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AN EREMOPHILANE SESQUITERPENOID FROM *PEDICULARIS STRIATA PALL* SSP. *ARACHNOIDEA*

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Key Word Index—*Pedicularis striata pall* spp. *arachnoidea*; Scrophulariaceae; eremophilane sesquiterpenoid; eremophila-10,11-dien-7α,13-diol.

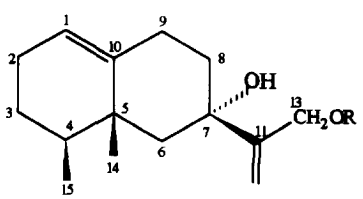
Abstract—A new sesquiterpenoid, eremophila-10,11-dien-7α,13-diol, has been isolated from *Pedicularis striata pall* ssp. *arachnoidea* and appropriately identified on the basis of spectral and chemical evidence. Copyright ©1996 Elsevier Science Ltd

INTRODUCTION

In a previous study, we reported on the isolation and characterization of two new phenylpropanoid glycosides, named pedicullariosides M and N, along with two known phenylpropanoid glycosides from *Pedicularis striata pall* ssp. *arachnoidea* [1]. In a further investigation of the chemical constituents of the title plant, we have now isolated a new secondary metabolite, the first sesquiterpenoid-type constituent in *Pedicularis*, eremophila-10,11-dien-7α,13-diol (**1**).

RESULTS AND DISCUSSION

Compound **1** gave IR absorption bands for the presence of hydroxyl groups (3316 cm^{-1}) and a terminal double bond (1645, 842 cm^{-1}). A molecular ion peak at *m/z* 236.3569 (HRMS) and 15 carbon signals in the ^{13}C NMR and DEPT spectra established the molecular formula as $C_{15}H_{24}O_2$. ^{13}C NMR signals at δ 65.6 (CH_2) and 74.5 (C) clearly indicated the presence of a primary and tertiary hydroxyl group, respectively. The 400 MHz ^1H NMR spectrum (Table 1) showed two methyl groups at δ 0.88 (3H, *d*, *J* = 6.4 Hz, H-15) and 0.84 (3H, *s*, H-14). Three olefinic protons at δ 5.38 (1H, *m*, H-1), 5.25 (1H, *s*, H-12) and 5.27 (1H, *s*, H-12) together with four signals for sp^2 carbons at δ 142.2 (C), 120.9 (CH), 150.5 (C), 113.2 (CH_2) established a trisubstituted and a terminal double bond, which are not conjugated (λ_{max} = 211 nm, lg ε 2.94). In the ^1H NMR spectrum of the monoacetate **1a**,



1 R=H
1a R=Ac

Table 1. ^1H NMR (400 MHz; $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) data of compound **1***

H	δ	J [Hz]	C	δ	DEPT
1	5.38 *dt*	8.8, 2.4	1	120.9	CH
2	1.90–2.04 *m*		2	25.7	CH_2
3	1.35–1.41 *m*		3	26.5	CH_2
4	1.44 *dq*	12.8, 6.4	4	41.3	CH
6α	1.39 *d*	13.0	5	37.9	C
6β	2.38 *dd*	13.0, 2.4	6	48.3	CH_2
8α	1.54 *dt*	12.8, 4.8	7	74.5	C
8β	2.28 *ddd*	12.8, 5.2, 2.9	8	37.8	CH_2
9α	2.10 *ddd*	12.8, 4.8, 2.9	9	30.2	CH_2
9β	2.37 *m*†		10	142.2	C
12	5.25 *s*		11	150.5	C
12′	5.27 *s*		12	113.2	CH_2
13	4.23 *d*	12.7	13	65.6	CH_2
13′	4.53 *d*	12.7	14	18.5	CH_3
14	0.84 *s*		15	16.8	CH_3
15	0.88 *d*	6.4			

*Assignment from ^1H–H COSY, ^1H–^{13}C COSY and ^{13}C–^1H long range COSY spectra.

†Signal partially overlapped.

H-13 and H-13′ are shifted downfield by 0.25 ppm and 0.17 ppm, respectively, suggesting the presence of a hydroxyl group at C-13. Based on the data above, **1** must be a functionalized carbobicyclic sesquiterpenoid [2–4].

