Tabelle 1. Flüchtige Inhaltsstoffe aus *Adoxa moschatellina*

Verbindung	Flächenprozent*
trans-2-Hexenal (**1**)	42,0
cis-3-Hexenol (**2**)	21,0
Benzylalkohol (**3**)	13,5
n-Hexanol (**4**)	12,5
2-Hexenol (**5**)	10,0

* Die Summe der identifizierten Riechstoffe (*ca* 20% des Extrakts) wurde als 100 Flächen-% gesetzt. Weiterhin wurden noch gefunden: *n*-Alkane von C-20 bis C-27 sowie Eicosan- und Docosansäuremethylester.

mit exaltierenden Geruchseigenschaften konnten in *A. moschatellina* nicht nachgewiesen werden.

EXPERIMENTELLES

Gaschromatographie. 50 m Glaskapillare WG 11 (FFAP-Phase). Trägergas: He; Vordruck: 2, 3 bar; Programmierung: 60–220°, Rate 4°/min.

Massenspektrometrie. Hewlett–Packard 5992A, GC–MS-System, 70 eV.

Gewinnung des Extraktes. Die frisch gesammelten Blütenstände (10 g) wurden unzerkleinert in einer Soxhlet-Apparatur unter einer Argon-Atmosphäre 8 Stdn. mit 1,1,2-Trichlor-1,2,2-trifluorethan (Kp 47,6°) extrahiert. Nach Abdampfen des Lösungsmittels über eine 15 cm Vigreux-Kolonne verblieben *ca* 70 mg Rückstand als gelbes Öl.

Danksagung—Herrn Dr. E. Klein von der DRAGOCO-Geschäftsleitung danken wir für sein förderndes Interesse.

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ANTIMICROBIAL ACTIVITY OF THE HELIANGOLIDE CHROMOLAENIDE AND RELATED SESQUITERPENE LACTONES

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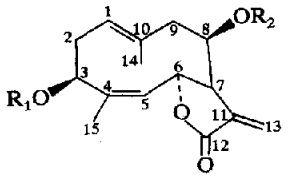
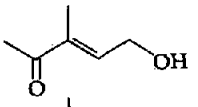
Key Word Index—Chromolaenide derivatives; sesquiterpene lactones; heliangolides; antimicrobial activity; proof of stereochemistry.

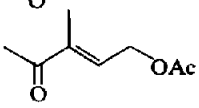
Some sesquiterpene lactones are known to exhibit antimicrobial activity [1, 2]. More recently, it has been noted that the pseudoguainolide carpesiolin inhibits the growth of *Xanthomonas oryzae* [3]. Here, we report on the antimicrobial activity of the heliangolide chromolaenide **1**, isolated from *Chromolaena glaberrima* (DC.) King et Robinson [4] and its derivatives, against *Staphylococcus aureus*.

The results are summarized in Table 1. It is apparent that there is a clear dependence between antimicrobial activity and the presence of the α-methylene-γ-lactone group. As already established [5–8], the growth inhibition of microorganisms is caused by the alkylation of their nucleophilic centers (R-SH) with the unsaturated lactone moiety. This observation is congruent with our results, because the only inactive compound was **3**, which is the one with no unsaturated lactone.

Chromolaenide **1** and the corresponding acetate **2** were the more active. This is reasonable because compounds with an unsaturated ester group close to the unsaturated lactone show enhanced activity due to anchimeric assistance [9]. The acetate of chromolaenide **2** was more potent than chromolaenide **1** itself. Also compound **5** showed more inhibition than **4**. This result can be explained by the fact that acetates are more lipophilic than the related alcohols. This undoubtedly indicates a problem of transport and not a problem of reactivity. Similar observations have been described before in the literature for cytotoxic

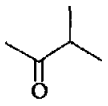


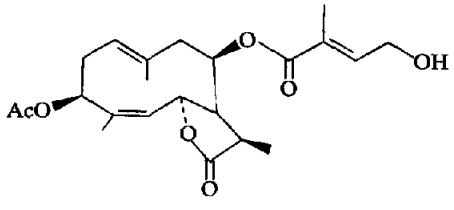
1 R_1 = Ac; R_2 = 

2 R_1 = Ac; R_2 = 

4 $R_1 = R_2 = H$

5 $R_1 = R_2 = Ac$

6 R_1 = Ac; R_2 = 



3

Table 1. Antimicrobial activity of chromolaenide and related compounds

Compound	MIC* (μg/ml)
1	200
2	100
3	>1000
4	1000
5	600

*Minimum inhibitory concentration against *Staphylococcus aureus*. Compounds **1** and **2** were inactive against *Escherichia coli*, *Klebsiella pneumoniae* and *Candida* sp. at the 1000 μg/ml level.

compounds [9, 10].

Compounds **1** and **2** were inactive against *Escherichia coli*, *Klebsiella pneumoniae* (Gram-negative) and *Candida* sp. (yeast), so that it appears that these two lactones are only effective against Gram-positive bacteria.

EXPERIMENTAL

Isolation of chromolaenide. The heliangolide **1** was extracted from the aerial part of the plant *Chromolaena glaberrima* (DC.) King et Robinson collected in June 1977, in Alajuela, Costa Rica. The dried material was extracted and worked according to the method described by Herz [11]. Chromolaenide **1** was eluted with C_6H_6–EtOAc (4:1) from a Si gel column and crystallized from petrol–CH_2Cl_2 as colourless prisms, mp 144–146° (lit. [4] mp 138°). The ^{1}H NMR, IR and MS were in complete agreement with those reported [4].

Derivatives of chromolaenide. Acetylation of lactone **1** produced the diacetate **2**, mp 127–128° (lit. [4] mp 127°). The reduction of **1** with $NaBH_4$ in MeOH at 0° afforded **3** as a colourless oil. These two compounds showed spectroscopic data consistent with those in the literature [4]. The diol **4** was prepared by saponification of **1** according to the procedure of Mabry [12]. Acetylation of the diol gave rise to the diacetate **5**. The ^{1}H NMR of **5** is identical to the one obtained from the diacetate prepared from peucephyllin **6** by a similar series of reactions [13–14]. This represents unequivocal proof of the stereochemistry of chromolaenide **1**. The structure and relative stereochemistry of peucephyllin were fully established by single crystal X-ray analysis [15].

Microorganisms. The organisms utilized in this study included (a) *Staphylococcus aureus* ATCC 6538P (Gram-positive), (b) *Escherichia coli* isolated from a case of colibacillosis in chickens (Gram-negative), (c) *Klebsiella pneumoniae* ATCC 10031 (Gram-negative), (d) *Candida* sp. (yeast), a donation from Facultad de Microbiología, Universidad de Costa Rica.

Antimicrobial testing. The determination of the minimum inhibitory concn was carried out according to the method developed by Mitscher [15].

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