLC) was obtained. The major component **2c** was isolated by prep. TLC (silica gel, $CHCl_3$–Me_2CO, 4:1, × 2). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3490, 1760, 1660, 1620. (Calc. for $C_{15}H_{20}O_4$: MW 264. Found MW (MS) 264.) Other significant peaks at MS were at m/z (rel. int.): 246 $[M - H_2O]^+$, 233 $[M - MeO]^+$, 228 $[M - 2H_2O]^+$, 215 $[M - H_2O - MeO]^+$, 79 (64.9).

Oxidation of **2a**. A soln of **2a** (60 mg) in CH_2Cl_2 (5 ml) was stirred for 1 hr with pyridinium dichromate (300 mg). The soln was percolated through a tonsil column using as eluent a mixture of $CHCl_3$–hexane (4:1). The residue was crystallized from Me_2CO–hexane (38 mg), mp 158–160°; UV λ_{max}^{EtOH} 223 nm (ε 16 500); $[\alpha]_D + 2.29$ (c 0.174, $CHCl_3$); IR ν_{max}^{film} cm^{-1}: 1760, 1733, 1680, 1620. (Calc. for $C_{17}H_{20}O_5$: MW 304. Found MW (CIMS) 304.) Other significant peaks at the EIMS were at m/z 262 $[M - C_2H_2O]^+$, 244 $[M - AcOH]^+$, 226 $[M - AcOH - H_2O]^+$, 215 $[M - AcOH - MeO]^+$ 91 (83), 79 (84), 43 (100).

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