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SESQUITERPENE LACTONES FROM *ACHILLEA ABROTANOIDES*

MILUTIN STEFANOVIĆ, VERICA DJERMANOVIĆ,* MOMČILO GORUNVIĆ,† MIODRAG DJERMANOVIĆ, SLOBODAN MACURA and SLOBODAN MILOSAVLJEVIĆ

Department of Chemistry and Physical Chemistry, Faculty of Science, University of Belgrade, Studentski trg 16, P.O Box 550, 11001 Belgrade, Yugoslavia; *Institute for Chemistry, Technology and Metallurgy, Njegoševa 12, 11000 Belgrade, Yugoslavia; †Institute for Pharmacognosy, Faculty of Pharmacy, Dr. Subotića 8, P. O. Box 146, 11000 Belgrade, Yugoslavia

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Key Word Index—*Achillea abrotanoides*; Compositae; guaianolides; 1β,10β-epoxydesacetoxymatricarin.

Abstract—The isolation of desacetoxymatricarin, desacetyl matricarin and 1β,10β-epoxydesacetoxymatricarin (a new guaianolide) from *Achillea abrotanoides* Vis. is reported. The configuration of the epoxy ring in this lactone was determined by comparison of its ^{13}C and ^{1}H NMR data to those of diastereomeric 1α,10α-epoxydesacetoxymatricarin, the epoxidation product of desacetoxymatricarin. A flavonoid centaureidin was also detected in this extract.

INTRODUCTION

In the course of our chemotaxonomic examination of Yugoslavian plants we investigated a chloroform extract of the aerial parts of *Achillea abrotanoides* which has not been studied before. The genus *Achillea*, well known for the medicinal properties of some members, has received much attention. A number of γ-lactones have been isolated from *Achillea* species [1]. The major constituents are guaianolides with cross-conjugated cyclopentadienone systems. According to the configuration at C-11, they are divided into the achillin (11β-Me) and matricarin (11α-Me) series. These types of guaianolides have also been found in numerous *Artemisia* and some other species [1].

RESULTS AND DISCUSSION

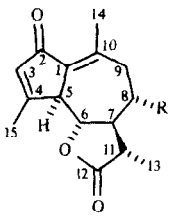
Silica gel column chromatography afforded three γ-lactones (**1**, **2** and **3**) and a flavonoid **6**. Lactones **1** and **2** were readily assigned as desacetoxymatricarin and desacetylmatricarin, respectively, by identity of their spectra to those published [2–5]. Flavonoid **6** was identified as centaureidin [6, 7] by means of ^{1}H NMR, UV and mass spectra. The gross structure of the remaining lactone **3** (EIMS: M^+ at *m/z* 262, corresponding to molecular formula $C_{15}H_{18}O_4$), based on IR (see Experimental) and NMR (^{1}H and ^{13}C, Table 1) spectral data, was the same as that of 1,10-epoxyachillin (**6**) isolated from *Artemisia lanata*, the guaianolide belonging to the 11β-Me series [8]. However, in that lactone the stereochemistry of the epoxy ring has not been determined. Different magnitudes of $J_{11-H,13-H}$ in **3** and **6** (i.e. 6.9 and 8 Hz in **3** and **6**, respectively) could be rationalized in terms of different relative configurations at C-11. By analogy with $J_{11,13}$ in the previously studied 11α-Me guaianolides with a *trans*-positioned (6β-H,7α-H) lactone ring [9], ranging from 6.6 to 6.9 Hz, lactone **3** could be assigned to the matricarin series. The large coupling between 7-H and 11-H in the ^{1}H NMR spectrum of **3** ($J_{7,11}=12.2$ Hz, Table 1) also fits this proposal. Epoxidation of the major lactone **1** by means of *m*-chloroperbenzoic acid (using a standard procedure [10]) afforded almost exclusively 1,10-epoxy lactone **4** which, according to the NMR data (Table 1), exhibited different stereochemistry of the epoxy ring in comparison to that in the natural epoxide **3**, also obtained as a minor product in this reaction. In the ^{13}C NMR spectrum of the natural epoxide **3**, the signals of β- and γ-carbons (with respect to the epoxy ring), i.e. C-5, C-6, C-8 and C-9, are shifted upfield in comparison to the same carbons in the synthetic epoxide **4** (see $\Delta\delta_C$ values in Table 1). This is fully in agreement with a β-oriented epoxide in **3**, i.e. *syn* to the pseudoaxial 6β- and 8β-hydrogens [11–13]. Consequently, the α-configuration could be assigned to the epoxy-ring in **4**. An additional proof for this stereochemical assignment was obtained in the ^{1}H NMR spectra of these compounds. Thus, a downfield shift of 6β-H in **3** (i.e. $\delta_{6\text{-H}}(\mathbf{3})-\delta_{6\text{-H}}(\mathbf{4})=0.28$ ppm) is effected by the *syn*-oriented β-epoxide [14].

