Pergamon

Phytochemistry, Vol. 42, No. 4, pp. 1231–1233, 1996

0031-9422/96 $15.00 + 0.00

S0031-9422(96)00142-2

SESQUITERPENE LACTONES FROM *ARTEMISIA LERCHIANA*

MILKA N. TODOROVA and MARIA L. KRASTEVA

Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria

(*Received in revised form* 23 *January* 1996)

Key Word Index—*Artemisia lerchiana*; Asteraceae; sesquiterpene lactones; eudesmanolides; guaianolides.

Abstract—The aerial parts of *Artemisia lerchiana* afforded, in addition to the known sesquiterpene lactones artemorin, ridentin A, ridentin 3-acetate and artecalin, two new eudesmanolides and two new guaianolides: 3β-acetoxy-1β-hydroxyarbusculin, 3-acetylridentin B, 4α,8α-dihydroxy-1α,5αH-guaia-2,10(14),11(13)-trien-12,6-olide and 2β-hydroxyepiligustrin. Their structures were established by spectroscopic methods.

INTRODUCTION

In continuation of our chemical research of Bulgarian *Artemisia* species, we have now studied the lactone composition of *A. lerchiana* Weber. Although *Artemisia* species have been investigated widely, *A. lerchiana* has so far been the object of only two early studies [1, 2], possibly due to its limited occurrence in Bulgaria, Romania and Russia [3]. We now wish to report that the Bulgarian *A. lerchiana* contains eight sesquiterpene lactones, four of which are new natural products. However, we could detect neither santonin nor desacetylmatricarin previously reported to be present in *A. lerchiana* of Russian origin [1, 2].

RESULTS AND DISCUSSION

The chloroform extract of the aerial parts of *A. lerchiana* afforded, after careful separation by column chromatography and preparative TLC, the new lactones **1**–**4** as well as the germacranolides artemorin [4], ridentin A [5] and ridentin 3-acetate [6] and the eudesmanolide artecalin [7].

Lactone **1** was assigned the molecular formula $C_{17}H_{24}O_6$ (*m/z* 324, M^+); its IR spectrum revealed the presence of an α-methylene-γ-lactone moiety (1760 cm^{-1}) and hydroxyl and acetate groups (3600, 1730 and 1250 cm^{-1}). The ^1H NMR spectrum (Table 1) was very similar to that of 1β-hydroxyarbusculin (**5**) [8] except for the presence of the signals of the acetoxy group (δ 2.10) and the corresponding geminal proton (δ 4.85, *dd*). The location of the ester group at C-3 was deduced from spin decoupling experiments and its β-orientation followed from the coupling pattern of the signal for H-3. All these data agreed with the structure of 3β-acetoxy-1β-hydroxyarbusculin for lactone **1**.

The structure of lactone **2** again followed from the molecular formula ($C_{17}H_{22}O_5$, *m/z* 306) and the ^1H NMR data (Table 1). The latter proved to be very close to those of the eudesmanolide ridentin B (**6**) [9]. However, the signals at δ 2.14 and 5.19 revealed that an acetoxy group was present in **2**, and its position at C-3 was established by decoupling experiments. Thus, the lactone **2** was identified as 3β-acetylridentin B.

The mass spectra of the lactones **3** and **4** were identical, showing the parent peak at *m/z* 262 in agreement with the molecular formula $C_{15}H_{18}O_4$. The successive loss of two molecules of water was the most prominent feature in the spectra of both **3** and **4**. Their ^1H NMR data (Table 1) indicated close structural similarity. Extensive decoupling experiments revealed the complete proton connectivities and pointed to the proposed *cis*-guaiane skeleton with a 12,6-α-methylene-γ-lactone moiety, a hydroxyl group at C-8 and an exomethylene group at C-10. The magnitude of the coupling constants of H-5 to H-8 were in full agreement with an antiperiplanar disposition of H-5/H-6/H-7/H-8. The α-orientation of the C-8 hydroxyl group was additionally supported by the downfield shift of one of the H-13 signals. Furthermore, the ^1H NMR data showed structural differences in the five-membered rings of **3** and **4**, although they both contained a double bond and a hydroxyl group. The lack of a signal of a carbinolic proton, and the chemical shift of the C-4 methyl group (δ 1.39, *s*) indicated that in **3** the hydroxyl group was located at C-4. Further, the two downfield signals at δ 5.64 (*dd*) and 5.87 (*dd*) were assigned to olefinic protons at C-2 and C-3. However, the double bond in **4** was trisubstituted, as shown by the signals for one olefinic proton (δ 5.62, *d*) and the corresponding vinylic methyl group (δ 1.93). The presence of a β-oriented hydroxyl group at C-2 clearly followed from decoupling experiments. Final proof of the structures **3** and **4** was provided by correlation of their spectroscopic data with those of the known

Table 1. ^{1}H NMR spectral data for compounds **1–4** (250 MHz, $CDCl_3$)

