

Sesquiterpene Lactones from *Achillea chrysocoma* and *Achillea coarctata*

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Achillea chrysocoma, *Achillea coarctata*, Sesquiterpene Lactones

The aerial parts of *A. chrysocoma* and *A. coarctata* afforded 22 and 9 sesquiterpene lactones, respectively. All the compounds described are new for the studied species. The lactones **5**, **6** and **12** are new for the genus *Achillea*.

Introduction

The genus *Achillea* (Asteraceae) includes about 100 species and subspecies, distributed mostly across the southern parts of the European continent (Richardson, 1976). In Bulgaria there are 20 species, of which *A. thracica*, *A. clypeolata*, *A. chrysocoma* and *A. coarctata* are grouped in the section Filipendulinae (Nedelcheva, 1997). These yellow flowering taxa are restricted to the Balkan peninsula and *A. thracica* is endemic to Bulgaria (Richardson, 1976), which could be the reason for the little interest they all have received. A survey of the literature showed that these species have been studied so far for their flavonoid content (Stosic *et al.*, 1988; Ivancheva *et al.*, 1990) and essential oil composition (Tasic *et al.*, 1998; Sinic *et al.*, 1999). Recently we have investigated seven collections of *A. clypeolata* growing in different regions of Bulgaria and showed the existence of two well defined chemotypes regarding the content of sesquiterpene lactones. (Todorova *et al.*, 1998; Todorova and Tsankova, 1999). These results prompted us to extend our investigation on other *Achillea* species of the section Filipendulinae and the sesquiterpene lactone profile of *A. chrysocoma* and *A. coarctata* is described in the present paper.

Experimental

Plant material

The plant material was collected during the flowering stage in August 1998 from Slavjanka mountain (*A. chrysocoma*) and Prevala village (*A.*

coarctata). Voucher specimens were deposited in the Herbarium of the Institute of Botany, Bulgarian Academy of Sciences, Sofia.

Extraction and isolation

The air-dried flowers and leaves of *A. chrysocoma* (110 g) and *A. coarctata* (44 g) were extracted with CHCl₃ (twice with 250 and 150 ml, respectively) to give, after evaporation of the solvent under reduced pressure brownish gums (5.0 g and 1.8 g, respectively). These extracts were then worked up as described previously (Todorova *et al.*, 1998) to give the corresponding lactone fractions : L. chrys. (1.1 g) and L. coarct. (218 mg). Subsequent separation of these fractions by CC on silica gel (100 g and 20 g) using solvent mixtures CHCl₃-MeOH with increasing polarity and further purification by CC and prep. TLC of selected sub-fractions (IR control) yielded the individual compounds. Thus, fraction L. chrys. afforded: **1** (10 mg), **2** (7 mg), **3** and **4** (7 mg), **5** (4 mg), **6** (2 mg), **7** (2 mg), **8** (1 mg), **9** (2 mg), **10** (2 mg), **11** (3 mg), **12** (1 mg), **13** (4 mg), **14** (3 mg), **15** (2 mg), **16** (3 mg), **17** (2 mg), **18** and **19** (4 mg mixture), **20** (2 mg), **21** (3 mg) and **22** (1 mg). The fraction L. coarct. afforded: **1** (4 mg), **2** (2 mg), **21** (2 mg), **22** (3 mg), **23** (3 mg), **24** (2 mg), **25** (1 mg), **26** (1 mg) and **27** (2 mg).