Finally, the preferential attack of the epoxidation reagent from the less hindered α-side in **1**, yielding predominantly the α-epoxidation product **4**, was in accordance with the above stereochemical proposal.

EXPERIMENTAL

Plant material. Achillea abrotanoides Vis. (Specimen No 130887) was collected in summer 1987 at mountain Bjelasica (Montenegro), Yugoslavia.

Isolation. A crude $CHCl_3$ extract (11), obtained from the powdered air-dried aerial parts (1.5 kg) of *A. abrotanoides*, using the standard procedure [15], was chromatographed on a silica gel column, eluting with toluene. Compounds, eluted in the following order: **3**, **1**, **5** and **2**, were isolated from the crude fractions by crystallization. The identification of the known compounds, i.e. desacetoxymatricarin [**1**, mp (uncorr) 208°, 202 mg], desacetylmatricarin [**2**, mp (uncorr) 154°, 24 mg] and centaureidin [**5**, mp (uncorr) 203°, 31 mg], is based on the identity of their spectral data to the published ones [2–7].



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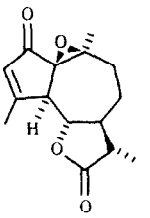
2 R = OH



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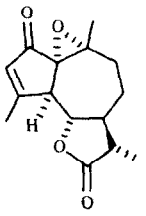

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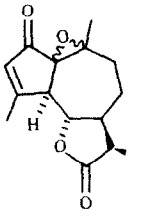
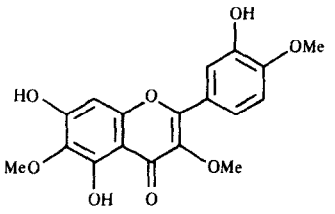


6 [8]



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Scheme 1.

Table 1 ^1H (500 MHz) and ^{13}C (125 MHz) NMR data of epoxides **3** and **4** (in $CDCl_3$ + TMS)*

	3		4		
H/C	δ_H	δ_C	δ_H	δ_C	$\Delta\delta_C$†
1	—	67.0	—	67.4	−0.4
2	—	201.0	—	201.5	−0.5
3	6.20 *dq*	133.1	6.20 *dq*	132.6	+0.5
4	—	176.6	—	177.1	−0.5
5	3.03 *ddq*	49.3	2.89 *d*	53.0	−3.7
6	4.05 *dd*	80.3	3.77 *t*	85.9	−5.6
7	1.44 *ddt*	56.2	1.85 *m*	54.4	+1.8
8α	1.67 *ddt*		1.99 *dddd*		
8		22.1		24.6	−2.5
8β	1.54 *ddt*		1.43 *dddd*		
9α	2.02 *ddd*		1.58 *br t*		
9		34.6		38.9	−4.3
9β	2.22 *ddd*		2.39 *ddd*		
10	—	65.3	—	66.3	−1.0
11	2.24 *dq*	40.8	2.27 *dq*	41.2	−0.4
12	—	178.1	—	178.5	−0.4
13	1.22 *d*	12.3	1.25 *d*	12.4	−0.1
14	1.76 *s*	18.9	1.76 *d*	17.3	+1.6
15	2.37 *t*	21.0	2.39 *dd*	21.4	−0.4

$J_{H,H}$ (Hz)- in **3**: 3, 15 = 1.3, 3, 5 = 2.2, 5, 6 = 10.3, 5, 15 = 1.3, 6, 7 = 9.6; 7, 8α = 2.7; 7, 8β = 12.2, 7, 11 = 12.2; 8α, 8β = 13.8, 8α, 9α = 2.3; 8α, 9β = 5.6; 8β, 9α = 11.9, 8β, 9β = 2.3, 9α, 9β = 15.7, 11, 13 = 6.9; in **4**: 3, 15 = 1.3, 3, 5 = 0.6; 5, 6 = 10.4, 5, 15 = 0.7; 6, 7 = 10.4; 7, 8α = 3.4, 7, 8β = 11.0; 7, 11 = 12.4, 8α, 8β = 14.0, 8α, 9α = 1.5, 8α, 9β = 7.1 8β, 9α = 12.4, 8β, 9β = 1.4, 9α, 9β = 12.8; 11, 13 = 6.9, 9α, 14 = 0.8.

*The spectral assignments are based on 2D heteronuclear ^{13}C–^1H shift correlated spectroscopy (HECTCOR)

†$\Delta\delta_C = \delta_C(3) - \delta_C(4)$

1β,10β-Epoxydesacetoxymatricarin (**3**, 20 mg) was isolated from the crude fraction by crystallization from Me_2CO–Et_2O; mp (uncorr) 207°. (Found: C, 68.3; H, 7.0. $C_{15}H_{18}O_4$ requires C, 68.7; H, 6.9%); IR ν_{max}^{KBr} cm^{-1}: 1775, 1700, 1605; EIMS (probe) 70 eV, *m/z* (rel. int.): 262 $[M]^+$ (93), 233 (13), 219 (17), 205 (27.5), 192 (15), 177 (19), 151 (87), 122 (35.5), 111 (34), 109 (100), 91 (33), 55 (51), 53 (30), 43 (46), 41 (66), 39 (33); ^1H and ^{13}C NMR: see Table 1.