The ^1H–^1H correlations observed in 2D ^1H–^1H COSY spectrum combined with 2D ^1H–^{13}C COSY spectrum enable us to establish the following subunits: >C=CHCH$_2$CH$_2$CH(CH$_3$)–, –CH$_2$CH$_2$– CH$_2$=C(CH$_2$OH)–, –CH$_2$– and >CMe. The connections of the subunits were determined from detailed analysis of the ^{13}C–^1H long range COSY optimized for a J_{C-H} coupling constant value of 8 Hz. The carbon at δ_c 142.2 (C-10) showed cross peaks with Me-14 and H-9, indicating the connection of C-10 to C-9 and C-5. The quarternary carbon at δ_c 37.9 (C-5) showed $^3J_{C-H}$ connection with H-15, whereas the carbon at δ_c 41.3 (C-4) showed $^3J_{C-H}$ connection with H-14. The sp^3 quarternary carbon at δ_c 74.5 (C-7) showed correlation with H-12 whereas the carbon at δ_c 150.5 (C-11) showed correlation with H-6. The above results are consistent with an eremophilane skeleton.

The relative stereochemistry of compound **1** was determined by ^1H NMR and NOE difference spectra. The large coupling constant (J = 12.8 Hz) between H-3 axial and H-4 shows that Me-15 is equatorial. The strong enhancement of H-15 (12.2%) on irradiation of H-14 indicates that Me-14 is axial. Irradiation of H-14 and H-9β (axial) caused enhancements (7.1% and 9.3%, respectively) of H-12, suggesting that the α-hydroxymethylvinyl group has the β configuration. In addition, irradiation of H-8α (δ 1.54 ppm) caused enhancement of H-6α (δ 1.39 ppm). Consequently, compound **1** is identified as eremophila-10,11-dien-7α,13-diol.

EXPERIMENTAL

General. ^1H NMR and ^{13}C NMR: 400 and 100 MHz, respectively, in the FT mode.

Plant material. Pedicularis striata pall ssp. *arachnoidea* was collected in Gansu Province, P. R. China, in August 1991. The plant was identified by Prof. Zhao Runeng (Pharmacognosy Department, Lanzhou Medical College, Lanzhou, P. R. China). A voucher specimen (LMC 91-086) was deposited in the Herbarium of the Pharmacognosy Department, Lanzhou Medical College, Lanzhou, P. R. China.

Extraction and isolation. Dried root (2.5 kg) was extracted with 95% EtOH at room temp. for 3 days. After concn of the combined extracts nearly to dryness under red. pres., hot water was added and the insoluble material was removed by filtration through celite. The filtrate was consecutively extracted with petrol and *n*-BuOH. The petrol portion (40 g) was chromatographed over a silica gel (200–300 mesh) column eluting with petrol (60–90°)-Me$_2$CO (4:1) to yield compound **1** (50 mg).

Eremophila-10,11-*dien*-7α,13-*diol* (**1**). Powder, mp 88–90°, $[\alpha]_D^{20}$ −9.77 (*c* 0.58, MeOH). UV λ_{max}^{MeOH} nm (lg ε): 208 (2.93), 211 (2.94); IR ν_{max}^{KBr} cm^{-1}: 3316 (OH), 2959, 1644 (C=C), 1602, 1451, 1433, 1059, 843; EI-MS *m/z* (rel. int.): 236 [M]$^+$, (8.3), 218 [M–H$_2$O]$^+$, (31), 200 [M–2H$_2$O]$^+$, (100), 185 (35), 158 (33), 121 (44), 107 (37), 91 (47), 70 (52), 55 (50); HR-MS *m/z*: 236.3569 (calcd for C$_{15}$H$_{24}$O$_2$, 236.3558); ^1H NMR and ^{13}C NMR: Table 1.

Acetylation of **1.** Compound 1 (15 mg) was acetylated with pyridine and Ac$_2$O for 12 hr at room temp. After addition of CH$_2$Cl$_2$, the residue was chromatographed on silica gel (petrol–Me$_2$CO 6:1) affording **1a** (10 mg). Oil; EI-MS *m/z*: 278 [M]$^+$, 235 [M−Ac]$^+$, 219 [M−AcO]$^+$, 185, 121, 107, 91, 55; ^1H NMR (CDCl$_3$, 400 MHz): δ 0.86 (3H, *s*, H-14), 0.88 (3H, *d*, J=6.4 Hz, H-15), 1.34 −1.41 (2H, *m*, H-3), 1.35 (1H, *d*, J=13.2, H-6), 1.44 (1H, *dq*, J=13.2 and 6.4 Hz, H-4), 1.57 (1H, *dt*, J=13.2 and 5.0 Hz, H-8), 1.90–2.03 (2H, *m*, H-2), 2.10 (1H, *m*, H-9), 2.11 (3H, *s*, CH$_3$CO), 2.21 (1H, *dd*, J=13.2 and 2.4 Hz, H-6), 2.24 (1H, *m*, H-8), 2.37 (1H, *m*, H-9), 4.48 and 4.47 (1H each, *d*, J=13.7 Hz, H-13), 5.26 and 5.38 (1H each, *brs*, H-12), 5.37 (1H, *dt*, J=8.9 and 2.4 Hz, H-1).

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