Results and Discussion

The above-ground parts of *A. chrysocoma* and *A. coarctata* were extracted with chloroform and the extracts obtained were worked up as described



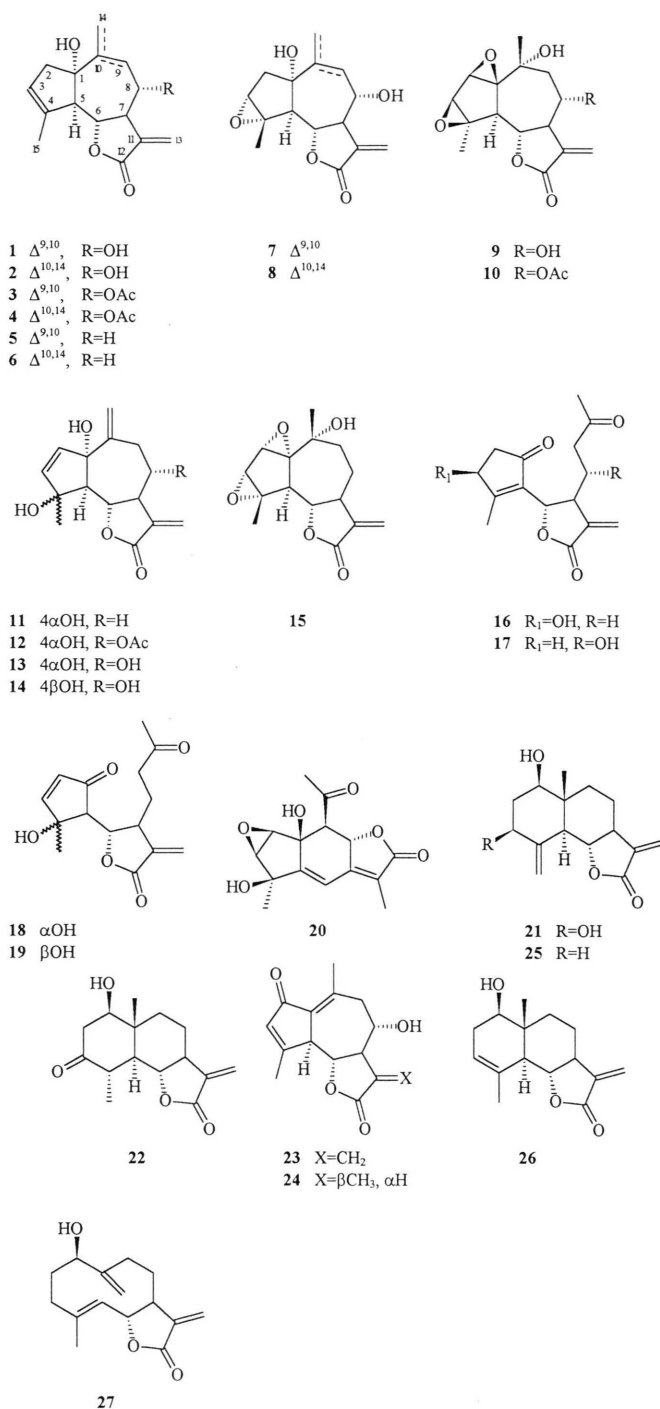


Fig. 1. **1**: rupicolin-A; **2**: rupicolin-B; **3**: 8-acetylrupicolin-A; **4**: 8-acetylrupicolin-B; **5**: 8-deoxyrupicolin-A; **6**: 8-deoxyrupicolin-B; **7**: $3\alpha,4\alpha$ -epoxyrupicolin-A; **8**: $3\alpha,4\alpha$ -epoxyrupicolin-B; **9**: rupin-A; **10**: rupin-B; **11**: $1\alpha,4\alpha$ -dihydroxy-2,10(14),11(13)-triene-12,6 α -olide; **12**: $1\alpha,4\alpha$ -dihydroxybishopsolicepolide; **13**: desacetyl- $1\alpha,4\alpha$ -dihydroxybishopsolicepolide; **14**: desacetyl- $1\alpha,4\beta$ -dihydroxybishopsolicepolide; **15**: artecenin; **16**: iso-secotanapartholide; **17**: arteludovinolide-A; **18**: secotanapartholide-A; **19**: secotanapartholide-B; **20**: acrifolide; **21**: ridentin-B; **22**: artecadin; **23**: 11,13-dehydridesacetylmaticarin; **24**: 8α -hydroxyachillin; **25**: reynosin; **26**: santamarin; **27**: artemorin.