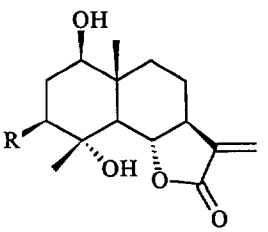
H	1	2	3	4
1	3.62 *dd*	3.63 *dd*	3.56 *br d*	2.96 *dd*
2α	2.06 *m**	2.24 *ddd*	5.64 *dd*	4.78 *m*
2β	1.68 *ddd*	1.60 *m**		
3	4.85 *dd*	5.19 *dd*	5.87 *dd*	5.62 *br s*
5	1.83 *d*	2.11 *m*†	2.67 *dd*	2.90 *dd*
6	4.17 *dd*	4.08 *dd*	4.12 *dd*	3.96 *dd**
7	2.61 *ddddd*	2.55 *ddddd*	3.00 *dddd*	2.83 *dddd*
8α	2.06 *m**	2.11 *m*†		
8β	1.58 *m*	1.60 *m**	3.83 *ddd*	3.96 *ddd**
9α	1.31 *ddd*	1.35 *ddd*	2.18 *dd*	2.37 *dd*
9β	2.06 *m**	1.60 *m**	2.90 *dd*	2.64 *dd*
13	6.14 *d*	6.11 *d*	6.37 *d**	6.28 *d*
13′	5.48 *d*	5.43 *d*	6.37 *d**	6.16 *d*
14	1.01 *s*	0.85 *s*	4.98 *br s* 4.80 *br s*	5.14 *br s* 5.04 *br s*
15	1.39 *s*	5.19 *br s* 5.02 *br s*	1.39 *s*	1.93 *s*
OAc	2.10 *s*	2.14 *s*		

*,†Overlapped signals.

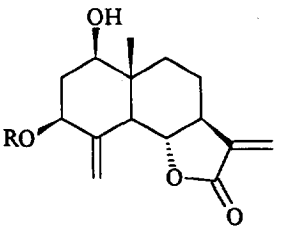
J [Hz]: **1**: 1,2α = 3.8; 1,2β = 2α,2β = 2β,3 = 8β,9α = 9α,9β = 12.0; 2α,3 = 4.9; 5,6 = 6,7 = 7,8α = 11.4; 7,8β = 7,13 = 3.2; 7,13′ = 3.0; 8α,9α = 3.7; **2**: 1,2α = 2α,3 = 4.5; 1,2β = 2α,2β = 12.0; 2β,3 = 11.4; 5,6 = 6,7 = 7,8α = 10.8; 7,8β = 7,13′ = 3.0; 7,13 = 3.2; 8β,9α = 9α,9β = 12.8; 8α,9α = 3.7; **3**: 1,2 = 2.7; 1,3 = 1.6; 1,5 = 9.7; 2,3 = 8,9β = 5.7; 5,6 = 11.3; 6,7 = 9.0; 7,8 = 8,9α = 10.0; 9α,9β = 12.4; 7,13 = 7,13′ = 3.2; **4**: 1,2 = 6.0; 1,5 = 8.5; 5,6 = 6,7 = 7,8 = 9.5; 8,9α = 5.1; 8,9β = 3.3; 9α,9β = 14.0; 7,13 = 3.5; 7,13′ = 3.1.

lactones **7** [10] and **8** (epiligustrin) [11]. Accordingly, **3** was the 8α-hydroxyl derivative of **7**, and **4** was 2β-hydroxyepiligustrin. We suggest the name lerchianin for lactone **3**.

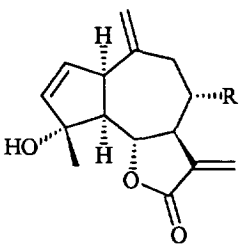
Artemisia lerchiana is included in sect. Seriphidium of the genus Artemisia, representatives of which are known to produce mainly 11,13-dihydrosesquiterpene lactones [12]. In contrast, all the lactones isolated from Bulgarian *A. lerchiana* possess an α-methylene-γ-lactone moiety, and this fact could be of taxonomical



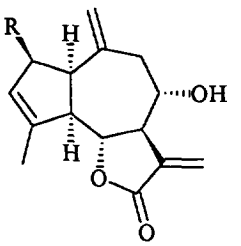
1 R=OAc
5 R=H



2 R=Ac
6 R=H



3 R=OH
7 R=H



4 R=OH
8 R=H

interest. The co-occurrence of germacranolides, guaianolides and eudesmanolides in the investigated sample is not unexpected, although eudesmanolides are found to dominate in species of sect. Seriphidium.

EXPERIMENTAL

The plant material was collected in August 1994 on the north Bulgarian Black Sea coast. The voucher specimen (SOM-Co-318) is deposited in the Herbarium of the Institute of Botany, Bulgarian Academy of Sciences.

