

Sesquiterpene Lactones from *Achillea collina* Becker

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Z. Naturforsch. **57c**, 568–570 (2002); received March 15, 2002

Achillea collina, Asteraceae, Sesquiterpene Lactones

Aerial parts of *Achillea collina* afforded, in addition to five known sesquiterpene lactones two new germacranolides and one new eudesmanolide, the structures of which were elucidated by spectroscopic methods.

Introduction

The species of genus *Achillea*, particularly those belonging to the *Achillea millefolium* group have received a lot of attention so far, due to their use in traditional medicine. Among the numerous chemical compounds isolated from the *A. millefolium* species, the sesquiterpene lactones are usually one of the major constituents (Seaman, 1982). Continuing our chemotaxonomic examination of Bulgarian *Achillea* taxa, we have undertaken an investigation of the chloroform extract of *Achillea collina* Becker, a tetraploid species of the *A. millefolium* group. Previous chemical studies on this species revealed the presence of lactones belonging to the guaiane type only. The main lactones were reported to be artabsin derivatives (Verzar-Petri *et al.*, 1980; Kastner *et al.*, 1991a; Kastner *et al.*, 1991b; Kubelka *et al.*, 1999), although a matricin derivative (Verzar-Petri *et al.*, 1980) and a matricarin derivative (Glasl *et al.*, 1994) were also isolated. In contrast, we could not detect any other lactones but germacranolides and eudesmanolides. In the present paper, we wish to report the isolation of three new sesquiterpene lactones, **2**, **4** and **5**, in addition to the known lactones **1**, **3**, **6**, **7** and **8**.

Experimental

Plant material

The above ground parts of *A. collina* were collected from Rodopa mountain in July 1995. The plant material was identified by Dr. R. Taskova,

Institute of Botany, Bulgarian Academy of Sciences, and a voucher specimen (CO-528) was deposited in the Herbarium of the same Institute.

Extraction and isolation

The air-dried plant material (60 g) was extracted with chloroform (2 × 500 ml) to give, after evaporation of the solvent under reduced pressure, a brownish gum (2.0 g). It was then defatted by dissolving in 50% aq. MeOH (20 ml). After filtration, the filtrate was first extracted with hexane (3 × 25 ml), then concentrated by evaporation the methanol, and finally extracted with chloroform (3 × 10 ml) to give, after removing the solvent the crude lactone fraction (0.7 g). It was separated into 9 fractions by column chromatography (CC) on silica gel (100 g) using chloroform-acetone mixtures as eluents. Selected fractions (IR control) were subjected further to repeated CC and/or prep TLC to yield **1** (2 mg), **2** (16 mg), **3** (11 mg), **4** (3 mg), **5** (6 mg), **6** (2 mg), **7** (10 mg) and **8** (4 mg).

8α-tigloyloxy-11β,13-dihydroparthenolide (**2**): oil, EIMS (70 eV), *m/z* (rel. int.): 348 [M]⁺ (1), C₂₀H₂₈O₅; 248 [M-100]⁺ (31); 220 [248-28]⁺ (23); 83 (100), 55 (64). ¹H NMR: in Table I.

8-acetylshonachalin A (**4**): oil, EIMS (70 eV), *m/z* (rel. int.): 308 [M]⁺ (1) C₁₇H₂₄O₅, 248 [M-60]⁺ (10), 230 [M-60-18]⁺ (100), 215 (22), 202 (32), 174 (57), 149 (61), 121 (62), 95 (78), 69 (77), 55 (83). ¹H NMR: in Table I.

8-acetylartapshin (**5**): oil; EIMS (70 eV), *m/z* (rel. int.): 308 [M]⁺ (1) C₁₇H₂₄O₅, 290 [M-18]⁺ (6), 248 [M-60]⁺ (12), 230 (70), 215 (20), 159 (30), 107 (29), 91 (35). ¹H NMR: in Table I.

Results and Discussion

The chloroform extract of the aerial parts of *A. collina* was worked up as described in the Experimental, to give the following lactones in order of their elution: 11 β H,13-dihydroparthenolide (**1**) (Ruangrunsi and Rivepiboon, 1988), **2**, balchanolide (**3**) (Suchy *et al.*, 1963), **4**, **5**, 1 β -hydroperoxy-8 α -hydroxygermacra-4,10(14)-diene-6 β ,7 α ,11 β H-12,6-olide (**6**) (Marco, 1989), 8 α -hydroxy-11 β H,13-dihydrobalchanin (**7**) (Fernandez *et al.*, 1987) and artapshin (**8**) (Fernandez *et al.*, 1987).

Compound **2**, isolated as an oil, was a germacranolide, the structure of which followed from the ^1H NMR spectrum (Table I). The latter indicated an 8 α -tigloyloxy derivative of **1**. The presence of the tigloyl ester moiety was further confirmed by the MS spectrum which displayed, alongside a molecular ion (m/z 348) with very low intensity a fragment at m/z 248 due to loss of the aliphatic acid ($\text{C}_5\text{H}_8\text{O}_2$). Moreover, the ^1H NMR data were very similar to those described for the lactones **9** (Jakupovic *et al.*, 1992) and **10** (Talapatra *et al.*, 1970). However, the chemical shift of the H-8 signal in **2** (δ 4.96) which appeared in the same region as that in **10** (δ 4.85) indicated that the hydroxyl group in **9** is replaced by a tigloyl group. The configuration at C-5/ C-8 and C-11 followed from the observed coupling constants, and from their good coincidence with those of the germacranolides **9** and **10**. Accordingly, the new lactone **2** was identified as 8 α -tigloyloxy-11 β H,13-dihydroparthenolide.