in Experimental to give the sesquiterpene lactones **1–27**. They were identified spectroscopically (^1H NMR, IR and MS) by comparison with our own spectra and literature values, as well as by TLC comparison with some authentic samples. Thus, the following lactones were isolated from *A. chrysocoma*: rupicolin-A (**1**) and -B (**2**) (Irwin and Geissman, 1973), 8-acetylrupicolin-A (**3**) and -B (**4**) (Greger *et al.*, 1986), 8-deoxyrupicolin-A (**5**) and -B (**6**) (De Gutierrez *et al.*, 1990), 3 α , 4 α -epoxyrupicolin-A (**7**) and -B (**8**) (Todorova *et al.*, 1998), rupin-A (**9**) and -B (**10**) (Milosavljevic *et al.*, 1994), 1 α , 4 α -dihydroxy-2, 10 (14), 11 (13)-triene-12,6 α -olide (**11**) (Jakupovic *et al.*, 1991), 1 α , 4 α -dihydroxybishopsolicopolide (**12**) (Singh *et al.*, 1985), desacetyl-1 α ,4 α -dihydroxybishopsolicopolide (**13**) (Jakupovic *et al.*, 1988), desacetyl-1 α ,4 β -dihydroxybishopsolicopolide (**14**) (Milosavljevic *et al.*, 1994), artecenin (**15**) (Bohlmann and Zdero, 1982), iso-secotanapartholide (**16**) (Huneck *et al.*, 1986), arteludovicinolide-A (**17**) (Jakupovic *et al.*, 1991), secotanapartholide-A (**18**) and -B (**19**) (Bohlmann and Zdero, 1982), acrifolide (**20**) (Todorova *et al.*, 2000), ridentin-B (**21**) (Irwin and Geissman, 1973) and artecenin (**22**) (Geissman *et al.*, 1969). All these compounds are described for the first time as constituents of *A. chrysocoma* and the lactones **5**, **6** and **12** are new for the genus *Achillea*. Their characteristic patterns are the guaiane skeleton, as all the lactones but ridentin-B (**21**) and artecenin (**22**) are guaianolides; the presence of an α -methylene- γ -lactone ring trans-fused at C-6, the only exception being acrifolide (**20**) and the high degree of oxidation of the carbon skeleton. Lack of germacranolides which represent the

simplest biosynthetic class of sesquiterpene lactones should be emphasized. The most biosynthetically advanced compound discovered is acrifolide (**20**). It is also noteworthy that guaianolides with cross-conjugated cyclopentadienone system of the matricarin or achillin series have not been detected in *A. chrysocoma* even in traces, although this type of lactones are reported in many *Achillea* species (Connolly and Hill, 1991).

In contrast, *A. coarctata* was found to contain only nine sesquiterpene lactones which belong to three skeletal classes. We succeeded in isolation of the guaianolides **1**, **2**, 11,13-dehydrodesacetylmaticarin (**23**) (Ohno *et al.*, 1980) and 8 α -hydroxyachillin (**24**) (Bohlmann and Zdero, 1972), the eudesmanolides **21**, **22**, reynosin (**25**) (Samek *et al.*, 1973) and santamarin (**26**) (Appendino *et al.*, 1982), and the germacranolide artemorin (**27**) (Sanz *et al.*, 1989). The eudesmanolides are not considered as typical constituents of *Achillea* species (Connolly and Hill, 1991) and this type of lactones has not been reported so far in taxa of the section Filipendulinae.

The results described above show that *A. chrysocoma* produces biogenetically more advanced and structurally more diversified sesquiterpene lactones with great variety of oxidation functionalities, a fact which may be connected with the higher ploidy of this taxon ($2n = 54$). The lactones of the diploid species *A. coarctata* ($2n = 18$) are in much smaller number and not as variable in oxidation. Two guaianolides (**1** and **2**) and two eudesmanolides (**21** and **22**) are the only compounds shared by both *A. chrysocoma* and *A. coarctata*.

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