The air-dried aerial parts of *A. lerchiana* (380 g) were extracted with EtOH and the total extract was worked-up as described in ref. [13] to give the crude lactone fr. (10 g). Five g of the latter were sepd by CC on silica gel using $CHCl_3$–Me_2CO with increasing polarity. The lactone-containing frs (IR monitoring) were further purified by CC and prep. TLC to give 7 mg artemorin, 8 mg artecalin, 50 mg ridentin A, 20 mg ridentin 3-acetate, 14 mg **1**, 15 mg **2**, 6 mg **3** and 8 mg **4**.

3β-Acetoxy-1β-hydroxyarbusculin (**1**). Mp 180–182° (hexane–Et_2O), IR ν_{max}^{KBr} cm^{-1}: 3450, 1760, 1725, 1650, 1240; EIMS *m/z* (rel. int.): 324 $[M]^+$ (2), 306 $[M-H_2O]^+$ (25), 264 $[M-HOAc]^+$ (2), 246 $[M-H_2O-HOAc]^+$ (10), 208 (60), 189 (30), 43 (100); ^1H NMR: Table 1.

3-Acetylridentin B (**2**). Mp 169–171° (hexane–Et_2O), IR ν_{max}^{KBr} cm^{-1}: 3500, 1760, 1725, 1650, 1240; EIMS *m/z* (rel. int.): 306 $[M]^+$ (1), 288 $[M-H_2O]^+$ (12), 264 $[M-42]^+$ (40), 246 $[M-HOAc]^+$ (60), 43 (100); ^1H NMR: Table 1.

4α,8α-Dihydroxy-1α,5αH-guaia-2,10(14),11(13)-trien-12,6-olide (*lerchianin*) (**3**). Oil, IR ν_{max}^{film} cm^{-1}: 3600, 1760, 1630; EIMS *m/z* (rel. int.): 262 $[M]^+$ (7), 247 $[M-Me]^+$ (100), 229 $[247-H_2O]^+$ (5), 211 $[229-H_2O]^+$ (6), 183 (11), 162 (9), 91 (24), 69 (34), 55 (37), 43 (90); ^1H NMR: Table 1.

2β-Hydroxyepiligustrin (**4**). Oil, IR ν_{max}^{film} cm^{-1}: 3600, 1760, 1630; EIMS *m/z* (rel. int.): 262 $[M]^+$ (2), 247 $[M-Me]^+$ (10), 229 $[247-H_2O]^+$ (3), 211 $[229-H_2O]^+$ (4), 183 (7), 162 (60), 91 (26), 69 (55), 55 (61), 43 (100); ^1H NMR: Table 1.

Acknowledgements—The authors are grateful for the financial support of the project provided by the Bulgarian National Research Foundation. We thank Frau Iris Klaiber, Institute of Chemistry, Hohenheim University, Stuttgart, Germany, for the mass spectra.

REFERENCES

1. Goryaev, M. I., Sazonova, R. N., Polyakov, P. P. and Belova, E. A. (1959) *Trudy Inst. Khim. Nauk, Akad. Nauk Kaz. SSR* **4**, 68.
2. Rybalko, K. S., Massagetov, P. S. and Evstratova, R. I. (1963) *Med. Prom. SSSR* **17**, 41.
3. Tutin, T. G., Persson, K. and Gutterman, W. (1976) in *Flora Europeae* (Tutin, T. G., Heywood, V. H., Burges, N. A., Moore, D. M., Valentine, D. H., Walters, S. M. and Webb, D. A., eds), Vol. 4, p. 178. Cambridge University Press, Cambridge, U.K.
4. Geissman, T. A. (1970) *Phytochemistry* **9**, 2377.
5. Irwin, M. A., Lee, K. H., Simpson, R. F. and Geissman, T. A. (1969) *Phytochemistry* **8**, 2009.
6. Marco, J. A., Sanz-Cervera, J. F., Manglino, E., Sancenon, F., Rustaiyan, A. and Kardar, M. (1993) *Phytochemistry* **34**, 1561.
7. Geissman, T. A., Griffin, T. S. and Irwin, M. A. (1969) *Phytochemistry* **8**, 1297.
8. Samek, Z., Holub, M., Grabarczyk, H., Drozdz, B. and Herout, V. (1973) *Collect. Czech. Chem. Commun.* **38**, 1971.
9. Irwin, M. A. and Geissman, T. A. (1973) *Phytochemistry* **12**, 871.
10. Zdero, C., Bohlmann, F. and Muller, M. (1987) *Phytochemistry* **26**, 2763.
11. Ito, K., Sakakibara, J. and Haruna, M. (1982) *Phytochemistry* **21**, 715.
12. Kelsey, R. G. and Shafizadeh, F. (1979) *Phytochemistry* **18**, 1591.
13. Todorova, M. and Ognyanov, I. (1989) *Phytochemistry* **28**, 1115.