1α,10α-Epoxydesacetoxymatricarin (**4**) was obtained as a main product by reaction of **1** (50 mg) with *m*-chloroperbenzoic acid in CH_2Cl_2–Et_2O (1:1, 10 ml) at room temp. (overnight) according to the standard procedure [10] Lactone **4** (32 mg) was isolated by crystallization from Et_2O; mp (uncorr) 155° (Found: C, 68.4, H, 7.1 $C_{15}H_{18}O_4$ requires: C, 68.7, H, 6.9%), IR ν_{max}^{KBr} cm^{-1}: 1770, 1712, 1620; EIMS (probe) 70 eV, *m/z* (rel. int.) 262 $[M]^+$ (86), 233 (15), 219 (15.5), 205 (26), 192 (19), 151 (88), 123 (21), 122 (41), 111 (32), 109 (100), 91 (21), 69 (57.5), 55 (58), 53 (38), 43 (36), 41 (69), ^1H and ^{13}C NMR: see Table 1

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AN ANTIFUNGAL TRITERPENOID FROM *MOLLUGO PENTAPHYLLA*

MATTHIAS HAMBURGER, GUY DUDAN, A. G. RAMACHANDRAN NAIR,† R. JAYAPRAKASAM† and KURT HOSTETTMANN*

Institut de Pharmacognosie et Phytochimie, Ecole de Pharmacie de l'Université de Lausanne, 2 rue Vuillermet, CH-1005 Lausanne, Switzerland; †Department of Chemistry, Pondicherry University, Pondicherry 605 006, India

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Key Word Index—*Mollugo pentaphylla*, Molluginaceae; hopane, mollugogenol A; mollugogenol B, antifungal.

Abstract—An antifungal compound was isolated from the aerial parts of *Mollugo pentaphylla* and identified as mollugogenol A, along with the inactive major triterpenoid mollugogenol B. The structures were established by spectroscopic methods (UV, DCIMS, EIMS, ^{1}H and ^{13}C NMR) and comparison with authentic samples.

INTRODUCTION

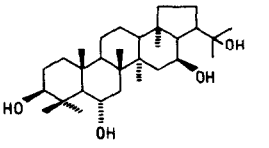
Continuing our search for biologically active compounds from traditional medicinal plants, we have undertaken an investigation of *Mollugo pentaphylla* L. (Syn. *M. stricta* L.) (Molluginaceae). This annual herb is eaten in India as a pot herb and reportedly contains carotenes, vitamin C, and a saponin [1, 2]. In the course of earlier phytochemical investigations of *M. pentaphylla*, the three novel flavone C-glycosides mollupentin, mollupentin 6-C-xyloside and isomollupentin 8-C-xyloside have been characterized [3, 4].

RESULTS AND DISCUSSION

The ethyl acetate soluble part of an aqueous ethanolic extract of *M. pentaphylla* contained an antifungal compound, evidenced by a bioassay on TLC using the plant pathogenic fungus *Cladosporium cucumerinum* [5]. Successive fractionation of the extract on silica gel and Sephadex LH 20 yielded the antifungal compound **1**, along with the inactive triterpene **2**.

The molecular formula of **1**, $C_{30}H_{52}O_4$, was derived from the DCIMS and the ^{13}C NMR spectra. The presence of three secondary and one tertiary hydroxyl groups was indicated by the successive elimination of four molecules of water observed in the DCI mass spectrum and the resonances of four oxygen bearing sp^3 carbons at δ78.17 (*d*), 67.79 (*d*), 67.29 (*d*) and 70.92 (*s*), respectively. Confirming evidence was obtained from the ^{1}H NMR spectrum, which showed signals of three secondary alcohols at δ4.1 (H-6$_{ax}$), 3.78 (H-16$_{ax}$) and 3.22 (H-3$_{ax}$) The multiplicities as determined by the DEPT spectra suggested a hopane or lupane-type skeleton. Compound **1** was finally identified as mollugogenol A by comparison with reported ^{13}C NMR data [6] and co-TLC with an authentic sample, previously isolated from *M. disticha* [7].

Compound **2**, $C_{30}H_{48}O_2$, exhibited a UV spectrum indicative of a heteroannular diene chromophore similar to hop-15,17(21)dienes [8]. The hopane skeleton and the positions of the functional groups were established by ^{13}C NMR and extensive ^{1}H NMR studies (COSY and NOE difference spectroscopy). Carbon resonances were assigned with the aid of DEPT spectra and data reported for related triterpenoids [9]. Compound **2** was found to be identical with mollugogenol B.



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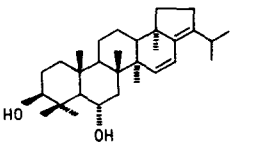

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