The MS and ^1H NMR data of the lactone **4** clearly showed that we were again dealing with

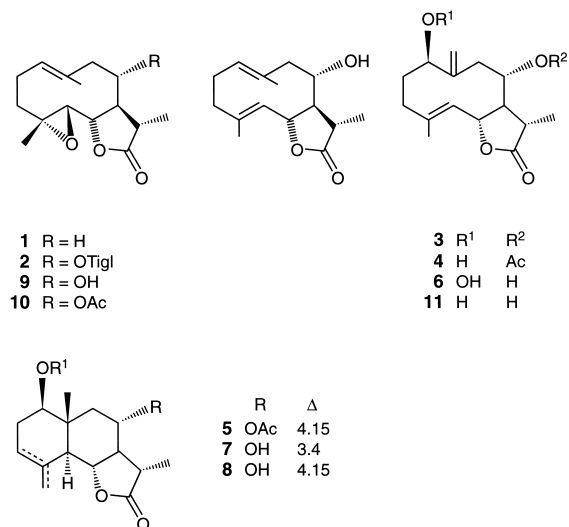


Fig. 1. **1**: 11 β ,13-dihydroparthenolide; **2**: 8 α -tigloyloxy-11 β ,13-dihydroparthenolide; **3**: balchanolide; **4**: 8-acetylshonachalin A; **5**: 8-acetylartapshin; **6**: 1 β -hydroperoxy-8 α -hydroxygermacra-4,10(14)-dien-6 β ,7 α ,11 β H-12,6-olide; **7**: 8 α -hydroxy-11 β ,13-dihydrobalchanin; **8**: artapshin; **9**: 8 α -hydroxy-4 α ,5 β -epoxy-11 β H-germacr-1(10)-en-12,6 α -olide; **10**: lanuginolide; **11**: shonachalin A.

11 β H,13-dihydrogermacranolide bearing a hydroxyl group and an acetate ester side chain. The location of these substituents at C-1 and C-8, respectively, and the stereochemistry followed from the ^1H NMR spectra (Table I) and COSY experiment. Furthermore, the ^1H NMR data of **4** were, with the exception of the chemical shift of the H-8 signal, in good accordance with those described for shonachalin A (**11**) (Serkerov and

Table I. ^1H NMR spectral data of lactones **2**, **4** and **5** in CDCl_3 (250 MHz).

H	2	4	5
1	5.22 brdd (14.1,13.0)	3.85 brs	3.52 dd (4.0, 11.7)
5	2.64 d (8.9)	5.19 d (9.8)	1.90–2.00*
6	4.02 t (8.9)	4.45 t (9.8)	4.13 t (10.9)
7	2.30–2.45*	2.25–2.45*	1.85–2.00*
8	4.96 brdd (6.8, 12.6)	5.07 brt (9.8)	5.12 ddd(10.7, 10.7, 4.5)
11	2.60 dq (6.9, 11.0)	2.48 dq (6.7, 11.5)	2.54 dq (6.6, 11.5)
13	1.43 d (6.9)	1.35 d (6.7)	1.30 d (6.6)
14	1.83 brs	5.27 brs (2H)	0.88 s
15	1.30 s	1.69 s	4.85 brs; 5.00 brs
OR	1.82 brd (6.9)	2.10 s	2.07 s
	1.86 brs		
	6.89 qq (6.9, 1.2)		

* Overlapped signal.

Aleskerova, 1985). Hence, the new germacranolide **4** was identified as 8-acetylshonachalin A.

The structure of the lactone **5** could be readily deduced from its ^1H NMR spectrum. It was very close to that of artapshin (**8**) (Fernandez *et al.*, 1987) but the observed downfield shift of the H-8 signal to δ 5.12 and the additional methyl singlet at δ 2.07 suggested the presence of an acetate instead of the hydroxyl group at C-8. This conclusion was further confirmed by the MS fragments at m/z 290 $[\text{M}-18]^+$, 248 $[\text{M}-60]^+$ and 230 $[\text{M}-60-18]^+$. Compound **5** is thus the 8-acetate of the known lactone artapshin (**8**).

As it was mentioned above, the species of the *A. millefolium* group are recognized as having significant medicinal properties and for pharmaceutical reasons much attention was focused on the content of proazulenes which are precursors of chamazulene. Based on chemical and cytological investigations of different *A. millefolium* taxa collected throughout Central Europe, the Vienna

school demonstrated that guaianolides (both proazulene and nonazulenogenic) characterized all diploid species, but only *A. collina* and *A. ceretamica* of the tetraploid species (Kubelka *et al.*, 1999). In contrast, *A. collina* of Bulgarian origin was proved to produce germacranolides and eudesmanolides only. Moreover, not even one of them has been found in *Achillea* species so far. Taking into account the observed difference in the sesquiterpene pattern on one hand, and on the other – the generally recognized polymorphism, introgression and high ecological plasticity of the taxa belonging to the *A. millefolium* group, one could presume that the Bulgarian species *A. collina* represent a new chemotype.

Acknowledgements

The partial support of this work by the National Foundation for Scientific Research of Bulgaria (Project X-911) is gratefully acknowledged.

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